Supporting information

Total Synthesis of (+)-Mycalamide A

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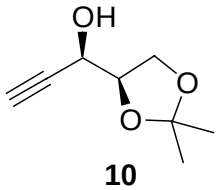
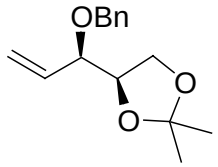


10

(+)-(2*R*,3*R*)-1,2-*O*-Isopropylidene-4-pentyne-1,2,3-triol (10)

To a –30 ˚C solution of *p*-nitrobenzoic acid (0.156 g, 0.934 mmol) and powdered PPh_3 (0.245 g, 0.934 mmol) in toluene (10 mL) was added a solution of *anti*-alcohol **9** (0.178 g, 0.779 mmol) in toluene (3 mL), and followed by a solution of DEAD in toluene (0.424 mL, 40%, 0.934 mmol). The mixture was stirred for 17 h at –30 ˚C, then poured into saturated $NaHCO_3$ (20 mL). The phases were separated and the aqueous phase was further extracted with Et_2O (2 x 40 mL). The combined organic extracts were washed with brine (20 mL), dried ($MgSO_4$) and concentrated. The resulting yellow solid was diluted with Et_2O (9 mL) and hexane (30 mL), and filtered. The filter cake was washed with Et_2O, and combined filtrate and washings were evaporated to provide a viscous oil. Purification of the crude product by flash chromatography (9% EtOAc/hexane) provided *syn-p*-nitrobenzoate (0.462 g, >100%) as a yellow solid, which was used without further purification in a next experiment.

To a 0 ˚C solution of *syn-p*-nitrobenzoate (0.462 g, <0.779 mmol) in MeOH (12 mL) was added K_2CO_3 (0.419 g, 3.03 mmol), and the suspension was stirred for 15 min at rt. After neutralization with AcOH, the solvent was removed to give a colorless oil. The resulting oil was diluted with H_2O (30 mL), and extracted with EtOAc (2 x 50 mL). The combined organic extracts were washed with brine (30 mL), dried ($MgSO_4$) and concentrated. Purification of the crude product by flash chromatography (25% EtOAc/hexane) provided *β*-acetylenic alcohol **10** (98.6 mg, 81% for 2 steps), of which structure was confirmed by comparison with reported spectral data [1)].



11

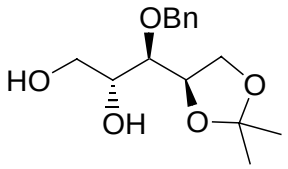
(–)-(3*R*,4*R*)-3-Benzyloxy-4,5-isopropylidenedioxypentene (11)

To a 0 ˚C suspension of $LiAlH_4$ (3.89 g, 0.103 mol) in Et_2O (250 mL) was added a solution of *β*-acetylenic alcohol **10** (14.5 g, 0.0929 mol) in Et_2O (30 mL). The mixture was stirred for 2 h at rt, then cooled to 0 ˚C and H_2O (3.89 mL) was slowly added. After 30 min, 15% NaOH (3.89 mL) and H_2O (11.7 mL) were added and the resulting solution was stirred for an additional 10 h at rt. $MgSO_4$ (4 g) was added, and the mixture was filtered through Celite and concentration to provide olefin (12.34 g). The crude olefin was used without further purification in a next experiment.

To a 0 ˚C suspension of NaH (3.46 g, 60 % in oil, 0.0864 mmol) in DMF (180 mL) was added a solution of a crude olefin (12.34 g) in DMF (40 mL), followed by BnBr (11.2 mL, 0.0944 mmol).

The mixture was stirred for 1.5 h at rt, and H_2O (50 mL) was added over 15 min. The phases were separated and the aqueous phase was further extracted with Er_2O (2 x 100 mL). The combined organic extracts were washed with brine (50 mL), dried ($MgSO_4$) and concentrated. Purification of the crude product by flash chromatography (6% EtOAc/hexane) provided benzyl ether **11** (18.75 g, 98% for 2 steps) as a colorless oil.

Data for **11** ;$[\alpha]^{28}_D$= –27.46˚ (c 0.97, $CHCl_3$); IR (neat) 1635 cm^{-1}; ^1H NMR (300 MHz, $CDCD_3$) δ 1.36 (s, 3 H), 1.40 (s, 3 H), 3.75 (dd, *J*= 8.5, 6.6 Hz, 1 H), 3.84 (dd, *J*= 7.4, 6.9 Hz, 1 H), 3.95 (dd, *J*= 8.5, 6.6 Hz, 1 H), 4.21 (q, *J*= 6.6 Hz, 1 H), 4.48 (d, *J*= 12.4 Hz, 1 H), 4.69 (d, *J*= 12.4 Hz, 1 H), 5.34 (ddd, *J*= 0.8, 1.4, 18.1 Hz, 1 H), 5.36 (ddd, *J*= 0.8, 1.4, 9.1 Hz, 1 H), 5.73 (ddd, *J*= 7.7, 11.0, 18.7 Hz, 1 H), 7.26-7.37 (m, 5H) ; ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.38, 134.34, 128.34, 127.79, 127.55, 120.04, 109.68, 80.97, 77.40, 70.25, 65.68, 26.36, 25.25; LRMS *m/z* 233 (M^+–15) ; HRMS calcd for $C_{14}H_{17}O_3$ 233.1177, found 233.1154; *Anal*. Calcd for $C_{15}H_{20}O_3$: C, 72.55; H, 8.11. Found : C, 72.60; H, 8.08.

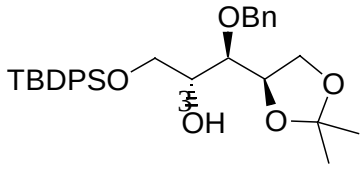


12 ($\alpha:\beta$ = 8:1)

(2*RS*,3*R*,4*R*)-3-Benzyloxy-4,5-isopropylidenedioxy-1,2-pentanediol (12)

To a solution of olefin **11** (2.43 g, 9.78 mmol) in ^tBuOH-H_2O (30 mL, 1:1, v/v) were added NMO (1.72 g, 14.7 mmol) and OsO_4 (0.124 g, 0.489 mmol). The mixture was stirred for 10 h at rt, then saturated Na_2SO_3 was added. The solution was stirred for an additional 1 h. The resulting mixture was extracted with EtOAc. The combined organic extracts were washed with brine, dried over $MgSO_4$ and concentrated. Purification of the crude product by flash chromatography (80% EtOAc/hexane) provided diol diastereomers **12** (2.76 g, 100%) in a 8:1 ratio.

Partial data for **12** ; IR (neat) 3420 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$), δ 1.38 (s, 3 H), 1.46 (s, 3 H), 2.97 (br s, 2 H), 3.59-3.69 (m, 2 H), 3.71-3.79 (m, 2 H), 3.87 (dd, *J*= 8.5, 7.4 Hz, 1 H), 4.04 (dd, *J*= 8.5, 6.6 Hz, 1 H), 4.32-4.43 (m, 1 H), 4.67 (d, *J*= 11.8 Hz, 0.1 H), 4.68 (d, *J*= 11.5 Hz, 0.9 H), 4.76 (d, *J*= 11.3 Hz, 0.9 H), 4.82 (d, *J*= 11.5 Hz, 0.1 H), 7.27-7.39 (m, 5 H); LRMS *m/z* 267 (M^+–15); HRMS calcd for $C_{14}H_{19}O_5$ 267.1231, found : 267.1223.

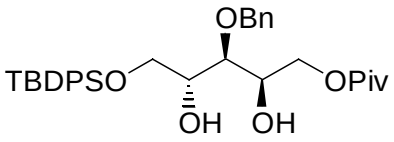


13

(+)-(2*R*,3*R*,4*R*)-3-Benzyloxy-1-*tert*-butyldiphenylsilyloxy-4,5-isopropylidenedioxy-2-pentol (13)

To a solution of diol **12** (0.475 g, 1.68 mmol, a 8:1 mixture of diastereomers) in CH_2Cl_2 (12 mL) were added Et_3N (0.305 mL, 2.18 mmol), TBDPSCl (0.524 mL, 2.02 mmol) and DMAP (10.3 mg, 0.084 mmol). The mixture was stirred for 10 h at rt, and quenched by H_2O. The resulting solution was extracted with Et_2O. The combined organic extracts were washed with brine, dried over $MgSO_4$ and concentrated to provide a yellow solid. The crude product was recrystallized from Et_2O-hexane to yield TBDPS ether **13** (0.531 g, 61%) as a colorless powder.

Data for **13** ; mp115-117 °C; $[\alpha]^{28}_D$= +6.86˚ (c 1.02, $CHCl_3$); IR (neat) 3550 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.07 (s, 9 H), 1.36 (s, 3 H), 1.43 (s, 3 H), 2.71 (d, *J*= 4.7 Hz, 1 H), 3.51 (t, *J*= 6.0 Hz, 1 H), 3.73-3.85 (m, 4 H), 4.01 (dd, *J*= 8.5, 6.4 Hz, 1 H), 4.31 (dt, *J*= 7.7, 6.2 Hz, 1 H), 4.55 (d, *J*= 11.3 Hz, 1 H), 4.74 (d, *J*= 11.5 Hz, 1 H), 7.19-7.47 (m, 11 H), 7.62-7.66 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.38, 135.78, 133.18, 133.12, 130.06, 128.48, 128.14, 127.99, 127.79, 109.01, 79.24, 77.60, 73.94, 71.98, 66.43, 64.85, 26.89, 26.42, 25.62, 19.21; LRMS *m/z* 505 (M^+–15); HRMS calcd for $C_{30}H_{37}O_5Si$ 505.2408, found : 505.2411; *Anal*. Calcd for $C_{31}H_{40}O_5Si$: C, 71.50 ; H, 7.74. Found : C, 71.34 ; H, 7.81.



14

(–)-(2*R*,3*S*,4*R*)-3-Benzyloxy-1-*tert*-butyldiphenylsilyloxy-2,4-dihydroxypentan-5-yl pivalate (14)

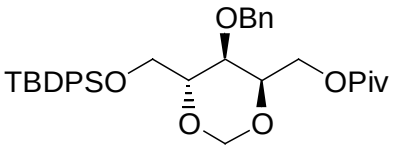
A solution of acetonide **13** (6.93 g, 13.3 mmol) in AcOH-THF-H_2O (40 mL, 3:1:1, v/v) was stirred for 6 h at 55 ˚C. The solution was cooled to rt, and then poured into saturated $NaHCO_3$. The resulting solution was extracted with EtOAc. The combined organic extracts were washed with brine, dried over $MgSO_4$ and concentrated. Purification of the crude product by flash chromatography (80% EtOAc/hexane) provided a triol (6.28 g, 98%) as a colorless oil.

Data for the triol ; $[\alpha]^{26}_D$= –5.00˚ (c 1.16, $CHCl_3$) ; IR (neat) 3400 cm^{-1} ; ^1H NMR (300 MHz, $CDCl_3$) δ 1.08 (s, 9 H), 2.22 (br s, 1 H), 2.92-2.96 (m, 2 H), 3.59 (dd, *J*= 3.2, 6.4 Hz, 1 H), 3.63-3.73 (m, 2 H), 3.77 (dd, *J*= 6.1, 10.4 Hz, 1 H), 3.85 (dd, *J*= 4.4, 10.4 Hz, 1 H), 3.88-3.97 (m, 2 H), 4.51 (d, *J*= 11.3 Hz, 1 H), 4.56 (d, *J*= 11.3 Hz, 1 H), 7.16-7.21 (m, 2 H), 7.26-7.30 (m, 3 H), 7.35-7.48 (m, 6 H), 7.63-7.66 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.60, 135.72, 135.69, 133.08, 13 2.99, 130.03, 128.57, 128.20, 128.10, 127.96, 78.07, 73.44, 71.62, 64.83, 64.04, 26.85,

19.14; LRMS *m/z* 423 (M^+–57); HRMS calcd for $C_{24}H_{27}O_5Si$ 423.1626, found : 423.1645; *Anal*. Calcd for $C_{28}H_{36}O_5Si$:C, 69.96 ; H, 7.54. Found : C, 69.99 ; H, 7.63.

To a solution of the triol (1.21 g, 2.51 mmol) in CH_2Cl_2 (10 mL) were added pyridine (2 mL, 24.7 mmol) and PivCl (0.324 mL, 2.63 mmol). The mixture was stirred for 10 h at rt. After the solvent was removed, the resulting crude oil was purified by flash chromatography (20% EtOAc/hexane) to provide pivalate **14** (1.27 g, 89%) as a colorless oil.

Data for **14** ; $[\alpha]^{20}_D$= –4.50˚ (c 1.20, $CHCl_3$); IR (neat) 3450, 1725 cm^{-1} ; ^1H NMR (300 MHz, $CDCl_3$) δ 1.08 (s, 9 H), 1.21 (s, 9 H), 2.79 (br s, 2 H), 3.58 (dd, *J*= 1.9, 7.1 Hz, 1 H), 3.78 (dd, *J*= 5.5, 10.4 Hz, 1 H), 3.87 (dd, *J*= 3.8, 10.4 Hz, 1 H), 3.90-3.97 (m, 1 H), 4.12 (dd, *J*= 5.5, 12.7 Hz, 1 H), 4.11-4.15 (m, 1 H), 4.25 (dd, *J*= 8.8, 12.6 Hz, 1 H), 4.53 (s, 2 H), 7.14-7.18 (m, 2 H), 7.26-7.29 (m, 3 H), 7.32-7.48 (m, 6 H), 7.63-7.66 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 178.46, 137.54, 135.64, 135.61, 132.97, 132.83, 129.95, 128.45, 128.05, 127.96, 127.88, 77.22, 73.59, 71.36, 69.10, 64.92, 64.67, 38.61, 27.05, 26.76, 19.06; LRMS *m/z* 489 (M^+–75); HRMS calcd for $C_{29}H_{33}O_5Si$ 489.2095, found : 489.2127; *Anal*. Calcd for $C_{33}H_{44}O_6Si$: C,70.17 ; H, 7.85. Found : C, 70.00 ; H, 7.81.

