Syntheses of ($\pm$)-Haedoxan A, D, E and Their Stereoisomers

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Received December 12, 1988

The naturally occurring insecticides, haedoxans A and D, as well as the artificial congener, haedoxan E, and nine of their stereoisomers were synthesized in racemic form.

The structure, 1-acetoxy/hydroxy-6-aryl-2-aryloxy-3,7-dioxabicyclo[3.3.0]octane, is the representative framework of a series of unique lignans responsible to the insecticidal activity of the plant, *Phryma leptostachya* L. (Fig. 1). Construction of the framework was accomplished by the syntheses of ($\pm$)-(1*S**,2*S**,5*R**,6*S**)-phrymarolin II (**5**)¹⁾ and natural (+)-

(1*S*,2*S*,5*R*,6*S*)-phrymarolin I (**4**).^{2,3} The 2*S*-configuration of **4** has been revised to 2*R* based on recent NOESY experiments.⁴ Our effort on the *Phryma* lignans has been extended to the syntheses of the insecticidal neolignans, (+)-haedoxan A⁵ and D,⁶ in succession to the preparation of the benzodioxane moiety⁷ involved in these molecules. The strategy de-

Fig. 1.

Fig. 2.

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Fig. 3.

veloped for the synthesis of ($\pm$)-phymarolin II (Fig. 2) was successfully employed for the haedoxan syntheses (Fig. 3). In this paper, the syntheses of ($\pm$)-haedoxan A (**1a**), D (**2a**) and the congener, haedoxan E (**3a**), as well as their stereoisomers are described.

The reaction of ($\pm$)-2,3-*trans*-2,3-dihydro-1,4-benzodioxine aldehyde **6**⁷⁾ with the lithium enolate of β -vinyl- γ -butyrolactone (**7**)⁸⁾ generated by lithium diisopropylamide (LDA) in tetrahydrofuran (THF) at -75°C gave a mixture of 2,3-*trans*-lactonic alcohols (**8a**~**d**) in an appreciable yield. The mixture was almost quantitatively silylated with *tert*-butyldimethylsilyl triflate (TBDMSOTf) and 2,6-lutidine⁹⁾ in methylene chloride at -30°C to afford a mixture of four diastereoisomeric *tert*-butyldimethylsilylated alcohols (TBDMS-ethers, **9a**~**9d**). A conventional method using *tert*-butyldimethylchlorosilane-imidazole was inefficient for silylation of the benzyl alcohols. The mixture of TBDMS-ethers was separated into three portions, *i.e.*, each of the *threo*-isomers, **9c** and **9d**, and a mixture of the *erythro*-isomers, **9a** and **9b**, in 12%, 18%, and 55% yields, respectively, by means of medium-pres-

sure liquid chromatography using silica gel. After desilylating each of the isolates, the stereochemistries of aldols **8a**, **8b**, **8c** and **8d** were assigned on the basis of the coupling constants, $J_{threo}=6\sim9\text{ Hz}$ and $J_{erythro}=2\sim4\text{ Hz}$, which have been established by House *et al.*¹⁰⁾ A lithium aluminum hydride reduction of the mixture of **9a** and **9b** gave a mixture of diols (**10a** and **10b**) in a quantitative yield. The inseparable diastereoisomeric diols were together oxidized with a catalytic amount of osmium tetroxide in the presence of a slight excess of *N*-methylmorpholine *N*-oxide¹¹⁾ in a solvent system of *tert*-BuOH–Me₂CO–H₂O, and followed by successive oxidation with sodium periodate in aqueous methanol and with silver carbonate–Celite¹²⁾ in refluxing benzene. A mixture of 2-hydroxymethyl-lactones (**11a** and **11b**) obtained as a resinous material was treated with mesyl chloride and triethylamine in benzene, and followed by 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) to furnish a mixture of α -methylenelactones (**12a** and **12b**) in 86% yield. These methylenelactones were separated into each of the diastereoisomers by medium-pressure liquid chro-

matography using a silica gel column (benzene–EtOAc=95:5). A catalytic osmium oxidation of **12a**, using *N*-methylmorpholine *N*-oxide as a reoxidant¹¹⁾ in a solvent system of *tert*-BuOH–Me₂CO–THF–H₂O, quantitatively furnished 2 α -hydroxyl lactone-glycol **13a**, which possessed the required configuration for constructing the 3,7-dioxabicyclo[3.3.0]octane framework. The stereoselective oxidation would be controlled by the attack of the oxidant from the less hindered α -side of the molecule. After removing the protecting TBDMS group of **13a** with tetra-*n*-butylammonium fluoride¹³⁾ in THF at room temperature, triol **14a** was dehydrated by treating with a catalytic amount of 10-camphorsulfonic acid in methylene chloride at room temperature to furnish the key intermediary 1 α -hydroxy-6 α -[(2'*R**,3'*R**)-6'-methoxy-2'-methoxymethyl-

3'-(3'',4''-methylenedioxy)phenyl-2',3'-dihydro-1',4'-benzodioxin-7'-yl]-3,7-dioxabicyclo[3.3.0]octane-2-one (**15a**)¹⁴⁾ in 84% yield. The diastereoisomer, 1 α -hydroxy-6 α -[(2'*S**,3'*S**)-6'-methoxy-2'-methoxymethyl-3'-(3'',4''-methylenedioxy)phenyl-2',3'-dihydro-1',4'-benzodioxin-7'-yl]-3,7-dioxabicyclo[3.3.0]octane-2-one (**15b**),¹⁴⁾ was obtained in 78% overall yield from **12b** by a series of reactions applied to **12a**. Desilylation of *threo*-silyl ether **13d** at room temperature furnished triol **14d** in a poor yield (26%), due to the inapposite product (**16**, 54%) resulting from intramolecular transesterification of the benzyloxy anion produced by desilylation of **13d**. This transesterification of the *threo*-isomer was overcome by carrying out the desilylation reaction at 0°C, whereby *threo*-isomer **13c** afforded **15a** in 63% yield. The transesterifica-

Fig. 4.

Fig. 5.

tion would be unfavorable to *erythro*-isomers **13a** and **13b**, since steric hindrance between the aromatic group and the hydroxymethyl group in a *cis*-arrangement on the γ -butyrolactone ring set the generated benzyloxide anion remote from the lactonic carbonyl group (Fig. 4).

