First Stereocontrolled Syntheses of Unsymmetrically Substituted Bislactone Lignans: Stereocontrolled Syntheses of Four Possible Isomers of Methyl 4,8-Dioxoxanthoxylol

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An efficient method for stereocontrolled syntheses of the unsymmetrically substituted bislactone subgroup of the furofuran lignan has been developed based on a stereoselective aldol reaction of the acid anhydride **8** or **9** and an aromatic aldehyde employing methyl 4,8-dioxoxanthoxylol (**1a**), 4,8-dioxofargesin (**1b**), methyl 4,8-dioxopiperitol (**2a**) and their isomer **3a** as the representative examples of the axial−equatorial **1**, diequatorial **2**, and diaxial **3** types of this series.

Introduction

Lignans of the furofuran series **I** (4,8-dioxo-3,7-dioxabicyclo[3.3.0]octane), **II** (4-oxo-3,7-dioxabicyclo[3.3.0]-octane) and **III** (3,7-dioxabicyclo[3.3.0]octane) are of considerable interest because of their wide range of biological activities (Figure 1).[1] Some of the naturally occurring bislactones (series **I**) have been reported to modulate the functions of central nervous systems by inhibition of catechol-*O*-methyltransferase, dopamine β-hydroxylase, and dopa decarboxylase (Figure 1).[2] Monolactone furofurans (series **II**) and simple furofurans (series **III**) have been also known to exhibit inhibition activity of phosphodeesterase and antagonistic activity of platelet aggregation factor.[3] Although much effort has been devoted to developing an efficient method for syntheses of the furofuran series of lignans and several ingenious ones have been reported,[4] only a little attention has been devoted to syntheses of the bislactone subgroup **I**; some nonstereocontrolled ones including those based on the oxidative dimerization of the cinnamic acid derivatives,[5] the reaction of 2,5-bis(trimethylsilyloxy)-furans with benzaldehydes,[6] and aldol reaction of *N*,*N*,*N*′,*N*′-tetraethylsuccindiamide and aromatic aldehydes have been reported.[7] In connection with our synthetic studies in search of new compounds having intriguing biological activities from lignans,[8] we have been interested in synthesis of the bislactone subgroup

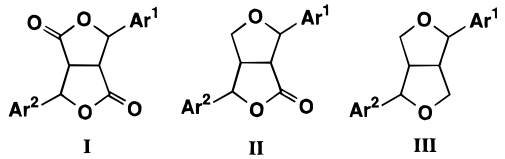

Figure 1.

of furofuran lignans. In this paper, we report the full account of our efforts to stereocontrolled syntheses of this group of lignans.[9]

Results and Discussion

There are four stereoisomers in this series of lignans having two different aryl groups, which are exemplified by **1a**, **1b**, **2a**, and **3a** (Figure 2). We selected these four compounds as the representative examples of these stereoisomers and envisaged that they would be synthesized *via* the key intermediates **4**−**7**, respectively, based on the strategy illustrated in Scheme 1. The four contiguous carbon centers of these key intermediates would be stereochemically defined based on (i) the stereoselective reduction of the carbonyl group at C-1 of keto ester **10**, which defines the relative stereochemistry between C-1 and C-2; (ii) the stereoselective aldol reaction of the acid anhydride **8** or **9** with veratraldehyde, which defines the relative stereochemistry among C-2, C-3, and C-4. Moreover, the alkoxy anion generated in the aldol reaction was expected to subsequently attack the carbonyl carbon atom of the acid anhydride intramolecularly to afford the γ-lactone skeleton (Scheme 1).

(i) Preparation of the Key Intermediates 8 and 9. According to the strategy, the intermediate **10** was first synthesized. The Michael addition reaction of the anion generated by treatment of the cyanohydrin **11**[8d]

[⊗] Abstract published in *Advance ACS Abstracts,* February 1, 1997.

(1) Reviews: (a) *Chemistry of lignans*; Rao, C. B. S., Ed.; Andhra Univ. Press: India, 1978. (b) *Lignans*; Ayres, D. C.; Loike, J. D., Ed.; Cambridge University Press: New York, 1990. (c) Ward, R. S. *Chem. Soc. Rev.* **1982**, *11*, 75.

(2) Kumada, Y.; Naganawa, H.; Iimura, H.; Matsuzaki, M.; Takeuchi, T.; Umezawa, H. *J. Antibiot.* **1976**, 882.

(3) MacRae, W. D.; Towers, G. H. N. *Phytochemistry* **1984**, 1207.

(4) (a) Pelter, A.; Ward, R. S.; Watson, D. J.; Collins, P. *J. Chem. Soc., Perkin Trans. 1* **1982**, 175. (b) Pelter, A.; Ward, R. S.; Collins, P.; Venkateswarlu, R.; Kay, I. T. *J. Chem. Soc., Perkin Trans. 1* **1985**, 587. (c) Till, C. P.; Whiting, D. *J. Chem. Soc., Chem. Commun.* **1984**, 590. (d) Stevens, D. R.; Whiting, D. A. *Tetrahedron Lett.* **1986**, *27*, 4629. (e) Stevens, D. R.; Till, C. P.; Whiting, D. A. *J. Chem. Soc., Perkin Trans. 1* **1992**, 185. (f) Bradley, H. M.; Knight, D. W. *J. Chem. Soc., Chem. Commun.* **1991**, 1641. (g) Takano, S.; Ohkawa, T.; Tamori, S.; Satoh, S.; Ogasawara, K. *J. Chem. Soc., Chem. Commun.* **1988**, 189. (h) Takano, S.; Samizu, K.; Ogasawara, K. *Synlett* **1993**, 785. (i) Suginome, H.; Orito, K.; Yorita, K.; Ishikawa, M.; Shimoyama, N.; Sasaki, T. *J. Org. Chem.* **1995**, *60*, 3052.

(5) (a) Cartwright, N. J.; Haworth, R. D. *J. Chem. Soc.* **1944**, 535. (b) Iguchi, M.; Nishiyama, A.; Eto, H.; Terada, Y.; Yamamura, S. *Chem. Lett.* **1979**, 1397.

(6) Brownbridge, P.; Chan, T.-H. *Tetrahedron Lett.* **1980**, *21*, 3427.

(7) Mahalanabis, K. K.; Mumtaz, M.; Snieckus, V. *Tetrahedron Lett.* **1982**, *23*, 3975.

(8) (a) Ogiku, T.; Seki, M.; Takahashi, M.; Ohmizu, H.; Iwasaki, T. *Tetrahedron Lett.* **1990**, *31*, 5487. (b) Ogiku, T.; Yoshida, S.; Kuroda, T.; Ohmizu, H.; Iwasaki, T. *Synlett* **1992**, 651. (c) Ogiku, T.; Yoshida, S.; Takahashi, M.; Kuroda, T.; Ohmizu, H.; Iwasaki, T. *Bull. Chem. Soc., Jpn.* **1992**, *65*, 3495. (d) Ogiku, T.; Yoshida, S.; Ohmizu, H.; Iwasaki, T. *J. Org. Chem.* **1995**, *60*, 4585. (e) Ogiku, T.; Yoshida, S.; Takahashi, M.; Kuroda, T.; Ohmizu, H.; Iwasaki, T. *Tetrahedron Lett.* **1992**, *33*, 4473. (f) Ogiku, T.; Yoshida, S.; Takahashi, M.; Kuroda, T.; Ohmizu, H.; Iwasaki, T. *Tetrahedron Lett.* **1992**, *33*, 4477. (g) Ogiku, T.; Yoshida, S.; Ohmizu, H.; Iwasaki, T. *J. Org. Chem.* **1995**, *60*, 1148.

(9) (a) Yoshida, S.; Ogiku, T.; Ohmizu, H.; Iwasaki, T. *Tetrahedron Lett.* **1995**, *36*, 1455. (b) Yoshida, S.; Ogiku, T.; Ohmizu, H.; Iwasaki, T. *Tetrahedron Lett.* **1995**, *36*, 1459.

