Supporting Text

General

All reactions were carried out under Ar in flame-dried glassware. The solvents used were purified by distillation over the drying agents indicated and were transferred under Ar: THF, Et_2O (Mg-anthracene), CH_2Cl_2 (P_4O_{10}), MeCN, Et_3N (CaH_2), MeOH (Mg), DMF, DMA (Desmodur, dibutyltin dilaurate), hexane, toluene (Na/K).

Flash Chromatography. Merck silica gel 60 (230-400 mesh). IR: Nicolet FT-7199 spectrometer, wavenumbers ($\tilde{\nu}$) in cm^{-1}. MS (EI): Finnigan MAT 8200 (70 eV), ESI-MS: Finnigan MAT 95, accurate mass determinations: Bruker APEX III FT-MS (7 T magnet). Melting points: Gallenkamp melting point apparatus (uncorrected). Elemental analyses: H. Kolbe, Mülheim/Ruhr. Unless stated otherwise, all commercially available compounds (Fluka, Lancaster, Aldrich) were used as received. NMR: Spectra were recorded on a Bruker DPX 300, AV 400, or DMX 600 spectrometer in the solvents indicated; chemical shifts (δ) are given in ppm relative to TMS, coupling constants (J) in Hz. The solvent signals were used as references and the chemical shifts converted to the TMS scale ($CDCl_3$: $\delta_C \equiv 77.0$ ppm; residual $CHCl_3$ in $CDCl_3$: $\delta_H \equiv 7.24$ ppm; CD_2Cl_2: $\delta_C \equiv 53.8$ ppm; residual CH_2Cl_2 in CD_2Cl_2: $\delta_H \equiv 5.32$ ppm). *Where indicated, the signal assignments are unambiguous*; the numbering scheme is arbitrary and is shown in the inserts. The assignments are based upon 1D and 2D spectra recorded using the following pulse sequences from the Bruker standard pulse program library: DEPT; COSY (*cosygs* and *cosydqtp*); HSQC (*invietgssi*) optimized for $^1J(C,H) = 145$ Hz; HMBC (*inv4gslplrnd*) for correlations via $^nJ(C,H)$; HSQC-TOCSY (*invietgsml*) using an MLEV17 mixing time of 120 ms.

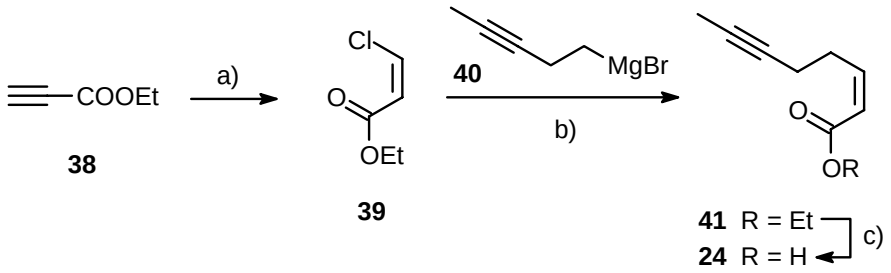
Bioassay. Murine NIH/3T3 fibroblasts (CRL-1658 from American Type Culture Collection) were cultured at 37°C and 5% CO_2 in Dulbecco's modified Eagle's medium supplemented with 4 mM L-glutamine, 4.5 g/liter glucose, and 10 % bovine calf serum. Cells (2×10^4) were seeded on coverslips in one well of a 24-well plate. After adapting and attaching overnight the cells were incubated with 1, 5, or 10 μM of the corresponding compound for 18 h. Before and after each fixation or staining step, the cells were washed three times with TPBS (0.2% Tween 20 in

phosphate-buffered saline). Cells were fixed with 3.7% formalin in PBS. For blocking unspecific epitopes, fixed cells were incubated with 1% powdered milk in PBS. Actin filaments were stained for 1 h with a solution of 77 nM TRITC-labeled phalloidin (P1951 from Sigma) in TPBS. Cell nuclei were stained with DAPI [2-(4-amidinophenyl)-6-indolecarbamidine dihydrochloride; D9542 from Sigma]. Cells were visualized and photographed at a Zeiss Axiophot fluorescence microscope.

Carboxylic Acid Building Blocks

Acids **23** (1) and **26** (2) were prepared by following the literature routes.

Analogues:



Scheme 4. a) LiCl, HOAc, MeCN, reflux, 60%; b) $Fe(acac)_3$ cat., THF, –30°C, 78%; c) NaOH, MeOH, 74%.

Ethyl (*Z*)-3-chloro-2-propenoate (39). See ref. 3. A mixture of ethyl propiolate **38** (2 g, 20.4 mmol, 2.04 ml), dry lithium chloride (0.95 g) and acetic acid (1.3 ml) in MeCN (25 ml) was refluxed for 18 h. The reaction was allowed to cool and water added (100 ml). Solid K_2CO_3 was added until no further CO_2 evolution occurred. The organic layer was separated and the aqueous phase extracted with MTBE (3 × 100 ml). The combined organic extracts were dried (Na_2SO_4) and evaporated. Purification of the residue by flash chromatography gave **39** as a colorless liquid (1.66 g, 60 %). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.32 (t, 3H, *J* = 7.1 Hz), 4.25 (q, 2H, *J* = 7.1 Hz), 6.20 (1H, d, *J* = 8.2 Hz), 6.71 (1H, d, *J* = 8.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.4, 132.3,

121.5, 60.7, 14.2; MS (EI) *m*/*z* (rel. intensity): 106 (9), 99 (42), 91 (34), 89 (100), 61 (20), 45 (14); HRMS (CI) *m*/*z* 135.0210 $(M + H)^+$; calcd. for $C_5H_7ClO_2$: 135.0212.

Ethyl (*Z*)-2-octen-6-ynoate (41). Magnesium turnings (433 mg, 17.8 mmol) were stirred with I_2 for 1 h. THF (2 ml) was added and a solution of 5-pentynyl bromide (2.3 g, 16.0 mmol) in THF (17 ml) was added dropwise to maintain a constant reflux. After complete addition, the mixture was refluxed for 1.5 h before allowing to cool. The solution of the Grignard reagent **40** thus formed was quickly added in one portion to a solution of chloride **39** (1 g, 7.4 mmol) and $Fe(acac)_3$ (565 mg, 10 mol%) in THF (15 ml) at –30°C. After 10 min the reaction was allowed to warm to room temperature before quenching with sat. aq. NH_4Cl. The organic layers were separated and the aqueous phase was extracted with MTBE. The combined organic layers were dried (Na_2SO_4), the solvent was evaporated and the residue purified by flash chromatography (20:1 hexane:EtOAc) to give **41** as a volatile light yellow oil (964 mg, 78%). IR (ATR) 2981, 2920, 1716, 1646, 1445, 1414, 1388, 1332, 1283, 1216, 1188, 1163, 1096, 1030, 821 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.28 (t, 3H, *J* = 7.1 Hz), 1.77 (t, 3H, *J* = 2.5 Hz), 2.27 (m, 2H), 2.82 (dd, 2H, *J* = 7.2, 1.7 Hz), 4.16 (q, 2H *J* = 7.1 Hz), 5.81 (ddd, 1H *J* = 1.7, 1.7, 11.4 Hz), 6.32 (dd, 1H *J* = 7.2, 11.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 3.5, 14.3, 18.4, 28.4, 59.9, 76.4, 78.0, 120.7, 148.3, 166.3; HRMS (CI, *iso*-butane): calcd. for $C_{10}H_{15}O_2$ ($M^+ + H$): 167.1072; found 167.1073.

(*Z*)-2-Octen-6-ynoic acid (24). To a stirred solution of ester **41** (773 mg, 4.65 mmol) in MeOH (10 ml) was added an aq. 1 M solution of NaOH (12.4 ml, 12.4 mmol). The reaction was allowed to stir overnight before removal of the methanol under vacuum. The aqueous layer was washed with MTBE and the organic phases were discarded. The aqueous layer was acidified to pH 1 with 2 M HCl and extracted with CH_2Cl_2 (3×). The combined organic phases were dried (Na_2SO_4) and evaporated and the residue was purified by Kugelrohr distillation to give **24** as a colorless liquid (571 mg, 74%). IR (ATR) 2970, 2921, 1737, 1695, 1432, 1366, 1287, 1231, 1217, 1204, 1110, 924, 826, 722 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.77 (t, 3H, *J* = 2.5 Hz), 2.23-2.32 (m, 2H), 2.82 (dd, 2H, *J* = 7.1, 1.7 Hz), 5.84 (ddd, 1H, *J* = 11.5, 1.6, 1.6 Hz), 6.44 (ddd, 1H, *J* = 11.5, 7.1,

7.1 Hz), 11.5 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 3.5, 18.4, 28.7, 76.7, 77.7, 120.0, 151.3, 171.8; HRMS (CI, *iso*-butane): calcd. for $C_8H_{11}O_2$ (M^+ + H): 139.0759; found 139.0760.

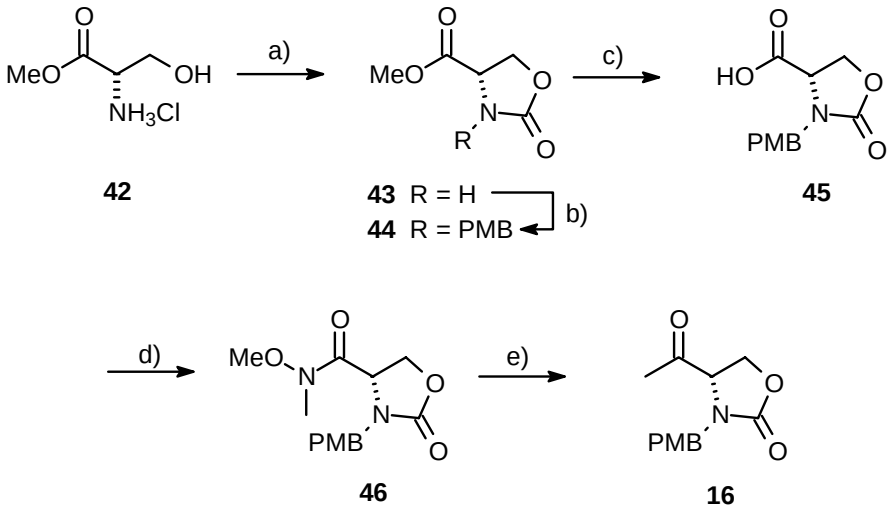
6-Octynoic Acid (25). A mixture of 6-octynol (500 mg, 3.96 mmol), TEMPO (43 mg, 0.28 mmol), sodium chlorite (900 mg, 80%, 7.92 mmol), acetonitrile (20 ml), and phosphate buffer (15 ml, 0.67 M, pH = 6.7) was heated to 35°C before dilute bleach (50 mg, 12% NaOCl diluted in 2 ml water, 2 mol%) was added. After stirring for 4 d at 35°C the conversion was complete as checked by GC-MS and the reaction mixture was cooled to room temperature. After diluting with water (30 ml), the pH was adjusted to ≈ 9.0 with 1 M NaOH and the resulting mixture was poured into a cold (0°C) Na_2SO_3 solution (1.2 g in 20 ml of water). After stirring for 0.5 h at room temperature, the mixture was diluted with MTBE, the organic layer was separated and discarded. The aqueous layer was then acidified with 3 M HCl to pH 1 and extracted three times with MTBE. The combined organic layers were washed with water and brine, dried (Na_2SO_4) and evaporated to yield white crystals. Purification of the residue by flash chromatography (ethyl acetate/hexane, 1/6) afforded acid **25** as a white solid (340 mg, 62% yield). IR (film) 3037, 2945, 1706, 1458, 1415, 1313, 937 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.49–1.57 (m, 2H), 1.70–1.76 (m, 2H), 1.77 (t, 3H, *J* = 2.6 Hz), 2.13–2.19 (m, 2H), 2.38 (t, 2H, *J* = 7.5 Hz), 11.68 (bs, 1H, OH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 3.4, 18.4, 23.8, 28.3, 33.6, 76.0, 78.5, 180.2; MS (EI) *m/z* (rel. intensity) 140 (19), 94 (46), 81 (100), 67 (35), 53 (53). HRMS: ($C_8H_{12}O_2$) calcd.: 140.083730, found: 140.083832.

8-Decynoic Acid (27). Prepared analogously from 8-decynol (279 mg, 51%). IR (neat): 3200-2500 (br), 2936, 2849, 1691, 933 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.36 (t, *J* = 7.4 Hz, 2H), 2.44-2.11 (m, 2H), 1.79 (s, 3H), 1.66 (qt, *J* = 7.4 Hz, 2H), 1.49-1.36 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 179.4 (C), 78.7 (C), 75.1 (C), 33.6 (CH_2), 28.4 (CH_2), 28.2 (CH_2), 28.0 (CH_2), 24.2 (CH_2), 18.3 (CH_2), 3.0 (CH_3); MS (EI) *m/z* (rel. intensity) 150 (2), 108 (14), 93 (17), 81 (23), 68 (100). HRMS ($C_{10}H_{17}O_2$): calcd. for (M^+ + H): 169.1229; found 169.1230.

Ketone Building Blocks

Ketone **8** and its 16-epimer **15** were prepared by the route outlined in ref. 1.

The preparation of the analogous oxygen containing heterocycle **16** is depicted in Scheme 5; the preparation of the antipode **17** followed the same route using the epimeric serine ester as the starting material.



42 **43** R = H **44** R = PMB **45** **46** **16**

Scheme 5. a) triphosgene, Et_3N, CH_2Cl_2, 0°C, quant.; b) NaH, PMBBr, THF, –15°C, 56%; c) aq. KOH, 1,4-dioxane, 97%; d) MeONH(Me)·HCl, BOP, Et_3N, CH_2Cl_2, quant.; e) MeMgBr, THF, –40°C, 96%, ee = 97% (after recrystallization from MTBE).

Methyl (4*S*)-2-oxo-1,3-oxazolidine-4-carboxylate (43). See ref. 4. To a stirred suspension of serine methyl ester hydrochloride **42** (5 g, 32.1 mmol) in CH_2Cl_2 (75 ml) at 0°C was added triethylamine (13.4 ml, 96.3 mmol) over 5 min. The reaction was stirred for 10 min before a solution of triphosgene (3.2 g, 10.9 mmol) in CH_2Cl_2 (25 ml) was added dropwise over 2 h. The reaction was stirred for 30 min, diluted with Et_2O (75 ml) and cooled to –78°C to precipitate all Et_3NHCl salts. The mixture was filtered and then concentrated to approx. 10 ml when it was applied carefully to a 2.5 cm depth column of silica (prepacked EtOAc) in a 100 ml sinter funnel. The solution was washed through the column with EtOAc (300 ml) and concentrated to give **43**

as a colorless oil in quantitative yield (4.65 g). $[\alpha]_D^{20} = -2.0$ (*c* 0.62, EtOH); IR (ATR) 3296, 2959, 1732, 1480, 1438, 1399, 1366, 1213, 1115, 1056, 1007, 954, 920, 825, 766 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.82 (s, 3H), 4.43 (dd, 1H, *J* = 9.5, 4.5 Hz), 4.57 (dd, 1H, *J* = 8.9, 4.5 Hz), 4.60 (d, 1H, *J* = 9.5 Hz), 6.38 (br s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 53.2, 53.8, 66.8, 159.1, 170.6; MS (EI) *m*/*z* (rel. intensity): 145 (7), 86 (100) 58 (11), 42 (55); HRMS (EI) *m*/*z* 145.0372 $(M)^+$; calcd. for $C_5H_7NO_4$: 145.0375.

Methyl (4*S*)-3-(4-methoxybenzyl)-2-oxo-1,3-oxazolidine-4-carboxylate (44). To a slurry of NaH (0.61 g, 25.3 mmol) in THF (50 ml) at –15°C was added a solution of **43** (3.5 g, 24.1 mmol) in THF (30 ml). The reaction was allowed to stir for 3 h before a solution of PMBBr (8.5 g, 42 mmol) in THF (20 ml) was added dropwise. The reaction was stirred for 16 h, quenched with aq. sat. NH_4Cl (40 ml) and the aqueous phase extracted with MTBE (2 × 40 ml). The combined organic layers were dried (Na_2SO_4) and concentrated to a colorless oil. Purification by flash chromatography (3:1, hexane:EtOAc) gave **44** as a white solid (3.57 g, 56%). mp 65-67°C; $[\alpha]_D^{20} = -25.0$ (*c* 0.45, EtOH); IR (ATR) 2973, 2959, 1732, 1613, 1585, 1515, 1466, 1435, 1415, 1364, 1316, 1302, 1285, 1245, 1209, 1174, 1113, 1086, 1048, 1025, 1009, 980, 966, 946, 921, 870, 837, 828, 814, 756, 744, 715, 671 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.76 (s, 3H), 3.81 (s, 3H), 4.09 (dd, 1H, *J* = 9.4, 5.1 Hz), 4.18 (d, 1H, *J* = 14.7 Hz), 4.32 (dd, 1H, *J* = 9.0, 5.1 Hz), 4.38 (dd, 1H, *J* = 9.4, 9.0 Hz), 4.84 (d, 1H, *J* = 14.7 Hz), 6.87 (app. d, 2H, *J* = 8.6 Hz), 7.19 (app. d, 2H, *J* = 8.6 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 46.8, 52.9, 55.4, 55.9, 64.4, 114.3, 127.1, 130.0, 157.6, 159.6, 170.0; MS (EI) *m*/*z* (rel. intensity): 265 (28), 179 (30), 162 (14), 135 (16), 134 (37), 121 (100), 78 (11); HRMS (EI) *m*/*z* 265.0952 $(M)^+$; calcd. for $C_{13}H_{15}NO_5$: 265.0950.

(4*S*)-3-(4-Methoxybenzyl)-2-oxo-1,3-oxazolidine-4-carboxylic acid (45). To a solution of **44** (3.38 g, 12.7 mmol) in 1,4-dioxane (50 ml) was added an aqueous KOH solution (2.15 g in 35 ml of H_2O, 38 mmol). After 1 h the reaction was acidifed with 2 M HCl and diluted with MTBE (200 ml). The aqueous layer was extracted with MTBE (2 × 100 ml), the combined organic phases were washed with brine, dried (Na_2SO_4) and concentrated to an oil. Repeated treatment of the oil with toluene/CH_2Cl_2 (2:1) followed by re-evaporation resulted in removal of residual

water and isolation of product **45** as a white solid (3.1 g, 97%). mp 116-118°C; $[\alpha]_D^{20} = -28.1$ (*c* 1.0, EtOH); IR (film) 3440, 2958, 2934, 2838, 2722, 2611, 2509, 1743, 1689, 1612, 1587, 1514, 1470, 1444, 1419, 1365, 1294, 1268, 1248, 1197, 1179, 1116, 1101, 1030, 971, 834, 813, 762, 746, 677 cm^{-1}; ^1H NMR (300 MHz, $[D]_6$-DMSO) δ 3.76 (s, 3H), 4.09 (d, 1H, *J* = 15.1 Hz), 4.14 (dd, 1H, *J* = 9.4, 4.4 Hz), 4.29 (dd, 1H, *J* = 8.9, 4.4 Hz), 4.47 (t, 1H, *J* = 9.4 Hz), 4.62 (d, 1H, *J* = 15.1 Hz), 6.93 (app. d, 2H, *J* = 8.7 Hz), 7.21 (app. d, 2H, *J* = 8.7 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 45.8, 55.1, 55.8, 64.5, 114.0, 127.7, 129.4, 157.3, 158.8, 171.3; MS (EI) *m*/*z* (rel. intensity): 251 (58), 206 (5), 179 (81), 162 (15), 134 (94), 121 (100), 78 (16), 77 (15); HRMS (EI) *m*/*z* 251.0794 $(M)^+$; calcd. for $C_{12}H_{13}NO_5$: 251.0793.

