

# **Synthesis of (–)-6,7-Dideoxysqualestatin H5 by Carbonyl Ylide Cycloaddition–Rearrangement and Cross-electrophile Coupling**

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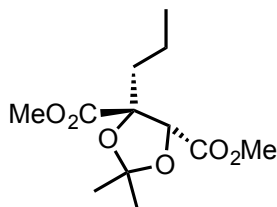
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## 1. General Techniques

All reactions requiring anhydrous conditions were carried out under an atmosphere of argon in flame-dried glassware. Tetrahydrofuran (THF), dichloromethane (DCM), ether (Et<sub>2</sub>O) and ethyl acetate (EtOAc) were obtained from Grubbs' drying stills.<sup>1</sup> MeOH was dried over 4Å MS for at least 24 h. Petrol (petroleum ether) 30–40 °C was used in flash column chromatography. Flash column chromatography was carried out using silica gel (VWR chemicals, BDH) in accordance with Still's method,<sup>2</sup> monitored by thin layer chromatography (TLC) (Merck 60 F<sub>254</sub>) plates. TLC plates were viewed using ultraviolet light ( $\lambda_{\text{max}} = 254/365 \text{ nm}$ ) and immersion in KMnO<sub>4</sub>, anisaldehyde or vanillin stains, followed by heating. Reverse phase HPLC was carried out using Phenomenex - Luna 5u C18(2)100A (column 250 x 10 mm). Except where stated otherwise, commercially available reagents were used as received. "Freshly distilled" refers to distillation over CaH<sub>2</sub> using a short-path distillation apparatus under a nitrogen atmosphere. Melting points (m.p.) were obtained using an Electrothermal melting point apparatus to the nearest 0.1 °C and are uncorrected. Optical rotations were recorded on a Perkin-Elmer 241 polarimeter, with a path length of 10 cm in CHCl<sub>3</sub> or MeOH.  $[\alpha]_{\text{D}}^{25}$  values are given in 10<sup>-1</sup> deg cm<sup>2</sup> g<sup>-1</sup>. Concentrations (*c*) are given in grams/cm<sup>3</sup>. Infrared spectra were obtained using a PerkinElmer FT-IR spectrometer (Universal ATR Sampling Accessory), with absorption maxima quoted in wavenumbers (cm<sup>-1</sup>). Peak intensities are described as broad (br), weak (w), medium (m) or strong (s). Nuclear magnetic resonance (<sup>1</sup>H NMR and <sup>13</sup>C NMR) spectra were recorded on Bruker Avance UltraShield AVC 500 and AVX 500 (500 MHz) spectrometers in CDCl<sub>3</sub>, referenced to residual CHCl<sub>3</sub> singlet at  $\delta$  7.27 and CD<sub>3</sub>OD quintet at  $\delta$  3.31 for <sup>1</sup>H NMR spectra, and to the central line of CDCl<sub>3</sub> triplet at 77.16 as well as the central line of CD<sub>3</sub>OD heptet at 49.0 for <sup>13</sup>C NMR spectra. Chemical shifts are quoted in parts per million (ppm). Coupling constants (*J*) are measured in Hertz (Hz). The splittings are quoted as singlet (s), doublet (d), triplet (t), quartet (q), or multiplet (m). The <sup>13</sup>C NMR peaks were assigned by standard methods using HSQC. Stereochemical assignments were based on NOE studies and X-ray crystallography. Low resolution mass spectra were obtained using electrospray ionization (ESI). High resolution mass spectra were obtained by electrospray ionization (ESI) using tetraoctylammonium bromide or sodium dodecyl sulfate as the lock mass.

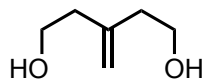
## 2. Experimental

### (4*R*,5*R*)-Dimethyl 2,2-dimethyl-4-propyl-1,3-dioxolane-4,5-dicarboxylate (SI-1)



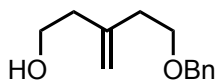
A stirred solution of dimethyl-2,3-*O*-isopropylidene-*L*-tartrate (**11**) (4.76 g, 21.8 mmol), 1-iodopropane (2.00 mL, 20.5 mmol) and freshly distilled HMPA (20 mL) in THF (100 mL) was cooled to  $-78\text{ }^{\circ}\text{C}$ . To this reaction mixture was added dropwise a pre-cooled ( $-78\text{ }^{\circ}\text{C}$ ) solution of LDA [freshly prepared by adding dropwise *n*-BuLi (17 mL, 1.6 M in hexanes, 27 mmol) to a solution of freshly distilled *i*-Pr<sub>2</sub>NH (3.2 g, 30 mmol) in THF (100 mL) at  $0\text{ }^{\circ}\text{C}$ ] over 1 h. The reaction mixture was further stirred for 48 h at  $-78\text{ }^{\circ}\text{C}$ , then quenched at that temperature with sat. aq NH<sub>4</sub>Cl (50 mL) and extracted with EtOAc (3x100 mL). The combined organic layers were washed with sat. aq CuSO<sub>4</sub> (100 mL), dried (MgSO<sub>4</sub>), evaporated under reduced pressure and purified by column chromatography to give alkylated tartrate **SI-1** (3.51 g, 66%) as a colourless oil;  $R_f$  0.4 (10% Et<sub>2</sub>O in petrol);  $[\alpha]_{\text{D}}^{25} = -54.6$  ( $c$  1.0, CHCl<sub>3</sub>); IR (film,  $\nu_{\text{max}}$  cm<sup>-1</sup>) 2963 s, 2859 s, 1736 s, 1655 m, 1561 m, 1459 s, 1375 m, 1214 s, 1104 s, 1023 s, 849 m; <sup>1</sup>H NMR (500 MHz; CDCl<sub>3</sub>)  $\delta$  4.40 (1H, s, CHCO<sub>2</sub>Me), 3.74 (3H, s, CO<sub>2</sub>Me), 3.65 (3H, s, CO<sub>2</sub>Me), 2.05 (1H, ddd,  $J$  14,  $J$  12,  $J$  5, CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 1.72 (1H, ddd,  $J$  14,  $J$  12,  $J$  5, CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 1.55 (3H, s, CH<sub>3</sub>C), 1.52–1.43 (1H, m, CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 1.36 (3H, s, CH<sub>3</sub>C), 1.32–1.24 (1H, m, CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 0.89 (3H, t,  $J$  7, CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>); <sup>13</sup>C NMR (125 MHz; CDCl<sub>3</sub>)  $\delta$  171.7 (CO<sub>2</sub>Me), 167.9 (CO<sub>2</sub>Me), 111.7 (CCH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 86.7 (C(CH<sub>3</sub>)<sub>2</sub>), 80.8 (CHCO<sub>2</sub>Me), 52.44 (CO<sub>2</sub>Me), 52.40 (CO<sub>2</sub>Me), 38.3 (CCH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 26.76 (CMe), 26.73 (CMe), 17.4 (CCH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 14.1 (CCH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>); HRMS  $m/z$  (M+Na<sup>+</sup>), found 261.1335 C<sub>12</sub>H<sub>21</sub>O<sub>6</sub> requires 261.1333.

### 3-Methylenepentane-1,5-diol (**13**)



To a solution of freshly distilled TMEDA (13.9 g, 120 mmol) in Et<sub>2</sub>O (30 mL) was added dropwise *n*-BuLi (48 mL, 2.5 M in hexanes, 120 mmol) at 0 °C and stirred for 15 min. A solution of 3-methyl-3-butenol (**12**) (5.17 g, 60.0 mmol) in Et<sub>2</sub>O (20 mL) was then added dropwise *via* cannula over 15 min and the reaction mixture allowed to reach rt over 30 min. The reaction mixture was then vigorously stirred for 15 h at rt to give a pale yellow suspension, diluted with freshly distilled THF (30 mL) and cooled to –78 °C before addition of dry paraformaldehyde (1.89 g, 63.0 mmol) in one portion. The reaction mixture was then allowed to warm to rt (1 h) and stirred vigorously overnight. The reaction mixture was then quenched with sat. aq NH<sub>4</sub>Cl (50 mL) and the aq layer was extracted with CHCl<sub>3</sub>/*i*-PrOH (8:2, 5x100 mL), the combined organic layers were dried (MgSO<sub>4</sub>), evaporated under reduced pressure and the residue purified by column chromatography to give diol **13**<sup>3</sup> (4.27 g, 61%) as a light yellow oil; *R*<sub>f</sub> 0.33 (EtOAc); IR (film,  $\nu_{\text{max}}$  cm<sup>-1</sup>) 3317 br, 2926 s, 2360 m, 1645 w, 1435 w, 1040 s; <sup>1</sup>H NMR (500 MHz; CDCl<sub>3</sub>)  $\delta$  4.99 (2H, s, CH<sub>2</sub>=C), 3.77 (4H, q, *J* 6, 2xCH<sub>2</sub>OH), 2.34 (4H, t, *J* 6, 2xCH<sub>2</sub>CH<sub>2</sub>OH), 1.82 (2H, t, *J* 5, 2xCH<sub>2</sub>OH); <sup>13</sup>C NMR (125 MHz; CDCl<sub>3</sub>)  $\delta$  143.1 (CH<sub>2</sub>=C), 114.4 (CH<sub>2</sub>=C), 60.8 (CH<sub>2</sub>OH), 39.0 (CH<sub>2</sub>CH<sub>2</sub>OH); HRMS *m/z* (M+Na<sup>+</sup>) found 139.0735, C<sub>6</sub>H<sub>12</sub>NaO<sub>2</sub> requires 139.0730.

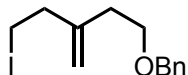
### 5-(Benzyloxy)-3-methylenepentan-1-ol (**14**)



To a stirred solution of diol **13** (1.74 g, 15.0 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (20 mL) was added Ag<sub>2</sub>O (5.21 g, 22.5 mmol) and benzyl bromide (2.82 g, 16.5 mmol) at rt. After 12 h, the reaction mixture was filtered, evaporated under reduced pressure and purified by column chromatography to give benzyl ether **14** (2.52 g, 81%) as a light yellow oil; *R*<sub>f</sub> 0.43 (40% EtOAc in petrol); IR (film,  $\nu_{\text{max}}$  cm<sup>-1</sup>) 3339 br, 2935 m, 2861 s, 2360 m, 2341 w, 1645 m, 1099 s; <sup>1</sup>H NMR (500 MHz; CDCl<sub>3</sub>)  $\delta$  7.37–7.28 (5H, m, 5xArCH), 4.94 (2H, d, *J* 9, CH<sub>2</sub>=C), 4.53 (2H, s, CH<sub>2</sub>Ph), 3.73 (2H, t, *J* 6, CH<sub>2</sub>OH), 3.62 (2H, t, *J* 7, CH<sub>2</sub>OBn), 2.38 (2H, t, *J* 7, CH<sub>2</sub>CH<sub>2</sub>OH), 2.33 (2H, t, *J* 6, CH<sub>2</sub>CH<sub>2</sub>OBn), 1.82 (1H, br. s, OH); <sup>13</sup>C NMR

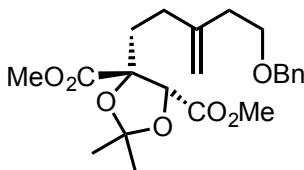
(125 MHz; CDCl<sub>3</sub>)  $\delta$  143.5 (CH<sub>2</sub>=C), 138.3 (ArC), 128.5 (ArCH), 127.9 (ArCH), 127.8 (ArCH), 113.6 (CH<sub>2</sub>=C), 73.2 (CH<sub>2</sub>Ph), 69.1 (CH<sub>2</sub>OBn), 60.6 (CH<sub>2</sub>OH), 39.8 (CH<sub>2</sub>), 35.8 (CH<sub>2</sub>); HRMS  $m/z$  (M+Na<sup>+</sup>) found 229.1196, C<sub>13</sub>H<sub>18</sub>NaO<sub>2</sub> requires 229.1199.

**(((5-Iodo-3-methylenepentyl)oxy)methyl)benzene (15)**



To a solution of PPh<sub>3</sub> (2.30 g, 8.77 mmol) and imidazole (1.66 g, 24.4 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (37 mL) was added iodine (3.10 g, 12.2 mmol) at 0 °C. After 15 min, benzyl ether **14** (2.30 g, 11.1 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (6 mL) was added dropwise. The ice bath was removed and the suspension was stirred for 2 h at rt. H<sub>2</sub>O (30 mL) was then added and the aq layer extracted with CH<sub>2</sub>Cl<sub>2</sub> (2x30 mL), the combined organic layers were dried (MgSO<sub>4</sub>), evaporated under reduced pressure and the residue purified by column chromatography to give iodide **15** (3.50 g, quant.) as a colourless oil, *R<sub>f</sub>* 0.21 (20% CH<sub>2</sub>Cl<sub>2</sub> in petrol); IR (film,  $\nu_{\max}$  cm<sup>-1</sup>) 2826 s, 1645 m, 1595 m, 1495 m, 1453 s, 1361 s, 1098 s; <sup>1</sup>H NMR (500 MHz; CDCl<sub>3</sub>)  $\delta$  7.38–7.25 (5H, m, ArH), 4.91 (2H, d, *J* 12, C=CH<sub>2</sub>), 4.53 (2H, s, CH<sub>2</sub>Ph), 3.59 (2H, t, *J* 7, CH<sub>2</sub>OBn), 3.26 (2H, t, *J* 8, CH<sub>2</sub>I), 2.63 (2H, t, *J* 8, ICH<sub>2</sub>CH<sub>2</sub>), 2.36 (2H, t, *J* 7, OBnCH<sub>2</sub>CH<sub>2</sub>); <sup>13</sup>C NMR (125 MHz; CDCl<sub>3</sub>)  $\delta$  145.3 (C=CH<sub>2</sub>), 138.4 (ArC), 128.5 (ArCH), 127.8 (ArCH), 127.75 (ArCH), 113.0 (C=CH<sub>2</sub>), 73.2 (CH<sub>2</sub>Ph), 68.9 (CH<sub>2</sub>OBn), 40.7 (ICH<sub>2</sub>CH<sub>2</sub>), 35.7 (CH<sub>2</sub>CH<sub>2</sub>OBn), 3.54 (ICH<sub>2</sub>); HRMS  $m/z$  (M+Na<sup>+</sup>) found 339.0215, C<sub>13</sub>H<sub>17</sub>INaO requires 339.0216.

