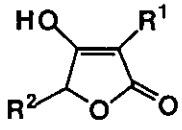
2(3*H*)-AND 2(5*H*)-FURANONES. VII.[1] CHIRALITY TRANSFER ON THE TETRONIC ACID TEMPLATES

Takefumi Momose, Naoki Toyooka,* Morihiro Nishio, Hiroyuki Shinoda, Hiromi Fujii,[#] and Hironobu Yanagino[#]

Faculty of Pharmaceutical Sciences, Toyama Medical and Pharmaceutical University, Sugitani 2630, Toyama 930-0194, Japan
[#]Faculty of Pharmaceutical Sciences, Kinki University, Kowakae 3-4-1, Higashi-Osaka, Osaka 577-8502, Japan

Abstract - The chirality transfer on the β-tetronic acid templates has been examined *via* highly diastereoselective alkylation or the Michael reaction at the α-position of the acids. Synthetic utility of this transfer procedure was demonstrated by the formal synthesis of (+)-cassiol and enantiodivergent synthesis of *O*-methyljoubertiamine.

β-Tetronic acids (**1**) are one of the attractive building blocks for the syntheses of several classes of natural products[2] due to the presence of multifunctionality in the molecule. Previously, we have demonstrated the efficient preparation of **1** (R^1, R^2 = H),[3] and investigated the reactivity of its congeners at the α-position.[4] However, most fundamental studies in the alkylation on the system have been reported only to a small extent.[5] Recently, we reported our preliminary results on the selective allylation at the α-position of optically active α-methyltetronic acids *via* direct allylation and the Claisen rearrangement of allyl tetronates concomitantly formed in the preceding direct allylation.[6] In this paper, we wish to report a full account of detail examination on the alkylation of optically active α,γ-disubstituted tetronic acids and the Michael reaction as another carbon-chain homologation at the α-position. As a synthetic utility of this method, formal synthesis of (+)-cassiol[7] and enantiodivergent synthesis of *O*-methyljoubertiamine[8] were accomplished.



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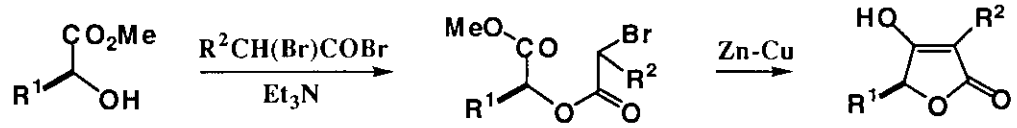
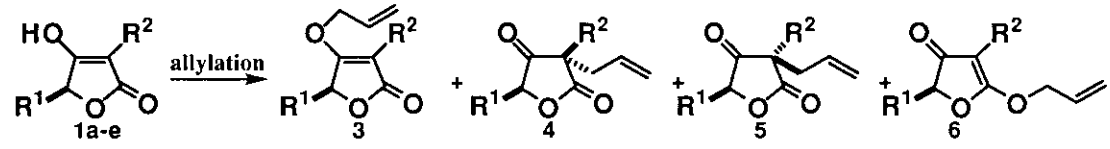
The starting optically active α,γ-disubstituted tetronic acids (**1a**)-(**1e**) were prepared from commercially available methyl lactate, L-phenylalanine and L-valine by employing the intramolecular Reformatsky reaction[9] as shown below.



2a: R^1=R^2=Me **1a**: R^1=R^2=Me
2b: R^1=Bn, R^2=Me **1b**: R^1=Bn, R^2=Me
2c: R^1=*i*-Pr, R^2=Me **1c**: R^1=*i*-Pr, R^2=Me
2d: R^1=*i*-Pr, R^2=Ph **1d**: R^1=*i*-Pr, R^2=Ph
2e: R^1=*i*-Pr, R^2=*p*-$MeOC_6H_4$ **1e**: R^1=*i*-Pr, R^2=*p*-$MeOC_6H_4$

First, we examined the allylation of tetronic acids (**1a**)-(**1e**) under the various conditions, and the results are summarized in Table 1.

Table 1: Allylation of optically active α,γ-disubstituted tetronic acids



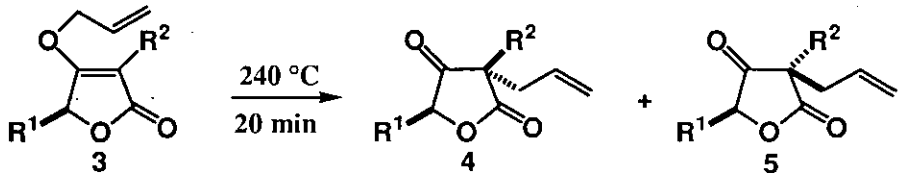
entry	R^1	R^2	Temp (°C)	Time (h)	Yield (%)[e]			Diastereomeric excess
					3	**4**[d]	**5**	**6**	(% de)
1[a]	Me	Me(**1a**)	80	4	31(**3a**)	22(**4a**)	18(**5a**)	--	10
2[b]	Me	Me(**1a**)	10	8	42(**3a**)	29(**4a**)	8(**5a**)	2.5(**6a**)	56
3[a]	Bn	Me(**1b**)	80	4	28(**3b**)	33(**4b**)	16(**5b**)	--	35
4[b]	Bn	Me(**1b**)	10	8	39(**3b**)	30(**4b**)	5(**5b**)	2.4(**6b**)	70
5[a]	*i*-Pr	Me(**1c**)	80	4	26(**3c**)	39(**4c**)	13(**5c**)	--	50
6[c]	*i*-Pr	Me(**1c**)	30	11	29(**3c**)	61(**4c**)	3(**5c**)	--	90
7[c]	*i*-Pr	Me(**1c**)	-15	48	25(**3c**)	73(**4c**)	1(**5c**)	--	96
8[b]	*i*-Pr	Me(**1c**)	10	8	39(**3c**)	42(**4c**)	2(**5c**)	1.3(**6c**)	90
9[c]	*i*-Pr	Ph(**1d**)	30	15	14(**3d**)	77(**4d**)	2(**5d**)	--	94
10[c]	*i*-Pr	Ph(**1d**)	-5	284	12(**3d**)	73(**4d**)	1(**5d**)	--	96
11[c]	*i*-Pr	*p*-$MeOC_6H_4$(**1e**)	30	24	16(**3e**)	78(**4e**)	3(**5e**)	--	93
12[c]	*i*-Pr	*p*-$MeOC_6H_4$(**1e**)	-15	240	11(**3e**)	85(**4e**)	1(**5e**)	--	98

Reactions were conducted as follows: a; Procedure A: tetronic acid (1 mmol), DMF (1 mL), K_2CO_3 (0.6 mmol), allyl bromide (1.2 mmol); b; Procedure B: tetronic acid (2 mmol), HMPA (2 mL), Ag_2O (1.2 mmol), allyl bromide (2.4 mmol); c; Procedure C: tetronic acid (1 mmol), DMF (2 mL), K_2CO_3 (0.53 mmol), molecular sieves 4A (10 mg). d: The stereochemistry of the major *C*-allyl product (R^1 = *i*-Pr, R^2 = Me) was assigned to bc **8c** on the basis of NOESY experiment. e: Yields of **3**, **4**, **5**, and **6** were isolated ones, respectively.

Although the reaction was conducted at 80 °C (entries, 1, 3, 5, procedure A), the racemization at the γ-position of the *C*-allyl products (**4a**), (**4b**), and (**4c**) was observed, at 30 °C in the presence of molecular sieves 4A (entries 6, 9, 11, procedure C), no racemization at the γ-position was observed.[10] The use of Ag_2O instead of K_2CO_3 in HMPA (entries 2, 4, 8, procedure B) was also effective, and racemization at the γ-position was not observed.[11] The diastereomeric excess of the *C*-allyl products was improved when the reaction was performed under the procedure C below 0 °C (entries 7, 10, 12). In this case, longer reaction time was needed for the completion of the reaction (entry 9 vs 10, and entry 11 vs 12).

The Claisen rearrangement of allyl tetronates (**3**) proceeded smoothly to give the ketones (**4**) and (**5**), and the results are summarized in Table 2.

Table 2: Claisen rearrangement of allyl tetronates

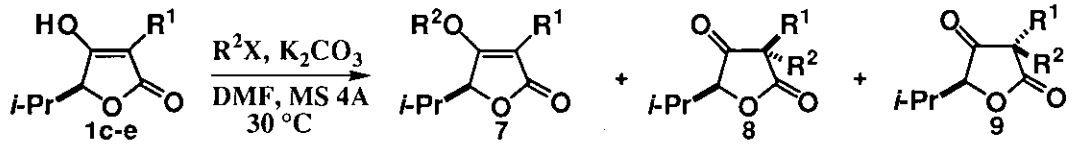


R^1	R^2	Yield (%)[a] 4	5
Me	Me(**3a**)	56(**4a**)	14(**5a**)
Bn	Me(**3b**)	56(**4b**)	18(**5b**)
i-Pr	Me(**3c**)	58(**4c**)	7(**5c**)

a: Yields of **4** and **5** were isolated ones, respectively.

In the above rearrangement, no racemization at the γ-position of the rearranged products (**4a-c**) was observed again.[11] In this way, the selective allylation at the α-position of α-substituted tetronic acid was achieved by the direct allylation and the Claisen rearrangement of the allyl tetronate. Thus, the chirality of L-amino acids was efficiently transferred into the α-position of the α-substituted β-tetronic acids to give the keto lactones (**5a-e**) bearing the chiral quaternary center. Furthermore, alkylation with other alkylating agents was also examined under the procedure C in Table 1, and the results are summarized in Table 3.

Table 3: Alkylation of optically active α,γ-disubstituted tetronic acids

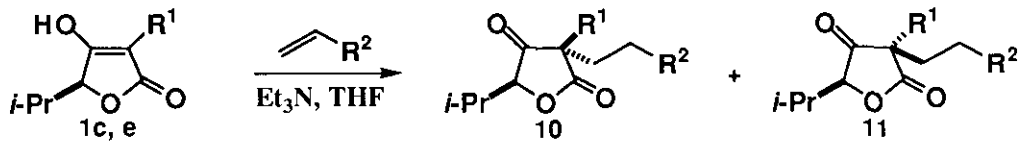


R^1	R^2	Time (h)	Yield (%)[b] 7	8	9	Diastereomeric excess (% de)
Me(**1c**)	Bn	7	32(**7a**)	65(**8a**)	1 (**9a**)[a]	96
Ph(**1d**)	Me	24	25(**7b**)	63(**8b**)	5 (**9b**)	85
Ph(**1d**)	Bn	20	22(**7c**)	75(**8c**)	1 (**9c**)[a]	97
p-$MeOC_6H_4$(**1e**)	Me	36	24(**7d**)	70(**8d**)	4 (**9d**)	88
p-$MeOC_6H_4$(**1e**)	Bn	36	19(**7e**)	78.6(**8e**)	0.4 (**9e**)[a]	99

a: Ratio of **8** and **9** was determined by the integration of the C_5-methine proton of the ^1H NMR spectrum of the crude products. b: Yields of **7**, **8**, and **9** were isolated ones, respectively.

Next, we examined the Michael reaction of **1c** and **1e** as another carbon-chain homologation at the α-position on the system, and the results are summarized in Table 4.

Table 4: Michael reaction of optically active α,γ-disubstituted tetronic acids

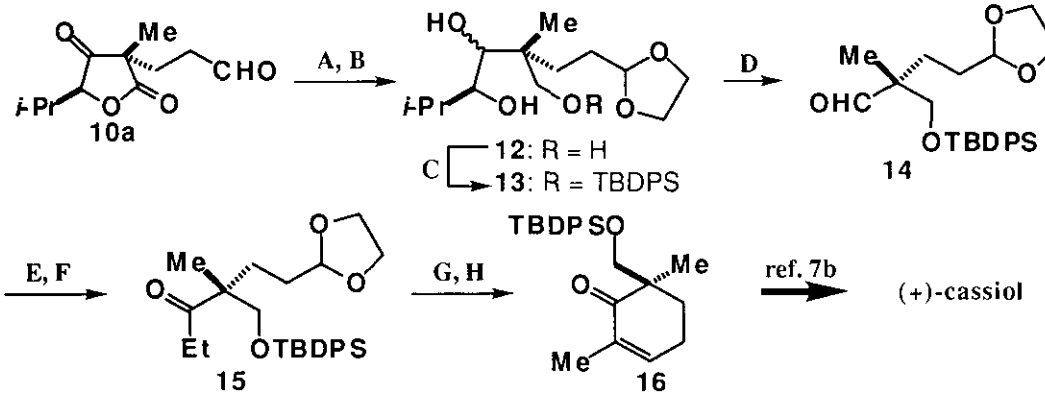


R^1	R^2	Temp (°C)	Time (h)	Yield (%)[c] 10	11	Diastereomeric excess (% de)
Me(**1c**)	CHO[a]	0	5	96(**10a**)	1(**11a**)	97
Me(**1c**)	COMe	30	11	96(**10b**)	3(**11b**)	94
Me(**1c**)	CO_2Me	30	24	--	--	--
Me(**1c**)	CN	30	24	--	--	--
p-$MeOC_6H_4$(**1e**)	CHO	0	24	41(**10c**)	5(**11c**)[b]	78
p-$MeOC_6H_4$(**1e**)	COMe	30	24	90(**10d**)	8(**11d**)	84
p-$MeOC_6H_4$(**1e**)	CO_2Me	30	24	--	--	--
p-$MeOC_6H_4$(**1e**)	CN	30	24	--	--	--

a: The chemical yield and diastereomeric excess of the reaction were determined after acetalization of the crude product with ethylene glycol and *p*-TsOH in benzene; see experimental section. b: Ratio of **10** and **11** was determined by the integration of the C_5-methine proton of the ^1H NMR spectrum of the crude products. c: Yields of **10** and **11** were isolated ones, respectively.

