Supporting Information

Total Synthesis of Kendomycin: A Macro–*C*–glycosidation Approach

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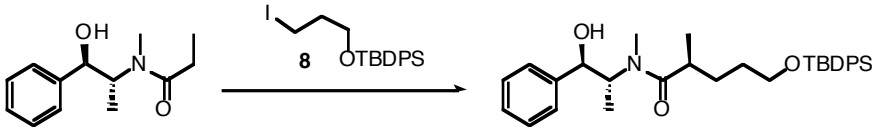
General:

Unless otherwise noted, all reactions were conducted in flame-dried glassware under an argon atmosphere using anhydrous solvent (either distilled or passed through an activated alumina column or activated molecular sieves column). Commercially available reagents were used without further purification. Thin layer chromatography (TLC) was performed using EM Science silica gel 60 F_{254} plates and visualized using UV light, anisaldehyde, ceric sulfate or potassium permanganate. Flash chromatography was performed on EM Science silica gel 60 (40-63 μm) using the indicated solvent system. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$, unless otherwise noted, on a Varian Mercury 300 MHz, a Varian Inova 400 MHz or a Varian Inova 500 MHz spectrometer. Chemical shifts in ^{1}H NMR spectra were reported in parts per million (ppm) on the δ scale from an internal standard of residual chloroform (7.27 ppm). Data for ^{1}H NMR are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constant in Herts (Hz) and integration. Data for ^{13}C NMR spectra are reported in terms of chemical shift in ppm from the central peak of $CDCl_3$ (77.23 ppm). Infrared (IR) spectra were recorded on a Nicolet 730 FT-IR spectrometer and reported in frequency of the absorption (cm^{-1}). High resolution mass spectra (HRMS) were obtained from the Princeton University Mass Spectrometry Facility and UCR Mass Spectrometry Facility. Optical rotations were measured on a Perkin-Elmer 341 polarimeter at 589 nm. Melting point was measured on a Mel-Temp apparatus without further calibration.



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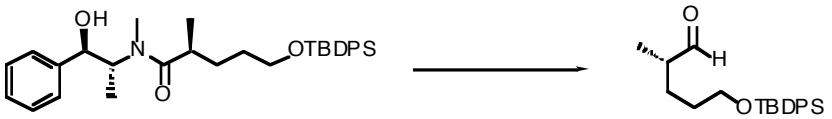
Aldehyde 9: A flask was charged with anhydrous lithium chloride (25.0 g, 590 mmol), diisopropylamine (31.3 mL, 225 mmol) and THF (100 mL). The resulting suspension was cooled to –78 °C, and a solution of *n*-BuLi (2.5 M in hexanes, 88.0 mL, 0.22 mol) was added. The suspension was warmed briefly to 0 °C and then cooled to –78 °C. An ice-cooled solution of amide **7** (22.1 g, 100 mmol) in THF (300 mL) was added to the reaction via cannula. The reaction mixture was stirred at –78 °C for 1 h, at 0 °C for 15 min, and at 23 °C for 5 min and finally cooled to 0 °C, whereupon the known alkyl iodide **8**[1] (38.2 g, 90.0 mmol) in THF (50 mL) was added. The reaction mixture was stirred at 0 °C for 20 h and then quenched by the addition of half saturated aqueous NH_4Cl solution. The mixture was extracted with EtOAc (3 X 250 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. Purification of the residue by flash column chromatography (silica gel, hexanes / EtOAc = 1 / 1) afforded the amide (39.0 g, 83%) as a light yellow gel: (Rotation isomers were observed) $[\alpha]_D^{23}$ –34.3 (*c* 2.20, $CHCl_3$); IR (Film) 3375, 2932, 2858, 1618, 1472, 1111 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.62-7.71 (m, 4H), 7.24-7.45 (m, 11H), 4.61 (br t, *J* = 6.7 Hz, 1H), 4.42 (br s, 1H), 3.63 (m, 2H), 2.79 (s, 3H), 2.59 (m, 1H), 1.68 (m, 1H), 1.56 (m, 1H), 1.47 (m, 2H), 1.13 (d, *J* = 7.0 Hz, 3H), 1.09 (d, *J* = 6.9 Hz, 3H), 1.07 (s, 9H); ^{13}C NMR (125 MHz,

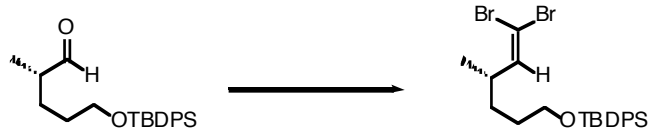
[1] Swindell, C. S.; Patel, B. P. *Tetrahedron Lett.* **1987**, *28*, 5275.

$CDCl_3$) δ 179.1, 142.7, 135.8, 135.7, 134.1, 129.8, 129.7, 128.5, 127.8, 127.7, 127.0, 126.4, 77.4, 76.6, 63.8, 36.4, 30.3, 30.2, 27.0, 19.4, 17.4, 14.6; HRMS-EI (m/z): [M – *t*-Bu]$^+$ calc'd for $C_{28}H_{34}O_3SiN$, 460.2308, found 460.2287.



9

To a suspension of lithium aluminum hydride (95%, 3.55 g, 88.8 mmol) in hexanes (200 mL) was added EtOAc (12.9 mL, 133 mmol) at 0 °C slowly over a period of 2 h, and the resulting suspension was cooled to –78 °C. A solution of the amide (20.0 g, 38.6 mmol) in THF (132 mL) was added and the reaction mixture was warmed to 0 °C. After being stirred for 1 h at 0 °C, the reaction mixture was transferred by cannula to a solution of trifluoroacetic acid (60.0 mL, 780 mmol) in 1 *N* aqueous HCl solution (960 mL), and the reaction flask was rinsed with an additional portion of THF (10 mL). The resulting biphasic mixture was stirred at 23 °C for 5 min and then diluted with 1 *N* aqueous HCl solution (1700 mL), and the layers were separated. The aqueous layer was extracted with EtOAc (3 X 360 mL). The combined organic layers were neutralized by the careful addition of saturated aqueous $NaHCO_3$ solution (600 mL). The aqueous layer (pH 7-8) was separated and extracted with EtOAc (100 mL). The combined organic extracts were dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. Purification of the residue by flash column chromatography (silica gel, hexanes / EtOAc = 10 / 1) afforded aldehyde **9** as a colorless liquid: $[\alpha]_D^{23}$ +15 (*c* 0.35, $CHCl_3$); IR (Film) 2932, 2858, 1727, 1428, 1112, 702 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.62 (d, *J* = 2.0 Hz, 1H), 7.67-7.68 (m, 4H), 7.38-7.44 (m, 6H), 3.71 (t, *J* = 6.0 Hz, 2H), 2.34 (m, 1H), 1.81 (m, 1H), 1.60 (m, 2H), 1.47 (m, 1H), 1.09 (d, *J* = 7.0 Hz, 3H), 1.07 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.4, 135.8, 134.1, 129.8, 127.8, 63.7, 46.2, 30.0, 27.1, 27.0, 19.4, 13.5; HRMS-EI (m/z): [M – *t*-Bu]$^+$ calc'd for $C_{18}H_{21}O_2Si$, 297.1311, found 297.1302.



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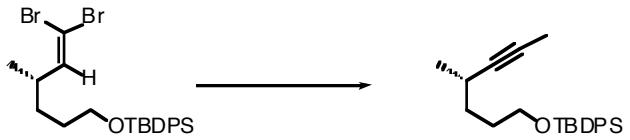
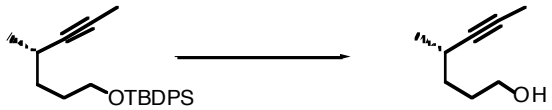
Aldehyde 10: A flask was charged zinc dust (5.0 g, 77 mmol), carbon tetrabromide (25.0 g, 75.4 mmol), triphenylphosphine (20.0 g, 76.2 mmol) and CH_2Cl_2 (300 mL). The resulting suspension was stirred at 23 °C overnight. To this suspension was added a solution of aldehyde **9** in CH_2Cl_2 (100 mL). After being stirred for 2 h, the mixture was diluted with hexanes (200 mL) and filtered to remove insoluble material. The filtrate was concentrated *in vacuo* and purified by flash column chromatography (silica gel, hexanes / EtOAc = 15 / 1) to afford the dibromoolefin (16.4 g, 83% for two steps) as a colorless liquid: $[\alpha]_D^{23}$ +2.30 (*c* 1.30, $CHCl_3$); IR (Film) 2931, 2857, 1428, 1111, 823, 701 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.70-7.73 (m, 4H), 7.40-7.50 (m, 6H), 6.20 (d, *J* = 9.4 Hz, 1H), 3.70 (t, *J* = 6.2 Hz, 2H), 2.48 (m, 1H), 1.60 (m, 2H), 1.45 (m, 2H), 1.11 (s, 9H), 1.04

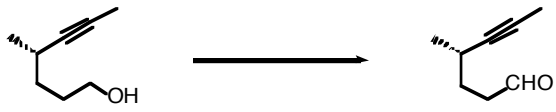
(d, J = 6.8 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.4, 135.8, 134.2, 129.8, 127.8, 87.7, 63.9, 38.3, 32.5, 30.3, 27.1, 19.5, 19.4; HRMS-EI (m/z): [M – t-Bu]$^+$ calc'd for $C_{19}H_{21}OBr_2Si$, 450.9728, found 450.9754.



