ENANTIOSELECTIVE SYNTHESIS AND CYCLOISOMERIZATION OF 1-BICYCLO[1.1.0]BUTAN-1-YL ALKYLAMINES

by

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This dissertation demonstrates the synthesis and application of 1-bicyclo[1.1.0]butyl alkylamines. The enantioselective synthesis of 1-bicyclo[1.1.0]butan-1-yl alkylamines was achieved by cyclopropanation to enantiomerically enriched propargyl amides. The enantioselective addition of alkynes to imines proceeded well for most *N*-diphenylphosphinyl 1-bicyclo[1.1.0]butyl alkylamines, but the cyclopropanation suffered from the formation of cyclopropane byproducts. A series of silyl-substituted bicyclo[1.1.0]butanes could be synthesized by this methodology in high, reproducible yields. When tethered to an activated alkyne, the silyl-substituted bicyclo[1.1.0]butane undergoes cyclization to form a pyrrolidine.

In the application of the 1-bicyclo[1.1.0]butyl alkylamines, a palladium(0)-catalyzed cycloisomerization of bicyclo[1.1.0]butanes and methylenecyclopropanes has been developed. 3-Azaspiro[bicyclo[3.1.0]hexane-6,1'-cyclopropane] is obtained with excellent stereoselectivity. A novel 2,3,3*a*,6*a*-tetrahydrocyclopenta[*c*]pyrrol-4(1*H*)-one is the product of the cycloisomerization and carbonylation sequence.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF SCHEMES

LIST OF ABBREVIATIONS

AIBN	2,2′-Azobis(2-methylpropionitrile)
Ac	Acetyl
n-Bu	*n*-Butyl
t-Bu	*tert*-Butyl
Cbz	Carboxybenzyl
COD	1,5-Cyclooctadiene
Cp	Cyclopentadienyl
Cy	Cyclohexyl
DCM	Dichloromethane
DFT	Density functional theory
DMF	*N*,*N*'-dimethyl formamide
DMP	Dess–Martin periodinane
DMSO	Dimethyl sulfoxide
DPP	Diphenylphosphinyl
dppp	1,3-Bis(diphenylphosphino)propane
dba	Dibenzylideneacetone
Et	Ethyl
HOMO	Highest Occupied Molecular Orbital

LG	Leaving group
LiHMDS	Lithium bis(trimethylsilyl)amide
LUMO	Lowest Unoccupied Molecular Orbital
Ms	Methylsulfonyl
MCP	Methylenecyclopropane
Ph	Phenyl
Piv	Pivaloyl
*i*Pr	*iso*-Propyl
SFC	Supercritical Fluid Chromatography
TBAF	Tetra-*n*-butylammonium fluoride
TBS	tert-Butyldimethylsilyl
TEEDA	*N,N,N′,N′*-Tetraethylethylenediamine
TES	Triethylsilyl
Tf	Trifluoromethanesulfonyl
TFE	Trifluoroethanol
THF	Tetrahydrofuran
TIPS	Tri-*iso*-propylsilyl
TLC	Thin Layer Chromatography
TMEDA	*N,N,N′,N′*-Tetramethylethylenediamine
TMM	Trimethylenemethane
TMS	Trimethylsilyl
Ts	4-Toluenesulfonyl

1. ENANTIOSELECTIVE SYNTHESIS OF 1-BICYCLO[1.1.0]BUTAN-1-YL ALKYLAMINES

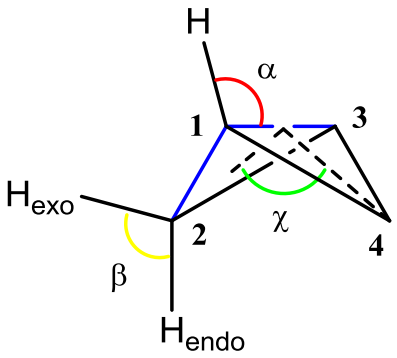
Bicyclo[1.1.0]butane is one of the most strained small carbon ring systems, and it can serve as an attractive building block for the synthesis of complex organic molecules.[1,2] Our group has taken advantage of this high strain energy and used bicyclo[1.1.0]butane as a precursor for the synthesis of pyrrolidines and azepines.[3] New developments in this area, specifically, an access to enantiomerically pure 1-bicyclo[1.1.0]butan-1-yl alkylamines starting materials, would add significantly to the repertoire of chemical transformations of bicyclo[1.1.0]butane substrates.

1.1 FUNDAMENTAL PROPERTIES OF BICYCLO[1.1.0]BUTANES

1.1.1 Structure of bicyclo[1.1.0]butanes.

The structure of bicyclo[1.1.0]butane has been elucidated by different methods including microwave[4], NMR[5], X-ray[5] and computations.[6-8] These studies revealed some interesting facets of bicyclo[1.1.0]butane. First, the C-C bond lengths are in agreement among different methods. Compared to straight-chain aliphatic (1.52-1.54Å) and cyclopropanes (1.51Å)[9], bicyclo[1.1.0]butanes have a shorter C-C bond length. This observation suggests that the central bond of bicyclo[1.1.0]butane [C1-C3] may contain some multiple-bond character.[1] Also, the bridgehead C-H bond has a similar length to a vinyl C-H bond (1.077 Å), which corresponds to the acidic nature of this bridgehead proton.[10] Finally, the geometry of the bridgehead carbon directs the substituents on C1 and C3 into one hemisphere.

Table 1. Structural information for bicyclo[1.1.0]butane.[5,6]

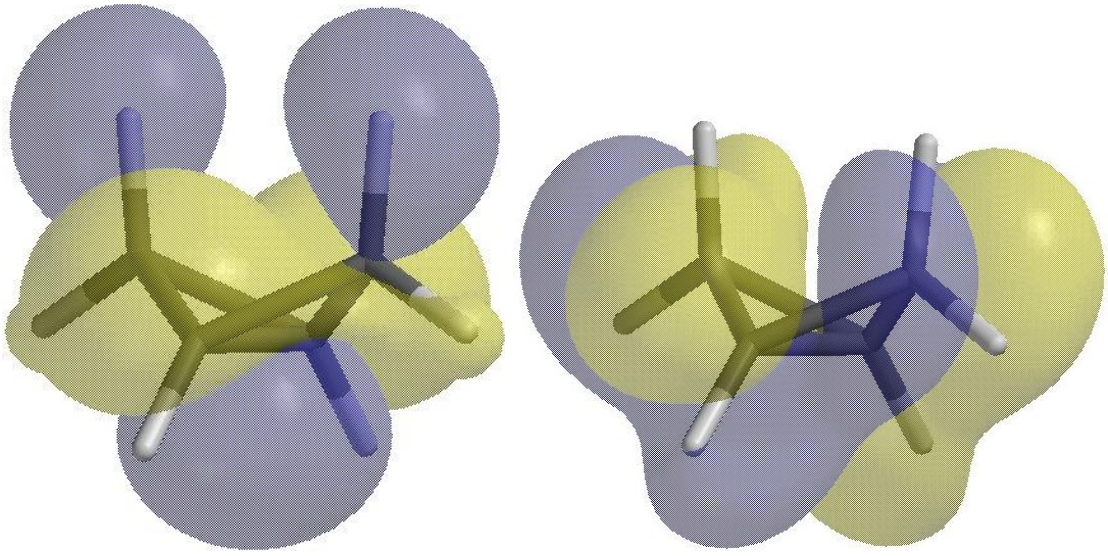


Method[a]	α	β	λ	C_1C_2	C_1C_3	C_1H_1	C_2H_{exo}	C_2H_{endo}
NMR	128.0	110.2	128.0	1.507	1.507	1.142	1.194	1.167
Electron Diffraction	125.5	111.6	122.8	1.507	1.502	1.108	1.106	1.106
Microwave	128.2	115.3	122.4	1.498	1.497	1.071	1.093	1.093

[a]Angles are given in degrees and bond lengths in Å.

1.1.2 Frontier orbitals of bicyclo[1.1.0]butane.

Many calculations of molecular orbitals of bicyclo[1.1.0]butane have been published since 1960.[7,11-14] These studies suggest that both HOMO and LUMO are associated with a π-like central C-C bond (Figure 1). *Ab initio* calculations show that the central bond has 96% *p*-character (cyclopropane 86%).[13]



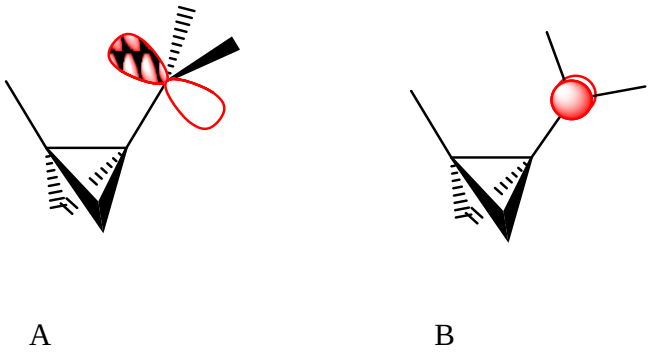
HOMO LUMO

Figure 1. HOMO and LUMO of bicyclo[1.1.0]butane.[a]
[a]Representation of the frontier orbitals calculated at the B3LYP/6-31G* level using Spartan 14.

1.1.3 The nature of the central bond in bicyclo[1.1.0]butane.

To further support the hypothesis of the significant *p*-character of the central bond, NMR studies have been performed. The C_1-H_1 coupling constant ($^1J_{CH}$ = 205 Hz) corresponds to a C-H bond hybrid having 40% *s*-character.[15] The $^1J_{CC}$ values for C_1-C_3 are exceptionally low (-5.4 to 17.5 Hz).[16] Using some approximations, Pomerantz *et al.*[17] calculated that the central bond has

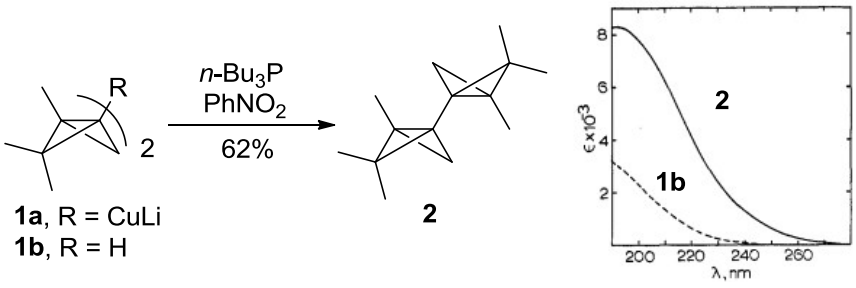
89% *p*-character. Additionally, Schleyer *et al.* used a GVB/3-21G optimized geometry to calculate that the central bond has *ca.* 4% biradical character (bicyclo[1.1.0]butane).[18]



A B

Figure 2. Two 1-bicyclo[1.1.0]butyl cation conformers used in *ab initio* calculations.

Because of the high π-character attributed to the C1-C3 bond, the conjugation between a cation and the central bond is expected to be significant. Using *ab initio* calculations, Greensburg[19] showed that the A^+ conformer is 32 kcal/mol more stable than the B^+ conformer (Figure 3). However, the corresponding A^- conformer is only 0.12 kcal/mol more stable than the B^- conformer. Subsequent calculations showed that the lower stabilization energy is caused by poor orbital overlap in the B conformer.[20]



Scheme 1. Synthesis of bicyclo[1.1.0]butane dimer **2.**

Experimental evidence for the *π*-character of the central bond also exists. For example, Moore *et al.*[21] synthesized a bicyclo[1.1.0]butane dimer **2** via oxidative coupling of Cu-derivative **2** (Scheme 1). UV/VIS analysis indicated that the λ_{max} was located at 190 nm as a

result of a red shift from the monobicylobutane **1b**. This result indicated that the two central bonds were conjugated.

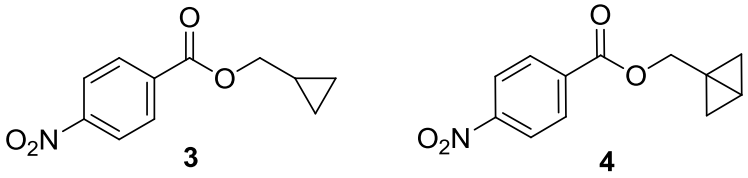


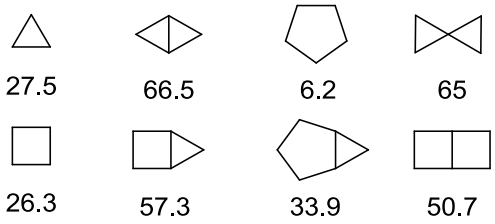
Figure 3. Bicyclo[1.1.0]butyl and cyclopropyl *p*-nitrobenzoate esters.

Wiberg *et al.*[1] have shown that solvolysis of **4** is 1000 times faster than that of the analogous cyclopropyl derivative **3** (Figure 3). The major solvolysis products of **4** resulted from an acid-catalyzed hydration of the central bond.

1.1.4 Strain energy in bicyclo[1.1.0]butane

Bicyclo[1.1.0]butane is one of the most strained bicyclic systems. Its strain energy ranges from 63.9 to 66.5 kcal/mol and depends on the substituents attached to the bicycle.[22-25] For example, the central bond of bicyclo[1.1.0]butane can be in conjugation with substituents having a π-system, which leads to an overall stabilization of the system.

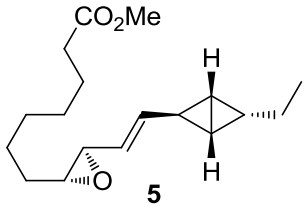
Table 2. Strain energies for common strained molecules (in kcal/mol).[26]



Bicyclo[1.1.0]butane does not follow the additivity rule for the strain of bicyclic systems; it has an extra 8.9 kcal/mol of strain energy generated from the fusion of the two cyclopropane

rings. In 1976, Holloway *et al.*[27] explained the extra strain energy by considering the non-bonding 1,3-carbon/carbon interactions (Dunitz-Schomaker hypothesis[28]) in cyclobutane (18 kcal/mol in cyclobutane). Recently, Baric and Maksic[29] challenged this idea by indicating that this extra strain energy is simply caused by an increase in Baeyer strain. The high strain energy makes bicyclo[1.1.0]butane a reactive building block for organic synthesis. By releasing the strain of the bicyclo[1.1.0]butane, a diene or cyclobutene can be obtained.

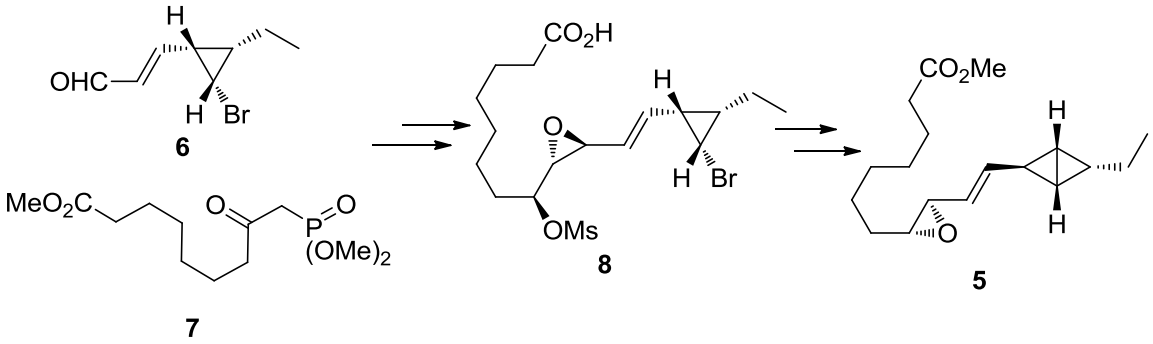
1.1.5 Bicyclo[1.1.0]butane in nature



5

Figure 4. Structure of a bicyclo[1.1.0]butane fatty acid methyl ester.

The high strain energy and acid sensitivity make bicyclo[1.1.0]butane a challenging structural motif for synthesis and isolation. The first compound bearing a bicyclo[1.1.0]butane group derived from a living organism was reported by Barsh *et al.*[30] in 2007. The authors identified a dual-function protein encoded in the cyanobacterium Anabaena PCC 7120. They reconstituted this protein in *E. coli in vitro* and found that it could consume 9-hydroperoxylinoleic acid and produce the bicyclo[1.1.0]butane fatty acid **5**. This unique structure with unknown bioactivity drew the attention of the scientific community, and led chemists to work on its total synthesis. In 2011, the total synthesis of **5** was achieved by Sulikowski *et al.*[31] in 13 steps (Scheme 2). The sequence featured a key cascade reaction that furnished the bicyclo[1.1.0]butane and epoxide functionality of **5** from carboxylic acid **8** in 20% yield.



Scheme 2. Total synthesis of bicyclo[1.1.0]butane fatty acid **5** by Sulikowski *et al*.

1.2 SYNTHESIS OF BICYCLO[1.1.0]BUTANES

1.2.1 Retrosynthetic analysis of bicyclo[1.1.0]butanes

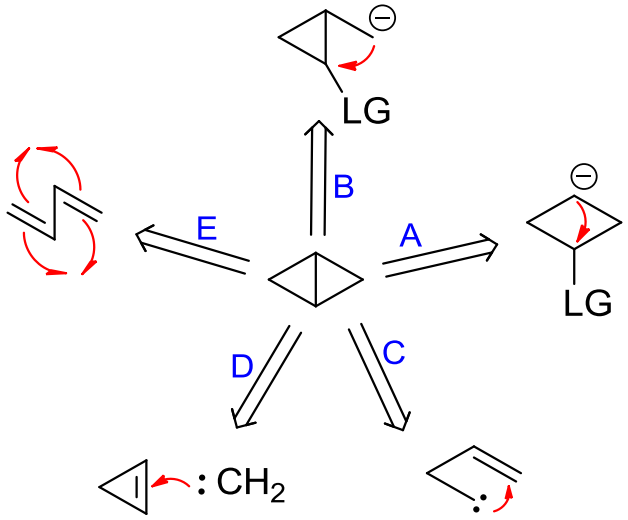


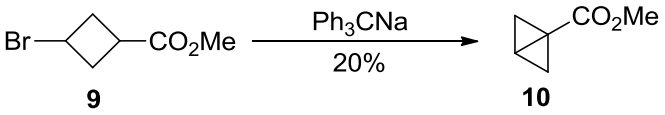
Figure 5. Several synthetic pathways towards bicyclo[1.1.0]butane.

As shown in Figure 5, bicyclo[1.1.0]butanes can be assembled by several different methods. Anionic pathways involving formation of either the central bond (A)[32-36] or lateral bond

(B)[37-39] are possible. An alternative way is carbene insertion into a double bond (path C[40-41] and D[42-47]). Furthermore, isomerization of a diene under photochemical conditions offers a unique pathway towards bicyclo[1.1.0]butane (path E)[48,49].

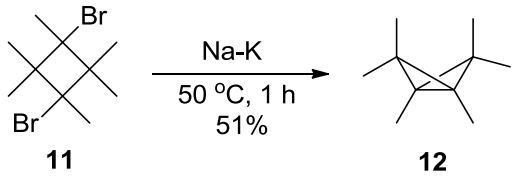
1.2.2 Synthesis of bicyclo[1.1.0]butanes by connecting the central bond

In 1959, Wiberg *et al.*[32] reported the first synthesis of a bicyclo[1.1.0]butane. Treatment of 2-bromocyclobutyl methylcarboxylate with triphenylmethide led to the formation of bicyclo[1.1.0]butanebutyl methylcarboxylate (Scheme 3).



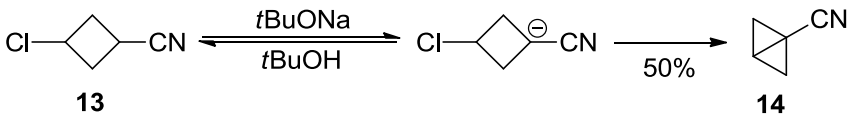
Scheme 3. First synthesis of a bicyclo[1.1.0]butane.

Hamon *et al.*[33] reported that a Wurtz-type reaction could also be used in the synthesis of bicyclo[1.1.0]butane. Precursor **11** was treated with sodium-potassium amalgam to afford bicyclo[1.1.0]butane **12** (Scheme 4).



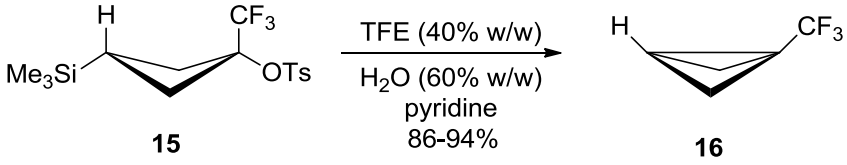
Scheme 4. Bicyclo[1.1.0]butane synthesis by Wurtz-type reaction.

Similar protocols using the displacement of a halogen from an activated cyclobutane species have been reported.[34,35] This reaction was shown to be a stereospecific process, proceeding with inversion.[34]



Scheme 5. Synthesis of 1-cyanobicyclo[1.1.0]butane.

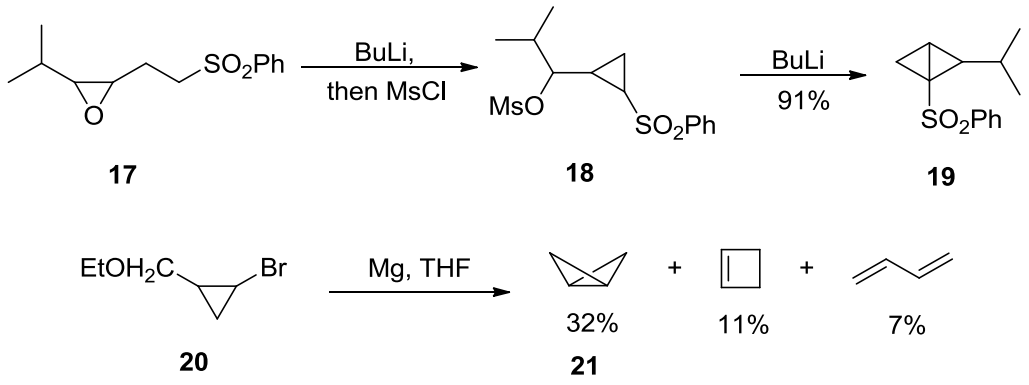
Recently, Tilley *et al.*[36] reported that 1,3-γ-silyl elimination could furnish the bicyclo[1.1.0]butane system (Scheme 6). The authors stated that the electron-withdrawing trifluoroalkyl group on the bridgehead carbon was crucial for the formation of the desired bicyclo[1.1.0]butane.



Scheme 6. Synthesis of 1-trifluoromethylbicyclo[1.1.0]butane **16**.

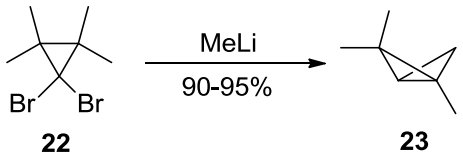
1.2.3 Synthesis of bicyclo[1.1.0]butanes by connecting the lateral bond

Although connecting the central bond is the most common way to synthesize bicyclo[1.1.0]butanes, synthesis of the lateral bond is also an effective way to access the bicyclo[1.1.0]butane system. Gaoni *et al.*[37] reported a highly efficient method utilizing a substrate bearing an epoxide and sulfonyl group (**17**). Treatment of **17** with *n*-BuLi and MsCl afforded cyclopropane **18**. Treatment with a second equivalent of butyllithium led to intramolecular displacement of the mesylate to afford bicyclo[1.1.0]butane **19** in good yield. In another case[38], the intramolecular nucleophilic substitution with substrate **20** can generate **21**, even though **20** has a poor leaving group (ethoxy).



Scheme 7. Synthesis of bicyclo[1.1.0]butane by connecting the lateral bond.

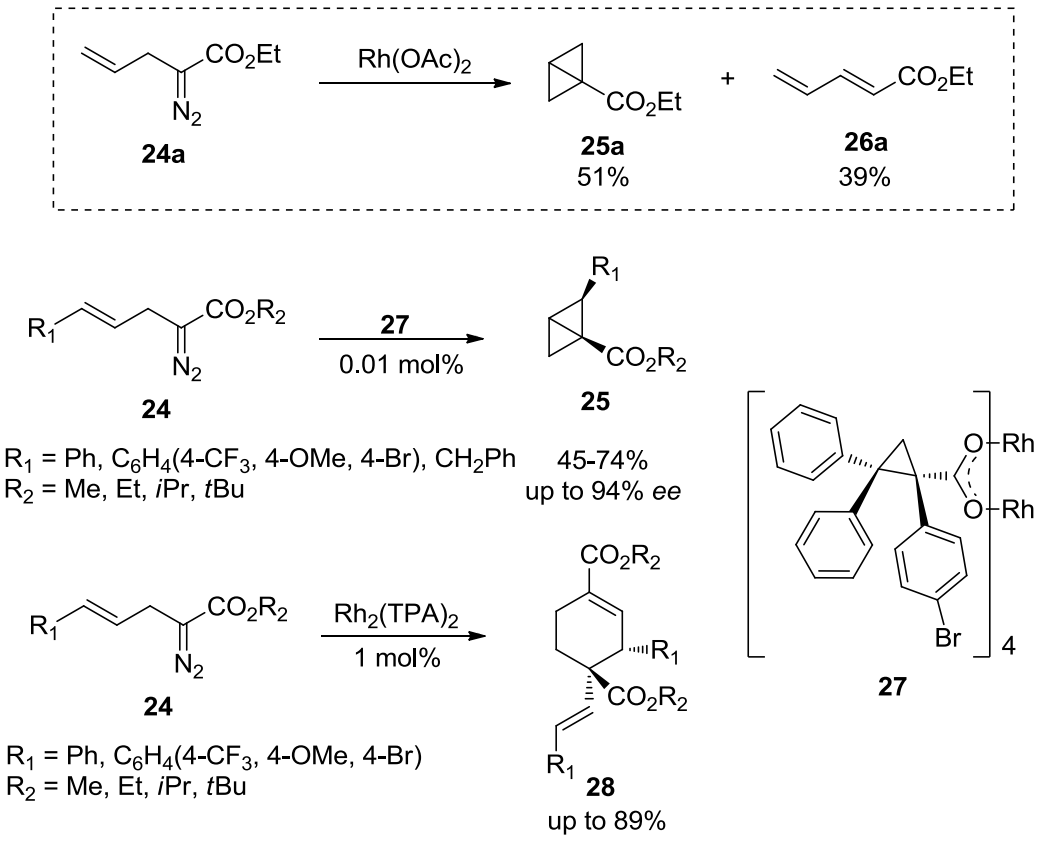
Carbene insertion of a cyclopropylidene generated by treatment of dibromocyclopropane **22** with methyllithium into an adjacent CH bond is another method to connect the lateral bond (Scheme 8).[39]



Scheme 8. Synthesis of bicyclo[1.1.0]butane by carbene insertion into a CH-bond.

1.2.4 Synthesis of bicyclo[1.1.0]butanes by simultaneous formation of lateral and central bonds

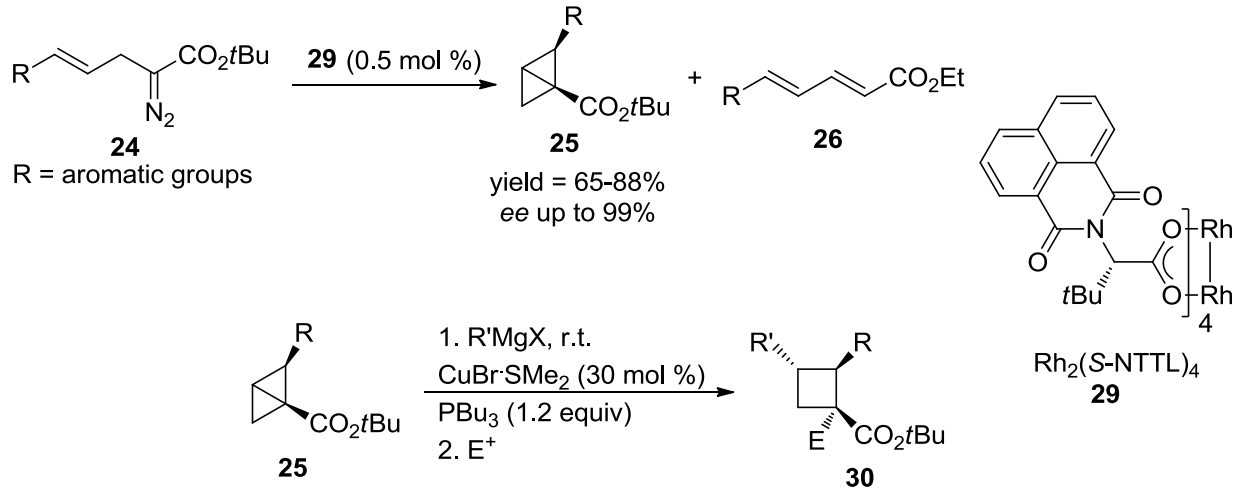
Another popular method for constructing the bicyclo[1.1.0]butane system is the addition of carbenes to alkenes. Ganem *et al.*[40] obtained bicyclo[1.1.0]butane ester **25a** as a byproduct when they treated the substituted α-diazoester **24a** with rhodium(II) acetate to provide the corresponding *cis*-enoate **26a**.



Scheme 9. Synthesis of bicyclo[1.1.0]butane by cyclopropanation to a CC-double bond.

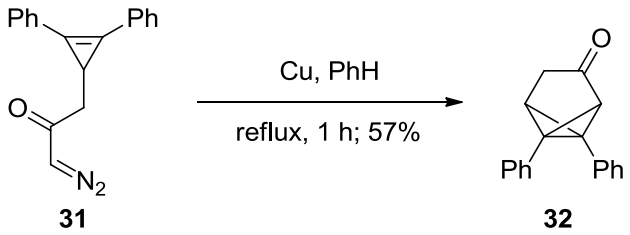
In 2013, Davies group[41] published an advanced enantioselective synthesis protocol of 2-arylbicyclo[1.1.0]butane carboxylates **25**. With a low catalyst loading (0.01 mol%), product **25** can be obtained with up to 94% *ee*. Furthermore, this rhodium-catalyzed reaction can be controlled by alternating the rhodium catalysts to afford cyclohexene **28** with high levels of diastereoselectivity (Scheme 9).

In 2013, Fox *et al.*[42] independently reported an similar enantioselective cyclopropanation of α-diazoesters **24** that gave various enantiomerically enriched bicyclo[1.1.0]butanes **25**. The new catalyst **29** eliminated the formation product **26** and greatly increased the yield of **25**. It is worth mentioning that **25** can subsequently engage in a homoconjugate and enolate trapping sequence to afford functionalized cyclobutanes **30** with high diastereoselectivity (Scheme 10).



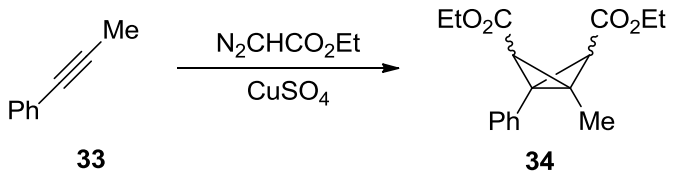
Scheme 10. Enantioselective synthesis of **26** and cyclobutane **30**.

1.2.5 Synthesis of bicyclo[1.1.0]butanes by carbene addition



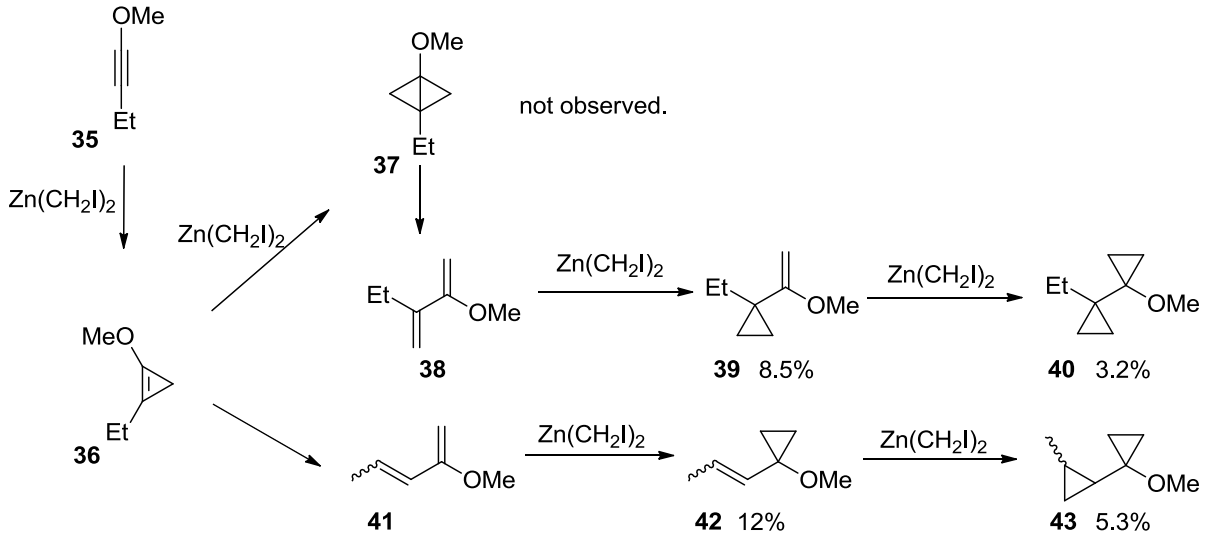
Scheme 11. Synthesis of bicyclo[1.1.0]butane *via* carbene addition to cyclopropene.

The addition of carbenes to alkynes or cyclopropenes is the most straightforward method to synthesize bicyclo[1.1.0]butanes, and this method provides the most possibilities for the synthesis of functionalized bicyclo[1.1.0]butanes. Some reactions utilize carbenes formed by the decomposition of diazo compounds[41] under thermal[44] or UV conditions[45] (Scheme 11). Unfortunately, this type of carbene addition is not a stereospecific process. The products formed are mixtures of *endo*- and *exo*-isomers (Scheme 12).[46]



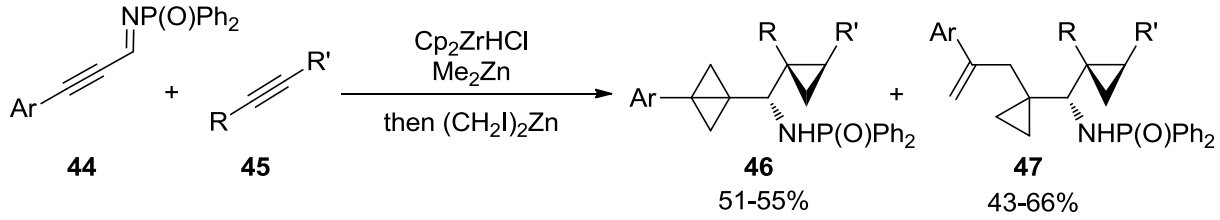
Scheme 12. Synthesis of bicyclo[1.1.0]butane by carbene addition to alkyne.

Other carbene sources such as the common Simmons-Smith zinc carbenoid were also explored. Schwartz *et al.*[47] treated 1-methoxy 1-butyne with zinc carbenoid. Only a mixture of cyclopropanated products was obtained under these conditions, and no formation of bicyclo[1.1.0]butane was observed. The result was explained by the isomerization of the corresponding cyclopropene **36** and bicyclo[1.1.0]butane **37** (Scheme 13).



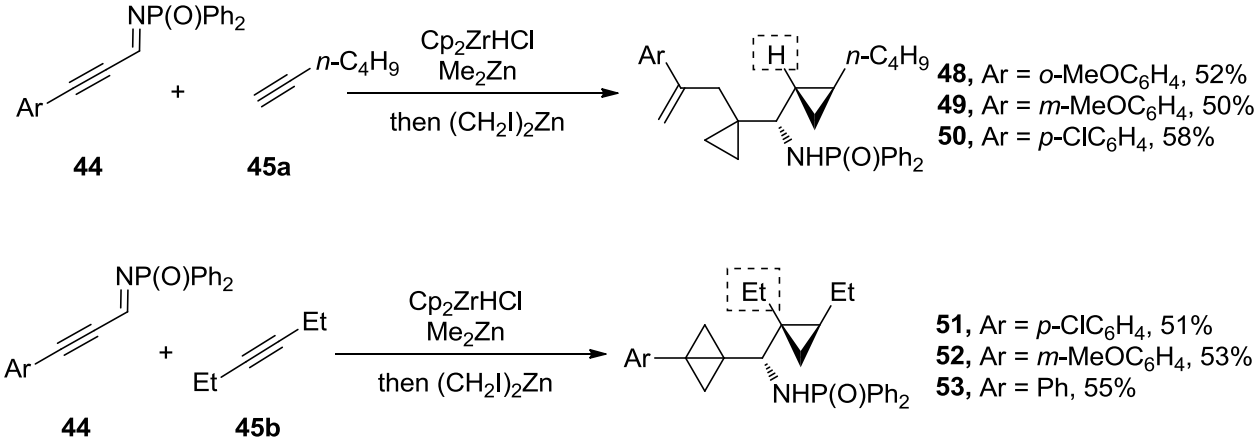
Scheme 13. Proposed mechanism for the cyclopropanation of **35**.

The potential of Simmons-Smith reagents for the synthesis of bicyclo[1.1.0]butanes was explored by our group.[48] As shown in Scheme 14, the "CH_2" unit is delivered after the addition of Schwartz reagent to the propargyl imine. The corresponding bicyclo[1.1.0]butane and dicyclopropylmethylamines were obtained in good yield.



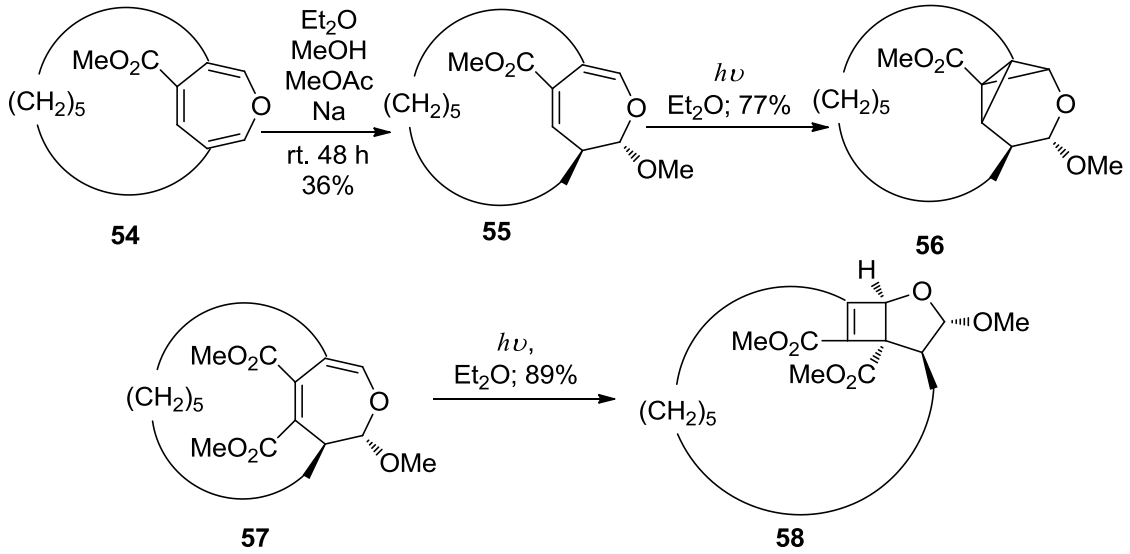
Scheme 14. One-pot synthesis of bicyclo[1.1.0]butane and dicyclopropylmethylamines.

The formation of the two products **46** and **47** depended on the steric environment at the α-position of the propargyl amide (Scheme 14). Only disubstituted alkyne **45b** was able to undergo this transformation effectively to afford bicyclo[1.1.0]butane **51-53**. The rearranged product **47** resulted from the addition of two additional methylene groups to **46** under the Simmons-Smith cyclopropanation conditions.



Scheme 15. Different products obtained depending on the steric environment at the α-position of the propargyl amide.

1.2.6 Synthesis of bicyclo[1.1.0]butanes by photochemical activation of diene



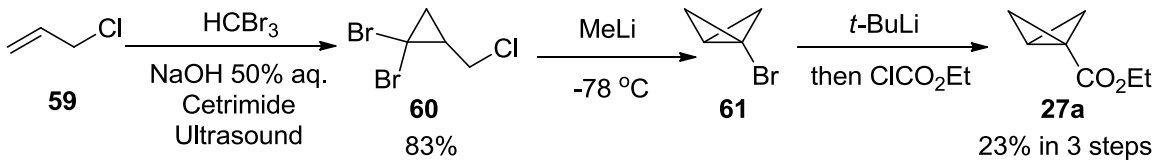
54 **55** **56** **57** **58**

Scheme 16. Photochemical activation of dienes **55** and **57**.

Photochemical activation of a diene is a unique route to synthesize the bicyclo[1.1.0]butane skeleton. This reaction is substrate dependent, and it is rarely used as a synthetic method. As shown in Scheme 16, two similar dienes **55** and **57** give completely different products.[49,50]

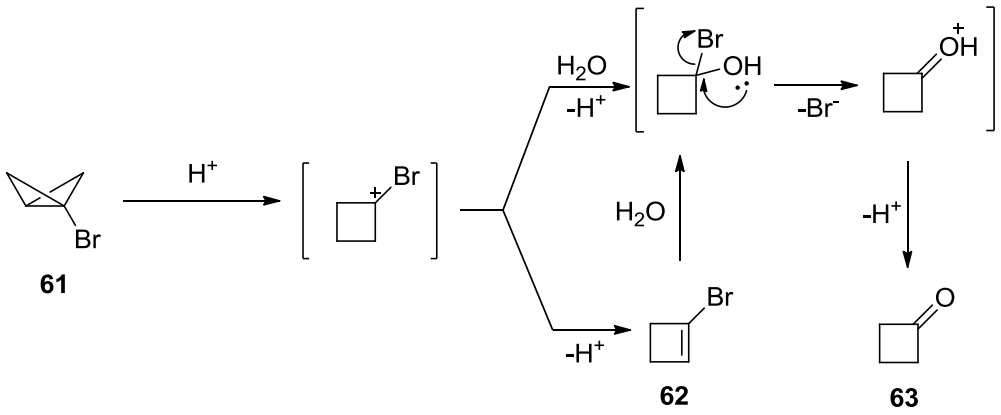
1.2.7 Bicyclo[1.1.0]butyllithium reagent

Due to the high *s*-character of the bridgehead carbon of bicyclo[1.1.0]butane, the lithium-bromide exchange reaction of **61** should be facile. Because bromide **61** is air-sensitive and volatile, a one-pot reaction for formation of **61** followed by a lithium-bromide exchange reaction and trapping with a suitable electrophile is the best solution for these problems.[51]



Scheme 17. Synthesis of bicyclo[1.1.0]butane by a one-pot halogen exchange reaction.

In 1985, Szeimies *et al.*[51] reported a one-pot reaction for formation of bicyclo[1.1.0]butane ethyl ester **27a** (Scheme 17). They treated dibromocyclopropane with 1 equivalent of methyllithium, which formed 1-bromobicyclo[1.1.0]butane **61**. The product was subsequently treated with *tert*-butyllithium followed by the addition of ethyl chloroformate to afford the bicyclo[1.1.0]butane ethyl ester **27a** in good yield.



Scheme 18. Synthesis of cyclobutanone from bicyclo[1.1.0]butane.

In 1999, Brinker *et al.*[52] used 1-bromobicyclo[1.1.0]butane **61** as a precursor to cyclobutanone, which is difficult to obtain using other methods. The mechanism of this transformation is shown in Scheme 18.

Our group explored the one-pot formation of bicyclo[1.1.0]butanes from dibromocyclopropanes extensively and found this method to be one of the most effective ways to access the bicyclo[1.1.0]butane system (Figure 6). By utilizing several different electrophiles and

various substitutions on the dibromocyclopropane, a series of bicyclo[1.1.0]butanes could be obtained in good yields.[53]

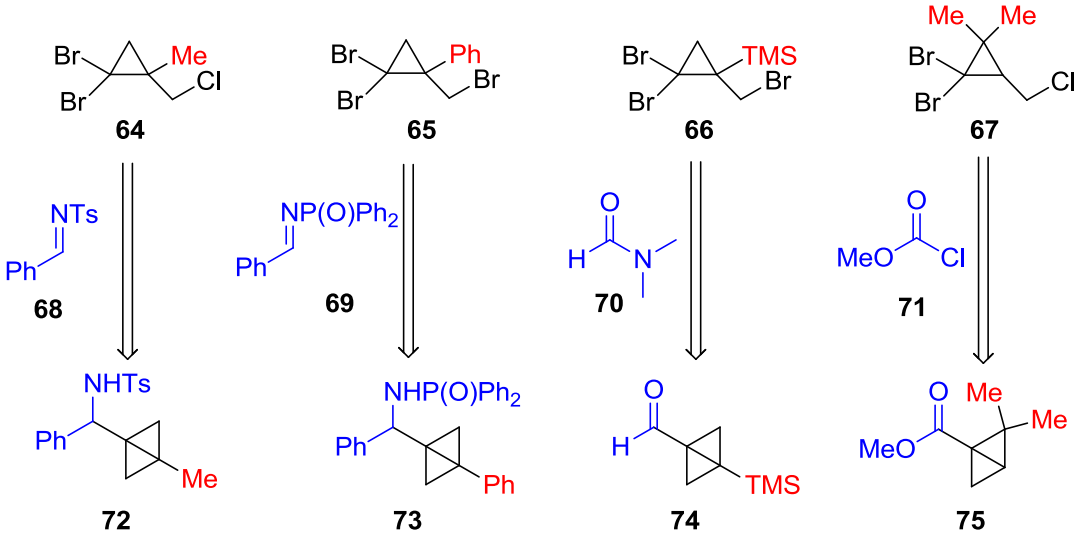


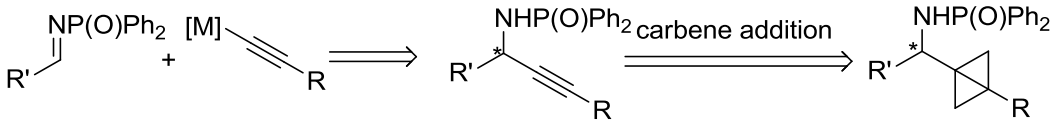
Figure 6. Several bicyclo[1.1.0]butanes synthesized from the halogen exchange reaction.

1.3 RESULTS AND DISCUSSION

Previously, our group has utilized bicyclo[1.1.0]butane derivatives in the synthesis of complex molecules.[3,54] However, all methodologies involved racemic bicyclo[1.1.0]butane-containing starting materials and consequently afforded racemic products. In order to make bicyclo[1.1.0]butane a more useful synthetic tool for organic synthesis, we sought to develop an effective way to access optically active bicyclo[1.1.0]butane derivatives.

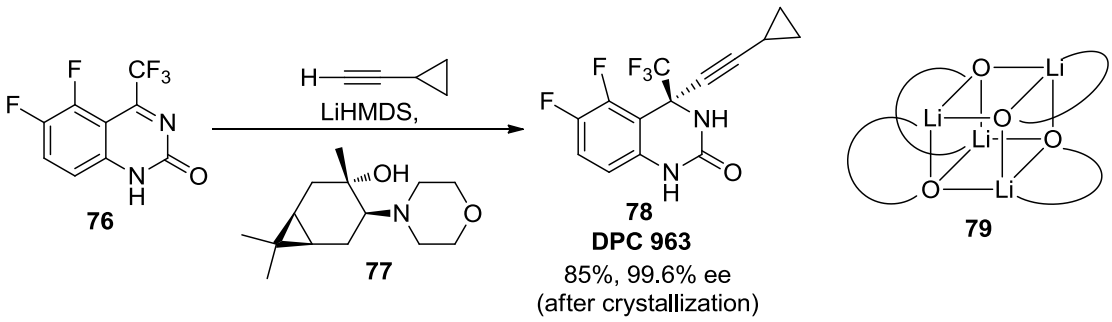
1.3.1 Enantioselective alkynyl addition to imines.

Because the direct addition of bicyclo[1.1.0]butyllithium to imines suffers from low enantioselectivity,[53] we decided to apply dicarbene addition to an enantiomerically enriched propargyl amine as our new strategy towards the enantiomerically enriched bicylo[1.1.0]butanes (Scheme 19).



Scheme 19. Dicarbene addition of enantiomerically enriched amine.

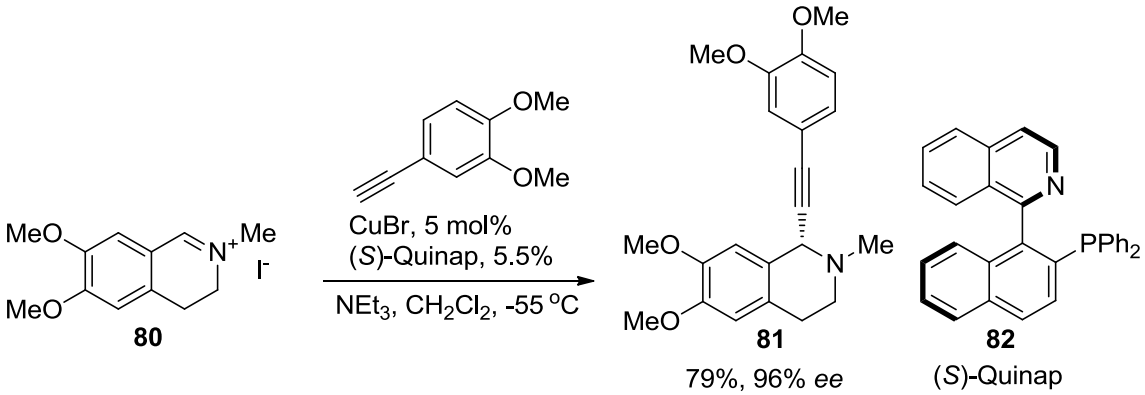
Recently, propargyl amines have been used as precursors of many useful intermediates towards pharmaceutical compounds.[55-57] Traditional synthetic methods usually involve deprotonation of the alkyne by a strong base such as butyllithium or an organomagnesium compound. The resulting alkynyllithium or magnesium reagent will undergo nucleophilic addition to imines. Drawbacks to this methodology are fast background addition processes and the incompatibility of strong bases with certain substrates.[58]



Scheme 20. Enantioselective synthesis of DPC 963 using chiral ligand **77**.

There are a few examples of alkynyllithium reagents undergoing enantioselective additions to ketimines. Nugent reported a procedure using 4-*β*-morpholinocaran-3*α*-ol **77** as a

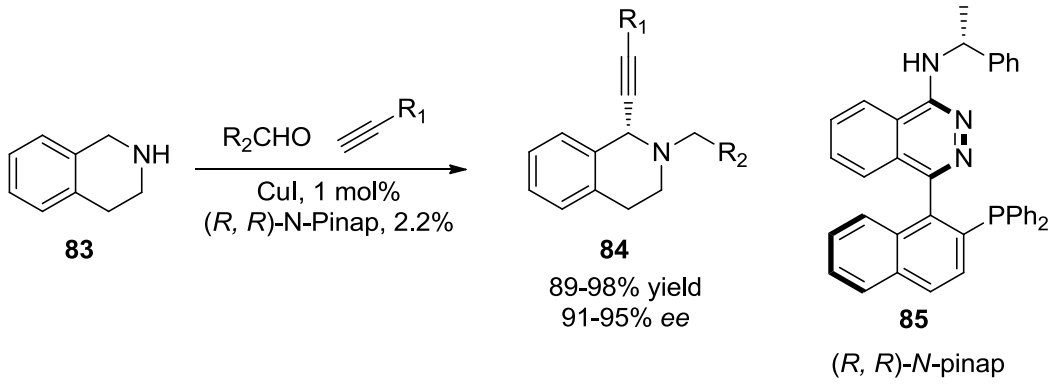
chiral ligand to control the addition of lithium cyclopropylacetylide to an unprotected *N*-acylketimine **76** (Scheme 20). The product of this reaction, DPC 963, is an anti-HIV drug candidate.[59] In 2014, Collum *et al.*[60] revealed that cubic tetramers **79** are the dominant forms in various lithium amino alkoxides and responsible for high enantioselectivities of the nucleophilic additions.



Scheme 21. Total synthesis of (S)-(-)-homolaudanosine.

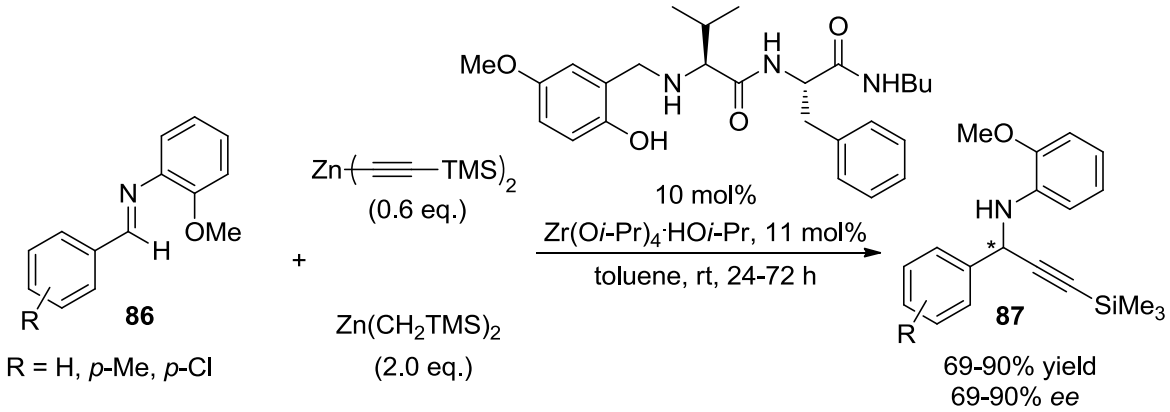
Most enantioselective processes reported to date involve copper (I) species. Knochel and coworkers[61] established a method using a copper (I) catalyst for the addition of an alkyne to an imine. Schreiber *et al.*[62] found that ligands such as Quinap **82** yielded propargyl amines in high yields and *ee*'s. This reaction later was applied to the total synthesis of (*S*)-(-)-homolaudanosine (Scheme 21).

In 2014, Ma *et al.*[63] developed a high enantioselective synthesis of tetrahydroquinoline synthesis utilizing 1,2-unsubstituted tetrahydroquinolines with *N*-pinap **85** as the chiral ligand. This methodology utilized an *in situ* iminium-ion-isomerization process and opened up an efficient entry to many tetrahydroisoquinoline alkaloids.



Scheme 22. Ma's synthesis of tetrahydroquinoline.

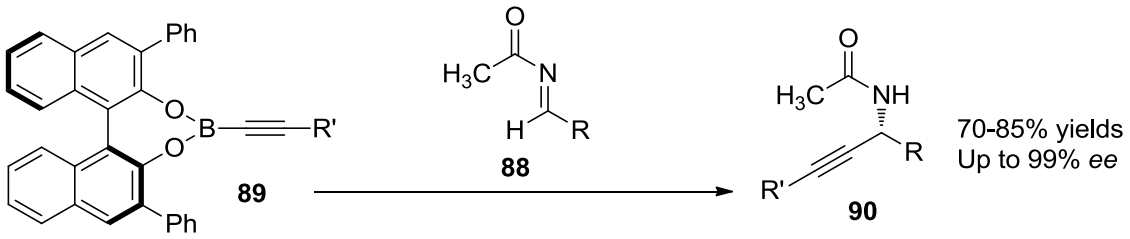
Besides the numerous copper catalysts used for the asymmetric addition of alkynes, Hoveyda *et al.*[64] utilized a peptide-based ligand in combination with a zirconium species to catalyze the addition of a mixed alkynyl zinc reagent to various *N*-aryl aromatic imines.



