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Divergent synthesis of stereodefined benzocyclobutene and indoline derivatives via sequential Cu- and Pd-catalysis

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List of abbreviations

Ac	Acetyl
APCI	Atmospheric Pressure Chemical Ionisation
aq	Aqueous
Ar	Aryl
$B_2(pin)_2$	4,4,4',4',5,5,5',5'-Octamethyl-2,2'-bis-(1,3,2-dioxaborolane)
BCB	Benzocyclobutene
Boc	*tertiary*-Butoxycarbonyl
Bn	Benzyl
Bpin	4,4,5,5-Tetramethyl-1,3,2-dioxaborolane
Bu	Butyl
CuTC	Copper(I) thiophene-2-carboxylate
Cp*	Pentamethylcyclopentadiene
DFT	Density functional theory
DME	1,2-Dimethyoxyethane
DMF	*N*,*N*-Dimethylformamide
DMSO	Dimethyl sulfoxide
dr	Diastereomeric ratio
E	Electrophile
Equiv.	Equivalent
ee	enantiomeric excess
ES	Electrospray
Et	Ethyl
FT/IR	Fourier Transform Infrared Spectroscopy
GC	Gas chromatography
h	Hour
HPLC	High performance liquid chromatography
HRMS	High resolution mass spectrometry
IMes	1,3-Bis(2,4,6-trimethylphenyl)imidazol-2-ylidene
IPr	1,3-Bis(2,6-diisopropylphenyl)imidazol-2-ylidene
m	Meta
m/z	Mass/charge ratio
Me	Methyl
min	Minute
M.p.	Melting point
MS	Mass spectrometry

NHC	*N*-Heterocyclic carbene
NMR	Nuclear magnetic resonance
o	Ortho
p	Para
Pent	Pentyl
Ph	Phenyl
PMP	Para-Methoxyphenyl
t	Tertiary
TEBA	Benzyltriethylammonium chloride
THF	Tetrahydrofuran
TLC	Thin layer chromatography

Abstract

The synthesis of stereodefined benzocyclobutene (BCB) and indoline derivatives is described. Both scaffolds can be accessed using the same palladium catalyst from a common homoallylic borylated amine intermediate. Notably, to our knowledge this represents the first Suzuki-mediated four-membered ring closure. The common intermediate is easily accessed using the Cu-catalysed borylative technology developed in our laboratory. Preliminary results on an enantioselective variant are described. The products can easily be further manipulated into advanced material industrial intermediates. Overall, this sequential approach offers an unprecedented, mild, and general access to BCBs for which very few synthetic options are currently available, and a rapid access to medicinally relevant indolines.

Declaration

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You let me know the most important basis of organic chemistry. Congratulations on officially becoming a father! If I have a chance, I will visit you in Japan!

In 2020, we experienced a very difficult year, and lockdown caused us not to have enough time for research. But my family members supported and encouraged me to continue research. I love my parents, grandparents and uncles. It is you who gave me the strongest support. Thank you! I love all of you!

Introduction

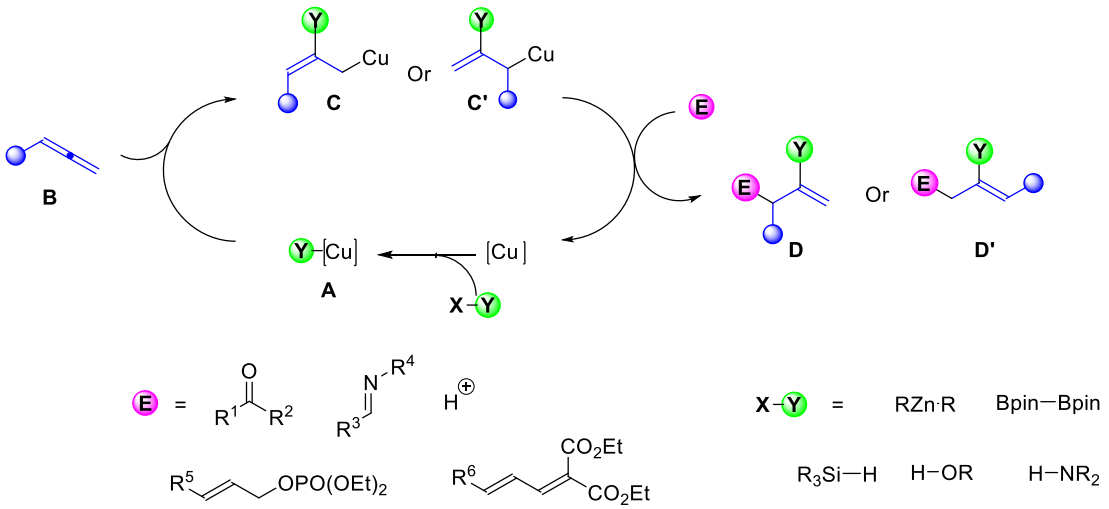
Chirality is one of the most important attributes of Nature. Molecular chiral recognition plays a vital role in life. The two enantiomers of a compound have different biological activities due to different interactions with the chiral environment of living organisms (for example, enzyme, cell membrane receptors etc.).[1] Therefore, drug properties are all closely related to chirality. From January 2004 to June 2006, enantiomerically pure drugs represented 66% of all FDA drugs.[2]

There are two main methods for synthesizing enantiopure chiral compounds: biological and non-biological. Biological methods use enzymatic synthesis to mimic Nature's way of preparing chiral substances. However, due to the complex and specific nature of enzymes, enantiopure chiral compounds are difficult to prepare this way on a large scale. Also, due to the substrate specificity of enzymes, only certain 'compatible' chiral compounds can be produced. For the establishment of drug molecular libraries, biosynthesis has therefore certain limitations. Non-biological methods generally refer to the stereocontrolled synthesis of chiral compounds using chemical means. Common methods include: asymmetric synthesis (chiral auxiliaries, chiral ligands), chiral resolution (kinetic, chromatography, crystallisation), and chiral pool starting materials.[2] The cost required to manually resolve a racemic mixture is high and difficult to operate on a large scale. Besides, resolution inevitably leads to the loss of half of the material. Asymmetric synthesis building on chiral pool starting material is perhaps the most straightforward method, but is limited by the availability and cost of the desired starting material. Therefore, the development of asymmetric synthesis has become a focus of chemists over the last decades.[3] Asymmetric synthesis using chiral ligands potentially offers the most atom and step economic way of controlling chirality. Only a catalytic amount of enantiopure chiral material is required, and the latter may be recycled at the end of the process.

An asymmetric synthesis catalysed by precious metals has been greatly developed in the past fifty years. In 2001, the Nobel Prize in Chemistry was awarded to William Standish Knowles, Noyori Ryōji, and K. Barry Sharpless, in recognition for their contributions to enantiomeric catalytic hydrogenation and oxidation. The unique atomic structure and chemical properties of precious metals have opened new directions in asymmetric synthesis. This type of reaction can produce enantiopure chiral compounds on a large scale using a small quantity of a stereodefined catalyst, and therefore has been widely used in industry.[4] However, the high cost of precious metals, the limit of their supply, and the environmental impact of their own refinement industry are concerning limitations. There is a global urge to reduce the carbon footprint of the chemical industry, transition metal catalysis should therefore shift towards the use of abundant and environmentally benign elements.

Recently, due to their low cost, mild reaction conditions, and environmental friendliness, copper-catalysed reactions have expanded widely.[5] Copper has gradually made its appearance in important precious metal-catalysed reactions, replacing palladium, ruthenium, rhodium and iridium. In particular, copper has recently been used to generate versatile allyl-copper species in a catalytic fashion, an important advance that circumvents the need to work with stoichiometric amounts of organometallic reagents.[6] Allenes are more reactive than olefins and alkynes. They have become a reagent of choice for the synthesis of complex molecules.[7] When a copper complex is coordinated, an allene metalation occurs, and the resulting allylcopper intermediate is nucleophilic, so various electrophiles can be trapped, offering a vast array of asymmetric processes. The high reactivity of allenes make them an ideal and readily available chemical feedstock for allylation chemistry. Although potential regioselectivity issues due to the presence of two contiguous double bonds adds a layer of complexity, high selectivities have been described.[5]

The general mechanism for the copper-catalysed functionalisation of allenes proceeds via initial formation of a copper–element complex **A** (**Scheme 1**). Then, intermediate **A** undergoes addition across the terminal double bond of the allene.[5] In this step, the regioselectivity is usually governed by steric factors, with the bulky ligated copper atom being on the terminal carbon atom of the chain.[8] However, the reactive allyl-copper intermediates may undergo isomerization through metalotropic rearrangement (**C** and **C**'). The allyl-copper intermediate can then be trapped with various electrophiles in an α- or γ-addition fashion. Chiral induction by the surrounding ligands is possible at this stage, overall delivering selectively functionalized products.[9] Copper-boron complexes are known to take part in such chemistries, and offer interesting boron-containing products that can easily undergo further transformations.[5]



Scheme 1 Copper-catalysed functionalisation of allenes allows access to diverse collections of enantioenriched organic molecules.

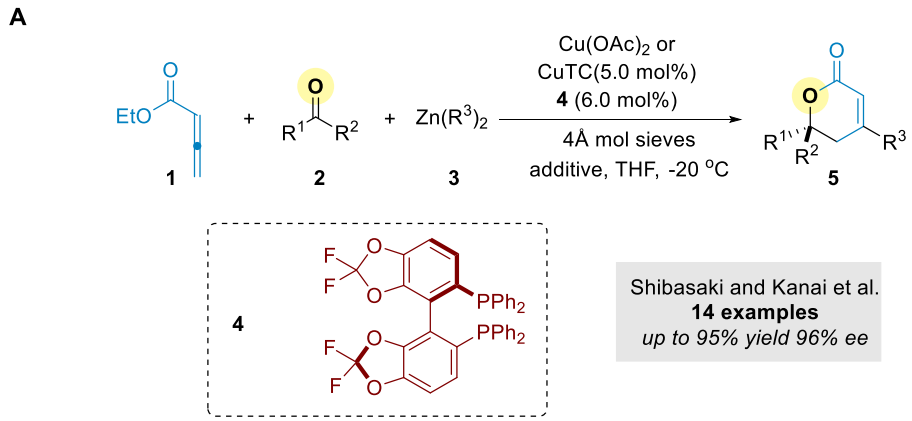
Allyl copper borylated species have attracted the attention of many research groups around the world due to their unique potential for stereoselectivity, the breadth of compatible electrophiles, and the versatility of the boron-containing products. Research groups such as the groups of Procter, Hoveyda, Buchwald, and Kanai[10] have extensively use borylated allyl-copper species with a wide range of electrophiles as detailed in the next section of this introduction. Benzocyclobutene and indolines,

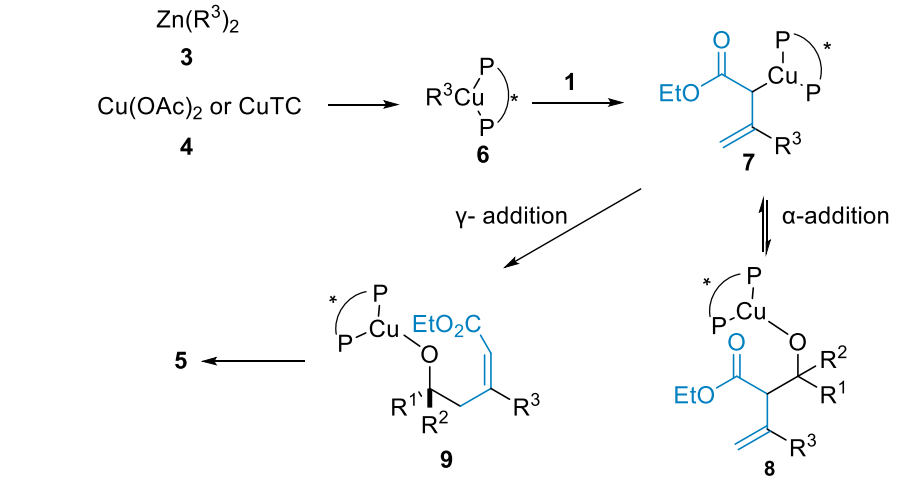
as common active intermediates, are widely used in the material industry and pharmaceutical industry. How they are synthesized and applied will be in the remaining section of this introduction.

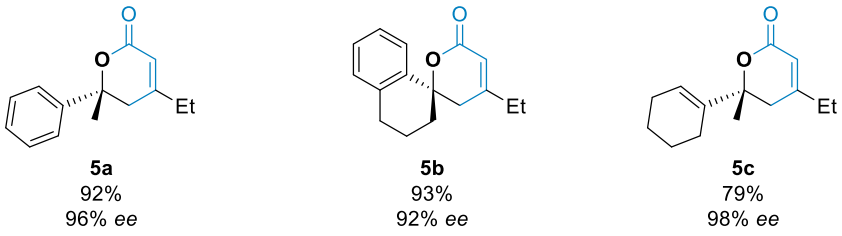
Copper-catalysed enantioselective functionalisation of allenes

Carbonyls as electrophiles

In 2007, Kanai and Shibasaki reported that copper-catalysed multi-component coupling of allenic esters **1** with ketones **2** and dialkylzinc reagents **3** can provide δ-lactones **5** with excellent enantioselectivity (**Scheme 2**).[11] A chiral phosphine-ligated alkylcopper(I) complex **6** is formed upon transmetallation with the dialkylzinc reagent **3**. Addition to the allenic ester **1** forms allyl copper **7** (**Scheme 2**). The reaction of **7** with ketones follows two possible pathways: kinetic α-addition to form aldol adduct **8**, or γ-addition to form thermodynamically favoured **9**. In fact, a mixture of **8** and **9** is initially formed, but retroaldol reaction of **8** makes the α-addition path reversible. **9** then selectively cyclizes to the desired lactone **5**. Coordinating additives (such as DMSO or HMPA) promote the retro-aldol, which is essential for high yields. The reaction range is wide and, interestingly, even α,β-unsaturated ketone electrophiles are tolerated.

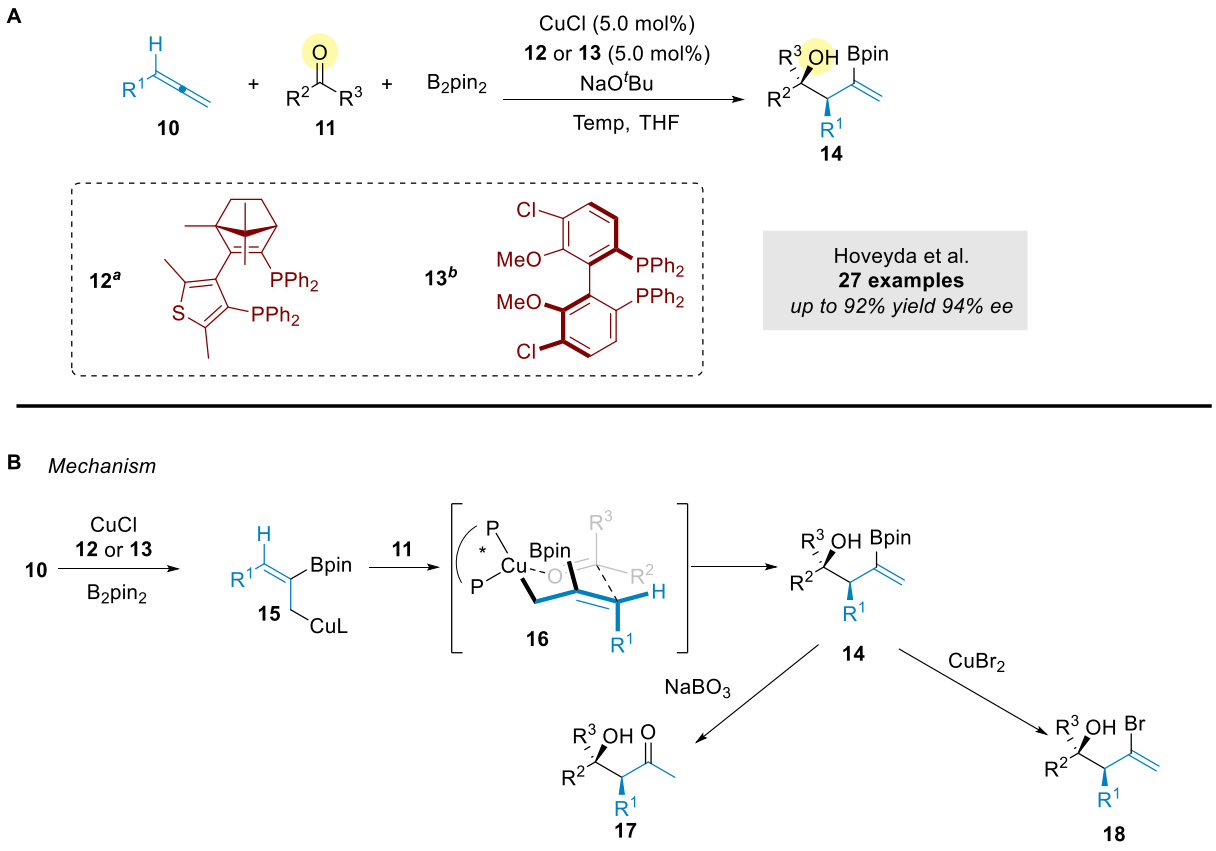






Scheme 2 Kanai and Shibasaki's carbocupration of allenic esters and subsequent enantioselective coupling to ketones.

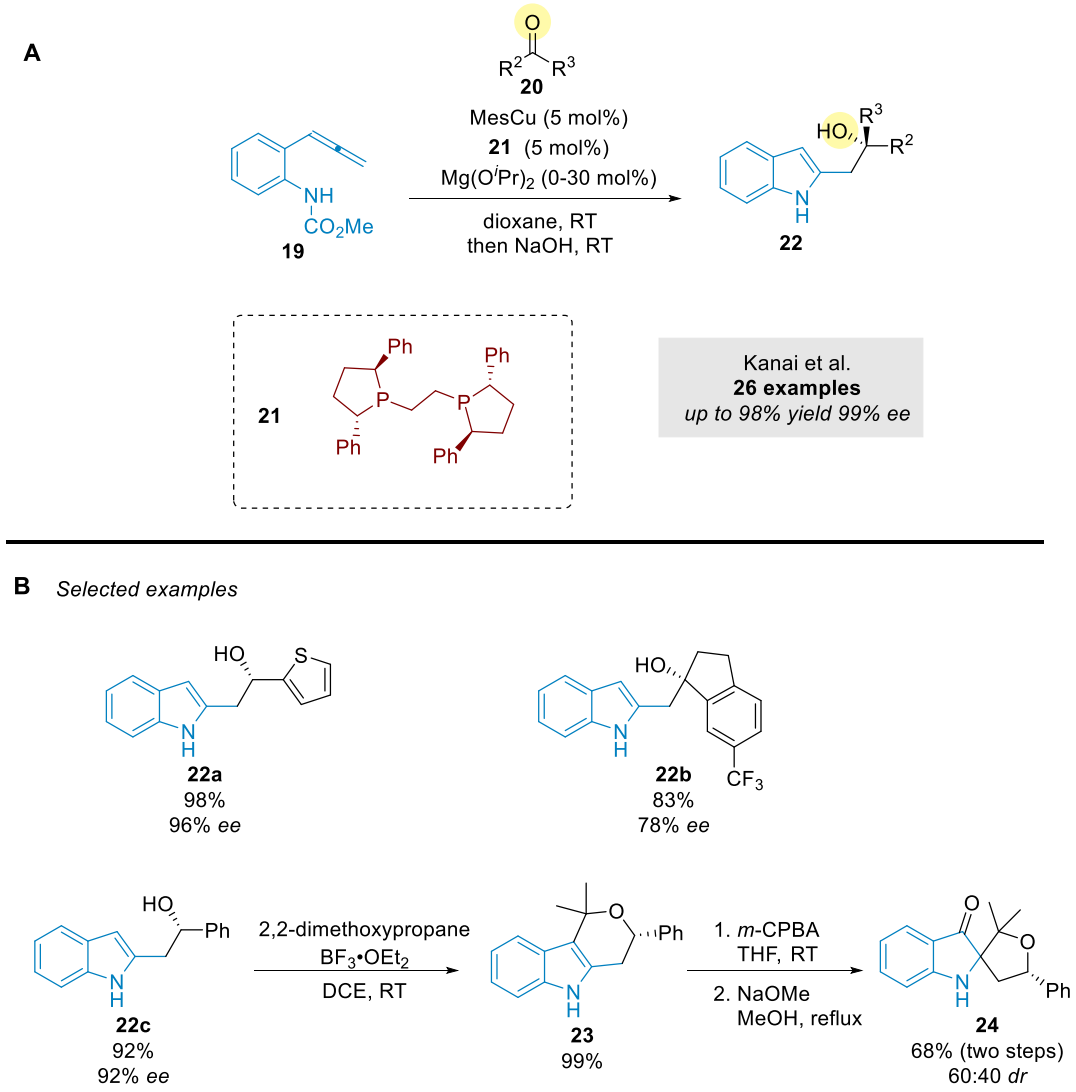
Hoveyda and co-workers reported in 2013 the enantioselective copper-catalysed borylative coupling of aldehydes or ketones **11** with aryl or alkyl substituted allenes **10** (**Scheme 3**).[12] Allene borocupration generates an *in situ* allyl copper **15**, which captures the carbonyl electrophile. *Syn* products are obtained through the proposed 6-membered transition state structure **16**, where the large substituent on the carbonyl is placed in a pseudo-equatorial position. The resulting vinylboronate-containing products **14** were not isolated as such, but oxidized or brominated *in situ* to obtain the corresponding β-hydroxyketone **17** or alkenyl bromide **18** respectively, which are more stable and easier to purify. The enantioselective addition reaction of ketones gives tertiary alcohols. Interestingly, when using α,β-unsaturated ketones, although there may be a competitive 1,4-allylation pathway, almost only 1,2-allylation is observed, and borocupration of **11** is not observed.



Scheme 3 Hoveyda's borocupration of allenes and subsequent enantioselective coupling to aldehydes and ketones. Enantiomeric ratio given for the major diastereomer. [a]Ligand **12** was used at 4 °C; [b]ligand **13** was used at 22 °C.

In 2014, Kanai and co-workers developed an intramolecular aminocupration of allenes **19**, followed by enantioselective trapping of the organocuprate with external ketones and aldehydes **20** to provide functionalized indoles **22** (**Scheme 4**).[13] In some cases, the addition of Mg(O^{i}Pr)$_2$ facilitates the liberation of the copper alkoxide

resulting from the addition onto the carbonyl, and helps the turnover of the catalyst. The synthetic utility of the products was demonstrated with **22c**, which was converted into the tetrahydropyranoindole and indoline based pharmacophores **23** and **24**.



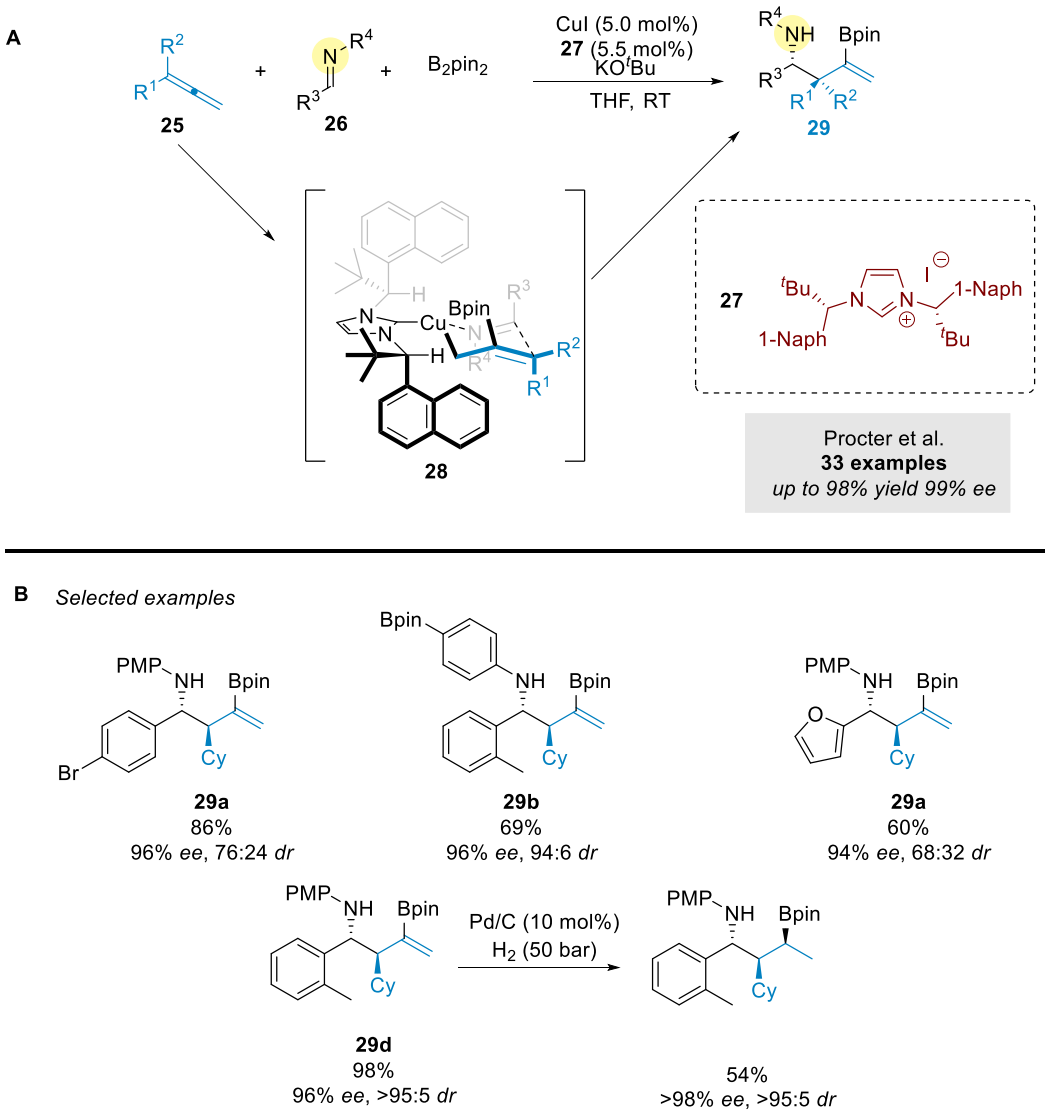
Scheme 4 Kanai's intramolecular aminocupration of allenes and subsequent enantioselective coupling to aldehydes and ketones.

Imines as electrophiles

In the breadth of potential electrophiles that could be attacked by the generated allyl copper species, imines are particularly interesting because of the value and

versatility of the resulting amines. Enantiomerically pure highly functionalized amines are commonly encountered in natural products, pharmaceutical molecules and proteins, and are used in the fields of medicine and crop protection. In 2008, 85% of the US top selling drugs contained nitrogen, 80% of which were amines.[14] As for amine compounds with four-membered rings and five-membered rings, they are often used in the development of optoelectronic materials, polymer synthesis and the construction of polycyclic molecules.[15]

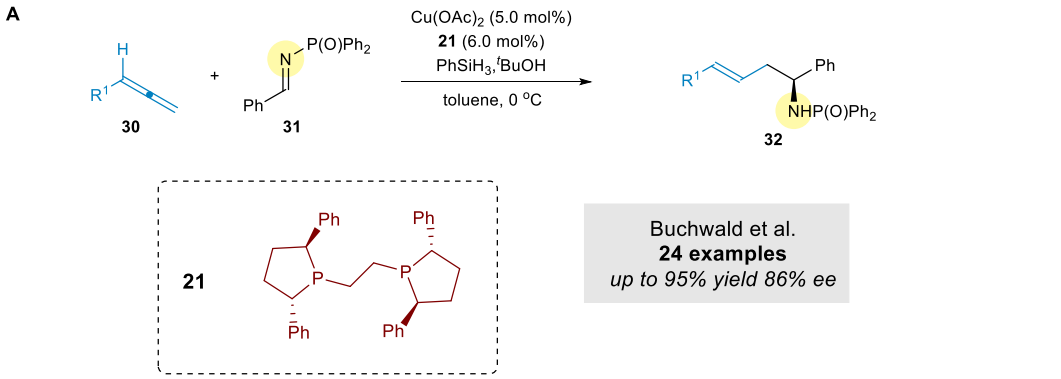
Procter and co-workers reported in 2016 the enantioselective copper-catalysed three-component coupling of allenes **25**, B_2pin_2, and aldimines **26** (**Scheme 5**).[16] This method delivers functionalized homoallylic amines with high diastereo- and enantiomeric control, excellent functional group tolerance, and high yields. Allyl copper intermediate **28** is generated *in situ* through regioselective borocupration of allene **25**. Computational chemical analysis suggests a chair-like transition state structure **28**, where the substituent on the imine is pseudo-axial. The target products are stable enough to be purified by column chromatography, presumably owing to a stabilizing interaction between the nitrogen and the boron atoms. The target product **29** can be further functionalized by oxidation to form the corresponding β-amino ketone, and by hydrogenation to form three consecutive stereocentres.

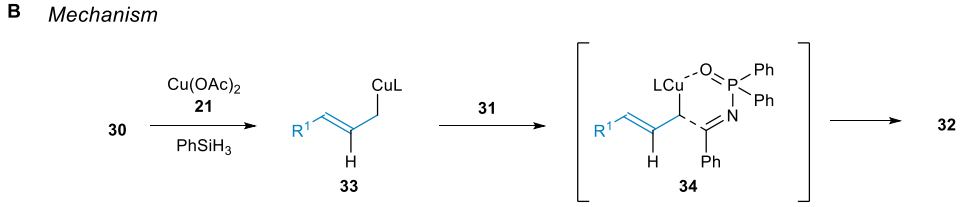


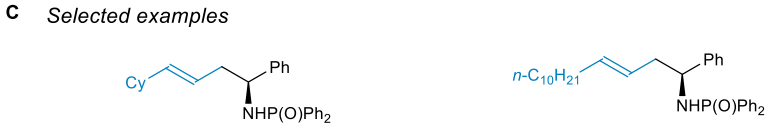
Scheme 5 Procter's borocupration of allenes and subsequent enantioselective coupling to imines. Enantiomeric ratio given for the major diastereomer.

Soon after, Buchwald and co-workers reported the copper-catalysed regio-, diastereo- and enantioselective reductive allylation of aldimines **31** to synthesize branched or linear homoallyl amines (**Scheme 6**).[17] Using *N*-diphenylphosphine oxide-protected imines and chiral ligand (*S*,*S*)-Ph-BPE **21**, they performed the linear variant of the enantioselective allylation for two examples. A copper hydride intermediate is formed *in situ* by transmetallation with the hydrosilane, hydrocupration of allene **30** and subsequent rapid isomerization leads to the formation of thermodynamically favoured terminal *E*-allylcopper intermediate **33**. In

the case of *N*-phosphonyl imines, transition state **34** supported by DFT studies is proposed, which involves the coordination of copper to the oxygen of the phosphine oxide, and transfer of the allyl fragment through the copper-bound carbon to selectively provide linear products.



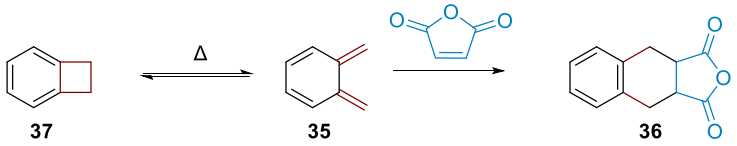




Scheme 6 Buchwald's hydrocupration of allenes and subsequent enantio- and regioselective coupling to aldimines.

Construction of benzofused four-membered rings

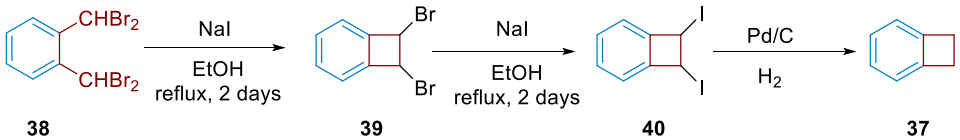
In 1909, Hans Finkelstein first reported the relationship between the kinetic reactivity and thermodynamic stability of benzocyclobutene **37**.[20] It attracted the attention of theoretical chemists who discovered the many important properties of benzocyclobutenes (BCBs) such as their applications as synthetic thermosetting plastics (**Scheme 7**).



Scheme 7 BCB thermolysis followed by Diels-Alder reaction.

BCBs are now often used in polymerization reactions to form thermoset or thermoplastic materials.[18] The polymerization products have high-density two-dimensional network structures, and at the same time have flexible segments, resulting in overall good processing abilities.[19]

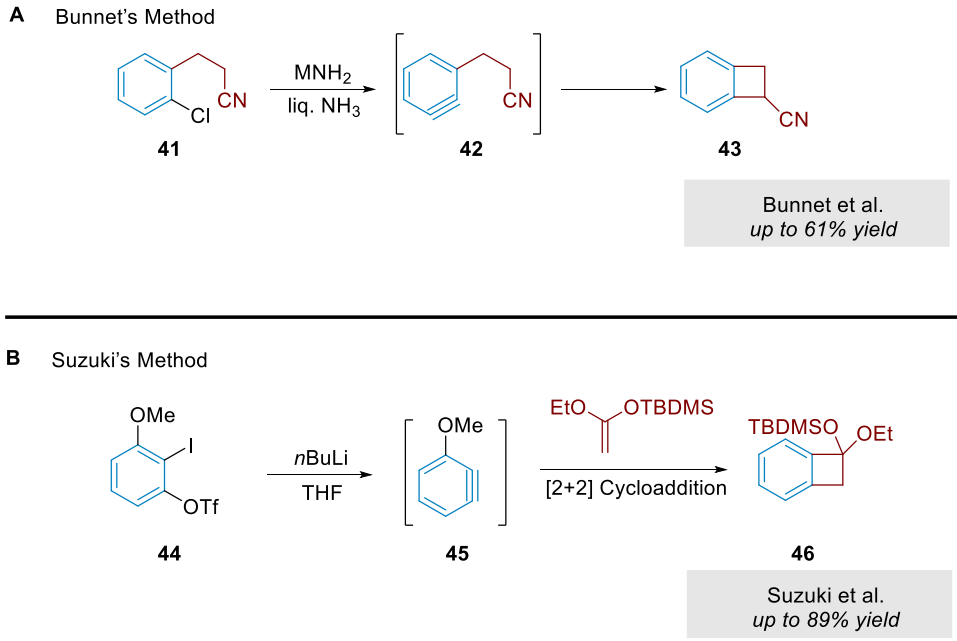
In 1956, Cava and co-workers reported a method for synthesizing BCB **37** (**Scheme 8**),[21] using 1,2-bis(bromomethyl)-benzene with sodium iodide and ethanol. The resulting bromides can then be exchanged for iodides before being reduced by palladium on charcoal to give the desired BCB. However, the long reaction time make this process unpractical.



Scheme 8 Cava's method to synthesize BCB.

Owing to the strong reactivity of benzyne, Bunnett reported in 1962 that benzyne

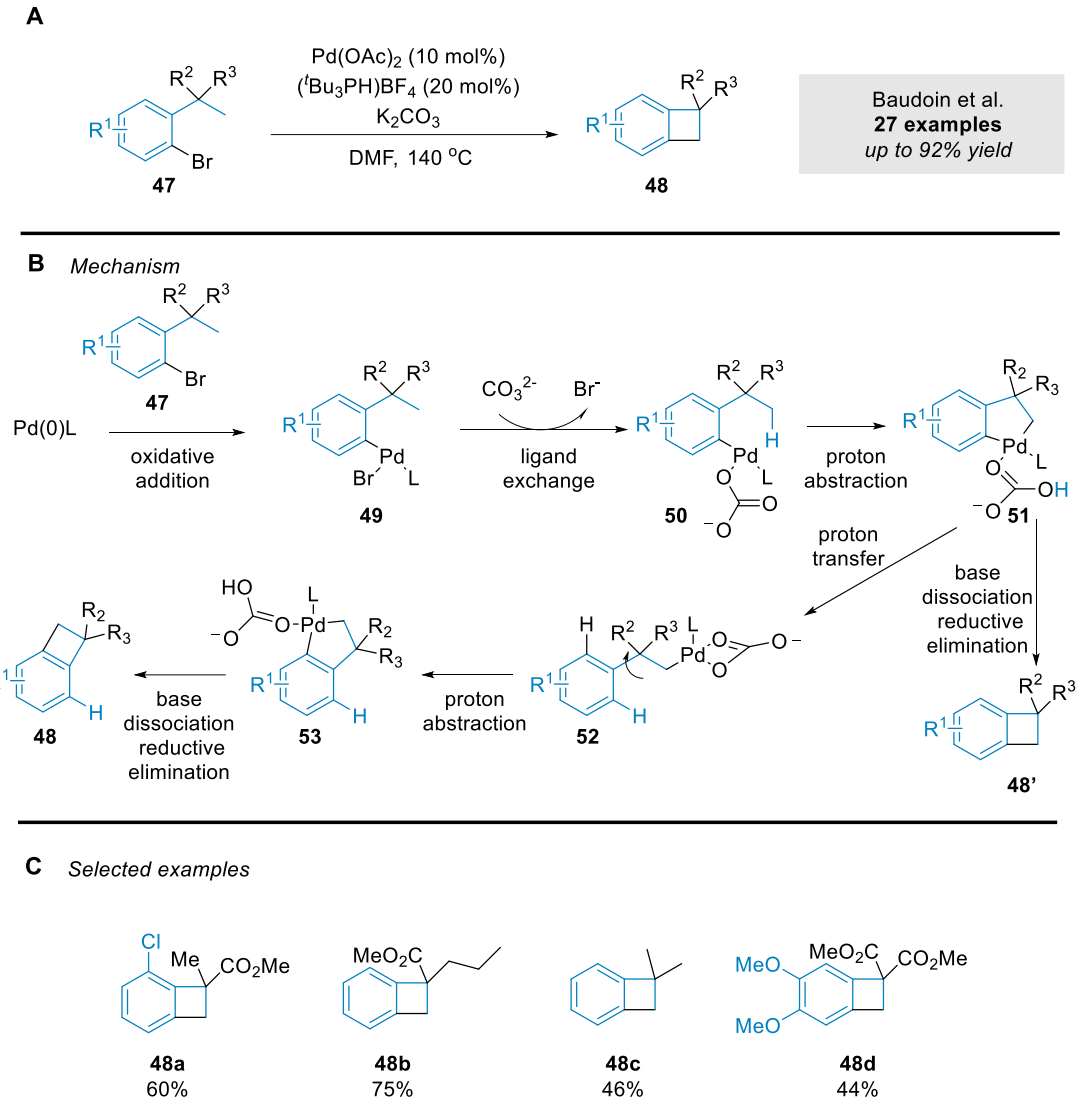
precursor **41** could be used to synthesize BCBs with a yield up to 61% (**Scheme 9A**).[22] In 1994, Suzuki and co-workers improved this method by using the more efficient benzyne precursor **44**, and by leveraging the [2+2] cycloaddition reaction to generate substituted BCBs in up to 89% yield (**Scheme 9B**).[22] However, due to the difficulty of preparing benzyne intermediates and their associated hazards, the prospect of industrial application is poor.



