The University Of Sheffield.

An Alkyne Diboration-6π-Electrocyclisation Strategy to Pyridine Boronic Acid Derivatives

A thesis submitted to the University of Sheffield in partial fulfilment of the degree of Doctor of Philosophy.

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“Imagination is far more important than knowledge. For knowledge is limited to all we now know and understand, while imagination embraces the entire world, and all there ever will be to know and understand.”

Albert Einstein

Abstract

*N*itrogen based heterocyclic compounds constitute important building blocks for organic synthesis since they are found in many pharmaceutical and agrochemical targets. In this regard, heteroaromatic boronic acid derivatives are one of the most valuable classes of intermediates in synthetic chemistry. Their value lies in their unique combination of high stability and rich reactivity, allowing them to participate in a wide range of functionalisation reactions. The present study aims to provide new and easy methodologies for the synthesis of small heterocycles, such as pyridine derivatives, bearing Carbon–Boron bonds that could be further functionalised to give rise to more complex molecules.

This project starts with the idea of synthesising a group of starting materials bearing an enyne and an oxime group. Importantly, in the context of boronic acid derivatives, we envisaged that we could take advantage of catalytic diborylation methodology to transform these readily available yne-ene-oximes into pyridine boronic esters via a 6π-electrocyclic reaction upon heating. The electrocyclisation of oximes is an important sub-set of disrotatory 6π-electrocyclisation reactions because it offers a synthetic strategy to pyridines through *de novo* ring synthesis. Furthermore, this transformation has never been performed before in the presence of a boron moiety.

This apparently straightforward transformation has raised a great number of questions about the relationship between substrate stereochemistry and the efficiency of electrocyclic reactions. Specifically, even though the effect of substituted hexatrienes in electrocyclic reactions has been broadly studied, much less is understood about the related transformation using oximes. We report herein a combined experimental and theoretical study of the synthesis of borylated heterocycles through a thermally promoted disrotatory 6π-electrocyclization of oxime ether stereoisomers and the surprising finding that the efficiency of the ring closure step is dependent on oxime stereochemistry.

Finally, we have used automated parallel library synthesis to demonstrate the broad chemistry of these diverse heterocyclic boronate building blocks. Using Sanofi´s internal compound profiling workflow, we have shown potential points for diversification in these compound series which give access to improved physicochemical and eADME properties.

Acknowledgements

*F*irst of all I would like to thank you *Joe*. Thank you for giving me the opportunity to join your group to do my PhD and live this huge adventure. After some months of desperation and torture I must admit I had the time of my life. Thanks a lot.

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Frankfurt's family, *let's get it started*.

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Last but not least, big thanks to the *United Kingdom* and *Germany*, the two countries who *adopted* me during these three years, it has been a terrifying and exciting adventure.

List of abbreviations

Ac	Acetyl
acac	Acetylaceonate
Alk	Alkyl
Ar	Aryl
B_2pin_2	Bis-pinacolatodiboron
Bn	Benzyl
Boc	tert-Butyloxycarbonyl
Bu	Butyl
^oC	Degree Celsius
cat.	Catalyst
Cat	Catechol
cod	1,5-Cyclooctadiene
Cp	Cyclopentane
Cy	Cyclohexyl
Dan	1,8 - Diaminonaphtalene
dba	Dibenzylideneacetone
DFT	Density Functional Theory
DMP	Dimethoxyphenol
dppf	1,1’-Bis(diphenylphosphino)ferrocene
DMF	Dimethyl formamide
DMSO	Dimethyl sulfoxide
equiv.	Equivalent
Et	Ethyl

EtOAc	Ethyl acetate
FTIR	Fourier transform infrared
h	hour
HRMS	High resolution mass spectroscopy
HFIP	Hexafluoroisopropanol
LC-MS	Liquid chromatography – Mass spectroscopy
LiTEBH	Lithium triethyl boro hydride
M	Metal
Me	Methyl
min	Minute
MW	Microwave-assisted reaction
NBE	Norbornene
NBS	*N*-bromosuccinimide
NMR	Nuclear magnetic resonance spectroscopy
o-DCB	1,2-dichlorobenzene
o-Tol	*orto*-Toluene
OAc	Acetate
Pin	Pinacol
Ph	Phenyl
^{i}Pr	Isopropyl
R	Alkyl group
RSM	Recovered starting material
r.t.	Room temperature
SM	Starting material
TBSCl	tert-Butyl silyl chloride

TBDPS	tert-Butyldiphenylsilyl
Tf	Trifuoromethanesulfonate
THF	Tetrahydrofuran
THP	Tetrahydropyran
TLC	Thin layer chromatography
TMS	Trimethylsilyl
Ts	Tosyl (p-Toluenesulfonyl)
X	Halogen

Table of contents

CHAPTER 1:

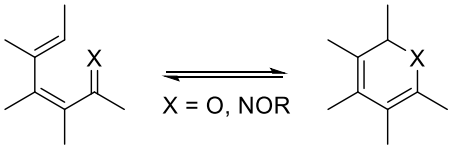
Synthesis of pyridines through 6π-electrocyclic reactions

1. Introduction

The objective of this project relied on the synthesis of pyridine boronic ester heterocycles through the disrotatory 6π-electrocyclisation of azatriene moieties. This approach to pyridine heterocycles has been exploited recently in several catalytic syntheses where conjugated oximes are the proposed intermediates that are formed transiently in the reaction. The examples of azaelectrocyclic transformations from oxime moieties are, however, not extremely abundant in the literature; and most of these have been employed in the synthesis of alkaloids.

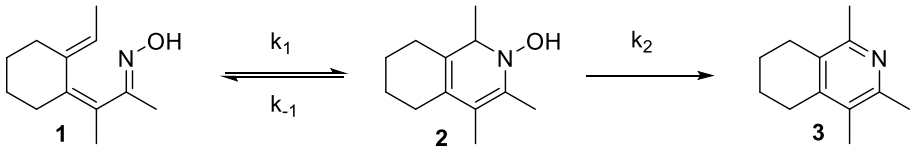
First azaelectrocyclic transformations: Thermal cyclisation of *cis*-dienone-oximes

Even though the thermal equilibrium between *cis*-dienones (X=O) and 2*H*-pyrans was well established,[1] it was not until the late 1970's that this same principle was applied in the synthesis of nitrogen based heterocycles using oxime derivatives (X= NOR). By analogy, these compounds could enter into equilibrium with their valence isomers 1,2-dihydropyridines (Scheme 1).[2]



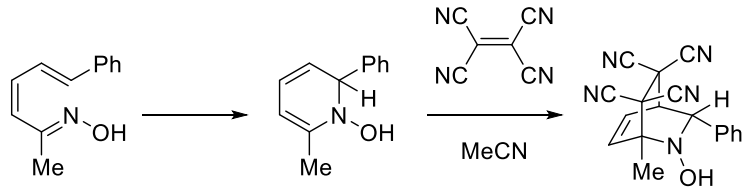
Scheme 1. *Thermal equilibrium between* cis*-dienones and 2H-pyrans.*

In this regard, Ringele and coworkers reported the transformation of aldoxime **1** to 5,6,7,8-tetrahydropyridine derivative **3** at 70 °C, via 6π-electrocyclisation tandem H_2O elimination (Scheme 2). They studied the rates of this reaction, concluding that the cyclisation was the rate determining step in this reaction ($k_2 >> k_1$); followed by elimination of water.



Scheme 2. *Proposed mechanism of 6π-electrocyclisation of oxime trienes.*

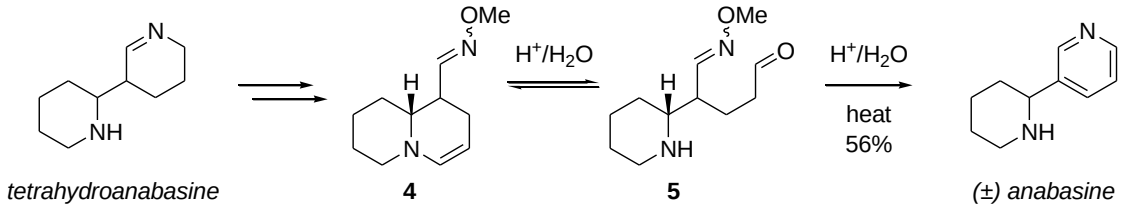
Evidence for the intermediacy of the 1,2-dihydropyridines **2**, was gathered by trapping the methyl substituted oxime intermediate through a cycloaddition reaction shown in scheme 3.



Scheme 3. *Cycloadduct formation via cycloaddition reaction with tetracyanoethylene.*

Thermal and microwave-assisted 6π-electrocyclisation of aldoximes

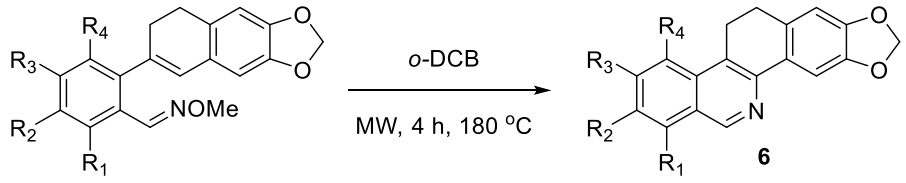
One of the first applications of this methodology was reported in the late 1990's by Wanner and Koomen.[3] The racemic total synthesis of natural products anabasine and 5-piperidylanabasine were achieved starting from tetrahydroanabasine via an unexpected rearrangement of **4** under acidic conditions, and an oxime induced aromatisation process (Scheme 4).



tetrahydroanabasine **4** **5** *(±) anabasine*

Scheme 4. *Synthesis of (±) anabasine.*

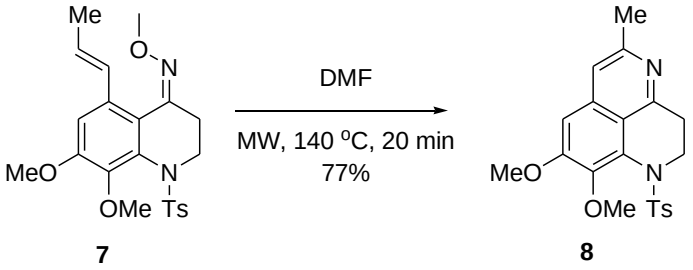
As described previously, the use of oximes towards the synthesis of heterocycles via electrocyclic reactions has been focused mostly in the synthesis of alkaloids. In the last decade, Hibino and coworkers reported a list of bioactive nitrogen based fused heterocycles that could be synthesised using a microwave-assisted 6π-electrocyclisation of aldoximes, via the formation of a new carbon-nitrogen bond.[4,5] One of the most recent examples was reported in 2011; the total synthesis of benzo[*c*]phenanthridine alkaloids **6** based on a thermal electrocyclic reaction of aza 6π-electron systems. The reported methodology turned out to be a great success and a number of derivatives were accessed in good to excellent yields (Scheme 5).[6]



Scheme 5. *Thermal electrocyclic reaction of aza 6π-electron systems.*

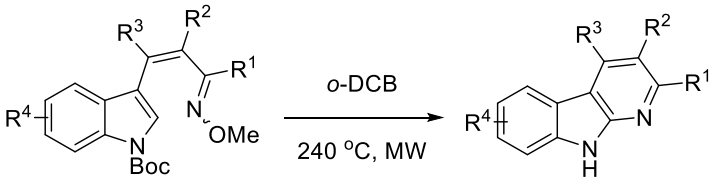
The efficiency of this transformation was found to be dependent on the mode of thermal promotion used; microwave promoted conditions proved to be the method of choice for a broader variety of substrates.

Similarly, in the late 2016, Kaufmann reported another interesting alkaloid synthesis based on a 6π-azaelectrocyclisation strategy.[7] The retrosynthetic analysis of the pyridine core present in **8** was envisaged as a thermal aza-cyclisation of the oxime **7** (Scheme 6). This substrate proved to be very sensitive to the reaction conditions and time. The authors noted that longer times contributed to lower yields due to decomposition. The stereochemistry of the oxime starting material was tentatively assigned as *Z* based on nOe analysis.



Scheme 6. *Synthesis of 5-methylaaptamine intermediate via an azaelectrocyclisation reaction.*

Inspired by this work, the Moody group investigated the possibility to synthesise α-carbolines from easily accessible 3-acyl indoles via thermal 6π-electrocyclisation using microwave-irradiation (Scheme 7).[8]



Scheme 7. *6π-electrocyclisation of 3-acyl indole derivatives.*

The transformation was found to be efficient only at 240 °C and both *E* and *Z* alkenes were successfully transformed into the desired carbolines in moderate to good yields. However, the authors noted that this class of substrates underwent facile and reversible oxime ether

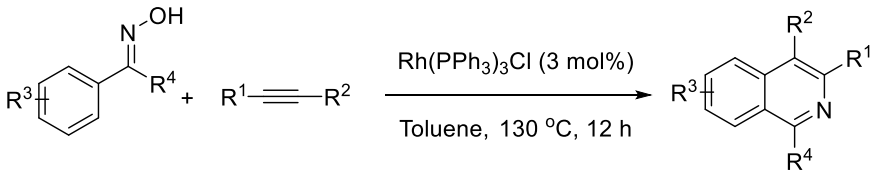
isomerisation. A limitation to this chemistry appeared to be that only electron rich indoles furnished the desired products.

Metal catalysed cycloadditions to pyridines that involve the cyclisation of oximes.

In light of the high temperatures required to promote the aza 6π-electrocyclisation reactions, a great number of researchers have focused their attention on the development of metal catalysed variants that would perhaps allow this transformation to be performed under milder conditions. These metal catalysed methodologies are strongly oriented towards the synthesis of highly substituted pyridines from the corresponding acyclic oximes.

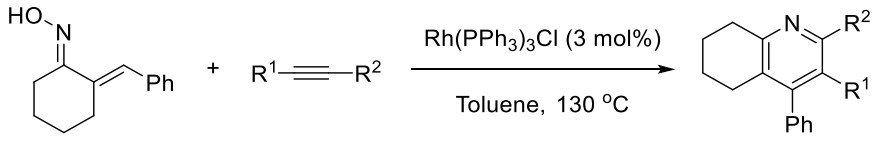
Rhodium catalysed C-H activation of ketoximes

One of the first approaches towards a metal catalysed pyridine synthesis was reported by Chen in 2009. They described an easy access to isoquinolines and tetrahydroisoquinolines via one-pot rhodium catalysed C-H activation of aromatic ketoximes and alkynes, in moderate to good yields (Scheme 8).[9]



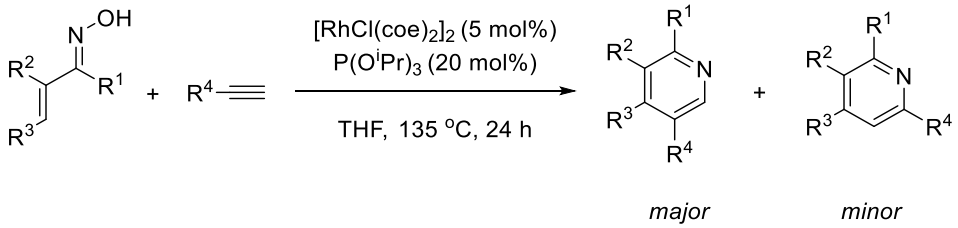
Scheme 8. *Rh (I) C-H activation of aromatic ketoximes.*

Inspired by Ellman's rhodium catalysed work that required an oxidation of the dihydropyridine product,[10] this group proposed a direct chelation-assisted activation of a C-H bond that avoided the need for further oxidation. A vast number of functionalities on the aromatic ring were accommodated and gratifyingly the reaction appeared to be highly regioselective, with only one regioisomer being isolated when unsymmetrical alkynes were tested. Surprisingly the use of terminal alkynes gave poor yields even though the regioselectivity was still excellent and only one product was obtained. Something particularly interesting is the applicability of this methodology to α-exocyclic unsaturated ketoximes giving as a result tetrahydropyridine derivatives (Scheme 9).



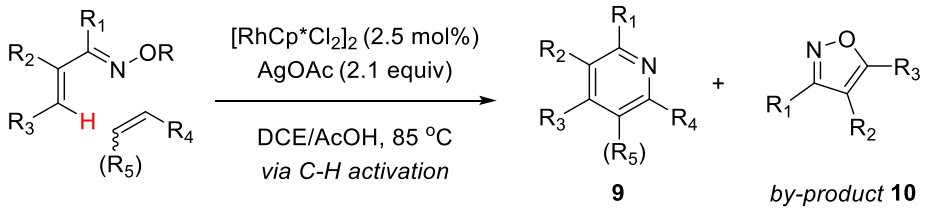
Scheme 9. *Reaction of ketoximes possesing an α-exocyclic double bond.*

Similarly, Chiba also reported a rhodium (III) catalysed C-H activation of aromatic *O*-acyl ketoximes and internal alkynes.[11] Nonetheless, a methodology that was compatible with terminal alkynes was still needed. Ellman reported in 2012 an extended methodology of their rhodium (I) catalysed dihydropyridine-oxidation synthesis providing access to pyridine derivatives in a one-pot method using terminal alkynes.[12] By using triisopropylphosphite as a ligand they were able to suppress the undesired homodimerisation of terminal alkynes. Different branched ketoximes were tested and found to be effective in this methodology and medium to good regioselectivities were obtained (Scheme 10).



Scheme 10. *Rh (I) C-H functionalisation to access pyridine derivatives. Regioselectivities 10:1>*

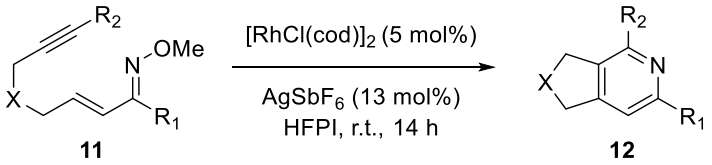
In order to access full stereoselectivity on the rhodium(I) catalysed formation of pyridines reported by Ellman, Neely and Rovis described in 2013 an improved strategy that allowed the synthesis of pyridines with enhanced regioselectivity.[13] They envisaged that the use of α,β-unsaturated oximes and alkenes (instead of alkynes) together with an external oxidant could represent an alternative means to obtain these heterocycles (Scheme 11).



Scheme 11*. Rhodium (III) catalysed regioselective synthesis of substituted pyridines.*

Interestingly, the reaction is highly dependent on the nature of the oxime moiety. They observed that when R = H or an acetate group, only isoxazole by-product **10** is obtained. Changing this group to pivaloyl derivative, however, allows the formation of pyridine **9** in good yields and excellent regioselectivities, generally by using electron-deficient alkenes.

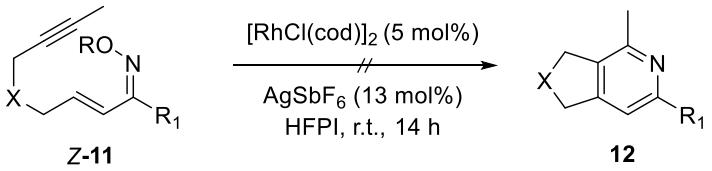
Another interesting approach towards the formation of bycyclic pyridines using rhodium(I) catalysis was reported by Hanzawa in 2009.[14] It allows the synthesis of novel pyridine scaffolds **12** via a [4+2] cycloaddition reaction of ω-alkynyl-vinyl oximes **11** by cationic rhodium catalyst in moderate to excellent yields (Scheme 12).



Scheme 12. *Synthesis of pyridines via [4,2]cycloaddition reaction of ω-alkynyl-vinyl oximes (X = heteroatom).*

The fused five-membered saturated pyridine products represent an interesting precursor in contrast of the highly studied fused aromatic heterocycles, such as isoquinolines. It is interesting to note that the corresponding intramolecular Diels-Alder reaction was not observed in the absence of the Rh(I) catalyst.

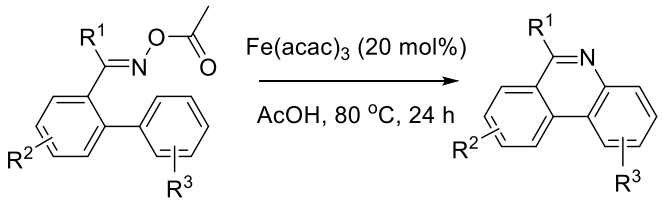
Interestingly, the submission of the Z-oxime isomer of the precursor **11** into the catalytic system led only to the recovery of the starting substrate (Scheme 13).



Scheme 13. *No reaction was observed when the corresponding Z-oxime isomer was submitted to the reaction conditions.*

Iron (III) catalysed cyclisation of biaryl oximes.

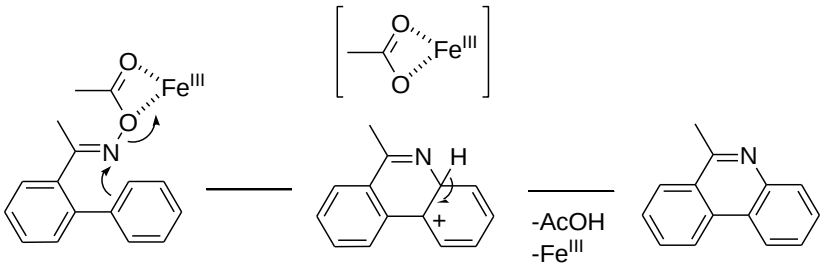
Yokishai reported in 2013 a new iron (III) catalysed protocol for the cyclisation of ortho-aryl *O*-acetyl oximes (Scheme 14).[15]



Scheme 14. *Iron (III) catalysed cyclisation of biaryl oximes.*

It is worth highlighting that the use of other metallic salts was not successful: Ni(II), Co(III) or Mn(III) were tested and found to be inefficient in promoting the desired cyclisation. Other solvents like DMSO or toluene proved to be ineffective and lowering the catalyst loading to 10 or 5 mol% did not make a huge difference in the yield obtained. However, attempts to try to lower the temperature dramatically diminished the efficiency of the reaction. Several groups were tested in both aromatic rings and in the position adjacent to the ketoxime moiety, and the reaction seemed tolerant to a range of groups.

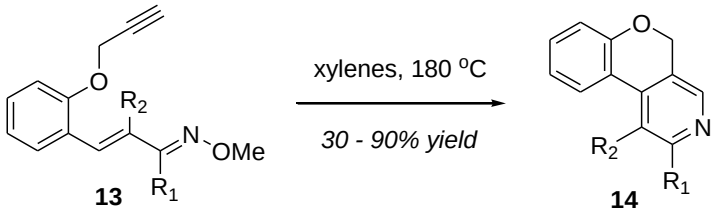
They also observed that when a mixture of *E* and *Z* ketoximes were subjected to the reaction conditions a good yield of the cyclised product was obtained, showing that ketoxime stereochemistry did not have an effect on the reactivity. The proposed mechanism included a Friedel-Crafts activation of the acyl group that, after electrophilic attack of the aromatic ring, furnished the desired heterocycle (Scheme 15).



Scheme 15. *Proposed Friedel-Crafts like mechanism.*

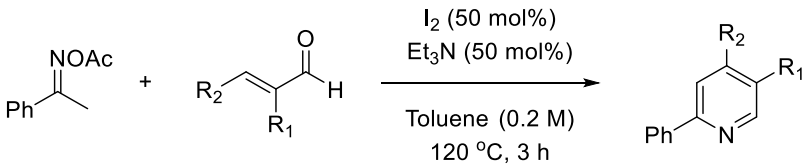
Metal free approaches to pyridines from oximes

One of the first approaches to *[c]*-annellated pyridines via an intramolecular hetero Diels-Alder reaction was described by Moody in 2007.[16] The transformation involved the reaction of a α,β-unsaturated oxime ether **13**, as the diene, together with acetylenic dienophiles, readily prepared from salicylaldehyde derivatives. The described pyridine products **14** were only obtained in moderate yields after the cycloaddition reaction (Scheme 16).



Scheme 16. *Synthesis of [c]annellated pyridines via intramolecular Diels-Alder reaction.*

Another interesting study of the synthesis of pyridines from the corresponding acyclic oximes and the corresponding α,β-unsaturated derivatives without the use of metal catalysis was reported by Huang in 2016 with yields up to 90% (Scheme 17).[17]

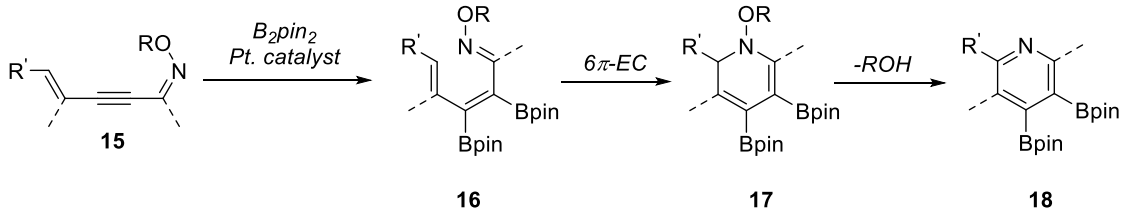


Scheme 17. *Metal-free synthesis of polysubstituted pyridines from oximes and acroleins.*

They used a combination of iodine and trimethylamine as a way to activate the N-O bond. The proposed radical pathway was confirmed by the use of radical scavengers, which dramatically blocked the reaction. Further studies on the detailed mechanism of this transformation have not yet been disclosed. To their delight, the obtained pyridine products showed great derivatisation especially towards C-H activation methodologies.

2. Project overview: Aims

In an effort to devise a new approach to pyridine boronic esters, we planned to prepare a series of ene-yne-oxime ethers **15** that we could simultaneously functionalise and cyclise (Scheme 18). In order to activate the alkyne towards electrocyclisation, we envisaged that we could take advantage of a catalytic diborylation methodology.[18] Upon formation of substrate **16**, bearing an activated diboryl alkene group, we hypothesised that after heating and elimination of the corresponding methanol derivative we would furnish the desired heterocyclic boronate **18**. It is important to highlight that this key transformation step had never been performed before in the presence of a boronic ester.



Scheme 18. *Catalytic alkyne diborylation - 6π-electrocyclisation strategy to pyridine boronic acid derivatives.*

Last but not least, the ultimate challenge to address would be the differentiation of both boronates at the end of the synthetic sequence towards further selective coupling reactions.

We expected to develop a straightforward, step-wise synthetic route to a broad spectrum of pyridine boronic esters using easily accessible starting materials and well established organic chemistry.

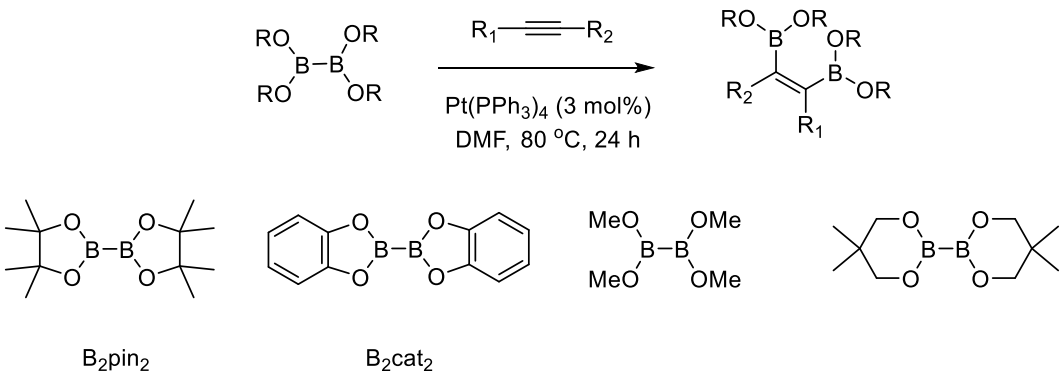
CHAPTER 2: Metal-catalysed borylations: Addition of diboron ester derivatives to alkynes.

1. Introduction

Platinum-catalysed diboration of alkynes

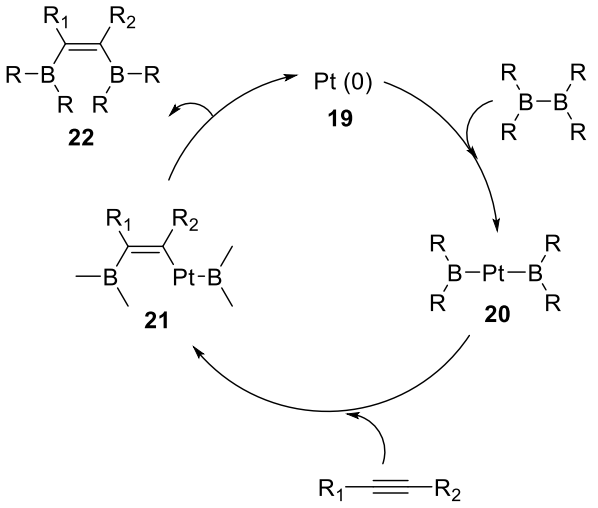
The diboration of unsaturated compounds was first explored using diboron tetrahalides. Although boron tetrahalides B_2X_4 (X= F, Cl, Br, I) have a very well established reactivity with alkynes, they suffer from low stability and preparative difficulties.[19] However, tetraorganodiborane compounds such as B_2R_4, are stable molecules when substituted by sterically hindered R groups such as -^{t}Bu or -CH_2-^{t}Bu. The most stable R groups are those in which good π-donor groups are attached to boron, such as amido (NR'_2) or alkoxy (OR') derivatives.

One of the first attempts to obtain *syn*-selective addition of diboron ester derivatives to alkynes was reported by Miyaura and Suzuki in the early 1990s.[18] These compounds are characterised by a weak energy B–B bond that needs the help of a transition metal to promote the addition of these compounds to unsaturated organic molecules through the formation of an intermediate metal-boron complex. The required alkoxy(diborons) can be prepared easily starting from (amido)diborons and the corresponding alcohols, and these are added to both internal and terminal alkynes efficiently in the presence of a platinum (0) catalyst (Scheme 19). The pinacol ester boron derivative (B_2pin_2) was chosen as the optimal reagent for this transformation due to its high stability allowing the easy handling in air.



Scheme 19. *Pt-catalysed diboration of alkynes.*

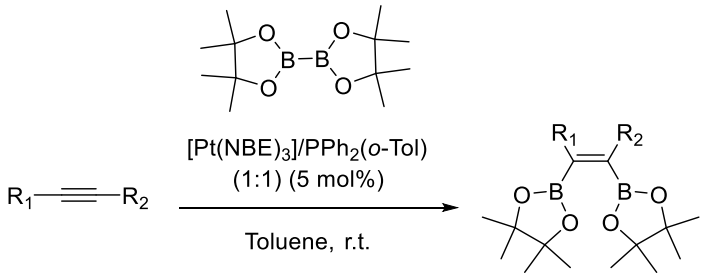
The proposed mechanism of the *syn*-selective diboration reaction involves the oxidative addition of the boron-boron bond to the platinum (0) complex to generate intermediate **20**. Notably, intermediates such as **20** have been isolated and fully characterised by x-ray analysis.[20] Coordination of the alkyne followed by *syn*-insertion to the Pt-B bond leads to **21**. Reductive elimination furnished the desired *syn*-bis-boryl alkene **22**, regenerating the Pt (0) complex **19** and completing the catalytic cycle (Scheme 20).



Scheme 20. *Catalytic cycle of platinum (0) diboration of alkynes.*

Preliminary results indicated that only platinum(0) complexes could successfully promote this transformation; Pd(0), Ni(II), Rh(I) or Co(I) which are useful catalysts for similar metalations were also tested, however, with ineffective results.[21,22,23] The reaction was compatible with both internal and terminal alkynes and it was completed within 24 h at 80 ^{o}C in DMF to provide isomerically pure 1,2-*cis*-alkene diboronic esters. The stereochemistry of the products was confirmed by nOe spectroscopy.

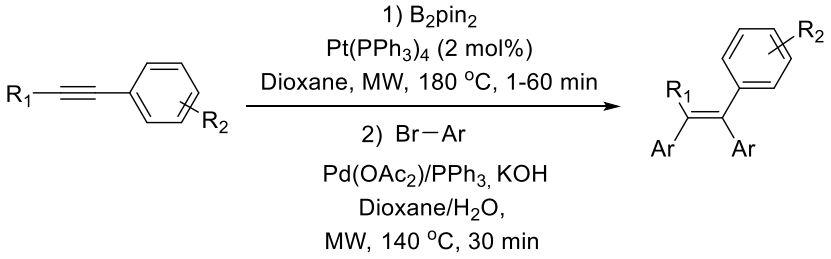
More recently, Marder *et al.* documented a highly efficient method that allowed alkyne diborations to be run at room temperature and using less polar solvents such as toluene.[24] They studied a monophosphine catalyst system generated from [Pt(NBE)$_3$] and one equivalent of a free phosphine ligand (Scheme 21).



Scheme 21. *Pt-catalysed diboration of alkynes at r.t.*

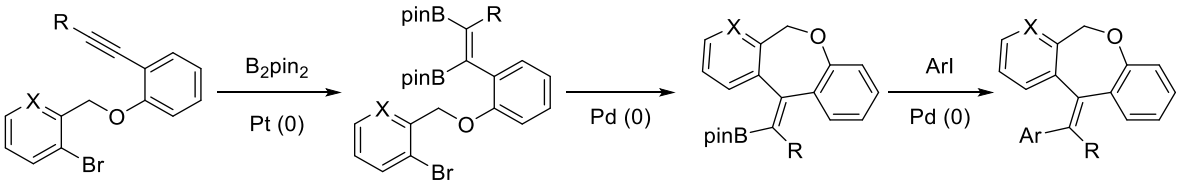
It was found that this reaction was more efficient in the presence of Pt(0) complexes bearing electron donating phosphine ligands. A wide variation in reactivity was observed across different phosphine ligands, and the reaction proved to be very sensitive to changes in size and basicity; for example, catalysts based on PCy_3 and P^tBu_3 show markedly different reactivities. Whereas the later phosphine is more basic than the former, it turned out to be too sterically hindered to allow the catalyst to interact with other reagents.

One of the most attractive characteristics of these diborated compounds is that they can undergo a range of Pd-catalysed coupling reactions. In the last decade, Kappe *et al.* developed a series of efficient microwave-assisted one-pot diboration/Suzuki cross-coupling reactions that furnished a series of multisubstituted alkenes through *in situ* formation of bis(boryl)alkene derivatives.[25] The boration reaction was efficiently performed by Pt(0) catalyst in dioxane, at 180 °C for 1-60 min under microwave conditions, followed by the corresponding Suzuki reaction with a large number of arylhalides (Scheme 22).



Scheme 22. *Microwave-assisted one-pot diboration/Suzuki cross-coupling. Yields 21-98%*

One of the most attractive applications of this chemistry was reported by Coghlan and co-workers who were able to synthesise a number of benzopyridyloxepines via *syn*-stereoselective diboration of highly substituted alkynes, bearing a number of different functional groups, followed by an intra- and an intermolecular Suzuki coupling sequence furnishing a geometrically pure exocyclic alkene (Scheme 23).[26]

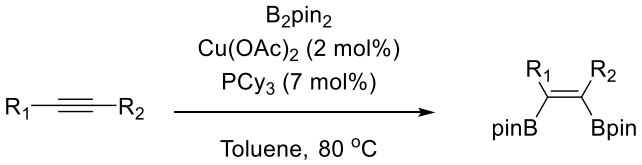


Scheme 23. *Syn-stereoselective diboration followed by an intra- and an intermolecular Suzuki sequence.*

Copper-catalysed boration of alkynes and arynes

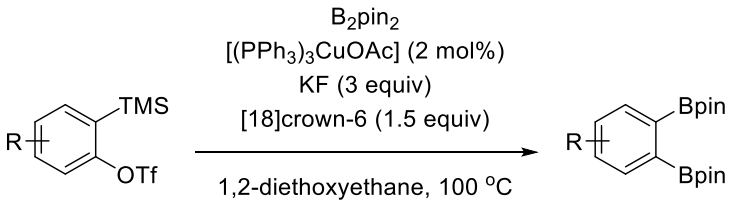
The formation of C–B bonds using copper (I) catalysis has been also broadly exploited. In this way, nucleophilic borylcopper species act as reaction intermediates.[27] The broad scope of this reaction makes it a universal method to obtain bis-borylated alkenes in a more economical way than the previously reported platinum (0) reaction.

Takaki and coworkers reported in 2012 a diboration reaction of alkynes with bis(pinacolato)diboron in the presence of a ligand (PCy_3) and the commercially available $Cu(OAc)_2$ catalyst (Scheme 24).[28] The reaction was tolerant of electron rich aryl groups and internal highly hindered alkynes furnishing the vicinal boronates in moderate to excellent yields.



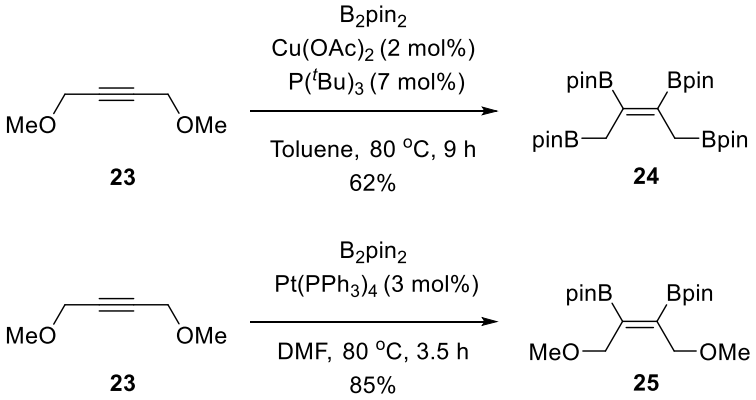
Scheme 24. *Cu-catalysed diborylation of alkynes.*

This reaction was also applicable to transiently generated arynes. Diborylation of aromatic compounds is an under-explored area and so this discovery was of great interest. The corresponding bis-borylated benzene was produced in good yield from the in situ generated benzyne with bis(pinacolato)diboron in the presence of [(PPh_3)CuOAc] (Scheme 25). Although the scope of this reaction is narrow, and is only applicable to aliphatic substitution in the benzyne adduct, this represents one of the first methods to directly obtain bis-borylated aromatic species by this strategy.



Scheme 25. *Cu-catalysed diborylation of arynes. Yields up tp 80%.*

A rather surprising feature of this chemistry was uncovered when it was applied to propargyl ether substrates. In an effort to synthesise the corresponding diborylated adduct, 1,4-dimethoxy-2-butyne **23** was instead converted exclusively into the tetraborylated product **24**, where the –OMe groups where replaced by –Bpin groups under copper catalysis. When applying this discovery to the reaction under Pt catalysis only the expected diborated product **25** was furnished (Scheme 26).



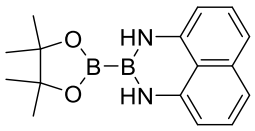
Scheme 26. *Cu or Pt-catalysed reaction of 1,4-dimethoxy-2-butyne with (pin)B-B(pin).*

The mechanism of this unexpected transformation could be explained by formation of the corresponding borylallene by β-alkoxide elimination from an alkenyl copper species.

Addition of unsymmetrical diboron to alkynes

Transition metal catalysed diborations of unsaturated organic compounds using symmetrical diborons give products with two available boron groups. This can therefore have the inconvenience of requiring a subsequent regioselective reaction at one of the boron groups. For instance, Suzuki Miyaura coupling of diboration products of terminal alkynes with B_2pin_2 has selectivity towards the terminal boron group. The result is a monoborylated adduct that can be further used in a second coupling reaction. Products derived from internal alkynes represent more of a challenge however.

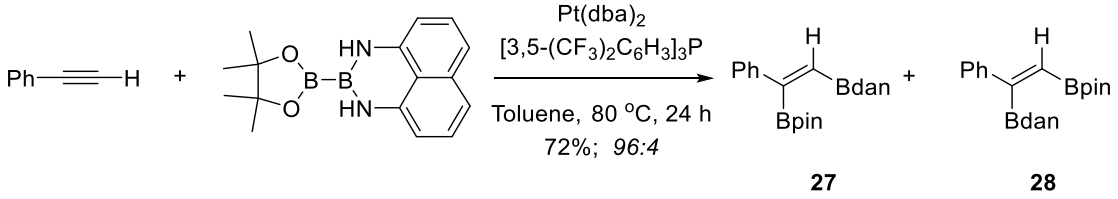
Recently, Iwadate and Suginome reported a regioselective diboration of alkynes using unsymmetrical diborons, compounds that have different groups at each boron atom.[29] Specifically, they reported the reactivity of (pin)B–B(dan) **26** (Figure 1).



26

Figure 1*. (pin)B–B(dan) reagent.*

This unsymmetrical diboron was prepared using a 1:1:1 ratio of tetrakis(dimethylamino)diboron with 1,8-diaminonaphthalene and pinacol, with a catalytic amount of HCl (10%). After screening some transition metals they found Pt, as reported before in these type of reactions, to be the most efficient transition metal to promote this transformation. In addition, among all the phosphine ligands examined tris[3,5-bis(trifluoromethyl)phenyl]phosphine showed selectivity for incorporating the most reactive pinacolborane in the internal position of the product alkene. For instance, when studying the diboration of phenylacetylene using unsymmetrical diboron under the conditions described above they obtained **27** and **28** in a 96:4 ratio (Scheme 27).

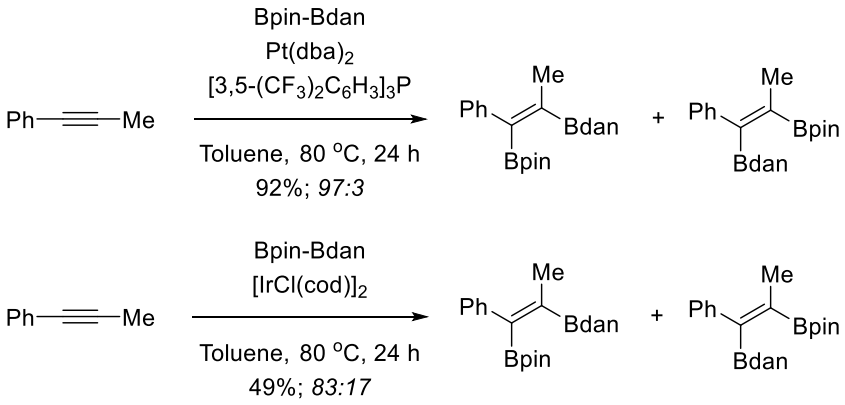


27 **28**

Scheme 27. *Diboration of phenylacetylene using unsymmetrical diboron.*

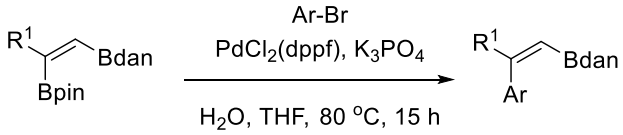
It is worth highlighting that a neutral Ir(I) complex showed a good catalytic activity and even higher selectivity than the Pt complexes. This was an unexpected result due to the fact that Ir had never been used for catalytic diborations before.

Suginome also studied the scope of this reaction. Good results were achieved with both aryl- and alkyl-substituted alkynes. Arylalkynes bearing electron-withdrawing or electron-donating groups at either *ortho*, *para* or *meta* positions gave rise to a 1,2-diboration product in high yield and selectivity. Even heterocyclic reagents, such as ethynylthiophene furnished successfully the corresponding product. Surprisingly, when studying an internal unsymmetrical alkyne, the product was achieved with higher regioselectivity when using Pt complexes (Scheme 28).



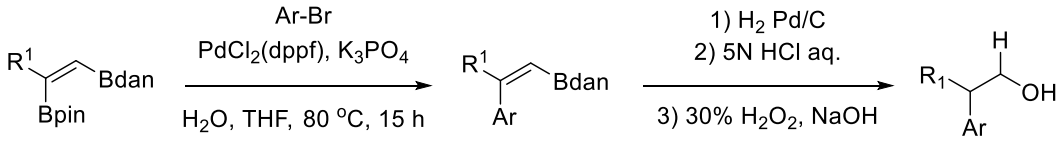
Scheme 28. *Diboration of internal alkyne using platinum and iridium catalysts.*

The obtained products were subjected to Suzuki-Miyaura coupling with aryl halides to prove that compounds bearing both B-pin and B-dan could be differentiated. In these cases, the internal Bpin group reacted smoothly, leaving the Bdan group untouched. This was in contrast with the early reported diboration of terminal alkynes using B_2pin_2 whereby the products underwent coupling with the terminal Bpin group (Scheme 29).



Scheme 29. *Internal selective Suzuki-Miyaura coupling of Bpin-Bdan species.*

It is worth highlighting that the cross-coupled products can be further utilised for the synthesis of the corresponding alcohols via Pd/C-catalysed hydrogenation followed by deprotection of –Bdan group using HCl and subsequent H_2O_2 oxidation (Scheme 30).

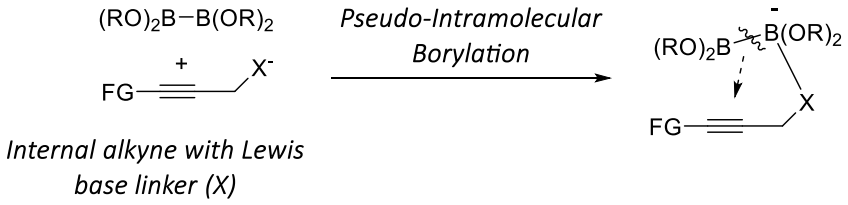


Scheme 30. *Synthesis of β-ethanols.Yields up to 70-80%.*

Diborylation of alkynes in a *trans*-fashion.

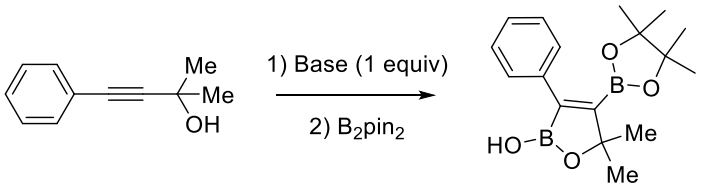
One of the main characteristic features of the reaction of unsaturated molecules with tetraorganodiborane compounds is that the resulting products have both boron species on the same face of the resulting alkenes. In all reported cases the reactions are triggered by interaction between a vacant orbital of boron and a π-orbital of the corresponding alkyne, and therefore the *cis*-addition predominates.

One of the areas that has been more recently studied is the addition of diboron species in a *trans*-fashion. Although *trans*-hydroboration of alkynes and Pd-catalysed *trans*-silaboration of terminal alkynes were well established, *trans*-diboration of unsaturated C-C bonds took far longer to discover.[30,31] In this regard, Uchiyama and co-workers presented in 2014 the first *trans*-selective diborylation of alkynes.[32] Their method consisted of a pseudo-intramolecular reaction of diboronic ester, propargyl alcohol and a base without the use of any catalyst (Scheme 31). The mechanism would allow a considerable lowering in the activation energy by coordination of the lithium propargyl alkoxide with the diboron species. After the first borylation, the intramolecular second borylation is strongly energetically favored compared to an intermolecular equivalent. Consequently the more thermodynamically stable *trans* adduct is formed.



Scheme 31. *Pseudo-intramolecular diborylation of alkynes.*

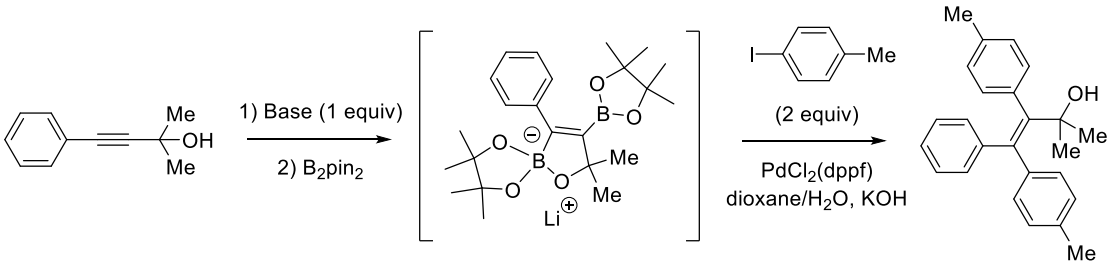
Surprisingly, the present transformation gave as a result an oxaborole ring. Two determining features were the temperature of the reaction and the concentration of the base. At room temperature only traces of the product were found in the reaction mixture, however at higher temperatures the yield of the product increased dramatically. Use of MeLi and ^{n}BuLi gave comparable results whereas the use of non lithiated bases furnished only small amounts of the desired product (Scheme 32).



Scheme 32. *Trans-diborylation of alkynes.*

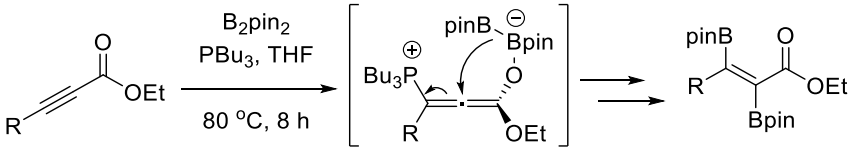
When studying the scope of the reaction they found that electronic effects at acetylene carbons had little or no influence on the reactivity. Heterocyclic propargylic alcohols were also tested with good results, as were primary and secondary aliphatic substituents. No formation of the corresponding *cis*-isomer was detected. Tertiary alkyl groups slowed down the reaction, presumably due to steric hindrance.

At this point, a sequential diborylation/Suzuki-Miyaura cross-coupling in one-pot was studied. The borate intermediate was directly subjected to the conditions to couple with 4-iodotoluene, that furnished the desired olefin in good yield (Scheme 33). This result gave a successful strategy for the regiocontrolled synthesis of tetrasubstituted olefins in good yields.



Scheme 33. *Sequential trans-diboration/Suzuki Miyaura cross-coupling process.*

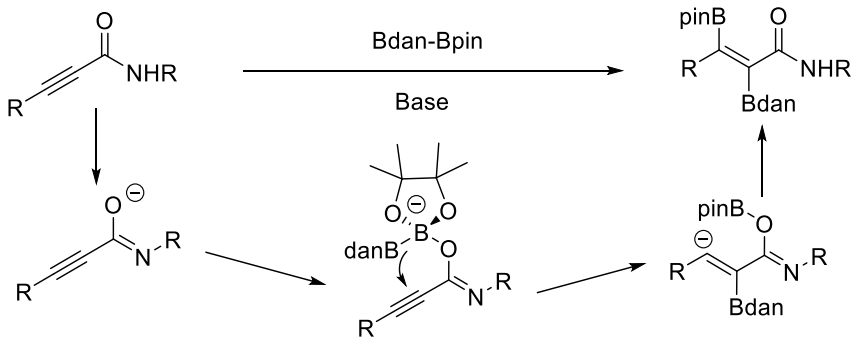
Alternatively, in 2015, Sawamura, Ohmiya and co-workers reported an *anti*-selective diboration of alkynoates using phosphine organocatalysis.[33] The limitation of this methodology relies on the mechanism, which requires the formation of the allenoate phosphonate to facilitate the addition in a *trans*-fashion. Nonetheless, a wide range of aromatic R groups bearing different electronic properties were successfully used. However, alkyl groups furnished the desired *trans*-product in lower yields (Scheme 34).



Scheme 34. *Anti-selective diboration of alkynoates using phosphine organocatalysis.*

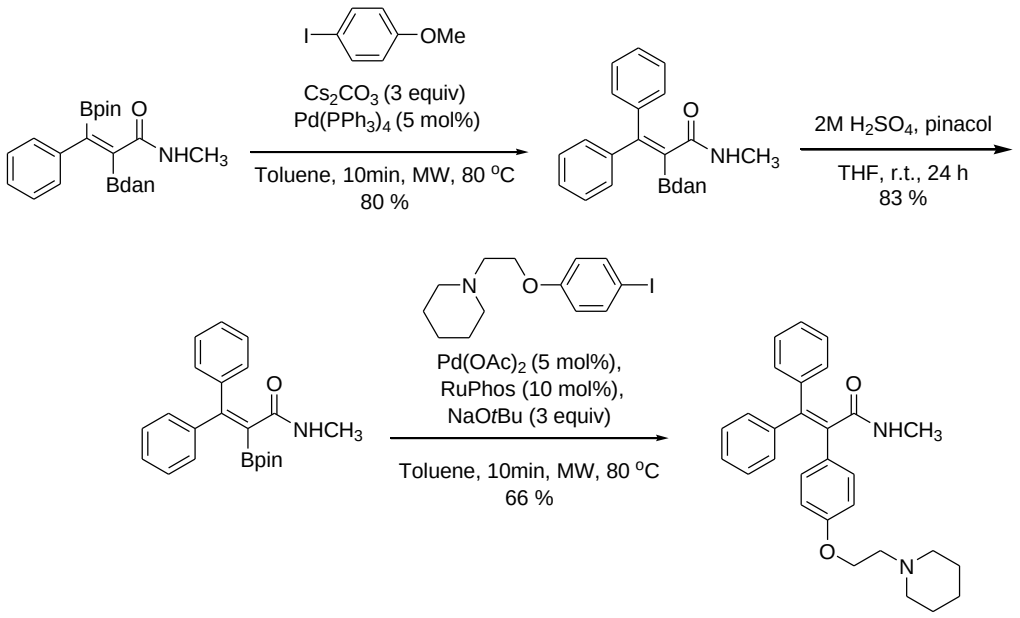
In order to overcome some of these limitations, earlier this year, Santos and collaborators reported a very elegant transition metal free *trans*-diboration of alkylamides using

unsymmetrical (Bpin-Bdan) diboron species.[34] The bespoke methodology involved a complete regioselective addition of the boronates, where the Bdan and the Bpin are added exclusively on the α- and β-position with respect to the carbonyl group, respectively (Scheme 35). Stereoselectivity was fully confirmed by means of X-ray analysis.



Scheme 35. *trans-Diboration of alkylamides.*

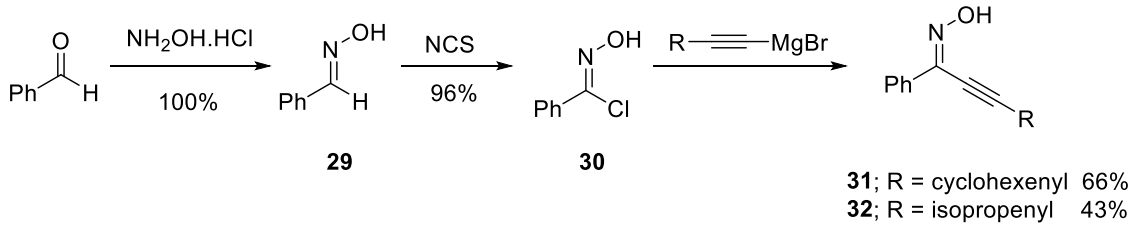
As explained before, the motivation for generating unsymmetrical olefinic diboron species relies on their potential to be orthogonally functionalised. In this example, fully substituted alkenes were obtained after a set of two completely selective palladium catalysed Suzuki couplings (Scheme 36).



Scheme 36. *Synthesis of fully substituted alkenes via orthogonal Suzuky coupling reactions.*

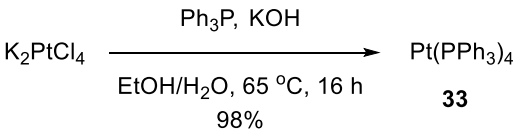
2. Investigations towards the diborylation of yneoxime ethers.

The initial objective of this project was the development of an efficient route to yne-ene-oximes, the starting materials for our methodology study. The first attempted preparation of α,β-acetylenic ketoximes **31** and **32** was performed following the report by Shearing.[35] Benzaldehyde was condensed with the desired oxime to obtain **29** and chlorinated using *N*-chlorosuccinimide. The obtained chloro oxime **30** was then reacted with the *in situ* formed Grignard reagent furnishing our desired starting materials. Using this approach, cyclohexenyl and isopropenyl derivatives were synthesised in good yield (Scheme 37).



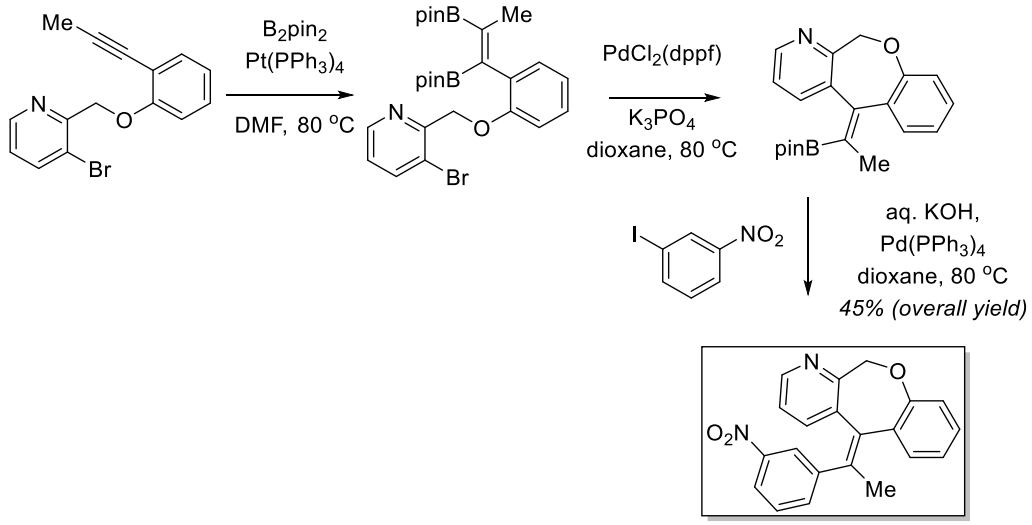
Scheme 37. *Synthetic route to hydroxyl oximes **31** and **32**.*

With our starting materials in hand, we focused our attention on the diboration reaction. We began by preparing the platinum catalyst using conditions previously established in the literature. Potassium tetrachloroplatinate(II) was efficiently transformed into the desired tetrakis(triphenyl phosphine) platinum(0) **33** in a 98% yield using excess of triphenylphosphine under basic conditions in a mixture of ethanol/water at 65 °C (Scheme 38). The formation of this catalyst could be scaled up to 2 grams and it proved to be stable for several months if stored in the refrigerator under a nitrogen atmosphere.



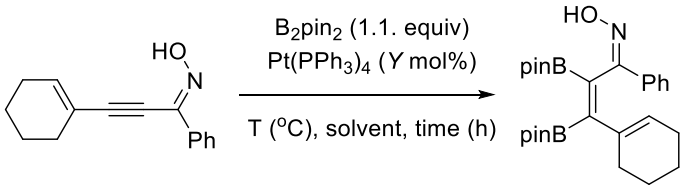
Scheme 38. *Synthesis of tetrakis(triphenyl phosphine) platinum (0).*

With respect to the diboration reaction, we were aware that our substrates could prove to be challenging as they contained an internal alkyne and a basic nitrogen atom. Moreover, this reaction had never been performed before in the presence of an oxime. As discussed earlier, Coghlan and co-workers had successfully performed a diboration reaction in the presence of a pyridine showing the compatibility of the catalyst with basic N-atoms, and so we chose to start with this procedure (Scheme 39).[26]



Scheme 39. *Syn-stereoselective diboration followed by an intra and an intermolecular Suzuki sequence.*

Coghlan used quite a high catalyst loading to perform this transformation (8 mol%), possibly because of the many functionalities present in this system. Applying these conditions to our oximes however, proved to be ineffective and the desired diboronic ester derivative was never formed. In all cases reported in table 1 we only recovered starting material.

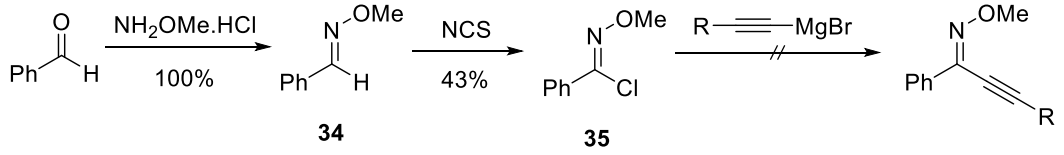


Entry	*Y*	*Solvent*	*T (°C)*	*Time (h)*	*Yield [%]*
1	8	DMF	80	24	**0%**
2	8	DMF	80	72	**0%**
3	3	DMF	80	16	**0%**
4	3	Toluene	100	16	**0%**

Table 1. *Diboration optimisation conditions.*

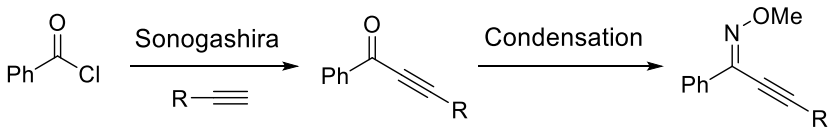
We envisaged that the free hydroxyl group could be interfering with the metal catalyst and so the decision was taken to change the oxime moiety into an *O*-methyl oxime ether. For the synthesis of *O*-methyl oximes, the condensation reaction was performed using *O*-methyl hydroxylamine hydrochloride. Chlorination of **34**, however, proved to be problematic. The reaction was slower in the case of *O*-methyl oxime relative to the parent oxime, and so more

equivalents of *N*-chlorosuccinimide were added over time to furnish the compound **35**. Unfortunately however, the subsequent nucleophilic attack of the Grignard reagent did not occur under these conditions, even using different terminal alkynes (Scheme 40).



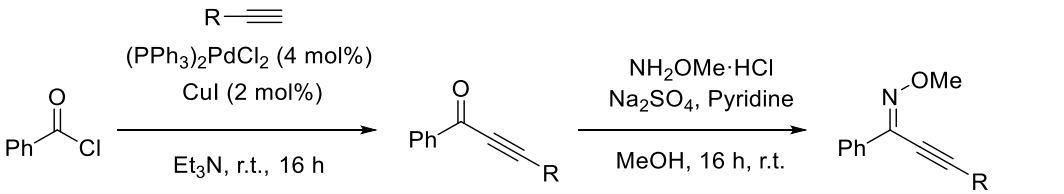
Scheme 40. *Proposed synthetic route to O-methyl oxime substrates.*

In considering alternative routes to the key substrates, we were attracted to a report by Larock *et al.*,[36] who showed that phenyl ynones could be formed from the well-known Sonogashira coupling reaction using benzoyl chloride and terminal alkynes (Scheme 41). Ynones could then be successfully transformed into the corresponding *O*-methyl oximes.



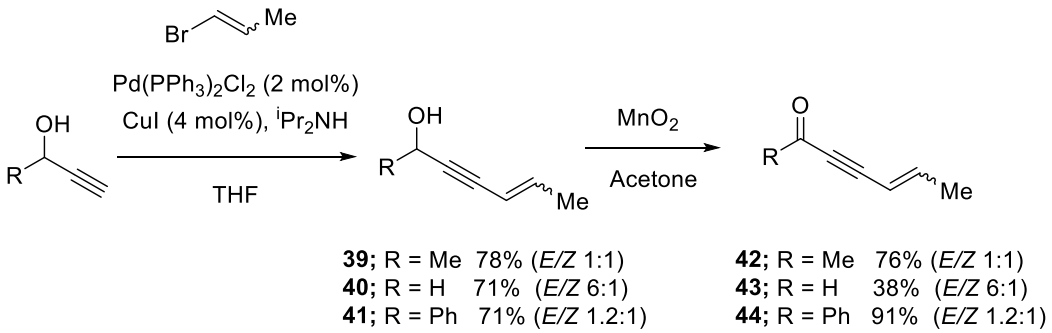
Scheme 41. *Proposed route by Larock to form acetylenic O-methyl oximes.*

In the event, a range of terminal alkynes were smoothly transformed into phenyl substituted ynones in good to excellent yields (Scheme 42). The isopropenyl alkyne substrate was very prone to Glaser coupling, and so an increase in yield might have occurred had we resorted to using an excess of terminal alkyne. Nonetheless, all the reactions could be performed on gram scale so at this stage we decided to progress these towards the oxime forming reaction. With regard to the condensation step, all three ynones furnished the desired *O*-methyl oximes in very good yields and as geometrically pure products (Scheme 42; yields over two steps).



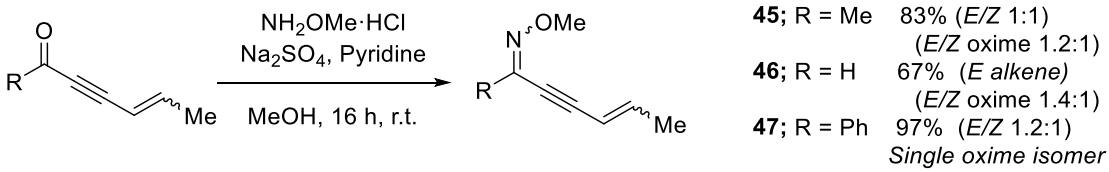
Scheme 42. *Synthetic route to compounds **36**, **37** and **38**.*

In an effort to broaden the scope of oximes for the diboration study, we employed a small family of readily available propargyl alcohols in a coupling-oxidation procedure to prepare ynones **42, 43** and **44** (Scheme 43).



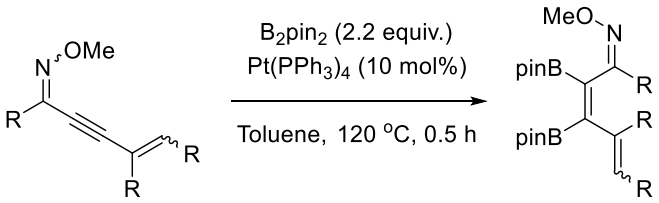
***Scheme 43**. Synthesis of ynones **42, 43** and **44** via a Sonogashira coupling – oxidation procedure.*

Ynones **42** - **44** were successfully transformed into the corresponding oximes in good to excellent yields. Despite their rather low boiling point, we were able to synthesise Me- and H-substituted oximes in a sufficient amount to study the subsequent transformations in detail. As will become important later, we noted in these cases that a mixture of oxime isomers was evident in all cases **45** – **47** (Scheme 44). This is in contrast to when we use phenyl substituted ketoximes (**36** to **38**), where a single oxime isomer was consistently obtained.



***Scheme 44.** Synthesis of ketoximes **45, 46** and **47**.*

Pleasingly, alkynes bearing the *O*-methyl oxime ethers turned out to be good substrates in the diboration step, and compounds **36-38** and **45**-**47** were successfully transformed into the corresponding diboronic ester derivatives (**48** to **53**) (Table 2).



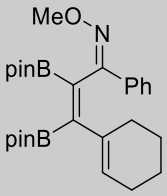
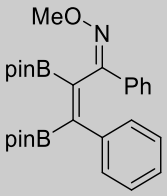
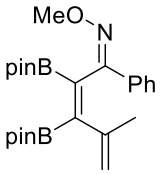
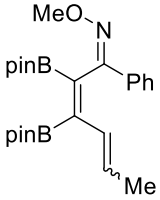
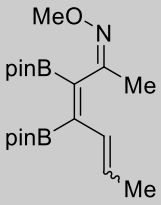
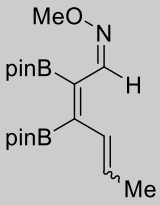
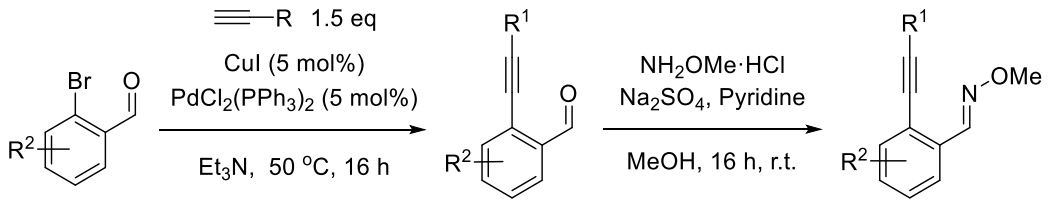
Compound	*Product*	*Yield*	*Compound*	*Product*	*Yield*
48		72%	**49**		74%
50		68%	**51**		82%* (*E/Z* alkene 1.2:1)
52		49%* (*E/Z alkene* 1:1)	**53**		34%* (*E alkene*)

Table 2. *Diboration of O-methyl oxime substrates.* **1.1 eq. B_2pin_2*

It is interesting to note that there was a profound solvent effect observed in this reaction; while the products were formed in toluene at 120 °C, the previously reported solvent, dimethylformamide, proved to be ineffective. At this stage the high catalyst loading gave us good results and so efforts to decrease the loading were not explored. Products **48** to **50** were obtained in good yields after Kugelrohr distillation at 150 °C. For this group of compounds 2.2 equivalents of B_2pin_2 were necessary and all attempts to reduce the amount of this reagent were unsuccessful. The three products were obtained in good yield as amorphous solids (Table 2). On the other hand, compounds **51**, **52** and **53** could be purified on florisil and a reduction of the equivalents of boronic ester reagent to 1.1 was effective.

Last but not least, we focused our attention on the synthesis of 2-alkynyl benzaldehyde derivatives. These substrates would, upon diborylation and cyclisation, furnish isoquinoline boronate esters, giving us the opportunity to study other pyridine derivatives. The synthesis of 2-alkynylbenzaldehyde derivatives was broadly precedented in the literature. [37,38,39]



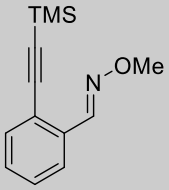
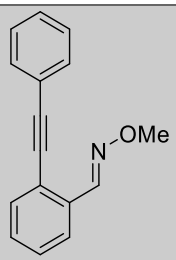
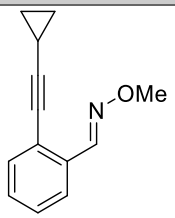
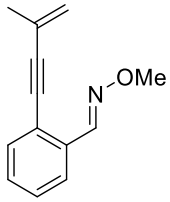
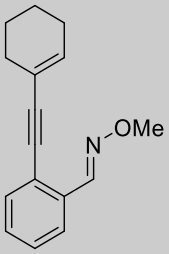
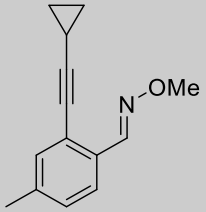
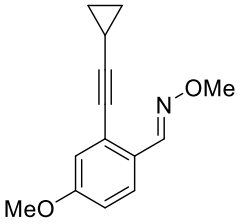
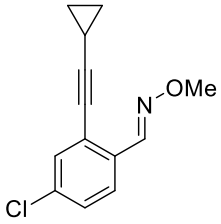
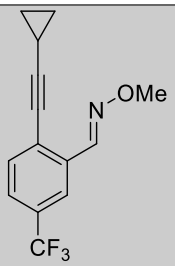
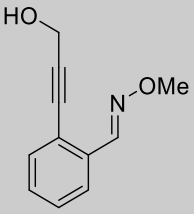
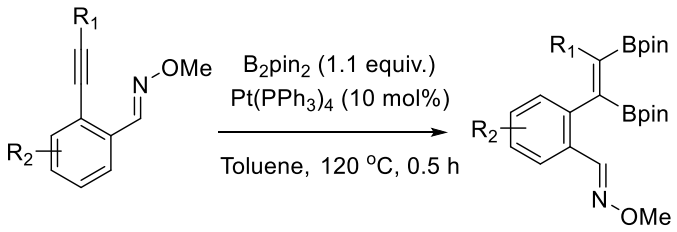
Compound	Product	Yield	Compound	Product	Yield
54		71%	**55**		72%
56		74%	**57**		68%
58		82%	**59**		44%
60		70%	**61**		55%
62		38%	**63**		81%

***Table 3**. Sonogashira coupling reaction-O-methyl oxime formation. Yields over two steps.*

Pleasingly, commercially available 2-bromobenzaldehyde was transformed into a large number of derivatives in excellent yield under standard Sonogashira coupling conditions. Furthermore,

the desired ethynylbenzaldehyde derivatives were successfully condensed to the oxime precursors in good yields over two steps (Table 3).[40]



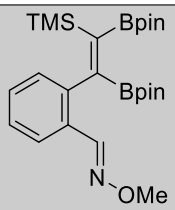
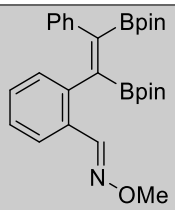
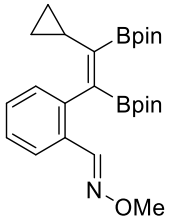
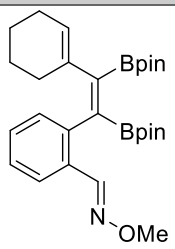
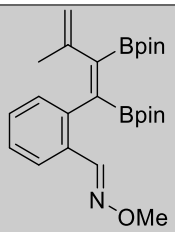
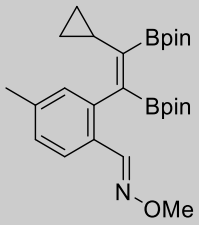
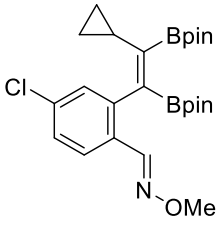
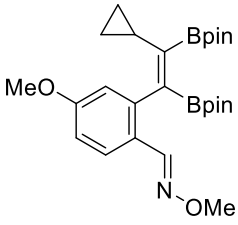
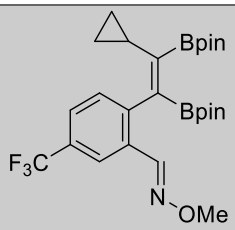
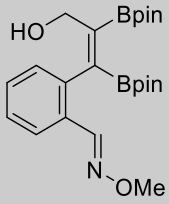
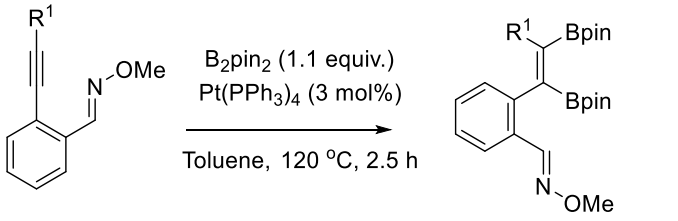
Compound	*Product*	*Yield*	*Compound*	*Product*	*Yield*
64		72%	**65**		82%
66		99%	**67**		85%
68		73%	**69**		51%
70		86%	**71**		76%
72		61%	**73**		73%

***Table 4**. Diboration of 2-alkynyl aryloximes.*

We were delighted to observe that the diboration methodology optimised at the outset of these studies was applicable to all the benzaldehyde derived *O*-methyl oximes (Table 4).

A range of alkynes were effective in the Pt-catalysed diboration and a great number of functionalities were tolerated in the aromatic ring. Both electron-donating and electron-withdrawing groups furnished the desired molecules in good to excellent yields (**69**-**72**) and even the unprotected propargyl alcohol afforded **73** in excellent yield (Table 4).

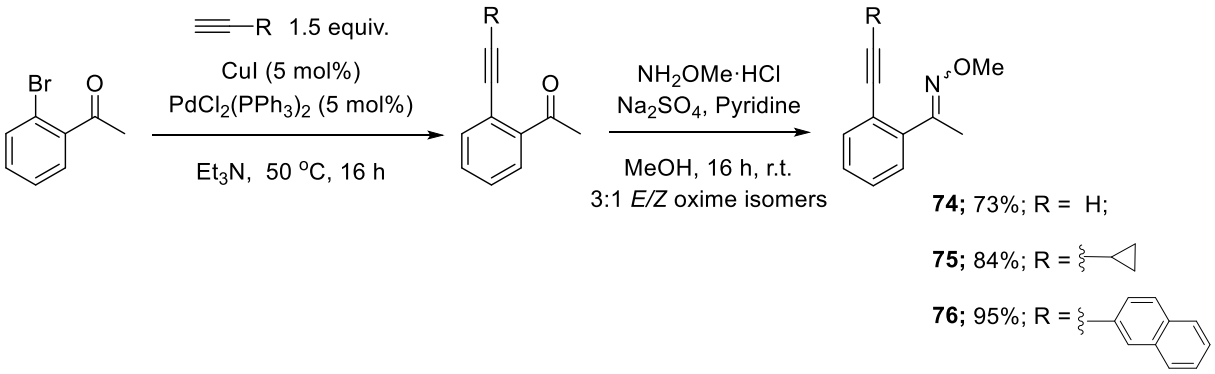
A relatively high catalyst loading was used in our scoping studies so that the reactions were complete in 30 min. However, we found it possible to lower the catalyst loading to 3 mol% and this had only a minor effect on the reaction yield over a slightly increased reaction time of 2.5 h (Scheme 45).



67; R^1= cyclohexene 72%
68; R^1= Isopropenyl 60%

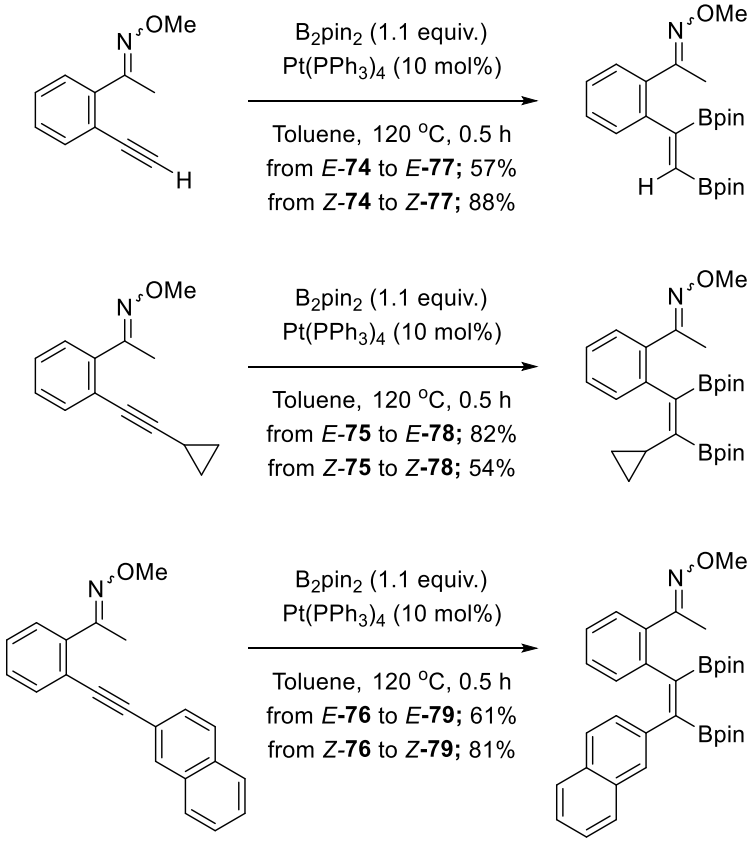
Scheme 45. *Lowering the catalyst loading.*

We next decided to explore the suitability of ketoximes to deliver more substituted heterocyclic derivatives. Me-substituted ketoximes were synthesised from the Sonogashira reaction with commercially available 2'-bromoacetophenone with the corresponding alkyne followed by condensation using methoxylamine hydrochloride. Three different substitutions were chosen on the alkyne moiety: a terminal acetylene **74** (formed by desilylation reaction of TMS acetylene), alkyl-substituted **75** (cyclopropyl) and a rather sterically hindered naphtalene derivative **76**. The three derivatives were succesfully obtained in excellent yields over two (or three) steps and as an expected mixture of oxime ether isomers (Scheme 46).



Scheme 46. *Synthetic route to compounds* ***74***, ***75*** *and* ***76****.*

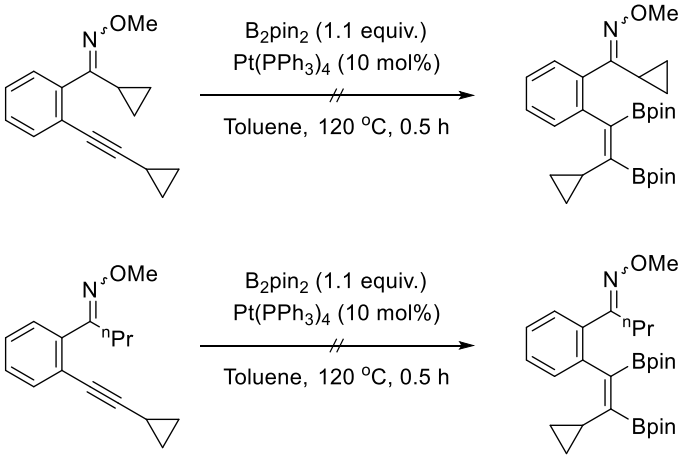
Gratifyingly, these isomers could be separated upon careful column chromatography purification and thus studied individually in the diborylation step (Scheme 47).



Scheme 47. *Platinum catalysed diborylation of E and Z-methyl substituted ketoximes.*

In the event, the six studied substrates furnished the desired vicinal diborylalkene azatrienes in good to excellent yields. To our delight, *E*-**76** was synthesised as a crystalline solid and, in this regard, we could unabiguously assign the stereochemistry of the oxime moiety using X-ray analysis (further discussion in *Chapter 3 – Investigations into the 6π-electrocyclisation of borylated azatrienes)*.

Higher homologues of our ketoxime substrates were studied in this transformation as well. Unfortunately these substrates turned out to be very prone to protodeborylation and thus we could not isolate the diboronate esters cleanly, although ^{1}H NMR spectroscopy did confirm their formation (Scheme 48).

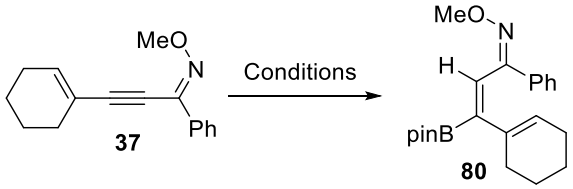


Scheme 48. *Homologus ketoximes as a limitation for our tandem methodology.*

3. Investigations towards the hydroboration of alkynes.

Together with the addition of two boronic ester units, we were interested in the incorporation of a single boron moiety by alkyne hydroboration. This hydroboration reaction could provide some advantages. The first and the most obvious one could be the fact that the differentiation between two boronic esters in the product would be avoided, potentially simplifying any further coupling studies on these substrates.

Even though hydroboration reactions have been broadly studied we found it difficult to successfully apply any of the reported conditions to our substrates (Table 5).

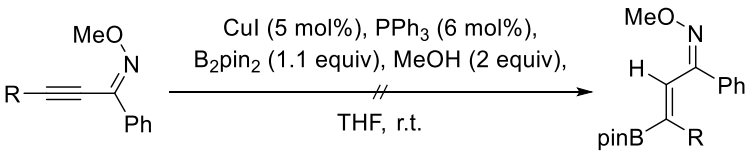


Entry	*Conditions*	*Solvent*	*T (°C)*	*Time (h)*	*Yield*
1	H-Bpin	THF/ CH_2Cl_2	55 /r.t	24	0%
3	B_2pin_2, Cp_2ZrHCl* (10 mol%)	Et_3N	55	16	0%
4	B_2pin_2, Cp_2ZrHCl* (10 mol%)	Toluene	100	16	0%
5	CuCl (5 mol%), PPh_3 (6 mol%), NaO^tBu (20 mol%) B_2pin_2 (1.1 equiv), MeOH (2 equiv)	THF	r.t.	16	**80**; 66%

Table 5. *Hydroboration optimisation.* **Prepared in situ*

First methodologies that we studied used only the hydroborating agent H-Bpin in different solvents and temperatures. None of them furnished the product, and recovery of starting material was observed in each case. We also explored a zirconium catalysed hydroboration.[41] The Zr-catalyst had to be prepared *in situ* using LiTEBH and Cp_2ZrCl_2 since it is very unstable.[42] Unfortunately, Zr-catalysed hydroboration was unsuccessful and as we were unable to confirm if this was due to poor reactivity or catalyst quality we decided to not pursue this strategy further. We then uncovered a very interesting paper from Yun that used a copper salt together with B_2pin_2 and an excess of MeOH to furnish hydroborated alkene derivatives from alkyne precursors.[43] Gratifyingly, applying these conditions to compound **37** provided **80** in good yield as a white solid.

Encouraged by the success in forming compound **80** we studied the transformation into precursors **36** and **38**. (Scheme 49).



36; R = Ph
38; R = ispropenyl

Scheme 49. *Hydroboration of **36** and **38**.*

Unlike boronic ester **80**, these two substrates failed to deliver the hydroboration product. The desired compounds could be identified in the crude mixtures via LC-MS analysis, but isolation and purification were very tedious and the results were not reproducible.

Even though the hydroboration strategy was ultimately abandoned, this first substrate **80** was a crystalline solid and gave us the opportunity to conduct an X-ray analysis that gave us a solid state structure of these borylated polyolefin systems (further discussion in *Chapter 3 – Investigations into the 6π-electrocyclisation of borylated azatrienes)*.

With all these precursors in hand, the next step was the study of effective conditions to promote the desired cyclisation and formation of the corresponding heterocyclic boronates.

4. Conclusions

Studies conducted on this aspect of the project highlighted that the use of alkyne oximes bearing a free hydroxyl were ineffective in platinum catalysed diborylation reactions. In contrast, alkynes bearing the corresponding oxime ethers functioned well, allowing us to carry out a great number of diborylations on a range of different substrates, and this methodology seems general.

Optimised conditions could be applied to linear oxime derivatives as well as to benzene tethered substrates. Even some methyl ketoximes were employed at this stage with successful results. The use of higher homologues, however, has proven to be challenging and we have not been able to obtain the corresponding vicinal borylated alkenes in sufficient purity.

In contrast, our preliminary studies on hydroboration techniques suggest this transformation is very substrate dependent and thus, a decision was made to not pursue this aspect of the project further. Importantly, one of the compounds obtained through this strategy was isolated as a crystalline solid, and this will be shown later to have provided significant insight in the later part of this project.

Most of the studied intermediates are unstable to column chromatography on silica but could be purified on florisil instead. Once purified, the products are stable and can be stored in a refrigerator over several months.

CHAPTER 3: Investigations into the 6π-electrocyclisation of borylated azatrienes

1. Introduction

The thermally promoted disrotatory 6π-electrocyclisation of conjugated trienes to form cyclohexa-1,3-dienes is an established transformation that has attracted many theoretical and experimental studies over the years. A notable aspect of these investigations is the finding that the electrocyclisation rate can be influenced by the introduction of substituents on the triene substrate.[44,45,46] In general, it has been found that the incorporation of groups in a *cis* configuration at the termini of the triene chain significantly retarded the cyclisation rate. This observation has been explained in terms of reducing the propensity for the substrate to adopt the reactive s-*cis*,s-*cis* conformation (Figure 2).

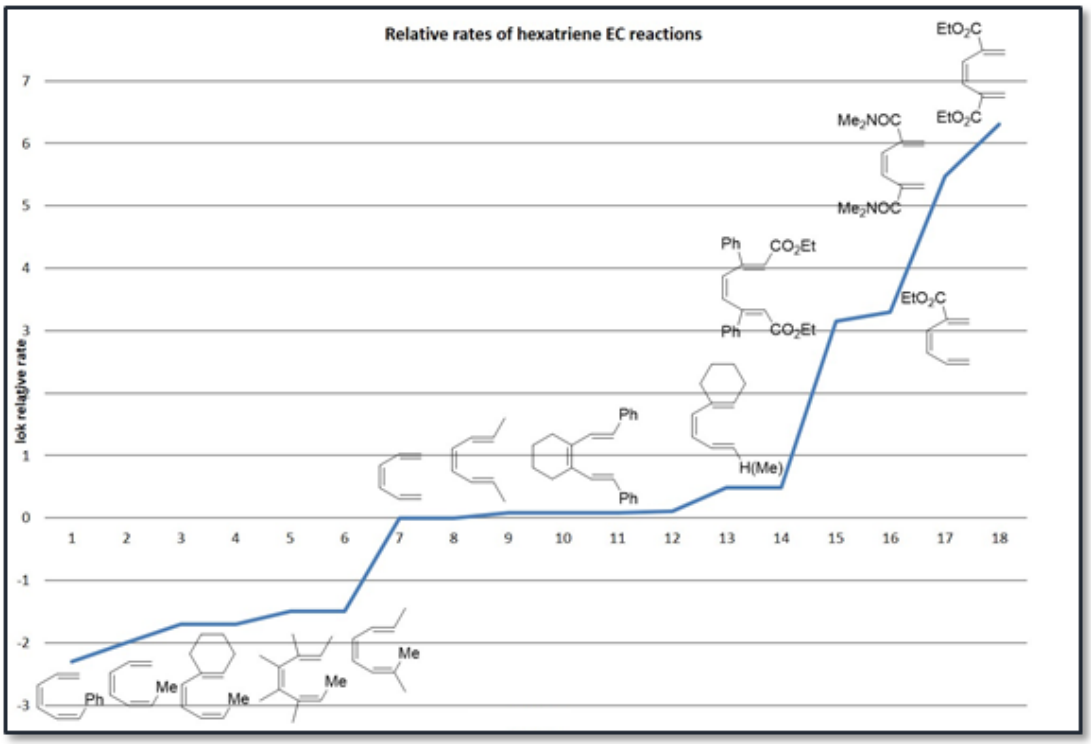


Figure 2. *Electrocyclisation rates for substituted hexatrienes .*[47]

Figure 2 shows a series of hexatriene examples and their approximate relative electrocyclisation rates. Substrates bearing no substituents at the end terminus exhibit a substantial increase on the reaction rate; which is especially favoured when electron withdrawing groups are present adjacent to the reactive positions. The addition of groups at

the end of the triene dramatically decreases the reaction rate; even when those are *trans* oriented. However, when groups are incorporated at the termini in a *cis* fashion, the reaction rate drops significantly. To the best of our knowledge, the electrocyclisation of a hexatrienes bearing a *cis-cis* conformation at the triene terminus are unprecedented.

In this regard, while the influence of substituents and geometrical effects in electrocyclisation reactions of trienes has been studied in some detail, much less is known about the related reaction bearing heteroatoms instead. To exemplify this, Otero described in 1999 a theoretical study on some imine based hexatrienes and the effect the stereochemistry of the C=N bond has on the transformation.[48] The increased activation energy is appreciable in the case of *Z*-dienimine, where the rotation of the C=N bond constitutes a huge hindrance on the electrocyclic reaction.

The dependence of oxime stereochemistry on the efficiency of electrocyclisation of azatrienes is intriguing and has never been deeply studied to the best of our knowledge. The existence of *syn* and *anti* oximes was first reported by Phillips and Lustig in 1958 using early NMR techniques, however, they had rarely been isolated as pure separated forms (Figure 3).[49]

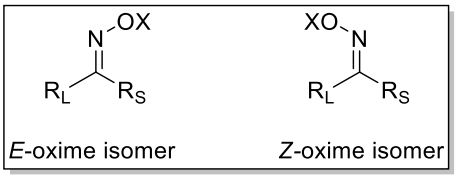


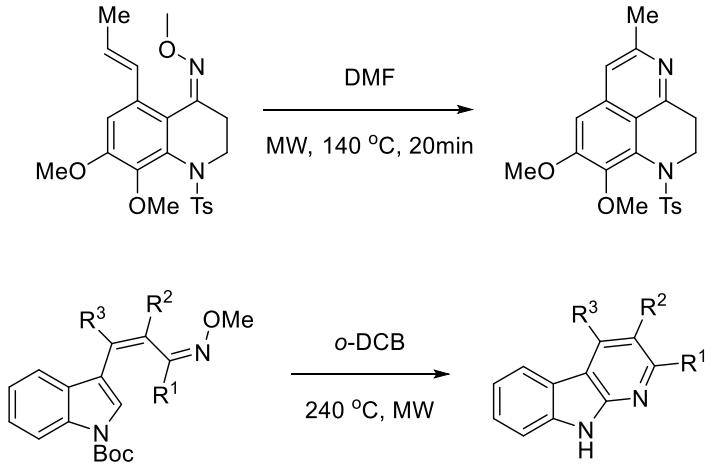
***Figure 3**. E and Z oxime isomers.*

One of the first assignment of oxime configuration was achieved by Huntress and Walker and they observed that *syn* and *anti* oximes of phenyl 2-pyridyl ketoxime had considerably different melting points (which is observed as well by some of our *E/Z* mixture of oximes).[50] In this regard, Murmann studied in the early 1960s for the first time the rates of isomerisation of these species (*X = H*) in the molten state at 175 °C.[51] In this case the results showed a great propensity of both oximes to equilibrate under thermal conditions. In contrast, the replacement of the hydroxyl for a methoxy group (*X = Me*) on the nitrogen atom makes oxime ether isomers configurationally stable and thus significantly more resistant to thermal equilibration.[52] In this regard, McCarty and coworkers reported in 1966 a study of a group of *syn* and *anti* oxime ethers heated separately at 230 °C for over a week without any detectable isomerisation.

Like many electrocyclic reactions, the cyclisation of aldoxime and ketoxime derived azatrienes takes place at elevated temperatures.[53,5] The correlation of oxime stereochemistry with the ease of cyclisation is complicated for unsubstituted oximes (*X = H*) because, as explained above, these species are very prone to *E/Z* isomerisation under elevated thermal conditions. However, this explanation can definitely not be applied in the case of oxime ethers.

The electrocyclisation of oxime ether based azatrienes has been dominated in the literature by arene tethered examples (see *Chapter 1*: *Synthesis of pyridines through 6π-electrocyclic reactions*) and these processes are generally quite efficient. Although the C=N configuration has generally not been unambiguously characterised in these cases, it can be assumed that the *E*-configuration predominates, particularly in the case of aldoximes (Figure 3, $R_s = H$).

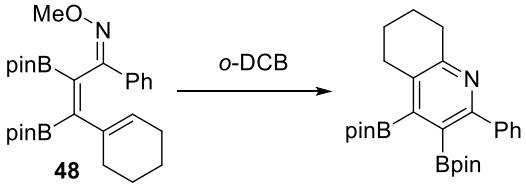
Electrocyclisation reactions of substrates that have been assigned *Z*-oxime stereochemistry are rare. Kaufman successfully cyclised a tetralone derived oxime with *syn* stereochemistry (apparently assigned using nOe techniques) while Moody showed that 3-indolyl alkenyloximes could be transformed to α-carbolines (Scheme 50).[7,8] The starting material is described as *Z*-oxime via X-ray analysis, although these systems are reported by Moody to be prone to isomerisation upon loss of the Boc-group – which does in fact take place during the cyclisation reaction.



Scheme 50. *Azaelectrocyclic reactions bearing a Z-oxime moiety.*

2. Studies on the synthesis of pyridine boronic ester derivatives from oxime trienes

The first attempts to perform the desired electrocyclisation of compounds **48** to **53** were clearly focused on the impact that the boron ester moiety would have on this transformation. The first trials to perform the desired transformation consisted of simply subjecting the precursors to high temperatures. Inspired by Hibino and co-workers who performed similar cyclisations on highly functionalised and complex substrates, we started our investigations using compound **48** in *o*-DCB at high temperatures using either sealed Schlenck tubes or microwave irradiation (Table 6).

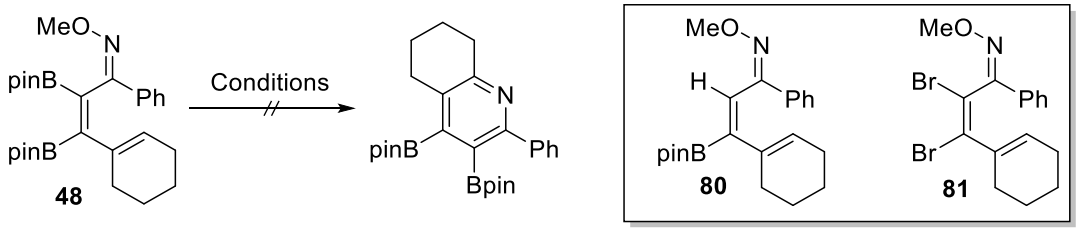


Entry	*Heating conditions*	*T (°C)*	*Time (h)*	*Product*
1	Schlenk tube	180	16	***RSM***
2	Schlenk tube	180	24	***RSM***
3	Schlenk tube	180	48	**Complex mixtures**
4	Schlenk tube	200	24	***RSM***
5	MW	180	3	**Complex mixtures**
6	MW	160	3	***RSM***

Table 6*. Investigations into 6π-electrocyclisation.*

To our surprise, boronic esters seemed to be stable at high temperatures but none of the conditions successfully furnished the expected product. After extensive heating, precursors appeared to decompose whereas milder conditions returned only starting material. None of the studied conditions seemed successful and not even the use of microwave irradiation, a heating system that generally offers excellent results, promoted the desired transformation.[6]

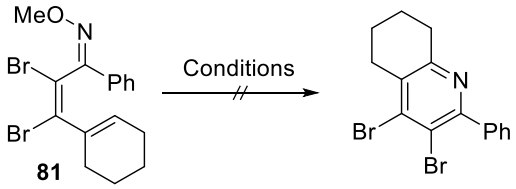
Inspired by Ellman, Chiba and Cheng who used rhodium catalysed C-H functionalisation of ketoxime derivatives to synthesise pyridine analogues, we envisaged a strategy involving the use of π-philic acids to promote the transformation in our systems.[12,11,54] We screened a number of different copper catalysts that could assist our electrocyclic process (Table 7)



Entry	*Lewis acid*	*Solvent*	*T (°C)*	*Time (h)*	*Product*
1	CuBr.DMS	Toluene	120	72	**80;** 10% + RSM
2	$CuCl_2$	Toluene	120	16	Complex mixtures
3	$Cu(acac)_2$	Toluene	120	16	Complex mixtures
4	NBS	DCM	r.t.	24	**81;** 18% + RSM

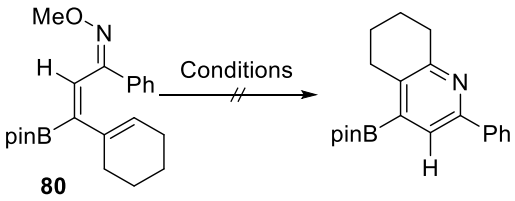
Table 7. *Lewis acid screening.*

None of the chosen Lewis acids appeared to facilitate the reaction and some undesired by-products were obtained instead. Copper bromide dimethylsulfide complex appeared to furnish the undesired protodeborylated product in low yield and the divalent salts $CuCl_2$ or $Cu(acac)_2$ decomposed the mixture. The regiochemistry of **80** was assigned by comparison with the hydroborated adduct obtained by Yun´s methodology (see *Chapter 2, Section 3 - Investigations towards the hydroboration of alkynes*).[43] When changing to NBS, we obtained an unexpected dibrominated substrate **81**. Trying to exploit our discovery we thought that a route to dihalogenated pyridines would be of high interest. However, no product was isolated after submitting this substrate to high temperatures; this compound appeared to be inert to cyclisation as well (Scheme 51).



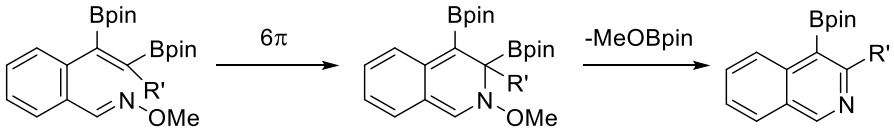
Scheme 51. *6π-electrocyclisation of by-product **81**.*

Since this transformation has never been performed before in the presence of boronic esters, we envisaged that maybe the use of highly hindered *cis*-diborylalkenes could be somehow obstructing the transformation. In this regard, monoborylated compound **80** was submitted to different heating conditions; however this compound appeared to be inert to this transformation as well (Scheme 52).



Scheme 52. *6π-electrocyclisation of compound* ***80****.*

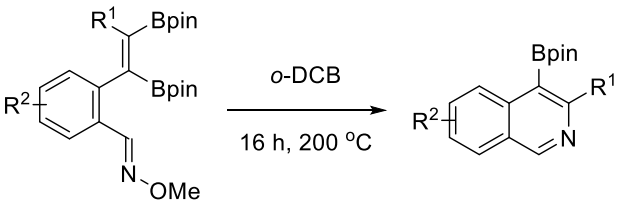
The failure of these substrates to deliver the expected heterocycles prompted us to examine a different group of molecules. Specifically, benzaldehyde derivatives **64**-**73** were subjected to high temperatures and pleasingly, all substrates underwent the key cyclisation step giving rise to a large number of functionalised isoquinoline derivatives after elimination of MeOBpin (Scheme 53) (further discussion in *Chapter 3*, *Section 3 – The importance of oxime stereochemistry on the efficiency of electrocyclic reactions*).[55]



Scheme 53. *Proposed mechanism for key cyclisation step.*

This set of substrates represent an interesting way to obtain isoquinoline boronic ester derivatives. Moreover, since the later elimination removes one of the Bpin fragments, the need to selectively functionalise the vicinal boronic ester framework is avoided.

1,2-Dichlorobenzene proved to be the optimal solvent to perform this transformation and a reaction temperature of 200 °C led to complete conversion across a series of examples within 16 h (Table 8).



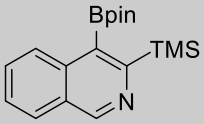
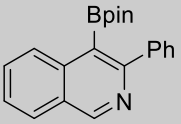
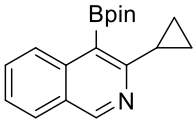
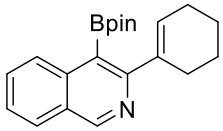
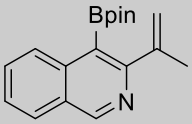
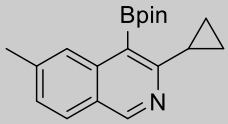
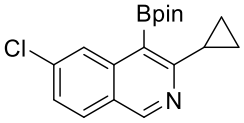
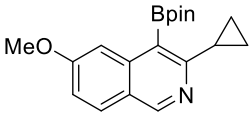
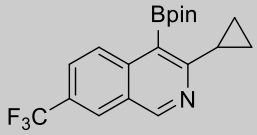
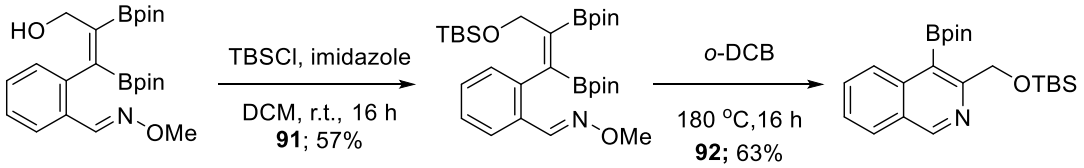
Compound	*Product*	*Yield*	*Compound*	*Product*	*Yield*
82		52%*	**83**		79%
84		88%	**85**		90%
86		61%	**87**		58%
88		75%	**89**		68%
90		91%			

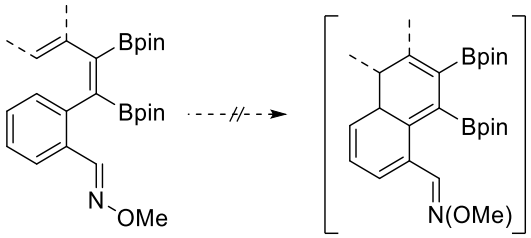
Table 8. *6π-electrocyclisation scope.* ** Reaction performed at 180 °C*

We observed that the silyl-substituted triene **64** required the use of slightly lower temperatures to avoid protodesilylation and the free alcohol bearing substrate **73** required protection as a TBS-ether **91**[56] to avoid protodeborylation during the electrocyclisation process (Scheme 54).



