Asymmetric Synthesis of Azepine-Fused Cyclobutanes from Yne-Methylenecyclopropanes Involving Cyclopropanation/C−C Cleavage/Wagner−Meerwein Rearrangement and Reaction Mechanism

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ABSTRACT: Ring expansion of in situ generated cyclopropylmethyl cations via Wagner−Meerwein rearrangement to cyclobutanes is widely used in synthesis. However, the cyclopropylmethyl cations generated are planar, which would lead to loss of chiral information in the case of chiral precursors, making an asymmetric version of such ring expansion difficult. In the present work, a gold(I)-catalyzed asymmetric cyclopropanation/C−C cleavage/Wagner−Meerwein rearrangement of easily affordable yne-methylenecyclopropanes (1,6-yney-MCPs) has been developed to synthesize 3-azabicyclo[5.2.0]nonadiene, a bicyclic 7/4 ring (azepine fused with cyclobutane) with a bridgehead aryl substituent. This reaction overcomes the challenging loss of chirality from the Wagner−Meerwein rearrangement. Density functional theory calculations indicate that the chirality of the final product comes from the first cyclopropanation step in this reaction. The chirality in the resultant cyclopropane is lost in the following C−C cleavage step, generating rigid, planar cyclopropylmethyl carboxylation intermediate. Then, only one carbon of the cyclopropyl group in the cyclopropylmethyl carboxylation intermediate can migrate via ring expansion in the Wagner−Meerwein rearrangement process, and consequently, the chirality in the cyclopropane generated in the first step is transferred to the final product.

INTRODUCTION

Many natural products with significant biological and medicinal activities have cyclobutane motif. Therefore, significant efforts have been devoted by many chemists to develop methods to synthesize cyclobutanes. Developing more synthetic methods to cyclobutanes, especially their asymmetric versions are highly required so that synthetic chemists have more tools in their efficient target-, diversity-, and function-oriented syntheses.

A widely used method to access four-membered rings is the ring expansion of in situ generated cyclopropylmethyl cations via the Wagner−Meerwein rearrangement. One of the efficient ways of generating cyclopropylmethyl cations is using methylenecyclopropanes (MCPs) as precursors. The MCP ring expansion can be directly triggered by transition-metal (such as Pt, Pd, and Au) coordination to the alkene part of MCPs. Another way to achieve ring expansion is through cycloisomerization by connecting MCP with alkynes. For example, in 2008, a gold-catalyzed cycloisomerization of 1,6-yney-MCPs to four-membered carbocycle-embedded polycyclic compounds via a key cyclopropylmethyl carboxylation intermediate was accomplished by Toste (Scheme 1a). In 2014, a series of gold-catalyzed cycloisomerizations of 1,5-yney-MCPs through MCP expansions were also reported by Gagné, one representative example of which is shown in Scheme 1b. Recently, Shi has found that 1,7-yney-MCPs can be converted to two different cycloisomerization products by using two different gold catalysts, in which a ring expansion of cyclopropylmethyl carboxylation intermediate was also involved (Scheme 1c). One drawback of the ring expansion of MCPs is that these reactions are difficult to be advanced to their asymmetric versions. The main reason is that these reactions generate planar achiral cyclopropylmethyl carboxylation intermediates, which then undergo ring expansion via the Wagner−Meerwein rearrangement to give racemic four-membered products. This could be the reason why only moderate enantioselectivity has been realized when Gagné and co-workers developed the asymmetric version of their reaction shown in Scheme 1b.

Here, we report our advance in this field, a new MCP ring expansion to form 3-azabicyclo[5.2.0]nonadienes enantioselectively. This reaction not only provides a new way to four-membered rings, but also leads to the challenging seven-membered heterocycles, in this case the azepine derivatives (fused with the four-membered rings), which are widely found...
in a variety of bioactive natural products and pharmaceutically important compounds. Furthermore, we achieved the asymmetric version of this 7/4 ring synthesis by overcoming the “planar cyclopropylmethyl carbocation” challenge mentioned above. In addition to reporting the development of our asymmetric cyclization/rearrangement reaction, we also present here the reaction mechanism, especially as to how the chirality from the first cyclopropanation step is transferred (and not lost) to the final product in the Wagner–Meerwein rearrangement. We point out here that, for $R^1 = H$, the reaction in Scheme 1d gave cyclopropanation products, as demonstrated by Shi and co-workers. Therefore, we decided to develop this reaction as a general method to synthesize bicyclic 7/4 compounds as our research project.

**Reaction Optimizations.** First, we screened reaction conditions for the present reaction by using nitrogen-tethered MCP 1a as the model substrate. The reaction was initially tested in 1,2-dichloroethane (DCE) by using a commercially available Au(I) salt as the catalyst. To our delight, the expected 3-azabicyclo[5.2.0]nonadiene 2a was obtained in 99% yield (Table 1, entry 1). Structure of product 2a was further confirmed by the X-ray crystal analysis. If the reaction time was reduced to 1 h, mostly starting material remained. We also tested newly prepared Au catalyst with either JohnPhos or BuXPhos ligand, observing that the reaction gave comparable yields of 2a (Table 1, entries 2 and 3). It was also worth mentioning that a simpler triphenylphosphine (PPh$_3$) ligand could be used in this transformation (Table 1, entry 4). With these observations in hand, we next studied whether this reaction could be advanced to its asymmetric version, even though previous reports of such rearrangement had encountered limited success. We chose L1 ($O^\prime$-(S)-(1,1′-dinaphthyl-2,2′-diyl)-N,N-di-i-propyl-phosphoramidite) as the chiral ligand, which had previously proven to be efficient in asymmetric gold-catalyzed cycloisomerization of 1,6-enynes. The reaction of 1a using L1 as chiral ligand gave the target product, but the e.e. was just 7% (Table 1, entry 5). We then tested the reaction using the gold catalyst and L2 ([R]-MeO-3,5-(t-Bu)$_2$-MeOBIPHEP) ligand, finding that the reaction afforded 2a product in 97% yield and 78% e.e. (Table 1, entry 6). Through screening counter anions of the catalysts (Table 1, entries 7–11) and reaction solvents (Table 1, entries 12–15), we found that a combination of hexafluoroantimonate anion and toluene solvent gave the best results: 96% reaction yield and 96% e.e. (Table 1, entry 14).

**Reaction Scope.** With the optimized reaction conditions (Table 1, entry 14) in hand, we then carried out reaction of 1a in a larger scale. We found that in 0.2 mmol scale, product 2a was obtained in 99% yield and 99% e.e. (Table 2, entry 1). Moreover, 2a could be also synthesized in gram scale, with the same yield and e.e. value (see Experimental Section). After that, we studied the scope of the present cascade reaction. We found that substrates bearing electron-donating substituents on aryl rings linked to the alkene motif ($R^1$ and $R^2$) could also give rise to products 2b and 2c in high yields and enantiomeric excess values, respectively (Table 2, entries 2 and 3). For substrate 1d with an electron-withdrawing CF$_3$ group in the aryl ring, the reaction only gave a complex mixture under asymmetric conditions (Table 2, entry 4). We found that this substrate gave cyclopropanation product (±)-3d when no chiral ligand was used (using (MeCN)Au(JohnPhos)SbF$_6$ as the catalyst in DCE solvent; Table 2, entry 4).

