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Studies on the structure–enantioselectivity relationships in the catalytic asymmetric intramolecular cyclopropanation reaction of α-diazo-β-keto sulfones possessing a methyl-substituted phenyl group

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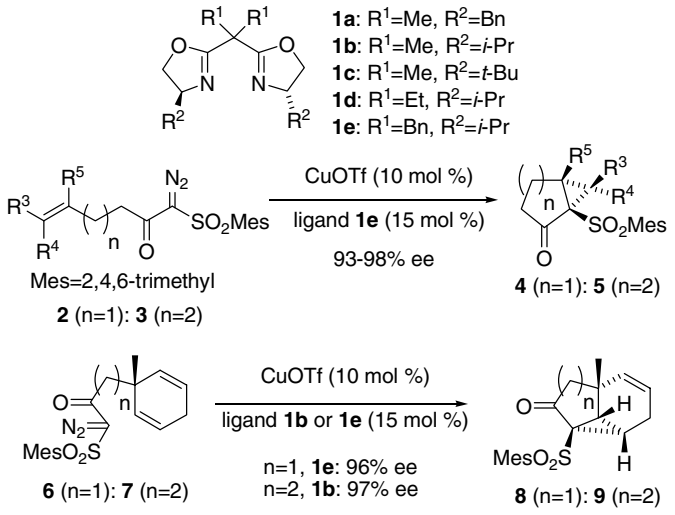
Abstract—This manuscript describes studies on structure–enantioselectivity relationships in the catalytic asymmetric intramolecular cyclopropanation (IMCP) reaction of α-diazo-β-keto sulfones possessing a methyl-substituted phenyl group. Enantioselectivity of the IMCP reaction of the α-diazo-β-keto sulfones was varied by the position of a methyl group on the phenyl group in the substrate, and the 2,3-dimethylphenyl sulfone **11h** provided the product **12h** in 95% yield with 93% ee. This yield is superior to that of the substrate with a mesityl sulfone **11b**, and the product **12h** is useful because alkylation of its cyclopropane-opened β-keto sulfone derivative **15h** provides the C-alkylated product as a major product.

1. Introduction

We have reported asymmetric catalysis of the intramolecular cyclopropanation (IMCP) reaction of various α-diazo-β-keto sulfones **2**, **3**, **6**, **7**, and have succeeded in preparing 2-oxobicyclo[3.1.0]hexanes **4**,[1] 2-oxobicyclo[4.1.0]heptanes **5**,[3] tricyclo[4.3.0.0]nonenes **8**,[1] and tricyclo[4.4.0.0]decenes **9**[1,3] in high yield with excellent enantioselectivity (Scheme 1). This asymmetric reaction possesses wide applicability[4–7] and generates a highly crystalline product, providing enantiopure chiral building blocks for the asymmetric total synthesis of natural products. The asymmetric total syntheses of (−)-malyngolide,[5] (+)-allocyathin B_2,[6] and (−)-methyl jasmonate[7] in an enantiomerically pure form have been reported utilizing this catalytic asymmetric IMCP reaction from our laboratory; however, during our studies on the asymmetric total synthesis of enantiopure (−)-methyl jasmonate,[7] we encountered a problem in that the attempted C-alkylation of β-keto sulfone **10**, which was derived from the corresponding cyclopropane **4** (R^3=R^4=R^5=H), afforded an O-alkylated product as a major product (Scheme 2).

To overcome this problem, we devised the new substrate **11c** possessing a less bulky 1-naphthyl group to attain good selectivity both in the IMCP reaction (83% ee, Table 1, entry 3) and in the C-alkylation of the corresponding β-keto sulfone derivative **13** (Scheme 3), and succeeded in utilizing it for the asymmetric total synthesis of enantiopure (−)-methyl jasmonate.[7]



Scheme 1. Asymmetric catalysis of α-diazo-β-keto sulfones **2**, **3**, **6**, and **7**.

The substrates **11a–d** that have been prepared to date and the results of their IMCP reactions are summarized in

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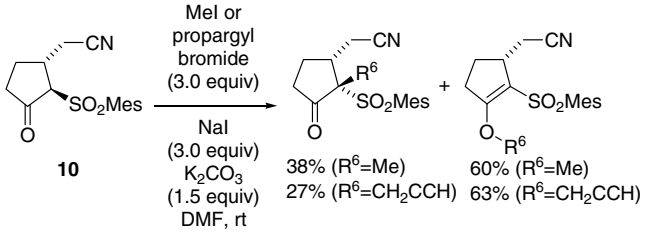
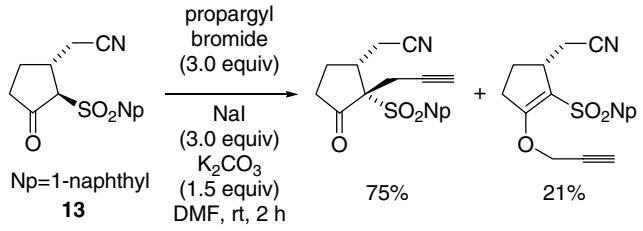


Scheme 2. Alkylation of **10**.



Scheme 3. Alkylation of **13**.

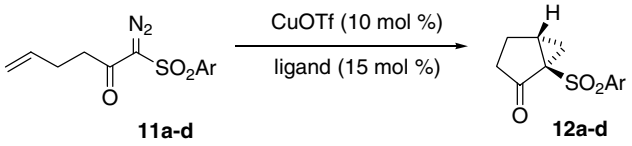
Table 1. Results of the substrates with a 1-naphthyl group **11c** or a 2,4-dimethylphenyl group **11d** are rather unsatisfactory because the enantioselectivity situates between those of the phenyl sulfone **11a** (73% ee, entry 1) and the mesityl sulfone **11b** (93% ee, entry 2). In addition, although many successful examples for the catalytic asymmetric IMCP of α-diazo ketones,[2,8] α-diazo acetates,[2] and α-diazo acetamidates[2,8] have been reported, the catalytic asymmetric IMCP reaction of the α-diazo-β-keto compound providing a bicyclo[3.1.0]hexane system with high enantioselectivity is limited,[1,4,6,7,9] thereby drawing our attention to further studies.

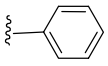
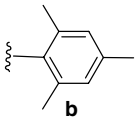
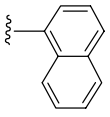
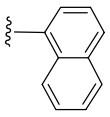
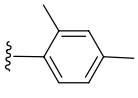
We report herein studies on structure–enantioselectivity relationships in the catalytic asymmetric IMCP reaction of the α-diazo-β-keto sulfones possessing a methyl-substituted phenyl group and disclose the new substrate which afforded a result superior to those previously reported.

2. Results and discussion

We prepared all the new α-diazo-β-keto sulfones **11e–l** (Table 2) possessing a methyl-substituted phenyl group according to our reported method[1,7] as shown in Scheme 4. Thus, the dianion of aryl methyl sulfone **14e–l**[10] was reacted with ethyl 4-pentenoate to produce the corresponding β-keto sulfone,[11] which was converted to the α-diazo-β-keto sulfone **11e–l** in 72–88% yield. Use of the mono-anion

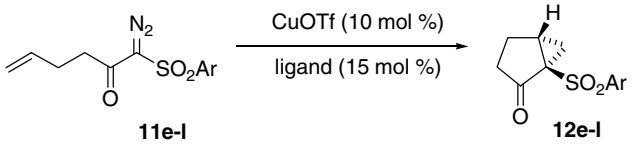
Table 1. Asymmetric catalysis of α-diazo-β-keto sulfones **11a–d**



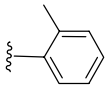
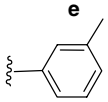
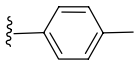
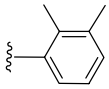
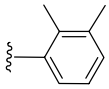
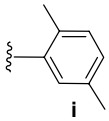
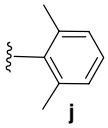
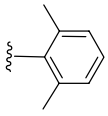
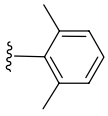
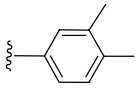
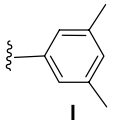
Entry	Ar	Ligand	Yield (%)	ee[a] (%)	Temperature (°C)	Time (h)
1[b]	 **a**	**1e**	61	73	rt	2
2[b]	 **b**	**1e**	87	93	rt, 50	2, 2.5[c]
3[d]	 **c**	**1d**	93	83	50	5
4[d]		**1e**	82	79	50	2
5[d]	 **d**	**1e**	97	81	50	5

[a] All the products have (1*R*)-configuration. ee was determined by HPLC analysis. See Experimental for the conditions.
[b] Ref. 1.
[c] Reaction was carried out at the indicated temperatures for the indicated times, respectively.
[d] Ref. 7.

