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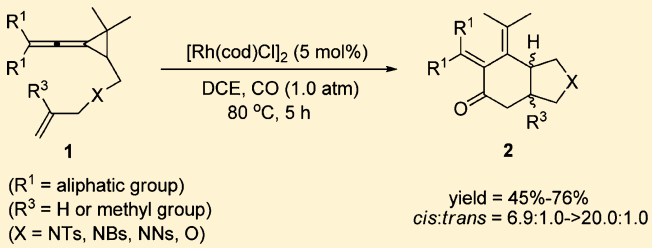
Rhodium(I)-Catalyzed Pauson–Khand-type [3 + 2 + 1] Cycloaddition Reaction of Ene-Vinylidenecyclopropanes and CO: A Highly Regio- and Stereoselective Synthetic Approach for the Preparation of Aza- and Oxa-Bicyclic Compounds

Bei-Li Lu, Yin Wei, and Min Shi*

State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 345 Lingling Road, Shanghai 200032, People's Republic of China

Supporting Information

ABSTRACT: In this paper, a novel Rh(I)-catalyzed Pauson–Khand-type [3 + 2 + 1] cycloaddition reaction of ene-vinylidenecyclopropanes (Ene-VDCPs) and carbon monoxide (CO) has been developed to furnish a series of aza- and oxa-bicyclic compounds in moderate to good yields in a highly regio- and diastereoselective manner, which provides an alternative and efficient synthetic approach for the access of bicyclic cyclohexanone frameworks. The substrate scope and limitations and a plausible mechanism are discussed.



INTRODUCTION

Since the first paper reported by Khand and Pauson and their co-workers in 1971, the Pauson–Khand reaction has become a powerful synthetic tool in organic chemistry and other related areas.[1] Recently, a metal-catalyzed Pauson–Khand reaction for the coupling of enynes with carbon monoxide (CO) has been developed as an efficient protocol to afford bicyclic frameworks, which are important structural motifs in many biologically active compounds.[2] Among the employed metal catalysts, rhodium complexes[3] have achieved remarkable progress and have attained great popularity thus far, probably due to their mild conditions, low catalyst loadings, and good control of stereoselectivities. Moreover, dienes,[4] allenes,[5] heteroalkenes,[6] and the recently reported cyclopropanes[7] and cyclopropenes[8] could be also used as alkene sources to produce Pauson–Khand-type reaction products in the presence of an alkyne. However, employing novel substrates and further optimizing the catalysts and reaction conditions for Pauson–Khand-type reactions are still highly desirable, enabling the discovery of unprecedented reaction modes.

Vinylidenecyclopropanes (VDCPs) bearing an allene moiety connected with a highly strained cyclopropane have been fascinating building blocks in organic synthesis and have attracted much interest from organic chemists. In the past few years, the chemistry of VDCPs has been extensively studied due to their unique structural and electronic properties.[9,10] Recently, we reported a rhodium(I)-catalyzed intramolecular cycloaddition of yne- and ene-vinylidenecyclopropanes (Yne- and Ene-VDCPs) to provide functionalized polycyclic compounds containing cyclobutene or azacyclooctene moieties in a highly regio- and diastereoselective manner.[10l] In view of the significant biological properties of the cyclic units, we attempted to develop a practical Pauson–Khand-type reaction using functionalized VDCPs as the substrates. It can be envisioned that the control of regio- and stereoselectivity in this reaction might be difficult because different potential reaction sites, including allene, alkene, and cyclopropane, existed in the starting materials. Herein, we wish to report a highly regio- and diastereoselective Rh(I)-catalyzed intramolecular Pauson–Khand-type [3 + 2 + 1] cycloaddition reaction of Ene-VDCPs and CO to give aza- or oxa-bicyclic cyclohexanone derivatives.

RESULTS AND DISCUSSION

Initially, the Ene-VDCP **1a** was used as a model substrate to examine the Pauson–Khand-type [3 + 2 + 1] cycloaddition reaction with a rhodium(I) catalyst under a carbon monoxide atmosphere, and the results are summarized in Table 1. As a first try, no reaction happened by using $RhCl(CO)(PPh_3)_2$ as the catalyst (Table 1, entry 1). However, when 5 mol % of $[Rh(CO)_2Cl]_2$ was used as the catalyst, the Pauson–Khand-type [3 + 2 + 1] cycloaddition product **2a** was obtained in 56% yield with an 11.0:1.0 ratio of the diastereoselectivity (Table 1, entry 2). An X-ray diffraction study of the major diastereomer of **2a** was carried out, and its configuration has been unambiguously determined as cis. The related CIF data are presented in the Supporting Information, and an ORTEP drawing is shown in Figure 1.[11] Then we screened a variety of rhodium complexes in 1,2-dichloroethane (DCE) and found that the yield of **2a** was quite sensitive to the rhodium complex employed. In the case of IPrRh(cod)Cl (IPr = 1,3-bis(2,6-

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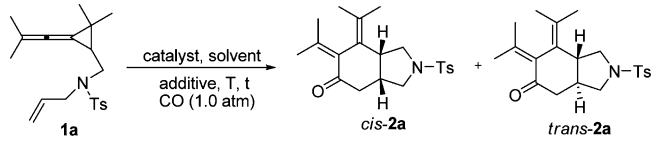
Table 1. Optimization of the Reaction Conditions for Rh(I)-Catalyzed Pauson–Khand-Type [3 + 2 + 1] Cycloaddition Reactions of Ene-VDCP 1a



entry[a]	cat.	additive (amt (mol %))	solvent	T (°C)	t (h)	yield (%)[b] (cis:trans)
1	$RhCl(CO)(PPh_3)_2$		DCE	80	24	*c*
2	$[Rh(CO)_2Cl]_2$		DCE	80	5	56 (11.1:1.0)
3	IPrRh(cod)Cl		DCE	80	5	45 (10.0:1.0)
4	$Rh(cod)_2SbF_6$		DCE	80	5	62 (11.1:1.0)
5	$[Rh(cod)Cl]_2$		DCE	80	5	76 (12.5:1.0)
6	$[Rh(cod)Cl]_2$/dppp		DCE	80	5	68 (9.1:1.0)
7	$[Rh(cod)Cl]_2$/dppf		DCE	80	5	71 (8.3:1.0)
8	$[Rh(cod)Cl]_2$/DPEPhos		DCE	80	24	*d*
9	$[Rh(cod)Cl]_2/PPh_3$		DCE	80	24	*e*
10	$[Rh(cod)Cl]_2$		THF	70	24	trace
11	$[Rh(cod)Cl]_2$		dioxane	80	5	20 (4.7:1.0)
12	$[Rh(cod)Cl]_2$		DMF	80	24	complex
13	$[Rh(cod)Cl]_2$		CH_2Cl_2	35	12	31[f] (11.8:1.0)
14	$[Rh(cod)Cl]_2$		$CHCl_3$	50	24	23 (6.3:1.0)
15	$[Rh(cod)Cl]_2$		DCE	60	12	59 (11.8:1.0)
16	$[Rh(cod)Cl]_2$	NMO (1.0)	DCE	80	5	75 (11.8:1.0)
17[g]	$[Rh(cod)Cl]_2$		DCE	80	5	72 (4.4:1.0)
18[h]	$[Rh(cod)Cl]_2$		DCE	80	5	76 (11.8:1.0)
19[i]	$[Rh(cod)Cl]_2$		DCE	80	5	64 (11.1:1.0)
20[j]	$[Rh(cod)Cl]_2$		DCE	80	5	59 (12.5:1.0)

[a]All reactions were carried out using **1a** (0.1 mmol) in the presence of catalyst (5 mol %) in various solvents (1.0 mL), for entries 6–9, using 10 mol % ligands. Abbreviations: dppp = 1,3-bis(diphenylphosphino)propane, dppf = 1,1′-bis(diphenylphosphino)ferrocene, DPEPhos = bis[(2-diphenylphosphino)phenyl] ether, NMO = 4-methylmorpholine *N*-oxide. [b]Isolated yield. [c]84% of **1a** was recovered. [d]54% azacyclooctene derivative was obtained, and 29% of **1a** was recovered. [e]86% of **1a** was recovered. [f]22% of **1a** was recovered. [g]CO (5.0 atm). [h]Using 10 mol % catalyst. [i]The reaction was carried out in 2.0 mL of DCE. [j]The reaction was carried out in 0.5 mL of DCE.

