Bicyclic β -Hydroxytetrahydrofurans as Precursors of Medium Ring Lactones

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Supporting Information

Table of Contents

	<i>page</i>
General Methods.....	S3
1. General procedure for the preparation of 3-alkenols 1c , 1e and 1f	S3
1.1. 2-Cyclohexenylbutan-1-ol (1c).....	S4
1.2. 2-(<i>E</i>)-Cycloheptenylpropan-1-ol (1e).....	S4
1.3. 2-(<i>E</i>)-Cycloheptenylbutan-1-ol (1f).....	S5
2. General procedure for the epoxidation of the 3-alkenols 1a-g : Preparation of the epoxyalcohols 2a-g	S6
2.1. 2-(7-Oxa-bicyclo[4.1.0]hept-1-yl)ethanol (2a).....	S6
2.2. 2-(7-Oxa-bicyclo[4.1.0]hept-1-yl)propan-1-ol (2b).....	S6
2.3. 2-(7-Oxa-bicyclo[4.1.0]hept-1-yl)butan-1-ol (2c).....	S7
2.4. 2-(8-Oxa-bicyclo[5.1.0]oct-1-yl)ethanol (2d).....	S7
2.5. 2-(8-Oxa-bicyclo[5.1.0]oct-1-yl)propan-1-ol (2e).....	S8
2.6. 2-(8-Oxa-bicyclo[5.1.0]octan-1-yl)butan-1-ol (2f).....	S8
2.7. 2-(5-Methyl-7-oxa-bicyclo[4.1.0]heptan-1-yl)ethanol (2g).....	S9
3. General procedure for the base-promoted cyclization of epoxyalcohols 2a-f : Preparation of the bicyclic β -hydroxyethers 3a-f	S9
3.1. 7 α H-Octahydro-benzofuran-3 α -ol (3a).....	S9
3.2. 3 β -Methyl-7 α H-octahydro-benzofuran-3 α -ol (3b) and 3 α -Methyl-7 α H-octahydro-benzofuran-3 α -ol (3b').....	S10

	<i>page</i>
3.3. 3 β -Ethyl-7 α <i>H</i> -octahydro-benzofuran-3 α -ol (3c) and 3 α -Ethyl-7 α <i>H</i> -octahydro-benzofuran-3 α -ol (3c').....	S10
3.4. 8 α <i>H</i> -Octahydro-cyclohepta[<i>b</i>]furan-3 α -ol (3d).....	S11
3.5. Base-promoted cyclization of epoxyalcohols 2g/2g'	S12
4. General procedure for the ruthenium tetraoxide-promoted oxidative cleavage of β -hydroxyethers 3a-c and 3e,f (PROTOCOL A).....	S13
4.1. Oxonane-2,7-dione (7a).....	S13
4.2. 8-Ethyl-oxonane-2,7-dione (7c).....	S14
4.3. 9-Ethyl-oxecane-2,8-dione (7f).....	S15
5. General procedure for the ruthenium tetraoxide-promoted oxidative cleavage of β -hydroxyethers 3a,b and 3d-f (PROTOCOL B).....	S15
5.1. Oxonane-2,7-dione (7a).....	S15
5.2. 8-Methyl-oxonane-2,7-dione (7b).....	S15
5.3. 9-Methyl-oxecane-2,8-dione (7e).....	S15
5.4. 9-Ethyl-oxecane-2,8-dione (7f).....	S16
6. Preparation of β -hydroxyethers 9a and 9b	S16
7. Reaction of β -hydroxyethers 9a with Ruthenium Tetraoxide.....	S16
8. Reaction of β -hydroxyethers 9b with Ruthenium Tetraoxide.....	S17
<i>Figures S1 – S14. NMR spectra of 3-alkenols 1a-g</i>	S19
<i>Figures S15 – S28. NMR spectra of epoxyalcohols 2a-g</i>	S33
<i>Figures S29 – S34. NMR spectra of 3g, 3g', 4, 5 and 6</i>	S47
<i>Figures S35 – S55. NMR spectra of β-hydroxyethers 3a-f</i>	S53
<i>Figures S56 – S67. NMR spectra of keto-lactones 7a, 7b and 7d-f</i>	S74
9. References.....	S86

General Methods. Ruthenium trichloride ($\text{RuCl}_3 \cdot n\text{H}_2\text{O}$), thallium trinitrate ($\text{TTN} \cdot 3\text{H}_2\text{O}$),¹ Oxone[®] and sodium periodate (NaIO_4) were used as received. Calculations were based on $n = 1$. Other known compounds used in this research were also purchased from standard chemical suppliers and were dried and/or purified by usual methods. Column chromatography was performed using silica gel Acros 230-400 mesh. TLC analyses were performed with silica gel plates Merck using iodine, vanilline solution or *p*-anisaldehyde solution for visualization.

1. General procedure for the preparation of 3-alkenols 1c, 1e and 1f. The 3-alkenols **1c**, **1e** and **1f** were prepared from commercially available cyclohexanone and cycloheptanone, using classical methodologies, as outlined in the Scheme 1 shown below.

To a stirred suspension of zinc² (3.90 g, 60.0 mmol), benzene (50 mL), the cycloketone (55.0 mmol) and iodine (one crystal) was added the α -bromoester (58.0 mmol). The mixture was refluxed (CAUTION! A vigorous reflux is observed in the beginning) for 2.5-3.0 hours and 10% aqueous H_2SO_4 solution was added at 0°C . The aqueous phase was extracted with AcOEt (three times) and the combined organic extracts were washed with brine and dried over anhydrous MgSO_4 . When necessary, the

β -hydroxyester was separated from the unreacted starting materials by distillation under reduced pressure.

To a stirred solution of the β -hydroxyester (50.0 mmol) in anhydrous Et₂O (50 mL) at 0°C were added SOCl₂³ (4.74 mL, 65.0 mmol) and dry pyridine (10 drops). The mixture was stirred under nitrogen (48 h for **1c**, 18 h for **1e** and **1f**) at room temperature and saturated aqueous NaHCO₃ was added. The aqueous phase was extracted with ethyl acetate (three times) and the combined organic phases were washed with brine (twice) and dried over anhydrous MgSO₄. The solvent was removed under reduced pressure and the crude product was distilled. It is noteworthy that the β,γ -unsaturated esters were obtained along with minor amounts of the corresponding α,β -unsaturated esters (less than 8%, determined by CG in the crude product).

To a stirred suspension of LiAlH₄ (36.0 mmol, 1.0 equivalents) in anhydrous THF (36 mL) at 0°C was added dropwise a solution of the β,γ -unsaturated ester (36.0 mmol) in anhydrous THF (36 mL). The mixture was stirred for 3.0-3.5 hours at room temperature and water was carefully added dropwise at 0°C, followed by 10% aqueous H₂SO₄ solution. The aqueous phase was extracted with ethyl acetate (twice) and the combined organic phases were washed with brine and dried with anhydrous MgSO₄. The solvent was removed under reduced pressure and the crude product was purified by flash chromatography (hexanes:AcOEt 7:3 as eluent), affording the corresponding 3-alkenols **1c**, **1e** or **1f** in the yields shown in Scheme 1.

The spectroscopic data for 3-alkenols **1c**, **1e** and **1f** are listed below.

1.1. 2-Cyclohexenylbutan-1-ol (1c): viscous colorless oil; IR (film) 3379 cm⁻¹; LRMS *m/z* (%) 154 (8.8, M⁺); ¹H NMR (300 MHz, CDCl₃) δ 0.85 (t, *J* = 7.4 Hz, 3H), 1.25-1.39 (m, 2H), 1.54-2.26 (m, 9H, H-OH), 3.41-3.52 (m, 2H), 5.53-5.56 (m, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 11.9, 22.1, 22.8, 23.0, 24.7, 25.4, 52.2, 63.9, 125.3, 136.9; HRMS [ESI(+)] *m/z* [M+Na⁺] calcd. for C₁₀H₁₈O: 177.1250; found: 177.1253.

1.2. 2-(E)-Cycloheptenylpropan-1-ol (1e): viscous colorless oil; IR (film) 3357 cm⁻¹; LRMS *m/z* (%) 154 (12, M⁺); ¹H NMR (500 MHz, CDCl₃) δ 0.97 (d, *J* = 6.9 Hz, 3H), 1.43-1.49 (m, 4H), 1.73-1.79 (m, 2H), 1.82 (br s, H-OH), 2.07-2.15 (m, 4H), 2.30 (sextet, *J* = 6.9 Hz, 1H), 3.42 (d, *J* = 6.9

Hz, 2H), 5.69 (t, $J = 6.5$ Hz, 1H); ^{13}C NMR (125 MHz, CDCl_3) δ 15.2, 27.2, 28.2, 29.2, 32.7, 45.5 (CH), 64.9, 128.8, 145.3; HRMS [ESI(+)] m/z $[\text{M}+\text{Na}^+]$ calcd. for $\text{C}_{10}\text{H}_{18}\text{O}$: 177.1250; found: 177.1251.