Table 2. Asymmetric catalysis of α-diazo-β-keto sulfones **11e–l**



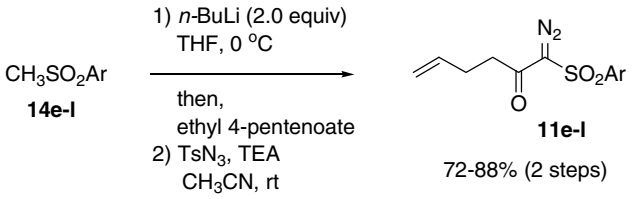
11e-l **12e-l**

Entry	Ar	Ligand	Yield (%)	ee[a] (%)	Temperature (°C)	Time (h)
1	 **e**	**1e**	98	86	50	3
2	 **f**	**1e**	97	77	50	3
3	 **g**	**1e**	95	69	50	3
4	 **h**	**1d**	***95***	***93***	50	2
5		**1e**	82	91	50	3
6	 **i**	**1e**	90	82	50	5
7	 **j**	**1d**	83	90	50	3
8		**1e**	82	91	50	96
9		**1e**	72	83	70	48
10	 **k**	**1e**	94	72	50	5
11	 **l**	**1e**	91	62	50	5

[a] All the products have (1*R*)-configuration. ee was determined by HPLC analysis. See Experimental for the conditions.

of **14e–l** resulted in low yield, probably because deprotonation of the rather acidic methylene proton in the product by the mono-anion occurred.[11]

As all the IMCP reactions of various α-diazo-β-keto sulfones **11e–l** were sluggish, the reactions were carried out at 50 °C or 70 °C (Table 2, entry 9); thus, the conditions were the same as those used for the IMCP reaction of **2** (Scheme 1). Since ligand **1e** provided the best ee in the IMCP reactions of **11a**, **11b**, and **11d**, ligand **1e** was used for all the reactions in Table 2. Nevertheless, the IMCP reaction with ligand **1d** sometimes gives a better result than



Scheme 4. Preparation of **11e–l**.

that with ligand **1e**, as shown in entry 3 of Table 1; hence, the IMCP reaction with ligand **1d** was further carried out for the substrate which afforded the product with over 90% ee (Table 2, entries 4 and 7).

First, we carried out the IMCP reactions of **11e–g** possessing a methylphenyl sulfone (entries 1–3). The reactions of **11e–g** smoothly produced the corresponding **12e–g** in excellent yield with the ee ranging from 69% ee to 86% ee.

The IMCP reaction of the 2-methylphenyl sulfone **11e** (entry 1) was the most enantioselective among the monosubstituted phenyl sulfones **11e–g** (entries 1–3), affording the product **12e** with 86% ee. This ee was higher than that of the phenyl sulfone **11a** (73% ee, Table 1, entry 1) and the 2,4-dimethylphenyl sulfone **11d** (81% ee, Table 1, entry 5), but lower than that of the mesityl sulfone **11b** (93% ee, Table 1, entry 2).

Enantioselectivity of the IMCP reaction of the 3-methylphenyl sulfone **11f** (entry 2) was slightly higher than that of the phenyl sulfone **11a**, but lower than the 2-methylphenyl sulfone **11e** (entry 1).

In the case of the 4-methylphenyl sulfone **11g** (entry 3), the enantioselectivity was lowest among the entries 1–3 and lower than that of the phenyl sulfone **11a**. The ee of the products in entries 1–3 was in the order: 2-methylphenyl sulfone **12e** > 3-methylphenyl sulfone **12f** > 4-methylphenyl sulfone **12g**.

Next, we carried out the IMCP reaction of dimethylphenyl sulfones **11h–l** (entries 4–11). The IMCP reaction of the 2,3-dimethylphenyl sulfone **11h** (entry 5) afforded the product **12h** with 91% ee, and the reaction of **11h** with ligand **1d** (entry 4) gave the product **12h** with the highest ee (93% ee), and this ee was the same as that of the mesityl sulfone **11b** (Table 1, entry 2); furthermore, the yield in entry 4 was better than that in entry 2 of Table 1. That is, the 2,3-dimethylphenyl sulfone **11h** was the best substrate which gave the 2-oxobicyclo[3.1.0]hexane system.

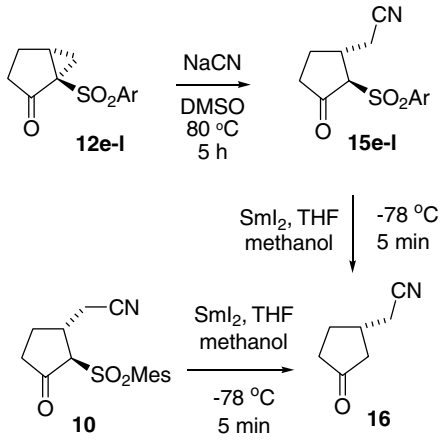
Enantioselectivity of the IMCP reaction of the 2,5-dimethylphenyl sulfone **11i** (82% ee, entry 6) was comparable with that of 2,4-dimethylphenyl sulfone **11d** (81% ee, Table 1, entry 5). The reaction of the 2,6-dimethylsulfone **11j** (entry 8) afforded a product with 91% ee; hence, the reaction with ligand **1d** was also carried out, but the enantioselectivity was not increased (90% ee, entry 7). Interestingly, compared with entry 7, the reaction of **11j** (entry 8) was very slow and required 96 h to be completed. This was reduced to 48 h by the elevated temperature (entry 9). Nonetheless, these results were unusual because the reaction of **11b** possessing a more bulky mesityl sulfone with ligand **1e** was completed in 2.5 h at 50 °C (Table 1, entry 2). Consequently, now we are investigating this long-reaction time induced by the 2,6-dimethylsulfonyl group in **11j** and ligand **1e**.

The IMCP reaction of other substrates, the 3,4-dimethylsulfone **11k** (entry 10) and the 3,5-dimethylsulfone **11l** (entry 11) gave less productive results, affording products with 72% ee and 62% ee, respectively.

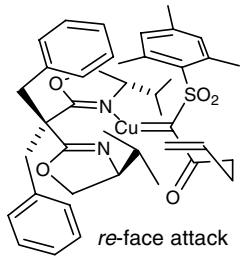
In summary of the results in Table 2, all the substrates with the 2-methyl substituted phenyl sulfone **11e**, **11h–j** (entries 1, 4–9) afforded products with over 82% ee, and other substrates lacking a methyl substituent at their 2-position. **11f**, **11g**, **11k**, **11l** (entries 2, 3, 10, 11, respectively) gave products with less than 77% ee. This trend of the structure–enantioselectivity relationship is consistent with that in Table 1, indicating that the 2-methyl group of the phenyl sulfonyl group is important to attain the high enantioselectivity in the IMCP reaction of **11**.