(4*S*)-*N*-Methoxy-3-(4-methoxybenzyl)-*N*-methyl-2-oxo-1,3-oxazolidine-4-carboxamide (46). To a solution of **45** (1.0 g, 4 mmol) in CH_2Cl_2 was added BOP (1.8 g, 4 mmol) shortly followed by Et_3N (0.58 ml, 4.2 mmol). The reaction was stirred for 10 min before *N*,*O*-dimethylhydroxylamine hydrochloride (0.43 g, 4.4 mmol) was added along with another portion of Et_3N (0.58 ml, 4.2 mmol). The mixture was stirred overnight and was quenched with sat. aq. NH_4Cl, the aqueous phase was extracted with CH_2Cl_2 (3×) and the combined organics were dried (Na_2SO_4) and evaporated. The residue was purified by flash chromatography (1:2, hexane:EtOAc) to give **46** as a light yellow oil in quantitative yield (1.17 g). $[\alpha]_D^{20} = -4.5$ (*c* 0.37, EtOH); IR (film) 3478, 2941, 2839, 1755, 1673, 1612, 1586, 1514, 1443, 1419, 1376, 1323, 1304, 1249, 1210, 1178, 1116, 1083, 1034, 997, 960, 846, 762, 559 cm^{-1}; ^1H NMR (400 MHz, $[D]_6$-DMSO) δ 3.12 (s, 3H), 3.51 (s, 3H), 3.76 (s, 3H), 4.01 (d, 1H, *J* = 14.9 Hz), 4.19 (dd, 1H, *J* = 6.6, 2.2 Hz), 4.47-4.55 (m, 2H), 4.62 (d, 1H, *J* = 14.9 Hz), 6.93 (app. d, 2H, *J* = 8.7 Hz), 7.21 (app. d, 2H, *J* = 8.7 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 32.0, 45.7, 53.9, 54.9, 61.2, 64.2, 113.9, 127.6, 129.4, 157.6, 158.7, 169.0; MS (EI) *m*/*z* (rel. intensity): 294 (7), 263 (23), 162 (6), 121 (100), 78 (6), 55 (7); HRMS (ESI) *m*/*z* 317.1112 $(M + Na)^+$; calcd. for $C_{14}H_{18}N_2O_5$ + Na: 317.1113.

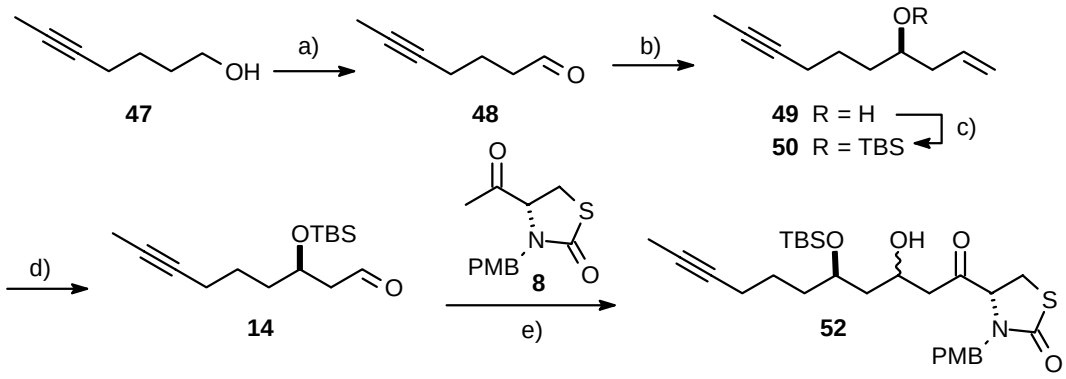
(4*S*)-4-Acetyl-3-(4-methoxybenzyl)-1,3-oxazolidin-2-one (16). To a solution of **46** (2.4 g, 8.2 mmol) in THF (25 ml) at –40°C was added MeMgBr (2.9 ml, 3M in Et_2O, 8.6 mmol). The reaction was stirred at –40°C for 1 h and then allowed to warm to –20°C for 2 h. The reaction

was quenched with sat. aq. NH_4Cl, the organic phase was separated and the aqueous layer extracted with EtOAc (3×), the combined organic phases were dried (Na_2SO_4) and evaporated, and the residue was purified by flash chromatography (1:1, hexane:EtOAc) to give **16** as a white solid (1.95 g, 96%). Chiral LC/MS showed that the product had an ee of 77.3%. The material was recrystallized from MTBE to give white crystals of 97.2% ee. mp 65-67°C; $[\alpha]_D^{20} = -26.5$ (*c* 1.0, $CHCl_3$); IR (film) 3002, 2935, 2838, 1756, 1725, 1612, 1586, 1514, 1443, 1412, 1362, 1304, 1248, 1207, 1176, 1115, 1077, 1038, 846, 754 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.07 (s, 3H), 3.81 (s, 3H), 4.06 (dd, 1H, *J* = 9.8, 5.6 Hz), 4.11 (d, 1H, *J* = 14.6 Hz), 4.13 (dd, 1H, *J* = 8.9, 5.6 Hz), 4.43 (dd, 1H, *J* = 9.8, 8.9 Hz), 4.80 (d, 1H, *J* = 14.6 Hz), 6.87 (app. d, 2H, *J* = 8.7 Hz), 7.16 (app. d, 2H, *J* = 8.7 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.9, 47.1, 55.4, 62.4, 63.5, 114.4, 126.9, 130.1, 157.8, 159.7, 204.3; MS (EI) *m*/*z* (rel. intensity): 249 (6), 206 (9), 121 (100), 91 (3), 78 (5), 77 (4); HRMS (ESI) *m*/*z* 272.0895 $(M + Na)^+$; calcd. for $C_{13}H_{15}NO_4$ + Na: 272.0898.

Aldol Reactions

The preparation of compound **10** followed the route published in ref.[1]

Aldol route to building block **52**:



Scheme 6. a) PCC, MS 4Å, CH_2Cl_2, 84%; b) (–)-Ipc_2B(allyl), Et_2O, –100°C; c) TBSCl, imidazole, DMF, 68%, ee = 91% (GC) (over both steps); d) O_3, MeOH, –78°C, then PPh_3, 67%; e) ketone **8**, $TiCl_4$, $(i\text{Pr})_2\text{NEt}$, 78°C→0°C, 70%, dr = 1:1.7.

5-Heptynal (48). See ref. 5. To a stirred suspension of PCC (10.6 g, 50 mmol) and powdered MS 4Å in CH_2Cl_2 (23 ml) was added dropwise a solution of 5-heptynol **47** (1.75 g, 15.6 mmol) in CH_2Cl_2 (23 ml). The reaction was allowed to stir for 8 h and then filtered through a short Celite column. The solvent was carefully evaporated at 0°C to give **48** as a colorless oil (1.45 g, 84%). IR (ATR) 2937, 2921, 2859, 2724, 1721, 1437, 1411, 1391, 1364, 1334, 1156, 1071, 1033, 925, 866, 796, 688 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.77 (t, 3H, *J* = 2.6 Hz), 1.81 (t, 2H, *J* = 7.1 Hz), 2.21 (m, 2H), 2.57 (dt, 2H, *J* = 7.1, 1.5 Hz), 9.80 (t, 1H, *J* = 1.5 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 3.3, 18.2, 21.5, 23.9, 42.8, 77.9, 202.1.

(1*R*)-1-Allyl-5-heptynyl *tert*-butyl(dimethyl)silyl ether (50). To a stirred solution of (–)-Ipc_2B(allyl) (6, 7) (25.4 ml, 0.5 M soln. in Et_2O, 12.7 mmol) at –100°C was added a solution of 5-heptynal **48** (1.4 g, 12.7 mmol) in diethyl ether (20 ml). The reaction was allowed to stir for 1 h at –100°C and then quenched with MeOH (1 ml). The solvent was removed under vacuum at 0°C and the residue dissolved in MeOH (26 ml). 8-Hydroxyquinoline (2.3 g) was added and the reaction stirred overnight. The yellow precipitate formed was filtered off and the filtrate evaporated to dryness. Purification of the residue by flash chromatography (40:1, hexane:EtOAc) gave **49** as a light brown oil (1.93 g). The crude material was dissolved in DMF (20 ml) followed by the addition of TBSCl (2.4 g, 15.88 mmol) and imidazole (1.7 g, 25.4 mmol). The reaction was stirred overnight before it was diluted with hexane (250 ml). The solution was successively washed with 5% aq. HCl., sat. aq. $NaHCO_3$, water and brine followed by drying (Na_2SO_4) of the organic phase and evaporation of the solvent. The residue was purified by flash chromatography (40:1, hexane:EtOAc) to give **50** as a colorless oil (2.05 g, 68%). $[\alpha]_D^{20} = +9$ (*c* 0.07, $CHCl_3$); IR (ATR) 2952, 2929, 2857, 1472, 1462, 1435, 1361, 1254, 1088, 1005, 938, 911, 880, 834, 808, 772, 665 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.06 (s, 6H), 0.89 (s, 9H), 1.53 (m, 4H), 1.78 (t, 3H, *J* = 2.5 Hz), 2.12 (m, 2H), 2.22 (ddd, 2H, *J* = 7.1, 5.9, 1.2 Hz), 3.72 (m, 1H), 5.02 (s, 1H), 5.06 (m, 1H), 5.82 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ –4.4, –4.3, 3.6, 18.2, 18.9, 24.9, 26.0, 36.0, 41.9, 71.8, 75.7, 79.3, 116.8, 135.4; MS (EI) *m*/*z* (rel. intensity): 225 (4), 209 (5), 185 (3), 133 (14), 99, (22), 93, (44), 75 (100), 73 (67); HRMS (CI) *m*/*z* 267.2141 $(M + H)^+$; calcd. for

$C_{16}H_{30}OSi$: 267.2144; the enantiomeric excess (91% ee) was determined by chiral GC of alcohol **49**.

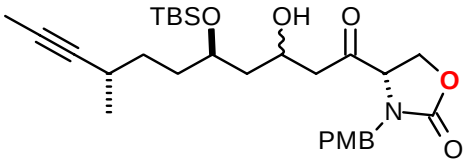
(3*R*)-3-{[*tert*-Butyl(dimethyl)silyl]oxy}-7-nonynal (14). A stirred solution of **50** (2.01 g, 8.43 mmol) and Sudan Red 7B (enough to give red color) in MeOH (100 ml) at –78°C was treated with ozone until the red color disappeared. Argon was bubbled through the solution for 15 min before triphenylphosphine (3.3 g, 1.5 eq.) was added and the reaction left to stir overnight. The solvent was evaporated and the residue purified by flash chromatography (100% hexane → 20:1, hexane:EtOAc) to give **14** as a colorless oil (1.51 g, 67%). $[\alpha]_D^{20} = -7.8$ (*c* 0.7, $CHCl_3$); IR (film) 2954, 2930, 2858, 2712, 1713, 1472, 1463, 1436, 1409, 1389, 1376, 1361, 1295, 1256, 1217, 1098, 1027, 1006, 939, 837, 811, 776, 680, 665 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.07 (s, 3H), 0.09 (s, 3H), 0.88 (s, 9H), 1.46-1.70 (m, 6H), 1.78 (t, 3H, *J* = 2.5 Hz), 2.15 (dddd, 2H, *J* = 9.2, 5.1, 2.5, 2.5 Hz), 2.52 (dd, 1H, *J* = 2.4, 1.5 Hz), 2.54 (t, 1H, *J* = 2.4 Hz), 4.23 (tt, 1H, *J* = 5.7 Hz), 9.82 (t, 1H, *J* = 2.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ –4.3, –4.0, 18.4, 19.1, 24.9, 26.1, 37.2, 51.1, 68.2, 76.4, 77.6, 79.0, 202.6; MS (EI) *m*/*z* (rel. intensity): 211 (50), 169 (41), 167 (32), 157 (13), 129 (10), 119 (19), 101 (100), 93 (56), 75 (64), 59 (39); HRMS (CI) *m*/*z* 269.1933 $(M + H)^+$; calcd. for $C_{15}H_{28}O_2Si$: 269.1936.

(4*R*)-4-((5*R*)-5-{[*tert*-Butyl(dimethyl)silyl]oxy}-3-hydroxy-9-undecynoyl)-3-(4-methoxy benzyl)-1,3-thiazolidin-2-one (52). To a solution of ketone **8** (332 mg, 1.25 mmol) in CH_2Cl_2 (5 ml) at –78°C was added $TiCl_4$ (1 M in CH_2Cl_2, 1.35 ml, 1.35 mmol). The reaction was allowed to stir for 20 min before $(iPr)_2NEt$ (1 M in CH_2Cl_2, 1.7 ml, 1.7 mmol) was introduced. After stirring for 2 h at –78°C the reaction was warmed to 0°C and allowed to stir for 3 h. The reaction was cooled to –78°C and a solution of aldehyde **14** (160 mg, 0.66 mmol) in CH_2Cl_2 (4 ml) was added dropwise. After stirring for 3 h at –78°C, the reaction was quenched with aq. NH_4Cl and the mixture allowed to warm to room temperature before water was added to dissolve salts. The organic layer was separated and the aqueous phase extracted with CH_2Cl_2 (3×). The combined organic layers were washed with aq. $NaHCO_3$ and brine, dried (Na_2SO_4) and concentrated. The residue was purified by flash chromatography (2:1, hexane:EtOAc) to give **52** as a mixture of diastereoisomers (colorless oil, 247 mg, 70%, dr = 1:1.7). IR (ATR) 3456, 2943, 2930, 2856,

1724, 1670, 1611, 1586, 1513, 1462, 1441, 1390, 1360, 1303, 1248, 1174, 1108, 1073, 1031, 1004, 938, 834, 809, 775, 713, 662 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.08 & 0.09 (2s, 6H), 0.87 & 088 (2s, 9H), 1.40-1.71 (m, 6H), 1.75 (t, 3H, *J* = 2.5 Hz), 2.07-2.15 (m, 2H), 2.28 (dd, 0.7H, *J* = 15.4, 3.6 Hz), 2.46 (dd, 0.3H, *J* = 16.1, 4.1 Hz), 2.56 (dd, 0.3H, *J* = 16.1, 7.8 Hz), 2.61 (dd, 0.7H, *J* = 15.4, 8.8 Hz), 3.15 & 3.22 (2dd, 1H, *J* = 11.5, 3.6 Hz), 3.40-3.48 (ddd, 1.3H, *J* = 11.5, 9.3, 2.0 Hz), 3.73 (br s, 0.7H), 3.75 & 3.76 (s, 3H), 3.82 & 3.83 (2d, 1H, *J* = 14.7 Hz), 3.91-4.03 (m, 1H), 4.16-4.23 (m, 0.6H), 4.25 (dd, 0.7H, *J* = 9.5, 3.6 Hz), 4.33-4.41 (m, 0.7H), 4.94 & 5.03 (2d, 1H, *J* = 14.7 Hz), 6.78-6.84 (m, 2H), 7.07-7.15 (m, 2H); ^{13}C NMR (100 MHz,$CDCl_3$) δ –4.8, –4.7, –4.6, –4.1, 3.4, 17.9, 18.6, 18.7, 24.1, 25.0, 25.8, 26.9, 27.2, 35.2, 36.6, 41.2, 42.5, 46.4, 46.5, 47.2, 47.3, 55.2, 65.3, 65.7, 65.8, 67.0, 70.9, 71.9, 75.9, 78.6, 78.7, 114.1, 114.2, 127.5, 127.6, 129.8, 130.1, 159.4, 171.7, 171.8, 205.6, 205.7; MS (EI) *m*/*z* (rel. intensity): 515 (1), 476 (1), 458 (3), 265 (1), 222 (7), 211 (4), 121 (100); HRMS (ESI) *m*/*z* 556.2523 $(M + Na)^+$; calcd. for $C_{28}H_{43}NO_5SSi$ + Na: 556.2528.

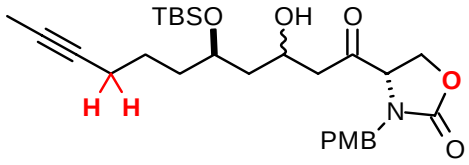
The following compounds were prepared analogously:

(4*S*)-4-((5*R*,8*S*)-5-{[*tert*-Butyl(dimethyl)silyl]oxy}-3-hydroxy-8-methyl-9-undecynoyl)-3-(4-methoxybenzyl)-1,3-oxazolidin-2-one (54). The procedure was adopted from the previous aldol reaction using **16** (159 mg, 0.64 mmol), and aldehyde **7** (2.1 ml, 0.25 M in CH_2Cl_2, 0.5 mmol). Colorless oil (200 mg, 71%, dr = 3.3:1). IR (film) 3458, 2953, 2930, 2857, 1758, 1612, 1586, 1514, 1471, 1462, 1443, 1414, 1372, 1304, 1250, 1177, 1114, 1075, 1037, 837, 811, 776 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.050 & 0.056 (2s, 6H), 0.85 (s, 9H), 1.09 (d, 3H, *J* = 6.9 Hz), 1.22-1.39 (m, 2H), 1.43-1.63 (m, 3H), 1.73 (d, 3H, *J* = 2.2 Hz), 1.74-1.80 (m, 1H), 2.15 (dd, 0.8H, *J* = 15.5, 3.5 Hz), 2.26-2.35 (m, 1H), 2.40 (dd, 0.2H, *J* = 11.5, 4.0 Hz), 2.50 (dd, 0.8H, *J* = 15.5, 8.8 Hz), 3.69 (br s, 1H), 3.74 (s, 3H), 3.90-3.97 (m, 1H), 4.00 (d, 1H, *J* = 14.7 Hz), 4.13-4.21 (m, 2.2H), 4.27-4.36 (m, 1.8H), 4.68 (d, 0.8H, *J* = 14.6 Hz), 4.77 (d, 0.2H, *J* = 14.7 Hz), 6.77-6.82 (m, 2H), 7.07-7.14 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ –4.9, –4.8, –4.7, –4.1, 3.3, 17.8, 21.3, 21.4, 25.7, 25.9, 26.0, 32.1, 33.0, 33.8, 35.4, 41.3, 42.4, 46.6, 46.8, 47.1, 55.1, 61.9, 62.4, 63.1, 63.3, 64.9, 65.2, 67.2, 67.8, 71.1, 72.4,



75.9, 77.3, 83.2, 83.3, 114.1, 114.2, 127.0, 127.1, 129.9, 130.1, 167.9, 159.5, 205.6, 205.9; MS (EI) *m*/*z* (rel. intensity): 513 (0.5), 456 (15), 239 (3), 225 (2), 121 (100); HRMS (ESI) *m*/*z* 554.2910 $(M + Na)^+$; calcd. for $C_{29}H_{45}NO_6Si$ + Na: 554.2913.

(4*S*)-4-((5*R*)-5-{[*tert*-Butyl(dimethyl)silyl]oxy}-3-hydroxy-9-undecynoyl)-3-(4-methoxy benzyl)-1,3-oxazolidin-2-one (55). The standard procedure was used with aldehyde **14** (250 mg, 1.04 mmol) and ketone **16** (311 mg, 1.25 mmol). The crude product was purified by flash chromatography (2:1, hexane:EtOAc) to give two partially separated fractions of the major isomer **55a** (358 mg, 67%, dr = 9.3:1) and the minor isomer **55b** (39 mg, 7%, dr = 1.6:1). Overall isomer ratio dr = 7:1.

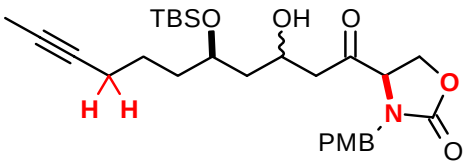


Major isomer 55a: IR (ATR) 3460, 2952, 2930, 2857, 1745, 1612, 1586, 1514, 1412, 1371, 1303, 1247, 1176, 1074, 1033, 911, 835, 809, 774, 730, 664 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.05 (d, 6H, *J* = 2.0 Hz), 0.84 (s, 9H), 1.36-1.49 (m, 3H), 1.51-1.67 (m, 3H), 1.72 (t, 3H, *J* = 2.5 Hz), 2.06-2.12 (m, 2H), 2.15 (dd, 1H, *J* = 15.5, 3.6 Hz), 2.50 (dd, 1H, *J* = 15.5, 8.8 Hz), 3.68 (br 2, 1H), 3.74 (s, 3H), 3.91-3.98 (m, 1H), 4.00 (d, 1H, *J* = 14.7 Hz), 4.12-4.21 (m, 2H), 4.27-4.36 (m, 2H), 4.68 (d, 1H, *J* = 14.7 Hz), 6.79 (app. d, 2H, *J* = 8.6 Hz), 7.11 (app. d, 2H, *J* = 8.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ –4.9, –4.7, 3.3, 17.8, 18.6, 24.9, 25.7, 35.1, 41.2, 46.8, 55.1, 62.4, 63.1, 65.2, 70.7, 75.9, 78.5, 114.1, 127.1, 130.1, 157.7, 159.5, 205.8; MS (EI) *m*/*z* (rel. intensity): 499 (0.4), 442 (3), 249 (3), 206 (4), 169 (4), 121 (100); HRMS (ESI) *m*/*z* 540.2753 $(M + Na)^+$; calcd. for $C_{28}H_{43}NO_6Si$ + Na: 540.2757.