1.3. 2-(*E*)-Cycloheptenylbutan-1-ol (1f): viscous colorless oil; IR (film) 3355 cm^{-1} ; LRMS m/z (%) 168 (14, M^+); ^1H NMR (300 MHz, CDCl_3) δ 0.85 (t, $J = 7.4$ Hz, 3H), 1.23-1.58 (m, 6H), 1.72-1.80 (m, 2H), 2.03-2.17 (m, 5H), 3.41 (dd, $J = 8.8$ and 10.5 Hz, 1H), 3.47 (dd, $J = 5.3$ and 10.5 Hz, 1H), 5.70 (t, $J = 6.5$ Hz, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ 12.2, 22.0, 27.2, 27.5, 28.5, 28.6, 32.8, 54.2, 63.7, 131.1, 143.5; HRMS [ESI(+)] m/z $[\text{M}+\text{Na}^+]$ calcd. for $\text{C}_{11}\text{H}_{20}\text{O}$: 191.1406; found: 191.1405.

The 3-alkenols **1a**, **1b**, **1d** and **1g** are known compounds. Spectral data are in agreement with literature.⁴⁻⁷ For experimental details see Ferraz, H. M. C.; Longo, Jr., L. S.; Zukerman-Schpector, J. *J. Org. Chem.* **2002**, 67, 3518-3521 (Supporting Information).

2-Cyclohexenylethanol (1a):⁴ viscous colorless oil; ^1H NMR (300 MHz, CDCl_3) δ 1.52-1.67 (m, 4H), 1.77 (br s, OH), 1.92-2.04 (m, 4H), 2.21 (t, $J = 6.3$ Hz, 2H), 3.66 (t, $J = 6.3$ Hz, 2H), 5.51-5.54 (m, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ 22.4, 22.9, 25.3, 28.1, 41.2, 60.3, 124.3, 134.1.

2-Cyclohex-1-enyl-propan-1-ol (1b):⁵ viscous colorless oil; ^1H NMR (300 MHz, CDCl_3) δ 0.99 (d, $J = 6.9$ Hz, 3H), 1.54-1.66 (m, 4H, OH), 1.89-2.05 (m, 4H), 2.26 (sextet, $J = 6.9$ Hz, 1H), 3.43-3.51 (m, 2H), 5.52-5.54 (m, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ 15.4, 22.7, 22.9, 25.2, 25.3, 43.9, 65.4, 123.3, 138.6.

2-Cyclohept-1-enyl-ethanol (1d):⁶ viscous colorless oil; ^1H NMR (300 MHz, CDCl_3) δ 1.44-1.52 (m, 4H), 1.71-1.78 (m, 2H, OH), 2.08-2.15 (m, 4H), 2.24 (t, $J = 6.2$ Hz, 2H), 3.63 (t, $J = 6.2$ Hz, 2H), 5.66 (t, $J = 6.4$ Hz, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ 26.9, 27.4, 28.4, 32.5, 32.6, 43.4, 60.2, 129.6, 140.8.

2-(4-Methylcyclohex-1-en-1-yl)ethanol (1g):⁷ viscous colorless oil; ¹H NMR (300 MHz, CDCl₃) δ 0.95 (d, *J* = 6.3 Hz, 3H), 1.16-1.29 (m, 1H), 1.54-1.74 (m, 3H, OH), 1.96-2.11 (m, 3H), 2.21 (t, *J* = 6.3 Hz, 2H), 3.65 (t, *J* = 6.3 Hz, 2H), 5.47-5.49 (m, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 21.7, 28.2, 28.4, 31.2, 33.9, 40.8, 60.3, 123.8, 133.8.

2. General procedure for the epoxidation of the 3-alkenols 1a-g: Preparation of the epoxyalcohols 2a-g. To a solution of the 3-alkenol **1a-g** (1.0 mmol) in acetone (2.0 mL) and H₂O (2.0 mL), were added NaHCO₃ (4.0 mmol) and Oxone[®] (1.5 mmol). The mixture was stirred at room temperature for 5-20 minutes and distilled water (*ca.* 10 mL) was added. The aqueous phase was extracted with AcOEt (three times) and the combined organic phases were washed with brine, dried over anhydrous MgSO₄ and. The solvent was removed under reduced pressure to afford the corresponding epoxyalcohols **2a-g**.

The epoxyalcohols **2a-g** showed to be slightly unstable, and therefore must be employed in the next step immediately after isolation.

2.1. 2-(7-Oxa-bicyclo[4.1.0]hept-1-yl)ethanol (2a). The 3-alkenol **1a** (0.446 g, 3.54 mmol), acetone (7.0 mL), H₂O (7.0 mL), NaHCO₃ (1.19 g, 14.2 mmol) and OXONE[®] (3.26 g, 5.31 mmol) were stirred at room temperature for 10 minutes following the general procedure. The crude product was purified by flash chromatography (eluent, 50% AcOEt in hexanes) giving the epoxyalcohol **2a** (0.380 g, 2.68 mmol, 76%).

2a: colorless oil; IR (film) 3390 cm⁻¹; LRMS *m/z* (%) 142 (2.6, M⁺); ¹H NMR (300 MHz, CDCl₃) δ mixture of 2 diastereomers: 1.16-1.47 (m, 4H), 1.68-1.98 (m, 4H), 2.64 (brs, 1H), 3.16 (d, *J* = 3.4 Hz, 1H), 3.65-3.83 (m, 2H), ¹³C NMR (125 MHz, CDCl₃) δ 19.5, 19.8, 24.4, 28.7, 38.6, 57.7, 58.8, 59.6.

2.2. 2-(7-Oxa-bicyclo[4.1.0]hept-1-yl)propan-1-ol (2b). The 3-alkenol **1b** (0.350 g, 2.50 mmol), acetone (5 mL), H₂O (5 mL), NaHCO₃ (0.840 g, 10.0 mmol) and Oxone[®] (3.75 g, 5.31 mmol) were stirred at room temperature for 10 minutes following the general procedure. The crude product was purified by flash chromatography (eluent,

50% AcOEt in hexanes) giving a 1:1 diastereomeric mixture of the epoxyalcohol **2b** (0.309 g, 1.98 mmol, 79%).

2b: colorless oil; IR (film) 3420 cm^{-1} ; LRMS m/z (%) 156 (3.3, M^+); ^1H NMR (300 MHz, CDCl_3) δ mixture of 2 diastereomers: 0.93 and 0.98 (d, $J = 7.0$ Hz, d, $J = 7.1$ Hz, 3H), 1.15-1.59 (m, 4H), 1.77-2.10 (m, 4H, 1H), 2.38 (br s, 1H), 2.77 (br s, 1H), 2.98 (dd, $J = 1.2$ and 3.3 Hz, 1H), 3.19 (d, $J = 2.4$ Hz, 1H), 3.39-3.48 (m, 2H), 3.55 (dd, $J = 5.5$ and 10.8 Hz, 1H), 3.71 (dd, $J = 7.4$ and 10.8 Hz, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ mixture of 2 diastereomers: 12.8 and 13.1, 19.4 and 19.6, 20.1 and 20.2, 24.1 and 24.7, 24.7 and 26.9, 41.1 and 42.7, 56.7 and 57.5, 62.4 and 63.0, 64.6 and 64.8.

2.3. 2-(7-Oxa-bicyclo[4.1.0]hept-1-yl)butan-1-ol (2c). The 3-alkenol **1c** (0.380 g, 2.47 mmol), acetone (5 mL), H_2O (5 mL), NaHCO_3 (0.830 g, 9.88 mmol) and Oxone[®] (3.71 g, 2.28 mmol) were stirred for 20 minutes following the general procedure. The crude product was purified by flash chromatography (eluent, 50% AcOEt in hexanes) giving a 3:1 diastereomeric mixture of the epoxyalcohol **2c** (0.352 g, 2.07 mmol, 84%).

2c: colorless oil; IR (film) 3435 cm^{-1} ; LRMS m/z (%) 170 (0.8, M^+); ^1H NMR (300 MHz, CDCl_3) δ mixture of 2 diastereomers: 0.95 and 0.96 (t, $J = 7.3$ Hz, t, $J = 7.4$ Hz, 3H), 1.16-1.52 (m, 6H), 1.60-2.04 (m, 5H), 2.33 (br s, 1H), 2.60 (br s, 1H), 2.94 (dd, $J = 1.3$ and 3.2 Hz, 1H), 3.17 (dd, $J = 1.2$ and 3.3 Hz, 1H), 3.39-3.45 (m, 1H), 3.50-3.64 (m, 2H), 3.76-3.82 (m, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ mixture of 2 diastereomers: 12.0 and 12.1, 19.5 and 19.6, 20.1 and 20.3, 21.3 and 21.5, 23.3 and 24.7, 24.7 and 27.6, 50.3 and 48, 58.5 and 56.6, 61.6 and 62.4, 63.9 and 62.7.

2.4. 2-(8-Oxa-bicyclo[5.1.0]oct-1-yl)ethanol (2d). The alkenol **1d** (0.332 g, 2.73 mmol), acetone (4.7 mL), H_2O (4.7 mL), NaHCO_3 (0.796 g, 9.48 mmol) and Oxone[®] (2.19 g, 3.56 mmol) were stirred for 5 min following the general procedure. The crude product was purified by flash chromatography (eluent, 50% AcOEt in hexanes) giving the epoxyalcohol **2d** (0.303 g, 1.94 mmol, 82%). This epoxide is slightly unstable in solution of CDCl_3 .