All the products **12e–l** in Table 2 were converted to **16** (Scheme 5) to determine their absolute configuration by comparing their sign of the specific rotations with that of the known compound **16**.[7] Thus, reactions of **12e–l** with sodium cyanide in DMSO at 80 °C smoothly produced the β-keto sulfones **15e–l**, respectively, and their subsequent desulfonylations with SmI_2 successfully afforded **16**. The specific rotations of all the products **16** had a minus sign, indicating that all the products **12e–l** in Table 2 possess (1*R*) configuration. This sense of enantioselectivity is well explained by the previously proposed model A (Fig. 1).[1]

From this model, the 2-methyl group of the phenyl sulfonyl group is surmised to be important for the high enantioselectivity because the increased steric hindrance around the carbene center would prevent its reaction from the *si*-face. Nevertheless, a careful analysis and discussion is required to account for the observed structure–enantioselectivity relationship because various factors could influence the enantioselectivity, and the rationale as well as the quan-



Scheme 5. Conversion of **12e–l** to **16**.



model A (for entry 2, Table 1)

Figure 1. Proposed model A.[1]

titative analysis await further studies on this IMCP reaction and theoretical calculations.

To explore the utility of **11h** as a chiral building block, alkylation of **15h** was examined (Scheme 6). β-Keto sulfone **15h**, obtained by the reaction of **11h** with sodium cyanide in DMSO at 80 °C (Scheme 5), was subjected to the alkylation reaction (Scheme 6). The reaction of **15h** with methyl iodide provided C-methylated product **17C** (66%) and O-methylated product **17O** (27%), and the reaction with propargyl bromide afforded C-propargylated product **18C** (58%) and O-propargylated product **18O** (33%), indicating that **11h** is superior to the corresponding mesityl sulfone **10** (Scheme 2) in the C-alkylation selectivity.

3. Conclusion

In summary, structure–enantioselectivity relationships in the catalytic asymmetric IMCP reaction of the α-diazo-β-keto sulfones possessing a methyl-substituted phenyl group have been studied. The enantioselectivity was varied by the position of the methyl group on the phenyl sulfone, and the 2-methyl group of the phenyl sulfonyl group was important to attain the high enantioselectivity in the IMCP reactions of new substrates**11a**–**l**. The sense of enantioselectivity in all the IMCP reactions of **11e**–**l** was well explained by the previously proposed model A. The new chiral building block **12h** was produced in 95% yield with 93% ee, and the alkylation reaction of its cyclopropane-opened derivative **15h** showed a good C-alkylation selectivity. These results are superior to those obtained to date, thereby making the new chiral building block **12h** useful for the asymmetric total synthesis of natural products. Studies on the use of **12h** are now ongoing in our laboratory and will be reported in due course.

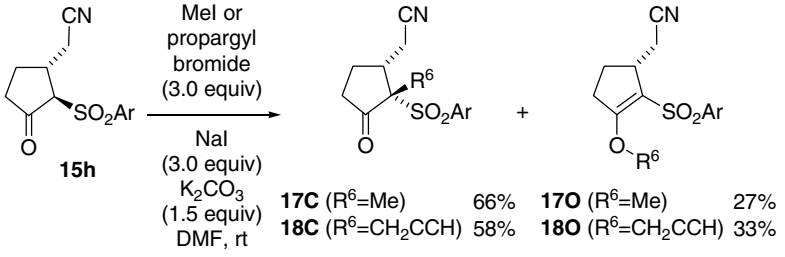
4. Experimental

4.1. General procedures

^{1}H and ^{13}C NMR spectra were recorded on a JEOL AL-400 spectrometer. ^{1}H and ^{13}C chemical shifts are reported in ppm downfield from tetramethylsilane (TMS, δ scale) with the solvent resonances as internal standards. The following abbreviations were used to explain the multiplicities: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; band, several overlapping signals; b, broad. IR spectra were recorded on a JASCO FT/IR-8300. Melting points (mp) are uncorrected, recorded on a Yamato capillary melting point apparatus equipped with a digital thermometer. Optical rotations were measured using a 2 mL cell with a 1 dm path length on a JASCO DIP-1000. Chiral HPLC analysis was performed on a JASCO PU-980 and UV-970. Mass spectrometric analyses and elemental analyses were provided at the Materials Characterization Central Laboratory, Waseda University. All reactions were carried out under an argon atmosphere with dry, freshly distilled solvents under anhydrous conditions, unless otherwise noted. All reactions were monitored by thin-layer chromatography carried out on 0.25 mm E. Merck silica gel plates (60F-254) using UV light as visualizing agent and phosphomolybdic acid and heat as developing agents. E. Merck silica gel (60, particle size 0.040–0.063 mm) was used for flash column chromatography. Preparative thin-layer chromatography (PTLC) separations were carried out on self-made 0.3 mm E. Merck silica gel plates (60F-254). THF was distilled from sodium/benzophenone ketyl and methylene chloride (CH_2Cl_2), benzene was distilled from calcium hydride. Toluene was distilled from sodium. Acetonitrile was distilled from CaH_2 under reduced pressure. $(CuOTf)_2C_6H_6$ and all other reagents were purchased from Aldrich, TCI, or Kanto Chemical Co. Ltd.

4.2. 1-(2-Methylphenylsulfonyl)-5-hexen-2-one

Procedure A: To a solution of methyl 2-methylphenyl sulfone (300.0 mg, 1.76 mmol) in THF (8 mL) was added *n*-BuLi (2.21 mL, 3.52 mmol) at 0 °C, and the solution was stirred for 1.5 h at room temperature. To this stirred solution was added ethyl 4-pentenoate (237.0 mg, 1.85 mmol) in THF (1 mL × 2) via a cannula. The reaction mixture was stirred at 0 °C for 1 h and quenched with saturated aqueous NH_4Cl solution (5 mL), and extracted with Et_2O (3 mL × 2). The combined organic layer was washed with brine (5 mL), dried over Na_2SO_4, and evaporated. The



Scheme 6. Alkylation of **15h**.

residue was purified by flash chromatography (hexane/ethyl acetate = 4/1) to afford 1-(2-methylphenylsulfonyl)-5-hexen-2-one (408.0 mg, 92%) as a white solid: mp 30–32 °C (CH_2Cl_2/hexane); IR (KBr) ν_{max} 1684, 884, 734 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.93 (d, $J = 8.1$ Hz, 1H), 7.54 (dd, $J = 7.6$, 7.6 Hz, 1H), 7.37 (dd, $J = 7.6$, 8.1 Hz, 1H), 7.35 (d, $J = 7.6$ Hz, 1H), 5.74 (ddt, $J = 6.6$, 10.0, 17.0 Hz, 1H), 5.04 (dd, $J = 1.7$, 17.0 Hz, 1H), 4.98 (dd, $J = 1.7$, 10.0 Hz, 1H), 4.19 (s, 2H), 2.81 (t, $J = 7.1$ Hz, 2H), 2.69 (s, 3H), 2.30 (dt, $J = 6.6$, 7.1 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 197.1, 137.6, 136.6, 134.2, 134.1, 132.7, 130.1, 126.6, 115.6, 66.0, 43.4, 27.0, 20.2; HRMS(FAB): calcd for $C_{13}H_{16}O_3S$+H 253.0898, found 253.0904.

