230, 202. Anal. Calcd for $C_{19}H_{17}NO_3S$: C, 67.25; H, 5.01. Found: C, 67.16; H, 5.05.

**Acknowledgment.** We thank Dr. Bernard J. Banks for helpful discussion and Pfizer Central Research, the Science and Engineering and Research Council (UK), the Atlantic Richfield Foundation, and Northwestern University for generous support of our programs.

**Registry No.** 1 (R′ = Me), 75-07-0; 1 (R′ = $Me_2CH$), 78-84-2; **2** (R′ = $Me_2CH$, X = SPh), 100683-56-5; **6**, 60595-16-6; **7**, 67808-90-6; **8a**, 67808-91-7; **8b**, 92339-58-7; **10a**, 92339-69-0; **10b**, 92339-70-3; **10c**, 100683-57-6; **10d**, 92339-67-8; **10e**, 92339-68-9; **10f**, 100683-58-7; **10g** (isomer 1), 100683-59-8; **10g** (isomer 2), 100683-60-1; **10h**, 92339-71-4; **10i**, 92339-72-5; **10j**, 100683-61-2; **10k**, 100683-62-3; **10l**, 92339-75-8; **11**, 92339-73-6; $FCH_2CONH_2$, 640-19-7; $PhCH_2NHTs$, 1576-37-0; TsNa, 657-84-1; $MeO_2CCH_2CO_2Me$, 108-59-8; PhAc, 98-86-2; potassium phthalimide, 1074-82-4; 5α-cholestan-3b-ol, 80-97-7; 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose, 582-52-5.

# Stereocontrolled Synthesis of Polyfunctionalized *trans*-Hydrindan Systems: A Model Study toward Anisatin

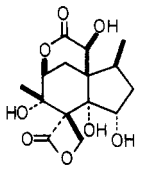
Haruki Niwa,* Tatsuya Mori, Takashi Hasegawa, and Kiyoyuki Yamada

*Department of Chemistry, Faculty of Science, Nagoya University, Chikusa, Nagoya 464, Japan*

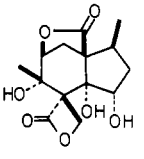
*Received July 2, 1985*

A model study toward the synthesis of anisatin (1) and its derivative, noranisatin (2), is described. A γ-lactone triol **3**, a model compound of **2**, has been prepared in highly regio- and stereocontrolled manners. Treatment of an enone **4** with osmium tetraoxide gives an angularly functionalized *trans*-hydrindan derivative **5**, which is converted into an olefinic acetate **9** by a four-step procedure. Epoxidation of **9** with *m*-CPBA and subsequent methanolysis give a cyclic ether **11**. Reaction of a ketone **12**, obtained from **11** by Collins oxidation, with methylmagnesium iodide gives almost exclusively the desired alcohol **13a**, while the reaction of **12** with methyllithium gives the undesired alcohol **13b** as a major product. The desired alcohol **13a** is transformed into **3** by a two-step sequence involving ruthenium tetraoxide oxidation of the tetrahydrofuran ring in **13a**. The stereostructures of **13a** and **13b** were unambiguously established by X-ray crystallographic analysis of crystalline **13b**.

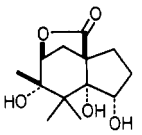
Anisatin (1), a poisonous principle isolated from the seeds of Japanese star anise, *Illicium Anisatum L.* (Shikimi in Japanese), is a highly oxygenated sesquiterpene having an unusual spiro-β-lactone ring.[1,2] The structure of **1** was elucidated in 1965 by chemical and spectral means coupled with X-ray analysis of a derivative of **1**.[2] Noranisatin (**2**), an oxidation product of **1**, played an important role in the structural determination.[2] Anisatin (**1**) has been known as one of the most toxic compounds of plant origin and furthermore, recent neurochemical studies have shown **1** to be the specific antagonist of γ-aminobutyric acid (GABA).[3]



1



2

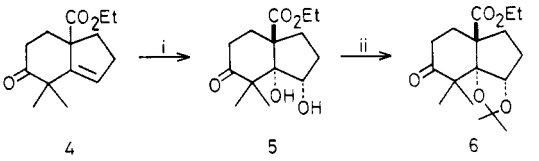


3

The unique structure and characteristic biological properties of anisatin (**1**) prompt us to attempt the total synthesis of **1**. Although anisatin (**1**) has not yet been prepared by total synthesis, a model study toward **1** has been reported recently.[4]

In this paper, we report our own model studies directed toward the synthesis of **1** and **2**. We present here a stereocontrolled construction of a polyfunctionalized *trans*-hydrindan skeleton, which possesses five asymmetric centers with desired functionality and correct stereo-

