Pergamon

SCIENCE DIRECT®

Tetrahedron Letters 44 (2003) 9007–9011

TETRAHEDRON LETTERS

Enantioselective intramolecular cyclopropanation of α-diazo-β-keto sulfones: asymmetric synthesis of bicyclo[4.1.0]heptanes and tricyclo[4.4.0.0]decenes

Masahiro Honma and Masahisa Nakada*

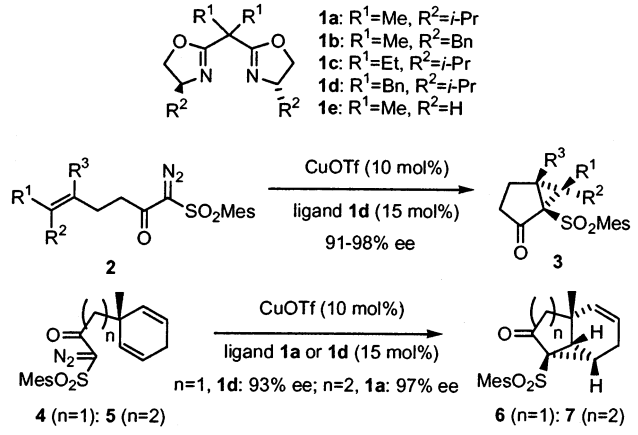
Department of Chemistry, School of Science and Engineering, Waseda University, 3-4-1 Ohkubo, Shinjuku-ku, Tokyo 169-8555, Japan

Received 25 August 2003; revised 24 September 2003; accepted 30 September 2003

Abstract—Catalytic asymmetric synthesis of some new chiral building blocks useful for natural product synthesis is described. The intramolecular cyclopropanation (IMCP) reaction of α-diazo-β-keto sulfones affording bicyclo[4.1.0]heptanes such as **9a–d** is found to proceed with high enantioselectivity (93–98% ee). The yield is moderate due to the competing intramolecular C–H insertion reaction. As intramolecular C–H insertion reaction is not observed in the reaction of the substrates possessing a quaternary carbon at the allylic position, the reactions of **19a** and **19b** proceed with high enantioselectivity (95% ee) and yield. It was also found that the substrates possessing an ether group, such as **19a** and **19b**, could be used in this enantioselective IMCP reaction.

The preparation of new chiral building blocks is important for the synthesis of many bioactive natural products because such new compounds enable easier and more efficient natural product synthesis. We have recently reported a highly enantioselective intramolecular cyclopropanation (IMCP) reaction of α-diazo-β-keto sulfones (Scheme 1).[1] This catalytic enantioselective reaction easily affords products, bicyclo[3.1.0]hexanes **3**, tricyclo[4.3.0.0]nonenes **6**, and tricyclo[4.4.0.0]decenes **7**. Since these products are highly crystalline and purified easily by a single recrystallization to be enantiomerically pure compounds, this catalytic enantioselective IMCP reaction would be advantageous for the preparation of new chiral building blocks.

We have reported extensive studies on enantioselective IMCP reactions of the substrates **2** and **4** to generate cyclopentanone derivatives.[1] However, enantioselective IMCP reactions to generate cyclohexanone derivatives other than the reaction of **5** have not been examined (Scheme 1). Since cyclohexanone derivatives are useful building blocks for the synthesis of many natural products, asymmetric synthesis of such compounds is very important. Accordingly, we decided to carry out studies on the enantioselective IMCP reactions to prepare chiral building blocks possessing six-membered-ring systems, and herein we report enantioselective preparation of new chiral bicyclo[4.1.0]hexanes and tricyclo[4.4.0.0]-decenes.



Scheme 1. Enantioselective intramolecular cyclopropanation (IMCP) of α-diazo-β-keto sulfones.

Keywords: asymmetric synthesis; cyclopropanation; enantioselection; intramolecular reaction.