4.3. 1-Diazo-1-(2-methylphenylsulfonyl)-5-hexen-2-one 11e

Procedure B: To a solution of 1-(2-methylphenylsulfonyl)-5-hexen-2-one (300.0 mg, 1.19 mmol) in CH_3CN (5 mL) was added triethylamine (0.40 mL, 2.85 mmol) at 0 °C and then a solution of *p*-toluenesulfonyl azide (280.0 mg, 1.42 mmol) in CH_3CN (2.5 mL × 2) via a cannula. The reaction mixture was stirred at room temperature for 8 h. The solution was concentrated under vacuum and diluted with ether (20 mL). This solution was washed with 0.1 M KOH aqueous solution (5 mL), and the organic was separated, washed with brine (5 mL), dried over Na_2SO_4, and evaporated. The residue was purified by flash chromatography (hexane/EtOAc = 20/1) to afford 1-diazo-1-(2-methylphenylsulfonyl)-5-hexen-2-one **11e** (288.0 mg, 87%) as a greenish yellow solid: IR (KBr) ν_{max} 1676, 917, 806, 763 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.12 (d, $J = 7.8$ Hz, 1H), 7.55 (dd, $J = 7.6$, 7.6 Hz, 1H), 7.42 (dd, $J = 7.6$, 7.8 Hz, 1H), 7.37 (d, $J = 7.6$ Hz, 1H), 5.61 (ddt, $J = 6.6$, 10.0, 17.0 Hz, 1H), 4.92 (dd, $J = 1.5$, 17.0 Hz, 1H), 4.84 (dd, $J = 1.5$, 10.0 Hz, 1H), 2.61 (s, 3H), 2.54 (t, $J = 7.1$ Hz, 2H), 2.35 (dt, $J = 6.6$, 7.1 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 187.9, 137.1, 135.8, 134.1, 133.0, 130.2, 126.6, 115.6, 38.0, 27.4, 20.0, 19.9: HRMS(FAB): calcd for $C_{13}H_{14}N_2O_3S$+H 279.0803, found 279.0812.

4.4. (1*R*,5*R*)-1-(2-Methylphenylsulfonyl)bicyclo[3.1.0]hexan-2-one 12e

Procedure C: A toluene azeotroped $[CuOTf]_2{\cdot}C_6H_6$ (9.3 mg, 0.0179 mmol, 10 mol % as CuOTf) was placed in a dried flask (10 mL) under Ar atmosphere and to this flask was added toluene (3 mL) and then a solution of toluene azeotroped ligand **1e** (22.3 mg, 0.0537 mmol, 15 mol %) in toluene (0.5 mL × 2) via a cannula. The mixture was stirred at room temperature for 0.5 h and then to the light blue solution was added a solution of toluene azeotroped 1-diazo-1-(2-methylphenylsulfonyl)-5-hexen-2-one **11e** (100.0 mg, 0.359 mmol) in toluene (0.5 mL × 2) via a cannula. The reaction mixture was stirred at 50 °C for 3 h, quenched with a mixture of saturated aqueous NH_4Cl solution (1 mL) and NH_4OH aqueous solution (1.5 mL), and extracted with ether (1 mL × 2). The combined organic layer was washed with brine (1 mL), dried over Na_2SO_4, and evaporated. The residue was purified by flash chromatography (hexane/EtOAc = 3/1) to afford (1*R*,5*R*)-1-(2-methylphenylsulfonyl)bicyclo[3.1.0]hexan-2-one **12e** (88.0 mg, 98%, 86% ee) as a white solid. The absolute configuration was determined as described in the text. Ee was determined by HPLC (254 nm); Daicel CHIRALPAK AS-H 0.46 cm ∅ × 25 cm; hexane/2-propanol = 4/1; flow rate = 0.5 mL/min; retention time: 48.0 min for the minor enantiomer, 50.0 min for the major enantiomer: mp 90–92 °C (hexane/CH_2Cl_2); $[\alpha]_D^{25} = -35.4$ (*c* 1.00, $CHCl_3$, 86% ee); IR (KBr) ν_{max}: 1736, 968, 816 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.08 (d, $J = 7.8$ Hz, 1H), 7.50 (dd, $J = 7.3$, 7.3 Hz, 1H), 7.38 (dd, $J = 7.3$, 7.8 Hz, 1H), 7.30 (d, $J = 7.3$ Hz, 1H), 3.08–3.00 (m, 1H), 2.70 (s, 3H), 2.40–2.20 (m, 4H), 2.15–2.00 (m, 1H), 1.63 (dd, $J = 5.6$, 5.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 203.5, 138.3, 137.6, 133.6, 132.5, 131.4, 126.3, 53.4, 33.5, 30.7, 20.8, 20.3; HRMS(FAB): calcd for $C_{13}H_{14}O_3S$+H 251.0742, found 251.0752.

4.5. 1-(3-Methylphenylsulfonyl)-5-hexen-2-one

This compound was prepared and purified by the previously described *Procedure A*, and was obtained as a colorless oil (93%): IR (neat) ν_{max} 1684, 858, 732 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.78–7.64 (m, 2H), 7.63–7.35 (m, 2H), 5.70 (ddt, $J = 6.6$, 10.0, 17.0 Hz, 1H), 5.01–4.89 (m, 2H), 4.11 (s, 2H), 2.74 (t, $J = 6.8$ Hz, 2H), 2.38 (s, 3H), 2.24 (dt, $J = 6.6$, 6.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 197.3, 139.5, 138.3, 136.0, 135.0, 129.0, 128.3, 125.2, 115.6, 66.6, 43.2, 26.8, 21.2; HRMS(FAB): calcd for $C_{13}H_{16}O_3S$+H 253.0898, found 253.0901.

4.6. 1-Diazo-1-(3-methylphenylsulfonyl)-5-hexen-2-one 11f

This compound was prepared and purified by the previously described *Procedure B*, and was obtained as a greenish yellow oil (86%): IR (neat) ν_{max} 1658, 916, 846 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.83–7.70 (m, 2H), 7.55–7.43 (m, 2H), 5.72 (ddt, $J = 6.3$, 10.0, 16.0 Hz, 1H), 5.05–4.88 (m, 2H), 2.66 (t, $J = 7.0$ Hz, 2H), 2.46 (s, 3H), 2.31 (dt, $J = 6.3$, 7.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 187.7, 141.7, 139.8, 136.0, 134.9, 133.7, 129.2, 127.4, 115.7, 38.1, 27.4, 21.3: HRMS(FAB): calcd for $C_{13}H_{14}N_2O_3S$+H 279.0803, found 279.0812.

4.7. (1*R*,5*R*)-1-(3-Methylphenylsulfonyl)bicyclo[3.1.0]hexan-2-one 12f

This compound was prepared and purified by the previously described *Procedure A*, and was obtained as a white solid (97%, 77% ee). Ee was determined by HPLC (254 nm); Daicel CHIRALCEL OD-H 0.46 cm ∅ × 25 cm; hexane/2-propanol = 20/1; flow rate = 0.5 mL/min; retention time: 53.0 min for the major enantiomer, 56.0 min for the minor enantiomer; mp 90–92 °C (hexane/CH_2Cl_2); $[\alpha]_D^{26} = -35.8$ (*c* 1.50, $CHCl_3$, 77% ee) ; IR (KBr) ν_{max} 1718, 923, 826 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.91–7.77 (m, 2H), 7.60–7.32 (m, 2H), 3.07–3.00 (m, 1H), 2.34 (s, 3H), 2.40–2.20 (m, 4H), 2.15–1.98 (m, 1H), 1.54 (dd, $J = 5.6$, 5.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 203.4, 139.2, 139.1, 134.5, 129.0, 128.9, 125.9, 53.1, 33.6, 31.1, 20.4, 20.2; HRMS(FAB): calcd for $C_{13}H_{14}O_3S$+H 251.0742, found 251.0744.