To a solution of the dibromoolefin (11.2 g, 21.9 mmol) in THF (80 mL) at –78 °C was added a solution of n-BuLi (2.5 M in hexanes, 20.0 mL, 50 mmol). The reaction mixture was stirred at –78 °C for 1 h, then 23 °C for 40 min, followed by the addition of MeI (3.70 mL, 59.0 mmol). After being stirred at room temperature for 8 h, the reaction was quenched by the addition of saturated aqueous NH_4Cl solution and extracted with Et_2O (3 X 100 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. Purification of the residue by flash column chromatography (silica gel, hexanes / EtOAc = 50 / 1) afforded the alkyne (8.01 g, 100%) as a colorless oil: $[\alpha]_D^{23}$ +15.3 (*c* 1.30, $CHCl_3$); IR (Film) 2961, 2931, 2858, 1473, 1428, 1112 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67-7.70 (m, 4H), 7.37-7.43 (m, 6H), 3.69 (t, J = 6.4 Hz, 2H), 2.37 (m, 1 H), 1.79 (d, J = 2.4 Hz, 3H), 1.75 (m, 1H), 1.66 (m, 1H), 1.48 (m, 2H), 1.13 (d, J = 7.0 Hz, 3H), 1.06 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.8, 134.3, 129.7, 127.8, 84.0, 75.8, 64.0, 33.7, 30.6, 27.1, 25.9, 21.7, 19.4, 3.7; HRMS (m/z): [M + H]$^+$ calc'd for $C_{24}H_{33}OSi$, 365.2301, found 365.2286.



To a solution of the alkyne (8.93 g, 24.5 mmol) in THF (30 mL) was added TBAF (1.0 M in THF, 30.0 mL, 30 mmol). After being stirred at room temperature for 5 h, the reaction mixture was poured into saturated aqueous NH_4Cl solution and extracted with Et_2O (3 X 50 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. Purification of the residue by flash column chromatography (silica gel, hexanes / EtOAc = 1 / 3) afforded the alcohol (3.08 g, 99.6%) as a colorless liquid: $[\alpha]_D^{23}$ +30.5 (*c* 2.00, $CHCl_3$); IR (Film) 3340, 2966, 2921, 2871, 1455, 1057 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.66 (t, J = 6.4 Hz, 2H), 2.39 (m, 1H), 1.78 (d, J = 2.4 Hz, 3H), 1.74 (m, 1H), 1.64 (m, 1H), 1.46 (m, 2H), 1.13 (d, J = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 83.7, 76.1, 63.0, 33.6, 30.8, 26.0, 21.7, 3.7; HRMS (m/z): [M + H]$^+$ calc'd for $C_8H_{15}O$, 127.1117, found 127.1125.



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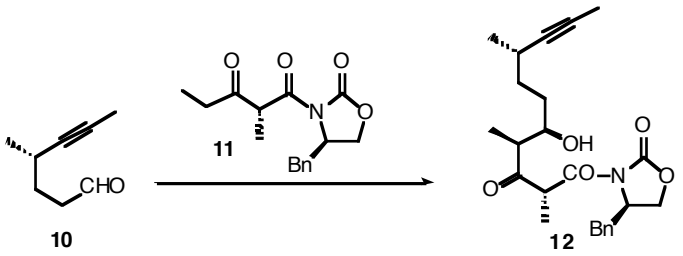
To a solution of the alcohol (1.51 g, 12.0 mmol) in CH_2Cl_2 (20 mL) was added Dess-Martin reagent (10.2 g, 24.0 mmol) in three portions. When the starting material was completely consumed (monitored by TLC), the reaction mixture was poured into saturated aqueous $NaHCO_3$ solution (10 mL). The organic layer was washed with saturated $NaHCO_3$ and brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo* at 0 °C to a volume of 5 mL. The resulting solution containing the volatile and unstable aldehyde **10** was dried over molecular sieves and used in the next step without further purification (*ca.* 85%, estimated by ^{1}H NMR): ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.83 (t, J = 1.5 Hz, 1H), 2.62 (m, 2H), 2.46 (m, 1H), 1.80 (s, 3H), 1.79 (m, 1H), 1.66 (m, 1H), 1.18 (d, J = 6.6 Hz, 3H).

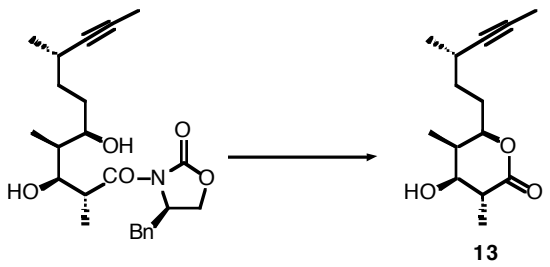


Aldol 12: A stirred suspension of anhydrous, acid-free $Sn(OTf)_2$ (3.62 g, 8.70 mmol) in CH_2Cl_2 (35 mL) at 25 °C was treated with triethylamine (1.21 mL, 8.70 mmol) and then immediately cooled to –20 °C. After 5 min, a solution of the β-keto imide **11**[2] (2.40 g, 8.30 mmol) in CH_2Cl_2 (15 mL) was added dropwise over a period of 10 min. The resulting suspension was stirred for 1 h and then cooled to –78 °C prior to the addition of aldehyde **10** from the previous step. The mixture was stirred at –78 °C for 1 h and then poured into a cooled and vigorously stirred 1:1 mixture of CH_2Cl_2 and 1 *N* aqueous $NaHSO_4$. After extracted with CH_2Cl_2 (3 X 75 mL), the combined organic layers were washed with saturated aqueous $NaHCO_3$, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. Purification of the mixture (*dr* = 7 : 1 determined by ^{1}H NMR) by flash column chromatography (silica gel, hexanes / EtOAc = 2 / 1) afforded the diastereomerically pure aldol **12** (2.82 g, 82%) as a colorless liquid: $[\alpha]_D^{23}$ +51.2 (*c* 1.77, $CHCl_3$); IR (Film) 3565, 2969, 1780, 1713, 1391, 1360 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.15-7.37 (m, 5H), 4.88 (q, J = 7.4 Hz, 1H), 4.77 (m, 1H), 4.28 (t, J = 8.1 Hz, 1H), 4.20 (dd, J = 9.1, 2.9 Hz, 1H), 3.95 (m, 1H), 3.32 (dd, J = 13.5, 3.0 Hz, 1H), 2.80 (m, 2H), 2.43 (m, 1H), 1.79 (d, J = 2.2 Hz, 3H), 1.70 (m, 1H), 1.55 (m, 1H), 1.50 (d, J = 7.3 Hz, 3H), 1.45 (m, 2H), 1.26 (d, J = 7.3 Hz, 3H), 1.15 (d, J = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 212.3, 170.5, 153.8, 135.2, 129.6, 129.2, 127.6, 83.5, 76.2, 71.1, 66.7, 55.5, 52.1, 48.6, 38.1, 33.6, 31.7, 25.8, 21.6, 13.1, 10.2, 3.7; HRMS (m/z): $[M + H]^+$ calc'd for $C_{24}H_{32}NO_5$, 414.2280, found 414.2265.

[2] Evans, D. A.; Clark, J. S.; Metternich, R.; Novack, V. J.; Sheppard, G. S. *J. Am. Chem. Soc.* **1990**, *112*, 866.