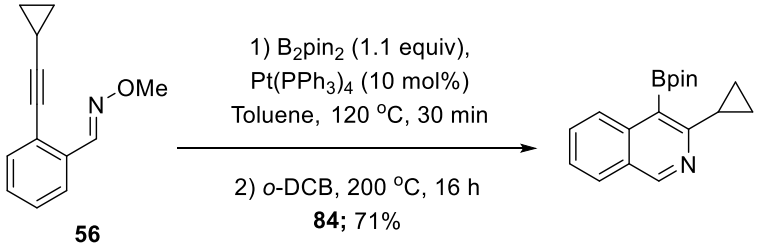
Scheme 54. *TBS ether protection of substrate **92**.*

Notably, chemoselective electrocyclisation was observed in the reactions of **83, 85** and **86,** and the corresponding naphthalenes were not observed in any of these cases (Scheme 55).



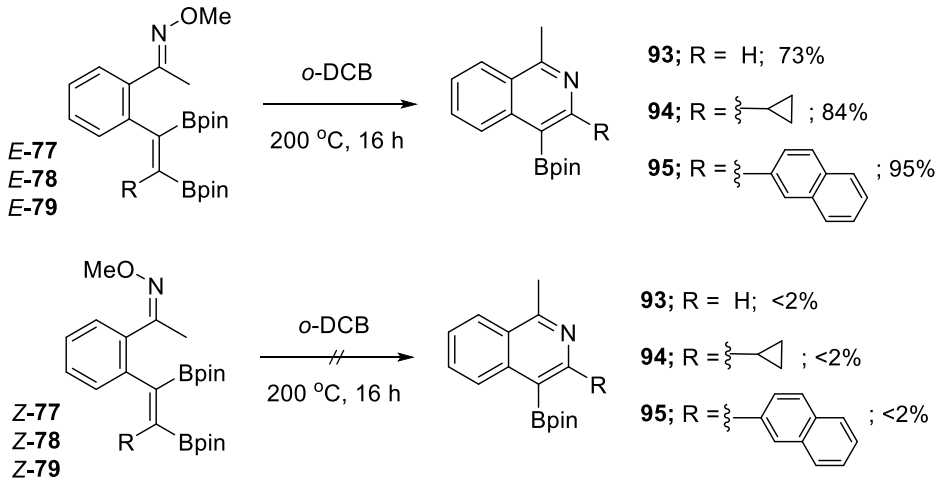
Scheme 55. *Formation of naphthalene derivatives was not observed in any case.*

We envisaged that this two-step strategy to boronic esters could be telescoped into a more direct one-pot method. In order to confirm this, we subjected alkyne **56** to B_2pin_2 in the presence of the Pt-catalyst. Subsequent addition of *o*-DCB and heating the mixture at 200 °C for 16 h resulted in clean formation of the isoquinoline product **84** in good yield (Scheme 56).



Scheme 56. *One-pot method.*

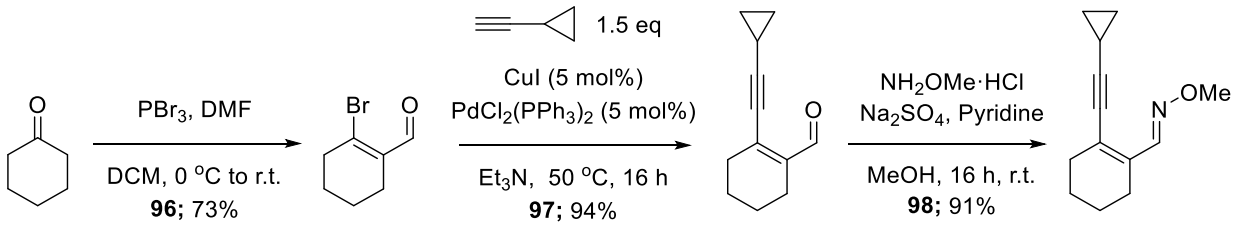
We next decided to explore the suitability of ketoximes to deliver more substituted heterocyclic products. Diboryl alkene substrates *E/Z*-**77-79** were successfully synthesised in good yields using our established route. Moreover, and as observed before, only the *E*-diborylated ketoxime furnished the isoquinoline derivative in good yields. The *Z*-substituted diborylalkenes failed to furnish the desired heterocycle, even after extensive heating. Unreacted starting material was recovered in all cases (Scheme 57).



Scheme 57. *6π-electrocyclisations of –Me substituted ketoxime azatrienes.*

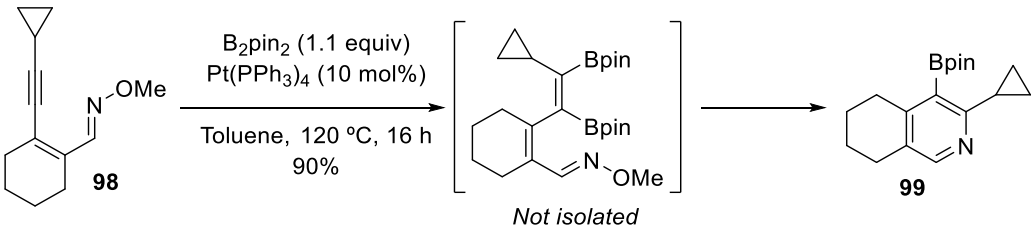
The main objective at the very start of this project was the synthesis of pyridine boronic acid derivatives. Since the bespoke transformation was found to be quite challenging our model substrate was modified in order to prove our hypothesis: experimental results suggested that oxime stereochemistry could play a role in determining electrocyclisation efficiency. As our understanding of this reactivity was growing, we focused our attention into the design of a reactive model that could furnish pyridine rather than isoquinoline boronic esters. 5,6,7,8-Tetrahydropyridine boronate derivatives were the chosen molecules to focus on. These kinds of heterocyclic structures are common in bioactive drugs and pharmaceuticals, but there is a lack of easy and versatile ways to obtain these, although their 1,2,3,4-tetrahydroisoquinoline partners can be formed by hydrogenation of isoquinolines.

The planned synthetic route included synthesis of **96** via a Vilsmeier-Haack reaction to introduce the β-bromo α,β-unsaturated aldehyde functionality.[57,58] Following our established route **97** was transformed into the desired *O*-methyl oxime **98** in excellent yield and as a single isomer (Scheme 58).



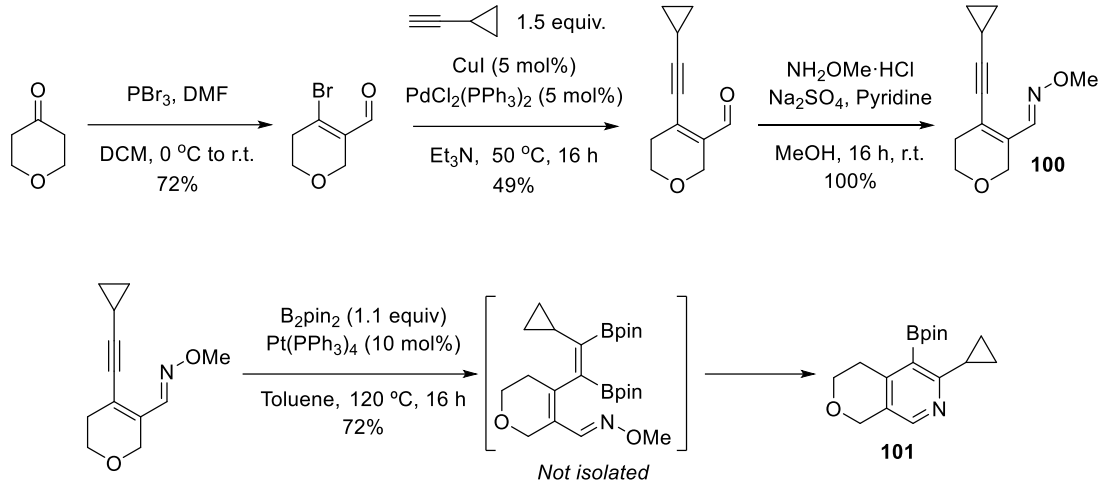
Scheme 58. *Synthetic route to compound* ***98****.*

O-Methyl oxime precursor was subjected to B_2pin_2 in the presence of the Pt-catalyst and we were delighted to observe that it directly furnished the cyclised tetrahydropyridine boronate **99** in an excellent yield after 16 hours. Electrocyclisation occurred at 120 °C in this non-aromatic precursor (Scheme 59).



Scheme 59. *Synthesis of 5,6,7,8-tetrahydroquinoline* ***99****.*

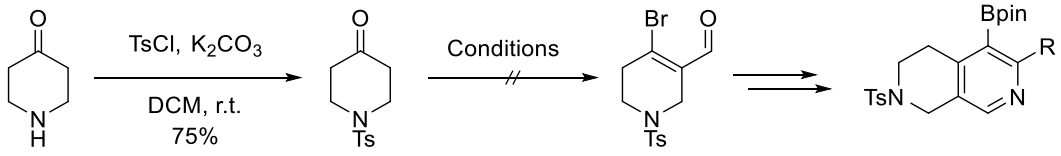
To our delight this methodology could be applied to other heterocyclic structures; a route to functionalisable 3,4-dihydro-1*H*-pyrano[3,4-c]pyridines is shown in scheme 60.



Scheme 60. *Route to functionalisable 3,4-dihydro-1H-pyrano[3,4-c]pyridine boronic ester* ***101****.*

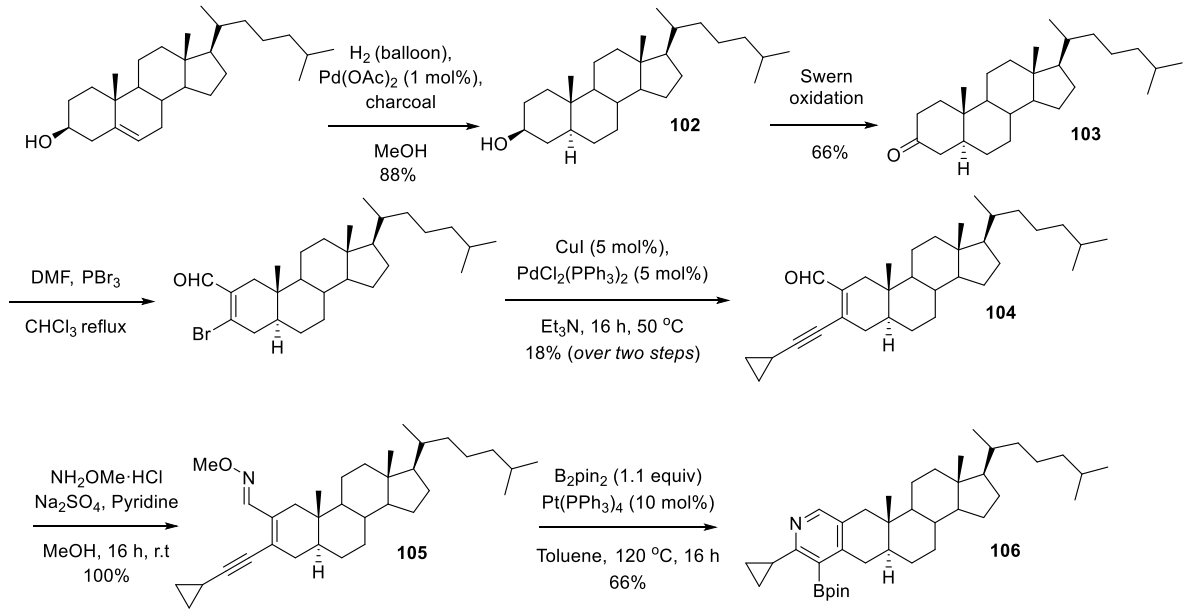
Oxime **100** was synthesised in excellent yield and as a single isomer. Once again, and as expected, the cyclised scaffold **101** was obtained directly without isolation of the diboronate intermediate. Noteworthy, this is the first time a fused tetrahydropyrano-pyridine boronate has been synthesised; no other examples of this scaffold can be found in the literature.

Challenged by the success of these previous examples we envisioned we could apply the bespoke strategy to the synthesis of novel piperidine fused pyridines. In the event, unprotected piperidinone was tosylated in good yield so as to avoid possible problems during the subsequent modifications. It is worth highlighting that, even if the next two reactions were precedented once in the literature, we were unable to reproduce the published results successfully. The first Vilsmeier-Haack reaction turned out to be very sensitive, not reproducible and the product, which was seldom isolated, proved to be very unstable. We were unable to successfully perform the following Sonogashira reaction in any case (Scheme 61).



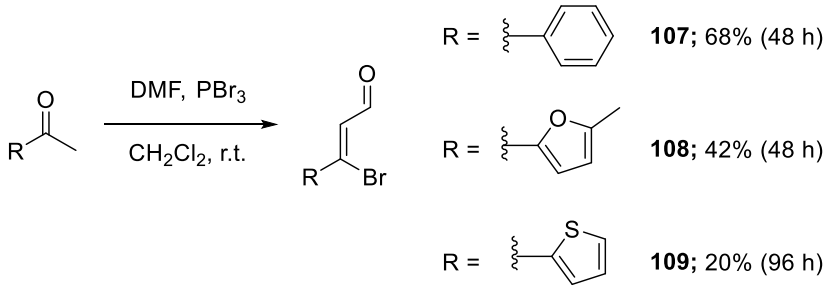
Scheme 61. *Planned synthetic route to piperidine fused pyridine boronic esters.*

Following the same principle, we chose to perform a late-stage modification of cholesterol in order to test that this method is applicable to highly complex molecules. Commercially available cholesterol was selectively hydrogenated to avoid any potential complications with the alkene moiety.[59] Swern oxidation furnished our ketone precursor **103** in good yield. Substrate **103** was synthesised as established in the literature and furnished **104** in an encouraging 18% yield over two steps. It is important to highlight that the formation of the β-bromo α,β-unsaturated aldehyde functionality in similar cholesterol derivatives has been highly precedented in the literature.[57,60] Unfortunately, we were only able to obtain and isolate our alkynyl intermediate **104** using a *one-pot* procedure after the subsequent Sonogashira coupling transformation. Pleasingly, *O*-methyl oxime precursor **105** was formed quantitatively and subsequent diborylation-cyclisation occurred as expected at 120 °C in good yield furnishing a functionalisable novel derivative **106** (Scheme 62).



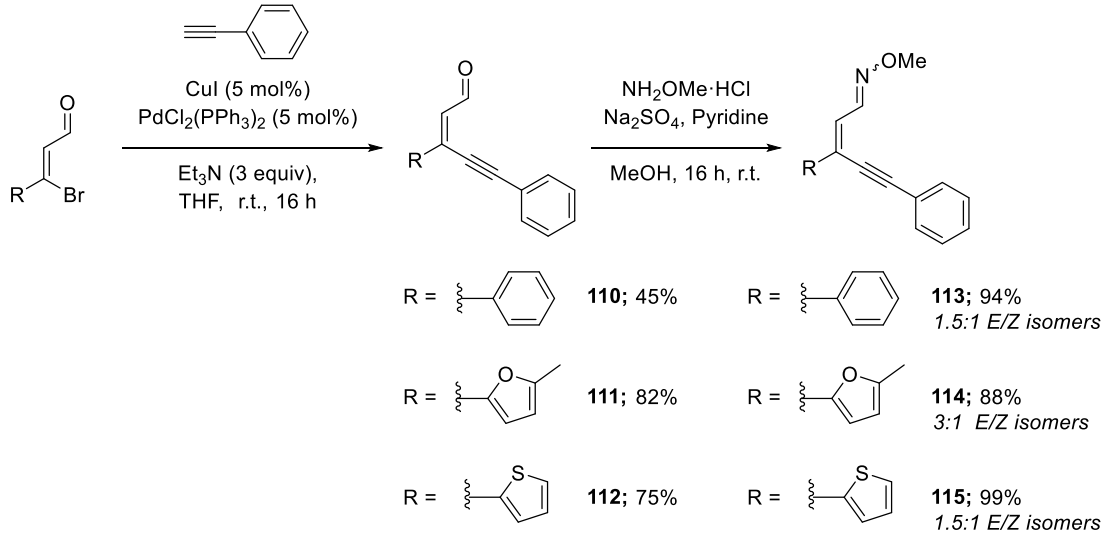
Scheme 62. *Synthetic route to pyridine boronic ester cholesterol derivative* ***106****.*

From a synthetic viewpoint, the study of an effective synthetic route to pure pyridine boronic ester scaffolds was still of huge interest. Highly encouraged by our previous results we envisaged that the diboration of yne-ene-oxime ethers should ideally form our long desired pyridine boronic esters. Different aryl substituted acetophenone derivatives were chosen as potential starting materials to perform the initial incorporation of a β-bromo α,β-unsaturated aldehyde via a known Vilsmeier-Haack reaction. This reaction, though, turned out to be a tedious and a rather slow transformation (Scheme 63).[61]



Scheme 63. *Vilsmeier-Haack reaction to access β-bromo α,β-unsaturated aldehydes.*

In spite of the low yield at this very first stage of the route, subsequent Sonogashira coupling reaction using phenyl acetylene followed by methoxyamine hydrochloride condensation delivered compounds **113**-**115** in good yields and as an expected *E/Z* mixture of oxime isomers (Scheme 64).

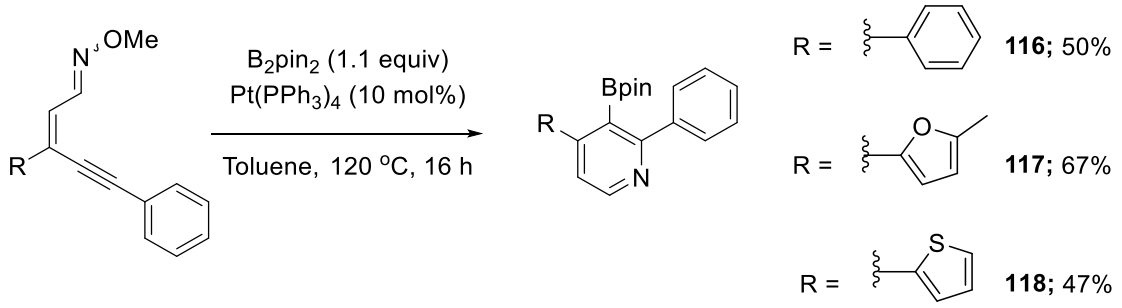


Scheme 64. *Synthesis of O-methyl oximes **113**, **114** and **115**.*

The successful synthesis of pyridine boronic esters via this electrocyclisation strategy would represent a novel and hitherto unexplored route to this class of heterocycles. Notably, access to functionalised pyridine boronic ester analogues is not straightforward. More specifically, these are classically furnished after a high number of steps via C-X borylation of pre-functionalised scaffolds.

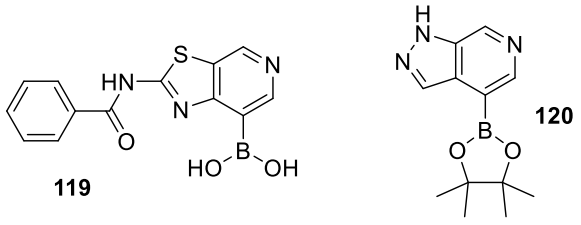
Gratifyingly, our tandem platinum catalysed diborylation – electrocyclisation reaction of compounds **113** to **115** successfully delivered the corresponding pyridines (Scheme 65). Compounds **116** to **118**, bearing different aryl groups in the 4th position were synthesised in average yield. Generally, and as expected, these scaffolds were again furnished by heating at 120 °C overnight, without isolation of the intermediate alkyne diborylation product. It is also

important to note that the product yields reflected the ratio of oxime isomers from the starting materials, based on the assumption that only the *E*-oxime was reactive (further discussion in *Chapter 3*, *Section 3 – The importance of oxime stereochemistry on the efficiency of electrocyclic reactions*).



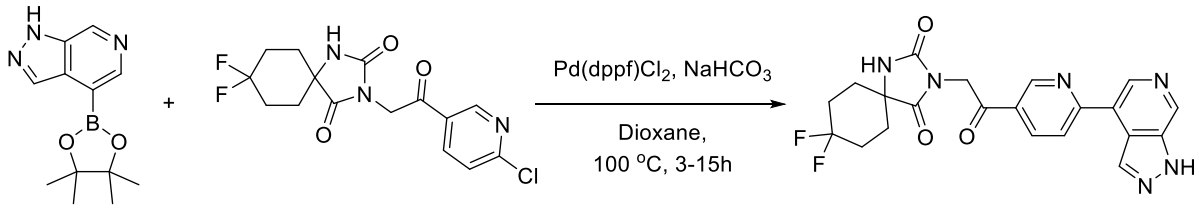
Scheme 65. *Synthesis of phenyl boronic ester pyridines.*

Encouraged by these results we next decided to broaden the scope of this method. In this context, we were particularly interested in the annellation of a heterocyclic moiety to the central pyridine ring. Thienopyridines, thiazolopyridines, furopyridines and pyrazolopyridines, although not naturally abundant, constitute synthetic targets of interest as replacements of the highly exemplified isoquinoline scaffold. The main challenge remains still the development of a synthetic route to further functionalisable scaffolds; since their accessibility has been found to be limited. For example, Bennett successfully synthesised a thiazolepyridine boronic acid derivative **119** for use as a beta-lactamase inhibitor[62] and Shishido showed an unsubstituted pyrazolopyridine pinacol ester **120** as a TRPM8 antagonist (Scheme 66).[63] Both approaches relied, once more, on the elaboration of a prefunctionalised scaffold through C-X borylation.



Scheme 66. *Examples of fused heterocyclic pyridine boronic esters present in the literature.*

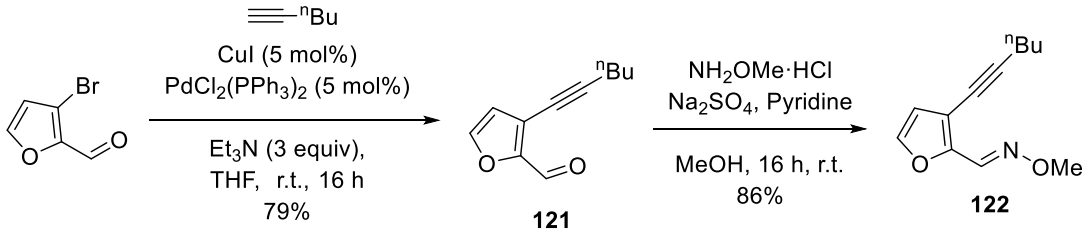
Pyrazolopyridine **120** was successfully employed in a subsequent palladium catalysed Suzuki-coupling reaction delivering a highly complex heterocycle (Scheme 67).



***Scheme 67**. Examples of fused heterocyclic pyridine boronic esters present in the literature.*

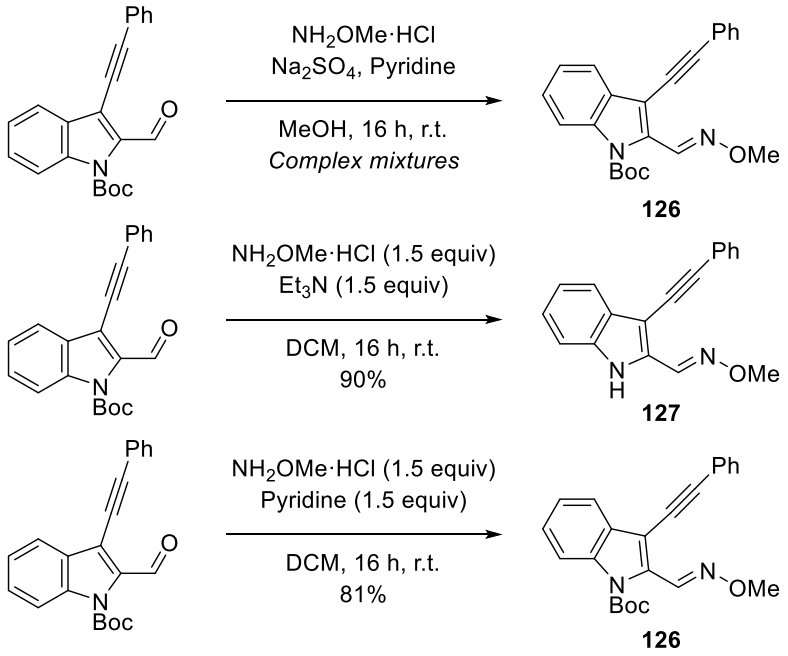
We envisaged that the successful application of the tandem Pt-catalysed diborylation/6π-electrocyclisation on heterocyclic substrates would give access to functionalisable fused heterocycles of this type. Specifically, the direct synthesis of annellated pyridine heterocycles bearing a boronic ester moiety - to the best of our knowledge – has never been performed in such a short reaction sequence.

Inspired by our reported route, yne-ene-heterocyclic oxime ethers were submitted to our established conditions. In the event, furan derivative **121** could be successfully transformed into the desired oxime **122** in excellent yield and as a single isomer (Scheme 68).



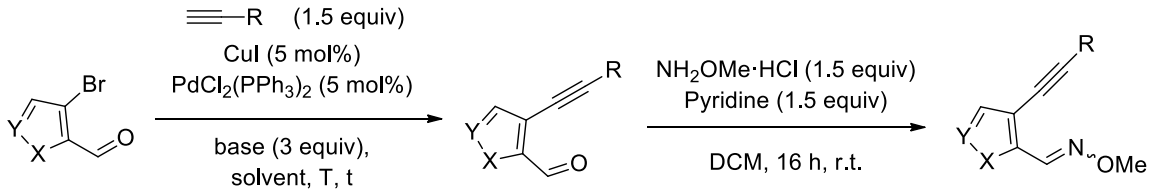
***Scheme 68.** Synthesis of (E)-3-(hex-1-yn-1-yl)furan-2-carbaldehyde O-methyl oxime.*

Other substrates, however, proved to be more challenging. Even though the Sonogashira coupling of some of the analogues required little optimisation (see experimental procedures for more details) most of them furnished the expected product in good yields. The condensation, to our surprise, turned out to be not as straightforward as expected. Some substrates, such as the indole derivatives, gave mixtures of products when we applied the conventional condensation conditions (Scheme 69). When we changed the protic methanol solvent to dichloromethane the reaction offered much better results. Interestingly, the transformation is base dependant. In the presence of Et_3N the Boc deprotected free indole derivative **127** was obtained as major product. Using pyridine as a base gave the expected – NBoc protected indole **126** in excellent yield (Scheme 69).



Scheme 69. *Synthesis of O-methyl oxime indoles.*

With the optimised conditions in hand we were able to furnish all the *O*-methyl oxime derivatives described in table 9. Substrates **122**, **125-127** were obtained as single oxime isomers – confirmed by comparison of our ^{1}H and ^{13}C NMR spectroscopic data with similar compounds from the literature. These reports had also highlighted the propensity of oximes to adopt the less sterically hindered *trans* configuration.[64] In this regard, *Z*-oxime isomers of all the pyrazole derivatives (**128** to **132**) were indeed observed by ^{1}H NMR spectroscopy but their isolation was never investigated because they were formed in such small quantities (to see accurate ratios check *Chapter 7: Experimental procedures*).



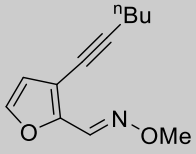
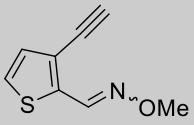
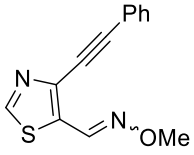
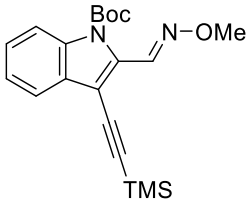
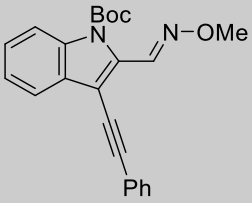
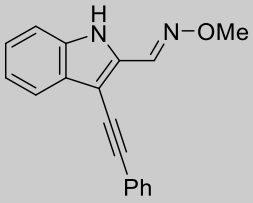
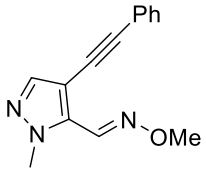
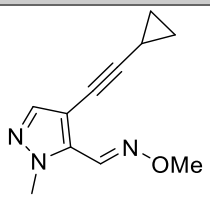
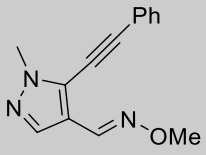
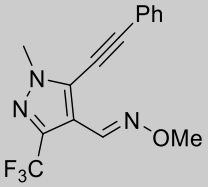
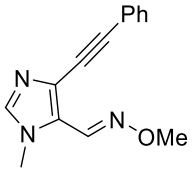
Compound	*Product*	*Yield*	*Compound*	*Product*	*Yield*
122		68%	**123**	 1/2 *E/Z* oxime isomers	95%
124	 1:5 *E/Z* oxime isomers	85%	**125**		64%
126		62%	**127**		68%
128		63%	**129**		72%
130		51%	**131**		27%
132		82%			

Table 9. *Synthesis of heterocyclic O-methyl oximes.* *Yields over two steps.*

In contrast, substrates **123** and **124** were obtained as mixture of oxime isomers. At first glance, one would expect the major oxime isomer should be the *E*-product. Unexpectedly however, the stereochemistry of the major **124** isomer was unambiguously assigned as *Z* via X-ray

crystallography (Figure 4). Although this result is intriguing and the nature of this observation is unclear, it is not the first time that the *Z*-aldoxime has been formed as the major component in heterocyclic systems. Otto and Opatz reported recently the synthesis of similar thiophene oximes where similar *E/Z* ratio was once again observed.[65]

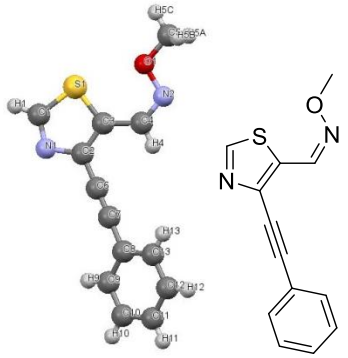
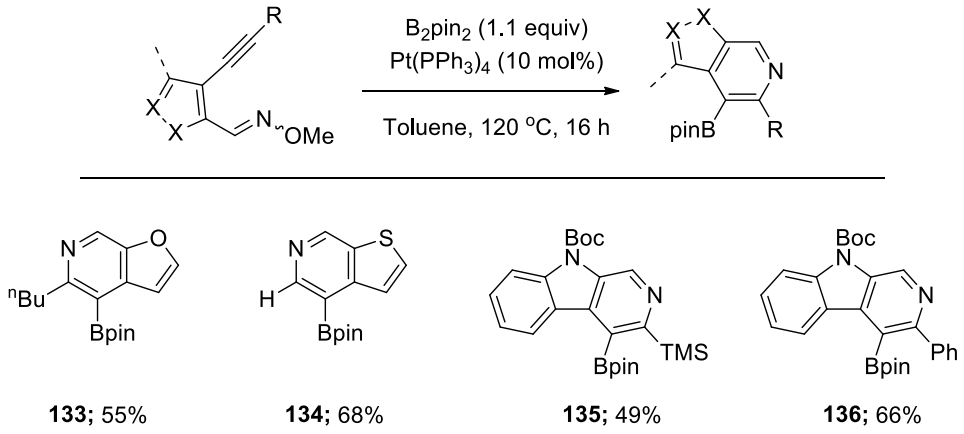


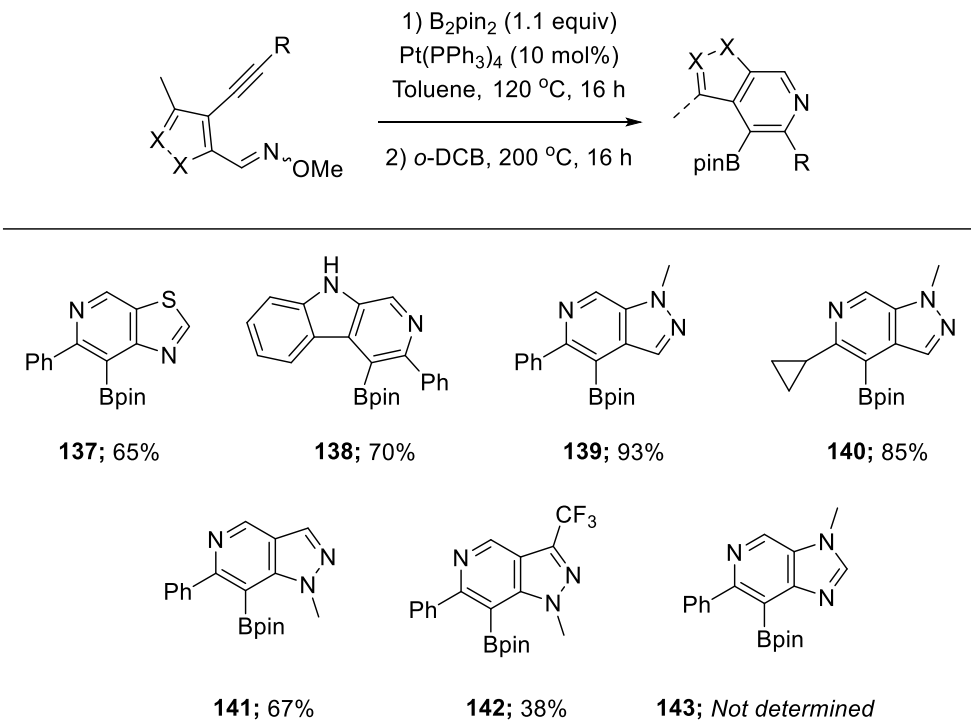
Figure 4. *X-ray structure of compound Z-**124**.*

Gratifyingly, furopyridine **133**, thienopyridine **134**, indolopyridine derivatives **135**, **136** and **138**, thiazolopyridine **137** and pyrazolopyridines **139** – **142** were formed in good to excellent yields (Scheme 71 and 72). Upon using our one-pot protocol, products **133** to **136** were synthesised in a direct manner, furnishing the heterocyclic boronates in a single step after heating over night at 120 °C (Scheme 70).



Scheme 70. *Fused-heterocyclic boronic ester synthesis at 120 °C overnight.*

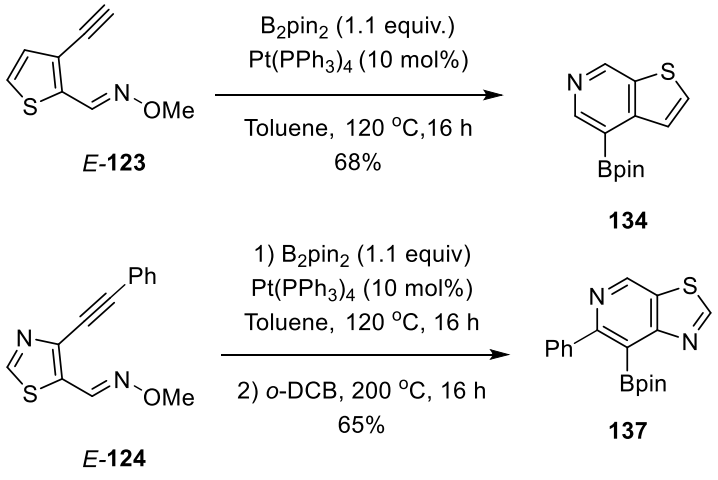
In contrast, substrates **137** to **143**, led to their corresponding cyclised products only after extensive heating at 200 °C. Nonetheless, the different pyrazole derivatives were obtained in good to excellent yields (Scheme 71).



Scheme 71. *Fused-heterocyclic boronic ester synthesis.*

Even though substrate **143** could not be isolated in analytically pure form due to its high polarity, product formation was clearly confirmed by LC-MS and ^{1}H NMR spectroscopy. We also noted that substrate **142** bearing a $-CF_3$ group led to a surprising low yield after the diboration-cyclisation sequence; this compound was extremely prone to protodeborylation and a significant amount of non-borylated pyrazolo-pyridine was obtained at the same time.

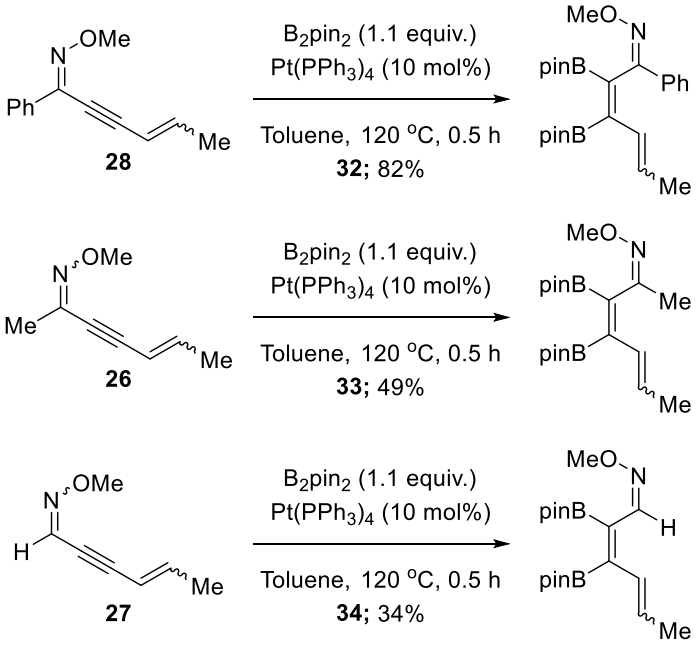
Since substrates **123** and **124** were synthesised as a mixture of oxime isomers, once again, only the *E*-isomer of both substrates furnished the desired heterocycle upon heating (Scheme 72).



Scheme 72. *Thermal electrocyclisation of compounds E-**123** and E-**124**.*

3. The importance of oxime ether stereochemistry on the efficiency of 6π-electrocyclisation reactions.

The first substrates that gave us an indication that oxime stereochemistry could have an impact on electrocyclisation efficiency arose when we examined the diboration of Ph-, H- and Me- substituted yne-oxime ethers. Specifically, we noted that the diborylation of **26** and **27** proceeded in a dramatically lower yield compared to the same transformation in the case of **28**. We suspected that the low yield in the latter two cases could arise because some of the product was undergoing electrocyclisation to a pyridine derivative which we had not isolated (Scheme 73).



***Scheme 73**. Platinum catalysed diborylation of substrates **26, 27** and **28**.*

In this regard, a decision was made to re-examine the diborylation of **26** that had proceeded in low yield when submitted to B_2pin_2 in the presence of the platinum catalyst (Scheme 73). The mass balance recovery from this reaction was unusually low. Moreover, upon closer inspection of the ^1H NMR spectra of both the starting materials and the products, we noted some interesting changes. Oxime **26** was observed as a mixture of four compounds (or isomers); a 1:1 mixture of *E*- and *Z*-alkenes (arising from 1:1 *E/Z*-1-bromo propene) and a 1:1.2 mixture of *E*- and *Z*-oxime isomers (Figure 5).

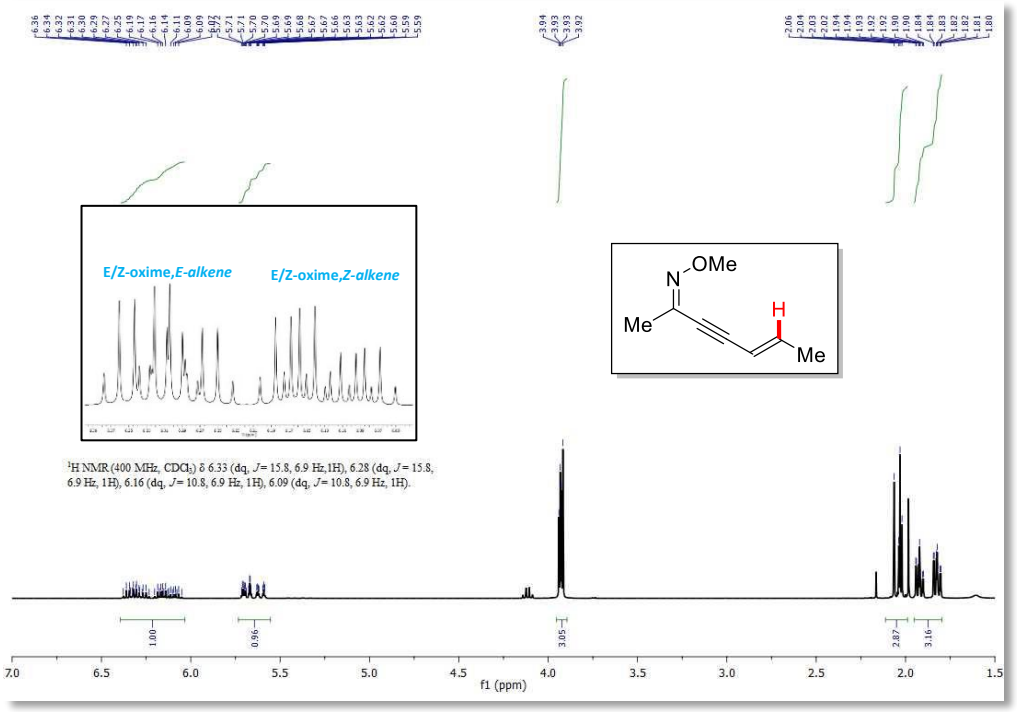


Figure 5. *NMR spectra of compound* ***26****.*

The NMR spectrum shown in Figure 5 shows the four signals for one of the alkenyl protons and the four differentiable singlets for the methyl oximes. After subjecting compound **26** to diboration conditions, the major compound isolated after chromatography appeared to be a mixture of two products only (Figure 6). The ^{1}H NMR spectrum showed only two singlets for the methoxy group adjacent to the nitrogen and the expanded area shows that the two products are a mixture of *cis* and *trans* alkenes. This data suggested that one oxime isomer had undergone diboration as expected (leading to an *E/Z*-olefin mixture of diborylated azatrienes) but that the other oxime isomer had undergone a different transformation that led to a product that could not be isolated by chromatography (hence, yields <50%). This apparent different reactivity of ketoxime isomer pairs was unknown, to the best of our knowledge.

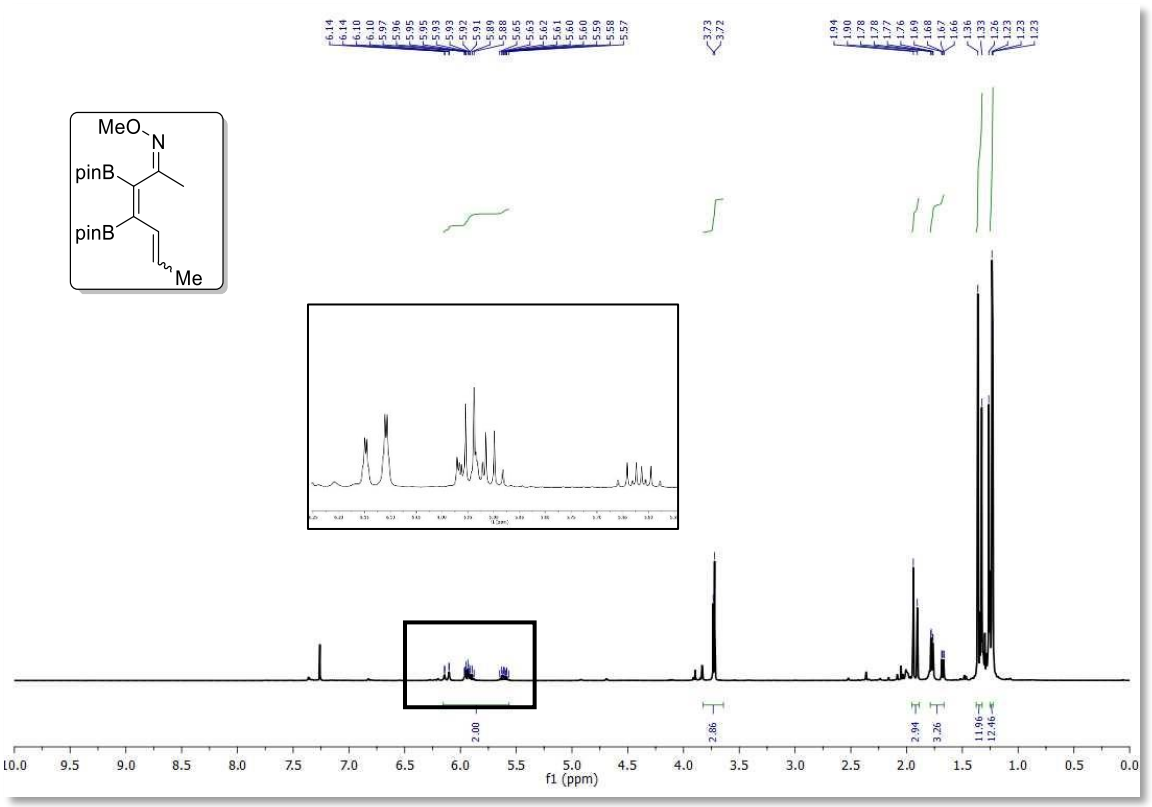
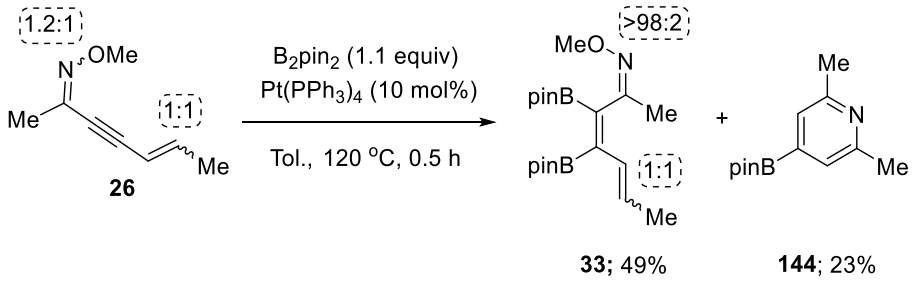


Figure 6. *NMR spectra of compound* ***33****.*

The next logical step was to repeat the reaction and to carefully analyse the crude ^{1}H NMR spectrum of the reaction mixture. As shown in Figure 7, the crude spectrum showed that there was another product in the mixture, which was later confirmed by LC-MS analysis to be 2,6-dimethyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-pyridine. This compound was formed by apparent electrocyclisation and regioselective protodeborylation of one of the oxime isomers of the starting material (Scheme 74 and Figure 7). In the crude ^{1}H NMR spectrum, we could unambiguously assign the peaks for this pyridine boronic ester by correlating them with literature data.[66] Pyridine boronic ester **144** was isolated in a low 23% yield due to its extremely high polarity.



Scheme 74*. Diboration reaction of* ***26****.*

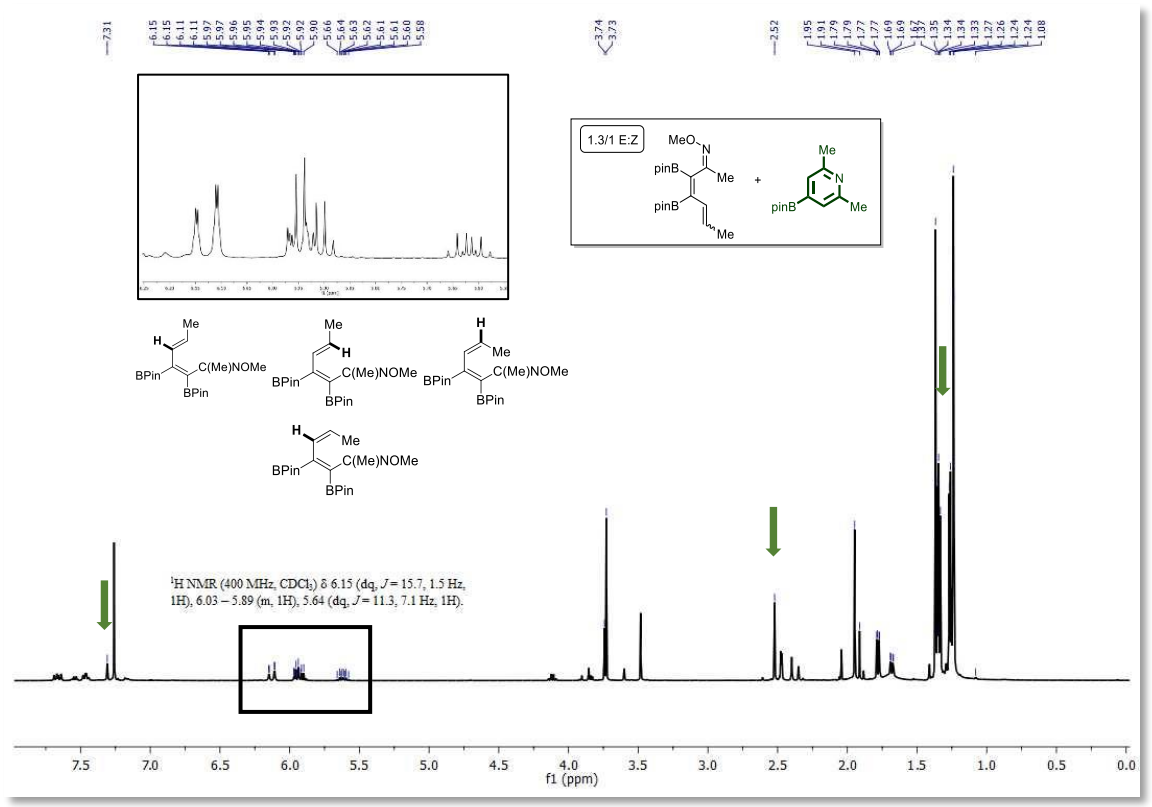


Figure 7. *^{1}H NMR spectra of crude diboration reaction of **26**.*

The results obtained in the cyclisation of *E/Z*-**26** suggested that oxime stereochemistry played a role in determining electrocyclisation efficiency. Since substrates **29**-**34** did not undergo this electrocyclic reaction and were single oxime isomers we decided to continue our investigations by assigning the stereochemistry of this class of precursors. Unfortunately, it proved to be impossible to crystallise any of the diborylated products (**29**-**34**) as they were isolated as foams. However, hydroborated substrate **80** was found to be crystalline and X-ray analysis showed it to have *E*-oxime stereochemistry (Figure 8). This compound, like substrates **29-34**, was found to be inert to 6π-electrocyclisation. This result prompted us to hypothesise that oxime ethers bearing the alkoxide *cis*-to the azatriene array would be less reactive than oximes with a *trans*-alkoxy (with respect to the azatriene moiety).

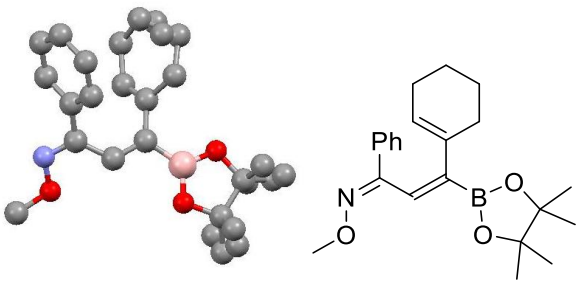
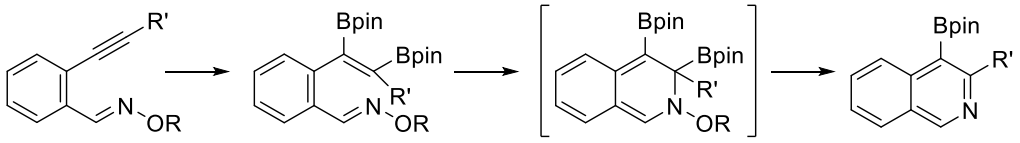


Figure 8. *X-ray structure of* ***80****.*

This hypothesis was consistent with the observation that intermediates bearing a phenyl group in the centre of the molecule underwent smooth cyclisation, as they would have the required *E* oxime configuration leaving the reacting site free to perform the desired electrocyclisation reaction (Scheme 75).



Scheme 75. *Synthesis of boronic ester derivatives from E-oxime azatrienes.*

Support for the configurational assignment of these substrates was provided when **64** was found to be a crystalline solid, allowing us to confirm the stereochemistry by X-ray crystallography (Figure 9).

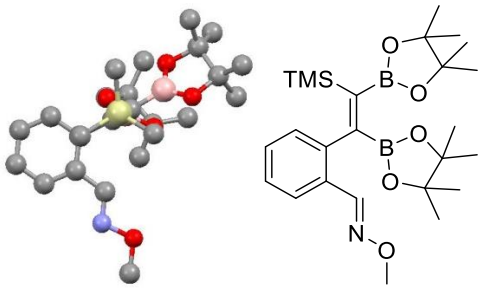
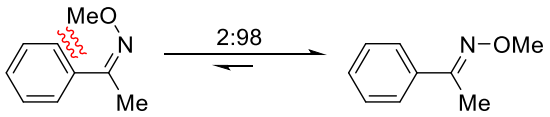


Figure 9. *X-ray structure of E-****64****.*

In order to fully investigate our hypothesis, we also prepared a series of substrates of this compound class that could provide both oxime isomers. Accordingly, methyl ketoximes *E/Z*-**77-79** were synthesised in good yields from their separable mixture of yne-ene-*E/Z* oximes **74-76**.

The proper stereochemical assignment of our pair of oxime isomers was crucial to the further understanding of our observations. In this regard, we focused our attention on the studies made by Karabatsos and co-workers who reported a list of *O*-methyl acetophenones and their preferred configuration together with their assigned ^{1}H NMR spectra.[64] Due to steric

hindrance, these acetophenone derivatives prefer the *trans* configuration, the ratio is shown in scheme 76.



***Scheme 76**. Conformational preference of acetophenone O-methyl oximes.*

In order to assign the correct stereochemistry to alkynyl oximes *E/Z*-**74-76** and diboryl alkenes *E/Z*-**77-79**, we compared our ^{1}H NMR spectra with those reported by Karabatsos. Precisely, the methoxy group adjacent to the nitrogen atom was correlated with the acetophenone derivatives reported by Karabatsos (Column 2), and the results for our alkynyl *E/Z*- **74-76** isomers (Column 3) and our diborylalkene examples *E/Z*- **77**-**79** (Column 4) are shown in table 10.

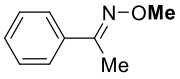
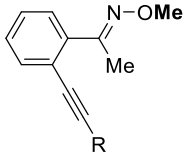
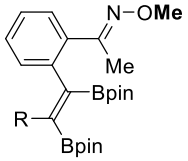
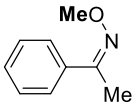
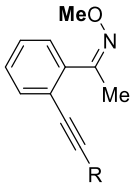
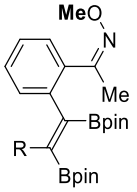
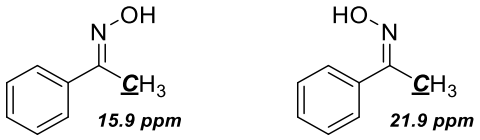
E - Substrate			
^{1}H signal (ppm) *-O**CH₃** (Solvent)*	*3.98 (neat)* *3.95 (CCl_4)* *3.96 (C_6H_6)*	*E-**74**; H : 4.00 ($CDCl_3$)* *E-**75**; Cyclop: 4.00 ($CDCl_3$)* *E-**76**; 2-Napht: 4.04 ($CDCl_3$)*	*E-**77**; H : 3.96 ($CDCl_3$)* *E-**78**; Cycloprop: 3.96 ($CDCl_3$)* *E-**79**; 2-Napht: 3.78 ($CDCl_3$)*
Z - Substrate			
^{1}H signal (ppm) *-O**CH₃** (Solvent)*	*3.82 (neat)* *3.73 (CCl_4)* *3.82 (C_6H_6)*	*Z-**74**; H : 3.81 ($CDCl_3$)* *Z -**75**; Cyclop: 3.81 ($CDCl_3$)* *Z -**76**; 2-Napht: 3.85 ($CDCl_3$)*	*Z -**77**; H : 3.79 ($CDCl_3$)* *Z -**78**; Cycloprop: 3.76 ($CDCl_3$)* *Z-**79**; 2-Napht: 3.61 ($CDCl_3$)*

***Table 10.** ^{1}H NMR correlation of E/Z-acetophenone ketoximes **74-79**.*

Table 10 shows that the ^{1}H NMR shifts of the *O*-methyl substituent of our major isomer closely matches the values reported by Karabatsos for the *trans* configuration. These signals appear to be more deshielded relative to those obtained for the *cis* isomers. One can observe that, once again, the results for our minor *cis* isomers also correlate well to those reported.

Another interesting way to assign the stereochemistry of our molecules is by comparative ^{13}C NMR analysis. Capoor and Fraser reported a series of substituted oximes (C=N–*OH*) and the

correlation between certain groups and their carbon NMR shift.[67] Interestingly, and to our delight, acetophenone oximes were described and the results closely matched our experimental observations (Scheme 77 and Table 11). In this regard, the ^{13}C NMR of the methyl group adjacent to the nitrogen atom was correlated between the acetophenone derivatives reported by Capoor and Fraser (Column 2), and the results for our alkynyl *E/Z*- **74-76** isomers (Column 3) and our diborylalkene examples *E/Z*- **77-79** (Column 4) are shown in table 11.



E-oxime isomer ***Z***-oxime isomer

Scheme 77*. [13]C NMR shifts of adjacent methyl groups in acetophenone ketoximes.*

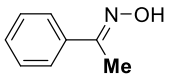
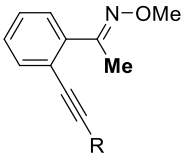
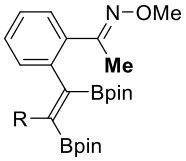
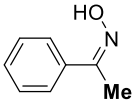
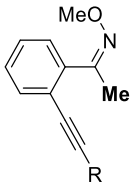
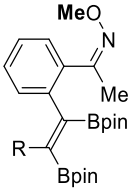
E - Substrate			
^{13}C signal *($CDCl_3$)* -***CH_3*** (ppm)	*15.9*	*E-**74**; H : 16.1* *E-**75**; Cycloprop: 15.9* *E-**76**; 2-Napht: 16.2*	*E-**77**; H : 16.5* *E-**78**; Cycloprop: 16.4* *E-**79**; 2-Napht: 15.2*
Z - Substrate			
^{13}C signal *($CDCl_3$)* -***CH_3*** (ppm)	*21.9*	*Z-**74**; H : 21.3* *Z -**75**; Cycloprop: 21.2* *Z -**76**; 2-Napht: 21.5*	*Z -**77**; H : 22.1* *Z -**78**; Cycloprop: 21.8* *Z-**79**; 2-Napht: 21.4*

Table 11. *[13]C NMR correlation of -Me E/Z-acetophenone ketoximes **74-79**.*

We could finally unambiguously assign the configuration of the major oxime isomer of these substrates when crystals of *E*-**76** were formed, allowing us to confirm the stereochemistry by X-ray crystallography (Figure 10).

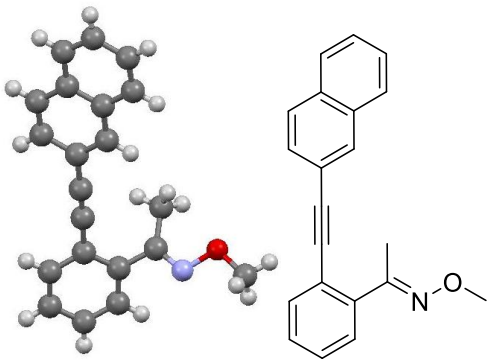
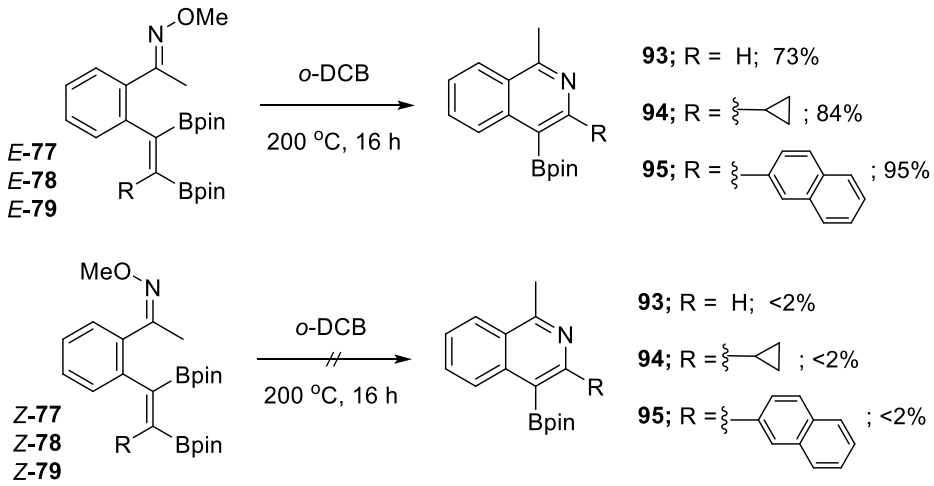


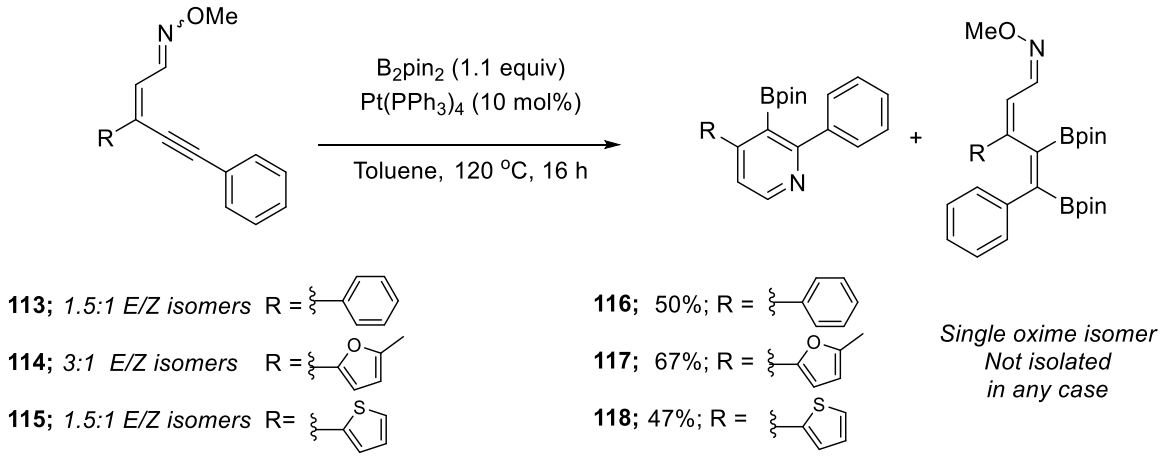
Figure 10. *X-ray structure of E-**76**.*

Having made and assigned the stereochemistry of *E*/*Z*-***74*** - ***79***, we decided to employ them in the electrocyclisation reaction. Addition of *o*-DCB and heating each of the compounds at 200 °C for 16 h resulted in clean formation of the isoquinoline products **93, 94** and **95** in excellent yield in the case of the substrates assigned as *E.* In contrast, oximes *Z*-***77***-***79*** failed to provide any isoquinoline; we were able to recover more than 60% of the starting material (Scheme 78). No conversion was observed, even after prolonged heating.



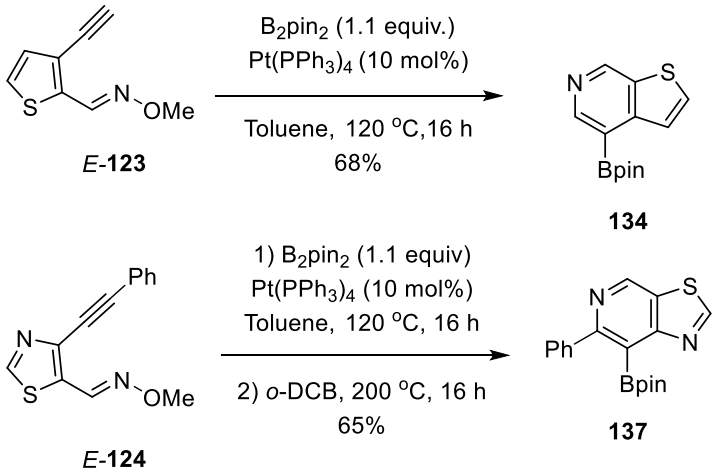
Scheme 78*. 6π-electrocyclisation of –Me substituted ketoxime azatrienes.*

We were now able to interpret some of the surprising results obtained in our earlier work. For example, the diboration-EC reactions only had delivered the corresponding 2,3,4-trisubstituted pyridines in modest overall yield. However, these reactions were carried out using a mixture of oxime isomers. Indeed, on close inspection of the crude NMR spectra, the *Z*-oxime ether isomers were discernible after overnight heating, highlighting their relatively poor reactivity in comparison to the *E*-isomers. These *Z*-diborylated molecules, however, turned out to be quite unstable and prone to decomposition and protodeborylation at room temperature, so they were never isolated and fully characterised (Scheme 79).



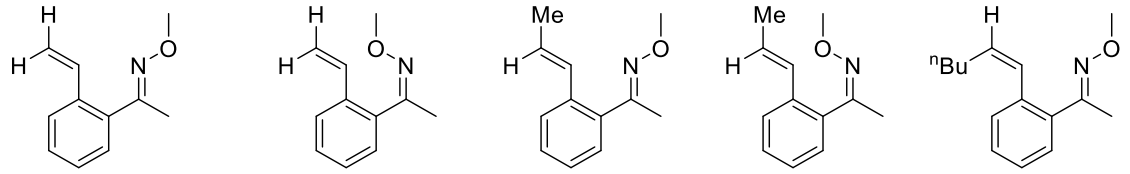
***Scheme 79**. Synthesis of phenyl boronic ester pyridines and the observation of the unreactive diborylated Z-isomer in the crude ^{1}H NMR spectra.*

This observation also applied to heteroaromatic ring tethered azatrienes (compounds **133** to **143**). While all substrates obtained mainly as single oxime ether isomers smoothly furnished the corresponding heterocyclic boronates in consistently good yields, only the *E*-oxime isomer of intermediates *E*-**123** and *E*-**124** furnished the desired thienopyridine **134** and thiazolopyridine **137** upon heating (Scheme 80). This issue will be addressed later in *Chapter 4 – Photochemical isomerisation/cyclisation of oxime trienes*).



***Scheme 80**. Thermal electrocyclisation of compounds E-**123** and E-**124**.*

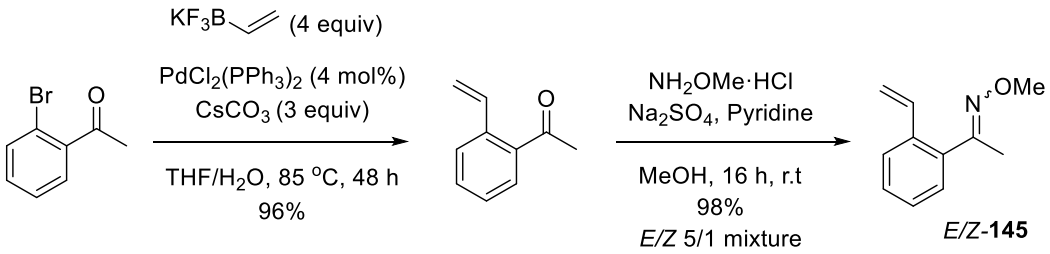
Research to date has been focused only on borylated azatrienes performing the desired transformation. In order to study the full picture on how both the oxime and the pendant olefin residues affect the electrocyclic reaction we decided to synthesise a series of simple hydrocarbon decorated 2-alkenyl acetophenone oxime ethers (Scheme 81).



145; *E*-oxime unsubstituted alkene | **145;** *Z*-oxime unsubstituted alkene | **146;** *E*-oxime *trans*-alkene | **146;** *Z*-oxime *trans*-alkene | **148;** *E*-oxime *cis*-alkene

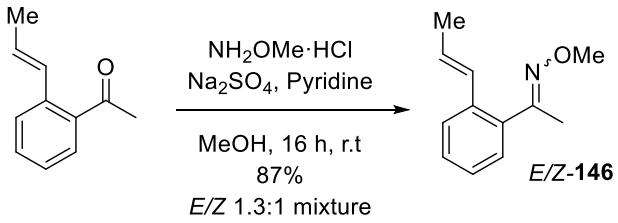
Scheme 81. *Benzene tethered olefin methyl oximes.*

The route to separable *E/Z*-**145** consisted of a Suzuki coupling reaction between 2-bromoacetophenone and the corresponding trifluoroboronate partner. Subsequent condensation gave the desired compounds in excellent yield (Scheme 82).



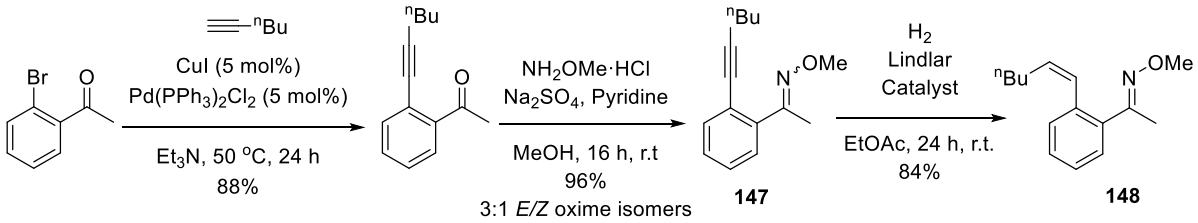
Scheme 82. *Synthetic route to compound E/Z-**145.***

Substrates *E*-**146** and *Z*-**146** were obtained by condensation of the commercially available *(E)*-1-(2-(prop-1-en-1-yl)phenyl)ethan-1-one, and separation of the oxime ethers.



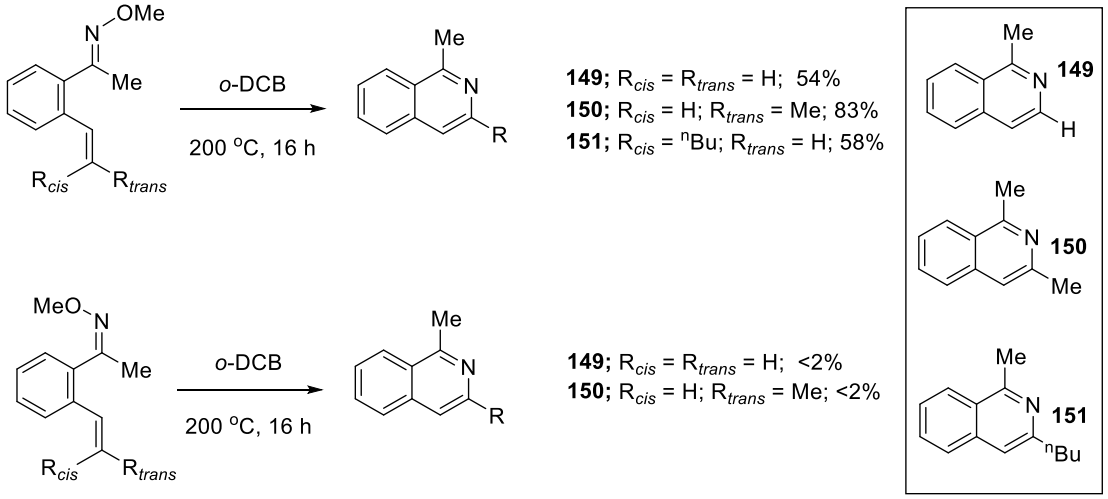
Scheme 83. *Synthetic route to compound E/Z-**146.***

Substrate **148** was produced using the route described in scheme 84. In this case, only the *E*-oxime isomer was isolated in pure form, the small quantities of the *Z* isomer that were produced made it difficult to access clean material. *E*-**147** was submitted to an alkyne reduction to provide the corresponding *cis* alkene *E*-**148** using a Lindlar reduction (Scheme 84).



Scheme 84. *Synthetic route to compound E-**148.***

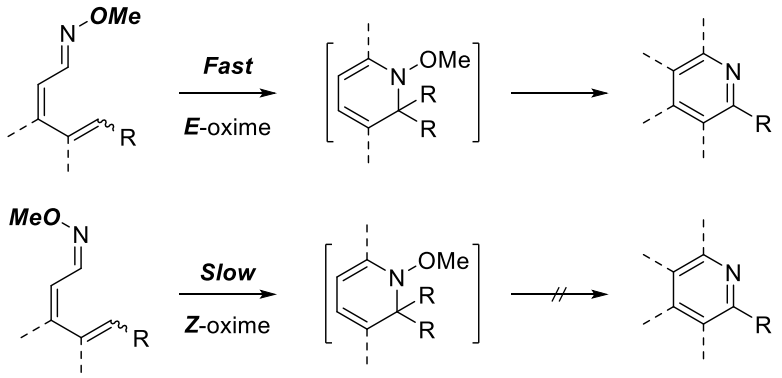
The 6π-electrocyclisation of substrates **145, 146** and **148** was studied by heating samples in 1,2-dichlorobenzene at 200 °C overnight; the results are shown in scheme 85. Oxime ether isomers *E/Z*-**145** showed a dramatic difference in reactivity under these conditions, with the *E*-isomer delivering isoquinoline **149** in 54% yield, while *Z*-isomer **145** failed to generate any detectable quantities of the same product. In contrast, substrates *trans-E*-**146** and *cis-E*-**148** were both found to undergo cyclisation to deliver the expected products **150** and **151**, albeit with the *Z*-alkene isomer providing a slightly lower 58 % yield. Once more, *trans-Z*-**146** proved to be inert to these conditions; the desired isoquinoline was not observed.



Scheme 85. *Electrocyclisation of benzene tethered olefin oximes.*

4. DFT calculations

As observed throughout our studies, it has been experimentally demonstrated that the rate of thermally promoted disrotatory 6π-electrocyclisation of conjugated pentadiene oxime ethers appears to be dependent on the stereochemistry of the C=N bond. Surprisingly however, this transformation is relatively insensitive to the stereochemistry or extent of substitution of the 5-alkenyl moiety (Scheme 86).



Scheme 86. *The effect of oxime stereochemistry on the efficiency of electrocyclic reactions.*

In order to further understand the origin of these observations, we decided to turn our attention to theoretical calculations. Thanks to our collaborative work with the group of Prof Enrique Gómez-Bengoa (Spain) we have been able to study the computed free activation energy of the cyclisation of various reaction substrates, namely **146** (*cis* and *trans*), **79**, **52** and **53**, with a special focus on explaining the general insensitivity of the reaction to the stereochemistry at the alkenyl terminus, and the high sensitivity to the stereochemistry of the oxime.

The Gómez-Bengoa group's calculations were performed at M06-2x/6-311+G(d,p)-IEFPCM(Toluene) level of theory, and are summarised in Figure 11. First, the *Z*- and *E*- isomeric forms of all initial oxime substrates show very similar relative stabilities, with differences between them of only 0-0.6 kcal/mol (Figure 11).

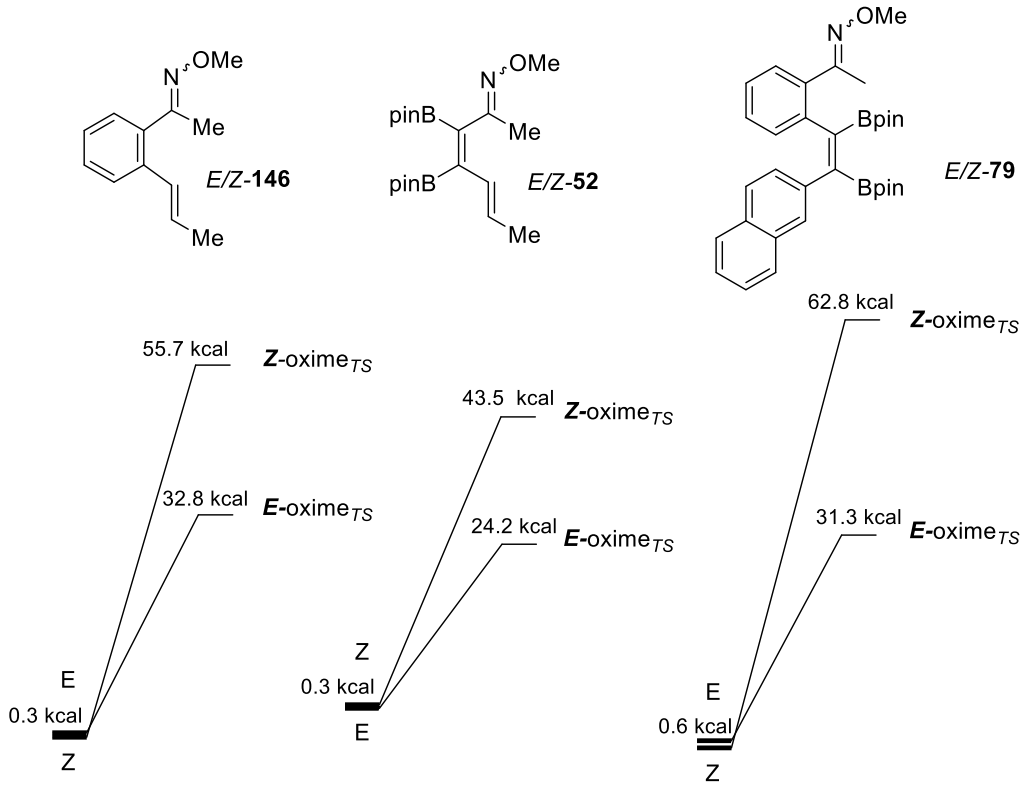
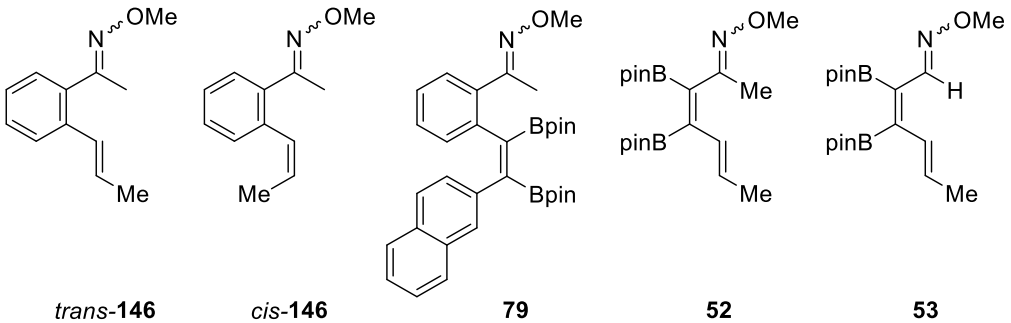


Figure 11. *Relative stabilities of oxime pairs E/Z-**146**, **52** and **79** (kcal/mol).*

Also, in agreement with the experimental results, but surprisingly, the activation energies for the cyclisation of the *Z*-oxime isomers are between 20 and 30 kcal/mol higher than those of their *E*-counterparts, which corresponds to *ten or more orders* of magnitude lower reaction rate (Figure 12). The reaction barriers for the *E*-isomers range from 24 kcal/mol (**52**) to 33 kcal/mol (**146**). These barriers are easily surmountable at the experimental temperatures typically used for the cyclisation reaction (up to 200 °C when using benzene-tethered substrates, presumably due to the need to break the aromaticity of the phenyl ring in the TS). Meanwhile, *Z*-oximes afford activation energies over 40 kcal/mol (even as high as 63 kcal/mol), meaning that this general kind of substrates will probably never react, whatever the experimental conditions employed. Thus, the stereochemistry of the oximes is crucial for the reactivity, and the reasons underlying these exceptional energy differences between *E*- and *Z*-cyclisations will be discussed later. Interestingly, oxime **52**, derived from a ketone, presents moderately higher activation barrier than the less sterically demanding substrate **53**, derived from an aldehyde, confirming the sensitivity of the process to changes at the imine position. In any case, the activation barrier of **53** is still low (24.3 kcal/mol) and ketone-oximes present good reactivity in general. Even though these substrates (**52** and **53**) are theoretically suitable substrates for cyclisation, they are problematic to obtain experimentally pure due to their high polarity and susceptibility to protodeborylation upon purification.

In contrast to the oxime moiety, the computational data also predict that the structural features on the alkene terminus do not exert any significant effect on the cyclisations, consistent with the experimental results discussed above. For example, *cis*-*E*-**146** presents slightly *lower* activation energy than the *trans* isomer *trans*-*E*-**146** (32.0 *vs* 32.8 kcal/mol, Figure 12), confirming the surprising finding that *cis*-alkenes can be as good substrates (or even better) as *trans*-alkenes in this specific reaction. In fact, the highly hindered butyl derivative **148** shows good reactivity (Scheme 85), in spite of its significant steric hindrance. Furthermore, any substitution on the alkene seems to be well tolerated, and tetrasubstituted derivative **79** shows comparable, slightly lower activation barrier than the simplest *E*-alkene **146**. Thus, the substitution degree and pattern of the alkene have no significant impact on the reactivity.



	trans-**146**	*cis*-**146**	**79**	**52**	**53**
TS ***E***-oxime	32.8 kcal	32.0 kcal	31.3 kcal	24.2 kcal	19.7 kcal
TS ***Z***-oxime	55.7 kcal	66.0 kcal	62.8 kcal	43.5 kcal	43.4 kcal

Figure 12. *Computed Free activation energies (kcal/mol) for cyclisations of oximes E and Z of different substrates, computed at M06-2X/6-311+G(d,p)(IEFPCM,toluene)*

To find an explanation for the above findings, we analysed the structures of the four different transition states of compound *trans/cis-E/Z*-**146** (Figure 13). As expected, all the cyclisations are disrotatory, and present very homogeneous C-N bond forming distances, ranging from 1.90 Å to 1.94 Å. The transition states of the two *E*-oxime isomers (*trans*-*E*-**146** and *cis*-*E*-**146**, Figure 12) are structurally very similar, and so are their barriers (32.8 and 32.0 kcal/mol). Inspection of the planarity of the reacting alkene provides an explanation for the good performance of hindered *Z*-alkenes. The PhCCMe dihedral angle θ_1 is close to 0° in the initial state of the double bond, but the value increases to 56° due to partial pyramidalisation during the transition state (*cis*-*E*-**146**), releasing part of the steric repulsion between the eclipsed aryl and methyl substituents.

Inspection of the oxime moiety during the transition state is also very instructive. The isomeric **TS**-*trans*-*E*-**146** and **TS**-*trans*-*Z*-**146** are structurally very different, as are their energies (32.8 *vs*

55.7 kcal/mol, Figure 12). We hypothesise that the lone pair of the oxime-nitrogen is actively participating in the electrocylisation, and its orientation is thus crucial for the reactivity. In **TS**-*trans*-*E*-**146**, the iminic nitrogen lone pair is pointing towards the terminal carbon of the double bond (see tentative disposition, Figure 13 in red), whereas in **TS**-*trans*-*Z*-**146**, the lone pair is pointing almost orthogonal to the forming C-N bond. We measured the dihedral θ_2 and θ_3, describing the position of the alkene terminal carbon with respect to the oxime plane (see description of the angles in Figure 13). In its ideal position, the lone pair should be aligned with the forming C-N bond, forming dihedral angles θ_2 = 0° and θ_3 = 180°. Confirming our hypothesis, the favoured structures **TS**-*trans*-*E*-**146** and **TS**-*cis*-*E*-**146** approach these values (θ_2 < 10° and θ_3 = 163°), whereas a clear deviation from them is observed in structures **TS**-*trans*-*Z*-**146** and **TS**-*cis*-*Z*-**146** (θ_2 > 50° and θ_3 < 120°).

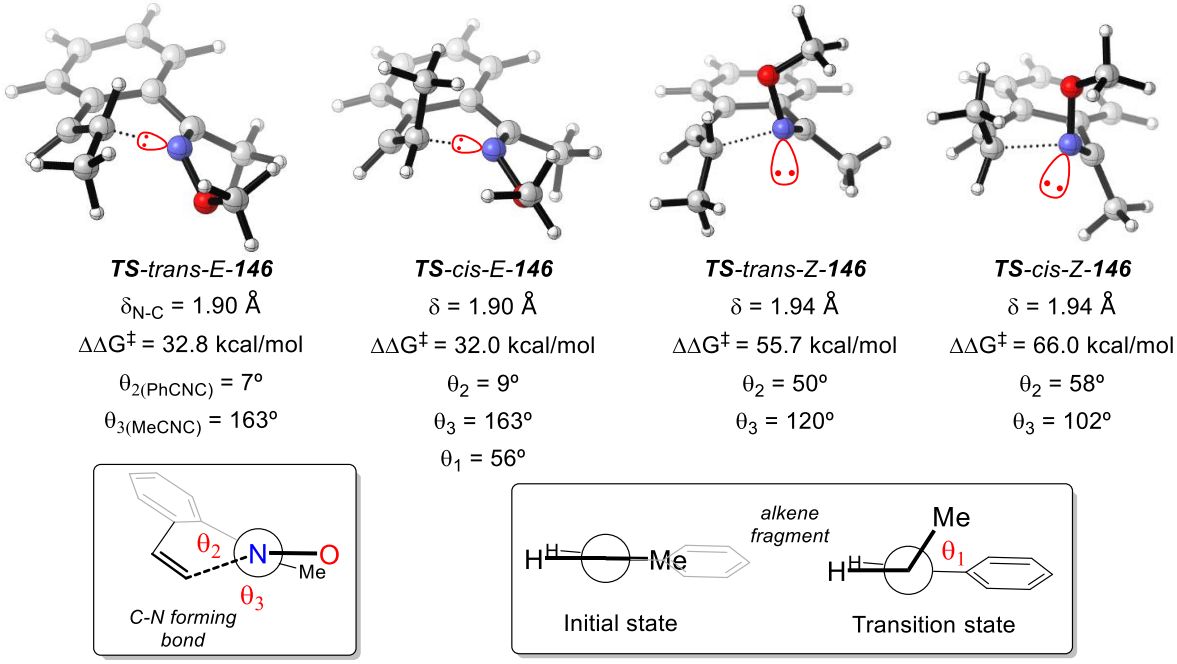


Figure 13. *Structural features of the isomeric transition structures of compound* ***146***

During the transition state of the cyclisation, the nitrogen lone pair donates into the alkene antibonding π*orbital, as evidenced in the plotted orbital interaction diagram for **TS**-*trans*-*E*-**146** (**B**, Figure 14). This interaction is lacking in **TS**-*trans*-*Z*-**146**, where the lone pair is not participating in the transition state (**C**). Also, the electronegative region (red in the ESP diagrams) of reacting oxime Z is large around the lone pairs of nitrogen and oxygen (**D**, Figure 14), showing the free electrons of nitrogen away from the forming C-N bond area. Meanwhile, there is an absence of negative charge around nitrogen in the **TS**-*trans*-*E*-**146** (**A**), since its lone pair is involved in bonding.

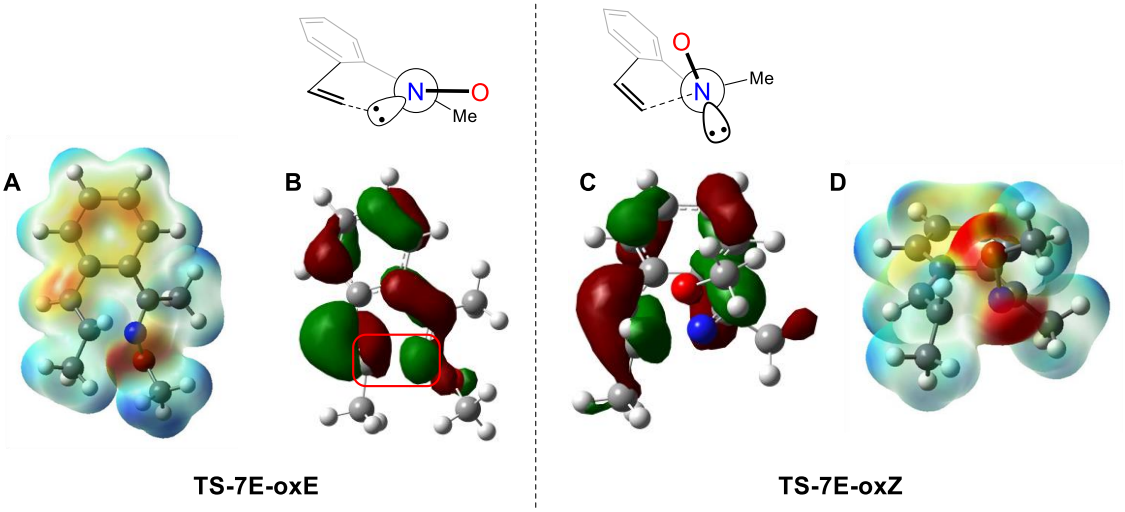


***Figure 14**. Orbital interaction diagrams (**B** and **C**) and Electrostatic Potential maps (**A** and **D**) for the cyclisation transition states of the isomeric E- and Z- **146**- oximes*

5. Conclusions

The 6π-electrocyclisation of oxime-based azatrienes has proven to be challenging. This reaction is very substrate dependent and requires high temperatures. Efforts to promote this process with the help of Lewis acids failed.

Benzaldehyde derived oximes are generally effective substrates for electrocyclisation, furnishing a number of isoquinoline boronates in good to excellent yields. The reaction was found to be tolerant of electron-donating and electron-withdrawing groups in the aromatic ring, and to a number of substitutions adjacent to the pyridine nitrogen. More challenging protected TBS ether furnished a further functionalisable heterocycle in very good yield and even substituted acetophenone *O*-methyl oximes reacted as expected to form fully substituted pyridine derivatives.

5,6,7,8-Tetrahydropyridine boronic ester derivatives have been obtained using our tandem methodology. Cyclohexanone and THP derivatives have been transformed into our desired heterocycles in a small number of steps and great yields. Piperidinone derivatives, however, turned out to be challenging precursors and the successful synthesis of the final product could not be accessed throughout our studies.

The synthesis of a diverse number of fused heterocyclic pyridine boronic ester has been achieved for the first time. In this regard, furanopyridines, thienopyridines, indolopyridine derivatives, thiazolopyridines and pyrazolopyridines have been obtained in good to excellent yields. These substrates are valuable precursors to further highly functionalised structures (further discussion in Chapter 5 – *Design, synthesis and profiling of novel annellated pyridine derivatives).*

We conclude that there is a relationship between the stereochemistry of ketoximes and their reactivity towards electrocyclic reactions. It has been experimentally shown that the configuration of this group affects its reactivity, but not that of the alkene at the azatriene terminus. Specifically, our studies show that the *E* oxime ether isomer - with respect to the azatriene moiety - is highly reactive towards electrocyclisation.

Thanks to the DFT calculations performed by the group of Professor E. Gómez-Bengoa in the University of the Basque Country (Spain) some of the surprising stereochemical aspects of this transformation could be successfully understood.

Using computational methods, we have identified a $N_{\text{lone pair}} \rightarrow$ C=C π^* orbital interaction between the reacting termini of the azatriene that lowers the energy of the transition state in electrocyclisation of *E*-oximes. This orbital interaction is not available in the case of the corresponding *Z*-oxime isomers, and the transition states for cyclisation are significantly higher in these cases. In contrast, the stereochemistry and extent of substitution at the pendant alkene do not play a significant role in modulating reactivity as partial pyramidalisation at the transition state offers a means by which steric congestion can be relieved during the electrocyclisation process.

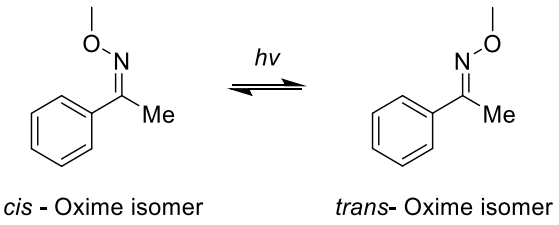
CHAPTER 4:

Photochemical isomerisation/cyclisation of *Z*-oxime ether azatrienes.

1. Introduction

Isomerisation of the carbon – nitrogen double bond of an imine (C=N) has been a subject of great interest throughout the years. Even though the thermal isomerisation of imines had been studied in detail many years ago, it was only much more recently that investigations into C=N bond isomerisation were undertaken in the excited photochemical state.

One of the first studies in this field was conducted in the early 1970s by Padwa and Albrecht. In this regard, they were interested in studying both the thermally and photochemically promoted interconversion of imine isomers. At that time, McCarty had already reported that the substituents on the nitrogen atom contribute significantly to the thermal configurational stability of this functional group.[51] Specifically, the exceptional configurational stability of oxime methyl ethers was highlighted and compared to, for instance, their *N*-aryl or *N*-alkyl partners. This thermal configurational stability made those compounds perfect analogues to study the C=N bond isomerisation under photochemical conditions since their isomerisation could not be affected by heating. The rapid *cis* – *trans* isomerisation of acetophenone derived ketoximes under ultraviolet irradiation (254 nm) was first reported in 1972 (Scheme 87).[68,69]

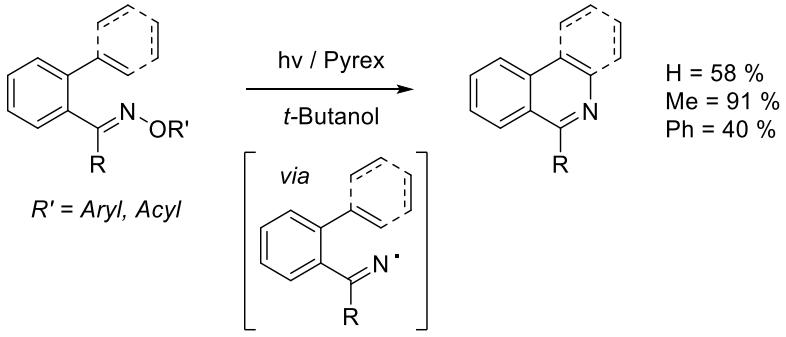


Scheme 87. *cis – trans Isomerisation of acetophenone ketoximes under ultraviolet irradiation.*

Pure *cis*-oxime isomer was submitted to the reaction conditions. Satisfyingly, a quick isomerisation was detected and both isomers could be readily separated using chromatographic techniques. Moreover, isomerically pure oximes were tested once again towards thermal interconversion. No isomerisation was noted after more than 5 days at elevated temperatures.

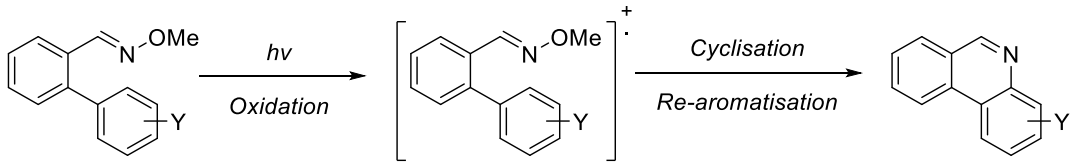
Photochemically induced electrocyclisation of azatrienes

The use of photochemistry for the synthesis of six membered ring nitrogen heterocycles has been dominated by the use of *N-O-aryl* and *N-O-acyl* based oxime azatrienes. Photolysis of these groups under UV irradiation has been broadly reported. Cleavage of the corresponding N–O bond results in the formation of the highly reactive iminyl radical intermediate that smoothly reacts in an intramolecular fashion, leading to aromatic substitution and furnishing a new C–N bond (Scheme 88).[70,71,72,73,74] This methodology has been broadly applied towards the synthesis of phenanthridine-type heterocycles.



Scheme 88. *Proposed mechanism for the intramolecular cyclisation of iminyl radicals.*

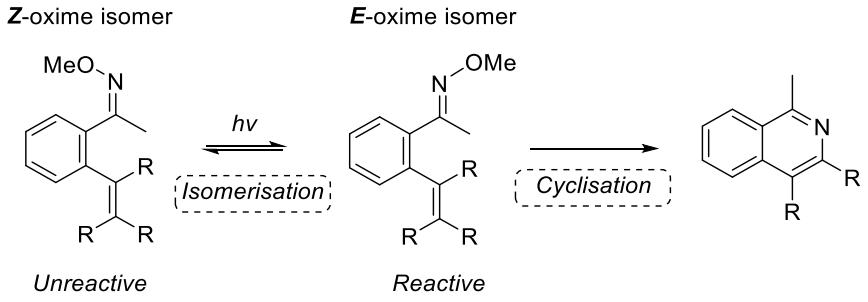
After an extensive search, it appears that the use of oxime methyl ethers in azaelectrocyclic reactions under photochemical conditions is rare. As an example, Lijser and co-workers studied a series of 2'-arylbenzaldehyde oxime ether precursors to furnish phenanthridine derivatives.[75] Curiously enough, they did not report the previously described initial N-O bond homolytic cleavage as the reaction mechanism. The theoretical mechanistic studies of this transformation concluded that the first step involves an oxidation step to form a radical cation intermediate (Scheme 89). Immediately after the nucleophilic attack of the benzene ring occurs, the methoxy radical is eliminated. Furthermore, a small amount of unreacted *Z*-oxime was observed as a by-product in some cases – highlighting, as already reported before, the existence of an equilibrium between the two isomeric species under photochemical irradiation.



Scheme 89. *Catalytic oxidative cyclisation under photoinduced conditions.*

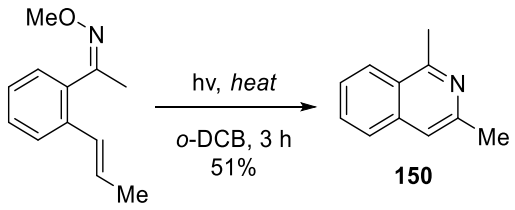
2. Results and discussion

Inspired by these studies, we envisaged that photochemistry could be a useful tool for promoting our transformation in the case of thermally unreactive *Z*-oxime substrates. Our planned strategy consisted of a *Z/E* switch via photochemical isomerisation followed by an *in situ* cyclisation on to the desired heterocycle (Scheme 90).



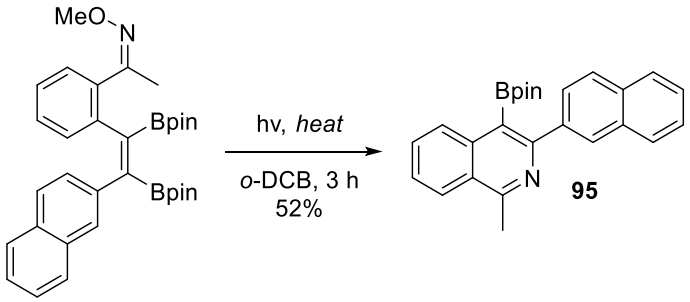
Scheme 90. *Photochemically induced Z/E isomerisation followed by a 6π-electrocyclisation.*

Firstly, substrate *Z*-**146** was subjected to irradiation under a high pressure 300 W ultraviolet lamp in *o*-DCB. To our delight, full conversion to the isoquinoline was detected after 3 hours (Scheme 91). Isoquinoline **150** was isolated in an encouraging 51% yield from the previously unreactive *Z*-**146** precursor. It is important to underline that this was the very first time we were able to isolate any cyclised adduct from the corresponding *Z*-oxime partner.



Scheme 91. *Photochemically promoted elecrocyclisation of Z-**146**.*

Since simple alkenes were stable to irradiation, the next logical step was to apply this methodology to diborylalkene azatrienes. In this regard, we were unsure about the impact of irradiation on our borylated adducts. The behaviour of carbon – boron bonds under photochemical conditions has been poorly studied over the years. Some examples from the early 1970s report C – B cleavage under the specified conditions (ultraviolet irradiation, 35 °C, CCl_4).[76] However, the boron handle was, in all cases, coordinated to a nitrogen atom. Consequently, we decided to challenge substrate *Z*-**79** (Scheme 92). To our delight, the reaction was complete in 3 hours giving complete conversion to the corresponding isoquinoline boronate **95**. No trace of protodeborylation adduct was observed both via NMR spectroscopy and LCMS analysis.



Scheme 92. *Photochemically promoted elecrocyclisation of Z-**79.***

Encouraged by this results we decided to further study this transformation. Photochemical conditions are able to significantly decrease activation energies of thermal reactions since they offer an alternative pathway to high energy intermediates. In this regard, we were unsure if the transformation was indeed proceeding through an *isomerisation/cyclisation* pathway or, simply via a photochemical promoted electrocyclisation reaction. In this regard, the photochemical cyclisation of *Z*-**79** was monitored via LC-MS analysis and ^{1}H NMR spectroscopy. Firstly, figures 15-16 show the LC-MS and the ^{1}H NMR spectra of pure *Z*-**79** and *E*-**79** as a reference point.