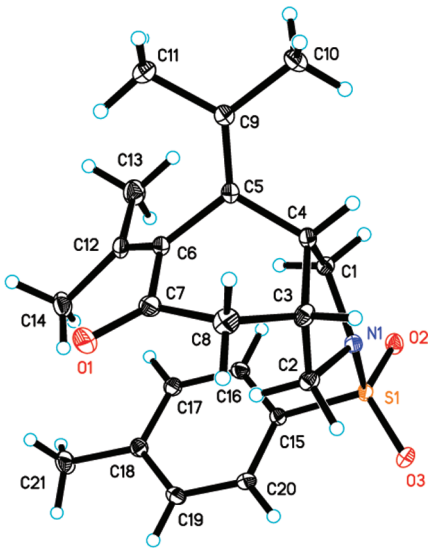


Figure 1. ORTEP drawing of *cis*-**2a**.

diisopropylphenyl)imidazol-2-ylidene) and a cationic rhodium complex such as $Rh(cod)_2SbF_6$, adduct **2a** was afforded in 45% and 62% yields as cis and trans isomeric mixtures, respectively (Table 1, entries 3 and 4). However, when $[Rh(cod)Cl]_2$ was used as the catalyst, the reaction afforded **2a** in 76% yield exclusively with a higher diastereoselectivity (cis:trans = 12.5:1.0) in DCE at 80 °C (Table 1, entry 5), and no other kinds of products such as the azacyclooctene derivatives reported by our group previously[10l] were observed. The reaction for the formation of azacyclooctene derivatives was carried out in toluene/acetonitrile (2/1) in the presence of $[RhCl(CO)_2]_2$ and CO, suggesting that the coordinative acetonitrile solvent can significantly affect the reaction outcome. Other catalyst systems, such as $[Rh(cod)Cl]_2$/diphosphine ligand (dppp or dppf), produced **2a** in reduced yields (Table 1, entries 6 and 7). $[Rh(cod)Cl]_2$/DPEPhos did not catalyze this Pauson–Khand-type [3 + 2 + 1] cycloaddition reaction, and the azacyclooctene derivative[10l] was formed in 54% yield and 29% of **1a** was recovered (Table 1, entry 8). $[Rh(cod)Cl]_2/PPh_3$ was also not an efficient catalyst system (Table 1, entry 9). We next attempted to optimize the reaction conditions by using $[Rh(cod)Cl]_2$ as the catalyst in various solvents. Among the examined solvents, DCE was found to be the optimal solvent and other solvents such as tetrahydrofuran (THF), dioxane, DMF, CH_2Cl_2, and $CHCl_3$ were not suitable for this reaction, suggesting the strong solvent effect on this reaction (Table 1, entries 10–14). Reducing the reaction temperature to 60 °C diminished the yield of **2a** (Table 1, entry 15). 4-Methylmorpholine *N*-oxide (NMO), which can lead to dissociation of CO from the metal center and allow coordination of the olefin to accelerate the reaction rate,[12] has been also used as an additive in this Pauson–Khand-type [3 + 2 + 1] cycloaddition reaction, affording **2a** in 75% yield with 11.8:1.0 diastereoselectivity (cis:trans) (Table 1, entry 16). Furthermore, carrying out the reaction under a higher pressure

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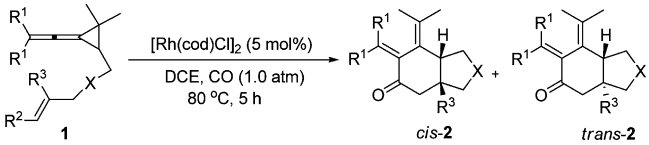
of CO was less efficient for the production of **2a** (Table 1, entry 17). Increasing the employed amount of catalyst $[Rh(cod)Cl]_2$ to 10 mol % did not improve the yield of **2a** (Table 1, entry 18). We also examined the impact of the concentration of the reaction mixtures on the reaction outcomes and found that the yields of **2a** became lower either by increasing or decreasing the concentration of the substrates (Table 1, entries 19 and 20). Therefore, the best reaction conditions have been identified as to carry out the reaction in 1.0 mL of DCE at 80 °C using 0.1 mmol of substrate **1a** in the presence of 5 mol % $[Rh(cod)Cl]_2$ and under 1.0 atm CO atmosphere.

Having these optimal reaction conditions in hand, we next examined the generality of this highly regio- and diastereoselective intramolecular reaction of Ene-VDCPs **1**, and the results are summarized in Table 2. In the cases of Ene-VDCPs **1b–e**

Table 2. Rh(I)-Catalyzed Pauson–Khand-Type [3 + 2 + 1] Cycloaddition Reaction of Ene-VDCPs 1 under the Optimal Conditions



entry[a]	1; R^1, R^1	R^2	R^3	X	product, yield (%)[b] (cis:trans)
1	**1b**; $-(CH_2)_5-$	H	H	NTs	**2b**, 73 (16.7:1.0)
2	**1c**; $-(CH_2)_4-$	H	H	NTs	**2c**, 46 (16.7:1.0)
3	**1d**; $-(CH_2)_6-$	H	H	NTs	**2d**, 50 (9.5:1.0)
4	**1e**; C_4H_9/C_4H_9	H	H	NTs	**2e**, 55 (11.8:1.0)
5	**1f**; CH_3/CH_3	H	H	NBs	**2f**, 64 (15.4:1.0)
6	**1g**; CH_3/CH_3	H	H	NNs	**2g**, 54 (6.9:1.0)
7	**1h**; $-(CH_2)_5-$	H	H	NBs	**2h**, 69 (>20.0:1.0)
8	**1i**; $-(CH_2)_5-$	H	H	NNs	**2i**, 48 (12.5:1.0)
9	**1j**, CH_3/CH_3	H	CH_3	NTs	**2j**, 63 (>20.0:1.0)
10	**1k**; $-(CH_2)_5-$	H	CH_3	NBs	**2k**, 57 (>20.0:1.0)
11	**1l**; CH_3/CH_3	H	H	O	**2l**, 45 (>20.0:1.0)
12	**1m**; CH_3/CH_3	C_6H_5	H	NTs	complex
13	**1n**; CH_3/CH_3	H	C_6H_5	NTs	complex

[a]All reactions were carried out using **1** (0.2 mmol) in the presence of $[Rh(cod)CI]_2$ (5 mol %) in DCE (2.0 mL) under a CO atmosphere (1.0 atm) at 80 °C for 5 h. Abbreviations: Ts = 4-toluenesulfonyl, Bs = 4-bromobenzenesulfonyl, Ns = 4-nitrobenzenesulfonyl. [b]Isolated yield.

(R^2 = H, R^3 = H, X = NTs), regardless of whether R^1 is a cyclic substituent ($-(CH_2)_5-$ = cyclohexyl, $-(CH_2)_4-$ = cyclopentyl, $-(CH_2)_6-$ = cycloheptyl) or a noncyclic substituent (C_4H_9 = butyl), these Rh(I)-catalyzed reactions proceeded smoothly to give the desired products **2b–e** in moderate to good yields (46–73%) with high diastereoselectivities ((9.5–16.7):1.0) (Table 2, entries 1–4). Changing the substituent at the nitrogen atom from Ts to Bs and Ns (Bs = 4-bromobenzenesulfonyl, Ns = 4-nitrobenzenesulfonyl) produced the corresponding bicyclic cyclohexanone derivatives **2f–i** in 48–69% yields with (6.9–20.0):1.0 diastereoselectivities (Table 2, entries 5–8). As for substrates **1j,k** bearing a methyl group at the internal position of the alkene moiety, this Rh(I)-catalyzed Pauson–Khand-type [3 + 2 + 1] cycloaddition reaction could also proceed smoothly to give the desired products **2j,k** in moderate yields and excellent cis diastereoselectivities (Table 2, entries 9 and 10). The structure of **2k** was unambiguously determined by an X-ray diffraction study. Its CIF data are presented in the Supporting Information, and an ORTEP drawing is shown in Figure 2.[13] Furthermore, the

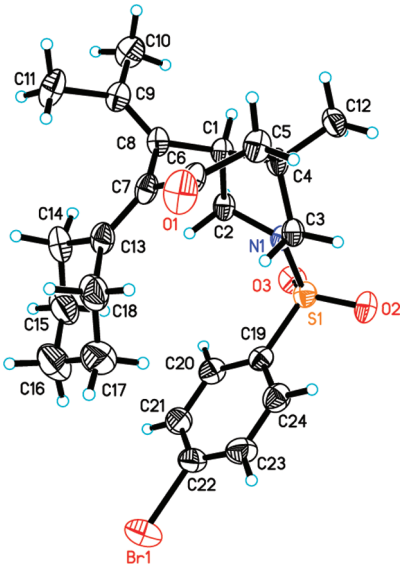


Figure 2. ORTEP drawing of *cis*-**2k**.

oxygen-tethered Ene-VDCP **1l** could be also successfully applied in this reaction under the optimal reaction conditions, furnishing the corresponding oxa-bicyclic adduct **2l** in 45% yield and excellent diastereoselectivity (Table 2, entry 11). However, this reaction was not suitable for substrates **1m,n** (R^2 = C_6H_5 or R^3 = C_6H_5). The large phenyl group may affect the coordination of the metal catalyst with the alkene moiety and further affect the cyclometalation process, giving complex product mixtures. Meanwhile, the electronic effect of the phenyl group may also have some influence on this process (Table 2, entries 12 and 13).

Moreover, when a methyl group was introduced at the terminal position of the alkene substituent, this Pauson–Khand-type [3 + 2 + 1] cycloaddition reaction for substrate **1o** proceeded efficiently to give the desired product **2o** in 52% yield with high diastereoselectivity (Scheme 1, eq 1). The structure of the major diastereomer **2o** was also characterized by an X-ray diffraction study. Its CIF data are presented in the Supporting Information, and an ORTEP drawing is shown in Figure 3.[14] Extending the length of the tethered alkene moiety, we found that the expected 6,6-fused azabicyclic derivative **2p** could be produced in 46% yield with a 16.7:1.0 diastereoselectivity (Scheme 1, eq 2). On the basis of the X-ray diffraction study, the major diastereomer of **2p** was identified as having a trans onfiguration (Figure 4),[15] which is different from the case for the 5,6-fused azabicyclic derivatives (the major diastereomer is cis).

