Total Synthesis of the Reputed Structure of Alcyonin and Reassignment of its Structure

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Supporting Information

Experimental procedures and characterization data for the preparation of compounds 3, 6, 8–14[1]

(3*R*,4*R*)-dihydroxy-4-(1*R*,3*R*,3a*R*,7*R*,7a*R*)-(7-isopropyl-4-methyl-3-prop-2-ynyl-1,3,3a,6,7,7a-hexahydroisobenzofuran-1-yl)pentyl alcohol (8). 4-(*N* , *N* -Dimethylamino)pyridine (12 mg, 0.11 mmol) was added to a solution of epoxy alcohol **6** (340 mg, 1.1 mmol), pyridine (11 mL), and Ac_2O (0.12 mL, 1.3 mmol) and the solution was maintained at room temperature. After 30 min, the reaction mixture was added to saturated aqueous NH_4Cl (120 mL), the resulting mixture was extracted with ethyl acetate (120 mL), the organic extract was washed sequentially with saturated aqueous $CuSO_4$ (2 ¥ 100 mL) and brine (2 ¥ 100 mL), dried (Na_2SO_4), filtered, and concentrated. The residue was purified by flash chromatography on silica gel (80:20 hexane–ethyl acetate) to afford 370 mg (95%) of acetic acid (*2R*,*3R*)-*2*-[3-(1*R*,3*R*,3a*R*,7*R*,7a*R*)-(7-isopropyl-4-methyl-3-prop-2-ynyl-1,3,3a,6,7,7a-hexahydroisobenzofuran-1-yl)-3-methyloxiranyl]ethyl ester as a clear yellow oil: $[a]^{23}_{D}$ +15.7, $[a]^{23}_{577}$ +16.4, $[a]^{23}_{546}$ +18.4, $[a]^{23}_{435}$ +30.0, $[a]^{23}_{405}$ +35.1 (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz,

[1] General experimental details have been described: MacMillan, D. W. C. ; Overman, L. E.; Pennington, L. D. *J. Am. Chem. Soc.* **2001**, *123*, 9033–9044.

$CDCl_3$) d 5.40-5.39 (m, 1 H), 4.29-4.19 (m, 2 H), 3.89 (ddd, *J* = 4.9, 4.9, 4.9 Hz, 1 H), 3.64 (d, *J* = 8.9 Hz, 1 H), 2.91 (dd, *J* = 9.2, 2.9 Hz, 1 H), 2.62 (ddd, *J* = 16.9, 5.5, 2.6 Hz, 1 H), 2.59-2.54 (m, 1 H), 2.54 (ddd, *J* = 16.9, 4.5, 2.6 Hz, 1 H), 2.46-2.40 (m, 1 H), 2.13-2.02 (m, 1 H), 2.06 (s, 3 H), 2.05-1.98 (m, 1H), 2.00 (dd, *J* = 2.6 Hz, 1H), 1.97-1.89 (m, 1 H), 1.86-1.77 (m, 1 H), 1.67 (d, *J* = 1.1 Hz, 3 H), 1.66-1.58 (m, 1 H), 1.37 (s, 3 H), 1.28-1.21 (m, 1 H), 0.95 (d, *J* = 6.7 Hz, 3H), 0.87 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) d 171.2, 132.4, 120.9, 81.8, 81.4, 80.3, 70.4, 62.4, 61.4, 61.1, 45.7, 42.7, 37.5, 29.2, 28.6, 26.2, 24.1, 22.1, 21.4, 21.2, 20.5, 18.2; IR (film) 3307, 2963, 1740, 1449, 1383, 1365, 1240, 1094, 1041 cm^{-1}; HRMS (CI) *m/z* 361.2377 (M+H, 361.2380 calcd for $C_{22}H_{32}O_4$).

Following the general method of Giner,[2] trifluoroacetic acid (0.08 mL, 1.0 mmol) was added dropwise to a solution of the epoxy ester (370 mg, 1.0 mmol) and PhMe (20 mL) at 0 °C. After 2 h, H_2O (20 mL, 1.1 mol) was added, and the resulting mixture was stirred for 1.5 h and then quenched with saturated aqueous $NaHCO_3$ (15 mL). Ethyl acetate (50 mL) was added, the layers were separated, the aqueous layer was washed with ethyl acetate (2 ¥ 50 mL), and the combined organic extracts were dried (Na_2SO_4), filtered, and concentrated.

A THF solution of $LiAlH_4$ (3.4 ml of a 1.0M solution, 3.4 mmol) was added dropwise to a solution of this mixture of crude acetoxy diols and THF (10 mL) at rt. After 45 min, the reaction mixture was cooled to 0 °C and treated dropwise with Rochelles's salt (30 mL), stirred for 1h at rt, and extracted with ethyl acetate (100 mL). The organic extract was washed brine (100 mL), dried (Na_2SO_4), filtered, and concentrated to afford pure **8**, 330 mg (95%, 2 steps) as a clear yellow oil: $[a]^{23}_{D}$ +7.7, $[a]^{23}_{577}$ +7.9, $[a]^{23}_{546}$ +8.5, $[a]^{23}_{435}$ +13.1, $[a]^{23}_{405}$ +14.8 (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) d 5.53-5.49 (m, 1 H), 4.03-4.00 (m, 1 H), 3.92 (d, *J* = 3.5

[2] Giner, J.-L.; Faraldos, J. A. *J. Org. Chem.* **2002**, *67*, 2717–2720.

Hz, 1H), 3.89-3.85 (m, 3 H), 3.68 (s, 1 H), 3.08 (s, 1 H), 2.99-2.97 (m, 1 H), 2.78 (ddd, *J* = 17.3, 3.9, 2.6 Hz, 1 H), 2.72-2.66 (m, 1 H), 2.56 (ddd, *J* = 17.3, 4.2, 2.6 Hz, 1 H), 2.41 (ddd, *J* = 10.7, 7.6, 3.5, Hz, 1 H), 2.02-1.93 (m, 1 H), 1.92-1.83 (m, 1 H), 1.80-1.67 (m, 3H), 1.69 (d, *J* = 1.5 Hz, 3 H), 1.47-1.33 (m, 1 H), 1.25 (dd, *J* = 7.0, 1 H), 1.04 (s, 3 H), 0.96 (d, *J* = 7.0 Hz, 3H), 0.79 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) d 130.3, 123.6, 87.4, 81.0, 80.5, 76.6, 75.7, 72.0, 61.8, 46.7, 41.7, 39.4, 32.9, 27.6, 25.1, 23.6, 22.6, 22.2, 18.6, 17.1; IR (film) 3420, 3310, 2959, 2244, 2119, 1730, 1666, 1463, 1441, 1368, 1304, 1093, 1068 cm^{-1}; HRMS (CI) *m/z* 337.2367 (M+H, 337.2380 calcd for $C_{20}H_{32}O_4$).

2,2-Dimethylpropionic acid 2-[(4*R*,5*R*)-5-(1*R*,3*R*,3a*R*,7*R*,7a*R*)-(7-isopropyl-4-methyl-3-prop-2-ynyl-1,3,3a,6,7,7a-hexahydroisobenzofuran-1-yl)-5-methyl-2-oxo-[1,3]dioxolan-4-yl]ethyl ester (9). Pivaloyl chloride (0.15 mL, 1.2 mmol) was added dropwise to a solution of **8** (330 mg, 0.98 mmol) and pyridine (1.2 mL) at rt. After 20 min, the reaction mixture was added to saturated aqueous NH_4Cl (10 mL) and the resulting mixture was extracted with ethyl acetate (2 ¥ 30 mL). The organic extract was washed sequentially with saturated aqueous $CuSO_4$ (2 ¥ 20 mL) and brine (2 ¥ 20 mL), dried (Na_2SO_4), filtered, and concentrated. The residue was purified by flash chromatography on silica gel (80:20 hexane–ethyl acetate) to afford 400 mg (98%) of 2,2-dimethylpropionic acid (3*R*,4*R*)-dihydroxy-4-(1*R*,3*R*,3a*R*,7*R*,7a*R*)-(7-isopropyl-4-methyl-3-prop-2-ynyl-1,3,3a,6,7,7a-hexahydroisobenzofuran-1-yl)pentyl ester (**8a**) as a clear yellow oil: $[a]^{23}_{D}$ -15.8, $[a]^{23}_{577}$ -16.6, $[a]^{23}_{546}$ -18.9, $[a]^{23}_{435}$ -31.7, $[a]^{23}_{405}$ -38.7 (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) d 5.53-5.49 (m, 1 H), 4.31-4.20 (m, 2 H), 3.89 (d, *J* = 3.5 Hz, 1 H), 3.87 (dd, *J* = 10.7, 2.1 Hz, 1H), 3.76 (ddd, *J* = 8.4, 8.4, 4.0, 1 H), 3.32 (s, 1 H), 3.03 (s, 1 H), 2.74 (ddd, *J* = 17.3, 3.9, 2.6 Hz, 1 H), 2.73-2.66 (m, 1 H), 2.54 (ddd, *J* = 17.3, 4.1, 2.6 Hz, 1 H), 2.40 (ddd, *J* = 10.6, 7.6, 3.5, Hz, 1 H), 2.12 (dd, *J* = 2.6, 1 H), 2.02-1.93 (m, 1 H), 1.92-1.81 (m, 2H), 1.80-