* Corresponding author. Tel.: +813-5286-3240; fax: +813-5286-3240; e-mail: mnakada@waseda.jp

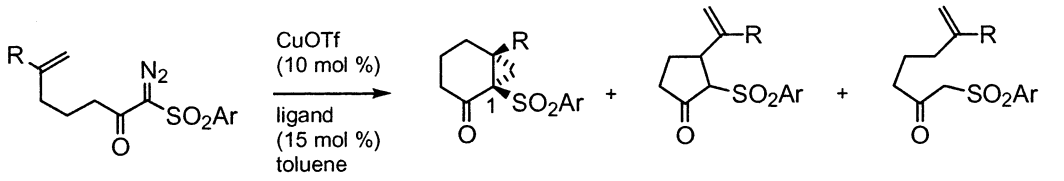
0040-4039/$ - see front matter © 2003 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2003.09.215

First, the most simple substrate, **8a**, was prepared,[2] and its enantioselective IMCP reaction was investigated. The reaction of **8a** was carried out in toluene with the asymmetric catalyst prepared in situ by $(CuOTf)_2$–C_6H_6 and bisoxazoline ligand **1a**.

The reaction of **8a** with **1a** completed at room temperature within 2 h to provide **9a** with high enantioselectivity (92% ee,[3] 58%, entry 1, Table 1). However, some by-products formed. The structure of the major by-product was elucidated as **10a** by ^1H, ^{13}C NMR, HRMS, and IR.[4] Thus, the reaction of **8a** accompanied C–H insertion reaction, forming **10a**. Another by-product, **11a**, which is a denitrogen product of **8a**, was also obtained as an inseparable mixture with **10a** (**10a**:**11a** = 20:1). The mechanism for the formation of **11a** has not yet been clarified.

To improve the yield of **9a**, the reaction condition for **8a** was examined. First, other copper catalysts, that is, $(CuOTf)_2$–toluene (entry 2) and $CuSbF_6$ (entry 3), were examined. However, neither the enantioselectivity nor yield increased, and by-products **10a** and **11a** formed again.[5] Then, the reaction of **8a** was examined in other solvents. THF, CH_2Cl_2, $(CH_2Cl)_2$, and benzene (entry 4, 5, 6, 7) were found to be applicable for this reaction, but the yield was somewhat lowered in all cases.[6]

Table 1. Enantioselective IMCP reaction of α-diazo-β-keto sulfones **8a–d**



8a: R=H, Ar=Ph
8b: R=Me, Ar=Ph
8c: R=H, Ar=Mes
8d: R=Me, Ar=Mes

9a: R=H, Ar=Ph
9b: R=Me, Ar=Ph
9c: R=H, Ar=Mes
9d: R=Me, Ar=Mes

10a: R=H, Ar=Ph
10b: R=Me, Ar=Ph
10c: R=H, Ar=Mes
10d: R=Me, Ar=Mes

11a: R=H, Ar=Ph
11b: R=Me, Ar=Ph
11c: R=H, Ar=Mes
11d: R=Me, Ar=Mes

Entry	Product	Ligand	Solvent	Temp. (°C)[a]	Time (h)[a]	Ee (%)[b] **9**	Yield (%)[c]	
							9	**10**+**11** (**10**/**11**)[d]
1	**9a**	**1a**	Toluene	rt	2	**92 (1*R*)**[e]	**58**	19 (20/1)
2[f]	**9a**	**1a**	Toluene	rt	1.5	88 (1*R*)[e]	43	8 (8/1)
3[g]	**9a**	**1a**	Toluene	rt, 50	2, 96	86 (1*R*)[e]	50	26 (>99/1)
4	**9a**	**1a**	THF	rt	2	92 (1*R*)[e]	33	9 (2/1)
5	**9a**	**1a**	CH_2Cl_2	rt	12	92 (1*R*)[e]	52	11 (11/1)
6	**9a**	**1a**	$(CH_2Cl)_2$	rt	72	93 (1*R*)[e]	44	6 (3/1)
7	**9a**	**1a**	Benzene	rt	2	91 (1*R*)[e]	50	13 (20/1)
8	**9a**	**1b**	Toluene	rt	4	91 (1*R*)[e]	53	16 (9/1)
9	**9a**	**1c**	Toluene	rt	17	88 (1*R*)[e]	28	14 (30/1)
10	**9a**	**1d**	Toluene	rt	14	89 (1*R*)[e]	41	14 (14/1)
11	**9a**	**1e**	Toluene	rt	11	0	34	5 (3/1)
12	**9a**	None	Toluene	rt, 50	3, 5	0	26	9 (1/1)
13	**9b**	**1a**	Toluene	rt	17	87 (1*R*)[e]	44	14 (8/1)
14	**9b**	**1b**	Toluene	rt	12	68 (1*R*)[e]	42	14 (14/1)
15	**9b**	**1c**	Toluene	rt	7	84 (1*R*)[e]	35	10 (8/1)
16	**9b**	**1d**	Toluene	rt	2	**93 (1*R*)**[e]	**62**	15 (18/1)
17	**9b**	**1e**	Toluene	rt	3	0	31	4 (2/1)
18	**9c**	**1a**	Toluene	50	1.5	90 (1*R*)[e]	36	19 (4/1)
19	**9c**	**1b**	Toluene	50	3.5	67 (1*R*)[e]	16	14 (2/1)
20	**9c**	**1c**	Toluene	50	2	94 (1*R*)[e]	23	8 (4/1)
21	**9c**	**1d**	Toluene	50	16	**98 (1*R*)**[e]	**31**	17 (4/1)
22	**9c**	**1e**	Toluene	50	6	0	33	14 (1/1)
23	**9d**	**1a**	Toluene	50	1.5	90 (1*R*)[e]	41	12 (4/1)
24	**9d**	**1b**	Toluene	50	1.5	84 (1*R*)[e]	32	29 (2/1)
25	**9d**	**1c**	Toluene	50	3.5	94 (1*R*)[e]	26	10 (3/1)
26	**9d**	**1d**	Toluene	50	4	**98 (1*R*)**[e]	**43**	15 (3/1)
27	**9d**	**1e**	Toluene	50	3	0	32	26 (1/1)

