Lanthanoid(II) or -(III) Alkoxide-Promoted Reactions of Silyl Ketene Acetals with Aldehydes

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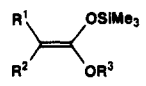
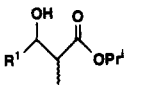
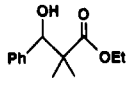
Lanthanoids have attracted much attention in organic synthesis.[1] Lanthanoid salts, in particular, have been expected to serve as unique Lewis acids and have been applied to many synthetic reactions such as the Friedel–Crafts reaction,[2] the hetero Diels–Alder reaction,[3] the Michael addition,[4] the ring opening reaction of oxiranes,[5] and the hydro- and silylcyanation of aldehydes.[6] There are also some examples of their use in the aldol reaction.[7] However, poor diastereoselectivity is a major limitation of lanthanoid-promoted aldol reactions, except the Cp''_2-YbCl–TMSCl-catalyzed reaction of aromatic aldehydes[7c] and the Eu(III)-catalyzed reaction of α-alkoxy aldehydes.[7e,f] A successful enantioselective reaction has never been achieved. In addition, all the lanthanoid catalysts reported so far have been limited to trivalent compounds. In our work on the application of lanthanoids to organic synthesis (see ref 8 for previous work), we have found that divalent samarium alkoxides promote the aldol reaction of silyl ketene acetals with aldehydes with better diastereoselectivity than do the corresponding trivalent lanthanoids.[9] We now report these results.







2 R^1 = H, R^2 = Me, R^3 = Pr^i

3 R^1 = Me, R^2 = H, R^3 = Pr^i

4 R^1 = H, R^2 = Me, R^3 = Me

5 R^1 = R^2 = Me, R^3 = Et

6 R^1 = Ph

7 R^1 = CH=CHPh

8 R^1 = n-C_5H_{11}

9 R^1 = $CHMe_2$

11

The reaction of the (*E*)-trimethylsilyl ketene acetal of isopropyl propionate (**2**)[10] with benzaldehyde in the presence of an equimolar amount of ytterbium(III) chloride proceeded at −78 °C in dichloromethane to give aldol **6** in 98% yield (anti/syn = 56:44) after desilylation. The results obtained with various ytterbium and samarium compounds under similar conditions are summarized in Table I. Of the trivalent compounds, $YbCl_3$ and $Yb(OTf)_3$ produced good yields, but the anti to syn selectivity was quite low (runs 1 and 2). The yields decreased with trivalent alkoxides, although the selectivity was slightly improved (run 4). It is noteworthy that the reaction was also promoted by divalent samarium compounds in good yields; in these reactions, the selectivity depended on the ligands (runs 5–7). Thus, samarium(II) menthoxide (**1**), prepared from SmI_2 and sodium menthoxide,[11] showed a better yield and better anti selectivity than the corresponding samarium(III) alkoxide (runs 7 vs 4). In contrast, the reaction with SmI_2 and free menthol was less selective (86% yield, 72:28).

Since divalent samarium menthoxide (**1**) promoted the reaction of **2** with benzaldehyde, the effect of the catalyst concentration on the yield and selectivity was investigated (Table II). Interestingly, the selectivity decreased when the amount of catalyst **1** was decreased, and when 5 mol% of **1** was used the selectivity was the same as that obtained with samarium(III) menthoxide (run 5 in Table II vs run 4 in Table I).

The reactions of (*E*)-silyl ketene acetal **2** with various aldehydes were carried out with stoichiometric (method A) and catalytic amounts (20 mol%, method B) of Sm(II) menthoxide (**1**) as shown in Table III. The yields of products **6–9** were higher in the catalytic reaction than those in the stoichiometric reaction because of the formation of pinacol as a byproduct of the divalent samarium reaction.[12] With respect to the selectivity, the catalytic reaction provided a lower anti to syn ratio for products **6** and **7** (runs 1–4), but it showed higher selectivity in the reactions of the aliphatic aldehydes (runs 5–8).