We then investigated substituent effects in the alkyne moiety of yne-MCPs. We found substrates 1e–h, in which the aryl rings had either electron-donating or electron-withdrawing substituents, had high reactivities, and gave excellent enantioselectivities (Table 2, entries 5–8). The absolute configuration of 2b was determined by X-ray structure of 2h in 99% e.e., which had an R configuration. Substrates 1i–k (Table 2, entries 9–11) with alkene substituents in the alkyne moiety of yne-MCPs also gave corresponding products in high yields (from 90 to 97%) and enantiomeric excess values (from 90 to 97%). To our surprise, no reaction took place for I1 in which the alkyne moiety was substituted by an ester group...
In this case, most 11 could be recovered back after 12 h of reaction under standard reaction conditions. It was interesting to note that when the R group in the substrate was a methyl group, a mixture of 7/4 compound 2m and cyclopropanation product 3m was obtained, with a ratio of 1.3/1 and in 86% total yield (Table 2, entry 13). Moreover, this reaction showed low enantioselectivities because 2m and 3m had 27 and 64% e.e., respectively. We then studied substrates with different tethers. For both the nitrogen-tethered yne-MCP with a para-nitrobenzenesulfonyl-protecting group (1n) and the oxygen-tethered yne-MCP (1o), the desired cyclization/rearrangement products 2n (84% yield, 82% e.e.) and 2o (47% yield, 43% e.e.) were obtained (Table 2, entries 14 and 15). It was reported that the tether in the similar gold-catalyzed cycloisomerization cannot be NBoc, and we did not test such substrates. For some reactions to give solid products (2a, 2c, 2e, and 2f), we directly measured enantiomeric excess values of the reaction mixture once reactions finished and found that these results were the same as those enantiomeric excess values from the purified solid products. This indicates that the high enantioselectivity of the present reactions were not artifacts from the purified products.

**Computational Investigation.** To gain more insights into the mechanism and chirality transfer processes in this cyclopropanation/rearrangement reaction, density functional theory (DFT) calculations at the PCM(toluene)/M06-2X/6-311+G(d,p) (SDD for Au)//B3LYP/6-31G(d) (SDD for Au) level have been executed. We first chose yne-MCP 1a to investigate its reaction mechanism. The para-toluenesulfonyl-protecting group in 1a and the ligand in the Au(I) catalyst
used were simplified as a smaller methanesulfonyl group and trimethylphosphine, respectively. The energy profile (Figure 1a) was drawn based on the relative Gibbs free energies in toluene solution ($\Delta G_{\text{sol-Toluene}}$). Other computed values such as enthalpies are given in the Supporting Information. The first step of the catalytic cycle is the well-known endo cycloisomerization of 1,6-enyne, starting from a complex of Au(I) catalyst and substrate (INT1-Ph) to give INT2-Ph via a cyclopropanation transition state TS1-Ph. This step is an endergonic process of 5.2 kcal/mol with a computed activation free energy of 19.6 kcal/mol. The newly formed tricyclic intermediate INT2-Ph with an elongated carbon–carbon (C–C) bond length of 2.19 Å can be regarded as a nonclassical carbocation (Figure 1b), considering that C1–C5 in this intermediate does not form a regular cyclopropane structure (this intermediate could also be regarded as a C1 cation). The two phenyl groups in this intermediate are in a cis configuration. Then, this C1–C5 bond in INT2-Ph easily breaks up via TS3-Ph to generate a ring-expanded intermediate INT4-Ph with an activation free energy of 4.0 kcal/mol. We have to mention here that TS3-Ph has a computed imaginary frequency of 52.9 cm$^{-1}$, suggesting that this corresponds a rotation of Ph group at C1 position (intrinsic reaction coordinate (IRC) could not be run here) so that the C1–C5 bond can be further broken to give INT4-Ph.

We can locate both reactant and product in this step by geometry optimizations of structures with slightly changed C1–C5 distances that are shorter or greater than 2.48 Å.

**Table 2. Reaction Scope**

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate</th>
<th>Product $^b$</th>
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</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1a, Ar = Ph</td>
<td>2a, 99 %, 99 % e.e.</td>
<td>9</td>
<td>1i, R$^1$ = R$^2$ = H</td>
<td>2i, 82 %, 90 % e.e.</td>
</tr>
<tr>
<td>2</td>
<td>1b, Ar = 4-MeC$_6$H$_4$</td>
<td>2b, 99 %, 98 % e.e.</td>
<td>10</td>
<td>1j, R$^1$ = Me, R$^2$ = H</td>
<td>2j, 68 %, 97 % e.e.</td>
</tr>
<tr>
<td>3</td>
<td>1c, Ar = 4-MeO$_2$C$_6$H$_4$</td>
<td>2c, 97 %, 97 % e.e.</td>
<td>11 $^c$</td>
<td>1k, R$^1$ = H, R$^2$ = Me</td>
<td>2k, 85 %, 97 % e.e.</td>
</tr>
<tr>
<td>4</td>
<td>1d, Ar = 4-CF$_3$C$_6$H$_4$</td>
<td>3d, mixture (89 %)</td>
<td>12</td>
<td>1l, R = CO$_2$Me</td>
<td>N.R.</td>
</tr>
<tr>
<td>5</td>
<td>1e, R = 4-MeC$_6$H$_4$</td>
<td>2e, 95 %, 98 % e.e.</td>
<td>13 $^c$</td>
<td>1m, R = Me</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>1f, R = 4-MeOC$_6$H$_4$</td>
<td>2f, 96 %, 99 % e.e.</td>
<td>14</td>
<td>1n</td>
<td>2n, 84 %, 82 % e.e.</td>
</tr>
<tr>
<td>7</td>
<td>1g, R = 4-CF$_3$C$_6$H$_4$</td>
<td>2g, 93 %, 99 % e.e.</td>
<td>15</td>
<td>1o, Ar = 4-MeOC$_6$H$_4$</td>
<td>2o, 47 %, 43 % e.e.</td>
</tr>
</tbody>
</table>

$^a$Reaction conditions: 0.2 mmol 1, 2.5 mol % L$_2$(AuSbF$_6$)$_2$, toluene (0.05 M), 30 °C, 12 h. $^b$Isolated yields and enantiomeric excess (e.e.) values were determined by high-performance liquid chromatography (HPLC). $^c$When (MeCN)Au(JohnPhos)SbF$_6$ and 1,2-dichloroethane (DCE) were used, (+)-3d was obtained in 89% yield. $^d$1 h. $^e$3 h. $^f$0.6 mmol scale (0.05 M). N.R. = no reaction.
Later discussion of TS3-H in Figure 2, we can see a real C1–C5 bond breaking by IRC with the computed imaginary frequency of 409.4 cm\(^{-1}\).

