Enantiodifferentiating Functionalization of *cis*-Cycloalkane-1,2-diols and *cis*-*endo*-5-Norbornen-2,3-ylenebis(methanol) via Chiral Spiroacetals Derived from *l*-Menthone

Toshiro Harada, Isao Wada, and Akira Oku*

Department of Chemistry, Kyoto Institute of Technology, Matsugasaki, Sakyo-ku, Kyoto 606, Japan

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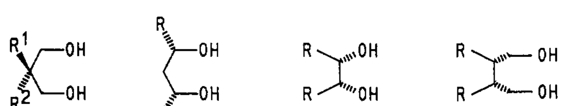
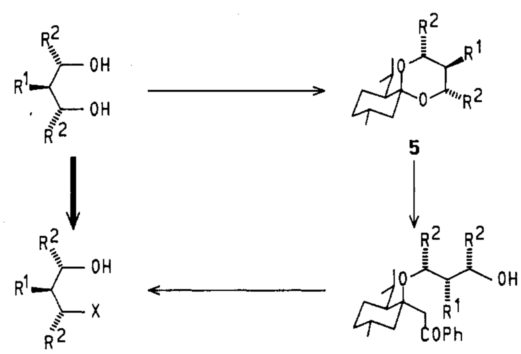
The enantiodifferentiating transformation of a prochiral hydroxyl group in *cis*-cycloalkane-1,2-diols and *cis*-*endo*-5-norbornen-2,3-ylenebis(methanol) (**16**) is presented. The reactions of the bis(trimethylsilyl) derivatives of 1,2-diols **6a–d** with *l*-menthone in the presence of trimethylsilyl trifluoromethanesulfonate gave one of the two diastereomeric spiroacetals selectively (>3:1). The major spiroacetal was treated with acetophenone enol trimethylsilyl ether in the presence of titanium tetrachloride to give the ring-cleavage product which was produced by the selective cleavage of the equatorial C–O bond of the starting spiroacetal accompanied by the introduction of the benzoylmethyl group. After protection of the hydroxyl group as a methoxymethyl ether, the chiral auxiliary was removed under basic conditions to give monomethoxymethyl ether derivatives **10a–d** (>95% ee). By a similar method, mono tetrahydropyranyl ether derivative **22** (95% ee) was obtained by starting from **16**.

Enantiodifferentiating transformation of a prochiral hydroxyl group of 2-substituted 1,3-propanediols **1** and *meso*-diols such as **2–4** provides versatile chiral building blocks which can be incorporated into diverse target structures.[1] While this type of asymmetric synthesis is common in enzymatic transformation,[2] examples of the chemical transformation are rare.[3] The problem of substrate specificities in enzymatic methods can be overcome by the nonenzymatic approach. In this regard, we recently reported a general method for enantiodifferentiating functionalization of symmetrical diols **1** and **2** utilizing a highly selective ring-cleavage reaction of chiral spiroacetals **5** derived from *l*- or *d*-menthone (Scheme I).[4] In the present paper, we report extension of this methodology to the enantiodifferentiating conversion of specific types of *meso*-1,2- and -1,4-diols.



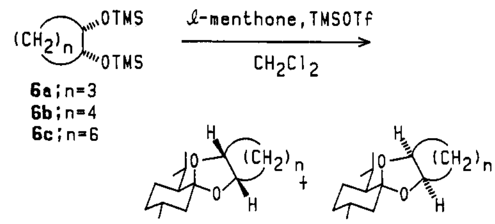
1 2 3 4

Scheme I



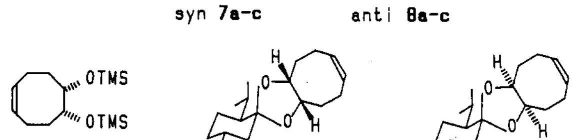
Results and Discussion

Enantiodifferentiating Transformation of *cis*-1,2-Cycloalkanediols. The reactions of bis(trimethylsilyl ethers) **6a–d** with *l*-menthone in the presence of a catalytic amount of trimethylsilyl trifluoromethanesulfonate (TMSOTf) (eq 1)[5] proceeded slowly at −85 °C in comparison with the acetalization of 2-substituted propanediol bis(trimethylsilyl ethers) studied previously[4a] and did not go to completion even after 2 days. However, the reaction at −40 °C proceeded with a reasonable rate to give a mixture of spiroacetals **7a–d** and **8a–d** in a high yield with 100% conversion of the starting materials (Table I). *syn*-Spiroacetals **7a–d** and *anti*-spiroacetals **8a–d** in which the ring fused to the 1,3-dioxolane ring is oriented syn and anti to the isopropyl group, respectively, were separated by flash or medium-pressure silica gel column chromatography.



(1)

syn **7a–c** anti **8a–c**



6d **7d** **8d**

As shown in Table I, stereoselectivities higher than 3:1 were observed in all reactions by choosing a proper reaction temperature. In the reaction of cyclopentanediol derivative **6a**, the moderate syn selectivity observed at −85 °C was significantly improved at −40 °C (entries 1 and 2). On the other hand, cyclohexanediol derivative **6b** showed a higher syn selectivity at a lower temperature (entries 3 and 4).

(1) (a) Scott, J. W. In *Asymmetric Synthesis*; Morrison, J. D., Scott, J. W. Eds.; Academic Press: New York, 1984; Vol. 4, p 1. (b) Hanessian, S. *Total Synthesis of Natural Products: The "Chiron" Approach*; Pergamon Press: Oxford, 1983.

(2) (a) Fischli, A. In *Modern Synthetic Methods*; Scheffold, R., Ed.; Otto Salle Verlag: Frankfurt, 1980; Vol. 2, p 269. (b) Lok, K. P.; Jakovac, I. J.; Jones, J. B. *J. Am. Chem. Soc.* **1985**, *107*, 2521 and references cited therein.

(3) (a) Mukaiyama, T.; Tanabe, Y.; Shimizu, M. *Chem. Lett.* **1984**, 401. (b) Ichikawa, J.; Asami, M.; Mukaiyama, T. *Ibid.* **1984**, 949. (c) Schreiber, S. L.; Wang, Z. *J. Am. Chem. Soc.* **1985**, *107*, 5303. (d) Schreiber, S. L.; Goulet, M. T.; Schulte, G. *Ibid.* **1987**, *109*, 4718.

(4) (a) Harada, T.; Hayashiya, T.; Wada, I.; Iwa-ake, N.; Oku, A. *J. Am. Chem. Soc.* **1987**, *109*, 527. (b) Harada, T.; Wada, I.; Oku, A. *Tetrahedron Lett.* **1987**, *28*, 4181. (c) Harada, T.; Sakamoto, K.; Ikemura, N. *Ibid.* **1988**, *29*, 3097.

(5) Tsunoda, T.; Suzuki, M.; Noyori, R. *Tetrahedron Lett.* **1980**, *21*, 1357.

0022-3263/89/1954-2599$01.50/0

Table I. Preparation of Spiroacetals 7 and 8

entry	starting material	reactn condtns temp, °C	reactn condtns time, h	products	yield,[a] % (conversn, %)	ratio 7:8
1	**6a**	−85	44	**7a**, **8a**	80 (86)	1.5:1
2	**6a**	−40	10	**7a**, **8a**	98 (100)	7.0:1
3	**6b**	−85	48	**7b**, **8b**	74 (65)	6.8:1
4	**6b**	−40	22	**7b**, **8b**	96 (100)	2.0:1
5	**6c**	−85	65	**7c**, **8c**	88 (61)	1:4.9
6	**6c**	−40	19	**7c**, **8c**	100 (100)	1:1.2
7	**6d**	−40	51	**7d**, **8d**	85 (100)	3.1:1

[a] Yield refers to isolated yield based on bis(trimethylsilyl ether) **6** consumed.