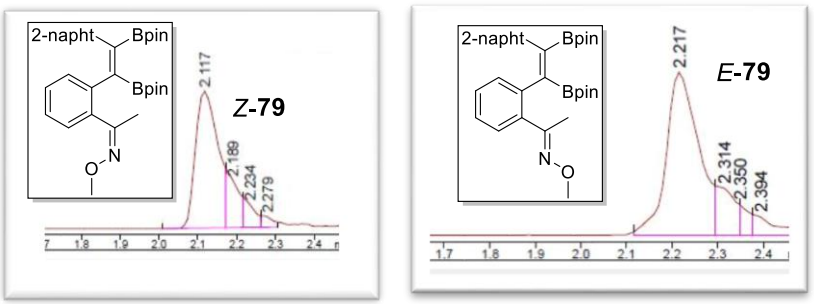


Figure 15*. LC-MS of pure Z-**79** and E-**79** substrate.*

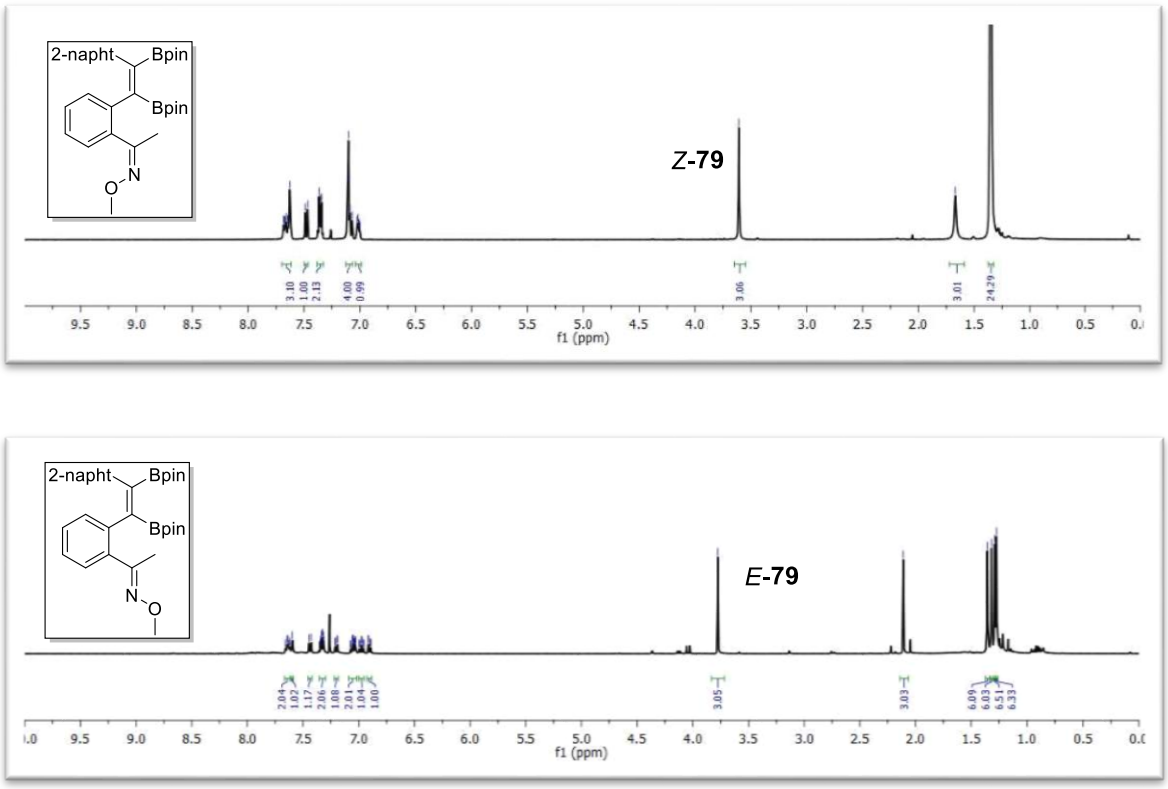


Figure 16. *^{1}H NMR spectra of pure Z-**79** and E-**79** substrate*

Compound *Z*-**79** in *o*-DCB was submitted to ultraviolet irradiation. The reaction was stopped after regular time intervals and a sample of the crude was analysed using both LC-MS and NMR spectroscopy techniques. Figure 17 shows the evolution of the transformation after 20 and 40 minutes respectively.

After 20 minutes (as observed in Figure 17), one can unambiguously discern in the LC-MS the formation of an equilibrium between *Z*-**79** and *E*-**79**. To our delight, it was also possible to identify the slow formation of the expected isoquinoline boronic ester **95**. All these compounds could also be clearly identified in the ^{1}H NMR spectrum of the same sample (Figure 19). Characteristic peaks (-protons corresponding to -O*Me* and –*Me*) of the three compounds in question could be clearly discerned (see experimental procedures for more details).

After 40 minutes (as observed in Figure 17) the equilibrium between *Z*-**79** and *E*-**79** was unambiguously clear; both oxime isomers were present in an approximate 1:1 mixture, as judged by the crude ^{1}H NMR spectrum in Figure 19. Furthermore, the synthesis of the isoquinoline boronate seems to proceed smoothly and a 33% NMR conversion could be estimated (Figure 19).

Subsequent Figure 18 show reaction times of 60 and 80 minutes respectively.

After an hour not much difference is observed, nonetheless, one can undoubtly spot the increase on the conversion to the heterocyclic boronate **95**.

After 80 minutes, interestingly, 50% conversion is achieved (Figure 18 and 19). No detectable amount of protodeborylation product is observed at this stage, neither via LC/MS or NMR analysis.

Since a 50% conversion was observed around 80 min, we decided to keep checking the transformation to detect when the reaction was complete.

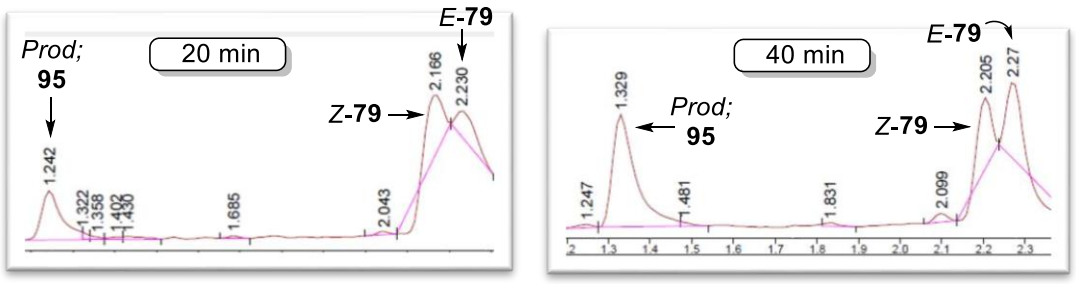


Figure 17. *LC/MS monitoring of the photochemical formation of* ***95*** *after 20 and 40 minutes.*

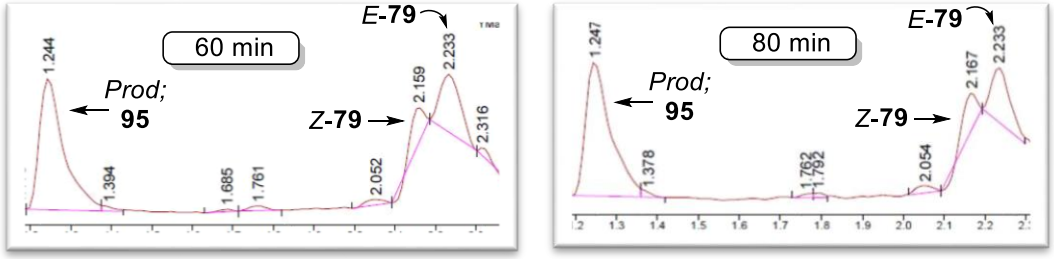


Figure 18. *LC/MS monitoring of the photochemical formation of* ***95*** *after 60 and 80 minutes.*

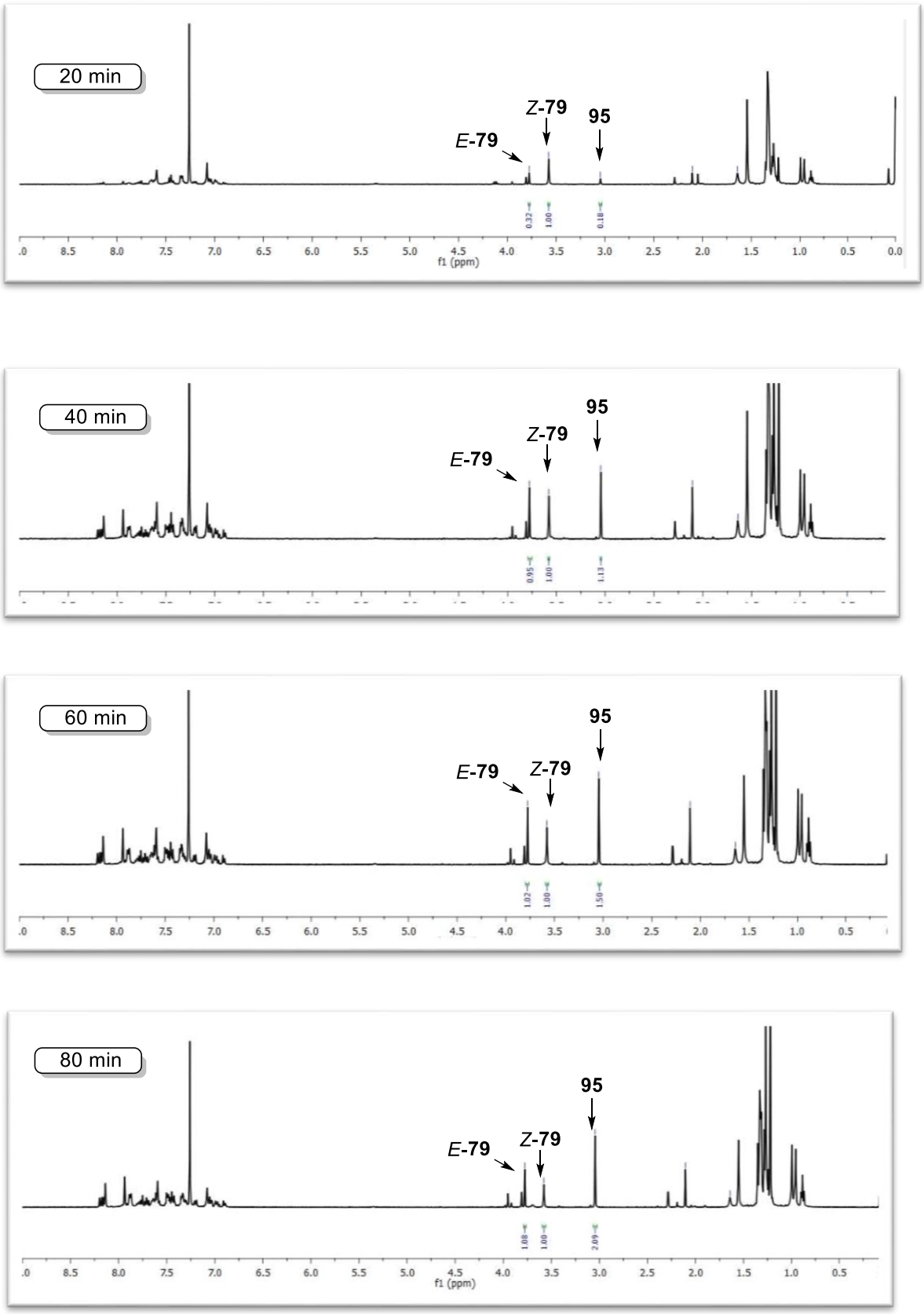


Figure 19. *^{1}H NMR monitoring of the photochemical formation of* ***95*** *over 20 –80 minutes. Main peaks for characterisation assigned accordingly.*

After 140 min the conversion was total and, gratifyingly, only the final product can be detected in both LC/MS and ^{1}H NMR spectra of the crude (Figure 20 and 21-*top*). Comparable NMR of the crude NMR at 140 min and the pure sample of isoquinoline **95** can be found in Figure 21-*down*.

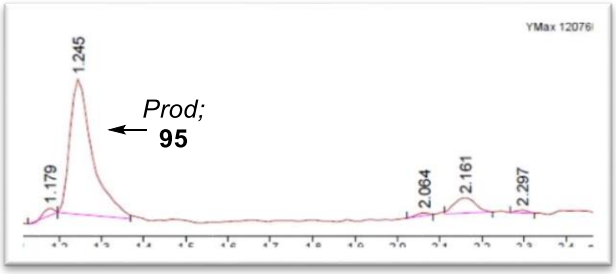


Figure 20. *LC/MS monitoring of the photochemical formation of* ***95*** *after 140 minutes.*

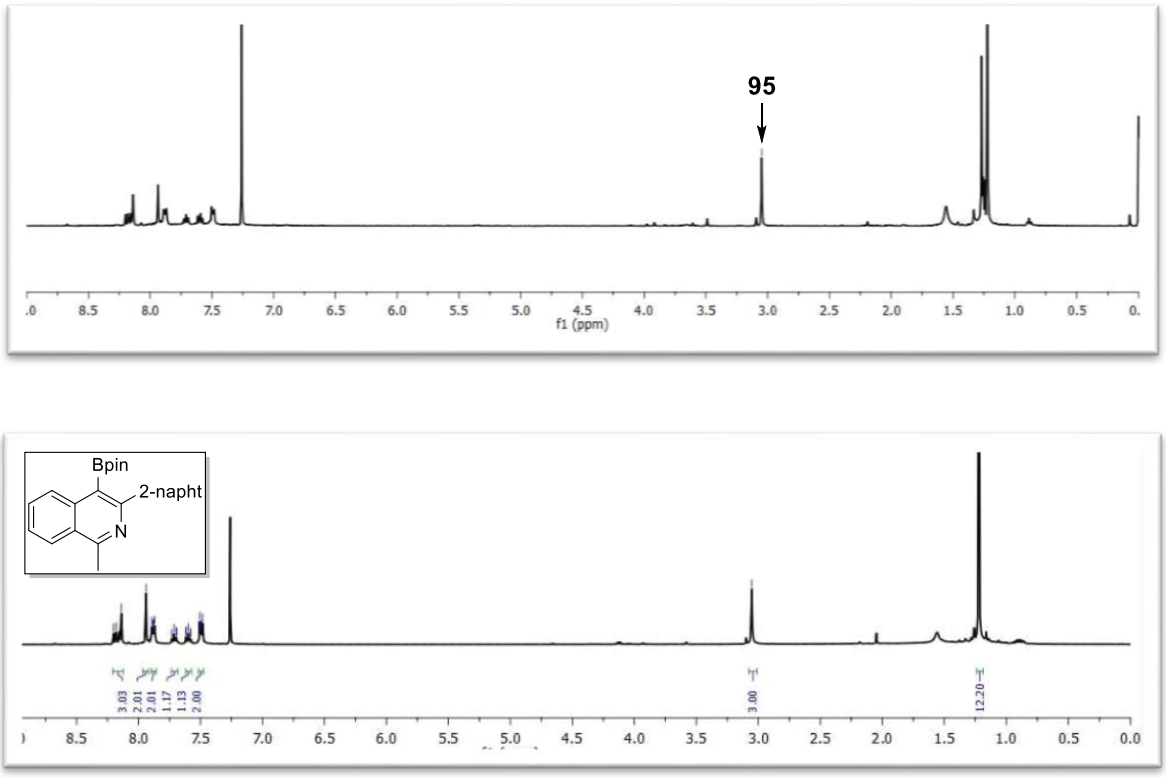
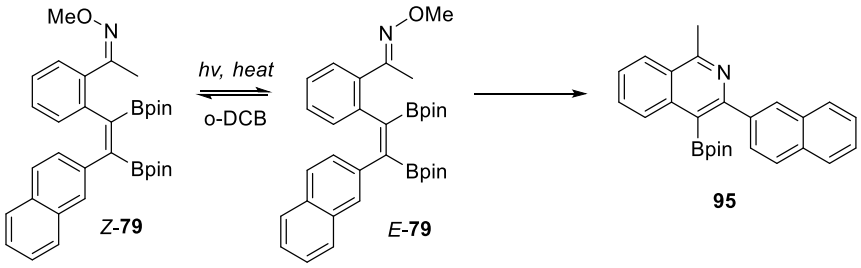


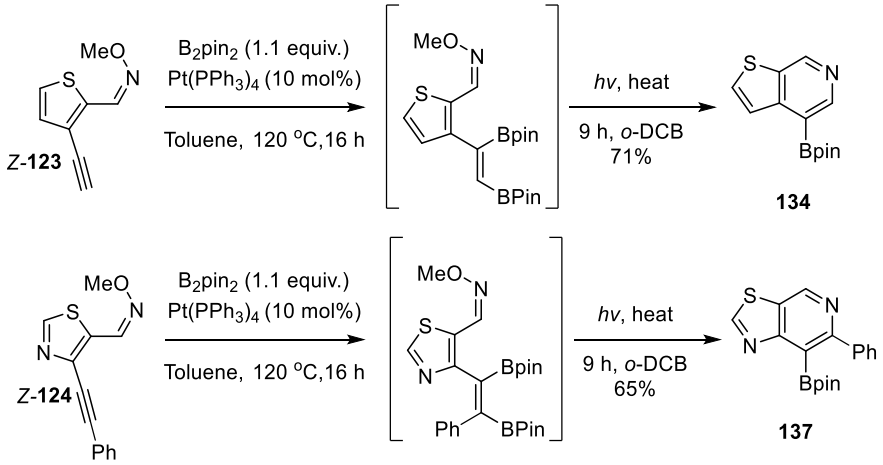
Figure 21. *^{1}H NMR monitoring of the photochemical transformation after 140 minutes showing full conversion to* ***95****, compared to the ^{1}H NMR spectra of pure naphtalene boronic ester* ***95****.*

These studies suggest that the reaction follows a *Z/E*-oxime ether isomerisation, followed by a 6π-electrocyclisation reaction to furnish the cyclised adduct (Scheme 93). This result, once again, is in support of our hypothesis that oxime stereochemistry dictates the efficiency of electrocyclisation.



Scheme 93. *Photochemical induced Z/E isomerisation followed by a 6π-electrocyclisation to furnish* ***95****.*

Encouraged by these results, we envisioned we could take advantage of this methodology to fully promote the synthesis of the cyclised adducts of some of the thermally unreactive Z-azatrienes described earlier. We were especially interested in using this photochemical methodology with the substrates that were synthesised with the Z-oxime ethers as the major components. For example, substrates **123** and **124** were synthesised from a mixture of oxime isomers with the *Z*-oxime being the major isomer observed. Therefore, substrates *Z*-**123** and *Z*-**124** were submitted to our newly developed photochemical conditions and we were delighted to observe that both fused heterocyclic boronates were smoothly obtained (Scheme 94).



Scheme 94. *Photochemical isomerisation-cyclisation strategy to compounds* ***134*** *and* ***137.***

It is worth noting that, in this case, both diborylalkenes were unstable to purification. Therefore, we directly used the crude azatrienes in the cyclisation step. Accordingly, the solvent was simply evaporated after diboration and 1,2,-dichlorobenzene added to the mixture followed by the submission to the photochemical conditions.

3. Conclusions

We have achieved the synthesis of pyridine boronic esters from the corresponding *Z*-oxime azatrienes – which were found to be thermally inert to this transformation in our preliminary studies. Azatrienes bearing different groups could successfully be transformed into the desired heterocycles in good to excellent yields. The boronic esters proved to be stable to these reaction conditions and the corresponding heterocyclic boronates were produced without evidence of significant undesired protodeborylated adducts.

The mechanism of this transformation, once again, confirmed the effect of oxime stereochemistry on the efficiency of electrocyclic reactions. A *Z/E* photochemical oxime ether isomerisation is observed followed by the formation of the isoquinoline derivative. Interestingly, additional heating was not required to promote cyclisation. Photochemical reactions are known to add a great amount of energy to the system and it was evident that the medium was heating during the reaction (solvent was observed to be boiling during photolysis). We therefore believe that this transformation proceeds indeed via a photochemical induced isomerisation followed by a thermally promoted electrocyclisation.

Last but not least, we could improve the yields obtained on the thermal synthesis of novel thienopyridine and thiazolopyridine boronic esters **134** and **137**. In this regard, it is much more convenient to obtain these scaffolds using photochemical conditions since the substrates are synthesised with the *Z*-oxime ethers as major components.

CHAPTER 5:

Design, synthesis and profiling of novel pyridine derivatives – *Industrial library production*

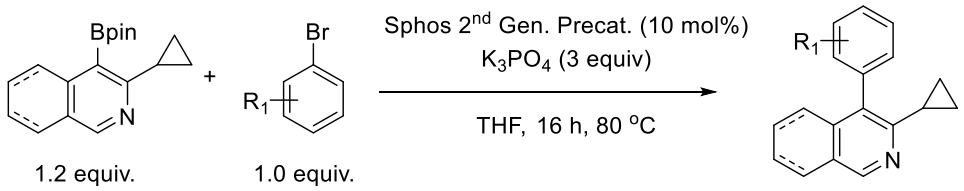
1. Introduction

The robust and rapid access to novel nitrogen-based heterocyclic compounds remains an attractive challenge for organic chemists since these motifs are part of many pharmaceutical and agrochemical target molecules.[77] In this context, pyridine boronic acid derivatives represent a valuable class of intermediates, as already described before, by constituting relevant precursors for the production of highly complex molecules.[78] Furthermore, the design and synthesis of groups of compounds that can be easily modified in order to access a desired combination of physicochemical properties is of great interest for medicinal chemists. Indeed, up to the 1990s, the clinical failure of drug candidates was mostly driven by inappropriate pharmacokinetic (PK) parameters and lack of clinical efficacy.[79] In 2000, the attrition rate due to PK was significantly reduced to ca 10%, while failure due to lack of efficacy and drug safety remained high.[80] One of the main reasons for this reduction was the improvement of the physicochemical and e-ADME profiling during the course of the lead optimisation process, combined with the acceptance that drug discovery is indeed a multi-parameter optimisation effort. Compound optimisation workflows nowadays include the early experimental assessment of intestinal absorption (e.g. CaCo profiling), inhibition of CYP3A4 enzyme, metabolic lability in microsome preparations (metabolic lability), solubility (important for effect limitations) and log D (lipohilicity). These parameters constitute an initial parameter screening for potentially active hits in the medicinal chemistry industry.

Throughout this PhD thesis, we have reported a novel synthetic pathway to access a broad group of different heterocyclic boronates from easily accessed starting materials. In this regard, where synthetically feasible, we have applied library synthesis to access a sufficiently large compound pool to optimise overall profiles in a chemical series with respect to biological activity, physicochemical and eADME properties.

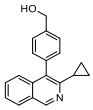
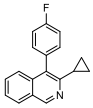
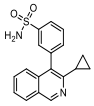
2. Results and discussion

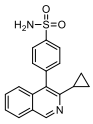
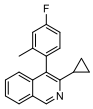
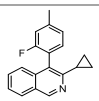
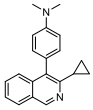
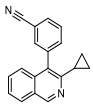
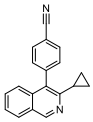
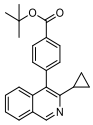
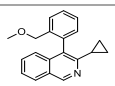
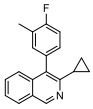
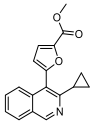
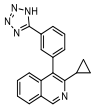
We began our studies by carrying out the Suzuki coupling of boronates **84** and **99** applied to a parallel library synthesis approach. Once the synthesis of the starting materials could be approached in an appropriate bigger scale (up to 10 grams) we optimised the reaction conditions for the corresponding coupling in the laboratory. In the event, the highest yield and broadest reagent scope was achieved using a 2nd generation S-phos precatalyst in combination with K_3PO_4 in THF (Scheme 95).



Scheme 95. *Suzuki coupling reaction between aryl bromides and pyridine boronic acid derivatives.*

Thanks to the automated library synthesis service provided by Sanofi we could complete the synthesis of compounds *A.01* to *A.34*. Reactions were performed in a heated stirring block of 96 positions on a 0.20 mmol scale by a specialised technician (see experimental section for detailed conditions, characterisation and purity values). Compounds *A.01* - *A.34* were characterised by ^{1}H NMR and LC-MS spectroscopy (see experimental section for detailed results) and subsequently subjected to physicochemical and eADME profiling to get logD, solubility, CaCo, CYP inhibition and metabolic lability data.

Entry	Chemical reference	Chemical compound	Molecular weight	Metabolic liability[a]	CaCO[b]	CYP inhibition[c]	Solubility[d]	Log D[e]
1	*A.01*		246.3	80	330.3	1.3	50	2.09
2	*A.02*		247.3	77	414.9	10.2	>2022	1.35
3	*A.03*		275.4	82	180.5	>30.0	7	2.48
4	*A.04*		263.3	50	119.3	>30.0	<4	4.65
5	*A.05*		324.4	20	151.8	>30.0	55	2.03

6	*A.06*		324.4	24	98.3	>30.0	4	2.05
7	*A.07*		277.3	58	93.6	>30.0	<4	5.06
8	*A.08*		263.3	65	119.6	>30.0	<4	4.66
9	*A.09*		277.3	94	162.2	>30.0	<4	4.84
10	*A.10*		288.4	84	116.4	>30.0	<4	4.99
11	*A.11*		270.3	79	182.7	>30.0	<4	3.76
12	*A.12*		270.3	63	168.4	>30.0	<4	3.85
13	*A.13*		345.5	18	NoVal	>30.0	<3	6.13
14	*A.14*		289.4	98	NoVal	>30.0	<4	4.22
15	*A.15*		277.3	50	113.0	>30.0	<4	5.02
16	*A.16*		277.3	73	89.1	>30.0	<4	5.25
17	*A.17*		293.3	100	8.3	>30.0	<4	3.39
18	*A.18*		249.2	65	365.8	>30.0	>2006	1.81
19	*A.19*		288.0	89	92.5	>30.0	<4	4.98
20	*A.20*		313.7	36	25.3	2.9	>392	0.84

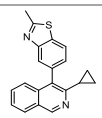
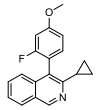
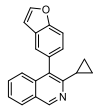
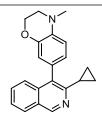
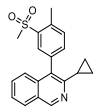
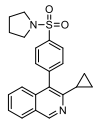
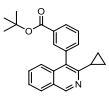
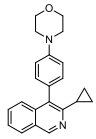
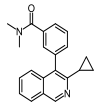
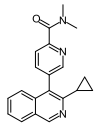
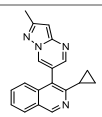
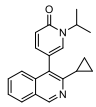
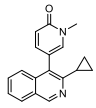
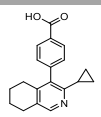
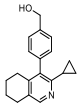
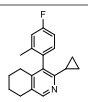
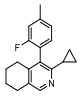
21	*A.21*		316.3	73	133.8	15.7	<3	4.14
22	*A.22*		293.3	71	133.8	>30.0	<3	4.27
23	*A.23*		285.4	35	98.4	8.3	<4	4.74
24	*A.24*		316.4	93	152.9	17.1	<3	4.44
25	*A.25*		337.4	64	217.8	>30.0	<3	3.10
26	*A.26*		378.5	99	265.9	6.7	<3	3.95
27	*A.27*		345.5	37	75.6	>30.0	<3	5.90
28	*A.28*		330.4	31	120.0	>30.0	<3	3.98
29	*A.29*		316.4	87	291.6	>30.0	187	2.41
30	*A.30*		317.4	72	437.1	>30.0	>1575	1.48
31	*A.31*		300.4	68	292.2	>30.0	37	2.40
32	*A.32*		304.4	33	337.2	>30.0	>1643	2.02
33	*A.33*		239.3	97	190.3	>30.0	>2089	1.73
34	*A.34*		276.3	5	280.8	>30.0	>1809	1.07

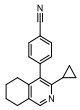
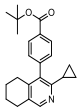
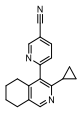
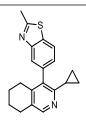
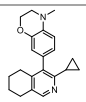
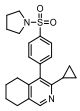
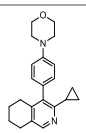
Table 12. *Physical and biological properties of compounds A.*

[a]Total metabolised (%), no CYP inhibitor added. [b]PTotal (10^{-7}cm/sec). [c]IC_{50} (INH) (uM) Isoform: CYP3A4 Substrate: Midazolam. [d]pH 6.4-8.4 (μM). [e] RP-Chromatography, MOPS Buffer pH: 7.4 T: 25 °C

Even though a high metabolic lability was observed for many of these compounds we could clearly influence the properties of the compounds by variation of residues in position 4 (Table 1). As expected, labile functionalities such as methyl esters (entry **17**) and substituted anilines (entries **10** and **19**) are rapidly metabolized. In comparison, hindered *tert*-butyl esters showed less metabolic lability (entries **13** and **27)**, at the expense of high log D values, and polar residues positively influenced the metabolic stability as expected (entries **5**, **6**, and **20**). A comparison of entries **20** and **23** further showed that compounds with opposite solubility and lipophilicity profiles can still show a similarly low metabolic lability. Compounds *A.32* and *A.34* both showed a decent overall profile with low metabolic lability, high CaCo values, no CYP3A4 inhibition and reasonable logD values accompanied by a high solubility.

We then subjected the tetrahydroisoquinoline boronate **99** to Suzuki couplings using the same conditions as for the isoquinolines (2nd generation S-Phos precatalyst, K_3PO_4, THF). Thanks to the automated library synthesis service provided by Sanofi we could complete the synthesis of compounds *B.01* to *B.29* (Table 13, see supplementary material for detailed procedures).

Entry	Chemical reference	Chemical compound	Molecular weight	Metabolic liability[a]	CaCO[b]	CYP inhibition[c]	Solubility[d]	Log D[e]
1	*B.01*		293.4	6	137.5	>30.0	>604	1.39
2	*B.02*		250.4	96	252.8	1.9	>1997	2.15
3	*B.03*		251.3	90	257.4	15.6	107	1.40
4	*B.04*		279.4	91	127.4	24.6	14	2.53
5	*B.05*		267.4	85	77.9	>30.0	<4	4.75
6	*B.06*		281.4	89	90.5	>30.0	<4	5.15
7	*B.07*		267.4	95	57.0	>30.0	<4	4.74
8	*B.08*		281.4	97	70.2	26.9	<4	5.01

9	*B.09*		274.4	90	150.7	>30.0	<4	3.87
10	*B.10*		274.4	93	135.3	>30.0	<4	3.94
11	*B.11*		349.5	36	23.8	>30.0	<3	6.24
12	*B.12*		293.4	98	141.4	13.7	<3	4.34
13	*B.13*		281.4	92	70.1	>30.0	<4	5.12
14	*B.14*		281.4	76	58.4	>30.0	<4	5.35
15	*B.15*		275.4	83	245.7	>30.0	166	2.49
16	*B.16*		297.4	100	26.5	>30.0	<3	3.60
17	*B.17*		320.5	97	100.9	7	<3	4.23
18	*B.18*		297.4	92	91.4	>30.0	<3	4.43
19	*B.19*		289.4	53	57.0	4.1	<4	4.83
20	*B.20*		320.4	97	113.8	8.0	<3	4.48
21	*B.21*		341.5	77	140.5	>30.0	<3	3.19
22	*B.22*		280.4	21	201.9	>30.0	>1783	1.11
23	*B.23*		382.5	100	111.6	4.4	<3	4.02
24	*B.24*		334.5	77	118.9	10.4	<3	4.02
25	*B.25*		320.4	98	183.0	>30.0	>1560	2.49

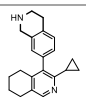
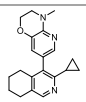
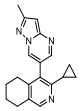
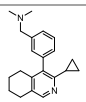
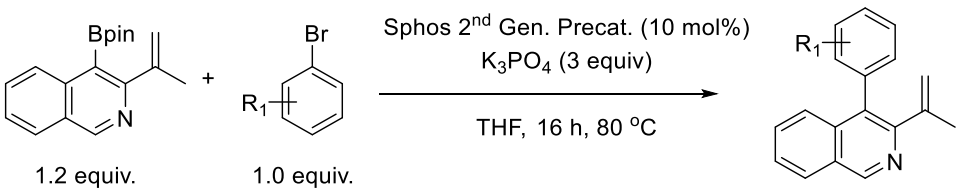
26	*B.26*		418.5	44	52.6	27.6	179	1.31
27	*B.27*		321.4	98	136.9	8.5	6	3.26
28	*B.28*		304.4	97	276.9	25.8	23	2.46
29	*B.29*		420.5	96	92.4	>30.0	>1189	2.21

Table 13. *Physical and biological properties of compounds B.*

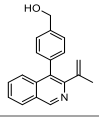
[a]Total metabolised (%), no CYP inhibitor added. [b]PTotal (10^{-7}cm/sec). [c]IC_{50} (INH) (uM) Isoform: CYP3A4 Substrate: Midazolam. [d]pH 6.4-8.4 (µM). [e] RP-Chromatography, MOPS Buffer pH: 7.4 T: 25 °C

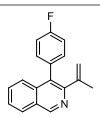
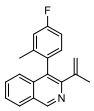
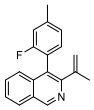
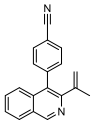
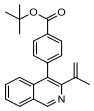
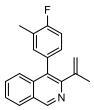
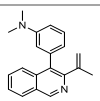
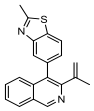
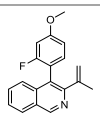
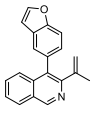
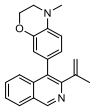
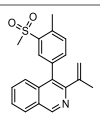
As expected, no dramatic difference was observed when changing from the isoquinoline core to the tetrahydroisoquinolines (Table 13); both scaffolds are highly hydrophobic, exhibiting rather high log D values. A peculiar result is the different metabolic lability obtained in both morpholine derivatives *A.28* and *B.24*, which might be an outlier due to the limited solubility of the compounds.

Finally, isoquinoline boronate **86** was subjected to Suzuki couplings using once again the automated library synthesis service provided by Sanofi (Scheme 96). In general, this set of compounds turned out to be more metabolically labile than the cyclopropyl analogues. Relevant structures and data points are presented in Table 14.



Scheme 96. *Suzuki coupling reaction between aryl bromides and pyridine boronic acid derivatives.*

Entry	Chemical reference	Chemical compound	Molecular weight	Metabolic lability[a]	CaCO[b]	CYP inhibition[c]	Solubility[d]	Log D[e]
1	*C.01*		246.3	82	243.4	<1.0	34	1.43
2	*C.02*		275.4	89	139.7	>30.0	59	1.79

3	*C.03*		263.3	76	110.3	>30.0	<4	3.82
4	*C.04*		277.3	90	94.2	>30.0	<4	4.23
5	*C.05*		263.3	88	NoVal	>30.0	<4	3.80
6	*C.06*		277.3	97	93.6	19.5	<4	4.16
7	*C.07*		270.3	61	178.8	>30.0	<4	2.99
8	*C.08*		270.3	77	199.4	>30.0	<4	3.07
9	*C.09*		345.5	35	53.3	>30.0	<3	5.26
10	*C.10*		277.3	97	145.0	>30.0	<4	4.19
11	*C.11*		277.3	70	94.8	>30.0	<4	4.38
12	*C.12*		288.4	98	112.0	6.1	6	4.11
13	*C.13*		316.4	93	141.9	6.8	<3	3.28
14	*C.14*		293.3	93	115.6	11.7	<3	3.62
15	*C.15*		285.4	47	81.6	4.2	<4	3.86
16	*C.16*		316.4	92	132.4	4.2	<3	3.57
17	*C.17*		337.4	68	194.5	21.7	36	2.41

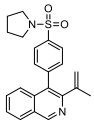
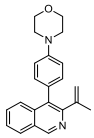
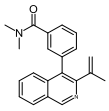
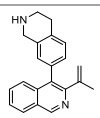
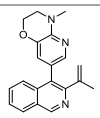
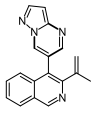
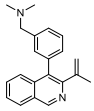
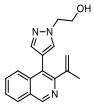
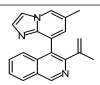
18	*C.18*		378.5	99	123.6	3.7	<3	3.25
19	*C.19*		345.5	59	60.5	>30.0	<3	5.04
20	*C.20*		330.4	61	154.1	13.9	6	3.15
21	*C.21*		316.4	92	194.7	27.8	>1580	1.79
22	*C.22*		414.4	23	64.8	16.9	>1207	0.72
23	*C.23*		317.4	92	189.4	15.3	7	2.42
24	*C.24*		300.4	85	285.2	>30.0	>1665	1.77
25	*C.25*		416.5	94	134.2	>30.0	>1201	1.52
26	*C.26*		279.4	35	162.6	>30.0	>282	0.40
27	*C.27*		299.4	98	152.1	19.8	>230	1.74
28	*C.28*		239.3	79	193.1	20.2	>2089	1.21

Table 14. *Physical and biological properties of compounds C.*

[a]Total metabolised (%), no CYP inhibitor added. [b]PTotal (10^{-7}cm/sec). [c]IC_{50} (INH) (uM) Isoform: CYP3A4 Substrate: Midazolam. [d]pH 6.4-8.4 (µM). [e] RP-Chromatography, MOPS Buffer pH: 7.4 T: 25 °C

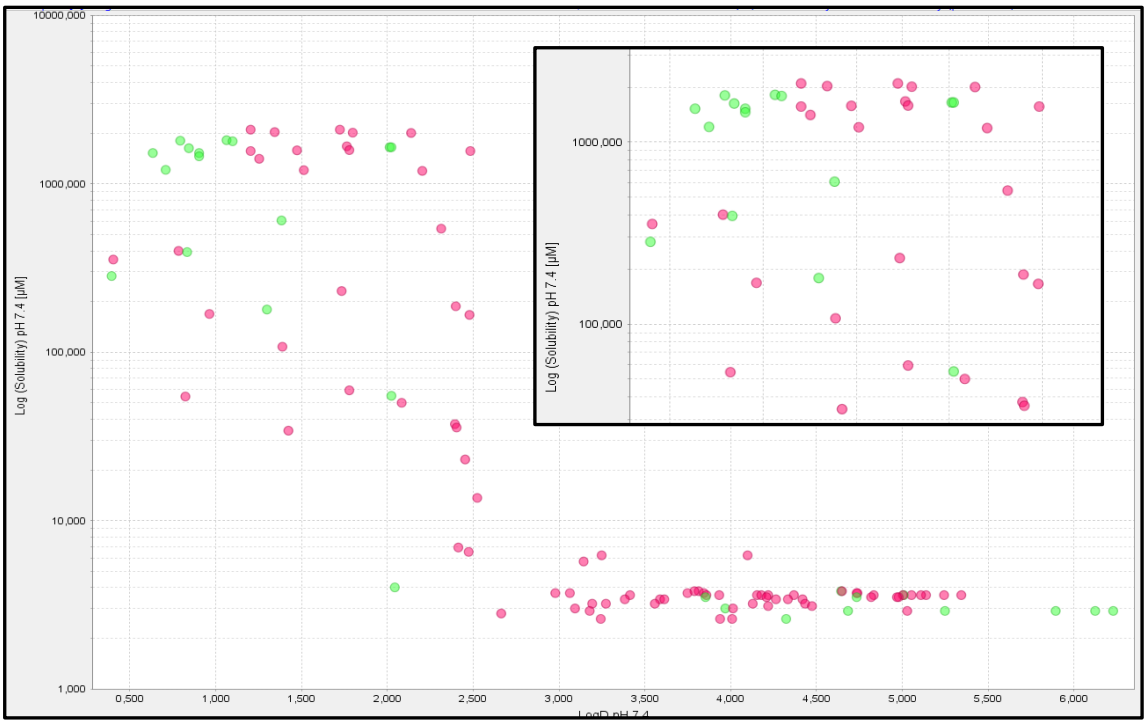
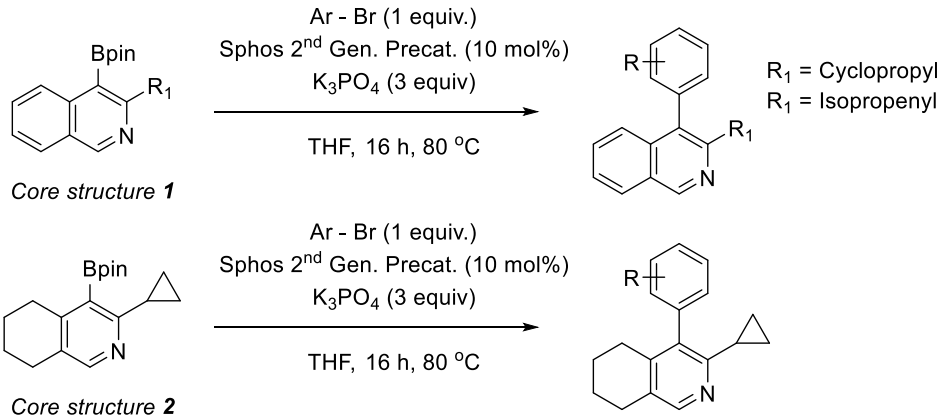


Figure 22. *Correlation log D vs Solubility. Point color: metabolic lability > 50 red; < 50 green.*

Correlations between the solubility and the log D of these analogues are illustrated in figure 22. As expected, no clear linear correlation is observed between log D and solubility values. However, compounds having a log D below the threshold of 2.5 show highly improved solubility. Several compounds in this region show improved metabolic lability (amplified graphic on the right hand side), highlighting the potential of the bespoke analogues to generate favourable ADME profiles. The high metabolic stability found for some of the substrates with log D values between 3.5 and 5.5 might be erratic due to their low solubility.



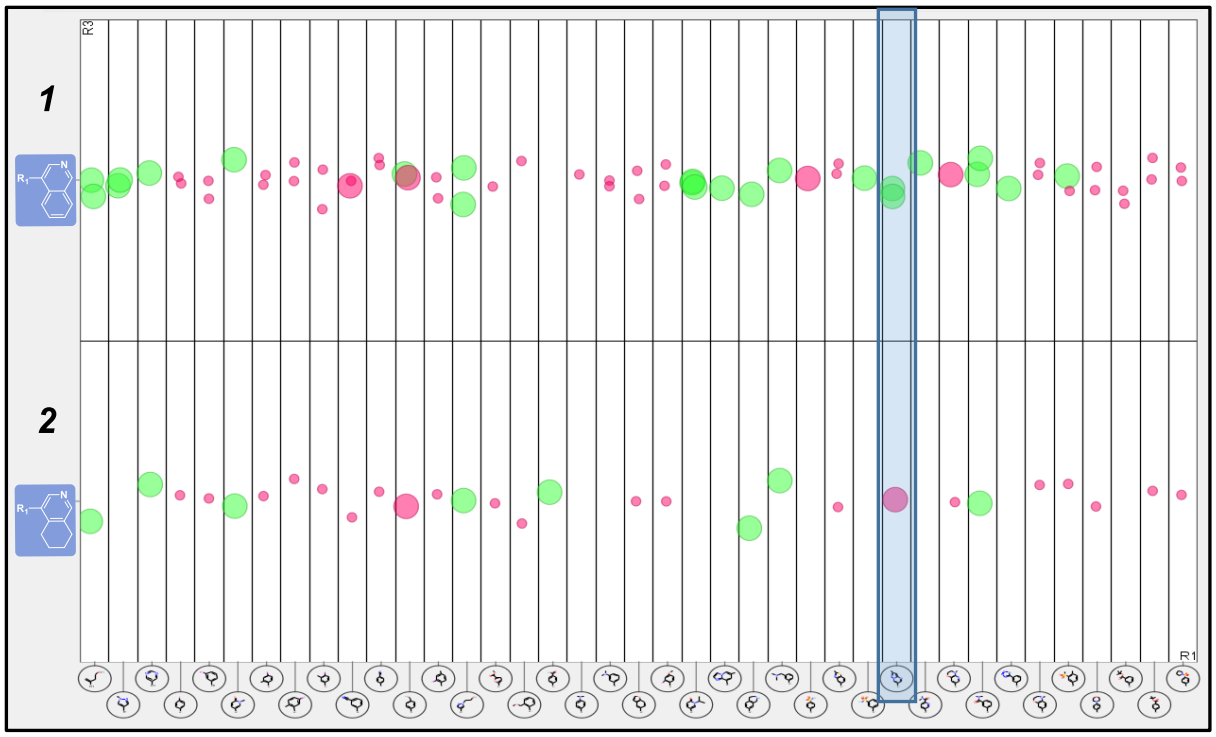
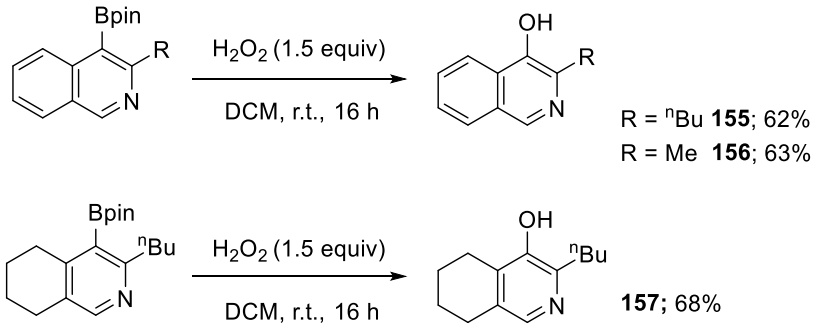


Figure 23. *R_1 group matrix. Point color: solubility (red < 25 µM; green > 25 µM). Point Size: log D (Big: <2.5). Core structure **1**: Isoquinoline R_1 = Cyclopropyl, Isopropenyl. Core structure **2**: Tetrahydropyridine R_1 = Cyclopropyl.*

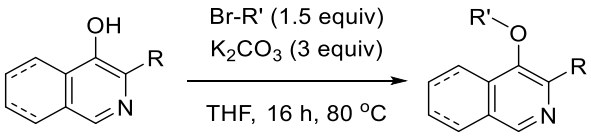
Figure 23 displays an R group matrix that correlates the R1 groups present in the two major core systems, together with their solubility and log D values. Interestingly, the structure of the core shows no dramatic influence when comparing the two sets of compounds. In contrast, the R1 groups have a pronounced influence on both parameters. At a glance, one can directly notice how all the soluble substrates (represented in green in the matrix) exhibit favourable log D values. However, the matrix also highlights a few outliers, and one pair where solubility changes significantly with reduction of the left hand side phenyl ring.

In a next step, we decided to investigate more hydrophilic ether derivatives obtained by alkylation of the corresponding hydroxy intermediates **155, 156** and **157**; both isoquinoline boronates **152** (-^{n}Bu) and **153** (-Me) as well as tetrahydroisoquinoline boronate **154** were transformed into the corresponding phenol intermediates by oxidative treatment with H_2O_2 in DCM (Scheme 97).

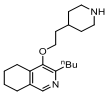
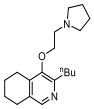
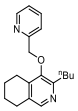


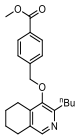
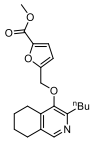
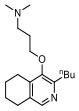
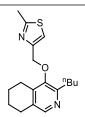
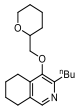
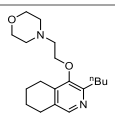
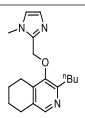
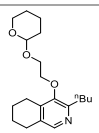
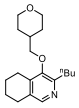
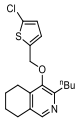
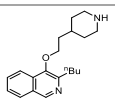
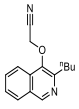
Scheme 97. *Synthesis of phenol-pyridine derivatives.*

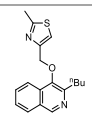
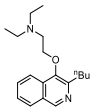
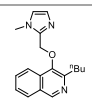
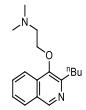
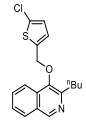
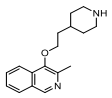
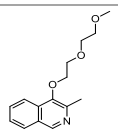
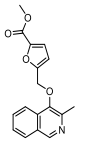
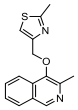
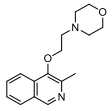
Compounds **155**, **156** and **157** were then subjected to alkylation reactions to obtain a series of 4-alkyloxy-isoquinoline and -tetrahydroisoquinoline derivatives (Scheme 98). Library synthesis service provided by Sanofi led to compounds *D.01* - *D.38*; the corresponding profiling data are shown in table 15.



Scheme 98. *Alkylation of phenol-pyridine derivatives using aryl bromide reagents.*

Entry	Chemical reference	Chemical compound	Molecular weight	Metabolic liability[a]	CaCO[b]	CYP inhibition[c]	Solubility[d]	Log D[e]
1	*D.01*		430.5	82	35.8	4.6	>1161	1.15
2	*D.02*		374.4	88	NoVal	<1.0	702	0.43
3	*D.03*		262.4	98	NoVal	>30.0	935	1.02
4	*D.04*		244.3	100	182.0	28.6	210	2.88
5	*D.05*		302.5	100	103.1	>30.0	808	1.40
6	*D.06*		296.4	100	158.4	6.0	393	3.16
7	*D.07*		261.4	96	63.2	>30.0	<4	5.40

8	*D.08*		353.5	100	1.9	>30.0	<3	4.68
9	*D.09*		295.4	99	116.7	>30.0	314	1.07
10	*D.10*		343.4	100	2.5	>30.0	41	3.69
11	*D.11*		290.5	96	NoVal	>30.0	>1721	1.03
12	*D.12*		316.5	100	172.0	5.7	299	3.45
13	*D.13*		303.5	99	160.5	12.5	150	4.35
14	*D.14*		318.5	100	165.1	4.8	1310	2.46
15	*D.15*		299.4	100	174.4	2.0	>1670	1.91
16	*D.16*		333.5	99	149.3	5.8	139	4.22
17	*D.17*		303.5	99	161.8	12.9	281	3.69
18	*D.18*		335.9	95	NoVal	9.5	<3	5.58
19	*D.19*		426.5	51	NoVal	17.2	>1172	1.03
20	*D.20*		258.3	98	138.1	>30.0	>1936	0.85
21	*D.21*		240.3	90	163.3	>30.0	>2081	2.62

22	*D.22*		312.4	97	NoVal	5.7	192	3.22
23	*D.23*		300.5	90	135.1	>30.0	>1664	2.00
24	*D.24*		295.4	100	198.5	5.0	>1693	1.71
25	*D.25*		272.4	79	129.3	>30.0	>1836	1.42
26	*D.26*		331.9	60	NoVal	18.5	<3	5.34
27	*D.27*		257.3	100	6.8	13.6	>1943	2.56
28	*D.28*		384.4	20	45.5	>30.0	>1301	-0.11
29	*D.29*		261.3	71	198.3	>30.0	>1913	0.89
30	*D.30*		216.2	44	144.4	>30.0	>2312	-0.55
31	*D.31*		198.2	80	239.8	>30.0	>2522	0.69
32	*D.32*		215.3	94	86.9	>30.0	<5	3.23
33	*D.33*		297.3	100	2.0	>30.0	137	1.88
34	*D.34*		270.4	82	NoVal	>30.0	>1849	1.40
35	*D.35*		272.4	47	NoVal	>30.0	>1834	0.63
36	*D.36*		253.3	36	170	12.8	>1974	0.22

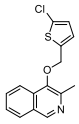
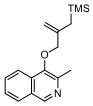
37	*D.37*		289.8	75	62.1	>30.0	<4	3.64
38	*D.38*		285.5	89	33.4	>30.0	<4	5.28

Table 15. *Physical and biological properties of compounds D.*

[a]Total metabolised (%), no CYP inhibitor added. [b]PTotal (10^{-7}cm/sec). [c]IC_{50} (INH) (uM) Isoform: CYP3A4 Substrate: Midazolam. [d]pH 6.4-8.4 (µM). [e] RP-Chromatography, MOPS Buffer pH: 7.4 T: 25 °C.

Generally, and as expected, this ether series was more soluble than the biaryl derivatives of the previous libraries. Again as expected, we observed a higher solubility for compounds with lower logD. The metabolic lability of the tetrahydroisoquinoline derivatives was significant, while there were some representatives of the isoquinoline series with lower logD exhibiting an improved metabolic lability. CaCo values were overall acceptable to good with a few exceptions (NoVal in this context means not tested). CYP inhibition was again influenced by the residues at position 4 – with little correlation to log D values.

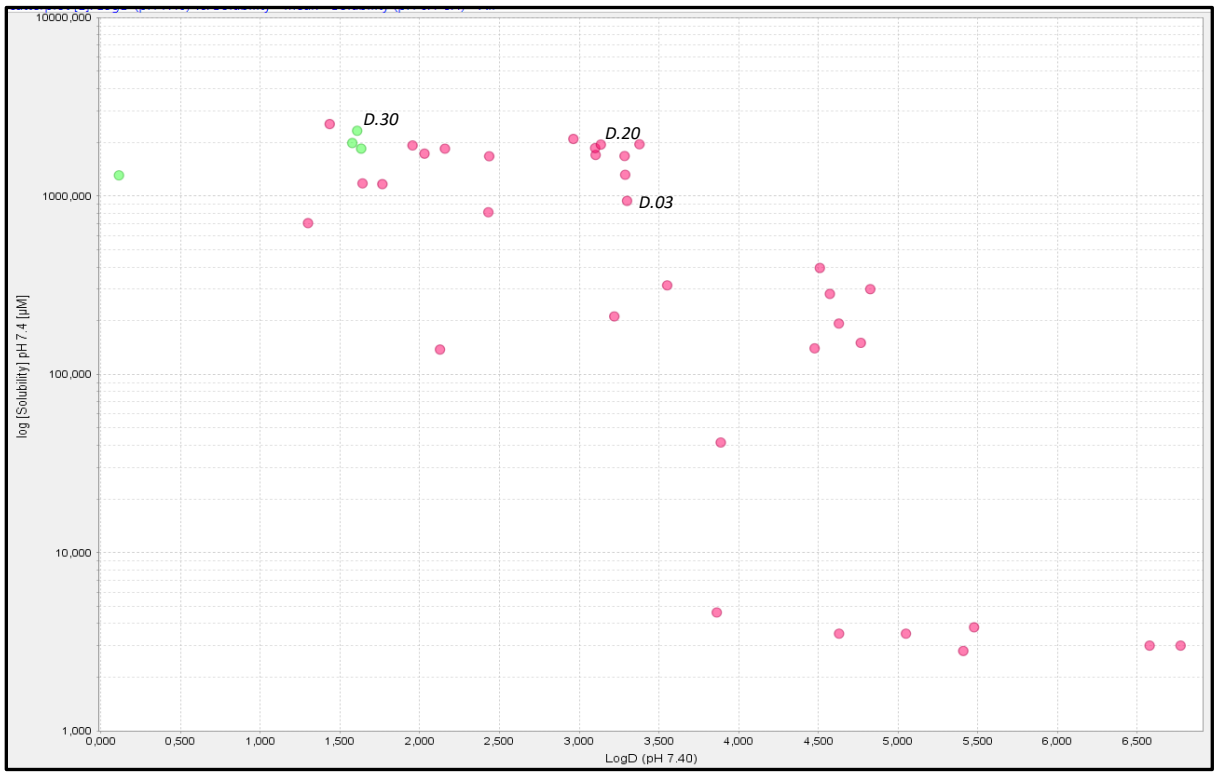
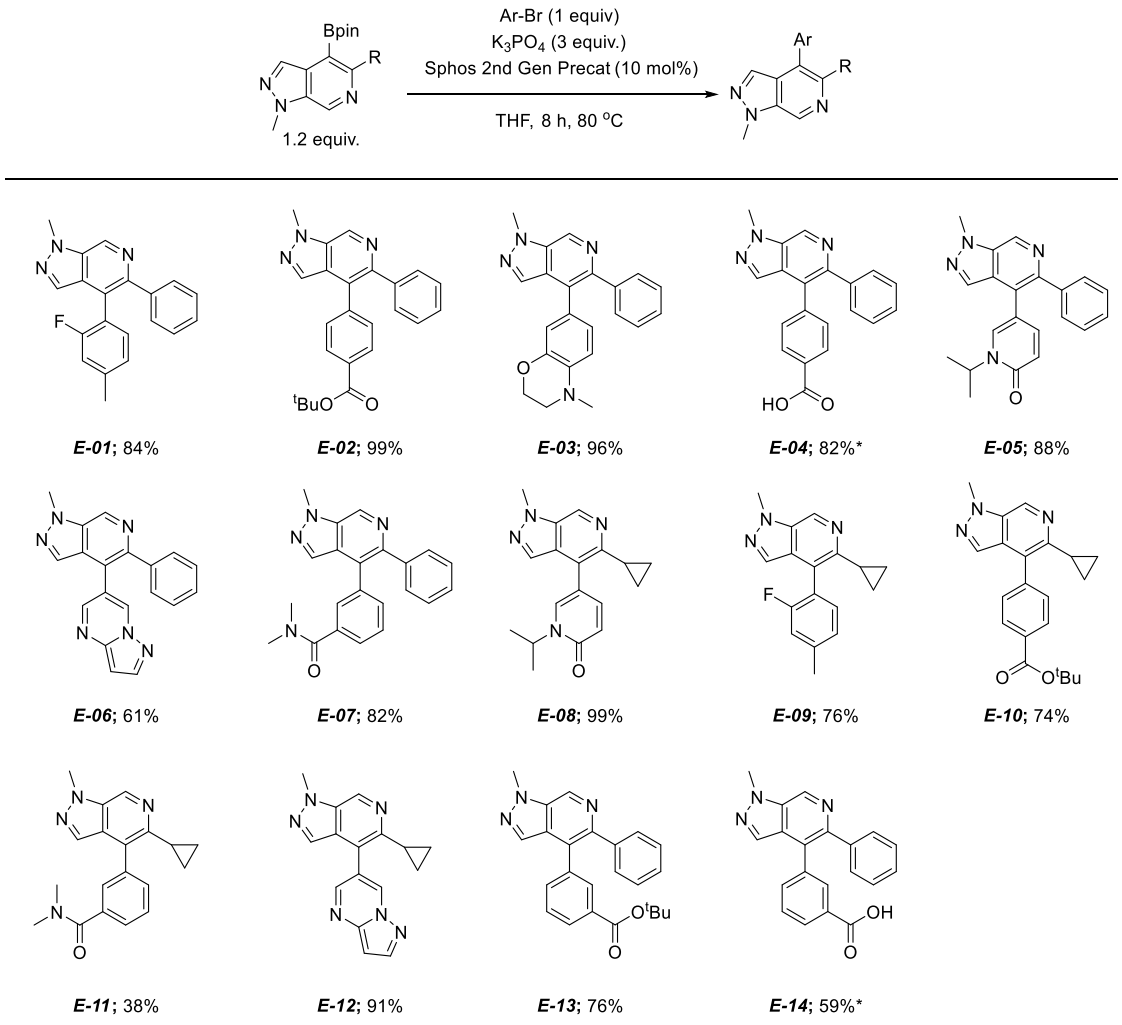


Figure 24. *Correlation log D vs Solubility. Point color: metabolic lability > 50 red; < 50 green.*

Correlations between the solubility and the log D of these analogues are illustrated in figure 24. As already mentioned before, there is not a clear linear correlation between the solubility and the log D values of these substrates. However, this set of compounds exhibits a much

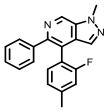
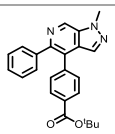
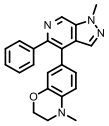
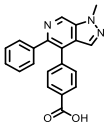
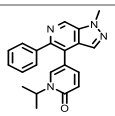
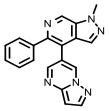
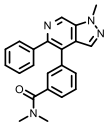
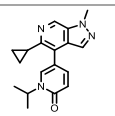
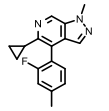
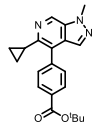
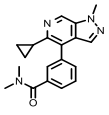
better solubility than its partners in groups *A*, *B* and *C*; represented by the number of compounds present on the upper left hand side of the graphic. Even though the amount of moderately metabolized examples seems rather low, there is a strong (and expected) effect of the different substitutions in position 3. Shorter alkyl chains, such as a methyl group, favour moderate labilities, while longer alkyl chains are rapidly and strongly metabolized. This effect is especially relevant when comparing substrates *D.03*, *D.20* and *D.30* (highlighted in the graph).



Scheme 99. *Synthesis of pyrazolopyridines* ***E-01*****-****E-14****. *Compounds* ***E-04*** *and* ***E-14****, obtained by the hydrolysis of the corresponding esters.*

Finally, we investigated the influence of the more polar pyrazolopyridine core on the properties of final compounds derived from a library of Suzuki couplings. Compounds *E.01* - *E.14* were manually synthesised in the lab in good to excellent yields using our optimised Suzuki-coupling conditions (See experimental section for further details) (Scheme 99).

Table 16 shows the list of isolated pyrazolopyridine derivatives *E.01* - *E.14* bearing modifications at positions 5 and 6.

Entry	*Chemical reference*	*Chemical compound*	*Molecular weight*	*Metabolic liability*[a]	*CaCO*[b]	*CYP inhibition*[c]	*Solubility*[d]	*Log D*[e]
1	*E.01*		317.4	88	136.0	28.2	<3	3.20
2	*E.02*		385.5	16	55.5	>30.0	<3	4.33
3	*E.03*		356.4	88	149.3	3.6	<3	2.67
4	*E.04*		329.4	5	NoVal	>30.0	>1518	0.64
5	*E.05*		344.4	36	206.9	>30.0	>1452	0.91
6	*E.06*		326.4	62	202.4	9.9	168	0.97
7	*E.07*		356.4	68	253.4	23.9	>1403	1.26
8	*E.08*		308.4	36	196.7	>30.0	>1621	0.85
9	*E.09*		281.3	96	119.1	>30.0	<4	3.42
10	*E.10*		349.4	17	47.8	>30.0	<3	4.69
11	*E.11*		320.4	56	218.4	>30.0	>1561	1.21

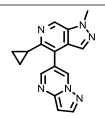
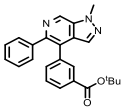
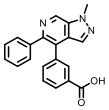
12	*E.12*		290.3	62	232.5	>30.0	54	0.83
13	*E.13*		385.5	67	84.0	5.2	NoVal	NoVal
14	*E.14*		329.4	6	102.8	>30.0	>1518	0.91

Table 16. *Physical and biological properties of compounds E.*

[a]Total metabolised (%), no CYP inhibitor added. [b]PTotal (10^{-7}cm/sec). [c]IC_{50} (INH) (uM) Isoform: CYP3A4 Substrate: Midazolam. [d]pH 6.4-8.4 (µM). [e] RP-Chromatography, MOPS Buffer pH: 7.4 T: 25 °C

Interestingly, the residue at position 5 (Ph vs Cyclopropyl) has little effect on the overall compound profile, while more polar aromatic groups added in position 6 clearly show a positive impact on the metabolic lability – however, this is again only the case for the previous examples carrying the *tert*-butoxycarbonyl residue, the pyridone moiety or certainly a carboxylic acid functionality. Solubility is slightly improved, indicating the effect of increasing the polarity on the ring. Overall, in terms of physchem and eADME profile, compounds *E.04*, *E.08* and *E.14* showed a promising profile to build on for further compound optimisation.

3. Conclusions.

We have successfully established an efficient route to 5,6- and 6,6- annellated pyridine boronates from easily accessible starting materials. The compounds are versatile intermediates, and more than 140 derivatives have been successfully synthesised using automated parallel library synthesis, either by Suzuki-coupling reactions of the corresponding boronic esters or by an *O*-alkylation transformation of the oxidised phenolic derivatives.

The ability to derivatise these diverse heteroaromatic compounds has been demonstrated and by using Sanofi´s internal compound profiling workflow. We have shown potential points for diversification in these compound series which give access to improved physicochemical and eADME properties.

Interestingly, we have been able to process and correlate the different results using R-group matrix and graphics. This represents a highly visual manner to rapidly classify the different substrates according to some of their first physicochemical profiling. Furthermore, we were able to join the sub-group of Suzuki coupling compounds in a structure similarity map (Figure 25). These kind of charts are useful tools to quickly assess how similar structures generally represent comparable interactions, properties and activities. Overall, we believe that these heterocyclic intermediates represent an interesting group of scaffolds for further compound optimisation.

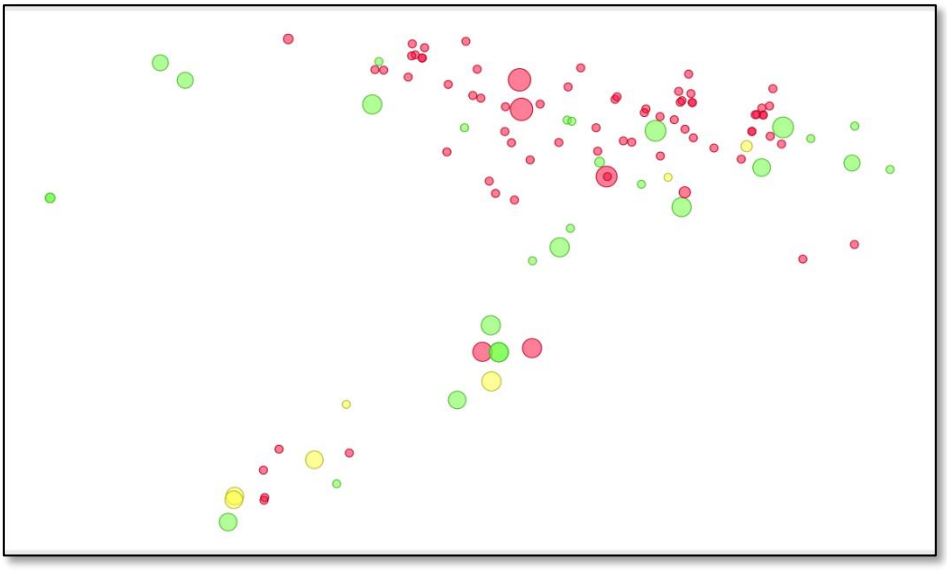


Figure 25. *Structure similarity map of the sub-group of Suzuki-coupling products.*

Color: log D. Green 2.0-3.5, Yellow < 2; Red > 3.5. Point size: solubility (big = high solubility); small low solubility.

CHAPTER 6: Final concluding remarks and future work

We have been able to carry out the diborylation of a large number of yne-oxime ethers and this process appears to be quite general. All the aproaches studied so far in this project promote the *cis*-addition of the bis-pinacolatodiboron species on the alkyne group. The achievement of easy methodologies for *trans*-diborylation remains a big challenge for organic chemists. The deep understanding of this transformation would represent the complete stereoselective control of the synthesis of fully substituted alkenes from alkynes. Unfortunately, even though we preliminary investigated the *trans*-borylation on some substrates, no real conclusions could be made at the end of this PhD project.

The key subsequent 6π-electrocyclisation has proved to be more challenging, with relatively low conversions to the appropriate pyridine boronates being observed in some cases. Nonetheless, we have been able to design a group of substrates that appear to be very reactive towards 6π-electrocyclisation after borylation, furnishing a group of boronate isoquinoline derivatives in good yields. This method provides an efficient and catalytic approach to isoquinoline boronic acid derivatives, an important class of compounds in the chemical sciences; together with tetrahydroisoquinolines derivatives such as the unique cholesterol boronic ester derivative. Pure pyridine rings were successfully furnished using this methodology, delivering a small set of 4-phenyl boronic ester pyridine examples. A great number of fused heterocyclic boronates were synthesised for the first time, delivering a group of novel compounds that could be straightaway derivatised to access highly complex scaffolds.

Our current hypothesis, borne out by experimental and theoretical data gathered thus far, is that the 6π-electrocyclisation efficiency is dramatically dictated by substrate oxime stereochemistry. Thanks to our collaborative work with the group of Prof Enrique Gomez-Bengoa, we could observe via DFT calculations how the lone pair of the oxime-nitrogen seems to be actively participating in the electrocylisation. Accordingly, its orientation appears to be crucial for the efficiency of this transformation.

Thanks to Sanofi's automated parallel library synthesis and internal compound profiling workflow, we have been able to design, study and profile a group of more than 140 pyridine compounds by derivatisation of our novel heterocyclic boronates.

CHAPTER 7: Experimental procedures

1. General considerations

All reactions were conducted in flame-dried glassware under ambient conditions unless otherwise stated.

Infrared (IR) spectra were recorded on a Perkin Elmer Paragon 100 FTIR spectrophotometer and Nicolet Nexus 470 FTIR spectrometer, ν_{max} in cm^{-1}. Samples were recorded neat or as thin films using sodium chloride plates as a dichloromethane solution. Bands are characterised as broad (br), strong (s), medium (m), or weak (w).

^{1}H NMR spectra were recorded on a Bruker AVIII HD 400 (400 MHz), Bruker AVI 400 (400 MHz), Bruker AMX-400 (400 MHz) or DPX-400 (400 MHz) supported by an Aspect 3000 data system. Chemical shifts are reported in parts per million (ppm) from tetramethylsilane with the residual protic solvent resonance as the internal standard ($CHCl_3$: δ 7.26, DMSO: δ 2.50) unless otherwise stated. Data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br = broad, m = multiplet), coupling constants (Hz), assignments).

^{13}C NMR spectra were recorded on a Bruker AVIII HD 400 (100.6 MHz), Bruker AVI 400 (100.6 MHz), Bruker AMX-400 (100.6 MHz) or DPX-400 (100.6 MHz) with complete proton decoupling. Chemical shifts are reported in ppm from tetramethylsilane with the solvent as the internal reference ($CHCl_3$: δ 77.16) unless otherwise stated.

^{19}F NMR spectra were recorded on a Bruker AVIII HD 400 (235.1 MHz) or Bruker AMX-400 (235.1 MHz).

^{11}B NMR spectra were recorded on a Bruker AVIII HD 400 (235.1 MHz).

High-resolution mass spectra (HRMS) recorded for accurate mass analysis, were performed on either a MicroMass LCT operating in Electrospray mode (TOF ES^+) or a MicroMass Prospec operating in FAB (FAB^+), EI (EI^+) or CI (CI^+) mode.

Photochemistry was performed under ultraviolet irradiation using an OSRAM ultra vitalux qw5 lamp – 300W (220-220V).

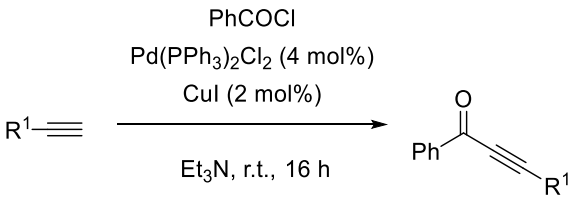
Automated library production was performed in Sanofi's premises. Reactions were carried out according to an established protocole (see individual protocoles exemplified below) using 4 mL vial heating and stirring racks containing up to 96 available positions. Reactions were followed

by LC-MS and, upon completion, solvent evaporation was performed using Hettich CombiDancer machine. Next, complete workup process was carried out using RG24 tubes (24 ml volume, thick-walled test tubes with screw caps) in stirring racks that allow phase mixing and separation. Then, organic phase was dried by passage through XTR Chromabond columns and filtration over filter columns. Finally, each compounds were purified by reverse phase chromatography and characterized by NMR and LC-MS.

Thin layer chromatography (TLC) was performed on aluminium backed plates pre-coated with silica (0.2 mm, Merck DC-alufolien Kieselgel 60 F254) which were developed using standard visualizing agents: UV light or potassium permanganate. Flash chromatography was performed on silica-gel (BDH Silica Gel 60 43-60). Melting points, performed on recrystallised solids, were recorded on a Gallenkamp melting point apparatus and are uncorrected. All solvents and reagents were purified using standard laboratory techniques according to methods published in “Purification of Laboratory Chemicals” by Perrin, Armarego and Perrin (Pergamon Press, 1966).

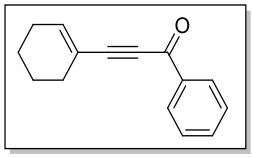
2. Experimental procedures.

General procedure A



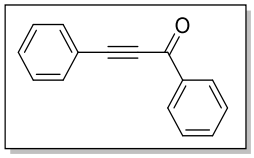
To a round bottomed flask was added CuI (2 mol%), $PdCl_2(PPh_3)_2$ (0.4 mol%) and Et_3N (0.25 M). The flask was flushed with N_2 and terminal alkyne (1.0 eq.) was added to the stirred suspension followed by the immediate addition of benzoyl chloride (1.3 eq.). The resulting mixture was stirred at room temperature overnight. Water was added and the aqueous layer was extracted with hexane. The organic phase was dried over anhydrous $MgSO_4$, filtered and the solvent was removed *in vacuo*. The residue was purified by flash column chromatography on silica gel eluting with petroleum ether (40/60) and ethyl acetate to afford the corresponding ynones.

Synthesis of 3-cyclohexenyl-1-phenylprop-2-yn-1-one[36]



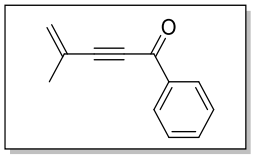
Following general procedure A, using ethynylcyclohexane (2.65 g, 25.0 mmol), CuI (95 mg, 0.5 mmol), $PdCl_2(PPh_3)_2$ (70 mg, 0.1 mmol) in Et_3N (50 mL), followed by the immediate addition of benzoyl chloride (4.57 g, 32.5 mmol) afforded the desired product as an orange oil (5.01 g, 79%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 – 8.10 (m, 2H, CH_{ar}), 7.63 – 7.54 (m, 1H, CH_{ar}), 7.53 – 7.44 (m, 2H, CH_{ar}), 6.63 – 6.54 (m, 1H, C*H*=C), 2.33 – 2.24 (m, 2H, CH_2), 2.24 – 2.17 (m, 2H, CH_2), 1.75 – 1.60 (m, 4H, CH_2 x 2). ^{13}C NMR (101 MHz, $CDCl_3$) δ 178.2, 142.7, 137.1, 133.8, 129.5, 128.5, 119.2, 95.8, 85.2, 28.4, 26.2, 22.0, 21.1.

Synthesis of 1,3-diphenyl-2-propyn-1-one[36]



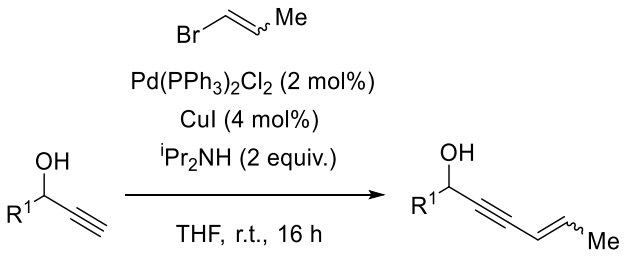
Following general procedure A, using phenylacetylene (1.02 g, 10.0 mmol) CuI (38 mg, 0.2 mmol), $PdCl_2(PPh_3)_2$ (23 mg, 0.04 mmol) in Et_3N (20 mL), followed by the immediate addition of benzoyl chloride (1.83 g, 13.0 mmol) afforded the desired product as a white solid (1.49 g, 72%). M.p.: 49 – 50 °C (lit:[81] 46 – 47 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 – 8.20 (m, 2H), 7.73 – 7.67 (m, 2H), 7.67 – 7.61 (m, 1H), 7.56 – 7.47 (m, 3H), 7.46 – 7.39 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 178.1, 136.9, 134.1, 133.1, 130.8, 129.6, 128.7, 128.7, 120.2, 93.1, 86.9.

Synthesis of 4-methyl-1-phenylpent-4-en-2-yn-1-one (25)[82]



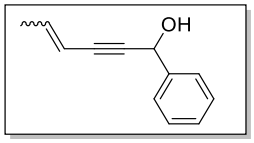
Following general procedure A, using 2-methyl-1-buten-3-yne (1.74 g, 26.3 mmol) CuI (100 mg, 0.53 mmol), $PdCl_2(PPh_3)_2$ (74 mg, 0.11 mmol) in Et_3N (51 mL), followed by the immediate addition of benzoyl chloride (4.80 g, 34.1 mmol) afforded the desired product as a pale brown oil (1.83 g, 41%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 – 8.01 (m, 2H), 7.71 – 7.56 (m, 1H), 7.55 – 7.45 (m, 2H), 5.71 (dq, *J* = 2.0, 1.0 Hz, 1H), 5.59 (dq, *J* = 2.0, 1.5 Hz, 1H), 2.05 (dd, *J* = 1.5, 1.0, 3H). ^{3}C NMR (101 MHz, $CDCl_3$) δ 178.2, 136.8, 134.1, 129.6, 128.6, 127.8, 125.0, 93.9, 85.7, 22.4.

General procedure B



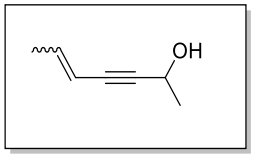
To a round bottomed flask was added CuI (4 mol%), $PdCl_2(PPh_3)_2$ (2 mol%) and diisopropylamine (2.0 eq.) in THF (0.2 M). The flask was flushed with N_2 and 1-bromo-1-propene (5.0 eq.) was added to the stirred suspension followed by the immediate addition of terminal alkyne (1.0 eq). The resulting mixture was stirred at room temperature overnight. Saturated NH_4Cl (aq.) was added and the aqueous layer was extracted with Et_2O. The organic phase was washed with aqueous HCl, saturated $NaHCO_3$ (aq.) and water. The organic phase was dried over anhydrous $MgSO_4$, filtered and the solvent was removed *in vacuo*. The residue was purified by flash column chromatography on silica gel eluting with pentane and Et_2O to afford the corresponding alcohols.

*Synthesis of 1-phenylhex-4-en-2-yn-1-ol (**41**)* [83]



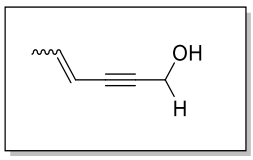
Following general procedure B, using benzyl alcohol (1.25 g, 9.47 mmol), CuI (72 mg, 0.38 mmol), $PdCl_2(PPh_3)_2$ (133 mg, 0.19 mmol), diisopropylamine (1.92 g, 18.9 mmol) and 1-bromo-1-propene (5.72 g, 47.3 mmol) in THF (48 mL) afforded the desired product as a yellow oil, and as a 1:1 mixture of *E/Z* isomers (1.17 g, 71%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 – 7.54 (m, 4H, C*H*$_{ar}$), 7.43 – 7.33 (m, 6H, C*H*$_{ar}$), 6.29 – 6.18 (br, 1H, =C*H E*), 6.06 (dq, *J* = 11.0, 7.0 Hz, 1H, =C*H Z*), 5.68 – 5.55 (m, 2H, C*H*=CH x 2), 2.25– 2.17 (m, 2H, C*H*OH x 2), 1.92 (dd, *J* = 7.0, 1.5 Hz, 3H, C*H*$_3$), 1.82 (dd, *J* = 7.0, 1.5 Hz, 3H, C*H*$_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 140.8, 139.6, 128.6 (x2C), 128.4 (x2C), 126.7 (x2C), 110.0, 109.4, 93.2, 86.9, 85.5, 83.5, 65.3, 65.1, 18.7, 16.1.

*Synthesis of hept-5-en-3-yn-2-ol (**39**)*



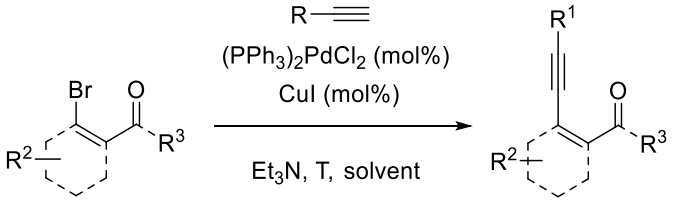
Following general procedure B, using 3-butyn-2-ol (1.05 g, 15.0 mmol), CuI (114 mg, 0.6 mmol), $PdCl_2(PPh_3)_2$ (211 mg, 0.3 mmol), diisopropylamine (3.04 g, 30.0 mmol) and 1-bromo-1-propene (9.07 g, 75.0 mmol) in THF (75 mL) afforded the desired product as a yellow oil and as a 1:1 mixture of *E/Z* isomers (1.53 g, 95%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.15 (dq, *J* = 15.0, 6.5 Hz, 1H, =C*H E*), 5.99 (dq, *J* = 11.0, 7.0 Hz, 1H, =C*H Z*), 5.54 – 5.46 (m, 2H, C*H*=CH), 4.73 – 4.59 (m, 2H, C*H*-OH), 1.87 (dd, *J* = 7.0, 2.0 Hz, 3H, C*H*$_3$), 1.78 (dd, *J* = 7.0, 2.0 Hz, 3H, C*H*$_3$), 1.50 (d, *J* = 6.5 Hz, 3H, C*H*$_3$), 1.46 (d, *J* = 6.5 Hz, 3H, C*H*$_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 140.2, 139.0, 110.1, 109.4, 95.6, 89.2, 82.8, 80.7, 59.0, 58.8, 24.6, 24.4, 18.6, 15.9. HRMS: *m/z* $[MH]^+$ $C_7H_{11}O$ calcd. 111.0804, found 111.0807. FTIR: ν_{max}/ cm^{-1} (neat) 3347 (br), 2983 (m), 2329 (w), 1670 (w), 1442 (m), 1074 (s).

*Synthesis of hex-4-en-2-yn-1-ol (**40**)*[83]



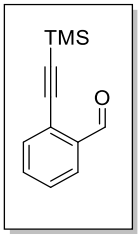
Following general procedure B, using propargyl alcohol (841 mg, 15.0 mmol), CuI (114 mg, 0.6 mmol), $PdCl_2(PPh_3)_2$ (211 mg, 0.3 mmol), diisopropylamine (3.04 g, 30.0 mmol) and 1-bromo-1-propene (9.07 g, 75.0 mmol) in THF (75 mL) afforded the desired product as a yellow oil, as a 6:1 mixture of *E/Z* isomers (1.03 g, 71%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.17 (dq, *J* = 15.5, 7.0 Hz, 1H=C*H E*), 6.01 (dq, *J* = 11.0, 7.0 Hz, 1H=C*H Z*), 5.54 – 5.47 (m, 2H), 4.43 (d, *J* = 2.0 Hz, 2H), 4.36 (d, *J* = 1.5 Hz, 2H), 1.87 (dd, *J* = 7.0, 1.5 Hz, 3H), 1.78 (dd, *J* = 7.0, 1.5 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 140.5, 139.3, 110.1, 109.4, 85.4 (x2 C), 84.5 (x2 C), 51.7, 51.7, 18.6, 16.0.

General procedure C



To a round bottomed flask was added CuI (5 mol%), $PdCl_2(PPh_3)_2$ (5 mol%), Et_3N (3 equiv.) and solvent. The flask was flushed with N_2 and the corresponding (hetero)aryl halide (1.0 eq.) was added to the stirred suspension followed by the immediate addition of terminal alkyne (1.5 eq.). The resulting mixture was stirred at the corresponding temperature until the reaction was complete. Saturated NH_4Cl (aq.) was added and the aqueous layer was extracted with ethyl acetate. The organic phase was washed with aqueous HCl and brine. The organic phase was dried over anhydrous $MgSO_4$, filtered and the solvent was removed *in vacuo*. The residue was purified by flash column chromatography on silica gel eluting with petroleum ether (40/60) and ethyl acetate to afford the corresponding 2-alkynyl aldehydes.

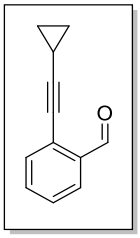
Synthesis of 2-(2-(trimethylsilyl)ethynyl)benzaldehyde [37]



Following general procedure C, using 2-bromobenzaldehyde (1.00 g, 5.4 mmol), CuI (51 mg, 0.27 mmol), $PdCl_2(PPh_3)_2$ (190 mg, 0.27 mmol) and trimethylsilylacetylene (796 mg, 8.1 mmol) in Et_3N (22 mL), the desired product was isolated as a white solid (909 mg, 83%). M.p.: 50 – 51 °C (lit:[84] 44– 48 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.58 (s, 1H, C*H*O), 8.00 – 7.82 (m, 1H, CH_{ar}),

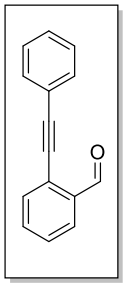
7.64 – 7.51 (m, 2H, C*H*$_{ar}$), 7.48 – 7.43 (m, 1H, C*H*$_{ar}$), 0.31 (s, 9H, Si(C*H*$_3$)$_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.9, 136.2, 133.7, 133.5, 128.8, 126.9, 126.8, 102.5, 100.1, -0.2.

Synthesis of 2-(2-cyclopropylethynyl)benzaldehyde[39]



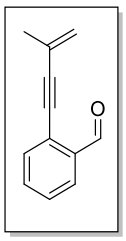
Following general procedure C, using 2-bromobenzaldehyde (1.00 g, 5.4 mmol), CuI (51 mg, 0.27 mmol), $PdCl_2(PPh_3)_2$ (190 mg, 0.27 mmol) and cyclopropylacetylene (535 mg, 8.1 mmol) in Et_3N (22 mL) the desired product was isolated as an orange oil (815 mg, 89%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.49 (s, 1H, C*H*O), 7.90 – 7.82 (m, 1H, C*H*$_{ar}$), 7.53 – 7.44 (m, 2H, C*H*$_{ar}$), 7.36 (td, *J* = 7.5, 1.5 Hz, 1H, C*H*$_{ar}$), 1.55 – 1.48 (m, 1H, C*H*), 0.97 – 0.91 (m, 2H, C*H*$_2$), 0.88 – 0.83 (m, 2H, C*H*$_2$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.2, 136.1, 133.7, 133.3, 127.9, 127.8, 127.0, 101.3, 71.5, 8.9, 0.4.

Synthesis of 2-(2-phenylethynyl)benzaldehyde[39]



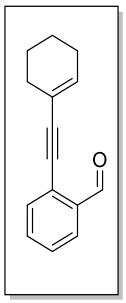
Following general procedure C, using 2-bromobenzaldehyde (500 mg, 2.7 mmol), CuI (27 mg, 0.14 mmol), $PdCl_2(PPh_3)_2$ (98 mg, 0.14 mmol) and phenylacetylene (418 mg, 4.1 mmol) in Et_3N (11 mL) afforded the desired product as an orange oil (351 mg, 63%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.68 (d, *J* = 1.0 Hz, 1H, C*H*O), 8.00 – 7.96 (m, 1H, C*H*$_{ar}$), 7.70 – 7.66 (m, 1H, C*H*$_{ar}$), 7.62 (dd, *J* = 7.5, 1.5 Hz, 1H, C*H*$_{ar}$), 7.61 – 7.58 (m, 2H, C*H*$_{ar}$), 7.51 – 7.46 (m, 1H, C*H*$_{ar}$), 7.44 – 7.40 (m, 3H, C*H*$_{ar}$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.8, 135.9, 133.8, 133.3, 131.7, 129.1, 128.7, 128.6, 127.3, 126.9, 122.3, 96.3, 84.9.

Synthesis of 2-(2-isopropenylethynyl)benzaldehyde[38]



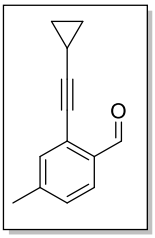
Following general procedure C, using 2-bromobenzaldehyde (500 mg, 2.7 mmol), CuI (27 mg, 0.14 mmol), $PdCl_2(PPh_3)_2$ (98 mg, 0.14 mmol) and isopropenylacetylene (271 mg, 4.1 mmol) in Et_3N (11 mL) afforded the desired product as an orange oil (455 mg, 99%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.54 (d, *J* = 1.0 Hz, 1H, C*H*O), 7.92 (dt, *J* = 8.0, 1.0 Hz, 1H, CH_{ar}), 7.59 – 7.47 (m, 2H, CH_{ar}), 7.50 – 7.36 (m, 1H, CH_{ar}), 5.48 (br, 1H, C=C*H*), 5.41 – 5.35 (m, 1H, C=C*H*), 2.07 – 1.95 (m, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.8, 135.8, 133.8, 133.2, 128.6, 127.2, 126.9, 126.3, 123.4, 97.5, 83.8, 23.2.

Synthesis of 2-(2-cyclohexenylethynyl)benzaldehyde[39]



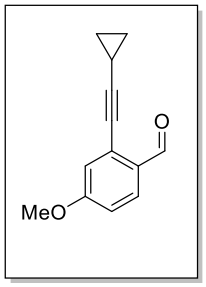
Following general procedure C, using 2-bromobenzaldehyde (500 mg, 2.7 mmol), CuI (27 mg, 0.14 mmol), $PdCl_2(PPh_3)_2$ (98 mg, 0.14 mmol) and cyclohexenylacetylene (435 mg, 4.1 mmol) in Et_3N (11 mL) afforded the desired product as a pale orange oil (407 mg, 72%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.54 (d, *J* = 1.0 Hz, 1H, C*H*O), 7.91 – 7.87 (m, 1H, CH_{ar}), 7.54 – 7.50 (m, 2H, CH_{ar}), 7.41 – 7.36 (m, 1H, CH_{ar}), 6.32 – 6.28 (m, 1H, C=C*H*), 2.28 – 2.22 (m, 2H, CH_2), 2.20 – 2.14 (m, 2H, CH_2), 1.74 – 1.61 (m, 4H, CH_2). ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.1, 136.9, 135.6, 133.7, 133.0, 128.1, 127.6, 127.1, 120.3, 98.5, 82.4, 29.0, 25.8, 22.2, 21.4.

Synthesis of 2-(2-cyclopropylethynyl)-4-methylbenzaldehyde



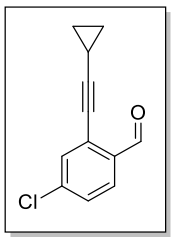
Following general procedure C, using 2-bromo-4-methylbenzaldehyde (223 g, 1.1 mmol), CuI (11 mg, 0.06 mmol), $PdCl_2(PPh_3)_2$ (42 mg, 0.06 mmol) and cyclopropylacetylene (112 mg, 1.7 mmol) in Et_3N (5 mL) afforded the desired product as an orange oil (67 mg, 33%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.42 (d, *J* = 1.0 Hz, 1H, C*H*O), 7.77 (d, *J* = 8.0 Hz, 1H, CH_{ar}), 7.31 – 7.27 (m, 1H, CH_{ar}), 7.22 – 7.10 (m, 1H, CH_{ar}), 2.37 (s, 3H, CH_3), 1.51 (tt, *J* = 8.0, 5.0 Hz, 1H, C*H*), 0.97 – 0.90 (m, 2H, CH_2), 0.88 – 0.82 (m, 2H, CH_2). ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.8, 144.7, 133.9, 133.7, 128.9, 127.9, 127.1, 100.7, 71.6, 21.6, 8.9, 0.3. HRMS: *m/z* $[MH]^+$ $C_{13}H_{13}O$ calcd. 185.0961, found 185.0959. FTIR: ν_{max}/ cm^{-1} (neat) 2926 (w), 2218 (w), 1778 (m), 1688 (s), 1597 (s), 1257 (m).

Synthesis of 2-(2-cyclopropylethynyl)-4-methoxybenzaldehyde



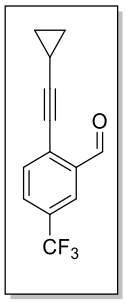
Following general procedure C, using 2-bromo-4-methoxybenzaldehyde (325 g, 1.5 mmol), CuI (15 mg, 0.08 mmol), $PdCl_2(PPh_3)_2$ (53 mg, 0.08 mmol) and cyclopropylacetylene (152 mg, 2.3 mmol) in Et_3N (6 mL) afforded the desired product as a pale yellow oil (225 mg, 74%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.33 (d, *J* = 1.0 Hz, 1H, C*H*O), 7.83 (d, *J* = 8.5 Hz, 1H, CH_{ar}), 6.93 (d, *J* = 2.5 Hz, 1H, CH_{ar}), 6.88 (ddd, *J* = 8.5, 2.5, 1.0 Hz, 1H, CH_{ar}), 3.86 (s, 3H, CH_3), 1.55 – 1.47 (m, 1H, C*H*), 0.97 – 0.91 (m, 2H, CH_2), 0.89 – 0.81 (m, 2H, CH_2). ^{13}C NMR (101 MHz, $CDCl_3$) δ 190.8, 163.8, 130.0, 129.9, 129.2, 117.0, 114.9, 101.1, 71.5, 55.6, 8.9, 0.3. HRMS: *m/z* $[MH]^+$ $C_{13}H_{13}O_2$ calcd. 201.0910, found 201.0907. FTIR: ν_{max}/ cm^{-1} (neat) 2943 (w), 2161 (w), 1684 (s), 1600 (s), 1380 (m), 1259 (m).

Synthesis of 2-(2-cyclopropylethynyl)-4-chlorobenzaldehyde



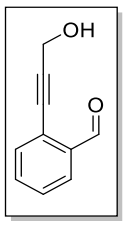
Following general procedure C, using 2-bromo-4-chlorobenzaldehyde (201 mg, 0.9 mmol), CuI (10 mg, 0.05 mmol), $PdCl_2(PPh_3)_2$ (35 mg, 0.05 mmol) and cyclopropylacetylene (93 mg, 1.4 mmol) in Et_3N (6 mL) afforded the desired product as an orange oil (125 mg, 67%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.41 (d, *J* = 1.0 Hz, 1H, C*H*O), 7.80 (d, *J* = 8.5 Hz, 1H, CH_{ar}), 7.46 (d, *J* = 2.0 Hz, 1H, CH_{ar}), 7.33 (ddd, *J* = 8.5, 2.0, 1.0 Hz, 1H, CH_{ar}), 1.55 – 1.46 (m, 1H, C*H*), 0.99 – 0.93 (m, 2H, CH_2), 0.89 – 0.84 (m, 2H, CH_2). ^{13}C NMR (101 MHz, $CDCl_3$) δ 190.9, 140.1, 134.4, 133.0, 129.3, 128.4, 128.3, 102.8, 70.4, 9.1, 0.3. HRMS: *m/z* $[MH]^+$ $C_{12}H_{10}{}^{35}ClO$ calcd. 205.0415, found 205.0415. FTIR: ν_{max}/ cm^{-1} (neat) 2130 (w), 1689 (s), 1614 (m), 1328 (s), 1169 (s).

Synthesis of 2-(2-cyclopropylethynyl)-5-trifluoromethylbenzaldehyde



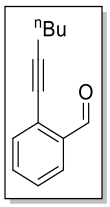
Following general procedure C, using 2-bromo-5-trifluoromethylbenzaldehyde (304 g, 1.2 mmol), CuI (11 mg, 0.06 mmol), $PdCl_2(PPh_3)_2$ (40 mg, 0.06 mmol) and cyclopropylacetylene (119 mg, 1.8 mmol) in Et_3N (6 mL) afforded the desired product as yellow oil (128 mg, 45%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.49 (s, 1H, C*H*O), 8.16 – 8.12 (m, 1H, CH_{ar}), 7.73 (br, 1H, CH_{ar}), 7.59 (d, *J* = 8.0 Hz, 1H, CH_{ar}), 1.58 – 1.50 (m, 1H, C*H*), 1.03 – 0.95 (m, 2H, CH_2), 0.94 – 0.87 (m, 2H, CH_2). ^{13}C NMR (101 MHz, $CDCl_3$) δ 190.7, 136.2, 133.9, 131.1, 129.9 (q, *J* = 33.5 Hz), 129.8 (q, *J* = 4.0 Hz), 124.2 (q, *J* = 4.0 Hz), 120.7 (q, *J* = 272.0 Hz), 104.5, 70.7, 9.2, 0.4. ^{19}F NMR (377 MHz, $CDCl_3$) δ -63.1. HRMS: *m/z* $[MH]^+$ $C_{13}H_{10}F_3O$ calcd. 239.0683, found 239.0678. FTIR: ν_{max}/ cm^{-1} (neat) 2229 (w), 1699 (s), 1614 (m), 1328 (s), 1168 (s), 1128 (s).

Synthesis of 2-(3-hydroxy-1-propynyl)benzaldehyde[85]



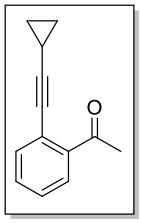
Following general procedure C, using 2-bromobenzaldehyde (500 mg, 2.7 mmol), CuI (27 mg, 0.14 mmol), $PdCl_2(PPh_3)_2$ (98 mg, 0.14 mmol) and propargyl alcohol (230 mg, 4.1 mmol) in Et_3N (11 mL) afforded the desired product as an orange oil (372 mg, 84%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.48 (d, *J* = 1.0 Hz, 1H, C*H*O), 7.89 (dt, *J* = 8.0, 1.0 Hz, 1H, CH_{ar}), 7.59 – 7.51 (m, 2H, CH_{ar}), 7.48 – 7.39 (m, 1H, CH_{ar}), 4.56 (d, *J* = 6.0 Hz, 2H, CH_2). ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.7, 136.0, 133.8, 133.5, 128.9, 127.5, 126.0, 94.4, 81.3, 51.6.

Synthesis of 2-(hex-1-yn-1-yl)benzaldehyde[86]



Following general procedure C, using 2-bromobenzaldehyde (8.0 g, 43.2 mmol), CuI (412 mg, 2.2 mmol), $PdCl_2(PPh_3)_2$ (1.6 g, 2.2 mmol) and hex-1-yne (5.3 g, 64.8 mmol) in Et_3N (173 mL), at 50 °C over night, the desired product was isolated as a dark orange oil (8.1 g, 99%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.54 (br, 1H, C*H*O), 7.91 – 7.85 (m, 1H, CH_{ar}), 7.54 – 7.48 (m, 2H, CH_{ar}), 7.41 – 7.35 (m, 1H, CH_{ar}), 2.49 (t, *J* = 7.0 Hz, 2H, CH_2), 1.63 (tt, *J* = 7.0, 6.0 Hz, 2H, CH_2), 1.55 – 1.46 (m, 2H, CH_2), 0.96 (t, *J* = 7.5 Hz, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.2, 136.0, 133.7, 133.3, 128.0, 127.9, 126.9, 98.2, 76.3, 30.6, 22.1, 19.3, 13.6.

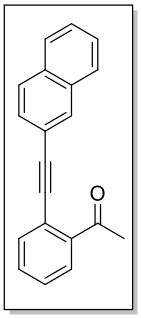
Synthesis of 2-(2-cyclopropylethynyl)acetophenone



Following general procedure C, using 2-bromoacetophenone (1.69 g, 8.5 mmol), CuI (76 mg, 0.4 mmol), $PdCl_2(PPh_3)_2$ (281 mg, 0.4 mmol) and cyclopropylacetylene (846 mg, 12.8 mmol) in

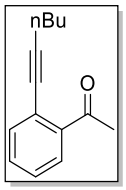
Et_3N (34 mL) afforded the desired product as an orange oil (1.33 g, 85%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (ddd, *J* = 7.5, 1.5, 0.5 Hz, 1H, C*H*$_{ar}$), 7.48 – 7.44 (m, 1H, C*H*$_{ar}$), 7.41 – 7.36 (m, 1H, C*H*$_{ar}$), 7.33 – 7.28 (m, 1H, C*H*$_{ar}$), 2.70 (s, 3H, C*H*$_3$), 1.50 (tt, *J* = 8.0, 5.0 Hz, 1H, C*H*), 0.94 – 0.87 (m, 2H, C*H*$_2$), 0.87 – 0.81 (m, 2H, C*H*$_2$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 200.9, 141.0, 134.0, 131.1, 128.4, 127.4, 122.5, 99.8, 74.9, 30.0, 8.6, 0.5. HRMS: *m/z* $[MH]^+$ $C_{13}H_{13}O$ calcd. 184.0883, found 184.0885. FTIR: ν_{max}/ cm^{-1} (neat) 2926 (w), 2226 (w), 1680 (s), 1356 (s), 1243 (s).

Synthesis of 1-(2-(naphthalen-2-ylethynyl)phenyl)ethan-1-one[87]



Following general procedure C, using 2-iodoacetophenone (2.0 g, 8.1 mmol), CuI (77.4 mg, 0.4 mmol), $PdCl_2(PPh_3)_2$ (291 mg, 0.4 mmol) and 2-ethynylnaphtalene (1.6 g, 10.6 mmol) in Et_3N (35 mL) afforded the desired product as a yellow foam (2.2 g, 98%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (s, 1H, C*H*$_{ar}$), 7.86 – 7.81 (m, 3H, C*H*$_{ar}$), 7.78 (dd, *J* = 8.0, 1.0 Hz, 1H, C*H*$_{ar}$), 7.69 (d, *J* = 7.5 Hz, 1H, C*H*$_{ar}$), 7.60 (dd, *J* = 8.5, 1.5 Hz, 1H, C*H*$_{ar}$), 7.53 – 7.48 (m, 3H, C*H*$_{ar}$), 7.42 (td, *J* = 7.5, 1.0 Hz, 1H, C*H*$_{ar}$), 2.84 (s, 3H, C*H*$_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 200.3, 140.8, 134.0, 133.1, 133.0, 131.6, 131.4, 128.8, 128.3, 128.2, 128.1, 127.9, 127.8, 127.0, 126.7, 121.8, 120.2, 95.4, 88.9, 30.0.

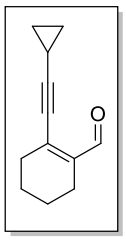
Synthesis of 1-(2-(hex-1-yn-1-yl)phenyl)ethan-1-one[88]



Following general procedure C, using 2-bromoacetophenone (5.0 g, 25.1 mmol), CuI (239 mg, 1.3 mmol), $PdCl_2(PPh_3)_2$ (900 mg, 1.3 mmol) and hex-1-yne (3.1 g, 38.0 mmol) in Et_3N (60 mL) afforded the desired product as a dark yellow oil (4.4 g, 88%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (dd, *J* = 8.0, 1.5 Hz, 1H, C*H*$_{ar}$), 7.47 (dd, *J* = 7.5, 1.0 Hz, 1H, C*H*$_{ar}$), 7.38 (td, *J* = 7.5, 1.5 Hz, 1H, C*H*$_{ar}$), 7.31 (td, *J* = 8.0, 1.0 Hz, 1H, C*H*$_{ar}$), 2.71 (s, 3H, C*H*$_3$), 2.46 (t, *J* = 7.0 Hz, 2H, C*H*$_2$), 1.65 –

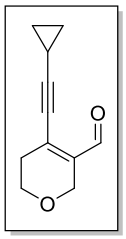
1.57 (m, 2H, CH_2), 1.53 – 1.43 (m, 2H, CH_2), 0.95 (t, J = 7.5 Hz, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 201.1, 141.1, 134.0, 131.1, 128.3, 127.5, 122.5, 96.9, 79.7, 30.5, 30.1, 22.1, 19.4, 13.6.

*Synthesis of 2-(2-cyclopropylethynyl)-1-cyclohexenecarboxaldehyde (**97**)*



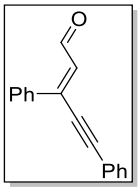
Following general procedure C, using 2-bromo-1-cyclohexenecarboxaldehyde[57] (227 mg, 1.2 mmol), CuI (11 mg, 0.06 mmol), $PdCl_2(PPh_3)_2$ (42 mg, 0.06 mmol) and cyclopropylacetylene (119 mg, 1.8 mmol) in Et_3N (5 mL) at 50 °C over night, the desired product was isolated as an orange oil (123 mg, 59%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.11 (s, 1H, C*H*O), 2.37 – 2.31 (m, 2H, CH_2), 2.24 – 2.19 (m, 2H, CH_2), 1.67 – 1.57 (m, 4H, CH_2), 1.46 – 1.39 (m, 1H, C*H*), 0.92 – 0.88 (m, 2H, CH_2), 0.80 – 0.75 (m, 2H, CH_2). ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.2, 141.7, 141.1, 104.0, 73.2, 32.7, 21.9, 21.9, 21.1, 9.1, 0.4. HRMS: *m/z* $[MH]^+$ $C_{12}H_{15}O$ calcd. 174.1039, found 174.1035. FTIR: ν_{max}/ cm^{-1} (neat) 2931 (m), 2210 (m), 1670 (s), 1600 (m), 1216 (m).