Intermediate INT4-Ph, which is also a nonclassical carbocation, is a special cyclopropylmethyl carbocation with memory of chirality (see discussion below).\(^{25}\) In this intermediate, C1 carbon is planar, sp\(^{2}\)-hybridized, suggesting this carbon has lost its chirality from INT2-Ph, in which C1 is sp\(^{3}\)-hybridized (C5 is weakly connected to C1). But the cyclopropane characteristic in INT4-Ph is almost lost because its C2–C3 bond is 1.68 Å (see Figure 1 for atom labeling). INT4-Ph can also be regarded as a homoallylic cation if we consider that C1–C2 has double-bond character. Therefore, C1–C2 and the aryl group linked to C1 form a plane and C3 is at the bottom of this plane. Since the following step is the Wagner–Meerwein rearrangement, only C3 migration (not C4, see below) can occur and the chirality from INT2-Ph is retained in INT5-Ph. Therefore, we can call INT4-Ph is a carbocation with memory of chirality. (Here, we mean that the chiral center at C1 is kept from INT2-Ph to INT5-Ph, even though this carbon temporarily becomes planar without chirality in the intermediate between INT2-Ph and INT5-Ph.) The computed activation free energy for the carbocation rearrangement from INT4-Ph to INT5-Ph, is only 1.0 kcal/mol.\(^{26}\) There is another possibility that intermediate INT4-Ph could form the C2–C3 bond and break the C2–C4 bond to form another homoallylic cation at C4, but this homoallylic cation rearrangement is prohibited sterically by the phenyl group adjacent to C2 and can be excluded for consideration (see more discussion in the Supporting Information).

After that, a [1,2]-hydride shift converts INT5-Ph to INT6-Ph, which is a complex of Au(I) catalyst and product, with an activation free energy of 7.7 kcal/mol. The [1,2]-hydride shift step is exergonic by 31.0 kcal/mol. The final product Pro2-Ph is liberated after an exchange reaction of INT6-Ph with substrate, which is slightly exergonic by 5.5 kcal/mol. In general, the cyclopropanation step is the rate-determining step and the enantioselectivity is determined here. This newly constructed chiral center is then retained completely in the subsequent Wagner–Meerwein rearrangement.

Figure 1. Computed energy surface for the reaction of 1a and the key structures of several stationary points (bond distances in angstrom, and most hydrogen atoms in (b) are omitted for clarification).
Ring Expansion vs [1,2]-Hydride Shift. Here we explain why cyclopropanation product, which was observed by Shi, was not generated in the present system. Our calculations indicated that the direct [1,2]-hydride shift in INT2-Ph, giving a tricyclic product Pro1-Ph, has a higher activation free energy compared to the irreversible C—C bond cleavage and migration in Figure 2a,b (6.1 vs 4.0 kcal/mol). Therefore, the formation of cyclopropanation product is disfavored, which agrees with our experiments. We computed the case for R1 = H, the Shi system, finding that the C—C bond cleavage is now requiring an activation free energy of 22.1 kcal/mol, while the [1,2]-hydride shift to give cyclopropanation product is still easy with a computed activation free energy of 7.6 kcal/mol. Certainly, the C—C bond cleavage in Shi’s work generates a secondary carbocation and is disfavored. While for yne-MCP with R1 = Ar group, this cation can be stabilized by the aromatic substituent and the C—C bond cleavage is easy and needs only 4.0 kcal/mol. Therefore, the stabilization of the carbocation by aryl ring is the key reason for the different reaction patterns for Shi’s work and the present work.

Chemoselectivities for Reactions of 1d and 1m. Now let us discuss the substituent effect found in substrates 1d and 1m to answer the question regarding less or no generation of 7/4 products (Table 2). Since both chemoselectivity determination reactions (through ring expansion and [1,2]-hydride shift) arise from the same intermediate, we simply compare these two transition states here. Chemoselectivity for the reaction of 1d was first investigated. As shown in Figure 3a, substrate 1d also gives a nonclassical cation intermediate INT2-CF3Ph. The electron-withdrawing CF3 group in the aryl ring has an influence on this nonclassical cation intermediate, in which a shorter elongated C—C bond of 2.14 Å is observed in INT2-CF3Ph compared to INT2-Ph (Figure 3b). This means that more cationic character is localized in the former species than that in the latter species. This can explain the [1,2]-hydride shift here is easier (3.5 kcal/mol here compared to 7.6 kcal/mol for INT2-Ph). Comparing to a phenyl group in INT4-Ph, this electron-withdrawing CF3 group also has less stabilization on the cation intermediate INT4-CF3Ph (−0.7 kcal/mol of INT4-CF3Ph vs −1.0 kcal/mol of INT4-Ph from INT2-Ph in ΔG_{sol-Toluene}). This makes the

Figure 2. Ring expansion vs [1,2]-hydride shift for R1 = Ph and R1 = H (bond distances in angstrom, and most hydrogen atoms in (b) are omitted for clarification).
expansion step become more difficult (its transition state is destabilized to some extent) than the direct [1,2]-hydride shift (6.2 kcal/mol of TS3-CF3Ph vs 3.5 kcal/mol of TS2-CF3Ph in ΔG_{sol-Toluene}‡), which can explain that only product 3d is obtained.

We also studied the reaction of substrate 1m in Figure 4a, which gave a mixture of two products 2m and 3m with a ratio of 1.3/1. As shown in Figure 4b, a nonclassical cation intermediate INT2-Me with a shorter elongated C−C bond of 2.15 Å is found comparing to INT2-Ph. We proposed that the present system with Me group could lose some conjugation with the carbene moiety compared to that in the previous system with Ph group, making C1−C5 become shorter and the carbene part in this intermediate have more positive charge. Therefore, [1,2]-hydride shift is also easier here (3.9 vs 7.6 kcal/mol for INT2-Ph). This shorter C−C bond also makes the ring expansion of INT2-Me (through TS3-Me) slightly more difficult than the direct [1,2]-hydride shift (through TS2-Me). Moreover, the computed energy difference of TS2-Me and TS3-Me (TS3-Me − TS2-Me) in ΔG_{sol-Toluene}‡ is only 1.6 kcal/mol, suggesting that both products can be generated. This is consistent with the experiment that a mixture of 2m and 3m was observed.