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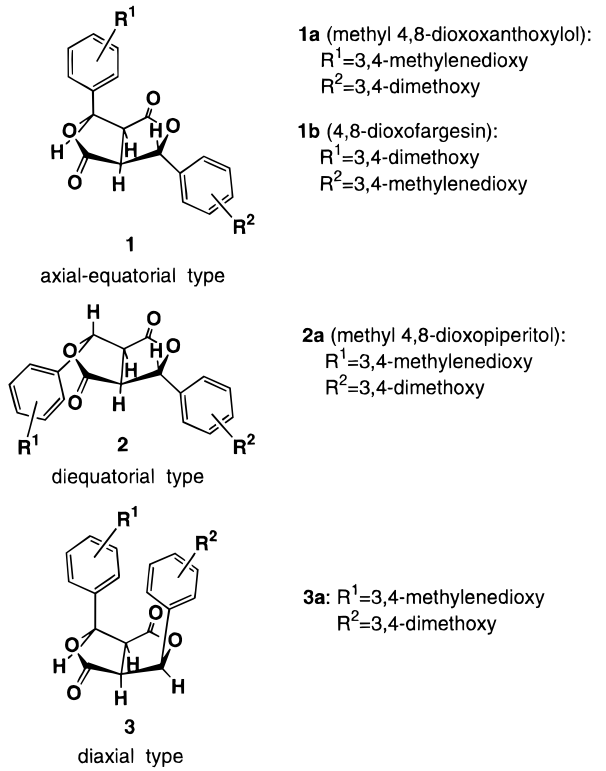


Figure 2.

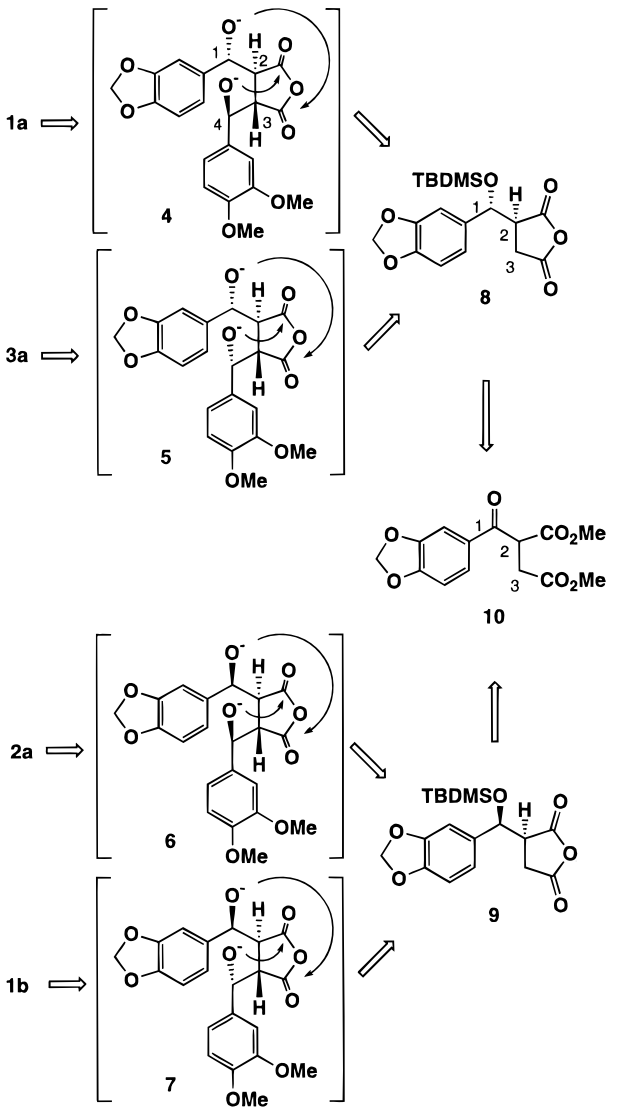
with LDA to dimethyl maleate in toluene at −70 °C followed by treatment of the resulting adduct with tetrabutylammonium fluoride−acetic acid (1:1) in THF at room temperature afforded the benzoyl succinate **10** in 85% yield (Scheme 2).

Reduction of the carbonyl group of **10** was next examined (Table 1). Reduction of **10** with $NaBH_4$ in MeOH at 0 °C provided the *anti*-hydroxy ester **12** in 55% yield along with the *trans*-lactone **13** (5%) generated *via* the initially yielded **14** (run 1). The corresponding *cis*-lactone was not produced in this reaction probably due to the unfavorable steric repulsion between the aryl and the methoxycarbonyl groups. A satisfactory result was obtained in the use of L-selectride in toluene at −70 °C, in which **12** was isolated in 92% yield as a sole product (run 2). This *anti*-selectivity would be explained by the Felkin−Ahn model illustrated in Figure 3, in which the hydride attacks the carbonyl group from the opposite side of the methoxycarbonyl group.

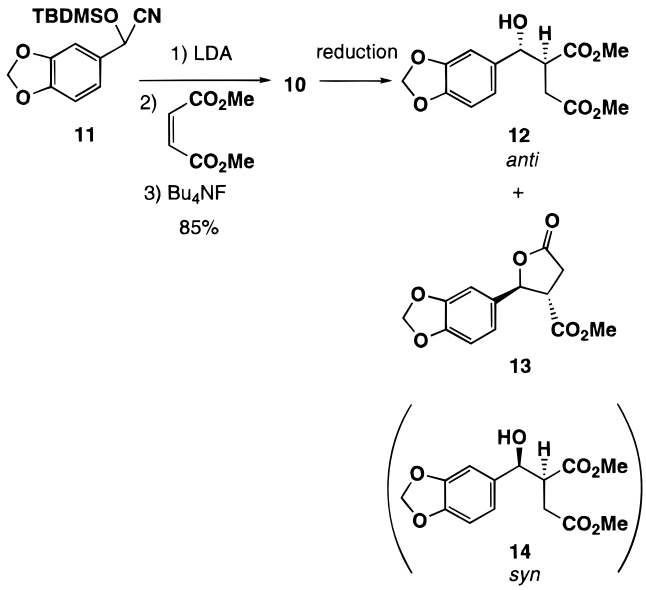
Treatment of **12** with TBDMSCl and imidazole in DMF followed by saponification of the diester **15** gave the diacid **16** in 81% yield. The diacid **16** was stirred in acetic anhydride at 60 °C for 30 min to afford the key intermediate **8** in 96% yield (Scheme 3).

On the other hand, Pd-catalyzed hydrogenation of **10** was examined in order to obtain the *syn*-hydroxy ester **14** selectively, because the Pd-catalyzed reduction of the *β*-keto ester has been reported to afford a *syn*-hydroxy ester in a highly stereoselective manner.[10] However, reduction of **10** under the similar conditions as those of the reported one gave unexpectedly the *anti*-hydroxy ester exclusively (run 3). Thus, an alternative method was examined. Nakata *et al*. have reported that the zinc-chelated reduction of the *β*-keto ester proceeded in a highly stereoselective manner to afford the *syn*-isomer (*erythro*-isomer) in good yield.[11] The method was applied

Scheme 1



Scheme 2



to the reduction of **10**, and the desired *trans*-lactone **13** was obtained in 79% yield along with the isomer **12** in 6% yield (run 4). We considered that the selectivity was

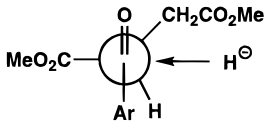
(10) Bolhofer, W. A. *J. Am. Chem. Soc.* **1953**, *75*, 4469.

(11) Nakata, T.; Oishi, T. *Tetrahedron Lett.* **1980**, *21*, 1641.

Table 1. Reduction of 10

run	reagent	solvent	temp (°C)	yield (%)[a] 12	13
1	$NaBH_4$	MeOH	0	55	5
2	L-Selectride	toluene	−70	92	−
3	H_2, Pd−C	AcOH	25	88	−
4	$Zn(BH_4)_2$	ether	−20−0	6	79

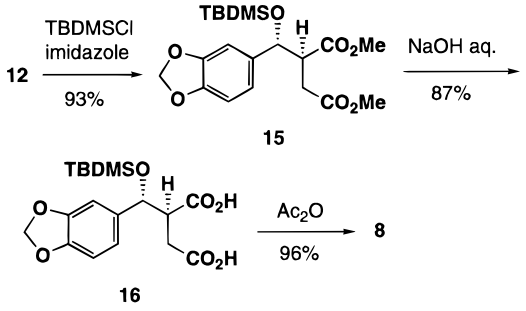
[a] Isolated yield.



Ar : 3,4-methylenedioxyphenyl

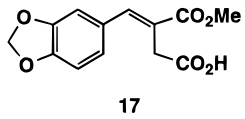
Figure 3.