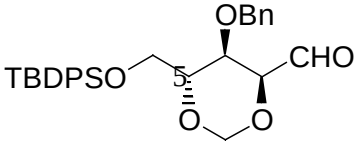


15

(+)-(2*S*,3*R*,4*R*)-3-Benzyloxy-5-*tert*-butyldiphenylsilyloxy-2,4-methylenedioxypentanal (15)

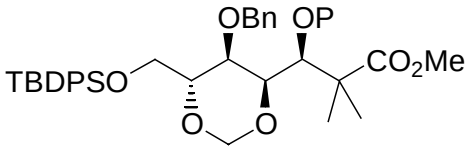
To a solution of diol **14** (0.340 g, 0.559 mmol) in CH_2Cl_2 (60 mL) was added freshly distilled dimethoxymethane (12 mL) followed by P_2O_5 (3.4 g). The mixture was vigorously stirred for 1.5 h, and poured into saturated $NaHCO_3$ at 0 ˚C. The phases were separated and the aqueous phase was further extracted with Et_2O. The combined organic extracts were washed with brine, dried over $MgSO_4$ and concentrated. Purification of the crude product by flash chromatography (9% EtOAc/hexane) provided a methylene acetal **15** (0.303 g, 88%) as a colorless oil.

Data for **15** ; $[\alpha]^{28}_D$= +12.82˚ (c 0.95, $CHCl_3$); IR (neat) 1730 cm^{-1} ; ^1H NMR (300 MHz, $CDCl_3$) δ 1.06 (s, 9 H), 1.19 (s, 9 H), 3.76 (dd, *J*= 3.8, 4.7 Hz, 1 H), 3.85-3.97 (m, 3 H), 4.17-4.24 (m, 2 H), 4.50 (dd, *J*= 9.1, 12.9 Hz, 1 H), 4.53 (d, *J*= 11.8 Hz, 1 H), 4.64 (d, *J*= 11.8 Hz, 1 H), 4.86 (d, *J*= 6.3 Hz, 1 H), 4.94 (d, *J*= 6.3 Hz, 1 H), 7.26-7.44 (m, 11 H), 7.64-7.68 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 178.56, 137.71, 135.84, 135.76, 133.23, 133.12, 130.03, 128.64, 128.14, 128.11, 127.96, 88.27, 75.22, 72.42, 72.18, 70.69, 62.63, 61.63, 38.75, 27.15, 26.83, 19.21; LRMS *m/z* 519 (M^+–57); HRMS calcd for $C_{30}H_{35}O_6Si$ 519.2200, found : 519.2200; *Anal*. Calcd for $C_{34}H_{44}O_6Si$: C,70.79 ; H, 7.68. Found : C, 70.62 ; H, 7.67.

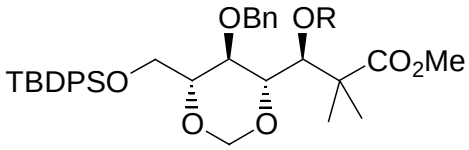


16

To a 0 ˚C solution of **15** (1.22 g, 2.12 mmol) in THF (13 mL) was added DIBAL-H (4.96 mL, 4.66 mmol) dropwise. The solution was stirred for 1 h at that temperature. H_2O (5 mL) was added to quench the reaction. After 20 min Et_2O (10 mL) and hexane (10 mL) were added. The resulting mixture was allowed to warm to rt and stirred for 10 h, then dried ($MgSO_4$) and filterd through Celite. The filtrate was concentrated to afford a crude oil. Purification of the crude product by flash chromatography (33% EtOAc/hexane) provided an alcohol (1.04 g, 99%) as a colorless oil.
Data for the alcohol ; $[\alpha]^{27}_D$= +0.75˚ (c 1.05, $CHCl_3$); IR (neat) 3425 cm^{-1} ; ^1H NMR (300 MHz, $CDCl_3$) δ 1.08 (s, 9 H), 1.83-1.85 (m, 1 H), 3.62-3.71 (m, 2 H), 3.89-3.96 (m, 4 H), 3.98-4.01 (m, 1 H), 4.46 (d, *J*= 11.5 Hz, 1 H), 4.67 (d, *J*= 11.8 Hz, 1 H), 4.83 (d, *J*= 6.3 Hz, 1 H), 4.91 (d, *J*= 6.3 Hz, 1 H), 7.25-7.48 (m, 11 H), 7.64-7.68 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.53, 135.78, 135.72, 133.09, 129.99, 128.66, 128.25, 128.20, 127.93, 127.90, 88.23, 75.04, 74.41, 71.97, 70.83, 62.18, 61.01, 26.82, 19.15 ; LRMS *m/z* 435 (M^+–57); HRMS calcd for $C_{25}H_{27}O_5Si$ 435.1626, found : 435.1610 ; *Anal*. Calcd for $C_{29}H_{36}O_5Si$: C,70.69 ; H, 7.36. Found : C, 70.83 ; H, 7.51.
To a –78 ˚C solution of $(COCl)_2$ (0.080 mL, 0.917 mmol) in CH_2Cl_2 (5 mL) was added a solution of DMSO (0.141 mL, 1.99 mmol) in CH_2Cl_2 (3 mL) dropwise over 10 min. The mixture was stirred for 30 min, then a solution of the above alcohol (0.377 g, 0.765 mmol) in CH_2Cl_2 (3 mL) was added dropwise. The mixture was stirred for 1 h at –78 ˚C, then Et_3N (0.553 mL, 3.97 mmol) was added. The solution was stirred for 20 min at –78 ˚C, then warmed to –30 ˚C and quenched by H_2O (3 mL). The phases were separated and the aqueous phase was further extracted with Et_2O. The combined organic extracts were washed with brine, dried over $MgSO_4$ and concentrated, producing crude aldehyde **16** (0.38 g). Due to the instability of the crude aldehyde **16**, it was immediately used without further purification.



17a : P = TMS
17b : P = H



18a : P = TMS
18b : P = H

(+)-Methyl (3*S*,4*R*,5*R*,6*S*)-5-Benzyloxy-7-*tert*-butyldiphenylsilyloxy-2,2-dimethyl-4,6-methylenedioxy-3-trimethylsilyloxyheptanoate (17a)

(–)-Methyl (3*S*,4*R*,5*R*,6*R*)-5-Benzyloxy-7-*tert*-butyldiphenylsilyloxy-2,2-dimethyl-3-hydroxy-4,6-methylenedioxy-heptanoate (17b)

(–)-Methyl (3*S*,4*R*,5*R*,6*R*)-5-Benzyloxy-7-*tert*-butyldiphenylsilyloxy-2,2-dimethyl-4,6-methylenedioxy-3-trimethylsilyloxyheptanoate (18a)

(–)-Methyl (3*S*,4*R*,5*R*,6*S*)-5-Benzyloxy-7-*tert*-butyldiphenylsilyloxy-2,2-dimethyl-3-hydroxy-4,6-methylenedioxyheptanoate (18b)

(entry 3)

To a water bath cooled suspention of $Yb(OTf)_3$ (47 mg, 0.076 mmol) in CH_2Cl_2 (30 mL) was added a mixture of the crude aldehyde **16** (0.38 g) and methyl trimethylsilyl dimethylketene acetal (0.39 mL, 1.92 mmol) in CH_2Cl_2 (10 mL) dropwise. The mixture was stirred for 48 h at rt and saturated $NaHCO_3$ (10 mL) was added. The phases were separated and the aqueous phase was further extracted with EtOAc. The combined organic extracts were washed with brine, dried over $MgSO_4$ and concentrated. The crude product was purified by flash chromatography. Elution with a 10:1 mixture of hexane-EtOAc afforded aldol **17a** and **18a** (**17a**: 0.261 g, 51% for 2 steps; **18a**: 0.125 g, 25% for 2 steps) as a colorless oil. Elution with a 6:1 mixture of hexane-EtOAc afforded aldol **17b** and **18b** (**17b**: 35.7 mg, 8% for 2 steps; **18b**: 24.0 mg, 5% for 2 steps) as a colorless oil.

Data for **17a** ; $[\alpha]^{27}_D$= +19.09˚ (c 0.54, $CHCl_3$) ; IR (neat) 1735 cm^{-1} ; ^1H NMR (500 MHz, $CDCl_3$) δ 0.06 (s, 9 H), 1.08 (s, 9 H), 1.13 (s, 3 H), 1.23 (s, 3 H), 3.60 (s, 3 H), 3.82 (dd, *J*= 4.4, 5.5 Hz, 1 H), 3.87 (dd, *J*= 4.8, 11.0 Hz, 1 H), 3.89 (t, *J*= 4.8 Hz, 1 H), 3.93 (dd, *J*= 5.1, 11.0 Hz, 1 H), 4.23 (q, *J*= 5.3 Hz, 1 H), 4.45 (d, *J*= 5.1 Hz, 1 H), 4.50 (d, *J*= 11.7 Hz, 1 H), 4.64 (d, *J*= 11.7 Hz, 1 H), 4.77 (d, *J*= 5.9 Hz, 1 H), 5.15 (d, *J*= 5.9 Hz, 1 H), 7.24-7.44 (m, 11 H), 7.67-7.71 (m, 4 H) ; ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.48, 138.18, 135.82, 135.70, 133.40, 133.21, 129.86, 128.42, 127.96, 127.85, 127.82, 127.75, 89.94, 75.89, 74.50, 74.27, 71.93, 71.88, 62.68, 51.86, 47.71, 26.96, 21.89, 21.87, 19.36, 0.87; LRMS *m/z* 649 (M^+–15); HRMS calcd for $C_{36}H_{49}O_7Si_2$ 649.3014, found : 649.3003 ; *Anal*. Calcd for $C_{37}H_{52}O_7Si_2$: C,66.82 ; H, 7.88. Found : C, 66.84 ; H, 7.98.

Data for **17b** ; $[\alpha]^{27}_D$= –6.03˚ (c1.03, $CHCl_3$); IR (neat) 3500, 1720 cm^{-1} ; ^1H NMR (300 MHz, $CDCl_3$) δ 1.08 (s, 9 H), 1.17 (s, 3 H), 1.19 (s, 3 H), 3.50 (d, *J*= 3.8 Hz, 1 H), 3.63 (s, 3 H), 3.74 (t, *J*= 3.3 Hz, 1 H), 3.84-3.91 (m, 4 H), 4.16-4.21 (m 1 H), 4.51 (d, *J*= 11.5 Hz, 1 H), 4.72 (d, *J*= 11.8 Hz, 1 H), 4.86 (d, *J*= 5.8 Hz, 1 H), 5.00 (d, *J*= 5.8 Hz, 1 H), 7.27-7.48 (m, 11 H), 7.64-7.67 (m, 4 H) ; ^{13}C NMR (75 MHz, $CDCl_3$) δ 177.71, 137.39, 135.70, 135.66, 133.02, 132.97, 130.04, 128.64, 128.29, 128.17, 127.95, 89.40, 76.19, 74.85, 74.47, 72.21, 71.65, 62.43, 51.84, 46.36, 26.79, 21.78, 21.59, 19.14; LRMS *m/z* 535 (M^+–57); HRMS calcd for $C_{30}H_{35}O_7Si$ 535.2150, found : 535.2147 ; *Anal*. Calcd for $C_{34}H_{44}O_7Si$: C,68.88 ; H, 7.48. Found : C, 68.79 ; H, 7.46.

Data for **18a** ; $[\alpha]^{27}_D$= –1.64˚ (c 1.68, $CHCl_3$) ; IR (neat) 2932, 1732, 1252, 1113, 1042, 843, 735, 702 cm^{-1} ; ^1H NMR (500 MHz, $CDCl_3$) δ 0.21 (s, 9 H), 1.07 (s, 9 H), 1.20 (s, 3 H), 1.28 (s, 3 H), 3.41 (td, *J*= 2.4, 7.2 Hz, 1 H), 3.45 (d, *J*= 7.6 Hz, 1 H), 3.62 (s, 3 H), 3.82 (t, *J*= 7.2 Hz, 1 H), 3.92-3.93 (m, 2 H), 4.42 (s, 1 H), 4.59 (d, *J*= 4.8 Hz, 1 H), 4.72 (d, *J*= 3.6 Hz, 1 H), 5.15 (d, *J*= 4.8

Hz, 1 H), 7.19-7.21 (m, 2 H), 7.27-7.41 (m, 9 H), 7.67-7.70 (m, 2 H), 7.72-7.74 (m, 2 H) ; ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.3, 137.9, 135.9, 135.7, 133.5, 132.9, 129.7, 129.6, 128.4, 127.7, 127.6, 127.3, 92.8, 81.8, 79.2, 74.0, 73.5, 69.8, 63.4, 51.8, 48.2, 26.9, 21.9,19.3, 1.23; LRMS *m/z* 607 (M^+–57); HRMS calcd for $C_{33}H_{43}O_7Si_2$ 607.2545, found : 607.2552.

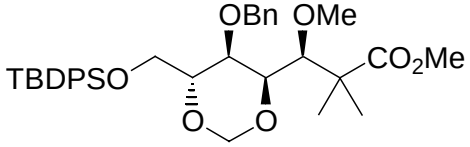
Data for **18b** ; $[\alpha]^{28}_D$= –3.09˚ (c 0.34, $CHCl_3$) ; IR (neat) 3452, 1732, 1084, 1040, 741, 702 cm^{-1} ; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.07 (s, 9 H), 1.20 (s, 3 H), 1.34 (s, 3 H), 3.42 (d, *J*= 10.9 Hz, 1 H), 3.74 (d, *J*= 10.9 Hz, 1 H), 3.48 (td, *J*= 2.4, 9.0 Hz, 1 H), 3.52 (d, *J*= 9.3 Hz, 1 H), 3.67 (s, 3 H), 3.89-3.97 (m, 3 H), 4.59 (d, *J*= 5.4 Hz, 1 H), 4.61 (d, *J*= 10.2 Hz, 1 H), 4.70 (d, *J*= 10.2 Hz, 1 H), 4.99 (d, *J*= 5.8 Hz, 1 H), 7.16-7.19 (m, 2 H), 7.27-7.45 (m, 9 H), 7.64-7.73 (m, 4 H) ; ^{13}C NMR (75 MHz, $CDCl_3$) δ 177.7, 138.0, 135.7, 133.3, 129.7, 129.7, 128.5, 127.9, 127.8, 127.6, 92.6, 81.5, 78.8, 74.9, 74.7, 69.4, 65.8, 63.2, 51.8, 44.5, 26.7, 24.3, 21.7, 19.2, 15.1; LRMS *m/z* 535 (M^+–57); HRMS calcd for $C_{30}H_{35}O_7Si$ 535.2150, found : 535.2186.