CONCLUSIONS

In conclusion, we have developed an efficient asymmetric synthetic method to azepine-fused cyclobutanes with bridgehead aryl substitutions, through a gold-catalyzed tandem cyclopropanation/C−C cleavage/Wagner–Meerwein rearrangement of yne-MCPs. DFT calculations reveal that the chirality is built in the cyclopropanation step. This chirality is temporarily lost in the followed C−C cleavage reaction to form planar cyclopropylmethyl carbocation. But this intermediate has very rigid structure and can only allow one carbon (not two) of the cyclopropyl group to migrate in the followed Wagner–Meerwein rearrangement. Consequently, chirality is regenerated in the Wagner–Meerwein rearrangement. The overall outcome of this C−C cleavage and Wagner–Meerwein rearrangement is that the chirality from cyclopropanation step is transferred to the final Wagner–Meerwein rearrangement.
product. Such a process can be regarded as chirality-
memorized Wagner–Meerwein rearrangement, even though the chirality of generated cyclopropane in the first step has been lost temporarily in the formed planar cyclopropylmethyl carbocation.

■ EXPERIMENTAL SECTION

Computational Methods. All calculations were performed with the Gaussian 09 program.27 Geometry optimizations of all minima and transition structures were carried out using the hybrid B3LYP functional23 with the SDD28 basis set and pseudopotential for Au and the 6-31+G(d)22 basis set for the other atoms. The keyword "SD" was used to specify that five d-type orbitals were used for all elements in the calculations. Frequency calculations at the same level were performed to confirm that each stationary point was either a minimum or a transition structure and to evaluate its zero-point energy and the thermal corrections at 298 K. To improve the calculation accuracy, single-point energy calculations were carried out using the M06-2X21,29 functional with the SDD basis set and pseudopotential for Au and the 6-311+G(d,p)22 basis set for the other atoms. Because experiments were performed in toluene (asymmetric product synthesis) and dichloroethane (DCE, racemic product synthesis), solvation energies in both solvents were taken into consideration. Solvation energies (ΔG_{solv}) were single-point energy differences in toluene and DCE from those in the gas phase, respectively. Single-point energies in toluene (ε = 2.3741) and DCE (ε = 10.125) were evaluated by default IEFPCM30 calculations. Gibbs free energies in solutions were obtained from sums of the large basis set gas-phase single-point energies, solvation energies (ΔG_{solv}), and the gas-phase Gibbs free energy corrections (at 298 K). The energy profile was drawn according to Gibbs free energies in the toluene solution (ΔG_{sol-Toluene}). Gibbs free energies in the DCE solution (ΔG_{sol-DCE}), Gibbs free energies, and enthalpies in the gas phase (ΔG_{gas} and ΔH_{gas}) have been all given in the Supporting Information. The computed structures were illustrated using CYL-
view.31 Most hydrogen atoms in computed structures are omitted for clarity.

General Methods. Air- and moisture-sensitive reactions were carried out in oven and flame-dried glassware sealed with rubber septa under a positive pressure of dry nitrogen. Similarly, sensitive liquids and solutions were transferred via syringe. Reactions were stirred using Teflon-coated magnetic stir bars. Elevated temperatures were maintained using thermostat-controlled silicone oil baths. Organic solutions were concentrated using a Büchi rotary evaporator with a desktop vacuum pump. Tetrahydrofuran (THF) and toluene were distilled from sodium and benzophenone prior to use. DCE was superdry (water ≤ 30 ppm), which could be purchased from J&K. Synthetic reagents were purchased from J&K and Acros Organics and used without further purification, unless otherwise indicated. Analytical thin-layer chromatography (TLC) was performed with 0.25 mm silica gel G plates with a 254 nm fluorescent indicator. The TLC plates were visualized by ultraviolet light and treatment with phosphomolybdic acid stain or KMnO4 stain followed by gentle heating. Purification of products was accomplished by flash chromatography on silica gel, and the purified compounds show a single spot by analytical TLC. NMR spectra were measured on Bruker ARX 400 (1H NMR at 400 MHz, 13C NMR at 101 MHz) nuclear magnetic resonance spectrometers. Data for 1H NMR spectra were reported as follows: chemical shift (ppm), referenced to residual

Figure 4. Chemoselectivity for the reaction of 1m (bond distances in angstrom, and most hydrogen atoms in (b) are omitted for clarification).
solvent peak (CDCl3 = δ 7.26 ppm, CD2Cl2 = δ 5.32 ppm, (CD3)2SO = δ 2.50 ppm; s = singlet, brs = broad singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doubles, dt = doublet of triplets, ddd = doublet of doublet of triplets, dm = doublet of multiplet, m = multiplet), coupling constant (Hz), and integration. Data for 13C{1H} NMR were reported in terms of chemical shifts (ppm) relative to residual solvent peak (CDCl3 = δ 77.16 ppm, CD2Cl2 = δ 35.84 ppm, (CD3)2SO = δ 39.52 ppm). Infrared spectra were recorded on a Mettler Toledo ReactIR iC10 system with a SiComp probe and were reported in wavenumbers (cm⁻¹).

To a stirred solution of S1 (3-phenylprop-2-yn-1-yl)benzenesulfonamide (1c) to a stirred solution of Reaction 1. The reaction was gradually allowed to warm to room temperature, monitored by TLC, and stirred for 2 h. Upon completion, the reaction mixture was concentrated and the crude product was purified by flash column chromatography on silica gel (eluted with pentane/2-propanol, 9:1) to afford S2 (1.72 g, 43.0 mmol, 60% in oil) and cyclopropyltriphenylphosphine (1.37 g, 4.3 mmol) in THF (8 mL) was added DIAD (272.7 mg, 1.4 mmol) at 0 °C. The reaction was gradually allowed to warm to room temperature, monitored by TLC, and stirred for 1 h. The reaction was quenched at 0 °C with saturated Na2CO3 solution and washed with ether (30 mL x 3). The crude product was purified by flash column chromatography on silica gel (eluted with pentane/2-propanol, 1:1) to afford S3 (9.7 mL, 69.3 mmol) in dry THF (70 mL), and the mixture was stirred at room temperature for about 30 min to generate the Grignard reagent. To a stirred solution of 2-(tert-butyldiphenylsilyl)oxy-1-(4-(trifluoromethyl)phenyl)ethan-1-one (S6, Scheme S1, Reaction 2). Magnesium (1.68 g, 69.1 mmol) and a piece of iodine crystal were placed in THF (52 mL) was added dropwise the newly prepared Grignard reagent at 0 °C. The reaction was gradually allowed to warm to room temperature, monitored by TLC, and stirred for 1 h. The reaction was quenched at 0 °C with saturated NH4Cl (10 mL) and washed with ether (30 mL x 3). The crude product was purified by flash column chromatography on silica gel (eluted with pentane/ethanol, 4:1) to afford S4 (7.93 g, 91%); light yellow oil, TLC Rf = 0.84 (PE/EtOAc, 9:1); 1H NMR (400 MHz, CDCl3) δ 7.95–7.37 (m, 4H), 4.20 (s, 2H), 1.11 (s, 9H); 13C{1H} NMR (101 MHz, CDCl3) δ 146.5, 137.8, 135.7, 134.6 (q, J = 36.2 Hz), 132.8, 130.2, 128.5, 128.0, 125.7 (q, J = 3.6 Hz), 123.7 (q, J = 272.8 Hz), 68.0, 26.8, 19.4; IR (neat) 3073, 3052, 2900, 2957, 2931, 2859, 1714, 1714, 1518, 1513, 1472, 1428, 1412, 1392, 1377, 1362, 1226, 885, 1127, 1134, 1112, 1067, 1017, 983 cm⁻¹; HRMS (ESI) calcd for C62H48NO1Si [(M + H)⁺] 660.1914, found 640.1916.