Minor isomer 55b (mixture of diastereomers): ^1H NMR (400 MHz, $CDCl_3$) δ 0.10 (2d, 6H), 0.89 (s, 9H), 1.40-1.72 (m, 6.4H), 1.78 (2s, 3H), 2.10-2.19 (m, 2.4H), 2.29-2.58 (m, 1.6H), 3.795 (2s, 3H), 3.92-4.02 (m, 1H), 4.06 (d, 1H, *J* = 14.6 Hz), 4.10-4.24 (m, 2.6H), 4.34-4.41 (m, 1.6H), 4.75 (d, 0.4H, *J* = 14.6 Hz), 4.85 (d, 0.6H, *J* = 14.7 Hz), 6.86 (2 app. d, 2H, *J* = 8.7 Hz), 7.17 (2 app. d, 2H, *J* = 8.7 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ –4.7, –4.6, –4.5, –3.5, 3.9, 17.9, 18.8, 24.1, 25.1, 25.2, 25.9, 35.2, 35.3, 36.8, 41.1, 41.2, 42.3, 46.8, 47.0, 47.2, 47.3, 55.3, 62.1, 62.7, 63.1,

63.4, 65.1, 65.3, 67.6, 70.9, 71.1, 72.4, 76.1, 78.6, 78.7, 114.3, 114.4, 127.0, 127.1, 127.2, 130.1, 130.3, 157.9, 159.6, 205.9, 206.1.

(4*R*)-4-((5*R*)-5-{[*tert*-Butyl(dimethyl)silyl]oxy}-3-hydroxy-9-undecynoyl)-3-(4-methoxy benzyl)-1,3-oxazolidin-2-one (56). The standard aldol procedure was used with aldehyde **14** (250 mg, 1.04 mmol) and ketone **17** (311 mg, 1.25 mmol). The product was obtained in form of two diastereomers. The major isomer **56a** was an colorless oil (163 mg, 30%) and the minor isomer **56b** was a white solid (147 mg, 27%) that were separable by chromatography (3:1, hexane:EtOAc).

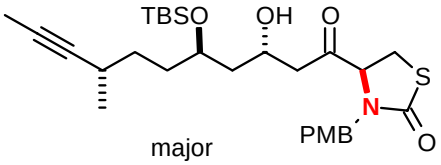


Major isomer 56a: $[\alpha]_D^{20} = -4.4$ (*c* 0.73, $CHCl_3$); IR (ATR) 3462, 2941, 2929, 2857, 1747, 1612, 1514, 1412, 1371, 1303, 1248, 1176, 1075, 1032, 835, 809, 774, 731, 663 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.09 (d, 6H, *J* = 4.6 Hz), 0.87 (s, 9H), 1.37-1.61 (m, 6H), 1.74 (t, 3H, *J* = 2.5 Hz), 2.07-2.14 (m, 2H), 2.21 (dd, 1H, *J* = 15.3, 3.7 Hz), 2.51 (dd, 1H, *J* = 15.3, 8.7 Hz), 3.51 (bs s, 1H), 3.77 (s, 3H), 3.90-3.97 (m, 1H), 4.02 (d, 1H, *J* = 14.7 Hz), 4.08-4.15 (m, 1H), 4.19 (m, 2H), 4.35 (m, 1H), 4.73 (d, 1H, *J* = 14.7 Hz), 6.81 (app. d, 2H, *J* = 8.6 Hz), 7.13 (app. d, 2H, *J* = 8.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ –4.8, –4.1, 3.3, 17.8, 18.6, 23.9, 25.7, 36.6, 42.4, 46.6, 46.8, 55.1, 62.4, 63.0, 67.7, 72.3, 75.9, 78.5, 114.1, 127.1, 130.0, 157.8, 159.5, 205.7; MS (EI) *m*/*z* (rel. intensity): 460 (1), 442 (6), 211 (4), 206 (3), 169 (3), 167 (3), 122 (8), 121 (100), 101 (9), 93 (7), 91 (2), 75 (9), 73 (7) 59 (4); HRMS (ESI) *m*/*z* 518.2935 $(M + H)^+$; calcd. for $C_{28}H_{43}NO_6Si$: 518.2937.

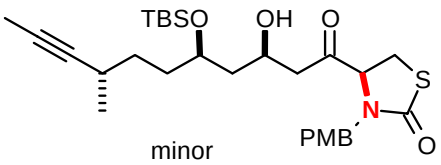
Minor isomer 56b: mp 77-79°C; $[\alpha]_D^{20} = +33.6$ (*c* 0.78, $CHCl_3$); IR (ATR) 3415, 2952, 2932, 2857, 1723, 1613, 1516, 1451, 1433, 1347, 1307, 1256, 1225, 1185, 1102, 1069, 1032, 1018, 941, 930, 838, 823, 808, 767, 753, 740, 726, 660 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.09 (s, 6H), 0.88 (s, 9H), 1.45 (m, 2H), 1.50 (ddd, 1H, *J* = 14.3, 5.2, 2.2 Hz), 1.58-1.73 (m, 3H), 1.76 (t, 3H, *J* = 2.5 Hz), 2.10-2.16 (m, 2H), 2.31 (dd, 1H, *J* = 15.9, 3.7 Hz), 2.49 (dd, 1H, *J* = 15.9, 8.5 Hz), 3.63 (br s, 1H), 3.78 (s, 3H), 3.95-4.01 (m, 1H), 4.04 (d, 1H, *J* = 14.7 Hz), 4.11 (dd, 1H, *J* = 9.6, 5.6 Hz), 4.19 (dd, 1H, *J* = 8.9, 5.6 Hz), 4.34-4.42 (m, 2H), 4.83 (d, 1H, *J* = 14.7 Hz), 6.84

(app. d, 2H, J = 8.6 Hz), 7.12 (app. d, 2H, J = 8.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ –4.8, –4.6, 3.4, 17.9, 18.7, 25.0, 25.7, 35.2, 41.1, 46.7, 47.2, 55.2, 62.0, 63.3, 64.9, 70.8, 76.0, 78.6, 114.2, 127.0, 110.0, 157.9, 159.5, 205.9; MS (EI) m/z (rel. intensity): 499 (0.8), 442 (11), 249 (6), 206 (8), 169 (8), 121 (100), 101 (12); HRMS (ESI) m/z 540.2751 $(M + Na)^+$; calcd. for $C_{28}H_{43}NO_6Si$ + Na: 540.2757.

Compound 57a (major isomer). $[\alpha]_D^{20}$ = +59.0 (c 1.38, $CHCl_3$). IR (neat) 3443, 2972, 1725, 1678, 1513, 1081 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.12 (d, J = 8.6 Hz, 2H), 6.85 (d, J = 8.8 Hz, 2H), 5.09 (d, J = 14.7 Hz, 1H), 4.48-4.39 (m, 1H), 4.13 (dd, J = 9.1, 4.0 Hz, 1H), 4.03-3.96 (m, 1H), 3.87 (d, J = 14.7 Hz, 1H), 3.79 (s, 3H), 3.60 (d, J = 2.0 Hz, 1H), 3.45 (dd, J = 11.4, 9.1 Hz, 1H), 3.25 (dd, J = 11.4, 3.8 Hz, 1H), 2.61 (dd, J = 16.4, 8.3 Hz, 1H), 2.43-2.30 (m, 1H), 2.38 (dd, J = 16.4, 3.8 Hz, 1H), 1.85-1.76 (m, 1H), 1.78 (d, J = 2.3 Hz, 3H), 1.70-1.60 (m, 2H), 1.53 (ddd, J = 14.4, 5.6, 2.3 Hz, 1H), 1.43-1.28 (m, 2H), 1.14 (d, J = 6.8 Hz, 3H), 0.89 (s, 9H), 0.10 (s, 3H), 0.09 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.2 (C), 171.8 (C), 159.5 (C), 129.9 (CH), 127.5 (C), 114.3 (CH), 83.4 (C), 76.0 (C), 71.1 (CH), 65.4 (CH), 64.9 (CH), 55.3 (CH_3), 47.3 (CH_2), 46.7 (CH_2), 41.3 (CH_2), 34.0 (CH_2), 33.1 (CH_2), 27.3 (CH_2), 26.1 (CH), 25.8 (CH_3), 21.4 (CH_3), 18.0 (C), 3.4 (CH_3), –4.6 (CH_3), –4.8 (CH_3). HRMS (ESI+) calcd for $C_{29}H_{45}NNaO_5SSi$ (M^+) 570.2683; found 570.2685.

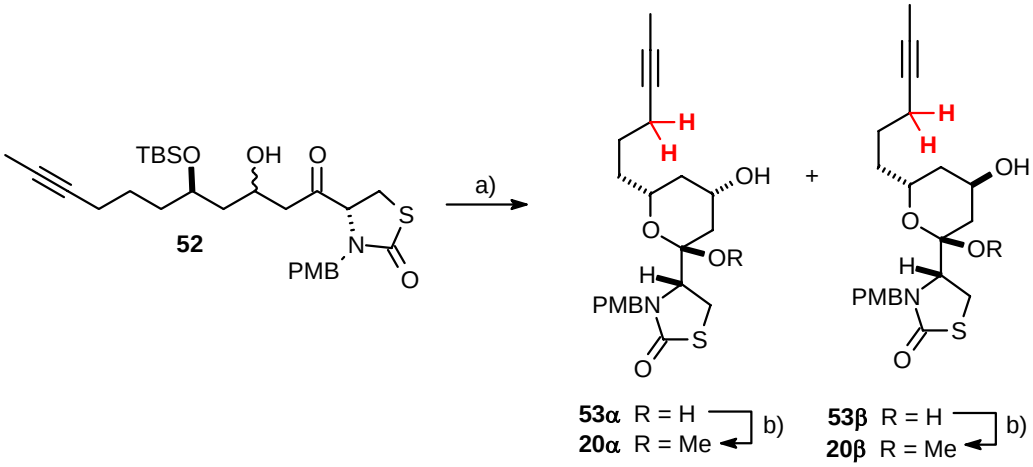


Compound 57b (minor isomer). $[\alpha]_D^{20}$ = +10.9 (c 1.16, $CHCl_3$). IR (neat) 3488, 2930, 2857, 1725, 1673, 1513, 1248 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.15 (d, J = 8.6 Hz, 2H), 6.83 (d, J = 8.6 Hz, 2H), 4.99 (d, J = 14.7 Hz, 1H), 4.27 (dd, J = 9.6, 3.5 Hz, 1H), 4.23-4.14 (m, 1H), 4.02-3.93 (m, 1H), 3.82 (d, J = 14.7 Hz, 1H), 3.79 (s, 3H), 3.59-3.56 (m, 1H), 3.46 (dd, J = 11.6, 9.6 Hz, 1H), 3.18 (dd, J = 11.6, 3.5 Hz, 1H), 2.61 (dd, J = 15.2, 8.8 Hz, 1H), 2.38-2.29 (m, 2H), 1.80-1.69 (m, 1H), 1.78 (d, J = 2.5 Hz, 3H), 1.62-1.48 (m, 3H), 1.47-1.37 (m, 1H), 1.35-1.23 (m, 1H), 1.13 (d, J = 6.8 Hz, 3H), 0.90 (s, 9H), 0.12 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 205.7 (C), 171.7 (C), 159.4 (C), 130.1 (CH), 127.7 (C), 114.2 (CH), 83.4 (C), 76.1 (C), 73.0 (CH), 68.5 (CH), 65.8 (CH), 55.3 (CH_3), 47.3 (CH_2), 46.3



(CH_2), 42.5 (CH_2), 35.6 (CH_2), 32.1 (CH_2), 26.8 (CH_2), 26.2 (CH), 25.8 (CH_3), 21.5 (CH_3), 17.9 (C), 3.4 (CH_3), –4.0 (CH_3), –4.8 (CH_3), HRMS (ESI+): calcd. for $C_{29}H_{45}NnaO_5SSi$ (M^+ + Na): 570.2683; found 570.2685.

Ketal Formations



Scheme 7. a) aq. HCl (1M), THF, quant., b) camphorsulfonic acid cat., MeOH, 92% (**20α**), 82% (**20β**).

(4*S*)-4-[(2*R*,4*S*,6*R*)-6-(4-Hexynyl)-4-hydroxy-2-methoxytetrahydro-2*H*-pyran-2-yl]-3-(4-methoxybenzyl)-1,3-thiazolidin-2-one (20α) and (4*S*)-4-[(2*R*,4*R*,6*R*)-6-(4-hexynyl)-4-hydroxy-2-methoxytetrahydro-2*H*-pyran-2-yl]-3-(4-methoxybenzyl)-1,3-thiazolidin-2-one (20β). To a stirred solution of **52** (325 mg, 0.61 mmol) in THF (12 ml) was added aq. HCl (1 M, 1.6 ml). The reaction was stirred overnight and then quenched with aq. $NaHCO_3$, the aqueous layer was extracted with CH_2Cl_2 (4×), the combined organic phases were washed with sat. aq. NaCl and dried (Na_2SO_4). After evaporation of the solvent the residue was purified by flash chromatography (1:1, hexane:EtOAc) to give the separable minor **53β** (88 mg) and major **53α** diastereomers (164 mg, 100% overall) in a dr = 1.9:1. The products were used without delay in the next reaction.

A catalytic amount of CSA was added to a solution of the major isomer **53α** (164 mg, 0.39 mmol) in methanol (4 ml). The reaction was stirred overnight before quenching with sat. aq. $NaHCO_3$. The aqueous phase was extracted with CH_2Cl_2 (3×), the combined organic layers were washed with brine, dried (Na_2SO_4) and evaporated. The residues was purified by flash chromatography (2:1, hexane:EtOAc) to give product **20α** (156 mg, 92%) as an oil. The minor isomer **20β** was prepared analogously as a white solid (60 mg, 82%).

Product 20α: $[\alpha]_D^{20}$ = +28.8 (*c* 0.74, $CHCl_3$); IR (ATR) 3441, 2943, 1738, 1666, 1611, 1585, 1511, 1442, 1402, 1364, 1302, 1245, 1216, 1199, 1174, 1107, 1070, 1030, 980, 938, 927, 894, 820, 756, 721, 665 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.21 (d, 1H, *J* = 11.7 Hz), 1.48 (dd, 1H, *J* = 12.4, 11.2 Hz), 1.50-1.68 (m, 2H), 1.74 (t, 3H, *J* = 2.5 Hz), 1.71-1.81 (m, 2H), 1.95-2.01 (m, 1H), 2.15-2.25 (m, 3H), 2.68 (br s, 1H), 3.04 (s, 3H), 3.20-3.29 (m, 2H), 3.54-3.62 (m, 1H), 3.78 (s, 3H), 3.83 (dd, 1H *J* = 8.5, 3.5 Hz), 3.98-4.08 (m, 1H), 4.23 (d, 1H, *J* = 14.5 Hz), 5.08 (d, 1H, *J* = 14.5 Hz), 6.85 (app. d, 2H, *J* = 8.6 Hz), 7.21 (app. d, 2H, *J* = 8.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 3.4, 18.8, 25.3, 25.4, 35.3, 36.9, 40.5, 47.2, 47.4, 55.2, 58.9, 64.3, 70.1, 76.0, 78.6, 102.9, 114.0, 128.7, 129.7, 159.1, 172.9; MS (EI) *m*/*z* (rel. intensity): 433 (0.5), 212 (10), 211 (77), 193 (9), 179 (14), 161 (24), 137 (71), 133 (45), 122 (13), 121 (100), 119 (62), 111 (19), 109 (13), 103 (14), 95 (34), 93 (10), 91 (14); HRMS (ESI) *m*/*z* 456.1819 $(M + Na)^+$; calcd. for $C_{23}H_{31}NO_5S$ + Na: 456.1820.

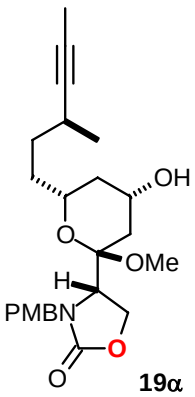
Product 20β: mp 127-129°C; $[\alpha]_D^{20}$ = +36.4 (*c* 0.55, $CHCl_3$); IR (ATR) 3547, 2935, 2833, 1738, 1662, 1608, 1585, 1510, 1436, 1403, 1366, 1366, 1305, 1287, 1241, 1210, 1199, 1174, 1099, 1087, 1063, 1033, 974, 953, 935, 924, 902, 886, 847, 839, 822, 808, 758, 662 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.46 (ddd, 1H, *J* = 14.1, 12.2, 2.7 Hz), 1.53-1.69 (m, 2H), 1.76 (t, 3H, *J* = 2.5 Hz), 1.74-1.83 (m, 2H), 1.86 (dd, 2H, *J* = 14.4, 3.7 Hz), 2.07 (ddd, 1H, *J* = 14.4, 2.3, 2.3 Hz), 2.18-2.28 (m, 2H), 3.15 (s, 3H), 3.21-3.32 (m, 2H), 3.65 (br d, 1H), 3.78 (dd, 1H, *J* = 8.8, 3.0 Hz), 3.80 (s, 3H), 3.90-3.98 (m, 1H), 4.15 (br s, 1H), 4.23 (d, 1H, *J* = 14.4 Hz), 5.09 (d, 1H, *J* = 14.4 Hz), 6.87 (app. d, 2H, *J* = 8.6 Hz), 7.22 (app. d, 2H, *J* = 8.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 3.5, 18.7, 25.3, 25.4, 32.4, 35.3, 37.8, 47.3, 47.7, 55.3, 58.9, 64.0, 66.1, 76.2, 78.5, 103.6, 114.1, 128.7, 129.8, 159.2, 172.8; MS (EI) *m*/*z* (rel. intensity): 433 (0.2), 212 (7), 211 (56),

193 (8), 179 (16), 161 (13), 137 (68), 133 (30), 122 (12), 121 (100), 119 (46), 111 (14), 109 (8), 103 (7), 95 (12), 93 (8), 91 (12); HRMS (ESI) *m*/*z* 456.1818 $(M + Na)^+$; calcd. for $C_{23}H_{31}NO_5S$ + Na: 456.1820.

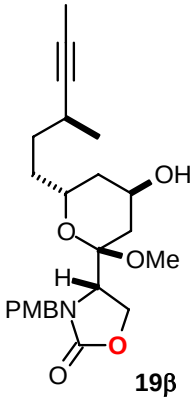
The following compounds were prepared analogously:

(4*R*)-4-{(2*R*,4*S*,6*R*)-4-Hydroxy-2-methoxy-6-[(3*S*)-3-methyl-4-hexynyl]tetrahydro-2*H*-pyran-2-yl}-3-(4-methoxybenzyl)-1,3-oxazolidin-2-one (19α) and (4*R*)-4-{(2*R*,4*R*,6*R*)-4-hydroxy-2-methoxy-6-[(3*S*)-3-methyl-4-hexynyl]tetrahydro-2*H*-pyran-2-yl}-3-(4-methoxybenzyl)-1,3-oxazolidin-2-one (19β). Prepared as described above by acid catalyzed cyclization of **54** to form the hemiketal as a mixture of diastereomers (32 mg, 15% + 149 mg, 72%), followed by separate methyl glycoside formation to give isomer **19α** (108 mg, 70%) as an oil and isomer **19β** (20 mg, 61%) as an oil.

Isomer 19α: $[\alpha]_D^{20}$ = +48.2 (*c* 0.69, $CHCl_3$); IR (film) 3428, 2941, 2871, 1752, 1612, 1513, 1441, 1416, 1362, 1303, 1246, 1208, 1175, 1141, 1082, 1033, 980, 844, 676 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.11 (d, 3H, *J* = 6.9 Hz), 1.19 (app. q, 1H, *J* = 11.6 Hz), 1.28-1.40 (m 2H), 1.50-1.59 (m, 1H), 1.61-1.71 (m, 1H), 1.69 (d, 3H, *J* = 2.3 Hz), 1.78-1.89 (m, 1H), 1.91-1.98 (br dd, 2H, *J* = 12.7, 4.5 Hz), 2.31-2.40 (m, 1H), 2.82 (br s, 1H), 2.96 (s, 3H), 3.48-3.56 (m, 1H), 3.70-3.75 (m, 1H), 3.73 (s, 3H), 3.94-4.16 (m, 4H), 4.75 (d, 1H, *J* = 14.4 Hz), 6.82 (app. d, 2H, *J* = 8.6 Hz), 7.23 (app. d, 2H, *J* = 8.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 3.6, 21.9, 26.2, 33.6, 34.3, 36.2, 40.8, 46.4, 48.0, 55.3, 55.9, 63.1, 64.5, 70.2, 76.4, 83.2, 101.9, 114.0, 128.3, 130.4, 158.9, 159.3; MS (EI) *m*/*z* (rel. intensity): 431 (1), 225 (39), 207 (21), 183 (2), 181 (3), 175 (15), 151 (27), 147 (37), 133 (55), 125 (10), 121 (100), 109 (24), 103 (13), 67 (14); HRMS (ESI) *m*/*z* 454.2201 $(M + Na)^+$; calcd. for $C_{24}H_{33}NO_6$ + Na: 454.2205.