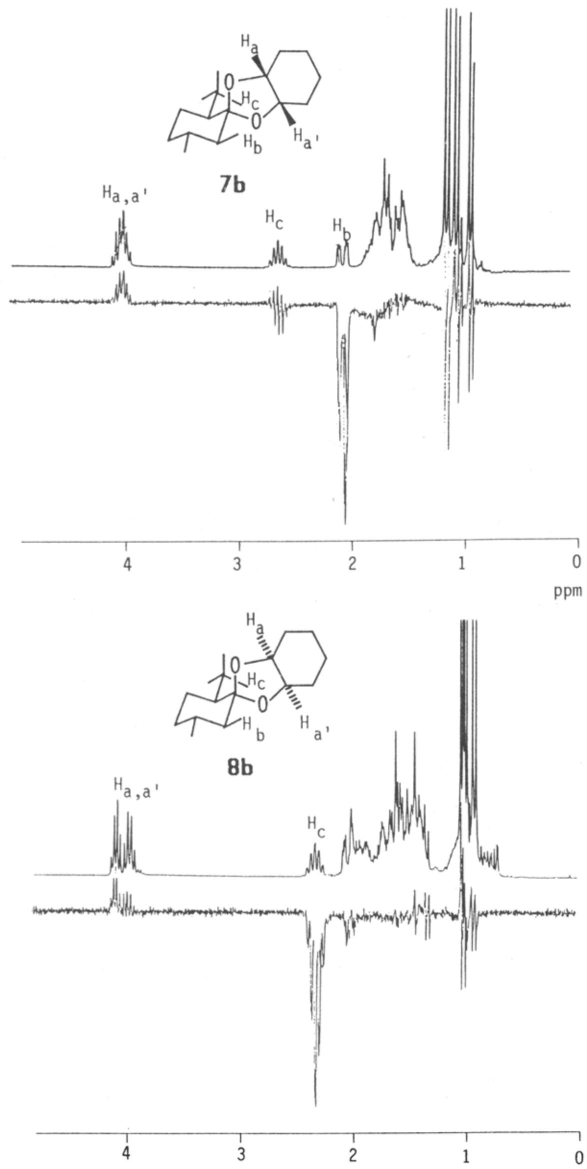


Figure 1. ^{1}H NMR spectra and NOE difference spectra of spiroacetals **7b** and **8b**.

While cyclooctenediol derivative **6d** gave syn isomer **7d** preferentially, the selectivity was reversed in the reaction of saturated analogue **6c** (entries 5–7).

In order to have an insight into factors that govern stereoselectivities in acetalization reactions, we performed the following equilibrium experiments.[6] Treatment of *syn*-**7b** with TMSOTf (20 mol %) in dichloromethane at −40 °C for 22 h gave a 2.0:1 mixture of **7b** and **8b** (75% yield). Since the ratio observed here was exactly the same as that in the acetalization reaction at −40 °C (entry 4), it is deduced that syn isomer **7** and anti isomer **8** are in equilibrium under the acetalization conditions at −40 °C. Results of the isomerization at −85 °C were somewhat contradictory. Starting from either pure **7b** or an equimolar mixture of **7b** and **8b**, the same ratio (**7b**:**8b** = 2.6:1) was observed after 22 h, indicating that they are in equilibrium under these conditions. Therefore, the higher selectivity (6.8:1) observed in the acetalization at −85 °C (entry 3) is at least partly attributed to kinetic control. The presence of unreacted *l*-menthone which can reversibly trap the catalyst TMSOTf may possibly retard the rate of isomerization at −85 °C. Indeed, when a similar isomerization experiment was performed in the presence of *l*-menthone (2 equiv), starting from **7b** (−85 °C, 22 h), a 3.1:1 mixture of **7b** and **8b** was obtained in a quantitative yield.

The stereochemistry of **7a–c** and **8a–c** was determined on the basis of the following observation of NOE in the ^{1}H NMR analysis. As shown in Figure 1, irradiation of the H_b proton of *syn*-**7b**, but not H_c, caused the NOE enhancement of H_a and $H_{a'}$. On the other hand, in *anti*-**8b**, the enhancement of H_a and $H_{a'}$ was observed when isopropyl methine (H_c) was irradiated. Similar results were obtained in **7a,c** and **8a,c**. The structure of **7d** was correlated with saturated analogue **7c** by the hydrogenation reaction (Pd/C). It should be noted that, with a pair of stereoisomers, anti spiroacetals **8a–d** were always eluted faster in silica gel column chromatography and possess a shorter retention time in capillary GLC (PEG 20M) than syn isomers **7a–d** (see Experimental Section).

The titanium tetrachloride promoted ring-cleavage reaction[7] of spiroacetal **7b** proceeded with high stereoselectivity to give **9b** (97% yield) as the sole detectable stereoisomer in 200-MHz ^{1}H NMR analysis (eq 2; $n = 4$). Judging from the stereochemistry of product **9b** at the carbinyl carbon of the cyclohexanediol moiety (vide infra), the less hindered equatorial C–O bond was cleaved selectively as observed in the ring-cleavage reaction of 1,3-dioxane analogue **5**.[4] The stereochemistry of **9b** at C(1) of the neomenthyl moiety was assigned tentatively in analogy with the previous study.[4a,8]

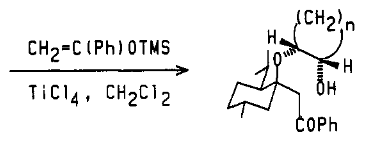
After protection of the hydroxyl group of **9b** as a methoxymethyl (MOM) or tetrahydropyranyl (THP) ether, the (1-benzoylmethyl)neomenthyl group was readily removed under basic conditions to give enantiomerically pure **10b** (>95% ee,[9] 90% overall yield) or **11** (>95% ee,[11]

(6) Hwu, J. R.; Wetzel, J. M. *J. Org. Chem.* **1985**, *50*, 3948.

(7) (a) McNamara, J. M.; Kishi, Y. *J. Am. Chem. Soc.* **1982**, *104*, 7371. (b) Bartlett, P. A.; Johnson, W. S.; Elliott, J. D. *Ibid.* **1983**, *105*, 2088. (c) Johnson, W. S.; Carckett, P. H.; Elliott, J. D.; Jagodzinsky, J. J.; Lindell, S. D.; Nataarjan, S. *Tetrahedron Lett.* **1984**, *25*, 3951 and references cited therein.

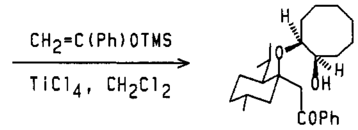
(8) A high equatorial selectivity was reported in the titanium tetrachloride promoted reaction between enol silyl ether and acetals derived from cyclohexanones. Nakamura, E.; Horiguchi, Y.; Shimada, J.; Kuwajima, I. *J. Chem. Soc., Chem. Commun.* **1983**, 796.

(9) The value was determined after the conversion to the corresponding (*R*)-(+)-MTPA ester.[10]

7a,b


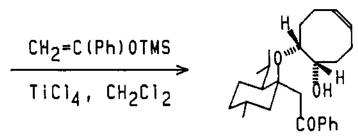
(2)

9a (n=3)
9b (n=4)

8c


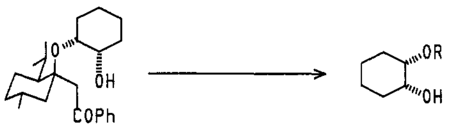
(3)

9c

7d


(4)

9d



(5)

9b

10b; R=MOM
11; R=THP

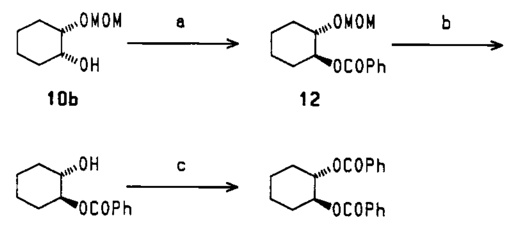
49% overall yield), respectively (eq 5).

In order to determine the absolute stereochemistry of **10b**, this material was transformed into (1*S*,2*S*)-1,2-cyclohexylene dibenzoate (**14**), whose stereochemistry has been clearly determined by utilizing the dibenzoate chirality rule (Scheme II).[12] Thus, *cis*-diol derivative **10b** was converted into trans derivative **12** by utilizing the Mitsunobu reaction.[13] Removal of the MOM group was performed under carefully controlled conditions (Me_3SiBr, molecular sieves 4A)[14] to minimize the racemization of both **12** and **13** under acidic conditions. Dibenzoate **14** obtained after a DCC esterification reaction of **13** showed $[\alpha]^{22}{}_D$ +102° (*c* 0.20, MeOH), which corresponds to 60% ee based on the previously predicted maximum rotation for this compound.[12]

We also examined the correlation of THP ether **11** to (*R*)-1-acetoxycyclohexanone (**15**) (Scheme III). Acetylation of **11** followed by removal of the THP group under weakly acidic conditions and the subsequent Collins oxidation gave **15**, which showed $[\alpha]^{22}{}_D$ +65.7° (*c* 1.11, $CHCl_3$).[15] Ridley et al. have reported $[\alpha]^{20}{}_D$ −85.1° for (*R*)-**15** which was obtained by kinetic resolution of racemic **15** by utilizing yeast reduction.[16] Judging from the highly established nature of the dibenzoate chirality rule, their assignment which was based on a negative Cotton effect in its ORD spectrum[17] is doubtful and ought to be reexamined.

