

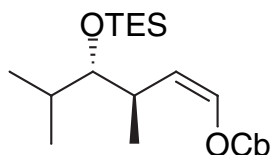
## Supplementary Material

**Diastereoselective Synthesis of Protected *syn* 1,3-Diols: Preparation of the C16-C24 Portion of Dolabelides**

Laurence Grimaud, Romain de Mesmay, and Joëlle Prunet\*

*Laboratoire de Synthèse Organique, UMR CNRS 7652, Ecole Polytechnique, DCSO, F-91128 Palaiseau, France***General**

Melting points were determined on a REICHERT apparatus and are uncorrected. Infrared spectra were obtained on a PERKIN-ELMER FT 1600 instrument and are reported in terms of frequency of absorption ( $\nu$ ,  $\text{cm}^{-1}$ ).  $^1\text{H}$  NMR spectra were recorded on a BRUKER WP 200 (200 MHz), or on a BRUKER AM 400 (400 MHz) instrument. The chemical shifts are expressed in parts per million (ppm) referenced to residual chloroform (7.27 ppm). Data are reported as follows:  $\delta$ , chemical shift; multiplicity (recorded as br, broad; s, singlet; d, doublet; t, triplet; q, quadruplet; hex., hexuplet; hept, heptuplet; oct, octuplet and m, multiplet), coupling constants ( $J$  in Hertz, Hz), and integration.  $^{13}\text{C}$  NMR spectra were recorded on the same instruments at 50.3 MHz and 100.6 MHz respectively. The chemical shifts are expressed in parts per million (ppm), reported from the central peak of deuteriochloroform (77.14 ppm). Mass spectra were obtained on a HEWLETT-PACKARD HP 5989B spectrometer *via* either direct introduction or GC/MS coupling with a HEWLETT-PACKARD HP 5890 chromatograph. Ionization was obtained either by electronic impact (EI) or chemical ionisation with ammonia (IC,  $\text{NH}_3$ ) or methane (IC,  $\text{CH}_4$ ). Mass spectral data are reported as  $m/z$ . Thin Layer Chromatography (TLC) was performed on precoated plate of silica gel 60F 254 or aluminium oxide 60F 254. Flash chromatography was performed on silica gel 60, 230-400 mesh. Microanalyses were performed by the Service de Microanalyse, Institut de Chimie des Substances Naturelles, C.N.R.S., F-91198, Gif sur Yvette.

**(1*E*,3*R*\*,4*S*\*)-(4-Triethylsilyloxy-1-*N,N*-diisopropylcarbamoyloxy-3,5-dimethylhex-1-enylsulfanyl)benzene ( $\pm$ )-6.**

To a  $-78^\circ\text{C}$  solution of 11 g of hydroxy vinylcarbamate ( $\pm$ )-**5** (42 mmol) and 12 mL of 2,6-lutidine (106 mmol, 2.5 equiv) in 100 mL of  $\text{CH}_2\text{Cl}_2$  was added dropwise 13 mL of TESOTf (55 mmol, 1.3 equiv). The mixture was stirred for 1 h at  $-78^\circ\text{C}$  then allowed to warm to  $20^\circ\text{C}$  over 1 h and partitioned between 100 mL of diethyl ether and 100 mL of saturated aqueous  $\text{NH}_4\text{Cl}$ . The aqueous phase was extracted with 3x100 mL of ether. The combined organic layers were washed with brine, dried over anhydrous  $\text{MgSO}_4$ , filtered and concentrated *in vacuo*. Purification by flash chromatography on silica gel (diethyl ether/petroleum ether 0:100 to 30:70) gave 16 g (100%) of the desired silyl ether as a colorless oil.

**$^1\text{H}$  NMR** (400 MHz,  $\text{CDCl}_3$ )  $\delta$  6.99 (d,  $J$  = 6.5 Hz, 1H), 4.86 (dd,  $J$  = 9.8, 6.5 Hz, 1H), 4.16-4.02 (m, 1H), 3.87-3.73 (m, 1H), 3.28 (dd,  $J$  = 6.7, 3.5 Hz, 1H), 2.87 (dq,  $J$  = 10.0, 6.7, 3.5 Hz, 1H), 1.75 (oct,

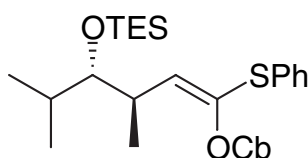
$J = 6.7$  Hz, 1H), 1.21-1.15 (m, 12H), 1.00 (d,  $J = 6.9$  Hz, 3H), 0.96 (t,  $J = 7.9$  Hz, 9H), 0.88, 0.85 (2d,  $J = 6.7$  Hz, 6H), 0.61 (q,  $J = 7.9$  Hz, 6H).

$^{13}\text{C}$  NMR (50 MHz,  $\text{CDCl}_3$ )  $\delta$  153.0, 134.5, 113.4, 81.6, 46.3, 33.7, 32.8, 20.9, 19.5, 19.2, 18.4, 6.5, 5.7.

IR (thin film) 2959, 1713, 1459, 1438, 1370, 1306, 1213, 1134, 1064, 1007, 740  $\text{cm}^{-1}$ .