After masking the 1-hydroxyl group of **15a** with TBDMSOTf and 2,6-lutidine⁹⁾ in methylene chloride, TBDMS-ether **17a** was reduced with diisobutylaluminium hydride (DIBAL) in toluene at -75°C to afford lactol **18a** in 94% yield. This lactol was fluorinated with 2-fluoro-1-methylpyridinium tosylate and triethylamine¹⁵⁾ in methylene chloride to give a mixture of the 2α - and 2β -fluoride (**19a**) in 81% yield (Fig. 5). The ratio of α/β -fluorides was estimated as 1/1 based on the comparable integrated intensities of the resonance signals of 2-H at 5.42 and 5.57 ppm, although the respective resonances remained to be assigned to the α/β -hydrogens. Trimethylsilyl triflate has catalyzed the reactions of 2,3,4,6-tetra-*O*-benzyl-D-glucopyranosyl fluoride with several trimethylsilylated alcohols.¹⁶⁾ The configuration of the anomeric carbon of the glucosides was primarily affected by the solvents used for glycosylation, irrespective of the stereochemistry of the anomeric carbon of the glucosyl fluorides used. The glycosylation reaction in ether resulted in predominant formation of α -glucosides from either α - or β -fluoride, whereas the reaction in acetonitrile favored the formation of β -glucosides. Treatment of mixed fluorides **19a** with *O*-trimethylsilyl (TMS) sesamol (**20**) in the presence of a catalytic amount of TMSOTf in ether at 0°C , which was followed by desilylation with tetra-*n*-butylammonium fluoride¹³⁾ in THF at room temperature, furnished ($\pm$)-haedoxan E (**3a**) along with ($\pm$)-isohaedoxan E (**29a**), in 25% and 61% yields, respectively. The reaction of **19a** with *O*-TMS-2-methoxy-4,5-methylenedioxyphenol (**21**) gave ($\pm$)-haedoxan D (**2a**) and ($\pm$)-isohaedoxan D (**28a**) in 19% and 72% yields, respectively. The stereochemical outcome of the α -isomers in the acetalization reaction was little improved by applying the

method developed for stereoselective preparation of α -ribofuranosides from 2,3,5-tri-*O*-benzyl- β -D-ribofuranosyl fluoride and various alcohols in the presence of tin(II) chloride-trityl perchlorate in ether.¹⁵⁾ Treatment of an equimolar mixture of fluorides **19a** with phenol **22** in ether in the presence of tin(II) chloride and trityl perchlorate, which was followed by desilylation of the products, furnished **2a** and **28a** in 25% and 55% yields, respectively. Acetalization of **19a** with 2,6-dimethoxy-3,4-methylenedioxyphenol (**23**) in ether in the presence of silver perchlorate and tin(II) chloride,¹⁷⁾ which was followed by deprotection of the 1-TBDMS group, gave ($\pm$)-haedoxan A (**1a**) and ($\pm$)-isohaedoxan A (**27a**) as well as the $2\alpha,6\beta$ -isomer in 17%, 16% and 10% yields, respectively. Stereoisomers **1b**, **2b**, **3b**, **27b**, **28b** and **29b** were also synthesized in appreciable yields from the other key intermediary lactone, **15b**. The 2,3-dihydro-1,4-benzodioxin framework of these stereoisomers should have a relative configuration opposite to that of the dihydrobenzodioxinyl involved in **1a**, **2a**, **3a**, **27a**, **28a** and **29a**.

The ^1H -NMR spectra of synthesized compounds **1a** and **2a**, but not of the other stereoisomers, were superimposable on those of natural (+)-haedoxan A and (+)-haedoxan D, respectively. Thus, racemic haedoxan A and D were synthesized by 15 steps in 4% and 3% yields, respectively. These stereo-controlled syntheses promised the establishment of the absolute configuration of natural haedoxans, employing *optically pure* β -vinyl- γ -butyrolactone³⁾ and 2,3-*trans*-2,3-dihydro-1,4-benzodioxine aldehyde.

Experimental

All melting points (mp) are uncorrected. Infrared (IR) spectra were determined on a Shimadzu IR-420 spectrophotometer. ^1H - and ^{13}C -NMR spectra were obtained on a JEOL FX-100 spectrometer. Low-resolution mass spectra (MS) were measured by an ESCO FMD-05A spectrometer at 70 eV.

Gravity column chromatography and medium-pressure liquid chromatography were done with Merck silica gel 60 (70~230 mesh ASTM) and Merck Lichroprep Si60, re-

spectively. Preparative TLC was performed with Merck silica gel 60 F₂₅₄ plates (0.5 mm thickness, 20 × 20 cm).

4-Ethenyl-3-[1'-hydroxy-1'-[6''-methoxy-2''-methoxymethyl-3'''-(3'''',4'''-methylenedioxyphenyl)-2'',3''-dihydro-1'',4''-benzodioxin-7''-yl]methyl]dihydro-2(3H)-furanones (8a~8d). LDA was prepared by adding a 15% solution of *n*-BuLi in *n*-hexane (4.20 ml, 6.74 mmol) to a solution of diisopropylamine (0.94 ml, 6.74 mmol) in dry THF (50 ml) at −30°C under argon and stirring for 15 min at −10°C. A solution of lactone **7** (0.76 g, 6.79 mmol) in THF (15 ml) was added in drops to the LDA solution at −75°C. After 30 min, aldehyde **6** (2.01 g, 5.61 mmol) dissolved in THF (15 ml) was also added in drops. After 3 hr, the reaction was quenched with 10% aqueous NH₄Cl. The mixture was warmed to room temperature and extracted with ether. The aqueous layer was re-extracted with AcOEt, and the combined extracts were washed with 5% aqueous NaHCO₃, dried over Na₂SO₄, and evaporated. The oily residue was chromatographed on silica gel eluted with benzene–EtOAc (4:1) to give a mixture of **8a~8d** (2.64 g, 5.61 mmol) as a viscous oil in a quantitative yield. IR $\nu_{\max}$ (CHCl₃) cm^{−1}: 3100~3650 (OH), 1760 (C=O), 1601, 1500, 1445, 1160, 1065, 1020. MS *m/z*: 470 (M⁺), 359, 358, 327, 326, 192, 161, 160 (base), 131, 103, 54. *Anal.* Found: C, 63.77; H, 5.56. Calcd. for C₂₅H₂₆O₉: C, 63.83; H, 5.53%.