Similarly, the reaction of (*Z*)-silyl ketene acetal **3**[10] with benzaldehyde in the presence of a stoichiometric amount of **1** at −78 °C gave aldol **6** in 80% yield (anti/syn = 81:19). The corresponding reactions of (*E*)-**2** and (*Z*)-**3** at ambient temperature afforded aldol **6** with selectivities of 70:30 (66% yield) and 55:45 (84% yield), respectively. In addition, the ratio of aldol **6** (65:35) did not change when the reaction with **1** was carried out at ambient temperature for 3 days. These results suggest that the anti product is formed kinetically as the major product, irrespective of the geometry of the starting silyl ketene acetal. This reaction is in marked contrast to the aldol reaction catalyzed by lanthanocene derivatives, in which anti and syn products were predominantly formed from (*E*)- and (*Z*)-acetals, respectively.[7c] Furthermore, anti selectivity was also observed in the reaction of the (*E*)-trimethylsilyl ketene acetal of methyl propionate (**4**) with racemic α-(*tert*-butyldimethylsilyloxy)propionaldehyde; the reaction cat-

(1) For recent reviews on lanthanoids in organic synthesis, see: (a) Molander, G. A. *Chem. Rev.* **1992**, *92*, 29. (b) Kagan, H. B.; Sasaki, M.; Collin, J. *Pure Appl. Chem.* **1988**, *60*, 1725. (c) Imamoto, T. *Yuki Gosei Kagaku Kyokai Shi* **1988**, *46*, 540.

(2) Mine, N.; Fujiwara, Y.; Taniguchi, H. *Chem. Lett.* **1986**, 357.

(3) Bednarski, M.; Danishefsky, S. *J. Am. Chem. Soc.* **1983**, *105*, 3716.

(4) Mikami, K.; Terada, M.; Nakai, T. *J. Org. Chem.* **1991**, *56*, 5456.

(5) Matsubara, S.; Onishi, H.; Utimoto, K. *Tetrahedron Lett.* **1990**, *31*, 6209.

(6) (a) Gu, J.-H.; Okamoto, M.; Terada, M.; Mikami, K.; Nakai, T. *Chem. Lett.* **1992**, 1169. (b) Ohno, H.; Mori, A.; Inoue, S. *Ibid.* **1993**, 375.

(7) (a) Takai, K.; Heathcock, C. H. *J. Org. Chem.* **1985**, *50*, 3247. (b) Vougioukas, A. E.; Kagan, H. B. *Tetrahedron Lett.* **1987**, *28*, 5513. (c) Gong, L.; Streitwieser, A. *J. Org. Chem.* **1990**, *55*, 6235. (d) Kobayashi, S. *Chem. Lett.* **1991**, 2087. (e) Terada, M.; Gu, J.-H.; Deka, D. C.; Mikami, K.; Nakai, T. *Ibid.* **1992**, 29. (f) Gu, J.-H.; Terada, M.; Mikami, K.; Nakai, T. *Tetrahedron Lett.* **1992**, *33*, 1465.

(8) (a) Yokoo, K.; Fukagawa, T.; Yamanaka, Y.; Taniguchi, H.; Fujiwara, Y. *J. Org. Chem.* **1984**, *49*, 3237. (b) Hou, Z.; Fujiwara, Y.; Jintoku, T.; Mine, N.; Yokoo, K.; Taniguchi, H. *Ibid.* **1987**, *52*, 3524. (c) Hou, Z.; Fujiwara, Y.; Taniguchi, H. *Ibid.* **1988**, *53*, 3118. (d) Hou, Z.; Takamine, K.; Aoki, O.; Shiraishi, H.; Fujiwara, Y.; Taniguchi, H. *Ibid.* **1988**, *53*, 6077. (e) Takaki, K.; Beppu, F.; Tanaka, S.; Tsubaki, Y.; Jintoku, T.; Fujiwara, Y. *J. Chem. Soc. Chem. Commun.* **1990**, 516. (f) Takaki, K.; Tanaka, S.; Fujiwara, Y. *Chem. Lett.* **1991**, 493. (g) Hou, Z.; Yamazaki, H.; Fujiwara, Y.; Taniguchi, H. *Organometallics* **1992**, *11*, 2711.

(9) Presented at the 63rd Annual Meeting of the Chemical Society of Japan, Osaka, March 28–31, 1992, Paper 1F343.

(10) Ratios of (*E*)- to (*Z*)-isomer were 86:14 for **2**, 15:85 for **3**, and 95:5 for **4**: (a) Chan, T. H.; Aida, T.; Lau, P. W. K.; Gorys, V.; Harpp, D. N. *Tetrahedron Lett.* **1979**, 4029. (b) Colvin, E. W. *Silicon Reagents in Organic Synthesis*; Academic Press: New York, 1988; pp 99–117.

(11) Kagan, H. B.; Namy, J. L. *Handbook on the Physics and Chemistry of Rare Earths*; Gschneidner, K. A., Jr.; Eyring, L., Eds.; North-Holland: Amsterdam, 1984; Vol. 6, p 534.

(12) (a) Souppe, J.; Namy, J. L.; Kagan, H. B. *Tetrahedron Lett.* **1983**, *24*, 765. (b) ref 8d.

