Supplementary Material (ESI) for Chemical Communications

Oxidative Radical Cyclisations for the Synthesis of γ-Lactones

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Introduction

^{1}H and ^{13}C NMR spectra were recorded on Bruker instruments (DPX-200, DPX-400, DQX-400 or DRX-500), using deuterochloroform as an internal deuterium lock. Chemical shifts are quoted in units of δ relative to tetramethylsilane (δ=0). Multiplets are indicated as s, singlet; d, doublet; t, triplet; q, quartet; qn, quintet; dd, double doublet; m, multiplet; br, broad, etc. Coupling constants *J* are quoted in Hz. Where useful, the FID was zero-filled (128 K) and sine-bell shifted (ssb = 30) prior to Fourier Transformation in order to provide baseline-resolved multiplets and easily identifiable coupling constants. Double Quantum Filtered and magnitude COSY and HMQC spectra were typically acquired with 256 slices in F_1 and 2048 points in F_2 (acquisition time approximately 20 min). ^{13}C spectra were recorded with proton decoupling; *J* resolved spin-echo APT or DEPT-135, and in some cases HMQC, were recorded to assist assignment.

Infrared spectra were recorded on a Perkin-Elmer 1600 series FTIR spectrometer calibrated relative to polystyrene absorption at 1630 cm^{-1}. The samples were prepared as a thin film or a solution in the solvent indicated.

Mass spectra were recorded by the Mass Spectrometry Service at the University of Cambridge Chemical Laboratory, or the Mass Spectrometry Service at the University of Oxford Chemistry Research Laboratory. Microanalyses were carried out by the Microanalytical Service at the University of Cambridge Chemical Laboratory.

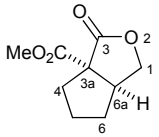
Optical specific rotations were measured on a Perkin-Elmer 241 polarimeter and are quoted in units of $^{\circ}10^{-1}cm^{2}g^{-1}$. The concentration (*c*) is expressed in g/0.1 dm^{3}.

Flash chromatography was carried out on silica gel [Merck 9385 Kieselgel 60 (230-400 ASTM)]. Analytical TLC was carried out on 0.25 mm thick plates precoated with Merck Kieselgel F_{254} silica gel and visualised by UV and aqueous potassium permanganate solution or ethanolic phosphomolybdic acid solution. Preparative layer chromatography was carried out on 1 mm thick plates of Merck Kieselgel PF_{254}.

Melting points were determined using a Kofler hot-stage apparatus and are uncorrected. Kugelrohr bulb-to-bulb distillations were carried out using a Büchi GKR-51 machine. Boiling points are oven temperatures.

The experimental procedures for the preparation of the lactone **2**, the methylenecyclopentane **3** and the methylcyclopentane **4** are representative.

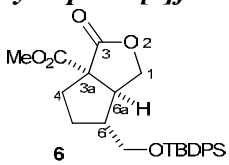
(3a*R**,6a*S**)-Methyl 3-oxohexahydro-1*H*-cyclopenta[*c*]furan-3a-carboxylate 2



2

Manganese(III) acetate (536 mg, 2.0 mmol) and copper(II) triflate (362 mg, 1.0 mmol) were added to a solution of dimethyl 4-pentenyl malonate **1** (200 mg, 1.0 mmol) in dry degassed acetonitrile (5 mL) (nitrogen bubbled through the solvent for 2 h prior to use). The resulting suspension was then heated to 80 °C for 24 h. Water (20 mL) and diethyl ether (20 mL) were added, the mixture was filtered and then extracted with diethyl ether (3 × 100 mL). The combined organics were then dried ($MgSO_4$), filtered and concentraed *in vacuo*. The resultant oil was then purified by flash column chromatography (gradient elution 5-20% diethyl ether/petroleum ether) to yield the *title compound* **2** (167.4 mg, 0.91 mmol, 91%) as a colourless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ=4.55 (dd, *J* (H, H)=9.3, 7.6 Hz, 1H; 1-H), 4.07 (dd, *J*(H, H)=9.3, 2.4 Hz, 1H; 1-H'), 3.77 (s, 3H; OCH_3), 3.14-3.06 (m, 1H; 6a-H), 2.42-2.32 (m, 1H; 4-H), 2.29-2.22 (m, 1H; 4-H'), 2.12-2.00 (m, 1H; 6-H), 1.88-1.77 (m, 1H; 5-H), 1.71-1.56 (m, 2H; 6-H', 5-H'); ^{13}C NMR (50 MHz, $CDCl_3$): δ=176.9 (C=O), 170.9 (C=O), 73.4 (1-C), 62.0 (3a-C), 53.5 (CH_3O), 46.0 (6a-C), 35.1 (4-C), 34.5 (6-C), 26.3 (5-C). Data consistent with literature.[1-3]

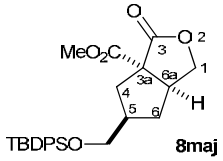
***(3a*R*, 6*R*, 6a*S*)-Methyl 6-(*tert*-butyldiphenylsilyloxymethyl)-3-oxohexahydro-1*H*-cyclopenta[*c*]furan-3a-carboxylate* 6**



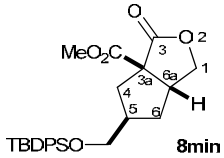
6

R_f 0.68 (EtOAc:hexane, 1:1); (Found: C, 68.83; H, 7.09%; $C_{26}H_{43}O_5Si$ requires C, 68.99; H 7.13); ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.65-7.59 (m, 4H; ArH), 7.47-7.36 (m, 6H; ArH), 4.48 (dd, ^2J (H, H)=9.4, ^3J (H, H)=6.8 Hz, 1H; 1-H), 4.23 (dd, ^2J (H, H)=9.4, ^3J (H, H)=1.6 Hz, 1H; 1-H'), 3.76 (s, 3H; OMe), 3.69 (dd, ^2J (H, H)=10.0, ^3J (H, H)=5.6 Hz, 1H; C*H*HOSi), 3.54 (dd, ^2J (H, H)=10.0, ^3J (H, H)=7.2 Hz, 1H; CH*H*OSi), 2.85 (td, ^3J (H, H)=6.8, 1.6 Hz, 1H; 6a-H), 2.53 (ddd, ^2J (H, H)=14.0, ^3J (H, H)=8.3, 5.5 Hz, 1H, 4-H), 2.19-2.09 (m, 2H), 1.77 (dddd, ^2J (H, H)=13.0, ^3J (H, H)=7.2, 7.2, 5.5 Hz, 1H), 1.58 (dq, ^2J (H, H)=13.0, ^3J (H, H)=8.3 Hz, 1H), 1.04 (s, 9H; $(CH_3)_3C$); ^{13}C NMR (100 MHz, $CDCl_3$): δ=176.5 (C), 170.3 (C), 135.5 (CH), 135.5 (CH), 133.2 (C), 133.1 (C), 129.9 (CH), 129.9 (CH), 127.8 (CH), 127.8 (CH), 72.0 (CH_2), 65.7 (CH_2), 61.4 (C), 53.1 (CH_3), 50.1 (CH), 49.5 (CH), 32.7 (CH_2), 29.1 (CH_2), 26.8 (CH_3), 19.2 (C); IR (film): 1775, 1741; MS (+ESI): *m/z* (%): Found: $(M+Na)^+$, 475.1908 (100), $C_{26}H_{32}O_5SiNa$ req. 475.1917.

***(3a*R*, 5*R*, 6a*S*)-Methyl 5-(*tert*-butyldiphenylsilyloxymethyl)-3-oxohexahydro-1*H*-cyclopenta[*c*]furan-3a-carboxylate* 8maj and *(3a*S*, 5*R*, 6a*R*)-methyl 5-((*tert*-butyldiphenylsilyloxy)methyl)-3-oxohexahydro-1*H*-cyclopenta[*c*]furan-3a-carboxylate* 8min**



8maj



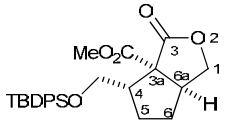
8min

The diastereomers were partly separable by flash chromatography.

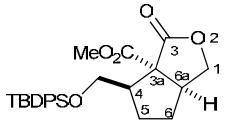
Minor diastereomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.64 (m, *J* (H, H)= 7.9, 1.5 Hz, 4H; ArH), 7.47-7.36 (m, 6H; ArH), 4.56 (dd, ^2J (H, H)= 9.2, ^3J (H, H)=6.6 Hz, 1H; 1-H), 4.07 (dd, ^2J (H, H)=9.2, ^3J (H, H)=1.7 Hz, 1H; 1-H'), 3.77 (s, 3H; OMe), 3.66-3.54 (m, 2H; CH_2OSi), 3.17-3.09 (m, 1H; 6a-H), 2.44-2.31 (m, 1H; 4-H), 2.27-2.15 (m, 2H; 5-H, 6-H), 1.99-1.89 (m, 1H; 4-H'), 1.32-1.24 (m, 1H; 6-H'), 1.05 (s, 9H; $(CH_3)_3C$); ^{13}C NMR (100 MHz, $CDCl_3$): δ=176.5 (3-C), 170.5 (C), 135.6 (CH), 133.4 (C), 129.7 (CH), 127.7 (CH), 71.4 (1-C), 65.4 (CH_2OSi), 60.8 (3a-C), 53.2 (OMe), 47.2 (6a-C), 44.0 (5-C), 36.2 (6-C), 35.9 (4-C), 26.9 (CH_3), 19.3 (C); IR (film):1776, 1744; MS (+ESI): *m/z* (%): Found: $(M+Na)^+$, 475.1912 (100), $C_{26}H_{32}O_5SiNa$ req. 475.1911.

Major diastereomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.66-7.61 (m, 4H; ArH), 7.47-7.36 (m, 6H; ArH), 4.50 (dd, ^2J (H, H)=9.3, ^3J (H, H)=7.7 Hz, 1H; 1-H), 4.15 (dd, ^2J (H, H)= 9.3, ^3J (H, H)=2.5 Hz, 1H; 1-H'), 3.79 (s, 3H; OMe), 3.63 (dd, ^2J (H, H)=10.2, ^3J (H, H)=5.5 Hz, 1H; C*H*HOSi), 3.57 (dd, *J* (H, H)= 10.2, ^3J (H, H)=6.0 Hz, 1H; CH*H*OSi), 3.13-3.05 (m, 1H; 6^a-H), 2.69 (ddd, ^2J (H, H)=13.9, ^3J (H, H)=8.0, 1.5 Hz, 1H; 4-H), 2.45-2.32 (m, 1H; 5-H), 2.27-2.17 (m, 1H; 6-H), 1.97 (dd, ^2J (H, H)=13.9, ^3J (H, H)= 10.3 Hz, 1H; 4-H'), 1.48-1.38 (m, 1H; 6-H'), 1.05 (s, 9H; $(CH_3)_3C$); ^{13}C NMR (100 MHz, $CDCl_3$): 176.3 (3-C), 170.2 (C), 135.5 (CH), 133.5 (C), 129.7 (CH), 127.7 (CH), 73.5 (1-C), 65.5 (CH_2OSi), 61.3 (3a-C), 53.1 (OMe), 44.3 (6a-C), 41.5 (5-C), 37.2 (6-C), 36.7 (4-C), 26.9 (CH_3), 19.3 (C); IR (film): 1778, 1743; MS (+ESI): *m/z* (%): Found: $(M+Na)^+$, 475.1919 (100), $C_{26}H_{32}O_5SiNa$ req. 475.1911.

***(3a*S*, 4S*, 6a*S*)-Methyl 4-(*tert*-butyldiphenylsilyloxymethyl)-3-oxohexahydro-1H-cyclopenta[c]furan-3a-carboxylate* 10maj and *(3a*S*, 4R*, 6a*S*)-methyl 4-(*tert*-butyldiphenylsilyloxymethyl)-3-oxohexahydro-1H-cyclopenta[c]furan-3a-carboxylate* 10min**



10maj



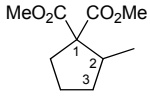
10min

The diastereomers were partly separable by flash chromatography.

Major diastereomer **10maj**: mp 97.3-98.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.69-7.62 (m, 4H; ArH), 7.48-7.38 (m, 6H; ArH), 4.47 (dd, ^2J (H, H)=9.2, ^3J (H, H)=6.1 Hz, 1H; 1-H), 4.16 (dd, ^2J (H, H)=9.2, ^3J (H, H)= 0.8 Hz, 1H; 1-H'), 3.79 (dd, ^2J (H, H)=10.4, ^3J (H, H)=6.0 Hz, 1H; C*H*HOSi), 3.71 (dd, ^2J (H, H)=10.4, ^3J (H, H)=4.0 Hz, 1H; 1'-H), 3.63 (s, 3H; OMe), 3.43-3.36 (m, 1H; 6a-H), 2.89-2.82 (m, 1H; 4-H), 2.32 (ddt, J (H, H)=13.3, 9.6, 8.0 Hz, 1H; 6-H), 1.93-1.79 (m, 2H; 5-H, 5-H'), 1.64-1.54 (m, 1H; 6-H'), 1.07 (s, 9H; $(CH_3)_3C$); ^{13}C NMR (100 MHz, $CDCl_3$): δ=175.5 (3-C), 167.9 (C), 135.7 (CH), 135.6 (CH), 133.1 (C) 133.1 (C), 129.8 (CH), 129.8 (CH), 127.7 (CH), 73.2 (1-C), 63.9 (3a-C), 63.8 (CH_2OSi), 52.9 (OMe), 49.3 (4-C), 44.2 (6a-C), 31.6 (6-C), 29.7 (5-C), 26.8 (CH_3), 19.1 (C); IR (KBr): 1776, 1732; MS (+ESI): *m/z* (%): 475.2 ($(M+Na)^+$, 90); Found: $(M+Na)^+$, 475.1921, $C_{26}H_{32}O_5SiNa$ req. 475.1911;

Minor diastereomer **10min**: ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.71-7.67 (app dt, J (H, H)= 7.9, 1.5 Hz; ArH), 7.45-7.35 (m, 6H; ArH), 4.56 (app t, ^2J (H, H)=8.9, ^3J (H, H)=8.9, 1H; 1-H), 4.03-3.97 (m, 2H; 1-H', C*H*HOSi), 3.88 (dd, ^2J (H, H)=10.5, ^3J (H, H)=6.3 Hz, 1H; CH*H*OSi), 3.74 (s, 3H; OMe), 3.34-3.27 (m, 1H; 6a-H), 2.99-2.91 (m, 1H; 4-H), 2.07-1.91 (m, 2H; 5-H, 6-H), 1.79-1.65 (m, 2H; 5-H', 6-H'), 1.05 (s, 9H; $(CH_3)_3C$); ^{13}C NMR (100 MHz, $CDCl_3$): δ=174.0 (3-C), 171.0 (C), 135.7 (CH), 135.6 (CH)), 133.4 (C), 129.6 (CH), 129.6 (CH), 127.6 (CH), 72.3 (1-C), 62.6 (CH_2OSi), 61.5 (3a-C), 53.2 (OMe), 49.4 (4-C), 46.9 (6a-C), 31.3 (6-C), 28.7 (5-C), 26.7 (CH_3), 19.3 (C); IR (film): 1774, 1737; MS (+ESI): *m/z* (%): 453.3 ($(M+H)^+$, 100); Found: $(M+Na)^+$, 475.1915, $C_{26}H_{32}O_5SiNa$ req. 475.1911.