Scheme 9 Synthesis of BCBs using benzyne intermediates.

Recently, Baudoin and co-workers reported a method of synthesizing BCBs by C(sp^3)-H activation (**Scheme 10**).[23] According to DFT calculations and control experiments, Pd(0) first performs oxidative addition with aryl halides **49**, then undergoes ligand exchange with carbonate **50**. According to DFT calculations, carbonate can stabilize the central metal palladium more than other anions. The newly formed palladium intermediate **50** undergoes proton abstraction, forming the stable cyclized palladium intermediate **51**. **51** can directly undergo reductive elimination to form a four-membered ring product, or undergo a proton transfer, proton abstraction, and reductive elimination, to finally get a different isomer of the product. This method is more general and compatible with chlorine- and fluorine-carbon bonds. The authors believe that the carbonate anion plays an

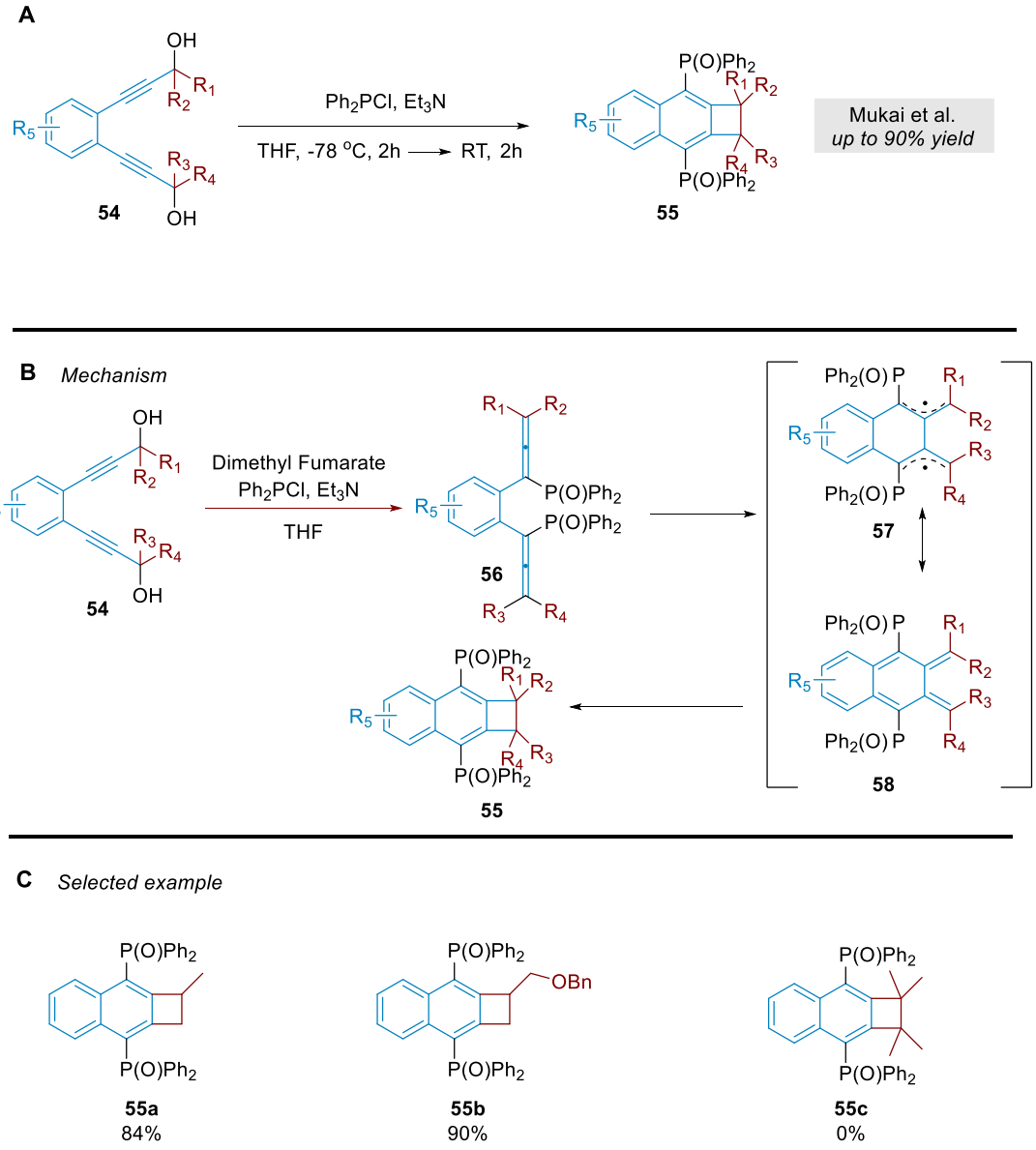
important coordination role in the formation of key metal centre intermediates. However, the method is limited to a CR_2-CH_2 substitution pattern on the four-membered ring's C(sp^3) carbons.



Scheme 10 Baudoin's C(sp^3)-H activation strategy for the synthesis of BCBs.

In 2006, Mukai and co-workers used phosphinylallene intermediates **56** produced from bis-propargyl alcohols **54** and chlorodiphenylphosphine to access BCBs **55**[24] (**Scheme 11**). Mukai and co-workers believe that the mechanism of the reaction may involve the double radical species (**57**). This species will spontaneously undergo ring closure to form **55**. The authors changed the functional groups of the starting materials: when the four functional groups were replaced with methyl groups, the

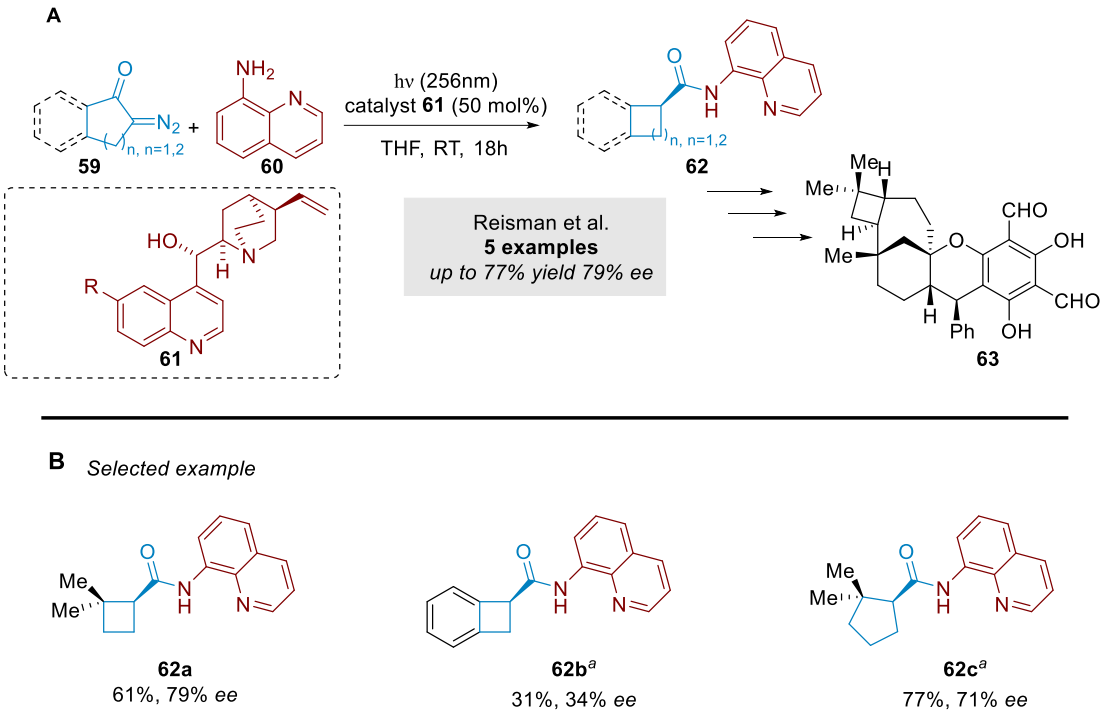
reaction could not be detected (**55c**). The specificity of the starting materials restrains the applicability of this method.



Scheme 11 Mukai's intramolecular cycloaddition strategy for the synthesis of BCBs.

The strategies reviewed so far offer efficient access to BCBs. However, enantiocontrol when constructing BCBs chiral aliphatic C(sp^3) carbons remains elusive. (+)-Psiguadial B is a chiral diformyl phloroglucinol meroterpenoid with a four-membered ring, which can effectively inhibit the proliferation of cancer cells. In their total synthesis

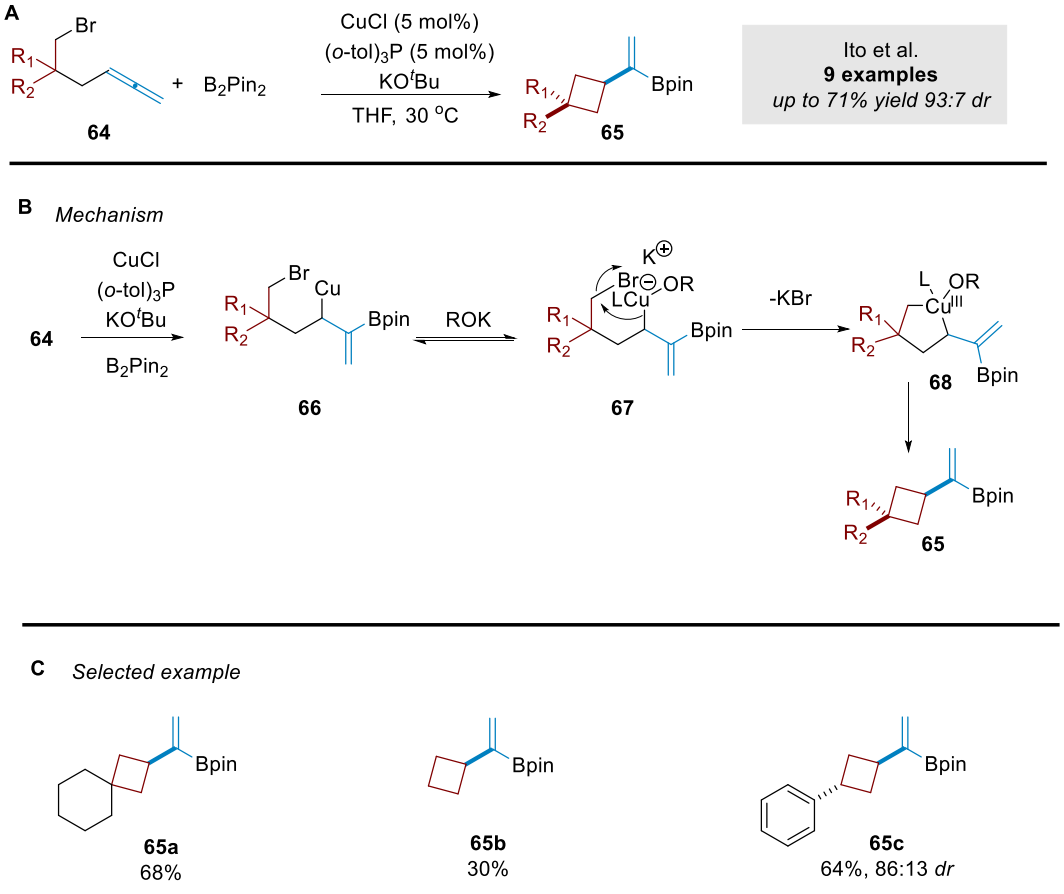
of (+)-Psiguadial B, Reisman and co-workers developed a tandem Wolff rearrangement/ketene addition to access cyclobutane intermediate **62a** in 61% yield and 79% ee (**Scheme 12**).[25] The enantioselectivity is proposed to arise from a chiral counter anion-controlled stereoselective protonation of the final enolate intermediate. Reisman and co-workers were surprised to find that scaling up the reaction had no significant impact and the reaction was applied to a small selection of substrates. This methodology is the first to address the challenge of making enantiopure BCBs. In this total synthesis, (+)-Psiguadial B was finally reached in 15 steps with a total yield of 1.3%.



Scheme 12 Reisman's tandem Wolff rearrangement/ketene addition strategy for the enantioselective synthesis of a BCB key intermediate. [a] Using different ligand photocatalysts.

In addition to the above methods that can synthesize BCBs, low-cost metals can also catalyse the synthesis of four-membered rings. Ito and co-workers reported that boron-containing cyclobutane compounds can be synthesized in one step using

cuprous chloride as a catalyst and (*o*-tol)$_3$P as a ligand, allene, and B_2pin_2 (**Scheme 13**).[26] The mechanism they proposed based on control reactions and DFT calculations is that the copper catalyst first generates Cu-Bpin species under the action of a strong base. This species reacts with allene to generate intemediates **66** by borocupration. After **66** has reversibly coordinated with the alkoxide, it undergoes intramolecular oxidative addition to generate **68**. The final reductive elimination gives the desired product **65**. The reaction product displays a vinyl boronic ester handle which can contribute to further functionalization. At the same time, the reaction exhibits a high degree of regio- and diastereo- control.

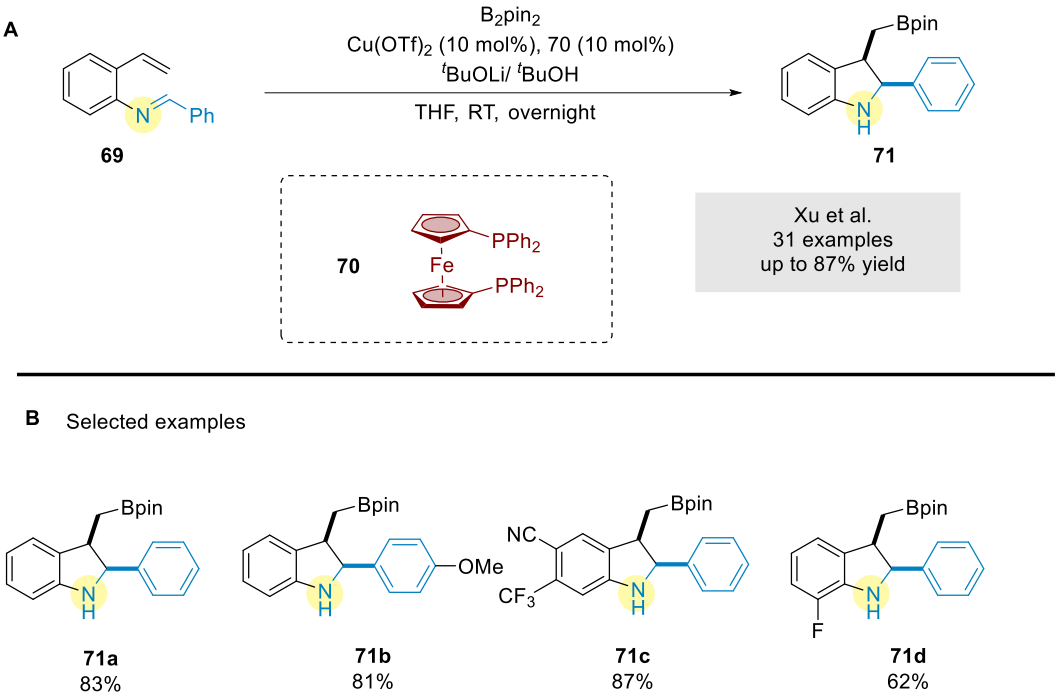


Scheme 13 Ito's Cu-catalysed borylative synthesis of cyclobutanes.

Construction of indolines

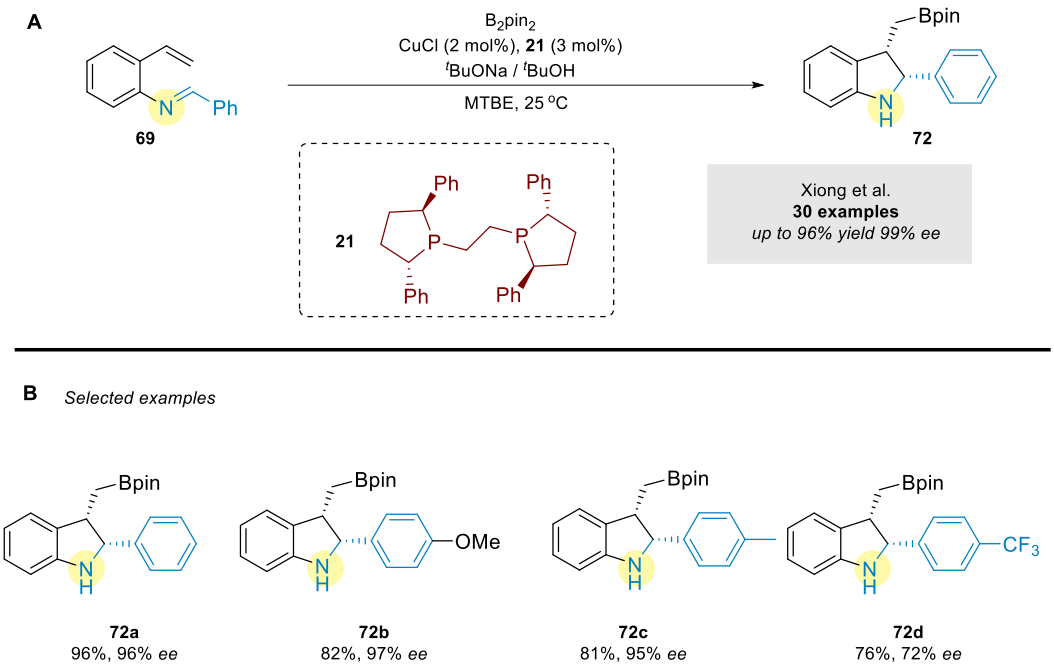
Indolines are common industrial synthetic intermediates, which are widely used in dyes, solar photovoltaic cell photosensitizers, and pharmaceutical intermediates.[27] Indoline is present as a skeleton in many natural products and medicines. The synthesis of indoline scaffolds has therefore become an important topic. Since boronic acid-based functional groups are easily converted into other functional groups (notably using Suzuki-Miyaura couplings), more synthetic chemists have begun to invest the synthesis of boron-containing indolines in recent years.

In 2018, Shen, Xu and co-workers reported a copper-catalysed diastereoselective borylative cyclization of substituted *N*-(2-vinylaryl) benzaldimines **69** (**Scheme 15**).[28] The catalytic cycle begins with the formation *in situ* of a copper alkoxide, typically copper tert-butoxide, which undergoes transmetalation with B_2pin_2. Subsequent chemoselective migratory insertion into the double bond forms the key organocopper intermediate which couples with the electrophilic aldimine to give the borylated product with concomitant regeneration of the catalyst. The *cis*-diastereoselectivity was exclusively observed across a wide range of substrates.



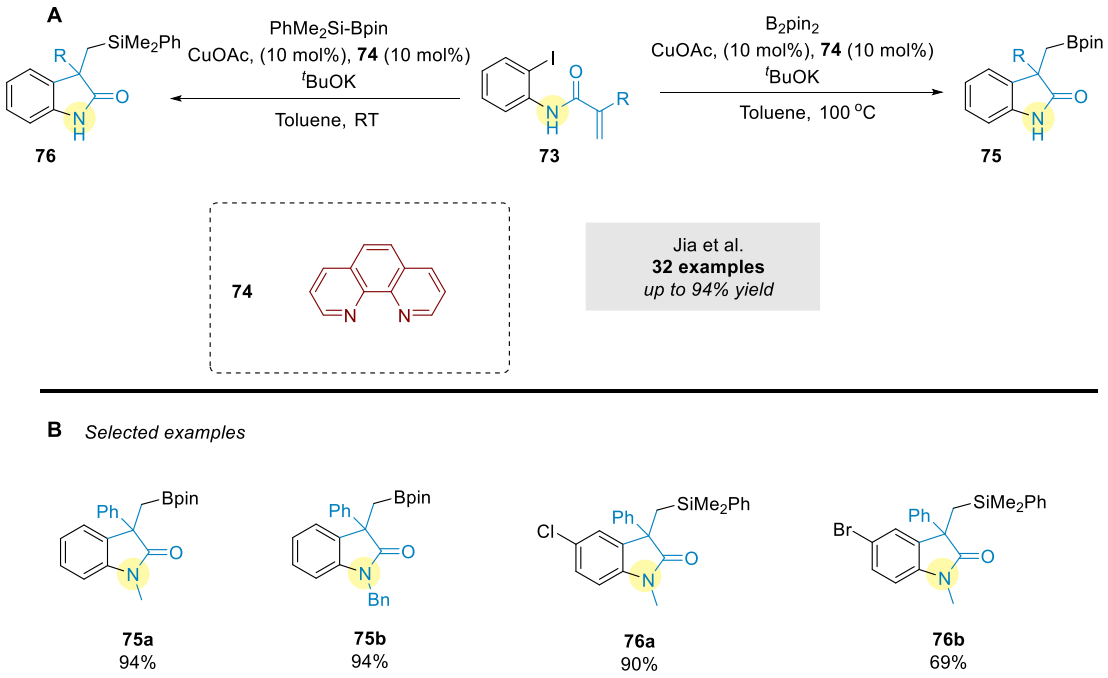
Scheme 15 Shen and Xu's copper-catalysed diastereoselective strategy for the synthesis of borylated indolines.

At the same time in 2018, Xiong and co-workers developed another copper-catalysed enantio- and diastereoselective borylative cyclization to access enantioenriched 2,3-disubstituted indolines **72** (**Scheme 16**).[29] Similar to Shen's and Xu's article, it uses the same starting material **69**, but it is worth noting that Xiong and co-workers use chiral ligand **21** to achieve an enantioselective reaction. *Cis*-diastereomers were also exclusively obtained in all cases, and high enantioselectivities were shown across a wide range of substrates. However, specially designed starting materials were also used, which restricts this strategy to a certain extent.



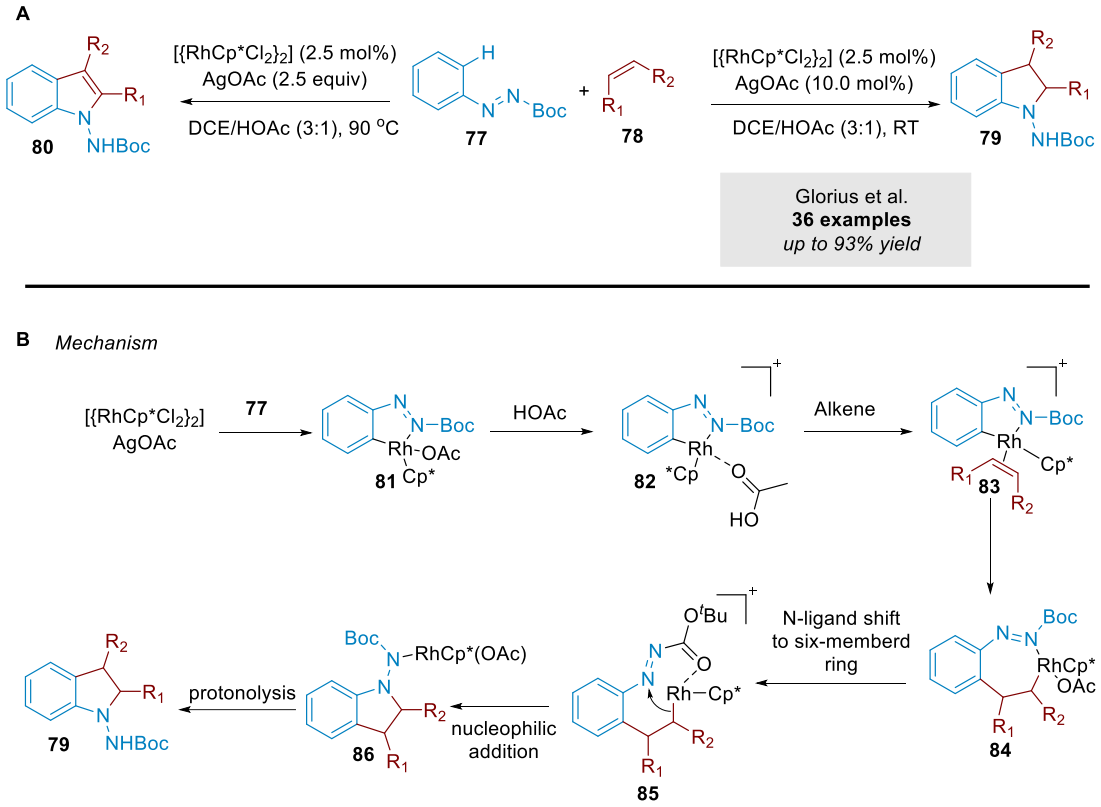
Scheme 16 Xiong's copper-catalysed diastereo- and enantioselective borylative synthesis of indolines.

In 2020, Jia and co-workers developed a synthetic methodology that uses cuprous acetate, and only needs to change B_2Pin_2 to $PhMe_2$-Si-Bpin to synthesize different indolinones under the same catalytic conditions (**Scheme 17**).[30]



Scheme 17 Jia's copper-catalysed strategy for the synthesis of indolinones.

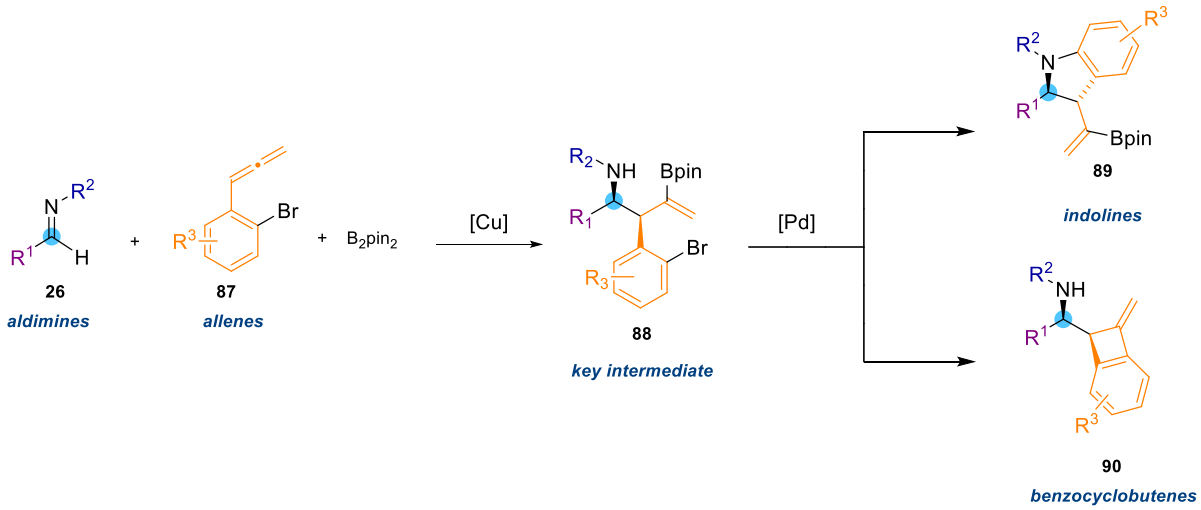
In 2014, Glorius and co-workers developed a ruthenium-catalysed one-step synthesis of 1-aminoindoline derivatives at room temperature (**Scheme 18**).[31] Glorius and co-workers used diazene compounds **77** and olefins **78** as starting materials and use hydrocarbon activation as the strategy to efficiently synthesize 1-aminoindoline derivatives **79**. The mechanism they proposed is that the ruthenium catalyst ([{RhCp*Cl_2}$_2$]) generates ([{RhCp*$(OAc)_2$}$_2$]) in the presence of silver acetate, and a directed C-H bond activation generates **81**. With the help of acetic acid, **81** undergoes ligand dissociation, olefin coordination and insertion reaction to generate **84**. **84** is a seven-membered metalacyclic compound, which easily rearranges into a more stable cyclic compound **85**. The ruthenium intermediate undergoes nucleophilic addition with the diazene bond at this point to form **86**, which protonates to yield **79**. This reaction can directly generate 1-aminoindole **80** without changing the catalyst and solvent when increasing the amounts of silver acetate oxidant and increasing the temperature.



Scheme 18 Glorius's Rh-catalysed strategy for the synthesis of indolines.

Project Aims

In spite of the synthetic value of BCBs, very few general methods exist for their preparation. Most importantly, there is no general method for the catalytic enantioselective synthesis of BCBs, a stereogenic centre at one of the two C(sp^3) positions of the four-membered ring. We envisaged that the products of our copper-catalysed multicomponent coupling refer to scheme earlier could serve as ideal precursors to BCBs, via a hypothetical and not yet reported intramolecular Suzuki-Miyaura cyclisation (**Scheme 19**). Moreover, we realized that the same precursors could also give access to medicinally important indolines through a Buchwald-Hartwig cyclisation. Such indolines would have an unprecedented substitution pattern, with notably a vinyl boronate handle for further derivatization. Overall, valuable BCBs and indolines would be selectively obtained in an enantio- and diastereoselective manner, from readily accessible aldimines, allene, and B_2pin_2. The possibility of easily tuning the substituents of each component promises the generation of varied building blocks for total synthesis and polymer science.

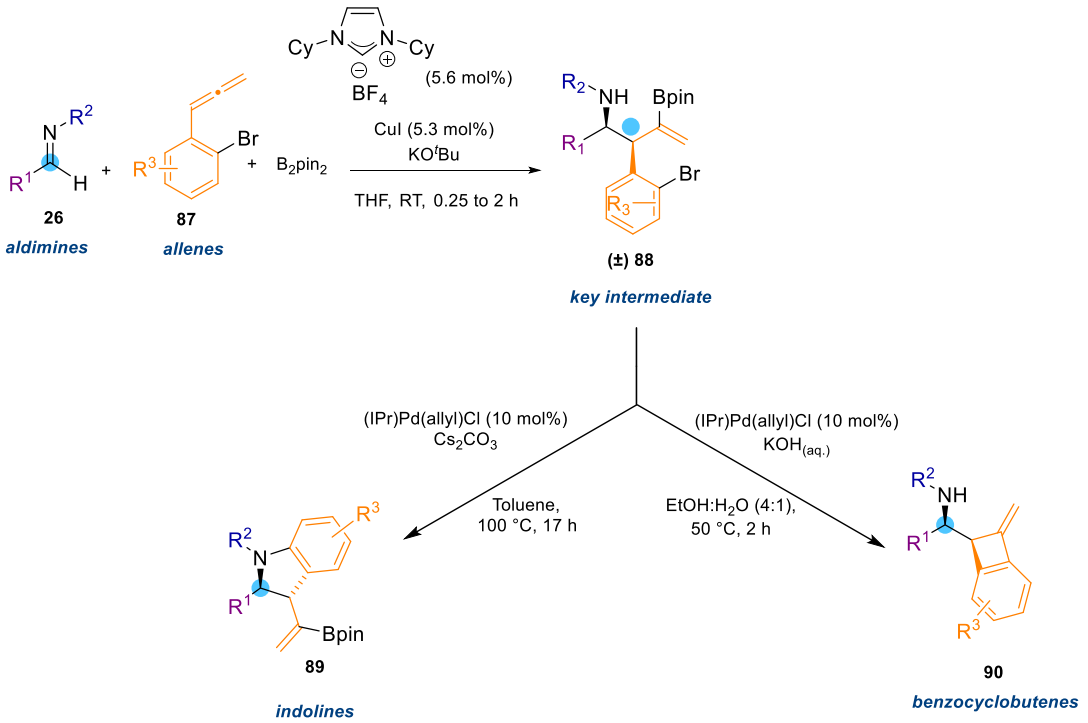


Scheme 19 Project design

The reaction conditions for a racemic version of this project were optimized by PhD student Fabien Talbot. The copper-catalysed borylative cross-coupling could occur at room temperature in only a few minutes, giving the homoallylic amine key precursor **88** in quantitative yield and moderate diastereoselectivity (**Scheme 20**). However, the diastereomeric ratio was found to improve upon purification by column chromatography due to the instability of the minor *anti* diastereisomer on silica.

The cyclobutarene formation was achieved using allyl[1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene]chloropalladium(II) as catalyst, potassium hydroxide as a base, in an aqueous ethanol solution (EtOH:H_2O =4:1). To our knowledge, this represents the first four-membered ring cyclisation using a palladium-catalysed Suzuki-Miyaura coupling. Notably, the reaction conditions are significantly milder than most of the recent methodologies used to access cyclobutarenes relying on C-H activation.

The indoline counterpart was also successfully accessed by only changing the base to caesium carbonate, solvent to toluene, and temperature to 100 ℃. The higher reaction temperature needed may be attributed to a low basicity of caesium carbonate over potassium hydroxide, and the change in selectivity, by the absence of water which is known to favour Suzuki couplings by hydrolysing *in situ* boronic esters, to boronic acids.



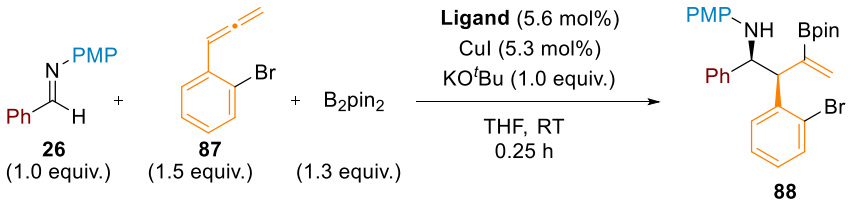
Scheme 20 Optimized racemic reaction conditions copper-catalyzed reaction intermediates, indolines and benzocyclobutenes.

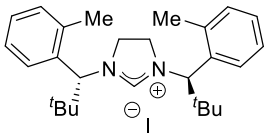
To be able to control the enantioselectivity of a process is a highly desirable feature, as different enantiomers may have different biological properties (*vide supra*). Therefore, one of the project aims is to develop a highly enantioselective copper-catalysed borylative step that would afford intermediate **88** in an enantiopure form, and retain the enantiopurity through both palladium-catalysed steps. Once optimal conditions are found, the second aim of this project is to explore the substrate scope of this process.

Optimisation of Enantioselectivity

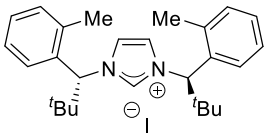
The asymmetric environment of the catalyst induced by the ligand is the key factor to control the enantioselectivity of a reaction. The copper-catalyzed borylative coupling of allenes and imines reaction is believed to occur via a six-membered ring transition state, as previously reported by Procter and co-workers.[14] *N*-Heterocyclic carbenes

(NHC) ligands in previous studies have led to good catalytic properties and excellent stereoselectivities in copper-catalysed borylative coupling.[16] Commercially available NHC ligands were therefore tried first. For most of the NHC ligands, the copper-catalysed three-component coupling reaction displayed a good yield (60-99%) (**Scheme 21**). The products were formed with good diastereoselective (typically 80:20), and the distereomeric ratio of the products was increased upon purification by column chromatography (up to >20:1). Unfortunately, enantioselectivities were low (1%-30% *ee*). Notably, ligands that displayed high enantioselectivity in previous, related systems studied by our group were not efficient here.[16] However, compared to previous studies, alkyl allenes are here replaced with aryl allenes, which have different electronic properties. It is believed that the electronic effect of the starting material has an important influence on the reaction. Aryl phosphine ligands are generally considered to be weaker sigma donors than NHCs, which may result in a different catalytic behaviour. When using **21** (S,S-Ph-BPE), a phosphine-based ligand widely encountered in enantioselective copper-catalysed borylative couplings (*vide supra*), the yield was improved to 70%, with a promising 68% *ee* (**Scheme 21**).