1.72 (m, 1H), 1.70 (d, *J* = 1.5 Hz, 3 H), 1.70-1.60 (m, 1 H), 1.45-1.38 (m, 1 H), 1.20 (s, 9H), 1.03 (s, 3 H), 0.97 (d, *J* = 6.8 Hz, 3H), 0.80 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) d 178.6, 130.1, 123.2, 86.7, 80.8, 80.2, 75.6, 72.4, 71.6, 61.8, 46.5, 41.5, 39.1, 38.7, 30.3, 27.3, 27.2, 24.8, 23.3, 22.4, 21.9, 18.1, 16.9; IR (film) 3496, 3309, 2960, 2249, 1725, 1480, 1462, 1366, 1286, 1162, 1094, 1070, 1035 cm^{-1}; HRMS (CI) *m/z* 421.2962 (M+H, 421.2955 calcd for $C_{25}H_{40}O_5$).

A solution of this pivalate derivative (380 mg, 0.90 mmol), pyridine (0.19 mL) and CH_2Cl_2 (19 mL) was cooled to 0 °C and solid trisphosgene was added by portions until TLC (70:30 hexane–ethyl acetate) indicated completion of the reaction. The reaction then was quenched with saturated aqueous NH_4Cl (5.0 with saturated aqueous $CuSO_4$ (2 ¥ 10 mL) and brine (2 ¥ 10 mL), dried (Na_2SO_4), filtered, and concentrated. The residue was purified by flash chromatography on silica gel (85:15 hexane–ethyl acetate) to afford 394 mg (97%) of **9** as a colorless solid: $[a]^{23}_{D}$ -4.7, $[a]^{23}_{577}$ -5.2, $[a]^{23}_{546}$ -6.1, $[a]^{23}_{435}$ -9.1, $[a]^{23}_{405}$ -11.0 (*c* 0.9, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) d 5.54-5.50 (m, 1 H), 5.03 (dd, *J* = 10.6, 3.1 Hz, 1H), 4.31-4.24 (m, 1 H), 4.22-4.15 (m, 1H), 3.84-3.79 (m, 2 H), 2.68 (ddd, *J* = 17.3, 4.3, 2.6 Hz, 1 H), 2.68-2.58 (m, 1H), 2.48 (ddd, *J* = 17.3, 5.2, 2.6 Hz, 1 H), 2.42-2.36 (m, 1 H), 2.04 (dd, *J* = 2.6, 1 H), 2.04-1.87 (m, 4 H), 1.78-1.70 (m, 1H), 1.71 (d, *J* = 1.3 Hz, 3 H), 1.49-1.40 (m, 1 H), 1.36 (s, 3 H), 1.21 (s, 9H), 0.97 (d, *J* = 6.8 Hz, 3H), 0.80 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) d 178.3, 153.5, 130.1, 123.1, 86.3, 82.6, 81.1, 80.2, 77.4, 70.8, 60.7, 46.7, 41.7, 38.8, 38.7, 29.1, 27.5, 27.1, 24.9, 23.2, 22.3, 21.7, 18.7, 16.9; IR (film) 3310, 2962, 1806, 1729, 1480, 1462, 1387, 1367, 1285, 1234, 1158, 1084, 1036 cm^{-1}; HRMS (CI) *m/z* 446.2663 (M+H, 446.2668 calcd for $C_{26}H_{38}O_6$).

2,2-Dimethylpropionic acid (3*R*,4*R*)-bis-(*tert*-butyldimethylsiloxy)-4-(1*R*,3*R*,3a*R*,7*R*,7a*R*)-(7-isopropyl-4-methyl-3-prop-2-ynyl-1,3,3a,6,7,7a-hexahydroisobenzofuran-1-yl)pentyl ester (10). A solution of pivalate **8a** (120 mg, 0.28 mmol), 2,6-lutidine (0.81 mL, 7.1 mmol) and CH_2Cl_2 (1.6 mL) was treated dropwise with *tert*-butyldimethylsilyl trifluoromethanesulfonate (0.67 mL, 2.8 mmol). The resulting mixture was stirred at rt for 24 h, quenched with saturated aqueous $NaHCO_3$ (5.0 mL), diluted with EtOAc (10 mL), the layers were separated, and the aqueous layer was extracted with EtOAc (2 ¥ 10 mL). The combined organic extracts were dried (Na_2SO_4), filtered, and concentrated. The residue was purified by flash chromatography on silica gel (98:2 hexane–ethyl acetate) to afford 165 mg (89%) of **10** as a pale yellow oil: $[a]^{23}_{D}$ +8.3, $[a]^{23}_{577}$ +8.7, $[a]^{23}_{546}$ +10.0, $[a]^{23}_{435}$ +17.7, $[a]^{23}_{405}$ +21.4 (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) d 5.48-5.44 (m, 1 H), 4.23 (d, *J* = 3.9 Hz, 1H), 4.19 (ddd, *J* = 11.9, 7.8, 4.2 Hz, 1 H), 4.00 (ddd, *J* = 10.5, 9.5, 6.39 Hz, 1H), 3.81 (ddd, *J* = 4.7, 7.4, 7.4 Hz, 1 H), 3.63 (dd, *J* = 9.7, 1.8 Hz, 1H), 2.62-2.45 (m, 3H), 2.45-2.36 (m, 1H), 2.31-2.16 (m, 2 H), 2.02-1.94 (m, 1 H), 1.96 (dd, *J* = 2.6 Hz, 1H), 1.91-1.77 (m, 2 H), 1.70-1.67 (m, 3 H), 1.50-1.42 (m, 1 H), 1.25 (s, 3 H), 1.19 (s, 9H), 0.94 (d, *J* = 7.0 Hz, 3H), 0.92 (s, 9H), 0.89 (s, 9H), 0.77 (d, *J* = 7.0 Hz, 3H), 0.17 (s, 3H), 0.16 (s, 3H), 0.07 (s, 3H), 0.06 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) d 178.6, 131.3, 122.4, 83.3, 82.3, 81.4, 79.5, 78.2, 69.3, 63.0, 47.8, 41.7, 39.0, 38.7, 31.9, 27.6, 27.3, 26.5, 26.1, 25.5, 23.3, 22.8, 21.7, 18.7, 17.7, -1.2, -1.3, -3.5, -3.9; IR (film) 2957, 2934, 2860, 1729, 1463, 1386, 1366, 1285, 1254, 1158, 1092, 1004 cm^{-1}; HRMS (ESI) *m/z* 671.4524 (M+Na, 671.4503 calcd for $C_{37}H_{68}O_5Si_2$).