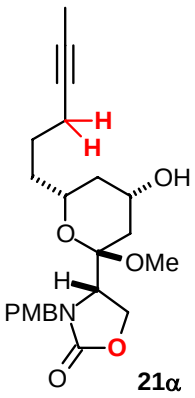
19α



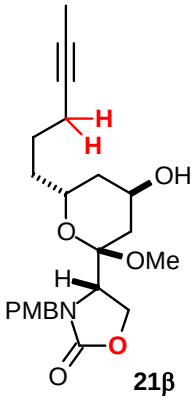
19β

Isomer 19β: $[\alpha]_D^{20}$ = +59.0 (*c* 0.26, $CHCl_3$); IR (KBr) 3516, 2971, 2935, 2919, 1747, 1611, 1584, 1512, 1463, 1435, 1415, 1394, 1368, 1305, 1241, 1207, 1173, 1107, 1084, 1033, 1019, 977, 877, 839, 765, 753, 675 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.20 (d, 3H, *J* = 6.9), 1.41-1.52 (m, 2H), 1.57-1.66 (m, 1H), 1.71-1.79 (m, 1H), 1.77 (d, 3H, 2.4), 1.80-1.97 (m, 3H), 2.40-2.49 (m, 1H), 3.13 (s, 3H), 3.59 (d, 1H, *J* = 9.4 Hz), 3.73 (dd, 1H, *J* = 9.5, 4.8 Hz), 3.81 (s, 3H), 3.93 (dddd, 1H, *J* = 11.8, 9.2, 2.8, 2.8 Hz) 4.14 (t, 1H, *J* = 9.5 Hz), 4.17 (d, 1H, *J* = 14.3 Hz), 4.23 (dd, 2H, *J* = 9.4, 4.8 Hz), 4.81 (d, 1H, *J* = 14.4 Hz), 6.87-6.92 (m, 2H), 7.28-7.34 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 3.6, 21.9, 26.3, 31.6, 33.5, 34.2, 38.1, 46.6, 48.3, 55.4, 56.1, 62.9, 64.1, 66.2, 76.4, 83.2, 102.3, 114.1, 128.2, 130.4, 158.8, 159.5; MS (EI) *m*/*z* (rel. intensity): 431 (0.35), 225 (51), 207 (13), 175 (11), 151 (34), 147 (25), 133 (45), 131 (2), 125 (16), 121 (100), 109 (14), 105 (10), 67 (14); HRMS (ESI) *m*/*z* 432.2385 $(M + H)^+$; calcd. for $C_{24}H_{33}NO_6$: 432.2386.

(4*S*)-4-[(2*R*,4*S*,6*R*)-6-(4-Hexynyl)-4-hydroxy-2-methoxytetrahydro-2*H*-pyran-2-yl]-3-(4-methoxybenzyl)-1,3-oxazolidin-2-one (21α) and (4*S*)-4-[(2*R*,4*R*,6*R*)-6-(4-hexynyl)-4-hydroxy-2-methoxytetrahydro-2*H*-pyran-2-yl]-3-(4-methoxybenzyl)-1,3-oxazolidin-2-one (21β). Prepared as described above by acid catalyzed cyclization of aldol product **55** (315 mg, 0.61 mmol) to form the hemiketal as two diastereomers (41 mg, 17% + 198 mg, 83%), which were separately transformed into the corresponding methyl glycosides. The major isomer **21α** (207 mg, 91%) was obtained as a wax and the minor isomer **21β** (22 mg, 56%) as a solid.



21α



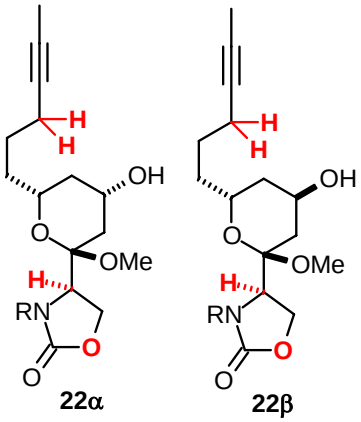
21β

Isomer 21α: $[\alpha]_D^{20}$ = +53.2 (*c* 0.43, $CHCl_3$); IR (film) 3433, 2943, 2837 1750, 1612, 1586, 1513, 1486, 1440, 1416, 1362, 1303, 1246, 1203, 1175, 1140, 1114, 1082, 1032, 982, 845, 767, 677 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.20 (app. q, 1H, *J* = 11.8 Hz), 1.33 (app. t, 1H, *J* = 11.8 Hz), 1.43-1.65 (m, 2H), 1.71

(t, 3H, *J* = 2.3 Hz), 1.72-1.79 (m, 2H), 1.92-1.99 (m, 2H), 2.09-2.23 (m, 2H), 2.98 (s, 3H), 3.36 (br s, 1H), 3.51-3.59 (m, 1H), 3.74 (s, 3H), 3.74-3.79 (dd, 1H, *J* = 9.6, 5.1 Hz), 4.01 (dd, 1H, *J* = 15.5, 4.5 Hz), 4.09 (app. t, 1H, *J* = 9.4 Hz), 4.13-4.19 (m, 2H), 4.75 (d, 1H, *J* = 14.5 Hz), 6.83 (app. d, 2H, *J* = 8.6 Hz), 7.22 (app. d, 2H, *J* = 8.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 3.3, 18.6, 25.2, 35.1, 35.8, 40.3, 46.1, 47.7, 55.1, 55.8, 62.9, 63.8, 69.9, 75.9, 78.5, 101.6, 113.8, 128.0, 129.9, 158.8, 159.1; MS (EI) *m*/*z* (rel. intensity): 417 (1), 211 (51), 179 (10), 169 (3), 167 (3), 161 (14), 137 (49), 133 (35), 121 (100), 119 (47), 111 (17), 103 (12), 95 (26), 91 (12), 71 (10); HRMS (ESI) *m*/*z* 440.2053 $(M + Na)^+$; calcd. for $C_{23}H_{32}NO_6$ + Na: 440.2049.

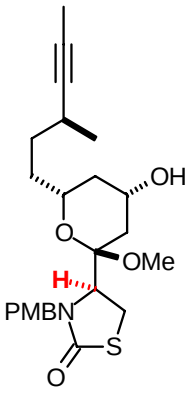
Isomer 21β: mp 126-128°C; $[\alpha]_D^{20} = +55.1$ (*c* 0.32, $CHCl_3$); IR (ATR) 3524, 2952, 2915, 2888, 2843, 1741, 1611, 1584, 1511, 1431, 1413, 1391, 1368, 1334, 1305, 1240, 1209, 1184, 1174, 1164, 1105, 1080, 1062, 1052, 1027, 1003, 978, 949, 926, 882, 841, 826, 801, 764, 752, 719, 674 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.46 (ddd, 1H, *J* = 14.1, 12.2, 2.7 Hz), 1.52-1.71 (m, 3H), 1.72-1.91 (m, 5H), 1.78 (t, 3H, *J* = 2.5 Hz), 2.17-2.32 (m, 2H), 3.15 (s, 3H), 3.60 (br s, 1H), 3.75 (dd, 1H, *J* = 9.5, 4.8 Hz), 3.81 (s, 3H), 3.92-4.00 (m, 1H), 4.14 (app. t, 2H, *J* = 9.5 Hz), 4.18 (d, 1H, *J* = 14.4 Hz), 4.23 (dd, 1H, *J* = 9.4, 4.8 Hz), 4.80 (d, 1H, *J* = 14.4 Hz), 6.89 (app. d, 2H, *J* = 8.6 Hz), 7.28 (app. d, 2H, *J* = 8.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 3.6, 18.9, 25.3, 31.6, 35.3, 37.9, 46.6, 48.2, 55.3, 56.1, 62.9, 64.0, 66.0, 76.2, 78.5, 102.3, 114.1, 128.2, 130.2, 158.7, 159.4; MS (EI) *m*/*z* (rel. intensity): 418 (0.22), 367 (2), 212 (4), 211 (31), 193 (4), 179 (10), 161 (8), 137 (40), 133 (21), 121 (100), 119 (30), 111 (10); HRMS (ESI) *m*/*z* 440.2046 $(M + Na)^+$; calcd. for $C_{23}H_{31}NNaO_6$: 440.2049.

(4*R*)-4-[(2*R*,4*S*,6*R*)-6-(4-Hexynyl)-4-hydroxy-2-methoxytetrahydro-2*H*-pyran-2-yl]-3-(4-methoxybenzyl)-1,3-oxazolidin-2-one (22α) and (4*R*)-4-[(2*R*,4*R*,6*R*)-6-(4-hexynyl)-4-hydroxy-2-methoxytetrahydro-2*H*-pyran-2-yl]-3-(4-methoxybenzyl)-1,3-oxazolidin-2-one (22β). Prepared as described above by acid catalyzed cyclization of aldol product **56** (315 mg, 0.61 mmol) to form the hemiketal as a two diastereomers (81 mg, 76% + 9 mg, 8%), which were separately transformed into the corresponding methyl glycosides **22α** (77 mg, 92%) and **22β** (58 mg, 88%).



Isomer 22α: $[\alpha]_D^{20}$ = +30.6 (*c* 0.41, $CHCl_3$); IR (ATR) 3520, 2942, 2838, 1745, 1612, 1585, 1513, 1439, 1410, 1366, 1303, 1287, 1229, 1175, 1103, 1080, 1026, 957, 886, 819, 766, 751, 735, 717, 675 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.38-1.50 (m, 2H), 1.51-1.62 (m, 3H), 1.65 (dd, 1H, *J* = 14.4, 3.7 Hz), 1.73 (t, 3H, *J* = 2.5 Hz), 1.77-1.88 (m, 2H), 2.07-2.13 (m, 2H), 3.07 (s, 3H), 3.64 (br s, 1H), 3.78 (s, 3H), 3.81 (dd, 1H, *J* = 9.3, 4.7 Hz), 3.83-3.89 (m, 1H), 4.12-4.26 (m, 4H), 4.94 (d, 1H, *J* = 15.2 Hz), 6.86 (app. d, 2H, *J* = 8.5 Hz), 7.17 (app. d, 2H, *J* = 8.5 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 3.4, 18.8, 24.9, 32.5, 34.6, 37.4, 46.2, 47.9, 53.8, 55.3, 63.6, 64.2, 65.2, 75.9, 78.5, 102.1, 114.2, 128.1, 128.9, 158.9, 159.3; MS (EI) *m*/*z* (rel. intensity): 417 (0.3), 211 (53), 193 (8), 179 (19), 161 (15), 151 (9), 138 (7), 137 (80), 121 (100), 119 (56), 111 (17), 109 (10), 95 (14), 93 (10), 91 (13); HRMS (ESI) *m*/*z* 440.2046 $(M + Na)^+$; calcd. for $C_{23}H_{31}NO_6$ + Na: 440.2049.

Isomer 22β: $[\alpha]_D^{20}$ = +30.0 (*c* 0.41, $CHCl_3$); IR (ATR) 3442, 2970, 2946, 1739, 1612, 1513, 1440, 1413, 1365, 1229, 1217, 1175, 1141, 1113, 1082, 1022, 963, 819, 751 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.20 (ddd, 1H, *J* = 11.8 Hz), 1.27-1.35 (m, 1H), 1.39-1.49 (m, 1H), 1.52-1.61 (m, 3H), 1.74 (t, 3H, *J* = 2.5 Hz), 1.92-2.03 (m, 2H), 2.07-2.13 (m, 2H), 2.53 (br s, 1H), 2.97 (s, 3H), 3.47-3.55 (m, 1H), 3.79 (s, 3H), 3.85 (dd, 1H, *J* = 7.3, 6.8 Hz), 4.03 (dddd, 1H, *J* = 10.4, 10.4, 4.3, 4.3 Hz), 4.18-4.26 (m, 3H), 4.92 (d, 1H, *J* = 15.3 Hz), 6.86 (app. d, 2H, *J* = 8.6 Hz), 7.18 (app. d, 2H, *J* = 8.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 3.4, 18.8, 24.9, 34.7, 36.9, 40.1, 46.1, 47.7, 53.5, 55.3, 64.3, 69.8, 75.9, 78.6, 101.8, 114.2, 128.4, 128.9, 159.2; MS (EI) *m*/*z* (rel. intensity): 417 (0.5), 211 (51), 193 (7), 179 (12), 161 (21), 151 (7), 137 (64), 133 (43), 121 (100), 119 (60), 111 (18), 109 (13), 103 (15), 95 (34), 93 (11), 91 (15), 71 (11); HRMS (ESI) *m*/*z* 440.2046 $(M + Na)^+$; calcd. for $C_{23}H_{31}NO_6$ + Na: 440.2049.



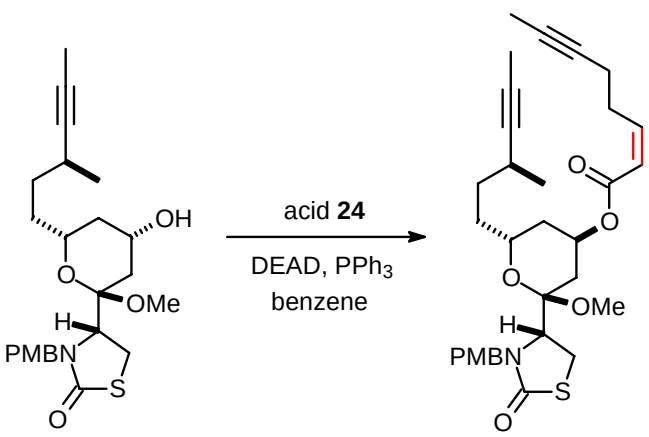
(+)-(*S*)-3-(4-Methoxybenzyl)-4-((2*R*,4*S*,6*R*)-tetrahydro-4-hydroxy-2-methoxy-6-((*S*)-3-methylhex-4-ynyl)-2H-pyran-2-yl)thiazolidin-2-one (58). $[\alpha]_D^{20}$ = +57.2 (c 0.95, $CHCl_3$). IR (neat) 3433, 2970, 2943, 1672, 1512, 1029 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.15 (d, *J* = 8.3 Hz, 2H), 6.87 (d, *J* = 8.7 Hz, 2H), 5.23 (d, *J* = 15.4 Hz, 1H), 4.22 (d, *J* = 15.4 Hz, 1H), 4.15-4.01 (m, 1H), 3.94 (dd, *J* = 8.3, 4.5 Hz, 1H), 3.80 (s, 3H), 3.59-3.47 (m, 1H), 3.39-3.31 (m, 2H), 3.01 (s, 3H), 2.40-2.28 (m, 1H), 2.10 (ddd, *J* = 12.8, 4.9, 1.9 Hz, 1H), 1.98 (dt, *J* = 12.4, 2.3 Hz, 1H), 1.76 (d, *J* = 2.6 Hz, 3H), 1.73-1.15 (m, 7H), 1.11 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.3 (C), 159.0 (C), 128.6 (C), 128.5 (CH), 114.1 (CH), 102.4 (C), 82.2 (C), 76.0 (C), 69.9 (CH), 64.6 (CH), 56.9 (CH), 55.3 (CH_3), 47.7 (CH_3), 46.7 (CH_2), 40.0 (CH_2), 37.7 (CH_2), 33.3 (CH_2), 32.8 (CH_2), 26.2 (CH_2), 25.9 (CH), 21.4 (CH_3), 3.5 (CH_3). HRMS (ESI+): calcd for $C_{24}H_{33}NNaO_5S$ (M^+ + Na): 470.1975; found 470.1977.

Diyne Formations

The synthesis of diyne **11** en route to Lat-B followed the previously described route (1).

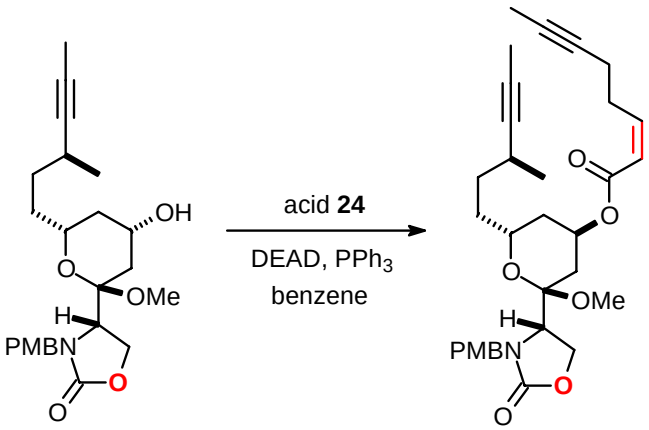
Analogues by Esterification with Inversion of Configuration.

(2*R*,4*R*,6*R*)-6-(4-Hexynyl)-2-methoxy-2-[(4*S*)-3-(4-methoxybenzyl)-2-oxo-1,3-thiazolidin-4-yl]tetrahydro-2*H*-pyran-4-yl (*Z*)-2-octen-6-ynoate (59). To a solution of alcohol **10α** (49 mg, 0.11 mmol) in benzene (5 ml) was added the acid **24** (30 mg, 0.22 mmol), triphenylphosphine (286 mg, 1.1 mmol) and DEAD (85 µL, 0.55 mmol) at room temperature. The reaction was allowed to stir overnight before the solvent was evaporated and the residue purified by flash chromatography (4:1 & 8:1, hexane:EtOAc) to give the title compound as a colorless oil



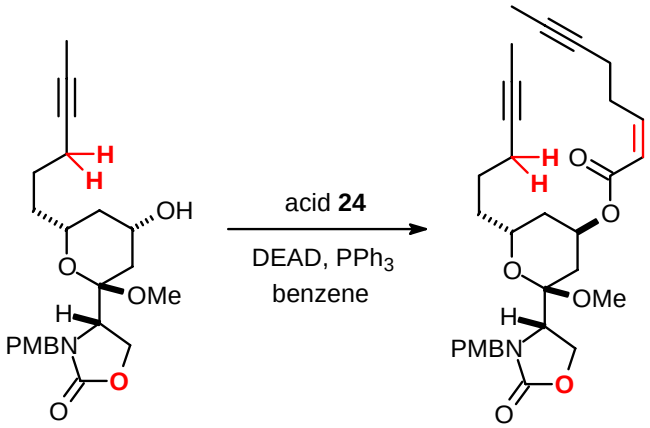
(38 mg, 61%). $[\alpha]_D^{20}$ = +33 (*c* 0.18, $CHCl_3$); IR (ATR) 2919, 1742, 1708, 1671, 1611, 1512, 1443, 1402, 1371, 1286, 1240, 1195, 1170, 1122, 1090, 1030, 821, 759 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.20 (d, 3H, *J* = 6.9 Hz), 1.75-189 (m, 10H), 1.94 (dd, 1H, *J* = 15.0, 4.3 Hz), 2.13 (ddd, 1H, *J* = 15.0, 1.9, 1.9 Hz), 2.24-2.34 (m, 3H) 2.41-2.48 (m, 1H), 2.84 (dd, 2H, *J* = 7.2, 1.7 Hz) 3.09 (s, 3H), 3.24 (d, 1H, *J* = 6.2 Hz), 3.78-3.84 (m, 4H), 3.88-3.96 (m, 1H), 4.20-4.34 (m, 3H), 5.12 (d, 1H, *J* = 14.3 Hz), 5.21-5.26 (m, 1H), 5.82 (dd, 1H, *J* = 11.6, 1.7 Hz), 6.30 (dd, 1H, *J* = 11.6, 7.3 Hz), 6.89 (app. d, 2H, *J* = 8.6 Hz) 7.27 (app. d, 2H, *J* = 8.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 3.5, 3.6, 18.6, 21.9, 25.4, 26.3, 28.5, 30.2, 33.5, 34.2, 34.8, 47.5 (2x), 55.3, 59.2, 66.1, 66.2, 76.4 (2x), 78.1, 83.3, 101.7, 114.1 (2x), 121.3, 128.9, 129.9 (2x), 147.9, 159.2, 165.9, 173.2; MS (EI) *m*/*z* (rel. intensity): 398 (2), 345 (18), 207 (49), 175 (21), 147 (27), 133 (32), 121 (100), 93 (11), 91 (11); HRMS (EI) *m*/*z* 590.2552 $(M + Na)^+$; calcd. for $C_{32}H_{41}NO_6S$ + Na: 590.2552.