Further transformations of product **2a** are shown in Scheme 2. As can be seen from Scheme 2, the corresponding epoxy product **3a** could be obtained in 72% yield with 15.4:1.0 diastereoselectivity upon subjecting **2a** to a conventional O_3 oxidation procedure (Scheme 2, eq 1).[16] Moreover, the

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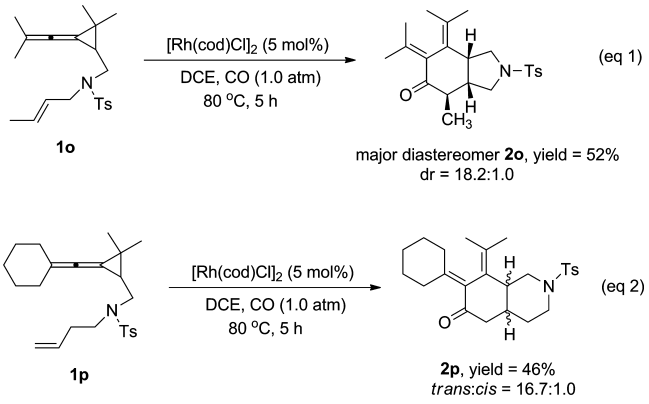
Scheme 1. Rh(I)-Catalyzed Pauson–Khand-Type [3 + 2 + 1] Cycloaddition Reactions of Ene-VDCPs 1o,p



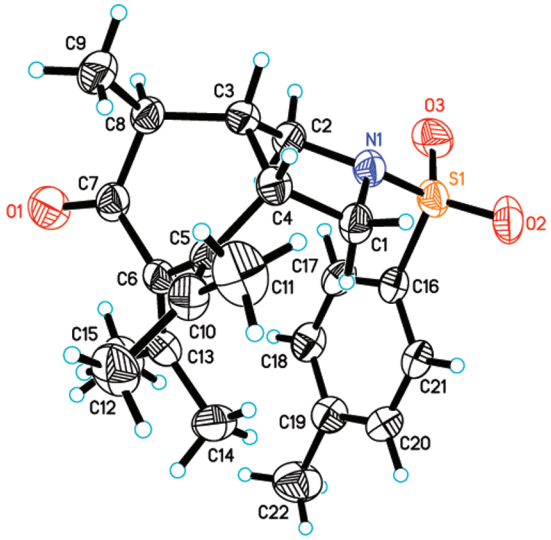


Figure 3. ORTEP drawing of the major diastereomer **2o**.

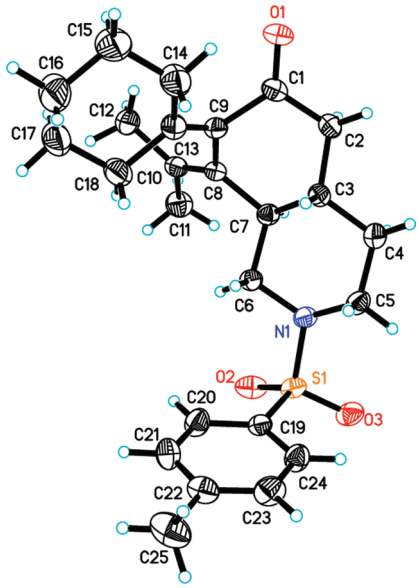
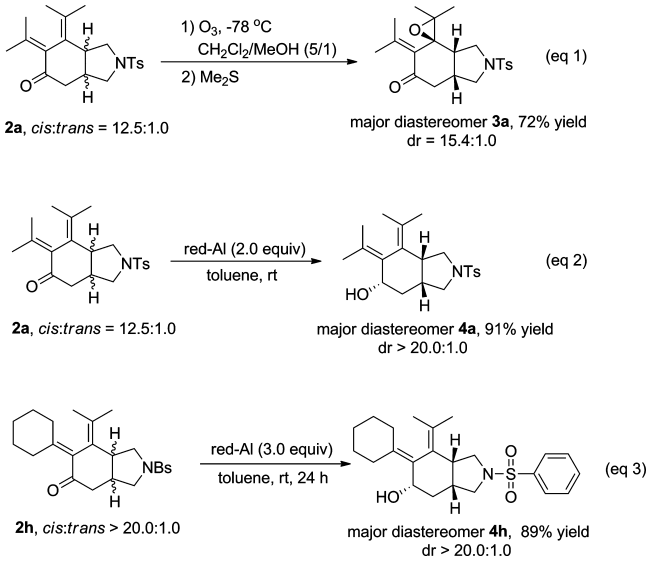


Figure 4. ORTEP drawing of *trans*-**2p**.

carbonyl group in product **2a** could be easily reduced by treatment with Red-Al reagent in toluene, thus giving the

Scheme 2. Transformations of Products 2a,h



corresponding alcohol derivative **4a** in high yield and stereoselectivity (Scheme 2, eq 2). When the Bs substituent was introduced at the nitrogen atom, in addition to the reduction of the carbonyl group, the bromine atom also underwent hydrogenolysis to the to give the corresponding product **4h** smoothly (Scheme 2, eq 3).[17] The structures of the major diastereomers **3a** and **4h** were confirmed by X-ray diffraction studies, and their CIF data are presented in the Supporting Information.[18,19]

On the basis of the above results, a plausible mechanism for the formation of azabicyclic cyclohexanone derivatives **2** is outlined in Scheme 3. The selective coordination of the internal double bonds of the allene and alkene moieties in substrate **1a** to the rhodium(I) complex gives intermediate **A**. Insertion of the rhodium(I) center into the distal C–C bond of cyclopropane produces the (π-allyl)(σ-alkyl)Rh^{III} intermediate **B**.[7a,e,8] Subsequent isomerization of intermediate **B** affords the rhodacyclobutane intermediate **C**,[20] which undergoes insertion of CO and the intramolecular C=C bond to give intermediate **D** or **D′**. Then product **2a** could be obtained from intermediate **D** or **D′** via reductive elimination along with the regeneration of the rhodium(I) catalyst (Scheme 3).

In summary, we have developed an efficient Rh(I)-catalyzed Pauson–Khand-type [3 + 2 + 1] cycloaddition reaction of Ene-VDCPs **1** under a CO atmosphere to produce the corresponding 5,6-fused or 6,6-fused bicyclic cyclohexanone derivatives in moderate to good yields with high diastereoselectivities. Our findings in this paper offer an easy one-pot process to construct complex bicyclic structures, which are important building blocks in organic synthesis. The scope and limitations of this reaction have been carefully examined, and the possible reaction mechanism has been discussed. Further applications of this practical rhodium-catalyzed Pauson–Khand-type [3 + 2 + 1] cycloaddition reaction and more detailed mechanistic investigations are under way in our laboratory.

EXPERIMENTAL SECTION

General Methods. Melting points were obtained with a Yanagimoto micro melting point apparatus and are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded for solutions in $CDCl_3$ with

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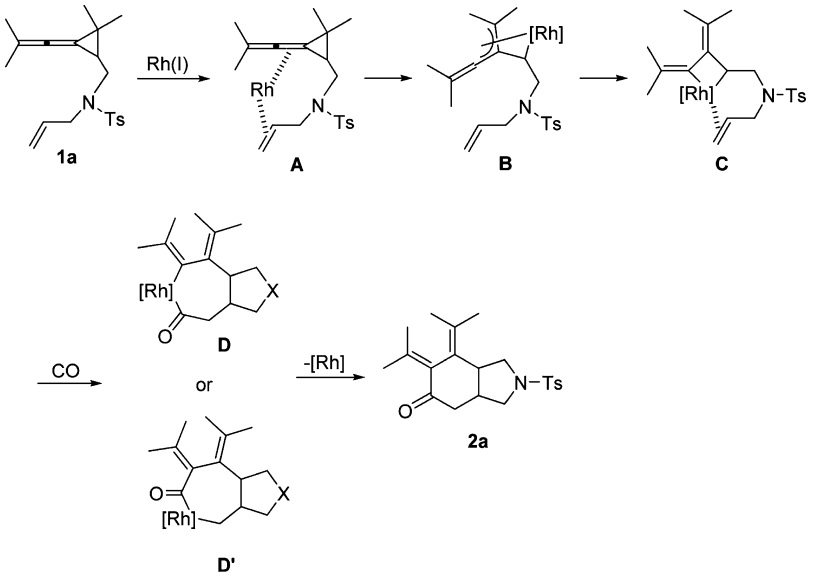
Scheme 3. Plausible Mechanism for the Formation of 2a



tetramethylsilane (TMS) as internal standard; *J* values are in Hz. Mass and HRMS spectra were recorded by the EI, ESI, or MALDI method. Organic solvents used were dried by standard methods when necessary. Commercially obtained reagents were used without further purification. All reactions were monitored by TLC with Huanghai GF_{254} silica gel coated plates. Flash column chromatography was carried out using 300−400 mesh silica gel at increased pressure. All reactions were performed under 1.0 atm of carbon monoxide using standard Schlenk techniques. The substrates **1a−d,f−j,o** are all known compounds, and the detailed spectroscopic data are included in the previous literature.[10l]

Typical Procedure for the Preparation of the Ene-Vinylidenecyclopropanes 1e,k,m,n. *N-Allyl-N-((3-(2-butylhex-1-enylidene)-2,2-dimethylcyclopropyl)methyl)-4-tolylsulfonamide (**1e**).* Under an argon atmosphere, triphenylphosphine (165 mg, 0.63 mmol) and *N*-allyl-4-methylbenzenesulfonamide (139 mg, 0.66 mmol) were added into a Schlenk tube. Then, 5.0 mL of tetrahydrofuran (THF) was added and the reaction mixture was cooled to 0 °C. (3-(2-Butylhex-1-enylidene)-2,2-dimethylcyclopropyl)methanol (142 mg, 0.6 mmol),[21] which was dissolved in THF (1.0 mL), was added into the above Schlenk tube. Then diisopropyl azodicarboxylate (DIAD; 0.12 mL, 0.63 mmol) was added dropwise at 0 °C and the mixture warmed to room temperature naturally. On completion of the reaction, the solvent was removed under reduced pressure and the residue was purified by flash column chromatography. Yield: 147 mg, 57% of a yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz, TMS): δ 0.85−0.89 (m, 6H, $3CH_3$), 1.18 (s, 3H, CH_3), 1.20 (s, 3H, CH_3), 1.27−1.40 (m, 8H, $4CH_2$), 1.63 (t, J = 6.8 Hz, 1H, CH), 1.93−2.01 (m, 4H, $2CH_2$), 2.41 (s, 3H, CH_3), 3.16 (dd, J_1 = 6.8 Hz, J_2 = 14.4 Hz, 1H, CH), 3.52 (dd, J_1 = 6.8 Hz, J_2 = 14.4 Hz, 1H, CH), 3.87 (d, J = 6.0 Hz, 2H, CH_2), 5.11 (dd, J_1 = 1.6 Hz, J_2 = 10.4 Hz, 1H, CH), 5.18 (dd, J_1 = 1.6 Hz, J_2 = 17.2 Hz, 1H, CH), 5.61−5.71 (m, 1H, CH), 7.28 (d, J = 8.8 Hz, 2H, Ar), 7.71 (d, J = 8.8 Hz, 2H, Ar). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS): δ 13.9, 19.2, 21.4, 22.3, 23.9, 25.8, 29.5, 29.7, 29.9, 32.8, 32.9, 46.8, 49.6, 92.1, 108.3, 117.8, 127.1, 129.5, 133.3, 137.3, 143.0, 184.2. IR (CH_2Cl_2): ν 2957, 2924, 2871, 2858, 2005, 1599, 1455, 1345, 1260, 1159, 1091, 1017, 927, 799, 758, 660 cm^{-1}. MS (ESI): m/z 430 (M^+ + 1). HRMS (ESI): calcd for $C_{26}H_{40}NO_2S$ 430.277 43, found 430.276 42.