Scheme 3



not complete but acceptable and turned our focus on conversion of **13** into the corresponding *syn*-hydroxy ester.

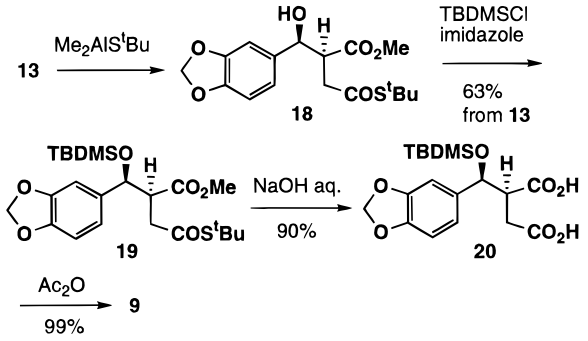
Usual treatment of **13** with NaOMe in methanol resulted in an elimination reaction to give the undesired half ester **17** quantitatively. This result indicated that the desired ring opening reaction of the γ-lactone **13** required a nucleophile which is less basic than NaOMe. Thus, the aluminum-mediated thioesterification was next examined.[12]



Treatment of **13** with dimethylaluminum *tert*-butyl sulfide in CH_2Cl_2 at 0 °C followed by protection of the hydroxyl group with a TBDMS group afforded **19** *via* **18** in 63% yield. The thioester **19** was saponified followed by treatment of the resulting diacid **20** with acetic anhydride to give the key intermediate **9** in 90% yield (Scheme 4).[13]

(ii) Aldol Reactions of the Acid Anhydrides 8 and 9 with Veratraldehyde. The aldol reactions of the acid anhydrides **8** and **9** with veratraldehyde, the key reactions of our strategy, were next examined (Schemes 5 and 6). The aldol reaction of **8** with veratraldehyde was first carried out employing LDA as a base. However, addition of LDA to a mixture of **8** and veratraldehyde in THF at −50 °C gave a mixture of **21** and its isomer **22** in only 8% yield,[14] the ratio of **21** to **22** being 44:56 (Table 2). Kuwajima *et al.* reported that the sterically hindered

Scheme 4



Scheme 5

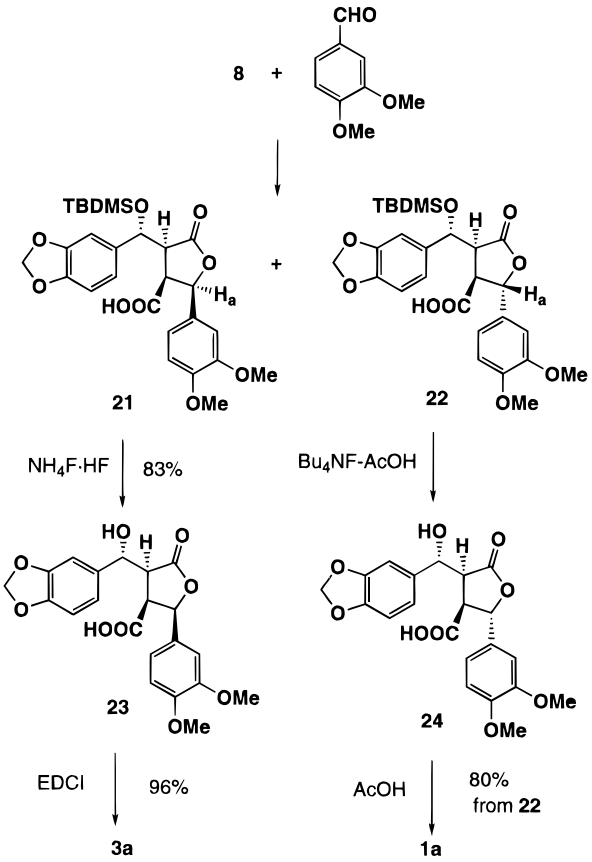


Table 2. Aldol Reaction of 8 with Veratraldehyde

run	base	solvent	temp (°C)	ratio[a] 21:22	yield (%)[b] 21 + 22
1	LDA	THF	−50	44:56	8
2	LiHMDS	THF	−50	47:53	54
3	LiHMDS	THF	−100	62:38	71
4	NaHMDS	THF	−50	56:44	67
5	NaHMDS	THF	−100	81:19	77
6	KHMDS	THF	−50	8:92	70
7	KHMDS	THF	−100	8:92	85
8	KHMDS	toluene	−50	6:94	73
9	KHMDS	toluene	−90	5:95	82

[a] Determined by HPLC analysis of the crude reaction product. [b] Isolated yield as a mixture of **21** and **22**.

alkoxide was effective as a base in the aldol reaction of the succinic anhydride derivatives with aldehydes.[15] Thus, the reaction using a metal amide of 1,1,1,3,3,3-hexamethyldisilazane (HMDS), the amine part of which was bulkier than that of LDA, was next examined. In the use of LiHMDS or NaHMDS at −50 °C, the combined yield of the products rose up to be 54% or 67%, respectively, as expected, but *anti*-selectivity was not obtained (run 2, 4). The *anti*-selectivity was found to be obtained

(12) Hatch, R. P.; Weinreb, S. M. *J. Org. Chem.* **1977**, *42*, 3960.
(13) The stereochemistry of **8** and **9** was unambiguously confirmed by X-ray crystallographic analysis of **21** and **3a**.
(14) Addition of veratraldehyde to a mixture of the acid anhydride and LDA in THF at −50 °C did not give the coupling products at all.
(15) Minami, N.; Kuwajima, I. *Tetrahedron Lett.* **1977**, *17*, 1423.

Table 3. Aldol Reaction of 9 with Veratraldehyde

run	base	solvent	temp (°C)	ratio[a] **25**:**26**	yield (%)[b] **25** + **26**
1	LiHMDS	THF	−100	77:23	66
2	NaHMDS	THF	−100	79:21	71
3	KHMDS	THF	−100	16:84	75
4	KHMDS	toluene	−90	13:87	81

[a] Determined by HPLC analysis of the crude reaction product. [b] Isolated yield as a mixture of **25** and **26**.

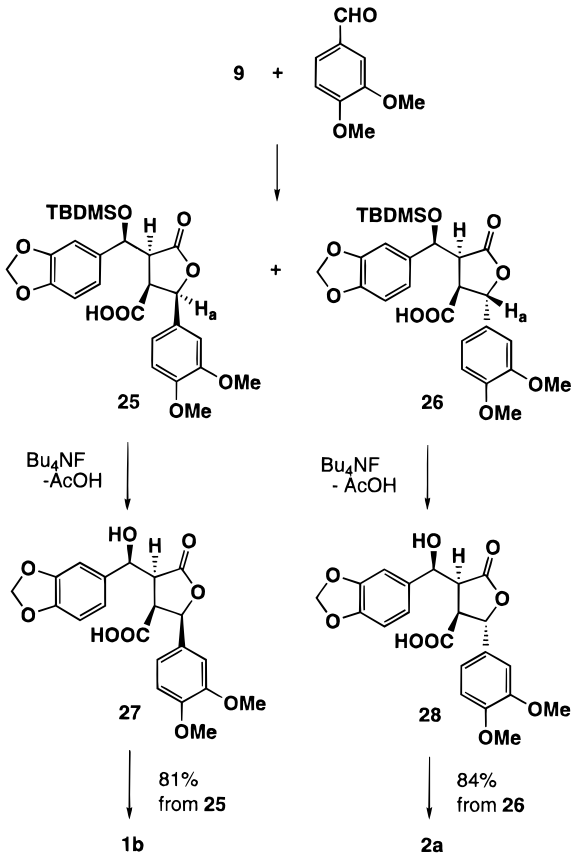
when the reaction was carried out at lower temperature (run 3, 5). Especially, in the use of NaHMDS at −100 °C, the ratio of **21** to **22** was 81:19 and pure **21** was isolated in 57% yield.[16] The ^{1}H NMR spectra of **21** and **22** showed the similar signals and their stereochemistry could not be fully characterized. However, stereochemistry of **21** could be determined by the X-ray crystallographic analysis. On the other hand, *syn*-selectivity was observed in the use of KHMDS (run 6−9). The selectivity was slightly improved in toluene (runs 8, 9). The best *syn*-selectivity was obtained in the case of KHMDS at −90 °C (run 9), in which pure **22** was isolated in 78% yield.[17]

