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

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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 due to the presence of multifunctionality in the molecule. Previously, we have demonstrated the efficient preparation of 1 (R1, R2 = 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 (+)-cassiol7 and enantiodivergent synthesis of O-methyljoubertiamine8 were accomplished.

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 reaction9 as shown below.
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

<table>
<thead>
<tr>
<th>Entry</th>
<th>R1</th>
<th>R2</th>
<th>Temp (°C)</th>
<th>Time (h)</th>
<th>Yield (%)</th>
<th>Diastereomeric excess (%)</th>
</tr>
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<tbody>
<tr>
<td>1a</td>
<td>Me</td>
<td>Me</td>
<td>80</td>
<td>4</td>
<td>31(3a)</td>
<td>22(4a) 18(5a)</td>
</tr>
<tr>
<td>2b</td>
<td>Me</td>
<td>Me</td>
<td>10</td>
<td>8</td>
<td>42(3a)</td>
<td>29(4a) 8(5a)</td>
</tr>
<tr>
<td>3a</td>
<td>Bn</td>
<td>Me</td>
<td>80</td>
<td>4</td>
<td>28(3b)</td>
<td>33(4b) 16(5b)</td>
</tr>
<tr>
<td>4b</td>
<td>Bn</td>
<td>Me</td>
<td>10</td>
<td>8</td>
<td>39(3b)</td>
<td>30(4b) 5(5b)</td>
</tr>
<tr>
<td>5a</td>
<td>i-Pr</td>
<td>Me</td>
<td>80</td>
<td>4</td>
<td>26(3c)</td>
<td>39(4c) 13(5c)</td>
</tr>
<tr>
<td>6c</td>
<td>i-Pr</td>
<td>Me</td>
<td>30</td>
<td>11</td>
<td>29(3c)</td>
<td>61(4c) 3(5c)</td>
</tr>
<tr>
<td>7c</td>
<td>i-Pr</td>
<td>Me</td>
<td>-15</td>
<td>48</td>
<td>25(3c)</td>
<td>73(4c) 1(5c)</td>
</tr>
<tr>
<td>8b</td>
<td>i-Pr</td>
<td>Me</td>
<td>10</td>
<td>8</td>
<td>39(3c)</td>
<td>42(4c) 2(5c)</td>
</tr>
<tr>
<td>9c</td>
<td>i-Pr</td>
<td>Ph</td>
<td>30</td>
<td>15</td>
<td>14(3d)</td>
<td>77(4d) 2(5d)</td>
</tr>
<tr>
<td>10c</td>
<td>i-Pr</td>
<td>Ph</td>
<td>-5</td>
<td>284</td>
<td>12(3d)</td>
<td>73(4d) 1(5d)</td>
</tr>
<tr>
<td>11c</td>
<td>i-Pr</td>
<td>p-MeOC6H4</td>
<td>30</td>
<td>24</td>
<td>16(3e)</td>
<td>78(4e) 3(5e)</td>
</tr>
<tr>
<td>12c</td>
<td>i-Pr</td>
<td>p-MeOC6H4</td>
<td>-15</td>
<td>240</td>
<td>11(3e)</td>
<td>85(4e) 1(5e)</td>
</tr>
</tbody>
</table>

Reactions were conducted as follows: a; Procedure A: tetronic acid (1 mmol), DMF (1 mL), K2CO3 (0.6 mmol), allyl bromide (1.2 mmol); b; Procedure B: tetronic acid (2 mmol), HMPA (2 mL), Ag2O (1.2 mmol), allyl bromide (2.4 mmol); c; Procedure C: tetronic acid (1 mmol), DMF (2 mL), K2CO3 (0.53 mmol), molecular sieves 4A (10 mg). d: The stereochemistry of the major C-allyl product (R1 = i-Pr, R2 = Me) was assigned to be 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 Ag2O instead of K2CO3 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 tetroxides (3) proceeded smoothly to give the ketones (4) and (5), and the results are summarized in Table 2.

Table 2: Claisen rearrangement of allyl tetroxides

<table>
<thead>
<tr>
<th>R⁺</th>
<th>R⁻</th>
<th>Yield (%)&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Me</td>
<td>Me(3a)</td>
<td>56(4a) 14(5a)</td>
</tr>
<tr>
<td>Bn</td>
<td>Me(3b)</td>
<td>56(4b) 18(5b)</td>
</tr>
<tr>
<td>i-Pr</td>
<td>Me(3c)</td>
<td>58(4c) 7(5c)</td>
</tr>
</tbody>
</table>

<sup>a</sup> Yields of 4 and 5 were isolated ones, respectively.