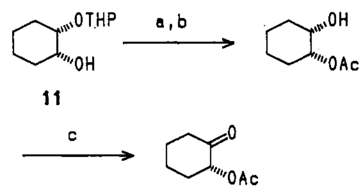
(10) Dale, J. A.; Dull, D. L.; Mosher, H. S. *J. Org. Chem.* **1969**, *34*, 2543.
(11) The value was determined after the conversion to the corresponding (*R*)-(+)-MTPA ester[10] followed by the removal of the THP group.
(12) Yamamoto, Y.; Fushimi, M.; Oda, J.; Inoue, Y. *Agric. Biol. Chem.* **1975**, *39*, 2223.
(13) Mitsunobu, O. *Synthesis* **1981**, 1.
(14) Hanessian, S.; Delorme, D.; Dufresne, Y. *Tetrahedron Lett.* **1984**, *25*, 2515.
(15) Partial racemization probably proceeded when the THP group was removed under acidic conditions.
(16) Crumbie, R. L.; Ridley, D. D.; Simpson, G. W. *J. Chem. Soc., Chem. Commun.* **1977**, 527.
(17) Ridley, D. D., The University of Sydney, personal communication, 1987.

Scheme II[a]



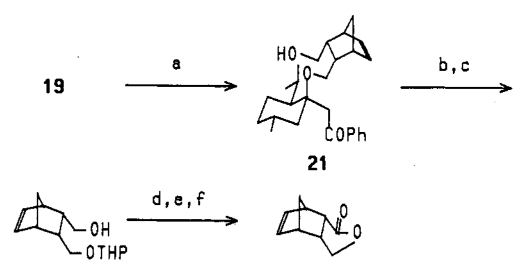
[a] (a) $PhCO_2H$, PPh_3, DEAD, THF, 40%. (b) Me_3SiBr, molecular sieves 4A, CH_2Cl_2, 73%. (c) $PhCO_2H$, DCC, DMAP, CH_2Cl_2, 88%.

Scheme III[a]



[a] (a) Ac_2O, Py, DMAP, 82%. (b) *p*-TsOH, aqueous THF, 74%. (c) CrO_3–Py_2, CH_2Cl_2, 24%.

Scheme IV[a]



[a] (a) CH_2=C(Ph)OTMS, $TiCl_4$, CH_2Cl_2, 86%. (b) DHP, PTSA, CH_2Cl_2. (c) *t*-BuOK, *t*-BuOH, 87%. (d) Swern oxidation. (e) *p*-TsOH, aqueous EtOH. (f) PCC, CH_2Cl_2, 18%.

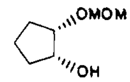
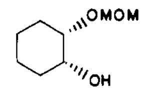
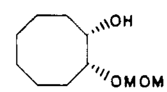
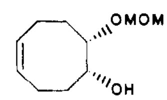
The titanium tetrachloride promoted ring-cleavage reaction of the major isomers **7b**, **8c**, and **7d** also proceeded with high stereoselectivities (>95% de) (eq 2–4), and the resulting ring-cleavage products **9a,c,d** were transformed into the mono-MOM derivatives **10a,c,d** with high optical purities (>95% ee)[9] by a similar procedure. These results are summarized in Table II. It should be noted that the enantiomer of **10a–d** can be prepared by utilizing *d*-menthone in the present reaction sequences.

Enantiodifferentiating Transformation of *cis*-*endo*-5-Norbornen-2,3-ylenebis(methanol) (16). As an application of the present methodology to *meso*-1,4-diols, we examined the enantiodifferentiating transformation of bicyclic diol **16**.[2b,18]

When bis(trimethylsilyl ether) **17** was treated with *l*-menthone in the presence of TMSOTf at temperatures from −85 to 0 °C, tetrahydrofuran derivative **18** was obtained in 31% yield without the formation of the desired spiroacetals (**19** and **20**) (eq 6). However, the acetal exchange reaction of *l*-menthone dimethyl acetal with diol **16** in the presence of molecular sieves 4A and a catalytic amount of *p*-toluenesulfonic acid proceeded effectively to give a mixture of spiroacetals **19** and **20** in the ratio of 6:1

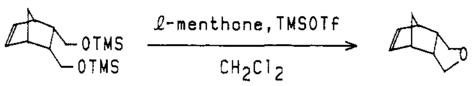
(18) An enantiodifferentiating transformation of *cis*-*endo*-5-norbornen-2,3-ylenebis(acetic acid) was reported: Nagao, T.; Inoue, T.; Fujita, E.; Terada, S.; Shiro, M. *Tetrahedron* **1984**, *40*, 1215.

Table II. Ring-Cleavage Reaction and Transformation to Mono-MOM Alcohol

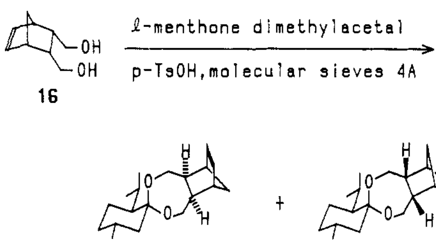
entry	spiroacetal	ring-cleavage product; yield, % (de, %)[a]	mono-MOM alcohol	yield, % (ee, %)[b]
1	**7a**	**9a**; 73 (>95)	 **10a**	75 (>95)
2	**7b**	**9b**; 97 (>95)	 **10b**	90 (>95)
3	**8c**	**9c**; 59 (>95)	 **10c**	52 (>95)
4	**7d**	**9d**; 69 (>95)	 **10d**	79 (>95)

[a] Determined by the 200-MHz ^{1}H NMR measurement. [b] Determined by the 200-MHz ^{1}H NMR analysis of the corresponding MTPA ester.

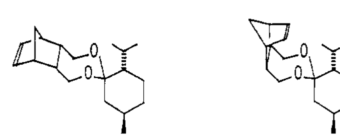
(85%) (eq 7). Their structures were determined tentatively on the basis of a molecular-model analysis. Thus, if the oxepane ring takes a chair-like conformation, the extended conformer of spiroacetal **19** (=**19′**) might be more stable than the folded one **20** (=**20′**).



17 **18** (6)



16 **19** + **20** (7)



19′ **20′**

The ring-cleavage reaction of **19** under the usual conditions proceeded stereoselectively to give keto alcohol **21** (>95% de) in 86% yield (Scheme IV). After protection of the free hydroxyl group as a THP ether, removal of the chiral auxiliary under basic conditions afforded the chiral derivative **22** with 95% ee.[11] The absolute configuration of **22** was determined after conversion of **22** into the known lactone **23** by a three-step sequence as shown in Scheme IV. Thus obtained lactone **23** showed $[\alpha]^{25}_D$ +136° (*c* 1.00, $CHCl_3$), which corresponds to 95% ee based on the maximum rotation value reported.[2b]

In summary, we have shown examples of nonenzymatic enantiodifferentiating transformations of symmetrical 1,2- and 1,4-diols utilizing commercially available *l*-menthone as a chiral auxiliary. It should be noted that the highly stereoselective ring-cleavage reaction is general in various types of spiroacetals derived from *l*-menthone including those possessing 1,3-dioxolane, 1,3-dioxane, and 1,3-dioxepine ring structures.

Experimental Section

Infrared spectra were measured on a JASCO IR-810 grating spectrophotometer. Unless otherwise noted, ^{1}H NMR spectra were measured in $CDCl_3$ as solvent on a Varian XL-200 instrument (200 MHz). Mass spectra were measured on a Hitachi M-80 mass spectrometer. Optical rotations were measured on a Union Giken PM-101 automatic digital polarimeter. Microanalyses were performed by the Microanalysis Center of Kyoto University. GLC analyses were performed by using a PEG-20M (20 m) capillary column. R_f values were obtained via Merck HPTLC plates (silica gel 60 F_{254}). Unless otherwise noted, flash chromatography was performed by using silica gel (Wakogel C-300) as an adsorbent and ethyl acetate in petroleum ether as an eluent, whose concentration is indicated in the parentheses. Medium-pressure column chromatography was performed by using a Merck Lobar column packed with 40–63-μm Li-Chroprep SI 60. Distillations were carried out with a Kugelrohr apparatus.