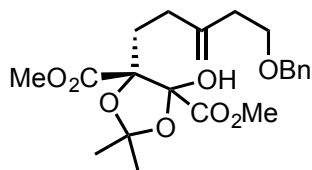
**(4*R*,5*R*)-Dimethyl 4-{5-(benzyloxy)-3-methylenepentyl}-2,2-dimethyl-1,3-dioxolane-4,5-dicarboxylate (16)**



A stirred solution of dimethyl-2,3-*O*-isopropylidene-*L*-tartrate **11** (873 mg, 4.0 mmol), iodide **15** (632 mg, 2 mmol) and freshly distilled HMPA (2.70 mL) in THF (10 mL) was cooled to -78 °C. To this reaction mixture was added dropwise a pre-cooled (-78 °C) solution of LDA [4.0 mmol, freshly prepared by adding dropwise *n*-BuLi (1.6 mL, 2.5 M

in hexanes, 4.0 mmol) to a solution of freshly distilled *i*-Pr<sub>2</sub>NH (405 mg, 4.0 mmol) in THF (10 mL) at 0 °C] over 1 h. The reaction mixture was further stirred for 48 h at –78 °C, and then quenched at the same temperature with sat. aq NH<sub>4</sub>Cl (20 mL), extracted with EtOAc (3x30 mL), washed with sat. aq CuSO<sub>4</sub> (30 mL). The combined organic layers were dried (MgSO<sub>4</sub>), evaporated under reduced pressure and purified by column chromatography to give alkylated tartrate **16** (637 mg, 78%) as a colourless oil; *R<sub>f</sub>* 0.48 (40% Et<sub>2</sub>O in petrol); [ $\alpha$ ]<sub>D</sub><sup>25</sup> = –61.4 (*c* 0.07, CHCl<sub>3</sub>); IR (film,  $\nu_{\text{max}}$  cm<sup>–1</sup>) 3066 w, 2991 m, 2858 w, 1756 s, 1739 s, 1647 w, 1453 m, 1382 m, 1209 s, 1103 s; <sup>1</sup>H NMR (500 MHz; CDCl<sub>3</sub>)  $\delta$  7.39–7.28 (5H, m, 5xArCH), 4.95 (1H, s, CHCO<sub>2</sub>Me), 4.78 (2H, d, *J* 16, CH<sub>2</sub>=C), 4.51 (2H, s, CH<sub>2</sub>Ph), 3.80 (3H, s, CO<sub>2</sub>Me), 3.80 (3H, s, CO<sub>2</sub>Me), 3.56 (2H, t, *J* 7, CH<sub>2</sub>OBn), 2.32 (2H, t, *J* 7, CH<sub>2</sub>CH<sub>2</sub>OBn), 2.21–2.11 (1H, m, 1H of CH<sub>2</sub>CH<sub>2</sub>C=C), 2.03–1.91 (2H, m, CH<sub>2</sub>CH<sub>2</sub>C=C), 1.81–1.74 (1H, m, 1H of CH<sub>2</sub>CH<sub>2</sub>C=C), 1.61 (3H, s, CH<sub>3</sub>C), 1.45 (3H, s, CH<sub>3</sub>C); <sup>13</sup>C NMR (125 MHz; CDCl<sub>3</sub>)  $\delta$  172.3 (CO<sub>2</sub>Me), 168.8 (CO<sub>2</sub>Me), 145.5 (CH<sub>2</sub>=C), 138.5 (ArC), 128.5 (ArCH), 127.8 (ArCH), 127.7 (ArCH), 112.8 (CH<sub>2</sub>=C), 111.0 (CMe<sub>2</sub>), 85.6 (CCO<sub>2</sub>Me), 80.2 (CHCO<sub>2</sub>Me), 72.9 (CH<sub>2</sub>Ph), 68.9 (CH<sub>2</sub>OBn), 53.0 (CO<sub>2</sub>Me), 52.5 (CO<sub>2</sub>Me), 36.4 (CH<sub>2</sub>), 32.7 (CH<sub>2</sub>), 30.4 (CMe), 27.8 (CMe), 26.1 (CH<sub>2</sub>CCO<sub>2</sub>Me); HRMS *m/z* (M+Na<sup>+</sup>) found 429.1886, C<sub>22</sub>H<sub>30</sub>NaO<sub>7</sub> requires 429.1884.

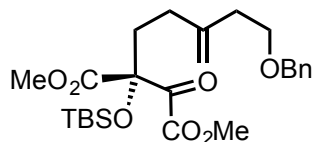
**(4*R*)-Dimethyl 4-{5-(benzyloxy)-3-methylenepentyl}-5-hydroxy-2,2-dimethyl-1,3-dioxolane-4,5-dicarboxylate (**17**)**



A pre-cooled (–78 °C) solution of alkylated tartrate **16** (5.45 g, 13.4 mmol) in THF (65 mL) was added dropwise over 1 h to a stirred solution of LDA [20.1 mmol, freshly prepared by adding dropwise *n*-BuLi (8 mL, 2.5 M in hexanes, 20 mmol) to a solution of freshly distilled *i*-Pr<sub>2</sub>NH (2.6 mL, 20 mmol) in THF (20 mL) at 0 °C] at –78 °C. After 30 min stirring at –78 °C, MoOPH<sup>4</sup> (8.7 g, 20 mmol) was added in one portion (by solid addition funnel) and the reaction mixture warmed to –40 °C over 15 min. The reaction was stirred at –40 °C for 24 h, then warmed to –20 °C and stirred for a further 3 h. The reaction

mixture was quenched by adding sat. aq Na<sub>2</sub>SO<sub>3</sub> solution and warmed to rt. The reaction mixture was diluted with Et<sub>2</sub>O (100 mL) and H<sub>2</sub>O (50 mL). The layers were separated and the aq layer extracted with Et<sub>2</sub>O (3x100 mL). The combined organic layers were washed with sat. aq CuSO<sub>4</sub> (50 mL), dried (MgSO<sub>4</sub>), evaporated under reduced pressure and the residue purified by column chromatography (15% EtOAc in petrol) to give a mixture of diastereomer of hydroxyacetone **17** (4.0 g, 71%) as a colourless oil; *R<sub>f</sub>* 0.32 and 0.25 (30% EtOAc in petrol);  $[\alpha]_D^{25} = -5.2$  (*c* 0.11, CHCl<sub>3</sub>); IR (film,  $\nu_{\max}$  cm<sup>-1</sup>) 3453 br, 2990 m, 2952 s, 2858 m, 1751 s, 1093 s; <sup>1</sup>H NMR (500 MHz; CDCl<sub>3</sub>)  $\delta$  7.36–7.28 (5H, m, 5xArCH), 4.81 (2H, d, *J* 6, CH<sub>2</sub>=C), 4.59 (1H, s, OH), 4.51 (2H, s, CH<sub>2</sub>Ph), 3.81 (3H, s, CO<sub>2</sub>Me), 3.69 (3H, s, CO<sub>2</sub>Me), 3.56 (2H, t, *J* 7, CH<sub>2</sub>OBn), 2.35 (2H, t, *J* 7, CH<sub>2</sub>CH<sub>2</sub>OBn), 2.24–2.03 (3H, m, CH<sub>2</sub>, 1H of CH<sub>2</sub>), 1.84 (1H, td, *J* 14, 7, 1H of CH<sub>2</sub>CCO<sub>2</sub>Me), 1.60 (3H, s, CH<sub>3</sub>C), 1.57 (3H, s, CH<sub>3</sub>C); <sup>13</sup>C NMR (125 MHz; CDCl<sub>3</sub>)  $\delta$  171.6 (CO<sub>2</sub>Me), 170.3 (CO<sub>2</sub>Me), 145.7 (CH<sub>2</sub>=C), 138.6 (ArC), 128.5 (ArCH), 127.8 (ArCH), 127.7 (ArCH), 113.7 (CH<sub>2</sub>=C), 110.9 (CMe<sub>2</sub>), 101.9 (HO–C–CO<sub>2</sub>Me), 91.0 (CCO<sub>2</sub>Me), 73.1 (CH<sub>2</sub>Ph), 68.9 (CH<sub>2</sub>OBn), 54.1 (CO<sub>2</sub>Me), 52.6 (CO<sub>2</sub>Me), 36.4 (CH<sub>2</sub>), 34.0 (CH<sub>2</sub>), 30.9 (CMe), 29.3 (CMe), 27.5 (CH<sub>2</sub>CCO<sub>2</sub>Me); HRMS *m/z* (M+Na<sup>+</sup>) found 445.1825, C<sub>22</sub>H<sub>30</sub>NaO<sub>8</sub> requires 445.1833.

**(*R*)-Dimethyl 2-{5-(benzyloxy)-3-methylenepentyl}-2-{{*tert*-butyldimethylsilyl}oxy}-3-oxosuccinate (**18**)**

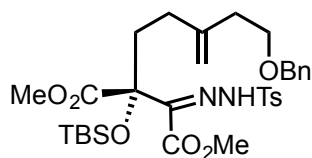


A mixture of hydroxyacetone **17** (537 mg, 1.27 mmol) and H<sub>2</sub>SO<sub>4</sub> (100 mL, 0.1 M in MeOH) was stirred at rt for 48 h. Pyridine (1.0 mL, 12.7 mmol) was then added dropwise, the mixture was concentrated under reduced pressure and the residue diluted with Et<sub>2</sub>O (200 mL) and filtered through a pad of Na<sub>2</sub>SO<sub>4</sub>. The filtrate was concentrated under reduced pressure to give crude hydroxyketone as a yellow oil, which was used in the next step without further purification. DMAP (15.5 mg, 0.13 mmol) was added to the above crude hydroxyketone, followed by a solution of 2,6-lutidine (0.44 mL, 3.82 mmol) in



CH<sub>2</sub>Cl<sub>2</sub> (3 mL). Finally, TBSOTf (0.87 mL, 3.81 mmol) was added. After 24 h at rt, H<sub>2</sub>O (10 mL) was added and the aq layer was extracted with CH<sub>2</sub>Cl<sub>2</sub> (3x20 mL). The combined organic layers were dried (MgSO<sub>4</sub>), evaporated under reduced pressure and the residue purified by column chromatography to give unsaturated ketone **18** (411 mg, 68%) as a colourless oil; *R<sub>f</sub>* 0.43 (10% EtOAc in petrol); [ $\alpha$ ]<sub>D</sub><sup>25</sup> = -2.6 (*c* 0.30, CHCl<sub>3</sub>); IR (film,  $\nu_{\max}$  cm<sup>-1</sup>) 3465 br, 2954 s, 2929 s, 2857 m, 1744 s, 1452 m, 1256 s; <sup>1</sup>H NMR (500 MHz; CDCl<sub>3</sub>)  $\delta$  7.36–7.28 (5H, m, 5xArCH), 4.82 (2H, s, CH<sub>2</sub>=C), 4.52 (2H, s, CH<sub>2</sub>Ph), 3.84 (3H, s, CO<sub>2</sub>Me), 3.76 (3H, s, CO<sub>2</sub>Me), 3.57 (2H, t, *J* 7, CH<sub>2</sub>OBn), 2.35 (2H, t, *J* 7, CH<sub>2</sub>CH<sub>2</sub>OBn), 2.27–2.20 (1H, m, 1 H of CH<sub>2</sub>CH<sub>2</sub>C=C), 2.19–1.98 (3H, m, 1 H of CH<sub>2</sub>CH<sub>2</sub>C=C and CH<sub>2</sub>CH<sub>2</sub>C=C), 0.88 (9H, s, SiMe<sub>3</sub>), 0.17 (3H, s, SiMe), 0.17 (3H, s, SiMe); <sup>13</sup>C NMR (125 MHz; CDCl<sub>3</sub>)  $\delta$  190.1 (C=O), 169.8 (CO<sub>2</sub>Me), 162.7 (CO<sub>2</sub>Me), 145.5 (CH<sub>2</sub>=C), 138.5 (ArC), 128.5 (ArCH), 127.8 (ArCH), 127.7 (ArCH), 111.3 (CH<sub>2</sub>=C), 83.8 (CCO<sub>2</sub>Me), 73.1 (CH<sub>2</sub>Ph), 68.9 (CH<sub>2</sub>OBn), 53.6 (CO<sub>2</sub>Me), 52.9 (CO<sub>2</sub>Me), 36.4 (CH<sub>2</sub>), 34.9 (CH<sub>2</sub>), 29.8 (CH<sub>2</sub>), 25.9 (CMe<sub>3</sub>), 18.9 (CMe<sub>3</sub>), -3.0 (SiMe), -3.3 (SiMe); HRMS *m/z* (M+Na<sup>+</sup>) found 501.2228, C<sub>25</sub>H<sub>38</sub>SiNaO<sub>7</sub> requires 501.2279.

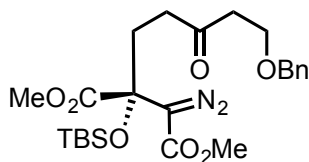
**(*R*)-Dimethyl 2-{5-(benzyloxy)-3-methylenepentyl}-2-{{*tert*-butyldimethylsilyl}oxy}-3-(2-tosylhydrazono)succinate (**19**)**



A mixture of unsaturated ketone **18** (3.2 g, 6.69 mmol) and TsNHNH<sub>2</sub> (1.87 g, 10.0 mmol) in THF (70 mL) was heated at 75 °C under reflux. After 24 h the mixture was concentrated under reduced pressure and purified by column chromatography to give hydrazone **19**<sup>5</sup> (3.48 g, 81%, 85% brsm) as a colourless glass; *R<sub>f</sub>* 0.45 (20% EtOAc in petrol); [ $\alpha$ ]<sub>D</sub><sup>25</sup> = -6.8 (*c* 0.51, CHCl<sub>3</sub>); IR (film,  $\nu_{\max}$  cm<sup>-1</sup>) 3215 br, 2952 m, 2929 m, 2856 s, 2360 m, 1757 s, 1702 s, 1170 s, 1086 s; <sup>1</sup>H NMR (500 MHz; CDCl<sub>3</sub>)  $\delta$  11.63 (1H, s, NH), 7.84 (2H, d, *J* 8, 2xArCH), 7.34 (4H, m, 4xArCH), 7.32–7.28 (3H, m, 3xArCH), 4.84 (1H, s, 1H of CH<sub>2</sub>=C), 4.80 (1H, s, 1H of CH<sub>2</sub>=C), 4.54 (2H, s, CH<sub>2</sub>Ph), 3.75 (3H, s,

CO<sub>2</sub>Me), 3.64 (3H, s, CO<sub>2</sub>Me), 3.59 (2H, t, *J* 7, CH<sub>2</sub>OBn), 2.40 (3H, s, *Me*-Ar), 2.34 (2H, t, *J* 7, CH<sub>2</sub>CH<sub>2</sub>OBn), 2.05–1.97 (3H, m, CH<sub>2</sub>CH<sub>2</sub>C=C and 1H CH<sub>2</sub>CH<sub>2</sub>C=C), 1.93–1.86 (1H, m, 1 H of CH<sub>2</sub>CH<sub>2</sub>C=C), 0.79 (9H, s, SiMe<sub>3</sub>), –0.10 (3H, s, SiMe), –0.24 (3H, s, SiMe); <sup>13</sup>C NMR (125 MHz; CDCl<sub>3</sub>) δ 172.3 (CO<sub>2</sub>Me), 161.8 (CO<sub>2</sub>Me), 146.0 (CH<sub>2</sub>=C), 144.8 (ArC), 138.6 (ArC), 136.9 (ArCMe), 135.3 (N=CCO<sub>2</sub>Me), 129.8 (ArCH), 128.5 (ArCH), 128.2 (ArCH), 127.8 (ArCH), 127.7 (ArCH), 110.5 (CH<sub>2</sub>=C), 80.2 (CCO<sub>2</sub>Me), 73.1 (CH<sub>2</sub>Ph), 69.0 (CH<sub>2</sub>OBn), 52.5 (CO<sub>2</sub>Me), 52.3 (CO<sub>2</sub>Me), 36.7 (CH<sub>2</sub>), 35.6 (CH<sub>2</sub>), 30.2 (CH<sub>2</sub>), 25.7 (CMe<sub>3</sub>), 21.7 (ArMe), 18.5 (CMe<sub>3</sub>), –3.1 (SiMe), –3.2 (SiMe); HRMS *m/z* (M+Na<sup>+</sup>) found 669.2642, C<sub>32</sub>H<sub>46</sub>N<sub>2</sub>NaO<sub>8</sub>SSi requires 669.2642.