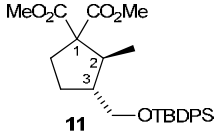
Dimethyl 2-methylcyclopentane-1,1-dicarboxylate 4



4

Manganese(III) acetate (536 mg, 2.0 mmol) was added to a solution of the malonate **1** (200 mg, 1.0 mmol) in dry degassed ethanol (50 mL) (nitrogen bubbled through the solvent for 2 h prior to use). The resulting suspension was then heated to 80 °C for 24 h. Water (50 mL) and diethyl ether (100 mL) were added and the mixture was filtered and then extracted with diethyl ether (3 × 100 mL). The combined organics were dried ($MgSO_4$), filtered and concentrated *in vacuo*. The resultant oil was purified by flash column chromatography (gradient elution 5-20% diethyl ether/petroleum ether) to yield the *title compound* **4** (132 mg, 0.66 mmol, 66%) as a colourless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ=3.72 (s, 3H; OCH_3), 3.71 (s, 3H; OCH_3), 2.68 (ddq, ^3J (H, H)=8.9, 7.0, 7.0 Hz, 1H; 2-H), 2.44 (ddd, ^3J (H, H)= 13.9, 8.8, 7.6 Hz, 1H; 5-H), 2.03 (ddd, ^3J (H, H)=13.9, 9.3, 4.7 Hz, 1H; 5-H'), 1.98-1.77 (m, 2H; 4-H, 3-H), 1.64-1.50 (m, 1H; 4-H'), 1.46-1.35 (m, 1H; 3-H'), 0.98 (d, ^3J (H, H)=7.0 Hz, 3H; 2-CCH_3). Data consistent with literature.[5]

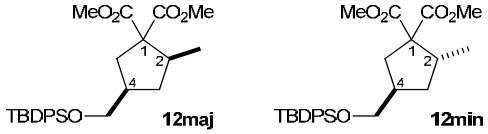
***(2S*, 3R*)-Dimethyl 3-(*tert*-butyldiphenylsilyloxymethyl)-2-methylcyclopentane-1,1-dicarboxylate* 11**



11

R_f 0.71 (EtOAc:hexane, 1:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.67-7.62 (m, 4H; ArH), 7.43-7.35 (m, 6H; ArH), 3.71 (s, 3H; OMe), 3.69 (s, 3H; OMe), 3.67 (dd, ^2J (H, H)=10.7, ^3J (H, H)=5.0 Hz, 1H; C*H*HOSi), 3.56 (dd, ^2J (H, H)=10.7, ^3J (H, H)=5.7 Hz, 1H; CH*H*OSi), 2.50 (dq, ^3J (H, H)=9.8, 7.0 Hz, 1H; 2-H), 2.35 (ddd, ^2J (H, H)=13.3, ^3J (H, H)=7.7, 7.7 Hz, 1H; 5-H), 2.05 (m, 2H), 1.87 (ddddd, ^2J (H, H)=9.8, ^3J (H, H)=8.6, 8.6, 5.7, 5.0 Hz, 1H), 1.57-1.42 (m, 1H), 1.04 (s, 9H; $(CH_3)_3C$), 0.95 (d, ^3J (H, H)=7.0 Hz, 3H; 2-CCH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ=172.9 (C), 172.1 (C), 135.6 (CH), 135.5 (CH), 133.8 (C), 133.7 (C), 129.6 (CH), 129.5 (CH), 127.6 (CH), 127.6 (CH), 65.7 (CH_2), 64.3 (C), 52.4 (CH_3), 51.9 (CH_3), 48.2 (CH), 33.3 (CH_2), 27.2 (CH_2), 26.8 (CH_3), 19.3 (C), 15.5 (CH_3); IR (film): 1731; MS (+ESI): *m/z* (%): Found: $(M+Na)^+$, 491.2234 (100), $C_{27}H_{36}O_5SiNa$ req. 491.2230.

***(2S*, 4R*)-Dimethyl 4-(*tert*-butyldiphenylsilyloxymethyl)-2-methylcyclopentane-1,1-dicarboxylate* 12maj and *(2R*, 4R*)-dimethyl 4-(*tert*-butyldiphenylsilyloxymethyl)-2-methylcyclopentane-1,1-dicarboxylate* 12min**



The diastereomers were partly separable by flash chromatography.

Major diastereomer **12maj**: ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.71-7.64 (m, 4H; ArH), 7.47-7.36 (m, 6H; ArH), 3.75 (s, 3H; OMe), 3.70 (s, 3H; OMe), 3.66 (d, ^3J (H, H)=5.9 Hz, 2H; CH_2OSi), 2.78 (ddq, ^3J (H, H)=13.8, 10.1, 7.0, 1H; 2-H), 2.36-2.13 (m, 3H; 5-H, 5-H', 4-H,), 2.08-1.99 (m, 1H; 3-H), 1. 30-1.17 (m, 1H; 3-H'), 1.08 (s, 9H; $(CH_3)_3C$), 1.00 (d, ^3J (H, H)=7.0 Hz, 3H; 2-CCH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ=173.1 (C), 171.9 (C), 135.6 (CH), 133.9 (C), 129.6 (CH), 127.6 (CH), 67.1 (CH_2OSi), 63.5 (1-C), 52.5 (OMe), 52.0 (OMe), 40.3 (4-C), 40.1 (2-C), 36.9 (3-C), 36.8 (5-C), 26.8 (CH_3), 19.3 (C), 16.9 (2-C*C*H_3); IR (film): 1732; MS (+ESI): *m/z* (%): 469.3 ($(M+H)^+$, 100); Found: $(M+Na)^+$, 491.2232, $C_{27}H_{36}O_5SiNa$ req. 491.2224.

minor diastereomer **12min**: ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.69-7.60 (m, 4H), 7.45-7.33 (m, 6H; ArH), 3.73 (s, 3H; OMe), 3.71 (s, 3H; OMe), 3.53 (dd, *J* (H, H)= 6.2, 1.8 Hz, 2H; CH_2OSi), 2.72 (ddq, ^3J (H, H)=10.4, 8.8, 7.2 Hz, 1H; 2-H), 2.64-2.48 (m, 2H; 5-H, 4-H), 1.85-1.77 (m, 2H; 5-H', 3-H), 1.64-1.54 (m, 1H; 3-H'), 1.07 (s, 9H; $(CH_3)_3C$), 1.01 (d, ^3J (H, H)=7.0 Hz, 3H; 2-CCH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ=172.7 (C), 171.7 (C), 135.7 (CH), 133.8 (C), 129.6 (CH), 127.6 (CH), 67.4 (CH_2OSi), 63.8 (1-C), 52.3 (OMe), 52.0 (OMe), 40.0 (2-C), 38.6 (4-C), 37.0 (5-C), 35.9 (3-C), 26.9 (CH_3), 19.3 (C) 16.3 (2-C*C*H_3); IR (film): 1733; MS (+ESI): *m/z* (%): 469.3 ($(M+H)^+$, 40); Found: $(M+Na)^+$, 491.2226, $C_{27}H_{36}O_5SiNa$ req. 491.2224.

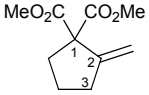
***(2S*, 5S*)-Dimethyl 2-(*tert*-butyldiphenylsilyloxymethyl)-5-methylcyclopentane-1,1-dicarboxylate* 13maj and *(2S*, 5R*)-dimethyl 2-(*tert*-butyldiphenylsilyloxymethyl)-5-methylcyclopentane-1,1-dicarboxylate* 13min**

The diastereomers were partly separable by flash chromatography.

major diastereomer **13maj**; ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.68-7.61 (m, 4H; ArH), 7.45-7.35 (m, 6H; ArH), 3.72-3.63 (m, 4H; C*H*HOSi, OMe), 3.56-3.51 (m, 1H; CH*H*OSi), 3.50 (s, 3H; OMe), 2.95-2.87 (m, 1H; 2-H), 2.87-2.76 (m, 1H; 5-H), 2.13-1.99 (m, 2H; 4-H, 3-H), 1.74-1.61 (m, 1H; 4-H'), 1. 35-1.25 (m, 1H; 3-H'), 1.05 (s, 9H; $(CH_3)_3C$), 0.94 (d, ^3J (H, H)=7.0 Hz, 3H; 5-CCH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ=(100 MHz, $CDCl_3$) 171.6 (C), 171.2 (C), 135.7 (CH), 135.7 (CH), 133.7 (C), 133.5 (C), 129.6 (CH), 129.5 (CH), 127.6 (CH), 127.6 (CH), 65.4 (1-C), 64.9 (CH_2OSi), 53.4 (OMe), 52.3 (OMe), 47.5 (2-C), 42.2 (5-C), 32.2 (3-C), 27.7 (4-C), 27.0 (CH_3), 19.8 (C), 17.8 (2-C*C*H_3); IR (film): 1731; MS (+ESI): *m/z* (%): 491.2 ($(M+Na)^+$, 100); Found: $(M+Na)^+$, 491.2227, $C_{27}H_{36}O_5SiNa$ req. 491.2224.

minor diastereomer **13min**: ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.69-7.60 (m, 4H; ArH), 7.45-7.33 (m, 6H; ArH), 4.03 (dd, ^2J (H, H)=9.7, ^2J (H, H)=4.6 Hz, 1H; C*H*HOSi), 3.65-3.51 (m, 7H; CH*H*OSi, 2 × OMe), 2.69 (m, 1H; 2-H), 2.56-2.44 (m, 1H; 5-H), 2.17-2.08 (m, 1H; 3-H), 1.98-1.80 (m, 2H; 4-H, 3-H'), 1.66-1.51 (m, 1H; 4-H'), 1.10-1.05 (m, 12H; $(CH_3)_3$C, 5-CCH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ=172.3 (C), 169.8 (C), 135.6 (CH), 135.6 (CH), 133.9, 133.8 (C), 129.6, 129.5 (CH), 127.7 (CH), 127.6 (CH), 65.3 (CH_2OSi), 64.6 (1-C), 52.5 (OMe), 51.8 (OMe), 50.5 (2-C), 43.8 (3-C), 32.4 (4-C), 31.4 (5-C), 27.0 (CH_3), 19.3 (C), 16.0 (5-C*C*H$_3$); IR (film): 1731; MS (+ESI): *m/z* (%): 491.2 ((M+Na)$^+$, 100); Found: (M+Na)$^+$, 491.2225, $C_{27}H_{36}O_5SiNa$ req. 491.2224.

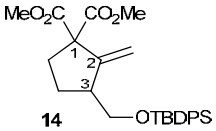
Dimethyl 2-methylenecyclopentane-1,1-dicarboxylate 3



3

Manganese(III) acetate (536 mg, 2.0 mmol) and copper(II) acetate (218 mg, 1.0 mmol) were added to a solution of the malonate **1** (200 mg, 1.0 mmol) in dry degassed DMSO (5 mL) (nitrogen bubbled through the solvent for 2 h prior to use). The resulting suspension was then heated to 80 °C for 24 h. Water (50 mL) and diethyl ether (100 mL) were added and the mixture was filtered and then extracted with diethyl ether (3 × 100 mL). The combined organics were washed with water (100 mL), dried ($MgSO_4$), filtered and then concentrated *in vacuo*. The resultant oil was purified by flash column chromatography (gradient elution 5-20% diethyl ether/petroleum ether) to yield in order of elution the *title compound* **3** (152 mg, 0.77 mmol, 77%) as a colourless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ=5.31 (d, J (H, H)=2.2 Hz, 1H; C=C*H*H), 5.28 (d, J (H, H)=2.2 Hz, 1H; C=CH*H*), 3.75 (s, 6H; OCH_3), 2.47 (tt, J (H, H)=7.3, 2.2 Hz, 2H; 3-H, 3-H'), 2.36 (t, J (H, H)=6.9 Hz, 2H; 5-H, 5-H'), 1.75 (qn, ^3J (H, H)=7.1 Hz, 2H; 4-H, 4-H'); and lactone **6** (13 mg, 0.07 mmol, 7%). Data consistent with literature.[4]

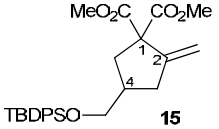
***Dimethyl 3-(*tert*-butyldiphenylsilyloxymethyl)-2-methylenecyclopentane-1,1-dicarboxylate* 14**



14

^{1}H NMR (400 MHz, $CDCl_3$): δ=7.67-7.62 (m, 4H; ArH), 7.41-7.34 (m, 6H; ArH), 5.36 (d, ^2J (H, H)=2.5 Hz, 1H; C=C*H*H), 5.21 (d, ^2J (H, H)= 2.1 Hz, 1H; C=CH*H*), 3.72 (m, 4H; OMe, C*H*HOSi), 3.71 (s, 3H, OMe), 3.55 (dd, ^2J (H, H)=10.1, ^3J (H, H)= 7.9 Hz, 1H; CH*H*OSi), 2.83 (m, 1H; 3-H), 2.41-2.34 (dt, J (H, H)= 6.6, 12.2 Hz, 1H; 5-H), 2.27-2.14 (m, 1H; 5-H'), 1.97-1.89 (m, 1H; 4-H), 1.75-1.66 (m, 1H; 4-H'), 1.04 (s, 9H; $(CH_3)_3$C); ^{13}C NMR (50 MHz, $CDCl_3$): δ=171.8 (C), 171.4 (C), 149.1 (C), 136.0 (CH), 134.1 (C), 130.0 (CH), 128.1 (CH), 113.9 (C=*C*H$_2$), 66.9 (CH_2OSi), 65.0 (6-C), 53.3 (OMe), 53.2 (OMe), 47.4 (3-C), 34.5 (5-C), 27.3 (CH_3), 19.7 (C); IR (film): 1735; MS (+ESI): *m/z* (%):Found (M+Na)$^+$, 489.2066 (100), $C_{27}H_{34}O_5SiNa$ req. 489.2068.

***Dimethyl 4-(*tert*-butyldiphenylsilyloxymethyl)-2-methylenecyclopentane-1,1-dicarboxylate* 15**

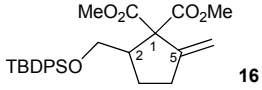


15

^{1}H NMR (400 MHz, $CDCl_3$): δ=7.72-7.67 (m, 4H; ArH), 7.49-7.38 (m, 6H; ArH), 5.35 (s, 1H; C=C*H*H), 5.30 (s, 1H; C=CH*H*), 3.78 (s, 3H; OMe), 3.76 (s, 3H; OMe), 3.70-3.50 (m, 2H; CH_2OSi), 2.65-2.57 (m, 2H; 3-H, 5-H), 2.50-2.30 (m, 2H; 3-H', 4-H), 2.17 (dd, ^2J (H, H)=12.8, ^3J (H, H)= 10.5, Hz, 1H; 5-H'), 1.10 (s, 9H; $(CH_3)_3$C); ^{13}C NMR (100 MHz, $CDCl_3$): δ=171.2 (C), 147.6 (2-C), 135.6 (CH), 133.7 (C),

129.7 (CH), 127.7 (CH), 112.5 (C=*C*H$_2$), 66.1 (CH$_2$OSi), 63.5 (1-C), 52.9 (OMe), 52.8 (OMe), 40.1 (4-C), 38.5 (5-C), 36.9 (3-C), 26.9 (CH$_3$), 19.3 (C); IR (film): 1735; MS (+ESI): *m/z* (%): 489.2 ((M+Na)$^+$, 100); Found: (M+Na)$^+$, 489.2068, $C_{27}H_{34}O_5SiNa$ req. 489.2068.