Bis(trimethylsilyl ether) (**6a–d** and **17**) was prepared by the reaction of the corresponding diol with hexamethyldisilazane (2.0 equiv) in the presence of a catalytic amount of TMSOTf (1 mol %) in THF at 0 °C for 0.5 h (>90% yield).[19] *l*-Menthone was purchased from Norse Laboratories Inc. and used after purification by flash chromatography (1% ether/petroleum ether).

General Procedure for the Preparation of Spiroacetals 7a–d and 8a–d. To a solution of **6a–d** (5.00 mmol) and *l*-menthone (5.50 mmol) in CH_2Cl_2 (4 mL) was added TMSOTf (1.00 mmol) at −85 or −40 °C under a nitrogen atmosphere, and the resulting solution was stirred for the period indicated in Table I at the same temperature. The reaction was quenched by the addition of pyridine (0.2 mL). After addition of water followed by extraction with petroleum ether, the combined organic layer was washed twice with water, dried over sodium sulfate, and concentrated in vacuo. The residue was purified by flash and/or medium-pressure column chromatography (1–2% ether/petroleum ether) to give **7a–d** and **8a–d**.

Spiroacetal 7a: oil; R_f 0.44 (5% ether/hexane); ^{1}H NMR (C_6D_6) δ 0.89 (3 H, d, *J* = 6.5 Hz, CH_3), 1.00–2.03 [20 H, m, including d (3 H, *J* = 7.0 Hz, CH_3) at 1.02 and d (3 H, *J* = 6.9 Hz, CH_3) at 1.12], 2.64 [1 H, d hept, *J* = 1.5 and 7.0 Hz, C*H*(CH_3)$_2$], 4.27 (1 H, t, *J* = 5.6 Hz, CHO), 4.42 (1 H, t, *J* = 5.6 Hz, CHO); IR (liquid film) 1115 (s), 1040 cm^{-1} (s); mass spectrum, *m/z* (relative intensity) 238 (M$^+$, 30), 223 (49), 181 (100), 153 (46), 67 (84); exact mass calcd for $C_{15}H_{26}O_2$ 238.1934, found 238.1939. Anal. Calcd for $C_{15}H_{26}O_2$: C, 75.58; H, 11.00. Found: C, 75.83; H, 11.29.

(19) Use of TMSOTf instead of chlorotrimethylsilane[20] remarkably accelerates the reaction.

(20) Sweeley, C. C.; Bentley, R.; Makita, M.; Wells, W. W. *J. Am. Chem. Soc.* **1963**, *85*, 2497.

Spiroacetal 8a: oil; R_f 0.47 (5% ether/hexane); ^{1}H NMR (C_6D_6) δ 0.89 (3 H, d, J = 6.4 Hz, CH_3), 1.01 (6 H, d, J = 6.9 Hz, 2 CH_3), 1.07–2.00 (14 H, m), 2.15 [1 H, d hept, J = 1.6 and 7.0 Hz, $CH(CH_3)_2$], 3.48 (2 H, m, 2 CHO); IR (liquid film) 1085 (s), 1010 cm^{-1} (s); mass spectrum, m/z (relative intensity) 238 (M^+, 8), 223 (6), 181 (4), 153 (100), 67 (47); exact mass calcd for $C_{15}H_{26}O_2$ 238.1934, found 238.1927. Anal. Calcd for $C_{15}H_{26}O_2$: C, 75.58; H, 11.00. Found: C, 75.62; H, 11.17.

Spiroacetal 7b: oil; R_f 0.39 (5% ether/hexane); ^{1}H NMR (C_6D_6) δ 0.89 (d, J = 6.4 Hz), 1.01 (1 H, t, J = 2.8 Hz), 1.04 (3 H, d, J = 7.0 Hz), 1.14 (3 H, d, J = 7.0 Hz), 1.35–1.89 (14 H, m), 2.05 (1 H, ddd, J = 2.0, 3.4, and 13.0 Hz), 2.64 (1 H, d hept, J = 1.6 and 7.0 Hz), 3.88–4.08 (2 H, m); IR (liquid film) 1115 (s), 1095 cm^{-1} (s); mass spectrum, m/z (relative intensity) 252 (M^+, 18), 237 (46), 195 (85), 167 (48), 81 (100); exact mass calcd for $C_{16}H_{28}O_2$ 252.2090, found 252.2090.

Spiroacetal 8b: oil; R_f 0.44 (5% ether/hexane); ^{1}H NMR (C_6D_6) δ 0.90 (3 H, d, J = 6.5 Hz), 0.96–1.12 [8 H, m, including d (3 H, J = 7.0 Hz) at 0.99 and d (3 H, J = 6.9 Hz) at 1.00], 1.29–2.09 (14 H, m), 2.32 (1 H, d hept, J = 1.7 and 7.0 Hz), 3.95 (1 H, q, J = 6.1 Hz), 4.08 (1 H, q, J = 6.1 Hz); IR (liquid film) 1115 (s), 1095 cm^{-1} (s); mass spectrum, m/z (relative intensity) 252 (M^+, 10), 237 (6), 167 (100), 81 (45); exact mass calcd for $C_{16}H_{28}O_2$ 252.2090, found 252.2084.

Spiroacetal 7c: oil; R_f 0.50 (5% ether/hexane); ^{1}H NMR (C_6D_6) δ 0.8–2.0 [28 H, m, including d (3 H, J = 6.6 Hz) at 0.93, d (3 H, J = 7.1 Hz) at 1.07, and d (3 H, J = 6.9 Hz) at 1.16], 2.07 (1 H, ddd, J = 2.0, 3.5, and 13.0 Hz), 3.94–4.16 (2 H, m); IR (liquid film) 1110 (s), 1090 (s), 1035 (s) cm^{-1}; mass spectrum, m/z (relative intensity) 280 (M^+, 61), 265 (56), 223 (100), 195 (85), 109 (32); exact mass calcd for $C_{18}H_{32}O_2$ 280.2404, found 280.2396.

Spiroacetal 8c: oil; R_f 0.51 (5% ether/hexane); ^{1}H NMR (C_6D_6) δ 0.92 (3 H, d, J = 6.5 Hz), 1.00–2.05 [26 H, m, including d (3 H, J = 7.0 Hz) at 1.08], 2.38 (1 H, d hept, J = 1.8 and 7.0 Hz), 4.13 (2 H, m); IR (liquid film) 1115 (s), 1040 (s), 1015 cm^{-1} (s); mass spectrum, m/z (relative intensity) 280 (M^+, 10), 265 (9), 223 (10), 195 (100), 109 (16); exact mass calcd for $C_{18}H_{32}O_2$ 280.2404, found 280.2395.

Spiroacetal 7d: oil; R_f 0.46 (5% ether/hexane); ^{1}H NMR (C_6D_6) δ 0.89 (3 H, d, J = 6.4 Hz), 0.97 (1 H, t, J = 13.4 Hz), 1.03 (3 H, d, J = 7.0 Hz), 1.10 (3 H, d, J = 7.0 Hz), 1.37–2.28 (15 H, m), 2.53 (1 H, d hept, J = 1.6 and 7.0 Hz), 4.10–4.36 (2 H, m), 5.51 (2 H, m); IR (liquid film) 1115 (s), 1090 cm^{-1} (s); mass spectrum, m/z (relative intensity) 278 (M^+, 48), 263 (30), 221 (52), 193 (49), 139 (23), 97 (100), 69 (81); exact mass calcd for $C_{18}H_{30}O_2$ 278.2247, found 278.2246.

Spiroacetal 8d: oil; R_f 0.50 (5% ether/hexane); ^{1}H NMR (C_6D_6) δ 0.83–1.09 [11 H, m, including d (3 H, J = 6.6 Hz) at 0.92, d (3 H, J = 6.9 Hz) at 1.01, and d (3 H, J = 6.7 Hz) at 1.05], 1.20–2.27 (15 H, m), 4.33 (2 H, m), 5.44 (2 H, m); IR (liquid film) 1115 (s), 1100 cm^{-1} (s); mass spectrum, m/z (relative intensity) 278 (M^+, 14), 263 (3), 193 (70), 139 (3), 69 (100); exact mass calcd for $C_{18}H_{30}O_2$ 278.2247, found 278.2250.