2,2-Dimethylpropionic acid (3*R*,4*R*)-bis-(*tert*-butyldimethylsiloxy)-4-(1*R*,3*R*,3a*R*,7*R*,7a*R*)-[3-(2-iodoallyl)-7-isopropyl-4-methyl-1,3,3a,6,7,7a-hexahydroisobenzofuran-1-yl]pentyl ester (11). A solution of alkyne **10** (110 mg, 0.18 mmol) and hexane (1.0 mL) was cooled to –25 °C, and then *B*-iodo-9-borabicyclo[3.3.1]nonane (0.42 mL of a 0.50M solution in hexane, 0.21 mmol) was added dropwise. After 4.5 h, the solution was allowed to warm to 0 °C and then treated dropwise with acetic acid (2.0 mL of a 1.0M solution in hexane). The resulting solution was stirred at 0 °C for 1 h, allowed to warm to rt, and then treated with a freshly prepared saturated aqueous solution of Na_2BO_3 (4.0 mL). The resulting mixture was stirred for 1 h, extracted with EtOAc (3 ¥ 10 mL), and the combined organic extracts were washed with brine (10 mL), dried (Na_2SO_4), filtered and concentrated. The residue was purified by flash chromatography on silica gel (98:2 hexane–ethyl acetate) to afford 110 mg (80%) of **11** as a clear pale yellow oil: $[a]^{23}_{D}$ +13.4, $[a]^{23}_{577}$ +13.7, $[a]^{23}_{546}$ +15.6, $[a]^{23}_{435}$ +26.2, $[a]^{23}_{405}$ +31.2 (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) d 6.14-6.12 (s, 1H), 5.75-5.73(s, 1H), 5.49-5.47 (m, 1 H), 4.18 (d, *J* = 3.3 Hz, 1H), 4.20-4.09 (m, 1 H), 3.94 (ddd, *J* = 10.4, 8.9, 7.4 Hz, 1H), 3.85 (ddd, *J* = 8.9, 8.9, 2.9 Hz, 1 H), 3.58 (dd, *J* = 8.2, 1.5 Hz, 1H), 2.85-2.72 (m, 2 H), 2.46 (dd, *J* = 7.8 Hz, 1H), 2.42-2.32 (m, 1 H), 2.21-2.10 (m, 2 H), 2.03-1.93 (m, 1 H), 1.90-1.79 (m, 2H), 1.70-1.68 (m, 3 H), 1.50-1.42 (m, 1 H), 1.24 (s, 3 H), 1.20 (s, 9H), 0.96 (d, *J* = 6.4 Hz, 3H), 0.92 (s, 9H), 0.89 (s, 9H), 0.76 (d, *J* = 6.7 Hz, 3H), 0.16 (s, 3H), 0.15 (s, 3H), 0.07 (s, 3H), 0.05 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) d 178.6, 131.4, 126.9, 122.7, 108.9, 83.1, 81.9, 79.3, 79.2, 78.3, 63.3, 52.0, 47.6, 41.9, 39.0, 38.7, 32.1, 27.4, 27.3, 26.8, 26.6, 26.4, 26.1, 23.4, 23.3, 21.8, 18.6, 18.3, 17.2, -1.1, -1.2, -3.5, -3.9; IR (film) 2957, 2934, 2895, 2860, 1729, 1621, 1463, 1386, 1366, 1285, 1254, 1158, 1092, 1004 cm^{-1}; HRMS (ESI) *m/z* 799.3599 (M+Na, 799.3626 calcd for $C_{37}H_{69}IO_5Si_2$).

(3*R*,4*R*)-Bis-(*tert*-butyldimethylsiloxy)-4-(1*R*,3*R*,3a*R*,7*R*,7a*R*)-[3-(2-iodoallyl)-7-isopropyl-4-methyl-1,3,3a,6,7,7a-hexahydroisobenzofuran-1-yl]pentanal (12). A solution of ester **11** (88 mg, 0.11 mmol) and toluene (1.8 mL) was cooled to –78 °C and treated dropwise with *i*-Bu_2AlH (95 mL of a 1.5M solution in toluene, 0.14 mmol). The solution was maintained at –78 °C for 10 min. Acetic acid (4.0 mL of a 1.0M solution in hexane, 4.0 mmol) was added dropwise at –78 °C and the reaction was allowed to warm to rt. This solution was diluted with EtOAc (4.0 mL), the layers were separated, the aqueous layer was extracted with EtOAc (2 × 10 mL), and the combined organic extracts were washed with saturated aqueous $NaHCO_3$, dried (Na_2SO_4), filtered, and concentrated to give the corresponding crude primary alcohol.

Dess-Martin periodinane[3] (180 mg, 0.30 mmol) was added in portion to a solution of the product from above and CH_2Cl_2 (8.0 mL), and the resulting mixture was stirred at room temperature. After 30 min, 1.5M aqueous $Na_2S_2O_3$ (5.0 mL) was added and the mixture was stirred vigorously. After 5 min, CH_2Cl_2 (10 mL) was added, and the organic layer was washed with 1.5M aqueous $Na_2S_2O_3$ (2 × 15 mL), brine (15 mL), dried (Na_2SO_4), filtered, and concentrated. The residue was purified by flash chromatography on silica gel (98:2 hexane–ethyl acetate) to afford 70 mg (90%, 2 steps) of **12** as a clear colorless oil: $[\alpha]^{23}_{D}$ +10.7, $[\alpha]^{23}_{577}$ +11.5, $[\alpha]^{23}_{546}$ +13.0, $[\alpha]^{23}_{435}$ +22.6, $[\alpha]^{23}_{405}$ +28.5 (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.81-9.79 (m, 1H), 6.13-6.11 (m, 1H), 5.80-5.77 (m, 1H), 5.50-5.48 (m, 1 H), 4.16-4.12 (m, 2H), 3.89 (ddd, *J* = 8.3, 8.3, 3.2 Hz, 1H), 3.15 (ddd, *J* = 19.0, 2.7, 0.1 Hz, 1 H), 2.97 (ddd, *J* = 19.0, 6.9, 1.5 Hz, 1H), 2.85-2.79 (m, 1 H), 2.69 (dd, *J* = 14.9, 8.8 Hz, 1H), 2.43 (dd, *J* = 7.6, 7.6 Hz, 1H), 2.25-2.19 (m, 1 H), 2.03-1.95 (m, 1 H), 1.93-1.85 (m, 1 H), 1.83-1.73 (m, 1H), 1.69 (s, 3 H), 1.49-1.41 (m, 1 H), 1.27 (s, 3 H), 0.94 (d, *J* = 6.8 Hz, 3H), 0.89 (s, 9H), 0.85 (s, 9H), 0.78 (d, *J* = 6.8

[3] Dess, D. B.; Martin, J. C. J. *Am. Chem. Soc.* **1991**, *113*, 7277–7287.

Hz, 3H), 0.14 (s, 3H), 0.10 (s, 3H), 0.09 (s, 3H), -0.04 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) d 203.3, 131.4, 126.7, 122.6, 108.8, 83.9, 81.8, 78.4, 74.0, 52.0, 49.0, 47.5, 41.2, 39.2, 27.5, 26.3, 26.4, 26.0, 25.9, 23.3, 23.2, 18.5, 18.1, 17.7, -1.4, -1.5, -3.9, -5.1; IR (film) 2957, 2930, 2895, 2860, 2714, 1725, 1621, 1463, 1386, 1254, 1096, 1004 cm^{-1}; HRMS (ESI) *m/z* 713.2877 (M+Na, 713.2894 calcd for $C_{32}H_{59}IO_4Si_2$).

(3*R*,7*R*,8*R*,11*S*,13*S*,14*S*,15*R*,16*R*)-13,14-Bis-(*tert*-butyldimethylsiloxy)-3-isopropyl-6,14-dimethyl-10-methylene-15-oxa-tricyclo[6.6.1.$0^{0,0}$]pentadec-5-en-11-ol (13). A mixture of the alkenyl iodide **12** (35 mg, 0.05 mmol), a 100:1 mixture of $CrCl_2$ and $NiCl_2$ (650 mg) and a dry, degassed 100:1 mixture of DMSO-Me_2S (45 mL) was stirred at room temperature for 5 days. The resulting dark green mixture was then transfered to a 1.0M solution of sodium serinate (60 mL) and EtOAc (30 mL) at 0 °C and the resulting mixture was stirred for 1 h at rt (purple solution). The layers were separated, the aqueous layer was extracted with EtOAc (2 ¥ 30 mL), and the combined organic extracts were washed with brine (2 ¥ 20 mL), dried (Na_2SO_4), filtered, and concentrated. The resulting residue was purified by silica gel chromatography (95:5 hexane–ethyl acetate) to afford 16 mg (55%) of **13** as a clear colorless oil: $[a]^{23}_{D}$ +82.3, $[a]^{23}_{577}$ +85.7, $[a]^{23}_{546}$ +97.8, $[a]^{23}_{435}$ +171.6, $[a]^{23}_{405}$ +210.7 (*c* 0.7, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) d 5.45-5.41 (m, 1H), 5.18 (dd, *J* = 1.8, 1.8 Hz, 1H), 5.09 (dd, *J* = 3.8, 3.8 Hz, 1 H), 4.91 (s, 1H), 4.02 (s, 1H), 3.86 (d, *J* = 8.1 Hz, 1 H), 3.74 (ddd, *J* = 11.3, 7.8, 4.2 Hz, 1 H), 2.94 (dd, *J* = 13.3, 9.1 Hz, 1H), 2.70 (dd, *J* = 15.5, 7.6 Hz, 1 H), 2.62 (dd, *J* = 7.2, 7.2 Hz, 1H), 2.48 (dd, *J* = 13.5, 4.1 Hz, 1H), 2.15 (dd, *J* = 11.8, 7.6 Hz, 1 H), 1.96-1.88 (m, 1 H), 1.87-1.69 (m, 3 H), 1.66 (s, 3H), 1.56-1.54 (m, 2 H), 1.46 (d, *J* = 6.7 Hz, 1 H), 1.40-1.32 (m, 1 H), 1.26 (s, 3H), 1.27-1.25 (m, 1H), 0.95 (s, 9H), 0.92 (s, 9H), 0.79 (d, *J* = 6.7 Hz, 3H), 0.20 (s, 3H), 0.14 (s, 3H), 0.13 (s, 3H), 0.11 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) d 153.9, 132.3, 121.1, 110.3, 85.9, 83.7, 81.5,