The *anti*-isomer **25** was similarly obtained as a major product in a moderate yield in the aldol reaction of **9** with veratraldehyde in THF at −100 °C utilizing LiHMDS or NaHMDS (Table 3, runs 1 and 2). The *anti*-selectivity was in the same level as that of the reaction of **8** with veratraldehyde. The corresponding *syn*-isomer **26** was obtained as a major product under the similar conditions employing KHMDS (run 3). The selectivity was slightly improved in toluene (run 4). Although the ^{1}H NMR spectra of **25** and **26** were similar, the signal of H_a of **26** was observed in the down field by 0.3 ppm compared with that of **25** probably due to the deshielding effect of the neighboring carbonyl group as was observed in the case of **21** (δ 5.44) and **22** (δ 5.67). Therefore the chemical structures of **25** and **26** seemed to be those as shown in Scheme 6. They were finally confirmed by conversion of **25** and **26** into the corresponding bislactones **1b** and **2a**, respectively.[18]

Although the chemical yields obtained in the above experiments were adequate, the selectivity in the case of the *anti*-isomers **21** and **25** was not necessarily satisfactory. However, we turned our attention to conversion of **21**, **22**, **25**, and **26** into the corresponding bislactones, because **21** related to the diaxial-type isomer **3a** being hitherto not synthesized, and **25** could be obtained more selectively by exchanging the aromatic aldehydes in the synthesis of **22**.

(iii) Conversion of the Lactone 21, 22, 25, and 26 into Bislactone 3a, 1a, 1b, and 2a. The compounds **22**, **25**, and **26** were easily converted into the corresponding alcohols **24**, **27**, and **28**, respectively, by treatment with TBAF−AcOH (1:1) in THF at room temperature. However, removal of the TBDMS group of **21** proceeded very slowly under the same reaction conditions to give only a trace of the desired compound **23** even after 3 days.

Scheme 6



This result indicates that the 3,4-dimethoxyphenyl and the carboxy groups occupying the *cis*-positions relative to each other shield the silyloxy group to retard the reaction. In order to find out an alternative, efficient method, we examined the deprotection reaction under the various conditions and found that treatment of **21** with NH_4F·HF in the mixed solvent of DMF and *N*-methylpyrrolidone (NMP) (10:1) for 2 days at room temperature brought about **23** in 83% yield.[19]

The lactonization of **24**, **27**, and **28** was successfully achieved by heating in AcOH at 40−50 °C for 30 min to give the desired bislactones **1a**, **1b**, and **2a** in good yields. However, the lactonization of **23** did not proceed at all under the same reaction conditions. Furthermore, the higher reaction temperature and/or the longer reaction period induced the isomerization reaction to afford a significant amount of **1a**.[20] Thus, the lactonization of **23** was examined under various nonacidic conditions, and it was found that the lactonization smoothly proceeded by treatment of **23** with 1-ethyl-3-[3-(dimethylamino)-propyl]carbodiimide hydrochloride (EDCI) in DMF at −20−0 °C to afford the diaxial bislactone **3a** in 96% yield. The structure of **3a** was unequivocally confirmed on the basis of X-ray crystallographic analysis. The stereochemistries of structure of **2a** were determined by comparison of ^{1}H NMR with those of diequatorial bislactone analogs reported in the literature.[6,21,22] Although **1a** and **1b** were proved to be the axial−equatorial type by comparison of reported ^{1}H NMR data,[6] the stere-

(16) In order to improve the selectivity, we tried to exchange the countercation of the enolate of acid anhydride **8** from Li to Mg, Sn or Zn by addition of the metal salts. But, the lithium enolate of **8** was so unstable that the enolate of these metals could not be generated.

(17) To the best of our knowledge, it has not been reported that a potassium countercation of an enolate enhances the stereoselectivity in its aldol reaction. The high *syn*-selectivity observed in the use of KHMDS in the present work would be elucidated by higher stability of the twist-boat transition structure leading to the *syn*-isomer than that of the chair transition structure leading to the *anti*-isomer.

(18) ^{1}H NMR data of **21**, **22**, **25**, and **26** were summarized in supporting information.

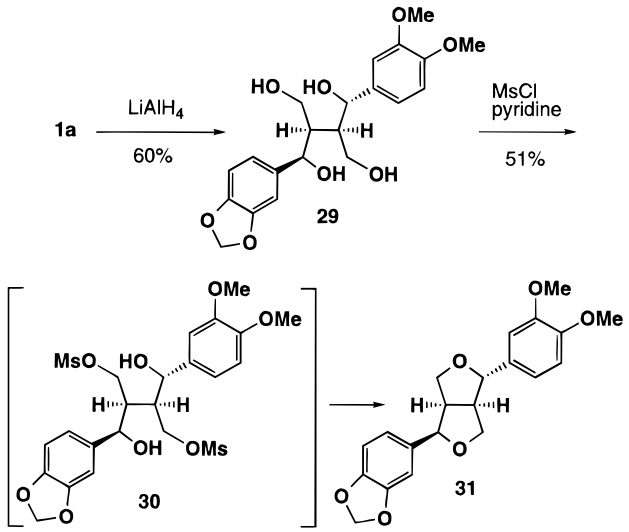
(19) Seki, M.; Kondo, K.; Kuroda, T.; Yamanaka, T.; Iwasaki, T. *Synlett* **1995**, 609.

(20) The isomerization of the bislactone under the acidic conditions was reported by Snieckus et al. See ref 7.

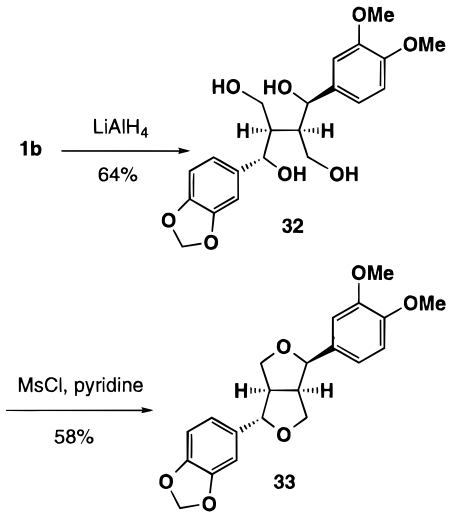
(21) The structure of the diequatorial bislactone **2b** ($R^1 = R^2 =$ 3,4-methylenedioxy) was determined by X-ray crystallographic analyses.

(22) Peterson, J. R.; Peterson, S.; Bakers, J. K.; Roger, R. D. *J. Crystallogr. Spectrosc. Res.* **1990**, *20*, 327.

Scheme 7



Scheme 8



ochemistries of **1a** and **1b** were difficult to distinguish based on their ^{1}H and ^{13}C NMR spectra. In order to determine their stereochemistries, **1a** and **1b** were converted into **31** and **33**, respectively (Schemes 7, 8). The chemical structure of **31** was confirmed to be methyl xanthoxylol on the basis of X-ray crystallographic analysis.[23] On the other hand, ^{1}H and ^{13}C NMR spectra of synthesized **33** were identical with those of methyl pluviatilol (fargesin) reported in the literature.[24] Thus, the stereochemistries of **1a** and **1b** were unequivocally confirmed as those shown in Figure 2.

As described above, we have achieved stereocontrolled syntheses of the four possible stereoisomers of the bislactone furofuran lignans having different aryl groups including the diaxial type which had never been synthesized. The present methodology should find wide application in the synthesis of a variety of bislactone furofuran lignans.