In the above rearrangement, no racemization at the γ-position of the rearranged products (4a-e) was observed again. In this way, the selective allylation at the α-position of α-substituted tetroxides was achieved by the direct allylation and the Claisen rearrangement of the allyl tetroxide. Thus, the chirality of L-amino acids was efficiently transferred into the α-position of the α-substituted β-tetroxides 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 tetroxides

<table>
<thead>
<tr>
<th>R&lt;sup&gt;1&lt;/sup&gt;</th>
<th>R&lt;sup&gt;2&lt;/sup&gt;</th>
<th>Time (h)</th>
<th>Yield (%)&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Diastereomeric excess (% de)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Me(1c)</td>
<td>Bn</td>
<td>7</td>
<td>32(7a)</td>
<td>65(8a)</td>
</tr>
<tr>
<td>Ph(1d)</td>
<td>Me</td>
<td>24</td>
<td>25(7b)</td>
<td>63(8b)</td>
</tr>
<tr>
<td>Ph(1d)</td>
<td>Bn</td>
<td>20</td>
<td>22(7c)</td>
<td>75(8c)</td>
</tr>
<tr>
<td>p-MeOC₆H₄(1e)</td>
<td>Me</td>
<td>36</td>
<td>24(7d)</td>
<td>70(8d)</td>
</tr>
<tr>
<td>p-MeOC₆H₄(1e)</td>
<td>Bn</td>
<td>36</td>
<td>19(7e)</td>
<td>78.6(8e)</td>
</tr>
</tbody>
</table>

<sup>a</sup> Ratio of 8 and 9 was determined by the integration of the C₅-methine proton of the <sup>1</sup>H NMR spectrum of the crude products. <sup>b</sup> 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

<table>
<thead>
<tr>
<th>R¹</th>
<th>R²</th>
<th>Temp (°C)</th>
<th>Time (h)</th>
<th>Yield (%)</th>
<th>Diastereomeric excess (%) de</th>
</tr>
</thead>
<tbody>
<tr>
<td>Me(1c) CHO</td>
<td>0</td>
<td>5</td>
<td>96(10a)</td>
<td>1(11a)</td>
<td>97</td>
</tr>
<tr>
<td>Me(1c) COMe</td>
<td>30</td>
<td>11</td>
<td>96(10b)</td>
<td>3(11b)</td>
<td>94</td>
</tr>
<tr>
<td>Me(1c) CO₂Me</td>
<td>30</td>
<td>24</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Me(1c) CN</td>
<td>30</td>
<td>24</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>p-MeOC₆H₄(1e) CHO</td>
<td>0</td>
<td>24</td>
<td>41(10c)</td>
<td>5(11c)b</td>
<td>78</td>
</tr>
<tr>
<td>p-MeOC₆H₄(1e) COMe</td>
<td>30</td>
<td>24</td>
<td>90(10d)</td>
<td>8(11d)</td>
<td>84</td>
</tr>
<tr>
<td>p-MeOC₆H₄(1e) CO₂Me</td>
<td>30</td>
<td>24</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>p-MeOC₆H₄(1e) CN</td>
<td>30</td>
<td>24</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
</tbody>
</table>

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 C₅-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 (Et₃N, 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-methyljoubertamine, and the synthetic schemes are shown below.

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.\textsuperscript{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 tetaacetate 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\textsuperscript{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 ([α]\textsuperscript{25}D -51.2° CHCl\textsubscript{3}; the value reported for the enantiomer: [α]\textsuperscript{25}D +50.3°, CHCl\textsubscript{3}, \textsuperscript{8c} [α]\textsuperscript{22}D -68.4°, MeOH\textsuperscript{8b}) in 66% yield, which was identical in its \textsuperscript{1}H-NMR and MS spectra with those reported.\textsuperscript{8}

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 \( \alpha,\gamma \)-disubstituted tetronic acids in detail, and selective alkylation at the \( \alpha \)-position was achieved by direct alkylation and the Claisen rearrangement of allyl tetronate. Furthermore, the Michael reaction of the acids as another carbon-chain homologation was accomplished, and the formal synthesis of \((+)-\)cassiol and the enantidivergent synthesis of \(O\)-methyljoubertiamine was achieved by utilizing this homologation reaction of \(1\) at the \(\alpha\)-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 \(\text{MgSO}_4\) unless otherwise specified.