(2*R*,4*R*,6*R*)-2-Methoxy-2-[(4*S*)-3-(4-methoxybenzyl)-2-oxo-1,3-oxazolidin-4-yl]-6-[(3*S*)-3-methyl-4-hexynyl]tetrahydro-2*H*-pyran-4-yl (*Z*)-2-octen-6-ynoate (60). Prepared as described above from alcohol **19** (100 mg, 0.23 mmol) and acid **24** (95 mg, 0.69 mmol) as a colorless syrup (53 mg, 42%). $[\alpha]_D^{20}$ = +60 (*c* 0.05, $CHCl_3$); IR (ATR) 2962, 1748, 1712, 1611, 1512, 1414, 1366, 1288, 1229, 1166, 1097, 1072, 1022, 865, 801, 766, 720 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.21 (d, 3H, *J* = 6.7 Hz), 1.42-1.64 (m, 3H), 1.76-1.92 (m, 10H), 1.98 (br d, 1H, *J* = 15.0 Hz), 2.24-2.31 (m, 2H), 2.41-2.49 (m 1H), 2.83 (dd, 2H, *J* = 7.3, 1.6 Hz), 3.09 (s, 3H), 3.79 (dd, 1H, *J* = 9.6, 5.3 Hz), 3.83 (s, 3H), 3.89-3.97 (m, 1H), 4.12 (app. t, 1H, *J* = 9.5 Hz), 4.18 (dd, 1H, *J* = 9.5, 5.3 Hz), 4.24 (d, 1H, *J* = 14.3 Hz), 4.81 (d, 1H, *J* = 14.3 Hz), 5.22-5.27 (m, 1H), 5.82 (dd, 1H, *J* = 11.6, 1.6 Hz), 6.31 (dd, 1H, *J* = 11.6, 7.3 Hz), 6.90 (app. d, 2H, *J* = 8.6 Hz), 7.33 (app d., 2H, *J* = 8.6 Hz); ^{13}C NMR (150 MHz, $CDCl_3$) δ 1.0, 3.4, 3.6, 18.5, 21.8, 26.2, 28.5, 29.3, 33.3, 34.1, 34.7, 46.7, 47.9, 55.3, 56.2, 63.0, 65.9, 66.0, 76.3, 78.0, 83.2, 100.2, 114.0, 121.1, 128.3, 130.3, 145.0, 159.0, 159.3, 165.8; MS (EI) *m*/*z* (rel.

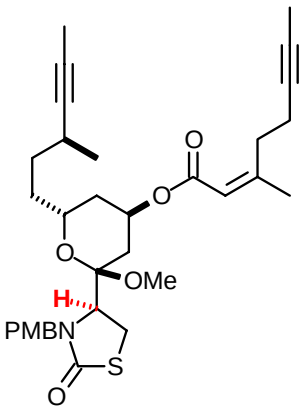


intensity): 382 (4), 345 (17), 225 (4), 207 (49), 175 (18), 147 (26), 133 (28), 121 (100); HRMS (ESI) *m*/*z* 574.2780 $(M + Na)^+$; calcd. for $C_{32}H_{41}NO_7$ + Na: 574.2780.

(2*R*,4*R*,6*R*)-6-(4-Hexynyl)-2-methoxy-2-[(4*S*)-3-(4-methoxybenzyl)-2-oxo-1,3-oxazolidin-4-yl]tetrahydro-2*H*-pyran-4-yl (*Z*)-2-octen-6-ynoate (61). Prepared as described above from



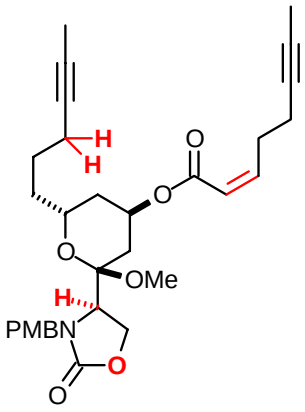
alcohol **21** (100 mg, 0.24 mmol) and acid **24** (133 mg, 0.96 mmol). Colorless syrup (83 mg, 65%). $[\alpha]_D^{20} = +39$ (*c* 0.16, $CHCl_3$); IR (ATR) 2919, 1747, 1712, 1611, 1513, 1437, 1414, 1368, 1230, 1165, 1130, 1098, 1073, 1036, 919, 820, 766, 753, 731 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.44-1.68 (m, 3H), 1.766 (t, 3H, *J* = 2.5 Hz), 1.776 (t, 3H, *J* = 2.5 Hz), 1.79-1.87 (m, 4H), 1.97 (ddd, 1H, *J* = 15.0, 1.8, 1.8 Hz), 2.20-2.31 (m, 4H), 2.82 (ddd 2H, *J* = 7.2, 1.6 Hz), 3.09 (s, 3H), 3.79 (dd, 1H, *J* = 9.7, 5.3 Hz), 3.81 (s, 3H), 3.90-3.98 (m, 1H), 4.11 (app. t, 1H, *J* = 9.5 Hz), 4.18 (dd, 1H, *J* = 9.5, 5.3 Hz), 4.23 (d, 1H, *J* = 14.4 Hz), 4.79 (d, 1H, *J* = 14.4 Hz), 5.20-5.25 (m, 1H), 5.81 (dd, 1H, *J* = 11.6, 1.7 Hz), 6.31 (dd, 1H, *J* = 11.6, 7.3 Hz), 6.88 (app. d, 2H, *J* = 8.6 Hz), 7.29 (app. d, 2H, *J* = 8.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 3.5, 3.6, 18.6, 18.9, 25.3, 28.6, 29.4, 34.7, 35.3, 46.8, 47.9, 55.3, 56.4, 63.1, 65.9, 66.0, 76.2, 76.4, 78.1, 78.6, 100.3, 114.1, 121.2, 128.4, 130.2, 148.2, 159.0, 159.4, 165.8; MS (EI) *m*/*z* (rel. intensity): 368 (5), 331 (20), 211 (4), 193 (41), 161 (15), 133 (30), 121 (100), 119 (21), ; HRMS (ESI) *m*/*z* 560.2623 $(M + Na)^+$; calcd. for $C_{31}H_{39}NO_7$ + Na: 560.2624.



(+)-(*Z*)-(2*R*,4*R*,6*R*)-2-((*S*)-3-(4-methoxybenzyl)-2-oxothiazolidin-4-yl)-tetrahydro-2-methoxy-6-((*S*)-3-methylhex-4-ynyl)-2H-pyran-4-yl 3-methyloct-2-en-6-ynoate (62). $[\alpha]_D^{20} = +59.0$ (c 1.04, $CHCl_3$). IR (neat) 2973, 1704, 1676, 1513, 1082 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.15 (d, *J* = 8.3 Hz, 2H), 6.86 (d, *J* = 8.7 Hz, 2H), 5.72 (d, *J* = 1.1 Hz, 1H), 5.24-5.11 (m, 2H), 4.26 (d, *J* = 15.5 Hz, 1H), 3.90 (dd, *J* = 9.4, 3.8

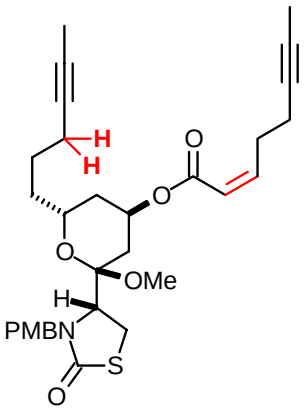
Hz, 2H), 3.80 (s, 3H), 3.41-3.18 (m, 2H), 3.09 (s, 3H), 2.89-2.72 (m, 2H), 2.40-2.29 (m, 3H), 2.03 (d, *J* = 3.4 Hz, 2H), 1.96 (d, J = 1.1 Hz, 3H), 1.86-1.78 (m, 1H), 1.77-1.74 (m, 6H), 1.73-1.34 (m, 5H), 1.11 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.0 (C), 165.7 (C), 159.0 (C), 158.0 (C), 128.8 (C), 128.6 (CH), 117.8 (CH), 114.1 (CH), 100.6 (C), 83.3 (C), 78.5 (C), 77.2 (C), 76.2 (C), 76.0 (C), 65.5 (CH), 65.4 (CH), 57.6 (CH), 55.3 (CH_3), 47.8 (CH_3), 46.9 (CH_2), 34.3 (CH_2), 33.4 (CH_2), 32.8 (CH_2), 32.7 (CH_2), 31.4 (CH_2), 26.3 (CH_2), 26.0 (CH), 25.6 (CH_3), 21.4 (CH_3), 17.9 (CH_2), 3.5 (CH_3). HRMS (ESI+): calcd. for $C_{33}H_{43}NnaO_6S$ (M^+ + Na): 604.2705; found 604.2709.

(+)-(*Z*)-(2*R*,4*R*,6*R*)-2-((*R*)-3-(4-Methoxybenzyl)-2-oxo-oxazolidin-4-yl)-6-(hex-4-ynyl)-tetrahydro-2-methoxy-2H-pyran-4-yl oct-2-en-6-ynoate (63). $[\alpha]_D^{20}$ = +57.7 (c 1.02, $CHCl_3$). IR



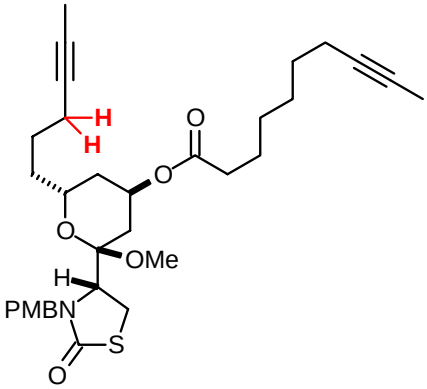
(neat) 2920, 1749, 1709, 1513, 1030 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19 (d, *J* = 8.6 Hz, 2H), 7.00 (dt, *J* = 15.7, 6.6 Hz, 1H), 6.85 (d, *J* = 8.6 Hz, 2H), 5.88 (dt, *J* = 15.7, 1.5 Hz, 1H), 5.19 (m, 1H), 4.88 (d, *J* = 15.2 Hz, 1H), 4.25-4.08 (m, 2H), 4.21 (d, *J* = 15.2 Hz, 1H), 3.91-3.83 (m, 1H), 3.83-3.77 (m, 1H), 3.79 (s, 3H), 3.07 (s, 3H), 2.44-2.37 (m, 2H), 2.35-2.27 (m, 2H), 2.15-2.08 (m, 2H), 1.96 (dt, *J* = 15.2, 1.9 Hz, 1H), 1.86-1.79 (m, 1H), 1.78 (t, *J* = 2.5 Hz, 3H), 1.74 (t, *J* = 2.5 Hz, 3H), 1.64 (dd, *J* = 15.2, 4.3 Hz, 2H), 1.57-1.41 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.7 (C), 159.2 (C), 159.0 (C), 147.4 (CH), 129.0 (CH), 128.5 (C), 122.5 (CH), 114.1 (CH), 99.9 (C), 78.5 (C), 77.5 (C), 76.6 (C), 75.9 (C), 66.6 (CH), 65.3 (CH), 64.2 (CH_2), 55.2 (CH_3), 54.2 (CH), 47.8 (CH_3), 46.2 (CH_2), 34.6 (CH_2), 34.2 (CH_2), 31.7 (CH_2), 30.7 (CH_2), 24.9 (CH_2), 18.8 (CH_2), 17.9 (CH_2), 3.4 (CH_3), 3.4 (CH_3). HRMS (ESI+): calcd. for $C_{31}H_{39}NNaO_7$ (M^+ + Na): 560.2624; found 560.2621.

Compound 64. Colorless syrup (38 mg, 52%). $[\alpha]_D^{20}$ = +32.6 (c 0.49, CH_2Cl_2). IR (neat) 2950, 2918, 1710, 1673, 1611, 1585, 1513, 1248, 1216, 1196, 1172, 1096, 824, 664 cm^{-1}; ^1H NMR (400 MHz, CD_2Cl_2) δ 7.21 (d, *J* = 8.6 Hz, 2H), 6.86 (d, *J* =8.0 Hz, 2H), 6.27 (dt, *J* = 11.6, 7.4 Hz, 1H),



5.76 (dt, *J* = 11.6, 1.8 Hz, 1H), 5.18 (m, 1 H), 5.00 (d, *J* = 14.6 Hz, 1H), 4.29 (d, *J* = 15.3 Hz, 1H), 3.91 (m, 1H), 3.82 (dd, *J* = 8.0, 4.2 Hz, 1H), 3.78 (s, 3H), 3.30-3.19 (m, 2H), 3.08 (s, 3H), 2.79 (qt, *J* = 7.2, 1.8 Hz, 2H), 2.28-2.17 (m, 4H), 2.07 (dt, *J* = 14.9, 2.1 Hz, 1H), 1.90 (dd, *J* = 14.9, 4.3 Hz, 1H), 1.83-1.70 (m, 3H), 1.74 (s, 3H), 1.72 (s, 3H), 1.67-1.49 (m, 3H); ^{13}C NMR (100 MHz, CD_2Cl_2) δ 169.2 (C), 166.4 (C), 159.9 (C), 148.4 (CH), 130.4 (2x CH), 129.7 (C), 121.9 (CH), 114.7 (2x CH), 102.3 (C), 79.3 (C), 78.7 (C), 76.9 (C), 76.6 (C), 66.8 (CH), 66.7 (CH), 60.1 (CH), 56.0 (CH_3), 48.1 (CH_3), 48.0 (CH_2), 36.0 (CH_2), 35.3 (CH_2), 30.8 (CH_2), 29.3 (CH_2), 26.1 (CH_2), 26.1 (CH_2), 19.5 (CH_2), 19.2 (CH_2), 4.0 (CH_3), 3.9 (CH_3). MS (EI) *m*/*z* (rel. intensity): (%) 384 (3), 331 (21), 193 (39), 161 (15), 133 (28), 121 (100), 93 (10), 91 (11), 77 (8), 55 (7). HRMS (ESI+): calcd. for $C_{31}H_{39}NNaO_6S$ (M^+ + Na): 576.2396; found 576.2390.

Compound 65. Colorless syrup (32 mg, 32%). $[\alpha]_D^{20}$ = +30.0 (c 0.3, CH_2Cl_2). ^1H NMR (400 MHz, CD_2Cl_2) δ 7.20 (d, *J* = 9.1 Hz, 2H), 6.86 (d, *J* = 8.4 Hz, 2H), 5.07 (m, 1H), 4.99 (d, *J* = 14.6 Hz, 1H), 4.28 (d, *J* = 14.6 Hz, 1H), 3.91 (m, 1H), 3.80 (dd, *J* =9.3, 2.8 Hz, 1H), 3.77 (s, 3H),

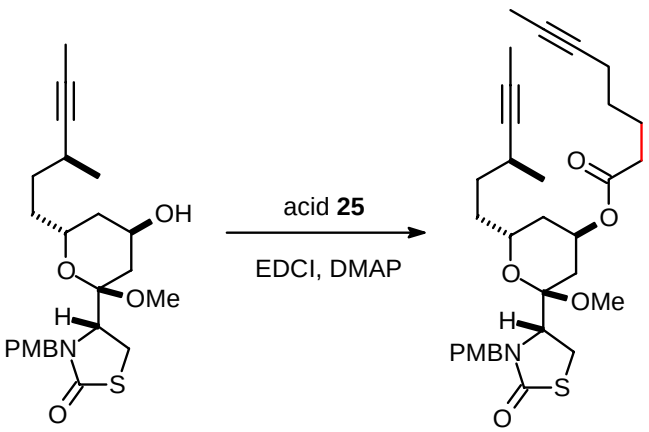


3.25 (dd, *J* = 11.8, 9.3 Hz, 1H), 3.20 (dd, *J* = 11.8, 3.4 Hz, 1H), 3.07 (s, 3H), 2.27-2.24 (m, 2H), 2.22-2.17 (m, 2H), 2.10-2.05 (m, 6H), 1.84 (dd, *J* = 15.2, 4.6 Hz, 1H), 1.74 (s, 3H), 1.72 (s, 3H), 1.83-1.30 (m, 11H); ^{13}C NMR (100 MHz, CD_2Cl_2) δ 173.7(C), 173.4 (C), 160.0 (C), 130.4 (2CH), 129.8 (CH), 114.7 (2CH), 102.3 (C), 79.8 (C), 79.3 (C), 76.4 (C), 75.9 (C), 66.9 (CH), 66.7 (CH), 60.1 (CH), 56.0 (CH_3), 48.1 (CH_3), 48.0 (CH_2), 36.0 (CH_2), 35.1 (CH_2), 35.4 (CH_2), 30.6 (CH_2), 29.7 (CH_2), 29.3 (CH_2), 26.2 (CH_2), 26.0 (CH_2), 25.6 (CH_2), 19.5 (CH_2), 19.3 (CH_2), 4.0 (CH_3), 3.9 (CH_3). MS (EI) *m*/*z* (rel. intensity): (%) 384 (4), 361 (42), 211 (37), 193 (90), 179

(13), 161(33), 133 (72), 121 (100), 109 (47). HRMS (ESI+): calcd. for $C_{33}H_{46}NO_6S_1$ (M^+ + H): 584.3046; found 584.3049.

Esterifications with Retention of Stereochemistry.

Compound 66. To a solution of **10β** (18 mg, 0.040 mmol) in CH_2Cl_2 (2 ml) were added acid **25** (6 mg, 0.040 mmol), DMAP (15 mg, 0.121 mmol), and EDCI·HCl (23 mg, 0.121 mmol). Two additional portions of acid **25** (6 mg each) were added after stirring for 1 and 2 h, respectively.



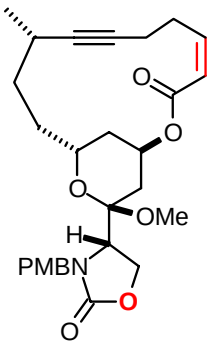
After stirring over night, the mixture was diluted with CH_2Cl_2 and extracted with aq. HCl (10%). The aqueous layer was extracted with CH_2Cl_2 and the combined organic phases were successively washed with aq. NaOH (10%), aq. HCl (10%), sat. aq. NH_4Cl, and brine. After drying (Na_2SO_4), the solvent was evaporated and the residue was purified by flash chromatography (ethyl acetate/hexane 1/5) to give diyne **66** as a colorless oil (18 mg, 78%). $[\alpha]_D^{20} = +50.7°$ (c=0.9, CH_2Cl_2). IR (ATR) 2943, 1727, 1673, 1512, 1247, 1092, 1032 cm^{-1}; ^1H NMR (400 MHz, CD_2Cl_2) δ 1.18 (d, 3H, *J* = 6.8 Hz), 1.4–1.9 (m, 17H), 2.06–2.16 (m, 3H), 2.29 (t, 2H, *J* = 7.5 Hz), 2.39–2.48 (m, 1H), 3.08 (s, 3H), 3.20–3.30 (m, 2H), 3.78–3.82 (m, 1H), 3.79 (s, 3H), 3.89–3.94 (m, 1H), 4.30 (d, 1H, *J* = 14.4 Hz), 5.03 (d, 1H, *J* = 14.4 Hz), 5.07–5.11 (m, 1H), 6.88 (d, 2H, *J* = 8.6 Hz), 7.25 (d, 2H, *J* = 8.6 Hz); ^{13}C NMR (100 MHz, CD_2Cl_2) δ 3.2, 3.3, 18.4, 21.6, 24.2, 25.4, 26.2, 28.5, 29.9, 33.4, 34.1, 34.3, 34.7, 47.3, 47.4, 55.3, 59.4, 66.1, 66.4, 75.5, 76.1, 83.3, 101.6, 114.0, 129.0, 129.8, 159.2, 172.7, 172.8; HRMS: ($C_{32}H_{43}N_1Na_1O_2S_1$, M + Na) calcd.: 592.270880, found: 592.27117.

Ring-Closing Alkyne Metathesis Reactions (RCAM)

The RCAM leading to Lat-A and Lat-B are described in refs. 1 and 2. For the formation of the "bare macrocycle" **36** by RCAM with [(*t*Bu)(Ar)N]$_3$Mo (**29**)/CH_2Cl_2 as the catalyst, see ref. 8.