*4-Bromo-N-((3-(cyclohexylidenemethylene)-2,2-dimethylcyclopropyl)methyl)-N-(2-methylallyl)benzenesulfonamide (**1k**).* Yield: 139 mg, 50% of a yellow oil. ^{1}H NMR ($CDCl_3$, 300 MHz, TMS): δ 1.14 (s, 3H, CH_3), 1.17 (s, 3H, CH_3), 1.53−1.59 (m, 7H, 7CH), 1.69 (s, 3H, CH_3), 2.10−2.14 (m, 4H, 4CH), 3.09 (dd, J_1 = 7.2 Hz, J_2 = 14.4 Hz, 1H, CH), 3.61 (dd, J_1 = 6.0 Hz, J_2 = 14.4 Hz, 1H, CH), 3.78 (s, 2H, 2CH), 4.88 (d, J = 9.3 Hz, 2H, 2CH), 7.63 (d, J = 8.7 Hz, 2H, Ar), 7.71 (d, J = 8.7 Hz, 2H, Ar). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS): δ 19.2, 19.9, 24.0, 25.9, 26.0, 27.3, 27.4, 29.2, 32.0, 32.3, 47.0, 53.1, 89.6, 106.1, 113.5, 127.1, 128.6, 132.1, 139.5, 140.3, 182.2. IR (CH_2Cl_2): ν 2925, 2854, 2007, 1716, 1575, 1471, 1447, 1388, 1343, 1260, 1161, 1098, 1068, 1010, 917, 798, 776, 735 cm^{-1}. MS (ESI): m/z 464 (M^+ + 1). HRMS (ESI): calcd for $C_{23}H_{30}BrNO_2S$ 463.1181, found 463.1178.

*N-Cinnamyl-N-((2,2-dimethyl-3-(2-methylprop-1-enylidene)-cyclopropyl)methyl)-4-tolylsulfonamide (**1m**).* Yield: 136 mg, 54% of a yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz, TMS): δ 1.19 (s, 3H, CH_3), 1.20 (s, 3H, CH_3), 1.68 (t, J = 6.8 Hz, 1H, CH), 1.73 (s, 6H, $2CH_3$), 2.39 (s, 3H, CH_3), 3.15 (dd, J_1 = 6.8 Hz, J_2 = 14.4 Hz, 1H, CH), 3.65 (dd, J_1 = 6.8 Hz, J_2 = 14.4 Hz, 1H, CH), 3.98−4.10 (m, 2H, CH_2), 5.93−6.01 (m, 1H, CH), 6.45 (d, J = 15.6 Hz, 1H, CH), 7.21−7.29 (m, 7H, Ar), 7.73 (d, J = 8.4 Hz, 2H, Ar). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS): δ 19.3, 21.2, 21.3, 21.5, 23.9, 25.9, 29.5, 46.7, 49.0, 89.7, 98.6, 124.4, 126.2, 127.1, 127.6, 128.4, 129.5, 133.0, 136.3, 137.4, 143.0, 185.3. IR (CH_2Cl_2): ν 2963, 2924, 2855, 2010, 1729, 1598, 1495, 1448, 1341, 1261, 1159, 1093, 1019, 969, 923, 800, 742, 695, 657 cm^{-1}. MS (ESI): m/z 422 (M^+ + 1). HRMS (ESI): calcd for $C_{26}H_{31}NNaO_2S$ 444.196 77, found 444.197 74.

*N-((2,2-Dimethyl-3-(2-methylprop-1-enylidene)cyclopropyl)-methyl)-4-methyl-N-(2-phenylallyl)benzenesulfonamide (**1n**).* Yield: 134 mg, 53% of a yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz, TMS): δ 1.09 (s, 3H, CH_3), 1.12 (s, 3H, CH_3), 1.56 (t, J = 6.8 Hz, 1H, CH), 1.60 (s, 3H, CH_3), 1.68 (s, 3H, CH_3), 2.42 (s, 3H, CH_3), 3.12 (dd, J_1 = 6.8 Hz, J_2 = 14.8 Hz, 1H, CH), 3.60 (dd, J_1 = 6.8 Hz, J_2 = 14.8 Hz, 1H, CH), 4.27 (s, 2H, CH_2), 5.29 (s, 1H, CH), 5.46 (s, 1H, CH), 7.28−7.33 (m, 5H, Ar), 7.37−7.39 (m, 2H, Ar), 7.68 (d, J = 8.4 Hz, 2H, Ar). ^{13}C NMR ($CDCl_3$, 75 MHz, TMS): δ 19.1, 21.16, 21.24, 21.4, 23.8, 25.7, 29.0, 47.2, 50.5, 89.6, 98.5, 114.5, 126.0, 127.1, 127.7, 128.2, 129.5, 137.0, 138.7, 142.5, 143.0, 185.2. IR (CH_2Cl_2): ν 2962, 2923, 2860, 2009, 1598, 1495, 1446, 1342, 1306, 1261, 1159, 1119, 1094, 1018, 931, 912, 803, 749, 707, 659 cm^{-1}. MS (ESI): m/z 422 (M^+ + 1). HRMS (ESI): calcd for $C_{26}H_{31}NNaO_2S$ 444.196 77, found 444.198 08.

Synthesis of the Vinylidenecyclopropane Derivative 2-(Allyloxymethyl)-1,1-dimethyl-3-(2-methylprop-1-enylidene)-cyclopropane (1l). Under an argon atmosphere, sodium hydride (36 mg, 0.9 mmol) and (2,2-dimethyl-3-(2-methylprop-1-enylidene)-cyclopropyl)methanol (91 mg, 0.6 mmol)[21] in THF (2.0 mL) were added into a Schlenk tube. After 20 min, allyl bromide (104 μL, 1.2 mmol) was added into the above Schlenk tube and the reaction mixture was warmed to 50 °C. On completion of the reaction the mixture was quenched by addition of water. The reaction solution was diluted with ether (10.0 mL × 3), and the organic layers were dried

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over anhydrous Na_2SO_4. The solvent was removed under reduced pressure and the residue was purified by a flash column chromatography. Yield: 70 mg, 61% of a yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz, TMS): δ 1.24 (s, 3H, CH_3), 1.28 (s, 3H, CH_3), 1.73 (s, 3H, CH_3), 1.75 (s, 3H, CH_3), 1.82 (dd, J_1 = 5.2 Hz, J_2 = 8.8 Hz, 1H, CH), 3.42 (dd, J_1 = 8.8 Hz, J_2 = 10.4 Hz, 1H, CH), 3.67 (dd, J_1 = 5.2 Hz, J_2 = 10.4 Hz, 1H, CH), 3.94−4.04 (m, 2H, 2CH), 5.16−5.19 (m, 1H, CH), 5.25−5.30 (m, 1H, CH), 5.87−5.96 (m, 1H, CH). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS): δ 19.1, 21.2, 21.6, 24.4, 26.1, 30.7, 69.3, 71.3, 89.2, 97.9, 116.7, 135.0, 185.4. IR (CH_2Cl_2): ν 2956, 2922, 2853, 1739, 1460, 1377, 1260, 1162, 1090, 1016, 863, 796, 700, 663 cm^{-1}. MS (%) (EI): m/z 192 (M^+, 32), 77 (100), 91 (74), 135 (71), 105 (47), 115 (46), 41 (43), 43 (35), 119 (33); HRMS (EI): calcd for $C_{13}H_{20}O$ 192.1514, found 192.1529.