Scheme 23. Hoveyda's methodology using a peptide-based ligand and Zr catalyst.

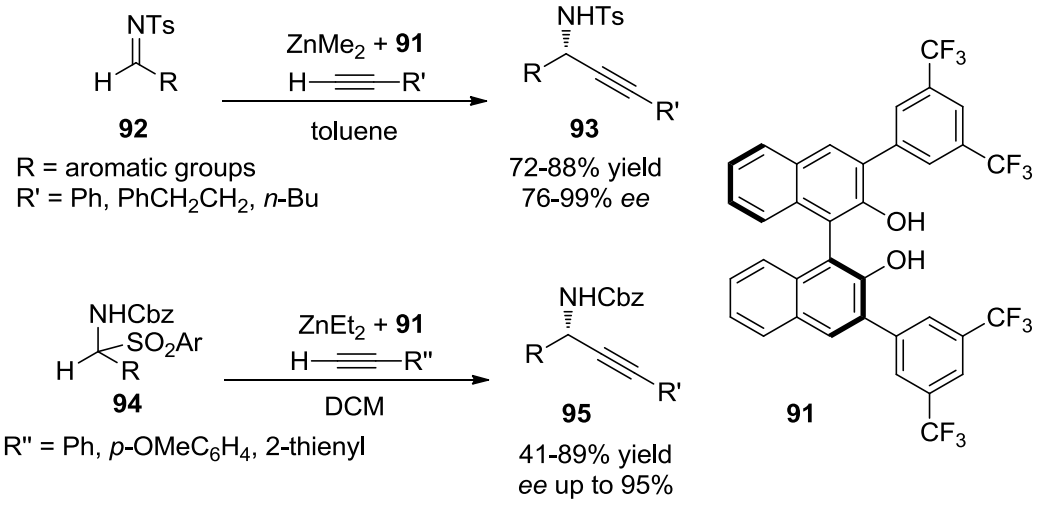
The majority of examples for the enantioselective addition of alkynes involve the use of unactivated imines, which have a slow background reaction and can be effectively enantiomerically catalyzed. Recently, many successful cases utilizing activated imines were also described.[65-67]

Wu and Chong reported that binaphthol-based alkynylboronates could undergo enantioselective addition to *N*-acylamine **88**. In this case, both boronate reagent and the imine have to be prepared and purified prior to the reaction (Scheme 24).[65]



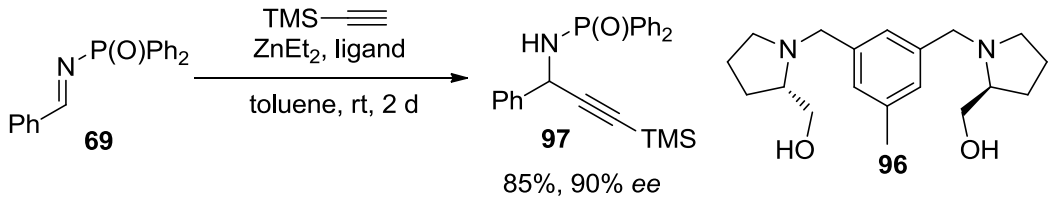
Scheme 24. Binaphthol-based alkynylboronate addition to *N*-acetylamine.

Alkynyl zinc reagents have been used extensively for the enantioselective addition to electron-deficient imines, including *N*-sulfonyl, *N*-acetyl and *N*-phosphonyl imines. Pedro *et al.* described an approach using binol-type ligand **91** as chiral catalyst in combination with an alkynyl zinc reagent to afford *N*-sulfonyl propargyl amines **93** with high yields and *ee*'s (Scheme 25).[66] In 2012, they applied this strategy to the synthesis of chiral *N*-Cbz protected amines.[67] These enantiomerically enriched propargylamines **95** are highly valuable synthetic intermediates.



Scheme 25. Enantioselective alkynyl zinc addition to *N*-tosyl and *N*-Cbz imine.

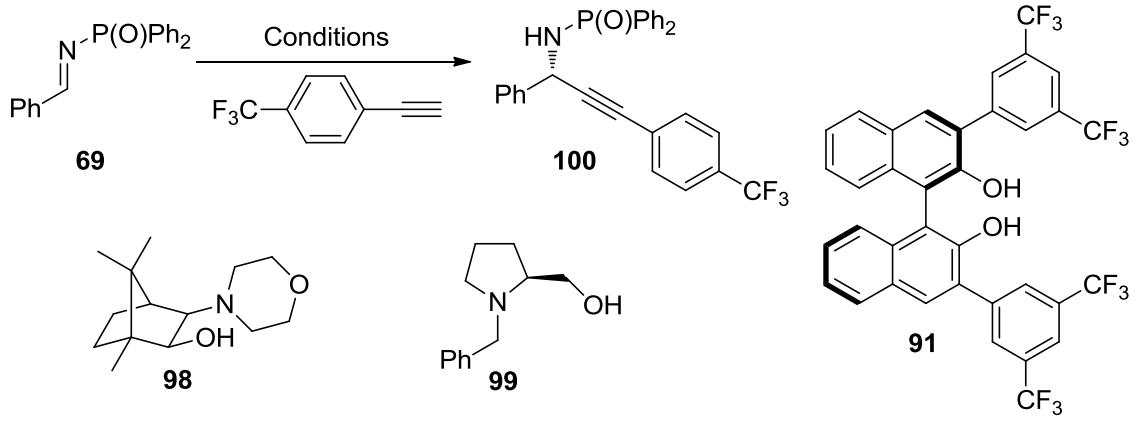
A similar approach using a proline-based ligand was reported by Wang *et al.*[67] As part of their methodology, they examined a series of different proline-type ligands and found that the C_2-symmetric ligand **96** catalyzed the addition of alkynyl zinc reagents to *N*-phosphinoyl imines in good yields and *ee*'s.[68]



Scheme 26. Enantioselective alkynyl zinc addition to *N*-phosphinoyl imine.

1.3.2 Enantioselective alkynyl addition to *N*-DPP imine.

We previously obtained favorable results when exploring the cyclopropanation of an *N*-DPP propargyl amide; therefore, we decided to use this method to access enantiomerically enriched bicyclo[1.1.0]butane substrates. A set of different ligands was examined for the addition of alkynyl zinc to imines. Diethyl zinc, *p*-trifluoromethyl phenyl acetylene and ligand were stirred for 2-6 h before the addition of the imine. After the addition of the imine, the mixture was stirred for another 12-48 h and quenched with saturated ammonium chloride solution. The products were then separated and analyzed by SFC (Chiralpak IA) (Scheme 27).



Scheme 27. Alkynyl zinc addition to *N*-phosphinoyl imine.

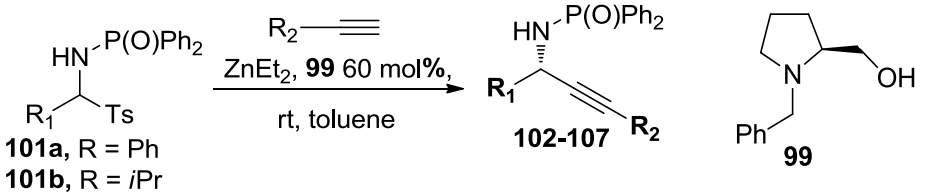
Table 3. Enantioselective alkynyl zinc addition to *N*-phosphinoyl imine.

Entry	Conditions	Yield (%)	*e.r.*[a] (*S:R*)[b]
1	$ZnMe_2$, rt, 48 h	86	-
2	$ZnMe_2$, **91** 20 mol%, rt, 48 h	15	53:47
3	$ZnMe_2$, **98** 10 mol%, rt, overnight	61	48:52
4	$ZnEt_2$, **99** 60 mol%, rt, overnight	65	93:7

[a]Enantiomeric ratio was determined by SFC analysis using a Chiralpak IA column. [b]Configurations were assigned according to the original paper.[68]

The results in Table 3 show that ligand **99** gave acceptable yield and enantiomeric ratio. We decided to use the commercially available ligand **99** as a chiral catalyst for the enantioselective additions of alkynes to imines.

Table 4. Enantioselective alkynyl zinc addition to *N*-phosphinoyl imine.



101a, R = Ph
101b, R = *i*Pr
101c, R = $PhCH_2CH_2$

Entry	Product	R_1	R_2	Conditions	Yield (%)	*e.r.*[a] (*S:R*)[b]
1	**102**	*i*-Pr	*p*-$CF_3C_6H_4$	12 h	78	93:7
2	**103**	Ph	*m*-ClC_6H_4	12 h	91	92:8
3	**104**	Ph	*c*-C_6H_{11}	48 h	67	69:31
4	**105**	*i*-Pr	*p*-BrC_6H_4	6 h	84	94:6
5	**106**	*i*-Pr	TIPS	24 h	84	92:8
6	**107**	$PhCH_2CH_2$	*p*-$CF_3C_6H_4$	24 h	82	98:2[c](86:14)

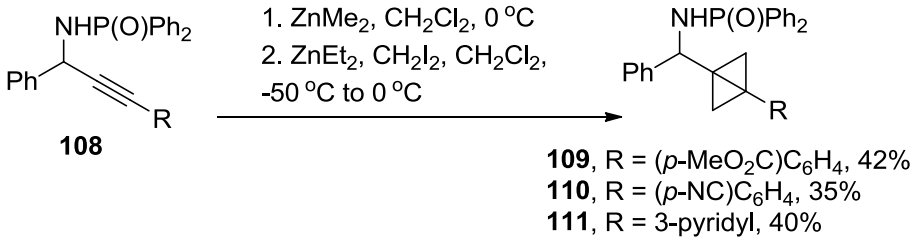
[a]Enantiomeric ratio was determined by SFC analysis using a Chiralpak IA column. [b]Configurations were tentatively assigned according to the original paper.[67] [c]*E.r.* was determined after recrystallization.

We further explored the substrate scope of this reaction. We used the imine tosyl adduct **101a-c** instead of the imine because some alkyl imines are not stable. The results are summarized in Table 4. As we expected, aromatic-substitued (entries 1, 2, and 4) and silyl-substituted alkyne (entry 5) gave good to excellent yield. Various substituents on the phenyl ring did not affect the *e.r.*. Alkyl-substituted alkyne (entry 3) only gave moderate yield and decreased enantioselectivity (69:31). When a smaller phenylethyl group was used (entry 6), a lower *e.r.* was observed.

However, we were able to increase the enantiomerical ratio to 98:2 by recrystallizing **104** in hexanes/dichloromethane.

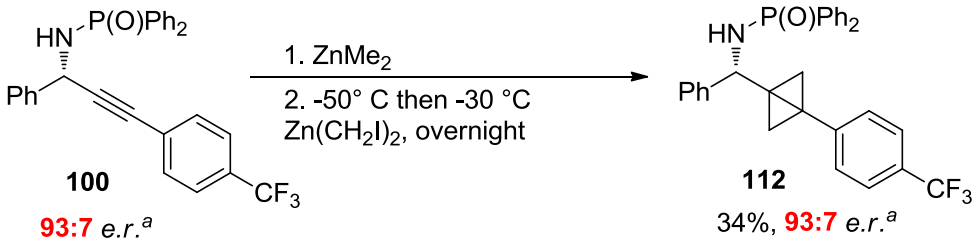
1.3.3 Cyclopropanation of enantiomerically enriched propargyl amide.

As stated in the introduction, our group has studied the cyclopropanation of alkynes (Scheme 28). However, the substrate scope of this reaction is limited to cases where the starting material is a conjugated propargyl phosphonyl amide with electron withdrawing substituents on the aryl group.[26]



Scheme 28. Carbene addition of propargyl amides.

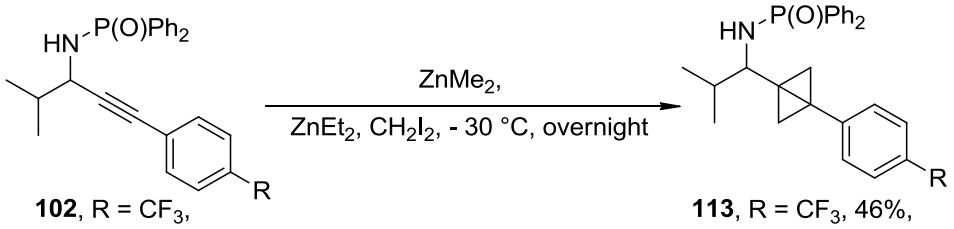
After obtaining the enantiomerically enriched propargyl amide **100** (Scheme 29), we subsequently treated **100** with a Simmons-Smith carbenoid to give bicyclo[1.1.0]butane **112** in 34% yield. After analysis by SFC using a chiral stationary phase the enantiomeric ratio of the bicyclo[1.1.0]butane product was equivalent to the propargyl amide starting material.



Scheme 29. Determination of *e.r.* after cyclopropanation.

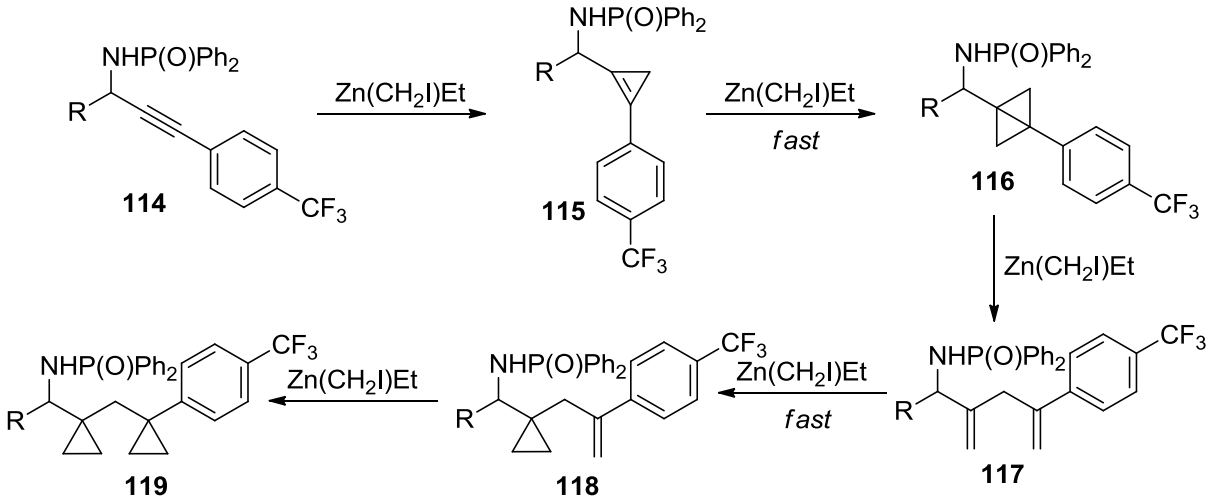
[a]Enantiomeric ratio was determined by SFC analysis using a Chiralpak IA column.

Although the chiral center was retained after cyclopropanation, this process still suffers from low and irreproducible yields. As shown in Scheme 30, substrate **102** undergoes cyclopropanation to form the bicyclo[1.1.0]butane products **113** in 46% yield. The yield was a slight improvement from substrate **100**,



Scheme 30. Cyclopropanation of substrates **102**.

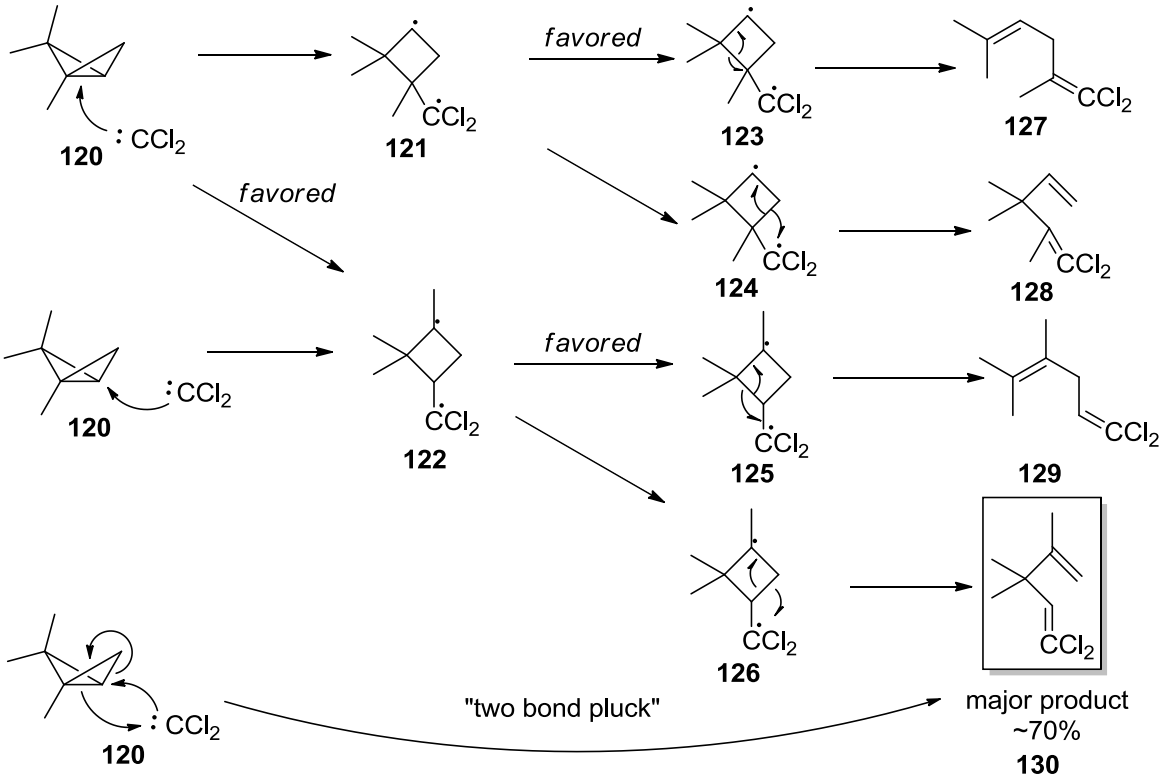
The reason for the low reaction yield is that the bicyclo[1.1.0]butane can undergo a subsequent carbenoid addition, which forms skipped diene **117**. Usually the skipped diene **117** cannot be observed in the product; it will be attacked by another equivalent of carbenoid to form products **118** and **119**. The mechanism of this transformation is shown in Scheme 31.



Scheme 31. Cyclopropanation of bicyclo[1.1.0]butane.

In 1985, Jackson *et al.*[69] described their studies on the cyclopropanation of bicyclo[1.1.0]butane. The author stated that if the mechanism is step-wise, **122** should be the

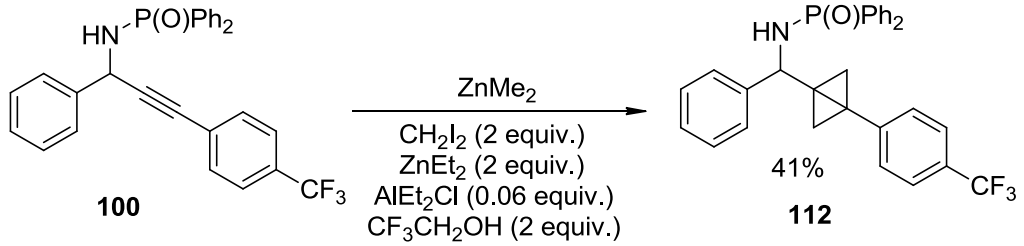
main product of the first step. Since **123** and **125** would form more substituted alkenes, **130** should be the main product of this reaction. Instead of the two suggested step-wise pathways, the author proposed another concerted route, the "two bond pluck", in which the central and lateral bonds open simultaneously. The concerted pathway was supported by the 70% yield of product **130** from the cyclopropanation of 1,2,2-trimethylbicyclo[1.1.0]butane (Scheme 32).



Scheme 32. Mechanism study of cyclopropanation of bicyclo[1.1.0]butane **110**.

First of all, we hoped that modifications of the cyclopropanation reaction would provide us with a more reliable access to bicyclo[1.1.0]butane-containing compounds. In 2004, Shi and co-workers[70] developed a novel class of zinc carbenoid reagents that offered efficient cyclopropanation of olefins. With the combination of Lewis acid catalyst such as $TiCl_4$, $SnCl_4$, $AlCl_3$ and $AlEtCl_2$, the reactivity of zinc reagents ($ROZnCH_2I$) increased dramatically. The mechanism of the acceleration is that Lewis acid can complex with oxygen to break the

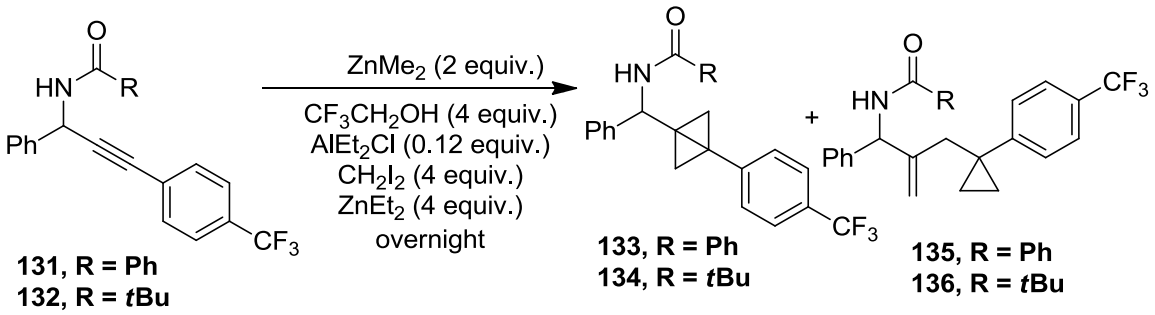
aggregated zinc reagents ($ROZnCH_2I$) and increase the electrophilicity of the generated zinc carbenoid.[71]



Scheme 33. Modification of cyclopropanation conditions of bicyclo[1.1.0]butane **100**.

The cyclopropanation of alkynes required excess reagent usage and had low conversion. Thus we examined the combination that increases the reactivity of zinc carbenoid the most, namely $AlEt_2Cl$ and CF_3CH_2OH. Despite the differences between simple olefins[70] and propagylic amines, the use of diethyl aluminum chloride and trifluoroethanol as additives gave a more consistent yield. We decided to use this condition for further reaction optimization (Scheme 33).

Table 5. Cyclopropanation of carbonyl-protected propargyl amides.



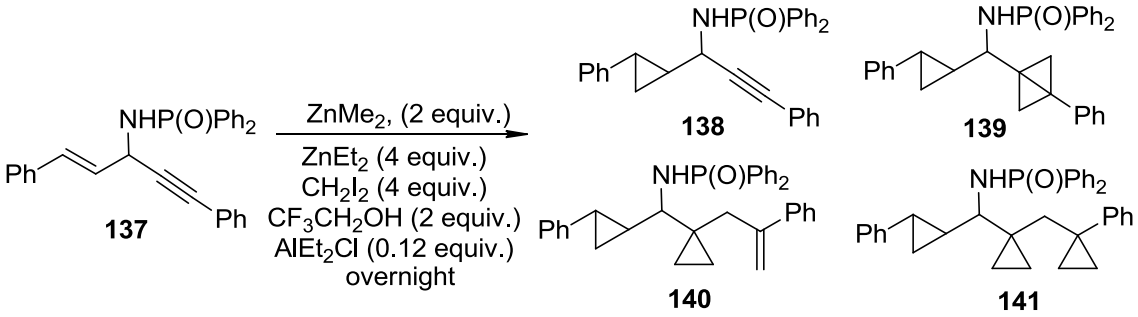
Entry	Starting Material	R	Product
1	**131**	Ph	**135**
2	**132**	*t*Bu	NR.

We next tested a series of carbonyl protecting groups under the optimized conditions. As shown in the Table 5, *N*-benzoyl amide **131** generated only rearranged products. *N*-Pivaloyl

amide **132** was unreactive under the reaction conditions. Because substrates with carbonyl protecting groups gave lower yields than the original propargyl amide, we continued to develop our methodology using DPP-protected starting materials.

Finally, we decided to test if the temperature could affect the selectivity of bicyclo[1.1.0]butane formation in the presence of other functional groups that are reactive toward carbenoids (Table 6). Cyclopropanation of both allyl and propargyl amides could be carried out above -40 ℃. At -30 ℃, the allyl amide was more reactive than the propargyl functionality and **138** could be obtained exclusively. At higher temperatures, **138**, **139** and **140** were obtained as an inseparable mixture, which means that the bicyclo[1.1.0]butane product has similar reactivity to the starting material propargyl amide. In summary, these results suggested that bicyclo[1.1.0]butane formation is difficult to perform in a selective fashion.

Table 6. Cyclopropanation of styrenal propargyl amide at different temperatures.

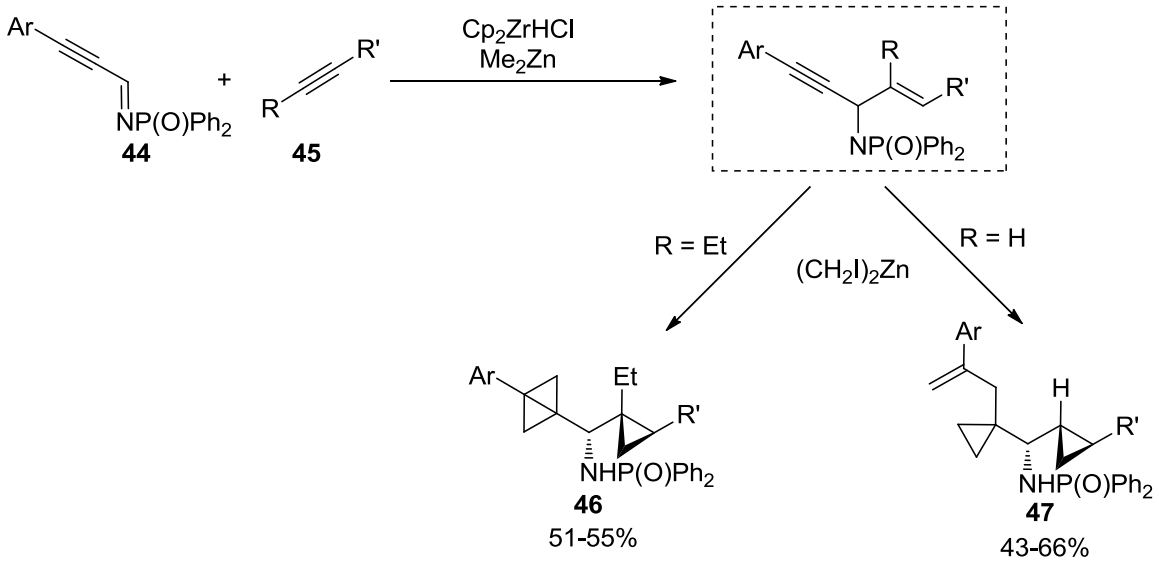


Entry	Conditions	Product	Yield
1	rt	**140**, **141** (1:10)	81%[a]
2	-20 ℃	**138**, **139**, **140** (~1:1:1)	62%[b]
3	-30 ℃	**138**	86%
4	-40 ℃	-	-

[a]**140** and **141** were obtained as an inseparable mixture, the ratio was determined by NMR. [b]**138** and **139** were obtained as an inseparable mixture, the yield was determined by NMR.

1.3.4 Cyclopropanation of silyl-substituted propargyl amide.

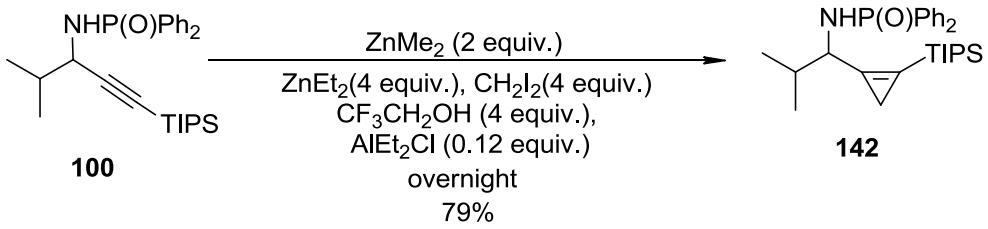
In **1.3.3**, we managed to use modified zinc reagents to solve the low conversion problem in the cyclopropanation of propagylic alkynes. but failed to keep the generated bicyclo[1.1.0]butane from reacting with excessive zinc carbenoids. In this section, we sought to design some substrates in order to solve the latter problem.



Scheme 34. Different product distribution in the one-pot cyclopropanation of propargylic amine.

As stated in **1.2.5**, our group investigated the cyclopropanation of *N*-DPP propargyl amides and found that the steric hindrance at the α-position was crucial for a selective formation of cyclopropanation products.[48] A simple structral change from hydrogen atom (**47**) to ethyl group (**46**) at *β*-position alternated the product distribution dramtically. In other word, the ethyl group blocked the resulting bicyclo[1.1.0]butane from reacting further with zinc carbenoid. These results implied that Simmons-Smith cyclopropanation of bicyclo[1.1.0]butanes is very sensitive to steric hindrance (Scheme 33) .

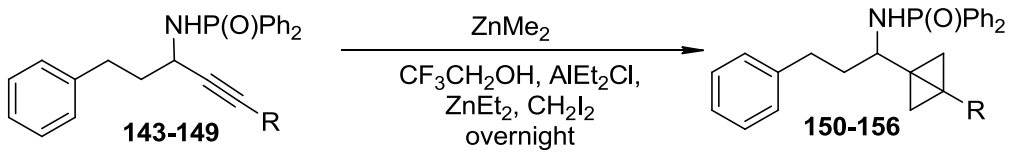
We decided to test substrates with larger steric hindrance, namely, alkynes bearing a TIPS protecting group. The results of the reaction of TIPS-protected propargyl amides are summarized in Scheme 34. Surprisingly, TIPS-substituted **106** gave the cyclopropene product **142** exclusively even at room temperature. Cyclopropene **142** is not decomposed upon storage at -20 ℃ for 6 months. The result indicated that the TIPS group imparts too much steric hindrance for cyclopropene **142**, which makes **142** resistant from reacting with zinc carbenoids to obtain a bicyclo[1.1.0]butane.

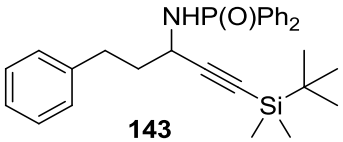
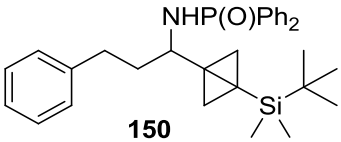
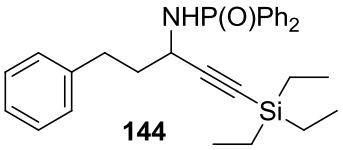
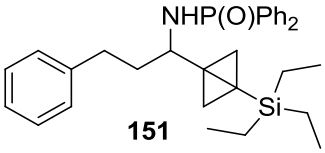
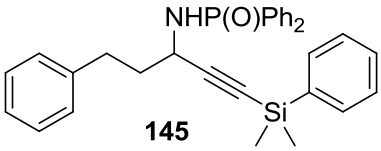
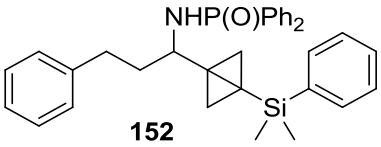
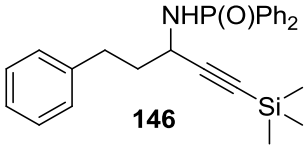
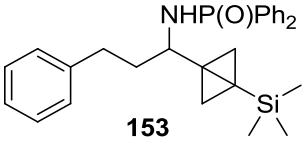
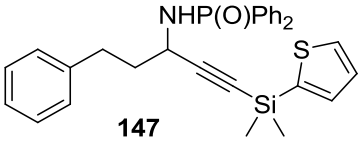
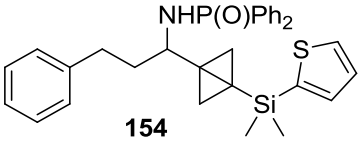
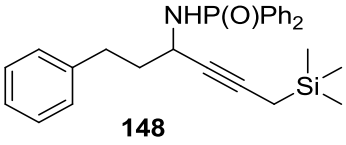
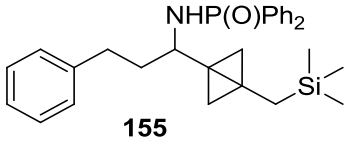
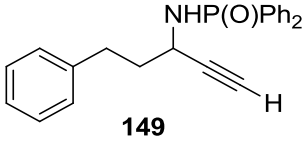
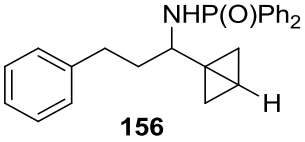


Scheme 35. Modification of cyclopropanation conditions of bicyclo[1.1.0]butane **100**.

Next, we reduced both the size of the substituents (Table 7). By reducing the size of the iso-propyl group to a smaller phenethyl group, we observed the formation of bicyclo[1.1.0]butanes. Furthermore, the reaction proceeded to the bicyclo[1.1.0]butanes and stopped without reacting further. For alkynes **143**-**147**, these reactions showed only one spot by TLC and gave excellent yields (75-92%). The reaction tolerated many silyl groups with sizes from trimethylsilyl to *tert*-butyldimethylsilyl. We also tested substrates with trimethylsilylmethyl (**148**) or hydrogen (**149**) substituents, which conveyed a similar electronic environment to other silyl alkynes. However, these substrates gave only decomposition products, suggesting a dominant role for steric effects in the cyclopropanation process.

Table 7. Cyclopropanation of a series of different silyl-substituted propargyl amides.



Starting materials	Products	Yield (%)
		91
		76
		86
		75
		92
		-[a]
		-[a]

[a]Products afforded as a messy mixture.

To our knowledge, this is the first case of a cyclopropanation reaction furnishing bicyclo[1.1.0]butane products with such high degree of selectivity. The combination of our modified reagents and substrate designs provided us an efficient route to these unique silyl-substituted bicyclo[1.1.0]butanes.

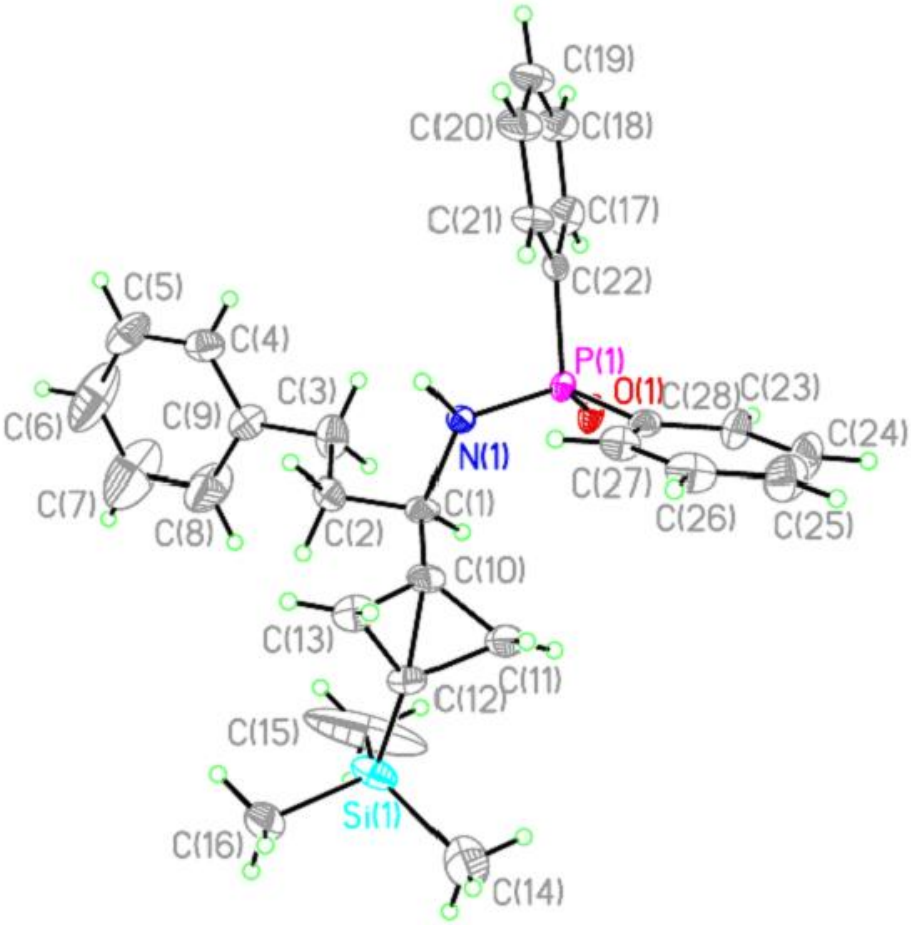
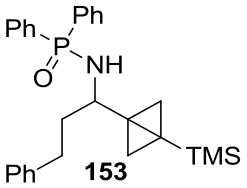
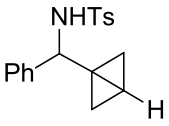
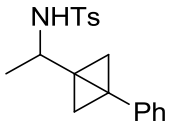


Figure 7. X-ray structure of **153**.

We managed to obtain an X-ray structure of our silyl-substituted bicyclo[1.1.0]butane **153**. Detailed structural information for several bicyclo[1.1.0]butane derivatives is summarized in Table 8.[53] As we stated in **1.1.1**, the substituents on the bicyclo[1.1.0]butane (C10 and C12) are restricted in the same hemisphere. As a result, we observed a strong interaction between the two substituents (trimethylsilyl and 3-phenyl-1-propyl DDP amide) on the bridgehead carbons

(Figure 7). Comparing to a similar bicyclo[1.1.0]butane bearing a hydrogen atom and a α-benzyl tosyl amide (**157**), the bond angles were enlarged by ~10 degrees each. Comparing to a conjugated bicyclo[1.1.0]butane **158**, the angle was increased by 23 degrees. We believed that this angle change along with the increased size of the substituent on C12 blocked the access to the *p*-orbital of the central bond and prevented the bicyclo[1.1.0]butane from further reaction with zinc carbenoids.

Table 8. Bond angles and lengths of **153**, **157**[53] and **158**[53].

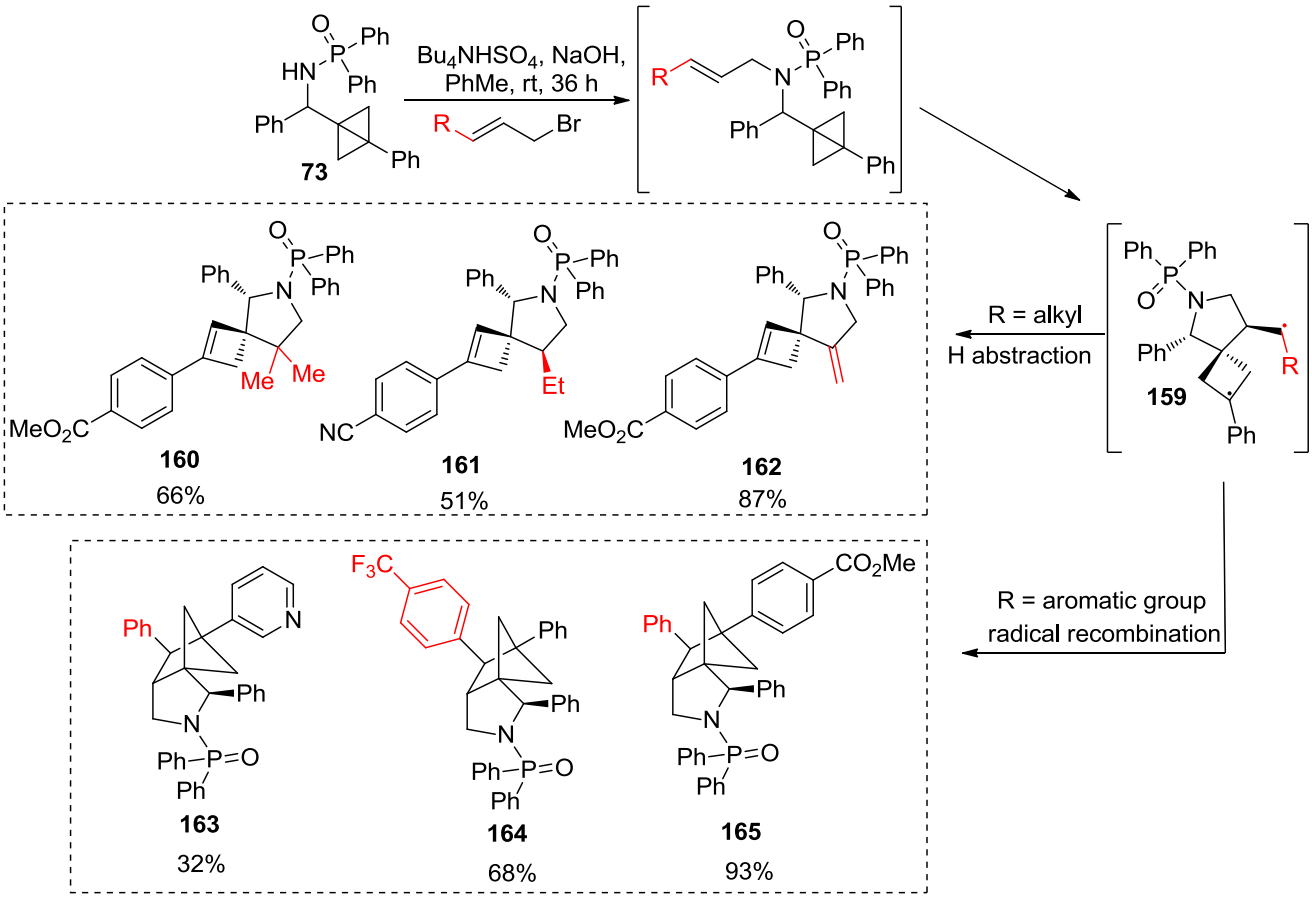
C-C Bond parameters	 **153**	 **157**[53]	 **158**[53]
C1-C10-C12 ( )	137.4	127.0	131.1
Si1-C12-C10 ( )	140.4	129.4	117.0
C10-C12 (Å)	1.505	1.456	1.518

Besides the bond angle, we also observed that the bond length of C10-C12 was expanded due to the interaction between C10 and C12 substituents, which again demonstrated the steric hindrance of the silyl group.

1.3.5 Ene reaction of silyl-substituted bicyclo[1.1.0]butane.

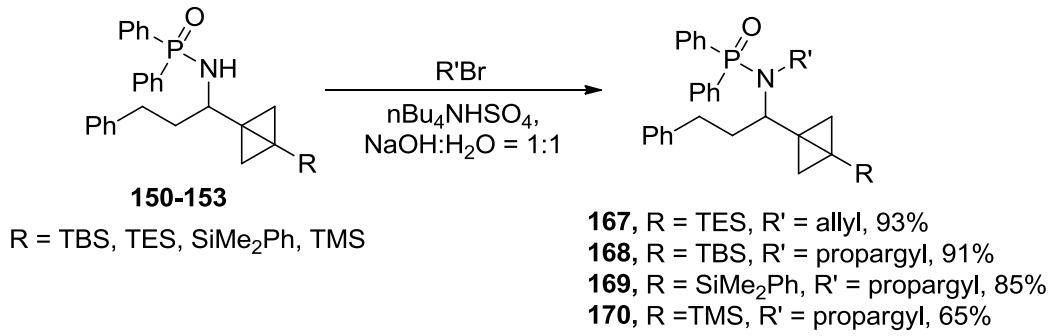
In 2006, our group reported a pericyclic cascade reaction using bicyclo[1.1.0]butane containing starting materials.[54] Depending on the substituent on the allyl bromide, the product was formed as a spirocyclic butene or tricyclic pyrrolidine system (Scheme 35). When the R group is an alkyl group, intermediate **159** has a short lifetime and undergoes H-abstraction to

form the spirocyclic butene **160-162**. However, when the R group is aromatic (**163-165**), intermediate **159** undergoes a radical recombination to form a C-C bond.



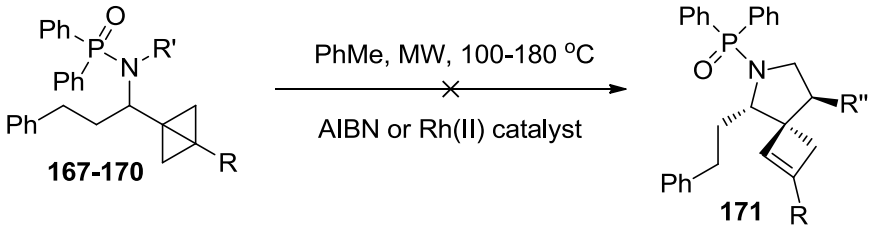
Scheme 36. Thermal ene reactions of bicyclo[1.1.0]butanes.[54]

We subsequently tried the cascade conditions with several allyl bromides and silyl-substituted bicyclo[1.1.0]butanes. The alkylated products were formed, but no cyclized products were found (Scheme 37). Subjecting the alkylated products to high temperatures or microwave conditions did not promote the cascade reactions. Furthermore, rhodium catalysts and radical initiators did not facilitate this reaction (Scheme 38).[3,53]



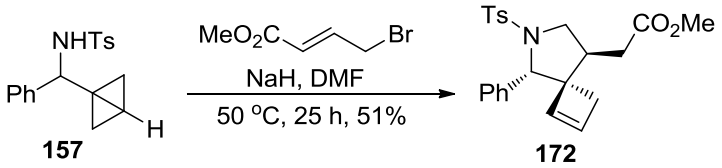
Scheme 37. Phase transfer alkylation of bicyclo[1.1.0]butanes **150-153**.

Since these silyl-substituted bicyclo[1.1.0]butanes have different HOMO/LUMO energies to the bicyclo[1.1.0]butanes with aromatic substitutions on the bridgehead carbon, the inertness of **167-170** was not unexpected. On the other hand, as we discussed in **1.3.4**, the X-ray structure revealed our silyl-substituted bicyclo[1.1.0]butane possessed strong steric hindrance that possibly blocked the anti-obital of the central bond of the fused ring system, which could also be detrimental to the pericyclic cascade reaction.



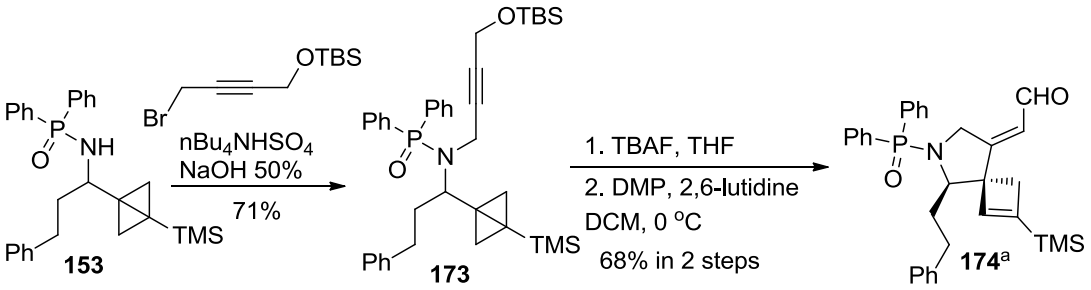
Scheme 38. Cyclization failure with prolonged heating or different catalysts.

Previously, our group developed the cyclization methodology using unactivated bicyclo[1.1.0]butane substrates such as **157** (Scheme 39).[53] Treatment of substrate **157** with sodium hydride in anhydrous dimethylformamide led to the formation of an alkylated amide that is converted to the cyclized product **172**. We expected silyl-substituted bicyclo[1.1.0]butanes to have properties similar to **157**.



Scheme 39. [2+2] ene reaction with unactivated bicyclo[1.1.0]butane.

However, when we attempted to carry out the reaction with compound **153**, we did not observe the formation of any alkylated or cyclized product. The decomposition of methyl 4-bromocrotonate indicated that the alkylation process was problematic. We sought to solve this issue by applying a 3-step (alkylation/deprotection/oxidation) strategy towards the synthesis of the activated propargyl functionality.

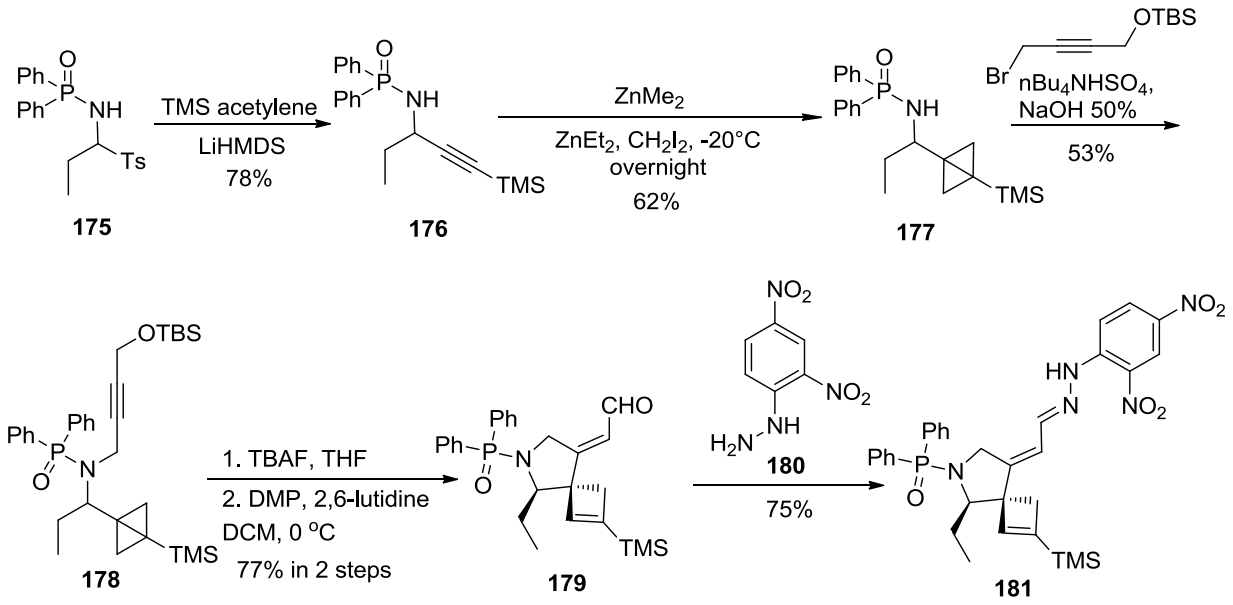


Scheme 40. [2+2] ene reaction with bicyclo[1.1.0]butane **174**.

[a]Structure assigned by comparing to X-ray structure a similar compound **180**.

This method involved a protected alcohol that can be easily oxidized to the aldehyde, which in turn can activate the conjugated propargyl alkyne.[53] Alkylation of amide **153** with TBS protected propargyl bromide using phase transfer conditions affords **173** in good yield (Scheme 40). The TBS group could be removed in nearly quantitative yield without any decomposition of the 1-trimethylsilyl bicyclo[1.1.0]butane. Subsequently, treating the propargyl alcohol with Dess-Martin reagent afforded the cyclized product **174** in high yield. It is worth mentioning that the ene-reaction happened simultaneously at 0 degrees, without the isolation of propargyl

aldehyde. We planned to obtain a crystal structure of **174**. Unfortunately, **174** slowly decomposed at room temperature and failed to crystallize.



Scheme 41. [2+2] ene reaction with silyl-substituted bicyclo[1.1.0]butane.

An alternative strategy with dinitrophenyl hydrazine was applied with substrate **175**. The alkyne addition provided TMS-substituted bicyclo[1.1.0]butane **176**. Switching the phenylethyl group to a smaller ethyl group did not affect the outcome of cyclopropanation. TMS-substituted bicyclo[1.1.0]butane **177** was obtained in 62% yield as the only product. The following alkylation/deprotection/ene reaction sequence produced the aldehyde **179** in high yield and as a single diastereomer. Hydrazone **181** was synthesized upon stirring **179** with (2,4-dinitrophenyl)hydrazine (**181**) in methanol at room temperature (Scheme 41).

The product was recrystallized from dichloromethane and hexanes to afford an orange crystal. As shown in Figure 8, we observed bond length differences between the double bond (1.343 Å) and the single bond (1.536 Å) on the cyclobutene ring. The ethyl group is located on

the same side with the double bond on the cyclobutene ring. This suggests that this reaction is a stereospecific formal ene reaction.

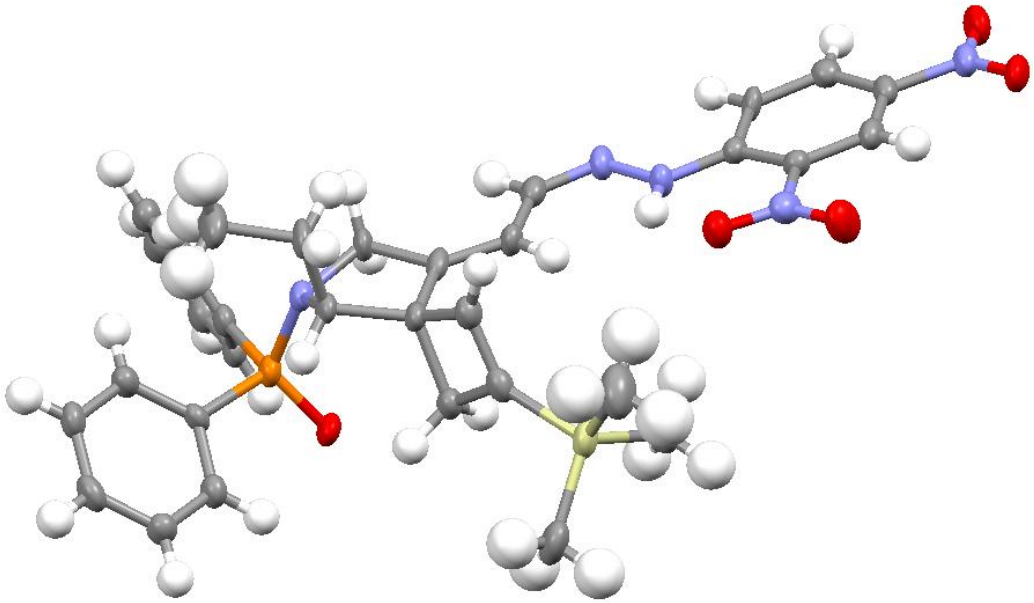
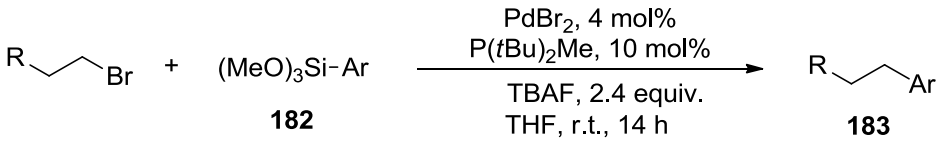


Figure 8. X-ray structure of **181**.