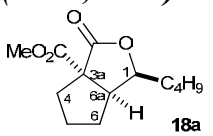
***Dimethyl 2-(*tert*butyldiphenylsilyloxymethyl)-5-methylenecyclopentane-1,1-dicarboxylate* 16**



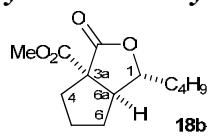
16

^{1}H NMR (400 MHz, $CDCl_3$): δ=7.68-7.64 (m, 4H; ArH), 7.46-7.36 (m, 6H; ArH), 5.29 (t, *J* (H, H)=2.4 Hz, 1H; C=C*H*H), 5.22 (t, *J* (H, H)=2.2 Hz, 1H; C=CH*H*), 3.82 (dd, ^2J (H, H)=10.2, ^3J (H, H)=4.9 Hz, 1H; C*H*HOSi), 3.71 (s, 3H; OMe), 3.58-3.51 (m, 4H; CH*H*OSi, OMe), 3.07-2.98 (m, 1H; 2-H), 2.65-2.55 (m, 1H; 4-H), 2.51-2.38 (m, 1H; 4-H'), 2.08 (ddd, ^2J (H, H)=12.2, ^3J (H, H)=6.3, 3.9 Hz, 1H; 3-H), 1.74 (ddd, ^2J (H, H)=12.2, ^3J (H, H)=9.3, 9.2 Hz, 1H; 3-H'), 1.06 (s, 9H; $(CH_3)_3C$); ^{13}C NMR (100 MHz, $CDCl_3$): δ=170.3 (C), 170.0 (C), 148.8 (5-C), 135.6 (CH), 133.7 (C), 129.6 (CH), 127.6 (CH), 111.9 (C=*C*H$_2$), 65.1 (1-C), 63.8 (CH$_2$OSi), 52.7 (OMe), 52.2 (OMe), 49.8 (2-C), 31.8 (4-C), 27.1 (3-C), 26.8 (CH$_3$), 19.3 (C); IR (film): 1734; MS (+ESI): *m/z* (%): 489.2 ((M+Na)$^+$, 100); Found: (M+Na)$^+$, 489.2072, $C_{27}H_{34}O_5SiNa$ req. 489.2068.

***(3a*R**, 6a*S**)-Methyl 3-oxo-1-butyl-hexahydro-1*H*-cyclopenta[c]furan-3a-carboxylate* 18**



18a

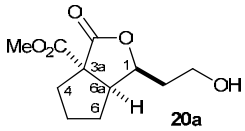


18b

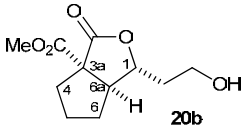
The lactones were isolated as a *ca* 2:1 mixture of inseparable diastereomers. Characterisation is on the mixture of diastereomers.

^{1}H NMR (400 MHz, $CDCl_3$): δ=4.65 (dt, ^3J (H, H)=7.2, 5.4 Hz, 1H; 1-H [d1]), 4.06 (ddd, ^3J (H, H)=7.9, 5.6, 4.0 Hz, 1H; 1-H [d2]), 3.77 (s, 6H; OCH_3 [d1, d2]), 2.97 (dt, ^3J (H, H)=13.2, 6.3 Hz, 1H; 6a-H [d1]), 2.79 (ddd, ^3J (H, H)=8.3, 3.7, 2.7 Hz, 1H; 6a-H [d2]), 2.43-2.31 (m, 2H; [d1, d2]), 2.30-2.22 (m, 2H; [d1, d2]), 2.00-1.93 (m, 1H; 6-H [d2]), 1.90-1.43 (m, 13H, [d1, d2]), 1.42-1.22 (m, 10H, [d1, d2]), 1.40-1.25 (m, 10H, [d1, d2]), 0.88 (3H, t, ^3J (H, H)=7.2 Hz, 6H; CH_2CH_3 [d1, d2]);^{13}C NMR (100 MHz, $CDCl_3$):δ=176.1 (C=O), 175.9 (C=O), 171.1 (C=O), 170.7 (C=O), 86.2 (CH), 81.2 (CH), 63.6 (C), 62.3 (C), 53.1 (CH_3), 53.0 (CH_3), 50.8 (CH), 50.1 (CH), 36.2 (CH_2), 35.5 (CH_2), 34.2 (CH_2), 34.1 (CH_2), 31.6 (CH_2), 31.4 (CH_2), 30.7 (CH_2), 27.1 (CH_2), 26.4 (CH_2), 25.8 (CH_2), 25.7 (CH_2), 25.0 (CH_2), 22.5 (CH_2), 22.4 (CH_2), 13.9 (CH_3); IR ($CDCl_3$): 2952, 2871, 1773 (C=O), 1742 (C=O); MS (+ESI): *m/z* (%): 277.1410 ((M+Na)$^+$, 100); Found: (M+Na)$^+$, 277.1410, $C_{14}H_{22}O_4Na$ req. 483. 277.1416).

***(3a*R**, 6a*S**)-Methyl 1-(2-hydroxyethyl)-3-oxohexahydro-1H-cyclopenta[c]furan-3a-carboxylate* 20**



20a



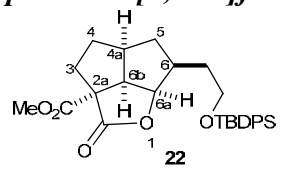
20b

Isolated as an inseparable 1.7:1 mixture of diastereomers. Characterisation is on the mixture of compounds.

R_f = 0.09 (hexane:EtOAc, 1:1); ^{1}H NMR (500 MHz, $CDCl_3$): δ=4.89 (ddd, ^3J (H, H)=9.8, 6.0, 4.0 Hz, 1H; 1-H [d1]), 4.32 (qn, ^3J (H, H)=4.2 Hz, 1H; 1-H [d2]) 3.88-3.80 (m, 4H; CH_2OH, [d1, d2]), 3.77 (s, 6H; OMe [d1, d2]), 2.98 (dt, ^3J (H, H)=7.0, 6.0 Hz, 1H; 6a-H [d1]), 2.86 (dt, ^3J (H, H)=4.2, 2.8 Hz, 1H; 6a-H [d2]), 2.45-2.32 (m, 2H), 2.98-2.20 (m, 2H), 2.05-1.90 (m, 2H), 1.89-1.80 (m, 2H), 1.75-1.65 (m, 3H), 1.62-1.52 9 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ=175.9 (C), 175.8 (C), 171.0 (C0, 170.5 (C), 83.2 (CH), 78.3 (CH), 63.4 (C), 62.2 (C), 59.8 (CH_2), 59.0 (CH_2), 53.2 (CH_3), 53.1 (CH_3), 50.7 (CH), 50.3 (CH), 38.8 (CH_2), 35.5 (CH_2), 34.1 (CH_2), 33.9 (CH_2), 33.7 (CH_2), 27.5 (CH_2), 26.4 (CH_2), 25.7 (CH_2);

1R ($CHCl_3$): 3423, 1769, 1739; MS (+ESI): *m/z* (%): Found: $(M+Na)^+$, 251.0882 (100), $C_{11}H_{16}O_5Na$ req. 251.0895.

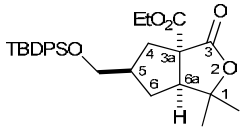
***(2a*S**, 4a*S**, 6*S**, 6a*R**, 6b*R**)-Methyl 6-(2-*tert*-butyldiphenylsilyloxyethyl)-2-oxo-hexahydro-pentaleno[1,6-bc]furan-2a-carboxylate* 22**



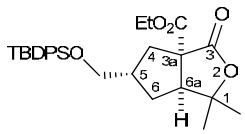
22

R_f = 0.84 (PE:EtOAc, 1:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.67-7.62 (m, 4H, ArH), 7.44-7.35 (m, 6H, ArH), 4.78 (dd, ^3J (H, H)=5.4, 4.4 Hz, 1H; 6a-H), 3.76 (s, 3H; OMe), 3.79-3.67 (m, 2H; CH_2OSi), 3.31 (dd, J (H, H)=9.8, 6.0 Hz, 1H), 2.74-2.64 (m, 1H), 2.55 (ddd, J (H, H)=14.0, 8.4, 6.6 Hz, 1H), 2.31 (dt, ^3J (H, H)=14.0, 7.0 Hz, 1H), 2.26-2.15 (m, 1H), 2.08-1.82 (m, 3H), 1.72-1.63 (m, 1H), 1.58-1.49 (m, 1H), 1.04 (s, 9H; $(CH_3)_3C$); ^{13}C NMR (125 MHz, $CDCl_3$): δ=176.4 (C), 170.6 (C), 135.5 (CH), 133.8 (C), 129.6 (CH), 127.7 (CH), 85.4 (CH), 62.3 (C), 62.2 (CH_2), 57.2 (CH), 53.0 (CH_3), 44.7 (CH), 44.1 (CH), 35.9 (CH_2), 35.5 (CH_2), 32.7 (CH_2), 32.1 (CH_2), 26.9 (CH_3), 19.2 (C); IR (film): 1772, 1742; MS (+ESI): *m/z* (%): Found: $(M+Na)^+$ 515.2208 (100), $C_{29}H_{36}O_5SiNa$ req. 515.2230.

***(3a*R**, 5*R**, 6a*S*)-Ethyl 5-((*tert*-butyldiphenylsilyloxy)methyl)-1,1-dimethyl-3-oxohexahydro-1H-cyclopenta[c]furan-3a-carboxylate* 24maj**



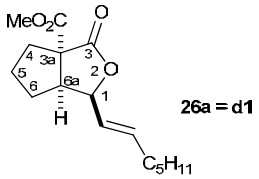
24maj



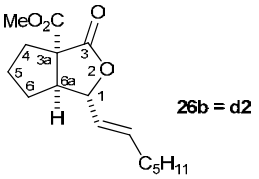
24min

Isolated as an inseparable 5:1 mixture of diastereomers; data for major diastereomer
R_f 0.63 (PE:EtOAc, 2:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.64-7.60 (m, 4H; ArH), 7.44-7.34 (m, 6H; ArH), 4.29-4.20 (m, 2H; OCH_2CH_3), 3.62 (dd, ^2J (H, H)=10.4, ^3J (H, H)= 5.8 Hz, 1H; C*H*HOSi), 3.59 (dd, ^2J (H, H)=10.4, ^3J (H, H)=6.0 Hz, 1H; CH*H*OSi), 2.94 (dd, J (H, H)=11.4, 7.4 Hz, 1H), 2.48-2.30 (m, 2H), 2.00-1.90 (m, 2H), 1.48-1.46 (m, 1H), 1.42 (s, 3H; 1-CCH_3), 1.37 (s, 3H; 1-CCH_3), 1.29 (t, ^3J (H, H)= 7.0 Hz, 3H; OCH_2CH_3), 1.03 (s, 9H; $(CH_3)_3C$); ^{13}C NMR (125 MHz, $CDCl_3$): δ=175.4 (C), 171.9 (C), 135.5 (CH), 133.5 (C), 129.7 (CH), 127.7 (CH), 83.8 (C), 65.4 (CH_2), 62.7 (C), 62.2 (CH_2), 55.8 (CH), 44.1 (CH), 38.8 (CH), 32.8 (CH_2), 29.4 (CH_2), 26.8 (CH_3), 24.4 (CH_3), 19.2 (C), 14.0 (CH_3); IR (film): 1769, 1732; MS (+ESI): *m/z* (%): Found: $(M + Na)^+$ 517.2398 (100), $C_{29}H_{38}O_5SiNa$ req. 517.2386.

***(3a*R**, 6a*S**)-Methyl 1-((*E*)-hept-1-enyl)-3-oxohexahydro-1*H*-cyclopenta[c]furan-3a-carboxylate* 26**



26a = d1

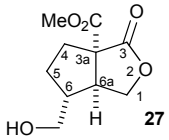


26b = d2

Isolated as an inseparable 1:1 mixture of diastereomers.
^{1}H NMR (500 MHz, $CDCl_3$): δ=5.84 (dtd, J (H, H)=15.4, 6.8, 0.9 Hz; 1H; CH=C*H*CH_2CH_2 [d1]), 5.74 5.84 (dd, ^3J (H, H)=15.3, 6.3 Hz; 1H; CH=C*H*CH_2CH_2 [d2]), 5.51 (ddt, J (H, H)=15.3, 7.8, 1.5 Hz; 1H; C*H*=$CHCH_2CH_2$ [d2]), 5.43 (ddt, J (H, H)=15.4, 7.0, 1.4 Hz; 1H; C*H*=$CHCH_2CH_2$ [d1]), 5.10 (t, ^3J (H, H)=7.0 Hz, 1H; 1-H [d1]), 4.44 (dd, ^3J (H, H)=8.0, 3.8 Hz, 1H; 1-H [d2]), 3.75 (s, 3H; OCH_3), 3.74 (s, 3H; OCH_3), 2.98 (dt, ^3J (H, H)=8.0, 7.0 Hz, 1H; 6a-H [d1]), 2.87 (dt, ^3J (H, H)=8.0, 3.1 Hz, 1H; 6a-H [d2]), 2.40-2.22 (m, 2H), 2.22-2.18 (m, 2H), 2.08-2.00 (m, 4H; CH=CHCH_2 [d1. d2]), 1.98-1.88 (m, 1H; 6-H [d2]), 1.86-1.80 (m, 1H), 1.75-1.53 (m, 6H), 1.40-1.32 (m, 4H; CH=$CHCH_2CH_2$ [d1, d2]), 1.30-1.20

(m, 8H; (C*H*$_2$)CH$_3$ [d1, d2]), 0.86 (t, ^3J (H, H)=6.7 Hz, 6H; CH$_2$C*H*$_3$ [d1, d2]); ^{13}C NMR (125 MHz, $CDCl_3$):δ=175.9 (C=O), 175.8 (C=O), 171.0 (C=O), 170.5 (C=O), 136.9 (CH), 135.8 (CH), 127.6 (CH), 123.6 (CH), 86.4 (CH), 81.6 (CH), 63.4 (C), 62.2 (C), 53.1 (CH), 51.7 (CH), 50.9 (CH), 35.5 (CH$_2$), 34.3 (CH$_2$), 33.4 (CH$_2$), 32.2 (CH$_2$), 32.0 (CH$_2$), 31.3 (CH$_2$), 31.2 (CH$_2$) 28.4 (CH$_2$), 28.4 (CH$_2$), 28.2 (CH$_2$), 26.2 (CH$_2$), 25.6 (CH$_2$), 22.4 (CH$_2$), 22.4 (CH$_2$), 14.0 (CH$_3$), 13.9 (CH$_3$); IR ($CDCl_3$): 2955, 2828, 2858, 1772 (C=O), 1740 (C=O); MS (+ESI): *m/z* (%): 303.1568 ((M+Na)$^+$, 100); Found: (M+Na)$^+$, 303. 1568, $C_{13}H_{22}O_5Na$ req. 303.1572.