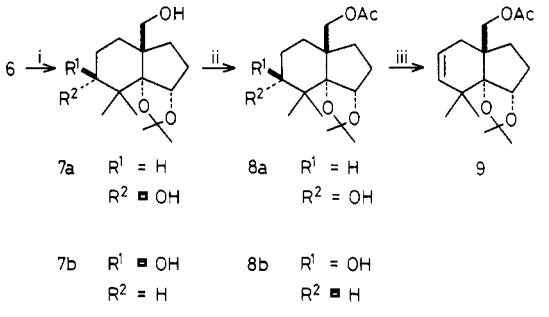
**Scheme I**[a]



4 5 6

[a] Reagents: i, $OsO_4$; ii, 2-methoxypropene, $H^+$.

**Scheme II**[a]



7a R¹ = H, R² = OH; 8a R¹ = H, R² = OH; 9

7b R¹ = OH, R² = H; 8b R¹ = OH, R² = H

[a] Reagents: i, $LiAlH_4$; ii, $Ac_2O$, pyridine; iii, $POCl_3$, pyridine.

(1) Lane, J. F.; Koch, W. T.; Leeds, N. S.; Gorin, G. *J. Am. Chem. Soc.* **1952**, *74*, 3211.

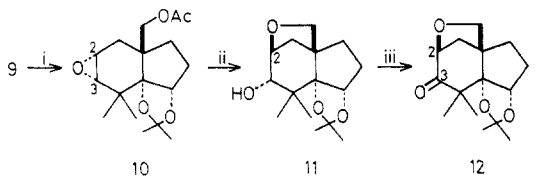
(2) (a) Yamada, K.; Takada, S.; Nakamura, S.; Hirata, Y. *Tetrahedron Lett.* **1965**, 4785. (b) Sakabe, N.; Hirata, Y.; Furusaki, A.; Tomiie, Y.; Nitta, I. *Tetrahedron Lett.* **1965**, 4795. (c) Yamada, K.; Takada, S.; Nakamura, S.; Hirata, Y. *Tetrahedron Lett.* **1965**, 4797. (d) Yamada, K.; Takada, S.; Nakamura, S.; Hirata, Y. *Tetrahedron* **1968**, *24*, 199.

(3) Kudo, Y.; Oka, J.; Yamada, K. *Neurosci. Lett.* **1981**, *25*, 83.

(4) Lindner, D. L.; Doherty, J. B.; Shoham, G.; Woodward, R. B. *Tetrahedron Lett.* **1982**, *23*, 5111. **Note Added in Proof**: The synthesis of (±)-8-deoxyanisatin has been reported after submission of our article, see: Kende, A. S.; Chen, J. *J. Am. Chem. Soc.* **1985**, *107*, 7184. See also: Kato, M.; Kitahara, H.; Yoshikoshi, A. *Chem. Lett.* **1985**, 1785.

0022-3263/86/1951-1015$01.50/0 

**Scheme III**[a]




[a] Reagents: i, *m*-CPBA; ii, $K_2CO_3$; iii, Collins.

chemistry among eight asymmetric centers of anisatin (**1**).

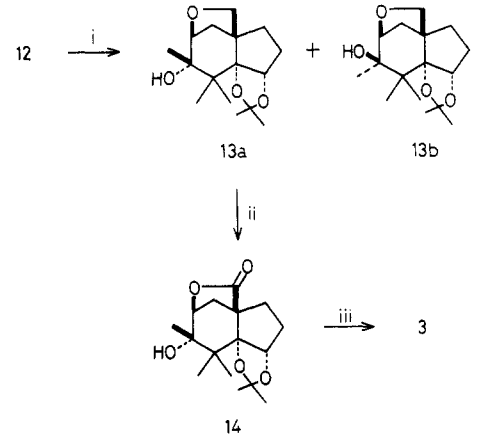
The central problem of the synthesis of **1** and **2** is elaboration of the spiro-β-lactone ring. Thus the first task has been focussed in the regio- and stereocontrolled construction of a highly functionalized *trans*-hydrindan skeleton, to which the spiro-β-lactone ring or the synthetic equivalent can be appended in the total synthesis of **1** and **2**.

We have chosen the enone **4**[5] as the starting material. Reaction of **4** with osmium tetraoxide in pyridine and tetrahydrofuran (THF) and subsequent hydrolysis of the resulting osmate ester with sodium hydrogen sulfite solution afforded the *cis*-diol **5** (mp 122–123 °C) as a sole product in almost quantitative yield (Scheme I). A trans ring fusion in **5**, expected on the basis of the analogous results[5] in *m*-CPBA epoxidation of **4**, was eventually confirmed by X-ray analysis using the further transformed compound **13b** (vide infra). Conversion of **5** into the acetonide **6** was effected with 2-methoxypropene[6] and *d*-camphorsulfonic acid in benzene in 88% yield.