MS (GC, CI  $\text{NH}_3$ )  $m/z$  386 ( $\text{MH}^+$ ), 372, 327, 313, 298, 260, 199, 187, 128, 86.

Anal. Calcd for  $\text{C}_{21}\text{H}_{43}\text{NO}_3\text{Si}$ : C, 65.40; H, 11.24. Found: C, 65.59; H, 11.03.



To a solution of 2.0 g (5.2 mmol) of the previous silyl ether, 1.6 mL (10 mmol, 2.0 equiv) of TMEDA and 4.5 g (20 mmol, 4.0 equiv) of diphenylsulfide in 20 mL of hexane at  $-78$  °C was added dropwise 6.1 mL (10 mmol, 2.0 equiv) of a 1.7 M solution of *t*-BuLi in pentane. The resulting solution was stirred for 2 h at  $-78$  °C. It was then quenched with 50 mL of a saturated aqueous  $\text{NH}_4\text{Cl}$  solution and the resulting mixture was allowed to warm to room temperature. The aqueous phase was extracted with 3x50 mL of ether. The combined organic layers were washed with brine, dried over anhydrous  $\text{MgSO}_4$ , filtered and concentrated *in vacuo*. Purification by flash chromatography on silica gel with a gradient of ether in petroleum ether (0:100, 10:90, 20:80) gave 2.3 g (90%) of sulfide ( $\pm$ )-6 as a colorless oil.

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.42-7.39, 7.29-7.25, 7.20-7.18 (m, 5H), 5.95 (d,  $J = 9.7$  Hz, 1H), 3.98-3.84 (m, 1H), 3.76-3.62 (m, 1H), 3.33 (dd,  $J = 6.8, 2.5$  Hz, 1H), 2.71 (dq,  $J = 9.7, 6.8, 2.5$  Hz, 1H), 1.73 (oct,  $J = 6.6$  Hz, 1H), 1.22-1.16 (m, 6H), 1.09 (d,  $J = 6.8$  Hz, 3H), 1.02-0.98 (m, 6H), 0.98 (t,  $J = 7.9$  Hz, 9H), 0.91 (d,  $J = 5.0$  Hz, 3H), 0.89 (d,  $J = 6.8$  Hz, 3H), 0.63 (q,  $J = 7.9$  Hz, 6H).

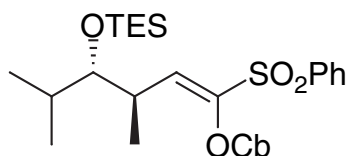
$^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  151.9, 139.0, 134.8, 132.3, 129.7, 128.7, 126.4, 81.4, 46.6, 46.1, 35.5, 33.3, 21.1, 20.4, 19.2, 19.1, 18.7, 7.1, 5.5.

IR (thin film) 2960, 2875, 1721, 1640, 1584, 1476, 1439, 1369, 1293, 1213, 1157, 1135, 1120, 1098, 1053, 1036  $\text{cm}^{-1}$ .

MS (GC, CI  $\text{NH}_3$ )  $m/z$  494 ( $\text{M}+\text{H}^+$ ), 421, 388, 349, 293, 257, 230, 187, 128.

Anal. Calcd for  $\text{C}_{27}\text{H}_{47}\text{NO}_3\text{SSi}$ : C, 65.67; H, 9.59. Found: C, 65.93; H, 9.59.

**(1*E*,3*R*\*,4*S*\*)-6-Benzenesulfonyl-6-*N,N*-diisopropylcarbamoyloxy-2,4-dimethylhex-5-en-3-ol ( $\pm$ )-7**



To a solution of 1.58 g (3.2 mmol) of sulfide ( $\pm$ )-6 in 30 mL of ethanol at  $-10$  °C was added a solution of 600 mg (0.48 mmol, 0.15 equiv) of ammoniumheptamolybdate tetrahydrate in 0.90 mL (9.6 mmol, 30 equiv) of a 33% aqueous solution of  $\text{H}_2\text{O}_2$ . The resulting solution was then allowed to warm to room temperature and stirred for 3 h. It was quenched with a crystal of  $\text{FeSO}_4$  and 30 mL of a saturated aqueous  $\text{NH}_4\text{Cl}$  solution, and stirred for one more hour. The aqueous phase was extracted with 3x50 mL of ether. The combined organic layers were washed with brine, dried over anhydrous  $\text{MgSO}_4$ , filtered and

concentrated *in vacuo*. Purification by flash chromatography on silica gel with a gradient of ether in petroleum ether (0:100, 10:90, 20:80, 30:70, 40:60) gave 1.28 g (100%) of the desired sulfone as a colorless oil.

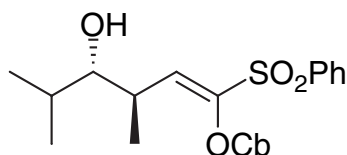
**<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) δ 7.89-7.86, 7.59-7.55, 7.49-7.45 (m, 5H), 6.88 (d, *J* = 10.1 Hz, 1H), 3.97-3.90 (m, 1H), 3.70-3.63 (m, 1H), 3.38 (dd, *J* = 5.7, 2.6 Hz, 1H), 2.56-2.48 (m, 1H), 1.68-1.60 (m, 1H), 1.21-1.17 (m, 6H), 1.09 (d, *J* = 6.8 Hz, 3H), 1.08-1.03 (m, 6H), 0.97 (t, *J* = 8.0 Hz, 9H), 0.82 (d, *J* = 6.8 Hz, 3H), 0.79 (d, *J* = 6.9 Hz, 3H), 0.62 (q, *J* = 8.0 Hz, 6H).