2d: colorless oil; IR (film) 3396 cm^{-1} ; LRMS m/z (%) 156 (1.5, M^+); ^1H NMR (500 MHz, CDCl_3) δ 1.35-1.56 (m, 6H), 1.74-2.04 (m, 6H), 2.69 (br s, 1H), 3.08 (dd, $J = 3.8$ and 7.0 Hz, 1H), 3.69 (ddd, $J = 4.7$, 7.1 and 11.3 Hz, 1H), 3.77 (ddd, $J = 5.0$, 6.5 and 11.3 Hz, 1H); ^{13}C NMR (125 MHz, CDCl_3) δ 24.3, 24.6, 29.0, 31.1, 33.4, 38.4, 59.2, 61.1, 63.3.

2.5. 2-(8-Oxa-bicyclo[5.1.0]oct-1-yl)propan-1-ol (2e). The 3-alkenol **1e** (0.423 g, 2.75 mmol), acetone (5.5 mL), H_2O (5.5 mL), NaHCO_3 (0.924 g, 11.0 mmol) and Oxone[®] (2.54 g, 4.13 mmol) were stirred for 8 min following the general procedure. The crude product was purified by flash chromatography (eluent, 50% AcOEt in hexanes) giving a 3:1 diastereomeric mixture of the epoxyalcohol **2e** (0.410 g, 2.41 mmol, 87%). This epoxide is slightly unstable in solution of CDCl_3 .

2e: colorless oil; IR (film) 3440 cm^{-1} ; LRMS m/z (%) 170 (1.9, M^+); ^1H NMR (500 MHz, CDCl_3) δ mixture of 2 diastereomers: 0.93 and 0.97 (d, $J = 7.0$ Hz, d, $J = 7.2$ Hz, 3H), 1.12-1.21 (m, 1H), 1.43-1.65 (m, 5H), 1.82-2.03 (m, 5H), 2.5 (br s, 1H), 2.96 (dd, $J = 3.6$ and 5.8 Hz, 1H), 3.15 (dd, $J = 2.6$ and 6.5 Hz, 1H), 3.43-3.49 (m, 2H), 3.53 (dd, $J = 5.2$ and 10.9 Hz, 1H), 3.75 (dd, $J = 7.9$ and 10.9 Hz, 1H); ^{13}C NMR (125 MHz, CDCl_3) δ mixture of 2 diastereomers: 13.1 and 13.2, 23.9 and 24.0, 24.2 and 24.5, 28.4 and 28.6, 28.8 and 31.0, 31.2 and 31.5, 42.5 and 43.1, 60.1 and 61.5, 65.1 and 65.3, 65.5 and 66.1.

2.6. 2-(8-Oxa-bicyclo[5.1.0]octan-1-yl)butan-1-ol (2f). The 3-alkenol **1f** (0.763 g, 4.54 mmol), acetone (9 mL), H_2O (9 mL), NaHCO_3 (1.53 g, 18.2 mmol) and Oxone[®] (4.19 g, 6.81 mmol) were stirred for 18 min following the general procedure. The crude product was purified by flash chromatography (eluent, 50% AcOEt in hexanes) giving a 7:3 diastereomeric mixture of the epoxyalcohol **2f** (0.677 g, 3.68 mmol, 81%). This epoxide is slightly unstable in solution of CDCl_3 .

2f: colorless oil; IR (film) 3430 cm^{-1} ; LRMS m/z (%) 184 (2.1, M^+); ^1H NMR (500 MHz, CDCl_3) δ mixture of 2 diastereomers: 0.94 and 0.95 (t, $J = 7.5$ Hz, t, $J = 7.0$ Hz, 3H), 0.96-1.07 (m, 1H), 1.31-2.08 (m,

12H), 2.63 (brs, 1H), 2.94 (dd, $J = 1.8$ and 6.4 Hz, 1H), 3.12 (dd, $J = 2.5$ and 6.5 Hz, 1H), 3.45-3.49 (m, 2H), 3.58-3.62 (m, 2H), 3.79-3.82 (m, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ mixture of diastereomers: 12.2 and 12.3, 21.3, 23.8 and 24.0, 24.1 and 24.2, 27.2 and 28.3, 28.5 and 31.0, 31.1 and 32.0, 49.3 and 51.0, 60.0 and 62.3, 63.2 and 64.3, 64.9 and 65.5.

2.7. 2-(5-Methyl-7-oxa-bicyclo[4.1.0]heptan-1-yl)ethanol (2g). The alkenol **1g** (0.386 g, 2.76 mmol), acetone (5.5 mL), H_2O (5.5 mL), NaHCO_3 (0.927 g, 11.0 mmol) and Oxone[®] (2.55 g, 4.14 mmol) were stirred for 10 min following the general procedure. The crude product was purified by flash chromatography (eluent, 50% AcOEt in hexanes) giving a 3:2 diastereomeric mixture of the epoxyalcohols **2g** and **2g'** (0.360 g, 2.31 mmol, 84%).

2g/2g': colorless oil; IR (film) 3441 cm^{-1} ; LRMS m/z (%) 141 (47, $\text{M}^+ - 15$); ^1H NMR (300 MHz, CDCl_3) δ mixture of 2 diastereomers: 0.86 and 0.87 (d, $J = 6.0$ Hz, d, $J = 6.7$ Hz, 3H), 0.90-2.15 (m, 9H), 2.55 (br s, 1H), 3.15 (d, $J = 5.4$ Hz, 1H), 3.18 (t, $J = 2.0$ Hz, 1H) 3.66-3.78 (m, 2H); ^{13}C NMR (75 MHz, CDCl_3) δ mixture of 2 diastereomers: 21.3 and 21.9, 24.1 and 27.9, 27.4 and 27.6, 29.2 and 29.4, 32.8 and 33.7, 37.7 and 39.0, 57.6 and 58.5, 58.9 and 58.9, 59.3 and 59.8.

3. General procedure for the base-promoted cyclization of epoxyalcohols 2a-f.
Preparation of the bicyclic β -hydroxyethers 3a-f. To a stirred solution of the epoxyalcohols **2a-f** (1 mmol) in 75% aqueous DMSO (20 mL) was added potassium hydroxide (10 eq., 0.56 g, 10 mmol). The mixture was stirred at $110\text{--}120^\circ\text{C}$ for 2 h and water (20 mL) was added dropwise. The aqueous phase was extracted with AcOEt (three times). The combined organic extracts were washed with H_2O followed by brine, dried over anhydrous MgSO_4 and the solvent was removed under reduced pressure.

3.1. 7 α H-Octahydro-benzofuran-3 α -ol (3a). The reaction was performed following the general procedure, using the epoxyalcohol **2a** (0.326 g, 2.30 mmol) in 75% aqueous DMSO (46 mL) and KOH (1.3 g, 23 mmol). The crude product was purified by flash

chromatography (eluent, 50% AcOEt in hexanes followed by AcOEt) to give **3a** (0.124 g, 0.873 mmol, 38%), together with minor amounts (*ca.* 4%) of the corresponding triol.

3a: colorless oil; IR (film) 3415 cm^{-1} ; LRMS m/z (%) 142 (17, M^+); ^1H NMR (300 MHz, CDCl_3) δ 1.25-1.90 (m, 9H), 2.08 (ddd, $J = 6.9, 9.0$ and 12.6 Hz, 1H), 2.54 (br s, H-OH), 3.64 (dd, $J = 5.3$ and 7.1 Hz, 1H), 3.93 (ddd, $J = 5.4, 8.7$ and 8.7 Hz, 1H), 4.03 (ddd, $J = 6.9, 8.7$ and 8.7 Hz, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ 21.6, 22.1, 28.3, 33.9, 37.3, 64.9, 77.4, 81.9; HRMS [ESI(+)] m/z [$\text{M}+\text{Na}^+$] calcd. for $\text{C}_8\text{H}_{14}\text{O}_2$: 165.0886; found: 165.0890.

3.2. 3 β -Methyl-7 α H-octahydro-benzofuran-3 α -ol (3b) and 3 α -Methyl-7 α H-octahydro-benzofuran-3 α -ol (3b'). The reaction was performed following the general procedure, using the epoxyalcohol **2b** (0.250 g, 1.60 mmol) in 75% aqueous DMSO (32 mL) and KOH (0.897 g, 16.0 mmol). The crude product was purified by flash chromatography (eluent, 50% AcOEt in hexanes) to give a 3:2 mixture of **3b** and **3b'** (0.207 g, 1.33 mmol, 83%), respectively (ratio determined by GC and ^1H NMR in the crude product). All attempts to separate the diastereoisomers were unsuccessful and the spectroscopic analyses were performed with the mixture of **3b** and **3b'**.