Synthesis of the Vinylidenecyclopropane Derivative *N*-(But-3-enyl)-*N*-((3-(cyclohexylidenemethylene)-2,2-dimethylcyclopropyl)methyl)-4-tolylsulfonamide (1p). Under an argon atmosphere, triphenylphosphine (165 mg, 0.63 mmol) and *N*-(but-3-en-1-yl)-4-methylbenzenesulfonamide (149 mg, 0.66 mmol) were added into a Schlenk tube. Then, 5.0 mL of THF was added and the reaction mixture was cooled to 0 °C. (3-(Cyclohexylidenemethylene)-2,2-dimethylcyclopropyl)methanol (115 mg, 0.6 mmol),[21] which was dissolved in THF (1.0 mL), was added into the above Schlenk tube. Then DIAD (0.12 mL, 0.63 mmol) was added dropwise at 0 °C and the mixture was warmed to room temperature naturally. On reaction completion, the solvent was removed under reduced pressure and the residue was purified by flash column chromatography. Yield: 113 mg, 47% of a yellow oil. ^{1}H NMR ($CDCl_3$, 300 MHz, TMS): δ 1.17 (s, 3H, CH_3), 1.21 (s, 3H, CH_3), 1.53−1.60 (m, 7H, 7CH), 2.10−2.16 (m, 4H, $2CH_2$), 2.27−2.36 (m, 2H, CH_2), 2.42 (s, 3H, CH_3), 2.99 (dd, J_1 = 7.8 Hz, J_2 = 14.4 Hz, 1H, CH), 3.19−3.31 (m, 2H, CH_2), 3.69 (dd, J_1 = 5.7 Hz, J_2 = 14.4 Hz, 1H, CH), 4.99−5.07 (m, 2H, CH_2), 5.64−5.78 (m, 1H, CH), 7.29 (d, J = 7.8 Hz, 2H, Ar), 7.71 (d, J = 7.8 Hz, 2H, Ar). ^{13}C NMR ($CDCl_3$, 75 MHz, TMS): δ 19.3, 21.4, 23.7, 26.00, 26.03, 27.2, 27.4, 29.5, 32.0, 32.3, 33.2, 46.6, 47.6, 89.8, 106.1, 116.7, 127.0, 129.6, 134.9, 137.2, 142.9, 182.1. IR (CH_2Cl_2): ν 2956, 2924, 2854, 2008, 1728, 1448, 1343, 1260, 1159, 1091, 1018, 918, 800, 746, 658 cm^{-1}. MS (ESI): m/z 400 (M^+ + 1). HRMS (ESI): calcd for $C_{24}H_{33}NNaO_2S$ 422.212 42, found 422.214 35.

Typical Procedure for the Preparation of 6,7-Bis(propan-2-ylidene)-2-tosylhexahydro-1*H*-isoindol-5(6*H*)-one (2a). Under an argon atmosphere, $[Rh(cod)Cl]_2$ (5.0 mg, 0.01 mmol) was added into a Schlenk tube. Then the atmosphere was pumped off and a balloon filled with CO was connected to the reaction flask. A solution of substrate **1a** (69 mg, 0.2 mmol) in 1,2-dichloroethane (DCE; 2.0 mL) was added into the Schlenk tube. The reaction mixture was stirred at 80 °C for 5 h. Then, the solvent was removed under reduced pressure and the residue was purified by flash column chromatography. Yield: 57 mg, 76% of a white solid. Mp: 138−140 °C. (*cis*-**2a**) ^{1}H NMR ($CDCl_3$, 300 MHz, TMS): δ 1.40 (s, 3H, CH_3), 1.44 (s, 3H, CH_3), 1.73 (s, 3H, CH_3), 1.77 (s, 3H, CH_3), 2.17−2.27 (m, 2H, 2CH), 2.33−2.41 (m, 2H, 2CH), 2.45 (s, 3H, CH_3), 2.71−2.82 (m, 1H, CH), 3.53 (t, J = 8.4 Hz, 1H, CH), 3.64−3.75 (m, 2H, 2CH), 7.32 (d, J = 7.8 Hz, 2H, Ar), 7.62 (d, J = 7.8 Hz, 2H, Ar) (7.74 (d, J = 7.8 Hz, 2H, Ar, *trans*-**2a**)). (*cis*-**2a**) ^{13}C NMR ($CDCl_3$, 100 MHz, TMS): δ 19.7, 21.3, 21.4, 21.7, 23.7, 34.5, 39.7, 40.5, 52.0, 53.3, 127.9, 128.1, 129.4, 131.2, 131.8, 131.9, 143.6, 148.5, 201.4. IR (CH_2Cl_2): ν 2982, 2923, 2854, 1684, 1598, 1439, 1368, 1344, 1254, 1185, 1162, 1094, 1032, 982, 832, 817, 735, 709, 682, 662, 611 cm^{-1}. MS (ESI): m/z 374 (M^+ + 1). HRMS (MALDI): calcd for $C_{21}H_{28}NO_3S$ 374.1797, found 374.1784.

*6-Cyclohexylidene-7-(propan-2-ylidene)-2-tosylhexahydro-1H-isoindol-5(6H)-one (**2b**).* Yield: 60 mg, 73% of a white solid. Mp: 134−135 °C. (*cis*-**2b**) ^{1}H NMR ($CDCl_3$, 300 MHz, TMS): δ 0.89−0.99 (m, 1H, CH), 1.07−1.17 (m, 1H, CH), 1.36−1.45 (m, 5H, CH_3 + 2CH), 1.50−1.59 (m, 2H, 2CH), 1.73 (s, 3H, CH_3), 1.77−1.80 (m, 2H, 2CH), 2.18−2.34 (m, 2H, 2CH), 2.38−2.48 (m, 6H, CH_3 + 3CH), 2.64−2.79 (m, 2H, 2CH), 3.58 (t, J = 8.1 Hz, 1H, CH), 3.65−3.76 (m, 2H, 2CH), 7.31 (d, J = 8.1 Hz, 2H, Ar), 7.65 (d, J = 8.1 Hz, 2H, Ar) (7.74 (d, J = 8.1 Hz, 2H, Ar, *trans*-**2b**)). (*cis*-**2b**) ^{13}C NMR ($CDCl_3$, 75 MHz, TMS): δ 19.7, 21.4, 21.8, 26.1, 27.0, 27.5, 29.9, 31.9, 34.6, 39.6, 40.5, 51.9, 53.3, 127.2, 127.9, 129.6, 129.8, 131.8, 132.1, 143.6, 154.4, 202.0. IR (CH_2Cl_2): ν 2926, 2855, 1682, 1597, 1473, 1448, 1347, 1165, 1096, 1039, 982, 840, 817, 739, 708, 665 cm^{-1}. MS (ESI): m/z 414 (M^+ + 1). HRMS (ESI): calcd for $C_{24}H_{31}NNaO_3S$ 436.191 69, found 436.190 60.

*6-Cyclopentylidene-7-(propan-2-ylidene)-2-tosylhexahydro-1H-isoindol-5(6H)-one (**2c**).* Yield: 37 mg, 46% of a white solid. Mp: 117−118 °C. (*cis*-**2c**) ^{1}H NMR ($CDCl_3$, 400 MHz, TMS): δ 1.50 (s, 3H, CH_3), 1.58−1.65 (m, 4H, 4CH), 1.74 (s, 3H, CH_3), 1.79−1.85 (m, 1H, CH), 1.97−2.06 (m, 1H, CH), 2.11−2.21 (m, 4H, 4CH), 2.42 (s, 3H, CH_3), 2.44−2.48 (m, 1H, CH), 2.76−2.83 (m, 2H, 2CH), 3.54 (t, J = 8.8 Hz, 1H, CH), 3.61−3.74 (m, 2H, 2CH), 7.29 (d, J = 8.4 Hz, 2H, Ar) (7.33 (d, J = 8.4 Hz, 2H, Ar, *trans*-**2c**)), 7.59 (d, J = 8.4 Hz, 2H, Ar) (7.74 (d, J = 8.4 Hz, 2H, Ar, *trans*-**2c**)). (*cis*-**2c**) ^{13}C NMR ($CDCl_3$, 100 MHz, TMS): δ 19.8, 21.4, 22.3, 24.8, 26.0, 33.3, 34.4, 35.0, 39.5, 40.6, 52.4, 53.2, 127.96, 128.02, 128.8, 129.4, 131.2, 131.5, 143.6, 163.7, 200.3. IR (CH_2Cl_2): ν 2955, 2925, 2856, 1684, 1600, 1473, 1452, 1347, 1184, 1164, 1095, 1035, 983, 817, 735, 710, 666 cm^{-1}. MS (ESI): m/z 400 (M^+ + 1). HRMS (MALDI): calcd for $C_{23}H_{30}NO_3S$ 400.1932, found 400.1941.

*6-Cycloheptylidene-7-(propan-2-ylidene)-2-tosylhexahydro-1H-isoindol-5(6H)-one (**2d**).* Yield: 43 mg, 50% of a white solid. Mp: 128−130 °C. (*cis*-**2d**) ^{1}H NMR ($CDCl_3$, 300 MHz, TMS): δ 1.29−1.47 (m, 7H, 7CH), 1.51 (s, 3H, CH_3), 1.54−1.58 (m, 1H, CH), 1.74 (s, 3H, CH_3), 1.77−1.82 (m, 1H, CH), 2.10−2.19 (m, 2H, 2CH), 2.31 (t, J = 9.9 Hz, 1H, CH), 2.38−2.46 (m, 6H, 6CH), 2.53−2.62 (m, 1H, CH), 2.68−2.78 (m, 1H, CH), 3.57 (t, J = 8.1 Hz, 1H, CH), 3.62−3.76 (m, 2H, 2CH), 7.30 (d, J = 8.1 Hz, 2H, Ar), 7.63 (d, J = 8.1 Hz, 2H, Ar) (7.73 (d, J = 8.1 Hz, 2H, Ar, *trans*-**2d**)). (*cis*-**2d**) ^{13}C NMR ($CDCl_3$, 100 MHz, TMS): δ 19.8, 21.5, 22.3, 26.0, 27.3, 28.9, 30.5, 32.6, 33.9, 34.9, 40.0, 41.1, 51.7, 53.3, 128.0, 128.1, 129.6, 131.3, 131.8, 132.0, 143.6, 158.6, 201.4. IR (CH_2Cl_2): ν 2960, 2924, 2854, 1725, 1680, 1596, 1531, 1452, 1347, 1260, 1164, 1094, 1017, 982, 859, 799, 708, 663 cm^{-1}. MS (ESI): m/z 428 (M^+ + 1). HRMS (ESI): calcd for $C_{25}H_{34}NO_3S$ 428.225 39, found 428.224 48.