The Michael reaction with acrolein or methyl vinyl ketone proceeded smoothly, however, with methyl acrylate or acrylonitrile the reaction did not proceed under the same condition (Et_3N, THF, 30 °C). The AM1 calculations {LUMOs for acrolein; -0.13877, for methyl vinyl ketone; -0.06805 (s-*trans*), for methyl acrylate; -0.01413 (s-*trans*), for acrylonitrile; 0.04971} on these α,β-unsaturated compounds suggested the low reactivity of methyl acrylate and acrylonitrile toward the Michael reaction.

Finally, we examined the synthetic utility of above Michael reaction for the synthesis of natural product, such as (+)-cassiol and *O*-methyljoubertiamine, and the synthetic schemes are shown below.

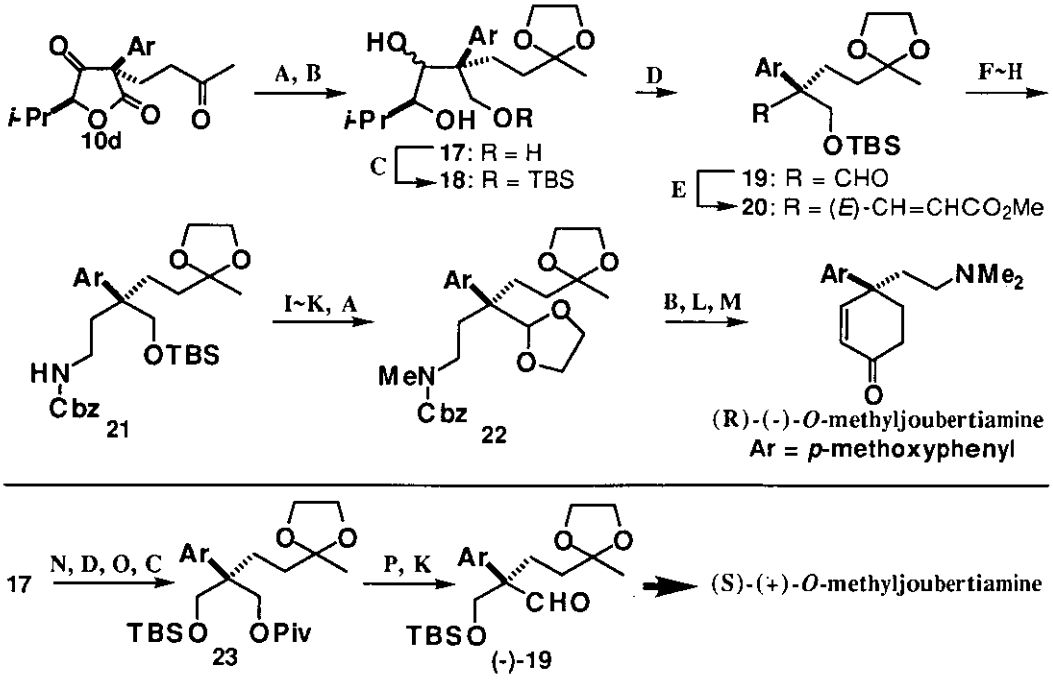


Formal synthesis of (+)-cassiol: Reagents and conditions: **A**: ethylene glycol, *p*-TsOH, benzene, reflux; **B**:$LiAlH_4$, THF; **C**: TBDPSCl, Et_3N, DMAP, CH_2Cl_2; **D**: $NaIO_4$, dioxane-H_2O=8:1; **E**: EtMgBr; **F**: Swern oxidn; **G**: *p*-TsOH, acetone; **H**: KOH, THF

The aldehyde (**10a**) was converted to the silyl ether (**13**) over three steps, and then the oxidative cleavage of the 1,2-glycol moiety in **13** afforded the aldehyde (**14**). After conversion of **14** to ethyl ketone (**15**),

deprotection of acetal moiety in **15** with acid followed by aldol cyclization of the resulting keto aldehyde gave the cyclohexenone (-)-(**16**), which has been converted to (+)-cassiol.[7b]

Next we examined the total synthesis of (-)-*O*-methyljoubertiamine. Selective protection of the side chain ketone in **10d** followed by the lithium aluminum hydride (LAH) reduction gave the triol (**17**). Selective protection of the primary hydroxyl group in **17** with *tert*-butyldimethylsilyl chloride and subsequent oxidative cleavage of the resulting 1,2-glycol (**18**) with lead tetraacetate provided the aldehyde (**19**). The Wittig-Horner reaction of **19** gave the *E*-olefin (**20**). Catalytic hydrogenation of **20** over 5% Pd-C followed by hydrolysis gave the acid, which was subjected to the modified Curtius rearrangement according to the Shioiri's protocol[12] using diphenylphosphoryl azide to afford the urethane (**21**). The *N*-methylation of **21** followed by deprotection with tetrabutylammonium fluoride and the Swern oxidation of the resulting alcohol gave the aldehyde, which gave the acetal (**22**) in 72% overall yield from **21**. Finally, the LAH reduction of **22** followed by sequential deprotection and cyclization gave (*R*)-(-)-*O*-methyljoubertiamine ($[\alpha]^{26}_D$ -51.2° $CHCl_3$; the value reported for the enantiomer: $[\alpha]^{25}_D$ +50.3°, $CHCl_3$,[8c] $[\alpha]^{22}_D$ -68.4°, MeOH[8b]) in 66% yield, which was identical in its ^{1}H-NMR and MS spectra with those reported.[8]



Enantiodivergent synthesis of *O*-methyljoubertiamine: *Reagents and conditions*: **A**: ethylene glycol, *p*-TsOH, benzene, reflux; **B**: $LiAlH_4$, THF; **C**: TBSCl, Et_3N, DMAP, CH_2Cl_2; **D**: $Pb(OAc)_4$, benzene; **E**: $Ph_3P{=}CHCO_2Me$, benzene, reflux; **F**: H_2, 5% Pd/C, MeOH; **G**: KOH, H_2O-MeOH; **H**: DPPA, Et_3N, then BnOH; **I**: NaH, MeI; **J**: TBAF; **K**: Swern oxidn; **L**: 10% HCl; **M**: NaOH; **N**: PivCl, Py, CH_2Cl_2; **O**: $NaBH_4$, MeOH; **P**: Super-Hydride, THF, 0 °C

The aldehyde (-)-(**19**) was also prepared from common starting material (**10d**). The spectral properties of (-)-**19** were identical with those of the aldehyde (+)-(**19**) prepared above.

In conclusion, we examined the alkylation reaction of optically active α,γ-disubstitued tetronic acids in detail, and selective allylation at the α-position was achieved by direct allylation and the Claisen rearrangement of allyltetronate. Furthermore, the Michael reaction of the acids as another carbon-chain homologation was accomplished, and the formal synthesis of (+)-cassiol and the enantiodivergent synthesis of *O*-methyljoubertiamine was achieved by utilizing this homologation reaction of **1** at the α-position.

EXPERIMENTAL

IR spectra were measured with a Shimadzu IR-435, JASCO A102 or Perkin-Elmer 1600 series FTIR spectrophotometer. ^{1}H NMR spectra were recorded at 270 MHz on a JEOL JNM-GSX 270 instrument with tetramethylsilane as an internal standard. MS spectra and HRMS spectra were measured on a JEOL JMS-100 or JMS D-200 spectrometer. Optical rotations were measured on a Union PM-101 or JASCO DIP-140 instrument. Chromatography was performed on a silica gel column (Merck Kieselgel 60 or Fuji-Davision BW-200) unless otherwise stated. The extracts were dried over $MgSO_4$ unless otherwise specified.

Methyl (2*S*)-2-(2-bromopropanoyloxy)propanoate (2a) To a stirred solution of methyl (*S*)-(-)-lactate (2.5 g, 24 mmol) in Et_2O (40 mL) were added Et_3N (5.0 mL, 36.2 mmol) and 2-bromopropionyl bromide (3.0 mL, 27.9 mmol) at 0 °C, and the resulting suspension was stirred at rt for 18 h. To the suspension was added Et_2O (150 mL), and the insoluble material was filtered through a celite pad. The filtrate was washed with satd $NaHCO_3$ (10 mL), brine (10 mL), 5% HCl (10 mL) and brine (10 mL), successively. The organic layer was dried and evaporated to give a pale yellow oil, which was purified by distillation under reduced pressure (105-110 °C/5 mmHg) to afford **2a** (4.61 g, 80%) as a colorless oil. IR ($CHCl_3$) 2990, 2950, 1750, 1270, 1150 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.54 and 1.55 (each 0.5H and 2.5H, each d, each J = 7.0 Hz), 1.86 and 1.87 (each 0.5H and 2.5H, each d, each J = 6.7 Hz), 3.76 and 3.77 (each 0.5H and 2.5H, each s), 4.42 and 4.46 (each 0.83H and 0.17H, each q, each J = 6.7 Hz), 5.16 and 5.20 (each 0.83H and 0.17H, each q, each J = 7.0 Hz).

Methyl (2*S*)-2-(2-bromopropanoyloxy)-3-phenylpropanoate (2b) To a stirred solution of 2-hydroxy-3-phenylpropanoic acid[13] (7.15 g, 43.1 mmol) in MeOH (70 mL) was added conc H_2SO_4 (0.2 mL), and the resulting solution was refluxed for 3.5 h. After cooling, the reaction mixture was diluted with CH_2Cl_2 (180 mL), and the organic layer was washed with 5% $NaHCO_3$ (60 mL). The aqueous layer was extracted with CH_2Cl_2 (60 mL x 2), and the organic layer and extracts were combined, dried, and evaporated to give a colorless oil, which was purified by distillation under reduced pressure (135-140 °C/5 mmHg) to afford the methyl ester (7.38 g, 96%) as a colorless solid (mp 46.0-47.0 °C). IR ($CHCl_3$) 3529, 3022, 2990, 1737, 1211, 1092 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.72 (1H, d, J = 6.5 Hz), 2.97 (1H, dd, J = 14.0, 6.5 Hz), 3.12 (1H, dd, J = 14.0, 4.6 Hz), 3.77 (3H, s), 4.46 (1H, td, J = 6.5, 4.6 Hz), 7.18-7.34 (5H, m); $[\alpha]^{16}_D$ -6.0° (*c* 1.08, $CHCl_3$).

To a stirred solution of the ester obtained above (3.73 g, 20.7 mmol) in Et_2O (45 mL) were added Et_3N (4.3 mL, 31.1 mmol) and 2-bromopropionyl bromide (2.4 mL, 22.3 mmol), and the resulting suspension was stirred at rt for 18 h. To the suspension was added Et_2O (100 mL), and the insoluble material was

filtered through a celite pad. The filtrate was washed with satd $NaHCO_3$ (30 mL), brine (30 mL), 5% HCl (30 mL) and brine (30 mL), successively. The organic layer was dried and evaporated to give a pale yellow oil, which was purified by distillation under reduced pressure (145-155 °C/0.1 mmHg) to afford **2b** (6.2 g, 95%) as a colorless oil. IR ($CHCl_3$) 3030, 2950, 2930, 1750, 1600, 1120, 1080 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.77 and 1.79 (each 1.5H, each d, each J = 7.0 Hz), 3.13 and 3.14 (each 0.5H, each dd, each J = 14.8, 9.0 Hz), 3.23 and 3.25 (each 0.5H, each dd, each J = 14.8, 4.7 Hz), 3.74 and 3.75 (each 1.5H, each s), 4.36 and 4.41 (each 0.5H, each q, each J = 7.0 Hz), 5.27 and 5.28 (each 0.5H, each dd, each J = 9.0, 4.7 Hz), 7.20-7.37 (5H, m).