12

Lactone 13: To a solution of aldol **12** (91.0 mg, 0.220 mmol) in anhydrous acetic acid (2.0 mL) at 5 °C was added $NaBH(OAc)_3$ (232 mg, 1.10 mmol). After being stirred for 3 h, the reaction was cooled to 0 °C, and quenched by the careful addition of saturated aqueous $NaHCO_3$. After extracted with Et_2O (4 X 25 mL), the combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. Purification of the residue by flash column chromatography (silica gel, hexanes / EtOAc = 2 / 1 to 1 / 1) afforded the diol (pure diastereomer 75.0 mg, $dr \geq 20 : 1$ determined by crude ^{1}H NMR, 82%) as a white solid: $[\alpha]_D^{23}$ -5.1 (*c* 0.93, $CHCl_3$); IR (Film) 3510, 2970, 1780, 1696, 1387, 1211 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28-7.37 (m, 3H), 7.21-7.22 (m, 2H), 4.72 (m, 1H), 4.25 (q, *J* = 8.1 Hz, 1H), 4.22 (dd, *J* = 8.8, 2.5 Hz, 1H), 4.01 (dd, *J* = 9.2, 2.2 Hz, 1H), 3.89 (qd, *J* = 7.0, 2.2 Hz, 1H), 3.82 (d, *J* = 9.8 Hz, 1H), 3.68 (br s, 1H), 3.26 (dd, *J* = 13.3, 3.3 Hz, 1H), 2.81 (dd, *J* = 13.6, 9.5 Hz, 1H), 2.75 (br s, 1H), 2.43 (m, 1H), 1.89 (m, 1H), 1.79 (d, *J* = 2.2 Hz, 3H), 1.68 (m, 1H), 1.61 (m, 1H), 1.55 (m, 1H), 1.47 (m, 1H), 1.29 (d, *J* = 6.9 Hz, 3H), 1.15 (d, *J* = 6.9 Hz, 3H), 0.87 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.2, 153.0, 135.1, 129.6, 129.2, 127.7, 83.8, 76.1, 73.9, 73.8, 66.4, 55.3, 39.7, 39.4, 38.0, 34.1, 30.7, 25.9, 21.7, 11.9, 10.3, 3.7; HRMS (m/z): $[M + H]^+$ calc'd for $C_{24}H_{34}NO_5$, 416.2437, found 416.2424.



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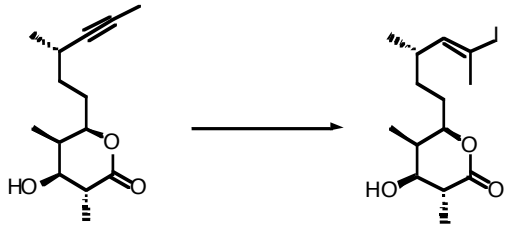
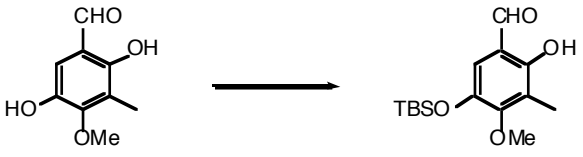
To a solution of the diol (580 mg, 1.40 mmol) in CH_2Cl_2 (15 mL) was added DBU (42 μL, 0.28 mmol). After being stirred at room temperature for 2 h, the reaction mixture was diluted with EtOAc (50 mL), washed with water and brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. Purification of the residue by flash column chromatography (silica gel, hexanes / EtOAc = 1 / 1) afforded lactone **13** (300 mg, 90%) as a colorless oil: $[\alpha]_D^{23}$ +101 (*c* 0.720, $CHCl_3$); IR (Film) 3445, 2970, 1707, 1457, 1213, 1099, 985 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.22 (m, 1H), 3.80 (dd, *J* = 10.3, 4.4 Hz, 1H), 2.44 (dd, *J* = 10.5, 7.0 Hz, 1H), 2.41 (m, 1H), 2.13 (m, 1H), 1.93 (m, 1H), 1.76 (d, *J* = 2.2 Hz, 3H), 1.61 (m, 1H), 1.53 (m, 1H), 1.44 (m, 1H), 1.37 (d, *J* = 6.9 Hz, 3H), 1.13 (d, *J* = 6.9 Hz, 3H), 0.96 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.2, 83.0, 79.8, 76.5, 73.8, 39.9, 37.5, 32.7, 30.0, 25.6, 21.5, 14.4, 4.7, 3.6; HRMS-EI (m/z): $[M]^+$ calc'd for $C_{14}H_{22}O_3$, 238.1569, found 238.1559.



13 **5**

Vinyl Iodide 5: To a suspension of $Pd(OAc)_2$ (22 mg, 0.10 mmol) in a mixture of hexanes and THF (5:1, 24 mL) was added PCy_3 (56 mg, 0.20 mmol). This suspension was stirred at room temperature until a homogenous yellow solution was formed. Then, a solution of lactone **13** (600 mg, 2.52 mmol) in hexanes-THF (1:1, 4 mL) was added via cannula followed by the addition of tributyltin hydride (1.34 mL, 5.00 mmol) over 30 min. Upon the complete consumption of lactone **13**, the reaction mixture was concentrated *in vacuo* and directly loaded onto a silica gel column. Purification by flash column chromatography (silica gel, hexanes / EtOAc = 8 / 1) afforded the vinyl stannane as a yellow liquid.

To a solution of the vinyl stannane in CH_2Cl_2 (10 mL) at 0 °C was added iodine (1.27 g, 5.00 mmol). After being stirred for 20 min, the reaction mixture was poured into a vigorously stirred solution of saturated aqueous $Na_2S_2O_3$ and extracted with Et_2O (3 X 30 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. Purification of the mixture (regioselectivity ≥ 7 : 1 determined by ^1H NMR) by flash column chromatography (silica gel, hexanes / EtOAc = 3 / 1) afforded pure (*E*)-vinyl iodide **5** (769 mg, 83% for two steps) as a colorless oil: $[\alpha]_D^{23}$ +68 (*c* 0.69, $CHCl_3$); IR (Film) 3440, 2953, 1710, 1457, 1376, 1215 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.93 (dq, *J* = 9.9, 1.5 Hz, 1H), 4.17 (m, 1H), 3.81 (m, 1H), 2.46 (dd, *J* = 10.5, 7.0 Hz, 1H), 2.42 (m, 1H), 2.37 (d, *J* = 1.5 Hz, 3H), 2.11 (m, 1H), 2.08 (d, *J* = 4.7 Hz, 1H), 1.75 (m, 1H), 1.64 (m, 1H), 1.45 (m, 1H), 1.39 (d, *J* = 7.0 Hz, 3H), 1.32 (m, 1H), 0.98 (d, *J* = 6.6 Hz, 3H), 0.96 (d, *J* = 7.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.8, 146.6, 93.3, 79.9, 74.0, 40.0, 37.4, 35.6, 32.6, 30.2, 28.0, 20.6, 14.4, 4.7; HRMS-EI (m/z): $[M + NH_4]^+$ calc'd for $C_{14}H_{27}O_3IN$, 384.1030, found 384.1045.



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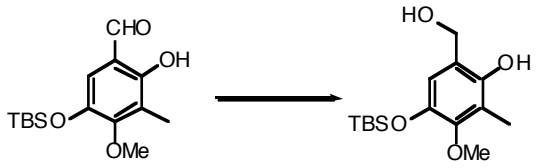
Benzyl Alcohol 15: To a solution of phenol **14**[3] (400 mg, 2.20 mmol) and imidazole (340 mg, 5.00 mmol) in CH_2Cl_2 (10 mL) was added TBSCl (375 mg, 2.50 mmol) at room temperature. After being stirred for 5 h, the reaction mixture was diluted with EtOAc (50 mL), washed with water and brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. Purification of the residue by flash column chromatography (silica gel, hexanes /

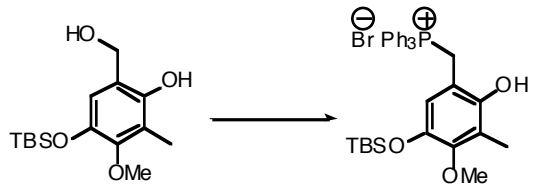
[3] Siddiqi, S. A.; Heckrodt, T. J. *Z.Naturforsch.(B)* **2003**, *58*, 328.

EtOAc = 8 / 1) afforded the monophenol (650 mg, 100 %) as a light yellow oil: IR (Film) 2956, 2931, 2859, 1651, 1474, 1319 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 11.19 (s, 1H), 9.69 (s, 1H), 6.84 (s, 1H), 3.83 (s, 3H), 2.16 (s, 3H), 1.02 (s, 9H), 0.19 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 195.3, 157.9, 156.6, 142.1, 121.2, 120.9, 116.1, 60.3, 25.9, 18.4, 8.5, -4.5; HRMS-EI (m/z): $[M]^+$ calc'd for $C_{15}H_{24}O_4Si$, 296.1444, found 296.1432.