(entry 1)

To a –78 ˚C solution of crude aldehyde **16** (53.0 mg) in CH_2Cl_2 (1 mL) was added $TiCl_4$ (0.0180 mL, 0.162 mmol), followed by methyl trimethylsilyl dimethylketene acetal (0.0330 mL, 0.162 mmol) in CH_2Cl_2 (1 mL) dropwise. The mixture was stirred for 1 h at –78 ˚C and quenched by H_2O. The phases were separated and the aqueous phase was further extracted with Et_2O. The combined organic extracts were washed with brine, dried over $MgSO_4$ and concentrated. Purification of the crude product by flash chromatography (20% EtOAc/hexane) provided aldol **17b** (40.4 mg, 63% for 2 steps).

(entry 5)

To a water bath cooled suspension of $Yb(OTf)_3$ (15 mg, 0.025 mmol) and TMSCl (0.030mL, 0.25 mmol) in CH_2Cl_2 (20 mL) was added a mixture of the crude aldehyde **16** (0.122 g) and methyl trimethylsilyl dimethylketene acetal (0.125 mL, 0.618 mmol) in CH_2Cl_2 (5 mL) dropwise. The mixture was stirred for 24 h at rt and quenched by saturated $NaHCO_3$ (10 mL). The phases were separated and the aqueous phase was further extracted with EtOAc. The combined organic extracts were washed with brine, dried over $MgSO_4$ and concentrated. The crude product was purified by flash chromatography. Elution with a 10:1 mixture of hexane-EtOAc afforded aldol **17a** (0.130 g, 79% for 2 steps) as a colorless oil. Elution with a 4:1 mixture of hexane-EtOAc afforded aldol **17b** (15.2 mg, 10% for 2 steps) as a colorless oil.



19

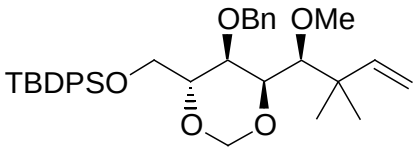
(+)-Methyl (3*S*,4*R*,5*R*,6*R*)-5-Benzyloxy-7-*tert*-butyldiphenylsilyloxy-2,2-dimethyl-3-methoxy-4,6-methylenedioxy-heptanoate (19)

To a solution of a crude mixture of **17a** and **17b** (16 mg) in MeOH (1 mL) was added CSA (1.0 mg, cat.). The mixture was stirred for 15 min at rt, then quenched by saturated $NaHCO_3$ (1 mL). The phases were separated and the aqueous phase was extracted with EtOAc. The combined organic extracts were washed with brine, dried over $MgSO_4$ and concentrated. Purification of the crude product by flash chromatography (14% EtOAc/hexane) provided alcohol **17b** (11.9 mg, 84% for 3 steps).

To a 0 ˚C suspension of NaH (53.7 mg, 1.34 mmol) in THF (13 mL) was added a solution of alcohol **17b** (0.531 g, 0.895 mmol) in THF (2 mL) dropwise. The mixture was stirred for 30 min at 0 ˚C, then warmed to rt and stirred for 1 h. After the solution was cooled to 0 ˚C, MeI (0.111 mL, 1.79 mmol) was added and the mixture was stirred for 30 min at 0 ˚C. The resulting mixture was allowed to warm to rt and stirred for an additional 4 h, then poured into saturated NH_4Cl at 0 ˚C. The phases were separated and the aqueous phase was extracted with Et_2O. The combined organic extracts were washed with brine, dried over $MgSO_4$ and concentrated. Purification of the crude product by flash chromatography (13% EtOAc/hexane) provided methyl ether **19** (0.519 mg, 95%).

Data for **19** ; $[\alpha]^{20}_D$= +28.18˚ (c 0.85, $CHCl_3$) ; IR (neat) 1720 cm^{-1} ; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.08 (s, 9 H), 1.17 (s, 3 H), 1.26 (s, 3 H), 3.38 (s, 3 H), 3.65 (s, 3 H), 3.83 (d, *J*= 2.7 Hz, 1 H), 3.86-3.93 (m, 3 H), 4.06-4.13(m, 2 H), 4.55 (d, *J*= 11.5 Hz, 1 H), 4.62 (d, *J*= 11.8 Hz, 1 H), 4.74 (d, *J*= 5.5 Hz, 1 H), 5.26 (d, *J*= 5.5 Hz, 1 H), 7.26-7.42 (m, 11 H), 7.67-7.73 (m, 4 H);

^{13}C NMR (75 MHz, $CDCl_3$) δ 177.62, 138.07, 135.92, 135.75, 133.65, 133.37, 129.83, 128.58, 128.08, 127.96, 127.84, 127.79, 90.01, 84.93, 75.40, 72.68, 72.58, 71.56, 63.30, 60.54, 51.81, 47.28, 26.83, 21.91, 21.76, 19.27 ; LRMS *m/z* 457 (M^+–149); HRMS calcd for $C_{24}H_{29}O_7Si$ 457.1681, found : 457.1666 ; *Anal*. Calcd for $C_{35}H_{46}O_7Si$: C,69.27 ; H, 7.64. Found : C, 69.27 ; H, 7.77.



20

(+)-(4*S*,5*R*,6*R*,7*R*)-6-Benzyloxy-8-*tert*-butyldiphenylsilyloxy-3,3-dimethyl-4-methoxy-5,7-methylenedioxyoct-1-ene (20)

To a 0 ˚C solution of ester **19** (0.0980 g, 0.162 mmol) in THF (5 mL) was added DIBAL-H (0.440 mL, 0.404 mmol) dropwise. The solution was stirred for 1 h at that temperature. H_2O (0.44 mL) was added to quench the reaction. After 20 min, Et_2O (5 mL) and hexane (5 mL) were added. The resulting mixture was allowed to warm to rt and stirred for 1 h, then dried ($MgSO_4$) and filterd

through Celite. The filtrate was concentrated to afford a crude solid. The crude product was recrystallized from Et_2O-hexane to provided an alcohol (0.0934 g, 100%) as colorless plates.

Data for the alcohol : mp 108-109 ˚C; $[\alpha]^{27}_D$= +30.36˚ (c 1.05, $CHCl_3$) ; IR (neat) 3450 cm^{-1} ; ^1H NMR (300 MHz, $CDCl_3$) δ 0.86 (s, 3 H), 0.94 (s, 3 H), 1.09 (s, 9 H), 2.99 (dd, *J*= 5.5, 6.9 Hz, 1 H), 3.37 (d, *J*= 2.5 Hz, 1 H), 3.43 (s, 3 H), 3.44-3.54 (m, 2 H), 3.92-3.96 (m, 3 H), 4.06-4.12(m, 1 H), 4.15 (dd, *J*= 2.2, 5.8 Hz, 1 H), 4.52 (d, *J*= 11.5 Hz, 1 H), 4.65 (d, *J*= 11.5 Hz, 1 H), 4.81 (d, *J*= 5.5 Hz, 1 H), 5.36 (d, *J*= 5.5 Hz,1 H), 7.25-7.45 (m, 11 H), 7.68-7.74 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.00, 135.96, 135.78, 133.67, 133.35, 129.86, 128.66, 128.14, 127.87, 127.82, 90.32, 86.98, 75.67, 72.88, 72.11, 71.63, 69.15, 63.39, 60.86, 40.51, 26.86, 23.95, 21.61, 19.30; LRMS *m/z* 521 (M^+–57); HRMS calcd for $C_{30}H_{37}O_6Si$ 521.2357, found : 521.2373 ; *Anal*. Calcd for $C_{34}H_{46}O_6Si$: C, 70.55 ; H, 8.00. Found : C, 70.61 ; H, 8.07.

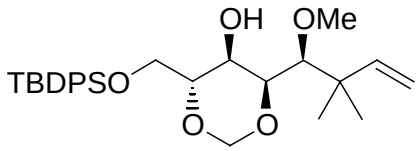
To a solution of the alcohol (0.613 g, 1.06 mmol) in DMSO (8 mL) were added Et_3N (1.03 mL, 7.41 mmol) and SO_3·Py (0.505 g, 3.18 mmol). The mixture was stirred for 2.5 h, and quenched by H_2O. The resulting mixture was extracted with Et_2O. The combined organic extracts were washed with brine, dried over $MgSO_4$ and concentrated. Purification of the crude product by flash chromatography (17% EtOAc/hexane) provided an aldehyde (0.593g, 97%) as a colorless oil.

Data for the aldehyde : $[\alpha]^{26}_D$= +25.40˚ (c 1.10, $CHCl_3$) ; IR (neat) 1722 cm^{-1} ; ^1H NMR (300 MHz, $CDCl_3$) δ 1.04 (s, 3 H), 1.08 (s, 3 H), 1.09 (s, 9 H), 3.46 (s, 3 H), 3.57 (d, *J*= 3.3 Hz, 1 H), 3.91-3.93 (m, 3 H), 4.00 (dd, *J*= 3.3, 5.8 Hz, 1 H), 4.06-4.11 (m, 1 H), 4.46 (d, *J*= 11.5 Hz, 1 H), 4.64 (d, *J*= 11.5 Hz, 1 H), 4.75 (d, *J*= 5.5 Hz, 1 H), 5.20 (d, *J*= 5.8 Hz,1 H), 7.26-7.43 (m, 11 H), 7.67-7.73 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.15, 138.04, 135.92, 135.73, 133.59, 133.24, 129.83, 128.64, 128.08, 128.02, 127.84, 127.79, 90.04, 86.98, 75.23, 72.76, 71.33, 63.12, 61.20, 50.38, 26.82, 19.68, 19.35, 19.24, 15.20; LRMS *m/z* 519 (M^+–57); HRMS calcd for $C_{30}H_{35}O_6Si$ 519.2200, found : 519.2189 ; *Anal*. Calcd for $C_{34}H_{44}O_6Si$: C, 70.79 ; H, 7.68. Found : C, 70.90 ; H, 7.67.

To a solution of $Ph_3P^+CH_3Br^-$(0.372 g, 1.04 mmol) in THF (8 mL) was added BuLi (0.680 mL, 1.53 M in hexane, 1.04 mmol) dropwise. The solution was warmed to 65 ˚C, and stirred for 15 min, then cooled to 0 ˚C. A solution of the aldehyde (0.200 g, 0.346 mmol) in THF (2 mL) was added at 0 ˚C and the mixture was stirred for 20 min. Saturated $NaHCO_3$ (5 mL) was added to quench the reaction and the resulting mixture was extracted with Et_2O. The combined organic extracts were washed with brine, dried over $MgSO_4$ and concentrated. Purification of the crude product by flash chromatography (9% EtOAc/hexane) provided olefin **20** (0.199 g, 100%) as a white solid.

Data for **20** : mp 86-87 ˚C; $[\alpha]^{22}_D$= +9.42˚ (c 0.85, $CHCl_3$); IR (neat) 1605 cm^{-1} ; ^1H NMR (300 MHz, $CDCl_3$) δ 1.00 (s, 3 H), 1.03 (s, 3 H), 1.08 (s, 9 H), 3.22 (d, *J*= 4.1 Hz, 1 H), 3.45 (s, 3 H), 3.77 (dd, *J*= 4.4, 6.0 Hz, 1 H), 3.85-3.93 (m, 2 H), 3.97 (t, *J*= 4.4 Hz, 1 H), 4.15 (q, *J*= 5.8 Hz, 1 H), 4.47 (d, *J*= 11.8 Hz, 1 H), 4.66 (d, *J*= 11.8 Hz, 1 H), 4.75 (d, *J*= 5.8 Hz, 1 H), 4.92 (dd, *J*= 1.6, 10.7 Hz, 1 H), 4.95 (dd, *J*= 1.6, 17.6 Hz, 1 H), 5.18 (d, *J*= 5.8 Hz,1 H), 5.88 (dd, *J*= 10.7, 17.6 Hz, 1 H), 7.31-7.43 (m, 11 H), 7.66-7.71 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 146.1, 138.2, 135.8, 135.7, 133.5, 133.3, 129.9, 128.6, 128.1, 127.9, 127.9, 127.8, 111.7, 90.0, 86.6, 74.7, 73.6, 72.0, 71.9,

62.8, 61.2, 42.1, 26.8, 25.3, 21.8, 1.92; LRMS *m/z* 517 (M^+–57); HRMS calcd for $C_{31}H_{37}O_5Si$ 517.2408, found : 517.2410.



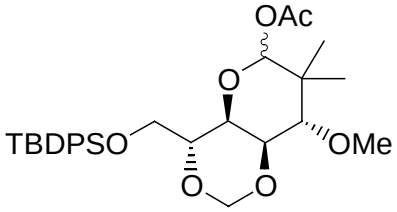
21

(+)-(2*R*,3*R*,4*R*,5*S*)-1-*tert*-Butyldiphenylsilyloxy-6,6-dimethyl-3-hydroxy-5-methoxy-2,4-methylenedioxyoct-7-en-3-ol (21)

Liquid NH_3 (30 mL) was distilled from Na (solid) via cannula to a –78 ˚C flask, and Li (solid) (0.130 g, 6.92 mmol) was added, immediately producing a blue solution. A solution of benzyl ether **20** (0.199 g, 0.346 mmol) in THF (9 mL) was added dropwise over 2 min. The mixture was stirred for 20 min, then NH_4Cl (solid) was added until the blue color disappeared. The solution was allowed to warm to rt and stand for at least 6 h, then quenched by H_2O. The resulting solution was extracted with EtOAc. The combined organic extracts were washed with brine, dried over $MgSO_4$ and concentrated to give a crude oil (0.176 g).

To a solution of crude product described above (0.176 g) in benzene (10 mL) was added DDQ (0.243 g, 1.04 mmol). The mixture was stirred for 3.5 h, then saturated NH_4Cl was added. The resulting solution was filterd through Celite and the filtrate was extracted with Et_2O. The combined organic extracts were washed with brine, dried over $MgSO_4$ and concentrated to give a crude oil. Purification of the crude product by flash chromatography (13% EtOAc/hexane) provided alcohol **21** (0.124 g, 74% for 2 steps) as a colorless oil.

Data for **21** : $[\alpha]^{22}_D$= +10.28˚ (c 0.50, $CHCl_3$); IR (neat) 3400, 1605 cm^{-1} ; ^1H NMR (300 MHz, $CDCl_3$) δ 1.05 (s, 9 H), 1.06 (s, 3 H), 1.09 (s, 3 H), 3.20 (d, *J*= 4.9 Hz, 1 H), 3.25 (d, *J*= 8.2 Hz, 1 H), 3.53 (s, 3 H), 3.82-3.94 (m, 4 H), 4.00-4.05 (m, 1 H), 4.79 (d, *J*= 6.0 Hz, 1 H), 4.94 (d, *J*= 6.0 Hz, 1 H), 4.98 (d, *J*= 11.3 Hz, 1 H), 4.99 (d, *J*= 17.0 Hz, 1 H), 5.97 (dd, *J*= 11.3, 17.0 Hz, 1 H), 7.37-7.46 (m, 6 H), 7.63-7.67 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 146.0, 135.7, 133.0, 132.8, 130.2, 128.0, 112.0, 89.8, 87.1, 77.7, 67.1, 62.2, 61.9, 42.1, 26.8, 25.7, 21.4, 19.1; LRMS *m/z* 427 (M^+–57); HRMS calcd for $C_{24}H_{31}O_5Si$ 427.1939, found : 427.1947.