Methyl (2*S*)-2-(2-bromopropanoyloxy)-3-methylbutanoate (2c) To a stirred solution of 2-hydroxy-3-methylbutanoic acid[14] (1.25 g, 10.6 mmol) in MeOH (10 mL) was added conc H_2SO_4 (0.05 mL), and the resulting solution was refluxed for 3.5 h. After cooling, the reaction mixture was diluted with CH_2Cl_2 (90 mL), and the organic layer was washed with 5% $NaHCO_3$ (30 mL). The aqueous layer was extracted with CH_2Cl_2 (30 mL x 2), and the organic layer and extracts were combined, dried, and evaporated to give a colorless oil, which was purified by distillation under reduced pressure (85-90 °C/40 mmHg) to afford the methyl ester (1.14 g, 84%) as a colorless oil. IR ($CHCl_3$) 3526, 2961, 2910, 1731, 1209, 1105 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.87 and 1.02 (each 3H, each d, each J = 7.0 Hz), 2.08 (1H, heptet of d, J = 7.0, 3.8 Hz), 2.71 (1H, d, J = 6.0 Hz), 3.80 (3H, s), 4.05 (1H, dd, J = 6.0, 3.8 Hz); $[\alpha]^{16}_D$ +27.2° (*c* 1.14, $CHCl_3$).

To a stirred solution of the ester obtained above (1.73 g, 13.1 mmol) in Et_2O (15 mL) were added Et_3N (2.8 mL, 20.3 mmol) and 2-bromopropionyl bromide (1.4 mL, 13.1 mmol), and the resulting suspension was stirred at rt for 18 h. To the suspension was added Et_2O (100 mL), and the insoluble material was filtered through a celite pad. The filtrate was washed with satd $NaHCO_3$ (10 mL), brine (10 mL), 5% HCl (10 mL) and brine (10 mL), successively. The organic layer was dried and evaporated to give a pale yellow oil, which was purified by distillation under reduced pressure (115-120 °C/5 mmHg) to afford **2c** (2.74 g, 79%) as a colorless oil. IR ($CHCl_3$) 2987, 2960, 1740, 1254, 1157, 1061 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.00 and 1.01 (each 0.45H and 2.55H, each d, each J = 7.0 Hz), 1.04 and 1.05 (each 2.55H and 0.45H, each d, each J = 7.0 Hz), 1.86 and 1.89 (each 0.45H and 2.55H, each d, each J = 7.0 Hz), 2.29 and 2.30 (each 0.18H and 0.82H, each heptet of d, each J = 7.0, 4.5 Hz), 3.76 and 3.78 (each 2.55H and 0.45H, each s), 4.44 and 4.50 (each 0.82H and 0.18H, each q, each J = 7.0 Hz), 4.90 and 4.91 (each 0.82H and 0.18H, each d, each J = 4.5 Hz).

Methyl (2*S*)-2-(2-bromo-2-phenylethanoyloxy)-3-methylbutanoate (2d) To a stirred solution of methyl 2-hydroxy-3-methylbutanoate (4.0 g, 30.3 mmol) in Et_2O (200 mL) were added Et_3N (9.4 mL, 68 mmol) and phenylacetyl chloride (6.0 g, 45 mmol), and the resulting suspension was stirred at rt for 18 h. The insoluble material was filtered through a celite pad, and the filtrate was washed with 10% HCl (20 mL), satd $NaHCO_3$ (20 mL) and brine (20 mL), successively. The organic layer was dried and evaporated to give a colorless oil, which was purified by column chromatography (hexane:acetone=50:1) to afford the ester (5.12 g, 68%) as a colorless oil. ^1H NMR ($CDCl_3$) δ 0.93 (6H, d, J = 6.8 Hz), 2.14-2.27 (1H, m), 3.71 (3H, s), 3.73 (3H, s), 4.85 (1H, d, J = 4.5 Hz), 7.31 (5H, m); $[\alpha]^{26}_D$ -34.4° (*c* 2.33, $CHCl_3$).

To a stirred solution of the ester obtained above (4.23 g, 16.9 mmol) in CCl_4 (50 mL) were added *N*-bromosuccinimide (NBS) (3.92 g, 22 mmol) and 2,2'-azobisisobutyronitrile (AIBN) (138.9 mg, 0.85 mmol), and the resulting solution was refluxed for 4 h. After cooling, the insoluble material was removed by filtration, and the filtrate was washed with 10% $Na_2S_2O_3$ in satd $NaHCO_3$ (15 mL x 2), and the organic layer was dried and evaporated to give a pale yellow oil, which was purified by column chromatography (hexane:acetone=40:1) to afford **2d** (5.6 g, 99%) as a colorless oil. IR ($CHCl_3$) 2984, 2963, 1742, 1232, 1129, 1061 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.97 (3H, d, J = 7.0 Hz), 1.01 and 1.02 (each 1.5H, each d, each J = 7.0 Hz), 2.19-2.39 (1H, m), 3.80 (3H, s), 4.93 (1H, d, J = 4.5 Hz), 5.47 (1H, s), 7.31 (5H, s).

Methyl (2*S*)-2-[2-(4-methoxyphenyl)ethanoyloxy]-3-methylbutanoate (2e) To a stirred solution of methyl 2-hydroxy-3-methylbutanoate (7.69 g, 60.3 mmol) in Et_2O (400 mL) were added Et_3N (15 mL, 108 mmol) and *p*-methoxyphenylacetyl chloride (12.2 g, 66.3 mmol), and the resulting suspension was stirred at rt for 18 h. The insoluble material was removed by filtration, and the filtrate was washed with 10% HCl (40 mL), satd $NaHCO_3$ (40 mL) and brine (40 mL), successively. The organic layer was dried and evaporated to give a colorless oil, which was purified by column chromatography (hexane:acetone=50:1) to afford the ester (15.38 g, 79%) as a colorless oil. To a stirred solution of the ester obtained above (1.59 g, 5.68 mmol) in CCl_4 (20 mL) were added NBS (1.31 g, 7.36 mmol) and AIBN (46.6 mg, 0.28 mmol), and the resulting solution was refluxed for 20 h. After cooling, the insoluble material was removed by filtration, and the filtrate was washed with 10% $Na_2S_2O_3$ in satd $NaHCO_3$ (10 mL x 2). The organic layer was dried and evaporated to give a pale yellow oil, which was purified by column chromatography (hexane:EtOAc=20:1) to afford **2e** (1.88 g, 92%) as a colorless oil. IR (neat) 2839, 1748, 1584, 1255, 1031 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.95 (3H, d, J = 7.0 Hz), 0.98 (1.5H, d, J = 7.0 Hz), 1.01 (1.5H, d, J = 7.0 Hz), 2.16-2.36 (1H, m), 3.69 and 3.74 (each 1.5H, s), 3.82 (3H, s), 4.91 and 4.92 (each 0.5H, d, J = 4.5 Hz), 5.45 (1H, s), 6.85-6.92 (2H, m), 7.48-7.56 (2H, m).

General procedure for the preparation of optically active tetronic acids (1a-c) To the suspension of zinc-copper couple (2 eq) and catalytic amount of iodine in THF was added a solution of the corresponding α-bromo ester (**2a-c**) in THF, and the resulting suspension was stirred at 50 °C for 30 min. The solvent was removed, and 5% HCl was added to the residue. The aqueous mixture was extracted with $CHCl_3$, and the $CHCl_3$ layer was extracted with 5% K_2CO_3. The basic aqueous layer was acidified with 5% HCl, and the resulting aqueous layer was extracted with $CHCl_3$. The combined $CHCl_3$ layer was dried and evaporated to give the corresponding tetronic acids (**1a-c**), which were purified by recrstallization.

(5*S*)-4-Hydroxy-3,5-dimethyl-2(5*H*)-furanone (1a) yield; 35%; mp; 129-130.5 °C (benzene); IR ($CHCl_3$) 3110, 2980, 2720, 1729, 1665 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.50 (3H, d, J = 6.5 Hz), 1.74 (3H, d, J = 1.0 Hz), 4.84 (1H, qd, J = 6.5, 1.0 Hz), 10.0-11.0 (1H, br); Anal. Calcd for $C_6H_8O_3$: C, 56.24; H, 6.29. Found: C, 56.11; H, 6.15; $[\alpha]^{18}_D$ +24.0° (*c* 1.04, $CHCl_3$).

(5*S*)-5-Benzyl-4-hydroxy-3-methyl-2(5*H*)-furanone (1b) yield; 20%; mp; 177.5-180 °C (ethyl acetate); IR (KBr) 3108, 2980, 2720, 1723, 1656 cm^{-1}; ^1H NMR (DMSO-d_6) δ 1.49 (3H, d, J = 1.0

Hz), 2.75 (1H, dd, J = 14.5, 3.3 Hz), 3.22 (1H, dd, J = 14.5, 3.3 Hz), 4.89 (1H, ddq, J = 7.5, 3.3, 1.0 Hz), 7.19-7.28 (5H, m); Anal. Calcd for $C_{12}H_{12}O_3$: C, 70.58; H, 5.92. Found: C, 70.55; H, 6.01; $[\alpha]^{18}_D$ -56.0° (*c* 1.00, $CHCl_3$).

(5*S*)-4-Hydroxy-3-methyl-5-(2-propyl)-2(5*H*)-furanone (1c) yield; 44%; mp; 116-118 ℃ (cyclohexane:benzene=3:1); IR ($CHCl_3$) 3110, 2963, 2720, 1725, 1658 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.82 and 1.10 (each 3H, each d, each J = 7.0 Hz), 1.75 (3H, d, J = 1.0 Hz), 2.25 (1H, heptet of d, J = 7.0, 3.0 Hz), 4.66 (1H, dq, J = 3.0, 1.0 Hz), 10.0-10.6 (1H, br); Anal. Calcd for $C_8H_{12}O_3$: C, 61.52; H, 7.74. Found: C, 61.28; H, 7.66; $[\alpha]^{18}_D$ -62.1° (*c* 1.03, $CHCl_3$).

General procedure for the preparation of optically active tetronic acids (1d-e) To the suspension of magnesium turnings (2 eq) and catalytic amounts of iodine in THF was added a solution of the corresponding α-bromo ester (**2d-e**) in THF, and the resulting suspension was stirred rt for 2 h. To the suspension was added 10% HCl, and the solvent was removed. The aqueous mixture was extracted with $CHCl_3$, and the $CHCl_3$ layer was extracted with 10% K_2CO_3. The basic aqueous layer was acidified with 10% HCl, and the resulting aqueous layer was extracted with $CHCl_3$. The combined $CHCl_3$ layer was dried and evaporated to give the corresponding tetronic acids (**1d-e**), which were purified by recrystallization.

(5*S*)-4-Hydroxy-3-phenyl-5-(2-propyl)-2(5*H*)-furanone (1d) yield; 38%; mp; 136-137 ℃ (isopropyl ether); IR (KBr) 2967, 2933, 2714, 1702, 1632, 1501 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.85 and 1.15 (each 3H, d, J = 7.0 Hz), 2.29-2.42 (1H, m), 4.76 (1H, d, J = 2.9 Hz), 7.25-7.43 (3H, m), 7.67 (2H, d, J = 8.5 Hz); HRMS calcd for $C_{13}H_{14}O_3$: 218.0942. Found: 218.0912; $[\alpha]^{18}_D$ -72.6° (*c* 2.37, $CHCl_3$).

(5*S*)-4-Hydroxy-3-(4-methoxyphenyl)-5-(2-propyl)-2(5*H*)-furanone (1e) yield; 43%; mp; 166.5-167.5 ℃ (ethyl acetate); IR (KBr) 1796, 1748, 1715, 1580 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.87 and 1.15 (each 3H, each d, each J = 7.0 Hz), 2.24-2.40 (1H, m), 3.80 (3H, s), 4.73 (1H, d-like, J = 2.5 Hz), 6.94 and 7.56 (each 2H, each d, each J = 9.0 Hz); HRMS calcd for $C_{14}H_{16}O_4$: 248.1049. Found: 248.1051; $[\alpha]^{18}_D$ -105.1° (*c* 0.52, MeOH).

General procedure for the allylation of tetronic acids (1a-e) Procedure A: To a stirred solution of the corresponding tetronic acid (**1a-e**) (1.0 mmol) in DMF (1 mL) was added K_2CO_3 (83 mg, 0.6 mmol), and the resulting suspension was stirred at rt for 30 min. To the suspension was added allyl bromide (0.1 mL, 1.2 mmol), and the suspension was stirred at 80 °C. To the suspension was added benzene (60 mL), and the insoluble material was removed by filtration. The filtrate was washed with H_2O (5 mL x 2), and the organic layer was dried and evaporated to give a pale yellow oil, which was purified by column chromatography (hexane:acetone=50:1~10:1) to afford the allylated products.

(5*S*)-3,5-Dimethyl-4-(2-propenyloxy)-2(5*H*)-furanone (3a) IR ($CHCl_3$) 2999, 2915, 1745, 1662, 1398, 1338 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.44 (3H, d, J = 6.5 Hz), 1.94 (3H, d, J = 1.0 Hz), 4.71 (1H, qq, J = 6.5, 1.0 Hz), 4.83 (2H, dt, J = 5.1, 1.2 Hz), 5.34 (1H, dq, J = 8.0, 1.2 Hz), 5.38 (1H, dq, J = 15.0, 1.2 Hz), 5.97 (1H, ddt, J = 15.0, 8.0, 5.1 Hz); HRMS calcd for $C_9H_{12}O_3$: 168.0787. Found: 168.0771; $[\alpha]^{21}_D$ +2.38° (*c* 1.47, $CHCl_3$).