0022-3263/93/1958-4771$04.00/0

Table I. Reactions of (*E*)-Silyl Ketene Acetal 2 with Benzaldehyde Promoted by Lanthanoid(II) or -(III) Salts[a]

run	lanthanoid	yield of 6 (%)	ratio (anti/syn)
1	$YbCl_3$	98	56:44
2	$Yb(OTf)_3$	96	49:51
3	$Sm(OPr^i)_3$	20	49:51
4	$Sm(O\text{-methyl})_3$	42	66:34
5	SmI_2	88	66:34
6	$Sm(O\text{-1-adamantyl})_2$	87	79:21
7	$Sm(O\text{-methyl})_2$ (1)	84	91:9

[a] Conditions: 2/benzaldehyde/Ln = 1.5:1:1, CH_2Cl_2, −78 °C, 4 h.

Table II. Samarium(II) Menthoxide (1)-Catalyzed Reactions of Silyl Ketene Acetal 2 with Benzaldehyde

run	amount of 1 (mol%)[a]	yield of 6 (%)	ratio (anti/syn)
1	100	84	91:9
2	50	96	89:11
3	20	95	83:17
4	10	74	80:20
5	5	56	67:33

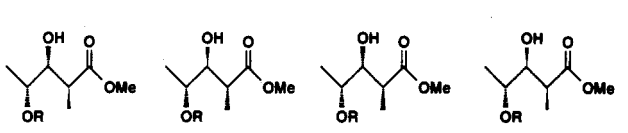
[a] Mol% based on the aldehyde.

Table III. Reactions of (*E*)-Silyl Ketene Acetal 2 with Various Aldehydes Promoted by Samarium(II) Methoxide (1)

run	aldehyde	method[a]	product	yield (%)	ratio (anti/syn)
1	benzaldehyde	A	6	84[b]	91:9
2	benzaldehyde	B	6	95	83:17
3	cinnamaldehyde	A	7	43[b]	71:29
4	cinnamaldehyde	B	7	60	69:31
5	hexanal	A	8	34[b]	74:26
6	hexanal	B	8	72	80:20
7	isobutyraldehyde	A	9	40[b]	61:39
8	isobutyraldehyde	B	9	68	84:16

[a] Method A: stoichiometric reaction. Method B: catalytic reaction (20 mol%). [b] A small amount of the corresponding pinacol was formed (<20%).

alyzed by 1 afforded products **10a–d** in a ratio of 64:22:0:14 (2,3-anti/syn = 86:14). The ratio changed to 35:25:19:21 with $Yb(OTf)_3$.[13]



10a 10b 10c 10d

Finally, we investigated the enantioselective reaction of the trimethylsilyl ketene acetal of ethyl isobutyrate (5) with benzaldehyde mediated by samarium(II) (L)-menthoxide (Table IV). Stoichiometric reaction in dichloromethane afforded product 11 in 81% yield and 19% ee (run 2). The reaction with 20 mol% catalyst gave a higher yield and a lower ee (run 3). The use of 2 equiv of the alkoxide resulted in an increase in the ee and a decrease in the yield, and hydrobenzoin was obtained as the major product (39%) (run 1). The reaction in toluene gave a higher ee but a lower yield than that in dichloromethane. The addition of free (L)-menthol improved both the yield and the ee and gave 11 in 85% yield and 52% ee (run 6). The absolute configuration of major epimer 11 was proved to be *R* on the basis of the optical rotation of the corresponding acid obtained by hydrolysis.[14]

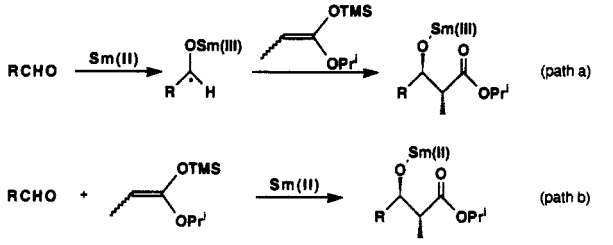
(13) The reaction with $Eu(dppm)_3$ was reported to exhibit a high nonchelation–syn selectivity: see ref 7e.

Table IV. Reactions of Silyl Ketene Acetal 5 with Benzaldehyde Promoted by Samarium(II) (L)-Menthoxide[a]

run	solvent	Sm[(L)-*O*-menthyl]$_2$ (equiv)[b]	(L)-menthol (equiv)[b]	yield of 11 (%)	ee (%)[c]
1	CH_2Cl_2	2.0	–	16	30
2	CH_2Cl_2	1.0	–	81	19
3	CH_2Cl_2	0.2	–	92	2
4	toluene	1.0	–	23	23
5	toluene	1.0	1.0	42	35
6	toluene	1.0	2.0	85	52

[a] Conditions: 5/benzaldehyde = 1.5:1 (runs 1–5) or 1:2 (run 6), −78 °C, 4 h. [b] Relative to the aldehyde. [c] Determined by HPLC (Daicel OD column).

