Supporting Information
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SUPPORTING INFORMATION

A Synthesis of (S)-(−)-Umbelactone and Related α,β-Butenolides

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Table of Contents

General details S2
Synthesis of the butenolides 1, 2, 18 and 23 S4
NMR spectra of the butenolides 1, 2, 18 and 23 S7
**General details.** Melting points were determined on a Stuart SMP10 electrothermal melting point apparatus and are uncorrected. Infrared spectra were recorded on a Perkin Elmer RX I FT-IR spectrometer as liquid films or as dilute solutions in spectroscopic grade chloroform or deuterochloroform between two sodium chloride plates. Proton NMR spectra were recorded on either a Bruker AVX300 (300 MHz) or Bruker DPX300 (300 MHz) spectrometer as dilute solutions in deuterochloroform. Chemical shifts are referenced to residual protonated solvent ($\delta_H = 7.26$ for CDCl$_3$) and are quoted in parts per million (ppm). The multiplicity of a signal is designated by one of the following abbreviations: s = singlet; d = doublet; t = triplet; q = quartet; br. = broad; m = multiplet; app. = apparent; obs. = obscured. All coupling constants, $J$, are reported in Hertz and quoted to the nearest 0.1 Hz. Carbon-13 NMR spectra were recorded on either a Bruker AVX300 (75 MHz) or a Bruker DPX300 (75 MHz) spectrometer as dilute solutions in deuterochloroform on a broad band decoupled mode. Chemical shifts are referenced to residual protonated solvent ($\delta_C = 77.0$ for CDCl$_3$) and are quoted in parts per million (ppm). Mass spectra were recorded on either a Micromass GCT Premier or a Waters Micromass LCT Premier spectrometer using electron ionisation (EI) at 70 eV or electrospray (ES) techniques, respectively.

All reactions were monitored by thin layer chromatography (TLC) using Polygram® Sil G/UV$_{254}$ pre-coated plastic sheets, which were visualised with ultraviolet light and then developed with basic potassium permanganate. Flash chromatography was performed on Davisil silica gel 60 as the stationary phase and the solvents employed were of analytical grade. Unless stated otherwise, all commercially available reagents were used as received. When necessary, commonly used organic solvents were dried prior to use. Tetrahydrofuran (THF) was distilled from sodium benzophenone ketyl. Dichloromethane was distilled from calcium hydride. Triethylamine was distilled from potassium hydroxide. Solvents were removed on a
Büchi rotary evaporator using water aspirator pressure. Brine refers to a saturated aqueous solution of sodium chloride. Petroleum ether refers to light petroleum ether boiling in the range 40-60 °C. Where necessary, reactions requiring anhydrous conditions were performed under an atmosphere of argon in oven dried apparatus. Ultrasonic reactions were conducted using a Decon® F5200b ultrasonicator.
General procedure for the synthesis of the butenolides 2, 18 and 23

Thionyl chloride (5 equiv) was added to a solution of the alcohol (1 equiv) in pyridine (0.10-0.06 M) and stirred at either 80 °C or 0 °C for 1 hour. The reaction mixture was cooled to room temperature and then concentrated in vacuo. The brown residue was diluted with ethyl acetate, and then washed sequentially with a 10% aqueous solution of HCl and a saturated aqueous solution of NaHCO₃. The organic extract was dried over MgSO₄, filtered and concentrated in vacuo.

\[ \text{(S)-5-} \text{( tert-Butyldimethylsilyloxy)methyl)-4-[3-(4-methoxybenzyl)oxy- propyl]-5H-furan-2-one (2).} \]

Following the general procedure using thionyl chloride (0.02 mL, 0.30 mmol), a 4:1 diastereoisomeric mixture of the alcohols 17 (26 mg, 0.06 mmol) and pyridine (1.0 mL), the resulting residue was purified by flash column chromatography on silica using 30% diethyl ether in petroleum ether as eluent to give the butenolide 2 (6.0 mg, 25%) as a pale yellow oil; \([\alpha]_{D}^{20} +4.6 \text{ (c 0.4 in CHCl}_3\); \(\nu_{\text{max}} \text{ (film/cm}^{-1}\) 2930, 1748, 1612, 1513, 1463, 1248, 1175 and 1099; \(\delta_{\text{H}} \text{ (300 MHz, CDCl}_3\) 7.25-7.22 (2H, m, ArH), 6.90-6.86 (2H, m, ArH), 5.79 (1H, dt, J 1.8 and 1.5, C=CH), 4.84 (1H, dt, J 3.5 and 1.8, CH), 4.43 (2H, s, PMPCH₂O), 3.93 (1H, dd, J 11.4 and 3.8, TBSOCHH), 3.87 (1H, dd, J 11.4 and 3.8, TBSOCHH), 3.81 (3H, s, OCH₃), 3.50 (2H, t, J 6.1, PMBOCH₂), 2.57-2.36 (2H, m, CH₂C=CH), 1.89 (2H, tt, J 7.6 and 6.1, PMBOCH₂CH₂), 0.84 (9H, s, SiC(CH₃)₃), 0.05 (3H, s, SiCH₃), 0.04 (3H, s, SiCH₃); \(\delta_{\text{C}} \text{ (75 MHz, CDCl}_3\) 173.1, 170.8, 159.3, 130.2, 129.3, 116.6, 113.8, 84.2, 72.7, 68.6, 61.8, 55.3, 27.3, 25.7, 25.2, 18.1, -5.5, -5.6; \(m/z \text{ (ES) 429.2100 (M}^{+}+\text{Na, 15%}, \text{C}_{22}\text{H}_{34}\text{O}_{5}\text{SiNa requires 429.2073).} \)
(S)-4-But-3-enyl-5-(tert-butyldimethylsilanyloxy-methyl)-5H-furan-2-one (18). Following the general procedure using thionyl chloride (0.04 mL, 0.50 mmol), a 4:1 diastereoisomeric mixture of the alcohols 16 (30 mg, 0.10 mmol) and pyridine (1.0 mL), the resulting residue was purified by flash column chromatography on silica using 10% diethyl ether in petroleum ether as eluent to give the butenolide 18 (24.0 mg, 85%) as a pale yellow oil; $[\alpha]_D^{20}$ -40.7 (c 1.38 in CHCl$_3$); $\nu_{\text{max}}$ (film/cm$^{-1}$) 3080, 2930, 2858, 1792, 1641 and 1471; $\delta$H (300 MHz, CDCl$_3$) 5.85 (1H, app. q, J 1.7, C=C-H), 5.81 (1H, ddt, J 16.8, 10.2 and 6.2, H$_2$C=CH), 5.13-5.03 (2H, m, H$_2$C=CH), 4.86 (1H, dt, J 3.6 and 1.5, CH), 3.93 (1H, dd, J 11.3 and 3.8, TBSOCH$_3$H), 3.89 (1H, dd, J 11.3 and 3.8, TBSOCH$_3$H), 2.60-2.33 (4H, m, CH$_2$=CHCH$_2$CH$_2$), 0.84 (9H, s, Si(CH$_3$)$_3$), 0.05 (3H, s, SiCH$_3$), 0.04 (3H, s, SiCH$_3$); $\delta$C (75 MHz, CDCl$_3$) 173.0, 170.3, 136.3, 116.9, 116.2, 84.1, 61.9, 30.9, 27.5, 25.7, 18.1, -5.6, -5.6; m/z (ES) 305.1549 (M$^+$+Na, 45%, C$_{15}$H$_{26}$O$_3$SiNa requires 305.1549).