1-(2-Cyclopropylidene-2-((tert-butyldiphenylsilyl)oxy)-1-(4-(trifluoromethyl)phenyl)ethan-1-yl)benzene (S4, Scheme S1, Reaction 2). To a stirred solution of S6 (7.92 g, 17.9 mmol) in THF (18 mL) was added. The reaction was monitored by TLC and stirred for 1 h at the same temperature. Then, the resulting mixture was quenched with water (60 mL) and extracted with ether (30 mL x 3). The combined organic phase was washed with brine and dried over Na2SO4, then filtered and concentrated. The residue was purified by flash column chromatography on silica gel (eluted with PE/EtOAc, 4:1) to afford S7 (6.69 g, 35.3 mmol, 66%); light yellow oil, TLC Rf = 0.77 (PE/EtOAc, 4:1); 1H NMR (400 MHz, CDCl3) δ 7.30–7.20 (m, 8H), 6.98 (s, 2H), 3.82 (s, 3H); 13C{1H} NMR (101 MHz, CDCl3) δ 141.6, 138.9, 138.6, 138.2, 132.2, 130.3, 128.9, 128.6, 128.3, 127.8, 126.7, 126.3, 125.8, 125.4 (q, J = 3.7 Hz), 124.4 (q, J = 271.7 Hz), 64.7, 4.7, 0.9; IR (KBr) 3289, 2949, 1614, 1574, 1469, 1409, 1361, 1325, 1211, 1171, 1145, 1073, 1051, 1011, 978 cm⁻¹; HRMS (ESI) calcd for C50H36F4NO5Si [(M + H)⁺] 777.16 ppm, CD2Cl2 = δ 77.16 ppm, CD2Cl2 = δ 35.84 ppm, (CD3)2SO = δ 39.52 ppm). Infrared spectra were recorded on a PerkinElmer model 341LC Polarimeter at 20 °C with visible light (λ = 589 nm) and 100 mm length cuvette.

For General Synthesis of Substrates, See Scheme S1, Reaction 1. To a stirred solution of 1-(2-cyclopropylidene-2-phenyl-4-(3-phenylprop-2-yn-1-yl)benzenesulfonamide (1a, Scheme S1, Reaction 1). The reaction was gradually allowed to warm to room temperature, monitored by TLC, and stirred for 1 h. The reaction was quenched at 0 °C with saturated NH4Cl (10 mL) and washed with ether (30 mL x 3). The crude product was purified by flash column chromatography on silica gel (eluted with pentane/2-propanol, 9:1) to afford S8 (4.82 g, 92%); light yellow oil, TLC Rf = 0.57 (PE/EtOAc, 1:1); 1H NMR (400 MHz, CDCl3) δ 7.84–7.74 (m, 4H), 7.32–7.22 (m, 2H), 7.05–6.98 (m, 2H), 6.69–6.90 (m, 2H), 4.48 (s, 2H), 4.10 (s, 2H), 3.82 (s, 3H), 2.31 (s, 3H), 1.50–1.43 (m, 2H), 1.22–1.16 (m, 2H); 13C{1H} NMR (101 MHz, CDCl3) δ 159.3, 154.2, 153.9, 151.7, 130.9, 128.7, 128.5, 127.9, 127.4, 127.0, 126.5, 114.0, 85.9, 82.3, 55.6, 30.0, 36.3, 21.5, 5.7, 1.6; IR (KBr) 3048, 2972, 2920, 2836, 1607, 1575, 1514, 1490, 1454, 1443, 1427, 1334, 1330, 1298, 1250, 1183, 1162, 1117, 1093, 1070, 1029, 990 cm⁻¹; HRMS (ESI) calcd for C23H20NO3S [(M + H)⁺] 458.1784, found 458.1785.
To a stirred solution of 4-methyl-N-(s, 3H), 1.54
6.92 (d, 1491, 1457, 1427, 1408, 1377, 1343, 1295, 127.2, 123.5, 128.4, 127.5, 126.4, 126.2, 125.2 (q, J = 3.7 Hz), 123.9 (q, J = 27.2 Hz),
4.59 (s, 2H), 2.33 (s, 3H), 1.65–1.80, 1.38–1.23 (m, 2H). 21C[H] NMR (101 MHz, CDCl3) δ 143.7, 137.0, 135.6, 131.7, 130.2 (q, J = 32.8 Hz), 129.6, 128.5, 128.2, 128.1, 127.5, 126.4, 126.2, 125.2 (q, J = 3.7 Hz), 123.9 (q, J = 27.2 Hz),
7.77 (m, 4H), 7.41
1.4 mmol), S8 (315.0 mg, 1.4 mmol), and PPh3 (544.4 mg, 2.1 mmol) in THF (9 mL) was added DIAD (416.9 mg, 2.1 mmol) at 0
°C. The reaction was gradually allowed to warm to room temperature, monitored by TLC, and stirred for 11 h. Upon completion, the reaction mixture was concentrated and the crude product was purified by flash column chromatography on silica gel (eluted with PE/DCM, 5:1) to afford 1d (346.0 mg, 50%): white solid, m.p. = 153–156 °C, TLC Rf = 0.44 (PE/EA, 5:1); 1H NMR (400 MHz, CDCl3) δ 8.02
7.33–7.36 (m, 2H), 7.34–7.24 (m, 3H), 7.02–6.91 (m, 2H), 6.82–6.73 (m, 2H), 4.50 (s, 2H), 4.10 (s, 2H), 3.79 (s, 3H), 3.23 (s, 3H), 1.53–1.47 (m, 2H), 1.26–1.18 (m, 2H). 21C[H] NMR (101 MHz, CDCl3) δ 159.7, 143.5, 137.2, 135.8, 132.9, 129.6, 128.5, 128.2, 128.1, 127.1, 124.6, 121.0, 114.6, 113.9, 85.7, 80.6, 55.4, 49.5, 36.3, 21.6, 5.7, 1.6 (d, J = 11.1 Hz, 1H), 151.0, 116.1, 110.0, 103.2 cm−1; HRMS (ESI) calcld for C25H20NO3S ([M + H]+) 405.1306, found 405.1303 cm−1; HRMS (ESI) calcld for C25H19NO3S ([M + H]+) 405.1283, found 405.1280 cm−1; 1H NMR (400 MHz, CDCl3) δ 7.88–7.77 (m, 4H), 7.53 (d, J = 8.1 Hz, 2H), 7.43–7.36 (m, 2H), 7.34–7.25 (m, 3H), 7.14 (d, J = 8.1 Hz, 2H),
9.22
IR (neat) 3051, 2957, 2919, 1603, 1496, 1454, 1343, 1292, 1159, 1094, 1031 cm⁻¹; HRMS (ESI) calcd for C₂₃H₂₄NO₅S ([M + H]⁺) 392.1679, found 392.1678.