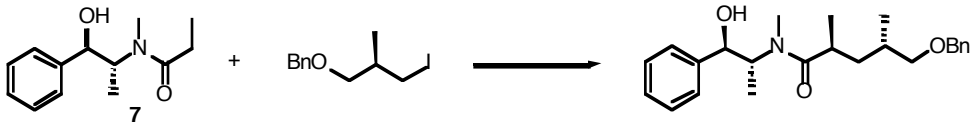
15

To a solution of the TBS ether (160 mg, 0.540 mmol) in CH_2Cl_2 (4 mL) at –78 °C was added DIBAL-H (1.0 M in hexanes, 1.50 mL, 1.5 mmol). After 2 h, the reaction was quenched by the addition of saturated aqueous potassium sodium tartrate (5 mL) and warmed to ambient temperature. After being stirred vigorously for 1 h, the mixture was diluted with H_2O and extracted with EtOAc (3 X 15 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. Purification of the residue by flash column chromatography (silica gel, hexanes / EtOAc = 1 / 3) afforded diol **15** (153 mg, 95%) as a white solid: IR (Film) 3504, 3325, 2949, 2930, 2857, 1487 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.99 (s, 1H), 6.41 (s, 1H), 4.75 (d, J = 4.9 Hz, 2H), 3.73 (s, 3H), 2.18 (s, 3H), 2.07 (br t, J = 4.9 Hz, 1H), 1.01 (s, 9H), 0.15 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 150.2, 149.2, 141.7, 120.2, 119.6, 117.1, 64.9, 60.2, 26.0, 18.4, 9.1, -4.4; HRMS-EI (m/z): $[M]^+$ calc'd for $C_{15}H_{26}O_4Si$, 298.1600, found 298.1586.

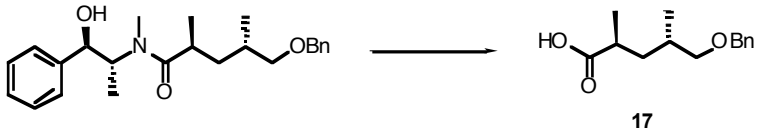


15 **16**

Triphenylphosphonium Bromide 16: A solution of diol **15** (502 mg, 1.70 mmol) and triphenylphosphine hydrobromide (650 mg, 1.90 mmol) in CH_3CN (3.5 mL) was stirred at room temperature for 2 h. The reaction mixture was cooled to 0 °C for 30 min at which point a fine white precipitate was formed. The solid was collected by filtering through a sintered glass funnel and washed with a small amount of cold CH_3CN. Drying the collected solid *in vacuo* afforded phosphonium salt **16** (815 mg, 78%) as a white powder: IR (Film) 3056, 2955, 2928, 1483, 1438, 1112 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.76-7.84 (m, 3H), 7.57-7.62 (m, 12H), 6.12 (d, J = 2.5 Hz, 1H), 5.31 (s, 1H), 5.13 (d, J = 13.0 Hz, 2H), 3.65 (s, 3H), 2.03 (s, 3H), 0.87 (s, 9H), -0.09 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 151.0, 150.2, 150.1, 142.6, 142.6, 135.1, 135.1, 134.5, 134.4, 130.3, 130.2, 124.2, 119.0, 119.0, 118.7, 118.0, 110.0, 60.3, 27.7, 27.4, 25.9, 18.4, 10.5.



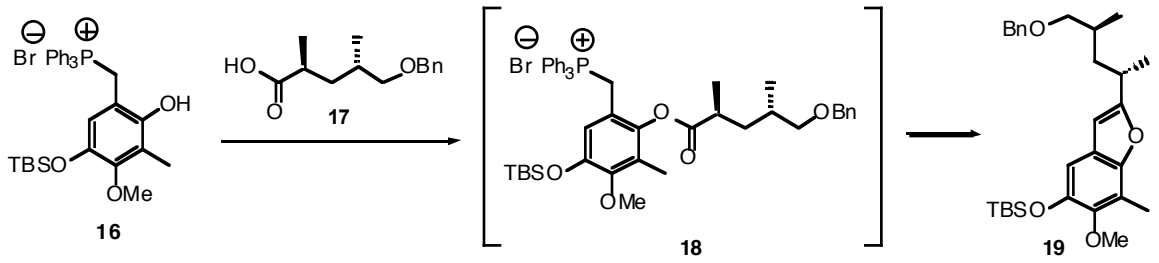
Carboxylic Acid 17: A solution of *n*-BuLi (2.5 M in hexanes, 7.20 mL, 18 mmol) was added to a suspension of lithium chloride (3.09 g, 72.0 mmol) and diisopropylamine (2.78 mL, 19.8 mmol) in THF (20 mL) at –78 °C. The resulting suspension was warmed to 0°C briefly and then was cooled to –78 °C. An ice-cooled solution of (*R*,*R*)-psudoephedrine propionamide **7** (1.99 g, 9.00 mmol) in THF (10 mL, followed by a 4 mL rinse) was added via cannula. The mixture was stirred at –78 °C for 1 h, at 0 °C for 15 min, and at 23 °C for 5 min. The mixture was cooled to 0°C, and a solution of the known iodide[4] (1.60 g, 5.50 mmol) in THF (5 mL) was then added via cannula. After being stirred for 12 h at 0 °C, the reaction mixture was treated with half saturated aqueous NH_4Cl solution (20 mL) and extracted with EtOAc (4 X 30 mL). The combined organic extracts were dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. Purification of the residue by flash column chromatography (silica gel, hexanes / EtOAc = 1 / 1) afforded the desired amide (1.94 g, 92%) as a yellow oil: (rotation isomers were observed) $[\alpha]_D^{23}$ –48 (*c* 0.75, $CHCl_3$); IR (Film) 3383, 2965, 2871, 1618, 1453, 1088 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.24-7.36 (m, 10H), 4.60 (d, *J* = 7.5 Hz, 1H), 4.50 (d, *J* = 12.0 Hz, 1H), 4.44 (d, *J* = 12.0 Hz, 1H), 4.38 (br s, 1H), 3.26 (dd, *J* = 9.0, 6.0 Hz, 1H), 3.20 (dd, *J* = 9.0, 6.0 Hz, 1H), 2.76 (s, 3H), 1.82 (m, 1H), 1.72 (m, 1H), 1.51 (m, 1H), 1.41 (m, 1H), 1.10 (d, *J* = 6.5 Hz, 3H), 1.06 (d, *J* = 7.0 Hz, 3H), 0.91 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 179.5, 142.8, 138.8, 128.5, 128.5, 127.9, 127.7, 127.1, 126.5, 76.7, 76.1, 73.3, 38.5, 34.5, 31.6, 17.8, 17.7, 14.6; HRMS-EI (m/z): $[M + H]^+$ calc'd for $C_{24}H_{34}O_3N$, 384.2533, found 384.2527.



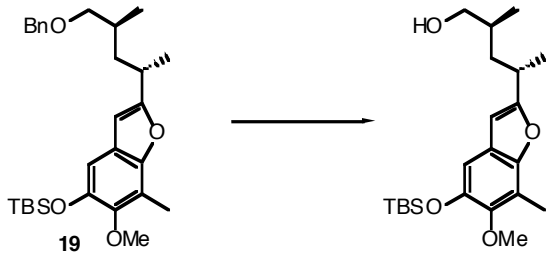
A 100-mL round-bottomed flask was charged with the amide (1.80 g, 4.70 mmol), aqueous tetra-*n*-butylammonium hydroxide solution (40% w/w, 15.3 g, 23.5 mmol), *t*-butyl alcohol (15 mL), and water (45 mL). The biphasic mixture was then heated under reflux for 24 h. The mixture was cooled to 23 °C and then partitioned between 0.5 *N* aqueous NaOH (300 mL) and Et_2O (25 mL). The aqueous layer was separated, extracted with Et_2O (2 X 25 mL), and then brought to pH = 1 by the addition of 3 *N* aqueous HCl solution. The acidified solution was saturated with NaCl and extracted with Et_2O (3 X 35 mL). The combined Et_2O extracts were washed with water, dried over anhydrous Na_2SO_4, and concentrated *in vacuo* to afford acid **17** (0.920 g, 83%) as a clear liquid: $[\alpha]_D^{23}$ +8.60 (*c* 1.70, $CHCl_3$); IR (Film) 3050, 2970, 1705, 1454, 1098, 698 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.28-7.39 (m, 5H), 4.52 (s, 2H), 3.34 (d, *J* = 5.9 Hz, 2H), 2.60 (m, 1H), 1.90 (m, 1H), 1.56 (m, 2H), 1.18 (d, *J* = 7.0 Hz, 3H), 0.94 (d, *J* = 6.6 Hz, 3H);

[4] Vong, B. G.; Abraham, S.; Xiang, A. X.; Theodorakis, E. A. *Org. Lett.* **2003**, *5*, 1617

^{13}C NMR (125 MHz, $CDCl_3$) δ 182.5, 138.6, 128.6, 127.8, 127.8, 75.9, 73.3, 38.1, 37.3, 31.5, 17.4, 17.3; HRMS-EI (m/z): $[M]^+$ calc'd for $C_{14}H_{20}O_3$, 236.1412, found 236.1414.

