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Supporting Information

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Total Synthesis of Neooxazolomycin

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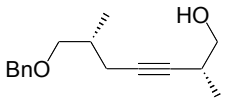
General. Where appropriate, reactions were performed in flame-dried glassware under argon atmosphere. All extracts were dried over $MgSO_4$ and concentrated by rotary evaporation below 30 °C at 25 Toor unless otherwise noted. Commercial reagents and solvents were used as supplied with following exceptions. *N*,*N*-Dimethyformamide (DMF), dichloromethane (CH_2Cl_2), acetonitrile (MeCN), and 1,3-dimethyl-3,4,5,6-tetrahydro-2(1*H*)-pyrimmidinone (DMPU) were distilled from CaH_2. Methanol (MeOH) was distilled from sodium. Thin-layer chromatography (TLC) was performed using glass-packed silica gel plates (0.2 or 0.5 mm thickness). Column chromatography was performed using silica gel (particle size 100-210 μm (regular), 40-50 μm (flush)). Optical rotations were recorded on a digital polarimeter at ambient temperature. Infrared spectra were measured on a Fourier transform infrared spectrometer. ^{1}H NMR (400 and 500 MHz) and ^{13}C NMR (100 MHz) spectra were measured using $CDCl_3$, C_6D_6, or CD_3OD, as solvent, and chemical shifts are reported as δ values in ppm based on internal $CHCl_3$ (7.26 ppm, ^{1}H; 77.0 ppm, ^{13}C), C_6H_6 (7.15 ppm, ^{1}H; 128.0 ppm, ^{13}C), H_2O (4.65 ppm, ^{1}H), or MeOH (49.9 ppm, ^{13}C). HRMS spectra were taken in EI or FAB mode.

Preparation of the Right Hand Segment

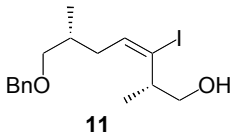


8

(2*R*,6*R*)-7-(Benzyloxy)-2,6-dimethylhept-3-yn-1-ol (8). To a solution of ((*R*)-2-methylbut-3-ynyloxy)(*tert*-butyl)diphenylsilane (**6**)[1] (35.0 g, 109 mmol) in THF (785 ml) was added *n*-BuLi (1.58 M in hexane, 60.0 ml, 94.1 mmol) at –78 °C over 5 min, and the mixture was allowed to warm to 0 °C and stirred for 30 min. A solution of (*S*)-3-(benzyloxy)-2-methylpropyl trifluoromethanesulfonate (**7**)[2] (22.6 g, 72.4 mmol) and DMPU (155 ml) in THF (145 ml) was added at –78 °C over 15 min, and stirring was continued at the same temperature for 30 min. The reaction was quenched with saturated $NaHCO_3$, and the reaction mixture was extracted with AcOEt. The extract was dried, concentrated, and chromatographed (SiO_2 1.2 kg, hexane/AcOEt = 100/1) to give a colorless oil (39.6 g) consisting of a 2:1 mixture of ((2*R*,6*R*)-6-((benzyloxy)methyl)-2-methylhept-3-ynyloxy)(*tert*-butyl)diphenylsilane, the desired coupling product, and **6**, which was used for the next reaction without further purification.

To a solution of the mixture (39.6 g) thus obtained in THF (300 ml) was added *n*-Bu_4NF (1.0 M in THF, 138 ml, 138 mmol), and the mixture was stirred at rt for 3.5 h. The reaction mixture was diluted with Et_2O, washed with saturated NH_4Cl, H_2O, and brine, dried, and concentrated. The residue was purified by column chromatography (SiO_2 900 g, hexane/AcOEt = 20/1 to 5/1) to give **8** (14.4 g, 81%) as a colorless oil: $[\alpha]_D^{26}$ +29.2 (*c* 1.00, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36-7.25 (m, 5H), 4.51 (s, 2H), 3.55-3.49 (m, 1H), 3.46-3.41 (m, 1H), 3.37 (d, *J* = 3.9 Hz, 1H), 3.35 (d, *J* = 2.9 Hz, 1H), 2.65-2.55 (m, 1H), 2.30 (ddd, *J* = 2.2, 5.6, 16.6 Hz, 1H), 2.18 (ddd, *J* = 2.2, 6.6, 16.6 Hz, 1H), 2.02-1.95 (m, 1H), 1.80 (brs, 1H), 1.12 (d, *J* = 6.8 Hz, 3H), 1.00 (d, *J* = 6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.5,

128.2 (2), 127.4, 127.4 (2), 82.6, 80.6, 74.3, 73.0, 67.1, 33.3, 29.6, 23.0, 17.4, 16.6; FTIR (neat) 3400, 1456, 1369, 1095 cm^{-1}; MS (EI) m/z 91 (100), 187, 215, 246 (M^+); HRMS (EI) calcd for $C_{16}H_{22}O_2$ (M^+) 246.1620, found 246.1600.

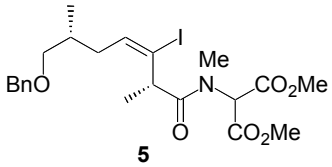


11

(*E*,2*S*,6*R*)-7-(Benzyloxy)-3-iodo-2,6-dimethylhept-3-en-1-ol (11). A mixture of **8** (3.05 g, 12.4 mmol) and 1,1,3,3-tetramethyldisilazane (TMDS) (2.40 ml, 13.6 mmol) was stirred at 0 °C for 5 min and at rt for 1 h. The reaction mixture was concentrated to give hydrodimethylsilyl ether **9** (3.82 g), a colorless oil: ^{1}H NMR (400 MHz, C_6D_6) δ 7.29-7.07 (m, 5H), 4.87–4.83 (m, 1H), 4.32 (s, 2H), 3.72 (dd, *J* = 5.6, 9.8 Hz, 1H), 3.48 (dd, *J* = 7.6, 9.5 Hz, 1H), 3.28 (dd, *J* = 6.8, 8.8 Hz, 1H), 3.21 (dd, *J* = 5.7, 8.8 Hz, 1H), 2.70–2.62 (m, 1H), 2.32 (ddd, *J* = 2.2, 5.6, 16.3 Hz, 1H), 2.18 (ddd, *J* = 2.2, 6.8, 16.3 Hz, 1H), 1.99-1.91 (m, 1H), 1.19 (d, *J* = 6.8 Hz, 3H), 1.01 (d, *J* = 6.8 Hz, 3H), 0.12 (d, *J* = 2.7 Hz, 6H).

To a solution of crude **9** (3.82 g) in THF (25 ml) was added Pt(DVDS) (0.10 M in xylene, 0.4 ml, 0.04 mmol) at 0 °C, and the mixture was stirred at rt for 1 h and concentrated to give siloxane **10** (3.90 g) as a yellow oil: ^{1}H NMR (400 MHz, C_6D_6) δ 7.30-7.07 (m, 5H), 5.72 (t, *J* = 7.1 Hz, 1H), 4.33 (s, 2H), 3.89 (dd, *J* = 5.0, 9.5 Hz, 1H), 3.79 (d, *J* = 9.5 Hz, 1H), 3.21 (dd, *J* = 5.9, 8.8 Hz, 1H), 3.16 (dd, *J* = 5.9, 8.8 Hz, 1H), 2.69-2.62 (m, 1H), 2.32 (dt, *J* = 7.0, 14.0 Hz, 1H), 1.95 (dt, *J* = 7.1, 14.0 Hz, 1H), 1.89–1.80 (m, 1H), 1.05 (d, *J* = 7.3 Hz, 3H), 0.97 (d, *J* = 6.8 Hz, 3H), 0.29 (s, 3H), 0.19 (s, 3H).

To a solution of crude **10** (3.90 g) in DMF (41 ml) and MeOH (8.3 ml) was added CsF (2.80 g, 18.60 mmol) at 0 °C, and the mixture was stirred under ultrasonication at 0 °C for 30 min until it became a clear solution. Iodine (3.15 g, 12.4 mmol) was added to this solution at 0 °C and the mixture was stirred at rt for 1 h. The reaction mixture was diluted with Et_2O, washed with saturated $Na_2S_2O_3$, H_2O, and brine, dried, and concentrated. The residue was subjected to flash chromatography (SiO_2 150 g, hexane/AcOEt = 10/1) to give **11** (3.79 g, 82%) as a colorless oil: $[\alpha]_D^{22}$ –1.7 (*c* 1.20, $CHCl_3$); ^{1}H NMR (400 MHz, C_6D_6) δ 7.29-7.07 (m, 5H), 6.31 (t, *J* = 7.8 Hz, 1H), 4.28 (d, *J* = 12.0 Hz, 1H), 4.24 (d, *J* = 12.0 Hz, 1H), 3.38-3.32 (m, 1H), 3.16-–3.10 (m, 1H), 3.07 (dd, *J* = 5.5, 9.3 Hz, 1H), 3.02 (dd, *J* = 6.3, 9.3 Hz, 1H), 2.13 (ddd, *J* = 6.3, 7.7, 14.1 Hz, 1H), 2.12-2.03 (m, 1H), 1.82 (dt, *J* = 14.1, 7.6 Hz, 1H), 1.65-1.57 (m, 1H), 0.75 (d, *J* = 6.6 Hz, 6H); ^{13}C NMR (100 MHz, C_6D_6) δ 142.1, 138.3, 128.2 (2), 127.4 (3), 111.3, 74.8, 73.0, 67.1, 40.1, 35.5, 33.7, 17.5, 16.9; FTIR (neat) 3417, 1454, 1367, 1090cm^{-1}; MS (EI) m/z 91 (100), 217, 247, 374 (M^+); HRMS (EI) calcd for $C_{16}H_{23}IO_2$ (M^+) 374.0743, found 374.0727.



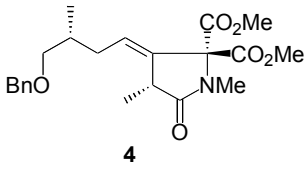
5

Dimethyl 2-((*E*,2*S*,6*R*)-7-(benzyloxy)-3-iodo-*N*,2,6-trimethylhept-3-enoylamino)malonate (5). To a solution of **11** (9.87 g, 26.4 mmol) in acetone (130 ml) was added Jones' reagent (5.8 M, 27.3 ml, 158 mmol) at –10 ºC over 15 min. After stirring at –10 ºC for 2 h, the reaction was quenched with 2-propanol (25 ml) and the reaction mixture was extracted with Et_2O. The ethereal layer was washed with H_2O, basified with 3 M NaOH at 0 °C, and extracted with H_2O. Combined aqueous layer was acidified to pH 1 by the addition of 3 M HCl at 0 °C, and extracted with Et_2O. The extract was washed with brine, dried, and concentrated to give the corresponding carboxylic acid (8.97 g) as a pale yellow oil.

To a solution of crude carboxylic acid (8.97 g) in CH_2Cl_2 (130 ml) was added $SOCl_2$ (5.8 ml, 79.2 mmol). After being stirred at rt for 18 h, the reaction mixture was concentrated to give the corresponding acid chloride (9.50 g).