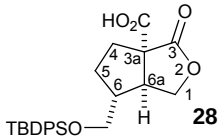
***(3aR*,6R*,6aS*)-Methyl 6-(hydroxymethyl)-3-oxohexahydro-1H-cyclopenta[c]furan-3a-carboxylate* 27**



27

Tetrabutyl ammonium fluoride (1.0 M, in THF, 300 μL, 0.30 mmol) was added dropwise to a solution of the[3.3.0]-bicyclic γ-lactone **6** (45 mg, 0.10 mmol) in THF (7 mL) buffered with acetic acid (17 μL, 0.30 mmol) at 0 °C. The reaction mixture is allowed to reach RT and stirred for 16 h. Water (40 mL) and diethyl ether (40 mL) were both added and the aqueous layer was extracted with diethyl ether (3 × 40 mL). The combined organic layers were dried ($MgSO_4$), filtered, and the solvent removed *in vacuo*. The resulting compound was purified by column chromatography (20% diethyl ether/petroleum ether) to give the *title compound* **27** as a colourless oil (19.2 mg, 90 μmol, 90%); (Found: C, 55.72; H, 6.65%; $C_{10}H_{14}O_5$ requires C, 56.07; H, 6.59); ^{1}H NMR (400 MHz, $CDCl_3$): δ=4.57 (dd, *J*(H, H)=9.4, 7.0 Hz, 1H; 1-H), 4.23 (dd, *J*(H, H)=9.3, 1.8 Hz, 1H; 1-H'), 3.78 (s, 3H; OMe), 3.72 (dd, *J*(H, H)=10.5, 5.8 Hz, 1H; C*H*HOH), 3.57 (dd, *J*(H, H)=10.5, 7.5 Hz, 1H; CH*H*OSi), 2.93 (td, ^3J(H, H)=6.9, 1.8 Hz, 1H; 6a-H), 2.57 (ddd, *J*(H, H)=14.2, 8.1, 6.4 Hz, 1H; 4-H), 2.25-2.09 (m, 2H; 6-H, 4-H'), 1.90-1.80 (m, 1H; 5-H), 1.72 (br s, 1H; OH), 1.64 (dq, *J*(H, H)=13.1, 7.6 Hz, 1H; 5-H'); ^{13}C NMR (100 MHz, $CDCl_3$): δ=176.5 (C), 170.4 (C), 72.1 (1-C), 64.6 (CH_2OH), 61.4 (3a-C), 53.2 (CH_3), 49.7 (6a-C), 49.3 (6-C), 32.8 (4-C), 29.0 (5-C); IR (film): 3431, 1768, 1738; MS (+ESI): *m/z*(%): 237.0737 ((M+Na)$^+$, 100); Found: (M+Na)$^+$, 237.0737, $C_{10}H_{14}O_5Na$ req. 237.0739.

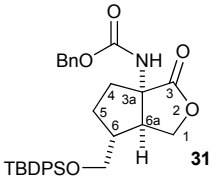
***(3aR*,6R*,6aS*)-6-(*tert*-Butyldiphenylsilyloxymethyl)-3-oxohexahydro-1H-cyclopenta[c]furan-3a-carboxylic acid* 28**



28

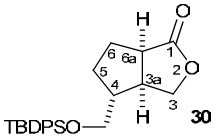
Aqueous 10% KOH solution (4 mL) was added to the γ-lactone **6** (452 mg, 1.0 mmol) in THF (20 mL) and the resulting mixture was stirred at RT for 16 h. Sulfate buffer (pH 2, 40 mL) was then added to acidify the mixture. The mixture was extracted with ether (5 × 50 mL), the organic layers combined, dried ($MgSO_4$), filtered, and the solvent removed *in vacuo*. The resulting compound was recrystallised (diethyl ether/hexane) to give the *title compound* **28** as a white crystalline solid (395 mg, 0.90 mmol, 90%); mp 118.0-118.5°C; ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.65-7.61 (m, 4H; ArH), 7.48-7.38 (m, 6H; ArH), 4.55 (dd, *J*(H, H)=9.3, 7.1 Hz, 1H; 1-H), 4.27 (dd, *J*(H, H)=9.3, 1.9 Hz, 1H; 1-H'), 3.71 (dd, *J*(H, H)= 10.3, 5.7 Hz, 1H; C*H*HOSi), 3.58 (dd, ^3J(H, H)=10.3, 7.5 Hz, 1H; CH*H*OSi), 3.00 (td, ^3J(H, H)=7.8, 1.6 Hz, 1H; 6a-H), 2.51 (ddd, *J*(H, H)=13.8, 8.1, 5.5 Hz, 1H; 4-H), 2.24-2.12 (m, 2H; 6a-H, 4-H'), 1.86-1.77 (m, 1H; 5-H), 1.58 (dq, *J*(H, H)=13.0, 8.3 Hz, 1H; 4-H'), 1.06 (s, 9H; $(CH_3)_3C$); ^{13}C NMR (50 MHz, $CDCl_3$): δ=176.7 (C), 175.4 (C), 136.0 CH), 133.5 (C), 130.4 (CH), 128.3 (CH), 72.7 (1-C), 66.1 (CH_2OSi), 61.9 (3a-C), 50.5 (6a-C), 50.1 (6-C), 33.2 (4-C), 27.3 (5-C), 27.3 (CH_3), 19.6 (C); IR (KBr): 3073, 1760, 1737; MS (+ESI): *m/z*(%): 502.2 ((M+Na+MeCN)$^+$, 60)); Found: (M+Na)$^+$, 461.1757, $C_{25}H_{30}O_5SiNa$ req. 461.1755.

***Benzyl (3aS*,6R*,6aS*)-6-((tert-butyldiphenylsilyloxy)methyl)-3-oxohexahydro-1H-cyclopenta[c]furan-3a-ylcarbamate* 31**



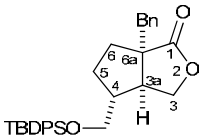
Diphenyl phosphoryl azide (15.8 μL, 0.074 mmol) was added to a solution of the [3.3.0]-bicyclic γ-lactone **28** (30.7 mg, 0.07 mmol) and triethylamine (10.7 μL, 0.077 mmol) in toluene (1 mL). The mixture was then heated to 110°C for 2 h, at which point benzyl alcohol (1 mL) was added, and the reaction was stirred at this temperature for a further 16h. Saturated aqueous $NaHCO_3$ (10 mL) and diethyl ether (20 mL) were then added and the aqueous layer was extracted with diethyl ether (2 × 20 mL). The combined organics were concentrated *in vacuo* and water was added (20 mL) and then concentrated *in vacuo* for azeotropic removal of the benzyl alcohol. Diethyl ether (20 mL) was then added and the solution was dried ($MgSO_4$), filtered and concentrated *in vacuo* to give the *title compound* **31** as a white solid (35.1 mg, 64 μmol, 92%); mp 113.5-114°C; NMR shows compound exists as rotomers; ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.63 (m, 4H; ArH), 7.48-7.30 (m, 11H; ArH), 5.22 (br s, 1H; NH), 5.10 (br s, 2H; C*H*$_2$Ar), 4.79 (t, *J*(H, H)=8.5 Hz, 1H; 1-H), 4.05 (d, *J*(H, H)=8.5 Hz, 1H; 1-H'), 3.66-3.55 (m, 2H; CH_2OSi), 2.81 (br s, 1H; 6a-H), 2.26-2.09 (m, 2H; 4-H, 6-H), 1.85-1.59 (m, 3H; 4-H', 5-H, 5-H'), 1.06 (9H, s, $(CH_3)_3$C); ^{13}C NMR (50 MHz, $CDCl_3$): δ=178.6 (C), 155.9 (C), 136.0 (CH), 133.7 (C), 130.3 (CH), 129.1 (CH), 128.8(CH), 128.7 (CH), 128.2 (CH), 73.9 (1-C), 67.7 (*C*H_2Ar), 65.9 (CH_2OSi), 51.8 (6-C), 48.6 (6a-C), 37.9 (4-C), 28.1 (5-C), 27.3 (CH_3), 19.6 (C); IR (KBr) 3465, 3314, 1753, 1713; MS (+ESI): *m/z* (%): 566.2 ((M+Na)$^+$, 100), Found: (M+Na)$^+$, 566.2333, $C_{32}H_{37}NO_5SiNa$ req. 566.2333.

***(3aS*,4R*,6aR*)-4-(tert-Butyldiphenylsilyloxymethyl)hexahydro-1H-cyclopenta[c]furan-1-one* 30**



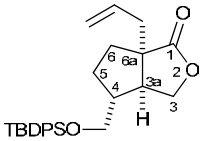
The [3.3.0]-bicyclic γ-lactone **5** (226 mg, 0.50 mmol) and LiCl (42 mg, 1.00 mmol) were dissolved in DMSO (0.9 mL) and water (9 μL, 0.50 mmol), the resulting mixture was heated to 160°C and stirred for 2 h. After cooling, water (30 mL) and diethyl ether (50 mL) were added and the aqueous layer extracted with ether (5 × 50 mL). The combined organic layers were washed with water (2 × 50 mL), brine (50 mL), dried ($MgSO_4$), filtered, and the solvent removed *in vacuo*. The resulting compound was purified *via* flash chromatography (gradient elution 5-20% diethyl ether/hexane) to give the *title compound* **30** as a white crystalline solid (178.2 mg, 90%); mp 51.7-52.3 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.66-7.62 (m, 4H), 7.48-7.37 (m, 6H), 4.40 (dd, *J*(H, H)=9.4, 7.3 Hz, 1H; 3-H), 4.19 (dd, ^{3}*J*(H, H)=9.4, 2.4 Hz, 1H; 3-H'), 3.68 (dd, *J*(H, H)=10.2, 5.8 Hz, 1H; C*H*HOSi), 3.54 (dd, ^{3}*J*(H, H)=10.2, 7.2 Hz, 1H; CH*H*OSi), 3.10 (td, ^{3}*J*(H, H)=9.5, 4.3 Hz, 1H' 6a-H), 2.69 (dddd, ^{3}*J*(H, H)=9.3, 7.2, 7.0, 2.3 Hz, 1H; 3a-H), 2.19-1.93 (m, 3H; 4-H, 6-H. 6-H'), 1.82-1.72 (m, 1H; 5-H), 1.56-1.46 (m, 1H; 5-H'), 1.06 (s, 9H; $(CH_3)_3$C); ^{13}C NMR (125 MHz, $CDCl_3$): δ=181.0 (C), 135.5 (CH), 133.3 (C), 129.8 (CH), 127.8 (CH), 72.4 (3-C), 65.9 (CH_2OSi), 48.9 (4-C), 44.5 (6a-C), 43.5 (3a-C), 29.1 (6-C), 28.4 (5-C), 26.8 (CH_3), 19.2 (C); IR (KBr) 1763; MS (+ESI): *m/z* (%): 458.3 ((M+Na+MeCN)$^+$, 100); Found (M+Na)$^+$, 417.1855, $C_{24}H_{30}O_5SiNa$ req. 417.1856.

(3aS*,4R*,6aS*)-6a-Benzyl-4-(*tert*-butyldiphenylsilyloxymethyl)hexahydro-1H-cyclopenta[c]furan-1-one



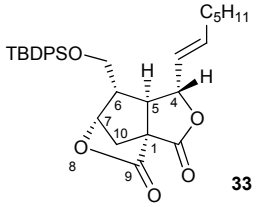
A solution of the [3.3.0]-bicyclic γ-lactone **30** (39.5 mg, 0.10 mmol) in dry THF (2 mL) was cooled to -78 °C and LiHMDS (300 μL 0f a 1.0 M solution in toluene, 0.3 mmol) was added dropwise and the solution was allowed to warm to -30°C and then cooled back down to -78°C. Benzyl bromide (35.6 μL, 0.3 mmol) was then added dropwise to the reaction mixture which was allowed to reach RT. over 16 h. Saturated aqueous NH_4Cl (20 mL) and diethyl ether (20 mL) were added and the aqueous layer was extracted with diethyl ether (3 × 20 mL). The combined organic layers were dried ($MgSO_4$), filtered, and the solvent removed *in vacuo*. The resulting compound was purified by flash chromatography (gradient elution 5-20% diethyl ether/hexane) to give the *title compound* as a colourless oil (43.3 mg, 89 μmol, 89%); ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.66-7.61 (m, 4H; ArH), 7.49-7.37 (m, 6H; ArH), 7.32-7.24 (m, 3H; ArH) 7.19-7.15 (m, 2H; ArH), 3.82 (dd, *J*(H, H)=9.2, 1.4 Hz, H; 3-H), 3.62 (dd, *J*(H, H)=10.2, 5.8 Hz, 1H; C*H*HOSi), 3.54 (dd, *J*(H, H)=10.2, 6.8 Hz, 1H; CH*H*OSi), 3.31-3.24 (m, 2H; 3-H', C*H*HAr), 2.66 (d, ^{2}*J*(H, H)=13.3 Hz, 1H; CH*H*Ar), 2.49 (t, 1H; ^{3}*J*(H, H)=6.9 Hz, 1H; 3a-H), 2.17 (app dt, *J*(H, H)=13.5, 7.4 Hz, 1H; 6-H), 2.05 (app sext, ^{3}*J*(H, H)=6.8 Hz, 1H; 4-H), 1.89 (ddd, *J*(H, H)=13.6, 7.6, 6.2 Hz, 1H; 6-H'), 1.73 (ddd, *J*(H, H)=13.0, 6.8, 6.2 Hz, 1H; 5-H), 1.64-1.49 (m, 1H; 5-H'), 1.07 (s, 9H; $(CH_3)_3$C); ^{13}C NMR (125 MHz, $CDCl_3$) δ=183.5 (C), 137.3 (C), 136.0 (CH), 133.8 (C), 130.3 (CH), 129.9 (CH), 129.1 (CH), 128.2 (CH), 127.6 (CH), 72.1 (3-C), 66.0 (CH_2OSi), 57.7 (6a-C), 50.8 (4-C), 46.9 (3a-C), 43.4 (*C*H_2Ar), 37.2 (6-C), 28.8 (5-C), 27.3 (CH_3), 19.7 (C); IR (film) 1765; MS (+ESI): *m/z*(%):548.3 ((M+Na+MeCN)$^+$, 100); Found (M+Na)$^+$, 507.2326, $C_{31}H_{36}O_3SiNa$ req. 507.2326.

(3aS*,4R*,6aS*)-6a-Allyl-4-(*tert*-butyldiphenylsilyloxymethyl)hexahydro-1H-cyclopenta[c]furan-1-one



Prepared as for (3a*S**,4*R**,6a*S**)-6a-benzyl-4-((tbutyldiphenylsilyloxy)methyl)hexahydro-1H-cyclopenta[*c*]furan-1-one using allylbromide in place of benzyl bromide.
^{1}H NMR (400 MHz, $CDCl_3$): δ=7.67-7.63 (m, 4H; ArH), 7.49-7.38 (m, 6H; ArH), 5.79-5.66 (m, 1H; C*H*=CH_2), 5.18-5.12 (m, 2H; CH=CH_2), 4.25 (dd, *J*(H, H)=9.4, 7.3 Hz, 1H; 3-H), 4.10 (dd, *J*(H, H)=9.4, 2.0 Hz, 1H; 3-H'), 3.67 (dd, *J*(H, H)=10.3, 5.7, 1H; C*H*HOSi), 3.55 (dd, *J*(H, H)=10.2, 7.2 Hz, 1H; CH*H*OSi), 2.51 (dd, *J*(H, H)=13.6, 6.8 Hz, 1H; C*H*HCH=CH_2), 2.42 (app td, ^{3}*J*(H, H)=7.0, 1.7, 1H; 3a-H), 2.25 (dd, *J*(H, H)=13.6, 8.0 Hz, 1H; CH*H*CH=CH_2), 2.16-2.00 (m, 2H; 4-H, 6-H), 1.82-1.65 (m, 2H; 5-H, 6-H'), 1.57-1.46 (m, 1H; 5-H'), 1.07 (s, 9H; $(CH_3)_3$C); ^{13}C NMR (125 MHz, $CDCl_3$): δ= 183.0 (C), 136.0 (CH), 133.8 (C), 133.3 (CH), 130.3 (CH), 128.2 (CH), 119.8 (CH), 72.2 (3-C), 66.2 (CH_2OSi), 55.7 (6a-C), 50.7 (4-C), 47.6 (3a-C), 41.3 (*C*H_2CH=CH_2), 35.9 (6-C), 28.9 (5-C), 27.3 (CH_3), 19.7 (C); IR (film): 1767; MS (+ESI): *m/z*(%): 498.3 ((M+Na+MeCN)$^+$, 80); Found (M+Na)$^+$, 457.2170, $C_{27}H_{34}O_3SiNa$ req. 457.2169.