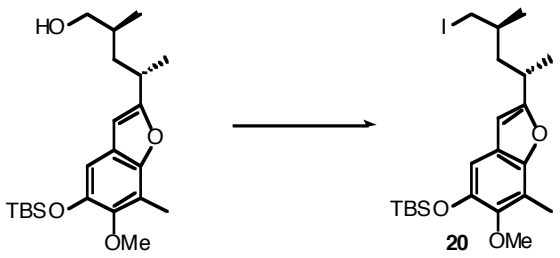


Benzofuran 19: To a solution of acid **17** (11 mg, 0.047 mmol) in CH_2Cl_2 (3 mL) was added triphenylphosphonium bromide **16** (30 mg, 0.050 mmol) and DCC (16 mg, 0.080 mmol). A crystal of DMAP (1.5 mg, 0.010 mmol) was added in one portion and the resulting mixture was stirred at room temperature for 12 h. After the removal of CH_2Cl_2 from the reaction mixture, toluene (8 mL) and triethylamine (0.50 mL) were added, and the solution was then heated to reflux for 30 min. The reaction mixture was cooled to room temperature, filtered through a silica pad, and concentrated *in vacuo*. Purification of the residue by column chromatography (silica gel, hexanes / EtOAc = 20 / 1) afforded benzofuran **19** (21 mg, 93%) as a colorless oil: $[\alpha]_D^{23}$ +14.3 (*c* 1.00, $CHCl_3$); IR (Film) 2957, 2930, 1442, 1418, 1255, 892 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28-7.36 (m, 5H), 6.78 (s, 1H), 6.21 (s, 1H), 4.51 (s, 2H), 3.77 (s, 3H), 3.37 (dd, *J* = 9.5, 6.0 Hz, 1H), 3.32 (dd, *J* = 9.5, 6.0 Hz, 1H), 3.00 (m, 1H), 2.41 (s, 3H), 1.91 (m, 1H), 1.65 (m, 2H), 1.28 (d, *J* = 6.9 Hz, 3H), 1.04 (s, 9H), 0.99 (d, *J* = 6.7 Hz, 3H), 0.19 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.3, 148.9, 146.8, 145.3, 138.9, 128.5, 127.7, 127.6, 123.6, 115.1, 108.1, 100.6, 76.0, 73.2, 60.6, 39.7, 31.4, 31.4, 26.0, 19.4, 18.5, 17.5, 9.4, -4.4; HRMS-EI (m/z): $[M]^+$ calc'd for $C_{29}H_{42}O_4Si$, 482.2852, found 482.2873.

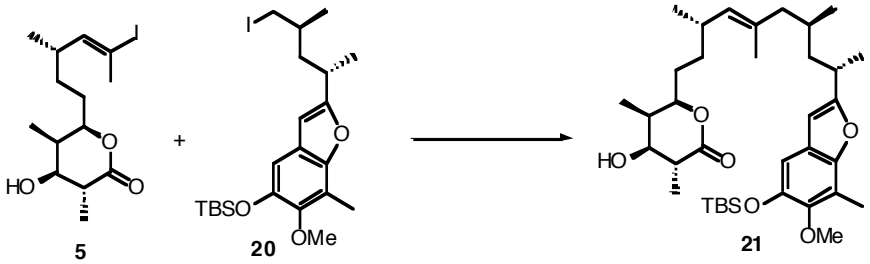


Alkyl Iodide 20: A flask containing a suspension of benzofuran **19** (1.30 g, 2.69 mmol) and Pd / C (5% w /w, 500 mg, 9 mol%) in MeOH / EtOAc (20 mL, 19 / 1) was charged with H_2 via a balloon. After stirred at room temperature for 30 min, the reaction mixture was filtered through a silica pad and concentrated *in vacuo*. Purification of the residue by flash column chromatography (silica gel, hexanes / EtOAc = 2 / 1) afforded the alcohol (1.06 g, 99%) as a colorless oil: $[\alpha]_D^{23}$ -3.9 (*c* 0.57, $CHCl_3$); IR (Film) 3341, 2930, 1442, 1353, 1255 894 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.78 (s, 1H), 6.24 (s, 1H), 3.78 (s, 3H), 3.55 (dd, *J* = 10.5, 5.6 Hz, 1H), 3.50 (dd, *J* = 10.6, 6.2 Hz, 1H), 3.03 (m, 1H), 2.42 (s, 3H), 1.77(m, 1H), 1.64 (m, 2H), 1.31 (d, *J* = 6.9 Hz, 3H), 1.04 (s, 9H), 0.96 (d, *J* = 6.9

Hz, 3H), 0.19 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.2, 148.9, 146.8, 145.3, 123.6, 115.2, 108.1, 100.6, 68.4, 60.7, 39.2, 33.5, 31.3, 26.0, 19.4, 18.5, 16.9, 9.4, -4.4; HRMS-EI (m/z): $[M]^+$ calc'd for $C_{22}H_{36}O_4Si$, 392.2383, found 392.2400.

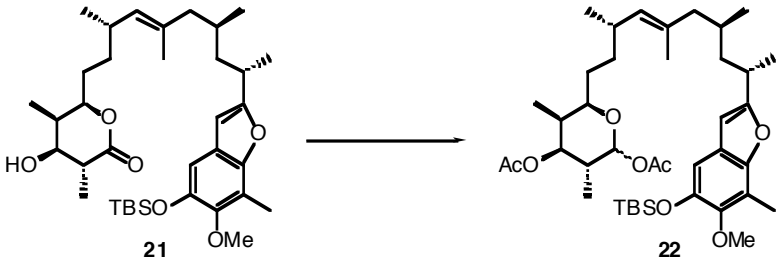


To a solution of triphenylphosphine (1.18 g, 4.50 mmol) in CH_2Cl_2 (20 mL) at 23 °C were added imidazole (400 mg, 6.00 mmol) and iodine (1.22 g, 4.80 mmol) sequentially. A solution of the alcohol (1.00 g, 2.55 mmol) in CH_2Cl_2 (10 mL) was added to the resulting suspension via cannula. After being stirred for 2 h, the reaction mixture was concentrated to a small volumn (*ca*. 5 mL), loaded onto a silica gel column, and eluted with 10% Et_2O-hexanes. The eluent was washed with saturated aqueous $Na_2S_2O_3$, dried over anhydrous $MgSO_4$, and concentrated *in vacuo* to give iodide **20** (1.23 g, 96 %) as a colorless liquid: $[\alpha]_D^{23}$ +21 (*c* 0.98, $CHCl_3$); IR (Film) 2929, 1442, 1254, 1214, 1201, 1116, 1034 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.80 (s, 1H), 6.26 (s, 1H), 3.79 (s, 3H), 3.29 (d, *J* = 4.6 Hz, 2H), 2.97 (m, 1H), 2.43 (s, 3H), 1.66 (m, 2H), 1.48 (m, 1H), 1.33 (d, *J* = 6.9 Hz, 3H), 1.05 (s, 9H), 0.99 (d, *J* = 6.5 Hz, 3H), 0.20 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.3, 149.0, 146.9, 145.4, 123.5, 115.3, 108.2, 101.0, 60.7, 42.7, 32.2, 31.4, 26.0, 21.1, 19.8, 18.5, 18.2, 9.5, -4.4; HRMS-EI (m/z): $[M]^+$ calc'd for $C_{22}H_{35}O_3SiI$, 502.1400, found 502.1386.

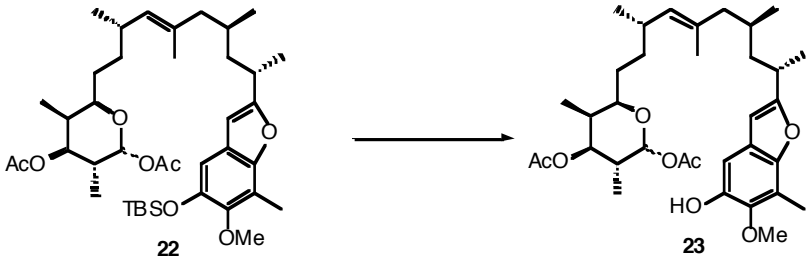


Alkene 21: To a solution of iodide **20** (526 mg, 1.05 mmol) in Et_2O (4 mL) at –78 °C was added rapidly *t*-BuLi (1.7 M in pentane, 1.23 mL, 2.1 mmol). After 3 min, a solution of *B*-methoxy-9-BBN (1.0 M in hexanes, 2.50 mL, 2.5 mmol) was added followed by THF (4 mL). The solution was stirred for 10 min at –78 °C and then allowed to warm to room temperature over 2 h. To this mixture at 25 °C were added an aqueous solution of K_3PO_4 (3.0 M, 0.83 mL, 2.5 mmol), vinyl iodide **5** (300 mg, 0.819 mmol) in DMF (5 mL), and $PdCl_2(dppf)•CH_2Cl_2$ (34 mg, 0.042 mmol). After being stirred in the dark for 18 h, the reaction mixture was diluted with H_2O and Et_2O. The aqueous layer was separated and extracted with Et_2O (2 X 50 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. Purification