Experimental Section

Dimethyl 2-[3,4-(Methylenedioxy)benzoyl]succinate (10). To LDA (38 mmol) in toluene (200 mL) were added dropwise successively the cyanohydrin **11** (10 g, 34 mmol) in toluene (20 mL) and dimethyl maleate (4.9 g, 34 mmol) in toluene (20 mL) at −70 °C under nitrogen atmosphere. The mixture was quenched by addition of aqueous AcOH (15%, 30 mL, 76 mmol). The organic layer was separated, and the aqueous layer was extracted with EtOAc (200 mL). The combined organic layer was washed with brine (100 mL) and dried ($MgSO_4$). After evaporation of the solvent, the residue was dissolved in THF (200 mL), and then AcOH (3.4 mL, 56 mmol) and Bu_4NF (1.0 M in THF, 51 mL) were added to the solution at room temperature. After 30 min, the solution was washed with water (100 mL), 10% citric acid (100 mL), and brine (100 mL) and then dried ($MgSO_4$). After evaporation of the solvent, the residue was purified by silica gel column chromatography using hexane/EtOAc (1:1) as an eluent to afford **10** as a syrup (8.5 g, 85%): IR (film) 1740, 1678 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 3.04 (d, 1H, J = 7.2 Hz), 3.06 (d, 1H, J = 7.2 Hz), 3.68, (s, 3H), 3.69 (s, 3H), 4.79 (t, 1H, J = 7.2 Hz), 6.06 (s, 2H), 6.88 (d, 1H, J = 8.2 Hz), 7.49 (d, 1H, J = 1.7 Hz), 7.68 (dd, 1H, J = 1.7, 8.2 Hz); MS m/z 294 (M$^+$). Anal. Calcd for $C_{14}H_{14}O_7$: C, 57.14; H, 4.80. Found: 56.75; H, 4.64.

Reduction of the Ketone 10. Reduction with L-Selectride. To a solution of **10** (1.1 g, 3.7 mmol) in THF (30 mL) was added dropwise L-Selectride (1 M in THF, 4.1 mL, 4.1 mmol) at −70 °C. After 1 h, the mixture was quenched by addition of AcOH (0.3 mL) in THF (1 mL) and diluted with EtOAc (50 mL). The mixture was washed with brine (50 mL), dried ($MgSO_4$), and concentrated *in vacuo*. Purification of the residue on silica gel chromatography using hexane/EtOAc (2:1) as an eluent afforded **dimethyl 2-(*S**)-[α(*R**)-hydroxy-3,4-(methylenedioxy)phenyl]succinate (12)** (1.0 g, 92%): mp 97−99 °C; IR (KBr) 3481, 1730, 1708 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.39 (dd, 1H, J = 5.1, 16.9 Hz), 2.57 (dd, 1H, J = 8.7, 16.9 Hz), 3.12 (m, 1H), 3.63 (s, 3H), 3.74 (s, 3H), 4.82 (d, 1H, J = 7.8 Hz), 5.96 (s, 2H), 6.80 (s, 2H), 6.84 (s, 1H); MS m/z 296 (M$^+$). Anal. Calcd for $C_{14}H_{16}O_7$: C, 56.76; H, 5.44. Found: C, 56.70; H, 5.41.

Reduction by Pd-Catalyzed Hydrogenation. A mixture of **10** (8.4 g, 29 mmol) and 5% Pd on carbon (615 mg) in acetic acid (40 mL) was stirred under hydrogen atmosphere (3.5 atom) for 5 h at room temperature. After removal of the catalyst by filtration the filtrate was concentrated *in vacuo*. The residue was purified on silica gel chromatography using hexane/EtOAc (2:1) as an eluent to afford **12** (7.5 g, 88%).

Reduction with Zn(BH$_4$)$_2$. To a suspension of $NaBH_4$ (303 mg, 8.0 mmol) in ether (30 mL) at room temperature under vigorous stirring was added $ZnCl_2$ (1 M in ether, 4.0 mL, 4.0 mmol). The mixture was vigorously stirred for 5 h. Insoluble materials were filtered off, and **10** (589 mg, 2.0 mmol) was added to the filtrate in dry ether (10 mL) at −20 °C. The mixture was allowed to warm slowly to 0 °C. After 2 h, excess reagent was decomposed by dropwise addition of AcOH until the evolution of hydrogen ceased. The solution was washed with brine (20 mL), dried ($MgSO_4$), and concentrated. The residue was chromatographed on silica gel using hexane/EtOAc (2:1) as an eluent to afford ***trans*-3-(methoxycarbonyl)-4-[3,4-(methylenedioxy)phenyl]butyrolactone (13)** (415 mg, 79%) and **12** (35 mg, 6%).

13: mp 103−104 °C; IR (KBr) 1778, 1734 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.93 (m, 2H), 3.32 (m, 1H), 3.77 (s, 3H), 5.55 (d, 1H, J = 7.5 Hz), 5.59 (s, 2H), 6.81 (s, 3H); MS m/z 264 (M$^+$). Anal. Calcd for $C_{13}H_{12}O_6$: C, 59.09; H, 4.58. Found: C, 59.17; H, 4.57.

Dimethyl 2(*S)-[α(*R**)-[(*tert*-Butyldimethylsilyl)oxy]-3,4-(methylenedioxy)phenyl]succinate (15).** To a solution of **12** (30 g, 0.101 mol) in DMF (300 mL) were added imidazole (16.5 g, 0.24 mol) and TBDMSCl (18.3 g, 0.12 mmol), and the mixture was stirred for 3 h at room temperature. The mixture was diluted with EtOAc (1 L), washed with water (1 L) and brine (1 L), and dried ($MgSO_4$). The solvent was evaporated *in vacuo* to dryness. The residue was purified on silica gel chromatography using hexane/EtOAc (4:1) as an eluent to afford **15** (38.6 g, 93%) as a syrup: IR (film) 1741 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ −0.21 (s, 3H), 0.01 (s, 3H), 0.84 (s, 9H), 2.23 (dd, 1H, J = 4.1, 16.7 Hz), 2.53 (dd, 1H, J = 10.8, 16.7 Hz), 3.14 (m, 1H), 3.59 (s, 3H), 3.71 (s, 3H), 4.76 (d, 1H, J = 8.0 Hz), 5.95 (s, 2H), 6.65−6.79 (m, 3H); MS m/z 410 (M$^+$).

(23) The author has deposited atomic coordinates for this structure with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.

(24) Pelter, A.; Ward, R. S.; Rao, E. V.; Sastry, K. V. *Tetrahedron* **1976**, *32*, 2783.

Anal. Calcd for $C_{20}H_{30}O_7Si$: C, 58.51; H, 7.37. Found: C, 58.15; H, 7.17.

2(*S)-[α(*R**)-[(*tert*-Butyldimethylsilyl)oxy]-3,4-(methylenedioxy)phenyl]succinic Acid (16).** A mixture of **15** (6.7 g, 16 mmol) in methanol (70 mL) and aqueous NaOH (2N, 16 mL, 32 mmol) was stirred for 1 day at room temperature. After evaporation of MeOH, the residue was dissolved in aqueous NaOH (2 N, 32 mL, 64 mmol), and the solution was stirred at 50 °C for 2 h. The reaction mixture was poured into a mixture of water (200 mL) and ether (200 mL). The aqueous layer was separated, acidified with aqueous HCl (2 N, 50 mL, 100 mmol), and extracted with EtOAc (400 mL). The organic layer was washed with brine, dried ($MgSO_4$), and concentrated *in vacuo*. The residue was crystallized from ether to give **16** (5.3 g, 87%): mp 182 °C; IR (KBr) 1713 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ −0.16 (s, 3H), 0.36 (s, 3H), 0.85 (s, 9H), 2.29 (dd, 1H, J = 4.3, 16.8 Hz), 2.46 (dd, 1H, J = 10.2, 16.8 Hz), 3.14 (m, 1H), 4.90 (d, 1H, J = 7.2 Hz), 5.94 (s, 2H), 6.72 (s, 2H), 6.82 (s, 1H); MS m/z 382 (M^+). Anal. Calcd for $C_{18}H_{26}O_7Si$: C, 56.52; H, 6.85. Found: C, 56.71; H, 6.83.

2(*S)-[α(*S**)[(*tert*-Butyldimethylsilyl)oxy]-3,4-(methylenedioxy)phenyl]succinic Acid (20).** The acid **20** was obtained in 90% yield from **19** according to the same procedure described above and was crystallized from ether: mp 160 °C; IR (KBr) 3400, 1712 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ −0.17 (s, 3H), −0.01 (s, 3H), 0.87 (s, 9H), 2.32 (dd, H, J = 2.4, 16.7 Hz), 2.93 (m, 2H), 5.17 (d, 1H, J = 3.3 Hz), 5.98 (s, 2H), 6.76 (s, 2H), 6.81 (s, 1H); MS m/z 382 (M^+). Anal. Calcd for $C_{18}H_{26}O_7Si$: C, 56.52; H, 6.85. Found: C, 56.38; H, 6.89.