78.1, 68.9, 49.2, 43.9, 42.5, 40.1, 38.7, 27.9, 27.5, 26.6, 26.0, 22.9, 22.8, 21.9, 18.9, 18.1, 15.7, -1.3, -1.5, -3.7, -5.1; IR (film) 2957, 2930, 2895, 2860, 1729, 1637, 1463, 1390, 1366, 1254, 1100, 1073, 1004 cm^{-1}; HRMS (CI) *m/z* 564.4034 (M, 564.4030 calcd for $C_{32}H_{60}O_4Si_2$).

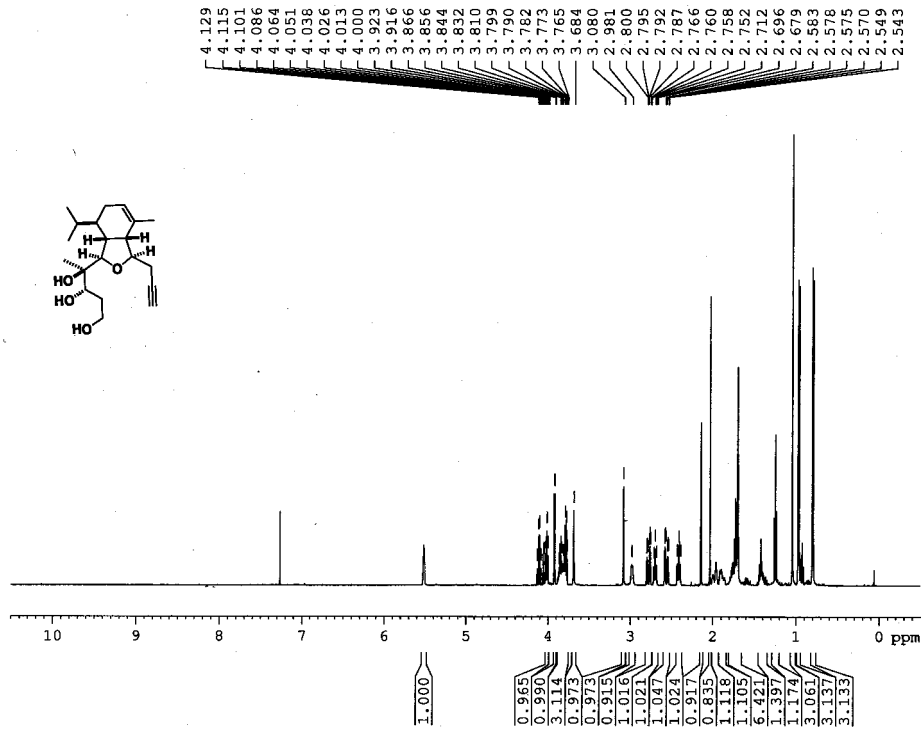
(6*R*,7*R*,8*R*,9*R*,12*S*,14*S*,15*R*,16*R*)-6-Isopropyl-3,9-dimethyl-13-methylene-15-oxatricyclo[6.6.1.$0^{0,0}$]pentadec-3-ene-9,10,12-triol (14). A solution of allylic alcohol **13** (17 mg, 0.03 mmol) and THF (0.6 mL) was treated at room temperature with *n*-Bu_4NF (0.3 mL of a 1.0M solution in THF, 0.30 mmol). After 4 h, saturated aqueous NH_4Cl (5.0 mL) was added, the aqueous layer was extracted with ethyl acetate (3 ¥ 5.0 mL), and the combined organic extracts were dried (Na_2SO_4), filtered, and concentrated. The residue was purified by flash chromatography on silica gel (50:50 hexane–ethyl acetate) to give 9.0 mg (88%) of **14** as a colorless solid: $[a]^{23}_{D}$ -31.6, $[a]^{23}_{577}$ -34.0, $[a]^{23}_{546}$ -39.6, $[a]^{23}_{435}$ -73.4, $[a]^{23}_{405}$ -91.3 (*c* 0.6, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) d 5.53-5.50 (m, 1H, H16), 5.48-5.45 (m, 1H, H12)), 5.17-5.14 (m, 1 H, H16), 4.37 (d, *J* = 5.6 Hz, 1H, H6), 4.12 (app q, *J* = 3.6 Hz, 1H, H9), 3.91 (d, *J* = 6.2 Hz, 1 H, H2), 3.85 (app t, *J* = 4.3 Hz, 1 H, H4), 2.73-2.66 (m, 1H), 2.67-2.54 (m, 2 H), 2.47 (dd, *J* = 14.2, 4.2 Hz, 1H), 2.35 (dd, *J* = 14.2, 3.0 Hz, 1 H), 2.13-1.97 (m, 2 H), 1.96-1.81 (m, 1 H), 1.69 (s, 3H), 1.70-1.67 (m, 1 H), 1.54-1.47 (m, 1 H), 1.31 (s, 3H), 1.25 (s, 3H), 0.92 (d, *J* = 6.8 Hz, 3H), 0.82 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) d 149.0, 132.2, 122.7, 115.3, 88.2, 82.2, 75.2, 73.0, 44.9, 40.3, 40.2, 40.0, 39.7, 29.9, 28.8, 23.1, 22.6, 22.4, 21.8, 19.4; IR (film) 3389, 2961, 2922, 2856, 1733, 1668, 1640, 1459, 1378, 1262, 1239, 1069, 1000 cm^{-1}; HRMS (ESI) *m/z* 559.2197 (M+Na, 559.2198 calcd for $C_{20}H_{32}O_4$).

Acetic acid (6*R*,7*R*,8*R*,9*R*,12*S*,14*S*,15*R*,16*R*)-9,12-dihydroxy-6-isopropyl-3,9-dimethyl-13-methylene-15-oxa-tricyclo[6.6.1.$0^{0,0}$]pentadec-3-en-10-yl ester (3). A solution of the triol **14** (8.0 mg, 0.024 mmol), dry pyridine (0.3 mL) and 4-(*N*,*N*-Dimethylamino)pyridine

(1.0 mg, 0.01 mmol) at 0 °C was treated with acetic anhydride until TLC analysis (70:30 hexane-ethyl acetate) showed complete consumption of the starting material. Saturated aqueous NH_4Cl (5.0 mL) was then added, the aqueous layer was extracted with ethyl acetate (3 ¥ 5.0 mL), and the combined organic extracts were washed sequentially with saturated aqueous $CuSO_4$ (2 ¥ 10 mL) and brine (2 ¥ 10 mL), dried (Na_2SO_4), filtered, and concentrated. The residue was purified by flash chromatography on silica gel (70:30 hexane–ethyl acetate) to give 6.0 mg (68%) of **3** as a clear colorless oil: $[a]^{23}_{D}$ -64.5, $[a]^{23}_{577}$ -68.7, $[a]^{23}_{546}$ -78.5, $[a]^{23}_{435}$ -147.1, $[a]^{23}_{405}$ -182.5 (*c* 0.4, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) d 5.63-5.61 (m, 1H, H16), 5.43-5.41 (m, 1H, H12), 5.23-5.21 (m, 1 H, H16), 4.99 (app t, *J* = 4.0 Hz, 1H, H4), 4.21-4.19 (m, 2H, H6 and H9), 3.84 (d, *J* = 8.4 Hz, 1 H, H2), 3.53-3.47 (m, 1 H), 3.02-2.98 (m, 1H), 2.77-2.71 (m, 1 H), 2.67-2.61 (m, 1H), 2.34 (app d, *J* = 3.5 Hz, 2 H), 2.15 (s, 3 H), 2.00-1.91 (m, 1 H), 1.88-1.83 (m, 1H), 1.80 (ddd, *J* = 16.1, 4.35, 4.3 Hz, 1 H), 1.68 (s, 3 H), 1.56-1.52 (m, 2H), 1.39 (s, 3H), 1.30-1.21 (m, 1H) , 0.91 (d, *J* = 6.2 Hz, 3H) , 0.83 (d, *J* = 6.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) d 172.7, 147.8, 132.2, 122.0 (C12), 115.1 (C6), 86.9 (C2), 81.1 (C9), 74.7, 73.8 (C4), 72.8 (C6), 44.6, 40.0, 39.6, 39.0, 37.5, 28.7, 22.9, 22.5, 22.0, 21.5, 21.3, 20.8; IR (film) 3443, 2961, 2926, 2872, 1714, 1640, 1440, 1374, 1262, 1096, 1069 cm^{-1}; HRMS (ESI) *m/z* 401.2310 (M+Na, 401.2304 calcd for $C_{22}H_{34}O_5$).