Synthesis of 4-(2-cyclopropylethynyl)-5,6-dihydro-2H-pyran-3-carboxaldehyde



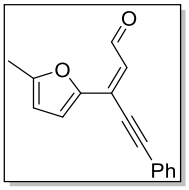
Following general procedure C, using 4-bromo-5,6-dihydro-2*H*-pyran-3-carboxaldehyde (116 mg, 0.6 mmol), CuI (6 mg, 0.03 mmol), $PdCl_2(PPh_3)_2$ (22 mg, 0.03 mmol) and cyclopropylacetylene (61 mg, 0.9 mmol) in Et_3N (5 mL) afforded the desired product as an orange oil (53 mg, 49%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.01 (s, 1H, C*H*O), 4.34 (t, J = 2.5 Hz, 2H, CH_2), 3.76 (t, J = 5.5 Hz, 2H, CH_2), 2.48 – 2.37 (m, 2H, CH_2), 1.45 (tt, J = 8.0, 5.0 Hz, 1H, C*H*), 0.98 – 0.89 (m, 2H, CH_2), 0.83 – 0.77 (m, 2H, CH_2). ^{13}C NMR (101 MHz, $CDCl_3$) δ 190.7, 139.7, 137.9, 105.5, 71.9, 63.5, 63.4, 31.5, 9.3, 0.5. HRMS: *m/z* $[MH]^+$ $C_{11}H_{13}O_2$ calcd. 176.0832, found 176.0832. FTIR: ν_{max}/ cm^{-1} (neat) 2834 (w), 2213 (m), 1668 (s), 1395 (m), 1264 (m).

Synthesis of (E)-3,5-diphenylpent-2-en-4-ynal[89]*(**110**)*



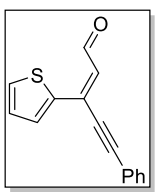
Following general procedure C, using (*E*)-3-bromo-3-phenylacrylaldehyde[61] (515 mg, 2.4 mmol), CuI (23 mg, 0.12 mmol), $PdCl_2(PPh_3)_2$ (87 mg, 0.12 mmol), ethynylbenzene (373 mg, 3.7 mmol) and Et_3N (748 mg, 7.3 mmol) in THF (24 mL) afforded the desired product as a yellow oil (252 mg, 45%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.42 (d, *J* = 8.0 Hz, 1H, C*H*O), 7.88 – 7.84 (m, 2H, CH_{ar}), 7.62 – 7.59 (m, 2H, CH_{ar}), 7.50 – 7.46 (m, 3H, CH_{ar}), 7.45 – 7.40 (m, 3H, CH_{ar}), 6.81 (d, *J* = 8.0 Hz, 1H, =C*H*). ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.2, 142.5, 135.7, 132.0, 131.1 (x2 C), 129.9, 128.9, 128.7, 127.2, 121.7, 102.2, 84.3.

*Synthesis of (Z)-3-(methylfuran-2-yl)-5-phenylpent-2-en-4-ynal (**111**)*



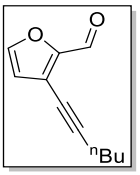
Following general procedure C, using (*E*)-3-bromo-3-(5methylfuran-2-yl)acrylaldehyde[61] (300 mg, 1.4 mmol), CuI (13 mg, 0.07 mmol), $PdCl_2(PPh_3)_2$ (50 mg, 0.07 mmol), ethynylbenzene (214 mg, 2.1 mmol) and Et_3N (427 mg, 4.2 mmol) in THF (14 mL) afforded the desired product as a yellow oil (269 mg, 82%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.27 (d, *J* = 8.5 Hz, 1H, C*H*O), 7.61 – 7.54 (m, 2H, CH_{ar}), 7.47 – 7.38 (m, 3H, CH_{ar}), 6.98 (d, *J* = 3.5 Hz, 1H, CH_{ar}), 6.69 (d, *J* = 8.5 Hz, 1H, =C*H*), 6.19 (dd, *J* = 3.5, 1.0 Hz, 1H, CH_{ar}) 2.39 (s, 1H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.4, 157.0, 149.6, 132.0, 130.4, 129.8, 128.7, 125.5, 121.6, 117.4, 109.6, 98.7, 81.9, 14.1. HRMS: *m/z* $[MH]^+$ $C_{16}H_{13}O_2$ calcd. 237.0910, found 237.0915. FTIR: ν_{max}/ cm^{-1} (neat) 3116 (w), 2831 (w), 2214 (m), 1656 (s), 1510 (m), 1140 (s), 1024 (s).

*Synthesis of (Z)-5-phenyl-3-(thiopen-2-yl)pent-2-en-4-ynal (**112**)*



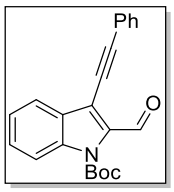
Following general procedure C, using (*E*)-3-bromo-3-(thiophen-2-yl)acrylaldehyde[61] (110 mg, 0.51 mmol), CuI (5 mg, 0.03 mmol), $PdCl_2(PPh_3)_2$ (18 mg, 0.03 mmol), ethynylbenzene (78 mg, 0.76 mmol) and Et_3N (115 mg, 1.5 mmol) in THF (5 mL) afforded the desired product as an intense yellow oil (90 mg, 75%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.31 (d, *J* = 8.0 Hz, 1H, C*H*O), 7.70 (d, *J* = 4.0 Hz, 1H, CH_{ar}), 7.63 – 7.59 (m, 2H, CH_{ar}), 7.51 (d, *J* = 5.0 Hz, 1H, CH_{ar}), 7.46 – 7.40 (m, 3H, CH_{ar}), 7.14 (dd, *J* = 5.0, 4.0 Hz, 1H, CH_{ar}), 6.68 (d, *J* = 8.0 Hz, 1H, =C*H*). ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.4, 141.2, 135.7, 132.0, 130.1, 130.0, 129.8, 128.7, 128.5, 128.3, 121.4, 100.4, 83.3. HRMS: *m/z* $[MH]^+$ $C_{15}H_{11}OS$ calcd. 239.0525, found 239.0528. FTIR: ν_{max}/ cm^{-1} (neat) 3103 (w), 2824 (w), 2203 (m), 1654 (s), 1554 (m), 1175 (s).

*Synthesis of 3-(hex-1-yn-1-yl)furan-2-carbaldehyde (**121**)*



Following general procedure C, using 3-bromofuran-2-carbaldehyde (200 mg, 1.1 mmol), CuI (11 mg, 0.06 mmol), $PdCl_2(PPh_3)_2$ (41 mg, 0.06 mmol) and hex-1-yne (141 mg, 1.7 mmol) in Et_3N (5 mL) at 50 °C over night, the desired product was isolated as a yellow oil (160 mg, 79%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.74 (s, 1H, C*H*O), 7.58 (d, *J* = 1.5 Hz, 1H, CH_{ar}), 6.53 (d, *J* = 1.5 Hz, 1H, CH_{ar}), 2.46 (t, *J* = 7.0 Hz, 1H, CH_2), 1.65 – 1.57 (m, 2H, CH_2), 1.52 – 1.43 (m, 2H, CH_2), 0.95 (t, *J* = 7.0 Hz, 1H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.1, 152.8, 147.4, 120.8, 115.4, 99.7, 69.7, 30.4, 22.0, 19.6, 13.6. HRMS: *m/z* $[MH]^+$ $C_{11}H_{13}O_2$ calcd. 177.0910, found 177.0911. FTIR: ν_{max}/ cm^{-1} (neat): 3379 (br), 2958 (m), 2233 (s), 1676 (s), 1420 (m).

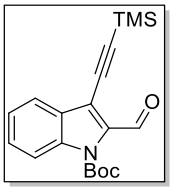
Synthesis of tert-butyl 2-formyl-3-(phenylethynyl)-1H-indole-1-carboxylate



Following general procedure C, using *tert*-butyl 3-bromo-2-formyl-1*H*-indole-1-carboxylate (600 mg, 1.9 mmol), CuI (18 mg, 0.09 mmol), $PdCl_2(PPh_3)_2$ (65 mg, 0.09 mmol) and ethynylbenzene (246 mg, 2.4 mmol) in Et_3N (4 mL) and THF (4 mL) at r.t. for 1.5 h, the desired product was isolated as an intense yellow oil (160 mg, 79%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.42 (s, 1H, C*H*O), 8.15 (d, *J* = 8.5 Hz, 1H, CH_{ar}), 7.89 (d, *J* = 8.0 Hz, 1H, CH_{ar}), 7.68 – 7.65 (m, 2H,

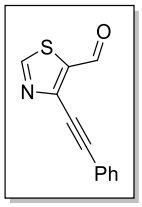
C*H*$_{ar}$), 7.54 (ddd, *J* = 8.5, 7.0, 1.5 Hz, 1H, C*H*$_{ar}$), 7.41 – 7.37 (m, 4H, C*H*$_{ar}$), 1.70 (s, 9H, C*H*$_3$ x3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 181.8, 149.3, 137.3, 137.1, 132.1, 129.1, 129.0, 128.7, 128.5, 124.1, 122.8, 122.0, 115.7, 113.3, 98.6, 85.9, 80.7, 28.1. HRMS: *m/z* $[MH]^+$ $C_{22}H_{20}NO_3$ calcd. 368.1257, found 368.1265. FTIR: ν_{max}/ cm^{-1} (neat): 2983 (w), 1732 (s), 1671 (s), 1533 (m), 1323 (s), 1125 (m).

Synthesis of tert-butyl 2-formyl-3-((trimethylsilyl)ethynyl)-1H-indole-1-carboxylate



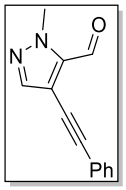
Following general procedure C, using *tert*-butyl 3-bromo-2-formyl-1*H*-indole-1-carboxylate (600 mg, 1.9 mmol), CuI (18 mg, 0.09 mmol), $PdCl_2(PPh_3)_2$ (65 mg, 0.09 mmol) and ethynylbenzene (246 mg, 2.4 mmol) in Et_3N (4 mL) and THF (4 mL) at r.t. for 1.5 h, the desired product was isolated as a yellow oil (160 mg, 79%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.30 (s, 1H, C*H*O), 8.10 (d, *J* = 8.5 Hz, 1H, C*H*$_{ar}$), 7.79 (d, *J* = 8.0 Hz, 1H, C*H*$_{ar}$), 7.51 (ddd, *J* = 8.5, 7.0, 1.5 Hz, 1H, C*H*$_{ar}$), 7.39 – 7.32 (m, 1H, C*H*$_{ar}$), 1.67 (s, 9H, C*H*$_3$ x3), 0.33 (s, 9H, C*H*$_3$ x3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 181.4, 149.3, 138.1, 137.2, 129.1, 128.9, 124.1, 122.1, 115.6, 113.6, 105.7, 95.3, 85.9, 28.1, 0.0. HRMS: *m/z* $[MH]^+$ $C_{19}H_{24}NO_3Si$ calcd. 364.1339, found 364.1351. FTIR: ν_{max}/ cm^{-1} (neat): 2959 (w), 2151 (m), 1750 (s), 1671 (s), 1523 (m), 1343 (s), 1155 (m).

Synthesis of 4-(phenylethynyl)thiazole-5-carbaldehyde



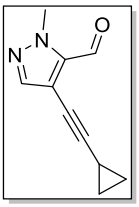
Following general procedure C, using 4-chlorothiazole-5-carbaldehyde (300 mg, 2.0 mmol), CuI (19 mg, 0.1 mmol), $PdCl_2(PPh_3)_2$ (73 mg, 0.1 mmol), Et_3N (416 mg, 4.0 mmol) and ethynylbenzene (311 mg, 3.1 mmol) in MeCN (20 mL) at 60 °C for 2 h, the desired product was isolated as a pale yellow oil (387 mg, 89%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.32 (br, 1H, C*H*O), 9.05 (d, *J* = 1.0 Hz, 1H, C*H*$_{ar}$), 7.65 – 7.59 (m, 2H, C*H*$_{ar}$), 7.47 – 7.39 (m, 3H, C*H*$_{ar}$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 182.9, 158.8, 145.4, 139.1, 132.2, 130.0, 128.7, 121.1, 96.6, 80.9. HRMS: *m/z* $[MH]^+$ $C_{12}H_8NOS$ calcd. 214.0321, found 214.0331. FTIR: ν_{max}/ cm^{-1} (neat): 3057 (w), 2827 (w), 2210 (m), 1670 (s), 1504 (m), 1322 (s), 1220 (m).

Synthesis of 1-methyl-4-(phenylethynyl)-1H-pyrazole-5-carbaldehyde



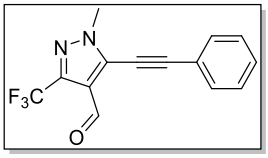
Following general procedure C, using 4-bromo-1-methyl-1*H*-pyrazole-5-carbaldehyde (300 mg, 1.6 mmol), CuI (15 mg, 0.08 mmol), $PdCl_2(PPh_3)_2$ (57 mg, 0.08 mmol), Et_3N (324 mg, 3.2 mmol) and ethynylbenzene (243 mg, 2.4 mmol) in MeCN (16 mL) at 60 °C for 2 h, the desired product was isolated as a yellow foam (250 mg, 75%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.08 (s, 1H, C*H*O), 7.66 (s, 1H, CH_{ar}), 7.56 – 7.47 (m, 2H, CH_{ar}), 7.40 – 7.34 (m, 3H, CH_{ar}), 4.18 (s, 3H, NCH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 179.5, 140.9, 138.6, 131.6, 128.9, 128.5, 122.4, 112.4, 95.0, 77.8, 39.8. HRMS: *m*/*z* $[MH]^+$ $C_{13}H_{11}N_2O$ calcd. 211.0866, found 211.0872. FTIR: ν_{max}/ cm^{-1} (neat): 3050 (w), 2960 (w), 2221 (m), 1685 (s), 1538 (m), 1367 (m), 1202 (m).

Synthesis of 4-(cyclopropylethynyl)-1-methyl-1H-pyrazole-5-carbaldehyde



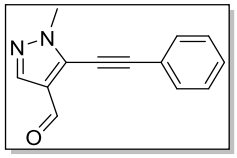
Following general procedure C, using 4-bromo-1-methyl-1*H*-pyrazole-5-carbaldehyde (2.0 g, 10.6 mmol), CuI (101 mg, 0.53 mmol), $PdCl_2(PPh_3)_2$ (379 mg, 0.53 mmol), Et_3N (2.2 g, 21.2 mmol) and ethynylcyclopropane (1.1 g, 15.9 mmol) in MeCN (106 mL) at 60 °C for 2 h, the desired product was isolated as a yellow oil (1.35 g, 73%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.93 (s, 1H, C*H*O), 7.49 (s, 1H, CH_{ar}), 4.12 (s, 3H, CH_3), 1.46 (td, *J* = 8.0, 4.0 Hz, 1H, C*H*), 0.94 – 0.88 (m, 2H, CH_2), 0.84 – 0.79 (m, 2H, CH_2). ^{13}C NMR (101 MHz, $CDCl_3$) δ 179.4, 140.6, 138.5, 113.0, 99.3, 63.8, 39.4, 8.5, 0.0. HRMS: *m*/*z* $[MH]^+$ $C_{10}H_{11}N_2O$ calcd. 175.0866, found 175.0868. FTIR: ν_{max}/ cm^{-1} (neat): 3014 (w), 2951 (w), 2232 (m), 1680 (s), 1430 (m), 1216 (m), 1198 (m).

Synthesis of 1-methyl-5-(phenylethynyl)-3-(trifluoromethyl)-1H-pyrazole-4-carbaldehyde



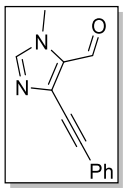
Following general procedure C, using 5-chloro-1-methyl-3-(trifluoromethyl)-1*H*-pyrazole-4-carbaldehyde (300 mg, 1.4 mmol), CuI (13 mg, 0.07 mmol), $PdCl_2(PPh_3)_2$ (51 mmol, 0.07 mmol), Et_3N (289 mg, 2.8 mmol) and ethynylbenzene (216 mg, 2.1 mmol) in MeCN (14 mL) at 60 °C for 24 h, the desired product was isolated as a white foam (115 mg, 30%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.06 (s, 1H, C*H*O), 7.65 – 7.60 (m, 2H, CH_{ar}), 7.49 – 7.42 (m, 3H, CH_{ar}), 4.07 (s, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 181.7, 141.0 (q, $^2J_{C\text{-}F}$ = 39.5 Hz), 132.1, 131.4, 130.5, 128.8, 121.5, 120.3 (q, $^1J_{C\text{-}F}$ = 270.0 Hz), 120.4, 102.5, 74.4, 38.0. ^{19}F NMR (376 MHz, $CDCl_3$) δ -61.3. HRMS: *m/z* $[MH]^+$ $C_{14}H_{10}F_3N_2O$ calcd. 279.0740, found 279.0746. FTIR: ν_{max}/ cm^{-1} (neat): 2833 (w), 2225 (m), 1688 (s), 1504 (m), 1307 (m), 1125 (s).

Synthesis of 1-methyl-5-(phenylethynyl)-1H-pyrazole-4-carbaldehyde



Following general procedure C, using 5-bromo-1-methyl-1*H*-pyrazole-4-carbaldehyde (300 mg, 1.6 mmol), CuI (15 mg, 0.08 mmol), $PdCl_2(PPh_3)_2$ (57 mg, 0.08 mmol), Et_3N (324 mg, 3.2 mmol) and ethynylbenzene (243 mg, 2.4 mmol) in MeCN (16 mL) at 60 °C for 2 h, the desired product was isolated as a pale brown foam (195 mg, 58%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.08 (s, 1H, C*H*O), 7.65 (s, 1H, CH_{ar}), 7.54 – 7.50 (m, 2H, CH_{ar}), 7.39 – 7.35 (m, 3H, CH_{ar}), 4.17 (s, 3H, NCH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 179.5, 140.9, 138.6, 131.6, 128.9, 128.5, 122.4, 112.4, 95.0, 77.8, 39.8. HRMS: *m/z* $[MH]^+$ $C_{13}H_{11}N_2O$ calcd. 211.0866, found 211.0865. FTIR: ν_{max}/ cm^{-1} (neat): 2959 (w), 2221 (m), 1695 (s), 1550 (m), 1366 (m), 1202 (m).

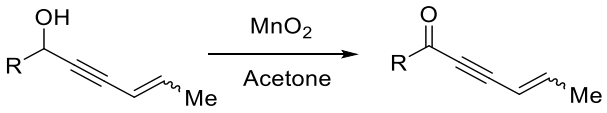
Synthesis of 1-methyl-4-(phenylethynyl)-1H-imidazole-5-carbaldehyde



Following general procedure C, using 4-bromo-1-methyl-1*H*-imidazole-5-carbaldehyde (250 mg, 1.3 mmol), CuI (13 mg, 0.07 mmol), $PdCl_2(PPh_3)_2$ (47 mg, 0.07 mmol), Et_3N (270 mg, 2.7 mmol) and ethynylbenzene (202 mg, 2.0 mmol) in MeCN (13 mL) at 60 °C for 2 h, the desired product was isolated as a pale yellow foam (247 mg, 88%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.03 (s, 1H, C*H*O), 7.57 (br, 3H, CH_{ar}), 7.38 (br, 3H, CH_{ar}), 3.95 (s, 3H, NCH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 179.7, 143.3, 137.3, 132.1, 131.9, 129.2, 128.5, 121.9, 94.5, 80.3, 34.5. HRMS: *m/z*

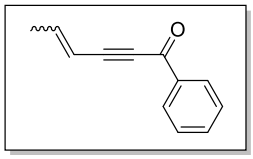
$[MH]^+$ $C_{13}H_{11}N_2O$ calcd. 211.0866, found 211.0868. FTIR: ν_{max}/ cm^{-1} (neat): 3116 (w), 2841 (w), 2217 (m), 1661 (s), 1510 (s), 1360 (m), 1321 (m), 1206 (m).

General procedure D



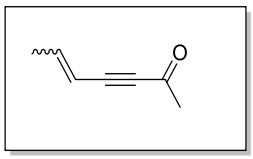
Corresponding alcohol (1.0 eq.) and manganese oxide (5.0 eq.) in acetone (0.1 M) were stirred at room temperature for 24 hours. The mixture was filtered and the solvent was evaporated to provide crude product. The residue was purified by flash column chromatography on silica gel eluting with petroleum ether (40/60) and ethyl acetate to afford the corresponding ynones.

*Synthesis of 1-phenylhex-4-en-2-yn-1-one (**44**)*[90]



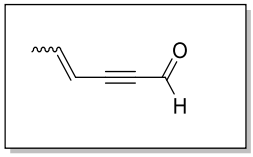
Following general procedure D, 1-phenylhex-4-en-2-yn-1-ol (1.11 g, 6.44 mmol) and manganese oxide (2.78 g, 32.2 mmol) in acetone (65 mL) afforded the desired product as a yellow oil, and as a 1:1 mixture of *E/Z* isomers (1.00 g, 91%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 – 8.12 (m, 4H, C*H*$_{ar}$), 7.67 – 7.59 (m, 2H, C*H*$_{ar}$), 7.55 – 7.46 (m, 4H, C*H*$_{ar}$), 6.66 (dq, *J* = 16.0, 7.0 Hz, 1H *E* C=C*H*), 6.43 (dq, *J* = 11.0, 7.0 Hz, 1H *Z* C=C*H*), 5.82 – 5.76 (m, 2H, C*H*=CH), 2.09 (dd, *J* = 7.0, 2.0 Hz, 3H, C*H*$_3$), 1.95 (dd, *J* = 7.0, 2.0 Hz, 3H, C*H*$_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 178.2, 178.1, 147.8, 146.1, 136.9 (x2 C), 134.0, 133.9, 129.5 (x2 C), 128.6, 128.5, 109.1, 108.4, 92.6, 92.0, 90.1, 85.9, 19.3, 17.0.

*Synthesis of hept-5-en-3-yn-2-one (**42**)*[91]



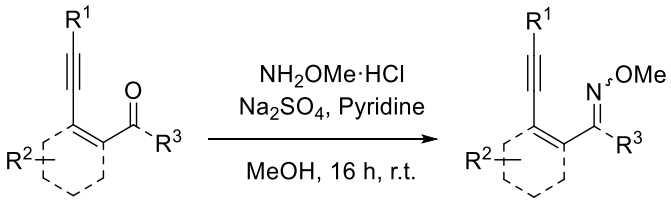
Following general procedure D, using hept-5-en-3-yn-2-ol (1.40 g, 12.6 mmol) and manganese oxide (5.45 g, 63.1 mmol) in acetone (125 mL) afforded the desired product as a yellow oil (1.00 g, 91%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.53 (dq, *J* = 16.0, 7.0 Hz, 1H, =C*H E*), 5.63 (dd, *J* = 16.0, 2.0 Hz, 1H), 2.37 (s, 3H, C*H*$_3$), 1.90 (dd, *J* = 7.0, 2.0 Hz, 3H, C*H*$_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 184.7, 147.6, 108.9, 89.8, 87.3, 32.6, 19.2.

*Synthesis of Hex-4-en-2-ynal (**43**)* [92]



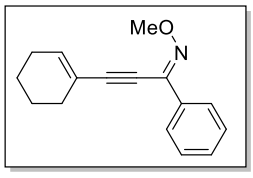
Following general procedure D, hex-4-en-2-yn-1-ol (440 mg, 4.56 mmol) and manganese oxide (1.97 g, 22.8 mmol) in acetone (46 mL) afforded the desired product as a yellow oil, and as a 6:1 mixture of *E/Z* isomers (225 mg, 52%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.36 (d, *J* = 1.0 Hz, 1H, C*H*O), 9.28 (d, *J* = 1.0 Hz, 1H, C*H*O), 6.60 (dq, *J* = 16.0, 7.0 Hz, 1H, =C*H E*), 6.47 – 6.37 (m, 1H, =C*H Z*), 5.73 – 5.62 (m, 2H, CH=C*H*), 1.99 (dd, *J* = 7.0, 2.0 Hz, 3H, CH_3), 1.91 (dd, *J* = 7.0, 2.0 Hz, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.8, 176.7, 149.2, 147.6, 108.7, 107.8, 94.7, 93.1, 92.0, 87.6, 19.4, 16.9.

General procedure E



Ketone/aldehyde (1.0 eq.), *O*-methylhydroxylamine hydrochloride (2.0 eq.), Na_2SO_4 (2.0 eq.) and pyridine (2.2 eq.) in solvent (0.45 M) were stirred at room temperature and the reaction was monitored via TLC analysis. Upon completion, the mixture was diluted with water, and extracted with ethyl acetate. The organic phase was dried over anhydrous $MgSO_4$, filtered and the solvent was removed *in vacuo*. The residue was purified by flash column chromatography on silica gel eluting with petroleum ether (40/60) and ethyl acetate to afford the corresponding *O*-methyl oximes.

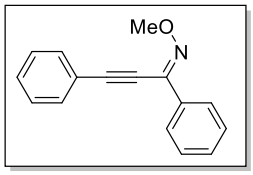
*Synthesis of (E) 3-(cyclohex-1-enyl)-1-phenylprop-2-yn-1-one O-methyl oxime (**37**)* [36]



Following general procedure E, using 3-cyclohexenyl-1-phenylprop-2-yn-1-one (2.18 g, 10.4 mmol), *O*-methylhydroxylamine hydrochloride (1.74 g, 20.8 mmol), Na_2SO_4 (2.95 g, 20.8 mmol) and pyridine (1.81 g, 22.9 mmol) in methanol (23 mL) afforded the desired product as a yellow

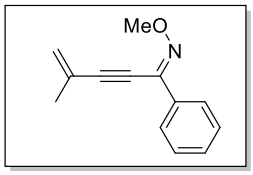
oil (2.28 g, 85%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 – 7.80 (m, 2H, CH_{ar}), 7.38 – 7.33 (m, 3H, CH_{ar}), 6.40 (tt, *J* = 4.0, 2.0 Hz, 1H, C*H* =CH), 4.09 (s, 3H, OCH_3), 2.33 – 2.23 (m, 2H, CH_2), 2.21 – 2.10 (m, 2H, CH_2), 1.74 – 1.57 (m, 4H, CH_2 x 2). ^{13}C NMR (101 MHz, $CDCl_3$) δ 140.2, 138.6, 133.8, 129.5, 128.3, 126.5, 120.0, 103.5, 77.1, 63.2, 28.9, 27.4, 25.9, 22.2.

*Synthesis of (E) 1,3-diphenylprop-2-yn-1-one O-methyl oxime (**36**)* [36]



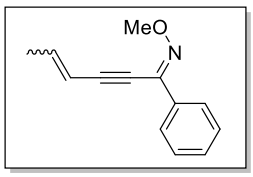
Following general procedure E, using 1,3-diphenyl-2-propyn-1-one (1.40 g, 6.8 mmol), *O*-methylhydroxylamine hydrochloride (1.14 g, 13.6 mmol), Na_2SO_4 (1.93 g, 13.6 mmol) and pyridine (1.18 g, 15.0 mmol) in methanol (15 mL) afforded the desired product as a white solid (1.23 g, 78%). M.p.: 42 – 44 °C (lit:[36] 40– 42 °C). ^{1}H (400 MHz, $CDCl_3$) δ 7.95 – 7.89 (m, 2H, CH_{ar}), 7.65 – 7.60 (m, 2H, CH_{ar}), 7.44 – 7.35 (m, 6H, CH_{ar}), 4.15 (s, 3H, OCH_3). ^{13}C (101 MHz, $CDCl_3$) δ 140.0, 133.6, 132.2, 129.7, 129.6, 128.5, 128.4, 126.5, 121.8, 101.2, 79.5, 63.2.

*Synthesis of (E) 4-methyl-1-phenylpent-4-en-2-yn O-methyloxime (**38**)* [93]



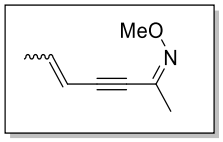
Following general procedure E, using 4-methyl-1-phenylpent-4-en-2-yn-1-one (1.82 g, 10.7 mmol), *O*-methylhydroxylamine hydrochloride (1.79 g, 21.4 mmol), Na_2SO_4 (3.04 g, 21.4 mmol) and pyridine (1.86 g, 23.5 mmol) in methanol (24 mL) afforded the desired product as a brown oil (1.72 g, 81%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 – 7.79 (m, 2H, CH_{ar}), 7.44 – 7.34 (m, 3H, CH_{ar}), 5.57 (dq, *J* = 2.0, 1.0 Hz, 1H, C*H*=C), 5.45 (dq, *J* =2.0, 1.5 Hz, 1H, C*H*=C), 4.11 (s, 3H, CH_3), 2.04 (dd, *J* = 1.5, 1.0 Hz, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.8, 133.6, 129.6, 128.4, 126.5, 125.9, 124.8, 102.3, 77.2, 63.1, 23.1.

*Synthesis of (E) 1-phenylhex-4-en-2-yn O-methyloxime (**47**)*



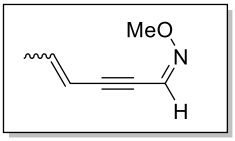
Following general procedure E, using 1-phenylhex-4-en-2-yn-1-one (992 mg, 5.8 mmol), *O*-methylhydroxylamine hydrochloride (1.00 g, 11.6 mmol), Na_2SO_4 (1.65 g, 11.6 mmol) and pyridine (1.00 g, 12.8 mmol) in methanol (13 mL) afforded the desired product as a brown oil, and as a 1.2:1 mixture of *E/Z* isomers (1.12 g, 97%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 – 7.80 (m, 4H, C*H*$_{ar}$), 7.41 – 7.34 (m, 6H, C*H*$_{ar}$), 6.44 (dq, *J* = 16.0, 7.0 Hz, 1H, =C*H E*), 6.24 (dq, *J* = 11.0, 7.0 Hz, 1H, =C*H Z*), 5.84 – 5.78 (m, 2H, =C*H*), 4.11 (s, 3H, OC*H*$_3$), 4.10 (s, 3H, OC*H*$_3$), 2.02 (dd, *J* = 7.0, 1.5 Hz, 3H, C*H*$_3$), 1.88 (dd, *J* = 7.0, 1.5 Hz, 3H, C*H*$_3$). HRMS: *m*/*z* $[MH]^+$ $C_{13}H_{14}NO$ calcd. 199.0992, found 199.0998. FTIR: ν_{max}/ cm^{-1} (neat) 2935 (w), 2194 (w).

*Synthesis of (E)/(Z) hept-5-en-3-yn-2-O-methyloxime (**45**)*



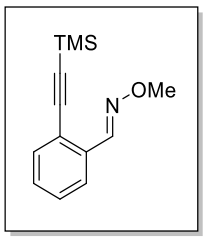
Following general procedure E, using hept-5-en-3-yn-2-ol (610 mg, 5.6 mmol), *O*-methylhydroxylamine hydrochloride (967 mg, 11.2 mmol), Na_2SO_4 (1.6 g, 11.2 mmol) and pyridine (973 mg, 12.3 mmol) in methanol (13 mL) afforded the desired product as a yellow oil and as a 1.2:1 mixture of *E/Z* olefin isomers and 1:1 mixture of *E/Z* oxime isomers (630 mg, 82%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.33 (dq, *J* = 16.0, 7.0 Hz, 1H, =C*H E*), 6.28 (dq, *J* = 16.0, 7.0 Hz, 1H, =C*H E*), 6.16 (dq, *J* = 11.0, 7.0 Hz, 1H, =C*H Z*), 6.09 (dq, *J* = 11.0, 7.0 Hz, 1H, =C*H Z*), 5.73 – 5.58 (m, 4H, C*H*=CH), 3.94 (s, 3H, OC*H*$_3$), 3.94 (s, 3H, OC*H*$_3$), 3.93 (s, 3H, OC*H*$_3$), 3.92 (s, 3H, OC*H*$_3$), 2.07 (s, 3H, C*H*$_3$), 2.04 (s, 3H, C*H*$_3$), 2.02 (s, 3H, C*H*$_3$), 1.99 (s, 3H, C*H*$_3$), 1.95 – 1.90 (m, 6H, C*H*$_3$), 1.86 – 1.80 (m, 6H, C*H*$_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.3, 142.5, 142.2, 142.1, 140.9, 137.8, 109.9, 109.9, 109.3, 109.2, 98.3, 96.2, 90.0, 89.3, 87.2, 85.5, 83.9, 79.5, 62.3, 62.3, 62.2, 62.2, 20.6, 20.6, 19.0, 18.9, 16.7, 16.5, 16.4, 16.4. HRMS: *m*/*z* $[MH]^+$ $C_8H_{12}NO$ calcd. 137.0835, found 137.0839. FTIR: ν_{max}/ cm^{-1} (neat) 2938 (w), 2204 (w), 1436 (m), 1304 (m), 1046 (s).

*Synthesis of (E)/(Z) hex-4-en-2-yn-1-O-methyloxime (**46**)*



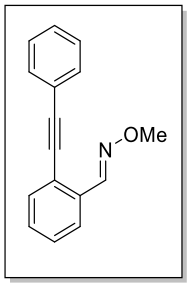
Following general procedure E, using hex-4-en-2-ynal (209 mg, 2.2 mmol), *O*-methylhydroxylamine hydrochloride (368 mg, 4.4 mmol), Na_2SO_4 (625 mg, 4.4 mmol) and pyridine (383 mg, 4.8 mmol) in methanol (5 mL) afforded the desired product as a yellow oil, and as a 1:1 mixture of *E/Z* oxime isomers (160 mg, 80%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 (d, *J* = 2.0 Hz, 1H, CN*H*), 6.78 (d, *J* = 2.0 Hz, 1H, CN*H*), 6.41 – 6.26 (m, 2H, =C*H*), 5.72 – 5.59 (m, 2H, =C*H*), 4.00 (s, 3H, OCH_3), 3.92 (s, 3H, OCH_3), 1.86 – 1.82 (m, 6H, CH_3 x 2). ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.8, 142.9, 133.4, 129.0, 109.8 (x2 C), 98.8, 93.5, 80.0, 77.7, 62.8, 62.5, 19.0, 18.9. HRMS: *m*/*z* $[MH]^+$ $C_7H_{10}NO$ calcd. 124.0750, found 124.0760. FTIR: ν_{max}/ cm^{-1} (neat) 2938 (w), 2191 (w), 1442 (m), 1329 (m), 1066 (s).

*Synthesis of (E) 2-(2-(trimethylsilyl)ethynyl)benzaldehyde O-methyl oxime (**54**)*



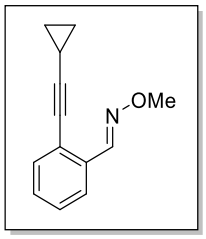
Following general procedure E, using 2-(2-(trimethylsilyl)ethynyl)benzaldehyde (545 mg, 2.7 mmol), *O*-methylhydroxylamine hydrochloride (451 mg, 5.4 mmol), Na_2SO_4 (767 mg, 5.4 mmol) and pyridine (470 mg, 5.9 mmol) in methanol (6 mL) afforded the desired product as a yellow oil (528 mg, 85%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (s, 1H, N=C*H*), 7.91 – 7.86 (m, 1H, CH_{ar}), 7.49 – 7.44 (m, 1H, CH_{ar}), 7.32 – 7.27 (m, 2H, CH_{ar}), 4.00 (s, 3H, OCH_3), 0.27 (s, 9H, SiCH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 147.2, 133.5, 132.8, 129.3, 128.7, 125.0, 122.9, 101.8, 100.3, 62.2, -0.1. HRMS: *m*/*z* $[MH]^+$ $C_{13}H_{17}NOSi$ calcd. 232.1152, found 232.1150. FTIR: ν_{max}/ cm^{-1} (neat) 2960 (w), 2156 (w), 1609 (w), 1448 (m), 1250 (m), 1053 (s).

*Synthesis of (E) 2-(2-phenylethynyl)benzaldehyde O-methyl oxime (**55**)* [40]



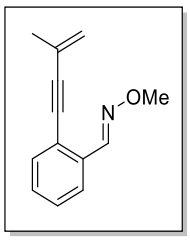
Following general procedure E, using 2-(2-phenylethynyl)benzaldehyde (336 mg, 1.6 mmol), *O*-methylhydroxylamine hydrochloride (267 mg, 3.2 mmol), Na_2SO_4 (454 mg, 3.2 mmol) and pyridine (278 mg, 3.5 mmol) in methanol (4 mL) afforded the desired product as a yellow oil (365 mg, 95%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.66 (s, 1H, N=C*H*), 7.96 – 7.90 (m, 1H, CH_{ar}), 7.58 – 7.51 (m, 3H, CH_{ar}), 7.40 – 7.30 (m, 5H, CH_{ar}), 4.02 (s, 3H, OCH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 147.3, 133.3, 132.5, 131.6, 129.5, 128.7, 128.5, 128.4, 125.2, 123.0, 122.8, 94.8, 86.3, 62.2.

*Synthesis of (E) 2-(2-cyclopropylethynyl)benzaldehyde O-methyl oxime (**56**)* [40]



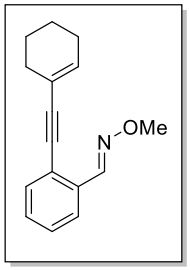
Following general procedure E, using 2-(2-cyclopropylethynyl)benzaldehyde (341 mg, 2.0 mmol), *O*-methylhydroxylamine hydrochloride (334 mg, 4.0 mmol), Na_2SO_4 (568 mg, 4.0 mmol) and pyridine (348 mg, 4.4 mmol) in methanol (5 mL) afforded the desired product as a bright yellow oil (352 mg, 90%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 (s, 1H, N=C*H*), 7.87 – 7.81 (m, 1H, CH_{ar}), 7.40 – 7.35 (m, 1H, CH_{ar}), 7.28 – 7.21 (m, 2H, CH_{ar}), 3.99 (s, 3H, OCH_3), 1.51 – 1.44 (m, 1H, C*H*), 0.93 – 0.85 (m, 2H, CH_2), 0.86 – 0.78 (m, 2H, CH_2). ^{13}C NMR (101 MHz, $CDCl_3$) δ 147.6, 133.2, 132.5, 129.3, 127.7, 125.0, 123.8, 99.4, 72.7, 62.1, 8.8, 0.3.

*Synthesis of (E) 2-(2-isopropenylethynyl)benzaldehyde O-methyl oxime (**57**)* [40]



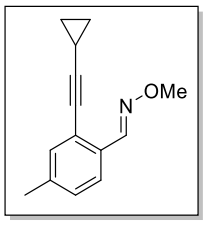
Following general procedure E, using 2-(2-isopropenylethynyl)benzaldehyde (451 mg, 2.7 mmol), *O*-methylhydroxylamine hydrochloride (451 mg, 5.4 mmol), Na_2SO_4 (767 mg, 5.4 mmol) and pyridine (470 mg, 5.9 mmol) in methanol (6 mL) afforded the desired product as an orange oil (489 mg, 93%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 (s, 1H, N=C*H*), 7.92 – 7.86 (m, 1H, CH_{ar}), 7.47 – 7.42 (m, 1H, CH_{ar}), 7.33 – 7.28 (m, 2H, CH_{ar}), 5.44 – 5.41 (m, 1H, =C*H*), 5.34 – 5.32 (m, 1H, =C*H*), 4.00 (s, 3H, OCH_3), 2.03 – 1.97 (m, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 147.3, 133.1, 132.5, 129.4, 128.4, 126.5, 125.2, 123.0, 122.6, 96.0, 85.1, 62.1, 23.4.

*Synthesis of (E) 2-(2-cyclohexenylethynyl)benzaldehyde O-methyl oxime (**58**)* [40]



Following general procedure E, using 2-(2-cyclohexenylethynyl)benzaldehyde (407 mg, 1.9 mmol), *O*-methylhydroxylamine hydrochloride (317 mg, 3.8 mmol), Na_2SO_4 (540 mg, 3.8 mmol) and pyridine (331 mg, 4.2 mmol) in methanol (5 mL) afforded the desired product as a brown oil (450 mg, 99%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56 (s, 1H, N=C*H*), 7.89 – 7.84 (m, 1H, CH_{ar}), 7.45 – 7.39 (m, 1H, CH_{ar}), 7.32 – 7.26 (m, 2H, CH_{ar}), 6.24 (tt, *J* = 4.0, 2.0 Hz, 1H, =C*H*), 3.99 (s, 3H, OCH_3), 2.27 – 2.20 (m, 2H, CH_2), 2.18 – 2.12 (m, 2H, CH_2), 1.72 – 1.59 (m, 4H, CH_2). ^{13}C NMR (101 MHz, $CDCl_3$) δ 147.5, 135.9, 132.9, 132.3, 129.4, 128.0, 125.1, 123.6, 120.5, 96.9, 83.7, 62.1, 29.1, 25.8, 22.3, 21.5.

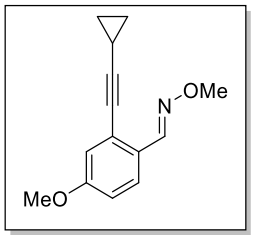
*Synthesis of (E) 2-(2-cyclopropylethynyl)-4-methylbenzaldehyde O-methyl oxime (**59**)*



Following general procedure E, using 2-(2-cyclopropylethynyl)-4-methylbenzaldehyde (56 mg, 0.3 mmol), *O*-methylhydroxylamine hydrochloride (50 mg, 0.6 mmol), Na_2SO_4 (85 mg, 0.6 mmol) and pyridine (52 mg, 0.7 mmol) in methanol (1 mL) afforded the desired product as a pale yellow oil (50 mg, 76%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.49 (s, 1H, N=C*H*), 7.73 (d, *J* = 8.0 Hz, 1H, CH_{ar}), 7.22 – 7.18 (m, 1H, CH_{ar}), 7.08 – 7.02 (m, 1H, CH_{ar}), 3.98 (s, 3H, OCH_3), 2.30 (s, 3H,

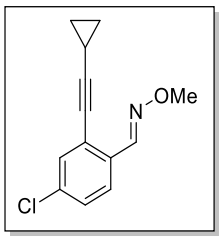
C*H*$_3$), 1.47 (tt, *J* = 8.0, 5.0 Hz, 1H, C*H*), 0.93 – 0.85 (m, 2H, C*H*$_2$), 0.83 – 0.78 (m, 2H, C*H*$_2$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 147.6, 139.5, 132.9, 130.4, 128.8, 124.9, 123.7, 98.9, 72.8, 62.0, 21.2, 8.8, 0.3. HRMS: *m*/*z* $[MH]^+$ $C_{14}H_{16}NO$ calcd. 214.1226, found 214.1224. FTIR: ν_{max}/ cm^{-1} (neat) 2923 (w), 2223 (w), 1611 (m), 1463 (m), 1262 (m), 1050 (s).

*Synthesis of (E) 2-(2-cyclopropylethynyl)-4-methoxybenzaldehyde O-methyl oxime (**60**)*



Following general procedure E, using 2-(2-cyclopropylethynyl)-4-methoxybenzaldehyde **(**205 mg, 1.0 mmol), *O*-methylhydroxylamine hydrochloride (167 mg, 2.0 mmol), Na_2SO_4 (284 mg, 2.0 mmol) and pyridine (174 mg, 2.2 mmol) in methanol (3 mL) afforded the desired product as a pale yellow oil (221 mg, 94%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.46 (s, 1H, N=C*H*), 7.77 (d, *J* = 9.0 Hz, 1H, C*H*$_{ar}$), 6.87 (d, *J* = 2.5 Hz, 1H, C*H*$_{ar}$), 6.84 – 6.79 (m, 1H, C*H*$_{ar}$), 3.96 (s, 3H, NOC*H*$_3$), 3.80 (s, 3H, COC*H*$_3$), 1.47 (tt, *J* = 8.0, 5.0 Hz, 1H, C*H*), 0.93 – 0.87 (m, 2H, C*H*$_{ar}$), 0.85 – 0.80 (m, 2H, C*H*$_{ar}$).^{13}C NMR (101 MHz, $CDCl_3$) δ 160.3, 147.3, 126.5, 126.1, 125.1, 116.2, 115.3, 99.2, 72.7, 61.9, 55.4, 8.8, 0.3. HRMS: *m*/*z* $[MH]^+$ $C_{14}H_{16}NO_2$ calcd. 230.1176, found 230.1175. FTIR: ν_{max}/ cm^{-1} (neat) 2938 (w), 2223 (w), 1607 (m), 1496 (m), 1217 (m), 1054 (s).

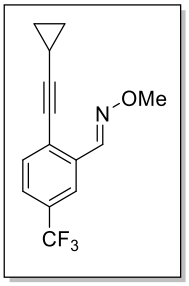
*Synthesis of (E) 2-(2-cyclopropylethynyl)-4-chlorobenzaldehyde O-methyl oxime (**61**)*



Following general procedure E, using 2-(2-cyclopropylethynyl)-4-chlorobenzaldehyde (105 mg, 0.5 mmol), *O*-methylhydroxylamine hydrochloride (84 mg, 1.0 mmol), Na_2SO_4 (142 mg, 1.0 mmol) and pyridine (87 mg, 1.1 mmol) in methanol (2 mL) afforded the desired product as a bright orange oil (99 mg, 83%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.45 (s, 1H, N=C*H*), 7.78 (d, *J* = 8.5 Hz, 1H, C*H*$_{ar}$), 7.35 (d, *J* = 2.0 Hz, 1H, C*H*$_{ar}$), 7.21 (ddd, *J* = 8.5, 2.0 Hz, 1H, C*H*$_{ar}$), 3.98 (s, 3H, OC*H*$_3$), 1.52 – 1.41 (m, 1H, C*H*), 0.94 – 0.88 (m, 2H, C*H*$_2$), 0.86 – 0.79 (m, 2H, C*H*$_2$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 146.6, 135.1, 132.1, 131.7, 128.1, 126.3, 125.2, 100.7, 71.6, 62.2, 8.9, 0.3. HRMS:

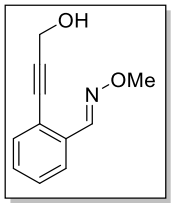
m/z $[MH]^+$ $C_{13}H_{13}{}^{35}ClNO$ calcd. 234.0680, found 234.0679. FTIR: ν_{max}/ cm^{-1} (neat) 2937 (w), 2225 (w), 1605 (m), 1462 (m), 1264 (w), 1050 (s).

*Synthesis of (E) 2-(2-cyclopropylethynyl)-5-trifluoromethylbenzaldehyde O-methyl oxime (**62**)*



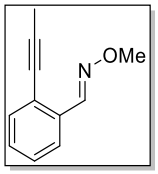
Following general procedure E, using 2-(2-cyclopropylethynyl)-5-trifluoromethylbenzaldehyde (127 mg, 0.5 mmol), *O*-methylhydroxylamine hydrochloride (84 mg, 1.0 mmol), Na_2SO_4 (142 mg, 1.0 mmol) and pyridine (87 mg, 1.1 mmol) in methanol (2 mL) afforded the desired product as a dark yellow oil (119 mg, 84%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.50 (s, 1H, N=C*H*), 8.12 (br, 1H, CH_{ar}), 7.52 – 7.45 (m, 2H, CH_{ar}), 4.02 (s, 3H, OCH_3), 1.50 (tt, *J* = 8.0, 5.0 Hz, 1H, C*H*), 0.98 – 0.90 (m, 2H, CH_2), 0.90 – 0.82 (m, 2H, CH_2). ^{13}C NMR (101 MHz, $CDCl_3$) δ 146.3, 133.8, 132.9, 129.5 (q, *J* = 33.0 Hz), 127.1, 125.6 (q, *J* = 3.5 Hz), 123.7 (q, *J* = 272.5 Hz), 122.1 (q, *J* = 4.0 Hz), 102.1, 71.9, 62.4, 9.0, 0.3. ^{19}F NMR (377 MHz, $CDCl_3$) δ -62.9. HRMS: *m/z* $[MH]^+$ $C_{14}H_{13}F_3NO$ calcd. 268.0944, found 268.0945. FTIR: ν_{max}/ cm^{-1} (neat) 2941 (w), 2226 (w), 1621 (m), 1318 (s), 1166 (m), 1051 (s).

*Synthesis of (E) 2-(3-hydroxy-1-propynyl)benzaldehyde O-methyl oxime (**63**)*



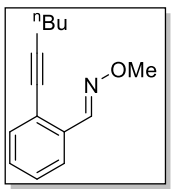
Following general procedure E, using 2-(3-hydroxy-1-propynyl)benzaldehyde (851 mg, 5.3 mmol), *O*-methylhydroxylamine hydrochloride (885 mg, 10.6 mmol), Na_2SO_4 (1.51 g, 10.6 mmol) and pyridine (925 mg, 11.7 mmol) in methanol (12 mL) afforded the desired product as a yellow oil (943 mg, 94%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 (s, 1H, N=C*H*), 7.92 – 7.83 (m, 1H, CH_{ar}), 7.48 – 7.41 (m, 1H, CH_{ar}), 7.34 – 7.27 (m, 2H, CH_{ar}), 4.52 (s, 2H, CH_2), 4.00 (s, 3H, OCH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 147.2, 133.4, 132.7, 129.5, 128.8, 125.2, 122.3, 92.8, 82.6, 62.2, 51.6. HRMS: *m/z* $[MH]^+$ $C_{11}H_{12}NO_2$ calcd. 190.0863, found 190.0860. FTIR: ν_{max}/ cm^{-1} (neat) 3404 (br), 2935 (w), 2231 (w), 1608 (w), 1448 (m), 1266 (m), 1050 (s), 1038 (s).

Synthesis of (E) 2-(prop-1-yn-1-yl)benzaldehyde O-methyl oxime



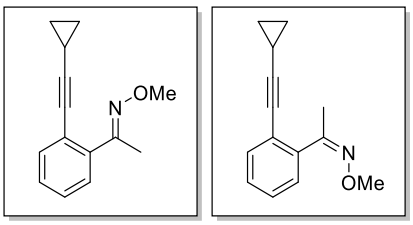
Following general procedure E, using 2-(hex-1-yn-1-yl)benzaldehyde (2.6 g, 14.0 mmol), *O*-methylhydroxylamine hydrochloride (2.4 g, 28.0 mmol), Na_2SO_4 (4.0 g, 28.0 mmol) and pyridine (2.5 g, 31.0 mmol) in methanol (31 mL) afforded the desired product as a dark orange oil (2.3 g, 77%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57 (s, 1H, N=C*H*), 7.88 – 7.82 (m, 1H, CH_{ar}), 7.42 – 7.35 (m, 1H, CH_{ar}), 7.28 – 7.23 (m, 2H, CH_{ar}), 3.99 (s, 3H, CH_3), 2.08 (s, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 147.7, 133.2, 132.4, 129.4, 127.8, 125.0, 123.9, 123.7, 91.7, 62.1, 4.5. HRMS: *m*/*z* $[MH]^+$ $C_{11}H_{12}NO$ calcd. 174.0913, found 174.0914. FTIR: ν_{max}/ cm^{-1} (neat): 2936 (w), 2246 (w), 1607 (w), 1477 (m), 1197 (m), 1051 (s).

Synthesis of (E) 2-(hex-1-yn-1-yl)benzaldehyde O-methyl oxime[40]



Following general procedure E, using 2-(hex-1-yn-1-yl)benzaldehyde (2.6 g, 14.0 mmol), *O*-methylhydroxylamine hydrochloride (2.4 g, 28.0 mmol), Na_2SO_4 (4.0 g, 28.0 mmol) and pyridine (2.5 g, 31.0 mmol) in methanol (31 mL) afforded the desired product as a dark orange oil (2.3 g, 77%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 (s, 1H, N=C*H*), 7.85 – 7.82 (m, 1H, CH_{ar}), 7.39 – 7.35 (m, 1H, CH_{ar}), 7.25 – 7.21 (m, 2H, CH_{ar}), 3.97 (s, 3H, CH_3), 2.42 (t, *J* = 7.0 Hz, 2H, CH_2), 1.63 – 1.54 (m, 2H, CH_2), 1.50 – 1.41 (m, 2H, CH_2), 0.93 (t, *J* = 7.5 Hz, 3H, CH_3).^{13}C NMR (101 MHz, $CDCl_3$) δ 147.6, 133.1, 132.5, 129.3, 127.7, 125.0, 124.0, 96.3, 77.6, 62.1, 30.8, 22.1, 19.3, 13.6.

*Synthesis of (E/Z) 2-(2-cyclopropylethynyl)acetophenone O-methyl oxime (E-**75** and Z-**75**)*

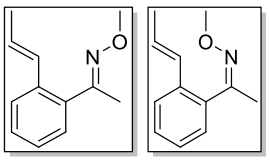


Following general procedure E, using 2-(2-cyclopropylethynyl)acetophenone (368 mg, 2.0 mmol), *O*-methylhydroxylamine hydrochloride (334 mg, 4.0 mmol), Na_2SO_4 (568 mg, 4.0 mmol) and pyridine (348 mg, 4.4 mmol) in methanol (5 mL) afforded the desired separable products *E*-**75** (293 mg, 70%) as a yellow oil and *Z*-**75** (50 mg, 12%) as a colourless oil.

E-**75**. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43 – 7.38 (m, 1H, C*H*$_{ar}$), 7.34 – 7.30 (m, 1H, C*H*$_{ar}$), 7.27 – 7.23 (m, 2H, C*H*$_{ar}$), 4.00 (s, 3H, OC*H*$_3$), 2.26 (s, 3H, C*H*$_3$), 1.45 (tt, *J* = 8.5, 5.0 Hz, 1H, C*H*), 0.89 – 0.84 (m, 2H, C*H*$_2$), 0.81 – 0.75 (m, 2H, C*H*$_2$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.2, 140.0, 133.0, 128.3, 128.3, 127.6, 122.4, 98.0, 74.4, 61.8, 15.9, 8.5, 0.4. HRMS: *m*/*z* $[MH]^+$ $C_{14}H_{16}NO$ calcd. 214.1226, found 214.1225. FTIR: ν_{max}/ cm^{-1} (neat) 2933 (w), 2227 (w), 1483 (w), 1260 (w), 1049 (s).

Z-**75**. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44 – 7.40 (m, 1H, C*H*$_{ar}$), 7.27 (dt, *J* = 7.5, 1.5 Hz, 1H, C*H*$_{ar}$), 7.23 (td, *J* = 7.5, 1.5 Hz, 1H, C*H*$_{ar}$), 7.11 – 7.09 (m, 1H, C*H*$_{ar}$), 3.81 (s, 3H, OC*H*$_3$), 2.18 (s, 3H, C*H*$_3$), 1.43 (tt, *J* = 8.0, 5.0 Hz, 1H, C*H*), 0.90 – 0.83 (m, 2H, C*H*$_2$), 0.81 – 0.75 (m, 2H, C*H*$_2$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.2, 138.9, 132.2, 128.0, 127.3, 126.7, 121.1, 97.0, 73.7, 61.7, 21.2, 8.7, 0.3. HRMS: *m*/*z* $[MH]^+$ $C_{14}H_{16}NO$ calcd. 214.1226, found 214.1224. FTIR: ν_{max}/ cm^{-1} (neat) 2931 (w), 2220 (w), 1479 (w), 1259 (w), 1050 (s).

*Synthesis of (E)/(Z)-1-(2-((E)-prop-1-en-1-yl)phenyl)ethan-1-one O-methyl oxime (E-**146** and Z-**146**)*



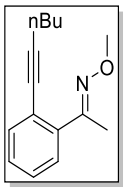
Following general procedure E, using *(E)*-1-(2-(prop-1-en-1-yl)phenyl)ethan-1-one (5.0 g, 31.2 mmol), *O*-methylhydroxylamine hydrochloride (5.3 g, 62.4 mmol), Na_2SO_4 (9.0 g, 62.4 mmol) and pyridine (5.7 g, 68.7 mmol) in methanol (70 mL) afforded the desired product as a 1.3:1 separable mixture of *E/Z* isomers (5.2 g, 87%).

E-**146**. Pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 (d, *J* = 8.0 Hz, 1H, C*H*$_{ar}$), 7.31 – 7.26 (m, 1H, C*H*$_{ar}$), 7.24 – 7.18 (m, 2H, C*H*$_{ar}$), 6.51 (dd, *J* = 16.0, 1.5 Hz, 1H, CH*H*), 6.16 (dq, *J* = 16.0, 6.5 Hz, 1H, CH*H*), 3.99 (s, 3H, OC*H*$_3$), 2.15 (s, 3H, C*H*$_3$), 1.88 (dd, *J* = 6.5, 1.5 Hz, 1H, C*H*$_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.2, 136.3, 135.9, 128.9, 128.7, 128.6, 127.8, 126.8, 126.1, 61.8, 18.8, 17.0.

Z-**146**. Colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (d, *J* = 7.5 Hz, 1H, C*H*$_{ar}$), 7.31 – 7.26 (m, 1H, C*H*$_{ar}$), 7.25 – 7.19 (m, 1H, C*H*$_{ar}$), 7.04 (d, *J* = 7.0 Hz, 1H, C*H*$_{ar}$), 6.30 (d, *J* = 16.0 Hz, 1H, CH*H*), 6.21 (dq, *J* = 16.0, 6.0 Hz, 1H, CH*H*), 3.80 (s, 3H, OC*H*$_3$), 2.13 (s, 3H, C*H*$_3$), 1.88 (dd, *J* = 6.0, 1.0 Hz, 3H, C*H*$_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.6, 134.7, 134.2, 128.4, 128.4, 127.7, 126.7, 126.4, 125.2, 61.7, 22.3, 18.7.

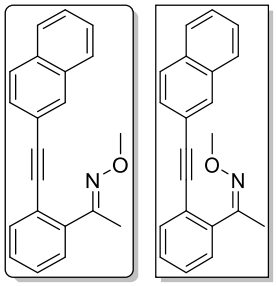
*E/*Z-**146.** HRMS: *m/z* $[MH]^+$ $C_{12}H_{16}NO$ calcd. 190.1226, found 190.1228. FTIR: ν_{max}/ cm^{-1} (neat): 2979 (w), 2603 (m), 1673 (m), 1475 (m), 1397 (m), 1172 (m), 1036 (s).

*Synthesis of (E)-1-(2-(hex-1-yn-1-yl)phenyl)ethan-1-one O-methyl oxime (**147**)*



Following general procedure E, using *(E)*-1-(2-(hex-1-yn-1-yl)phenyl)ethan-1-one (2.0 g, 10.0 mmol), *O*-methylhydroxylamine hydrochloride (1.70 g, 20.0 mmol), Na_2SO_4 (2.9 g, 20.0 mmol) and pyridine (1.8 g, 22.0 mmol) in methanol (25 mL) afforded the desired product as a 3:1 mixture of separable *E/Z* isomers (2.2 g, 96%). *E*-**147** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.33 (m, 1H, C*H*$_{ar}$), 7.27 – 7.24 (m, 1H, C*H*$_{ar}$), 7.21 – 7.17 (m, 2H, C*H*$_{ar}$), 3.92 (s, 3H, OC*H*$_3$), 2.34 (t, *J* = 7.0 Hz, 2H, C*H*$_2$), 2.20 (s, 3H, C*H*$_3$), 1.55 – 1.44 (m, 2H, C*H*$_2$), 1.45 – 1.35 (m, 2H, C*H*$_2$), 0.87 (t, *J* = 7.5 Hz, 3H, C*H*$_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.3, 140.0, 132.9, 128.3, 128.3, 127.6, 122.6, 95.1, 79.2, 61.8, 30.6, 22.0, 19.3, 16.0, 13.6. HRMS: *m/z* $[MH]^+$ $C_{15}H_{20}NO$ calcd. 230.1539, found 215.1542. FTIR: ν_{max}/ cm^{-1} (neat): 2932 (w), 2230 (w), 1482 (m), 1364 (m), 1318 (m) 1186 (w), 1048 (s).

*Synthesis of (E)/(Z)-1-(2-(naphtalen-2-ylethynyl)phenyl)ethan-1-one O-methyl oxime (E-**76** and Z-**76**)*

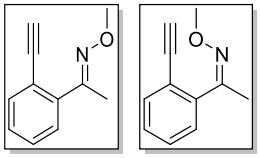


Following general procedure E, using 1-(2-(naphthalen-2-yl-ethynyl)phenyl)ethan-1-one (930 mg, 3.4 mmol), *O*-methylhydroxylamine hydrochloride (586 mg, 6.8 mmol), Na_2SO_4 (987 mg, 6.8 mmol) and pyridine (623 mg, 7.6 mmol) in methanol (10 mL) afforded the desired product as a 1.3:1 mixture of separable *E/Z* isomers (1.0 g, 97%).

E-**76**. Yellow solid. M.p.: 69 – 70 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (br, 1H, C*H*$_{ar}$), 7.85 – 7.79 (m, 3H, C*H*$_{ar}$), 7.64 – 7.61 (m, 1H, C*H*$_{ar}$), 7.55 (dd, *J* = 8.5, 1.5 Hz, 1H, C*H*$_{ar}$), 7.52 – 7.49 (m, 2H, C*H*$_{ar}$), 7.45 – 7.42 (m, 1H, C*H*$_{ar}$), 7.38 – 7.35 (m, 2H, C*H*$_{ar}$), 4.04 (s, 3H, C*H*$_3$), 2.41 (s, 3H, C*H*$_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.8, 140.1, 133.1, 133.0, 132.9, 131.3, 128.5 (x 2C), 128.2 (x 2C), 128.1, 127.9, 127.8, 126.8, 126.7, 121.7, 120.6, 94.1, 88.6, 62.0, 16.2. HRMS: *m/z* $[MH]^+$ $C_{21}H_{18}NO$ calcd. 300.1383, found 300.1381. FTIR: ν_{max}/ cm^{-1} (neat): 2936 (w), 2236 (w), 1597 (m), 1483 (m), 1268 (m), 1049 (s).

Z-**76**. Pale yellow foam. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (s, 1H, C*H*$_{ar}$), 7.85 – 7.79 (m, 3H, C*H*$_{ar}$), 7.65 – 7.62 (m, 1H, C*H*$_{ar}$), 7.56 (dd, *J* = 8.5, 1.5 Hz, 1H, C*H*$_{ar}$), 7.52 – 7.48 (m, 2H, C*H*$_{ar}$), 7.37 (td, *J* = 7.5, 1.5 Hz, 2H, C*H*$_{ar}$), 7.23 – 7.20 (m, 1H, C*H*$_{ar}$), 3.85 (s, 3H, C*H*$_3$), 2.32 (s, 3H, C*H*$_{ar}$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.9, 139.1, 133.0, 132.9, 132.2, 131.4, 128.3 (x2 C), 128.2, 128.1, 127.8 (x 2C), 126.9, 126.8 126.6, 120.6, 120.5, 93.0, 87.9, 61.8, 21.5. HRMS: *m/z* $[MH]^+$ $C_{21}H_{18}NO$ calcd. 300.1383, found 300.1382. FTIR: ν_{max}/ cm^{-1} (neat): 2935 (w), 2158 (w), 1598 (m), 1432 (m), 1268 (m), 1048 (s).

*Synthesis of (E)/(Z)-1-(2-ethynylphenyl)ethan-1-one O-methyl oxime (E-**74** and Z-**74**)*



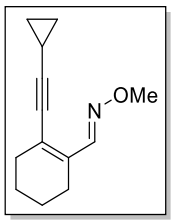
Following general procedure E, using 1-(2-ethynylphenyl)ethan-1-one (900 mg, 6.2 mmol), *O*-methylhydroxylamine hydrochloride (1.05 g, 12.4 mmol), Na_2SO_4 (1.8 g, 12.4 mmol) and

pyridine (1.1 g, 13.5 mmol) in methanol (15 mL) afforded the desired product as a 1.3:1 mixture of separable *E/Z* isomers (1.0 g, 94%).

E-***74***. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (d, *J* = 7.5 Hz, 1H, C*H*$_{ar}$), 7.37 – 7.35 (m, 2H, C*H*$_{ar}$), 7.34 – 7.30 (m, 1H, C*H*$_{ar}$), 4.00 (s, 3H, OC*H*$_3$), 3.24 (s, 1H, C*H*), 2.29 (s, 3H, C*H*$_3$).^{13}C NMR (101 MHz, $CDCl_3$) δ 156.6, 140.8, 133.7, 128.9, 128.4 (x2 C), 120.6, 82.2, 81.6, 61.9, 16.1. HRMS: *m/z* $[MH]^+$ $C_{11}H_{12}NO$ calcd. 174.0913, found 173.0914. FTIR: ν_{max}/ cm^{-1} (neat): 3285 (br), 2899 (w), 1442 (m), 1136 (m), 1187 (w), 1046 (s).

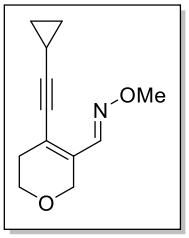
Z-***74***. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (dd, *J* = 8.0, 1.0 Hz, 1H, C*H*$_{ar}$), 7.38 (td, *J* = 8.0, 1.5 Hz, 1H), 7.30 (td, *J* = 7.5, 1.5 Hz, 1H, C*H*$_{ar}$), 7.15 (dd, *J* = 7.5, 1.0 Hz, 1H, C*H*$_{ar}$), 3.81 (s, 3H, OC*H*$_3$), 3.18 (s, 1H, C*H*), 2.21 (s, 3H, C*H*$_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.7, 139.7, 133.0, 128.8, 128.1, 126.7, 119.4, 81.6, 80.2, 61.8, 21.3. HRMS: *m/z* $[MH]^+$ $C_{11}H_{12}NO$ calcd. 174.0913, found 173.0918. FTIR: ν_{max}/ cm^{-1} (neat): 3282 (br), 2936 (w), 1432 (m), 1372 (w), 1084 (m), 1046 (s).

*Synthesis of (E) 2-(2-cyclopropylethynyl)-1-cyclohexenecarboxaldehyde O-methyl oxime (**98**)*



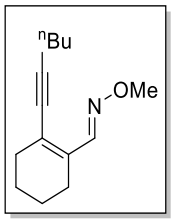
Following general procedure E, using 2-(2-cyclopropylethynyl)-1-cyclohexenecarboxaldehyde (114 mg, 0.7 mmol), *O*-methylhydroxylamine hydrochloride (109 mg, 1.3 mmol), Na_2SO_4 (186 mg, 1.3 mmol) and pyridine (122 mg, 1.5 mmol) in methanol (2 mL) afforded the desired product as a white solid (293 mg, 70%). M.p.: 60 – 61 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (s, 1H, N=C*H*), 3.88 (s, 3H, OC*H*$_3$), 2.32 – 2.28 (m, 2H, C*H*$_2$), 2.26 – 2.19 (m, 2H, C*H*$_2$), 1.65 – 1.58 (m, 4H, C*H*$_2$), 1.44 – 1.34 (m, 1H, C*H*), 0.87 – 0.80 (m, 2H, C*H*$_2$), 0.75 – 0.68 (m, 2H, C*H*$_2$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 150.3, 135.3, 126.1, 100.2, 74.4, 61.7, 31.5, 24.1, 22.2, 21.6, 8.9, 0.3. HRMS: *m/z* $[MH]^+$ $C_{13}H_{18}NO$ calcd. 204.1383, found 204.1379. FTIR: ν_{max}/ cm^{-1} (neat) 2930 (m), 2211 (w), 1600 (w), 1434 (w), 1274 (w), 1046 (s).

*Synthesis of (E) 4-(2-cyclopropylethynyl)- 5,6-dihydro-2H-pyran-3-carboxaldehyde O-methyl oxime (**100**)*



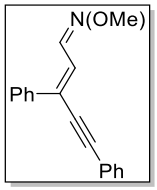
Following general procedure E, using 4-(2-cyclopropylethynyl)-5,6-dihydro-2*H*-pyran-3-carboxaldehyde (46 mg, 0.25 mmol), *O*-methylhydroxylamine hydrochloride (45 mg, 0.5 mmol), Na_2SO_4 (74 mg, 0.5 mmol) and pyridine (45 mg, 0.6 mmol) in methanol (2 mL) afforded the desired product (43 mg, 80%) as a white solid. M.p.: 45 – 47 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (s, 1H, N=C*H*), 4.37 (t, *J* = 2.0 Hz, 2H, CH_2), 3.87 (s, 3H, OCH_3), 3.76 (t, *J* = 5.5 Hz, 2H, CH_2), 2.34 – 2.29 (m, 2H, CH_2), 1.44 – 1.35 (m, 1H, C*H*), 0.90 – 0.84 (m, 2H, CH_2), 0.77 – 0.71 (m, 2H, CH_2). ^{13}C NMR (101 MHz, $CDCl_3$) δ 146.9, 133.8, 123.0, 101.3, 72.9, 64.4, 63.9, 62.0, 30.4, 9.0, 0.3. HRMS: *m/z* $[MH]^+$ $C_{12}H_{16}NO_2$ calcd. 206.1176, found 206.1173. FTIR: ν_{max}/ cm^{-1} (neat) 2935 (m), 2214 (m), 1425 (w), 1398 (w), 1057 (s).

Synthesis of (E) 2-(hex-1-yn-1-yl)-1-cyclohexenecarboxaldehyde O-methyl oxime



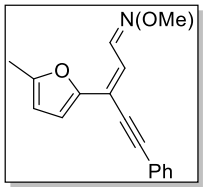
Following general procedure E, using 2-(hex-1-yn-1-yl)-1-cyclohexenecarboxaldehyde[58] (3.4 g, 17.9 mmol), *O*-methylhydroxylamine hydrochloride (3.1 g, 35.7 mmol), Na_2SO_4 (5.1 g, 35.7 mmol) and pyridine (3.2 g, 39.3 mmol) in methanol (40 mL) afforded the desired product as an intense orange oil (3.9 g, 99%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 (s, 1H, N=C*H*), 3.88 (s, 3H, OCH_3), 2.35 (t, *J* = 7.0 Hz, 2H, CH_2), 2.31 (br, 2H, CH_2), 2.27 – 2.24 (m, 2H, CH_2), 1.65 – 1.61 (m, 4H, CH_2 x2), 1.56 – 1.50 (m, 2H, CH_2), 1.46 – 1.39 (m, 2H, CH_2), 0.92 (t, *J* = 7.5 Hz, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 150.3, 135.1, 126.3, 97.1, 79.2, 61.7, 31.5, 30.9, 24.1, 22.2, 22.0, 21.6, 19.3, 13.6. HRMS: *m/z* $[MH]^+$ $C_{14}H_{22}NO$ calcd. 220.1696, found 220.1697. FTIR: ν_{max}/ cm^{-1} (neat) 2927 (m), 2215 (w), 1687 (w), 1458 (w), 1377 (w), 1046 (s).

Synthesis of (1E/Z, 2E)-3,5-diphenylpent-2-en-4-ynal O-methyl oxime[40] ***(113)***



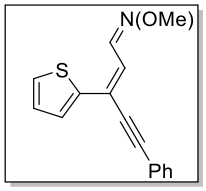
Following general procedure E, using (*Z*)-1-(2-ethynylphenyl)ethan-1-one (900 mg, 6.2 mmol), *O*-methylhydroxylamine hydrochloride (1.05 g, 12.4 mmol), Na_2SO_4 (1.8 g, 12.4 mmol) and pyridine (1.1 g, 13.5 mmol) in methanol (15 mL) afforded the desired product (1.0 g, 94%) as a 3:1 mixture of *E/Z* isomers. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.50 (d, *J* = 10.0 Hz, 1H, C*H*N *E*), 7.91 (d, *J* = 10.0 Hz, 1H, C*H*N *Z*), 7.84 – 7.81 (m, 2H, CH_{ar}), 7.79 – 7.76 (m, 2H, CH_{ar}), 7.59 – 7.56 (m, 4H, CH_{ar}), 7.49 (d, *J* = 10.0 Hz, 1H, =C*H Z*), 7.44 – 7.36 (m, 12H, CH_{ar}), 7.04 (d, *J* = 10.0 Hz, 1H, =C*H E*), 4.02 (s, 3H, OCH_3 *Z*), 4.00 (s, 3H, OCH_3 *E*). ^{13}C NMR (101 MHz, $CDCl_3$) δ 149.7, 146.2, 136.8, 131.8, 131.7 (x2 C), 130.4, 129.4, 129.3, 129.2, 129.1, 129.0, 128.7 (x2 C), 128.6, 128.5, 126.9, 126.5, 126.4, 122.6, 122.5, 119.7, 100.0, 99.1, 85.4, 85.3, 62.3 (x2 C).

*Synthesis of (1E/Z, 2Z)-3-(5-methylfuran-2-yl)-5-phenylpent-2-en-4-ynal O-methyl oxime (**114**)*



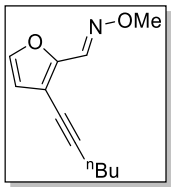
Following general procedure E, using (*Z*)-3-(5-methylfuran-2-yl)-5-phenylpent-2-en-4-ynal (231 mg, 1.0 mmol), *O*-methylhydroxylamine hydrochloride (167 mg, 2.0 mmol), Na_2SO_4 (281 g, 2.0 mmol) and pyridine (177 mg, 2.2 mmol) in methanol (3 mL) afforded the desired product (228 mg, 88%) as a 2:1 mixture of *E/Z* isomers. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (d, *J* = 10.5 Hz, 1H, C*H*N *E*), 7.77 (d, *J* = 10.0 Hz, 1H, C*H*N *Z*), 7.57 – 7.50 (m, 4H, CH_{ar}), 7.39 – 7.35 (m, 7H, CH_{ar} + , =C*H Z*), 6.95 (d, *J* = 10.5 Hz, 1H, =C*H E*), 6.70 (d, *J* = 3.0 Hz, 1H, CH_{ar} *Z*), 6.62 (d, *J* = 3.0 Hz, 1H, CH_{ar} *E*), 6.09 (dd, *J* = 3.0, 1.0 Hz, 1H, CH_{ar} *Z)*, 6.07 (dd, *J* = 3.0, 1.0 Hz, 1H, CH_{ar} *E*), 4.01 (s, 3H, OCH_3 *Z*), 3.96 (s, 3H, OCH_3 *E*), 2.36 (s, 3H, CH_3 *Z*), 2.34 (s, 3H, CH_3 *E*). ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.7, 154.1, 150.5 (x2 C), 149.2, 145.8, 131.8, 131.7, 129.2, 129.0, 128.5 (x2 C), 122.4, 122.3, 121.9, 119.6, 118.8, 114.9, 113.7, 112.1, 108.7, 108.4, 97.2, 96.6, 83.1, 83.0, 62.3, 62.2, 14.0, 13.9. HRMS: *m/z* $[MH]^+$ $C_{17}H_{16}NO_2$ calcd. 266.1176, found 266.1184. FTIR: ν_{max}/ cm^{-1} (neat): 2933 (w), 2213 (w), 1599 (m), 1443 (m), 1172 (s), 1021 (s).

*Synthesis of (1E/Z, 2Z)-5-phenyl-3-(thiophenyl)pent-2-en-4-ynal O-methyl oxime (**153**)*



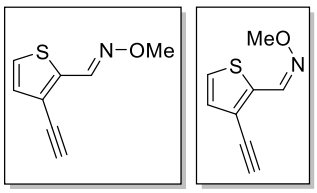
Following general procedure E, using (*Z*)-5-phenyl-3-(thiophenyl)pent-2-en-4-ynal (90 mg, 0.4 mmol), *O*-methylhydroxylamine hydrochloride (65 mg, 0.8 mmol), Na_2SO_4 (110 mg, 0.8 mmol) and pyridine (70 mg, 0.85 mmol) in methanol (2 mL) afforded the desired product as an orange oil and as a 1.7:1 mixture of *E/Z* isomers (100 mg, 99%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.39 (d, *J* = 10.2 Hz, 1H, C*H*N *E*), 7.82 – 7.78 (m, 1H, C*H*N *Z*), 7.59 – 7.54 (m, 4H, CH_{ar}), 7.52 (d, *J* = 4.0 Hz, 1H, CH_{ar} *Z*), 7.45 (d, *J* = 4.0 Hz, 1H, CH_{ar} *E*), 7.44 – 7.36 (m, 6H, CH_{ar}), 7.36 – 7.30 (m, 3H, CH_{ar} + , =C*H Z*), 7.06 (dd, *J* = 9.0, 4.0 Hz, 2H, CH_{ar}), 6.90 (d, *J* = 10.0 Hz, 1H, =C*H E*), 4.00 (s, 3H, OCH_3 *Z*), 3.97 (s, 3H, OCH_3 *E*). ^{13}C NMR (101 MHz, $CDCl_3$) δ 149.2, 145.6, 142.3 (x 2C), 131.8, 131.7, 129.3, 129.1, 128.6, 128.5, 127.9 (x2 C), 127.7, 127.3, 126.7, 126.6, 124.5, 124.2, 123.3, 122.3, 122.2, 117.6, 98.6, 97.9, 84.4, 84.3, 62.3 (x2 C). HRMS: *m/z* $[MH]^+$ $C_{16}H_{14}NOS$ calcd. 268.0791, found 268.0799. FTIR: ν_{max}/ cm^{-1} (neat): 2978 (m), 2253 (w), 1565 (m), 1326 (s), 1125 (s), 1046 (s).

*Synthesis of (E)-3-(hex-1-yn-1-yl)furan-2-carbaldehyde O-methyl oxime (**122**)*



Following general procedure E, using 3-(hex-1-yn-1-yl)furan-2-carbaldehyde (154 mg, 0.9 mmol), *O*-methylhydroxylamine hydrochloride (149 mg, 1.8 mmol), Na_2SO_4 (251 mg, 1.8 mmol) and pyridine (158 mg, 1.9 mmol) in methanol (3 mL) afforded the desired product as a yellow oil (155 mg, 86%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (s, 1H, N=C*H*), 7.36 (d, *J* = 2.0 Hz, 1H, CH_{ar}), 6.42 (d, *J* = 2.0 Hz, 1H, CH_{ar}), 4.00 (s, 3H, OCH_3), 2.40 (t, *J* = 7.0 Hz, 2H, CH_2), 1.62 – 1.53 (m, 2H, CH_2), 1.50 – 1.41 (m, 2H, CH_2), 0.94 (t, *J* = 7.5 Hz, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.6, 143.6, 137.5, 114.1, 111.6, 96.9, 70.4, 62.5, 30.6, 22.0, 19.3, 13.6. HRMS: *m/z* $[MH]^+$ $C_{12}H_{16}NO_2$ calcd. 206.1176, found 206.1177. FTIR: ν_{max}/ cm^{-1} (neat) 2934 (m), 2233 (w), 1493 (w), 1327 (w), 1145 (w), 1050 (s).

*Synthesis of (E)/(Z)-3-ethynylthiophene-2-carbaldehyde O-methyl oxime (E-**123** and Z-**123**)*



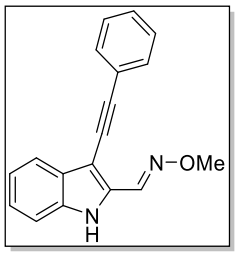
Following general procedure E, using 3-ethynylthiophene-2-carbaldehyde (3 g, 22.0 mmol), *O*-methylhydroxylamine hydrochloride (3.8 g, 44.1 mmol), Na_2SO_4 (6.3 g, 44.1 mmol) and pyridine (4.0 g, 48.5 mmol) in methanol (50 mL) afforded the desired product as an orange oil and as a 1:2.3 separable mixture of *E/Z* isomers (3.3 g, 91%).

E-**123**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.42 (d, *J* = 1.0 Hz, 1H, N=C*H*), 7.22 (dd, *J* = 5.0, 1.0 Hz, 1H, CH_{ar}), 7.05 (d, *J* = 5.0 Hz, 1H, CH_{ar}), 3.97 (s, 3H, OCH_3), 3.31 (s, 1H, CC*H*). ^{13}C NMR (101 MHz, $CDCl_3$) δ 142.7, 139.2, 130.2, 126.4, 122.7, 82.2, 76.9, 62.4.

Z-**123.** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, *J* = 1.0 Hz, 1H, N=C*H*), 7.42 (dd, *J* = 5.0, 1.0 Hz, 1H, CH_{ar}), 7.13 (d, *J* = 5.0 Hz, 1H, CH_{ar}), 4.10 (s, 3H, OCH_3), 3.37 (s, 1H, CC$H_,$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.9, 133.7, 129.9, 129.3, 123.8, 82.4, 76.9, 62.6.

*E/*Z-**123.** HRMS: *m/z* $[MH]^+$ C_8H_8NOS calcd. 166.0321, found 166.0320. FTIR: ν_{max}/ cm^{-1} (neat): 3287 (m), 2998 (m), 2107 (w), 1397 (m), 1247 (w), 1047 (s).

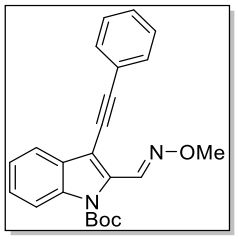
*Synthesis of (E)-3-(phenylethynyl)-1H-indole-2-carbaldehyde O-methyl oxime (**127**)*



Following general procedure E, using *tert*-butyl 2-formyl-3-(phenylethynyl)-1*H*-indole-1-carboxylate (100 mg, 0.3 mmol), *O*-methylhydroxylamine hydrochloride (27 mg, 0.32 mmol), and Et_3N (33 mg, 0.32 mmol) in dichloromethane (3 mL) afforded the desired product as a colourless oil (70 mg, 79%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.73 (br, 1H, N=C*H*), 8.39 (s, 1H, N*H*), 7.80 (d, *J* = 8.0 Hz, 1H, CH_{ar}), 7.59 – 7.56 (m, 2H, CH_{ar}), 7.40 – 7.29 (m, 5H), 7.23 – 7.18 (m, 1H, CH_{ar}), 4.02 (s, 3H, OCH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.3, 136.0, 132.9, 131.4, 128.8, 128.4, 128.1, 125.2, 123.6, 121.0, 120.6, 111.3, 102.5, 95.3, 81.1, 62.5. HRMS: *m/z* $[MH]^+$ $C_{18}H_{15}N_2O$

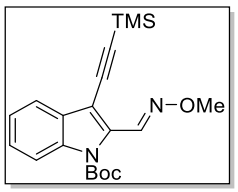
calcd. 275.1179, found 275.1189. FTIR: ν_{max}/ cm^{-1} (neat): 3422 (br), 2934 (w), 2205 (w), 1598 (w), 1455 (m), 1324 (m), 1047 (s).

*Synthesis of tert-butyl (E)-2-((methoxyimino)methyl)-3-(phenylethynyl)-1H-indole-1-carboxylate (**126**)*



Following general procedure E, using *tert*-butyl 2-formyl-3-(phenylethynyl)-1*H*-indole-1-carboxylate (90 mg, 0.26 mmol), *O*-methylhydroxylamine hydrochloride (33 mg, 0.39 mmol), and pyridine (32 mg, 0.39 mmol) in dichloromethane (3 mL) afforded the desired product as a yellow oil (79 mg, 81%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.62 (s, 1H, N=C*H*), 8.14 – 8.09 (m, 1H, CH_{ar}), 7.82 – 7.78 (m, 1H, CH_{ar}), 7.63 – 7.58 (m, 2H, CH_{ar}), 7.43 – 7.32 (m, 5H, CH_{ar}), 4.08 (s, 3H, OCH_3), 1.70 (s, 9H, CH_3 x 3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 149.6, 142.1, 135.9, 132.8, 131.7, 129.6, 128.4, 128.3, 126.3, 123.7 (x2 C), 120.6, 115.6, 105.9, 95.7, 85.4, 82.0, 62.5, 28.2. HRMS: *m/z* $[MH]^+$ $C_{23}H_{23}N_2O_3$ calcd. 375.1703, found 375.1711. FTIR: ν_{max}/ cm^{-1} (neat): 2936 (w), 1723 (s), 1451 (m), 1302 (s), 1054 (s).

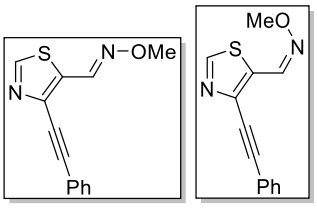
*Synthesis of tert-butyl(E)-2-((methoxyimino)methyl)-3-((trimethylsilyl)ethynyl)-1H-indole-1-carboxylate (**125**)*



Following general procedure E, using *tert*-butyl 2-formyl-3-((trimethylsilyl)ethynyl)-1*H*-indole-1-carboxylate (350 mg, 1.0 mmol), *O*-methylhydroxylamine hydrochloride (128 mg, 1.5 mmol), and pyridine (122 mg, 1.5 mmol) in dichloromethane (10 mL) afforded the desired product as a yellow oil (366 mg, 96%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.52 (s, 1H, N=C*H*), 8.06 (d, *J* = 8.0 Hz, 1H, CH_{ar}), 7.69 (dd, *J* = 7.5, 1.0 Hz, 1H, CH_{ar}), 7.39 – 7.34 (m, 1H, CH_{ar}), 7.30 (td, *J* = 7.5, 1.0 Hz, 1H, CH_{ar}), 4.04 (s, 3H, OCH_3), 1.67 (s, 9H, CH_3 x3), 0.30 (s, 9H, CH_3 x3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 149.5, 141.7, 135.7, 133.4, 129.7, 126.1, 123.6, 120.6, 115.4, 105.8, 101.5, 96.8, 85.3, 62.4,

28.1, 0.0. HRMS: *m/z* $[MH]^+$ $C_{20}H_{27}N_2O_3Si$ calcd. 371.1785, found 371.1795. FTIR: ν_{max}/ cm^{-1} (neat): 2932 (w), 2252 (w), 1730 (s), 1452 (m), 1331 (s), 1248 (s), 1055 (s).

*Synthesis of (E)/(Z)-4-(phenylethynyl)thiazole-5-carbaldehyde O-methyl oxime (E-**124** and Z-**124**)*

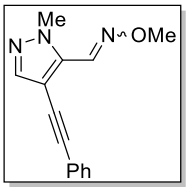


Following general procedure E, using 3-(phenylethynyl)thiazole-5-carbaldehyde (1.4 g, 6.6 mmol), *O*-methylhydroxylamine hydrochloride (811 mg, 9.9 mmol) and pyridine (839 mg, 9.9 mmol) in dichloromethane (65 mL) afforded the desired product as a pale yellow solid and as a 1:6 separable mixture of *E/Z* isomers (1.55 g, 99%).

E-**124.** Pale yellow solid. M.p.: 69 – 70 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.71 (s, 1H, N=C*H*), 8.48 (s, 1H, CH_{ar}), 7.60 – 7.56 (m, 2H, CH_{ar}), 7.40 – 7.36 (m, 3H, CH_{ar}), 4.00 (s, 3H, OCH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.2, 141.4, 138.8, 133.0, 131.8, 129.2, 128.5, 121.9, 94.9, 81.4, 62.7. HRMS: *m/z* $[MH]^+$ $C_{13}H_{11}N_2OS$ calcd. 243.0587, found 243.0595. FTIR: ν_{max}/ cm^{-1} (neat): 2936 (w), 2210 (w), 1500 (m), 1417 (m), 1371 (m), 1044 (s).

Z-**124.** Colourless solid. M.p.: 56 – 57 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.85 (br, 1H, N=C*H*), 8.08 (br, 1H, CH_{ar}), 7.62 – 7.59 (m, 2H, CH_{ar}), 7.41 – 7.36 (m, 3H, CH_{ar}), 4.13 (s, 3H, OCH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.0, 140.8, 137.9, 131.9, 129.3, 128.5, 126.4, 121.8, 95.1, 81.8, 62.8. HRMS: *m/z* $[MH]^+$ $C_{13}H_{11}N_2OS$ calcd. 243.0587, found 243.0594. FTIR: ν_{max}/ cm^{-1} (neat): 2937 (w), 2216 (w), 1596 (m), 1496 (m), 1459 (m), 1340 (m), 1052 (s).

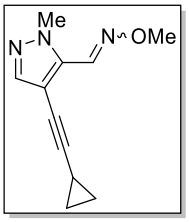
*Synthesis of (E)-1-methyl-4-(phenylethynyl)-1H-pyrazole-5-carbaldehyde O-methyl oxime (**128**)*



Following general procedure E, using 3-(phenylethynyl)thiazole-5-carbaldehyde (1.4 g, 6.6 mmol), *O*-methylhydroxylamine hydrochloride (811 mg, 9.9 mmol) and pyridine (839 mg, 9.9 mmol) in dichloromethane (65 mL) afforded the desired product as a pale yellow solid and as a 6:1 non-separable mixture of *E/Z* isomers (1.55 g, 99%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (s,

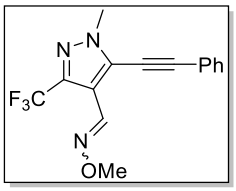
1H, N=C*H*), 7.63 (s, 0.14H, *Z*-CH_{ar}), 7.60 (s, 0.86H, *E*-CH_{ar}), 7.50 – 7.46 (m, 2H, CH_{ar}), 7.35 – 7.31 (m, 3H, CH_{ar}), 4.09 (s, 2.58H, *E*-OCH_3), 4.03 (s, 0.42H, *Z*-OCH_3), 4.02 (s, 2.58H, *E*-NCH_3), 3.86 (s, 0.42H, *Z*-NCH_3). ***E*-128.** ^{13}C NMR (101 MHz, $CDCl_3$) δ 140.6, 138.4, 135.7, 131.4, 128.4, 128.3, 123.1, 106.6, 93.6, 79.3, 62.6, 40.4. HRMS: *m/z* $[MH]^+$ $C_{14}H_{14}N_3O$ calcd. 240.1131, found 240.1138. FTIR: ν_{max}/ cm^{-1} (neat): 2940 (w), 2222 (w), 1497 (m), 1441 (m), 1375 (m), 1048 (s).

*Synthesis of (E)-1-methyl-4-(cyclopropylethynyl)-1H-pyrazole-5-carbaldehyde O-methyl oxime (**129**)*



Following general procedure E, using 1-methyl-4-(cyclopropylethynyl)-1H-pyrazole-5-carbaldehyde (1.3 g, 7.4 mmol), *O*-methylhydroxylamine hydrochloride (947 mg, 11.1 mmol) and pyridine (915 mg, 11.1 mmol) in dichloromethane (75 mL) afforded the desired product as a pale yellow oil and as a 10:1 non-separable mixture of *E/Z* oxime isomers (1.48 g, 98%). ***E*-129**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (s, 1H, N=C*H*), 7.44 (s, 1H, CH_{ar}), 4.04 (s, 3H, OCH_3), 3.98 (s, 3H, NCH_3), 1.46 – 1.38 (m, 1H, C*H*), 0.87 – 0.82 (m, 2H, CH_2), 0.78 – 0.74 (m, 2H, CH_2). ^{13}C NMR (101 MHz, $CDCl_3$) δ 140.4, 138.3, 135.4, 107.1, 97.5, 65.0, 62.3, 40.0, 8.5, 0.0. HRMS: *m/z* $[MH]^+$ $C_{11}H_{14}N_3O$ calcd. 204.1131, found 204.1131. FTIR: ν_{max}/ cm^{-1} (neat): 2941 (w), 2233 (w), 1484 (m), 1393 (s), 1180 (s), 1047 (s).

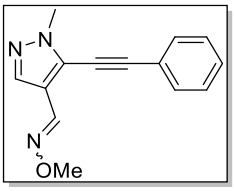
*Synthesis of (E)-1-methyl-5-(phenylethynyl)-3-(trifluoromethyl)-1H-pyrazole-4-carbaldehyde O-methyl oxime (**130**)*



Following general procedure E, using 1-methyl-5-(phenylethynyl)-3-(trifluoromethyl)-1*H*-pyrazole-4-carbaldehyde (195 mg, 0.7 mmol), *O*-methylhydroxylamine hydrochloride (90 mg, 1.1 mmol) and pyridine (87 mg, 1.1 mmol) in dichloromethane (7 mL) afforded the desired product as a pale orange oil and as a 5:1 non-separable mixture of *E/Z* oxime isomers (200 mg, 93%). ***E*-130**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (s, 1H, N=C*H*), 7.60 – 7.53 (m, 2H, CH_{ar}), 7.45 – 7.38 (m, 3H, CH_{ar}), 4.03 (s, 3H, CH_3), 3.99 (s, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.7, 135.6,

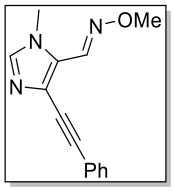
131.7, 129.8, 128.7, 126.6, 121.4, 120.8 (q, $^{1}J_{C\text{-}F}$ = 269.5 Hz), 115.4, 101.0, 75.9, 62.3, 38.1. ^{19}F NMR (376 MHz, $CDCl_3$) δ -61.3. HRMS: *m/z* $[MH]^+$ $C_{15}H_{13}F_3N_3O$ calcd. 243.0587, found 243.0595. FTIR: ν_{max}/ cm^{-1} (neat): 2917 (s), 2222 (w), 1458 (m), 1376 (s), 1234 (s), 1128 (s), 1039 (s).

*Synthesis of (E)-1-methyl-5-(phenylethynyl)-1H-pyrazole-4-carbaldehyde O-methyl oxime (**131**)*



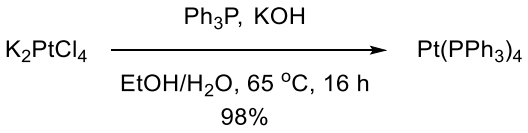
Following general procedure E, using 1-methyl-5-(phenylethynyl)-1*H*-pyrazole-4-carbaldehyde (100 mg, 0.5 mmol), *O*-methylhydroxylamine hydrochloride (61 mg, 0.7 mmol) and pyridine (59 mg, 0.7 mmol) in dichloromethane (5 mL) afforded the desired product as a bright yellow oil and as a 5.5:1 non-separable mixture of *E/Z* oxime isomers (107 mg, 94%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (s, 1H, N=C*H*), 7.63 (s, 0.15H, *Z*-CH_{ar}), 7.60 (s, 0.85H, *E*-CH_{ar}), 7.50 – 7.46 (m, 2H, CH_{ar}), 7.35 – 7.32 (m, 3H, CH_{ar}), 4.10 (s, 2.55H, *E*-OCH_3), 4.04 (s, 0.45H, *Z*-OCH_3), 4.02 (s, 2.55H, *E*-NCH_3), 3.87 – 3.86 (m, 0.45H, *Z*-NCH_3). *E*-**131**. ^{13}C NMR (101 MHz, $CDCl_3$) δ 140.6, 138.4, 135.7, 131.4, 128.4, 128.3, 123.1, 106.6, 93.6, 79.3, 62.6, 40.4. HRMS: *m/z* $[MH]^+$ $C_{14}H_{14}N_3O$ calcd. 240.1131, found 240.1136. FTIR: ν_{max}/ cm^{-1} (neat): 2938 (w), 2221 (w), 1685 (m), 1483 (s), 1377 (m), 1181 (m), 1050 (s).

*Synthesis of (E)-1-methyl-4-(phenylethynyl)-1H-imidazole-5-carbaldehyde O-methyl oxime (**132**)*



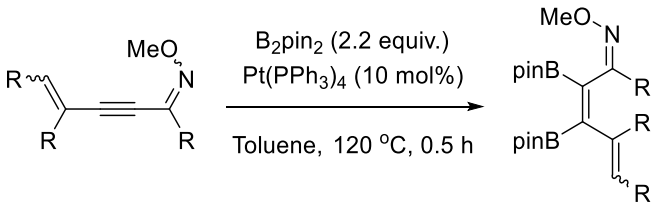
Following general procedure E, using 1-methyl-4-(phenylethynyl)-1*H*-imidazole-5-carbaldehyde (237 mg, 1.1 mmol), *O*-methylhydroxylamine hydrochloride (144 mg, 1.7 mmol) and pyridine (139 mg, 1.7 mmol) in dichloromethane (11 mL) afforded the desired product as a pale orange foam (252 mg, 93%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25 (s, 1H, N=C*H*), 7.63 (s, 1H, CH_{ar}), 7.52 – 7.48 (m, 2H, CH_{ar}), 7.32 – 7.29 (m, 3H, CH_{ar}), 3.94 (s, 3H, OCH_{ar}), 3.85 (s, 3H, NCH_{ar}). ^{13}C NMR (101 MHz, $CDCl_3$) δ 140.9, 139.0, 131.6, 128.6, 128.4, 127.8, 127.7, 122.6, 93.8, 80.8, 62.4, 35.4. HRMS: *m/z* $[MH]^+$ $C_{14}H_{14}N_3O$ calcd. 240.1131, found 240.1134. FTIR: ν_{max}/ cm^{-1} (neat): 2941 (w), 2218 (w), 1511 (w), 1422 (w), 1248 (m), 1043 (s).

Syntesis of tetrakis(triphenyl phosphine) platinum (0) (33)



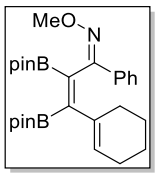
A suspension of triphenyl phosphine (1.56 g, 5.96 mmol) in ethanol (19 mL) was heated to 65 C. When the mixture had homogenized, a solution of potassium hydroxide (214.1 mg, 3.61 mmol) in a mixture of ethanol and water (4.25 mL, 4:1), was added. Then a solution of K_2PtCl_4 (530.2 mg, 1.20 mmol) in water (4.75 mL) was added over 5 minutes. A pale yellow precipitate is formed immediately and the reaction was left to stir over night. The reaction mixture was allowed to cool to room temperature before being filtered and the precipitate was washed sequentially with warm ethanol (20 mL), water (5 mL) and room temperature ethanol (5 mL) then dried *in vacuo*. Tetrakis(triphenylphosphine) platinum (0) (1.53 g, 98%) was isolated as a yellow solid.

General procedure F



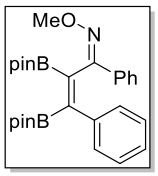
B_2Pin_2 (2.2. equiv) was added to a stirred solution of alkyne derivative (1.0 equiv.) in toluene (0.1 M). Then $Pt(PPh_3)_4$ (10 mol%) was added and the reaction was stirred at 120 °C for 30 min. The reaction mixture was allowed to cool to room temperature and the solvent was evaporated. The residue was purified by kugelrohr distillation at 150 °C or flash column chromatography on florisil eluting with petroleum ether (40/60) and ethyl acetate to afford the corresponding boronic esters.

*Synthesis of (E) 3-cyclohexenyl-2,3-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-phenylprop-2-en-1-O-methyl oxime (**48**)*



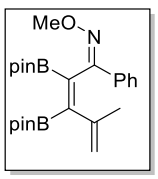
Following general procedure F, using 3-(cyclohex-1-enyl)-1-phenylprop-2-yn-1-one *O*-methyl oxime (598 mg, 2.5 mmol), B_2Pin_2 (1.40 g, 5.5 mmol) and $Pt(PPh_3)_4$ (290 mg, 0.25 mmol) in toluene (25 mL) afforded the desired product after kugelrohr distillation as a pale yellow foam (861 mg, 72%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 – 7.44 (m, 2H, CH_{ar}), 7.25 – 7.20 (m, 3H, CH_{ar}), 5.45 – 5.40 (m, 1H, =C*H*), 3.92 (s, 3H, OCH_3), 1.81 – 1.75 (m, 2H, CH_2), 1.64 – 1.55 (m, 2H, CH_2), 1.33 (s, 12H, CH_3 x 4), 1.29 (s, 12H, CH_3 x 4), 1.18 – 1.10 (m, 2H, CH_2), 1.08 – 0.97 (m, 2H, CH_2). ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.7, 154.4, 139.7, 136.9, 134.7, 128.2, 127.7, 127.4, 126.3, 83.9, 83.7, 61.6, 27.2, 25.3, 25.0, 24.7, 22.0, 21.4. ^{11}B NMR (128 MHz, $CDCl_3$) δ 29.8 (br). HRMS: *m/z* $[MH]^+$ $C_{28}H_{42}B_2NO_5$ calcd. 494.3249, found 494.3227. FTIR: ν_{max}/ cm^{-1} (neat) 2929 (m), 1444 (w), 1307 (s), 1138 (s), 1052 (s).

*Synthesis of (E) 2,3-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1,3-diphenylprop-2-en-1-O-methyl oxime (**49**)*



Following general procedure F, using 1,3-diphenylprop-2-yn-1-one *O*-methyl oxime (589 mg, 2.5 mmol), B_2Pin_2 (1.40 g, 5.5 mmol) and $Pt(PPh_3)_4$ (290 mg, 0.25 mmol) in toluene (25 mL) afforded the desired product after kugelrohr distillation as a white foam (899 mg, 74%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 – 7.29 (m, 2H, CH_{ar}), 7.13 – 6.94 (m, 7H, CH_{ar}), 3.94 (s, 3H, OCH_3), 1.33 (s, 12H, CH_3 x 4), 1.30 (s, 12H, CH_3 x 4). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.4, 141.5, 135.1, 128.2, 127.6, 127.5, 127.2, 127.1, 127.0, 84.1, 84.0, 61.8, 24.9, 24.7. ^{11}B NMR (128 MHz, $CDCl_3$) δ 30.3 (br). HRMS: m/z $[MNa]^+$ $C_{28}H_{38}B_2NO_5Na$ calcd. 512.2756, found 512.2765. FTIR: ν_{max}/ cm^{-1} (neat) 2979 (m), 1494 (w), 1496 (w), 1309 (s), 1140 (s), 1051 (s).

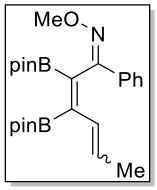
*Synthesis of (E) 4-methyl-2,3-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-phenylpenta-2,4-dien-1- O-methyl oxime (**50**).*



Following general procedure F, using 4-methyl-1-phenylpent-4-en-2-yn *O*-methyloxime (757 mg, 3.8 mol), B_2Pin_2 (2.13 g, 8.4 mmol) and $Pt(PPh_3)_4$ (434 mg, 0.4 mmol) in toluene (38 mL) afforded the desired product after kugelrohr distillation as an orange foam (1.15 g, 68%). ^{1}H

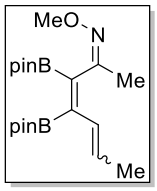
NMR (500 MHz, $CDCl_3$) δ 7.57 – 7.53 (m, 2H, C*H*$_{ar}$), 7.27 – 7.23 (m, 3H, C*H*$_{ar}$), 4.75 (dd, *J* = 2.0, 1.0 Hz, 1H, =C*H*), 4.63 (dq, *J* = 2.0, 1.5 Hz, 1H, =C*H*), 1.47 (dd, *J* = 1.5, 1.0 Hz, 3H, C*H*$_3$), 1.34 (s, 12H, C*H*$_3$ x 4), 1.27 (s, 12H, C*H*$_3$ x 4). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.6, 146.0, 135.9, 128.5, 127.8, 127.6, 114.2, 84.1, 83.9, 61.7, 25.0, 24.7, 21.5. ^{11}B NMR (128 MHz, $CDCl_3$) δ 29.8 (br). HRMS: *m/z* [MNa]$^+$ $C_{25}H_{37}{}^{11}B_2NO_5Na$ calcd. 454.2936, found 454.2950. FTIR: ν_{max}/ cm^{-1} (neat) 2978 (m), 1444 (w), 1308 (s), 1142 (s), 1053 (s).