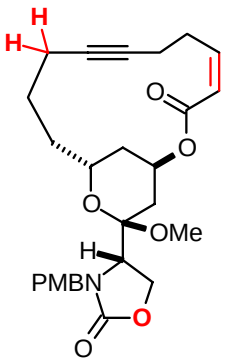
(4*R*)-3-(4-Methoxybenzyl)-4-[(1*R*,10*S*,13*R*,15*R*)-15-methoxy-10-methyl-3-oxo-2,14-dioxabicyclo[11.3.1]heptadec-4-en-8-yn-15-yl]-1,3-thiazolidin-2-one (67). Argon was bubbled through a toluene (62 ml, 0.001 M) solution of diyne **59** (35 mg, 61.6 μmol) for 1 h. Schrock's catalyst (*t*BuO)$_3$W≡CCMe$_3$ (**28**) was added (9 mg, 30 mol%) and the reaction stirred at 80°C for 2.5 h. Air was bubbled through the reaction for 10 min before the solvent was vaporated. The residue was purified by flash chromatography (4:1, hexane:EtOAc) to give cycloalkyne **67** as a colorless solid (13 mg, 41%). $[\alpha]_D^{20} = +43$ (*c* 0.09, $CHCl_3$); IR (film) 3059, 3031, 2961, 2933, 2874, 2836, 1702, 1667, 1610, 1584, 1512, 1449, 1403, 1374, 1356, 1326, 1290, 1247, 1215, 1197, 1173, 1125, 1091, 1049, 1031, 976, 829, 733, 661 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.15 (d, 3H, *J* = 6.9 Hz), 1.33-1.50 (m, 2H), 1.72-1.90 (m, 3H), 1.98 (dd, 1H, *J* = 15.0, 4.3 Hz), 2.09-2.15 (br d, 1H, *J* = 14.3 Hz), 2.16-2.25 (m, 2H), 2.31-2.55 (m, 3H), 3.16 (s, 3H), 3.24 (d, 2H, *J* = 6.6 Hz), 3.37-3.47 (m, 1H), 3.82 (s, 3H), 3.80-3.87 (m, 1H), 4.30 (d, 1H, *J* = 14.2 Hz), 4.90-4.97 (m, 1H), 5.09 (d, 1H, *J* = 14.2 Hz), 5.33 (br s, 1H), 5.81 (d, 1H, *J* = 11.8 Hz), 6.21 (dd, 1H, *J* = 11.8, 6.8 Hz), 6.87 (app. d, 2H, *J* = 8.6 Hz), 7.24 (app. d, 2H, *J* = 8.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.1, 22.2, 25.3, 26.7, 28.2, 30.0, 30.8, 33.7, 34.3, 47.4, 47.5, 55.3, 58.9, 65,3, 67.2, 80.6, 85.9, 101.9, 114.0, 122.9, 128.8, 130.1, 146.0, 159.1, 166.1, 173.0; MS (EI) *m*/*z* (rel. intensity): 482 (0.5), 291 (100), 273 (24), 241 (18), 231 (9), 223 (6), 217 (6), 213 (15), 199 (22), 189 (19), 145 (10), 121 (93), 91 (12), 79 (11), 77 (10), 55 (13); HRMS (ESI) *m*/*z* 536.2079 (M + Na)$^+$; calcd. for $C_{28}H_{35}NO_6S$ + Na: 536.2082.

(4*S*)-3-(4-Methoxybenzyl)-4-[(1*R*,10*S*,13*R*,15*R*)-15-methoxy-10-methyl-3-oxo-2,14-dioxabicyclo[11.3.1]heptadec-4-en-8-yn-15-yl]-1,3-oxazolidin-2-one (68). Prepared



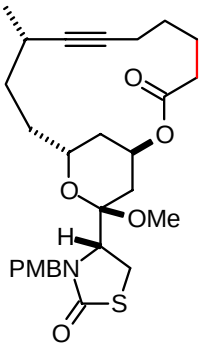
analogously from diyne **60** (45 mg, 82 μmol). Flash chromatography (1:1, hexane:EtOAc) afforded cycloalkyne **68** as a white solid (36 mg, 87%). $[\alpha]_D^{20}$ = +44 (*c* 0.09, $CHCl_3$); IR (ATR) 2955, 1733, 1693, 1609, 1509, 1444, 1413, 1397, 1375, 1346, 1281, 1217, 1170, 1130, 1092, 1073, 1025, 945, 889, 876, 828, 769, 751, 720 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.16 (d, 3H, *J* = 7.0 Hz), 1.26-1.36 (m, 2H), 1.39-1.49 (m, 1H), 1.72-1.91 (m, 4H), 2.05 (ddd, 1H, *J* = 16.9, 1.9 Hz), 2.09-2.16 (m, 1H), 2.17-2.25 (m, 1H), 2.30-2.46 (m, 2H), 2.47-2.56 (m, 1H), 3.16 (s, 3H), 3.33-3.46 (m, 1H), 3.80-3.86 (m, 1H), 3.82 (s, 3H), 4.12 (d, 1H, *J* = 9.5 Hz), 4.18 (dd, 1H, *J* = 9.5, 5.4 Hz), 4.27 (d, 1H, *J* = 14.3 Hz), 4.77 (d, 1H, *J* = 14.3 Hz), 4.91-4.99 (m, 1H), 5.3-5.35 (m, 1H), 5.81 (d, 1H, *J* = 11.7 Hz), 6.21 (ddd, 1H, *J* = 11.7, 10.5, 6.8 Hz), 6.79 (app. d, 2H, *J* = 8.6 Hz), 7.22 (app. d, 2H, *J* = 8.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.2, 22.3, 26.8, 28.4, 29.4, 30.9, 33.8, 34.3, 46.8, 48.0, 55.4, 56.3, 63.1, 65.3, 67.2, 80.7, 86.0, 100.7, 114.1, 122.9, 128.5, 130.4, 146.1, 159.0, 159.4, 166.2; MS (EI) *m*/*z* (rel. intensity): 466 (1), 291 (81), 273 (18), 241 (14), 223 (5), 213, (11), 199 (19), 121 (100); HRMS (ESI) *m*/*z* 520.2312 $(M + Na)^+$; calcd. for $C_{28}H_{35}NO_7$ + Na: 520.2311.

(4*S*)-3-(4-methoxybenzyl)-4-[(1*R*,13*R*,15*R*)-15-methoxy-3-oxo-2,14-dioxabicyclo[11.3.1] heptadec-4-en-8-yn-15-yl]-1,3-oxazolidin-2-one (69). Prepared analogously from diyne **61** (50



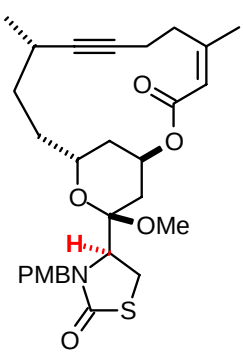
mg, 93 μmol). Flash chromatography (2:1, hexane:EtOAc) afforded cycloalkyne **69** as a cream solid (34 mg, 76%). $[\alpha]_D^{20}$ = +59 (*c* 0.1, $CHCl_3$); IR (ATR) 2931, 2862, 1740, 1694, 1611, 1514, 1446, 1424, 1410, 1355, 1323, 1292, 1245, 1208, 1142, 1114, 1093, 1068, 1028, 998, 963, 914, 894, 844, 826, 811, 765, 719 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.37 (ddd, 1H, *J* = 14.2, 11.7, 2.5 Hz), 1.59-1.74 (m, 2H), 1.76-1.97 (m, 3H), 2.05 (m, 2H), 2.16-2.25 (m, 1H), 2.27-2.32 (m, 2H), 2.36-2.45 (m, 2H), 3.19 (s, 3H), 3.35-3.45 (m, 1H), 3.82 (s, 3H), 3.85 (dd, *J* = 9.6, 5.3 Hz), 4.12 (dd, 1H, *J* = 9.6, 9.5 Hz), 4.19 (dd, 1H, *J* = 9.4, 5.3 Hz), 4.28 (d, 1H, *J* = 14.3 Hz), 4.78 (d, 1H, *J* = 14.3 Hz), 4.99 (dd, 1H, *J* = 11.9, 6.2 Hz), 5.30-5.35 (m, 1H), 5.81 (d, 1H, *J* = 11.7 Hz), 6.20 (ddd, 1H, *J* = 11.7, 11.0, 6.9 Hz),

6.87 (app. d, 2H, J = 8.6 Hz), 7.29 (app. d, 2H, J = 8.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.2, 19.8, 22.3, 28.4, 29.4, 34.3, 36.5, 46.8, 48.1, 55.4, 56.3, 63.1, 65.6, 67.3, 81.1, 81.7, 100.7, 114.1, 122.9, 128.5, 130.4, 146.1, 159.0, 159.4, 166.2; MS (EI) *m*/*z* (rel. intensity): 452 (1), 278 (18), 277 (100), 259 (16), 227 (22), 217 (5), 203 (5), 199 (18), 185 (17), 183 (2), 181 (5), 177 (3), 175 (15), 167 (5), 159 (8), 157 (8), 134 (4), 131 (10), 121 (95), 117 (7), 91 (14); HRMS (ESI) *m*/*z* 506.2158 $(M + Na)^+$; calcd. for $C_{27}H_{33}NO_7$ + Na: 506.2154.



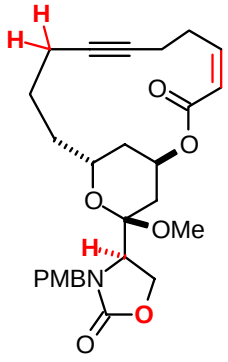
Compound 70. Prepared analogously from diyne **66**. Flash chromatography (ethyl acetate/hexane, 1/4) afforded cycloalkyne **70** as white crystals (8.6 mg, 73% yield). $[\alpha]_D^{20}$ = +64.8° (*c* 0.8, CH_2Cl_2). IR (ATR) 2933, 1725, 1672, 1512, 1446, 1248, 1093, 1031 cm^{-1}; ^{1}H NMR (400 MHz, CD_2Cl_2) δ 1.16 (d, 3H, J = 7.1 Hz), 1.32–1.45 (m, 3H), 1.68–1.85 (m, 6H), 1.92 (dd, 1H, J = 4.3, 14.9 Hz), 1.91–1.96 (m, 1H), 2.07 (dt, 1H, J = 2.3, 14.9 Hz), 2.18–2.21 (m, 1H), 2.25–2.31 (m, 1H), 2.37–2.44 (m, 1H), 2.54–2.64 (m, 1H), 3.17 (s, 3H), 3.21–3.30 (m, 2H), 3.79 (s, 3H), 3.84 (dd, 1H, J = 3.9, 8.3 Hz), 4.31 (d, 1H, J = 14.4 Hz), 4.60–4.67 (m, 1H), 5.00 (d, 1H, J = 14.4 Hz), 5.14–5.17 (m, 1H), 6.86 (d, 1H, J = 8.6 Hz), 7.22 (d, 1H, J = 8.6 Hz); ^{13}C NMR (100 MHz, CD_2Cl_2) δ 18.7, 22.5, 24.2, 25.5, 26.1, 28.0, 30.1, 30.4, 34.1, 34.4, 34.8, 47.4, 47.5, 55.3, 59.3, 65.0, 66.4, 81.2, 84.6, 101.9, 114.0, 129.1, 130.0, 159.2, 172.4, 172.6; MS (EI) *m*/*z* (rel. intensity): 293 (82), 275 (47), 243 (36), 191 (41), 121 (100). HRMS: ($C_{28}H_{38}N_1O_6S_1$, M+H) calcd.: 516.241986, found: 516.24222.

(+)-(*S*)-3-(4-Methoxybenzyl)-4-((*Z*,1*R*,10*S*,13*R*,15*R*)-15-methoxy-5,10-dimethyl-3-oxo-2,14-dioxa-bicyclo[11.3.1]heptadec-4-en-8-yn-15-yl)thiazolidin-2-one (71). $[\alpha]_D^{20}$ = +66.3 (*c* 1.17, $CDCl_3$). IR (neat) 2938, 1697, 1673, 1512, 1276, 1248 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.14 (d, J = 8.7 Hz, 2H), 6.85 (d, J = 8.7 Hz, 2H), 5.65 (d, J = 1.1 Hz, 1H), 5.28-5.21 (m, 1H), 5.15 (d, J = 15.1 Hz, 1H), 4.92-4.79 (m, 1H), 4.24 (d, J = 15.1 Hz, 1H), 3.90 (dd, J = 9.0, 3.8 Hz, 1H), 3.79 (s, 3H), 3.40-3.26 (m, 3H), 3.13 (s, 3H), 2.48-2.21 (m, 4H), 2.20-2.07 (m, 2H), 2.00 (dd, J = 15.4, 4.1 Hz, 1H), 1.88 (d, J = 1.5 Hz, 3H), 1.75-1.61 (m, 3H), 1.50-



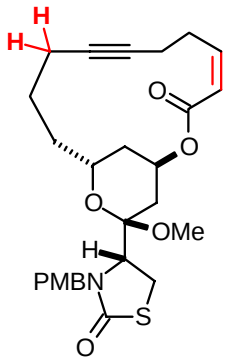
1.36 (m, 2H), 1.12 (d, J = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.9, 165.9, 159.0, 156.2, 128.9, 128.7, 119.1, 114.1, 101.0, 86.2, 80.9, 66.8, 65.0, 57.7, 55.3, 47.9, 47.0, 33.9, 33.8, 33.3, 31.2, 21.1, 26.4, 26.3, 25.1, 22.0, 19.0. HRMS (ESI+): calcd. for $C_{29}H_{37}NNaO_6S$ (M^+ + Na): 550.2235; found 550.2239.

(+)-(*R*)-3-(4-Methoxybenzyl)-4-((*Z*,1*R*,13*R*,15*R*)-15-methoxy-3-oxo-2,14-dioxa-bicyclo-[11.3.1]heptadec-4-en-8-yn-15-yl)oxazolidin-2-one (72). $[\alpha]_D^{20}$ = +46.2 (c 1.66, CH_2Cl_2). IR



(neat) 2936, 1750, 1701, 1513 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.20 (d, J = 8.3 Hz, 2H), 6.86 (d, J = 8.7 Hz, 2H), 6.27-6.15 (m, 1H), 5.81 (d, J = 11.7 Hz, 1H), 5.35-5.26 (m, 1H), 4.95-4.82 (m, 2H), 4.30-4.15 (m, 3H), 3.87 (dd, J = 9.2, 4.7 Hz, 1H), 3.79 (s, 3H), 3.50-3.35 (m, 1H), 3.14 (s, 3H), 2.51-2.35 (m, 2H), 2.27-2.16 (m, 2H), 2.03 (d, J = 14.7 Hz, 2H), 1.77-1.61 (m, 4H), 1.59-1.33 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.0, 159.2, 159.0, 146.1, 129.0, 128.5, 122.8, 114.1, 100.2, 81.6, 80.9, 66.8, 64.9, 64.3, 55.3, 54.0, 48.0, 46.2, 35.9, 34.1, 30.7, 28.4, 22.2, 19.6, 19.0. HRMS (ESI+): calcd. for $C_{27}H_{33}NNaO_7$ (M^+ + Na): 506.2155; found 506.2159.

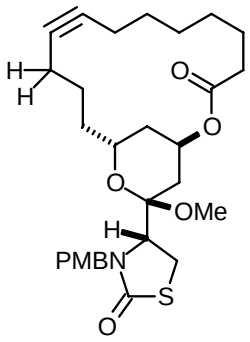
Compound 73. Colorless syrup (24 mg, 71%). $[\alpha]_D^{20}$ = +37.4 (c 0.74, CH_2Cl_2). IR (neat) 3031, 2937, 1702, 1671, 1611, 1585, 1512, 1248, 1198, 1034, 831 cm^{-1}; ^{1}H NMR (400 MHz, CD_2Cl_2) δ



7.20 (d, J = 8.6 Hz, 2H), 6.84 (d, J = 8.7 Hz, 2H), 6.19 (m, 1H), 5.72 (d, J = 11.7 Hz, 1H), 5.25 (m, 1H), 4.99 (d, J = 14.3 Hz, 1H), 4.94 (m, 1H), 4.32 (d, J = 14.4 Hz, 1H) 3.84 (dd, J = 8.6, 3.6 Hz, 1H), 3.77 (s, 3H), 3.27-3.20 (m, 2H), 3.16 (s, 3H), 2.42-2.33 (m, 2H), 2.25-2.24 (m, 2H), 2.18 (m, 1H), 2.13 (m, 1H), 1.98 (m, 1H), 1.93 (dd, J = 15.1, 4.3 Hz, 1H), 1.77 (m, 1H), 1.68-1.56 (m, 2H), 1.40 (ddd, J = 15.0, 12.0, 2.9 Hz, 1H); ^{13}C NMR (100 MHz, CD_2Cl_2) δ 173.0 (C), 166.3 (C), 159.6 (C), 146.4 (CH), 130.3 (2 CH), 129.4 (C), 123.0 (CH), 114.3 (2 CH), 102.3 (C), 82.0 (C), 81.3 (C), 67.7 (CH), 66.1 (CH), 59.6 (CH), 55.6 (CH_3), 47.9 (CH_3), 47.8 (CH_2), 36.8 (CH_2), 34.6 (CH_2), 30.4 (CH_2), 28.8 (CH_2), 25.8 (CH_2), 22.8 (CH_2), 20.0 (CH_2), 19.4 (CH_2). MS (EI) *m*/*z* (rel. intensity): 277 (97), 259 (16), 227 (23),

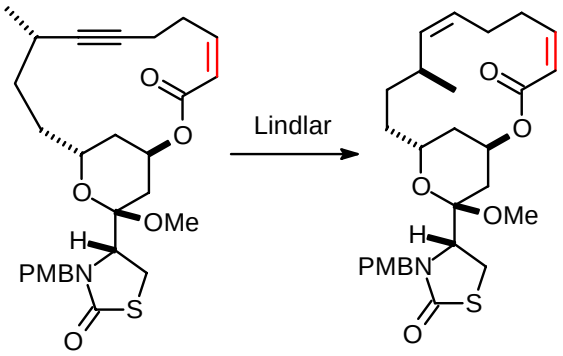
199 (19), 185 (17), 175 (15), 135 (15), 121 (100), 91 (14). HRMS (ESI+): calcd. for $C_{27}H_{34}NO_6S_1$ (M^+ + H): 500.2107; found 500.2108.

Compound 74. Colorless syrup (15 mg, 58%). $[\alpha]_D^{20}$ = +53.5 (c 0.65, CH_2Cl_2). ^{1}H NMR (400 MHz, CD_2Cl_2) δ 7.18 (d, *J* = 8.5 Hz, 2H), 6.85 (d, *J* = 9.3 Hz, 2H), 5.18 (m, 1H), 5.00 (d, *J* = 15.2 Hz, 1H), 4.30 (d, *J* = 13.5 Hz, 1H), 4.05 (t, *J* = 10.8 Hz, 1H), 3.83 (dd, *J* =9.0, 3.8 Hz, 1H), 3.77 (s, 3H), 3.31-3.21 (m, 2H), 3.17 (s, 3H), 2.43 (ddd, *J* = 14.7, 7.9, 3.6 Hz, 1H), 2.40 (m, 1H), 2.26-2.14 (m, 3H), 2.11-2.05 (m, 1H), 1.99 (dt, *J* = 14.8, 2.0 Hz, 1H), 1.93 (dd, *J* = 14.7, 4.0 Hz, 1H), 1.83-1.63 (m, 7H), 1.59-1.51 (m, 2H), 1.45 (ddd, *J* = 14.4, 11.6, 2.8 Hz, 1H), 1.40-1.32 (m, 3H); ^{13}C NMR (100 MHz, CD_2Cl_2) δ 173.5 (C), 173.4 (C), 160.0 (C), 130.4 (2CH), 129.8 (CH), 114.7 (2CH), 102.4 (C), 82.4 (C), 80.2 (C), 66.8 (CH), 65.7 (CH), 60.2 (CH), 56.0 (CH_3), 48.3 (CH_3), 48.2 (CH_2), 36.0 (CH_2), 35.1 (CH_2), 34.0 (CH_2), 31.0 (CH_2), 29.8 (CH_2), 29.2 (CH_2), 28.5 (CH_2), 26.2 (CH_2), 24.0 (CH_2), 18.8 (CH_2), 18.1 (CH_2). MS (EI) *m*/*z* (rel. intensity): (%) 498 (1), 307 (100), 289 (11), 275 (16), 257 (28), 121 (98). HRMS (ESI+): calcd. for $C_{29}H_{39}NNaO_6S_1$ (M^+ + Na): 552.2396; found 552.2399.