1.3.6 Hiyama cross-coupling of silyl-substituted bicyclo[1.1.0]butane

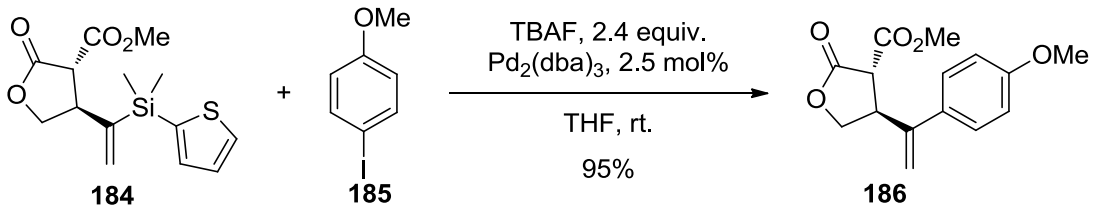
The high π-character of the central bond of bicyclo[1.1.0]butane has been highlighted in the first chapter. We expected this compound to have similar reactivity to a vinyl silane, which undergoes a Hiyama coupling in the presence of a fluoride activator and a palladium species.



Scheme 42. Hiyama coupling protocol using aryl silane and alkyl bromide.

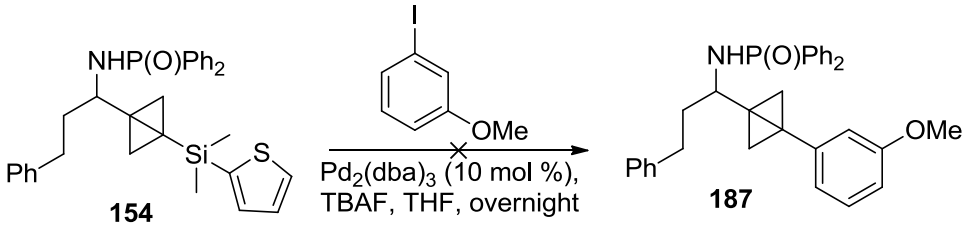
Hundreds of protocols for Hiyama couplings utilizing mild conditions and different silicon species have been reported in the last decade.[72] For example, a room-temperature Hiyama

cross-coupling of arylsilanes with alkyl bromides and iodides was reported by Fu *et al.* (Scheme 42).[73] Silicon functionalities such as dimethyl(2-thienyl)silyl have also been used in Hiyama-coupling partners (Scheme 43).



Scheme 43. Hiyama coupling using a dimethyl(2-thienyl)silyl group.

We began our explorations of the use of silyl-substituted bicyclo[1.1.0]butanes as Hiyama coupling partners using substrate **154** (Scheme 44). Unfortunately, subjecting compound **154** to Hiyama coupling conditions led to the decomposition. An explanation is that the palladium catalyst opens the bicyclo[1.1.0]butane ring and formed a palladium-carbene complex that decomposes under the reaction conditions.



Scheme 44. Hiyama coupling using a dimethyl(2-thienyl)silyl bicyclo[1.1.0]butane.

1.4 CONCLUSION

This chapter describes our methodologies for the enantioselective synthesis of 1-bicyclo[1.1.0]butan-1-yl alkylamines. Initial trials with the enantioselective addition of

bicyclo[1.1.0]butyllithium reagent to imines were unsuccessful. We developed an alternative route using cyclopropanation to enantiomerically enriched propargyl amides. The enantioselective addition of alkynes to imines proceeded well for most *N*-DPP amides. The cyclopropanation went well for conjugated propargyl amides with the stereocenter retained. This methodology enabled us an access to enantiomerically enriched 1-bicyclo[1.1.0]butan-1-yl alkylamines.

A series of silyl-substituted bicyclo[1.1.0]butanes could be synthesized by double cyclopropanation from propargyl amides without observation of byproduct. To our knowledge, this is the first case of a cyclopropanation reaction furnishing bicyclo[1.1.0]butane products in such high, reproducible yields. When tethered to an activated alkyne, the silyl-substituted bicyclo[1.1.0]butanes underwent cyclization to form pyrrolidines. This methodology also enables an unique pathway for the synthesis of multi-functional cyclobutene compound. Cyclobutane/cyclobutene-containing alkaloids have shown anticancer, antibiotical and other activities and may serve as potential lead drug candidates.[74] Despite various well-known methodologies developed for cyclobutane/cyclobutene synthesis, highly-substituted cyclobutenes remain challenging synthesis target[75]. However, our oxidation/pericyclic cascade reaction furnished a quaternary center in the cyclobutene at ease. This methodology could pave a unique pathway for the synthesis of multi-functional cyclobutene compounds such as welwitindolinone A isonitrile.[76-78]

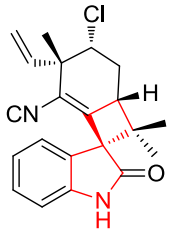


Figure 9. Welwitindolinone A isonitrile.

2. PALLADIUM-CATALYZED CYCLOISOMERIZATION OF 1-BICYCLO[1.1.0]BUTAN-1-YL ALKYLAMINES

Transition metals have been at the center of strained cyclopropane methodology development in the last few decades. For example, metal-catalyzed methylenecyclopropene (MCP) reactions have proven multifunctional and versatile in organic synthesis. Utilizing this transformation on bicyclo[1.1.0]butanes reveals some interesting reactivity of these species. This chapter will demonstrate some fundamental aspects of these transformations as well as applications of these strategies for bicyclo[1.1.0]butane derivatives.

2.1 FUNDAMENTAL PROPERTIES OF METHYLENECYCLOPROPANE

2.1.1 Transformation patterns of MCP

Similar to bicyclo[1.1.0]butane, MCP is a highly strained four-carbon unit that can undergo a variety of reactions by releasing its strain energy.[22] Metal catalysts can utilize the π character of the cyclopropane bond and the high thermodynamic driving force provided by the ring strain to initiate many fascinating transformations. This type of rearrangement reaction usually results in significant increase in structural complexity.[79]

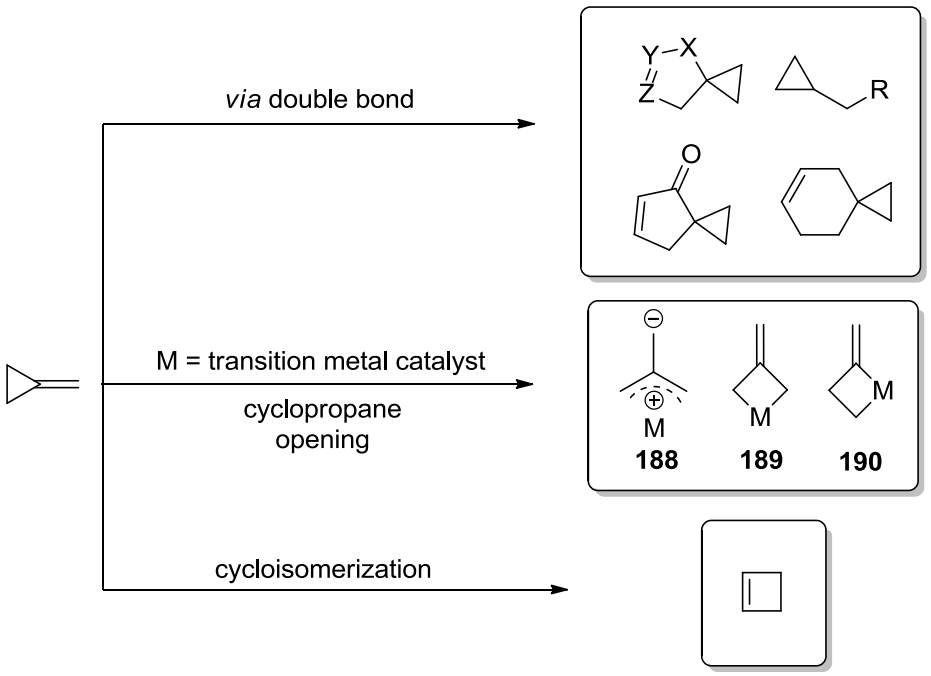


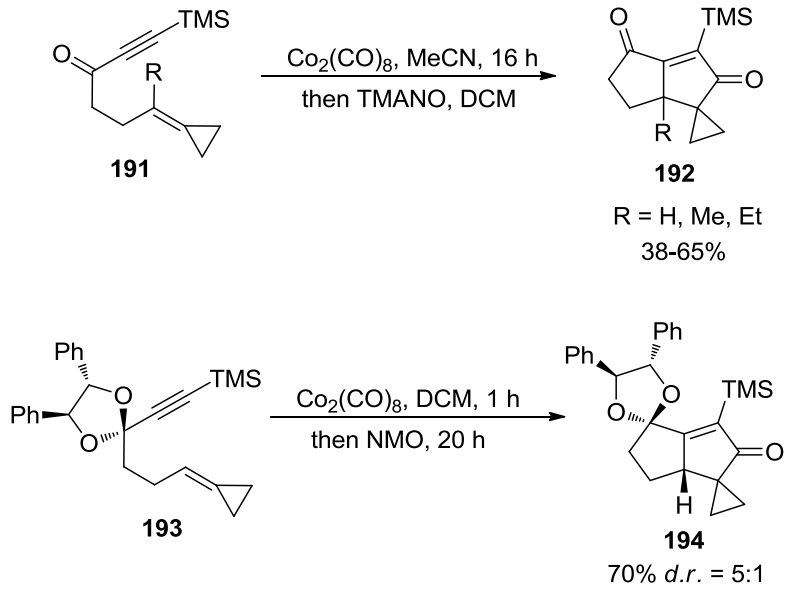
Figure 10. Metal-catalyzed MCP reaction pathways.

As shown in Figure 10, there are three major reaction patterns for MCP. The first pattern arises from the reactivity of the double bond in MCP. It can undergo carbometallation followed by *β*-elimination to afford the homoallylic or allylic compounds.[80] Alternatively, the double bond

may also react as a component in a Pauson-Khand,[81] Diels-Alder[82] or [3+2] dipolar cycloaddition[83], which furnish many spirocyclic compounds without cyclopropane ring opening. The second reaction pattern relies on the formation of a metallacyclobutane species or a metal trimethylenemethane (TMM) complex **188**. These highly reactive intermediates are produced by the insertion of the transition metal into the distal (**189**) or the proximal (**190**) bond, respectively. Finally, MCPs can undergo metal-catalyzed cycloisomerization to afford the cyclobutene.[84,85]

The following sections review several representative examples of metal-catalyzed MCP cycloaddition/isomerization reactions.

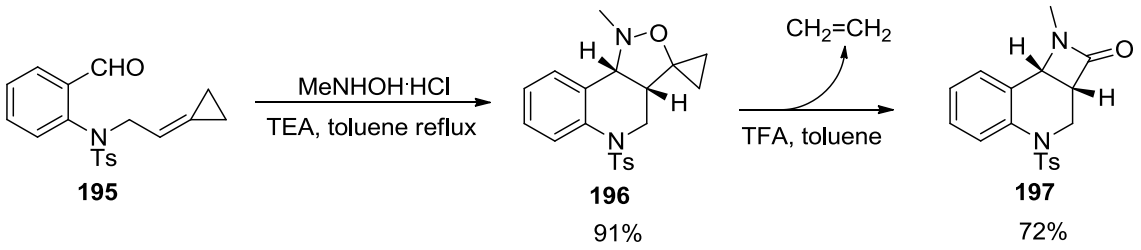
2.1.2 Cycloadditions with the conservation of cyclopropane ring



Scheme 45. Intramolecular Pauson-Khand reaction of enyne.

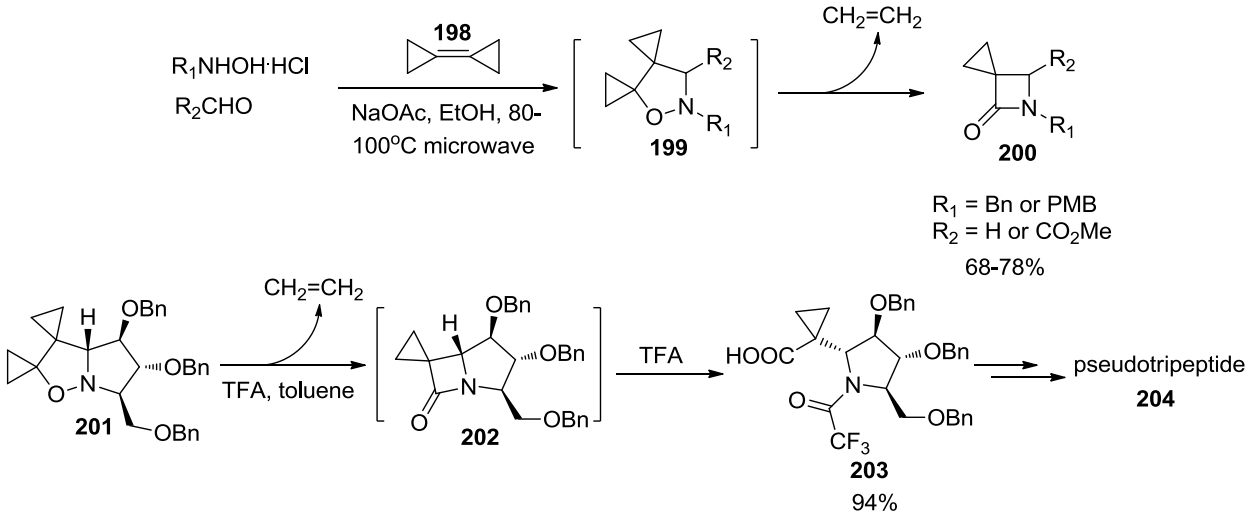
The Pauson-Khand reaction (PKR) is a cobalt/rhodium-mediated [2+2+1] cyclization of an alkyne, an alkene and a carbon monoxide that yields a cyclopentenone. In 2005, de Meijere and co-workers applied MCP moieties as alkenes in PKR precursors 1,6- and 1,7-enynes, which

furnished spirocyclopropanated bicyclo[3,3,0]octenone or bicyclo[4,3,0]nonenone in good yields.[86] Additionally, the authors found that a chiral auxiliary led an asymmetric induction in the cyclization step. Spiro(cyclopropanebicylo[3,3,0]octantenone) **194** can be obtained in enantiomerically pure form (Scheme 45).



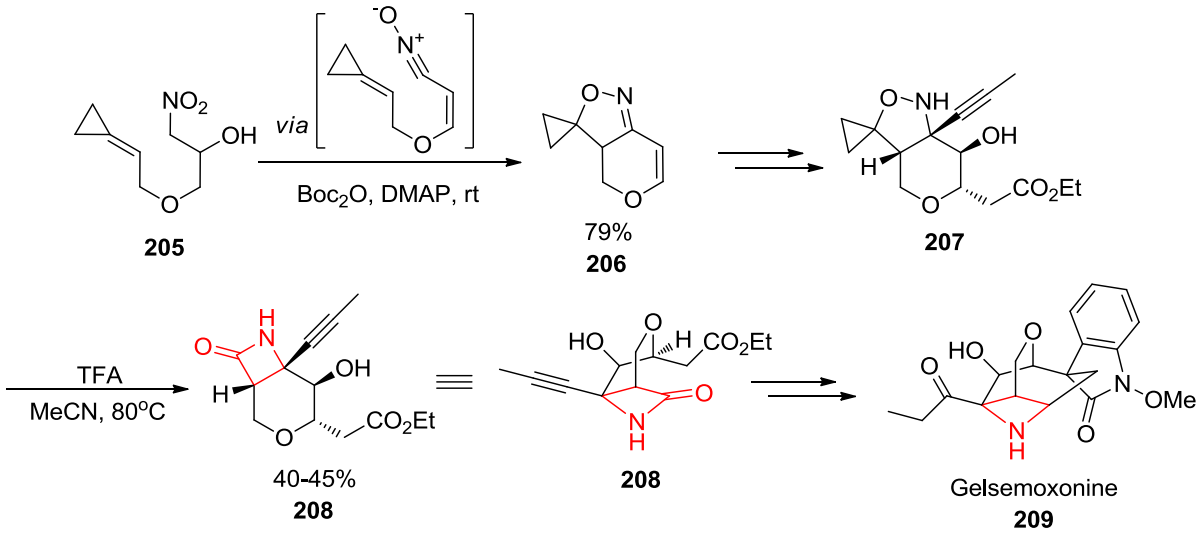
Scheme 46. 1,3-Dipolar addition of MCP with nitrones and acid-mediated ring contraction.

In 2000, Brandi *et al* investigated the 1,3-dipolar addition of MCP with various nitrones, providing 1,5-isoxazolidines in moderate yield.[87] An acid led these resulting isoxazolidines to form valuable *β*-lactams by ethylene extrusion. (Scheme 46)



Scheme 47. 1,3-Dipolar addition of BCP with nitrones and transformation of the adducts.

This cascade reaction was applied to bicyclopropylidene **198** (BCP) for the synthesis of *α*-spirocyclopropane-*β*-lactam.[88,89] Upon microwave heating in presence of NaOAc, the adducts of BCP and nitrone (*in situ* generated from aldehyde) gave cyclopropanated *β*-lactam **200** in good yield. Interestingly, pyrrolidine derivatives afforded *α*-cyclopropanated-*β*-homoprolines due to the instability of carbapenam skeleton in **202**. Additionally, the authors showed that these highly functionalized homoprolines were incorporated in the synthesis of a pseudotripeptide (Scheme 47).[90]



Scheme 48. Total synthesis of gelsemoxonine.

In 2013, Carreira's group published a 21-step total synthesis of gelsemoxonine, a natural product isolated from traditional Chinese medicine.[91] The author utilized Brandi's 1,3-dipolar addition and acid-promoted ring contraction sequence to obtain *β*-lactam **208**, which ultimately elaborated into the azetidine in **209**. A mechanistic study indicated that the reaction proceeds *via* a concerted pathway.[92] In 2015, Carreira *et al.* reported a full account of their studies on gelsemoxonine as well as an enantioseletive synthesis of key intermediate **206**.[93]

2.1.3 Metal-catalyzed MCP [3+2] cycloaddition reactions

The metal-catalyzed [3+2] cycloaddition of MCP and double bonds has been studied extensively since the pioneering studies of Noyori's and Binger's group in 1970s.[94-96] Motherwell and Nakamura independently reported examples of intramolecular [3+2] cycloaddition between MCPs with alkenes and alkynes in 1988.[97-98] These methodologies served as great procedures to construct highly functionalized cyclopentanes. (Figure 11)

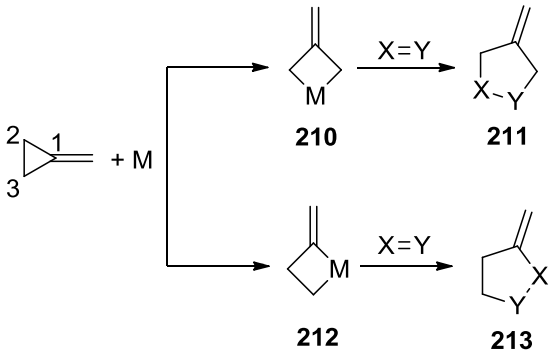
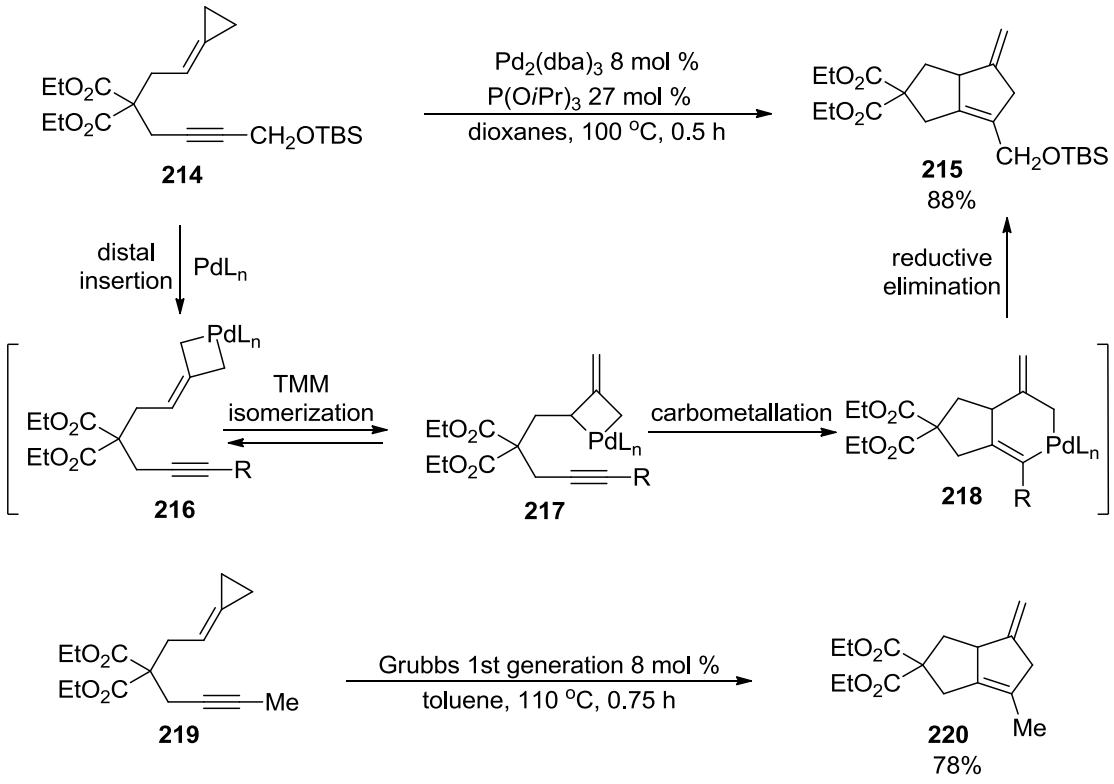


Figure 11. Metal-catalyzed MCP reaction pathways.

Generally, there are two different pathways for the [3+2] cycloaddition between MCP and double bonds. An oxidative insertion of the distal bond (C2-C3) would generate metallacyclobutane **210**. The carbonmetalation with double bonds and reductive elimination forms cyclopentane **211**. Alternatively, the proximal bond cleavage between C1 and C2 would lead to the formation of regioisomer **213** (Figure 11).

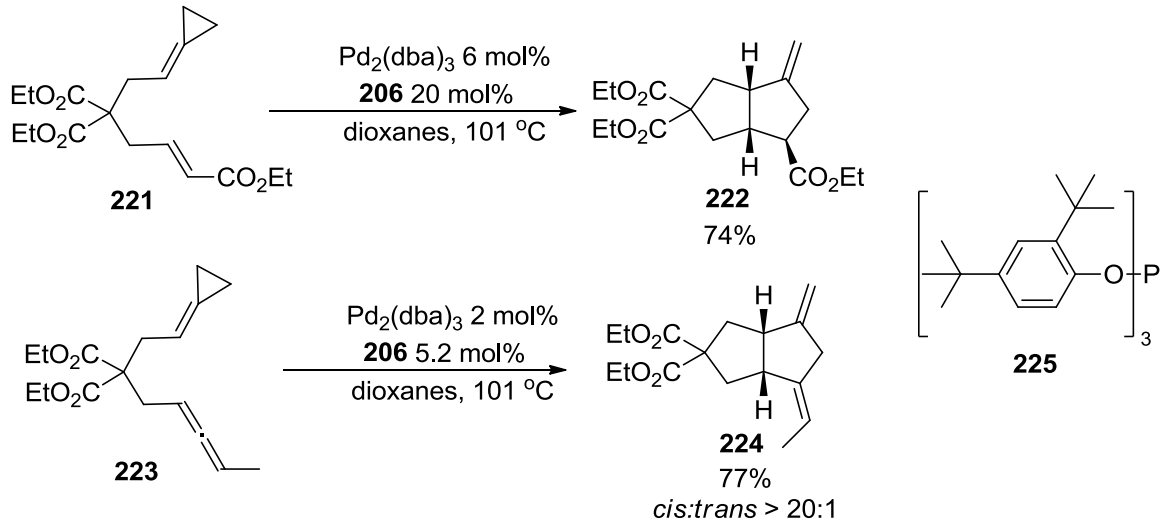
Mascareñas and co-workers published a series of papers on the [3+2] cycloaddition of alkyne/alkene/allene tethered MCPs in the presence of palladium catalysts.[99-103] In 2003, they found that the cyclization of **214** afforded **215** in good yield when treated with a palladium-phosphite complex.[99] Later they discovered that a Ruthenium-based catalyst was capable of

catalyzing the reaction in a similar fashion.[100] DFT studies suggested that these cyclizations are initiated by an oxidative insertion into the distal bond and followed by an isomerization *via* a TMM-Pd complex to give a palladacyclobutane intermediate **216**.[101] Intramolecular addition into the alkyne and reductive elimination leads to the formation of **218**. Additionally, the authors managed to combine the alkylation with the cycloaddition to a one-pot synthesis, which is a more simple and practical process (Scheme 49) .[102]



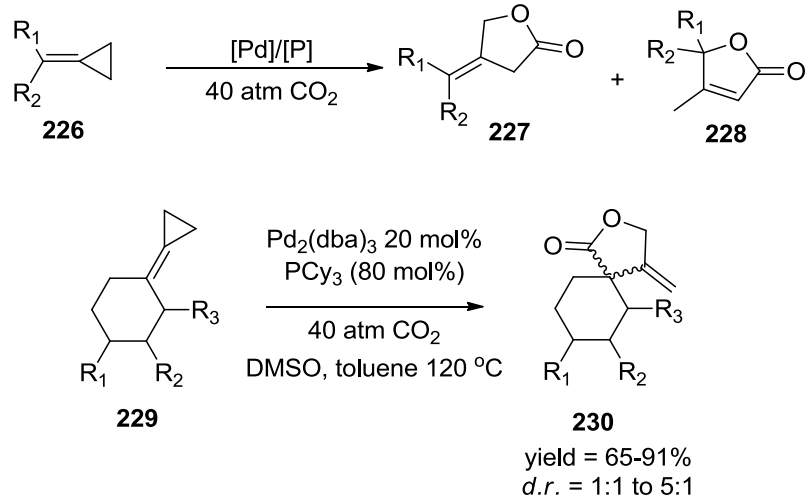
Scheme 49. Palladium-catalyzed [3+2] MCP cyclization with alkynes.

The electron-deficient alkene tethered MCP **221** furnished **222** in a highly diastereoselective fashion through a similar mechanism to alkynes.[102] On the other hand, the authors found the allene **223** could perform the cycloaddition with less catalyst loading (Scheme 50).[103]



Scheme 50. Palladium-catalyzed [3+2] MCP cyclization with alkenes/allenes.

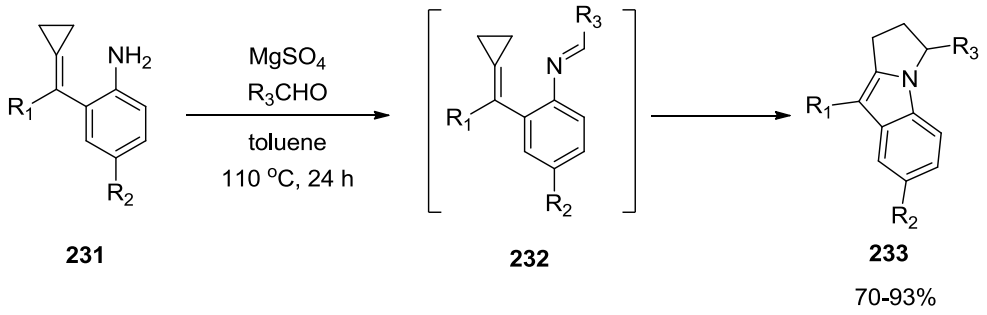
2.1.4 Heterocycle synthesis from MCP [3+2] cycloaddition



Scheme 51. Palladium-catalyzed [3+2] MCP cyclization with CO_2.

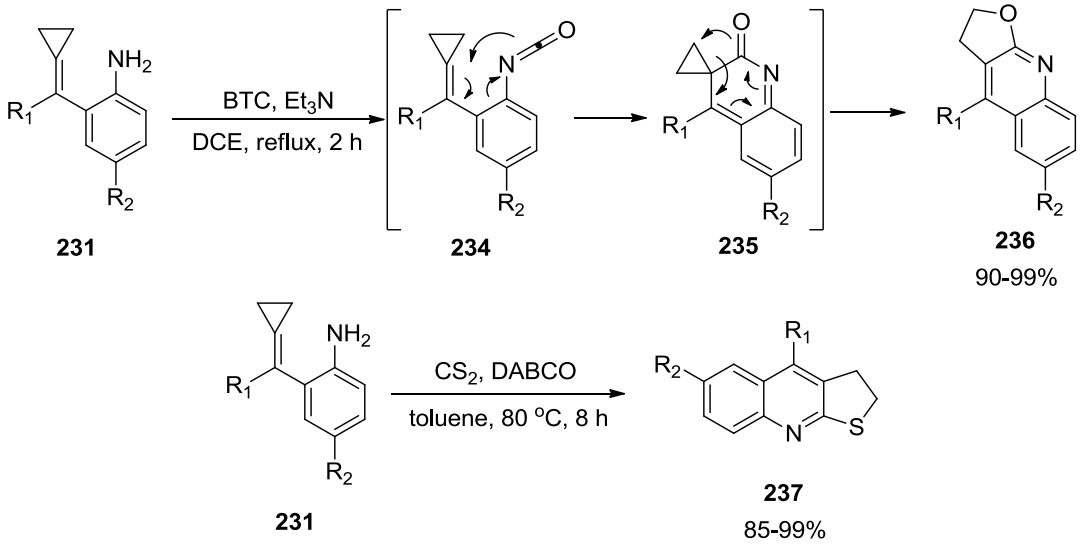
A C=X (X = N, O) double bond can also react with MCP in the presence of metal catalysts. An interesting example is Binger's lactone synthesis by a palladium-catalyzed cycloaddition between MCP and carbon dioxide.[104] However, this process afforded a mixture of regioisomers (**227** and **228**) and diastereomers. In 2011, Shi *et al.* published an optimized

procedure to synthesize spirocycliclactones **230** with complete regioselectivity.[105] This methodology offers a straightfoward strategy to these highly-substituted lactones, which usually took several steps to synthesize from ketones.



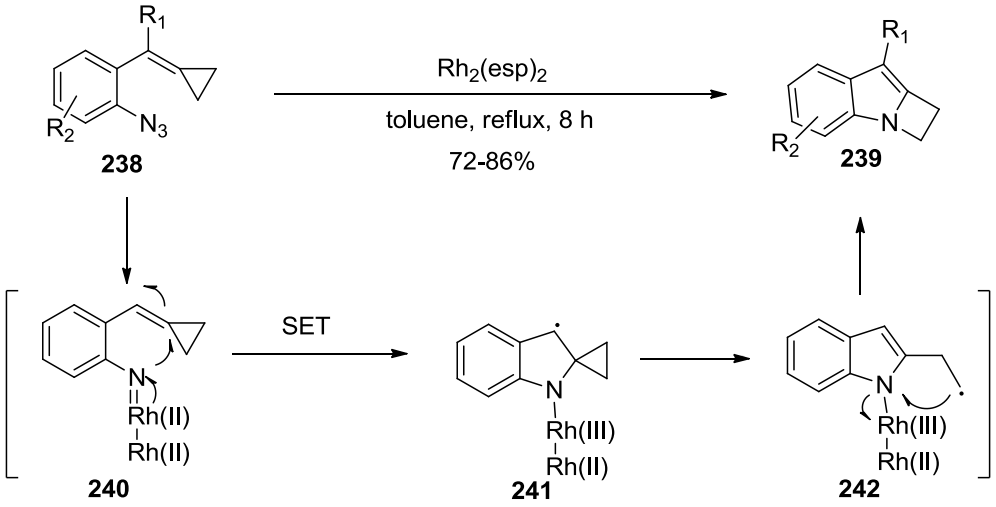
Scheme 52. Heat-induced [3+2] cycloaddition of *o*-aniline-tethered MCP.

Shi *et al.* developed a series of novel and efficient protocols utilizing intramolecular cycloadditions of *o*-aniline-tethered MCP.[106-108] In 2009, they reported a thermo-induced [3+2] cyclization from cyclopropane opening of *in situ* genertated imine **232**. Notably, many biologically active natural products possesses the same functionalized pyrrolo[1,2-*a*]indole core as **233**.[106] (Scheme 52)



Scheme 53. Heat-induced [3+2] synthesis of furoquinoline **236** and thienoquinoline **237**.

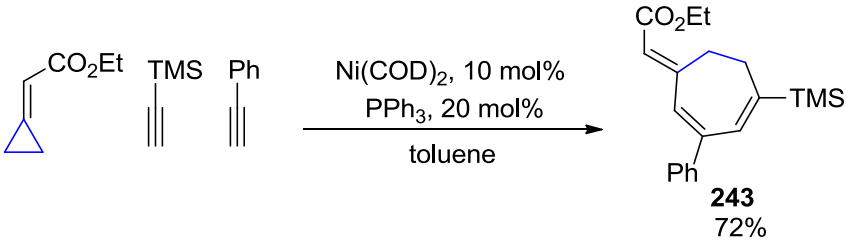
In 2016, their group published an approach for facile access to furoquinoline and thienoquinoline scaffolds from **231**.[107] Mechanistically, the starting anilines were transformed into isocyanates *in situ*. Next, the isocyanate-tethered **234** underwent a 6π-electrocyclization to form intermediate **235**, which further rearranged to product **236** through cleavage of the cyclopropane ring. Potential applications of products **236** and **237** were still under investigation.



Scheme 54. Rh(II)-catalyzed indole-fused azetidine synthesis.

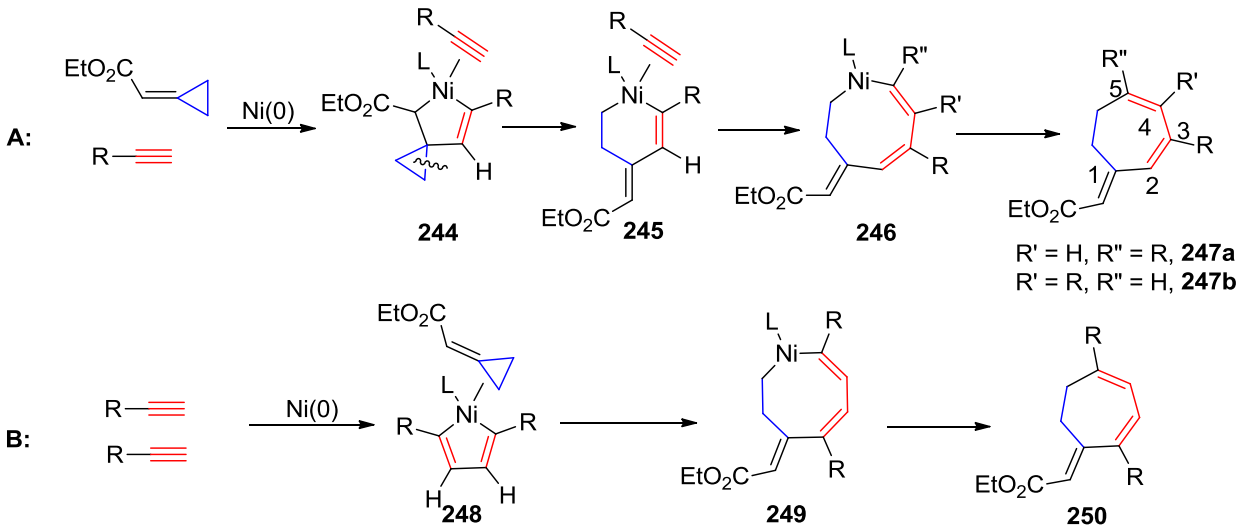
Another rhodium(II)-catalyzed protocol that converts othro-MCP-tethered phenyl azide into indole-fused azetidines was discovered by Shi and co-workers in 2016.[108] When the radical trapping reagent TEMPO was applied, the authors found the yield of **239** was dramatically diminished. This suggested a SET (single-electron-transfer) mechanism might be involved. The authors proposed a mechanism based on the experimental results and DFT studies. Upon the coordination of $Rh_2(esp)_2$, **238** releases N_2 and produces nitrene **240**. Subsequent SET and addition generates radical **241**, which is rearranged to give indole intermediate **242**. Another SET regenerates rhodium catalyst and furnishes indole-fused azetidines **239** as final product (Scheme 54).

2.1.5 Metal-catalyzed MCP [3+2+2] cycloaddition reactions



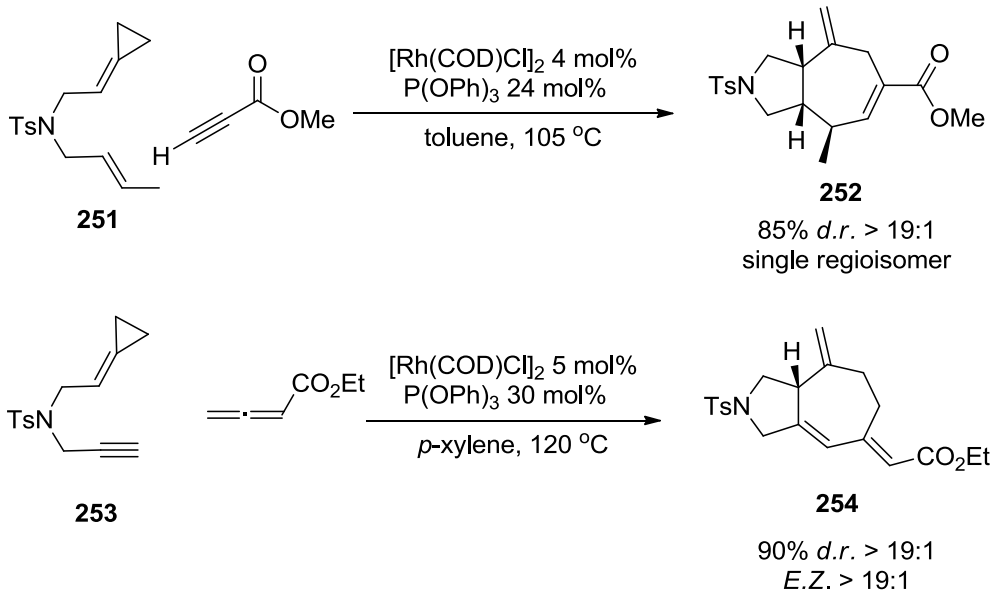
Scheme 55. Nickel-catalyzed [3+2+2] MCP cyclization with alkynes.

In 2004, Saito *et al.* first discovered a intermolecular [3+2+2] cycloaddition between MCP and alkynes.[109] The resulting seven-member ring carbocycles are prevalent among many nature products. Interestingly, nickel was used in this case and the product distribution was distinctively different from palladium-catalyzed cycloadditions because nickel prefers the proximal insertion to the distal insertion. Recently, this reaction was further developed as a 3-component reaction (2 different alkynes) with a good yield of a single regioisomer (Scheme 55).[110]



Scheme 56. Mechanisms of nickel-catalyzed [3+2+2] MCP cyclization with alkynes.

In 2015, a follow-up DFT study from Saito's group suggested two possible pathways depending on the different substitutions on the alkynes.[111] Alkyl-substituted alkynes prefer pathway A, and the regioselectivity is determined by the second insertion of acetylene (**246**). A bulkier R would generate 3,5-substituted **247a**, while a smaller R would afford a mixture of **247a** and **247b**. For pathway B, electron-deficient alkynes would couple with the nickel catalyst to form **248**, which ultimately determines regioselectivity of the 2,5-substituted **250**. These reactions provide a facile synthesis of 7-member ring carbocycles with decent regioselectivity. (Scheme 56)



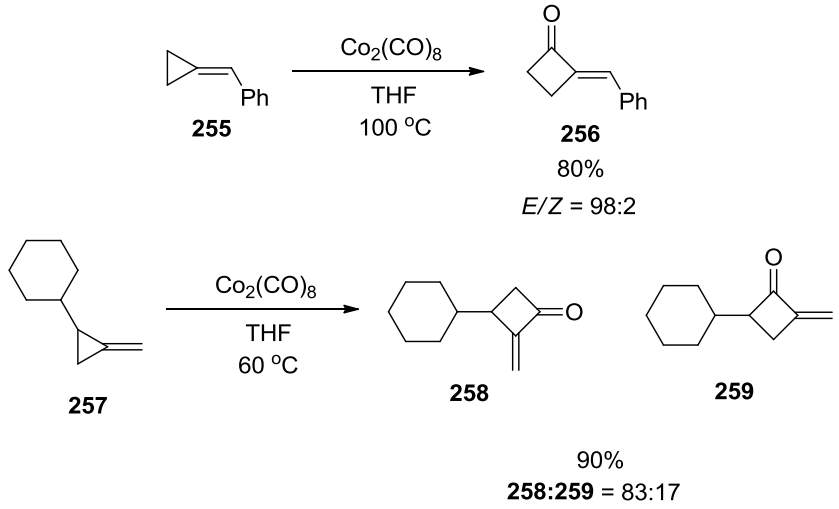
Scheme 57. Rhodium-catalyzed [3+2+2] MCP cyclization with alkynes.

In 2008, Evans *et al.* explored an intra/intermolecular [3+2+2] process for the preparation of *cis*–fused bicycloheptadienes **252** catalyzed by a rhodium phosphite complex.[112] The study was noteworthy for the fast stereospecific generation of three new stereogenic centers and the control of the regiochemistry. In 2015, the same authors published another [3+2+2]

cycloaddition utilizing allenes as a component to generate tri- or tetrasubstituted exocyclic olefins **254**, which provided a new route to the guaiane family of sesquiterpenes (Scheme 57).[113]

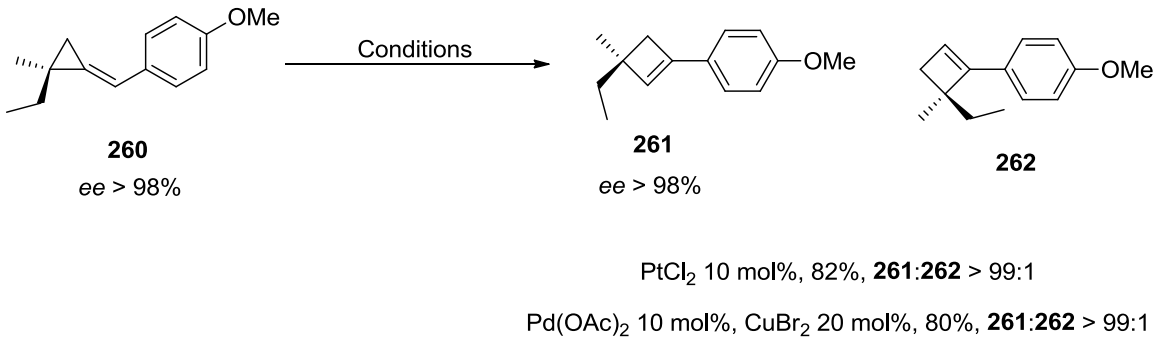
2.1.6 Metal-catalyzed MCP cycloisomerization reactions

De Meijere *et al.* developed a novel [3+1] ring expansion reaction that produces methylenecyclobutanones under mild conditions.[114] The carbonylation could be carried out under 1 atmosphere of CO (balloon) with 5 mol% of [$Co_2(CO)_8$]. Other metal carbonyls such as [$W(CO)_6$], [$Mo(CO)_6$], [$Fe(CO)_5$] and [$Cr(CO)_6$] gave poor yield. Notably, this is the first example of a cobalt catalyst effectively activating the δ bonds of a cyclopropane. (Scheme 58)



Scheme 58. Cobalt-catalyzed carbonylation of MCP.

In 2006, Fürstner reported a $PtCl_2$-catalyzed cycloisomerization of MCP into cyclobutene in moderate to good yield.[84] Shi *et al.* independently published the same ring-expansion transformation utilizing $Pd(OAc)_2$ and $CuBr_2$.[85] In 2009, Marek and co-workers proved that the rearrangement of enantiomerically pure MCP completely conserved the quaternary stereocenter with high regioselectivity (Scheme 59).[115]

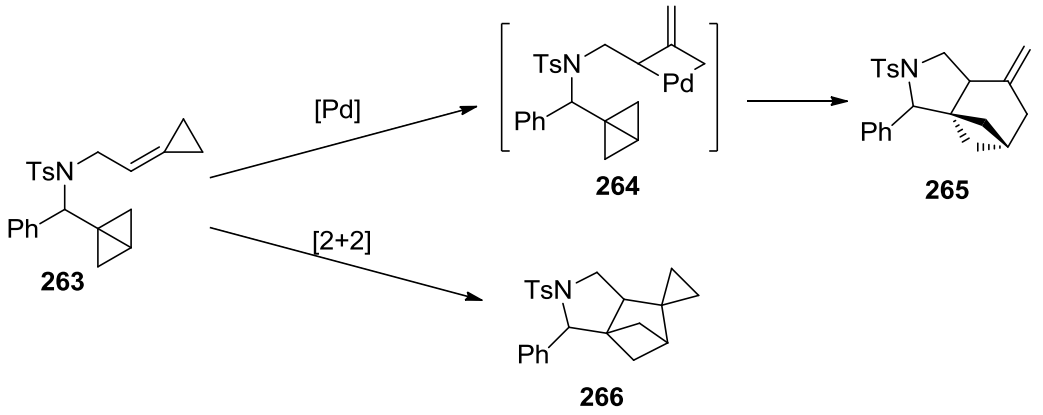


Scheme 59. Pd/Pt-catalyzed cycloisomerization of MCP.

2.2 RESULTS AND DISSCUSSION

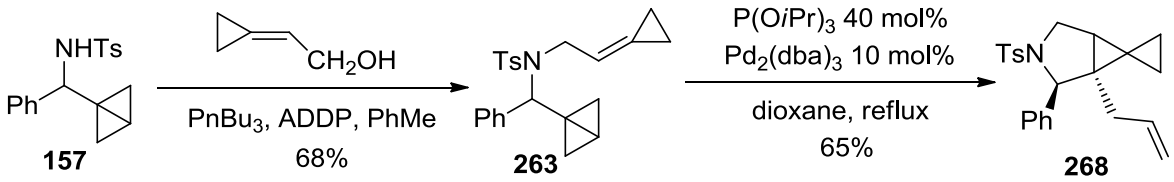
2.2.1 Pd-catalyzed cycloisomerization of bicyclo[1.1.0]butane and MCP

In the last several sections, we have discussed the reactivities of MCP extensively. Inspired by these fascinating examples, we planned to explore the interaction between MCP and bicyclo[1.1.0]butane. With the highly strained nature of both moieties, a great potential in organic synthesis can be envisioned.



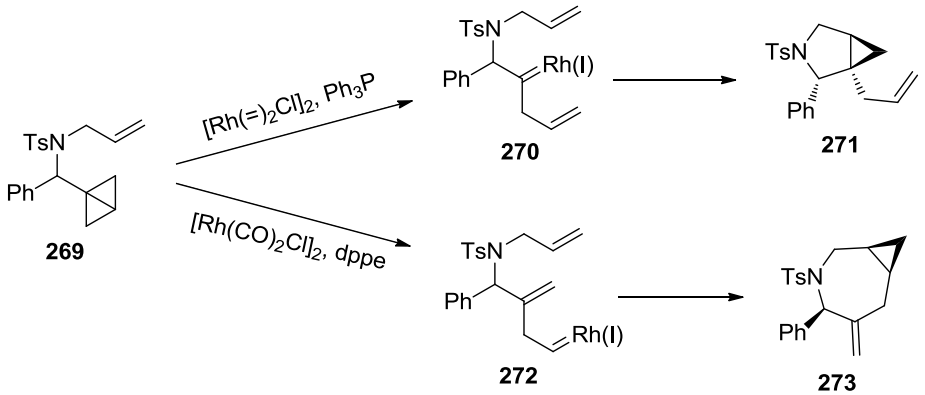
Scheme 60. Proposed palladium-catalyzed cycloisomerization of MCP and bicyclo[1.1.0]butane.

We imagined that the central bond of bicyclo[1.1.0]butane in **263** would serve as an alkene functionality to perform a formal [3+2] cycloaddition with MCP. A palladium catalyst could insert into the distal bond of MCP and isomerize to palladacyclobutane **264**. Next, the addition of bicyclo[1.1.0]butane and reductive elimination would afford our desired bicyclo[3.1.1]heptane **265**. On the other hand, **263** could also undergo a formal [2+2] cycloaddition to product cyclopropanated bicyclo[3.1.1]heptane **266**.



Scheme 61. Initial attempt of a palladium-catalyzed MCP cyclization.

Our initial attempt was carried out with substrate **263**, which was prepared from the Mistunobu reaction between **157** and 2-cyclopropylideneethanol. As shown in Scheme 61, A solution of **263** in dioxane was heated at reflux in the presence of 10 mol% $Pd_2(dba)_3$ and 40 mol% triisopropylphosphite. Surprisingly, we obtained **268** in 65% yield as the only product without the observation of **265** or **266**. Instead of forming the Pd-TMM complex with MCP, the palladium catalyst might open the bicyclo[1.1.0]butane ring into a carbene intermediate to provide the product **268**.



Scheme 62. Rhodium(I)-catalyzed cycloisomerization of **269**.

We were intrigued by this result because our group previously reported a rhodium-catalyzed cycloisomerization of bicyclo[1.1.0]butanes.[3] As depicted in Scheme 62, by tuning the ligands on the rhodium catalyst, bicyclo[1.1.0]butane **269** can generate two rhodium carbine species **270** and **272**. Subsequently, cyclopropanations produced pyrrolidine **271** or azepine **273**, respectively.

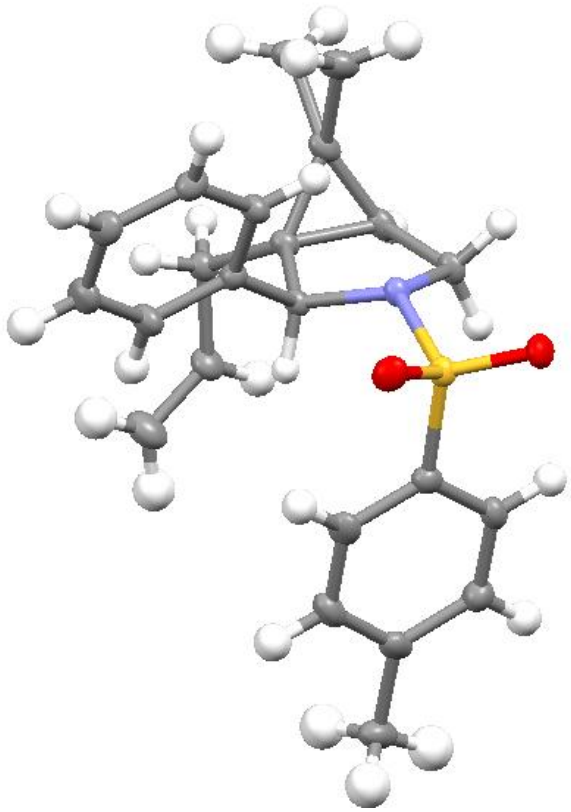


Figure 12. X-ray structure of **268**.

Recrystallization of **268** in dichloromethane and hexanes afforded a fine colorless crystal. The X-ray structure of **268** is displayed in Figure 12. The highly-strained spirocyclopropane ring is perpendicular to the pyrrolidine. Notably, the phenyl and allyl group are in a *trans* relationship. We observed a *cis* orientation of these groups in our previous rhodium-catalyzed cycloisomerization.

Having confirmed the structure of spirocyclopropane **268**, we further examined the reaction with substrate **269**, which provided **274** under our standard conditions. Interestingly, **274** is the opposite diastereomer of our previous rhodium-catalyzed cycloisomerization product **271**. On the other hand, we did not detect any azepine-type (**273**) product under our conditions. We noticed very similar H-NMR spectra of these two compounds except for the protons located in the pyrrolidine ring. The assignment of these protons are depicted in Figure 13.

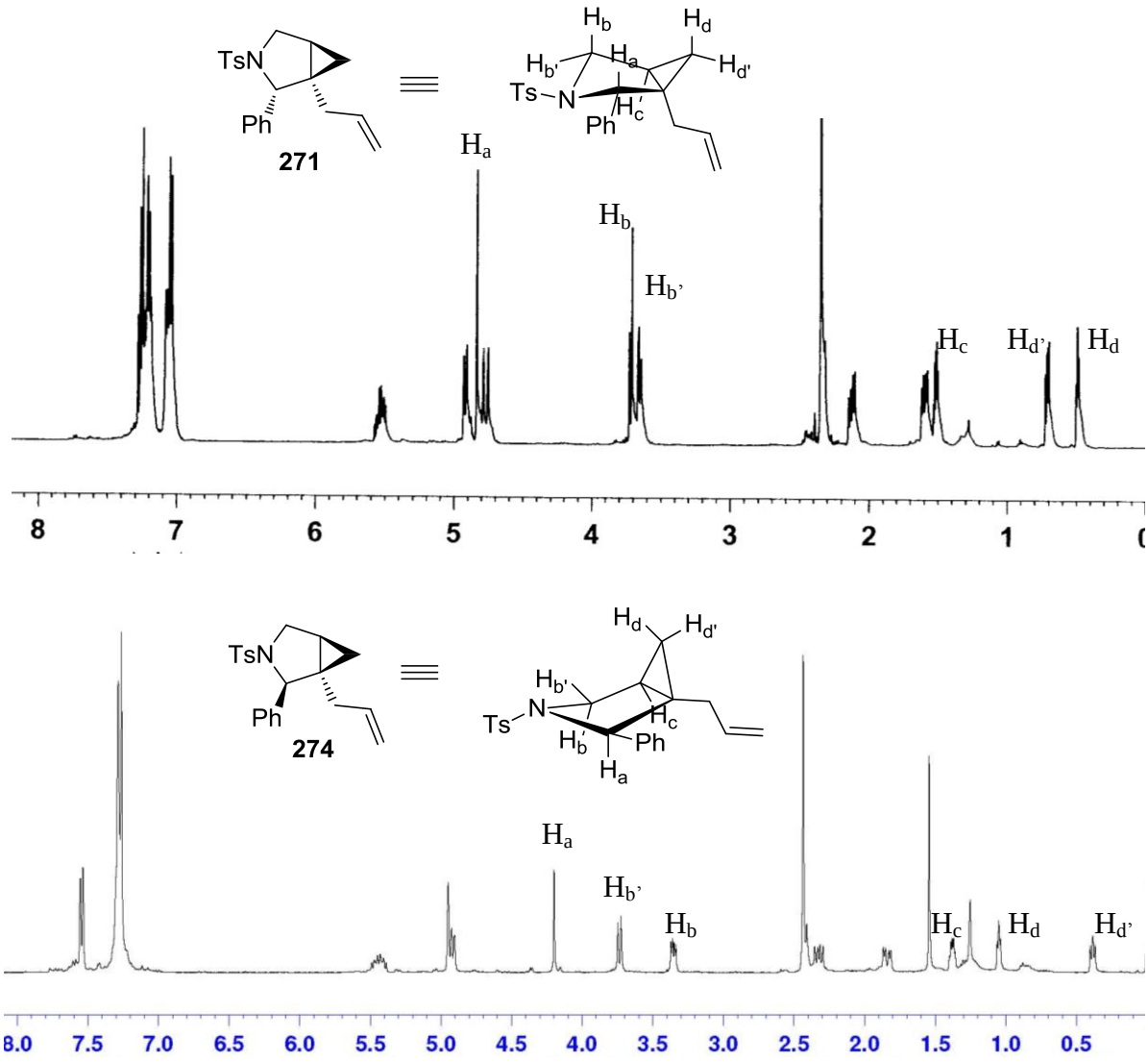
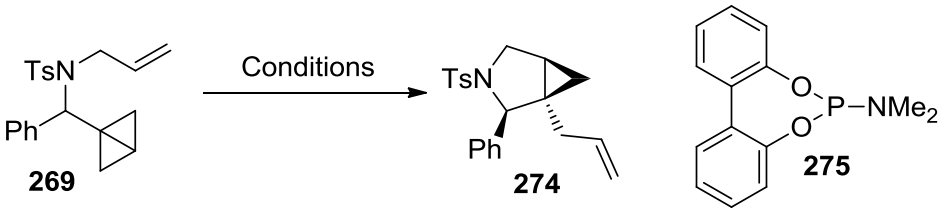


Figure 13. NMR spectra of diastereomers **271** and **274**.