Equilibrium Experiments between 7b and 8b. To a solution of **7b** (58.1 mg, 0.230 mmol) in CH_2Cl_2 (0.14 mL) was added 9 μL (0.046 mmol) of TMSOTf at −40 °C, and the resulting mixture was stirred at −40 °C for 22 h. After a workup similar to that described in the preparation of spiroacetals **7** and **8**, purification by flash chromatography (1% ether/petroleum ether) gave a mixture of **7b** and **8b** (43.8 mg, 75% yield), and the product ratio **7b**:**8b** was determined to be 2.0:1 by a GLC analysis. Other equilibrium experiments were performed by similar procedures.

Hydrogenation of Spiroacetal 7d. A mixture of **7d** (10.9 mg, 0.0391 mmol) and 10% Pd/C (11.0 mg) in 0.5 mL of ethanol was stirred under a hydrogen atmosphere (1 atm) at room temperature for 16 h. The usual workup followed by flash chromatography (1% ether/petroleum ether) gave **7c** (10.4 mg, 95%).

General Procedure for the Ring-Cleavage Reaction of Spiroacetals 7a, 7b, 7d, and 8c. To a solution of the spiroacetal (1.00 mmol) and acetophenone enol trimethylsilyl ether (1.05 mmol) in CH_2Cl_2 (30 mL) was added $TiCl_4$ (1.05 mmol, 1 M solution in CH_2Cl_2) at −85 °C, and the resulting yellow solution was stirred at the same temperature for 1 h. After the addition of pyridine or triethylamine (0.1 mL), the mixture was diluted with petroleum ether, poured into brine, and extracted twice with ethyl acetate. The extract was washed with aqueous $NaHCO_3$, dried over sodium sulfate, and concentrated in vacuo to give a crude oil, from which **9** was isolated by flash chromatography (5–20%).

Ring-cleavage product 9a: oil; ^{1}H NMR δ 0.68 (3 H, d, J = 6.9 Hz, CH_3), 0.82 (3 H, d, J = 6.0 Hz, CH_3), 0.89 (3 H, d, J = 6.8 Hz, CH_3), 1.33–1.90 (14 H, m), 1.95 [1 H, hept, J = 6.8 Hz, $CH(CH_3)_2$], 2.64 (1 H, d, J = 1.8 Hz, OH), 3.04 (1 H, d, J = 15.5 Hz, CH_2COPh), 3.57 (1 H, d, J = 15.5 Hz, CH_2COPh), 4.00 (2 H, m, 2 CHO), 7.46 (3 H, m, Ar), 7.90 (2 H, m, Ar); IR (liquid film) 3550 (br), 1690 (s), 1075 (s), 1005 (s), 755 (s), 690 cm^{-1} (s); mass spectrum, m/z (relative intensity) 358 (M^+, <1), 340 (2), 257 (37), 137 (76), 105 (100); exact mass calcd for $C_{23}H_{34}O_3$ 358.2909, found 358.2912.

Ring-cleavage product 9b: oil; ^{1}H NMR δ 0.66 (3 H, d, J = 6.8 Hz), 0.83 (3 H, d, J = 6.0 Hz), 0.92 (3 H, d, J = 6.9 Hz), 1.18–1.90 (16 H, m), 1.94 (1 H, br hept, J = ~7 Hz), 2.25 (1 H, br d, J = 3.6 Hz), 3.07 (1 H, d, J = 15.4 Hz), 3.59 (1 H, d, J = 15.3 Hz), 3.77 (2 H, m), 7.50 (3 H, m), 7.91 (2 H, m); IR (liquid film) 3575 (br), 1690 (s), 1055 (s), 1000 (s), 755 (s), 690 cm^{-1} (s); mass spectrum, m/z (relative intensity) 372 (M^+, <1), 189 (18), 137 (43), 105 (100); exact mass calcd for $C_{24}H_{36}O_3$ 372.2666, found 372.2654.

Ring-cleavage product 9c: oil; ^{1}H NMR δ 0.70 (3 H, d, J = 6.9 Hz), 0.83 (3 H, d, J = 6.1 Hz), 0.88 (3 H, d, J = 6.9 Hz), 1.22–1.89 (19 H, m), 1.98 (1 H, br hept, J = ~7 Hz), 2.17 (1 H, m), 2.95 (1 H, br s), 3.04 (1 H, d, J = 15.6 Hz), 3.64 (1 H, d, J = 15.6 Hz), 3.82 (2 H, m), 7.50 (3 H, m), 7.91 (2 H, m); IR (liquid film) 3560 (br), 1690 (s), 1030 (s), 1000 (s), 750 (s), 690 cm^{-1} (s); mass spectrum, m/z (relative intensity) 275 ($M^+ - C_8H_{13}O$, 6), 257 (50), 137 (61), 105 (100).

Ring-cleavage product 9d: oil; ^{1}H NMR δ 0.68 (3 H, d, J = 6.9 Hz), 0.80 (3 H, d, J = 6.2 Hz), 0.91 (3 H, d, J = 6.9 Hz), 1.35–2.17 (16 H, m), 3.66 (2 H, m), 3.18 (1 H, d, J = 15.8 Hz), 3.57 (1 H, d, J = 15.8 Hz), 4.02 (2 H, m), 5.66 (2 H, m), 7.50 (3 H, m), 7.94 (2 H, m); IR (liquid film) 3560 (br), 1690 (s), 1030 (s), 1000 (s), 755 (s), 725 (s), 690 cm^{-1} (s); mass spectrum, m/z (relative intensity) 398 (M^+, <1), 380 (2), 257 (46), 137 (61), 105 (100); exact mass calcd for $C_{26}H_{38}O_3$ 398.2822, found 398.2816.

General Procedure for the Conversion of 9a–d to Mono-MOM Derivatives 10a–d. To a solution of **9a–d** (1.00 mmol) and ethyldiisopropylamine (3.00 mmol) in CH_2Cl_2 (2 mL) was added chloromethyl methyl ether (2.00 mmol), and the mixture was stirred at room temperature for 2–14 h. After aqueous workup (aqueous $NaHCO_3$/ether), the crude mixture was purified by flash chromatography (2–3%) to give MOM ether derivatives of **9a–d**. This material was treated by a 0.5 N solution of *t*-BuOK (3 equiv) in *t*-BuOH at 60 °C for 2 h. The usual workup (brine/ethyl acetate) and purification by flash chromatography (4–20%) gave **10a–d**. Optical purities of these materials were analyzed by ^{1}H NMR in the form of the corresponding (*R*)-(+)-MTPA ester derivatives. Racemic **10a,b,d** were prepared by the reaction of the corresponding 1,2-cycloalkanediol with 0.5 equiv of chloromethyl methyl ether in the presence of ethyldiisopropylamine (0.75 equiv) and were converted into the corresponding diastereomixture of MTPA esters.

(1*S*,2*R*)-2-(Methoxymethoxy)cyclopentanol (10a): bp 150 °C/78 mmHg; ^{1}H NMR (C_6D_6) δ 1.49–1.87 (7 H, m), 3.09 (1 H, s, CH_3O), 3.66 (1 H, m, CHO), 3.96 (1 H, m, CHO), 4.41 (2 H, m, OCH_2O); IR (liquid film) 3470 (br), 1150 (s), 1110 (s), 1055 cm^{-1} (s); mass spectrum (CI, isobutane), m/z (relative intensity) 147 MH^+, 1, 115 (26), 101 (100). Anal. Calcd for $C_7H_{14}O_3$: C, 57.51; H, 9.65. Found: C, 56.99; H, 9.73.

(1*S*,2*R*)-2-(Methoxymethoxy)cyclopentyl (*R*)-α-methoxy-α-(trifluoromethyl)phenylacetate: oil; ^{1}H NMR (C_6D_6) δ 1.50–2.05 (6 H, m), 3.33 (3 H, s), 3.60 (3 H, q, J = 1.2 Hz), 4.11 (1 H, m), 4.58 (1 H, d, J = 6.7 Hz), 4.69 (1 H, d, J = 6.7 Hz), 5.40 (1 H, m), 7.40 (3 H, m), 7.64 (2 H, m).