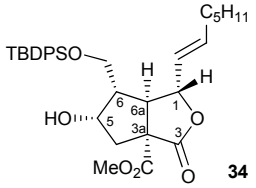
***(1*S*, 4*S*, 5*R*, 6*S*, 7*S*)-6-(*tert*-Butyldiphenylsilyloxymethyl)-4-((E)-hept-1-enyl)-3,8-dioxa-tricyclo[5.2.1.0^{1,5}]decane-2,9-dione* 33**



33

$[\alpha]_D^{20}$ = +11.3 (*c* 1.1, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.63-7.62 (m, 4H; ArH), 7.48-7.38 (m, 6H; ArH), 5.83 (dt, ^3J (H, H)=15.3, 6.8 Hz, 1H; CH=C*H*CH_2), 5.40 (dd, ^3J (H, H)=15.3, 7.5 Hz, 1H; C*H*=$CHCH_2$), 5.12 (s, 1H; 7-H), 4.72 (dd, ^3J (H, H)=7.5, 9.6 Hz, 1H;4-H), 3.70 (1H, dd, ^2J (H, H)=10.4, ^3J (H, H)=1.3 Hz, 1H; C*H*HOSi), 3.60 (dd, ^2J (H, H)=10.4, ^3J (H, H)=6.6 Hz, 1H; CH*H*OSi), 2.62-2.58 (m, 2H; 6-H, 10-H), 2.43 (d, ^2J (H, H)=10.9 Hz, 1H; 10-H'), 2.26 (dd, ^3J (H, H)=9.6, 4.7 Hz, 1H; 5-H), 1.98 (td, ^3J (H, H)=8.2, 6.8 Hz, 2H; CH=CHCH_2), 1.34-1.18 (6H, m), 1.06 (s, 9H; $(CH_3)_3$C), 0.86 (t, ^3J (H, H)=7.1 Hz, 3H; CH_2CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ=169.1 (C), 167.3 (C), 138.7 (CH=*C*HCH_2), 135.5 (CH), 135.4 (CH), 130.0 (C), 129.9 (C), 127.9 (CH), 127.8 (CH), 124.7 (*C*H=$CHCH_2$), 84.2 (4-C), 82.2 (7-C), 62.2 (*C*H_2OSi), 56.8 (1-C), 50.1 (5-C), 49.4 (6-C), 40.6 (10-C), 32.1 (CH=CH*C*H_2), 31.2 (CH_2), 28.2 (CH_2), 26.8 (C(*C*$H_3)_3$), 22.4 (CH_2), 19.2 (*C*$(CH_3)_3$), 14.0 (CH_2*C*H_3); IR ($CDCl_3$): 1813 (CO), 1783 (CO), 1728 (CO); MS (+ESI): *m/z* (%): Found: $(M+Na)^+$ 555.2335 (100), $C_{25}H_{34}NaO_3Si$ req. 555.2335.

***(1*S*, 3a*S*, 5*S*, 6*S*, 6a*R*)-Methyl 6-(*tert*-butyldiphenylsilyloxymethyl)-1-((E)-hept-1-enyl)-5-hydroxy-3-oxohexahydro-1*H*-cyclopenta[c]furan-3a-carboxylate* 34**



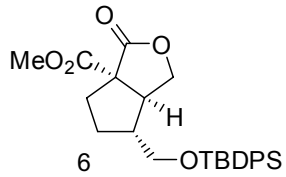
34

$[\alpha]_D^{20}$ = +22 (*c* 0.53, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.66-7.63 (m, 4H; ArH), 7.48-7.38 (m, 6H; ArH), 5.66 (dt, ^3J (H, H)=15.4, 6.7 Hz, 1H; CH=C*H*CH_2), 5.55 (dd, ^3J (H, H)=15.4, 7.2 Hz, 1H; C*H*=$CHCH_2$), 4.66 (d, ^3J (H, H)=7.2 Hz, 1H; 1-H), 4.42 (d, ^3J (H, H)=6.8, 4.2 Hz, 1H; 5-H), 3.96 (dd, ^2J (H, H)=10.7, ^3J (H, H)=6.4 Hz, 1H; C*H*HOSi) , 3.96 (dd, ^2J (H, H)=10.7, ^3J (H, H)=6.0 Hz, 1H; CH*H*OSi), 3.80 (s, 3H; OMe), 2.98 (dd, ^3J (H, H)=9.9, 8.0 Hz, 1H; 6a-H), 2.67 (dd, ^2J (H, H)=14.8, ^3J (H, H)=13.8 Hz, 1H; 4-H), 2.52 (d, ^3J (H, H)=4.2 Hz, 1H; OH), 2.28 (dd, ^2J (H, H)=14.8, ^3J (H, H)=4.1 Hz, 1H; 4-H'), 2.07 (m, 1H; 6-H), 2.01 (dt, ^3J (H, H)=7.1, 6.7 Hz, 2H; CH=CHCH_2), 1.37-1.20 (m, 6H), 1.06 (s, 9H; $(CH_3)_3$C), 0.88 (t, ^3J (H, H)=6.6 Hz, 3H; CH_2CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ=(100 MHz, $CDCl_3$) 175.3 (C), 171.5 (C), 135.7 (CH), 135.6 (CH), 135.5 (CH=*C*HCH_2), 135.5 (CH), 132.9 (CH), 132.7 (CH), 130.0 (C), 127.9 (C), 127.4 (*C*H=$CHCH_2$), 84.7 (4-C), 74.9 (7-C), 62.5 (*C*H_2OSi), 60.4 (1-C), 54.5 (6-C), 53.5 (OMe), 52.8 (5-C), 43.3 (8-C), 32.0 (CH=CH*C*H_2), 31.3 (CH_2), 28.4 (CH_2), 26.8 (C(*C*$H_3)_3$), 22.5 (CH_2), 19.1 (*C*$(CH_3)_3$), 14.0 (CH_2*C*H3); IR ($CDCl_3$): 3508 (OH), 1773 (CO), 1738 (CO); MS (+ESI): *m/z* (%): 587.2791 ($(M+Na)^+$, 100); Found: $(M+Na)^+$, 587.2791, $C_{28}H_{34}NaO_6Si$ req. 587.2805.

References

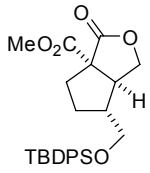
[1] T. Inoue, O. Kitagawa, A. Saito, T. Taguchi, *J. Org. Chem.* **1997**, *62*, 7384.
[2] D. P. Curran, T. M. Morgan, C. E. Schwartz, B. B. Snider, M. A. Dombroski, *J. Am. Chem. Soc.* **1991**, *113*, 6607.
[3] D. P. Curran, C. T. Chang, *J. Org. Chem.* **1989**, *54*, 3140.
[4] N. Monteiro, J. Gore, G. Balme, *Tetrahedron* **1992**, *48*, 10103.
[5] B. B. Snider, J. E. Merritt, M. A. Dombroski, B. O. Buckman, *J. Org. Chem.* **1991**, *56*, 5544.

1H NMR (400 MHz, CDCl3)



6

13 C NMR (100 MHz, CDCl3)



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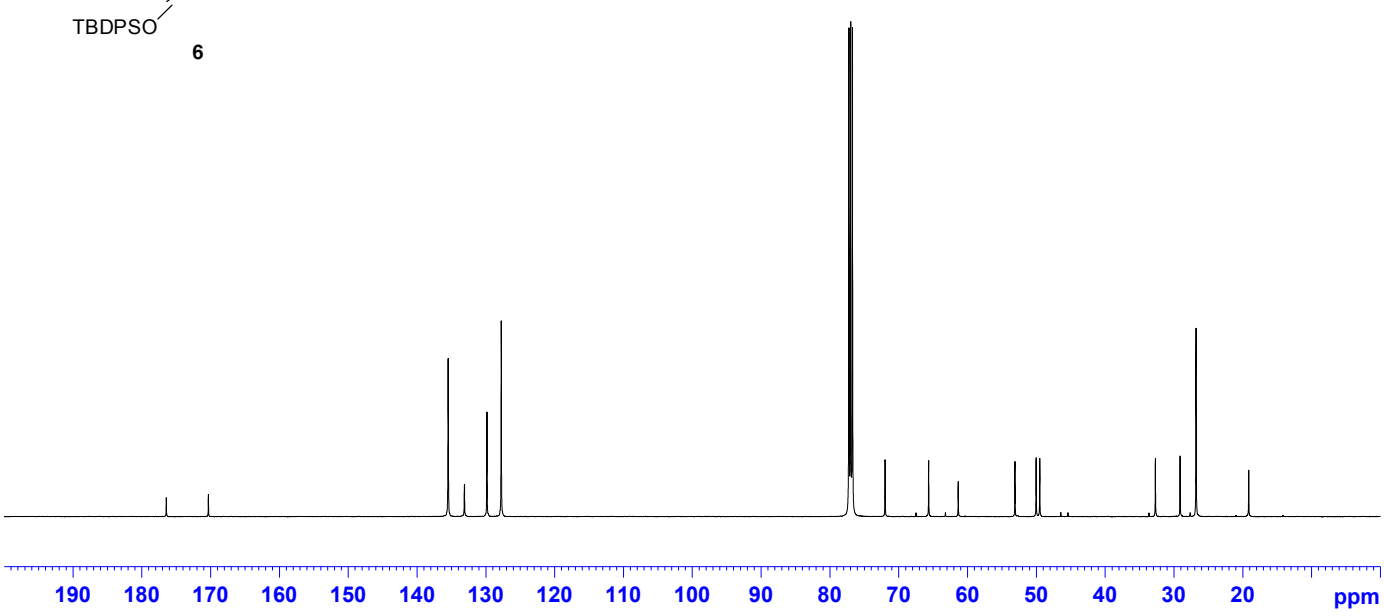
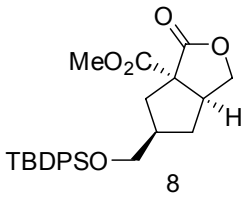
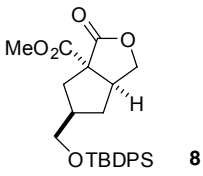


1H NMR (400 MHz, CDCl3)



8

13C NMR (100 MHz, CDCl3) with minor diastereomer present



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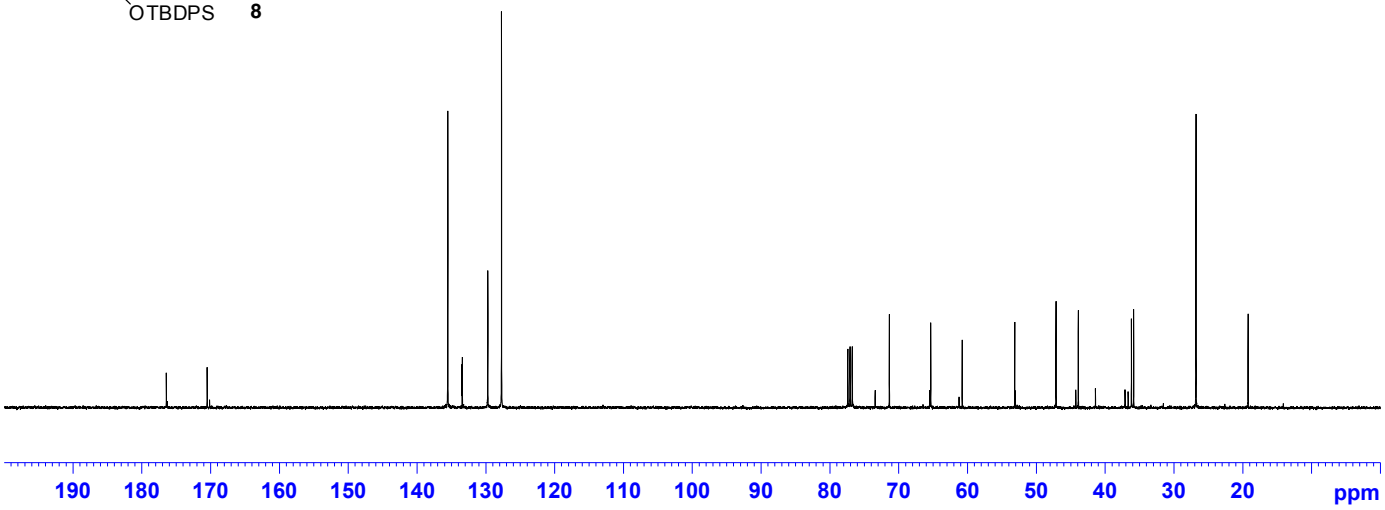
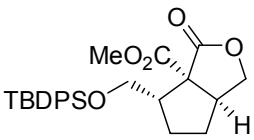
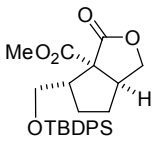


1H NMR (400 MHz, CDCl3)

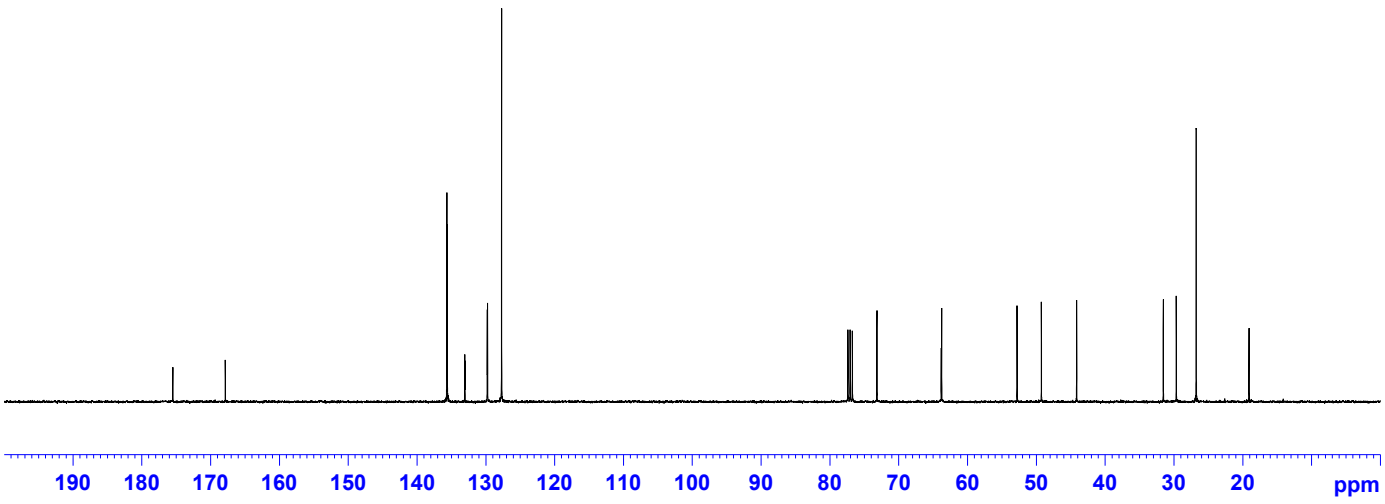


10maj

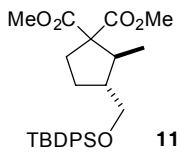
13C NMR (100 MHz, CDCl3)



10maj

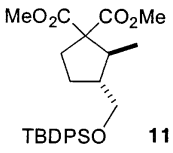


1H NMR (500 MHz, CDCl3)



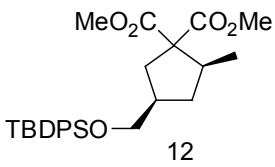
11

13C NMR (125 MHz, CDCl3)