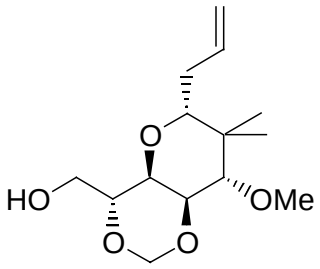
22

(1*R*,5*R*,6*R*,8*RS*,10*S*)-8-Acetoxy-5-(*tert*-butyldiphenylsilyloxy)methyl-9,9-dimethyl-10-methoxy-2,4,7-trioxabicyclo[4.4.0]decane (22)

Ozone was bubbled through a –78 ˚C solution of olefin **21** (54.0 mg, 0.111 mmol) in MeOH (10 mL) for 15 min. After removal of excess ozone, Me_2S (0.041 mL, 0.558 mmol) was added and the solution was stirred for 5 h. The solution was concentrated to afford a clear oil (33.5 mg). Due to the instability of the crude lactol , it was immediately used without further purification.

A mixture of crude lactol (33.5 mg) and Ac_2O (0.5 mL) in pyridine (1 mL) was stirred for 16 h. The solvent was removed to leave a crude oil. Purification of the crude product by flash chromatography (14% EtOAc/hexane) provided acetate diastereomers **22** (58.0 mg, 99% for 2 steps) in a 1.4:1 ratio, as a colorless oil.

Partial data for **22** : IR (neat) 1745 cm^{-1} ; ^1H NMR (300 MHz, $CDCl_3$) δ 0.97 (s, 1.3 H), 0.98 (s, 1.7 H), 1.07 (s, 9 H),1.17 (s, 1.7 H), 1.21 (s, 1.3 H), 2.07 (s, 1.3 H), 2.10 (s, 1.7 H), 3.04 (d, *J*= 4.4 Hz, 0.4 H), 3.23 (d, *J*= 3.6 Hz, 0.6 H), 3.42 (s, 1.3 H), 3.43 (s, 1.7 H), 3.81-4.21 (m, 5 H), 4.92 (d, *J*= 6.0 Hz, 0.4 H), 4.96 (d, *J*= 6.0 Hz, 0.6 H), 4.97 (d, *J*= 5.8 Hz, 0.4 H), 5.08 (d, *J*= 5.8 Hz, 0.6 H), 5.71 (s, 0.6 H), 5.78 (s, 0.4 H), 7.26-7.47 (m, 6 H), 7.65-7.70 (m, 4 H); LRMS *m/z* 471 (M^+–57); HRMS calcd for $C_{25}H_{31}O_7Si$ 471.1837, found : 471.1835 ; *Anal*. Calcd for $C_{29}H_{40}O_7Si$: C, 65.88 ; H, 7.62. Found : C, 66.03 ; H, 7.62.



23

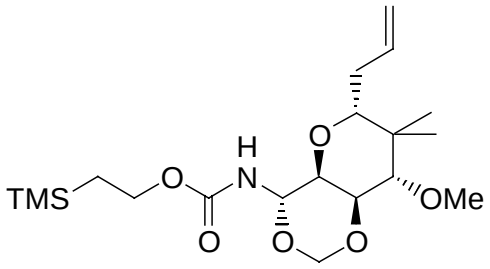
(+)-(1*R*,5*R*,6*R*,8*R*,10*S*)-5-(Hydroxy)methyl-10-methoxy-9,9-dimethyl -8-(prop-2-enyl)-2,4,7-trioxabicyclo[4.4.0]decane (23)

A suspension of acetate **22** (10.4 mg, 0.0197 mmol) and activated 4 Å mol. sieves (0.1 g) in CH_3CN (5 mL) was stirred for 30 min at 0 ˚C, and allyltrimethylsilane (0.019 mL, 0 118 mmol) was added. The solution was stirred for 20 min at 0 ˚C, and $BF_3{\cdot}Et_2O$ (7.0μL, 0.059 mmol) was added dropwise. The mixture was stirred for an additional 10 min, and quenched by saturated $NaHCO_3$ (5 mL). After the removal of 4 Å mol. sieves by Celite, the filtrate was extracted with EtOAc (3 x 10 mL). The combined organic extracts were washed with brine, dried over $MgSO_4$ and concentrated to give a crude oil. The crude product was purified by flash chromatography. Elution with a 7:1 mixture of hexane-EtOAc afforded a silyl ether (7.7 mg, 77%) as a colorless oil. Elution with a 2:1 mixture of hexane-EtOAc afforded alcohol **23** (0.9 mg, 17%) as a colorless oil. Data for the silyl ether : $[\alpha]^{26}_D$= +75.70˚ (c 1.02, $CHCl_3$); IR (neat) 1635 cm^{-1} ; ^1H NMR (300 MHz, $CDCl_3$) δ 0.87 (s, 3 H), 0.94 (s, 3 H), 1.30 (s, 9 H), 1.95-2.13 (m, 2 H), 2.98 (dd, *J*= 2.6, 9.5

Hz, 1 H), 3.14 (d, *J*= 10.2 Hz, 1 H), 3.44 (s, 3 H), 3.90 (ddd, *J*= 1.6, 5.3, 10.3 Hz, 1 H), 3.99 (dd, *J*= 5.5, 11.3 Hz, 1 H), 4.16 (dd, *J*= 1.6, 11.3 Hz, 1 H), 4.23 (dd, *J*= 6.9, 10.4 Hz, 1 H), 4.35 (dd, *J*= 6.9, 10.2 Hz, 1 H), 4.77 (d, *J*= 6.6 Hz, 1 H), 4.88 (d, *J*= 6.6 Hz,1 H), 5.07 (dt, *J*= 9.3, 0.9 Hz, 1 H), 5.09 (dt, *J*= 17.9, 0.9 Hz, 1 H), 5.87 (ddt, *J*= 6.6, 10.7, 17.9 Hz, 1 H), 7.28-7.79 (m, 6 H), 7.80-8.03 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 136.17, 135.89, 135.86, 129.83, 129.80, 127.82, 116.51, 87.24, 79.67, 78.44, 74.05, 73.52, 67.05, 63.80, 61.77, 41.45, 33.39, 26.80, 23.26, 19.30, 13.55; LRMS *m/z* 469 (M^+–41); HRMS calcd for $C_{27}H_{37}O_5Si$ 469.2408, found : 469.2427 ; *Anal*. Calcd for $C_{30}H_{42}O_5Si$: C, 70.54 ; H, 8.28. Found : C, 70.40 ; H, 8.05.

Data for **23**; $[\alpha]^{27}_D$= +79.83˚ (c 1.77, $CHCl_3$) ; IR (neat) 3458, 1641, 1178, 912, 841, 613 cm^{-1} ; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.89 (s, 3 H), 1.01 (s, 3 H), 2.00-2.08 (m, 2 H), 2.18 (ddd, *J*=2.0, 6.9, 13.8 Hz, 1 H), 3.28 (dd, *J*=2.2, 10.4 Hz, 1 H), 3.44 (d, *J*=10.2 Hz, 1 H), 3.58 (s, 3 H), 3.65-3.71(m, 1 H), 3.82-3.88 (m, 1 H), 4.01-4.03 (m, 2 H), 4.16 (dd, *J*=6.4, 10.2 Hz, 1 H), 4.86 (A of AB, *J*=6.8 Hz, 1 H), 5.02 (B of AB, *J*=6.8 Hz, 1 H), 5.04-5.09 (m, 2 H), 5.73-5.83 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 135.9, 117.1, 86.9, 78.5, 73.5, 72.9, 68.4, 63.4, 61.7, 41.6, 33.4, 23.1, 13.1; LRMS *m/z* 272 (M^+); *Anal*. Calcd for $C_{14}H_{24}O_5$: C, 61.74; H, 8.88. Found: C, 61.37 ; H, 8.63.

To a solution of crude products (64 mg, a mixture of the silyl ether and **23**) in THF (5 mL) was added TBAF (0.10 mL, 1 M in THF, 0.10 mmol). The solution was stirred for 6 h and saturated $NaHCO_3$ (1 mL) was added. The resulting mixture was extracted with EtOAc (3 x 7 mL). The combined organic extracts were washed with brine, dried over $MgSO_4$ and concentrated to give a crude oil. Purification of the crude product by flash chromatography (33% EtOAc/hexane) provided alcohol **23** (25.8 mg, 86% for 2 steps) as a colorless oil.



24

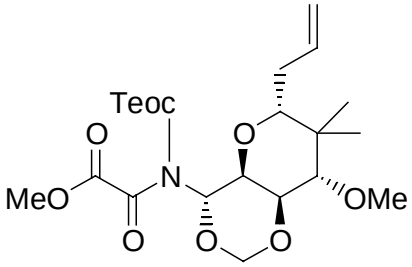
(+)-(1*R*,5*S*,6*S*,8*R*,10*S*)-9,9-Dimethyl-10-methoxy-8-(prop-2-enyl)-5-{*N*-[(2-trimethylsilyl)ethoxycarbonyl]amino}-2,4,7-trioxabicyclo[4.4.0]decane (24)

To a solution of alcohol **23** (5.5 mg, 0.0202 mmol) in acetone (0.5 mL) was added Jones reagent (approximately 0.06 mL, prepared in according to literature[37]). The mixture was stirred for 0.5 h, and *i*-PrOH (0.2 mL) was added. The solution was concentrated and diluted with Et_2O (3 mL). The resulting solution was washed with brine, dried ($MgSO_4$) and concentrated to afford a crude carboxylic acid (7.7 mg).

To a suspension of the carboxylic acid (7.7 mg) and activated 4 Å mol. sieves in THF (1.0 mL) were added Et_3N (8.5 μL, 0.0607 mmol), DPPA (4.5 μL, 0.0212 mmol) and freshly distilled

trimethylsilylethanol (14 μL, 0.101 mmol). The mixture was warmed to 65 ˚C, and stirred for 5.5 h. After filtration, the filtrate was washed with 5% citric acid aqueous solution, saturated $NaHCO_3$, and brine. The resulting solution was dried ($MgSO_4$) and concentrated. Purification of the crude product by flash chromatography (20% EtOAc/hexanes) provided carbamate **24** (6.3 mg, 78% for 2 steps) as a colorless oil.

Data for **24**; $[\alpha]^{27}_D$= +79.83˚ (c 1.77, $CHCl_3$); IR (neat) 3323, 1732, 1714, 1531, 1250, 1032, 860 cm^{-1} ; ^1H NMR (300 MHz, $CDCl_3$) δ 0.03 (s, 9 H), 086 (s, 3 H), 0.98 (s, 3 H), 0.96-1.01 (m, 2 H), 1.98-2.06 (m, 1 H), 2.15 (ddd, *J*=1.0, 6.0, 14.8 Hz, 1 H), 3.28 (d, *J*=9.6 Hz, 1 H), 3.42 (d, *J*=10.4 Hz, 1 H), 3.54 (s, 3 H), 3.76 (dd, *J*=7.2, 10.0 Hz, 1 H), 4.16-4.21 (m, 3 H), 4.83 (d, *J*=7.2 Hz, 1 H), 4.93 (d, *J*=10.0 Hz, 1 H), 5.00 (dd, *J*=0.8, 17.2 Hz, 1 H), 5.11 (d, *J*=6.8 Hz, 1 H), 5.24 (br d, *J*=8.0 Hz, 1 H), 5.50 (br t, *J*=9.0 Hz, 1 H), 5.64-5.74 (m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 135.8, 116.2, 86.6, 79.5, 78.5, 76.4, 74.7, 70.7, 63.9, 61.8, 41.6, 33.1, 23.0, 17.6, 13.3, –1.66; LRMS *m/z* 401 (M^+); HRMS calcd for $C_{19}H_{35}NO_6Si$ 401.2234, found : 401.2245.



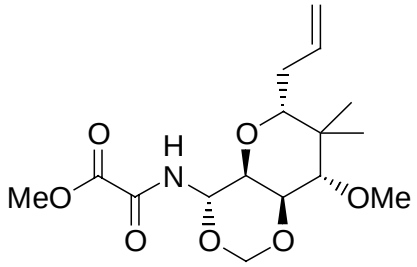
25

(+)-(1*S*,5*R*,6*S*,8*R*,10*S*)-10-Methoxy-5-{*N*-(methoxalyl)-*N*-[(2-trimethylsilyl)ethoxy-carbonyl]amino}-9,9-dimethyl -8-(prop-2-enyl)-2,4,7-trioxabicyclo[4.4.0]decane (25)

To a –78 ˚C mixture of carbamate **24** (111.6 mg, 278 μmol) and DMAP (44.2 mg, 362 μmol) in THF (2.0 mL) was added a solution of LHMDS in THF (0.56 mL, 1.0 M, 0.56 mmol) dropwise over 10 min. The resulting yellow solution was stirred for 0.5 h, at which time a solution of methyl chlorooxoacetate in CH_2Cl_2 (0.14 mL, 3.0 M, 0.42 mmol) was added dropwise. The mixture was stirred for 0.5 h at –78 ˚C, and warmed to 0 ˚C, and stirred for 1 h at 0 ˚C, The mixture was allowed to warm to rt, and poured into a slurry of SiO_2 in hexane-EtOAc (2:1, 10mL). The resulting suspension was vigorously stirred for 15 min, and filtered through Celite. The filtrate was concentrated to give a crude oil. Purification of the crude product by chromatography (25% EtOAc/hexane) provided imide **25** (105.8 mg, 78%; 90% yield based on the recoverd **24**) as a colorless oil, in addition to recovered carbamate **24** (14.5 mg, 13%).