(1*S,2*R**)-2-(Methoxymethoxy)cyclopentyl (*R*)-α-methoxy-α-(trifluoromethyl)phenylacetate**: oil; ^{1}H NMR (C_6D_6) δ 1.50–2.05 (6 H, m), 3.27 and 3.33 (3 H, s), 3.55 and 3.60 (3 H, q, J = 1.2 Hz), 4.11 (1 H, m), 4.05 and 4.58 (1 H, d, J = 6.8 and 6.7 Hz, respectively), 4.60 and 4.69 (1 H, d, J = 6.8 and 6.7 Hz, respectively), 5.40 (1 H, m), 7.40 (3 H, m), 7.64 (2 H, m).

(1*S*,2*R*)-2-(Methoxymethoxy)cyclohexanol (10b): bp 150 °C/55 mmHg; ^{1}H NMR δ 0.95–2.07 (8 H, m), 2.54 (1 H, d, *J* = 4.6 Hz), 3.39 (3 H, s), 3.51–3.39 (2 H, m), 4.72 (2 H, s); IR (liquid film) 3460 (br), 1150 (s), 1105 (s), 1035 cm^{-1} (s); mass spectrum (CI, isobutane, *m/z* (relative intensity) 161 (MH$^+$, 2), 115 (19), 97 (53), 45 (100). Anal. Calcd for $C_8H_{16}O_3$: C, 59.98; H, 10.07. Found: C, 60.17; H, 10.28.

(1*S*,2*R*)-2-(Methoxymethoxy)cyclohexyl (*R*)-α-methoxy-α-(trifluoromethyl)phenylacetate: ^{1}H NMR δ 1.20–2.10 (8 H, m), 3.34 (3 H, s), 3.58 (3 H, q, *J* = 1.2 Hz), 3.71 (1 H, m), 4.62 (1 H, d, *J* = 6.9 Hz), 5.41 (1 H, m), 7.38 (3 H, m), 7.50 (2 H, m).

(1*S,2*R**)-2-(Methoxymethoxy)cyclohexyl (*R*)-α-methoxy-α-(trifluoromethyl)phenylacetate**: ^{1}H NMR δ 1.20–2.10 (8 H, m), 3.34 and 3.27 (3 H, s), 3.55 and 3.58 (3 H, q, *J* = 1.2 Hz), 3.62 and 3.71 (1 H, m), 4.52 and 4.62 (1 H, d, *J* = 6.8 and 6.9 Hz, respectively), 4.58 and 4.69 (1 H, d, *J* = 6.8 and 6.9 Hz, respectively), 5.35 and 5.41 (1 H, m), 7.38 (3 H, m), 7.50 (2 H, m).

(1*R*,2*S*)-2-(Methoxymethoxy)cyclooctanol (10c): bp 175 °C/37 mmHg; ^{1}H NMR δ 1.34–2.08 (12 H, m), 3.39 (3 H, s), 3.72–3.95 (2 H, m), 4.68 (2 H, br s); IR (liquid film) 3460 (br), 1150 (s), 1095 (s), 1035 cm^{-1} (s); mass spectrum (CI, isobutane), *m/z* (relative intensity) 189 (MH$^+$, 1.5), 167 (24), 143 (45), 45 (100). Anal. Calcd for $C_{10}H_{20}O_3$: C, 63.79; H, 10.71. Found: C, 63.59; H, 10.96.

(1*R*,2*S*)-2-(Methoxymethoxy)cyclooctyl (*R*)-α-methoxy-α-(trifluoromethyl)phenylacetate: oil; ^{1}H NMR δ 1.38–2.31 (12 H, m), 3.26 (3 H, m), 3.55 (3 H, q, *J* = 1.2 Hz), 3.82 (1 H, br, d, *J* = 9.2 Hz), 4.46 (1 H, d, *J* = 6.9 Hz), 4.52 (1 H, d, *J* = 6.9 Hz), 5.38 (1 H, br d, *J* = 9.2 Hz), 7.39 (3 H, m), 7.52 (2 H, m).

(1*S*,2*R*)-2-(Methoxymethoxy)cyclooct-5-enol (10d): bp 170 °C/37 mmHg; ^{1}H NMR δ 1.41–2.24 (6 H, m), 2.28–2.77 (3 H, m), 3.39 (3 H, m), 3.69–4.20 (2 H, m), 4.66 (2 H, s), 5.63 (2 H, t, *J* = 4.8 Hz); IR (liquid film) 3460 (br), 1150 (s), 1040 (s), 730 cm^{-1} (s). Anal. Calcd for $C_{10}H_{18}O_3$: C, 64.49; H, 9.74. Found: C, 64.37; H, 9.97.

(1*S*,2*R*)-2-(Methoxymethoxy)cyclooct-5-enyl (*R*)-α-methoxy-α-(trifluoromethyl)phenylacetate: oil; ^{1}H NMR δ 1.46–2.14 (6 H, m), 2.48 (2 H, m), 3.32 (3 H, s), 3.55 (3 H, q, *J* = 1.0 Hz), 3.98 (1 H, dd, *J* = 4.0 and 7.7 Hz), 4.63 (2 H, AB, *J* = 7.0 Hz), 5.37 (1 H, dd, *J* = 5.3 and 8.6 Hz), 5.67 (2 H, m), 7.39 (3 H, m), 7.54 (2 H, m).

(1*S,2*R**)-2-(Methoxymethoxy)cyclooct-5-enyl (*R*)-α-methoxy-α-(trifluoromethyl)phenylacetate**: oil; ^{1}H NMR δ 1.46–2.14 (6 H, m), 2.48 (2 H, m), 3.24 and 3.32 (3 H, s), 3.55 (3 H, m), 3.90 and 3.98 (1 H, dd, *J* = 3.8 and 6.9 Hz, and 4.0 and 7.6 Hz, respectively), 4.53 and 4.63 (1 H, AB, *J* = 6.8 and 7.0 Hz, respectively), 5.37 (1 H, m), 5.67 (2 H, m), 7.39 (3 H, m), 7.54 (2 H, m).

(1*S*,2*S*)-1,2-Cyclohexylene Dibenzoate (14). To a solution of 247.4 mg (1.54 mmol) for **10b**, 190 mg (1.50 mmol) of benzoic acid, and 610 mg (2.30 mmol) of triphenylphosphine in THF (3 mL) was added a THF solution of diethyl azodicarboxylate (DEAD) (1.2 M, 2 mL, 2.3 mmol), and the resulting mixture was stirred at room temperature for 3 h. After concentration in vacuo, the crude mixture was purified by flash chromatography to give 163.0 mg (40%) of (1*S*,2*S*)-2-(methoxymethoxy)cyclohexyl benzoate (**12**) together with the recovery of **10b** (40%). To a mixture of 161.1 mg (0.609 mmol) of the benzoate and 200 mg of ground molecular sieves in CH_2Cl_2 (4 mL) was added 320 μL (2.44 mmol) of bromotrimethylsilane at −30 °C, and the total mixture was stirred at the same temperature for 2 h. Aqueous workup (aqueous $NaHCO_3$/ethyl acetate) followed by flash chromatography (10%) gave 110.5 mg (73%) of hydroxy benzoate **13**: ^{1}H NMR (60 MHz) δ 1.2–2.3 (9 H, m), 3.77 (1 H, m), 4.87 (1 H, m), 7.50 (3 H, m), 7.95 (2 H, m); IR (liquid film) 3560 (br), 1695 (s), 1285 (s), 715 cm^{-1} (s).

Hydroxy benzoate **13** (115.2 mg, 0.523 mmol) was dissolved in CH_2Cl_2 (1 mL) containing 96 mg (0.786 mmol) of benzoic acid. To the resulting solution were added successively 183 mg (0.888 mmol) of dicyclohexylcarbodiimide (DCC) and 4-(*N*,*N*-dimethylamino)pyridine (DMAP) (100 mg, 0.819 mmol) at room temperature. After being stirred for 1 h, the mixture was diluted with ether and filtered through a short column packed with Celite. The filtrate was washed with brine, dried over sodium sulfate, and purified by flash chromatography (2–5%) to give 149.4 mg (88%) of dibenzoate **14**: $[\alpha]^{22}_D$ +102° (*c* 0.2, MeOH) [lit.[12] $[\alpha]^{24}_D$ +125° (*c* 0.2, MeOH) (optical purity was estimated to be 73%)];[12] ^{1}H NMR δ 1.37–1.73 (6 H, m), 1.83 (2 H, m), 2.24 (2 H, m), 5.25 (2 H, m), 7.40 (6 H, m), 7.98 (4 H, m); IR (KBr) 1720 (s), 1110 (s), 715 cm^{-1} (s).