**Methyl (\(2S\))-2-(2-bromopropanoyloxy)propanoate** (2a) To a stirred solution of methyl \((S)-(-)\)-lactate (2.5 g, 24 mmol) in \(\text{Et}_2\text{O}\) (40 mL) were added \(\text{Et}_3\text{N}\) (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 \(\text{Et}_2\text{O}\) (150 mL), and the insoluble material was filtered through a celite pad. The filtrate was washed with satd \(\text{NaHCO}_3\) (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 (CHCl3) \(2990, 2950, 1750, 1270, 1150\) cm\(^{-1}\); \(^1 \)H NMR (CDCl3) \(\delta 1.54\) and \(1.55\) (each 0.5H and 2SH, 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 (\(2S\))-2-(2-bromopropanoyloxy)-3-phenylpropanoate** (2b) To a stirred solution of 2-hydroxy-3-phenylpropanoic acid\(^{15}\) (7.15 g, 43.1 mmol) in MeOH (70 mL) was added conc \(\text{H}_2\text{SO}_4\) (0.2 mL), and the resulting solution was refluxed for 3.5 h. After cooling, the reaction mixture was diluted with \(\text{CH}_2\text{Cl}_2\) (180 mL), and the organic layer was washed with 5% \(\text{NaHCO}_3\) (60 mL). The aqueous layer was extracted with \(\text{CH}_2\text{Cl}_2\) (60 mL \(\times\) 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 (CHCl3) 3529, 3022, 2990, 1737, 1211, 1092 cm\(^{-1}\); \(^1 \)H NMR (CDCl3) \(\delta 2.72\) (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); \(|\alpha|\text{D}^-6.0^\circ\) (c 1.08, CHCl3).

To a stirred solution of the ester obtained above (3.73 g, 20.7 mmol) in \(\text{Et}_2\text{O}\) (45 mL) were added \(\text{Et}_3\text{N}\) (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 \(\text{Et}_2\text{O}\) (100 mL), and the insoluble material was
filtered through a celite pad. The filtrate was washed with satd NaHCO₃ (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 (CHCl₃) 3030, 2950, 2930, 1750, 1600, 1120, 1080 cm⁻¹; ¹H NMR (CDCl₃) 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 (2S)-2-(2-bromopropanoxy)-3-methylbutanoate (2c)** To a stirred solution of 2-hydroxy-3-methylbutanoic acid¹⁴ (1.25 g, 10.6 mmol) in MeOH (10 mL) was added conc H₂SO₄ (0.05 mL), and the resulting solution was refluxed for 3.5 h. After cooling, the reaction mixture was diluted with CH₂Cl₂ (90 mL), and the organic layer was washed with 5% NaHCO₃ (30 mL). The aqueous layer was extracted with CH₂Cl₂ (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 (CHCl₃) 3526, 2961, 2910, 1731, 1209, 1105 cm⁻¹; ¹H NMR (CDCl₃) 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); [α]¹⁶D +27.2° (c 1.14, CHCl₃).

To a stirred solution of the ester obtained above (1.73 g, 13.1 mmol) in Et₂O (15 mL) were added Et₃N (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 Et₂O (100 mL), and the insoluble material was filtered through a celite pad. The filtrate was washed with satd NaHCO₃ (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 (CHCl₃) 2987, 2960, 1740, 1254, 1157, 1061 cm⁻¹; ¹H NMR (CDCl₃) 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 (2S)-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 Et₂O (200 mL) were added Et₃N (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 NaHCO₃ (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 (CDCl₃) 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); [α]²⁶D -34.4° (c 2.33, CHCl₃).
To a stirred solution of the ester obtained above (4.23 g, 16.9 mmol) in CCl₄ (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% Na₂S₂O₃ in satd NaHCO₃ (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 (CHCl₃) 2984, 2963, 1742, 1232, 1129, 1061 cm⁻¹; ¹H NMR (CDCl₃) 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 (IH, m), 3.80 (3H, s), 4.93 (IH, d, J = 4.5 Hz), 5.47 (1H, s), 7.31 (5H, s).

Methyl (2S)-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 Et₂O (400 mL) were added Et₃N (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 NaHCO₃ (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=20:1) 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 CCl₄ (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% Na₂S₂O₃ in satd NaHCO₃ (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 (CDCl₃) δ 0.95 (3H, d, J = 7.0 Hz), 0.98 (1.5H, d, J = 7.0 Hz), 2.16-2.36 (IH, m), 3.69 and 3.74 (each 3H, 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 CHCl₃, and the CHCl₃ layer was extracted with 5% K₂CO₃. The basic aqueous layer was acidified with 5% HCl, and the resulting aqueous layer was extracted with CHCl₃. The combined CHCl₃ layer was dried and evaporated to give the corresponding tetronic acids (1a-c), which were purified by recrystallization.