*Synthesis of 2,3-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-phenylhexa-2,4-dien-1-O-methyl oxime (**51**)*



Following general procedure F, using 4-methyl-1-phenylpent-4-en-2-yn *O*-methyloxime (757 mg, 3.8 mol), B_2Pin_2 (2.13 g, 8.4 mmol) and $Pt(PPh_3)_4$ (434 mg,.38 mmol) in toluene (38 mL) afforded the desired product as an orange foam and as 1.2:1 mix of *E/Z* alkenes (1.40 g, 82%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 – 7.60 (m, 2H, C*H*$_{ar}$), 7.56 – 7.53 (m, 2H, C*H*$_{ar}$), 7.28 – 7.26 (m, 3H, C*H*$_{ar}$), 7.25 – 7.23 (m, 3H, C*H*$_{ar}$), 6.04 (dd, *J* = 16.0, 1.5 Hz, 1H, =C*H E*), 5.90 (dq, *J* = 16.0, 6.5 Hz, 1H, =C*H E*), 5.73 (dq, *J* = 11.5, 1.5 Hz, 1H, =C*H Z*), 5.31 (dq, *J* = 11.5, 7.0 Hz, 1H, =C*H Z*), 3.89 (s, 3H, OC*H*$_3$), 3.89 (s, 3H, OC*H*$_3$), 1.62 (dd, *J* = 6.5, 1.5 Hz, 3H, C*H*$_3$), 1.59 (dd, *J* = 7.0, 1.5 Hz, 3H, C*H*$_3$), 1.39 (s, 12H, C*H*$_3$ x4), 1.35 (s, 12H, C*H*$_3$ x4), 1.24 (s, 12H, C*H*$_3$ x4), 1.19 (s, 12H, C*H*$_3$ x4). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.0, 158.2, 135.7, 135.5, 133.7, 133.2, 130.5, 128.7, 128.6, 128.5, 128.2, 127.9, 127.0, 126.9, 84.0 (x 2C), 83.8, 83.7, 61.9, 61.8, 25.4, 25.2, 24.6 (x 2C), 19.1, 15.4. ^{11}B NMR (128 MHz, $CDCl_3$) δ 29.8 (br). HRMS: *m/z* [MH]$^+$ $C_{25}H_{38}{}^{11}B_2NO_5$ calcd. 454.2931, found 454.2942. FTIR: ν_{max}/ cm^{-1} (neat): 2978 (w), 2251 (w), 1474 (m), 1328 (m), 1142 (s), 1049 (s).

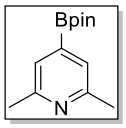
*Synthesis of 3,4-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hepta-3,5-dien-2-O-methyl oxime (**52**)*



Following general procedure F, using hept-5-en-3-yn-2-*O*-methyloxime (124 mg, 0.9 mmol), B_2Pin_2 (294 mg, 1.0 mmol) and $Pt(PPh_3)_4$ (35 mg, 0.03 mmol) in toluene (9 mL) afforded the

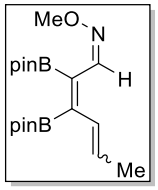
desired product as a yellow oil, and as a 1.3:1 mixture of *E/Z* isomers (140 mg, 41%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.12 (dd, *J* = 15.5, 1.5 Hz, =C*H E*), 5.97 – 5.87 (m, 2H, CH=C*H*), 5.61 (dq, *J* = 11.5, 7.0 Hz, 1H, =C*H Z*), 3.73 (s, 3H, OCH_3), 3.72 (s, 3H, OCH_3), 1.94 (s, 3H, CH_3), 1.90 (s, 3H, CH_3), 1.77 (dd, *J* = 6.5, 1.5 Hz, 3H, CH_3), 1.67 (dd, *J* = 7.0, 1.5 Hz, 3H, CH_3), 1.38 – 1.32 (m, 24H, CH_3 x 8), 1.28 – 1.21 (m, 24H CH_3 x 8). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.6, 158.2, 133.0, 132.9, 130.1, 128.9, 84.0, 83.7, 61.0, 61.0, 25.3, 25.1, 24.8, 24.7, 24.6, 24.6, 21.0, 19.7, 19.1, 15.4. ^{11}B NMR (128 MHz, $CDCl_3$) δ 29.9 (br). HRMS: *m/z* $[MH]^+$ $C_{20}H_{36}{}^{11}B_2NO_5$ calcd. 392.2780, found 392.02780. FTIR: ν_{max}/ cm^{-1} (neat) 2979 (m), 1316 (m), 1371 (m), 1137 (s), 1154 (s).

Synthesis of 2,6-dimethyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine[66] ***(144)***

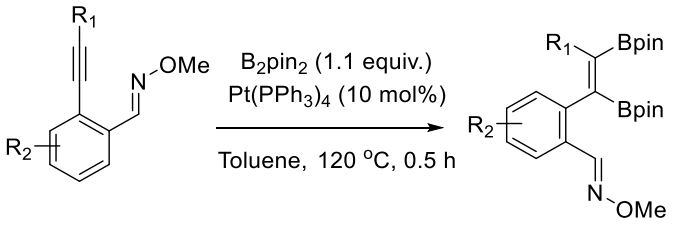


Following general procedure F, using (2*E*,5*E*)-hept-5-en-3-yn-2-one *O*-methyl oxime (105 mg, 0.8 mmol), B_2Pin_2 (218 mg, 0.85 mmol) and $Pt(PPh_3)_4$ (29 mg, 0.02 mmol) in toluene (8 mL) afforded the desired product as a white foam (86 mg, 48%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (s, 2H, CH_{ar}), 2.40 (s, 6H, CH_3), 1.34 (s, 12H, CH_3 x4). ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.1, 125.2, 84.3, 24.9, 24.3. ^{11}B NMR (128 MHz, $CDCl_3$) δ 30.9 (br).

*Synthesis of 2,3-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexa-2,4-dien-1-O-methyl oxime (**53**)*

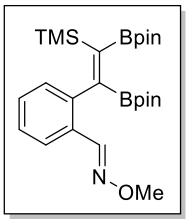


Following general procedure F, using hex-4-en-2-yn-1-O-methyloxime (100 mg, 0.8 mol), B_2Pin_2 (227 mg, 0.9 mmol) and $Pt(PPh_3)_4$ (23 mg, 0.02 mmol) in toluene (8 mL) afforded the desired product as a yellow oil (105 mg, 34%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 (s, 1H, NC*H*), 6.43 – 6.35 (m, 1H, CH=C*H*), 5.97 (dq, *J* = 15.5, 7.0 Hz, 1H, CH=C*H*), 3.84 (s, 3H, OCH_3), 1.80 (dd, *J* = 7.0, 2.0 Hz, 3H, CH_3), 1.33 (s, 12H, CH_3 x 4), 1.28 (s, 12H, CH_3 x 4). ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.8, 134.4, 131.5, 84.2, 83.8, 61.4, 25.1, 24.6, 19.3. ^{11}B NMR (128 MHz, $CDCl_3$) δ 30.7 (br). HRMS: *m/z* $[MH]^+$ $C_{19}H_{34}B_2NO_5$ calcd. 375.2690, found 376.2692. FTIR: ν_{max}/ cm^{-1} (neat) 2979 (m), 1557 (w), 1453 (w), 1313 (s), 1135 (s), 1052 (s).



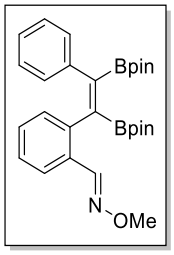
B_2Pin_2 (2.2. equiv) was added to a stirred solution of alkyne derivative (1.0 equiv.) in toluene (0.1 M). Then $Pt(PPh_3)_4$ (10 mol%) was added and the reaction was stirred at 120 °C for 30 min. The reaction mixture was allowed to cool to room temperature and the solvent was evaporated. The residue was purified by flash column chromatography on florisil eluting with petroleum ether (40/60) and ethyl acetate to afford the corresponding boronic esters.

*Synthesis of (E) 2-(1,2-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2 (trimethylsilyl)ethenyl)benzaldehyde O-methyl oxime (**54**)*



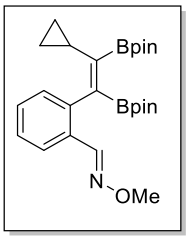
Following general procedure F, using 2-(2-(trimethylsilyl)ethynyl)benzaldehyde *O*-methyl oxime (212 mg, 0.9 mmol), B_2Pin_2 (254 mg, 1.0 mmol) and $Pt(PPh_3)_4$ (106 mg, 0.09 mmol) in toluene (9 mL) afforded the desired product as a white solid (260 mg, 58%). M.p.: 123.5 – 124.5 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (s, 1H, N=C*H*), 7.90 – 7.61 (m, 1H, CH_{ar}), 7.24 – 7.18 (m, 2H, CH_{ar}), 7.05 – 7.01 (m, 1H, CH_{ar}), 3.94 (s, 3H, OCH_3), 1.37 (s, 12H, CH_3 x 4), 1.18 (s, 12H, CH_3 x 4), -0.21 (s, 9H, Si(CH_3)$_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.2, 145.7, 129.5, 129.1, 129.0, 126.7, 124.9, 84.1, 83.7, 61.8, 25.7, 25.5, 24.8, 24.5, 0.3. ^{11}B NMR (128 MHz, $CDCl_3$) δ 28.6 (br). HRMS: *m/z* $[MH]^+$ $C_{25}H_{41}{}^{11}B_2NO_5Si$ calcd. 484.3086, found 484.3069. FTIR: ν_{max}/ cm^{-1} (neat) 2978 (m), 1519 (w), 1474 (m), 1456 (m), 1316 (m), 1123 (s), 1055 (m).

*Synthesis of (E) 2-(1,2-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-phenylethenyl)benzaldehyde O-methyl oxime (**55**)*



Following general procedure F, using 2-(2-phenylethynyl)benzaldehyde *O*-methyl oxime (140 mg, 0.6 mmol), B_2Pin_2 (166 mg, 0.7 mmol) and $Pt(PPh_3)_4$ (69 mg, 0.06 mmol) in toluene (6 mL) afforded the desired product as a pale yellow foam (240 mg, 82%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (s, 1H, N=C*H*), 7.66 – 7.63 (m, 1H, CH_{ar}), 7.10 – 6.98 (m, 5H, CH_{ar}), 6.90 – 6.85 (m, 3H, CH_{ar}), 3.90 (s, 3H, OCH_3), 1.34 (s, 6H, CH_3 x 2), 1.32 (s, 6H, CH_3 x 2), 1.27 (s, 6H, CH_3 x 2), 1.27 (s, 6H, CH_3 x 2). ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.3, 141.8, 140.8, 130.1, 129.8, 129.0, 128.6, 127.5, 126.3, 126.2, 125.2, 84.2, 84.1, 61.7, 25.0, 24.9, 24.8, 24.6. ^{11}B NMR (128 MHz, $CDCl_3$) δ 30.3 (br). HRMS: *m/z* $[MH]^+$ $C_{28}H_{38}{}^{11}B_2NO_5$ calcd. 490.2931, found 490.2943. FTIR: ν_{max}/ cm^{-1} (neat) 2979 (m), 1587 (w), 1310 (s), 1139 (s), 1053 (s).

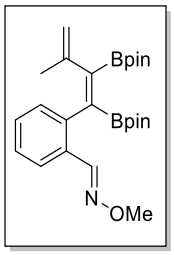
*Synthesis of (E) 2-(1,2-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-cyclopropylethenyl)benzaldehyde O-methyl oxime (**56**)*



Following general procedure F, using 2-(2-cyclopropylethynyl)benzaldehyde *O*-methyl oxime (139 mg, 0.7 mmol), B_2Pin_2 (183 mg, 0.8 mmol) and $Pt(PPh_3)_4$ (75 mg, 0.07 mmol) in toluene (7 mL) afforded the desired product as a pale yellow oil (314 mg, 99%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (s, 1H, N=C*H*), 7.86 (dd, *J* = 8.0, 1.5 Hz, 1H, CH_{ar}), 7.30 (td, *J* = 8.0, 1.5 Hz, 1H, CH_{ar}), 7.20 (td, *J* = 8.0, 1.0 Hz, 1H, CH_{ar}), 7.13 (dd, *J* = 8.0, 1.0 Hz, 1H, CH_{ar}), 3.94 (s, 3H, OCH_3), 1.35 (s, 12H, CH_3 x 4), 1.29 – 1.24 (m, 1H, C*H*), 1.19 (s, 12H, CH_3 x 4), 0.79 – 0.69 (m, 2H, CH_2), 0.62 – 0.55 (m, 2H, CH_2). ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.6, 142.9, 129.9, 129.8, 129.3, 126.2, 125.0, 83.9, 83.7, 61.8, 25.5, 25.4, 24.7, 24.6, 16.4, 7.4, 7.3. ^{11}B NMR (128 MHz, $CDCl_3$) δ 29.7 (br). HRMS:

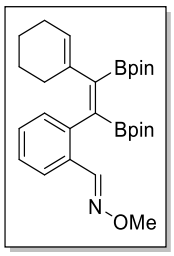
m/z [MH]$^+$ $C_{25}H_{38}{}^{11}B_2NO_5$ calcd. 454.2931, found 454.2934. FTIR: ν_{max}/ cm^{-1} (neat) 2979 (m), 1577 (w), 1474 (m), 1336 (m), 1305 (s), 1136 (s), 1053 (m).

*Synthesis of (E) 2-(1,2-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-isopropenylethenyl)benzaldehyde O-methyl oxime (**57**)*



Following general procedure F, using 2-(2-isopropenylethynyl)benzaldehyde *O*-methyl oxime (130 mg, 0.7 mmol), B_2Pin_2 (183 mg, 0.8 mmol) and $Pt(PPh_3)_4$ (75 mg, 0.07 mmol) in toluene (7 mL) afforded the desired product as a pale yellow foam (235 mg, 79%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (s, 1H, N=C*H*), 7.79 (dd, *J* = 7.5, 1.5 Hz, 1H, CH_{ar}), 7.25 – 7.14 (m, 2H, CH_{ar}), 7.06 – 7.00 (m, 1H, CH_{ar}), 4.77 – 4.74 (m, 1H, =C*H*), 4.61 – 4.58 (m, 1H, =C*H*), 3.93 (s, 3H, OCH_3), 1.47 – 1.46 (m, 3H, CH_3), 1.34 (s, 12H, CH_3 x 4), 1.22 (s, 12H, CH_3 x 4). ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.5, 145.4, 142.4, 129.4, 129.2, 129.1, 126.5, 125.1, 114.4, 84.0, 83.9, 61.7, 25.0, 24.8 (x2 C), 24.5, 22.6. ^{11}B NMR (128 MHz, $CDCl_3$) δ 30.2 (br). HRMS: *m/z* [MH]$^+$ $C_{25}H_{38}{}^{11}B_2NO_5$ calcd. 452.3003, found 452.3022. FTIR: ν_{max}/ cm^{-1} (neat) 2978 (m), 1587 (w), 1473 (m), 1309 (s), 1140 (s), 1056 (m).

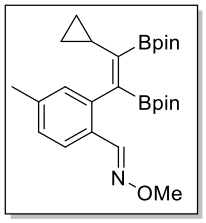
*Synthesis of (E) 2-(1,2-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-cyclohexenylethenyl)benzaldehyde O-methyl oxime (**58**)*



Following general procedure F, using 2-(2-cyclohexenylethynyl)benzaldehyde *O*-methyl oxime (123 mg, 0.5 mmol), B_2Pin_2 (152 mg, 0.6 mmol) and $Pt(PPh_3)_4$ (60 mg, 0.05 mmol) in toluene (5 mL) afforded the desired product as a pale yellow oil (219 mg, 85%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (s, 1H, N=C*H*), 7.77 (dd, *J* = 8.0, 1.5 Hz, 1H, CH_{ar}), 7.23 – 7.18 (m, 1H, CH_{ar}), 7.16 – 7.11 (m, 1H, CH_{ar}), 7.04 – 6.99 (m, 1H, CH_{ar}), 5.34 – 5.28 (m, 1H, =C*H*), 3.91 (s, 3H, OCH_3), 1.86 – 1.78 (m, 2H, CH_2), 1.63 – 1.55 (m, 2H, CH_2), 1.33 (s, 12H, CH_3 x 4), 1.31 (br, 4H, CH_2 x 2), 1.22 (s, 12H,

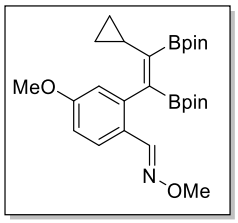
C*H*$_3$ x 4). ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.8, 142.9, 138.2, 129.6, 129.4, 128.9, 126.3, 126.2, 125.0, 83.9, 83.7, 61.7, 28.0, 25.4, 25.0, 24.8, 22.7, 21.9. ^{11}B NMR (128 MHz, $CDCl_3$) δ 30.3 (br). HRMS: *m/z* $[MH]^+$ $C_{28}H_{42}{}^{11}B_2NO_5$ calcd. 494.3244, found 494.3253. FTIR: ν_{max}/ cm^{-1} (neat) 2978 (m), 1579 (w), 1473 (m), 1324 (s), 1138 (s), 1054 (m).

*Synthesis of (E) 2-(1,2-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-cyclopropylethenyl)-4-methylbenzaldehyde O-methyl oxime (**59**)*



Following general procedure F, using 2-(2-cyclopropylethynyl)-4-methylbenzaldehyde *O*-methyl oxime (42 mg, 0.2 mmol), B_2Pin_2 (53 mg, 0.22 mmol) and $Pt(PPh_3)_4$ (22 mg, 0.02 mmol) in toluene (2 mL) afforded the desired product as a pale yellow oil (45 mg, 51%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (s, 1H, N=C*H*), 7.75 (d, *J* = 8.0 Hz, 1H, CH_{ar}), 7.00 (dd, *J* = 8.0, 1.5 Hz, 1H, CH_{ar}), 6.94 (br, 1H, CH_{ar}), 3.92 (s, 3H, OCH_3), 2.31 (s, 3H), 1.34 (s, 12H, CH_3 x 4), 1.31 – 1.28 (m, 1H, C*H*), 1.19 (s, 12H, CH_3 x 4), 0.77 – 0.72 (m, 2H, CH_2), 0.61 – 0.54 (m, 2H, CH_2).^{13}C NMR (101 MHz, $CDCl_3$) δ 148.6, 142.8, 139.1, 130.4, 127.2, 127.0, 124.9, 83.9, 83.7, 61.6, 25.4, 25.4, 24.8, 24.5, 21.5, 16.4, 7.4, 7.3. ^{11}B NMR (128 MHz, $CDCl_3$) δ 29.9 (br). HRMS: *m/z* $[MH]^+$ $C_{26}H_{40}{}^{11}B_2NO_5$ calcd. 468.3096, found 468.3095. FTIR: ν_{max}/ cm^{-1} (neat) 2978 (m), 1578 (w), 1460 (m), 1306 (s), 1144 (s), 1055 (m).

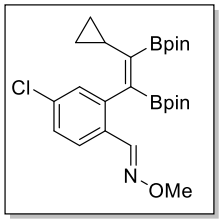
*Synthesis of (E) 2-(1,2-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-cyclopropylethenyl)-4-methoxybenzaldehyde O-methyl oxime (**60**)*



Following general procedure F, using 2-(2-cyclopropylethynyl)-4-methoxybenzaldehyde *O*-methyl oxime (95 mg, 0.4 mmol), B_2Pin_2 (112 mg, 0.44 mmol) and $Pt(PPh_3)_4$ (46 mg, 0.04 mmol) in toluene (4 mL) afforded the desired product as an orange oil (150 mg, 76%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (s, 1H, N=C*H*), 7.80 (d, *J* = 8.5 Hz, 1H, CH_{ar}), 6.75 (dd, *J* = 8.5, 2.5 Hz, 1H, CH_{ar}), 6.65 (d, *J* = 2.5 Hz, 1H, CH_{ar}), 3.91 (s, 3H, NOCH_3), 3.77 (s, 3H, COCH_3), 1.34 (s, 12H, CH_3 x

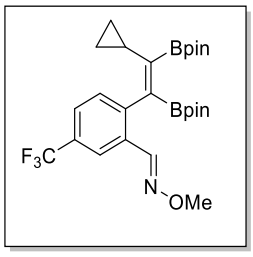
4), 1.33 – 1.29 (m, 1H, C*H*), 1.20 (s, 12H, CH_3 x 4), 0.79 – 0.69 (m, 2H, CH_2), 0.62 – 0.55 (m, 2H, CH_2). ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.3, 148.3, 144.6, 126.5, 122.6, 113.8, 113.3, 84.0, 83.7, 61.6, 55.2, 25.4 (x2C), 24.7, 24.6, 16.4, 7.5, 7.4. ^{11}B NMR (128 MHz, $CDCl_3$) δ 30.0 (br). HRMS: *m/z* $[MH]^+$ $C_{26}H_{40}{}^{11}B_2NO_5$ calcd. 484.3045, found 484.3049. FTIR: ν_{max}/ cm^{-1} (neat) 2979 (m), 1595 (m), 1463 (m), 1305 (s), 1137 (s), 1054 (s).

*Synthesis of (E) 2-(1,2-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-cyclopropylethenyl)-4-chlorobenzaldehyde O-methyl oxime (**61**)*



Following general procedure F, using 2-(2-cyclopropylethynyl)-4-chlorobenzaldehyde *O*-methyl oxime (93 mg, 0.4 mmol), B_2Pin_2 (112 mg, 0.44 mmol) and $Pt(PPh_3)_4$ (46 mg, 0.04 mmol) in toluene (4 mL) afforded the desired product as a yellow oil (168 mg, 86%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (s, 1H, N=C*H*), 7.80 (d, *J* = 8.5 Hz, 1H, CH_{ar}), 7.20 – 7.12 (m, 2H, CH_{ar}), 3.93 (s, 3H, OCH_3), 1.34 (s, 12H, CH_3 x 4), 1.26 – 1.24 (m, 1H, C*H*), 1.20 (s, 6H, CH_3 x 2), 1.20 (s, 6H, CH_3 x 2), 0.78 – 0.73 (m, 2H, CH_2), 0.65 – 0.60 (m, 2H, CH_2). ^{13}C NMR (101 MHz, $CDCl_3$) δ 147.5, 144.4, 135.0, 129.8, 128.5, 126.5, 126.4, 84.1, 83.9, 61.9, 25.5, 25.4, 24.7, 24.5, 16.5, 7.6, 7.5. ^{11}B NMR (128 MHz, $CDCl_3$) δ 29.5 (br). HRMS: *m/z* $[MH]^+$ $C_{25}H_{37}{}^{11}B_2NO_5{}^{35}Cl$ calcd. 488.2546, found 488.2552. FTIR: ν_{max}/ cm^{-1} (neat) 2979 (m), 1583 (w), 1472 (m), 1309 (s), 1142 (s), 1052 (m).

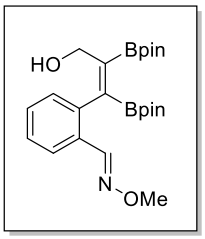
*Synthesis of (E) 2-(1,2-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-cyclopropylethenyl)-5-trifluoromethylbenzaldehyde O-methyl oxime (**62**)*



Following general procedure F, using 2-(2-cyclopropylethynyl)-5-trifluoromethylbenzaldehyde *O*-methyl oxime (110 mg, 0.4 mmol), B_2Pin_2 (112 mg, 0.44 mmol) and $Pt(PPh_3)_4$ (46 mg, 0.04 mmol) in toluene (4 mL) afforded the desired product as a dark yellow oil (131 mg, 61%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (s, 1H, N=C*H*), 8.15 (br, 1H, CH_{ar}), 7.52 (dd, *J* = 8.0, 1.5 Hz, 1H,

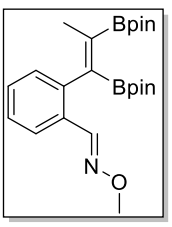
C*H*$_{ar}$), 7.24 (d, *J* = 8.0 Hz, 1H, C*H*$_{ar}$), 3.97 (s, 3H, OC*H*$_3$), 1.35 (s, 12H, C*H*$_3$ x 4), 1.32– 1.28 (m, 1H, C*H*), 1.20 (s, 12H, C*H*$_3$ x 4), 0.79 – 0.75 (m, 2H, C*H*$_2$), 0.63 – 0.59 (m, 2H, C*H*$_2$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 147.1, 146.3, 131.2, 130.6, 129.3 (q, *J* = 272.5 Hz), 128.4 (q, *J* = 65.0 Hz), 125.5 (q, *J* = 7.0 Hz), 122.2 (q, *J* = 7.0 Hz), 84.1, 84.0, 62.0, 25.5, 25.4, 24.7, 24.5, 16.6, 7.7, 7.5. ^{11}B NMR (128 MHz, $CDCl_3$) δ 29.7 (br). ^{19}F NMR (377 MHz, $CDCl_3$) δ -62.4. HRMS: *m/z* $[MH]^+$ $C_{26}H_{37}{}^{11}B_2F_3NO_5$ calcd. 522.2814, found 522.2810. FTIR: ν_{max}/ cm^{-1} (neat) 2982 (m), 1577 (w), 1317 (s), 1125 (s), 1052 (m), 850 (m).

*Synthesis of (E) 2-(1,2-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-(3-hydroxy-1-propenyl)benzaldehyde O-methyl oxime (**63**)*



Following general procedure F, using 2-(3-hydroxy-1-propynyl)benzaldehyde *O*-methyl oxime (122 mg, 0.7 mmol), B_2Pin_2 (183 mg, 0.8 mmol) and $Pt(PPh_3)_4$ (75 mg, 0.07 mmol) in toluene (7 mL) afforded the desired product as a dark orange oil (211 mg, 73%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (s, 1H, N=C*H*), 7.84 (dd, *J* = 7.5, 1.5 Hz, 1H, C*H*$_{ar}$), 7.29 (td, *J* = 7.5, 1.5 Hz, 1H, C*H*$_{ar}$), 7.21 (td, *J* = 7.5, 1.0 Hz, 1H, C*H*$_{ar}$), 7.05 – 7.00 (m, 1H, C*H*$_{ar}$), 3.97 (d, *J* = 6.0 Hz, 2H, C*H*$_2$), 3.94 (s, 3H, OC*H*$_3$), 2.13 (t, *J* = 6.0 Hz, 1H, C-O*H*), 1.35 (s, 12H, C*H*$_3$ x 4), 1.20 (s, 12H, C*H*$_3$ x 4). ^{13}C NMR (101 MHz, $CDCl_3$) δ 147.8, 140.8, 129.5, 129.1, 128.3, 126.9, 125.5, 84.3, 84.0, 63.7, 61.9, 25.0, 24.9, 24.7, 24.6. ^{11}B NMR (128 MHz, $CDCl_3$) δ 30.7 (br). HRMS: *m/z* $[MH]^+$ $C_{23}H_{36}{}^{11}B_2NO_6$ calcd. 444.2731, found 444.2734. FTIR: ν_{max}/ cm^{-1} (neat) 3465 (br), 2978 (m), 1603 (w), 1474 (m), 1312 (s), 1143 (s), 1052 (s).

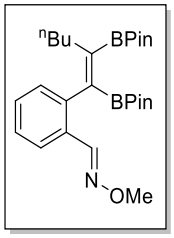
Synthesis of (E) 2-(1,2-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)prop-1-en-1-yl) benzaldehyde O-methyl oxime



Following general procedure F, using *(E)* 2-(prop-1-yn-1-yl)benzaldehyde *O*-methyl oxime (4.2 g, 24.3 mmol), B_2Pin_2 (6.8 g, 26.7 mmol) and $Pt(PPh_3)_4$ (754 mg, 0.6 mmol) in toluene (250 mL) afforded the desired product as an dark brown foam (10.3 g, 99%). ^{1}H NMR (400 MHz, $CDCl_3$) δ

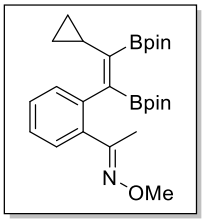
8.13 (s, 1H, N=C*H*), 7.87 (dd, *J* = 8.0, 1.5 Hz, 1H, CH_{ar}), 7.29 (td, *J* = 7.5, 1.5 Hz, 1H, CH_{ar}), 7.20 (td, *J* = 7.5, 1.0 Hz, 1H, CH_{ar}), 7.03 (dd, *J* = 8.0, 1.0 Hz, 1H, CH_{ar}), 3.94 (s, 3H, OCH_3), 1.53 (s, 3H, CH_3), 1.33 (s, *J* = 7.8 Hz, 12H, CH_3 x 4), 1.20 (s, *J* = 1.0 Hz, 6H, CH_3 x 2), 1.20 (s, 6H, CH_3 x 2). ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.1, 142.1, 129.4, 129.3, 128.8, 126.4, 125.2, 83.8, 83.7, 61.8, 24.9 (x2 C), 24.8, 24.6 (x2 C). ^{11}B NMR (160 MHz, $CDCl_3$) δ 30.1 (br). HRMS: *m/z* $[MH]^+$ $C_{23}H_{36}{}^{11}B_2NO_5$ calcd. 428.2774, found 428.2782. FTIR: ν_{max}/ cm^{-1} (neat) 2978 (m), 1517 (w), 1473 (m), 1332 (s), 1271 (s), 1144 (s), 1054 (m).

Synthesis of (E) 2-(1,2-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)(hex-1-en-1-yl) benzaldehyde O-methyl oxime



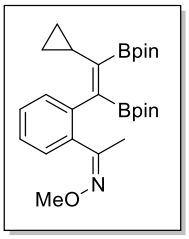
Following general procedure F, using *(E)* 2-(hex-1-yn-1-yl)benzaldehyde *O*-methyl oxime (2.2 g, 10.2 mmol), B_2Pin_2 (2.91 g, 11.2 mmol) and $Pt(PPh_3)_4$ (635 mg, 0.51 mmol) in toluene (100 mL) afforded the desired product as a dark orange oil (4.63 g, 97%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (s, 1H, N=C*H*), 7.85 (dd, *J* = 8.0, 1.5 Hz, 1H, CH_{ar}), 7.28 (dt, *J* = 7.5, 1.5 Hz, 2H, CH_{ar}), 7.19 (td, *J* = 7.5, 1.0 Hz, 1H, CH_{ar}), 7.01 (dd, *J* = 8.0, 1.0 Hz, 1H, CH_{ar}), 3.93 (s, 3H, OCH_3), 1.97 – 1.88 (m, 2H, CH_2), 1.34 (s, 12H, CH_3 x4), 1.24 – 1.20 (m, 2H, CH_2), 1.19 (s, 12H, CH_3 x4), 1.13 – 1.07 (m, 2H, CH_2), 0.71 (t, *J* = 7.5 Hz, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.3, 142.3, 129.5, 129.2, 129.1, 126.3, 125.0, 83.7 (x2 C), 61.7, 32.8, 31.0, 25.0 (x2 C), 24.7 (x2 C), 24.6 (x2 C), 22.8 (x2 C), 13.8. ^{11}B NMR (128 MHz, $CDCl_3$) δ 31.9 (br). HRMS: *m/z* $[MH]^+$ $C_{26}H_{42}{}^{11}B_2NO_5$ calcd. 470.3244, found 470.3259. FTIR: ν_{max}/ cm^{-1} (neat) 2977 (m), 1599 (w), 1467 (m), 1307 (s), 1146 (s), 1055 (s).

*Synthesis of (E) 2-(1,2-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2 cyclopropylethenyl)acetophenone O-methyl oxime (E-**78**)*



Following general procedure F, using *(E)* 2-(2-cyclopropylethynyl)acetophenone *O*-methyl oxime (95 mg, 0.45 mmol), B_2Pin_2 (127 mg, 0.5 mmol) and $Pt(PPh_3)_4$ (58 mg, 0.05 mmol) in toluene (4.5 mL) afforded the desired product as a pale yellow oil (172 mg, 82%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (dd, *J* = 7.5, 1.0 Hz, 1H, C*H*$_{ar}$), 7.31 – 7.26 (m, 1H, C*H*$_{ar}$), 7.20 (td, *J* = 7.5, 1.5 Hz, 1H, C*H*$_{ar}$), 7.13 (dd, *J* = 7.5, 1.0 Hz, 1H, C*H*$_{ar}$), 3.95 (s, 3H, OC*H*$_3$), 2.07 (s, 3H, CC*H*$_3$), 1.33 (s, 12H, C*H*$_3$ x 4), 1.20 1.20 (s, 6H, C*H*$_3$ x 2), 1.19 (s, 6H, C*H*$_3$ x 2) 0.95 – 0.86 (m, 1H, C*H*), 0.77 – 0.71 (m, 1H, CH*H*), 0.70 – 0.65 (m, 1H, CH*H*), 0.62 – 0.57 (m, 1H, CH*H*), 0.56 – 0.49 (m, 1H, CH*H*). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.0, 141.5, 137.1, 130.1, 128.1 (x2C), 126.0, 83.7, 83.6, 61.6, 25.5, 25.4, 24.7, 24.5, 16.4, 16.3, 7.3, 7.1.^{11}B NMR (128 MHz, $CDCl_3$) δ 29.8. HRMS: *m*/*z* $[MH]^+$ $C_{26}H_{40}{}^{11}B_2NO_5$ calcd. 468.3093, found 468.3084. FTIR: ν_{max}/ cm^{-1} (neat) 2978 (m), 1578 (w), 1442 (m), 1303 (s), 1137 (s), 1050 (s).

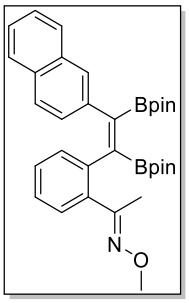
*Synthesis of (Z) 2-(1,2-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-cyclopropylethenyl)acetophenone O-methyl oxime (Z-**78**)*



Following general procedure F, using *(Z)* 2-(2-cyclopropylethynyl)acetophenone *O*-methyl oxime (25 mg, 0.11 mmol), B_2Pin_2 (30 mg, 0.12 mmol) and $Pt(PPh_3)_4$ (13 mg, 0.01 mmol) in toluene (1 mL) afforded the desired product as a pale orange oil (28 mg, 54%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 – 7.15 (m, 4H, C*H*$_{ar}$), 3.76 (s, 3H, OC*H*$_3$), 2.14 (s, 3H, CC*H*$_3$), 1.50 – 1.42 (m, 1H, C*H*), 1.33 (s, 12H, C*H*$_3$ x 4), 1.29 (s, 6H, C*H*$_3$ x 2), 1.19 (s, 6H, C*H*$_3$ x 2), 0.85 – 0.77 (m, 1H, CH*H*), 0.75 – 0.68 (m, 1H, CH*H*), 0.64 – 0.52 (m, 2H, C*H*$_2$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.9, 140.7, 135.0, 130.4, 127.8, 127.3, 125.5, 83.7, 83.6, 61.3, 25.6, 25.4, 25.0, 24.3, 21.8, 16.6, 7.7, 7.3. ^{11}B NMR (128 MHz, $CDCl_3$) δ 29.8 (br). HRMS: *m*/*z* $[MH]^+$ $C_{26}H_{40}{}^{11}B_2NO_5$ calcd. 468.3096,

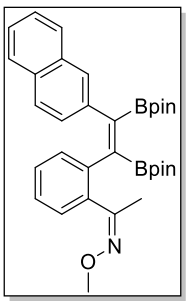
found 468.3099. FTIR: ν_{max}/ cm^{-1} (neat) 2979 (m), 1578 (w), 1437 (m), 1303 (s), 1137 (s), 1051 (m).

*Synthesis of (E)-1-(2-((Z)-2-(naphthalen-2-yl)-1,2-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)vinyl)phenyl)ethan-1-one O-methyl oxime (E-**79**)*



Following general procedure F, using *(E)*-1-(2-(naphtalen-2-yl-ethynyl)phenyl)ethan-1-one O-methyl oxime (150 mg, 0.50 mmol), B_2pin_2 (140 mg, 0.55 mmol) and $Pt(PPh_3)_4$ (62 mg, 0.05 mmol) in toluene (5 mL) afforded the desired product (170 mg, 61%) as a brown foam. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 – 7.61 (m, 2H, CH_{ar}), 7.60 (br, 1H, CH_{ar}), 7.44 (d, *J* = 8.5 Hz, 1H, CH_{ar}), 7.35 – 7.31 (m, 2H, CH_{ar}), 7.20 (dd, *J* = 8.0, 1.0 Hz, 1H, CH_{ar}), 7.09 – 7.02 (m, 2H, CH_{ar}), 6.98 (td, *J* = 7.5, 1.5 Hz, 1H, CH_{ar}), 6.90 (dd, *J* = 7.5, 1.0 Hz, 1H, CH_{ar}), 3.78 (s, 3H, OCH_3), 2.11 (s, 3H, CH_3), 1.36 (s, 6H, CH_3 x 2), 1.32 (s, 6H, CH_3 x 2), 1.29 (s, 6H, CH_3 x 2), 1.27 (s, 6H, CH_3 x 2). ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.9, 140.8, 139.5, 136.4, 133.2, 131.9, 131.2, 128.4, 127.9, 127.7, 127.6, 127.5, 127.4, 126.8, 126.0, 125.3, 125.1, 83.9, 83.7, 61.5, 25.3, 24.8, 24.7 (x2 C), 15.2. ^{11}B NMR (128 MHz, $CDCl_3$) δ 30.2 (br). HRMS: *m/z* $[MH]^+$ $C_{33}H_{42}{}^{11}B_2NO_5$ calcd. 554.3255, found 554.3257. FTIR: ν_{max}/ cm^{-1} (neat): 2977 (m), 2159 (m), 1530 (m), 1313 (s), 1143 (s), 1047 (s), 856 (s).

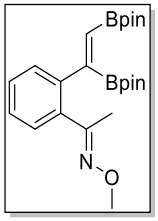
*Synthesis of (Z)-1-(2-((Z)-2-(naphthalen-2-yl)-1,2-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)vinyl)phenyl)ethan-1-one O-methyl oxime (Z-**78**)*



Following general procedure F, using *(Z)*-1-(2-(naphtalen-2-yl-ethynyl)phenyl)ethan-1-one O-methyl oxime (150 mg, 0.50 mmol), B_2pin_2 (140 mg, 0.55 mmol) and $Pt(PPh_3)_4$ (62 mg, 0.05 mmol) in toluene (5 mL) afforded the desired product as a white foam (225 mg, 81%). ^{1}H NMR

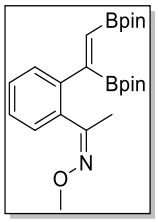
(400 MHz, $CDCl_3$) δ 7.70 – 7.62 (m, 3H, CH_{ar} x3), 7.48 (d, *J* = 8.5 Hz, 1H, CH_{ar}), 7.38 – 7.33 (m, 2H, CH_{ar} x2), 7.12 – 7.06 (m, 4H, CH_{ar} x4), 7.03 – 6.99 (m, 1H, CH_{ar}), 3.61 (s, 3H, OCH_3), 1.67 (s, 3H, CH_3), 1.36 (s, 24H, CH_3 x8). ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.9, 140.0, 138.8, 134.3, 133.3, 132.0, 131.0, 128.4, 128.0, 127.8, 127.7, 127.5, 127.4, 126.7, 125.8, 125.4 (x 2C), 84.1, 83.8, 60.9, 25.3 (x2 C), 25.0, 24.4, 21.4. ^{11}B NMR (128 MHz, $CDCl_3$) δ 30.4 (br). HRMS: *m/z* $[MH]^+$ $C_{33}H_{42}{}^{11}B_2NO_5$ calcd. 554.3255, found 554.3260. FTIR: ν_{max}/ cm^{-1} (neat): 2987 (m), 2167 (m), 1522 (m), 1310 (s), 1144 (s), 1047 (s).

*Synthesis of (E)-1-(2-((Z)-1,2-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)vinyl)phenyl)ethan-1-one O-methyl oxime (E-**77**)*



Following general procedure F, using *(E)*-1-(2-ethynylphenyl)ethan-1-one O-methyl oxime (200 mg, 1.20 mmol), B_2pin_2 (329 mg, 1.30 mmol) and $Pt(PPh_3)_4$ (144 mg, 0.12 mmol) in toluene (12 mL) afforded the desired product as a violet oil (280 mg, 57%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 (d, *J* = 7.5 Hz, 1H, CH_{ar}), 7.28 – 7.22 (m, 3H, CH_{ar}), 6.12 (s, 1H, C*H*=C), 3.96 (s, 3H, OCH_3), 2.11 (s, 3H, CH_3), 1.31 (s, 12H, CH_3 x4), 1.27 (s, 12H, CH_3 x4). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.1, 157.5, 143.7, 135.6, 129.0, 128.5, 126.9, 83.8, 83.5, 61.6, 24.9 (x 2C), 16.5. ^{11}B NMR (160 MHz, $CDCl_3$) δ 30.1 (br). HRMS: *m/z* $[MH]^+$ $C_{23}H_{36}{}^{11}B_2NO_5$ calcd. 428.2774, found 428.2792. FTIR: ν_{max}/ cm^{-1} (neat): 2977 (m), 1602 (w), 1328 (s), 1165 (s), 1049 (m).

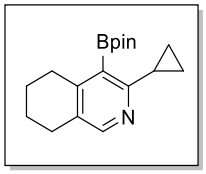
*Synthesis of (Z)-1-(2-((Z)-1,2-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)vinyl)phenyl)ethan-1-one O-methyl oxime (Z-**78**)*



Following general procedure F, using *(Z)*-1-(2-ethynylphenyl)ethan-1-one O-methyl oxime (200 mg, 1.20 mmol), B_2pin_2 (329 mg, 1.30 mmol) and $Pt(PPh_3)_4$ (144 mg, 0.12 mmol) in toluene (12 mL) afforded the desired product as a pale brown oil (432 mg, 88%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 – 7.26 (m, 1H, CH_{ar}), 7.25 – 7.22 (m, 2H, CH_{ar}), 7.14 – 7.11 (m, 1H, CH_{ar}), 6.02 (s, 1H,

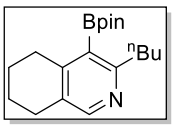
C*H*=C), 3.79 (s, 3H, OC*H*$_3$), 2.12 (s, 3H, C*H*$_3$), 1.30 (s, 12H, C*H*$_3$ x4), 1.29 (s, 12H, C*H*$_3$ x4). ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.1, 142.1, 133.8, 128.1, 127.9, 127.7, 126.5, 83.9, 83.5, 61.3, 24.9, 24.9, 22.1. ^{11}B NMR (160 MHz, $CDCl_3$) δ 30.2 (br). HRMS: *m/z* $[MNa]^+$ $C_{23}H_{35}{}^{11}B_2NO_5Na$ calcd. 450.2599, found 450.2600. FTIR: ν_{max}/ cm^{-1} (neat): 2979 (m), 1605 (w), 1335 (s), 1139 (s), 1051 (m).

*Synthesis of 3-cyclopropyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5,6,7,8-tetrahydroisoquinoline (**99**)*



Following general procedure F, using 2-(2-cyclopropylethynyl)-1-cyclohexenecarboxaldehyde *O*-methyl oxime (103 mg, 0.5 mmol), B_2Pin_2 (152 mg, 0.6 mmol) and $Pt(PPh_3)_4$ (60 mg, 0.05 mmol) in toluene (5 mL) afforded the cyclised product as a pale yellow oil (77 mg, 51%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (s, 1H, C*H*$_{ar}$), 2.77 (t, *J* = 5.5 Hz, 1H, C*H*$_2$), 2.64 (t, *J* = 5.5 Hz, 2H, C*H*$_2$), 2.14 – 2.02 (m, 1H, C*H*), 1.78 – 1.72 (m, 4H, C*H*$_2$), 1.38 (s, 12H, C*H*$_3$ x 4), 1.05 – 0.99 (m, 2H, C*H*$_2$), 0.86 – 0.82 (m, 2H, C*H*$_2$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.5, 150.6, 149.7, 128.6, 84.1, 29.0, 26.5, 25.0, 22.9, 22.5, 16.5, 9.1. ^{11}B NMR (128 MHz, $CDCl_3$) δ 32.5 (br). HRMS: *m/z* $[MH]^+$ $C_{18}H_{27}{}^{11}BNO_2$ calcd. 300.2133, found 300.2134. FTIR: ν_{max}/ cm^{-1} (neat) 2976 (m), 1560 (m), 1444 (m), 1370 (s), 1139 (s).

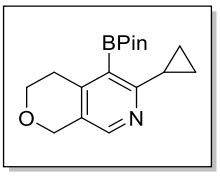
*Synthesis of 3-butyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5,6,7,8-tetrahydroisoquinoline (**152**)*



Following general procedure F, using (E) 2-(hex-1-yn-1-yl)-1-cyclohexenecarboxaldehyde O-methyl oxime (3.9 g, 17.6 mmol), B_2Pin_2 (5.0 g, 19.4 mmol) and $Pt(PPh_3)_4$ (658 mg, 0.53 mmol) in toluene (170 mL) afforded the cyclised product as a pale orange oil (4.5 g, 81%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (s, 1H, C*H*$_{ar}$), 2.80 – 2.71 (m, 4H, C*H*$_2$ x2), 2.66 (br, 2H, C*H*$_2$), 1.79 – 1.73 (m, 4H, C*H*$_2$ x2), 1.67 – 1.60 (m, 2H, C*H*$_2$), 1.41 – 1.35 (m, 14H, C*H*$_2$ + C*H*$_3$ x4), 0.91 (t, *J* = 7.5 Hz, 3H, C*H*$_3$).). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.9, 150.5, 150.1, 129.0, 84.1, 38.5, 33.4, 29.0, 26.5, 25.0, 23.0, 22.8, 22.5, 14.1.^{11}B NMR (160 MHz, $CDCl_3$) δ 32.2 (br). HRMS: *m/z* $[MH]^+$

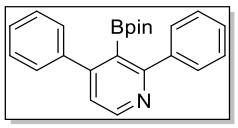
$C_{19}H_{31}{}^{11}BNO_2$ calcd. 316.2442, found 316.2452. FTIR : ν_{max}/ cm^{-1} (neat) 2930 (w), 1560 (m), 1475 (w), 1303 (m), 1138 (s).

*Synthesis of 6-cyclopropyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3,4-dihydro-1H-pyrano[3,4-c]pyridine (**101**)*



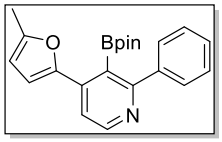
Following general procedure F, using 4-(2-cyclopropylethynyl)- 5,6-dihydro-2*H*-pyran-3-carboxaldehyde *O*-methyl oxime (81 mg, 0.4 mmol), B_2Pin_2 (110 mg, 0.43 mmol) and $Pt(PPh_3)_4$ (46 mg, 0.04 mmol) in toluene (4 mL) afforded the desired product as a pale yellow oil (86 mg, 72%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (s, 1H, CH_{ar}), 4.70 (br, 2H, CH_2), 3.93 (t, *J* = 6.0 Hz, 2H, CH_2), 2.90 (t, *J* = 6.0 Hz, 2H, CH_2), 2.26 (tt, *J* = 8.0, 5.0 Hz, 1H, C*H*), 1.39 (s, 12H, CH_3 x 4), 1.07 – 1.03 (m, 2H, CH_2), 0.92 – 0.86 (m, 2H, CH_2). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.6, 146.6, 146.6, 126.5, 84.2, 66.1, 65.0, 28.2, 24.9, 16.4, 9.7. ^{11}B NMR (128 MHz, $CDCl_3$) δ 32.1 (br). HRMS: *m/z* $[MH]^+$ $C_{17}H_{25}{}^{11}BNO_3$ calcd. 302.1922, found 302.1927. FTIR: ν_{max}/ cm^{-1} (neat) 2978 (m), 1564 m), 1443 (m), 1371 (s), 1140 (s).

*Synthesis of 2,4-diphenyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine (**116**)*



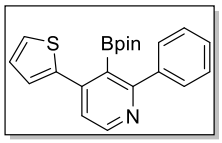
Following general procedure F, using (1*E/Z*, 2*E*)-3,5-diphenylpent-2-en-4-ynal *O*-methyl oxime (30 mg, 0.11 mmol), B_2Pin_2 (33 mg, 0.13 mmol) and $Pt(PPh_3)_4$ (14 mg, 0.01 mmol) in toluene (2 mL) afforded the cyclised product as a pale yellow foam (21 mg, 50%).^{1}H NMR (400 MHz, $CDCl_3$) δ 8.69 (d, *J* = 5.0 Hz, 1H, CH_{ar}), 7.73 – 7.69 (m, 2H, CH_{ar}), 7.53 – 7.49 (m, 2H, CH_{ar}), 7.46 – 7.39 (m, 6H, CH_{ar}), 7.23 (d, *J* = 5.0 Hz, 1H, CH_{ar}), 0.93 (s, 12H, CH_3 x4). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.4, 155.1, 149.0, 142.1, 140.8, 129.2, 128.8, 128.4, 128.3, 128.3, 128.1, 121.7, 84.3, 24.8.^{11}B NMR (160 MHz, $CDCl_3$) δ 31.5 (br). HRMS: *m/z* $[MH]^+$ $C_{23}H_{25}$ $^{11}BNO_2$ calcd. 358.1973, found 358.1985. FTIR: ν_{max}/ cm^{-1} (neat): 2973 (m), 1579 (w), 1543 (w), 1344 (s), 1144 (s).

*Synthesis of 4-(5-methylfuran-2-yl)-2-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine (**117**)*



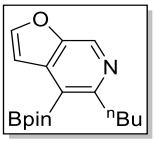
Following general procedure F, using (1*E*, 2*Z*)-3-(5-methylfuran-2-yl-phenylpent-2-yl)-en-4-ynal *O*-methyl oxime (55 mg, 0.2 mmol), B_2Pin_2 (59 mg, 0.23 mmol) and $Pt(PPh_3)_4$ (26 mg, 0.02 mmol) in toluene (2 mL) afforded the cyclised product as a pale orange foam (51 mg, 67%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.58 (d, *J* = 5.5 Hz, 1H, C*H*$_{ar}$), 7.64 – 7.57 (m, 2H, C*H*$_{ar}$), 7.43 – 7.35 (m, 4H, C*H*$_{ar}$), 6.86 (d, *J* = 3.5 Hz, 1H, C*H*$_{ar}$), 6.11 (dd, *J* = 3.5, 1.0 Hz, 1H, C*H*$_{ar}$), 2.40 (s, 3H, C*H*$_3$), 1.11 (s, 12H, C*H*$_3$ x4). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.8, 154.0, 151.4, 149.3, 142.5, 141.7, 129.4, 128.2, 127.9, 117.4, 111.1, 108.5, 84.3, 25.2, 14.2. ^{11}B NMR (128 MHz, $CDCl_3$) δ 31.2 (br). HRMS: *m/z* $[MH]^+$ $C_{22}H_{25}{}^{11}BNO_3$ calcd. 362.1922, found 362.1936. FTIR: ν_{max}/ cm^{-1} (neat): 2987 (w), 1604 (m), 1558 (m), 1295 (s), 1138 (s) 1121 (s).

*Synthesis of 2-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-4-(thiophen-2-yl)pyridine (**118**)*



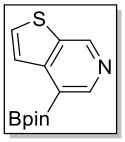
Following general procedure F, using (1*E*, 2*Z*)-5-phenyl-3-(thiophen-2-yl)pent-2-en-4-ynal *O*-methyl oxime (50 mg, 0.19 mmol), B_2Pin_2 (53 mg, 0.21 mmol) and $Pt(PPh_3)_4$ (23 mg, 0.02 mmol) in toluene (2 mL) afforded the cyclised product as a pale orange foam (51 mg, 67%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.67 (d, *J* = 5.0 Hz, 1H, C*H*$_{ar}$), 7.71 – 7.68 (m, 2H, C*H*$_{ar}$), 7.44 – 7.40 (m, 5H, C*H*$_{ar}$), 7.31 (d, *J* = 5.0 Hz, 1H, C*H*$_{ar}$), 7.10 (dd, *J* = 5.0, 3.5 Hz, 1H, C*H*$_{ar}$), 1.01 (s, 12H, C*H*$_3$ x4). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.9, 149.1, 147.1, 142.1, 141.9, 129.2, 128.5, 128.1, 128.0, 127.4, 127.2, 121.9, 84.5, 24.9. ^{11}B NMR (128 MHz, $CDCl_3$) δ 31.1 (br). HRMS: *m/z* $[MH]^+$ $C_{21}H_{23}{}^{11}BNO_2S$ calcd. 364.1537, found 364.1551. FTIR: ν_{max}/ cm^{-1} (neat): 2978 (w), 1565 (m), 1325 (s), 1141 (s), 1045 (s).

*Synthesis of 5-butyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)furo[2,3-c]pyridine (**133**)*



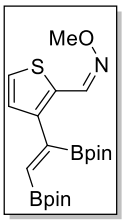
Following general procedure F, using (E)-3-(hex-1-yn-1-yl)furan-2-carbaldehyde *O*-methyl oxime (70 mg, 0.34 mmol), B_2Pin_2 (97 mg, 0.38 mmol) and $Pt(PPh_3)_4$ (42 mg, 0.03 mmol) in toluene (3.5 mL) afforded the cyclised product as a pale orange oil (56 mg, 55%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.78 (br, 1H, C*H*$_{ar}$), 7.69 (d, *J* = 2.0 Hz, 1H, C*H*$_{ar}$), 7.16 (dd, *J* = 2.0, 1.0 Hz, 1H, C*H*$_{ar}$), 3.18 – 3.12 (m, 2H, C*H*$_2$), 1.71 – 1.59 (m, 2H, C*H*$_2$), 1.46 – 1.40 (m, 2H, C*H*$_2$), 1.39 (s, 12H, C*H*$_3$ x4), 0.94 (t, *J* = 7.5 Hz, 3H, C*H*$_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.3, 150.0, 148.1, 140.6, 134.2, 108.3, 83.8, 37.6, 34.5, 25.0, 22.8, 14.0. ^{11}B NMR (160 MHz, $CDCl_3$) δ 31.3 (br). HRMS: *m/z* $[MH]^+$ $C_{17}H_{25}{}^{11}BNO_3$ calcd. 302.1922, found 302.1929. FTIR : ν_{max}/ cm^{-1} (neat) 2929 (w), 1591 (m), 1415 (m), 1369 (m), 1308 (m), 1139 (s).

*Synthesis of 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)thieno[3,2-c]pyridine (**134**)*



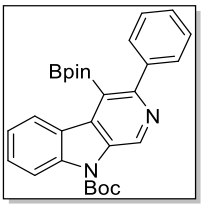
Following general procedure F, using *(E)*-3-ethynylthiophene-2-carbaldehyde *O*-methyl oxime (70 mg, 0.42 mmol), B_2Pin_2 (121 mg, 0.47 mmol) and $Pt(PPh_3)_4$ (53 mg, 0.04 mmol) in toluene (4.5 mL) afforded the cyclised product as a pale orange oil (35 mg, 32%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.21 (s, 1H, C*H*$_{ar}$), 8.88 (s, 1H, C*H*$_{ar}$), 7.96 (dd, *J* = 5.5, 1.0 Hz, 1H, C*H*$_{ar}$), 7.74 (d, *J* = 5.5 Hz, 1H, C*H*$_{ar}$), 1.40 (s, 12H, C*H*$_3$ x4). ^{13}C NMR (101 MHz, $CDCl_3$) δ 150.1, 149.2, 146.9, 136.0, 132.2, 125.3, 84.2, 25.0. ^{11}B NMR (160 MHz, $CDCl_3$) δ 31.0 (br). HRMS: *m/z* $[MH]^+$ $C_{13}H_{17}{}^{11}BNO_2S$ calcd. 262.1073, found 262.1063. FTIR: ν_{max}/ cm^{-1} (neat): 3073 (m), 2974 (m), 1594 (w), 1401 (m), 1181 (s), 1034 (s).

Synthesis of (Z)-3-((E)-1,2-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)vinyl)thiophene-2-carbaldehyde O-methyl oxime



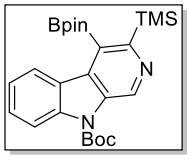
Following general procedure F, using *(Z)*-3-ethynylthiophene-2-carbaldehyde *O*-methyl oxime (70 mg, 0.42 mmol), B_2Pin_2 (121 mg, 0.47 mmol) and $Pt(PPh_3)_4$ (53 mg, 0.04 mmol) in toluene (4.5 mL) afforded the desired product as a pale yellow oil (135 mg, 74%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (br, 1H, N=C*H*), 7.37 (dd, *J* = 5.0, 0.5 Hz, 1H, CH_{ar}), 7.01 (d, *J* = 5.0 Hz, 1H, CH_{ar}), 6.12 (s, 1H, =C*H*), 4.04 (s, 3H, OCH_3), 1.32 (s, 12H, CH_3 x4), 1.31 (s, 12H, CH_3 x4). ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.2, 140.0, 129.2, 127.3, 125.6, 84.4, 83.8, 62.2, 24.9. ^{11}B NMR (160 MHz, $CDCl_3$) δ 30.0 (br). HRMS: *m/z* $[MNa]^+$ $C_{20}H_{31}{}^{11}B_2NO_5SNa$ calcd. 442.2007, found 442.2016. FTIR: ν_{max}/ cm^{-1} (neat): 2977 (m), 1596 (m), 1371 (s), 1137 (s), 1054 (s).

*Synthesis of tert-butyl 3-phenyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-9H-pyrido[3,4-b]indole-9-carboxylate (**136**)*



Following general procedure F, using *(E)*-2-((methoxyimino)methyl)-3-(phenylethynyl)-1*H*-indole-1-carboxylate (112 mg, 0.30 mmol), B_2Pin_2 (84 mg, 0.33 mmol) and $Pt(PPh_3)_4$ (41 mg, 0.03 mmol) in toluene (3 mL) afforded the cyclised product as a yellow oil (93 mg, 66%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.61 (s, 1H, CH_{ar}), 8.47 (d, *J* = 9.0 Hz, 2H, CH_{ar}), 7.72 – 7.67 (m, 2H, CH_{ar}), 7.60 (ddd, *J* = 8.5, 7.5, 1.0 Hz, 1H, CH_{ar}), 7.47 – 7.35 (m, 4H, CH_{ar}), 1.78 (s, 9H, CH_3 x3), 1.31 (s, 12H, CH_3 x4). ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.4, 150.5, 143.1, 139.8, 138.1, 135.5, 132.8, 129.5, 129.4, 128.1, 128.0, 125.0, 123.1, 122.5, 116.5, 84.9, 84.7, 28.4, 25.3. ^{11}B NMR (128 MHz, $CDCl_3$) δ 31.8 (br). HRMS: *m/z* $[MH]^+$ $C_{28}H_{32}{}^{11}B_2N_2O_4$ calcd. 471.2450, found 471.2462. FTIR: ν_{max}/ cm^{-1} (neat): 2980 (m), 1729 (s), 1556 (m), 1316 (s), 1123 (s), 1028 (m).

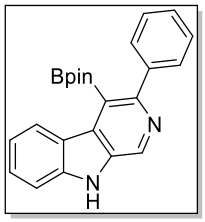
*Synthesis of tert-butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3-(trimethylsilyl)-9H-pyrido[3,4-b]indole-9-carboxylate (**135**)*



Following general procedure F, using *tert*-butyl *(E)*-2-((methoxyimino)methyl)-3-((trimethylsilyl)ethynyl)-1*H*-indole-1-carboxylate (90 mg, 0.24 mmol), B_2Pin_2 (69 mg, 0.27 mmol) and $Pt(PPh_3)_4$ (30 mg, 0.02 mmol) in toluene (2.5 mL) afforded the cyclised product after overnight heating as a pale yellow oil (55 mg, 49%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.72 (s,

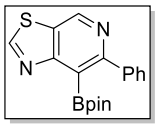
1H, C*H*$_{ar}$), 8.69 (d, *J* = 8.0 Hz, 1H, C*H*$_{ar}$), 8.46 (d, *J* = 8.5 Hz, 1H, C*H*$_{ar}$), 7.56 (ddd, *J* = 8.5, 7.0, 1.0 Hz, 1H, C*H*$_{ar}$), 7.39 – 7.32 (m, 1H, C*H*$_{ar}$), 1.77 (s, 9H, C*H*$_3$ x3), 1.55 (s, 12H, C*H*$_3$ x4), 0.46 (s, 9H, C*H*$_3$ x3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.0, 149.8, 138.5, 137.9, 133.0, 132.6, 128.4, 124.5, 122.7, 122.1, 115.6, 84.2, 84.1, 27.8, 25.3, 0.0. ^{11}B NMR (128 MHz, $CDCl_3$) δ 31.7 (br). HRMS: *m/z* $[MH]^+$ $C_{25}H_{36}{}^{11}BN_2O_4Si$ calcd. 467.2532, found 467.2549. FTIR: ν_{max}/ cm^{-1} (neat): 2979 (w), 1731 (s), 1459 (m), 1317 (s), 1147 (s), 1025 (m).

*Synthesis of 3-phenyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-9H-pyrido[3,4-b]indole (**138**)*



Following general procedure F, using *(E)*-3-(phenylethynyl)-1*H*-indole-2-carbaldehyde *O*-methyl oxime (50 mg, 0.18 mmol), B_2Pin_2 (50 mg, 0.2 mmol) and $Pt(PPh_3)_4$ (20 mg, 0.02 mmol) in toluene (2 mL). Subsequent addition of *o*-DCB (4 mL) after 3 h and further heating overnight at 200 °C afforded the cyclised product as a colourless oil (47 mg, 70%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.95 (s, 1H, C*H*$_{ar}$), 8.56 (d, *J* = 8.0 Hz, 1H, C*H*$_{ar}$), 8.40 (br, 1H, N*H*), 7.72 – 7.69 (m, 2H, C*H*$_{ar}$), 7.56 – 7.51 (m, 1H, C*H*$_{ar}$), 7.49 – 7.41 (m, 3H, C*H*$_{ar}$), 7.41 – 7.36 (m, 1H, C*H*$_{ar}$), 7.30 – 7.27 (m, 1H, C*H*$_{ar}$), 1.34 (s, 12H, C*H*$_3$ x4).^{13}C NMR (101 MHz, $CDCl_3$) δ 154.3, 144.0, 141.0, 133.8, 133.6, 132.6, 129.6, 128.3, 128.0, 127.6, 123.3, 122.7, 119.9, 111.5, 84.5, 25.3. ^{11}B NMR (128 MHz, $CDCl_3$) δ 31.1 (br). HRMS: *m/z* $[MH]^+$ $C_{23}H_{24}{}^{11}BN_2O_2$ calcd. 372.1957, found 372.1967. FTIR: ν_{max}/ cm^{-1} (neat): 2978 (m), 1440 (m), 1330 (s), 1137 (s), 1020 (s).

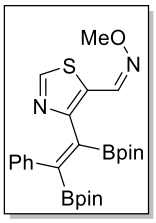
*Synthesis of 6-phenyl-7-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)thiazolo[5,4-c]pyridine (**137**)*



Following general procedure F, using *(E)*-4-(phenylethynyl)thiazole-5-carbaldehyde *O*-methyl oxime (50 mg, 0.21 mmol), B_2Pin_2 (59 mg, 0.23 mmol) and $Pt(PPh_3)_4$ (26 mg, 0.02 mmol) in toluene (2.0 mL). Subsequent addition of *o*-DCB (4 mL) after 3 h and further heating overnight at 200 °C afforded the cyclised product as a yellow oil (45 mg, 65%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.33 (s, 1H, C*H*$_{ar}$), 9.21 (s, 1H, C*H*$_{ar}$), 7.82 (br, 2H, C*H*$_{ar}$), 7.48 – 7.39 (m, 3H, C*H*$_{ar}$), 1.35 (s, 12H, C*H*$_3$ x4). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.6, 159.0, 158.9, 144.5, 141.8, 129.1, 128.5, 128.4,

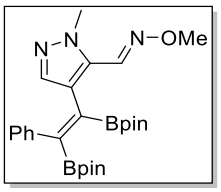
128.1, 84.9, 24.8. ^{11}B NMR (128 MHz, $CDCl_3$) δ 31.8 (br). HRMS: *m/z* $[MH]^+$ $C_{18}H_{20}{}^{11}BN_2O_2S$ calcd. 339.1333, found 339.1443. FTIR: ν_{max}/ cm^{-1} (neat): 2978 (m), 1534 (m), 1453 (m), 1380 (s), 1270 (s), 1140 (s), 1083 (m).

Synthesis of (Z)-4-((Z)-2-phenyl-1,2-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)vinyl)thiazole-5-carbaldehyde O-methyl oxime



Following general procedure F, using *(Z)*-4-(phenylethynyl)thiazole-5-carbaldehyde *O*-methyl oxime (89 mg, 0.37 mmol), B_2Pin_2 (103 mg, 0.40 mmol) and $Pt(PPh_3)_4$ (46 mg, 0.04 mmol) in toluene (4.0 mL) afforded the desired product as a pale yellow oil (45 mg, 25%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.74 (d, *J* = 1.0 Hz, 1H, N=C*H*), 7.41 (d, *J* = 1.0 Hz, 1H, CH_{ar}), 7.09 – 7.02 (m, 3H, CH_{ar}), 6.92 – 6.88 (m, 2H, CH_{ar}), 3.90 (s, 3H, OCH_3), 1.33 (s, 12H, CH_3 x4), 1.29 (s, 12H, CH_3 x4). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.3, 154.8, 140.9, 138.8, 128.2, 127.9, 126.6, 118.5, 84.3, 84.3, 62.0, 24.9, 24.8. ^{11}B NMR (128 MHz, $CDCl_3$) δ 30.3 (br). HRMS: *m/z* $[MH]^+$ $C_{25}H_{35}{}^{11}B_2N_2O_5S$ calcd. 497.2453, found 497.2433. FTIR: ν_{max}/ cm^{-1} (neat): 2977(w), 1598 (w), 1310 (s), 1139 (s), 1047 (m).

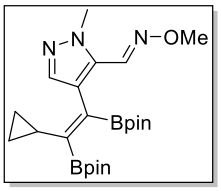
Synthesis of (E)-1-methyl-4-((Z)-2-phenyl-1,2-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)vinyl)-1H-pyrazole-5-carbaldehyde O-methyl oxime



Following general procedure F, using *(E)*-1-methyl-4-(phenylethynyl)-1H-pyrazole-5-carbaldehyde *O*-methyl oxime (100 mg, 0.42 mmol), B_2Pin_2 (121 mg, 0.47 mmol) and $Pt(PPh_3)_4$ (53 mg, 0.04 mmol) in toluene (4.5 mL) afforded the desired product as a yellow oil (181 mg, 88%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (s, 1H, N=C*H*), 7.14 – 7.05 (m, 3H, CH_{ar}), 7.00 – 6.96 (m, 3H, CH_{ar}), 3.89 (s, 3H, OCH_3), 3.81 (s, 3H, NCH_3), 1.31 (s, 12H, CH_3 x4), 1.30 (s, 12H, CH_3 x4). ^{13}C NMR (101 MHz, $CDCl_3$) δ 141.0, 139.7, 138.8, 130.2, 128.8, 127.8, 126.3, 123.8, 84.3, 84.1, 62.0, 40.0, 24.9. ^{11}B NMR (128 MHz, $CDCl_3$) δ 30.2 (br). HRMS: *m/z* $[MH]^+$ $C_{26}H_{38}{}^{11}B_2N_3O_5$ calcd.

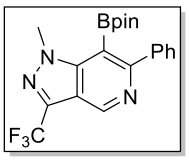
494.2998, found 494.3021. FTIR: ν_{max}/ cm^{-1} (neat): 2978 (w), 1459 (w), 1308 (s), 1140 (s), 1052 (s).

Synthesis of (E)-1-methyl-4-((Z)-2-cyclopropyl-1,2-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)vinyl)-1H-pyrazole-5-carbaldehyde O-methyl oxime



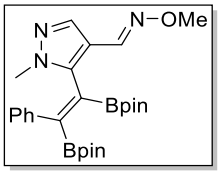
Following general procedure F, using *(E)*-1-methyl-4-(cyclopropylethynyl)-1H-pyrazole-5-carbaldehyde *O*-methyl oxime (1.4 g, 6.9 mmol), B_2Pin_2 (1.97 g, 0.47 mmol) and $Pt(PPh_3)_4$ (53 mg, 0.04 mmol) in toluene (4.5 mL) afforded the desired product as a yellow oil (181 mg, 88%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (s, 1H), 7.31 (s, 1H, C*H*$_{ar}$), 4.07 (s, 3H, OC*H*$_3$), 3.92 (s, 3H, NC*H*$_3$), 1.70 – 1.61 (m, 1H, C*H*), 1.33 (s, 12H, C*H*$_3$ x4), 1.22 (s, 12H, C*H*$_3$ x4), 0.80 – 0.75 (m, 2H, C*H*$_2$), 0.69 – 0.63 (m, 2H, C*H*$_2$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 140.6, 138.8, 130.7, 124.7, 84.0, 83.8, 62.1, 40.2, 25.4, 24.7, 16.7, 7.9. ^{11}B NMR (128 MHz, $CDCl_3$) δ 29.4 (br). HRMS: *m*/*z* [MH]$^+$ $C_{23}H_{38}{}^{11}B_2N_3O_5$ calcd. 458.2992, found 458.3009. FTIR: ν_{max}/ cm^{-1} (neat): 2978 (w), 1458 (w), 1345 (s), 1271 (s), 1112 (s), 1053 (s).

*Synthesis of 1-methyl-6-phenyl-7-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3-(trifluoromethyl)-1H-pyrazolo[4,3-c]pyridine (**142**)*



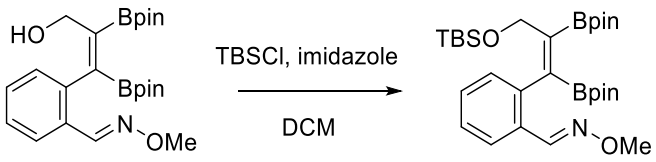
Following general procedure F, using *(E)*-1-methyl-5-(phenylethynyl)-3-(trifluoromethyl)-1*H*-pyrazole-4-carbaldehyde *O*-methyl oxime (100 mg, 0.33 mmol), B_2Pin_2 (93 mg, 0.36 mmol) and $Pt(PPh_3)_4$ (40 mg, 0.03 mmol) in toluene (3.5 mL) and subsequent addition of *o*-DCB (7 mL) afforded the cyclised product after over night heating at 200 °C as a colourless oil (50 mg, 38%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.23 (s, 1H, C*H*$_{ar}$), 7.67 – 7.59 (m, 2H, C*H*$_{ar}$), 7.50 – 7.39 (m, 3H, C*H*$_{ar}$), 4.27 (s, 3H, C*H*$_3$), 1.21 (s, 12H, C*H*$_3$ x4). ^{13}C NMR (176 MHz, DMSO) δ 159.1, 146.2, 143.7, 141.8, 132.31 (q, $^2J_{C\text{-}F}$ = 39 Hz), 129.2, 128.6, 128.1, 127.0, 122.8 (q, $^1J_{C\text{-}F}$ = 269 Hz), 85.0, 38.3, 24.9. ^{19}F NMR (376 MHz, $CDCl_3$) δ -60.7. ^{11}B NMR (128 MHz, $CDCl_3$) δ 22.3 (br). HRMS: *m*/*z* [MH]$^+$ $C_{20}H_{22}{}^{11}BF_3N_3O_2$ calcd. 404.1752, found 404.1756. FTIR: ν_{max}/ cm^{-1} (neat): 2938 (w), 1615 (m), 1511 (m), 1170 (s), 1111 (s).

Synthesis of (E)-1-methyl-5-((Z)-2-phenyl-1,2-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)vinyl)-1H-pyrazole-4-carbaldehyde O-methyl oxime



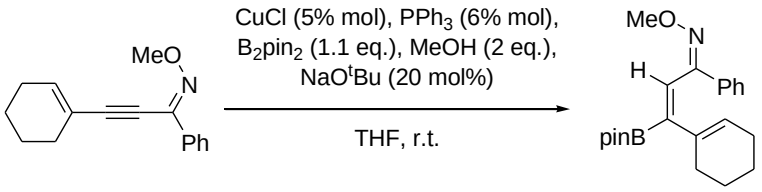
Following general procedure F, using *(E)*-1-methyl-5-(phenylethynyl)-1*H*-pyrazole-4-carbaldehyde *O*-methyl oxime (50 mg, 0.21 mmol), B_2Pin_2 (61 mg, 0.24 mmol) and $Pt(PPh_3)_4$ (27 mg, 0.02 mmol) in toluene (2.5 mL) afforded the desired product as a dark yellow oil (79 mg, 77%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (s, 1H, N=C*H*), 7.14 – 7.08 (m, 3H, CH_{ar}), 7.01 – 6.97 (m, 3H, CH_{ar}), 3.90 (s, 3H, OCH_{ar}), 3.82 (s, 3H, NCH_{ar}), 1.31 (s, 12H, CH_3 x4), 1.31 (s, 12H, CH_3 x4). ^{13}C NMR (101 MHz, $CDCl_3$) δ 141.1, 139.7, 138.8, 130.2, 128.8, 127.9, 126.3, 123.8, 84.3, 84.1, 62.0, 40.0, 24.9. ^{11}B NMR (128 MHz, $CDCl_3$) δ 29.1 (br). HRMS: *m/z* $[MH]^+$ $C_{26}H_{38}{}^{11}B_2N_3O_5$ calcd. 494.2998, found 494.3010. FTIR: ν_{max}/ cm^{-1} (neat): 2978 (w), 1458 (w), 1311 (s), 1212 (w), 1141 (s), 1053 (s).

*Synthesis of (E) 2-(1,2-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-(3-tert-butyldimethylsiloxy-1-propenyl)benzaldehyde O-methyl oxime (**91**)*

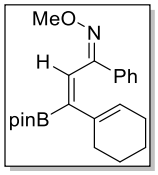


A solution of of 2-(1,2-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-(3-hydroxy-1-propenyl)benzaldehyde *O*-methyl oxime (112 mg, 0.25 mmol), *tert*-butyldimethylsilyl chloride (60 mg, 0.4 mmol) and imidazole (31 mg, 0.45 mmol) were stirred in dichloromethane (4 mL) at room temperature. Water was added and the product extracted with ethyl acetate. Removal of solvent and purification by silica gel chromatography afforded the desired product as a colourless oil (69 mg, 57%).[56] ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (s, 1H, N=C*H*), 7.84 – 7.84 (m, 1H, CH_{ar}), 7.30 – 7.24 (m, 1H, CH_{ar}), 7.22 – 7.18 (m, 1H, CH_{ar}), 7.04 – 6.98 (m, 1H, CH_{ar}), 4.08 – 3.94 (m, 2H, CH_2), 3.93 (s, 3H, OCH_3), 1.35 (s, 12H, CH_3 x 4), 1.19 (s, 12H, CH_3 x 4), 0.79 (s, 9H, C(CH_3)$_3$), -0.10 (s, 6H, Si(CH_3)$_2$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 147.9, 141.6, 129.3, 129.3, 128.7, 126.6, 125.2, 83.9, 83.8, 64.6, 61.7, 26.0, 25.3, 25.1, 24.8, 24.6, 18.5, -5.4. ^{11}B NMR (128 MHz, $CDCl_3$) δ 29.1 (br). HRMS: *m/z* $[MNa]^+$ $C_{29}H_{50}{}^{11}B_2NO_6Si$ calcd. 578.3480, found 578.3472. FTIR: ν_{max}/ cm^{-1} (neat) 2977 (m), 1606 (w), 1472 (m), 1311 (s), 1120 (s), 1055 (s).

General procedure G

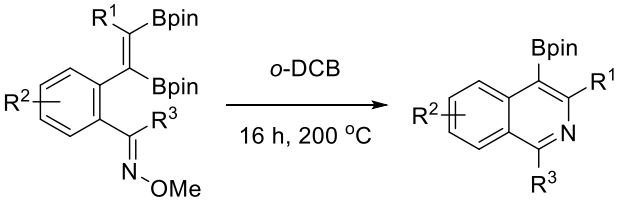


Synthesis of (E) 3-cyclohexenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-phenylprop-2-en-1-O-methyl oxime[43] ***(80)***



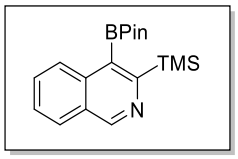
CuCl (20 mg, 0.2 mmol), NaO^{t}Bu (73 mg, 0.8 mmol) and triphenylphosphine (58 mg, 0.23 mmol) were added to a stirred solution of THF (15 mL). After the mixture was stirred at room temperature for 30 min, B_2Pin_2 (975 mg, 3.8 mmol) dissolved in THF (4.5 mL) was added. The reaction mixture was stirred for 10 min. Then, 3-(cyclohex-1-enyl)-1-phenylprop-2-yn-1-one *O*-methyl oxime[36] (459 mg, 1.9 mmol) was added followed by MeOH (0.04 mL, 1 mmol). The reaction was stirred until no starting material was detected by TLC analysis. The reaction mixture was filtered through a pad of Celite and concentrated. The residue was purified by flash column chromatography on silica gel eluting with petroleum ether (40/60) and ethyl acetate to afford 3-cyclohexenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-phenylprop-2-en-1 *O*-methyl oxime (422 mg, 60%) as a white solid. M.p.: 76 – 77 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 – 7.38 (m, 2H, C*H*$_{ar}$), 7.29 – 7.26 (m, 3H, C*H*$_{ar}$), 7.02 (s, 1H, =C*H*), 5.28 – 5.25 (m, 1H, =C*H*), 4.01 – 3.98 (m, 3H, OC*H*$_3$), 1.81 – 1.77 (m, 2H, C*H*$_2$), 1.70 – 1.65 (m, 2H, C*H*$_2$), 1.30 (s, 12H, C*H*$_3$ x 4), 1.12 – 1.06 (m, 4H, C*H*$_2$ x 2). ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.7, 138.1, 136.3, 131.9, 128.3, 127.9, 127.4, 127.3, 83.8, 62.3, 27.3, 25.3, 24.8, 22.1, 21.3. ^{11}B NMR (128 MHz, $CDCl_3$) δ 30.7 (br). HRMS: *m/z* $[MH]^+$ $C_{22}H_{31}{}^{11}BNO_3$ calcd. 368.2396, found 368.2394. FTIR: ν_{max}/ cm^{-1} (neat) 2977 (m), 1550 (w), 1443 (w), 1372 (m), 1319 (m), 1140 (s). 1047 (s).

General procedure H



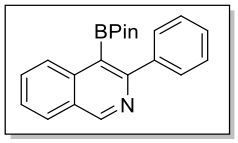
A solution of diboronic ester derivative in *o*-DCB (0.1 M) was stirred at 200 °C for 16 h. The reaction mixture was allowed to cool to room temperature and was filtered through silica gel. The residue was purified by flash column chromatography on silica gel eluting with petroleum ether (40/60) and ethyl acetate to afford the corresponding isoquinolines.

*Synthesis of 3-(trimethylsilyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)isoquinoline (**82**)*



Following general procedure H stirring at 180 °C for 16 h, using *(E)* 2-(1,2-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-(trimethylsilyl)ethenyl)benzaldehyde *O*-methyl oxime (97 mg, 0.2 mmol) in *o*-DCB (2 mL) afforded the desired product as a colorless foam (40 mg, 54%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.33 (s, 1H, C*H*$_{ar}$), 8.30 (dd, *J* = 8.5, 1.0 Hz, 1H, C*H*$_{ar}$), 7.89 (d, *J* = 8.0 Hz, 1H, C*H*$_{ar}$), 7.67 (ddd, *J* = 8.5, 7.0, 1.5 Hz, 1H, C*H*$_{ar}$), 7.57 (ddd, *J* = 8.0, 7.0, 1.0 Hz, 1H, C*H*$_{ar}$), 1.50 (s, 12H, C*H*$_3$ x 4), 0.45 (s, 9H, Si(C*H*$_3$)$_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.5, 152.5, 137.9, 130.2, 128.0, 127.0, 126.7, 126.6, 84.6, 25.7, 0.4. ^{11}B NMR (128 MHz, $CDCl_3$) δ 32.3 (br) . HRMS: *m/z* $[MH]^+$ $C_{18}H_{27}{}^{11}BNO_2Si$ calcd. 327.1935, found 327.1934. FTIR: ν_{max}/ cm^{-1} (neat) 2976 (m), 1569 (w), 1493 (m), 1235 (s), 1134 (s).

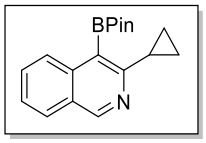
*Synthesis of 3-phenyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)isoquinoline (**83**)*



Following general procedure H, using *(E)* 2-(1,2-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-phenylethenyl)benzaldehyde *O*-methyl oxime (98 mg, 0.2 mmol) in *o*-DCB (2 mL) afforded the desired product as an orange oil (53 mg, 79%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.31 (s, 1H, C*H*$_{ar}$), 8.12 (dd, *J* = 8.5, 0.5 Hz, 1H, C*H*$_{ar}$), 7.98 (d, *J* = 8.0 Hz, 1H, C*H*$_{ar}$), 7.78 – 7.68 (m, 3H C*H*$_{ar}$), 7.61 – 7.56 (m, 1H, C*H*$_{ar}$), 7.49 – 7.38 (m, 3H, C*H*$_{ar}$), 1.31 (s, 12H, C*H*$_3$ x 4). ^{13}C NMR (101 MHz,

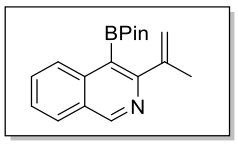
$CDCl_3$) δ 152.9, 139.5, 130.9, 129.5 (x2C), 128.3, 128.2 (x2C), 126.9 (x2C), 126.8, 126.4, 84.5, 25.0. ^{11}B NMR (128 MHz, $CDCl_3$) δ 32.0 (br). HRMS: *m/z* $[MH]^+$ $C_{21}H_{23}{}^{11}BNO_2$ calcd. 331.1853, found 331.1856. FTIR: ν_{max}/ cm^{-1} (neat) 2978 (m), 1555 (m), 1494 (m), 1312 (m), 1240 (s), 1134 (s).

*Synthesis of 3-cyclopropyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)isoquinoline (**84**)*



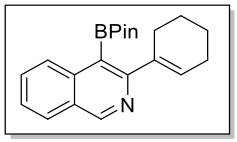
Following general procedure H, using *(E)* 2-(1,2-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-cyclopropylethenyl)benzaldehyde *O*-methyl oxime (121 mg, 0.27 mmol) in *o*-DCB (3 mL) afforded the desired product as an orange oil (69 mg, 88%). ^1H NMR (400 MHz, $CDCl_3$) δ 9.09 (s, 1H, CH_{ar}), 8.11 (dd, *J* = 8.5, 1.0 Hz, 1H, CH_{ar}), 7.84 (d, *J* = 8.0 Hz, 1H, CH_{ar}), 7.62 (ddd, *J* = 8.5, 7.0, 1.5 Hz, 1H, CH_{ar}), 7.45 (ddd, *J* = 8.0, 7.0, 1.0 Hz, 1H, CH_{ar}), 2.61 – 2.54 (m, 1H, C*H*), 1.49 (s, 12H, CH_3 x 4), 1.22 – 1.18 (m, 2H, CH_2), 1.02 – 0.96 (m, 2H, CH_2). ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.7, 153.8, 139.5, 130.4, 128.0, 126.3, 126.1, 125.5, 84.3, 25.0, 16.6, 9.9. ^{11}B NMR (128 MHz, $CDCl_3$) δ 32.8 (br). HRMS: *m/z* $[MH]^+$ $C_{18}H_{23}BNO_2$ calcd. 295.1853, found 295.1856. FTIR: ν_{max}/ cm^{-1} (neat) 2978 (m), 1619 (m), 1562 (m), 1495 (m), 1235 (s), 1134 (s).

*Synthesis of 3-isopropenyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)isoquinoline (**86**)*



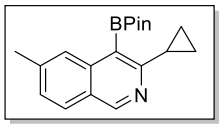
Following general procedure H, using *(E)* 2-(1,2-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-isopropenylethenyl)benzaldehyde *O*-methyl oxime (104 mg, 0.23 mmol) in *o*-DCB (2.5 mL) afforded the desired product as an orange oil (41 mg, 61%). ^1H NMR (400 MHz, $CDCl_3$) δ 9.19 (br, 1H, CH_{ar}), 8.01 (dd, *J* = 8.5, 1.0 Hz, 1H, CH_{ar}), 7.93 (d, *J* = 8.0 Hz, 1H, CH_{ar}), 7.66 (ddd, *J* = 8.5, 7.0, 1.5 Hz, 1H, CH_{ar}), 7.54 (ddd, *J* = 8.0, 7.0, 1.0 Hz, 1H, CH_{ar}), 5.27 – 5.25 (m, 1H, =C*H*), 5.18 – 5.16 (m, 1H, =C*H*), 2.33 – 2.31 (m, 3H, CH_3), 1.44 (s, 12H, CH_3 x 4). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.9, 152.5, 148.1, 139.3, 130.5, 128.1, 126.7, 126.6 (x2C), 117.0, 84.3, 24.9, 22.4. ^{11}B NMR (128 MHz, $CDCl_3$) δ 32.1 (br). HRMS: *m/z* $[MH]^+$ $C_{18}H_{23}{}^{11}BNO_2$ calcd. 295.1853, found 295.1853. FTIR: ν_{max}/ cm^{-1} (neat) 2978 (m), 1619 (m), 1558 (m), 1495 (m), 1311 (m), 1242 (s), 1135 (s).

*Synthesis of 3-cyclohexenyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)isoquinoline (**85**)*



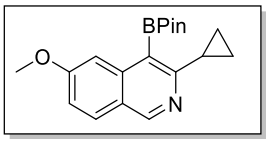
Following general procedure H, using *(E)* 2-(1,2-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-cyclohexenylethenyl)benzaldehyde *O*-methyl oxime (108 mg, 0.22 mmol) in *o*-DCB (2.5 mL) afforded the desired product as a yellow oil (66 mg, 90%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.17 (s, 1H, C*H*$_{ar}$), 8.03 (dd, *J* = 8.5, 1.0 Hz, 1H, C*H*$_{ar}$), 7.90 (br, 1H, C*H*$_{ar}$), 7.64 (ddd, *J* = 8.5, 7.0, 1.5 Hz, 1H, C*H*$_{ar}$), 7.51 (ddd, *J* = 8.0, 7.0, 1.0 Hz, 1H, C*H*$_{ar}$), 5.83 – 5.80 (m, 1H, =C*H*), 2.66 – 2.59 (m, 2H, C*H*$_2$), 2.23 – 2.16 (m, 2H, C*H*$_2$), 1.88 – 1.80 (m, 2H, C*H*$_2$), 1.76 – 1.69 (m, 2H, C*H*$_2$), 1.42 (s, 12H, C*H*$_3$ x 4). ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.9, 152.6, 142.3, 139.5, 130.4, 128.4, 128.1, 126.6, 126.5, 126.3, 84.2, 28.3, 25.8, 25.2, 22.8, 22.1. ^{11}B NMR (128 MHz, $CDCl_3$) δ 31.8 (br). HRMS: *m/z* $[MH]^+$ $C_{21}H_{27}{}^{11}BNO_2$ calcd. 335.2166, found 335.2167. FTIR: ν_{max}/ cm^{-1} (neat) 2978 (m), 1618 (w), 1557 (m), 1494 (m), 1309 (m), 1239 (s), 1134 (s).

*Synthesis of 3-cyclopropyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-6-methylisoquinoline (**87**)*



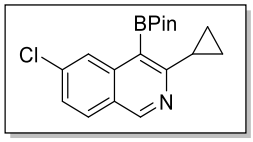
Following general procedure H, using *(E)* 2-(1,2-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-cyclopropylethenyl)-4-methylbenzaldehyde *O*-methyl oxime (23 mg, 0.05 mmol) in *o*-DCB (1 mL) afforded the desired product as a dark yellow oil (9 mg, 58%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.01 (s, 1H, C*H*$_{ar}$), 7.84 (d, *J* = 1.0 Hz, 1H, C*H*$_{ar}$), 7.73 (d, *J* = 8.5 Hz, 1H, C*H*$_{ar}$), 7.28 (dd, *J* = 8.5, 1.0 Hz, 1H, C*H*$_{ar}$), 2.55 – 2.48 (m, 4H, C*H*$_3$ + C*H*), 1.50 (s, 12H, C*H*$_3$ x 4), 1.19 – 1.16 (m, 2H, C*H*$_2$), 1.00 – 0.94 (m, 2H, C*H*$_2$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.5, 153.3, 140.5, 139.8, 127.8, 127.7, 125.3, 124.6, 84.3, 25.0, 22.5, 16.6, 9.8. ^{11}B NMR (128 MHz, $CDCl_3$) δ 32.4 (br). HRMS: *m/z* $[MH]^+$ $C_{19}H_{25}{}^{11}BNO_2$ calcd. 310.1976, found 310.1975. FTIR: ν_{max}/ cm^{-1} (neat) 2976 (m), 1625 (w), 1580 (w), 1496 (m), 1318 (m), 1244 (m), 1138 (s).

*Synthesis of 3-cyclopropyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-6-methoxyisoquinoline (**89**)*



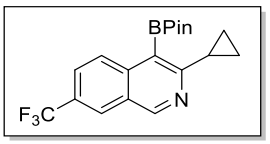
Following general procedure H, using *(E)* 2-(1,2-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-cyclopropylethenyl)-4-methoxybenzaldehyde *O*-methyl oxime (111 mg, 0.23 mmol) in *o*-DCB (2.5 mL) afforded the desired product as a dark yellow oil (51 mg, 68%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.93 (s, 1H, C*H*$_{ar}$), 7.72 (d, *J* = 9.0 Hz, 1H, C*H*$_{ar}$), 7.50 (d, *J* = 2.5 Hz, 1H, C*H*$_{ar}$), 7.08 (dd, *J* = 9.0, 2.5 Hz, 1H, C*H*$_{ar}$), 3.91 (s, 3H, OC*H*$_3$), 2.60 – 2.53 (m, 1H, C*H*), 1.49 (s, 12H, C*H*$_3$ x 4), 1.22 – 1.16 (m, 2H, C*H*$_2$), 1.00 – 0.94 (m, 2H, C*H*$_2$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.5, 161.0, 152.9, 141.6, 129.6, 122.0, 118.3, 104.6, 84.1, 55.2, 25.1, 16.6, 9.9. ^{11}B NMR (128 MHz, $CDCl_3$) δ 32.8 (br). HRMS: *m*/*z* $[MH]^+$ $C_{19}H_{25}{}^{11}BNO_3$ calcd. 326.1625, found 326.1625. FTIR: ν_{max}/ cm^{-1} (neat) 2975 (m), 1619 (s), 1566 (w), 1496 (m), 1317 (m), 1221 (s), 1127 (s).

*Synthesis of 3-cyclopropyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-6-chloroisoquinoline (**88**)*



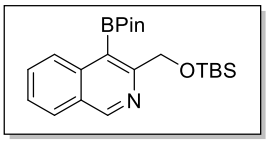
Following general procedure H, using *(E)* 2-(1,2-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-cyclopropylethenyl)-4-chlorobenzaldehyde *O*-methyl oxime (97 mg, 0.2 mmol) in *o*-DCB (2 mL) afforded the desired product as a pale yellow oil (49 mg, 75%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.04 (s, 1H, C*H*$_{ar}$), 8.17 (d, *J* = 2.0 Hz, 1H, C*H*$_{ar}$), 7.77 (d, *J* = 8.5 Hz, 1H, C*H*$_{ar}$), 7.39 (dd, *J* = 8.5, 2.0 Hz, 1H, C*H*$_{ar}$), 2.65 – 2.57 (m, 1H, C*H*), 1.49 (s, 12H, C*H*$_3$ x 4), 1.22 – 1.18 (m, 2H, C*H*$_2$), 1.03 – 0.98 (m, 2H, C*H*$_2$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.3, 153.6, 140.3, 136.6, 129.5, 126.5, 125.6, 124.3, 84.5, 25.0, 16.6, 10.3. ^{11}B NMR (128 MHz, $CDCl_3$) δ 32.4 (br). HRMS: *m*/*z* $[MH]^+$ $C_{18}H_{22}{}^{11}B^{35}ClNO_3$ calcd. 329.1000, found 329.1000. FTIR: ν_{max}/ cm^{-1} (neat) 2976 (m), 1609 (m), 1482 (m), 1371 (m), 1320 (m), 1234 (s), 1136 (s).

*Synthesis of 3-cyclopropyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-7 – trifluoromethylisoquinoline (**90**)*



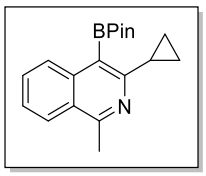
Following general procedure H, using *(E)* 2-(1,2-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-cyclopropylethenyl)-5-trifluoromethylbenzaldehyde *O*-methyl oxime (104 mg, 0.2 mmol) in *o*-DCB (2 mL) afforded the desired product as a dark yellow oil (66 mg, 91%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.16 (s, 1H, CH_{ar}), 8.29 (dd, *J* = 9.0, 0.5 Hz, 1H, CH_{ar}), 8.14 (br, 1H, CH_{ar}), 7.78 (dd, *J* = 9.0, 2.0 Hz, 1H, CH_{ar}), 2.68 – 2.61 (m, 1H, C*H*), 1.49 (s, 12H, CH_3 x 4), 1.25 – 1.21 (m, 2H, CH_2), 1.06 – 1.02 (m, 2H, CH_2). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.7, 154.5, 140.9, 127.7, 127.1 (q, *J* = 65.5 Hz) 125.9, 125.8 (q, *J* = 10.0 Hz), 125.2 (q, *J* = 286.0 Hz) 124.8, 84.5, 25.0, 16.7, 10.6. ^{11}B NMR (128 MHz, $CDCl_3$) δ 32.3 (br). ^{19}F NMR (377 MHz, $CDCl_3$) δ -62.6. HRMS: *m*/*z* $[MH]^+$ $C_{19}H_{22}{}^{11}BF_3NO_2$ calcd. 364.1694, found 364.1692. FTIR: ν_{max}/ cm^{-1} (neat) 2980 (m), 1634 (m), 1566 (w), 1440 (m), 1311 (s), 1122 (s), 850 (s).

*Synthesis of 3-(tert-butyldimethylsiloxymethyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)isoquinoline (**92**)*



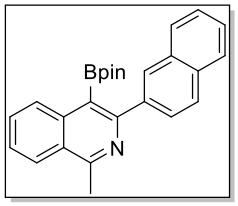
Following general procedure H stirring at 180 °C for 16 h, using *(E)* 2-(1,2-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-(3-tert-butyldimethylsiloxy-1-propenyl)benzaldehyde *O*-methyl oxime (55 mg, 0.1 mmol) in *o*-DCB (1 mL) afforded the desired product as a colorless oil (25 mg, 63%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.20 (s, 1H, CH_{ar}), 8.22 (dd, *J* = 8.5, 1.0 Hz, 1H, CH_{ar}), 7.92 (d, *J* = 8.0 Hz, 1H, CH_{ar}), 7.66 (ddd, *J* = 8.5, 7.0, 1.5 Hz, 1H, CH_{ar}), 7.54 (ddd, *J* = 8.0, 7.0, 1.0 Hz, 1H, CH_{ar}), 5.10 (s, 2H, CH_2), 1.49 (s, 12H, CH_3 x 4), 0.88 (s, 9H, C(CH_3)$_3$), 0.04 (s, 6H, Si(CH_3)$_2$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.0, 153.0, 151.7, 139.6, 130.4, 128.0, 127.0, 126.6, 84.3, 67.7, 26.1, 25.1, 18.6, -4.8. ^{11}B NMR (128 MHz, $CDCl_3$) δ 31.5 (br). HRMS: *m*/*z* $[MH]^+$ $C_{22}H_{35}{}^{11}BNO_3Si$ calcd. 400.2478, found 400.2478. FTIR: ν_{max}/ cm^{-1} (neat) 2987 (m), 1620 (w), 1571 (w), 1373 (m), 1238 (m), 1077 (m).

*Synthesis of 3-cyclopropyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1 –methylisoquinoline (**94**)*



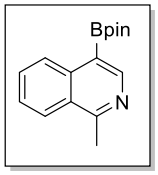
Following general procedure H, using *(E)* 2-(1,2-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-cyclopropylethenyl)benzophenone *O*-methyl oxime (110 mg, 0.24 mmol) in *o*-DCB (2.5 mL) afforded the desired product as a bright yellow foam (61 mg, 84%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (d, *J* = 8.5 Hz, 1H, C*H*$_{ar}$), 8.01 (d, *J* = 8.5 Hz, 1H, C*H*$_{ar}$), 7.60 – 7.56 (m, 1H, C*H*$_{ar}$), 7.45 – 7.40 (m, 1H, C*H*$_{ar}$), 2.84 (s, 3H, C*H*$_3$), 2.57 – 2.49 (m, 1H, C*H*), 1.48 (s, 12H, C*H*$_3$ x 4), 1.21 – 1.17 (m, 2H, C*H*$_2$), 0.95 – 0.89 (m, 2H, C*H*$_2$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.7, 159.4, 139.6, 129.7, 126.9, 125.7, 125.1 (x2C), 84.1, 25.0, 22.8, 16.5, 9.5. ^{11}B NMR (128 MHz, $CDCl_3$) δ 32.7 (br). HRMS: *m/z* $[MH]^+$ $C_{19}H_{25}BNO_2$ calcd. 310.1976, found 310.1977. FTIR: ν_{max}/ cm^{-1} (neat) 2976 (m), 1614 (w), 1502 (m), 1439 (m), 1252 (s), 1138 (s).

*Synthesis of 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3 –(naphtalene-2-yl)-1-methylisoquinoline (**95**)*



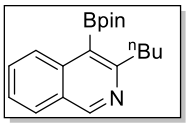
Following general procedure H, using *(E)*-1-(2-((Z)-2-(naphthalen-2-yl)-1,2-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)vinyl)phenyl)ethan-1-one O-methyl oxime (100 mg, 0.2 mmol) in *o*-DCB (2 mL) afforded the desired product as a dark yellow oil (68 mg, 95%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 – 8.13 (m, 3H, C*H*$_{ar}$), 7.96 – 7.92 (m, 2H, C*H*$_{ar}$), 7.91 – 7.86 (m, 2H, C*H*$_{ar}$), 7.74 – 7.68 (m, 1H, C*H*$_{ar}$), 7.63 – 7.57 (m, 1H, C*H*$_{ar}$), 7.52 – 7.46 (m, 2H, C*H*$_{ar}$), 3.05 (s, 3H, C*H*$_3$), 1.22 (s, 12H, C*H*$_3$ x4). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.4, 139.5, 133.1, 130.3, 128.6 (x2 C), 128.3 (x2 C), 128.0, 127.8, 127.5 (x2 C), 126.6, 126.0 (x3 C), 125.4 (x2 C), 84.3, 25.0, 22.7. ^{11}B NMR (128 MHz, $CDCl_3$) δ 31.4 (br). HRMS: *m/z* $[MH]^+$ $C_{26}H_{27}{}^{11}BNO_2$ calcd. 396.2134, found 396.2135. FTIR: ν_{max}/ cm^{-1} (neat) 2977 (m), 2103 (w), 1570 (m), 1505 (m), 1312 (m), 1257 (s), 1139 (s).

*Synthesis of 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)- 1-methylisoquinoline (**93**)*



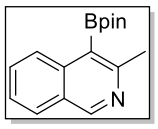
Following general procedure H, using *(E)*-1-(2-((Z)-1,2-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)vinyl)phenyl)ethan-1-one *O*-methyl oxime (115 mg, 0.27 mmol) in *o*-DCB (3 mL) afforded the desired product as a white foam (53 mg, 73%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.83 (s, 1H, C*H*$_{ar}$), 8.69 (d, *J* = 8.5 Hz, 1H, C*H*$_{ar}$), 8.13 (d, *J* = 8.5 Hz, 1H, C*H*$_{ar}$), 7.71 (ddd, *J* = 8.5, 7.0, 1.0 Hz, 1H, C*H*$_{ar}$), 7.60 – 7.56 (m, 1H, C*H*$_{ar}$), 2.98 (s, 3H, C*H*$_3$), 1.42 (s, 12H, C*H*$_3$ x4). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.8, 150.4, 139.2, 130.3, 128.1, 126.9, 126.6, 125.7, 83.9, 25.0, 22.9. ^{11}B NMR (160 MHz, $CDCl_3$) δ 31.5 (br). HRMS: *m*/*z* $[MH]^+$ $C_{16}H_{21}{}^{11}BNO_2$ calcd. 270.1665, found 270.1656. FTIR: ν_{max}/ cm^{-1} (neat): 2990 (m), 1573 (w), 1356 (s), 1123 (s).

*Synthesis of 3-butyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)isoquinoline (**152**)*



Following general procedure H, using *(E)* 2-(1,2-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hex-1-en-1-yl) benzaldehyde *O*-methyl oxime (4.3 g, 9.2 mmol) in *o*-DCB (90 mL) afforded the desired product as a dark orange oil (2.32 g, 81%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.18 (s, 1H, C*H*$_{ar}$), 8.11 (d, *J* = 8.5 Hz, 1H, C*H*$_{ar}$), 7.87 (d, *J* = 8.0 Hz, 1H, C*H*$_{ar}$), 7.66 – 7.60 (m, 1H, C*H*$_{ar}$), 7.48 (t, *J* = 7.5 Hz, 1H, C*H*$_{ar}$), 3.10 – 3.04 (m, 2H, C*H*$_2$), 1.81 – 1.71 (m, 2H, C*H*$_2$), 1.46 (s, 12H, C*H*$_3$ x4), 1.45 – 1.38 (m, 2H, C*H*$_2$), 0.94 (t, *J* = 7.5 Hz, 3H, C*H*$_3$).^{13}C NMR (101 MHz, $CDCl_3$) δ 160.8, 153.3, 139.8, 130.5, 128.1, 126.7, 126.1 (x 2C), 84.3, 38.5, 33.8, 25.0, 23.0, 14.1. ^{11}B NMR (128 MHz, $CDCl_3$) δ 32.3 (br). HRMS: *m*/*z* $[MH]^+$ $C_{19}H_{27}{}^{11}BNO_2$ calcd. 312.2129, found 312.2136. FTIR: ν_{max}/ cm^{-1} (neat) 2957 (m), 1562 (m), 1496 (m), 1314 (m), 1237 (m), 1144 (s).