(1*R*,2*S*)-2-(Tetrahydropyranyloxy)cyclohexanol (11). A CH_2Cl_2 (5 mL) solution of **9b** (49.9 mg, 0.134 mmol), dihydropyran (0.20 mmol), and pyridinium *p*-toluenesulfonate (PTS) (0.026 mmol) was stirred at room temperature for 40 h. After the usual workup, followed by flash chromatography (3%), the product was treated with *t*-BuOK in *t*-BuOH at 60 °C for 2 h as described above to give 13.2 mg (49% overall yield) of **11**: oil; ^{1}H NMR δ 1.15–1.95 (15 H, m), 3.48 (1 H, m), 3.64–4.00 (3 H, m), 4.58 and 4.74 (1 H, m); IR (liquid film) 3440 (br), 1120 (s), 1075 (s), 1025 cm^{-1} (s); mass spectrum, *m/z* (relative intensity) 182 ($M^+ - H_2O$, 0.5), 99 (16), 85 (100). The optical purity of **11** was analyzed by ^{1}H NMR after conversion to the corresponding (R)-(+)-MTPA ester derivative followed by removal of the THP group. **(1*R*,2*S*)-2-Hydroxycyclohexyl (*R*)-α-methoxy-α-(trifluoromethyl)phenylacetate**: oil; ^{1}H NMR δ 1.30–2.03 (9 H, m), 3.54 (3 H, q, *J* = 1.3 Hz), 3.84 (1 H, m), 5.23 (1 H, t, d, *J* = 2.8 and 6.6 Hz), 7.42 (3 H, m), 7.57 (2 H, m). **(1*R**,2*S**)-2-Hydroxycyclohexyl (*R*)-α-methoxy-α-(trifluoromethyl)phenylacetate**: oil; ^{1}H NMR 1.30–2.03 (9 H, m), 3.54 and 3.57 (3 H, q, *J* = 1.3 Hz), 3.84 (1 H, m), 5.23 (1 H, m), 7.42 (3 H, m), 7.57 (2 H, m).

(*R*)-2-Acetoxycyclohexanone (15). A mixture of 111.3 mg (0.556 mmol) of **11**, 15 mg of DMAP, Ac_2O (0.10 mL), and pyridine (1.0 mL) was stirred at room temperature for 15 min. The usual workup followed by purification by flash chromatography (5%) gave 110.1 mg (82%) of the acetyl derivative of **11**. This material (108.5 mg) was dissolved in 30% aqueous THF containing 30 mg of PTS, and the mixture was stirred at room temperature for 5 h. After the usual workup followed by purification by short flash chromatography (20–50%) to remove unreacted starting material (47.5 mg), crude (1*S*,2*R*)-2-acetoxycyclohexanol was treated with Collins' reagent prepared by the reaction of 358 mg (3.58 mmol) of CrO_3 and 0.58 mL (7.2 mmol) of pyridine in CH_2Cl_2 (9 mL) at room temperature for 1 h. The usual workup followed by flash chromatography (20% ether/petroleum ether) gave 11.1 mg (17% overall yield) of (*R*)-**15**:[16] $[\alpha]^{22}_D$ +65.7° (*c* 1.11, $CHCl_3$); ^{1}H NMR δ 1.50–2.60 [9 H, m, including s (3 H) at 2.14], 5.16 (1 H, d, *J* = 6.2 and 11.2 Hz); IR (KBr) 1750 (s), 1720 (s), 1230 (s), 1075 cm^{-1} (s).

Reaction of Bis(trimethylsilyl ether) 17 with *l*-Menthone. **17** (2.09 g, 6.98 mmol) was treated with *l*-menthone (1.19 g, 7.71 mmol) in CH_2Cl_2 at −85 °C for 2 h and then at 0 °C for 3 h. usual workup followed by flash chromatography (5%, ether/petroleum ether) gave **18**:[21] ^{1}H NMR δ 1.41 (1 H, d, *J* = 8.0 Hz), 1.51 (1 H, d, *J* = 8.0 Hz), 2.85 (4 H, m), 3.50 (4 H, m), 6.18 (2 H, m).

Spiroacetals 19 and 20. A mixture of *l*-menthone dimethyl acetal (3.18 g, 15.9 mmol), diol **16**[16] (9.79 mg, 4.89 mmol), ground molecular sieves 4A (20 mg), and *p*-toluenesulfonic acid (100 mg) was stirred at 80 °C for 20 h. After dilution with petroleum ether, the mixture was filtered, and the filtrate was washed with aqueous $NaHCO_3$. Concentration of the dried extracts followed by purification by flash chromatography (3%, ether/petroleum ether) gave a mixture of **19** and **20** (1.21 g, 85%), which was separated by medium-pressure column chromatography. **19**: oil; R_f 0.50 (5% ether/hexane); ^{1}H NMR (C_6D_6) δ 0.68 (1 H, dd, *J* = 12.4 and 13.6 Hz), 0.87 (3 H, d, *J* = 6.6 Hz, CH_3), 1.13 (3 H, d, *J* = 7.1 Hz, CH_3), 1.25 (3 H, d, *J* = 7.0 Hz, CH_3), 1.35–1.78 (8 H, m), 2.38 (2 H, br s, 2 CH), 2.55 (3 H, m), 2.87 [1 H, d hept, *J* = 2.0 and 7.2 Hz, $CH(CH_3)_2$], 3.25 (1 H, t, *J* = 12.3 Hz, CH_2O), 3.46 (1 H, t, *J* = 12.2 Hz, CH_2O), 3.57 (2 H, m, CH_2O), 5.81 (2 H, m, 2 CH=); IR (liquid film) 3060 (m), 1115 (s), 735 cm^{-1} (s); mass spectrum, *m/z* (relative intensity) 290 (M$^+$, 30), 275 (7), 205 (18), 119 (100), 91 (80); exact mass calcd for $C_{19}H_{30}O_2$ 290.2247, found 290.2251. Anal. Calcd for $C_{19}H_{30}O_2$: C, 78.57; H, 10.41. Found: C, 78.35; H, 10.62. **20**: oil; R_f 0.46 (5% ether/hexane); ^{1}H NMR (C_6D_6) δ 1.00 (3 H, d, *J* = 6.9 Hz, CH_3), 1.17 (3 H, d, *J* = 6.9 Hz, CH_3), 1.22 (3 H, d, *J* = 6.9 Hz, CH_3), 1.29–1.96 (9 H, m), 1.39 (2 H, br s), 1.56 (4 H, m), 3.34 (2 H, m, CH_2O), 3.60 (2 H, m, CH_2O), 5.86 (2 H, br s, 2 CH=); IR (KBr) 3055 (m), 1105 (s), 730 cm^{-1} (s);

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mass spectrum, m/z (relative intensity) 290 (M^+, 25), 275 (7), 205 (28), 119 (100), 91 (82); exact mass calcd for $C_{19}H_{30}O_2$ 290.2247, found 290.2244.

Ring-Cleavage Product 21. A ring-cleavage reaction was performed, starting from 157.8 mg (0.543 mmol) of **19**, by a procedure similar to the one described above. Flash chromatography (20–25%) gave 191.2 mg (86%) of **21**: oil; ^1H NMR δ 0.84 (3 H, d, J = 6.4 Hz, CH_3), 0.89 (3 H, d, J = 6.0 Hz, CH_3), 1.10–1.95 [13 H, m, including d (3 H, J = 6.4 Hz, CH_3) at 1.15], 2.05–2.56 (4 H, m), 2.80 (1 H, br s), 2.93 (1 H, d, J = 15.6 Hz, CH_2COPh), 2.93 (1 H, br s), 3.04 (1 H, m, CH_2O), 3.36 (3 H, m, CH_2O), 3.57 (1 H, d, J = 15.6 Hz, CH_2COPh), 6.09 (2 H, m, 2 CH=), 7.13 (3 H, m, Ar), 7.99 (2 H, m, Ar); IR (liquid film) 3560 (br) 1680 (s), 1020 (s), 1000 (s), 750 (s), 685 cm^{-1} (s); mass spectrum, 410 (M^+, <1), 257 (48), 137 (60), 105 (100); exact mass calcd for $C_{27}H_{38}O_3$ 410.2822, found 410.2821.