(5S)-4-Hydroxy-3,5-dimethyl-2(5H)-furanone (1a) yield; 35%; mp; 129-130.5 °C (benzene); IR (CHCl₃) 3110, 2980, 2720, 1729, 1665 cm⁻¹; ¹H NMR (CDCl₃) 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 C₅H₈O₃: C, 56.24; H, 6.29; [α]D +24.0° (c 1.04, CHCl₃).

(5S)-5-Benzyl-4-hydroxy-3-methyl-2(5H)-furanone (1b) yield; 20%; mp; 177.5-180 °C (ethyl acetate); IR (KBr) 3108, 2980, 2720, 1723, 1656 cm⁻¹; ¹H NMR (DMSO-d₆) 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; [α]_{D}^{18} -56.0° (c 1.00, CHCl_3).

(5S)-4-Hydroxy-3-methyl-5-(2-propyl)-2(5H)-furanone (1c) yield; 44%; mp; 116-118 °C (cyclohexane:benzene=3:1); IR (CHCl_3) 3110, 2963, 2720, 1725, 1658 cm⁻¹; ¹H NMR (CDCl_3) 6 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_{9}H_{12}O_3: C, 61.52; H, 7.74. Found: C, 61.28; H, 7.66; [α]_{D}^{18} -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% K₂CO₃. 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.

(5S)-4-Hydroxy-3-phenyl-5-(2-propyl)-2(5H)-furanone (1d) yield; 38%; mp; 136-137 °C (isopropyl ether); IR (KBr) 2967, 2933, 2714, 1702, 1632, 1501 cm⁻¹; ¹H NMR (CDCl_3) 6 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; [α]_{D}^{18} -72.6° (c 2.37, CHCl_3).

(5S)-4-Hydroxy-3-(4-methoxyphenyl)-5-(2-propyl)-2(5H)-furanone (1e) yield; 43%; mp; 166.5-167.5 °C (ethyl acetate); IR (KBr) 1796, 1748, 1715, 1580 cm⁻¹; ¹H NMR (CDCl_3) 6 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; [α]_{D}^{18} -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 K₂CO₃ (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 H₂O (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.

(5S)-3,5-Dimethyl-4-(2-propenyl-oxy)-2(5H)-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 C₉H₁₂O₃: 168.0787. Found: 168.0771; [α]_{D}^{21} +2.38° (c 1.47, CHCl_3).
(3S,5S)-3,5-Dimethyl-3-(2-propenyl)-2,4(3H,5H)-furandione (4a) IR (CHCl₃) 2990, 2915, 1798, 1756, 1640, 1068 cm⁻¹; ¹H NMR (CDCl₃) 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, 1.0 Hz), 5.66 (1H, dddd, J = 15.5, 10.5, 8.0, 7.1 Hz); HRMS calcd for C₉H₁₂O₃: 168.0787. Found: 168.0801; [α]D²¹⁺ = 37.3° (c 1.10, CHCl₃).

(3R,5S)-3,5-Dimethyl-3-(2-propenyl)-2,4(3H,5H)-furandione (5a) IR (CHCl₃) 2990, 2905, 1798, 1757, 1640, 1078 cm⁻¹; ¹H NMR (CDCl₃) 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 = 10.5 Hz), 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 C₉H₁₂O₃: 168.0787. Found: 168.0785.

(5S)-5-Benzyl-3-methyl-4-(2-propenyl)oxy)-2(5H)-furanone (3b) IR (CHCl₃) 2999, 2915, 1746, 1665, 1600, 1395, 1312 cm⁻¹; ¹H NMR (CDCl₃) 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, 12.0 Hz), 5.99 (1H, ddt, J = 13.0, 6.1, 5.2 Hz), 7.19-7.31 (5H, m); HRMS calcd for C₁₅H₁₆O₃: 244.1099. Found: 244.1073; [α]D²¹⁺ - 50.3° (c 0.98, CHCl₃).

(3S,5S)-5-Benzyl-3-methyl-3-(2-propenyl)-2,4(3H,5H)-furandione (4b) IR (CHCl₃) 3006, 2905, 1798, 1755, 1640, 1600, 1376 cm⁻¹; ¹H NMR (CDCl₃) 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 C₁₅H₁₆O₃: 244.1099. Found: 244.1104; [α]D²¹⁺ - 82.1° (c 1.12, CHCl₃).

(3R,5S)-5-Benzyl-3-methyl-3-(2-propenyl)-2,4(3H,5H)-furandione (5b) IR (CHCl₃) 3004, 2908, 1799, 1757, 1640, 1600, 1331 cm⁻¹; ¹H NMR (CDCl₃) 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 C₁₅H₁₆O₃: 244.1099. Found: 244.1129.