3-[1'-[(*tert*-Butyldimethylsilyl)oxy]-1'-[6''-methoxy-2''-methoxymethyl-3'''-(3'''',4'''-methylenedioxyphenyl)-2'',3''-dihydro-1'',4''-benzodioxin-7''-yl]methyl]-4-ethenyldihydro-2(3H)-furanones (9a~9d). To a stirred solution of **8a~8d** (2.64 g, 5.61 mmol) and 2,6-lutidine (1.31 ml, 11.25 mmol) in dry CH₂Cl₂ was added in drops *tert*-BuMe₂SiOTf (1.93 ml, 8.42 mmol) in a solution of CH₂Cl₂ (10 ml) at −40°C under argon. After 35 min at −30°C, the reaction was quenched with 5% aqueous NaHCO₃. The CH₂Cl₂ layer was separated and the aqueous layer was extracted with CH₂Cl₂. The combined extracts were dried over Na₂SO₄ and evaporated. The oily residue was purified by medium-pressure liquid chromatography on silica gel. Elution with 5% EtOAc in benzene first afforded a mixture of **9a** and **9b** (1.79 g, 3.07 mmol, 55% yield), was followed by **9c** (0.41 g, 0.70 mmol, 12% yield), and finally **9d** (0.58 g, 0.99 mmol, 18% yield). The mixture of **9a** and **9b**: mp 141~150°C. **9c**: mp 141~144°C. NMR δ_{H} (CDCl₃): −0.05 (3H, s), 0.12 (3H, s), 0.94 (9H, s), 2.71 (1H, dd, *J*=4, 8 Hz), 3.05 (1H, m), 3.27 (1H, dd, *J*=4, 10 Hz), 3.33 (3H, s), 3.59 (1H, dd, *J*=3, 10 Hz), 3.68 (3H, s), 3.81 (1H, dd, *J*=7, 9 Hz), 3.98 (1H, m), 4.14 (1H, dd, *J*=8, 9 Hz), 4.88~5.33 (4H, m), 5.52~5.88 (1H, m), 5.97 (2H, s), 6.41 (1H, s), 6.72~6.96 (3H, m), 7.18 (1H, s). **9d**: mp 142~145°C. NMR δ_{H} (CDCl₃): −0.06 (3H, s), 0.12 (3H, s), 0.93 (9H, s), 2.70 (1H, dd, *J*=4, 8 Hz), 3.00 (1H, deformed t, *J*=7 Hz), 3.26 (1H, dd, *J*=4, 11 Hz), 3.32 (3H, s), 3.63 (1H, dd, *J*=3, 11 Hz), 3.67 (3H, s), 3.68~4.14 (3H, m), 4.84~5.38 (4H, m), 5.50~5.92 (1H,

m), 5.96 (2H, s), 6.41 (1H, s), 6.72~6.96 (3H, m), 7.19 (1H, br. s). IR $\nu_{\max}$ (CHCl₃) cm^{−1}: 3350, 1760, 1601, 1500, 1445, 1160, 1065, 1021. *Anal.* Found: C, 63.71; H, 6.92. Calcd. for C₃₁H₄₀O₉Si: C, 63.70; H, 6.85%.

2-[1'-[(*tert*-Butyldimethylsilyl)oxy]-1'-[6''-methoxy-2''-methoxymethyl-3'''-(3'''',4'''-methylenedioxyphenyl)-2'',3''-dihydro-1'',4''-benzodioxin-7''-yl]methyl]-3-ethenyl-1,4-butanediols (10a and 10b). To a stirred slurry of LiAlH₄ (0.14 g, 3.68 mmol) in dry ether (30 ml) was added in drops a solution of a mixture of **9a** and **9b** (2.02 g, 3.46 mmol) in dry THF (30 ml) at −10°C under argon. After 30 min at −10°C, the excess reagent was decomposed by carefully adding EtOAc, and then 10% aqueous citric acid. The organic layer was separated and the aqueous layer was extracted with EtOAc. The combined organic extracts were washed with 5% aqueous NaHCO₃, dried over Na₂SO₄, and evaporated. The oily residue was chromatographed on silica gel eluted with *n*-hexane–EtOAc (1:1) to give a mixture of **10a** and **10b** (2.00 g, 3.40 mmol) as a viscous oil in 98% yield. IR $\nu_{\max}$ (CHCl₃) cm^{−1}: 3100~3650 (OH), 2950, 1602, 1502, 1445, 1255 (C–Si), 1197, 1155, 1068, 1043. *Anal.* Found: C, 62.81; H, 7.53. Calcd. for C₃₁H₄₄O₉Si: C, 63.24; H, 7.53%.

4-[1'-[(*tert*-Butyldimethylsilyl)oxy]-1'-[6''-methoxy-2''-methoxymethyl-3'''-(3'''',4'''-methylenedioxyphenyl)-2'',3''-dihydro-1'',4''-benzodioxin-7''-yl]methyl]-3-hydroxymethyldihydro-2(3H)-furanones (11a and 11b). A solution of a mixture of **10a** and **10b** (2.00 g, 3.40 mmol), *N*-methylmorpholine *N*-oxide monohydrate (0.52 g, 3.85 mmol) and 2% aqueous OsO₄ (1 ml) in a mixture of acetone (20 ml), *tert*-BuOH (5 ml) and water (5 ml) was stirred at room temperature for 18 hr under argon. Celite and aqueous NaHSO₃ (1 g/20 ml) were added, and the resulting mixture was filtered. The residue was washed well with acetone and the filtrate was concentrated under reduced pressure. The oily residue was taken up in EtOAc, washed with brine, dried over Na₂SO₄, and evaporated to give an oil (2.45 g).

The crude product was dissolved in MeOH (40 ml), and aqueous NaIO₄ (0.37 g, 1.73 mmol/10 ml) was added in drops at 0°C. After 20 min at 0°C, the reaction was worked up with 10% aqueous Na₂SO₃ (10 ml). The methanol was removed under reduced pressure, and the residue was extracted twice with EtOAc. The extracts were washed with brine, dried over Na₂SO₄, and evaporated to give an oil (2.05 g).

A mixture of the crude lactols and Ag₂CO₃/Celite (5.1 g, containing *c.* 5.1 mmol of Ag₂CO₃) in benzene (50 ml) was heated under reflux for 30 min. The mixture was then filtered and the residue was washed well with benzene. The filtrate was concentrated to give a mixture of **11a** and **11b** (1.96 g) as a viscous oil, which was used for the next step without further purifications. An analytically pure sample was obtained by preparative TLC on silica gel. IR $\nu_{\max}$ (CHCl₃) cm^{−1}: 835, 1067, 1250 (C–Si), 1310, 1500,

1602, 1702 (C=O), 3100~3600 (OH). *Anal.* Calcd. for $C_{30}H_{40}O_{10}Si$: C, 61.21; H, 6.85. Found: C, 61.04; H, 6.78%.