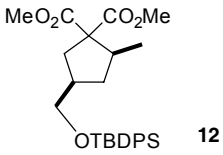
11

1H NMR (400 MHz, CDCl3) mixture of diastereomers



12

13C NMR (100 MHz, CDCl3) mixture of diastereomers



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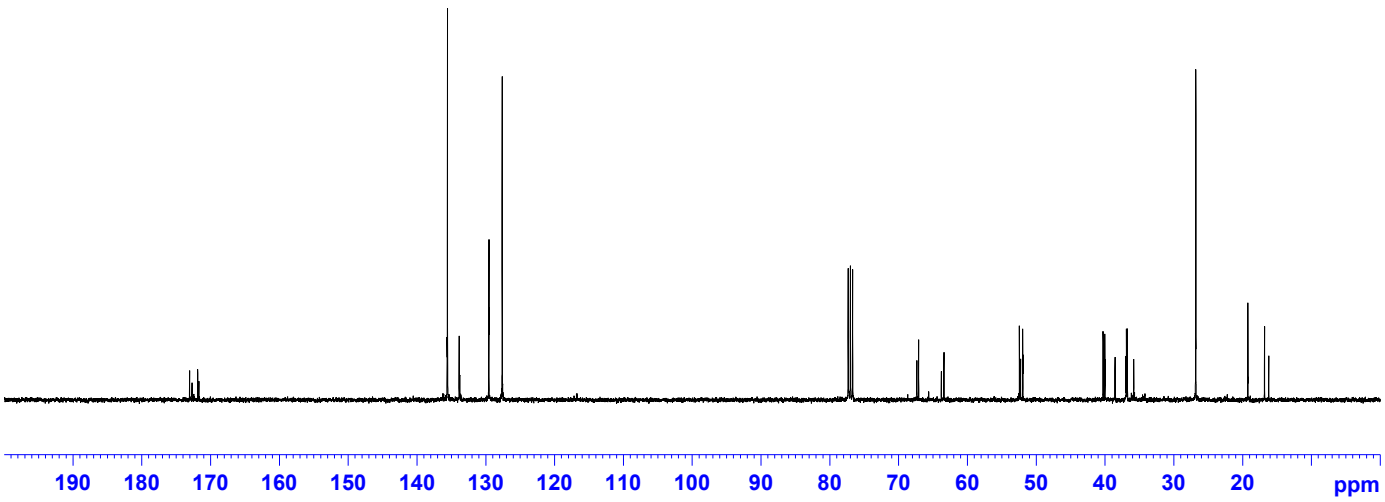
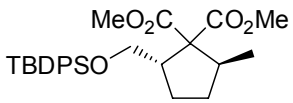
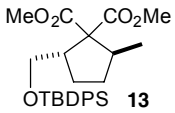


1H NMR (400 MHz, CDCl3)



13

13C NMR (100 MHz, CDCl3) mixture of diastereomers



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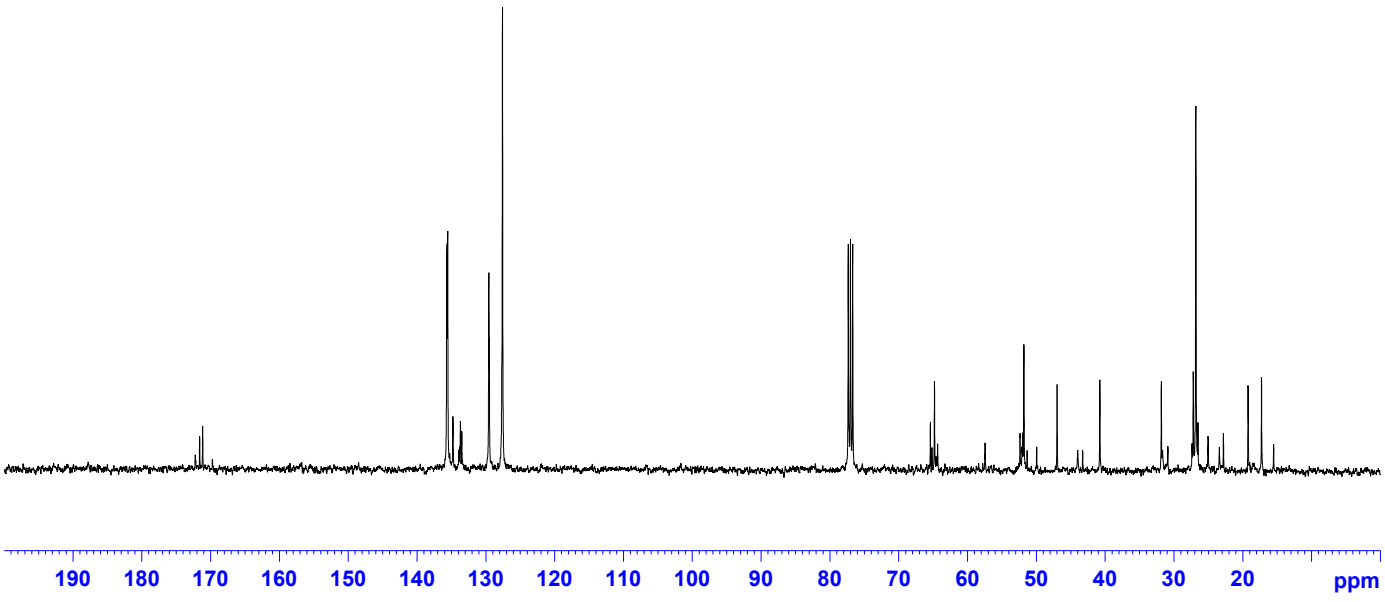
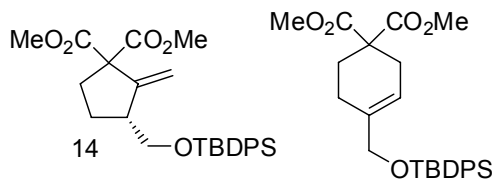
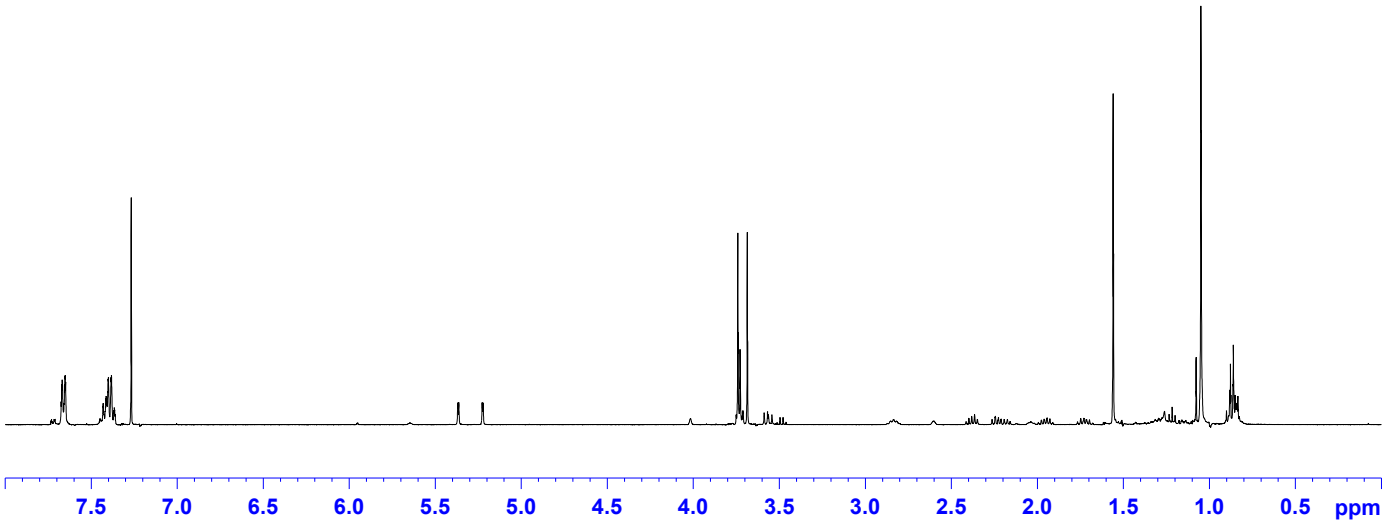
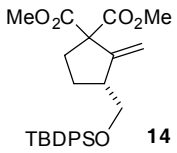


1H NMR (400 MHz, CDCl3) with the cyclohexene as a slight impurity





13 C NMR (50 MHz, CDCl3)



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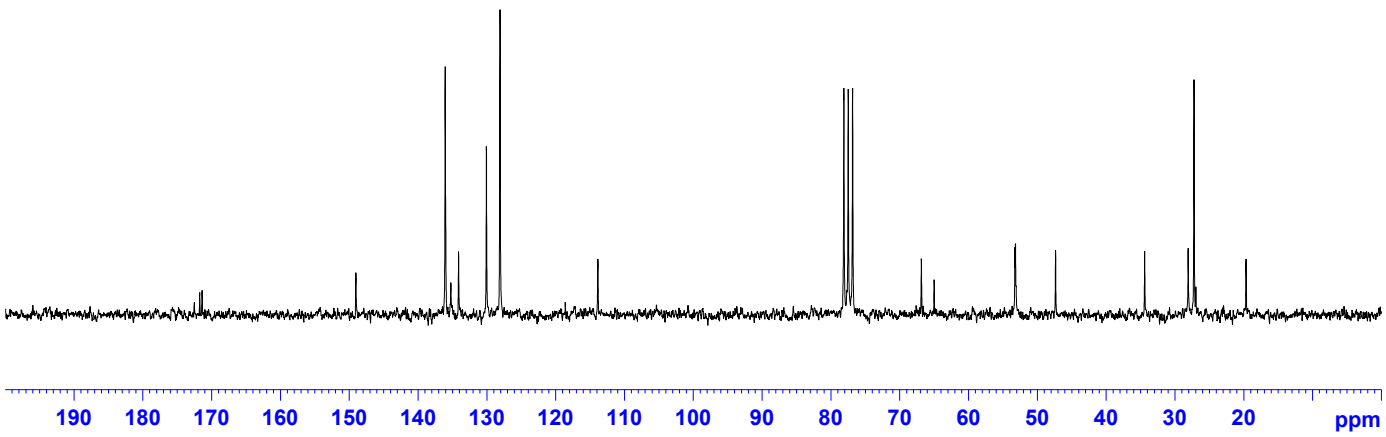
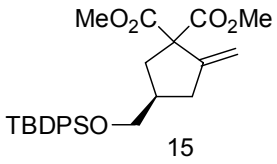
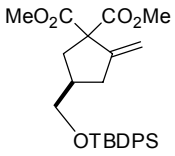


1H NMR (400 MHz, CDCl3)



15

13C NMR (100 MHz, CDCl3)



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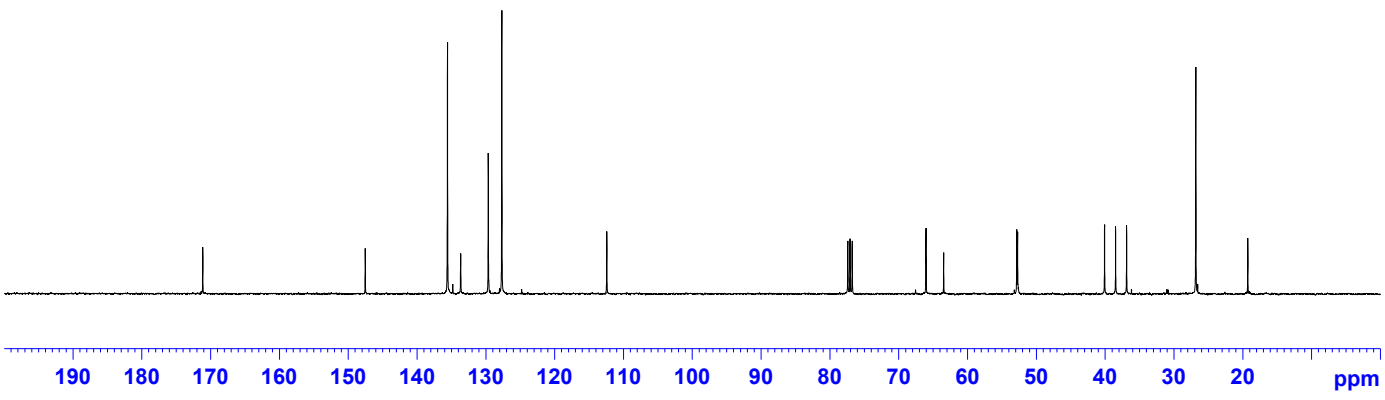
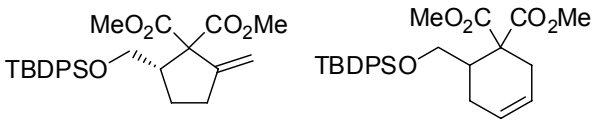
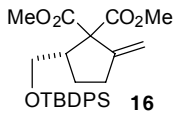


1H NMR (400 MHz, CDCl3)with the cyclohexene as a slight impurity



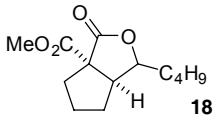
16

13C NMR (100 MHz, CDCl3)



16

1H NMR (500 MHz, CDCl3)



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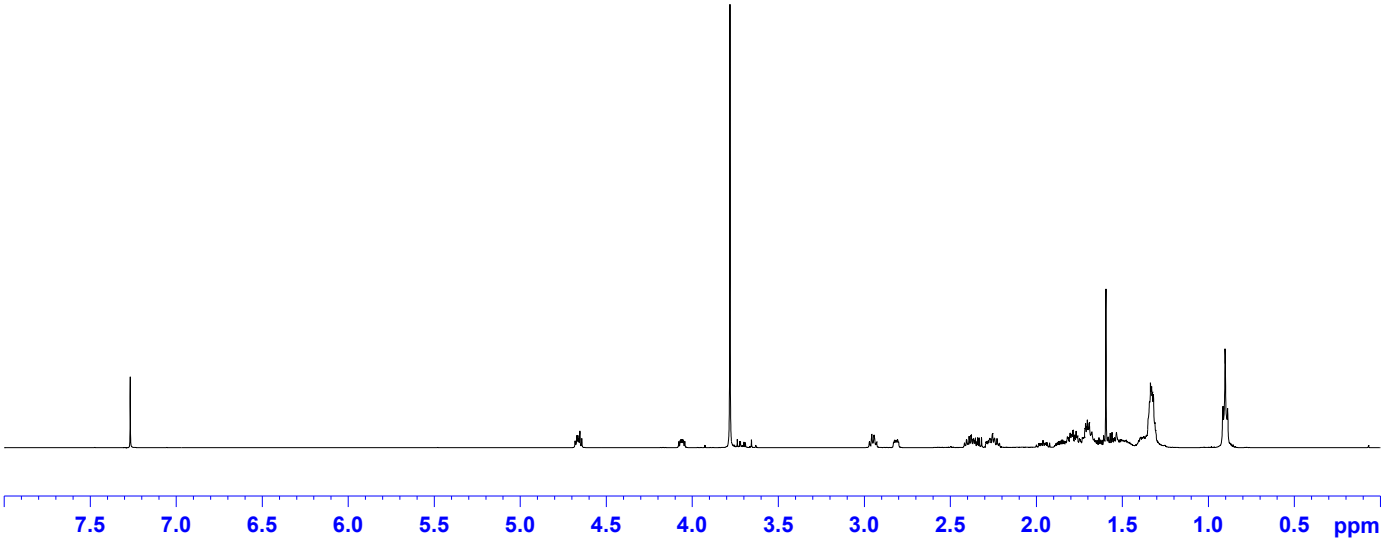
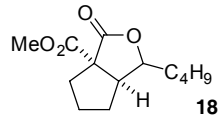