2(*S)-[α(*R**)-[(*tert*-Butyldimethylsilyl)oxy]-3,4-(methylenedioxy)phenyl]succinic Anhydride (8).** Suspension of **16** (25 g, 65 mmol) in Ac_2O was stirred for 20 min at 60 °C. After removal of the solvent under reduced pressure, the residue was crystallized from ether−hexane to afford **8** (22.8 g, 96%): mp 104−105 °C; IR (KBr) 1776 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ −0.08 (s, 3H), 0.09 (s, 3H), 0.89 (s, 9H), 2.97 (m, 2H), 3.42 (m, 1H), 5.12 (d, 1H, J = 3.9 Hz), 5.97 (s, 2H), 6.76 (s, 2H), 6.80 (s, 1H); MS m/z 364 (M^+). Anal. Calcd for $C_{18}H_{24}O_6Si$: C, 59.32; H, 6.64. Found: C, 59.20; H, 6.61.

2(*S)-[α(*S**)-[(*tert*-Butyldimethylsilyl)oxy]-3,4-(methylenedioxy)phenyl]succinic Anhydride (9).** The anhydride **9** was obtained in 99% yield from **20** according to the same procedure described above: mp 76 °C; IR (KBr) 1784 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ −0.11 (s, 3H), 0.05 (s, 3H), 0.89 (s, 9H), 2.62 (dd, 1H, J = 8.5, 17.2 Hz), 3.07−3.23 (m, 2H), 5.35 (s, 1H), 5.98 (s, 2H), 6.79 (s, 3H); MS m/z 364 (M^+). Anal. Calcd for $C_{18}H_{24}O_6Si$: C, 59.32; H, 6.64. Found: C, 59.08; H, 6.60.

Methyl Hydrogen (*E*)-2-[3,4-(methylenedioxy)benzylidene]succinate (17). To the solution of **13** (264 mg, 1.0 mmol) in MeOH was added NaOMe (59 mg 1.1 mmol), and the mixture was stirred for 30 min at 0 °C. After removal of the solvent under reduced pressure, the residue was crystallized from ether to afford **17** (263 mg, 100%): mp 180 °C; IR (KBr) 3490, 1706 cm^{-1}; ^1H NMR (δ in $CDCl_3$) 3.52 (s, 2H), 3.87 (s, 3H), 6.00 (s, 2H), 6.8−6.9 (m, 3H), 7.78 (s, 1H); MS m/z 264 (M^+). Anal. Calcd for $C_{13}H_{12}O_6$: C, 59.09; H, 4.58. Found: C, 58.88; H, 4.51.

***S*-*tert*-Butyl [3(*S**)-(Methoxycarbonyl)-4(*S**)-[3,4-(methylenedioxy)phenyl]-4-[(*tert*-butyldimethylsilyl)oxy]]butanethioate (19).** To a solution of trimethylaluminum (2 M in hexane, 2.3 mL, 4.6 mmol) in CH_2Cl_2 (15 mL) was added *tert*-butylmercaptan (0.52 mL, 4.6 mmol) at 0 °C under a nitrogen stream. The mixture was allowed to warm to room temperature and stirred for 20 min. To the mixture was added **13** (1.0 g, 3.8 mmol) in CH_2Cl_2 (10 mL) at room temperature. After 1 h, water (10 mL) was added to the mixture, and insoluble materials were filtered off by a Celite pad. The filtrate was washed with brine (50 mL), dried ($MgSO_4$), and concentrated *in vacuo*. The residue was dissolved in DMF (10 mL), and TBDMSCl (858 mg, 5.7 mmol) and imidazole (775 mg, 11.4 mml) were added to the solution at room temperature. After 5 h, the reaction mixture was poured into water (100 mL) and extracted with EtOAc (100 mL). The organic layer was washed with brine (100 mL), dried ($MgSO_4$), and concentrated *in vacuo*. Silica gel column chromatography of the residue using hexane/EtOAc (4:1) as an eluent afforded **19** (1.12 g, 63%): mp 101 °C; IR (KBr) 1740 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ −0.17 (s, 3H), 0.02 (s, 3H), 0.88 (s, 9H), 1.40 (s, 9H), 2.59 (d, 1H, J = 12.9 Hz), 2.95−3.13 (m, 2H), 3.63 (s, 3H), 5.05 (d, 1H, J = 4.1 Hz), 5.95 (s, 2H), 6.73 (s, 2H), 6.79 (s, 1H); MS m/z 468 (M^+). Anal. Calcd for $C_{23}H_{36}O_6SSi$: C, 58.94; H, 7.74. Found: C, 58.87; H, 7.72.

2(*S)-[α(*R**)-[(*tert*-Butyldimethylsilyl)oxy]-3,4-(methylenedioxy)benzyl]-3(*S**)-carboxy-4(*S**)-(3,4-dimethoxyphenyl)butyrolactone (22).** To a mixture of **8** (331 mg, 0.908 mmol) and veratraldehyde (166 mg, 1.0 mmol) in toluene (10 mL) was added KHMDS (0.5 M in toluene, 2.0 mL, 1.0 mmol) at −90 °C. The reaction mixture was stirred for 30 min at the same temperature. The mixture was quenched by addition of AcOH (0.6 mL, 10 mmol) in toluene (2 mL) and warmed to room temperature. The mixture was diluted with EtOAc (30 mL) and washed with water (30 mL), and the aqueous layer was extracted with EtOAc (30 mL). The combined organic layer was dried over $MgSO_4$ and evaporated to dryness *in vacuo*. The residue was chromatographed on silica gel using $CHCl_3$/EtOH (20:1) as an eluent to afford a mixture of **21** and **22** (1:19, 395 mg, 82%). Purification by silica gel chromatography using $CHCl_3$/EtOH (200:1−50:1) as an eluent afforded a pure **22** (375 mg, 78%) as a powder: IR (KBr) 3500, 1780, 1712 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ −0.23 (s, 3H), 0.11 (s, 3H), 0.91 (s, 9H), 3.21 (dd, 1H, J = 3.5, 8.9 Hz), 3.39 (dd, 1H, J = 8.0, 8.9 Hz), 3.88 (s, 3H), 3.89 (s, 3H), 5.13 (d, 1H, J = 3.5 Hz), 5.67 (d, 1H, J = 8.0 Hz), 5.96 (s, 2H), 6.6−7.0 (m, 6H); MS m/z 530 (M^+). Anal. Calcd for $C_{27}H_{34}O_9Si$: C, 61.11; H, 6.46. Found: C, 60.73; H, 6.34.

The compounds **21**, **25**, and **26** were synthesized in the same manner, and the experimental details were deposited in the Supporting Information.

2(*S)-[α(*R**)-[(*tert*-Butyldimethylsilyl)oxy]-3,4-(methylenedioxy)benzyl]-3(*S**)-carboxy-4(*R**)-(3,4-dimethoxyphenyl)butyrolactone (21)**: mp 221−222 °C; IR (KBr) 3450, 1760, 1720 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ −0.09 (s, 3H), 0.19 (s, 3H), 0.82 (s, 9H), 2.99 (dd, 1H, J = 5.5, 6.8 Hz), 3.30 (dd, 1H, J = 6.8, 8.3 Hz), 3.78 (s, 3H), 3.82 (s, 3H), 4.97 (d, 1H, J = 8.3 Hz), 5.44 (d, 1H, J = 5.5 Hz), 5.94 (d, 1H, J = 1.3 Hz), 5.95 (d, 1H, J = 1.3 Hz), 6.4−6.6 (m, 2H), 6.8 − 7.0 (m, 4H); MS m/z 530 (M^+). Anal. Calcd for $C_{27}H_{34}O_9Si$: C, 61.11; H, 6.46. Found: C, 61.04; H, 6.46.

2(*S)-[α(*S**)-[(*tert*-Butyldimethylsilyl)oxy]-3,4-(methylenedioxy)benzyl]-3(*S**)-carboxy-4(*R**)-(3,4-dimethoxyphenyl)butyrolactone (25)**: mp 188 °C; IR (KBr) 3420, 1790, 1714 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ −0.35 (s, 3H), −0.08 (s, 3H), 0.80 (s, 9H), 3.37 (dd, 1H, J = 6.7, 8.2 Hz), 3.78 (dd, 1H, J = 5.3, 6.7 Hz), 3.87 (s, 6H), 5.06 (d, 1H, J = 8.2 Hz), 5.51 (d, 1H, J = 5.3 Hz), 5.97 (d, 1H, J = 1.4 Hz), 5.99 (d, 1H, J = 1.4 Hz), 6.7 − 7.0 (m, 6H); MS m/z 530 (M^+). Anal. Calcd for $C_{27}H_{34}O_9Si$: C, 61.11; H, 6.46. Found: C, 60.97; H, 6.41.