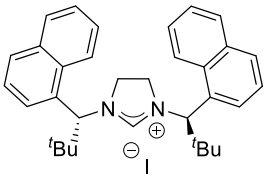




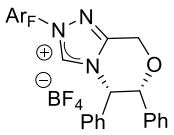
91
Crude ~60% (77:23 d.r.)
Isolated 44% (97:3 d.r.)
4% *ee*



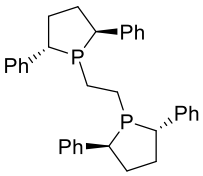
92
Crude ~70% (84:16 d.r.)
Isolated 56% (98:2 d.r.)
30% *ee*



93
Crude ~70% (78:22 d.r.)
Isolated 54% (96:4 d.r.)
5% *ee*



94
Crude 99% (67:33 d.r.)
Isolated 70% (89:11 d.r.)
1% *ee*

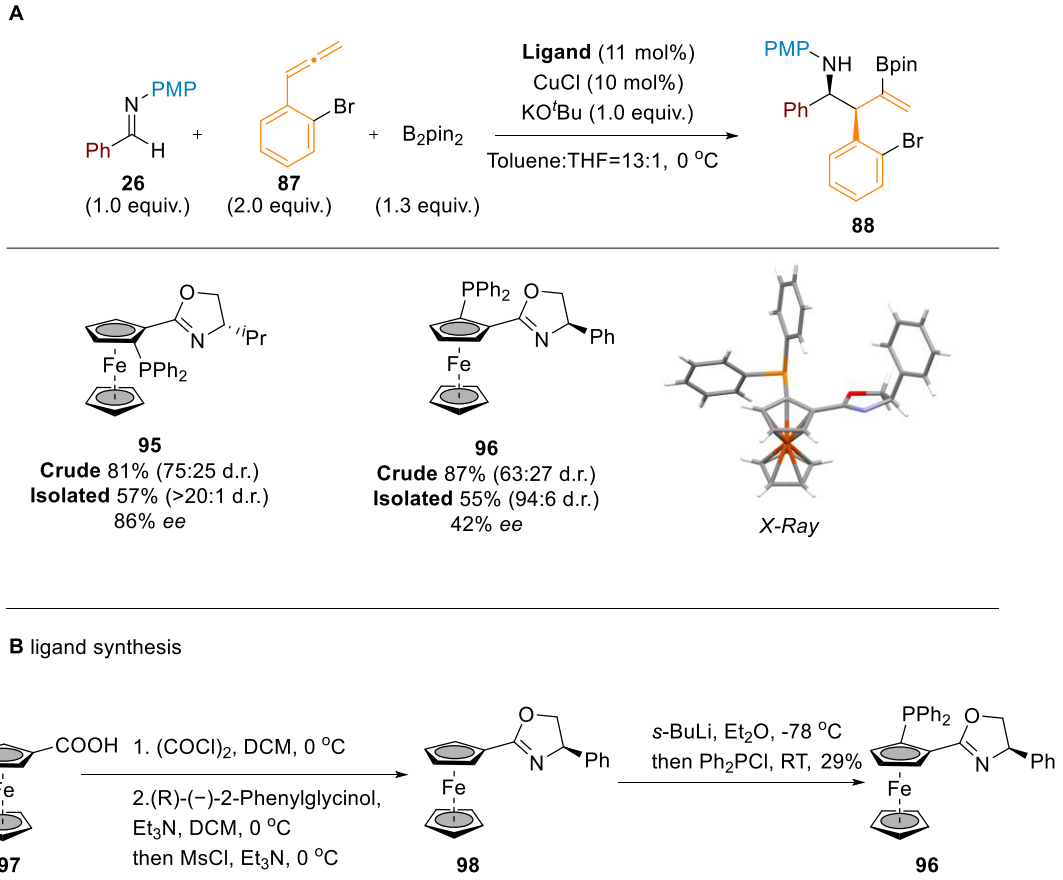


21
Crude ~70% (67:33 d.r.)
Isolated 53% (83:17 d.r.)
68% *ee*

Scheme 21 Ligand screening for the enantioselective copper-catalysed three-component coupling of allenes, aldimines and B_2pin_2. Crude yield and dr were determined by ^{1}H-NMR of the crude reaction mixture. Ee was determined by chiral high pressure liquid chromatography.

This result prompted the investigation of various phosphine ligands and the optimization of the reaction parameters around the most promising hits. It was found that high enantioselectivities could be reached using a ferrocene-based chiral P,N-ligand, copper(I) chloride in a toluene:THF mix at 0 ℃ (**Scheme 22**). After having explored various substitutions around the phosphine aryl groups, we set out to synthesise **96** containing a different group at the stereocentre. According to the

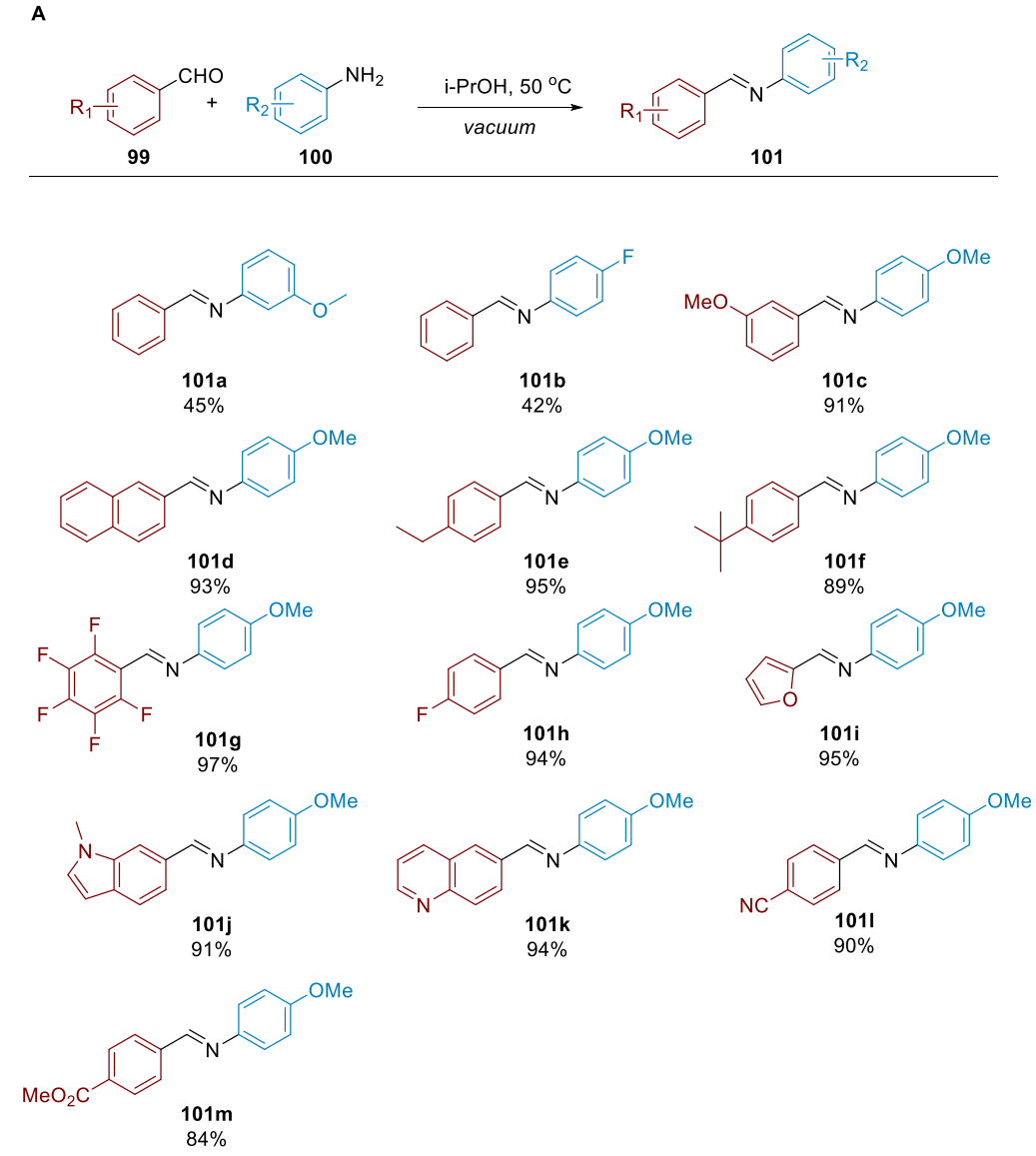
literature,[41] (*R*)-(−)-2-phenylglycinol and ferrocenecarboxylic acid were selected as starting materials. Ferrocenecarboxylic acid was converted to the acid chloride, then (*R*)-(−)-2-phenylglycinol was added to form an amide intermediate. The appending alcohol is then transformed to its corresponding mesylate *in situ* upon which cyclisation to the oxazoline spontaneously occurs. The purified ferrocene oxazoline is then subjected to a diastereoselective, directed lithiation using *sec*-BuLi and TMEDA, and the resulting organolithium is trapped by Ph_2PCl. The pure chiral ligand **96** was obtained after recrystallization. Unfortunately, no significant improvement was achieved using **96** (yield: 87%, d.r.: 63:37, *ee*: 42%) (**Scheme 22**). Based on the above experimental results, it is clear that the reaction is hard to render enantioselective through the use of chiral ligands.



Scheme 22 Ligand screening for the enantioselective, copper-catalysed three-component coupling of allenes, aldimines and B_2pin_2. Crude yield and dr were determined by ^{1}H-NMR of the crude reaction mixture. *Ee* was determined by chiral high pressure liquid chromatography.

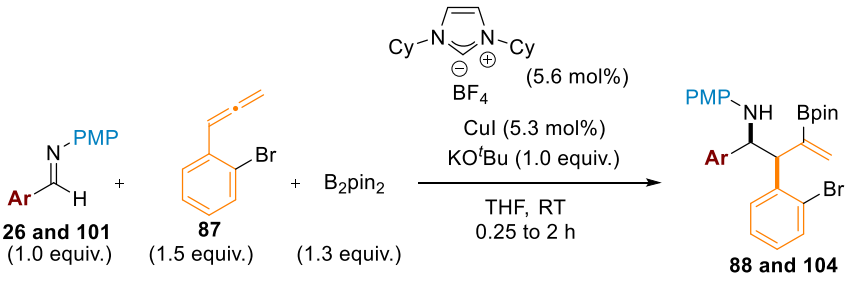
Substrate Scope

The optimized conditions for the racemic reaction were used to investigated, the scope of the racemic copper-catalysed borylative coupling was next investigated. To that purpose, a range of aldimine **101** starting materials was synthesised by condensation of aniline derivatives onto aromatic aldehydes (**Scheme 23.A**). A very practical process was employed: the two reactants were simply mixed in *iso*-propanol and removal of the alcohol *in vacuo* also removes the water from the system by azeotrope, thus driving the reaction towards the formation of aldimines. Crystallisation proved to be the purification method of choice here as aldimines tend to hydrolyse on silica. The aldimines were found to be all exclusively *E* isomers by comparison with the literature. The allene partner **103** was synthesized using a two-step procedure: cyclopropanation of the corresponding styrene **102** leads to a stable *gem*-dihalocyclopropane intermediate, which is then converted to the desired 2-bromophenyl allene by generation of a cyclopropyl carbene in a so-called Skattebøl rearrangement (**Scheme 23.B**).



Scheme 23 Aldimines and allenes starting material synthesis

Firstly, the C-substituent of the aldimine (R_1) was explored using *N*-substituted aldimines with a PMP protecting group (**Scheme 24**). Pleasingly, various functional groups were tolerated. Using phenyl-substituted aldimine (**26**) affords the desired product (**88**) with excellent yield (97%) and moderate diastereoselectivity (82:18 dr). Electron withdrawing group suchs as *p*-fluoro- (**104l**), *p*-chloro- (**104d**), *p*-bromo- (**104g**), *p*-trifluoromethyl- (**104e**), pentafluoro- (**104h**), *p*-cyano- (**104p**), and *p*-methylester (**104q**) substituents did not have obvious interference on the yield and diastereoselectivity of the reaction. The product yields remained high for all reactions (yield: 72-99%). As for aldimines with electron-donating groups, *o*-methyl- (**104b**), *o*-methoxy- (**104c**), *p*-ethyl- (**104j**) and *p*-tert-butyl-(**104k**) substituents, all substrates performed well in the reaction (yield: 66-87%). Benzofused ring substituents, such as 1-naphthyl- (**104a**), 2-naphthyl- (**104i**) groups were also well tolerated (yield: 90-95%). Finally, heterocyclic substituents were also tried. Here, furyl- (**104m**), indolyl- (**104n**) and quinolinyl- (**104o**) groups did not decrease significantly the yields from the rest of the scope (yield: 71-82%), although lower diastereoselectivity was observed. It is worth to mention that having a substituent in the *ortho* position greatly increased the diastereoselectivity (**104a**, **104b**, **104c**), presumably through a better spatial discrimination in the transition state. Throughout this range of substrates, the diastereoselectivity was found to be increased after purification by column chromatography, presumably due to the instability of the minor *anti* diastereoisomer on silica. The *anti* diastereoisomer could not be isolated after chromatography, and is thought to undergo a reverse elimination reaction regenerating the aldimine.

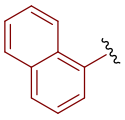


26 and 101 (1.0 equiv.) + **87** (1.5 equiv.) + B_2pin_2 (1.3 equiv.) → **88 and 104**

Ar =

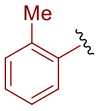
88

Crude 97% (82:18 dr)
Isolated 86% (86:14 dr)



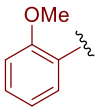
104a

Crude 90% (90:10 dr)
Isolated 80% (>20:1 dr)



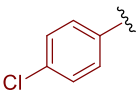
104b

Crude 90% (95:5 dr)
Isolated 81% (>20:1 dr)



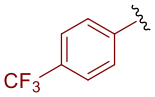
104c

Crude 93% (92:8 dr)
Isolated 84% (>20:1dr)



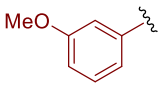
104d

Crude 86% (78:22 dr)
Isolated 60% (20:1 dr)

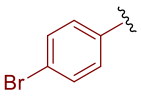


104e

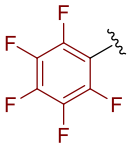
Crude 90% (79:21 dr)
Isolated 70% (>20:1 dr)



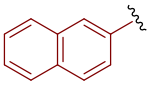
104f
Crude 99% (75:25 dr)
Isolated 70% (>20:1 dr)



104g
Crude 99% (79:21 dr)
Isolated 65% (>20:1 dr)

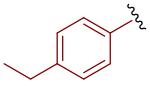


104h
Crude 72% (72:28 dr)
Isolated 48% (>20:1 dr)



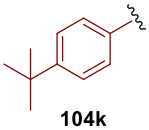
104i

Crude 95% (77:23 dr)
Isolated 61% (>20:1 dr)



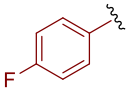
104j

Crude 82% (86:14 dr)
Isolated 60% (>20:1 dr)



104k

Crude 92% (89:11 dr)
Isolated 80% (>20:1 dr)

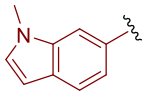


104l

Crude 94% (82:18 dr)
Isolated 64% (>20:1 dr)

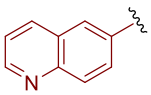
104m

Crude 71% (67:33 dr)
Isolated 38% (74:26 dr)



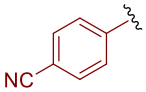
104n

Crude 71% (67:33 dr)
Isolated 38% (74:26 dr)



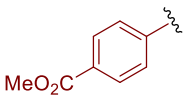
104o

Crude 82% (86:14 dr)
Isolated 60% (91:9 dr)



104p

Crude 76% (76:24 dr)
Isolated 66% (77:23 dr)



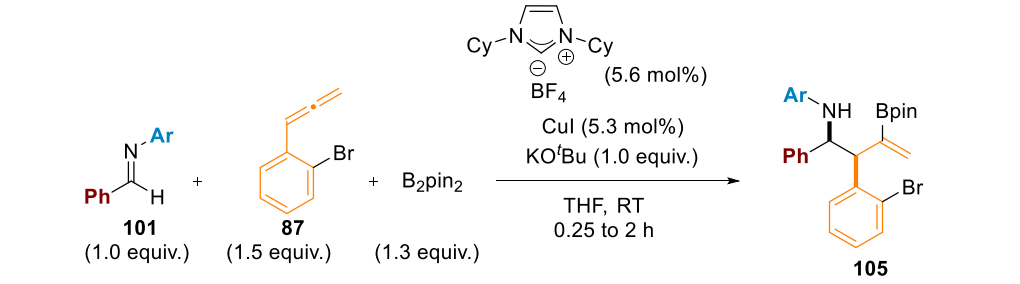
104q

Crude 75% (75:25 dr)
Isolated 66% (77:23 dr)

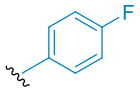
Scheme 24 Scope investigation for the racemic copper-catalysed three-component coupling of

allenes, aldimines and B_2pin_2. Variation of the C-substituent of the imine. Crude yield and dr were determined by ^{1}H-NMR of the crude reaction mixture using an internal standard ($MeNO_2$).

Secondly, the protecting group PMP of the imine was replaced with various *N*-aryl substituents (**Scheme 25**). *p*-Fluoro- (**105a**), morpholinyl- (**105b**) and m-methoxy-phenyl (**105c**) substituents were all tolerated in the reaction (yield: 74-95%). Since **105c** and the starting material aldimine are very close on TLC, the separation was very difficult, so the isolated yield is much lower than the crude yield. We also tried an imine with a dimethyl amino phenyl substituent (**105d**), but the yield was very low. We believe that the nitrogen lone pair of electrons has a significant basicity and coordinates with the copper catalyst, weakening the catalytic activity.

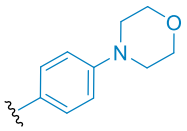


Ar =



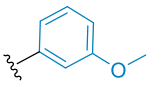
105a

Crude 95% (71:29 d.r.)
Isolated 65% (>20:1 d.r.)



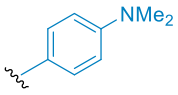
105b

Crude 74% (82:18 d.r.)
Isolated 70% (>20:1 d.r.)



105c

Crude 89% (74:26 d.r.)
Isolated 40% (72:28 d.r.)



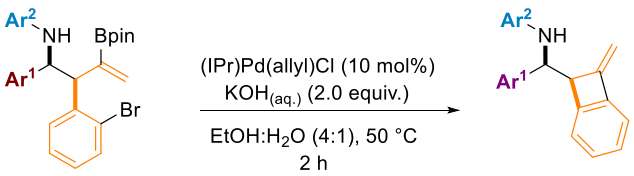
105a

Crude <10%
Isolated N/A

Scheme 25 Scope investigation for the racemic copper-catalysed three-component coupling of allenes, aldimines and B_2pin_2. Variation of the N-substituent of the imine. Crude yield and dr were determined by ^{1}H-NMR of the crude reaction mixture using an internal standard ($MeNO_2$).

From the above data, it is believed that the electronic parameters of the substrates have little effect on the three-component coupling reaction catalysed by copper.

Next, with a wide range of homoallylic intermediates in hand, the scope of the synthesis of four-membered rings in BCBs was investigated (**Scheme 26**). Substituents with electron donating groups, *m*-methoxy- (**106d**), *p*-ethyl- (**106f**) and *p*-tert-butyl- (**106e**) were tolerated and products were obtained in moderate yields (yield: 39-61%). For electron-withdrawing groups, such as *p*-fluoro- (**106g**), *p*-chloro- (**106b**) and *p*-trifluoromethyl- (**106c**), the yields obtained were slightly better (yield: 53-69%). In the presence of benzofused groups such as 2-naphthyl- (**106h**), furyl- (**106i**) and indolyl- (**106j**) the yield was not as high (yield: 34-49%). However, when *o*-methyl (**106a**) and *o*-methoxy (**106b**) and 1-naphthyl (**106m**) substituents were present, the yield was found to be particularly low (yield: 15-38%), presumably because of steric hindrance. When the PMP group on nitrogen was replaced with *p*-fluoro- (**106n**), morpholinyl- (**106o**) and m-methoxy- (**106p**) phenyl substituents, good yields were still obtained (>60%). Since **106k** is very close to the side-product (the indoline ring product) on TLC, separation by column chromatography or preparative TLC could not be achieved. Numerous solvent systems were tried, such as: 20% ethyl acetate in hexane, 30% ether in hexane, 50% dichloromethane in hexane, and 1% methanol in hexane. We tried to add 1% triethylamine to the mixed solvents without any positive effects. For **106l**, after the reaction, no product peaks were found in the crude NMR. We believe that pentafluorophenyl has distinctive electronic parameters which makes the reaction difficult. It was concluded from these results that the four-membered ring synthesized by the Suzuki-Miyara reaction is not greatly affected by electronic effects, but steric hindrance seriously affects the yield. Pleasingly, diastereomeric ratios were all retained unaffected by cyclization.



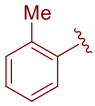
104 or 105

(1.0 equiv.)

106

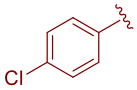
Ar^2 = PMP

Ar^1 =



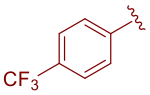
106a

Crude 15% (>20:1 dr)
Isolated 10% (>20:1 dr)



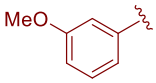
106b

Crude 60% (>20:1 dr)
Isolated 51% (>20:1 dr)



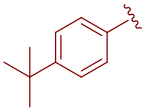
106c

Crude 69% (>20:1 dr)
Isolated 39% (>20:1 dr)



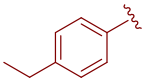
106d

Crude 55% (>20:1 dr)
Isolated 47% (>20:1 dr)



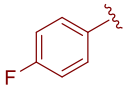
106e

Crude 61% (>20:1 dr)
Isolated 54% (>20:1 dr)



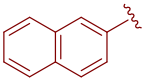
106f

Crude 39% (>20:1 dr)
Isolated 31% (>20:1 dr)



106g

Crude 53% (>20:1 dr)
Isolated 43% (>20:1 dr)

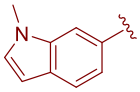


106h

Crude 49% (>20:1 dr)
Isolated 41% (>20:1 dr)

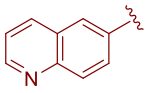
106i

Crude 38% (79:21 dr)
Isolated 30% (81:19 dr)



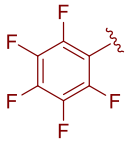
106j

Crude 34% (88.12 dr)
Isolated 28% (86:14 dr)



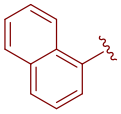
106k

Crude 35% (91:9 dr)
Isolated N/A



106l

Crude 0%
Isolated N/A

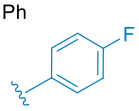


104m

Crude <5%
Isolated N/A

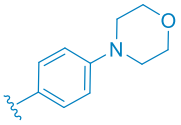
Ar^1 = Ph

Ar^2 =



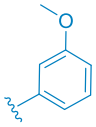
106n

Crude >60% (>20:1 dr)
Isolated 61% (>20:1 dr)



106o

Crude >60% (>20:1 dr)
Isolated 59% (>20:1 dr)

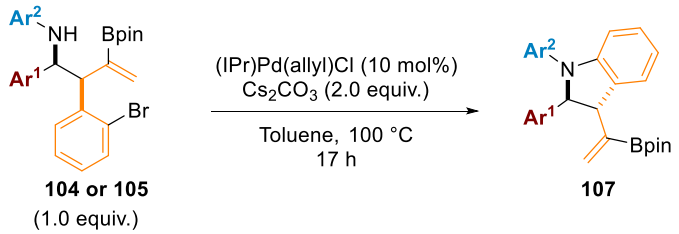


106p

Crude >60% (80:20 dr)
Isolated 63% (83:17 dr)

Scheme 26 Scope investigation for the palladium-catalysed formation of BCBs. Crude yield and dr were determined by ^{1}H-NMR of the crude reaction mixture using an internal standard ($MeNO_2$).

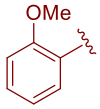
Then, the scope of the five-membered ring cyclisation was investigated (**Scheme 27**). For electron withdrawing groups, *p*-trifluoromethylphenyl (**107b**) was well tolerated. However, the presence of pentafluoro- (**107c**) and *p*-fluoro- (**107f**) phenyl led to average yields (yield: 54-55%). For electron-donating groups, the crude yields for *p*-ethyl- (**107d**) and *p*-tert-butyl- (**107l**) phenyl substrates reached a good level. However, due to the proximity on TLC of the four-membered ring side-product, we failed to separate the *p*-tert-butylphenyl (**107l**) crude product. For *ortho*-substituted groups groups, as with the Suzuki reaction, steric hindrance caused a sharp drop in yield **(107a**, **107j)**. For benzofused rings, 2-naphthyl- derivative (**107e**) can be obtained in 58% yield. For *p*-bromophenyl (**107k**), due to the two active carbon-bromine bonds, intramolecular cyclization did not occur. Fortunately, all heterocyclic compounds reacted, albeit in low yield, for example furyl-(**107g**) containing substrates, indolyl-(**107h**) and quinolinyl-(**107i**) containing substrates. But when separating the products, we encountered the same problem: the indoline product was very close to the four-membered ring side-product, which makes purification tedious. When the PMP-group was not used on nitrogen, *p*-fluoro-(**107m**), morpholinyl- (**107n**) and *m*-methoxy-(**107o**) phenyl substituents in substrates still led to good yields (>50%), although **107o** suffered from the same purification issues.



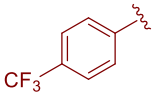
104 or 105
(1.0 equiv.)

107

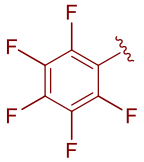
Ar^2 = PMP
Ar^1 =



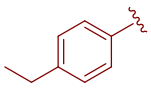
107a
Crude 44% (>20:1 dr)
Isolated 37% (>20:1 dr)



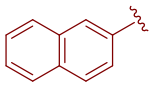
107b
Crude 70% (>20:1 dr)
Isolated 63% (>20:1 dr)



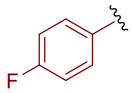
107c
Crude 55% (>20:1 dr)
Isolated 49% (>20:1 dr)



107d
Crude 66% (>20:1 dr)
Isolated *50%* (>20:1 dr)

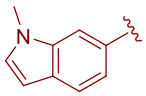


107e
Crude 58% (>20:1 dr)
Isolated 50% (>20:1 dr)

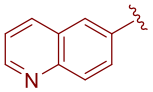


107f
Crude 54% (>20:1 dr)
Isolated 39% (>20:1 dr)

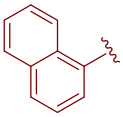
107g
Crude 36% (79:21 dr)
Isolated N/A



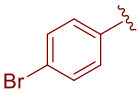
107h
Crude 42% (88:12 dr)
Isolated N/A



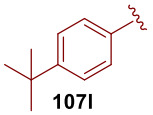
107i
Crude 36% (91:9 dr)
Isolated N/A



107j
Crude <5%
Isolated N/A

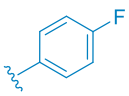


107k
Crude <5%
Isolated N/A

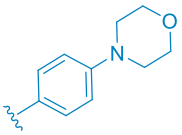


107l
Crude 60% (>20:1 dr)
Isolated N/A

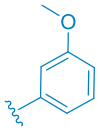
Ar^1 =Ph
Ar^2 =



107m
Crude 58% (>20:1 dr)
Isolated 50% (>20:1 dr)



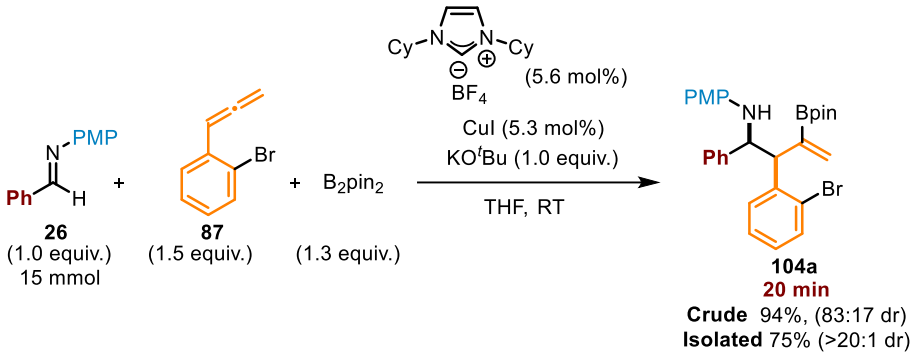
107n
Crude 53% (>20:1 dr)
Isolated 48% (>20:1 dr)



107o
Crude 53% (80:20 dr)
Isolated N/A

Scheme 27 Scope investigation for the palladium-catalysed formation of indolines. Crude yield and d.r. were determined by ^{1}H NMR of the crude reaction mixture using an internal standard ($MeNO_2$).

Finally, the practicality of the three-component coupling reaction catalysed by copper was explored. Under standard conditions, 15 mmol of starting material could be efficiently converted to product with an isolated yield of 75% in 20 minutes only. This demonstrates that the copper-catalysed three-component coupling reaction is amenable to large-scale production (**Scheme 28**).



Scheme 28 Gram-scale copper-catalysed three-component coupling of allenes, aldimines and B_2pin_2. Crude yield and dr were determined by ^{1}H-NMR of the crude reaction mixture using an internal standard (Me-NO_2).

Conclusion

A copper-catalysed multicomponent coupling of aryl allenes, aldimines and B_2pin_2 has been developed. The resulting products can be further transformed into synthetically useful BCBs and indolines.

The copper-catalysed reaction uses cuprous iodide and commercially available NHC ligands to form the catalytic species. At room temperature, the reaction displays a high yield and high diastereoselectivity after very short reaction times. The coupling reaction has a wide functional group tolerance including electron withdrawing groups, electron donating groups, fused rings and heterocycles. At the same time,

the coupling reaction is not affected when performed on a large scale. For the two palladium-catalysed cyclization reactions, there is no need to replace the catalyst, simply changing the base, solvent and temperature allows two very different molecular architectures to be accessed, selectiviely. The electronic properties of the substituent did not seem to overly affect either of the palladium-catalysed pathways.

In conclusion, the project has shown the potential of synthesising high-value amine compounds. At the same time, it provides a novel method to generate uncommon BCBs in a milder manner than the current existing methods. It also allows access to a wide range of medicinally relevant indolines displaying an unprecedented substitution pattern. Most importantly, both products can be accessed from the same versatile precursor, itself easily accessed via the copper-catalysed borylative coupling strategy developed in the Procter group.

Experimental data

General experimental information

All experiments were performed under an atmosphere of nitrogen, using anhydrous solvents, unless otherwise stated. All other solvents were purchased directly from commercial sources (anhydrous over molecular sieves). ^{1}H, ^{13}C, ^{11}B, ^{31}P and ^{19}F NMR spectra were recorded using 400 and 500 MHz Bruker NMR spectrometers at 298K, with chemical shift values being reported in ppm relative to the corresponding residual solvent signal (δ_H = 7.26 or δ_C = 77.1). All coupling constants (*J*) are reported in Hertz (Hz). Splitting patterns are assigned s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, and br. = broad. Mass spectra were obtained using positive and negative electrospray (ES±), atmospheric-pressure chemical ionisation (APCI) or gas chromatography (GC) techniques. Column chromatography was carried out using 35-70 μ, 60 Å silica gel. Routine TLC analysis was carried out on aluminium sheets coated with silica gel 60 F254, 0.2 mm thickness and plates were viewed using a 254 nm ultraviolet lamp and dipped in a solution of phosphomolybdic acid, potassium permanganate, *p*-anisaldehyde or ninhydrin (heated).

Synthesis of aldimines

General procedure A:

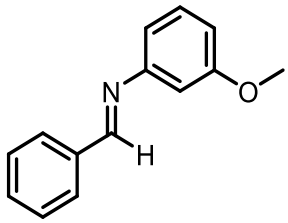
The corresponding aldehyde (1.05 equiv.) and amine (1.0 equiv.) were dissolved in 2-propanol (0.1 M) and stirred for 1 h to 24 h at room temperature (reaction monitored by TLC) after which the mixture was concentrated *in vacuo* to afford the crude product which was used without further purification unless otherwise stated.

General procedure B:

To a dry round bottom flask was added 4 Å molecular sieves (0.5 g per mmol). The

flask was then flame dried three times under vacuum with nitrogen refills. The amine (1.0 equiv.) and the aldehyde (1.05 equiv.) were added in MeOH (0.32 M) and the mixture was stirred for 16 h at room temperature. The resulting solution was then filtered through a pad of celite (Et_2O) and concentrated *in vacuo* to afford the crude product which was used without further purification unless otherwise stated.

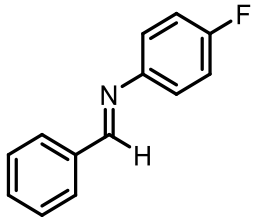
(E)-N-(3-Methoxyphenyl)-1-phenylmethanimine **101a**



As described in General Procedure B, benzaldehyde (1.06 mL, 1.05 mmol, 1.05 equiv.), *m*-methoxyaniline (1.12 mL, 10.0 mmol, 1.0 equiv.), molecular sieves, methanol (0.32M), after purification by column chromatography on silica gel (15% Et_2O in hexane), afforded the title compound as a yellow oil (0.95 g, 4.49 mmol, 45%). δ_H (400 MHz, $CDCl_3$) 3.86 (s, 3H, OC*H*$_3$), 6.80-6.86 (m, 3H, aryl *H*), 7.28-7.36 (m, 1H, aryl *H*), 7.45-7.53 (m, 3H, aryl *H*), 7.89-8.00 (m, 2H, aryl *H*), 8.48 (s, 1H, *H*C=N); δ_C (101 MHz, $CDCl_3$) 55.4 (O*C*H$_3$), 106.7 (aryl *C*H), 111.9 (aryl *C*H), 112.9 (aryl *C*H), 128.8 (aryl *C*H), 128.9 (aryl *C*H), 130.0 (aryl *C*H), 131.5 (aryl *C*H), 136.2 (aryl *C*), 153.4 (aryl *C*), 160.4 (CH$_3$O*C*), 160.6 (H*C*=N). MS (APCI) *m/z* 212.1 (M+H$^+$); HRMS $C_{14}H_{14}ON$ Expected 212.1070, Found 212.1069.

The data is in accordance with the literature.[32]

(E)-N-(4-Fluorophenyl)-1-phenylmethanimine **101b**

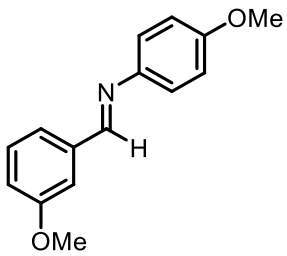


As described in General Procedure B, benzaldehyde (1.06 mL, 1.05 mmol, 1.05 equiv.),

p-fluoroaniline (0.99 mL, 10.0 mmol, 1.0 equiv.), molecular sieves, methanol (0.32 M), after purification by recrystallisation (CH_2Cl_2), afforded the title compound as a yellow powder (0.83 g, 4.19 mmol, 42%). δ_H (400 MHz, $CDCl_3$) 7.04-7.13 (m, 2H, FCC*H*), 7.16-7.24 (m, 2H, FCCHC*H*), 7.42-7.53 (m, 3H, aryl *H*), 7.83-7.97 (m, 2H, aryl *H*), 8.45 (s, 1H, *H*C=N); δ_C (101 MHz, $CDCl_3$) 116.0 (d, *J* = 22.6 Hz, FC*C*H), 122.4 (d, *J* = 8.2 Hz, FCCH*C*H), 128.9 (aryl *C*H), 128.9 (aryl *C*H), 131.6 (aryl *C*H), 148.2 (d, *J* = 2.9 Hz, FCCHCH*C*), 152.4 (d, *J* = 244.1 Hz, F*C*), 160.3 (aryl *C*), 160.3 (H*C*=N); δ_F (376 MHz, $CDCl_3$) -177.26 (*F*C); MS (APCI) *m/z* 200.1 ($M+H^+$); HRMS $C_{13}H_{11}FN$ Expected 200.0870, Found 200.0868.

The data is in accordance with the literature.[33]

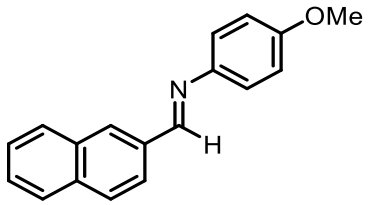
(E)-1-(3-Methoxyphenyl)-N-(4-methoxyphenyl)methanimine **101c**



As described in General Procedure A, *m*-anisaldehyde (1.21 mL, 10.5 mmol, 1.05 equiv.), *p*-anisidine (1.23 g, 10.0 mmol, 1.0 equiv.), 2-propanol (50 mL), afforded the title compound as a yellow powder (2.19 g, 9.12 mmol, 91%) without further purification. δ_H (400 MHz, $CDCl_3$) 3.83 (s, 3H, OCH_3), 3.88 (s, 3H, OCH_3), 6.91-6.98 (m, 2H, OCC*H*), 6.99-7.05 (m, 1H, aryl *H*), 7.20-7.28 (m, 2H, OCCHC*H*), 7.33-7.44 (m, 2H, aryl *H*), 7.49-7.54 (m, 1H, aryl *H*), 8.45 (s, 1H, *H*C=N); δ_C (101 MHz, $CDCl_3$) 55.4 (O*C*H_3), 55.5 (O*C*H_3), 111.7 (aryl *C*H), 114.5 (OC*C*H), 118.0 (aryl *C*H), 122.1 (aryl *C*H), 122.3 (OCCH*C*H), 129.7 (aryl *C*H), 138.0 (aryl *C*), 144.8 (OC(CH)$_2$*C*), 158.3 (CH_3O*C*), 158.4 (H*C*=N), 160.0 (CH_3O*C*); MS (APCI) *m/z* 242.1 ($M+H^+$); HRMS $C_{15}H_{16}NO_2$ Expected 242.1176, Found 242.1173.