[a] Reaction was carried out at the indicated temperatures for the indicated times, respectively.
[b] Ee determined by HPLC. For HPLC conditions, see Ref. 3.
[c] Isolated yields.
[d] Ratios determined by ^1H NMR.
[e] Absolute configuration of **9a–9d** was determined by X-ray crystallographic analysis.
[f] $(CuOTf)_2$·toluene was used.
[g] $CuSbF_6$ was used.

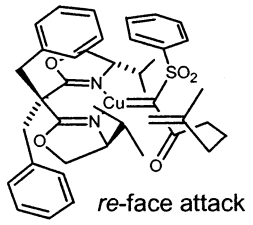
The reactions of **8a** with other ligands, **1b**, **1c**, and **1d** were examined. As shown in entries 8–10, enantioselectivity and yield was not improved in all cases. Though ligand **1d** was the most effective for the enantioselective IMCP reactions of **2** and **4** (Scheme 1),[1] ligand **1a** was found to be the best in the reaction of **8a**. The reaction of **8a** with the achiral ligand **1e** was carried out to prepare the racemic standard sample for HPLC analysis (entry 11), because the reaction of **8a** with no ligand was slow and required heating (entry 12). As a result, formation of **10a** and **11a** decreased, but the yield of **9a** did not increase.[7] It was found that by-products (**10** and **11**) always form (entries 1–12); therefore, the formation of **10** and **11** is not related to the type of copper salt or solvent, or the structure of the ligand.

Examined next was the reaction of **8b** (entries 13–17).[2] The reaction of **8b** with **1d** afforded **9b** highly enantioselectively (93% ee, 62%, entry 16)[a]. This result differs from that given in **8a**. Thus, ligand **1d** was best, showing relationships between the ligand and the enantioselectivity similar to those seen in the reactions of **2** and **4**.[1]

In the reactions of **2** and **4**, the mesitylsulfones had showed higher enantioselectivity compared with the corresponding phenylsulfones.[1] Therefore, the enantioselective IMCP reactions of mesitylsulfones **8c**[2] and **8d**[2] were investigated next. The products, **9c** and **9d**, were obtained with high enantioselectivity (98% ee,[3] entries 21 and 26) with ligand **1d**. The same trend in increment of enantioselectivity in the order of **1d**, **1c**, **1a**, and **1b**, that had been observed in the reaction of **2** and **4**, was found (entries 18–21, 23–26). Unfortunately, the yields of **9c** and **9d** were low, and formation of by-products, **10c**, **10d**, **11c**, and **11d**, could not be avoided.

As products **9a–d** were highly crystalline, the absolute structure of each was determined successfully by X-ray crystallographic analysis. These results and the $[\alpha]_D$ values of the products[3] indicate that all products in Table 1 possess 1*R* configuration, and the outcome of the enantioselectivity of **9** is well explained by model A (Fig. 1). Thus, the cyclopropanation reactions are thought to occur preferentially at the *re*-face (defined by the Cu=C–C arrangement) of the chiral catalyst–carbene complexes.