(3*S*,5*S*)-3,5-Dimethyl-3-(2-propenyl)-2,4(3*H*,5*H*)-furandione (4a) IR ($CHCl_3$) 2990, 2915, 1798, 1756, 1640, 1068 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.32 (3H, s), 1.50 (3H, d, *J* = 7.1 Hz), 2.45 (1H, ddt, *J* = 13.5, 8.0, 1.0 Hz), 2.51 (1H, ddt, *J* = 13.5, 7.1, 1.0 Hz), 4.63 (1H, q, *J* = 7.1 Hz), 5.16 (1H, dq-like, *J* = 15.5, 1.0 Hz), 5.17 (1H, dm, *J* = 10.5 Hz), 5.66 (1H, dddd, *J* = 15.5, 10.5, 8.0, 7.1 Hz); HRMS calcd for $C_9H_{12}O_3$: 168.0787. Found: 168.0801; $[\alpha]^{21.5}_D$ -37.3° (*c* 1.10, $CHCl_3$).

(3*R*,5*S*)-3,5-Dimethyl-3-(2-propenyl)-2,4(3*H*,5*H*)-furandione (5a) IR ($CHCl_3$) 2990, 2905, 1798, 1757, 1640, 1078 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.34 (3H, s), 1.45 (3H, d, *J* = 7.0 Hz), 2.47 and 2.51 (each 1H, each ddt, *J* = 13.5, 7.5, 1.0 Hz), 4.80 (1H, q, *J* = 7.0 Hz), 5.14 (1H, dm, *J* = 10.5Hz), 5.15 (1H, dq-like, *J* = 15.9, 1.0 Hz), 5.63 (1H, ddt, *J* = 15.9, 10.5, 7.5 Hz); HRMS calcd for $C_9H_{12}O_3$: 168.0787. Found: 168.0785.

(5*S*)-5-Benzyl-3-methyl-4-(2-propenyloxy)-2(5*H*)-furanone (3b) IR ($CHCl_3$) 2999, 2915, 1746, 1665, 1600, 1395, 1312 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.83 (3H, d, *J* = 1.0 Hz), 2.99 (1H, dd, *J* = 14.2, 6.9 Hz), 3.23 (1H, dd, *J* = 14.2, 3.8 Hz), 4.76 and 4.82 (each 1H, each ddt, *J* = 12.6, 5.2, 1.2 Hz), 4.84 (1H, ddq, *J* = 6.9, 3.8, 1.0 Hz), 5.36 (1H, dq, *J* = 6.1, 1.2 Hz), 5.41 (1H, dq, *J* = 13.0, 1.2 Hz), 5.99 (1H, ddt, *J* = 13.0, 6.1, 5.2 Hz), 7.19-7.31 (5H, m); HRMS calcd for $C_{15}H_{16}O_3$: 244.1099. Found: 244.1073; $[\alpha]^{21}_D$ -50.3° (*c* 0.98, $CHCl_3$).

(3*S*,5*S*)-5-Benzyl-3-methyl-3-(2-propenyl)-2,4(3*H*,5*H*)-furandione (4b) IR ($CHCl_3$) 3006, 2905, 1798, 1755, 1640, 1600, 1376 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.55 (3H, s), 2.33 and 2.39 (each 1H, ddt-like, *J* = 13.5, 7.0, 1.0 Hz), 3.13 and 3.26 (each 1H, dd, *J* = 14.0, 4.3 Hz), 4.82 (1H, t, *J* = 4.3 Hz), 5.12 (1H, dq-like, *J* = 17.6, 1.0 Hz), 5.13 (1H, dm, *J* = 9.5 Hz), 5.61 (1H, ddt, *J* = 17.6, 9.5, 7.0 Hz), 7.15-7.32 (5H, m); HRMS calcd for $C_{15}H_{16}O_3$: 244.1099. Found: 244.1104; $[\alpha]^{21}_D$ -82.1° (*c* 1.12, $CHCl_3$).

(3*R*,5*S*)-5-Benzyl-3-methyl-3-(2-propenyl)-2,4(3*H*,5*H*)-furandione (5b) IR ($CHCl_3$) 3004, 2908, 1799, 1757, 1640, 1600, 1331 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.27 (3H, s), 1.96 and 2.03 (each 1H, each dtt-like, *J* = 14.4, 7.0, 1.0 Hz), 3.06 (1H, dd, *J* = 15.0, 6.5 Hz), 3.24 (1H, dd, *J* = 15.0, 4.1 Hz), 4.96 (1H, dd, *J* = 6.5, 4.1 Hz), 5.01 (1H, dq-like, *J* = 15.8, 1.0 Hz), 5.02 (1H, dm, *J* = 9.0 Hz), 5.41 (1H, ddt, *J* = 15.8, 9.0, 7.0 Hz), 7.20-7.34 (5H, m); HRMS calcd for $C_{15}H_{16}O_3$: 244.1099. Found: 244.1129.

(5*S*)-3-Methyl-4-(2-propenyloxy)-5-(2-propyl)-2(5*H*)-furanone (3c) IR ($CHCl_3$) 2995, 2991, 1742, 1663, 1394, 1316 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.81 and 1.10 (each 3H, each d, each *J* = 7.0 Hz), 1.96 (3H, d, *J* = 1.0 Hz), 2.15 (1H, heptet of d, *J* = 7.0, 3.0 Hz), 4.53 (1H, dq, *J* = 3.0, 1.0 Hz), 4.82 and 4.85 (each 1H, each ddt, each *J* = 13.2, 5.0, 1.2 Hz), 5.34 (1H, dq, *J* = 10.5, 1.2 Hz), 5.40 (1H, dq, *J* = 17.0, 1.2 Hz), 5.97 (1H, ddt, *J* = 17.0, 10.5, 5.0 Hz); HRMS calcd for $C_{11}H_{16}O_3$: 196.1099. Found: 196.1119; $[\alpha]^{20}_D$ -46.0° (*c* 1.00, $CHCl_3$).

(3*S*,5*S*)-3-Methyl-3-(2-propenyl)-5-(2-propyl)-2,4(3*H*,5*H*)-furandione (4c) IR ($CHCl_3$) 2965, 2910, 1796, 1753, 1640 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.93 and 1.10 (each 3H, each d, each *J* = 7.0 Hz), 1.27 (3H, s), 2.27 (1H, heptet of d, *J* = 7.0, 4.0 Hz), 2.46 (2H, ddt, *J* = 13.0, 8.0, 1.0 Hz), 4.39 (1H, d, *J* = 4.0 Hz), 5.16 (1H, dq-like, *J* = 16.9, 1.0 Hz), 5.17 (1H, dm, *J* = 9.2 Hz), 5.65 (1H, ddt, *J*

= 16.9, 9.2, 8.0 Hz); HRMS calcd for $C_{11}H_{16}O_3$: 196.1099. Found: 196.1127; $[\alpha]^{20}_D$ -102.4° (*c* 2.07, $CHCl_3$).

(3*R*,5*S*)-3-Methyl-3-(2-propenyl)-5-(2-propyl)-2,4(3*H*,5*H*)-furandione (5c) IR ($CHCl_3$) 2961, 1795, 1753, 1640, 1374, 1328, 1299 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.98 and 1.11 (each 3H, d, *J* = 7.0 Hz), 1.33 (3H, s), 2.23 (1H, heptet of d, *J* = 7.0, 5.6 Hz), 2.46 and 2.49 (each 1H, ddt-like, each *J* = 14.5, 7.5, 1.0 Hz), 4.50 (1H, d, *J* = 5.6 Hz), 5.13 (1H, dm, *J* = 10.0 Hz), 5.17 (1H, dq-like, *J* = 17.0, 1.0 Hz), 5.71 (1H, ddt, *J* = 17.0, 10.0, 7.5 Hz); HRMS calcd for $C_{11}H_{16}O_3$: 196.1099. Found: 196.1113.

Procedure B: To a stirred solution of the corresponding tetronic acid (2.0 mmol) in HMPA (2 mL) was added Ag_2O (280 mg, 1.2 mmol), and the resulting suspension was sonicated at 10 °C for 30 min. To the suspension was added allyl bromide (0.21 mL, 2.4 mmol), and the suspension was sonicated at 10 °C for 8 h. To the suspension was added benzene (60 mL), and the insoluble material was removed by filtration. The filtrate was washed with H_2O (5 mL x 2), and the organic layer was dried and evaporated to give a pale yellow oil, which was purified by column chromatography (hexane:acetone=50:1~10:1) to afford the allylated products.

(5*S*)-3,5-Dimethyl-4-(2-propenyloxy)-2(5*H*)-furanone (3a) The spectroscopic data were identical with those of the sample obtained from procedure A; $[\alpha]^{21}_D$ +2.35° (*c* 1.09, $CHCl_3$).

(3*S*,5*S*)-3,5-Dimethyl-3-(2-propenyl)-2,4(3*H*,5*H*)-furandione (4a) The spectroscopic data were identical with those of the sample obtained from procedure A; $[\alpha]^{21.5}_D$ -41.8° (*c* 1.10, $CHCl_3$).

(3*R*,5*S*)-3,5-Dimethyl-3-(2-propenyl)-2,4(3*H*,5*H*)-furandione (5a) The spectroscopic data were identical with those of the sample obtained from procedure A.

(2*S*)-2,4-Dimethyl-5-(2-propenyloxy)-3(2*H*)-furanone (6a) IR ($CHCl_3$) 2920, 1590, 1463, 1440, 1414, 1342, 1299, 1144, 966 cm^{-1}.

(5*S*)-5-Benzyl-3-methyl-4-(2-propenyloxy)-2(5*H*)-furanone (3b) The spectroscopic data were identical with those of the sample obtained from procedure A; $[\alpha]^{21}_D$ -50.9° (*c* 1.00, $CHCl_3$).

(3*S*,5*S*)-5-Benzyl-3-methyl-3-(2-propenyl)-2,4(3*H*,5*H*)-furandione (4b) The spectroscopic data were identical with those of the sample obtained from procedure A; $[\alpha]^{21}_D$ -103.8° (*c* 1.06, $CHCl_3$).

(3*R*,5*S*)-5-Benzyl-3-methyl-3-(2-propenyl)-2,4(3*H*,5*H*)-furandione (5b) The spectroscopic data were identical with those of the sample obtained from procedure A.

(2*S*)-2-Benzyl-4-methyl-5-(2-propenyloxy)-3(2*H*)-furanone (6b) IR ($CHCl_3$) 2997, 2991, 1594, 1468, 1437, 1415, 1340, 1144 cm^{-1}.

(5*S*)-3-Methyl-4-(2-propenyloxy)-5-(2-propyl)-2(5*H*)-furanone (3c) The spectroscopic data were identical with those of the sample obtained from procedure A; $[\alpha]^{21}_D$ -47.0° (*c* 1.00, $CHCl_3$).

(3*S*,5*S*)-3-Methyl-3-(2-propenyl)-5-(2-propyl)-2,4(3*H*,5*H*)-furandione (4c) The spectroscopic data were identical with those of the sample obtained from procedure A; $[\alpha]^{21}_D$ -106.7° (*c* 1.27, $CHCl_3$).

(3*R*,5*S*)-3-Methyl-3-(2-propenyl)-5-(2-propyl)-2,4(3*H*,5*H*)-furandione (5c) The spectroscopic data were identical with those of the sample obtained from procedure A.

(2*S*)-4-Methyl-5-(2-propenyloxy)-2-(2-propyl)-3(2*H*)-furanone (6c) IR ($CHCl_3$) 2950, 2905, 1591, 1467, 1437, 1415, 1341, 1148 cm^{-1}.

Procedure C: To a stirred solution of the corresponding tetronic acid (1.0 mmol) in DMF (2 mL) were added K_2CO_3 (73 mg, 0.53 mmol) and molecular sieves 4A (10 mg), and the resulting suspension was stirred at 0 °C for 30 min. To the suspension was added allyl bromide (0.1 mL, 1.2 mmol), and the suspension was stirred at 30 °C or -15 °C. To the suspension was added benzene (60 mL), and the insoluble material was removed by filtration. The filtrate was washed with H_2O (5 mL x 2), and the organic layer was dried and evaporated to give a pale yellow oil, which was purified with column chromatography (hexane:acetone=50:1~10:1) to afford the allylated products.

(5*S*)-3-Methyl-4-(2-propenyloxy)-5-(2-propyl)-2(5*H*)-furanone (3c) The spectroscopic data and optical rotation were identical with those of the sample obtained from procedure B.