Data for **25** : $[\alpha]^{29}_D$= +63.74˚ (c 1.80, $CHCl_3$); IR (neat) 2955, 1714, 1715, 1541, 1252, 1177, 1128, 1109, 1084, 1030, 860, 839 cm^{-1} ; ^1H NMR (300 MHz, $CDCl_3$ referenced to 7.24 ppm) δ 0.032 (s, 3 H), 0.043 (s, 6 H), 0.86 (s, 3 H), 0.99 (s, 3 H), 1.08 (dd,*J*=3.6, 6.0 Hz, 1 H), 1.10 (dd, *J*= 3.6, 6.0 Hz, 1 H), 1.96-2.07 (m, 1 H), 2.10-2.18 (m, 1 H), 3.26 (dd, *J*=2.0, 10.0 Hz, 1 H), 3.44 (d, *J*=10.4 Hz, 1 H), 3.56 (s, 3 H), 3.87 (s, 3 H), 4.30 (dd, *J*= 7.2, 10.8 Hz, 1 H), 4.32 (dd, *J*= 3.6, 6.0

Hz, 1 H), 4.34 (dd, *J*= 3.2, 6.0 Hz, 1 H), 4.84 (dd, *J*= 7.2, 10.2 Hz, 1 H), 4.90-5.03 (m, 2 H), 4.95 (d, *J*= 6.8 Hz, 1 H), 5.09 (d, *J*= 6.8 Hz, 1 H), 5.66 (tdd, *J*=6.8, 10.0, 16.8 Hz, 1 H), 6.10 (d, *J*= 10.4 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.62, 160.96, 152.22, 135.59, 116.33, 87.60, 79.43, 78.77, 77.32, 75.05, 67.51, 61.84, 52.91, 41.66, 33.58, 23.06, 17.42, 13.27, –1.41, –1.54, –1.54; LRMS *m/z* 446 (M^+–41, $CH_2CH=CH_2$); HRMS calcd for $C_{19}H_{32}O_9NSi$ 446.1847, found : 446.1835.

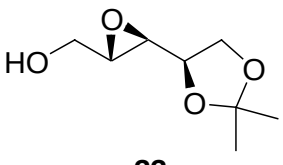


2

(+)-(1*S*,5*R*,6*S*,8*R*,10*S*)-10-Methoxy-5-{*N*-(methoxalyl)amino}-9,9-dimethyl-8-(prop-2-enyl)-2,4,7-trioxabicyclo[4.4.0]decane (2)

To a 0 ˚C solution of imide **25**(98.3 mg, 0.202 mmol) in THF (3.0 mL) was added TBAF (0.30 mL, 1.0 M, 0.30 mmol). After 5 min, a mixture of CH_2Cl_2 (10 mL) and H_2O (10 mL) was added. The aqueous phase was separated and further extracted with CH_2Cl_2 (2 x 10 mL). The combined organic extracts were dried (Na_2SO_4) and concentrated to afford a crude yellow solid. Purification of the crude product by flash chromatography (50% EtOAc/hexane) provided methyl oxalate **2** (64.5 mg, 93%) as a white solid, in addition to carbamate **24** (3.3 mg, 4.1%). The methyl oxalate **2** was used immediately in the next step.

Data for **2** : mp 168-170 ˚C; IR (KBr) 3315, 1738, 1701, 1541, 1263, 1182, 1123, 1103, 1076, 1036, 978, 907 cm^{-1} ; ^{1}H NMR (400 MHz, $CDCl_3$ referenced to 7.24 ppm) δ 0.88 (s, 3 H), 1.02 (s, 3 H), 1.97-2.05 (m, 1 H), 2.16 (dddd, *J*=1.6, 2.0, 6.0, 14.4 Hz, 1 H), 3.29 (dd, *J*=2.0, 10.0 Hz, 1 H), 3.46 (d, *J*=10.8 Hz, 1 H), 3.57 (s, 3 H), 3.91 (dd, *J*=6.8, 10.0 Hz, 1 H), 3.93 (s, 3 H), 4.25 (dd, *J*=6.4, 10.4 Hz, 1 H), 4.88 (d, *J*=6.8 Hz, 1 H), 4.88 (br d, *J*= 6.8 Hz, 1 H), 4.97 (dddd, *J*= 1.4, 1.4, 3.2, 17.2 Hz, 1 H), 5.15 (d, *J*= 7.2 Hz, 1 H), 5.63 (tdd, *J*=6.8, 10.4, 17.2 Hz, 1 H), 5.74 (dd, *J*= 10.0, 10.0 Hz, 1 H), 7.55 (d, *J*=9.2 Hz, 1 H) ; ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.98, 156.23, 135.45, 116.22, 86.69, 79.34, 78.67, 74.63, 74.11, 70.37, 61.78, 53.85, 41.71, 33.25, 23.11, 13.43; LRMS *m/z* 344 (M^++H); HRMS calcd for $C_{16}H_{26}O_7N$ 344.1709, found : 344.1711.

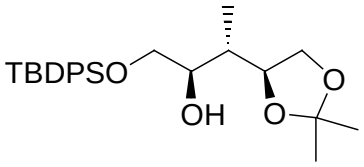


33

(2*R*,3*R*,4*R*)-2,3-epoxy-4,5-isopropylidenedioxypentanol (33)

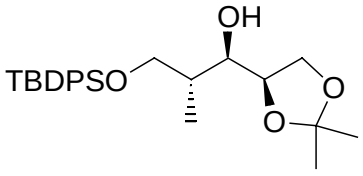
To a –78 ˚C solution of ethyl (S)-4,5-isoprorylidenedioxy-2-pentenoate (**32**)[2] (0.980 g, 4.91mmol)

in THF (20 mL) was added DIBAL-H in hexanes (10.3 mL, 1.0 M, 10.3 mmol). The mixture was stirred for 3.5 h at –78 ˚C, then H_2O (10 mL) was added. The solution was stirred for 30 min at –78 ˚C, at which time Et_2O (10 mL) and hexane (10 mL) were added. The solution was allowed to warm to rt, then filtered through Celite. The resulting clear solution was concentrated to afford a crude oil. Purification of the crude product by flash chromatography (50% EtOAc/hexane) provided (*S*)-4,5-isopropylidenedioxy-2-pentenol (0.682 g, 88%), in addition to recovered ester **32** (0.110 g, 11%). To a –40 ˚C suspension of $Ti(O^iPr)_4$ (0.110 mL, 0.374 mmol) and powdered activated 3 Å mol. sieves (0.2 g) in CH_2Cl_2 (5 mL) was added a solution of (+)-DIPT (0.087 mL, o.416 mmol) in CH_2Cl_2 (2 mL). The mixture was stirred for 40 min at –40 ˚C, then the solution of (*S*)-4,5-isopropylidenedioxy- 2-pentenol (0.658 g, 4.16 mmol) in CH_2Cl_2 (2 mL) was added. After 1.5 h, cumene hydroperoxide (1.84 mL, 12.5 mmol) was added dropwise over 3 min. The resulting solution was stirred for 89 h at –40 ˚C, then cooled to –78 ˚C and stirred for 10 min. Bu_3P (2.09 mL, 8.05 mmol) was added dropwise over 10 min to quench the reaction. The mixture was stirred for 30 min, then treated with citric acid monohydrate (ca. 87 mg, 0.42 mmol) dissolved in acetone-ether(1:9, 6 mL). The cooling bath was removed, and the resulting mixture was stirred for an additional 40 min. After filtration through a pad of Celite, the filtrate was dried over $MgSO_4$ and concentrated to give an oil. Purification of the oil by flash chromatography (33% EtOAc/hexanes) provided epoxide **33** (0.644 g, 89%). The identity of epoxide **33** was confirmed by comparison with reported spectral data [3) 4)]; $[\alpha]^{23}_D$= –21.36˚ (c 1.80, $CHCl_3$), literature[5)] $[\alpha]_D$= –21.5˚ (c 0.77, $CHCl_3$); IR (neat) 3435, 1637, 1376, 1217, 1058 cm^{-1} ; ^1H NMR (500 MHz, $CDCl_3$ referenced to 7.26 ppm) δ 1.37 (s, 3 H), 1.43 (s, 3 H), 1.89 (dd, *J*=5.5, 7.3 Hz, 1 H), 3.11 (dd, *J*=2.3, 4.6 Hz, 1 H), 3.15 (td, *J*=2.3, 3.7 Hz, 1 H), 3.68 (ddd, *J*=3.7, 7.4, 12.4 Hz, 1 H), 3.83-3.88 (m, 1 H), 3.95 (ddd, *J*=2.3, 5.0, 12.8 Hz, 1 H), 4.09 (dt, *J*=5.1, 6.9 Hz, 1 H), 4.11 (dd, *J*=6.4, 13.8 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 110.01, 75.13, 65.95, 60.79, 55.37, 54.99, 26.28, 25.47.



34

(1,2-diol)



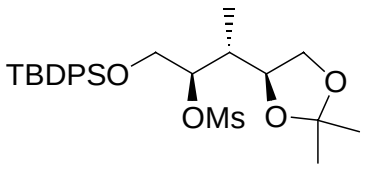
(1,3-diol)

(2*S*,3*S*,4*R*)-1-*tert*-Butyldiphenylsilyloxy-4,5-isopropylidenedioxy-3-methylpentan-2-ol (34, 1,2-diol)

(2*R*,3*R*,4*R*)-1-*tert*-Butyldiphenylsilyloxy-4,5-isopropylidenedioxy-2-methylpentan-3-ol (1,3-diol)

To a 0 ˚C solution of epoxide **33** (29.8 mg, 0.171 mmol) and Et_3N (0.119 mL, 0.856 mmol) in CH_2Cl_2 (5 mL) were added TBDPSCl (89.0 μL, 0.342 mmol) and DMAP (5.0 mg, 0.0409mmol). The mixture was stirred for 10 h at rt, then cooled to 0 ˚C, and quenched by H_2O (10 mL). The phases were separated and the aqueous phase was further extracted with Et_2O (3 x 30 mL). The combined organic extracts were washed with brine (30 mL), dried ($MgSO_4$), and concentrated. Purification of the crude product by flash chromatography (9% EtOAc/hexane) provided a silyl ether (173 mg, including any remaining silanol). To a –20 ˚C suspension of CuI (0.456 g, 2.40 mmol) in Et_2O (5 mL) was added MeLi (5.26 mL, 1.14 M in Et_2O, 5.99 mmol) dropwise over 5 min. When the yellow color had disappeared, the solution was cooled to –40 ˚C, then the silyl ether described above in Et_2O (2 mL) was added. The mixture was stirred for 1 h between –40 ˚C and –30 ˚C, quenching with a mixture of concd.NH_4OH and saturated NH_4Cl (1:9, 10 mL). The resulting mixture was allowed to warm to rt, and stirred for 20 min, then filtered through Celite. The phases were separated and the aqueous phase was further extracted with Et_2O (3 x 15 mL). The combined organic extracts were washed with brine (10 mL), dried ($MgSO_4$), and concentrated. Purification of the crude product by flash chromatography (9% EtOAc/hexane) provided a mixture of **34** and **1,3-diol** (64.6 mg, 0.151 mmol, 88% from **33**) in a 7:1 ratio.

Partial data for **34** and **1,3-diol**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.81 (d, *J*= 6.8 Hz, 2.6 H),1.00 (d, *J*= 6.8 Hz, 0.4 H), 1.06 (s, 1.1 H), 1.07 (s, 7.9 H), 1.33 (s, 2.6 H), 1.36 (s, 0.4 H), 1.38 (s, 2.6 H), 1.44 (s, 0.4 H), 1.78-1.88 (m, 0.1 H), 1.96 (dq, *J*= 13.6, 6.8 Hz, 0.9 H), 2.83 (d, *J*= 6.4 Hz, 0.1 H), 3.12 (d, *J*= 2.8 Hz, 0.9 H), 3.45-3.50 (m, 0.3 H), 3.56-3.59 (m, 0.3 H), 3.56-3.59 (m, 0.1 H), 3.61-3.67 (m, 1.8 H), 3.70 (dd, *J*= 10.4, 4.0 Hz, 0.9 H), 3.75 (dd, *J*= 10.0, 3.2 Hz, 0.9 H), 3.78 (dd, *J*= 10.4, 4.4 Hz, 0.1 H), 3.85 (t, *J*= 7.6 Hz, 0.1 H), 3.99 (dd, *J*= 10.0, 6.4 Hz, 0.1H), 4.02 (dd, *J*= 8.0, 6.0 Hz, 0.9 H), 4.12 (dt, *J*= 6.4, 7.6 Hz, 0.9 H), 4.22-4.27 (m, 0.1 H), 7.36-7.44 (m, 6 H), 7.67 (dd, *J*= 3.2, 1.6 Hz, 2 H), 7.69 (dd, *J*= 2.8, 1.2 Hz, 2 H).



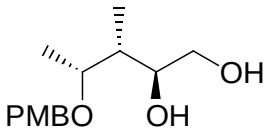
35

(–)-(2*S*,3*R*,4*R*)-1-*tert*-Butyldiphenylsilyloxy-4,5-isopropylidenedioxy-2-mesyloxy-3-methylpentane (35)

To a 0 ˚C solution of alcohols (0.205 g, 0.479 mmol; a 7:1 mixture of **34** and **1,3-diol**) in CH_2Cl_2 (5 mL) were added Et_3N (0.33 mL, 2.40 mmol) and MsCl (0.048 mL, 0.623 mmol). The mixture was stirred for 30 min, then poured into saturated $NaHCO_3$ (10 mL). The phases were separated

and the aqueous phase was further extracted with Et_2O (3 x 15 mL). The combined organic extracts were washed with brine (10 mL), dried ($MgSO_4$), and concentrated to give a yellow oil. The crude oil was chromatographed (11% EtOAc/hexane) to remove any remaining Et_3N, then recrystallized twice from Et_2O to yield methanesulfonate **35** (0.168 g, 69%) as colorless prisms.

Data for **35**: mp 113 ˚C; $[\alpha]^{23}_D$= –10.45˚ (c 0.60, $CHCl_3$) ; IR (KBr) 1360, 1176, 1113, 915, 703 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.90 (d, *J*= 7.2 Hz, 3 H), 1.06 (s, 9 H), 1.30 (s, 3 H), 1.36 (s, 3 H), 2.18 (ddq, *J*= 10.9, 6.8, 3.8 Hz, 1 H), 3.04 (s, 3 H), 3.59 (dd, *J*= 6.3, 7.4 Hz, 1 H), 3.85 (dd, *J*= 3.2, 11.7 Hz, 1 H), 3.89-4.02 (m, 3 H), 4.93 (m, 1 H), 7.40-7.48 (m, 6 H), 7.66-7.70 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 135.6, 135.5, 132.9, 132.7, 130.0, 127.9, 109.1, 85.7, 76.2, 67.8, 63.7, 39.5, 38.4, 26.7, 26.4, 19.0, 11.1 ; LRMS *m/z* 491 (M^+–15) ; *Anal*. Calcd for $C_{26}H_{38}O_6SSi$: C, 61.63 ; H, 7.56 ; S, 6.33. Found : C, 61.53 ; H, 7.67 ; S, 6.41.