Conversion of 3 to 19. Dess-Martin periodinane (4.7 mg, 0.03 mmol) was added to a solution of alcohol **9** (1.2 mg, 0.003 mmol), $NaHCO_3$ (4.7 mg, 0.05 mmol) and CH_2Cl_2 (0.5 mL), and the resulting mixture was stirred at room temperature. After 1 h, 1.5M aqueous $Na_2S_2O_3$ (1.0 mL) was added and the mixture was stirred vigorously for 5 min; then hexane (5.0 mL) was added and the organic layer was washed with 1.5 M aqueous $Na_2S_2O_3$ (2 ¥ 5.0 mL), brine (5.0 mL), dried (Na_2SO_4), filtered, and concentrated. The residue was purified by flash

chromatography on silica gel (70:30 hexane–ethyl acetate) to afford 1.0 mg (80%) of **19** as a clear colorless oil. $[\alpha]^{23}_{D}$ -64.5, $[\alpha]^{23}_{577}$ -68.7, $[\alpha]^{23}_{546}$ -78.5, $[\alpha]^{23}_{435}$ -147.1, $[\alpha]^{23}_{405}$ -182.5 (*c* 0.4, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.47-5.43 (m, 1H), 5.42-5.41 (m, 1H), 5.24 (dd, *J* = 9.5, 9.5 Hz, 1 H), 5.05-5.03 (m, 1H), 4.09-4.04 (m, 1H), 4.05 (d, *J* = 2.5 