**<sup>13</sup>C NMR** (100 MHz, CDCl<sub>3</sub>) δ 149.9, 143.7, 138.6, 133.7, 133.6, 128.8, 128.6, 80.4, 46.8, 46.7, 34.8, 33.3, 21.0, 20.0, 18.5, 18.4, 17.6, 7.0, 5.5.

**IR** (thin film) 3066, 2961, 2876, 1735, 1657, 1586, 1459, 1447, 1431, 1370, 1323, 1270, 1249, 1212, 1157, 1137, 1089, 1058, 1037 cm<sup>-1</sup>.

**MS** (GC, CI NH<sub>3</sub>) *m/z* 526 (M+H<sup>+</sup>), 496, 128.

**Anal.** Calcd for C<sub>27</sub>H<sub>47</sub>NO<sub>5</sub>Si: C, 61.67; H, 9.01. Found: C, 61.92; H, 9.08.



To 1.3 g (2.4 mmol) of the silyl ether was added 50 mL of a solution (HF/acetonitrile 5:95). The resulting solution was stirred for 3 h at room temperature and quenched with 50 mL of a saturated aqueous NaHCO<sub>3</sub> solution. The aqueous phase was extracted with 3x50 mL of ether. The combined organic layers were washed with brine, dried over anhydrous MgSO<sub>4</sub>, filtered and concentrated *in vacuo*. Purification by flash chromatography on silica gel with a gradient of ether in petroleum ether (40:60, 50:50, 60:40, 70:30) gave 890 mg (89%) of alcohol (±)-**7** as white crystals.

**mp** 68 °C.

**<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) δ 7.90-7.87, 7.59-7.55, 7.49-7.45 (m, 5H), 6.83 (d, *J* = 11.2 Hz, 1H), 4.06-3.99 (m, 1H), 3.61-3.54 (m, 1H), 3.28-3.27 (m, 2H), 2.52-2.41 (m, 1H), 1.79-1.69 (m, 1H), 1.20 (d, *J* = 6.8 Hz, 3H), 1.16 (d, *J* = 6.8 Hz, 3H), 1.07 (d, *J* = 6.8 Hz, 3H), 1.03 (d, *J* = 6.8 Hz, 3H), 0.96 (d, *J* = 6.9 Hz, 3H), 0.94 (d, *J* = 6.8 Hz, 3H), 0.73 (d, *J* = 6.7 Hz, 3H).

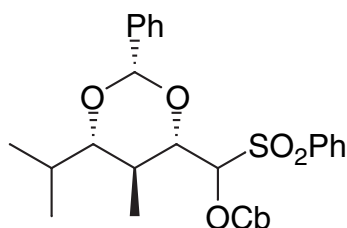
**<sup>13</sup>C NMR** (100 MHz, CDCl<sub>3</sub>) δ 150.4, 144.0, 137.8, 135.0, 134.9, 133.7, 133.6, 79.2, 47.3, 46.8, 35.4, 29.9, 20.9, 20.8, 20.1, 19.8, 16.6, 14.3.

**IR** (thin film) 3449, 2968, 2934, 2875, 1716, 1447, 1371, 1320, 1272, 1210, 1153, 1132, 1095, 1072, 1036 cm<sup>-1</sup>.

**MS** (GC, CI NH<sub>3</sub>) *m/z* 429 (M+NH<sub>4</sub><sup>+</sup>), 412 (M+H<sup>+</sup>), 128.

**Anal.** Calcd for C<sub>21</sub>H<sub>33</sub>NO<sub>5</sub>S: C, 61.28; H, 8.08. Found: C, 61.41; H, 8.19.

**(2*R*\*,4*R*\*(1*R*\*/*S*\*),5*R*\*,6*R*\*)-4-(Benzenesulfonyl-*N,N*-diisopropylcarbamoyloxymethyl)-6-isopropyl-5-methyl-2-phenyl[1,3]dioxane (±)-**8****



To a solution of 650 mg (1.6 mmol) of vinylsulfone ( $\pm$ )-**7** in 6 mL of THF at 0 °C was added 180  $\mu$ L (1.74 mmol, 1.1 equiv) of freshly distilled benzaldehyde, followed by 18 mg (0.16 mmol, 0.1 equiv) of *t*-BuOK, and the resulting solution was stirred for 15 min at 0 °C. This sequence (addition/stirring) was repeated twice and the reaction mixture was quenched with 10 mL of a saturated aqueous  $\text{NH}_4\text{Cl}$  solution. The layers were separated. The aqueous phase was extracted with 3x15 mL of ether. The combined organic layers were washed with brine, dried over anhydrous  $\text{MgSO}_4$ , filtered and concentrated *in vacuo*. The crude ketal (one major diastereomer > 95:5 by  $^1\text{H}$  NMR) was purified by recrystallization from ether to give 675 mg (83%) of a single diastereomer of ketal ( $\pm$ )-**8** as white crystals.