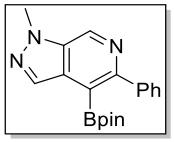
*Synthesis of 3-methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)isoquinoline (**153**)*



Following general procedure H, using *(E)* 2-(1,2-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)prop-1-en-1-yl) benzaldehyde *O*-methyl oxime (10.8 g, 25.3 mmol) in *o*-DCB (250 mL) afforded the desired product as a dark orange foam (6.1 g, 90%). ^{1}H NMR (400 MHz, $CDCl_3$) δ

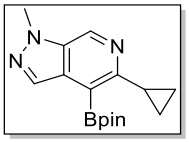
9.15 (s, 1H, C*H*$_{ar}$), 8.15 (d, *J* = 8.5 Hz, 1H, C*H*$_{ar}$), 7.88 (d, *J* = 8.0 Hz, 1H, C*H*$_{ar}$), 7.64 (ddd, *J* = 8.5, 7.0, 1.5 Hz, 1H, C*H*$_{ar}$), 7.49 (t, *J* = 7.5 Hz, 1H, C*H*$_{ar}$), 2.83 (s, 3H, C*H*$_3$), 1.47 (s, 12H, C*H*$_3$ x 4). ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.9, 153.3, 139.7, 130.5, 128.1, 126.6, 126.1, 126.0, 84.3, 25.0, 24.6. ^{11}B NMR (160 MHz, $CDCl_3$) δ 32.3 (br). HRMS: *m/z* $[MH]^+$ $C_{16}H_{21}{}^{11}BNO_2$ calcd. 300.1383, found 300.1381. FTIR: ν_{max}/ cm^{-1} (neat): 2976 (m), 1574 (m), 1454 (m), 1324 (m), 1133 (s).

*Synthesis of 1-methyl-5-phenyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazolo[3,4-c]pyridine (**139**)*



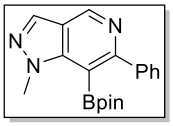
Following general procedure H, using *(E)*-1-methyl-4-((*Z*)-2-phenyl-1,2-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)vinyl)-1*H*-pyrazole-5-carbaldehyde *O*-methyl oxime (2.5 g, 5.0 mmol) in *o*-DCB (50 mL) afforded the desired product as a yellow foam (1.6 g, 93%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.02 (s, 1H, C*H*$_{ar}$), 8.23 (s, 1H, C*H*$_{ar}$), 7.68 – 7.63 (m, 2H, C*H*$_{ar}$), 7.45 – 7.36 (m, 3H, C*H*$_{ar}$), 4.21 (s, 3H, NC*H*$_3$), 1.32 (s, 12H, C*H*$_3$ x3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.6, 142.2, 134.6, 134.0, 133.9, 133.1, 129.7, 127.9, 127.8, 84.4, 36.1, 24.8. ^{11}B NMR (128 MHz, $CDCl_3$) δ 31.6 (br). HRMS: *m/z* $[MH]^+$ $C_{19}H_{23}{}^{11}BN_3O_2$ calcd. 336.1878, found 336.1888. FTIR: ν_{max}/ cm^{-1} (neat): 2971 (m), 1725 (w), 1562 (m), 1451 (s), 1319 (m), 1195 (s), 1070 (s).

*Synthesis of 5-cyclopropyl-1-methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazolo[3,4-c]pyridine (**140**)*



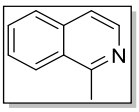
Following general procedure H, using *(E)*-1-methyl-4-((*Z*)-2-cyclopropyl-1,2-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)vinyl)-1*H*-pyrazole-5-carbaldehyde *O*-methyl oxime (2.4 g, 5.3 mmol) in *o*-DCB (55 mL) afforded the desired product as a white foam (1.3 g, 85%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.80 (s, 1H, C*H*$_{ar}$), 8.25 (s, 1H, C*H*$_{ar}$), 4.09 (s, 3H, NC*H*$_3$), 3.00 – 2.91 (m, 1H, C*H*), 1.41 (s, 12H, C*H*$_3$ x4), 1.10 – 1.07 (m, 2H, C*H*$_2$), 0.98 – 0.93 (m, 2H, C*H*$_2$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.6, 134.8, 134.4, 134.0, 133.5, 83.9, 35.8, 25.0, 15.3, 10.1. ^{11}B NMR (128 MHz, $CDCl_3$) δ 31.5 (br). HRMS: *m/z* $[MH]^+$ $C_{16}H_{23}{}^{11}BN_3O_2$ calcd. 300.1878, found 300.1886. FTIR: ν_{max}/ cm^{-1} (neat): 2975 (m), 1566 (m), 1475 (m), 1369 (m), 1326 (m), 1217 (m), 1122 (s), 1057 (s).

*Synthesis of 1-methyl-6-phenyl-7-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazolo[4,3-c]pyridine (**141**)*



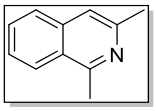
Following general procedure H, using *(E)*-1-methyl-5-((*Z*)-2-phenyl-1,2-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)vinyl)-1*H*-pyrazole-4-carbaldehyde *O*-methyl oxime (56 mg, 0.11 mmol) in *o*-DCB (1.5 mL) afforded the desired product as a brown foam (25 mg, 66%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.05 (s, 1H, C*H*$_{ar}$), 8.24 (s, 1H, C*H*$_{ar}$), 7.69 – 7.62 (m, 2H, C*H*$_{ar}$), 7.44 – 7.36 (m, 3H, C*H*$_{ar}$), 4.20 (s, 3H, NC*H*$_3$), 1.31 (s, 12H, C*H*$_3$ x4). ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.5, 141.9, 134.6, 134.0, 133.8, 133.2, 129.7, 127.9, 127.8, 84.4, 36.2, 24.8. ^{11}B NMR (128 MHz, $CDCl_3$) δ 31.5 (br). HRMS: *m/z* $[MH]^+$ $C_{19}H_{23}{}^{11}BN_3O_2$ calcd. 336.1878, found 336.1886. FTIR: ν_{max}/ cm^{-1} (neat): 2929 (w), 1563 (m), 1451 (m), 1359 (m), 1316 (m), 1216 (m), 1128 (s).

Synthesis of 1-methylisoquinoline[94] *(**149**)*



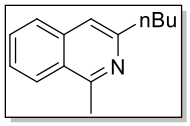
Following general procedure H, using *(E)*-1-(2-vinylphenyl)ethan-1-one *O*-methyl oxime (100 mg, 0.57 mmol) in *o*-DCB (5 mL) afforded the desired product as a yellow oil (82 mg, 54%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40 (d, *J* = 6.0 Hz, 1H, C*H*$_{ar}$), 8.13 (d, *J* = 8.5 Hz, 1H, C*H*$_{ar}$), 7.81 (d, *J* = 8.0 Hz, 1H, C*H*$_{ar}$), 7.71 – 7.65 (m, 1H, C*H*$_{ar}$), 7.63 – 7.58 (m, 1H, C*H*$_{ar}$), 7.51 (d, *J* = 6.0 Hz, 1H, C*H*$_{ar}$), 2.97 (s, 3H, C*H*$_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.6, 141.8, 135.9, 130.0, 127.5, 127.2, 127.0, 125.7, 119.3, 22.4.

Synthesis of 1,3-dimethylisoquinoline[94] *(**150**)*



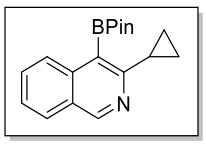
Following general procedure H, using *(E)*-1-(2-((E)-prop-1-en-1-yl)phenyl)ethan-1-one *O*-methyl oxime (100 mg, 0.53 mmol) in *o*-DCB (5 mL) afforded the desired product as a clear yellow oil (69 mg, 83%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (dd, *J* = 8.5, 1.0 Hz, 1H, C*H*$_{ar}$), 7.71 (d, *J* = 8.0 Hz, 1H), 7.63 (ddd, *J* = 8.5, 7.0, 1.5 Hz, 1H, C*H*$_{ar}$), 7.52 (ddd, *J* = 8.0, 7.0, 1.0 Hz, 1H), 7.35 (s, 1H), 2.96 (s, 3H), 2.67 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.1, 150.1, 136.8, 130.0, 126.6, 126.1, 125.6, 125.6, 117.3, 24.1, 22.2.

Synthesis of 3-butyl-1-methylisoquinoline[94] ***(151)***



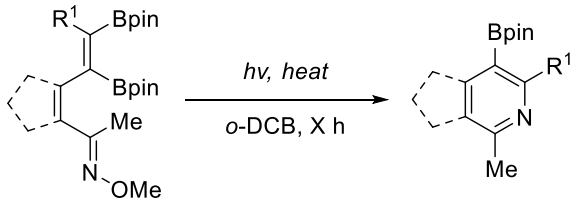
Following general procedure H, using *(E)*-1-(2-((Z)-hex-1-en-1-yl)phenyl)ethan-1-one *O*-methyl oxime (50 mg, 0.22 mmol) in *o*-DCB (3 mL) afforded the desired product as a pale yellow oil (73 mg, 58%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, *J* = 8.5 Hz, 1H), 7.73 (d, *J* = 8.0 Hz, 1H), 7.65 – 7.60 (m, 1H), 7.54 – 7.49 (m, 1H), 7.33 (s, 1H), 2.98 (s, 3H), 2.95 – 2.90 (m, 2H), 1.85 – 1.75 (m, 2H), 1.49 – 1.39 (m, 2H), 0.97 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.1, 154.6, 136.7, 129.8, 126.8, 126.1, 125.9, 125.6, 116.6, 38.0, 32.2, 22.6, 22.5, 14.1.

***General procedure I: Two steps/one pot reaction to obtain isoquinoline derivatives*.**



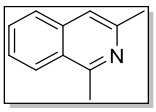
B_2pin_2 (640 mg, 2.5 mmol) was added to a stirred solution of 2-(2-cyclopropylethynyl)benzaldehyde *O*-methyl oxime (456 mg, 2.3 mmol) in toluene (15 mL). Then $Pt(PPh_3)_4$ (132 mg, 0.12 mmol) was added and the reaction was stirred at 120 °C for 1 h. The reaction mixture was allowed to cool to room temperature and *o*-DCB was added (30 mL). The reaction mixture was stirred at 200 °C for 16 h. The reaction mixture was allowed to cool to room temperature and was filtered through silica gel. The residue was purified by flash column chromatography on silica gel eluting with petroleum ether (40/60) and ethyl acetate to afford 3-cyclopropyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)isoquinoline (480 mg, 71%) as an orange oil. The compound showed identical spectroscopic to data to that described earlier.

General procedure J



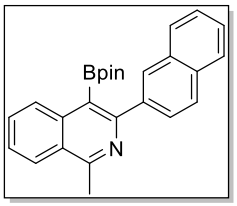
A solution of triene derivative in *o*-DCB (0.1 M) was stirred under a high pressure 300 W ultraviolet lamp for X hours. The reaction mixture was allowed to cool to room temperature and was filtered through silica gel. The residue was purified by flash column chromatography on silica gel eluting with petroleum ether (40/60) and ethyl acetate to afford the corresponding isoquinolines.

Synthesis of 1,3-dimethylisoquinoline[94] ***(150)***



Following general procedure J, using *(Z)*-1-(2-((E)-prop-1-en-1-yl)phenyl)ethan-1-one *O*-methyl oxime (40 mg, 0.21 mmol) in *o*-DCB (2.5 mL) afforded the desired product as a clear yellow oil (17 mg, 51%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (dd, *J* = 8.5, 1.0 Hz, 1H, C*H*$_{ar}$), 7.71 (d, *J* = 8.0 Hz, 1H), 7.63 (ddd, *J* = 8.5, 7.0, 1.5 Hz, 1H, C*H*$_{ar}$), 7.52 (ddd, *J* = 8.0, 7.0, 1.0 Hz, 1H), 7.35 (s, 1H), 2.96 (s, 3H), 2.67 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.1, 150.1, 136.8, 130.0, 126.6, 126.1, 125.6, 125.6, 117.3, 24.1, 22.2.

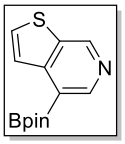
*Synthesis of 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3 –(naphtalene-2-yl)-1-methylisoquinoline (**95**)*



Following general procedure J, using *(Z)*-1-(2-((Z)-2-(naphthalen-2-yl)-1,2-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)vinyl)phenyl)ethan-1-one O-methyl oxime (140 mg, 0.25 mmol) in *o*-DCB (2.5 mL) afforded the desired product as a dark yellow oil (52 mg, 52%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 – 8.13 (m, 3H, C*H*$_{ar}$), 7.96 – 7.92 (m, 2H, C*H*$_{ar}$), 7.91 – 7.86 (m, 2H, C*H*$_{ar}$), 7.74 – 7.68 (m, 1H, C*H*$_{ar}$), 7.63 – 7.57 (m, 1H, C*H*$_{ar}$), 7.52 – 7.46 (m, 2H, C*H*$_{ar}$), 3.05 (s, 3H,

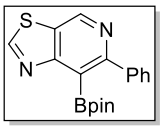
C*H*$_3$), 1.22 (s, 12H, C*H*$_3$ x4). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.4, 139.5, 133.1, 130.3, 128.6 (x2 C), 128.3 (x2 C), 128.0, 127.8, 127.5 (x2 C), 126.6, 126.0 (x3 C), 125.4 (x2 C), 84.3, 25.0, 22.7. ^{11}B NMR (128 MHz, $CDCl_3$) δ 31.4 (br). HRMS: *m/z* $[MH]^+$ $C_{26}H_{27}{}^{11}BNO_2$ calcd. 396.2134, found 396.2135. FTIR: ν_{max}/ cm^{-1} (neat) 2977 (m), 2103 (w), 1570 (m), 1505 (m), 1312 (m), 1257 (s), 1139 (s).

*Synthesis of 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)thieno[3,2-c]pyridine (**134**)*



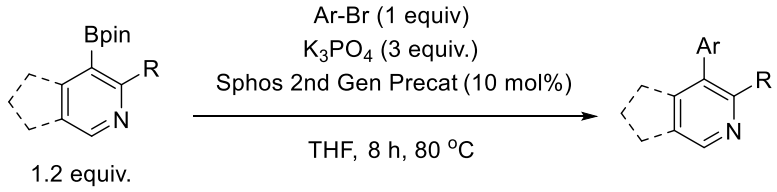
Following general procedure J, using *(Z)*-3-((*E*)-1,2-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)vinyl)thiophene-2-carbaldehyde *O*-methyl oxime (90 mg, 0.54 mmol) in o-DCB (5.5 mL) afforded the cyclised product as a pale orange oil (40 mg, 71%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.21 (s, 1H, C*H*$_{ar}$), 8.88 (s, 1H, C*H*$_{ar}$), 7.96 (d, *J* = 5.5,Hz, 1H, C*H*$_{ar}$), 7.74 (d, *J* = 5.5 Hz, 1H, C*H*$_{ar}$), 1.40 (s, 12H, C*H*$_3$ x4). ^{13}C NMR (101 MHz, $CDCl_3$) δ 150.1, 149.2, 146.9, 136.0, 132.2, 125.3, 84.2, 25.0. ^{11}B NMR (160 MHz, $CDCl_3$) δ 31.0 (br). HRMS: *m/z* $[MH]^+$ $C_{13}H_{17}{}^{11}BNO_2S$ calcd. 262.1073, found 262.1063. FTIR: ν_{max}/ cm^{-1} (neat): 3073 (m), 2974 (m), 1594 (w), 1401 (m), 1181 (s), 1034 (s).

*Synthesis of 6-phenyl-7-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)thiazolo[5,4-c]pyridine (**137**)*



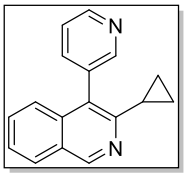
Following general procedure J, using *(E)*-4-(phenylethynyl)thiazole-5-carbaldehyde *O*-methyl oxime (50 mg, 0.21 mmol), B_2Pin_2 (59 mg, 0.23 mmol) and $Pt(PPh_3)_4$ (26 mg, 0.02 mmol) in toluene (2.0 mL). Subsequent addition of *o*-DCB (4 mL) to this mixture and cyclisation following general procedure E afforded the cyclised product as a yellow oil (42 mg, 60%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.33 (s, 1H, C*H*$_{ar}$), 9.21 (s, 1H, C*H*$_{ar}$), 7.82 (br, 2H, C*H*$_{ar}$), 7.48 – 7.39 (m, 3H, C*H*$_{ar}$), 1.35 (s, 12H, C*H*$_3$ x4). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.6, 159.0, 158.9, 144.5, 141.8, 129.1, 128.5, 128.4, 128.1, 84.9, 24.8. ^{11}B NMR (128 MHz, $CDCl_3$) δ 31.8 (br). HRMS: *m/z* $[MH]^+$ $C_{18}H_{20}{}^{11}BN_2O_2S$ calcd. 339.1333, found 339.1443. FTIR: ν_{max}/ cm^{-1} (neat): 2978 (m), 1534 (m), 1453 (m), 1380 (s), 1270 (s), 1140 (s), 1083 (m).

General procedure K



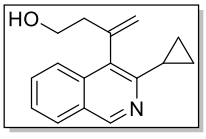
A vial was equipped with a magnetic stirring bar and charged with Sphos 2nd Generation precatalyst (10 mol%), the boronic ester derivative (1.2 equiv) and the aryl bromide (1 equiv.). Then, K_3PO_4 (3 equiv.) was added followed by the immediate addition of THF. The reaction mixture was allowed to stir at 80 °C for 16 h. At this point, water was added to the mixture, and the aqueous phase was extracted with dichloromethane. The organic phase was dried over anhydrous $MgSO_4$, filtered and the solvent was removed *in vacuo*. The residue was purified by flash column chromatography on silica gel eluting with heptanes and ethyl acetate to afford the corresponding isoquinolines.

*Synthesis of 3-cyclopropyl-4-(pyridin-3-yl)isoquinoline (A-**01**)*



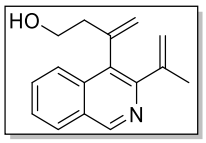
Following general procedure K, using 3-cyclopropyl-4-(4,4,5,5,-tetramethyl-1,3,2-dioxaborolan-2-yl)isoquinoline (67 mg, 0.23 mmol), 3-bromopyridine (30 mg, 0.19 mmol), K_3PO_4 (125 mg, 0.57 mmol) and Sphos 2nd Generation precatalyst (14 mg, 0.02 mmol) in THF (1.5 mL), the desired product was isolated as a yellow oil (42 mg, 90%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.16 (s, 1H, CH_{ar}), 8.72 (dd, *J* = 5.0, 1.5 Hz, 1H, CH_{ar}), 8.68 (d, *J* = 1.5 Hz, 1H, CH_{ar}), 7.94 (d, *J* = 8.0 Hz, 1H, CH_{ar}), 7.76 (dt, *J* = 8.0, 1.5 Hz, 1H, CH_{ar}), 7.54 (ddd, *J* = 8.5, 7.0, 1.5 Hz, 1H, CH_{ar}), 7.51 – 7.45 (m, 2H, CH_{ar}), 7.31 (d, *J* = 8.5 Hz, 1H, CH_{ar}), 1.83 – 1.76 (m, 1H, C*H*), 1.22 – 1.17 (m, 2H, CH_2), 0.91 – 0.81 (m, 2H, CH_2). ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.3, 152.5, 151.5, 148.9, 138.3, 135.5, 133.4, 130.6, 127.7, 126.4, 125.9, 125.9, 124.0, 123.5, 14.6, 10.0, 9.9. HRMS: *m/z* $[MH]^+$ $C_{17}H_{15}N_2$ calcd. 247.1230, found 247.1234. FTIR: ν_{max}/ cm^{-1} (neat): 3002 (w), 1617 (m), 1571 (m), 1452 (m), 1045 (s).

Synthesis of 3-(3-cyclopropylisoquinolin-4-yl)but-3-en-1-ol



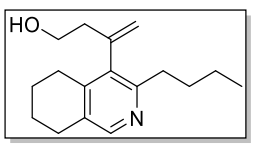
Following general procedure K, using 3-cyclopropyl-4-(4,4,5,5,-tetramethyl-1,3,2-dioxaborolan-2-yl)isoquinoline (117 mg, 0.40 mmol), 3-bromobut-3-en-1-ol (50 mg, 0.33 mmol), K_3PO_4 (217 mg, 1.0 mmol) and Sphos 2nd Generation precatalyst (24 mg, 0.03 mmol) in THF (3.3 mL), the desired product was isolated as a yellow oil (75 mg, 95%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.05 (s, 1H, C*H*$_{ar}$), 7.89 – 7.85 (m, 2H, C*H*$_{ar}$), 7.62 (ddd, *J* = 8.5, 7.0, 1.0 Hz, 1H, C*H*$_{ar}$), 7.47 (t, *J* = 7.5 Hz, 1H, C*H*$_{ar}$), 5.69 (d, *J* = 1.5 Hz, 1H, =CH*H*), 5.25 (d, *J* = 1.5 Hz, 1H, =CH*H*), 3.83 – 3.69 (m, 2H, C*H*$_2$), 2.87 – 2.68 (m, 2H, C*H*$_2$), 2.34 (tt, *J* = 8.0, 5.0 Hz, 1H, C*H*), 1.33 – 1.23 (m, 1H, CH*H*), 1.14 – 1.07 (m, 1H, CH*H*), 1.01 – 0.92 (m, 2H, C*H*$_2$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 151.4, 151.2, 142.2, 134.6, 130.4, 130.2, 127.7, 126.5, 125.7, 124.1, 119.0, 60.6, 41.5, 14.0, 10.1, 9.3. HRMS: *m*/*z* $[MH]^+$ $C_{16}H_{18}NO$ calcd. 240.1383, found 240.1386. FTIR: ν_{max}/ cm^{-1} (neat): 3322 (br), 3003 (w), 1619 (m), 1574 (m), 1422 (m), 1045 (s).

Synthesis of 3-(3-(prop-1-en-2-yl)isoquinolin-4-yl)but-3-en-1-ol



Following general procedure K, using 3-(prop-1-en-2-yl)-4-(4,4,5,5,-tetramethyl-1,3,2-dioxaborolan-2-yl)isoquinoline (117 mg, 0.40 mmol), 3-bromobut-3-en-1-ol (50 mg, 0.33 mmol), K_3PO_4 (217 mg, 0.99 mmol) and Sphos 2nd Generation precatalyst (24 mg, 0.03 mmol) in THF (3.3 mL), the desired product was isolated as a yellow oil (55 mg, 69%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.08 (s, 1H, C*H*$_{ar}$), 8.02 – 7.97 (m, 1H, C*H*$_{ar}$), 7.87 (d, *J* = 8.0 Hz, 1H, C*H*$_{ar}$), 7.59 (ddd, *J* = 8.5, 7.0, 1.5 Hz, 1H, C*H*$_{ar}$), 7.49 (ddd, *J* = 8.0, 7.0, 1.0 Hz, 1H, C*H*$_{ar}$), 5.59 (d, *J* = 1.5 Hz, 1H, =CH*H*), 5.31 – 5.28 (br, 1H, =CH*H*), 5.19 (d, *J* = 1.0 Hz, 1H, =CH*H*), 5.14 (br, 1H, =CH*H*), 3.66 – 3.58 (m, 2H, C*H*$_2$), 2.60 (t, *J* = 6.5 Hz, 2H, C*H*$_2$), 2.16 (s, 3H, C*H*$_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 151.4, 150.9, 144.9, 141.8, 135.2, 130.5, 130.1, 127.7, 127.3, 126.7, 125.2, 119.9, 117.9, 60.4, 41.1, 23.5. HRMS: *m*/*z* $[MH]^+$ $C_{16}H_{18}NO$ calcd. 240.1383, found 240.1386. FTIR: ν_{max}/ cm^{-1} (neat): 3320 (br), 2921 (br), 1616 (w), 1376 (m), 1139 (m), 1040 (s).

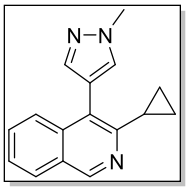
Synthesis of 3-(3-butyl-5,6,7,8-tetrahydroisoquinolin-4-yl)but-3-en-1-ol



Following general procedure K, using 3-butyl-4-(4,4,5,5,-tetramethyl-1,3,2-dioxaborolan-2-yl)-5,6,7,8-tetrahydroisoquinoline (125 mg, 0.40 mmol), 3-bromobut-3-en-1-ol (50 mg, 0.33 mmol), K_3PO_4 (217 mg, 0.99 mmol) and Sphos 2nd Generation precatalyst (24 mg, 0.03 mmol)

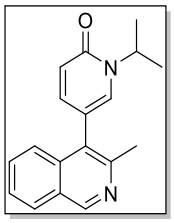
in THF (3.3 mL), the desired product was isolated as a yellow oil (53 mg, 62%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (s, 1H, C*H*$_{ar}$), 5.37 (br, 1H, -CH*H*), 4.93 (br, 1H, -CH*H*), 3.85 – 3.75 (m, 2H, C*H*$_2$), 2.74 – 2.57 (m, 6H, C*H*$_2$ x3), 2.49 (t, *J* = 6.5 Hz, 2H, C*H*$_2$), 1.74 (s, 4H, C*H*$_2$ x2), 1.67 – 1.59 (m, 2H, C*H*$_2$), 1.39 – 1.29 (m, 2H, C*H*$_2$), 0.89 (t, *J* = 7.5 Hz, 3H, C*H*$_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.6, 148.3, 143.7, 143.1, 136.2, 129.9, 116.2, 60.3, 40.3, 34.9, 32.7, 26.7, 26.5, 23.0, 22.8, 22.4, 14.0. HRMS: *m/z* $[MH]^+$ $C_{17}H_{26}NO$ calcd. 260.2009, found 260.2012. FTIR: ν_{max}/ cm^{-1} (neat): 3350 (br), 2928 (s), 1636 (w), 1450 (m), 1248 (m), 1112 (m), 1051 (s).

*Synthesis of 3-cyclopropyl-4-(1-methyl-1H-pyrazol-4-yl)isoquinoline (A-**18**)*



Following general procedure K, using 3-cyclopropyl-4-(4,4,5,5,-tetramethyl-1,3,2-dioxaborolan-2-yl)isoquinoline (105 mg, 0.35 mmol), 4-bromo-1-methyl-1H-pyrazole (50 mg, 0.30 mmol), K_3PO_4 (194 mg, 0.89 mmol) and Sphos 2nd Generation precatalyst (22 mg, 0.03 mmol) in THF (3.0 mL), the desired product was isolated as a yellow oil (47 mg, 64%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.64 (s, 1H, C*H*$_{ar}$), 8.31 (d, *J* = 8.0 Hz, 1H, C*H*$_{ar}$), 8.05 – 7.97 (m, 1H, C*H*$_{ar}$), 7.93 (d, *J* = 8.5 Hz, 1H, C*H*$_{ar}$), 7.87 – 7.81 (m, 1H, C*H*$_{ar}$), 7.72 (s, 1H, C*H*$_{ar}$), 7.67 (s, 1H, C*H*$_{ar}$), 4.12 (s, 3H, NC*H*$_3$), 2.28 (tt, *J* = 8.5, 5.5 Hz, 1H, C*H*), 1.34 – 1.26 (m, 2H, C*H*$_2$), 1.23 – 1.16 (m, 2H, C*H*$_2$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 146.4, 146.1, 139.9, 139.2, 136.6, 131.2, 130.4, 129.8, 128.5, 125.8, 125.4, 113.2, 39.3, 13.6, 10.3 (x 2C). HRMS: *m/z* $[MH]^+$ $C_{16}H_{16}N_3$ calcd. 250.1339, found 250.1339. FTIR: ν_{max}/ cm^{-1} (neat): 2722 (br), 1675 (s), 1565 (m), 1380 (m), 1127 (s).

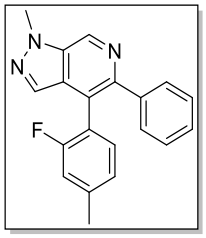
Synthesis of 1-isopropyl-5-(3-methylisoquinolin-4-yl)pyridin-2(1H)-one



Following general procedure K, using 3-methyl-4-(4,4,5,5,-tetramethyl-1,3,2-dioxaborolan-2-yl)isoquinoline (120 mg, 0.44 mmol), 5-bromo-1-isopropylpyridin-2(1H)-one (80 mg, 0.37 mmol), K_3PO_4 (243 mg, 1.10 mmol) and Sphos 2nd Generation precatalyst (27 mg, 0.04 mmol) in THF (3.7 mL), the desired product was isolated as a yellow oil (94 mg, 91%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.73 (s, 1H, C*H*$_{ar}$), 8.37 (d, *J* = 8.0 Hz, 1H, C*H*$_{ar}$), 8.06 (ddd, *J* = 8.5, 7.0, 1.0 Hz, 1H, C*H*$_{ar}$), 7.91 (t, *J* = 7.5 Hz, 1H, C*H*$_{ar}$), 7.77 (d, *J* = 8.5 Hz, 1H, C*H*$_{ar}$), 7.44 (d, *J* = 2.5 Hz, 1H, C*H*$_{ar}$), 7.35 (dd, *J* = 9.5, 2.5 Hz, 1H, C*H*$_{ar}$), 6.94 (d, *J* = 9.5 Hz, 1H, C*H*$_{ar}$), 5.45 – 5.35 (m, 1H, C*H*), 2.77 (s,

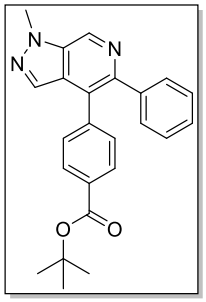
3H, C*H*$_3$), 1.43 (dd, *J* = 7.0, 2.5 Hz, 6H, C*H*$_3$ x 2). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.0, 147.1, 142.5, 140.4, 138.8, 136.8, 134.3, 131.4, 130.7, 130.1, 126.4, 124.8, 121.4, 113.1, 48.1, 22.1, 22.0, 18.3. HRMS: *m/z* $[MH]^+$ $C_{18}H_{19}N_2O$ calcd. 279.1492, found 279.1497. FTIR: ν_{max}/ cm^{-1} (neat): 2548 (br), 1658 (s), 1385 (m), 1132 (s).

*Synthesis of 4-(2-fluoro-4-methylphenyl)-1-methyl-5-phenyl-1H-pyrazolo[3,4-c]pyridine (E-**01**)*



Following general procedure K, using 1-methyl-5-phenyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-pyrazolo[3,4-c]pyridine (106 mg, 0.32 mmol), 1-bromo-2-fluoro-4-methylbenzene (50 mg, 0.26 mmol), K_3PO_4 (168 mg, 0.79 mmol) and Sphos 2nd Generation precatalyst (19 mg, 0.03 mmol) in THF (2.6 mL), the desired product was isolated as a yellow oil (60 mg, 72%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.04 (s, 1H, C*H*$_{ar}$), 7.82 (s, 1H, C*H*$_{ar}$), 7.44 – 7.38 (m, 2H, C*H*$_{ar}$), 7.28 – 7.22 (m, 3H, C*H*$_{ar}$), 7.10 (br, 1H, C*H*$_{ar}$), 6.94 – 6.89 (m, 2H, C*H*$_{ar}$), 4.23 (s, 3H, NC*H*$_3$), 2.37 (s, 3H, C*H*$_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.6 (d, , $^1J_{C\text{-}F}$ = 247.5 Hz), 147.6, 140.6 (d, $^3J_{C\text{-}F}$ = 8.0 Hz), 140.3, 135.8, 132.8, 132.5, 131.7 (d, $^4J_{C\text{-}F}$ = 4.0 Hz), 129.8, 129.7, 127.9, 127.2, 125.1 (d, $^4J_{C\text{-}F}$ = 3.0 Hz), 121.7 (d, $^2J_{C\text{-}F}$ = 16.0 Hz), 121.0, 116.6 (d, $^2J_{C\text{-}F}$ = 22.0 Hz), 36.3, 21.2. ^{19}F NMR (376 MHz, $CDCl_3$) δ -114.7. HRMS: *m/z* $[MH]^+$ $C_{20}H_{17}FN_3$ calcd. 318.1401, found 318.1402. FTIR: ν_{max}/ cm^{-1} (neat): 2939 (w), 1566 (w), 1410 (m), 1378 (m), 1235 (m).

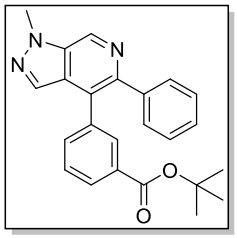
*Synthesis of tert-butyl 4-(1-methyl-5-phenyl-1H-pyrazolo[3,4-c]pyridin-4-yl)benzoate (E-**02**)*



Following general procedure K, using 1-methyl-5-phenyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-pyrazolo[3,4-c]pyridine (156 mg, 0.47 mmol), *tert*-butyl-4-bromobenzoate (100 mg, 0.39 mmol), K_3PO_4 (248 mg, 1.2 mmol) and Sphos 2nd Generation precatalyst (28 mg, 0.04 mmol) in THF (3.9 mL), the desired product was isolated as a yellow foam (148 mg, 99%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.04 (s, 1H, C*H*$_{ar}$), 7.97 (br, 2H, C*H*$_{ar}$), 7.88 (s, 1H, C*H*$_{ar}$), 7.38 – 7.35 (m, 3H, C*H*$_{ar}$), 7.27 – 7.23 (m, 4H, C*H*$_{ar}$), 4.25 (s, 3H, NC*H*$_3$), 1.61 (s, 9H, C*H*$_3$ x3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.5, 146.7, 141.6, 139.9, 136.0, 132.5 (x2 C), 131.2, 130.4, 130.1, 129.6, 129.2,

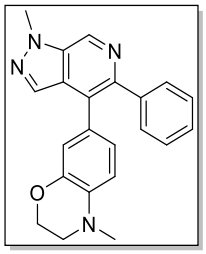
128.0, 127.3, 126.1, 81.2, 36.4, 28.2. HRMS: *m/z* $[MH]^+$ $C_{24}H_{24}N_3O_2$ calcd. 386.1863, found 386.1869. FTIR: ν_{max}/ cm^{-1} (neat): 2978 (w), 1710 (s), 1609 (m), 1463 (m), 1294 (s), 1162 (s), 1118 (s).

*Synthesis of tert-butyl 3-(1-methyl-5-phenyl-1H-pyrazolo[3,4-c]pyridin-4-yl)benzoate (E-**13**)*



Following general procedure K, using 1-methyl-5-phenyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-pyrazolo[3,4-c]pyridine (156 mg, 0.47 mmol), *tert*-butyl-3-bromobenzoate (100 mg, 0.39 mmol), K_3PO_4 (248 mg, 1.2 mmol) and Sphos 2nd Generation precatalyst (28 mg, 0.04 mmol) in THF (4.0 mL), the desired product was isolated as a white foam (114 mg, 76%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.04 (br, 1H, C*H*$_{ar}$), 8.02 – 8.00 (m, 1H, C*H*$_{ar}$), 7.98 – 7.92 (m, 2H, C*H*$_{ar}$), 7.41 – 7.33 (m, 4H, C*H*$_{ar}$), 7.25 – 7.21 (m, 3H, C*H*$_{ar}$), 4.26 (s, 3H, C*H*$_3$), 1.55 (s, 9H, C*H*$_3$ x3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.4, 146.8, 139.9, 137.3, 136.1, 134.2, 132.6, 132.4, 132.3, 131.1, 130.5, 129.3, 128.6, 128.5, 128.0, 127.2, 126.2, 81.2, 36.4, 28.2. HRMS: *m/z* $[MH]^+$ $C_{24}H_{24}N_3O_2$ calcd. 386.1863, found 386.1870. FTIR: ν_{max}/ cm^{-1} (neat): 2977 (w), 1709 (s), 1464 (m), 1368 (s), 1297 (s), 1160 (s).

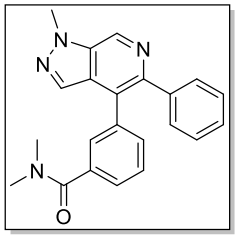
*Synthesis of 4-methyl-7-(1-methyl-5-phenyl-1H-pyrazolo[3,4-c]pyridin-4-yl)-3,4-dihydro-2H-benzo[b][1,4]oxazine (E-**03**)*



Following general procedure K, using 1-methyl-5-phenyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-pyrazolo[3,4-c]pyridine (88 mg, 0.26 mmol), 7-bromo-4-methyl-3,4-dihydro-2H-benzo[b][1,4]oxazine (50 mg, 0.22 mmol), K_3PO_4 (140 mg, 0.66 mmol) and Sphos 2nd Generation precatalyst (16 mg, 0.02 mmol) in THF (2.6 mL), the desired product was isolated as a white foam (75 mg, 96%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.94 (s, 1H, C*H*$_{ar}$), 8.00 (s, 1H, C*H*$_{ar}$), 7.42 (br, 2H, C*H*$_{ar}$), 7.30 – 7.20 (m, 3H, C*H*$_{ar}$), 6.79 (br, 1H, C*H*$_{ar}$), 6.71 (d, *J* = 8.5 Hz, 1H, C*H*$_{ar}$), 6.58 (d, *J* = 8.5 Hz, 1H, C*H*$_{ar}$), 4.31 – 4.28 (m, 2H, C*H*$_2$), 4.21 (s, 3H, C*H*$_3$), 3.32 – 3.29 (m, 2H, C*H*$_2$), 2.90 (s, 3H, C*H*$_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 146.2, 144.0, 140.6, 136.1, 136.0,

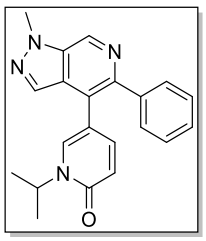
133.2, 131.0, 130.3, 129.6, 127.9, 127.2, 126.9, 126.5, 123.7, 117.5, 112.2, 64.8, 49.0, 38.6, 36.2. HRMS: *m/z* $[MH]^+$ $C_{22}H_{21}N_4O$ calcd. 357.1710, found 357.1714. FTIR: ν_{max}/ cm^{-1} (neat): 2536 (br), 1678 (m), 1616 (m), 1517 (m), 1437 (m), 1267 (m), 1054 (m).

*Synthesis of 3-(5-phenyl-1-methyl-1H-pyrazolo[3,4-c]pyridin-4-yl)-N,N-dimethylbenzamide (E-**07**)*



Following general procedure K, using 1-methyl-5-phenyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-pyrazolo[3,4-c]pyridine (88 mg, 0.26 mmol), 3-bromo-*N*,*N*-dimethylbenzamide (50 mg, 0.22 mmol), K_3PO_4 (140 mg, 0.66 mmol) and Sphos 2nd Generation precatalyst (16 mg, 0.02 mmol) in THF (2.2 mL), the desired product was isolated as a pink foam (64 mg, 82%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.03 (br, 1H, C*H*$_{ar}$), 7.88 (br, 1H, C*H*$_{ar}$), 7.54 – 7.46 (m, 2H, C*H*$_{ar}$), 7.43 (dt, *J* = 7.0, 2.0 Hz, 1H, C*H*$_{ar}$), 7.39 – 7.35 (m, 2H, C*H*$_{ar}$), 7.26 – 7.18 (m, 3H, C*H*$_{ar}$), 7.15 (br, 1H, C*H*$_{ar}$), 4.25 (s, 3H, NC*H*$_3$), 3.00 (s, 3H, NC*H*$_3$), 2.54 (s, 3H, NC*H*$_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.0, 146.7, 140.2, 137.2, 136.7, 136.0, 132.5, 132.4, 131.0, 130.6, 129.3, 129.1, 128.8, 128.1, 127.1, 126.7, 126.3, 39.3, 36.4, 35.3. HRMS: *m/z* $[MH]^+$ $C_{22}H_{21}N_4O$ calcd. 357.1710, found 357.1717. FTIR: ν_{max}/ cm^{-1} (neat): 3368 (br), 2530 (w), 1632 (s), 1493 (m), 1389 (s), 1214 (m).

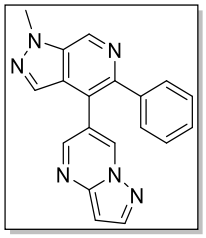
*Synthesis of 1-isopropyl-5-(1-methyl-5-phenyl-1H-pyrazolo[3,4-c]pyridin-4-yl)pyridin-2(1H)-one (E-**05**)*



Following general procedure K, using 1-methyl-5-phenyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-pyrazolo[3,4-c]pyridine (106 mg, 0.32 mmol), 5-bromo-1-isopropylpyridin-2(1*H*)-one (50 mg, 0.23 mmol), K_3PO_4 (147 mg, 0.69 mmol) and Sphos 2nd Generation precatalyst (17 mg, 0.02 mmol) in THF (2.3 mL), the desired product was isolated as an yellow oil (70 mg, 88%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.67 (s, 1H, C*H*$_{ar}$), 8.26 (s, 1H, C*H*$_{ar}$), 7.59 (dd, *J* = 9.5, 2.5 Hz, 1H, C*H*$_{ar}$), 7.52 – 7.47 (m, 3H, C*H*$_{ar}$), 7.41 – 7.36 (m, 2H, C*H*$_{ar}$), 7.18 (d, *J* = 2.5 Hz, 1H, C*H*$_{ar}$), 6.94 (d, *J* = 9.5 Hz, 1H, C*H*$_{ar}$), 5.18 (hept, *J* = 7.0 Hz, 1H, C*H*), 4.44 (s, 3H,

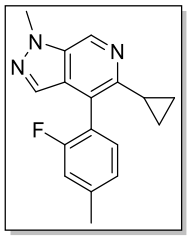
NCH_3), 1.07 (d, *J* = 7.0 Hz, 6H, CH_3 x2). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.8, 140.8, 140.1, 135.9, 135.0, 133.1, 131.3, 131.0, 130.6, 130.2, 129.6, 129.0, 126.4, 120.8, 114.0, 48.1, 37.6, 21.6 (x 2C). HRMS: *m/z* $[MH]^+$ $C_{21}H_{21}N_4O$ calcd. 345.1710, found 345.1716. FTIR: ν_{max}/ cm^{-1} (neat): 2546 (br), 1656 (m), 1529 (m), 1270 (m).

*Synthesis of 1-methyl-5-phenyl-4-(pyrazolo[1,5-a]pyrimidin-6-yl)-1H-pyrazolo[3,4-c]pyridine (E-**06**)*



Following general procedure K, using 1-methyl-5-phenyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-pyrazolo[3,4-c]pyridine (102 mg, 0.30 mmol), 6-bromopyrazolo[1,5-a]pyrimidine (50 mg, 0.25 mmol), K_3PO_4 (167 mg, 0.76 mmol) and Sphos 2nd Generation precatalyst (19 mg, 0.03 mmol) in THF (2.5 mL), the desired product was isolated as a red foam (50 mg, 61%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.13 (br, 1H, CH_{ar}), 8.74 (d, *J* = 2.0 Hz, 1H, CH_{ar}), 8.28 (d, *J* = 2.0 Hz, 1H) , CH_{ar}, 8.16 (d, *J* = 2.5 Hz, 1H, CH_{ar}), 8.03 (s, 1H, CH_{ar}), 7.44 – 7.38 (m, 2H, CH_{ar}), 7.32 – 7.28 (m, 3H, CH_{ar}), 6.73 (d, *J* = 2.5 Hz, 1H, CH_{ar}), 4.29 (s, 3H, NCH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 150.7, 147.7, 147.3, 145.8, 138.7, 136.1, 134.6, 133.4, 131.6, 130.4, 129.2, 128.6, 128.2, 119.1, 118.5, 97.4, 36.6. HRMS: *m/z* $[MH]^+$ $C_{19}H_{15}N_6$ calcd. 327.1353, found 327.1358. FTIR: ν_{max}/ cm^{-1} (neat): 3051 (br), 2934 (w), 1622 (m), 1468 (m), 1443 (m), 1281 (m), 1143 (m).

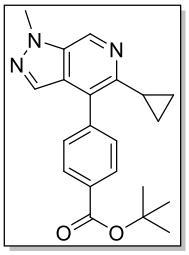
*Synthesis of 5-cyclopropyl-4-(2-fluoro-4-methylphenyl)-1-methyl-1H-pyrazolo[3,4-c]pyridine (E-**09**)*



Following general procedure K, using 5-cyclopropyl-1-methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-pyrazolo[3,4-c]pyridine (95 mg, 0.32 mmol), 1-bromo-2-fluoro-4-methylbenzene (50 mg, 0.26 mmol), K_3PO_4 (168 mg, 0.79 mmol) and Sphos 2nd Generation precatalyst (19 mg, 0.03 mmol) in THF (2.6 mL), the desired product was isolated as a yellow oil (56 mg, 76%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.63 (s, 1H, CH_{ar}), 7.99 (s, 1H, CH_{ar}), 7.32 (t, *J* = 7.5 Hz, 1H, CH_{ar}), 7.19 (dd, *J* = 7.5, 1.0 Hz, 1H, CH_{ar}), 7.14 (br, 1H, CH_{ar}), 4.35 (s, 3H, NCH_3), 2.50 (s,

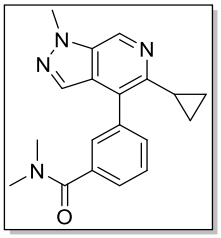
3H, CH_3), 2.27 – 2.19 (m, 1H, CH), 1.17 – 1.09 (m, 2H, CH_2), 1.08 – 0.96 (m, 2H, CH_2). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.4 (d, $^1J_{C\text{-}F}$ = 249.5 Hz), 143.7, 143.2 (d, $^3J_{C\text{-}F}$ = 8.0 Hz), 134.1, 133.1, 132.4, 130.8, 128.1, 127.0, 125.7, 117.5 (d, $^2J_{C\text{-}F}$ = 16.0 Hz), 117.1 (d, $^2J_{C\text{-}F}$ = 21.0 Hz), 37.4, 21.4, 12.5, 9.2, 9.0. ^{19}F NMR (376 MHz, $CDCl_3$) δ -75.9. HRMS: *m/z* $[MH]^+$ $C_{17}H_{17}FN_3$ calcd. 282.1401, found 282.1405. FTIR: ν_{max}/ cm^{-1} (neat): 3422 (br), 1672 (m), 1627 (m), 1414 (m), 1131 (s).

*Synthesis of tert-butyl 4-(5-cyclopropyl-1-methyl-1H-pyrazolo[3,4-c]pyridin-4-yl)benzoate (E-**10**)*



Following general procedure K, using 5-cyclopropyl-1-methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-pyrazolo[3,4-c]pyridine (140 mg, 0.47 mmol), *tert*-butyl-4-bromobenzoate (100 mg, 0.39 mmol), K_3PO_4 (248 mg, 1.2 mmol) and Sphos 2nd Generation precatalyst (28 mg, 0.04 mmol) in THF (3.9 mL), the desired product was isolated as a brown foam (101 mg, 74%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.83 (s, 1H, CH_{ar}), 8.16 – 8.13 (m, 2H, CH_{ar}), 7.69 (s, 1H, CH_{ar}), 7.63 – 7.60 (m, 2H, CH_{ar}), 4.17 (s, 3H, NCH_3), 2.08 (tt, *J* = 8.0, 5.0 Hz, 1H, CH), 1.64 (s, 9H, CH_3 x3), 1.14 – 1.10 (m, 2H, CH_2), 0.88 – 0.84 (m, 2H, CH_2). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.5, 147.8, 141.4, 135.3, 132.2, 131.4, 131.3, 129.9, 129.7, 128.9, 125.5, 81.3, 36.2, 28.3, 13.7, 9.7. HRMS: *m/z* $[MH]^+$ $C_{21}H_{24}N_3O_2$ calcd. 350.1863, found 350.1873. FTIR: ν_{max}/ cm^{-1} (neat): 2977 (w), 1708 (s), 1608 (m), 1477 (m), 1368 (m), 1295 (s), 1163 (s), 1117 (s).

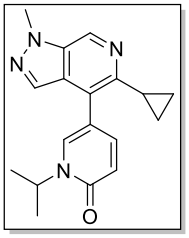
*Synthesis of 3-(5-cyclopropyl-1-methyl-1H-pyrazolo[3,4-c]pyridin-4-yl)-N,N-dimethylbenzamide (E-**11**)*



Following general procedure K, using 5-cyclopropyl-1-methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-pyrazolo[3,4-c]pyridine (79 mg, 0.26 mmol), 3-bromo-*N*,*N*-dimethylbenzamide (50 mg, 0.22 mmol), K_3PO_4 (140 mg, 0.66 mmol) and Sphos 2nd Generation precatalyst (16 mg, 0.02 mmol) in THF (2.2 mL), the desired product was isolated as a pale yellow oil (27 mg, 38%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.59 (s, 1H, CH_{ar}), 8.03 (s, 1H, CH_{ar}), 7.70 – 7.58 (m, 4H, CH_{ar}), 4.35 (s, 3H, NCH_3), 3.17 (s, 3H, CH_3), 3.07 (s, 3H, CH_3), 2.25 (tt, *J* = 7.5, 6.0 Hz,

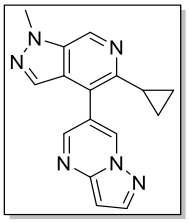
1H, C*H*), 1.14 – 1.07 (m, 4H, CH_2 x2). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.9, 142.8, 136.8, 134.2, 133.6, 132.9, 131.9, 131.4, 130.8, 129.5, 128.3, 128.2, 128.1, 39.7, 37.4, 35.7, 12.6, 9.9. HRMS: *m/z* $[MH]^+$ $C_{19}H_{21}N_4O$ calcd. 321.1710, found 321.1717. FTIR: ν_{max}/ cm^{-1} (neat): 2941 (br), 1620 (s), 1402 (m), 1271 (m), 1135 (s).

*Synthesis of 5-(5-cyclopropyl-1-methyl-1H-pyrazolo[3,4-c]pyridin-4-yl)-1-isopropylpyridin-2(1H)-one (E-**08**)*



Following general procedure K, using 5-cyclopropyl-1-methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-pyrazolo[3,4-c]pyridine (83 mg, 0.28 mmol), 5-bromo-isopropylpyridin-2(1*H*)-one (50 mg, 0.23 mmol), K_3PO_4 (147 mg, 0.69 mmol) and Sphos 2nd Generation precatalyst (17 mg, 0.02 mmol) in THF (2.3 mL), the desired product was isolated as a yellow oil (54 mg, 76%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.52 (s, 1H, CH_{ar}), 8.08 (s, 1H, CH_{ar}), 7.68 (d, *J* = 2.5 Hz, 1H, CH_{ar}), 7.60 (dd, *J* = 9.5, 2.5 Hz, 1H, CH_{ar}), 6.93 (d, *J* = 9.5 Hz, 1H, CH_{ar}), 5.42 (hept, *J* = 7.0 Hz, 1H, C*H*), 4.35 (s, 3H, CH_3), 2.27 (tt, *J* = 8.5, 5.5 Hz, 1H, C*H*), 1.45 (d, *J* = 7.0 Hz, 6H, CH_3 x2), 1.24 – 1.17 (m, 2H, CH_2), 1.15 – 1.09 (m, 2H, CH_2). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.7, 143.1, 139.7, 134.5, 134.5, 132.3, 131.3, 128.7, 127.4, 121.1, 113.5, 47.8, 37.4, 22.1, 12.7, 9.9. HRMS: *m/z* $[MH]^+$ $C_{18}H_{21}N_4O$ calcd. 309.1710, found 309.1716. FTIR: ν_{max}/ cm^{-1} (neat): 2985 (br), 1657 (s), 1598 (m), 1529 (m), 1266 (m), 1134 (s).

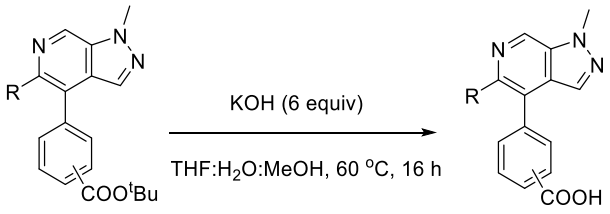
*Synthesis of 5-cyclopropyl-1-methyl-4-(pyrazolo[1,5-a]pyrimidin-6-yl)-1H-pyrazolo[3,4-c]pyridine (E-**12**)*



Following general procedure K, using 5-cyclopropyl-1-methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-pyrazolo[3,4-c]pyridine (91 mg, 0.30 mmol), 3-bromo-*N*,*N*-dimethylbenzamide (50 mg, 0.25 mmol), K_3PO_4 (161 mg, 0.76 mmol) and Sphos 2nd Generation precatalyst (18 mg, 0.03 mmol) in THF (2.5 mL), the desired product was isolated as a pale yellow oil (67 mg, 91%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.64 (s, 1H, CH_{ar}), 9.06 (d, *J* = 2.0 Hz, 1H, CH_{ar}), 8.71 (d, *J* = 2.5 Hz, 1H, CH_{ar}), 8.31 (d, *J* = 2.5 Hz, 1H, CH_{ar}), 8.16 (s, 1H, CH_{ar}), 6.92 (d, *J* =

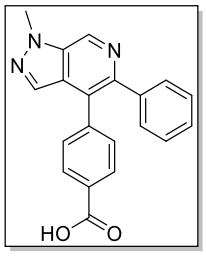
2.0 Hz, 1H, C*H*$_{ar}$), 4.39 (s, 3H, NC*H*$_3$), 2.37 – 2.25 (m, 1H, C*H*), 1.23 – 1.18 (m, 2H, C*H*$_2$), 1.17 – 1.09 (m, 2H, C*H*$_2$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 149.2, 147.7, 146.7, 144.0, 135.2, 134.4, 132.1, 131.6, 130.0, 124.3, 115.0, 98.3, 37.5, 12.7, 10.0. HRMS: *m/z* $[MH]^+$ $C_{16}H_{15}N_6$ calcd. 291.1353, found 291.1361. FTIR: ν_{max}/ cm^{-1} (neat): 3090 (br), 1672 (m), 1622 (m), 1500 (m), 1275 (m), 1135 (s).

General procedure L



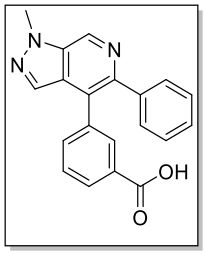
KOH (6.0 eq) was added to a stirred solution of the corresponding ester (1.0 eq.) in a mixture of THF:MeOH 1:1 (0.1 M). The reaction was heated at 60 °C overnight. Diluted aq. HCl (1 M) was added and the aqueous layer was extracted with ethyl acetate. The organic phase was dried over anhydrous $MgSO_4$, filtered and the solvent was removed *in vacuo*. The residue was purified by flash column chromatography on silica gel eluting with petroleum ether (40/60) and ethyl acetate to afford the corresponding acids.

*Synthesis of 4-(1-methyl-5-phenyl-1H-pyrazolo[3,4-c]pyridin-4-yl)benzoic acid (E-**04**)*



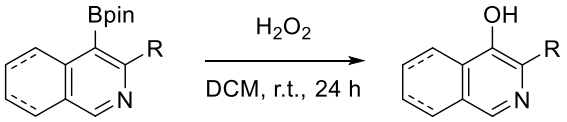
Following general procedure L, using *tert*-butyl 4-(1-methyl-5-phenyl-1H-pyrazolo[3,4-c]pyridin-4-yl)benzoate (70 mg, 0.18 mmol), KOH, (61 mg, 1.1 mmol) in THF:MeOH (2 mL), the desired product was isolated as a pale brown foam (49 mg, 82%). ^{1}H NMR (500 MHz, DMSO) δ 9.28 (s, 1H, C*H*$_{ar}$), 7.96 (s, 1H, C*H*$_{ar}$), 7.92 (d, *J* = 8.5 Hz, 2H, C*H*$_{ar}$), 7.42 (d, *J* = 8.5 Hz, 2H, C*H*$_{ar}$), 7.32 – 7.29 (m, 2H, C*H*$_{ar}$), 7.26 – 7.23 (m, 3H, C*H*$_{ar}$), 4.25 (s, 3H, NC*H*$_3$). ^{13}C NMR (126 MHz, DMSO) δ 167.0, 145.5, 141.5, 139.9, 135.6, 133.8, 131.7, 130.3, 130.2, 129.7, 129.5, 128.0, 127.7, 127.1, 125.1, 36.2. HRMS: *m/z* $[MH]^+$ $C_{20}H_{16}N_3O_2$ calcd. 330.1237, found 330.1245. FTIR: ν_{max}/ cm^{-1} (neat): 2919 (w), 1691 (s), 1612 (m), 1469 (m), 1406 (m), 1232 (s), 1069 (m)

*Synthesis of 4-(5-cyclopropyl-1-methyl-1H-pyrazolo[3,4-c]pyridin-4-yl)benzoic acid (E-**14**)*



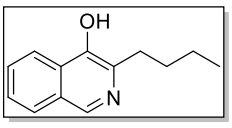
Following general procedure L, using *tert*-butyl 3-(1-methyl-5-phenyl-1H-pyrazolo[3,4-c]pyridin-4-yl)benzoate (76 mg, 0.20 mmol), KOH, (66 mg, 1.2 mmol) in THF:MeOH (2 mL), the desired product was isolated as a pale brown foam (38 mg, 59%). ^{1}H NMR (400 MHz, DMSO) δ 9.41 (s, 1H, C*H*$_{ar}$), 8.03 (s, 1H, C*H*$_{ar}$), 7.93 (d, *J* = 7.0 Hz, 1H, C*H*$_{ar}$), 7.85 (s, 1H, C*H*$_{ar}$), 7.57 – 7.49 (m, 2H, C*H*$_{ar}$), 7.34 – 7.27 (m, 5H, C*H*$_{ar}$), 4.29 (s, 3H, C*H*$_{3}$). ^{13}C NMR (101 MHz, DMSO) δ 167.3, 144.5, 138.5, 136.9, 134.0, 134.7, 133.4, 132.5, 131.7, 131.1, 130.9, 129.5, 129.3 (x2 C), 128.4, 128.1, 126.6, 37.0. HRMS: *m/z* [MH]$^{+}$ $C_{20}H_{16}N_3O_2$ calcd. 330.1237, found 330.1240. FTIR: ν_{max}/ cm^{-1} (neat): 2939 (w), 1691 (s), 1622 (m), 1499 (m), 1232 (s).

General procedure M[95]



To a stirred solution of the correponding aromatic boronate in dichloromethane (0.1 M) was slowly added a 30% (w/w) aqueous solution of hydrogen peroxide (1.5 equiv). The reaction was then stirred at room temperature during 24 h. Water was added and the organic layer was extracted with dichloromethane. The organic phase was dried over anhydrous $MgSO_4$, filtered and the solvent was removed *in vacuo*. The residue was purified by flash column chromatography on silica gel eluting with petroleum ether (40/60) and ethyl acetate to afford the desired products.

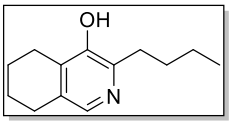
*Synthesis of 3-butylisoquinolin-4-ol (**155**)*



Following general procedure M, using 3-butyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)isoquinoline (2.8 g, 9.0 mmol) and H_2O_2 (377 mg, 11.1 mmol) in dichloromethane (90 mL) afforded the desired product as a pale yellow foam (1.1 g, 62%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.78 (s, 1H, C*H*$_{ar}$), 8.28 (d, *J* = 8.5 Hz, 1H, C*H*$_{ar}$), 7.89 (d, *J* = 8.0 Hz, 1H, C*H*$_{ar}$), 7.65 (t, *J* = 7.5 Hz,

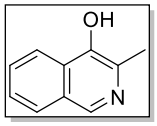
1H, C*H*$_{ar}$), 7.54 (t, *J* = 7.5 Hz, 1H, C*H*$_{ar}$), 2.99 – 2.94 (m, 2H, C*H*$_2$), 1.72 – 1.63 (m, 2H, C*H*$_2$), 1.30 – 1.20 (m, 2H, C*H*$_2$), 0.78 (t, *J* = 7.5 Hz, 3H, C*H*$_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 146.8, 141.0, 139.1, 129.9, 129.4, 128.4, 127.3, 126.9, 121.5, 31.4, 31.3, 22.7, 13.9. HRMS: *m*/*z* $[MH]^+$ $C_{13}H_{16}NO$ calcd. 202.1226, found 202.1230. FTIR : ν_{max}/ cm^{-1} (neat) 3110 (br), 2917 (m), 1586 (m), 1493 (m), 1359 (s), 1104 (s).

*Synthesis of 3-butyl-5,6,7,8-tetrahydroisoquinolin-4-ol (**157**)*



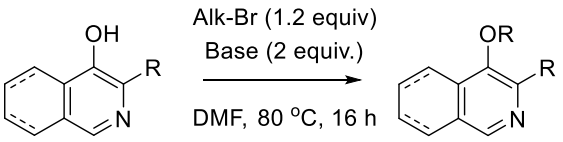
Following general procedure M, using 3-butyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5,6,7,8-tetrahydroisoquinoline (3.4 g, 10.8 mmol) and H_2O_2 (550 mg, 16.2 mmol) in dichloromethane (110 mL) afforded the desired product as a pale orange foam (1.5 g, 68%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (s, 1H, C*H*$_{ar}$), 2.76 – 2.72 (m, 2H, C*H*$_2$), 2.71 – 2.63 (m, 4H, C*H*$_2$ x2), 1.84 – 1.71 (m, 4H, C*H*$_2$), 1.62 (tt, *J* = 8.0, 6.5 Hz, 2H, C*H*$_2$), 1.38 – 1.28 (m, 2H, C*H*$_2$), 0.88 (t, *J* = 7.5 Hz, 3H, C*H*$_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 150.4, 146.3, 138.3, 135.3, 131.9, 31.6, 31.1, 26.2, 24.9, 24.6, 23.4, 22.8, 13.9. HRMS: *m*/*z* $[MH]^+$ $C_{13}H_{20}NO$ calcd. 206.1539, found 206.1543. FTIR : ν_{max}/ cm^{-1} (neat) 2931 (w), 2507 (br), 1595 (m), 1358 (m), 1207 (s), 1100 (s).

*Synthesis of 3-metylisoquinolin-4-ol (**156**)*



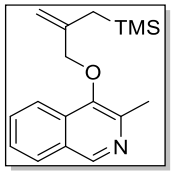
Following general procedure M, using 3-methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)isoquinoline (6.0 g, 22.3 mmol) and H_2O_2 (1.1 g, 33.4 mmol) in dichloromethane (225 mL) afforded the desired product as a brown foam (2.3 g, 63%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.83 (s, 1H, C*H*$_{ar}$), 8.10 (d, *J* = 8.5 Hz, 1H, C*H*$_{ar}$), 7.91 (d, *J* = 8.0 Hz, 1H, C*H*$_{ar}$), 7.70 – 7.65 (m, 1H), 7.58 – 7.53 (m, 1H, C*H*$_{ar}$), 2.67 (s, 3H, C*H*$_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 146.1, 141.5, 133.5, 130.4, 128.4, 128.2, 127.4, 127.1, 120.9, 17.3**.** HRMS: *m*/*z* $[MH]^+$ $C_{10}H_{10}NO$ calcd. 160.0757, found 160.0757. FTIR : ν_{max}/ cm^{-1} (neat) 3190 (br), 2530 (br), 1542 (m), 1412 (m), 1377 (m), 1088 (s).

General procedure N



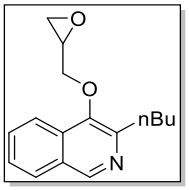
To a stirred solution of alcohol derivative and potassium carbonate (2 equiv.) or NaH (2 equiv.) in DMF (0.1 M) was slowly added corresponding alkyl halide (1.2 equiv). The reaction was then stirred at 80 °C during 3 h. Water was added and the organic layer was extracted with dichloromethane. The organic phase was dried over anhydrous $MgSO_4$, filtered and the solvent was removed *in vacuo*. The residue was purified by flash column chromatography on silica gel eluting with heptanes and ethyl acetate to afford the corresponding product.

Synthesis of 3-methyl-4-((2-((trimethylsilyl)methyl)allyl)oxy)isoquinoline



Following general procedure N, using 3-methylisoquinolin-4-ol (60 mg, 0.38 mmol), (2-(chloromethyl)allyl)trimethylsilane (74 mg, 0.45 mmol) and K_2CO_3 (104 mg, 0.75 mmol) in dimethylformamide (4 mL), the desired product was isolated as a pale yellow oil (45 mg, 42%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.90 (s, 1H, C*H*$_{ar}$), 7.96 (dd, *J* = 8.5, 0.5 Hz, 1H, C*H*$_{ar}$), 7.86 (d, *J* = 8.0 Hz, 1H, C*H*$_{ar}$), 7.59 (ddd, *J* = 8.5, 7.0, 1.0 Hz, 1H, C*H*$_{ar}$), 7.49 – 7.42 (m, 1H, C*H*$_{ar}$), 5.17 (br, *J* = 1.5 Hz, 1H, CH*H*), 4.84 – 4.76 (br, 1H, CH*H*), 4.23 (br, 2H, OC*H*$_2$), 2.59 (s, 3H, C*H*$_3$), 1.63 (br, 2H, C*H*$_2$), 0.00 (s, 9H, C*H*$_3$ x3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.9, 148.8, 145.2, 144.2, 132.7, 131.4, 130.2, 128.9, 127.8, 122.2, 110.7, 78.8, 24.9, 20.3, 0.0. HRMS: *m/z* $[MH]^+$ $C_{17}H_{24}NOSi$ calcd. 286.1622, found 286.1629. FTIR: ν_{max}/ cm^{-1} (neat): 3375 (br), 2954 (w), 1581 (w), 1381 (m), 1247 (m), 1101 (m), 1030 (s).

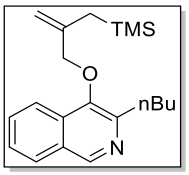
*Synthesis of 3-butyl-4-(oxiran-2-ylmethoxy)isoquinoline (D.**27**)*



Following general procedure N, using 3-butylisoquinolin-4-ol (70 mg, 0.35 mmol), 2-(bromomethyl)oxirane) (57 mg, 0.42 mmol) and NaH (17 mg, 0.70) in dimethylformamide (3.5 mL), the desired product was isolated as an orange oil (58 mg, 65%). ^{1}H NMR (400 MHz, $CDCl_3$)

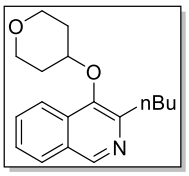
δ 9.03 (s, 1H, C*H*$_{ar}$), 8.11 (d, *J* = 8.5 Hz, 1H, C*H*$_{ar}$), 7.95 (d, *J* = 8.0 Hz, 1H, C*H*$_{ar}$), 7.70 (ddd, *J* = 8.5, 7.0, 1.0 Hz, 1H), 7.58 – 7.51 (m, 1H, C*H*$_{ar}$), 4.28 (dd, *J* = 11.0, 4.0 Hz, 1H, CH*H*), 3.95 (dd, *J* = 11.0, 6.0 Hz, 1H, CH*H*), 3.48 (ddd, *J* = 9.0, 4.0, 2.5 Hz, 1H, C*H*), 3.02 – 2.97 (m, 2H, C*H*$_2$), 2.97 – 2.94 (m, 1H, CH*H*), 2.79 (dd, *J* = 6.0, 2.5 Hz, 1H, CH*H*), 1.85 – 1.76 (m, 2H, C*H*$_2$), 1.50 – 1.40 (m, 2H, C*H*$_2$), 0.98 (t, *J* = 7.5 Hz, 3H, C*H*$_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.2, 147.8, 146.7, 131.1, 130.3, 128.8, 127.6, 126.6, 120.9, 75.3, 50.5, 44.5, 31.7 (x 2C), 22.9, 14.0. HRMS: *m/z* $[MH]^+$ $C_{16}H_{20}NO_2$ calcd. 258.1489, found 258.1495. FTIR: ν_{max}/ cm^{-1} (neat): 3364 (br), 2956 (w), 1578 (m), 1452 (m), 1374 (s), 1251 (m), 1164 (m), 1075 (m).

Synthesis of 3-butyl-4-((2-((trimethylsilyl)methyl)allyl)oxy)isoquinoline



Following general procedure N, using 3-butylisoquinolin-4-ol (60 mg, 0.30 mmol), (2-(chloromethyl)allyl)trimethylsilane (58 mg, 0.36 mmol) and NaH (14 mg, 0.60 mmol) in dimethylformamide (3.0 mL), the desired product was isolated as a colourless oil (17 mg, 18%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.02 (s, 1H, C*H*$_{ar}$), 8.03 (d, *J* = 8.5 Hz, 1H, C*H*$_{ar}$), 7.95 (d, *J* = 8.0 Hz, 1H, C*H*$_{ar}$), 7.67 (ddd, *J* = 8.5, 7.0, 1.0 Hz, 1H, C*H*$_{ar}$), 7.56 – 7.51 (m, 1H, C*H*$_{ar}$), 5.27 (d, *J* = 1.5 Hz, 1H, CH*H*), 4.89 (br, 1H, CH*H*), 4.32 (s, 2H, OC*H*$_2$), 4.23 (s, 2H, C*H*$_2$), 3.01 – 2.93 (m, 2H, C*H*$_2$), 1.84 – 1.76 (m, 2H, C*H*$_2$), 1.51 – 1.40 (m, 2H, C*H*$_2$), 0.97 (t, *J* = 7.5 Hz, 3H, C*H*$_3$), 0.09 (s, 9H, C*H*$_3$ x3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 149.4, 149.1, 148.6, 144.2, 132.7, 131.4, 130.1, 128.9, 127.8, 122.4, 110.5, 79.5, 33.2, 33.2, 24.8, 24.3, 15.4, 0.0. HRMS: *m/z* $[MH]^+$ $C_{20}H_{30}NOSi$ calcd. 329.2117, found 329.2124. FTIR: ν_{max}/ cm^{-1} (neat): 2955 (w), 1679 (w), 1578 (m), 1379 (m), 1248 (s), 1161 (m), 1078 (m).

Synthesis of 3-butyl-4-((tetrahydro-2H-pyran-4-yl)oxy)isoquinoline

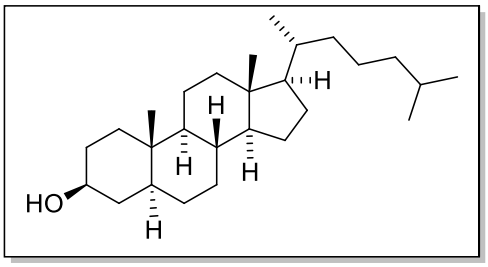


Following general procedure N, using 3-butylisoquinolin-4-ol (60 mg, 0.30 mmol), 4-bromotetrahydro-2*H*-pyran (59 mg, 0.36 mmol) and K_2CO_3 (82 mg, 0.60 mmol) in dimethylformamide (3.0 mL), the desired product was isolated as an orange oil (33 mg, 39%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.01 (s, 1H, C*H*$_{ar}$), 8.04 (d, *J* = 8.5 Hz, 1H, C*H*$_{ar}$), 7.94 (d, *J* = 8.0 Hz,

1H, CH_{ar}), 7.68 (ddd, *J* = 8.5, 7.0, 1.5 Hz, 1H, CH_{ar}), 7.54 (ddd, *J* = 8.0, 7.0, 1.0 Hz, 1H, CH_{ar}), 4.26 – 4.15 (m, 1H, OC*H*), 4.05 (dt, *J* = 12.0, 4.0 Hz, 2H, CH_2), 3.45 – 3.36 (m, 2H, CH_2), 3.03 – 2.97 (m, 2H, CH_2), 2.02 – 1.96 (m, 4H, CH_2 x2), 1.85 – 1.74 (m, 2H, CH_2), 1.49 – 1.38 (m, 2H, CH_2), 0.97 (t, *J* = 7.5 Hz, 3H, CH_3).^{13}C NMR (101 MHz, $CDCl_3$) δ 148.1, 147.6, 145.4, 132.1, 129.9, 128.6, 127.5, 126.4, 121.5, 79.6, 66.2 (x 2C), 33.4 (x 2C), 32.1, 31.5, 22.9, 14.1. HRMS: *m/z* $[MH]^+$ $C_{18}H_{24}NO_2$ calcd. 286.1802, found 286.1806. FTIR: ν_{max}/ cm^{-1} (neat): 3347 (br), 2955 (w), 1624 (w), 1576 (m), 1353 (m), 1250 (m), 1166 (m), 1088 (m).

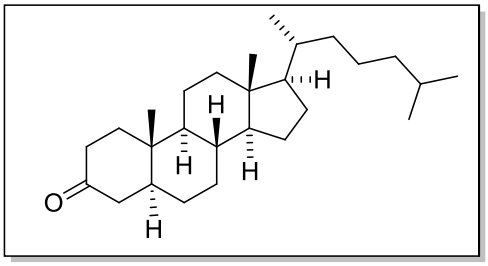
Cholesterol derivative synthesis

Synthesis of (3ß,5α)-cholestan-3-ol[59] ***(102)***



Charcoal (78.3 mg) and $Pd(OAc)_2$ (9 mg, 0.04 mmol) were added to a stirred solution of cholesterol (1.5 g, 3.9 mmol) in MeOH (5 mL) at 25 °C. The resulting mixture was stirred for 12 h under H_2 atmosphere (1 atm, balloon). The crude product was filtered and the solvent was evaporated. The residue was obtained with analitical purity as a white solid (1.3 g, 88%). M.p.: 137 – 138 °C (lit. 141.5 °C)[59]. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.62 – 3.50 (m, 1H, CHO*H*), 1.96 (dt, *J* = 12.5, 3.5 Hz, 1H, C*H*), 1.83 – 1.75 (m, 2H, CH_2), 1.74 – 1.62 (m, 1H, CH_2), 1.54 – 0.93 (m, 26H), 0.90 (d, *J* = 6.6 Hz, 3H, CH_3), 0.86 (dd, *J* = 6.6, 1.8 Hz, 6H, CH_3 x 2), 0.80 (s, 3H, CH_3), 0.65 (s, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 71.4, 56.5, 56.3, 54.4, 44.9, 42.6, 40.1, 39.5, 38.2, 37.0, 36.2, 35.8, 35.5, 35.5, 32.1, 31.6, 28.8, 28.3, 28.0, 24.2, 23.8, 22.8, 22.6, 21.3, 18.7, 12.3, 12.0.

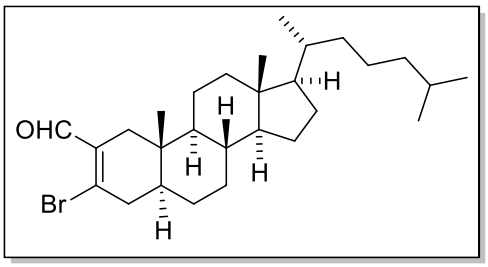
*Synthesis of cholestan-3-one (**103**)* [96]



Dimehtyl sulphoxide (668 mg, 8.6 mmol) and oxalyl chloride (52 mg, 4.1 mmol) were stirred in dichloromethane at -78 °C for 15 min. (3β,5α)-cholestan-3-ol (1.3 g, 3.4 mmol) was added

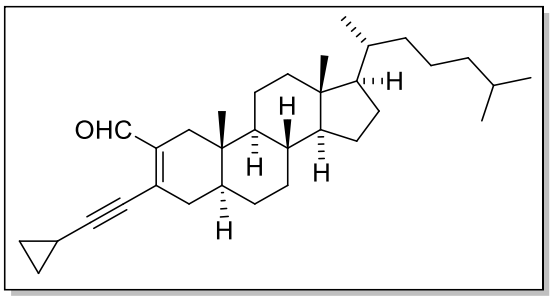
carefully and the resulting mixture was stirred for 1 h at -78 °C. Then triethylamine (986 mg, 9.8 mmol) was added dropwise and the solution was allowed to warm to room temperature and stirr overnight. Saturated $NaHCO_3$ was added and the crude product was extracted with dichloromethane. The organic phase was dried over anhydrous $MgSO_4$, filtered and the solvent was removed *in vacuo*. The residue was purified by flash column chromatography on silica gel eluting with petroleum ether (40/60) and ethyl acetate to afford cholestan-3-one (874 mg, 66%) as a white solid. M.p.: 129 – 130 °C (lit. 128 – 129)[96]. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.42 – 2.22 (m, 4H, C*H*$_2$), 2.11 – 1.96 (m, 4H, C*H*$_2$), 1.88 – 1.76 (m, 2H, C*H*$_2$), 1.73 – 1.65 (m, 2H, C*H*$_2$), 1.42 – 1.04 (m, 19H), 1.01 (s, 3H, C*H*$_3$), 0.90 (d, *J* = 6.5 Hz, 3H, C*H*$_3$), 0.87 (d, *J* = 1.5 Hz, 3H, C*H*$_3$), 0.85 (d, *J* = 1.5 Hz, 3H, C*H*$_3$), 0.68 (s, 3H, C*H*$_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 212.3, 56.3, 56.3, 53.8, 46.7, 44.8, 42.6, 39.9, 39.5, 38.6, 38.2, 36.2, 35.8, 35.7, 35.4, 31.7, 29.0, 28.3, 28.0, 24.2, 23.8, 22.8, 22.6, 21.5, 18.7, 12.1, 11.5.

Synthesis of 3-bromo-2-formyl-cholest-2-ene[60]



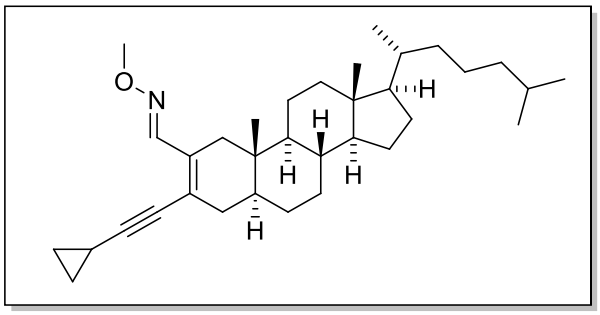
N,N-Dimethylformamide (152 mg, 2.1 mmol) was cooled to 0 °C in ice bath. Phosphorous tribromide (282 mg, 1.0 mmol) was added dropwise over a period of 10 min. A solution of cholestan-3-one (100 mg, 0.3 mmol) in chloroform (2 mL) was added dropwise and the reaction mixture was stirred for 12 h at 60 °C. The reaction mixture was then poured in ice water. Solid sodium hydrogen carbonate was carefully added to neutralize the acids and the mixture was extracted three times with DCM. The organic phase was dried over anhydrous $MgSO_4$, filtered and the solvent was removed *in vacuo*. The residue was used without further purification in the next step.

*Synthesis of 3-(2-cyclopropylethynyl)-2-formyl-cholest-2-ene (**104**)*



To a round bottomed flask was added CuI (3 mg, 0.01), $PdCl_2(PPh_3)_2$ (9 mg, 0.01)) and Et_3N (1 mL). 3-Bromo-2-formyl-cholest-2-ene (122 mg, 0.3 mmol) was added to the stirred suspension followed by the immediate addition of cyclopropylacetyelene (25 mg, 0.4 mmol). The resulting mixture was stirred at 50 ^oC overnight. Saturated NH_4Cl (aq.) was added and the aqueous layer was extracted with ethyl acetate. The organic phase was washed with aqueous HCl and brine. The organic phase was dried over anhydrous $MgSO_4$, filtered and the solvent was removed *in vacuo*. The residue was purified by flash column chromatography on silica gel eluting with petroleum ether (40/60) and ethyl acetate to furnish3-(2-cyclopropylethynyl)-2-formyl-cholest-2-ene (22 mg, 18% yield over two steps). ^1H NMR (400 MHz, $CDCl_3$) δ 10.11 (s, 1H), 2.48 (br, 1H), 2.28 – 2.20 (m, 1H), 2.12 – 2.07 (m, 1H), 1.98 (dt, *J* = 12.5, 3.5 Hz, 1H), 1.85 – 1.76 (m, 1H), 1.70 – 1.63 (m, 2H), 1.53 – 0.95 (m, 23H), 0.90 (d, *J* = 6.5 Hz, 3H), 0.87 (d, *J* = 1.5 Hz, 3H), 0.85 (d, *J* = 1.5 Hz, 3H), 0.79 – 0.75 (m, 4H), 0.66 (s, 3H), 0.65 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.6, 140.8, 140.1, 104.0, 72.9, 56.4, 56.2, 53.7, 42.5, 41.0, 39.8, 39.5, 37.5, 36.2, 36.1, 35.8, 35.5, 33.9, 31.5, 28.2, 28.0, 27.9, 24.2, 23.8, 22.8, 22.6, 21.03, 18.7, 12.0, 11.7, 9.1, 9.1, 0.4. HRMS: *m/z* $[MH]^+$ $C_{33}H_{51}O$ calcd. 462.3856, found 462.3863. FTIR: ν_{max}/ cm^{-1} (neat) 2925 (s), 2222 (m), 1674 (s), 1466 (m), 1381 (m).

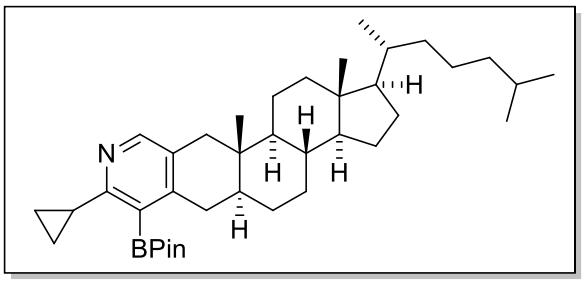
*Synthesis of 3-(2-cyclopropylethynyl)-2-formyl-cholest-2-ene O-methyl oxime (**105**)*



3-(2-Cyclopropylethynyl)-2-formyl-cholest-2-ene (20 mg, 0.04 mmol), *O*-methylhydroxylamine hydrochloride (7 mg, 0.08), Na_2SO_4 (11 mg, 0.08) and pyridine (7 mg, 0.09 mmol) in methanol

(1 mL) were stirred at room temperature and the reaction was monitored via TLC analysis. Upon completion, the mixture was diluted with water, and extracted with ethyl acetate. The organic phase was dried over anhydrous $MgSO_4$, filtered and the solvent was removed *in vacuo*. The residue was purified by flash column chromatography on silica gel eluting with petroleum ether (40/60) and ethyl acetate to afford 3-(2-cyclopropylethynyl)-2-formyl-cholest-2-ene *O*-methyl oxime (20 mg, 100%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (s, 1H), 3.88 (s, 3H), 2.53 – 2.48 (m, 1H), 2.15 – 2.08 (m, 1H), 2.02 – 1.94 (m, 2H), 1.81 – 1.76 (m, 1H), 0.90 (d, *J* = 6.5 Hz, 3H), 0.87 (d, *J* = 1.8 Hz, 3H), 0.85 (d, *J* = 1.7 Hz, 3H), 0.70 (s, 3H), 0.66 (s, 3H). *Only important peaks for identification are being shown.* ^{13}C NMR (101 MHz, $CDCl_3$) δ 150.8, 134.3, 125.1, 100.2, 74.1, 61.7, 56.4, 56.2, 53.8, 42.5, 41.2, 39.9, 39.5, 38.2, 36.2, 35.8, 35.5, 34.1, 31.5, 29.7, 28.2, 28.1, 28.0, 24.2, 23.8, 22.8, 22.6, 21.1, 18.7, 12.0, 11.8, 8.8, 0.3. HRMS: *m/z* $[MH]^+$ $C_{34}H_{54}NO$ calcd. 491.4122, found 491.4120. FTIR: ν_{max}/ cm^{-1} (neat) 2924 (s), 2031 (w), 1468 (m), 1059 (m).

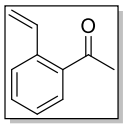
*Synthesis of **106***



B_2Pin_2 (14 mg, 0.06 mmol) was added to a stirred solution of 3-(2-cyclopropylethynyl)-2-formyl-cholest-2-ene *O*-methyl oxime (25 mg, 0.05) in toluene (1 mL). Then $Pt(PPh_3)_4$ (6 mg, 0.005 mmol) was added and the reaction was stirred at 120 °C for 24 h. The reaction mixture was allowed to cool to room temperature and the solvent was evaporated. The residue was purified by flash column chromatography on florisil eluting with petroleum ether (40/60) and ethyl acetate to afford **26** (19 mg, 66%) as a yellow oil.). ^{1}H NMR (400 MHz, $CDCl_3$) {selected peaks only see spectra for further details} δ 8.08 (s, 1H), 1.39 (s, 12H), 0.92 (d, *J* = 6.5 Hz, 3H), 0.87 (d, *J* = 1.5 Hz, 3H), 0.86 (d, *J* = 1.5 Hz, 3H), 0.69 (s, 3H), 0.67 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.5, 151.2, 148.8, 128.0, 84.1, 56.4, 56.3, 53.7, 42.5, 41.6, 40.8, 39.9, 39.5, 36.2, 35.8, 35.6, 34.8, 33.6, 31.6, 29.7, 28.8, 28.2, 28.0, 24.9, 24.9, 24.2, 23.9, 22.8, 22.6, 21.1, 18.7, 16.4, 12.0, 9.3, 9.2. ^{11}B NMR (128 MHz, $CDCl_3$) δ 32.4 (br). HRMS: *m/z* $[MH]^+$ $C_{39}H_{63}{}^{11}BNO2$ calcd. 588.4952, found 588.4952. FTIR: ν_{max}/ cm^{-1} (neat) 2927 (s), 1562 (m), 1443 (m), 1370 (s), 1139 (s).

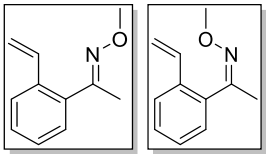
Experimental route to compounds** E-**145 and** Z-**145

Synthesis of 1-(2-vinylphenyl)ethan-1-one[97]



1-(2-Bromophenyl)ethanone (1 g, 5.0 mmol), potassium vinyltrifluoroborate (1.4 g, 10.0 mmol), $PdCl_2$ (108 mg, 0.15 mmol), PPh_3 (108 mg, 0.15 mmol), Cs_2CO_3 (4.9 g, 15.0 mmol), THF (8 mL) and H_2O (2 mL) were stirred under nitrogen atmosphere at 85 °C for 24 hours. Subsequently, water (20 mL) was added to the reaction mixture and the residue was extracted with ethyl acetate (50 mL x 3) and dried over anhydrous Na_2SO_4. After removing the solvent under reduced pressure, the crude product was purified by flash column chromatography on silica gel and eluted with petroleum ether (40/60) and ethyl acetate to afford 1-(2-vinylphenyl)ethanone (734 mg, 95%) as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (dd, *J* = 8.0, 1.0 Hz, 1H, C*H*$_{ar}$), 7.59 – 7.55 (m, 1H, C*H*$_{ar}$), 7.46 (td, *J* = 7.5, 1.0 Hz, 1H, C*H*$_{ar}$), 7.34 (td, *J* = 7.5, 1.5 Hz, 1H, C*H*$_{ar}$), 7.20 (dd, *J* = 17.5, 11.0 Hz, 1H, CH_2=C*H*), 5.64 (dd, *J* = 17.5, 1.0 Hz, 1H, CH=C*H*H), 5.35 (dd, *J* = 11.0, 1.0 Hz, 1H, CH=C*H*H), 2.58 (s, 3H, C*H*$_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 202.1, 137.7, 137.5, 135.9, 131.6, 128.7, 127.6, 127.5, 116.7, 29.9.

*Synthesis of (E)/(Z)-1-(2-vinylphenyl)ethan-1-one O-methyl oximes (E-***145** and *Z-***145**)



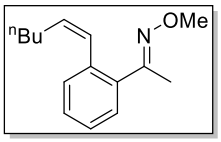
1-(2-Vinylphenyl)ethan-1-one (900 mg, 6.2 mmol) *O*-methylhydroxylamine hydrochloride (1.05 g, 12.4 mmol), Na_2SO_4 (1.8 g, 12.4 mmol)) and pyridine (1.1 g, 13.5 mmol) in methanol (15 mL) were stirred at room temperature and the reaction was monitored via TLC analysis. Upon completion, the mixture was diluted with water, and extracted with ethyl acetate. The organic phase was dried over anhydrous $MgSO_4$, filtered and the solvent was removed *in vacuo*. The residue was purified by flash column chromatography on silica gel eluting with petroleum ether (40/60) and ethyl acetate to afford a mixture of *(E)/(Z)*-1-(2-vinylphenyl)ethan-1-one *O*-methyl oximes (1.0 g, 94%).

E-**145.** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, *J* = 8.0 Hz, 1H, C*H*$_{ar}$), 7.36 – 7.31 (m, 1H, C*H*$_{ar}$), 7.30 – 7.26 (m, 1H, C*H*$_{ar}$), 7.26 – 7.23 (m, 1H, C*H*$_{ar}$), 6.88 (dd, *J* = 17.5, 11.0 Hz, 1H, CH_2=C*H*), 5.70 (dd, *J* = 17.5, 1.0 Hz, 1H, =C*H*H), 5.29 (dd, *J* = 11.0, 1.0 Hz, 1H, =C*H*H), 3.99 (s, 3H, OC*H*$_3$), 2.16 (s, 3H,

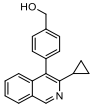
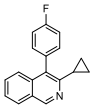
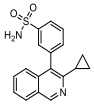
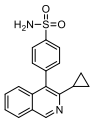
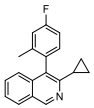
C*H*$_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.8, 136.5, 136.0, 135.0, 128.7, 128.6, 127.7, 126.1, 115.8, 61.8, 17.0. HRMS: *m*/*z* $[MH]^+$ $C_{11}H_{14}NO$ calcd. 176.1070, found 176.1069. FTIR : ν_{max}/ cm^{-1} (neat) 2937 (w), 1581 (w), 1365 (m), 1185 (w), 1071 (s).

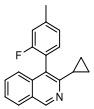
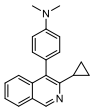
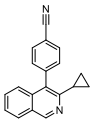
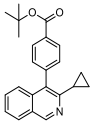
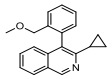
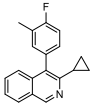
Z-**145.** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 – 7.58 (m, 1H, C*H*$_{ar}$), 7.34 – 7.27 (m, 2H, C*H*$_{ar}$), 7.10 – 7.05 (m, 1H, C*H*$_{ar}$), 6.62 (dd, *J* = 17.5, 11.0 Hz, 1H, C*H*$_{ar}$), 5.73 (dd, *J* = 17.5, 1.1 Hz, 1H, C*H*$_{ar}$), 5.28 (dd, *J* = 11.0, 1.0 Hz, 1H, C*H*$_{ar}$), 3.80 (s, 3H, OC*H*$_3$), 2.13 (s, 3H, C*H*$_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.2, 135.4, 134.4, 134.0, 128.4, 127.8, 126.4, 125.1, 115.6, 61.7, 22.3. HRMS: *m*/*z* $[MH]^+$ $C_{11}H_{14}NO$ calcd. 176.1070, found 176.1069. FTIR : ν_{max}/ cm^{-1} (neat) 2942 (w), 1580 (w), 1365 (m), 1181 (w), 1071 (s).

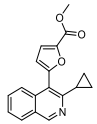
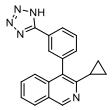
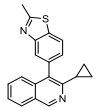
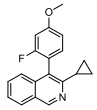
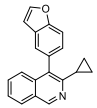
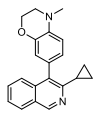
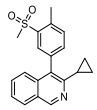
Experimental route to compound *E*-148

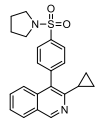
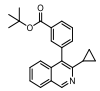
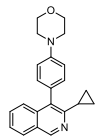
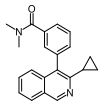
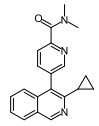
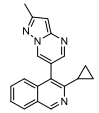
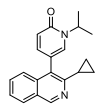
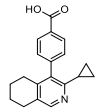


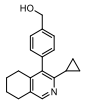
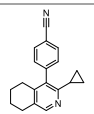
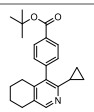
(E)-1-(2-(hex-1-yn-1-yl)phenyl)ethan-1-one *O*-methyl oxime (100 mg, 0.43 mmol), Lindlar Catalyst (1 equiv) in EtOAc (5 mL) were stirred at under H_2 admosphere at room temperature and the reaction was monitored via TLC analysis. Upon completion, the mixture was filtrated over celite, dried over anhydrous $MgSO_4$, filtered and the solvent was removed *in vacuo*. The residue was purified by flash column chromatography on silica gel eluting with petroleum ether (40/60) and ethyl acetate to afford compound *E*-**148** as a yellow oil (83 mg, 84%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 – 7.28 (m, 2H, C*H*$_{ar}$), 7.26 – 7.22 (m, 2H, C*H*$_{ar}$), 6.43 (d, *J* = 11.5 Hz, 1H, =C*H*), 5.69 (dt, *J* = 11.5, 7.5 Hz, 1H, =C*H*), 3.96 (s, 3H, OC*H*$_3$), 2.23 – 2.12 (m, 2H, C*H*$_2$), 2.10 (s, 3H, C*H*$_3$), 1.39 – 1.34 (m, 2H, C*H*$_2$), 1.31 – 1.24 (m, 2H, C*H*$_2$), 0.86 (t, *J* = 7.0 Hz, 3H, C*H*$_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.6, 137.3, 136.1, 134.0, 129.8, 128.4, 128.2, 127.5, 126.8, 61.7, 31.9, 28.3, 22.4, 16.7, 14.0. HRMS: *m*/*z* $[MH]^+$ $C_{15}H_{22}NO$ calcd. 232.1696, found 232.1701. FTIR : ν_{max}/ cm^{-1} (neat) 2956 (w), 1465 (w), 1364 (w), 1185 (w), 1049 (s

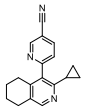
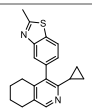
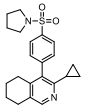
Reference	*Chemical compound*	*LC-MS purity*	*^{1}H NMR*
A.01		95	^{1}H NMR (400 MHz, $CDCl_3$) δ 9.16 (s, 1H, C*H*$_{ar}$), 8.72 (dd, *J* = 5.0, 1.5 Hz, 1H, C*H*$_{ar}$), 8.68 (d, *J* = 1.5 Hz, 1H, C*H*$_{ar}$), 7.94 (d, *J* = 8.0 Hz, 1H, C*H*$_{ar}$), 7.76 (dt, *J* = 8.0, 1.5 Hz, 1H, C*H*$_{ar}$), 7.54 (ddd, *J* = 8.5, 7.0, 1.5 Hz, 1H, C*H*$_{ar}$), 7.51 – 7.45 (m, 2H, C*H*$_{ar}$), 7.31 (d, *J* = 8.5 Hz, 1H, C*H*$_{ar}$), 1.83 – 1.76 (m, 1H, C*H*), 1.22 – 1.17 (m, 2H, C*H*$_2$), 0.91 – 0.81 (m, 2H, C*H*$_2$).
A.02		100	^{1}H NMR (600 MHz, DMSO) δ 9.37 (s, 1H, C*H*$_{ar}$), 9.33 (s, 1H, C*H*$_{ar}$), 8.94 (s, 2H, C*H*$_{ar}$), 8.16 (d, *J* = 8.0 Hz, 1H, C*H*$_{ar}$), 7.72 (ddd, *J* = 8.5, 7.0, 1.5 Hz, 1H, C*H*$_{ar}$), 7.64 (ddd, *J* = 8.0, 7.0, 1.0 Hz, 1H, C*H*$_{ar}$), 7.30 (dd, *J* = 8.5, 1.0 Hz, 1H, C*H*$_{ar}$), 1.74 (tt, *J* = 8.0, 4.0 Hz, 1H, C*H*), 1.12 – 1.08 (m, 2H, C*H*$_2$), 0.92 – 0.87 (m, 2H, C*H*$_2$).
A.03		98	1H NMR (600.05 MHz, DMSO-d6) δ ppm 9.29 (s, 1 H, C*H*$_{ar}$), 8.15 (d, J=8.0 Hz, 1 H, C*H*$_{ar}$), 7.69 (t, J=7.5 Hz, 1 H, C*H*$_{ar}$), 7.61 (t, J=7.0 Hz, 1 H, C*H*$_{ar}$), 7.53 (d, J=8.0 Hz, 2 H, C*H*$_{ar}$), 7.35 (m, 3 H, C*H*$_{ar}$), 4.63 (s, 2 H, C*H*$_2$), 1.87 (m, 1 H, C*H*), 1.06 (m, 2 H, C*H*$_2$), 0.85 (m, 2 H, C*H*$_2$).
A.04		100	^{1}H NMR (600 MHz, DMSO) δ 9.29 (s, 1H, C*H*$_{ar}$), 8.14 (d, *J* = 8.0 Hz, 1H, C*H*$_{ar}$), 7.74 – 7.67 (m, 1H, C*H*$_{ar}$), 7.65 – 7.59 (m, 1H, C*H*$_{ar}$), 7.48 – 7.39 (m, 4H, C*H*$_{ar}$), 7.30 (d, *J* = 8.5 Hz, 1H, C*H*$_{ar}$), 1.83 (tt, *J* = 8.0, 5.0 Hz, 1H, C*H*), 1.09 – 1.03 (m, 2H, C*H*$_2$), 0.89 – 0.82 (m, 2H, C*H*$_2$).
A.05		92	^{1}H NMR (600 MHz, DMSO) δ 9.30 (s, 1H, C*H*$_{ar}$), 8.14 (d, *J* = 8.0 Hz, 1H, C*H*$_{ar}$), 8.00 – 7.95 (m, 1H, C*H*$_{ar}$), 7.85 – 7.83 (m, 1H, C*H*$_{ar}$), 7.80 (t, *J* = 7.5 Hz, 1H, C*H*$_{ar}$), 7.69 (ddd, *J* = 8.0, 7.0, 1.0 Hz, 1H, C*H*$_{ar}$), 7.67 – 7.64 (m, 1H, C*H*$_{ar}$), 7.62 (ddd, *J* = 8.0, 7.0, 1.0 Hz, 1H, C*H*$_{ar}$), 7.46 (br, 2H, N*H*$_2$), 7.25 (d, *J* = 8.5 Hz, 1H, C*H*$_{ar}$), 1.81 – 1.74 (m, 1H, C*H*), 1.12 – 1.05 (m, 2H, C*H*$_2$), 0.87 (m, 2H, C*H*$_2$).
A.06		85	^{1}H NMR (600 MHz, DMSO) δ 9.30 (s, 1H, C*H*$_{ar}$), 8.15 (d, *J* = 8.0 Hz, 1H, C*H*$_{ar}$), 8.06 – 8.01 (m, 2H, C*H*$_{ar}$), 7.72 – 7.68 (m, 1H, C*H*$_{ar}$), 7.64 – 7.62 (m, 3H, C*H*$_{ar}$), 7.52 (br, 2H, N*H*$_2$), 7.24 (d, *J* = 8.3 Hz, 1H, C*H*$_{ar}$), 1.78 – 1.73 (m, 1H, C*H*), 1.12 – 1.03 (m, 2H, C*H*$_2$), 0.91 – 0.80 (m, 2H, C*H*$_2$).
A.07		99	^{1}H NMR (600 MHz, DMSO) δ 9.29 (s, 1H, C*H*$_{ar}$), 8.15 (d, *J* = 8.0 Hz, 1H, C*H*$_{ar}$), 7.68 (ddd, *J* = 8.5, 7.0, 1.0 Hz, 1H, C*H*$_{ar}$), 7.65 – 7.58 (m, 1H, C*H*$_{ar}$), 7.34 (m, 1H, C*H*$_{ar}$), 7.27 (dd, *J* = 8.5, 6.0 Hz, 1H, C*H*$_{ar}$), 7.22 (td, *J* = 8.5, 3.0 Hz, 1H, C*H*$_{ar}$), 7.13 (dd, *J* = 8.5, 1.0 Hz, 1H, C*H*$_{ar}$), 1.95 (s, 3H, C*H*$_3$), 1.67 (tt, *J* = 8.0, 5.0 Hz, 1H, C*H*), 1.12 – 1.05 (m, 1H, C*H*H), 1.04 – 0.98 (m, 1H, C*H*H), 0.95 – 0.76 (m, 2H, C*H*$_2$).