2(*S)-[α(*S**)-[(*tert*-butyldimethylsilyl)oxy]-3,4-(methylenedioxy)benzyl]-3(*S**)-carboxy-4(*S**)-(3,4-dimethoxyphenyl)butyrolactone (26)**: mp 168 °C; IR (KBr) 3400, 1780, 1740 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ −0.18 (s, 3H), 0.03 (s, 3H), 0.88 (s, 9H), 3.20 (dd, 1H, J = 4.2, 8.6 Hz), 3.45 (dd, 1H, J = 5.2, 8.6 Hz), 3.87 (s, 3H), 3.88 (s, 3H), 5.33 (d, 1H, J = 4.2 Hz), 5.81 (d, 1H, J = 5.2 Hz), 5.89 (d, 1H, J = 1.3 Hz), 5.92 (d, 1H, J = 1.3 Hz), 6.70 (d, 1H, J = 7.9 Hz), 6.8−6.9 (m, 5H); MS m/z 530 (M^+). Anal. Calcd for $C_{27}H_{34}O_9Si$: C, 61.11; H, 6.46. Found: C, 60.86; H, 6.38.

(1*S,2*S**,5*S**,6*R**)-2-(3,4-Dimethoxyphenyl)-6-[3,4-(methylenedioxy)phenyl]-4,8-dioxo-3,7-dioxabicyclo[3.3.0]-octane (1a).** To a solution of **22** (2.4 g, 4.5 mmol) in THF (50 mL) were added AcOH (0.42 mL, 7.4 mmol) and Bu_4NF (1.0 M in THF, 6.8 mL, 6.8 mmol) at room temperature. After stirring for 1 day, the mixture was diluted with $CHCl_3$ (100 mL), and the solution was washed with 10% citric acid (50 mL) and brine (100 mL). The organic layer was dried over $MgSO_4$ and evaporated to dryness *in vacuo*. The residue was dissolved in AcOH (5 mL), and the reaction mixture was stirred for 12 h at room temperature and for 30 min at 50 °C. The mixture was diluted with AcOEt (200 mL) and washed with brine (100 mL). The organic layer was dried over $MgSO_4$ and concentrated to dryness *in vacuo*. Silica gel column chromatography of the residue using hexane/EtOAc (1:1) as an eluent afforded **1a** (1.4 g, 80%): mp 198−199 °C; IR (KBr)

1792, 1760 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 3.77 (s, 3H), 3.79 (s, 3H), 3.94 (dd, 1H, J = 3.5, 10.1 Hz), 4.34 (d, 1H, J = 8.6, 10.1 Hz), 5.73 (d, 1H, J = 3.5 Hz), 5.94 (d, 1H, J = 8.6 Hz), 6.048 (d, 1H, J = 0.9 Hz), 6.051 (d, 1H, J = 0.9 Hz), 6.84 (dd, 1H, J = 0.5, 8.1 Hz), 6.920 (d, 1H, J = 1.8 Hz), 6.922 (d, 1H, J = 8.1 Hz), 6.95 (dd, 1H, J = 1.8, 8.3 Hz), 6.99 (d, 1H, J = 8.3 Hz), 7.00 (d, 1H, J = 0.5 Hz); ^{13}C NMR (100 MHz, DMSO-d_6) δ 45.84, 49.66, 55.53, 55.60, 80.21, 80.30, 101.12, 106.48, 107.92, 109.76, 111.75, 118.56, 119.60, 128.85, 130.89, 147.17, 147.28, 149.01, 149.29, 172.11, 175.05; MS *m/z* 398 (M^+). Anal. Calcd for $C_{21}H_{18}O_8$: C, 63.32; H, 4.55. Found: C, 63.14; H, 4.53.

(1*S,2*R**,5*S**,6*S**)-2-(3,4-Dimethoxyphenyl)-6-[3,4-(methylenedioxy)phenyl]-4,8-dioxo-3,7-dioxabicyclo[3.3.0]-octane (1b).** The bislactone **1b** was obtained from **25** in 81% yield in a same manner described above: mp 195−196 °C; IR (KBr) 1769 cm^{-1}; ^1H NMR NMR (400 MHz, DMSO-d_6) δ 3.76 (s, 3H), 3.77 (s, 3H), 3.91 (dd, 1H, J = 3.5, 10.1 Hz), 4.37 (dd, 1H, J = 8.6, 10.1 Hz), 5.72 (d, 1H, J = 3.5 Hz), 5.94 (d, 1H, J = 8.6 Hz), 6.05 (d, 1H, J = 1.0 Hz), 6.06 (d, 1H, J = 1.0 Hz), 6.88 (dd, 1H, J = 1.9, 8.6 Hz), 6.90 (d, 1H, J = 1.9 Hz), 6.92−6.97 (m, 3H), 7.03 (d, 1H, J = 1.6 Hz); ^{13}C NMR (100 MHz, DMSO-d_6) δ 45.86, 49.78, 55.36, 55.53, 80.09, 80.44, 101.33, 106.33, 108.24, 110.24, 111.32, 118.21, 120.20, 127.29, 132.47, 147.73, 147.82, 148.37, 148.87, 172.01, 175.09; MS *m/z* 398 (M^+). Anal. Calcd for $C_{21}H_{18}O_8$: C, 63.32; H, 4.55. Found: C, 63.19; H, 4.54.

(1*S,2*S**,5*S**,6*S**)-2-(3,4-Dimethoxyphenyl)-6-[3,4-(methylenedioxy)phenyl]-4,8-dioxo-3,7-dioxabicyclo[3.3.0]-octane (2a).** The bislactone **2a** was obtained from **26** in 84% yield in a same manner described above: mp 130 °C; IR (KBr) 1772 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 3.77 (s, 3H), 3.79 (s, 3H), 4.18 (dd, 1H, J = 2.9, 9.9 Hz), 4.24 (dd, 1H, J = 2.9, 9.9 Hz), 5.78 (br t, 2H, J = 2.9 Hz), 6.06 (s, 2H), 6.95 (d, 1H, J = 7.9 Hz), 6.94−7.00 (m, 3H), 7.02 (s, 1H), 7.09 (d, 1H, J = 1.3 Hz); ^{13}C NMR (100 MHz, DMSO-d_6) δ 47.88, 47.94, 55.54, 55.62, 81.57, 81.63, 101.30, 106.61, 108.14, 109.93, 111.66, 118.76, 120.59, 130.43, 131.95, 147.78, 147.80, 148.99, 149.34, 175.06, 175.09; MS *m/z* 398 (M^+). Anal. Calcd for $C_{21}H_{18}O_8$: C, 63.32; H, 4.55. Found: C, 63.05; H, 4.51.

2(*S)-[α(*R**)-Hydroxy-3,4-(methylenedioxy)benzyl]-3(*S**)-carboxy-4(*R**)-(3,4-dimethoxyphenyl)butyrolactone (23).** To a solution of **21** (467 mg, 0.88 mmol) in DMF−NMP (10:1, 10 mL) was added $NH_4F{\cdot}HF$ (251 mg, 4.4 mmol) at room temperature. The mixture was stirred for 2 days at room temperature. The mixture was diluted with EtOAc (40 mL) and washed with water (40 mL). The organic layer was dried over $MgSO_4$ and concentrated *in vacuo*. The residue was crystallized from EtOAc to give **23** (304 mg, 83%): mp 171−172 °C; IR (KBr) 3535, 1762, 1705 cm^{-1}; ^1H NMR (200 MHz, DMSO-d_6, D_2O exchange) δ 3.02 (dd, 1H, J = 5.3, 6.5 Hz), 3.57 (dd, 1H, J = 6.5, 8.9 Hz), 3.70 (s, 3H), 3.73 (s, 3H), 4.82 (d, 1H, J = 8.9 Hz), 5.63 (s, 1H, J = 5.3 Hz), 5.98 (s, 2H), 6.6−7.0 (m, 6H); MS *m/z* 416 (M^+). Anal. Calcd for $C_{21}H_{20}O_9$: C, 60.58; H, 4.84. Found: C, 60.43; H, 4.76.