4.8. 1-(4-Methylphenylsulfonyl)-5-hexen-2-one

This compound was prepared and purified by the previously described *Procedure A*, and was obtained as a white solid (90%): mp 31–33 °C (hexane/CH_2Cl_2); IR (KBr) ν_{max} 1644, 813, 735 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, $J = 8.0$ Hz, 2H), 7.36 (d, $J = 7.8$ Hz, 2H), 5.76 (ddt, $J = 6.8$, 10.0, 17.0 Hz, 1H), 5.08–4.95 (m, 2H), 4.15 (s, 2H), 2.80 (t, $J = 7.3$ Hz, 2H), 2.44 (s, 3H), 2.30 (dt, $J = 6.8$, 7.3 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.6, 145.3, 138.9, 135.9, 129.9, 127.2, 127.1, 115.7, 38.0, 27.4, 21.5; HRMS(FAB): calcd for $C_{13}H_{16}O_3S$+H 253.0898, found 253.0904.

4.9. 1-Diazo-1-(4-methylphenylsulfonyl)-5-hexen-2-one 11g

This compound was prepared and purified by the previously described *Procedure B*, and was obtained as a greenish-yellow oil (87%): IR (neat) ν_{max} 1654, 820, 740 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.85 (d, $J = 8.2$ Hz, 2H), 7.37 (d, $J = 8.2$ Hz, 2H), 5.72 (ddt, $J = 6.8$, 10.0, 17.0 Hz, 1H), 5.02–4.90 (m, 2H), 2.64 (t, $J = 7.5$ Hz, 2H), 2.45 (s, 3H), 2.30 (dt, $J = 6.8$, 7.5 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 187.6 145.3, 138.9, 135.9, 129.9, 127.2, 115.7, 38.0, 27.3, 21.5; HRMS(FAB): calcd for $C_{13}H_{14}N_2O_3S$+H 279.0803, found 279.0812.

4.10. (1*R*,5*R*)-1-(4-Methylphenylsulfonyl)bicyclo[3.1.0]-hexan-2-one 12g

This compound was prepared and purified by the previously described *Procedure C*, and was obtained as a white solid (95%, 69% ee). Ee was determined by HPLC (254 nm); Daicel CHIRALPAK AS-H 0.46 cm $\varnothing \times 25$ cm; hexane/2-propanol = 4/1; flow rate = 0.5 mL/min; retention time: 78.0 min for the major enantiomer, 82.0 min for the minor enantiomer; mp 96–98 °C (hexane/CH_2Cl_2); $[\alpha]_D^{28} = -25.2$ (c 0.75, $CHCl_3$, 69% ee); IR (KBr) ν_{max} 1731, 967, 810 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, $J = 8.0$ Hz, 2H), 7.34 (d, $J = 7.8$ Hz, 2H), 3.07–3.00 (m, 1H), 2.44 (s, 3H), 2.30–2.15 (m, 4H), 2.10–1.95 (m, 1H), 1.51 (dd, $J = 5.6$, 5.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 203.8, 144.7, 136.4, 129.5, 128.8, 53.2, 33.6, 31.0, 21.8, 20.3; HRMS(FAB): calcd for $C_{13}H_{14}O_3S$+H 251.0742, found 251.0740.

4.11. 1-(2,3-Dimethylphenylsulfonyl)-5-hexen-2-one

This compound was prepared and purified by the previously described *Procedure A*, and was obtained as a colorless oil (93%): IR (neat) ν_{max} 1690, 839, 730 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.83 (d, $J = 8.0$ Hz, 1H), 7.44 (d, $J = 7.5$ Hz, 1H), 7.36 (dd, $J = 7.5$, 8.0 Hz, 1H), 5.76 (ddt, $J = 7.0$, 10.0, 17.0 Hz, 1H), 5.02 (dd, $J = 1.5$, 17.0 Hz, 1H), 4.98 (dd, $J = 1.5$, 10.0 Hz, 1H), 4.20 (s, 2H), 2.81 (t, $J = 7.3$ Hz, 2H), 2.60 (s, 3H), 2.35 (s, 3H), 2.28 (dt, $J = 7.0$, 7.3 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 197.2, 139.7, 137.1, 136.2, 136.0, 135.7, 127.7, 125.9, 115.6, 66.3, 43.3, 26.9, 20.4, 16.1; HRMS(FAB): calcd for $C_{14}H_{18}O_3S$+H 267.1055, found 267.1062.

4.12. 1-Diazo-1-(2,3-dimethylphenylsulfonyl)-5-hexen-2-one 11h

This compound was prepared and purified by the previously described *Procedure B*, and was obtained as a greenish-yellow solid (95%): IR (KBr) ν_{max} 1678, 838, 739 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.00 (d, $J = 8.0$ Hz, 1H), 7.45 (d, $J = 7.5$ Hz, 1H), 7.30 (dd, $J = 7.5$, 8.0 Hz, 1H), 5.62 (ddt, $J = 6.8$, 9.0, 17.0 Hz, 1H), 4.89 (dd, $J = 1.5$, 17.0 Hz, 1H), 4.83 (dd, $J = 1.5$, 9.0 Hz, 1H), 2.53 (t, $J = 7.3$ Hz, 2H), 2.50 (s, 3H), 2.36 (s, 3H), 2.22 (dt, $J = 6.8$, 7.3 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 187.9, 139.8, 139.6, 135.8, 128.0, 127.8, 125.8, 125.7, 115.4, 37.8, 27.2, 20.3, 15.7: HRMS(FAB): calcd for $C_{14}H_{16}N_2O_3S$+H 293.0960, found 293.0966.

4.13. (1*R*,5*R*)-1-(2,3-Dimethylphenylsulfonyl)bicyclo[3.1.0]-hexan-2-one 12h

This compound was prepared and purified by the previously described *Procedure C*, and was obtained as a white solid (95%, 93% ee, using ligand **1d**). Ee was determined by HPLC (254 nm); Daicel CHIRALPAK AS-H 0.46 cm $\varnothing \times 25$ cm; hexane/2-propanol = 4/1; flow rate = 0.5 mL/min; retention time: 44.0 min for the minor enantiomer, 49.0 min for the major enantiomer; mp 99–101 °C (hexane/CH_2Cl_2); $[\alpha]_D^{26} = -37.2$ (c 1.02, $CHCl_3$, >99% ee); IR (KBr) ν_{max} 1732, 927, 863 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.97 (d, $J = 8.0$ Hz, 1H), 7.40 (d, $J = 7.6$ Hz, 1H), 7.27 (dd, $J = 7.6$, 8.0 Hz, 1H), 3.07–3.00 (m, 1H), 2.59 (s, 3H), 2.38–2.31 (m, 4H including δ 2.34, s, 3H), 2.30–2.16 (m, 3H), 2.14–2.00 (m, 1H), 1.64 (dd, $J = 5.4$, 5.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 203.5, 139.1, 136.4, 135.1, 129.1, 129.0, 53.4, 33.4, 31.1, 20.7, 20.6, 20.2, 16.6; HRMS(FAB): calcd for $C_{14}H_{16}O_3S$+H 265.0898, found 265.0898.

4.14. 1-(2,5-Dimethylphenylsulfonyl)-5-hexen-2-one

This compound was prepared and purified by the previously described *Procedure A*, and was obtained as a colorless oil (94%): IR (neat) ν_{max} 1642, 916, 831 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.64 (s, 1H), 7.24 (d $J = 7.6$ Hz, 1H), 7.14 (d, $J = 7.6$ Hz, 1H), 5.65 (ddt, $J = 6.8$, 10.0, 17.0 Hz, 1H), 4.94 (dd, $J = 1.5$, 17.0 Hz, 1H), 4.89 (dd, $J = 1.5$, 10.0 Hz, 1H), 4.11 (s, 2H), 2.71 (t, $J = 7.1$ Hz, 2H), 2.54 (s, 3H), 2.28 (s, 3H), 2.20 (dt, $J = 6.8$, 7.1 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 196.9, 136.3, 135.9, 134.7, 134.5, 132.5, 129.9, 129.8, 115.4, 65.8, 43.1, 26.7, 20.3, 19.4; HRMS(FAB): calcd for $C_{14}H_{18}O_3S$+H 267.1055, found 267.1057.