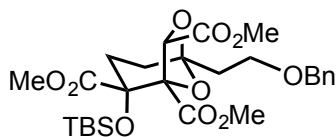
**(*R*)-Dimethyl 2-{5-(benzyloxy)-3-oxopentyl}-2-{{*tert*-butyldimethylsilyl}oxy}-3-diazosuccinate (**20**)**



A solution of hydrazone **19** (110 mg, 0.17 mmol) and sudan red 7B (~1 mg) in CH<sub>2</sub>Cl<sub>2</sub> (20 mL) was cooled to –78 °C. A stream of O<sub>3</sub> in oxygen was bubbled through the solution. Ozone treatment was terminated when the colour of reaction mixture was changed from red to light pink. The excess O<sub>3</sub> was removed by bubbling N<sub>2</sub> through the reaction mixture. After 5 min, Et<sub>3</sub>N (0.1 mL, 0.68 mmol) was added and reaction mixture was allowed to warm to rt. After 3 h, the reaction mixture was passed through a pad of silica, evaporated under reduced pressure and purified by column chromatography to give diazoketone **20** (67 mg, 80%) as a bright yellow oil; *R<sub>f</sub>* 0.54 (50% Et<sub>2</sub>O in petrol); [α]<sub>D</sub><sup>25</sup> = +1.4 (*c* 0.50, CHCl<sub>3</sub>); IR (film, ν<sub>max</sub> cm<sup>–1</sup>) 2954 m, 2857 m, 2360 s, 2341 m, 2098 s, 1748 m, 1710 s, 1135 s; <sup>1</sup>H NMR (500 MHz; CDCl<sub>3</sub>) δ 7.36–7.30 (5H, m, 5xArCH), 4.50 (2H, s, CH<sub>2</sub>Ph), 3.74–3.72 (8H, m, 2xCO<sub>2</sub>Me, CH<sub>2</sub>OBn), 2.70 (2H, t, *J* 6, O=C–CH<sub>2</sub>), 2.76–2.61 (1H, m, 1H of CH<sub>2</sub>), 2.52–2.46 (1H, m, 1H of CH<sub>2</sub>), 2.27–2.23 (2H, m, O=C–CH<sub>2</sub>), 0.87 (9H, s, SiMe<sub>3</sub>), 0.10 (3H, s, SiMe), 0.06 (3H, s, SiMe); <sup>13</sup>C NMR (125 MHz; CDCl<sub>3</sub>) δ 207.7 (C=O), 171.3 (CO<sub>2</sub>Me), 165.2 (N<sub>2</sub>CCO<sub>2</sub>Me), 138.2 (ArC), 128.5 (ArCH), 127.83 (ArCH), 127.82 (ArCH), 75.4 (TBSO-C-CO<sub>2</sub>Me), 73.4 (CH<sub>2</sub>Ph), 65.4 (CH<sub>2</sub>OBn),

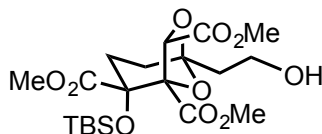
52.9 (CO<sub>2</sub>Me), 52.1 (CO<sub>2</sub>Me), 43.2 (O=C–CH<sub>2</sub>), 37.8 (O=C–CH<sub>2</sub>), 32.1 (CH<sub>2</sub>), 25.8 (CMe<sub>3</sub>), 18.6 (CMe<sub>3</sub>), –3.5 (SiMe), –3.9 (SiMe); HRMS *m/z* (M+Na<sup>+</sup>) found 515.2185, C<sub>24</sub>H<sub>36</sub>N<sub>2</sub>NaO<sub>7</sub>Si requires 515.2184.

**Trimethyl-(1*S*,2*R*,5*R*,7*S*)- 5-(2-(benzyloxy)ethyl)-2-{{*tert*-butyldimethylsilyl}oxy}-6,8-dioxabicyclo[3.2.1]octane-1,2,7-tricarboxylate (**21**)**



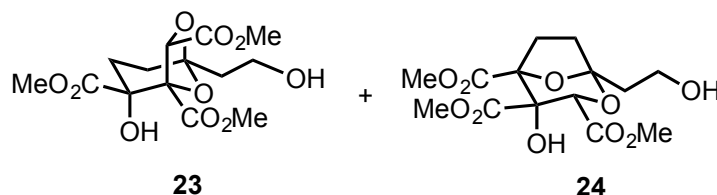
Rh<sub>2</sub>(OAc)<sub>4</sub> (~2 mg, cat.) was added to a stirred solution of diazoketone **20** (68 mg, 0.14 mmol) and freshly distilled methyl glyoxylate<sup>6</sup> (52 mg, 0.59 mmol) in toluene (0.5 mL) and heated to 110 °C. After 1 h, the reaction mixture was allowed to cool to rt, diluted with Et<sub>2</sub>O (10 mL), filtered through Celite and evaporated under reduced pressure.<sup>7</sup> Purification of the residue by column chromatography (20% Et<sub>2</sub>O in petrol) gave the major cycloadduct **21** (58 mg, 75%) as a colourless oil; *R<sub>f</sub>* 0.47 (50% Et<sub>2</sub>O in petrol); [α]<sub>D</sub><sup>25</sup> = +36.5 (*c* 0.21, CHCl<sub>3</sub>); IR (film, ν<sub>max</sub> cm<sup>–1</sup>) 2952 s, 2855 s, 1753 s, 1436 s, 1258 m, 1093 s, 831 s; <sup>1</sup>H NMR (500 MHz; CDCl<sub>3</sub>) δ 7.35–7.26 (5H, m, 5xArCH), 5.59 (1H, s, CHCO<sub>2</sub>Me), 4.51 (2H, d, *J* 6, CH<sub>2</sub>Ph), 3.82 (3H, s, CO<sub>2</sub>Me), 3.77 (2H, ddd, *J* 10, 10, 5, CH<sub>2</sub>OBn), 3.70 (3H, s, CO<sub>2</sub>Me), 3.66 (3H, s, CO<sub>2</sub>Me), 2.39 (1H, ddd, *J* 14, *J* 13, *J* 6, 1H<sub>endo</sub> of C<sup>(3)</sup>H<sub>2</sub>), 2.30 (2H, t, *J* 7, CH<sub>2</sub>CH<sub>2</sub>OBn), 2.01 (1H, td, *J* 13, *J* 6, 1H of C<sup>(4)</sup>H<sub>2</sub>), 1.81–1.75 (2H, m, 1H<sub>exo</sub> of C<sup>(3)</sup>H<sub>2</sub>, 1H of C<sup>(4)</sup>H<sub>2</sub>), 0.89 (9H, s, SiCMe<sub>3</sub>), 0.13 (3H, s, SiMe), 0.11 (3H, s, SiMe); NOE experiment: irradiation at δ 5.59 (CHCO<sub>2</sub>Me) saw enhancement at δ 2.39 (1H<sub>endo</sub> of C<sup>(3)</sup>H<sub>2</sub>); <sup>13</sup>C NMR (125 MHz; CDCl<sub>3</sub>) δ 173.3 (CO<sub>2</sub>Me), 169.6 (CO<sub>2</sub>Me), 166.8 (CO<sub>2</sub>Me), 138.5 (ArC), 128.5 (ArCH), 127.8 (ArCH), 127.7 (ArCH), 111.2 (O–C<sup>(5)</sup>–O), 90.4 (C<sup>(1)</sup>CO<sub>2</sub>Me), 77.4 (CHCO<sub>2</sub>Me), 77.2 (C<sup>(2)</sup>CO<sub>2</sub>Me), 73.2 (CH<sub>2</sub>Ph), 65.9 (CH<sub>2</sub>OBn), 52.7 (CO<sub>2</sub>Me), 52.54 (CO<sub>2</sub>Me), 52.52 (CO<sub>2</sub>Me), 37.5 (CH<sub>2</sub>), 30.0 (C<sup>(4)</sup>H<sub>2</sub>), 29.8 (C<sup>(3)</sup>H<sub>2</sub>), 26.0 (CMe<sub>3</sub>), 19.1 (CMe<sub>3</sub>), –2.7 (SiMe), –2.9 (SiMe); HRMS *m/z* (M+Na<sup>+</sup>) found 575.2286, C<sub>27</sub>H<sub>40</sub>NaO<sub>10</sub>Si requires 575.2283.

**Trimethyl (1*S*,2*R*,5*R*,7*S*)-2-*tert*-butyldimethylsilyloxy}-5-(2-hydroxyethyl)-6,8-dioxabicyclo [3.2.1]octane-1,2,7-tricarboxylate (**22**)**



To a solution of cycloadduct **21** (87 mg, 0.16 mmol) in MeOH (14 mL) was added a spatula tip of 10% Pd/C. The reaction mixture was stirred overnight under H<sub>2</sub> (balloon) at rt. The reaction mixture was then filtered through a pad of Celite (under N<sub>2</sub>), evaporated under reduced pressure and the residue purified by column chromatography to give alcohol **22** (71 mg, 98%) as a white solid; *R<sub>f</sub>* 0.20 (80% Et<sub>2</sub>O in petrol); Mp 111–113 °C;  $[\alpha]_D^{25} = +26.9$  (*c* 0.0013, CHCl<sub>3</sub>); IR (film,  $\nu_{\max}$  cm<sup>-1</sup>) 3528 br, 2954 w, 2928 w, 2854 w, 1753 s, 1726 s, 1438 w, 1262 s, 1096 s; <sup>1</sup>H NMR (500 MHz; CDCl<sub>3</sub>)  $\delta$  5.69 (1H, s, CHCO<sub>2</sub>Me), 4.01–3.97 (1H, m, 1H of CH<sub>2</sub>OH), 3.88–3.85 (1H, m, 1H of CH<sub>2</sub>OH), 3.84 (3H, s, CO<sub>2</sub>Me), 3.73 (3H, s, CO<sub>2</sub>Me), 3.72 (3H, s, CO<sub>2</sub>Me), 3.57 (1H, t, *J* 7, CH<sub>2</sub>OH), 2.35 (1H, ddd, *J* 14, *J* 13, *J* 6, 1H<sub>endo</sub> of C<sup>(3)</sup>H<sub>2</sub>), 2.16–2.13 (2H, m, CH<sub>2</sub>CH<sub>2</sub>OH), 1.94 (1H, td, *J*<sub>1</sub> 13, *J*<sub>2</sub> 6, 1H of C<sup>(4)</sup>H<sub>2</sub>), 1.83–1.72 (2H, m, 1H<sub>exo</sub> of C<sup>(3)</sup>H<sub>2</sub>, 1H of C<sup>(4)</sup>H<sub>2</sub>), 0.87 (9H, s, SiCMe<sub>3</sub>), 0.14 (3H, s, SiMe), 0.13 (3H, s, SiMe); <sup>13</sup>C NMR (125 MHz; CDCl<sub>3</sub>)  $\delta$  173.3 (CO<sub>2</sub>Me), 170.3 (CO<sub>2</sub>Me), 166.6 (CO<sub>2</sub>Me), 112.1 (O–C<sup>(5)</sup>–O), 90.0 (C<sup>(1)</sup>CO<sub>2</sub>Me), 77.6 (CHCO<sub>2</sub>Me), 57.3 (CH<sub>2</sub>OH), 52.9 (CO<sub>2</sub>Me), 52.8 (CO<sub>2</sub>Me), 52.6 (CO<sub>2</sub>Me), 38.8 (CH<sub>2</sub>), 30.8 (C<sup>(4)</sup>H<sub>2</sub>), 29.7 (C<sup>(3)</sup>H<sub>2</sub>), 25.9 (CMe<sub>3</sub>), 19.1 (CMe<sub>3</sub>), –2.6 (SiMe), –2.9 (SiMe); HRMS *m/z* (M+Na<sup>+</sup>) found 485.1813, C<sub>20</sub>H<sub>34</sub>NaO<sub>10</sub>Si requires 485.1813.

**Trimethyl (1*S*,2*R*,5*R*,7*S*)-2-hydroxy-5-(2-hydroxyethyl)-6,8-dioxabicyclo[3.2.1]octane-1,2,7-tricarboxylate (**23**) and Trimethyl (1*R*,3*S*,4*S*,5*R*)-4-hydroxy-1-(2-hydroxyethyl)-2,8-dioxabicyclo[3.2.1]octane-3,4,5-tricarboxylate (**24**)**



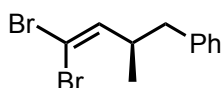
To a solution of alcohol **22** (20 mg, 0.043 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (0.32 mL) was added TFA (160 μL) and H<sub>2</sub>O (16 μL). The mixture was heated to 40 °C for 68 h, then concentrated under reduced pressure. To the residue was added toluene (3x1 mL) to azeotrope traces of TFA and H<sub>2</sub>O. To the residue was then added Na<sub>2</sub>CO<sub>3</sub> (6.9 mg, 0.065 mmol) in MeOH (1.0 mL) and stirred at rt. After 1 h toluene (0.4 mL), and TMSCHN<sub>2</sub> (28 μL, 2 M in Et<sub>2</sub>O, 0.056 mmol) was added dropwise.<sup>8</sup> After 30 min, AcOH (50 μL) was added dropwise, and the mixture then evaporated under reduced pressure. Purification of the residue by column chromatography (1% MeOH in CH<sub>2</sub>Cl<sub>2</sub>) gave unrearranged diol **23** (10 mg, 67%) and rearranged diol **24** (4.1 mg, 27%), both as colourless oils.