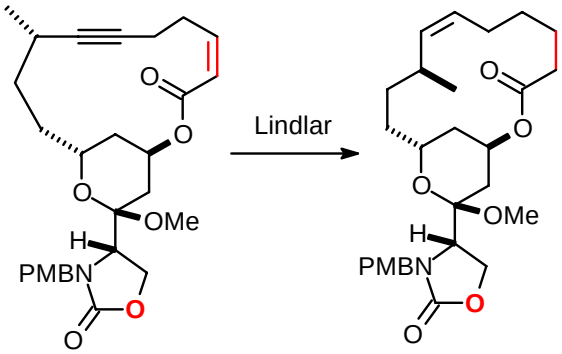
Lindlar Hydrogenations

(4*R*)-3-(4-Methoxybenzyl)-4-[(1*R*,10*S*,13*R*,15*R*)-15-methoxy-10-methyl-3-oxo-2,14-dioxabicyclo[11.3.1]heptadeca-4,8-dien-15-yl]-1,3-thiazolidin-2-one (75). Lindlar catalyst was added to a solution of cycloalkyne **67** (13 mg, 25 μmol) in CH_2Cl_2 (3 ml) and the resulting mixture was stirred vigorously under a hydrogen atmosphere (1 atm) overnight. The reaction conversion was 40% and so the catalyst and hydrogen were re-charged. After 4 days of repetitive recharging, the reaction was filtered through Celite, the filtrate was evaporated and the residue purified by flash chromatography (hexane:EtOAc, 10:1 → 8:1 → 6:1) to give alkene **75** as a colorless oil (8.5 mg, 65%). ^{1}H NMR

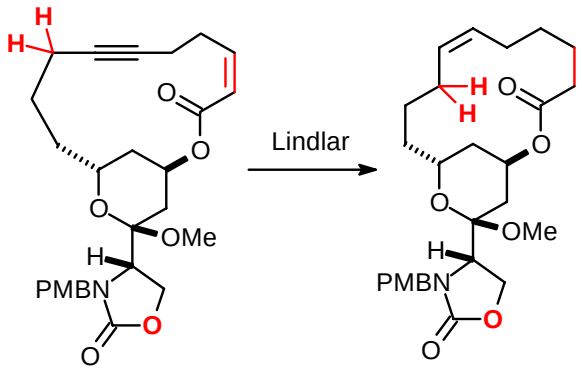


(300 MHz, $CDCl_3$) δ 0.99 (d, 3H, *J* = 6.5 Hz), 1.26-1.34 (m, 1H), 1.46-1.57 (m, 2H), 1.66-1.76 (m, 2H), 1.84 (dd, 1H, *J* = 13.2, 3.9 Hz), 1.91 (dd, 1H, *J* = 15.0, 3.7 Hz), 1.99-2.09 (m, 1H), 2.23 (dd, 1H, *J* = 11.4, 5.7 Hz), 2.29-2.40 (m, 2H), 2.66 (dd, 1H, *J* = 12.1, 3.4 Hz), 2.72-2.82 (m, 1H), 3.14 (s, 3H), 3.18-3.27 (m, 2H), 3.78-3.84 (m, 4H), 4.23-4.33 (m, 2H), 5.05-5.14 (m, 2H), 5.20 (br s, 1H), 5.33 (ddd, 1H, *J* = 11.3, 11.2, 3.2 Hz), 5.78 (d, 1H, *J* = 11.7 Hz), 6.20 (ddd, 1H, *J* = 11.7, 11.2, 6.3 Hz), 6.88 (app. d, 2H, *J* = 8.6 Hz), 7.23 (app. d, 2H, *J* = 8.6 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.2, 22.7, 25.4, 27.4, 29.3, 29.9, 31.0, 31.5, 32.4, 35.8, 47.6, 47.7, 55.4, 59.2, 63.4, 67.7, 102.4, 114.1, 122.1, 127.9, 128.9, 130.0, 130.2, 135.1, 144.6, 159.2, 166.2, 173.2.

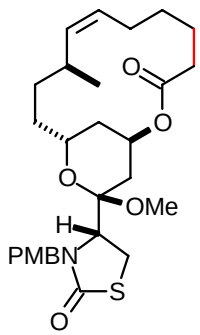
(4*S*)-3-(4-Methoxybenzyl)-4-[(1*R*,10*S*,13*R*,15*R*)-15-methoxy-10-methyl-3-oxo-2,14-dioxabicyclo[11.3.1]heptadeca-4,8-dien-15-yl]-1,3-oxazolidin-2-one (76). Lindlar catalyst was added to a solution of the cyclic alkyne **68** (30 mg, 60 μmol) in CH_2Cl_2 (5 ml) and the resulting mixture was stirred vigorously under a hydrogen atmosphere (1 atm) overnight. The reaction was filtered through Celite and the filtrate was evaporated. Purification of the residue by flash chromatography (2:1, hexane:EtOAc) gave the over-reduced product **76** as a colorless oil (23 mg, 76%). $[\alpha]_D^{20} = +95$ (*c* 0.08, $CHCl_3$); IR (ATR) 2930, 2861, 1749, 1727, 1612, 1513, 1438, 1366, 1325, 1242, 1226, 1174, 1152, 1131, 1112, 1092, 1041, 1023, 976, 960, 845, 820, 752 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.97 (d, 3H, *J* = 6.5 Hz), 1.20-1.38 (m, 3H), 1.44-1.69 (m, 3H), 1.71-1.93 (m, 7H), 2.12-2.28 (m, 2H), 2.61 (dd, 1H, *J* = 14.9, 4.7 Hz), 2.68-2.78 (m, 1H), 3.24 (s, 3H), 3.84 (dd, 1H, *J* = 9.8, 5.2 Hz), 3.82 (s, 3H), 3.95-4.03 (m, 1H), 4.13-4.20 (app. t, 1H, *J* = 9.5 Hz), 4.21-4.27 (m 2H), 4.79 (d, 1H, *J* = 14.4 Hz), 5.03 (app. t, 1H, *J* = 10.6 Hz), 5.22-5.27 (m, 1H), 5.44 (dd, 1H, *J* = 11.1, 4.7 Hz), 6.88 (app. d, 2H, *J* = 8.6 Hz), 7.29 (app. d, 2H, *J* = 8.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.0, 26.3, 28.5, 28.8, 29.8, 30.2, 31.3, 34.8, 34.9, 46.9, 48.1, 55.4, 56.6, 62.8, 63.1, 66.4, 100.6, 114.1, 128.4, 128.8, 130.3, 134.7, 159.4, 172.7; MS (EI) *m*/*z* (rel. intensity): 470 (3), 295 (100), 263 (15), 245 (33), 121 (85); HRMS (ESI) *m*/*z* 502.2804 $(M + H)^+$; calcd. for $C_{28}H_{39}NO_7$: 502.2804.



(4*S*)-3-(4-Methoxybenzyl)-4-[(1*R*,13*R*,15*R*)-15-methoxy-3-oxo-2,14-dioxabicyclo[11.3.1] heptadec-8-en-15-yl]-1,3-oxazolidin-2-one (77). Prepared as described above using the cyclic alkyne **69** (25 mg, 52 μmol). Flash chromatography (3:1 → 2:1, hexane:EtOAc) gave the over-reduced product **77** as a glassy solid (20 mg, 80%). IR (ATR) 2931, 2858, 1748, 1725, 1612, 1513, 1462, 1437, 1415, 1365, 1324, 1228, 1206, 1174, 1146, 1133, 1092, 1073, 1036, 974, 919, 817, 766, 753, 729 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 0.94 (d, 3H, *J* = 6.6 Hz), 1.35-1.18 (m, 4H), 1.65-1.42 (m, 3H), 1.89-1.67 (m, 6H), 2.23-2.10 (m. 2H), 2.58 (ddd, 1H, *J* = 15.0, 5.5, 4.0 Hz), 2.74-2.66 (m, 1H), 3.21 (s, 3H), 3.80 (s, 3H), 3.83-3.76 (m, 1H), 3.99-3.93 (m, 1H), 4.14 (t, 1H, *J* = 9.7 Hz), 4.23-4.20 (m, 2H), 4.76 (d, 1H, *J* = 14.3 Hz, 1H), 5.00 (t, 1H, *J* = 10.7 Hz), 5.22 (br s, 1H), 5.41 (td, 1H, *J* = 11.2, 4.8 Hz), 6.85 (d, 2H, *J* = 8.4 Hz), 7.26 (d, 2H, *J* = 8.8 Hz); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.9, 26.2, 28.4, 28.7, 29.7, 30.1, 31.2, 32.2, 34.7, 34.8, 46.8, 48.0, 55.3, 56.5, 62.7, 63.0, 66.3, 100.4, 114.0, 128.3, 128.8, 130.2, 134.5, 158.9, 159.3, 172.7; MS (EI) *m*/*z* (rel. intensity): 458 (1), 456 (2), 283 (45), 281 (100) 249 (11), 251 (4), 233 (13), 231 (35), 213 (9), 185 (6), 121 (84).

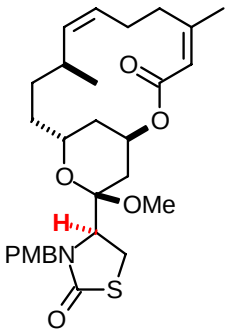


Compound 78. Prepared as described above from cycloalkyne **70** (8 mg, 0.016 mmol). Filtration of the catalyst and evaporation of the solvent provided product **78** in analytically pure form as a colorless oil (8 mg, quant.). $[\alpha]_D^{20}$ = +85.5° (c=0.8, $CHCl_3$). IR (ATR) 2926, 1728, 1674, 1513, 1248, 1091, 1031 cm^{-1}; ^{1}H NMR (400 MHz, CD_2Cl_2) δ 0.96 (d, 3H, *J* = 6.5 Hz), 1.18–1.90 (m, 11H), 1.98 (d, 2H, *J* = 3.5 Hz), 2.13–2.24 (m, 2H), 2.51–2.57 (m, 1H), 2.68–2.80 (m, 1H), 3.22 (s, 3H), 3.26–3.35 (m, 2H), 3.79 (s, 3H), 3.86 (dd, 1H, *J* = 8.9, 3.3 Hz), 3.96 (m, 1H), 4.31 (d, 1H, *J* = 14.4 Hz), 5.01 (d, 1H, *J* = 14.4 Hz), 5.02 (t, 1H, *J* = 11.0 Hz), 5.44 (dt, 1H, *J* = 11.0, 4.7 Hz), 6.88 (d, 2H, *J* = 8.8 Hz), 7.22 (d, 2H, *J* = 8.8 Hz); ^{13}C NMR (100 MHz, CD_2Cl_2) δ 21.7, 25.5, 26.2, 28.4, 28.7, 30.1, 30.5, 31.3, 32.3, 34.7, 34.9, 47.5, 47.5, 55.3,



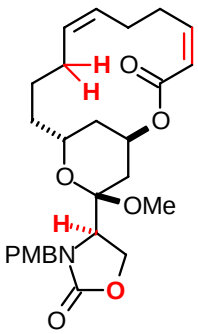
59.5, 62.8, 66.5, 101.9, 114.0, 128.8, 129.0, 129.8, 134.7, 159.3, 172.5, 172.7; MS (EI) *m/z* (rel. intensity): 295 (100), 263 (21), 245 (43), 121 (65). HRMS: ($C_{28}H_{40}N_1O_6S_1$, M+H) calcd.: 518.257636, found: 518.25753.

(+)-(*S*)-3-(4-Methoxybenzyl)-4-((1*R*,4*Z*,8*Z*,10*S*,13*R*,15*R*)-15-methoxy-5,10-dimethyl-3-oxo-2,14-dioxa-bicyclo[11.3.1]heptadeca-4,8-dien-15-yl)thiazolidin-2-one (79). $[\alpha]_D^{20}$ = +115.8 (*c*



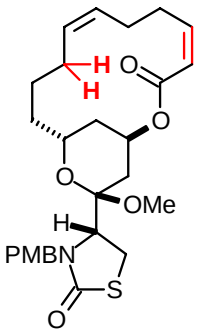
0.91, CH_2Cl_2). IR (neat) 2954, 1700, 1673, 1512, 1275, 1248, 1022 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.14 (d, *J* = 8.3 Hz, 2H), 6.86 (d, *J* = 8.8 Hz, 2H), 5.69 (d, *J* = 1.3 Hz, 1H), 5.26 (td, *J* = 11.2, 2.8 Hz, 1H), 5.18 (d, *J* = 15.7 Hz, 1H), 5.18-5.13 (m, 1H), 5.06 (td, *J* = 10.9, 1.5 Hz, 1H), 4.26 (d, *J* = 15.7 Hz, 1H), 4.20-4.08 (m, 1H), 3.90 (dd, *J* = 9.1, 4.0 Hz, 1H), 3.79 (s, 3H), 3.38-3.26 (m, 2H), 3.13 (s, 3H), 2.79-2.63 (m, 2H), 2.39-2.29 (m, 1H), 2.24 (dt, *J* = 15.4, 2.0 Hz, 1H), 2.20-2.07 (m, 2H), 1.97 (d, *J* = 15.4, 4.0 Hz, 1H), 1.91 (d, *J* = 15.4, 4.0 Hz, 1H), 1.76-1.11 (m, 6H), 0.92 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.9, 166.2, 159.0, 153.9, 135.2, 128.9, 128.4, 127.7, 118.9, 114.1, 101.3, 67.2, 63.0, 57.9, 55.3, 47.8, 46.8, 35.6, 34.9, 32.3, 31.5, 29.6, 26.5, 26.2, 24.4, 22.6, 22.0. HRMS (ESI+): calcd for $C_{29}H_{39}NNaO_6S$ (M^+ + Na): 552.2389; found 552.2396.

(+)-(*R*)-3-(4-Methoxybenzyl)-4-((1*R*,4*Z*,8*Z*,13*R*,15*R*)-15-methoxy-3-oxo-2,14-dioxa-bicyclo[11.3.1]heptadeca-4,8-dien-15-yl)oxazolidin-2-one (80). $[\alpha]_D^{20}$ = +53.3 (c 1.09, CH_2Cl_2).

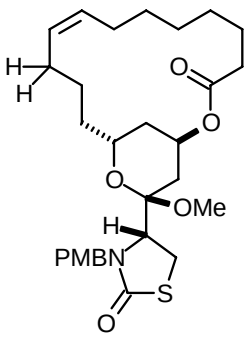


IR (neat) 2935, 1753, 1707, 1513 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.20 (d, *J* = 8.3 Hz, 2H), 6.86 (d, *J* = 8.7 Hz, 2H), 6.27-6.15 (m, 1H), 5.81 (d, *J* = 11.7 Hz, 1H), 5.35-5.26 (m, 1H), 4.95-4.82 (m, 2H), 4.30-4.15 (m, 3H), 3.87 (dd, *J* = 9.2, 4.7 Hz, 1H), 3.79 (s, 3H), 3.50-3.35 (m, 1H), 3.14 (s, 3H), 2.51-2.35 (m, 2H), 2.27-2.16 (m, 2H), 2.03 (d, *J* = 14.7 Hz, 2H), 1.77-1.61 (m, 4H), 1.59-1.33 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.0 (C), 159.2 (C), 159.0 (C), 145.5 (CH), 129.5 (CH), 129.0 (CH), 128.5 (C), 122.0 (CH), 114.1 (CH), 100.4 (C), 66.9 (CH), 64.2 (CH_2), 62.9 (CH), 55.3 (CH), 54.3 (CH_3), 47.9 (CH_3), 46.2 (CH_2), 34.1 (CH_2), 30.8 (CH_2), 30.8 (CH_2), 30.2 (CH_2), 27.3 (CH_2), 23.7 (CH_2), 21.8 (CH_2). HRMS (ESI+): calcd. for $C_{27}H_{35}NNaO_7$ (M^+ + Na): 508.2311; found 508.2308.

Compound 81. Colorless syrup (20 mg, quant.). $[\alpha]_D^{20}$ = +38.0 (*c* 0.75, CH_2Cl_2). IR (neat) 3030, 2955, 2936, 1709, 1665, 1611, 1585, 1512, 1249, 1196, 1031, 829 cm^{-1}; ^1H NMR (400 MHz, CD_2Cl_2) δ 7.20 (d, *J* = 8.8 Hz, 2H), 6.85 (d, *J* = 8.8 Hz, 2H), 6.25 (dt, *J* = 12.0, 8.0 Hz, 1H), 5.70 (d, *J* = 12.0 Hz, 1H), 5.39 (m, 2H), 5.19 (m, 1H), 4.99 (d, *J* = 13.2 Hz, 1H), 4.31 (d, *J* = 14.2 Hz, 1H), 4.22 (m, 1H), 3.79 (dd, *J* = 9.7, 2.8 Hz, 1H), 3.77 (s, 3H), 3.26-3.16 (m, 2H), 3.07 (s, 3H), 2.66 (m, 1H), 2.41-2.25 (m, 2H), 2.21 (dt, *J* = 15.3, 2.3 Hz, 1H), 2.17-2.12 (m, 3H), 1.87 (m, 2H), 1.80 (m, 2H), 1.63-1.52 (m, 2H), 1.47 (ddd, *J* = 13.9, 11.6, 2.3 Hz, 1H); ^{13}C NMR (100 MHz, CD_2Cl_2) δ 171.9 (C), 165.1 (C), 158.5 (C), 144.8 (CH), 129.1 (CH), 128.9 (CH), 128.3 (2 CH), 127.7 (C), 121.1 (CH), 113.2 (2 CH), 101.4 (C), 66.7 (CH), 62.7 (CH), 58.5 (CH), 54.5 (CH_3), 46.7 (CH_3), 46.6 (CH_2), 33.6 (CH_2), 30.6 (CH_2), 29.5 (CH_2), 29.1 (CH_2), 26.6 (CH_2), 24.6 (CH_2), 23.0 (CH_2), 21.1 (CH_2). *m*/*z* (EI) 279 (100), 261 (9), 247 (8), 229 (34), 201 (10), 133 (11), 121 (87). HRMS (ESI+): calcd. for $C_{27}H_{36}NO_6S_1$ (M^+ + H): 502.2263; found 502.2265.

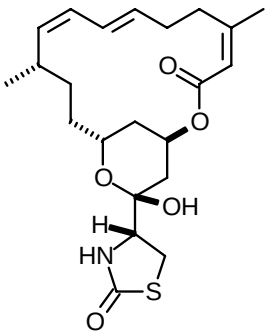


Compound 82. Colorless syrup (10 mg, quant.). $[\alpha]_D^{20}$ = +45.3 (*c* 0.5, CH_2Cl_2). ^1H NMR (400 MHz, CD_2Cl_2) δ 7.19 (d, *J* = 9.5 Hz, 2H), 6.85 (d, *J* = 9.5 Hz, 2H), 5.48 (m, 1H), 5.32 (m, 1H), 4.98 (d, *J* = 15.0 Hz, 1H), 4.29 (d, *J* = 16.3 Hz, 1H), 4.05 8m, 1H), 3.82 (dd, *J* = 8.8, 3.7 Hz, 1H), 3.77 (s, 3H), 3.29-3.21 (m, 2H), 3.14 (s, 3H), 2.40-2.23 (m, 3H), 2.03 (dt, *J* = 14.9, 2.0 Hz, 1H), 1.97-1.92 (m, 3H), 1.88 (dd, *J* = 14.9, 4.5 Hz, 1H), 1.85-1.74 (m, 2H), 1.73-1.60 (m, 3H), 1.55-1.48 (m, 2H), 1.46-1.32 (m, 7H); ^{13}C NMR (100 MHz, CD_2Cl_2) δ 173.3 (C), 173.0 (C), 159.6 (C), 131.1 (CH), 130.1 (2CH), 129.4 (CH), 114.3 (2CH), 102.0 (C), 66.3 (CH), 63.8 (CH), 59.8 (CH), 55.6 (CH_3), 47.8 (CH_3), 35.1 (CH_2), 34.7 (CH_2), 33.5 (CH_2), 30.6 (CH_2), 30.1 (CH_2), 29.6 (CH_2), 27.8 (CH_2), 27.1 (CH_2), 25.8 (CH_2), 25.2 (CH_2), 25.0 (CH_2), 23.7 (CH_2). MS (EI) *m*/*z* (rel. intensity): 500 (1), 309 (100), 291 (13), 277 (17), 259 (35), 121 (72). HRMS (ESI+): calcd. for $C_{29}H_{41}NNaO_6S_1$ (M^+ + Na): 554.2552; found 554.2549.