The data is in accordance with the literature.[34]

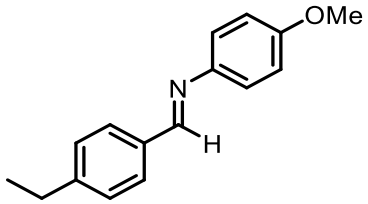
(E)-N-(4-Methoxyphenyl)-1-(naphthalen-2-yl)methanimine **101d**



As described in General Procedure A, 2-naphthaldehyde (1.64 g, 10.5 mmol, 1.05 equiv.), *p*-anisidine (1.23 g, 10.0 mmol, 1.0 equiv.), 2-propanol (50 mL), afforded the title compound as a yellow powder (2.43 g, 9.32 mmol, 93%) without further purification. δ_H (400 MHz, $CDCl_3$) 3.85 (s, 3H, OC*H*$_3$), 6.91-7.02 (m, 2H, OCC*H*), 7.27-7.34 (m, 2H, OCCHC*H*), 7.46-7.58 (m, 2H, aryl *H*), 7.84-7.99 (m, 3H, aryl *H*), 8.11-8.23 (m, 2H, aryl *H*), 8.65 (s, 1H, *H*C=N); δ_C (101 MHz, $CDCl_3$) 55.7 (O*C*H$_3$), 114.6 (OC*C*H), 122.4 (OCCH*C*H), 124.0 (aryl *C*H), 126.7 (aryl *C*H), 127.5 (aryl *C*H), 128.0 (aryl *C*H), 128.8 (aryl *C*H), 128.9 (aryl *C*H), 130.1 (aryl *C*H), 133.3 (aryl *C*), 134.3 (aryl *C*), 135.0 (aryl *C*), 145.0 (OC(CH)$_2$*C*), 158.5 (H*C*=N), 158.5 (CH$_3$O*C*); MS (APCI) *m/z* 262.1 (M+H$^+$); HRMS $C_{18}H_{16}NO$ Expected 262.1226, Found 262.1224.

The data is in accordance with the literature.[35]

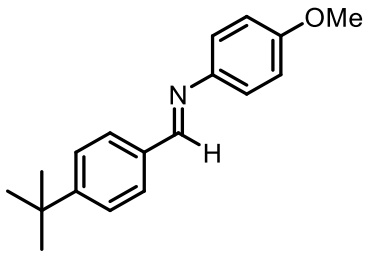
(E)-1-(4-Ethylphenyl)-N-(4-methoxyphenyl)methanimine **101e**



As described in General Procedure A, 4-ethylbenzaldehyde (1.44 mL, 10.5 mmol, 1.05 equiv.), *p*-anisidine (1.23 g, 10.0 mmol, 1.0 equiv.), 2-propanol (50 mL), afforded the title compound as a yellow powder (2.27 g, 9.49 mmol, 95%) without further purification. ν_{max} (thin film/cm^{-1}): 3059, 3028, 2962, 2837, 1621, 1608, 1501, 1308, 1245, 1030, 836, 739; δ_H (400 MHz, $CDCl_3$) 1.28 (t, *J* = 7.6 Hz, 3H, C*H*$_3$CH$_2$), 2.72 (q, *J* = 7.7 Hz, 2H, CH$_3$C*H*$_2$), 3.83 (s, 3H, OC*H*$_3$), 6.86-6.97 (m, 2H, OCC*H*), 7.18-7.25 (m, 2H, OCCHC*H*), 7.27-7.33 (m, 2H, CH$_3$CH$_2$CC*H*), 7.71-7.86 (m, 2H, CH$_3$CH$_2$CCHC*H*), 8.46 (s, 1H, *H*C=N); δ_C (101 MHz, $CDCl_3$) 15.5 (*C*H$_3$CH$_2$), 29.0 (CH$_3$*C*H$_2$), 55.6 (O*C*H$_3$), 114.5

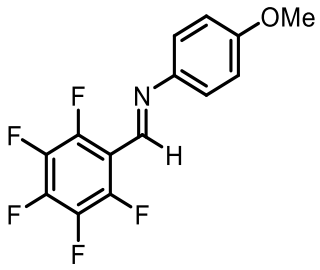
(OC*C*H), 122.3 (OCCH*C*H), 128.4 (CH_3CH_2C*C*H), 128.8 (CH_3CH_2CCHC*H*), 134.2 ($CH_3CH_2C(CH)_2$*C*), 145.2 ($OC(CH)_2$*C*), 147.9 (CH_3CH_2*C*), 158.2 (CH_3O*C*), 158.7 (H*C*=N); M.p.: 103-106 ℃ (IPA); MS (APCI) *m/z* 240.1 ($M+H^+$); HRMS $C_{16}H_{18}NO$ Expected 240.1383, Found 240.1381.

(E)-1-(4-(tert-Butyl)phenyl)-N-(4-methoxyphenyl)methanimine **101f**



As described in General Procedure A, 4-(tert-butyl)benzaldehyde (1.76 mL, 10.5 mmol, 1.05 equiv.), *p*-anisidine (1.23 g, 10.0 mmol, 1.0 equiv.), 2-propanol (50 mL), afforded the title compound as a yellow powder (2.37 g, 8.93 mmol, 89%) without further purification. ν_{max} (thin film/cm^{-1}): 2959, 2867, 1621, 1608, 1501, 1302, 1242, 1027, 839, 764 δ_H (400 MHz, $CDCl_3$) 1.36 (s, 9H, $C(CH_3)_3$), 3.83 (s, 3H, OCH_3), 6.86-6.97 (m, 2H, OCC*H*), 7.18-7.25 (m, 2H, OCCHC*H*), 7.44-7.53 (m, 2H, $(CH_3)_3CCCH$), 7.78-7.85 (m, 2H, $(CH_3)_3CCCHCH$), 8.46 (s, 1H, *H*C=N); δ_C (101 MHz, $CDCl_3$) 31.6 ($C(CH_3)_3$), 35.1 ($C(CH_3)_3$), 55.6 (OCH_3), 114.5 (OC*C*H), 122.3 (OCCH*C*H), 125.9 ($(CH_3)_3CCCH$), 128.5 ($(CH_3)_3CCCHCH$), 133.9 ($(CH_3)_3CC(CH)_2$*C*), 145.4 ($OC(CH)_2$*C*), 154.7 ($(CH_3)_3C$*C*), 158.2 (CH_3O*C*), 158.6 (H*C*=N); M.p.: 99-102 ℃ (IPA); MS (APCI) *m/z* 268.1 ($M+H^+$); HRMS $C_{18}H_{22}NO$ Expected 268.1696, Found 268.1693.

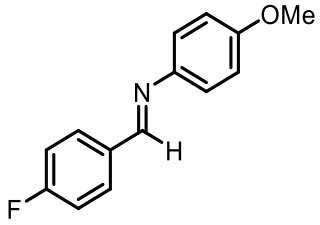
(E)-N-(4-Methoxyphenyl)-1-(perfluorophenyl)methanimine **101g**



As described in General Procedure A, 2,3,4,5,6-pentafluorobenzaldehyde (1.30 mL, 10.5 mmol, 1.05 equiv.), *p*-anisidine (1.23 g, 10.0 mmol, 1.0 equiv.), 2-propanol (50 mL), afforded the title compound as a yellow powder (2.92 g, 9.71 mmol, 97%) without further purification. δ_H (400 MHz, $CDCl_3$) 3.84 (s, 3H, OC*H*$_3$), 6.86-6.99 (m, 2H, OCC*H*), 7.18-7.32 (m, 2H, OCCHC*H*), 8.58 (s, 1H, *H*C=N); δ_C (101 MHz, $CDCl_3$) 55.7 (O*C*H$_3$), 114.7 (OCCH*C*H), 122.6 (OC*C*H), 144.2 (OC(CH)$_2$*C*), 146.0 (q, *J* = 2.9 Hz, H*C*=N), 159.6 (CH$_3$O*C*); δ_F (376 MHz, $CDCl_3$) -161.73 (*F*C), -150.52 (*F*C), -142.10 (*F*C); MS (APCI) *m/z* 302.0 (M+H$^+$); HRMS $C_{14}H_9NOF_5$ Expected 300.0599, Found 300.0594.

The data is in accordance with the literature.[36]

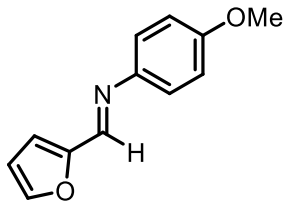
(E)-1-(4-Fluorophenyl)-N-(4-methoxyphenyl)methanimine **101h**



As described in General Procedure A, 4-fluorobenzaldehyde (1.13 mL, 10.5 mmol, 1.05 equiv.), *p*-anisidine (1.23 g, 10.0 mmol, 1.0 equiv.), 2-propanol (50 mL), afforded the title compound as a yellow powder (2.16 g, 9.43mmol, 94%) without further purification. δ_H (400 MHz, $CDCl_3$) 3.83 (s, 3H, OC*H*$_3$), 6.82-7.02 (m, 2H, OCC*H*), 7.15 (t, *J* = 8.6 Hz, 2H, aryl *H*), 7.20-7.37 (m, 2H, OCCHC*H*), 7.89 (dd, *J* = 8.7, 5.6 Hz, 2H, aryl *H*), 8.44 (s, 1H, *H*C=N); δ_C (101 MHz, $CDCl_3$) 55.6 (O*C*H$_3$), 114.5 (OC*C*H), 116.0 (d, *J* = 21.9 Hz, FC*C*H), 122.3 (OCCH*C*H), 130.6 (d, *J* = 8.8 Hz, FCCH*C*H), 132.9 (d, *J* = 3.0 Hz, FC(CH)$_2$*C*), 144.8 (OC(CH)$_2$*C*), 156.9 (H*C*=N), 158.5 (CH$_3$O*C*), 164.6 (d, *J* = 251.8 Hz, F*C*); δ_F (376 MHz, $CDCl_3$) -108.69 (*F*C); MS (APCI) *m/z* 230.1 (M+H$^+$); HRMS $C_{14}H_{13}NOF$ Expected 230.0976, Found 230.0976.

The data is in accordance with the literature.[37]

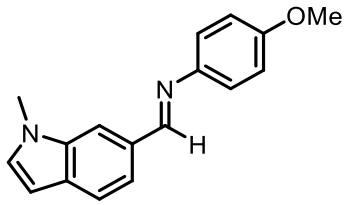
(E)-1-(Furan-2-yl)-N-(4-methoxyphenyl)methanimine **101i**



As described in General Procedure A, 2-furancarboxaldehyde (0.87 mL, 10.5 mmol, 1.05 equiv.), *p*-anisidine (1.23 g, 10.0 mmol, 1.0 equiv.), 2-propanol (50 mL), afforded the title compound as a black oil (1.79 g, 8.94 mmol, 89%) without further purification. δ_H (400 MHz, $CDCl_3$) 3.83 (s, 3H, OC*H*$_3$), 6.51-6.58 (m, 1H, furan *H*), 6.87-6.96 (m, 3H, OCC*H* + furan *H*), 7.21-7.31 (m, 2H, OCCHC*H*), 7.89 (d, *J* = 1.5 Hz, 1H, furan *H*), 8.31 (s, 1H, *H*C=N); δ_C (101 MHz, $CDCl_3$) 55.6 (O*C*H$_3$), 112.2 (furan *C*H), 114.6 (OC*C*H), 115.7 (furan *C*H), 122.5 (OCCH*C*H), 144.4 (OC(CH)$_2$*C*), 145.5 (furan *C*H), 145.9 (H*C*=N), 152.5 (furan *C*), 158.6 (CH$_3$O*C*); MS (APCI) *m/z* 202.1 ($M+H^+$); HRMS $C_{12}H_{12}NO_2$ Expected 202.0863, Found 202.0866.

The data is in accordance with the literature.[38]

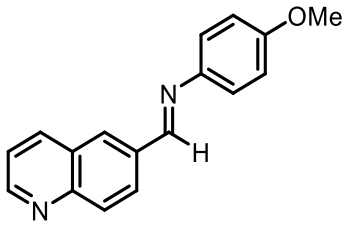
(E)-N-(4-Methoxyphenyl)-1-(1-methyl-1H-indol-6-yl)methanimine **101j**



As described in General Procedure A, 1-methyl-1H-indole-6-carbaldehyde (1.67 g, 10.5 mmol, 1.05 equiv.), *p*-anisidine (1.23 g, 10.0 mmol, 1.0 equiv.), 2-propanol (50 mL), afforded the title compound as a yellow powder (2.41 g, 9.14 mmol, 91%) without further purification. ν_{max} (thin film/cm^{-1}): 3096, 2833, 1681, 1502, 1419, 1180, 1086, 1032; δ_H (400 MHz, $CDCl_3$) 3.84 (s, 3H, OC*H*$_3$), 3.87 (s, 3H, NC*H*$_3$), 6.52 (dd, *J* = 3.1, 0.9 Hz, 1H, indole *H*), 6.91-6.99 (m, 2H, OCC*H*), 7.17 (d, *J* = 3.0 Hz, 1H,

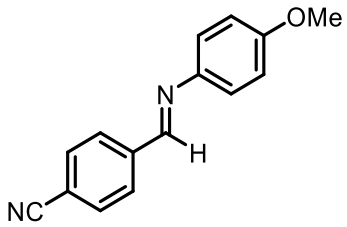
indole *H*), 7.22-7.31 (m, 2H, OCCHC*H*), 7.62 (dd, *J* = 8.3, 1.4 Hz, 1H, indole *H*), 7.68 (dd, *J* = 8.1, 0.7 Hz, 1H, indole *H*), 7.94 (s, 1H, indole *H*), 8.60 (s, 1H, *H*C=N); δ_C (101 MHz, $CDCl_3$) 33.2 (N*C*H_3), 55.6 (O*C*H_3), 101.5 (indole *C*H), 109.7 (indole *C*H), 114.5 (OC*C*H), 120.8 (indole *C*H), 121.6 (indole *C*H), 122.2 (OCCH*C*H), 130.4 (indole *C*), 131.3 (indole *C*), 131.5 (indole *C*H), 137.0 (indole *C*), 145.7 (OC(CH)$_2$*C*), 158.0 (CH_3O*C*), 160.1 (H*C*=N); M.p.: 104-105 ℃(IPA); MS (APCI) *m/z* 265.2 ($M+H^+$); HRMS $C_{17}H_{17}N_2O$ Expected 265.1335, Found 265.1329.

(E)-N-(4-Methoxyphenyl)-1-(quinolin-6-yl)methanimine **101k**



As described in General Procedure A, quinoline-6-carbaldehyde (1.65 g, 10.5 mmol, 1.05 equiv.), *p*-anisidine (1.23 g, 10.0 mmol, 1.0 equiv.), 2-propanol (50 mL), afforded the title compound as a yellow powder (2.46 g, 9.41 mmol, 94%) without further purification. ν_{max} (thin film/cm^{-1}): 3067, 3013, 2958, 2838, 1618, 1591, 1504, 1294, 1247, 1027, 834, 739; δ_H (400 MHz, $CDCl_3$) 3.84 (s, 3H, O*C*H_3), 6.92-6.99 (m, 2H, OCC*H*), 7.27-7.35 (m, 2H, OCCHC*H*), 7.44 (dd, *J* = 8.3, 4.2 Hz, 1H, quinoline *H*), 8.13-8.26 (m, 3H, quinoline *H*), 8.38 (dd, *J* = 8.8, 1.9 Hz, 1H, quinoline *H*), 8.65 (s, 1H, *H*C=N), 8.95 (dd, *J* = 4.3, 1.7 Hz, 1H, quinoline *H*); δ_C (101 MHz, $CDCl_3$) 55.6 (O*C*H_3), 114.6 (OC*C*H), 121.9 (quinoline *C*H), 122.5 (OCCH*C*H), 128.0 (quinoline *C*H), 128.3 (quinoline *C*), 129.9 (quinoline *C*H), 130.3 (quinoline *C*H), 134.9 (quinoline *C*), 136.8 (quinoline *C*H), 144.6 (OC(CH)$_2$*C*), 149.8 (quinoline *C*), 151.6 (quinoline *C*H), 157.2 (H*C*=N), 158.7 (CH_3O*C*); M.p.: 121-123 ℃ (IPA); MS (APCI) *m/z* 263.2 ($M+H^+$); HRMS $C_{17}H_{15}N_2O$ Expected 263.1179, Found 263.1186.

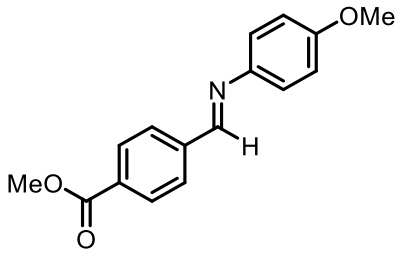
(E)-4-(((4-Methoxyphenyl)imino)methyl)benzonitrile **101l**



As described in General Procedure A, 4-formylbenzonitrile (1.38 g, 10.5 mmol, 1.05 equiv.), *p*-anisidine (1.23 g, 10.0 mmol, 1.0 equiv.), 2-propanol (50 mL), afforded the title compound as a yellow powder (2.12 g, 9.00 mmol, 90%) without further purification.; δ_H (400 MHz, $CDCl_3$) 3.84 (s, 3H, OC*H*$_3$), 6.88-7.01 (m, 2H, OCC*H*), 7.17-7.33 (m, 2H, OCCHC*H*), 7.67-7.79 (m, 2H, CNCCHC*H*), 7.88-8.04 (m, 2H, CNCC*H*), 8.51 (s, 1H, *H*C=N); δ_C (101 MHz, $CDCl_3$) 55.6 (O*C*H$_3$), 114.0 (aryl *C*), 114.6 (OCCH*C*H), 118.7 (N*C*), 122.7 (OC*C*H), 128.9 (CNC*C*H), 132.6 (CNCCH*C*H), 140.4 (CNC(CH)$_2$*C*), 143.8 (OC(CH)$_2$*C*), 155.5 (H*C*=N), 159.2 (CH$_3$O*C*); MS (APCI) *m/z* 237.2 ($M+H^+$); HRMS $C_{15}H_{13}N_2O$ Expected 237.1022, Found 237.1025.

The data is in accordance with the literature.[39]

Methyl (E)-4-(((4-methoxyphenyl)imino)methyl)benzoate **101m**



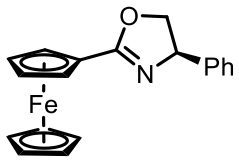
As described in General Procedure A, methyl 4-formylbenzoate (1.72 g, 10.5 mmol, 1.05 equiv.), *p*-anisidine (1.23 g, 10.0 mmol, 1.0 equiv.), 2-propanol (50 mL), afforded the title compound as a yellow powder (2.27 g, 8.41 mmol, 84%) without further purification.; δ_H (400 MHz, $CDCl_3$) 3.84 (s, 3H, OC*H*$_3$), 3.94 (s, 3H, CO_2C*H*$_3$), 6.91-6.97 (m, 2H, OCC*H*), 7.2-7.30 (m, 2H, OCCHC*H*), 7.91-7.97 (m, 2H, CO_2CH_3CCHC*H*), 8.09-8.15 (m, 2H, CO_2CH_3CC*H*), 8.53 (s, 1H, *H*C=N); δ_C (101 MHz, $CDCl_3$) 52.4 (CO_2*C*H$_3$), 55.6 (O*C*H$_3$), 114.6 (OCCH*C*H), 122.5 (OC*C*H), 128.5 (CO_2CH_3CCH), 130.1 (CO_2CH_3CCHCH), 132.1 (CO_2CH_3C(CH)$_2$*C*), 140.4 (OC(CH)$_2$*C*), 144.4 (CO_2CH_3C), 156.9

(H*C*=N), 158.9 (CH_3O*C*), 166.8 (*C*O_2CH_3); MS (APCI) *m/z* 270.2 ($M+H^+$); HRMS $C_{16}H_{16}NO_3$ Expected 270.1125, Found 270.1129.

The data is in accordance with the literature.[37]

Synthesis of Chiral Ligand

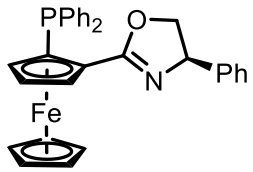
[(4R)-4,5-Dihydro-4-phenyl-2-oxazolyl]-Ferrocene **98**



An oven dried flask was charged with ferrocenecarboxylic acid (1.15 g, 5 mmol, 1.0 equiv.) dry CH_2Cl_2 (35 mL) and oxalyl chloride (1.9 g, 15 mmol, 3.0 equiv.) and stirred for 4 hours at RT under an inert atmosphere. The solvent was removed under reduced pressure. The product was taken up in dry CH_2Cl_2 (20 mL) and slowly added to a stirred mixture of (R)-(−)-2-phenylglycinol (0.892 g, 6.5 mmol, 1.3 equiv.), Et_3N (1.52 mL, 15 mmol, 3.0 equiv.) in dry CH_2Cl_2 (20 mL) at 0 °C under an inert atmosphere. Stirring was continued for 4 hours, after which MsCl (1.145 g, 10 mmol, 2.0 equiv.) and Et_3N (1.52 mL, 15 mmol, 3.0 equiv.) were added, with stirring continued for a further 3 hours. Aqueous $NaHCO_3$ (sat., 75 mL) and CH_2Cl_2 (75 mL) were added to the flask, and the layers separated. The aqueous layer was extracted with further portions of CH_2Cl_2 (2 x 25 mL), the organic layers combined, dried over $MgSO_4$ and the solvent removed under reduced pressure. Column chromatography (5% Et_2O in hexane) afforded the title compound as an orange solid (1.49 g, 4.5 mmol, 90%). ν_{max} (thin film/cm^{-1}): 3083, 3026, 2892, 1648, 1480, 1378, 1295, 1276, 1111, 822; δ_H (400 MHz, $CDCl_3$) 4.19 (t, *J* = 8.0 Hz, 1H, OCH_2CH), 4.25 (s, 5H, ferrocyl *H*), 4.38 (s, 2H, ferrocyl *H*), 4.69 (dd, *J* = 9.9, 8.3 Hz, 1H, OCH_2CH), 4.84 (s, 2H, ferrocyl *H*), 5.23 (dd, *J* = 9.9, 7.8 Hz, 1H, OCH_2CH), 7.24 – 7.39 (m, 5H, aryl *H*); δ_C (101 MHz, $CDCl_3$) 69.4 (ferrocyl *C*H), 69.4 (ferrocyl *C*H), 69.8 (ferrocyl *C*H), 70.1 (ferrocyl *C*), 70.2 (OCH_2CH), 70.6 (ferrocyl *C*H), 70.6 (ferrocyl *C*H), 74.7 (OCH_2CH), 126.8 (aryl *C*H),

127.7 (aryl *C*H), 128.9 (aryl *C*H), 142.8 (aryl *C*), 167.6 (*C*=N); MS (APCI) *m/z* 332 ($M+H^+$); HRMS $C_{19}H_{18}NOFe$ Expected 332.0732, Found 332.0726.

Ligand **96**



[(4R)-4,5-Dihydro-4-phenyl-2-oxazolyl]-ferrocene **98** (0.33 g, 1.0 mmol, 1.0 equiv.) was dissolved in dry Et_2O (10 mL) under argon atmosphere and cooled to -78 °C. At this temperature, TMEDA (0.15 g, 1.3 mmol, 1.3 equiv.) was added, followed by sBuLi (0.48 mL, 1.2 mmol, 1.2 equiv., 2.5 M sol. in hexane). The solution was stirred for 30 min. Ph_2PCl (0.29 g, 1.3 mmol, 1.3 equiv.) was then added, and the resulting mixture was continually stirred for 30 min then allowed to warm to room temperature over another 30 min. The reaction mixture was diluted with ether (20 mL), quenched with saturated aqueous $NaHCO_3$, extracted three times with Et_2O, and dried over $MgSO_4$. The solvent was removed under reduced pressure, and the resulting residue was purified by column chromatography. Special care was taken to avoid exposure of the purified ligand to air from this point (under nitrogen atmosphere). Purification by recrystallisation (Hexane), afforded the title compound as a dark red solid (0.149 g, 0.29 mmol, 29%). ν_{max} (thin film/cm^{-1}): 3053, 3027, 2895, 1643, 1475, 1380, 1268, 1202, 1124, 821, 697; δ_H (400 MHz, $CDCl_3$) 3.65 (s, 1H, ferrocyl *H*), 3.79 (t, *J* = 8.2 Hz, 1H, OCH_2CH), 4.25 (s, 5H, ferrocyl *H*), 4.39 (t, *J* = 2.6 Hz, 1H, ferrocyl *H*), 4.65 (dd, *J* = 9.8, 8.3 Hz, 1H, OCH_2CH), 5.01 (s, 1H, ferrocyl *H*), 5.06 (dd, *J* = 9.8, 8.1 Hz, 1H, OCH_2CH), 6.90 - 6.96 (m, 2H, aryl *H*), 7.14-7.29 (m, 8H, aryl *H*), 7.32-7.39 (m, 3H, aryl *H*), 7.44-7.52 (m, 2H, aryl *H*); δ_C (101 MHz, $CDCl_3$) 70.1 (OCH_2CH), 71.0 (d, J = 1.9 Hz, ferrocyl *C*H), 71.1 (OCH_2CH), 72.5 (d, *J* = 2.0 Hz, ferrocyl *C*H), 74.1 (d, *J* = 3.9 Hz, ferrocyl *C*H), 74.8 (d, *J* = 15.7 Hz, ferrocyl *C*), 75.0 (ferrocyl *C*H), 79.2 (d, *J* = 14.6 Hz, ferrocyl *C*), 127.0 (aryl *C*H), 127.5 (aryl *C*H), 128.3 (d, *J* = 6.7 Hz, aryl *C*H), 128.4 (aryl *C*H), 128.5 (aryl *C*H), 128.7 (aryl *C*H), 129.2 (aryl *C*H), 132.8 (d, *J* = 19.5 Hz, aryl *C*H),

134.9 (d, *J* = 21.4 Hz, aryl *C*H), 138.0 (d, *J* = 13.0 Hz, aryl *C*), 139.6 (d, *J* = 12.7 Hz, aryl *C*), 142.5 (aryl *C*), 167.1 (d, J = 2.6 Hz, *C*=N); δ_p (163 MHz, $CDCl_3$) -17.08 (*P*Ph_2); M.p. 181-183 ℃ (Et_2O); MS (APCI) *m/z* 516 ($M+H^+$); HRMS $C_{31}H_{27}NOPFe$ Expected 516.1174, Found 516.1179.

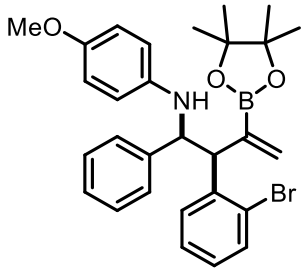
The data is in accordance with the literature [40].

Synthesis of homoallylic amines

General procedure A

To a solution of CuI (5.3 mol%) and 1,3-dicyclohexylimidazolium tetrafluoroborate salt (5.6 mol%) in dry THF (0.013 M) at room temperature under N_2, was added ^{t}BuOK (1.0 equiv.) as a 1.0 M solution in dry THF, and the reaction was stirred for 20 minutes at room temperature. B_2pin_2 (1.3 equiv.) in dry THF (0.325 mL) was then added and the resulting mixture stirred for 30 minutes. A solution of imine (1.0 equiv.) and 1-bromoaryl allene (1.5 equiv.) in dry THF (0.2 M) was then added dropwise at room temperature. The reaction was stirred at room temperature and monitored by TLC for 20 minutes to 2 hours before being filtered through a pad of silica, concentrated *in vacuo*, and purified by column chromatography on silica to afford the desired homoallylic amine. Nitromethane is used as an internal standard.

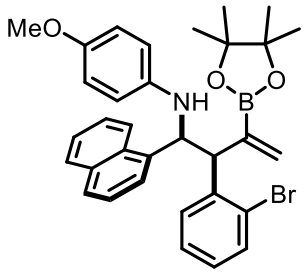
Rac-1S,2S-N-2-(2-Bromophenyl)-1-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)but-3-en-1-yl)-4-methoxyaniline **88**



Prepared according to General Procedure A on a 0.200 mmol scale (crude ^{1}H NMR: 97%, 82:18 dr). Column chromatography (5% Et_2O in hexane) afforded the title

compound as a yellow solid (95.1 mg, 0.172 mmol, 86%, 86:14 dr). ν_{max} (thin film/cm^{-1}): 3390, 3061, 3027, 2975, 2929, 2830, 1615, 1509, 1355, 1308, 1235, 1136, 816, 753, 698; δ_H (400 MHz, $CDCl_3$) 1.13 (s, 6H, BOCCH_3), 1.15 (s, 6H, BOCCH_3), 3.65 (s, 3H, OCH_3), 3.75 (br. s, 1H, N*H*), 4.37 (d, *J* = 10.4 Hz, 1H, C*H*C=CH_2), 4.96 (d, *J* = 10.4 Hz, 1H, C*H*CHC=CH_2), 5.51 (d, *J* = 2.8 Hz, 1H, C=CH_2), 5.77 (d, *J* = 3.0 Hz, 1H, C=CH_2), 6.36 (d, *J* = 8.9 Hz, 2H, OCC*H*), 6.61 (d, *J* = 8.9 Hz, 2H, OCCHC*H*), 7.02-7.07 (m, 1H, aryl *H*), 7.15-7.36 (m, 4H, aryl *H*), 7.44 (d, *J* = 7.2 Hz, 2H, aryl *H*), 7.55 (dd, *J* = 7.9, 1.3 Hz, 1H, aryl *H*), 7.69 (dd, *J* = 7.8, 1.6 Hz, 1H, aryl *H*); δ_C (101 MHz, $CDCl_3$) 24.7 (BOC*C*H_3), 24.9 (BOC*C*H_3), 55.8 (O*C*H_3), 57.1 (*C*HC=CH_2), 61.5 (*C*HCHC=CH_2), 83.6 (BO*C*CH_3), 114.7 (OCCH*C*H), 114.8 (OC*C*H), 126.4 (aryl *C*), 127.0 (aryl *C*H), 127.4 (aryl *C*H), 128.1 (aryl *C*H), 128.3 (aryl *C*H), 128.3 (aryl C*H*), 129.7 (aryl *C*H), 133.3 (aryl *C*H), 133.7 (C=*C*H_2), 140.6 (aryl *C*), 141.9 (OC$(CH)_2$*C*), 142.8 (aryl *C*), 152.0 (CH_3O*C*), (B*C*=CH_2 not observed); M.p.: 57-59 ℃ (Et_2O); MS (ES^+) *m/z* 566 ($M+Na^+$); HRMS $C_{29}H_{34}O_3NBBr$ Expected 534.1810, Found 534.1797.

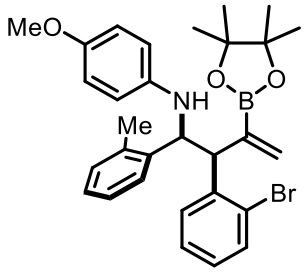
Rac-1S,2S-N-2-(2-Bromophenyl)-1-(naphthalen-1-yl)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)but-3-en-1-yl)-4-methoxyaniline **104a**



Prepared according to General Procedure A on a 0.200 mmol scale (crude ^{1}H NMR: 90%, 90:10 dr). Column chromatography (5% Et_2O in hexane) afforded the title compound as a brown oil (93.5 mg, 0.160 mmol, 80%, >20:1 dr). ν_{max} (thin film/cm^{-1}): 3410, 3060, 2977, 2831, 1686, 1509, 1466, 1357, 1311, 1238, 1167, 1137, 1037; δ_H (400 MHz, $CDCl_3$) 1.07 (s, 6H, BOCCH_3), 1.08 (s, 6H, BOCCH_3), 3.63 (s, 3H, OCH_3), 4.81 (d, *J* = 8.1 Hz, 1H, C*H*C=CH_2), 5.51-5.56 (d, *J* = 2.7 Hz, 1H, C=CH_2), 5.77 (d, *J* = 2.7 Hz, 1H, C=CH_2), 5.83 (d, *J* = 8.1 Hz, 1H, C*H*CHC=CH_2), 6.33-6.47 (m, 2H, OCC*H*),

6.54-6.66 (m, 2H, OCCHC*H*), 6.95–7.18 (m, 1H, aryl *H*), 7.27-7.43 (m, 2H, aryl *H*), 7.50 (ddt, *J* = 6.4, 3.4, 1.6 Hz, 2H, aryl *H*), 7.54-7.64 (m, 2H, aryl *H*), 7.73 (d, *J* = 8.1 Hz, 1H, aryl *H*), 7.80 (dd, *J* = 7.8, 1.7 Hz, 1H, aryl *H*), 7.87 (dd, *J* = 8.1, 1.4 Hz, 1H , aryl *H*), 8.59 (d, *J* = 8.5 Hz, 1H, aryl *H*); δ_C (101 MHz, $CDCl_3$) 24.6 (BOC*C*H_3), 24.7 (BOC*C*H_3), 55.7 (O*C*H_3), 55.8 (*C*HC=CH_2), 61.8 (*C*HCHC=CH_2), 83.6 (BO*C*CH_3), 114.7 (OCCH*C*H), 114.8 (OC*C*H), 123.7 (aryl *C*H), 125.2 (aryl *C*H), 125.7 (aryl *C*H), 125.8 (aryl *C*H), 127.0 (aryl *C*H), 127.0 (aryl *C*H), 127.7 (aryl *C*H), 128.1 (aryl *C*H), 129.0 (aryl *C*H), 129.6 (aryl *C*), 130.6 (aryl *C*H), 132.0 (aryl *C*), 132.7 (C=*C*H_2), 133.2 (aryl *C*H), 134.0 (aryl *C*), 138.2 (aryl *C*), 139.8 (aryl *C*), 141.8 (OC(CH)$_2$*C*), 152.0 (CH_3O*C*), (B*C*=CH_2 not observed); δ_B (128 MHz, $CDCl_3$) 30.8 (*B*OCCH$_3$); MS (APCI) *m/z* 582.2 ($M+H^+$); HRMS $C_{33}H_{36}O_3NBBr$ Expected 584.1966, Found 584.1960.

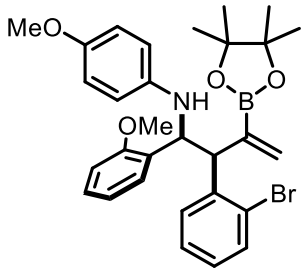
Rac-1S,2S-N-2-(2-Bromophenyl)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-(o-tolyl)but-3-en-1-yl)-4-methoxyaniline **104b**



Prepared according to General Procedure A on a 0.200 mmol scale (crude ^{1}H NMR: 90%, 95:5 dr). Column chromatography (5% Et_2O in hexane) afforded the title compound as a yellow oil (88.8 mg, 0.162 mmol, 81%, >20:1 dr). ν_{max} (thin film/cm^{-1}): 3406, 2963, 2327, 1511, 1446, 1258, 1140, 1027; δ_H (400 MHz, $CDCl_3$) 1.04 (s, 6H, BOCC*H*$_3$), 1.08 (s, 6H, BOCC*H*$_3$), 2.50 (s, 3H, Ar-C*H*$_3$), 3.65 (s, 3H, OC*H*$_3$), 3.78 (br. s, 1H, N*H*), 4.60 (d, *J* = 9.0 Hz, 1H, C*H*C=CH_2), 5.10 (d, *J* = 9.1 Hz, 1H, C*H*CHC=CH_2), 5.53 (d, *J* = 1.7 Hz, 1H, C=C*H*$_2$), 5.88 (d, *J* = 2.8 Hz, 1H, C=C*H*$_2$), 6.27-6.35 (m, 2H, OCC*H*), 6.57-6.67 (m, 2H, OCCHC*H*), 7.00-7.13 (m, 4H, aryl *H*), 7.26 (td, *J* = 7.3, 1.1 Hz, 1H, aryl *H*), 7.33-7.39 (m, 1H, aryl *H*), 7.50 (dd, *J* = 8.0, 1.3 Hz, 1H, aryl *H*), 7.62 (dd, *J* = 7.8, 1.7 Hz, 1H, aryl *H*); δ_C (101 MHz, $CDCl_3$) 20.2 (Ar-*C*H_3), 24.5 (BOC*C*H_3), 24.9 (BOC*C*H_3), 54.1 (*C*HC=CH_2), 55.8 (O*C*H_3), 57.9 (*C*HCHC=CH_2), 83.6 (BO*C*CH_3), 114.6 (OCCH*C*H),

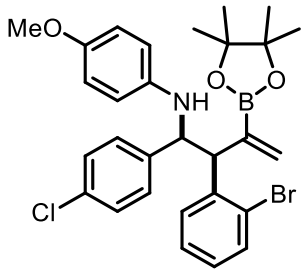
114.7 (OC*C*H), 126.1 (aryl *C*), 126.8 (aryl *C*H), 126.8 (aryl *C*H), 127.0 (aryl *C*H), 128.0 (aryl *C*H), 128.4 (aryl *C*H), 130.3 (aryl *C*H), 130.6 (aryl *C*H), 132.8 (C=*C*H_2), 133.2 (aryl *C*H), 135.9 (aryl *C*), 140.0 (OC(CH)$_2$*C*), 140.4 (aryl *C*), 141.8 (aryl *C*), 152.0 (CH_3O*C*), (B*C*=CH_2 not observed); δ_B (128 MHz, $CDCl_3$) 27.7 (*B*OCCH$_3$); MS (APCI) *m/z* 548.2 (M+H$^+$); HRMS $C_{30}H_{36}O_3NBBr$ Expected 548.1966, Found 548.1976.