DEPT QGPSP (125 MHz, CDCl3) mixture of diastereomers



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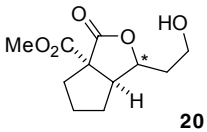
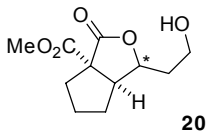
1H NMR (500 MHz, CDCl3) mixture of diastereomers



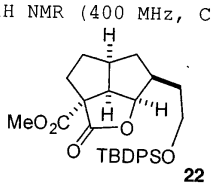
20

13 C NMR (125 MHz, CDCl3) mixture of diastereomers



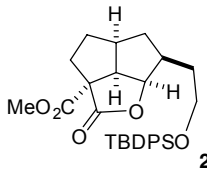
20

1H NMR (400 MHz, CDCl3)



22

13 C NMR (125 MHz, CDCl3)



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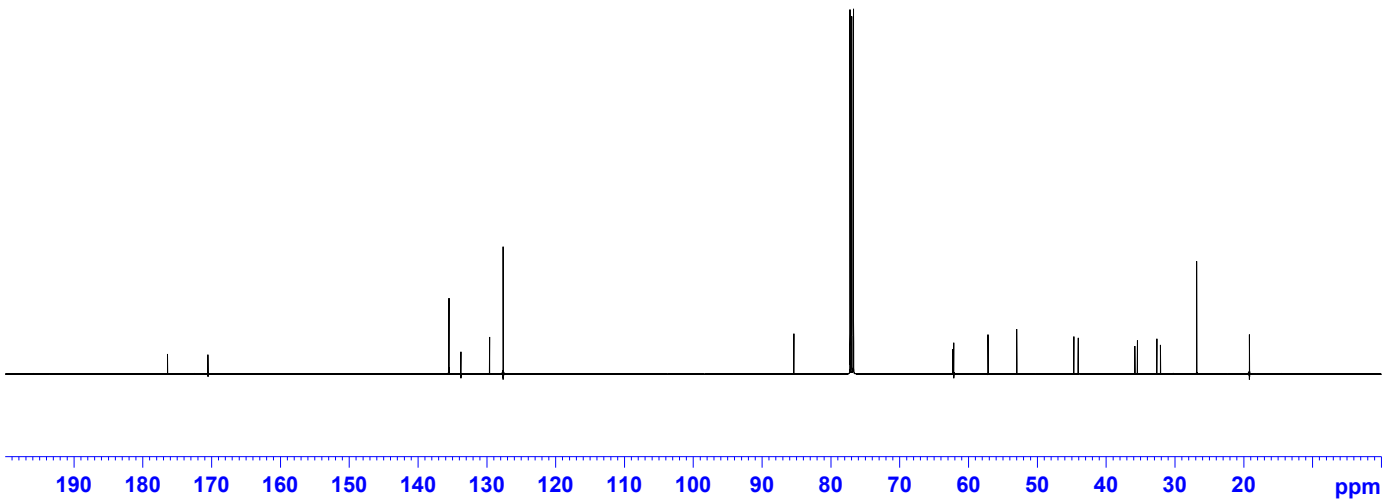
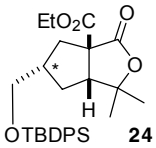
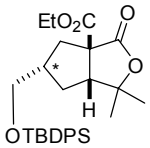


1H NMR (500 MHz, CDCl3) mixture of diastereomers



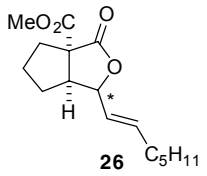
24

13 C NMR (125 MHz, CDCl3) mixture of diastereomers



24

1H NMR (500 MHz, CDCl3) mixture of diastereomers



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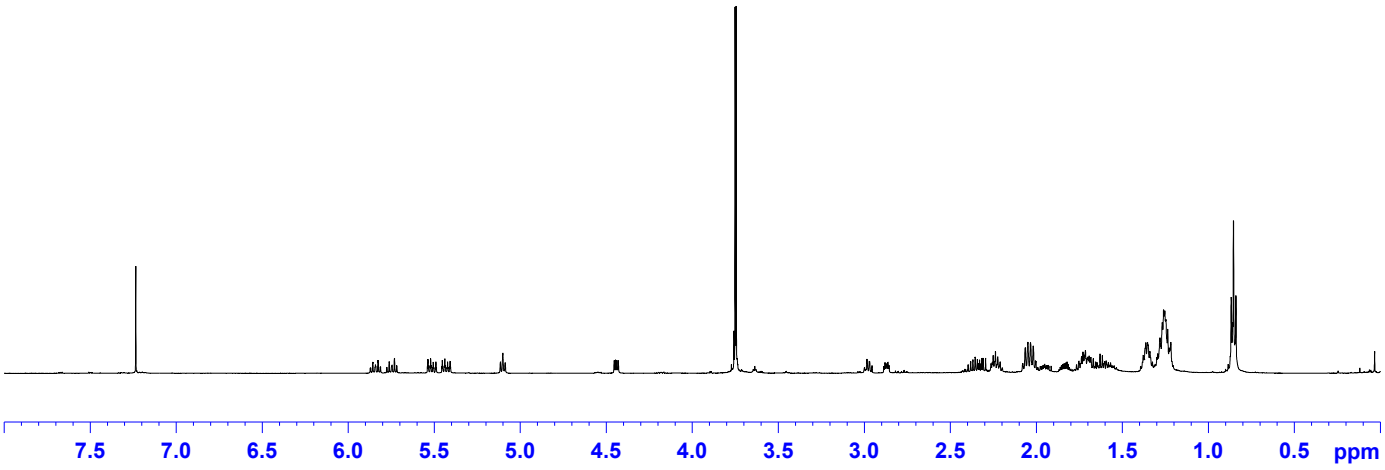
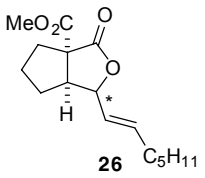
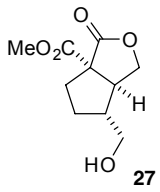


13 C NMR (125 MHz, CDCl3) mixtuer of diastereomers



26

1H NMR (400 MHz, CDCl3)



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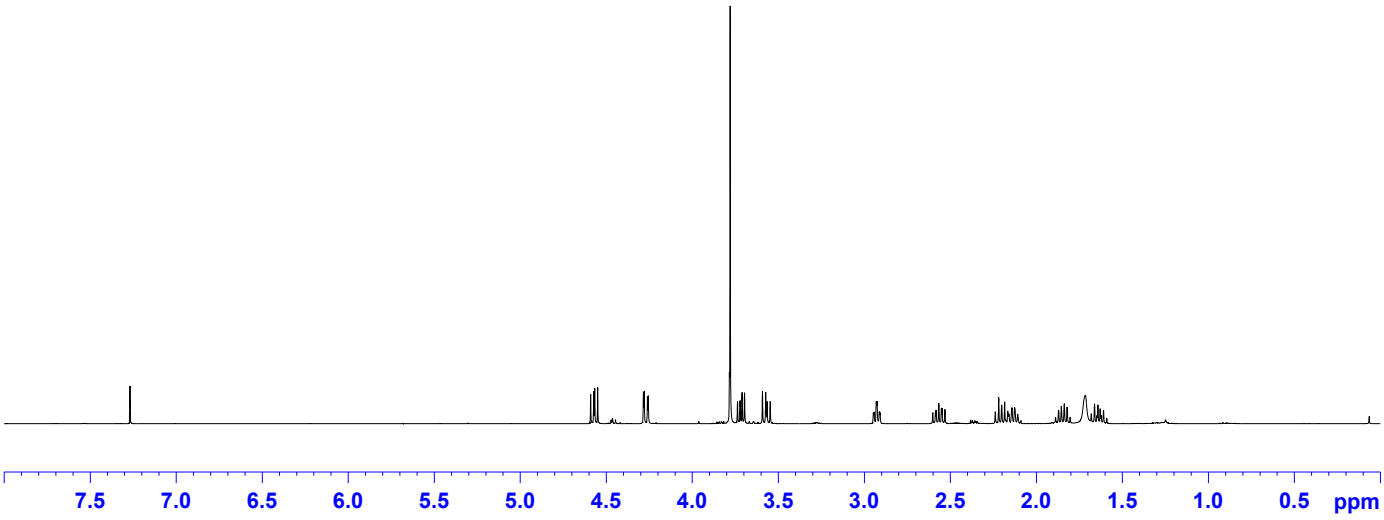
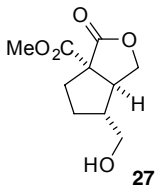
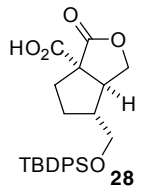


13 C NMR (100 MHz, CDCl3)



27

1H NMR (400 MHz, CDCl3)



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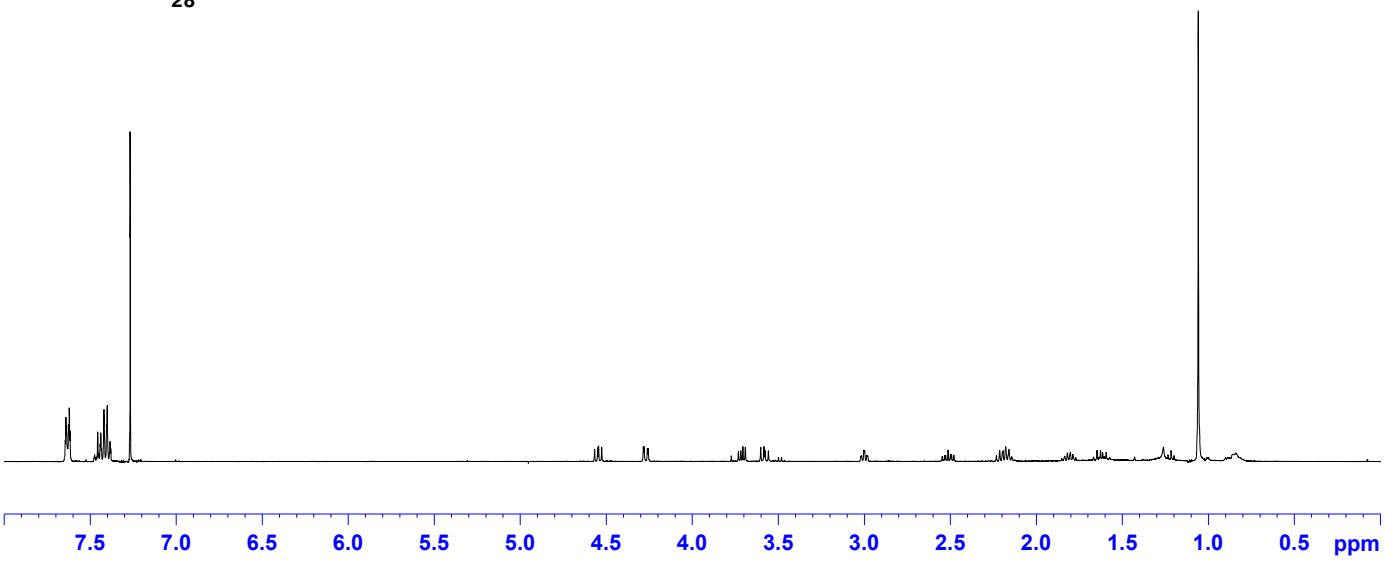
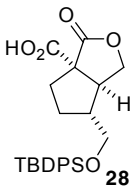


13 C NMR (50 MHz, CDCl3)



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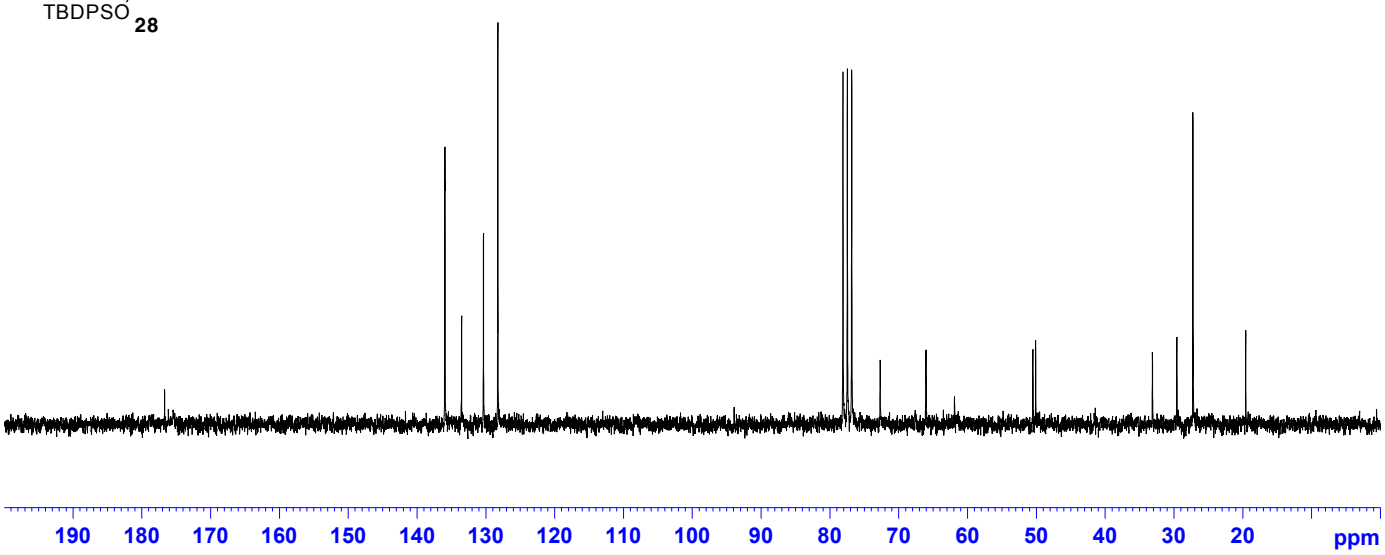

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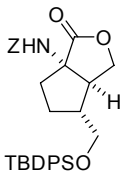
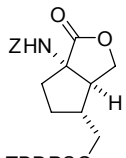
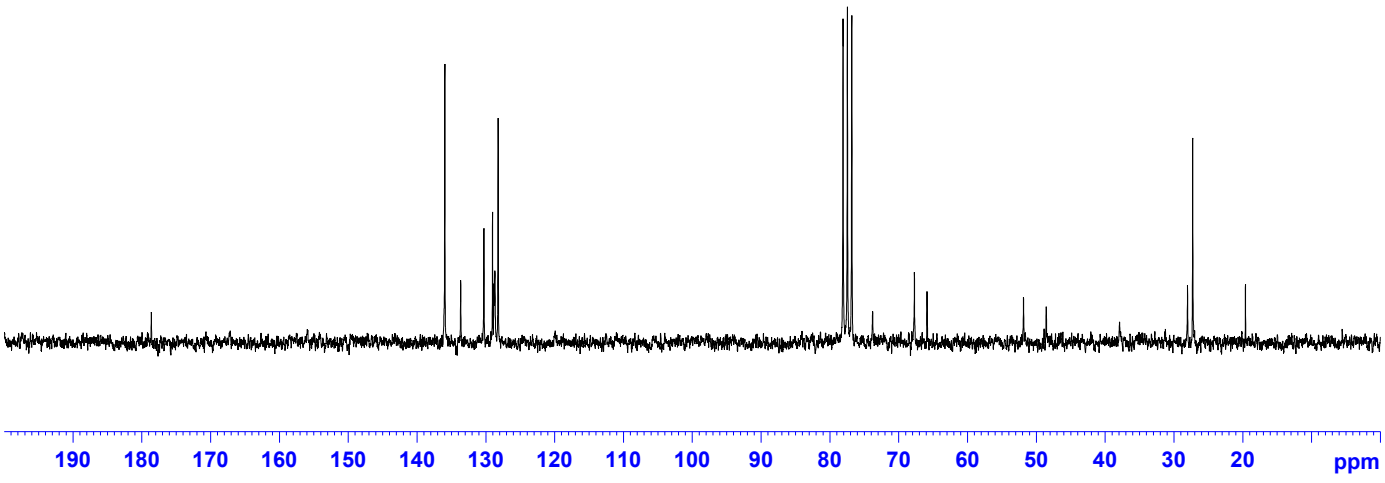