4.15. 1-Diazo-1-(2,5-dimethylphenylsulfonyl)-5-hexen-2-one 11i

This compound was prepared and purified by the previously described *Procedure B*, and was obtained as a greenish yellow oil (85%): IR (neat) ν_{max} 1670, 916, 730 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.81 (s, 1H), 7.23 (d, $J = 7.6$ Hz, 1H), 7.13 (d, $J = 7.6$ Hz, 1H), 5.52 (ddt, $J = 6.6$, 10.0, 17.0 Hz, 1H), 4.84 (dd, $J = 1.5$, 17.0 Hz, 1H), 4.75 (dd, $J = 1.5$, 10.0 Hz, 1H), 2.45 (t, $J = 6.9$ Hz,

2H), 2.43 (s, 3H), 2.29 (s, 3H), 2.08 (dt, $J = 6.6$, 6.9 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 187.8, 139.0, 136.0, 134.9, 134.1, 133.0, 130.3, 130.2, 115.4, 37.9, 27.4, 20.7, 19.5: HRMS(FAB): calcd for $C_{14}H_{16}N_2O_3S$+H 293.0960, found 293.0956.

4.16. (1*R*,5*R*)-1-(2,5-Dimethylphenylsulfonyl)bicyclo[3.1.0]-hexan-2-one 12i

This compound was prepared and purified by the previously described *Procedure C*, and was obtained as a white solid (90%, 82% ee). Ee was determined by HPLC (254 nm); Daicel CHIRALPAK AS-H 0.46 cm $\varnothing \times 25$ cm; hexane/2-propanol = 4/1; flow rate = 0.5 mL/min; retention time: 36.0 min for the major enantiomer, 39.0 min for the minor enantiomer; mp 96–98 °C (hexane/CH_2Cl_2); $[\alpha]_D^{28} = -43.0$ (c 1.05, $CHCl_3$, 82% ee); IR (KBr) ν_{max} 1740, 964, 882 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.88 (s, 1H), 7.29 (d, $J = 7.8$ Hz, 1H), 7.17 (d, $J = 7.8$ Hz, 1H), 3.06–2.90 (m, 1H), 2.64 (s, 3H), 2.40 (s, 3H), 2.39–2.14 (m, 4H), 2.12–1.99 (m, 1H), 1.60 (dd, $J = 5.4$, 5.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 203.4, 137.2, 136.1, 135.1, 134.3, 132.4, 131.6, 53.5, 33.5, 30.7, 20.8, 20.4, 20.3; HRMS(FAB): calcd for $C_{14}H_{16}O_3S$+H 265.0898, found 265.0909.

4.17. 1-(2,6-Dimethylphenylsulfonyl)-hex-5-en-2-one

This compound was prepared and purified by the previously described *Procedure A*, and was obtained as a white solid (87%): mp 39–41 °C (hexane/CH_2Cl_2); IR (KBr) ν_{max} 1718, 926, 832 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42–7.32 (m, 1H), 7.22–7.14 (m, 2H), 5.77 (ddt, $J = 6.8$, 10.0, 17.0 Hz, 1H), 5.04 (dd, $J = 1.7$, 17.0 Hz, 1H), 4.99 (dd, $J = 1.7$, 10.0 Hz, 1H), 4.16 (s, 2H), 2.83 (t, $J = 7.1$ Hz, 2H), 2.67 (s, 6H) 2.33 (dt, $J = 6.8$, 7.1 Hz. 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 197.4, 140.0, 136.0, 135.7, 133.2, 131.6, 115.9, 66.6, 43.8, 27.0, 22.9; HRMS(FAB): calcd for $C_{14}H_{18}O_3S$+H 267.1055, found 267.1057.

4.18. 1-Diazo-1-(2,6-dimethylphenylsulfonyl)-5-hexen-2-one 11j

This compound was prepared and purified by the previously described *Procedure B*, and was obtained as a greenish-yellow solid (83%): IR (KBr) ν_{max} 1671, 913, 832 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43–7.33 (m, 1H), 7.31–7.18 (m, 2H), 5.66 (ddt, $J = 6.8$, 11.0, 17.0 Hz, 1H), 4.95 (dd, $J = 1.2$, 17.0 Hz, 1H), 4.88 (dd, $J = 1.2$, 11.0 Hz, 1H), 2.70 (s, 6H), 2.50 (t, $J = 7.6$ Hz, 2H), 2.23 (dt, $J = 6.8$, 7.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 197.1, 140.1, 137.8, 135.8, 133.3, 130.2, 127.5, 115.8, 37.9, 27.4, 22.6: HRMS(FAB): calcd for $C_{14}H_{16}N_2O_3S$+H 293.0960, found 293.0962.

4.19. (1*R*,5*R*)-1-(2,6-Dimethylphenylsulfonyl)bicyclo[3.1.0]-hexan-2-one 12j

This compound was prepared and purified by the previously described *Procedure C*, and was obtained as a white solid (82%, 91% ee). Ee was determined by HPLC (254 nm); Daicel CHIRALCEL OD-H 0.46 cm $\varnothing \times 25$ cm; hexane/2-propanol = 4/1; flow rate = 0.5 mL/min; retention time: 21.0 min for the major enantiomer, 23.0 min for the minor enantiomer; mp 98–100 °C (hexane/CH_2Cl_2); $[\alpha]_D^{28} = -50.0$ (c 1.25, $CHCl_3$, 91% ee); IR (KBr) ν_{max} 1731, 874, 790 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36–7.28 (m, 1H), 7.18–7.11 (m, 2H), 3.05–2.96 (m, 1H) 2.73 (s, 6H), 2.48–2.38 (m, 1H), 2.32–2.18 (m, 3H), 2.12–2.02 (m, 1H), 1.66 (dd, $J = 5.6$, 5.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 204.0, 140.9, 132.8, 131.4, 129.6, 55.1, 33.4, 31.6, 23.3, 20.7, 20.4; HRMS(FAB): calcd for $C_{14}H_{16}O_3S$+H 265.0898, found 265.0897.

4.20. 1-(3,4-Dimethylphenylsulfonyl)-5-hexen-2-one

This compound was prepared and purified by the previously described *Procedure A*, and was obtained as a colorless oil (96%): IR (neat) ν_{max} 1680, 929, 818 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.61 (s, 1H), 7.58 (d, $J = 7.8$ Hz, 1H), 7.30 (d, $J = 7.8$ Hz, 1H), 5.76 (ddt, $J = 6.3$, 10.0, 18.0 Hz, 1H), 5.02 (dd, $J = 1.2$, 18.0 Hz, 1H), 4.98 (dd, $J = 1.2$, 10.0 Hz, 1H), 4.14 (s, 2H), 2.80 (t, $J = 7.3$ Hz, 2H), 2.40–2.26 (m, 8H including δ 2.34, s, 3H and δ 2.33, s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 197.4, 144.0, 138.1, 135.7, 130.3, 128.7, 128.6, 125.5, 115.6, 66.9, 43.1, 26.9, 19.9, 19.8; HRMS(FAB): calcd for $C_{14}H_{18}O_3S$+H 267.1055, found 267.1044.

4.21. 1-Diazo-1-(3,4-dimethylphenylsulfonyl)-5-hexen-2-one 11k

This compound was prepared and purified by the previously described *Procedure B*, and was obtained as a greenish-yellow oil (91%): IR (neat) ν_{max} 1734, 914, 823 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.70 (s, 1H), 7.66 (d, $J = 7.6$ Hz, 1H), 7.31 (d, $J = 7.6$ Hz, 1H), 5.73 (ddt, $J = 6.6$, 10.0, 17.0 Hz, 1H), 4.96 (dd, $J = 1.5$, 17.0 Hz, 1H), 4.92 (dd, $J = 1.5$, 10.0 Hz, 1H), 2.65 (t, $J = 7.6$ Hz, 2H), 2.33 (s, 6H), 2.28 (dt, $J = 6.6$, 7.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 187.4, 143.8, 138.9, 138.1, 135.8, 130.1, 127.6, 124.6, 115.3, 37.8, 27.2, 19.6, 19.5: HRMS(FAB): calcd for $C_{14}H_{16}N_2O_3S$+H 293.0960, found 293.0967.