Data for unrearranged diol **23**: *R<sub>f</sub>* 0.36 (5% MeOH in CH<sub>2</sub>Cl<sub>2</sub>): [α]<sub>D</sub><sup>25</sup> = +60.7 (*c* 0.59, CHCl<sub>3</sub>); IR (film, ν<sub>max</sub> cm<sup>-1</sup>) 3490 br, 2959 w, 1750 s, 1748 s, 1439 w, 1361 w, 1220 s, 1165 s, 1089 s; <sup>1</sup>H NMR (500 MHz; CDCl<sub>3</sub>) δ 5.56 (1H, s, CHCO<sub>2</sub>Me), 4.06–4.01 (1H, m, 1H of CH<sub>2</sub>OH), 3.93 (3H, s, CO<sub>2</sub>Me), 3.82–3.78 (1H, m, 1H of CH<sub>2</sub>OH), 3.75 (3H, s, CO<sub>2</sub>Me), 3.74 (3H, s, CO<sub>2</sub>Me), 2.29 (1H, ddd, *J* 13, *J* 8, *J* 7, 1H of CH<sub>2</sub>CH<sub>2</sub>OH), 2.19–2.16 (2H, m, 1H of CH<sub>2</sub>CH<sub>2</sub>OH, 1H *endo* C<sup>3</sup>H<sub>2</sub>), 1.98 (1H, ddd, *J* 7, *J* 7, *J* 13, 1H of C<sup>4</sup>H<sub>2</sub>), 1.84–1.78 (2H, m, 1H *exo* of C<sup>3</sup>H<sub>2</sub>, 1H of C<sup>4</sup>H<sub>2</sub>); <sup>13</sup>C NMR (125 MHz; CDCl<sub>3</sub>) δ 173.8 (CO<sub>2</sub>Me), 170.0 (CO<sub>2</sub>Me), 166.7 (CO<sub>2</sub>Me), 112.9 (O-C<sup>5</sup>-O), 89.2 (C<sup>1</sup>CO<sub>2</sub>Me), 77.8 (CHCO<sub>2</sub>Me), 73.8 (HOC<sup>2</sup>CO<sub>2</sub>Me), 56.9 (CH<sub>2</sub>OH), 53.9 (CO<sub>2</sub>Me), 53.3 (CO<sub>2</sub>Me), 53.0 (CO<sub>2</sub>Me), 38.6 (CH<sub>2</sub>CH<sub>2</sub>OH), 31.1 (C<sup>4</sup>H<sub>2</sub>), 29.3 (C<sup>3</sup>H<sub>2</sub>); HRMS *m/z* (M+Na<sup>+</sup>); found 371.0945, C<sub>14</sub>H<sub>20</sub>NaO<sub>10</sub> requires 371.0949.

Data for rearranged diol **24**: *R<sub>f</sub>* 0.34 (5% MeOH in CH<sub>2</sub>Cl<sub>2</sub>); [α]<sub>D</sub><sup>25</sup> = –13.8 (*c* 0.41, CHCl<sub>3</sub>); IR (film, ν<sub>max</sub> cm<sup>-1</sup>) 3517 br, 2957 w, 1737 s, 1439 w, 1271 s, 1130 s, 1096 s, 1060 s; <sup>1</sup>H NMR (500 MHz; CDCl<sub>3</sub>) δ 4.94 (1H, s, CHCO<sub>2</sub>Me), 4.05 (1H, ddd, *J* 12, *J* 8, *J* 3, 1H of

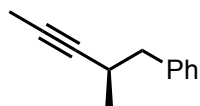
CH<sub>2</sub>OH), 3.91 (3H, s, CO<sub>2</sub>Me), 3.84 (1H, ddd, *J* 12, *J* 6, *J* 3, 1H of CH<sub>2</sub>OH), 3.79 (3H, s, CO<sub>2</sub>Me), 3.77 (3H, s, CO<sub>2</sub>Me), 3.14 (1H, ddd, *J* 13, *J* 9, *J* 3, 1H *endo* of C<sup>6</sup>H<sub>2</sub>), 2.30–2.07 (5H, m, 1H *exo* of C<sup>6</sup>H<sub>2</sub>, 2H C<sup>7</sup>H<sub>2</sub>, CH<sub>2</sub>CH<sub>2</sub>OH), 1.92 (2H, br s, CH<sub>2</sub>OH, COHCO<sub>2</sub>Me); <sup>13</sup>C NMR (125 MHz; CDCl<sub>3</sub>) δ 170.0 (CO<sub>2</sub>Me), 168.7 (CO<sub>2</sub>Me), 167.4 (CO<sub>2</sub>Me), 109.5 (O-C<sup>1</sup>-O), 88.2 (C<sup>5</sup>CO<sub>2</sub>Me), 74.94 (C<sup>4</sup>CO<sub>2</sub>MeOH), 74.88 (CHCO<sub>2</sub>Me), 58.9 (CH<sub>2</sub>OH), 53.7 (CO<sub>2</sub>Me), 53.1 (CO<sub>2</sub>Me), 53.0 (CO<sub>2</sub>Me), 38.9 (CH<sub>2</sub>CH<sub>2</sub>OH), 32.5 (C<sup>7</sup>H<sub>2</sub>), 29.1 (C<sup>6</sup>H<sub>2</sub>); HRMS *m/z* (M+Na<sup>+</sup>): found 371.0948, C<sub>14</sub>H<sub>20</sub>NaO<sub>10</sub> requires 371.0949.

**(*R*)-(4,4-Dibromo-2-methylbut-3-en-1-yl)benzene (SI-2)**



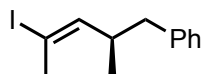
A stirred solution of CBr<sub>4</sub> (44.8 g, 135 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (100 mL) was cooled to 0 °C and a solution of PPh<sub>3</sub> (72.7 g, 277 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (100 mL) was then added dropwise over 30 min. The reaction mixture was stirred at 0 °C for 10 min, and then a solution of *R*-2-methyl-3-phenylpropanal<sup>9</sup> (10.0 g, 67.5 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (150 mL) was added over 10 min *via* cannula. The solution was stirred at 0 °C for 1 h, and then H<sub>2</sub>O (500 mL) added. The aq layer was extracted with CH<sub>2</sub>Cl<sub>2</sub> (2x200 mL), the combined organic layers were dried (MgSO<sub>4</sub>) and concentrated under reduced pressure. Purification of the residue by column chromatography (petrol) gave dibromoalkene **SI-2** (18.3 g, 89%) as a colourless oil. *R<sub>f</sub>* 0.54 (petrol); [α]<sub>D</sub><sup>25</sup> = −41.9 (*c* 2.0, CHCl<sub>3</sub>); IR (film, ν<sub>max</sub> cm<sup>−1</sup>) 3085 w, 3062 m, 3026 s, 2963 s, 2926 s, 2869 m, 1944 w, 1614 m, 1495 s, 1374 m, 1089 m; <sup>1</sup>H NMR (500 MHz; CDCl<sub>3</sub>) δ 7.31–7.13 (5H, m, ArCH), 6.25 (1H, d, *J* 9, CH=C), 2.78–2.69 (2H, m, 1 H of CH<sub>2</sub> and CHMe), 2.56 (1H, dd, *J* 7, 13, 1H of CH<sub>2</sub>Ph), 1.00 (3H, d, *J* 7, CH<sub>3</sub>); <sup>13</sup>C NMR (125 MHz; CDCl<sub>3</sub>) δ 143.4 (CH=C), 139.3 (ArC), 129.3 (ArCH), 128.4 (ArCH), 126.4 (ArCH), 88.2 (CH=CBr<sub>2</sub>), 42.0 (CH<sub>2</sub>Ar), 40.1 (CHCH<sub>3</sub>), 18.6 (CH<sub>3</sub>); HRMS *m/z* (M<sup>+</sup>): found 301.9309, C<sub>11</sub>H<sub>12</sub><sup>79</sup>Br<sub>2</sub> requires 301.9306.

**(*R*)-(2-Methylpent-3-yn-1-yl)benzene (6)**



To a stirred solution of dibromoalkene **SI-2** (3.44 g, 11.3 mmol) in dry THF (30 mL) was added *n*-BuLi (10.4 mL, 2.5 M in hexanes, 26 mmol) at  $-78\text{ }^{\circ}\text{C}$ . The resulting mixture was warmed to rt. After 30 min at rt, freshly distilled MeI (2.1 mL, 34 mmol) was added. After 1 h at rt the reaction mixture was quenched with sat. aq  $\text{NH}_4\text{Cl}$  (30 mL), the layers separated and the aq layer extracted with  $\text{Et}_2\text{O}$  (3x30 mL). The combined organic layers were dried ( $\text{MgSO}_4$ ) and concentrated under reduced pressure. Purification of the residue by column chromatography (petrol) gave alkyne **6**<sup>10</sup> (1.72 g, 96%) as a colourless oil.  $R_f$  0.22 (petrol);  $[\alpha]_{\text{D}}^{25} = -61.0$  ( $c$  1.0,  $\text{CHCl}_3$ ) [lit.<sup>10</sup>  $[\alpha]_{\text{D}}^{25} = -56$  ( $c$   $4.8 \times 10^{-4}$ ,  $\text{CH}_2\text{Cl}_2$ )]; IR (film,  $\nu_{\text{max}}$   $\text{cm}^{-1}$ ) 3028 m, 2968 s, 2919 s, 2360 m, 1726 m, 1603 m, 1495 s, 1086 s;  $^1\text{H}$  NMR (500 MHz;  $\text{CDCl}_3$ )  $\delta$  7.37–7.26 (5H, m, ArCH), 2.91–2.85 (1H, m,  $\text{CH}_2\text{Ph}$ ), 2.74–2.68 (2H, m,  $\text{CHCH}_3$ , 1H of  $\text{CH}_2\text{Ph}$ ), 1.84 (3H, d,  $J$  3,  $\text{CCH}_3$ ), 1.20 (3H, d,  $J$  7,  $\text{CHCH}_3$ );  $^{13}\text{C}$  NMR (125 MHz;  $\text{CDCl}_3$ )  $\delta$  140.0 (ArC), 129.3 (ArCH), 128.2 (ArCH), 126.2 (ArCH), 83.5 ( $\text{C}\equiv\text{CCH}_3$ ), 76.5 ( $\text{C}\equiv\text{CCH}_3$ ), 43.6 ( $\text{CH}_2\text{Ph}$ ), 28.0 ( $\text{CHCH}_3$ ), 20.9 ( $\text{CHCH}_3$ ), 3.6 ( $\text{C}\equiv\text{CCH}_3$ ); HRMS  $m/z$  ( $\text{M}+\text{Na}^+$ ) found 181.0982,  $\text{C}_{12}\text{H}_{14}\text{Na}$  requires 181.0988.

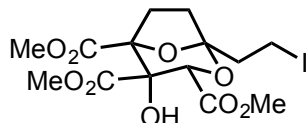
**(*R,E*)-(4-Iodo-2-methylpent-3-en-1-yl)benzene (4)**



A suspension of  $\text{Cp}_2\text{ZrCl}_2$  (585 mg, 2.0 mmol, 2.0 equiv) in THF (4.00 mL) was cooled to  $0\text{ }^{\circ}\text{C}$ . To this solution was added  $\text{LiEt}_3\text{BH}$  (2.0 mL, 1.0 M in THF, 2.0 mmol) dropwise.<sup>11</sup> The reaction mixture was stirred at rt shielded from light. After 1 h, alkyne **6** (158 mg, 1.00 mmol) in THF (1 mL) was added dropwise. The reaction mixture was stirred at  $50\text{ }^{\circ}\text{C}$  for 1 h and then allowed to reach rt.<sup>12</sup> The reaction mixture was then cooled to  $-20\text{ }^{\circ}\text{C}$  and solution of  $\text{I}_2$  (254 mg, 1.0 mmol) in THF (1 mL) was added dropwise. The reaction was allowed to reach rt, stirred for 30 min and poured into sat. aq  $\text{NaHCO}_3$  (10 mL). The layers were separated and the aq layer extracted with  $\text{Et}_2\text{O}$  (3x30 mL), the combined organic layers were dried ( $\text{MgSO}_4$ ) and evaporated under reduced pressure. The residue was purified by column chromatography to give *E*-alkenyl iodide **4** (212 mg, 74%) as a

colourless oil;  $R_f$  0.50 (petrol);  $[\alpha]_D^{25} = -127.3$  ( $c$  1.0,  $\text{CHCl}_3$ ); IR (film,  $\nu_{\text{max}}$   $\text{cm}^{-1}$ ) 3026 w, 2959 s, 2924 s, 2360 s, 2341 m, 1452 s, 1039 m;  $^1\text{H}$  NMR (500 MHz;  $\text{CDCl}_3$ )  $\delta$  7.30–7.12 (5H, m, ArCH), 6.01 (1H, dq,  $J$  10, 2, CH=Cl), 2.69–2.59 (1H, m, CHCH<sub>3</sub>), 2.58–2.55 (2H, m, CH<sub>2</sub>Ph), 2.10 (3H, d,  $J$  2, CH=CICH<sub>3</sub>), 1.01 (3H, d,  $J$  6, CHCH<sub>3</sub>);  $^{13}\text{C}$  NMR (125 MHz;  $\text{CDCl}_3$ )  $\delta$  146.1 (CH=Cl), 140.1 (ArC), 129.3 (ArCH), 128.3 (ArCH), 126.1 (ArCH), 93.6 (CH=Cl), 43.3 (CH<sub>2</sub>Ph), 38.2 (CHCH<sub>3</sub>), 27.6 (CH=CICH<sub>3</sub>), 20.2 (CHCH<sub>3</sub>); HRMS  $m/z$  ( $\text{M}+\text{Na}^+$ ) found 309.0109,  $\text{C}_{12}\text{H}_{15}\text{INa}$  requires 309.0111.