**mp** 143 °C.

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.85-7.83, 7.49-7.45, 7.34-7.28 (m, 10H), 6.18 (d,  $J$  = 4.6 Hz, 1H), 5.50 (s, 1H), 4.18 (dd,  $J$  = 10.0, 4.6 Hz, 1H), 4.15-4.05 (m, 1H), 3.75-3.65 (m, 1H), 3.36 (dd,  $J$  = 10.0, 2.1 Hz, 1H), 2.22 (tq,  $J$  = 10.0, 6.7 Hz, 1H), 2.08 (septd,  $J$  = 6.9, 2.1 Hz, 1H), 1.25-1.17 (m, 9H), 1.16-1.13 (m, 3H), 1.09 (d,  $J$  = 6.9 Hz, 3H), 1.00 (d,  $J$  = 6.7 Hz, 3H), 0.97 (d,  $J$  = 6.9 Hz, 3H).

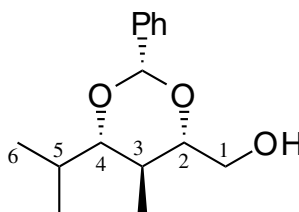
$^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  151.4, 138.3, 138.1, 133.4, 129.5, 128.4, 128.3, 127.8, 126.1, 100.3, 87.1, 85.7, 80.0, 46.7, 46.3, 33.0, 28.1, 21.1, 20.8, 20.3, 20.1, 14.7, 11.8.

**IR** (thin film) 3066, 3035, 2969, 2935, 2876, 1719, 1585, 1448, 1432, 1370, 1327, 1213, 1153, 1073, 1039  $\text{cm}^{-1}$ .

**MS** (GC, CI  $\text{NH}_3$ )  $m/z$  536 ( $\text{M}+\text{NH}_4^+$ ), 518 ( $\text{M}+\text{H}^+$ ), 412, 394, 270, 128.

**Anal.** Calcd for  $\text{C}_{28}\text{H}_{39}\text{NO}_6\text{S}$ : C, 64.96; H, 7.59. Found: C, 64.59; H, 7.58.

**(2*R*\*,4*R*\*,5*R*\*,6*R*\*)-(6-Isopropyl-5-methyl-2-phenyl[1,3]dioxan-4-yl)carbaldehyde ( $\pm$ )-**9****



To a solution of 130 mg (0.25 mmol) of carbamate ( $\pm$ )-**8** in 2 mL of THF at room temperature was added 29 mg (0.75 mmol, 3.0 equiv) of  $\text{LiAlH}_4$ . The resulting mixture was stirred at reflux for 1 h. It was then quenched with 10 mL of a saturated aqueous potassium/sodium tartrate solution and diluted with 10 mL of ether. The resulting mixture was stirred until the organic phase became clear. The aqueous phase was extracted with 3x10 mL of ether. The combined organic layers were washed with brine, dried over anhydrous  $\text{MgSO}_4$ , filtered and concentrated *in vacuo*. Purification by flash chromatography on silica gel with a gradient of ether in petroleum ether (20:80, 30:70, 40:60, 50:50) gave 51 mg (81%) of the desired alcohol as a colorless oil.

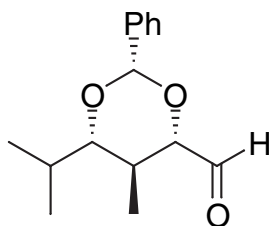
$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.53-7.51, 7.39-7.36 (m, 5H), 5.60 (s, 1H), 3.90-3.86 (m, 1H), 3.72-3.68 (m, 1H), 3.61 (ddd,  $J$  = 10.0, 6.1, 2.5 Hz, 1H), 3.37 (dd,  $J$  = 10.0, 2.1 Hz, 1H), 2.19-2.17 (m, 1H), 2.02 (septd,  $J$  = 6.9, 2.1 Hz, 1H), 1.87 (tq,  $J$  = 10.0, 6.7 Hz, 1H), 1.09 (d,  $J$  = 6.9 Hz, 3H), 0.98 (d,  $J$  = 6.9 Hz, 3H), 0.85 (d,  $J$  = 6.7 Hz, 3H).

$^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  138.9, 128.6, 128.1, 126.1, 100.4, 85.6, 82.4, 63.4, 31.6, 28.3, 20.2, 14.8, 11.6.

**IR** (thin film) 3422, 2967, 2932, 2875, 2840, 1453, 1401, 1349, 1311, 1214, 1184, 1154, 1112, 1086, 1068, 1029  $\text{cm}^{-1}$ .