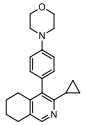
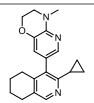
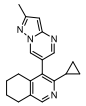
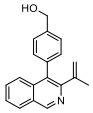
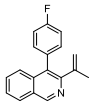
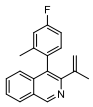
A.08		99	1H NMR (600.05 MHz, DMSO-d6) δ ppm 9.29 (s, 1 H, C*H*$_{ar}$), 8.14 (d, J=8.0 Hz, 1 H, C*H*$_{ar}$), 7.65 (m, 3 H, C*H*$_{ar}$), 7.36 (t, J=8.5, 1 H, C*H*$_{ar}$), 7.27 (m, 3 H, C*H*$_{ar}$), 1.82 (m, 1 H, C*H*), 1.06 (m, 2 H, C*H*$_2$), 0.87 (m, 2 H, C*H*$_2$)
A.09		100	^{1}H NMR (600 MHz, DMSO) δ 9.28 (s, 1H, C*H*$_{ar}$), 8.13 (d, *J* = 8.0 Hz, 1H, C*H*$_{ar}$), 7.69 (ddd, *J* = 8.5, 7.0, 1.0 Hz, 1H, C*H*$_{ar}$), 7.64 – 7.58 (m, 1H, C*H*$_{ar}$), 7.32 (t, *J* = 7.5 Hz, 1H, C*H*$_{ar}$), 7.27 (dd, *J* = 9.0, 6.0 Hz, 2H, C*H*$_{ar}$), 7.24 (dd, *J* = 7.5, 1.0 Hz, 1H, C*H*$_{ar}$), 2.45 (s, 3H, C*H*$_3$), 1.85 – 1.76 (m, 1H, C*H*), 1.09 – 1.02 (m, 2H, C*H*$_2$), 0.91 – 0.81 (m, 2H, C*H*$_2$).
A.10		98	^{1}H NMR (600 MHz, DMSO) δ 9.29 (s, 1H, C*H*$_{ar}$), 8.17 (d, *J* = 8.0 Hz, 1H, C*H*$_{ar}$), 7.73 (t, *J* = 7.5 Hz, 1H, C*H*$_{ar}$), 7.64 (t, *J* = 7.5 Hz, 1H, C*H*$_{ar}$), 7.46 (d, *J* = 8.5 Hz, 1H, C*H*$_{ar}$), 7.24 (d, *J* = 8.5 Hz, 2H, C*H*$_{ar}$), 6.98 (d, *J* = 8.5 Hz, 2H, C*H*$_{ar}$), 3.02 (s, 6H, C*H*$_3$ x2), 2.06 – 1.88 (m, 1H, C*H*), 1.08 – 1.01 (m, 2H, C*H*$_2$), 0.92 – 0.79 (m, 2H, C*H*$_2$).
A.11		100	^{1}H NMR (600 MHz, DMSO) δ 9.31 (s, 1H, C*H*$_{ar}$), 8.15 (d, *J* = 8.0 Hz, 1H, C*H*$_{ar}$), 8.01 (dt, *J* = 7.5, 1.5 Hz, 1H, C*H*$_{ar}$), 7.93 (t, *J* = 1.5 Hz, 1H, C*H*$_{ar}$), 7.81 (t, *J* = 7.5 Hz, 1H, C*H*$_{ar}$), 7.77 (dt, *J* = 7.5, 1.5 Hz, 1H, C*H*$_{ar}$), 7.70 (ddd, *J* = 8.5, 7.0, 1.5 Hz, 1H, C*H*$_{ar}$), 7.63 (ddd, *J* = 8.0, 7.0, 1.0 Hz, 1H, C*H*$_{ar}$), 7.24 (dd, *J* = 8.5, 1.0 Hz, 1H, C*H*$_{ar}$), 1.77 – 1.70 (m, 1H, C*H*), 1.11 – 1.03 (m, 2H, C*H*$_2$), 0.95 – 0.79 (m, 2H, C*H*$_2$).
A.12		99	^{1}H NMR (600 MHz, DMSO) δ 9.31 (s, 1H, C*H*$_{ar}$), 8.15 (d, *J* = 8.0 Hz, 1H, C*H*$_{ar}$), 8.09 – 8.04 (m, 2H, C*H*$_{ar}$), 7.69 (ddd, *J* = 8.5, 7.0, 1.5 Hz, 1H, C*H*$_{ar}$), 7.66 – 7.60 (m, 3H, C*H*$_{ar}$), 7.23 (dd, *J* = 8.5, 1.0 Hz, 1H, C*H*$_{ar}$), 1.79 – 1.69 (m, 1H, C*H*), 1.10 – 1.04 (m, 2H, C*H*$_2$), 0.89 – 0.82 (m, 2H, C*H*$_2$).
A.13		99	^{1}H NMR (600 MHz, DMSO) δ 9.30 (s, 1H, C*H*$_{ar}$), 8.15 (d, *J* = 8.0 Hz, 1H, C*H*$_{ar}$), 8.13 – 8.09 (m, 2H, C*H*$_{ar}$), 7.68 (ddd, *J* = 8.5, 7.0, 1.5 Hz, 1H, C*H*$_{ar}$), 7.64 – 7.59 (m, 1H, C*H*$_{ar}$), 7.57 – 7.52 (m, 2H, C*H*$_{ar}$), 7.27 (d, *J* = 8.5 Hz, 1H, C*H*$_{ar}$), 1.83 – 1.74 (m, 1H, C*H*), 1.60 (s, 9H, C*H*$_3$ x3), 1.10 – 1.03 (m, 2H, C*H*$_2$), 0.88 – 0.81 (m, 2H, C*H*$_2$).
A.14		100	^{1}H NMR (600 MHz, DMSO) δ 9.28 (s, 1H, C*H*$_{ar}$), 8.13 (d, *J* = 8.0 Hz, 1H, C*H*$_{ar}$), 7.69 – 7.62 (m, 2H, C*H*$_{ar}$), 7.61 – 7.58 (m, 1H, C*H*$_{ar}$), 7.54 (td, *J* = 7.5, 1.5 Hz, 1H, C*H*$_{ar}$), 7.50 (td, *J* = 7.5, 1.5 Hz, 1H, C*H*$_{ar}$), 7.26 (dd, *J* = 7.5, 1.5 Hz, 1H, C*H*$_{ar}$), 7.10 (dd, *J* = 8.5, 1.0 Hz, 1H, C*H*$_{ar}$), 4.09 (d, *J* = 12.5 Hz, 1H, C*H*H), 3.99 (d, *J* = 12.5 Hz, 1H, C*H*H), 3.02 (s, 3H, C*H*$_3$), 1.69 – 1.62 (m, 1H, C*H*), 1.11 – 0.98 (m, 2H, C*H*$_2$), 0.89 – 0.77 (m, 2H, C*H*$_2$).
A.15		94	^{1}H NMR (600 MHz, DMSO) δ 9.29 (s, 1H, C*H*$_{ar}$), 8.14 (d, *J* = 8.0 Hz, 1H, C*H*$_{ar}$), 7.68 (ddd, *J* = 8.5, 7.0, 1.5 Hz, 1H, C*H*$_{ar}$), 7.64 – 7.58 (m, 1H, C*H*$_{ar}$), 7.49 (dd, *J* = 8.5, 6.0 Hz, 1H, C*H*$_{ar}$), 7.27 (td, *J* = 8.5, 3.0 Hz, 1H, C*H*$_{ar}$), 7.16 – 7.09 (m, 2H, C*H*$_{ar}$), 1.90 (s, 3H, C*H*$_3$), 1.71 – 1.62 (m, 1H, C*H*), 1.16 – 1.03 (m, 1H, C*H*H), 1.03 – 0.98 (m, 1H, CH*H*), 0.94 – 0.78 (m, 2H, C*H*$_2$).
A.16		97	1H NMR (600.05 MHz, DMSO-d6) δ ppm 9.28 (s, 1 H, C*H*$_{ar}$), 8.13 (d, J=8.0 Hz, 1 H, C*H*$_{ar}$), 7.69 (t, J=7.5, 1 H, C*H*$_{ar}$), 7.61 (t, J=7.0, 1 H, C*H*$_{ar}$), 7.33 (m, 3 H, C*H*$_{ar}$), 7.24 (ddd, J=8.0, 5.0, 2.2 Hz, 1 H, C*H*$_{ar}$), 2.34 (m, 3 H, C*H*$_3$), 1.85 (m, 1 H, C*H*), 1.05 (m, 2 H, C*H*$_2$), 0.86 (m, 2H, C*H*$_2$).

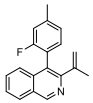
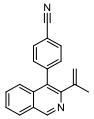
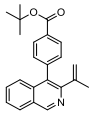
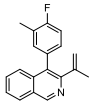
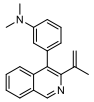
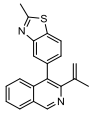
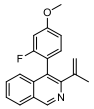
A.17		96	^{1}H NMR (600 MHz, DMSO) δ 9.33 (s, 1H, C*H*$_{ar}$), 8.15 (d, *J* = 8.0 Hz, 1H, C*H*$_{ar}$), 7.77 (ddd, *J* = 8.5, 7.0, 1.5 Hz, 1H, C*H*$_{ar}$), 7.65 (ddd, *J* = 8.0, 7.0, 1.0 Hz, 1H, C*H*$_{ar}$), 7.58 (d, *J* = 3.5 Hz, 1H, C*H*$_{ar}$), 7.51 (dd, *J* = 8.5, 1.0 Hz, 1H, C*H*$_{ar}$), 7.01 (d, *J* = 3.5 Hz, 1H, C*H*$_{ar}$), 3.85 (s, 3H, OC*H*$_3$), 2.02 (tt, *J* = 8.0, 5.0 Hz, 1H, C*H*), 1.19 – 1.01 (m, 2H, C*H*$_2$), 1.01 – 0.87 (m, 2H, C*H*$_2$).
A.18		96	^{1}H NMR (600 MHz, DMSO) δ 9.23 (s, 1H, C*H*$_{ar}$), 8.12 (d, *J* = 7.5 Hz, 1H, C*H*$_{ar}$), 7.97 (s, 1H, C*H*$_{ar}$), 7.75 – 7.71 (m, 1H, C*H*$_{ar}$), 7.68 (d, *J* = 8.5 Hz, 1H, C*H*$_{ar}$), 7.64 – 7.59 (m, 2H, C*H*$_{ar}$), 3.98 (s, 3H, C*H*$_3$), 2.31 – 2.15 (m, 1H, C*H*), 1.10 – 1.00 (m, 2H, C*H*$_2$), 0.94 – 0.87 (m, 2H, C*H*$_2$).
A.19		95	1H NMR (600.05 MHz, DMSO-d6) δ ppm 9.29 (s, 1 H, C*H*$_{ar}$), 8.15 (d, J=8.0 Hz, 1 H, C*H*$_{ar}$), 7.71 (t, J=7.5 Hz, 1 H, C*H*$_{ar}$), 7.62 (t, J=7.0 Hz, 1 H, C*H*$_{ar}$), 7.41 (m, 2 H, C*H*$_{ar}$), 6.92 (br d, J=8.0 Hz, 1 H, C*H*$_{ar}$), 6.76 (br s, 1 H, C*H*$_{ar}$), 6.71 (d, J=7.0 Hz, 1 H, C*H*$_{ar}$), 2.96 (s, 6 H, C*H*$_3$ x2), 1.95 (m, 1 H, C*H*), 1.06 (m, 2 H, C*H*$_2$), 0.87 (m, 2 H, C*H*$_2$).
A.20		100	1H NMR (600.05 MHz, DMSO-d6) δ ppm 9.30 (s, 1 H, C*H*$_{ar}$), 8.21 (dt, J=8.0, 1.5 Hz, 1 H, C*H*$_{ar}$), 8.15 (d, J=8.0 Hz, 1 H, C*H*$_{ar}$), 8.06 (t, J=1.5 Hz, 1 H, C*H*$_{ar}$), 7.84 (t, J=7.5 Hz, 1 H, C*H*$_{ar}$), 7.65 (m, 3 H, C*H*$_{ar}$), 7.32 (d, J=7.5 Hz, 1 H, C*H*$_{ar}$), 1.84 (m, 1 H, C*H*), 1.09 (m, 2 H, C*H*$_{a2}$), 0.86 (m, 2 H, C*H*$_2$).
A.21		99	1H NMR (600.05 MHz, DMSO-d6) δ ppm 9.34 (s, 1 H, C*H*$_{ar}$), 8.24 (d, J=8.0 Hz, 1 H, C*H*$_{ar}$), 8.18 (d, J=8.5 Hz, 1 H, C*H*$_{ar}$), 7.93 (s, 1 H, C*H*$_{ar}$), 7.69 (t, J=7.0 Hz, 1 H, C*H*$_{ar}$), 7.64 (t, J=7.0 Hz, 1 H, C*H*$_{ar}$), 7.42 (dd, J=8.0, 1.5 Hz, 1 H, C*H*$_{ar}$), 7.33 (d, J=8.5 Hz, 1 H, C*H*$_{ar}$), 2.86 (s, 3 H, C*H*$_3$), 1.87 (m, 1 H, C*H*), 1.08 (m, 2 H, C*H*$_2$), 0.85 (m, 2 H, C*H*$_2$).
A.22		98	^{1}H NMR (600 MHz, DMSO) δ 9.28 (s, 1H, C*H*$_{ar}$), 8.14 (d, *J* = 8.0 Hz, 1H, C*H*$_{ar}$), 7.70 (ddd, *J* = 8.5, 7.0, 1.5 Hz, 1H, C*H*$_{ar}$), 7.64 – 7.58 (m, 1H, C*H*$_{ar}$), 7.35 (t, *J* = 8.5 Hz, 1H, C*H*$_{ar}$), 7.30 (d, *J* = 8.5 Hz, 1H, C*H*$_{ar}$), 7.08 (dd, *J* = 11.5, 2.5 Hz, 1H, C*H*$_{ar}$), 7.01 (dd, *J* = 8.5, 2.5 Hz, 1H, C*H*$_{ar}$), 3.88 (s, 3H, OC*H*$_3$), 1.88 – 1.80 (m, 1H, C*H*), 1.08 – 1.02 (m, 2H, C*H*$_2$), 0.92 – 0.82 (m, 2H, C*H*$_2$).
A.23		99	^{1}H NMR (600 MHz, DMSO) δ 9.32 (s, 1H, C*H*$_{ar}$), 8.16 (d, *J* = 8.0 Hz, 1H, C*H*$_{ar}$), 8.11 (d, *J* = 2.0 Hz, 1H, C*H*$_{ar}$), 7.80 (d, *J* = 8.5 Hz, 1H, C*H*$_{ar}$), 7.75 – 7.65 (m, 2H, C*H*$_{ar}$), 7.62 (t, *J* = 7.5 Hz, 1H, C*H*$_{ar}$), 7.31 (dd, *J* = 8.5, 1.5 Hz, 2H, C*H*$_{ar}$), 7.05 (d, *J* = 2.0 Hz, 1H, C*H*$_{ar}$), 1.92 – 1.83 (m, 1H, C*H*), 1.14 – 0.99 (m, 2H, C*H*$_2$), 0.86 – 0.77 (m, 2H, C*H*$_2$).
A.24		98	^{1}H NMR (600 MHz, DMSO) δ 9.27 (s, 1H, C*H*$_{ar}$), 8.15 (d, *J* = 8.0 Hz, 1H, C*H*$_{ar}$), 7.73 (t, *J* = 7.5 Hz, 1H, C*H*$_{ar}$), 7.62 (t, *J* = 7.5 Hz, 1H, C*H*$_{ar}$), 7.48 (d, *J* = 8.5 Hz, 1H, C*H*$_{ar}$), 6.88 (d, *J* = 8.0 Hz, 1H, C*H*$_{ar}$), 6.79 (dd, *J* = 8.0, 2.0 Hz, 1H, C*H*$_{ar}$), 6.69 (d, *J* = 2.0 Hz, 1H, C*H*$_{ar}$), 4.31 (dd, *J* = 5.0, 4.0 Hz, 2H, C*H*$_2$), 3.36 – 3.31 (m, 2H, C*H*$_2$), 2.93 (s, 3H, C*H*$_3$), 2.06 – 2.00 (m, 1H, C*H*), 1.07 – 1.01 (m, 2H, C*H*$_2$), 0.93 – 0.83 (m, 2H, C*H*$_2$).
A.25		98	^{1}H NMR (600 MHz, DMSO) δ 9.31 (s, 1H, C*H*$_{ar}$), 8.16 (d, *J* = 8.0 Hz, 1H, C*H*$_{ar}$), 7.88 (d, *J* = 1.5 Hz, 1H, C*H*$_{ar}$), 7.74 – 7.59 (m, 4H, C*H*$_{ar}$), 7.31 (d, *J* = 8.5 Hz, 1H, C*H*$_{ar}$), 3.32 (s, 3H, SC*H*$_3$), 2.77 (s, 3H, C*H*$_3$), 1.84 – 1.75 (m, 1H, C*H*), 1.08 (m, 2H, C*H*$_2$), 0.87 (m, 2H, C*H*$_2$).

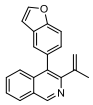
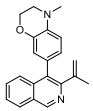
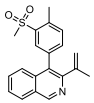
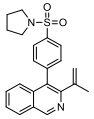
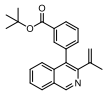
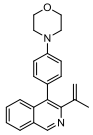
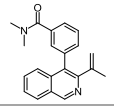
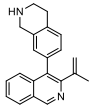
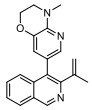
A.26		99	^{1}H NMR (600 MHz, DMSO) δ 9.31 (s, 1H, C*H*$_{ar}$), 8.15 (d, *J* = 8.0 Hz, 1H, C*H*$_{ar}$), 8.03 – 7.98 (m, 2H, C*H*$_{ar}$), 7.70 (ddd, *J* = 8.5, 7.0, 1.5 Hz, 1H, C*H*$_{ar}$), 7.69 – 7.66 (m, 2H, C*H*$_{ar}$), 7.63 (ddd, *J* = 8.0, 7.0, 1.0 Hz, 1H, C*H*$_{ar}$), 7.25 (dd, *J* = 8.5, 1.0 Hz, 1H, C*H*$_{ar}$), 3.30 – 3.22 (m, 4H, C*H*$_2$ x2), 1.80 – 1.70 (m, 5H, C*H*$_2$ x2 + C*H*), 1.12 – 1.04 (m, 2H, C*H*$_2$), 0.90 – 0.82 (m, 2H, C*H*$_2$).
A.27		96	^{1}H NMR (600 MHz, DMSO) δ 9.31 (s, 1H, C*H*$_{ar}$), 8.16 (d, *J* = 8.0 Hz, 1H, C*H*$_{ar}$), 8.08 – 8.03 (m, 1H, C*H*$_{ar}$), 7.88 (t, *J* = 1.5 Hz, 1H, C*H*$_{ar}$), 7.73 (t, *J* = 7.5 Hz, 1H, C*H*$_{ar}$), 7.71 – 7.66 (m, 2H, C*H*$_{ar}$), 7.64 – 7.60 (m, 1H, C*H*$_{ar}$), 7.25 (dd, *J* = 8.5, 1.0 Hz, 1H, C*H*$_{ar}$), 1.82 – 1.74 (m, 1H, C*H*), 1.55 (s, 9H, C*H*$_3$ x3), 1.15 – 1.00 (m, 2H, C*H*$_2$), 0.92 – 0.79 (m, 2H, C*H*$_2$).
A.28		98	^{1}H NMR (600 MHz, DMSO) δ 9.29 (s, 1H, C*H*$_{ar}$), 8.16 (d, *J* = 8.0 Hz, 1H, C*H*$_{ar}$), 7.72 (t, *J* = 7.5 Hz, 1H, C*H*$_{ar}$), 7.63 (t, *J* = 7.5 Hz, 1H, C*H*$_{ar}$), 7.43 (d, *J* = 8.5 Hz, 1H, C*H*$_{ar}$), 7.29 – 7.24 (m, 2H, C*H*$_{ar}$), 7.17 – 7.13 (m, 2H, C*H*$_{ar}$), 3.82 – 3.76 (m, 4H, C*H*$_2$ x2), 3.27 – 3.20 (m, 4H, C*H*$_2$ x2), 2.01 – 1.93 (m, 1H, C*H*), 1.08 – 1.01 (m, 2H, C*H*$_2$), 0.91 – 0.81 (m, 2H, C*H*$_2$).
A.29		99	^{1}H NMR (600 MHz, DMSO) δ 9.31 (s, 1H, C*H*$_{ar}$), 8.16 (d, *J* = 8.0 Hz, 1H, C*H*$_{ar}$), 7.75 – 7.69 (m, 1H, C*H*$_{ar}$), 7.67 (t, *J* = 7.5 Hz, 1H, C*H*$_{ar}$), 7.65 – 7.61 (m, 1H, C*H*$_{ar}$), 7.55 (dt, *J* = 7.5, 1.5 Hz, 1H, C*H*$_{ar}$), 7.51 – 7.46 (m, 1H, C*H*$_{ar}$), 7.40 (t, *J* = 1.5 Hz, 1H, C*H*$_{ar}$), 7.34 – 7.29 (m, 1H, C*H*$_{ar}$), 2.99 (s, 6H, C*H*$_3$ x2), 1.89 – 1.80 (m, 1H, C*H*), 1.10 – 1.02 (m, 2H, C*H*$_2$), 0.90 – 0.83 (m, 2H, C*H*$_2$).
A.30		99	^{1}H NMR (600 MHz, DMSO) δ 9.33 (s, 1H, C*H*$_{ar}$), 8.62 (dd, *J* = 2.0, 1.0 Hz, 1H, C*H*$_{ar}$), 8.17 (d, *J* = 8.0 Hz, 1H, C*H*$_{ar}$), 8.01 (dd, *J* = 8.0, 2.0 Hz, 1H, C*H*$_{ar}$), 7.78 (dd, *J* = 8.0, 1.0 Hz, 1H, C*H*$_{ar}$), 7.73 (ddd, *J* = 8.5, 7.0, 1.5 Hz, 1H, C*H*$_{ar}$), 7.67 – 7.62 (m, 1H, C*H*$_{ar}$), 7.32 (dd, *J* = 8.5, 1.0 Hz, 1H, C*H*$_{ar}$), 3.07 (d, *J* = 2.5 Hz, 6H, C*H*$_3$ x2), 1.83 – 1.75 (m, 1H, C*H*), 1.18 – 1.06 (m, 2H, C*H*$_2$), 0.94 – 0.83 (m, 2H, C*H*$_2$).
A.31		97	^{1}H NMR (600 MHz, DMSO) δ 9.35 (s, 1H, C*H*$_{ar}$), 9.21 (dd, *J* = 2.0, 1.0 Hz, 1H, C*H*$_{ar}$), 8.49 (d, *J* = 2.0 Hz, 1H, C*H*$_{ar}$), 8.17 (d, *J* = 8.0 Hz, 1H, C*H*$_{ar}$), 7.72 (ddd, *J* = 8.5, 7.0, 1.5 Hz, 1H, C*H*$_{ar}$), 7.68 – 7.62 (m, 1H, C*H*$_{ar}$), 7.52 (d, *J* = 8.5 Hz, 1H, C*H*$_{ar}$), 6.66 (s, 1H, C*H*$_{ar}$), 2.49 (s, 3H, C*H*$_3$), 1.99 – 1.91 (m, 1H, C*H*), 1.14 – 1.07 (m, 2H, C*H*$_2$), 0.98 – 0.83 (m, 2H, C*H*$_2$).
A.32		100	^{1}H NMR (600 MHz, DMSO) δ 9.29 (s, 1H, C*H*$_{ar}$), 8.16 (d, *J* = 8.0 Hz, 1H, C*H*$_{ar}$), 7.83 (d, *J* = 2.5 Hz, 1H, C*H*$_{ar}$), 7.81 – 7.76 (m, 1H, C*H*$_{ar}$), 7.65 (t, *J* = 7.0 Hz, 1H, C*H*$_{ar}$), 7.58 (d, *J* = 8.5 Hz, 1H, C*H*$_{ar}$), 7.43 (dd, *J* = 9.0, 2.5 Hz, 1H, C*H*$_{ar}$), 6.58 (d, *J* = 9.0 Hz, 1H, C*H*$_{ar}$), 5.21 – 5.13 (m, 1H, C*H*), 2.10 – 2.00 (m, 1H, C*H*), 1.34 (d, *J* = 7.0 Hz, 6H, C*H*$_3$ x2), 1.13 – 1.02 (m, 2H, C*H*$_2$), 1.02 – 0.90 (m, 2H, C*H*$_2$).
B.01		96	1H NMR (600.05 MHz, DMSO-d6) δ ppm 8.26 (s, 1 H, C*H*$_{ar}$), 8.07 (m, 2 H, C*H*$_{ar}$), 7.41 (m, 2 H, C*H*$_{ar}$), 2.78 (br, 2H, C*H*$_2$), 2.37 – 2.22 (m, 2H, C*H*$_2$), 1.74 – 1.68 (m, 2H, C*H*$_2$), 1.67 – 1.62 (m, 2H, C*H*$_2$), 1.57 – 1.52 (m, 1H, C*H*), 1.02 – 0.86 (m, 2H, C*H*$_2$), 0.86 – 0.66 (m, 2H, C*H*$_2$).
B.02		100	1H NMR (600.05 MHz, DMSO-d6) δ ppm 8.75 (br, 1 H, C*H*$_{ar}$), 8.63 (s, 1 H, C*H*$_{ar}$), 8.35 (s, 1 H, C*H*$_{ar}$), 7.97 (d, J=7.5 Hz, 1 H, C*H*$_{ar}$), 7.72 (dd, J=8.0, 5.0 Hz, 1 H, C*H*$_{ar}$), 2.81 (m, 2 H, C*H*$_2$), 2.35 (m, 2 H, C*H*$_2$), 1.70 (m, 4 H, C*H*$_2$ x2), 1.60 (m, 1 H, C*H*), 0.97 (m, 2 H, C*H*$_2$), 0.82 (m, 2 H, C*H*$_2$).

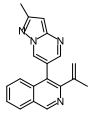
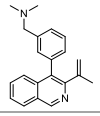
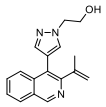
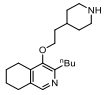
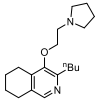
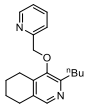
B.03		100	1H NMR (600.05 MHz, DMSO-d6) δ ppm 9.29 (s, 1 H, C*H*$_{ar}$), 8.82 (s, 2 H, C*H*$_{ar}$), 8.33 (s, 1 H, C*H*$_{ar}$), 2.79 (t, J=6.0 Hz, 2 H, C*H*$_2$), 2.35 (t, J=6.0 Hz, 2 H, C*H*$_2$), 1.69 (m, 4 H, C*H*$_2$ x2), 1.57 (m, 1 H, C*H*), 0.95 (m, 2 H, C*H*$_2$), 0.80 (m, 2 H, C*H*$_2$).
B.04		92	1H NMR (600.05 MHz, DMSO-d6) d ppm 8.27 (s, 1 H, C*H*$_{ar}$), 7.46 (m, 2 H, C*H*$_{ar}$), 7.22 (m, 2 H, C*H*$_{ar}$), 4.57 (s, 2 H, C*H*$_2$), 2.82 – 2.76 (m, 2H, C*H*$_2$), 2.34 (m, 2 H, C*H*$_2$), 1.68 (m, 5 H, C*H*$_2$ x2 + C*H*), 0.97 (m, 2 H, C*H*$_2$), 0.81 (m, 2 H, C*H*$_2$).
B.05		99	1H NMR (600.05 MHz, DMSO-d6) δ ppm 8.29 (s, 1 H, C*H*$_{ar}$), 7.35 (m, 4 H, C*H*$_{ar}$), 2.80 (t, J=6.0 Hz, 2 H, C*H*$_2$), 2.34 (t, J=6.0 Hz, 2 H, C*H*$_2$), 1.68 (m, 5 H, C*H*$_2$ x2 + C*H*), 0.96 (m, 2 H, C*H*$_2$), 0.82 (m, 2 H, C*H*$_2$).
B.06		100	1H NMR (600.05 MHz, DMSO-d6) δ ppm 8.31 (s, 1 H, C*H*$_{ar}$), 7.28 (d, J=9.5 Hz, 1 H, C*H*$_{ar}$), 7.17 (d, J=7.0 Hz, 2 H, C*H*$_{ar}$), 2.81 (t, J=6.0 Hz, 2 H, C*H*$_2$), 2.34 (m, 1 H, C*H*H), 2.11 (m, 1 H, CH*H*), 2.00 (s, 3 H, C*H*$_3$), 1.69 (m, 4 H, C*H*$_2$ x2), 1.52 (m, 1 H, C*H*), 1.02 (m, 1 H, CH*H*), 0.98 (m, 1 H, CH*H*), 0.87 (m, 1 H, CH*H*), 0.83 (m, 1 H, CH*H*).
B.07		100	1H NMR (600.05 MHz, DMSO-d6) δ ppm 8.30 (s, 1 H, C*H*$_{ar}$), 7.58 (td, J=8.0, 6.0 Hz, 1 H, C*H*$_{ar}$), 7.30 (td, J=8.5, 2.0 Hz, 1 H, C*H*$_{ar}$), 7.20 – 7.17 (m, 1H, C*H*$_{ar}$), 7.13 (br, 1 H, C*H*$_{ar}$), 2.80 (t, J=6.0 Hz, 2 H, C*H*$_2$), 2.36 (m, 2 H, C*H*$_2$), 1.68 (m, 5 H, C*H*$_2$ x2 + C*H*), 0.97 (m, 2 H, C*H*$_2$), 0.83 (m, 2 H, C*H*$_2$)
B.08		98	1H NMR (600.05 MHz, DMSO-d6) d ppm 8.28 (s, 1 H, C*H*$_{ar}$), 7.20 (m, 3 H, C*H*$_{ar}$), 2.78 (br, 2H, C*H*$_2$), 2.40 (s, 3H, C*H*$_3$), 2.39 – 2.34 (m, 1H, CH*H*), 2.30 – 2.23 (m, 1H, CH*H*), 1.73 – 1.68 (m, 2H, C*H*$_2$), 1.69 – 1.64 (m, 2H, C*H*$_2$), 1.63 – 1.59 (m, 1H, C*H*). 0.95 (m, 2 H, C*H*$_2$), 0.81 (m, 2 H, C*H*$_2$).
B.09		99	1H NMR (600.05 MHz, DMSO-d6) δ ppm 8.31 (s, 1 H, C*H*$_{ar}$), 7.95 – 7.92 (m, 1H, C*H*$_{ar}$), 7.82 (br, 1H, C*H*$_{ar}$), 7.74 (t, *J* = 8.0 Hz, 1H, C*H*$_{ar}$), 7.66 – 7.63 (m, 1H, C*H*$_{ar}$), 2.80 (t, J=6.0 Hz, 2 H, C*H*$_2$), 2.37 (dt, *J* = 12.0, 6.0 Hz, 1H, CH*H*), 2.27 (dt, *J* = 12.0, 6.0 Hz, 1H, CH*H*), 1.68 (m, 4 H, C*H*$_2$ x2), 1.57 (m, 1 H, C*H*), 0.95 (m, 2 H, C*H*$_2$), 0.80 (m, 2 H, C*H*$_2$).
B.10		99	1H NMR (600.05 MHz, DMSO-d6) δ ppm 8.30 (s, 1 H, C*H*$_{ar}$), 8.00 (m, 2 H, C*H*$_{ar}$), 7.52 (m, 2 H, C*H*$_{ar}$), 2.79 (t, J=6.0 Hz, 2 H, C*H*$_2$), 2.30 (t, J=6.0, 2 H, C*H*$_2$), 1.68 (m, 4 H, C*H*$_2$ x2), 1.53 (m, 1 H, C*H*), 0.95 (m, 2 H, C*H*$_2$), 0.80 (m, 1 H, CH*H*), 0.79 (m, 1 H, CH*H*).
B.11		83	1H NMR (600.05 MHz, DMSO-d6) δ ppm 8.29 (s, 1 H, C*H*$_{ar}$), 8.04 (m, 2 H, C*H*$_{ar}$), 7.42 (m, 2 H, C*H*$_{ar}$), 2.79 (t, J=6.0 Hz, 2 H, C*H*$_2$), 2.31 (t, J=6.0 Hz, 2 H, C*H*$_2$), 1.76 (m, 1 H, C*H*), 1.68 (m, 4 H, C*H*$_2$ x2), 1.57 (s, 9 H, C*H*$_3$ x3), 0.96 (m, 2 H, C*H*$_2$), 0.79 (m, 2 H, C*H*$_2$).
B.12		99	1H NMR (600.05 MHz, DMSO-d6) δ ppm 8.30 (s, 1 H, C*H*$_{ar}$), 7.56 (m, 1 H, C*H*$_{ar}$), 7.47 (m, 2 H, C*H*$_{ar}$), 7.17 (m, 1 H, C*H*$_{ar}$), 4.07 (q, J=12.0, Hz, 2 H, OC*H*$_2$), 3.13 (br, 3 H, C*H*$_3$), 2.81 (t, J=6.0, Hz, 2 H, C*H*$_2$), 2.29 (dt, J=18.0, 6.0 Hz, 1 H, CH*H*), 2.20 (m, 1 H, CH*H*), 1.69 (m, 4 H, C*H*$_2$ x2), 1.48 (m, 1 H, C*H*), 1.00 (br, 2 H, C*H*$_2$), 0.85 (br, 1 H, CH*H*), 0.80 (br, 1 H, CH*H*).
B.13		100	1H NMR (600.05 MHz, DMSO-d6) δ ppm 8.31 (s, 1 H, C*H*$_{ar}$), 7.43 (dd, J=8.5, 6.0 Hz, 1 H, C*H*$_{ar}$), 7.20 (td, J=8.5, 3.0 Hz, 1 H, C*H*$_{ar}$), 7.03 (dd, J=9.5, 3.0 Hz, 1 H, C*H*$_{ar}$), 2.80 (t, J=6.0 Hz, 2 H, C*H*$_2$), 2.38 (dt, *J* = 12.0, 6.0 Hz, 1H, CH*H*), 2.11 (dt, *J* = 12.0, 6.0 Hz, 1H,

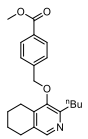
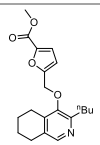
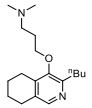
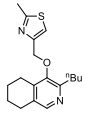
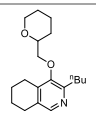
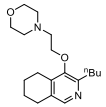
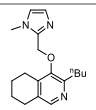
			CH*H*), 1.95 (s, 3 H, C*H*$_3$), 1.70 (m, 4 H, C*H*$_2$ x2), 1.52 (m, 1 H, C*H*), 1.02 (m, 1 H, CH*H*), 0.97 (m, 1 H, CH*H*), 0.85 (m, 2 H, C*H*$_2$).
B.14		100	1H NMR (600.05 MHz, DMSO-d6) δ ppm 8.29 (s, 1 H, C*H*$_{ar}$), 7.33 – 7.26 (m, 1H, C*H*$_{ar}$), 7.23 – 7.18 (m, 1H, C*H*$_{ar}$), 7.15 – 7.09 (m, 1H, C*H*$_{ar}$), 2.80 (t, J=6.0 Hz, 2 H, C*H*$_2$), 2.36 (m, 2 H, C*H*$_2$), 2.29 (s, 3 H, C*H*$_3$), 1.68 (m, 5 H, C*H*$_2$ x2 + C*H*), 0.97 (m, 2 H, C*H*$_2$), 0.84 (m, 2 H, C*H*$_2$).
B.15		99	1H NMR (600.05 MHz, DMSO-d6) δ ppm 9.19 (dd, *J* = 2.0, 1.0 Hz, 1H), 8.48 (dd, J=8.0, 2.0 Hz, 1 H, C*H*$_{ar}$), 8.31 (s, 1 H, C*H*$_{ar}$), 7.73 (dd, J=8.0, 1.0 Hz, 1 H, C*H*$_{ar}$), 2.78 (t, J=6.0 Hz, 2 H, C*H*$_2$), 2.30 (m, 2 H, C*H*$_2$), 1.68 (m, 4 H, C*H*$_2$ x2), 1.49 (m, 1 H, C*H*), 0.93 (m, 2 H, C*H*$_2$), 0.77 (m, 2 H, C*H*$_2$).
B.16		100	1H NMR (600.05 MHz, DMSO-d6) δ ppm 8.28 (s, 1 H, C*H*$_{ar}$), 7.48 (d, J=3.5 Hz, 1 H, C*H*$_{ar}$), 6.84 (d, J=3.5 Hz, 1 H, C*H*$_{ar}$), 3.83 (s, 3 H, OC*H*$_3$), 2.73 (t, J=6.0 Hz, 2 H, C*H*$_2$), 2.47 (t, *J* = 6.0 Hz, 2H, C*H*$_2$), 1.76 (m, 1 H, C*H*), 1.69 (m, 4 H, C*H*$_2$ x2), 0.93 (m, 2 H, C*H*$_2$), 0.84 (m, 2 H, C*H*$_2$).
B.17		100	1H NMR (600.05 MHz, DMSO-d6) δ ppm 8.35 (s, 1 H, C*H*$_{ar}$), 8.19 (d, J=8.0 Hz, 1 H, C*H*$_{ar}$), 7.84 (s, 1 H, C*H*$_{ar}$), 7.30 (dd, J=8.0, 1.5 Hz, 1 H, C*H*$_{ar}$), 2.83 (m, 5 H, C*H*$_3$ + C*H*$_2$), 2.40 (m, 2 H, C*H*$_2$), 1.69 (m, 5 H, C*H*$_2$ + C*H*), 1.01 (m, 2 H, C*H*$_2$), 0.83 (m, 2 H, C*H*$_2$).
B.18		98	1H NMR (600.05 MHz, DMSO-d6) δ ppm 8.28 (s, 1 H, C*H*$_{ar}$), 7.24 (t, J=8.5 Hz, 1 H, C*H*$_{ar}$), 7.01 (m, 1 H, C*H*$_{ar}$), 6.94 (dd, J=8.5, 2.5 Hz, 1 H, C*H*$_{ar}$), 3.83 (s, 3 H, OC*H*$_3$), 2.78 (m, 2 H, C*H*$_2$), 2.40 (m, 1 H, CH*H*), 2.29 (m, 1 H, CH*H*), 1.68 (m, 5 H, C*H*$_2$ x2 + C*H*), 0.95 (m, 2 H, C*H*$_2$), 0.83 (m, 2 H, C*H*$_2$).
B.19		100	1H NMR (600.05 MHz, DMSO-d6) δ ppm 8.33 (s, 1 H, C*H*$_{ar}$), 8.09 (d, J=2.0 Hz, 1 H, C*H*$_{ar}$), 7.76 (d, J=8.5 Hz, 1 H, C*H*$_{ar}$), 7.58 (m, 1 H, C*H*$_{ar}$), 7.20 (dd, J=8.5, 1.5 Hz, 1 H, C*H*$_{ar}$), 7.03 (dd, J=2.0, 1.0 Hz, 1 H, C*H*$_{ar}$), 2.84 (t, J=6.0 Hz, 2 H, C*H*$_2$), 2.38 (m, 2 H, C*H*$_2$), 1.68 (m, 5 H, C*H*$_2$ x2 + C*H*), 1.00 (m, 2 H, C*H*$_2$), 0.84 (m, 2H, C*H*$_2$).
B.20		100	1H NMR (600.05 MHz, DMSO-d6) δ ppm 8.26 (s, 1 H, C*H*$_{ar}$), 6.81 (d, J=8.0 Hz, 1 H, C*H*$_{ar}$), 6.66 (dd, J=8.0, 2.0 Hz, 1 H, C*H*$_{ar}$), 6.58 (d, J=2.0 Hz, 1 H, C*H*$_{ar}$), 4.27 (m, 2 H, C*H*$_2$), 3.29 (m, 2 H, C*H*$_2$), 2.88 (s, 3 H, NC*H*$_3$), 2.80 (m, 2 H, C*H*$_2$), 2.45 (m, 2 H, C*H*$_2$), 1.82 (m, 1 H, C*H*), 1.68 (m, 4 H, C*H*$_2$ x2), 1.00 (m, 2 H, C*H*$_2$), 0.92 (m, 2 H, C*H*$_2$).
B.21		100	1H NMR (600.05 MHz, DMSO-d6) δ ppm 8.32 (s, 1 H, C*H*$_{ar}$), 7.77 (d, J=2.0 Hz, 1 H, C*H*$_{ar}$), 7.63 (d, J=8.0 Hz, 1 H, C*H*$_{ar}$), 7.55 (dd, J=8.0, 2.0 Hz, 1 H, C*H*$_{ar}$), 3.28 (s, 3 H, SC*H*$_3$), 2.80 (t, J=6.0 Hz, 2 H, C*H*$_2$), 2.72 (s, 3 H, C*H*$_3$), 2.34 (t, J=6.0 Hz, 2 H, C*H*$_2$),), 1.69 (m, 4 H, C*H*$_2$ x2), 1.60 (m, 1 H, C*H*), 0.97 (m, 2 H, C*H*$_2$), 0.83 (m, 2 H, C*H*$_2$).
B.22		100	1H NMR (600.05 MHz, DMSO-d6) δ ppm 8.31 (s, 1 H, C*H*$_{ar}$), 7.73 (d, J=2.5 Hz, 1 H, C*H*$_{ar}$), 7.35 (dd, J=9.0, 2.5 Hz, 1 H, C*H*$_{ar}$), 6.53 (d, J=9.0 Hz, 1 H, C*H*$_{ar}$), 3.47 (s, 3 H, C*H*$_3$), 2.80 (m, 2 H, C*H*$_2$), 2.63 (m, 1 H, CH*H*), 2.47 (m, 1H, CH*H*), 1.95 (m, 1 H, C*H*), 1.71 (m, 4 H, C*H*$_2$ x2), 1.04 (m, 1 H, CH*H*), 0.96 (m, 1 H, CH*H*), 0.95 (m, 2H, C*H*$_2$).
B.23		100	1H NMR (600.05 MHz, DMSO-d6) δ ppm 8.31 (s, 1 H, C*H*$_{ar}$), 7.94 (m, 2 H, C*H*$_{ar}$), 7.55 (m, 2 H, C*H*$_{ar}$), 3.22 (m, 4 H, C*H*$_2$ x2), 2.80 (t, J=6.0 Hz, 2 H, C*H*$_2$), 2.31 (t, J=6.0 Hz, 2 H, C*H*$_2$), 1.68 (m, 8 H, C*H*$_2$ x4), 1.56 (m, 1 H, C*H*), 0.94 (m, 2 H, C*H*$_2$), 0.79 (m, 2 H, C*H*$_2$).

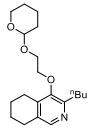
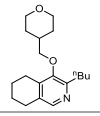
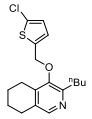
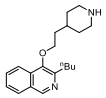
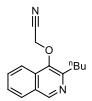
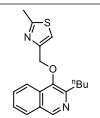
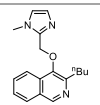
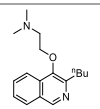
B.24		96	1H NMR (600.05 MHz, DMSO-d6) δ ppm 8.31 (s, 1 H, C*H*$_{ar}$), 7.14 (m, 2 H, C*H*$_{ar}$), 7.08 (m, 2 H, C*H*$_{ar}$), 3.76 (m, 4 H, C*H*$_2$ x2), 3.19 (m, 4 H, C*H*$_2$ x2), 2.83 (br, 2 H, C*H*$_2$), 2.43 (br, 2 H, C*H*$_2$), 1.79 (m, 1 H, C*H*), 1.69 (m, 4 H, C*H*$_2$ x2), 1.02 (m, 2 H, C*H*$_2$), 0.92 (m, 2 H, C*H*$_2$).
B.25		99	1H NMR (600.05 MHz, DMSO-d6) δ ppm 8.33 (s, 1H, C*H*$_{ar}$), 7.60 (t, *J* = 8.0 Hz, 1H, C*H*$_{ar}$), 7.50 – 7.47 (m, 1H, C*H*$_{ar}$), 7.40 – 7.34 (m, 1H, C*H*$_{ar}$), 7.31 (br, 1H, C*H*$_{ar}$), 2.99 (s, 3 H, C*H*$_3$), 2.93 (s, 3 H, C*H*$_3$), 2.82 (m, 2 H, C*H*$_2$), 2.38 (m, 2 H, C*H*$_2$), 1.70 (m, 5 H, C*H*$_2$ x2 + C*H*), 0.98 (m, 2 H, C*H*$_2$), 0.85 (m, 2 H, C*H*$_2$).
B.26		93	1H NMR (600.05 MHz, DMSO-d6) δ ppm 9.04 (br, 1 H, C*H*$_{ar}$), 8.22 (s, 1 H, C*H*$_{ar}$), 7.37 (d, J=8.0 Hz, 1 H, C*H*$_{ar}$), 7.16 (d, J=8.0 Hz, 1 H, C*H*$_{ar}$), 7.14 (s, 1 H, C*H*$_{ar}$), 4.34 (br, 2 H, C*H*$_2$), 3.46 (m, 2H, C*H*$_2$), 3.08 – 3.05 (m, 2H, C*H*$_2$), 2.75 (m, 2 H, C*H*$_2$), 2.29 (m, 1 H, CH*H*), 2.20 (m, 1 H, CH*H*), 1.67 (m, 4 H, C*H*$_2$ x2), 1.57 (m, 1 H, C*H*), 0.96 (m, 1 H, CH*H*), 0.92 (m, 1 H, CH*H*), 0.75 (m, 2 H, C*H*$_2$)
B.27		98	1H NMR (600.05 MHz, DMSO-d6) δ ppm 8.31 (s, 1 H, C*H*$_{ar}$), 7.58 (d, J=2.0 Hz, 1 H, C*H*$_{ar}$), 7.02 (br, 1 H, C*H*$_{ar}$), 4.28 (m, 2 H, C*H*$_2$), 3.55 (m, 2 H, C*H*$_2$), 3.12 (s, 3 H, C*H*$_3$), 2.82 (m, 2 H, C*H*$_2$), 2.48 (m, 2H, C*H*$_2$), 1.84 (m, 1 H, C*H*), 1.70 (m, 4 H, C*H*$_2$ x2), 1.02 (m, 2 H, C*H*$_2$), 0.93 (m, 2 H, C*H*$_2$).
B.28		97	1H NMR (600.05 MHz, DMSO-d6) δ ppm 9.09 (d, J=2.0 Hz, 1 H, C*H*$_{ar}$), 8.39 (d, J=2.0 Hz, 1 H, C*H*$_{ar}$), 8.34 (s, 1 H, C*H*$_{ar}$), 6.61 (s, 1 H, C*H*$_{ar}$), 2.80 (m, 2 H, C*H*$_2$), 2.56 (m, 1 H, CH*H*), 2.46 (s, 3H, C*H*$_3$), 2.43 (m, 1 H, CH*H*), 1.80 (m, 1 H, C*H*), 1.70 (m, 4 H, C*H*$_2$ x2), 0.98 (m, 2 H, C*H*$_2$), 0.84 (m, 2 H, C*H*$_2$).
B.29		96	1H NMR (600.05 MHz, DMSO-d6) δ ppm 8.26 (s, 1H, C*H*$_{ar}$), 7.64 – 7.60 (m, 1H, C*H*$_{ar}$), 7.55 (d, *J* = 7.5 Hz, 1H, C*H*$_{ar}$), 7.40 – 7.36 (m, 2H, C*H*$_{ar}$). 4.34 (m, 2 H, C*H*$_2$), 2.80 – 2.74 (m, 8H, C*H*$_3$ x2+ C*H*$_2$), 2.31 (m, 2 H, C*H*$_2$), 1.67 (m, 4 H, C*H*$_2$ x2), 1.57 (m, 1 H, C*H*), 0.95 (m, 2 H, C*H*$_2$), 0.76 (m, 2 H, C*H*$_2$).
C.01		96	1H NMR (600.05 MHz, DMSO-d6) δ ppm 9.49 (s, 1 H, C*H*$_{ar}$), 8.78 (dd, J=5.0, 1.5 Hz, 1 H, C*H*$_{ar}$), 8.71 (d, J=2.0 Hz, 1 H, C*H*$_{ar}$), 8.29 (d, J=8.0 Hz, 1 H, C*H*$_{ar}$), 8.10 (d, J=7.5 Hz, 1 H, C*H*$_{ar}$), 7.78 (m, 3 H, C*H*$_{ar}$), 7.44 (d, J=7.5 Hz, 1 H, C*H*$_{ar}$), 5.18 (s, 1 H, =CH*H*), 4.73 (s, 1 H, =CH*H*), 2.02 (s, 3 H, C*H*$_3$).
C.02		92	1H NMR (600.05 MHz, DMSO-d6) δ ppm 9.51 (s, 1 H, C*H*$_{ar}$), 8.31 (d, J=8.0 Hz, 1 H, C*H*$_{ar}$), 7.83 (t, J=8.0 Hz, 1 H, C*H*$_{ar}$), 7.78 (t, J=7.5 Hz, 1 H, C*H*$_{ar}$), 7.48 (m, 3 H, C*H*$_{ar}$), 7.31 (d, J=8.0 Hz, 2 H, C*H*$_{ar}$), 5.22 (s, 1 H, =CH*H*), 4.94 (br s, 1 H, =CH*H*), 4.61 (s, 2 H, C*H*$_2$), 1.92 (s, 3 H, C*H*$_3$).
C.03		100	1H NMR (600.05 MHz, DMSO-d6) δ ppm 9.49 (s, 1 H, C*H*$_{ar}$), 8.29 (d, J=8.0 Hz, 1 H, C*H*$_{ar}$), 7.80 (m, 2 H, C*H*$_{ar}$), 7.47 (d, J=8.5 Hz, 1 H, C*H*$_{ar}$), 7.38 (m, 4 H, C*H*$_{ar}$), 5.21 (s, 1 H, =CH*H*), 4.88 (s, 1 H, =CH*H*), 1.94 (s, 3 H, C*H*$_3$)
C.04		98	1H NMR (600.05 MHz, DMSO-d6) δ ppm 9.48 (s, 1 H, C*H*$_{ar}$), 8.27 (d, J=8.0 Hz, 1 H, C*H*$_{ar}$), 7.76 (m, 2 H, C*H*$_{ar}$), 7.24 (m, 3 H, C*H*$_{ar}$), 7.16 (td, J=8.5, 3.0 Hz, 1 H, C*H*$_{ar}$), 5.18 (s, 1 H, =CH*H*), 4.86 (s, 1 H, =CH*H*), 1.95 (s, 3 H, C*H*$_3$), 1.91 (s, 3 H, C*H*$_3$).

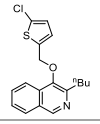
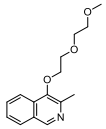
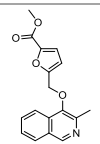
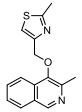
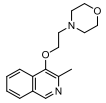
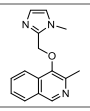
C.05		99	1H NMR (600.05 MHz, DMSO-d6) δ ppm 9.47 (s, 1 H, C*H*ar), 8.28 (d, J=8.0 Hz, 1 H, C*H*ar), 7.78 (m, 2 H, C*H*ar), 7.56 (td, J=8.0, 6.5 Hz, 1 H, C*H*ar), 7.46 (d, J=8.5 Hz, 1 H, C*H*ar), 7.31 (t, J=8.5 Hz, 1 H, C*H*ar), 7.25 (d, J=9.5 Hz, 1 H, C*H*ar), 7.20 (dt, J=7.5, 1.0 Hz, 1 H, C*H*ar), 5.19 (s, 1 H, =CH*H*), 4.86 (s, 1 H, =CH*H*), 1.98 (m, 3 H, C*H*3).
C.06		99	1H NMR (600.05 MHz, DMSO-d6) δ ppm 9.41 (s, 1 H, C*H*ar), 8.22 (d, J=8.0 Hz, 1 H, C*H*ar), 7.74 (m, 2 H, C*H*ar), 7.38 (d, J=8.0 Hz, 1 H, C*H*ar), 7.20 (m, 3 H, C*H*ar), 5.11 (m, 1 H, =CH*H*), 4.76 (s, 1 H, =CH*H*), 2.42 (s, 3 H, C*H*3), 2.01 (s, 3 H, C*H*3).
C.07		99	1H NMR (600.05 MHz, DMSO-d6) δ ppm 9.47 (s, 1 H, C*H*ar), 8.27 (d, J=8.0 Hz, 1 H, C*H*ar), 7.95 (m, 1 H, C*H*ar), 7.90 (d, J=1.0 Hz, 1 H, C*H*ar), 7.74 (m, 4 H, C*H*ar), 7.39 (d, J=8.5 Hz, 1 H, C*H*ar), 5.17 (m, 1 H, =CH*H*), 4.77 (s, 1 H, =CH*H*), 2.00 (s, 3 H, C*H*3).
C.08		99	1H NMR (600.05 MHz, DMSO-d6) δ ppm 9.46 (s, 1 H, C*H*ar), 8.27 (d, J=7.5 Hz, 1 H, C*H*ar), 7.99 (m, 2 H, C*H*ar), 7.77 (m, 2 H, C*H*ar), 7.60 (m, 2 H, C*H*ar), 7.37 (d, J=8.0 Hz, 1 H, C*H*ar), 5.15 (s, 1 H, =CH*H*), 4.75 (s, 1 H, =CH*H*), 2.00 (m, 3 H, C*H*3).
C.09		100	1H NMR (600.05 MHz, DMSO-d6) δ ppm 9.47 (s, 1 H, C*H*ar), 8.27 (d, J=8.0 Hz, 1 H, C*H*ar), 8.03 (m, 2 H, C*H*ar), 7.76 (m, 2 H, C*H*ar), 7.50 (m, 2 H, C*H*ar), 7.42 (d, J=8.5 Hz, 1 H, C*H*ar), 5.16 (s, 1 H, =CH*H*), 4.80 (s, 1 H, =CH*H*), 1.98 (s, 3 H, C*H*3), 1.59 (s, 9 H, C*H*3 x3).
C.10		100	1H NMR (600.05 MHz, DMSO-d6) δ ppm 9.47 (s, 1 H, C*H*ar), 8.27 (d, J=8.0 Hz, 1 H, C*H*ar), 7.76 (m, 2 H, C*H*ar), 7.42 (dd, J=8.5, 6.0 Hz, 1 H, C*H*ar), 7.23 (m, 2 H, C*H*ar), 7.09 (dd, J=9.5, 3.0 Hz, 1 H, C*H*ar), 5.18 (s, 1 H, =CH*H*), 4.86 (s, 1 H, =CH*H*), 1.98 (s, 3 H, C*H*3), 1.87 (s, 3 H, C*H*3).
C.11		99	1H NMR (600.05 MHz, DMSO-d6) δ ppm 9.47 (s, 1 H, C*H*ar), 8.28 (d, J=8.0 Hz, 1 H, C*H*ar), 7.78 (m, 2 H, C*H*ar), 7.48 (d, J=8.0 Hz, 1 H, C*H*ar), 7.28 (m, 2 H, C*H*ar), 7.20 (t, J=6.5, 1 H, C*H*ar), 5.21 (s, 1 H, =CH*H*), 4.90 (s, 1 H, =CH*H*), 2.30 (s, 3 H, C*H*3), 1.94 (s, 3 H, C*H*3).
C.12		89	1H NMR (600.05 MHz, DMSO-d6) δ ppm 9.55 (s, 1 H, C*H*ar), 8.34 (d, J=8.0 Hz, 1 H, C*H*ar), 7.88 (t, J=7.5 Hz, 1 H, C*H*ar), 7.80 (t, J=7.5 Hz, 1 H, C*H*ar), 7.61 (d, J=8.5 Hz, 1 H, C*H*ar), 7.34 (t, J=8.0 Hz, 1 H, C*H*ar), 6.87 (d, J=6.5 Hz, 1 H, C*H*ar), 6.71 (s, 1 H, C*H*ar), 6.66 (d, J=7.0 Hz, 1 H, C*H*ar), 5.27 (s, 1 H, =CH*H*), 5.06 (s, 1 H, =CH*H*), 2.92 (s, 6 H, C*H*3 x2), 1.92 (s, 3 H, C*H*3).
C.13		99	1H NMR (600.05 MHz, DMSO-d6) δ ppm 9.55 (s, 1 H, C*H*ar), 8.33 (d, J=7.5 Hz, 1 H, C*H*ar), 8.18 (d, J=8.0 Hz, 1 H, C*H*ar), 7.89 (d, J=1.5 Hz, 1 H, C*H*ar), 7.83 (t, J=7.5 Hz, 1 H, C*H*ar), 7.79 (d, J=7.5 Hz, 1 H, C*H*ar), 7.50 (d, J=8.0 Hz, 1 H, C*H*ar), 7.38 (dd, J=8.0, 1.5 Hz, 1 H, C*H*ar), 5.19 (s, 1 H, =CH*H*), 4.93 (s, 1 H, =CH*H*), 2.84 (s, 3 H, C*H*3), 1.94 (s, 3 H, C*H*3).
C.14		98	1H NMR (600.05 MHz, DMSO-d6) δ ppm 9.43 (s, 1 H, C*H*ar), 8.24 (d, J=8.0 Hz, 1 H, C*H*ar), 7.75 (m, 2 H, C*H*ar), 7.42 (d, J=8.5 Hz, 1 H, C*H*ar), 7.28 (t, J=8.5 Hz, 1 H, C*H*ar), 7.00 (dd, J=11.0, 3.0 Hz, 1 H, C*H*ar), 6.93 (dd, J=8.5, 3.0 Hz, 1 H, C*H*ar), 5.15 (s, 1 H, =CH*H*), 4.80 (s, 1 H, =CH*H*), 3.96 (s, 3 H, OC*H*3), 2.01 (s, 3 H, C*H*3).

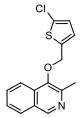
C.15		99	1H NMR (600.05 MHz, DMSO-d6) δ ppm 9.55 (s, 1 H, C*H*$_{ar}$), 8.33 (d, J=8.0 Hz, 1 H, C*H*$_{ar}$), 8.10 (d, J=2.0 Hz, 1 H, C*H*$_{ar}$), 7.81 (m, 2 H, C*H*$_{ar}$), 7.75 (d, J=8.0 Hz, 1 H, C*H*$_{ar}$), 7.65 (d, J=1.5 Hz, 1 H, C*H*$_{ar}$), 7.50 (d, J=8.5 Hz, 1 H, C*H*$_{ar}$), 7.29 (dd, J=8.0, 1.5 Hz, 1 H, C*H*$_{ar}$), 7.03 (dd, J=2.0, 1.0 Hz, 1 H, C*H*$_{ar}$), 5.21 (br, 1 H, =CH*H*), 4.96 (br, 1 H, =CH*H*), 1.89 (s, 3 H, C*H*$_3$).
C.16		92	1H NMR (600.05 MHz, DMSO-d6) δ ppm 9.51 (s, 1 H, C*H*$_{ar}$), 8.33 (d, J=8.5 Hz, 1 H, C*H*$_{ar}$), 7.89 (t, J=8.0 Hz, 1 H, C*H*$_{ar}$), 7.80 (m, 1 H, C*H*$_{ar}$), 7.68 (d, J=8.5 Hz, 1 H, C*H*$_{ar}$), 6.82 (d, *J* = 8.0 Hz, 1H, C*H*$_{ar}$), 6.75 (dd, *J* = 8.0, 2.0 Hz, 1H, C*H*$_{ar}$), 6.66 (d, *J* = 2.0 Hz, 1H, C*H*$_{ar}$), 5.32 (br, 1 H, =CH*H*), 5.09 (br, 1 H, =CH*H*), 4.29 (dd, J=5.0, 3.5 Hz, 2 H, C*H*$_2$), 3.33 (dd, *J* = 5.0, 3.5 Hz, 2H, C*H*$_2$), 2.92 (s, 3 H, NC*H*$_3$), 1.88 (s, 3 H, C*H*$_3$).
C.17		99	1H NMR (600.05 MHz, DMSO-d6) δ ppm 9.49 (s, 1 H, C*H*$_{ar}$), 8.29 (d, J=8.0 Hz, 1 H, C*H*$_{ar}$), 7.81 (m, 3 H, C*H*$_{ar}$), 7.63 (m, 2 H, C*H*$_{ar}$), 7.48 (d, J=7.5 Hz, 1 H, C*H*$_{ar}$), 5.20 (s, 1 H, =CH*H*), 4.82 (s, 1 H, =CH*H*), 3.27 (s, 3 H, SC*H*$_3$), 2.75 (s, 3 H, C*H*$_3$), 1.96 (s, 3 H, C*H*$_3$).
C.18		95	1H NMR (600.05 MHz, DMSO-d6) δ ppm 9.47 (s, 1 H, C*H*$_{ar}$), 8.28 (d, J=8.0 Hz, 1 H, C*H*$_{ar}$), 7.93 (m, 2 H, C*H*$_{ar}$), 7.78 (m, 2 H, C*H*$_{ar}$), 7.63 (m, 2 H, C*H*$_{ar}$), 7.43 (d, J=8.0 Hz, 1 H, C*H*$_{ar}$), 5.15 (s, 1 H, =CH*H*), 4.75 (s, 1 H, =CH*H*), 3.24 (m, 4 H, C*H*$_2$ x2), 1.97 (s, 3 H, C*H*$_3$), 1.69 (m, 4 H, C*H*$_2$ x2).
C.19		95	1H NMR (600.05 MHz, DMSO-d6) δ ppm 9.49 (s, 1 H, C*H*$_{ar}$), 8.29 (d, J=8.0 Hz, 1 H, C*H*$_{ar}$), 8.01 (m, 1 H, C*H*$_{ar}$), 7.81 (m, 3 H, C*H*$_{ar}$), 7.65 (m, 2 H, C*H*$_{ar}$), 7.42 (d, J=8.5 Hz, 1 H, C*H*$_{ar}$), 5.18 (s, 1 H, =CH*H*), 4.82 (s, 1 H, =CH*H*), 1.96 (s, 3 H, C*H*$_3$), 1.54 (s, 9 H, C*H*$_3$ x3).
C.20		89	1H NMR (600.05 MHz, DMSO-d6) δ ppm 9.51 (s, 1 H, C*H*$_{ar}$), 8.32 (d, J=7.5 Hz, 1 H, C*H*$_{ar}$), 7.83 (m, 2 H, C*H*$_{ar}$), 7.62 (d, J=8.5 Hz, 1 H, C*H*$_{ar}$), 7.21 (m, 2 H, C*H*$_{ar}$), 7.09 (m, 2 H, C*H*$_{ar}$), 5.28 (br, 1 H, =CH*H*), 5.03 (br, 1 H, =CH*H*), 3.78 (m, 4 H, C*H*$_2$ x2), 3.22 (m, 4 H, C*H*$_2$ x2), 1.87 (s, 3 H, C*H*$_3$).
C.21		93	1H NMR (600.05 MHz, DMSO-d6) δ ppm 9.51 (s, 1 H, C*H*$_{ar}$), 8.31 (d, J=8.0 Hz, 1 H, C*H*$_{ar}$), 7.84 (m, 1 H, C*H*$_{ar}$), 7.78 (t, J=7.5 Hz, 1 H, C*H*$_{ar}$), 7.60 (m, 1 H, C*H*$_{ar}$), 7.48 (m, 3 H, C*H*$_{ar}$), 7.36 (m, 1 H, C*H*$_{ar}$), 5.21 (s, 1 H, =CH*H*), 4.88 (s, 1 H, =CH*H*), 2.98 (s, 3 H, NC*H*$_3$), 2.94 (s, 3 H, NC*H*$_3$), 1.95 (s, 3 H, C*H*$_3$).
C.22		89	1H NMR (600.05 MHz, DMSO-d6) δ ppm 9.39 (s, 1 H, C*H*$_{ar}$), 9.07 (br, 1 H, N*H*), 8.22 (d, J=7.5 Hz, 1 H, C*H*$_{ar}$), 7.72 (m, 2 H, C*H*$_{ar}$), 7.41 – 7.36 (m, 2H, C*H*$_{ar}$), 7.26 (dd, *J* = 7.5, 2.0 Hz, 1H, C*H*$_{ar}$), 7.22 (br, 1H, C*H*$_{ar}$), 5.12 (s, 1 H, =CH*H*), 4.81 (s, 1 H, =CH*H*), 4.34 (m, 2 H, C*H*$_2$), 3.48 (m, 2 H, C*H*$_2$), 3.11 (m, 2 H, C*H*$_2$), 1.99 (s, 3 H, C*H*$_3$).
C.23		97	1H NMR (600.05 MHz, DMSO-d6) δ ppm 9.47 (s, 1 H, C*H*$_{ar}$), 8.28 (d, J=8.0 Hz, 1 H, C*H*$_{ar}$), 7.85 (t, J=7.5 Hz, 1 H, C*H*$_{ar}$), 7.77 (t, J=7.5 Hz, 1 H, C*H*$_{ar}$), 7.64 (d, J=8.5 Hz, 1 H, C*H*$_{ar}$), 7.62 (d, J=2.0 Hz, 1 H, C*H*$_{ar}$), 7.13 (br, 1 H, C*H*$_{ar}$), 5.28 (s, 1 H, =CH*H*), 4.97 (s, 1 H, =CH*H*), 4.31 (m, 2 H, C*H*$_2$), 3.60 (m, 2 H, C*H*$_2$), 3.16 (s, 3 H, NC*H*$_3$), 1.99 (s, 3 H, C*H*$_3$).

C.24		99	1H NMR (600.05 MHz, DMSO-d6) δ ppm 9.47 (s, 1 H, C*H*$_{ar}$), 9.15 (d, J=2.0 Hz, 1 H, C*H*$_{ar}$), 8.45 (d, J=2.0 Hz, 1 H, C*H*$_{ar}$), 8.27 (d, J=7.5 Hz, 1 H, C*H*$_{ar}$), 7.78 (m, 2 H, C*H*$_{ar}$), 7.67 (d, J=8.0 Hz, 1 H, C*H*$_{ar}$), 6.62 (s, 1 H, C*H*$_{ar}$), 5.20 (s, 1 H, =CH*H*), 4.82 (s, 1 H, =CH*H*), 2.47 (s, 3H, C*H*$_3$), 2.07 (s, 3 H, C*H*$_3$).
C.25		83	1H NMR (600.05 MHz, DMSO-d6) δ ppm 9.40 (s, 1 H, C*H*$_{ar}$), 8.22 (d, J=8.0 Hz, 1 H, C*H*$_{ar}$), 7.73 (m, 2 H, C*H*$_{ar}$), 7.61 (m, 2 H, C*H*$_{ar}$), 7.47 (m, 3 H, C*H*$_{ar}$), 5.09 (s, 1 H, =CH*H*), 4.72 (s, 1 H, =CH*H*), 4.31 (m, 2 H, C*H*$_2$), 2.75 (m, 6 H, NC*H*$_3$ x2), 1.99 (s, 3 H, C*H*$_3$).
C.26		89	^{1}H NMR (600 MHz, DMSO) δ 9.42 (s, 1H, C*H*$_{ar}$), 8.27 (d, *J* = 8.0 Hz, 1H, C*H*$_{ar}$), 7.90 (s, 1H, C*H*$_{ar}$), 7.88 – 7.84 (m, 2H, C*H*$_{ar}$), 7.80 – 7.70 (m, 1H, C*H*$_{ar}$), 7.54 (s, 1H, C*H*$_{ar}$), 5.29 (br, 1H, =CH*H*), 5.05 (br, 1H, =CH*H*), 4.25 (t, *J* = 6.0 Hz, 2H, C*H*$_2$), 3.81 (t, *J* = 6.0 Hz, 2H, C*H*$_2$), 1.92 (s, 3H, C*H*$_3$).
C.27		95	1H NMR (600.05 MHz, DMSO-d6) δ ppm 9.54 (s, 1 H), 8.85 (s, 1 H, C*H*$_{ar}$), 8.38 (s, 1 H, C*H*$_{ar}$), 8.30 (d, J=7.5 Hz, 1 H, C*H*$_{ar}$), 8.10 (s, 1 H, C*H*$_{ar}$), 7.93 (s, 1 H, C*H*$_{ar}$), 7.74 (m, 2 H, C*H*$_{ar}$), 7.41 (d, J=8.5 Hz, 1 H, C*H*$_{ar}$), 4.98 (s, 1 H, =CH*H*), 4.65 (s, 1 H, =CH*H*), 2.48 (s, 3H, C*H*$_3$), 2.03 (s, 3 H, C*H*$_3$).
D.01		73	1H NMR (600.05 MHz, DMSO-d6) δ ppm 8.57 (br s, 1 H, N*H*), 8.28 (br s, 1 H, C*H*$_{ar}$), 3.92 (t, *J* = 6.5 Hz, 2H, C*H*$_2$), 3.29 (br, 2H, C*H*$_2$), 2.93 – 2.78 (m, 8H, C*H*$_2$ x4), 1.89 (br, 2H, C*H*$_2$), 1.83 – 1.79 (m, 1H, C*H*), 1.78 – 1.71 (m, 6H, C*H*$_2$ x3), 1.65 – 1.59 (m, 2H, C*H*$_2$), 1.40 – 1.31 (m, 4H, C*H*$_2$ x2), 0.91 (t, *J* = 7.5 Hz, 3H, C*H*$_3$).
D.02		100	1H NMR (600.05 MHz, DMSO-d6) δ ppm 8.93 (br s, 1 H, N*H*), 8), 8.23 (s, 1 H, C*H*$_{ar}$), 4.73 (q, J=6.5 1 H, C*H*), 4.35 (m, 2 H, C*H*$_2$), 4.26 (m, 2 H, C*H*$_2$), 2.76 (t, J=5.5, 2 H, C*H*$_2$), 2.70 (m, 2 H, C*H*$_2$), 2.63 (m, 2 H, C*H*$_2$), 1.73 (m, 4 H, C*H*$_2$ x2), 1.58 (m, 2 H, C*H*$_2$), 1.33 (sxt, J=7.5 Hz, 2 H, C*H*$_2$), 0.91 (t, J=7.5 Hz, 3 H, C*H*$_3$).
D.03		100	1H NMR (600.05 MHz, DMSO-d6) δ ppm 8.01 (s, 1 H, C*H*$_{ar}$), 7.55 (br, 1 H, NH*H*), 7.47 (br, 1 H, NH*H*), 4.15 (s, 2 H, C*H*$_2$), 2.70 (m, 2 H, C*H*$_2$), 2.68 (m, 4 H, C*H*$_2$ x2), 1.70 (m, 4 H, C*H*$_2$ x2), 1.62 (m, 2 H, C*H*$_2$), 1.32 (sxt, J=7.5, 2 H, C*H*$_2$), 0.89 (t, J=7.0 Hz, 3 H, C*H*$_3$).
D.04		100	1H NMR (600.05 MHz, DMSO-d6) δ ppm 8.07 (s, 1 H, C*H*$_{ar}$), 4.94 (s, 2 H, C*H*$_2$), 2.71 (m, 6 H, C*H*$_2$ x3), 1.72 (m, 4 H, C*H*$_2$ x2), 1.62 (m, 2 H, C*H*$_2$), 1.32 (sxt, J=7.5, 2 H, C*H*$_2$), 0.90 (t, J=7.0 Hz, 3 H, C*H*$_3$).
D.05		100	1H NMR (600.05 MHz, DMSO-d6) δ ppm 7.99 (s, 1 H, C*H*$_{ar}$), 3.89 (m, 2 H, C*H*$_2$), 2.70 (m, 4 H, C*H*$_2$ x2), 2.68 (m, 6 H, C*H*$_2$ x3), 2.61 (m, 2 H, C*H*$_2$), 1.75 (br, 2 H, C*H*$_2$), 1.71 (m, 6 H, C*H*$_2$ x3), 1.62 (m, 2 H, C*H*$_2$), 1.33 (m, 2 H, C*H*$_2$), 0.90 (t, J=7.5 Hz, 3 H, C*H*$_3$).
D.06		95	1H NMR (600.05 MHz, DMSO-d6) δ ppm 8.58 (d, J=5.0 Hz, 1 H, C*H*$_{ar}$), 8.02 (s, 1 H, C*H*$_{ar}$), 7.89 (td, J=7.5, 1.0 Hz, 1 H, C*H*$_{ar}$), 7.64 (d, J=7.5 Hz, 1 H, C*H*$_{ar}$), 7.38 (ddd, J=7.5, 5.0, 1.0 Hz, 1 H, C*H*$_{ar}$), 4.89 (m, 2 H, C*H*$_2$), 2.69 (m, 6 H, C*H*$_2$ x3), 1.71 (m, 4 H, C*H*$_2$ x2), 1.59 (m, 2 H, C*H*$_2$), 1.27 (m, 2 H, C*H*$_2$), 0.85 (t, J=7.5 Hz, 3 H, C*H*$_3$).

D.07		88	1H NMR (600.05 MHz, DMSO-d6) δ ppm 7.97 (s, 1 H, C*H*$_{ar}$), 3.51 (m, 2 H, C*H*$_2$), 2.66 (m, 6 H, C*H*$_2$ x3), 2.03 (m, 1 H, C*H*), 1.70 (m, 4 H, C*H*$_2$ x2), 1.60 (m, 2 H, C*H*$_2$), 1.31 (sxt, J=7.5 Hz, 2 H, C*H*$_2$), 1.03 (d, J=6.5 Hz, 6 H, C*H*$_3$ x2), 0.89 (t, J=7.5 Hz, 3 H, C*H*$_3$).
D.08		93	1H NMR (600.05 MHz, DMSO-d6) δ ppm 8.02 (m, 1 H, C*H*$_{ar}$), 7.93 (d, J=8.5 Hz, 2 H, C*H*$_{ar}$), 7.63 (d, J=8.5 Hz, 2 H, C*H*$_{ar}$), 4.92 (s, 2 H, C*H*$_2$), 3.87 (m, 3 H, OC*H*$_3$), 2.69 (m, 6 H, C*H*$_2$ x3), 1.71 (m, 4 H, C*H*$_2$ x2), 1.59 (m, 2 H, C*H*$_2$), 1.27 (m, 2 H, C*H*$_2$), 0.84 (t, J=7.5 Hz, 3 H, C*H*$_3$).
D.09		100	1H NMR (600.05 MHz, DMSO-d6) δ ppm 8.01 (s, 1 H, C*H*$_{ar}$), 4.07 (m, 2 H, C*H*$_2$), 2.70 (m, 6 H, C*H*$_2$ x3), 1.72 (m, 4 H, C*H*$_2$ x2), 1.62 (m, 2 H, C*H*$_2$), 1.56 (s, 3 H, PC*H*$_3$), 1.54 (s, 3 H, PC*H*$_3$), 1.32 (m, 2 H, C*H*$_2$), 0.89 (t, J=7.5 Hz, 3 H, C*H*$_3$).
D.10		86	1H NMR (600.05 MHz, DMSO-d6) δ ppm 8.01 (s, 1 H, C*H*$_{ar}$), 7.30 (d, J=3.5 Hz, 1 H, C*H*$_{ar}$), 6.72 (d, J=3.5 Hz, 1 H, C*H*$_{ar}$), 4.90 (s, 2 H, C*H*$_2$), 3.82 (m, 3 H, OC*H*$_3$), 2.68 (br, 4 H, C*H*$_2$ x2), 2.61 (m, 2 H, C*H*$_2$), 1.71 (m, 4 H, C*H*$_2$ x2), 1.56 (m, 2 H, C*H*$_2$), 1.28 (m, 2 H, C*H*$_2$), 0.86 (t, J=7.5 Hz, 3 H, C*H*$_3$).
D.11		88	1H NMR (600.05 MHz, DMSO-d6) δ ppm 7.98 (s, 1 H, C*H*$_{ar}$), 3.77 (m, 2 H, C*H*$_2$), 2.72 (m, 2 H, C*H*$_2$), 2.67 (m, 6 H, C*H*$_2$ x3), 2.39 (br, 6 H, NC*H*$_3$ x2), 1.94 (m, 2 H, C*H*$_2$), 1.71 (m, 4 H, C*H*$_2$ x2), 1.61 (m, 2 H, C*H*$_2$), 1.32 (s, J=7.5 Hz, 2 H, C*H*$_2$), 0.90 (t, J=7.5 Hz, 3 H, C*H*$_3$).
D.12		93	1H NMR (600.05 MHz, DMSO-d6) δ ppm 8.00 (s, 1 H, C*H*$_{ar}$), 7.54 (s, 1 H, C*H*$_{ar}$), 4.83 (s, 2 H, C*H*$_2$), 2.67 (m, 4 H, C*H*$_2$ x2), 2.67 (s, 5 H, C*H*$_2$ + C*H*$_3$), 1.71 (m, 4 H, C*H*$_2$ x2), 1.58 (m, 2 H, C*H*$_2$), 1.29 (m, 2 H, C*H*$_2$), 0.87 (t, J=7.5 Hz, 3 H, C*H*$_3$).
D.13		90	1H NMR (600.05 MHz, DMSO-d6) δ ppm 7.96 (s, 1 H, C*H*$_{ar}$), 3.92 (m, 2 H, C*H*$_2$), 3.68 (m, 4 H, C*H*$_2$ x2), 3.59 (tdd, J=8.5, 4.0 Hz, 1 H, C*H*), 2.68 (m, 6 H, C*H*$_2$ x3), 1.82 (m, 2 H, C*H*$_2$), 1.70 (m, 4 H, C*H*$_2$ x2), 1.61 (m, 2 H, C*H*$_2$), 1.49 (m, 2 H, C*H*$_2$), 1.31 (m, 2 H, C*H*$_2$), 0.89 (t, J=7.5 Hz, 3 H, C*H*$_3$).
D.14		96	1H NMR (600.05 MHz, DMSO-d6) δ ppm 7.97 (s, 1 H, C*H*$_{ar}$), 3.84 (m, 2 H, C*H*$_2$), 3.59 (m, 4 H, C*H*$_2$ x2), 2.68 (m, 8 H, C*H*$_2$ x4), 2.40 (m, 4 H, C*H*$_2$ x2), 1.70 (m, 4 H, C*H*$_2$ x2), 1.61 (m, 2 H, C*H*$_2$), 1.32 (m, 2 H, C*H*$_2$), 0.90 (t, J=7.5 Hz, 3 H, C*H*$_3$).
D.15		100	1H NMR (600.05 MHz, DMSO-d6) δ ppm 8.00 (s, 1 H, C*H*$_{ar}$), 7.20 (d, J=1.0 Hz, 1 H, C*H*$_{ar}$), 6.86 (d, J=1.0 Hz, 1 H, C*H*$_{ar}$), 4.85 (s, 2 H, C*H*$_2$), 3.73 (s, 3 H, NC*H*$_3$), 2.68 (br, 2 H, C*H*$_2$), 2.58 (m, 4 H, C*H*$_2$ x2), 1.69 (m, 4 H, C*H*$_2$ x2), 1.56 (m, 2 H, C*H*$_2$), 1.27 (s, J=7.5 Hz, 2 H, C*H*$_2$), 0.86 (t, J=7.5 Hz, 3 H, C*H*$_3$).

D.16		97	1H NMR (600.05 MHz, DMSO-d6) δ ppm 7.97 (s, 1 H, C*H*$_{ar}$), 4.68 (t, *J* = 3.5 Hz, 1H, C*H*), 3.94 – 3.86 (m, 3H, C*H*$_2$ + CH*H*), 3.79 (ddd, *J* = 11.5, 9.0, 3.0 Hz, 1H, CH*H*), 3.68 (ddd, *J* = 11.0, 6.0, 3.0 Hz, 1H, CH*H*), 3.45 (dd, *J* = 11.0, 5.0 Hz, 1H, CH*H*), 2.74 – 2.65 (m, 6H, C*H*$_2$ x3), 1.80 – 1.73 (m, 1H, CH*H*), 1.70 (dt, *J* = 6.5, 3.5 Hz, 4H, C*H*$_2$ x2), 1.67 – 1.58 (m, 3H, C*H*$_2$ + CH*H*), 1.55 – 1.43 (m, 4H, C*H*$_2$ x2), 1.35 – 1.28 (m, 2H, C*H*$_2$), 0.89 (t, *J* = 7.5 Hz, 3H, C*H*$_3$).
D.17		100	1H NMR (600.05 MHz, DMSO-d6) δ ppm 7.97 (s, 1 H, C*H*$_{ar}$), 3.89 (m, 2 H, C*H*$_2$), 3.59 (m, 4 H, C*H*$_2$ x2), 2.66 (m, 6 H, C*H*$_2$ x3), 2.01 (m, 1 H, C*H*), 1.71 (m, 6 H, C*H*$_2$ x3), 1.61 (m, 2 H, C*H*$_2$), 1.40 (m, 2 H, C*H*$_2$), 1.31 (s, J=7.5 Hz, 2 H, C*H*$_2$), 0.89 (t, J=7.5 Hz, 3 H, C*H*$_3$).
D.18		93	1H NMR (600.05 MHz, DMSO-d6) δ ppm 8.02 (s, 1 H, C*H*$_{ar}$), 7.06 (m, 2 H, C*H*$_{ar}$), 4.94 (s, 2 H, C*H*$_{ar}$), 2.67 (m, 6 H, C*H*$_2$ x3), 1.71 (m, 4 H, C*H*$_2$ x2), 1.59 (m, 2 H, C*H*$_2$), 1.30 (m, 2 H, C*H*$_2$), 0.88 (t, J=7.5 Hz, 3 H, C*H*$_3$).
D.19		97	^{1}H NMR (600 MHz, DMSO) δ 9.15 (s, 1H, C*H*$_{ar}$), 8.53 (br, 1H, N*H*), 8.16 (d, *J* = 8.0 Hz, 1H, C*H*$_{ar}$), 8.04 (d, *J* = 8.5 Hz, 1H, C*H*$_{ar}$), 7.84 (d, *J* = 7.5 Hz, 1H, C*H*$_{ar}$), 7.68 (t, *J* = 7.5 Hz, 1H, C*H*$_{ar}$), 4.02 (t, *J* = 6.5 Hz, 2H, C*H*$_2$), 3.31 (br, 2H, C*H*$_2$), 2.94 – 2.88 (m, 4H, C*H*$_2$ x2), 2.88 – 2.81 (m, 1H, C*H*), 1.95 (br, 2H, C*H*$_2$), 1.88 – 1.84 (m, 2H, C*H*$_2$), 1.76 – 1.71 (m, 2H, C*H*$_2$), 1.41 – 1.35 (m, 4H, C*H*$_2$ x2), 0.94 (t, *J* = 7.5 Hz, 3H, C*H*$_3$).
D.20		100	1H NMR (600.05 MHz, DMSO-d6) δ ppm 9.10 (s, 1 H, C*H*$_{ar}$), 8.11 (br, 2 H, N*H*$_2$), 7.79 (m, 2 H, C*H*$_{ar}$), 7.65 (m, 1 H, C*H*$_{ar}$), 7.49 (m, 1 H, C*H*$_{ar}$), 4.36 (s, 2 H, C*H*$_2$), 2.91 (m, 2 H, C*H*$_2$), 1.74 (m, 2 H, C*H*$_2$), 1.38 (s, J=7.5 Hz, 2 H, C*H*$_2$), 0.93 (t, J=7.5 Hz, 3 H, C*H*$_3$).
D.21		92	1H NMR (600.05 MHz, DMSO-d6) δ ppm 9.16 (s, 1 H, C*H*$_{ar}$), 8.16 (d, J=8.0 Hz, 1 H, C*H*$_{ar}$), 8.04 (dd, J=8.5, 1.0 Hz, 1 H, C*H*$_{ar}$), 7.85 (ddd, J=8.0, 7.0, 1.0 Hz, 1 H, C*H*$_{ar}$), 7.68 (t, J=7.5 Hz, 1 H, C*H*$_{ar}$), 5.17 (s, 2 H, C*H*$_2$), 2.95 (m, 2 H, C*H*$_2$), 1.75 (m, 2 H, C*H*$_2$), 1.37 (m, 2 H, C*H*$_2$), 0.93 (t, J=7.5, 3 H, C*H*$_3$).
D.22		90	1H NMR (600.05 MHz, DMSO-d6) δ ppm 9.08 (s, 1 H, C*H*$_{ar}$), 8.12 (m, 2 H, C*H*$_{ar}$), 7.78 (ddd, J=8.5, 7.0, 1.0 Hz, 1 H, C*H*$_{ar}$), 7.62 (m, 2 H, C*H*$_{ar}$), 5.04 (s, 2 H, C*H*$_2$), 2.88 (m, 2 H, C*H*$_2$), 2.70 (s, 3 H, C*H*$_3$), 1.68 (m, 2 H, C*H*$_2$), 1.34 (s, J=7.5 Hz, 2 H, C*H*$_2$), 0.91 (t, J=7.5 Hz, 3 H, C*H*$_3$).
D.24		91	1H NMR (600.05 MHz, DMSO-d6) δ ppm 9.09 (s, 1 H, C*H*$_{ar}$), 8.12 (d, J=8.0 Hz, 1 H, C*H*$_{ar}$), 7.99 (dd, J=8.5, 1.0 Hz, 1 H, C*H*$_{ar}$), 7.78 (t, J=8.0 Hz, 1 H, C*H*$_{ar}$), 7.64 (m, 1 H, C*H*$_{ar}$), 7.23 (d, J=1.0 Hz, 1 H, C*H*$_{ar}$), 6.88 (d, J=1.0 Hz, 1 H, C*H*$_{ar}$), 5.08 (s, 2 H, C*H*$_2$), 3.76 (s, 3 H, NC*H*$_3$), 2.77 (m, 2 H, C*H*$_2$), 1.65 (m, 2 H, C*H*$_2$), 1.32 (s, J=7.5 Hz, 2 H, C*H*$_2$), 0.90 (t, J=7.5 Hz, 3 H, C*H*$_3$).
D.25		89	1H NMR (600.05 MHz, DMSO-d6) δ ppm 9.06 (s, 1 H), 8.10 (m, 2 H), 7.78 (m, 1 H), 7.63 (t, J=7.5 Hz, 1 H), 4.02 (m, 2 H), 2.92 (m, 2 H, C*H*$_2$), 2.74 (m, 2 H), 2.28 (s, 6 H), 1.73 (m, 2 H, C*H*$_2$), 1.37 (sxt, J=7.5 Hz, 2 H, C*H*$_2$), 1.23 (m, 1 H), 0.93 (t, J=7.0 Hz, 3 H, C*H*$_3$).

D.26		92	1H NMR (600.05 MHz, DMSO-d6) δ ppm 9.10 (s, 1 H, C*H*$_{ar}$), 8.13 (d, J=8.0 Hz, 1 H, C*H*$_{ar}$), 8.02 (dd, J=8.5, 1.0 Hz, 1 H, C*H*$_{ar}$), 7.80 (t, J=8.0 1 H, C*H*$_{ar}$), 7.65 (t, J=7.5 Hz, 1 H, C*H*$_{ar}$), 7.08 (s, 2 H, C*H*$_{ar}$), 5.18 (s, 2 H, C*H*$_2$), 2.86 (m, 2 H, C*H*$_2$), 1.68 (m, 2 H, C*H*$_2$), 1.34 (s, J=7.5 Hz, 2 H, C*H*$_2$), 0.91 (t, J=7.5 Hz, 3 H, C*H*$_3$).
D.29		91	1H NMR (600.05 MHz, DMSO-d6) δ ppm 9.03 (s, 1 H, C*H*$_{ar}$), 8.16 (d, J=8.5 Hz, 1 H, C*H*$_{ar}$), 8.09 (d, J=8.0 Hz, 1 H, C*H*$_{ar}$), 7.76 (ddd, J=8.5, 7.0, 1.5 Hz, 1 H, C*H*$_{ar}$), 7.62 (t, J=7.5 Hz, 1 H, C*H*$_{ar}$), 4.11 (m, 2 H, C*H*$_2$), 3.80 (m, 2 H, C*H*$_2$), 3.64 (m, 2 H, C*H*$_2$), 3.52 (m, 2 H, C*H*$_2$), 3.29 (s, 3 H, OC*H*$_3$), 2.59 (s, 3 H, C*H*$_3$).
D.30		96	1H NMR (600.05 MHz, DMSO-d6) δ ppm 9.06 (s, 1 H, C*H*$_{ar}$), 8.12 (d, J=8.0 Hz, 1 H, C*H*$_{ar}$), 8.10 (d, J=8.5 Hz, 1 H, C*H*$_{ar}$), 7.80 (m, 2 H, C*H*$_{ar}$ + NH*H*), 7.64 (t, J=7.5 Hz, 1 H, C*H*$_{ar}$), 7.53 (br, 1 H, NH*H*), 4.37 (s, 2 H, C*H*$_2$), 2.60 (s, 3 H, C*H*$_3$).
D.31		100	1H NMR (600.05 MHz, DMSO-d6) δ ppm 9.13 (s, 1 H, C*H*$_{ar}$), 8.16 (d, J=8.0 Hz, 1 H, C*H*$_{ar}$), 8.05 (d, J=8.5 Hz, 1 H, C*H*$_{ar}$), 7.85 (ddd, J=8.5, 7.0, 1.0 Hz, 1 H, C*H*$_{ar}$), 7.68 (ddd, J=8.0, 7.0, 1.0 Hz, 1 H, C*H*$_{ar}$), 5.18 (s, 2 H, C*H*$_2$), 2.63 (s, 3 H, C*H*$_3$).
D.32		81	1H NMR (600.05 MHz, DMSO-d6) δ ppm 9.02 (s, 1 H, C*H*$_{ar}$), 8.10 (d, J=8.0 Hz, 1 H, C*H*$_{ar}$), 8.01 (d, J=8.5 Hz, 1 H, C*H*$_{ar}$), 7.78 (ddd, J=8.5, 7.0, 1.5 Hz, 1 H, C*H*$_{ar}$), 7.63 (t, J=7.5, 1 H, C*H*$_{ar}$), 3.74 (d, J=6.0 Hz, 2 H, C*H*$_2$), 2.57 (s, 3 H, C*H*$_3$), 2.20 (m, 1 H, C*H*), 1.12 (d, J=7.0 Hz, 6 H, C*H*$_3$ x2).
D.33		100	1H NMR (600.05 MHz, DMSO-d6) δ ppm 9.06 (s, 1 H, C*H*$_{ar}$), 8.12 (d, J=8.0 Hz, 1 H, C*H*$_{ar}$), 7.98 (d, J=8.5 Hz, 1 H, C*H*$_{ar}$), 7.76 (ddd, J=8.5, 7.0, 1.10 Hz, 1 H, C*H*$_{ar}$), 7.63 (t, J=7.5, 1 H, C*H*$_{ar}$), 7.29 (d, J=3.5 Hz, 1 H, C*H*$_{ar}$), 6.71 (d, J=3.5 Hz, 1 H, C*H*$_{ar}$), 5.13 (s, 2 H, C*H*$_2$), 3.84 (s, 3 H, OC*H*$_3$), 2.50 (s, 3 H, C*H*$_3$).
D.34		100	1H NMR (600.05 MHz, DMSO-d6) δ ppm 9.05 (s, 1 H, C*H*$_{ar}$), 8.11 (d, J=8.0 Hz, 1 H, C*H*$_{ar}$), 8.09 (d, J=8.5 Hz, 1 H, C*H*$_{ar}$), 7.77 (ddd, J=8.5, 7.0, 1.0 Hz, 1 H, C*H*$_{ar}$), 7.62 (m, 2 H, C*H*$_{ar}$), 5.05 (s, 2 H, C*H*$_2$), 2.70 (s, 3 H, C*H*$_3$), 2.56 (s, 3 H, C*H*$_3$).
D.35		92	1H NMR (600.05 MHz, DMSO-d6) δ ppm 9.02 (s, 1 H, C*H*$_{ar}$), 8.19 (d, J=8.5 Hz, 1 H, C*H*$_{ar}$), 8.09 (d, J=8.0 Hz, 1 H, C*H*$_{ar}$), 7.78 (m, 1 H, C*H*$_{ar}$), 7.62 (t, J=7.5 Hz, 1 H, C*H*$_{ar}$), 4.07 (t, J=5.5 Hz, 2 H, C*H*$_2$), 3.61 (m, 4 H, C*H*$_2$ x2), 2.78 (t, J=5.5 Hz, 2 H, C*H*$_2$), 2.60 (s, 3 H, C*H*$_3$), 2.50 (m, 4 H, C*H*$_2$ x2).
D.36		96	1H NMR (600.05 MHz, DMSO-d6) δ ppm 9.05 (s, 1 H, C*H*$_{ar}$), 8.12 (d, J=8.0 Hz, 1 H, C*H*$_{ar}$), 7.96 (d, J=8.5 Hz, 1 H, C*H*$_{ar}$), 7.77 (ddd, J=8.5, 7.0, 1.0 Hz, 1 H, C*H*$_{ar}$), 7.63 (ddd, J=8.0, 7.0, 1.0 Hz, 1 H, C*H*$_{ar}$), 7.22 (d, J=1.0 Hz, 1 H, C*H*$_{ar}$), 6.87 (d, J=1.0 Hz, 1 H, C*H*$_{ar}$), 5.09 (s, 2 H, C*H*$_2$), 3.75 (s, 3 H, NC*H*$_3$), 2.43 (s, 3 H, C*H*$_3$).

D.37		93	1H NMR (600.05 MHz, DMSO-d6) δ ppm 9.06 (s, 1 H, C*H*$_{ar}$), 8.12 (d, J=8.0 Hz, 1 H, C*H*$_{ar}$), 8.00 (d, J=8.5 Hz, 1 H, C*H*$_{ar}$), 7.79 (ddd, J=8.5, 7.0, 1.0 Hz, 1 H, C*H*$_{ar}$), 7.64 (t, J=7.5, 1 H, C*H*$_{ar}$), 7.08 (m, 2 H, C*H*$_{ar}$), 5.18 (s, 2 H, C*H*$_2$), 2.56 (s, 3 H, C*H*$_3$).

CHAPTER 8: References

(1) Bott, R. *J. Am. Chem. Soc.* **1966**, *88*, 619.
(2) P. Schiess, H.L. Chia, P. R. *Tetrahedron Lett.* **1972**, 313.
(3) Wanner, M. J.; Koomen, G. *J. Org. Chem.* **1996**, *61*, 5581.
(4) Choshi, T.; Kumemura, T.; Nobuhiro, J.; Hibino, S. *Tetrahedron Lett.* **2008**, *49*, 3725.
(5) Mura, K. O.; Hoshi, T. C.; Atanabe, S. W.; Atoh, Y. S.; Obuhiro, J. N.; Ibino, S. H. *Chem. Pharm. Bull.* **2008**, *56*, 237.
(6) Ishihara, Y.; Azuma, S.; Choshi, T.; Kohno, K.; Ono, K.; Tsutsumi, H.; Ishizu, T.; Hibino, S. *Tetrahedron* **2011**, *67*, 1320.
(7) D. Heredia, Larghi, E, Kaufman, T. *Eur. J. Org. Chem.* **2016**, 1397.
(8) Markey, S. J.; Lewis, W.; Moody, C. J. *Org. Lett.* **2013**, *15*, 6306.
(9) Parthasarathy, K.; Cheng, C.-H. *J. Org. Chem.* **2009**, *74*, 9359.
(10) Colby, D. a.; Bergman, R. G.; Ellman, J. a. *J. Am. Chem. Soc.* **2008**, *130*, 3645.
(11) Too, P. C.; Wang, Y. F.; Chiba, S. *Org. Lett* **2010**, *12*, 5688.
(12) Martin, R. M.; Bergman, R. G.; Ellman, J. a. *J. Org. Chem.* **2012**, *77*, 2501.
(13) Esters, O.; Neely, J. M.; Rovis, T. *J. Am. Chem. Soc.* **2013**, *135*, 66.
(14) Saito, A.; Hironaga, M.; Oda, S.; Hanzawa, Y. *Tetrahedron Lett.* **2007**, *48*, 6852.
(15) Deb, I.; Yoshikai, N. *Org. Lett.* **2013**, *15*, 4254.
(16) Hurst, T. E.; Miles, T. J.; Moody, C. J. *Tetrahedron* **2008**, *64*, 874.
(17) Huang, H.; Cai, J.; Tang, L.; Wang, Z.; Li, F.; Deng, G. *J. Org. Chem.* **2016**, *81*, 1499.
(18) Ishiyama, T.; Matsuda, N.; Miyaura, N.; Suzuki, A. *J. Am. Chem. Soc.* **1993**, *115*, 11018.
(19) Kerrlgan, J.; Parsons, T.; Urry, G.; Schlesinger, H. I. *J. Am. Chem. Soc.* **1958**, *3573*, 6368.
(20) Ishiyama, T.; Matsuda, N.; Murata, M.; Ozawa, F.; Suzuki, A.; Miyaura, N. *Organometallics* **1996**, *15*, 713.
(21) Satoh, M. Y. N. *Tetrahedron* **1989**, 3789.
(22) Sato, M.; Miyaura, N.; Suzuki, A. *Tetrahedron Lett.* **1990**, *31*, 231.
(23) Gridnev, I. D.; Miyaura, N.; Suzuki, A. *Organometallics* **1993**, *12*, 589.
(24) Thomas, R. L.; Souza, F. E. S.; Marder, T. B. *J. Chem. Soc.; Dalt. Trans.* **2001**, 1650.
(25) Prokopcová, H.; Ramírez, J.; Fernández, E.; Kappe, C. O. *Tetrahedron Lett.* **2008**, *49*, 4831.
(26) Carson, M. W.; Giese, M. W.; Coghlan, M. J. *Org. Lett.* **2008**, *10*, 2701.
(27) Okuno, Y.; Yamashita, M.; Nozaki, K. *Angew. Chem. Int. Ed.* **2011**, *50*, 920.
(28) Yoshida, H.; Kawashima, S.; Takemoto, Y.; Okada, K.; Ohshita, J.; Takaki, K. *Angew. Chem. Int. Ed.* **2012**, *51*, 235.
(29) Iwadate, N.; Suginome, M. *J. Am. Chem. Soc.* **2010**, *132*, 2548.
(30) Ohmura, T.; Yamamoto, Y.; Miyaura, N. *J. Am. Chem. Soc.* **2000**, *122*, 4990.
(31) Ohmura, T.; Oshima, K.; Suginome, M. *Chem. Commun.* **2008**, 1416.
(32) Nagashima, Y.; Hirano, K.; Takita, R.; Uchiyama, M. *J. Am. Chem. Soc.* **2014**, *136*, 8532.
(33) Nagao, K.; Ohmiya, H.; Sawamura, M. *Org. Lett.* **2015**, *17*, 1304.
(34) Verma, A.; Snead, R. F.; Dai, Y.; Slebodnick, C.; Yang, Y.; Yu, H.; Yao, F.; Santos, W. L. *Angew. Chem. Int. Ed.* **2017**, *56*, 1.
(35) Hamlet, Z.; Rampersad, M. *Tetrahedron Lett.* **1970**, 2101.

(36) Waldo, J. P.; Larock, R. C. *Org. Lett.* **2005**, *7*, 5203.
(37) Mariaule, G.; Newsome, G.; Toullec, P. Y.; Belmont, P.; Michelet, V. *Org. Lett.* **2014**, 19.
(38) Daiki, H.; Noguchi, K.; Tanaka, K. *Angew. Chem. Int. Ed.* **2009**, *48*, 8129.
(39) Zhu, S.; Zhang, Z.; Huang, X.; Jiang, H.; Guo, Z. *Chem. Eur. J.* **2013**, *19*, 4695.
(40) Gao, H.; Zhang, J. *Adv. Synth. Catal.* **2009**, *351*, 85.
(41) Winternheimer, D. J.; Merlic, C. a. *Org. Lett.* **2010**, *12*, 2508.
(42) Zhao, Y.; Snieckus, V. *Org. Lett.* **2014**, *16*, 390.
(43) Kim, H. R.; Yun, J. *Chem. Commun.* **2011**, *47*, 2943.
(44) Ring, T. E.; Spangler, W.; Jondahl, P. *J. Org. Chem.* **1973**, *38*, 2478.
(45) Guner, V. A.; Houk, K. N.; Davies, I. W. *J. Med. Chem.* **2004**, *69* (14), 8024.
(46) Yu, T.; Fu, Y.; Liu, L.; Guo, Q. *J. Org. Chem.* **2006**, *71* (5), 6157.
(47) Marvell, E. N.; Caple, G. *Tetrahedron* **1973**, *29*, 3797.
(48) Rodriguez-Otero Jesús. *J. Org. Chem.* **1999**, *64* (18), 6842.
(49) Lustig, E. *J. Phys. Chem.* **1961**, *65*, 491.
(50) Walter, C.; Huntress, E. *J. Am. Chem. Soc.* **1948**, *70*, 3702.
(51) Murmann, R. K.; Vassian, E. G. *J. Org. Chem.* **1962**, *27* (7), 4309.
(52) Curtin, D. Y.; Grubbs, E. J.; Mccarty, C. G. *J. Am. Chem. Soc.* **1966**, No. 88, 2775.
(53) Hosokawa, T.; Shimo, N.; Maeda, K.; Sonoda, A.; Murahashi, S. *Tetrahedron Lett.* **1976**, *17* (5), 383.
(54) Parthasarathy, K.; Jeganmohan, M.; Cheng, C.-H. *Org. Lett.* **2008**, *10*, 325.
(55) Mora-Radó, H.; Bialy, L.; Czechtizky, W.; Méndez, M.; Harrity, J. P. A. *Angew. Chem. Int. Ed.* **2016**, *55*, 5834.
(56) Higashino, M.; Ikeda, N.; Shinada, T.; Sakaguchi, K.; Ohfune, Y. *Tetrahedron Lett.* **2011**, *52*, 422.
(57) Gogoi, J.; Gogoi, P.; Boruah, R. C. *Eur. J. Org. Chem.* **2014**, 3483.
(58) Zhang, Y.; Herndon, J. W. *Org. Lett.* **2003**, *5*, 2043.
(59) Felpin, F. X.; Fouquet, E. *Chem. Eur. J.l* **2010**, *16*, 12440.
(60) Gogoi, S.; Shekarrao, K.; Duarah, A.; Bora, T. C.; Gogoi, S.; Boruah, R. C. *Steroids* **2012**, *77*, 1438.
(61) Wang, G.; Chen, X.; Miao, G.; Yao, W. *J. Org. Chem.* **2013**, *78*, 6223.
(62) Application, I.; Under, P.; Patent, T. H. E.; Treaty, C. **2016**, No. 12.
(63) Application, I.; Under, P.; Patent, T. H. E.; Treaty, C. **2015**, No. 12.
(64) Karabatsos. Gj; Hsi, N. *Tetrahedron* **1967**, *23*, 1079.
(65) Otto, N.; Opatz, T. *Beilstein J. Org. Chem.* **2012**, *8*, 1105.
(66) Sadler, S. A.; Tajuddin, H.; Mkhalid, I. A. I.; Batsanov, A. S.; Albesa-Jove, D.; Cheung, M. S.; Maxwell, A. C.; Shukla, L.; Roberts, B.; Blakemore, D. C.; Lin, Z.; Marder, T. B.; Steel, P. G. *Org. Biomol. Chem.* **2014**, *12*, 7318.
(67) Fraser, R. R.; Capoor., R. *Can. J. Chem.* **1983**, *61*, 2616.
(68) Padwa, A.; Albrecht, F. *J. Am. Chem. Soc.* **1972**, *94* (3), 1000.
(69) Padwa, A.; Albrecht, F. *J. Org. Chem.* **1974**, *39* (16), 2361.
(70) Jiang, H.; An, X.; Tong, K.; Zheng, T.; Zhang, Y.; Yu, S. *Angew. Chem. Int. Ed.* **2015**, *54*, 4055.
(71) Alonso, R.; Campos, P. J.; Rodr, M. A. *Tetrahedron* **2010**, *66*, 8828.
(72) Liu, X.; Qing, Z.; Cheng, P.; Zheng, X.; Zeng, J.; Xie, H. *Molecules* **2016**, *21*, 1609.
(73) Mcburney, R. T.; Walton, J. C. *Beilstein J. Org. Chem.* **2013**, *9*, 1083.