4-[1'-[(*tert*-Butyldimethylsilyl)oxy]-1'-[6''-methoxy-2''-methoxymethyl-3''-(3''',4'''-methylenedioxyphenyl)-2'',3''-dihydro-1'',4''-benzodioxin-7''-yl]methyl]-3-methylenedihydro-2(3H)-furanones (**12a**~**12d**). Methanesulfonyl chloride (0.39 ml, 5.10 mmol) was added to a stirred solution of a mixture of **11a** and **11b** (1.96 g) and triethylamine (0.95 ml, 6.80 mmol) in dry benzene (50 ml) at 0°C. After 2.5 hr at room temperature, diazabicyclo[5.4.0]undec-7-ene (0.78 g, 5.10 mmol) was added, and stirring was continued for 45 min. The mixture was then diluted with EtOAc, washed successively with 10% aqueous citric acid and 5% aqueous $NaHCO_3$, dried over Na_2SO_4 , and evaporated. The oily residue was chromatographed on silica gel with 5% EtOAc in benzene as the eluant to give a mixture of **12a** and **12b** (1.67 g, 2.93 mmol) in 86% overall yield from diols **10a** and **10b**. The mixture was separated by medium-pressure liquid chromatography on silica gel eluted with the same solvent to first afford **12b** (0.53 g, *Rf* 0.49, 10% EtOAc in benzene), then a mixture of **12a** and **12b** (0.18 g), and finally **12a** (0.96 g, *Rf* 0.44, 10% EtOAc in benzene).

12a. A viscous oil. NMR δ_H ($CDCl_3$): -0.19 (3H, s), 0.04 (3H, s), 0.87 (9H, s), 3.08~3.40 (2H, m), 3.33 (3H, s), 3.62 (1H, dd, $J=3$, 12 Hz), 3.71 (3H, s), 3.96 (1H, m), 4.07~4.38 (2H, m), 4.99 (1H, d, $J=8$ Hz), 5.05 (1H, d, $J=6$ Hz), 5.33 (1H, br. s), 5.97 (2H, s), 6.22 (1H, br. s), 6.45 (1H, s), 6.74~6.90 (3H, m), 6.96 (1H, s). IR ν_{max} ($CHCl_3$) cm^{-1} : 2950, 1755 (C=O), 1600, 1504, 1493, 1465, 1448, 1309, 1253 (C-Si), 1195, 1163, 1121, 1095, 1067, 1039, 857, 837.

12b. A viscous oil. NMR δ_H ($CDCl_3$): -0.19 (3H, s), 0.03 (3H, s), 0.87 (9H, s), 3.12~3.42 (3H, m), 3.33 (3H, s), 3.54 (1H, dd, $J=3$, 12 Hz), 3.71 (3H, s), 3.98 (1H, m), 4.09~4.26 (2H, m), 4.95 (1H, d, $J=8$ Hz), 5.04 (1H, d, $J=7$ Hz), 5.34 (1H, br. s), 5.97 (2H, s), 6.23 (1H, br. s), 6.45 (1H, s), 6.74~6.89 (3H, m), 6.95 (1H, s). *Anal.* Calcd. for $C_{30}H_{38}O_9Si$: C, 63.14; H, 6.71. Found: C, 62.82; H, 6.70%.

12c. A viscous oil. NMR δ_H ($CDCl_3$): -0.16 (3H, s), 0.00 (3H, s), 0.90 (9H, s), 3.16~3.41 (2H, m), 3.34 (3H, s), 3.55 (1H, dd, $J=3$, 11 Hz), 3.72 (3H, s), 3.97 (1H, m), 4.13 (1H, dd, $J=8$, 9 Hz), 4.49 (1H, dd, $J=4$, 9 Hz), 4.97 (1H, d, $J=8$ Hz), 5.12 (1H, d, $J=5$ Hz), 5.42 (1H, d, $J=2$ Hz), 5.98 (2H, s), 6.24 (1H, d, $J=2$ Hz), 6.44 (1H, s), 6.72~6.94 (3H, m), 7.04 (1H, s).

12d. mp 120~124°C. NMR δ_H ($CDCl_3$): -0.16 (3H, s), 0.00 (3H, s), 0.89 (9H, s), 3.12~3.44 (2H, m), 3.33 (3H, s), 3.66 (1H, dd, $J=3$, 11 Hz), 3.72 (3H, s), 3.88~4.24 (2H, m), 4.47 (1H, dd, $J=5$, 9 Hz), 5.00 (1H, d, $J=9$ Hz), 5.11 (1H, d, $J=5$ Hz), 5.40 (1H, d, $J=2$ Hz), 5.99 (2H, s), 6.23 (1H, d, $J=2$ Hz), 6.44 (1H, s), 6.72~6.98 (3H, m), 7.06 (1H, s).

2''-methoxymethyl-3''-(3''',4'''-methylenedioxyphenyl)-2'',3''-dihydro-1'',4''-benzodioxin-7''-yl]methyl]-3-hydroxy-3-(hydroxymethyl)dihydro-2(3H)-furanone (**13a**). A solution of **12a** (0.13 g, 0.23 mmol), *N*-methylmorpholine *N*-oxide monohydrate (0.04 g, 0.30 mmol) and 2% aqueous OsO_4 (0.2 ml) in a mixture of acetone (6 ml), THF (0.5 ml), *tert*-BuOH (2 ml) and water (2 ml) was stirred at room temperature in the dark for 14 hr under argon. Celite and aqueous $NaHSO_3$ (0.2 g/10 ml) were added, and the mixture was filtered. The residue was washed well with acetone, and the filtrate was concentrated under reduced pressure. The residue was taken up in EtOAc, washed with brine, dried over Na_2SO_4 , and concentrated. The oily residue was chromatographed on silica gel eluted with *n*-hexane-EtOAc (1:2) to give **13a** (0.13 g, 0.22 mmol) as a viscous oil in 96% yield. NMR δ_H ($CDCl_3$): -0.26 (3H, s), 0.10 (3H, s), 0.91 (9H, s), 2.52~2.76 (1H, br.), 2.92~3.16 (2H, m), 3.27 (1H, dd, $J=3$, 11 Hz), 3.33 (3H, s), 3.63 (1H, dd, $J=3$, 11 Hz), 3.73 (3H, s), 3.84~4.24 (5H, m), 5.00 (1H, d, $J=8$ Hz), 5.28 (1H, d, $J=8$ Hz), 5.98 (2H, s), 6.47 (1H, s), 6.80~6.96 (3H, m), 7.00 (1H, s). IR ν_{max} ($CHCl_3$) cm^{-1} : 838, 1018 (C-O), 1040 (C-O), 1250 (C-Si), 1315, 1495, 1602, 1777 (C=O), 3200~3600 (OH). *Anal.* Calcd. for $C_{30}H_{40}O_{11}Si$: C, 59.59; H, 6.67. Found: C, 59.42; H, 6.71%.