*6-(Nonan-5-ylidene)-7-(propan-2-ylidene)-2-tosylhexahydro-1H-isoindol-5(6H)-one (**2e**).* Yield: 50 mg, 55% of a white solid. Mp: 114−116 °C. (*cis*-**2e**) ^{1}H NMR ($CDCl_3$, 300 MHz, TMS): δ 0.89−0.95 (m, 6H, 6CH), 1.06−1.21 (m, 2H, 2CH), 1.25−1.40 (m, 6H, 6CH), 1.48 (s, 3H, CH_3), 1.68−1.89 (m, 6H, CH_3+3CH), 2.08−2.17 (m, 2H, 2CH), 2.30−2.38 (m, 2H, 2CH), 2.43 (s, 3H, CH_3), 2.48−2.56 (m, 1H, CH), 2.62−2.70 (m, 1H, CH), 3.54 (t, J = 8.4 Hz, 1H, CH), 3.59−3.71 (m, 2H, 2CH), 7.30 (d, J = 7.8 Hz, 2H, Ar) (7.34 (d, J = 7.8 Hz, 2H, Ar, *trans*-**2e**)), 7.64 (d, J = 7.8 Hz, 2H, Ar) (7.73 (d, J = 7.8 Hz, 2H, Ar, *trans*-**2e**)). (*cis*-**2e**) ^{13}C NMR ($CDCl_3$, 100 MHz, TMS): δ 13.75, 13.84, 19.8, 21.5, 22.0, 23.2, 23.5, 28.5, 31.2, 31.4, 33.9, 35.0, 40.0, 41.2, 51.7, 53.3, 127.80, 127.84, 129.6, 131.3, 132.2, 132.3, 143.5, 156.4, 201.1. IR (CH_2Cl_2): ν 2956, 2928, 2858, 1683, 1585, 1458, 1347, 1163, 1095, 1038, 981, 816, 735, 709, 664 cm^{-1}. MS (ESI): m/z 458 (M^+ + 1). HRMS (MALDI): calcd for $C_{27}H_{40}NO_3S$ 458.2734, found 458.2723.

*2-(4-Bromophenylsulfonyl)-6,7-bis(propan-2-ylidene)hexahydro-1H-isoindol-5(6H)-one (**2f**).* Yield: 56 mg, 64% of a white solid. Mp: 173−174 °C. (*cis*-**2f**) ^{1}H NMR ($CDCl_3$, 300 MHz, TMS): δ 1.44 (s, 3H, CH_3), 1.45 (s, 3H, CH_3), 1.74 (s, 3H, CH_3), 1.86 (s, 3H, CH_3) (1.90 (s, 3H, CH_3, *trans*-**2f**)), 2.19−2.31 (m, 2H, 2CH), 2.37−2.49 (m, 2H, 2CH), 2.73−2.83 (m, 1H, CH), 3.53 (t, J = 8.1 Hz, 1H, CH), 3.64−3.76 (m, 2H, 2CH), 7.60 (d, J = 8.4 Hz, 2H, Ar), 7.68 (d, J = 8.4 Hz, 2H, Ar). (*cis*-**2f**) ^{13}C NMR ($CDCl_3$, 100 MHz, TMS): δ 19.7, 21.4, 21.8, 23.8, 34.5, 39.8, 40.5, 52.2, 53.3, 127.8, 128.0, 129.4, 131.7, 132.1, 132.2, 133.3, 148.7, 201.1. IR (CH_2Cl_2): ν 2983, 2923, 2852, 1684, 1600, 1574, 1471, 1439, 1348, 1255, 1167, 1093, 1068, 1034, 1009, 982, 822, 737, 706, 619 cm^{-1}. MS (ESI): m/z 438 (M^+ + 1). HRMS (MALDI): calcd for $C_{20}H_{25}NO_3SBr$ 438.0739, found 438.0733.

*2-(4-Nitrophenylsulfonyl)-6,7-bis(propan-2-ylidene)hexahydro-1H-isoindol-5(6H)-one (**2g**).* Yield: 44 mg, 54% of a yellow solid. Mp: 158−159 °C. (*cis*-**2g**) ^{1}H NMR ($CDCl_3$, 300 MHz, TMS): δ 1.47 (s, 3H, CH_3), 1.48 (s, 3H, CH_3), 1.75 (s, 3H, CH_3), 1.85 (s, 3H, CH_3)

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(1.89 (s, 3H, CH_3, *trans*-**2g**)), 2.24 (dd, J_1 = 3.0 Hz, J_2 = 16.8 Hz, 1H, CH), 2.43−2.50 (m, 2H, 2CH), 2.58−2.66 (m, 1H, CH), 2.73−2.85 (m, 1H, CH) (2.91−2.97 (m, 1H, CH, *trans*-**2g**)), 3.54 (t, J = 9.3 Hz, 1H, CH), 3.64−3.74 (m, 2H, 2CH), 7.95 (d, J = 8.7 Hz, 2H, Ar) (8.04 (d, J = 8.7 Hz, 2H, Ar, *trans*-**2g**)), 8.38 (d, J = 8.7 Hz, 2H, Ar). (*cis*-**2g**) ^{13}C NMR ($CDCl_3$, 100 MHz, TMS): δ 19.8, 21.4, 21.8, 23.8, 34.7, 40.0, 40.6, 52.4, 53.1, 124.0, 127.5, 128.9, 131.9, 132.6, 140.8, 148.3, 150.1, 200.8. IR (CH_2Cl_2): ν 2025, 2855, 1685, 1603, 1530, 1472, 1441, 1349, 1309, 1255, 1168, 1095, 1037, 1013, 982, 857, 822, 736, 688, 664, 621 cm^{-1}. MS (ESI): m/z 405 (M^+ + 1). HRMS (MALDI): calcd for $C_{20}H_{25}N_2O_5S$ 405.1475, found 405.1479.

*2-(4-Bromophenylsulfonyl)-6-cyclohexylidene-7-(propan-2-ylidene)hexahydro-1H-isoind-ol-5(6H)-one (**2h**).* Yield: 66 mg, 69% of a white solid. Mp: 155−156 °C. (*cis*-**2h**) ^{1}H NMR ($CDCl_3$, 300 MHz, TMS): δ 0.88−1.12 (m, 2H, 2CH), 1.46 (s, 3H, CH_3), 1.50−1.60 (m, 4H, 4CH), 1.74 (s, 3H, CH_3), 1.79−1.86 (m, 2H, 2CH), 2.21−2.37 (m, 2H, 2CH), 2.40−2.49 (m, 3H, 3CH), 2.69−2.80 (m, 2H, 2CH), 3.58 (t, J = 8.4 Hz, 1H, CH), 3.66−3.78 (m, 2H, 2CH), 7.63 (d, J = 8.7 Hz, 2H, Ar), 7.67 (d, J = 8.7 Hz, 2H, Ar). (*cis*-**2h**) ^{13}C NMR ($CDCl_3$, 100 MHz, TMS): δ 19.8, 21.9, 26.0, 27.2, 27.8, 30.0, 32.0, 34.6, 39.6, 40.4, 52.0, 53.3, 127.1, 128.0, 129.4, 129.7, 132.3, 132.4, 133.9, 154.7, 201.8. IR (CH_2Cl_2): ν 2927, 2854, 1682, 1595, 1574, 1471, 1448, 1388, 1351, 1266, 1248, 1169, 1095, 1068, 1041, 1009, 982, 820, 738, 706, 613 cm^{-1}. MS (ESI): m/z 478 (M^+ + 1). HRMS (ESI): calcd for $C_{23}H_{28}BrNNaO_3S$ 500.086 55, found 500.086 89.

*6-Cyclohexylidene-2-(4-nitrophenylsulfonyl)-7-(propan-2-ylidene)hexahydro-1H-isoindol-5(6H)-one (**2i**).* Yield: 43 mg, 48% of a yellow solid. Mp: 138−140 °C. (*cis*-**2i**) ^{1}H NMR ($CDCl_3$, 300 MHz, TMS): δ 0.83−0.96 (m, 1H, CH), 1.00−1.10 (m, 1H, CH), 1.35−1.45 (m, 1H, CH), 1.47 (s, 3H, CH_3), 1.53−1.65 (m, 3H, 3CH), 1.74 (s, 3H, CH_3), 1.82−1.87 (m, 2H, 2CH), 2.23−2.32 (m, 2H, 2CH), 2.43−2.51 (m, 1H, CH), 2.56−2.65 (m, 2H, 2CH), 2.73−2.85 (m, 2H, 2CH), 3.60 (t, J = 9.0 Hz, 1H, CH), 3.68−3.77 (m, 2H, 2CH), 7.98 (d, J = 8.7 Hz, 2H, Ar) (8.05 (d, J = 8.7 Hz, 2H, Ar, *trans*-**2i**)), 8.38 (d, J = 8.7 Hz, 2H, Ar). (*cis*-**2i**) ^{13}C NMR ($CDCl_3$, 100 MHz, TMS): δ 19.8, 21.9, 26.0, 27.3, 27.7, 30.1, 32.0, 34.8, 39.9, 40.5, 52.2, 53.2, 124.3, 127.0, 128.9, 129.9, 132.8, 141.4, 150.1, 154.3, 201.5. IR (CH_2Cl_2): ν 2927, 2855, 1681, 1601, 1530, 1474, 1447, 1401, 1350, 1312, 1265, 1168, 1095, 1043, 1012, 982, 857, 819, 735, 688, 614 cm^{-1}. MS (ESI): m/z 445 (M^+ + 1). HRMS (ESI): calcd for $C_{23}H_{28}N_2NaO_5S$ 467.161 11, found 467.162 07.