Rac-1S,2S-N-2-(2-Bromophenyl)-1-(2-methoxyphenyl)-3-(4,4,5,5-tetramethyl-1,3,2-di oxaborolan-2-yl)but-3-en-1-yl)-4-methoxyaniline **104c**



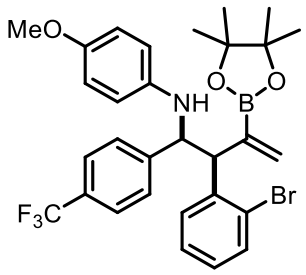
Prepared according to General Procedure A on a 0.200 mmol scale (crude ^{1}H NMR: 93%, 92:8 dr). Column chromatography (5% Et_2O in hexane) afforded the title compound as a yellow oil (94.6 mg, 0.168 mmol, 84%, >20:1 dr). ν_{max} (thin film/cm^{-1}): 3439, 2964, 2940, 2373, 1511, 1446, 1357, 1259, 1140, 1127; δ_H (400 MHz, $CDCl_3$) 1.13 (s, 6H, BOCC*H*$_3$), 1.14 (s, 6H, BOCC*H*$_3$), 3.66 (s, 3H, OC*H*$_3$), 3.91 (s, 3H, Ar-OC*H*$_3$), 4.16 (br. s, 1H, N*H*), 4.83 (d, *J* = 10.0 Hz, 1H, C*H*C=CH_2), 5.27 (d, *J* = 10.0 Hz, 1H, C*H*CHC=CH_2), 5.66 (d, *J* = 3.2 Hz, 1H, C=C*H*$_2$), 5.79 (d, *J* = 3.0 Hz, 1H, C=C*H*$_2$), 6.43-6.52 (m, 2H, OCC*H*), 6.59-6.68 (m, 2H, OCCHC*H*), 6.79-6.87 (m, 2H, aryl *H*), 7.01 (td, *J* = 7.6, 1.7 Hz, 1H, aryl *H*), 7.10-7.19 (m, 1H, aryl *H*), 7.19-7.33 (m, 2H, aryl *H*), 7.52 (dd, *J* = 8.0, 1.3 Hz, 1H, aryl *H*), 7.70 (dd, *J* = 8.0, 1.7 Hz, 1H, aryl *H*); δ_C (101 MHz, $CDCl_3$) 24.7 (BOC*C*H$_3$), 24.8 (BOC*C*H$_3$), 53.4 (*C*HC=CH_2), 55.5 (Ar-OC*H*$_3$), 55.8 (OC*H*$_3$) 83.4 (BO*C*CH$_3$), 110.9 (aryl *C*H), 114.7 (OCCH*C*H), 114.9 (OC*C*H), 120.4 (aryl *C*H), 126.5 (aryl *C*), 127.0 (aryl *C*H), 127.6 (aryl *C*H), 128.0 (aryl *C*H), 129.9 (aryl *C*H), 129.9 (aryl *C*), 130.1 (aryl *C*H), 132.4 (C=*C*H_2), 132.9 (aryl *C*H), 141.7 (aryl *C*), 142.1 (OC(CH)$_2$*C*), 151.8 (CH_3O*C*), 157.7 (CH_3O*C*), (B*C*=CH_2 not observed); δ_B (128 MHz, $CDCl_3$) 27.6 (*B*OCCH$_3$); MS (APCI) *m/z* 564.1 (M+H$^+$); HRMS $C_{30}H_{36}O_4NBBr$ Expected 564.1915, Found 564.1907.

Rac-1S,2S-N-2-(2-Bromophenyl)-1-(4-chlorophenyl)-3-(4,4,5,5-tetramethyl-1,3,2-diox aborolan-2-yl)but-3-en-1-yl)-4-methoxyaniline **104d**



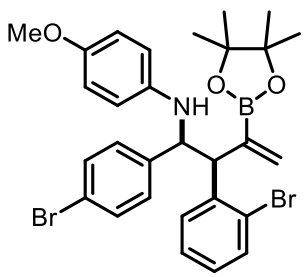
Prepared according to General Procedure A on a 0.200 mmol scale (crude ^{1}H NMR: 69%, 80:20 dr). Column chromatography (5% Et_2O in hexane) afforded the title compound as a yellow oil (68.2 mg, 0.120 mmol, 60%, 87:13 dr). ν_{max} (thin film/cm^{-1}): 2975, 2825, 1511, 1489, 1358, 1314, 1238, 1138, 1037; δ_H (400 MHz, $CDCl_3$) 1.13 (s, 6H, BOCC*H*$_3$), 1.15 (s, 6H, BOCC*H*$_3$), 3.66 (s, 3H, OC*H*$_3$), 3.76 (br. s, 1H, N*H*), 4.33 (d, *J* = 10.4 Hz, 1H, C*H*C=CH$_2$), 4.90 (d, *J* = 10.4 Hz, 1H, C*H*CHC=CH$_2$), 5.51 (d, *J* = 2.8 Hz, 1H, C=C*H*$_2$), 5.82 (d, *J* = 2.8 Hz, 1H, C=C*H*$_2$), 6.30-6.38 (m, 2H, OCC*H*), 6.58-6.67 (m, 2H, OCCHC*H*), 7.06 (td, *J* = 7.6, 1.6 Hz, 1H, aryl *H*), 7.20-7.28 (m, 3H, aryl *H*), 7.36-7.43 (m, 2H, aryl *H*), 7.56 (dd, *J* = 8.0, 1.3 Hz, 1H, aryl *H*), 7.63 (dd, *J* = 7.9, 1.7 Hz, 1H, aryl *H*); δ_C (101 MHz, $CDCl_3$) 24.8 (BOC*C*H$_3$), 24.8 (BOC*C*H$_3$), 55.8 (O*C*H$_3$), 56.6 (*C*HC=CH$_2$), 61.1 (*C*HCHC=CH$_2$), 83.7 (BO*C*CH$_3$), 114.7 (OCCH*C*H), 114.9 (OC*C*H), 126.3 (aryl *C*), 127.4 (aryl *C*H), 128.2 (aryl *C*H), 128.4 (aryl *C*H), 129.4 (aryl *C*H), 129.7 (aryl *C*H), 132.6 (aryl *C*), 133.4 (aryl *C*H), 134.0 (C=*C*H$_2$), 140.3 (aryl *C*), 141.4 (aryl *C*), 141.5 (OC(CH)$_2$*C*), 152.2 (CH$_3$O*C*), (B*C*=CH$_2$ not observed); δ_B (128 MHz, $CDCl_3$) 28.6 (*B*OCCH$_3$); MS (APCI) *m/z* 568.1 (M+H$^+$); HRMS $C_{29}H_{33}O_3NBBrCl$ Expected 568.1420, Found 568.1423.

Rac-1S,2S-N-2-(2-Bromophenyl)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-(4-(trifluoromethyl)phenyl)but-3-en-1-yl)-4-methoxyaniline **104e**



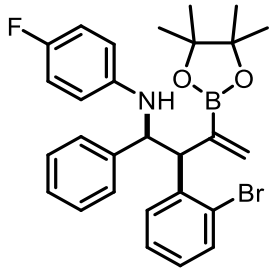
Prepared according to General Procedure A on a 0.500 mmol scale (crude ^{1}H NMR: 90%, 79:21 dr). Column chromatography (5% Et_2O in hexane) afforded the title compound as a yellow solid (246 mg, 0.410 mmol, 82%, 87:13 dr). ν_{max} (thin film/cm^{-1}): 3397, 2978, 2926, 2853, 1511, 1446, 1358, 1323, 1239, 1163, 1124, 1038; δ_H (400 MHz, $CDCl_3$) 1.11 (s, 6H, BOCC*H*$_3$), 1.12 (s, 6H, BOCC*H*$_3$), 3.66 (s, 3H, OC*H*$_3$), 3.78 (br. s, 1H, N*H*), 4.37 (d, *J* = 10.4 Hz, 1H, C*H*C=CH$_2$), 4.96 (d, *J* = 10.4 Hz, 1H, C*H*CHC=CH$_2$), 5.52 (d, *J* = 2.7 Hz, 1H, C=C*H*$_2$), 5.84 (d, *J* = 2.7 Hz, 1H, C=C*H*$_2$), 6.29-6.37 (m, 2H, OCC*H*), 6.59-6.65 (m, 2H, OCCHC*H*), 7.07 (td, *J* = 7.7, 1.7 Hz, 1H, aryl *H*), 7.26 (m, 1H, aryl *H*), 7.50-7.65 (m, 6H, aryl *H*); δ_C (101 MHz, $CDCl_3$) 24.7 (BOC*C*H$_3$), 24.8 (BOC*C*H$_3$), 55.8 (O*C*H$_3$), 56.2 (*C*HC=CH$_2$), 61.5 (*C*HCHC=CH$_2$), 83.7 (BO*C*CH$_3$), 114.8 (OCCH*C*H), 114.8 (OC*C*H), 124.4 (q, *J* = 271.6 Hz, F$_3$*C*), 125.2 (q, *J* = 3.8 Hz, CF$_3$C*C*H), 126.3 (aryl *C*), 127.5 (aryl *C*H), 128.3 (CF$_3$CCH*C*H), 128.8 (aryl *C*H), 129.3 (q, *J* = 31.6 Hz, *C*CF$_3$), 129.4 (aryl *C*H) 133.5 (aryl *C*H), 134.2 (C=*C*H$_2$), 140.2 (aryl *C*), 141.3 (OC(CH)$_2$*C*), 147.1 (CF$_3$C(CH)$_2$*C*), 152.3 (CH$_3$O*C*), (B*C*=CH$_2$ not observed); δ_B (128 MHz, $CDCl_3$) 30.2 (*B*OCCH$_3$); δ_F (376 MHz, $CDCl_3$) -62.3 (*F*$_3$C); M.p.: 89-91 ℃ (Et_2O); MS (APCI) *m/z* 602.3 (M+H$^+$); HRMS $C_{30}H_{33}O_3NBBrF_3$ Expected 602.1683, Found 602.1689.

Rac-1S,2S-N-2-(2-Bromophenyl)-1-(4-bromophenyl)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)but-3-en-1-yl)-4-methoxyaniline **104g**



Prepared according to General Procedure A on a 0.500 mmol scale (crude ^{1}H NMR: 70%, 79:21 dr). Column chromatography (5% Et_2O in hexane) afforded the title compound as a yellow solid (199 mg, 0.325 mmol, 65%, >20:1 dr). ν_{max} (thin film/cm^{-1}): 3400, 2978, 2926, 1682, 1510, 1446, 1371, 1314, 1239, 1166, 1138, 1037; δ_H (400 MHz, $CDCl_3$) 1.13 (s, 6H, BOCC*H*$_3$), 1.15 (s, 6H, BOCC*H*$_3$), 3.67 (s, 3H, OC*H*$_3$), 3.84 (br. s, 1H, N*H*), 4.32 (d, *J* = 10.4 Hz, 1H, C*H*C=CH$_2$), 4.87 (d, *J* = 10.4 Hz, 1H, C*H*CHC=CH$_2$), 5.51 (d, *J* = 2.8 Hz, 1H, C=C*H*$_2$), 5.82 (d, *J* = 2.8 Hz, 1H, C=C*H*$_2$), 6.29-6.38 (m, 2H, OCC*H*), 6.58-6.70 (m, 2H, OCCHC*H*), 7.02-7.11 (m, 1H, aryl *H*), 7.20-7.26 (m, 1H, aryl *H*), 7.32-7.36 (m, 2H, aryl *H*), 7.37-7.43 (m, 2H, aryl *H*), 7.50-7.71 (m, 2H, aryl *H*); δ_C (101 MHz, $CDCl_3$) 24.8 (BOC*C*H$_3$), 55.8 (O*C*H$_3$), 56.5 (*C*HC=CH$_2$), 61.3 (*C*HCHC=CH$_2$), 83.7 (BO*C*CH$_3$), 114.8 (OCCH*C*H), 114.9 (OC*C*H), 120.9 (aryl *C*), 126.3 (aryl *C*), 127.5 (aryl *C*H), 128.2 (aryl *C*H), 129.5 (aryl *C*H), 130.2 (aryl *C*H), 131.4 (aryl *C*H), 133.4 (aryl *C*H), 134.0 (C=*C*H$_2$), 140.4 (aryl *C*), 141.5 (aryl *C*), 141.9 (OC(CH)$_2$*C*), 152.3 (CH$_3$O*C*), (B*C*=CH$_2$ not observed); δ_B (128 MHz, $CDCl_3$) 30.2 (*B*OCCH$_3$); M.p.: 79-82 ℃ (Et_2O); MS (APCI) *m/z* 612.2 (M+H$^+$); HRMS $C_{29}H_{32}O_3NBBr_2Na$ Expected 634.0734, Found 634.0716.

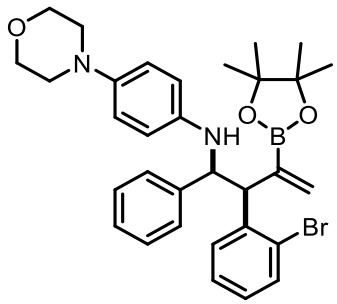
Rac-1S,2S-N-(2-(2-Bromophenyl)-1-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)but-3-en-1-yl)-4-fluoroaniline **105a**



Prepared according to General Procedure A on a 1.000 mmol scale (crude ^{1}H NMR: 95%, 79:21 dr). Column chromatography (5% Et_2O in hexane) afforded the title compound as a yellow solid (339 mg, 0.65 mmol, 65%, >20:1 dr). ν_{max} (thin film/cm^{-1}): 3411, 2976, 2929, 1612, 1454, 1357, 1264, 1166, 1137; δ_H (500 MHz, $CDCl_3$) 1.14 (s, 6H, BOCC*H*$_3$), 1.16 (s, 6H, BOCC*H*$_3$), 3.90 (br. s, 1H, N*H*), 4.40 (d, *J* = 10.4 Hz, 1H,

C*H*C=CH_2), 4.99 (d, *J* = 10.4 Hz, 1H, C*H*CHC=CH_2), 5.53 (d, *J* = 2.9 Hz, 1H, C=C*H*$_2$), 5.79 (d, *J* = 2.8 Hz, 1H, C=C*H*$_2$), 6.30-6.38 (m, 2H, FCC*H*), 6.65-6.79 (m, 2H, FCCHC*H*), 7.01-7.08 (m, 1H, aryl *H*), 7.17-7.35 (m, 4H, aryl *H*), 7.41-7.46 (m, 2H, aryl *H*), 7.55 (dd, *J* = 8.0, 1.3 Hz, 1H, aryl *H*), 7.68 (dd, *J* = 7.9, 1.7 Hz, 1H, aryl *H*); δ_C (126 MHz, $CDCl_3$) 24.7 (BOC*C*H_3), 24.9 (BOC*C*H_3), 57.1 (*C*HC=CH_2), 61.3 (*C*HCHC=CH_2), 83.7 (BO*C*CH_3), 114.3 (d, *J* = 7.2 Hz, FCCH*C*H), 115.4 (d, *J* = 22.3 Hz, FC*C*H), 126.3 (aryl *C*), 127.2 (aryl *C*H), 127.4 (aryl *C*H), 128.2 (aryl *C*H), 128.2 (aryl *C*H), 128.3 (aryl *C*H), 129.6 (aryl *C*H), 133.3 (aryl *C*H), 133.8 (C=*C*H_2), 140.5 (aryl *C*), 142.4 (aryl *C*), 143.9 (d, *J* = 1.9 Hz, FC(CH)$_2$*C*), 155.7 (d, *J* = 235.6 Hz, F*C*), (B*C*=CH_2 not observed); δ_B (128 MHz, $CDCl_3$) 31.9 (*B*OCCH$_3$); δ_F (376 MHz, $CDCl_3$) -128.2 (*F*C); M.p.: 55-57 ℃ (Et_2O); MS (APCI) *m/z* 522.2 ($M+H^+$); HRMS $C_{28}H_{31}O_2NBBrF$ Expected 522.1610, Found 522.1607.

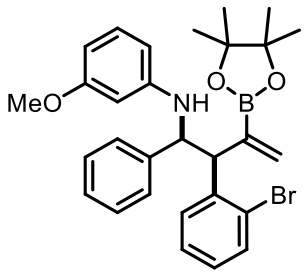
Rac-1S,2S-N-((1S,2S)-2-(2-Bromophenyl)-1-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)but-3-en-1-yl)-4-morpholinoaniline **105b**



Prepared according to General Procedure A on a 1.000 mmol scale (crude ^{1}H NMR: 74%, 82:18 dr). Column chromatography (20% Et_2O in hexane) afforded the title compound as a yellow solid (295 mg, 0.5 mmol, 50%, >20:1 dr). ν_{max} (thin film/cm^{-1}): 3399, 2975, 2856, 1615, 1450, 1359, 1266, 1166, 1139; δ_H (400 MHz, $CDCl_3$) 1.13 (s, 6H, BOCC*H*$_3$), 1.15 (s, 6H, BOCC*H*$_3$), 2.89-2.97 (m, 4H, N(C*H*$_2$)$_2$), 3.75-3.84 (m, 4H, O(C*H*$_2$)$_2$), 3.82 (br. s, 1H, N*H*), 4.37 (d, *J* = 10.3 Hz, 1H, C*H*C=CH_2), 4.97 (d, *J* = 10.4 Hz, 1H, C*H*CHC=CH_2), 5.51 (d, *J* = 2.9 Hz, 1H, C=C*H*$_2$), 5.77 (d, *J* = 2.9 Hz, 1H, C=C*H*$_2$), 6.34-6.42 (m, 2H, CH_2NCCHC*H*), 6.60-6.73 (m, 2H, CH_2NCC*H*), 7.02-7.08 (m, 1H, aryl *H*), 7.14-7.28 (m, 4H, aryl *H*), 7.41-7.47 (m, 2H, aryl *H*), 7.55 (dd, *J* = 8.0, 1.3 Hz, 1H, aryl *H*), 7.68 (dd, *J* = 7.8, 1.7 Hz, 1H, aryl *H*); δ_C (101 MHz, $CDCl_3$) 24.7 (BOC*C*H_3), 24.9

(BOCCH_3), 51.2 (N(CH_2)$_2$), 57.1 (CHC=CH_2), 61.2 (CHCHC=CH_2), 67.2 (O(CH_2)$_2$), 83.6 (BOCCH$_3$), 114.6 (CH_2NCCHCH), 118.1 (CH_2NCCH), 126.4 (aryl C), 127.0 (aryl CH), 127.4 (aryl CH), 128.1 (aryl CH), 128.3 (aryl CH), 128.3 (aryl CH), 129.7 (aryl CH), 133.3 (aryl CH), 133.7 (C=CH$_2$), 140.6 (aryl C), 142.2 (aryl C), 142.8 (CH_2NC(CH)$_2$$C$), 143.4 ($CH_2NC$), (B$C$=$CH_2$ not observed); δ_B (128 MHz, $CDCl_3$) 29.3 (BOCCH$_3$); M.p.: 113-115 ℃ (Et_2O); MS (APCI) *m/z* 589.2 ($M+H^+$); HRMS $C_{32}H_{39}O_3N_2BBr$ Expected 589.2232, Found 589.2236.

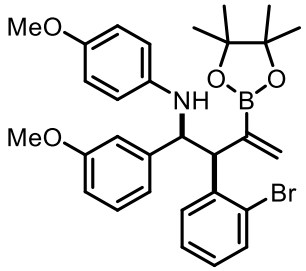
Rac-1S,2S-N-(2-(2-Bromophenyl)-1-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)but-3-en-1-yl)-3-methoxyaniline **105c**



Prepared according to General Procedure A on a 1.000 mmol scale (crude ^{1}H NMR: 89%, 75:25 dr). Column chromatography (5% Et_2O in hexane) afforded the title compound as a yellow solid (213 mg, 0.400 mmol, 40%, 75:25 dr). ν_{max} (thin film/cm^{-1}): 3407, 2976, 2833, 1612, 1453, 1357, 1269, 1161, 1138; δ_H (400 MHz, $CDCl_3$) 1.10 (s, 6H, BOCCH_3 **minor**), 1.13 (s, 6H, BOCCH_3 **major**), 1.16 (s, 6H, BOCCH_3 **major**), 1.17 (s, 6H, BOCCH_3 **minor**), 3.63 (s, 3H, OCH_3 **major**), 3.66 (s, 3H, OCH_3 **minor**), 4.03 (s, 2H, NH **major** + NH **minor**), 4.38 (d, J = 10.3 Hz, 1H, CHC=CH_2 **major**), 4.52 (d, J = 10.3 Hz, 1H, CHC=CH_2 **minor**), 4.99 (d, J = 10.5 Hz, 1H, CHCHC=CH_2 **minor**), 5.05 (d, J = 10.5 Hz, 1H, CHCHC=CH_2 **major**), 5.53 (d, J = 2.9 Hz, 1H, C=CH_2 **major**), 5.79 (d, J = 2.9 Hz, 1H, C=CH_2 **major**), 5.86 (d, J = 2.9 Hz, 1H, C=CH_2 **minor**), 5.99 (t, 1H, aryl H **major**), 6.04 (d, J = 2.9 Hz, 1H, C=CH_2 **minor**), 6.05 (d, J = 1.9 Hz, 1H, aryl H **minor**), 6.09 (t, J = 2.3 Hz, 1H, aryl H **minor**), 6.11-6.20 (m, 3H, 1 aryl H **major** + 2 aryl H **minor**), 6.85-6.97 (m, 3H, 1 aryl H **major** + 2 aryl H **minor**), 7.01-7.13 (m, 3H, 2 aryl H **major** + 2 aryl H **minor**), 7.14-7.30 (m, 7H, 4 aryl H **major** + 3 aryl H **minor**), 7.33

(dd, *J* = 8.0, 1.3 Hz, 1H, aryl *H* **minor**), 7.41-7.47 (m, 2H, aryl *H* **major**), 7.55 (dd, *J* = 8.0, 1.3 Hz, 1H, aryl *H* **major**), 7.69 (dd, *J* = 7.9, 1.7 Hz, 1H, aryl *H* **major**), 7.81 (dd, *J* = 7.9, 1.7 Hz, 1H, aryl *H* **minor**); δ_C (101 MHz, $CDCl_3$) 24.7 (BOC*C*H_3 **minor**), 24.7 (BOC*C*H_3 **major**), 24.8 (BOC*C*H_3 **minor**), 24.9 (BOC*C*H_3 **major**), 55.0 (O*C*H_3 **major**), 55.0 (O*C*H_3 **minor**), 56.4 (*C*HC=CH_2 **minor**), 57.0 (*C*HC=CH_2 **major**), 60.6 (*C*HCHC=CH_2 **major** + *C*HCHC=CH_2 **minor**), 83.6 (BO*C*CH_3 **major**), 83.8 (BO*C*CH_3 **minor**), 99.5 (aryl *C*H **major**), 102.6 (aryl *C*H, **major**), 106.8 (aryl *C*H **major** + aryl *C*H **minor**), 125.6 (aryl *C* **minor**), 126.3 (aryl *C* **major**), 126.8 (aryl *C*H **minor**), 127.1 (aryl *C*H **major**), 127.2 (aryl *C*H **minor**), 127.3 (aryl *C*H **minor**), 127.4 (aryl *C*H **major**), 127.6 (aryl *C*H **major**), 127.7 (aryl *C*H **minor**), 128.0 (aryl *C*H **minor**), 128.1 (aryl *C*H **minor**), 128.2 (aryl *C*H **major**), 128.3 (aryl *C*H **major**), 129.7 (aryl *C*H **major** + aryl *C*H **minor**), 129.7 (aryl *C*H **major** + aryl *C*H **minor**), 130.3 (aryl *C*H **minor**), 132.8 (aryl *C*H **minor**), 132.9 (C=*C*H_2 **minor**), 133.3 (aryl *C*H **major**), 133.8 (C=*C*H_2 **major**), 140.5 (aryl *C* **major**), 141.5 (aryl *C* **minor**), 141.9 (aryl *C* **minor**), 142.5 (aryl *C* **major**), 148.7 (aryl *C* **minor**), 148.8 (aryl *C* **major**), 160.6 (CH_3O*C* **major**) 160.6 (CH_3O*C* **minor**), (B*C*=CH_2 not observed); δ_B (128 MHz, $CDCl_3$) 30.5 (*B*OCCH_3 **major** + *B*OCCH_3 **minor**); M.p.: 61-62 ℃ (Et_2O); MS (APCI) *m/z* 534.2 ($M+H^+$); HRMS $C_{29}H_{34}O_3NBBr$ Expected 534.1810, Found 534.1811.

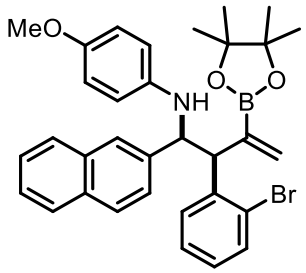
Rac-1S,2S-N-(2-(2-Bromophenyl)-1-(3-methoxyphenyl)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)but-3-en-1-yl)-4-methoxyaniline **104f**



Prepared according to General Procedure A on a 1.000 mmol scale (crude ^{1}H NMR: 99%, 75:25 dr). Column chromatography (5% Et_2O in hexane) afforded the title compound as a yellow solid (395 mg, 0.7 mmol, 70%, >20:1 dr). ν_{max} (thin film/cm^{-1}):

3409, 2976, 2883, 1633, 1468, 1358, 1241, 1166, 1138; δ_H (400 MHz, $CDCl_3$) 1.15 (s, 6H, BOCC*H*$_3$), 1.17 (s, 6H, BOCC*H*$_3$), 3.67 (s, 3H, OC*H*$_3$), 3.78 (s, 3H, OC*H*$_3$), 4.37 (d, *J* = 10.3 Hz, 1H, C*H*C=CH$_2$), 4.93 (d, *J* = 10.3 Hz, 1H, C*H*CHC=CH$_2$), 5.53 (d, *J* = 2.9 Hz, 1H, C=C*H*$_2$), 5.79 (d, *J* = 2.9 Hz, 1H, C=C*H*$_2$), 6.32-6.45 (m, 2H, OCC*H*), 6.57-6.67 (m, 2H, OCCHC*H*), 6.67-6.77 (m, 1H, aryl *H*), 6.95-7.09 (m, 3H, aryl *H*), 7.13-7.28 (m, 2H, aryl *H*), 7.55 (dd, *J* = 8.0, 1.3 Hz, 1H, aryl *H*), 7.67 (dd, *J* = 7.8, 1.7 Hz, 1H, aryl *H*), (N*H* not observed); δ_C (101 MHz, $CDCl_3$) 24.8 (BOC*C*H$_3$), 24.9 (BOC*C*H$_3$), 55.2 (O*C*H$_3$), 55.8 (O*C*H$_3$), 57.0 (*C*HC=CH$_2$), 61.5 (*C*HCHC=CH$_2$), 83.6 (BO*C*CH$_3$), 112.3 (aryl *C*H), 114.0 (aryl *C*H), 114.7 (NHC*C*H), 114.8 (NHCCH*C*H), 120.8 (aryl *C*H), 126.4 (aryl *C*), 127.4 (aryl *C*H), 128.1 (aryl *C*H), 129.1 (aryl *C*H), 129.7 (aryl *C*H), 133.3 (aryl *C*H), 133.5 (C=*C*H$_2$), 140.6 (aryl *C*), 142.0 (aryl *C*), 144.6 (aryl *C*), 152.0 (aryl *C*), 159.7 (aryl *C*), (B*C*=CH$_2$ not observed); δ_B (128 MHz, $CDCl_3$) 30.7 (*B*OCCH$_3$); M.p.: 100-102 ℃ (Et_2O); MS (APCI) *m/z* 550.2; HRMS $C_{30}H_{36}O_4NBBr$ Expected 564.1915, Found 564.1919.

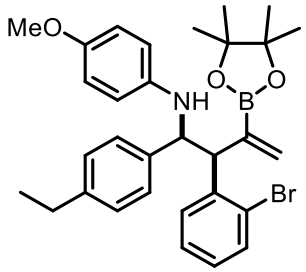
Rac-1S,2S-N-(2-(2-Bromophenyl)-1-(naphthalen-2-yl)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)but-3-en-1-yl)-4-methoxyaniline **104i**



Prepared according to General Procedure A on a 1.000 mmol scale (crude ^{1}H NMR: 95%, 78:22 dr). Column chromatography (5% Et_2O in hexane) afforded the title compound as a yellow solid (362 mg, 0.61 mmol, 61%, >20:1 dr). ν_{max} (thin film/cm^{-1}): 3404, 2976, 2831, 1693, 1460, 1358, 1237, 1169, 1138; δ_H (400 MHz, $CDCl_3$) 1.06 (s, 6H, BOCC*H*$_3$), 1.10 (s, 6H, BOCC*H*$_3$), 3.65 (s, 3H, OC*H*$_3$), 3.91 (br. s, 1H, N*H*), 4.52 (d, *J* = 10.5 Hz, 1H, C*H*C=CH$_2$), 5.16 (d, *J* = 10.6 Hz, 1H, C*H*CHC=CH$_2$), 5.55 (d, *J* = 2.9 Hz, 1H, C=C*H*$_2$), 5.78 (d, *J* = 2.9 Hz, 1H, C=C*H*$_2$), 6.40-6.47 (m, 2H, OCC*H*), 6.53-6.68 (m, 2H,

OCCHC*H*), 7.05-7.12 (m, 1H, aryl *H*), 7.26-7.33 (m, 1H, aryl *H*), 7.41-7.50 (m, 2H, aryl *H*), 7.55-7.68 (m, 2H, aryl *H*), 7.74-7.83 (m, 4H, aryl *H*), 7.94-7.99 (m, 1H, aryl *H*); δ_C (101 MHz, $CDCl_3$), 24.7 (BOC*C*H_3), 55.7 (O*C*H_3), 56.9 (*C*HC=CH_2), 61.8 (*C*HCHC=CH_2), 83.5 (BO*C*CH_3), 114.7 (OCCH*C*H), 114.9 (OC*C*H), 125.5 (aryl *C*H), 125.8 (aryl *C*H), 126.3 (aryl *C*H), 126.4 (aryl *C*), 127.5 (aryl *C*H), 127.5 (aryl *C*H), 127.7 (aryl *C*H), 128.0 (aryl C*H*), 128.1 (aryl *C*H), 128.1 (aryl *C*H), 129.6 (aryl *C*H), 133.0 (aryl *C*), 133.3 (aryl *C*H), 133.5 (aryl *C*), 133.8 (C=*C*H_2), 140.4 (aryl *C*), 140.7 (aryl *C*), 141.9 (OC(CH)$_2$*C*), 152.1 (CH_3O*C*), (B*C*=CH_2 not observed); δ_B (128 MHz, $CDCl_3$) 31.4 (*B*OCCH_3); M.p.: 57-58 ℃ (Et_2O); MS (APCI) *m/z* 584.2 ($M+H^+$); HRMS $C_{33}H_{36}O_3NBBr$ Expected 584.1966, Found 584.1969.

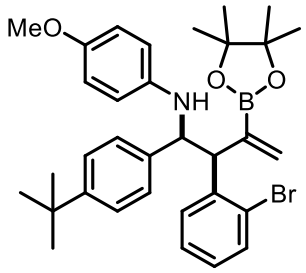
Rac-1S,2S-N-(2-(2-Bromophenyl)-1-(4-ethylphenyl)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)but-3-en-1-yl)-4-methoxyaniline **104j**



Prepared according to General Procedure A on a 1.000 mmol scale (crude ^{1}H NMR: 84%, 87:13 dr). Column chromatography (5% Et_2O in hexane) afforded the title compound as a yellow solid (366 mg, 0.65 mmol, 65%, >20:1 dr). ν_{max} (thin film/cm^{-1}): 3400, 2974, 2831, 1702, 1466, 1358, 1237, 1166, 1138; δ_H (400 MHz, $CDCl_3$) 1.13 (s, 6H, BOCC*H*$_3$), 1.15 (s, 6H, BOCC*H*$_3$), 1.21 (td, *J* = 7.3, 2.5 Hz, 3H, CH_2CH_3), 2.60 (q, *J* = 7.6 Hz, 2H, C*H*$_2$CH$_3$), 3.66 (s, 3H, OC*H*$_3$), 3.74 (br. s, 1H, N*H*), 4.38 (d, *J* = 10.4 Hz, 1H, C*H*C=CH_2), 4.90 (d, *J* = 10.4 Hz, 1H, C*H*CHC=CH_2), 5.52 (d, *J* = 2.9 Hz, 1H, C=C*H*$_2$), 5.80 (d, *J* = 2.9 Hz, 1H, C=C*H*$_2$), 6.32-6.41 (m, 2H, OCC*H*), 6.57-6.66 (m, 2H, OCCHC*H*), 6.99-7.11 (m, 3H, aryl *H*), 7.19-7.29 (m, 1H, aryl *H*), 7.33-7.38 (m, 2H, aryl *H*), 7.55 (dd, *J* = 8.0, 1.3 Hz, 1H, aryl *H*), 7.66 (dd, *J* = 7.9, 1.7 Hz, 1H, aryl *H*); δ_C (101 MHz, $CDCl_3$) 15.4 (CH_2CH_3), 24.8 (BOC*C*H_3), 24.9 (BOC*C*H_3), 28.6 (*C*H_2CH$_3$) 55.8 (O*C*H_3), 56.6

(*C*HC=CH_2), 61.3 (*C*HCHC=CH_2), 83.5 (BO*C*CH_3), 114.6 (OCCH*C*H), 114.7 (OC*C*H), 126.3 (aryl *C*), 127.3 (aryl *C*H), 127.7 (aryl *C*H), 128.0 (aryl *C*H), 128.2 (aryl *C*H), 129.6 (aryl *C*H), 133.3 (aryl *C*H), 133.5 (C=*C*H_2), 139.7 (aryl *C*), 140.9 (aryl *C*), 142.0 (OC(CH)$_2$*C*), 142.6 (CH_3CH_2*C*), 151.9 (CH_3O*C*), (B*C*=CH_2 not observed); δ_B (128 MHz, $CDCl_3$) 30.8 (*B*OCCH_3); M.p.: 63-65 ℃ (Et_2O); MS (APCI) *m/z* 562.2 ($M+H^+$); HRMS $C_{31}H_{38}O_3NBBr$ Expected 562.2123, Found 562.2125.

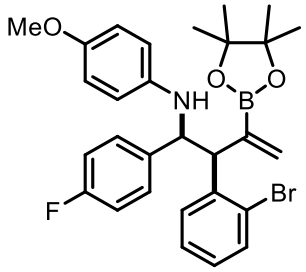
Rac-1S,2S-N-(2-(2-Bromophenyl)-1-(4-(tert-butyl)phenyl)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)but-3-en-1-yl)-4-methoxyaniline **104k**



Prepared according to General Procedure A on a 1.000 mmol scale (crude ^{1}H NMR: 92%, 90:10 dr). Column chromatography (5% Et_2O in hexane) afforded the title compound as a yellow solid (472 mg, 0.8 mmol, 80%, >20:1 dr). ν_{max} (thin film/cm^{-1}): 3408, 2966, 2831, 1697, 1465, 1358, 1237, 1166, 1137; δ_H (400 MHz, $CDCl_3$) 1.12 (s, 6H, BOCCH_3), 1.13 (s, 6H, BOCCH_3), 1.29 (s, 9H, C(CH_3)$_3$), 3.67 (s, 3H, OCH_3), 3.79 (br. s, 1H, N*H*), 4.41 (d, *J* = 10.4 Hz, 1H, C*H*C=CH_2), 4.88 (d, *J* = 10.4 Hz, 1H, C*H*CHC=CH_2), 5.54 (d, *J* = 2.8 Hz, 1H, C=CH_2), 5.82 (d, *J* = 2.8 Hz, 1H, C=CH_2), 6.32-6.42 (m, 2H, OCC*H*), 6.57-6.67 (m, 2H, OCCHC*H*), 6.99-7.09 (m, 1H, aryl *H*), 7.16-7.30 (m, 3H, aryl *H*), 7.31-7.39 (m, 2H, aryl *H*), 7.55 (dd, *J* = 8.0, 1.3 Hz, 1H, aryl *H*), 7.61 (dd, *J* = 7.9, 1.7 Hz, 1H, aryl *H*); δ_C (101 MHz, $CDCl_3$) 24.8 (BOC*C*H_3), 24.9 (BOC*C*H_3), 31.6 (C(*C*H_3)$_3$), 34.5 (*C*(CH$_3$)$_3$), 55.8 (O*C*H_3), 56.2 (*C*HC=CH_2), 61.4 (*C*HCHC=CH_2), 83.5 (BO*C*CH_3), 114.6 (OCCH*C*H), 114.7 (OC*C*H), 125.1 (aryl *C*H), 126.3 (aryl *C*), 127.3 (aryl *C*H), 128.0 (aryl *C*H), 128.0 (aryl *C*H), 129.6 (aryl *C*H), 133.3 (aryl *C*H), 133.4 (C=*C*H_2), 139.4 (aryl *C*), 141.0 (aryl *C*), 142.0 (OC(CH)$_2$*C*), 149.5 (*C*C(CH$_3$)$_3$), 151.9 (CH_3O*C*), (B*C*=CH_2 not observed); δ_B (128 MHz, $CDCl_3$) 31.2 (*B*OCCH_3); M.p.: 85-87 ℃ (Et_2O); MS (APCI)

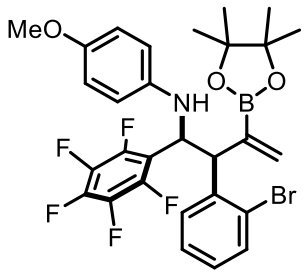
m/z 590.2 ($M+H^+$); HRMS $C_{33}H_{42}O_3NBBr$ Expected 590.2436, Found 590.2441.