Hz, 1H), 2.99-2.90 (m, 2H), 2.89-2.85 (m, 1 H), 2.66 (dd, *J* = 15.2, 5.2 Hz, 1H), 2.54 (dd, *J* = 12.7, 9.3 Hz, 1H), 2.47-2.43 (m, 1 H), 2.14 (s, 3 H), 2.03-1.96 (m, 1H), 1.88-1.70 (m, 2H), 1.65-1.63 (m, 3 H), 1.40-1.23 (m, 2H), 1.29 (s, 3H), 0.98 (d, *J* = 6.8 Hz, 3H) , 0.80 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.0, 133.0, 121.4, 115.1, 104.0, 83.8, 82.3, 86.0, 78.9, 46.1, 45.1, 43.5, 41.9, 38.8, 30.0, 28.3, 23.0, 22.7, 22.3, 21.6, 20.4, 17.0; IR (film) 3424, 2961, 2934, 2856, 1714, 1459, 1440, 1374, 1239, 1143, 1073, 1023 cm^{-1}; HRMS (ESI) *m/z* 399.2149 (M+Na, 399.2148 calcd for $C_{22}H_{32}O_5$).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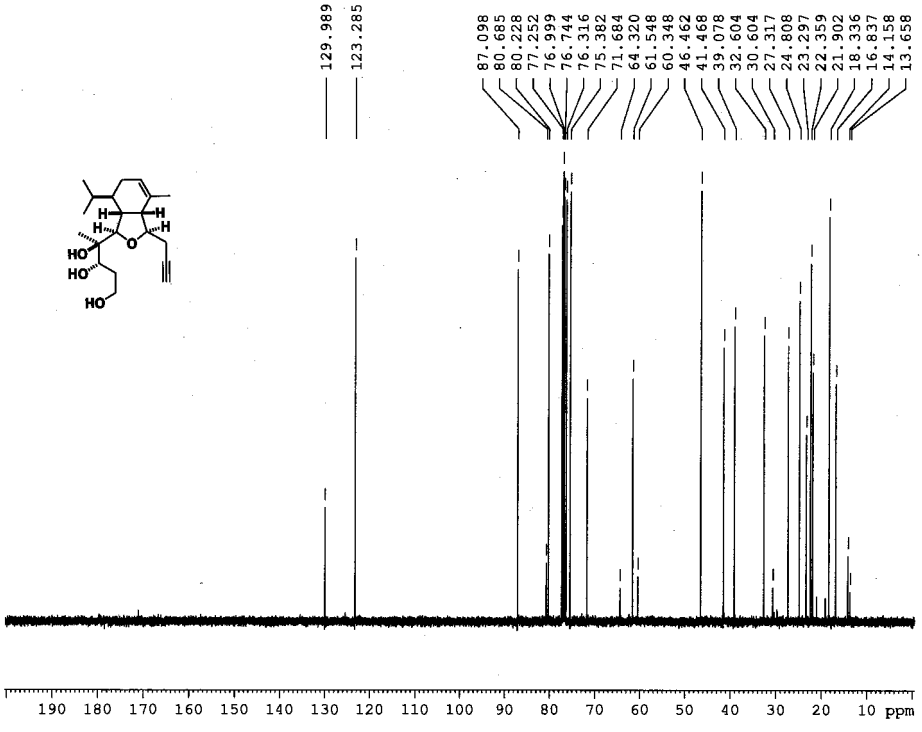
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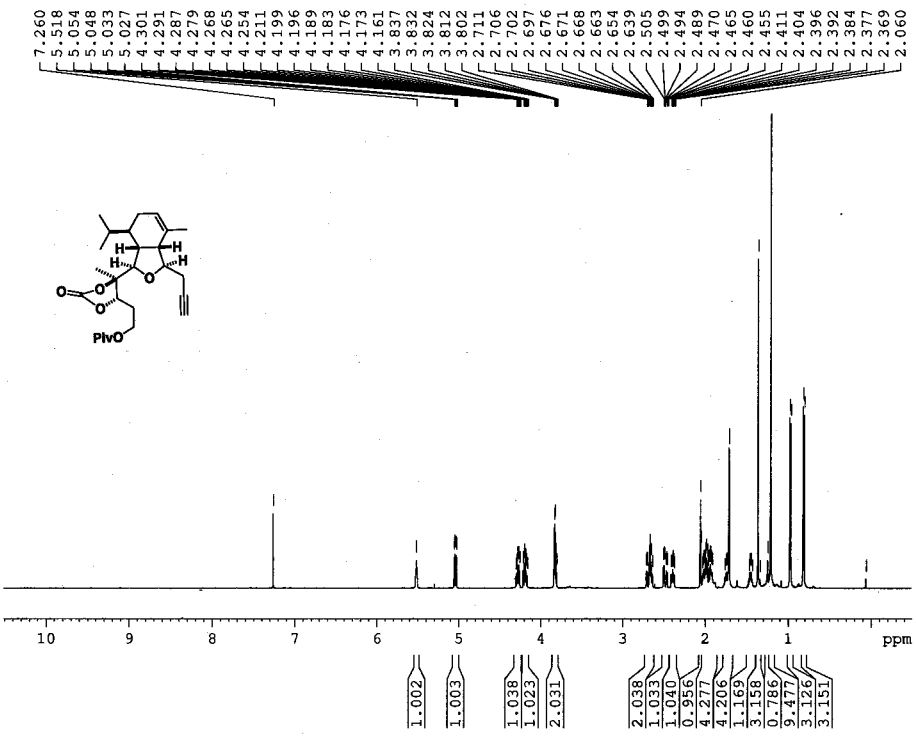
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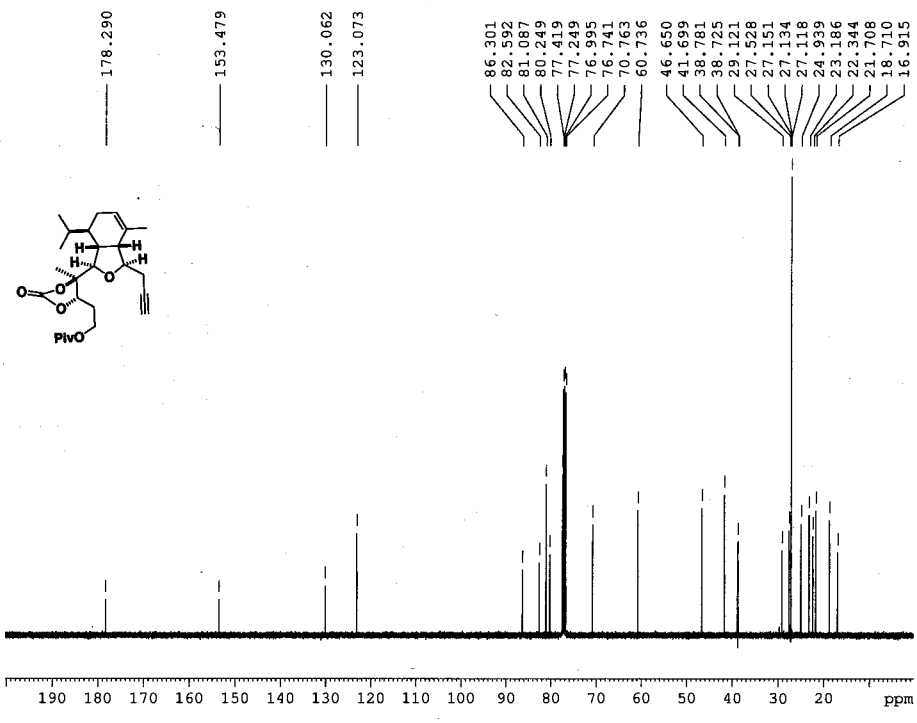
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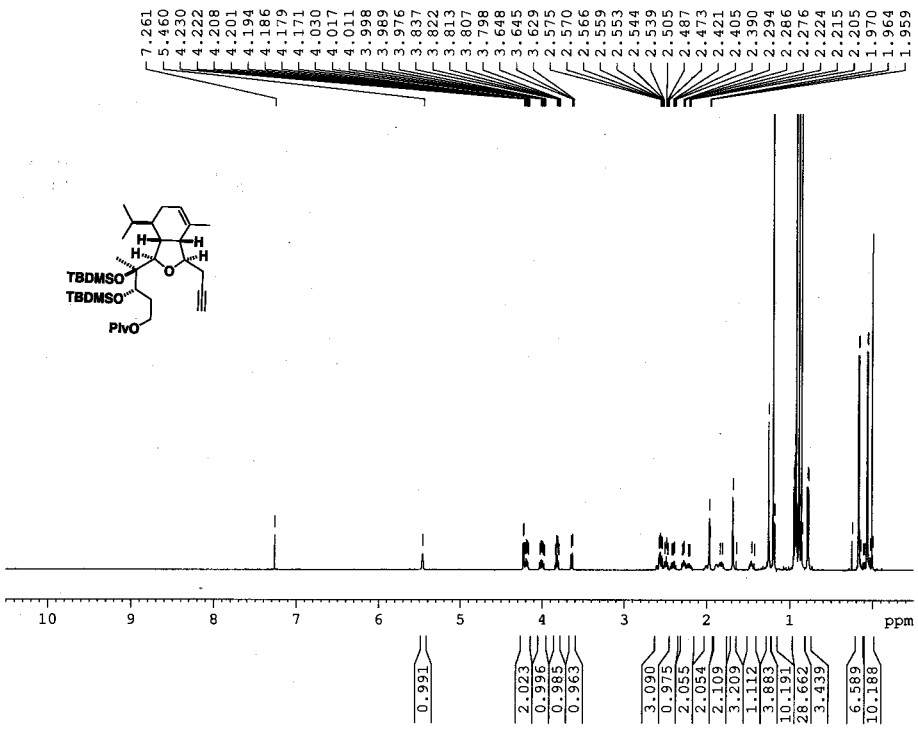