We also investigated other enantioselective IMCP reactions to prepare new tricyclic cyclopropanes, that is, the reactions of the substrates providing new tricyclo[4.4.0.0]decenes. We are interested in the IMCP reactions of **19a** and **19b**, because the corresponding products **20a** and **20b** would be good chiral building blocks for the synthesis of bioactive polycyclic natural products.[8] However, an ether group in the substrate could react with the carbene complex to form oxonium ylide, reducing the yield of the desired product.[9] Therefore, we prepared phenylsulfones **19a** and **19b**, possessing a bulky TBS ether and a less bulky benzyl ether, respectively, to examine the possibility of forming **20a** and **20b** by this catalytic enantioselective IMCP reaction.[10] The preparation of **19a** is shown in Scheme 2.

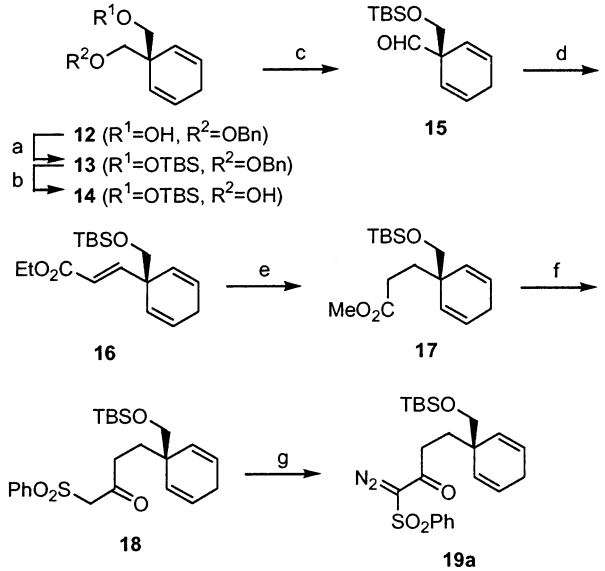


model A (for entry 16, Table 1)

Figure 1. Proposed model A.

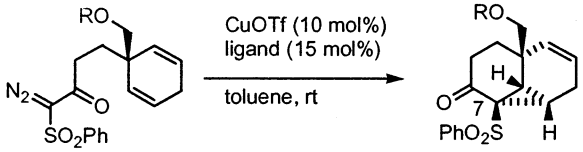
The known alcohol **12**[11] was converted to TBS ether **13** (97%), followed by debenzylation to afford **14** (94%). Dess–Martin oxidation[12] of **14** gave **15** in 90% yield, and the following Horner–Wadsworth–Emmons reaction generated **16** (99%). Alkene **16** was reduced by magnesium (88%), and the resultant **17** was reacted with methylsulfone to afford **18** (92%). Keto sulfone **18** was easily converted to diazo compound **19a** by TsN_3 and triethylamine (90%). The same operations described above provided **19b** as well.

As shown in Table 2, the IMCP reaction of **19a** with ligand **1a** proceeded smoothly at room temperature, and **20a** was obtained with high enantioselectivity (95% ee, 89%, entry 1). The reaction of **19a** with ligand **1d** resulted in slightly reduced enantioselectivity (93% ee, 86% yield, entry 2). The reaction of **19b** with ligand **1a** also formed **20b** with high enantioselectivity (95% ee), but the yield was somewhat lowered (73%, entry 3). In



Scheme 2. *Reagents and conditions*: (a) TBSCl, imidazole, DMAP, DMF, CH_2Cl_2, rt, 10 h, 97%; (b) Li, liq. NH_3, THF, –20°C, 20 min, 94%; (c) Dess–Martin reagent, $NaHCO_3$, CH_2Cl_2, rt, 2 h, 90%; (d) $(EtO)_2P(O)CH_2CO_2Et$, *t*-BuOK, THF, –78°C to 0°C, 99%; (e) Mg, MeOH, 0°C, 88%; (f) CH_3SO_2Ph, *n*-BuLi, THF, 0°C, 92%; (g) TsN_3, TEA, CH_3CN, 0°C to rt, 6 h, 90%.