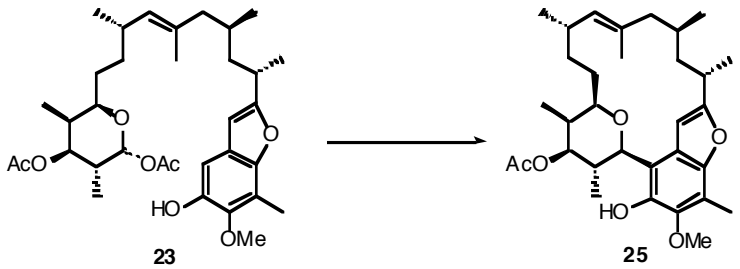
of the residue by flash column chromatography (silica gel, hexanes / EtOAc = 2 / 1) afforded alkene **21** (433 mg, 86%) as a white foam: $[\alpha]_D^{23}$ +32 (*c* 0.66, $CHCl_3$); IR (Film) 3459, 2928, 1716, 1443, 1418, 1352 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.79 (s, 1H), 6.22 (s, 1H), 4.88 (d, *J* = 9.5 Hz, 1H), 4.16 (m, 1H), 3.79 (m, 1H), 3.78 (s, 3H), 3.01 (m, 1H), 2.44 (m, 1H), 2.41 (s, 3H), 2.36 (m, 1H), 2.15 (br s, 1H), 2.11 (m, 1H), 2.08 (m, 1H), 1.77 (m, 2H), 1.71 (m, 1H), 1.60 (m, 1H), 1.56 (s, 3H), 1.49 (m, 1H), 1.45 (m, 1H), 1.39 (d, *J* = 7.1 Hz, 3H), 1.35 (m, 2H), 1.28 (d, *J* = 6.8 Hz, 3H), 1.04 (s, 9H), 0.95 (d, *J* = 6.7 Hz, 3H), 0.93 (d, *J* = 7.1 Hz, 3H), 0.83 (d, *J* = 6.2 Hz, 3H), 0.19 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.0, 164.7, 148.9, 146.6, 145.2, 133.1, 132.5, 123.6, 115.1, 108.0, 100.3, 80.2, 74.0, 60.7, 48.2, 43.2, 40.0, 37.5, 33.3, 32.3, 31.4, 30.4, 28.3, 26.0, 21.5, 19.7, 19.3, 18.5, 16.3, 14.5, 9.4, 4.6, -4.4; HRMS-EI (m/z): $[M]^+$ calc'd for $C_{36}H_{58}O_6Si$, 614.4003, found 614.4014.



Diacetate 22: To a solution of alkene **21** (400 mg, 0.650 mmol) in toluene (10 mL) at –78 °C was added DIBAL-H (1.0 M in hexanes, 1.60 mL, 1.6 mmol). The reaction mixture was stirred at –78 °C for 2 h, quenched by the addition of MeOH, and warmed to room temperature. After saturated aqueous potassium sodium tartrate (5 mL) was added, the mixture was vigorously stirred for 1 h, diluted with H_2O, and extracted with Et_2O (3 X 50 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and concentrated *in vacuo* to give the crude lactol. To a solution of the crude lactol in pyridine (5 mL) was added acetic anhydride (0.50 mL, 5.3 mmol) at room temperature. The reaction mixture was stirred for 8 h and concentrated *in vacuo*. Purification of the residue by flash column chromatography (silica gel, hexanes / EtOAc = 4 / 1) afforded diacetate **22** (361 mg, 5 : 1 diastereomers, 79% for both diastereomers) as a colorless liquid: $[\alpha]_D^{23}$ +39 (*c* 0.57, $CHCl_3$); IR (Film) 2929, 1746, 1456, 1222, 1031, 893 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.79 (s, 1H), 6.21 (s, 1H), 5.34 (d, *J* = 9.2 Hz, 1H), 4.87 (d, *J* = 9.5 Hz, 1H), 4.67 (dd, *J* = 11.3, 4.9 Hz, 1H), 3.77 (s, 3H), 3.53 (m, 1H), 3.00 (m, 1H), 2.41 (s, 3H), 2.34 (m, 1H), 2.15 (m, 1H), 2.13 (s, 3H), 2.10 (s, 3H), 2.05 (m, 2H), 1.96 (m, 1H), 1.75 (m, 1H), 1.70 (m, 1H), 1.60 (m, 1H), 1.56 (m, 1H), 1.54 (s, 3H), 1.48 (m, 1H), 1.33 (m, 1H), 1.30 (m, 1H), 1.27 (d, *J* = 7.0 Hz, 3H), 1.04 (s, 9H), 0.92 (d, *J* = 6.5 Hz, 3H), 0.88 (d, *J* = 7.0 Hz, 3H), 0.87 (d, *J* = 7.0 Hz, 3H), 0.83 (d, *J* = 6.5 Hz, 3H), 0.19 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.6, 169.7, 164.8, 148.9, 146.7, 145.2, 132.9, 132.7, 123.7, 115.1, 108.1, 100.3, 96.8, 77.1, 75.9, 60.7, 48.3, 43.1, 35.0, 33.6, 33.5, 32.5, 31.4, 29.9, 28.4, 26.0, 21.4, 21.3, 21.2, 19.7, 19.2, 18.5, 16.3, 12.2, 9.4, 6.2, -4.4; HRMS-EI (m/z): $[M]^+$ calc'd for $C_{40}H_{64}O_8Si$, 700.4371, found 700.4348.

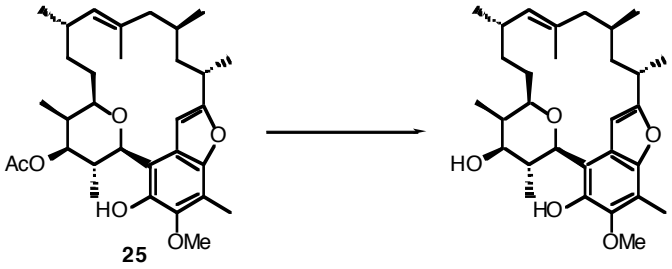


Phenol 23: To a solution of diacetate **22** (450 mg, 0.640 mmol) in THF (5 mL) was added TBAF (1.0 M in THF, 1.00 mL, 1.0 mmol). After stirring at room temperature for 10 min, the reaction was quenched by the addition of saturated aqueous NH_4Cl solution, and the mixture was extracted with Et_2O (3 X 25 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. Purification of the residue by flash column chromatography (silica gel, hexanes / EtOAc = 2 / 1) afforded phenol **23** (344 mg, 5 : 1 diastereomers, 91%) as a colorless liquid: $[\alpha]_D^{23}$ +31 (*c* 0.75, $CHCl_3$); IR (Film) 3448, 2927, 1745, 1457, 1362, 1225 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.87 (s, 1H), 6.23 (s, 1H), 5.71 (br s, 1H), 5.34 (d, *J* = 9.2 Hz, 1H), 4.86 (d, *J* = 9.4 Hz, 1H), 4.68 (dd, *J* = 11.4, 4.9 Hz, 1H), 3.82 (s, 3H), 3.51 (m, 1H), 2.99 (m, 1H), 2.45 (s, 3H), 2.32 (m, 1H), 2.13 (m, 1H), 2.12 (s, 3H), 2.09 (s, 3H), 2.04 (m, 2H), 1.95 (m, 1H), 1.74 (m, 1H), 1.68 (m, 1H), 1.57 (m, 2H), 1.53 (s, 3H), 1.48 (m, 1H), 1.33 (m, 1H), 1.26 (d, *J* = 6.8 Hz, 3H), 1.23 (m, 1H), 0.91 (d, *J* = 6.7 Hz, 3H), 0.88 (d, *J* = 6.9 Hz, 3H), 0.87 (d, *J* = 6.4 Hz, 3H), 0.82 (d, *J* = 6.3Hz, 3H); ^{13}C NMR (100Hz, $CDCl_3$) δ 170.6, 169.6, 164.9, 147.9, 145.3, 142.6, 132.9, 132.6, 124.3, 114.0, 102.2, 100.4, 96.7, 77.4, 77.1, 75.8, 61.5, 48.2, 43.0, 35.0, 33.5, 32.4, 31.4, 29.8, 28.3, 21.3, 21.1, 21.1, 19.7, 19.2, 16.2, 12.1, 9.5, 6.1; HRMS-EI (m/z): $[M]^+$ calc'd for $C_{34}H_{50}O_8$, 586.3506, found 586.3528.