*3a-Methyl-6,7-bis(propan-2-ylidene)-2-tosylhexahydro-1H-isoindol-5(6H)-one (**2j**).* Yield: 49 mg, 63% of a white solid. Mp: 138−139 °C. (*cis*-**2j**) ^{1}H NMR ($CDCl_3$, 400 MHz, TMS): δ 1.18 (s, 3H, CH_3), 1.42 (s, 3H, CH_3), 1.45 (s, 3H, CH_3), 1.72 (s, 3H, CH_3), 1.77 (s, 3H, CH_3), 2.17 (d, J = 16.0 Hz, 1H, CH), 2.25 (d, J = 16.0 Hz, 1H, CH), 2.44 (s, 3H, CH_3), 2.46−2.50 (m, 2H, CH_2), 3.08 (d, J = 9.2 Hz, 1H, CH), 3.21 (t, J = 8.4 Hz, 1H, CH), 3.67 (t, J = 9.2 Hz, 1H, CH), 7.32 (d, J = 8.0 Hz, 2H, Ar), 7.62 (d, J = 8.0 Hz, 2H, Ar). (*cis*-**2j**) ^{13}C NMR ($CDCl_3$, 100 MHz, TMS): δ 19.8, 21.2, 21.4, 21.9, 23.6, 28.0, 41.7, 47.6, 49.0, 51.6, 59.1, 127.8, 127.9, 129.4, 131.3, 131.4, 132.0, 143.6, 147.6, 201.1. IR (CH_2Cl_2): ν 2956, 2926, 2855, 1686, 1599, 1454, 1349, 1166, 1093, 1032, 845, 817, 738, 664 cm^{-1}. MS (ESI): m/z 388 (M^+ + 1). HRMS (MALDI): calcd for $C_{22}H_{30}NO_3S$ 388.1938, found 388.1941.

*2-(4-Bromophenylsulfonyl)-6-cyclohexylidene-3a-methyl-7-(propan-2-ylidene)hexahydro-1H-isoindol-5(6H)-one (**2k**).* Yield: 56 mg, 57% of a white solid. Mp: 150−151 °C. (*cis*-**2k**) ^{1}H NMR ($CDCl_3$, 300 MHz, TMS): δ 0.96−1.13 (m, 2H, 2CH), 1.17 (s, 3H, CH_3), 1.48 (s, 3H, CH_3), 1.54−1.66 (m, 4H, 4CH), 1.73 (s, 3H, CH_3), 1.80−1.84 (m, 2H, 2CH), 2.24 (d, 2H, J = 4.2 Hz, 2CH), 2.27−2.33 (m, 1H, CH), 2.59 (t, J = 8.1 Hz, 1H, CH), 2.66−2.75 (m, 2H, 2CH), 3.14 (d, J = 9.6 Hz, 1H, CH), 3.23 (t, J = 8.1 Hz, 1H, CH), 3.69 (t, J = 9.6 Hz, 1H, CH), 7.64 (d, J = 8.4 Hz, 2H, Ar), 7.68 (d, J = 8.4 Hz, 2H, Ar). (*cis*-**2k**) ^{13}C NMR ($CDCl_3$, 100 MHz, TMS): δ 19.8, 21.9, 26.0, 27.2, 27.8, 30.0, 32.0, 34.6, 39.6, 40.4, 52.0, 53.3, 127.1, 128.0, 129.4, 129.7, 132.3, 132.4, 133.9, 154.7, 201.8. IR (CH_2Cl_2): ν 2955, 2924, 2853, 1683, 1595, 1574, 1471, 1449, 1388, 1351, 1260, 1168, 1090, 1067, 1036, 1009, 823, 805, 738 cm^{-1}. MS (ESI): m/z 493 (M^+ + 1). HRMS (ESI): calcd for $C_{24}H_{30}BrNO_3S$ 491.1130, found 491.1147.

*6,7-Bis(propan-2-ylidene)hexahydroisobenzofuran-5(1H)-one (**2l**).* Yield: 20 mg, 45% of a yellow oil. (*cis*-**2l**) ^{1}H NMR ($CDCl_3$, 400 MHz, TMS): δ 1.53 (s, 3H, CH_3), 1.72 (s, 3H, CH_3), 1.80 (s, 3H, CH_3), 2.19 (s, 3H, CH_3), 2.29 (dd, J_1 = 2.0 Hz, J_2 = 16.4 Hz, 1H, CH), 2.55 (dd, J_1 = 6.0 Hz, J_2 = 16.4 Hz, 1H, CH), 2.64−2.73 (m, 1H, CH), 3.16 (t, J = 9.2 Hz, 1H, CH), 3.29 (dd, J_1 = 6.8 Hz, J_2 = 9.2 Hz, 1H, CH), 3.65−3.72 (m, 1H, CH), 3.96 (t, J = 8.0 Hz, 1H, CH), 4.08 (t, J = 8.0 Hz, 1H, CH). (*cis*-**2l**) ^{13}C NMR ($CDCl_3$, 100 MHz, TMS): δ 19.8, 21.99, 22.02, 24.3, 35.8, 40.3, 41.2, 72.2, 73.2, 128.6, 131.1, 132.3, 148.9, 202.0. IR (CH_2Cl_2): ν 2963, 2924, 2855, 1683, 1599, 1437, 1415, 1369, 1327, 1252, 1198, 1190, 1162, 1096, 1062, 1048, 1019, 981, 932, 830, 745, 693, 672 cm^{-1}. MS (%) (EI): m/z 220 (M^+, 21), 175 (100), 133 (50), 91 (47), 105 (37), 147 (36), 77 (36), 134 (30), 119 (30); HRMS (EI): calcd for $C_{14}H_{20}O_2$ 220.1463, found 220.1466.

*4-Methyl-6,7-bis(propan-2-ylidene)-2-tosylhexahydro-1H-isoindol-5(6H)-one (**2o**).* Yield: 40 mg, 52% of a white solid. Mp: 135−137 °C. (major diastereomer **2o**) ^{1}H NMR ($CDCl_3$, 300 MHz, TMS): δ 1.05 (d, J = 7.2 Hz, 3H, CH_3), 1.42 (s, 3H, CH_3), 1.46 (s, 3H, CH_3), 1.71 (s, 3H, CH_3), 1.75 (s, 3H, CH_3), 2.09−2.18 (m, 1H, CH), 2.33−2.41 (m, 1H, CH), 2.44 (s, 3H, CH_3), 2.62−2.72 (m, 2H, 2CH), 3.45 (dd, J_1 = 7.2 Hz, J_2 = 9.6 Hz, 1H, CH), 3.50−3.64 (m, 2H, 2CH), 7.32 (d, J = 8.1 Hz, 2H, Ar), 7.66 (d, J = 8.1 Hz, 2H, Ar). (major diastereomer **2o**) ^{13}C NMR ($CDCl_3$, 100 MHz, TMS): δ 16.9, 19.7, 21.0, 21.4, 21.7, 22.7, 39.2, 43.1, 45.3, 51.4, 53.3, 127.1, 127.8, 129.5, 131.7, 132.1, 132.6, 143.6, 144.3, 204.8. IR (CH_2Cl_2): ν 2975, 2926, 2872, 2855, 1682, 1599, 1473, 1448, 1371, 1344, 1163, 1093, 1030, 982, 966, 836, 816, 735, 708, 662, 609 cm^{-1}. MS (ESI): m/z 388 (M^+ + 1). HRMS (MALDI): calcd for $C_{22}H_{30}NO_3S$ 388.1948, found 388.1941.

*7-Cyclohexylidene-8-(propan-2-ylidene)-2-tosyloctahydroisoquinolin-6(7H)-one (**2p**).* Yield: 39 mg, 46% of a white solid. Mp: 176−177 °C. (*trans*-**2p**) ^{1}H NMR ($CDCl_3$, 300 MHz, TMS): δ 1.15−1.39 (m, 3H, 3CH), 1.42−1.59 (m, 6H, 3CH + CH_3), 1.64−1.75 (m, 3H, 3CH), 1.82 (s, 3H, CH_3), 1.88−1.92 (m, 1H, CH), 2.00−2.10 (m, 3H, 3CH), 2.18−2.36 (m, 2H, 2CH), 2.39−2.49 (m, 5H, CH_3 + 2CH), 2.70−2.77 (m, 1H, CH), 3.91−4.02 (m, 2H, 2CH), 7.31 (d, J = 7.8 Hz, 2H, Ar), 7.66 (d, J = 7.8 Hz, 2H, Ar) (7.74 (d, J = 8.4 Hz, 2H, Ar, *cis*-**2p**)). (*trans*-**2p**) ^{13}C NMR ($CDCl_3$, 100 MHz, TMS): δ 20.2, 21.5, 22.2, 26.2, 27.6, 28.3, 29.9, 30.0, 31.8, 36.8, 44.6, 44.9, 46.2, 49.8, 124.9, 127.4, 129.6, 131.8, 134.0, 135.3, 143.4, 148.8, 203.8. IR (CH_2Cl_2): ν 2922, 2851, 1689, 1611, 1448, 1344, 1307, 1186, 1162, 1104, 1091, 1025, 990, 950, 841, 729 cm^{-1}. MS (ESI): m/z 428 (M^+ + 1). HRMS (ESI): calcd for $C_{25}H_{33}NNaO_3S$ 450.207 34, found 450.207 46.