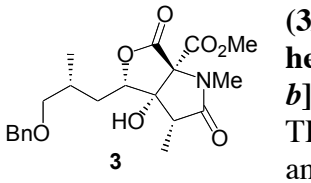
To a solution of dimethyl 2-(methylamino)malonate[3] (10.6 g, 66.0 mmol) in toluene (130 ml) at 0 °C was added a solution of crude acid chloride (9.50 g) in toluene (130 ml). After

being stirried at 0 °C for 3 h, the reaction mixture was diluted with Et_2O, washed with 0.5 M HCl, H_2O, saturated $NaHCO_3$, dried, and concentrated. The residue was purified by flash chromatography (SiO_2 350 g, hexane/AcOEt = 5/1 to 4/1) to give **5** (8.73 g, 62%) as an yellow oil: $[\alpha]_D^{25}$ –31.0 (*c* 1.21, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37-7.26 (m, 5H), 6.36 (t, *J* = 6.6 Hz, 1H), 6.04 (s, 1H), 4.49 (s, 2H), 3.79 (s, 3H), 3.79 (s, 3H), 3.65 (q, *J* = 6.6 Hz, 1H), 3.34 (dd, *J* = 5.4, 9.3 Hz, 1H), 3.26 (dd, *J* = 7.0, 9.3 Hz, 1H), 3.04 (s, 3H), 2.31 (dt, *J* = 15.6, 5.9 Hz, 1H), 2.04 (dt, *J* = 15.6, 8.3 Hz, 1H), 1.95-1.86 (m, 1H), 1.22 (d, *J* = 6.6 Hz, 3H), 1.89 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.2, 166.7, 166.4, 141.7, 138.2, 128.2 (2), 127.5, 127.4 (2), 100.0, 74.6, 73.0, 60.2, 52.8, 52.7, 43.8, 35.3, 33.4, 33.2, 17.3, 16.9; FTIR (neat) 1753, 1664, 1446, 1205, 1110, 1031 cm^{-1}; MS (EI) m/z 91 (100), 160, 162, 404, 440, 500, 531 (M^+); HRMS (EI) calcd for $C_{22}H_{30}INO_6$ (M^+) 531.1118, found 531.1113.



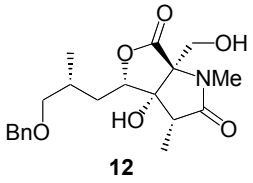
4

(*R*,*E*)-Dimethyl 3-((*R*)-4-(benzyloxy)-3-methylbutylidene)-1,4-dimethyl-5-oxopyrrolidine-2,2-dicarboxylate (4). To a solution of **5** (2.91g, 5.48 mmol) in DMF (247 ml) and H_2O (27 ml) were added *n*-Bu_4NBr (1.17 g, 5.48 mmol), K_2CO_3 (3.03 g, 21.9 mmol), $Pd(OAc)_2$ (61.5 mg, 0.274 mmol), and triphenylphosphine (287 mg, 1.10 mmol) and the mixture was degassed. After being heated for 1.5 h, the reaction mixture was cooled to rt and extracted with Et_2O. The extract was washed with H_2O, dried, concentrated, and chromatographed (SiO_2 130 g, hexane/AcOEt = 5/1 to 3/1) to give **4** (1.87 g, 84%) as a pale yellow oil: $[\alpha]_D^{25}$ +0.2 (*c* 1.25, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36-7.27 (m, 5H), 5.88 (dt, *J* = 2.1, 6.5 Hz, 1H), 4.48 (s, 2H), 3.79 (s, 3H), 3.76 (s, 3H), 3.29 (d, *J* = 5.9 Hz, 2H), 3.14 (q, *J* = 7.1 Hz, 1H), 2.93 (s, 3H), 2.30-2.22 (m, 1H), 2.08–2.01 (m, 1H), 1.91 (sex, *J* = 6.6 Hz, 1H), 1.33 (d, *J* = 7.3 Hz, 3H), 0.95 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.6, 167.8, 167.5, 138.3, 133.0, 129.2, 128.2 (2), 127.40, 127.39 (2), 75.5, 74.6, 73.0 (2), 53.19, 53.16, 38.3, 33.9, 32.7, 28.3, 17.5, 17.1; FTIR (neat) 3489, 1749, 1444, 1377, 1250, 1066 cm^{-1}; MS (EI) m/z 91, 182, 238, 344 (100), 403 (M^+); HRMS (EI) calcd for $C_{22}H_{29}NO_6$ (M^+) 403.1995, found 403.1996.



3

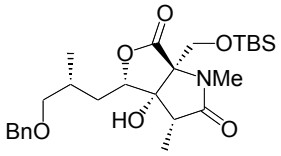
(3*R*,3a*S*,4*S*,6a*R*)-Methyl 4-((*R*)-3-(benzyloxy)-2-methylpropyl)-hexahydro-3a-hydroxy-1,3-dimethyl-2,6-dioxo-1*H*-furo[3,4-*b*]pyrrole-6a-carboxylate (3). To a solution of **4** (1.78 g, 4.41 mmol) in THF (33 ml) and H_2O (11 ml) were added NMO (2.27 g, 19.4 mmol) and OsO_4 (0.15 M in H_2O, 12.0 ml, 1.76 mmol). After being stirred at rt for 48 h, the reaction mixture was diluted with Et_2O, washed with saturated $Na_2S_2O_3$, H_2O, and brine, dried, and concentrated. The residue was subjected to flash chromatography (SiO_2 80 g, hexane/AcOEt = 3/1) to give **3** (1.57 g, 88%) as a colorless oil: $[\alpha]_D^{26}$ +17.0 (*c* 1.17, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38-7.28 (m, 5H), 4.55 (d, *J* = 12.0 Hz, 1H), 4.50 (d, *J* = 12.0 Hz, 1H), 4.37 (t, *J* = 7.0 Hz, 1H), 4.24 (s, 1H), 3.86 (s, 3H), 3.42 (dd, *J* = 4.4, 9.0 Hz, 1H), 3.25 (t, *J* = 8.7 Hz, 1H), 2.92 (s, 3H), 2.53 (q, *J* = 7.4 Hz, 1H), 2.06 (ddd, *J* = 5.7, 6.8, 14.6 Hz, 1H), 1.92–1.82 (m, 1H), 1.76 (dt, *J* = 14.6, 6.5 Hz, 1H), 1.15 (d, *J* = 7.6 Hz, 3H), 1.00 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.2, 167.7, 166.2, 137.2, 128.5 (2), 128.0, 127.9 (2), 86.5, 82.0, 75.8, 75.1, 73.4, 53.5, 45.4, 32.6, 30.3, 27.3, 18.4, 11.0; FT-IR (neat) 3352, 2956, 1782, 1693, 1454, 1365, 1269, 1085 cm^{-1}; MS (EI) m/z 91, 185(100), 405 (M^+); HRMS (EI) calcd for $C_{21}H_{27}NO_7$ (M^+) 405.1788, found 405.1787.



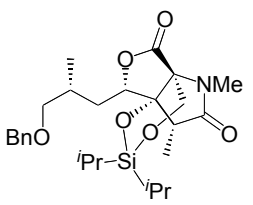
12

(3*R*,3a*S*,4*S*,6a*S*)-4-((*R*)-3-(Benzyloxy)-2-methylpropyl)-dihydro-3a-hydroxy-6a-(hydroxymethyl)-1,3-dimethyl-1*H*-furo[3,4-*b*]pyrrole-2,6(3*H*,6a*H*)-dione (12). To a solution of **3** (270 mg, 0.667 mmol) in THF (16 ml) was added 4 M LiOH (3.6 ml), and the mixture was stirred at rt for 20 min. The reaction mixture was washed with Et_2O, acidified with 1 M HCl to pH 1, and extracted with Et_2O. The extract was washed with brine, dried, and concentrated to give the corresponding carboxylic acid (245 mg) as a colorless solid.

To a solution of DMF (78 µl, 1.00 mmol) in CH_2Cl_2 (1.0 ml) was added $(COCl)_2$ (252 µl, 2.94 mmol) and the reaction mixture was stirred at 0 °C for 1 h. After evaporation of the solvent, the residue was dissolved in MeCN (1.0 ml) and THF (1.7 ml), and a solution of the carboxylic acid (245 mg) in THF (2.7 ml) was added at 0 °C. After stirred for 1 h, $NaBH_4$ (2.00 M in DMF, 1.0 ml, 2.00 mmol) was added at –78 °C, and the mixture was allowed to warm to rt over 12 h. The reaction was quenched with 1 M HCl at 0 °C, and the reaction mixture was extracted with Et_2O. The extract was washed with saturated $NaHCO_3$, dried, concentrated, and chromatographed (SiO_2 20g, hexane/AcOEt = 2/1) to give **12** (142.8 mg, 57%): $[\alpha]_D^{25}$ +44.5º (*c* 1.14, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38-7.29 (m, 5H), 4.53 (s, 2H), 4.45 (s, 1H), 4.32 (t, *J* = 7.0 Hz, 1H), 3.99 (dd, *J* = 6.6, 12.3 Hz, 1H), 3.91 (dd, *J* = 5.5, 12.3 Hz, 1H), 3.43 (dd, *J* = 4.6, 9.0 Hz, 1H), 3.33 (t, *J* = 6.1 Hz, 1H), 3.28 (t, *J* = 8.4 Hz, 1H), 2.87 (s, 3H), 2.50 (q, *J* = 7.6 Hz, 1H), 2.01 (ddd, *J* = 5.6, 6.8, 14.4 Hz, 1H), 1.89-1.82 (m, 1H), 1.74 (ddd, *J* = 6.1, 7.2, 14.4 Hz, 1H), 1.21 (d, *J* = 7.8 Hz, 3H), 1.01 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.2, 171.5, 137.2, 128.5 (2), 128.0, 127.9 (2), 86.6, 80.7, 75.2, 73.5, 71.8, 58.9, 45.6, 32.4, 30.2, 26.1, 18.4, 11.6; FT-IR (neat) 3394, 2943, 1768, 1679, 1457, 1389, 1232, 1078, 1108 cm^{-1}; MS (EI) m/z 91, 157 (100), 377 (M^+); HRMS (EI) calcd for $C_{20}H_{27}NO_6$ (M^+) 377.1813, found 377.1818.

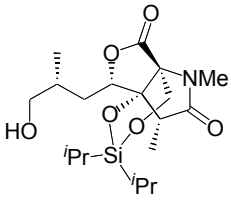


(3*R*,3a*S*,4*S*,6a*S*)-4-((*R*)-3-(Benzyloxy)-2-methylpropyl)-6a-(*tert*-butyldimethylsiloxymethyl)-dihydro-3a-hydroxy-1,3-dimethyl-1*H*-furo[3,4-*b*]pyrrole-2,6(3*H*,6a*H*)-dione. To a solution of **12** (30.8 mg, 0.082 mmol) in CH_2Cl_2 (1.0 ml) was added TBSOTf (35 µl, 0.163 mmol), and the mixture was stirred for 30 min. The reaction mixture was diluted with Et_2O, washed with H_2O, dried, and concentrated. The residue was purified by preparative TLC (SiO_2, hexane/AcOEt = 1/1) to give the corresponding mono-TBS ether (35.0 mg, 87%) as colorless crystals: mp 104-105 °C (EtOH); $[\alpha]_D^{25}$ +31.2º (*c* 1.14, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36-7.26 (m, 5H), 4.50 (s, 2H), 4.32 (dd, *J* = 4.4, 8.5 Hz, 1H), 4.07 (d, *J* = 11.0 Hz, 1H), 3.89 (s, 1H), 3.96 (d, *J* = 11.0 Hz, 1H), 3.40 (dd, *J* = 4.8, 9.3 Hz, 1H), 3.30 (dd, *J* = 6.3, 9.0 Hz, 1H), 2.84 (s, 3H), 2.45 (q, *J* = 7.6 Hz, 1H), 1.99-1.89 (m, 2H), 1.73–1.66 (m, 1H), 1.24 (d, *J* = 7.6 Hz, 3H), 1.02 (d, *J* = 6.6 Hz, 3H), 0.89 (s, 9H), 0.13 (s, 3H), 0.12 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.1, 171.0, 138.0, 128.3 (2), 127.6 (3), 86.8, 80.3, 75.0, 73.2, 71.4, 59.8, 45.1, 32.2, 30.4, 25.9, 25.8 (3), 18.2, 18.1, 11.6, -5.5, -5.7; FTIR (neat) 3294, 1763, 1662, 1456 cm^{-1}; MS (EI) m/z 91(100), 434, 491 (M^+); HRMS (EI) calcd for $C_{26}H_{41}NO_6Si$ (M^+) 491.2703, found 491.2698.

