The Methoxyallene Approach to Oxacycles, Part 2: Stereoselective Synthesis of 2,3-Disubstituted Oxepanes

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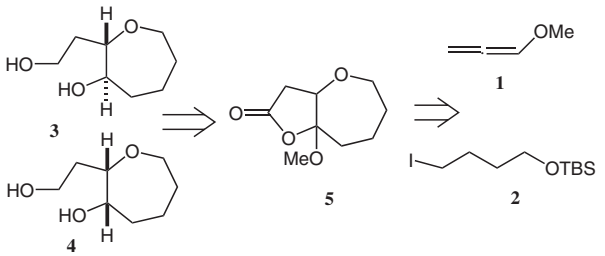
Dedicated to Professor P. J. Kocienski for the experience in allene chemistry we gained under his guidance at the University of Southampton.

Abstract: 2,3-Disubstituted oxepanes **3** and **4** were stereoselectively synthesized from methoxyallene (**1**) and iodide **2**. The *trans* stereochemistry of diol **3** was established by NMR studies of the bicyclic precursor **10**, while the *cis* stereochemistry of **4** was secured by using the highly diastereoselective reducing agent L-Selectride.

Key words: natural products, methoxyallene, Michael addition, oxepanes, toxins

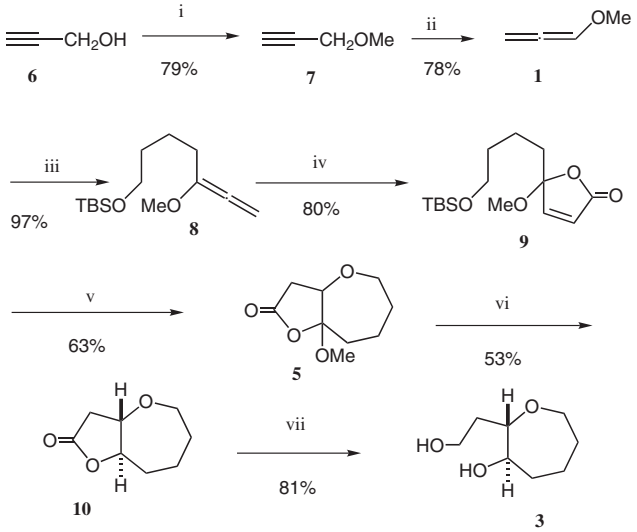
Fused polycyclic ethers with *trans-syn-trans* stereochemistry are the common framework of various marine polyether compounds, including brevetoxins,[1] maitotoxin,[2] and ciguatoxins.[3] Their unusual molecular architecture makes them challenging synthetic targets for organic chemists. We recently reported a new method for the synthesis of oxacycles using either methoxyallene[4a] or furan[4b,c] as starting material. In this paper, we report a full account of the methoxyallene approach, describing the stereoselective synthesis of *trans*- and *cis*-2,3-disubstituted oxepanes **3** and **4** following the retrosynthetic analysis depicted in Scheme 1.



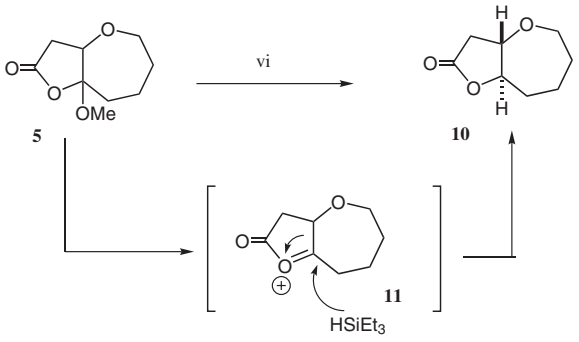
Scheme 1

trans-2,3-Disubstituted oxepane **3** was synthesized from propargyl alcohol (**6**) via methoxyallene (**1**) as detailed in Scheme 2.