First of all, we assigned H_b and $H_{b'}$ by examing the vicinal H-H coupling between $H_b/H_{b'}$ and H_c. $^3J_{HH}$ of H_b/H_c (**271**) and $H_{b'}/H_c$ (**274**) were close to 0 Hz so the dihedral angles of these C-H bond should be ~90 º. Second of all, $H_{b'}$ in **271** and **274** were both around 3.7 ppm because they adopted a similar equatorial position. Comparing to **274**, two axial protons (H_a and H_b) in **271** shifted downfield. The shielding effect of cyclopropane rings should be responsible for this shift.[115] In **271** both protons were *cis* to the cyclopropane ring and much closer than the protons that were *trans* to the cyclopropane ring in **274**. Additionally, in **271** H_a shifted downfield due to the anisotropic effect of the *trans* allyl group.[116] This explains why H_a had a larger $\Delta\delta$ value (0.6 ppm for H_a, 0.4 ppm for H_b). Finally, we also observed the shielding effect of the phenyl ring to the protons located at the cyclopropanes.[117] As shown in Figure 12, the phenyl ring in **274** was perpendicular to the pyrrolidine ring and adjacent to the endo proton H_d. Comparing to **271**, The current on the phenyl ring shifted H_d downfield (0.6 ppm) and $H_{d'}$ upfield (-0.3 ppm).

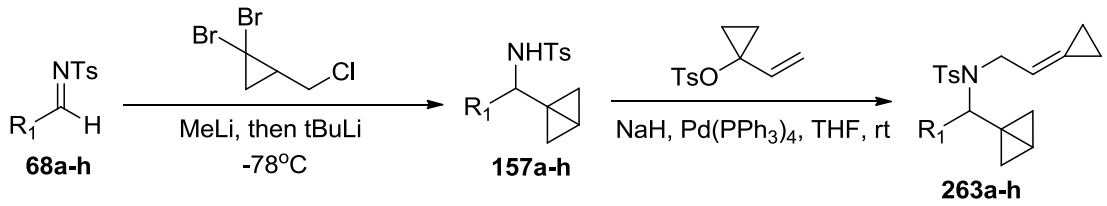
We next optimized the reaction conditions (Table 9). When the palladium (II) catalysts were applied, no product was observed. (entry 1). The yield was lower with palladium catalyst such as $Pd(PPh_3)_4$ (entry 2). **275** and triphenylphosphite reduced the yield dramatically (entries 3 and 4). When the phosphine ligand DPPP or P(*n*Bu)$_3$ was used, the yield was also diminished (entries 5 and 6). Addition of the bulkier P(*i*Pr)$_3$ improved the yield of **274** to 81% (entry 7). By reducing the catalyst and ligand loading to 10 mol%, the yield remained excellent (entry 8). The reaction was completed in less than 45 min in a microwave reactor. When only 5% catalyst was applied, a high concentration (0.1 M) was required to generate **274** in a high yield (entry 9). Finally, the bulkier P(*t*Bu)$_3$ ligand had a detrimental effect, while the smaller ligand PCy_3 gave 82% of **274** (entries 10 and 11). Additionally, solvents such as toluene and DMF provided no improvement.

Table 9. Reaction conditions optimizations for the cycloisomerization of **224**.



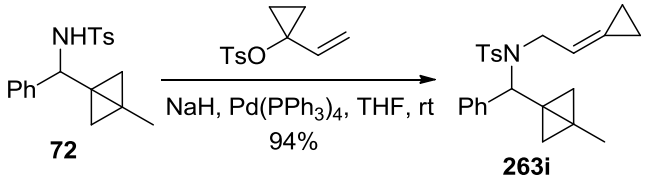
Entry[a]	Catalyst	Ligand	Yield[b]
1	20 mol % $PdCl_2$	40 mol % P(O*i*Pr)$_3$	0%
2	20 mol % $Pd(PPh_3)_4$	-	35%
3	10 mol % $Pd_2(dba)_3$	40 mol % $P(OPh)_3$	0%
4	20 mol % $Pd(dba)_2$	40 mol % **226**	15%
5	20 mol % $Pd(dba)_2$	20 mol % DPPP	42%
6	20 mol % $Pd(dba)_2$	40 mol % P*n*Bu$_3$	34%
7[c,d]	20 mol % $Pd(dba)_2$	40 mol % P*i*Pr$_3$	81%
8[c]	10 mol % $Pd(dba)_2$	20 mol % P*i*Pr$_3$	82%
9[c,d]	5 mol % $Pd(dba)_2$	10 mol % P*i*Pr$_3$	84%
10[c,e]	5 mol % $Pd(Pt Bu_3)_2$	-	0%
11[c,e]	5 mol % $Pd(PCy_3)_2$	-	82%

[a] Reaction was heated to reflux in 1,4-dioxanes for 2 h, concentration = 0.02M. [b] All yields are isolated yields. [c] Reaction was heated at 130 ℃ in a microwave reactor for 30-45 min. [d] Concentration = 0.1 M. [e] Concentration = 0.05 M.



157a, R_1 = *p*-C_6H_4Cl, 61%
157b, R_1 = fural, 75%
157c, R_1 = *m,m*-$C_6H_3(OMe)_2$, 66%
157d, R_1 = o-C_6H_4Cl, 25%
157e, R_1 = *i*Pr, 72%
157f, R_1 = cyclopropyl, 33%
157g, R_1 = CH_2OPMB, 55%
157h, R_1 = Me, 40%

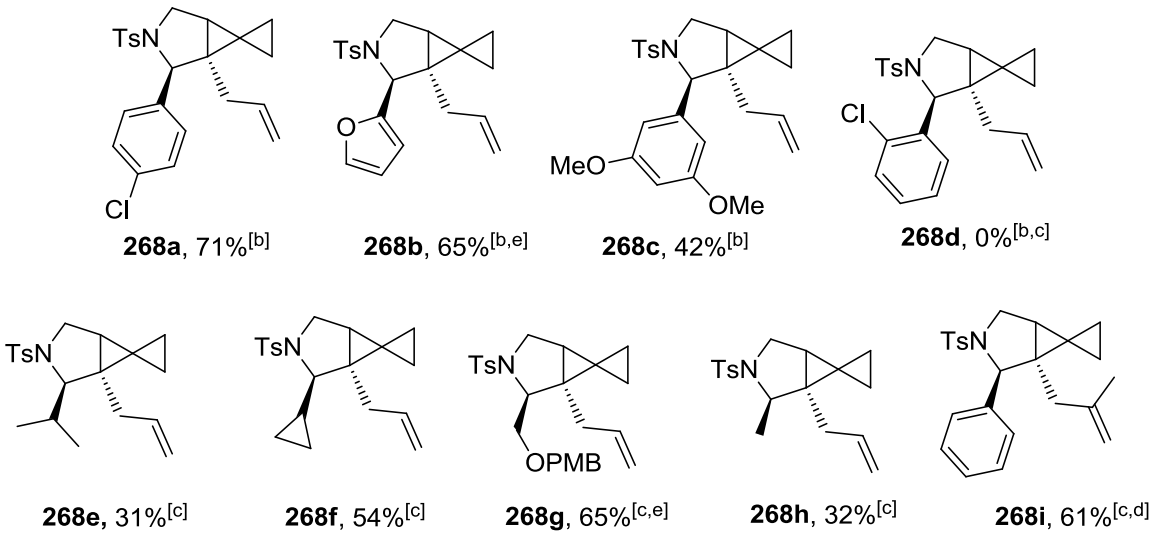
263a, R_1 = *p*-C_6H_4Cl, 85%
263b, R_1 = fural, 83%
263c, R_1 = *m,m*-$C_6H_3(OMe)_2$, 91%
263d, R_1 = o-C_6H_4Cl, 93%
263e, R_1 = *i*Pr, 90%
263f, R_1 = cyclopropyl, 76%
263g, R_1 = CH_2OPMB, 62%
263h, R_1 = Me, 45%



Scheme 63. Precursor synthesis of various bicyclo[1.1.0]butanes **263a-i**.

After identifying optimized conditions, we synthesized a set of 1-bicyclo[1.1.0]butan-1-yl alkylamines **157a-i** through the addition of bicyclo[1.1.0]butyllithium reagent in moderate to good yields (Scheme 63). Due to the high volatility of 2-cyclopropylideneethanol, we applied a Tsuji-Trost type reaction for the alkylation of **157a-i**. The vinylcyclopropyl tosylate formed a π-allyl-Pd(II) complex and attacked by the tosyl amide to generate **263a-i** in excellent yields. Morever, we also prepared methyl-susbstituted **263i** in 94% yield.

Table 10. Palladium-catalyzed isomerization of various bicyclo[1.1.0]butanes.[a]



[a] Reaction was heated to 130 ℃ with microwave reactor in 1,4-dioxanes for 30 min at 0.05 M concentration. [b] Condition A = 10 mol % $Pd(dba)_2$, 20 mol % P*i*Pr_3. [c] Condition B = 10 mol % $Pd(dba)_2$, 20 mol % P(O*i*Pr)$_3$. [d] Reaction was carried out in toluene. [e] concentration = 0.1 M.

We next explored the scope of the methodology using substrates **263a-i**. (Table 11). All reactions proceeded in excellent stereoselectivity (**268a-i** were obtained as a single diastereomer). The yield decreased considerably as the substituent on the aromatic group moved closer to the

bicyclo[1.1.0]butane (**268a-d**). The aliphatic substrates generally formed spirocyclopropanes in good yield under the original conditions rather than our optimized conditions (entries **268e-i**). The yield of these substrates decreased dramatically when the size of α-group was too large or too small (**268e** and **268h**). Only **268f** and **268g** gave moderate yields. We were surprised that the methyl-substituted biyclo[1.1.0]butane underwent the cyclopropanation with good yield, despite having a very hindered bicyclo[1.1.0]butane core (**268i**).

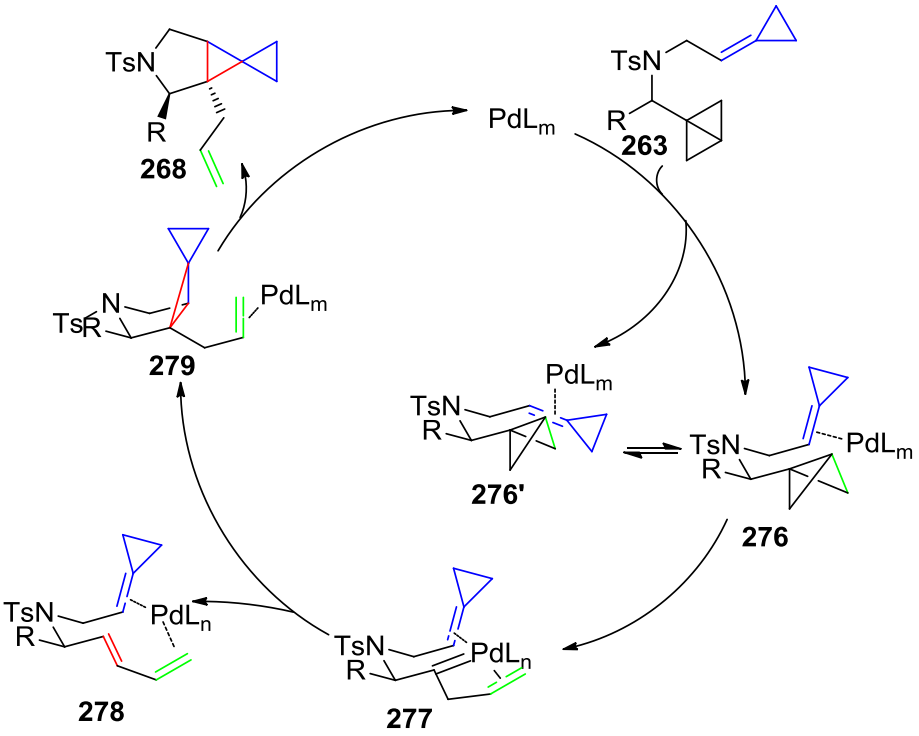
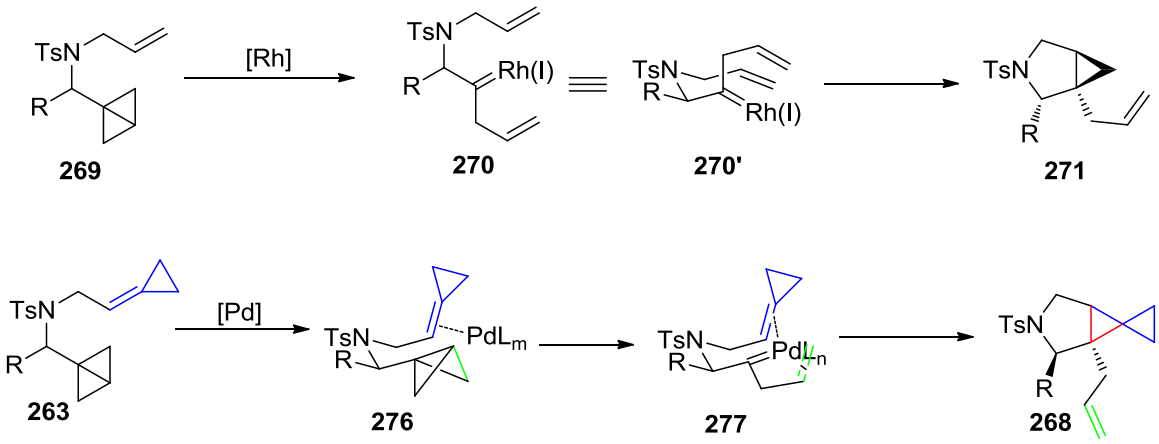


Figure 14. Proposed reaction pathway.

Our proposed palladium-induced reaction pathway of the bicyclo[1.1.0]butane is illustrated in Figure 14. Precomplexation of MCP **263** and palladium catalyst gave intermediate **276** or **276'**. Although palladium could cleave the lateral bond in MCP, the bicyclo[1.1.0]butane core was released probably due to a much higher strain energy (66 kcal/mol). And palladium catalyst was unable to activate **276'** due to steric hindrance between bicyclo[1.1.0]butane and

MCP. The central bond and lateral bond of bicyclo[1.1.0]butane in **276** rearranged to form the allyl-carbene intermediate **277**. The highly reactive palladium-carbene reacts with MCP spontaneously and leads to the formation of **279**. Alternatively, the unproductive hydride migration pathway provides the side-product diene **278**.

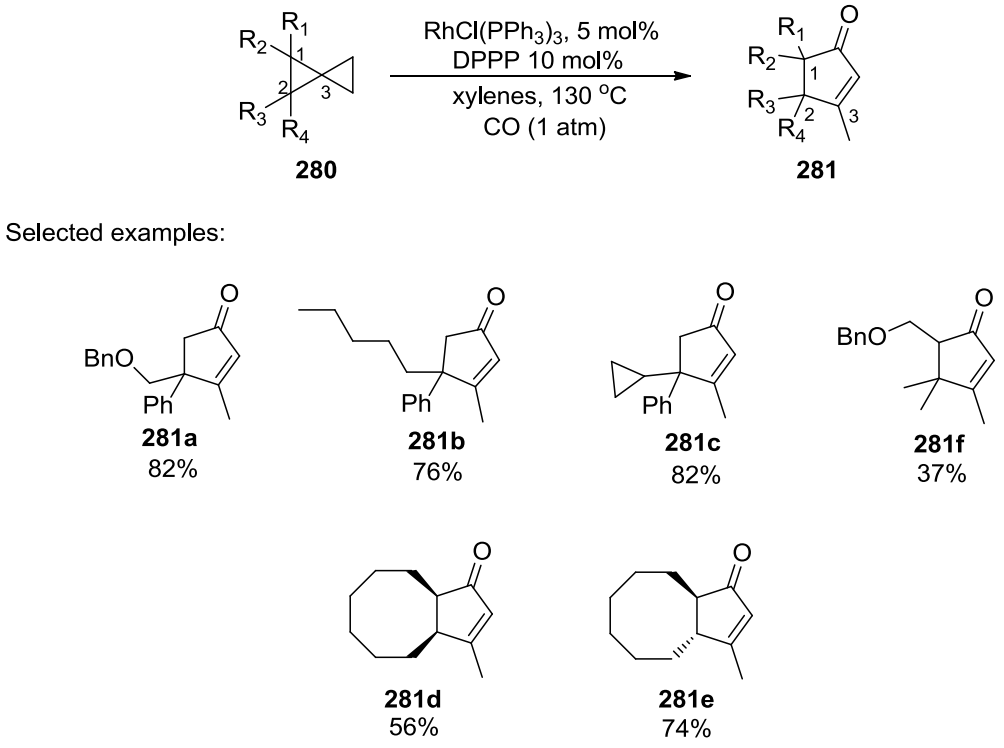


Scheme 64. Proposed mechanism for the formation of two diastereomers.

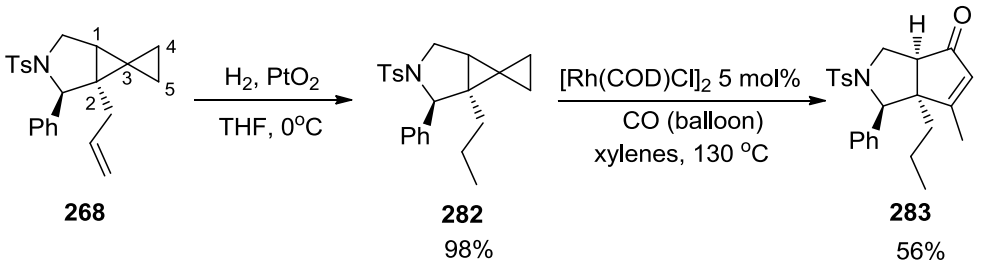
Furthermore, we rationalized the origin of diastereoselectivities of Pd and Rh catalysts in Scheme 64. Since the reaction led to the pyrrolidine without forming any azepine isomers, the palladium catalyst could not generate an external metal-carbene complex like our previous rhodium-catalyzed cycloisomerization process. One interpretation from this is that the coordination between palladium and MCP/allyl was essential for the generation of palladium-carbene species **277**. However, rhodium catalysts can insert into bicyclo[1.1.0]butanes and provide rhodium-carbene species **270'** without such directing groups.[118-119] The selectivity of rhodium catalyst can be explained by thermodynamic stability of conformer **270'**. On the other hand, the coordination of MCP and palladium directed the bicyclo[1.1.0]butane opening. And the less sterically hindered intermediate **276** produced palladium-carbene **277** which furnished **268** simultaneously. Thus **268** can be considered as a kinetically-controlled product.

2.2.2 Rhodium-catalyzed carbonylation of spiropentanes

Intrigued by the formation of spiropentanes, we further explored the utility of the 3-azaspiro[bicyclo[3.1.0]hexane-6,1'-cyclopropane] scaffold. Most of the methodologies of spiropentanes demand a heteroatom or an activating group on the cyclopropane. However, Murakami *et al.* developed a rhodium-catalyzed carbonylation reaction involving two consecutive σ-bond cleavages (C1-C3 and C4-C5) of inactivated spiropentane.[120] As depicted in Scheme 65, the carbonylation protocol provided gem-di-substituted products (**281a-c**) in good yield but cyclooctane-fused (**281d** and **281e**) and tri-substituted (**281f**) products in moderate to low yield.



Scheme 65. Murakami's rhodium-catalyzed carbonylation of spiropentanes.

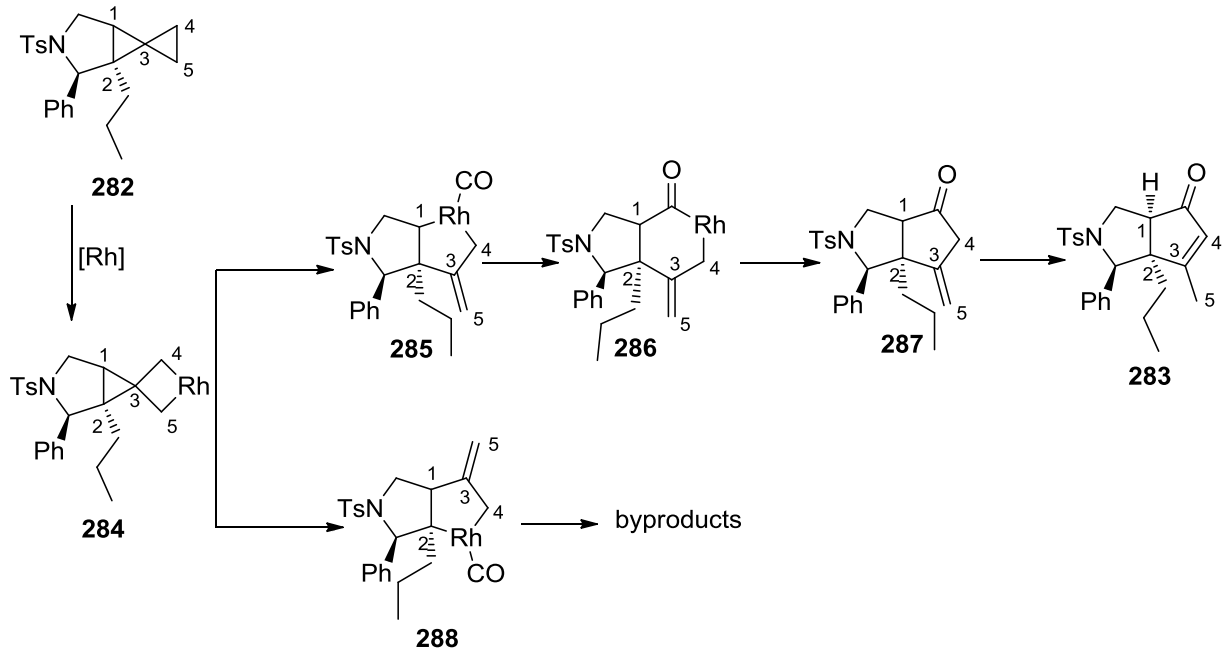


Scheme 66. Rhodium-catalyzed carbonylation of spiropentane **223**.

Our concern for the reaction was that **268** is a tri-substituted and cyclopentane-fused spirocyclopentane, which might give a poor yield according to Murakami's substrate scope. Another concern was that the allyl group in **268** might coordinate with rhodium and fail to activate the spirocyclopropane because the allyl group was in the opposite position of spirocyclopropane.

We decided to test the reaction with hydrogenated product **282** to avoid the potential detrimental effect of the allyl to the carbonylation sequence. The hydrogenation with platinum dioxide at low temperature (0 ℃) gave **282** almost quantitatively without the hydrogenation of the spirocyclopropanes. Refluxing **282** in presence of rhodium catalyst under one atmosphere carbon monoxide furnished cyclopentenone **283** in decent yield (Scheme 66).

Mechanistically, the rhodium catalyst opens C4-C5 bond in spirocyclopentane **282** to generate rhodacyclobutane **284**. Next, the migrations of C1 and C2 lead to the formation of **285** and **288**, respectively. Since C2 possesses more steric hindrance than C1, **285** is the predominant intermediate. Carbonyl insertion and reductive elimination produces **287**, which further isomerizes to furnish our final product **283**. On the other hand, due to excessive steric on tertiary C2, the carbonylation does not occur on **288** (Scheme 67) .



Scheme 67. Proposed pathways for rhodium-catalyzed carbonylation of spiropentane **282**.

Murakami obtained an excellent yield on the gem-di-substituted substrates because the large steric hindrance on C2 drove the migration to occur at C1 almost entirely. For other substrates however, there were no such dramatic differences between C1 and C2, which led to the formation of many C1-migration by-products. We believed that the *cis* phenyl group in **282** provided extra steric hindrance to force C1 migration over C2 migration, which benefited the overall yield of our product **283**.

Recrystallization of **283** from dichloromethane and hexanes provided a fine colorless crystal. The butterfly-shape X-ray structure confirmed our proposed structure of **283** (Figure 15). The orientation of *n*-propyl and phenyl group remained the same during the carbonylation process.

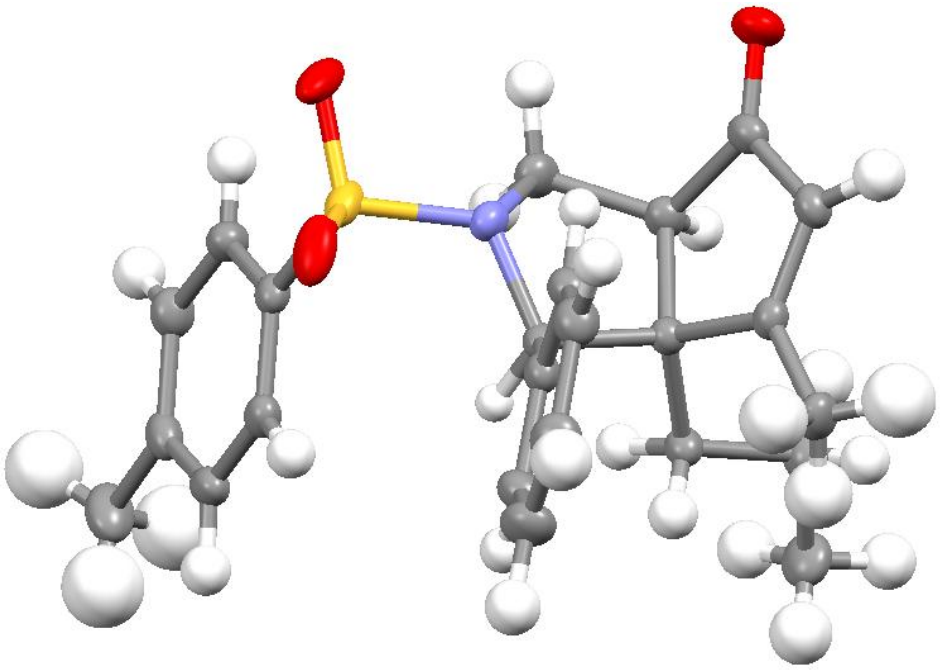
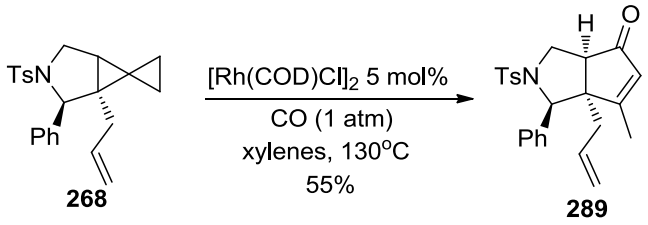


Figure 15. X-ray structure of **283**.

Additionally, **268** can also afford carbonylation product **289** with a decent yield (55%). The coordination of the allyl group did not affect the carbonylation process.



Scheme 68. Rhodium-catalyzed carbonylation of spiropentane **268**.

2.3 CONCLUSION

We have developed a palladium-catalyzed cycloisomerization reaction of bicyclo[1.1.0]butane and MCP. The unique pathway gave spiropentanes as single diastereomers

which happens to be the opposite diastereomer of our previous rhodium-catalyzed process. These methodologies enabled a diastereoselective access to a variety of 3-azabicyclo[3.1.0]hexane scaffolds that possessed a quaternary stereocenter. This demonstrates that 1-bicyclo[1.1.0]butan-1-yl alkylamines could be applied into the synthesis of multifunctional molecules and potentially served as precursors to pharmacologically active heterocycles such as indolizomycin[121], boceprevir[122], cycloclavine[123-127] or duocamycin A[128] (Figure 16).

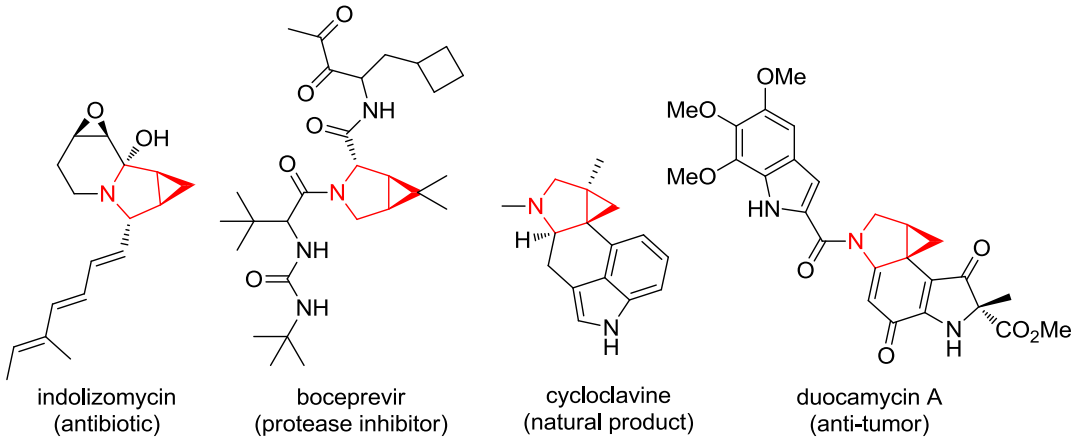


Figure 16. Examples of several biologically active compounds with a 3-azabicyclo[3.1.0]hexane core.

The cycloisomerization and carbonylation sequences allow a rapid synthesis of a multifunctionalized 3-azabicyclo[3.3.0]octane scaffold. This carbonylation process benefited from the extra steric hindrance provided by the substitutions on the pyrrolidine ring. Finally, this methodology enables a brand new pathway towards the synthesis of complex natural product such as paucidisine[129], mubironine C[130], lycopalhine A[131-133] and obscurinine[134].

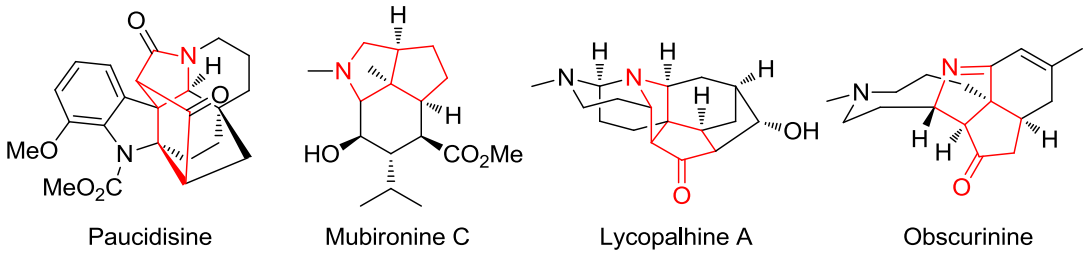


Figure 17. Examples of several natural products with a 3-azabicyclo[3.3.0]octane core.

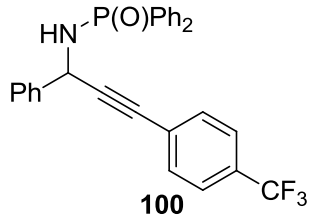
3. EXPERIMENTAL SECTION

General. All reactions were performed under an Argon atmosphere and all glassware was dried in an oven at 140 ℃ for 2 h prior to use. Reactions carried out at -78 ℃ employed a CO_2/acetone bath. THF and Et_2O were distilled over sodium/benzophenone ketyl, (-)-sparteine was distilled from CaH_2, and CH_2Cl_2 and toluene were purified using an alumina column filtration system.

Reactions were monitored by TLC analysis (pre-coated silica gel 60 F254 plates, 250 m layer thickness) and visualization was accomplished with a 254 nm UV light and by staining with a PMA solution (5 g of phosphomolybdic acid in 100 mL of 95% EtOH), *p*-anisaldehyde solution (2.5 mL of *p*-anisaldehyde, 2 mL of AcOH, and 3.5 mL of conc. H_2SO_4 in 100 mL of 95% EtOH), Vaughn's reagent (4.8 g of $(NH_4)_6Mo_7O_{24}•4H_2O$ and 0.2 g of $Ce(SO_4)_2$ in 100 mL of a 3.5 N H_2SO_4 solution) or a $KMnO_4$ solution (1.5 g of $KMnO_4$ and 1.5 g of K_2CO_3 in 100 mL of a 0.1% NaOH solution). Flash chromatography on SiO_2 was used to purify the crude reaction mixtures.

^1H spectra were obtained at 400 or 500 MHz in $CDCl_3$ unless otherwise noted. Chemical shifts were reported in parts per million with the residual solvent peak used as an internal standard. ^1H NMR spectra were obtained and are tabulated as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), number of protons,

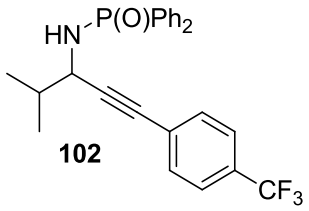
and coupling constant(s). ^{13}C NMR spectra were run at 100 or 125 MHz using a proton-decoupled pulse sequence with a d_1 of 3 sec, and are tabulated by observed peak. SFC analyses were performed using a Mettler-Toledo Model Analytix SFC.



100

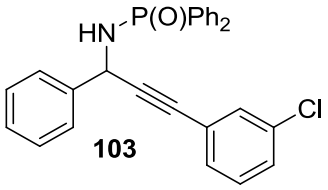
***P,P*-Diphenyl-*N*-(1-phenyl-3-(4-(trifluoromethyl)phenyl)prop-2-yn-1-yl)phosphinic amide (100)**. To a solution of dimethyl zinc (29 mg, 0.30 mmol) in anhydrous toluene (1.0 mL) was added 4-(trifluoromethyl)phenylacetylene (0.068 g, 0.40 mmol) and (*S*)-(-)-1-benzyl-2-pyrrolidinemethanol (0.012 g, 0.06 mmol). The mixture was stirred at room temperature for 1 h and added a solution of imine (306 mg, 0.10 mmol) in toluene (2.0 mL). The reaction was stirred at rt overnight and quenched by NH_4Cl. The mixture was extracted with EtOAc, washed with brine and dried (Na_2SO_4). The organic layers were concentrated and purified by chromatography on SiO_2 (EtOAc: hexanes = 4:1) to afford **100** (30.9 mg, 65%) as a white solid: IR (ATR) 3125.7, 3086.1, 2905.8, 1591.5, 1574.8, 1446.2, 1313.8, 1174.1, 1159.2, 1149.8, 1075.3, 1026.9, 997.0, 943.0, 719.4, 700.7, 691.4 cm^{-1}; Mp 195℃; *e.r.*= 93:7 (*S*:*R*), SFC condition: Chiralpak IA column, sc CO_2/MeOH = 70/30, flow rate = 2.5 mL/min, wavelength = 240 nm, t_R = 2.7 min (*S*) and 3.1 min (*R*); $[\alpha]_D$ -43 (*c* 1.40, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 8.07-8.03 (m, 2 H), 7.88-7.83 (m, 2 H), 7.65 (d, 2 H, *J* = 7.6 Hz), 7.56 (d, 2 H, *J* = 8.0 Hz), 7.54-7.32 (m, 11 H), 5.42 (t, 1 H, *J* = 9.6 Hz), 3.54 (dd, 1 H, *J* = 8.4, 9.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.9 (d, *J* = 5 Hz), 132.3 (d, *J* = 10, 78 Hz), 132.1 (d, *J* = 3 Hz), 132.0, 128.8, 128.6 (d, *J* = 2, 13 Hz),

128.2, 127.3, 126.5, 125.1 (q, J = 4 Hz), 91.5, 84.3, 47.1; HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{28}H_{21}NOF_3P$ 498.1211, found 498.1209.



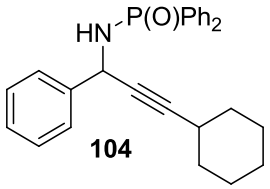
102

***N*-(4-Methyl-1-(4-(trifluoromethyl)phenyl)pent-1-yn-3-yl)-*P,P*-diphenylphosphinic amide (102**). To a solution of diethyl zinc (75 mg, 0.60 mmol) in anhydrous toluene (1.0 mL) was added 4-(trifluoromethyl)phenylacetylene (0.102 g, 0.6 mmol) and (*S*)-(-)-1-benzyl-2-pyrrolidinemethanol (0.012 g, 0.06 mmol). The mixture was stirred at room temperature for 1 h and added a solution of imine tosyl adduct **101b** (0.046 g, 0.1 mmol) in toluene (2.0 mL). The reaction was stirred at room temperature for 12 h and quenched by NH_4Cl. The mixture was extracted with EtOAc, washed with brine and dried (Na_2SO_4). The organic layers were concentrated and purified by chromatography on SiO_2 (EtOAc: hexanes = 4: 1) to afford **102** (34.5 mg, 78%) as a white solid: IR (ATR) 3172.3, 2959.8, 1612.2, 1437.0, 1327.1, 1185.4, 1122.0, 1103.4, 1066.1, 838.7, 749.3, 723.2, 693.4 cm^{-1}; Mp 196-199℃; *e.r.*= 93:7 (*S*:*R*), SFC condition: Chiralpak IB column, sc CO_2/MeOH = 91/9, flow rate = 3.5 mL/min, wavelength = 240 nm, t_R = 3.2 min (*S*) and 3.9 min (*R*); $[\alpha]_D$ -83.4 (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09-8.01 (m, 2 H), 7.92-7.86 (m, 2 H), 7.58-7.45 (m, 10 H), 4.08 (dt, 1 H, J = 9.6, 4.8 Hz), 3.30 (app t, 1 H, J = 10.0 Hz), 2.10 (m, 1 H), 1.12 (d, 3 H, J = 6.8 Hz), 1.06 (d, 3 H, J = 6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 132.4 (dd, J = 78, 127 Hz), 132.3 (d, J = 10, 110 Hz), 132.0 (t, J = 3 Hz), 131.9, 129.9 (q, J = 32 Hz), 128.5 (dd, J = 13, 1 Hz), 126.8, 125.1 (q, J = 4 Hz), 124.0 (q, J = 271 Hz), 91.3 (d, J = 6 Hz), 83.2, 49.7, 34.8 (d, J = 4 Hz), 19.4, 17.3; HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{25}H_{23}NOF_3P$ 464.1367, found 464.1354.



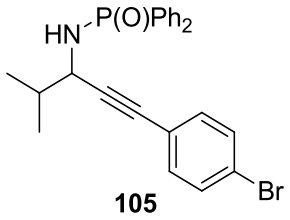
103

***N*-(3-(3-Chlorophenyl)-1-phenylprop-2-ynyl)-*P,P*-diphenylphosphinic amide (103).** To a solution of diethyl zinc (75 mg, 0.60 mmol) in anhydrous toluene (1.0 mL) was added 3-chlorophenylacetylene (81.5 mg, 0.6 mmol) and (*S*)-(-)-1-benzyl-2-pyrrolidinemethanol (0.012 g, 0.06 mmol). The mixture was stirred at room temperature for 1 h and added a solution of imine tosyl adduct **101a** (0.046 g, 0.1 mmol) in toluene (2.0 mL). The reaction was stirred at room temperature for 12 h and quenched by NH_4Cl. The mixture was extracted with EtOAc, washed with brine and dried (Na_2SO_4). The organic layers were concentrated and purified by chromatography on SiO_2 (EtOAc: hexanes = 4: 1) to afford **103** (39.8 mg, 91%) as a white solid: IR (ATR) 3144.3, 2855.4, 2848.0, 1589.9, 1560.0, 1472.4, 1450.1, 1435.2, 1185.4, 1123.9, 1107.1, 1060.5, 991.6, 784.7, 747.4, 725.0, 695.2, 680.3 cm^{-1}; Mp 165-166℃; *e.r.* = 92:8 (*S*:*R*), SFC condition: Chiralpak IA column, sc CO_2/MeOH = 75/25, flow rate = 2.5 mL/min, wavelength = 240 nm, t_R = 3.5 min (*S*) and 4.0 min (*R*); $[\alpha]_D$ -50.8 (*c* 1.24, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 8.11-8.06 (m, 2 H), 7.90-7.85 (m, 2 H), 7.70-7.67 (d, 2 H, *J* = 8 Hz), 7.58-7.49 (m, 4 H), 7.44-7.37 (m, 4 H), 7.34-7.23 (m, 5 H), 5.43 (t, *J* = 9.6 Hz), 3.61 (t, *J* = 9.6, 4.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.04 (d, *J* = 5 Hz), 134.1, 132.2 (dd, *J* = 49, 129 Hz), 132.1 (t. *J* = 3 Hz), 131.6, 131.3 (dd, *J* = 10, 88 Hz), 129.8, 129.5, 128.8, 128.7, 128.6 (d, *J* = 13 Hz), 128.1, 127.3, 124.4, 90.1 (d, *J* = 5 Hz), 84.2, 47.1; HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{27}H_{21}NOClP$ 464.0947, found 464.0967.



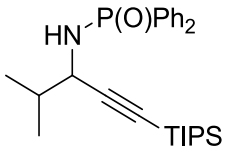
104

***N*-(3-Cyclohexyl-1-phenylprop-2-ynyl)-*P,P*-diphenylphosphinic amide (104).** To a solution of diethyl zinc (75 mg, 0.6 mmol) in anhydrous toluene (1.0 mL) was added cyclohexylacetylene (64.6 mg, 0.6 mmol) and (*S*)-(-)-1-benzyl-2-pyrrolidinemethanol (12 mg, 0.06 mmol). The mixture was stirred at room temperature for 1 h and added a solution of imine tosyl adduct **101a** (0.046 g, 0.1 mmol) in toluene (2.0 mL). The reaction was stirred at room temperature for 48 h and quenched by NH_4Cl. The mixture was extracted with EtOAc, washed with brine and dried (Na_2SO_4). The organic layers were concentrated and purified by chromatography on SiO_2 (EtOAc: hexanes = 4: 1) to afford **104** (27.7 mg, 67%) as a white solid: IR (ATR) 3153.6, 3054.9, 2926.3, 2849.8, 1491.1, 1448.2, 1437.0, 1260.0, 1187.3, 1148.1, 1123.9, 1109.0, 1092.2, 1068.0, 1053.1, 1027.0, 997.2, 930.1, 900.2, 889.1, 825.7, 803.3, 749.3, 738.1, 723.2, 695.2 cm^{-1}; Mp 158-159℃; *e.r.* = 69:31 (*S*:*R*), SFC condition: Chiralpak IB column, sc CO_2/MeOH = 90/10, flow rate = 4.0 mL/min, wavelength = 220 nm, t_R = 5.3 min (*S*) and 6.0 min (*R*); $[\alpha]_D$ -12.6 (*c* 1.12, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.11-8.06 (m, 2 H), 7.86-7.81 (m, 2 H), 7.65 (d, 2 H, *J* = 8 Hz), 7.56-7.54 (m, 1 H), 7.52-7.47 (m, 3 H), 7.43-7.40 (m, 2 H), 7.37-7.34 (m, 2 H), 7.29-7.26 (m, 2 H), 5.18 (t, *J* = 8.0 Hz), 3.43 (t, *J* = 7.6 Hz), 2.45 (m, 1 H), 1.93-1.81 (m, 2 H), 1.74-1.72 (m, 2 H), 1.56-1.53 (m, 1 H), 1.50-1.46 (m, 2 H), 1.46-1.32 (m,3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.08 (d, *J* = 4 Hz), 132.5 (dd, *J* = 130, 76 Hz), 132.3 (d, *J* = 10, 104 Hz), 131.9 (dd, *J* = 7, 3 Hz), 128.5 (d, *J* = 2 Hz), 128.4, 127.7, 127.3, 90.3, 79.7 (d, *J* = 7 Hz), 46.8, 32.6, 25.9, 24.9; HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{27}H_{28}NOP$ 436.1806, found 436.1806.



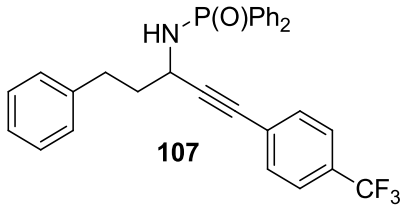
105

***N*-(1-(4-Bromophenyl)-4-methylpent-1-yn-3-yl)-*P,P*-diphenylphosphinic amide (105).** To a solution of diethyl zinc (75 mg, 0.60 mmol) in anhydrous toluene (1.0 mL) was added 4-bromophenylacetylene (109 mg, 0.6 mmol) and (*S*)-(-)-1-benzyl-2-pyrrolidinemethanol (0.012 g, 0.06 mmol). The mixture was stirred at room temperature for 1 h and added a solution of imine tosyl adduct **101b** (0.043 g, 0.1 mmol) in toluene (2.0 mL). The reaction was stirred at room temperature for 6 h and quenched by NH_4Cl. The mixture was extracted with EtOAc, washed with brine and dried (Na_2SO_4). The organic layers were concentrated and purified by chromatography on SiO_2 (EtOAc: hexanes = 4: 1) to afford **105** (37.9 mg, 84%) as a white solid: IR (ATR) 3159.2, 2956.1, 2868.5, 1483.6, 1437.0, 1187.3, 1122.0, 1109.0, 1068.0, 1010.2, 922.6, 892.8, 823.8, 749.3, 723.2, 697.1 cm^{-1}; Mp 194-195℃; *e.r.*= 94:6 (*S*:*R*), SFC condition: Chiralpak IB column, sc CO_2/MeOH = 90/10, flow rate = 4.0 mL/min, wavelength = 240 nm, t_R = 5.4 min (*S*) and 6.0 min (*R*); $[\alpha]_D$ -101.2 (*c* 1.03, $CHCl_3$); mp 194-195; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06-8.00 (m, 2 H), 7.91-7.86 (m, 2 H), 7.53-7.43 (m, 8 H), 7.23 (d, 2 H, *J* = 8.4 Hz), 4.04 (ddd,1 H, *J* = 6.4, 5.2, 4.8 Hz), 3.28 (dd, *J* = 10.4, 8.8 Hz), 2.12-2.08 (m, 1 H), 1.10 (d, 3 H, *J* = 6.8 Hz), 1.04 (d, 3 H, *J* = 6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 133.1, 132.4 (dd, *J* = 129, 95 Hz), 132.2 (d, *J* = 10, 96 Hz), 132.0, 131.5, 128.6 (dd, *J* =13, 2 Hz), 122.4, 121.9, 89.8 (d, *J* = 6 Hz), 83.5, 49.8, 34.9 (d, *J* = 4 Hz), 19.4, 17.2; HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{24}H_{23}NOPBr$ 474.0598, found 474.0598.



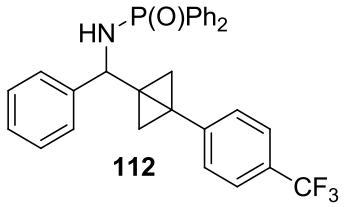
106

***N*-(4-Methyl-1-(triisopropylsilyl)pent-1-yn-3-yl)-*P,P*-diphenylphosphinic amide (106).** To a solution of diethyl zinc (75 mg, 0.60 mmol) in anhydrous toluene (1.0 mL) was added triisopropylsilylacetylene (110 mg, 0.6 mmol) and (*S*)-(-)-1-benzyl-2-pyrrolidinemethanol (0.012 g, 0.06 mmol). The mixture was stirred at 5 ℃ for 1 h and added a solution of imine tosyl adduct **101b** (0.043 g, 0.1 mmol) in toluene (2.0 mL). The reaction was stirred at rt for 24 h and quenched by NH_4Cl. The mixture was extracted with EtOAc, washed with brine and dried (Na_2SO_4). The organic layers were concentrated and purified by chromatography on SiO_2 (EtOAc: hexanes = 4: 1) to afford **106** (38.1 mg, 84%) as a white solid: IR (ATR) 3183.5, 3056.7, 2954.2, 2939.3, 2862.9, 2165.8, 2158.3, 1461.3, 1437.0, 1383.0, 1189.1, 1123.9, 1109.0, 1071.7, 1027.0, 1017.7, 997.2, 883.5, 751.1, 747.4, 723.2, 693.4, 678.4 cm^{-1}; Mp 86-87℃; *e.r.*= 92:8 (*S*:*R*), SFC condition: Chiralpak IA column, sc CO_2/MeOH = 90/10, flow rate = 4.0 mL/min, wavelength = 220 nm, t_R = 2.1 min (*R*) and 2.6 min (*S*); $[\alpha]_D$ -89.0 (*c* 0.87, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 8.09-8.02 (m, 2 H), 7.89-7.82 (m, 2 H), 7.56-7.43 (m, 6 H), 3.86 (dt,1 H, *J* = 10.4, 4.8 Hz), 3.22 (t, *J* = 10.4 Hz), 2.06-2.00 (m ,1 H), 1.11(m, 21 H), 1.06 (d, 3 H, *J* = 6.8 Hz), 1.00 (d, 3 H, *J* = 6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 132.6 (dd, *J* = 154, 126 Hz), 132.3 (d, *J* = 10, 121 Hz), 131.9 (t, *J* = 3 Hz), 128.5 (dd, *J* = 13, 4 Hz), 106.9 (d, *J* = 9 Hz), 84.8, 50.2, 34.9 (d, *J* = 2 Hz), 19.4, 18.6, 16.8, 11.2; HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{27}H_{40}NOPSi$ 476.2515, found 476.2511.



107

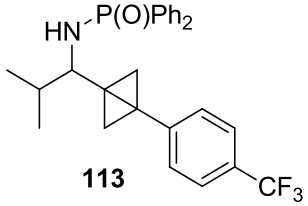
***P,P*-Diphenyl-*N*-(5-phenyl-1-(4-(trifluoromethyl)phenyl)pent-1-yn-3-yl)phosphinic amide (107).** To a solution of diethyl zinc (75 mg, 0.60 mmol) in anhydrous toluene (1.0 mL) was added 4-(trifluoromethyl)phenylacetylene (102 mg, 0.6 mmol) and (*S*)-(-)-1-benzyl-2-pyrrolidinemethanol (0.012 g, 0.06 mmol). The mixture was stirred at room temperature for 1 h and added a solution of imine tosyl adduct **101c** (0.049 g, 0.1 mmol) in toluene (2.0 mL). The reaction was stirred at room temperature for 24 h and quenched by NH_4Cl. The mixture was extracted with EtOAc, washed with brine and dried (Na_2SO_4). The organic layers were concentrated and purified by chromatography on SiO_2 (EtOAc: hexanes = 4: 1) to afford **107** (41.3 mg, 82%) as a white solid: IR (ATR) 3144.3, 2928.1, 2859.2, 1614.1, 1437.0, 1328.9, 1321.5, 1185.4, 1163.0, 1123.9, 1110.9, 1103.4, 1094.1, 1081.0, 1068.0, 1015.8, 965.5, 840.6, 749.3, 725.0, 698.9, 693.4 cm^{-1}; Mp 188-189℃; *e.r.*= 98:2 (*S*:*R*) (after recrystallization), SFC condition: Chiralpak IB column, sc CO_2/MeOH = 85/15, flow rate = 3.5 mL/min, wavelength = 240 nm, t_R = 4.2 min (*S*) and 5.1 min (*R*); $[\alpha]_D$ -47.0 (*c* 0.84, $CHCl_3$) (70% *ee* sample); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.99-7.95 (m, 2 H), 7.87-7.83 (m, 2 H), 7.59-7.57 (m, 2 H), 7.54-7.43 (m, 8 H), 7.28-7.26 (m, 2 H), 7.20-7.18 (m , 3 H), 4.25-4.20 (m, 1 H), 3.34 (dd, *J* = 10.5, 7.5 Hz), 2.92-2.85 (m, 2 H), 2.27- 2.16 (m, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.9, 132.2 (dd, *J* = 10, 93 Hz), 132.2 (dd, *J* = 129, 85 Hz), 132.1 (t, *J* = 2.5 Hz), 131.9, 130.0 (q, *J* = 45 Hz), 128.6 (dd, *J* = 12.5, 1.3 Hz), 128.5 (overlap), 126.6, 126.1, 125.2 (q, *J* = 3.8 Hz), 123.9 (q, *J* = 270 Hz), 92.4 (d, *J* = 6.3 Hz), 82.9, 43.7, 40.0 (d, *J* = 3.8 Hz), 32.1; HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{30}H_{25}NOF_3P$ 526.1524, found 526.1524.



112

***P,P*-Diphenyl-*N*-(phenyl(3-(4-(trifluoromethyl)phenyl)bicyclo[1.1.0]butan-1-yl)methyl) phosphinic amide (112)**. To a cold solution of **100** (220 mg, 0.46 mmol) in anhydrous CH_2Cl_2 (6 mL) was added Me_2Zn (44 mg, 0.46 mmol) in anhydrous CH_2Cl_2 (1 mL). The reaction mixture was stirred at 0 ℃ for 1 h, cooled to -50 ℃ and added a cold solution of Et_2Zn (114 mg, 0.93 mmol) in anhydrous DCM (5 mL). The mixture was stirred for 10 min and added CH_2I_2 (501 mg, 1.85 mmol). The reaction was stirred at -30 ℃ overnight, quenched with saturated NH_4Cl and extracted with DCM. The combined organic layers were washed with water and brine and dried ($MgSO_4$). The product was concentrated and purified by chromatography on SiO_2 (EtOAc: hexanes = 4: 1) to afford **112** (74 mg, 32%) as a white solid: IR (ATR) 3285.6, 3086.1, 3067.5, 3054.5, 3037.7, 3030.2, 1647.4, 1626.9, 1591.5, 1574.8, 1559.8, 1446.2, 1313.8, 1272.8, 1203.9, 1174.1, 1159.2, 1149.8, 1075.3, 1026.9, 997.0, 943.0, 935.5, 916.9, 864.7, 812.5, 764.1, 719.4, 700.7, 691.4 cm^{-1}; Mp 124-126℃; *e.r.*= 93:7 (*S*:*R*), SFC condition: Chiralpak IA column, sc CO_2/MeOH = 75/25, flow rate = 2.5 mL/min, wavelength = 240 nm, t_R = 3.1 min (*S*) and 3.9 min (*R*); $[\alpha]_D$ -28.5 (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91-7.86 (m, 2 H), 7.64-7.59 (m, 2 H), 7.53-7.40 (m, 4 H), 7.46-7.28 (m, 4 H), 7.18-7.10 (m, 3 H), 6.95 (d, 2 H, *J* = 8.0 Hz), 6.76 (d, 2 H, *J* = 8.4 Hz), 4.64 (t, 1 H, *J* = 8.4 Hz), 3.46 (dd, 1 H, *J* = 7.2, 4.8 Hz), 2.24 (d, 1 H, *J* = 6.8, 5.6 Hz), 2.00 (d, 1 H, *J* = 6.4 Hz), 1.03 (s, 1 H), 0.95 (s, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.7, 139.9 (d, *J* = 6 Hz), 132.6 (dd, *J* = 128, 88 Hz), 132.0 (dd, *J* = 18, 9 Hz), 131.8 (t, *J* = 3 Hz), 128.4 (dd, *J* = 12, 7 Hz), 128.2, 127.5, 126.9, 125.6, 124.9 (q, *J* = 4 Hz), 55.1, 34.2, 31.5,

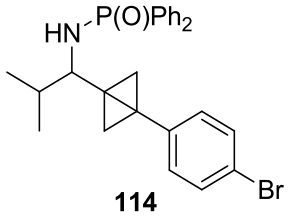
30.0 (q, J = 5 Hz), 20.4; HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{30}H_{25}NOF_3P$ 526.1524, found 526.1525.