(3*S*,5*S*)-3-Methyl-3-(2-propenyl)-5-(2-propyl)-2,4(3*H*,5*H*)-furandione (4c) The spectroscopic data and optical rotation were identical with those of the sample obtained from procedure B.

(3*R*,5*S*)-3-Methyl-3-(2-propenyl)-5-(2-propyl)-2,4(3*H*,5*H*)-furandione (5c) The spectroscopic data were identical with those of the sample obtained from procedure A.

(5*S*)-3-Phenyl-4-(2-propenyloxy)-5-(2-propyl)-2(5*H*)-furanone (3d) IR (neat) 1795, 1752, 1654 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.92 and 1.18 (each 3H, each d, each J = 6.8 Hz), 2.21-2.33 (1H, m), 4.47 (2H, d, J = 5.5 Hz), 4.75 (1H, d, J = 2.9 Hz), 5.14-5.26 (2H, m), 5.73-5.88 (1H, m), 7.30-7.48 (5H, m); HRMS calcd for $C_{16}H_{18}O_3$: 258.1256. Found: 258.1267; $[\alpha]^{26}_D$ -71.0° (*c* 0.91, $CHCl_3$).

(3*R*,5*S*)-3-Phenyl-3-(2-propenyl)-5-(2-propyl)-2,4(3*H*,5*H*)-furandione (4d) IR (neat) 1797, 1752, 1641 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.76 and 0.95 (each 3H, d, J = 6.8 Hz), 1.99 (1H, m), 2.82 and 2.92 (2H, ABq of d, J = 13.3, 7.1 Hz), 4.35 (1H, d, J = 5.4 Hz), 5.15-5.24 (2H, m), 5.62-5.77 (1H, m), 7.28-7.55 (5H, m); HRMS calcd for $C_{16}H_{18}O_3$: 258.1256. Found: 258.1255; $[\alpha]^{26}_D$ -169.5° (*c* 1.12, $CHCl_3$).

(3*S*,5*S*)-3-Phenyl-3-(2-propenyl)-5-(2-propyl)-2,4(3*H*,5*H*)-furandione (5d) IR (neat) 1798, 1754, 1642 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.96 and 1.11 (each 3H, d, J = 6.8 Hz), 2.29-2.36 (1H, m), 2.79 and 2.89 (2H, ABq of d, J = 13.9, 7.8 Hz), 4.49 (1H, d, J = 4.2 Hz), 5.08-5.22 (2H, m), 5.63-5.73 (1H, m), 7.26-7.43 (5H, m); HRMS calcd for $C_{16}H_{18}O_3$: 258.1256. Found: 258.1231; $[\alpha]^{26}_D$ -9.3° (*c* 0.15, $CHCl_3$).

(5*S*)-3-(4-Methoxyphenyl)-4-(2-propenyloxy)-5-(2-propyl)-2(5*H*)-furanone (3e) IR (neat) 2967, 1795, 1751, 1660, 1608, 1513 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.90 and 1.17 (each 3H, d, J = 6.8 Hz), 2.17-2.34 (1H, m), 3.82 (3H, s), 4.48 (1H, d, J = 5.4 Hz), 5.16-5.29 (2H, m), 5.74-5.88 (1H, m), 6.92 and 7.39 (each 2H, d, J = 8.8 Hz); HRMS calcd for $C_{17}H_{20}O_4$: 288.1362. Found: 288.1389; $[\alpha]^{26}_D$ -48.7° (*c* 1.32, $CHCl_3$).

(3*R*,5*S*)-3-(4-Mehthoxyphenyl)-3-(2-propenyl)-5-(2-propyl)-2,4(3*H*,5*H*)-furandione (4e) IR (neat) 2967, 1796, 1751, 1608, 1513 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.77 and 0.96 (each 3H, each d, each J = 6.8 Hz), 1.98 (1H, octet, J = 5.8 Hz), 2.78 and 2.87 (2H, ABq of d, J = 13.2, 7.8 Hz), 3.80 (3H, s), 5.15-5.22 (2H, m), 5.61-5.76 (1H, m), 6.89 and 7.43 (each 2H, each d, each J = 9.0 Hz); HRMS calcd for $C_{16}H_{18}O_3$: 288.1362. Found: 288.1385; $[\alpha]^{26}_D$ -144.7° (*c* 1.01, $CHCl_3$).

(3*S*,5*S*)-3-Phenyl-3-(2-propenyl)-5-(2-propyl)-2,4(3*H*,5*H*)-furandione (5e) IR (neat) 1798, 1754, 1642 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.96 and 1.11 (each 3H, each d, each J = 6.8 Hz), 2.29-2.36 (1H, m), 2.79 and 2.89 (2H, ABq of d, J = 13.9, 7.8 Hz), 4.49 (1H, d, J = 4.2 Hz), 5.08-5.22 (2H, m), 5.63-5.73 (1H, m), 7.26-7.43 (5H, m); HRMS calcd for $C_{16}H_{18}O_3$: 258.1256. Found: 258.1231; $[\alpha]^{26}_D$ -9.3° (*c* 0.15, $CHCl_3$).

General procedure for the Claisen rearrangement of the allyl tetronates (3a-c) The allyl tetronate was heated at 240 °C for 20 min, and the product was purified by column chromatography (hexane:acetone=50:1) to afford the *C*-allylated product. Spectroscopic properties (IR and ^1H NMR) and optical rotations were identical with those of the authentic sample obtained from the direct allylation (Procedure B or C).

General procedure for the alkylation of tetronic acids (1c-e) To a stirred solution of the corresponding tetronic acid (1.0 mmol) in DMF (2 mL) were added K_2CO_3 (69 mg, 0.5 mmol) and molecular sieves 4A (10 mg), and the resulting suspension was stirred at rt for 30 min. To the suspension was added alkyl halide (1.2 mmol), and the suspension was stirred at 30 °C. To the suspension was added benzene (60 mL), and the insoluble material was removed by filtration. The filtrate was washed with H_2O (5 mL x 2), and the organic layer was dried and evaporated to give a pale yellow oil, which was purified by column chromatography (hexane:acetone=50:1~10:1) to afford the allylated products.

(5*S*)-3-Methyl-4-phenylmethoxy-5-(2-propyl)-2(5*H*)-furanone (7a) IR (neat) 2967, 1748, 1667 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.67 and 0.95 (each 3H, each d, each J = 6.8 Hz), 2.00 (3H, s), 2.11-2.22 (1H, m), 4.57 (1H, d, J = 1.2 Hz), 5.34 and 5.39 (2H, ABq, J = 1.5 Hz), 7.33-7.42 (5H, m); HRMS calcd for $C_{15}H_{18}O_3$: 246.1254. Found: 246.1244; $[\alpha]^{26}_D$ -52.5° (*c* 1.22, $CHCl_3$).

(3*S*,5*S*)-3-Benzyl-3-methyl-5-(2-propyl)-2,4-(3*H*,5*H*)-furandione (8a) IR (neat) 2926, 2938, 1800, 1753 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.83 and 0.95 (each 3H, each d, each J = 6.8 Hz), 1.37 (3H, s), 2.06-2.18 (1H, m), 2.99 and 3.10 (2H, ABq, J = 2.9 Hz), 3.48 (1H, d, J = 3.9 Hz), 7.08-7.37 (5H, m); HRMS calcd for $C_{15}H_{18}O_3$: 246.1254. Found: 246.1266; $[\alpha]^{26}_D$ -101.3° (*c* 1.21, $CHCl_3$).

(5*S*)-4-Methoxy-3-phenyl-5-(2-propyl)-2(5*H*)-furanone (7b) IR (neat) 2966, 1748, 1660 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.90 and 1.17 (each 3H, each d, each J = 6.8 Hz), 2.20-2.31 (1H, m), 3.76 (3H, s), 4.73 (1H, d, J = 2.7 Hz), 7.31-7.46 (5H, m); HRMS calcd for $C_{14}H_{16}O_3$: 232.1100. Found: 232.1111; $[\alpha]^{26}_D$ -38.1° (*c* 2.70, $CHCl_3$).

(3*R*,5*S*)-3-Methyl-3-phenyl-5-(2-propyl)-2,4-(3*H*,5*H*)-furandione (8b) IR (neat) 2969, 1798, 1754, 1493 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.84 and 0.96 (each 3H, each d, each J = 6.6 Hz), 1.68 (3H, s), 1.87-2.00 (1H, m), 4.53 (1H, d, J = 6.1 Hz), 7.28-7.47 (5H, m); HRMS calcd for $C_{14}H_{16}O_3$: 232.1100. Found: 232.1097; $[\alpha]^{26}_D$ -156.0° (*c* 2.67, $CHCl_3$).

(3*S*,5*S*)-3-Methyl-3-phenyl-5-(2-propyl)-2,4-(3*H*,5*H*)-furandione (9b) IR (neat) 2969, 1798, 1754, 1447 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.97 and 1.14 (each 3H, each d, each J = 6.8 Hz), 1.62 (3H, s), 2.31-2.42 (1H, m), 4.66 (1H, d, J = 3.4 Hz), 7.31-7.39 (5H, m); HRMS calcd for $C_{14}H_{16}O_3$: 232.1100. Found: 232.1098; $[\alpha]^{26}_D$ -51.5° (*c* 0.46, $CHCl_3$).

(5*S*)-3-Phenyl-4-phenylmethoxy-5-(2-propyl)-2(5*H*)-furanone (7c) IR (neat) 2966, 2932, 1749, 1658 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.89 and 1.17 (each 3H, each d, each *J* = 6.8 Hz), 2.22-2.33 (1H, m), 4.74 (1H, d, *J* = 2.7 Hz), 4.98 (2H, s), 7.13-7.47 (10H, m); HRMS calcd for $C_{14}H_{16}O_3$: 232.1100. Found: 232.1098; $[\alpha]^{26}_D$ -10.9° (*c* 3.31, $CHCl_3$).

(3*R*,5*S*)-3-Benzyl-3-phenyl-5-(2-propyl)-2,4-(3*H*,5*H*)-furandione (8c) IR (neat) 2968, 1795, 1751 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.65 and 0.84 (each 3H, each d, each *J* = 6.8 Hz), 1.91 (1H, m), 3.37 and 3.50 (2H, ABq, *J* = 12.9 Hz), 3.65 (1H, d, *J* = 4.9 Hz), 7.19-7.65 (10H, m); HRMS calcd for $C_{14}H_{16}O_3$: 232.1100. Found: 232.1098; $[\alpha]^{26}_D$ -146.8° (*c* 1.67, $CHCl_3$).

(5*S*)-4-Methoxy-3-(4-methoxyphenyl)-5-(2-propyl)-2(5*H*)-furanone (7d) IR (neat) 2965, 1748, 1657, 1608, 1514 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.97 and 1.14 (each 3H, each d, each *J* = 6.8 Hz), 1.62 (3H, s), 2.31-2.42 (1H, m), 4.66 (1H, d, *J* = 3.4 Hz), 7.31-7.39 (5H, m); HRMS calcd for $C_{15}H_{18}O_4$: 262.1204. Found: 262.1178; $[\alpha]^{26}_D$ -41.3° (*c* 1.08, $CHCl_3$).

(3*R*,5*S*)-3-Methyl-3-(4-methoxyphenyl)-5-(2-propyl)-2,4-(3*H*,5*H*)-furandione (8d) IR (neat) 2968, 1792, 1751, 1608, 1513 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.84 and 0.96 (each 3H, d, *J* = 6.8 Hz), 1.87 (3H, s), 1.94 (1H, m), 3.80 (3H, s), 4.49 (1H, d, *J* = 6.3 Hz), 6.90 and 7.36 (each 2H, d, *J* = 8.9 Hz); HRMS calcd for $C_{15}H_{18}O_4$: 262.1204. Found: 262.1225; $[\alpha]^{26}_D$ -130.1° (*c* 1.70, $CHCl_3$).

(3*S*,5*S*)-3-Methyl-3-(4-methoxyphenyl)-5-(2-propyl)-2,4-(3*H*,5*H*)-furandione (9d) IR (neat) 2967, 1798, 1753, 1608, 1512 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.96 and 1.13 (each 3H, d, *J* = 6.8 Hz), 1.58 (3H, s), 2.33-2.40 (1H, m), 3.79 (3H, s), 4.66 (1H, d, *J* = 3.7 Hz), 6.89 and 7.30 (each 2H, d, *J* = 8.8 Hz); HRMS calcd for $C_{15}H_{18}O_4$: 262.1204. Found: 262.1171; $[\alpha]^{26}_D$ -67.7° (*c* 0.26, $CHCl_3$).