Lithium aluminum hydride reduction of **6** in THF gave two diastereomeric diols, **7a** (mp 140–141 °C) and **7b** (mp 159–160 °C), in 40% and 52% yield, respectively (Scheme II). Stereochemical assignment of the secondary hydroxyl groups in **7a** and **7b** was based on their $^1H$ NMR and IR spectra. Selective monoacetylation of the primary hydroxyl groups in **7a** and **7b** with acetic anhydride and pyridine afforded the monoacetates, **8a** and **8b**, in 83% and 65% yield, respectively. Dehydration of **8a** and **8b** with phosphorus oxychloride and pyridine gave the olefinic acetate **9** in 78% yield from **8a** and 90% yield from **8b**, respectively.

Epoxidation of **9** with *m*-CPBA in dichloromethane proceeded in highly stereoselective manner to give the epoxy acetate **10** (mp 86–87 °C) as a sole product in 97% yield (Scheme III). Although the stereochemistry of **10** could not clearly be established by spectral means in this stage, we assumed that the peracid attacked from the less hindered side of **9** to give the desired epoxide **10**. The correctness of the stereochemical assignment for **10** was substantiated by subsequent conversion of **10** to the cyclic ether **11**. Thus, treatment of **10** with anhydrous potassium carbonate in methanol afforded directly **11** in 80% yield. This result clearly indicated the epoxide ring in **10** to be oriented at the α-side, i.e., anti to the acetoxyl group, as predicted. Although there were two possible modes for the epoxide ring opening in **10**, we assumed that the rigid conformation of **10** would favor trans diaxial ring opening at C-2 by the primary hydroxyl group to give the desired **11**. This assumption was confirmed by the conversion of **11** into the ketone **12**. Collins oxidation of **11** provided **12** (mp 84–85 °C) in 81% yield. In the $^1H$ NMR spectrum of **12**, a signal due to the C-2 proton appeared at δ 4.33 as a doublet ($J$ = 6.8 Hz), indicating that the epoxide ring opening in **10** occurred at C-2 and not at C-3.

**Scheme IV**[a]




[a] Reagents: i, $CH_3MgI$ (or $CH_3Li$); ii, $RuCl_3$, $NaIO_4$; iii, $H_2O$, $H^+$.

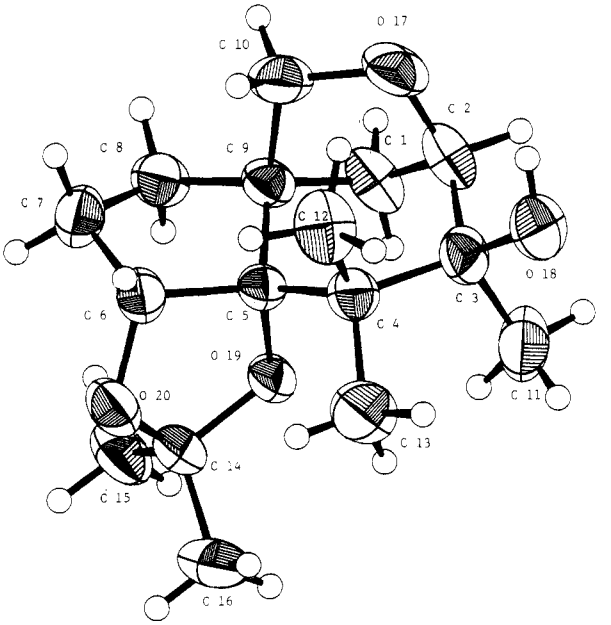



**Figure 1.** ORTEP drawing of **13b**.

The remaining problem in the present study is introduction of a methyl group into the C-3 ketone group in **12** with correct stereochemistry. Reaction of **12** with methyllithium in THF afforded two diastereomeric alcohols, **13a** (mp 115–116 °C) and **13b** (mp 103–105 °C) in 16% and 74% yield, respectively (Scheme IV). In order to confirm the structures of **13a** and **13b** unambiguously, single-crystal X-ray analysis using the major product **13b** was performed. A computer-generated perspective drawing of the final X-ray model of **13b** is shown in Figure 1. The X-ray analysis of **13b** revealed that the hydrindan skeleton was fused in trans as expected and that the newly introduced methyl group at C-3 possessed the undesired stereochemistry, i.e., the methyl group was anti to the tetrahydrofuran ring. This result clearly indicated that **13a**, the minor product of this reaction is the desired compound. In marked contrast to this undesired result using methyllithium as methylating agent, the reaction of **12** with methylmagnesium iodide in ether gave a 23:1 mixture of the desired alcohol, **13a** (92%) and the undesired one, **13b** (4%).