**MS** (GC, CI  $\text{NH}_3$ )  $m/z$  268 ( $\text{M}+\text{NH}_4^+$ ), 251 ( $\text{M}+\text{H}^+$ ), 145.

**Anal.** Calcd for  $\text{C}_{15}\text{H}_{22}\text{O}_3$ : C, 71.97; H, 8.86. Found: C, 72.31; H, 8.94.



To a solution of 152 mg (0.53 mmol, 1.5 equiv) of IBX in 1 mL of DMSO (dissolved for 20 min) was added a solution of 90 mg (0.35 mmol) of the alcohol in 1 mL of THF. The resulting mixture was stirred for 3 h at room temperature. The same amount of IBX was added and the reaction mixture was stirred for an additional 3 h. It was then diluted with 10 mL of water and the white precipitate was filtered (rinsed several times with ether). The aqueous phase was extracted with 3x10 mL of ether. The combined organic layers were washed with brine, dried over anhydrous  $\text{MgSO}_4$ , filtered and concentrated *in vacuo*. Purification by flash chromatography on silica gel with a gradient of ether in petroleum ether (30:70, 40:60, 50:50) gave 64 mg (74%) of aldehyde ( $\pm$ )-**9** as white crystals.

**mp** 36 °C.

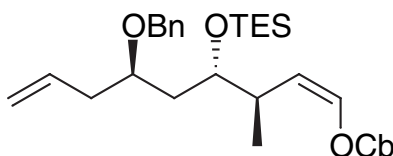
**$^1\text{H}$  NMR** (400 MHz,  $\text{CDCl}_3$ )  $\delta$  9.67 (d,  $J$  = 2.4 Hz, 1H), 7.55-7.53, 7.41-7.38 (m, 5H), 5.63 (s, 1H), 3.89 (dd,  $J$  = 10.5, 2.4 Hz, 1H), 3.42 (dd,  $J$  = 9.9, 2.2 Hz, 1H), 2.06 (septd,  $J$  = 6.9, 2.2 Hz), 2.02-1.92 (m, 1H), 1.10 (d,  $J$  = 6.9 Hz, 3H), 0.98 (d,  $J$  = 6.9 Hz, 3H), 0.92 (d,  $J$  = 6.6 Hz, 3H).

**$^{13}\text{C}$  NMR** (50 MHz,  $\text{CDCl}_3$ )  $\delta$  199.6, 138.4, 128.9, 128.3, 126.2, 100.2, 85.9, 85.1, 31.0, 28.4, 20.1, 14.8, 10.9.

**IR** (thin film) 2968, 1738, 1454, 1404, 1215, 1114, 1030  $\text{cm}^{-1}$ .

**MS** (GC, CI  $\text{NH}_3$ )  $m/z$  266 ( $\text{M}+\text{NH}_4^+$ ), 249 ( $\text{M}+\text{H}^+$ ), 160, 143.

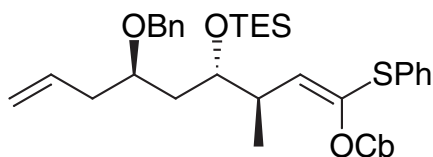
**(1*E*,3*R*,4*R*,6*R*)-(6-Benzoyloxy-1-*N,N*-diisopropylcarbamoyloxy-4-triethylsilyloxy-3-methylnona-1,8-dienylsulfanyl)benzene **15****



To a solution of 760 mg (1.9 mmol) of vinylcarbamates **14** and **14dia** and 440  $\mu\text{L}$  (3.8 mmol, 2.0 equiv) of 2,6-lutidine in 10 mL of  $\text{CH}_2\text{Cl}_2$  at  $-78^\circ\text{C}$  was added dropwise 510  $\mu\text{L}$  (2.2 mmol, 1.2 equiv) of triethylsilyl trifluoromethanesulfonate. The resulting solution was stirred for 1 h at  $-78^\circ\text{C}$  and was allowed to warm to room temperature over one more hour. It was then quenched with 10 mL of a saturated aqueous  $\text{NH}_4\text{Cl}$  solution. The aqueous phase was extracted with 3x10 mL of ether. The combined organic layers were washed with brine, dried over anhydrous  $\text{MgSO}_4$ , filtered and concentrated *in vacuo*. Purification by flash chromatography on silica gel with a gradient of ether in petroleum ether (0:100, 10:90, 20:80) gave 832 mg (86%) of two inseparable diastereomers in a 1:1 ratio of the desired silylated vinyl carbamate as a colorless oil.

**$^1\text{H}$  NMR** (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.33-7.32 (m, 20H), 7.04 (d,  $J$  = 6.6 Hz, 1H), 7.02 (d,  $J$  = 6.6 Hz, 1H), 5.83 (ddt,  $J$  = 17.2, 10.2, 7.0 Hz, 1H), 5.80 (m, 1H), 5.12-5.05 (m, 4H), 4.77 (dd,  $J$  = 9.9, 5.5 Hz, 1H), 4.75 (dd,  $J$  = 9.9, 6.5 Hz, 1H), 4.59 (d,  $J$  = 11.5 Hz, 2H), 4.44 (d,  $J$  = 11.5 Hz, 1H), 4.43 (d,  $J$  = 11.5 Hz, 1H), 4.10-3.90 (m, 2H), 3.89-3.85 (m, 2H), 3.87 (dt,  $J$  = 8.1, 3.5 Hz, 1H), 3.78 (td,  $J$  = 6.8, 2.8 Hz, 1H), 3.62 (tt,  $J$  = 6.3, 5.4 Hz, 1H), 3.52 (tt,  $J$  = 6.5, 5.6 Hz, 1H), 2.81-2.72 (m, 2H), 2.37-2.27 (m, 4H), 1.74-

1.54 (m, 4H), 1.25-1.23 (m, 24H), 1.02 (d,  $J = 7.0$  Hz, 3H), 1.00 (d,  $J = 7.0$  Hz, 3H), 0.96 (t,  $J = 7.9$  Hz, 9H), 0.95 (t,  $J = 7.9$  Hz, 9H), 0.62 (q,  $J = 7.9$  Hz, 12H).