Propargyl alcohol (**6**) was O-methylated with dimethyl sulfate giving 3-methoxyprop-1-yne (**7**).[5] Isomerization of **7** with potassium *tert*-butoxide afforded methoxyallene (**1**) in high yield.[6] Sequential metalation, alkylation, metalation and carboxylation of **1** afforded, after acidic work-up,[7] butenolide **9** (78% from **1**). Removal of the TBS group of **9** with TBAF then gave the bicyclic compound **5** as a single isomer through an intramolecular Michael addition (63% yield). Finally, reduction of **5** with Et_3SiH (3.0 equiv) in the presence of TMSOTf (2.4 equiv)[8] in CH_2Cl_2 gave compound **10** in 53% yield, presumably via oxonium ion intermediate **11** (Scheme 3; note that the stereochemical course of this reaction does not depend on whether the ring junction of **5** is *cis* or *trans*).



Scheme 2 *Reagents and conditions*: (i) Me_2SO_4, NaOH; (ii) *t*-BuOK (10%); (iii) *n*-BuLi/THF, –30 °C, **2**; (iv) *t*-BuLi/THF, –70 °C, 1 h, CO_2; 10% H_2SO_4–Et_2O, 0 °C, 1 h; (v) TBAF/THF, r.t., 2 h; (vi) TMSOTf, Et_3SiH, CH_2Cl_2, r.t., 6 h; (vii) LAH, Et_2O, r.t.



Scheme 3

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The structure of **10** was determined from its ^1H and ^{13}C NMR, NOE, NOESY, COSY and HMBC spectra (Figure 1).

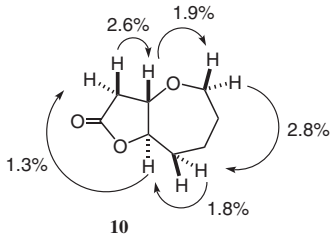


Figure 1 NOE correlations for **10**

The synthesis of *cis*-oxepane diol **4** was achieved using the highly diastereoselective L-Selectride reduction of ketone **13** (Scheme 4).

Bicyclic lactone **5** was opened using $LiAlH_4$ in the presence of $BF_3{\cdot}OEt_2$ to afford a 91% yield of **11** as a mixture of diastereoisomeric diols (**3** and **4**). Selective protection of the primary alcohol of **11** afforded **12** in 86% yield, which was oxidized with tetrapropylammonium perruthenate (TPAP) to give ketone **13** in 95% yield. Reduction of **13** with L-Selectride afforded stereoselectively alcohol **14** (76% yield). The *tert*-butyldimethylsilyl (TBS) protecting group of **14** was removed by tetrabutylammonium fluoride (TBAF) to give finally the desired *cis*-diol **4** in 78% yield.

In conclusion, a new and efficient method for the stereoselective synthesis of *trans*- and *cis*-2,3-disubstituted oxepanes **3** and **4** from methoxyallene has been developed. Work is now in progress towards the enantioselective synthesis of highly substituted oxepanes, precursors of biologically active natural products.

IR spectra were recorded in a Perkin-Elmer 1640FT spectrometer. ^1H and ^{13}C NMR spectra were recorded on a Bruker AMX spectrometer at 400 and 100.61 MHz, respectively, using TMS as internal standard (chemical shifts in δ values, *J* in Hz). Mass spectrometry was carried out with a Hewlett Packard 5988A spectrometer. Flash chromatography (FC) was performed on silica gel (Merck 60, 230–400 mesh); analytical TLC was performed on plates precoated with silica gel (Merck 60 F254, 0.25 mm).

3-Methoxypropyne (7)

To a mixture of propargyl alcohol **6** (168 g, 174 mL, 2.99 mol) and H_2O (132 mL) was added a 50% aq solution of NaOH (330 g), and the mixture was stirred with a mechanical stirrer. The temperature was brought from 70 °C to which it had risen to 40 °C, and was kept below 60 °C during addition of dimethyl sulfate (225 g, 169 mL, 1.78 mol). After stirring at 50–60 °C for 2 h, distillation gave a product that came over at 61–62 °C, which was dried ($CaCl_2$) overnight. Finally, redistillation of this product at atmospheric pressure using a Dufton column and a cooled receiver afforded 166.4 g of **7** (79%); colorless oil; bp 60 °C/760 Torr.

^1H NMR ($CDCl_3$): δ = 4.01 (2 H, s, CH_2), 3.31 (3 H, s, OCH_3), 2.35 (1 H, s, CH).

^{13}C NMR ($CDCl_3$): δ = 79.2 (C), 74.3 (CH), 59.2 (CH_2), 57.0 (CH_3).