Scheme I



As mentioned above, the reaction of silyl ketene acetals with aldehydes depends remarkably on the oxidation state of the lanthanoid catalysts and amount used. The reaction process can presumably be explained as follows. When benzaldehyde and silyl ketene acetals **2–5** are treated separately with samarium(II) menthoxide (1), the aldehyde is converted to pinacol in quantitative yield, and the acetals are recovered unchanged. Therefore, the reaction is probably initiated by electron transfer from 1 to the aldehyde to give a ketyl radical. The reaction of the ketyl radical with the acetal[15] leads to the aldolate by a loss of trimethylsilyl radical, as depicted in Scheme I (path a). In the catalytic reaction, a trivalent samarium species, formed in the initial step,[16] catalyzes the aldol reaction. Thus, when 1 is used in small amounts (~5%), the diastereoselectivity decreases to the same level obtained with Sm(III) menthoxide. However, the reaction with 20 mol% of the catalyst or more shows better than expected selectivity. Accordingly, an alternative process in which divalent samarium menthoxide (1) directly promotes the reaction without being oxidized to Sm(III) may be involved (path b).[17] Further work is necessary to determine which mechanism is operating.

In summary, we have demonstrated that samarium(II) compounds promote the aldol reactions of silyl ketene acetals with aldehydes in good yield with better diastereoselectivity than the corresponding reactions with trivalent lanthanoids and that anti aldols are formed preferentially from both (*E*) and (*Z*)-acetals. In addition, moderate enantioselectivity is observed when samarium(II) (L)-menthoxide is used.

(14) (a) Matell, M. *Arkiv Kemi* **1949**, *1*, 455; *Chem. Abstr.* **1950**, *44*, 4446e. (b) Guette, M.; Capillon, J.; Guette, J.-P. *Tetrahedron* **1973**, *29*, 3659.

(15) Generation of ketyl radicals by SmI_2 and subsequent trapping with olefinic compounds have been reported: (a) Otsubo, K.; Inanaga, J.; Yamaguchi, M. *Tetrahedron Lett.* **1986**, *27*, 5763. (b) Enholm, E. J.; Trivellas, A. *Ibid.* **1989**, *30*, 1063.

(16) The active trivalent samarium catalyst for the Oppenauer reaction was formed in situ from SmI_2: Collin, J.; Namy, J. L.; Kagan, H. B. *New. J. Chem.* **1986**, *10*, 229.

(17) The greenish-blue color typical of divalent samarium species remains unchanged until quenching.

Experimental Section

^1H and ^{13}C NMR spectra were recorded on JEOL JNM-FX90A and JNM-EX270 spectrometers in $CDCl_3$ solution unless otherwise noted, and chemical shifts are reported in ppm on the δ scale relative to internal tetramethylsilane. IR spectra were measured on a Perkin-Elmer 1600-FTIR spectrophotometer. Mass spectra were obtained on a Shimadzu GCMS QP-1000 apparatus at 70 eV. HPLC analyses were performed on a Shimadzu LC-9A instrument with 15 cm × 0.46 cm i.d. Shimadzu ODS-H and 25 cm × 0.46 cm i.d. Daicel Chiralcel OD columns. Optical rotations were measured on a Horiba SPEA-200 polarimeter.

Prior to use, dichloromethane was distilled from P_2O_5, tetrahydrofuran from sodium/benzophenone ketyl, and toluene from $LiAlH_4$ under N_2. Trimethylsilyl ketene acetals **2–5** were prepared according to the literature method.[10] Ytterbium(III) chloride and samarium(III) isopropoxide were purchased and dried prior to use. Ytterbium(III) trifluoromethanesulfonate was prepared by the reported methods.[18] Samarium(II) menthoxide and 1-adamantanoxide were generated as described below[11] and were used in the reaction without removal of NaI.