36

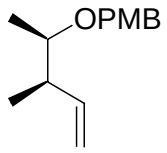
(–)-(2*R*,3*R*,4*R*)-4-(4-Methoxybenzyl)oxy-3-methylpentan-1,2-diol (36)

To a solution of methanesulfonate **35** (1.23 g, 2.42 mmol) in THF (10 mL) was added TBAF (3.6 mL, 1.0 M in THF, 3.6 mmol). The mixture was stirred for 50 min, then saturated K_2CO_3 (10 mL) was added. The mixture was stirred for an additional 10 min. The phases were separated and the aqueous phase was further extracted with Et_2O (3 x 20 mL). The combined organic extracts were washed with brine, dried ($MgSO_4$), and concentrated, providing the intermediate (crude) epoxide (0.46 g) which was used immediately in the next step.

To a 23 ˚C bath cooled suspension of $LiAlH_4$ (0.184 g, 4.85 mmol) in Et_2O (10 mL) was added a solution of the crude epoxide in Et_2O (2 mL) dropwise. The mixture was stirred for 12 h at rt, then cooled to 0 ˚C, and H_2O (0.18 mL) was added. After 15 min, 15% NaOH (0.18 mL) and H_2O (0.55 mL) were added and the resulting solution was stirred for an additional 2 h at rt. $MgSO_4$ (0.5 g) was added, and the solution was filterd through Celite and concentrated to afford a crude alcohol (0.42 g). This crude alcohol was immediately used without further purification.

To a 0 ˚C suspension of NaH (0.485 g, 12.1 mmol) in DMF (5 mL) was added the solution of the crude alcohol (0.42 g) in DMF (2 mL). The mixture was stirred for 1 h at 0 ˚C, and warmed to rt, then MPMCl (0.43 mL, 3.15 mmol) was added. The solution was stirred for 7 h at rt, then cooled to 0 ˚C. H_2O (5 mL) was added slowly to quench the reaction. The resulting solution was extracted with Et_2O (3 x 15 mL). The combined organic extracts were washed with brine (15 mL), dried ($MgSO_4$) and concentrated to afford a crude *p*-methoxybenzyl ether (1.0 g) which was dissolved in AcOH-THF-H_2O (3:1:1, 5 mL). The mixture was warmed to 55 ˚C, and stirred for 9 h. After the removal of the solvents by azeotropic distillation , the residue was purified by flash chromatography (50% EtOAc/hexane) to provide diol **36** (0.482 g, 78% from **35**) as a colorless oil.

Data for **36**: $[\alpha]^{24}_D$= –10.00˚ (c 1.09, $CHCl_3$); IR (neat) 3414, 1613, 1512, 1246, 1038, 822, 421 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.85 (d, *J*= 7.2 Hz, 3 H), 1.23 (d, *J*= 6.3 Hz, 3 H), 1.98-2.10 (m, 1 H), 2.25 (br s, 1 H), 3.51 (dd, *J*= 5.7, 11.4 Hz, 1 H), 3.66-3.79 (m, 3 H), 3.81 (s, 3 H), 4.16 (br s, 1 H), 4.44 (d, *J*= 10.8 Hz, 1 H), 4.55 (d, *J*= 10.8 Hz, 1 H), 6.88 (d, *J*= 8.7 Hz, 2 H), 7.25 (d, *J*= 8.7 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.4, 130.1, 129.3, 113.9, 77.6, 70.2, 64.8, 55.1, 37.8, 14.4, 12.2; LRMS *m/z* 254 (M^+) ; HRMS calcd for $C_{14}H_{22}O_4$ 254.1518, found : 254.1504.



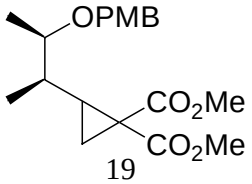
37

(+)-(3*R*,4*R*)-4-(4-Methoxybenzyl)oxy-3-methylpentene (37)

To a mixture of diol **36** (1.46 g, 5.75 mmol) and K_2CO_3 (3.18 g, 23.0 mmol) in benzene (50 mL) was added $Pb(OAc)_4$ (5.61 g, 12.6 mmol). The mixture was stirred for 1.5 h and then filtered through Celite. The filtrate was concentrated to give a colorless oil which was used immediately in the next step.

To a 0 ˚C suspension of $MePPh_3^+Br^-$ (3.08 g, 8.62 mmol) in THF (20 mL) was added BuLi (6.48 mL, 1.33 M in hexane, 8.62 mmol) dropwise over 5 min. The resulting yellow solution was warmed to rt and stirred for 20 min. After the yellow solids had dissipated, a solution of crude aldehyde in THF (10 mL) was added at 0 ˚C. The solution was allowed to warm to rt and stirred for 2 h. Saturated NH_4Cl (15 mL) was added to quench the reaction. The phases were separated and the aqueous phase was further extracted with EtOAc (3 x 50 mL). The combined organic extracts were washed with brine, dried ($MgSO_4$) and concentrated to give a crude oil. Purification of the crude oil by flash chromatography (5% EtOAc/hexane) provided alkene **37** (0.834 g, 69% for 2 steps) as a colorless oil.

Data for **37**: $[\alpha]^{29}_D$= +2.20˚ (c 1.16, $CHCl_3$); IR (neat) 1614, 1514, 1456, 1248, 1092, 1038, 822 cm^{-1} ; ^1H NMR (400 MHz, $CDCl_3$ referenced to 7.24 ppm) δ 7.26 (td, *J*=2.5, 8.4 Hz, 2 H), 6.86 (td, *J*=2.8, 8.4 Hz, 2 H), 5.81 (ddd, *J*=7.6, 10.8, 18.0 Hz, 1 H), 5.04 (ddd, *J*=1.6, 2.0, 17.6 Hz, 1 H), 5.01 (ddd, *J*=1.2, 2.0, 10.0 Hz, 1 H), 4.51 (d, *J*=11.2 Hz, 1 H), 4.41 (d, *J*=11.2 Hz, 1 H), 3.80 (s, 3 H), 3.34 (qd, *J*=6.4, 12.4 Hz, 1 H), 2.36 (ddq, *J*=6.8, 6.8, 6.8 Hz, 1 H), 1.12 (d, *J*=6.0 Hz, 3 H), 1.03 (d, *J*=6.8 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ158.86, 140.74, 131.04, 128.98, 114.31, 113.96, 78.07, 70.27, 55.21, 43.04, 16.69; LRMS *m/z* 220 (M^+); *Anal*. Calcd for $C_{14}H_{20}O_2$: C, 76.33 ; H, 9.15. Found : C, 76.45 ; H, 9.09.

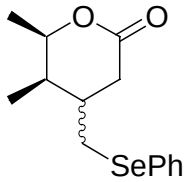


38

(2*RS*)-2-[(1*R*,2*R*)-2-(4-Methoxybenzyl)oxy-1-methylpropyl]cyclopropane-1,1-dimethyl dicarboxylate (38)

To a suspension of CuOTf (31.8 mg, 63.2 μmol) in toluene-CH_2Cl_2 (1:1, 20 mL) were added alkene **37** (1.39 g, 6.32 mmol) and dimethyl diazomalonate[6](100 mg, 0.632 mmol). The solution was plunged into an oil bath at 110 ˚C and the mixture was heated at reflux for 12 hours. The solvent was removed *in vacuo* to afford a green oil. Purification of the crude oil by flash chromatography (20% EtOAc/hexane) provided cyclopropane **38** (179 mg, 81%, dr =3:1) as a colorless oil.

Data for **38**: IR(neat) 1728, 1514, 1437, 1300, 1248, 1213, 1132, 1035 cm^{-1} ; ^1H NMR (600 MHz, $CDCl_3$) δ 7.26 (d, *J*=7.2 Hz, 0.25 x 2 H), 7.25 (d, *J*=9.0 Hz, 0.75 x 2 H), 6.87 (dd, *J*=1.8, 7.2 Hz, 0.25 x 2 H), 6.86 (d, *J*=8.4 Hz, 0.75 x 2 H), 4.52(d, *J*=11.4 Hz, 0.25 H), 4.51 (d, *J*=11.4 Hz, 0.75 H), 4.37 (d, *J*=11.4 Hz, 0.25 H), 4.36 (d, *J*=10.8 Hz, 0.75 H), 3.80 (s, 3 H), 3.75 (s, 0.25 x 3 H), 3.72 (s, 0.25 x 3 H), 3.72 (s, 0.75 x 3 H), 3.69 (s, 0.75 x 3 H), 3.49 (dq, *J*=3.6, 6.0 Hz, 0.75 H), 3.47 (dq, *J*=4.2, 6.0 Hz, 0.25 H), 2.10 (dt, *J*=8.4, 8.4 Hz, 0.75 H), 1.94 (td, *J*=9.0, 10.8 Hz, 0.25 H), 1.53 (dd, *J*=4.8, 8.4 Hz, 0.25 H), 1.43 (dd, *J*=4.8, 8.4 Hz, 0.75 H), 1.40 (dd, *J*=4.2, 9.0 Hz, 0.75 H), 1.34 (dd, *J*=4.2, 9.0 Hz, 0.25 H)1.26-1.19 (m, 0.75 H), 1.18-1.12 (m, 0.25 H), 1.19 (d, *J*=6.0 Hz, 0.25 x 3 H), 1.11 (d, *J*=6.0 Hz, 0.75 x 3 H), 1.03 (d, *J*=6.6 Hz, 0.75 x 3 H), 1.00 (d, *J*=6.6 Hz, 0.25 x 3 H) ; ^{13}C NMR (150 MHz, $CDCl_3$) δ171.07, 170.63, 169.19, 169.04, 159.23, 159.16, 131.31, 131.15, 129.37, 129.35, 113.88, 113.83, 77.84, 77.42, 70.97, 70.58, 55.43, 55.41, 52.73, 52.67, 52.61, 52.53, 38.45, 38.37, 34.76, 33.51, 33.17, 32.89, 21.46, 20.33, 17.23, 16.94, 14.88, 14.39 ; LRMS *m/z* 350 (M^+); *Anal*. Calcd for $C_{19}H_{26}O_6$: C, 65.13 ; H, 7.48. Found : C, 64.85 ; H, 7.52.



27

(3*RS*,4*R*,5*R*)-4,5 –Dimethyl-3-phenylselenylmethylpentano-5-lactone (27)

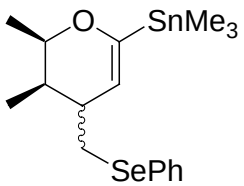
To a solution of cyclopropane **38** (0.395 g, 1.13 mmol) in MeCN-H_2O (10:1, 10 mL) was added ceric ammonium nitrate (1.86 g, 3.39 mmol) in one portion. After 2 h, the reaction was quenched by the addition of saturated $NaHCO_3$ (15 mL) and $NaHSO_3$ (0.4 g). The mixture was stirred vigorously for a further 15 min and then filtered. The filter cake was washed several times with EtOAc, and the combined filtrate and washings were extracted with EtOAc (3 x 50 mL). The organic extracts were washed with brine, dried ($MgSO_4$) and concentrated to afford a crude oil.

Purification of the crude oil by flash chromatography (33% EtOAc/hexane) provided alcohols (240.8 mg, dr =3:1, 93%) as a colorless oil.

Data for alcohols (dr = 3:1): IR(neat) 3437, 1728, 1439, 1298, 1215, 1134, 912 cm^{-1} ; ^1H NMR (400 MHz, $CDCl_3$) δ 3.85-3.78 (br, 1 H), 3.77 (s, 0.25 x 3 H), 3.75 (s, 0.75 x 3 H), 3.73 (s, 3 H), 1.95 (dt, *J*=8.0, 8.0 Hz, 0.25 H), 1.92 (dt, *J*=9.2, 9.2 Hz, 0.75 H), 1.88 (br s, 0.75 H), 1.79 (br s, 0.25 H), 1.57 (dd, *J*=4.8, 8.0 Hz, 0.25 H), 1.44 (dd, *J*=4.8, 9.6 Hz, 1 H), 1.39 (dd, *J*=4.8, 8.0 Hz, 0.75 H), 1.29-1.20 (m, 0.75 H), 1.22 (d, *J*=6.4 Hz, 0.25 x 3 H), 1.15 (d, *J*=6.4 Hz, 0.75 x 3 H), 1.02 (d, *J*=7.2 Hz, 0.75 x 3 H), 0.99 (d, *J*=6.4 Hz, 0.25 x 3 H) ; ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.62, 170.31, 169.11, 71.31, 70.11, 52.67, 52.62, 52.57, 52.52, 34.70, 33.29, 32.80, 31.64, 21.23, 20.90, 20.19, 19.67, 14.40, 13.88; LRMS *m/z* 231 (M^++H) ; HRMS calcd for $C_{11}H_{19}O_5$ 231.1123, found : 231.1238.

To a suspension of $(PhSe)_2$ (1.56 g, 5.00 mmol) in EtOH (15 mL) was added $NaBH_4$ (0.36 g, 9.52 mmol). After the yellow color had dissipated a solution of the alcohol (0.24 g) in EtOH (5 mL) was added. The mixture was heated at reflux and stirred for 16 hours. The reaction was diluted with 10% HCl (15 mL) and which was stirred for a further 5 min and then extracted with EtOAc (3 x 80 mL). The combined organic extracts were washed with saturated $NaHCO_3$ (50 mL), and brine(50 mL), then dried ($MgSO_4$) and concentrated. Purification of the crude product by column chromatography (33% EtOAc/hexane) provided lactones (0.29 g, a mixture of three compounds). The mixture of lactones (0.29 g) and LiI (0.35 g) in DMF (5 mL) was plunged into an oil bath at 150 ˚C and stirred for 12 hours. The solution was diluted with H_2O (15 mL) and then extracted with Et_2O (3 x 30 mL). The combined organic extracts were washed with H_2O, and brine, then dried ($MgSO_4$) and concentrated. Purification of the crude oil by column chromatography (33% EtOAc/hexane) provided an unseparated mixture of lactone **27** (0.28 g, 83%) as a pale yellow oil.