Mono-THP Derivative 22. This material was prepared, starting from **21**, in 87% overall yield by a procedure similar to the one described in the preparation of **11**. **22**: ^1H NMR δ 1.15–1.80 (9 H, m), 2.54 (2 H, m), 2.82 (2 H, m), 3.08–3.85 (6 H, m), 4.56 (1 H, br s), 6.03 (2 H, br s); IR (liquid film) 3410 (br), 3060 (m), 1030 (s), 730 cm^{-1} (s). The optical purity of **22** was also determined after the conversion of **22** into the corresponding (R)-(+)-MTPA ester followed by the removal of the THP group. **(R)-MTPA ester**: oil; ^1H NMR δ 1.30 (1 H, br d, J = 8.4 Hz), 1.48 (1 H, t, d, J = 1.7 and 8.4 Hz), 2.32–2.63 (2 H, m), 2.80 (1 H, br s), 2.91 (1 H, br s), 3.35 (2 H, d, J = 7.3 Hz), 3.53 (3 H, q, J = 1.2 Hz), 4.04 (1 H, dd, J = 6.4 and 10.6 Hz), 4.18 (1 H, dd, J = 9.4 and 10.6 Hz), 6.08 (1 H, dd, J = 3.2 and 5.6 Hz), 6.16 (1 H, dd, J = 3.2 and 5.6 Hz), 7.42 (3 H, m), 7.50 (3 H, m). **Mono (R)-MTPA ester derived from diol 16**: oil; ^1H NMR δ 1.30 (1 H, m), 1.48 (1 H, m), 2.3–2.6 (2 H, m), 2.84 (1 H, br), 2.91 (1 H, br s), 3.33 and 3.35 [2 H, br d (J = 7.4 Hz) and d, respectively], 3.53 and 3.55 (3 H, q, J = 1.2 Hz), 4.0–4.25 (2 H, m), 6.12 (2 H, m), 7.42 (3 H, m), 7.50 (3 H, m).

(2S,3R)-Lactone 23. To a solution of oxalyl chloride (98 μL, 1.12 mmol) in CH_2Cl_2 (1 mL) were added a CH_2Cl_2 solution (0.27 mL) of dimethyl sulfoxide (196 mg, 78.1 mmol) and a CH_2Cl_2 solution (0.27 mL) of **22** (110.2 mg, 0.426 mmol) at –75 °C, and the mixture was stirred for 20 min. To this was added 330 μL (2.37 mmol) of triethylamine, and then the mixture was stirred at room temperature for 1 h. After aqueous workup (brine/CH_2Cl_2), the crude material was dissolved in aqueous 30% EtOH (10 mL) containing 23 mg of PTS and the mixture was heated at 50 °C for 40 min. After aqueous workup (brine/ethyl acetate) followed by concentration in vacuo, the crude mixture was treated with pyridinium chlorochromate (150 mg, 0.70 mmol) in CH_2Cl_2 (3 mL) at room temperature for 3 h. After the usual workup, purification by flash chromatography (50%) gave 11.5 mg (18% overall yield) of **23**: oil; $[\alpha]^{25}_D$ +136° (c 1.00, $CHCl_3$) [lit.[2b] $[\alpha]^{25}_D$ +143.2 (c 5.2, $CHCl_3$)]; ^1H NMR ($CDCl_3$) δ 1.45 (1 H, br d, J = 8.4 Hz), 1.64 (1 H, br d, J = 8.4 Hz), 3.00–3.37 (4 H, m), 3.78 (1 H, dd, J = 3.1 and 9.5 Hz), 4.29 (1 H, dd, J = 8.2 and 9.5 Hz), 6.30 (2 H, br s); IR (liquid film) 1750 (s), 1175 (s), 1045 (s), 1000 cm^{-1} (s).

Registry No. 6a, 41235-26-1; **6b**, 39789-20-3; **6c**, 119972-72-4; **6d**, 119972-73-5; **7a**, 119972-74-6; **7b**, 119972-75-7; **7c**, 119972-76-8; **7d**, 119972-77-9; **8a**, 120053-10-3; **8b**, 120053-11-4; **8c**, 120053-12-5; **8d**, 120053-13-6; **9a**, 119972-78-0; **9b**, 119972-79-1; **9c**, 119972-80-4; **9d**, 119972-81-5; **10a**, 120053-14-7; **10b**, 120053-15-8; **10c**, 119972-82-6; **10d**, 119972-83-7; **11**, 120053-19-2; **11** acetate, 119972-90-6; **12**, 119972-88-2; **13**, 120053-18-1; **14**, 58502-00-4; (R)-**15**, 64363-90-2; **16**, 699-97-8; **16** (mono (R)-MTPA ester), 119972-97-3; **17**, 119972-91-7; **18**, 43187-61-7; **19**, 119972-92-8; **20**, 120142-40-7; **21**, 119972-94-0; **22**, 119972-95-1; **22** ((R)-MTPA ester), 119972-96-2; **23**, 95340-88-8; l-menthone, 14073-97-3; acetophenone enol, 13735-81-4; (1S,2R)-2-(methoxymethoxy)cyclopentyl (R)-α-methoxy-α-(trifluoromethyl)phenylacetate, 119972-84-8; (1R,2S)-2-(methoxymethoxy)cyclopentyl (R)-α-methoxy-α-(trifluoromethyl)phenylacetate, 120053-16-9; (1S,2R)-2-(methoxymethoxy)cyclohexyl (R)-α-methoxy-α-(trifluoromethyl)phenylacetate, 119972-85-9; (1R,2S)-2-(methoxymethoxy)cyclohexyl (R)-α-methoxy-α-(trifluoromethyl)phenylacetate, 120053-17-0; (1R,2S)-2-(methoxymethoxy)cyclooctyl (R)-α-methoxy-α-(trifluoromethyl)phenylacetate, 119972-86-0; (1S,2R)-2-(methoxymethoxy)cyclooct-5-enyl (R)-α-methoxy-α-(trifluoromethyl)phenylacetate, 119972-87-1; (1R,2S)-2-(methoxymethoxy)cyclooct-5-enyl (R)-α-methoxy-α-(trifluoromethyl)phenylacetate, 120142-38-3; (1R,2S)-2-hydroxycyclohexyl (R)-α-methoxy-α-(trifluoromethyl)phenylacetate, 119972-89-3; (1S,2R)-2-hydroxycyclohexyl (R)-α-methoxy-α-(trifluoromethyl)phenylacetate, 120142-39-4; l-menthone dimethyl acetal, 119972-93-9.

Carbon–Carbon Bond Formation in Reactions of PhIO•HBF_4/Silyl Enol Ether Adduct with Alkenes or Silyl Enol Ethers

Viktor V. Zhdankin, Michelle Mullikin, Rik Tykwinski, Bruce Berglund, and Ronald Caple*

Department of Chemistry, University of Minnesota, Duluth, Minnesota 55812

Nikolai S. Zefirov* and Anatoly S. Koz'min

Department of Chemistry, Moscow State University, Moscow 119899, USSR

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A new method for generation of reactive α-ketomethyl aryliodonium intermediates from silyl enol ethers and PhIO·HBF_4 has been developed. Reactions of PhIO·HBF_4/silyl enol ether adduct with alkenes (1-hexene, cyclohexene, α-methylstyrene, allyltrimethylsilane, 2,3-dimethyl-2-butene) yielded products of allylic alkylation or (in case of 2,3-dimethyl-2-butene) a substituted dihydrofuran. Reactions of adducts from PhIO/HBF_4 and silyl enol ethers of acetophone, p-chloroacetophenone, p-methylacetophenone, and p-nitroacetophenone with various silyl enol ethers led to unsymmetrical 1,4-butanediones as major products.

There is a considerable current interest in polyvalent iodine chemistry.[1] Although I(III) reagents have been used for solution of a wide variety of synthetic tasks, the main application is usually connected with different oxidations.[1] But in recent years it has been shown that polyvalent iodine chemistry can be applied for more complicated purposes such as transformation of alkenes[2,3] or

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