1-Hydroxy-6-[6'-methoxy-2'-methoxymethyl-3'-(3'',4''-methylenedioxyphenyl)-2'',3''-dihydro-1'',4''-benzodioxin-7''-yl]-3,7-dioxabicyclo[3.3.0]octan-2-ones (**15a** and **15b**). A 1 M solution of *n*-Bu₄NF in THF (0.27 ml, 0.27 mmol) was added to a solution of **13a** (0.13 g, 0.22 mmol) in dry THF (5 ml) at 0°C, and the mixture was stirred for 1.5 hr at 0°C. The reaction was quenched by 10% aqueous NH_4Cl , and the mixture was then extracted twice with EtOAc. The extracts were washed with brine, dried over Na_2SO_4 , and evaporated. The oily residue was chromatographed on silica gel eluted with EtOAc-THF (3:1) to give triol **14a** as a viscous oil (0.67 g).

The triol was dissolved in dry CH_2Cl_2 (10 ml), and a catalytic amount of CSA (c. 20 mg) was added. After 16 hr at room temperature, the reaction was quenched by adding one drop of triethylamine. The solvent was removed under reduced pressure, and the oily residue was chromatographed on silica gel with *n*-hexane-EtOAc (1:2) as the eluant to give lactone **15a** (0.09 g, 0.19 mmol) as white crystals in 87% yield, mp 177~179°C. NMR δ_H ($CDCl_3$): 2.98 (1H, s), 3.12 (1H, m), 3.27 (1H, dd, $J=5$, 11 Hz), 3.33 (3H, s), 3.58 (1H, dd, $J=3$, 11 Hz), 3.73 (3H, s), 3.97 (1H, m), 4.18 (2H, s), 4.34 (1H, dd, $J=6$, 11 Hz), 4.65 (1H, dd, $J=9$, 10 Hz), 4.96 (1H, d, $J=8$ Hz), 5.10 (1H, d, $J=5$ Hz), 5.97 (2H, s), 6.49 (1H, s), 6.72~6.92 (3H, m), 7.14 (1H, s). IR ν_{max} ($CHCl_3$) cm^{-1} : 3100~3650 (OH), 1777 (C=O), 1601, 1502, 1495, 1469, 1450, 1335, 1255, 1200, 1170, 1125, 1073, 1042, 1205. MS m/z : 472 (M^+), 192 (base), 162, 161, 160, 135, 131, 103. *Anal.* Found: C, 60.99; H, 5.17. Calcd. for $C_{24}H_{24}O_{10}$: C, 61.02; H, 5.08%.

4-[1'-[(*tert*-Butyldimethylsilyl)oxy]-1'-[6''-methoxy-

In the same manner as that just described, lactone **15b** was obtained in 78% overall yield from **14b**, mp 180~182°C. NMR δ_{H} (CDCl_3): 3.12 (1H, m), 3.24 (1H, s), 3.29 (1H, dd, $J=4$, 10 Hz), 3.32 (3H, s), 3.54 (1H, dd, $J=2$, 10 Hz), 3.72 (3H, s), 4.09 (1H, m), 4.16 (2H, s), 4.34 (1H, dd, $J=6$, 10 Hz), 4.65 (1H, dd, $J=9$, 10 Hz), 4.93 (1H, d, $J=8$ Hz), 5.08 (1H, d, $J=5$ Hz), 5.97 (2H, s), 6.48 (1H, s), 6.84 (3H, s), 7.14 (1H, s).

1-[(*tert*-Butyldimethylsilyl)oxy]-6-[6'-methoxy-2'-methoxymethyl-3'-(3'',4''-methylenedioxyphenyl)-2',3'-dihydro-1',4'-benzodioxin-7'-yl]-3,7-dioxabicyclo[3.3.0]octan-2-ones (**17a** and **17b**). *tert*-BuMe₂SiOTf (0.37 ml, 1.61 mmol) dissolved in dry CH_2Cl_2 (2 ml) was added in drops to a stirred solution of **15a** (381 mg, 0.807 mmol) and 2,6-lutidine (0.28 ml, 2.42 mmol) in dry CH_2Cl_2 (6 ml) at -10°C under argon. The reaction mixture was gradually warmed up to room temperature and allowed to stand for 17 hr. The mixture was then diluted with ether (30 ml) and washed successively with aqueous $\text{Cu}(\text{NO}_3)_2$ (3 g/12 ml $\times$ 2), water and 5% aqueous NaHCO_3 . The extract was dried over Na_2SO_4 and evaporated. The oily residue was chromatographed on silica gel with 7% EtOAc in benzene as the eluant to give **17a** (370 mg, 0.645 mmol) as a colorless viscous oil in 78% yield. NMR δ_{H} (CDCl_3): 0.05 (3H, s), 0.17 (3H, s), 0.80 (9H, s), 2.97 (1H, m), 3.30 (1H, dd, $J=6$, 11 Hz), 3.34 (3H, s), 3.54 (1H, dd, $J=3$, 11 Hz), 3.72 (3H, s), 3.99 (1H, m), 4.08 (1H, d, $J=10$ Hz), 4.24 (1H, d, $J=10$ Hz), 4.33 (1H, dd, $J=4$, 10 Hz), 4.58 (1H, dd, $J=8$, 9 Hz), 4.95 (1H, d, $J=8$ Hz), 5.02 (1H, d, $J=5$ Hz), 5.97 (2H, s), 6.47 (1H, s), 6.72~6.88 (3H, m), 7.10 (1H, s).

17b. A viscous oil. NMR δ_{H} (CDCl_3): 0.07 (3H, s), 0.18 (3H, s), 0.82 (9H, s), 2.93 (1H, m), 3.27 (1H, dd, $J=4$, 11 Hz), 3.34 (3H, s), 3.58 (1H, dd, $J=3$, 11 Hz), 3.73 (3H, s), 3.97 (1H, m), 4.06 (1H, d, $J=10$ Hz), 4.25 (1H, d, $J=10$ Hz), 4.37 (1H, dd, $J=4$, 10 Hz), 4.57 (1H, dd, $J=8$, 9 Hz), 4.98 (1H, d, $J=8$ Hz), 5.05 (1H, d, $J=5$ Hz), 5.98 (2H, s), 6.48 (1H, s), 6.75~6.90 (3H, m), 7.10 (1H, s).