To a solution of 535 mg (1.0 mmol) of the previous carbamates, 310  $\mu$ L (2.1 mmol, 2.0 equiv) of TMEDA and 900 mg (4.0 mmol, 4.0 equiv) of diphenylsulfide in 5 mL of hexane at  $-78^{\circ}\text{C}$  was added dropwise 1.2 mL (2.0 mmol, 2.0 equiv) of a 1.7 M solution of *t*-BuLi in pentane. The resulting solution was stirred for 2 h at  $-78^{\circ}\text{C}$ . It was then quenched with 10 mL of a saturated aqueous  $\text{NH}_4\text{Cl}$  solution and the resulting mixture was allowed to warm to room temperature. The aqueous phase was extracted with 3x10 mL of ether. The combined organic layers were washed with brine, dried over anhydrous  $\text{MgSO}_4$ , filtered and concentrated *in vacuo*. Purification by flash chromatography on silica gel with a gradient of ether in petroleum ether (0:100, 10:90, 20:80) gave 302 mg (47%) of **15dia** and 296 mg (46%) of the desired sulfide **15** as colorless oils. **15**:

**$^1\text{H}$  NMR** (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.40-7.21 (m, 10H), 5.84 (ddt,  $J = 17.2, 10.3, 7.0$  Hz, 1H), 5.82 (d,  $J = 9.8$  Hz, 1H), 5.12 (dd,  $J = 17.2, 1.8$  Hz, 1H), 5.08 (d,  $J = 10.3$  Hz, 1H), 4.63 (d,  $J = 11.4$  Hz, 1H), 4.46 (d,  $J = 11.4$  Hz, 1H), 3.94 (dt,  $J = 8.3, 3.4$  Hz, 1H), 3.93-3.87 (m, 1H), 3.67-3.63 (m, 2H), 2.63 (dq,  $J = 9.9, 6.9, 3.4$  Hz, 1H), 2.45-2.37 (m, 2H), 1.75-1.55 (m, 2H), 1.22-1.19 (m, 6H), 1.06 (d,  $J = 6.9$  Hz, 3H), 1.03-1.00 (m, 6H), 0.94 (t,  $J = 7.7$  Hz, 9H), 0.58 (q,  $J = 7.8$  Hz, 6H).

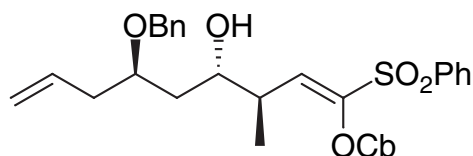
**$^{13}\text{C}$  NMR** (100 MHz,  $\text{CDCl}_3$ )  $\delta$  151.7, 134.5, 132.2, 131.8, 129.5, 128.8, 128.3, 127.5, 126.4, 117.2, 75.7, 71.9, 70.3, 46.5, 46.3, 39.5, 38.5, 38.2, 21.1, 20.4, 15.6, 7.0, 5.2.

**IR** (thin film) 3063, 2961, 2875, 1720, 1641, 1584, 1455, 1439, 1369, 1298, 1242, 1213, 1135, 1035  $\text{cm}^{-1}$ .

**MS** (CI  $\text{NH}_3$ )  $m/z$  643 ( $\text{M}+\text{NH}_4^+$ ), 626 ( $\text{M}+\text{H}^+$ ), 481, 389, 367, 238, 202, 130, 128.

**Anal.** Calcd for  $\text{C}_{36}\text{H}_{55}\text{NO}_4\text{SSi}$ : C, 69.07; H, 8.86. Found: C, 69.23; H, 9.01.

**(1*E*,3*R*,4*R*,6*R*)-(1-Benzenesulfonyl-6-benzyloxy-1-*N,N*-diisopropylcarbamoyloxy-3-methyl nona-1,8-dien-4-ol 16**



To a solution of 573 mg (0.9 mmol) of sulfide **15** in 5 mL of ethanol at  $-10^{\circ}\text{C}$  was added 210 mg (0.14 mmol, 0.15 equiv) of ammoniumheptamolybdate tetrahydrate and 130  $\mu$ L (2.7 mmol, 3 equiv) of a 33% aqueous  $\text{H}_2\text{O}_2$  solution. The resulting solution was then allowed to warm to room temperature and stirred for 18 h. It was quenched with 10 mL of a saturated aqueous  $\text{NH}_4\text{Cl}$  solution. The aqueous phase was extracted with 3x10 mL of ether. The combined organic layers were washed with brine, dried over anhydrous  $\text{MgSO}_4$ , filtered and concentrated *in vacuo*. Purification by flash chromatography on silica gel with a gradient of ether in petroleum ether (0:100, 10:90, 20:80, 30:70, 40:60) gave 522 mg (60%) of the desired sulfone **16** as a colorless oil.