(5*S*)-3-(4-Methoxyphenyl)-4-phenylmethoxy-5-(2-propyl)-2-(5*H*)-furanone (7e) IR (neat) 2966, 1748, 1659, 1608, 1514 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.89 and 1.16 (each 3H, d, *J* = 6.8 Hz), 2.19-2.36 (1H, m), 3.82 (3H, s), 4.73 (1H, d, *J* = 2.9 Hz), 5.00 (2H, s), 6.93 and 7.40 (each 2H, d, *J* = 8.8 Hz), 7.14-7.39 (5H, m); HRMS calcd for $C_{21}H_{22}O_4$: 338.1519. Found: 338.1545; $[\alpha]^{26}_D$ -1.64° (*c* 1.23, $CHCl_3$).

(3*R*,5*S*)-3-(4-Methoxyphenyl)-3-benzyl-5-(2-propyl)-2,4-(3*H*,5*H*)-furandione (8e) IR (neat) 2967, 1794, 1750, 1510, 1256 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.67 and 0.86 (each 3H, each d, each *J* = 6.8 Hz), 1.89-1.96 (1H, m), 3.34 and 3.46 (2H, ABq, *J* = 13.2 Hz), 3.66 (1H, d, *J* = 4.9 Hz), 3.82 (3H, s), 6.92 and 7.56 (each 2H, each d, each *J* = 9.0 Hz), 7.18-7.37 (5H, m); HRMS calcd for $C_{21}H_{22}O_4$: 338.1519. Found: 338.1519; $[\alpha]^{26}_D$ -132.2° (*c* 1.51, $CHCl_3$).

General procedure for the Michael reaction of tetronic acids (1c) and (1e) To a stirred solution of the corresponding tetronic acid (1.0 mmol) in THF (2 mL) were added Et_3N (0.14 mL, 1.0 mmol) and α,β-unsaturated compound (2.0 mmol), and the resulting solution was stirred at rt for 5~24 h. The solvent was removed, and the residue was purified by column chromatography (hexane:acetone=8:1~5:1) to afford the products.

(3*S*,5*S*)-3-[2-(1,3-Dioxolan-2-yl)ethyl]-3-methyl-5-(2-propyl)-2,4-(3*H*,5*H*)-furandione (10a) IR (neat) 2880, 1797, 1753, 1224, 1141, 1031 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.96 and 1.11 (each 3H, each d, each *J* = 7.0 Hz), 1.28 (3H, s), 1.58-1.74 (2H, m), 1.88 (2H, t, *J* = 7.8 Hz), 2.17-2.35 (1H, m),

3.79-3.97 (4H, m), 4.52 (1H, d, J = 4.4 Hz), 4.81 (1H, t, J = 4.2 Hz); HRMS calcd for $C_{21}H_{22}O_4$: 338.1519. Found: 338.1519; $[\alpha]^{26}_D$ -110.9° (*c* 1.25, $CHCl_3$).

(3*R*,5*S*)-3-[2-(1,3-Dioxolan-2-yl)ethyl]-3-methyl-5-(2-propyl)-2,4-(3*H*,5*H*)-furandione (11a) IR (neat) 2968, 1798, 1754 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.00 and 1.13 (each 3H, each d, each J = 6.8 Hz), 1.34 (3H, s), 1.66-1.73 (2H, m), 1.84-1.91 (2H, m), 2.16-2.33 (1H, m), 3.81-3.97 (4H, m), 4.52 (1H, d, J = 5.4 Hz), 4.84 (1H, t, J = 4.4 Hz); HRMS calcd for $C_{21}H_{22}O_4$: 338.1519. Found: 338.1519; $[\alpha]^{26}_D$ -57.8° (*c* 0.41, $CHCl_3$).

(3*S*,5*S*)-3-Methyl-3-(3-oxobutyl)-5-(2-propyl)-2,4-(3*H*,5*H*)-furandione (10b) IR (neat) 2969, 1795, 1752, 1717, 1094, 1006 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.94 and 1.11 (each 3H, d, J = 6.8 Hz), 1.26 (3H, s), 2.00 (3H, t, J = 7.5 Hz), 2.14 (3H, s), 2.20-2.31 (1H, m), 2.51-2.57 (2H, m), 4.62 (1H, d, J = 4.4 Hz); HRMS calcd for $C_{21}H_{22}O_4$: 338.1519. Found: 338.1519; $[\alpha]^{26}_D$ -112.2° (*c* 1.55, $CHCl_3$).

(3*R*,5*S*)-3-Methyl-3-(3-oxobutyl)-5-(2-propyl)-2,4-(3*H*,5*H*)-furandione (11b) IR (neat) 2970, 1795, 1751, 1718, 1105 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.10 and 1.13 (each 3H, each d, each J = 6.8 Hz), 1.33 (3H, s), 1.93-2.02 (2H, m), 2.15 (3H, s), 2.22-2.32 (1H, m), 2.51-2.59 (2H, m), 4.54 (1H, d, J = 5.4 Hz); HRMS calcd for $C_{21}H_{22}O_4$: 338.1519. Found: 338.1519; $[\alpha]^{26}_D$ -55.5° (*c* 0.56, $CHCl_3$).

(3*R*,5*S*)-3-(2-Formylethyl)-3-(4-methoxyphenyl)-5-(2-propyl)-2,4-(3*H*,5*H*)-furandione (10c) IR (neat) 2892, 1792, 1751, 1579, 1220, 1132 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.98 and 1.13 (each 3H, each d, each J = 6.8 Hz), 2.19-2.47 (2H, m), 2.59-2.69 (1H, m), 3.80 (3H, s), 4.57 (1H, d, J = 3.7 Hz), 6.90 and 7.30 (each 2H, each d, each J = 8.8 Hz); HRMS calcd for $C_{21}H_{22}O_4$: 338.1519. Found: 338.1519; $[\alpha]^{26}_D$ -55.5° (*c* 0.56, $CHCl_3$).

(3*R*,5*S*)-3-(4-Methoxyphenyl)-3-(3-oxobutyl)-5-(2-propyl)-2,4-(3*H*,5*H*)-furandione (10d) IR (neat) 1796, 1748, 1715, 1580 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.78 and 0.94 (each 3H, each d, each J = 7.0 Hz), 1.83-1.98 (1H, m), 2.08 (3H, s), 2.26-2.47 (3H, m), 2.55-2.69 (1H, m), 3.80 (3H, s), 4.50 (1H, d, J = 6.0 Hz), 6.89 and 7.37 (each 2H, each d, each J = 9.0 Hz); HRMS calcd for $C_{18}H_{22}O_5$: 318.1467. Found: 318.1447; $[\alpha]^{26}_D$ -136.8° (*c* 0.89, $CHCl_3$).

(3*S*,5*S*)-3-(4-Methoxyphenyl)-3-(3-oxobutyl)-5-(2-propyl)-2,4-(3*H*,5*H*)-furandione (11d) IR (neat) 2968, 1791, 1747, 1714, 1514, 1187 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.98 and 1.13 (each 3H, each d, each J = 7.0 Hz), 2.09 (3H, s), 2.14-2.43 (4H, m), 2.55-2.68 (1H, m), 3.80 (3H, s), 4.55 (1H, d, J = 4.0 Hz), 6.90 and 7.29 (each 2H, each d, each J = 9.0 Hz); HRMS calcd for $C_{18}H_{22}O_5$: 318.1467. Found: 318.1447; $[\alpha]^{26}_D$ -15.7° (*c* 0.90, $CHCl_3$).

(4*R*,6*S*)-5,6-Dihydroxy-4-hydroxymethyl-4,7-dimethyloctanal ethylene acetal (12) To a stirred solution of **10a** (441.7 mg, 2.08 mmol) in benzene (20 mL) were added ethylene glycol (0.23 mL, 4.16 mmol) and *p*-TsOH•H_2O (46.5 mg, 0.021 mmol), and the resulting mixture was refluxed for 50 min. After cooling, the reaction was quenched with satd $NaHCO_3$ (10 mL), and the organic layer was separated. The aqueous layer was extracted with benzene (15 mL x 3), and the organic layer and extracts were combined, dried, and evaporated to give a colorless oil, which was used directly in the next step.

To a stirred suspension of $LiAlH_4$ (150.6 mg, 3.96 mmol) in THF (20 mL) was added a solution of the acetal obtained above (502.2 mg, 1.96 mmol) in THF (15 mL) at 0 °C, and the resulting suspension was stirred at rt for 30 min and then refluxed for 5 h. After cooling, to the suspension was added 10 % NaOH (4 mL), and the insoluble material was filtered through a celite pad. The filtrate was dried and evaporated to give a colorless oil, which was purified by column chromatography ($CHCl_3$:EtOH=40:1~30:1) to afford a mixture of the diastereoisomers (6:1) of **12** (506.1 mg, 93% combined yield) as a colorless solid, mp 71.5-72.5 °C for major alcohol and mp 67.5-68.5 °C for minor alcohol, respectively. Major alcohol; IR (nujol) 3350, 2950, 1130 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.97 (3H, s), 0.91 and 1.01 (each 3H, each d, each J = 7.0 Hz), 1.50-1.81 (4H, br m), 2.15 (1H, heptet, J = 7.0 Hz), 2.38 (1H, d, J = 6.0 Hz), 3.40 (1H, dd, J = 8.5, 6.9 Hz), 3.58 (2H, s), 3.62 (1H, dd, J = 8.5, 2.5 Hz), 3.84-4.02 (4H, m), 4.88 (1H, t-like, J = 4.5 Hz); Anal. Calcd for $C_{13}H_{26}O_5$: C, 59.2; H, 9.99. Found: C, 59.67; H, 9.69; $[\alpha]^{26}_D$ -9.9° (*c* 0.94, $CHCl_3$).

Minor alcohol; IR (nujol) 3400, 2950, 1130 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.85 (3H, s), 0.92 and 1.00 (each 3H, each d, each J = 7.0 Hz), 1.24-1.36 (1H, m), 1.58-1.74 (3H, m), 1.79 (1H, heptet, J = 7.0 Hz), 2.20 (1H, br), 3.29 and 3.37 (2H, ABq, J = 8.0 Hz), 3.30 (1H, br), 3.47 (1H, d, J = 7.0 Hz), 3.60 (1H, m), 3.84-4.02 (5H, m), 4.87 (1H, t-like, J = 4.5 Hz); Anal. Calcd for $C_{13}H_{26}O_5$: C, 59.2; H, 9.99. Found: C, 59.40; H, 9.69; $[\alpha]^{26}_D$ +12.3° (*c* 1.84, $CHCl_3$).

(4*R*,6*S*)-4-(*tert*-Butyldiphenylsilyloxymethyl)-5,6-dihydroxy-4,7-dimethyloctanal ethylene acetal (13) To a stirred solution of **12** (683 mg, 2.61 mmol) in CH_2Cl_2 (10 mL) were added Et_3N (0.55 mL, 3.91 mmol), DMAP (31.8 mg, 0.26 mmol) and TBDPSCl (0.82 mL, 2.78 mmol) at 0 °C, and the resulting mixture was stirred at rt for 3 h. To the mixture was added Et_2O (30 mL), and the insoluble material was filtered through a celite pad. The filtrate was evaporated to give a pale yellow oil, which was purified by column chromatography (hexane:EtOAc=30:1~5:1) to afford **13** (1.11 g, 86%) as a colorless oil. IR (neat) 3500, 3060, 1595, 1110 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.91 and 0.99 (each 3H, each d, each J = 7.0 Hz), 0.92 (3H, s), 1.08 (9H, s), 1.35-1.83 (4H, br m), 2.17-2.27 (1H, m), 3.16 (1H, d, J = 6.0 Hz), 3.47 (1H, dd, J = 8.0, 6.0 Hz), 3.58 (1H, br), 3.61 (2H, s), 3.81-3.97 (4H, m), 4.81 (1H, t-like, J = 4.5 Hz), 7.37-7.46 (6H, m), 7.63-7.67 (4H, m).

(2*R*)-2-(*tert*-Butyldiphenylsilyloxymethyl)-2-methylpentanedial 5-ethylene acetal (14) To a stirred solution of **13** (601.4 mg, 1.20 mmol) in dioxane (12 mL) and H_2O (1.5 mL) was added $NaIO_4$ (462 mg, 2.16 mmol) at 0 °C, and the resulting suspension was stirred for 6 h at rt. To the reaction mixture were added H_2O (10 mL) and 10% $Na_2S_2O_3$ in satd $NaHCO_3$ (5 mL), and the aqueous mixture was extracted with CH_2Cl_2 (20 mL x 3). The organic extracts were combined, dried, and evaporated to give a colorless oil, which was purified by column chromatography (hexane:EtOAc=10:1~5:1) to afford **14** (247.5 mg, 48%) along with the starting diol (290.9 mg, 48%) as a colorless oil, respectively. IR (neat) 3070, 2700, 1730, 1590, 1150 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.04 (9H, s), 1.07 (3H, s), 1.48-1.76 (4H, m), 3.59 and 3.72 (2H, ABq, J = 10.0 Hz), 3.82-3.97 (4H, m), 4.82 (1H, t-like, J = 4.0 Hz), 7.35-7.44 (6H, m), 7.60-7.64 (4H, m), 9.57 (1H, s); Anal. Calcd for $C_{13}H_{26}O_5$: C, 59.2; H, 9.99. Found: C, 59.40; H, 9.69; $[\alpha]^{26}_D$ +2.54° (*c* 0.89, $CHCl_3$).