(S)-5-(tert-Butyldimethylsilanyloxymethyl)-4-methyl-5H-furan-2-one (23).$^1$ Following the general procedure using thionyl chloride (0.14 mL, 20 mmol), a 4:1 diastereoisomeric mixture of the alcohols 22 (101 mg, 0.388 mmol) and pyridine (5.0 mL), the resulting residue was purified by flash column chromatography on silica using 40% diethyl ether in petroleum ether as eluent to give the butenolide 23 (53.0 mg, 57%) as a colourless oil; $[\alpha]_D^{20}$ -64.7 (c 1.0 in CHCl$_3$) [lit.$^{1a}$ $[\alpha]_D^{20}$ -52.1 (c 1.3 in CHCl$_3$); lit.$^{1b}$ $[\alpha]_D^{20}$ -11.2 (c 1.8 in CHCl$_3$); lit.$^{1c}$ $[\alpha]_D^{20}$ -10.5 (c 1.80 in CHCl$_3$)]; $\nu_{\text{max}}$ (film/cm$^{-1}$) 2929, 2856, 1759, 1731 and 1649; $\delta$H (300 MHz, CDCl$_3$) 5.83 (1H, q, J 1.5, C=CH), 4.83-4.80 (1H, m, CH$_3$), 3.93 (1H, dd, J 11.4 and 3.8, TBSOCH$_3$H), 3.89 (1H, dd, J 11.4 and 3.8, TBSOCH$_3$H), 2.10 (3H, dd, J 2.0, H$_2$C=CH).
Borontrifluoride diethyl etherate (0.10 mL, 0.61 mmol, 6 equiv) was added to a solution of the silyl ether 23 (23 mg, 0.10 mmol, 1 equiv) in chloroform (1.0 mL, 0.1 M) and stirred at room temperature for 30 minutes. The reaction mixture was quenched with water (2 mL), diluted with ethyl acetate (5 mL), and the separated aqueous phase was extracted with ethyl acetate (2 x 5 mL). The combined organic extracts were dried over MgSO₄, filtered and concentrated in vacuo. The residue was purified by flash column chromatography on silica using 50% ethyl acetate in hexane as eluent to give the (S)-(−)-umbelactone (1) (5.0 mg, 43%) as a white solid; mp 62-63 °C (lit. 2 65 °C; lit. 3 60-62 °C; lit. 4 62-64 °C) (1:1 ethyl acetate/petroleum ether); [α]D²⁰ -9.3 (c 0.5 in CHCl₃) [lit. 4 [α]D²⁰ -11.86 (c 1.57 in CHCl₃); lit. 5 [α]D -67.8 (c 4.28 in EtOH); lit. 1b [α]D²⁰ -10.6 (c 1.0 in CHCl₃); lit. 1c [α]D²⁰ -9.3 (c 1.0 in CHCl₃)]; νmax (CDCl₃/cm⁻¹) 3607, 2928, 2360, 2256, 1758 and 1648; δH (300 MHz, CDCl₃) 5.89 (1H, dq, J 1.5 and 0.4, C=CH), 4.91 (1H, dddq, J 4.3, 3.0, 0.7 and 0.4, CH), 4.07 (1H, ddd, J 12.6, 3.0 and 0.6, HOCHH), 3.78 (1H, dd, J 12.6 and 4.3, HOCHH), 2.11 (3H, dd, J 1.5 and 0.7, CH₃), 1.92 (1H, s, OH); δC (75 MHz, CDCl₃) 173.0, 165.9, 118.2, 85.1, 61.4, 13.9; m/z (EI) 98.0369 (M⁺-CH₂O, 100%, C₅H₆O₂ requires 98.0368).
TBSO

23
\((S)-(-)-1\)
References