113

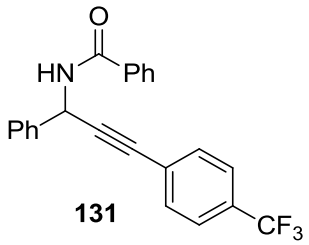
***N*-(2-Methyl-1-(3-(4-(trifluoromethyl)phenyl)bicyclo[1.1.0]butan-1-yl)propyl)-*P*,*P*-diphenylphosphinic amide (113)**. To a cold solution of **102** (34.5 mg, 0.08 mmol) in anhydrous CH_2Cl_2 (6 mL) was added Me_2Zn (7.5 mg, 0.08 mmol) in anhydrous CH_2Cl_2 (1 mL). The reaction mixture was stirred at 0 ℃ for 1 h, cooled to -50 ℃ and added a solution of Et_2Zn (19 mg, 0.16 mmol) in anhydrous DCM (5 mL). The mixture was added CH_2I_2 (84.5 mg, 0.31 mmol) in this temperature. The reaction mixture was stirred at -30 ℃ overnight, quenched with saturated NH_4Cl and extracted with DCM. The combined organic layers were washed with water and brine and dried ($MgSO_4$). The product was concentrated and purified by chromatography on SiO_2 (EtOAc: hexanes = 4: 1) to afford **113** (17.0 mg, 46%) as a yellowish solid: IR (ATR) 3204.0, 3190.9, 3183.5, 2957.9, 2926.3, 2883.4, 2870.3, 1614.1, 1437.0, 1323.3, 1185.4, 1163.0, 1118.3, 1062.4, 842.5, 751.1, 723.2, 697.1, 685.9 cm^{-1}; Mp 117-118℃; ^1H NMR (400 MHz, $CDCl_3$) δ 7.61-7.36 (m, 13 H), 7.49-7.38 (m, 1 H), 3.25 (ddd, J = 10.4, 6.4, 3.2 Hz), 2.76 (dd, 1 H, J = 10.8, 2.8 Hz), 2.32 (d, 1 H, J = 6.8 Hz), 2.20-2.12 (m, 1 H), 2.13 (d, 1 H, J = 6.4 Hz), 1.21 (s, 1 H), 1.12 (s, 1 H), 1.00 (d, 3 H, J = 6.8 Hz), 0.95 (d, 3 H, J = 6.8 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.2, 132.2 (dd, J = 134, 130 Hz), 132.0 (d, J = 10, 30 Hz), 131.8 (dd, J = 10, 3 Hz), 128.3 (dd, J =13, 7 Hz), 127.2 (q, J = 32 Hz), 126.1, 125.2, (q, J = 4 Hz), 124.5 (q, J = 270 Hz),

54.8, 34.9 (d, J = 3 Hz), 33.3, 30.6, 29.0 (d, J = 10 Hz), 19.0, 17.4, 17.1; HRMS (ESI) m/z: [M + Na]$^+$ Calcd for $C_{27}H_{27}NOPF_3$ 492.1680, found 492.1666.



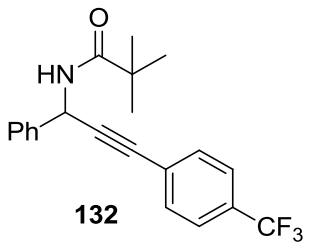
114

***N*-(1-(3-(4-Bromophenyl)bicyclo[1.1.0]butan-1-yl)-2-methylpropyl)-*P*,*P*-diphenylphosphinic amide (114).** To a cold solution of **105** (32 mg, 0.07 mmol) in anhydrous CH_2Cl_2 (6 mL) was added Me_2Zn (6.8 mg, 0.07 mmol) in anhydrous CH_2Cl_2 (1 mL). The reaction mixture was stirred at 0 ℃ for 1 h, cooled to -50 ℃ and added a solution of Et_2Zn (17.5 mg, 0.14 mmol) in anhydrous DCM (5 mL). The mixture was added CH_2I_2 (77 mg, 0.28 mmol) in this temperature. The reaction mixture was stirred at -30 ℃ overnight, quenched with saturated NH_4Cl and extracted with DCM. The combined organic layers were washed with water and brine and dried ($MgSO_4$). The product was concentrated and purified by chromatography on SiO_2 (EtOAc: hexanes = 4: 1) to afford **114** (22.3 mg, 66%) as a yellowish solid: IR (ATR) 3198.4, 3058.6, 2956.1, 2926.3, 2868.5, 1589.9, 1481.8, 1437.0, 1187.3, 1122.0, 1107.1, 1069.9, 1008.3, 904.0, 829.4, 751.1, 723.2, 697.1 cm^{-1}; Mp 121-123 ℃; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.65-7.60 (m, 2 H), 7.49-7.38 (m, 10 H), 7.15 (d, 2 H, J = 8.5 Hz), 3.25 (ddd, J = 10.0, 6.4, 3.2 Hz), 2.73 (dd, 1 H, J = 10.0, 2.8 Hz), 2.21 (d, 1 H, J = 7.0 Hz), 2.21-2.15 (m, 1 H), 2.05 (d, 1 H, J = 7.0 Hz), 1.14 (s, 1 H), 1.05 (s, 1 H), 1.01 (d, 3 H, J = 7.0 Hz), 0.94 (d, 3 H, J = 7.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 136.6, 133.6, 132.3 (d, J = 10 Hz), 132.0 (d, J = 10 Hz), 128.4 (t, J = 10 Hz), 127.6, 126.3, 118.8, 54.9, 34.9, 33.1, 30.1, 27.3 (d, J = 10 Hz), 19.1, 17.3, 16.5; HRMS (ESI) m/z: [M + H]$^+$ Calcd for $C_{26}H_{28}NOBrP$ 480.1092, found 480.1082.



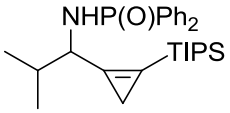
131

***N*-(1-Phenyl-3-(4-(trifluoromethyl)phenyl)prop-2-ynyl)benzamide (131)**. To an ice-cooled MeOH (5.0 mL) was added AcCl (0.71 mL, 10 mmol). The colorless solution was stirred at 0 ℃ for 15 min, warmed to room temperature, and stirred for a further 5 min. The resulting solution of 2 N HCl in MeOH was added **100** (144 mg, 0.30 mmol), stirred at room temperature for 12 h, and concentrated to dryness. The residue was dissolved in CH_2Cl_2 (5.0 mL) and concentrated to dryness, and the residue was dissolved in CH_2Cl_2 (1.0 mL) and treated with PhCOCl (80 μL, 0.69 mmol), (*i*Pr)$_2$NEt (0.18 mL, 1.0 mmol) and DMAP (6.0 mg, 0.048 mmol). The reaction mixture was stirred at room temperature for 1 h, concentrated to 0.5 mL, and purified by column chromatography on SiO_2 (EtOAc: hexanes = 1: 9) to afford **131** (96.6 mg, 85%) as a white solid: IR (ATR) 3284.1, 3064.2, 1634.6, 1522.8, 1487.4, 1319.6, 1166.8, 1123.9, 1105.3, 1066.1, 1015.8, 840.6, 693.4 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, 2 H, *J* = 7.2 Hz), 7.59 (d, 2 H, *J* = 7.2 Hz), 7.49 (s, 4 H), 7.43 (m 1 H), 7.37-7.30 (m, 5 H), 6.47 (d, 1 H, *J* = 8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.6, 138.6, 133.6, 132.1, 131.9, 130.3 (q, *J* = 33 Hz), 128.9, 128.6, 128.3, 127.4, 127.2, 126.4, 125.2 (q, *J* = 4 Hz), 89.8, 83.6, 45.6; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{23}H_{17}NOF_3$ 380.1262, found 380.1275.



132

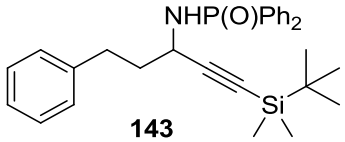
***N*-(1-Phenyl-3-(4-(trifluoromethyl)phenyl)prop-2-ynyl)pivalamide (132).** To an ice-cooled MeOH (5.0 mL) was added AcCl (0.71 mL, 10 mmol). The colorless solution was stirred at 0 ℃ for 15 min, warmed to room temperature, and stirred for a further 5 min. The resulting solution of 2 N HCl in MeOH was added **100** (144 mg, 0.30 mmol), stirred at room temperature for 12 h, and concentrated to dryness. The residue was dissolved in CH_2Cl_2 (5.0 mL) and concentrated to dryness, and the residue was dissolved in CH_2Cl_2 (1.0 mL) and treated with PivCl (86 μL, 0.69 mmol), $(i\text{Pr})_2\text{NEt}$ (0.18 mL, 1.0 mmol) and DMAP (6.0 mg, 0.048 mmol). The reaction mixture was stirred at room temperature for 1 h, concentrated to 0.5 mL, and purified by column chromatography on SiO_2 (EtOAc: hexanes = 1: 9) to afford **132** (99.1 mg, 92%) as a white solid: IR (ATR) 3297.2, 2965.4, 2632.7, 1517.2, 1319.6, 1202.2, 1181.7, 1164.9, 1157.5, 1123.9, 1101.5, 1064.3, 1015.8, 842.5, 745.5, 736.2, 719.4, 697.1 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.56 (s, 4 H), 7.54-7.53 (d, 2 H, J = 8.0 Hz), 7.40-7.37 (m, 2 H), 7.34-7.33-7.32 (m, 1 H), 6.29 (m, 2 H), 1.24 (s, 9 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.3, 132.1, 130.2 (q, J = 32.5 Hz), 128.8, 128.2, 126.9, 126.4, 125.2 (q, J = 3.8 Hz), 123.9 (q, J = 270 Hz), 89.8, 83.3, 45.0, 38.8, 27.4; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{21}H_{21}NOF_3$ 360.1575, found 360.1582.



142

***N*-(2-Methyl-1-(2-(triisopropylsilyl)cycloprop-1-en-1-yl)propyl)-*P*,*P*-diphenylphosphinic amide (142).** To a cooled solution of **106** (45 mg, 0.10 mmol) in anhydrous CH_2Cl_2 (2.0 mL) was added Me_2Zn (19 mg, 0.20 mmol) in anhydrous CH_2Cl_2 (1.0 mL). The reaction mixture was stirred at 0 ℃ for 1 h, cooled to -50 ℃ and added a cold solution of Et_2Zn (50 mg, 0.40 mmol) and trifluoroethanol (29 μL, 0.40 mmol) in anhydrous dichloromethane (5 mL). Then, diethyl

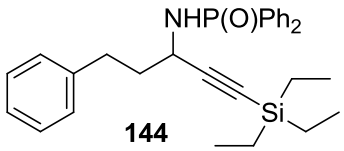
aluminum chloride (0.012 mL, 0.012 mmol) and CH_2I_2 (107 mg, 0.40 mmol) was added at this temperature. The reaction mixture was stirred at 0 ℃ overnight, quenched with saturated NH_4Cl and extracted with dichloromethane (3×10 mL). The combined organic layers were washed with water and brine and dried ($MgSO_4$). The product was concentrated and purified by chromatography on SiO_2 to afford **142** as a white semisolid (37 mg, 79%): IR (ATR) 2954.2, 2939.3, 2862.9, 1785.6, 1589.9, 1461.3, 1437.0, 1383.0, 1191.0, 1122.0, 1109.0, 1069.9, 1010.2, 997.2, 881.6, 749.3, 723.2, 695.2, 678.4 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.87-7.80 (m, 4 H), 7.51-7.38 (m, 6 H), 4.18-4.12 (m, 1 H), 3.29 (t, 1 H, *J* = 7.6 Hz), 2.15-2.07 (m, 1 H), 1.01-0.94 (m, 23 H), 0.84-0.82 (m, 5 H), 0.83 (d, 1 H, *J* = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 132.7 (dd, *J* = 126, 137 Hz), 132.1 (dd, *J* = 10, 91 Hz), 131.8 (dd, *J* = 3, 6 Hz), 131.7, 128.4 (d, *J* = 13 Hz), 104.9, 55.4, 34.6 (d, *J* = 3 Hz), 19.2, 18.8, 18.7, 18.2, 11.5, 7.9; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{28}H_{43}NOSiP$ 468.2852 found 468.2845.



143

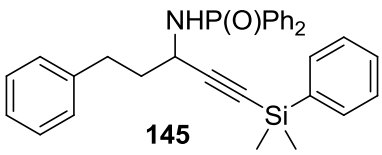
***N*-(1-(*tert*-Butyldimethylsilyl)-5-phenylpent-1-yn-3-yl)-*P*,*P*-diphenylphosphinicamide (143).** To a solution of diethyl zinc (0.15 g, 1.2 mmol) in anhydrous toluene (1.0 mL) was added (tert-butyldimethylsilyl)acetylene (0.17 g, 1.2 mmol) and (*S*)-(-)-1-benzyl-2-pyrrolidinemethanol (24 mg, 0.12 mmol). The mixture was stirred at room temperature for 1 h and added a solution of **101c** (0.10 g, 0.20 mmol) in anhydrous toluene (2.0 mL). The reaction was stirred at room temperature for 24 h and quenched by NH_4Cl. The mixture was extracted with EtOAc, washed with brine and dried (Na_2SO_4). The organic layers were concentrated and purified by chromatography on SiO_2 (EtOAc : hexanes = 4 :1) to afford **143** (35 mg, 36%) as a colorless oil:

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86-7.81 (m, 2 H), 7.72-7.66 (m, 2 H), 7.39-7.29 (m, 6 H), 7.14-7.11 (m, 2 H), 7.09-7.03 (m, 3 H), 3.87-3.79 (m, 1 H), 3.04 (t, 1 H, *J* = 9.2 Hz), 2.72-2.63 (m, 2 H), 2.02-1.88 (m, 2 H), 0.84 (s, 9 H), 0.01 (s, 6 H).



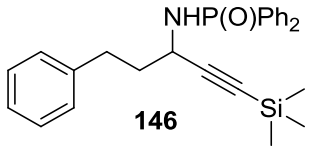
144

***P,P*-Diphenyl-*N*-(5-phenyl-1-(triethylsilyl)pent-1-yn-3-yl)phosphinic amide (144).** To a solution of diethyl zinc (0.15 g, 1.2 mmol) in anhydrous toluene (1.0 mL) was added triethylsilylacetylene (0.17 g, 1.2 mmol) and (*S*)-(-)-1-benzyl-2-pyrrolidinemethanol (24 mg, 0.12 mmol). The mixture was stirred at room temperature for 1 h and added a solution of **101c** (0.10 g, 0.20 mmol) in anhydrous toluene (2.0 mL). The reaction was stirred at room temperature for 24 h and quenched by NH_4Cl. The mixture was extracted with EtOAc, washed with brine and dried (Na_2SO_4). The organic layers were concentrated and purified by chromatography on SiO_2 (EtOAc : hexanes = 4 :1) to afford **144** (45 mg, 47%) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99-7.94 (m, 2 H), 7.84-7.79 (m, 2 H), 7.52-7.41 (m, 6 H), 7.25-7.21 (m, 2 H), 7.17-7.14 (m, 3 H), 3.97-3.95 (m, 1 H), 3.17 (t, 1 H, *J* = 10.0 Hz), 2.85-2.76 (m, 2 H), 2.13-2.03 (m, 1 H), 2.03-2.00 (m, 1 H), 1.02 (t, 9 H, *J* = 8.0 Hz), 0.61 (q, 6 H, *J* = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.3, 132.4 (dd, *J* = 130, 135 Hz), 132.1 (dd, *J* = 10, 105 Hz), 128.5 (d, *J* = 11, 12 Hz), 128.5, 128.4, 125.9, 101.7 (d, *J* = 8 Hz), 85.8, 44.1, 40.6 (d, *J* = 2 Hz), 32.1, 7.53, 4.4;



145

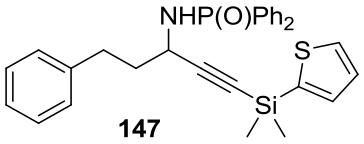
***N*-(1-(Dimethylsilyl)-5-phenylpent-1-yn-3-yl)-*P,P*-diphenylphosphinic amide (145).** To a solution of diethyl zinc (0.15 g, 1.2 mmol) in anhydrous toluene (1.0 mL) was added phenyldimethylsilylacetylene (0.20 g, 1.2 mmol) and (*S*)-(-)-1-benzyl-2-pyrrolidinemethanol (24 mg, 0.12 mmol). The mixture was stirred at room temperature for 1 h and added a solution of **101c** (0.10 g, 0.20 mmol) in anhydrous toluene (2.0 mL). The reaction was stirred at room temperature for 24 h and quenched by NH_4Cl. The mixture was extracted with EtOAc, washed with brine and dried (Na_2SO_4). The organic layers were concentrated and purified by chromatography on SiO_2 (EtOAc : hexanes = 4 :1) to afford **145** (67 mg, 66%) as a colorless oil: IR (ATR) 3144.8, 3055.3, 2954.6, 2921.1, 2857.7, 1452.2, 1437.2 ,1427.9, 1247.1, 1187.4, 1122.2, 1111.0, 1092.4, 1071.9, 837.0, 816.5, 779.2, 749.4, 725.1, 697.2 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.97-7.92 (m, 2 H), 7.83-7.76 (m, 2 H), 7.65-7.62 (m, 2 H), 7.49-7.45 (m, 2 H), 7.40-7.38 (m, 6 H), 7.26-7.20 (m, 3 H), 7.16-7.14 (m, 3 H), 4.02-3.98 (m, 1 H), 3.26 (t, 1 H, *J* = 9.6 Hz), 2.85-2.77 (m, 2 H), 2.16-2.12 (m, 1 H), 2.07-2.01 (m, 1 H), 0.43 (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.9, 137.8, 134.6, 133.1 (t, *J* = 128 Hz), 133.1 (dd, *J* = 10, 100 Hz), 132.9, 130.4, 129.4 (d, *J* = 13 Hz), 129.4, 129.3, 128.8, 126.8, 109.1 (d, *J* = 7 Hz), 87.5, 44.9, 41.1 (d, *J* = 2 Hz), 32.9, 0.1, 0.0; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{31}H_{33}NOSiP$ (M+H) 494.2069, found 494.2077.



146

***P,P*-Diphenyl-*N*-(5-phenyl-1-(trimethylsilyl)pent-1-yn-3-yl)phosphinic amide (146).** To a solution of diethyl zinc (0.15 g, 1.2 mmol) in anhydrous toluene (1.0 mL) was added trimethylsilylacetylene (0.12 g, 1.2 mmol) and (*S*)-(-)-1-benzyl-2-pyrrolidinemethanol (24 mg,

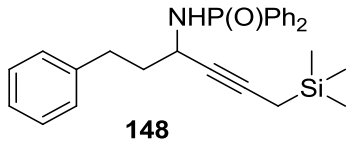
0.12 mmol). The mixture was stirred at room temperature for 1 h and added a solution of hydrocinnamyl substrate **101c** (0.10 g, 0.20 mmol) in anhydrous toluene (2.0 mL). The reaction was stirred at room temperature for 24 h and quenched by NH_4Cl. The mixture was extracted with EtOAc, washed with brine and dried (Na_2SO_4). The organic layers were concentrated and purified by chromatography on SiO_2 (EtOAc : hexanes = 4 :1) to afford **146** (54 mg, 61%) as a colorless oil: IR (ATR) 3056.7, 2954.2, 2920.7, 2167.7, 2160.2, 1437.0, 1246.9, 1185.4, 1122.0, 1109.0, 1090.4, 1071.7, 840.6, 749.3, 723.2, 695.2 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.80-7.75 (m, 2 H), 7.66-7.61 (m, 2 H), 7.29-7.25 (m, 6 H), 7.08-7.03 (m, 2 H), 7.00-6.94 (m, 3 H), 3.79-3.71 (m,1 H), 2.98 (t, 1 H, *J* = 9.6 Hz), 2.65-2.56 (m, 2 H), 1.93-1.82 (m, 2 H), 0.00 (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.2, 132.4 (d, *J* = 124, 129 Hz), 132.2 (d, *J* = 10, 102 Hz), 132.0, 128.6, 128.5. 128.4 (d, *J* = 3 Hz), 126.0, 106.5 (d, *J* = 7 Hz), 88.6, 43.9, 40.3 (d, *J* = 3 Hz), 32.0, 0.0; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{26}H_{31}NOSiP$ 432.1913, found 432.1912.



147

***N*-(1-(Dimethyl(thiophen-2-yl)silyl)-5-phenylpent-1-yn-3-yl)-*P,P*-diphenylphosphinic amide (147).** To a solution of diethyl zinc (0.15 g, 1.2 mmol) in anhydrous toluene (1.0 mL) was added dimethyl(2-thienyl)silylacetylene (0.20 g, 1.2 mmol) and (*S*)-(-)-1-benzyl-2-pyrrolidinemethanol (24 mg, 0.12 mmol). The mixture was stirred at room temperature for 1 h and added a solution of **101c** (0.10 g, 0.20 mmol) in anhydrous toluene (2.0 mL). The reaction was stirred at room temperature for 24 h and quenched by NH_4Cl. The mixture was extracted with EtOAc, washed with brine and dried (Na_2SO_4). The organic layers were concentrated and purified by chromatography on SiO_2 (EtOAc : hexanes = 4 :1) to afford **147** (64.3 mg, 63%) as a colorless

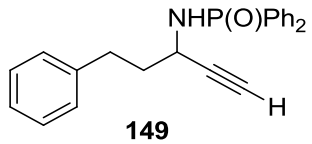
oil: IR (ATR) 2954.6, 2921.1, 3150.4, 3055.3, 2169.8, 2160.5, 1452.2, 1437.2, 1405.6, 1249.0, 1211.7, 1187.4, 1122.2, 1109.2, 1086.8, 1071.9, 995.4, 835.1, 810.9, 781.1, 747.5, 723.3, 697.2 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97-7.92 (m, 2 H), 7.84-7.79 (m, 2 H), 7.65 (d, 1 H, *J* = 4.8 Hz), 7.48 (t, 2 H, *J* = 7.6 Hz), 7.43-7.37 (m, 5 H), 7.23-7.20 (m, 3 H), 7.17-7.14 (m, 3 H), 4.00-3.95 (m, 1 H), 3.22 (bs, 1 H), 2.83-2.76 (m, 2 H), 2.16-2.12 (m, 1 H), 2.07-2.03 (m, 1 H), 0.47 (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.8, 136.1, 135.0, 132.0 (dd, *J* = 10, 99 Hz), 131.8 (d, *J* = 12 Hz), 131.2, 128.3 (d, *J* = 13 Hz), 128.3, 128.2, 128.1, 125.7, 108.0 (d, *J* = 7 Hz), 86.0, 43.8, 39.9, 31.7, 0.0 (d, *J* = 4 Hz); HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{29}H_{31}NOSSiP$ 500.1633, found 500.1628.



148

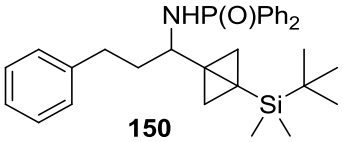
***P,P*-Diphenyl-*N*-(1-phenyl-6-(trimethylsilyl)hex-4-yn-3-yl)phosphinic amide (148).** To a solution of diethyl zinc (0.15 g, 1.2 mmol) in anhydrous toluene (1.0 mL) was added propargyltrimethylsilane (0.14 g, 1.2 mmol) and (*S*)-(-)-1-benzyl-2-pyrrolidinemethanol (24 mg, 0.12 mmol). The mixture was stirred at room temperature for 1 h and added a solution of **101c** (0.1 g, 0.2 mmol) in anhydrous toluene (2.0 mL). The reaction was stirred at room temperature for 24 h and quenched by NH_4Cl. The mixture was extracted with EtOAc, washed with brine and dried (Na_2SO_4). The organic layers were concentrated and purified by chromatography on SiO_2 (EtOAc : hexanes = 4 :1) to afford **148** (68 mg, 76%) as a yellowish oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97-7.92 (m, 2 H), 7.86-7.81 (m, 2 H), 7.49-7.241 (m, 6 H), 7.26-7.21 (m, 2 H), 7.17-7.14 (m, 3 H), 3.95-3.86 (m,1 H), 3.11 (t, 1 H, *J* = 9.2 Hz), 2.82-2.71 (m, 2 H), 2.10-2.08 (m, 1 H), 1.99-1.96 (m, 1 H), 1.49 (d, 2 H, *J* = 2.0 Hz), 0.13 (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ

141.4, 132.5 (dd, *J* = 100, 127 Hz), 132.0 (dd, *J* = 9, 68 Hz), 131.8, 128.4 (dd, *J* = 4, 13 Hz), 128.4, 128.3, 125.8, 82.3, 79.4 (d, *J* = 9 Hz), 44.0, 41.1 (d, *J* = 3 Hz), 32.1, 7.1, -2.0.



149

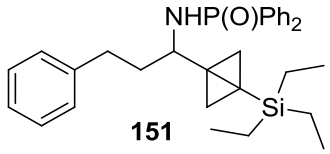
***P,P*-Diphenyl-*N*-(5-phenylpent-1-yn-3-yl)phosphinic amide (149).** To a solution of amide **146** (50 mg, 0.11 mmol) in THF was added TBAF (1 M in THF, 0.24 mL, 0.24 mmol). The mixture was stirred at room temperature for 2 h, quenched with water, and extracted with EtOAc for 3 times. The organic layers were washed with brine and dried (Na_2SO_4). The product was concentrated to afford **149** as a yellowish oil (38 mg, 91%) without further purification: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96-7.91 (m, 2 H), 7.87-7.82 (m, 2 H), 7.52-7.42 (m, 6 H), 7.25-7.21 (m, 2 H), 7.18-7.15 (m, 3 H), 3.95-3.88 (m, 1 H), 3.18 (t, 1 H, *J* = 9.6 Hz), 2.82-2.75 (m, 2 H), 2.38 (s, 1 H), 2.14-2.05 (m, 2 H);



150

***N*-(1-(3-(*tert*-Butyldimethylsilyl)bicyclo[1.1.0]butan-1-yl)-3-phenylpropyl)-*P,P*-diphenyl-phosphinic amide (150).** To a cooled solution of amide **143** (35 mg, 0.07 mmol) in anhydrous CH_2Cl_2 (2.0 mL) was added Me_2Zn (14 mg, 0.15 mmol) in anhydrous CH_2Cl_2 (1.0 mL). The reaction mixture was stirred at 0 ℃ for 1 h, cooled to -30 ℃ and added a cold solution of Et_2Zn (36 mg, 0.30 mmol) and trifluoroethanol (22 μl, 0.29 mmol) in anhydrous dichloromethane (5.0 mL). Then, diethyl aluminum chloride (1 M in hexanes, 0.0090 mL, 0.0090 mmol) and CH_2I_2 (79 mg, 0.29 mmol) was added at this temperature. The reaction mixture was stirred overnight,

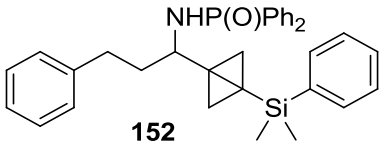
quenched with saturated NH_4Cl and extracted with dichloromethane (3×10 mL). The combined organic layers were washed with water and brine and dried ($MgSO_4$). The product was concentrated and purified by chromatography on SiO_2 (EtOAc : hexanes = 4 :1) to afford **150** as a colorless oil slowly solidified (33 mg, 91%): IR (ATR) 3215.6, 3057.2, 2949.0, 2924.8, 2852.1, 1707.5, 1452.2, 1437.2, 1249.0, 1183.7, 1122.2, 1109.2, 1092.4, 1071.9, 829.5, 807.2, 768.0, 749.4, 723.3, 697.2 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.97-7.87 (m, 4 H), 7.52-7.42 (m, 6 H), 7.26-7.22 (m, 2 H), 7.17-7.15 (m, 3 H), 3.68-3.60 (m, 1 H), 2.97-2.88 (m, 2 H), 2.78-2.74 (m, 1 H), 1.81-1.73 (m, 2 H), 1.26 (d, 1 H, *J* = 6.4 Hz), 1.03 (d, 1 H, *J* = 6.4 Hz), 0.88 (s, 9 H), 0.23 (s, 1 H), 0.19 (s, 1 H), -1.05 (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.2, 132.3 (dd, *J* = 10, 52 Hz), 131.8, 128.7, 128.5, 128.4, 128.3, 125.8, 50.8, 33.6, 32.3, 29.7, 26.4, 17.8, 0.0, -1.0, -6.0, -6.6; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{31}H_{41}NOSiP$ 502.2695, found 502.2707.



151

***P,P*-Diphenyl-*N*-(3-phenyl-1-(3-(triethylsilyl)bicyclo[1.1.0]butan-1-yl)propyl)phosphinic amide (151).** To a cooled solution of amide **144** (45 mg, 0.096 mmol) in anhydrous CH_2Cl_2 (2.0 mL) was added Me_2Zn (18 mg, 0.19 mmol) in anhydrous CH_2Cl_2 (1.0 mL). The reaction mixture was stirred at 0 ℃ for 1 h, cooled to -30 ℃ and added a cold solution of Et_2Zn (47 mg, 0.38 mmol) and trifluoroethanol (28 μl, 0.38 mmol) in anhydrous dichloromethane (5.0 mL). Then, diethyl aluminum chloride (1 M in hexanes, 0.011 mL, 0.011 mmol) and CH_2I_2 (0.10 g, 0.38 mmol) was added at this temperature. The reaction mixture was stirred overnight, quenched with saturated NH_4Cl and extracted with dichloromethane (3×10 mL). The combined organic layers were washed with water and brine and dried ($MgSO_4$). The product was concentrated and

purified by chromatography on SiO_2 (EtOAc : hexanes = 4 :1) to afford **151** as a white semisolid (37 mg, 76%): IR (ATR) 3172.7, 3057.2, 3023.6, 2949.0, 2932.3, 2909.9, 2872.6, 1452.2, 1437.2, 1187.4, 1122.2, 1109.2, 1077.5, 769.9, 751.2, 721.4, 695.3 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.97-7.88 (m, 4 H), 7.49-7.43 (m, 6 H), 7.24-7.22 (m, 2 H), 7.17-7.15 (m, 3 H), 3.61-3.59 (m, 1 H), 2.98-2.90 (m, 2 H), 2.77-2.75 (m, 1 H), 1.78-1.73 (m, 1 H), 1.24 (d, 1 H, *J* = 6.8 Hz), 0.99 (d, 1 H, *J* = 6.4 Hz), 0.84 (t, 9 H, *J* = 8.0 Hz), 0.44 (q, 6 H, *J* = 8.0 Hz), 0.20 (s, 1 H), 0.17 (s, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.0, 134.0, 133.2 (dd, *J* = 58, 129 Hz), 132.3 (dd, *J* = 7, 4 Hz) 131.8 (dd, *J* = 2, 8 Hz), 128.4 (d, *J* = 15 Hz), 128.4, 128.3, 125.8, 51.2, 38.0 (d, *J* = 3 Hz), 33.5, 32.3, 30.5, 23.5 (d, *J* = 5 Hz), 7.5, 4.1, -1.2; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{33}H_{36}NOSiP$ 502.2679, found 502.2686.



152

***N*-(1-(3-(Dimethyl(phenyl)silyl)bicyclo[1.1.0]butan-1-yl)-3-phenylpropyl)-*P*,*P*-diphenyl-phosphinic amide (152)**. To a cooled solution of amide **145** (50.0 mg, 0.10 mmol) in anhydrous CH_2Cl_2 (2.0 mL) was added Me_2Zn (19 mg, 0.20 mmol) in anhydrous CH_2Cl_2 (1.0 mL). The reaction mixture was stirred at 0 ℃ for 1 h, cooled to -30 ℃ and added a cold solution of Et_2Zn (50 mg, 0.41 mmol) and trifluoroethanol (29 μl, 0.41 mmol) in anhydrous dichloromethane (5.0 mL). Then, diethyl aluminum chloride (1 M in hexanes, 0.012 mL, 0.012 mmol) and CH_2I_2 (0.11 g, 0.41 mmol) was added at this temperature. The reaction mixture was stirred overnight, quenched with saturated NH_4Cl and extracted with dichloromethane (3×10 mL). The combined organic layers were washed with water and brine and dried ($MgSO_4$). The product was concentrated and purified by chromatography on SiO_2 (EtOAc : hexanes = 4 :1) to afford **152** as a white semisolid (45 mg, 86%): IR (ATR) 2950.9, 2941.6, 2923.0, 2917.4, 2867.0, 2857.7,

2852.1, 3167.2, 1437.2, 1187.4, 1122.2, 1111.0, 1092.4, 827.7, 812.8, 747.5, 725.1, 699.0 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.92-7.82 (m, 4 H), 7.50-7.48 (m, 2 H), 7.44-7.42 (m, 6 H), 7.25-7.22 (m, 5 H), 7.19-7.17 (m, 1 H), 7.11-7.09 (m, 2 H), 3.59-3.54 (m, 1 H), 2.92-2.88 (m, 1 H), 2.72 (dd, 1 H, *J* = 6.8, 10.0 Hz), 2.64-2.58 (m, 1 H), 1.64-1.61 (m, 1 H), 1.38 (d, 1 H, *J* = 6.8 Hz), 1.11 (d, 1 H, *J* = 6.8 Hz), 0.34 (s, 1 H), 0.30 (s, 1 H), 0.26 (s, 3 H), 0.22 (s, 3 H); HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{33}H_{37}NOSiP$ 522.2382, found 522.2382

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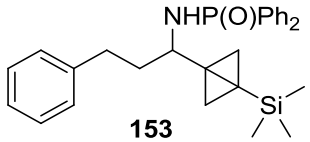
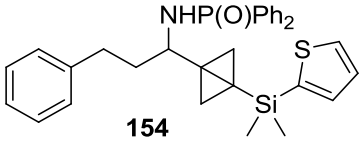


153

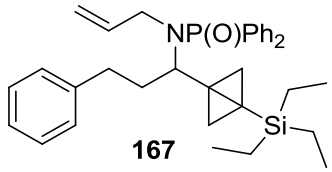
***P,P*-Diphenyl-*N*-(3-phenyl-1-(3-(trimethylsilyl)bicyclo[1.1.0]butan-1-yl)propyl)phosphinic amide (153).** To a cooled solution of amide **146** (43.0 mg, 0.10 mmol) in anhydrous CH_2Cl_2 (2.0 mL) was added Me_2Zn (19 mg, 0.20 mmol) in anhydrous CH_2Cl_2 (1.0 mL). The reaction mixture was stirred at 0 ℃ for 1 h, cooled to -30 ℃ and added a cold solution of Et_2Zn (49 mg, 0.40 mmol) and trifluoroethanol (29 μl, 0.40 mmol) in anhydrous dichloromethane (5.0 mL). Then, diethyl aluminum chloride (1 M in hexanes, 0.012 mL, 0.012 mmol) and CH_2I_2 (0.11 g, 0.40 mmol) was added at this temperature. The reaction mixture was stirred overnight, quenched with saturated NH_4Cl and extracted with dichloromethane (3×10 mL). The combined organic layers were washed with water and brine and dried ($MgSO_4$). The product was concentrated and purified by chromatography on SiO_2 (EtOAc : hexanes = 4 :1) to afford **153** as a yellowish semisolid (34 mg, 75%): IR (ATR) 3176.0, 3054.9, 3023.2, 2946.8, 2922.5, 2861.0, 2853.6, 1437.0, 1246.9, 1185.4, 1122.0, 1109.0, 1092.2, 835.0, 747.4, 723.2, 695.2 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.02-7.93 (m, 4 H), 7.55-7.49 (m, 6 H), 7.29-7.28 (m, 2 H), 7.22-7.20 (m, 3 H), 3.68-3.65 (m, 1 H), 3.07-2.97 (m, 2 H), 2.83-2.76 (m, 1 H), 1.86-1.77 (m, 2 H), 1.33 (d, 1 H, *J* =

6.8 Hz), 1.04 (d, 1 H, *J* = 6.8 Hz), 0.26 (s, 1 H), 0.24 (s, 1 H), 0.00 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.0, 133.6 (d, *J* = 10 Hz), 133.0 (d, *J* = 10 Hz), 132.8, 129.5 (d, *J* = 10 Hz), 129.4 (overlap), 129.3, 126.8, 51.9, 39.1, 34.0, 33.3, 31.1, 25.1 (d, *J* = 7 Hz), 1.9, 0.0; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{28}H_{35}NOSiP$ 460.2226, found 460.2222.



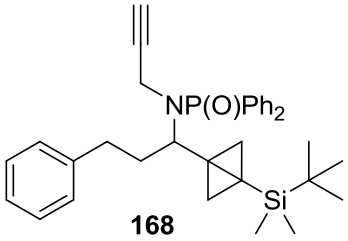
154

***N*-(1-(3-(Dimethyl(thiophen-2-yl)silyl)bicyclo[1.1.0]butan-1-yl)-3-phenylpropyl)-*P*,*P*-diphenylphosphinic amide (154).** To a cooled solution of amide **147** (50.0 mg, 0.10 mmol) in anhydrous CH_2Cl_2 (2.0 mL) was added Me_2Zn (19 mg, 0.20 mmol) in anhydrous CH_2Cl_2 (1.0 mL). The reaction mixture was stirred at 0 ℃ for 1 h, cooled to -30 ℃ and added a cold solution of Et_2Zn (50 mg, 0.41 mmol) and trifluoroethanol (29 µl, 0.41 mmol) in anhydrous dichloromethane (5.0 mL). Then, diethyl aluminum chloride (1 M in hexanes, 0.012 mL, 0.012 mmol) and CH_2I_2 (0.11 g, 0.41 mmol) was added at this temperature. The reaction mixture was stirred overnight, quenched with saturated NH_4Cl and extracted with dichloromethane (3×10 mL). The combined organic layers were washed with water and brine and dried ($MgSO_4$). The product was concentrated and purified by chromatography on SiO_2 (EtOAc : hexanes = 4 :1) to afford **154** as a white semisolid (48 mg, 92%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95-7.85 (m, 4 H), 7.53-7.50 (m, 2 H), 7.48-7.43 (m, 6 H), 7.27-7.26 (m, 2 H), 7.21-7.13 (m, 4 H), 7.06 (dd, 1 H, *J* = 3.2, 4.8 Hz), 3.68-3.59 (m, 1 H), 2.98-2.89 (m, 1 H), 2.73 (dd, 1 H, *J* = 7.2, 10.0 Hz), 2.68-2.60 (m, 1 H), 1.70-7.62 (m, 2 H), 1.47 (d, 1 H, *J* = 6.8 Hz), 1.19 (d, 1 H, *J* = 6.8 Hz), 0.39 (s, 1 H), 0.35 (s, 4 H, overlap), 0.32 (s, 3 H).



167

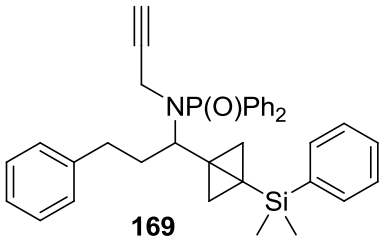
***N*-Allyl-*P,P*-diphenyl-*N*-(3-phenyl-1-(3-(triethylsilyl)bicyclo[1.1.0]butan-1-yl) propyl) phosphinic amide (167).** Amide **151** (15 mg, 0.030 mmol), allyl bromide (36 mg, 0.30 mmol) and Bu_4NHSO_4 (5 mg, 0.015 mmol) were dissolved in PhMe (1.0 mL) and treated with a 50 % NaOH solution (1.0 mL). The reaction mixture was vigorously stirred at room temperature for 1.5 h, diluted with water, and extracted (3x) with EtOAc. The combined organic layers were washed with water and brine, dried (Na_2SO_4) and concentrated. The residue was purified by chromatography on SiO_2 (EtOAc : hexanes = 4 :1) to afford the product **167** (15 mg, 93%) as a yellowish oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96-7.87 (m, 4 H), 7.48-7.44 (m, 6 H), 7.29-7.27 (m, 2 H), 7.18-7.16 (m, 3 H), 6.01-5.97 (m, 1 H), 4.95 (s, 1 H), 4.92 (d, 1 H, *J* = 7.2 Hz), 4.00-3.96 (m, 1 H), 3.82-3.77 (m, 2 H), 3.15-3.06 (m, 1 H), 2.50-2.43 (m, 1 H), 2.09-2.05 (m, 1 H), 1.45-1.38 (m, 1 H), 1.25 (d, 1 H, *J* = 6.4 Hz), 1.12 (d, 1 H, *J* = 6.8 Hz), 0.82 (d, 9 H, *J* = 8.0 Hz), 0.43 (s, 1 H), 0.42 (q, 6 H, *J* = 8.0 Hz), 0.27 (s, 1 H) 0.02 (s, 1 H).



168

***N*-(1-(3-(*tert*-Butyldimethylsilyl)bicyclo[1.1.0]butan-1-yl)-3-phenylpropyl)-*P,P*-diphenyl-*N*-(prop-2-yn-1-yl)phosphinic amide (168).** Amide **150** (0.015 g, 0.030 mmol), propargyl bromide (36 mg, 0.29 mmol) and Bu_4NHSO_4 (0.0051 g, 0.015 mmol) were dissolved in PhMe (1.0 mL) and treated with a 50 % NaOH solution (1.0 mL). The reaction mixture was vigorously stirred at room temperature for 1.5 h, diluted with water, and extracted (3x) with EtOAc. The

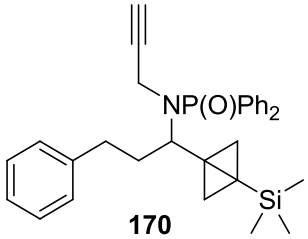
combined organic layers were washed with water and brine, dried (Na_2SO_4), and concentrated. The residue was purified by chromatography on SiO_2 (EtOAc : hexanes = 4 :1) to afford the product **168** (14 mg, 91%) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03-7.91 (m, 4 H), 7.54-7.44 (m, 6 H), 7.29-7.23 (m, 2 H), 7.20-7.18 (m, 3 H), 4.15-4.11 (m, 1 H), 3.91-3.85 (m, 2 H), 3.25-3.16 (m, 1 H), 2.48-2.41 (m, 1 H), 2.31-2.26 (m, 1 H), 2.17 (s, 1 H), 1.36 (d, 1 H, *J* = 6.8 Hz), 1.33-1.30 (m, 1 H), 1.17 (d, 1 H, *J* = 6.8 Hz), 0.88 (s, 9 H), 0.47 (s, 1 H), 0.34 (s, 1 H), -0.12 (s, 3 H), 0.35 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.4, 133.0 (d, *J* = 10 Hz), 132.8 (d, *J* = 9 Hz), 131.8 (d, *J* = 8 Hz), 128.5 (d, *J* = 9 Hz), 128.3, 125.8, 82.6, 71.2, 56.8, 34.9, 33.7, 33.1, 32.1, 31.9, 26.4, 19.7, 17.8, -1.6, -6.0, -6.8; HRMS (ESI) *m/z* calcd. for $C_{36}H_{39}NOSiP$ (M+H) 560.2539, found 560.2554.



169

***N*-(1-(3-(Dimethyl(phenyl)silyl)bicyclo[1.1.0]butan-1-yl)-3-phenylpropyl)-*P,P*-diphenyl-*N*-(prop-2-yn-1-yl)phosphinic amide (169).** Amide **152** (0.015 g, 0.029 mmol), propargyl bromide (34 mg, 0.29 mmol) and Bu_4NHSO_4 (0.005 g, 0.014 mmol) were dissolved in PhMe (1.0 mL) and treated with a 50 % NaOH solution (1.0 mL). The reaction mixture was vigorously stirred at room temperature for 1.5 h, diluted with water, and extracted (3x) with EtOAc. The combined organic layers were washed with water and brine, dried (Na_2SO_4), and concentrated. The residue was purified by chromatography on SiO_2 (EtOAc : hexanes = 4 :1) to afford the product **169** (14 mg, 85%) as a colorless oil: IR (ATR) 3304.6, 3299.0, 3291.6, 3282.3, 3054.9, 3023.2, 2948.6, 2924.4, 2851.7, 1716.6, 1692.4, 1601.1, 1591.7, 1468.7, 1459.4, 1453.8, 1437.0, 1248.8, 1181.7, 1120.2, 1107.1, 1081.0, 1071.7, 1047.5, 829.4, 767.9, 751.1, 725.0 cm^{-1}; ^{1}H

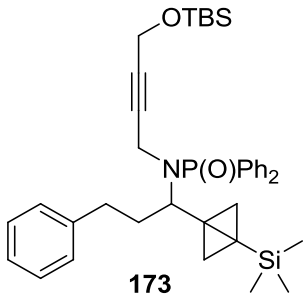
NMR (400 MHz, $CDCl_3$) δ 8.03-7.98 (m, 2 H), 7.95-7.90 (m, 2 H), 7.53-7.41 (m, 6 H), 7.39-7.37 (m, 2 H), 7.26-7.23 (m, 5 H), 7.10-7.08 (m, 1 H), 7.06-7.03 (m, 2 H), 4.14-4.07 (m, 1 H), 3.87-3.76 (m, 2 H), 3.19-3.11 (m, 1 H), 2.34-2.16 (m, 2 H), 2.13 (s, 1 H), 1.39 (d, 1 H, *J* = 6.4 Hz), 1.27 (d, 1 H, *J* = 6.4 Hz), 1.13-1.09 (m, 1 H), 0.56 (s, 1 H), 0.45 (s, 1 H), 0.19 (s, 3 H), 0.15 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.1, 138.5, 133.0 (d, *J* = 10 Hz),132.7, 132.5, 132.2 (d, *J* = 9 Hz), 132.1 (d, *J* = 10 Hz), 131.3 (d, *J* = 21 Hz), 129.2, 128.7, 128.6 (d, *J* = 10 Hz), 128.5, 128.0, 125.9, 82.7 (d, *J* = 7 Hz), 71.4, 56.8 (d, *J* = 3 Hz), 35.0, 33.6 (d, *J* = 4 Hz), 33.1, 32.3 (d, *J* = 6 Hz), 21.9 (d, *J* = 2 Hz), 0.0, -2.1, -2.5; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{34}H_{43}NOSiP$ 540.2852, found 540.2854.



170

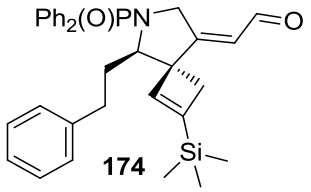
***P,P*-Diphenyl-*N*-(3-phenyl-1-(3-(trimethylsilyl)bicyclo[1.1.0]butan-1-yl)propyl)-*N*-(prop-2-yn-1-yl)phosphinic amide (170).** Amide **153** (0.015 g, 0.033 mmol), propargyl bromide (39 mg, 0.33 mmol) and Bu_4NHSO_4 (0.006 g, 0.016 mmol) were dissolved in PhMe (1.0 mL) and treated with a 50 % NaOH solution (1.0 mL). The reaction mixture was vigorously stirred at room temperature for 1.5 h, diluted with water, and extracted (3x) with EtOAc. The combined organic layers were washed with water and brine, dried (Na_2SO_4) and concentrated. The residue was purified by chromatography on SiO_2 (EtOAc : hexanes = 4 :1) to afford the product **170** (11 mg, 65%) as a yellowish oil: ^1H NMR (400 MHz, $CDCl_3$) δ 8.11-8.06 (m, 2 H), 8.04-7.99 (m, 2 H), 7.60-7.53 (m, 6 H), 7.34-7.32 (m, 2 H), 7.28-7.25 (m, 3 H), 4.21-4.19 (m, 1 H), 3.98-3.93 (m, 2 H), 3.35-3.28 (m, 1 H), 2.54-2.49 (m, 1 H), 2.41-2.33 (m, 1 H), 2.25 (s, 1 H), 1.45 (d, 1 H, *J* = 6.8 Hz), 1.40-1.35 (m, 1 H), 1.25 (d, 1 H, *J* = 6.4 Hz), 0.52 (s, 1 H), 0.43 (s, 1 H), 0.00 (s, 9 H);

^{13}C NMR (100 MHz, $CDCl_3$) δ 143.5, 134.0 (dd, *J* = 9, 10 Hz), 133.7, 133.5, 133.0 (dd, *J* = 3, 8 Hz), 132.8, 132.4, 132.2, 129.6, 129.5, 129.4, 126.9, 83.7 (d, *J* = 7 Hz), 72.3, 57.9 (d, *J* = 2 Hz), 35.4, 34.8 (d, *J* = 5 Hz), 34.2, 33.3 (d, *J* = 6 Hz), 32.8, 22.4 (d, *J* = 3 Hz), 1.3, 0.0.



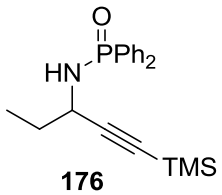
173

***N*-(4-((*tert*-Butyldimethylsilyl)oxy)but-2-yn-1-yl)-*P,P*-diphenyl-*N*-(3-phenyl-1-(3-(trimethyl-silyl)bicyclo[1.1.0]butan-1-yl)propyl)phosphinic amide (173).** Amide **153** (0.040 g, 0.087 mmol), propargyl bromide (69 mg, 0.26 mmol) and Bu_4NHSO_4 (0.015 g, 0.044 mmol) were dissolved in PhMe (1.0 mL) and treated with a 50 % NaOH solution (1.0 mL). The reaction mixture was vigorously stirred at room temperature overnight, diluted with water, and extracted (3x) with EtOAc. The combined organic layers were washed with water and brine, dried (Na_2SO_4), and concentrated. The residue was purified by chromatography on SiO_2 (EtOAc : hexanes = 3 :1) to afford the product **173** (40 mg, 71%) as a yellowish oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (ddd, 4 H, *J* = 7.2, 12.0, 25.2 Hz), 7.60-7.50 (m, 6 H), 7.36-7.32 (m, 2 H), 7.27-7.23 (m, 3 H), 4.27 (s, 2 H), 4.25-4.21 (m, 1 H), 4.00-3.93 (m, 2 H), 3.26 (dt, 1 H, *J* = 4.0, 12.8 Hz), 2.56 (dt, 1 H, *J* = 4.8, 13.2 Hz), 2.46-2.33 (m, 1 H), 1.44 (d, 1 H, *J* = 6.8 Hz), 1.23 (d, 1 H, *J* = 6.4 Hz), 0.96 (s, 9 H), 0.51 (s, 1 H), 0.44 (s, 1 H), 0.14 (s, 6 H), 0.00 (s, 9 H).



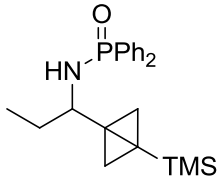
174

(*Z*)-2-(6-(Diphenylphosphoryl)-5-phenethyl-2-(trimethylsilyl)-6-azaspiro[3.4]oct-1-en-8-ylidene)acetaldehyde (174). To 1 mL anhydrous THF was added TBAF (0.12 mL, 0.12 mmol, 1 M solution in THF) and TBS protected alcohol **173** (40 mg, 0.062 mmol). The mixture was then stirred at 0 ℃ for 1 h and concentrated. The product was purified by chromatography to afford the primary alcohol (32 mg, 98%) without further characterization. To a solution of primary alcohol (10 mg, 0.019 mmol) was added 2,6-lutidine (0.011 mL, 0.095 mmol). The mixture was cooled to 0 ℃, added Dess-Martin periodinane (16 mg, 0.038 mmol) and stirred at this temperature for 8 h. The reaction was quenched by a 1:1 solution of saturated $Na_2S_2O_3$ and $NaHCO_3$ solution and extracted with EtOAc for 3 times. The combined organic layer was washed with brine and dried ($MgSO_4$). The product was concentrated and purified by chromatography on SiO_2 (EtOAc : hexanes = 4 :1) afford the product as a colorless oil (6.9 mg, 69 %): ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.64 (d, 2 H, *J* = 6.4 Hz), 7.95-7.87 (m, 4 H), 7.55-7.45 (m, 6 H), 7.24-7.22 (m, 2 H), 7.18-7.14 (m, 1 H), 7.06-7.04 (m, 2 H), 6.34 (s, 1 H), 6.06 (br d, *J* = 6.0 Hz), 4.39 (ddq, 2 H, *J* = 2.4, 8.8, 18.0 Hz), 3.77 (q, 1 H, *J* = 6.8 Hz), 2.91 (d, 1 H, *J* = 13.2 Hz), 2.65 (m, 1 H), 2.54 (d, 1 H, *J* = 13.2 Hz), 2.54 (s, 1 H), 2.35 (m, 1 H), 1.71 (m, 1 H), 0.10 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 190.4, 170.0, 159.7, 143.7, 141.7, 132.5 (dd, *J* = 9, 10 Hz), 132.1 (dd, *J* = 3, 14 Hz), 128.8 (dd, *J* = 13, 15 Hz), 128.4, 128.2, 126.0, 118.7, 65.1, 62.7, 49.9, 48.6, 35.5, 32.9, -2.4.



176

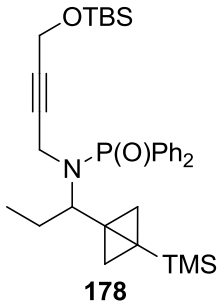
***P,P*-Diphenyl-*N*-(1-(trimethylsilyl)pent-1-yn-3-yl)phosphinic amide (176).** To a solution of lithium bistrimethylsilyl amide (0.408 g, 2.4 mmol) in anhydrous hexanes (5 mL) was added trimethylsilyl acetylene (0.355 g, 3.6 mmol). The mixture was stirred at -78 ℃ for 15 min and added a solution of imine adduct (0.50 g, 1.21 mmol) in THF (4.0 mL). The reaction was stirred at room temperature for 6 h and quenched by NH_4Cl. The mixture was extracted with EtOAc, washed with brine, and dried (Na_2SO_4). The organic layers were concentrated and purified by chromatography on SiO_2 (EtOAc : hexanes = 4 : 1) to afford the product **176** as a yellowish solid (0.336 g, 78%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86-7.80 (m, 2 H), 7.71-7.65 (m, 2 H), 7.33-7.23 (m, 6 H), 3.72-3.69 (m, 1 H), 3.23 (t, 1 H, *J* = 9.6 Hz), 1.69-1.59 (m, 1 H), 1.57-1.54 (m, 1 H), 0.84 (t, 3 H, *J* = 8.4 Hz), 0.00 (s, 9 H); HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{20}H_{27}NOSiP$ 356.1600, found 356.1603.