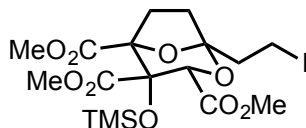
**Trimethyl (1*R*,3*S*,4*S*,5*R*)-4-hydroxy-1-(2-iodoethyl)-2,8-dioxabicyclo[3.2.1]octane-3,4,5-tricarboxylate (**25**)**



A vial was charged with  $\text{PPh}_3$  (4.0 mg, 0.014 mmol) and imidazole (2.0 mg, 0.028 mmol) in  $\text{CH}_2\text{Cl}_2$  (0.1 mL) at 0 °C. To the solution was added  $\text{I}_2$  (4.0 mg, 0.014 mmol) and the vial was sealed. A solution of diol **24** (4.5 mg, 0.013 mmol) in  $\text{CH}_2\text{Cl}_2$  (0.1 mL) was added to the mixture. After 12 h,  $\text{H}_2\text{O}$  (0.5 mL) was added to the reaction mixture and the aq layer extracted with  $\text{CH}_2\text{Cl}_2$  (3x2 mL). The combined organic layers were dried ( $\text{MgSO}_4$ ), concentrated by blowing nitrogen and purified by column chromatography (30–70% EtOAc in petrol) to give iodide **25** (5.3 mg, 90%) as a colourless glass;  $R_f$  0.47 (70% EtOAc in petrol);  $[\alpha]_D^{25} = -11.6$  ( $c$  0.50,  $\text{CHCl}_3$ ); IR (film,  $\nu_{\text{max}}$   $\text{cm}^{-1}$ ) 3469 br, 2955 w, 1765 s, 1738 s, 1439 s;  $^1\text{H}$  NMR (500 MHz;  $\text{CDCl}_3$ )  $\delta$  4.90 (1H, s,  $\text{CHCO}_2\text{Me}$ ), 3.90 (3H, s,  $\text{CO}_2\text{Me}$ ), 3.79 (3H, s,  $\text{CO}_2\text{Me}$ ), 3.76 (3H, s,  $\text{CO}_2\text{Me}$ ), 3.67 (1H, s, OH), 3.38 (2H, ddd,  $J$  10,  $J$  5,  $J$  5,  $\text{CH}_2\text{I}$ ), 3.14 (1H, ddd,  $J$  15,  $J$  10,  $J$  5, 1H *endo* of  $\text{C}^6\text{H}_2$ ), 2.59 (2H, ddd,  $J$  10,  $J$  10,  $J$  5,  $\text{CH}_2\text{CH}_2\text{I}$ ), 2.23 (1H, ddd,  $J$  10,  $J$  10,  $J$  5, 1H *exo* of  $\text{C}^6\text{H}_2$ ), 2.11 (2H, ddd,  $J$  15,  $J$  10,  $J$  5,  $\text{C}^7\text{H}_2$ );  $^{13}\text{C}$  NMR (125 MHz;  $\text{CDCl}_3$ )  $\delta$  170.0 ( $\text{CO}_2\text{Me}$ ), 168.6 ( $\text{CO}_2\text{Me}$ ), 167.3 ( $\text{CO}_2\text{Me}$ ), 108.6 (O-C<sup>1</sup>-O), 88.2 ( $\text{C}^5\text{CO}_2\text{Me}$ ), 75.0 ( $\text{C}^4\text{CO}_2\text{MeOH}$ ), 74.9 ( $\text{CHCO}_2\text{Me}$ ), 53.6 ( $\text{CO}_2\text{Me}$ ), 53.1 ( $\text{CO}_2\text{Me}$ ), 52.9 ( $\text{CO}_2\text{Me}$ ), 41.9 ( $\text{CH}_2\text{CH}_2\text{OH}$ ), 31.8 ( $\text{C}^6\text{H}_2$ ), 29.0 ( $\text{C}^7\text{H}_2$ ), –3.42 ( $\text{CH}_2\text{I}$ ); HRMS  $m/z$  ( $\text{M}+\text{Na}^+$ ): found 480.9965,  $\text{C}_{14}\text{H}_{19}\text{O}_9\text{INa}$  requires 480.9966.

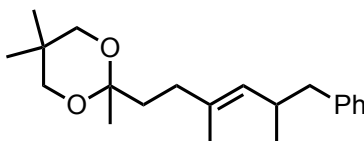


**Trimethyl (1*R*,3*S*,4*S*,5*R*)-1-(2-iodoethyl)-4-((trimethylsilyl)oxy)-2,8-dioxabicyclo[3.2.1]octane-3,4,5-tricarboxylate (SI-3)**



A vial was charged with iodoalcohol **25** (5.0 mg, 0.011 mmol), imidazole (1.3 mg, 0.019 mmol) and DMAP (0.1 mg, 0.0011 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (0.1 mL) and sealed. To the solution was added TMSCl (2.2  $\mu$ L, 0.018 mmol) dropwise and allowed to stir at rt overnight. The mixture was then loaded directly onto a column and purified by column chromatography (10–80% Et<sub>2</sub>O in petrol) to give alkyl iodide **SI-3** (5.5 mg, 95%) as colourless glass; *R<sub>f</sub>* 0.71 (80% Et<sub>2</sub>O in petrol);  $[\alpha]_D^{25} = -14.60$  (*c* 0.273, CHCl<sub>3</sub>); IR (film,  $\nu_{\max}$  cm<sup>-1</sup>) 2955 w, 2917 s, 2850 s, 1767 s, 1739 s, 1438 s; <sup>1</sup>H NMR (500 MHz; CDCl<sub>3</sub>)  $\delta$  4.85 (1H, s, CHCO<sub>2</sub>Me), 3.84 (3H, s, CO<sub>2</sub>Me), 3.76 (3H, s, CO<sub>2</sub>Me), 3.73 (3H, s, CO<sub>2</sub>Me), 3.42 (2H, ddd, *J* 15, *J* 10, *J* 5, CH<sub>2</sub>I), 3.18 (1H, ddd, *J* 15, *J* 10, *J* 5, 1H *endo* of C<sup>6</sup>H<sub>2</sub>), 2.57 (2H, dd, *J* 10, *J* 2, CH<sub>2</sub>CH<sub>2</sub>I), 2.15 (1H, ddd, *J* 15, *J* 10, *J* 5, 1H *exo* of C<sup>6</sup>H<sub>2</sub>), 2.00 (2H, ddd, *J* 15, *J* 10, *J* 5, C<sup>7</sup>H<sub>2</sub>), 0.08 (9H, s, OTMS); <sup>13</sup>C NMR (125 MHz; CDCl<sub>3</sub>)  $\delta$  170.8 (CO<sub>2</sub>Me), 169.4 (CO<sub>2</sub>Me), 167.7 (CO<sub>2</sub>Me), 108.2 (O-C<sup>1</sup>-O), 88.4 (C<sup>5</sup>CO<sub>2</sub>Me), 78.4 (C<sup>4</sup>CO<sub>2</sub>MeOH), 75.8 (CHCO<sub>2</sub>Me), 52.78 (CO<sub>2</sub>Me), 52.75 (CO<sub>2</sub>Me), 52.6 (CO<sub>2</sub>Me), 42.3 (CH<sub>2</sub>CH<sub>2</sub>OH), 32.3 (C<sup>6</sup>H<sub>2</sub>), 30.0 (C<sup>7</sup>H<sub>2</sub>), -2.25 (OTMS), -2.36 (CH<sub>2</sub>I); HRMS *m/z* (M+Na<sup>+</sup>): found 553.03588, C<sub>17</sub>H<sub>27</sub>INaO<sub>9</sub>Si requires 553.03612.

**(*E*)-2-(3,5-Dimethyl-6-phenylhex-3-en-1-yl)-2,5,5-trimethyl-1,3-dioxane (SI-5)**

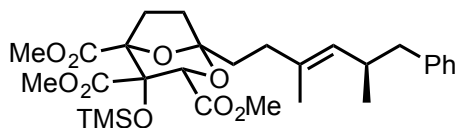


To a Schlenk tube was added Mn dust (1.5 mg, 0.027 mmol), NiI<sub>2</sub>(bpy)<sup>13</sup> (0.13 mg, 0.00028 mmol), alkyl iodide **SI-4**<sup>14</sup> (4 mg, 0.014 mmol) and alkenyl iodide ( $\pm$ )-**4** (4 mg, 0.014 mmol) and the flask evacuated and refilled with argon (x3). DMPU (0.1 mL) was added to the reaction mixture, followed by freshly distilled TMSCl (0.4  $\mu$ L, 0.0028 mmol). The reaction mixture was then allowed to stir vigorously at rt overnight. H<sub>2</sub>O (2 mL) was then added and the aq layer extracted with EtOAc (3 x 5 mL). The combined organic

layers were washed with brine (5 mL), dried (MgSO<sub>4</sub>), filtered, evaporated under reduced pressure and the residue purified by column chromatography (1% EtOAc in petrol) to give alkene (*E*)-**SI-5** (3.8 mg, 85%, 3:1 *E/Z*) as a colourless oil; *R<sub>f</sub>* 0.59 (1% EtOAc in petrol); IR (film,  $\nu_{\text{max}}$  cm<sup>-1</sup>) 3027 s, 2954 s, 2925 s, 2864 s, 1495 m, 1252 m, 1121 s, 1089 s; <sup>1</sup>H NMR (500 MHz; CDCl<sub>3</sub>)  $\delta$  7.27–7.22 (2H, m, ArCH), 7.19–7.14 (3H, m, ArCH), 5.20 (1H, dq, *J* 9, *J* 2, HC=C), 3.50 (2H, d, *J* 11, CH<sub>2</sub>O), 3.45–3.37 (2H, m, CH<sub>2</sub>O), 2.75–2.69 (1H, m, CHCH<sub>3</sub>), 2.59–2.55 (2H, m, CH<sub>2</sub>Ph), 2.46–2.42 (2H, m, H<sub>2</sub>C=C), 2.05–2.01 (2H, m, CH<sub>2</sub>), 1.53 (3H, d, *J* 2, C=CCH<sub>3</sub>), 1.45 (3H, s, OCCH<sub>3</sub>), 1.05 (3H, d, *J* 7, CHCH<sub>3</sub>), 1.04 (3H, s, CH<sub>3</sub>CCH<sub>3</sub>), 0.73 (3H, s, CH<sub>3</sub>CCH<sub>3</sub>); <sup>13</sup>C NMR (125 MHz; CDCl<sub>3</sub>)  $\delta$  141.3 (C=CH), 134.2 (C=CH), 130.2 (ArC), 129.4 (2xArCH), 128.1 (2xArCH), 125.7 (ArCH), 99.1 (O-CMe-O), 70.6 (OCH<sub>2</sub>), 70.50 (OCH<sub>2</sub>), 44.2 (CH<sub>2</sub>Ph), 36.5 (CHCH<sub>3</sub>), 34.7 (CH<sub>2</sub>), 33.4 (CH<sub>2</sub>), 30.1 (OCCH<sub>3</sub>), 26.0 (CH<sub>3</sub>CCH<sub>3</sub>), 22.9 (CH<sub>3</sub>CCH<sub>3</sub>), 21.1 (CHCH<sub>3</sub>), 20.9 (C=CCH<sub>3</sub>), 16.4 (CH<sub>3</sub>CCH<sub>3</sub>); HRMS *m/z* (M+H<sup>+</sup>) found 317.2475, C<sub>21</sub>H<sub>33</sub>O<sub>2</sub> requires 317.2475.

Discernible data for (*Z*)-**SI-5**: <sup>1</sup>H NMR (500 MHz; CDCl<sub>3</sub>)  $\delta$  5.14 (1H, d, *J* 9, HC=C), 1.97 (3H, d, *J* 2, C=CCH<sub>3</sub>), 1.42 (3H, s, OCCH<sub>3</sub>), 1.07 (3H, d, *J* 7, CHCH<sub>3</sub>), 1.06 (3H, s, CH<sub>3</sub>CCH<sub>3</sub>), 0.71 (3H, s, CH<sub>3</sub>CCH<sub>3</sub>); <sup>13</sup>C NMR (125 MHz; CDCl<sub>3</sub>)  $\delta$  134.1 (C=CH), 131.3 (ArC), 125.8 (ArCH), 98.9 (O-CMe-O), 70.5 (OCH<sub>2</sub>), 70.47 (OCH<sub>2</sub>), 44.4 (CH<sub>2</sub>Ph), 35.8 (CHCH<sub>3</sub>), 23.6 (CH<sub>3</sub>CCH<sub>3</sub>), 22.7 (CH<sub>3</sub>CCH<sub>3</sub>), 21.0 (CHCH<sub>3</sub>), 20.8 (C=CCH<sub>3</sub>).

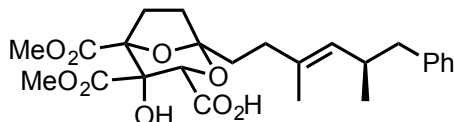
**Trimethyl (1*S*,3*S*,4*S*,5*R*)-1-((*R,E*)-3,5-dimethyl-6-phenylhex-3-en-1-yl)-4-(((trimethylsilyl)oxy)-2,8-dioxabicyclo[3.2.1]octane-3,4,5-tricarboxylate (26)**



To a Schlenk tube was added Mn dust (8.4 mg, 0.152 mmol), NiI<sub>2</sub>(bpy)<sup>13</sup> (0.9 mg, 0.0019 mmol, 2.5 mol%), hydroxy iodide **25** (35 mg, 0.076 mmol) and alkenyl iodide **4** (21.8 mg, 0.076 mmol) and the flask evacuated and refilled with argon (x3). DMF (0.2 mL) was added to the reaction mixture, followed by freshly distilled TMSCl (1.9  $\mu$ L, 0.015 mmol).

The reaction mixture was then allowed to stir vigorously at rt overnight. H<sub>2</sub>O (3 mL) was then added and the aq layer extracted with EtOAc (3x5 mL). The combined organic layers were washed with brine (5 mL), dried (MgSO<sub>4</sub>) and evaporated under reduced pressure. The residue was purified by column chromatography (30% EtOAc in petrol) to give *E*-alkene **26** (28.1 mg, 66%) as a colourless oil; *R<sub>f</sub>* 0.51 (30% EtOAc in petrol);  $[\alpha]_{\text{D}}^{25} = -42.10$  (*c* 0.073, CHCl<sub>3</sub>); IR (film,  $\nu_{\text{max}}$  cm<sup>-1</sup>) 3025 s, 2956 s, 2920 s, 2850 s, 2358 w, 2342 w, 2331 w, 1770 s, 1739 s, 1453 s, 1274 s, 1204 s, 846 s; <sup>1</sup>H NMR (500 MHz; CDCl<sub>3</sub>)  $\delta$  7.26–7.22 (2H, m, ArCH), 7.18–7.11 (3H, m, ArCH), 5.02 (1H, dq, *J* 9, *J* 1, HC=C), 4.84 (1H, s, CHCO<sub>2</sub>Me), 3.85 (3H, s, CO<sub>2</sub>Me), 3.76 (3H, s, CO<sub>2</sub>Me), 3.74 (3H, s, CO<sub>2</sub>Me), 3.20–3.14 (1H, m, H<sub>endo</sub> of C<sup>6</sup>H<sub>2</sub>), 2.67–2.60 (1H, m, CHCH<sub>3</sub>), 2.52 (2H, dd, *J* 7, *J* 4 CH<sub>2</sub>Ph), 2.24–2.07 (3H, m, 1H<sub>exo</sub> of C<sup>6</sup>H<sub>2</sub> and 2H, C<sup>7</sup>H<sub>2</sub>), 2.02–1.93 (4H, m, CH<sub>2</sub>CH<sub>2</sub>), 1.47 (3H, d, *J* 1, CCH<sub>3</sub>), 0.93 (3H, d, *J* 7, CHCH<sub>3</sub>), 0.10 (9H, s, OTMS); <sup>13</sup>C NMR (125 MHz; CDCl<sub>3</sub>)  $\delta$  171.3 (CO<sub>2</sub>Me), 169.8 (CO<sub>2</sub>Me), 168.0 (CO<sub>2</sub>Me), 141.3 (C=CH), 133.4 (C=CH), 130.3 (ArC), 129.4 (2xArCH), 128.1 (2xArCH), 125.7 (ArCH), 108.8 (O-C<sup>1</sup>-O), 88.4 (C<sup>5</sup>CO<sub>2</sub>Me), 78.5 (C<sup>4</sup>CO<sub>2</sub>MeOTMS), 75.8 (CHCO<sub>2</sub>Me), 52.8 (CO<sub>2</sub>Me), 52.7 (CO<sub>2</sub>Me), 52.6 (CO<sub>2</sub>Me), 44.1 (CH<sub>2</sub>Ph), 35.3 (CHCH<sub>3</sub>), 34.6 (C<sup>6</sup>H<sub>2</sub>), 33.3 (C<sup>7</sup>H<sub>2</sub>), 31.5 (CCH<sub>2</sub>CH<sub>2</sub>CMe), 30.3 (CH<sub>2</sub>), 20.9 (CHCH<sub>3</sub>), 16.5 (C=CCH<sub>3</sub>), 2.34 (OTMS); HRMS *m/z* (M+Na<sup>+</sup>) found 585.2489, C<sub>29</sub>H<sub>42</sub>O<sub>9</sub>NaSi requires 585.2490.