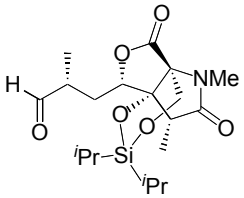


Protection of 12 as its Dioxasilinane. To a solution of **12** (82.0 mg, 0.277 mmol) in 1,2-dichloroethane (2.5 ml) were added 2,6-lutidine (267 µl, 2.290 mmol) and diisopropyl bis(trifluoromethanesulfonate) (225 µl, 0.762 mmol), and the mixture was refluxed for 2 h. The reaction mixture was diluted with Et_2O, washed with H_2O, 0.5 M HCl, and saturated $NaHCO_3$, dried, and concentrated. The residue was purified by column chromatography (SiO_2 6.2 g, hexane/AcOEt = 3/1) to give the corresponding dioxasilinane (135.5 mg, 100%) as a colorless oil: $[\alpha]_D^{25}$ +50.7 (*c* 1.025, $CHCl_3$); ^{1}H NMR (300 MHz,

$CDCl_3$) δ 7.39-7.23 (m, 5H), 4.47 (d, *J* = 13.8 Hz, 3H), 4.35 (dd, *J* = 2.9, 4.5 Hz, 1H), 3.94 (d, 11.4 Hz, 1H), 3.42 (dd, *J* = 5.0, 9.3 Hz, 1H), 3.31 (dd, *J* = 6.0, 9.3 Hz, 1H), 2.87 (s, 3H), 2.51 (q, *J* = 7.5 Hz, 1H), 2.11-1.86 (m, 2H), 1.81-1.55 (m, 1H), 1.28 (d, *J* = 7.5 Hz, 3H), 1.05-0.96 (m, 17H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.5, 171.1, 138.3, 128.4 (2), 127.7, 127.6 (2), 85.6, 82.3, 74.7, 67.4, 61.2, 45.3, 32.5, 30.7, 25.9, 18.0, 16.8, 16.6, 13.6, 11.7; FTIR (neat) 1780, 1705, 1462, 1377, 1209, 1093 cm^{-1}; MS (EI) m/z 91(100), 269, 327, 383, 418, 446, 489 (M^+); HRMS (EI) calcd for $C_{26}H_{39}NO_6Si$ (M^+) 489.2527, found 489.2542.

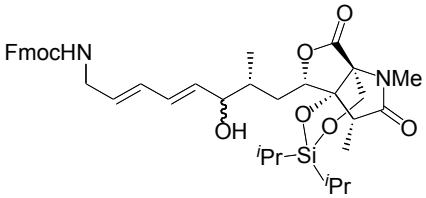


Debenzylation. A solution of the cyclic silyl ether of **12** (118.6 mg, 0.242 mmol) in MeOH (2.0 ml) was stirred with 10% Pd/C (12 mg) at rt under H_2 atmosphere. After 1.5 h, the reaction mixture was filtered through Celite pad and concentrated to give the corresponding primary alcohol (96.7 mg, 100%) as a colorless oil, which was used for the next reaction without purification: $[\alpha]_D^{22}$ +44.8 (*c* 1.74, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.49 (d, *J* = 10.8 Hz, 1H), 4.37 (d, *J* = 10.5 Hz, 1H), 3.94 (d, *J* = 11.4 Hz, 1H), 3.62 (dd, *J* = 4.2, 10.5 Hz, 1H), 3.51 (dd, *J* = 5.7, 10.5 Hz, 1H), 2.88 (s, 3H), 2.58 (q, *J* = 7.5, 1H), 2.03-1.60 (m, 4H), 1.30 (d, *J* = 7.8 Hz, 3H), 1.14-0.95 (m, 17H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.6, 171.9, 86.5, 83.3, 68.4, 68.0, 62.2, 46.1, 33.6, 32.7, 26.9, 18.4, 17.8, 17.7, 17.6, 17.5, 14.5, 14.2, 12.8; FTIR (neat) 3440, 1784, 1710, 1466, 1388, 1091 cm^{-1}; MS (EI) m/z 189, 244 (100), 256, 328, 356, 399 (M^+); HRMS (EI) calcd for $C_{19}H_{33}NO_6Si$ (M^+) 399.2077, found 399.2059.



13

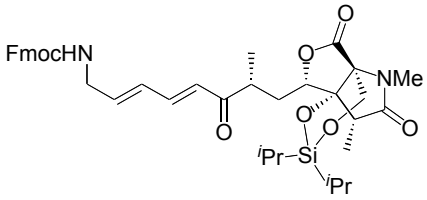
Aldehyde 13. To a solution of the primary alcohol (92.4 mg, 0.231 mmol) in CH_2Cl_2 (2.0 ml) was added Dess-Martin periodinane (146.9 mg, 347 μmol), and the mixture was stirred at rt for 4.5 h. The reaction was quenched with saturated $Na_2S_2O_3$ at 0 °C and the reaction mixture was extracted with Et_2O. The extract was washed with $NaHCO_3$, dried, concentrated. The residue was subjected to flash chromotography (SiO_2 2.0 g, hexane/AcOEt = 3/1) to give aldehyde **13** (76.4 mg, 83%) as a pale yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.68 (s, 1H), 4.69 (d, *J* = 11.8 Hz, 1H), 4.30 (d, *J* = 10.8 Hz, 1H), 3.95 (d, *J* = 11.7 Hz, 1H), 2.87 (s, 3H), 2.81-2.61 (m, 2H), 2.24 (dd, *J* = 8.7, 15.2 Hz, 1H), 1.74 (dd, *J* = 10.5, 15.2 Hz, 1H), 1.32 (d, *J* = 7.8 Hz, 3H), 1.26 (d, *J* = 7.3 Hz, 3H), 1.93-1.17 (m, 14 H).



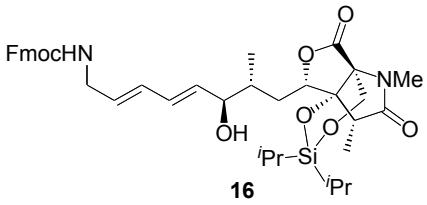
15 *R*:*S* = 1:1

Nozaki-Hiyama-Kishi Reaction of 13 with 14. A mixture of $NiCl_2$ (3.0 mg, 23 μmol) and $CrCl_2$ (56.9 mg, 463 μmol) in THF-DMSO (3:1) (3.0 ml) was stirred for 10 min. To this mixture were added a solution of **13** (46.0 mg, 116 μmol) in THF-DMSO (3:1) (0.6 ml), and **14** (85.0 mg, 197 μmol). After stirring at rt for 20 h, the reaction was quenched with H_2O at 0 °C, and the reaction mixture was filtered through Celite pad. The filtrate was extracted with AcOEt, dried, and concentrated. The residue was again reacted with **14** (85.0 mg, 197 μmol) using $NiCl_2$ (3.0 mg, 23 μmol) and $CrCl_2$ (56.9 mg, 463 μmol) in THF-DMSO (3:1) (3.6 ml) in the same manner as described above. After being stirred at rt for 16 h, the reaction was quenched with H_2O filtered through Celite pad, extracted with AcOEt, dried, and concentrated. The residue was purified by preparative TLC (hexane/AcOEt = 1/1) to give recovered **13** (6.4 mg, 14%) and **15**, a colorless oil, (59.7 mg, 73%; 85% based on recovered **13**) as a 1:1 epimeric mixture: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, *J* = 7.3 Hz, 2H), 7.61 (d, *J* = 7.3 Hz, 2H), 7.40 (t, *J* = 7.3 Hz,

2H), 7.30 (t, *J* = 7.3 Hz, 2H), 6.28-6.10 (m, 2H), 5.77-5.63 (m, 2H), 5.32 (brs, 0.5H), 5.24 (brs, 0.5H), 4.50 (d, *J* = 11.7 Hz, 1H), 4.41 (d, *J* = 6.8 Hz, 1H), 4.34 (t, *J* = 8.0, 1H), 4.23 (t, *J* = 6.8 Hz, 1H), 4.04 (brs, 1H), 3.99-3.86 (m, 3H), 2.87 (s, 3H), 2.52 (q, *J* = 7.3 Hz, 1H), 2.00-1.80 (m, 3H), 1.70-1.53 (m, 1H), 1.28 (d, *J* = 7.8 Hz, 3H), 1.15-0.92 (m, 17H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.7, 171.0, 156.4, 144.0 (2), 141.3 (2), 134.7, 134.0, 130.9, 127.7 (2), 127.0 (2), 125.1 (2), 120.0 (2), 85.8, 82.4, 68.0, 67.6, 66.7, 61.3, 47.2, 45.0, 42.7, 35.7, 31.1, 26.0, 25.6, 16.9, 16.7, 13.7, 13.3, 13.0, 12.1; FT-IR (neat) 3347, 2950, 1781, 1709, 1529, 1452, 1387, 1247, 1089, 913, 739 cm^{-1}; MS (EI) m/z 44, 122, 178(100), 269, 326, 368, 462, 603, 684, 702 (M^+); HRMS (EI) calcd. for $C_{39}H_{50}N_2O_8Si$ (M^+) 702.3377, found: 702.3337.

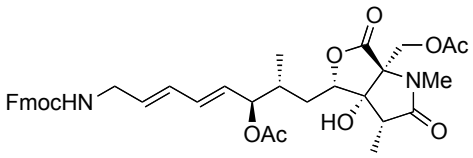


Oxidation of 15. To a solution of **15** (59.7 mg, 85 mmol) in CH_2Cl_2 (2 ml) was added Dess-Martin periodinane (54.0 mg, 127 mmol), and the mixture was stirred at rt for 2 h. The reaction was quenched with saturated $Na_2S_2O_3$ at 0 °C, the reaction mixture was extracted with Et_2O. The extract was washed with saturated $NaHCO_3$, dried, and concentrated. The residue was purified by preparative TLC (hexane/AcOEt = 1/1) to afford the corresponding ketone (51.8 mg, 87%) as a colorless oil: $[\alpha]_D^{25}$ +18.0 (*c* 1.04, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, *J* = 7.8 Hz, 2H), 7.59 (d, *J* = 7.3 Hz, 2H), 7.40 (t, *J* = 7.8 Hz, 2H), 7.31 (d, *J* = 7.3 Hz, 2H), 7.20 (dd, *J* = 11.0, 15.4 Hz, 1H), 6.35-6.09 (m, 3H), 4.99 (brs, 1H), 4.47 (d, *J* = 11.7, 3H), 4.22 (t, *J* = 6.4 Hz, 1H), 4.07 (d, *J* = 9.3 Hz, 1H), 3.93 (d, *J* = 11.7 Hz, 2H), 3.86-3.70 (m, 1H), 3.08 (t, *J* = 6.8 Hz, 1H), 2.84 (s, 3H), 2.63 (q, *J* = 7.6 Hz, 1H), 2.30 (t, *J* = 12.2 Hz, 1H), 1.71 (t, *J* = 12.9 Hz, 1H), 1.30 (d, *J* = 7.3 Hz, 3H), 1.21 (d, *J* = 7.3 Hz, 3H), 1.13-0.96 (m, 14 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.1, 174.5, 170.9, 143.8 (2), 142.3, 141.3 (2), 140.2, 129.2, 128.4, 127.7 (2), 127.0 (2), 124.9 (2), 120.0 (2), 85.2, 82.3, 67.4, 66.8, 61.2, 60.3, 47.2, 44.9, 40.4, 31.1, 25.9, 23.7, 22.9, 21.0, 18.7, 16.8, 14.2, 13.6, 13.3, 11.8; FTIR (neat) 3530, 1780, 1705, 1597, 1526, 1458, 1244, 1086 cm^{-1}; MS (FAB) m/z 89, 137, 154 (100), 289, 307, 391, 460, 505, 613, 700 (M^+); HRMS (FAB) calcd for $C_{39}H_{48}N_2O_8Si$ (M^+) 700.3180, found 700.3115.