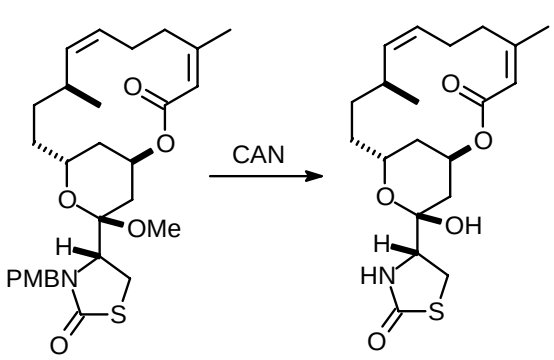
Latrunculins and Latrunculin Analogues

Latrunculin A (1). For the preparation see ref. 2. $[\alpha]_D^{20}$ = +145 (c 0.05 CH_2Cl_2); IR (ATR) 3302, 2952, 2854, 1670, 1435, 1377, 1351, 1279, 1231, 1190, 1060, 1050, 1029, 985, 953, 904, 865,



806, 753, 726, 686, 663 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.98 (d, 3H, *J* = 6.31 Hz), 1.01-1.14 (m, 1H), 1.24-1.98 (m, 6H), 1.93 (s, 3H), 2.04-2.07 (m, 1H), 2.23-2.34 (m, 2H), 2.62-2.77 (m, 2H), 2.86-2.95 (m, 1H), 3.37-3.52 (m, 1H), 3.82-3.93 (m, 2H), 4.2-4.3 (m, 1H), 5.01 (dd, 1H, *J* = 10.7, 10.6 Hz), 5.42 (m, 1H), 5.65-5.69 (m, 1H), 5.69 (br s, 1H), 5.74 (s, 1H), 5.97 (dd, 1H, *J* = 10.7, 10.6 Hz), 6.40 (dt, 1H, *J* = 14, 12 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.6, 24.5, 28.7, 29.2, 30.5, 31.0, 31.5, 31.8, 32.7, 34.9, 61.4, 62.3, 68.2, 97.3, 117.3, 126.0, 127.2, 131.8, 136.5, 158.4, 165.4, 174.8; MS (EI) *m*/*z* (rel. intensity): 403 (28), 385 (15), 335 (41), 334 (23), 333 (100), 327 (13), 315 (15), 301 (17), 285 (10), 205 (11), 175 (11), 170 (14), 159 (11), 147 (14), 135 (12), 133 (14), 131 (14), 121 (19), 119 (15), 117 (16), 109 (11), 107 (25), 105 (19), 93 (30), 91 (22), 81 (30), 79 (41), 55 (25); HRMS (ESI+) *m*/*z* 444.18233 (M+Na); calcd. for $C_{22}H_{31}NaSO_5N$: 444.182065.

Latrunculin B (2). CAN (31 mg, 0.057 mmol) was added to a vigorously stirred suspension of compound **83** (12 mg, 0.023mmol)[1] in acetonitrile/water (2:1, 0.5 ml). After 20 min the mixture became homogeneous and stirring was continued for additional 3 h. The solution was extracted three times with CH_2Cl_2, the combined organic layers were dried (Na_2SO_4) and evaporated, and the residue was purified by flash chromatography (ethyl acetate/hexane, 1/2) to give latrunculin B as a colorless oil (7 mg, 78%). $[\alpha]_D^{20}$ = +122° (*c* = 0.55, $CHCl_3$); IR (ATR) 3328, 2952, 1678, 1278, 1092,

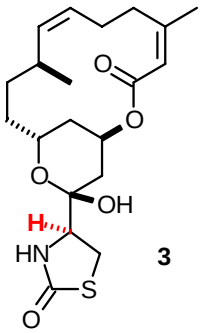


83 **Lat-B (2)**

1057 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.95 (d, 3H, *J* = 6.3 Hz), 1.07–2.39 (m, 11H), 1.90 (d, 3H, *J* = 1.3 Hz), 2.60–2.80 (m, 2H), 3.39 (dd, 1H, *J* = 6.3, 11.6 Hz), 3.47 (dd, 1H, *J* = 8.8, 11.6 Hz), 3.81–3.85 (m, 1H), 3.87 (s, 1H, OH), 4.24 (br t, 1H, *J* = 10.6 Hz), 5.05 (dt, 1H, *J* = 1.5, 11.2

Hz), 5.25 (dt, 1H, J = 3.0, 11.2 Hz), 5.43–5.46 (m, 1H), 5.68 (d, 1H, J = 1.3 Hz), 5.77 (s, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.2, 24.0, 26.9, 28.7, 28.8, 30.9, 31.2, 31.4, 35.3, 35.8, 61.3, 62.5, 68.7, 97.8, 117.8, 127.4, 135.8, 154.5, 165.3, 174.7.

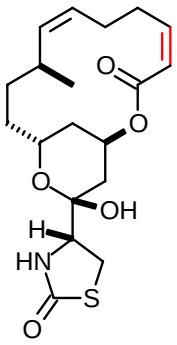
16-*epi*-Latrunculin B (3). $[\alpha]_D^{24}$ = +85 (c 0.24, $CHCl_3$) [lit $[\alpha]_D^{24}$ = +76 (c 0.2, $CHCl_3$)] (9). IR (neat) 3342, 2923, 2854, 1685, 1260, 1029, 796 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.67 (d, J =



3

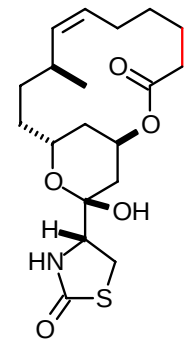
1.3 Hz, 1H), 5.51 (br s, 1H), 5.31-5.21 (m, 1H), 5.24 (dd, J = 11.4, 2.8 Hz, 1H), 5.08-5.00 (m, 1H), 4.39-4.30 (m, 1H), 3.86 (ddd, J = 8.4, 8.4, 1.0 Hz, 1H), 3.40 (dd, J = 11.1, 8.6 Hz, 1H), 3.28 (dd, J = 11.6, 8.3 Hz, 1H), 3.28 (br s, 1H), 2.80 (ddd, J = 12.9, 12.1, 4.8 Hz, 1H), 2.69-2.57 (m, 1H), 2.48-2.35 (m, 1H), 2.25-2.12 (m, 2H), 2.03-1.92 (m, 2H), 1.76-1.46 (m, 5H), 1.42-1.36 (m, 1H), 1.18-1.09 (m, 1H), 0.97 (d, J = 6.6 Hz, 3H); ^{13}C NMR (75 MHz, CD_2Cl_2) δ 175.1, 165.9, 155.7, 135.8, 128.3, 118.4, 97.0, 68.1, 63.3, 63.2, 36.0, 35.9, 32.8, 31.6, 29.9, 29.5, 29.4, 27.1, 24.5, 22.4. HRMS (EI): calcd. for $C_{20}H_{29}NO_5SNa$ (M^+ + Na): 418.1664; found 418.1664.

(4*R*)-4-[(1*R*,10*S*,13*R*,15*R*)-15-Hydroxy-10-methyl-3-oxo-2,14-dioxabicyclo[11.3.1] heptadeca-4,8-dien-15-yl]-1,3-thiazolidin-2-one (30). Prepared analogously; white crystals (2.6

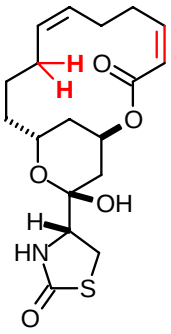


mg, 41%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 0.93 (d, 3H, J = 6.4 Hz), 1.08 (ddd, 1H, J = 14.9, 11.0, 4.0 Hz), 1.31-1.39 (m, 1H), 1.47 (dddd, 1H, J = 14.4, 10.7, 3.7, 3.6 Hz), 1.51 (ddd, 1H, J = 14.0, 11.6, 2.3 Hz), 1.70 (dd, 1H, J = 13.4, 4.0 Hz), 1.73 (m, 1H), 1.91 (dd, 1H, J = 14.7, 3.1 Hz), 1.99-2.17 (m, 3H), 2.32 (dd, 1H, J = 12.5, 4.2 Hz), 2.44 (dd, 1H, J = 12.5, 4.2 Hz), 2.61-2.69 (m, 1H), 3.37 (dd, 1H, J = 11.7, 6.2 Hz), 3.44 (dd, 1H, J = 11.7, 8.8 Hz), 3.81 (dd, 1H, J = 8.8, 6.2 Hz), 4.23 (br t, 1H, J = 10.8 Hz), 5.02 (m, 1H), 5.25 (ddd, 1H), 5.45 (br s, 1H), 5.81 (d, 1H, J = 11.7 Hz), 5.83 (NH, br s, 1H), 6.18 (ddd, 1H, J = 11.7, 11.6, 5.7 Hz); ^{13}C NMR (150 MHz, $CDCl_3$) δ 22.3, 27.5, 28.6, 28.7, 31.0, 31.1, 31.4, 31.7, 35.4, 61.5, 62.5, 68.8, 97.8, 121.2, 127.2, 135.8, 144.1, 165.3, 174.9; LCMS (ESI) *m*/*z* 785 (2, 2M + Na), 404 (100, M+Na), 382 (2), 364 (12), 346 (7).

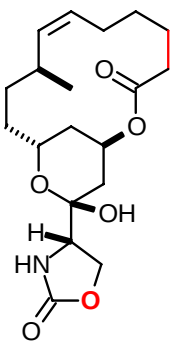
Compound 31. Colorless crystals (4 mg, 80% yield). $[\alpha]_D^{20}$ = +95.5° (c 0.4, $CHCl_3$). IR (ATR) 2929, 1678, 1227, 1091 cm^{-1}. ^1H NMR (400 MHz, CD_2Cl_2) δ 0.93 (d, 3H, *J* = 6.5 Hz), 1.01–2.02 (m, 13H), 2.20–2.32 (m, 2H), 2.55–2.71 (m, 2H), 3.42 (dd, 1H, *J* = 6.3, 11.6 Hz), 3.51 (dd, 1H, *J* = 8.8, 11.6 Hz), 3.87 (dd, 1H, *J* = 1.0, 6.3 Hz), 4.00–4.07 (m, 1H), 4.29 (bs, 1H, OH), 4.99 (t, 1H, , *J* = 10.8 Hz), 5.34–5.41 (m, 2H), 5.70 (bs, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.0, 26.3, 28.3, 28.4, 28.9, 30.1, 31.2, 31.6, 31.8, 34.5, 34.6, 61.3, 61.9, 68.8, 97.5, 128.1, 135.3, 171.2, 174.1; MS (EI) *m/z* (rel. intensity): 281 (63), 263 (100), 245 (42), 227 (17), 195 (14), 161 (10). HRMS: ($C_{19}H_{29}N_1Na_1O_5S_1$, M+Na) calcd.:403.166415, found: 406.16692.



Compound 32. Colorless syrup (5 mg, 45%). ^1H NMR (400 MHz, CD_2Cl_2) δ 6.21 (m, 1H), 5.79 (d, *J* = 12.9 Hz, 1H), 5.61 (m, 1H), 5.43-5.24 (m, 2H), 4.27 (m, 1H), 3.78 (t, *J* = 7.6 Hz, 1H), 3.52 (m, 1H), 3.44 (dd, *J* = 11.5, 8.6 Hz, 1H), 3.37 (dd, *J* = 11.6, 6.6 Hz, 1H), 2.44-2.32 (m, 2H), 2.28 (m, 1H), 2.08-2.03 (m, 2H), 2.00-1.95 (m, 2H), 1.91 (dd, *J* = 15.1, 3.2 Hz, 1H), 1.79-1.74 (m, 1H), 1.56-1.46 (m, 4H), 1.45-1.34 (m, 2H); ^{13}C NMR (75 MHz, CD_2Cl_2): δ 174.6 (C), 165.7 (C), 144.9 (CH), 129.9 (CH), 129.6 (C), 121.7 (CH), 98.1 (C), 69.0 (CH), 62.5 (CH), 62.2 (CH), 35.3 (CH_2), 31.7 (CH_2), 31.6 (CH_2), 31.1 (CH_2), 29.1 (CH_2), 27.7 (CH_2), 24.1 (CH_2), 22.3 (CH_2); HRMS (ESI+): calcd. for $C_{18}H_{25}NNaO_5S_1$ (M^+ + Na): 390.1351; found 390.1352.

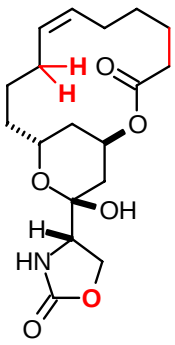


((4*S*)-4-[(1*R*,10*S*,13*R*,15*R*)-15-Hydroxy-10-methyl-3-oxo-2,14-dioxabicyclo[11.3.1] heptadeca-4,8-dien-15-yl]-1,3-oxazolidin-2-one (33). White solid (8 mg, 61%). $[\alpha]_D^{20}$ = +89 (*c* 0.04, $CHCl_3$); IR (ATR) 3564, 3293, 2922, 2856, 1752, 1727, 1459, 1402, 1360, 1326, 1225, 1188, 1176, 1156, 1111, 1083, 1064, 1055, 1026, 1003, 974, 941, 927, 911, 890, 875, 855, 838, 795, 768, 750, 723, 672 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 0.77-0.84 (m, 1H), 0.95 (d, 3H, *J* = 6.5 Hz), 1.06 (dddd, 1H, *J* = 14.2, 10.5, 4.0, 4.0 Hz), 1.33-1.49 (m, 4H), 1.56-1.64 (m, 2H), 1.68 (dd, 1H, *J* = 13.5, 3.9 Hz), 1.81-1.91 (m, 4H), 1.93 (dd, 1H, *J* = 14.5, 2.0 Hz), 2.26 (m, 1H), 2.34

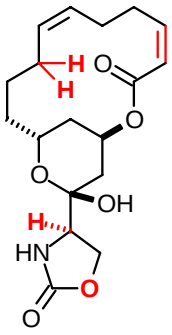


(ddd, 1H, *J* = 15.3, 11.6, 3.9 Hz), 2.60 (ddd, 1H, *J* = 15.3, 5.5, 3.8 Hz), 2.64-2.72 (m, 1H), 3.81 (dd, 1H, *J* = 8.4, 4.7 Hz), 4.02-4.07 (m 1H), 4.43-4.49 (m, 2H), 4.99 (app. t, 1H, *J* = 10.8 Hz), 5.36 (dd, 1H, *J* = 11.3, 4.5 Hz), 5.38-5.41 (m, 1H), 5.50 (br s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 22.3, 26.4, 28.41, 28.42, 30.1, 31.1, 31.6, 32.3, 34.5, 34.6, 59.2, 61.7, 65.7, 68.8, 96.6, 128.0, 135.4, 159.5, 171.2; MS (EI) *m*/*z* (rel. intensity): 367 (8), 349 (8), 281 (32), 263 (100), 245 (37), 221 (18), 195 (17), 137 (14), 95 (29), 81 (40), 67 (39), 55 (56); HRMS (ESI) *m*/*z* 390.1889 (M + Na)$^+$; calcd. for $C_{19}H_{29}NO_6$ + Na: 390.1892.

(4*S*)-4-[(1*R*,13*R*,15*R*)-15-Hydroxy-3-oxo-2,14-dioxabicyclo[11.3.1]heptadec-8-en-15-yl]-1,3-oxazolidin-2-one (34). Prepared analogously; prep-HPLC gave compound **34** as a colorless syrup



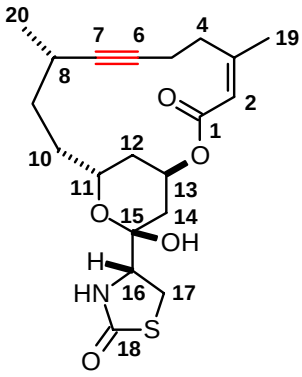
(8.8 mg, 81%) which turned out rather unstable in $CDCl_3$ solution. $[\alpha]_D^{20}$ = +51 (*c* 0.04, $CHCl_3$); IR (ATR) 3561, 3289, 2929, 2858, 1733, 1715, 1441, 1407, 1360, 1327, 1245, 1222, 1176, 1144, 1103, 1077, 1055, 1037, 1022, 1000, 976, 914, 873, 852, 794, 769, 727 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.27-1.33 (m, 1H), 1.35-1.49 (m, 4H), 1.55-1.66 (m, 3H), 1.78-1.94 (m, 8H), 2.24-2.30 (m, 1H), 2.35 (ddd, 1H, *J* = 15.3, 11.3, 4.0 Hz), 2.42-2.50 (m, 1H), 2.60 (ddd, 1H, *J* = 15.3, 5.8, 3.9 Hz), 3.81 (dd, 1H, *J* = 7.5, 5.6 Hz), 4.05-4.11 (m, 1H), 4.44 (d, 1H, *J* = 2.5 Hz), 4.46 (br s, 1H), 5.23 (ddd, 1H, *J* = 11.3, 11.3, 4.0 Hz), 5.34 (br s, 1H), 5.38-5.41 (m, 1H), 5.44-5.50 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 22.3, 23.7, 26.1, 27.8, 29.9, 31.3, 32.1, 34.4, 34.5, 59.1, 61.2, 65.7, 68.8, 96.6, 129.3, 129.7, 164.1, 171.1; MS (EI) *m*/*z* (rel. intensity): 353 (5), 335 (12), 317 (6), 267 (24), 251 (97), 249 (100), 231 (29), 207 (13), 181 (9), 135 (15); HRMS (ESI) *m*/*z* 376.1740 (M + Na)$^+$; calcd. for $C_{18}H_{25}NO_6$ + Na: 376.1736.



(+)-(*R*)-4-((1*R*,4*Z*,8*Z*,13*R*,15*R*)-15-Hydroxy-3-oxo-2,14-dioxa-bicyclo[11.3.1]heptadeca-4,8-dien-15-yl)oxazolidin-2-one (35). $[\alpha]_D^{20}$ = +58.1 (c 1.1, $CHCl_3$). IR (neat) 3337, 2924, 2858, 1747, 1706 cm^{-1}; ^{1}H NMR (400 MHz, CD_2Cl_2) δ 8.51 (s, 1H), 6.28-6.20 (m, 1H), 5.75 (d, *J* = 11.6 Hz, 1H), 5.51 (dd, *J* = 6.1, 2.0 Hz, 1H), 5.42-5.33 (m, 1H), 5.31-5.20 (m, 1H), 4.36 (t, *J* = 9.0 Hz, 1H), 4.34-4.27 (m, 1H), 4.24 (dd, *J* = 9.1, 6.1 Hz, 1H), 3.98-3.84 (m, 2H), 3.79 (ddd, *J* = 9.0, 5.9, 1.3 Hz, 1H), 3.33 (d, *J* = 1.0 Hz, 1H), 2.51-1.20 (m, 12H); ^{13}C

NMR (100 MHz, CD_2Cl_2) δ 165.9 (C), 159.7, 145.6 (CH), 129.8 (CH), 129.8 (CH), 121.8 (CH), 96.4 (C), 68.3 (CH), 66.1 (CH_2), 62.5 (CH), 60.6 (CH), 35.4 (CH_2), 32.6 (CH_2), 31.5 (CH_2), 31.0 (CH_2), 27.6 (CH_2), 24.2 (CH_2), 22.4 (CH_2).

Compound 13. Cerium ammonium nitrate (26 mg, 0.047 mmol) was added to a vigorously stirred suspension of cycloalkyne **12** (10 mg, 0.019 mmol) in acetonitrile/water (2:1, 0.5 ml).



After 20 min the mixture became homogeneous and stirring was continued for additional 4 h. The solution was extracted three times with CH_2Cl_2, the combined organic layers were dried (Na_2SO_4) and the solvent was evaporated. Purification by flash chromatography (ethyl acetate/hexane, 1/2) afforded derivative **13** as a pale yellow oil (5 mg, 80%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.74 (s, 1H, *J* = 1.2 Hz, H-2), 5.68 (s, 1H, –NH), 5.35 (quint., 1H, *J* = 2.9 Hz, H-13), 4.71 (ddt, 1H, *J* = 11.6, 6.8, 1.8 Hz, H-11), 3.80 (ddd, 1H, *J* = 9.0, 6.1, 1.1 Hz, H-16), 3.79 (s, 1H, -OH), 3.47 (dd, 1H, *J* = 11.7, 8.9 Hz, H-17a), 3.39 (dd, 1H, *J* = 11.7, 6.0 Hz, H-17b), 2.90 (ddd, 1H, *J* = 12.7, 8.5, 8.0 Hz, H-4a), 2.59 (dddd, 1H, *J* = 12.6, 7.3, 5.1, 1.0 Hz, H-4b), 2.45 (m, 1H, H-8), 2.33-2.37 (m, 2H, H-5), 2.30 (ddt, 1H, *J* = 14.2, 3.1, 1.8 Hz, H-12a), 2.10 (ddd, 1H, *J* = 14.7, 2.8, 2.0 Hz, H-14a), 1.95 (dd, 1H, *J* = 14.7, 3.5 Hz, H-14b), 1.87 (d, 3H, *J* = 1.4 Hz, H-19), 1.44-1.67 (m, 4H, H-9, H-10), 1.37 (ddd, 1H, *J* = 14.3, 11.7, 2.6 Hz, H-12b), 1.14 (d, 3H, *J* = 7.0 Hz, H-20); ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.7 (s, C-18), 165.3 (s, C-1), 156.1 (s, C-3), 118.2 (d, C-2), 97.7 (s, C-15), 86.3 (s, C-7), 79.6 (s, C-6), 68.8, d, C-13), 63.9 (d, C-11), 61.6 (d, C-16), 34.1 (t, C-10), 33.4 (t, C-12), 32.7 (t, C-4), 31.4 (t, C-14), 31.3 (t, C-9), 28.8 (t, C-17), 25.6 (d, C-8), 24.2 (q, C-19), 22.7 (q, C-20), 18.3 (t, C-5).

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