1-[(*tert*-Butyldimethylsilyl)oxy]-2-hydroxy-6-[6'-methoxy-2'-methoxymethyl-3'-(3'',4''-methylenedioxyphenyl)-2',3'-dihydro-1',4'-benzodioxin-7'-yl]-3,7-dioxabicyclo[3.3.0]octanes (**18a** and **18b**). A 1 M solution of iso-Bu₂AlH in hexane (0.815 ml, 0.815 mmol) was added in drops to a stirred solution of **17a** (308 mg, 0.526 mmol) in dry toluene (10 ml) at -75°C under argon. After 1 hr at -75°C , the reaction was quenched by MeOH (0.5 ml). The mixture was then diluted with ether, washed successively with 0.5 N HCl and 5% aqueous NaHCO_3 , dried over Na_2SO_4 , and evaporated. The oily residue was chromatographed on silica gel with *n*-hexane-EtOAc (2:1) as the eluant to give **18a** (290 mg, 0.493 mmol) as a viscous oil in 94% yield. NMR δ_{H} (CDCl_3): 0.04~0.28 (6H, s $\times$ 4), 0.84~0.92 (9H, s $\times$ 2), 2.28~2.52 (1H, m), 3.12~3.36 (1H, m), 3.33 (3H, s), 3.48~3.76 (1H, m), 3.71 (3H, s), 3.80~4.30 (5H, m), 4.65~5.27 (3H, m), 5.98 (2H,

s), 6.48 (1H, s), 6.80~6.92 (3H, m), 7.17 (1H, s).

18b. A viscous oil. NMR δ_{H} (CDCl_3): 0.05~0.28 (6H, s $\times$ 4), 0.76~0.96 (9H, s $\times$ 2), 2.28~2.68 (1H, m), 3.16~3.37 (1H, br.), 3.34 (3H, s), 3.46~3.76 (2H, m), 3.71 (3H, s), 3.84~4.32 (5H, m), 4.75 (1H, d, $J=8$ Hz), 4.82~5.02 (1H, d $\times$ 2, $J=8$ each), 5.02~5.25 (2H, m), 5.98 (2H, s), 6.47 (1H, s), 6.72~6.92 (3H, m), 7.08~7.20 (1H, s $\times$ 2).

1-[(*tert*-Butyldimethylsilyl)oxy]-2-fluoro-6-[6'-methoxy-2'-methoxymethyl-3'-(3'',4''-methylenedioxyphenyl)-2',3'-dihydro-1',4'-benzodioxin-7'-yl]-3,7-dioxabicyclo[3.3.0]octane (**19a**). A solution of **18a** (290 mg, 0.493 mmol), 2-fluoro-1-methylpyridinium tosylate (0.21 g, 0.74 mmol) and triethylamine (0.137 ml, 0.986 mmol) in dry CH_2Cl_2 (10 ml) was stirred at room temperature for 1.5 hr. The solvent was removed under reduced pressure, and the residue was chromatographed on silica gel. Elution with *n*-hexane-EtOAc (3:1) afforded **19a** (236 mg, 0.400 mmol) as a white powder in 81% yield. NMR δ_{H} (CDCl_3): 0.09 (6H, s), 0.80~0.92 (9H, s $\times$ 2), 2.53~2.78 (1H, m), 3.10~3.40 (1H, m), 3.13 (3H, s), 3.40~3.65 (2H, m), 3.70 (3H, s), 3.80~4.48 (4H, m), 4.64~5.04 (2H, m), 5.42 (0.5H, d, $J=64$ Hz), 5.57 (0.5H, d, $J=64$ Hz), 5.97 (2H, s), 6.46 (1H, s), 6.70~6.96 (3H, m), 7.10~7.20 (1H, s $\times$ 2).

1-Hydroxy-6-[6'-methoxy-2'-methoxymethyl-3'-(3'',4''-methylenedioxyphenyl)-2',3'-dihydro-1',4'-benzodioxin-7'-yl]-2-(2'''-methoxy-3'''',4'''-methylenedioxyphenoxy)-3,7-dioxabicyclo[3.3.0]octanes (**2a**, **2b**, **28a** and **28b**).

Method A. Trimethylsilyl trifluoromethanesulfonate (7.5 μl , 0.004 mmol) was injected via a syringe into a solution of fluoride **19a** (50 mg, 0.085 mmol) and silyl ether **21** (29 mg, 0.121 mmol) in dry ether (2 ml) at 0°C . After 4 hr at 0°C , one drop of triethylamine was added, and the mixture was concentrated under reduced pressure. The crude product was purified by preparative TLC on silica gel developed with 10% EtOAc in benzene to give **25a** (50 mg, 0.068 mmol) in 80% yield.

A 2 α /2 β mixture of silyl ethers **25a** was dissolved in dry THF (1 ml), and a 1 M solution of *n*-Bu₄NF in THF (0.10 ml, 0.10 mmol) was added. After 1.5 hr at room temperature, the mixture was diluted with CH_2Cl_2 , washed with 10% aqueous NH_4Cl , dried over Na_2SO_4 , and concentrated. The residue was purified by preparative TLC on silica gel developed with 20% EtOAc in benzene to give **2a** (7.8 mg, 0.013 mmol) along with **28a** (30.7 mg, 0.049 mmol) in 19% and 72% yields, respectively).

Method B. A mixture of fluoride **19a** (39 mg, 0.066 mmol), 2-methoxy-4,5-methylenedioxyphenol (**22**, 13 mg, 0.079 mmol), TrClO_4 (27 mg, 0.079 mmol), SnCl_2 (26 mg, 0.133 mmol) and pulverized 4A molecular sieves in dry ether (3 ml) was stirred at $0\sim5^\circ\text{C}$ for 5.5 hr. The reaction was then quenched by adding 5% aqueous NaHCO_3 , and the resulting mixture was filtered through a pad of celite with the aid of ether. The ethereal layer was separated, washed with 0.5 N aqueous NaOH, dried over Na_2SO_4 , and concentrated. The oily residue was purified by pre-

parative TLC on silica gel developed with 10% EtOAc in benzene to give **25a** (39 mg, 0.053 mmol) in 80% yield.

Silyl ethers **25a** were desilylated with *n*-Bu₄NF in THF to give **2a** and **28a** in a ratio of 31:69 (determined by HPLC).