IR (film) 3418 cm^{-1} ; LRMS m/z (%) 156 (3.7, M^+); **3b**: colorless oil; ^1H NMR (300 MHz, CDCl_3) δ 0.93 (d, $J = 6.9$ Hz, 3H), 1.25-1.90 (m, 8H, H-OH), 2.20-2.34 (m, 1H), 3.42 (dd, $J = 8.5$ and 10.2 Hz, 1H), 3.66 (d, $J = 2.3$ Hz, 1H), 4.09 (t, $J = 8.8$ Hz, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ 9.3, 20.2, 20.7, 25.9, 28.3, 44.0, 71.8, 75.2, 80.4. **3b'**: colorless oil; ^1H NMR (300 MHz, CDCl_3) δ 0.98 (d, $J = 6.9$ Hz, 3H), 1.25-1.90 (m, 8H, H-OH), 2.20-2.34 (m, 1H), 3.56 (t, $J = 8.4$ Hz, 1H), 3.73 (dd, $J = 5.7$ and 8.3 Hz, 1H), 4.11 (t, $J = 8.4$ Hz, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ 10.5, 22.1, 22.2, 29.5, 32.8, 38.0, 72.7, 78.2, 83.0; HRMS [ESI(+)] m/z [$\text{M}+\text{Na}^+$] calcd. for $\text{C}_9\text{H}_{16}\text{O}_2$: 179.1043; found: 179.1044.

3.3. 3 β -Ethyl-7 α H-octahydro-benzofuran-3 α -ol (3c) and 3 α -Ethyl-7 α H-octahydro-benzofuran-3 α -ol (3c'). The reaction was performed following the general procedure, using the epoxyalcohol **2c** (0.589 g, 3.46 mmol) in 75% aqueous DMSO (70

mL) and KOH (1.94 g, 34.6 mmol). The crude product was purified by flash chromatography (eluent, 50% AcOEt in hexanes) to give a 3:1 mixture of **3c** and **3c'** (0.441 g, 2.59 mmol, 75%), respectively (ratio determined by GC and ^1H NMR in the crude product). Analytical samples of the diastereomeric bicyclic β -hydroxyethers **3c** and **3c'** were obtained performing a second flash chromatography (gradient elution, 0-50% AcOEt in hexanes).

3c: viscous colorless oil; IR (film) 3420 cm^{-1} ; LRMS m/z (%) 170 (1.9, M^+); ^1H NMR (300 MHz, CDCl_3) δ 0.92 (d, $J = 7.4\text{ Hz}$, 3H), 1.18-1.65 (m, 9H, H-OH), 1.85-1.95 (m, 1H), 2.10 (qd, $J = 5.1$ and 9.6 Hz , 1H), 3.46 (dd, $J = 8.6$ and 10.0 Hz , 1H), 3.64-3.66 (m, 1H), 4.14 (t, $J = 8.8\text{ Hz}$, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ 12.8, 19.4, 20.1, 20.7, 25.9, 28.7, 51.8, 71.0, 75.6, 80.7 (CH).

3c': viscous colorless oil; IR (film) 3426 cm^{-1} ; LRMS m/z (%) 170 (1.5, M^+); ^1H NMR (300 MHz, CDCl_3) δ 0.92 (d, $J = 7.5\text{ Hz}$, 3H), 1.21-1.39 (m, 4H), 1.40-1.70 (m, 4H), 1.75-1.95 (m, 2H), 2.00-2.12 (m, 1H, H-OH), 3.64 (t, $J = 8.4\text{ Hz}$, 1H), 3.70 (dd, $J = 5.7$ and 8.5 Hz , 1H), 4.13 (t, $J = 8.5\text{ Hz}$, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ 12.9, 20.0, 22.1, 22.3, 29.3, 33.2, 45.5, 71.5, 78.4, 83.6.

The HRMS analysis was performed for the diastereomeric mixture of β -hydroxyethers **3c** and **3c'**: HRMS [ESI(+)] m/z [$\text{M}+\text{Na}^+$] calcd. for $\text{C}_9\text{H}_{16}\text{O}_2$: 193.1199; found: 193.1201.

3.4. 8 α H-Octahydro-cyclohepta[b]furan-3 α -ol (3d). The reaction was performed following the general procedure, using the epoxyalcohol **2d** (0.485 g, 3.11 mmol) in 75% aqueous DMSO (60 mL) and KOH (1.74 g, 31.1 mmol). The crude product was purified by flash chromatography (eluent, 50% AcOEt in hexanes) to give **3d** (0.329 g, 2.11 mmol, 68%).

3d: colorless oil; IR (film) 3443 cm^{-1} ; LRMS m/z (%) 156 (21, M^+); ^1H NMR (500 MHz, CDCl_3) δ 1.28- 2.01 (m, 12H, H-OH), 3.74 (dd, $J = 2.8$ and 10.8 Hz , 1H), 3.86 (ddd, $J = 5.4$, 8.4 and 11.2 Hz , 1H), 3.95 (td, $J =$

1.6 and 8.4 Hz, 1H); ^{13}C NMR (125 MHz, CDCl_3) δ 23.2, 25.3, 30.9, 33.1, 38.4, 42.7, 66.4, 83.1, 90.7; Anal. Calcd. for $\text{C}_9\text{H}_{16}\text{O}_2$: C, 69.19%; H, 10.32%; found: 68.83%; H, 9.95%.

3.5. Base-promoted cyclization of epoxyalcohols **2g/2g'.** To a stirred solution of the epoxyalcohols **2g/2g'** (0.171 g, 1.10 mmol) in 75% aqueous DMSO (22 mL) was added potassium hydroxide (10 equivalents, 0.616 g, 11.0 mmol). The mixture was stirred at 110-120°C for 2 hours and water was added dropwise. The aqueous phase was extracted with ethyl acetate (three times) and the combined organic extracts were washed with water followed by brine, dried over anhydrous magnesium sulfate and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (40-60% AcOEt in hexanes, gradient elution, followed by AcOEt) giving a 2:1 mixture of ethers **3g** and **4**, respectively (0.051 g, 0.327 mmol, 30%), along with a 4:1 mixture of the ether **3g'** and the allylic alcohol **5**, respectively, (0.022 g, 0.141 mmol, 13%) and the glycolic derivative **6** (0.033 g, 0.190 mmol, 17%).

It is noteworthy that *ca.* 15% of the starting epoxyalcohol **2g** were observed in the ^1H NMR spectra of mixture of products **3g** and **4**.

6β-Methyl-7αβH-octahydrobenzofuran-3αβ-ol (3g**):**⁴ IR (film) 3410 cm^{-1} ; LRMS m/z (%) 156 (20, M^+); ^1H NMR (500 MHz, CDCl_3) δ 0.91 (d, $J = 6.7$ Hz, 3H), 1.14-1.20 (m, 1H), 1.31 (ddd, $J = 3.6, 11.5$ and 14.8 Hz, 1H), 1.49-1.71 (m, 4H, OH), 1.85-2.04 (m, 3H), 3.63 (t, $J = 3.3$ and 3.3 Hz, 1H), 3.87 (dd, $J = 8.8$ and 17 Hz, 1H), 3.98 (ddd, $J = 4.0, 8.8$ and 10 Hz, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ 21.7, 26.2, 29.8, 34.0, 34.4, 39.9, 64.9, 75.1, 80.2.

7α-Methyl-1-oxaspiro[3.5]nonan-5β-ol (4**):** IR (film) 3410 cm^{-1} ; LRMS m/z (%) 156 (20, M^+); ^1H NMR (500 MHz, CDCl_3) δ 0.94 (d, $J = 7.0$ Hz, 3H), 1.16-2.22 (m, 7H, H-OH), 2.61-2.74 (m, 2H); 3.82-3.91 (m, 1H), 4.41-4.54 (m, 2H); ^{13}C NMR (75 MHz, CDCl_3) δ 19.8, 26.0, 27.3, 28.4, 32.1, 35.9, 65.6, 71.2, 88.5.

6α-Methyl-7αβH-octahydrobenzofuran-3αβ-ol (3g'**):** IR (film) 3389 cm^{-1} ; LRMS m/z (%) 156 (27, M^+); ^1H NMR (300 MHz, CDCl_3) δ 0.93

(d, $J = 6.6$ Hz, 3H), 0.82-1.07 (m, H of the ring), 1.35-1.95 (m, H of the ring), 2.06-2.30 (m, 2H), 3.72 (dd, $J = 6.4$ and 10.8 Hz, 1H), 3.94-4.10 (m, 2H); ^{13}C NMR (75 MHz, CDCl_3) δ 21.7, 30.0, 31.6, 33.3, 35.2, 38.9, 65.0, 79.2, 84.0.

***trans*-(2-(2'-Hydroxyethyl)-5-methylcyclohex-2-enol (5):**⁸ IR (film) 3314 cm^{-1} ; LRMS m/z (%) 156 (13, M^+); ^1H NMR (300 MHz, CDCl_3) δ 0.97 (d, $J = 6.5$ Hz, 3H), 1.34 (ddd, $J = 3.9$, 11.1 and 15.0 Hz, 1H), 1.55-1.65 (m, 1H), 1.80-1.95 (m, 2H), 2.09-2.28 (m, 2H), 2.37-2.44 (m, 1H), 3.31 (br s, H-OH), 3.60 (ddd, $J = 3.9$, 9.0 and 10.4 Hz, 1H), 3.81 (dt, $J = 5.0$ and 10.4 Hz, 1H), 4.03 (br s, 1H), 5.63-5.66 (m, 1H); ^{13}C NMR (125 MHz, CDCl_3) δ 21.5, 22.8, 34.4, 39.2, 39.8, 62.6, 67.4, 128.4, 136.3.