(5S)-3-Methyl-4-(2-propenyl)-5-(2-propyl)-2(5H)-furanone (3c) IR (CHCl₃) 2995, 2991, 1742, 1663, 1394, 1316 cm⁻¹; ¹H NMR (CDCl₃) 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 C₁₁H₁₆O₃: 196.1099. Found: 196.1119; [α]D²⁰⁺ - 46.0° (c 1.00, CHCl₃).

(3S,5S)-3-Methyl-3-(2-propenyl)-5-(2-propyl)-2,4(3H,5H)-furandione (4c) IR (CHCl₃) 2965, 2910, 1796, 1753, 1640 cm⁻¹; ¹H NMR (CDCl₃) 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
(3S,5S)-3-Methyl-3-(2-propenyl)-5-(2-propyl)-2,4(3H,5H)-furandione (5c) IR (CHCl₃) ν 2961, 1795, 1753, 1640, 1374, 1328, 1299 cm⁻¹; ¹H NMR (CDCl₃) 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), 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 C₁₁H₁₆O₃: 196.1099. Found: 196.1127.

Procedure B: To a stirred solution of the corresponding tetronic acid (2.0 mmol) in HMPA (2 mL) was added Ag₂O (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 H₂O (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.

(3S)-3,5-Dimethyl-4-(2-propenyl)-2(5H)-furanone (3a) The spectroscopic data were identical with those of the sample obtained from procedure A; [α]²¹D +2.35° (c 1.09, CHCl₃).

(3S,5S)-3,5-Dimethyl-3-(2-propenyl)-2,4(3H,5H)-furandione (4a) The spectroscopic data were identical with those of the sample obtained from procedure A; [α]²¹D -41.8° (c 1.10, CHCl₃).

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

(2S)-2,4-Dimethyl-5-(2-propenyl)-3(2H)-furanone (6a) IR (CHCl₃) ν 2920, 1590, 1463, 1440, 1414, 1342, 1299, 1144, 966 cm⁻¹.

(5S)-5-Benzyl-3-methyl-4-(2-propenyl)-2(5H)-furanone (3b) The spectroscopic data were identical with those of the sample obtained from procedure A; [α]²¹D -50.9° (c 1.00, CHCl₃).

(3S,5S)-5-Benzyl-3-methyl-3-(2-propenyl)-2,4(3H,5H)-furandione (4b) The spectroscopic data were identical with those of the sample obtained from procedure A; [α]²¹D -103.8° (c 1.06, CHCl₃).

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

(2S)-2-Benzyl-4-methyl-3-(2-propenyl)-3(2H)-furanone (6b) IR (CHCl₃) ν 2997, 2991, 1594, 1468, 1437, 1415, 1340, 1144 cm⁻¹.

(5S)-3-Methyl-4-(2-propenyl)-5-(2-propyl)-2(5H)-furanone (3c) The spectroscopic data were identical with those of the sample obtained from procedure A; [α]²¹D -47.0° (c 1.00, CHCl₃).

(3S,5S)-3-Methyl-3-(2-propenyl)-5-(2-propyl)-2,4(3H,5H)-furandione (4c) The spectroscopic data were identical with those of the sample obtained from procedure A; [α]²¹D -106.7° (c 1.27, CHCl₃).

(3R,5S)-3-Methyl-3-(2-propenyl)-5-(2-propyl)-2,4(3H,5H)-furandione (5c) The spectroscopic data were identical with those of the sample obtained from procedure A.
(2S)-4-Methyl-5-(2-propenyl)-2-(2-propyl)-3(2H)-furanone (6c) IR (CHCl₃) 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 K₂CO₃ (73 mg, 0.53 mmol) and molecular sieves 4Å (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 H₂O (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.

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

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

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

(5S)-3-Phenyl-4-(2-propenyl)-5-(2-propyl)-2(5H)-furanone (3d) IR (neat) 1795, 1752, 1654 cm⁻¹; ¹H NMR (CDCl₃) 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 C₁₆H₁₈O₃: 258.1256. Found: 258.1267; [α]D25 -110° (c 0.91, CHCl₃).

(3R,5S)-3-Phenyl-3-(2-propenyl)-5-(2-propyl)-2,4(3H,5H)-furandione (4d) IR (neat) 1797, 1752, 1641 cm⁻¹; ¹H NMR (CDCl₃) 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 C₁₆H₁₈O₃: 258.1256. Found: 258.1255; [α]D25 -169.5° (c 1.12, CHCl₃).