177

***P,P*-Diphenyl-*N*-(1-(3-(trimethylsilyl)bicyclo[1.1.0]butan-1-yl)propyl)phosphinic amide (177).** To a cooled solution of **176** (0.33 g, 0.93 mmol) in anhydrous CH_2Cl_2 (15 mL) was added Me_2Zn (0.18 g, 1.8 mmol) in anhydrous CH_2Cl_2 (5 mL). The reaction mixture was stirred at 0 ℃ for 1 hour, cooled to -30 ℃ and treated with a cold solution of Et_2Zn (0.46 g, 3.7 mmol) in anhydrous CH_2Cl_2 (2 mL). Then, CH_2I_2 (1.0 g, 3.7 mmol) were slowly added in this temperature. The reaction mixture was stirred overnight, quenched with sat. NH_4Cl, and extracted with

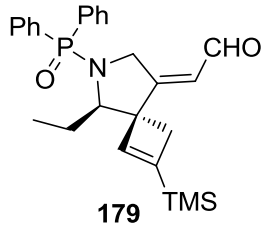
CH_2Cl_2 (3×10 mL). The combined organic layers were washed with water and brine and dried ($MgSO_4$). The product was concentrated and purified by chromatography on SiO_2 (EtOAc : hexanes = 4 : 1) to afford the product as a white solid (0.22 g, 62 %): ^{1}H NMR (400 MHz, CDCl3) δ 7.91-7.83 (m, 4 H), 7.42-7.36 (m, 6 H), 3.46 (m, 1 H), 2.83 (t, 1 H, *J* = 8.4 Hz), 1.45 (p, 2 H, *J* = 6.8 Hz), 1.23 (d, 1 H, *J* = 9.2 Hz), 1.02 (t, 3 H, *J* = 6.8 Hz), 0.99 (d, 1 H, *J* = 9.2 Hz), 1.15 (d, 2 H, *J* = 6.4 Hz), -0.05 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 134.2, 133.8, 132.9, 132.5, 132.4, 132.0, 131.9, 131.6, 128.4, 128.3, 128.2, 52.4, 32.8, 30.2, 29.0 (d, *J* = 4 Hz), 24.0 (d, *J* = 7 Hz), 10.7, -1.01; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{22}H_{31}NOSiP$ 384.1913, found 384.1918; IR(ATR) 3176, 3055, 2954, 2926, 2870, 1437, 1247, 1187, 1122, 1107, 1060, 1010, 997, 954, 835, 749, 721, 695 cm^{-1}.



178

***N*-(4-((*tert*-Butyldimethylsilyl)oxy)but-2-yn-1-yl)-*P,P*-diphenyl-*N*-(1-(3-(trimethylsilyl)-bicyclo[1.1.0]butan-1-yl)propyl)phosphinic amide (178).** Amide (0.10 g, 0.26 mmol), TBS-protected propargyl bromide (0.21 g, 0.78 mmol) and Bu_4NHSO_4 (0.044 g, 0.13 mmol) were dissolved in toluene (3.0 mL) and treated with a 50 % aq NaOH solution (3.0 mL). The reaction mixture was vigorously stirred at rt overnight, diluted with water, and extracted (3x) with EtOAc. The combined organic layers were washed with water, brine, dried (Na_2SO_4), and concentrated. The product was purified by chromatography on SiO_2 (EtOAc : hexanes = 4 : 1) to afford the product **178** as a yellowish oil (78 mg, 53%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (ddd, 2 H, *J* =

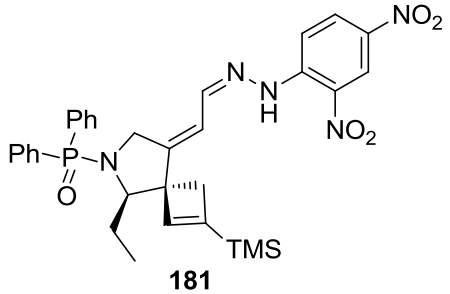
1.2, 8.0, 12.0 Hz), 7.93 (ddd, 2 H, *J* = 1.2, 8.0, 12.0 Hz), 7.53-7.45 (m, 6 H), 4.28 (t, 2 H, *J* = 1.6 Hz), 4.10 (ddt, 1 H, *J* = 1.6, 8.8, 18.4 Hz), 3.83 (ddt, 1 H, *J* = 2.0, 8.8, 18.4 Hz), 3.65 (dt, 1 H, *J* = 2.8, 8.8 Hz), 2.05 (m, 1 H), 1.39 (d, 1 H, *J* = 6.8 Hz), 1.16 (d, 1 H, *J* = 6.8 Hz), 1.14-1.08 (m, 1 H), 1.08 (t, 3 H, *J* = 6.4 Hz), 0.93 (s, 9 H), 0.45 (s, 1 H), 0.37 (s, 1 H), 0.12 (s, 6 H), -0.06 (s, 9 H); ^{13}C NMR (125 MHz, CDCl3) δ 132.9 (dd, *J* = 10.0, 20.0 Hz), 132.0 (dd, *J* = 126, 33 Hz), 131.8 (dd, *J* = 11, 2.5 Hz), 128.3 (dd, *J* = 1.3, 12.5 Hz), 83.1 (d, *J* = 6.3 Hz), 81.2, 57.9, 51.7, 34.0, 32.1 (d, *J* = 6.3 Hz), 31.7, 25.8, 24.3 (d, *J* = 5 Hz), 21.5 (d, *J* = 2.5 Hz), 18.3, 11.4, -1.2, -5.2 (d, *J* = 7.5 Hz); HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{32}H_{49}NO_2Si_2P$ 566.3040, found 566.3046; IR(ATR) 2950, 2926, 2896, 2874, 2855, 1461, 1437, 1371, 1361, 1340, 1249, 1206, 1139, 1118, 1103, 1068, 913, 831, 775, 749, 721, 695 cm^{-1}.



179

(*Z*)-2-(6-(Diphenylphosphoryl)-5-ethyl-2-(trimethylsilyl)-6-azaspiro[3.4]oct-1-en-8-ylidene)-acetaldehyde (**179**) To 1 mL anhydrous THF was added TBAF (0.28 mL, 0.28 mmol, 1 M solution in THF) and **178** (78 mg, 0.14 mmol). The mixture was then stirred at 0 ℃ for 1 h and concentrated. The product was purified by chromatography on SiO_2 (EtOAc : hexanes = 3:1) to afford the corresponding propargyl alcohol (60 mg, 96%) without further purification: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09-8.01 (m, 4 H), 7.60-7.54 (m, 6 H), 4.48-4.36 (m, 1 H), 4.32 (s, 2 H), 4.14 (dd, 1 H, *J* = 15.2, 24.0 Hz), 3.90 (dd, 1 H, *J* = 15.2, 24.0 Hz), 3.62 (t, 1 H, *J* = 12.8 Hz), 2.04 (dt, 1 H, *J* = 14.0, 9.6 Hz), 1.47 (d, 1 H, *J* = 8.8 Hz), 1.25 (d, 1 H, *J* = 8.8 Hz), 1.21-1.15 (m, 1 H), 1.17 (t, 3 H, *J* = 4.0 Hz), 0.58 (s, 1 H), 0.47(s, 1 H), 0.00 (s, 9 H). To a solution of

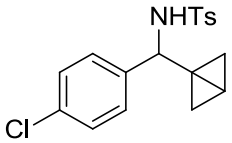
propargyl alcohol (60 mg, 0.13 mmol) was added 2,6-lutidine (0.078 mL, 0.66 mmol). The mixture was cooled to 0 ℃, treated with Dess-Martin periodinane (113 mg, 0.27 mmol) and stirred at this temperature for 8 h. The reaction was quenched by a 1:1 solution of saturated $Na_2S_2O_3$ and $NaHCO_3$ and extracted with EtOAc for 3 times. The combined organic layer was washed with brine and dried ($MgSO_4$). The product was concentrated and purified by chromatography on SiO_2 (EtOAc : hexanes = 3:1) to afford **179** as a colorless oil (48 mg, 80%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.63 (d, 1 H, *J* = 6.4 Hz), 7.96-7.86 (m, 4 H), 7.51-7.45 (m, 6 H), 6.31 (s, 1 H), 6.03 (br d, 1 H, J = 6.4 Hz), 4.37 (ddd, 1 H, *J* = 2.0, 9.2, 13.2 Hz), 4.32 (ddd, 1 H, *J* = 2.0, 9.2, 13.2 Hz), 3.6 (q, 1 H, *J* = 7.2 Hz), 2.8 (d, 1 H, *J* = 12.8 Hz), 2.52 (d, 1 H, *J* = 12.8 Hz), 1.48-1.40 (m, 2 H), 0.80 (t, 3 H, *J* = 7.2 Hz), 0.10 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 190.6, 170.8 (d, *J* = 5 Hz), 159.4, 144.0, 132.7, 132.6 (dd, *J* = 17, 9 Hz), 132.1 (dd, *J* = 17, 3 Hz), 131.4, 128.8 (dd, *J* = 20, 12 Hz), 118.6, 66.6, 62.7 (d, *J* = 3 Hz), 50.1, 48.8 (d, *J* = 4 Hz), 26.5 (d, *J* = 5 Hz), 11.0, -2.3; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{26}H_{33}NO_2SiP$ 450.2018, found 450.2007; IR(ATR) 3059, 2956, 2934, 2928, 2878, 2872, 2855, 1676, 1614, 1590, 1437, 1247, 1184, 1122, 1107, 1072, 911, 839, 751, 725, 693, 677 cm^{-1}.



181

((*Z*)-8-((*Z*)-2-(2-(2,4-Dinitrophenyl)hydrazono)ethylidene)-5-ethyl-2-(trimethylsilyl)-6-azaspiro[3.4]oct-1-en-6-yl)diphenylphosphine oxide (**181**) To solution of the aldehyde **179** (40 mg, 0.089 mmol) in methanol (1 mL) was added (2,4-dinitrophenyl)hydrazine (18 mg, 0.089

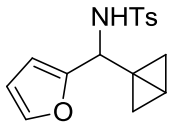
mmol). The mixture was stirred at room temperature overnight. The product is concentrated and purified by chromatography to afford the hydrazone **181** as a yellow oil (42 mg, 75%). An orange color crystal was obtained by slowly crystallizing a solution of **181** in dichloromethane and hexanes: ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.5 (s, 1 H), 9.13 (d, 1 H, *J* = 2.4 Hz), 8.31 (dd, 1 H, *J* = 9.6, 2.0 Hz), 7.99-7.88 (m, 5 H), 7.57-7.48 (m, 6 H), 7.15 (d, 1 H, *J* = 10.8 Hz), 6.39-6.35 (m, 2 H), 4.25 (dd, 1 H, *J* = 16.0, 8.0 Hz), 4.13 (dd, 1 H, *J* = 16.0, 8.0 Hz), 3.61 (q, 1 H, *J* = 6.0 Hz), 2.91 (d, 1 H, *J* = 12.8 Hz), 2.58 (d, 1 H, *J* = 12.8 Hz), 1.46 (m, 2 H), 0.82 (t, 1 H, *J* = 7.2 Hz), 0.14 (s, 9 H); HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{32}H_{36}N_5O_5NaSiP$ 652.2121 found 652.2118; IR(ATR) 3122, 3116, 3111, 3103, 3100, 3090, 3083, 3075, 3055, 2956, 2924, 2874, 2854, 1616, 1590, 1437, 1422, 1333, 1310, 1247, 1183, 1122, 1107, 1077, 1070, 1025, 1008, 997, 911, 902, 839, 753, 723, 692, 677 cm^{-1}.



157a

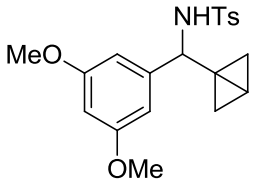
***N*-(Bicyclo[1.1.0]butan-1-yl(4-chlorophenyl)methyl)-4-methylbenzenesulfonamide (157a)**.[53] To a -78 ℃ solution of tribromo cyclopropane (2.5 g, 10 mmol) in Et_2O (100 mL) was added a 1.6 M solution of MeLi in ether (6.3 mL, 10 mmol). After 1 h, MeBr was removed *in vacuo*. Then, a 1.7 M solution of *t*-BuLi in pentane (12 mL, 20 mmol) was added dropwise at -78 ℃. After 1 hr, sulfonyl imine (1.5 g, 5.0 mmol) in THF (2 x 3.5 mL) was added. The reaction mixture was then gradually warmed to rt. After 30 min, the reaction mixture was quenched with $NaHCO_3$ (20 mL). The aqueous layer was extracted with Et_2O (3 x 50 mL). The combined organic fractions were dried ($MgSO_4$), filtered and concentrated *in vacuo*. Purification by chromatography on SiO_2 (EtOAc : hexanes = 1 : 4) afforded **157a** as a white solid (1.06 g, 61%):

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.60 (d, 2 H, *J* = 8.1 Hz), 7.20-7.13 (m, 4 H), 7.03 (d, 2 H, *J* = 8.4 Hz), 5.28 (d, 2 H, *J* = 6.6 Hz), 4.73 (d, 2 H, *J* = 6.9 Hz), 2.40 (s, 3 H), 1.46 (dd, 1 H, *J* = 3.0, 6.0 Hz), 1.26-1.22 (m, 2 H), 0.62 (s, 1 H), 0.53 (s, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.6, 138.03, 137.8, 133.5, 129.6, 128.6, 128.4, 127.3, 57.5, 32.6, 31.5, 21.6, 14.1, 1.9; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{18}H_{19}NO_2SCl$ 348.0825, found 348.0829.



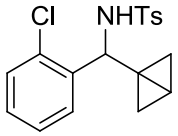
157b

***N*-(Bicyclo[1.1.0]butan-1-yl(furan-2-yl)methyl)-4-methylbenzenesulfonamide (157b)**[53]. To a -78 ℃ solution of tribromo cyclopropane (2.5 g, 10 mmol) in Et_2O (100 mL) was added a 1.6 M solution of MeLi in ether dropwise (6.3 mL, 10 mmol). After 1 h, MeBr was removed *in vacuo*. Then, a 1.7 M solution of *t*-BuLi in pentane (12 mL, 20 mmol) was added dropwise at -78 ℃. After 1 hr, sulfonyl imine (1.2 g, 5.0 mmol) in THF (2 x 3.5 mL) was added. The reaction mixture was then gradually warmed to rt. After 30 min, the reaction mixture was quenched with $NaHCO_3$ (20 mL). The aqueous layer was extracted with Et_2O (3 x 50 mL). The combined organic fractions were dried ($MgSO_4$), filtered and concentrated *in vacuo*. Purification by chromatography on SiO_2 (EtOAc : hexanes = 1 : 4) afforded **157b** as a yellowish solid (1.14 g, 75%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, 2 H, *J* = 8.0 Hz), 7.22 (d, 2 H, *J* = 8.0 Hz), 7.16 (d, 1 H, *J* = 0.8 Hz), 6.17 (dd, 1 H, *J* = 1.6, 2.8 Hz), 6.05 (d, 1 H, *J* = 2.8 Hz), 5.16 (d, 1 H, *J* = 8.0 Hz), 4.91 (d, 1 H, *J* = 8.0 Hz), 2.40 (s, 3 H), 1.44-1.42 (m, 3 H), 0.58 (s, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.3, 143.3, 142.2, 137.9, 129.5, 127.2, 110.2, 107.3 ,52.1, 32.4, 32.0, 21.6, 12.9, 2.0; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{16}H_{18}NO_3S$ 304.1007, found 304.1033.



157c

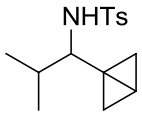
***N*-(Bicyclo[1.1.0]butan-1-yl(3,5-dimethoxyphenyl)methyl)-4-methylbenzenesulfonamide (157c).**[53] To a -78 ℃ solution of tribromo cyclopropane (2.5 g, 10 mmol) in Et_2O (100 mL) was added a 1.6 M solution of MeLi in ether (6.3 mL, 10 mmol). After 1 h, MeBr was removed *in vacuo*. Then, a 1.7 M solution of *t*-BuLi in pentane (12 mL, 20 mmol) was added dropwise at -78 ℃. After 1 hr, sulfonyl imine (1.6 g, 5.0 mmol) in THF (2 x 3.5 mL) was added. The reaction mixture was then gradually warmed to rt. After 30 min, the reaction mixture was quenched with $NaHCO_3$ (20 mL). The aqueous layer was extracted with Et_2O (3 x 50 mL). The combined organic fractions were dried ($MgSO_4$), filtered and concentrated *in vacuo*. Purification by chromatography on SiO_2 (EtOAc : hexanes = 1 : 4) afforded **157c** as a yellowish solid (1.23 g, 66%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, 2 H, *J* = 8.0 Hz), 7.18 (d, 2 H, *J* = 8.0 Hz), 6.25 (s, 1 H), 6.22 (s, 2 H), 5.45 (d, 1 H, *J* = 6.8 Hz), 4.69 (d, 1 H, *J* = 7.2 Hz), 3.66 (s, 6 H), 2.38 (s, 3 H), 1.50-1.49 (m, 1 H), 1.35-1.30 (m, 1 H), 1.30 (s, 1 H), 0.60 (s, 1 H), 0.54 (s, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.8, 143.3, 141.9, 138.0, 129.5, 127.3, 105.1, 99.6, 58.0, 55.3, 32.4, 31.9, 21.6, 14.1, 1.9; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{20}H_{24}NO_4S$ 374.1426 found 374.1398.



157d

***N*-(Bicyclo[1.1.0]butan-1-yl(2-chlorophenyl)methyl)-4-methylbenzenesulfonamide (157d).** To a -78 ℃ solution of tribromo cyclopropane (2.5 g, 10 mmol) in Et_2O (100 mL) was added a

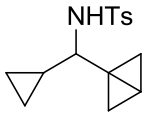
1.6 M solution of MeLi in ether (6.3 mL, 10 mmol). After 1 h, MeBr was removed *in vacuo*. Then, a 1.7 M solution of *t*-BuLi in pentane (12 mL, 20 mmol) was added dropwise at -78 ℃. After 1 hr, sulfonyl imine (1.5 g, 5.0 mmol) in THF (2 x 3.5 mL) was added. The reaction mixture was then gradually warmed to rt. After 30 min, the reaction mixture was quenched with $NaHCO_3$ (20 mL). The aqueous layer was extracted with Et_2O (3 x 50 mL). The combined organic fractions were dried ($MgSO_4$), filtered and concentrated *in vacuo*. Purification by chromatography on SiO_2 (EtOAc : hexanes = 1 : 4) afforded **157d** as a white solid (0.45 g, 25%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, 2 H, *J* = 8.4 Hz), 7.23-7.19 (m, 2 H), 7.15 (d, 2 H, *J* = 8.0 Hz), 7.10-7.07 (m, 2 H), 5.60 (d, 1 H, *J* = 7.2 Hz), 5.28 (d, 1 H, *J* = 7.2 Hz), 2.36 (s, 3 H), 1.44 (dd, 1 H, *J* = 2.8, 6.0 Hz), 1.38 (s, 1 H), 1.19 (dd, 1 H, *J* = 2.8, 6.4 Hz), 0.61 (s, 1 H), 0.48 (s, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.4, 137.3, 136.6, 132.4, 129.6, 129.5, 128.8, 128.6, 127.3, 126.8, 54.9, 33.4, 30.7, 21.6, 13.8, 2.3; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{18}H_{19}NO_2SCl$ 348.0825, found 348.0847.



157e

***N*-(1-(Bicyclo[1.1.0]butan-1-yl)-2-methylpropyl)-4-methylbenzenesulfonamide (157e).**[53] To a -78 ℃ solution of tribromo cyclopropane (2.5 g, 10 mmol) in Et_2O (100 mL) was added a 1.6 M solution of MeLi in ether (6.3 mL, 10 mmol). After 1 h, MeBr was removed *in vacuo*. Then, a 1.7 M solution of *t*-BuLi in pentane (12 mL, 20 mmol) was added dropwise at -78 ℃. After 1 hr, sulfonyl imine (1.1 g, 5.0 mmol) in THF (5 mL) was added. The reaction mixture was then gradually warmed to rt. After 30 min, the reaction mixture was quenched with $NaHCO_3$ (20 mL). The aqueous layer was extracted with Et_2O (3 x 50 mL). The combined organic fractions were

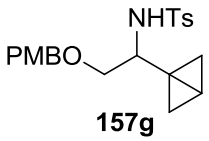
dried ($MgSO_4$), filtered and concentrated *in vacuo*. Purification by chromatography on SiO_2 (EtOAc : hexanes = 1 : 4) afforded **157e** as a yellowish solid (1.01 g, 72%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, 2 H, *J* = 8.0 Hz), 7.32 (d, 2 H, *J* = 8.0 Hz), 4.63 (d, 1 H, *J* = 8.8 Hz), 3.43 (dd, 1 H, *J* = 5.6, 8.8 Hz), 2.46 (s, 3 H), 1.85 (ds, 1 H, *J* = 5.6, 6.8 Hz), 1.43 (d, 1 H, *J* = 2.8 Hz), 0.93 (s, 1 H), 0.92 (dd, 6 H, *J* = 5.6, 6.8 Hz), 0.62 (s, 1 H), 0.41 (s, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.3, 138.5, 129.6, 126.9, 58.6, 34.6, 33.6, 28.9, 21.6, 18.9, 18.7, 11.6, -0.2; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{15}H_{22}NO_2S$ 280.1371, found 280.1394.



157f

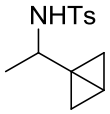
***N*-(Bicyclo[1.1.0]butan-1-yl(cyclopropyl)methyl)-4-methylbenzenesulfonamide (157f).** To a -78 ℃ solution of tribromo cyclopropane (2.5 g, 10 mmol) in Et_2O (100 mL) was added a 1.6 M solution of MeLi in ether (6.3 mL, 10 mmol). After 1 h, MeBr was removed *in vacuo*. Then, a 1.7 M solution of *t*-BuLi in pentane (12 mL, 20 mmol) was added dropwise at -78 ℃. After 1 hr, sulfonyl imine (1.1 g, 5.0 mmol) in THF (5 mL) was added. The reaction mixture was then gradually warmed to rt. After 30 min, the reaction mixture was quenched with $NaHCO_3$ (20 mL). The aqueous layer was extracted with Et_2O (3 x 50 mL). The combined organic fractions were dried ($MgSO_4$), filtered and concentrated *in vacuo*. Purification by chromatography on SiO_2 (EtOAc : hexanes = 1 : 4) afforded **157f** as a yellowish solid (0.46 g, 33%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (d, 2 H, *J* = 8.0 Hz), 7.06 (d, 2 H, *J* = 8.0 Hz), 4.61 (d, 1 H, *J* = 6.8 Hz), 2.97 (t, 1 H, *J* = 7.2 Hz), 2.2 (s, 3 H), 1.33 (dd, 1 H, *J* = 2.8, 6.0 Hz), 1.13 (dd, 1 H, *J* = 2.8, 6.0 Hz), 1.03 (s, 1 H), 0.62-0.57 (m, 1 H), 0.25 (s, 1 H), 0.22-0.16 (m, 2 H), 0.14 (s, 1 H), 0.05-0.00 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.6, 137.9, 128.9, 126.6, 57.0, 30.9 (d, *J* = 3.0 Hz), 20.9, 15.0,

11.5, 2.2, 2.1, 0.0; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{15}H_{20}NO_2S$ 278.1215, found 278.1217; IR (ATR) 3288, 3258, 3252, 3247, 3239, 3003, 2997, 2917, 2898, 2878, 2867, 1597, 1456, 1435, 1405, 1398, 1387, 1320, 1316, 1305, 1286, 1156, 1133, 1094, 1016, 986, 958, 908, 885, 809 cm^{-1}.



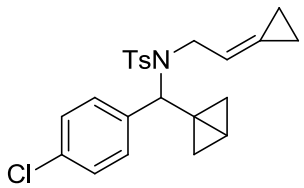
157g

***N*-(1-(Bicyclo[1.1.0]butan-1-yl)-2-((4-methoxybenzyl)oxy)ethyl)-4-methylbenzenesulfonamide (157g)**. To a -78 ℃ solution of tribromo cyclopropane (2.5 g, 10 mmol) in Et_2O (100 mL) was added a 1.6 M solution of MeLi in ether (6.3 mL, 10 mmol). After 1 h, MeBr was removed *in vacuo*. Then, a 1.7 M solution of *t*-BuLi in pentane (12 mL, 20 mmol) was added dropwise at -78 ℃. After 1 hr, sulfonyl imine (1.7 g, 5.0 mmol) in THF (5 mL) was added. The reaction mixture was then gradually warmed to rt. After 30 min, the reaction mixture was quenched with $NaHCO_3$ (20 mL). The aqueous layer was extracted with Et_2O (3 x 50 mL). The combined organic fractions were dried ($MgSO_4$), filtered and concentrated *in vacuo*. Purification by chromatography on SiO_2 (EtOAc : hexanes = 1 : 4) afforded **157g** as a yellowish solid (1.07 g, 55%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, 2 H, *J* = 8.0 Hz), 7.16 (d, 2 H, *J* = 8.0 Hz), 7.06 (d, 2 H, *J* = 8.4 Hz), 6.79 (d, 2 H, *J* = 8.4 Hz), 4.91 (d, 1 H, *J* = 7.6 Hz), 4.23 (s, 2 H), 3.75-3.62 (m, 1 H), 3.74 (s, 3 H), 3.37 (dd, 1 H, *J* = 4.8, 9.6 Hz), 3.30 (dd, 1 H, *J* = 4.8, 9.6 Hz), 2.33 (s, 3 H), 1.42 (dd, 1 H, *J* = 2.8, 6.0 Hz), 1.13 (dd, 1 H, *J* = 2.8, 6.0 Hz), 1.29 (s, 1 H), 0.39 (s, 1 H), 0.32 (s, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.3, 143.2, 138.0, 129.7, 129.5, 129.3, 127.2, 113.8, 72.8, 71.3, 55.3, 52.8, 31.4, 31.3, 21.5, 11.1, 1.7; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{21}H_{26}NO_4S$ 388.1583, found 388.1580; IR (ATR) 3279, 3271, 2924, 2863, 1610, 1512, 1456, 1452, 1439, 1420, 1405, 1322, 1301, 1243, 1156, 1087, 1031, 967 cm^{-1}.



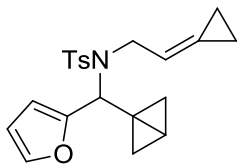
157h

***N*-(1-(Bicyclo[1.1.0]butan-1-yl)ethyl)-4-methylbenzenesulfonamide (157h).** To a -78 ℃ solution of tribromo cyclopropane (2.5 g, 10 mmol) in Et_2O (100 mL) was added a 1.6 M solution of MeLi in ether (6.3 mL, 10 mmol). After 1 h, MeBr was removed *in vacuo*. Then, a 1.7 M solution of *t*-BuLi in pentane (12 mL, 20 mmol) was added dropwise at -78 ℃. After 1 hr, sulfonyl imine (1.0 g, 5.0 mmol) in THF (5 mL) was added. The reaction mixture was then gradually warmed to rt. After 30 min, the reaction mixture was quenched with $NaHCO_3$ (20 mL). The aqueous layer was extracted with Et_2O (3 x 50 mL). The combined organic fractions were dried ($MgSO_4$), filtered, and concentrated *in vacuo*. Purification by chromatography on SiO_2 (EtOAc : hexanes = 1 : 4) afforded **157h** as a yellowish solid (0.50 g, 40%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.79 (d, 2 H, *J* = 8.1 Hz), 7.32 (d, 2 H, *J* = 8.1 Hz), 4.55 (d, 1 H, *J* = 7.2 Hz), 3.83 (p, 1 H, *J* = 7.2 Hz), 2.45 (s, 3 H), 1.51 (dd, 1 H, *J* = 3.0, 6.0 Hz), 1.31-1.27 (m, 2 H), 1.16 (d, 3 H, *J* = 7.2 Hz), 0.44 (s, 1 H), 0.41 (s, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.5, 136.7, 127.9, 125.5, 48.2, 30.6, 28.2, 19.9, 18.8, 12.0, 0.0; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{13}H_{18}NO_2S$ 252.1058, found 252.1030; IR (ATR) 2954, 2947, 2924, 2867, 2852, 1597, 1448, 1420, 1411, 1377, 1322, 1303, 1288, 1154, 1107, 1083, 1044, 1033, 1020, 969, 951, 911, 889, 863, 815, 802 cm^{-1}.



263a

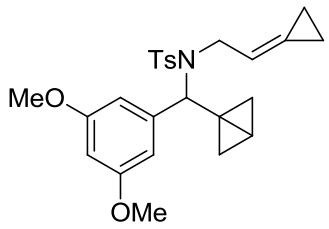
***N*-(Bicyclo[1.1.0]butan-1-yl(4-chlorophenyl)methyl)-*N*-(2-cyclopropylideneethyl)-4-methyl-benzenesulfonamide (263a).** A solution of **157a** (219 mg, 0.63 mmol) in THF (3 mL) was added to an ice-cooled suspension of NaH (22.4 mg, 0.84 mmol, 90% in mineral oil) in THF (3 mL). After stirring at rt for 20 min the solution was transferred *via* cannula over a solution of tosylate (100 mg, 0.420 mmol) and $Pd(PPh_3)_4$ (22.2 mg, 0.021 mmol) in THF (2 mL) previously stirred for 15 min at rt. The reaction mixture was allowed to stir for 3 h at rt, poured into water and extracted with ether. The combined organic layers were dried, filtered and concentrated and the crude product was purified by chromatography on SiO_2 (Et_2O : hexanes = 1 : 100 to 1 : 20) to give **263a** as a colorless oil (148 mg, 85%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.59 (d, 2 H, *J* = 8.1 Hz), 7.22-7.18 (m, 4 H), 7.13 (d, 2 H, *J* = 8.7 Hz), 5.61 (d, 1 H, *J* = 2.8, 6.3 Hz), 5.21 (d, 1 H, *J* = 6.6 Hz), 2.4 (s, 3 H), 1.55 (dd, 1 H, *J* = 3.0, 6.3 Hz), 1.47 (s, 1 H), 1.24 (dd, 1 H, *J* = 3.0, 6.3 Hz), 0.98-0.94 (m, 4 H), 0.69 (s, 1 H), 0.57 (s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.1, 138.6, 138.1, 133.3, 129.4, 129.2, 128.5, 127.4, 125.2, 115.6, 62.0, 47.9, 34.2, 32.0, 21.6, 12.1, 3.8, 2.4, 1.9; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{23}H_{25}NO_2SCl$ 414.1295, found 414.1282; IR (ATR) 2978, 2926, 2867, 1596, 1489, 1435, 1405, 1335, 1305, 1288, 1156, 1117, 1090, 1027, 1012, 951, 910, 897, 848, 813, 762, 746, 731 cm^{-1}.



263b

***N*-(Bicyclo[1.1.0]butan-1-yl(furan-2-yl)methyl)-*N*-(2-cyclopropylideneethyl)-4-methyl benzenesulfonamide (263b).** A solution of **157b** (190 mg, 0.63 mmol) in THF (3 mL) was added to an ice-cooled suspension of NaH (22.4 mg, 0.84 mmol, 90% in mineral oil) in THF (3

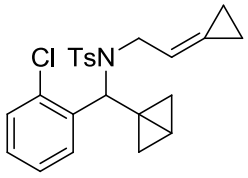
mL). After stirring at rt for 20 min the solution was transferred *via* cannula over a solution of tosylate (100 mg, 0.420 mmol) and $Pd(PPh_3)_4$ (22.2 mg, 0.021 mmol) in THF (2 mL) previously stirred for 15 min at rt. The reaction mixture was allowed to stir for 3 h at rt, poured into water and extracted with ether. The combined organic layers were dried, filtered and concentrated and the crude product was purified by chromatography on SiO_2 (Et_2O : hexanes = 1 : 100 to 1 : 20) to give **263b** as a colorless oil (129 mg, 83%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (d, 2 H, *J* = 8.0 Hz), 7.22-7.19 (m, 3 H), 6.25-6.22 (m, 1 H), 6.17 (d, 1 H, *J* = 3.3 Hz), 5.58 (tt, 1 H, *J* = 2.1, 6.3 Hz), 5.52 (s, 1 H), 4.15 (dd, 2 H, *J* = 1.2, 6.6 Hz), 2.39 (s, 3 H), 1.60-1.57 (m, 2 H), 1.49 (dd, 1 H, *J* = 1.8, 5.4 Hz), 0.98-0.94 (m, 4 H), 0.66 (s, 1 H), 0.60 (s, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.4, 142.9, 141.9, 138.4, 129.3, 127.5, 124.6, 115.5, 110.3, 108.5, 56.8, 47.1, 33.8, 32.6, 21.6, 11.2, 3.3, 2.3, 1.8; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{21}H_{24}NO_3S$ 370.1477, found 370.1493; IR (ATR) 2975, 2924, 2880, 2865, 2852, 1596, 1495, 1435, 1398, 1387, 1379, 1362, 1340, 1325, 1308, 1290, 1273, 1159, 1133, 1118, 1098, 1090, 1070, 1033, 1008, 928, 915, 893, 884 cm^{-1}.



263c

***N*-(Bicyclo[1.1.0]butan-1-yl(3,5-dimethoxyphenyl)methyl)-N-(2-cyclopropylideneethyl)-4-methylbenzenesulfonamide (263c).** A solution of **157c** (235 mg, 0.63 mmol) in THF (3 mL) was added to an ice-cooled suspension of NaH (17.9 mg, 0.67 mmol, 90% in mineral oil) in THF (3 mL). After stirring at rt for 20 min the solution was transferred *via* cannula over a solution of tosylate (100 mg, 0.420 mmol) and $Pd(PPh_3)_4$ (22.2 mg, 0.021 mmol) in THF (2 mL) previously

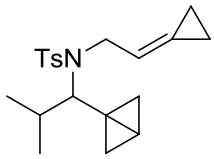
stirred for 15 min at rt. The reaction mixture was allowed to stir for 3 h at rt, poured into water and extracted with ether. The combined organic layers were dried, filtered and concentrated and the crude product was purified by chromatography on SiO_2 (Et_2O : hexanes = 1 : 100 to 1 : 20) to give **263c** as a colorless oil (168 mg, 91%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (d, 2 H, *J* = 8.4 Hz), 7.62 (d, 2 H, *J* = 8.4 Hz), 6.30 (s, 3 H), 5.65 (m, 1 H), 5.27 (s, 1 H), 4.19 (d, 2 H, *J* = 6.4 Hz), 3.66 (s, 6 H), 2.39 (s, 3 H), 1.60 (dd, 1 H, *J* = 2.8, 6.0 Hz), 1.53 (s, 1 H), 1.34 (dd, 1 H, *J* = 2.8, 6.0 Hz), 0.98-0.96 (m, 4 H), 0.71 (s, 1 H), 0.60 (s, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.6, 142.9, 141.8, 138.6, 129.3, 127.4, 124.9, 115.7, 106.1, 99.3, 62.5, 55.2, 47.8, 33.9, 32.4, 21.5, 12.1, 3.8, 2.3, 1.8; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{25}H_{30}NO_4S$ 440.1896, found 440.1895; IR (ATR) 2930, 2837, 1596, 1458, 1443, 1428, 1335, 1322, 1316, 1303, 1290, 1204, 1154, 1096, 1066, 1059, 1027, 1020, 1001, 925, 908, 897, 880, 837, 813 cm^{-1}.



263d

***N*-(Bicyclo[1.1.0]butan-1-yl(2-chlorophenyl)methyl)-N-(2-cyclopropylideneethyl)-4-methylbenzenesulfonamide (263d).** A solution of **157d** (219 mg, 0.63 mmol) in THF (3 mL) was added to an ice-cooled suspension of NaH (22.4 mg, 0.84 mmol, 90% in mineral oil) in THF (3 mL). After stirring at rt for 20 min the solution was transferred *via* cannula over a solution of tosylate (100 mg, 0.420 mmol) and $Pd(PPh_3)_4$ (22.2 mg, 0.021 mmol) in THF (2 mL) previously stirred for 15 min at rt. The reaction mixture was allowed to stir for 3 h at rt, poured into water and extracted with ether. The combined organic layers were dried, filtered and concentrated and the crude product was purified by chromatography on SiO_2 (Et_2O : hexanes = 1 : 100 to 1 : 20)

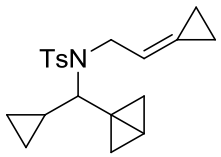
to give **263d** as a colorless oil (162 mg, 93%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (d, 2 H, *J* = 8.0 Hz), 7.51-7.48 (m, 1 H), 7.51-7.48 (m, 1 H), 7.27-7.25 (m, 1 H), 7.18-7.12 (m, 4 H), 5.68 (s, 2 H), 4.40 (dd, 1 H, *J* = 1.2, 16.0 Hz), 4.29 (dd, 1 H, *J* = 6.8, 16.0 Hz), 2.37 (s, 3 H), 1.63 (dd, 1 H, *J* = 2.4, 6.4 Hz), 1.55 (s, 1 H), 1.13 (dd, 1 H, *J* = 2.8, 6.0 Hz), 0.98-0.92 (m, 4 H), 0.69 (s, 1 H), 0.54 (s, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.9, 138.1, 137.3, 132.9, 129.8, 129.5, 129.2, 128.6, 127.5, 126.7, 125.1, 115.6, 59.9, 48.8, 35.6, 31.2, 21.6, 11.9, 3.7, 2.4, 1.9; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{23}H_{25}NO_2SCl$ 414.1295, found 414.1294; IR (ATR) 3024, 1597, 1481, 1421, 1321, 1141, 1098, 1025, 1012, 916, 887, 805, 717, 736, 748, 763 cm^{-1}.



263e

***N*-(1-(Bicyclo[1.1.0]butan-1-yl)-2-methylpropyl)-*N*-(2-cyclopropylideneethyl)-4-methyl benzenesulfonamide (263e).** A solution of **157e** (176 mg, 0.63 mmol) in THF (3 mL) was added to an ice-cooled suspension of NaH (22.4 mg, 0.84 mmol, 90% in mineral oil) in THF (3 mL). After stirring at rt for 20 min the solution was transferred *via* cannula over a solution of tosylate (100 mg, 0.420 mmol) and $Pd(PPh_3)_4$ (22.0 mg, 0.021 mmol) in THF (2 mL) previously stirred for 15 min at rt. The reaction mixture was allowed to stir for 3 h at rt, poured into water and extracted with ether. The combined organic layers were dried, filtered and concentrated and the crude product was purified by chromatography on SiO_2 (Et_2O : hexanes = 1 : 100 to 1 : 20) to give **263e** as a colorless oil (131 mg, 90%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (d, 2 H, *J* = 8.0 Hz), 7.23 (d, 2 H, *J* = 8.0 Hz), 5.79 (bs, 1 H), 4.13 (dd, 1 H, *J* = 7.6, 15.6 Hz), 4.02 (dd, 1 H, *J* = 6.4, 16.0 Hz), 3.85 (d, 1 H, *J* = 10.4 Hz), 2.40 (s, 3 H), 1.90-1.87 (m, 1 H), 1.55-1.53 (m, 1 H),

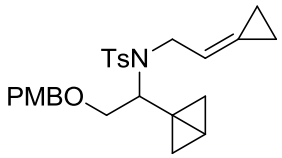
1.03 (bs, 4 H), 0.99 (d, 1 H, *J* = 6.4 Hz), 0.97-0.94 (m, 1 H), 0.88 (dd, 1 H, *J* = 6.8, 11.2 Hz), 0.80 (d, 1 H, *J* = 6.8 Hz), 0.35 (s, 1 H), 0.15 (s, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.6, 139.2, 129.2, 127.5, 124.4, 115.9, 64.2, 46.2, 31.1, 30.9, 29.8, 21.5, 21.1, 20.5, 11.4, 5.1, 2.4, 1.7; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{20}H_{28}NO_2S$ 346.1841, found 346.1842; IR (ATR) 2977, 2973, 2956, 2924, 2870, 1733, 1724, 1719, 1596, 1493, 1465, 1458, 1448, 1437, 1387, 1333, 1303, 1286, 1154, 1117, 1090, 1020, 1012, 1001, 975, 960, 926, 904, 887, 811 cm^{-1}.



263f

***N*-(Bicyclo[1.1.0]butan-1-yl(cyclopropyl)methyl)-*N*-(2-cyclopropylideneethyl)-4-methyl-benzenesulfonamide (263f).** A solution of **157f** (175 mg, 0.63 mmol) in THF (3 mL) was added to an ice-cooled suspension of NaH (22.4 mg, 0.84 mmol, 90% in mineral oil) in THF (3 mL). After stirring at rt for 20 min the solution was transferred *via* cannula over a solution of tosylate (100 mg, 0.420 mmol) and $Pd(PPh_3)_4$ (22.0 mg, 0.021 mmol) in THF (2 mL) previously stirred for 15 min at rt. The reaction mixture was allowed to stir for 3 h at rt, poured into water and extracted with ether. The combined organic layers were dried, filtered and concentrated and the crude product was purified by chromatography on SiO_2 (Et_2O : hexanes = 1 : 100 to 1 : 20) to give **263f** as a colorless oil (110 mg, 76%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (d, 2 H, *J* = 8.0 Hz), 7.09 (d, 2 H, *J* = 8.0 Hz), 5.71 (bs, 1 H), 4.08-4.05 (m, 2 H), 3.26 (d, 1 H, *J* = 9.6 Hz), 2.4 (s, 3 H), 1.55 (dd, 1 H, *J* = 2.8, 6.0 Hz), 1.42 (s, 1 H), 1.06 (dd, 1 H, *J* = 2.8, 6.0 Hz), 0.87-0.80 (m, 5 H), 0.37-0.33 (m, 2 H), 0.29-0.22 (m, 3 H), 0.02-0.00 (m, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.7, 139.1, 129.3, 127.4, 124.1, 116.6, 64.1, 46.3, 33.3, 31.2, 21.5, 13.8, 11.3, 5.7, 3.4, 2.4, 1.8;

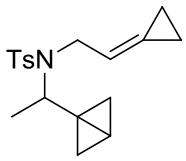
HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{20}H_{26}NO_2S$ 344.1684, found 344.1672; IR (ATR) 3001, 2997, 2977, 2951, 2921, 2869, 1597, 1456, 1435, 1396, 1379, 1333, 1305, 1288, 1154, 1131, 1118, 1092, 1021, 1007, 979, 962, 939, 925, 897, 859, 813, 772 cm^{-1}.



263g

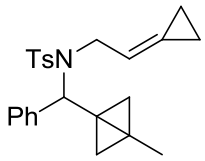
***N*-(1-(Bicyclo[1.1.0]butan-1-yl)-2-((4-methoxybenzyl)oxy)ethyl)-*N*-(2-cyclopropylidene-ethyl)-4-methylbenzenesulfonamide (263g).** A solution of **157g** (244 mg, 0.63 mmol) in THF (3 mL) was added to an ice-cooled suspension of NaH (22.4 mg, 0.84 mmol, 90% in mineral oil) in THF (3 mL). After stirring at rt for 20 min the solution was transferred *via* cannula over a solution of tosylate (100 mg, 0.420 mmol) and $Pd(PPh_3)_4$ (22.0 mg, 0.021 mmol) in THF (2 mL) previously stirred for 15 min at rt. The reaction mixture was allowed to stir for 3 h at rt, poured into water and extracted with ether. The combined organic layers were dried, filtered and concentrated and the crude product was purified by chromatography on SiO_2 (Et_2O : hexanes = 1 : 100 to 1 : 20) to give the product **263g** as a colorless oil (118 mg, 62%): ^1H NMR (300 MHz, $CDCl_3$) δ 7.63 (d, 2 H, *J* = 8.1 Hz), 7.13 (d, 2 H, *J* = 8.1 Hz), 7.08 (d, 2 H, *J* = 8.4 Hz), 6.79 (d, 2 H, *J* = 8.7 Hz), 5.69 (m, 1 H), 4.31-4.19 (m, 3 H), 4.06 (d, 2 H, *J* = 6.6 Hz), 3.74 (s, 3 H), 3.49 (dd, 1 H, *J* = 6.0, 9.6 Hz), 3.37 (dd, 1 H, *J* = 8.4, 9.6 Hz), 2.32 (s, 3 H), 1.48-1.43 (m, 2 H), 1.01 (dd, 1 H, *J* = 3.0, 6.3 Hz), 0.95-0.89 (m, 4 H), 0.38 (s, 1 H), 0.29 (s, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.4, 142.9, 138.6, 130.1, 129.5, 129.4, 127.5, 124.7, 116.4, 113.9, 72.7, 70.4, 57.8, 55.4, 46.6, 32.7, 31.0, 21.6, 8.9, 3.2, 2.4, 1.9; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{26}H_{32}NO_4S$ 454.2052, found 454.2061; IR (ATR) 2917, 2885, 2863, 2848, 1717, 1707, 1700, 1605, 1584,

1512, 1497, 1465, 1458, 1437, 1405, 1361, 1333, 1303, 1286, 1273, 1249, 1158, 1098, 1090, 1029, 1007 cm^{-1}.



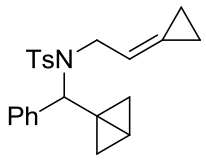
263h

***N*-(1-(Bicyclo[1.1.0]butan-1-yl)ethyl)-*N*-(2-cyclopropylideneethyl)-4-methylbenzene-sulfonamide (263h).** A solution of **157h** (158 mg, 0.63 mmol) in THF (3 mL) was added to an ice-cooled suspension of NaH (22.4 mg, 0.84 mmol, 90% in mineral oil) in THF (3 mL). After stirring at rt for 20 min the solution was transferred *via* cannula over a solution of tosylate (100 mg, 0.42 mmol) and $Pd(PPh_3)_4$ (22.2 mg, 0.021 mmol) in THF (2 mL) previously stirred for 15 min at rt. The reaction mixture was allowed to stir for 3 h at rt, poured into water and extracted with ether. The combined organic layers were dried, filtered and concentrated and the crude product was purified by chromatography on SiO_2 (Et_2O : hexanes = 1 : 100 to 1 : 20) to give **263h** as a colorless oil (60 mg, 45%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.73 (d, 2 H, *J* = 8.4 Hz), 7.13 (d, 2 H, *J* = 8.7 Hz), 5.88-5.83 (m, 1 H), 4.37 (q, 1 H, *J* = 6.9 Hz), 4.22 (dd, 1 H, *J* = 7.2, 15.9 Hz), 4.12 (ddt, 1 H, *J* = 1.5, 5.7, 15.9 Hz), 2.44 (s, 3 H), 1.56 (dd, 1 H, *J* = 3.0, 6.3 Hz), 1.29-1.26 (m, 1 H), 1.23 (dd, 1 H, *J* = 3.0, 6.3 Hz), 1.13 (d, 3 H, *J* = 6.9 Hz), 1.09-1.05 (m, 4 H), 0.48 (d, 2 H, *J* = 3.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.8, 139.0, 129.4, 127.3, 124.2, 116.6, 54.7, 45.6, 34.3, 30.3, 21.6, 17.9, 11.8, 2.4, 2.2, 1.9; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{18}H_{24}NO_2S$ 318.1528, found 318.1514; IR (ATR) 3049, 3038, 3031, 3018, 2977, 2949, 2928, 2880, 2874, 1597, 1493, 1450, 1437, 1390, 1357, 1333, 1303, 1288, 1150, 1120, 1096, 1066, 1019, 1003, 988, 958, 887, 872, 857, 813, 770 cm^{-1}.



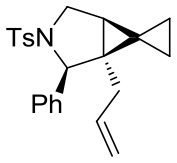
263i

***N*-(2-Cyclopropylideneethyl)-4-methyl-*N*-((3-methylbicyclo[1.1.0]butan-1-yl)(phenyl) methyl)benzenesulfonamide (263i).** A solution of tosyl amide **72**[53] (206 mg, 0.63 mmol) in THF (3 mL) was added to an ice-cooled suspension of NaH (22.4 mg, 0.84 mmol, 90% in mineral oil) in THF (3 mL). After stirring at rt for 20 min the solution was transferred *via* cannula over a solution of tosylate (100 mg, 0.42 mmol) and $Pd(PPh_3)_4$ (22.2 mg, 0.021 mmol) in THF (2 mL) previously stirred for 15 min at rt. The reaction mixture was allowed to stir for 3 h at rt, poured into water and extracted with ether. The combined organic layers were dried, filtered and concentrated and the crude product was purified by chromatography on SiO_2 (Et_2O : hexanes = 1 : 100 to 1 : 20) to give **263i** as a colorless oil (155 mg, 94%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.59 (d, 2 H, *J* = 8.1 Hz), 7.22-7.18 (m, 4 H), 7.13 (d, 2 H, *J* = 8.7 Hz), 5.61 (d, 1 H, *J* = 2.8, 6.3 Hz), 5.21 (d, 1 H, *J* = 6.6 Hz), 2.4 (s, 3 H), 1.55 (dd, 1 H, *J* = 3.0, 6.3 Hz), 1.47 (s, 1 H), 1.24 (dd, 1 H, *J* = 3.0, 6.3 Hz), 0.98-0.94 (m, 4 H), 0.69 (s, 1 H), 0.57 (s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.1, 138.6, 138.1, 133.3, 129.4, 129.2, 128.5, 127.4, 125.2, 115.6, 62.0, 47.9, 34.2, 32.0, 21.6, 12.1, 3.8, 2.4, 1.9; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{23}H_{25}NO_2SCl$ 414.1295, found 414.1282; IR (ATR) 2919, 2852, 1493, 1452, 1407, 1374, 1333, 1303, 1288, 1156, 1137, 1118, 1090, 1020, 1010, 1003, 975, 895, 813 cm^{-1}.



263

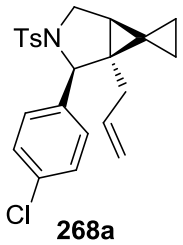
***N*-(Bicyclo[1.1.0]butan-1-yl(phenyl)methyl)-*N*-(2-cyclopropylideneethyl)-4-methylbenzene-sulfonamide** (**263**)[53] To a 0 ℃ solution of tosyl amide **157**[53] (80 mg, 0.26 mmol), alcohol (68 mg, 0.77 mmol), and 1,1'-(azodicarbonyl) dipiperidine (73 mg, 0.28 mmol) was added tri-butyl phosphine (0.068 mL, 0.26 mmol). After 24 h, the mixture was added another portion of 1,1'-(azodicarbonyl) dipiperidine (73 mg, 0.28 mmol) and tri-butyl phosphine (0.068 mL, 0.26 mmol). After 30 h, the reaction mixture was added 15 mL hexanes. The solid was filtered and the filtrate was concentrated and purified by column chromatography (EtOAc : hexanes = 1:19 to 1:9) to yield **263** as a colorless oil slowly crystallized in freezer (89 mg, 92%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, 2 H, *J* = 11.2 Hz), 7.26-7.14 (m, 7 H), 5.61 (tt, 1 H, *J* = 8.4, 2.8 Hz), 5.35 (s, 1 H), 4.21 (d, 1 H, *J* = 8.8 Hz), 2.39 (s, 3 H), 1.58 (dd, 1 H, *J* = 8.8, 4.0 Hz), 1.49 (bs, 1 H), 1.27 (dd, 1 H, *J* = 8.8, 4.0 Hz), 0.98-0.92 (m, 4 H), 0.70 (s, 1 H), 0.56 (s, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.1, 131.6, 136.9, 127.5, 126.5, 126.0, 125.6, 123.3, 113.9, 60.7, 46.1, 32.3, 30.2, 19.7, 10.5, 1.8, 0.5.



268

1-Allyl-2-phenyl-3-tosyl-3-azaspiro[bicyclo[3.1.0]hexane-6,1'-cyclopropane] (**268**) To a solution of **263** (10 mg, 0.026 mmol) in 0.5 mL dioxane was added tris(dibenzylideneacetone) dipalladium powder (3.0 mg, 2.6 μmol) and triisopropyl phosphite (3.0 mg, 0.01 mmol). The

solution was degassed and then heated at 110 ℃ in the oil bath. After 3h, the mixture was concentrated and purified by chromatography (EtOAc : hexanes = 1:20) to afford **268** as a colorless semisolid (6.5 mg, 65%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (d, 2 H, *J* = 8.0 Hz), 7.33-7.20 (m, 7 H), 5.49-5.39 (m, 1 H), 4.98 (d, 1 H, *J* = 10.8 Hz), 4.95 (s, 1 H), 4.42 (s, 1 H), 3.66 (d, 1 H, *J* = 9.6 Hz), 3.43 (dd, 1 H, *J* = 9.6, 4.8 Hz), 2.44 (s, 3 H), 2.34 (dd, 1 H, *J* = 14.8, 8.0 Hz), 1.94 (dd, 1 H, *J* = 15.2, 4.8 Hz), 1.46 (d, 1 H, *J* = 4.8 Hz), 0.95-0.87 (m, 2 H), 0.54 (p, 1 H, *J* = 4.4 Hz), 0.46 (p, 1 H, *J* = 4.4 Hz);^{13}C NMR (100 MHz, $CDCl_3$) δ 143.5, 138.1, 134.9, 129.3, 128.3, 127.8, 127.5, 127.2, 117.3, 66.6, 51.0, 37.6, 35.2, 24.1, 21.6, 21.4, 3.9, 3.0; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{23}H_{24}NO_2S$ 378.1528, found 378.1517; IR (ATR) 3068, 3033, 2997, 2971, 2954, 2926, 2867, 2846, 1597, 1491, 1454, 1437, 1361, 1346, 1338, 1301, 1290, 1161, 1090, 1023, 1012, 997, 919, 837, 813, 703 cm^{-1}.

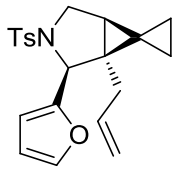


268a

1-Allyl-2-(4-chlorophenyl)-3-tosyl-3-azaspiro[bicyclo[3.1.0]hexane-6,1'-cyclopropane] (268a)

To a solution of **263a** (20 mg, 0.048 mmol) in 0.90 mL dioxane was added bis(dibenzylideneacetone)palladium (2.8 mg, 4.8 μmol, 56 μL in 50 mg/mL solution in dioxane) and triisopropyl phosphine (1.6 mg, 9.7 μmol, 35 μL in 45 mg/mL solution in dioxane). The solution was carefully degassed and then heated at 130 ℃ in microwave. After 30 mins, the mixture was concentrated and purified by chromatography (EtOAc : hexanes = 1:100 to 1:20) to afford **268a** as a colorless oil (14.2 mg, 71%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.61 (d, 2 H, *J* = 8.4 Hz), 7.34-7.27 (m, 7 H), 5.62-5.55 (m, 1 H), 5.02 (s, 1 H), 4.97 (s, 1 H), 4.44 (s, 1 H), 3.68 (d, 1 H, *J* = 9.6 Hz), 3.45 (dd, 1 H, *J* = 5.1, 9.6 Hz), 2.48 (s, 3 H), 2.33 (dd, 1 H, *J* = 8.4, 15.6 Hz),

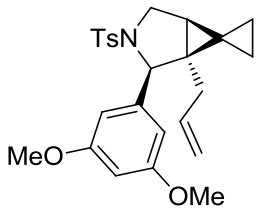
1.98 (dd, 1 H, *J* = 3.3, 15.6 Hz), 1.50 (d, 1 H, *J* = 4.8 Hz), 0.93 (t, 1 H, *J* = 7.2 Hz), 0.62-0.56 (m, 1 H), 0.53-0.47 (m, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.7, 136.8, 134.7, 132.9, 132.6, 129.4, 129.1, 128.2, 127.7, 117.5, 66.0, 50.9, 37.4, 35.1, 24.2, 21.6, 21.3, 3.9, 2.9; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{23}H_{25}NO_2SCl$ 414.1295, found 414.1277; IR (ATR) 3068, 2990, 2975, 2954, 2926, 2913, 2880, 2869, 1637, 1597, 1491, 1469, 1448, 1437, 1424, 1411, 1346, 1303, 1292, 1163, 1089, 1059, 1025, 1014, 999, 982, 928, 919, 893, 839, 829, 822, 813, 725, 710 cm^{-1}.