4-Methyl-N-(5-methylhex-4-en-2-yn-1-yl)benzenesulfonamide (SI6, Scheme S1, Reaction 4). C6H6 (285.6 mg, 1.50 mmol) and PMBPh2 (133.4 mg, 0.49 mmol) were dissolved in pyridine (50 mL). 1-Bromo-2-methylprop-1-ene (2.1 mL, 20.5 mmol) was added to the resulting solution at 0 °C. After stirring for 5 min, 4-methyl-N-(prop-2-yn-1-yl)benzenesulfonamide (SI5) (20.9 g, 10.0 mmol) in THF (8 mL) was added to the solution at 0 °C. The reaction was gradually allowed to warm to 25 °C. The reaction was monitored by TLC and stirred for 18 h. Upon completion, 2 M HCl solution (50 mL) was added to quench the reaction. The resulting mixture was extracted with ether (30 mL × 3), and the combined organic phase was washed with brine, dried over Na₂SO₄, then filtered and concentrated. The crude product was purified by flash column chromatography on silica gel (eluted with PE/EA, 10:1) to afford SI6 (121.1 g, 46%); yellow solid, m.p. = 69–72 °C; TLC Rf = 0.25 (PE/EA, 9:1); ¹H NMR (400 MHz, CDCl₃) δ 7.78 (d, J = 8.2 Hz, 2H), 7.30 (d, J = 8.2 Hz, 2H), 5.03 (s, 1H), 4.64 (t, J = 5.4 Hz, 1H), 3.97 (d, J = 5.4 Hz, 2H), 2.42 (s, 3H), 1.74 (s, 3H), 1.70 (s, 3H); ¹³C{¹H} NMR (100 MHz, CDCl₃) δ 149.8, 143.7, 136.8, 129.8, 127.5, 104.2, 85.0, 83.0, 34.1, 24.8, 21.6, 21.0; IR (neat) 3280, 3035, 2921, 2853, 1595, 1432, 1323, 1244, 1153, 1089, 1047 cm⁻¹; HRMS (ESI) calcd for C₂₃H₂₄NO₅S ([M + H]⁺) 364.1053, found 364.1049.

N-(2-Cyclopropylidene-2-phenylethyl)-4-methyl-N-(5-methylhex-4-en-2-yn-1-yl)benzenesulfonamide (SI7, Scheme S1, Reaction 1). To a stirred solution of SI6 (290.0 mg, 1.11 mmol), SI3 (175.6 mg, 1.11 mmol), and PPh₃ (434.6 mg, 1.71 mmol) in THF (7 mL) was added DIAD (330.6 mg, 1.6 mmol) at 0 °C. The reaction was gradually allowed to warm to room temperature, monitored by TLC, and stirred for 4 h. Upon completion, the reaction mixture was concentrated and the crude product was purified by flash column chromatography on silica gel (eluted with PE/EA, 10:1) to afford SI1 (274.4 mg, 61%); light yellow solid, m.p. = 110–113 °C; TLC Rf = 0.54 (PE/EA, 9:1); ¹H NMR (400 MHz, CDCl₃) δ 7.83–7.87 (m, 1H, 4H), 7.40–7.42 (m, 2H), 3.95 (d, J = 1.2 Hz, 2H), 2.42 (s, 3H), 1.73 (s, 3H), 1.59 (s, 3H), 1.51–1.44 (m, 2H), 1.23–1.15 (m, 2H); ¹³C{¹H} NMR (100 MHz, CDCl₃) δ 149.0, 144.0, 137.9, 136.1, 129.8, 128.6, 128.5, 127.5, 127.6, 121.4, 104.6, 84.09, 84.08, 49.77, 36.6, 24.7, 21.6, 21.0, 5.6, 1.8; IR (neat) 3054, 2976, 2911, 2872, 1637, 1579, 1497, 1451, 1400, 1380, 1346, 1331, 1308, 1290, 1241, 1106, 1186, 1162, 1144, 1093, 1038, 1026, 1001, 989 cm⁻¹; HRMS (ESI) calcd for C₂₃H₂₁NO₅S ([M + H]⁺) 406.1385, found 406.1381.