2a [(±)-haedoxan D]. mp 155~157°C (ether). NMR δ_H (CDCl₃): 1.62 (1H, br.), 2.64 (1H, m), 3.28 (1H, dd, *J*=5, 11 Hz), 3.34 (3H, s), 3.58 (1H, dd, *J*=3, 11 Hz), 3.72 (3H, s), 3.74 (1H, d, *J*=11 Hz), 3.77 (3H, s), 3.87~4.15 (2H, m), 4.29 (1H, d, *J*=11 Hz), 4.44 (1H, dd, *J*=8, 10 Hz), 4.92 (1H, d, *J*=6 Hz), 4.96 (1H, d, *J*=8 Hz), 5.17 (1H, s), 5.88 (2H, s), 5.98 (2H, s), 6.47 (1H, s), 6.53 (1H, s), 6.76 (1H, s), 6.80~6.98 (3H, m), 7.28 (1H, s).

28a. mp 172~173°C. NMR δ_H (CDCl₃): 2.62 (1H, br.), 2.72 (1H, q, *J*=7 Hz), 3.27 (1H, dd, *J*=4, 11 Hz), 3.33 (3H, s), 3.58 (1H, dd, *J*=3, 11 Hz), 3.71 (3H, s), 3.79 (3H, s), 3.98 (1H, m), 4.05 (1H, d, *J*=10 Hz), 4.20 (2H, d, *J*=7 Hz), 4.57 (1H, d, *J*=10 Hz), 4.97 (1H, d, *J*=8 Hz), 5.02 (1H, d, *J*=7 Hz), 5.34 (1H, s), 5.87 (2H, s), 5.97 (2H, s), 6.47 (1H, s), 6.54 (1H, s), 6.74 (1H, s), 6.80~6.90 (3H, m), 7.18 (1H, s). Anal. Found: C, 61.13; H, 5.18. Calcd. for C₃₂H₃₂O₁₃: C, 61.54; H, 5.16%.

Compounds **2b** and **28b**, isomers of the benzodioxane part of **2a** and **28a**, were obtained from **19b** by "method A" for synthesizing **2a** and **28a**.

2b. mp 194~196°C. NMR δ_H (CDCl₃): 1.70 (1H, br.), 2.63 (1H, m), 3.28 (1H, dd, *J*=4, 11 Hz), 3.33 (3H, s), 3.54 (1H, dd, *J*=3, 11 Hz), 3.71 (3H, s), 3.73 (1H, d, *J*=10 Hz), 3.75 (3H, s), 3.84~4.15 (3H, m), 4.29 (1H, d, *J*=10 Hz), 4.43 (1H, dd, *J*=7, 10 Hz), 4.88 (1H, d, *J*=6 Hz), 4.94 (1H, d, *J*=8 Hz), 5.16 (1H, s), 5.87 (2H, s), 5.96 (2H, s), 6.45 (1H, s), 6.52 (1H, s), 6.76 (1H, s), 6.78~6.95 (3H, m), 7.26 (1H, s).

28b. mp 147~149°C. NMR δ_H (CHCl₃): 2.72 (1H, m), 2.79 (1H, br.), 3.29 (1H, dd, *J*=4, 11 Hz), 3.33 (3H, s), 3.54 (1H, dd, *J*=3, 11 Hz), 3.71 (3H, s), 3.78 (3H, s), 3.96 (1H, m), 4.04 (1H, d, *J*=10 Hz), 4.20 (2H, d, *J*=7 Hz), 4.55 (1H, d, *J*=10 Hz), 4.93 (1H, d, *J*=8 Hz), 5.00 (1H, d, *J*=6 Hz), 5.33 (1H, s), 5.87 (2H, s), 5.97 (2H, s), 6.46 (1H, s), 6.54 (1H, s), 6.73 (1H, s), 6.77~6.94 (3H, m), 7.18 (1H, s).

1-Hydroxy-6-[6'-methoxy-2'-methoxymethyl-3'-(3'',4''-methylenedioxyphenyl)-2',3'-dihydro-1',4'-benzodioxin-7'-yl]-2-(3''',4'''-methylenedioxyphenoxy)-3,7-dioxabicyclo[3.3.0]octanes (3a, 3b, 29a and 29b). Compounds **3a** and **29a** were obtained via **26a** by "method A" from fluoride **19a** and *O*-trimethylsilylsesamol (**20**) in 25% and 61% yields, respectively.

3a [(±)-haedoxan E]. mp 158~159°C (ether). NMR δ_H (CDCl₃): 2.58 (1H, m), 3.10 (1H, d, *J*=1 Hz), 3.27 (1H, dd, *J*=4, 11 Hz), 3.35 (3H, s), 3.58 (1H, dd, *J*=3, 11 Hz), 3.72 (3H, s), 3.77 (1H, dd, *J*=1, 10 Hz), 3.88~4.13 (2H, m), 4.32 (1H, d, *J*=10 Hz), 4.36 (1H, dd, *J*=6, 10 Hz), 4.92 (1H, d, *J*=6 Hz), 4.98 (1H, d, *J*=8 Hz), 5.27 (1H, s), 5.92 (2H, s), 5.97 (2H, s), 6.47 (1H, s), 6.48~6.96 (6H, m), 7.27 (1H, s). NMR δ_C (CDCl₃): 55.7 (q), 58.2 (d), 59.5 (q), 70.9 (t), 71.2 (t), 76.5 (d), 77.2 (t), 83.9 (d), 92.1 (s), 99.9

(d), 100.5 (d), 101.2 (t × 2), 103.4 (d), 107.6 (d), 108.0 (d), 108.4 (d), 109.8 (d), 115.1 (d), 121.2 (d), 122.9 (s), 130.5 (s), 136.9 (s), 143.0 (s), 143.3 (s), 148.0 (s × 3), 150.5 (s), 151.3 (s). Anal. Found: C, 62.74; H, 5.31. Calcd. for C₃₁H₃₀O₁₂: C, 62.62; H, 5.09%.

29a. mp 169~171°C. NMR δ_H (CDCl₃): 2.48 (1H, br.), 2.72 (1H, m), 3.27 (1H, dd, *J*=4, 11 Hz), 3.33 (3H, s), 3.58 (1H, dd, *J*=3, 11 Hz), 3.72 (3H, s), 3.87~4.31 (3H, m), 4.26 (1H, dd, *J*=8, 9 Hz), 4.45 (1H, d, *J*=11 Hz), 4.95 (1H, d, *J*=6 Hz), 4.97 (1H, d, *J*=8 Hz), 5.41 (1H, s), 5.90 (2H, s), 5.97 (2H, s), 6.48 (1H, s), 6.52~6.97 (6H, m), 7.16 (1H, s).

Compounds **3b** and **29b**, isomers of the benzodioxane part of **3a** and **29a**, were obtained from **19b** by "method A" for producing **2a** and **28a**.