Oxidation of **13a** with ruthenium tetraoxide[7] generated in situ from ruthenium trichloride and sodium metaper-

(5) Halsall, T. G.; McHale, P. J.; Mendez, A. M. *J. Chem. Soc., Perkin Trans. 1* **1978**, 1606.
(6) Newman, M. S.; Vander Zwan, M. C. *J. Org. Chem.* **1973**, *38*, 2910.
(7) Carlsen, P. H. J.; Katsuki, T.; Martin, V. S.; Sharpless, K. B. *J. Org. Chem.* **1981**, *46*, 3936.

iodate gave the γ-lactone **14** in 93% yield (Scheme IV). Finally, acid hydrolysis of **14** in 2 M hydrochloric acid afforded the γ-lactone triol **3** in quantitative yield.

In the present study, an efficient synthetic route has been set up toward a highly functionalized *trans*-hydrindan skeleton having five asymmetric centers contained in anisatin (**1**) and noranisatin (**2**), in regio- and stereocontrolled manners.

## Experimental Section

Melting points are uncorrected. Infrared (IR) spectra were obtained with a JASCO Model IRS spectrophotometer in $CHCl_3$. Proton nuclear magnetic resonance ($^1H$ NMR) spectra were recorded on a JEOL FX-90QE (90 MHz) spectrometer in $CDCl_3$. Chemical shifts are expressed in ppm downfield from internal tetramethylsilane (δ 0.0). Significant $^1H$ NMR data are tabulated in order: multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad), coupling constant in Hz, and number of protons. Exact mass spectra were measured on a JEOL JMS-DX 300 instrument. Fuji-Davison silica gel BW-80 was used for column chromatography. Merck precoated silica gel $60F_{254}$ plates, 0.25 mm thickness, were used for analytical thin-layer chromatography (TLC) and Merck silica gel $PF_{254}$ for preparative TLC. Reactions, except for those performed in aqueous solvents, were carried out in a dry nitrogen atmosphere. Unless otherwise stated, materials were obtained from commercial suppliers and used without further purification. Tetrahydrofuran (THF) and ether were freshly distilled from sodium–benzophenone ketyl under nitrogen. Pyridine, benzene, and dichloromethane were distilled from calcium hydride under nitrogen. Unless otherwise noticed, the solution obtained by extractive workup were washed with saturated brine, dried over anhydrous sodium sulfate, and concentrated under reduced pressure.

**Preparation of *cis*-Diol 5.** To a solution of enone **4**[5] (137 mg, 0.58 mmol) in pyridine (2 mL) was added a solution of $OsO_4$ (295 mg, 1.16 mmol) in THF (6 mL) at room temperature. The mixture was stirred at room temperature for 3 h, and a solution of $NaHSO_3$ (0.6 g, 5.8 mmol) in 3 mL of pyridine–$H_2O$ (1:2) was added. After being stirred for 1 h, the mixture was extracted with ethyl acetate (3 × 30 mL). The combined organic layers were washed successively with saturated $CuSO_4$ solution, water, and saturated brine, dried, and concentrated to give an oily residue. Purification by preparative TLC (ether) afforded 160 mg (99%) of **5**: mp 122–123 °C (hexane–ether); IR 3480, 1705 $cm^{-1}$; $^1H$ NMR δ 1.02 (s, 3 H), 1.18 (s, 3 H), 1.32 (t, $J$ = 7.1, 3 H), 1.84 (d, $J$ = 4.3, 1 H, OH), 3.55 (s, 1 H, OH), 4.14 (m, 2 H), 4.96 (ddd, $J$ = 4.3, 4.3, 9.4, 1 H). Anal. Calcd for $C_{14}H_{22}O_5$: C, 62.21; H, 8.21. Found: C, 62.00; H, 8.49.

**Preparation of Acetonide 6.** To a solution of **5** (123 mg, 0.46 mmol) in benzene (2 mL) were added freshly prepared 2-methoxypropene[6] (0.22 mL, 2.3 mmol) and *d*-camphorsulfonic acid (ca. 2 mg). The mixture was stirred at room temperature for 3 h, diluted with saturated $NaHCO_3$ solution (2 mL), and extracted with ether (4 × 10 mL). Removal of solvent gave an oily residue, which was purified by column chromatography (15:1 → 2:1 hexane–ether) to give 124 mg (88%) of **6** as a colorless oil: IR 1710 $cm^{-1}$; $^1H$ NMR δ 1.05 (s, 3 H), 1.23 (s, 3 H), 1.30 (t, $J$ = 7.0, 3 H), 1.51 (s, 6 H), 4.09 (m, 2 H), 4.82 (d, $J$ = 7.9, 1 H); exact mass calcd for $C_{17}H_{26}O_5$ ($M^+$) $m/z$ 310.1780, found $m/z$ 310.1750.