(3S,5S)-3-Phenyl-3-(2-propenyl)-5-(2-propyl)-2,4(3H,5H)-furandione (5d) IR (neat) 1798, 1754, 1642 cm⁻¹; ¹H NMR (CDCl₃) 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 C₁₆H₁₈O₃: 258.1256. Found: 258.1231; [α]D25 -9.3° (c 0.15, CHCl₃).

(5S)-3-(4-Methoxyphenyl)-4-(2-propenyl)-5-(2-propyl)-2(5H)-furanone (3e) IR (neat) 2967, 1795, 1751, 1660, 1608, 1513 cm⁻¹; ¹H NMR (CDCl₃) 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 C₁₇H₂₀O₄: 288.1362. Found: 288.1389; [α]D25 -48.7° (c 1.32, CHCl₃).

(3R,5S)-3-(4-Methoxyphenyl)-3-(2-propenyl)-5-(2-propyl)-2,4(3H,5H)-furandione (4e) IR (neat) 2967, 1796, 1751, 1608, 1513 cm⁻¹; ¹H NMR (CDCl₃) 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 C₁₆H₁₈O₃: 288.1362. Found: 288.1385; [α]D25 -144.7° (c 1.01, CHCl₃).
(3S,5S)-3-Phenyl-3-(2-propenyl)-5-(2-propyl)-2,4(3H,5H)-furandione (5e) IR (neat) 1798, 1754, 1642 cm⁻¹; ¹H NMR (CDCl₃) 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 C₁₆H₁₈O₃: 258.1256. Found: 258.1231; [α]₂₆⁰ ~ -9.3° (c 0.15, CHCl₃).

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 K₂CO₃ (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 H₂O (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:l) to afford the allylated products.

(3S,5S)-3-Methyl-4-phenylmethoxy-5-(2-propyl)-2(5H)-furanone (7a) IR (neat) 2967, 1748, 1667 cm⁻¹; ¹H NMR (CDCl₃) 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 C₁₅H₁₈O₃: 246.1254. Found: 246.1244; [α]₂₆⁰ ~ -52.5° (c 1.22, CHCl₃).

(3R,5S)-3-Methyl-3-phenyl-5-(2-propyl)-2,4-(3H,5H)-furandione (8b) IR (neat) 2969, 1798, 1754, 1493 cm⁻¹; ¹H NMR (CDCl₃) δ 0.84 and 0.96 (each 3H, each d, each J = 6.8 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 C₁₄H₁₆O₃: 232.1101. Found: 232.1111; [α]₂₆⁰ ~ -38.1° (c 2.70, CHCl₃).

(3S,5S)-3-Methyl-3-phenyl-5-(2-propyl)-2,4-(3H,5H)-furandione (9b) IR (neat) 2969, 1798, 1754, 1447 cm⁻¹; ¹H NMR (CDCl₃) 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 C₁₄H₁₆O₃: 232.1100. Found: 232.1098; [α]₂₆⁰ ~ -51.5° (c 0.46, CHCl₃).
The solvent was removed, and the residue was purified by column chromatography to afford the products.

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 Et₃N (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.
extracts were combined, dried, and evaporated to give a colorless oil, which was used directly in the next step.

After cooling, the reaction was quenched with satd NaHCO₃ solution of p-TsOH-H₂O (46.5 mg, 0.021 mmol), and the resulting mixture was refluxed for 50 min. After cooling, the reaction was quenched with satd NaHCO₃ (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 LiAlH₄ (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 (CHCl₃: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) 3500, 3060, 1595, 1130 cm⁻¹;¹H NMR (CDCl₃) 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 C₁₃H₂₆O₅: C, 59.2; H, 9.99. Found: C, 59.67; H, 9.69; [α]D²⁰ -9.9° (c 0.94, CHCl₃).

Minor alcohol; IR (nujol) 3400, 2950, 1130 cm⁻¹;¹H NMR (CDCl₃) 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 C₁₃H₂₆O₅: C, 59.2; H, 9.99. Found: C, 59.40; H, 9.69; [α]D²⁰ +12.3° (c 1.84, CHCl₃).

(4R,6S)-4-(tert-Butyldiphenylsilyloxyethyl)-5,6-dihydroxy-4,7-dimethyloctanal ethylene acetal (13) To a stirred solution of 12 (683 mg, 2.61 mmol) in CH₂Cl₂ (10 mL) were added Et₃N (0.55 mL, 3.91 mmol), DMAP (31.8 mg, 0.26 mmol) and TBDPSCI (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 Et₂O (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 (CDCl₃) 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).