**$^1\text{H}$  NMR** (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.92-7.90, 7.61-7.59, 7.52-7.48, 7.37-7.31 (4m, 10H), 6.84 (d,  $J = 10.9$  Hz, 1H), 5.80 (ddt,  $J = 17.2, 10.1, 7.2$  Hz, 1H), 5.13-5.08 (m, 2H), 4.65 (d,  $J = 11.2$  Hz, 1H), 4.44 (d,  $J =$

11.2 Hz, 1H), 4.01-3.96 (m, 1H), 3.87-3.78 (m, 2H), 3.77-3.60 (m, 1H), 3.31 (br d,  $J = 5.7$  Hz, 1H), 2.46-2.25 (m, 3H), 1.69-1.61 (m, 1H), 1.47-1.40 (m, 1H), 1.20-1.17 (m, 12H), 1.01 (d,  $J = 6.8$  Hz, 3H).

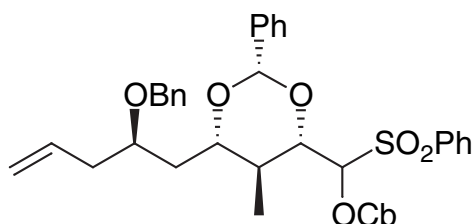
$^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  150.0, 144.5, 138.2, 137.8, 133.7, 133.5, 133.4, 128.8, 128.7, 128.4, 127.7, 127.6, 117.8, 78.3, 73.6, 70.7, 47.0, 46.6, 38.7, 38.2, 37.7, 20.9, 19.9, 15.8.

IR (thin film) 3456 (br), 3065, 2971, 2934, 1734, 1640, 1585, 1496, 1447, 1371, 1321, 1210, 1154, 1036  $\text{cm}^{-1}$ .

MS (CI  $\text{NH}_3$ )  $m/z$  544 ( $\text{M}+\text{H}^+$ ), 340, 270, 222, 205, 198, 178, 161, 128, 102, 86.

Anal. Calcd for  $\text{C}_{30}\text{H}_{41}\text{NO}_6\text{S}$ : C, 66.27; H, 7.60. Found: C, 66.23; H, 7.57.

**(2*S*,4*S*(1*R*/*S*),5*S*,6*S*(2*R*))-4-(Benzenesulfonyl-*N,N*-diisopropylcarbamoyloxymethyl)-6-(2-benzoyloxypent-4-enyl)-5-methyl-2-phenyl[1,3]dioxane 17**



To a solution of 312 mg (0.55 mmol) of vinylsulfone **16** in 2 mL of THF at 0°C was added 70  $\mu\text{L}$  (0.65 mmol, 1.2 equiv) of freshly distilled benzaldehyde, followed by 6 mg (0.06 mmol, 0.1 equiv) of *t*-BuOK, and the resulting solution was stirred for 15 min at 0°C. This sequence (addition/stirring) was repeated twice. The reaction mixture was quenched with 10 mL of a saturated aqueous  $\text{NH}_4\text{Cl}$  solution and diluted with  $\text{Et}_2\text{O}$ . The layers were separated. The aqueous phase was extracted with 3x10 mL of  $\text{Et}_2\text{O}$ . The combined organic layers were washed with brine, dried over anhydrous  $\text{MgSO}_4$ , filtered and concentrated *in vacuo*. Purification by flash chromatography on silica gel with a gradient of ether in petroleum ether (50:50, 60:40, 70:30) gave 306 mg (86%) of the desired ketal **17** as white crystals.

mp 48-49 °C.

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.87-7.85, 7.54-7.50, 7.37-7.20 (3m, 15H), 6.18 (d,  $J = 4.6$  Hz, 1H), 5.95-5.87 (ddt,  $J = 14.2, 10.2, 7.1$  Hz, 1H), 5.51 (s, 1H), 5.14-5.09 (m, 2H), 4.54 (s, 2H), 4.20 (dd,  $J = 10.2, 4.5$  Hz, 1H), 4.14-4.03 (m, 1H), 3.83 (m, 1H), 3.68-3.56 (m, 1H), 2.53-2.50 (m, 1H), 2.39-2.36 (m, 2H), 2.16-1.92 (m, 3H), 1.21-1.17 (m, 12H), 1.00 (d,  $J = 6.5$  Hz, 3H).

$^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  151.0, 137.9, 137.3, 134.4, 133.2, 128.3, 128.2, 128.1, 128.0, 127.6, 127.5, 127.4, 127.2, 125.9, 116.9, 99.9, 86.5, 79.7, 78.9, 74.7, 70.5, 46.5, 46.0, 37.5, 36.1, 35.6, 20.8, 20.5, 12.0.

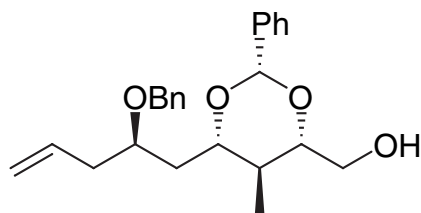
IR (thin film) 3066, 2961, 2876, 1735, 1657, 1586, 1459, 1447, 1431, 1370, 1323, 1270, 1249, 1212, 1157, 1137, 1089, 1058, 1037  $\text{cm}^{-1}$ .