**Preparation of Diols 7a and 7b.** To a solution of **6** (124 mg, 0.40 mmol) in THF (1.2 mL) was added a 1.0 M solution of $LiAlH_4$ (2.0 mL, 2.0 mmol) in THF at room temperature. The mixture was stirred for 3 h and cooled to 0 °C. To the mixture was added 850 mg of anhydrous NaF, and the mixture was stirred for an additional 30 min at room temperature. The mixture was cooled again to 0 °C and water (0.4 mL) was added. The mixture was stirred for 30 min at room temperature and filtered through a pad of Celite. The Celite filter cake was washed thoroughly with ethyl acetate (100 mL). The combined organic solutions were concentrated under reduced pressure to give a white solid. Purification by column chromatography (2:1 → 1:3 hexane–ether) gave 43.5 mg (40%) of **7a** [$R_f$ 0.35 (ether)] and 55.8 mg (52%) of **7b** [$R_f$ 0.20 (ether)]. **7a**: mp 140–141 °C (hexane–ether); IR 3670, 3490 $cm^{-1}$; $^1H$ NMR δ 0.94 (s, 3 H), 1.28 (s, 3 H), 1.56 (s, 3 H), 1.61 (s, 3 H), 3.15 (d, $J$ = 10.8, 1 H), 3.37 (dd, $J$ = 10.8, 2.9, 1 H), 3.93 (d, $J$ = 10.8, 1 H), 4.14 (d, $J$ = 10.8, 1 H, OH), 4.53 (m, 1 H); exact mass calcd for $C_{14}H_{23}O_4$ ($M^+ - CH_3$) $m/z$ 255.1596, found $m/z$ 255.1621. **7b**: mp 159–160 °C ($CHCl_3$–ether); IR 3670, 3480 $cm^{-1}$; $^1H$ NMR δ 0.90 (s, 3 H), 1.23 (s, 3 H), 1.54 (s, 6 H), 3.20 (d, $J$ = 10.8, 1 H), 3.84 (m, 1 H), 4.00 (d, $J$ = 10.8, 1 H), 4.52 (br d, $J$ = 7.2, 1 H); exact mass calcd for $C_{14}H_{23}O_4$ ($M^+ - CH_3$) $m/z$ 255.1596, found $m/z$ 255.1623.

**Preparation of Monoacetates 8a and 8b.** A mixture of **7a** (79.1 mg, 0.29 mmol), acetic anhydride (0.33 mL), and pyridine (1.5 mL) was stirred for 3 h at 0 °C and then ice (0.5 g) was added. The mixture was stirred for an additional 15 min at 0 °C and concentrated in vacuo to give an oily residue, which was purified by column chromatography (25:1 $CHCl_3$–ether) to afford 76.1 mg (83%) of **8a** as a colorless oil: IR 3520, 1737 $cm^{-1}$; $^1H$ NMR δ 0.99 (s, 3 H), 1.29 (s, 3 H), 1.55 (s, 3 H), 1.62 (s, 3 H), 2.08 (s, 3 H), 3.39 (dt, $J$ = 10.8, 2.9, 1 H), 3.66 (d, $J$ = 11.5, 1 H), 4.00 (d, $J$ = 10.8, 1 H, OH), 4.44 (d, $J$ = 11.5, 1 H), 4.57 (d, $J$ = 5.4, 1 H); exact mass calcd for $C_{17}H_{28}O_5$ ($M^+$) $m/z$ 312.1937, found $m/z$ 312.1954.

Acetylation of **7b** (112 mg, 0.41 mmol) and purification of the crude product by the procedure as described above gave 83.7 mg (65%) of **8b** as a colorless oil: IR 3640, 3460, 1736 $cm^{-1}$; $^1H$ NMR δ 0.95 (s, 3 H), 1.24 (s, 3 H), 1.54 (s, 6 H), 2.07 (s, 3 H), 3.74 (d, $J$ = 10.8, 1 H), 3.90 (m, 1 H), 4.49 (d, $J$ = 10.8, 1 H), 4.56 (d, $J$ = 6.8, 1 H); exact mass calcd for $C_{17}H_{28}O_5$ ($M^+$) $m/z$ 312.1937, found $m/z$ 312.1947.