General Procedure for the Samarium(II) Menthoxide-Promoted Reaction of a Silyl Ketene Acetal with an Aldehyde. A THF solution of SmI_2 (0.1 M, 40 mL) was added under N_2 to sodium menthoxide (8.0 mmol), prepared from menthol and NaH in THF (5 mL), and the mixture was stirred for 2 h at ambient temperature. The solvent was evaporated under reduced pressure to leave a black precipitate, which was then suspended in dichloromethane (15 mL). The resulting greenish-blue slurry was cooled to −78 °C. A solution of aldehyde (4.0 mmol) and trimethylsilyl ketene acetal (6.0 mmol) in dichloromethane (5 mL) was added to the slurry, and the mixture was stirred for 4 h under N_2. The mixture was quenched with water and warmed to ambient temperature. After addition of 2 N HCl (10 mL), the mixture was extracted with $CHCl_3$ (3 × 20 mL), and the combined organic layer was washed with brine, dried over anhydrous $MgSO_4$, and concentrated in vacuo. The residue was dissolved in THF (10 mL) and treated with 2 N HCl (1 mL) to complete desilylation. The mixture was extracted again with diethyl ether, and the extract was washed with brine, dried over anhydrous $MgSO_4$, and concentrated in vacuo. The diastereomer ratio and yield of the products were determined by NMR analysis of the crude mixture and by GC with eicosane and tetracosane as internal standards, respectively. The aldols were isolated as colorless oils by medium-pressure liquid chromatography (silica gel) and were identified by comparison of their NMR, IR, and MS spectra with the reported data.[19]

The reaction with other lanthanoid compounds were carried out under the similar conditions. Physical properties of the products are recorded below.

Isopropyl 3-Hydroxy-2-methyl-3-phenylpropionate (6).[19b] Anti isomer: ^1H NMR δ 7.34–7.25 (m, 5 H), 5.05 (hep, J = 6.3 Hz, 1 H), 4.73 (dd, J = 8.3, 4.6 Hz, 1 H), 3.10 (d, J = 4.6 Hz, 1 H), 2.77 (dq, J = 8.3, 7.3 Hz, 1 H), 1.24 (d, J = 6.3 Hz, 3 H), 1.21 (d, J = 6.3 Hz, 6 H), 1.03 (d, J = 7.3 Hz, 3 H); ^{13}C NMR δ 175.4, 142.9, 128.4, 127.1, 127.0, 68.0, 47.9, 31.5, 21.7, 14.5; MS, m/z 222 (M^+); IR (neat) 3500, 1730 cm^{-1}. Syn isomer: ^1H NMR δ 7.37–7.22 (m, 5 H), 5.05 (dd, J = 4.3, 3.2 Hz, 1 H), 4.99 (hep, J = 6.3 Hz, 1 H), 3.03 (d, J = 3.2 Hz, 1 H), 2.74 (dq, J = 4.3, 7.3 Hz, 1 H), 1.24 (d, J = 6.3 Hz, 3 H), 1.20 (d, J = 6.3 Hz, 3 H), 1.03 (d, J = 7.3 Hz, 3 H); ^{13}C NMR δ 175.0, 142.8, 128.3, 127.5, 126.7, 74.5, 67.5, 47.5, 21.5, 11.7; MS, m/z 222 (M^+); IR (neat) 3450, 1730 cm^{-1}.

Isopropyl 3-Hydroxy-2-methyl-5-phenyl-4-pentenoate (7). Anti isomer: ^1H NMR (C_6D_6) δ 7.24–7.01 (m, 5 H), 6.55 (d, J = 15.9 Hz, 1 H), 6.10 (dd, J = 15.9, 6.3 Hz, 1 H), 5.04 (hep, J = 6.2 Hz, 1 H), 4.31 (dd, J = 6.6, 6.3 Hz, 1 H), 2.60 (br s, 1 H), 2.58 (dq, J = 6.6, 7.2 Hz, 1 H), 1.12 (d, J = 7.2 Hz, 3 H), 1.00 (d, J = 6.2 Hz, 3 H), 0.95 (d, J = 6.2 Hz, 3 H); ^{13}C NMR (C_6D_6) δ 175.0, 141.8, 132.1, 129.3, 128.8, 128.2, 127.1, 74.9, 68.0, 46.7, 21.9, 14.0; MS, m/z 248 (M^+); IR (neat) 3446, 1729 cm^{-1}. Anal. Calcd for $C_{15}H_{20}O_3$: C, 72.55; H, 8.11. Found: C, 72.40; H, 8.08. Syn isomer: ^1H NMR (C_6D_6) δ 7.37–7.04 (m, 5 H), 6.64 (d, J = 15.8 Hz, 1 H), 6.09 (dd, J = 15.8, 5.7 Hz, 1 H), 4.97 (hep, J = 6.2 Hz, 1 H), 4.47 (dd, J = 5.7, 4.8 Hz, 1 H), 2.50 (dq, J = 4.8, 7.3 Hz, 1 H), 2.45 (br s, 1 H), 1.20 (d, J = 7.3 Hz, 3 H), 0.98 (d, J = 6.2 Hz, 6H); ^{13}C NMR (C_6D_6) δ 174.6, 142.2, 131.4, 129.9, 128.8, 127.8, 126.0, 73.3, 67.8, 45.8, 21.7, 11.9; MS, m/z 248 (M^+); IR (neat) 3450, 1726 cm^{-1}. Anal. Calcd for $C_{15}H_{20}O_3$: C, 72.55; H, 8.11. Found: C, 72.35; H, 8.13.