Rac-1S,2S-N-(2-(2-Bromophenyl)-1-(4-fluorophenyl)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)but-3-en-1-yl)-4-methoxyaniline **104l**



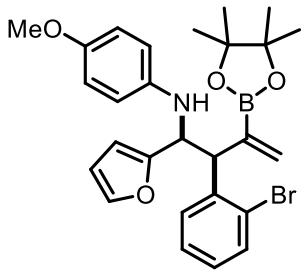
Prepared according to General Procedure A on a 1.000 mmol scale (crude ^1H NMR: 94%, 82:18 dr). Column chromatography (5% Et_2O in hexane) afforded the title compound as a yellow solid (353 mg, 0.64 mmol, 64%, >20:1 dr). ν_{max} (thin film/cm^{-1}): 3404, 2977, 2831, 1603, 1466, 1357, 1236, 1166, 1136; δ_H (400 MHz, $CDCl_3$) 1.14 (s, 6H, BOCCH_3), 1.16 (s, 6H, BOCCH_3), 3.66 (s, 3H, OCH_3), 3.75 (br. s, 1H, N*H*), 4.34 (d, *J* = 10.3 Hz, 1H, C*H*C=CH_2), 4.94 (d, *J* = 10.3 Hz, 1H, C*H*CHC=CH_2), 5.52 (d, *J* = 2.9 Hz, 1H, C=CH_2), 5.81 (d, *J* = 2.9 Hz, 1H, C=CH_2), 6.31-6.40 (m, 2H, OCC*H*), 6.58-6.67 (m, 2H, OCCHC*H*), 6.92-7.01 (m, 2H, aryl *H*), 7.03-7.07 (m, 1H, aryl *H*), 7.20-7.28 (m, 1H, aryl *H*), 7.37-7.46 (m, 2H, aryl *H*), 7.55 (dd, *J* = 7.9, 1.3 Hz, 1H, aryl *H*), 7.66 (dd, *J* = 7.9, 1.7 Hz, 1H, aryl *H*); δ_C (101 MHz, $CDCl_3$) 24.7 (BOC*C*H_3), 24.8 (BOC*C*H_3), 55.7 (O*C*H_3), 56.9 (*C*HC=CH_2), 60.9 (*C*HCHC=CH_2), 83.6 (BO*C*CH_3), 114.6 (OCCH*C*H), 114.8 (OC*C*H), 114.9 (d, *J* = 21.0 Hz, FC*C*H), 126.3 (aryl *C*), 127.4 (aryl *C*H), 128.1 (aryl *C*H), 129.4 (aryl *C*H), 129.7 (d, *J* = 7.9 Hz, FCCH*C*H), 133.3 (aryl *C*H), 133.8 (C=*C*H_2), 138.4 (d, *J* = 3.0 Hz, FC$(CH)_2$*C*), 140.4 (aryl *C*), 141.6 (OC$(CH)_2$*C*), 152.1 (CH_3O*C*), 161.9 (d, *J* = 243 Hz, F*C*), (B*C*=CH_2 not observed); δ_B (128 MHz, $CDCl_3$) 32.1 (*B*OCCH_3); δ_F (376 MHz, $CDCl_3$) -116.17 (*F*C); M.p.: 94-97 ℃ (Et_2O); MS (APCI) *m/z* 552.2 ($M+H^+$); HRMS $C_{29}H_{33}O_3NFBBr$ Expected 552.1715, Found 552.1721.

Rac-1S,2S-N-(2-(2-Bromophenyl)-1-(perfluorophenyl)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)but-3-en-1-yl)-4-methoxyaniline **104h**



Prepared according to General Procedure A on a 1.00 mmol scale (crude ^{1}H NMR: 81%, 76:24 dr). Column chromatography (5% Et_2O in hexane) afforded the title compound as a yellow solid (380 mg, 0.61 mmol, 61%, >20:1 dr). ν_{max} (thin film/cm^{-1}): 3393, 2978, 2833, 1651, 1468, 1357, 1241, 1168, 1138; δ_H (400 MHz, $CDCl_3$) 1.15 (s, 12H, BOCC*H*$_3$), 3.69 (s, 3H, OC*H*$_3$), 3.79 (br. s, 1H, N*H*), 4.75 (d, *J* = 11.2 Hz, 1H, C*H*C=CH$_2$), 5.47 (d, *J* = 11.2 Hz, 1H, C*H*CHC=CH$_2$), 5.76 (d, *J* = 2.6 Hz, 1H, C=C*H*$_2$), 5.90 (d, *J* = 2.6 Hz, 1H, C=C*H*$_2$), 6.46-6.59 (m, 2H, OCC*H*), 6.65-6.77 (m, 2H, OCCHC*H*), 7.02-7.07 (m, 1H, aryl *H*), 7.20-7.31 (m, 1H, aryl *H*), 7.54 (dd, *J* = 8.0, 1.3 Hz, 1H, aryl *H*), 7.61 (dd, *J* = 7.9, 1.6 Hz, 1H, aryl *H*); δ_C (101 MHz, $CDCl_3$), 24.6 (BOC*C*H$_3$), 24.8 (BOC*C*H$_3$), 52.2 (*C*HC=CH$_2$), 53.2 (*C*HCHC=CH$_2$), 55.8 (O*C*H$_3$), 83.8 (BO*C*CH$_3$), 114.5 (OC*C*H), 115.1 (OCCH*C*H), 126.0 (aryl *C*), 127.2 (aryl *C*H), 128.2 (aryl *C*H), 129.3 (aryl *C*H), 133.2 (aryl *C*H), 134.5 (C=*C*H$_2$), 140.0 (aryl *C*), 140.3 (OC(CH)$_2$*C*), 152.8 (CH$_3$O*C*), (*C*F, B*C*=CH$_2$ not observed); δ_B (128 MHz, $CDCl_3$) 31.9 (*B*OCCH$_3$); δ_F (376 MHz, $CDCl_3$) -155.99 (*F*C); M.p.: 59-61 ℃ (Et_2O); MS (APCI) *m/z* 625.0 (M+H$^+$); HRMS $C_{29}H_{29}O_3NF_5BBr$ Expected 624.1339, Found 624.1341.

Rac-1S,2S-N-(2-(2-Bromophenyl)-1-(furan-2-yl)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)but-3-en-1-yl)-4-methoxyaniline **104m**

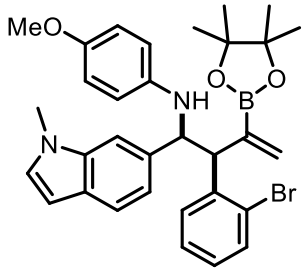


Prepared according to General Procedure A on a 1.000 mmol scale (crude ^{1}H NMR: 71%, 70:30 dr). Column chromatography (15% Et_2O in hexane) afforded the title

compound as a yellow solid (380 mg, 0.38 mmol, 38%, 70:30 dr). ν_{max} (thin film/cm^{-1}): 3387, 2976, 2831, 1609, 1467, 1358, 1238, 1166, 1137; δ_H (400 MHz, $CDCl_3$) 1.16 (s, 6H, BOCC*H*$_3$ **minor**), 1.20 (s, 6H, BOCC*H*$_3$ **minor**), 1.22 (s, 6H, BOCC*H*$_3$ **major**), 1.23 (s, 6H, BOCC*H*$_3$ **major**), 3.69 (s, 3H, OC*H*$_3$ **major**), 3.72 (s, 3H, OC*H*$_3$ **minor**), 4.60 (d, *J* = 10.4 Hz, 1H, C*H*C=CH$_2$ **major**), 4.69 (d, *J* = 10.4 Hz, 1H, C*H*C=CH$_2$ **minor**), 5.11 (d, *J* = 10.4 Hz, 1H, C*H*CHC=CH$_2$ **minor**), 5.23 (d, *J* = 10.4 Hz, 1H, C*H*CHC=CH$_2$ **major**), 5.75 (d, *J* = 3.0 Hz, 1H, C=C*H*$_2$ **major**), 5.82 (d, *J* = 3.2 Hz, 2H, C=C*H*$_2$ **major** + C=C*H*$_2$ **minor**), 5.93 (d, *J* = 3.0 Hz, 1H, furan *H* **minor**), 5.99 (d, *J* = 3.0 Hz, 1H, C=C*H*$_2$ **minor**), 6.09 (dd, *J* = 3.3, 1.8 Hz, 1H, furan *H* **minor**), 6.20 (d, *J* = 3.2 Hz, 1H, furan *H* **major**), 6.24 (dd, *J* = 3.2, 1.8 Hz, 1H, furan *H* **major**), 6.54 (m, 2H, OCC*H* **major**), 6.60-6.74 (m, 6H, OCCHC*H* **major** + OCCHC*H* **minor** + OCC*H* **minor**), 6.94-7.08 (m, 2H, 1 aryl *H* **major** + 1 aryl *H* **minor**), 7.19 (dd, *J* = 1.8, 0.9 Hz, 1H, furan *H* **minor**), 7.20-7.27 (m, 2H, 1 aryl *H* **major** + 1 aryl *H* **minor**), 7.33 (dd, *J* = 1.8, 0.9 Hz, furan *H* **major**), 7.45 (dd, *J* = 8.0, 1.3 Hz, 1H, aryl *H* **minor**), 7.55 (dd, *J* = 8.0, 1.3 Hz, 1H, aryl *H* **major**), 7.69 (dd, *J* = 7.9, 1.7 Hz, 1H, aryl *H* **major**), 7.73 (dd, *J* = 7.9, 1.7 Hz, 1H, aryl *H* **minor**); δ_C (101 MHz, $CDCl_3$) 24.7 (BOC*C*H$_3$ **minor**), 24.8 (BOC*C*H$_3$ **major**), 24.9 (BOC*C*H$_3$ **major**), 24.9 (BOC*C*H$_3$ **minor**), 53.8 (*C*HC=CH$_2$ **minor**), 54.9 (*C*HC=CH$_2$ **major**), 55.5 (*C*HCHC=CH$_2$ **major**), 55.6 (*C*HCHC=CH$_2$ **minor**), 55.7 (O*C*H$_3$ **major**), 55.8 (O*C*H$_3$ **minor**), 83.6 (BO*C*CH$_3$ **major**), 83.7 (BO*C*CH$_3$ **minor**), 107.1 (furan *C*H **minor**), 108.0 (furan *C*H **major**), 109.9 (furan *C*H **major**), 110.0 (furan *C*H **minor**), 114.6 (OCCH*C*H **major** + OCCH*C*H **minor**), 115.2 (OC*C*H **major**), 115.4 (OC*C*H **minor**), 125.3 (aryl *C* **minor**), 126.1 (aryl *C* **major**), 127.2 (aryl *C*H, **minor**), 127.3 (aryl *C*H **major**), 127.7 (aryl *C*H **minor**), 128.0 (aryl *C*H **major**), 129.3 (aryl *C*H **major**), 129.8 (aryl *C*H **minor**), 132.3 (C=*C*H$_2$ **minor**), 132.9 (C=*C*H$_2$ **major**), 133.0 (aryl *C*H **minor**), 133.1 (aryl *C*H **major**), 140.5 (aryl *C* **major**), 141.3 (furan *C*H **minor**), 141.4 (furan *C*H **major**), 141.5 (aryl *C* **minor**), 141.6 (OC(CH)$_2$*C* **minor** + OC(CH)$_2$*C* **major**), 152.4 (CH$_3$O*C* **major**), 152.4 (CH$_3$O*C* **minor**), 154.9 (furan *C* **minor**), 155.0 (furan *C* **major**) (B*C*=CH$_2$ not observed); δ_B (128 MHz, $CDCl_3$) 29.9 (*B*OCCH$_3$ **major** + *B*OCCH$_3$ **minor**); M.p.: 101-102 ℃ (Et_2O); MS (APCI) *m/z* 524.2 ($M+H^+$); HRMS $C_{27}H_{32}BBrNO_4$ Expected 524.1602, Found

524.1607.

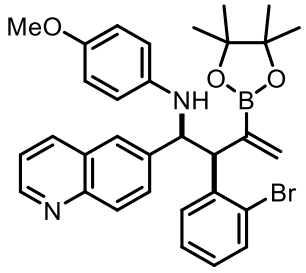
Rac-1S,2S-N-(2-(2-Bromophenyl)-1-(1-methyl-1H-indol-6-yl)-3-(4,4,5,5-tetramethyl-1, 3,2-dioxaborolan-2-yl)but-3-en-1-yl)-4-methoxyaniline **104n**



Prepared according to General Procedure A on a 1.00 mmol scale (crude ^{1}H NMR: 56%, 75:25 dr). Column chromatography (30% Et_2O in hexane) afforded the title compound as a yellow solid (287 mg, 0.9800 mmol, 49%, 80:20 dr). ν_{max} (thin film/cm^{-1}): 3398, 2976, 2831, 1611, 1467, 1356, 1238, 1166, 1138; δ_H (400 MHz, $CDCl_3$) 1.02 (s, 6H, BOCCH_3 **major**), 1.05 (s, 6H, BOCCH_3 **major**), 1.08 (s, 6H, BOCCH_3 **minor**), 1.14 (s, 6H, BOCCH_3 **minor**), 3.64 (s, 6H, NCH_3 **major** + NCH_3 **minor**), 3.66 (s, 3H, OCH_3 **minor**), 3.76 (s, 3H, OCH_3 **major**), 4.44 (d, *J* = 10.4 Hz, 1H, C*H*C=CH_2 **major**), 4.62 (d, *J* = 10.4 Hz, 1H, C*H*C=CH_2 **minor**), 4.98-5.05 (m, 2H, C*H*CHC=CH_2 **major** + C*H*CHC=CH_2 **minor**), 5.47 (d, *J* = 2.9 Hz, 1H, C=CH_2 **major**), 5.75 (d, *J* = 3.0 Hz, 1H, C=CH_2 **major**), 5.81 (d, *J* = 2.9 Hz, 1H, C=CH_2 **minor**), 5.99 (d, *J* = 3.0 Hz, 1H, C=CH_2 **minor**), 6.32 (dd, *J* = 3.0, 0.8 Hz, 1H, aryl *H* **minor**), 6.36-6.46 (m, 3H, OCC*H* **major** + aryl *H* **major**), 6.47-6.68 (m, 6H, OCC*H* **minor** + OCCHC*H* **major** + OCCHC*H* **minor**), 6.84-6.96 (m, 4H, aryl *H* **minor**), 6.98 (d, *J* = 3.1 Hz, 1H, aryl *H* **major**), 7.06 (td, 1H, *J* = 7.6, 1.6 Hz, aryl *H* **major**), 7.11 (s, 1H, aryl *H* **minor**), 7.15-7.30 (m, 3H, 2 aryl *H* **major** + aryl *H* **minor**), 7.34 (d, *J* = 8.2 Hz, 1H, aryl *H* **minor**), 7.41 (s, 1H, aryl *H* **major**), 7.51 (d, *J* = 8.2 Hz, 1H, aryl *H* **major**), 7.56 (dd, *J* = 7.9, 1.4 Hz, 1H, aryl *H* **major**), 7.70 (dd, *J* = 7.9, 1.7 Hz, 1H, aryl *H* **major**), 7.82 (dd, *J* = 7.9, 1.7 Hz, 1H, aryl *H* **minor**), (N*H* not observed); δ_C (101 MHz, $CDCl_3$), 24.7 (BOC*C*H_3 **major**), 24.8 (BOC*C*H_3 **major**), 24.8 (BOC*C*H_3 **minor**), 24.8 (BOC*C*H_3 **minor**), 32.9 (N*C*H_3 **minor**), 33.0 (N*C*H_3 **major**), 55.8 (O*C*H_3 **major**), 55.9 (O*C*H_3 **minor**), 56.7 (*C*HC=CH_2 **minor**), 57.3 (*C*HC=CH_2 **major**), 62.3 (*C*HCHC=CH_2 **minor**), 62.4 (*C*HCHC=CH_2 **major**), 83.4 (BO*C*CH_3 **major**), 83.7 (BO*C*CH_3

minor), 100.6 (aryl *C*H **minor**), 100.8 (aryl *C*H **major**), 108.1 (aryl *C*H **minor**), 108.8 (aryl *C*H **major**), 114.5 (aryl *C*H **minor**), 114.6 (OCCH*C*H **major**), 114.7 (OCCH*C*H **minor**), 114.9 (OC*C*H **major**), 115.3 (OC*C*H **minor**), 119.7 (aryl *C*H **minor**), 120.2 (aryl *C*H **minor**), 120.4 (aryl *C*H **major**), 120.4 (aryl *C*H **major**), 126.4 (aryl *C* **major**), 127.0 (aryl *C* **minor**), 127.4 (aryl *C*H **major**), 127.5 (aryl C*H* **minor**), 127.6 (aryl *C*H **minor**), 127.9 (aryl *C*H **major**), 128.0 (aryl *C*H **major**), 128.6 (aryl *C*, **minor**), 128.6 (aryl *C* **major**), 129.7 (aryl *C*H **major**), 130.4 (aryl *C*H **minor**), 131.7 (C=*C*H_2 **minor**), 132.8 (aryl *C*H **minor**), 133.3 (C=*C*H_2 **major**), 133.3 (aryl *C*H **major**), 135.9 (aryl *C* **minor**), 136.3 (aryl *C* **major**), 136.9 (aryl *C* **minor**), 137.2 (aryl *C* **major**), 141.1 (aryl *C* **major**), 141.8 (aryl *C* **minor**), 141.9 (OC(CH)$_2$*C* **minor**), 142.3 (OC(CH)$_2$*C* **major**), 151.9 (CH_3O*C* **major**), 152.0 (CH_3O*C* **minor**), (B*C*=CH_2 not observed); δ_B (128 MHz, $CDCl_3$) 29.6 (*B*OCCH_3 **major** + *B*OCCH_3 **minor**); M.p.: 110-112 ℃ (Et_2O); MS (APCI) *m/z* 587.3 ($M+H^+$); HRMS $C_{32}H_{37}BBrN_2O_3$ Expected 587.2075, Found 587.2081.

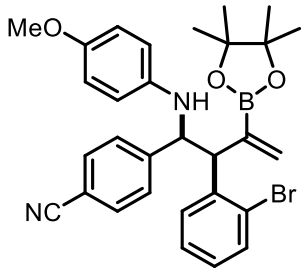
Rac-1S,2S-N-(2-(2-Bromophenyl)-1-(quinolin-6-yl)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)but-3-en-1-yl)-4-methoxyaniline **104o**



Prepared according to General Procedure A on a 1.00 mmol scale (crude ^{1}H NMR: 35%, 89:11 dr). Column chromatography (20% EtOAc in hexane) afforded the title compound as a yellow oil (176 mg, 0.600 mmol, 30%, 91:9 dr). ν_{max} (thin film/cm^{-1}): 3392, 2975, 2854, 1618, 1464, 1357, 1238, 1165, 1135; δ_H (400 MHz, $CDCl_3$) 0.99 (s, 6H, BOCCH_3), 1.04 (s, 6H, BOCCH_3), 3.63 (s, 3H, OCH_3), 4.47 (d, *J* = 10.4 Hz, 1H, C*H*C=CH_2), 5.11 (d, *J* = 10.4 Hz, 1H, C*H*CHC=CH_2), 5.51 (d, *J* = 2.8 Hz, 1H, C=CH_2), 5.78 (d, *J* = 2.8 Hz, 1H, C=CH_2), 6.34-6.43 (m, 2H, OCC*H*), 6.55-6.64 (m, 2H, OCCHC*H*), 7.08 (td, *J* = 7.7, 1.6 Hz, 1H, aryl *H*), 7.21-7.39 (m, 2H, aryl *H*), 7.57 (dd, *J* = 8.0, 1.4 Hz, 1H,

aryl *H*), 7.70 (dd, *J* = 8.0, 1.4 Hz, 1H, aryl *H*), 7.85 (dd, *J* = 8.8, 1.9 Hz, 1H, aryl *H*), 7.91 (d, *J* = 1.9 Hz, 1H, aryl *H*), 8.04 (d, *J* = 8.9 Hz, 1H, aryl *H*), 8.10 (d, *J* = 8.3 Hz, 1H, aryl *H*), 8.86 (dd, *J* = 4.2, 1.7 Hz, 1H, aryl *H*); δ_C (101 MHz, $CDCl_3$) 24.7 (BOC*C*H_3), 24.7 (BOC*C*H_3), 55.8 (O*C*H_3), 56.6 (*C*HC=CH_2), 61.8 (*C*HCHC=CH_2), 83.6 (BO*C*CH_3), 114.7 (OCCH*C*H), 114.9 (OC*C*H), 121.0 (aryl *C*H), 126.4 (aryl *C*), 127.0 (aryl *C*H), 127.5 (aryl *C*H), 128.2 (aryl *C*H), 129.4 (aryl *C*H), 129.5 (aryl *C*H), 130.2 (aryl *C*H), 133.5 (aryl *C*H), 134.0 (C=*C*H_2), 136.1 (aryl *C*H), 140.4 (aryl *C*), 141.3 (aryl *C*), 141.6 (OC(CH)$_2$*C*), 148.1 (aryl *C*), 150.1 (aryl *C*H), 152.3 (CH_3O*C*) (aryl *C*, B*C*=CH_2 not observed); δ_B (128 MHz, $CDCl_3$) 32.1 (*B*OCCH_3); MS (APCI) *m/z* 585.3 ($M+H^+$); HRMS $C_{32}H_{35}BBrN_2O_3$ Expected 585.1919, Found 585.1920.

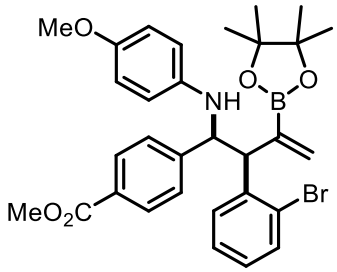
Rac-1S,2S-4-(2-(2-Bromophenyl)-1-((4-methoxyphenyl)amino)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)but-3-en-1-yl)benzonitrile **104p**



Prepared according to General Procedure A on a 1.00 mmol scale (crude ^{1}H NMR: 76%, 76:24 dr). Column chromatography (15% EtOAc in hexane) afforded the title compound as a yellow oil (368 mg, 0.66 mmol, 66%, 77:23 dr). ν_{max} (thin film/cm^{-1}): 3394, 2977, 2832, 1627, 1466, 1357, 1237, 1166, 1136;; δ_H (400 MHz, $CDCl_3$) 1.08 (s, 6H, BOCC*H*$_3$ **minor**), 1.13 (s, 6H, BOCC*H*$_3$ **major**), 1.16 (s, 6H, BOCC*H*$_3$ **major**), 1.17 (s, 6H, BOCC*H*$_3$ **minor**), 3.66 (s, 3H, OC*H*$_3$ **major**), 3.67 (s, 3H, OC*H*$_3$ **minor**), 4.35 (d, *J* = 10.2 Hz, 1H, C*H*C=CH_2 **major**), 4.45 (d, *J* = 10.0 Hz, 1H, C*H*C=CH_2 **minor**), 4.95 (d, *J* = 10.0 Hz, 1H, C*H*CHC=CH_2 **minor**), 5.00 (d, *J* = 10.2 Hz, 1H, C*H*CHC=CH_2 **major**), 5.52 (d, *J* = 2.7 Hz, 1H, C=C*H*$_2$ **major**), 5.82 (d, *J* = 2.7 Hz, 1H, C=C*H*$_2$ **major**), 5.88 (d, *J* = 2.8 Hz, 1H, C=C*H*$_2$ **minor**), 6.05 (d, *J* = 2.8 Hz, 1H, C=C*H*$_2$ **minor**), 6.28-6.35 (m, 2H, OCC*H* **major**), 6.38-6.44 (m, 2H, OCC*H* **minor**), 6.58-6.68 (m, 4H, OCCHC*H* **major** + OCCHC*H* **minor**), 6.93-7.00 (m, 1H, aryl *H* **minor**), 7.04-7.10 (m, 1H, aryl *H* **major**), 7.21-7.28

(m, 2H, aryl *H* **major**), 7.33 (dd, *J* = 8.0, 1.4 Hz, 1H, aryl *H* **minor**), 7.35-7.40 (m, 2H, aryl *H* **minor**), 7.53-7.59 (m, 8H, 4 aryl *H* **major** + 3 aryl *H* **minor**), 7.63 (dd, *J* = 7.9, 1.7 Hz, 1H, aryl *H* **major**), 7.80 (dd, *J* = 7.9, 1.7 Hz, 1H, aryl *H* **minor**), (N*H* not observed); δ_C (101 MHz, $CDCl_3$), 24.7 (BOC*C*H_3 **minor**), 24.7 (BOC*C*H_3 **major**), 24.8 (BOC*C*H_3 **minor**), 24.8 (BOC*C*H_3 **major**), 55.7 (O*C*H_3 **major**), 55.8 (O*C*H_3 **minor**), 56.2 (*C*HC=CH_2 **minor**), 56.5 (*C*HC=CH_2 **major**), 61.3 (*C*HCHC=CH_2 **major**), 61.4 (*C*HCHC=CH_2 **minor**), 83.8 (BO*C*CH_3 **major**), 83.9 (BO*C*CH_3 **minor**), 110.6 (aryl *C* **minor**), 110.9 (aryl *C* **major**), 114.6 (aryl *C*H **minor**), 114.7 (OCCH*C*H **minor**), 114.8 (OCCH*C*H **major**), 114.8 (OC*C*H **minor**), 114.8 (OC*C*H **major**), 119.1 (aryl *C* **major**), 119.2 (aryl *C* **minor**), 125.6 (aryl *C* **minor**), 126.3 (aryl *C* **major**), 127.5 (aryl *C*H **minor**), 128.2 (aryl *C*H **minor**), 128.4 (aryl *C*H **major**), 128.5 (aryl *C*H, **major**), 129.1 (aryl *C*H **major**), 129.3 (aryl *C*H **major**), 130.2 (aryl *C*H **minor**), 131.8 (aryl *C*H **minor**), 132.1 (aryl *C*H **major**), 133.0 (aryl *C*H **minor**), 133.1 (C=*C*H_2 **minor**), 133.5 (aryl *C*H **major**), 134.3 (C=*C*H_2 **major**), 139.6 (aryl *C* **major**), 140.7 (aryl *C* **minor**), 140.9 (OC(CH)$_2$*C* **minor**), 141.0 (OC(CH)$_2$*C* **major**), 148.2 (*C*N **minor**), 149.0 (*C*N **major**), 152.3 (CH_3O*C* **minor**), 152.5 (CH_3O*C* **major**), (B*C*=CH_2 not observed); δ_B (128 MHz, $CDCl_3$) 24.1 (*B*OCCH_3 **major** + *B*OCCH_3 **minor**); MS (APCI) *m/z* 559.3 ($M+H^+$); HRMS $C_{30}H_{33}BBrN_2O_3$ Expected 559.1762, Found 559.1762.

Rac-1S,2S-Methyl 4-(2-(2-bromophenyl)-1-((4-methoxyphenyl)amino)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)but-3-en-1-yl)benzoate **104q**



Prepared according to General Procedure A on a 1.00 mmol scale (crude ^{1}H NMR: 75%, 75:25 dr). Column chromatography (15% EtOAc in hexane) afforded the title compound as a yellow oil (368 mg, 0.66 mmol, 66%, 77:23 dr). ν_{max} (thin film/cm^{-1}):

3391, 2977, 2850, 1610, 1467, 1357, 1237, 1167, 1137; δ_H (400 MHz, $CDCl_3$) 1.09 (s, 6H, BOCC*H*$_3$ **minor**), 1.13 (s, 6H, BOCC*H*$_3$ **major**), 1.16 (s, 6H, BOCC*H*$_3$ **major**), 1.17 (s, 6H, BOCC*H*$_3$ **minor**), 3.65 (s, 3H, OC*H*$_3$ **major**), 3.66 (s, 3H, OC*H*$_3$ **minor**), 3.83 (s, 3H, CO_2CH_3 **minor**), 3.88 (s, 3H, CO_2CH_3 **major**), 4.37 (d, *J* = 10.3 Hz, 1H, C*H*C=CH_2 **major**), 4.49 (d, *J* = 10.0 Hz, 1H, C*H*C=CH_2 **minor**), 4.97 (d, *J* = 10.1 Hz, 1H, C*H*CHC=CH_2 **minor**), 5.05 (d, *J* = 10.3 Hz, 1H, C*H*CHC=CH_2 **major**), 5.51 (d, *J* = 2.9 Hz, 1H, C=C*H*$_2$ **major**), 5.76 (d, *J* = 2.8 Hz, 1H, C=C*H*$_2$ **major**), 5.87 (d, *J* = 2.7 Hz, 1H, C=C*H*$_2$ **minor**), 6.03 (d, *J* = 2.9 Hz, 1H, C=C*H*$_2$ **minor**), 6.31-6.37 (m, 2H, OCC*H* **major**), 6.39-6.49 (m, 2H, OCC*H* **minor**), 6.57-6.67 (m, 4H, OCCHC*H* **major** + OCCHC*H* **minor**), 6.89-7.00 (m, 1H, aryl *H* **minor**), 7.01-7.10 (m, 1H, aryl *H* **major**), 7.19-7.28 (m, 4H, aryl *H* **major** + 3 aryl *H* **minor**), 7.31 (dd, *J* = 8.0, 1.3 Hz, 1H, aryl *H* **minor**), 7.50-7.59 (m, 3H, aryl *H* **major**), 7.69 (dd, *J* = 7.9, 1.7 Hz, 1H, aryl *H* **major**), 7.74-7.79 (m, 2H, aryl *H* **minor**), 7.81 (dd, *J* = 7.9, 1.7 Hz, 1H, aryl *H* **minor**),7.92-8.00 (m, 2H, aryl *H* **major**), (N*H* **major**, N*H* **minor** not observed); δ_C (101 MHz, $CDCl_3$), 24.7 (BOC*C*H$_3$ **major**), 24.7 (BOC*C*H$_3$ **minor**), 24.8 (BOC*C*H$_3$ **minor**), 24.9 (BOC*C*H$_3$ **major**), 52.0 (CO_2CH_3 **minor**), 52.1 (CO_2CH_3 **major**), 55.8 (OCH$_3$ **major**), 55.8 (OCH$_3$ **minor**), 56.3 (*C*HC=CH_2 **minor**), 57.2 (*C*HC=CH_2 **major**), 61.3 (*C*HCHC=CH_2 **major**), 61.5 (*C*HCHC=CH_2 **minor**), 83.7 (BO*C*CH$_3$ **major**), 83.9 (BO*C*CH$_3$ **minor**), 114.7 (OCCH*C*H **major**), 114.8 (OCCH*C*H **minor**), 114.8 (OC*C*H **minor**), 114.9 (OC*C*H **major**), 125.6 (aryl *C* **minor**), 126.4 (aryl *C* **major**), 127.3 (aryl *C*H **minor**), 127.5 (aryl *C*H **major**), 127.8 (aryl *C*H **major**), 128.0 (aryl *C*H, **minor**), 128.3 (aryl *C* **major**), 128.3 (aryl *C* **minor**), 128.7 (aryl *C*H **minor**), 129.0 (aryl *C*H **major**), 129.3 (aryl *C*H **minor**), 129.5 (aryl *C*H **major**), 129.7 (aryl *C*H **major**), 130.3 (aryl *C*H **minor**), 132.8 (C=*C*H$_2$ **minor**), 132.9 (aryl *C*H **minor**), 133.4 (aryl *C*H **major**), 134.1 (C=*C*H$_2$ **major**), 140.0 (aryl *C* **major**), 141.1 (aryl *C* **minor**), 141.2 (OC(CH)$_2$*C* **minor**), 141.5 (OC(CH)$_2$*C* **major**), 147.9 (aryl *C* **minor**), 148.7 (aryl *C* **major**), 152.2 (CH$_3$O*C* **minor**), 152.3 (CH$_3$O*C* **major**), 167.2 (*C*O$_2$CH$_3$ **minor**), 167.2 (*C*O$_2$CH$_3$ **major**), (B*C*=CH_2 not observed); δ_B (128 MHz, $CDCl_3$) 21.8 (*B*OCCH$_3$ **major** + *B*OCCH$_3$ **minor**); MS (APCI) *m/z* 592.2 ($M+H^+$); HRMS $C_{31}H_{36}BBrNO_5$ Expected 592.1864, Found 592.1862.

Synthesis of *N*-(2-(2-bromophenyl)-1-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)but-3-en-1-yl)-4-methoxyaniline (88) (gram-scale)

Procedure

To a solution of CuI (0.151 g, 0.795 mmol, 5.3 mol%) and 1,3-dicyclohexylimidazolium tetrafluoroborate salt (0.268 g, 0.84 mmol, 5.6 mol%) in dry THF (60 ml, 0.013 M) at room temperature under N_2, was added ^{t}BuOK (15 ml, 15 mmol, 1.0 equiv.) as a 1.0 M solution in dry THF, and the reaction was stirred for 20 minutes at room temperature. B_2pin_2 (4.95 g, 19.5 mmol, 1.3 equiv.) in dry THF (60 mL) was then added and the resulting mixture stirred for 30 minutes. A solution of (*E*)-*N*-(4-methoxyphenyl)-1-phenylmethanimine (**26**) (3.17 g, 15.0 mmol, 1.0 equiv.) and 1-bromoaryl allene (**87**) (4.39 g, 22.5 mmol, 1.5 equiv.) in dry THF (75 ml, 0.2 M) was then added dropwise at room temperature. The reaction was stirred at room temperature and monitored by TLC to 20 minutes before being filtered through a pad of silica, concentrated *in vacuo*, and purified by column chromatography on silica to afford the desired N-(2-(2-bromophenyl)-1-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)but-3-en-1-yl)-4-methoxyaniline (**88**). Nitromethane is used as an internal standard.

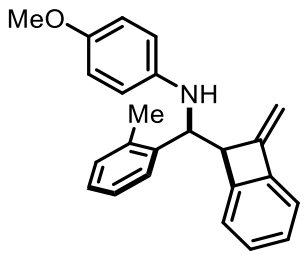
Synthesis of cyclobutarenes

General procedure B

To a solution of the homoallylic amine (1.0 equiv.) in ethanol (0.1 M) were successively added $KOH_{(aq.)}$ (2.0 equiv.) as a 0.5 M solution in H_2O, and a solution of (IPr)Pd(allyl)Cl (10 mol%) in ethanol (0.017 M). The vial was sealed and stirred at

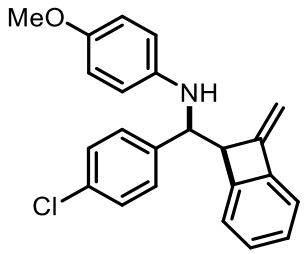
50 °C for 17 h, before being cooled down, diluted with water, extracted with Et_2O three times, dried over $MgSO_4$, and concentrated *in vacuo* to afford the crude product. Purification by silica chromatography afforded the desired cyclobutarene. Nitromethane is used as an internal standard.

4-Methoxy-N-((S)-((S)-8-methylenebicyclo[4.2.0]octa-1,3,5-trien-7-yl)(o-tolyl)methyl)aniline **106a**



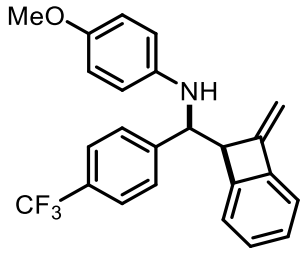
Prepared according to General Procedure B on a 55 µmol scale (crude ^1H NMR: 15%, >20:1 dr). Column chromatography (5% Et_2O in hexane) afforded the title compound as a yellow oil (1.9 mg, 5.5 µmol, 10%, >20:1 dr). ν_{max} (thin film/cm^{-1}): 3404, 3060, 2919, 2853, 1671, 1513, 1447, 1290, 1243, 1172, 1160, 1036; δ_H (400 MHz, $CDCl_3$) 2.52 (s, 3H, Ar-C*H*$_3$), 3.66 (s, 3H, OC*H*$_3$), 3.84 (br. s, 1H, N*H*), 4.24 (d, *J* = 5.4 Hz, 1H, C*H*C=CH$_2$), 4.77 (s, 1H, C*H*CHC=CH$_2$), 4.89 (s, 1H, C=C*H*$_2$), 5.29 (s, 1H, C=C*H*$_2$), 6.28-6.37 (m, 2H, OCC*H*), 6.58-6.66 (m, 2H, OCCHC*H*), 6.96-7.11 (m, 1H, aryl *H*), 7.17 – 7.25 (m, 5H, aryl *H*), 7.30 (t, *J* = 7.5 Hz, 1H, aryl *H*), 7.50 (dt, *J* = 5.5, 3.5 Hz, 1H, aryl *H*); δ_C (101 MHz, $CDCl_3$) 19.4 (Ar-*C*H$_3$), 55.6 (O*C*H$_3$), 55.8 (*C*HC=CH$_2$), 56.3 (*C*HCHC=CH$_2$), 103.2 (C=*C*H$_2$), 114.7 (OCCH*C*H), 114.8 (OC*C*H), 118.8 (aryl *C*H), 124.1 (aryl *C*H), 126.2 (aryl *C*H), 126.6 (aryl *C*H), 127.0 (aryl *C*H), 128.6 (aryl *C*H), 129.2 (aryl *C*H), 130.9 (aryl *C*H), 140.8 (aryl *C*), 142.0 (OC(CH)$_2$*C*), 145.0 (*C*=CH$_2$), 146.3 (aryl *C*), 146.4 (aryl *C*), 152.0 (CH$_3$O*C*); MS (APCI) *m/z* 342.1 ($M+H^+$); HRMS $C_{24}H_{24}ON$ Expected 342.1852, Found 342.1861.