**Preparation of Olefinic Acetate 9.** To a solution of **8a** (13.0 mg, 0.042 mmol) in pyridine (1.0 mL) was added freshly distilled $POCl_3$ (70 μL, 0.76 mmol). The mixture was heated at 100 °C with stirring for 1 h and cooled to 0 °C. Ice (0.5 g) was added and then the mixture was diluted with saturated $NaHCO_3$ solution (2 mL). The mixture was extracted with ethyl acetate (4 × 5 mL). Removal of solvent gave an oily residue, which was purified by column chromatography (10:1 hexane–ether) to yield 9.5 mg (78%) of **9** as a colorless oil: IR 1735 $cm^{-1}$; $^1H$ NMR δ 1.05 (s, 3 H), 1.15 (s, 3 H), 1.51 (s, 3 H), 1.53 (s, 3 H), 2.06 (s, 3 H), 2.20 (m, 2 H), 3.82 (br d, $J$ = 10.8, 1 H), 4.07 (d, $J$ = 10.8, 1H), 4.70 (d, $J$ = 7.2, 1 H), 5.27 (dt, $J$ = 10.8, 2.5, 1 H), 5.54 (ddd, $J$ = 10.8, 5.0, 3.6, 1 H); exact mass calcd for $C_{17}H_{26}O_4$ ($M^+$) $m/z$ 294.1831, found $m/z$ 294.1835.

Dehydration of **8b** (23.0 mg, 0.074 mmol) and purification of the crude product by the procedure as described above gave 19.6 mg (90%) of **9**.

**Preparation of Epoxy Acetate 10.** To a solution of **9** (29.1 mg, 0.099 mmol) in dichloromethane (3.0 mL) was added *m*-CPBA (55 mg, 0.32 mmol) at 0 °C. The mixture was stirred at 0 °C for 30 min and at room temperature for 7 h, and diluted with saturated $Na_2S_2O_3$ solution (2 mL) and $NaHCO_3$ solution (1 mL). The mixture was extracted with chloroform (5 × 5 mL). Removal of solvent gave an oily residue, which was purified by column chromatography (5:1 hexane–ether) to give 29.8 mg (97%) of **10**: mp 86–87 °C (hexane); IR 1740 $cm^{-1}$; $^1H$ NMR δ 1.12 (s, 3 H), 1.30 (s, 3 H), 1.48 (s, 3 H), 1.50 (s, 3 H), 2.08 (s, 3 H), 2.79 (d, $J$ = 4.0, 1 H), 3.26 (ddd, $J$ = 4.0, 4.0, 4.0, 1 H), 3.80 (d, $J$ = 10.8, 1 H), 4.16 (d, $J$ = 10.8, 1 H), 4.66 (br d, $J$ = 7.2, 1 H); exact mass calcd for $C_{16}H_{23}O_5$ ($M^+ - CH_3$) $m/z$ 295.1546, found $m/z$ 295.1569.

**Preparation of Cyclic Ether 11.** A mixture of **10** (22.8 mg, 0.074 mmol) and anhydrous $K_2CO_3$ (104 mg, 0.74 mmol) in methanol (3.0 mL) was stirred at room temperature for 1 h and concentrated under reduced pressure. The residue was diluted with water (2 mL) and the mixture was extracted with ether (3 × 5 mL). Removal of solvent gave an oily residue, which was purified by preparative TLC (1:2 hexane–ether) to afford 15.8 mg (80%) of **11** as a colorless oil: IR 3580 $cm^{-1}$; $^1H$ NMR δ 1.18 (s, 3 H), 1.31 (s, 3 H), 1.50 (s, 6 H), 3.44 (d, $J$ = 10.0, 1 H), 3.96 (d, $J$ = 10.0, 1 H), 3.44 (m, 1 H), 4.44 (t, $J$ = 5.4, 1 H), 4.76 (t, $J$ = 3.6, 1 H); exact mass calcd for $C_{15}H_{24}O_4$ ($M^+$) $m/z$ 268.1675, found $m/z$ 268.1648.

**Preparation of Ketone 12.** To a mixture of **11** (24.5 mg, 0.091 mmol) and dry Celite (190 mg) in dichloromethane (0.5 mL) was added a 1.2 M solution of Collins reagent ($CrO_3$·2Py) (2.2 mL, 2.6 mmol) in dichloromethane. The mixture was stirred at room temperature for 1 h, diluted with ether (5 mL), and passed through a short column of Florisil. The column was washed thoroughly with ether (20 mL). The combined organic solutions were washed with saturated $CuSO_4$ solution (3 × 1 mL). Removal of solvent gave an oily residue, which was purified by column chromatog-

raphy (15:2 hexane–ether) to give 19.8 mg (81%) of **12**: mp 84–85 °C (hexane); IR 1720 $cm^{-1}$; $^1H$ NMR $\delta$ 1.18 (s, 3 H), 1.43 (s, 3 H), 1.46 (s, 3 H), 1.52 (s, 3 H), 3.67 (d, $J$ = 9.0, 1 H), 4.15 (d, $J$ = 9.0, 1 H), 4.33 (d, $J$ = 6.8, 1 H), 4.84 (m, 1 H). Anal. Calcd for $C_{15}H_{22}O_4$: C, 67.65; H, 8.33. Found C, 67.40; H, 8.60.