MS (GC, CI  $\text{NH}_3$ )  $m/z$

Anal. Calcd for  $\text{C}_{37}\text{H}_{47}\text{NO}_7\text{S}$ : C, 68.38; H, 7.29. Found: C, 68.53; H, 7.31.



**(2*S*,4*S*,5*S*,6*S*(2*R*))-6-(2-benzoyloxypent-4-enyl)-5-methyl-2-phenyl[1,3]dioxan-4-yl)carbaldehyde **18****



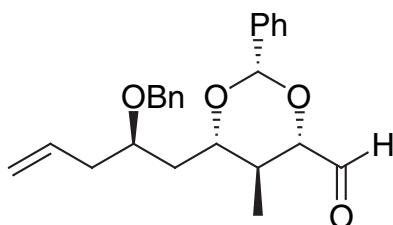
To a solution of 256 mg (0.39 mmol) of carbamate **17** in 2 mL of THF at room temperature was added 45 mg (1.2 mmol, 3.0 equiv) of LiAlH<sub>4</sub>. The resulting mixture was stirred at reflux for 1 h. It was then quenched with 10 mL of a saturated aqueous potassium/sodium tartrate solution and diluted with 10 mL of ether. The resulting mixture was stirred until the organic phase became clear. The aqueous phase was extracted with 3x10 mL of ether. The combined organic layers were washed with brine, dried over anhydrous MgSO<sub>4</sub>, filtered and concentrated *in vacuo*. Purification by flash chromatography on silica gel with a gradient of ether in petroleum ether (40:60, 50:50, 60:40, 70:30) gave 121 mg (80%) of the desired alcohol as a colorless oil.

**<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) δ 7.51-7.27 (m, 10H), 6.00-5.88 (ddt, *J* = 14.1, 10.1, 7.2 Hz, 1H), 5.59 (s, 1H), 5.15 (d, *J* = 15.9 Hz, 1H), 5.12 (d, *J* = 8.2 Hz, 1H), 4.57 (s, 2H), 3.95-3.82, 3.72-3.67, 3.63-3.55 (3m, 5H), 2.56-2.30 (m, 3H), 2.00-1.91, 1.82-1.74, 1.72-1.58 (3m, 3H), 0.88 (d, *J* = 6.6 Hz, 3H).

**<sup>13</sup>C NMR** (100 MHz, CDCl<sub>3</sub>) δ 138.6, 137.8, 134.6, 128.9, 128.5, 128.4, 127.9, 127.7, 125.2, 116.5, 99.8, 86.5, 79.0, 79.7, 74.7, 70.5, 37.5, 36.1, 35.6, 12.0.

**IR** (thin film) 3319 (br), 3030, 2919, 2849, 1602, 1461, 1373, 1261, 1073, 1032 cm<sup>-1</sup>.

**MS** (GC, CI NH<sub>3</sub>) *m/z* 383 (M+H<sup>+</sup>), 372, 243, 220, 78, 61.



To a solution of 130 mg (0.5 mmol, 1.5 equiv) of IBX in 1 mL of DMSO (dissolved for 20 min) was added a solution of 120 mg (0.3 mmol) of the previous alcohol in 1 mL of THF. The resulting mixture was stirred for 3 h at room temperature. It was then diluted with 10 mL of water and the white precipitate was filtered (rinsed several times with ether). The aqueous phase was extracted with 3x10 mL of ether. The combined organic layers were washed with brine, dried over anhydrous MgSO<sub>4</sub>, filtered and concentrated *in vacuo*. Purification by flash chromatography on silica gel with a gradient of ether in petroleum ether (30:70, 40:60, 50:50) gave 73 mg (61%) of the desired aldehyde **18** as a colorless oil.

**<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) δ 9.66 (d, *J* = 2.1 Hz, 1H), 7.54-7.28 (m, 10H), 5.98-5.85 (ddt, *J* = 14.1, 10.2, 7.1 Hz, 1H), 5.63 (s, 1H), 5.17-5.11 (m, 2H), 4.59 (d, *J* = 11.6 Hz, 1H), 4.55 (d, *J* = 11.6 Hz, 1H), 3.94-3.82 (m, 2H), 3.64 (td, *J* = 9.8, 3.4 Hz, 1H), 2.56-2.43 (m, 2H), 2.06-1.84, 1.81-1.71, 1.66-1.59 (3m, 3H), 0.95 (d, *J* = 6.6 Hz, 3H).

**<sup>13</sup>C NMR** (100 MHz, CDCl<sub>3</sub>) δ 199.3, 138.5, 137.5, 134.5, 128.9, 128.3, 128.2, 127.7, 127.5, 126.0, 117.3, 99.7, 84.8, 78.9, 74.2, 70.7, 38.7, 36.2, 33.5, 11.2.



**IR** (thin film) 3066, 3032, 2957, 2925, 2868, 1738, 1640, 1596, 1454, 1403, 1364, 1251, 1096, 1069, 1028  $\text{cm}^{-1}$ .

**MS** (GC, CI  $\text{NH}_3$ )  $m/z$  381 ( $\text{M}+\text{H}^+$ ), 354, 282, 275, 257.