4.22. (1*R*,5*R*)-1-(3,4-Dimethylphenylsulfonyl)bicyclo[3.1.0]-hexan-2-one 12k

This compound was prepared and purified by the previously described *Procedure C*, and was obtained as a white solid (94%, 72% ee). Ee was determined by HPLC (254 nm); Daicel CHIRALPAK AS-H 0.46 cm $\varnothing \times 25$ cm; hexane/2-propanol = 4/1; flow rate = 0.5 mL/min; retention time: 62.0 min for the major enantiomer, 65.0 min for the minor enantiomer; mp 92–94 °C (hexane/CH_2Cl_2); $[\alpha]_D^{28} = -42.3$ (c 1.09, $CHCl_3$, 72% ee); IR (KBr) ν_{max} 1656, 892, 754 cm^{-1} ; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.78 (s, 1H), 7.75 (d, $J = 8.0$ Hz, 1H), 7.29 (d, $J = 8.0$ Hz, 1H), 3.06–2.97 (m, 1H), 2.34 (s, 3H), 2.33 (s, 3H), 2.29–2.13 (m, 4H), 2.10–1.94 (m, 1H), 1.51 (dd, $J = 5.6$, 5.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 203.5, 143.4, 137.6, 130.0, 129.4, 127.8, 126.2, 53.2, 33.6,

31.0, 20.3, 20.0, 19.7; HRMS(FAB): calcd for $C_{14}H_{16}O_3S$+H 265.0898, found 265.0886.

4.23. 1-(3,5-Dimethylphenylsulfonyl)-5-hexen-2-one

This compound was prepared and purified by the previously described *Procedure A*, and was obtained as a colorless oil (98%): IR (neat) ν_{max} 1720, 730, 684 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.47 (s, 2H), 7.28 (s, 1H), 5.76 (ddt, $J = 6.8$, 10.0, 17.0 Hz, 1H), 5.03 (dd, $J = 1.2$, 17.0 Hz, 1H), 4.99 (dd, $J = 1.2$, 10.0 Hz, 1H), 4.13 (s, 2H), 2.81 (t, $J = 7.3$ Hz, 2H), 2.39 (s, 6H), 2.32 (dt, $J = 6.8$, 7.3 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 197.3, 139.4, 138.3, 136.1, 135.9, 125.5, 115.7, 67.0, 43.2, 27.0, 21.1; HRMS(FAB): calcd for $C_{14}H_{18}O_3S$+H 267.1055, found 267.1052.

4.24. 1-Diazo-1-(3,5-dimethylphenylsulfonyl)-5-hexen-2-one 11l

This compound was prepared and purified by the previously described *Procedure B*, and was obtained as a greenish-yellow oil (90%): IR (neat) ν_{max} 1734, 858, 786 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.55 (s, 2H), 7.28 (s, 1H), 5.72 (ddt, $J = 6.3$, 9.8, 16.0 Hz, 1H), 4.97 (dd, $J = 1.2$, 16.0 Hz, 1H), 4.93 (dd, $J = 1.2$, 9.8 Hz, 1H), 2.66 (t, $J = 7.6$ Hz, 2H), 2.41 (s, 6H), 2.30 (dt, $J = 6.3$, 7.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 197.2, 141.8, 139.7, 136.1, 135.8, 124.6, 115.7, 38.1, 27.5, 21.2, 14.1: HRMS(FAB): calcd for $C_{14}H_{16}N_2O_3S$+H 293.0960, found 293.0962.

4.25. (1*R*,5*R*)-1-(3,5-Dimethylphenylsulfonyl)bicyclo[3.1.0]-hexan-2-one 12l

This compound was prepared and purified by the previously described *Procedure C*, and was obtained as a white solid (91%, 62% ee). Ee was determined by HPLC (254 nm); Daicel CHIRALPAK AS-H 0.46 cm $\varnothing \times 25$ cm; hexane/2-propanol = 4/1; flow rate = 0.5 mL/min; retention time: 33.0 min for the major enantiomer, 35.0 min for the minor enantiomer; mp 95–97 °C (hexane/CH_2Cl_2); $[\alpha]_D^{28} = -41.0$ (c 1.37, $CHCl_3$, 62% ee); IR (KBr) ν_{max} 1716, 982, 882 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.64 (s, 2H), 7.26 (s, 1H), 3.07–2.99 (m, 1H), 2.40 (s, 6H), 2.38–2.15 (m, 4H), 2.11–1.98 (m, 1H), 1.53 (dd, $J = 5.4$, 5.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 203.4, 139.1, 138.8, 135.5, 126.2, 53.1, 33.6, 31.0, 21.2, 20.3; HRMS(FAB): calcd for $C_{14}H_{16}O_3S$+H 265.0898, found 265.0900.

4.26. (1*R*,2*R*)-[2-(2,3-Dimethylbenzenesulfonyl)-3-oxocyclopentyl]acetonitrile 15h

To a solution of **12h** (300.0 mg, 1.13 mmol) in DMSO (10 mL) was added sodium cyanide (61.2 mg, 1.25 mmol) and the reaction mixture was stirred at 80 °C for 5 h. After the starting material disappeared, the reaction mixture was quenched with saturated aqueous $NaHCO_3$ solution (10 mL) and extracted with ethyl acetate (3 mL × 2). The combined organic layer was washed with brine (5 mL), dried over Na_2SO_4, and evaporated. The residue was purified by flash chromatography (hexane/ethyl acetate = 4/1) to afford **15h** (323.0 mg, 98%) as a white solid: mp 108–110 °C (hexane/CH_2Cl_2); $[\alpha]_D^{25} = -33.0$ (c 1.15, $CHCl_3$, 93% ee); IR (KBr) ν_{max} 1735, 1457, 844 743 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.82 (d, $J = 8.0$ Hz, 1H), 7.48 (d, $J = 7.6$ Hz, 1H), 7.31 (dd, $J = 7.6$, 8.0 Hz, 1H), 3.76 (d, $J = 9.8$ Hz, 1H), 3.37–3.23 (m, 1H), 3.00 (dd, $J = 5.8$, 17.0 Hz, 1H), 2.81 (dd, $J = 3.8$, 17.0 Hz, 1H), 2.66–2.28 (m, 9H including δ 2.60, s, 3H and δ 2.37, s, 3H), 1.88–1.73 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 203.8, 139.8, 136.6, 136.1, 135.9, 129.2, 125.8, 116.9, 70.9, 38.7, 34.1, 25.7, 22.3, 20.5, 16.3; HRMS(FAB): calcd for $C_{15}H_{17}NO_3S$+H 292.1007, found 292.1017.

4.27. (*R*)-(3-Oxocyclopentyl)acetonitrile (16)

Compound **16** was obtained from **12e–l** according to the procedure in Ref. 6.

Compound **16** was obtained from **12e** in 55% yield (2 steps): $[\alpha]_D^{24} = -70.1$ (c 1.20, $CHCl_3$, >99% ee).

Compound **16** was obtained from **12f** in 49% yield (2 steps). $[\alpha]_D^{23} = -70.0$ (c 1.20, $CHCl_3$, >99% ee).

Compound **16** was obtained from **12g** in 56% yield (2 steps). $[\alpha]_D^{26} = -69.9$ (c 1.20, $CHCl_3$, >99% ee).