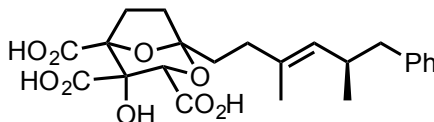
**(1*S*,3*S*,4*S*,5*R*)-1-((*R,E*)-3,5-Dimethyl-6-phenylhex-3-en-1-yl)-4-hydroxy-4,5-bis(methoxycarbonyl)-2,8-dioxabicyclo[3.2.1]octane-3-carboxylic acid (**27**)**



To a solution of siloxytriester **26** (18 mg, 0.032 mmol) in THF (0.1 mL) was added a solution of TBAF (60  $\mu$ L, 1.0 M in THF, 0.064 mmol) at rt. After 4 h, H<sub>2</sub>O (2 mL) was added and the aq layer was extracted with EtOAc (3x5 mL). The combined organic layers were dried (MgSO<sub>4</sub>) and evaporated under reduced pressure. The residue was purified by column chromatography (5% MeOH in CH<sub>2</sub>Cl<sub>2</sub>) to give hydroxyacid **27**<sup>15</sup> (10.3 mg, 67%) as a colourless glass; *R<sub>f</sub>* 0.37 (10% EtOAc in CH<sub>2</sub>Cl<sub>2</sub>);  $[\alpha]_{\text{D}}^{25} = -96.4$  (*c* 0.1, MeOH); IR

(film,  $\nu_{\max}$   $\text{cm}^{-1}$ ) 3437 br, 3026 s, 2954 s, 2919 s, 2850 s, 1739 s, 1690 s, 1625 s, 1438 s, 1204 w, 1124 w, 700 s;  $^1\text{H}$  NMR (500 MHz;  $\text{CD}_3\text{OD}$ )  $\delta$  7.26–7.19 (2H, m, ArCH), 7.16–7.10 (3H, m, ArCH), 5.03 (1H, d,  $J$  9, HC=C), 4.85 (1H, s,  $\text{CHCO}_2\text{Me}$ ), 3.80 (3H, s,  $\text{CO}_2\text{Me}$ ), 3.72 (3H, s,  $\text{CO}_2\text{Me}$ ), 3.08–3.01 (1H, m,  $\text{H}_{\text{endo}}$  of  $\text{C}^6\text{H}_2$ ), 2.69–2.57 (1H, m,  $\text{CHCH}_3$  and 1H of  $\text{CH}_2\text{Ph}$ ), 2.47 (1H, dd,  $J$  7, 13,  $\text{CH}_2\text{Ph}$ ), 2.20–2.09 (2H, m,  $\text{C}^7\text{H}_2$ ), 2.08–1.93 (4H, m,  $\text{CCH}_2\text{CH}_2$ ), 1.90–1.83 (1H, m,  $\text{H}_{\text{exo}}$  of  $\text{C}^6\text{H}_2$ ), 1.43 (3H, d,  $J$  1,  $\text{CCH}_3$ ), 0.96 (3H, d,  $J$  7,  $\text{CHCH}_3$ );  $^{13}\text{C}$  NMR (125 MHz;  $\text{CD}_3\text{OD}$ )  $\delta$  171.8 ( $\text{CO}_2\text{Me}$ ), 170.7 ( $\text{CO}_2\text{Me}$ ), 169.5 ( $\text{CO}_2\text{Me}$ ), 142.4 ( $\text{C}=\text{CH}$ ), 134.9 (ArC), 131.8 ( $\text{C}=\text{CH}$ ), 130.3 (2xArCH), 129.0 (2xArCH), 126.7 (ArCH), 110.0 ( $\text{O}-\text{C}^1-\text{O}$ ), 89.4 ( $\text{C}^5\text{CO}_2\text{Me}$ ), 76.6 ( $\text{C}^4\text{CO}_2\text{Me}$ ), 75.7 ( $\text{CHCO}_2\text{Me}$ ), 53.3 ( $\text{CO}_2\text{Me}$ ), 52.9 ( $\text{CO}_2\text{Me}$ ), 45.1 ( $\text{CH}_2\text{Ph}$ ), 36.3 ( $\text{CHCH}_3$ ), 35.9 ( $\text{C}^6\text{H}_2$ ), 34.6 ( $\text{C}^7\text{H}_2$ ), 31.9 ( $\text{CCH}_2\text{CH}_2\text{CMe}$ ), 30.3 ( $\text{CH}_2$ ), 21.4 ( $\text{CHCH}_3$ ), 16.1 ( $\text{C}=\text{CCH}_3$ ); HRMS  $m/z$  ( $\text{M}-\text{H}$ ) $^+$  found 475.1973,  $\text{C}_{25}\text{H}_{31}\text{O}_9$  requires 475.1974.

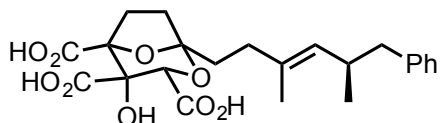
**(1*S*,3*S*,4*S*,5*R*)-1-((*R,E*)-3,5-Dimethyl-6-phenylhex-3-en-1-yl)-4-hydroxy-2,8-dioxabicyclo[3.2.1]octane-3,4,5-tricarboxylic acid (**2**)**



To a solution of 6,7-dideoxysqualestatin H5 dimethyl ester **27** (6.0 mg, 0.013 mmol) in dioxane (0.6 mL) was added  $\text{H}_2\text{O}$  (0.91 mg, 0.050 mmol), and  $\text{KO}t\text{-Bu}$  (14.1 mg, 0.13 mmol). The reaction mixture was heated at 110  $^\circ\text{C}$  for 24 h. The solvent was evaporated, and  $\text{H}_2\text{O}$  (5 mL) was added. The aq mixture was washed with  $\text{Et}_2\text{O}$  (1x5 mL), acidified with 0.1 M  $\text{HCl}$  (2 mL), and extracted with  $\text{EtOAc}$  (2x10 mL). The combined organic layers were dried ( $\text{MgSO}_4$ ) and evaporated under reduced pressure. The residue was purified by reverse phase (C18) HPLC eluting with  $\text{MeOH}/\text{H}_2\text{O}/\text{AcOH}$  (850:150:2,  $t_{\text{R}}$  = 10:00 min) to give 6,7-dideoxysqualestatin H5 (**2**)<sup>15</sup> (2.7 mg 48%) as a colourless glass;  $[\alpha]_{\text{D}}^{25} = -50.6$  ( $c$  0.13,  $\text{MeOH}$ )<sup>16</sup>; IR (film,  $\nu_{\max}$   $\text{cm}^{-1}$ ) 3381 br, 2957 w, 2490 br, 1732 s, 1452 w, 1119 s, 972 s;  $^1\text{H}$  NMR (500 MHz;  $\text{CD}_3\text{OD}$ )  $\delta$  7.24–7.11 (5H, m, ArCH), 5.04 (1H, d,  $J$  9, HC=C), 4.87 (1H, s,  $\text{CHCO}_2\text{Me}$ ), 3.22–3.15 (1H, m,  $\text{H}_{\text{endo}}$  of  $\text{C}^6\text{H}_2$ ), 2.68–2.62 (1H, m,  $\text{CHCH}_3$ ), 2.59 (1H, dd,  $J$  6,  $J$  13,  $\text{CH}_2\text{Ph}$ ), 2.48 (1H, d,  $J$  8, 13,  $\text{CH}_2\text{Ph}$ ), 2.23–2.11

(2H, m,  $C^7H_2$ ), 2.09–1.93 (4H, m,  $CH_2CH_2C=C$ ), 1.90–1.83 (1H, m,  $1H_{exo}$  of  $C^6H_2$ ), 1.43 (3H, d,  $J$  1,  $CCH_3$ ), 0.96 (3H, d,  $J$  6,  $CHCH_3$ );  $^{13}C$  NMR (125 MHz;  $CD_3OD$ )  $\delta$  173.5 ( $CO_2H$ ), 172.4 ( $CO_2H$ ), 171.1 ( $CO_2H$ ), 142.4 ( $C=CH$ ), 135.0 (ArC), 131.7 ( $C=CH$ ), 130.3 (2x ArCH), 129.0 (2xArCH), 126.7 (ArCH), 109.8 ( $O-C^1-O$ ), 89.5 ( $C^5CO_2Me$ ), 76.2 ( $C^4CO_2Me$ ), 75.9 ( $CHCO_2Me$ ), 45.1 ( $CH_2Ph$ ), 36.5 ( $CHCH_3$ ), 35.9 ( $C^6H_2$ ), 34.7 ( $C^7H_2$ ), 32.2 ( $CCH_2CH_2CMe$ ), 30.3 ( $CH_2$ ), 21.4 ( $CHCH_3$ ), 16.1 ( $C=CCH_3$ ); HRMS  $m/z$  ( $M-H$ )<sup>+</sup> found 447.1660,  $C_{23}H_{27}O_9$  requires 447.1661.

### 3. Tabular Comparison of NMR Data between Natural and Synthetic 6,7-dideoxysqualstatin H5 (2)



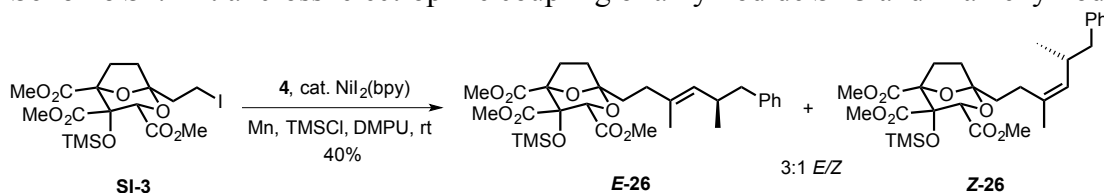
<sup>1</sup> H NMR – (500 MHz, CD <sub>3</sub> OD)	
Natural Isolate <sup>17</sup>	Synthetic
7.23 (2H, t, <i>J</i> 7)	7.24–7.20 (2H, m)
7.17–7.10 (3H, m)	7.15–7.12 (3H, m)
5.04 (1H, m)	5.04 (1H, d, <i>J</i> 9)
3.18 (1H, m)	3.22–3.15 (1H, m, H <sub>endo</sub> of C <sup>6</sup> H <sub>2</sub> )
2.66 (1H, m)	2.58 (1H, dd, <i>J</i> 13, 6)
2.59 (1H, dd, <i>J</i> 13, 6)	2.59 (1H, dd, <i>J</i> 13, 6)
2.47 (1H, dd, <i>J</i> 13, 8)	2.48 (1H, d, <i>J</i> 13, 8)
2.23–2.09 (2H, m)	2.23–2.11 (2H, m)
2.0–1.90 (4H, m)	2.09–1.93 (4H, m)
1.87 (1H, m)	1.90–1.83 (1H, m, 1H <sub>exo</sub> of C <sup>6</sup> H <sub>2</sub> )
1.44 (3H, d, <i>J</i> 1)	1.43 (3H, d, <i>J</i> 1)
0.96 (3H, d, <i>J</i> 7)	0.96 (3H, d, <i>J</i> 6)

<sup>13</sup> C NMR – (100 MHz, CD <sub>3</sub> OD)	
Natural Isolate <sup>17</sup>	Synthetic
173.1	173.5
172.1	172.4
170.8	171.1
142.3	142.4
134.9	135.0
131.7	131.7
130.2	130.3
128.9	129.0
126.6	126.7
109.8	109.8
89.3	89.5
76.0	76.2
75.7	75.9
45.0	45.1
36.3	36.5
35.8	35.9
34.6	34.7
32.0	32.2
30.3	30.3
21.3	21.4
16.0	16.1

#### 4. Optimization of Cross-Electrophile Coupling Conditions

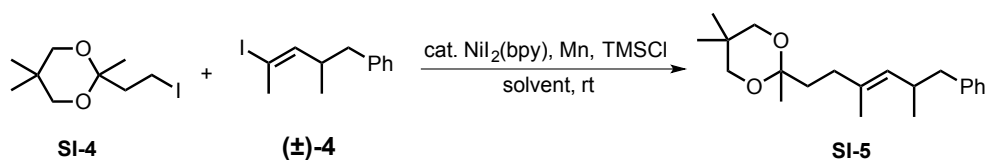
Initial cross-electrophile coupling, between equimolar quantities of TMS-protected alkyl iodide **SI-3** and *E*-alkenyl iodide **4** under the conditions reported by Weix and co-workers for alkyl and alkenyl halides,<sup>13</sup> gave an inseparable 3:1 mixture of *E*-**26** and *Z*-**26**<sup>18</sup> in 40% yield (Scheme S1).

**Scheme S1.** Initial cross-electrophile coupling of alkyl iodide **SI-3** and *E*-alkenyl iodide **4**



Optimization of the reaction conditions used alkyl iodide **SI-4**<sup>14</sup> and *E*-alkenyl iodide **4** (Table S1). Under Weix's conditions,<sup>13</sup> equimolar quantities of iodides **SI-4** and **4** gave alkene **SI-5** as a 3:1 *E*:-*Z*-mixture in 70–85% yields (3 runs, Table 1, entry 1), whereas with 2 equiv of alkyl iodide **SI-4**, alkene **SI-5** formed with improved *E*:-*Z*-selectivity (6:1) in 77% yield (entry 2). Alkyl iodide **SI-4** was still consumed if the reaction temperature was lowered from rt to –20 °C, or the solvent changed to *N,N*-dimethylacetamide,<sup>13</sup> but only traces of or no alkene **SI-5**, respectively, were observed. However, on changing the solvent to DMF,<sup>19</sup> alkene **SI-5** was obtained with high *E*:-*Z*-selectivity (17:1-20:1) in 86–88% yields (entries 3 and 4).