Methyl 4-((N-(2-Cyclopropylidene-2-phenylethyl)-4-methylphenylsulfonyl)amino)but-2-ynoate (II, Scheme S1, Reaction 5). To a stirred solution of SI5 (328.7 mg, 1.66 mmol), SI3 (252.0 mg, 1.66 mmol), and PPh₃ (618.0 mg, 2.4 mmol) in THF (10 mL) was added DIAD (476.6 mg, 2.4 mmol) at 0 °C. The reaction was gradually allowed to warm to room temperature, monitored by TLC, and stirred for 6 h. Upon completion, the reaction mixture was concentrated and the residue was purified by flash column chromatography on silica gel (eluted with PE/EA, 20:1) to afford crude SI₂ (292.8 mg, 1.1 mmol), and PMBPh₂ (133.4 mg, 0.49 mmol) were dissolved in pyridine (8 mL). 1-Bromo-2-methylprop-1-ene (2.1 mL, 20.5 mmol) was added to the resulting solution at 0 °C. After stirring for 5 min, 4-methyl-N-(prop-2-yn-1-yl)benzenesulfonamide (SI5) (20.9 g, 10.0 mmol) in THF (8 mL) was added DIAD (332.2 mg, 1.6 mmol) at 0 °C. The reaction was gradually allowed to warm to room temperature, monitored by TLC, and stirred for 6 h. Upon completion, the reaction mixture was concentrated and the crude product was purified by flash column chromatography on silica gel (eluted with PE/DCM, 2:1) to afford SI₂ (320.5 mg, 63%); white solid, m.p. = 132–135 °C; TLC Rf = 0.44 (PE/EA, 9:1); ¹H NMR (400 MHz, CDCl₃) δ 8.38–8.32 (m, 2H, 8.12–8.06 (m, 2H), 7.78–7.72 (m, 2H), 7.41–7.35 (m, 2H), 7.31–7.26 (m, 1H), 5.46–5.33 (m, 2H), 5.26 (dd, J = 16.4, 3.1 Hz, 1H), 4.46 (s, 2H), 4.08 (d, J = 1.1 Hz, 2H), 1.54–1.48 (m, 2H), 1.23–1.17 (m, 2H); ¹³C{¹H} NMR (100 MHz, CDCl₃) δ 150.3, 144.4, 136.9, 129.4, 129.0, 128.6, 128.0, 127.6, 126.3, 124.1, 110.4, 112.5, 84.9, 82.1, 49.7, 36.2, 5.7, 1.6; IR (neat) 3105, 3053, 2978, 2968, 1607, 1536, 1498, 1476, 1453, 1426, 1401, 1348, 1330, 1288, 1240, 1191, 1164, 1105, 1044, 1027, 1010, 982, 944 cm⁻¹; HRMS (ESI) calcd for C₂₃H₁₉NO₅S ([M + H]⁺) 409.1217, found 409.1217.
1-(1-Cyclopentyliden-2-(3-phenylprop-2-yn-1-yl)oxo)ethy-4-methoxybenzene (10, Scheme 5, Reaction 7). To a stirred solution of NaH (31.99 mg, 0.80 mmol, 60% in oil) and n-Bu3NLi (369.2 mg, 1.0 mmol) in DMF (2 mL) was added dropwise 44 (190.4 mg, 1.0 mmol) in DMF (3 mL) at 0 °C. The reaction was stirred at 0 °C for 30 min, then (3-bromoprop-1-yn-1-yl)benzene (321) (60.9 mg, 0.35 mmol) was added dropwise at the same temperature. The reaction was gradually allowed to warm to room temperature, monitored by TLC, and stirred for 2 h. The reaction was quenched with water (60 mL) and extracted with ether (30 mL × 3). The combined organic phase was washed with brine and dried over Na2SO4, then filtered and concentrated. The crude product was purified by flash column chromatography on silica gel (eluted with PE/EA, 70:1) to afford 10 (173.0 mg, 57%): yellow oil (some impurities could be found in the final product, but all efforts to purify it failed), TLC Rf = 0.62 (PE/EA, 5:1); 1H NMR (400 MHz, CDCl3) δ 7.75–7.69 (m, 2H), 7.48–7.44 (m, 2H), 7.34–7.31 (m, 3H), 6.92–6.88 (m, 2H), 4.72 (s, 2H), 4.37 (s, 2H), 3.82 (s, 3H), 1.53–1.47 (m, 2H), 1.29–1.24 (m, 2H); 13C{1H} NMR (101 MHz, CDCl3) δ 158.8, 131.9, 131.0, 128.5, 128.4, 127.3, 125.1, 123.0, 122.8, 113.8, 86.3, 85.6, 71.3, 57.2, 55.4, 5.4, 1.0; IR (neat) 2956, 2921, 2870, 2850, 1512, 1492, 1461, 1378, 1249, 1181, 1081 cm−1; HRMS (ESI) calculated for C18H16O (M + H)+ 280.1285, found 280.1286.

Racemic Product Synthesis, General Procedure A (5 mol % Catalyst). Under nitrogen, the commercially available (MeCN)Au(2−PrOH) = 90/10, 1.0 mL/min, 220 nm, 25 °C), tR = 7.42 min (minor), 9.40 min (major); δ = 201.2°C (δ = 0.50, CHCl3).

2b: white solid, m.p. = 66–69 °C, TLC Rf = 0.53 (PE/EA, 5:1); 1H NMR (400 MHz, CDCl3) δ 7.38–7.28 (m, 6H), 7.27–7.22 (m, 1H), 7.20 (d, δ = 8.0 Hz, 2H), 7.15–7.10 (m, 2H), 7.06 (d, δ = 8.0 Hz, 2H), 6.69 (d, δ = 10.6 Hz, 1H), 5.28 (d, δ = 10.6 Hz, 1H), 4.44 (dd, δ = 12.1, 1.6 Hz, 1H), 3.20 (d, δ = 12.1 Hz, 1H), 3.10 (d, δ = 16.0, 9.4 Hz, 1H), 2.50 (d, δ = 16.0, 7.8, 4.1 Hz, 1H), 2.41 (s, 3H), 2.35 (s, 3H), 2.32–2.23 (m, 2H); 13C{1H} NMR (101 MHz, CDCl3) δ 146.1, 144.1, 144.1, 140.3, 140.0, 136.7, 136.3, 130.0, 129.9, 129.3, 128.5, 127.9, 127.4, 127.3, 127.1, 126.9, 106.8, 59.4, 55.5, 31.6, 29.2, 21.7, 21.3; IR (neat) 3051, 2935, 2923, 2854, 1654, 1612, 1599, 1513, 1495, 1445, 1424, 1401, 1347, 1321, 1290, 1241, 1224, 1184, 1163, 1116, 1091, 1031, 1020, 983, 918 cm−1; HRMS (ESI) calculated for C29H27F2NO2S (M + H)+ 442.1835, found 442.1835.

(R)-1-(4-Methoxyphenyl)-6-phenyl-3-ethyl-3-azabicyclo[5.2.0]nona-4,6-diene (2e). Following general procedure B, 18.8 mg of 1c was used, and the reaction time was 12 h. After flash column chromatography on silica gel (eluted with PE/EA, 20:1), 1.0578 g of 2a was obtained in 99% yield and 99% e.e., as determined by HPLC analysis.

(R)-6-Phenyl-1-(t-poly)-3-ethyl-3-azabicyclo[5.2.0]nona-4,6-diene (2b). Following general procedure B, 88.2 mg of 1b was used, and the reaction time was 12 h. After flash column chromatography on silica gel (eluted with PE/EA, 20:1), 87.6 mg of 2b was obtained in 99% yield and 99% e.e., as determined by HPLC analysis (chiral OD-H, hexane/i-PrOH = 90/10, 1.0 mL/min, 220 nm, 25 °C), tR = 7.42 min (minor), 9.40 min (major); δ = 201.2°C (δ = 0.50, CHCl3).

2c: white solid, m.p. = 65–68 °C, TLC Rf = 0.53 (PE/EA, 5:1); 1H NMR (400 MHz, CDCl3) δ 7.79–7.58 (m, 6H), 7.27–7.22 (m, 1H), 7.19 (d, δ = 8.0 Hz, 2H), 7.17–7.11 (m, 2H), 6.80–6.74 (m, 2H), 6.71 (d, δ = 10.6 Hz, 1H), 5.29 (d, δ = 10.6 Hz, 1H), 4.44 (dd, δ = 12.2, 1.6 Hz, 1H), 3.80 (d, δ = 12.2 Hz, 1H), 3.10 (d, δ = 16.0, 9.4, 9.4 Hz, 1H), 2.50 (d, δ = 16.0, 8.1, 3.7 Hz, 1H), 2.41 (s, 3H), 2.32–2.23 (m, 2H); 13C{1H} NMR (101 MHz, CDCl3) δ 158.9, 146.2, 144.1, 140.3, 136.4, 134.9, 130.0, 129.9, 128.6, 128.5, 127.9, 127.1, 127.0, 113.9, 106.7, 59.1, 55.5, 5.3, 21.9; IR (neat) 3043, 2925, 2844, 1609, 1505, 1452, 1345, 1245, 1168, 1085, 1031, 985, 917 cm−1; HRMS (ESI) calculated for C29H27F2NO2S (M + H)+ 442.1835, found 442.1835.