1-(2'-Hydroxyethyl)-4-methylcyclohexane-1,2-diol (6): white solid; mp = 104.6-104.7 $^{\circ}\text{C}$; IR (KBr) 3333 cm^{-1} ; LRMS m/z 174 (M^+ , 0.7%); ^1H NMR (300 MHz, CD_3OD) δ 0.87 (d, $J = 6.5$ Hz, 3H), 1.25-1.84 (m, 9H, H-OH), 3.59 (br s, 1H), 3.73-3.81 (m, 2H); ^{13}C NMR (125 MHz, CD_3OD) δ 22.6, 26.7, 30.5, 33.4, 38.4, 42.1, 58.8, 72.4, 73.5; HRMS [ESI(+)] m/z [$\text{M}+\text{Na}^+$] calcd. for $\text{C}_9\text{H}_{18}\text{O}_3$: 197.1148; found: 197.1152.

4. General procedure for the ruthenium tetroxide-promoted oxidative cleavage of β -hydroxyethers 3a-c and 3e,f (PROTOCOL A). To 7.0 mL of a 3:2:2 mixture of $\text{H}_2\text{O}/\text{CCl}_4/\text{CH}_3\text{CN}$, respectively, was added 1 mmol of β -hydroxyethers **3**, 4.1 mmol of NaIO_4 and 2.4-3.0 mol% of $\text{RuCl}_3 \cdot n\text{H}_2\text{O}$, according to the data shown in Table 2. The mixture was magnetically stirred at rt for 75-90 min and 10 mL of distilled H_2O was added. The aqueous phase was extracted with CH_2Cl_2 (three times) and the combined organic phases were washed with brine (twice) and concentrated by removing part of the solvent under reduced pressure. The resulting residue was then filtered through a small silica gel pad (*ca.* 10cm), washing with CH_2Cl_2 . The filtrate was dried over anhydrous MgSO_4 and the solvent was removed under reduced pressure affording the corresponding keto-lactones.

4.1. Oxonane-2,7-dione (7a). The reaction was performed following the general procedure, stirring the β -hydroxyether **3a** (0.144 g, 1.01 mmol), $\text{RuCl}_3 \cdot n\text{H}_2\text{O}$ (3.0

mol%, *ca.* 0.006 g), NaIO₄ (0.886 g, 4.14 mmol) in 7.0 mL of a 3:2:2 mixture of H₂O/CCl₄/CH₃CN at rt for 90 min, leading to the keto-lactone **7a** (0.025 g, 0.162 mmol, 16%) as a colorless oil. Spectral data are in agreement with literature.⁹

4.2. 8-Ethyl-oxonane-2,7-dione (7c). The reaction was performed following the general procedure, stirring a 3:1 mixture of β -hydroxyethers **3c** and **3c'** (0.175 g, 1.03 mmol), RuCl₃.*n*H₂O (3.0 mol%, *ca.* 0.006 g), NaIO₄ (0.903 g, 4.22 mmol) in 7.0 mL of a 3:2:2 mixture of H₂O/CCl₄/CH₃CN at rt for 90 min. The crude product was purified by flash chromatography (gradient elution, 0-30% AcOEt in hexanes) affording the keto-lactone **7c** (0.117 g, 0.636 mmol, 62%).

7c: colorless oil; IR (film) 1741, 1712 cm⁻¹; LRMS *m/z* (%) 184 (0.7, M⁺); ¹H NMR (500 MHz, CDCl₃) δ 0.87 (d, *J* = 7.4 Hz, 3H), 1.35-1.43 (m, 1H), 1.64-1.97 (m, 5H), 2.31-2.46 (m, 4H), 3.10-3.16 (m, 1H), 4.07 (t, *J* = 10.5 Hz, 1H), 4.64 (dd, *J* = 7.3 and 10.5 Hz, 1H); ¹³C NMR (125 MHz, CDCl₃) δ 11.6, 21.7, 23.5, 24.1, 34.7, 42.3, 52.1, 65.4, 174.4, 213.5; Anal. Calcd. for C₁₀H₁₆O₃: C, 65.19%; H, 8.75%; found: C, 64.81%; H, 8.85%.

4.3. 9-Ethyl-oxecane-2,8-dione (7f). The reaction was performed following the general procedure, stirring a 7:3 mixture of β -hydroxyethers **3f** and **3f'** (0.179 g, 0.973 mmol), RuCl₃.*n*H₂O (3.0 mol%, *ca.* 0.006 g), NaIO₄ (0.853 g, 3.99 mmol) in 7.0 mL of a 3:2:2 mixture of H₂O/CCl₄/CH₃CN at rt for 90 min. The crude product was purified by flash chromatography (eluent, 20% AcOEt in hexanes) affording the keto-lactone **7f** (0.128 g, 0.646 mmol, 66%).

7f: colorless oil; IR (film) 1739, 1715 cm⁻¹; LRMS *m/z* (%) 198 (2.0, M⁺); ¹H NMR (500 MHz, CDCl₃) δ 0.88 (t, *J* = 7.4 Hz, 3H), 1.14-1.18 (m, 1H), 1.34-1.39 (m, 1H), 1.49-1.66 (m, 4H), 1.72-1.77 (m, 1H), 1.87-1.90 (m, 1H), 2.22-2.29 (m, 2H), 2.36 (td, *J* = 4.7 and 13.8 Hz, 1H), 2.64 (ddd, *J* = 3.2, 9.4 and 14.8 Hz, 1H), 3.17-3.23 (m, 1H), 4.05 (dd, *J* = 10.4 and 11.3 Hz, 1H), 4.39 (dd, *J* = 5.6 and 10.4 Hz, 1H); ¹³C NMR (125 MHz, CDCl₃) δ 11.8, 21.6, 22.3, 23.0, 24.8, 34.9, 43.5, 50.3, 66.2, 173.1, 214.9; Anal. Calcd. for C₁₁H₁₈O₃: C, 66.64%; H, 9.15%; found: C, 66.92%; H, 9.24%.

5. General procedure for the ruthenium tetraoxide-promoted oxidative cleavage of β -hydroxyethers **3a,b and **3d-f** (PROTOCOL B).** To 7.0 mL of a 3:2:2 mixture of $\text{H}_2\text{O}/\text{CCl}_4/\text{CH}_3\text{CN}$, respectively, was added 1 mmol of β -hydroxyethers **3**, 4.1 mmol of NaIO_4 and 3.0 mol% of $\text{RuCl}_3 \cdot n\text{H}_2\text{O}$, according to the data shown in Table 2. The mixture was magnetically stirred at rt for 90 min and 10 mL of saturated aqueous solution of $\text{Na}_2\text{S}_2\text{O}_3$ was added. The resulting solution was filtered under Celite[®], washing with CH_2Cl_2 . The aqueous phase was extracted with CH_2Cl_2 (three times) and the combined organic phases were washed with brine (twice) and dried over anhydrous MgSO_4 . The solvent was removed under reduced pressure affording the corresponding keto-lactones.

5.1. Oxonane-2,7-dione (7a). The reaction was performed following the general procedure, stirring the β -hydroxyether **3a** (0.290 g, 2.04 mmol), $\text{RuCl}_3 \cdot n\text{H}_2\text{O}$ (3.0 mol%, *ca.* 0.013 g), NaIO_4 (1.79 g, 8.36 mmol) in 14.0 mL of a 3:2:2 mixture of $\text{H}_2\text{O}/\text{CCl}_4/\text{CH}_3\text{CN}$ at rt for 90 min, leading to the keto-lactone **7a** (0.166 g, 1.06 mmol, 52%) as a colorless oil. Spectral data are in agreement with literature.⁹

5.2. 8-Methyl-oxonane-2,7-dione (7b). The reaction was performed following the general procedure, stirring a 3:2 mixture of β -hydroxyethers **3b** and **3b'** (0.219 g, 1.40 mmol), $\text{RuCl}_3 \cdot n\text{H}_2\text{O}$ (3.0 mol%, *ca.* 0.009 g), NaIO_4 (1.23 g, 5.74 mmol) in 9.8 mL of a 3:2:2 mixture of $\text{H}_2\text{O}/\text{CCl}_4/\text{CH}_3\text{CN}$ at rt for 90 min. The crude product was purified by flash chromatography (gradient elution, 0-30% AcOEt in hexanes) affording the keto-lactone **7b** (0.180 g, 1.06 mmol, 76%) as a colorless oil.

5.3. 9-Methyl-oxecane-2,8-dione (7e). The reaction was performed following the general procedure, stirring a 2:3 mixture of β -hydroxyethers **3e** and **3e'** (0.172 g, 1.01 mmol), $\text{RuCl}_3 \cdot n\text{H}_2\text{O}$ (3.0 mol%, *ca.* 0.007 g), NaIO_4 (0.886 g, 4.14 mmol) in 7.0 mL of a 3:2:2 mixture of $\text{H}_2\text{O}/\text{CCl}_4/\text{CH}_3\text{CN}$ at rt for 90 min. The crude product was purified by flash chromatography (eluent, 20% AcOEt in hexanes) affording the keto-lactone **7e** (0.117 g, 0.636 mmol, 63%) as a colorless oil.

5.4. 9-Ethyl-oxecane-2,8-dione (7f). The reaction was performed following the general procedure, stirring a 7:3 mixture of β -hydroxyethers **3f** and **3f'** (0.085 g, 0.462 mmol), $\text{RuCl}_3 \cdot n\text{H}_2\text{O}$ (3.0 mol%, *ca.* 0.003 g), NaIO_4 (0.404 g, 1.89 mmol) in 7.0 mL of a 3:2:2 mixture of $\text{H}_2\text{O}/\text{CCl}_4/\text{CH}_3\text{CN}$ at rt for 90 min, leading to the keto-lactone **7f** (0.079 g, 0.40 mmol, 86%) as a colorless oil.