(2R)-2-(tert-Butyldiphenylsilyloxyethyl)-2-methylpentanedial 5-ethylene acetal (14) To a stirred solution of 13 (601.4 mg, 1.20 mmol) in dioxane (12 mL) and H₂O (1.5 mL) was added NaIO₄ (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 H₂O (10 mL) and 10% Na₂S₂O₃ in satd NaHCO₃ (5 mL), and the aqueous mixture was extracted with CH₂Cl₂ (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 (CDCl₃) 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 C₁₃H₂₆O₅: C, 59.2; H, 9.99. Found: C, 59.40; H, 9.69; [α]D²⁰ +2.54° (c 0.89, CHCl₃).
(4R)-4-(tert-Butyldiphenylsiloxymethyl)-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 NH4Cl (1.5 mL), and the aqueous layer was separated. The organic layer was extracted with CH2Cl2 (10 mL x 6). The combined CH2Cl2 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 CH2Cl2 (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 CH2Cl2 (3 mL) at -78 °C, and the stirring was continued at -78 °C for 40 min. To the mixture was added Et3N (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 Et2O (20 mL), and the insoluble material was removed by filtration. The filtrate was washed with H2O (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, 1668, 1589 cm⁻¹; ¹H NMR (CDCl₃) 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 C27H36O4Si: 454.2537 Found: 454.2514; [α]²⁶D +2.66° (c 0.97, CHCl₃).

(6R)-4-(tert-Butyldiphenylsiloxymethyl)-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·H2O (23 mg, 0.12 mmol) at 0 °C, and the resulting mixture was refluxed for 18 h. After cooling, satd NaHCO₃ (6 mL) was added to the reaction mixture, and the volatiles were removed. The residue was extracted with CH2Cl2 (20 mL x 3), and the combined CH2Cl2 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 H2O (2 mL) at 0 °C, and the resulting mixture was refluxed for 7 h. After cooling, the aqueous layer was extracted with CH2Cl2 (20 mL x 3), and the combined CH2Cl2 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 (CDCl₃) 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 C25H32O2Si: 392.2169 Found: 392.2138; [α]²⁶D -15.2° (c 1.00, CHCl₃), [α]²⁶D -23.8° (c 1.00, MeOH), lit.,[b] [α]²⁴D -23.6° (c 1.80, MeOH).

(1S,3S)-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·H2O (38 mg, 0.20 mmol), and the mixture was refluxed for 30 min using the Dean-Stark apparatus. After cooling, satd NaHCO₃ (10 mL) was added, and the organic layer was separated. The aqueous layer was extracted with CH2Cl2 (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 LiAlH₄ (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 (CHCl₃:EtOH=30:1) to afford a mixture of the diastereoisomers of 17 (714.4 mg, 98%) as a colorless oil. IR (neat) 3446, 2955, 1610, 1514, 1057 cm⁻¹; ¹H NMR (CDCl₃) 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).

(IS,3S)-3-(tert-Butyldimethylsilyloxyethyl)-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 CH₂Cl₂ (8 mL) were added TBSCI (525 mg, 3.49 mmol), Et₃N (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 CH₂Cl₂ (100 mL), and the organic layer was washed with H₂O (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) 3405, 1611, 1465 cm⁻¹; ¹H NMR (CDCl₃) δ 0.90 (each 3H, each d, each J = 9.0 Hz), 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).

(2S)-2-((tert-Butyldimethylsilyloxyethyl)-5,5-ethylenedioxy-2-(4-methoxyphenyl)-hexanol (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 CH₂Cl₂ (20 mL) and 10% Na₂S₂O₃ in satd NaHCO₃ (6 mL), and the organic layer was separated. The aqueous layer was extracted with CH₂Cl₂ (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, 2965, 1610, 1514, 1057 cm⁻¹; ¹H NMR (CDCl₃) δ 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 C₂₂H₃₀O₅Si: 408.2332 Found: 408.2344; [α]Dⁿ +36.3° (c 1.55, CHCl₃).

Methyl (4S)-(2E)-4-((tert-butyldimethylsilyloxyethyl)-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) to afford 20 (343.1 mg, 94%) as a colorless oil. IR (neat) 3052, 2925, 1513, 1007 cm⁻¹; ¹H NMR (CDCl₃) δ 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 C₂₅H₄₀O₆Si: 464.2592 Found: 464.2591; [α]Dⁿ +6.1° (c 1.16, CHCl₃).