(R)-1,6-Diphenyl-1-(t-poly)-3-ethyl-3-azabicyclo[5.2.0]nona-4,6-diene (2a). Following general procedure B, 85.6 mg of 1a was used, and the reaction time was 12 h. After flash column chromatography on silica gel (eluted with PE/EA, 20:1), 85.1 mg of 2a was obtained in 99% yield and 99% e.e., as determined by HPLC analysis.
(R)-1-Phenyl-3-ethyl-5,6-(4-trifluoromethylphenyl)phenyl-3-azabicyclo[5.2.0]-2,4-diene (2). Following general procedure B, 81.3 mg of 2 was obtained in 85% yield and 97% e.e., as determined by HPLC analysis (chiral OD-H, hexane/\(\alpha\)-PrOH = 90/10, 0.5 mL/min, 220 nm, 25 °C), \(t_{R} = 12.01\) min (minor), 14.73 min (major); \(\alpha = -223.3^\circ\) (c = 0.50, CHCl₃). 2g: colorless oil, TLC, \(R_f = 0.52\) (PE/EA, 5:1); 1H NMR (400 MHz, CDCl₃) \(\delta 7.37\) (d, \(J = 8.3\) Hz, 2H), 7.32–7.25 (m, 5H), 6.58 (d, \(J = 8.6\) Hz, 2H), 6.65 (d, \(J = 10.7\) Hz, 1H), 5.27 (d, \(J = 10.7\) Hz, 1H), 4.66 (d, \(J = 10.5\) Hz, 1H), 2.37 (m, 2H), 1.21 (m, 2H), 2.74 (m, 2H), 1.12 (m, 2H), 0.80 (m, 3H), 0.67 (m, 3H), 0.34 (m, 3H). HRMS (ESI) calcd for \(\text{C}_{24}\text{H}_{26}\text{N}_{2}\text{O}_{2}\) ([M + H]⁺) 392.1679, found 392.1680.

(R)-6-(4-Methoxyphenyl)-1-phenyl-3-tosyl-3-azabicyclo[5.2.0]-2,4-diene (2). Following general procedure B, 90.9 mg of 1 was used, and the reaction time was 12 h. After flash column chromatography on silica gel (eluted with PE/EA, 20:1), 62.0 mg of 2 was obtained in 82% yield and 90% e.e., as determined by HPLC analysis (chiral OD-H, hexane/\(\alpha\)-PrOH = 90/10, 0.5 mL/min, 220 nm, 25 °C), \(t_{R} = 13.17\) (major), 16.32 min (minor); \(\alpha = -241.9^\circ\) (c = 0.51, CHCl₃). 2b: white solid, m.p. = 44–47 °C, TLC, \(R_f = 0.55\) (PE/EA, 5:1); 1H NMR (400 MHz, CDCl₃) \(\delta 7.30\) (d, \(J = 8.3\) Hz, 2H), 7.25–7.18 (m, 3H), 7.17–7.09 (m, 4H), 6.63 (d, \(J = 10.6\) Hz, 1H), 6.35 (d, \(J = 17.5\), 10.9 Hz, 1H), 5.37–5.27 (m, 2H), 5.10 (d, \(J = 10.6\) Hz, 1H), 4.47 (d, \(J = 12.1\), 1.5 Hz, 1H), 3.17 (d, \(J = 12.1\) Hz, 1H), 2.86 (d, \(J = 15.7\), 9.4 Hz, 1H), 2.71 (d, \(J = 15.7\), 8.4, 3.5 Hz, 1H), 2.35 (s, 3H), 2.35–2.24 (m, 2H), 1.57 (s, 3H), 1.49 (s, 3H). HRMS (ESI) calcd for \(\text{C}_{25}\text{H}_{28}\text{N}_{2}\text{OS}\) ([M + H]⁺) 406.1835, found 406.1836.

Reaction of 11: following general procedure B, 81.3 mg of 11 was used, and the reaction time was 12 h. Only 66.2 mg of 11 was recollected in 81% yield.

(R)-6-Methyl-1-phenyl-3-ethyl-3-tosyl-3-azabicyclo[5.2.0]-2,4-diene (2m) and (15R)-6-Methyl-1-phenyl-3-ethyl-3-azaspiro[4.1.0]heptane-7,1’-cyclopropane-4-ene (3m). Following a simple procedure (the reaction time was 0.6 h) the general procedure B, 219.3 mg of 1 was used, and the reaction time was 1 h. After flash column chromatography on silica gel (eluted with PE/EA, 20:1), 187.7 mg of 2m + 3m was obtained in 86% yield with 2m/3m = 1:3.1, which was determined by crude H NMR, 2m: 276 e.e., as
determined by HPLC analysis (chiral OD-H, hexane/-i-PrOH = 90/10, 1.0 mL/min, 220 nm, 25 °C), tR, 6.45 min (major), 7.59 min (minor); α = −28.6° (c = 0.25, CHCl3); colorless oil, TLC, Rf = 0.52 (PE/EA, 5:1); 1H NMR (400 MHz, CDCl3) δ 7.32 (d, J = 8.1 Hz, 2H), 7.27–7.15 (m, 3H), 4.64 (d, J = 10.5 Hz, 1H), 4.85 (d, J = 10.5 Hz, 1H), 3.52 (d, J = 11.2 Hz, 1H), 2.94 (d, J = 11.2 Hz, 1H), 2.42 (s, 3H), 1.07 (s, 3H), 1.00 (s, 3H), 3.02 (d, J = 11.9 Hz, 1H), 2.75–2.64 (m, 1H), 2.56–2.48 (m, 1H), 2.39 (s, 3H), 2.26–2.19 (m, 2H), 1.71 (s, 3H), 13C{1H} NMR (101 MHz, CDCl3) δ 141.1, 143.7, 142.6, 135.3, 131.0, 128.5, 127.7, 126.8, 125.7, 124.0, 109.0, 59.0, 55.4, 30.5, 26.3, 21.6, 18.4; IR (neat) 3020, 2920, 2856, 1730, 1610, 1493, 1451, 1348, 1242, 1163, 1094, 1058, 938 cm−1; HRMS (ESI) calcld for C17H18NO3S ([M + H]+) 305.1536, found 305.1536.

**REFERENCES**


(29) It had been proved that the M06-2X functional was reliable in calculations of late-transition-metal-catalyzed reactions (Au, Pt, and Ir), see: Kang, R.; Lai, W.; Yao, J.; Shaik, S.; Chen, H. How Accurate Can a Local Coupled Cluster Approach Be in Computing the Activation Energies of Late-Transition-Metal-Catalyzed Reactions with Au, Pt, and Ir? *J. Chem. Theory Comput.* 2012, 8, 3119.