1-Methoxypropadiene (1)

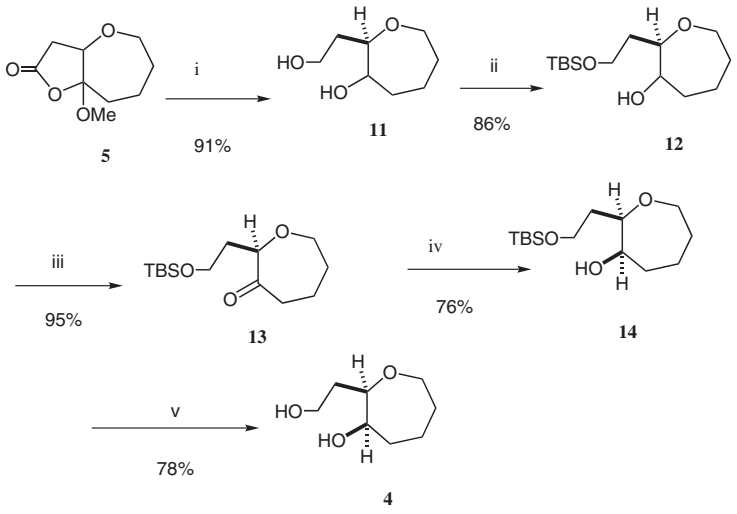
t-BuOK (13.8 g, 0.118 mol) was added in one portion to propargyl ether **7** (83 g, 1.18 mol) in a 250 mL round-bottomed flask fitted with a double surface condenser and a mechanical stirrer. After heating in an oil bath at 70 °C for 3 h, the mixture was allowed to cool to r.t., the condenser and the mechanical stirrer were removed and the reaction flask was connected to a receiver cooled with liquid N_2. Vacuum distillation without heating afforded a colorless oil that was dried over KOH, kept in a refrigerator for 1 h, and then distilled under N_2, affording 64.8 g of **1** (78%); colorless oil; bp 50 °C/760 Torr.

^1H NMR ($CDCl_3$): δ = 6.75 (1 H, t, *J* = 5.9 Hz, CH), 5.45 (2 H, d, *J* = 5.9 Hz, CH_2), 3.39 (3 H, s, OCH_3).

^{13}C NMR ($CDCl_3$): δ = 201.8 (C), 122.8 (CH), 91.0 (CH_2), 55.7 (CH_3).

4-Dimethyl-*tert*-butylsiloxy-1-iodobutane (2)

A solution of *tert*-butyldimethylsilyl chloride (25 g, 0.166 mol) in MeCN (200 mL) was added to a solution of NaI (37.3 g, 0.249 mol) in THF (50 mL). The mixture was stirred for 7 days at r.t. in the dark, poured into hexane (200 mL), and the hexane layer was



Scheme 4 *Reagents and conditions*: (i) $BF_3{\cdot}OEt_2$, $LiAH_4$, Et_2O, r.t.; (ii) TBSCl, DMF, imidazole, DMAP; (iii) TPAP, NMO, CH_2Cl_2; (iv) L-Selectride, THF, –78 °C; (v) TBAF/THF, r.t., 2 h.

washed with $NaHCO_3$ solution containing a little $Na_2S_2O_3$ (100 mL). The aqueous and MeCN layers were separated and sequentially extracted with hexane (2 × 100 mL). The combined hexane layers were washed with brine (50 mL), dried (Na_2SO_4), and the solvent was removed. Vacuum distillation of the residue afforded 40 g of **2** (76%); bp 132–134 °C/15 Torr.

^{1}H NMR ($CDCl_3$): δ = 3.61 (2 H, t, *J* = 6.2 Hz, CH_2-4), 3.20 (2 H, t, *J* = 7.0 Hz, CH_2-1), 1.88 (2 H, m, CH_2), 1.61 (2 H, m, CH_2), 0.87 (9 H, s, *t*-C_4H_9), 0.02 [6 H, s, $(CH_3)_2Si$].

^{13}C NMR ($CDCl_3$): δ = 61.9 (C-4), 33.4 (C-2), 30.2 (C-3), 25.9 [C(*C*$H_3)_3$], 25.7 [C(*C*$H_3)_3$], 25.6 [C(*C*$H_3)_3$], 18.2 (C), 7 (C-1), –5.4 (CH_3Si).