31

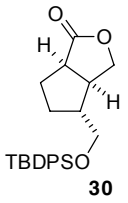
13 C NMR (50 MHz, CDCl3)



31

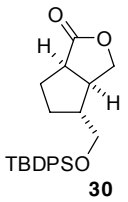


1H NMR (400 MHz, CDCl3)

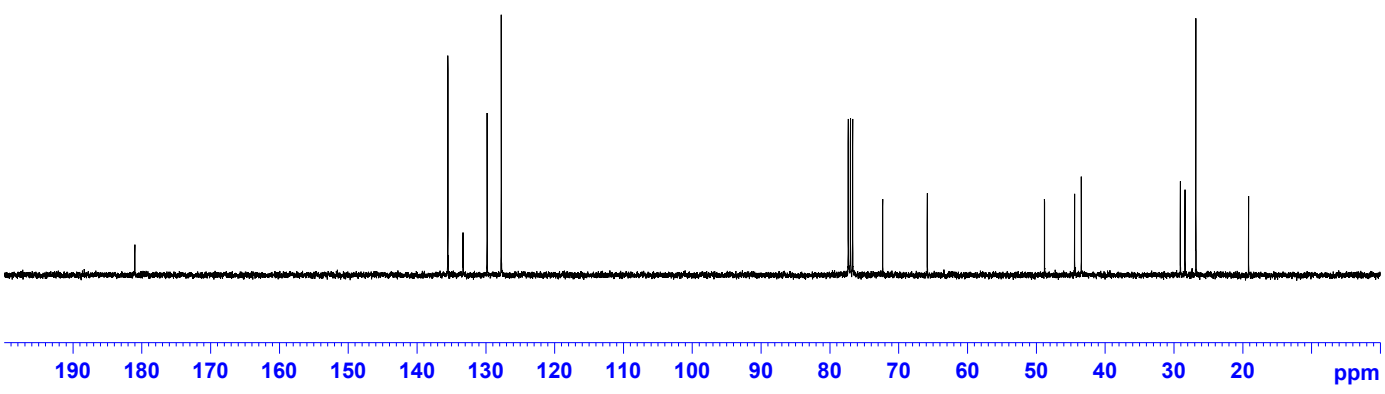


30

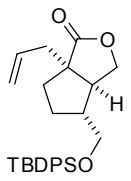
13C NMR (100 MHz, CDCl3)



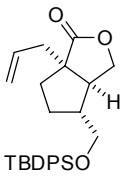
30

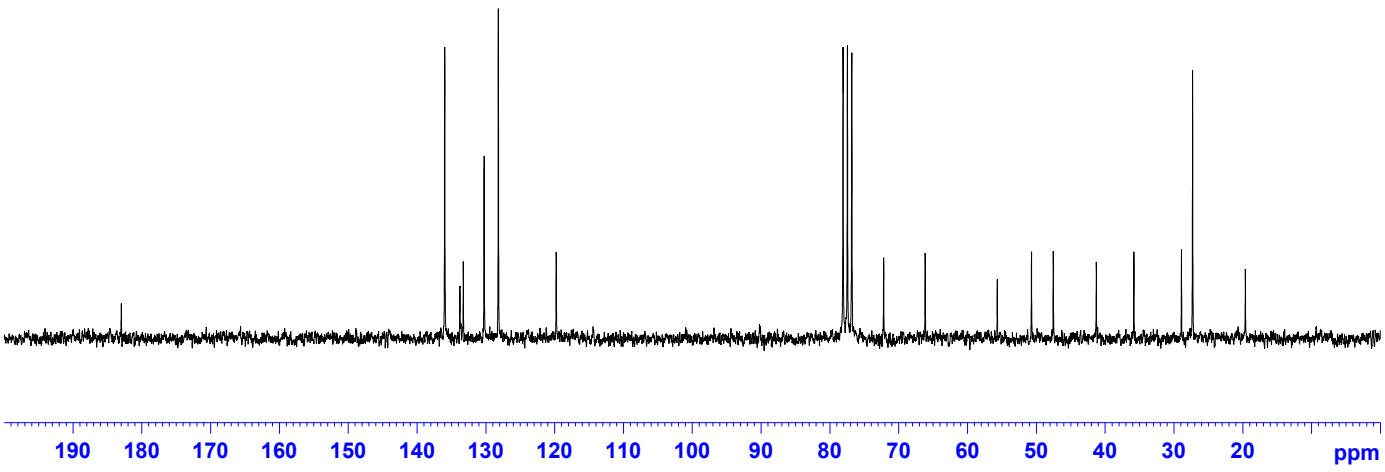


1H NMR (400 MHz, CDCl3)

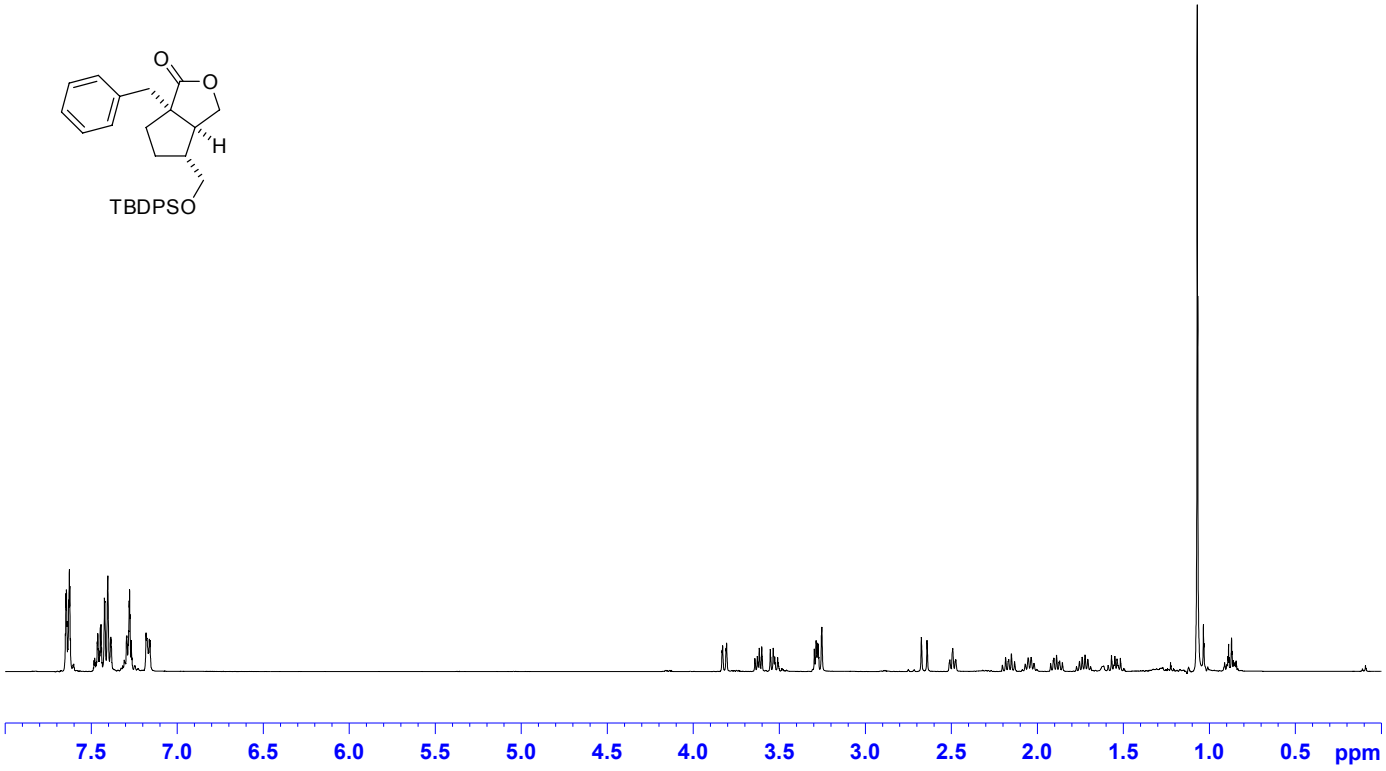


13C NMR (50 MHz, CDCl3)

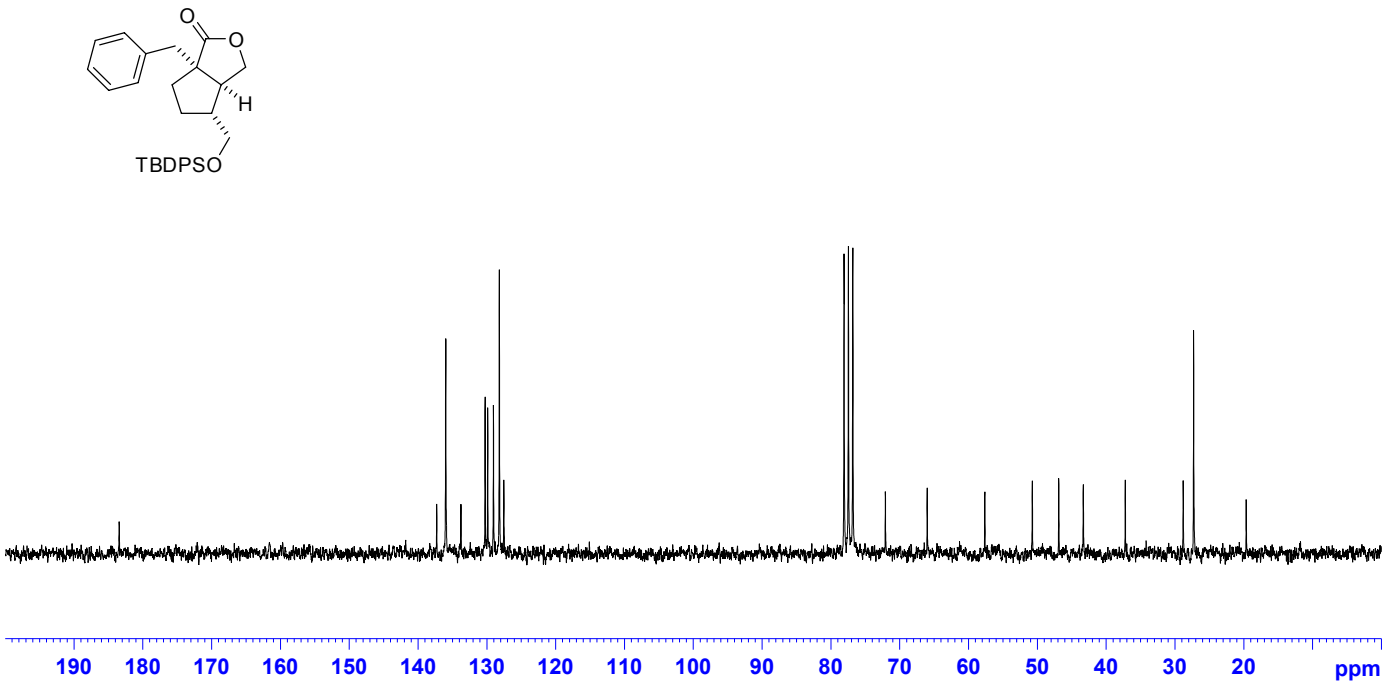




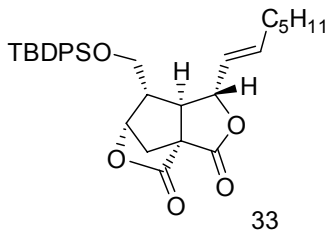
1H NMR (400 MHz, CDCl3)



13C NMR (50 MHz, CDCl3)



1H NMR (500 MHz, CDCl3)



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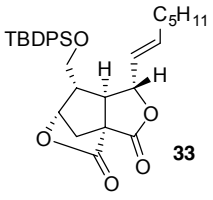
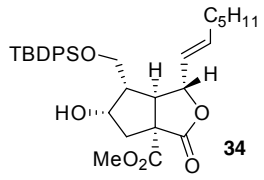
13C NMR (125 MHz, CDCl3)



33

1H NMR (500 MHz, CDCl3)



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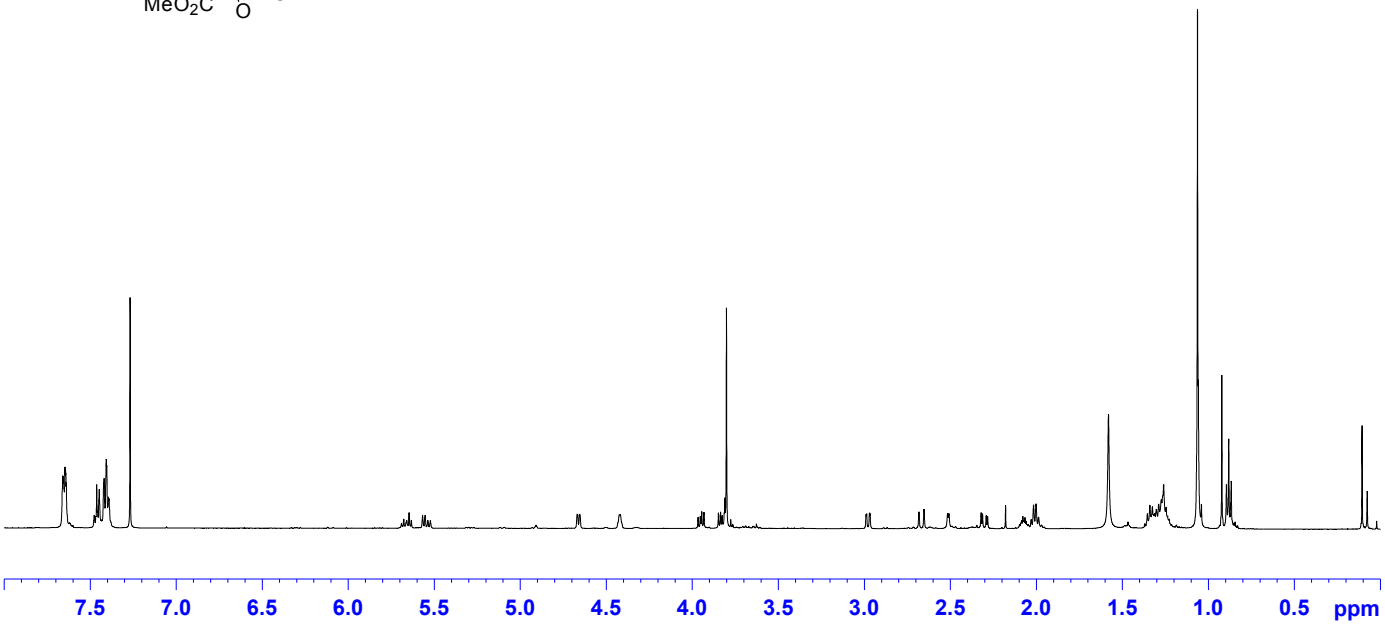
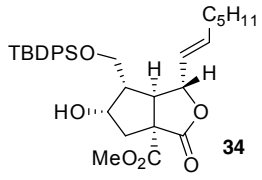


13 C NMR (125 MHz, CDCl3)



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