Isopropyl 3-Hydroxy-2-methylcaprylate (8). Anti isomer: ^1H NMR δ 5.05 (hep, J = 6.0 Hz, 1 H), 3.61 (m, 1 H), 2.63 (d, J = 7.5 Hz, 1 H), 2.45 (dq, J = 7.0, 6.5 Hz, 1 H), 1.60–0.89 (m, 14 H), 1.25 (d, J = 6.0 Hz, 3 H), 1.19 (d, J = 6.0 Hz, 3 H); ^{13}C NMR δ 175.5, 73.4, 67.8, 45.3, 34.8, 31.8, 25.2, 22.6, 21.8, 14.2, 14.0; MS, m/z 216 (M^+); IR (neat) 3450, 1730 cm^{-1}. Anal. Calcd for $C_{12}H_{24}O_3$: C, 66.62; H, 11.18. Found: C, 66.61; H, 11.12. Syn isomer: ^1H NMR δ 5.04 (hep, J = 7.5 Hz, 1 H), 3.92 (m, 1 H), 2.63 (br s, 1 H), 2.52 (dq, J = 4.1, 6.9 Hz, 1 H), 1.55–0.89 (m, 14 H), 1.16 (d, J = 7.5 Hz, 6 H); ^{13}C NMR δ 175.7, 71.7, 67.8, 44.4, 33.8, 31.8, 25.6, 22.5, 21.7, 13.9, 10.7; MS, m/z 216 (M^+); IR (neat) 3450, 1720 cm^{-1}. Anal. Calcd for $C_{12}H_{24}O_3$: C, 66.62; H, 11.18. Found: C, 66.47; H, 11.34.

Isopropyl 2,4-Dimethyl-3-hydroxyvalerate (9). Anti isomer: ^1H NMR δ 5.05 (hep, J = 6.2 Hz, 1 H), 3.35 (dt, J = 6.0, 6.5 Hz, 1 H), 2.69 (d, J = 6.5 Hz, 1 H), 2.60 (dq, J = 6.0, 6.2 Hz, 1 H), 1.71 (m, 1 H), 1.25 (d, J = 6.2 Hz, 6 H), 1.20 (d, J = 6.2 Hz, 3 H), 0.96 (d, J = 6.5 Hz, 3 H), 0.93 (d, J = 6.5 Hz, 3 H); ^{13}C NMR δ 176.0, 78.4, 67.9, 42.7, 31.3, 21.8, 19.7, 16.7, 14.9; MS, m/z 188 (M^+); IR (neat) 3500, 1720 cm^{-1}. Anal. Calcd for $C_{10}H_{20}O_3$: C, 63.80; H, 10.71. Found: C, 63.42; H, 11.15. Syn isomer: ^1H NMR δ 5.11 (hep, J = 6.4 Hz, 1 H), 3.56 (m, 1 H), 2.67 (d, J = 4.0 Hz, 1 H), 2.58 (dq, J = 3.8, 6.3 Hz, 1 H), 1.64 (m, 1 H), 1.24 (d, J = 6.4 Hz, 6 H), 1.13 (d, J = 6.3 Hz, 3 H), 0.98 (d, J = 6.5 Hz, 3 H), 0.88 (d, J = 6.5 Hz, 3 H); ^{13}C NMR δ 176.1, 76.7, 67.8, 42.0, 30.6, 21.7, 19.0, 18.4, 10.4; MS, m/z 188 (M^+); IR (neat) 3450, 1720 cm^{-1}. Anal. Calcd for $C_{10}H_{20}O_3$: C, 63.80; H, 10.71. Found: C, 63.55; H, 10.88.