LRMS: *m*/*z* (%) = 257 (100), 215 (94), 189 (14), 185 (62), 147 (27), 129 (19), 85 (15), 83 (23), 75 (35), 73 (21).

HRMS: *m*/*z* calcd for $C_{10}H_{23}IOSi$: 314.0563; found: 314.0550.

3-Methoxy-7-*tert*-butyldimethylsiloxyhepta-1,2-diene (8)

n-BuLi (28.5 mL of a 2.6 M solution in hexane, 0.075 mol) was added at –25 °C to 1-methoxypropadiene (**1**; 5.4 g, 0.078 mol) in THF (30 mL). The mixture was stirred for 1 h at –25 °C and then cooled to –30 °C. Iodide **2** (18.03 g, 0.057 mol) was added to the mixture at this temperature, and after stirring for a further 4 h, the mixture was poured into a separating funnel containing sat. aq $NaHCO_3$ solution (33 mL) and hexane (66 mL). The organic layer was washed with H_2O (16 mL), brine (33 mL), and dried (Na_2SO_4). The solvent was removed, and the residue was filtered through basic alumina using 5% Et_3N in hexane as eluent, affording 9.5 g of **8** (97%); colorless oil.

IR (KBr): 2970, 2940, 2860, 1965, 1470, 1265, 1110, 840, 780 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 5.35 (2 H, d, *J* = 2.3 Hz, CH_2-1), 3.36 (3 H, s, OCH_3), 2.12–2.31 (2 H, m, CH_2-4), 1.46–1.66 (6 H, m), 0.86 (9 H, s, *t*-C_4H_9), 0.02 [6 H, s, $(CH_3)Si$].

^{13}C NMR ($CDCl_3$): δ = 199.5 (C), 135.2 (C), 89.8 (CH_2), 63.1 (CH_2), 56.0 (OCH_3), 32.5 (CH_2), 31.8 (CH_2), 26.1 [C(*C*$H_3)_3$], 23.1 (CH_2), 18.5 (C), –5.2 (CH_3Si).

5-[4-(*tert*-Butyldimethylsiloxy)butyl]-5-methoxy-5*H*-furan-2-one (9)

t-BuLi (6.9 mL of a 1.7 M solution in pentane, 11.7 mmol) was added to a solution of **8** (2.9 g, 11.3 mmol) in THF (15 mL) at –70 °C, and the mixture was stirred for 1 h. Dry CO_2 was then bubbled through it for 15 min, after which it was poured into a mixture of 10% H_2SO_4 (10%, 75 mL) and Et_2O (30 mL) at 0 °C. After stirring at this temperature for 1 h, the organic layer was separated and the aqueous phase was extracted with Et_2O (2 × 50 mL). The combined organic layers were washed with brine and dried (Na_2SO_4). The solvent was evaporated, and the residue was chromatographed on silica gel with 1:3 Et_2O–hexane as eluent, affording 1.9 g of **9** (80%); yellowish oil; R_f 0.65 (40% EtOAc–hexane).

^{1}H NMR ($CDCl_3$): δ = 7.11 (1 H, d, *J* = 5.7 Hz, CH-4), 6.21 (1 H, d, *J* = 5.7 Hz, CH-3), 3.58 (2 H, t, *J* = 6.0 Hz, OCH_2), 3.20 (3 H, s, OCH_3), 1.38–1.93 (6 H, m), 0.86 (9 H, s, *t*-C_4H_9), 0.02 [6 H, s, $(CH_3)_2Si$].

^{13}C NMR ($CDCl_3$): δ = 169.9 (C=O), 153.4 (CH-4), 124.8 (CH-3), 111.2 (C), 62.6 (CH_2), 51.1 (OCH_3), 36.7 (CH_2), 32.5 (CH_2), 25.9 [C(*C*$H_3)_3$], 19.7 (CH_2), 18.9 (C), –5.3 (CH_3Si), –5.4 (CH_3Si).

LRMS: *m*/*z* (%) = 269 (38), 253 (25), 243 (20), 216 (18), 215 (100), 213 (11), 211 (11), 201 (14), 187 (21), 185 (10), 171 (35), 155 (14), 154 (12).