6. Preparation of β -hydroxyethers 9a and 9b. The β -hydroxyethers **9a** and **9b** were prepared by thallium triacetate-mediated cyclization of commercially available (-)-isopulegol and (+)-neoisopulegol, respectively, according to a previously described procedure.¹⁰ Spectral data are in agreement with literature.¹⁰

(1R,3S,4R,8R)-3,9-Oxa-*p*-menthanol-8 (9a):¹⁰ ^1H NMR (300 MHz, CDCl_3) δ 0.80-0.98 (m, 1H), 0.89 (d, $J = 6.6$ Hz, 3H), 1.25 (ddd, $J = 3.5, 11.6$ and 14.8 Hz, 1H), 1.30-1.42 (m, 1H), 1.44 (s, 3H), 1.59-1.79 (m, 4H), 1.93-2.00 (m, 1H), 3.65 (d, $J = 8.7$ Hz, 1H), 3.80 (d, $J = 8.7$ Hz, 1H), 4.09 (q, $J = 3.2$ Hz, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ 22.2, 22.9, 26.5, 27.9, 32.8, 37.5, 47.6, 78.0, 78.1, 79.8.

(1R,3R,4R,8R)-3,9-Oxa-*p*-menthanol-8 (9b):¹⁰ ^1H RMN (300 MHz, CDCl_3) δ 0.88-1.20 (m, 3H), 0.99 (d, $J = 6.6$ Hz, 3H), 1.26 (s, 3H), 1.34-1.55 (m, 2H), 1.74-1.86 (m, 3H), 2.04-2.12 (m, 1H), 3.24 (dt, $J = 4.0$ and 10.9 Hz, 1H), 3.68 (d, $J = 9.3$ Hz, 1H), 3.88 (d, $J = 9.3$ Hz, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ 22.0, 22.8, 22.9, 31.1, 34.5, 40.4, 56.7, 78.1, 81.3, 82.3.

7. Reaction of β -hydroxyethers 9a with Ruthenium Tetraoxide. To a solution of **9a** (0.227 g, 1.34 mmol) in 10.5 mL of a mixture of $\text{H}_2\text{O}:\text{CCl}_4:\text{CH}_3\text{CN}$ (3:2:2) was added NaIO_4 (1.17 g, 5.49 mmol) and $\text{RuCl}_3 \cdot n\text{H}_2\text{O}$ (0.014 g, 5.0 mol%). The reaction mixture was magnetically stirred at rt for 30 min. Then, water was added and the aqueous phase was extracted with CH_2Cl_2 (three times). The combined organic phases were washed with brine (twice) and dried over anhydrous MgSO_4 . The solvent was removed under reduced pressure and the crude product was purified by flash

chromatography (gradient elution 0-20% AcOEt in hexanes) affording **10** (0.101 g, 0.656 mmol, 48%).

2-Acetyl-5-methyl-cyclohexanone (10):¹¹ colorless oil; ¹H NMR (300 MHz, CDCl₃) δ 1.00 (d, *J* = 6.5 Hz, 3H), 1.18-1.32 (m, 1H), 1.70-1.85 (m, 2H), 1.94-2.03 (m, 1H), 2.13 (s, 3H), 2.30-2.43 (m, 3H), 5.9 (s, 1H); ¹³C NMR (125 MHz, CDCl₃) δ 21.3, 23.8, 25.1, 28.0, 30.9, 39.2, 106.5, 181.6, 199.0. Dione **10** exists predominantly in the enol form.^{11b}

8. Reaction of β-hydroxyethers **9b with Ruthenium Tetraoxide.** To a solution of **9b** (1.03 g, 6.06 mmol) in 42 mL of a mixture of H₂O:CCl₄:CH₃CN (3:2:2) was added NaIO₄ (5.17 g, 24.2 mmol) and RuCl₃·*n*H₂O (0.063 g, 5.0 mol%). The reaction mixture was magnetically stirred at rt for 4 hours. Then, water was added and the aqueous phase was extracted with CH₂Cl₂ (three times). The combined organic phases were washed with brine (twice) and dried over anhydrous MgSO₄. The solvent was removed under reduced pressure and the crude product was purified by flash chromatography (gradient elution 0-50% AcOEt in hexanes) affording the dione **10**¹¹ (0.371 g, 2.41 mmol, 40%), the ceto-formate **11** (0.129 g, 0.701 mmol, 12%) and the α-hydroxy-lactone **12** (0.162 g, 0.880 mmol, 15%).

Formic acid 2-acetyl-5-methyl-cyclohexyl ester (11): viscous colorless oil; IR (film) 1722 cm⁻¹; LRMS *m/z* 185 (11, M⁺+1); ¹H NMR (500 MHz, CDCl₃) δ 0.95 (d, *J* = 6.6 Hz, 3H), 0.93-1.07 (m, 2H), 1.37 (dq, *J* = 3.6 and 13.2 Hz, 1H), 1.55-1.61 (m, 1H), 1.73-1.78 (m, 1H), 1.97 (qd, *J* = 3.6 and 13.2 Hz, 1H), 2.11-2.16 (m, 1H), 2.18 (s, 3H), 2.63 (ddd, *J* = 3.8, 10.6 and 12.7 Hz, 1H), 5.10 (dt, *J* = 4.5 and 10.9 Hz, 1H); ¹³C NMR (125 MHz, CDCl₃) δ 21.8, 27.8, 29.3, 30.8, 33.3, 39.3, 55.1, 73.1, 160.3, 209.5; Anal. Calcd for C₁₀H₁₆O₃: C, 65.19; H, 8.75. Found: C, 65.20; H, 8.70.

3-Hydroxy-3,6-dimethyl-hexahydro-benzofuran-2-one (12): white solid; IR (KBr) 3471, 1764 cm⁻¹; LRMS *m/z* 140 (8.7, M⁺); ¹H NMR (300 MHz, CDCl₃) δ 0.99-1.13 (m, 1H), 1.03 (d, *J* = 6.6 Hz,

3H), 1.20-1.37 (m, 2H), 1.31 (s, 3H), 1.55-1.65 (m, 1H), 1.81-2.01 (m, 3H), 2.22-2.29 (m, 1H), 2.97 (br s, H-OH), 3.81 (dt, $J = 3.9$ and 11.0 Hz, 1H); ^{13}C NMR (125 MHz, CDCl_3) δ 18.1, 22.0, 22.5, 31.3, 33.8, 38.7, 53.6, 74.8, 79.9, 180.5; Anal. Calcd for $\text{C}_{10}\text{H}_{16}\text{O}_3$: C, 65.19; H, 8.75. Found: C, 64.95; H, 8.35.

Figure S1. ^1H NMR spectrum of **1a** (CDCl_3 , TMS, 300 MHz)

Figure S2. ^{13}C NMR spectrum of **1a** (CDCl_3 , TMS, 75 MHz)

Figure S3. ^1H NMR spectrum of **1b** (CDCl_3 , TMS, 300 MHz)

Figure S4. ^{13}C NMR spectrum of **1b** (CDCl_3 , TMS, 75 MHz)

Figure S5. ^1H NMR spectrum of **1c** (CDCl_3 , TMS, 300 MHz)

Figure S6. ^{13}C NMR spectrum of **1c** (CDCl_3 , TMS, 75 MHz)

Figure S7. ^1H NMR spectrum of **1d** (CDCl_3 , TMS, 300 MHz)

Figure S8. ^{13}C NMR spectrum of **1d** (CDCl_3 , TMS, 75 MHz)

Figure S9. ^1H NMR spectrum of **1e** (CDCl_3 , TMS, 500 MHz)

Figure S10. ^{13}C NMR spectrum of **1e** (CDCl_3 , TMS, 125 MHz)

Figure S11. ^1H NMR spectrum of **1f** (CDCl_3 , TMS, 300 MHz)

Pulse Sequence: s2pu1
 Solvent: CDCl₃
 Ambient temperature
 INOVA-300 "inovai"
 Relax. delay 0.300 sec
 Pulse 45.0 degrees
 Acq. time 1.765 sec
 Width 18859.0 Hz
 1040 repetitions
 OBSERVE C13, 75.4216832 MHz
 DECOUPLE H1, 299.9483516 MHz
 Power 35 dB
 continuously on
 WALTZ-16 modulated
 DATA PROCESSING
 Line broadening 1.0 Hz
 FT size 131072
 Total time 1 hr, 10 min, 46 sec

Figure S12. ¹³C NMR spectrum of **1f** (CDCl₃, TMS, 75 MHz)

Figure S13. ^1H NMR spectrum of **1g** (CDCl_3 , TMS, 300 MHz)

Figure S14. ^{13}C NMR spectrum of **1g** (CDCl_3 , TMS, 75 MHz)

Figure S15. ^1H NMR spectrum of **2a** (CDCl_3 , TMS, 300 MHz)

Figure S16. ^{13}C NMR spectrum of **2a** (CDCl_3 , TMS, 125 MHz)