16

Compound 16. To a solution of the ketone (40.0 mg, 57 μmol) in THF (2 ml) was added L-Selectride (1 M solution in THF, 63 μl, 63 μmol) at –78 °C, and the mixture was stirred at –78 °C for 30 min. The reaction was quenched with saturated NH_4Cl, and the reaction mixture was extracted with AcOEt, dried, and concentrated. The residue was purified by flash chromatography (SiO_2 1.2g, hexane/AcOEt = 2/1 to 1/1) to give **16** (38.4 mg, 96%) as a colorless oil: $[\alpha]_D^{21}$ +6.3 (*c* 0.814, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, *J* = 7.3 Hz, 2H), 7.60 (d, *J* = 7.3 Hz, 2H), 7.39 (t, *J* = 7.3 Hz, 2H), 7.30 (t, *J* = 7.3 Hz, 2H), 6.28-6.03 (m, 2H), 5.76-5.58 (m, 2H), 5.38 (brs, 1H), 4.49 (d, *J* = 11.7 Hz, 1H), 4.40 (d, *J* = 7.3 Hz, 1H), 4.38-4.30 (m, 1H), 4.23 (t, *J* = 6.8 Hz, 1H), 4.04 (brs, 1H), 3.91 (d, *J* = 11.7 Hz, 2H), 3.86-3.72 (m, 1H), 2.86 (s, 3H), 2.52 (q, *J* = 7.8 Hz, 1H), 2.05 (dd, *J* = 6.36, 15.1 Hz, 1H), 1.97-1.81 (m, 2H), 1.69-1.52 (m, 1H), 1.27 (d, *J* = 7.32 Hz, 3H), 1.12-0.95 (m, 17H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.6, 171.9, 157.2, 144.9 (2), 142.2 (2), 135.5, 131.8, 131.2, 128.6 (2), 127.9 (2), 126.0 (2), 120.8 (2), 87.5, 83.2, 68.5, 67.6, 62.2, 48.2, 45.9, 43.5, 36.8, 31.7, 26.9, 18.6, 17.8, 17.5, 14.5, 14.2, 13.0; FTIR (neat) 3216, 1781, 1704, 1454, 1249, 1089 cm^{-1}; MS (FAB) m/z 55, 136, 178, 179(100), 270, 368, 463, 507, 685, 702 (M^+); HRMS (FAB) calcd for $C_{39}H_{50}N_2O_8Si$ (M^+) 702.3337, found 702.3300.

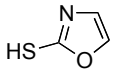


2

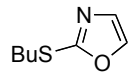
Right hand segment 2. To a solution of **16** (38.4 mg, 54.7 μmol) in MeCN (3.3 ml) was added a mixture of 46% HF-pyridine-H_2O (1:4:2) (1.2 ml), and the mixture was stirred at rt for 20 min. The reaction was quenched with saturated $NaHCO_3$, and the reaction mixture was extracted with AcOEt, dried, and concentrated to give the corresponding triol (39.3 mg) as a yellow viscous oil, which was used for the next reaction without purification.

Crude triol (39.3 mg) was dissolved in pyridine (2ml) and Ac_2O (0.1 ml, 1.06 mmol) was added. After being stirred at rt for 16 h, the reaction mixture was diluted with Et_2O, washed with H_2O, dried, and concentrated. The residue was purified by preparative TLC (SiO_2, hexane/AcOEt = 1/10) to give **2** (34.1 mg, 92%) as a colorless viscous oil: $[\alpha]_D^{23}$ +3.0 (*c* 1.65, CH_2Cl_2) (lit.[4] $[\alpha]_D^{23}$ +3.6 (*c* 0.6, CH_2Cl_2)); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.76 (d, *J* = 7.6 Hz, 2H), 7.60 (d, *J* = 7.6 Hz, 2H), 7.40 (d, *J* = 7.6 Hz, 2H), 7.32 (d, *J* = 7.6 Hz, 2H), 6.22 (dd, *J* = 10.5, 15.1 Hz, 1H), 6.13 (dd, *J* = 10.8, 14.7 Hz, 1H), 5.74 (dt, *J* = 6.9, 15.1 Hz, 1H), 5.57 (dd, *J* = 7.1, 15.1 Hz, 1H), 5.24 (brs, 1H), 5.20 (t, *J* = 6.0 Hz, 1H), 4.71 (d, *J* = 13.0 Hz, 1H), 4.41 (d, *J* = 6.9 Hz, 2H), 4.30 (q, *J* = 4.3 Hz, 1H), 4.26 (d, *J* = 12.8 Hz, 1H), 4.23 (t, *J* = 6.9 Hz, 1H), 3.88-3.77 (m, 2H), 2.88 (s, 3H), 2.61 (s, 1H), 2.42 (q, *J* = 7.7 Hz, 1H), 2.09 (s, 3H), 2.07 (s, 3H), 1.99-1.88 (m, 2H), 1.67-1.58 (m, 1H), 1.25 (d, *J* = 7.6 Hz, 3H), 1.02 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.5, 170.3, 170.2, 169.7, 156.3, 143.9 (2), 141.3 (2), 132.7, 131.3, 130.5, 128.7, 127.7 (2), 127.0 (2), 125.1 (2), 120.0 (2), 86.7, 80.2, 71.4, 66.8, 57.8, 47.3, 44.2, 42.6, 40.9, 34.0, 30.5, 26.1, 20.9, 11.0; FT-IR (neat) 3340, 2937, 1770, 1703, 1528, 1450, 1382, 1232, 1018, 740 cm^{-1}; MS (FAB) m/z 69, 137, 154 (100), 289, 307, 391, 460, 550, 615, 674 (M^+); HRMS (FAB) calcd for $C_{37}H_{42}N_2O_{10}Si$ (M^+) 674.2840, found 674.2855. The spectral data were identical with those reported.[4]

Preparation of the Left Hand Segment



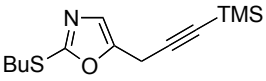
Oxazole-2-thiol. To a suspension of KSCN (7.57 g, 39.5 mmol) in MeCN (167 ml) was added concentrated HCl (8.14 g). After stirring at rt for 30 min, the precipitates were removed by filtration through Celite pad. To the resulting solution of HSCN was added 2,2-diethoxyethanol (**18**) (7.00 g, 52.2 mmol) and the mixture was refluxed for 4 h. After being cooled to rt, the reaction mixture was concentrated and chromatographed (SiO_2, hexane/AcOEt = 2/3) to give oxazole-2-thiol (5.25g, 100%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 (s, 1H), 6.92 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.4, 116.0; FTIR ($CDCl_3$) 3123, 2170, 1588, 1481, 1259, 1481, 1259, 1169, 1087 cm^{-1}; HRMS (FAB) calcd for C_3H_4NOS (M^++H) 102.0013, found 102.0024.



19

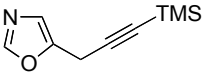
2-(Butylthio)oxazole (19). To a suspension of KH, prepared by washing oil-dispersed KH (35 % in oil, 8.7 g, 73.9 mmol) with hexaene, in THF (200 ml) was added a solution of oxazole-2-thiol (5.0 g 49.3 mmol) in THF (200 ml) at –60 °C, and the mixture was stirred at the same temperature for 30 min. To this mixture was added *n*-BuI (16.1 ml, 147.4 mmol), and the mixture was allowed to warm gradually to rt and stirring was continued for 2 h. The reaction was quenched by the addition of saturated NH_4Cl (50 ml) and H_2O (40 ml) and the reaction mixture was extracted with Et_2O, dried, and concentrated. The residue was purified by column chromatography (SiO_2 300 g, hexane/AcOEt = 20/1) to give **19** (6.0 g, 79%) as a yellow oil: ^{1}H NMR (400 MHz $CDCl_3$) δ 7.64 (s, 1H), 7.10 (s, 1H), 3.17 (t, *J* = 7.3 Hz, 2H), 1.74 (q, *J* = 7.3 Hz, 2H), 1.47 (sextet, *J* = 7.3 Hz, 2H), 0.94 (t, 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.8, 139.7, 128.2. 32.2, 31.5, 21.7, 13.5; FTIR (neat) 3128, 2961 1488, 1318, 1161, 1096 cm^{-1}; HRMS (FAB) calcd for $C_7H_{11}NOS$ (M^+) 157.0561,

found 157.0559.

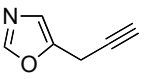


20

2-Butylthio-5-(3-trimethylsilyl-prop-2-ynyl)oxazole (20). To a solution of **19** (6.0 g, 38.2 mmol) in THF (60 ml) was added *t*-BuLi (1.41 M in hexane, 29.8 ml, 42.0 mmol) at –78 °C. After stirring for 30 min, the solution was transferred into a suspension of CuCN (1.52 g, 17.1 mmol) and LiCl (1.42 g, 33.8 mmol) in THF (120 ml) at –78 °C, and stirring was continued at –78 °C for 30 min. To this mixture was added (3-bromoprop-1-ynyl)trimethylsilane (10.8 ml, 76.4 mmol), and the mixture was stirred at rt for 2 h. The reaction was quenched with saturated NH_4Cl, and the reaction mixture was extracted with Et_2O, washed with brine, dried, and concentrated. The residue was purified by column chromatography (SiO_2 g, hexane/Et_2O = 95/5) to afford **20** (9.3 g, 94%) as a yellow oil: ^{1}HNMR (400 MHz, $CDCl_3$) δ 6.87 (s, 1H), 3.61 (s, 2H), 3.15 (t, 2H, *J* = 7.3 Hz), 1.74 (quint, *J* = 7.3 Hz, 2H), 1.47 (sextet, *J* = 7.3 Hz, 2H), 0.94 (t, *J* = 7.3 Hz, 3H), 0.15 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.0, 148.6, 124.9, 99.3, 87.2, 32.4, 31.7, 21.9, 17.9, 13.7, –0.07; FTIR (neat) 3126, 2962, 2183, 1929, 1608, 1497, 1254, 1497 cm^{-1}; HRMS (FAB) calcd. for $C_{13}H_{21}NOSSi$ (M^+) 267.1114, found: 267.1125. The spectral data were identical with those reported.[5]

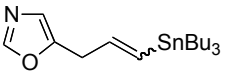


5-(3-(Trimethylsilyl)prop-2-ynyl)oxazole. Raney-Ni (W2) (40 g) was deactivated by heating at reflux in EtOH-acetone (1:1) (500 ml) for 1 h. To this suspension of Raney-Ni was added **20** (8.0 g, 29.9 mmol), and the mixture was refluxed for 36 h. The reaction mixture was filtered through Celite pad, which was then washed with Et_2O and acetone. The filtrate and washing were combined, concentrated, and chromatographed (SiO_2 250 g, hexane/AcOEt = 90/10) to afford 5-(3-(trimethylsilyl)prop-2-ynyl)oxazole (4.93 g, 92%) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (s, 1H), 7.00 (s, 1H), 3,66 (s, 2H), 0.18 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.8, 147.7, 123.4, 99.2, 87.5, 23.4, 17.7; FTIR (neat) 3132, 2959, 2185, 1604, 1511, 1254, 1103, 1031 cm^{-1}; HRMS (EI) calcd for $C_9H_{13}NOS$ (M^+) 179.0766, found 179.0751. The spectral data were identical with those reported.[5]



21

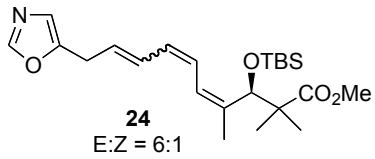
5-(Prop-2-ynyl)oxazole (21). To a solution of 5-(3-(trimethylsilyl)prop-2-ynyl)oxazole (4.6 g, 25.6 mmol) in CH_2Cl_2-MeOH-H_2O (7:4:1) (445 ml) was added Ag(OTf) (1.3 g, 5.1 mmol), and the mixture was stirred at rt for 36 h. The reaction was quenched with saturated NH_4Cl and the reaction mixture was extracted with CH_2Cl_2, dried, and concentrated. The residue was purified by column chromatography (SiO_2 120 g, hexane/Et_2O = 10/1 to 3/1) to give **21** (2.0 g, 73%) as a colorless oil: bp 70-72 (20 mmHg); ^{1}HNMR (400 MHz $CDCl_3$) δ 7.82 (s, 1H), 7.0 (s, 1H), 3.7 (s, 2H), 2.17 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.6, 147.0, 123.3, 70. 16.2; FTIR (neat) 3728, 1699, 1539, 1262, 1107 cm^{-1}; HRMS (EI) calcd for C_6H_5NO (M^+) 107.0371, found 107.0325.