Methyl 4-(*tert*-Butyldimethylsilyloxy)-3-hydroxy-2-methylvalerate. The reaction was carried out using stoichiometric amounts of **1** as above, and the aldols were obtained in 50% total yield.[20] 2,3-Anti-3,4-syn isomer (**10a**)[7e]: ^1H NMR δ 3.39 (dq, J = 2.8, 7.0 Hz, 1 H), 3.66 (s, 3 H), 3.33 (m, 1 H), 2.53 (dq, J = 8.0, 7.0 Hz, 1 H), 2.38 (br s, 1 H), 1.12 (d, J = 7.0 Hz, 3 H), 1.10 (d, J = 7.0 Hz, 3 H), 0.86 (s, 9 H), 0.08 (s, 6 H); ^{13}C NMR δ 175.7, 77.5, 68.0, 51.6, 43.1, 40.9, 25.8, 20.4, 14.1, −4.0; MS, m/z 171, 159, 131, 115; IR (neat) 3500, 1745, 1258, 1100 cm^{-1}. Anal. Calcd for $C_{13}H_{28}O_4Si$: C, 56.49; H, 10.21. Found: C, 56.86; H, 10.38. 2,3-Anti-3,4-anti isomer (**10b**):[7e] ^1H NMR δ 3.78 (dq, J = 8.0, 7.0 Hz, 1 H), 3.67 (s, 3 H), 3.52 (m, 1 H), 2.58 (dq, J = 7.5, 7.0 Hz, 1 H), 1.18 (d, J = 4.3 Hz, 1 H), 1.17 (d, J = 7.0 Hz, 3 H), 1.15 (d, J = 7.0 Hz, 3 H), 0.88 (s, 9 H), 0.06 (s, 6 H); ^{13}C NMR δ 176.5, 77.8, 76.2, 51.5, 43.6, 40.1, 25.8, 20.7, 13.0, −4.1; MS, m/z 159, 131, 115; IR (neat) 3550, 1742, 1258, 1100 cm^{-1}. Anal. Calcd for $C_{13}H_{28}O_4Si$: C, 56.49; H, 10.21. Found: C, 56.15; H, 10.44. 2,3-Syn-3,4-syn isomer (**10c**):[7e] ^1H NMR δ 3.88 (dq, J = 5.5, 7.0 Hz, 1 H), 3.70 (br s, 1 H), 3.68 (s, 3 H), 3.51 (m, 1 H), 2.68 (dq, J = 5.5, 7.0 Hz, 1 H), 1.20 (d, J = 7.0 Hz, 3 H), 1.13 (d, J = 7.0 Hz, 3 H), 0.87 (s, 9 H), 0.04 (s, 6 H); ^{13}C NMR δ 175.8, 77.8, 68.9, 51.6, 40.9, 40.1, 25.8, 18.4, 12.0, −4.4; MS, m/z 171, 159, 131, 115; IR (neat) 3530, 1742, 1258, 1097 cm^{-1}. Anal. Calcd for $C_{13}H_{28}O_4Si$: C, 56.49; H, 10.21. Found: C, 56.46; H, 10.21. 2,3-Syn-3,4-anti isomer (**10d**):[7e] ^1H NMR δ 3.70 (dq, J = 7.5, 7.0 Hz, 1 H), 3.68 (s, 3 H), 3.65 (m, 1 H), 3.57 (m, 1 H), 2.44 (dq, J = 5.5, 7.0 Hz, 1 H), 1.19 (d, J = 7.0 Hz, 3 H), 1.17 (d, J = 7.0 Hz, 3 H), 0.87 (s, 9 H), 0.05 (s, 6 H): ^{13}C NMR δ 175.8, 78.4, 70.0, 51.2, 41.9, 40.1, 25.9, 19.4, 11.2, −4.3; MS, m/z 159, 131, 115; IR (neat) 3520, 1742, 1260, 1100 cm^{-1}. Anal. Calcd for $C_{13}H_{28}O_4Si$: C, 56.49; H, 10.21. Found: C, 56.47; H, 10.41.

(18) Forsberg, J. H.; Spaziano, V. T.; Balasubramanian, T. M.; Liu, G. K.; Kinsley, S. A.; Duckworth, C. A.; Poteruca, J. J.; Brown, P. S.; Miller, J. L. *J. Org. Chem.* **1987**, *52*, 1017.

(19) (a) Heathcock, C. H.; Pirrung, M. C.; Sohn, J. E. *J. Org. Chem.* **1979**, *44*, 4294. (b) Heathcock, C. H.; Davidsen, S. K.; Hug, K. T.; Flippin, L. A. *Ibid.* **1986**, *51*, 3027.

(20) The stereochemistry at C_3 and C_4 was tentatively assigned by comparison of the NMR spectra with those of related compounds: see ref 4.