HRMS: *m*/*z* calcd for $C_{15}H_{29}O_4Si$: 301.1835; found: 301.1845.

7-Methoxy-2,8-dioxabicyclo[5.3.0]decan-9-one (5)

TBAF (0.83 mL of 1.0 M in THF, 0.83 mmol) was added to a solution of furanone **9** (125 mg, 0.416 mmol) in THF (5 mL) and the mixture was stirred at r.t. for 2.5 h. It was then poured into sat. aq $NaHCO_3$ solution (10 mL) and extracted with Et_2O (3 × 10 mL). The combined organic layers were washed with brine (10 mL), dried (Na_2SO_4), and the solvent was evaporated. The residue was chromatographed on silica gel with 1:2.5 Et_2O–hexane as eluent, affording 50 mg of **5** (63%); yellowish oil; R_f 0.52 (40% EtOAc–hexanes).

IR (KBr): 2960, 2880, 1780, 1470, 1310, 1220, 1120, 1100, 1000, 960, 905 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 4.17 (1 H, ddt, *J* = 12.2, 2.15, 1.79 Hz, CH-1), 3.91 (1 H, dd, *J* = 7.9, 2.0 Hz, CH_a-3), 3.37 (1 H, m, CH_b-3), 3.31 (3 H, s, OCH_3), 3.01 (1 H, dd, *J* = 18.7, 7.8 Hz, CH_a-10), 2.46 (1 H, dd, *J* = 18.7, 2.0 Hz, CH_b-10), 2.39 (1 H, dd, *J* = 14.7, 8.1 Hz, CH_a-6), 1.65–1.85 (4 H, m), 1.45 (1 H, m).

^{13}C NMR ($CDCl_3$): δ = 174.6 (C=O), 114.5 (C-7), 84.4 (CH-1), 74.7 (CH_2), 50.0 (OCH_3), 36.6 (CH_2), 31.6 (CH_2), 30.3 (CH_2), 20.8 (CH_2).

LRMS: *m*/*z* (%) = 187 ([M^+ + 1], 13), 186 ([M^+], 16), 167 (11), 165 (14), 163 (13), 161 (10), 159 (10), 156 (14), 154 (52), 153 (100).

HRMS: *m*/*z* calcd for $C_9H_{15}O_4$: 187.0970; found: 187.0970.

2,8-Dioxabicyclo[5.3.0]decan-9-one (10)

TMSOTf (0.09 mL, 0.48 mmol) and Et_3SiH (0.09 mL, 0.597 mmol) were added dropwise to a solution of **7** (37 mg, 0.20 mmol) in CH_2Cl_2 (5 mL) at r.t., and the mixture was stirred for 6 h. H_2O (5 mL) and a few drops of pyridine were added, and the product was extracted with Et_2O (5 × 5 mL). The organic layer was washed with H_2O (2 × 5 mL) and dried (Na_2SO_4). The solvent was evaporated, and the residue was chromatographed on silica gel with 30–50% EtOAc–hexanes as eluent, affording 16 mg of **10** (52%); colorless oil; R_f 0.54 (60% EtOAc– hexanes).

^{1}H NMR ($CDCl_3$): δ = 4.20 (1 H, ddd, *J* = 10.7, 8.0, 5.7 Hz, CH-1), 4.09 (1 H, dt, *J* = 10.7, 8.0 Hz, CH-7), 3.90 (1 H, m, CH_a-3), 3.77 (1 H, m, CH_b-3), 2.74 (1 H, dd, *J* = 16.9, 7.8 Hz, CH_a-10), 2.59 (1 H, dd, *J* = 16.9, 10.5 Hz, CH_b-10), 2.34 (1 H, m, CH_a-6), 1.7–2.0 (4 H, m), 1.5–2.0 (1 H, m, CH_b-6).

^{13}C NMR ($CDCl_3$): δ = 173.4 (C=O), 84.4 (H-7), 77.0 (H-1), 71.1 (CH_2-3), 36.5 (CH_2-10), 30.4 (CH_2-6), 28.2 (CH_2-4), 22.3 (CH_2-5).