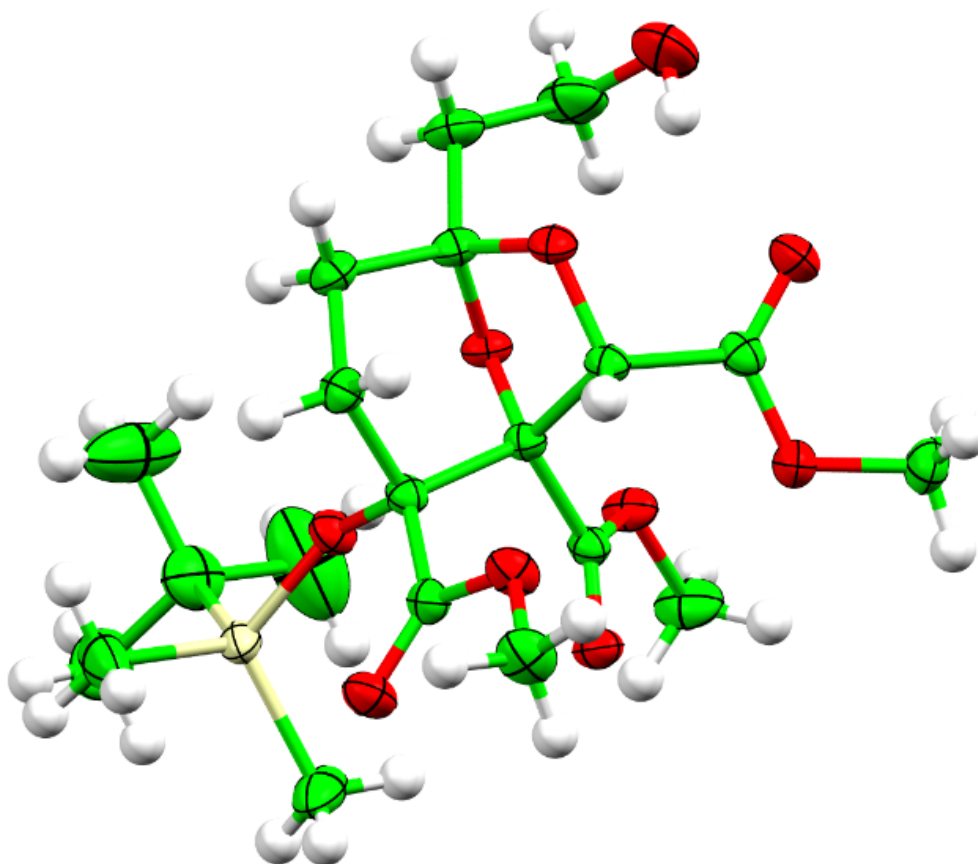
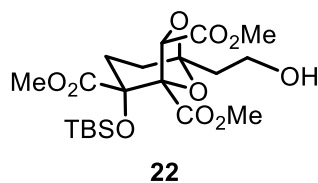
**Table S1.** Effect of reactants ratio and solvent on stereoselectivity (and yield) of alkene **SI-5**.



entry <sup>a</sup>	alkyl iodide <b>SI-4</b> (equiv)	alkenyl iodide ( $\pm$ )- <b>4</b> (equiv)	solvent	alkene <b>SI-5</b> <i>E</i> :- <i>Z</i> - (yield)
1	1	1	DMPU	3:1 <sup>b</sup> (70–85%)
2	2	1	DMPU	6:1 (77%)
3	1	1	DMF	17:1 (86%)
4	2	1	DMF	20:1 (88%)

<sup>a</sup> 0.15 M in ( $\pm$ )-**4**; <sup>b</sup> *E*:-*Z*- 1.5:1 at 0.05 M.

## 5. Single Crystal X-ray Diffraction Determination



**Fig.1** Crystal structure of **22** with ellipsoids at 50% probability.

Compound **22** was crystallized *via* vapour diffusion by dissolving 5 mg of **22** in ethyl acetate (*c.a.* 50  $\mu$ L) and using pentane as the volatile component. Low temperature<sup>20</sup> single crystal X-ray diffraction studies were carried out at 150 K on **22** using CuK $\alpha$  radiation on an Oxford Diffraction SuperNova diffractometer equipped with an area detector and graphite monochromator, within the University of Oxford Chemistry



Department. Raw frame data were reduced using CrysAlisPro(Agilent) and the structures were solved using superflip.<sup>21</sup> Full-matrix least-squares refinement of the structures were carried out using CRYSTALS.<sup>22,23</sup> The Flack x parameter<sup>24,26</sup> refined to -0.01(2) and Bayesian analysis of the Bijvoet pairs<sup>26</sup> gave the Hooft y parameter as 0.01(1) and the probability that the structure was the correct hand of >99.99% given that the crystal was enantiopure, thus determining the absolute configuration. Crystallographic data have been deposited with the Cambridge Crystallographic Data Centre (CCDC 1544840) and copies of these data can be obtained free of charge via [www.ccdc.cam.ac.uk/data\\_request/cif](http://www.ccdc.cam.ac.uk/data_request/cif).

## Crystal Data

$a = 9.57910(10) \text{ \AA}$   $\alpha = 90^\circ$

$b = 8.51190(10) \text{ \AA}$   $\beta = 100.9121(15)^\circ$

$c = 15.0831(2) \text{ \AA}$   $\gamma = 90^\circ$

<b>Volume</b>	1207.584(16) $\text{\AA}^3$	<b>Crystal Class</b>	monoclinic
<b>Space group</b>	P 2 <sub>1</sub>	<b>Z =</b>	2
<b>Formula</b>	C <sub>20</sub> H <sub>34</sub> O <sub>10</sub> Si <sub>1</sub>	<b>M<sub>r</sub></b>	462.57
<b>Cell determined from</b>	16487 reflections	<b>Cell <math>\theta</math> range =</b>	5 - 76°
<b>Temperature</b>	150K		
<b>Shape</b>	block		
<b>Colour</b>	clear_pale_colourless	<b>Size</b>	0.24 × 0.32 × 0.50 mm
<b>D<sub>x</sub></b>	1.27 Mg m <sup>-3</sup>	<b>F000</b>	496.000
<b><math>\mu</math></b>	1.297 mm <sup>-1</sup>		
<b>Absorption correction</b>	multi-scan		
<b>T<sub>min</sub></b>	0.55	<b>T<sub>max</sub></b>	0.73

## Data Collection

**Diffractometer** Oxford Diffraction SuperNova; CuK $\alpha$  radiation (1.5418  $\text{\AA}$ )

<b>Scan type</b>	$\omega$ scans
<b>Reflections measured</b>	24093
<b>Independent reflections</b>	4839
<b>R<sub>int</sub></b>	0.0186
<b><math>\theta_{\max}</math></b>	76.2262
<b>h =</b>	-11 $\rightarrow$ 12
<b>k =</b>	-10 $\rightarrow$ 9
<b>l =</b>	-18 $\rightarrow$ 18

## Refinement

<b><math>\Delta\rho_{\min}</math> =</b>	-0.19 e $\text{\AA}^{-3}$
<b><math>\Delta\rho_{\max}</math> =</b>	0.17 e $\text{\AA}^{-3}$
<b>Reflections used</b>	4839
<b>Cutoff: I &gt;</b>	-10.00 $\sigma$ (I)
<b>Parameters refined</b>	284
<b>S =</b>	1.00
<b>R-factor</b>	0.025
<b>weighted R-factor</b>	0.066
<b><math>\Delta/\sigma_{\max}</math></b>	0.0005
<b>Flack parameter</b>	0.015(17)
<b>Refinement on</b>	F <sup>2</sup>
<b>w =</b>	$1/[\sigma^2(F_{\text{obs}}^2) + (0.040 \times P)^2 + 0.250 \times P + 0.000 + 0.000 \times \sin\theta]$ , $P = 0.333 \times \max(F_{\text{obs}}^2, 0) + 0.667 \times F_{\text{calc}}^2$

## Parameters

<b>Label</b>	<b>x</b>	<b>y</b>	<b>z</b>	<b>U<sub>iso</sub>/equiv</b>	<b>Occupancy</b>
<b>Si1</b>	0.31645(3)	0.25016(7)	0.12547(2)	0.0262	1.0000
<b>O2</b>	0.21516(10)	0.31311(12)	0.19454(6)	0.0267	1.0000
<b>C3</b>	0.16491(12)	0.27634(15)	0.27319(8)	0.0220	1.0000
<b>C4</b>	0.25026(13)	0.14205(16)	0.32465(8)	0.0239	1.0000
<b>O5</b>	0.21668(10)	0.12108(12)	0.40560(6)	0.0301	1.0000
<b>C6</b>	0.27204(18)	0.01845(19)	0.45432(11)	0.0379	1.0000
<b>O7</b>	0.32862(10)	0.05899(14)	0.29232(7)	0.0330	1.0000
<b>C8</b>	0.00844(13)	0.22252(16)	0.24885(9)	0.0273	1.0000
<b>C9</b>	0.08850(13)	0.35790(18)	0.20930(9)	0.0296	1.0000
<b>C10</b>	0.05184(12)	0.50573(17)	0.26521(9)	0.0262	1.0000

<b>O11</b>	0.05524(9)	0.47250(12)	0.35865(6)	0.0263	1.0000
<b>C12</b>	0.08534(12)	0.43509(16)	0.40342(8)	0.0219	1.0000
<b>C13</b>	0.17131(12)	0.43592(15)	0.32527(8)	0.0199	1.0000
<b>O14</b>	0.09198(8)	0.54790(12)	0.26603(6)	0.0233	1.0000
<b>C15</b>	0.32664(12)	0.48742(16)	0.34999(8)	0.0214	1.0000
<b>O16</b>	0.34199(9)	0.63984(12)	0.33727(7)	0.0285	1.0000
<b>C17</b>	0.48673(15)	0.69851(19)	0.35638(13)	0.0413	1.0000
<b>O18</b>	0.42109(9)	0.39644(12)	0.37619(7)	0.0289	1.0000
<b>C19</b>	0.13327(13)	0.55508(17)	0.47770(8)	0.0251	1.0000
<b>O20</b>	0.26685(10)	0.53177(13)	0.51690(6)	0.0299	1.0000
<b>C21</b>	0.31850(15)	0.62204(19)	0.59760(9)	0.0334	1.0000
<b>O22</b>	0.05748(11)	0.65470(15)	0.49905(8)	0.0424	1.0000
<b>C23</b>	0.14701(15)	0.6436(2)	0.23155(10)	0.0354	1.0000
<b>C24</b>	0.11425(18)	0.7942(2)	0.28395(14)	0.0468	1.0000
<b>O25</b>	0.16425(16)	0.79455(18)	0.36703(10)	0.0633	1.0000
<b>C26</b>	0.25433(19)	0.0594(2)	0.07308(13)	0.0498	1.0000
<b>C27</b>	0.50842(14)	0.2420(3)	0.17797(10)	0.0473	1.0000
<b>C28</b>	0.2898(2)	0.4126(3)	0.03833(11)	0.0485	1.0000
<b>C29</b>	0.1324(2)	0.4264(4)	0.00416(15)	0.0907	1.0000
<b>C30</b>	0.3428(4)	0.5687(3)	0.08403(19)	0.0929	1.0000
<b>C31</b>	0.3728(2)	0.3784(3)	0.03687(12)	0.0588	1.0000
<b>H61</b>	0.23286(18)	0.02452(19)	0.50847(11)	0.0566	1.0000
<b>H62</b>	0.37450(18)	0.01436(19)	0.46811(11)	0.0559	1.0000
<b>H63</b>	0.24161(18)	0.10753(19)	0.41490(11)	0.0568	1.0000
<b>H81</b>	0.01828(13)	0.18311(16)	0.30189(9)	0.0318	1.0000
<b>H82</b>	0.00225(13)	0.14003(16)	0.20475(9)	0.0330	1.0000
<b>H91</b>	0.18703(13)	0.32821(18)	0.20957(9)	0.0359	1.0000
<b>H92</b>	0.07923(13)	0.37715(18)	0.14775(9)	0.0350	1.0000
<b>H121</b>	0.09031(12)	0.33092(16)	0.43191(8)	0.0240	1.0000
<b>H171</b>	0.48442(15)	0.80165(19)	0.33095(13)	0.0605	1.0000
<b>H172</b>	0.51969(15)	0.70120(19)	0.42079(13)	0.0596	1.0000
<b>H173</b>	0.54855(15)	0.63196(19)	0.32952(13)	0.0629	1.0000
<b>H211</b>	0.41823(15)	0.60473(19)	0.61602(9)	0.0517	1.0000
<b>H212</b>	0.27284(15)	0.58454(19)	0.64479(9)	0.0509	1.0000
<b>H213</b>	0.30172(15)	0.72868(19)	0.58928(9)	0.0533	1.0000
<b>H231</b>	0.24672(15)	0.6160(2)	0.23198(10)	0.0412	1.0000
<b>H232</b>	0.13613(15)	0.6629(2)	0.16984(10)	0.0438	1.0000

<b>H241</b>	0.17150(18)	0.8766(2)	0.24669(14)	0.0562	1.0000
<b>H242</b>	0.01275(18)	0.8216(2)	0.28997(14)	0.0564	1.0000
<b>H262</b>	0.30437(19)	0.0357(2)	0.02527(13)	0.0735	1.0000
<b>H263</b>	0.26223(19)	-0.0265(2)	0.11399(13)	0.0750	1.0000
<b>H261</b>	0.15657(19)	0.0649(2)	0.04905(13)	0.0765	1.0000
<b>H273</b>	0.56825(14)	0.2547(3)	0.13302(10)	0.0701	1.0000
<b>H271</b>	0.52942(14)	0.3233(3)	0.22121(10)	0.0726	1.0000
<b>H272</b>	0.53523(14)	0.1422(3)	0.20973(10)	0.0726	1.0000
<b>H291</b>	0.0957(2)	0.3250(4)	0.02913(15)	0.1343	1.0000
<b>H293</b>	0.1178(2)	0.5033(4)	0.05095(15)	0.1348	1.0000
<b>H292</b>	0.0820(2)	0.4549(4)	0.04238(15)	0.1352	1.0000
<b>H302</b>	0.4444(4)	0.5604(3)	0.11085(19)	0.1403	1.0000
<b>H301</b>	0.3235(4)	0.6519(3)	0.03962(19)	0.1381	1.0000
<b>H303</b>	0.2882(4)	0.5909(3)	0.13026(19)	0.1395	1.0000
<b>H312</b>	0.4725(2)	0.3748(3)	0.01007(12)	0.0856	1.0000
<b>H313</b>	0.3591(2)	0.4607(3)	0.08191(12)	0.0876	1.0000
<b>H311</b>	0.3471(2)	0.2763(3)	0.06370(12)	0.0867	1.0000
<b>H251</b>	-0.113(3)	0.720(3)	0.3955(18)	0.0943	1.0000