(4*R*)-4-(*tert*-Butyldiphenylsilyloxymethyl)-4-methyl-5-oxoheptanal ethylene acetal (15) To a stirred solution of **14** (200.8 mg, 0.47 mmol) in THF (3 mL) was added EtMgBr (0.71 mL, 1.01 M in THF) at 0 °C, and the reaction mixture was stirred at rt for 3 h. The reaction was quenched with satd NH_4Cl (1.5 mL), and the aqueous layer was extracted with CH_2Cl_2 (10 mL x 6). The combined CH_2Cl_2 layer was dried and evaporated to give a colorless oil, which was used directly in the next step. To a stirred solution of oxalyl chloride (0.04 mL, 0.42 mmol) in CH_2Cl_2 (3 mL) was added DMSO (0.065 mL, 0.85 mmol) at -78 °C, and the reaction mixture was stirred at -78 °C for 10 min. To the mixture was added a solution of the oil obtained above in CH_2Cl_2 (3 mL) at -78 °C, and the stirring was continued at -78 °C for 40 min. To the mixture was added Et_3N (0.19 mL, 1.26 mmol) at -78 °C, and the reaction temperature was gradually increased to rt for 1 h. To the resulting suspension was added Et_2O (20 mL), and the insoluble material was removed by filtration. The filtrate was washed with H_2O (2 mL x 2), dried, and evaporated to give a pale yellow oil, which was purified by column chromatography (hexane:EtOAc=10:1~5:1) to afford **15** (130 mg, 61%) as a colorless oil. IR (neat) 3071, 1707, 1589, 1112 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.02 (3H, s), 1.03 (9H, s), 1.18 (3H, s), 1.48-1.55 (4H, m), 1.68-1.82 (1H, m), 2.48 and 2.53 (each 1H, each d, each *J* = 10.0 Hz), 3.81-3.95 (4H, m), 4.78 (1H, t-like, *J* = 4.0 Hz), 7.34-7.46 (6H, m), 7.58-7.63 (4H, m); HRMS calcd for $C_{27}H_{36}O_4Si$: 454.2537 Found: 454.2514; $[\alpha]^{26}_D$ +2.66° (*c* 0.97, $CHCl_3$).

(6*R*)-4-(*tert*-Butyldiphenylsilyloxymethyl)-2,6-dimethyl-2-cyclohexenone (16) To a stirred solution of **15** (142 mg, 0.31 mmol) in acetone (20 mL) was added *p*-TsOH• H_2O (23 mg, 0.12 mmol) at 0 °C, and the resulting mixture was refluxed for 18 h. After cooling, satd $NaHCO_3$ (6 mL) was added to the reaction mixture, and the volatiles were removed. The residue was extracted with CH_2Cl_2 (20 mL x 3), and the combined CH_2Cl_2 layer was dried and evaporated to give a colorless oil, which was used directly in the next step.

To a stirred solution of the oil obtained above in THF (20 mL) was added KOH (45 mg, 0.94 mmol) in H_2O (2 mL) at 0 °C, and the resulting mixture was refluxed for 7 h. After cooling, the aqueous layer was extracted with CH_2Cl_2 (20 mL x 3), and the combined CH_2Cl_2 layer was dried and evaporated to give a colorless oil, which was purified by column chromatography (hexane:EtOAc=50:1) to afford **16** (118.3 mg, 92%) as a colorless oil. IR (neat) 3071, 1668, 1589 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.03 (9H, s), 1.08 (3H, s), 1.76 (3H, d-like, *J* = 1.5 Hz), 1.77-1.86 (1H, m), 2.21-2.37 (3H, m), 3.50 (1H, d, J = 9.5 Hz), 3.87 (1H, d, *J* = 9.5 Hz), 6.66 (1H, br), 7.35-7.42 (6H, m), 7.61-7.79 (4H, m); HRMS calcd for $C_{25}H_{32}O_2Si$: 392.2169 Found: 392.2138; $[\alpha]^{26}_D$ -15.2° (*c* 1.00, $CHCl_3$), $[\alpha]^{26}_D$ -23.8° (*c* 1.00, MeOH), lit.,[7b] $[\alpha]^{24}_D$ -23.6° (*c* 1.80, MeOH).

(1*S*,3*S*)-6,6-Ethylenedioxy-2-hydroxy-3-hydroxymethyl-3-(4-methoxyphenyl)-1-(2-propyl)heptanol (17) To a stirred solution of **10d** (632 mg, 1.99 mmol) in benzene (30 mL) were added ethylene glycol (0.17 mL, 3.05 mmol) and *p*-TsOH•H_2O (38 mg, 0.20 mmol), and the mixture was refluxed for 30 min using the Dean-Stark apparatus. After cooling, satd $NaHCO_3$ (10 mL) was added, and the organic layer was separated. The aqueous layer was extracted with CH_2Cl_2 (10 mL x 3), and the organic layer and extracts were combined, dried, and evaporated to give a colorless oil, which was used directly in the next step.

To a suspension of $LiAlH_4$ (151.2 mg, 3.98 mmol) in THF (40 mL) was added a solution of the oil obtained above in THF (20 mL) at 0 °C, and the resulting suspension was refluxed for 4.5 h. After cooling, aqueous 10% NaOH solution was added to the suspension at 0 °C, and the insoluble material was removed by filtration. The filtrate was dried and evaporated to give a colorless oil, which was purified by column chromatography ($CHCl_3$:EtOH=30:1) to afford a mixture of the diastereoisomers of **17** (714.4 mg, 98%) as a colorless oil. IR (neat) 3405, 1611, 1465 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.83 and 0.90 (each 3H, each d, each J = 7.0 Hz), 1.31 (3H, s), 1.50 (2H, t, J = 7.5 Hz), 1.62-1.77 (1H, m), 1.81-1.95 (1H, m), 1.98-2.11 (1H, m), 2.95 (1H, d, J = 5.0 Hz), 3.42 (1H, t. J = 6.5 Hz), 3.73 (1H, d, J = 5.0 Hz), 3.79 (3H, s), 3.85-4.00 (4H, m), 4.28 (1H, d, J = 11.5 Hz), 6.88 and 7.20 (each 2H, each d, each J = 9.0 Hz).

(1*S*,3*S*)-3-(*tert*-Butyldimethylsilyloxymethyl)-6,6-ethylenedioxy-2-hydroxy-3-(4-methoxyphenyl)-1-(2-propyl)heptanol (18) To a stirred solution of **17** (1.07 g, 2.9 mmol) in CH_2Cl_2 (8 mL) were added TBSCl (525 mg, 3,49 mmol), Et_3N (0.73 mL, 5.22 mmol) and DMAP (35.4 mg, 0.29 mmol) at 0 °C, and the resulting mixture was stirred at rt for 15 h. To the mixture was added CH_2Cl_2 (100 mL), and the organic layer was washed with H_2O (10 mL x 2), dried, and evaporated to give a pale yellow oil, which was purified by column chromatography (hexane:EtOAc=50:1) to afford **18** (1.4 g, 99%) as a colorless oil. IR (neat) 3446, 2955, 1610, 1514, 1057 cm^{-1}.

(2*S*)-2-(*tert*-Butyldimethylsilyloxymethyl)-5,5-ethylenedioxy-2-(4-methoxyphenyl)-hexanal (19) To a stirred solution of **18** (52.4 mg, 0.11 mmol) in benzene (2 mL) was added $Pb(OAc)_4$ (108.4 mg, 0.22 mmol), and the resulting suspension was stirred at rt for 5 min. To the suspension were added CH_2Cl_2 (20 mL) and 10% $Na_2S_2O_3$ in satd $NaHCO_3$ (6 mL), and the organic layer was separated. The aqueous layer was extracted with CH_2Cl_2 (10 mL x 3), and the organic layer and extracts were combined, dried, and evaporated to give a pale yellow oil, which was purified by column chromatography (hexane:EtOAc=50:1) to afford **19** (39.4 mg, 89%) as a colorless solid (mp 57.0-57.5 °C). IR (KBr) 3068, 2821, 1721 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.02 (6H, s), 0.84 (9H, s), 1.29 (3H, s), 1.33-1.55 (2H, m), 1.98-2.18 (2H, m), 3.80 (3H, s), 3.81-3.94 (4H, m), 3.93 (1H, d, J = 10.0 Hz), 4.18 (1H, d, J = 10.0 Hz), 6.88 (2H, d, J = 7.0 Hz), 7.10 (2H, d, J = 7.0 Hz), 9.55 (1H, s); HRMS calcd for $C_{22}H_{36}O_5Si$: 408.2332 Found: 408.2344; $[\alpha]^{26}_D$ +36.3° (*c* 1.55, $CHCl_3$).

Methyl (4*S*)-(2*E*)-4-(*tert*-butyldimethylsilyloxymethyl)-7,7-ethylenedioxy-4-(4-methoxyphenyl)-2-octenoate (20) To a stirred solution of **19** (322.5 mg, 0.79 mmol) in benzene (7 mL) was added methyl (triphenylphosphoranylidene)acetate (1.06 g, 3.17 mmol), and the resulting suspension was refluxed for 18 h. After cooling, the solvent was removed, and the residue was purified by column chromatography (hexane:acetone=30:1~20:1) to afford **20** (343.1 mg, 94%) as a colorless oil. IR (neat) 2952, 1725, 1513, 1007 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.02 (6H, s), 0.84 (9H, s), 1.29 (3H, s), 1.44-1.54 (2H, m), 1.92-2.03 (2H, m), 3.73 (3H, s), 3.79 (3H, s), 3.82-3.97 (6H, m), 5.85 (1H, d, J = 16.0 Hz), 6.83 (2H, d, J = 9.0 Hz), 7.13 (1H, d, J = 16.0 Hz), 7.16 (2H, d, J = 7.0 Hz); HRMS calcd for $C_{25}H_{40}O_6Si$: 464.2592 Found: 464.2591; $[\alpha]^{26}_D$ +6.1° (*c* 1.16, $CHCl_3$).

(3*S*)-3-(*tert*-Butyldimethylsilyloxymethyl)-6,6-ethylenedioxy-3-(4-methoxyphenyl)-*N*-(phenylmethoxycarbonyl)heptanamine (21) To a stirred solution of **20** (400 mg, 0.86 mmol) in

MeOH (10 mL) was added 5% Pd-C (100 mg), and the resulting suspension was stirred at rt for 2 h under a hydrogen atmosphere. The catalyst was filtered through a celite pad, and the filtrate was evaporated to give a colorless oil, which was used directly in the next step.

To a stirred solution of the oil obtained above in MeOH (12 mL) was added a solution of KOH (227.7 mg, 3.45 mmol) in H_2O (4 mL), and the resulting mixture was stirred at 45 °C for 2 h. After cooling, 10% HCl was added to the mixture at 0 °C, and MeOH was removed. The aqueous layer was extracted with $CHCl_3$ (20 mL x 3), and the organic extracts were combined, dried, and evaporated to give a colorless oil, which was used directly in the next step.

To a stirred solution of the oil obtained above in toluene (6 mL) were added Et_3N (0.14 mL, 1.01 mmol) and DPPA (0.22 mL, 1.02 mmol), and the resulting mixture was heated at 80 °C for 1 h. To the mixture was added benzyl alcohol (0.13 mL, 1.26 mmol), and the reaction mixture was refluxed for 16 h. After cooling, the solvent was removed, and the residue was purified by column chromatography (hexane:acetone=20:1~10:1) to afford **21** (389 mg, 81%) as a colorless oil. IR (neat) 3348, 3033, 1713, 1515 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.02 (6H, s), 0.86 (9H, s), 1.26 (3H, s), 1.33-1.45 (2H, m), 1.72-1.83 (2H, m), 1.87-1.96 (2H, m), 3.03-3.14 (2H, m), 3.66-3.92 (6H, m), 3.77 (3H, s), 4.78 (1H, br), 5.04 (2H, s), 6.83 (2H, d, J = 9.0 Hz), 7.14 (2H, d, J = 9.0 Hz), 7.32 (5H, s); Anal. Calcd for $C_{31}H_{47}NO_6Si$: C, 66.75; H, 8.49; N, 2.51 Found: C, 66.20; H, 8.17; N, 2.96; $[\alpha]^{26}_D$ +1.81° (*c* 2.77, $CHCl_3$).