(3S)-3-((tert-Butyldimethylsilyloxyethyl)-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 H2O (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 CHCl3 (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 Et3N (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) to afford 21 (389 mg, 81%) as a colorless oil. IR (neat) 3348, 3033, 1713, 1515 cm⁻¹; ¹H NMR (CDCl3) 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 C31H45N06Si: C, 66.75; H, 8.49; N, 2.51 Found: C, 66.20; H, 8.17; N, 2.96; [α]26D +1.81° (c 2.77, CHCl3).

(3S)-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 CH2Cl2 (10 mL) and 3% HCl, and the organic layer was separated. The aqueous layer was extracted with CH2Cl2 (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 21 (82.8 mg, 0.15 mmol) in benzene (0.5 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 CH2Cl2 (10 mL) and 3% HCl, and the organic layer was separated. The aqueous layer was extracted with CH2Cl2 (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 (CDCl3) 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 C31H47NO6Si: C, 66.75; H, 8.49; N, 2.51 Found: C, 66.20; H, 8.17; N, 2.96; [α]26D +1.81° (c 2.77, CHCl3).

(2S)-5,5-Ethylenedioxy-2-[N-methyl-N-(phenylmetoxycarbonyl)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 CH2Cl2 (50 mL) and H2O (5 mL), and the organic layer was separated. The aqueous layer was extracted with CH2Cl2 (5 mL x 3), 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 oxaly chloride (0.05 mL, 0.53 mmol) in CH$_2$Cl$_2$ (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$_2$Cl$_2$ (2 mL) at -78 °C, and the mixture was stirred at -78 °C for 30 min. To the mixture was added Et$_3$N (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$_2$O (60 mL), and the insoluble material was removed by filtration. The filtrate was washed with H$_2$O (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$_2$O (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$_2$Cl$_2$ (2 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=15:1) to afford 22 (162.9 mg, 94%) as a colorless oil. IR (neat) 1694, 1514, 857, 832 cm$^{-1}$; $^1$H NMR (CDCl$_3$) $\delta$ 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$_2$H$_{37}$N$_{2}$O$_7$: 499.2568. Found: 499.2531; $\alpha$D$^2$D -0.02° (c 1.70, CHCl$_3$).

(-)-O-Methyljoubertamine 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$_2$O (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$_2$O$_3$, hexane:CHCl$_3$=5:1) to afford (-)-O-methyljoubertamine (18 mg, 66%) as a colorless oil. IR (neat) 1684 cm$^{-1}$; $^1$H NMR (CDCl$_3$) $\delta$ 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$_7$: 273.1751. Found: 273.1719; $\alpha$D$^2$D -51.2° (c 0.34, CHCl$_3$); $\alpha$D$^2$D -65.3° (c 0.34, MeOH); lit.,$^8c$ $\alpha$D$^2$D -50.3° (c 0.003, CHCl$_3$), lit.,$^8b$ $\alpha$D$^2$D -68.4° (c 1.40, MeOH); lit.,$^8a$ $\alpha$D$^2$D -51° (c 1.45, MeOH).

(2'S)-2'-[(tert-Butyl(dimethyl)silyloxy)methyl]-5',5'-ethylenedioxy-2'-
(4-methoxyphenyl)heptyl 2,2-dimethylopropanoate (23) To a stirred solution of 17 (123 mg, 0.33 mmol) in CH$_2$Cl$_2$ (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$_2$Cl$_2$ (20 mL) and H$_2$O (2 mL), and the organic layer was separated. The aqueous layer was extracted
with CH₂Cl₂ (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% Na₂S₂O₃ in satd NaHCO₃ (10 mL) and CH₂Cl₂ (10 mL), and the organic layer was separated. The aqueous layer was extracted with CH₂Cl₂ (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 NaBH₄ (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 CH₂Cl₂ (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 CH₂Cl₂ (5 mL) were added TBSCl (231 mg, 1.53 mmol), Et₃N (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, Et₂O (50 mL) and H₂O (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 (CDCl₃) 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 C₁₇H₂₃NÔ₂: 273.1727. Found: 273.1719; [α]D²₀ -9.6° (c 0.91, CHCl₃).

(2R)-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 LiEt₃BH (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 H₂O (5 mL) and CH₂Cl₂ (30 mL), and the organic layer was separated. The aqueous layer was extracted with CH₂Cl₂ (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 CH₂Cl₂ (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 CH₂Cl₂ (1 mL) at -78 °C, and the stirring was continued at -78 °C for 30 min. To the mixture was added Et₃N (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 Et₂O (30 mL), and the insoluble material was removed by filtration. The filtrate was washed with H₂O (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; [α]D²₀ -35.6° (c 0.95, CHCl₃).
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REFERENCES AND NOTES


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.

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 confirmed by the comparison of the optical rotations with those of 4a-c obtained from procedure C (see experimental section).


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