Compound **16** was obtained from **12h** in 55% yield (2 steps). $[\alpha]_D^{27} = -70.2$ (c 1.20, $CHCl_3$, >99% ee).

Compound **16** was obtained from **12i** in 51% yield (2 steps). $[\alpha]_D^{24} = -70.1$ (c 1.20, $CHCl_3$, >99% ee).

Compound **16** was obtained from **12j** in 51% yield (2 steps). $[\alpha]_D^{28} = -69.9$ (c 1.20, $CHCl_3$, >99% ee).

Compound **16** was obtained from **12k** in 50% yield (2 steps). $[\alpha]_D^{26} = -70.0$ (c 1.20, $CHCl_3$, >99% ee).

Compound **16** was obtained from **12l** in 54% yield (2 steps). $[\alpha]_D^{25} = -70.1$ (c 1.20, $CHCl_3$, >99% ee).

4.28. (1*R*,2*RS*)-[2-(2,3-Dimethylbenzenesulfonyl)-2-methyl-3-oxocyclopentyl]acetonitrile (17C); (*R*)-[2-(2,3-dimethylbenzenesulfonyl)-3-methoxy-2-cyclopentenyl]acetonitrile 17O

To a solution of **15h** (100 mg, 0.343 mmol) in DMF (3 mL) were added potassium carbonate (71.0 mg, 0.514 mmol) and methyl iodide (0.064 mL, 1.03 mmol) successively, and the reaction mixture was stirred at room temperature for 2 h. The reaction mixture was quenched with saturated aqueous NH_4Cl solution (10 mL) and extracted with ether (3 mL × 2). The combined organic layer was washed with brine (5 mL), dried over Na_2SO_4, and evaporated. The residue was purified by flash chromatography (hexane/ethyl acetate = 4/1) to afford **17C** (69.1 mg, 66%, dr = 5:1) as a white solid and **17O** (28.2 mg, 27%) as a white solid.

Compound **17C**: IR (KBr) ν_{max} 1751, 1461, 919, 835 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): major product: δ 7.68 (d,

$J = 8.1$ Hz, 1H), 7.44 (d, $J = 7.3$ Hz, 1H), 7.32–7.26 (m, 1H), 3.51–3.40 (m, 1H), 2.92 (dd, $J = 4.4$, 17.0 Hz, 1H), 2.89–2.28 (m, 10H including δ 2.48, s, 3H and δ 2.33, s, 3H), 1.72–1.56 (m, 1H), 1.27 (s, 3H); minor product: δ 7.61 (d, $J = 8.1$ Hz, 1H), 7.44 (d, $J = 7.3$ Hz, 1H), 7.32–7.26 (m, 1H), 3.51–3.40 (m, 1H), 2.92 (dd, $J = 4.4$, 17.0 Hz, 1H), 2.89–2.28 (m, 10H including δ 2.48, s, 3H and δ 2.33, s, 3H), 1.72–1.56 (m, 1H), 1.30 (s, 3H); HRMS(FAB): calcd for $C_{16}H_{19}NO_3S$+H 306.1164, found 306.1150.

Compound **17O**: mp 113–115 °C (CH_2Cl_2–hexane); $[\alpha]_D^{25} = -17.9$ (c 0.72, $CHCl_3$, 93% ee); IR (KBr) ν_{max} 1457, 946, 801 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.89 (d, $J = 7.8$ Hz, 1H), 7.37 (d, $J = 7.3$ Hz, 1H), 7.25 (dd, $J = 7.3$, 7.8 Hz, 1H), 3.75 (s, 3H), 3.30–3.20 (m, 1H), 2.77 (dd, $J = 3.6$, 17.0 Hz, 1H), 2.70–2.45 (m, 6H including δ 2.52, s, 3H), 2.48–2.20 (m, 4H including δ 2.33, s, 3H), 1.97–1.83 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.5, 140.2, 139.1, 136.3, 134.6, 127.0, 125.4, 118.4, 111.3, 58.2, 40.0, 29.2, 25.5, 23.4, 20.4, 15.8; HRMS(FAB): calcd for $C_{16}H_{19}NO_3S$+H 306.1164, found 306.1161.

4.29. (1*R*,2*RS*)-[2-(2,3-Dimethylbenzenesulfonyl)-3-oxo-2-(2-propynyl)cyclopentyl]acetonitrile (18C); (*R*)-[2-(2,3-dimethylbenzenesulfonyl)-3-(2-propynyloxy)-2-cyclopentenyl]-acetonitrile 18O

To a solution of **15h** (100.0 mg, 0.343 mmol) in DMF (2 mL) were added potassium carbonate (71.0 mg, 0.514 mmol), sodium iodide (154.0 mg, 1.03 mmol), and propargyl bromide (0.094 mL, 1.03 mmol) successively, and the reaction mixture was stirred at room temperature for 3 h. The reaction mixture was quenched with saturated aqueous NH_4Cl solution (3 mL) and extracted with ether (1 mL × 2). The combined organic layer was washed with brine (5 mL), dried over Na_2SO_4, and evaporated. The residue was purified by flash chromatography (hexane/ethyl acetate = 4/1) to afford **18C** (65.5 mg, 58%, dr = 10:1) and **18O** as white solids (37.2 mg, 33%).

Compound **18C**: IR (KBr) ν_{max} 2262, 1660, 832, 767 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): major product: δ 7.68 (d, $J = 8.0$ Hz, 1H), 7.49 (d, $J = 7.3$ Hz, 1H), 7.28 (dd, $J = 7.3$, 8.0 Hz, 1H), 3.67–3.54 (m, 1H), 3.06–2.90 (m, 2H), 2.83 (dd, $J = 2.6$, 17.0 Hz, 1H), 2.67–2.30 (m, 10H, including δ 2.49, s, 3H and δ 2.36, s, 3H), 2.08 (dd, $J = 2.6$, 2.6 Hz, 1H), 2.01–1.88 (m, 1H); minor product: δ 7.62 (d, $J = 8.0$ Hz, 1H), 7.49 (d, $J = 7.3$ Hz, 1H), 7.28 (dd, $J = 7.3$, 8.0 Hz, 1H), 3.67–3.54 (m, 1H), 3.06–2.90 (m, 2H), 2.67–2.30 (m, 11H including δ 2.60, dd, $J = 2.5$, 17.0 Hz, 1H and δ 2.49, s, 3H and δ 2.34, s, 3H), 2.06 (dd, $J = 2.5$, 2.5 Hz, 1H), 2.01–1.88 (m, 1H); HRMS(FAB): calcd for $C_{18}H_{19}NO_3S$+H 330.1164, found 330.1161.

Compound **18O**: mp 119–121 °C (CH_2Cl_2–hexane); $[\alpha]_D^{25} = -11.2$ (c 0.94, $CHCl_3$, 93% ee); IR (KBr) ν_{max} 2124, 1454, 792, 709 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.91 (d, $J = 8.0$ Hz, 1H), 7.37 (d, $J = 7.6$ Hz, 1H), 7.24 (dd, $J = 7.6$, 8.0 Hz, 1H), 4.50 (d, $J = 2.2$ Hz, 2H), 3.32–3.23 (m, 1H), 2.86–2.71 (m, 2H including δ 2.81, dd, $J = 3.9$, 17.0 Hz, 1H), 2.64–2.39 (m, 6H including δ 2.52, s, 3H), 2.38–2.19 (m, 4H including δ 2.33, s, 3H), 1.90 (dddd, $J = 3.4$, 7.8, 9.0, 9.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.9, 140.0, 139.1, 136.5, 134.7, 127.2, 125.5, 118.3, 114.3, 76.9, 76.8, 58.0, 39.8, 29.1, 25.7, 23.3, 20.4, 16.0; HRMS(FAB): calcd for $C_{18}H_{19}NO_3S$+H 330.1164, found 330.1150.

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