Table 2. Enantioselective IMCP reaction of α-diazo-β-keto sulfones **19a** and **19b**



19a (R=TBS)
19b (R=Bn)

20a (R=TBS)
20b (R=Bn)

Entry	Product	Ligand	Time (h)	Ee (%)[a]	Yield (%)[b]
1	**20a**	**1a**	0.5	95 (7*R*)[c]	89
2	**20a**	**1d**	3	93 (7*R*)[c]	86
3	**20b**	**1a**	1	95 (7*R*)[d]	73
4	**20b**	**1d**	1	89 (7*R*)[d]	31

[a] Ee determined by HPLC. For HPLC conditions, see Ref. 13.
[b] Isolated yields.
[c] Absolute configuration determined by X-ray crystallographic analysis.
[d] Absolute configuration determined by the comparison of optical rotation.

the reaction of **19b**, the result obtained with **1a** (95% ee, 73%, entry 3) was superior to that obtained with **1d** (89% ee, 31%, entry 4). This reduced yield of **20b** may be explained by the oxonium ylide formation;[14] however, no product corresponding to the oxonium ylide formation was isolated.

X-Ray crystallographic analysis of the crystalline *p*-bromobenzoate[15] derived from **20a** was successfully carried out (Fig. 2). This analysis unambiguously elucidated the absolute structure of **20a**. The absolute structure of **20b** was determined as shown in Table 2 through comparison of the $[\alpha]_D$ value of **20b** with that of the same compound derived from **20a**.[16] That is, **20a** was desilylated with TBAF (quant.), and the resultant alcohol was treated with benzyl trichloroacetimidate and TMSOTf to afford **20b** (52%).

Based on the structure determination described above, the C-7 configuration of both compounds, **20a** and **20b**, is confirmed as *R*; hence, the outcome of the enantioselectivity of **20a** and **20b** is found to be well explained by model A′ shown in Figure 3. In the reactions of **20a** and **20b**, the steric repulsion between the 1,4-cyclohexadiene moiety and the isopropyl group of the ligand is so large that the less bulky ligand **1a** and phenyl sulfone would be effective enough to achieve high enantioselectivity.

In summary, highly enantioselective preparation of some new chiral building blocks has been developed. The enantioselective IMCP reaction of α-diazo-β-keto sulfones affording bicyclo[4.1.0]heptanes such as **9a**–**d** is found to proceed with high enantioselectivity (93–98% ee) and moderate yield. As C–H insertion reaction is not observed in the reaction of the substrates possessing a quaternary carbon at the allylic position, the reactions of **19a** and **19b** proceed with high enantioselectivity (95% ee) and yield. It was also found that the substrates possessing an ether group, such as **19a** and **19b**, could be used in this enantioselective IMCP reaction. Work on natural product synthesis using the new enantiomerically pure compounds described herein is now in progress, and the details will be reported in due course.

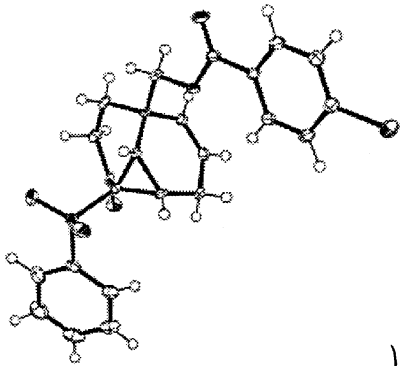
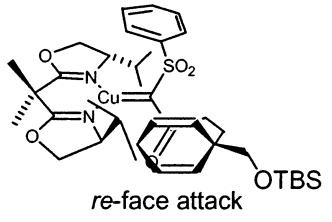


Figure 2. X-Ray crystal structure of the *p*-bromobenzoate derived from **20a**.



model A' (for entry 1, Table 2)

Figure 3. Proposed model A′.

Acknowledgements

We thank Material Characterization Central Laboratory, Waseda University, for technical support of the X-ray crystallographic analysis. This work was financially supported in part by 21COE 'Practical Nano-Chemistry'.