268b

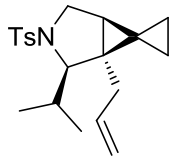
1-Allyl-2-(furan-2-yl)-3-tosyl-3-azaspiro[bicyclo[3.1.0]hexane-6,1'-cyclopropane] (268b). To a solution of **263b** (20 mg, 0.054 mmol) in 0.50 mL dioxane was added bis(dibenzylideneacetone)palladium (3.1 mg, 5.4 μmol, 62 μL in 50 mg/mL solution in dioxane) and triisopropyl phosphine (1.8 mg, 11 μmol, 39 μL in 45 mg/mL solution in dioxane). The solution was carefully degassed and then heated at 130 ℃ in microwave. After 30 mins, the mixture was concentrated and purified by chromatography (EtOAc : hexanes = 1:100 to 1:20) to afford **268b** as a colorless oil (13.0 mg, 65%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, 2 H, *J* = 8.0 Hz), 7.25 (d, 2 H, *J* = 8.0 Hz), 7.20 (s, 1 H), 6.23 (s, 2 H), 5.53-5.51 (m, 1 H), 4.93 (s, 1 H), 4.89 (s, 1 H), 4.47 (s, 1 H), 3.60 (d, 1 H, *J* = 9.6 Hz), 3.46 (dd, 1 H, *J* = 4.8, 9.6 Hz), 2.42 (s, 3 H), 2.26 (dd, 1 H, *J* = 8.0, 15.2 Hz), 2.05 (dd, 1 H, *J* = 6.0, 15.2 Hz), 1.50 (d, 1 H, *J* = 4.8 Hz), 1.10-1.06 (m, 1 H), 0.9-0.85 (m, 1 H), 0.72-0.65 (m, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.5, 143.1, 142.0, 134.5, 134.2, 129.2, 127.9, 117.1, 110.1, 109.9, 60.1, 50.5, 36.2, 35.1, 23.3, 21.5, 20.7, 4.3, 3.6; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{21}H_{24}NO_3S$ 370.1477, found 370.1492; IR

(ATR) 2993, 2951, 2921, 2865, 2850, 1801, 1793, 1784, 1778, 1774, 1760, 1752, 1733, 1728, 1719, 1702, 1685, 1638, 1597, 1493, 1465, 1458, 1448, 1437, 1348, 1305, 1288, 1223, 1182, 1161, 1092, 1031, 1012, 917, 885, 837, 813, 800,734, 708 cm^{-1}.



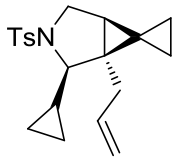
268c

1-Allyl-2-(3,5-dimethoxyphenyl)-3-tosyl-3-azaspiro[bicyclo[3.1.0]hexane-6,1'-cyclopropane] (268c). To a solution of **263c** (20 mg, 0.045 mmol) in 0.90 mL dioxane was added bis(dibenzylideneacetone)palladium (2.6 mg, 4.5 μmol, 53 μL in 50 mg/mL solution in dioxane) and triisopropyl phosphine (1.5 mg, 9.1 μmol, 33 μL in 45 mg/mL solution in dioxane). The solution was carefully degassed and then heated at 130 ℃ in microwave. After 30 mins, the mixture was concentrated and purified by chromatography (EtOAc : hexanes = 1 : 20) to afford the product **268c** as a colorless oil (8.4 mg, 42%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.63 (d, 2 H, *J* = 8.1 Hz), 7.31 (d, 2 H, *J* = 10.2 Hz), 6.49 (d, 2 H, *J* = 2.1 Hz), 6.35 (t, 1 H, *J* = 2.1 Hz), 5.65-5.52 (m, 1 H), 5.03, (d, 1 H, *J* = 9.6 Hz), 4.98 (s, 1 H), 4.42 (s, 1 H), 3.79 (s, 6 H), 3.67 (d, 1 H, *J* = 9.6 Hz), 3.50 (dd, 1 H, *J* = 4.8, 9.6 Hz), 2.47 (s, 3 H), 2.41 (dd, 1 H, *J* = 8.4, 15.3 Hz), 1.99 (dd, 1 H, *J* = 5.1, 15.3 Hz), 1.49 (d, 1 H, *J* = 5.1 Hz), 1.04-1.01 (m, 1 H), 0.99-0.92 (m, 1 H), 0.61-0.51 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.0, 143.5, 140.5, 134.9, 133.1, 129.3, 128.2, 117.4, 106.2, 99.2, 66.7, 55.2, 51.0, 37.7, 35.3, 24.1, 21.6, 21.4, 4.1, 3.2; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{25}H_{30}NO_4S$ 440.1896, found 440.1902; IR (ATR) 2993, 2954, 2932, 2874, 2850, 2837, 1748, 1637, 1596, 1493, 1458, 1428, 1402, 1346, 1305, 1292, 1260, 1202, 1152, 1090, 1059, 1029, 1014, 993, 939, 925, 889, 839, 815, 738 cm^{-1}.



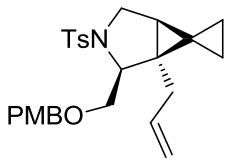
268e

1-Allyl-2-isopropyl-3-tosyl-3-azaspiro[bicyclo[3.1.0]hexane-6,1'-cyclopropane] (268e). To a solution of **263e** (20 mg, 0.058 mmol) in 0.90 mL dioxane was added bis(dibenzylideneacetone)palladium (3.4 mg, 5.8 μmol, 67 μL in 50 mg/mL solution in dioxane) and triisopropyl phosphine (1.9 mg, 12 μmol, 42 μL in 45 mg/mL solution in dioxane). The solution was carefully degassed and then heated at 130 ℃ in microwave. After 30 mins, the mixture was concentrated and purified by chromatography (EtOAc : hexanes = 1 : 20) to afford **268e** as a colorless oil (6.2 mg, 31%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, 2 H, *J* = 8.0 Hz), 7.36 (d, 2 H, *J* = 8.0 Hz), 5.38-5.27 (m, 1 H), 4.87 (d, 1 H, *J* = 10.4 Hz), 4.77 (d, 1 H, *J* = 16.8 Hz), 3.86 (dd, 1 H, *J* = 6.8, 12.8 Hz), 3.49 (d, 1 H, *J* = 9.2 Hz), 3.21 (dd, 1 H, *J* = 3.2, 12.8 Hz), 2.47 (s, 3 H), 2.08-1.99 (m, 1 H), 2.01 (d, 2 H, *J* = 7.6 Hz), 1.36 (dd, 1 H, *J* = 3.2, 6.8 Hz), 1.10 (d, 3 H, *J* = 6.8 Hz), 0.97-0.91 (m, 2 H), 0.79-0.75 (m, 1 H), 0.75 (d, 3 H, *J* = 6.4 Hz), 0.68-0.64 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.3, 136.3, 135.2, 129.6, 128.1, 116.9, 72.0, 51.5, 39.3, 39.2, 29.1, 28.4, 27.1, 21.5, 19.9, 5.2, 4.9; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{20}H_{28}NO_2S$ 346.1841, found 346.1855; IR (ATR) 2956, 2923, 2885, 2878, 2870, 2848, 2099, 2093, 1653, 1646, 1637, 1596, 1512, 1508, 1489, 1465, 1458, 1450, 1420, 1363, 1340, 1303, 1286, 1260, 1236, 1160, 1122, 1090, 1051, 1021, 995, 977, 911 cm^{-1}.



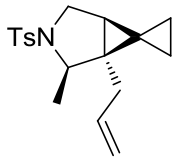
268f

1-Allyl-2-cyclopropyl-3-tosyl-3-azaspiro[bicyclo[3.1.0]hexane-6,1'-cyclopropane] (**268f**) To a solution of **263f** (20 mg, 0.058 mmol) in 0.90 mL dioxane was added bis(dibenzylideneacetone)palladium (3.3 mg, 5.8 μmol, 67 μL in 50 mg/mL solution in dioxane) and triisopropyl phosphite (2.7 mg, 12 μmol, 71 μL in 38 mg/mL solution in dioxane). The solution was carefully degassed and then heated at 130 ℃ in microwave. After 30 mins, the mixture was concentrated and purified by chromatography (EtOAc : hexanes = 1 : 20) to afford **268f** as a colorless oil (10.8 mg, 54%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, 2 H, *J* = 8.0 Hz), 7.26 (d, 2 H, *J* = 8.0 Hz), 5.68-5.60 (m, 1 H), 4.99 (s, 1 H), 4.95 (d, 1 H, *J* = 9.2 Hz), 3.64 (dd, 1 H, *J* = 4.4, 9.6 Hz), 3.56 (d, 1 H, *J* = 9.6 Hz), 2.88 (d, 1 H, *J* = 9.2 Hz), 2.49 (dd, 1 H, *J* = 8.0, 15.2 Hz), 2.41 (s, 3 H), 2.08 (dd, 1 H, *J* = 5.6, 15.2 Hz), 1.44 (d, 1 H, *J* = 4.4 Hz), 0.94-0.90 (m, 2 H), 0.82-0.77 (m, 1 H), 0.75-0.70 (m, 1 H), 0.58-0.54 (m, 1 H), 0.45-0.41 (m, 1 H), 0.37-0.32 (m, 1 H), 0.19-0.17 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.0, 137.9, 135.3, 129.2, 127.6, 117.2, 67.5, 51.1, 37.0, 51.1, 37.0, 36.1, 23.7, 21.7, 20.8, 11.5, 6.1, 4.3, 3.5, 2.6; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{20}H_{26}NO_2S$ 344.1684, found 344.1667; IR (ATR) 3008, 3005, 2997, 2971, 2951, 2926, 2917, 2889, 2872, 2859, 2850, 2121, 2114, 2106, 2101, 2091, 2073, 1638, 1597, 1491, 1458, 1448, 1439, 1431, 1342, 1299, 1288, 1258, 1225, 1159, 1118, 1103, 1090, 1061, 1042, 1025, 1008, 993, 964, 945, 934, 921, 902, 872, 856, 841, 833, 811 cm^{-1}.



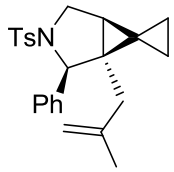
268g

1-Allyl-2-(((4-methoxybenzyl)oxy)methyl)-3-tosyl-3-azaspiro[bicyclo[3.1.0]hexane-6,1'-cyclopropane] (**268g**). To a solution of **263g** (20 mg, 0.044 mmol) in 0.50 mL dioxane was added bis(dibenzylideneacetone)palladium (2.5 mg, 4.4 μmol, 51 μL in 50 mg/mL solution in dioxane) and triisopropyl phosphite (2.0 mg, 8.8 μmol, 54 μL in 38 mg/mL solution in dioxane). The solution was carefully degassed and then heated at 130 ℃ in microwave. After 30 mins, the mixture was concentrated and purified by chromatography (EtOAc : hexanes = 1 : 20) to afford **268g** as a colorless oil (13.0 mg, 65%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, 2 H, *J* = 8.0 Hz), 7.34 (d, 2 H, *J* = 8.0 Hz), 7.23 (d, 2 H, *J* = 8.8 Hz), 6.91 (d, 2 H, *J* = 8.4 Hz), 5.54-5.44 (m, 1 H), 4.85 (d, 1 H, *J* = 4.4 Hz), 4.82 (s, 1 H), 4.53 (d, 1 H, *J* = 11.6 Hz), 4.33 (d, 1 H, *J* = 11.6 Hz), 4.06 (dd, 1 H, *J* = 2.0, 6.8 Hz), 3.85 (s, 3 H), 3.66 (dd, 2 H, *J* = 8.8, 16.0 Hz), 3.44 (d, 1 H, *J* = 9.6 Hz), 3.30 (dd, 1 H, *J* = 4.8, 9.6 Hz), 2.61 (dd, 1 H, *J* = 8.0, 14.8 Hz), 2.48 (s, 3 H), 2.02 (dd, 2 H, *J* = 5.6, 14.8 Hz), 1.33 (d, 1 H, *J* = 5.2 Hz), 0.85-0.81 (m, 1 H), 0.76-0.71 (m, 2 H), 0.66-0.62 (m, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.2, 143.5, 135.1, 132.9, 130.6, 129.5, 129.2, 128.1, 116.6, 113.7, 72.8, 70.5, 61.6, 55.3, 51.3, 36.4, 36.0, 24.5, 21.6, 21.6, 4.2, 3.7; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{26}H_{32}NO_4S$ 454.2052, found 454.2064; IR (ATR) 2971, 2954, 2947, 2926, 2923, 2883, 2876, 2869, 2857, 2852, 2101, 1653, 1646, 1638, 1610, 1597, 1586, 1512, 1491, 1463, 1458, 1441, 1420, 1342, 1303, 1243, 1159, 1090, 1029, 1012, 913, 815, 708 cm^{-1}.



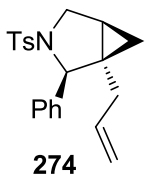
268h

1-Allyl-2-methyl-3-tosyl-3-azaspiro[bicyclo[3.1.0]hexane-6,1'-cyclopropane] (**268h**). To a solution of **263h** (20 mg, 0.063 mmol) in 0.90 mL dioxane was added bis(dibenzylideneacetone)palladium (3.6 mg, 6.3 μmol, 72 μL in 50 mg/mL solution in dioxane) and triisopropyl phosphite (2.9 mg, 12.6 μmol, 77 μL in 38 mg/mL solution in dioxane). The solution was carefully degassed and then heated at 130 ℃ in microwave. After 30 mins, the mixture was concentrated and purified by chromatography (EtOAc : hexanes = 1 : 20) to afford **268h** as a colorless oil (6.4 mg, 32%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, 2 H, *J* = 8.4 Hz), 7.35 (d, 2 H, *J* = 7.6 Hz), 5.63-5.55 (m, 1 H), 4.96 (d, 1 H, *J* = 5.2 Hz), 4.92 (s, 1 H), 3.50 (d, 1 H, *J* = 9.6 Hz), 3.37 (dd, 1 H, *J* = 6.4, 12.4 Hz), 3.25 (dd, 1 H, *J* = 4.4, 9.2 Hz), 2.48 (s, 3 H), 2.32 (dd, 1 H, *J* = 7.2, 15.2 Hz), 2.12 (dd, 1 H, *J* = 6.4, 15.2 Hz), 1.35 (d, 1 H, *J* = 6.4 Hz), 1.35-1.33 (m, 1 H), 0.99 (dt, 1 H, *J* = 4.4, 4.8 Hz), 0.90 (dt, 1 H, *J* = 4.4, 5.2 Hz), 0.77 (dt, 1 H, *J* = 4.4, 5.2 Hz), 0.69 (dt, 1 H, *J* = 4.0, 4.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.2, 134.9, 133.8, 129.4, 127.8, 116.8, 59.3, 50.9, 35.8, 35.0, 23.2, 21.6, 20.2, 16.0, 3.9, 3.2; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{18}H_{23}NO_2S$ 318.1528, found 318.1531; IR (ATR) 2977, 2960, 2926, 2887, 2878, 2867, 2857, 2850, 2110, 2097, 2084, 1653, 1638, 1597, 1514, 1491, 1458, 1452, 1420, 1376, 1344, 1303, 1288, 1260, 1236, 1161, 1109, 1092, 1074, 1029, 1020, 1007, 966, 913, 844, 815 cm^{-1}.



268i

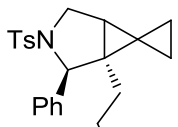
1-(2-Methylallyl)-2-phenyl-3-tosyl-3-azaspiro[bicyclo[3.1.0]hexane-6,1'-cyclopropane] (268i). To a solution of **263i** (20 mg, 0.051 mmol) in 0.90 mL toluene was added bis(dibenzylideneacetone)palladium (2.9 mg, 5.1 μmol, 58 μL in 50 mg/mL solution in toluene) and triisopropyl phosphite (2.4 mg, 10 μmol, 62 μL in 38 mg/mL solution in toluene). The solution was carefully degassed and then heated at 130 ℃ in microwave. After 30 mins, the mixture was concentrated and purified by chromatography (EtOAc : hexanes = 1 : 20) to afford **268i** as a colorless oil (12.2 mg, 61%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, 2 H, *J* = 7.2 Hz), 7.40-7.25 (m, 7 H), 4.79 (s, 1 H), 4.70 (s, 1 H), 4.50 (s, 1 H), 3.73 (d, 1 H, *J* = 9.6 Hz), 3.52 (dd, 1 H, *J* = 4.8, 9.2 Hz), 2.49 (s, 3 H), 2.42 (d, 1 H, *J* = 15.2 Hz), 1.80 (d, 1 H, *J* = 16.0 Hz), 1.52 (d, 1 H, *J* = 4.8 Hz), 1.35 (s, 3 H), 0.94-0.90 (m, 2 H), 0.58-0.52 (m, 1 H), 0.45-0.40 (m, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.5, 142.7, 138.5, 132.2, 129.4, 128.3, 127.7, 127.4, 127.0, 113.8, 65.3, 50.8, 39.3, 36.2, 26.2, 22.1, 21.5, 21.0, 3.6, 2.8; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{24}H_{28}NO_2S$ 394.1841, found 394.1840; IR (ATR) 2956, 2921, 2852, 1722, 1648, 1597, 1493, 1450, 1377, 1348, 1303, 1290, 1163, 1090, 1075, 1051, 1023, 1014, 898, 891, 839, 816, 738, 708, 699 cm^{-1}.



274

1-Allyl-2-phenyl-3-tosyl-3-azabicyclo[3.1.0]hexane (274). To a solution of **269** (20 mg, 0.056 mmol) in 0.5 mL dioxane was added bis(dibenzylideneacetone)palladium (1.6 mg, 2.8 μmol, 62

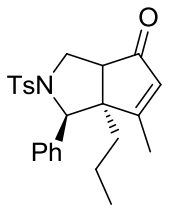
μL in 26 mg/mL solution in dioxane) and triisopropylphosphine (0.93 mg, 5.7 μmol, 28 μL in 33 mg/mL solution in dioxane). The solution was degassed and then heated at 130 ℃ in the microwave reactor. After 45 mins, the mixture was concentrated and purified by chromatography (EtOAc : hexanes = 1:100 to 1:20) to afford the product as a colorless oil (16.8 mg, 84%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, 2 H, *J* = 8.0 Hz), 7.33-7.27 (m, 5 H), 7.26-7.22 (m, 2 H), 5.57-5.50 (m, 1 H), 4.95 (s, 1 H), 4.91 (d, 1 H, *J* = 8.0 Hz), 4.20 (s, 1 H), 3.73 (d, 1 H, *J* = 9.2 Hz), 3.43 (dd, 1 H, *J* = 9.2, 4.4 Hz), 2.44 (s, 3 H), 2.33 (dd, 1 H, *J* = 14.8, 8.0 Hz), 1.84 (dd, 1 H, *J* = 15.2, 5.2 Hz), 1.38 (q, 1 H, *J* = 4.0 Hz), 1.05 (t, 1 H, *J* = 4.4 Hz), 0.39 (t, 1 H, *J* = 6.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.5, 138.7, 134.3, 132.7, 129.4, 128.2, 128.0, 127.6, 127.4, 117.7, 66.9, 52.4, 35.3, 21.6, 19.3, 11.9; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{21}H_{22}NO_2S$ 352.1371, found 352.1353; IR (ATR) 3062, 3029, 2997, 2971, 2965, 2958, 2921, 2880, 2869, 2861, 2854, 1638, 1597, 1493, 1452, 1435, 1349, 1303, 1290, 1161, 1107, 1092, 1040, 1027, 1016, 915, 815, 772 cm^{-1}.



282

2-Phenyl-1-propyl-3-tosyl-3-azaspiro[bicyclo[3.1.0]hexane-6,1'-cyclopropane] (282). To a 0 ℃ suspension of platinum oxide (6.0 mg, 26 μmol) in 5 ml THF hydrogenated with H_2 under room temperature for 15 mins. After this, a solution of **268** (0.20 g, 0.53 mmol) was added dropwise, and the mixture was stirred at this temperature for 30 mins. The mixture was concentrated and purified by chromatography on SiO_2 (EtOAc : hexanes = 1 : 20) to afford **282** as a colorless oil (0.176 g, 88%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.54-7.50 (m, 2 H), 7.26-7.08 (m, 7 H), 4.29 (s, 1 H), 7.58 (d, 1 H, *J* = 9.3 Hz), 3.35 (dd, 1 H, *J* = 4.5, 7.8 Hz), 2.36 (s, 3 H),

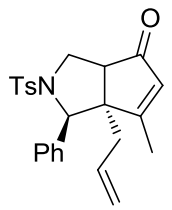
1.53-1.48 (m, 1 H), 1.32-1.25 (m, 1 H), 1.11-1.19 (m, 3 H), 0.88-0.75 (m, 2 H), 0.67 (dt, 3 H, *J* = 1.5, 6.9 Hz), 0.45-0.43 (m, 1 H), 0.37-0.33 (s, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.5, 138.3, 132.8, 129.3, 128.2, 127.8, 127.5, 127.1, 67.0, 51.0, 38.0, 32.7, 24.3, 21.6, 21.0, 19.4, 14.0, 3.9, 3.1; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{23}H_{28}NO_2S$ 382.1841, found 382.1871; IR (ATR) 3061, 2965, 2912, 2901, 2867, 2846, 1491, 1439, 1411, 1336, 1326, 1308, 1291, 1095, 1021, 1009, 921, 823, 810, 791 cm^{-1}.



283

6-Methyl-1-phenyl-6a-propyl-2-tosyl-1,3,3a,6a-tetrahydrocyclopenta[c]pyrrol-4(2*H*)-one (283). To a solution of **282** (40 mg, 0.1 mmol) in xylenes was added chloro-(1,5-cyclooctadiene)rhodium(I) dimmer (2.6 mg, 5.2 μmol) and DPPP (4.4 mg, 10 μmol) and degassed by bubbling CO through the solution. The resulting reaction mixture was heated at 130 ℃ for 3 h under CO atmosphere (CO : N_2 = 1:1 balloon). The mixture was then purified by chromatography on SiO_2 (acetone : hexanes = 2 : 5) to afford **283** as a colorless oil (24 mg, 56%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 (d, 2 H, *J* = 8.0 Hz), 7.17-7.16 (m, 5 H), 7.05 (d, 2 H, *J* = 7.2 Hz), 5.92 (s, 1 H), 4.09-4.08 (m, 1 H), 4.00 (dd, 1 H, *J* = 2.0, 10.0 Hz), 3.40-3.35 (m, 2 H), 2.69 (d, 1 H, *J* = 8.4 Hz), 2.42 (s, 3 H), 1.74-1.70 (m, 1 H), 1.65-1.61 (m, 1 H), 1.27-1.14 (m, 1 H), 1.05 (s, 3 H), 1.03-0.94 (m, 1 H), 0.93 (s, 3 H, *J* = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.8, 180.0, 143.6, 136.7, 133.3, 129.3, 128.6, 128.1, 128.1, 128.0, 72.0, 63.2, 52.5, 49.0, 37.5, 21.5, 18.0, 15.6, 14.4; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{24}H_{28}NO_3S$ 410.1790, found 410.1774; IR (ATR) 3057, 2969, 2962, 2926, 2919, 2854, 1700, 1614, 1597, 1469, 1454, 1363, 1351, 1312,

1299, 1199, 1184, 1159, 1128, 1111, 1090, 1033, 1023, 1014, 1007, 988, 904, 874, 865, 856, 833, 824, 811, 785, 759 cm^{-1}.



289

6a-Allyl-6-methyl-1-phenyl-2-tosyl-1,3,3a,6a-tetrahydrocyclopenta[c]pyrrol-4(2*H*)-one (289). To a solution of **268** (10 mg, 26 μmol) in xylenes (1 mL) was added chloro-(1,5-cyclooctadiene)rhodium(I) dimmer (0.66 mg, 1.3 μmol) and degassed by bubbling CO through the solution for 5 mins. The resulting reaction mixture was heated at 130 ℃ for 6 h under CO atmosphere (CO balloon). The mixture was then purified by chromatography on SiO_2 (EtOAc : hexanes = 1:100 to 1:20) to afford **289** as a colorless oil (5.9 mg, 55%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (dd, 2 H, *J* = 1.6, 6.8 Hz), 7.29-7.19 (m, 5 H), 7.07 (dd, 1 H, *J* = 1.6, 6.8 Hz), 5.94 (d, 1 H, *J* = 1.2 Hz), 5.48-5.40 (m, 1 H), 5.16-5.08 (m, 2 H), 4.14 (s, 1 H), 4.01 (dd, 1 H, *J* = 1.6, 10.0 Hz), 3.34 (dd, 1 H, *J* = 8.4, 9.6 Hz), 2.72 (dd, 1 H, *J* = 1.6, 8.4 Hz), 2.52-2.41 (m, 2 H), 2.43 (s, 3 H), 1.09 (d, 3 H, *J* = 1.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.4, 179.2, 143.7, 136.6, 133.6, 132.9, 132.0, 129.3, 128.6, 128.2, 128.1, 128.0, 120.5, 71.0, 62.5, 52.7, 48.9, 39.5, 21.6, 15.6; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{24}H_{26}NO_3S$ 408.1633, found 408.1602; IR (ATR) 2951, 2921, 2867, 2848, 2060, 2048, 1702, 1612, 1597, 1491, 1467, 1454, 1374, 1349, 1303, 1292, 1199, 1184, 1163, 1090, 1021, 1008, 925, 867, 839, 816 cm^{-1}.

APPENDIX A

X-RAY DATA FOR 153

Table 11. Crystal data and structural refinement for **153**.

Identification code	yan1	
Chemical formula	$C_{28}H_{34}NOPSi$	
Formula weight	459.62	
Temperature	100(2) K	
Wavelength	1.54178 Å	
Crystal size	0.020 x 0.090 x 0.130 mm	
Crystal habit	colorless plate	
Crystal system	monoclinic	
Space group	P 1 21/c 1	
Unit cell dimensions	a = 10.5991(3) Å	α = 90°
	b = 20.9441(7) Å	β = 92.369(2)°
	c = 23.2304(8) Å	γ = 90°
Volume	5152.5(3) $Å^3$	

Z	8	
Density (calculated)	1.185 Mg/cm^3	
Absorption coefficient	1.532 mm^{-1}	
Theta range for data collection	3.81 to 63.30 °	
Index ranges	-12<=h<=12, -24<=k<=23, -26<=l<=26	
Reflections collected	48198	
Independent reflections	8292 [R(int) = 0.0702]	
Coverage of independent reflections	98.7%	
Absorption correction	multi-scan	
Max. and min. transmission	0.9700 and 0.8257	
Structure solution technique	direct methods	
Structure solution program	SHELXS-97 (Sheldrick, 2008)	
Refinement method	Full-matrix least-squares on F2	
Refinement program	SHELXL-97 (Sheldrick, 2008)	
Function minimized	Σ w(Fo2 - Fc2)2	
Data / restraints / parameters	8292 / 0 / 590	
Goodness-of-fit on F2	1.823	
Δ/σmax	0.003	
Final R indices	6063 data; I>2σ(I)	R1 = 0.0885, wR2 = 0.2198
	all data	R1 = 0.1165, wR2 = 0.2325

Weighting scheme	$w=1/[\sigma^2(F_o^2)+(0.0780P)^2+0.0000P]$ where $P=(F_o^2+2F_c^2)/3$
Largest diff. peak and hole	1.639 and -0.475 eÅ^{-3}
R.M.S. deviation from mean	0.109 eÅ^{-3}

Table 12. Atomic coordinates and equivalent isotropic displacement parameters for **153**.

U(eq) is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x/a	y/b	z/c	U(eq) (Å^2)
P1	0.63098(8)	0.35474(5)	0.16016(4)	0.0223(3)
Si1	0.71943(13)	0.27991(7)	0.42326(5)	0.0459(4)
O1	0.5100(2)	0.38306(13)	0.17764(13)	0.0327(7)
N1	0.7486(3)	0.36560(16)	0.20672(13)	0.0262(8)
C1	0.7372(4)	0.36273(19)	0.26955(17)	0.0291(9)
C2	0.8089(4)	0.41808(19)	0.29670(18)	0.0315(10)
C3	0.7530(4)	0.4826(2)	0.2794(2)	0.0485(13)
C4	0.9015(4)	0.5758(2)	0.2743(2)	0.0461(12)
C5	0.9652(5)	0.6271(3)	0.2985(3)	0.0640(17)
C6	0.9510(7)	0.6413(3)	0.3541(4)	0.117(4)
C7	0.8733(9)	0.6053(4)	0.3869(4)	0.148(5)
C8	0.8093(7)	0.5538(4)	0.3625(3)	0.092(3)
C9	0.8214(4)	0.5386(2)	0.3053(2)	0.0394(11)

	x/a	y/b	z/c	U(eq) ($Å^2$)
C10	0.7777(4)	0.2987(2)	0.29237(18)	0.0331(10)
C11	0.7045(5)	0.2380(2)	0.2964(2)	0.0474(12)
C12	0.7733(4)	0.2659(2)	0.34990(19)	0.0365(10)
C13	0.8963(4)	0.2753(2)	0.3200(2)	0.0427(11)
C14	0.6090(6)	0.2137(4)	0.4410(3)	0.107(3)
C15	0.6392(12)	0.3569(5)	0.4285(3)	0.220(8)
C16	0.8538(5)	0.2801(3)	0.4748(2)	0.0657(17)
C17	0.6282(4)	0.4436(2)	0.0728(2)	0.0421(12)
C18	0.6735(5)	0.4745(2)	0.0249(2)	0.0468(13)
C19	0.7837(5)	0.4539(2)	0.0010(2)	0.0483(13)
C20	0.8470(5)	0.4006(2)	0.0234(2)	0.0511(13)
C21	0.7981(4)	0.3688(2)	0.06988(18)	0.0367(10)
C22	0.6892(4)	0.39029(18)	0.09599(17)	0.0266(9)
C23	0.4968(4)	0.2491(2)	0.1210(2)	0.0403(11)
C24	0.4807(5)	0.1855(2)	0.1063(2)	0.0563(15)
C25	0.5782(6)	0.1438(2)	0.1127(2)	0.0560(15)
C26	0.6933(5)	0.1643(2)	0.1349(2)	0.0481(13)
C27	0.7110(4)	0.2280(2)	0.15021(19)	0.0367(10)
C28	0.6119(4)	0.27079(19)	0.14344(17)	0.0299(9)
P1'	0.13267(9)	0.39080(5)	0.16437(5)	0.0268(3)

	x/a	y/b	z/c	U(eq) ($Å^2$)
Si1'	0.23006(13)	0.45270(7)	0.42797(5)	0.0428(4)
O1'	0.0113(2)	0.36346(13)	0.18246(13)	0.0337(7)
C1'	0.2402(4)	0.37907(19)	0.27303(19)	0.0303(10)
N1'	0.2509(3)	0.37751(16)	0.21042(16)	0.0327(8)
C2'	0.3074(4)	0.3203(2)	0.2984(2)	0.0391(11)
C3'	0.2408(5)	0.2582(2)	0.2798(3)	0.0668(18)
C4'	0.3956(5)	0.1733(3)	0.2600(3)	0.0581(15)
C5'	0.4571(5)	0.1170(3)	0.2735(3)	0.0711(19)
C6'	0.4304(5)	0.0846(3)	0.3215(3)	0.0663(18)
C7'	0.3439(5)	0.1084(3)	0.3574(3)	0.0611(15)
C8'	0.2844(5)	0.1653(2)	0.3445(2)	0.0482(13)
C9'	0.3088(4)	0.1983(2)	0.2956(2)	0.0402(12)
C10'	0.2856(4)	0.4412(2)	0.29765(18)	0.0311(10)
C11'	0.2163(4)	0.5025(2)	0.30443(19)	0.0411(11)
C12'	0.2847(4)	0.4716(2)	0.35617(19)	0.0340(10)
C13'	0.4076(4)	0.4618(2)	0.3255(2)	0.0383(11)
C14'	0.2071(11)	0.5287(5)	0.4714(4)	0.087(4)
C15'	0.3416(9)	0.4042(6)	0.4709(4)	0.098(5)
C16'	0.0748(8)	0.4122(5)	0.4216(4)	0.073(3)
C14"	0.104(2)	0.5029(11)	0.4388(10)	0.097(7)

	x/a	y/b	z/c	U(eq) ($Å^2$)
C15"	0.3607(13)	0.4741(7)	0.4767(6)	0.045(4)
C16"	0.2213(18)	0.3612(9)	0.4356(8)	0.076(6)
C17'	0.1331(4)	0.2996(2)	0.0805(3)	0.0568(15)
C18'	0.1763(5)	0.2699(3)	0.0310(3)	0.0713(19)
C19'	0.2713(5)	0.2952(3)	0.0013(2)	0.0591(15)
C20'	0.3260(5)	0.3527(2)	0.0190(2)	0.0546(14)
C21'	0.2812(4)	0.3828(2)	0.0671(2)	0.0402(11)
C22'	0.1860(4)	0.35678(19)	0.09854(18)	0.0309(10)
C23'	0.0044(4)	0.5002(2)	0.1290(2)	0.0395(11)
C24'	0.9938(5)	0.5651(2)	0.1172(2)	0.0546(14)
C25'	0.0992(6)	0.6043(2)	0.1279(2)	0.0562(16)
C26'	0.2101(6)	0.5812(2)	0.1489(2)	0.0506(14)
C27'	0.2214(5)	0.5155(2)	0.16020(18)	0.0402(11)
C28'	0.1180(4)	0.47554(19)	0.15061(18)	0.0310(10)

Table 13. Bond lengths (Å) for **153**.

P1-O1	1.485(3)	P1-N1	1.633(3)
P1-C22	1.798(4)	P1-C28	1.810(4)
Si1-C16	1.823(5)	Si1-C15	1.829(7)
Si1-C12	1.843(5)	Si1-C14	1.872(7)

N1-C1	1.471(5)	N1-H1B	0.88
C1-C10	1.499(6)	C1-C2	1.510(6)
C1-H1A	1.0	C2-C3	1.522(6)
C2-H2A	0.99	C2-H2B	0.99
C3-C9	1.492(6)	C3-H3A	0.99
C3-H3B	0.99	C4-C5	1.376(8)
C4-C9	1.378(6)	C4-H4A	0.95
C5-C6	1.340(10)	C5-H5A	0.95
C6-C7	1.372(11)	C6-H6A	0.95
C7-C8	1.383(9)	C7-H7A	0.95
C8-C9	1.376(7)	C8-H8A	0.95
C10-C13	1.472(6)	C10-C11	1.494(6)
C10-C12	1.505(6)	C11-C12	1.531(6)
C11-H11A	0.99	C11-H11B	0.99
C12-C13	1.515(6)	C13-H13A	0.99
C13-H13B	0.99	C14-H14A	0.98
C14-H14B	0.98	C14-H14C	0.98
C15-H15A	0.98	C15-H15B	0.98
C15-H15C	0.98	C16-H16A	0.98
C16-H16B	0.98	C16-H16C	0.98
C17-C22	1.387(6)	C17-C18	1.391(7)

C17-H17A	0.95	C18-C19	1.383(7)
C18-H18A	0.95	C19-C20	1.392(7)
C19-H19A	0.95	C20-C21	1.386(6)
C20-H20A	0.95	C21-C22	1.400(6)
C21-H21A	0.95	C23-C28	1.382(6)
C23-C24	1.386(6)	C23-H23A	0.95
C24-C25	1.355(8)	C24-H24A	0.95
C25-C26	1.374(8)	C25-H25A	0.95
C26-C27	1.392(6)	C26-H26A	0.95
C27-C28	1.385(6)	C27-H27A	0.95
P1'-O1'	1.485(3)	P1'-N1'	1.638(3)
P1'-C22'	1.799(4)	P1'-C28'	1.809(4)
Si1'-C14"	1.72(2)	Si1'-C15"	1.808(13)
Si1'-C15'	1.824(9)	Si1'-C12'	1.832(4)
Si1'-C16'	1.851(8)	Si1'-C14'	1.906(9)
Si1'-C16"	1.927(19)	C1'-N1'	1.464(6)
C1'-C10'	1.493(6)	C1'-C2'	1.528(6)
C1'-H1'A	1.0	N1'-H1'B	0.88
C2'-C3'	1.533(6)	C2'-H2'A	0.99
C2'-H2'B	0.99	C3'-C9'	1.486(6)
C3'-H3'A	0.99	C3'-H3'B	0.99

C4'-C9'	1.368(7)	C4'-C5'	1.376(8)
C4'-H4'A	0.95	C5'-C6'	1.347(9)
C5'-H5'A	0.95	C6'-C7'	1.359(8)
C6'-H6'A	0.95	C7'-C8'	1.375(7)
C7'-H7'A	0.95	C8'-C9'	1.363(7)
C8'-H8'A	0.95	C10'-C13'	1.486(6)
C10'-C11'	1.490(6)	C10'-C12'	1.501(6)
C11'-C12'	1.522(6)	C11'-H11C	0.99
C11'-H11D	0.99	C12'-C13'	1.525(6)
C13'-H13C	0.99	C13'-H13D	0.99
C14'-H14D	0.98	C14'-H14E	0.98
C14'-H14F	0.98	C15'-H15D	0.98
C15'-H15E	0.98	C15'-H15F	0.98
C16'-H16D	0.98	C16'-H16E	0.98
C16'-H16F	0.98	C14''-H14G	0.98
C14''-H14H	0.98	C14''-H14I	0.98
C15''-H15G	0.98	C15''-H15H	0.98
C15''-H15I	0.98	C16''-H16G	0.98
C16''-H16H	0.98	C16''-H16I	0.98
C17'-C22'	1.379(6)	C17'-C18'	1.399(8)
C17'-H17B	0.95	C18'-C19'	1.352(8)

C18'-H18B	0.95	C19'-C20'	1.391(8)
C19'-H19B	0.95	C20'-C21'	1.385(7)
C20'-H20B	0.95	C21'-C22'	1.382(6)
C21'-H21B	0.95	C23'-C28'	1.385(6)
C23'-C24'	1.391(6)	C23'-H23B	0.95
C24'-C25'	1.400(8)	C24'-H24B	0.95
C25'-C26'	1.344(8)	C25'-H25B	0.95
C26'-C27'	1.405(7)	C26'-H26B	0.95
C27'-C28'	1.390(6)	C27'-H27B	0.95

Table 14. Bond angles (°) for **153**.

O1-P1-N1	114.07(16)	O1-P1-C22	113.02(18)
N1-P1-C22	102.29(17)	O1-P1-C28	110.88(17)
N1-P1-C28	110.68(18)	C22-P1-C28	105.27(18)
C16-Si1-C15	107.9(5)	C16-Si1-C12	110.2(2)
C15-Si1-C12	111.4(3)	C16-Si1-C14	109.6(3)
C15-Si1-C14	110.0(5)	C12-Si1-C14	107.8(3)
C1-N1-P1	124.0(3)	C1-N1-H1B	118.0
P1-N1-H1B	118.0	N1-C1-C10	110.7(3)
N1-C1-C2	108.8(3)	C10-C1-C2	114.1(3)
N1-C1-H1A	107.7	C10-C1-H1A	107.7

C2-C1-H1A	107.7	C1-C2-C3	112.8(3)
C1-C2-H2A	109.0	C3-C2-H2A	109.0
C1-C2-H2B	109.0	C3-C2-H2B	109.0
H2A-C2-H2B	107.8	C9-C3-C2	114.5(4)
C9-C3-H3A	108.6	C2-C3-H3A	108.6
C9-C3-H3B	108.6	C2-C3-H3B	108.6
H3A-C3-H3B	107.6	C5-C4-C9	122.0(5)
C5-C4-H4A	119.0	C9-C4-H4A	119.0
C6-C5-C4	119.6(6)	C6-C5-H5A	120.2
C4-C5-H5A	120.2	C5-C6-C7	120.5(6)
C5-C6-H6A	119.7	C7-C6-H6A	119.7
C6-C7-C8	119.7(7)	C6-C7-H7A	120.1
C8-C7-H7A	120.1	C9-C8-C7	120.9(6)
C9-C8-H8A	119.6	C7-C8-H8A	119.6
C8-C9-C4	117.2(5)	C8-C9-C3	120.5(5)
C4-C9-C3	122.2(5)	C13-C10-C11	97.2(4)
C13-C10-C1	132.8(4)	C11-C10-C1	130.0(4)
C13-C10-C12	61.2(3)	C11-C10-C12	61.4(3)
C1-C10-C12	134.7(4)	C10-C11-C12	59.6(3)
C10-C11-H11A	117.8	C12-C11-H11A	117.8
C10-C11-H11B	117.8	C12-C11-H11B	117.8

H11A-C11-H11B	114.9	C10-C12-C13	58.4(3)
C10-C12-C11	59.0(3)	C13-C12-C11	93.9(4)
C10-C12-Si1	140.4(3)	C13-C12-Si1	135.1(3)
C11-C12-Si1	131.0(3)	C10-C13-C12	60.5(3)
C10-C13-H13A	117.7	C12-C13-H13A	117.7
C10-C13-H13B	117.7	C12-C13-H13B	117.7
H13A-C13-H13B	114.8	Si1-C14-H14A	109.5
Si1-C14-H14B	109.5	H14A-C14-H14B	109.5
Si1-C14-H14C	109.5	H14A-C14-H14C	109.5
H14B-C14-H14C	109.5	Si1-C15-H15A	109.5
Si1-C15-H15B	109.5	H15A-C15-H15B	109.5
Si1-C15-H15C	109.5	H15A-C15-H15C	109.5
H15B-C15-H15C	109.5	Si1-C16-H16A	109.5
Si1-C16-H16B	109.5	H16A-C16-H16B	109.5
Si1-C16-H16C	109.5	H16A-C16-H16C	109.5
H16B-C16-H16C	109.5	C22-C17-C18	121.0(5)
C22-C17-H17A	119.5	C18-C17-H17A	119.5
C19-C18-C17	120.0(4)	C19-C18-H18A	120.0
C17-C18-H18A	120.0	C18-C19-C20	120.2(5)
C18-C19-H19A	119.9	C20-C19-H19A	119.9
C21-C20-C19	119.0(5)	C21-C20-H20A	120.5

C19-C20-H20A	120.5	C20-C21-C22	121.7(4)
C20-C21-H21A	119.2	C22-C21-H21A	119.2
C17-C22-C21	118.0(4)	C17-C22-P1	119.0(3)
C21-C22-P1	122.9(3)	C28-C23-C24	120.4(5)
C28-C23-H23A	119.8	C24-C23-H23A	119.8
C25-C24-C23	120.4(5)	C25-C24-H24A	119.8
C23-C24-H24A	119.8	C24-C25-C26	120.2(4)
C24-C25-H25A	119.9	C26-C25-H25A	119.9
C25-C26-C27	120.2(5)	C25-C26-H26A	119.9
C27-C26-H26A	119.9	C28-C27-C26	119.9(4)
C28-C27-H27A	120.1	C26-C27-H27A	120.1
C23-C28-C27	118.9(4)	C23-C28-P1	119.3(3)
C27-C28-P1	121.8(3)	O1'-P1'-N1'	113.48(17)
O1'-P1'-C22'	113.22(18)	N1'-P1'-C22'	103.24(18)
O1'-P1'-C28'	111.06(18)	N1'-P1'-C28'	109.87(19)
C22'-P1'-C28'	105.43(19)	C14"-Si1'-C15"	109.5(9)
C14"-Si1'-C15'	138.4(8)	C15"-Si1'-C15'	48.2(6)
C14"-Si1'-C12'	106.0(8)	C15"-Si1'-C12'	104.7(5)
C15'-Si1'-C12'	113.3(3)	C14"-Si1'-C16'	66.5(8)
C15"-Si1'-C16'	145.0(6)	C15'-Si1'-C16'	110.1(5)
C12'-Si1'-C16'	109.8(3)	C14"-Si1'-C14'	45.3(8)

C15''-Si1'-C14'	64.7(6)	C15'-Si1'-C14'	105.6(6)
C12'-Si1'-C14'	110.7(3)	C16'-Si1'-C14'	107.0(5)
C14''-Si1'-C16''	123.6(10)	C15''-Si1'-C16''	103.2(7)
C15'-Si1'-C16''	55.2(7)	C12'-Si1'-C16''	108.5(6)
C16'-Si1'-C16''	60.4(7)	C14'-Si1'-C16''	140.8(7)
N1'-C1'-C10'	111.3(3)	N1'-C1'-C2'	108.2(4)
C10'-C1'-C2'	114.6(3)	N1'-C1'-H1'A	107.5
C10'-C1'-H1'A	107.5	C2'-C1'-H1'A	107.5
C1'-N1'-P1'	123.8(3)	C1'-N1'-H1'B	118.1
P1'-N1'-H1'B	118.1	C1'-C2'-C3'	111.8(4)
C1'-C2'-H2'A	109.2	C3'-C2'-H2'A	109.2
C1'-C2'-H2'B	109.2	C3'-C2'-H2'B	109.2
H2'A-C2'-H2'B	107.9	C9'-C3'-C2'	115.7(4)
C9'-C3'-H3'A	108.4	C2'-C3'-H3'A	108.4
C9'-C3'-H3'B	108.4	C2'-C3'-H3'B	108.4
H3'A-C3'-H3'B	107.4	C9'-C4'-C5'	121.0(6)
C9'-C4'-H4'A	119.5	C5'-C4'-H4'A	119.5
C6'-C5'-C4'	120.5(6)	C6'-C5'-H5'A	119.8
C4'-C5'-H5'A	119.8	C5'-C6'-C7'	119.6(5)
C5'-C6'-H6'A	120.2	C7'-C6'-H6'A	120.2
C6'-C7'-C8'	120.0(6)	C6'-C7'-H7'A	120.0

C8'-C7'-H7'A	120.0	C9'-C8'-C7'	121.3(5)
C9'-C8'-H8'A	119.3	C7'-C8'-H8'A	119.3
C8'-C9'-C4'	117.7(5)	C8'-C9'-C3'	121.9(5)
C4'-C9'-C3'	120.4(5)	C13'-C10'-C11'	97.4(4)
C13'-C10'-C1'	132.8(4)	C11'-C10'-C1'	129.7(4)
C13'-C10'-C12'	61.4(3)	C11'-C10'-C12'	61.2(3)
C1'-C10'-C12'	134.6(4)	C10'-C11'-C12'	59.8(3)
C10'-C11'-H11C	117.8	C12'-C11'-H11C	117.8
C10'-C11'-H11D	117.8	C12'-C11'-H11D	117.8
H11C-C11'-H11D	114.9	C10'-C12'-C11'	59.1(3)
C10'-C12'-C13'	58.8(3)	C11'-C12'-C13'	94.4(4)
C10'-C12'-Si1'	138.3(3)	C11'-C12'-Si1'	130.7(3)
C13'-C12'-Si1'	134.9(3)	C10'-C13'-C12'	59.8(3)
C10'-C13'-H13C	117.8	C12'-C13'-H13C	117.8
C10'-C13'-H13D	117.8	C12'-C13'-H13D	117.8
H13C-C13'-H13D	114.9	Si1'-C14'-H14D	109.5
Si1'-C14'-H14E	109.5	H14D-C14'-H14E	109.5
Si1'-C14'-H14F	109.5	H14D-C14'-H14F	109.5
H14E-C14'-H14F	109.5	Si1'-C15'-H15D	109.5
Si1'-C15'-H15E	109.5	H15D-C15'-H15E	109.5
Si1'-C15'-H15F	109.5	H15D-C15'-H15F	109.5

H15E-C15'-H15F	109.5	Si1'-C16'-H16D	109.5
Si1'-C16'-H16E	109.5	H16D-C16'-H16E	109.5
Si1'-C16'-H16F	109.5	H16D-C16'-H16F	109.5
H16E-C16'-H16F	109.5	Si1'-C14"-H14G	109.5
Si1'-C14"-H14H	109.5	H14G-C14"-H14H	109.5
Si1'-C14"-H14I	109.5	H14G-C14"-H14I	109.5
H14H-C14"-H14I	109.5	Si1'-C15"-H15G	109.5
Si1'-C15"-H15H	109.5	H15G-C15"-H15H	109.5
Si1'-C15"-H15I	109.5	H15G-C15"-H15I	109.5
H15H-C15"-H15I	109.5	Si1'-C16"-H16G	109.5
Si1'-C16"-H16H	109.5	H16G-C16"-H16H	109.5
Si1'-C16"-H16I	109.5	H16G-C16"-H16I	109.5
H16H-C16"-H16I	109.5	C22'-C17'-C18'	119.5(5)
C22'-C17'-H17B	120.2	C18'-C17'-H17B	120.2
C19'-C18'-C17'	121.4(5)	C19'-C18'-H18B	119.3
C17'-C18'-H18B	119.3	C18'-C19'-C20'	119.9(5)
C18'-C19'-H19B	120.1	C20'-C19'-H19B	120.1
C21'-C20'-C19'	118.6(5)	C21'-C20'-H20B	120.7
C19'-C20'-H20B	120.7	C22'-C21'-C20'	121.9(5)
C22'-C21'-H21B	119.0	C20'-C21'-H21B	119.0
C17'-C22'-C21'	118.6(4)	C17'-C22'-P1'	117.6(4)

C21'-C22'-P1'	123.7(3)	C28'-C23'-C24'	119.9(5)
C28'-C23'-H23B	120.1	C24'-C23'-H23B	120.1
C23'-C24'-C25'	118.7(5)	C23'-C24'-H24B	120.7
C25'-C24'-H24B	120.7	C26'-C25'-C24'	122.3(5)
C26'-C25'-H25B	118.9	C24'-C25'-H25B	118.9
C25'-C26'-C27'	119.1(5)	C25'-C26'-H26B	120.5
C27'-C26'-H26B	120.5	C28'-C27'-C26'	120.0(5)
C28'-C27'-H27B	120.0	C26'-C27'-H27B	120.0
C23'-C28'-C27'	120.1(4)	C23'-C28'-P1'	119.8(3)
C27'-C28'-P1'	120.1(3)		

Table 15. Torsion angles (°) for **153**.

O1-P1-N1-C1	38.6(4)	C22-P1-N1-C1	161.0(3)
C28-P1-N1-C1	-87.2(3)	P1-N1-C1-C10	98.3(4)
P1-N1-C1-C2	-135.6(3)	N1-C1-C2-C3	64.5(5)
C10-C1-C2-C3	-171.4(4)	C1-C2-C3-C9	179.9(4)
C9-C4-C5-C6	0.9(9)	C4-C5-C6-C7	-0.2(13)
C5-C6-C7-C8	0.2(16)	C6-C7-C8-C9	-0.8(15)
C7-C8-C9-C4	1.4(11)	C7-C8-C9-C3	179.4(8)
C5-C4-C9-C8	-1.4(8)	C5-C4-C9-C3	179.4(4)
C2-C3-C9-C8	-74.6(7)	C2-C3-C9-C4	103.4(5)

N1-C1-C10-C13	98.6(5)	C2-C1-C10-C13	-24.6(6)
N1-C1-C10-C11	-84.7(5)	C2-C1-C10-C11	152.2(4)
N1-C1-C10-C12	-171.9(4)	C2-C1-C10-C12	65.0(6)
C13-C10-C11-C12	51.5(3)	C1-C10-C11-C12	126.1(5)
C11-C10-C12-C13	117.6(4)	C1-C10-C12-C13	123.1(6)
C13-C10-C12-C11	-117.6(4)	C1-C10-C12-C11	119.3(6)
C13-C10-C12-Si1	124.1(6)	C11-C10-C12-Si1	118.3(6)
C1-C10-C12-Si1	1.0(9)	C10-C11-C12-C13	-49.1(3)
C10-C11-C12-Si1	132.0(5)	C16-Si1-C12-C10	116.3(5)
C15-Si1-C12-C10	3.3(8)	C14-Si1-C12-C10	124.1(6)
C16-Si1-C12-C13	-23.6(5)	C15-Si1-C12-C13	96.1(7)
C14-Si1-C12-C13	-143.1(5)	C16-Si1-C12-C11	154.8(4)
C15-Si1-C12-C11	-85.5(7)	C14-Si1-C12-C11	35.3(5)
C11-C10-C13-C12	-51.7(3)	C1-C10-C13-C12	125.8(5)
C11-C12-C13-C10	49.6(3)	Si1-C12-C13-C10	-131.6(5)
C22-C17-C18-C19	-2.6(7)	C17-C18-C19-C20	2.5(8)
C18-C19-C20-C21	-0.2(7)	C19-C20-C21-C22	-2.1(7)
C18-C17-C22-C21	0.4(6)	C18-C17-C22-P1	176.8(4)
C20-C21-C22-C17	2.0(7)	C20-C21-C22-P1	-174.3(4
O1-P1-C22-C17	7.2(4)	N1-P1-C22-C17	-115.9
C28-P1-C22-C17	128.4(3)	O1-P1-C22-C21	176.5(3)

N1-P1-C22-C21	60.4(4)	C28-P1-C22-C21	-55.3(4)
C28-C23-C24-C25	-1.2(8)	C23-C24-C25-C26	1.1(9)
C24-C25-C26-C27	-0.7(8)	C25-C26-C27-C28	0.4(7)
C24-C23-C28-C27	0.8(7)	C24-C23-C28-P1	178.1(4)
C26-C27-C28-C23	-0.5(7)	C26-C27-C28-P1	-177.7(4)
O1-P1-C28-C23	31.1(4)	N1-P1-C28-C23	158.7(3)
C22-P1-C28-C23	-91.5(4)	O1-P1-C28-C27	151.7(3)
N1-P1-C28-C27	-24.1(4)	C22-P1-C28-C27	85.7(4)
C10'-C1'-N1'-P1'	-99.3(4)	C2'-C1'-N1'-P1'	133.9(3)
O1'-P1'-N1'-C1'	-38.3(4)	C22'-P1'-N1'-C1'	161.3(3)
C28'-P1'-N1'-C1'	86.7(4)	N1'-C1'-C2'-C3'	-65.7(5)
C10'-C1'-C2'-C3'	169.4(4)	C1'-C2'-C3'-C9'	171.9(5)
C9'-C4'-C5'-C6'	1.8(8)	C4'-C5'-C6'-C7'	-1.3(9)
C5'-C6'-C7'-C8'	-0.1(9)	C6'-C7'-C8'-C9'	1.0(8)
C7'-C8'-C9'-C4'	-0.6(7)	C7'-C8'-C9'-C3'	177.0(5)
C5'-C4'-C9'-C8'	-0.8(7)	C5'-C4'-C9'-C3'	178.5(5)
C2'-C3'-C9'-C8'	95.0(6)	C2'-C3'-C9'-C4'	-87.4(6)
N1'-C1'-C10'-C13'	-97.6(5)	C2'-C1'-C10'-C13'	25.6(7)
N1'-C1'-C10'-C11'	86.1(5)	C2'-C1'-C10'-C11'	-150.8(4)
N1'-C1'-C10'-C12'	172.6(4)	C2'-C1'-C10'-C12'	-64.2(6)
C13'-C10'-C11'-C12'	-51.5(3)	C1'-C10'-C11'-C12'	125.8(5)

C13'-C10'-C12'-C11'	117.9(4)	C1'-C10'-C12'-C11'	118.8(5)
C11'-C10'-C12'-C13'	-117.9(4)	C1'-C10'-C12'-C13'	123.3(5)
C13'-C10'-C12'-Si1'	-124.1(5)	C11'-C10'-C12'-Si1'	118.1(5)
C1'-C10'-C12'-Si1'	-0.7(8)	C10'-C11'-C12'-C13'	49.3(3)
C10'-C11'-C12'-Si1'	-129.3(5)	C14"-Si1'-C12'-C10'	109.9(9)
C15"-Si1'-C12'-C10'	134.3(6)	C15'-Si1'-C12'-C10'	83.9(6)
C16'-Si1'-C12'-C10'	-39.6(6)	C14'-Si1'-C12'-C10'	157.6(6)
C16"-Si1'-C12'-C10'	24.7(8)	C14"-Si1'-C12'-C11'	-23.0(9)
C15"-Si1'-C12'-C11'	-138.7(6)	C15'-Si1'-C12'-C11'	170.9(6)
C16'-Si1'-C12'-C11'	47.3(6)	C14'-Si1'-C12'-C11'	-70.6(6)
C16"-Si1'-C12'-C11'	111.7(7)	C14"-Si1'-C12'-C13'	159.0(9)
C15"-Si1'-C12'-C13'	43.3(7)	C15'-Si1'-C12'-C13'	-7.2(7)
C16'-Si1'-C12'-C13'	-130.7(6)	C14'-Si1'-C12'-C13'	111.3(6)
C16"-Si1'-C12'-C13'	-66.4(7)	C11'-C10'-C13'-C12'	51.4(3)
C1'-C10'-C13'-C12'	-125.8(5)	C11'-C12'-C13'-C10'	-49.5(3)
Si1'-C12'-C13'-C10'	129.0(5)	C22'-C17'-C18'-C19'	1.8(9)
C17'-C18'-C19'-C20'	-1.7(9)	C18'-C19'-C20'-C21'	0.1(8)
C19'-C20'-C21'-C22'	1.3(8)	C18'-C17'-C22'-C21'	-0.4(7)
C18'-C17'-C22'-P1'	-176.9(4)	C20'-C21'-C22'-C17'	-1.1(7)
C20'-C21'-C22'-P1'	175.1(4)	O1'-P1'-C22'-C17'	-17.3(4)
N1'-P1'-C22'-C17'	105.8(4)	C28'-P1'-C22'-C17'	138.9(4)

O1'-P1'-C22'-C21'	166.4(3)	N1'-P1'-C22'-C21'	-70.5(4)
C28'-P1'-C22'-C21'	44.8(4)	C28'-C23'-C24'-C25'	-0.3(7)
C23'-C24'-C25'-C26'	0.2(8)	C24'-C25'-C26'-C27'	0.5(8)
C25'-C26'-C27'-C28'	-1.2(7)	C24'-C23'-C28'-C27'	-0.3(7)
C24'-C23'-C28'-P1'	-178.6(4)	C26'-C27'-C28'-C23'	1.1(7)
C26'-C27'-C28'-P1'	179.4(3)	O1'-P1'-C28'-C23'	-32.5(4)
N1'-P1'-C28'-C23'	-158.9(3)	C22'-P1'-C28'-C23'	90.4(4)
O1'-P1'-C28'-C27'	149.2(3)	N1'-P1'-C28'-C27'	22.8(4)
C22'-P1'-C28'-C27'	-87.8(4)		

APPENDIX B

X-RAY DATA FOR 181

Table 16. Crystal data and structure refinement for **181**.