22
E:Z = 6:1

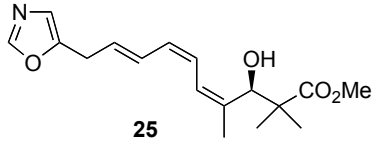
5-((*E*,*Z*))-3-(Tributylstannyl)allyl)oxazole (22). A mixture of **21** (200 mg, 1.88 mmol), *n*-Bu_3SnH (1.0 ml, 3.76 mmol), and AIBN (46.4 mg, 0.282 mg) was heated at 90 °C for 14 h, and chromatographed (SiO_2 50 g, hexane/Et_3N = 50:1 to hexane/AcOEt 20/1) to give a 6:1 E/Z-mixture of **22** (657 mg, 88%): The spectral data for the *E*-isomer; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (s, 2H), 6.78 (s, 2H), 6.54-6.61 (m, 1H), 5.95-6.16 (m, 3H), 3.52 (d, *J* = 2.9 Hz, 2H), 3.41 (d, *J* = 1 Hz, 2H), 1.46-1.54 (m, 12H), 1.26-1.38 (m, 12H), 0.93 (t, 30H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151 (150.2), 141.5 (141.4), 132.8 (132.4), 122.4 (122.23), 33.7, 29.0, 27.2, 13.7, 9.4; FTIR (neat) 3124, 2959, 2186, 1598, 1509, 1376, 1103 cm^{-1}; HRMS (EI) calcd for

$C_{18}H_{33}NOSn$ (M^+) 399.1585, found 399.1577.



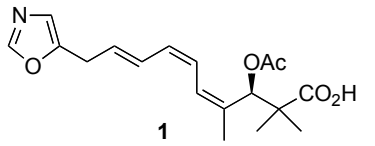
24
E:Z = 6:1

Stille coupling of 22 with 23 giving 24. To a stirred solution $PdCl_2(MeCN)_2$ (3.84 mg, 16.2 μmol) in degassed DMF (4 ml) at rt were added a solution of (*R*,4*Z*,6*Z*)-methyl 3-(*tert*-butyldimethylsilyl)oxy-7-iodo-2,2,4-trimethylhepta-4,6-dienoate (**23**) (240 mg, 0.540 mmol) in degassed DMF (2 ml) and subsequently a solution of **22** (261.6 mg, 0.652 mmol) in degassed DMF (2 ml). After being stirred at rt for 4 d, the reaction mixture was diluted with 10% NH_4OH (8 ml) and stirring was continued for several minutes. The mixture was extracted with AcOEt, washed with brine, dried, concentrated, and chromatographed (SiO_2 20 g, hexane/AcOEt = 3/1/) to give **24** (179 mg, 79%), a pale yellow oil, as an inseparable 6:1 *E*/*Z*-mixture: The spectral data for the *E*-isomer; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (s, 1H), 6.81 (s, 1H), 6.68 (dd, *J* = 14.6, 11.2 Hz, 1H), 6.41 (d, *J* = 12.2 Hz, 1H), 6.25 (dd, *J*= 11.0, 11.9 Hz, 1H), 5.96 (dd, *J* = 10.8, 11.2 Hz, 1H), 5.77 (dt, *J* = 7.3, 14.6 Hz, 1H), 5.00 (s, 1H), 3.63 (s, 3H), 3.52 (d, 2H, *J* = 6.8 Hz), 1.84 (s, 3H), 1.22 (s, 3H), 1.10 (s, 3H), 0.87 (s, 9H), 0.02 (s, 3H), –0.04 (s, 3H); ^{13}C NMR (100 MHz $CDCl_3$) δ 177.0, 150.9, 150.3, 139.0, 128.3, 127.5, 126.0, 124.3, 122.5, 122.3, 73.8, 51.7, 49.4, 29.0, 25.7, 22.3, 21.2, 20.1,20.1. 18.0, HRMS (EI) calcd for $C_{23}H_{37}NO_4Si$ (M^+) 419.2528, found 419.2488. The spectral data were identical with those reported.[4]



25

(*R*,4*Z*,6*Z*,8*E*)-Methyl 3-Hydroxy-2,2,4-trimethyl-10-(oxazol-5-yl)deca-4,6,8-trienoate (25). To a solution of **24** (170 mg, 0.41 mmol) in MeCN (10 ml) was added 47% HF (0. 8 ml) at 0 °C, and the mixture was stirred at rt for 6 h. The reaction mixture was basified with saturated $NaHCO_3$ at 0 °C, extracted with AcOEt, washed with brine, dried, and concentrated. The residue was purified by column chromatography (SiO_2 10 g, hexane/AcOEt = 2/1) followed by recrystallization from hexane to give **25** (100 mg, 80%) as colorless needles: mp 102-102 °C (lit.[4] mp 102-102 °C); $[\alpha]_D^{21}$ +100.6 (*c* 0.7, CH_2Cl_2) (lit.[4] $[\alpha]_D$ +102.1 (*c* 1.0, CH_2Cl_2)]; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (s, 1H], 6.81 (s, 1H), 6.67 (dd, *J* = 15.2, 11.2 Hz, 1H), 6.44 (d, *J* = 11.7 Hz, 1H), 6.21 (dd, *J* = 11.1, 11.7 Hz, 1H), 5.96 (dd, *J* = 11.1, 12.1 Hz, 1H), 5.77 (dd, *J* = 7.0, 14.5 Hz, 1H), 4.77 (dd, *J* = 6.4 Hz, 1H), 3.72 (s, 3H), 3.52 (d, 2H, *J* = 6.8 Hz, 2H), 3.33 (d, *J* = 6.8 Hz, 1H), 1.80 (s, 3H), 1.27 (s, 3H), 1.16 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.3, 150.7, 150.4, 137.7, 128.5, 128.2, 127.9, 124.9, 124.8, 122.5, 74.6, 52.2, 46.9, 29.0, 24.31, 21.0, 19.7; FT-IR (neat) 3474, 2951, 2246, 1736, 1512, 1469, 1142, 833, 649, 493 cm^{-1}; HRMS (EI) calcd for $C_{17}H_{23}NO_4$ (M^+) 305.1681, found 305.1621. The spectral data were identical with those reported.[4]

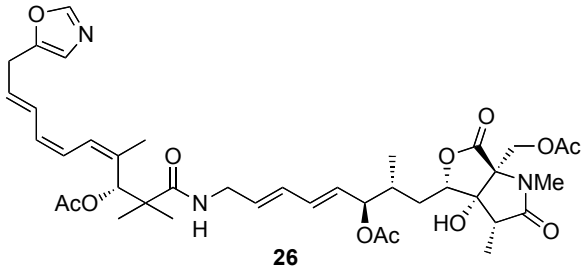


1

(*R*,4*Z*,6*Z*,8*E*)-3-Acetoxy-2,2,4-trimethyl-10-(oxazol-5-yl)deca-4,6,8-trienoic acid (1). To a solution of **25** (60 mg, 0.196 mmol) in THF-MeOH-H_2O (3:1:1) (4.8 ml) was added LiOH (28 mg, 0.57 mmol) at 0 °C, and the mixture was stirred at rt for 24 h. The reaction mixture was acidified by 10% HCl at 0 °C and extracted with AcOEt. The extract was washed with brine, dried, and concentrated to give the corresponding hydroxy acid (50 mg) as a pale yellow oil, which was used for the next reaction without purification.

To a solution of crude hydroxy acid (50 mg) in pyridine (162 μl) was added Ac_2O (162 μl, 1.70 mmol) at 0 °C, and the mixture was stirred at rt for 20 h. A solution of $NaHCO_3$ (142 mg) in MeOH (1.0 ml) was added to the reaction mixture and stirring was continued for 1 h. The reaction mixture was extracted with AcOEt, washed with brine, dried, concentrated, and

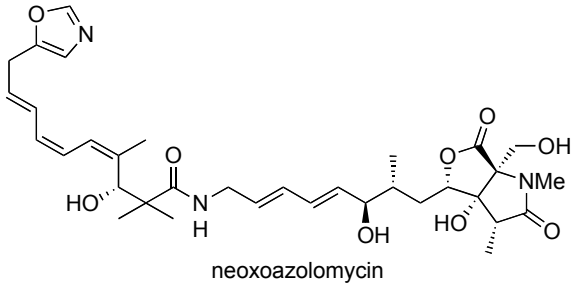
chromatographed (SiO_2 2 g, $CHCl_3$/MeOH = 1/19) to give **1** (65 mg, 100%) as a yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (s, 1H), 6.82 (s, 1H), 6.63 (dd, *J* = 7.0, 14.4 Hz, 1H), 6.52 (d, *J* = 12.2 Hz, 1H), 6.36 (dd, *J* = 11.0, 11.5 Hz, 1H), 6.01 (s, 1H), 5.98 (dd, *J* = 11.0, 11.6 Hz, 1H), 5.77 (dt, *J* = 7.0, 14.4 Hz, 1H), 3.51 (d, *J* = 6.8 Hz, 2H), 2.05 (s, 3H), 1.82 (s, 3H), 1.26 (s, 3H), 1,22 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 180.4, 170, 150.8, 150.6, 133.2, 128.7, 128.6, 126.4,124.3, 122.3, 75.8, 47.3, 29.0, 23.1, 21.0, 20.8, 20.7; FTIR (neat) 3528, 2923, 2532, 1749, 1512, 1471, 1370, 1271 cm^{-1}; HRMS (EI) calcd for $C_{18}H_{23}NO_5$ (M^+) 333.1603, found 333.1573. The spectral data were identical with those reported.[4]