Ethyl 2,2-Dimethyl-3-hydroxy-3-phenylpropionate (11).[21] Trimethylsilyl ketene acetal 5 was added at −78 °C under N_2 to a suspension of samarium(II) (L)-menthoxide, prepared from SmI_2 and (L)-menthol as described above, and the mixture was stirred for 10 min. Then, benzaldehyde was added to the mixture. Steps similar to those used in the general procedure were followed. The ee was determined by HPLC [Daicel Chiralcel OD column; eluent: hexane/2-propanol = 98:2; flow rate: 1.0 mL/min; 40 °C; t_R = 9.5 min (major) and 11.5 (minor)]: ^{1}H NMR (C_6D_6) δ 7.40–7.22 (m, 5 H), 4.93 (d, J = 4.2 Hz, 1 H), 3.95 (q, J = 7.2 Hz, 2 H), 2.78 (d, J = 4.2 Hz, 1 H), 1.26 (s, 3 H), 1.11 (s, 3 H), 0.95 (t, J = 7.2 Hz, 3 H); MS m/z 222 (M^+); IR (neat): 3510, 1720 cm^{-1}. Compound 11 (20% ee) was hydrolyzed to 2,2-dimethyl-3-hydroxy-3-phenylpropionic acid by the treatment with aqueous NaOH in THF: colorless needles; mp 141–142 °C (from ethyl acetate) [lit.[14a] 134 °C]; $[\alpha]^{25}_D$ −4.47° (c 0.45, MeOH) [lit.[14a,b] −17.5° (AcOH) and −5.2° (MeOH) for pure R epimer]; ^{1}H NMR (DMSO-d_6) δ 12.1 (br s, 1 H), 7.31–7.23 (m, 5 H), 5.50 (s, 1 H), 4.83 (s, 1 H), 1.01 (s, 3 H), 0.88 (s, 3 H); ^{13}C NMR (DMSO-d_6) δ 178.0, 142.2, 127.6, 127.4, 127.1, 76.6, 47.1, 21.6, 19.7; IR (Nujol): 3400, 1690 cm^{-1}. Anal. Calcd for $C_{11}H_{14}O_3$: C, 68.02; H, 7.26. Found: C, 67.96; H, 7.23.

(21) Smith, A. B., III; Levenberg, P. A. *Synthesis* 1981, 567.

Additions and Corrections

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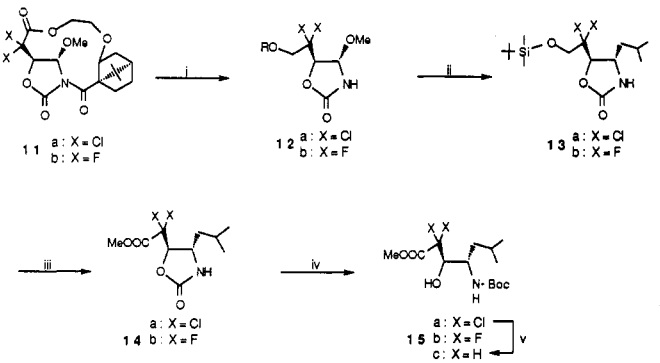
Peter Wipf* and Yuntae Kim. Stereoselective Synthesis of the Functionalized Spirocyclic Core of Aranorosin.

Page 1649, column 2, Scheme I and line 9. The addition of $BnOCH_2Li$ to dienone 10 was performed at −100 °C.

Takuya Yamamoto, Seigo Ishibuchi, Tadao Ishizuka, Mamoru Haratake, and Takehisa Kunieda*. Stereoselective Intramolecular Radical Addition of Polyhaloacetyl Functions to 2-Oxazolones. A Facile Synthesis of Statine and Its 2,2-Dichloro and 2,2-Difluoro Analogues.

Page 1998, Scheme II. The following footnotes should be added to Scheme II.

Scheme II[a]



[a] (i) (1) $LiBH_4$/MeOH, (2) TBDMSCl/imidazole; (ii) i-BuCuCN-MgBr, LiCl/BF_3·OEt_2; (iii) (1) n-Bu_4NF·$3H_2O$, (2) CrO_3/H_2SO_4–$(Me)_2CO$–H_2O, (3) CH_2N_2; (iv) (1) HCl/Δ, (2) $(Boc)_2O$/NEt_3, DMAP, (3) CH_2N_2; (v) n-Bu_3SnH/AIBN.

Lyndon A. M. Cornelius, Richard G. A. Bone, Riley H. Hastings, Matthew A. Deardorff, Randall A. Scharlach, Brett E. Hauptmann, Charles J. Stankovic, and Harold W. Pinnick*. Synthesis of 2-Acetylbicyclo[2.2.1]heptene.

Page 3188. The middle initial of Charles Stankovic should be J.