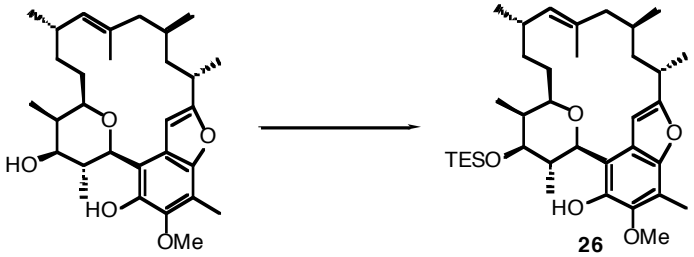
Macrocycle 25: A flamed dried flask was charged with activated molecular sieves (power, 4 Å, 500 mg) under argon. A solution of phenol **23** (200 mg, 0.34 mmol) in freshly distilled chloroform (30 mL) was added via cannula followed by two additional portions of rinse (2 X 15 mL) to assist the transfer. The reaction mixture was cooled to –5 °C, and $SnCl_4$ (1.0 M in CH_2Cl_2, 0.45 mL, 0.45 mmol) was added via a syringe. After stirring at –5 °C for 2 h and at room temperature for 12 h, the reaction was quenched by the addition of solid $NaHCO_3$. The reaction mixture was filtered through a silica gel pad and concentrated *in vacuo*. Purification of the residue by flash column chromatography (silica gel, hexanes / EtOAc = 10 / 1) afforded macrocycle **25** (75 mg, 42%) as a colorless liquid: $[\alpha]_D^{23}$ +41 (*c* 0.22, $CHCl_3$); IR (Film) 3442, 2927, 1724, 1455, 1385, 1240 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.56 (s, 1H), 5.58 (s, 1H), 4.87 (dd, *J* = 10.9, 4.7 Hz, 1H),

4.64 (d, J = 9.9 Hz, 1H), 4.60 (d, J = 9.5 Hz, 1H), 3.84 (s, 3H), 3.51 (d, J = 10.5 Hz, 1H), 3.08 (m, 1H), 2.46 (s, 3H), 2.45 (m, 1H), 2.22 (m, 1H), 2.10 (m, 1H), 2.09 (s, 3H), 2.03 (m, 1H), 1.63 (s, 3H), 1.58 (dd, J = 13.0, 2.0 Hz, 1H), 1.44 (m, 1H), 1.39 (d, J = 6.6 Hz, 3H), 1.37 (m, 1H), 1.32 (m, 1H), 1.28 (m, 4H), 1.02 (d, J = 7.0 Hz, 3H), 0.81 (d, J = 6.5 Hz, 3H), 0.79 (d, J = 6.6 Hz, 3H), 0.77 (d, J = 6.6 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.9, 160.0, 148.5, 141.9, 131.8, 129.2, 122.3, 115.6, 112.9, 104.9, 79.6, 77.6, 77.5, 77.4, 61.7, 44.0, 42.0, 37.1, 36.4, 33.8, 32.7, 31.7, 31.1, 27.8, 22.0, 21.4, 21.2, 19.8, 18.9, 12.9, 9.7, 7.5; HRMS-EI (m/z): $[M]^+$ calc'd for $C_{32}H_{46}O_6$, 526.3294, found 526.3290.



25

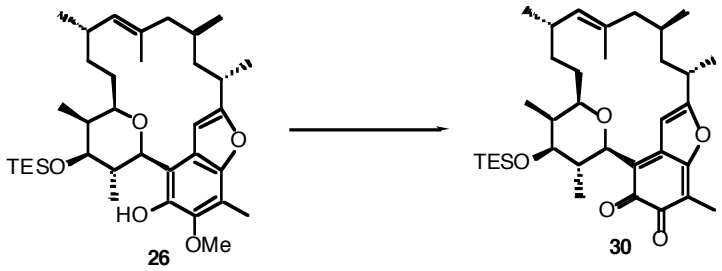
TES Ether 26: To a solution of macrocycle **25** (35 mg, 0.066 mmol) in MeOH (5 mL) was added NaOMe (10 mg, 0.19 mmol). After the mixture was stirred at 25 °C for 15 h, acetic acid (11 μL, 0.20 mmol) was added. The resulting solution was concentrated *in vacuo* and purified by flash column chromatography (silica gel, hexanes / EtOAc = 1 / 1) to afford the alcohol (28 mg, 87%) as a white foam: $[\alpha]_D^{23}$ +88 (*c* 0.12, $CHCl_3$); IR (Film) 3446, 2925, 1455, 1324, 1107 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.55 (s, 1H), 5.56 (s, 1H), 4.60 (d, J = 9.5 Hz, 1H), 4.55 (d, J = 10.1 Hz, 1H), 3.84 (s, 3H), 3.65 (dd, J = 10.4, 4.9 Hz, 1H), 3.44 (d, J = 9.7 Hz, 1H), 3.09 (m, 1H), 2.46 (s, 3H), 2.44 (m, 1H), 2.24 (m, 1H), 1.92 (m, 1H), 1.81 (m, 1H), 1.63 (s, 3H), 1.59 (m, 2H), 1.44 (m, 2H), 1.39 (d, J = 6.7 Hz, 3H), 1.26-1.36 (m, 4H), 1.04 (d, J = 6.4 Hz, 3H), 0.91 (d, J = 6.4 Hz, 3H), 0.83 (d, J = 6.5 Hz, 3H), 0.77 (d, J = 6.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.0, 148.5, 141.9, 141.8, 131.7, 129.2, 122.4, 116.0, 112.7, 105.0, 78.0, 77.6, 77.5, 61.7, 44.0, 42.0, 39.8, 38.9, 33.9, 32.7, 31.7, 31.4, 27.7, 22.0, 21.2, 19.8, 18.9, 13.0, 9.7, 6.8; HRMS-EI (m/z): $[M]^+$ calc'd for $C_{30}H_{44}O_5$, 484.3189, found 484.3185.



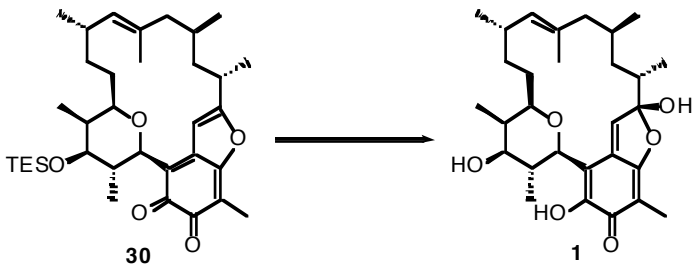
26

To a mixture of the alcohol (26 mg, 0.050 mmol) and triethylamine (0.050 mL, 0.36 mmol) in CH_2Cl_2 (5 mL) at 0 °C was added TESOTf (14 μL, 0.060 mmol) over 10 min. When TLC analysis indicated complete consumption of the starting alcohol (ca. 0.5 h), the reaction was quenched by the addition of saturated aqueous $NaHCO_3$ (0.02 mL). After concentration of the mixture *in vacuo*, the residue was purified by flash column

chromatography (silica gel, hexanes / EtOAc = 8 / 1) to afford TES ether **26** (31 mg, 98%) as a colorless oil: $[\alpha]_D^{23}$ +33 (*c* 0.080, $CHCl_3$); IR (Film) 2954, 2876, 1456, 1380, 1324, 1106 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.56 (s, 1H), 5.54 (s, 1H), 4.60 (d, *J* = 9.0 Hz, 1H), 4.52 (d, *J* = 10.5 Hz, 1H), 3.83 (s, 3H), 3.62 (dd, *J* = 10.0, 4.5 Hz, 1H), 3.41 (d, *J* = 11.0 Hz, 1H), 3.07 (m, 1H), 2.46 (m, 1H), 2.45 (s, 3H), 2.22 (m, 1H), 1.82 (m, 1H), 1.76 (m, 1H), 1.62 (s, 3H), 1.59 (m, 2H), 1.44 (m, 2H), 1.38 (d, *J* = 7.0 Hz, 3H), 1.26-1.36 (m, 4H), 1.03 (d, *J* = 6.5 Hz, 3H), 0.98 (t, *J* = 8.0 Hz, 9H), 0.83 (d, *J* = 6.5 Hz, 3H), 0.81 (d, *J* = 7.0 Hz, 3H), 0.76 (d, *J* = 6.5 Hz, 3H), 0.64 (q, *J* = 8.0 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.8, 148.5, 141.8, 141.6, 131.7, 129.2, 122.5, 116.4, 112.5, 105.1, 78.1, 77.9, 77.7, 61.6, 44.0, 42.0, 41.1, 39.0, 33.9, 32.8, 31.7, 31.5, 27.7, 22.1, 21.2, 19.8, 19.0, 13.5, 9.7, 7.2, 7.1, 5.3; HRMS-EI (m/z): $[M]^+$ calc'd for $C_{36}H_{58}O_5Si$, 598.4054, found 598.4043.