References

1. Honma, M.; Sawada, T.; Fujisawa, Y.; Utsugi, M.; Watanabe, H.; Umino, A.; Matsumura, T.; Hagihara, T.; Takano, M.; Nakada, M. *J. Am. Chem. Soc.* **2003**, *125*, 2860–2861.
2. For the preparation of sulfones, see Ref. 1.
3. Ee was determined by HPLC (254 nm); **9a**: $[\alpha]_D^{21}$ −97.4 (*c* 1.27, $CHCl_3$, 99% ee); Daicel Chiral Cell OD-H 0.46 cm ϕ×25 cm; hexane/isopropanol = 3/1; flow rate = 0.5 mL/min; retention time: 22.8 min for *ent*-**9a**, 25.0 min for **9a**. **9b**: $[\alpha]_D^{23}$ −139.8 (*c* 0.98, $CHCl_3$, >99% ee); Daicel Chiral Cell AS-H 0.46 cm ϕ×25 cm; hexane/isopropanol = 3/1; flow rate = 0.5 mL/min; retention time: 38.4 min for **9b**, 48.9 min for *ent*-**9b**. **9c**: $[\alpha]_D^{28}$ +30.3 (*c* 1.11, $CHCl_3$, >99.5% ee); Daicel Chiral Cell AS-H 0.46 cm ϕ×25 cm; hexane/isopropanol = 3/1; flow rate = 0.5 mL/min; retention time: 22.5 min for **9c**, 25.9 min for *ent*-**9c**. **9d**: $[\alpha]_D^{22}$ −191.6 (*c* 1.03, $CHCl_3$, >99.5% ee); Daicel Chiral Cell AS-H 0.46 cm ϕ×25 cm; hexane/isopropanol = 3/1; flow rate = 0.5 mL/min; retention time: 13.1 min for *ent*-**9d**, 16.2 min for **9d**.
4. **10a**: IR(KBr): 2932, 1748, 1448, 1308, 1150, 1080, 824 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 7.88$ (d, $J = 7.8$ Hz, 2H), 7.68 (t, $J = 7.3$ Hz, 1H), 7.58 (dd, $J = 7.8$, 7.3 Hz, 2H), 5.88 (ddd, $J = 17.1$, 10.5, 6.3 Hz, 1H), 5.13 (d, $J = 17.1$ Hz, 1H), 5.11 (d, $J = 10.5$ Hz, 1H), 3.59–3.54 (m, 2H), 2.51–2.32 (m, 3H), 1.82–1.71 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 205.8$, 138.0, 137.7, 134.1, 129.0, 129.0, 116.1, 73.9, 41.3, 38.4, 26.3; HRMS (FAB): *m*/*z* calcd for $C_{13}H_{14}O_3SH^+$ 251.0742, found 251.0770. **10a**–**d** were obtained as a single diastereomer. The relative configuration of **10a**–**d** is surmised to be *trans* on the basis of their thermodynamic stability. Ee of **10a**–**d** was not determined.
5. Also examined catalyst was CuI, but many unidentified products formed.
6. The product was obtained as a complex mixture when Et_2O, DMF, or DMSO was used as the solvent.
7. Other examples using achiral ligand **1e** (entries 17, 22 and 27) show no improvement of the by-product formation and yield.
8. These chiral building blocks would be useful for the total synthesis of the natural products possessing a hydroxy group at C-19 such as oubain, which has been used for more than two centuries in the clinical treatment of congestive heart failure, and bufadienolides, which exhibit potent antitumor activity. For the structure of oubain, see: Arnaud, M. *Compt. Rend. Acad.* **1888**, *107*, 1011. For the structure of recently isolated bufadienolides possessing a formyl group at C-19, see: Watanabe, K.; Mimaki, Y.; Sakagami, H.; Sashida, Y. *J. Nat. Prod.* **2003**, *66*, 236–241.
9. Reviews: (a) Padwa, A. *J. Organomet. Chem.* **2001**, *617–618*, 3–16.; (b) Doyle, M. P.; Forbes, D. C. *Chem. Rev.* **1998**, *98*, 911–935; (c) Padwa, A.; Krumpe, K. E. *Tetrahedron* **1992**, *48*, 5385–5453; (d) Padwa, A.; Hornbuckle, S. F. *Chem. Rev.* **1991**, *91*, 263–309; (e) Adams, J.; Spero, D. M. *Tetrahedron* **1991**, *47*, 1765–1808; (f) Doyle, M. P. *Chem. Rev.* **1986**, *86*, 919–939.