**Preparation of Alcohols 13a and 13b. (a) Reaction of 12 with $CH_3Li$.** To a stirred solution of **12** (19.8 mg, 0.074 mmol) in THF (2 mL) was added a 1.25 M solution of $CH_3Li$ (1.2 mL, 1.5 mmol) in ether at 0 °C and the mixture was stirred at 0 °C for 1 h. The mixture was diluted with saturated $NH_4Cl$ solution (1 mL) and extracted with ethyl acetate (3 × 5 mL). Removal of solvent afforded an oily residue, which was separated by column chromatography (15:2 → 5:1 hexane–ether) to give 3.4 mg (16%) of **13a** [$R_f$ 0.50 (1:2 hexane–ether)] and 15.5 mg (74%) of **13b** [$R_f$ 0.25 (1:2 hexane–ether)]. **13a**: mp 115–116 °C (hexane–ether); IR 3540 $cm^{-1}$; $^1H$ NMR $\delta$ 1.13 (s, 3 H), 1.18 (s, 3 H), 1.28 (s, 3 H), 1.52 (s, 6 H), 3.05 (br s, 1 H, OH), 3.41 (d, $J$ = 9.0, 1 H), 3.94 (d, $J$ = 9.0, 1 H), 3.99 (d, $J$ = 5.4, 1 H), 4.82 (m, 1 H); exact mass calcd for $C_{16}H_{26}O_4$ ($M^+$) $m/z$ 282.1831, found $m/z$ 282.1813. **13b**: mp 103–105 °C (hexane–ether); IR 3600, 3500 $cm^{-1}$; $^1H$ NMR $\delta$ 1.06 (s, 3 H), 1.14 (s, 3 H), 1.28 (s, 3 H), 1.49 (s, 6 H), 3.44 (d, $J$ = 9.0, 1 H), 3.94 (d, $J$ = 7.2, 1 H), 3.99 (d, $J$ = 9.0, 1 H), 4.85 (m, 1 H); exact mass calcd for $C_{16}H_{26}O_4$ ($M^+$) $m/z$ 282.1831, found $m/z$ 282.1841.

**(b) Reaction of 12 with $CH_3MgI$.** To a stirred solution of $CH_3MgI$ (from 73 mg of Mg) in ether (10 mL) was added a solution of **12** (20 mg, 0.075 mmol) in ether (3 mL) at 0 °C and the mixture was stirred at 0 °C for 1 h. Workup and separation by the procedure as described above gave 19.5 mg (92%) of **13a** and 0.8 mg (4%) of **13b**.

**Single-Crystal X-ray Analysis of Alcohol 13b.** Crystals of alcohol **13b** were obtained by slow crystallization from hexane–ether. $D_{measd}$ was measured by floatation. Crystal data of **13b** were as follows: $C_{16}H_{26}O_4$, $M_r$ = 282.18; monoclinic space group $P2_1/c$, $a$ = 10.875 (1) Å, $b$ = 12.135 (1) Å, $c$ = 12.175 (2) Å, $\beta$ = 108.82 (1)°; $V$ = 1520.8 (3) Å$^3$; $D_{calcd}$ = 1.233 g/cm$^3$, $D_{measd}$ = 1.243 g/cm$^3$; $Z$ = 4; crystal size, 0.4 × 0.4 × 0.2 mm. A total 3939 reflections with $2\theta \leq 126°$ were collected on a RIGAKU AFC-5R automated four-circle diffractometer using graphite monochromated Cu K$\alpha$ radiation (1.54178 Å). Structure was solved by Monte–Carlo direct method[8] with the aid of MULTAN 78 program system[9] using 2325 non zero unique reflections and refined by full-matrix least-square program. Non-H atoms were assigned with anisotropic thermal parameters. All H atoms were located in a difference Fourier map and refined with the equivalent isotropic thermal parameters to those for the bonded atoms. The final unweighted $R$ factor was 0.055 after minimizing $\sum w(|F_o|^2 - |F_c|^2)^2$ with $w = 1/\sigma^2(F_o^2)$; $w_R$ = 0.05, $S = [\sum w(|F_o|^2 - |F_c|^2)^2/(m - n)]^{1/2}$ = 1.8; $\Delta\rho_{max}$ = 0.47 e Å$^{-3}$. Atomic scattering factors were from ref 10. ORTEP 78 program[11] was employed in drawing the computer-generated molecular structure. All crystallographic calculations were performed on a FACOM M-382 computer, operated by Computation Center of Nagoya University. A computer-generated perspective drawing of **13b** is given in Figure 1. Tables I, II, III, and IV contain the fractional coordinates, thermal parameters, bond angles, and bond distances.[12]