(3*S*)-3-(*tert*-Butyldimethylsilyloxymethyl)-6,6-ethylenedioxy-3-(4-methoxyphenyl)-*N*-methyl-*N*-(phenylmetoxycarbonyl)heptanamine To a stirred suspension of 60% NaH (35 mg, 0.88 mmol) in benzene (0.5 mL) was added a solution of **21** (82.8 mg, 0.15 mmol) in benzene (1 mL) and DMF (0.1 mL) at 0 °C, and the resulting suspension was stirred at rt for 10 min. To the suspension was added MeI (0.094 mL, 1.51 mmol), and the suspension was stirred at rt for 2 h. To the suspension were added CH_2Cl_2 (10 mL) and 3% HCl, and the organic layer was separated. The aqueous layer was extracted with CH_2Cl_2 (5 mL x 3), the organic layer and extracts were combined, dried, and evaporated to give a pale yellow oil, which was purified by column chromatography (hexane:acetone=20:1) to afford the urethane (72.2 mg, 85%) as a colorless oil. IR (neat) 1704, 1039 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.02 (6H, s), 0.87 (9H, s), 1.24 (3H, s), 1.28 (3H, s), 1.33-1.46 (2H, m), 1.69-1.98 (4H, br m), 2.81 and 2.85 (each 3H, s), 2.95-3.23 (2H, m), 3.64-3.92 (6H, m), 3.76 (3H, s), 5.08 and 5.09 (each 2H, s), 6.71 and 6.85 (each 1H, d, J = 9.0 Hz), 7.10 and 7.22 (each 1H, d, J = 9.0 Hz), 7.29 (5H, s); Anal. Calcd for $C_{32}H_{49}NO_6Si$: C, 67.21; H, 8.64; N, 2.45 Found: C, 67.16; H, 8.44; N, 2.91; $[\alpha]^{26}_D$ +6.5° (*c* 1.31, $CHCl_3$).

(2*S*)-5,5-Ethylenedioxy-{2-[*N*-methyl-*N*-(phenylmethoxycarbonyl)]amino}ethyl-2-(4-methoxyphenyl)hexanal ethylene acetal (22) To a stirred solution of the silyl ether obtained above (220.9 mg, 0.39 mmol) in THF (2 mL) was added TBAF (0.47 mL, 1M in THF) at 0 °C, and the resulting mixture was stirred at rt for 3 h. To the mixture were added CH_2Cl_2 (50 mL) and H_2O (5 mL), and the organic layer was separated. The aqueous layer was extracted with CH_2Cl_2 (5 mL x 3), and the organic layer and extracts were combined, dried, and evaporated to give a colorless oil, which was purified by column chromatography (hexane:acetone=10:1~5:1) to afford the alcohol (159.5 mg, 90%) as

a colorless oil. To a stirred solution of oxalyl chloride (0.05 mL, 0.53 mmol) in CH_2Cl_2 (1.5 mL) was added DMSO (0.08 mL, 1.05 mmol) at -78 °C, and the reaction mixture was stirred at -78 °C for 5 min. To the mixture was added a solution of the alcohol obtained above (159.5 mg, 0.35 mmol) in CH_2Cl_2 (2 mL) at -78 °C, and the mixture was stirred at -78 °C for 30 min. To the mixture was added Et_3N (0.25 mL, 1.6 mmol) at -78 °C, and the reaction temperature was gradually increased to 0 °C. To the resulting suspension was added Et_2O (60 mL), and the insoluble material was removed by filtration. The filtrate was washed with H_2O (2 mL x 2), and the organic layer was dried and evaporated to give a pale yellow oil, which was used directly in the next step.

To a stirred solution of the aldehyde obtained above in benzene (10 mL) were added ethylene glycol (0.04 mL, 0.7 mmol) and *p*-TsOH•H_2O (6.7 mg, 0.035 mmol), and the mixture was refluxed for 30 min using the Dean-stark apparatus. After cooling, satd $NaHCO_3$ (6 mL) was added, and the organic layer was separated. The aqueous layer was extracted with CH_2Cl_2 (10 mL x 3), and the organic layer and extracts were combined, dried, and evaporated to give a pale yellow oil, which was purified by column chromatography (hexane:acetone=15:1) to afford **22** (162.9 mg, 94%) as a colorless oil. IR (neat) 1694, 1514, 857, 832 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.25 and 1.32 (each 3H, each s), 1.47-1.72 (2H, m), 1.81-2.15 (6H, m), 2.90 (3H, s), 3.15-3.44 (2H, m), 3.77 (3H, s), 3.64-3.98 (8H, br m), 4.90 and 4.96 (each 2H, each s), 5.11 (2H, s), 6.75 and 6.86 (each 2H, each d, each J = 9.0 Hz), 7.25-7.45 (5H, m); HRMS calcd for $C_{28}H_{37}NO_7$: 499.2568. Found: 499.2531; $[\alpha]^{26}_D$ -0.02° (*c* 1.70, $CHCl_3$).

(-)-*O*-Methyljoubertiamine To a stirred suspension of $LiAlH_4$ (30 mg, 0.79 mmol) in THF (4 mL) was added a solution of **22** (50 mg, 0.1 mmol) in THF (2 mL) at 0 °C, and the resulting suspension was stirred at rt for 14 h. To the suspension was added 10% NaOH solution at 0 °C, and the insoluble material was filtered through a celite pad. The filtrate was evaporated to give a colorless oil, which was used directly in the next step.

To the amine obtained above was added 10% HCl (0.5 mL), and the mixture was stirred at 50 °C for 8 h. After cooling, the aqueous solution was washed with Et_2O (5 mL x 2). To the resulting mixture were added THF (4 mL) and 10% NaOH solution (1 mL), and the resulting solution was stirred at rt for 3 h. The THF was removed by evaporation, and the aqueous layer was extracted with $CHCl_3$ (10 mL x 4), and combined $CHCl_3$ layer was dried and evaporated to give a colorless oil, which was purified by column chromatography (Al_2O_3, hexane:$CHCl_3$=5:1) to afford (-)-*O*-methyljoubertiamine (18 mg, 66%) as a colorless oil. IR (neat) 1684 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.94-2.34 (4H, m), 2.17 (6H, s), 3.81 (3H, s), 6.15 (1H, d, J = 10.0 Hz), 6.88 and 7.21 (each 2H, each d, each J = 9.0 Hz), 7.12 (1H, d, J = 10.0 Hz); HRMS calcd for $C_{17}H_{23}NO_2$: 273.1727. Found: 273.1719; $[\alpha]^{26}_D$ -51.2° (*c* 0.34, $CHCl_3$); $[\alpha]^{26}_D$ -65.3° (*c* 0.34, MeOH); lit.,[8c] $[\alpha]^{26}_D$ -50.3° (*c* 0.003, $CHCl_3$), lit.,[8b] $[\alpha]^{26}_D$ -68.4° (*c* 1.40, MeOH); lit.,[8a] $[\alpha]^{25}_D$ -51° (*c* 1.45, MeOH)..

(2'*S*)-2'-(*tert*-Butyldimethylsilyloxymethyl)-5',5'-ethylenedioxy-2'-(4-methoxyphenyl)heptyl 2,2-dimethylpropanoate (23) To a stirred solution of **17** (123 mg, 0.33 mmol) in CH_2Cl_2 (2 mL) were added pivaloyl chloride (0.045 mL, 0.37 mmol) and pyridine (0.04 mL, 0.5 mmol) at 0 °C, and the resulting suspension was stirred at rt for 16 h. To the mixture were added CH_2Cl_2 (20 mL) and H_2O (2 mL), and the organic layer was separated. The aqueous layer was extracted

with CH_2Cl_2 (5 mL x 2), and the organic layer and extracts were combined, dried, and evaporated to give a pale yellow oil, which was used directly in the next step.

To a stirred solution of the oil obtained above in benzene (7 mL) was added $Pb(OAc)_4$ (329 mg, 0.67 mmol) at 0 °C, and the resulting suspension was stirred at rt for 10 min. To the suspension were added 10% $Na_2S_2O_3$ in satd $NaHCO_3$ (10 mL) and CH_2Cl_2 (10 mL), and the organic layer was separated. The aqueous layer was extracted with CH_2Cl_2 (20 mL x 2), and the organic layer and extracts were combined, dried, and evaporated to give a colorless oil, which was used directly in the next step.

To a stirred solution of the aldehyde obtained above in MeOH (5 mL) was added $NaBH_4$ (6.6 mg, 0.17 mmol) at 0 °C, and the mixture was stirred at 0 °C for 20 min. To the mixture was added 5% HCl, and MeOH was removed by evaporation. The residue was extracted with CH_2Cl_2 (10 mL x 5), and the organic extracts were combined, dried, and evaporated to give a colorless oil, which was used directly in the next step.

To a stirred solution of the alcohol obtained above in CH_2Cl_2 (5 mL) were added TBSCl (231 mg, 1.53 mmol), Et_3N (0.29 mL, 2.06 mmol) and DMAP (4.5 mg, 0.036 mmol) at 0 °C, and the mixture was refluxed for 18 h. After cooling, Et_2O (50 mL) and H_2O (5 mL) were added to the reaction mixture, and the organic layer was separated, dried, and evaporated to give a pale yellow oil, which was purified by column chromatography (hexane:acetone=50:1) to afford **23** (111.3 mg, 66%) as a colorless oil. IR (neat) 1684 cm^{-1}; ^1H NMR ($CDCl_3$) δ -0.03 and 0.00 (each 3H, each s), 0.85 (9H, s), 1.10 (9H, s), 1.26 (3H, s), 1.34-1.44 (2H, m), 1.69-1.90 (2H, m), 3.70-3.91 (6H, m), 3.78 (3H, s), 4.24 and 4.32 (2H, ABq, J = 10.5 Hz), 6.82 and 7.13 (each 2H, each d, each J = 9.0 Hz); HRMS calcd for $C_{17}H_{23}NO_2$: 273.1727. Found: 273.1719; $[\alpha]^{26}_D$ -9.6° (*c* 0.91, $CHCl_3$).

(2*R*)-2-(*tert*-Butyldimethylsilyloxymethyl)-5,5-ethylenedioxy-2-(4-methoxyphenyl)-hexanal (19) To a stirred solution of **23** (61.3 mg, 0.12 mmol) in THF (2 mL) was added $LiEt_3BH$ (0.15 mL, 1M in THF, 0.149 mmol) at 0 °C, and the reaction mixture was stirred at rt for 30 min. To the mixture were added H_2O (5 mL) and CH_2Cl_2 (30 mL), and the organic layer was separated. The aqueous layer was extracted with CH_2Cl_2 (10 mL x 5), and the organic layer and extracts were combined, dried, and evaporated to give a colorless oil, which was used directly in the next step.

To a stirred solution of oxalyl chloride (0.016 mL, 0.19 mmol) in CH_2Cl_2 (1 mL) was added DMSO (0.027 mL, 0.38 mmol) at -78 °C, and the resulting mixture was stirred at -78 °C for 10 min. To the mixture was added a solution of the alcohol obtained above in CH_2Cl_2 (1 mL) at -78 °C, and the stirring was continued at -78 °C for 30 min. To the mixture was added Et_3N (0.08 mL, 0.56 mmol) at -78 °C, and the reaction temperature was gradually increased to 0 °C. To the resulting suspension was added Et_2O (30 mL), and the insoluble material was removed by filtration. The filtrate was washed with H_2O (5 mL x 2), and the organic layer was dried and evaporated to give a pale yellow oil, which was purified by column chromatography (hexane:EtOAc=50:1) to afford (-)-**19** (19 mg, 37%) as a colorless solid (mp 55.0-56.0 °C). The spectroscopic properties (IR, ^1H NMR and MS) of (-)-**19** were good accordance with those of (+)-**19**; $[\alpha]^{26}_D$ -35.6° (*c* 0.95, $CHCl_3$).

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REFERENCES AND NOTES

1. The previous paper entitled "Di-π-methane rearrangement of the α-substituted 4-benzylfuran-2(5*H*)-one system" [O. Muraoka, G. Tanabe, M. Higashiura, T. Minematsu, and T. Momose, *J. Chem. Soc. Perkin Trans., 1*, **1995**, 1437] constitutes Part VI of this series.
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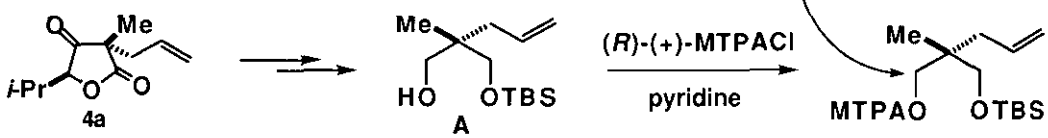
10. The enantiomeric excess of the *C*-allyl product (**4a**) obtained from procedure C was determined by the ^{1}H NMR spectrum of the MTPA ester of the alcohol (A) derived from **4a**.

4.17 and **4.20** (each d) for racemic compound derived from dimethyl methylmalonate
4.17 (d) only for optically pure compound derived from **4a** by procedure C



11. The enantiomeric excess of the *C*-allyl products (**4a**), (**4b**), and (**4c**) obtained from procedure B or Claisen rearrangement of corresponding allyl tetronates **3a-c** was comfirmed by the comparison of the optical rotations with those of **4a-c** obtained from procedure C (see experimental section).

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