26

Compound 26. To a solution of **2** (28.4 mg, 40 μmol) in CH_2Cl_2 (0.5 ml) was added DBU (12.4 μl, 80 μmol) at rt and the mixture was stirred at rt for 30 min to afford the corresponding free amine. To a solution of carboxylic acid **1** (14.0 mg, 40 μmol) in CH_2Cl_2 (0.5 ml) was added *N,N*-bis(2-oxo-3-oxazolidinyl)phosphorodiamidic chloride (12.0 mg, 40 μmol) and Et_3N (14 μl, 120 μmol). The mixture was stirred at rt for 3 h to give mixed anhydride. The above-mentioned solution of the free amine was transferred to the anhydride, and the mixture was stirred at rt for 1 h. The reaction mixture was extracted with CH_2Cl_2, washed with H_2O and brine, dried, and concentrated. The residue was purified by preparative TLC ($CHCl_3$/MeOH =10:1) to give (18.3 mg, 60%) of **26** as a pale yellow oil: $[\alpha]_D^{23}$ +48.9 (*c* 0.7, CH_2Cl_2) (lit.[4] $[\alpha]_D$ +43.3 (*c* 0.6, CH_2Cl_2)]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.81 (s, 1H), 6.90 (s, 1H), 6.62 (dd, *J* = 14.0, 12.5 Hz, 1H), 6.48 (br d, *J* = 12.0 Hz, 1H), 6.34 (dd, *J* = 11.0, 12.0 Hz, 1H), 6.12-6.20 (m, 3H), 5.99 (t, *J* = 11.0 Hz, 1H), 5.86 (s, 1H), 5.80 (dt, *J* = 7.0, 15.0 Hz, 1H), 5.66 (dt, *J* = 8.0, 14.5 Hz, 1H), 5.56 (dd, *J* = 7.0, 8.0 Hz, 1H,), 5.20 (t, *J* = 5.0 Hz, 1H), 4.71 (d, *J* = 13.0 Hz, 1H), 4.30 (dd, *J* = 4.8, 8.5 Hz, 1H), 4.24 (d, *J* = 13.0 Hz, 1H), 3.87-3.93 (m, 2H), 3.52 (br d, *J* = 7.0 Hz, 1H), 2.86 (s, 3H), 2.41 (q, *J* = 8.0 Hz, 1H), 2.08 (s, 9H), 1.89-1.96 (m, 2H), 1.79 (s, 3H), 1.65 (s, 3H), 1.26 (d, *J* = 7.5 Hz, 3H), 1.22 (s, 3H), 1.21 (s, 3H), 1.02 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (100 MHz $CDCl_3$) δ 174.9, 174.6, 170.2, 170.1, 169.8, 169.6, 150.9, 150.5, 133.4, 132.7, 131.2, 130.8, 128.8, 128.7, 128.2, 126.5, 124.3, 122.4, 86.7, 80.3, 77.5, 77.4, 71.3, 57,8, 46.8, 44.4, 41.5, 34.0, 30.6, 29.7, 29.0, 26.2, 23.7, 21.8, 21.2, 20.9, 16.4, 11.0; FTIR ($CDCl_3$) 3370, 1740, 1531, 1428, 1371, 1242 cm^{-1}; HRMS (FAB) calcd for $C_{40}H_{53}N_3O_{12}Na$ [$(M+Na)^+$] 790.3552, found 790.3539. The spectral data were identical with those reported.[4]

Completion of the Total Synthesis

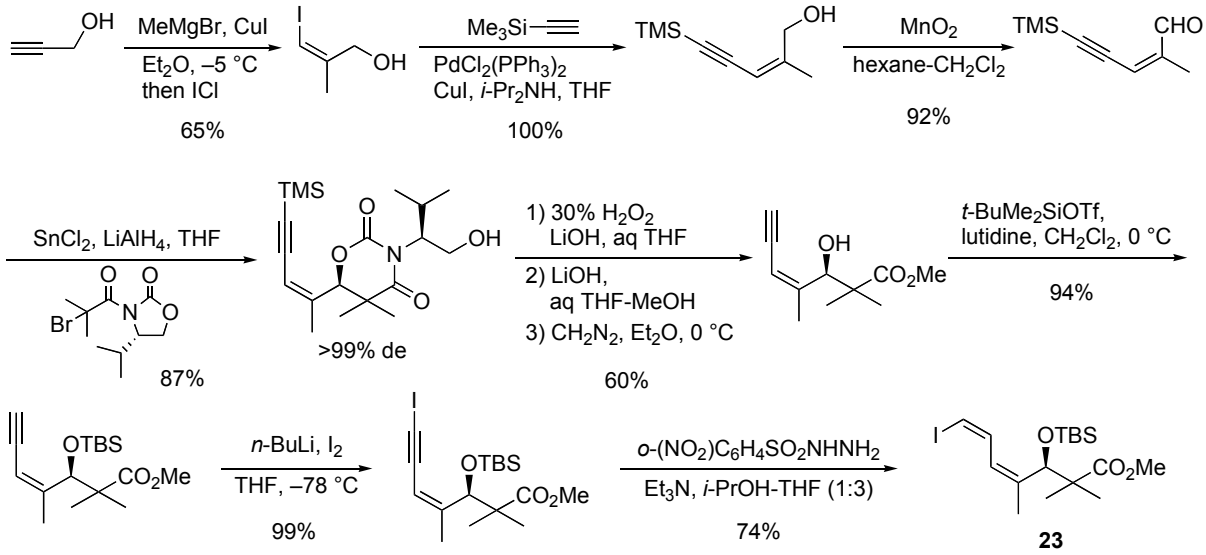


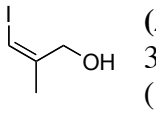
neoxoazolomycin

Neooxazolomycin. To a solution of **30** (6.0 mg 8.0 μmol) in THF-H_2O (3:1) (0.5 ml) at 0 °C was added LiOH (3.3 mg 80.0 μmol). After being stirred at rt for 1 h, the reaction mixture was acidified to pH 1-2 by the addition of 0.1 M HCl at 0 °C. The reaction mixture was extracted with AcOEt, washed with brine, dried and concentrated. The residue was purified by preparative TLC ($CHCl_3$/MeOH = 10/1) to give neooxazolomycin (3.0 mg, 59%) as a pale yellow oil: $[\alpha]_D^{23}$ +23.8 (*c* 0.08, MeOH), $[\alpha]_D^{23}$ +36.3 (*c* 0.08, CH_2Cl_2); ^{1}H NMR (500 MHz, CD_3OD) δ 8.10 (s, 1H), 6.86 (s, 1H), 6.72 (dd, *J* = 12.0, 14.5 Hz, 1H), 6.46 (d, *J* = 11.7 Hz, 1H), 6.28 (t, *J* = 11.5 Hz, 1H), 6.22 (d, *J* = 14.4 Hz, 2H), 5.96 (t, *J* = 11.3 Hz, 1H), 5.79 (dt, *J* = 7.3, 15.1 Hz, 1H), 5.64-5.72 (m, 2H), 4.71 (s, 1H),

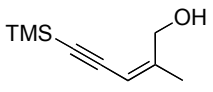
4.62 (br s, 1H), 4.38 (dd, J = 3.7, 9.4 Hz, 1H), 3.96 (t, J = 6.4 Hz, 1H), 3.96 (d, J = 12.6 Hz, 1H), 3.86 (d, J = 5.6 Hz, 2H), 3.77 (d, J = 12.4 Hz, 1H), 3.56 (d, J = 8.9 Hz, 2H), 2.83 (s, 3H), 2.44 (dd, J = 7.3, 15.1 Hz, 1H), 1.95 (dt, J = 4.8, 14.8 Hz, 1H), 1.80 (s, 3H), 1.74-1.82 (m, 1H), 1.55 (dt, J = 8.0, 15.0 Hz, 1H), 1.25 (d, J = 8.0 Hz, 3H), 1.25 (s, 3H), 1.06 (s, 3H), 0.97 (d, J = 6.9 Hz, 3H); ^{13}C NMR (125 MHz $CDCl_3$) δ 178.4, 173.2, 158.3, 153.1, 152.8, 140.0, 135.3, 132.3, 132.1, 130.6, 129.7, 129.5, 129.0, 125.7, 125.2, 122.6, 88.8, 81.6, 77.4, 75.5, 74.3, 56.9, 46.9, 45.9, 42.1, 37.5, 32.2, 29.6, 26.3, 26.0, 22.1, 20.1, 17.4, 11.6; FTIR ($CDCl_3$) 3370, 1740, 1531, 1428, 1371, 1242 cm^{-1}; HRMS (FAB) calcd for $C_{34}H_{48}N_3O_9$ [(M+H)$^+$] 642.3390, found 642.3401. The spectral data were identical with those reported.[4]

Preparation of (*R*,4*Z*,6*Z*)-Methyl 3-(*tert*-Butyldimethylsilyl)oxy-7-iodo-2,2,4-trimethylhepta-4,6-dienoate (23)



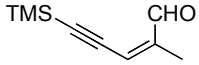


(*Z*)-3-Iodo-2-methylprop-2-en-ol. To a suspension of propargyl alcohol (2.0 g, 35.6 mmol) and CuI (6.78 g, 35.6 mmol) in Et_2O (100 ml) was added MeMgBr (1.65 M in Et_2O, 45 ml, 74.8 mmol) at –5 °C. The mixture was gradually allowed to warm to rt and stirred for 2 h. After addition of ICl (5.78 g, 35.6 mmol) at –5 °C, the mixture was gradually allowed to warm to rt and stirring was continued for additional 16 h. The reaction was quenched with saturated NH_4Cl at 0 °C. The reaction mixture was filtered through Celite pad and the filtrate was extracted with Et_2O. The extract was washed with brine, dried, concentrated, and chromatographed (SiO_2 150 g, hexane/AcOEt = 5/1) to give (*Z*)-3-iodo-2-methylprop-2-en-ol[6] (4.60 g, 65%) as a pale yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.99 (s, 1H), 4.20 (s, 2H), 1.98 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.1, 74.9, 68.1, 21.6; FTIR (neat) 3419, 2911, 2187, 2012, 1618, 1283, 1137, 1046 cm^{-1}; HRMS (EI) calcd for C_4H_7OI (M^+) 197.9541, found 197.9515.

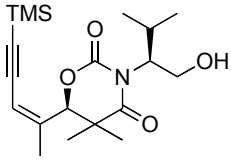


(*Z*)-2-Methyl-5-(trimethylsilyl)pent-2-en-4-yn-1-ol. To a solution of (*Z*)-3-iodo-2-methylprop-2-en-ol (4.0 g, 20.2 mmol) in degassed THF (102 ml) were added (trimethylsilyl)acerylene (5.6 ml, 40.8 mmol), diisopropylamine (24 ml, 153.7 mmol), $PdCl_2(PPh_3)_2$ (288.2 mg. 0.4 mmol), and CuI (272 mg, 1.6 mmol) at rt. After being stirred at rt for 1 h under ultrasonication, the reaction mixture was diluted with Et_2O, washed with saturated $NaHCO_3$, dried, and concentrated. The residue was purified by column chromatography (SiO_2 180 g, hexane/AcOEt = 10/1 to 5/1) to afford (*Z*)-2-methyl-5-(trimethylsilyl)pent-2-en-4-yn-1-ol (3.46 g, 100%) as a red brown oil: ^{1}HNMR

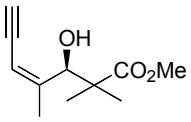
(400 MHz $CDCl_3$) δ 5.41 (s, 1H), 4.36 (d, *J* = 6.4 Hz, 2H), 1.88 (s, 3H), 0.19 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.9, 106.7, 101.6, 64.1, 20.3; FTIR (neat) 3393, 2143, 1629, 1448, 1254, 1100 cm^{-1}; HRMS (EI) calcd for $C_9H_{16}OSi$ (M^+) 168.1034, found 168.0964.



(*Z*)-2-Methyl-5-(trimethylsilyl)pent-2-en-4-ynal. To a solution of (*Z*)-2-methyl-5-(trimethylsilyl)pent-2-en-4-yn-1-ol (2.0 g, 11.8 mmol) in hexane-CH_2Cl_2 (1:1) (60 ml) was added activated MnO_2 (14.4 g, 177 mmol) at rt. After stirring at rt for 24 h, the reaction mixture was filtered through Celite pad and concentrated to give (*Z*)-2-methyl-5-(trimethylsilyl)pent-2-en-4-ynal (1.8 g, 92%) as a brown oil, which was used for the next reaction without further purification: ^1H NMR (400 MHz, $CDCl_3$) δ 10.25 (s, 1H), 6.53 (s, 1H), 1.86 (s, 3H), 0.22 (s, 9H). ^{13}C NMR (100 MHz $CDCl_3$) δ 192.5, 147.4, 125.8, 106.5, 92.3, 15.5; FTIR (neat) 3557, 3357, 2138, 1697, 1257, 1100 cm^{-1}.