Typical Procedure for the Synthesis of 3,3-Dimethyl-5-(propan-2-ylidene)-2-tosylhexahydrospiro[isoindole-4,2-oxiran]-6(5*H*)-one (3a). The compound **2a** (0.1 mmol, 37 mg, 1.0 equiv) was dissolved in dichloromethane and methanol (v/v, 5.0 mL/1.0 mL). The solution was cooled to −78 °C, and O_3 was directed into the solution until it turned deep blue. The resulting solution was then bubbled with argon to remove the excess O_3. Dimethyl sulfide (0.5 mmol, 5.0 equiv) was added, and the solution was warmed to room temperature and stirred for 3 h. The residue was washed successively with water and brine. The combined organic layers were dried over anhydrous Na_2SO_4 and filtered. Then, the solvent was removed under reduced pressure and the residue was purified by flash column chromatography. Yield: 28 mg, 72% of a white solid. Mp: 159−161 °C. (major diastereomer **3a**) ^{1}H NMR ($CDCl_3$, 400 MHz, TMS): δ 1.21 (s, 3H, CH_3), 1.41 (s, 3H, CH_3), 1.54 (s, 3H, CH_3), 1.69 (s, 3H, CH_3), 2.23 (t, J = 9.6 Hz, 1H, CH), 2.33 (d, J = 15.6 Hz, 1H, CH), 2.46 (s, 3H, CH_3), 2.67−2.70 (m, 2H, 2CH), 2.83−2.90 (m, 2H, 2CH), 3.50 (t, J = 9.6 Hz, 1H, CH), 3.62 (t, J = 11.6 Hz, 1H, CH), 7.36 (d, J = 8.4 Hz, 2H, Ar), 7.65 (d, J = 8.4 Hz, 2H, Ar). (major diastereomer **3a**) ^{13}C NMR ($CDCl_3$, 100 MHz, TMS): δ 20.1, 20.8, 21.5, 22.9, 24.6, 34.8, 40.4, 43.8, 49.2, 53.0, 64.3, 67.6, 128.1, 129.2, 129.6, 131.1, 144.0, 147.2, 201.1. IR (CH_2Cl_2): ν 3001, 2964, 2927, 2877, 2851, 1693, 1626, 1598, 1444, 1377, 1345, 1165, 1093, 1039,

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983, 832, 818, 736, 711, 665, 611 cm^{-1}. MS (ESI): m/z 390 (M^+ + 1). HRMS (ESI): calcd for $C_{21}H_{27}NNaO_4S$ 412.155 30, found 412.156 50.

Typical Procedure for the Synthesis of 6,7-Bis(propan-2-ylidene)-2-tosyloctahydro-1*H*-isoindol-5-ol (4a). Under an argon atmosphere, a solution of compound **2a** (0.1 mmol, 37 mg, 1.0 equiv) in toluene (2.0 mL) was added into the Schlenk tube. Then Red-Al (39 μL, 0.2 mmol, 2.0 equiv) was added into the above Schlenk tube and the reaction mixture was stirred for 2 h at room temperature. On reaction completion the reaction was quenched by addition of water. The reaction solution was diluted with ether (10.0 mL × 3), and the organic layers were dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure, and the residue was purified by flash column chromatography. Yield: 34 mg, 91% of a white solid. Mp: 167−169 °C. (major diastereomer **4a**) ^{1}H NMR ($CDCl_3$, 300 MHz, TMS): δ 1.41−1.47 (m, 4H, CH + CH_3), 1.50 (s, 3H, CH_3), 1.61−1.69 (m, 4H, CH + CH_3), 1.86 (s, 3H, CH_3), 2.09 (d, J = 6.9 Hz, 1H, OH), 2.41−2.53 (m, 4H, CH_3 + CH), 2.90 (t, J = 8.4 Hz, 1H, CH), 3.15 (t, J = 8.4 Hz, 2H, 2CH), 3.35−3.45 (m, 2H, 2CH), 4.37−4.41 (m, 1H, CH), 7.33 (d, J = 8.1 Hz, 2H, Ar), 7.69 (d, J = 8.1 Hz, 2H, Ar). (major diastereomer **4a**) ^{13}C NMR ($CDCl_3$, 100 MHz, TMS): δ 19.6, 20.0, 21.5, 22.1, 23.1, 35.9, 37.4, 40.2, 50.8, 54.1, 70.7, 128.0, 128.5, 129.4, 130.3, 132.1, 132.30, 132.32, 143.6. IR (CH_2Cl_2): ν 3521, 2955, 2922, 2854, 1598, 1448, 1369, 1341, 1305, 1261, 1159, 1089, 1042, 1007, 949, 804, 734, 708 cm^{-1}. MS (ESI): m/z 398 (M^+ + Na). HRMS (ESI): calcd for $C_{21}H_{29}NO_3S$ 375.1868, found 375.1871.

*6-Cyclohexylidene-2-(phenylsulfonyl)-7-(propan-2-ylidene)-octahydro-1H-isoindol-5-ol (**4h**).* Yield: 36 mg, 89% of a white solid. Mp: 129−131 °C. (major diastereomer **4h**) ^{1}H NMR ($CDCl_3$, 400 MHz, TMS): δ 1.17−1.34 (m, 2H, 2CH), 1.40−1.52 (m, 5H, CH_3 + 2CH), 1.58−1.60 (m, 1H, CH), 1.62−1.75 (m, 7H, CH_3 + 4CH), 1.92−2.04 (m, 2H, 2CH), 2.18 (d, J = 6.8 Hz, 1H, OH), 2.53−2.60 (m, 1H, CH), 2.78−2.82 (m, 1H, CH), 2.89 (dd, J_1 = 6.8 Hz, J_2 = 9.2 Hz, 1H, CH), 3.15−3.24 (m, 2H, 2CH), 3.43 (dd, J_1 = 2.8 Hz, J_2 = 9.6 Hz, 1H, CH), 3.51 (dd, J_1 = 9.2 Hz, J_2 = 16.4 Hz, 1H, CH), 4.45−4.49 (m, 1H, CH), 7.52−7.56 (m, 2H, Ar), 7.60−7.64 (m, 1H, Ar), 7.82 (d, J = 8.0 Hz, 2H, Ar). (major diastereomer **4h**) ^{13}C NMR ($CDCl_3$, 100 MHz, TMS): δ 19.6, 22.1, 26.7, 27.9, 28.5, 30.4, 32.7, 35.0, 36.9, 39.7, 51.8, 54.2, 69.6, 128.0, 128.4, 128.7, 129.8, 132.7, 134.7, 141.2. IR (CH_2Cl_2): ν 3518, 2955, 2924, 2853, 1998, 1602, 1507, 1459, 1260, 1223, 1157, 1093, 1013, 911, 836, 800, 750, 721 cm^{-1}. MS (ESI): m/z 424 (M^+ + Na). HRMS (ESI): calcd for $C_{23}H_{31}NO_3S$ 401.2025, found 401.2021.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Figures giving compound characterization data and figures giving ORTEP drawings and CIF files giving X-ray crystal data of *cis*-**2a** (CCDC 865612), *cis*-**2k** (CCDC 868900), major diastereomer **2o** (CCDC 826605), *trans*-**2p** (CCDC 867084), major diastereomer **3a** (CCDC 858045), and major diastereomer **4h** (CCDC 874178). This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: Mshi@mail.sioc.ac.cn. Fax: 86-21-64166128.

Notes

The authors declare no competing financial interest.

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(14) The crystal data of major diastereomer **2o** have been deposited with the CCDC as file 826605: empirical formula $C_{22}H_{29}NO_3S$, formula weight 387.52, crystal color colorless, crystal dimensions 0.353 × 0.268 × 0.043 mm, crystal system orthorhombic, lattice type primitive, lattice parameters a = 9.1187(7) Å, b = 20.3918(15) Å, c = 23.2981(18) Å, α = 90°, β = 90°, and γ = 90°, V = 4330.5(6) Å^3, space group *Pbca*; Z = 8, D_{calcd} = 1.189 g/cm, F_{000} = 1664, final R indices ($I > 2\sigma(I)$) R1 = 0.0567 and wR2 = 0.1290.

(15) The crystal data of *trans*-**2p** have been deposited with the CCDC as file 867084: empirical formula $C_{25}H_{33}NO_3S$, formula seight 427.58, crystal color colorless, crystal dimensions 0.321 × 0.165 × 0.112 mm, crystal system orthorhombic, lattice parameters a = 8.1706(5) Å, b = 12.2862(7) Å, c = 23.6896(12) Å, α = 90°, β = 90°, and γ = 90°, V = 2378.1(2) Å^3, space group $P2_12_12_1$, Z = 4; D_{calcd} = 1.194 g/cm^3, F_{000} = 920, final R indices ($I > 2\sigma(I)$) R1 = 0.0489 and wR2 = 0.1220.

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(18) The crystal data of major diastereomer **3a** have been deposited with the CCDC as file 858045: empirical formula $C_{21}H_{27}NO_4S$, formula weight 389.50, crystal color colorless, crystal dimensions 0.258 × 0.137 × 0.069 mm, crystal system monoclinic, lattice parameters a = 19.2333(13) Å, b = 8.4368(6) Å, c = 12.4042(8) Å, α = 90°, β = 96.411(2)°, and γ = 90°, V = 2000.2(2) Å^3, space group $P2_1/c$, Z = 4, D_{calcd} = 1.293 g/cm^3, F_{000} = 832, final R indices ($I > 2\sigma(I)$) R1 = 0.0541 and wR2 = 0.1354.

(19) The crystal data of major diastereomer **4h** have been deposited with the CCDC as file 874178: empirical formula $C_{23}H_{31}NO_3S$, formula weight 401.55, crystal color colorless, crystal dimensions 0.231 × 0.207 × 0.115 mm, crystal system orthorhombic, lattice parameters a = 14.689(3) Å, b = 9.005(2) Å, c = 32.942(8) Å, α = 90°, β = 90°, and γ = 90°, V = 4357.3(17) Å^3, space group *Pbca*; Z = 8, D_{calcd} = 1.224 g/cm^3, F_{000} = 1728, final R indices ($I > 2\sigma(I)$) R1 = 0.0493 and wR2 = 0.1180.

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