N-((S)-(4-Chlorophenyl)((S)-8-methylenebicyclo[4.2.0]octa-1,3,5-trien-7-yl)methyl)-4-methoxyaniline **106b**



Prepared according to General Procedure B on a 0.150 mmol scale (crude ^{1}H NMR: 67%, >20:1 dr). Column chromatography (5% Et_2O in hexane) afforded the title compound as a yellow oil (35.1 mg, 0.0970 mmol, 65%, >20:1 dr). ν_{max} (thin film/cm^{-1}): 3402, 3064, 2924, 2851, 1668, 1510, 1444, 1286, 1239, 1186, 1179, 1037; δ_H (400 MHz, $CDCl_3$) 3.67 (s, 3H, OC*H*$_3$), 3.86 (s, 1H, N*H*), 4.23 (d, *J* = 5.8 Hz, 1H, C*H*C=CH$_2$), 4.60 (d, *J* = 5.8 Hz, 1H, C*H*CHC=CH$_2$), 4.78 (s, 1H, C=C*H*$_2$), 5.30 (s, 1H, C=C*H*$_2$), 6.33-6.42 (m, 2H, OCC*H*), 6.60-6.69 (m, 2H, OCCHC*H*), 6.99 (d, *J* = 7.3 Hz, 1H, aryl *H*), 7.17-7.24 (m, 2H, aryl *H*), 7.29 (t, *J* = 7.5 Hz, 1H, aryl *H*), 7.34 (d, *J* = 8.5 Hz, 2H, aryl *H*), 7.40 (d, *J* = 8.5 Hz, 2H, aryl *H*); δ_C (101 MHz, $CDCl_3$) 55.8 (O*C*H$_3$), 57.9 (*C*HC=CH$_2$), 59.4 (*C*HCHC=CH$_2$), 103.8 (C=*C*H$_2$), 114.8 (OCCH*C*H), 115.0 (OC*C*H), 119.0 (aryl *C*H), 123.7 (aryl *C*H), 128.4 (aryl *C*H), 128.8 (aryl *C*H), 128.9 (aryl *C*H), 129.3 (aryl *C*H), 132.9 (aryl *C*), 141.6 (OC(CH)$_2$*C*), 141.7 (aryl *C*), 144.9 (*C*=CH$_2$), 145.9 (aryl *C*), 146.0 (aryl *C*), 152.3 (CH$_3$O*C*); MS (APCI) *m/z* 362.1 (M+H$^+$); HRMS $C_{23}H_{21}ONCl$ Expected 362.1306, Found 361.1301.

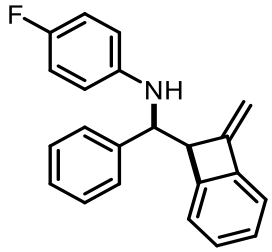
4-Methoxy-N-((S)-((S)-8-methylenebicyclo[4.2.0]octa-1,3,5-trien-7-yl)(4-(trifluoromethyl)phenyl)methyl)aniline **106c**



Prepared according to General Procedure B on a 0.150 mmol scale (crude ^{1}H NMR: 47%, >20:1 dr). Column chromatography (5% Et_2O in hexane) afforded the title compound as a yellow oil (23.1 mg, 58.5 µmol, 39%, >20:1 dr). ν_{max} (thin film/cm^{-1}):

3392, 2954, 2922, 2852, 1510, 1446, 1323, 1240, 1162, 1110, 1038; δ_H (400 MHz, $CDCl_3$) 3.67 (s, 3H, OCH_3), 3.89 (s, 1H, N*H*), 4.26 (d, *J* = 5.6 Hz, 1H, C*H*C=CH_2), 4.69 (d, *J* = 5.6 Hz, 1H, C*H*CHC=CH_2), 4.80 (s, 1H, C=CH_2), 5.32 (s, 1H, C=CH_2), 6.33-6.45 (m, 2H, OCC*H*), 6.61-6.75 (m, 2H, OCCHC*H*), 6.96 (d, *J* = 7.3 Hz, 1H, aryl *H*), 7.17-7.27 (m, 2H, aryl *H*), 7.31 (t, *J* = 7.5 Hz, 1H, aryl *H*), 7.49-7.67 (m, 4H, aryl *H*); δ_C (101 MHz, $CDCl_3$) 55.8 (OCH_3), 57.7 (*C*HC=CH_2), 59.7 (*C*HCHC=CH_2), 103.9 (C=*C*H_2), 114.8 (OCCH*C*H), 114.9 (OC*C*H), 119.1 (aryl *C*H), 123.6 (aryl *C*H), 124.4 (q, *J* = 271.3 Hz, *C*F_3), 125.7 (q, *J* = 3.9 Hz, CF_3C*C*H), 127.4 (CF_3CCH*C*H), 128.9 (aryl *C*H), 129.4 (aryl *C*H), 129.9 (q, *J* = 32.6 Hz, CF_3*C*), 141.4 (OC(CH)$_2$*C*), 144.9 (aryl *C*), 145.7 (*C*=CH_2), 145.8 (aryl *C*), 147.4 (CF_3C(CH)$_2$*C*), 152.4 (CH_3O*C*); δ_F (376 MHz, $CDCl_3$) -62.3 (*F*C); MS (APCI) *m/z* 396.2 ($M+H^+$); HRMS $C_{24}H_{21}ONF_3$ Expected 396.1570, Found 396.1570.

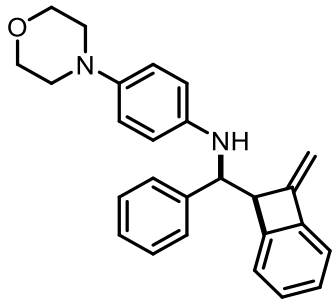
4-Fluoro-N-((S)-((S)-8-methylenebicyclo[4.2.0]octa-1,3,5-trien-7-yl)(phenyl)methyl)aniline **106n**



Prepared according to General Procedure B on a 0.200 mmol scale (crude ^{1}H NMR: ~60%, >20:1 dr). Column chromatography (5% Et_2O in hexane) afforded the title compound as a yellow oil (38 mg, 0.122 mmol, 61%, >20:1 dr). ν_{max} (thin film/cm^{-1}): 3410, 3028, 2913, 1505, 1445, 1313, 1280, 1172, 1108, 1027; δ_H (400 MHz, $CDCl_3$) 3.99 (br. s, 1H, N*H*), 4.27 (d, *J* = 5.8 Hz, 1H, C*H*C=CH_2), 4.64 (d, *J* = 5.9 Hz, 1H, C*H*CHC=CH_2), 4.77 (s, 1H, C=CH_2), 5.30 (s, 1H, C=CH_2), 6.34-6.40 (m, 2H, FCCHC*H*), 6.74 (t, *J* = 8.9 Hz, 2H, FCC*H*), 7.00 (d, *J* = 7.3 Hz, 1H, aryl *H*), 7.16-7.26 (m, 2H, aryl *H*), 7.26-7.33 (m, 2H, aryl *H*), 7.34-7.41 (m, 2H, aryl *H*), 7.42-7.50 (m, 2H, aryl *H*); δ_C (101 MHz, $CDCl_3$) 58.0 (*C*HC=CH_2), 59.7 (*C*HCHC=CH_2), 103.7 (C=*C*H_2), 114.5 (d, *J* = 7.4 Hz, FCCH*C*H), 114.6 (d, *J* = 24.0 Hz, FC*C*H), 119.0 (aryl *C*H), 123.8 (aryl *C*H), 126.9 (aryl *C*H), 127.5 (aryl *C*H), 128.8 (aryl CH), 129.3 (aryl *C*H), 142.7 (aryl *C*), 144.0 (aryl *C*), 145.0

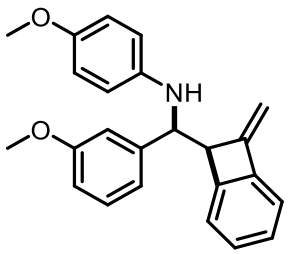
(*C*=CH_2), 146.1 (d, *J* = 3.1 Hz FCCHCH*C*), 155.8 (d, *J* = 234.0 Hz F*C*) (aryl *C*H, NHCH*C* not observed); δ_F (376 MHz, $CDCl_3$) -128.17 (dt, *J* = 8.6, 4.2 Hz, *F*C); MS (APCI) *m/z* 316.1 ($M+H^+$); HRMS $C_{22}H_{19}NF$ Expected 316.1496, Found 316.1493.

N-((S)-((S)-8-Methylenebicyclo[4.2.0]octa-1,3,5-trien-7-yl)(phenyl)methyl)-4-morpholi noaniline **106o**



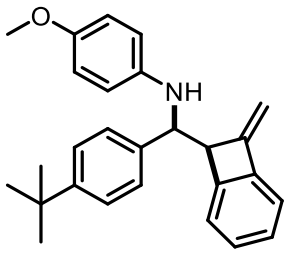
Prepared according to General Procedure B on a 0.200 mmol scale (the reaction time is 4h) (crude ^1H NMR: ~60%, >20:1 dr). Column chromatography (15% Et_2O in hexane) afforded the title compound as a yellow oil (45 mg, 0.118 mmol, 59%, >20:1 dr). ν_{max} (thin film/cm^{-1}): 3400, 2958, 2891, 2854, 1513, 1448, 1320, 1265, 1171, 1117, 1028; δ_H (400 MHz, $CDCl_3$) 2.84-3.05 (m, 4H, N(C*H*$_2$)$_2$), 3.76-3.80 (m, 4H, O(C*H*$_2$)$_2$), 3.93 (br. s, 1H, N*H*), 4.27 (d, *J* = 5.9 Hz, 1H, C*H*C=CH_2), 4.64 (d, *J* = 5.8 Hz, 1H, C*H*CHC=CH_2), 4.75 (s, 1H, C=C*H*$_2$), 5.29 (s, 1H, C=C*H*$_2$), 6.43 (d, *J* = 8.4 Hz, 2H, CH_2NCC*H*), 6.69 (d, *J* = 8.4 Hz, 2H, CH_2NCCHC*H*), 7.01 (d, *J* = 7.6 Hz, 1H, aryl *H*), 7.14-7.25 (m, 2H, aryl *H*), 7.25-7.28 (m, 2H, aryl *H*), 7.34-7.38 (m, 2H, aryl *H*), 7.44-7.49 (m, 2H, aryl *H*); δ_C (101 MHz, $CDCl_3$) 51.2 (N(*C*H$_2$)$_2$), 58.0 (*C*HC=CH_2), 59.8 (*C*HCHC=CH_2), 67.2 (O(*C*H$_2$)$_2$), 103.6 (C=*C*H$_2$), 114.7 (CH_2NCCH*C*H), 118.2 (CH_2NC*C*H), 118.9 (aryl *C*H), 123.8 (aryl *C*H), 127.0 (aryl *C*H), 127.3 (aryl *C*H), 128.6 (aryl *C*H), 128.7 (aryl *C*H), 129.2 (aryl *C*H), 142.2 (aryl *C*), 143.1 (CH_2NC(CH)$_2$*C*), 143.5 (CH_2N*C*), 144.9 (*C*=CH_2), 146.2 (aryl *C*), 146.4 (aryl *C*); MS (APCI) *m/z* 383.2 ($M+H^+$); HRMS $C_{26}H_{27}ON_2$ Expected 383.2118, Found 383.2115.

4-Methoxy-N-((S)-(3-methoxyphenyl)((S)-8-methylenebicyclo[4.2.0]octa-1,3,5-trien-7-yl)methyl)aniline **106d**



Prepared according to General Procedure B on a 0.200 mmol scale (crude ^{1}H NMR: 55%, >20:1 dr). Column chromatography (5% Et_2O in hexane) afforded the title compound as a yellow oil (33 mg, 0.094 mmol, 47%, >20:1 dr). ν_{max} (thin film/cm^{-1}): 2931, 2832, 1508, 1460, 1313, 1237, 1176, 1113, 1038; δ_H (400 MHz, $CDCl_3$) 3.67 (s, 3H, OC*H*$_3$), 3.81 (s, 3H, OC*H*$_3$), 3.85 (br. s, 1H, N*H*), 4.27 (d, *J* = 5.8 Hz, 1H, C*H*C=CH$_2$), 4.59 (d, *J* = 5.8 Hz, 1H, C*H*CHC=CH$_2$), 4.79 (s, 1H, C=C*H*$_2$), 5.30 (s, 1H, C=C*H*$_2$), 6.38-6.48 (m, 2H, OCC*H*), 6.60-6.69 (m, 2H, OCCHC*H*), 6.82 (d, *J* = 8.2 Hz, 1H, aryl *H*), 7.01-7.12 (m, 3H, aryl *H*), 7.12-7.33 (m, 4H, aryl *H*); δ_C (101 MHz, $CDCl_3$) 55.4 (O*C*H$_3$), 55.8 (O*C*H$_3$), 58.0 (*C*HC=CH$_2$), 60.0 (*C*HCHC=CH$_2$), 103.6 (C=*C*H$_2$), 112.6 (aryl *C*H), 112.6 (aryl *C*H), 114.8 (NHCCH*C*H), 115.0 (NHC*C*H), 119.0 (aryl *C*H), 119.4 (aryl *C*H), 123.8 (aryl *C*H), 128.6 (aryl *C*H), 129.2 (aryl *C*H), 129.7 (aryl *C*H), 142.0 (aryl *C*), 145.0 (NH*C*), 145.0 (aryl *C*), 146.2 (*C*=CH$_2$), 146.4 (aryl *C*), 152.1 (aryl *C*), 160.0 (aryl *C*); MS (APCI) *m/z* 358.1 (M+H$^+$); HRMS $C_{24}H_{24}O_2N$ Expected 358.1802, Found 358.1799.

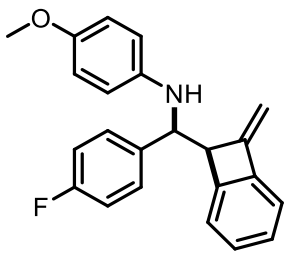
N-((S)-(4-(tert-Butyl)phenyl)((S)-8-methylenebicyclo[4.2.0]octa-1,3,5-trien-7-yl)methyl)-4-methoxyaniline **106e**



Prepared according to General Procedure B on a 0.200 mmol scale (the reaction time is 3.5h) (crude ^{1}H NMR: 61%, >20:1 dr). Column chromatography (5% Et_2O in hexane) afforded the title compound as a yellow oil (41 mg, 0.108 mmol, 54%, >20:1 dr). ν_{max} (thin film/cm^{-1}): 3404, 2958, 2830, 1509, 1460, 1334, 1236, 1179, 1111, 1037; δ_H

(400 MHz, $CDCl_3$) 1.34 (s, 9H, C(CH_3)$_3$), 3.66 (s, 3H, OCH_3), 3.86 (br. s, 1H, N*H*), 4.26 (d, *J* = 5.9 Hz, 1H, C*H*C=CH_2), 4.60 (d, *J* = 5.9 Hz, 1H, C*H*CHC=CH_2), 4.73 (s, 1H, C=CH_2), 5.28 (s, 1H, C=CH_2), 6.38-6.48 (m, 2H, OCC*H*), 6.60-6.69 (m, 2H, OCCHC*H*), 6.99-7.06 (m, 1H, aryl *H*), 7.11-7.33 (m, 3H, aryl *H*), 7.37 (s, 4H, aryl *H*); δ_C (101 MHz, $CDCl_3$) 31.6 (C(CH_3)$_3$), 34.6 (*C*(CH_3)$_3$), 55.8 (OCH_3), 58.2 (*C*HC=CH_2), 59.6 (*C*HCHC=CH_2), 103.5 (C=*C*H_2), 114.7 (OCCH*C*H), 114.9 (OC*C*H), 118.9 (aryl *C*H), 123.9 (aryl *C*H), 125.6 (aryl *C*H), 126.6 (aryl *C*H), 128.5 (aryl *C*H), 129.1 (aryl *C*H), 140.0 (aryl *C*), 142.1 (OC(CH)$_2$*C*), 145.0 (aryl *C*), 146.4 (*C*=CH_2), 146.6 (aryl *C*), 150.1 (aryl *C*), 152.0 (CH_3O*C*); MS (APCI) *m/z* 384.3 ($M+H^+$); HRMS $C_{27}H_{30}NO$ Expected 384.2322, Found 384.2318.

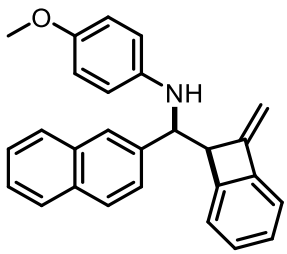
N-((S)-(4-Fluorophenyl)((S)-8-methylenebicyclo[4.2.0]octa-1,3,5-trien-7-yl)methyl)-4-methoxyaniline **106g**



Prepared according to General Procedure B on a 0.200 mmol scale (crude ^{1}H NMR: 53%, >20:1 dr). Column chromatography (5% Et_2O in hexane) afforded the title compound as a yellow oil (30 mg, 0.086 mmol, 43%, >20:1 dr). ν_{max} (thin film/cm^{-1}): 3404, 2904, 2831, 1508, 1460, 1237, 1179, 1113, 1036; δ_H (400 MHz, $CDCl_3$) 3.67 (s, 3H, OCH_3), 3.87 (br. s, 1H, N*H*), 4.23 (d, *J* = 6.0 Hz, 1H, C*H*C=CH_2), 4.60 (d, *J* = 6.0 Hz, 1H, C*H*CHC=CH_2), 4.75 (s, 1H, C=CH_2), 5.29 (s, 1H, C=CH_2), 6.33-6.46 (m, 2H, OCC*H*), 6.59-6.69 (m, 2H, OCCHC*H*), 6.97-7.10 (m, 3H, aryl *H*), 7.13-7.34 (m, 3H, aryl *H*), 7.38-7.46 (m, 2H, aryl *H*); δ_C (101 MHz, $CDCl_3$) 55.8 (OCH_3), 58.0 (*C*HC=CH_2), 59.5 (*C*HCHC=CH_2), 103.8 (C=*C*H_2), 114.8 (OCCH*C*H), 115.0 (OC*C*H), 115.5 (d, *J* = 21.2 Hz, FC*C*H), 119.0 (aryl *C*H), 123.6 (aryl *C*H), 128.5 (d, *J* = 7.9 Hz, FCCH*C*H), 128.7 (aryl *C*H), 129.3 (aryl *C*H), 138.7 (d, *J* = 3.0 Hz, FC(CH)$_2$*C*), 141.7 (OC(CH)$_2$*C*), 144.9 (*C*=CH_2), 146.0 (aryl *C*), 146.0 (aryl *C*), 152.3 (CH_3O*C*), 162.2 (d, *J* = 244.7 Hz, F*C*); δ_F (376 MHz, $CDCl_3$) -115.69 (s, *F*C); MS (APCI) *m/z* 346.1 ($M+H^+$); HRMS $C_{23}H_{21}NFO$ Expected

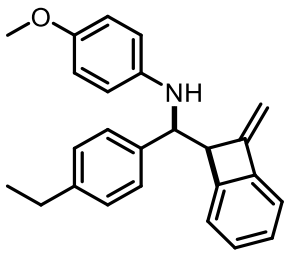
346.1602, Found 346.1599.

4-Methoxy-N-((S)-((S)-8-methylenebicyclo[4.2.0]octa-1,3,5-trien-7-yl)(naphthalen-2-yl)methyl)aniline **106h**



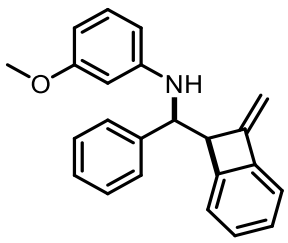
Prepared according to General Procedure B on a 0.200 mmol scale (crude ^{1}H NMR: 49%, >20:1 dr). Column chromatography (5% Et_2O in hexane) afforded the title compound as a yellow oil (30 mg, 0.081 mmol, 41%, >20:1 dr). ν_{max} (thin film/cm^{-1}): 3401, 2951, 2830, 1509, 1460, 1368, 1239, 1176, 1125, 1036; δ_H (400 MHz, $CDCl_3$) 3.65 (s, 3H, OC*H*$_3$), 3.98 (br. s, 1H, N*H*), 4.37 (d, *J* = 5.7 Hz, 1H, C*H*C=CH$_2$), 4.73-4.83 (m, 2H, C*H*CHC=CH$_2$ + C=C*H*$_2$), 5.31 (s, 1H, C=C*H*$_2$), 6.39-6.53 (m, 2H, OCC*H*), 6.56-6.67 (m, 2H, OCCHC*H*), 6.96-7.02 (m, 1H, aryl *H*), 7.11-7.36 (m, 3H, aryl *H*), 7.42-7.58 (m, 2H, aryl *H*), 7.59-7.69 (m, 1H, aryl *H*), 7.81-8.00 (m, 4H, aryl *H*); δ_C (101 MHz, $CDCl_3$) 55.8 (OC*H*$_3$), 58.0 (*C*HC=CH$_2$), 60.2 (*C*HCHC=CH$_2$), 103.7 (C=*C*H$_2$), 114.8 (OCCH*C*H), 115.0 (OC*C*H), 119.0 (aryl *C*H), 123.8 (aryl *C*H), 125.3 (aryl *C*H), 125.7 (aryl *C*H), 125.8 (aryl *C*H), 126.2 (aryl *C*H), 127.9 (aryl *C*H), 128.1 (aryl *C*H), 128.5 (aryl *C*H), 128.7 (aryl *C*H), 129.3 (aryl *C*H), 133.2 (aryl *C*), 133.7 (aryl *C*), 140.8 (aryl *C*), 142.0 (OC(CH)$_2$*C*), 145.0 (aryl *C*), 146.2 (*C*=CH$_2$), 146.4 (aryl *C*), 152.2 (CH$_3$O*C*); MS (APCI) *m/z* 378.1 (M+H$^+$); HRMS $C_{27}H_{24}NO$ Expected 378.1852, Found 378.1852.

N-((S)-(4-Ethylphenyl)((S)-8-methylenebicyclo[4.2.0]octa-1,3,5-trien-7-yl)methyl)-4-m ethoxyaniline **106f**



Prepared according to General Procedure B on a 0.200 mmol scale (crude ^{1}H NMR: 39%, >20:1 dr). Column chromatography (5% Et_2O in hexane) afforded the title compound as a yellow oil (22mg, 0.061 mmol, 31%, >20:1 dr). ν_{max} (thin film/cm^{-1}): 3402, 2961, 2830, 1508, 1459, 1235, 1176, 1112, 1036; δ_H (400 MHz, $CDCl_3$) 1.25 (t, *J* = 7.6 Hz, 3H, CH_2CH_3), 2.66 (q, *J* = 7.6 Hz, 2H, CH_2CH_3), 3.66 (s, 3H, OCH_3), 4.25 (d, *J* = 5.9 Hz, 1H, $CHC=CH_2$), 4.60 (d, *J* = 6.0 Hz, 1H, $CHCHC=CH_2$), 4.74 (s, 1H, $C=CH_2$), 5.28 (s, 1H, $C=CH_2$), 6.35-6.48 (m, 2H, OCC*H*), 6.59-6.68 (m, 2H, OCCHC*H*), 7.00-7.06 (m, 1H, aryl *H*), 7.14-7.24 (m, 4H, aryl *H*), 7.24-7.31 (m, 1H, aryl *H*), 7.32-7.40 (m, 2H, aryl *H*); δ_C (101 MHz, $CDCl_3$) 15.6 (CH_2CH_3), 28.6 (CH_2CH_3), 55.8 (OCH_3), 58.2 ($CHC=CH_2$), 59.7 ($CHCHC=CH_2$), 103.5 ($C=CH_2$), 114.7 (OCCH*C*H), 114.9 (OC*C*H), 118.9 (aryl *C*H), 123.8 (aryl *C*H), 126.9 (aryl *C*H), 128.1 (aryl *C*H), 128.5 (aryl *C*H), 129.1 (aryl *C*H), 140.3 (aryl *C*), 142.1 ($OC(CH)_2C$), 143.2 (aryl *C*), 144.9 (aryl *C*), 146.4 ($C=CH_2$), 146.6 (aryl *C*), 152.0 (CH_3OC); MS (APCI) *m/z* 356.2 ($M+H^+$); HRMS $C_{25}H_{26}NO$ Expected 356.2009, Found 356.2005.

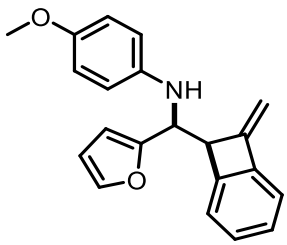
3-Methoxy-N-((S)-((S)-8-methylenebicyclo[4.2.0]octa-1,3,5-trien-7-yl)(phenyl)methyl) aniline **106p**



Prepared according to General Procedure B on a 0.200 mmol scale (crude ^{1}H NMR: >60%, 80:20 dr). Column chromatography (5% Et_2O in hexane) afforded the title compound as a yellow oil (41 mg, 0.122 mmol, 63%, 83:17 dr). ν_{max} (thin film/cm^{-1}): 3410, 2931, 2833, 1506, 1450, 1302, 1208, 1159, 1106, 1041; δ_H (400

MHz, $CDCl_3$) 3.62-3.71 (m, 6H, OC*H*$_3$ **major** + OC*H*$_3$ **minor**), 4.15 (br. s, 2H, N*H* **major** + N*H* **minor**), 4.23 (d, *J* = 7.8 Hz, 1H, C*H*C=CH_2 **minor**), 4.30 (d, *J* = 6.1 Hz, 1H, C*H*C=CH_2 **major**), 4.67 (d, *J* = 7.8 Hz, 1H, C*H*CHC=CH_2 **minor**), 4.73 (d, *J* = 5.9 Hz, 1H, C*H*CHC=CH_2 **major**), 4.79 (s, 1H, C=C*H*$_2$ **major**), 4.97 (s, 1H, C=C*H*$_2$ **minor**), 5.32 (s, 2H, C=C*H*$_2$ **major** + C=C*H*$_2$ **minor**), 6.00-6.28 (m, 5H, 3 aryl *H* **major** + 2 aryl *H* **minor**), 6.69 (d, *J* = 7.4 Hz, 1H, aryl *H* **minor**), 6.90-7.11 (m, 4H, 2 aryl *H* **major** + 2 aryl *H* **minor**), 7.15-7.65 (m, 16H, 8 aryl *H* **major** + 8 aryl *H* **minor**); δ_C (101 MHz, $CDCl_3$) 55.0 (O*C*H$_3$ **major**), 55.0 (O*C*H$_3$ **minor**), 57.5 (*C*HC=CH_2 **minor**), 57.9 (*C*HC=CH_2 **major**), 59.0 (*C*HCHC=CH_2 **major**), 60.6 (*C*HCHC=CH_2 **minor**), 99.7 (aryl *C*H **major**), 99.7 (aryl *C*H **minor**), 102.8 (aryl *C*H **major**), 103.0 (aryl *C*H **minor**), 103.7 (C=*C*H$_2$ **major**), 104.1 (C=*C*H$_2$ **minor**), 106.8 (aryl *C*H **major**), 106.9 (aryl *C*H **minor**), 118.8 (aryl *C*H **minor**), 119.0 (aryl *C*H **major**), 123.3 (aryl *C*H **minor**), 123.9 (aryl *C*H **major**), 126.9 (aryl *C*H **major**), 127.1 (aryl *C*H **minor**), 127.4 (aryl *C*H **major**), 127.5 (aryl *C*H **minor**), 128.5 (aryl *C*H **minor**), 128.6 (aryl *C*H **minor**), 128.7 (aryl *C*H **major**), 128.7 (aryl *C*H **major**), 129.0 (aryl *C*H **minor**), 129.2 (aryl *C*H **major**), 129.8 (aryl *C*H **major**), 129.9 (aryl *C*H **minor**), 142.3 (aryl *C* **minor**), 142.8 (aryl *C* **major**), 144.7 (*C*=CH_2 **minor**), 145.0 (*C*=CH_2 **major**), 146.0 (aryl *C* **major**), 146.2 (aryl *C* **major**), 146.5 (aryl *C* **minor**), 146.9 (aryl *C* **minor**), 148.7 (aryl *C* **minor**), 149.0 (aryl *C* **major**), 156.7 (CH_3O*C* **major**), 156.7 (CH_3O*C* **minor**); MS (APCI) *m/z* 328.1 ($M+H^+$); HRMS $C_{23}H_{22}NO$ Expected 328.1696, Found 328.1695.

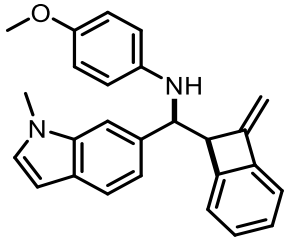
N-((S)-Furan-2-yl((S)-8-methylenebicyclo[4.2.0]octa-1,3,5-trien-7-yl)methyl)-4-methoxyaniline **106i**



Prepared according to General Procedure B on a 0.200 mmol scale (the reaction time is 4h) (crude ^{1}H NMR: 38%, 79:21 dr). Column chromatography (5% Et_2O in hexane)

afforded the title compound as a yellow oil (19 mg, 0.06 mmol, 30%, 81:19 dr). ν_{max} (thin film/cm^{-1}): 3387, 2931, 2831, 1509, 1461, 1238, 1159, 1114, 1071; δ_H (400 MHz, $CDCl_3$) 3.55-3.70 (m, 8H, OC*H*$_3$ **major** + OC*H*$_3$ **minor** + N*H* **major** + N*H* **minor**), 4.28 (d, *J* = 8.0 Hz, 1H, C*H*C=CH$_2$ **minor**), 4.33 (d, *J* = 6.8 Hz, 1H, C*H*C=CH$_2$ **major**), 4.54-4.66 (m, 3H, C*H*CHC=CH$_2$ **minor** + C*H*CHC=CH$_2$ **major** + C=C*H*$_2$ **major**), 4.97 (s, 1H, C=C*H*$_2$ **minor**), 5.19 (s, 1H, C=C*H*$_2$ **major**), 5.24 (s, 1H, C=C*H*$_2$ **minor**), 6.06-6.09 (m, 1H, aryl *H* **minor**), 6.11-6.16 (m, 1H, aryl *H* **major**), 6.21-6.27 (m, 2H, aryl *H* **major** + aryl *H* **minor**), 6.40-6.51 (m, 4H, OCC*H* **major** + OCC*H* **minor**), 6.57-6.66 (m, 4H, OCCHC*H* **major** + OCCHC*H* **minor**), 6.75 (d, *J* = 7.3 Hz, aryl *H* **minor**), 7.01-7.23 (m, 7H, 4 aryl *H* **major** + 3 aryl *H* **minor**), 7.29-7.35 (m, 2H, aryl *H* **major** + aryl *H* **minor**); δ_C (101 MHz, $CDCl_3$) 54.8 (O*C*H$_3$ **major**), 55.1 (O*C*H$_3$ **minor**), 55.3 (*C*HC=CH$_2$ **major** + *C*HC=CH$_2$ **minor**), 55.8 (*C*HCHC=CH$_2$ **major**), 55.8 (*C*HCHC=CH$_2$ **minor**), 103.4 (C=*C*H$_2$ **major**), 104.2 (C=*C*H$_2$ **minor**), 106.7 (aryl *C*H **major**), 106.9 (aryl *C*H **minor**), 110.4 (aryl *C*H **minor**), 110.4 (aryl *C*H **major**), 114.8 (OCCH*C*H **major**), 114.8 (OCCH*C*H **minor**), 115.5 (OC*C*H **major** + OC*C*H **minor**), 118.8 (aryl *C*H **minor**), 118.9 (aryl *C*H **major**), 123.0 (aryl *C*H **minor**), 123.7 (aryl *C*H **major**), 128.4 (aryl *C*H **minor**), 128.6 (aryl *C*H **major**), 129.1 (aryl *C*H **minor**), 129.2 (aryl *C*H **major**), 141.6 (aryl *C*H **minor** + *C*=CH$_2$ **minor**), 141.7 (aryl *C*H **major** + *C*=CH$_2$ **major**), 144.7 (OC(CH)$_2$*C* **minor**), 145.0 (OC(CH)$_2$*C* **major**), 146.1 (aryl *C* **major**), 146.4 (aryl *C* **major**), 146.5 (aryl *C* **minor**), 146.7 (aryl *C* **minor**), 152.6 (CH$_3$O*C* **major** + CH$_3$O*C* **minor**), 155.5 (aryl *C* **minor**), 155.9 (aryl *C* **major**); MS (APCI) *m/z* 318.2 (M+H$^+$); HRMS $C_{21}H_{20}NO_2$ Expected 318.1489, Found 318.1489.

4-Methoxy-N-((S)-(1-methyl-1H-indol-6-yl)((S)-8-methylenebicyclo[4.2.0]octa-1,3,5-trien-7-yl)methyl)aniline **106j**



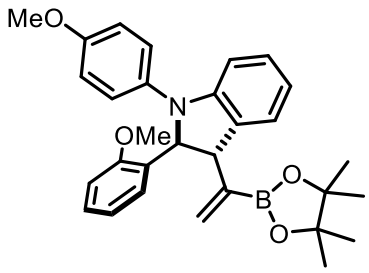
Prepared according to General Procedure B on a 0.200 mmol scale (the reaction time is 3h) (crude ^{1}H NMR: 34%, 88:12 dr). Column chromatography (5% Et_2O in hexane) afforded the title compound as a yellow oil (21 mg, 0.06 mmol, 28%, 86:14 dr). ν_{max} (thin film/cm^{-1}): 3399, 2927, 2830, 1508, 1465, 1319, 1237, 1179, 1114, 1036; δ_H (400 MHz, $CDCl_3$) 3.62-3.65 (m, 6H, OC*H*$_3$ **major** + OC*H*$_3$ **minor**), 3.73 (s, 3H, NC*H*$_3$ **minor**), 3.76 (s, 3H, NC*H*$_3$ **minor**), 3.95 (s, 2H, N*H* **major** + N*H* **minor**), 4.26 (d, *J* = 8.1 Hz, 1H, C*H*C=CH$_2$ **minor**), 4.33 (d, *J* = 5.8 Hz, 1H, C*H*C=CH$_2$ **major**), 4.65 (d, *J* = 8.1 Hz, 1H, C*H*CHC=CH$_2$ **minor**), 4.74 (d, *J* = 5.9 Hz, 1H, C*H*CHC=CH$_2$ **major**), 4.76 (s, 1H, C=C*H*$_2$ **major**), 5.00 (s, 1H, C=C*H*$_2$ **minor**), 5.28 (s, 1H, C=C*H*$_2$ **major**), 5.30 (s, 1H, C=C*H*$_2$ **minor**), 6.42-6.53 (m, 5H, OCC*H* **major** + OCC*H* **minor** + aryl *H* **major**), 6.57-6.66 (m, 4H, OCCHC*H* **major** + OCCHC*H* **minor**), 7.00-7.09 (m, 3H, aryl *H* **major** + aryl *H* **minor**), 7.13-7.31 (m, 10H, aryl *H* **major** + aryl *H* **minor**), 7.35 (s, 1H, aryl *H* **minor**), 7.42 (s, 1H, aryl *H* **major**), 7.56-7.65 (m, *2*H, aryl *H* **major** + aryl *H* **minor**); δ_C (101 MHz, $CDCl_3$) 33.0 (N*C*H$_3$ **minor**), 33.0 (N*C*H$_3$ **major**), 55.8 (O*C*H$_3$ **major**), 55.8 (O*C*H$_3$ **minor**), 58.2 (*C*HC=CH$_2$ **minor**), 58.7 (*C*HC=CH$_2$ **major**), 60.7 (*C*HCHC=CH$_2$ **major**), 62.5 (*C*HCHC=CH$_2$ **minor**), 100.8 (aryl *C*H **minor**), 100.9 (aryl *C*H **major**), 103.5 (C=*C*H$_2$ **major**), 103.8 (C=*C*H$_2$ **minor**), 107.4 (aryl *C*H **major**), 107.7 (aryl *C*H **minor**), 114.7 (OCCH*C*H **major**), 114.8 (OCCH*C*H **minor**), 115.1 (OC*C*H **major**), 115.2 (OC*C*H **minor**), 118.7 (aryl *C*H **minor**), 118.8 (aryl *C*H **major**), 118.9 (aryl *C*H **major**), 119.1 (aryl *C*H **minor**), 120.8 (aryl *C*H **minor**), 121.0 (aryl *C*H **major**), 123.5 (aryl *C*H **minor**), 123.9 (aryl *C*H **major**), 128.0 (aryl *C* **major**), 128.0 (aryl *C* **minor**),128.3 (aryl *C*H **minor**), 128.5 (aryl *C*H **major**), 128.9 (aryl *C*H **minor**), 129.0 (aryl *C*H **major**), 129.0 (aryl *C*H **minor**), 129.1 (aryl *C*H **major**), 136.4 (aryl *C* **minor**), 137.0 (aryl *C* **major**), 137.1 (aryl *C* **minor**), 137.3 (aryl *C* **major**), 142.1 (OC(CH)$_2$*C* **minor**), 142.4 (OC(CH)$_2$*C* **major**), 144.8 (*C*=CH$_2$ **minor**), 145.0 (*C*=CH$_2$ **major**), 146.5 (aryl *C* **major**), 146.8 (aryl *C* **major**), 147.1 (aryl *C* **minor**), 147.5 (aryl *C* **minor**), 152.0 (CH$_3$O*C* **major**), 152.1 (CH$_3$O*C* **minor**); MS (APCI) *m/z* 258.1 (M+H$^+$); HRMS $C_{26}H_{25}N_2O$ Expected 381.1961, Found 381.1958.