Identification code	yan4a	
Empirical formula	C23 H25 N O2 S	
Formula weight	379.50	
Temperature	100(2) K	
Wavelength	1.54178 Å	
Crystal system	Triclinic	
Space group	P -1	
Unit cell dimensions	a = 7.8396(2) Å	a= 89.908(2) °.
	b = 8.6125(4) Å	b= 81.344(2) °.
	c = 16.8418(5) Å	g = 62.948(2) °.
Volume	998.30(6) $Å^3$	
Z	2	
Density (calculated)	1.262 Mg/m^3	
Absorption coefficient	1.570 mm^{-1}	

F(000)	404
Crystal size	0.21 x 0.16 x 0.12 mm^3
Theta range for data collection	2.66 to 71.73 °.
Index ranges	-9<=h<=9, -9<=k<=10, -20<=l<=20
Reflections collected	11041
Independent reflections	3610 [R(int) = 0.0231]
Completeness to theta = 71.73 °	92.3 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.8340 and 0.7340
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3610 / 0 / 244
Goodness-of-fit on F^2	2.394
Final R indices [I>2sigma(I)]	R1 = 0.0643, wR2 = 0.2729
R indices (all data)	R1 = 0.0654, wR2 = 0.2738
Largest diff. peak and hole	0.507 and -1.260 e.$Å^{-3}$

Table 17. Atomic coordinates and equivalent isotropic displacement parameters for **181**.

U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x (10^4)	y (10^4)	z (10^4)	U(eq) ($Å^2$ x 10^3)
S	4631(1)	3660(1)	3400(1)	18(1)
N	6302(3)	4018(3)	2842(1)	16(1)
O(1)	3497(3)	5202(3)	3939(1)	23(1)
C(1)	7815(4)	2533(4)	2279(2)	15(1)

O(2)	3707(3)	3106(3)	2869(1)	25(1)
C(2)	9474(4)	3012(4)	2094(2)	17(1)
C(3)	8992(4)	4827(4)	1876(2)	20(1)
C(4)	7728(5)	6249(5)	1414(2)	29(1)
C(5)	9925(5)	5598(5)	1273(2)	30(1)
C(6)	9098(4)	4454(4)	2734(2)	20(1)
C(7)	7213(4)	4878(4)	3277(2)	19(1)
C(8)	11484(4)	1529(4)	1807(2)	20(1)
C(9)	12183(4)	194(4)	2416(2)	25(1)
C(10)	12573(5)	-1459(5)	2307(3)	34(1)
C(11)	7981(5)	519(4)	1178(2)	23(1)
C(12)	7437(5)	159(5)	478(2)	27(1)
C(13)	6017(5)	1477(5)	134(2)	25(1)
C(14)	5134(4)	3159(4)	496(2)	23(1)
C(15)	5660(4)	3534(4)	1198(2)	20(1)
C(16)	7107(4)	2209(4)	1540(2)	18(1)
C(17)	6211(4)	2187(4)	4720(2)	21(1)
C(18)	7284(5)	777(4)	5141(2)	24(1)
C(19)	8012(4)	-943(4)	4817(2)	24(1)
C(20)	7637(5)	-1207(4)	4058(2)	28(1)
C(21)	6545(5)	182(4)	3633(2)	24(1)
C(22)	5857(4)	1882(4)	3967(2)	20(1)
C(23)	9193(5)	-2480(5)	5267(2)	31(1)

Table 18. Bond lengths [Å] for **181**.

S-O(2)	1.436(2)	C(7)-H(7B)	0.9900
S-O(1)	1.437(2)	C(8)-C(9)	1.506(4)
S-N	1.641(2)	C(8)-H(8A)	0.9900
S-C(22)	1.764(3)	C(8)-H(8B)	0.9900
N-C(1)	1.492(3)	C(9)-C(10)	1.320(5)
N-C(7)	1.495(3)	C(9)-H(9A)	0.9500
C(1)-C(16)	1.512(4)	C(10)-H(10A)	0.9500
C(1)-C(2)	1.525(4)	C(10)-H(10B)	0.9500
C(1)-H(1A)	1.0000	C(11)-C(16)	1.390(4)
C(2)-C(3)	1.491(4)	C(11)-C(12)	1.392(4)
C(2)-C(8)	1.514(4)	C(11)-H(11A)	0.9500
C(2)-C(6)	1.539(4)	C(12)-C(13)	1.381(5)
C(3)-C(6)	1.487(4)	C(12)-H(12A)	0.9500
C(3)-C(4)	1.487(4)	C(13)-C(14)	1.383(5)
C(3)-C(5)	1.491(4)	C(13)-H(13A)	0.9500
C(4)-C(5)	1.528(4)	C(14)-C(15)	1.394(4)
C(4)-H(4A)	0.9900	C(14)-H(14A)	0.9500
C(4)-H(4B)	0.9900	C(15)-C(16)	1.391(4)
C(5)-H(5A)	0.9900	C(15)-H(15A)	0.9500
C(5)-H(5B)	0.9900	C(17)-C(18)	1.390(4)
C(6)-C(7)	1.502(4)	C(17)-C(22)	1.389(4)
C(6)-H(6A)	1.0000	C(17)-H(17A)	0.9500
C(7)-H(7A)	0.9900	C(18)-C(19)	1.399(5)

C(18)-H(18A)	0.9500	C(21)-C(22)	1.395(4)
C(19)-C(20)	1.394(5)	C(21)-H(21A)	0.9500
C(19)-C(23)	1.509(4)	C(23)-H(23A)	0.9800
C(20)-C(21)	1.388(5)	C(23)-H(23B)	0.9800
C(20)-H(20A)	0.9500	C(23)-H(23C)	0.9800

Table 19. Bond angles [°] for **181**.

O(2)-S-O(1)	119.88(14)	C(8)-C(2)-C(1)	116.9(2)
O(2)-S-N	107.66(12)	C(3)-C(2)-C(6)	58.8(2)
O(1)-S-N	105.68(13)	C(8)-C(2)-C(6)	122.1(2)
O(2)-S-C(22)	107.38(15)	C(1)-C(2)-C(6)	107.3(2)
O(1)-S-C(22)	108.83(14)	C(6)-C(3)-C(4)	137.5(3)
N-S-C(22)	106.73(13)	C(6)-C(3)-C(5)	134.5(3)
C(1)-N-C(7)	110.6(2)	C(4)-C(3)-C(5)	61.8(2)
C(1)-N-S	116.71(19)	C(6)-C(3)-C(2)	62.23(19)
C(7)-N-S	115.56(18)	C(4)-C(3)-C(2)	142.4(3)
N-C(1)-C(16)	113.8(2)	C(5)-C(3)-C(2)	134.4(3)
N-C(1)-C(2)	103.6(2)	C(3)-C(4)-C(5)	59.2(2)
C(16)-C(1)-C(2)	114.0(2)	C(3)-C(4)-H(4A)	117.8
N-C(1)-H(1A)	108.4	C(5)-C(4)-H(4A)	117.8
C(16)-C(1)-H(1A)	108.4	C(3)-C(4)-H(4B)	117.8
C(2)-C(1)-H(1A)	108.4	C(5)-C(4)-H(4B)	117.8
C(3)-C(2)-C(8)	120.2(2)	H(4A)-C(4)-H(4B)	115.0
C(3)-C(2)-C(1)	118.0(2)	C(3)-C(5)-C(4)	59.0(2)

C(3)-C(5)-H(5A)	117.9	C(2)-C(8)-H(8B)	108.9
C(4)-C(5)-H(5A)	117.9	H(8A)-C(8)-H(8B)	107.8
C(3)-C(5)-H(5B)	117.9	C(10)-C(9)-C(8)	124.7(3)
C(4)-C(5)-H(5B)	117.9	C(10)-C(9)-H(9A)	117.7
H(5A)-C(5)-H(5B)	115.0	C(8)-C(9)-H(9A)	117.7
C(3)-C(6)-C(7)	116.6(2)	C(9)-C(10)-H(10A)	120.0
C(3)-C(6)-C(2)	58.99(19)	C(9)-C(10)-H(10B)	120.0
C(7)-C(6)-C(2)	108.0(2)	H(10A)-C(10)-H(10B)	120.0
C(3)-C(6)-H(6A)	119.3	C(16)-C(11)-C(12)	120.6(3)
C(7)-C(6)-H(6A)	119.3	C(16)-C(11)-H(11A)	119.7
C(2)-C(6)-H(6A)	119.3	C(12)-C(11)-H(11A)	119.7
N-C(7)-C(6)	104.3(2)	C(13)-C(12)-C(11)	120.5(3)
N-C(7)-H(7A)	110.9	C(13)-C(12)-H(12A)	119.8
C(6)-C(7)-H(7A)	110.9	C(11)-C(12)-H(12A)	119.8
N-C(7)-H(7B)	110.9	C(12)-C(13)-C(14)	119.1(3)
C(6)-C(7)-H(7B)	110.9	C(12)-C(13)-H(13A)	120.4
H(7A)-C(7)-H(7B)	108.9	C(14)-C(13)-H(13A)	120.4
C(9)-C(8)-C(2)	113.1(2)	C(13)-C(14)-C(15)	121.0(3)
C(9)-C(8)-H(8A)	108.9	C(13)-C(14)-H(14A)	119.5
C(2)-C(8)-H(8A)	108.9	C(15)-C(14)-H(14A)	119.5
C(9)-C(8)-H(8B)	108.9	C(16)-C(15)-C(14)	119.9(3)
C(16)-C(15)-H(15A)	120.0	C(11)-C(16)-C(15)	119.0(3)
C(14)-C(15)-H(15A)	120.0	C(11)-C(16)-C(1)	118.2(3)

C(15)-C(16)-C(1)	122.8(3)	C(20)-C(21)-C(22)	118.7(3)
C(18)-C(17)-C(22)	119.4(3)	C(20)-C(21)-H(21A)	120.6
C(18)-C(17)-H(17A)	120.3	C(22)-C(21)-H(21A)	120.6
C(22)-C(17)-H(17A)	120.3	C(17)-C(22)-C(21)	120.9(3)
C(17)-C(18)-C(19)	121.0(3)	C(17)-C(22)-S	119.8(2)
C(17)-C(18)-H(18A)	119.5	C(21)-C(22)-S	119.2(2)
C(19)-C(18)-H(18A)	119.5	C(19)-C(23)-H(23A)	109.5
C(20)-C(19)-C(18)	118.2(3)	C(19)-C(23)-H(23B)	109.5
C(20)-C(19)-C(23)	120.5(3)	H(23A)-C(23)-H(23B)	109.5
C(18)-C(19)-C(23)	121.3(3)	C(19)-C(23)-H(23C)	109.5
C(21)-C(20)-C(19)	121.7(3)	H(23A)-C(23)-H(23C)	109.5
C(21)-C(20)-H(20A)	119.1	H(23B)-C(23)-H(23C)	109.5
C(19)-C(20)-H(20A)	119.1		

Table 20. Anisotropic displacement parameters for **181**.

The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U^{11} + ... + 2 h k a^*b^*U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}	($Å^2$x 10^3)
S	11(1)	19(1)	21(1)	0(1)	-2(1)	-7(1)	
N	11(1)	17(1)	20(1)	-1(1)	-2(1)	-6(1)	
O(1)	16(1)	21(1)	25(1)	-1(1)	0(1)	-3(1)	
C(1)	11(1)	14(1)	20(1)	1(1)	-3(1)	-6(1)	
O(2)	19(1)	34(1)	27(1)	3(1)	-5(1)	-17(1)	
C(2)	14(1)	16(1)	22(1)	3(1)	-5(1)	-7(1)	
C(3)	12(1)	16(1)	32(2)	3(1)	-4(1)	-6(1)	
C(4)	24(2)	27(2)	39(2)	12(1)	-7(1)	-14(2)	

C(5)	20(2)	29(2)	44(2)	12(2)	-4(1)	-13(2)
C(6)	14(1)	16(1)	30(2)	-2(1)	-4(1)	-7(1)
C(7)	15(1)	18(1)	26(2)	-2(1)	-4(1)	-10(1)
C(8)	14(1)	19(2)	26(2)	2(1)	-2(1)	-7(1)
C(9)	18(1)	20(2)	31(2)	3(1)	-5(1)	-4(1)
C(10)	25(2)	22(2)	51(2)	5(2)	-12(2)	-7(2)
C(11)	25(2)	18(2)	28(2)	1(1)	-9(1)	-10(1)
C(12)	32(2)	24(2)	30(2)	-2(1)	-7(1)	-16(2)
C(13)	25(2)	31(2)	25(2)	1(1)	-7(1)	-17(1)
C(14)	17(1)	30(2)	22(2)	6(1)	-5(1)	-11(1)
C(15)	19(1)	17(1)	24(2)	2(1)	-5(1)	-8(1)
C(16)	17(1)	20(2)	18(1)	3(1)	-4(1)	-10(1)
C(17)	18(1)	19(2)	25(2)	-3(1)	1(1)	-9(1)
C(18)	22(2)	26(2)	23(2)	3(1)	-3(1)	-10(1)
C(19)	18(1)	21(2)	31(2)	5(1)	2(1)	-10(1)
C(20)	22(2)	18(2)	39(2)	-1(1)	1(1)	-8(1)
C(21)	24(2)	25(2)	29(2)	0(1)	-2(1)	-18(1)
C(22)	16(1)	21(2)	24(2)	4(1)	-1(1)	-9(1)
C(23)	25(2)	25(2)	38(2)	11(1)	0(1)	-8(2)

Table 21. Hydrogen coordinates and isotropic displacement parameters for **181**.

	x(10^4)	y(10^4)	z(10^4)	U(eq) (Å^2 x 10^3)
H(1A)	8270	1448	2576	18
H(4A)	6891	7413	1703	35
H(4B)	7166	5930	992	35

H(5A)	10693	4884	766	36
H(5B)	10418	6368	1477	36
H(6A)	10210	4413	2972	24
H(7A)	7445	4403	3808	22
H(7B)	6375	6158	3358	22
H(8A)	11473	941	1304	24
H(8B)	12410	2017	1680	24
H(9A)	12356	569	2915	30
H(10A)	12417	-1880	1815	41
H(10B)	13010	-2228	2719	41
H(11A)	8957	-400	1409	28
H(12A)	8048	-1002	236	33
H(13A)	5652	1233	-345	30
H(14A)	4155	4071	263	27
H(15A)	5032	4693	1444	24
H(17A)	5724	3350	4946	25
H(18A)	7527	984	5656	29
H(20A)	8142	-2367	3826	33
H(21A)	6271	-22	3124	29
H(23A)	9317	-2055	5784	47
H(23B)	10487	-3165	4947	47
H(23C)	8541	-3217	5363	47

APPENDIX C

X-RAY DATA FOR 268

Table 22. Crystal data and structure refinement for **268**.

Identification code	yan5	
Empirical formula	C32 H36 N5 O5 P Si	
Formula weight	629.72	
Temperature	100(2) K	
Wavelength	1.54178 Å	
Crystal system	Triclinic	
Space group	P -1	
Unit cell dimensions	a = 11.1144(18) Å	a= 88.012(7) °.
	b = 12.2142(18) Å	b= 69.895(8) °.
	c = 13.799(2) Å	g = 72.721(7) °.
Volume	1675.0(4) $Å^3$	
Z	2	
Density (calculated)	1.249 Mg/m^3	
Absorption coefficient	1.449 mm^{-1}	

F(000)	664
Crystal size	0.09 x 0.06 x 0.02 mm^3
Theta range for data collection	3.80 to 67.68 °.
Index ranges	-13<=h<=8, -13<=k<=13, -15<=l<=15
Reflections collected	8530
Independent reflections	4306 [R(int) = 0.0529]
Completeness to theta = 67.68 °	70.8 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9716 and 0.8806
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4306 / 0 / 401
Goodness-of-fit on F^2	1.171
Final R indices [I>2sigma(I)]	R1 = 0.0712, wR2 = 0.1572
R indices (all data)	R1 = 0.1137, wR2 = 0.1738
Largest diff. peak and hole	0.593 and -0.468 e.$Å^{-3}$

Table 23. Atomic coordinates and equivalent isotropic displacement parameters for **268**.

U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x(10^4)	y(10^4)	z(10^4)	U(eq) ($Å^2$ x 10^3)
P(1)	8395(1)	2556(1)	1993(1)	32(1)
Si(1)	1880(1)	5984(1)	3658(1)	39(1)
O(1)	7510(3)	2344(3)	3024(2)	35(1)
N(1)	8101(4)	3890(3)	1619(3)	28(1)

C(1)	9228(5)	1568(4)	-35(4)	35(1)
O(2)	2840(3)	8836(3)	4871(3)	42(1)
N(2)	6504(4)	7476(3)	4838(3)	33(1)
C(2)	9055(5)	972(4)	-793(4)	38(1)
N(3)	5167(3)	8112(3)	5117(3)	31(1)
O(3)	1218(3)	10172(3)	5932(3)	54(1)
C(3)	7968(5)	558(4)	-559(4)	38(1)
O(4)	1851(3)	12416(3)	8314(3)	49(1)
N(4)	2401(4)	9569(3)	5612(4)	40(1)
C(4)	7038(5)	736(4)	430(4)	36(1)
O(5)	3775(4)	11951(3)	8565(3)	48(1)
N(5)	3034(4)	11819(3)	8120(3)	39(1)
C(5)	7227(5)	1312(4)	1197(4)	34(1)
C(6)	8304(4)	1744(4)	975(4)	27(1)
C(7)	10457(5)	1620(4)	2729(4)	34(1)
C(8)	11742(5)	1360(4)	2744(4)	38(1)
C(9)	12710(5)	1712(4)	1968(4)	38(1)
C(10)	12385(5)	2292(4)	1175(4)	36(1)
C(11)	11093(5)	2555(4)	1156(4)	36(1)
C(12)	10104(5)	2223(4)	1945(4)	32(1)
C(13)	8383(6)	4528(5)	-561(4)	62(2)
C(14)	7256(5)	5189(4)	409(4)	38(1)
C(15)	6928(4)	4428(4)	1299(3)	31(1)

C(16)	8129(4)	4778(4)	2319(4)	34(1)
C(17)	6662(4)	5494(4)	2809(4)	31(1)
C(18)	5865(4)	5120(4)	2283(4)	31(1)
C(19)	4589(4)	6020(5)	2268(4)	34(1)
C(20)	3725(5)	5531(4)	2922(4)	33(1)
C(21)	4858(4)	4502(4)	3024(4)	35(1)
C(22)	1256(5)	4748(5)	3603(4)	55(2)
C(23)	1006(6)	7244(5)	3126(5)	71(2)
C(24)	1682(5)	6368(5)	5011(4)	50(2)
C(25)	6151(4)	6322(4)	3588(4)	32(1)
C(26)	6906(5)	6660(4)	4120(4)	35(1)
C(27)	4648(4)	9026(4)	5831(4)	27(1)
C(28)	3298(4)	9741(4)	6096(4)	29(1)
C(29)	2778(5)	10650(4)	6841(4)	33(1)
C(30)	3590(5)	10869(4)	7305(4)	32(1)
C(31)	4937(5)	10219(4)	7043(4)	33(1)
C(32)	5449(4)	9300(4)	6317(3)	30(1)

Table 24. Bond lengths [Å] for **268**.

P(1)-O(1)	1.490(3)	Si(1)-C(22)	1.854(5)
P(1)-N(1)	1.665(4)	Si(1)-C(24)	1.862(5)
P(1)-C(6)	1.794(5)	Si(1)-C(20)	1.864(5)
P(1)-C(12)	1.799(5)	N(1)-C(15)	1.480(5)
Si(1)-C(23)	1.837(6)	N(1)-C(16)	1.491(6)

C(1)-C(2)	1.391(7)	C(7)-H(7A)	0.9500
C(1)-C(6)	1.397(6)	C(8)-C(9)	1.393(7)
C(1)-H(1A)	0.9500	C(8)-H(8A)	0.9500
O(2)-N(4)	1.244(5)	C(9)-C(10)	1.376(7)
N(2)-C(26)	1.293(6)	C(9)-H(9A)	0.9500
N(2)-N(3)	1.379(5)	C(10)-C(11)	1.385(6)
C(2)-C(3)	1.379(6)	C(10)-H(10A)	0.9500
C(2)-H(2A)	0.9500	C(11)-C(12)	1.404(7)
N(3)-C(27)	1.361(6)	C(11)-H(11A)	0.9500
N(3)-H(3B)	0.8800	C(13)-C(14)	1.527(7)
O(3)-N(4)	1.231(5)	C(13)-H(13A)	0.9800
C(3)-C(4)	1.377(7)	C(13)-H(13B)	0.9800
C(3)-H(3A)	0.9500	C(13)-H(13C)	0.9800
O(4)-N(5)	1.239(5)	C(14)-C(15)	1.523(6)
N(4)-C(28)	1.441(6)	C(14)-H(14A)	0.9900
C(4)-C(5)	1.396(7)	C(14)-H(14B)	0.9900
C(4)-H(4A)	0.9500	C(15)-C(18)	1.530(6)
O(5)-N(5)	1.231(5)	C(15)-H(15A)	1.0000
N(5)-C(30)	1.476(6)	C(16)-C(17)	1.522(6)
C(5)-C(6)	1.385(6)	C(16)-H(16A)	0.9900
C(5)-H(5A)	0.9500	C(16)-H(16B)	0.9900
C(7)-C(8)	1.376(6)	C(17)-C(25)	1.347(6)
C(7)-C(12)	1.389(7)	C(17)-C(18)	1.492(6)

C(18)-C(19)	1.521(6)	C(24)-H(24B)	0.9800
C(18)-C(21)	1.590(6)	C(24)-H(24C)	0.9800
C(19)-C(20)	1.342(7)	C(25)-C(26)	1.436(6)
C(19)-H(19)	1.03(5)	C(25)-H(25A)	0.9500
C(20)-C(21)	1.535(6)	C(26)-H(26A)	0.9500
C(21)-H(21A)	0.9900	C(27)-C(32)	1.398(6)
C(21)-H(21B)	0.9900	C(27)-C(28)	1.419(6)
C(22)-H(22A)	0.9800	C(28)-C(29)	1.384(6)
C(22)-H(22B)	0.9800	C(29)-C(30)	1.360(6)
C(22)-H(22C)	0.9800	C(29)-H(29A)	0.9500
C(23)-H(23A)	0.9800	C(30)-C(31)	1.394(6)
C(23)-H(23B)	0.9800	C(31)-C(32)	1.376(6)
C(23)-H(23C)	0.9800	C(31)-H(31A)	0.9500
C(24)-H(24A)	0.9800	C(32)-H(32A)	0.9500

Table 25. Bond angles [°] for **268**.

O(1)-P(1)-N(1)	118.55(18)	C(22)-Si(1)-C(24)	110.9(3)
O(1)-P(1)-C(6)	110.9(2)	C(23)-Si(1)-C(20)	110.8(3)
N(1)-P(1)-C(6)	103.5(2)	C(22)-Si(1)-C(20)	108.1(2)
O(1)-P(1)-C(12)	110.8(2)	C(24)-Si(1)-C(20)	105.8(2)
N(1)-P(1)-C(12)	101.9(2)	C(15)-N(1)-C(16)	105.8(3)
C(6)-P(1)-C(12)	110.6(2)	C(15)-N(1)-P(1)	121.1(3)
C(23)-Si(1)-C(22)	111.4(3)	C(16)-N(1)-P(1)	116.0(3)
C(23)-Si(1)-C(24)	109.6(3)	C(2)-C(1)-C(6)	120.0(4)

C(2)-C(1)-H(1A)	120.0	C(4)-C(5)-H(5A)	119.3
C(6)-C(1)-H(1A)	120.0	C(5)-C(6)-C(1)	118.5(4)
C(26)-N(2)-N(3)	114.9(4)	C(5)-C(6)-P(1)	118.0(4)
C(3)-C(2)-C(1)	120.6(5)	C(1)-C(6)-P(1)	123.5(3)
C(3)-C(2)-H(2A)	119.7	C(8)-C(7)-C(12)	121.1(5)
C(1)-C(2)-H(2A)	119.7	C(8)-C(7)-H(7A)	119.4
C(27)-N(3)-N(2)	120.1(4)	C(12)-C(7)-H(7A)	119.4
C(27)-N(3)-H(3B)	120.0	C(7)-C(8)-C(9)	119.8(5)
N(2)-N(3)-H(3B)	120.0	C(7)-C(8)-H(8A)	120.1
C(2)-C(3)-C(4)	120.1(5)	C(9)-C(8)-H(8A)	120.1
C(2)-C(3)-H(3A)	119.9	C(10)-C(9)-C(8)	119.9(5)
C(4)-C(3)-H(3A)	119.9	C(10)-C(9)-H(9A)	120.1
O(3)-N(4)-O(2)	121.5(4)	C(8)-C(9)-H(9A)	120.1
O(3)-N(4)-C(28)	118.9(4)	C(9)-C(10)-C(11)	120.6(5)
O(2)-N(4)-C(28)	119.6(4)	C(9)-C(10)-H(10A)	119.7
C(3)-C(4)-C(5)	119.4(5)	C(11)-C(10)-H(10A)	119.7
C(3)-C(4)-H(4A)	120.3	C(10)-C(11)-C(12)	120.0(5)
C(5)-C(4)-H(4A)	120.3	C(10)-C(11)-H(11A)	120.0
O(5)-N(5)-O(4)	124.8(4)	C(12)-C(11)-H(11A)	120.0
O(5)-N(5)-C(30)	117.6(4)	C(7)-C(12)-C(11)	118.6(5)
O(4)-N(5)-C(30)	117.6(5)	C(7)-C(12)-P(1)	118.5(4)
C(6)-C(5)-C(4)	121.4(5)	C(11)-C(12)-P(1)	122.8(4)
C(6)-C(5)-H(5A)	119.3	C(14)-C(13)-H(13A)	109.5

C(14)-C(13)-H(13B)	109.5	C(25)-C(17)-C(18)	125.1(4)
H(13A)-C(13)-H(13B)	109.5	C(25)-C(17)-C(16)	126.6(5)
C(14)-C(13)-H(13C)	109.5	C(18)-C(17)-C(16)	108.3(4)
H(13A)-C(13)-H(13C)	109.5	C(17)-C(18)-C(15)	103.9(4)
H(13B)-C(13)-H(13C)	109.5	C(17)-C(18)-C(19)	116.3(4)
C(15)-C(14)-C(13)	112.8(4)	C(15)-C(18)-C(19)	122.0(4)
C(15)-C(14)-H(14A)	109.0	C(17)-C(18)-C(21)	112.7(4)
C(13)-C(14)-H(14A)	109.0	C(15)-C(18)-C(21)	117.3(4)
C(15)-C(14)-H(14B)	109.0	C(19)-C(18)-C(21)	84.4(4)
C(13)-C(14)-H(14B)	109.0	C(20)-C(19)-C(18)	96.4(4)
H(14A)-C(14)-H(14B)	107.8	C(20)-C(19)-H(19)	130(3)
N(1)-C(15)-C(14)	111.9(4)	C(18)-C(19)-H(19)	134(3)
N(1)-C(15)-C(18)	103.5(4)	C(19)-C(20)-C(21)	92.9(4)
C(14)-C(15)-C(18)	111.9(4)	C(19)-C(20)-Si(1)	135.6(4)
N(1)-C(15)-H(15A)	109.8	C(21)-C(20)-Si(1)	130.6(4)
C(14)-C(15)-H(15A)	109.8	C(20)-C(21)-C(18)	86.2(3)
C(18)-C(15)-H(15A)	109.8	C(20)-C(21)-H(21A)	114.3
N(1)-C(16)-C(17)	104.1(4)	C(18)-C(21)-H(21A)	114.3
N(1)-C(16)-H(16A)	110.9	C(20)-C(21)-H(21B)	114.3
C(17)-C(16)-H(16A)	110.9	C(18)-C(21)-H(21B)	114.3
N(1)-C(16)-H(16B)	110.9	H(21A)-C(21)-H(21B)	111.4
C(17)-C(16)-H(16B)	110.9	Si(1)-C(22)-H(22A)	109.5
H(16A)-C(16)-H(16B)	108.9	Si(1)-C(22)-H(22B)	109.5

H(22A)-C(22)-H(22B)	109.5	N(2)-C(26)-H(26A)	115.5
Si(1)-C(22)-H(22C)	109.5	C(25)-C(26)-H(26A)	115.5
H(22A)-C(22)-H(22C)	109.5	N(3)-C(27)-C(32)	120.4(4)
H(22B)-C(22)-H(22C)	109.5	N(3)-C(27)-C(28)	121.7(4)
Si(1)-C(23)-H(23A)	109.5	C(32)-C(27)-C(28)	117.8(4)
Si(1)-C(23)-H(23B)	109.5	C(29)-C(28)-C(27)	121.0(5)
H(23A)-C(23)-H(23B)	109.5	C(29)-C(28)-N(4)	116.5(4)
Si(1)-C(23)-H(23C)	109.5	C(27)-C(28)-N(4)	122.6(4)
H(23A)-C(23)-H(23C)	109.5	C(30)-C(29)-C(28)	119.0(4)
H(23B)-C(23)-H(23C)	109.5	C(30)-C(29)-H(29A)	120.5
Si(1)-C(24)-H(24A)	109.5	C(28)-C(29)-H(29A)	120.5
Si(1)-C(24)-H(24B)	109.5	C(29)-C(30)-C(31)	122.1(4)
H(24A)-C(24)-H(24B)	109.5	C(29)-C(30)-N(5)	119.3(4)
Si(1)-C(24)-H(24C)	109.5	C(31)-C(30)-N(5)	118.5(5)
H(24A)-C(24)-H(24C)	109.5	C(32)-C(31)-C(30)	118.9(5)
H(24B)-C(24)-H(24C)	109.5	C(32)-C(31)-H(31A)	120.5
C(17)-C(25)-C(26)	125.4(4)	C(30)-C(31)-H(31A)	120.5
C(17)-C(25)-H(25A)	117.3	C(31)-C(32)-C(27)	121.1(4)
C(26)-C(25)-H(25A)	117.3	C(31)-C(32)-H(32A)	119.5
N(2)-C(26)-C(25)	129.1(4)	C(27)-C(32)-H(32A)	119.5

Table 26. Anisotropic displacement parameters for **268**.

The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U^{11} + ... + 2 h k a^*b^*U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}	($Å^2 x\ 10^3$)
P(1)	29(1)	31(1)	26(1)	-8(1)	0(1)	-6(1)	
Si(1)	29(1)	42(1)	33(1)	-9(1)	0(1)	-3(1)	
O(1)	32(2)	35(2)	25(2)	-4(2)	5(2)	-8(1)	
N(1)	26(2)	28(2)	24(2)	-3(2)	-1(2)	-6(2)	
C(1)	30(2)	32(3)	38(4)	-8(2)	-5(3)	-10(2)	
O(2)	37(2)	42(2)	40(2)	-10(2)	-7(2)	-9(2)	
N(2)	31(2)	28(2)	30(3)	-5(2)	-2(2)	-2(2)	
C(2)	35(3)	34(3)	33(3)	-11(2)	-3(3)	-4(2)	
N(3)	25(2)	33(2)	29(3)	-11(2)	-4(2)	-6(2)	
O(3)	32(2)	46(2)	74(3)	-14(2)	-14(2)	0(2)	
C(3)	48(3)	29(3)	36(4)	-10(2)	-14(3)	-8(2)	
O(4)	40(2)	37(2)	45(3)	-12(2)	11(2)	-6(2)	
N(4)	33(2)	31(2)	47(3)	1(2)	-6(2)	-8(2)	
C(4)	31(3)	38(3)	37(4)	-6(2)	-7(3)	-14(2)	
O(5)	55(2)	44(2)	32(2)	-15(2)	-2(2)	-13(2)	
N(5)	42(3)	32(3)	30(3)	-6(2)	3(2)	-10(2)	
C(5)	34(3)	34(3)	28(3)	-7(2)	-5(2)	-9(2)	
C(6)	28(2)	21(3)	31(3)	-6(2)	-9(2)	-7(2)	
C(7)	32(3)	33(3)	28(3)	-8(2)	0(2)	-7(2)	
C(8)	40(3)	39(3)	31(3)	-6(2)	-9(3)	-8(2)	
C(9)	32(3)	42(3)	38(4)	-7(3)	-10(3)	-10(2)	
C(10)	32(3)	35(3)	35(4)	-6(2)	-4(3)	-9(2)	

C(11)	35(3)	32(3)	30(3)	-6(2)	-1(2)	-8(2)
C(12)	32(2)	29(3)	28(3)	-11(2)	-2(2)	-7(2)
C(13)	72(4)	50(4)	34(4)	-8(3)	8(3)	-8(3)
C(14)	39(3)	34(3)	24(3)	-11(2)	1(2)	1(2)
C(15)	34(3)	29(3)	19(3)	-6(2)	2(2)	-8(2)
C(16)	29(2)	31(3)	29(3)	-14(2)	3(2)	-5(2)
C(17)	30(2)	27(3)	21(3)	1(2)	3(2)	-1(2)
C(18)	29(2)	28(3)	25(3)	-6(2)	4(2)	-8(2)
C(19)	29(3)	31(3)	36(3)	-6(3)	-7(3)	-5(2)
C(20)	34(3)	29(3)	34(3)	-7(2)	-12(3)	-5(2)
C(21)	30(2)	33(3)	33(3)	-8(2)	-1(2)	-10(2)
C(22)	40(3)	73(4)	36(4)	-16(3)	4(3)	-16(3)
C(23)	68(4)	64(4)	56(5)	-6(3)	-12(4)	5(3)
C(24)	50(3)	47(3)	41(4)	-14(3)	1(3)	-17(3)
C(25)	24(2)	33(3)	28(3)	-9(2)	1(2)	-6(2)
C(26)	34(3)	30(3)	29(3)	-1(2)	3(2)	-8(2)
C(27)	23(2)	25(3)	26(3)	-1(2)	-2(2)	-7(2)
C(28)	25(2)	30(3)	29(3)	-2(2)	-4(2)	-11(2)
C(29)	29(2)	27(3)	31(3)	-1(2)	1(2)	-4(2)
C(30)	37(3)	26(3)	24(3)	-3(2)	0(2)	-9(2)
C(31)	35(3)	32(3)	29(3)	2(2)	-6(2)	-14(2)
C(32)	24(2)	36(3)	19(3)	-8(2)	1(2)	-2(2)

Table 27.Hydrogen coordinates and isotropic displacement parameters for **268**.

	x ($x10^4$)	y ($x10^4$)	z ($x10^4$)	U(eq) ($Å^2 x10^3$)
H(1A)	9976	1856	-205	42
H(2A)	9691	849	-1478	45
H(3B)	4650	7928	4832	37
H(3A)	7860	150	-1082	46
H(4A)	6277	469	590	43
H(5A)	6603	1410	1885	41
H(7A)	9798	1384	3265	41
H(8A)	11970	940	3282	46
H(9A)	13592	1552	1985	45
H(10A)	13053	2514	637	44
H(11A)	10876	2961	609	43
H(13A)	8566	5059	-1102	92
H(13B)	8108	3930	-806	92
H(13C)	9197	4170	-397	92
H(14A)	7523	5813	633	45
H(14B)	6437	5548	237	45
H(15A)	6611	3818	1094	37
H(16A)	8682	5257	1923	40
H(16B)	8495	4415	2853	40
H(19)	4400(40)	6780(40)	1910(40)	37(14)
H(21A)	4905	3760	2723	42
H(21B)	4891	4435	3732	42

H(22A)	1361	4567	2886	82
H(22B)	304	4944	4037	82
H(22C)	1773	4078	3856	82
H(23A)	1108	7039	2416	106
H(23B)	1395	7867	3126	106
H(23C)	49	7500	3553	106
H(24A)	2007	7028	5022	75
H(24B)	2203	5712	5275	75
H(24C)	730	6566	5447	75
H(25A)	5214	6714	3804	38
H(26A)	7829	6225	3915	42
H(29A)	1868	11115	7025	40
H(31A)	5493	10408	7359	39
H(32A)	6361	8844	6143	36

APPENDIX D

X-RAY DATA FOR 283

Table 28. Crystal data and structure refinement for **283**.

Identification code	yan6	
Empirical formula	C24 H27 N O3 S	
Formula weight	409.53	
Temperature	150(2) K	
Wavelength	1.54178 Å	
Crystal system	Monoclinic	
Space group	P 21/c	
Unit cell dimensions	a = 12.1214(2) Å	a= 90 °.
	b = 14.4706(2) Å	b= 110.5600(10) °.
	c = 13.0421(2) Å	g = 90 °.
Volume	2141.92(6) $Å^3$	
Z	4	
Density (calculated)	1.270 Mg/m^3	
Absorption coefficient	1.537 mm^{-1}	

F(000)	872
Crystal size	0.21 x 0.15 x 0.09 mm^3
Theta range for data collection	3.89 to 72.13 °.
Index ranges	-14<=h<=14, -16<=k<=17, -15<=l<=15
Reflections collected	15495
Independent reflections	4034 [R(int) = 0.0171]
Completeness to theta = 70.00 °	98.4 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.8741 and 0.7385
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4034 / 0 / 370
Goodness-of-fit on F^2	1.659
Final R indices [I>2sigma(I)]	R1 = 0.0347, wR2 = 0.1212
R indices (all data)	R1 = 0.0360, wR2 = 0.1235
Largest diff. peak and hole	0.311 and -0.331 e.$Å^{-3}$

Table 29. Atomic coordinates and equivalent isotropic displacement parameters for **283**.

U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x (10^4)	y (10^4)	z (10^4)	U(eq) ($Å^2$ x 10^3)
S(1)	4751(1)	2336(1)	9149(1)	28(1)
O(1)	1863(1)	-377(1)	8502(1)	36(1)
N(1)	3758(1)	1640(1)	8308(1)	24(1)
C(1)	4045(1)	644(1)	8443(1)	29(1)

O(2)	5001(1)	1952(1)	10221(1)	43(1)
C(2)	3059(1)	223(1)	7489(1)	24(1)
O(3)	4314(1)	3258(1)	8914(1)	41(1)
C(3)	1930(1)	48(1)	7721(1)	25(1)
C(4)	965(1)	463(1)	6829(1)	25(1)
C(5)	1371(1)	958(1)	6170(1)	22(1)
C(6)	2717(1)	936(1)	6548(1)	20(1)
C(7)	3322(1)	1865(1)	7117(1)	20(1)
C(8)	622(1)	1464(1)	5169(1)	29(1)
C(9)	3168(1)	694(1)	5617(1)	24(1)
C(10)	2652(1)	-190(1)	4982(1)	30(1)
C(11)	3238(1)	-430(1)	4159(1)	38(1)
C(12)	1733(1)	2885(1)	7366(1)	25(1)
C(13)	977(1)	3640(1)	7054(1)	30(1)
C(14)	1034(1)	4230(1)	6233(1)	34(1)
C(15)	1843(1)	4071(1)	5729(1)	36(1)
C(16)	2606(1)	3313(1)	6037(1)	29(1)
C(17)	2542(1)	2714(1)	6850(1)	22(1)
C(18)	6103(1)	2723(1)	7914(1)	25(1)
C(19)	7100(1)	2631(1)	7640(1)	28(1)
C(20)	8047(1)	2084(1)	8270(1)	28(1)
C(21)	7969(1)	1634(1)	9186(1)	30(1)
C(22)	6966(1)	1703(1)	9458(1)	26(1)

C(23)	6036(1)	2251(1)	8817(1)	22(1)
C(24)	9117(1)	1963(1)	7952(2)	45(1)

Table 30. Bond lengths [Å] for **283**.

S(1)-O(3)	1.4277(11)	C(7)-C(17)	1.5141(14)
S(1)-O(2)	1.4340(10)	C(7)-H(7)	1.003(16)
S(1)-N(1)	1.6547(10)	C(8)-H(8A)	0.96(2)
S(1)-C(23)	1.7621(12)	C(8)-H(8B)	0.98(3)
O(1)-C(3)	1.2154(15)	C(8)-H(8C)	0.99(3)
N(1)-C(1)	1.4800(15)	C(9)-C(10)	1.5336(15)
N(1)-C(7)	1.4912(13)	C(9)-H(9A)	1.005(16)
C(1)-C(2)	1.5170(15)	C(9)-H(9B)	0.924(18)
C(1)-H(1A)	0.984(19)	C(10)-C(11)	1.5204(19)
C(1)-H(1B)	1.015(16)	C(10)-H(10A)	1.00(2)
C(2)-C(3)	1.5238(16)	C(10)-H(10B)	0.950(18)
C(2)-C(6)	1.5445(14)	C(11)-H(11B)	1.037(19)
C(2)-H(2)	0.993(17)	C(11)-H(11C)	0.97(2)
C(3)-C(4)	1.4582(16)	C(11)-H(11A)	0.93(2)
C(4)-C(5)	1.3391(17)	C(12)-C(13)	1.3915(17)
C(4)-H(4)	0.966(19)	C(12)-C(17)	1.3929(17)
C(5)-C(8)	1.4941(15)	C(12)-H(12)	0.926(17)
C(5)-C(6)	1.5296(14)	C(13)-C(14)	1.3899(19)
C(6)-C(9)	1.5362(15)	C(13)-H(13)	0.982(18)
C(6)-C(7)	1.5859(14)	C(14)-C(15)	1.379(2)

C(14)-H(14)	0.94(2)	C(20)-C(21)	1.3924(18)
C(15)-C(16)	1.3995(18)	C(20)-C(24)	1.5055(18)
C(15)-H(15)	0.98(2)	C(21)-C(22)	1.3851(18)
C(16)-C(17)	1.3922(17)	C(21)-H(21)	0.980(18)
C(16)-H(16)	0.945(17)	C(22)-C(23)	1.3917(16)
C(18)-C(19)	1.3819(19)	C(22)-H(22)	0.908(18)
C(18)-C(23)	1.3879(17)	C(24)-H(24A)	1.01(3)
C(18)-H(18)	0.945(17)	C(24)-H(24B)	1.01(3)
C(19)-C(20)	1.3985(19)	C(24)-H(24C)	0.92(3)
C(19)-H(19)	0.947(18)		

Table 31. Bond angles [°] for **283**.

O(3)-S(1)-O(2)	120.42(7)	N(1)-C(1)-H(1B)	108.2(10)
O(3)-S(1)-N(1)	107.28(5)	C(2)-C(1)-H(1B)	112.7(9)
O(2)-S(1)-N(1)	105.41(6)	H(1A)-C(1)-H(1B)	110.0(13)
O(3)-S(1)-C(23)	107.84(6)	C(1)-C(2)-C(3)	114.09(10)
O(2)-S(1)-C(23)	108.08(6)	C(1)-C(2)-C(6)	107.36(9)
N(1)-S(1)-C(23)	107.14(5)	C(3)-C(2)-C(6)	105.09(9)
C(1)-N(1)-C(7)	108.55(9)	C(1)-C(2)-H(2)	112.7(9)
C(1)-N(1)-S(1)	115.38(7)	C(3)-C(2)-H(2)	107.2(9)
C(7)-N(1)-S(1)	117.83(8)	C(6)-C(2)-H(2)	110.1(9)
N(1)-C(1)-C(2)	102.06(9)	O(1)-C(3)-C(4)	127.30(11)
N(1)-C(1)-H(1A)	111.9(11)	O(1)-C(3)-C(2)	125.38(11)
C(2)-C(1)-H(1A)	111.8(10)	C(4)-C(3)-C(2)	107.31(9)

C(5)-C(4)-C(3)	111.09(10)	H(8B)-C(8)-H(8C)	100(2)
C(5)-C(4)-H(4)	126.6(10)	C(10)-C(9)-C(6)	115.21(10)
C(3)-C(4)-H(4)	122.3(10)	C(10)-C(9)-H(9A)	107.6(9)
C(4)-C(5)-C(8)	125.12(11)	C(6)-C(9)-H(9A)	107.9(9)
C(4)-C(5)-C(6)	111.92(10)	C(10)-C(9)-H(9B)	110.0(10)
C(8)-C(5)-C(6)	122.94(10)	C(6)-C(9)-H(9B)	108.7(11)
C(5)-C(6)-C(9)	112.66(9)	H(9A)-C(9)-H(9B)	107.1(14)
C(5)-C(6)-C(2)	103.18(9)	C(11)-C(10)-C(9)	111.67(11)
C(9)-C(6)-C(2)	113.92(9)	C(11)-C(10)-H(10A)	109.8(11)
C(5)-C(6)-C(7)	113.53(9)	C(9)-C(10)-H(10A)	113.0(11)
C(9)-C(6)-C(7)	109.14(9)	C(11)-C(10)-H(10B)	111.1(10)
C(2)-C(6)-C(7)	104.08(8)	C(9)-C(10)-H(10B)	108.2(10)
N(1)-C(7)-C(17)	112.34(9)	H(10A)-C(10)-H(10B)	102.8(14)
N(1)-C(7)-C(6)	103.84(8)	C(10)-C(11)-H(11B)	109.4(11)
C(17)-C(7)-C(6)	115.54(9)	C(10)-C(11)-H(11C)	109.3(11)
N(1)-C(7)-H(7)	109.2(8)	H(11B)-C(11)-H(11C)	106.9(16)
C(17)-C(7)-H(7)	109.8(8)	C(10)-C(11)-H(11A)	113.1(13)
C(6)-C(7)-H(7)	105.7(8)	H(11B)-C(11)-H(11A)	105.6(16)
C(5)-C(8)-H(8A)	116.2(14)	H(11C)-C(11)-H(11A)	112.4(18)
C(5)-C(8)-H(8B)	110.2(13)	C(13)-C(12)-C(17)	120.16(11)
H(8A)-C(8)-H(8B)	108(2)	C(13)-C(12)-H(12)	121.2(10)
C(5)-C(8)-H(8C)	113.4(15)	C(17)-C(12)-H(12)	118.6(10)
H(8A)-C(8)-H(8C)	107.5(19)	C(12)-C(13)-C(14)	120.08(12)

C(12)-C(13)-H(13)	120.1(9)	C(20)-C(19)-H(19)	118.6(11)
C(14)-C(13)-H(13)	119.8(9)	C(21)-C(20)-C(19)	118.72(11)
C(15)-C(14)-C(13)	120.07(12)	C(21)-C(20)-C(24)	120.44(13)
C(15)-C(14)-H(14)	121.4(12)	C(19)-C(20)-C(24)	120.82(13)
C(13)-C(14)-H(14)	118.5(12)	C(22)-C(21)-C(20)	121.06(11)
C(14)-C(15)-C(16)	120.17(12)	C(22)-C(21)-H(21)	117.3(10)
C(14)-C(15)-H(15)	122.1(11)	C(20)-C(21)-H(21)	121.7(10)
C(16)-C(15)-H(15)	117.8(11)	C(21)-C(22)-C(23)	119.04(11)
C(17)-C(16)-C(15)	119.96(12)	C(21)-C(22)-H(22)	119.4(11)
C(17)-C(16)-H(16)	120.9(10)	C(23)-C(22)-H(22)	121.5(11)
C(15)-C(16)-H(16)	119.1(10)	C(18)-C(23)-C(22)	120.96(11)
C(16)-C(17)-C(12)	119.55(11)	C(18)-C(23)-S(1)	119.63(9)
C(16)-C(17)-C(7)	118.89(11)	C(22)-C(23)-S(1)	119.41(9)
C(12)-C(17)-C(7)	121.51(10)	C(20)-C(24)-H(24A)	111.2(17)
C(19)-C(18)-C(23)	119.27(11)	C(20)-C(24)-H(24B)	106.2(18)
C(19)-C(18)-H(18)	118.1(10)	H(24A)-C(24)-H(24B)	106(2)
C(23)-C(18)-H(18)	122.7(10)	C(20)-C(24)-H(24C)	103(2)
C(18)-C(19)-C(20)	120.93(11)	H(24A)-C(24)-H(24C)	126(3)
C(18)-C(19)-H(19)	120.4(11)	H(24B)-C(24)-H(24C)	103(2)

Table 32. Anisotropic displacement parameters for **283**.

The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U^{11} + ... + 2 h k a^*b^*U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
S(1)	20(1)	42(1)	22(1)	-11(1)	7(1)	-2(1)

O(1)	42(1)	37(1)	31(1)	8(1)	16(1)	-5(1)
N(1)	19(1)	31(1)	19(1)	-1(1)	5(1)	-1(1)
C(1)	22(1)	33(1)	27(1)	5(1)	4(1)	2(1)
O(2)	27(1)	85(1)	19(1)	-9(1)	9(1)	-11(1)
C(2)	22(1)	22(1)	25(1)	3(1)	7(1)	2(1)
O(3)	28(1)	42(1)	50(1)	-25(1)	9(1)	2(1)
C(3)	29(1)	22(1)	25(1)	0(1)	11(1)	-3(1)
C(4)	20(1)	26(1)	29(1)	-3(1)	10(1)	-3(1)
C(5)	20(1)	21(1)	22(1)	-3(1)	5(1)	0(1)
C(6)	19(1)	21(1)	20(1)	0(1)	7(1)	-1(1)
C(7)	19(1)	24(1)	19(1)	-2(1)	8(1)	-2(1)
C(8)	24(1)	30(1)	27(1)	3(1)	1(1)	0(1)
C(9)	24(1)	25(1)	23(1)	-4(1)	11(1)	-3(1)
C(10)	32(1)	28(1)	31(1)	-8(1)	12(1)	-5(1)
C(11)	43(1)	38(1)	36(1)	-14(1)	17(1)	-2(1)
C(12)	25(1)	25(1)	26(1)	-1(1)	11(1)	-1(1)
C(13)	28(1)	29(1)	34(1)	-3(1)	13(1)	2(1)
C(14)	36(1)	26(1)	38(1)	1(1)	10(1)	7(1)
C(15)	48(1)	28(1)	36(1)	8(1)	17(1)	2(1)
C(16)	33(1)	27(1)	31(1)	0(1)	17(1)	-3(1)
C(17)	21(1)	22(1)	22(1)	-3(1)	7(1)	-3(1)
C(18)	25(1)	22(1)	24(1)	-1(1)	5(1)	-4(1)
C(19)	33(1)	29(1)	24(1)	-2(1)	12(1)	-10(1)

C(20)	25(1)	30(1)	32(1)	-10(1)	13(1)	-8(1)
C(21)	23(1)	30(1)	34(1)	0(1)	8(1)	2(1)
C(22)	25(1)	31(1)	23(1)	3(1)	7(1)	-1(1)
C(23)	20(1)	26(1)	21(1)	-5(1)	7(1)	-3(1)
C(24)	33(1)	59(1)	50(1)	-18(1)	25(1)	-11(1)

Table 33. Hydrogen coordinates and isotropic displacement parameters for **283**.

	x(10^4)	y(10^4)	z(10^4)	U(eq) (Å^2 x 10^3)
H(1A)	4824(16)	512(12)	8401(13)	37(4)
H(1B)	4023(14)	440(12)	9180(13)	33(4)
H(2)	3288(14)	-370(12)	7238(12)	29(4)
H(4)	149(16)	362(12)	6740(13)	38(4)
H(7)	4013(13)	1961(10)	6875(12)	20(3)
H(8A)	890(20)	1466(17)	4565(19)	65(6)
H(8B)	510(20)	2103(18)	5351(19)	65(6)
H(8C)	-210(20)	1254(19)	4890(20)	76(7)
H(9A)	4046(14)	613(11)	5946(13)	30(4)
H(9B)	3028(15)	1190(12)	5142(14)	34(4)
H(10A)	2692(17)	-729(15)	5468(16)	50(5)
H(10B)	1828(16)	-104(11)	4628(13)	34(4)
H(11B)	2876(16)	-1036(14)	3756(15)	44(5)
H(11C)	4066(19)	-549(14)	4545(16)	47(5)
H(11A)	3113(18)	12(16)	3614(17)	55(6)
H(12)	1721(13)	2494(11)	7924(13)	24(3)

H(13)	387(15)	3749(11)	7400(13)	33(4)
H(14)	517(18)	4734(16)	6039(16)	53(5)
H(15)	1910(16)	4476(14)	5155(15)	43(5)
H(16)	3145(14)	3207(11)	5674(13)	29(4)
H(18)	5493(14)	3111(12)	7475(13)	33(4)
H(19)	7146(15)	2925(12)	7008(14)	35(4)
H(21)	8621(16)	1261(12)	9668(14)	38(4)
H(22)	6938(14)	1406(12)	10062(14)	34(4)
H(24A)	9850(30)	1880(20)	8620(20)	85(8)
H(24B)	9000(30)	1360(20)	7530(20)	101(9)
H(24C)	9010(30)	2400(20)	7410(30)	95(10)

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