3b. Resinous. NMR δ_H (CDCl₃): 2.62 (1H, m), 3.11 (1H, d, *J*=1 Hz), 3.29 (1H, dd, *J*=5, 11 Hz), 3.34 (3H, s), 3.55 (1H, dd, *J*=3, 11 Hz), 3.72 (3H, s), 3.77 (1H, dd, *J*=1, 9 Hz), 3.90~4.19 (2H, m), 4.32 (1H, d, *J*=9 Hz), 4.35 (1H, dd, *J*=7, 9 Hz), 4.88 (1H, d, *J*=6 Hz), 4.95 (1H, d, *J*=8 Hz), 5.28 (1H, s), 5.92 (2H, s), 5.98 (2H, s), 6.47 (1H, s), 6.52~6.96 (6H, m), 7.27 (1H, s).

29b. mp 156~158°C. NMR δ_H (CDCl₃): 2.45 (1H, br.), 2.75 (1H, m), 3.29 (1H, dd, *J*=5, 11 Hz), 3.33 (3H, s), 3.55 (1H, dd, *J*=3, 11 Hz), 3.72 (3H, s), 3.90~4.16 (3H, m), 4.27 (1H, dd, *J*=8, 9 Hz), 4.45 (1H, d, *J*=10 Hz), 4.93 (1H, d, *J*=6 Hz), 4.95 (1H, d, *J*=8 Hz), 5.42 (1H, s), 5.91 (2H, s), 5.98 (2H, s), 6.48 (1H, s), 6.52~6.92 (6H, m), 7.16 (1H, s).

1-Hydroxy-6-[6'-methoxy-2'-methoxymethyl-3'-(3'',4''-methylenedioxyphenyl)-2',3'-dihydro-1',4'-benzodioxin-7'-yl]-2-(2''',6'''-dimethoxy-3'''',4'''-methylenedioxyphenoxy)-3,7-dioxabicyclo[3.3.0]octanes (1a, 1b, 27a and 27b). Compounds **1a** and **27a** were obtained in 17% and 16% yields, respectively, by the reaction between fluoride **19a** and 2,6-dimethoxy-3,4-methylenedioxyphenol (**23**) by a similar procedure to that of "method B", using AgClO₄ instead of TrClO₄.

1a [(±)-haedoxan A]. mp 173~175°C. NMR δ_H (CDCl₃): 1.64 (1H, br.), 2.63 (1H, m), 3.27 (1H, dd, *J*=4, 11 Hz), 3.34 (3H, s), 3.58 (1H, dd, *J*=3, 11 Hz), 3.71 (1H, d, *J*=10 Hz), 3.72 (3H, s), 3.77 (3H, s), 3.88~4.13 (3H, m), 4.00 (3H, s), 4.28 (1H, d, *J*=10 Hz), 4.55 (1H, dd, *J*=7, 9 Hz), 4.91 (1H, d, *J*=5 Hz), 4.98 (1H, d, *J*=8 Hz), 5.22 (1H, s), 5.85 (2H, s), 5.97 (2H, s), 6.27 (1H, s), 6.47 (1H, s), 6.79~6.96 (3H, m), 7.28 (1H, s). Anal. Found: C, 60.65; H, 5.69. Calcd. for C₃₃H₃₄O₁₄: C, 60.55; H, 5.24%.

27a. mp 196~198°C. NMR δ_H (CDCl₃): 2.70 (2H, m), 3.27 (1H, dd, *J*=4, 11 Hz), 3.33 (3H, s), 3.57 (1H, dd, *J*=3, 11 Hz), 3.72 (3H, s), 3.78 (3H, s), 3.99 (1H, m), 4.00 (3H, s), 4.07 (1H, d, *J*=10 Hz), 4.16 (1H, dd, *J*=8, 9 Hz), 4.33 (1H, dd, *J*=6, 9 Hz), 4.61 (1H, d, *J*=10 Hz), 4.95 (1H, d, *J*=8 Hz), 5.09 (1H, d, *J*=7 Hz), 5.35 (1H, s), 5.84 (2H, q, *J*=1 Hz), 5.97 (2H, s), 6.27 (1H, s), 6.46 (1H, s), 6.72~6.96 (3H, m), 7.21 (1H, s).

2a, 6β-isomer. Resinous. NMR δ_H (CDCl₃): 3.07 (1H, m),

m), 3.28 (1H, dd, $J=4$, 11 Hz), 3.34 (3H, s), 3.44~3.68 (2H, m), 3.71 (3H, s), 3.79 (3H, s), 3.83~4.16 (4H, m), 4.98 (1H, d, $J=8$ Hz), 5.17 (1H, s), 5.31 (1H, d, $J=5$ Hz), 5.86 (2H, s), 5.98 (2H, s), 6.44 (1H, s), 6.52 (1H, s), 6.73 (1H, s), 6.76~6.93 (3H, m), 7.17 (1H, s).

Compounds **1b** and **27b**, isomers of the benzodioxane part of **1a** and **27a**, were obtained from **19b** by "method A" for producing **2a** and **28a**.

1b. mp 139~140°C. NMR δ_{H} (CDCl_3): 2.63 (1H, m), 3.29 (1H, dd, $J=4$, 11 Hz), 3.33 (3H, s), 3.54 (1H, dd, $J=3$, 11 Hz), 3.71 (3H, s), 3.72 (1H, d, $J=10$ Hz), 3.76 (3H, s), 3.84~4.12 (3H, m), 4.00 (3H, s), 4.28 (1H, d, $J=10$ Hz), 4.56 (1H, dd, $J=7$, 9 Hz), 4.87 (1H, d, $J=6$ Hz), 4.94 (1H, d, $J=8$ Hz), 5.20 (1H, s), 5.84 (2H, s), 5.96 (2H, s), 6.26 (1H, s), 6.46 (1H, s), 6.72~6.95 (3H, m), 7.27 (1H, s).

27b. mp 157~158°C. NMR δ_{H} (CDCl_3): 2.52~2.84 (2H, m), 3.28 (1H, dd, $J=4$, 11 Hz), 3.33 (3H, s), 3.53 (1H, dd, $J=3$, 11 Hz), 3.71 (3H, s), 3.77 (3H, s), 3.98 (1H, m), 4.00 (3H, s), 4.03 (1H, d, $J=10$ Hz), 4.15 (1H, dd, $J=8$, 9 Hz), 4.34 (1H, dd, $J=6$, 9 Hz), 4.60 (1H, d, $J=10$ Hz), 4.93 (1H, d, $J=8$ Hz), 5.07 (1H, d, $J=7$ Hz), 5.35 (1H, s), 5.84 (2H, s), 5.96 (2H, s), 6.27 (1H, s), 6.45 (1H, s), 6.68~6.94 (3H, m), 7.20 (1H, s).

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