Synthesis of indolines

General procedure C

(IPr)Pd(allyl)Cl (10 mol%) and Cs_2CO_3 (2.0 equiv.) were added to a round bottom vial and flushed with N_2. A solution of the homoallylic amine (1.0 equiv.) in dry toluene (0.1 M) was then added. The vial was sealed and stirred at 100 °C for 17 h, before being cooled down and filtered through a plug of silica and concentrated *in vacuo* to afford the crude product, which was purified by column chromatography to afford the desired indoline. Nitromethane is used as an internal standard.

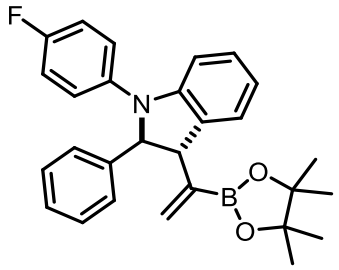
Rac-(2S,3S)-2-(2-Methoxyphenyl)-1-(4-methoxyphenyl)-3-(1-(4,4,5,5-tetramethyl-1,3, 2-dioxaborolan-2-yl)vinyl)indoline **107a**



Prepared according to General Procedure B on a 55 µmol scale (crude ^{1}H NMR: 44%, >20:1 dr). Column chromatography (5% Et_2O in hexane) afforded the title compound as a yellow oil (9.8 mg, 20 µmol, 37%, >20:1 dr). ν_{max} (thin film/cm^{-1}): 2923, 2853, 2175, 1510, 1459, 1370, 1311, 1243, 1167, 1140, 1033; δ_H (400 MHz, $CDCl_3$) 1.10 (s, 6H, BOCC*H*$_3$), 1.16 (s, 6H, BOCC*H*$_3$), 3.74 (s, 3H, OC*H*$_3$), 3.76 (s, 3H, Ar-OC*H*$_3$), 3.79 (d, *J* = 6.2 Hz, 1H, C*H*C=CH$_2$), 5.54 (d, *J* = 6.1 Hz, 1H, C*H*CHC=CH$_2$), 5.62 (d, *J* = 3.1 Hz, 1H, C=C*H*$_2$), 5.83 (d, *J* = 3.1 Hz, 1H, C=C*H*$_2$), 6.68 (t, *J* = 7.3 Hz, 1H, aryl *H*), 6.75-6.81 (m, 2H, OCCHC*H*), 6.82-6.91 (m, 3H, aryl *H*), 6.95 (d, *J* = 7.3 Hz, 1H, aryl *H*), 7.01-7.09 (m, 1H, aryl *H*), 7.10-7.21 (m, 3H, OCC*H* + aryl *H*), 7.41 (d, *J* = 7.8 Hz, 1H, aryl *H*); δ_C (101 MHz, $CDCl_3$) 24.7 (BOC*C*H$_3$), 24.8 (BOC*C*H$_3$), 55.5 (O*C*H$_3$), 55.6 (Ar-O*C*H$_3$), 57.3 (*C*HC=CH$_2$), 69.0 (*C*HCHC=CH$_2$), 83.4 (BO*C*CH$_3$), 108.7 (aryl *C*H), 110.8 (aryl *C*H), 114.3 (OCCH*C*H), 118.6 (aryl *C*H), 120.8 (aryl *C*H), 122.0 (OC*C*H), 124.9 (aryl *C*H), 127.3 (aryl *C*H), 127.5 (aryl *C*H), 127.9 (aryl *C*H), 129.4 (C=*C*H$_2$), 131.8 (aryl *C*),

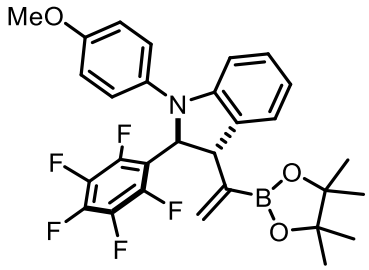
133.2 (aryl *C*), 138.4 (OC(CH)$_2$*C*), 149.1 (aryl *C*), 155.0 (aryl *C*), 155.0 (CH_3O*C*), (B*C*=CH_2 not observed); δ_B (128 MHz, $CDCl_3$) 27.3 (*B*OCCH_3); MS (APCI) *m/z* 484.1 ($M+H^+$); HRMS $C_{30}H_{35}BNO_4$ Expected 484.2654, Found 484.2656.

Rac-(2S,3S)-1-(4-Fluorophenyl)-2-phenyl-3-(1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan -2-yl)vinyl)indoline **107m**



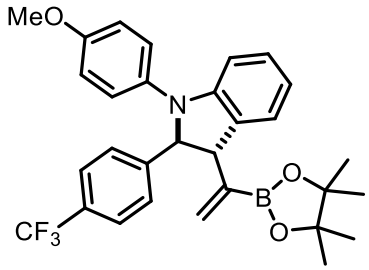
Prepared according to General Procedure B on a 0.2 mmol scale (crude ^{1}H NMR: 58%, >20:1 dr). Column chromatography (5% Et_2O in hexane) afforded the title compound as a yellow oil (22 mg, 0.499 mmol, 25%, >20:1 dr). ν_{max} (thin film/cm^{-1}): 2976, 2929, 1506, 1458, 1361, 1310, 1224, 1166, 1135, 1035; δ_H (500 MHz, $CDCl_3$) 1.13 (s, 6H, BOCC*H*$_3$), 1.20 (s, 6H, BOCC*H*$_3$), 3.88 (d, *J* = 6.0 Hz, 1H, C*H*C=CH_2), 5.01 (d, *J* = 6.0 Hz, 1H, C*H*CHC=CH_2), 5.52 (d, *J* = 3.0 Hz, 1H, C=C*H*$_2$), 5.91 (d, *J* = 3.0 Hz, 1H, C=C*H*$_2$), 6.76 (t, *J* = 7.3 Hz, 1H, aryl *H*), 6.88 – 6.95 (m, 3H, FCCHC*H* + aryl *H*), 6.98 (d, *J* = 7.4 Hz, 1H, aryl *H*), 7.08-7.16 (m, 3H, FCC*H* + aryl *H*), 7.20-7.25 (m, 1H, aryl *H*), 7.28 (t, *J* = 7.8 Hz, 2H, aryl *H*), 7.34-7.39 (m, 2H, aryl *H*); δ_C (126 MHz, $CDCl_3$) 24.6 (BOC*C*H$_3$), 25.0 (BOC*C*H$_3$), 57.9 (*C*HC=CH_2), 75.6 (*C*HCHC=CH_2), 83.7 (BO*C*CH_3), 108.7 (aryl *C*H), 115.7 (d, *J* = 18.0 Hz, FC*C*H), 119.4 (aryl *C*H), 122.2 (d, *J* = 8.0 Hz, FCCH*C*H), 125.4 (aryl *C*H), 126.7 (aryl *C*H), 127.3 (aryl *C*H), 127.7 (aryl *C*H), 128.7 (aryl *C*H), 131.1 (C=*C*H_2), 131.9 (aryl *C*), 140.9 (d, *J* = 2.5 Hz, FC(CH)$_2$*C*), 143.3 (aryl *C*), 148.9 (aryl *C*), 158.5 (d, *J* = 241.1 Hz, F*C*), (B*C*=CH_2 not observed); δ_B (128 MHz, $CDCl_3$) 30.4 (*B*OCCH_3); δ_F (376 MHz, $CDCl_3$) -120.79 (s, *F*C); MS (APCI) *m/z* 442.2 ($M+H^+$); HRMS $C_{28}H_{30}BFNO_2$ Expected 442.2348, Found 442.2348.

Rac-(2S,3S)-1-(4-Methoxyphenyl)-2-(perfluorophenyl)-3-(1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)vinyl)indoline **107c**



Prepared according to General Procedure B on a 0.200 mmol scale (the reaction time is 14 h) (crude ^{1}H NMR: 55%, >20:1 dr). Column chromatography (3% Et_2O in hexane) afforded the title compound as a yellow oil (53 mg, 0.098 mmol, 49%, >20:1 dr). ν_{max} (thin film/cm^{-1}): 2977, 2837, 1502, 1441, 1311, 1282, 1167, 1136, 1035; δ_H (400 MHz, $CDCl_3$) 1.10 (s, 6H, BOCC*H*$_3$), 1.20 (s, 6H, BOCC*H*$_3$), 3.78 (s, 3H, OC*H*$_3$), 4.31 (d, *J* = 8.9 Hz, 1H, C*H*C=CH$_2$), 5.54 (d, *J* = 9.0 Hz, 1H, C*H*CHC=CH$_2$), 5.73 (d, *J* = 2.9 Hz, 1H, C=C*H*$_2$), 6.01 (d, *J* = 2.9 Hz, 1H, C=C*H*$_2$), 6.54 (d, *J* = 7.9 Hz, 1H, aryl *H*), 6.73 (t, *J* = 7.4 Hz, 1H, aryl *H*), 6.80-6.88 (m, 2H, OCCHC*H*), 6.97 (d, *J* = 7.4 Hz, 1H, aryl *H*), 7.04 (t, *J* = 7.4 Hz, 1H, aryl *H*), 7.09-7.19 (m, 2H, OCC*H*); δ_C (101 MHz, $CDCl_3$) 24.7 (BOC*C*H$_3$), 24.7 (BOC*C*H$_3$), 54.8 (*C*HC=CH$_2$), 55.5 (O*C*H$_3$), 66.1 (*C*HCHC=CH$_2$), 83.7 (BO*C*CH$_3$), 108.0 (aryl *C*H), 114.8 (OCCH*C*H), 118.8 (aryl *C*H), 124.5 (aryl *C*H), 125.5 (OC*C*H*)*, 127.9 (aryl *C*H), 130.6 (aryl *C*), 132.3 (C=*C*H$_2$), 136.8 (OC(CH)$_2$*C*), 150.4 (aryl *C*), 156.9 (CH$_3$O*C*), (*C*F, B*C*=CH$_2$ not observed); δ_B (128 MHz, $CDCl_3$) 30.1 (*B*OCCH$_3$); δ_F (376 MHz, $CDCl_3$) -155.51 (s, *F*C); MS (APCI) *m/z* 544.2 (M+H$^+$); HRMS $C_{29}H_{27}BNO_3F_5Na$ Expected 566.1896, Found 566.1897.

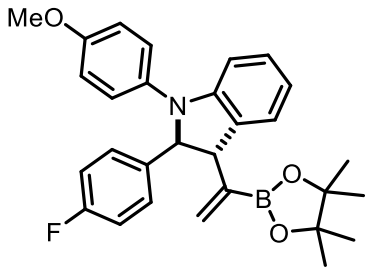
Rac-(2S,3S)-1-(4-Methoxyphenyl)-3-(1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)vinyl)-2-(4-(trifluoromethyl)phenyl)indoline **107b**



Prepared according to General Procedure B on a 0.200 mmol scale (crude ^{1}H NMR: 70%, >20:1 dr). Column chromatography (3.5% Et_2O in hexane) afforded the title

compound as a yellow oil (65 mg, 0.125 mmol, 63%, >20:1 dr). ν_{max} (thin film/cm^{-1}): 3044, 2977, 2932, 2836, 1508, 1459, 1321, 1274, 1162, 1108, 1035; δ_H (400 MHz, $CDCl_3$) 1.13 (s, 6H, BOCC*H*$_3$), 1.23 (s, 6H, BOCC*H*$_3$), 3.76 (s, 3H, OC*H*$_3$), 4.31 (d, *J* = 7.0 Hz, 1H, C*H*C=CH$_2$), 5.10 (d, *J* = 7.0 Hz, 1H, C*H*CHC=CH$_2$), 5.57 (d, *J* = 2.9 Hz, 1H, C=C*H*$_2$), 5.97 (d, *J* = 3.0 Hz, 1H, C=C*H*$_2$), 6.72-6.87 (m, 4H, OCCHC*H* + aryl *H*), 6.97 (d, *J* = 7.2 Hz, 1H, aryl *H*), 7.06-7.17 (m, 3H, OCC*H* + aryl *H*), 7.50-7.60 (m, 4H, aryl *H*); δ_C (101 MHz, $CDCl_3$) 24.6 (BOC*C*H$_3$), 25.0 (BOC*C*H$_3$), 55.5 (O*C*H$_3$), 58.0 (*C*HC=CH$_2$), 75.9 (*C*HCHC=CH$_2$), 83.7 (BO*C*CH$_3$), 108.6 (aryl *C*H), 114.6 (OCCH*C*H), 119.1 (aryl *C*H), 123.0 (OC*C*H), 124.4 (q, *J* = 272.0 Hz, *C*F$_3$), 125.0 (aryl *C*H), 125.5 (q, *J* = 3.8 Hz, CF$_3$C*C*H), 127.4 (F$_3$CCCH*C*H), 127.9 (aryl *C*H), 129.6 (q, *J* = 32.2 Hz, CF$_3$*C*), 131.2 (OC(CH)$_2$*C*), 131.7 (C=*C*H$_2$), 137.9 (aryl *C*), 147.6 (CF$_3$C(CH)$_2$*C*), 150.1 (aryl *C*), 156.0 (CH$_3$O*C*), (B*C*=CH$_2$ not observed); δ_B (128 MHz, $CDCl_3$) 31.1 (*B*OCCH$_3$); δ_F (376 MHz, $CDCl_3$) -62.31 (s, *F*$_3$C); MS (APCI) *m/z* 544.2 (M+H$^+$); HRMS $C_{30}H_{31}BNO_3F_3Na$ Expected 544.2241 Found 544.2240.

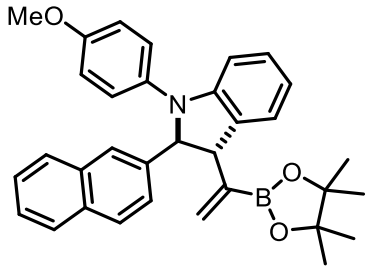
Rac-(2S,3S)-2-(4-Fluorophenyl)-1-(4-methoxyphenyl)-3-(1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)vinyl)indoline **107f**



Prepared according to General Procedure B on a 0.200 mmol scale (crude ^{1}H NMR: 54%, >20:1 dr). Column chromatography (5% Et_2O in hexane) then preparative TLC (2% EtOAc + 1% Et_3N in hexane, 500 µm) afforded the title compound as a yellow oil (37-mg, 0.078 mol, 39%, >20:1 dr). ν_{max} (thin film/cm^{-1}): 3044, 2957, 2855, 1509, 1458, 1362, 1311, 1272, 1154, 1104, 1036; δ_H (400 MHz, $CDCl_3$) 1.11 (s, 6H, BOCC*H*$_3$), 1.20 (s, 6H, BOCC*H*$_3$), 3.75 (s, 3H, OC*H*$_3$), 3.89 (d, *J* = 6.9 Hz, 1H, C*H*C=CH$_2$), 4.99 (d, *J* = 7.2 Hz, 1H, C*H*CHC=CH$_2$), 5.54 (d, *J* = 3.1 Hz, 1H, C=C*H*$_2$), 5.92 (d, *J* = 3.1 Hz, 1H, C=C*H*$_2$), 6.68-6.75 (m, 2H, aryl *H*), 6.75-6.82 (m, 2H, OCCHC*H*), 6.90-6.99 (m, 3H, aryl *H*),

7.03-7.12 (m, 3H, OCC*H* + aryl *H*), 7.29-7.38 (m, 2H, aryl *H*); δ_C (101 MHz, $CDCl_3$) 24.6 (BOC*C*H_3), 25.0 (BOC*C*H_3), 55.6 (O*C*H_3), 58.1 (*C*HC=CH_2), 75.7 (*C*HCHC=CH_2), 83.7 (BO*C*CH_3), 108.3 (aryl *C*H), 114.5 (OCCH*C*H), 115.3 (d, *J* = 21.2 Hz, FC*C*H), 118.9 (aryl *C*H), 123.9 (OC*C*H), 125.0 (aryl *C*H), 127.7 (aryl *C*H), 128.7 (d, *J* = 8.0 Hz, FCCH*C*H), 131.4 (C=*C*H_2), 131.5 (aryl *C*), 138.0 (OC$(CH)_2$*C*), 139.0 (d, *J* = 3.0 Hz, FC$(CH)_2$*C*), 150.2 (aryl *C*), 155.9 (CH_3O*C*), 162.1 (d, *J* = 244.6 Hz, F*C*), (B*C*=CH_2 not observed); δ_B (128 MHz, $CDCl_3$) 28.0 (*B*OCCH_3); δ_F (376 MHz, $CDCl_3$) -115.77 (*F*C); MS (APCI) *m/z* 472.3 ($M+H^+$); HRMS $C_{29}H_{31}BNO_3F$ Expected 472.2454, Found 472.2459.

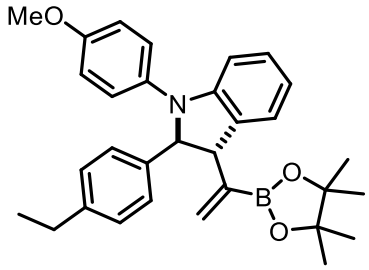
Rac-(2S,3S)-1-(4-Methoxyphenyl)-2-(naphthalen-2-yl)-3-(1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)vinyl)indoline **107e**



Prepared according to General Procedure B on a 0.200 mmol scale (crude ^{1}H NMR: 58%, >20:1 dr). Column chromatography (5% Et_2O in hexane) afforded the title compound as a yellow oil (50 mg, 0.100 mol, 50%, >20:1 dr). ν_{max} (thin film/cm^{-1}): 2974, 2926, 2854, 1508, 1458, 1361, 1311, 1242, 1167, 1137, 1035; δ_H (400 MHz, $CDCl_3$) 1.09 (s, 6H, BOCCH_3), 1.20 (s, 6H, BOCCH_3), 3.72 (s, 3H, OCH_3), 4.00 (d, *J* = 6.9 Hz, 1H, C*H*C=CH_2), 5.16 (d, *J* = 6.9 Hz, 1H, C*H*CHC=CH_2), 5.55 (d, *J* = 3.0 Hz, 1H, C=CH_2), 5.93 (d, *J* = 3.0 Hz, 1H, C=CH_2), 6.69-6.83 (m, 4H, OCCHC*H* + 2 aryl *H*), 6.98 (d, *J* = 7.1 Hz, 1H, aryl *H*), 7.10 (t, *J* = 7.5 Hz, 1H, aryl *H*), 7.13-7.19 (m, 2H, OCC*H*), 7.39-7.46 (m, 2H, aryl *H*), 7.63 (dd, *J* = 8.4, 1.5 Hz, 1H, aryl *H*), 7.72-7.83 (m, 4H, aryl *H*); δ_C (101 MHz, $CDCl_3$) 24.6 (BOC*C*H_3), 25.0 (BOC*C*H_3), 55.5 (O*C*H_3), 58.0 (*C*HC=CH_2), 76.5 (*C*HCHC=CH_2), 83.6 (BO*C*CH_3), 108.4 (aryl *C*H), 114.5 (OCCH*C*H), 118.8 (aryl *C*H), 123.8 (OC*C*H), 125.0 (aryl *C*H), 125.3 (aryl *C*H), 125.6 (aryl *C*H), 125.9 (aryl *C*H), 126.0 (aryl *C*H), 127.7 (aryl *C*H), 127.8 (aryl *C*H), 128.0 (aryl *C*H), 128.4 (aryl *C*H), 131.2 (C=*C*H_2), 131.7 (aryl *C*), 133.1 (aryl *C*), 133.5 (aryl *C*), 138.3 (OC$(CH)_2$*C*), 141.0 (aryl *C*), 150.3

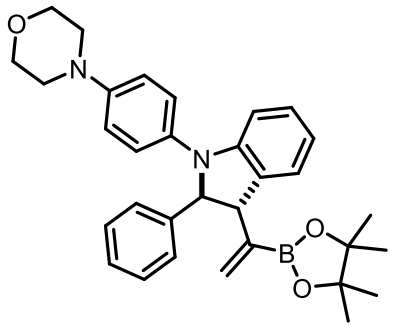
(aryl *C*), 155.8 (CH_3OC), (B*C*=CH_2 not observed); δ_B (128 MHz, $CDCl_3$) 28.9 (*B*$OCCH_3$); MS (APCI) *m/z* 504.3 ($M+H^+$); HRMS $C_{33}H_{35}BNO_3$ Expected 504.2705, Found 504.2710.

Rac-(2S,3S)-2-(4-Ethylphenyl)-1-(4-methoxyphenyl)-3-(1-(4,4,5,5-tetramethyl-1,3,2-di oxaborolan-2-yl)vinyl)indoline **107d**



Prepared according to General Procedure B on a 0.200 mmol scale (crude ^1H NMR: 66%, >20:1 dr). Column chromatography (5% Et_2O in hexane) then preparative TLC (2% EtOAc + 1% Et_3N in hexane, 500 μm) afforded the title compound as a yellow oil (48 mg, 0.100 mmol, 50%, >20:1 dr). ν_{max} (thin film/cm^{-1}): 2973, 2930, 2834, 1508, 1458, 1369, 1310, 1241, 1167, 1137, 1036; δ_H (400 MHz, $CDCl_3$) 1.12 (s, 6H, BOCC*H*$_3$), 1.18-1.24 (m, 9H, BOCC*H*$_3$ + CH_2C*H*$_3$), 2.60 (q, *J* = 7.6 Hz, 2H, C*H*$_2$$CH_3$), 3.74 (s, 3H, OC*H*$_3$), 3.88 (d, *J* = 6.6 Hz, 1H, C*H*C=CH_2), 4.98 (d, *J* = 6.6 Hz, 1H, C*H*CHC=CH_2), 5.54 (d, *J* = 3.1 Hz, 1H, C=C*H*$_2$), 5.90 (d, *J* = 3.0 Hz, 1H, C=C*H*$_2$), 6.70 (t, *J* = 7.5 Hz, 1H, aryl *H*), 6.75-6.81 (m, 3H, OCCHC*H* + aryl *H*), 6.95 (d, *J* = 7.5 Hz, 1H, aryl *H*), 7.02-7.16 (m, 5H, OCC*H* + aryl *H*), 7.24-7.30 (m, 2H, aryl *H*); δ_C (101 MHz, $CDCl_3$) 15.6 (CH_2*C*H_3), 24.6 (BOC*C*H_3), 25.0 (BOC*C*H_3), 28.6 (*C*H_2CH_3), 55.6 (O*C*H_3), 57.9 (*C*HC=CH_2), 75.8 (*C*HCHC=CH_2), 83.6 (BO*C*CH_3), 108.3 (aryl *C*H), 114.5 (OCCH*C*H), 118.7 (aryl *C*H), 123.3 (OC*C*H), 125.1 (aryl *C*H), 126.9 (aryl *C*H), 127.6 (aryl *C*H), 128.0 (aryl *C*H), 130.9 (C=*C*H_2), 131.8 (aryl *C*), 138.3 (OC(CH)$_2$*C*), 140.7 (aryl *C*), 143.0 (aryl *C*), 150.0 (aryl *C*), 155.5 (CH_3OC), (B*C*=CH_2 not observed); δ_B (128 MHz, $CDCl_3$) 31.1 (*B*$OCCH_3$); MS (APCI) *m/z* 482.3 ($M+H^+$); HRMS $C_{31}H_{27}BNO_3$ Expected 482.2861, Found 482.2866.

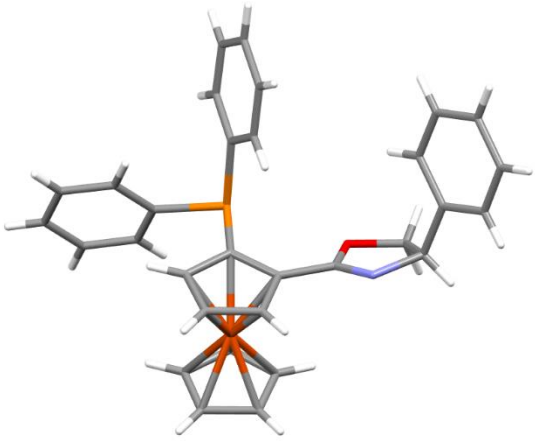
Rac-4-(4-((2S,3S)-2-Phenyl-3-(1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)vinyl)ind olin-1-yl)phenyl)morpholine **107n**



Prepared according to General Procedure B on a 0.200 mmol scale (the reaction time is 23 h) (crude ^{1}H NMR: 42%, >20:1 dr). Column chromatography (15% EtOAc in hexane) afforded the title compound as a yellow oil (39 mg, 0.100 mmol, 38%, >20:1 dr). ν_{max} (thin film/cm^{-1}): 2974, 2925, 2854, 1512, 1450, 1370, 1310, 1258, 1168, 1136, 1050; δ_H (400 MHz, $CDCl_3$) 1.12 (s, 6H, BOCC*H*$_3$), 1.20 (m, 6H, BOCC*H*$_3$), 3.03-3.09 (m, 4H, OCH$_2$C*H*$_2$N), 3.77-3.85 (m, 4H, OC*H*$_2$CH$_2$N), 3.88 (d, *J* = 6.4 Hz, 1H, C*H*C=CH$_2$), 5.02 (d, *J* = 6.4 Hz, 1H, C*H*CHC=CH$_2$), 5.52 (d, *J* = 3.2 Hz, 1H, C=C*H*$_2$), 5.90 (d, *J* = 3.1 Hz, 1H, C=C*H*$_2$), 6.70 (t, *J* = 7.4 Hz, 1H, aryl *H*), 6.76-6.85 (m, 3H, CH$_2$NCCHC*H* + aryl *H*), 6.95 (d, *J* = 7.3 Hz, 1H, aryl *H*), 7.03-7.13 (m, 3H, CH$_2$NCC*H* + aryl *H*), 7.15-7.29 (m, 3H, aryl *H*), 7.34-7.41 (m, 2H, aryl *H*); δ_C (101 MHz, $CDCl_3$) 24.6 (BOC*C*H$_3$), 25.0 (BOC*C*H$_3$), 50.1 (OCH$_2$*C*H$_2$N), 57.9 (*C*HC=CH$_2$), 67.1 (O*C*H$_2$CH$_2$N), 75.6 (*C*HCHC=CH$_2$), 83.6 (BO*C*CH$_3$), 108.4 (aryl *C*H), 116.8 (NCCH*C*H), 118.7 (aryl *C*H), 122.5 (NC*C*H), 125.2 (aryl *C*H), 126.9 (aryl *C*H), 127.1 (aryl *C*H), 127.6 (aryl *C*H), 128.5 (aryl *C*H), 131.0 (C=*C*H$_2$), 131.8 (aryl *C*), 137.9 (CH$_2$NC(CH)$_2$*C*), 143.6 (aryl *C*), 147.0 (CH$_2$N*C*), 149.7 (aryl *C*), (B*C*=CH$_2$ not observed); δ_B (128 MHz, $CDCl_3$) 31.1 (*B*OCCH$_3$); MS (APCI) *m/z* 509.3 (M+H$^+$); HRMS $C_{32}H_{38}BN_2O_3$ Expected 509.2970, Found 509.2971.

X-Ray Crystal Structures

Crystal data and structure refinement for Ligand 96.



Identification code	Ligand **96**
Empirical formula	$C_{31}H_{26}FeNOP$
Formula weight	515.35
Temperature/K	150.00(10)
Crystal system	monoclinic
Space group	$P2_1$
a/Å	8.1809(2)
b/Å	14.4600(2)
c/Å	10.2698(2)
α/°	90
β/°	92.683(2)
γ/°	90
Volume/Å^3	1213.54(4)
Z	2
ρ_{calc}g/cm^3	1.410
μ/mm^{-1}	5.795
F(000)	536.0
Crystal size/mm^3	0.05 × 0.05 × 0.05
Radiation	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	8.62 to 151.734
Index ranges	-8 ⩽ h ⩽ 10, -18 ⩽ k ⩽ 17, -12 ⩽ l ⩽ 12
Reflections collected	11961
Independent reflections	4869 [R_{int} = 0.0255, R_{sigma} = 0.0287]
Data/restraints/parameters	4869/1/316
Goodness-of-fit on F^2	1.094
Final R indexes [I>=2σ (I)]	R_1 = 0.0272, wR_2 = 0.0718
Final R indexes [all data]	R_1 = 0.0282, wR_2 = 0.0722
Largest diff. peak/hole / e Å^{-3}	0.21/-0.26
Flack parameter	-0.011(2)

References

[1] Solomon and Fryhles organic chemistry. Wiley (Students edition), Chapter 5 (Stereochemistry), Section 5.11 (Chiral drugs).

[2] Medicinal Chemistry: The Modern Drug Discovery Process. Pearson. Chapter 13 (Aspects in Pharmaceutical Synthesis). Section 13.2 (Stereochemistry).

[3] Corey, Kurti - Enantioselective Chemical Synthesis - Methods, Logic, and Practice

[4] (a)O. Korpiun, K. Mislow, *J. Am. Chem. Soc.*, **1967**, *89*, 4784-4786;(b) M. Kitamura, T. Ohkuma, S. Inoue, N. Sayo, H. Kobayashi, S. Akutagama, T. Ohta, H. Takaya, R. Noyori, *J. Am. Chem. Soc.*, **1988**, *110*, 629-631;(c) T. Katsuki, K. B. Sharpless, , *J. Am. Chem. Soc.*, **1980**, *102*, 5974-5976.

[5] For recent reviews, see: (a) D. S. Muller, I. Marek, *Chem. Soc. Rev.*, **2016**, *45*, 4552–4566; (b) X. Zhu, S. Chiba, *Chem. Soc. Rev.*, **2016**, *45*, 4504–4523; (c) M. Shibasaki, M. Kanai, *Chem. Rev.*, **2008**, *108*, 2853–2873; (d) S. Thapa, B. Shrestha, S. K. Gurung, R. Giri, *Org. Biomol. Chem.*, **2015**, *13*, 4816– 4827; (e) C. Maaliki, E. Thiery, J. Thibonnet, *Eur. J. Org. Chem.*, **2017**, *2*, 209–228; (f) N. Yoshikai, E. Nakamura, *Chem. Rev.*, **2012**, *112*, 2339–2372. For selected recent publications, see: (a) R. P. Jumde, F. Lanza, M. J. Veenstra, S. R. Harutyunyan, *Science*, **2016**, *352*, 433–437; (b) Y. Yang, I. B. Perry, S. L. Buchwald, *J. Am. Chem. Soc.*, **2016**, *138*, 9787–9790; (c) K. Kubota, Y. Watanabe, K. Hayama, H. Ito, *J. Am. Chem. Soc.*, **2016**, *138*, 4338–4341; (d) K. Hojoh, H. Ohmiya, M. Sawamura, *J. Am. Chem. Soc.*, **2017**, *139*, 2184–2187.

[6] A. P. Pulis, K. Yeung, D. J. Procter, *Chem. Sci.* **2017**, *8*, 5240–5247.

[7] E. Soriano, I. Fernandez, *Chem. Soc. Rev.,***2014**, *43*, 3041–3105.

[8] F. Meng, B. Jung, F. Haeffner, A. H. Hoveyda, *Org. Lett.* **2013**, *15*, 1414–1417.

[9] Y. Shimizu and M. Kanai, *Tetrahedron Lett.*, **2014**, *55*, 3727– 3737.

[10] (a) K. Yeung, R. E. Ruscoe, J. Rae, A. P. Pulis, D. J. Procter, *Angew. Chem. Int. Ed.*, **2016**, *55*, 11912–11916; (b) F. Meng, B. Jung, F. Haeffner, A. H. Hoveyda, *Org. Lett.* **2013**, *15*, 1414–1417**;** (c) R. Y. Liu, Y. Yang, S. L. Buchwald, *Angew. Chem. Int. Ed.*, **2016**, *55*, 14077–14080; (d) P. K. Chikkade, Y. Shimizu, M. Kanai, *Chem. Sci.*,

2014, *5*, 1585–1590.

[11] K. Oisaki, D. Zhao, M. Kanai, M. Shibasaki, *J. Am. Chem. Soc.*, **2007**, *129*, 7439–7443.

[12] F. Meng, H. Jang, B. Jung, A. H. Hoveyda, *Angew. Chem. Int. Ed.*, **2013**, *52*, 5046–5051.

[13] P. K. Chikkade, Y. Shimizu, M. Kanai, *Chem. Sci.*, **2014**, *5*, 1585–1590.

[14] N. A. McGrath, M Brichacek, J. T. Njardarson,*J. Chem. Ed.*, **2010**, *87*, 1348-1349.

[15] S, Kobayashi, H, Ishitani. *Chemical Reviews*, **1999**, *99*, 1069-1094.

[16] (a) K. Yeung, R. E. Ruscoe, J. Rae, A. P. Pulis, D. J. Procter, *Angew. Chem. Int. Ed.*, **2016**, *55*, 11912–11916. (b) J. Rae, K. Yeung, J. J. W. McDouall, D. J. Procter, *Angew. Chem. Int. Ed.*, **2016**, *55*, 1102–1107.

[17] R. Y. Liu, Y. Yang, S. L. Buchwald, *Angew. Chem. Int. Ed.*, **2016**, *55*, 14077–14080

[18] L. S. Tan, N. Venkatasubramanian, P. T. Mather, M. D. Houtz, C. L.Benner, *J. Polym. Sci. A Polym. Chem.*, **1998**, *36*, 2637-2651.

[19] M. F. Farona, *Science*, **1996**, *21*, 505-555.

[20] H. Finkelstein, Über Ein Derivat Des Benzocyklobutans, University of Strasbourg, 1909.

[21] M. P. Cava, D. R. Napier, *J. Am. Chem. Soc.*, **1957**, *79*, 1701-1705.

[22] (a) J. F. Bunnett, J. A. Skorcz, *J. Org. Chem.*, **1962**, *27*, 3836–3843. (b) T. Hosoya, T. Hasegawa, Y. Kuriyama, T. Matsumoto, K. Suzuki, *Synlett,* **1995**, *2*, 177–179.

[23] (a) G. Dyker, *Angew. Chem. Int. Ed.* **1994**, *33*, 103–105. (b) O. Baudoin, A. Herrbach, F. Guéritte, *Angew. Chem. Int. Ed.*, **2003**, *42*, 5736–5740. (c) M. Chaumontet, R. Piccardi, N. Audic, J. Hitce, J.-L. Peglion, E. Clot, O. Baudoin, *J. Am. Chem. Soc. ,***2008**, *130*, 15157–15166.

[24] S. Kitagaki, Y. Okumura, C. Mukai, *Tetrahedron*, **2006**, *62*, 10311-10320.

[25] L. M. Chapman, J. C. Beck, C. R. Lacker, L. Wu, S. E. Reisman, *J. Org. Chem.*, **2018**, *83*, 11, 6066–6085.

[26] Y. Ozawa, H. Iwamoto, H. Ito, *Chem. Commun.*, **2018**, *54*, 4991-4994.

[27] For selected examples, see: (a) J. L. Stanton, M. H. Ackerman, *J. Med. Chem.*,

1983, *26*, 986-989; (b) P. Melnyk, B. Legrand, J. Gasche, P. Ducrot, C. Thal, *Tetrahedron*, **1995**, *51*, 1941-1952; (c) Y. H. Kim, J. Y. Choi, *Tetrahedron Lett.*, **1996**, *37*, 5543-5546; (d) Y. Kiryu, S. Itoh, K. Kaneko, H. Katayama, *Chem. Pharm. Bull.*, **1998**, *46*, 1810-1813.

[28] H. M. Wang, H. Zhou, Q. S. Xu, T. S. Liu, C. L. Zhuang, M. H. Shen, H. D. Xu, *Org. Lett.*, **2018**, *20*, 1777-1780.

[29] G. Zhang, A. Cang, Y. Wang, Y. Li, G. Xu, Q. Zhang, *Org. Lett.*, **2018,** *20*, 1798-1801.

[30] R. X., Liang, R. Y. Chen, C. Zhong, J. W. Zhu, Z. Y. Cao, Y. X. Jia, *Org. Lett.* **2020**, *22*, 3215-3218.

[31] D. Zhao, S. Vásquez-Céspedes, F. Glorius, *Angew. Chem. Int. Ed.*, **2015**, *54*, 1657-1661.

[32] J. Barluenga, F. Aznar, C. Valdes, *Angew. Chem. Int. Ed.* **2004**, 43, 343.

[33] A. Kumar, A. G. Samuelson, *J. Organomet. Chem.* **2010**, *3,* 338.

[34] J. Bain, P. Cho, A. Voutchkova-Kostal, *Green Chem.* **2015**, 17, 2271.

[35] Y. F. Zhang, B. Wu, Z. J. Shi, *Chem. Eur. J.* **2016**, 22, 17808.

[36] D. Yu, L. Lu, Q. Shen, *Org. Lett.*, **2013**, *15*, 940.

[37] J. A. Leitch, T. Rogova, F. Duarte, D. J. Dixon, *Angew. Chem. Int. Ed.* **2020**, 59, 4121.

[38] R. Sala, F. Roudesly, L. F. Veiros, G. Broggini, J. Oble, G. Poli, *Adv. Synth. Catal.* **2020**, 362, 2486.

[39] J. C. Anderson, G. P. Howell, R. M. Lawrence, Wilson C. S., *J. Org. Chem.* **2005**, 70, 5665.

[40] W. Yuan, S. Ma, *Adv. Synth. Catal.* **2012**, *354*, 1867.

[41] R. A. Arthurs, C. J. Richards, *Org. Lett.* **2017**, 19, 702.