HRMS: *m*/*z* calcd for $C_8H_{12}O_3$: 156.0786; found: 156.0780.

***trans*-2-(2-Hydroxyethyl)-3-hydroxyoxepane (3)**

To a solution of lactone **10** (0.028 g, 0.18 mmol) in anhyd Et_2O (3 mL) at 0 °C was added $LiAlH_4$ (0.033 g, 0.89 mmol) and the mixture was stirred at 0 °C to r.t. for 18 h. Excess of $LiAlH_4$ was destroyed by adding a few drops of H_2O at 0 °C. After filtration and extraction with EtOAc, the aqueous phase was saturated with NaCl and extracted with EtOAc. The combined organic phases were dried (Na_2SO_4). Filtration and evaporation of solvent afforded a residue, which was chromatographed on silica gel with EtOAc as eluent, affording 23 mg of diol **3** (81%); colorless oil.

^{1}H NMR ($CDCl_3$): δ = 3.96 (1 H, q, *J* = 4.9 Hz, CH-3), 3.32–3.72 (2 H, m, CH_2), 3.63–3.52 (2 H, m, CH_2-7), 3.40–3.35 (1 H, m, CH-2), 2.03–1.90 (2 H, m, CH_2), 1.80–1.52 (6 H, m, CH_2-4, CH_2-5, CH_2-6).

^{13}C NMR ($CDCl_3$): δ = 84.7 (H-2), 75.3 (H-3), 71.2 (CH_2-7), 60.7 (CH_2-2′), 36.3 (CH_2-1′), 35.8 (CH_2-4), 30.3 (CH_2-6), 20.5 (CH_2-5).

HRMS: *m*/*z* calcd for $C_8H_{14}O_2$ [M – H_2O]: 142.0994; found: 142.0991.

***cis- and trans*-2-(2-Hydroxyethyl)-3-hydroxyoxepane (11)**

To a solution of **5** (4.4 g, 23.5 mmol) in anhyd Et_2O (200 mL) at r.t. was added $BF_3{\cdot}OEt_2$ (7 mL, 56.4 mmol) and the mixture was stirred for 1 h. It was then cooled to 0 °C before adding $LiAlH_4$ (8.9 g, 235 mmol). The end of the reaction was monitored by TLC analysis. At the end of the reaction, excess $LiAlH_4$ was carefully destroyed by adding a few drops of H_2O at 0 °C. After filtration and extraction with EtOAc, the aqueous phase was saturated with NaCl and extracted with EtOAc. The combined organic phases were dried (Na_2SO_4). Filtration and evaporation of solvent afforded a residue which was chromatographed on silica gel with EtOAc as eluent, giving 3.4 g of diol **11** (as an inseparable mixture of diols **3** and **4**); yield: 91%; colorless oil.

***cis- and trans*-2-(2-*tert*-Butyldimethylsilyloxyethyl)-3-hydroxyoxepane (12)**

To a solution of diol **11** (2.2 g 13.5 mmol) in DMF (80 mL) were added imidazole (1.8 g, 27 mmol), DMAP (catalytic amount) and TBSCl (2.2 g, 14.8 mmol). The mixture was stirred at r.t. overnight, quenched with aq NH_4Cl solution and extracted with Et_2O. The organic phase was washed with H_2O and brine. After drying (Na_2SO_4) and evaporation of solvent, the residue was chromatographed on silica gel using 20% EtOAc–hexane as eluent, to afford 3.2 g of diastereomeric alcohols **12** (86%); colorless oil.

2-(2-*tert*-Butyldimethylsilyloxyethyl)oxepane-3-one (13)

To a solution of alcohol **12** (4.79 g, 17.48 mmol) in anhyd CH_2Cl_2 (250 mL) at r.t. were added powdered molecular sieves (10.6 g), 4-methylmorpholine *N*-oxide (NMO, 4.09 g, 34.96 mmol) and a catalytic amount of TPAP. The mixture was stirred at r.t. for 48 h, the solvent was removed by rotary evaporation, and the residue was chromatographed on silica gel using 15% EtOAc–hexane as eluent to afford 4.06 g of ketone **13** (95%); colorless oil.