Figure S17. ¹H NMR spectrum of **2b** (CDCl₃, TMS, 300 MHz)

Figure S18. ^{13}C NMR spectrum of **2b** (CDCl_3 , TMS, 75 MHz)

Figure S19. ¹H NMR spectrum of **2c** (CDCl₃, TMS, 300 MHz)

Figure S20. ^{13}C NMR spectrum of **2c** (CDCl_3 , TMS, 75 MHz)

Figure S21. ^1H NMR spectrum of **2d** (CDCl_3 , TMS, 500 MHz)

Current Data Parameters
 NAME LuizSidney
 EXPNO 30
 PROCNO 1

F2 - Acquisition Parameters
 Date_ 20021114
 Time 9.53
 INSTRUM spect
 PROBHD 5 mm Multinuc1
 PULPROG zgpg30
 TD 65536
 SOLVENT CDCl3
 NS 353
 DS 4
 SWH 32679.738 Hz
 FIDRES 0.498653 Hz
 AQ 1.0027508 sec
 RG 32768
 DM 15.300 usec
 DE 6.00 usec
 TE 300.0 K
 D1 1.00000000 sec
 d11 0.03000000 sec
 d12 0.0002000 sec

===== CHANNEL f1 =====
 NUC1 13C
 P1 13.30 usec
 PL1 0.00 dB
 SF01 125.7716224 MHz

===== CHANNEL f2 =====
 CPDPRG2 waltz16
 NUC2 1H
 PCPD2 116.00 usec
 PL2 0.00 dB
 PL12 20.87 dB
 PL13 20.00 dB
 SF02 500.1320005 MHz

F2 - Processing parameters
 SI 32768
 SF 125.7578042 MHz
 NDN EM
 SSB 0
 LB 1.00 Hz
 GB 0
 PC 1.40

1D NMR plot parameters
 CX 23.00 cm
 CY 15.00 cm
 F1P 230.000 ppm
 F1 28924.29 Hz
 F2P -10.000 ppm
 F2 -1257.58 Hz
 PPMCM 10.43478 ppm/cm
 HZCM 1312.25537 Hz/cm

Figure S22. ^{13}C NMR spectrum of **2d** (CDCl_3 , TMS, 125 MHz)

Figure S23. ^1H NMR spectrum of **2e** (CDCl_3 , TMS, 500 MHz)

Figure S24. ^{13}C NMR spectrum of **2e** (CDCl_3 , TMS, 125 MHz)

Figure S25. ^1H NMR spectrum of **2f** (CDCl_3 , TMS, 500 MHz)

Figure S26. ^{13}C NMR spectrum of **2f** (CDCl_3 , TMS, 75 MHz)

Figure S27. ¹H NMR spectrum of **2g** and **2g'** (CDCl₃, TMS, 300 MHz)

Figure S28. ^{13}C NMR spectrum of **2g** and **2g'** (CDCl_3 , TMS, 75 MHz)

(ca. 15% of epoxyalcohol **2g**)

Figure S29. ^1H NMR spectrum of **3g** and **4** (CDCl_3 , TMS, 300 MHz)

Figure S30. ^{13}C NMR spectrum of **3g** and **4** (CDCl_3 , TMS, 75 MHz)

Figure S31. ^1H NMR spectrum of **3g'** and **5** (CDCl_3 , TMS, 300 MHz)

Figure S32. ^{13}C NMR spectrum of **3g'** and **5** (CDCl_3 , TMS, 75 MHz)

Figure S33. ^1H NMR spectrum of **6** (CD_3OD , TMS, 300 MHz)

Current Data Parameters
 NAME LuizSidney
 EXPNO 1
 PROCNO 1

F2 - Acquisition Parameters

Date_ 500000
 Time 10.18
 INSTRUM spect
 PROBHD 5 mm Dual 13
 PULPROG zgpg30
 TD 65536
 SOLVENT MeOH
 NS 142
 DS 2
 SWH 32679.738 Hz
 FIDRES 0.498653 Hz
 AQ 1.0027508 sec
 RG 32768
 DW 15.300 usec
 DE 6.00 usec
 TE 300.0 K
 d11 0.0300000 sec
 d12 0.0000200 sec
 PL13 17.00 dB
 D1 1.00000000 sec
 CPDPRG2 waltz16
 PCPD2 105.00 usec
 SF02 500.1320005 MHz
 NUC2 1H
 PL2 0.00 dB
 PL12 17.00 dB
 P1 7.20 usec
 DE 6.00 usec
 SF01 125.7715724 MHz
 NUC1 13C
 PL1 1.00 dB

F2 - Processing parameters

SI 32768
 SF 125.7576153 MHz
 WDN EM
 SSB 0
 LB 1.00 Hz
 GB 0
 PC 1.40

1D NMR plot parameters

CX 22.00 cm
 F1P 230.000 ppm
 F1 28924.25 Hz
 F2P -10.000 ppm
 F2 -1257.58 Hz
 PPMCM 10.90909 ppm/cm
 HZCM 1371.90125 Hz/cm

Figure S34. ^{13}C NMR spectrum of 6 (CD_3OD , TMS, 300 MHz)

Figure S35. ^1H NMR spectrum of **3a** (CDCl_3 , TMS, 300 MHz)

Figure S36. ^{13}C NMR spectrum of **3a** (CDCl_3 , TMS, 75 MHz)

Figure S37. ^1H NMR spectrum of **3b** and **3b'** (CDCl_3 , TMS, 300 MHz)

Figure S38. ^{13}C NMR spectrum of **3b** and **3b'** (CDCl_3 , TMS, 75 MHz)

Figure S39. ^1H NMR spectrum of **3c** (CDCl_3 , TMS, 300 MHz)

Figure S40. ^{13}C NMR spectrum of **3c** (CDCl_3 , TMS, 75 MHz)

24/09/2002 (1 hora)

Current Data Parameters

NAME	LuizSidney
EXPNO	26
PROCNO	1

F2 - Acquisition Parameters

Date_	500000
Time	10.05
INSTRUM	spect
PROBHD	5 mm Dui113
PULPROG	cosy45
TD	2048
SOLVENT	CDCl3
NS	8
DS	16
SWH	2777.778 Hz
FIDRES	1.356337 Hz
AQ	0.3686900 sec
RG	256
DN	180.000 usec
DE	6.00 usec
TE	300.0 K
D1	1.50000000 sec
P1	8.00 usec
DO	0.0000300 sec
DE	8.00 usec
SFO1	300.1312484 MHz
NUC1	1H
PL1	1.00 dB
INO	0.0003600 sec

F1 - Acquisition parameters

ND0	1
TD	256
SFO1	300.1313 MHz
FIDRES	10.850883 Hz
SH	9.255 ppm

F2 - Processing parameters

S1	2048
SF	300.1309923 MHz
WDW	SINE
SSB	0
LB	0.00 Hz
GB	0
PC	1.00

F1 - Processing parameters

S1	1024
MC2	0F
SF	300.1300106 MHz
WDW	SINE
SSB	0
LB	0.00 Hz
GB	0

2D NMR plot parameters

CX2	15.00 cm
CX1	15.00 cm
F2PLO	4.512 ppm
F2LO	1354.28 Hz
F2PHI	0.490 ppm
F2H1	147.14 Hz
F1PLO	4.501 ppm
F1LO	1350.95 Hz
F1PHI	0.506 ppm
F1H1	151.95 Hz
F2PPMCM	0.26814 ppm/cm
F2HZCM	80.47598 Hz/cm
F1PPMCM	0.26633 ppm/cm
F1HZCM	79.93336 Hz/cm

Figure S41. COSY spectrum of **3c** (CDCl₃, TMS, 300 MHz)

Figure S42. ^1H NMR spectrum of **3c'** (CDCl_3 , TMS, 300 MHz)

Figure S43. ^{13}C NMR spectrum of **3c'** (CDCl_3 , TMS, 75 MHz)

25/09/2002 (1 hora)

Current Data Parameters

NAME	Lui25.
EXPNO	10
PROCNO	1

F2 - Acquisition Parameters

Date_	500000
Time	1.20
INSTRUM	spect
PROBHD	5 mm Duol 13
PULPROG	cosy45
TD	2048
SOLVENT	CDCl3
NS	16
DS	16
SWH	2976.190 Hz
FIDRES	1.453218 Hz
AQ	0.3441140 sec
RG	64
DM	168.000 usec
DE	6.00 usec
TE	300.0 K
D1	1.50000000 sec
P1	8.00 usec
DO	0.00000300 sec
DE	6.00 usec
SFO1	300.1312305 MHz
NUC1	1H
PL1	1.00 dB
IN0	0.00033600 sec

F1 - Acquisition parameters

NO0	1
TD	100
SFO1	300.1312 MHz
FIDRES	29.761904 Hz
SW	9.916 ppm

F2 - Processing parameters

SI	2048
SF	300.1299963 MHz
MDM	SINE
SSB	0
LB	0.00 Hz
GB	0
PC	1.00

F1 - Processing parameters

SI	1024
NC2	0F
SF	300.1299967 MHz
MDM	SINE
SSB	0
LB	0.00 Hz
GB	0

2D NMR plot parameters

CX2	15.00 cm
CX1	15.00 cm
F2PL0	4.311 ppm
F2L0	1293.86 Hz
F2PH1	0.496 ppm
F2H1	148.72 Hz
F1PL0	4.305 ppm
F1L0	1291.96 Hz
F1PH1	0.509 ppm
F1H1	152.64 Hz
F2PMCM	0.25436 ppm/cm
F2HZCM	76.34236 Hz/cm
F1PMCM	0.25307 ppm/cm
F1HZCM	75.95486 Hz/cm