**Preparation of γ-Lactone 14.** A mixture of **13a** (8.3 mg, 0.029 mmol), $RuCl_3 \cdot H_2O$ (3.3 mg, 0.015 mmol), and $NaIO_4$ (50 mg, 0.23 mmol) in $CCl_4$ (0.8 mL), $CH_3CN$ (0.8 mL), and phosphate buffer (0.05 M, pH 6.8; 1.2 mL) was stirred at room temperature for 14 h and then isopropyl alcohol (0.1 mL) was added. The mixture was stirred vigorously for an additional 10 min, and extracted with dichloromethane (5 × 5 mL). The combined organic layers were dried and concentrated to give a crude product. Purification by column chromatography (1:1 hexane–ether) gave 8.1 mg (93%) of **14** as a colorless oil: IR 3520, 1775 $cm^{-1}$; $^1H$ NMR $\delta$ 1.14 (s, 3 H), 1.17 (s, 3 H), 1.23 (s, 3 H), 1.51 (s, 6 H), 2.21 (dd, $J$ = 5.4, 12.6, 1 H), 2.83 (d, $J$ = 12.6, 1 H), 3.25 (br s, 1 H, OH), 4.33 (d, $J$ = 5.4, 1 H), 4.75 (d, $J$ = 7.2, 1 H); exact mass calcd for $C_{16}H_{24}O_5$ ($M^+$) $m/z$ 296.1624, found $m/z$ 296.1618.

**Preparation of γ-Lactone Triol 3.** A mixture of **14** (7.0 mg, 0.024 mmol) and 2 M hydrochloric acid (2 mL) was stirred at 90 °C for 3 h and concentrated in vacuo to leave an oily residue, which was diluted with ethyl acetate (10 mL). The organic solution was washed with saturated $NaHCO_3$ solution, dried, and concentrated to give a crude product. Purification by column chromatography (ether) gave 7.5 mg (quantitative) of **3** as a colorless oil: 3560, 1780 $cm^{-1}$; $^1H$ NMR $\delta$ 1.14 (s, 3 H), 1.20 (s, 3 H), 1.27 (s, 3 H), 2.82 (d, $J$ = 12.6, 1 H), 2.84 (br s, 1 H, OH), 3.46 (br s, 1 H, OH), 4.33 (d, $J$ = 5.4, 1 H), 4.45 (br t, $J$ = 7.2, 1 H); exact mass calcd for $C_{13}H_{18}O_4$ ($M^+ - H_2O$) $m/z$ 238.1205, found $m/z$ 238.1207.

**Acknowledgment.** The X-ray crystal analysis was performed by Drs. C. Katayama and H. Kigoshi of Department of Chemistry, Faculty of Science, Nagoya University, to whom we are grateful.

**Registry No.** **1**, 5230-87-5; **2**, 5230-95-5; (±)-**3**, 100604-40-8; (±)-**4**, 69586-19-2; (±)-**5**, 100604-30-6; (±)-**6**, 100604-31-7; (±)-**7a**, 100604-32-8; (±)-**7b**, 100758-91-6; (±)-**8a**, 100604-33-9; (±)-**8b**, 100758-92-7; (±)-**9**, 100604-34-0; (±)-**10**, 100604-35-1; (±)-**11**, 100604-36-2; (±)-**12**, 100604-37-3; (±)-**13a**, 100604-38-4; (±)-**13b**, 100758-93-8; (±)-**14**, 100604-39-5.

**Supplementary Material Available:** Tables of the fractional coordinates, thermal parameters, bond angles, and bond distances (Tables I–IV) for alcohol **13b** (4 pages). Ordering information is given on any current masthead page.

(8) Furusaki, A. *Acta Crystallogr., Sect. A: Found. Crystallog.* **1979**, *A35*, 220.

(9) Main, P.; Hull, S. E.; Lessinger, L.; Germain, G.; Declercq, J. P.; Woolfson, M. M. "MULTAN 78, a System of Computer Programs for the Automatic Solution of Crystal Structures from X-ray Diffraction Data"; University of York, England, 1978.

(10) "International Tables for X-ray Crystallography"; Kynoch Press: Birmingham, England, 1974; Vol. 4.

(11) Johnson, C. K. "ORTEP, Crystallographic Illustration Program"; Repo t ORNL-3794, Oak Ridge National Laboratory: Oak Ridge, TN, 1965.

(12) Supplementary material.