(*R*)-3-((*S*)-1-Hydroxy-3-methylbutan-2-yl)-5,5-dimethyl-6-((*Z*)-5-(trimethylsilyl)pent-2-en-4-yn-2-yl)-1,3-oxazinane-2,4-dione. $LiAlH_4$ (342 mg, 9.0 mmol) was added portionwise to a suspension of anhydrous $SnCl_2$ (3.42 g, 18.0 mmol), dried at 120 °C for 2 h in vacuo prior to use, in THF (18 ml) at rt. After stirring at rt for 20 min, a dark gray material was precipitated. To this suspension was added (*S*)-3-(2-bromo-2-methylpropanoyl)-4-isopropyloxazolidin-2-one (3.0 g, 10.8 mmol) in THF (18 ml) at rt, and the mixture was stirred at rt for 45 min. A solution of (*Z*)-2-methyl-5-(trimethylsilyl)pent-2-en-4-ynal (1.5 g, 9 mmol) in THF (18 ml) was then added at rt, and stirring was continued at rt for 16 h. The reaction was quenched with H_2O at 0 °C, and most of the THF was evaporated. The residue was extracted with Et_2O, washed with brine, dried, concentrated, and chromatographed (SiO_2 150 g, haxane/AcOEt = 10/1 to 5/1) to give (*R*)-3-((*S*)-1-hydroxy-3-methylbutan-2-yl)-5,5-dimethyl-6-((*Z*)-5-(trimethylsilyl)pent-2-en-4-yn-2-yl)-1,3-oxazinane-2,4-dione (2.87 g, 87%) as a colorless solid: $[\alpha]_D^{23}$ +8.1 (*c* 1.0, CH_2Cl_2) (lit.[4] $[\alpha]_D$ +8.1 (*c* 1.0, CH_2Cl_2)]; ^1H NMR (400 MHz, $CDCl_3$) δ 5.66 (s, 1H), 5.50 (s, 1H), 4.42(ddd, 1H, *J* = 2.7, 7.9, 10.6 Hz), 4.08 (m, 1H), 3.82 (br d, 1H, *J* = 12.2 Hz), 2.75 (br d, 1H, *J* = 7.8 Hz), 2.43-2.28 (m, 1H), 1.94 (s, 3H), 1.33 (s, 3H), 1.25 (s, 3H), 1.06 (d, 3H, *J*= 6.8Hz), 0.86 (d, 3H, J= 6.84), 0.15 (s, 9H); ^{13}C (400 Mhz, $CDCl_3$) δ 175.9, 152.2, 144.4, 113.7, 102.3, 101.5, 81.2, 62. 8. 43.6, 26,1, 22.3, 22.3, 20.1, 19.4; FTIR (neat), 3559, 1712, 1479, 1260 cm^{-1}; HRMS (EI) calcd for 365.2022 (M^+) found: 365.2018. The spectral data were identical with those reported.[4]

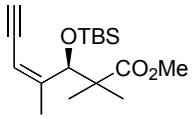


(*R*,*Z*)-Methyl 3-Hydroxy-2,2,4-trimethylhept-4-en-6-ynoate. To a solution of **21** (2.20 g, 6.03 mmol) in THF (90 ml) and H_2O (30 ml) were added 30% H_2O_2 (4.10 g, 36.1 mmol) and LiOH (506 mg, 12.1 mmol) at 0 °C, and the mixture was stirred at rt for 24 h. The reaction was quenched with 1.5 M Na_2SO_3 at 0 °C, and most of the THF was evaporated. The residue was diluted with H_2O, washed with CH_2Cl_2, acidified to pH 1, and extracted with AcOEt. The extract was washed with brine, dried, and concentrated to give a yellow oily residue (1.40 g).

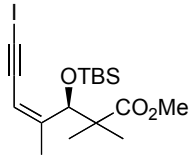
The residue (1.40 g) was dissolved in THF-MeOH-H_2O (3:1:1) (90 ml) and LiOH (568 mg, 13.6 mmol) was added. After being stirred at rt for 24 h, the reaction mixture was concentrated, extracted with AcOEt, washed with brine, dried, and concentrated to give the corresponding hydroxy acid as a yellow oil (1.20 g), which was used for the next reaction without purification.

To a solution of crude hydroxy acid (1.20 g) in Et_2O (30 ml) was added ethereal CH_2N_2 at 0 °C, and the mixture was stirred at 0 °C for 10 min. The reaction mixture was concentrated and chromtatographed (SiO_2 40 g, hexane/AcOEt = 7/1) to give (*R*,*Z*)-methyl 3-hydroxy-2,2,4-trimethylhept-4-en-6-ynoate (700 mg, 60%) as a colorless oil: $[\alpha]_D^{22}$ –18.3 (*c* 1.1,

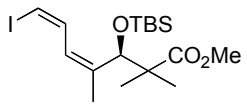
CH_2Cl_2) (lit.[4] $[\alpha]_D$ –26.6 (*c* 0.94, CH_2Cl_2)); ^{1}HNMR (400 MHz, $CDCl_3$) δ 5.47 (s, 1H), 5,30 (s, 1H), 4.87 (d, 1 H, *J* = 7.3 Hz), 3.73 (s, 3H), 3.61 (d, 1H, *J* = 7.3 Hz), 3.07 (d, 1H, *J* = 1.9 Hz), 1.75 (s, 3H), 1.35 (s, 3H), 1.18 (s, 3H); ^{13}C (400 MHz $CDCl_3$), δ 178.2, 151.4, 108.7, 81.8, 80.5, 52.1, 46.5, 24,4, 20.6, 18.1; FTIR (neat) 3494, 2094, 1735, 1469, 1142, 1050 cm^{-1}. HRMS (EI) calcd for $C_{11}H_{16}O_3$ (M^+) 196.1162, found 196.1092.



(*R*,*Z*)-Methyl 3-(*tert*-Buthyldimethylsilyloxy)-2,2,4-trimethylhept-4-en-6-ynoate. To a solution of (*R*,*Z*)-methyl 3-hydroxy-2,2,4-trimethylhept-4-en-6-ynoate (600 mg, 3.1 mmol) in CH_2Cl_2 (13 ml) were added 2,6-lutidine (1.4 ml, 12.4 mmol) and TBSOTf (2.7 ml, 7.9 mmol) at 0 °C. The mixture was allowed to warm to rt and stirred for additional 0.5 h. The reaction was quenched with saturated NH_4Cl at 0 ° C, and the reaction mixture was extracted with CH_2Cl_2. The extract was washed with brine, dried, concentrated, and chromatographed (SiO_2 30 g, hexane/AcOEt = 100/1) to give (*R*,*Z*)-methyl 3-(*tert*-buthyldimethylsilyloxy)-2,2,4-trimethylhept-4-en-6-ynoate (900 mg, 94 %) as a colorless oil: $[\alpha]_D^{22}$ +115.3 (*c* 1.1, CH_2Cl_2) (lit.[4] $[\alpha]_D$ +114.3 (*c* 1.2, CH_2Cl_2)]; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.44 (s, 1H), 5.15 (s, 1H), 3.66 (s, 3H), 3.13 (d, 1H, *J* = 1.5 Hz), 1.80 (s, 3H), 1,21 (s, 3H), 1.18 (s, 3H), 0.87 (s, 9H), 0.06 (s, 3H), –0.02 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.2, 153.1, 108.8, 82.2, 80.9, 52.0, 49.4, 26.9, 22.9, 21.0, 18.9, 18.3; FTIR (neat) 3311, 1735, 1468, 1256, 1136, 1083 cm^{-1}; HRMS (EI) calcd for $C_{17}H_{30}O_3Si$ (M^+) 310.1965, found 310.1938. The spectral data were identical with those reported.[4]



(*R*,*Z*)-Methyl 3-(*tert*-Buthyldimethylsilyloxy)-7-iodo-2,2,4-trimethylhept-4-en-6-ynoate. To a solution of (*R*,*Z*)-methyl 3-(*tert*-buthyldimethylsilyloxy)-2,2,4-trimethylhept-4-en-6-ynoate (600 mg, 1.94 mmol) in THF (10 ml) was added *n*-BuLi (1.6 M in hexane, 1.34 ml, 2.14 mmol) at –78 °C. After stirring at –78 °C for 1 h, a solution of I_2 (984 mg, 3.88 mmol) in THF (2 ml) was added and stirring was continued at –78 °C for 1 h. The mixture was allowed to warm to rt, and the reaction was quenched with saturated $Na_2S_2O_3$ at 0 °C. The reaction mixture was extracted with AcOEt, washed with brine, dried, concentrated, and chromatographed (SiO_2 50 g, hexane/AcOEt = 7/1) gave (*R*,*Z*)-methyl 3-(*tert*-buthyldimethylsilyloxy)-7-iodo-2,2,4-trimethylhept-4-en-6-ynoate (841 mg, 99%) as a pale yellow oil. $[\alpha]_D^{23}$ +93.4 (*c* 1.0, CH_2Cl_2) (lit.[4] $[\alpha]_D$ +97.6 (*c* 1.3, CH_2Cl_2)]; ^{1}HNMR (400 MHz, $CDCl_3$) δ 5.55 (s, 1H), 5.10 (s, 1H), 3.67 (s, 3H), 1.80 (s, 3H), 1.20 (s, 3H), 1.16 (s, 3H), 0.88 (s, 9H), 0.06 (s, 3H), 0.01 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.7, 154.0, 109.6, 91.4, 76.5, 51.8, 49.0, 25.7, 22.4, 20.9, 18.4, 18.0; FTIR (neat) 1736, 1468, 1388, 1255, 1137, 1079, 1000 cm^{-1}; HRMS (EI) calcd for $C_{17}H_{29}O_3SiI$ (M^+) 436.0931, found 436.0922. The spectral data were identical with those reported.[4]

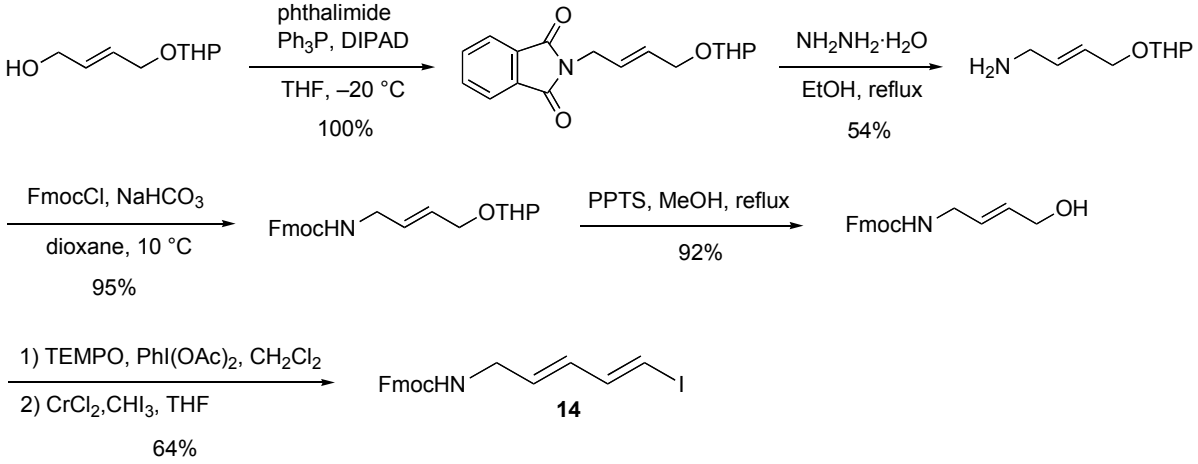


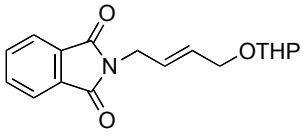
23

(*R*,4*Z*,6*Z*)-Methyl 3-(*tert*-Butyldimethylsilyloxy)-7-iodo-2,2,4-trimethylhepta-4,6-dienoate (23). To a solution of (*R*,*Z*)-methyl 3-(*tert*-buthyldimethylsilyloxy)-7-iodo-2,2,4-trimethylhept-4-en-6-ynoate (800 mg, 1.84 mmol) in THF-*i*-PrOH (1:1) (10 ml) were added Et_3N (0.384 ml, 2.76 mmol) and *o*-nitrobenzenesulfonyl hydrazide[7] (654 mg, 3.00 mmol) at rt. The mixture was stirred under dark at rt for 12 h. The reaction mixture was diluted with AcOEt, washed with H_2O and brine, dried, and concentrated. The residue was purified by flash chromatography (SiO_2 15 g, hexane/AcOEt = 100/1) to give the recovered starting material (120 mg, 15%) and **23** (600 mg, 74 %) as a pale yellow oil: $[\alpha]_D^{23}$ +77.5 (*c* 1.35, CH_2Cl_2) (lit.[4] $[\alpha]_D$ +78.2 (*c* 1.1, CH_2Cl_2)]; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.00 (br d, *J* = 8.3 Hz), 6.25