(74) Portela-cubillo, F.; Lymer, J.; Scanlan, E. M.; Scott, J. S.; Walton, J. C. *Tetrahedron* **2008**, *64* (52), 11908.
(75) Hofstra, J. L.; Grassbaugh, B. R.; Tran, Q. M.; Armada, N. R.; Lijser, H. J. P. De. *J. Org. Chem.* **2015**, *80*, 256.
(76) Hancock, K.; Dickinson, D. *J. Am. Chem. Soc.* **1973**, *95*, 280.
(77) Goetz, A. E.; Garg, N. K. *Nat. Chem.* **2013**, *5* (1), 54.
(78) Bentley, K. W. *Nat. Prod. Rep.* **2005**, *22*, 249.
(79) Prentis, R. A.; Lis, Y.; Walker, S. R. *Br. J. Clin. Pharmac.* **1988**, *25*, 387.
(80) Kola, I.; Landis, J. *Nat. Rev. drug Discov.* **2004**, *3*, 711.
(81) Park, A.; Park, K.; Kim, Y.; Lee, S. *Org. Lett.* **2011**, *13*, 944.
(82) Van Den Hoven BG; Ali, B.; Alper, H. *J. Org. Chem.* **2000**, *65*, 4131.
(83) Matheu, M. I.; Castillo, S.; Maseras, F.; Pe, P. J. *J. Am. Chem. Soc.* **2014**.
(84) Alfonsi, M.; Dell'Acqua, M.; Facoetti, D.; Arcadi, A.; Abbiati, G.; Rossi, E. *Eur. J. Org. Chem.* **2009**, *2009*, 2852.
(85) Shu, X.-Z.; Zhao, S.-C.; Ji, K.-G.; Zheng, Z.-J.; Liu, X.-Y.; Liang, Y.-M. *Eur. J. Org. Chem.* **2009**, 117.
(86) Tiwari, R. K.; Verma, A. K.; Choudhary, D.; Saunthwal, R. K.; Rustagi, V.; Patel, M. *J. Org. Chem.* **2013**, *78*, 6657.
(87) Guo, B.; Zheng, L.; Yang, L.; Hua, R. *J. Org. Chem.* **2014**, *79*, 4352.
(88) Sanjuµn, A. M.; Rashid, M. A.; García-garcía, P.; Martínez-, A.; Fernµndez-rodríguez, M. A.; Rodríguez, F.; Sanz, R. *Chem. Eur. J.* **2015**, *21*, 3042.
(89) Isogai, Y.; Khan, F. N.; Asao, N. *Tetrahedron* **2009**, *65* (46), 9575.
(90) Hansen, E. C.; Lee, D. *Org. lett.* **2004**.
(91) Ch, C. H.; Our, D. *J. Org. Chem.* **1977**, *42*, 6.
(92) Li, X.; Peng, F.; Zhou, M.; Mo, M.; Zhao, R.; Shao, Z. *Chem. Commun.* **2014**, 1745.
(93) Dolliver, D. D.; Bhattarai, B. T.; Pandey, A.; Lanier, M. L.; Bordelon, A. S.; Adhikari, S.; Dinser, J. a.; Flowers, P. F.; Wills, V. S.; Schneider, C. L.; Shaughnessy, K. H.; Moore, J. N.; Raders, S. M.; Snowden, T. S.; McKim, A. S.; Fronczek, F. R. *J. Org. Chem.* **2013**, *78*, 3676.
(94) Chu, H.; Sun, S.; Yu, J.; Cheng, J. *Chem. Commun.* **2015**, *51*, 13327.
(95) Voisin, A. S.; Bouillon, A.; Lancelot, J.-C.; Rault, S. *Tetrahedron* **2005**, *61*, 1417.
(96) Barton, C-N, C. *J. Chem. Soc.* **1956**, 3500.
(97) Hu, Y.; Xie, Y.; Shen, Z.; Huang, H. *Angew. Chem. Int. Ed.* **2017**, *56*, 2473.

CHAPTER 8: *Appendix*

X-ray crystal structure for *(E) 3-cyclohexenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-phenylprop-2-en-1-O-methyl oxime (80)*

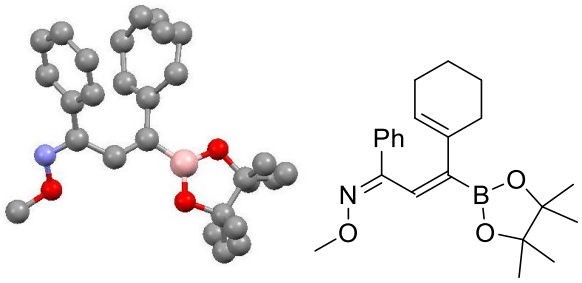


Table 1. Crystal data and structure refinement for OHJ271_0m_a.

Identification code	OHJ271_0m_a	
Empirical formula	C22 H30 B N O3	
Formula weight	367.28	
Temperature	100(2) K	
Wavelength	1.54178 Å	
Crystal system	Monoclinic	
Space group	$P2_1/c$	
Unit cell dimensions	a = 6.3288(2) Å	a= 90°.
	b = 19.6124(5) Å	b= 90.4590(10)°.
	c = 16.6749(4) Å	g = 90°.
Volume	2069.67(10) $Å^3$	
Z	4	
Density (calculated)	1.179 Mg/m^3	
Absorption coefficient	0.604 mm^{-1}	
F(000)	792	
Crystal size	0.320 x 0.110 x 0.110 mm^3	
Theta range for data collection	3.479 to 66.679°.	
Index ranges	-7<=h<=7, -23<=k<=23, -19<=l<=19	
Reflections collected	35016	
Independent reflections	3666 [R(int) = 0.0313]	
Completeness to theta = 67.000°	99.1 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.98 and 0.54	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3666 / 69 / 294	

Goodness-of-fit on F^2	1.036
Final R indices [I>2sigma(I)]	R1 = 0.0767, wR2 = 0.1866
R indices (all data)	R1 = 0.0823, wR2 = 0.1921
Extinction coefficient	n/a
Largest diff. peak and hole	0.938 and -1.015 e.$Å^{-3}$

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for OHJ271_0m_a. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
B(1)	3104(5)	4325(1)	7332(2)	22(1)
O(1)	3109(3)	4311(1)	8141(1)	29(1)
O(2)	1924(4)	4838(1)	7022(1)	52(1)
O(3)	9348(3)	3005(1)	7761(1)	29(1)
N(1)	8703(3)	2600(1)	7099(1)	23(1)
C(1)	4418(4)	3813(1)	6810(2)	21(1)
C(2)	5618(4)	3344(1)	7191(1)	22(1)
C(3)	6912(4)	2807(1)	6815(1)	20(1)
C(4)	6159(4)	2418(1)	6098(1)	18(1)
C(5)	7541(4)	2278(1)	5473(2)	21(1)
C(6)	6867(4)	1900(1)	4818(2)	23(1)
C(7)	4826(4)	1647(1)	4778(1)	22(1)
C(8)	3446(4)	1786(1)	5401(2)	22(1)
C(9)	4096(4)	2174(1)	6054(1)	20(1)
C(10)	4398(4)	3880(1)	5922(1)	19(1)
C(11)	6194(4)	3954(1)	5518(2)	23(1)
C(12)	6319(4)	3975(2)	4618(2)	31(1)
C(13)	4271(4)	3715(2)	4219(3)	26(1)
C(14)	2387(6)	4068(2)	4616(2)	26(1)
C(13')	4158(5)	4128(3)	4243(4)	26(1)
C(14')	2550(9)	3649(3)	4628(2)	26(1)
C(15)	2277(4)	3859(1)	5503(1)	25(1)
C(16)	961(4)	5197(1)	7654(2)	29(1)
C(17)	1825(4)	4868(1)	8428(2)	26(1)
C(18)	-1226(7)	4882(3)	7476(3)	42(1)
C(19)	775(10)	5966(2)	7551(3)	41(1)
C(20)	2843(8)	5277(3)	9106(3)	36(1)
C(21)	1(7)	4477(3)	8823(3)	36(1)
C(18')	-1331(7)	5442(4)	7623(5)	41(1)
C(19')	2337(11)	5841(3)	7557(5)	40(1)
C(20')	3625(9)	5341(3)	8697(4)	36(1)
C(21')	375(11)	4713(4)	9128(4)	36(1)
C(22)	10911(4)	2634(2)	8199(2)	29(1)

Table 3. Bond lengths [Å] and angles [°] for OHJ271_0m_a.

B(1)-O(1)	1.350(3)
B(1)-O(2)	1.353(3)
B(1)-C(1)	1.571(4)
O(1)-C(17)	1.444(3)
O(2)-C(16)	1.410(3)
O(3)-N(1)	1.417(3)
O(3)-C(22)	1.426(3)
N(1)-C(3)	1.290(3)
C(1)-C(2)	1.348(4)
C(1)-C(10)	1.486(3)
C(2)-C(3)	1.477(3)
C(2)-H(2)	0.9500
C(3)-C(4)	1.494(3)
C(4)-C(9)	1.392(3)
C(4)-C(5)	1.394(3)
C(5)-C(6)	1.385(4)
C(5)-H(5)	0.9500
C(6)-C(7)	1.385(4)
C(6)-H(6)	0.9500
C(7)-C(8)	1.389(4)
C(7)-H(7)	0.9500
C(8)-C(9)	1.388(3)
C(8)-H(8)	0.9500
C(9)-H(9)	0.9500
C(10)-C(11)	1.334(4)
C(10)-C(15)	1.509(3)
C(11)-C(12)	1.503(4)
C(11)-H(11)	0.9500
C(12)-C(13')	1.529(3)
C(12)-C(13)	1.539(3)
C(12)-H(12A)	0.9900
C(12)-H(12B)	0.9900
C(12)-H(12C)	0.9900
C(12)-H(12D)	0.9900
C(13)-C(14)	1.534(3)
C(13)-H(13A)	0.9900

C(13)-H(13B)	0.9900
C(14)-C(15)	1.538(3)
C(14)-H(14A)	0.9900
C(14)-H(14B)	0.9900
C(13')-C(14')	1.531(3)
C(13')-H(13C)	0.9900
C(13')-H(13D)	0.9900
C(14')-C(15)	1.528(3)
C(14')-H(14C)	0.9900
C(14')-H(14D)	0.9900
C(15)-H(15A)	0.9900
C(15)-H(15B)	0.9900
C(15)-H(15C)	1.01(8)
C(15)-H(15D)	1.06(8)
C(16)-C(19)	1.523(4)
C(16)-C(18')	1.528(4)
C(16)-C(17)	1.540(4)
C(16)-C(19')	1.542(4)
C(16)-C(18)	1.543(4)
C(17)-C(21')	1.522(4)
C(17)-C(20)	1.525(4)
C(17)-C(20')	1.534(4)
C(17)-C(21)	1.538(4)
C(18)-H(18A)	0.9800
C(18)-H(18B)	0.9800
C(18)-H(18C)	0.9800
C(19)-H(19A)	0.9800
C(19)-H(19B)	0.9800
C(19)-H(19C)	0.9800
C(20)-H(20A)	0.9800
C(20)-H(20B)	0.9800
C(20)-H(20C)	0.9800
C(21)-H(21A)	0.9800
C(21)-H(21B)	0.9800
C(21)-H(21C)	0.9800
C(18')-H(18D)	0.9800
C(18')-H(18E)	0.9800
C(18')-H(18F)	0.9800

C(19')-H(19D)	0.9800
C(19')-H(19E)	0.9800
C(19')-H(19F)	0.9800
C(20')-H(20D)	0.9800
C(20')-H(20E)	0.9800
C(20')-H(20F)	0.9800
C(21')-H(21D)	0.9800
C(21')-H(21E)	0.9800
C(21')-H(21F)	0.9800
C(22)-H(22A)	0.9800
C(22)-H(22B)	0.9800
C(22)-H(22C)	0.9800

O(1)-B(1)-O(2)	113.1(2)
O(1)-B(1)-C(1)	123.0(2)
O(2)-B(1)-C(1)	123.8(2)
B(1)-O(1)-C(17)	108.62(19)
B(1)-O(2)-C(16)	109.1(2)
N(1)-O(3)-C(22)	107.88(18)
C(3)-N(1)-O(3)	110.89(19)
C(2)-C(1)-C(10)	122.0(2)
C(2)-C(1)-B(1)	118.2(2)
C(10)-C(1)-B(1)	119.7(2)
C(1)-C(2)-C(3)	126.7(2)
C(1)-C(2)-H(2)	116.6
C(3)-C(2)-H(2)	116.6
N(1)-C(3)-C(2)	123.8(2)
N(1)-C(3)-C(4)	114.0(2)
C(2)-C(3)-C(4)	122.0(2)
C(9)-C(4)-C(5)	119.1(2)
C(9)-C(4)-C(3)	120.8(2)
C(5)-C(4)-C(3)	120.1(2)
C(6)-C(5)-C(4)	120.3(2)
C(6)-C(5)-H(5)	119.8
C(4)-C(5)-H(5)	119.8
C(5)-C(6)-C(7)	120.7(2)
C(5)-C(6)-H(6)	119.7
C(7)-C(6)-H(6)	119.7

C(6)-C(7)-C(8)	119.1(2)
C(6)-C(7)-H(7)	120.5
C(8)-C(7)-H(7)	120.5
C(9)-C(8)-C(7)	120.7(2)
C(9)-C(8)-H(8)	119.7
C(7)-C(8)-H(8)	119.7
C(8)-C(9)-C(4)	120.1(2)
C(8)-C(9)-H(9)	119.9
C(4)-C(9)-H(9)	119.9
C(11)-C(10)-C(1)	120.9(2)
C(11)-C(10)-C(15)	121.8(2)
C(1)-C(10)-C(15)	117.3(2)
C(10)-C(11)-C(12)	124.0(2)
C(10)-C(11)-H(11)	118.0
C(12)-C(11)-H(11)	118.0
C(11)-C(12)-C(13')	111.1(3)
C(11)-C(12)-C(13)	111.8(2)
C(11)-C(12)-H(12A)	109.3
C(13)-C(12)-H(12A)	109.3
C(11)-C(12)-H(12B)	109.3
C(13)-C(12)-H(12B)	109.3
H(12A)-C(12)-H(12B)	107.9
C(11)-C(12)-H(12C)	109.4
C(13')-C(12)-H(12C)	109.4
C(11)-C(12)-H(12D)	109.4
C(13')-C(12)-H(12D)	109.4
H(12C)-C(12)-H(12D)	108.0
C(14)-C(13)-C(12)	108.6(3)
C(14)-C(13)-H(13A)	110.0
C(12)-C(13)-H(13A)	110.0
C(14)-C(13)-H(13B)	110.0
C(12)-C(13)-H(13B)	110.0
H(13A)-C(13)-H(13B)	108.3
C(13)-C(14)-C(15)	109.6(3)
C(13)-C(14)-H(14A)	109.7
C(15)-C(14)-H(14A)	109.7
C(13)-C(14)-H(14B)	109.7
C(15)-C(14)-H(14B)	109.7

H(14A)-C(14)-H(14B)	108.2
C(12)-C(13')-C(14')	107.6(4)
C(12)-C(13')-H(13C)	110.2
C(14')-C(13')-H(13C)	110.2
C(12)-C(13')-H(13D)	110.2
C(14')-C(13')-H(13D)	110.2
H(13C)-C(13')-H(13D)	108.5
C(15)-C(14')-C(13')	108.4(4)
C(15)-C(14')-H(14C)	110.0
C(13')-C(14')-H(14C)	110.0
C(15)-C(14')-H(14D)	110.0
C(13')-C(14')-H(14D)	110.0
H(14C)-C(14')-H(14D)	108.4
C(10)-C(15)-C(14')	110.0(3)
C(10)-C(15)-C(14)	113.0(2)
C(10)-C(15)-H(15A)	109.0
C(14)-C(15)-H(15A)	109.0
C(10)-C(15)-H(15B)	109.0
C(14)-C(15)-H(15B)	109.0
H(15A)-C(15)-H(15B)	107.8
C(10)-C(15)-H(15C)	107(4)
C(14')-C(15)-H(15C)	123(4)
C(10)-C(15)-H(15D)	110(4)
C(14')-C(15)-H(15D)	107(4)
H(15C)-C(15)-H(15D)	98(6)
O(2)-C(16)-C(19)	116.4(3)
O(2)-C(16)-C(18')	123.2(4)
O(2)-C(16)-C(17)	105.3(2)
C(19)-C(16)-C(17)	122.5(3)
C(18')-C(16)-C(17)	119.4(4)
O(2)-C(16)-C(19')	94.8(3)
C(18')-C(16)-C(19')	106.0(4)
C(17)-C(16)-C(19')	103.6(3)
O(2)-C(16)-C(18)	92.8(3)
C(19)-C(16)-C(18)	107.8(3)
C(17)-C(16)-C(18)	107.8(3)
O(1)-C(17)-C(21')	116.6(4)
O(1)-C(17)-C(20)	114.1(3)

O(1)-C(17)-C(20')	97.8(3)
C(21')-C(17)-C(20')	110.3(5)
O(1)-C(17)-C(21)	101.1(3)
C(20)-C(17)-C(21)	105.0(3)
O(1)-C(17)-C(16)	103.71(19)
C(21')-C(17)-C(16)	121.0(4)
C(20)-C(17)-C(16)	123.0(3)
C(20')-C(17)-C(16)	104.4(3)
C(21)-C(17)-C(16)	107.8(3)
C(16)-C(18)-H(18A)	109.5
C(16)-C(18)-H(18B)	109.5
H(18A)-C(18)-H(18B)	109.5
C(16)-C(18)-H(18C)	109.5
H(18A)-C(18)-H(18C)	109.5
H(18B)-C(18)-H(18C)	109.5
C(16)-C(19)-H(19A)	109.5
C(16)-C(19)-H(19B)	109.5
H(19A)-C(19)-H(19B)	109.5
C(16)-C(19)-H(19C)	109.5
H(19A)-C(19)-H(19C)	109.5
H(19B)-C(19)-H(19C)	109.5
C(17)-C(20)-H(20A)	109.5
C(17)-C(20)-H(20B)	109.5
H(20A)-C(20)-H(20B)	109.5
C(17)-C(20)-H(20C)	109.5
H(20A)-C(20)-H(20C)	109.5
H(20B)-C(20)-H(20C)	109.5
C(17)-C(21)-H(21A)	109.5
C(17)-C(21)-H(21B)	109.5
H(21A)-C(21)-H(21B)	109.5
C(17)-C(21)-H(21C)	109.5
H(21A)-C(21)-H(21C)	109.5
H(21B)-C(21)-H(21C)	109.5
C(16)-C(18')-H(18D)	109.5
C(16)-C(18')-H(18E)	109.5
H(18D)-C(18')-H(18E)	109.5
C(16)-C(18')-H(18F)	109.5
H(18D)-C(18')-H(18F)	109.5

H(18E)-C(18')-H(18F)	109.5
C(16)-C(19')-H(19D)	109.5
C(16)-C(19')-H(19E)	109.5
H(19D)-C(19')-H(19E)	109.5
C(16)-C(19')-H(19F)	109.5
H(19D)-C(19')-H(19F)	109.5
H(19E)-C(19')-H(19F)	109.5
C(17)-C(20')-H(20D)	109.5
C(17)-C(20')-H(20E)	109.5
H(20D)-C(20')-H(20E)	109.5
C(17)-C(20')-H(20F)	109.5
H(20D)-C(20')-H(20F)	109.5
H(20E)-C(20')-H(20F)	109.5
C(17)-C(21')-H(21D)	109.5
C(17)-C(21')-H(21E)	109.5
H(21D)-C(21')-H(21E)	109.5
C(17)-C(21')-H(21F)	109.5
H(21D)-C(21')-H(21F)	109.5
H(21E)-C(21')-H(21F)	109.5
O(3)-C(22)-H(22A)	109.5
O(3)-C(22)-H(22B)	109.5
H(22A)-C(22)-H(22B)	109.5
O(3)-C(22)-H(22C)	109.5
H(22A)-C(22)-H(22C)	109.5
H(22B)-C(22)-H(22C)	109.5

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for OHJ271_0m_a. The anisotropic displacement factor exponent takes the form: $-2p^2[\ h^2\ a^{*2}U^{11} + ...\ + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
B(1)	30(2)	17(1)	19(1)	-1(1)	-3(1)	-2(1)
O(1)	39(1)	30(1)	17(1)	3(1)	5(1)	16(1)
O(2)	98(2)	40(1)	18(1)	-8(1)	-6(1)	43(1)
O(3)	37(1)	24(1)	27(1)	-5(1)	-16(1)	-2(1)
N(1)	28(1)	19(1)	21(1)	-2(1)	-8(1)	-3(1)
C(1)	28(1)	16(1)	20(1)	-2(1)	-2(1)	-1(1)
C(2)	32(1)	18(1)	17(1)	-4(1)	-3(1)	-2(1)
C(3)	27(1)	14(1)	18(1)	0(1)	-4(1)	-2(1)
C(4)	23(1)	13(1)	17(1)	1(1)	-4(1)	4(1)
C(5)	21(1)	18(1)	25(1)	0(1)	-2(1)	2(1)
C(6)	29(1)	21(1)	19(1)	-1(1)	2(1)	7(1)
C(7)	31(1)	17(1)	18(1)	-4(1)	-8(1)	5(1)
C(8)	22(1)	18(1)	27(1)	-2(1)	-6(1)	1(1)
C(9)	22(1)	17(1)	21(1)	-1(1)	1(1)	2(1)
C(10)	25(1)	12(1)	19(1)	-2(1)	-3(1)	2(1)
C(11)	22(1)	20(1)	26(1)	2(1)	-4(1)	1(1)
C(12)	28(1)	37(2)	26(1)	5(1)	2(1)	1(1)
C(15)	21(1)	29(1)	24(1)	-6(1)	0(1)	0(1)
C(16)	42(2)	24(1)	20(1)	3(1)	7(1)	13(1)
C(17)	33(1)	24(1)	20(1)	-7(1)	-3(1)	9(1)
C(18)	56(2)	30(2)	39(2)	-1(1)	-5(2)	12(2)
C(19)	56(2)	29(1)	38(2)	0(1)	-3(2)	13(2)
C(20)	50(2)	39(2)	19(2)	-5(1)	1(1)	10(2)
C(21)	50(2)	40(2)	18(2)	-3(1)	2(1)	11(2)
C(18')	56(2)	29(1)	38(2)	0(1)	-4(2)	13(2)
C(19')	56(2)	28(2)	37(2)	0(1)	-3(2)	13(2)
C(20')	50(2)	39(2)	18(2)	-6(2)	0(1)	10(2)
C(21')	50(2)	39(2)	18(2)	-4(1)	2(1)	11(2)
C(22)	27(1)	37(2)	25(1)	2(1)	-10(1)	-2(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for OHJ271_0m_a.

	x	y	z	U(eq)
H(2)	5634	3362	7760	26
H(5)	8952	2442	5496	25
H(6)	7816	1813	4391	28
H(7)	4375	1383	4331	27
H(8)	2044	1614	5380	27
H(9)	3131	2273	6472	24
H(11)	7472	3997	5816	27
H(12A)	7520	3690	4441	37
H(12B)	6587	4449	4443	37
H(12C)	6837	3530	4418	37
H(12D)	7340	4330	4455	37
H(13A)	4284	3818	3638	32
H(13B)	4157	3215	4287	32
H(14A)	1062	3936	4337	31
H(14B)	2547	4569	4574	31
H(13C)	4198	4052	3656	32
H(13D)	3763	4609	4342	32
H(14C)	1180	3679	4339	32
H(14D)	3058	3172	4598	32
H(15A)	1292	4169	5784	30
H(15B)	1698	3391	5539	30
H(15C)	1460(120)	4280(40)	5670(40)	30
H(15D)	1300(110)	3490(40)	5780(40)	30
H(18A)	-1680	5008	6932	63
H(18B)	-2252	5054	7864	63
H(18C)	-1136	4385	7518	63
H(19A)	2188	6171	7563	62
H(19B)	-71	6156	7987	62
H(19C)	88	6068	7035	62
H(20A)	3208	4971	9550	54
H(20B)	1849	5624	9293	54
H(20C)	4127	5499	8910	54

H(21A)	-685	4182	8425	53
H(21B)	-1031	4803	9033	53
H(21C)	558	4198	9264	53
H(18D)	-1585	5689	7120	62
H(18E)	-1596	5746	8078	62
H(18F)	-2280	5048	7651	62
H(19D)	3832	5717	7608	61
H(19E)	1977	6172	7974	61
H(19F)	2076	6042	7027	61
H(20D)	4482	5113	9109	54
H(20E)	3030	5762	8919	54
H(20F)	4512	5452	8236	54
H(21D)	-628	4355	8972	54
H(21E)	-401	5126	9275	54
H(21F)	1221	4557	9588	54
H(22A)	10256	2236	8452	44
H(22B)	11532	2928	8614	44
H(22C)	12020	2482	7833	44

Table 6. Hydrogen bonds for OHJ271_0m_a [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
C(21)-H(21A)...O(3)#1	0.98	2.56	3.410(6)	145.1
C(21)-H(21A)...O(3)#1	0.98	2.56	3.410(6)	145.1

Symmetry transformations used to generate equivalent atoms:

#1 x-1,y,z

X-ray crystal structure for *(E) 2-(1,2-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2 (trimethylsilyl)ethenyl)benzaldehyde O-methyl oxime (54)*

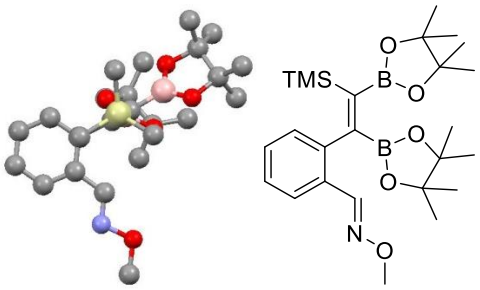


Table 1. Crystal data and structure refinement for orjhm1_a.

Identification code	orjhm1_a	
Empirical formula	C25 H41 B2 N O5 Si	
Formula weight	485.30	
Temperature	296(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P-1	
Unit cell dimensions	a = 10.9500(6) Å	a= 92.971(4)°.
	b = 14.0922(8) Å	b= 95.156(4)°.
	c = 28.9607(15) Å	g = 108.157(3)°.
Volume	4214.1(4) $Å^3$	
Z	6	
Density (calculated)	1.147 Mg/m^3	
Absorption coefficient	0.117 mm^{-1}	
F(000)	1572	
Crystal size	0.320 x 0.210 x 0.210 mm^3	
Theta range for data collection	0.708 to 25.000°.	
Index ranges	-13<=h<=13, -16<=k<=16, -34<=l<=34	
Reflections collected	68436	
Independent reflections	14805 [R(int) = 0.2946]	
Completeness to theta = 25.000°	99.9 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.98 and 0.94	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	14805 / 0 / 955	
Goodness-of-fit on F^2	1.058	
Final R indices [I>2sigma(I)]	R1 = 0.1282, wR2 = 0.1878	

R indices (all data)	R1 = 0.2263, wR2 = 0.2365
Extinction coefficient	n/a
Largest diff. peak and hole	0.387 and -0.437 e.Å^{-3}

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for orjhm1_a. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Si(1A)	2678(2)	7149(1)	80(1)	24(1)
B(1A)	5366(6)	9512(5)	1088(2)	21(1)
B(2A)	5160(6)	7497(5)	627(2)	22(2)
O(1A)	6305(3)	10335(3)	983(1)	25(1)
O(2A)	5419(3)	9368(3)	1553(1)	26(1)
O(3A)	6356(3)	8011(3)	858(1)	24(1)
O(4A)	5067(4)	6529(3)	468(1)	27(1)
O(5A)	1446(4)	8566(3)	1973(1)	40(1)
N(1)	1322(4)	9039(4)	1561(2)	30(1)
C(1A)	4045(5)	7948(4)	516(2)	20(1)
C(2A)	4197(5)	8877(4)	719(2)	18(1)
C(3A)	3267(5)	9439(4)	593(2)	20(1)
C(4A)	3306(5)	9876(4)	174(2)	27(1)
C(5A)	2476(5)	10407(4)	43(2)	26(1)
C(6A)	1546(6)	10472(4)	324(2)	28(1)
C(7A)	1472(5)	10033(4)	740(2)	25(1)
C(8A)	2337(5)	9519(4)	880(2)	21(1)
C(9A)	2239(5)	9048(4)	1320(2)	26(1)
C(10A)	340(6)	8472(7)	2214(2)	63(3)
C(11A)	6358(6)	10284(4)	1793(2)	26(1)
C(12A)	7223(5)	10704(4)	1405(2)	24(1)
C(13A)	7747(6)	11833(4)	1435(2)	31(2)
C(14A)	8303(6)	10256(5)	1362(2)	39(2)
C(15A)	5590(6)	10942(5)	1945(2)	40(2)
C(16A)	7080(6)	10002(5)	2213(2)	46(2)
C(17A)	7035(5)	7269(4)	945(2)	24(1)
C(18A)	6366(5)	6444(4)	552(2)	25(1)
C(19A)	6971(6)	6623(5)	99(2)	35(2)
C(20A)	6222(6)	5381(4)	681(2)	38(2)
C(21A)	8467(5)	7760(4)	926(2)	28(1)
C(22A)	6769(6)	6944(5)	1433(2)	36(2)
C(23A)	1208(6)	7553(5)	-12(2)	43(2)
C(24A)	3407(6)	7118(4)	-473(2)	31(2)

C(25A)	2100(5)	5867(4)	281(2)	28(1)
Si(1B)	7285(2)	6236(1)	3191(1)	24(1)
B(1B)	4800(6)	5912(5)	2658(2)	21(2)
B(2B)	4476(6)	3892(5)	2225(2)	19(1)
O(1B)	4167(3)	4224(3)	1813(1)	24(1)
O(2B)	3694(3)	2965(3)	2300(1)	22(1)
O(3B)	5042(4)	6875(3)	2541(1)	30(1)
O(4B)	3524(3)	5441(3)	2699(1)	22(1)
O(5B)	8792(4)	5293(4)	1422(1)	47(1)
N(1B)	8790(5)	4627(4)	1772(2)	30(1)
C(1B)	5894(5)	5428(4)	2759(2)	20(1)
C(2B)	5714(5)	4482(4)	2569(2)	19(1)
C(3B)	6627(5)	3905(4)	2668(2)	19(1)
C(4B)	6433(5)	3257(4)	3022(2)	25(1)
C(5B)	7225(5)	2698(4)	3127(2)	26(1)
C(6B)	8311(5)	2801(4)	2887(2)	24(1)
C(7B)	8504(5)	3426(4)	2532(2)	24(1)
C(8B)	7682(5)	3971(4)	2413(2)	20(1)
C(9B)	7886(6)	4608(4)	2025(2)	29(1)
C(10B)	9777(6)	5284(5)	1136(2)	43(2)
C(11B)	2586(5)	2698(4)	1937(2)	22(1)
C(12B)	3169(5)	3363(4)	1547(2)	25(1)
C(13B)	2235(6)	3754(5)	1258(2)	41(2)
C(14B)	3893(6)	2873(5)	1233(2)	36(2)
C(15B)	1536(5)	2999(5)	2145(2)	34(2)
C(16B)	2165(5)	1594(4)	1806(2)	29(1)
C(17B)	3780(6)	7018(4)	2426(2)	28(1)
C(18B)	3888(6)	8092(4)	2588(2)	33(2)
C(19B)	3449(6)	6832(5)	1900(2)	35(2)
C(20B)	2882(5)	6216(4)	2697(2)	24(1)
C(21B)	2877(6)	6555(4)	3204(2)	32(2)
C(22B)	1520(5)	5753(4)	2465(2)	31(2)
C(23B)	6534(6)	6407(5)	3727(2)	36(2)
C(24B)	8649(6)	5740(5)	3328(2)	41(2)
C(25B)	7959(6)	7467(4)	2949(2)	39(2)
Si(1C)	2693(2)	462(1)	3474(1)	21(1)
O(1C)	5375(3)	3843(3)	4614(1)	24(1)
O(2C)	6401(3)	2673(3)	4532(1)	26(1)

O(3C)	5875(3)	637(3)	3729(1)	21(1)
O(4C)	5279(3)	455(3)	4463(1)	21(1)
O(5C)	1336(4)	1622(3)	5360(1)	28(1)
N(1C)	1121(4)	2074(3)	4951(1)	24(1)
B(1C)	5297(6)	2922(5)	4424(2)	18(1)
B(2C)	5105(6)	828(4)	4041(2)	20(1)
C(1C)	4025(5)	1307(4)	3919(2)	18(1)
C(2C)	4094(5)	2233(4)	4103(2)	19(1)
C(3C)	3056(5)	2700(4)	3984(2)	18(1)
C(4C)	3079(5)	3216(4)	3584(2)	22(1)
C(5C)	2147(5)	3662(4)	3460(2)	24(1)
C(6C)	1136(5)	3582(4)	3736(2)	25(1)
C(7C)	1110(5)	3082(4)	4132(2)	22(1)
C(8C)	2049(5)	2644(4)	4262(2)	17(1)
C(9C)	2032(5)	2149(4)	4700(2)	20(1)
C(10C)	282(6)	1536(5)	5626(2)	40(2)
C(11C)	6579(5)	4215(4)	4933(2)	22(1)
C(12C)	7398(5)	3579(4)	4753(2)	21(1)
C(13C)	8178(5)	4040(5)	4368(2)	33(2)
C(14C)	8253(6)	3296(5)	5128(2)	37(2)
C(15C)	6196(6)	4016(5)	5420(2)	35(2)
C(16C)	7149(6)	5327(4)	4897(2)	31(2)
C(17C)	6814(5)	232(4)	3971(2)	21(1)
C(18C)	6206(5)	-92(4)	4434(2)	21(1)
C(19C)	5440(5)	-1194(4)	4424(2)	27(1)
C(20C)	7175(5)	218(4)	4869(2)	25(1)
C(21C)	6929(5)	-627(4)	3656(2)	27(1)
C(22C)	8088(5)	1058(4)	4043(2)	29(1)
C(23C)	3355(6)	618(4)	2906(2)	32(2)
C(24C)	1092(5)	667(5)	3448(2)	34(2)
C(25C)	2433(6)	-840(4)	3633(2)	29(1)

Table 3. Bond lengths [Å] and angles [°] for orjhm1_a.

Si(1A)-C(24A)	1.856(6)
Si(1A)-C(25A)	1.862(6)
Si(1A)-C(23A)	1.870(6)
Si(1A)-C(1A)	1.889(5)
B(1A)-O(1A)	1.358(7)
B(1A)-O(2A)	1.370(7)
B(1A)-C(2A)	1.587(8)
B(2A)-O(3A)	1.374(7)
B(2A)-O(4A)	1.388(7)
B(2A)-C(1A)	1.559(8)
O(1A)-C(12A)	1.471(6)
O(2A)-C(11A)	1.470(6)
O(3A)-C(17A)	1.479(6)
O(4A)-C(18A)	1.463(6)
O(5A)-N(1)	1.412(5)
O(5A)-C(10A)	1.425(7)
N(1)-C(9A)	1.270(7)
C(1A)-C(2A)	1.362(7)
C(2A)-C(3A)	1.505(7)
C(3A)-C(4A)	1.389(7)
C(3A)-C(8A)	1.398(7)
C(4A)-C(5A)	1.385(7)
C(4A)-H(4A)	0.9300
C(5A)-C(6A)	1.381(8)
C(5A)-H(5A)	0.9300
C(6A)-C(7A)	1.380(7)
C(6A)-H(6A)	0.9300
C(7A)-C(8A)	1.405(7)
C(7A)-H(7A)	0.9300
C(8A)-C(9A)	1.463(7)
C(9A)-H(9A)	0.9300
C(10A)-H(10A)	0.9600
C(10A)-H(10B)	0.9600
C(10A)-H(10C)	0.9600
C(11A)-C(15A)	1.506(8)
C(11A)-C(16A)	1.527(7)

C(11A)-C(12A)	1.556(7)
C(12A)-C(13A)	1.508(7)
C(12A)-C(14A)	1.515(8)
C(13A)-H(13A)	0.9600
C(13A)-H(13B)	0.9600
C(13A)-H(13C)	0.9600
C(14A)-H(14A)	0.9600
C(14A)-H(14B)	0.9600
C(14A)-H(14C)	0.9600
C(15A)-H(15A)	0.9600
C(15A)-H(15B)	0.9600
C(15A)-H(15C)	0.9600
C(16A)-H(16A)	0.9600
C(16A)-H(16B)	0.9600
C(16A)-H(16C)	0.9600
C(17A)-C(21A)	1.512(7)
C(17A)-C(22A)	1.531(7)
C(17A)-C(18A)	1.538(7)
C(18A)-C(19A)	1.521(7)
C(18A)-C(20A)	1.526(8)
C(19A)-H(19A)	0.9600
C(19A)-H(19B)	0.9600
C(19A)-H(19C)	0.9600
C(20A)-H(20A)	0.9600
C(20A)-H(20B)	0.9600
C(20A)-H(20C)	0.9600
C(21A)-H(21A)	0.9600
C(21A)-H(21B)	0.9600
C(21A)-H(21C)	0.9600
C(22A)-H(22A)	0.9600
C(22A)-H(22B)	0.9600
C(22A)-H(22C)	0.9600
C(23A)-H(23A)	0.9600
C(23A)-H(23B)	0.9600
C(23A)-H(23C)	0.9600
C(24A)-H(24A)	0.9600
C(24A)-H(24B)	0.9600
C(24A)-H(24C)	0.9600

C(25A)-H(25A)	0.9600
C(25A)-H(25B)	0.9600
C(25A)-H(25C)	0.9600
Si(1B)-C(23B)	1.859(6)
Si(1B)-C(24B)	1.857(6)
Si(1B)-C(25B)	1.862(6)
Si(1B)-C(1B)	1.900(5)
B(1B)-O(3B)	1.367(7)
B(1B)-O(4B)	1.366(7)
B(1B)-C(1B)	1.565(8)
B(2B)-O(1B)	1.358(7)
B(2B)-O(2B)	1.362(7)
B(2B)-C(2B)	1.578(8)
O(1B)-C(12B)	1.477(6)
O(2B)-C(11B)	1.473(6)
O(3B)-C(17B)	1.468(6)
O(4B)-C(20B)	1.471(6)
O(5B)-N(1B)	1.416(5)
O(5B)-C(10B)	1.421(6)
N(1B)-C(9B)	1.279(7)
C(1B)-C(2B)	1.364(7)
C(2B)-C(3B)	1.492(7)
C(3B)-C(4B)	1.394(7)
C(3B)-C(8B)	1.407(7)
C(4B)-C(5B)	1.368(7)
C(4B)-H(4B)	0.9300
C(5B)-C(6B)	1.402(7)
C(5B)-H(5B)	0.9300
C(6B)-C(7B)	1.377(7)
C(6B)-H(6B)	0.9300
C(7B)-C(8B)	1.386(7)
C(7B)-H(7B)	0.9300
C(8B)-C(9B)	1.463(7)
C(9B)-H(9B)	0.9300
C(10B)-H(10D)	0.9600
C(10B)-H(10E)	0.9600
C(10B)-H(10F)	0.9600
C(11B)-C(16B)	1.494(7)

C(11B)-C(15B)	1.506(7)
C(11B)-C(12B)	1.557(7)
C(12B)-C(13B)	1.515(7)
C(12B)-C(14B)	1.530(8)
C(13B)-H(13D)	0.9600
C(13B)-H(13E)	0.9600
C(13B)-H(13F)	0.9600
C(14B)-H(14D)	0.9600
C(14B)-H(14E)	0.9600
C(14B)-H(14F)	0.9600
C(15B)-H(15D)	0.9600
C(15B)-H(15E)	0.9600
C(15B)-H(15F)	0.9600
C(16B)-H(16D)	0.9600
C(16B)-H(16E)	0.9600
C(16B)-H(16F)	0.9600
C(17B)-C(19B)	1.523(7)
C(17B)-C(18B)	1.527(8)
C(17B)-C(20B)	1.548(7)
C(18B)-H(18A)	0.9600
C(18B)-H(18B)	0.9600
C(18B)-H(18C)	0.9600
C(19B)-H(19D)	0.9600
C(19B)-H(19E)	0.9600
C(19B)-H(19F)	0.9600
C(20B)-C(22B)	1.506(7)
C(20B)-C(21B)	1.522(7)
C(21B)-H(21D)	0.9600
C(21B)-H(21E)	0.9600
C(21B)-H(21F)	0.9600
C(22B)-H(22D)	0.9600
C(22B)-H(22E)	0.9600
C(22B)-H(22F)	0.9600
C(23B)-H(23D)	0.9600
C(23B)-H(23E)	0.9600
C(23B)-H(23F)	0.9600
C(24B)-H(24D)	0.9600
C(24B)-H(24E)	0.9600

C(24B)-H(24F)	0.9600
C(25B)-H(25D)	0.9600
C(25B)-H(25E)	0.9600
C(25B)-H(25F)	0.9600
Si(1C)-C(23C)	1.854(6)
Si(1C)-C(25C)	1.856(6)
Si(1C)-C(24C)	1.859(6)
Si(1C)-C(1C)	1.904(5)
O(1C)-B(1C)	1.358(7)
O(1C)-C(11C)	1.472(6)
O(2C)-B(1C)	1.374(7)
O(2C)-C(12C)	1.467(6)
O(3C)-B(2C)	1.361(7)
O(3C)-C(17C)	1.467(6)
O(4C)-B(2C)	1.377(7)
O(4C)-C(18C)	1.459(6)
O(5C)-N(1C)	1.409(5)
O(5C)-C(10C)	1.423(6)
N(1C)-C(9C)	1.268(6)
B(1C)-C(2C)	1.559(8)
B(2C)-C(1C)	1.558(8)
C(1C)-C(2C)	1.361(7)
C(2C)-C(3C)	1.504(7)
C(3C)-C(4C)	1.395(7)
C(3C)-C(8C)	1.409(7)
C(4C)-C(5C)	1.387(7)
C(4C)-H(4C)	0.9300
C(5C)-C(6C)	1.402(7)
C(5C)-H(5C)	0.9300
C(6C)-C(7C)	1.376(7)
C(6C)-H(6C)	0.9300
C(7C)-C(8C)	1.389(7)
C(7C)-H(7C)	0.9300
C(8C)-C(9C)	1.478(7)
C(9C)-H(9C)	0.9300
C(10C)-H(10G)	0.9600
C(10C)-H(10H)	0.9600
C(10C)-H(10I)	0.9600

C(11C)-C(16C)	1.508(7)
C(11C)-C(15C)	1.523(7)
C(11C)-C(12C)	1.554(7)
C(12C)-C(13C)	1.516(7)
C(12C)-C(14C)	1.519(7)
C(13C)-H(13G)	0.9600
C(13C)-H(13H)	0.9600
C(13C)-H(13I)	0.9600
C(14C)-H(14G)	0.9600
C(14C)-H(14H)	0.9600
C(14C)-H(14I)	0.9600
C(15C)-H(15G)	0.9600
C(15C)-H(15H)	0.9600
C(15C)-H(15I)	0.9600
C(16C)-H(16G)	0.9600
C(16C)-H(16H)	0.9600
C(16C)-H(16I)	0.9600
C(17C)-C(22C)	1.502(7)
C(17C)-C(21C)	1.520(7)
C(17C)-C(18C)	1.577(7)
C(18C)-C(19C)	1.515(7)
C(18C)-C(20C)	1.522(7)
C(19C)-H(19G)	0.9600
C(19C)-H(19H)	0.9600
C(19C)-H(19I)	0.9600
C(20C)-H(20D)	0.9600
C(20C)-H(20E)	0.9600
C(20C)-H(20F)	0.9600
C(21C)-H(21G)	0.9600
C(21C)-H(21H)	0.9600
C(21C)-H(21I)	0.9600
C(22C)-H(22G)	0.9600
C(22C)-H(22H)	0.9600
C(22C)-H(22I)	0.9600
C(23C)-H(23G)	0.9600
C(23C)-H(23H)	0.9600
C(23C)-H(23I)	0.9600
C(24C)-H(24G)	0.9600

C(24C)-H(24H)	0.9600
C(24C)-H(24I)	0.9600
C(25C)-H(25G)	0.9600
C(25C)-H(25H)	0.9600
C(25C)-H(25I)	0.9600

C(24A)-Si(1A)-C(25A)	110.3(3)
C(24A)-Si(1A)-C(23A)	110.5(3)
C(25A)-Si(1A)-C(23A)	105.5(3)
C(24A)-Si(1A)-C(1A)	105.2(2)
C(25A)-Si(1A)-C(1A)	108.2(2)
C(23A)-Si(1A)-C(1A)	117.1(3)
O(1A)-B(1A)-O(2A)	113.7(5)
O(1A)-B(1A)-C(2A)	122.7(5)
O(2A)-B(1A)-C(2A)	122.9(5)
O(3A)-B(2A)-O(4A)	112.3(5)
O(3A)-B(2A)-C(1A)	125.3(5)
O(4A)-B(2A)-C(1A)	122.3(5)
B(1A)-O(1A)-C(12A)	107.0(4)
B(1A)-O(2A)-C(11A)	106.3(4)
B(2A)-O(3A)-C(17A)	107.1(4)
B(2A)-O(4A)-C(18A)	106.7(4)
N(1)-O(5A)-C(10A)	109.2(4)
C(9A)-N(1)-O(5A)	110.3(5)
C(2A)-C(1A)-B(2A)	117.4(5)
C(2A)-C(1A)-Si(1A)	127.9(4)
B(2A)-C(1A)-Si(1A)	114.7(4)
C(1A)-C(2A)-C(3A)	122.0(5)
C(1A)-C(2A)-B(1A)	125.6(5)
C(3A)-C(2A)-B(1A)	112.3(5)
C(4A)-C(3A)-C(8A)	118.4(5)
C(4A)-C(3A)-C(2A)	119.4(5)
C(8A)-C(3A)-C(2A)	122.2(5)
C(5A)-C(4A)-C(3A)	121.5(5)
C(5A)-C(4A)-H(4A)	119.2
C(3A)-C(4A)-H(4A)	119.2
C(6A)-C(5A)-C(4A)	119.8(5)
C(6A)-C(5A)-H(5A)	120.1

C(4A)-C(5A)-H(5A)	120.1
C(5A)-C(6A)-C(7A)	119.9(6)
C(5A)-C(6A)-H(6A)	120.1
C(7A)-C(6A)-H(6A)	120.1
C(6A)-C(7A)-C(8A)	120.5(5)
C(6A)-C(7A)-H(7A)	119.8
C(8A)-C(7A)-H(7A)	119.8
C(3A)-C(8A)-C(7A)	119.8(5)
C(3A)-C(8A)-C(9A)	120.3(5)
C(7A)-C(8A)-C(9A)	119.9(5)
N(1)-C(9A)-C(8A)	120.5(6)
N(1)-C(9A)-H(9A)	119.7
C(8A)-C(9A)-H(9A)	119.7
O(5A)-C(10A)-H(10A)	109.5
O(5A)-C(10A)-H(10B)	109.5
H(10A)-C(10A)-H(10B)	109.5
O(5A)-C(10A)-H(10C)	109.5
H(10A)-C(10A)-H(10C)	109.5
H(10B)-C(10A)-H(10C)	109.5
O(2A)-C(11A)-C(15A)	106.5(5)
O(2A)-C(11A)-C(16A)	108.9(4)
C(15A)-C(11A)-C(16A)	110.9(5)
O(2A)-C(11A)-C(12A)	102.2(4)
C(15A)-C(11A)-C(12A)	113.6(5)
C(16A)-C(11A)-C(12A)	113.9(5)
O(1A)-C(12A)-C(13A)	109.6(4)
O(1A)-C(12A)-C(14A)	106.6(4)
C(13A)-C(12A)-C(14A)	110.4(5)
O(1A)-C(12A)-C(11A)	101.6(4)
C(13A)-C(12A)-C(11A)	114.0(5)
C(14A)-C(12A)-C(11A)	113.9(5)
C(12A)-C(13A)-H(13A)	109.5
C(12A)-C(13A)-H(13B)	109.5
H(13A)-C(13A)-H(13B)	109.5
C(12A)-C(13A)-H(13C)	109.5
H(13A)-C(13A)-H(13C)	109.5
H(13B)-C(13A)-H(13C)	109.5
C(12A)-C(14A)-H(14A)	109.5

C(12A)-C(14A)-H(14B)	109.5
H(14A)-C(14A)-H(14B)	109.5
C(12A)-C(14A)-H(14C)	109.5
H(14A)-C(14A)-H(14C)	109.5
H(14B)-C(14A)-H(14C)	109.5
C(11A)-C(15A)-H(15A)	109.5
C(11A)-C(15A)-H(15B)	109.5
H(15A)-C(15A)-H(15B)	109.5
C(11A)-C(15A)-H(15C)	109.5
H(15A)-C(15A)-H(15C)	109.5
H(15B)-C(15A)-H(15C)	109.5
C(11A)-C(16A)-H(16A)	109.5
C(11A)-C(16A)-H(16B)	109.5
H(16A)-C(16A)-H(16B)	109.5
C(11A)-C(16A)-H(16C)	109.5
H(16A)-C(16A)-H(16C)	109.5
H(16B)-C(16A)-H(16C)	109.5
O(3A)-C(17A)-C(21A)	109.2(4)
O(3A)-C(17A)-C(22A)	106.0(4)
C(21A)-C(17A)-C(22A)	110.7(5)
O(3A)-C(17A)-C(18A)	101.7(4)
C(21A)-C(17A)-C(18A)	114.6(5)
C(22A)-C(17A)-C(18A)	113.8(5)
O(4A)-C(18A)-C(19A)	106.9(4)
O(4A)-C(18A)-C(20A)	107.8(4)
C(19A)-C(18A)-C(20A)	110.1(5)
O(4A)-C(18A)-C(17A)	103.5(4)
C(19A)-C(18A)-C(17A)	113.4(5)
C(20A)-C(18A)-C(17A)	114.6(5)
C(18A)-C(19A)-H(19A)	109.5
C(18A)-C(19A)-H(19B)	109.5
H(19A)-C(19A)-H(19B)	109.5
C(18A)-C(19A)-H(19C)	109.5
H(19A)-C(19A)-H(19C)	109.5
H(19B)-C(19A)-H(19C)	109.5
C(18A)-C(20A)-H(20A)	109.5
C(18A)-C(20A)-H(20B)	109.5
H(20A)-C(20A)-H(20B)	109.5

C(18A)-C(20A)-H(20C)	109.5
H(20A)-C(20A)-H(20C)	109.5
H(20B)-C(20A)-H(20C)	109.5
C(17A)-C(21A)-H(21A)	109.5
C(17A)-C(21A)-H(21B)	109.5
H(21A)-C(21A)-H(21B)	109.5
C(17A)-C(21A)-H(21C)	109.5
H(21A)-C(21A)-H(21C)	109.5
H(21B)-C(21A)-H(21C)	109.5
C(17A)-C(22A)-H(22A)	109.5
C(17A)-C(22A)-H(22B)	109.5
H(22A)-C(22A)-H(22B)	109.5
C(17A)-C(22A)-H(22C)	109.5
H(22A)-C(22A)-H(22C)	109.5
H(22B)-C(22A)-H(22C)	109.5
Si(1A)-C(23A)-H(23A)	109.5
Si(1A)-C(23A)-H(23B)	109.5
H(23A)-C(23A)-H(23B)	109.5
Si(1A)-C(23A)-H(23C)	109.5
H(23A)-C(23A)-H(23C)	109.5
H(23B)-C(23A)-H(23C)	109.5
Si(1A)-C(24A)-H(24A)	109.5
Si(1A)-C(24A)-H(24B)	109.5
H(24A)-C(24A)-H(24B)	109.5
Si(1A)-C(24A)-H(24C)	109.5
H(24A)-C(24A)-H(24C)	109.5
H(24B)-C(24A)-H(24C)	109.5
Si(1A)-C(25A)-H(25A)	109.5
Si(1A)-C(25A)-H(25B)	109.5
H(25A)-C(25A)-H(25B)	109.5
Si(1A)-C(25A)-H(25C)	109.5
H(25A)-C(25A)-H(25C)	109.5
H(25B)-C(25A)-H(25C)	109.5
C(23B)-Si(1B)-C(24B)	110.3(3)
C(23B)-Si(1B)-C(25B)	109.8(3)
C(24B)-Si(1B)-C(25B)	107.3(3)
C(23B)-Si(1B)-C(1B)	105.0(3)
C(24B)-Si(1B)-C(1B)	116.6(3)

C(25B)-Si(1B)-C(1B)	107.8(2)
O(3B)-B(1B)-O(4B)	113.0(5)
O(3B)-B(1B)-C(1B)	122.8(5)
O(4B)-B(1B)-C(1B)	124.1(5)
O(1B)-B(2B)-O(2B)	114.5(5)
O(1B)-B(2B)-C(2B)	123.0(5)
O(2B)-B(2B)-C(2B)	122.3(5)
B(2B)-O(1B)-C(12B)	106.1(4)
B(2B)-O(2B)-C(11B)	106.9(4)
B(1B)-O(3B)-C(17B)	106.8(4)
B(1B)-O(4B)-C(20B)	107.0(4)
N(1B)-O(5B)-C(10B)	109.0(4)
C(9B)-N(1B)-O(5B)	109.6(5)
C(2B)-C(1B)-B(1B)	118.9(5)
C(2B)-C(1B)-Si(1B)	127.8(4)
B(1B)-C(1B)-Si(1B)	113.1(4)
C(1B)-C(2B)-C(3B)	124.3(5)
C(1B)-C(2B)-B(2B)	121.7(5)
C(3B)-C(2B)-B(2B)	113.9(5)
C(4B)-C(3B)-C(8B)	117.8(5)
C(4B)-C(3B)-C(2B)	119.5(5)
C(8B)-C(3B)-C(2B)	122.7(5)
C(5B)-C(4B)-C(3B)	122.4(5)
C(5B)-C(4B)-H(4B)	118.8
C(3B)-C(4B)-H(4B)	118.8
C(4B)-C(5B)-C(6B)	119.7(5)
C(4B)-C(5B)-H(5B)	120.2
C(6B)-C(5B)-H(5B)	120.2
C(7B)-C(6B)-C(5B)	118.5(5)
C(7B)-C(6B)-H(6B)	120.8
C(5B)-C(6B)-H(6B)	120.8
C(6B)-C(7B)-C(8B)	122.1(5)
C(6B)-C(7B)-H(7B)	118.9
C(8B)-C(7B)-H(7B)	118.9
C(7B)-C(8B)-C(3B)	119.4(5)
C(7B)-C(8B)-C(9B)	121.1(5)
C(3B)-C(8B)-C(9B)	119.5(5)
N(1B)-C(9B)-C(8B)	120.2(5)

N(1B)-C(9B)-H(9B)	119.9
C(8B)-C(9B)-H(9B)	119.9
O(5B)-C(10B)-H(10D)	109.5
O(5B)-C(10B)-H(10E)	109.5
H(10D)-C(10B)-H(10E)	109.5
O(5B)-C(10B)-H(10F)	109.5
H(10D)-C(10B)-H(10F)	109.5
H(10E)-C(10B)-H(10F)	109.5
O(2B)-C(11B)-C(16B)	109.2(4)
O(2B)-C(11B)-C(15B)	106.2(4)
C(16B)-C(11B)-C(15B)	111.2(5)
O(2B)-C(11B)-C(12B)	101.5(4)
C(16B)-C(11B)-C(12B)	114.9(4)
C(15B)-C(11B)-C(12B)	113.1(5)
O(1B)-C(12B)-C(13B)	108.6(4)
O(1B)-C(12B)-C(14B)	105.8(4)
C(13B)-C(12B)-C(14B)	110.5(5)
O(1B)-C(12B)-C(11B)	102.8(4)
C(13B)-C(12B)-C(11B)	115.5(5)
C(14B)-C(12B)-C(11B)	112.9(5)
C(12B)-C(13B)-H(13D)	109.5
C(12B)-C(13B)-H(13E)	109.5
H(13D)-C(13B)-H(13E)	109.5
C(12B)-C(13B)-H(13F)	109.5
H(13D)-C(13B)-H(13F)	109.5
H(13E)-C(13B)-H(13F)	109.5
C(12B)-C(14B)-H(14D)	109.5
C(12B)-C(14B)-H(14E)	109.5
H(14D)-C(14B)-H(14E)	109.5
C(12B)-C(14B)-H(14F)	109.5
H(14D)-C(14B)-H(14F)	109.5
H(14E)-C(14B)-H(14F)	109.5
C(11B)-C(15B)-H(15D)	109.5
C(11B)-C(15B)-H(15E)	109.5
H(15D)-C(15B)-H(15E)	109.5
C(11B)-C(15B)-H(15F)	109.5
H(15D)-C(15B)-H(15F)	109.5
H(15E)-C(15B)-H(15F)	109.5

C(11B)-C(16B)-H(16D)	109.5
C(11B)-C(16B)-H(16E)	109.5
H(16D)-C(16B)-H(16E)	109.5
C(11B)-C(16B)-H(16F)	109.5
H(16D)-C(16B)-H(16F)	109.5
H(16E)-C(16B)-H(16F)	109.5
O(3B)-C(17B)-C(19B)	107.6(5)
O(3B)-C(17B)-C(18B)	108.5(5)
C(19B)-C(17B)-C(18B)	110.5(5)
O(3B)-C(17B)-C(20B)	102.4(4)
C(19B)-C(17B)-C(20B)	113.4(5)
C(18B)-C(17B)-C(20B)	113.8(5)
C(17B)-C(18B)-H(18A)	109.5
C(17B)-C(18B)-H(18B)	109.5
H(18A)-C(18B)-H(18B)	109.5
C(17B)-C(18B)-H(18C)	109.5
H(18A)-C(18B)-H(18C)	109.5
H(18B)-C(18B)-H(18C)	109.5
C(17B)-C(19B)-H(19D)	109.5
C(17B)-C(19B)-H(19E)	109.5
H(19D)-C(19B)-H(19E)	109.5
C(17B)-C(19B)-H(19F)	109.5
H(19D)-C(19B)-H(19F)	109.5
H(19E)-C(19B)-H(19F)	109.5
O(4B)-C(20B)-C(22B)	108.4(4)
O(4B)-C(20B)-C(21B)	106.4(4)
C(22B)-C(20B)-C(21B)	110.6(5)
O(4B)-C(20B)-C(17B)	101.6(4)
C(22B)-C(20B)-C(17B)	115.0(4)
C(21B)-C(20B)-C(17B)	114.0(5)
C(20B)-C(21B)-H(21D)	109.5
C(20B)-C(21B)-H(21E)	109.5
H(21D)-C(21B)-H(21E)	109.5
C(20B)-C(21B)-H(21F)	109.5
H(21D)-C(21B)-H(21F)	109.5
H(21E)-C(21B)-H(21F)	109.5
C(20B)-C(22B)-H(22D)	109.5
C(20B)-C(22B)-H(22E)	109.5

H(22D)-C(22B)-H(22E)	109.5
C(20B)-C(22B)-H(22F)	109.5
H(22D)-C(22B)-H(22F)	109.5
H(22E)-C(22B)-H(22F)	109.5
Si(1B)-C(23B)-H(23D)	109.5
Si(1B)-C(23B)-H(23E)	109.5
H(23D)-C(23B)-H(23E)	109.5
Si(1B)-C(23B)-H(23F)	109.5
H(23D)-C(23B)-H(23F)	109.5
H(23E)-C(23B)-H(23F)	109.5
Si(1B)-C(24B)-H(24D)	109.5
Si(1B)-C(24B)-H(24E)	109.5
H(24D)-C(24B)-H(24E)	109.5
Si(1B)-C(24B)-H(24F)	109.5
H(24D)-C(24B)-H(24F)	109.5
H(24E)-C(24B)-H(24F)	109.5
Si(1B)-C(25B)-H(25D)	109.5
Si(1B)-C(25B)-H(25E)	109.5
H(25D)-C(25B)-H(25E)	109.5
Si(1B)-C(25B)-H(25F)	109.5
H(25D)-C(25B)-H(25F)	109.5
H(25E)-C(25B)-H(25F)	109.5
C(23C)-Si(1C)-C(25C)	109.7(3)
C(23C)-Si(1C)-C(24C)	111.3(3)
C(25C)-Si(1C)-C(24C)	106.6(3)
C(23C)-Si(1C)-C(1C)	105.6(2)
C(25C)-Si(1C)-C(1C)	106.5(2)
C(24C)-Si(1C)-C(1C)	116.8(2)
B(1C)-O(1C)-C(11C)	107.6(4)
B(1C)-O(2C)-C(12C)	107.3(4)
B(2C)-O(3C)-C(17C)	108.6(4)
B(2C)-O(4C)-C(18C)	108.7(4)
N(1C)-O(5C)-C(10C)	108.6(4)
C(9C)-N(1C)-O(5C)	110.5(4)
O(1C)-B(1C)-O(2C)	113.1(5)
O(1C)-B(1C)-C(2C)	123.3(5)
O(2C)-B(1C)-C(2C)	123.6(5)
O(3C)-B(2C)-O(4C)	113.1(5)

O(3C)-B(2C)-C(1C)	123.8(5)
O(4C)-B(2C)-C(1C)	122.7(5)
C(2C)-C(1C)-B(2C)	122.3(5)
C(2C)-C(1C)-Si(1C)	126.2(4)
B(2C)-C(1C)-Si(1C)	111.5(4)
C(1C)-C(2C)-C(3C)	122.4(5)
C(1C)-C(2C)-B(1C)	122.6(5)
C(3C)-C(2C)-B(1C)	114.9(5)
C(4C)-C(3C)-C(8C)	117.8(5)
C(4C)-C(3C)-C(2C)	119.6(5)
C(8C)-C(3C)-C(2C)	122.6(4)
C(5C)-C(4C)-C(3C)	121.8(5)
C(5C)-C(4C)-H(4C)	119.1
C(3C)-C(4C)-H(4C)	119.1
C(4C)-C(5C)-C(6C)	119.6(5)
C(4C)-C(5C)-H(5C)	120.2
C(6C)-C(5C)-H(5C)	120.2
C(7C)-C(6C)-C(5C)	119.0(5)
C(7C)-C(6C)-H(6C)	120.5
C(5C)-C(6C)-H(6C)	120.5
C(6C)-C(7C)-C(8C)	121.6(5)
C(6C)-C(7C)-H(7C)	119.2
C(8C)-C(7C)-H(7C)	119.2
C(7C)-C(8C)-C(3C)	120.1(5)
C(7C)-C(8C)-C(9C)	120.6(5)
C(3C)-C(8C)-C(9C)	119.3(5)
N(1C)-C(9C)-C(8C)	120.4(5)
N(1C)-C(9C)-H(9C)	119.8
C(8C)-C(9C)-H(9C)	119.8
O(5C)-C(10C)-H(10G)	109.5
O(5C)-C(10C)-H(10H)	109.5
H(10G)-C(10C)-H(10H)	109.5
O(5C)-C(10C)-H(10I)	109.5
H(10G)-C(10C)-H(10I)	109.5
H(10H)-C(10C)-H(10I)	109.5
O(1C)-C(11C)-C(16C)	108.1(4)
O(1C)-C(11C)-C(15C)	106.3(4)
C(16C)-C(11C)-C(15C)	110.0(5)

O(1C)-C(11C)-C(12C)	102.5(4)
C(16C)-C(11C)-C(12C)	114.7(5)
C(15C)-C(11C)-C(12C)	114.3(5)
O(2C)-C(12C)-C(13C)	105.7(4)
O(2C)-C(12C)-C(14C)	109.7(4)
C(13C)-C(12C)-C(14C)	110.3(5)
O(2C)-C(12C)-C(11C)	102.3(4)
C(13C)-C(12C)-C(11C)	113.0(5)
C(14C)-C(12C)-C(11C)	115.1(4)
C(12C)-C(13C)-H(13G)	109.5
C(12C)-C(13C)-H(13H)	109.5
H(13G)-C(13C)-H(13H)	109.5
C(12C)-C(13C)-H(13I)	109.5
H(13G)-C(13C)-H(13I)	109.5
H(13H)-C(13C)-H(13I)	109.5
C(12C)-C(14C)-H(14G)	109.5
C(12C)-C(14C)-H(14H)	109.5
H(14G)-C(14C)-H(14H)	109.5
C(12C)-C(14C)-H(14I)	109.5
H(14G)-C(14C)-H(14I)	109.5
H(14H)-C(14C)-H(14I)	109.5
C(11C)-C(15C)-H(15G)	109.5
C(11C)-C(15C)-H(15H)	109.5
H(15G)-C(15C)-H(15H)	109.5
C(11C)-C(15C)-H(15I)	109.5
H(15G)-C(15C)-H(15I)	109.5
H(15H)-C(15C)-H(15I)	109.5
C(11C)-C(16C)-H(16G)	109.5
C(11C)-C(16C)-H(16H)	109.5
H(16G)-C(16C)-H(16H)	109.5
C(11C)-C(16C)-H(16I)	109.5
H(16G)-C(16C)-H(16I)	109.5
H(16H)-C(16C)-H(16I)	109.5
O(3C)-C(17C)-C(22C)	107.1(4)
O(3C)-C(17C)-C(21C)	107.9(4)
C(22C)-C(17C)-C(21C)	109.5(5)
O(3C)-C(17C)-C(18C)	103.0(4)
C(22C)-C(17C)-C(18C)	114.2(4)

C(21C)-C(17C)-C(18C)	114.5(4)
O(4C)-C(18C)-C(19C)	106.5(4)
O(4C)-C(18C)-C(20C)	108.2(4)
C(19C)-C(18C)-C(20C)	109.8(4)
O(4C)-C(18C)-C(17C)	103.3(4)
C(19C)-C(18C)-C(17C)	114.6(4)
C(20C)-C(18C)-C(17C)	113.9(4)
C(18C)-C(19C)-H(19G)	109.5
C(18C)-C(19C)-H(19H)	109.5
H(19G)-C(19C)-H(19H)	109.5
C(18C)-C(19C)-H(19I)	109.5
H(19G)-C(19C)-H(19I)	109.5
H(19H)-C(19C)-H(19I)	109.5
C(18C)-C(20C)-H(20D)	109.5
C(18C)-C(20C)-H(20E)	109.5
H(20D)-C(20C)-H(20E)	109.5
C(18C)-C(20C)-H(20F)	109.5
H(20D)-C(20C)-H(20F)	109.5
H(20E)-C(20C)-H(20F)	109.5
C(17C)-C(21C)-H(21G)	109.5
C(17C)-C(21C)-H(21H)	109.5
H(21G)-C(21C)-H(21H)	109.5
C(17C)-C(21C)-H(21I)	109.5
H(21G)-C(21C)-H(21I)	109.5
H(21H)-C(21C)-H(21I)	109.5
C(17C)-C(22C)-H(22G)	109.5
C(17C)-C(22C)-H(22H)	109.5
H(22G)-C(22C)-H(22H)	109.5
C(17C)-C(22C)-H(22I)	109.5
H(22G)-C(22C)-H(22I)	109.5
H(22H)-C(22C)-H(22I)	109.5
Si(1C)-C(23C)-H(23G)	109.5
Si(1C)-C(23C)-H(23H)	109.5
H(23G)-C(23C)-H(23H)	109.5
Si(1C)-C(23C)-H(23I)	109.5
H(23G)-C(23C)-H(23I)	109.5
H(23H)-C(23C)-H(23I)	109.5
Si(1C)-C(24C)-H(24G)	109.5

Si(1C)-C(24C)-H(24H)	109.5
H(24G)-C(24C)-H(24H)	109.5
Si(1C)-C(24C)-H(24I)	109.5
H(24G)-C(24C)-H(24I)	109.5
H(24H)-C(24C)-H(24I)	109.5
Si(1C)-C(25C)-H(25G)	109.5
Si(1C)-C(25C)-H(25H)	109.5
H(25G)-C(25C)-H(25H)	109.5
Si(1C)-C(25C)-H(25I)	109.5
H(25G)-C(25C)-H(25I)	109.5
H(25H)-C(25C)-H(25I)	109.5

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for orjhm1_a. The anisotropic displacement factor exponent takes the form: $-2p^2[\ h^2\ a^{*2}U^{11} + ...\ + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
Si(1A)	23(1)	22(1)	26(1)	-1(1)	-1(1)	9(1)
B(1A)	18(3)	23(4)	24(3)	1(3)	0(3)	10(3)
B(2A)	25(4)	23(4)	18(3)	4(3)	4(3)	7(3)
O(1A)	28(2)	26(2)	16(2)	2(2)	-1(2)	3(2)
O(2A)	27(2)	28(2)	18(2)	6(2)	-2(2)	5(2)
O(3A)	21(2)	19(2)	35(2)	6(2)	0(2)	12(2)
O(4A)	26(2)	22(2)	35(2)	6(2)	-4(2)	11(2)
O(5A)	33(3)	69(3)	21(2)	18(2)	9(2)	16(2)
N(1)	25(3)	48(3)	17(2)	6(2)	3(2)	12(3)
C(1A)	21(3)	20(3)	22(3)	7(2)	6(2)	8(3)
C(2A)	17(3)	23(3)	16(3)	9(2)	6(2)	8(2)
C(3A)	19(3)	17(3)	19(3)	-2(2)	-2(2)	2(2)
C(4A)	25(3)	31(4)	25(3)	7(3)	5(2)	8(3)
C(5A)	28(3)	27(3)	25(3)	12(3)	0(3)	9(3)
C(6A)	27(3)	27(4)	31(3)	0(3)	-4(3)	12(3)
C(7A)	22(3)	31(4)	24(3)	-1(3)	3(2)	11(3)
C(8A)	25(3)	21(3)	18(3)	0(2)	2(2)	11(3)
C(9A)	26(3)	34(4)	17(3)	0(2)	3(2)	8(3)
C(10A)	25(4)	136(8)	22(3)	29(4)	11(3)	12(4)
C(11A)	32(4)	22(3)	19(3)	3(2)	1(2)	3(3)
C(12A)	22(3)	24(3)	26(3)	3(2)	2(2)	10(3)
C(13A)	40(4)	26(4)	23(3)	3(3)	3(3)	2(3)
C(14A)	28(4)	42(4)	48(4)	-11(3)	-1(3)	14(3)
C(15A)	39(4)	49(4)	31(3)	-8(3)	7(3)	13(3)
C(16A)	50(4)	45(4)	29(3)	20(3)	-18(3)	-1(4)
C(17A)	29(3)	26(3)	25(3)	4(2)	1(2)	20(3)
C(18A)	22(3)	22(3)	31(3)	4(2)	-3(2)	7(3)
C(19A)	37(4)	42(4)	33(3)	3(3)	7(3)	22(3)
C(20A)	30(4)	31(4)	56(4)	6(3)	-10(3)	17(3)
C(21A)	24(3)	20(3)	44(4)	0(3)	-1(3)	14(3)
C(22A)	44(4)	42(4)	27(3)	7(3)	1(3)	23(3)
C(23A)	23(4)	40(4)	64(4)	-19(3)	-10(3)	15(3)
C(24A)	42(4)	27(4)	23(3)	5(3)	-2(3)	8(3)

C(25A)	22(3)	32(4)	33(3)	4(3)	7(3)	10(3)
Si(1B)	23(1)	27(1)	23(1)	1(1)	2(1)	7(1)
B(1B)	26(4)	14(4)	24(3)	1(3)	6(3)	8(3)
B(2B)	21(4)	19(4)	19(3)	1(3)	0(3)	11(3)
O(1B)	32(2)	24(2)	16(2)	6(2)	-2(2)	9(2)
O(2B)	20(2)	24(2)	21(2)	7(2)	-4(2)	3(2)
O(3B)	20(2)	29(2)	44(2)	11(2)	4(2)	10(2)
O(4B)	26(2)	16(2)	29(2)	6(2)	5(2)	10(2)
O(5B)	51(3)	76(4)	38(2)	40(2)	28(2)	40(3)
N(1B)	30(3)	42(3)	23(3)	14(2)	7(2)	17(3)
C(1B)	19(3)	22(3)	19(3)	8(2)	4(2)	5(3)
C(2B)	20(3)	28(3)	15(3)	9(2)	7(2)	13(3)
C(3B)	23(3)	20(3)	17(3)	2(2)	1(2)	12(3)
C(4B)	20(3)	33(4)	29(3)	16(3)	9(2)	15(3)
C(5B)	30(3)	24(3)	26(3)	12(2)	3(3)	12(3)
C(6B)	23(3)	20(3)	33(3)	4(2)	-1(3)	13(3)
C(7B)	24(3)	24(3)	26(3)	1(2)	3(2)	12(3)
C(8B)	27(3)	14(3)	20(3)	2(2)	3(2)	8(3)
C(9B)	28(3)	37(4)	31(3)	13(3)	8(3)	20(3)
C(10B)	35(4)	75(5)	34(4)	21(3)	14(3)	35(4)
C(11B)	18(3)	22(3)	22(3)	0(2)	-3(2)	4(3)
C(12B)	29(3)	21(3)	23(3)	-2(2)	-2(2)	9(3)
C(13B)	46(4)	41(4)	37(4)	3(3)	-17(3)	20(3)
C(14B)	46(4)	37(4)	23(3)	-2(3)	10(3)	6(3)
C(15B)	26(4)	44(4)	31(3)	-5(3)	1(3)	12(3)
C(16B)	24(3)	29(4)	32(3)	-2(3)	-4(3)	8(3)
C(17B)	27(3)	27(4)	31(3)	6(3)	1(3)	11(3)
C(18B)	34(4)	19(3)	44(4)	4(3)	-1(3)	8(3)
C(19B)	44(4)	39(4)	26(3)	11(3)	2(3)	21(3)
C(20B)	28(3)	21(3)	33(3)	8(2)	8(3)	20(3)
C(21B)	42(4)	31(4)	30(3)	9(3)	8(3)	19(3)
C(22B)	25(3)	30(4)	39(3)	9(3)	4(3)	9(3)
C(23B)	41(4)	38(4)	28(3)	2(3)	4(3)	13(3)
C(24B)	34(4)	44(4)	40(4)	-8(3)	-5(3)	12(3)
C(25B)	43(4)	31(4)	32(3)	8(3)	2(3)	-3(3)
Si(1C)	22(1)	19(1)	24(1)	2(1)	2(1)	8(1)
O(1C)	19(2)	24(2)	31(2)	-1(2)	-4(2)	14(2)
O(2C)	22(2)	20(2)	34(2)	-1(2)	-1(2)	9(2)

O(3C)	23(2)	30(2)	20(2)	8(2)	5(2)	20(2)
O(4C)	25(2)	23(2)	23(2)	7(2)	4(2)	18(2)
O(5C)	33(2)	41(3)	18(2)	15(2)	7(2)	19(2)
N(1C)	28(3)	33(3)	16(2)	10(2)	2(2)	15(2)
B(1C)	22(4)	21(4)	17(3)	6(3)	7(3)	11(3)
B(2C)	34(4)	11(3)	17(3)	0(2)	4(3)	10(3)
C(1C)	24(3)	20(3)	15(3)	6(2)	7(2)	12(3)
C(2C)	23(3)	24(3)	17(3)	11(2)	9(2)	13(3)
C(3C)	17(3)	16(3)	22(3)	0(2)	2(2)	7(2)
C(4C)	23(3)	23(3)	24(3)	6(2)	2(2)	10(3)
C(5C)	33(4)	24(3)	21(3)	11(2)	7(3)	13(3)
C(6C)	28(3)	26(3)	26(3)	2(2)	-1(3)	15(3)
C(7C)	19(3)	29(3)	20(3)	0(2)	5(2)	10(3)
C(8C)	17(3)	18(3)	18(3)	2(2)	2(2)	7(2)
C(9C)	24(3)	18(3)	22(3)	4(2)	0(2)	11(3)
C(10C)	40(4)	60(5)	24(3)	19(3)	8(3)	16(4)
C(11C)	20(3)	22(3)	23(3)	0(2)	-5(2)	7(3)
C(12C)	14(3)	22(3)	25(3)	-2(2)	-4(2)	5(3)
C(13C)	25(3)	38(4)	33(3)	3(3)	4(3)	5(3)
C(14C)	35(4)	34(4)	36(4)	2(3)	-11(3)	9(3)
C(15C)	43(4)	37(4)	24(3)	2(3)	1(3)	10(3)
C(16C)	33(4)	19(3)	38(3)	-3(3)	-10(3)	9(3)
C(17C)	24(3)	27(3)	18(3)	8(2)	-1(2)	16(3)
C(18C)	30(3)	18(3)	18(3)	4(2)	1(2)	14(3)
C(19C)	32(4)	21(3)	30(3)	5(2)	4(3)	9(3)
C(20C)	31(3)	27(3)	19(3)	3(2)	-2(2)	14(3)
C(21C)	31(3)	37(4)	22(3)	2(3)	5(2)	21(3)
C(22C)	30(4)	34(4)	26(3)	10(3)	7(3)	13(3)
C(23C)	39(4)	28(4)	27(3)	5(3)	-5(3)	8(3)
C(24C)	29(4)	29(4)	41(4)	-5(3)	-2(3)	7(3)
C(25C)	37(4)	25(3)	25(3)	1(3)	5(3)	9(3)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for orjhm1_a.

	x	y	z	U(eq)
H(4A)	3903	9811	-25	32
H(5A)	2545	10719	-233	32
H(6A)	972	10811	233	34
H(7A)	845	10077	929	30
H(9A)	2853	8754	1424	31
H(10A)	227	9118	2262	94
H(10B)	461	8216	2509	94
H(10C)	-413	8021	2032	94
H(13A)	8254	12038	1182	47
H(13B)	8280	12076	1725	47
H(13C)	7042	12102	1416	47
H(14A)	7965	9541	1365	59
H(14B)	8964	10524	1618	59
H(14C)	8662	10420	1075	59
H(15A)	5170	11129	1675	60
H(15B)	6160	11534	2122	60
H(15C)	4951	10583	2133	60
H(16A)	7384	9461	2118	69
H(16B)	6507	9798	2447	69
H(16C)	7803	10571	2337	69
H(19A)	6439	6144	-143	52
H(19B)	7817	6550	137	52
H(19C)	7041	7288	18	52
H(20A)	5733	5244	943	57
H(20B)	7062	5319	760	57
H(20C)	5779	4911	422	57
H(21A)	8600	8085	643	42
H(21B)	8894	7260	935	42
H(21C)	8816	8247	1187	42
H(22A)	7028	7525	1652	54
H(22B)	7249	6503	1518	54
H(22C)	5861	6602	1434	54

H(23A)	1435	8196	-136	64
H(23B)	868	7599	280	64
H(23C)	565	7072	-227	64
H(24A)	4146	6892	-422	47
H(24B)	3671	7778	-579	47
H(24C)	2781	6667	-703	47
H(25A)	1334	5474	86	43
H(25B)	1907	5911	597	43
H(25C)	2761	5555	265	43
H(4B)	5738	3203	3193	30
H(5B)	7045	2251	3356	31
H(6B)	8887	2456	2966	29
H(7B)	9209	3484	2366	29
H(9B)	7356	5000	1963	35
H(10D)	10607	5539	1317	64
H(10E)	9744	5696	884	64
H(10F)	9645	4609	1012	64
H(13D)	1851	4115	1459	62
H(13E)	1570	3201	1088	62
H(13F)	2692	4193	1044	62
H(14D)	4333	3347	1028	54
H(14E)	3287	2302	1052	54
H(14F)	4511	2660	1421	54
H(15D)	1308	2637	2413	51
H(15E)	790	2847	1919	51
H(15F)	1841	3706	2235	51
H(16D)	2890	1406	1721	44
H(16E)	1501	1427	1548	44
H(16F)	1833	1242	2066	44
H(18A)	4291	8247	2903	49
H(18B)	3040	8160	2572	49
H(18C)	4401	8545	2391	49
H(19D)	4092	7308	1751	52
H(19E)	2617	6905	1815	52
H(19F)	3429	6165	1802	52
H(21D)	2485	5983	3368	48
H(21E)	2393	7016	3221	48
H(21F)	3750	6879	3342	48

H(22D)	1536	5426	2167	46
H(22E)	1124	6267	2423	46
H(22F)	1031	5271	2656	46
H(23D)	7188	6818	3961	53
H(23E)	6137	5766	3838	53
H(23F)	5891	6727	3658	53
H(24D)	9240	6163	3576	61
H(24E)	9090	5729	3057	61
H(24F)	8321	5073	3422	61
H(25D)	7296	7778	2905	58
H(25E)	8266	7366	2656	58
H(25F)	8663	7892	3162	58
H(4C)	3738	3262	3397	27
H(5C)	2193	4013	3196	29
H(6C)	492	3862	3652	30
H(7C)	448	3037	4318	27
H(9C)	2693	1892	4792	24
H(10G)	159	2179	5672	61
H(10H)	464	1306	5923	61
H(10I)	-490	1066	5464	61
H(13G)	8544	3567	4233	50
H(13H)	8861	4634	4493	50
H(13I)	7625	4210	4132	50
H(14G)	7728	2923	5347	55
H(14H)	8867	3894	5286	55
H(14I)	8706	2893	4987	55
H(15G)	5611	4374	5492	53
H(15H)	6955	4238	5642	53
H(15I)	5779	3311	5434	53
H(16G)	7246	5453	4578	47
H(16H)	7979	5573	5079	47
H(16I)	6584	5663	5013	47
H(19G)	4982	-1310	4694	41
H(19H)	6019	-1584	4422	41
H(19I)	4832	-1387	4148	41
H(20D)	7577	932	4895	37
H(20E)	7824	-104	4847	37
H(20F)	6735	23	5138	37

H(21G)	6086	-1105	3570	41
H(21H)	7475	-946	3819	41
H(21I)	7298	-371	3382	41
H(22G)	8378	1234	3746	43
H(22H)	8714	834	4221	43
H(22I)	7987	1633	4208	43
H(23G)	4190	525	2933	49
H(23H)	3437	1279	2816	49
H(23I)	2782	130	2675	49
H(24G)	1165	1312	3338	52
H(24H)	809	640	3752	52
H(24I)	475	155	3238	52
H(25G)	1700	-1287	3440	44
H(25H)	2276	-879	3953	44
H(25I)	3187	-1027	3587	44

X-ray crystal structure for (E)/(Z)-1-(2-(naphtalen-2-ylethynyl)phenyl)ethan-1-one O-methyl oxime (76)

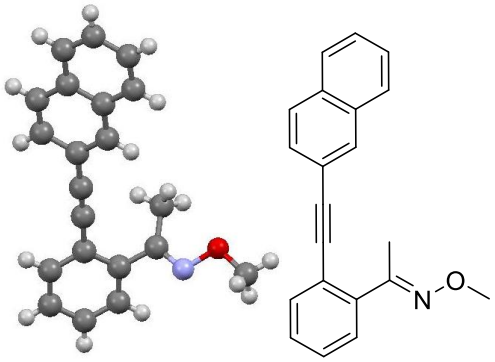


Table 1. Crystal data and structure refinement for fftcoe2043_a.

Identification code	fftcoe2043_a	
Empirical formula	C21 H17 N O	
Formula weight	299.36	
Temperature	100(2) K	
Wavelength	1.54178 Å	
Crystal system	Orthorhombic	
Space group	Pbca	
Unit cell dimensions	a = 12.4635(5) Å	a= 90°.
	b = 7.1150(2) Å	b= 90°.
	c = 36.3193(13) Å	g = 90°.
Volume	3220.7(2) $Å^3$	
Z	8	
Density (calculated)	1.235 Mg/m^3	
Absorption coefficient	0.590 mm^{-1}	
F(000)	1264	
Crystal size	0.380 x 0.090 x 0.035 mm^3	
Theta range for data collection	2.433 to 66.594°.	
Index ranges	-14<=h<=12, -8<=k<=8, -43<=l<=38	
Reflections collected	13114	
Independent reflections	2821 [R(int) = 0.0709]	
Completeness to theta = 66.594°	98.8 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.92 and 0.74	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2821 / 0 / 210	
Goodness-of-fit on F^2	1.029	

Final R indices [I>2sigma(I)]	R1 = 0.0479, wR2 = 0.0986
R indices (all data)	R1 = 0.0786, wR2 = 0.1113
Extinction coefficient	n/a
Largest diff. peak and hole	0.195 and -0.201 e.Å^{-3}

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for fftcoe2043_a. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
N(1)	4450(1)	8213(2)	5802(1)	19(1)
O(1)	3676(1)	7728(2)	6075(1)	23(1)
C(1)	8310(2)	5960(3)	6588(1)	17(1)
C(2)	7753(2)	6285(3)	6910(1)	17(1)
C(3)	8210(2)	5843(3)	7257(1)	20(1)
C(4)	7660(2)	6198(3)	7591(1)	26(1)
C(5)	8130(2)	5769(3)	7921(1)	35(1)
C(6)	9156(2)	4969(3)	7934(1)	38(1)
C(7)	9715(2)	4619(3)	7618(1)	31(1)
C(8)	9258(2)	5052(3)	7269(1)	22(1)
C(9)	9811(2)	4734(3)	6935(1)	24(1)
C(10)	9358(2)	5173(3)	6606(1)	22(1)
C(11)	7858(2)	6396(3)	6236(1)	17(1)
C(12)	7506(2)	6722(3)	5936(1)	16(1)
C(13)	7120(2)	7145(3)	5574(1)	16(1)
C(14)	7857(2)	7461(3)	5291(1)	20(1)
C(15)	7519(2)	7941(3)	4940(1)	23(1)
C(16)	6437(2)	8128(3)	4867(1)	24(1)
C(17)	5694(2)	7822(3)	5144(1)	22(1)
C(18)	6015(2)	7316(3)	5498(1)	18(1)
C(19)	5191(2)	6965(3)	5786(1)	17(1)
C(20)	5221(2)	5232(3)	6020(1)	30(1)
C(21)	2900(2)	9199(3)	6083(1)	28(1)

Table 3. Bond lengths [Å] and angles [°] for fftcoe2043_a.

N(1)-C(19)	1.283(2)
N(1)-O(1)	1.423(2)
O(1)-C(21)	1.425(2)
C(1)-C(2)	1.379(3)
C(1)-C(10)	1.422(3)
C(1)-C(11)	1.433(3)
C(2)-C(3)	1.416(3)
C(2)-H(2)	0.9500
C(3)-C(4)	1.417(3)
C(3)-C(8)	1.423(3)
C(4)-C(5)	1.370(3)
C(4)-H(4)	0.9500
C(5)-C(6)	1.401(4)
C(5)-H(5)	0.9500
C(6)-C(7)	1.366(3)
C(6)-H(6)	0.9500
C(7)-C(8)	1.424(3)
C(7)-H(7)	0.9500
C(8)-C(9)	1.411(3)
C(9)-C(10)	1.360(3)
C(9)-H(9)	0.9500
C(10)-H(10)	0.9500
C(11)-C(12)	1.198(3)
C(12)-C(13)	1.432(3)
C(13)-C(14)	1.396(3)
C(13)-C(18)	1.409(3)
C(14)-C(15)	1.383(3)
C(14)-H(14)	0.9500
C(15)-C(16)	1.381(3)
C(15)-H(15)	0.9500
C(16)-C(17)	1.383(3)
C(16)-H(16)	0.9500
C(17)-C(18)	1.394(3)
C(17)-H(17)	0.9500
C(18)-C(19)	1.488(3)
C(19)-C(20)	1.498(3)

C(20)-H(20A)	0.9800
C(20)-H(20B)	0.9800
C(20)-H(20C)	0.9800
C(21)-H(21A)	0.9800
C(21)-H(21B)	0.9800
C(21)-H(21C)	0.9800

C(19)-N(1)-O(1)	110.62(16)
N(1)-O(1)-C(21)	107.24(15)
C(2)-C(1)-C(10)	119.39(18)
C(2)-C(1)-C(11)	121.52(18)
C(10)-C(1)-C(11)	119.09(18)
C(1)-C(2)-C(3)	120.88(18)
C(1)-C(2)-H(2)	119.6
C(3)-C(2)-H(2)	119.6
C(2)-C(3)-C(4)	121.79(19)
C(2)-C(3)-C(8)	118.97(18)
C(4)-C(3)-C(8)	119.23(19)
C(5)-C(4)-C(3)	120.2(2)
C(5)-C(4)-H(4)	119.9
C(3)-C(4)-H(4)	119.9
C(4)-C(5)-C(6)	120.8(2)
C(4)-C(5)-H(5)	119.6
C(6)-C(5)-H(5)	119.6
C(7)-C(6)-C(5)	120.7(2)
C(7)-C(6)-H(6)	119.6
C(5)-C(6)-H(6)	119.6
C(6)-C(7)-C(8)	120.4(2)
C(6)-C(7)-H(7)	119.8
C(8)-C(7)-H(7)	119.8
C(9)-C(8)-C(3)	118.99(18)
C(9)-C(8)-C(7)	122.3(2)
C(3)-C(8)-C(7)	118.7(2)
C(10)-C(9)-C(8)	121.06(19)
C(10)-C(9)-H(9)	119.5
C(8)-C(9)-H(9)	119.5
C(9)-C(10)-C(1)	120.70(19)
C(9)-C(10)-H(10)	119.6

C(1)-C(10)-H(10)	119.6
C(12)-C(11)-C(1)	177.7(2)
C(11)-C(12)-C(13)	178.0(2)
C(14)-C(13)-C(18)	119.02(17)
C(14)-C(13)-C(12)	119.22(17)
C(18)-C(13)-C(12)	121.73(17)
C(15)-C(14)-C(13)	121.06(18)
C(15)-C(14)-H(14)	119.5
C(13)-C(14)-H(14)	119.5
C(16)-C(15)-C(14)	119.94(19)
C(16)-C(15)-H(15)	120.0
C(14)-C(15)-H(15)	120.0
C(15)-C(16)-C(17)	119.87(19)
C(15)-C(16)-H(16)	120.1
C(17)-C(16)-H(16)	120.1
C(16)-C(17)-C(18)	121.25(18)
C(16)-C(17)-H(17)	119.4
C(18)-C(17)-H(17)	119.4
C(17)-C(18)-C(13)	118.86(18)
C(17)-C(18)-C(19)	119.65(17)
C(13)-C(18)-C(19)	121.49(17)
N(1)-C(19)-C(18)	114.43(17)
N(1)-C(19)-C(20)	124.12(18)
C(18)-C(19)-C(20)	121.39(17)
C(19)-C(20)-H(20A)	109.5
C(19)-C(20)-H(20B)	109.5
H(20A)-C(20)-H(20B)	109.5
C(19)-C(20)-H(20C)	109.5
H(20A)-C(20)-H(20C)	109.5
H(20B)-C(20)-H(20C)	109.5
O(1)-C(21)-H(21A)	109.5
O(1)-C(21)-H(21B)	109.5
H(21A)-C(21)-H(21B)	109.5
O(1)-C(21)-H(21C)	109.5
H(21A)-C(21)-H(21C)	109.5
H(21B)-C(21)-H(21C)	109.5

Symmetry transformations used to generate equivalent atoms:

X-ray crystal structure for (Z)-(4)phenylethynyl)thiazole-5-carbaldehyde O-methyl oxime (124)

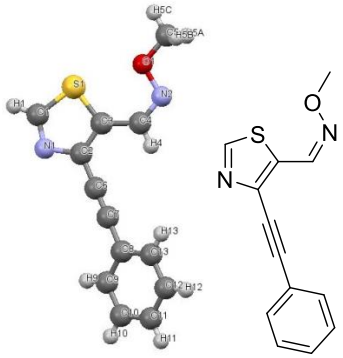


Table 1 Crystal data and structure refinement for ojh366v_fs.

Identification code	ojh366v_fs
Empirical formula	$C_{13}H_{10}N_2OS$
Formula weight	242.29
Temperature/K	99.99
Crystal system	monoclinic
Space group	$P2_1/n$
a/Å	13.2137(6)
b/Å	5.1696(2)
c/Å	17.6579(8)
α/°	90
β/°	109.0220(10)
γ/°	90
Volume/Å^3	1140.34(9)
Z	4
ρ_{calc}g/cm^3	1.411
μ/mm^{-1}	2.384
F(000)	504.0
Crystal size/mm^3	0.11 × 0.11 × 0.02
Radiation	CuKα (λ = 1.54178)
2Θ range for data collection/°	7.328 to 133.236
Index ranges	-15 ≤ h ≤ 15, -6 ≤ k ≤ 6, -19 ≤ l ≤ 21
Reflections collected	12586
Independent reflections	2006 [R_{int} = 0.0221, R_{sigma} = 0.0149]
Data/restraints/parameters	2006/0/155
Goodness-of-fit on F^2	1.057
Final R indexes [I>=2σ (I)]	R_1 = 0.0276, wR_2 = 0.0718
Final R indexes [all data]	R_1 = 0.0297, wR_2 = 0.0733
Largest diff. peak/hole / e Å^{-3}	0.24/-0.35

Table 2 Fractional Atomic Coordinates (×10^4) and Equivalent Isotropic Displacement Parameters (Å^2×10^3) for ojh366v_fs. U_{eq} is defined as 1/3 of of the trace of the orthogonalised U_{IJ} tensor.

Atom	*x*	*y*	*z*	U(eq)
S1	7695.9(3)	-135.7(6)	3347.9(2)	14.69(12)
O1	5760.3(8)	871(2)	2229.5(6)	20.5(2)
N1	8653.3(9)	1685(2)	4761.5(7)	16.4(3)
N2	5428.6(9)	3106(2)	2535.7(7)	17.5(3)
C1	8718.9(11)	-66(3)	4246.4(8)	16.7(3)
C2	7726.8(10)	3108(3)	4438.2(8)	13.9(3)
C3	7104.7(10)	2430(3)	3668.7(8)	13.6(3)
C4	6120.7(10)	3718(3)	3212.4(8)	16.0(3)
C5	4868.8(11)	-149(3)	1588.9(9)	19.9(3)
C6	7445.7(11)	5061(3)	4903.6(8)	15.1(3)
C7	7185.3(11)	6626(3)	5310.7(8)	16.0(3)
C8	6881.4(11)	8478(3)	5802.7(8)	14.5(3)
C9	7640.5(11)	10172(3)	6293.2(8)	15.8(3)
C10	7337.8(11)	11995(3)	6754.1(8)	16.9(3)
C11	6274.6(11)	12182(3)	6721.6(8)	16.7(3)
C12	5521.3(11)	10491(3)	6243.3(8)	18.1(3)
C13	5817.4(11)	8626(3)	5790.4(8)	17.5(3)

Table 3 Anisotropic Displacement Parameters (Å^2×10^3) for ojh366v_fs. The Anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U_{11}+2hka^*b^*U_{12}+\ldots]$.

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
S1	14.76(19)	15.8(2)	13.22(19)	-2.44(12)	4.08(13)	1.91(12)
O1	16.6(5)	22.9(6)	18.4(5)	-7.3(4)	0.8(4)	3.9(4)
N1	15.9(6)	17.7(6)	15.5(6)	-0.3(5)	4.9(5)	0.7(5)
N2	16.9(6)	16.4(6)	18.8(6)	-0.7(5)	5.3(5)	2.6(5)
C1	14.5(7)	18.8(7)	16.1(7)	-0.1(5)	4.2(5)	1.8(5)
C2	14.8(6)	13.9(7)	13.9(6)	0.5(5)	6.0(5)	-1.5(5)
C3	15.2(6)	12.7(7)	14.7(6)	-1.1(5)	7.5(5)	-1.1(5)
C4	15.7(7)	15.4(7)	17.0(7)	-0.5(5)	5.6(5)	0.7(5)
C5	17.9(7)	23.4(8)	14.8(7)	-3.8(6)	0.4(6)	-1.6(6)
C6	17.0(7)	15.3(7)	12.0(7)	1.0(5)	3.4(5)	-1.0(5)
C7	18.5(7)	15.8(7)	12.3(6)	2.4(5)	2.9(5)	0.6(6)
C8	21.0(7)	12.4(7)	10.2(6)	2.6(5)	5.5(5)	2.7(6)
C9	18.3(7)	15.4(7)	14.2(7)	2.5(5)	6.1(5)	1.1(5)
C10	22.6(7)	14.1(7)	13.4(7)	-0.1(5)	5.0(5)	-1.8(6)
C11	24.7(7)	14.0(7)	12.8(6)	2.1(5)	8.0(5)	4.3(6)
C12	18.1(7)	18.1(7)	19.3(7)	2.2(6)	7.6(6)	2.7(6)
C13	19.9(7)	15.7(7)	14.4(7)	0.6(5)	2.3(5)	-0.6(6)

Table 4 Bond Lengths for ojh366v_fs.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
S1	C1	1.7170(14)	C3	C4	1.4492(19)
S1	C3	1.7257(13)	C6	C7	1.204(2)
O1	N2	1.4048(15)	C7	C8	1.4355(19)

O1	C5	1.4410(16)	C8	C9	1.399(2)
N1	C1	1.3060(18)	C8	C13	1.4012(19)
N1	C2	1.3818(18)	C9	C10	1.387(2)
N2	C4	1.2853(18)	C10	C11	1.3906(19)
C2	C3	1.3846(19)	C11	C12	1.386(2)
C2	C6	1.4256(19)	C12	C13	1.388(2)

Table 5 Bond Angles for ojh366v_fs.

Atom	Atom	Atom	Angle/˚	Atom	Atom	Atom	Angle/˚
C1	S1	C3	89.13(7)	N2	C4	C3	129.90(13)
N2	O1	C5	108.98(10)	C7	C6	C2	176.99(15)
C1	N1	C2	109.40(12)	C6	C7	C8	179.45(16)
C4	N2	O1	110.09(11)	C9	C8	C7	120.45(12)
N1	C1	S1	116.56(11)	C9	C8	C13	119.27(13)
N1	C2	C3	115.68(12)	C13	C8	C7	120.28(13)
N1	C2	C6	120.07(12)	C10	C9	C8	120.20(13)
C3	C2	C6	124.21(12)	C9	C10	C11	120.24(13)
C2	C3	S1	109.22(10)	C12	C11	C10	119.78(13)
C2	C3	C4	124.57(12)	C11	C12	C13	120.54(13)
C4	C3	S1	126.20(10)	C12	C13	C8	119.92(13)

Table 6 Hydrogen Atom Coordinates (Å×10^4) and Isotropic Displacement Parameters (Å^2×10^3) for ojh366v_fs.

Atom	*x*	*y*	*z*	U(eq)	
H1	9303	-1240	4363		20
H4	5963	5249	3450		19
H5A	4584	1198	1185		30
H5B	4308	-712	1803		30
H5C	5108	-1625	1343		30
H9	8366	10073	6311		19
H10	7859	13121	7093		20
H11	6065	13465	7026		20
H12	4796	10609	6225		22
H13	5299	7450	5473		21

Crystal structure determination of ojh366v_fs

Crystal Data for $C_{13}H_{10}N_2OS$ (*M* =242.29 g/mol): monoclinic, space group $P2_1/n$ (no. 14), *a* = 13.2137(6) Å, *b* = 5.1696(2) Å, *c* = 17.6579(8) Å, *β* = 109.0220(10)°, *V* = 1140.34(9) Å^3, *Z* = 4, *T* = 99.99 K, μ(CuKα) = 2.384 mm^{-1}, *Dcalc* = 1.411 g/cm^3, 12586 reflections measured (7.328° ≤ 2Θ ≤ 133.236°), 2006 unique (R_{int} = 0.0221, R_{sigma} = 0.0149) which were used in all calculations. The final R_1 was 0.0276 (I > 2σ(I)) and wR_2 was 0.0733 (all data).

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for fftcoe2043_a. The anisotropic displacement factor exponent takes the form: $-2p^2[\ h^2\ a^{*2}U^{11} + ...\ + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
N(1)	14(1)	25(1)	18(1)	-2(1)	1(1)	-2(1)
O(1)	17(1)	27(1)	26(1)	0(1)	6(1)	2(1)
C(1)	18(1)	13(1)	20(1)	1(1)	-1(1)	-2(1)
C(2)	17(1)	12(1)	22(1)	1(1)	-2(1)	-1(1)
C(3)	28(1)	10(1)	21(1)	-1(1)	-3(1)	-3(1)
C(4)	42(1)	15(1)	22(1)	0(1)	2(1)	-3(1)
C(5)	64(2)	21(1)	21(1)	-3(1)	0(1)	-8(1)
C(6)	67(2)	21(1)	26(1)	5(1)	-24(1)	-10(1)
C(7)	43(1)	16(1)	34(1)	2(1)	-21(1)	-4(1)
C(8)	28(1)	12(1)	27(1)	-1(1)	-9(1)	-3(1)
C(9)	16(1)	17(1)	39(1)	-2(1)	-7(1)	3(1)
C(10)	20(1)	18(1)	28(1)	-3(1)	0(1)	1(1)
C(11)	15(1)	14(1)	21(1)	-2(1)	2(1)	-1(1)
C(12)	13(1)	16(1)	20(1)	-2(1)	3(1)	1(1)
C(13)	16(1)	13(1)	18(1)	-3(1)	1(1)	1(1)
C(14)	18(1)	19(1)	22(1)	-2(1)	1(1)	3(1)
C(15)	25(1)	23(1)	21(1)	-1(1)	7(1)	1(1)
C(16)	30(1)	27(1)	16(1)	2(1)	-4(1)	3(1)
C(17)	19(1)	25(1)	22(1)	0(1)	-2(1)	3(1)
C(18)	19(1)	16(1)	18(1)	-2(1)	1(1)	1(1)
C(19)	14(1)	20(1)	18(1)	-1(1)	-3(1)	1(1)
C(20)	20(1)	30(1)	40(1)	11(1)	9(1)	4(1)
C(21)	19(1)	30(1)	34(1)	-5(1)	6(1)	6(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (Å^{2}x 10^3) for fftcoe2043_a.

	x	y	z	U(eq)
H(2)	7054	6812	6899	21
H(4)	6962	6734	7586	32
H(5)	7756	6018	8144	42
H(6)	9467	4666	8166	45
H(7)	10412	4083	7631	37
H(9)	10510	4204	6941	29
H(10)	9745	4952	6385	27
H(14)	8603	7344	5340	24
H(15)	8030	8142	4750	28
H(16)	6203	8466	4627	29
H(17)	4951	7960	5091	26
H(20A)	5306	5591	6279	45
H(20B)	5826	4441	5945	45
H(20C)	4549	4532	5990	45
H(21A)	3253	10386	6146	41
H(21B)	2352	8909	6268	41
H(21C)	2561	9311	5840	41