Figure S44. COSY spectrum of **3c'** (CDCl₃, TMS, 300 MHz)

25/09/2002 (2 horas)

Current Data Parameters
 NAME LuizS.
 EXPNO 11
 PROCNO 1

F2 - Acquisition Parameters
 Date_ 500000
 Time 2.12
 INSTRUM spect
 PROBHD 5 mm Dui 13
 PULPROG hnce
 TD 2048
 SOLVENT CDCl3
 NS 64
 DS 16
 SWH 20060.320 Hz
 FIDRES 9.604844 Hz
 AQ 0.0510452 sec
 RG 11505.2
 CH 24.900 usec
 DE 6.00 usec
 TE 300.0 K
 D11 0.03000000 sec
 D1 1.50000000 sec
 D12 0.0002000 sec
 PL2 0.00 dB
 P3 8.60 usec
 SF02 300.1312305 MHz
 NS2 1H
 D0 0.00000300 sec
 P2 15.40 usec
 D2 0.00345000 sec
 P1 7.70 usec
 D3 0.00230000 sec
 PL12 22.00 dB
 DE 6.00 usec
 SF01 75.4760204 MHz
 PL1 13C
 PL1 4.00 dB
 CPDPRG2 waltz16
 PCPD2 105.00 usec
 IN0 0.00016794 sec

F1 - Acquisition parameters
 NS0 2
 TD 128
 SF01 300.1312 MHz
 FIDRES 23.260112 Hz
 CH 9.520 ppm

F2 - Processing parameters
 SI 2048
 SF 75.4677471 MHz
 WDW 65INE
 SSB 0
 LB 0.00 Hz
 GB 0
 PC 1.40

F1 - Processing parameters
 SI 1024
 SF 300.1299562 MHz
 WDW 65INE
 SSB 0
 LB 0.00 Hz
 GB 0

2D NMR plot parameters
 CX2 15.00 cm
 CX1 15.00 cm
 F2H0 99.984 ppm
 F2L0 7538.01 Hz
 F2PHI -0.285 ppm
 F2HI -21.53 Hz
 F1H0 5.004 ppm
 F1L0 1501.81 Hz
 F1PHI -0.005 ppm
 F1HI -1.38 Hz
 F2H2CH 6.67794 ppm/cm
 F2H2CH 503.96962 Hz/cm
 F1H2CH 0.33390 ppm/cm
 F1H2CH 100.21257 Hz/cm

Figure S45. HETCOR spectrum of **3c'** (CDCl₃, TMS, 300 MHz)

Figure S46. ¹H NMR spectrum of **3d** (CDCl₃, TMS, 500 MHz)

Figure S47. ^{13}C NMR spectrum of **3d** (CDCl_3 , TMS, 125 MHz)

Figure S48. ^1H NMR spectrum of **3e** (CDCl_3 , TMS, 500 MHz)

3e

Figure S49. ^{13}C NMR spectrum of **3e** (CDCl_3 , TMS, 125 MHz)

Figure S50. ^1H NMR spectrum of **3e'** (CDCl_3 , TMS, 500 MHz)

Figure S51. ^{13}C NMR spectrum of **3e'** (CDCl_3 , TMS, 125 MHz)

Figure S52. ^1H NMR spectrum of **3f** (CDCl_3 , TMS, 500 MHz)

Figure S53. ^{13}C NMR spectrum of **3f** (CDCl_3 , TMS, 125 MHz)

Figure S54. ^1H NMR spectrum of **3f** and **3f'** (CDCl_3 , TMS, 300 MHz)

Figure S55. ^{13}C NMR spectrum of **3f** and **3f'** (CDCl_3 , TMS, 75 MHz)

Figure S56. ^1H NMR spectrum of **7a** (CDCl_3 , TMS, 200 MHz)

Figure S57. ^{13}C NMR spectrum of **7a** (CDCl_3 , TMS, 50 MHz)

Figure S58. ^1H NMR spectrum of **7b** (CDCl_3 , TMS, 500 MHz)

Pulse Sequence: s2pul
 Solvent: CDCl₃
 Ambient temperature
 INOVA-300 "inova1"
 Relax. delay 0.200 sec
 Pulse 45.0 degrees
 Acq. time 1.765 sec
 Width 18859.0 Hz
 560 repetitions
 OBSERVE C13, 75.4216817 MHz
 DECOUPLE H1, 299.9483516 MHz
 Power 35 dB
 continuously on
 WALTZ-16 modulated
 DATA PROCESSING
 Line broadening 1.0 Hz
 FT size 131072
 Total time 1 hr, 7 min, 21 sec

Figure S59. ¹³C NMR spectrum of **7b** (CDCl₃, TMS, 75 MHz)

Figure S60. ^1H NMR spectrum of **7c** (CDCl_3 , TMS, 500 MHz)

Figure S61. ^{13}C NMR spectrum of **7c** (CDCl_3 , TMS, 125 MHz)

Figure S62. ¹H NMR spectrum of **7d** and **8** (CDCl₃, TMS, 200 MHz)

Figure S63. ¹³C NMR spectrum of **7d** and **8** (CDCl₃, TMS, 50 MHz)

Figure S64. ^1H NMR spectrum of **7e** (CDCl_3 , TMS, 500 MHz)

Pulse Sequence: s2pu1
 Solvent: CDCl₃
 Ambient temperature
 INOVA-300 "inova1"
 Relax. delay 0.500 sec
 Pulse 45.0 degrees
 Acq. time 1.765 sec
 Width 18859.0 Hz
 512 repetitions
 OBSERVE C13, 75.4216841 MHz
 DECOUPLE H1, 299.9483516 MHz
 Power 35 dB
 continuously on
 WALTZ-16 modulated
 DATA PROCESSING
 Line broadening 1.0 Hz
 FT size 131072
 Total time 1 hr, 17 min, 36 sec

Figure S65. ¹³C NMR spectrum of 7e (CDCl₃, TMS, 75 MHz)

Current Data Parameters
NAME LuizSidney
EXPNO 8
PROCNO 1

F2 - Acquisition Parameters
Date_ 20030117
Time 11.49
INSTRUM spect
PROBHD 5 mm Dual 13C/
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 0
SWH 5175.983 Hz
FIDRES 0.078979 Hz
AQ 6.3308277 sec
RG 101.6
DW 96.600 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec

===== CHANNEL f1 =====
NUC1 1H
P1 10.50 usec
PL1 -3.00 dB
SF01 500.1322016 MHz

F2 - Processing parameters
SI 32768
SF 500.1299952 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00

1D NMR plot parameters
CX 23.00 cm
CY 12.50 cm
F1P 9.000 ppm
F1 4501.17 Hz
F2P -0.500 ppm
F2 -250.06 Hz
PPMCM 0.41304 ppm/cm
HZCM 206.57542 Hz/cm

Figure S66. ¹H NMR spectrum of **7f** (CDCl₃, TMS, 500 MHz)

Figure S67. ^1H NMR spectrum of **7f** (CDCl_3 , TMS, 125 MHz)

9. References

- (1) WARNING! Thallium salts are toxic and must be handled with care.
- (2) Zinc powder was activated by washing several times with 10% aqueous HCl, water, saturated aqueous HgCl₂, water and acetone. The zinc obtained was then dried in an oven (ca. 120°C) and stored in a desiccator.
- (3) Thionyl chloride was distilled from linseed oil (50 g of SOCl₂/20 g of linseed oil).
- (4) (a) Benkeser R.A.; Arnold, Jr., C.; Lambert, R.F.; Thomas, O.H. *J. Am. Chem. Soc.* **1955**, 77, 6042; (b) Barluenga, J.; Alvarez, F.; Concellon, J.M.; Yus, M. *Synthesis* **1986**, 654.
- (5) Barluenga, J.; Alvarez, F.; Concellon, J.M.; Yus, M. *J. Chem. Res. (M)* **1987**, 3264.
- (6) Lillie, T.S.; Ronald, R.C. *J. Org. Chem.* **1985**, 50, 5884.
- (7) Ferraz, H. M. C.; Longo, Jr., L. S.; Zukerman-Schpector, J. *J. Org. Chem.* **2002**, 67, 3518.
- (8) Spectroscopic data of a pure sample of allylic alcohol **5**, obtained in a test of the base promoted-cyclization of epoxyalcohols **2g/2g'** using NaH in THF.
- (9) Das, J.; Chandrasekaran, S. *Tetrahedron* **1994**, 50, 11709.
- (10) Ferraz, H. M. C.; Grazini, M. V. A.; Ribeiro, C. M. R.; Brocksom, U.; Brocksom, T. J. *J. Org. Chem.* **2000**, 65, 2606.
- (11) (a) Descotes, G.; Yvon, Q. *Bull. Soc. Chim. Fr.* **1968**, 8, 3395; (b) Snider, B. B.; Shi, Z. *J. Am. Chem. Soc.* **1992**, 114, 1790.