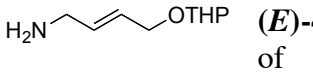
(d, 1H, J = 6.3 Hz), 6.12 (d, 1H, J = 10.3 Hz), 4.91 (br s, 1H), 3.63 (s, 3H), 1.84 (s, 3H), 1.23 (s, 3H), 1.10 (s, 3H), 0.88 (s, 9H), 0.02 (s, 3H), -0.04 (s, 3H); FTIR (neet) 1741, 1469, 1386,1260, 1091, 1012 cm^{-1}; HRMS (EI) calcd for $C_{17}H_{31}O_3SiI$ (M^+) 438.1087, found 438.1072. The spectral data were identical with those reported.[4]

Preparation of (9*H*-Fluoren-9-yl)methyl (2*E*,4*E*)-5-Iodopenta-2,4-dienylcarbamate (14)

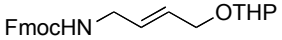




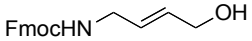
2-((*E*)-4-(Tetrahydro-2*H*-pyran-2-yloxy)but-2-enyl)isoindoline-1,3-dione. To a solution of (*E*)-4-(tetrahydro-2*H*-pyran-2-yloxy)but-2-en-1-ol[8] (5.00 g, 29.0 mmol) in THF (137 ml) were added triphenylphosphine (9.14 g, 34.8 mmol), phthalimide (5.12 g, 34.8 mmol), and diisopropyl azodicarboxylate (DIAD) (6.75 ml, 34.8 mmol) at –20 °C. After stirring at rt for 1 h, SiO_2 (54 g) was added, and the mixture was concentrated. The residue was subjected to column chromatography (SiO_2 270 g, hexane/AcOEt = 10/1 to 6/1) to afford 2-((*E*)-4-(tetrahydro-2*H*-pyran-2-yloxy)but-2-enyl)isoindoline-1,3-dione (8.74 g, 100%) as a colorless solid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, J = 2.9 Hz, 1H), 7.84 (d, J = 2.9 Hz, 1H), 7.72 (d, J = 2.9 Hz, 1H), 7.71 (d, J = 2.9 Hz, 1H), 5.84-5.81 (m, 2H), 4.61 (t, J = 3.4, 1H), 4.30 (d, J = 4.6 Hz, 2H), 4.23-4.19 (m, 1H), 3.97-3.93 (m, 1H), 3.86-3.80 (m, 1H), 3.50-3.46 (m, 1H), 1.82–1.50 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.7 (2), 134.2, 133.8, 132.1, 130.4, 125.5, 123.5, 123.2 (2), 97.9, 66.6, 62.1, 39.1, 30.5, 25.5, 19.4; FTIR (neat) 3801, 3464, 1699, 1606, 1389, 1190, 1024, 802, 715 cm^{-1}; MS (EI) m/z 85, 200 (100), 217, 301 (M^+).



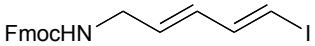
(*E*)-4-(Tetrahydro-2*H*-pyran-2-yloxy)but-2-en-1-amine. To a solution of 2-((*E*)-4-(tetrahydro-2*H*-pyran-2-yloxy)but-2-enyl)isoindoline-1,3-dione (8.50 g, 28.2 mmol) in EtOH (320 ml) was added hydrazine monohydrate (2.0 ml, 42.3 mmol), and the mixture was refluxed for 1 h. Most of the EtOH was removed in vacuo, and the residue was dissolved in $CHCl_3$ and filtered through Celite pad. The filtrate was concentrated and chromatographed (SiO_2 150 g, $CHCl_3$/MeOH = 20/1) to give (*E*)-4-(tetrahydro-2*H*-pyran-2-yloxy)but-2-en-1-amine (2.58 g, 54%) as a pale yellow solid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.89-5.83 (m, 1H), 5.75-5.68 (m, 1H), 4.65 (t, J = 3.5 Hz, 1H), 4.25 (dd, J = 1.2, 12.2 Hz, 0.5H), 4.23 (dd, J = 1.0, 12.2 Hz, 0.5H), 3.99-3.94 (m, 1H), 3.91-3.85 (m, 1H), 3.54-3.49 (m, 1H), 3.32 (dd, J = 1.0, 5.5 Hz, 2H), 1.88-1.45 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 134.6, 125.9, 97.9, 67.3, 62.2, 43.6, 30.6, 25.4, 19.5; FTIR (neat) 1566, 1442, 1124, 1026 cm^{-1}; MS (FAB) m/z 43, 69, 70, 85 (100), 172 (M^++H).



(9*H*-Fluoren-9-yl)methyl (*E*)-4-(Tetrahydro-2*H*-pyran-2-yloxy)but-2-enylcarbamate. To a solution of (*E*)-4-(tetrahydro-2*H*-pyran-2-yloxy)but-2-en-1-amine (2.00 g, 11.7 mmol) in 1,4-dioxane (117 ml) were added $NaHCO_3$ (2.94 g, 35.0 mmol) and 9-fluorenylmethyl chloroformate (5.43 g, 17.5 mmol). After being stirred at rt for 5 h, the reaction mixture was extracted with Et_2O, washed with saturated $NaHCO_3$ and brine, dried, and concentrated. The residue was purified by column chromatography (SiO_2 300 g, hexane/AcOEt = 10/1 to 6/1) to give (9*H*-fluoren-9-yl)methyl (*E*)-4-(tetrahydro-2*H*-pyran-2-yloxy)but-2-enylcarbamate (4.36 g, 95%) as a colorless solid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, *J* = 7.6 Hz, 2H), 7.59 (d, *J* = 7.3 H, 2H), 7.40 (t, *J* = 7.3 Hz, 2H), 7.31 (t, *J* = 7.4 Hz, 2H), 5.75 (s, 2H), 4.85 (s, 1H), 4.63 (s, 1H), 4.41 (d, *J* = 6.8 Hz, 2H), 4.23 (d, *J* = 11.5 Hz, 1H), 4.22 (s, 1H), 3.95 (d, *J* = 11.5 Hz, 1H), 3.88-3.83 (m, 3H), 3.52-3.48 (m, 1H), 1.87-1.52 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.0, 143.7 (2), 141.1 (2), 128.8, 128.4, 127.5 (2), 126.9 (2), 124.8 (2), 119.8 (2), 98.0, 66.8, 66.6, 62.1, 47.2, 30.5, 25.4, 19.4; FTIR (neat) 3327, 1714, 1529, 1450, 1246, 1130, 1074, 1024 cm^{-1}; MS (EI) m/z 178 (100), 393 (M^+); HRMS (EI) calcd for $C_{24}H_{27}NO_4$ (M^+) 393.1940, found 393.1936.



(9*H*-Fluoren-9-yl)methyl (*E*)-4-Hydroxybut-2-enylcarbamate. To a solution of (9*H*-fluoren-9-yl)methyl (*E*)-4-(tetrahydro-2*H*-pyran-2-yloxy)but-2-enylcarbamate (4.30 g, 10.9 mmol) in MeOH (36 ml) was added PPTS (550 mg, 2.19 mmol), and the mixture was refluxed for 24 h. The After being cooled to rt, reaction mixture was diluted with Et_2O, washed with saturated $NaHCO_3$ and brine, dried, concentrated, and chromatographed (SiO_2 175 g, hexane/AcOEt = 100/ 1 to 80/1) to give (9*H*-fluoren-9-yl)methyl (*E*)-4-hydroxybut-2-enylcarbamate (3.10 g, 92%) as colorless crystals: mp 115-116 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, *J* = 7.6 Hz, 2H), 7.59 (d, *J* = 7.3 H, 2H), 7.40 (t, *J* = 7.4 Hz, 2H), 7.31 (t, *J* = 7.4 Hz, 2H), 5.80-5.71 (m, 2H), 4.84 (bs, 1H), 4.43 (d, *J* = 6.6 Hz, 2H), 4.23-4.20 (m, 1H), 4.15 (bs, 1H), 3.83 (bs, 2H), 1.41 (bs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.1, 143.8 (2), 141.2 (2), 131.0, 127.7, 127.6 (2), 126.9 (2), 124.8 (2), 119.8 (2), 66.6, 62.8, 47.2, 42.3; FTIR (neat) 3315, 1685, 1514, 1444, 1261, 1146, 1092 cm^{-1}; MS (EI) m/z 178 (100), 309 (M^+); HRMS (EI) calcd for $C_{19}H_{19}NO_3$ (M^+) 309.1365, found 309.1355.



14

(9*H*-Fluoren-9-yl)methyl (2*E*,4*E*)-5-Iodopenta-2,4-dienylcarbamate (14). To a solution of (9*H*-fluoren-9-yl)methyl (*E*)-4-hydroxybut-2-enylcarbamate (500 mg, 1.62 mmol) in CH_2Cl_2 (16 ml) were added $PhI(OAc)_2$ (1.72 g, 5.34 mmol) and TEMPO (50.5 mg, 0.32 mmol). After being stirred at rt for 4.5 h, the reaction mixture was diluted with CH_2Cl_2, washed with saturated $Na_2S_2O_3$ and brine, dried, and concentrated to give the corresponding aldehyde (1.70 g), which was used for the next reaction without purification.

To a suspension of $CrCl_2$ (2.79 g, 22.9 mmol) in THF (30 ml) at 0 °C were added CHI_3 (2.09 g, 5.28 mmol) and crude aldehyde (1.70 g), and the mixture was stirred at rt for 1.5 h. The reaction was quenched with saurated $Na_2S_2O_3$ (30 ml), and the reacrtion mixtur was extracted with AcOEt. The extract was washed with brine, dried, and concentrated. The residue was purified by column chromatography (SiO_2 30 g, hexane/AcOEt = 40/1 to 10/1) to give **14** (450 mg, 64%) as pale yellow crystals ($CHCl_3$): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, *J* = 7.6 Hz, 2H), 7.58 (d, *J* = 7.1 H, 2H), 7.40 (t, *J* = 7.6 Hz, 2H), 7.32–7.29 (m, 1H), 7.00 (dd, *J* = 10.5, 14.4 Hz, 1H), 6.32 (d, *J* = 14.4 Hz, 1H), 6.10-6.04 (m, 1H), 5.75-5.65 (m, 1H), 4.82 (bs, 1H), 4.43 (d, *J* = 6.7 Hz, 2H), 4.22 (t, *J* = 6.7 Hz, 1H), 3.8 (bs, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.0, 144.1, 143.8 (2), 141.2 (2), 131.4, 130.3, 127.6 (2), 127.0 (2), 124.9 (2), 120.2 (2), 79.6, 66.7, 47.3, 42.3; FTIR (neat) 3317, 3053, 1687, 1531, 1442, 1263, 1146, 1263, 1146 cm^{-1}; MS (EI) m/z 178 (100), 256, 367, 431 (M^+); HRMS (EI) calcd for $C_{20}H_{18}NIO_2$ (M^+) 431.0382, found 431.0381.

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