***ortho*-Quinone 30:** A solution of TES ether **26** (30 mg, 0.050 mmol) in DMF (*degassed*, 5.0 mL) was added to 5 vials (each vial containing IBX 8.4 mg, 0.030 mmol) in 1.0 mL portion under argon. After being stirred in the *dark* for 36 h, the reaction mixtures were combined, directly loaded onto a silica gel column, and eluted (hexanes / EtOAc = 10 / 1). Collection of purple fractions and evaporation of the solvent afforded *ortho*-quinone **30** (18 mg, 62%) as an intensely blue liquid which was used immediately in the next reaction: IR (CH_2Cl_2, Film) 2955, 2925, 1652, 1586, 1456, 1376 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.13 (s, 1H), 4.74 (d, *J* = 9.5 Hz, 1H), 4.18 (d, *J* = 10.5 Hz, 1H), 3.50 (dd, *J* = 10.5, 5.0 Hz, 1H), 3.28 (d, *J* = 9.5 Hz, 1H), 2.92 (m, 1H), 2.32 (d, *J* = 16.5 Hz, 1H), 2.26 (m, 1H), 1.93 (s, 3H), 1.79 (m, 1H), 1.71 (m, 1H), 1.64 (s, 3H), 1.61 (m, 2H), 1.43 (m, 2H), 1.29-1.44 (m, 4H), 1.26 (d, *J* = 7.0 Hz, 3H), 0.98 (t, *J* = 8.0 Hz, 9H), 0.93 (d, *J* = 7.0 Hz, 3H), 0.92 (d, *J* = 6.0 Hz, 3H), 0.91 (d, *J* = 6.5 Hz, 3H), 0.75 (d, *J* = 6.5 Hz, 3H), 0.62 (q, *J* = 8.0 Hz, 6H).



Kendomycin (1): A solution of *ortho*-quinone **30** (18 mg, 0.030 mmol) in CH_3CN (5.0 mL) was added to 5 polypropylene microtubes in 1.0 mL portion. Aqueous HF (0.1 M,

0.08 mL, 0.08 mmol) was added to each of the tubes, and the resulting mixtures were stirred at room temperature upon which the originally purple solutions slowly turned yellow. After TLC analysis indicated complete consumption of the starting material (ca. 5 h), the reaction mixtures were poured into 2% aqueous $NaHCO_3$ and extracted with EtOAc (50 mL). The organic layer was washed three times with 2% aqueous $NaHCO_3$ and once with brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. Purification of the residue by flash column chromatography (silica gel, hexanes / EtOAc = 3 / 1 to 1 / 1) afforded kendomycin (**1**) (7.5 mg, 50%) as a yellow powder: MP 232-236 ^oC, (lit. 241-241.5 ^oC,[5] 258 ^oC[6]); $[\alpha]_D^{23}$ –84 (*c* 0.20, MeOH), {lit. $[\alpha]_D^{20}$ –82.4 (*c* 0.514, MeOH),[5] $[\alpha]_D^{25}$ –80 (*c* 2.71, MeOH)[6]}; IR (Film) 3335, 2927, 1614, 1590, 1575, 1328, 1099 cm^{-1}; ^1H NMR (500 MHz, CD_3COCD_3) δ 8.09 (s, 1H), 7.19 (s, 1H), 6.53 (s, 1H), 4.64 (d, *J* = 10.0 Hz, 1H), 4.36 (d, *J* = 10.0 Hz, 1H), 3.93 (d, *J* = 4.5 Hz, 1H), 3.56 (dt, *J* = 9.5, 4.5 Hz, 1H), 3.53 (ddd, *J* = 11.0, 2.0, 1.0 Hz, 1H), 2.42 (m, 1H), 2.36 (m, 1H), 2.12 (d, *J* = 16.0 Hz, 1H), 1.97 (m, 1H), 1.88 (m, 1H), 1.84 (s, 3H), 1.71 (m, 1H), 1.67 (m, 1H), 1.63 (m, 1H), 1.61 (s, 3H), 1.57 (m, 2H), 1.45 (ddd, *J* = 13.0, 11.0, 3.0 Hz, 1H), 1.33 (m, 1H), 1.25 (m, 1H), 0.95 (d, *J* = 7.0 Hz, 3H), 0.94 (d, *J* = 6.5 Hz, 3H), 0.89 (d, *J* = 6.5 Hz, 3H), 0.87 (d, *J* = 6.5 Hz, 3H), 0.71 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, CD_3COCD_3) δ 182.1, 168.6, 146.8, 141.3, 132.1, 130.2, 129.9, 119.1, 111.0, 104.2, 78.7, 77.7, 76.3, 46.1, 41.4, 40.8, 39.7, 38.1, 35.9, 33.6, 33.4, 26.5, 22.7, 19.9, 19.7, 13.3, 12.6, 7.6, 7.2; HRMS-EI (m/z): $[M]^+$ calc'd for $C_{29}H_{42}O_6$, 486.2981, found 486.2978.

[5] Y. Funahashi, N. Kawamura and T. Ishimaru, *Jap. Pat.* 08 231 551 [A2 960 910], 1996 (*Chem. Abstr.,* 1997, **125**, 6553)

Comparison of the NMR Spectral Data of Natural[6] and Synthetic Kendomycin

^{1}H NMR

Natural	**Synthetic**
8.10 (s, 1H)	8.09 (s, 1H)
7.19 (s, 1H)	7.19 (s, 1H)
6.54 (s, 1H)	6.53 (s, 1H)
4.63 (d, *J* = 9.0 Hz, 1H)	4.64 (d, *J* = 10.0 Hz, 1H)
4.35 (d, *J* = 10.0 Hz, 1H)	4.36 (d, *J* = 10.0 Hz, 1H)
3.95 (d, *J* = 4.5 Hz, 1H)	3.93 (d, *J* = 4.5 Hz, 1H)
3.56 (dt, *J* = 10.0, 4.5 Hz, 1H)	3.56 (dt, *J* = 9.5, 4.5 Hz, 1H)
3.52 (ddd, *J* = 11.0, 2.0, 1.0 Hz, 1H)	3.53 (ddd, *J* = 11.0, 2.0, 1.0 Hz, 1H)
2.41 (m, 1H)	2.42 (m, 1H)
2.35 (m, 1H)	2.36 (m, 1H)
2.12 (m, 1H)	2.12 (d, *J* = 16.0 Hz, 1H)[7]
1.96 (m, 1H)	1.97 (m, 1H)
1.88 (m, 1H)	1.88 (m, 1H)
1.84 (s, 3H)	1.84 (s, 3H)
1.70 (m, 1H)	1.71 (m, 1H)
1.65 (m, 1H)	1.67 (m, 1H)
1.62 (m, 1H)	1.63 (m, 1H)
1.60 (s, 3H)	1.61 (s, 3H)
1.57 (m, 2H)	1.57 (m, 2H)
1.45 (ddd, *J* = 13.0, 11.0, 3.0 Hz, 1H)	1.45 (ddd, *J* = 13.0, 11.0, 3.0 Hz, 1H)
1.32 (m, 1H)	1.33 (m, 1H)
1.25 (m, 1H)	1.25 (m, 1H)
0.95 (d, *J* = 7.0 Hz, 3H)	0.95 (d, *J* = 7.0 Hz, 3H)
0.94 (d, *J* = 7.0 Hz, 3H)	0.94 (d, *J* = 6.5 Hz, 3H)
0.88 (d, *J* = 7.0 Hz, 3H)	0.89 (d, *J* = 6.5 Hz, 3H)
0.86 (d, *J* = 7.0 Hz, 3H)	0.87 (d, *J* = 6.5 Hz, 3H)
0.71 (d, *J* = 7.0 Hz, 3H)	0.71 (d, *J* = 7.0 Hz, 3H)

^{13}C NMR

Natural	**Synthetic**	**Natural**	**Synthetic**
182.1	182.1	40.8	40.8
168.6	168.6	39.7	39.7
146.8	146.8	38.1	38.1
141.4	141.3	35.8	35.9
132.1	132.1	33.6	33.6
130.2	130.2	33.4	33.4
129.9	129.9	26.5	26.5
119.1	119.1	22.7	22.7
111.0	111.0	19.9	19.9
104.2	104.2	19.7	19.7
78.7	78.7	13.3	13.3
77.7	77.7	12.7	12.6
76.3	76.3	7.6	7.6
46.1	46.1	7.2	7.2
41.4	41.4		

[6] Bode, H. B.; Zeeck, A. *J. Chem. Soc.-Perkin Trans. 1* **2000**, 323

[7] Zeeck also observed C15-H^{a} to be a doublet (*J* = 17.0 Hz) in pyridine-d_5