### Thermal Parameters

<b>Label</b>	<b>U<sub>11</sub></b>	<b>U<sub>22</sub></b>	<b>U<sub>33</sub></b>	<b>U<sub>23</sub></b>	<b>U<sub>13</sub></b>	<b>U<sub>12</sub></b>
<b>Si1</b>	0.01902(14)	0.0348(2)	0.02496(15)	0.00725(14)	0.00464(11)	0.00320(13)
<b>O2</b>	0.0293(4)	0.0279(5)	0.0246(4)	0.0015(4)	0.0094(3)	0.0029(4)
<b>C3</b>	0.0210(5)	0.0229(7)	0.0231(5)	-0.0011(4)	0.0063(4)	-0.0009(4)
<b>C4</b>	0.0237(6)	0.0198(6)	0.0279(6)	-0.0022(5)	0.0044(4)	-0.0027(5)
<b>O5</b>	0.0381(5)	0.0232(5)	0.0309(5)	0.0056(4)	0.0110(4)	0.0049(4)
<b>C6</b>	0.0487(9)	0.0267(7)	0.0388(8)	0.0093(6)	0.0095(6)	0.0060(6)
<b>O7</b>	0.0337(5)	0.0285(5)	0.0377(5)	0.0007(4)	0.0094(4)	0.0085(4)
<b>C8</b>	0.0229(6)	0.0256(7)	0.0330(6)	-0.0044(5)	0.0043(5)	-0.0047(5)
<b>C9</b>	0.0194(6)	0.0344(8)	0.0335(6)	-0.0029(5)	0.0007(5)	-0.0018(5)
<b>C10</b>	0.0170(5)	0.0306(7)	0.0306(6)	0.0013(5)	0.0036(4)	0.0006(5)
<b>O11</b>	0.0175(4)	0.0320(5)	0.0301(4)	-0.0005(4)	0.0066(3)	0.0007(3)
<b>C12</b>	0.0186(5)	0.0212(6)	0.0265(6)	0.0002(4)	0.0061(4)	-0.0001(4)
<b>C13</b>	0.0186(5)	0.0177(6)	0.0234(5)	0.0011(4)	0.0038(4)	0.0001(4)

<b>O14</b>	0.0175(4)	0.0239(4)	0.0287(4)	0.0051(4)	0.0050(3)	0.0014(3)
<b>C15</b>	0.0199(5)	0.0205(6)	0.0245(5)	-0.0020(4)	0.0057(4)	-0.0008(4)
<b>O16</b>	0.0211(4)	0.0204(5)	0.0438(5)	0.0014(4)	0.0058(4)	-0.0033(3)
<b>C17</b>	0.0253(6)	0.0278(8)	0.0701(11)	0.0013(7)	0.0073(7)	-0.0083(6)
<b>O18</b>	0.0210(4)	0.0241(5)	0.0400(5)	-0.0033(4)	0.0014(4)	0.0017(3)
<b>C19</b>	0.0254(6)	0.0244(6)	0.0271(6)	-0.0011(5)	0.0093(4)	-0.0020(5)
<b>O20</b>	0.0273(4)	0.0332(5)	0.0281(4)	-0.0069(4)	0.0023(3)	0.0008(4)
<b>C21</b>	0.0356(7)	0.0321(8)	0.0299(6)	-0.0060(6)	-0.0002(5)	-0.0046(6)
<b>O22</b>	0.0356(5)	0.0417(7)	0.0489(6)	-0.0187(5)	0.0050(4)	0.0103(5)
<b>C23</b>	0.0247(6)	0.0366(8)	0.0430(7)	0.0052(6)	0.0017(5)	0.0088(6)
<b>C24</b>	0.0380(8)	0.0301(9)	0.0690(11)	0.0020(7)	0.0017(7)	0.0113(6)
<b>O25</b>	0.0652(9)	0.0555(9)	0.0659(9)	-0.0145(7)	0.0039(7)	0.0311(7)
<b>C26</b>	0.0446(8)	0.0495(10)	0.0572(10)	-0.0278(9)	0.0146(7)	-0.0085(8)
<b>C27</b>	0.0227(6)	0.0830(13)	0.0358(7)	-0.0090(9)	0.0046(5)	-0.0033(8)
<b>C28</b>	0.0530(10)	0.0637(12)	0.0325(7)	0.0099(8)	0.0181(7)	0.0044(9)
<b>C29</b>	0.0607(13)	0.165(3)	0.0515(11)	0.0514(16)	0.0236(10)	0.0477(16)
<b>C30</b>	0.173(3)	0.0458(13)	0.0739(15)	0.0100(12)	0.0600(18)	-0.0127(17)
<b>C31</b>	0.0484(10)	0.0965(17)	0.0358(8)	0.0050(10)	0.0190(7)	-0.0117(10)

## Distances

<b>Si1 O2</b>	1.6422(9)Å	<b>Si1 C26</b>	1.8543(18)Å
<b>Si1 C27</b>	1.8606(14)Å	<b>Si1 C28</b>	1.8916(19)Å
<b>O2 C3</b>	1.3974(14)Å	<b>C3 C4</b>	1.5288(17)Å
<b>C3 C8</b>	1.5436(16)Å	<b>C3 C13</b>	1.5645(17)Å
<b>C4 O5</b>	1.3323(15)Å	<b>C4 O7</b>	1.1998(17)Å
<b>O5 C6</b>	1.4437(17)Å	<b>C6 H61</b>	0.963Å
<b>C6 H62</b>	0.965Å	<b>C6 H63</b>	0.974Å
<b>C8 C9</b>	1.5285(19)Å	<b>C8 H81</b>	0.946Å
<b>C8 H82</b>	0.961Å	<b>C9 C10</b>	1.5184(19)Å
<b>C9 H91</b>	0.978Å	<b>C9 H92</b>	0.963Å
<b>C10 O11</b>	1.4439(15)Å	<b>C10 O14</b>	1.4214(14)Å
<b>C10 C23</b>	1.5138(19)Å	<b>O11 C12</b>	1.4235(14)Å
<b>C12 C13</b>	1.5605(15)Å	<b>C12 C19</b>	1.5213(17)Å
<b>C12 H121</b>	0.983Å	<b>C13 O14</b>	1.4239(14)Å

<b>C13 C15</b>	1.5281(16)Å	<b>C15 O16</b>	1.3238(16)Å
<b>C15 O18</b>	1.1996(15)Å	<b>O16 C17</b>	1.4503(16)Å
<b>C17 H171</b>	0.957Å	<b>C17 H172</b>	0.963Å
<b>C17 H173</b>	0.963Å	<b>C19 O20</b>	1.3191(15)Å
<b>C19 O22</b>	1.1993(17)Å	<b>O20 C21</b>	1.4453(16)Å
<b>C21 H211</b>	0.954Å	<b>C21 H212</b>	0.958Å
<b>C21 H213</b>	0.926Å	<b>C23 C24</b>	1.507(2)Å
<b>C23 H231</b>	0.985Å	<b>C23 H232</b>	0.970Å
<b>C24 O25</b>	1.424(3)Å	<b>C24 H241</b>	0.996Å
<b>C24 H242</b>	0.987Å	<b>O25 H251</b>	0.860(17)Å
<b>C26 H262</b>	0.960Å	<b>C26 H263</b>	0.950Å
<b>C26 H261</b>	0.939Å	<b>C27 H273</b>	0.973Å
<b>C27 H271</b>	0.946Å	<b>C27 H272</b>	0.986Å
<b>C28 C29</b>	1.527(3)Å	<b>C28 C30</b>	1.538(4)Å
<b>C28 C31</b>	1.531(2)Å	<b>C29 H291</b>	0.980Å
<b>C29 H293</b>	0.954Å	<b>C29 H292</b>	0.956Å
<b>C30 H302</b>	0.983Å	<b>C30 H301</b>	0.968Å
<b>C30 H303</b>	0.966Å	<b>C31 H312</b>	0.965Å
<b>C31 H313</b>	0.968Å	<b>C31 H311</b>	0.970Å

## Angles

<b>O2 Si1 C26</b>	112.07(7)°	<b>O2 Si1 C27</b>	113.40(6)°
<b>C26 Si1 C27</b>	111.12(10)°	<b>O2 Si1 C28</b>	100.60(7)°
<b>C26 Si1 C28</b>	110.73(10)°	<b>C27 Si1 C28</b>	108.40(9)°
<b>Si1 O2 C3</b>	143.63(8)°	<b>O2 C3 C4</b>	111.19(10)°
<b>O2 C3 C8</b>	109.85(10)°	<b>C4 C3 C8</b>	107.50(10)°
<b>O2 C3 C13</b>	104.17(9)°	<b>C4 C3 C13</b>	115.33(10)°
<b>C8 C3 C13</b>	108.73(9)°	<b>C3 C4 O5</b>	111.52(10)°
<b>C3 C4 O7</b>	123.36(11)°	<b>O5 C4 O7</b>	124.86(12)°
<b>C4 O5 C6</b>	116.59(11)°	<b>O5 C6 H61</b>	108.141°
<b>O5 C6 H62</b>	109.925°	<b>H61 C6 H62</b>	111.298°
<b>O5 C6 H63</b>	106.926°	<b>H61 C6 H63</b>	110.894°
<b>H62 C6 H63</b>	109.548°	<b>C3 C8 C9</b>	111.10(11)°
<b>C3 C8 H81</b>	108.057°	<b>C9 C8 H81</b>	110.827°
<b>C3 C8 H82</b>	108.140°	<b>C9 C8 H82</b>	109.112°

**H81 C8 H82** 109.556°  
**C8 C9 H91** 108.612°  
**C8 C9 H92** 110.137°  
**H91 C9 H92** 108.244°  
**C9 C10 O14** 109.63(10)°  
**C9 C10 C23** 113.27(11)°  
**O14 C10 C23** 109.16(11)°  
**O11 C12 C13** 103.17(9)°  
**C13 C12 C19** 115.11(10)°  
**C13 C12 H121** 110.219°  
**C3 C13 C12** 113.53(10)°  
**C12 C13 O14** 100.48(9)°  
**C12 C13 C15** 116.47(10)°  
**C10 O14 C13** 103.75(9)°  
**C13 C15 O18** 122.28(11)°  
**C15 O16 C17** 115.91(11)°  
**O16 C17 H172** 109.090°  
**O16 C17 H173** 110.786°  
**H172 C17 H173** 109.156°  
**C12 C19 O22** 123.97(12)°  
**C19 O20 C21** 116.48(10)°  
**O20 C21 H212** 108.480°  
**O20 C21 H213** 112.574°  
**H212 C21 H213** 109.597°  
**C10 C23 H231** 109.610°  
**C10 C23 H232** 106.589°  
**H231 C23 H232** 109.104°  
**C23 C24 H241** 105.379°  
**C23 C24 H242** 110.651°  
**H241 C24 H242** 108.255°  
**Si1 C26 H262** 109.755°  
**H262 C26 H263** 109.710°  
**H262 C26 H261** 108.904°  
**Si1 C27 H273** 111.373°  
**H273 C27 H271** 108.872°  
**H273 C27 H272** 107.475°  
**Si1 C28 C29** 109.92(15)°  
**C29 C28 C30** 109.8(2)°

**C8 C9 C10** 110.39(10)°  
**C10 C9 H91** 109.506°  
**C10 C9 H92** 109.904°  
**C9 C10 O11** 109.52(11)°  
**O11 C10 O14** 104.00(9)°  
**O11 C10 C23** 110.84(11)°  
**C10 O11 C12** 108.22(9)°  
**O11 C12 C19** 109.01(10)°  
**O11 C12 H121** 111.865°  
**C19 C12 H121** 107.516°  
**C3 C13 O14** 107.49(9)°  
**C3 C13 C15** 108.38(9)°  
**O14 C13 C15** 109.90(9)°  
**C13 C15 O16** 112.06(10)°  
**O16 C15 O18** 125.65(11)°  
**O16 C17 H171** 106.721°  
**H171 C17 H172** 111.153°  
**H171 C17 H173** 109.918°  
**C12 C19 O20** 111.16(10)°  
**O20 C19 O22** 124.84(12)°  
**O20 C21 H211** 109.099°  
**H211 C21 H212** 107.752°  
**H211 C21 H213** 109.220°  
**C10 C23 C24** 115.54(12)°  
**C24 C23 H231** 107.800°  
**C24 C23 H232** 108.058°  
**C23 C24 O25** 113.07(15)°  
**O25 C24 H241** 104.729°  
**O25 C24 H242** 114.088°  
**C24 O25 H251** 101(2)°  
**Si1 C26 H263** 114.651°  
**Si1 C26 H261** 109.670°  
**H263 C26 H261** 103.898°  
**Si1 C27 H271** 109.292°  
**Si1 C27 H272** 112.612°  
**H271 C27 H272** 107.061°  
**Si1 C28 C30** 109.29(13)°  
**Si1 C28 C31** 110.76(15)°

**C29 C28 C31 108.27(15)°**

**C28 C29 H291 110.342°**

**H291 C29 H293 109.199°**

**H291 C29 H292 108.174°**

**C28 C30 H302 109.852°**

**H302 C30 H301 112.446°**

**H302 C30 H303 110.232°**

**C28 C31 H312 107.906°**

**H312 C31 H313 107.973°**

**H312 C31 H311 107.456°**

**C30 C28 C31 108.82(19)°**

**C28 C29 H293 111.008°**

**C28 C29 H292 107.877°**

**H293 C29 H292 110.192°**

**C28 C30 H301 108.534°**

**C28 C30 H303 108.327°**

**H301 C30 H303 107.329°**

**C28 C31 H313 111.199°**

**C28 C31 H311 110.685°**

**H313 C31 H311 111.443°**



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18. Discernible data for Z-**26**:  $^1\text{H}$  NMR (500 MHz;  $\text{CDCl}_3$ )  $\delta$  4.98 (1H, d,  $J$  9,  $\text{HC}=\text{C}$ ), 4.85 (1H, s,  $\text{CHCO}_2\text{Me}$ ), 0.08 (9H, s, OTMS);  $^{13}\text{C}$  NMR (125 MHz;  $\text{CDCl}_3$ )  $\delta$  171.34 ( $\text{CO}_2\text{Me}$ ), 133.7 ( $\text{C}=\text{CH}$ ), 131.6 (ArC), 129.5 (2xArCH), 125.7 (ArCH), 108.6 ( $\text{O}-\text{C}^1-\text{O}$ ), 78.5 ( $\text{C}^4\text{CO}_2\text{MeOTMS}$ ), 75.9 ( $\text{CHCO}_2\text{Me}$ ), 52.4 ( $\text{CO}_2\text{Me}$ ), 44.3 ( $\text{CH}_2\text{Ph}$ ), 35.6 ( $\text{CHCH}_3$ ), 34.4 ( $\text{C}^6\text{H}_2$ ), 32.1 ( $\text{C}^7\text{H}_2$ ), 31.7 ( $\text{CCH}_2\text{CH}_2\text{CMe}$ ), 30.4 ( $\text{CH}_2$ ), 21.0 ( $\text{CHCH}_3$ ), 14.3 ( $\text{C}=\text{CCH}_3$ ), 1.18 (OTMS).
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## 6. Spectra