(1*S,2*R**,5*S**,6*R**)-2-(3,4-Dimethoxyphenyl)-6-[3,4-(methylenedioxy)phenyl]-4,8-dioxo-3,7-dioxabicyclo[3.3.0]-octane (3a).** To a solution of **23** (58 mg, 0.14 mmol) in DMF (1.0 mL) was added EDCI (40 mg, 0.21 mmol) at −20 °C. The mixture was stirred for 1 h at room temperature. The mixture was diluted with $CHCl_3$ (50 mL), washed with water (50 mL), dried ($MgSO_4$), and concentrated. The residue was chromatographed on silica gel using $CHCl_3$/EtOH (40:1) as an eluent to afford **3a** (53 mg, 96%): mp 228−230 °C; IR (KBr) 1777 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 3.773 (s, 3H), 3.774 (s, 3H), 4.13 (m, 2H), 5.81 (br t, 2H, J = 7.8 Hz), 6.05 (d, 1H, J = 0.9 Hz), 6.06 (d, 1H, J = 0.9 Hz), 6.78−6.85 (m, 3H), 6.88 (d, 1H, J = 2.0 Hz), 6.93 (d, 1H, J = 7.9 Hz), 6.97 (d, 1H, J = 8.3 Hz); ^{13}C NMR (100 MHz, DMSO-d_6) δ 46.89, 46.98, 55.37, 55.43, 78.57, 78.80, 101.07, 106.37, 107.88, 109.84, 111.27, 118.14, 119.21, 127.36, 128.99, 147.01, 147.10, 148.26, 148.70, 171.91, 172.06; MS *m/z* 398 (M^+). Anal. Calcd for $C_{21}H_{18}O_8$: C, 63.32; H, 4.55. Found: C, 63.02; H. 4.44.

(1*S,2*R**,3*R**,4*R**)-2,3-Bis(hydroxymethyl)-1-(3,4-dimethoxyphenyl)-4-[3,4-(methylenedioxy)phenyl]butane-1,4-diol (29).** To a suspension of LAH (1.2 g, 33 mmol) in THF (100 mL) was added **1a** (1.3 g, 3.3 mmol) in THF (20 mL) at 60 °C. After refluxing for 1 h, the mixture was quenched by addition of 10% NaOH (2.4 mL). The insoluble materials were filtered off by a Celite pad. The filtrate was evaporated to dryness *in vacuo*. The residue was purified by silica gel chromatography using chloroform/EtOH (20:1) as an eluent to afford **29** (798 mg, 60%): mp 159−160 °C; IR (KBr) 3328 cm^{-1}; ^1H NMR (200 MHz, DMSO-d_6, D_2O exchange) δ 1.69 (m, 1H), 1.96 (m, 1H), 3.5−3.7 (m, 4H), 3.62 (s, 3H), 3.75 (s, 3H), 4.32 (d, 1H, J = 8.4 Hz), 4.72 (d, 1H, J = 3.7 Hz), 5.93 (s, 1H), 5.94 (s, 1H), 6.24 (d, 1H, J = 1.3 Hz), 6.4−6.9 (m, 5H); MS *m/z* 406 (M^+). Anal. Calcd for $C_{21}H_{26}O_8$: C, 62.06, H, 6.45. Found: C, 61.87; H, 6.42.

(1*R,2*R**,3*R**,4*S**)-2,3-Bis(hydroxymethyl)-1-(3,4-dimethoxyphenyl)-4-[3,4-(Methylenedioxy)phenyl]butane-1,4-diol (32).** The tetraol **32** was obtained in 64% yield from **1b** according to the same procedure described above: mp 153−155 °C; IR (KBr) 3314 cm^{-1}; ^1H NMR (200 MHz, DMSO-d_6, D_2O exchange) δ 1.78 (m, 1H), 1.92 (m, 1H), 3.5−3.7 (m, 4H), 3.72 (s, 6H), 4.35 (d, 1H, J = 7.5 Hz), 4.70 (d, 1H, J = 3.7 Hz), 5.95 (s, 1H), 5.97 (s, 1H), 6.4−6.8 (m, 6H); MS *m/z* 406 (M^+). Anal. Calcd for $C_{21}H_{26}O_8$: C, 62.06; H, 6.45. Found: C, 61.95; H, 6.46.

(1*R,2*S**,5*R**,6*R**)-2-(3,4-Dimethoxyphenyl)-6-[3,4-(methylenedioxy)phenyl]-3,7-dioxabicyclo[3.3.0]octane (31, methylxanthoxylol).** To a solution of **29** (700 mg, 1.7 mmol) in CH_2Cl_2 (15 mL) containing pyridine (1.4 mL, 17 mmol) was added MsCl (0.4 mL in 5.2 mmol) in CH_2Cl_2 (2 mL) at 0 °C. The mixture was stirred at 0 °C for 2 h and at room temperature for 1 day. The mixture was diluted with CH_2Cl_2, washed with water (50 mL), 10% citric acid (50 mL), and brine (50 mL), dried ($MgSO_4$), and concentrated. The residue was purified on silica gel chromatography using hexane/AcOEt (4:1) as an eluent to afford **31** (325 mg, 51%): mp 115−116 °C; IR (KBr) 1594, 1521, 1243, 1037 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.90 (m, 1H), 3.28−3.36 (m, 2H), 3.81−3.86 (m, 2H), 3.87 (s, 3H), 3.90 (s, 3H), 4.11 (dd, 1H, J = 0.9, 9.5 Hz), 4.42 (d, 1H, J = 7.1 Hz), 4.84 (d, 1H, J = 5.4 Hz), 5.96 (s, 2H), 6.79 (d, 1H, J = 7.9 Hz), 6.81 (dd, 1H, J = 0.8, 1.5 Hz), 6.84 (d, 1H, J = 7.9 Hz), 6.87−6.89 (m, 2H), 6.91 (dd, 1H, J = 1.7, 6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 50.19, 54.55, 55.94, 55.99, 69.68, 70.96, 82.09, 87.63, 100.99, 106.43, 108.16, 109.25, 111.11, 118.52, 118.72, 132.32, 133.68, 146.60, 147.67, 148.80, 149.30; MS *m/z* 370 (M^+). Anal. Calcd for $C_{21}H_{22}O_6$: C, 68.10; H, 5.99. Found: C, 67.91; H, 5.97.

(1*R,2*R**,5*R**,6*S**)-2-(3,4-Dimethoxyphenyl)-6-[3,4-(methylenedioxy)phenyl]-4,8-dioxo-3,7-dioxabicyclo[3.3.0]-octane (33, methyl pluviatilol).** **33** was obtained in 58% yield from **32** according to the same procedure described above: mp 145 °C; IR (KBr) 1591, 1517, 1231, 1028 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.87 (m, 1H), 3.28−3.37 (m, 2H), 3.80−3.91 (m, 2H), 4.11 (dd, 1H, J = 1.1, 9.5 Hz), 4.43 (d, 1H, J = 7.0 Hz), 4.86 (d, 1H, J = 5.4 Hz), 3.88 (s, 3H), 3.91 (s, 3H), 4.12 (d, 1H, J = 9.3 Hz), 5.95 (s, 2H), 6.77 (d, 1H, J = 7.8 Hz), 6.82 (dd, 1H, J = 1.6, 7.8 Hz), 6.85 (br s, 2H), 6.87 (d, 1H, J = 1.6 Hz), 6.92 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 50.20, 54.64, 55.94, 55.97, 69.76, 71.05, 82.06, 87.69, 101.04, 106.55, 108.16, 109.09, 111.14, 117.76, 119.54, 131.00, 135.23, 147.22, 147.98, 148.10, 148.93; MS *m/z* 370 (M^+). Anal. Calcd for $C_{21}H_{22}O_6$: C, 68.10; H, 5.99. Found: C, 68.02; H, 5.95.

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Supporting Information Available: X-ray ORTEP diagram of **3a**, **21**, and **31**; ^1H and ^{13}C NMR spectra of **1a**, **1b**, **2a**, **3a**, **31**, and **33**; tables of characterization of **1a**, **1b**, **2a**, **3a**, **21**, **22**, **25**, and **26** by ^1H NMR; experimental details of syntheses of **21**, **25**, and **26** (19 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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