10. Since the reaction of **7** was sluggish as previously reported, the IMCP reaction of the mesityl sulfones corresponding to **19a** and **19b** was not examined.
11. Zutterman, F.; Mungheer, D. W. R.; Clercq, P. D.; Vanderwalle, M. *Tetrahedron* **1979**, *35*, 2389–2396.
12. (a) Dess, D. B.; Martin, J. C. *J. Org. Chem.* **1991**, *113*, 7277–7287; (b) Frigerio, M.; Santagostino, M.; Sputore, S. *J. Org. Chem.* **1999**, *64*, 4537–4538.
13. Ee was determined by HPLC (254 nm); **20a**: Daicel Chiral Cell OD-H 0.46 cm ϕ×25 cm; hexane/isopropanol = 9/1; flow rate = 0.5 mL/min; retention time: 12.2 min for *ent*-**20a**, 15.2 min for **20a**. **20b**: Daicel Chiral Cell OD-H 0.46 cm ϕ×25 cm; hexane/isopropanol = 9/1; flow rate = 0.5 mL/min; retention time: 23.1 min for *ent*-**20b**, 25.0 min for **20b**.
14. Structure of some by-products was not fully characterized.
15. TBS ether **20a** was desilylated by TBAF (quant.), and the resultant alcohol was converted with *p*-bromobenzoyl chloride and pyridine to the crystalline *p*-bromobenzoate (93%).
16. **20a**: $[\alpha]_D^{25}$ +80.9 (*c* 0.11, $CHCl_3$, 96% ee); IR(KBr): 2956, 2932, 2896, 2860, 1708, 1448, 1310, 1286, 1258, 1180, 1152, 1118, 1086, 840, 778, 756 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 7.85$ (d, $J = 8.1$ Hz, 2H), 7.64 (t, $J = 7.3$ Hz, 1H), 7.53 (dd, $J = 8.1$, 7.3 Hz, 2H), 5.63 (ddd, $J = 10.5$, 3.4, 2.4 Hz, 1H), 5.24 (d, $J = 10.5$ Hz, 1H), 3.64 (d, $J = 9.5$ Hz, 1H), 3.62 (d, $J = 9.5$ Hz, 1H), 2.65 (d, $J = 9.8$ Hz, 1H), 2.50–2.35 (m, 1H), 2.25–2.10 (m, 3H), 2.07–1.95 (m, 2H), 1.60–1.50 (m, 1H), 0.93 (s, 9H), 0.09 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 201.3$, 139.4, 133.6, 128.8, 128.7, 128.3, 126.3, 69.9, 48.4, 36.2, 35.0, 31.3, 27.0, 25.9, 22.4, 19.8, 18.4, −5.3; HRMS (FAB): *m*/*z* calcd for $C_{23}H_{32}O_4SSiH^+$ 433.1869, found 433.1869. **20b**: $[\alpha]_D^{37}$ + 130.7 (*c* 0.64, $CHCl_3$, 95% ee); IR(KBr): 2864, 1706, 1448, 1310, 1288, 1182, 1152, 1086 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 7.83$ (d, $J = 8.3$ Hz, 2H), 7.62 (t, $J = 7.3$ Hz, 1H), 7.48 (dd, $J = 8.3$, 7.3 Hz, 2H), 7.45–7.30 (m, 5H), 5.68 (ddd, $J = 10.3$, 3.4, 2.4 Hz, 1H), 5.30 (d, $J = 10.3$ Hz, 1H), 4.62 (d, $J = 12.2$ Hz, 1H), 4.58 (d, $J = 12.2$ Hz, 1H), 3.53 (d, $J = 8.8$ Hz, 1H), 3.50 (d, $J = 8.8$ Hz, 1H), 2.75 (d, $J = 9.8$ Hz, 1H), 2.52–2.44 (m, 1H), 2.26 (dd, $J = 8.3$, 7.3 Hz, 1H), 2.17–2.12 (m, 2H), 2.06–1.95 (m, 2H), 1.60–1.54 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 201.1$, 139.3, 137.9, 133.6, 128.8, 128.7, 128.4, 128.2, 127.7, 127.6, 126.5, 77.0, 73.5, 48.6, 36.0, 33.9, 31.8, 27.6, 22.7, 19.7; HRMS (FAB): *m*/*z* calcd for $C_{24}H_{24}O_4SH^+$ 409.1473, found 409.1456. **20b** (from **20a**): $[\alpha]_D^{34}$ +130.7 (*c* 0.77, $CHCl_3$, 95% ee).