^{1}H NMR ($CDCl_3$): δ = 4.24–4.18 (1 H, ddt, *J* = 8.5, 4.8, 1.8 Hz, CH-2), 3.89–3.86 (1 H, dd, *J* = 8.8, 4.2 Hz, CH-4), 3.73–3.70 (2 H, dd, *J* = 6.8, 5.4 Hz, CH_2-2′), 3.32–3.25 (1 H, dt, *J* = 2.3, 9.1 Hz, CH-7), 2.94–2.87 (1 H, dt, *J* = 9.9, 2.6 Hz, CH-7), 2.40–2.35 (1 H, dq, *J* = 5.0, 1.9 Hz, CH-1′), 1.96–1.86 (3 H, m, CH-1′, CH_2-6), 1.85–1.69 (2 H, m, CH_2-5), 0.87 (9 H, s, *t*-C_4H_9Si), 0.03 (6 H, s, CH_3Si).

^{13}C NMR ($CDCl_3$): δ = 274.1 (C=O), 84.0 (CH), 73.1 (CH_2), 58.5 (CH_2), 41.5 (CH_2), 36.0 (CH_2), 31.2 (CH_2), 25.9 [C(*C*H_3)$_3$Si], 23.8 (CH_2), 18.3 (CSi), –5.4 (CH_3Si).

HRMS: *m*/*z* calcd for $C_{14}H_{29}O_3Si$: 273.1886; found: 273.1894.

2-(2-*tert*-Butyldimethylsilyloxyethyl)-3-hydroxyoxepane (14)

To a solution of ketone **13** (0.03 g, 0.111 mmol) at –78 °C was added L-Selectride (0.278 mL of 1.0 M solution in THF, 0.278 mmol). At the end of the reaction (TLC control), aq sat. NH_4Cl solution (2 mL) was added and the mixture was stirred at r.t. for 30 min and extracted with EtOAc. After drying (Na_2SO_4) the extract and evaporation of the solvent, the residue was chromatographed on silica gel using 10% EtOAc–hexane to afford 23 g of alcohol **14** (76%); colorless oil.

^{1}H NMR ($CDCl_3$): δ = 3.80–3.61 (6 H, m), 1.92–1.80 (2 H, m), 1.72–1.53 (6 H, m), 0.88 (9 H, s, *t*-C_4H_9Si), 0.04 [6 H, s, $(CH_3)_2Si$].

^{13}C NMR ($CDCl_3$): δ = 76.0 (CH-2), 71.8 (CH-3), 69.3 (CH_2-7), 59.5 (CH_2-2′), 36.6 (CH_2-1′), 36.0 (CH_2-4), 30.1 (CH_2-6), 25.9 [C(*C*H_3)$_3$Si], 19.6 (CH_2-5), 18.2 (CSi), –5.4 [$(CH_3)_2Si$].

HRMS: *m*/*z* calcd for $C_{14}H_{31}O_3Si$: 275.2042; found: 275.2051.

***cis*-2-(2-Hydroxyethyl)-3-hydroxyoxepane (4)**

TBAF (0.055 mL of a 1.0 M sln in THF, 0.055 mmol) was added to a solution of alcohol **14** (0.015g, 0.055 mmol) in THF (1 mL) and the mixture was stirred at r.t. At the end of the reaction (TLC control), aq sat. solution of $NaHCO_3$ (3 mL) was added and the product was extracted with EtOAc. The aqueous phase was saturated with NaCl and extracted with EtOAc. The combined organic phases were dried (Na_2SO_4). Filtration and evaporation of solvent afforded a residue, which was chromatographed on silica gel with EtOAc as eluent, providing 8.7 mg of diol **4** (78%); colorless oil.

^{1}H NMR ($CDCl_3$): δ = 3.82–3.65 (6 H, m), 2.49 (2 H, br s), 2.04–2.00 (4 H, m), 1.99–1.51 (4 H, m).

^{13}C NMR ($CDCl_3$): δ = 77.9 (CH-2), 71.9 (CH-3), 69.3 (CH_2-7), 60.3 (CH_2-2′), 36.7 (CH_2-1′), 35.5 (CH_2-4), 29.8 (CH_2-6), 19.4 (CH_2-5).

HRMS: *m*/*z* calcd for $C_8H_{16}O_3$: 160.1099; found: 160.1107.

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