Data for **27** (dr = 3:2) : IR(neat) 1732, 1240, 1209, 1096, 1003, 739, 692 cm^{-1} ; ^1H NMR (600 MHz, $CDCl_3$) δ 7.52-7.49 (m, 2 H), 7.28-7.27 (m, 3 H), 4.50 (dq, *J*=3.6, 6.6 Hz, 0.6 H), 4.43 (dq, *J*=2.4, 6.6 Hz, 0.4 H), 3.03 (dd, *J*=6.0, 12.0 Hz, 0.6 H), 2.96 (dd, *J*=7.2, 12.6 Hz, 0.6 H), 2.89 (dd, *J*=6.6, 14.4 Hz, 0.4 H), 2.84 (dd, *J*=7.2, 12.6 Hz, 0.4 H), 2.74 (dd, *J*=5.4, 18.0 Hz, 0.4 H), 2.67 (dd, *J*=6.6, 16.8 Hz, 0.6 H), 2.37 (dd, *J*=9.6, 16.2 Hz, 0.6 H), 2.27-2.21 (m, 0.4 H), 2.17 (dd, *J*= 12.6, 18.0 Hz, 0.4 H), 2.08-2.04 (m, 0.4 H), 1.96-1.86 (m, 0.6 x 2 H), 1.33 (d, *J*=6.6 Hz, 0.4 x 3 H), 1.28 (d, *J*=6.6 Hz, 0.6 x 3 H), 0.95 (d, *J*=7.2 Hz, 0.6 x 3 H), 0.83 (d, *J*=7.2 Hz, 0.4 x 3 H) ; ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.06, 170.39, 133.18, 133.09, 133.08, 129.36, 129.29, 129.14, 127.46, 127.45, 127.44, 80.28, 75.86, 37.34, 37.19, 36.86, 34.33, 34.24, 33.83, 32.28, 31.03, 18.49, 16.98, 13.91, 4.20; LRMS *m/z* 298 (M^+); HRMS calcd for $C_{14}H_{18}O_2Se$ 298.0472, found : 298.0470.



26

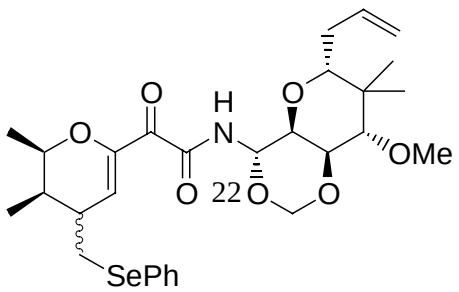
(2*R*,3*R*,4*RS*)-3,4-Dihydro-2,3 –dimethyl-4-phenylselenylmethyl-6-trimethylstannyl-2*H*-pyran (26)

To a –78 ˚C solution of lactone **27** (114.3 mg, 0.384 mmol) in THF (2.5 mL) was added KHMDS (1.00 mL, 0.5 M in toluene, 0.500 mmol) dropwise over 20 min. After 15 min, HMPA (0.100 mL, 0.575 mmol) was added and the mixture stirred for 2 hours at that temperature. A solution of $PhNTf_2$ (0.164 mg, 0.460 mmol, recrystallized from CH_2Cl_2-hexane) in THF (2 mL) was added dropwise and the mixture stirred at 0 ˚C for 1 hour and at rt for 2 hours. The solvent was removed to give an oily residue, which was dissolved in Et_2O (10 mL) and H_2O (10mL). The separated aqueous phase was extracted with Et_2O (3 x 20 mL). The combined organic extracts were washed with brine (10 mL), dried ($MgSO_4$) and concentrated to afford a crude enol triflate (163 mg), which was used immediately in the next step.

To a solution of the crude enol triflate (163 mg) in THF (15 mL) was added a solution of $(Me_3Sn)_2$ in THF (0.580 mL, 1.0 M, 0.580 mmol) followed by $Pd(PPh_3)_4$ (22.2 mg, 19.2 μmol) and LiCl (162.6 mg, 3.84 mmol). The mixture was stirred under reflux for 12 hours. Saturated $NaHCO_3$ (10 mL) was added to the mixture and the phases were separated. The aqueous phase was further extracted with Et_2O (3 x 20 mL). The combined organic extracts were washed with brine (20 mL), dried ($MgSO_4$) and concentrated to give a crude oil. Purification of the crude oil by chromatography on alumina deactivated by 5% water eluting with petroleum ether provided dihydropyran **26** (143.5 mg, 84%) as a colorless oil.

Data for **26** (dr = 3:1): IR(neat) 2970, 2922, 2876, 1603, 1578, 1477, 1437, 1379, 1252, 1070, 1022, cm^{-1} ; ^1H NMR (400 MHz, $CDCl_3$) δ 7.50-7.47 (m, 2 H), 7.33-7.19 (m, 3 H), 4.73-4.64 (m, 0.75 H), 4.49-4.41 (m, 0.25 H), 3.95 (dq, *J*=1.6, 6.4 Hz, 0.25 H), 3.78 (dq, *J*=2.4, 6.4 Hz, 0.75 H), 2.96 (dd, *J*=6.0, 12.4 Hz, 1 H), 2.84 (dd, *J*=8.0, 11.2 Hz, 0.75 + 0.25 x 2 H), 2.73-2.66 (m, 0.25 H), 1.93-1.88 (m, 0.75 H), 1.85-1.77 (m, 1 H), 1.18 (d, *J*= 6.0 Hz, 0.25 x 3 H), 1.14 (d, *J*=6.8 Hz, 0.75 x 3 H), 0.82 (d, *J*=7.2 Hz, 0.75 x 3 H), 0.75 (d, *J*=6.8 Hz, 0.25 x 3 H), 0.13 (s, 9 H) ; ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.48, 132.59, 132.50, 130.60, 128.95, 128.92, 126.65, 125.43, 112.64, 75.55, 70.60, 39.77, 38.44, 35.08, 34.80, 34.27, 33.95, 31.49, 30.38, 18.57, 17.51, 13.08, 5.32, -9.64; LRMS *m/z* 446 (M^+); HRMS calcd for $C_{17}H_{26}OSeSn$ 446.0171, found :.446.0154.

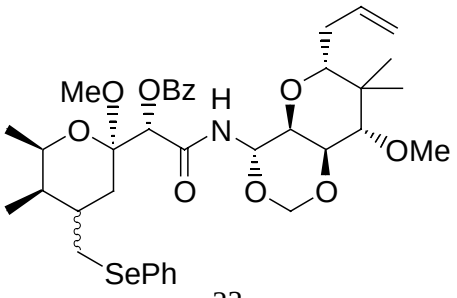
Data for the major isomer of **2** : mp < 30 ˚C; $[\alpha]^{26}_D$= +51.86˚ (c 1.10, $CHCl_3$) ; IR (neat) 2970, 2920, 2876, 1578, 1477, 1456, 1437, 1379, 1252, 1070, 1022, cm^{-1} ; ^1H NMR (400 MHz, $CDCl_3$) δ 7.50-7.47 (m, 2 H), 7.26-7.20 (m, 3 H), 4.74-4.64 (m, 1 H), 3.78 (dq, *J*=2.4, 6.4 Hz, 1 H), 2.97 (dd, *J*=6.0, 12.4 Hz, 1 H), 2.84 (dd, *J*=8.8, 12.0 Hz, 1 H), 1.93-1.88 (m, 1 H), 1.84-1.77 (m, 1 H), 1.14 (d, *J*=6.4 Hz, 3 H), 0.82 (d, *J*=6.8 Hz, 3 H), 0.13 (s, 9 H) ; ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.47, 132.59, 130.60, 128.91, 126.65, 125.42, 112.63, 70.59, 39.77, 35.08, 34.80, 30.37, 17.50, 13.07, –9.66.



(1*S*,5*R*,6*S*,8*R*,10*S*)-10-Methoxy-9,9-dimethyl-5-{[(2*R*,3*R*,4*RS*)-2,3–dimethyl-4-phenylselenylmethyl-3,4-dihydro-2*H*-pyran-6-yl]oxoethanamido}-8-(prop-2-enyl)-2,4,7-trioxabicyclo[4.4.0]decane (39)

To a –78 ˚C solution of left segment **26** (51.6 mg, 0.116 mmol) in THF (0.65 mL) was added BuLi (0.20 mL, 0.57 M in THF, 0.12 mmol) dropwise over 10 min. After 15 min TMEDA (0.11 mL) was added and the solution was stirred for 30 min, and then a cold solution of right segment **2** (22.9 mg, 66.8 μmol) in THF (0.25 mL x 2) was added *via* cannula. The mixture was stirred for 2.5 hours at that temperature before being poured onto ice-cooled saturated aqueous NH_4Cl (7 mL) and stirred vigorously for 10 min. The separated aqueous phase was further extracted with CH_2Cl_2 (30 mL x 3). The combined organic extracts were dried (Na_2SO_4) and concentrated to give a crude yellow oil (71.5 mg). Purification of the crude oil by flash chromatography (33% EtOAc/hexane) provided the title compound **39** (19.6 mg, 50%) as a colorless oil.

Data for **39** (dr = 12.5:1): IR(neat) 3364, 2878, 1695, 1674, 1522, 1107, 1074, 1024, 739, 694 cm^{-1} ; ^1H NMR (400 MHz, $CDCl_3$) δ 7.54-7.47 (m, 3 H), 7.29-7.23 (m, 3 H), 7.14 (dd, *J*=1.2, 5.0 Hz, 0.93 H), 7.07 (dd, *J*= 1.6, 2.2 Hz, 0.07 H), 5.71 (dd, *J*=9.5, 9.5 Hz, 0.07 H), 5.70 (dd, *J*=9.5, 9.5 Hz, 0.93 H), 5.61(tdd, *J*=6.8, 10.0, 16.8 Hz, 1 H), 5.16 (d, *J*=7.1 Hz, 1 H), 4.89 (d, *J*=6.8 Hz, 1 H), 4.86 (dd, *J*=1.6, 9.5 Hz, 0.07 H), 4.78 (dd, *J*=1.2, 10.0 Hz, 0.93 H), 4.25 (dd, *J*=6.6, 10.2 Hz, 1 H), 4.09 (dq, *J*=1.2, 6.4 Hz, 0.07 H), 4.00 (dq, *J*=2.2, 6.3 Hz, 0.93 H), 3.92 (dd, *J*=6.7, 9.8 Hz, 0.07 H), 3.91 (dd, *J*=6.6, 9.8 Hz, 0.93 H), 3.57 (s, 3 H), 3.46 (d, *J*=10.2 Hz, 0.07 H), 3.45 (d, *J*=10.2 Hz, 0.93 H), 3.29 (dd, *J*=2.0, 10.0 Hz, 0.07 H), 3.27 (dd, *J*=2.0, 10.0 Hz, 0.93 H), 3.06 (dd, *J*=5.9, 12.4 Hz, 0.93 H), 3.03-2.92 (m, 0.07 x 2 H), 2.88 (dd, *J*=8.5, 12.7 Hz, 0.93 H), 2.89-2.81 (m, 0.07 H), 2.88 (dd, *J*=8.5, 12.7 Hz, 0.93 H), 2.27-2.21 (m, 1 H), 2.13 (ddm, *J*=6.6, 12.4 Hz, 1 H), 2.06-1.95 (m, 2 H), 1.38 (d, *J*=6.6 Hz, 0.07 x 3 H), 1.31 (d, *J*=6.6 Hz, 0.93 x 3 H), 1.01 (s, 3 H), 0.88 (s, 3 H), 0.86 (d, *J*=7.2 Hz, 0.93 x 3 H) ; ^{13}C NMR (100 MHz, $CDCl_3$) for the major isomer δ 179.84, 160.43, 147.47, 135.44, 133.29, 129.38, 129.14, 127.35, 124.37, 116.24, 86.72, 79.40, 78.77, 74.61, 73.81, 72.11, 70.24, 61.83, 41.66, 40.01, 34.34, 33.24, 32.78, 23.19, 16.99, 13.54, 13.20; LRMS *m/z* 593 (M^+); HRMS calcd for $C_{29}H_{39}NO_7Se$ 593.1892, found : 593.1901.

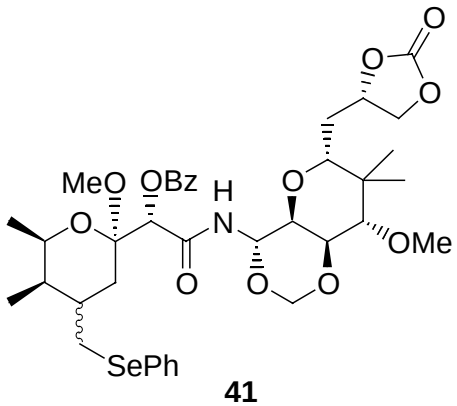


(4*RS*)-7-Benzoyl-4-phenylselenylmethyl-15-(prop-2-enyl)-mycalamide A

To a –90 ˚C solution of ketone **39** (21.3 mg, 35.9 μmol) in (1.5 mL) was added $LiBH(sBu)_3$ (0.47 mL, 0.23 M in THF, 0.108 mmol) dropwise over 20 min. After stirring at –90 ˚C for 15 min the reaction was quenched by the addition of brine (3 mL) and CH_2Cl_2 (3 mL). The mixture was stirred vigorously for a further 20 min. The separated aqueous phase was extracted with CH_2Cl_2 (10 mL x 3), dried (Na_2SO_4) and concentrated to give a colorless oil, which was used immediately in the next step. The residue was dissolved in a mixture of CH_2Cl_2 (2.3 mL) and MeOH (0.2 mL) to which CSA (2 mg) was added. The mixture was stirred for 18 hours before K_2CO_3 (8 mg) was added. The solution was then stirred for 40 min and poured onto saturated aqueous $NaHCO_3$ (3 mL). The phases were separated and the aqueous phase was further extracted with CH_2Cl_2 (10 mL x 3). The combined organic extracts were dried (Na_2SO_4) and concentrated to give a yellow oil, which was used immediately in the next step. To a solution of the crude oil in CH_2Cl_2 (1 mL) were added DMAP (8.8 mg, 72 μmol), $^{i}Pr_2NEt$ (63 μL, 0.36 mmol) and benzoyl chloride (12 μL, 0.10 mmol). The mixture was stirred for 1 hour at rt, and then MeOH (0.05 mL) was added. After stirring for 10 min, brine (3 mL) was added and the mixture was extracted with CH_2Cl_2 (10 mL x 3). The combined organic extracts were dried (Na_2SO_4) and concentrated to give a yellow solid. Purification of the crude solid by flash chromatography (33% EtOAc/hexane) provided benzoates (19.8 mg, 75% for 3 steps, a mixture of 5 diastereoisomers) as a colorless solid. The diastereoisomers were separated by column chromatography (33% EtOAc/hexane) to give the title compounds **40** (11.0 mg, a 5.4:1 mixture of diastereoisomers at C4, 42 % for 3 steps).