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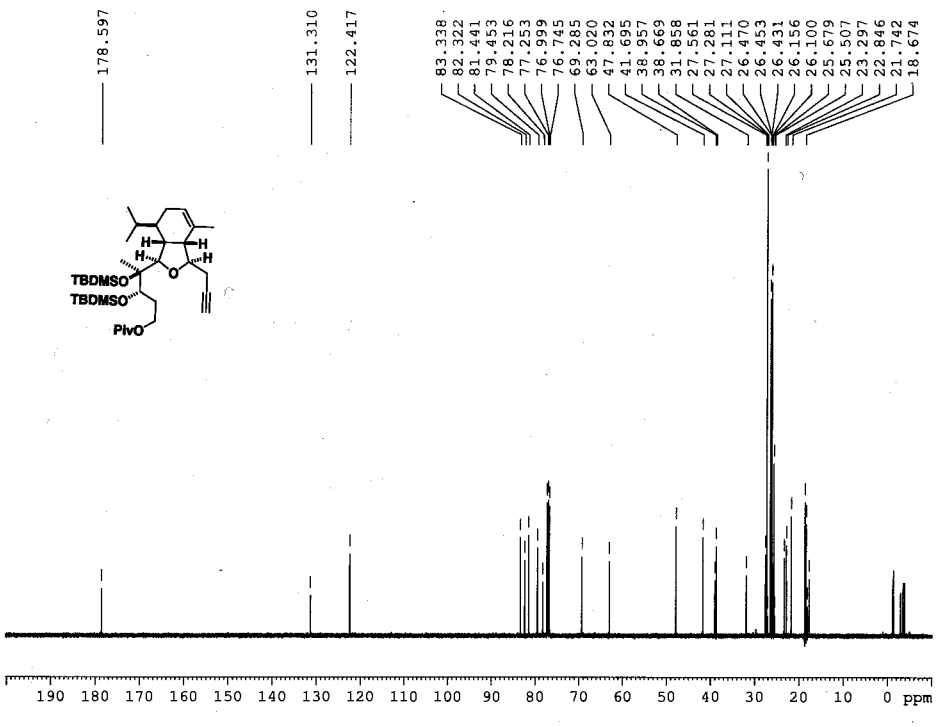
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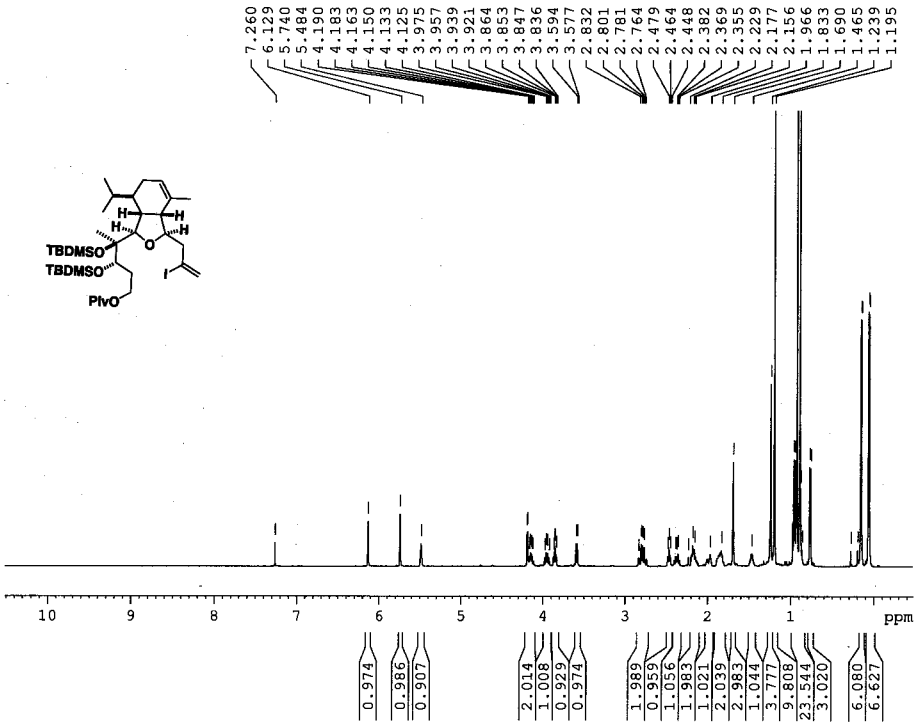
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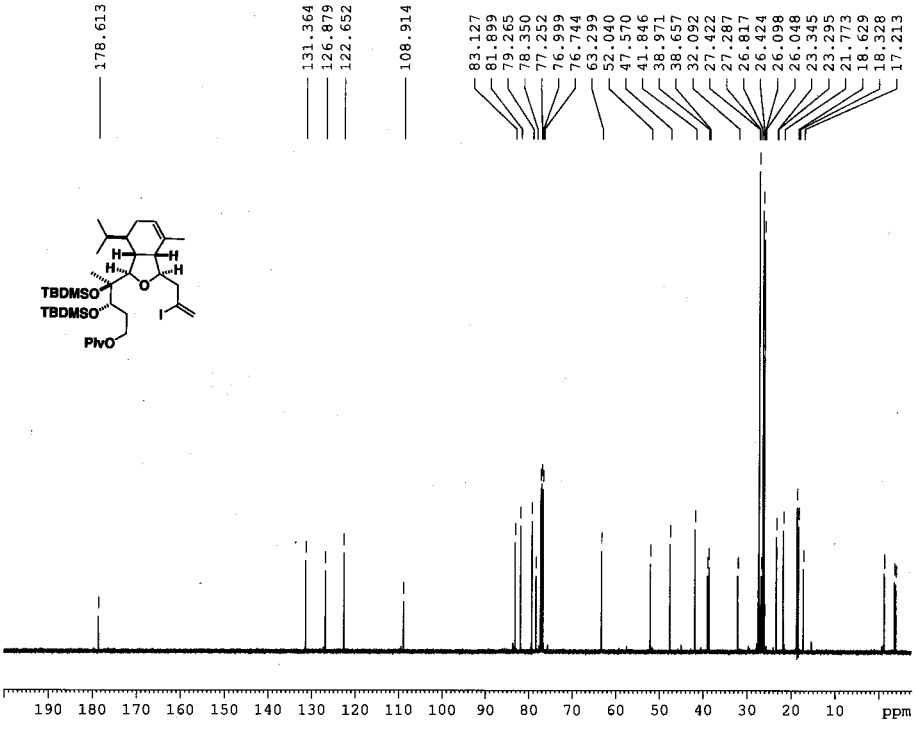
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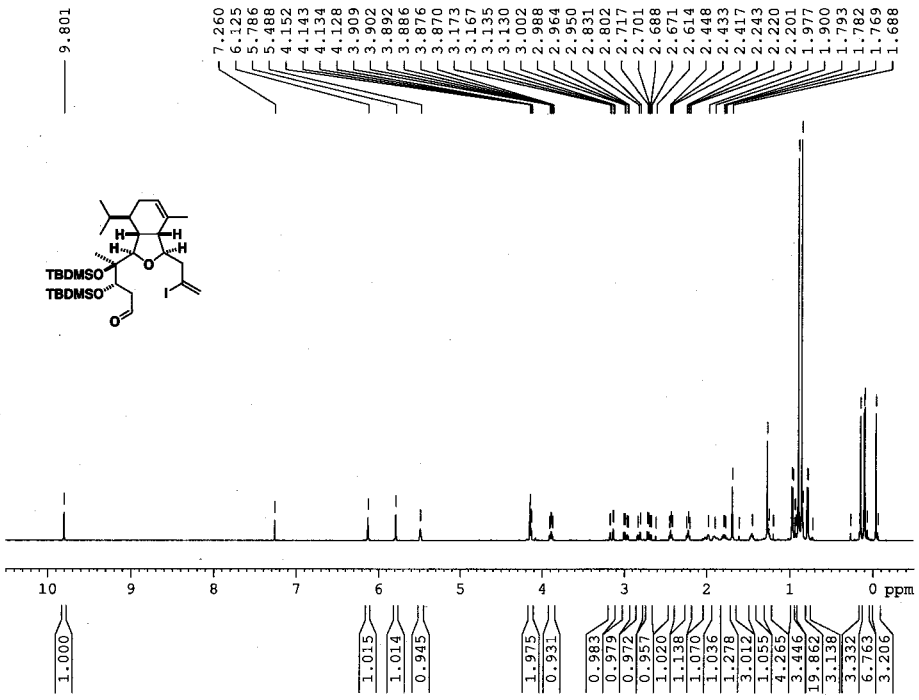
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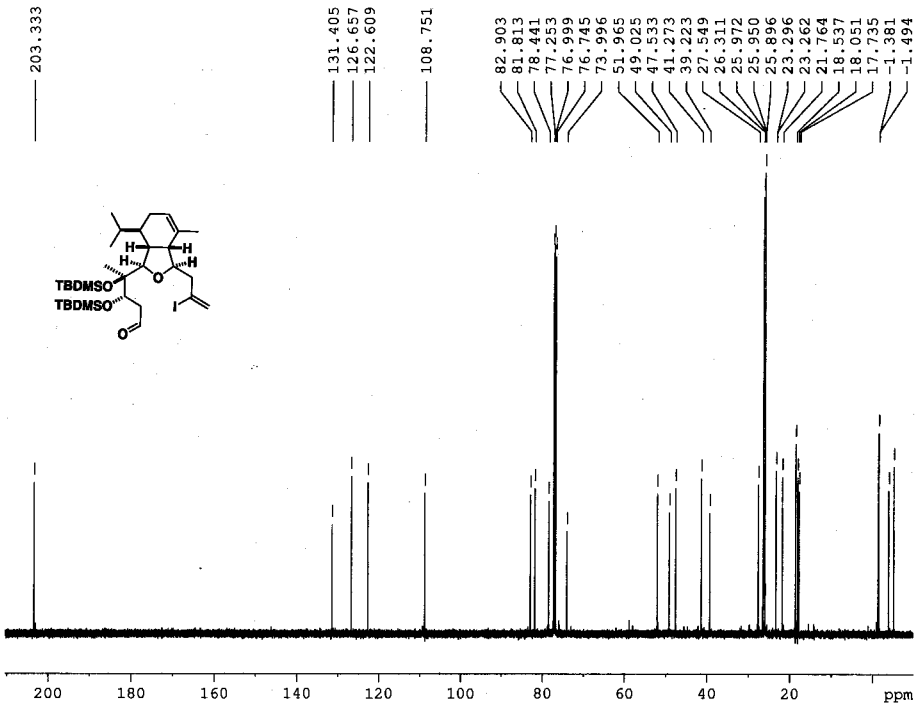
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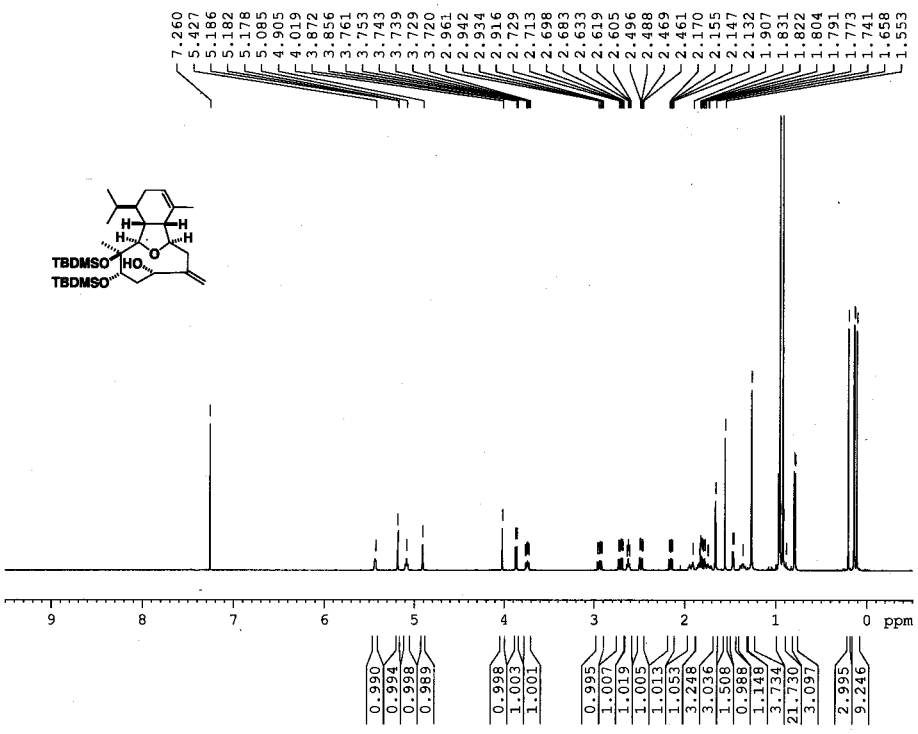
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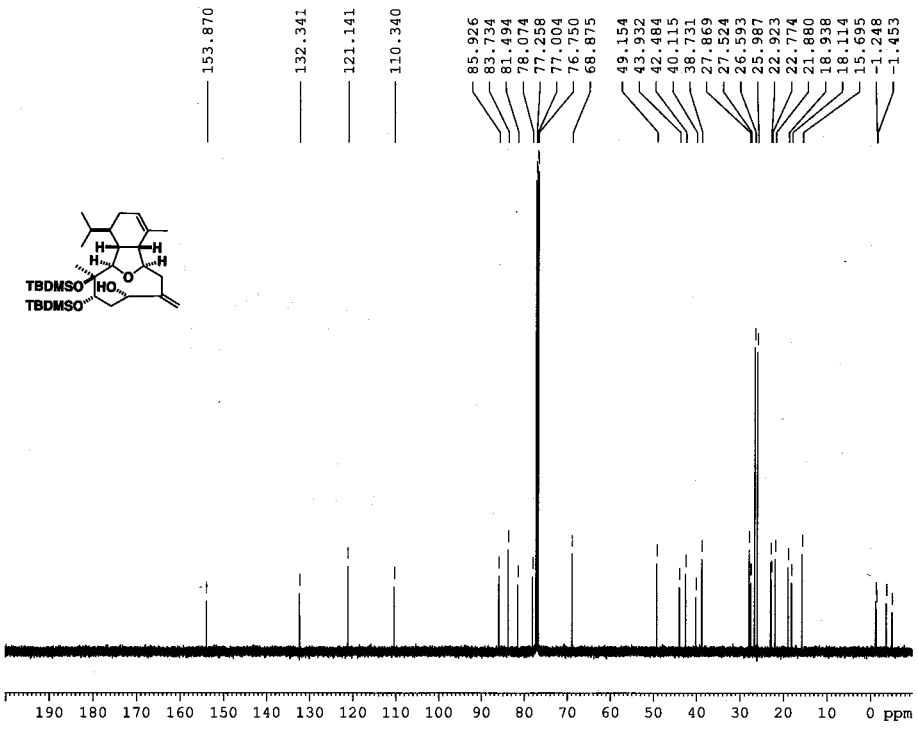
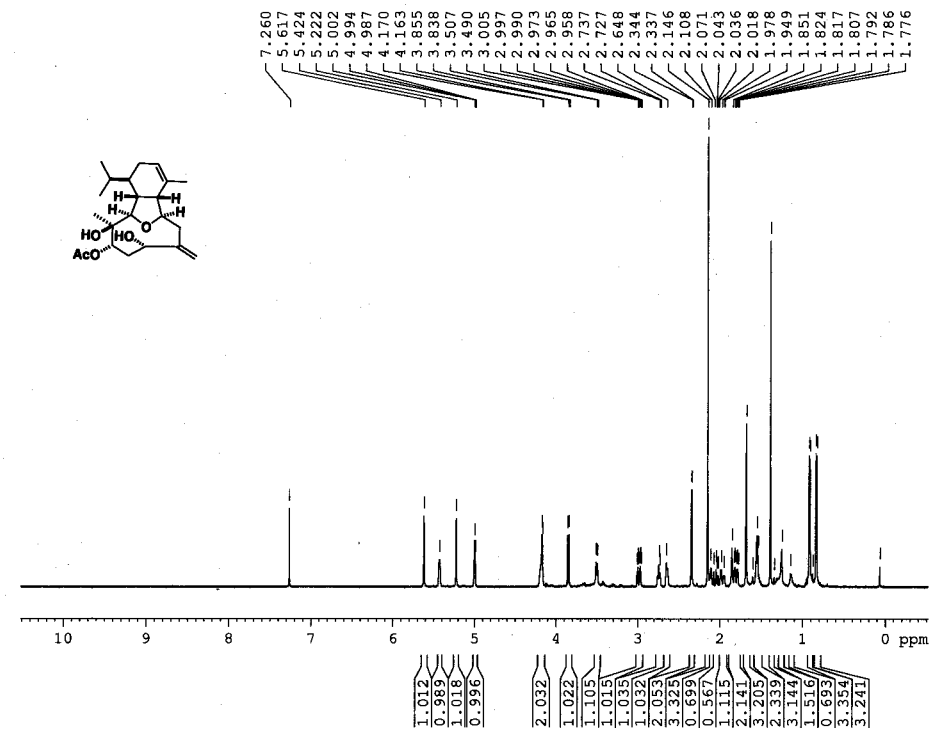
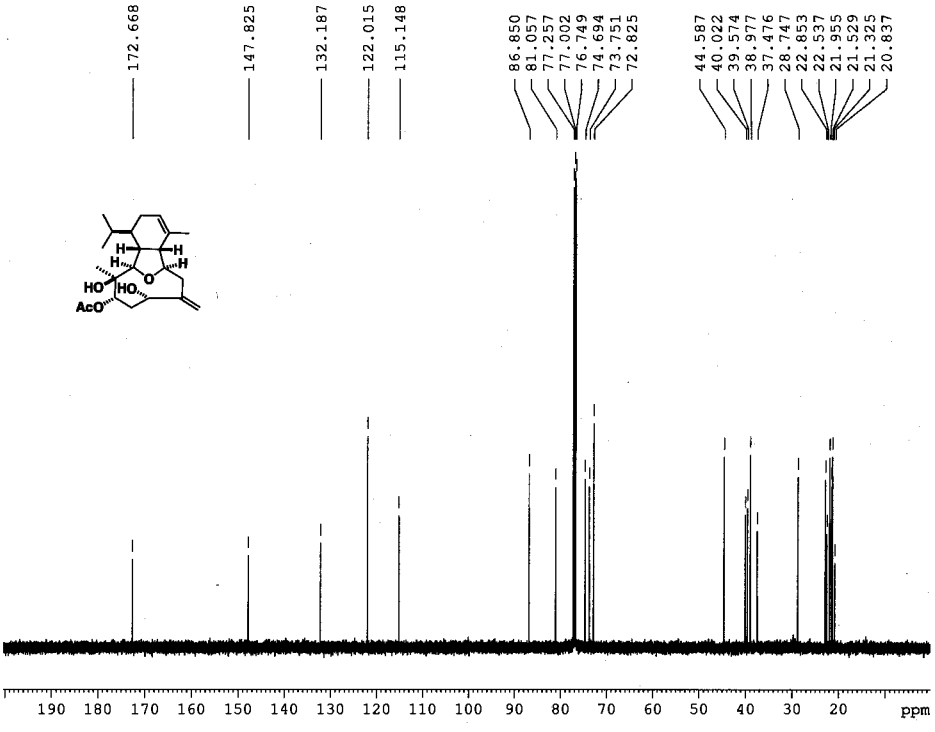
2.469
2.461
2.170
2.155
2.147
2.132
1.907
1.831
1.822
1.804
1.791
1.773
1.741
1.658
1.553
TBDMSO
TBDMSO
HO
9 8 7 6 5 4 3 2 1 0 ppm
0.990
0.994
0.998
0.989
0.998
1.003
1.001
0.995
1.007
1.019
1.005
1.013
1.053
3.248
3.036
1.508
0.988
1.148
3.734
21.730
3.097
2.995
9.246