Data for **40** (dr = 13:1): mp 70-75 ˚C; IR(KBr) 3362, 1732, 1699, 1522, 1269, 1107, 1034, 739, 710 cm^{-1} ; ^1H NMR (600 MHz, C_6D_6 referenced to 7.16 ppm) δ 8.31 (ddd, *J*=1.8, 1.8, 7.2 Hz, 2 H), 7.50-7.48 (m, 0.93 x 2 H), 7.48-7.46 (m, 0.07 x 2 H), 7.31 (d, *J*=9.6 Hz, 0.93 H), 7.06-6.91 (m, 6 H), 6.08-6.02 (m, 0.07 H), 6.00-5.95 (m, 0.93 H), 5.94 (s, 0.07 H), 5.93 (t, *J*=10.2 Hz, 0.07 H), 5.93 (t, *J*=10.2 Hz, 0.93 H), 5.89 (s, 0.93 H), 4.97 (dddd, *J*=1.8, 1.8, 3.6, 6.7 Hz, 0.93 H), 4.95 (dd, *J*=1.2, 2.1 Hz, 0.93 H), 4.60 (d, *J*=7.2 Hz, 0.07 H), 4.58 (d, *J*=7.2 Hz, 0.93 H), 4.54 (d, *J*=7.2 Hz, 0.07 H), 4.52 (d, *J*=7.2 Hz, 0.93 H), 4.32 (dd, *J*=6.8, 10.3 Hz, 1 H), 4.29 (dd, *J*=6.8, 10.4 Hz, 1 H), 3.77 (dd, *J*=6.6, 10.2 Hz, 0.93 H), 3.73 (dq, *J*=2.4, 6.6 Hz, 0.93 H), 3.81 (dd, *J*=6.8, 9.7 Hz, 0.07 H), 3.56-3.54 (m, 0.07 x 2 H), 3.54 (dd, *J*=3.0, 10.2 Hz, 0.93 H), 3.31 (dd, *J*=7.2, 12.6 Hz, 0.93 H), 3.27 (s, 0.07 x 3 H), 3.26 (s, 0.93 x 3 H), 3.16 (dd, *J*=9.0, 12.6 Hz, 0.93 H), 3.07 (d, *J*=10.2 Hz, 0.93 H), 3.06 (d, *J*=10.8 Hz, 0.07 H), 2.89 (s, 0.07 x 3 H), 2.84 (dd, *J*=5.8, 11.9 Hz, 0.07 H), 2.82 (s, 0.93 x 3 H), 2.79 (dd, *J*=11.9, 14.4 Hz, 0.07 H), 2.47-2.38 (m, 0.07 H), 2.29 (dd, *J*=3.6, 13.5 Hz, 0.07 H), 2.27 (dd, *J*=6.0, 14.4 Hz, 0.93 H), 2.24 (mddd, *J*=1.8, 2.4, 12.6 Hz, 0.093 H), 2.17-2.11 (m, 0.07 H), 2.09 (qdd, *J*=3.0, 5.4, 15.0 Hz, 0.93 H), 2.04 (mdd, *J*=7.8, 15.8 Hz, 0.07 H), 2.01-1.95 (m, 0.93 H), 1.90-1.86 (m, 0.93 H), 1.85 (t, *J*=13.0 Hz, 0.07 H), 1.63-1.60 (m, 0.07 H), 1.60-1.55 (m, 0.93 H),0.94 (d, *J*=7.2 Hz, 0.93 x 3 H), 0.86 (s, 0.07 x 3 H), 0.85 (d, *J*=6.6 Hz, 0.93 x 3 H), 0.84 (s, 0.93 x 3H), 0.84 (d, *J*=7.8 Hz, 0.07 x 3 H), 0.79 (d, *J*=7.2 Hz, 0.07 x 3 H), 0.78 (s, 0.07 x 3 H), 0.77

(s, 0.93 x 3 H) ; ^{13}C NMR (150 MHz, $CDCl_3$) for the major isomer δ 166.40, 165.58, 137.10, 133.30, 133.16, 131.00, 130.41, 130.29, 129.26, 128.61, 126.95, 115.99, 99.92, 86.76, 78.98, 78.53, 75.35, 74.41, 73.03, 72.08, 64.73, 61.28, 47.51, 41.58, 38.24, 35.08, 34.24, 34.20, 28.95, 23.11, 18.28, 13.63, 13.10; LRMS *m/z* 731 (M^+); HRMS calcd for $C_{37}H_{49}NO_9Se$ 731.2573, found : 731.2554.



41

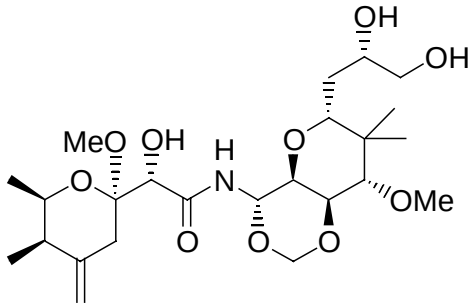
(4*RS*)-7-Benzoyl-17,18-*O*-carbonyldioxy-4-phenylselenylmethylmycalamide A (41)

To a well stirred suspension of $(DHQ)_2PYR$ (3.6 mg, 4.1 μmol), $K_3Fe(CN)_6$ (13.5 mg, 41.0 μmol) and K_2CO_3 (5.7 mg, 4.1 μmol) in ^{t}BuOH-H_2O (1:1, 1 mL) was added OsO_4 (1% in water, 5 μL, 0.1 μmol) at 0 ˚C. The solution was stirred for 2h and poured onto alkene **40** (3.0 mg, 4.1 μmol) in a 10 mL flask at –10 ˚C. The mixture was stirred for 4 hours at –10 ˚C before saturated aqueous Na_2SO_3 (2 mL) was added. The resulting colorless solution was extracted with EtOAc (10 mL x 3). The combined organic extracts were dried (Na_2SO_4) and concentrated to give a white solid (13 mg), which was used immediately in the next step.

To a solution of the crude diol (13 mg) in CH_2Cl_2 (1 mL) were added Et_3N (5.7 μL, 41.0 μmol) and a solution of triphosgene (4.9 mg, 16.4 μmol) in CH_2Cl_2 (0.3 mL). The mixture was stirred for 2 hours and poured onto a mixture of CH_2Cl_2 (2 mL) and saturated aqueous $NaHCO_3$ (2 mL). The phases were separated and the aqueous phase was further extracted with CH_2Cl_2 (4 mL x 3). The combined organic extracts were dried (Na_2SO_4) and concentrated to give a crude oil. Purification of the crude oil by flash chromatography (40% EtOAc/hexane) provided carbonates (3.1 mg, 94% for 2 steps, C17*α*:C17*β*= 4.8:1) as a white oil. The diastereoisomers were separated by HPLC (SiO_2, 30% EtOAc/hexane) to afford carbonate **41** (1.8 mg).

Data for **41** (C4*α*:C4*β*=11:1): IR(neat) 3352, 2959, 2930, 1799, 1732, 1699, 1271, 1124, 1107, 1092, 1069, 1036, 712 cm^{-1} ; ^{1}H NMR (400 MHz, C_6D_6 referenced to 7.15 ppm) δ 8.30 (dd, *J*=2.8, 7.6 Hz, 2 H), 7.54 (d, *J*=7.1 Hz, 0.92 x 2 H), 7.53 (d, *J*=8.3 Hz, 0.08 x 2 H), 7.31 (d, *J*=11.0 H, 1 H), 7.12-6.95 (m, 6 H), 5.79 (s, 0.08 H), 5.76 (s, 0.92 H), 4.50 (t, *J*=9.5 Hz, 1 H), 4.81-4.74 (m, 0.08 x 2 H), 4.76-4.69 (m, 0.92 x 2 H), 4.61 (t, *J*=8.5 Hz, 0.08 H), 4.54 (t, *J*=8.3 Hz, 0.92 H), 4.52 (d, *J*=6.8 Hz, 0.92 H), 4.51 (d, *J*=6.9 Hz, 0.08 H), 4.40 (d, *J*=6.8 Hz, 0.92 H), 4.39 (d, *J*=6.9 Hz, 0.08 H), 4.19 (dd, *J*=7.1, 10.7 Hz, 0.08 H), 4.18 (dd, *J*=6.8, 10.5 Hz, 0.08 H), 3.68 (dd, *J*=7.1, 10.0 Hz, 0.08 H), 3.71 (dq, *J*=2.4, 6.2 Hz, 0.92 H), 3.68 (dd, *J*=7.1, 10.0 Hz, 0.08 H), 3.54 (dd, *J*=8.0, 8.0 Hz,

0.08 H), 3.54 (dd, *J*=6.2, 8.3 Hz, 0.08 H), 3.53 (dd, *J*=6.1, 8.5 Hz, 0.92 H), 3.24 (s, 3 H), 3.23 (dd, *J*=6.6, 12.4 Hz, 0.92 H), 3.14 (dd, *J*=9.0, 12.4 Hz, 0.92 H), 3.09 (d, *J*=10.5 Hz, 0.92 H), 3.06 (d, *J*=10.1 Hz, 0.08 H), 2.83 (dd, *J*=6.5, 11.9 Hz, 0.08 H), 2.79-2.77 (m, 0.08 H), 2.82 (s, 0.08 x 3 H), 2.78 (s, 0.92 x 3 H), 2.38-2.30 (m, 0.08 H), 2.24 (dd, *J*=11.3, 14.8 Hz, 0.08 H), 2.25 (dd, *J*=2.8, 11.7 Hz, 0.92 H), 2.19 (dd, *J*=3.2, 13.0 Hz, 0.08 H), 2.04 (dd, *J*=6.1, 14.1 Hz, 0.92 H), 1.96-1.88 (m, 1 H),1.65-1.54 (m, 2 H), 1.16 (dd, *J*=10.0, 13.9 Hz, 1 H), 0.88 (d, *J*=7.1 Hz, 0.92 x 3 H), 0.83 (d, *J*=6.3Hz, 0.92 x 3 H), 0.82 (d, *J*=6.9 Hz, 0.08 x 3 H), 0.72 (d, *J*=7.1 Hz, 0.08 x 3 H), 0.66 (s, 3H), 0.82 (d, *J*=6.9 Hz, 0.08 x 3 H), 0.72 (d, *J*=7.1 Hz, 0.08 x 3 H), 0.66 (s, 3 H), 0.54 (s, 3 H) ; ^{13}C NMR (150 MHz, C_6D_6 referenced to 128 ppm) for the major isomer δ 166.84, 165.49, 133.80, 133.28, 132.64, 130.77, 130.10, 129.77, 129.45, 129.01, 128.44, 127.34, 127.19, 99.89, 86.83, 78.30, 74.92, 74.80, 74.73, 72.74, 72.56, 69.88, 64.91, 62.75, 61.39, 47.73, 41.27, 38.45, 34.78, 34.38, 33.85, 30.56, 28.67, 22.79, 18.28, 13.03; LRMS *m/z* 791 (M^+); HRMS calcd for $C_{38}H_{49}NO_{12}Se$ 791.2420, found : 791.2412.



1a

Mycalamide A (1a)

To a solution of carbonate **41** (2.1 mg, 2.6 μmol) in MeOH-H_2O-CH_2Cl_2 (3:1:1, 1 mL) was added $NaIO_4$ (5.7 mg, 26 μmol) in one portion. The mixture was stirred for 2 hours, and then diluted with EtOAc (10 mL) and Et_3N (0.5 mL), washed with H_2O (2 mL x 2), dried (Na_2SO_4) and concentrated to give a white solid. The residue was dissolved in toluene (0.25 mL), whereupon Et_3N (0.25 mL) was added. After refluxing for 10 min, the reaction was poured onto saturated aqueous $NaHCO_3$ (2 mL), and extracted with Et_2O (5 mL x 3). The combined organic extracts were dried (Na_2SO_4) and concentrated to afford a yellow oil. To a solution of the crude oil in MeOH (0.5 mL) was added a

solution of LiOH (0.05 mL, 1.0 M) in H_2O. The mixture was stirred for 2 hours and concentrated to yield a white residue, which was dissolved in EtOAc (10 mL). The solution was washed with H_2O (2 mL x 2), dried (Na_2SO_4) and concentrated to give a white oil. Purification of the crude oil by pipette column chromatography provided micalamide A (0.9 mg, 69% for 3 steps).

Data for **1a**: $[\alpha]^{32}_D$= –98.9˚ (c 0.2, $CHCl_3$) ; IR(neat) 3392, 2924, 2852, 1682, 1521, 1456, 1382, 1195, 1093, 1034 cm^{-1} ; ^{1}H NMR (500 MHz, $CDCl_3$ referenced to 7.26 ppm) δ 7.49 (d, *J*=9.7 Hz, 1 H), 5.89 (t, *J*=9.7 Hz, 1 H), 5.16 (d, *J*=6.9 Hz, 1 H), 4.90 (d, *J*=6.9 Hz, 1 H), 4.87 (s, 1 H), 4.78 (s, 1 H), 4.32 (s, 1 H), 4.24 (dd, *J*=6.4, 10.1 Hz, 1 H), 4.01 (dq, *J*=2.7, 6.5 Hz, 1 H), 3.87 (dd, *J*=6.9, 10.1 Hz, 1 H), 3.78 (br s, 1 H), 3.76 (m, 1 H), 3.66 (dd, *J*=4.2, 7.8 Hz, 1 H), 3.59 (m, 1 H), 3.58 (s, 3 H), 3.48 (d, *J*=10.1 Hz, 1 H), 3.40 (dd, *J*=5.5, 10.6 Hz, 1 H), 3 32 (s, 3 H), 3.18 (br s, 1 H), 2.39 (m, 2 H), 2 27 (dq, *J*=2.8, 6.9 Hz, 1 H), 2 23 (br s, 1 H), 1.56 (m, 2 H), 1.21 (d, *J*=6.4 Hz, 3 H), 1.02 (d, *J*=7.3 Hz, 3 H), 1.00 (s, 3 H), 0.89 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.59, 145.45, 110.57, 99.68, 86.75, 79.02, 78.99, 74.30, 73.69, 72.82, 71.45, 71.21, 69.73, 66.44, 61.76, 48.90, 41.56, 41.24, 33.67, 31.91, 23.04, 17.82, 13.50, 11.97; LRMS *m/z* 502 (M^- – H); HRMS calcd for $C_{24}H_{40}NO_{10}$ 502.2652, found : 502.2659.

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