153.870
132.341
121.141
110.340
85.926
83.734
81.494
78.074
77.258
77.004
76.750
68.875
49.154
43.932
42.484
40.115
38.731
27.869
27.524
26.593
25.987
22.923
22.774
21.880
18.938
18.114
15.695
-1.248
-1.453
TBDMSO
TBDMSO
HO
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


7.260
5.617
5.424
5.222
5.002
4.994
4.987
4.170
4.163
3.855
3.838
3.507
3.490
3.005
2.997
2.990
2.973
2.965
2.958
2.737
2.727
2.648
2.344
2.337
2.146
2.108
2.071
2.043
2.036
2.018
1.978
1.949
1.851
1.824
1.817
1.807
1.792
1.786
1.776
HO
HO
AcO
10 9 8 7 6 5 4 3 2 1 0 ppm
1.012
0.989
1.018
0.996
2.032
1.022
1.105
1.015
1.035
1.032
2.053
3.325
0.699
0.567
1.115
2.141
3.205
2.339
3.144
1.516
0.693
3.354
3.241


172.668
147.825
132.187
122.015
115.148
86.850
81.057
77.257
77.002
76.749
74.694
73.751
72.825
44.587
40.022
39.574
38.977
37.476
28.747
22.853
22.537
21.955
21.529
21.325
20.837
HO
HO
AcO
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm