JOURNAL OF THE AMERICAN CHEMICAL SOCIETY
J. Am. Chem. Soc., 1996, 118(37), 8860-8870, DOI:10.1021/ja961888n

Supplementary Material

Synthesis, X-ray Structure, and Properties of Fluorocyclopropane Analogs of the Duocarmycins Incorporating the 9,9-Difluoro-1,2,9,9a-tetrahydrocyclopropa[*c*]benzo[*e*]indol-4-one (F_2CBI) Alkylation Subunit

Dale L. Boger* and Tracy J. Jenkins
Department of Chemistry, The Scripps Research Institute
10550 North Torrey Pines Road, La Jolla, California 92037

3-[*N*-(*tert*-Butyloxycarbonyl)-*N*-(3-methyl-2-buten-1-yl)]amino-1-benzyloxynaphthalene (5). A suspension of NaH (0.53 g, 22.0 mmol) in anhydrous DMF (10 mL) at 25 °C under Ar was treated with a solution of **4**[24] (5.98 g, 17.0 mmol) in DMF (50 mL), and the reaction mixture was stirred at 25 °C for 0.5 h. The mixture was cooled to 0 °C, and 4-bromo-2-methyl-2-butene (5.9 mL, 51.0 mmol) was added slowly to the mixture. The mixture was allowed to warm to 25 °C and was stirred for 14 h before being poured into H_2O (60 mL). The organic layer was separated and the aqueous layer extracted with EtOAc (3 × 50 mL). The combined organic solutions were washed with H_2O (70 mL), saturated aqueous NaCl (100 mL), dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography (SiO_2, 15% EtOAc–hexane) gave **5** (6.91 g, 7.10 g theoretical, 97%) as a white solid: mp 89–90.5 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.25 (d, 1H, J = 8.1 Hz, C8-H), 7.71 (d, 1H, J = 7.4 Hz, C5-H), 7.45 (m, 7H), 7.22 (br s, 1H, C4-H), 6.77 (br s, 1H, C2-H), 5.30 (m, 1H, C2′-H), 5.20 (s, 2H, CH_2Ph), 4.25 (br d, 2H, J = 6.6 Hz, C1′-H), 1.67 (s, 3H, CH_3), 1.51 (s, 3H, CH_3), 1.42 (s, 9H, $C(CH_3)_3$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 154.8, 154.4, 140.5, 136.7, 134.3, 134.1, 128.4, 127.8, 127.2, 127.1, 126.6, 124.8, 123.9, 121.9, 120.9, 116.7, 105.9, 79.9, 70.0, 48.2, 28.2 (3C), 25.3, 17.7; IR (solid film) ν_{max} 2974, 1694, 1412, 1163 cm^{-1}; FABHRMS (NBA–NaI) *m/z* 417.2291 (M^+, $C_{27}H_{31}NO_3$ requires 417.2304).

Anal. Calcd for $C_{27}H_{31}NO_3$: C, 77.67; H, 7.48; N, 3.35. Found: C, 77.30; H, 7.60; N, 3.30.

3-[*N*-(*tert*-Butyloxycarbonyl)-*N*-(formylmethyl)]amino-1-benzyloxynaphthalene (6). A solution of **5** (3.31 g, 7.94 mmol) in 5:1 CH_2Cl_2–CH_3OH (350 mL) at –78 °C was treated with a stream of 3% O_3/O_2 (160 L/h, 4 min). The reaction mixture was quenched quickly with the addition of 14 mL of Me_2S and the resulting mixture was stirred at 25 °C (12 h) before the solvent was removed in vacuo. Chromatography (SiO_2, 10–20% EtOAc–hexane gradient elution) yielded **6** (2.55 g, 3.15 g theoretical, 81%) as a white solid: mp 96.0–98.0 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.73 (s, 1H, CHO), 8.27 (dd, 1H, J = 1.5, 7.9 Hz, C8-H), 7.71 (dd, 1H, J = 1.4, 7.4 Hz, C5-H), 7.43 (m, 7H), 7.23 (br s, 1H, C4-H), 6.85 (br s, 1H, C2-H), 5.22 (s, 2H, CH_2Ph), 4.39 (s, 2H, CH_2CHO), 1.42 (s, 9H, $C(CH_3)_3$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 198.1, 154.8, 140.3, 136.7, 134.1, 128.7, 128.1, 127.43, 127.39, 127.0, 125.4, 124.4, 122.1, 116.5, 105.4, 81.6, 70.3, 60.5, 28.2 (3C); IR (solid film) ν_{max} 2976, 1736, 1693, 1368 cm^{-1}; FABHRMS (NBA–NaI) *m/z* 414.1672 (M + Na$^+$, $C_{24}H_{25}NO_4$ requires 414.1681).

Anal. Calcd for $C_{24}H_{25}NO_4$: C, 73.64; H, 6.44; N, 3.58. Found: C, 73.50; H, 6.41; N, 3.67.

3-[*N*-(*tert*-Butyloxycarbonyl)-*N*-(3,3-difluoro-2-hydroxy-3-phenylsulfonyl-1-propyl)]amino-1-benzyloxynaphthalene (7). A solution of **6** (33.1 mg, 0.085 mmol) and $PhSO_2CF_2H$ (31.0 mg, 0.16 mmol) in anhydrous THF (3.5 mL) and HMPA (0.5 mL) was cooled to –78 °C under Ar. A solution of 1.14 M LiHMDS in THF (200 μL, 0.20 mmol) was added dropwise and the resulting orange solution was allowed to warm to 25 °C and stirred for 4 h. The reaction mixture was poured into saturated aqueous NaCl (10 mL) and extracted with Et_2O (3 × 15 mL). The organic layers were combined, dried ($MgSO_4$), filtered, and concentrated under reduced pressure. Chromatography (SiO_2, 10% EtOAc–hexane) afforded recovered **6** (10.0 mg, 30%) and **11** (25.2 mg, 49.4 mg theoretical, 51%; 73% based on recovered **6**) as a white foam: mp 45–46.5 °C; ^{1}H NMR

($CDCl_3$, 400 MHz) δ 8.29 (d, 1H, J = 7.8 Hz, C8-H), 7.94 (d, 1H, J = 7.5 Hz, C5-H), 7.76 (m, 2H, C-6 and C-7H), 7.47 (m, 10H), 7.18 (br s, 1H, C4-H), 6.72 (br s, 1H, C2-H), 5.25 (d, 1H, J = 11.6 Hz, C*H*HPh), 5.21 (d, 1H, J = 11.5 Hz, CH*H*Ph), 4.65 (m, 1H, OH), 4.50 (m, 1H, C2′-H), 4.31 (br t, 1H, J = 6.0 Hz, C1′-H), 3.89 (br d, 1H, J = 14.0 Hz, C1′-H), 1.36 (s, 9H, $C(CH_3)_3$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 154.9, 139.6, 136.6, 135.3, 134.1, 133.2, 130.7, 129.1, 128.7, 128.6, 128.0, 127.6, 127.3, 127.0, 125.5, 122.6, 122.1, 117.6, 105.6, 81.9, 70.1, 69.4 (t, J = 84.0 Hz), 51.0 (d, J = 12.0 Hz), 28.2 (3C); ^{19}F NMR ($CDCl_3$, 376 MHz) δ –112.0 (dd, J = 40.0, 240.0 Hz), –116.9 (d, J = 240.0 Hz); IR (solid film) ν_{max} 3390, 1771, 1367 cm^{-1}; FABHRMS (NBA–CsI) *m/z* 716.0899 ($M + Cs^+$, $C_{31}H_{31}F_2NO_6S$ requires 716.0894).

Anal. Calcd for $C_{31}H_{31}F_2NO_6S$: C, 63.80; H, 5.35; N, 2.40. Found: C, 63.48; H, 5.11; N, 2.41.

3-[*N*-(*tert*-Butyloxycarbonyl)-*N*-(3,3-difluoro-2-methanesulfonyloxy-3-phenylsulfonyl-1-propyl)]amino-1-benzyloxynaphthalene (8). A solution of **7** (205 mg, 0.35 mmol) in CH_2Cl_2 (5 mL) was cooled to –30 °C under Ar and treated with Et_3N (0.30 mL, 3.5 mmol). After stirring for 5 min, MsCl (98 μL, 0.70 mmol) was added and the reaction mixture stirred for an additional 5 h. The reaction mixture was quenched by addition of saturated aqueous NH_4Cl (10 mL). The organic layer was removed and the aqueous layer was extracted with EtOAc (3 × 15 mL). The organic solutions were combined, dried ($MgSO_4$), filtered and concentrated under reduced pressure. Chromatography (SiO_2, 10% EtOAc–hexane) yielded **8** (202 mg, 232 mg theoretical, 87%) as a beige foam: mp 54.5–56.0 °C; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.28 (dd, 1H, J = 1.2, 7.1 Hz, C8-H), 7.90 (d, 1H, J = 7.7 Hz, C5-H), 7.75 (m, 2H, C6 and C7-H), 7.32–7.58 (m, 11 H), 7.00 (d, 1H, J = 1.4 Hz, C2-H), 5.76 (br m, 1H, C2′-H), 5.24 (s, 2H, CH_2Ph), 4.44 (m, 1H, C1′-H), 4.28 (m, 1H, C1′-

H), 3.04 (s, 3H, CH_3SO_2), 1.42 (s, 9H, $C(CH_3)_3$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 154.6, 154.3, 140.1, 137.0, 135.9, 134.1, 132.0, 130.8, 129.4, 128.5, 127.9, 127.5, 126.8, 125.3, 124.0, 122.1, 119.2, 117.0, 116.3, 106.5, 81.7, 74.6 (t, J = 86.4 Hz), 70.2, 60.3, 50.1, (d, J = 15.0 Hz), 39.0, 28.2 (3C), 21.0, 14.1; ^{19}F NMR ($CDCl_3$, 376 MHz) δ –106.7 (d, J = 240.0 Hz), –110.8 (br d, J = 240.0 Hz); IR (solid film) ν_{max} 1699, 1368, 1160 cm^{-1}; FABHRMS (NBA–CsI) *m/z* 794.0678 ($M + Cs$, $^+$ $C_{32}H_{33}F_2NO_8S_2$ requires 794.0670).

Anal. Calcd for $C_{32}H_{33}F_2NO_8S_2$: C, 58.08; H, 5.03; N, 2.12. Found: C, 58.45; H, 5.16; N, 2.02.

3-[*N*-(*tert*-Butyloxycarbonyl)-*N*-(3,3-difluoro-2-propen-1-yl)]amino-1-benzyloxynaphthalene (9). A solution of **8** (116 mg, 0.17 mmol) in CH_3OH (4 mL) cooled to 0 °C under Ar was treated with Na_2HPO_4 (99 mg, 0.70 mmol) and 5% Na(Hg) (500 mg, 1.1 mmol). After vigorous stirring at 0 °C for 1 h, the reaction mixture was allowed to warm to 25 °C where Et_2O (20 mL) was added. The solid Hg residue was removed by filtration through a cotton wool plug and the etheral solution was concentrated under reduced pressure. Chromatography (SiO_2, 3% EtOAc–hexane) afforded **9** as a colorless oil (57 mg, 74 mg theoretical, 77%) which crystallized in the refrigerator to give a white solid: mp 57.0–59.0 °C; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.27 (dd, 1H, J = 1.0, 8.0 Hz, C8-H), 7.75 (dd, 1H, J = 1.2, 8.7 Hz, C5-H), 7.50 (m, 2H, C6 and C7-H), 7.43 (m, 5H, C_6H_5), 7.21 (s, 1H, C4-H), 6.73 (s, 1H, C2-H), 5.23 (s, 2H, CH_2Ph), 4.46 (dtd, 1H, J = 1.9, 7.8, 24.2 Hz, C2′-H), 4.49 (dd, 1H, J = 1.7, 1.7, C1′-H), 4.27 (dd, 1H, J = 1.7, 1.7, C1′-H), 1.43 (s, 9H, $C(CH_3)_3$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 160.0, 157.1, 154.8, 154.4, 154.2, 139.8, 136.8, 134.2, 128.6, 128.0, 127.5, 127.4, 126.9, 125.3, 124.4, 122.1, 117.1, 105.7, 80.8, 76.0 (dd, J = 86.8, 87.2 Hz), 70.3, 43.7 (d, J = 28.0 Hz), 28.2 (3C); ^{19}F NMR ($CDCl_3$, 376 MHz) δ –87.6 (d, J = 44.0 Hz),

–89.0 (dd, J = 24.2, 44.0 Hz); IR (film) ν_{max} 1746, 1703, 1581 cm^{-1}; FABHRMS (NBA–NaI) *m/z* 425.1815 (M^+, $C_{25}H_{25}F_2NO_3$ requires 425.1803).

Anal. Calcd for $C_{25}H_{25}F_2NO_3$: C, 70.57; H, 5.92; N, 3.29. Found: C, 70.82; H, 5.88; N, 3.05.

3-[*N*-(3,3-Difluoro-2-propen-1-yl)]amino-1-benzyloxynapthalene (10). A solution of **9** (700 mg, 1.64 mmol) in EtSH (4.0 mL) under Ar was treated with BF_3•Et_2O (305 μL, 2.45 mmol) and the resulting solution was stirred at 25 °C for 1 h before being quenched by the addition of H_2O (5 mL). The aqueous layer was extracted with Et_2O (3 × 5 mL) and the combined organic solutions were washed with saturated aqueous NaCl (15 mL), dried ($MgSO_4$), filtered and concentrated under reduced pressure. Chromatography (SiO_2, 5% EtOAc–hexane) gave **10** (480 mg, 530 mg theoretical, 91%) as a rust colored viscous oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.13 (dd, 1H, J = 0.5, 8.4 Hz, C8-H), 7.56 (d, 1H, J = 8.2 Hz, C5-H), 7.50 (m, 2H, C6 and C7-H), 7.38 (m, 5H, C_6H_5), 7.19 (ddd, 1H, J = 1.2, 4.9, 7.6 Hz, NH), 6.46 (d, 1H, J = 1.8 Hz, C4-H), 6.28 (d, 1H, J = 1.9 Hz, C2-H), 5.18 (br s, 2H, CH_2Ph), 4.47 (dtd, 1H, J = 2.0, 7.7, 24.7 Hz, C2′-H), 3.86 (dd, 1H, J = 1.8, 1.8 Hz, C1′-H), 3.84 (dd, 1H, J = 1.8, 1.8 Hz, C1′-H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 159.7, 156.8, 155.2, 153.9, 145.2, 136.8, 135.8, 128.3, 127.8, 127.1, 126.9, 125.6, 121.9, 121.4, 120.4, 97.8, 97.5, 76.7 (t, J = 78.0 Hz), 69.6, 36.6 (d, J = 24.0 Hz); ^{19}F NMR ($CDCl_3$, 376 MHz) δ –87.2 (d, J = 44.0 Hz), –88.9 (dd, J = 24.7, 44.0 Hz); IR (film) ν_{max} 3406, 2922, 2852, 1741, 1629 cm^{-1}; FABHRMS (NBA) *m/z* 325.1268 (M^+, $C_{20}H_{17}F_2NO$ requires 325.1278).

3-[*N*-(3,3-Difluoro-2-propen-1-yl)acetamido]-1-benzyloxynaphthalene (11). A solution of **10** (149 mg, 0.46 mmol) in dioxane (5 mL) under Ar was treated with DMAP (50 mg, 0.40 mmol), pyridine (0.37 mL, 4.6 mmol) and Ac_2O (0.2 mL, 2.3 mmol) and stirred at 25 °C for 19 h. The reaction solution was quenched by the addition of 10% aqueous HCl (10 mL) and EtOAc (10

mL). The aqueous layer was removed and extracted with EtOAc (3 × 5 mL). The organic solutions were combined, washed with saturated aqueous NaCl (15 mL), dried ($MgSO_4$), and concentrated under reduced pressure. Chromatography (SiO_2, 15% EtOAc–hexane) afforded **11** (162 mg, 169 mg theoretical, 96%) as a pale yellow oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.33 (dd, 1H, J = 1.6, 8.1 Hz, C8-H), 7.77 (dd, 1H, J = 1.7, 7.5 Hz, C5-H), 7.52 (m, 5H, C_6H_5), 7.38 (m, 2H, C6 and C7-H), 7.20 (d, 1H, J = 1.6 Hz, C4-H), 6.57 (d, 1H, J = 1.6 Hz, C2-H), 5.25 (s, 2H, CH_2Ph), 4.43 (dtd, 1H, J = 1.9, 7.9, 24.8 Hz, C2′-H), 4.32 (dd, 1H, J = 1.6, 1.6 Hz, C1′-H), 4.30 (m, 1H, C1′-H), 1.82 (s, 3H, CH_3CO); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.0, 160.0, 157.1, 155.1, 139.4, 135.9, 133.8, 128.2, 127.7, 127.2, 127.1, 126.9, 125.7, 124.7, 121.9, 118.6, 105.0, 74.9 (dd, J = 75.2, 91.6 Hz), 69.8, 41.8 (d, J = 28 Hz), 22.0; ^{19}F NMR ($CDCl_3$, 376 MHz) δ –87.0 (d, J = 40.0 Hz), –89.1 (dd, J = 24.8, 40.0 Hz); IR (film) ν_{max} 2928, 1745, 1660, 1413 cm^{-1}; FABHRMS (NBA–NaI) *m/z* 368.1740 (M + H$^+$, $C_{22}H_{19}F_2NO$ requires 368.1470).

2-[*N*-(3,3-Difluoro-2-propen-1-yl)acetamido]-4-benzyloxy-1-nitronaphthalene (12). A mixture of **11** (581 mg, 1.58 mmol) and Bu_4NNO_3 (1.20 g, 3.90 mmol) in CH_2Cl_2 (20 mL) under Ar was treated with TFAA (0.25 mL). After stirring at 25 °C for 16 h, additional TFAA (10 μL) was added and the reaction mixture was stirred at 25 °C for an additional 4 h. The solution was quenched by the addition of saturated aqueous $NaHCO_3$ (20 mL) and $CHCl_3$ (10 mL). The organic layer was removed and the aqueous layer extracted with $CHCl_3$ (3 × 15 mL). The combined organic solutions were dried ($MgSO_4$), filtered and concentrated under pressure. Chromatography (SiO_2, 10% EtOAc–hexane) gave **12** (457 mg, 652 mg theoretical, 70%) as a yellow oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.42 (d, 1H, J = 8.0 Hz, C8-H), 7.79 (d, 1H, J = 8.2 Hz, C5-H), 7.71 (dt, 1H, J = 1.3, 6.9 Hz, C6 or C7-H), 7.65 (dt, 1H, J = 1.3, 6.9 Hz, C7 or C6-H), 7.42 (m, 5H, C_6H_5), 6.55 (s, 1H, C3-H),

5.32 (d, 1H, J = 16.7 Hz, C*H*HPh), 5.29 (d, 1H, J = 16.7 Hz, CH*H*Ph), 4.43 (m, 2H, C1′-H), 4.05 (m, 1H, C2′-H), 1.83 (s, 3H, CH_3CO); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.0, 160.4, 157.5, 156.8, 154.6, 140.0, 135.0, 132.4, 129.8, 128.7, 128.4, 127.6, 127.1, 125.7, 125.2, 122.6, 121.9, 105.0, 74.5 (dd, J = 72.4, 93.6 Hz), 70.9, 42.1 (d, J = 29.6 Hz), 22.0; ^{19}F NMR ($CDCl_3$, 376 MHz) δ –85.6 (d, J = 36.0 Hz), –88.5 (dd, J = 28.0, 36.0 Hz); IR (film) ν_{max} 2928, 1746, 1674, 1525 cm^{-1}; FABHRMS (NBA) *m/z* 413.1319 ($M + H^+$, $C_{22}H_{18}F_2N_2O_4$ requires 413.1313). The regiochemistry of the nitration was confirmed by ^1H NMR employing 1D-NOE, 2D-NOE and HMBC experiments. Carbon-carbon connectivity from the HMBC study showed connectivity of the NO_2 bearing carbon (δ 157.5) to the C2 (δ 132.6) and the C8a carbon (δ 125.8). This was further supported by ^1H NMR NOE experiments where irradiation of the C3-H resonance (δ 6.55) resulted in a 5% enhancement of the OCH_2Ph resonance at δ 5.30 and a 4% enhancement of the CH_3CO resonance at δ 1.83. Similarly, the 2D-NOE experiment showed diagnostic crosspeaks of C3-H with OCH_2Ph and CH_3CO.

Occasionally, the isomeric nitration product, 3-[*N*-(3,3-difluoro-2-propen-2-yl)acetamido]-1-benzyloxy-2-nitronaphthalene (*ca.* 10%), could be isolated: ^1H NMR ($CDCl_3$, 400 MHz) δ 8.21 (dd, 1H, J = 2.3, 7.8 Hz, C8-H), 7.91 (dd, 1H, J = 2.1, 6.8 Hz, C5-H), 7.70 (m, 2H, C6 and C7-H), 7.53 (s, 1H, C4-H), 5.03 (m, 5H, C_6H_5), 5.28 (d, 1H, J = 13.9 Hz, C*H*HPh), 5.25 (d, 1H, J = 13.9 Hz, CH*H*Ph), 4.55 (m, 2H, C2′-H and C1′-H), 3.94 (m, 1H, C2′-H), 1.91 (s, 3H, CH_3CO); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.6, 160.8, 157.9, 155.0, 148.4, 140.7, 135.4, 133.9, 131.1, 129.6, 129.0, 128.9, 128.8, 128.7, 128.6, 128.3, 125.6, 123.6, 78.8, 74.6 (dd, J = 92.8, 93.2 Hz), 42.4 (d, J = 30.0 Hz), 22.4; ^{19}F NMR ($CDCl_3$, 376 MHz) δ –85.9 (d, J = 40.0 Hz), –88.8 (dd, J = 28.0, 40.0 Hz); IR (film) ν_{max} 3066, 2888, 1746, 1681, 1538 cm^{-1}; FABHRMS (NBA–NaI) *m/z* 413.1357 ($M + H^+$,

$C_{22}H_{18}F_2N_2O_4$ requires 413.1313).

For 3-[*N*-(*tert*-butyloxycarbonyl)-*N*-(3,3-difluoro-2-methanesulfonyloxy-1-propyl)]amino-1-benzyloxynaphthalene: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.27 (dd, 1H, *J* = 1.3, 7.6 Hz, C8-H), 7.75 (dd, 1H, *J* = 1.4, 7.5 Hz, C5-H), 7.45 (m, 7H), 7.25 (d, 1H, *J* = 1.3 Hz, C4-H), 6.84 (d, 1H, *J* = 1.5 Hz, C2-H), 5.87 (dt, 1H, *J* = 2.9, 54.1 Hz, CF_2H), 5.25 (s, 2H, OCH_2Ph), 5.18 (m, 1H, C2′-H), 4.15 (dd, 1H, *J* = 14.9, 14.9 Hz, C1′-H), 3.97 (dd, 1H, *J* = 14.9, 14.9 Hz, C1′-H), 2.99 (s, 3H, CH_3SO_2), 1.39 (s, 9H, $C(CH_3)_3$); IR (film) ν_{max} 3418, 2962, 1703, 1581, 1260 cm^{-1}; FABHRMS (NBA–NaI) *m/z* (M^+, $C_{26}H_{29}F_2NO_6S$ requires 521.1684).

For 3-[*N-tert*-butyloxycarbonyl)-*N*-(3,3-difluoro-3-phenylsulfonyl-2-tosyloxy-1-propyl)]amino-1-benzyloxynaphthalene: ^{1}H NMR ($CDCl_3$, 250 MHz) δ 8.23 (d, 1H, *J* = 7.5 Hz, C8-H), 7.76 (d, 1H, *J* = 7.6 Hz, C5-H), 7.60–7.68 (m, 6H), 7.28–7.47 (m, 10H), 7.12 (br s, 1H, C4-H), 6.97 (br s, 1H, C2-H), 5.76 (m, 1H, C2′-H), 5.18 (s, 2H, CH_2Ph), 4.52 (m, 1H, C1-H), 4.13 (m, 1H, C1′-H), 2.53 (s, 3H, CH_3), 1.45 (s, 9H, $C(CH_3)_3$).

For 3[*N*-(*tert*)-butyloxycarbonyl)-*N*-(3,3-difluoro-2-hydroxy-1-propyl)]amino-1-benzyloxynaphthalene: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.30 (dd, 1H, *J* = 2.0, 7.6 Hz, C8-H), 7.74 (dd, 1H, *J* = 2.0, 7.4 Hz, C5-H), 7.51 (m, 2H, C6 and C7-H), 7.40 (m, 6H), 6.70 (s, 1H, C2-H), 5.70 (dt, 1H, *J* = 3.3, 55.4 Hz, CF_2H), 5.24 (s, 2H, OCH_2Ph), 5.11 (br s, 1H, OH), 4.11 (m, 1H, C2′-H), 3.98 (m, 1H, C1′-H), 3.74 (d, 1H, *J* = 15.0 Hz, C1′-H), 1.37 (s, 9H, $C(CH_3)_3$); IR (film) ν_{max} 3430, 2924, 1693, 1367 cm^{-1}; FABHRMS (NBA–NaI) *m/z* 443.1895 (M^+, $C_{25}H_{27}F_2NO_4$ requires 443.1980).

For 3-(5-difluoromethyl-oxazolidinon-3-yl)-1-benzyloxynaphthalene: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.26 (d, 1H, *J* = 8.2 Hz, C8-H), 7.76 (d, 1H, *J* = 2.0 Hz, C4-H), 7.71 (d, 1H, *J* = 8.0 Hz, C5-

H), 7.33–7.56 (m, 7H), 7.05 (d, 1H, J = 1.9 Hz, C2-H), 5.28 (s, 2H, CH_2Ph), 4.82 (m, 1H, C5′-H), 4.23 (m, 2H, C4′-H); IR (film) ν_{max} 2924, 1764, 1417 cm^{-1}; FABHRMS (NBA–NaI) *m/z* 369.1104 (M^+, $C_{21}H_{17}F_2NO_3$ requires 369.1176).

For **20a**: ^1H NMR ($CDCl_3$, 400 MHz) δ 8.58 (d, 1H, J = 8.2 Hz, C9-H), 8.00 (d, 1H, J = 8.4 Hz, C6-H), 7.64 (dt, 1H, J = 1.1, 7.6 Hz, C7-H), 7.52 (dt, 1H, J = 1.2, 7.6 Hz, C8-H), 7.37 (s, 1H, C4-H), 4.78 (dd, 1H, J = 1.7, 7.6 Hz, C1′-H), 4.77 (dd, 1H, J = 1.7, 7.6 Hz, C1′-H), 4.51 (dtd, 1H, J = 1.2, 7.4, 24.0 Hz, C2′-H), 4.38 (q, 2H, J = 7.2 Hz, CH_2CH_3), 2.69 (s, 3H, CH_3), 1.44 (t, 3H, J = 7.2 Hz, CH_2CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 160.3, 157.4, 154.5, 154.1, 136.0, 129.2, 127.2, 126.8, 125.0, 123.5, 121.9, 121.7, 102.3, 75.1 (dd, J = 24.2, 24.2 Hz), 65.1, 37.2 (d, J = 7.1 Hz), 14.3, 13.8; ^{19}F NMR ($CDCl_3$, 376 MHz) δ –85.1 (d, J = 36.0 Hz), –86.1 (dd, J = 24.0, 36.0 Hz); IR (film) ν_{max} 2929, 1748, 1233 cm^{-1}; FABHRMS (NBA–NaI) *m/z* 347.1198 ($M + H^+$, $C_{18}H_{16}F_2N_2O_3$ requires 347.1207).

For **20b**: ^1H NMR ($CDCl_3$, 400 MHz) δ 8.59 (d, 1H, J = 8.2 Hz, C9-H), 7.97 (d, 1H, J = 8.3 Hz, C6-H), 7.63 (t, 1H, J = 7.0 Hz, C7-H), 7.51 (t, 1H, J = 7.3 Hz, C8-H), 7.34 (s, 1H, C4-H), 4.80 (m, 2H, C1′-H_2), 4.52 (m, 1H, C2′-H), 2.65 (s, 3H, CH_3), 1.56 (s, 9H, $C(CH_3)_3$).

For **21**: ^1H NMR ($CDCl_3$, 400 MHz) δ 8.19 (dd, 1H, J = 2.2, 7.0 Hz, C8-H), 7.71–7.81 (m, 3H), 7.27 (s, 1H, C3-H), 4.53 (m, 2H, C1′-H and C2′-H), 4.05 (m, 1H, C1′-H), 1.92 (s, 3H, CH_3CO), 1.61 (s, 9H, $C(CH_3)_3$).

For 1-amino-4-[(*tert*-butyloxycarbonyl)oxy]-2-[*N*-(3,3-difluoro-2-propen-1-yl)acetamido]naphthalene (**22**): ^1H NMR ($CDCl_3$, 400 MHz) δ 7.96 (dd, 1H, J = 1.8, 6.5 Hz, C5-H), 7.83 (dd, 1H, J = 2.0, 6.6 Hz, C8-H), 7.57 (m, 2H, C6 and C7-H), 6.98 (s, 1H, C3-H), 4.48 (m, 2H, C1′-H and C2′-H), 4.15 (m, 1H, C1′-H), 4.31 (br s, 2H, NH_2), 1.89 (s, 3H, CH_3CO), 1.57 (s, 9H,

$C(CH_3)_3$); ^{19}F NMR ($CDCl_3$, 376 MHz) δ –86.2 (d, J = 40.0 Hz), –88.2 (dd, J = 24.0, 40.0 Hz); IR (film) ν_{max} 3360, 1747, 1250 cm^{-1}; FABHRMS (NBA–NaI) *m/z* 415.1445 ($M + Na^+$, $C_{20}H_{22}F_2N_2O_4$ requires 415.1455).

DNA Alkylation Studies: Selectivity and Efficiency. Eppendorf tubes containing singly ^{32}P 5′-end-labeled w794 DNA[58] (9 μL) in TE buffer (10 mM Tris, 1 mM EDTA, pH 7.5) were treated with agents in DMSO (1 μL, at the specified concentrations). The solutions were mixed by vortexing and brief centrifugation and subsequently incubated at 25 or 4 °C for 72 h. The modified DNA was separated from unbound agent by EtOH precipitation of the DNA. The EtOH precipitations were carried out by adding *t*-RNA as a carrier (1 μL, 10 μg/μL), 3 M NaOAc (0.1 volume) and –20 °C EtOH (2.5 volumes). The solutions were mixed and chilled at –78 °C in a REVCO freezer for 1 h or longer. The DNA was reduced to a pellet by centrifugation at 4 °C for 15 min and washed with –20 °C 70% EtOH in TE buffer containing 0.2 M NaCl. The pellets were dried on a Savant Speed Vac concentrator and resuspended in TE buffer (10 μL). The solutions of alkylated DNA were warmed at 100 °C for 30 min to induce cleavage at the adenine N3 alkylation sites. After brief centrifugation, formamide dye solution (5 μL) was added. Prior to electrophoresis, the samples were denatured by warming at 100 °C for 5 min, placed in an ice bath, centrifuged briefly, and the supernatant (2.8 μL) was loaded onto a gel. Sanger dideoxynucleotide sequencing reactions were run as standards adjacent to the agent treated DNA reaction samples. Polyacrylamide gel electrophoresis (PAGE) was run on an 8% sequencing gel under denaturing conditions (19:1 acrylamide: *N,N′*-methylenebisacrylamide, 8 M urea) in TBE buffer (100 mM Tris, 100 mM boric acid, 0.2 mM Na_2EDTA). PAGE was pre-run for 30 min with formamide dye solution prior to loading the samples. Autoradiography of dried gels were carried out at –78 °C using Kodak X-Omat

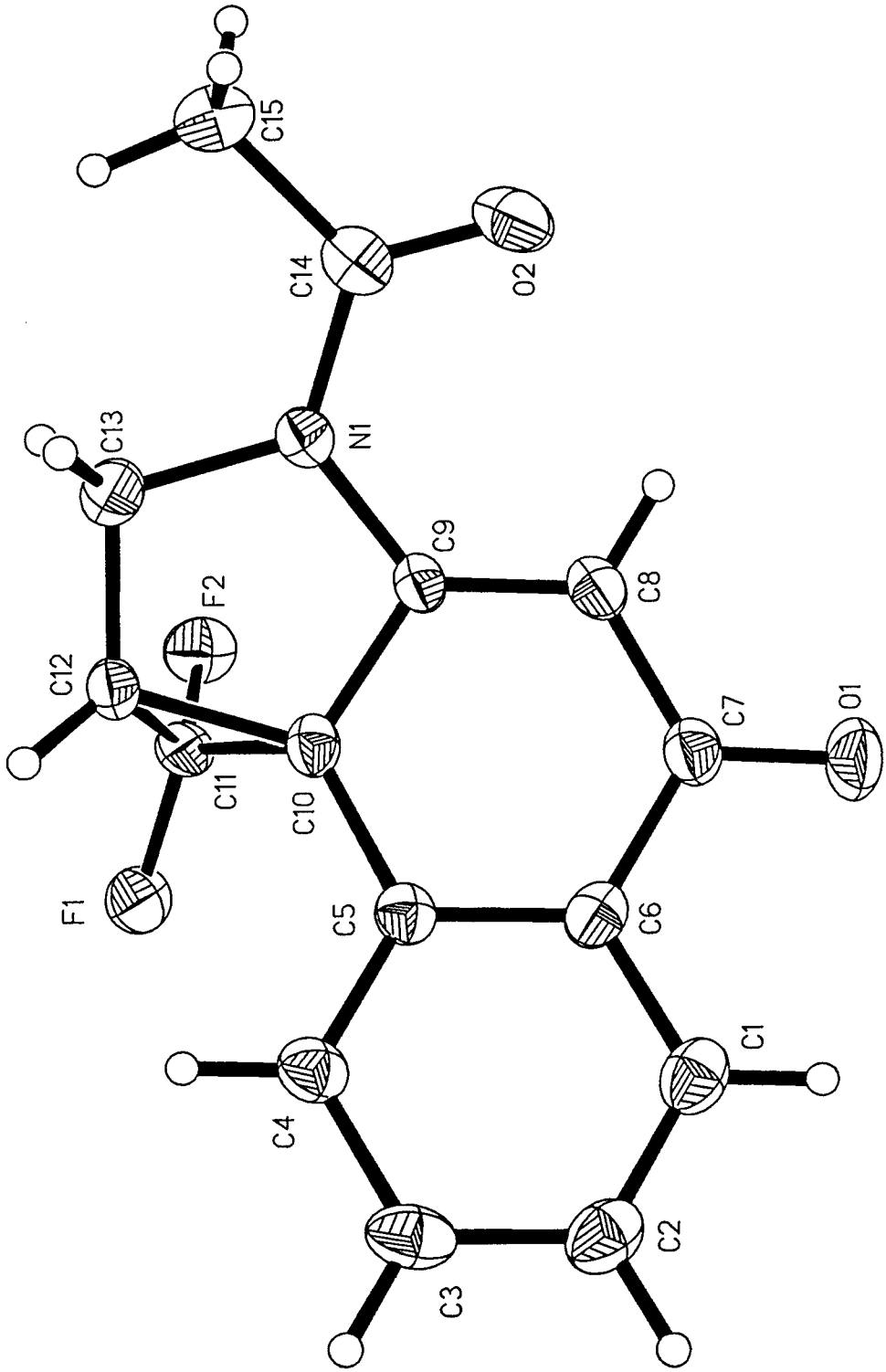
AR film and a Picker Spectra™ intensifying screen.

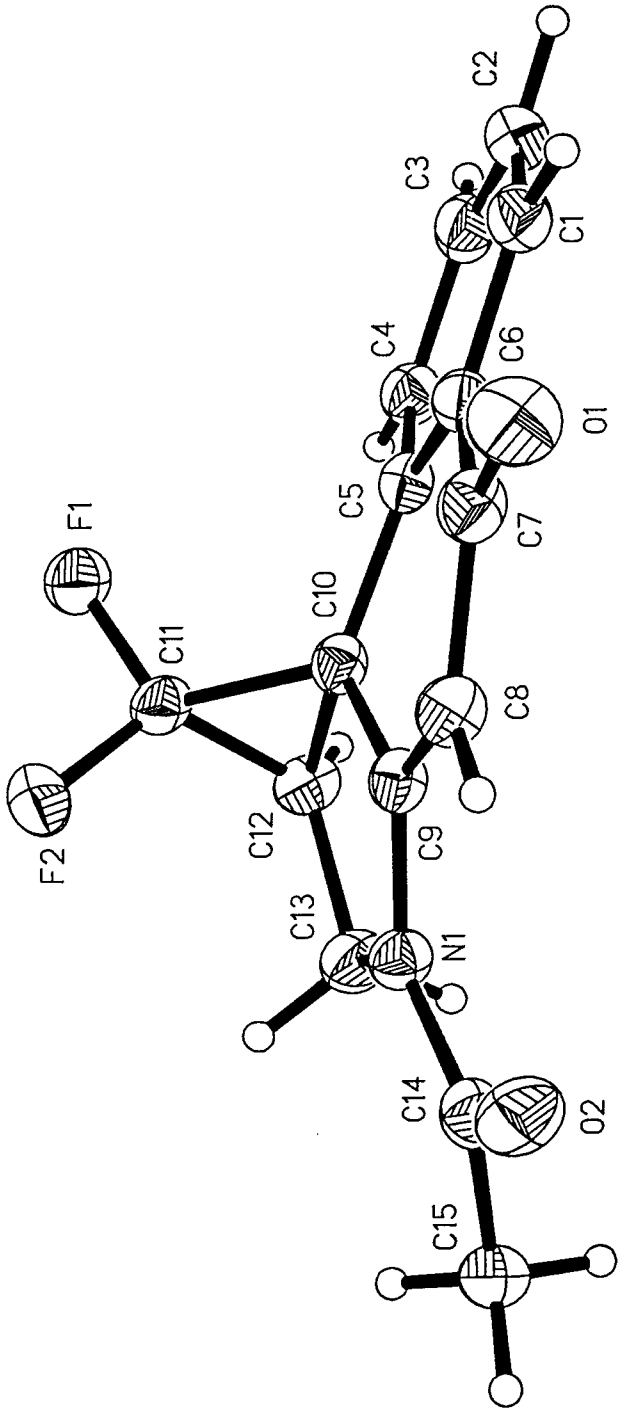
Table 1. In vitro cytotoxic activity of BOC derivatives.

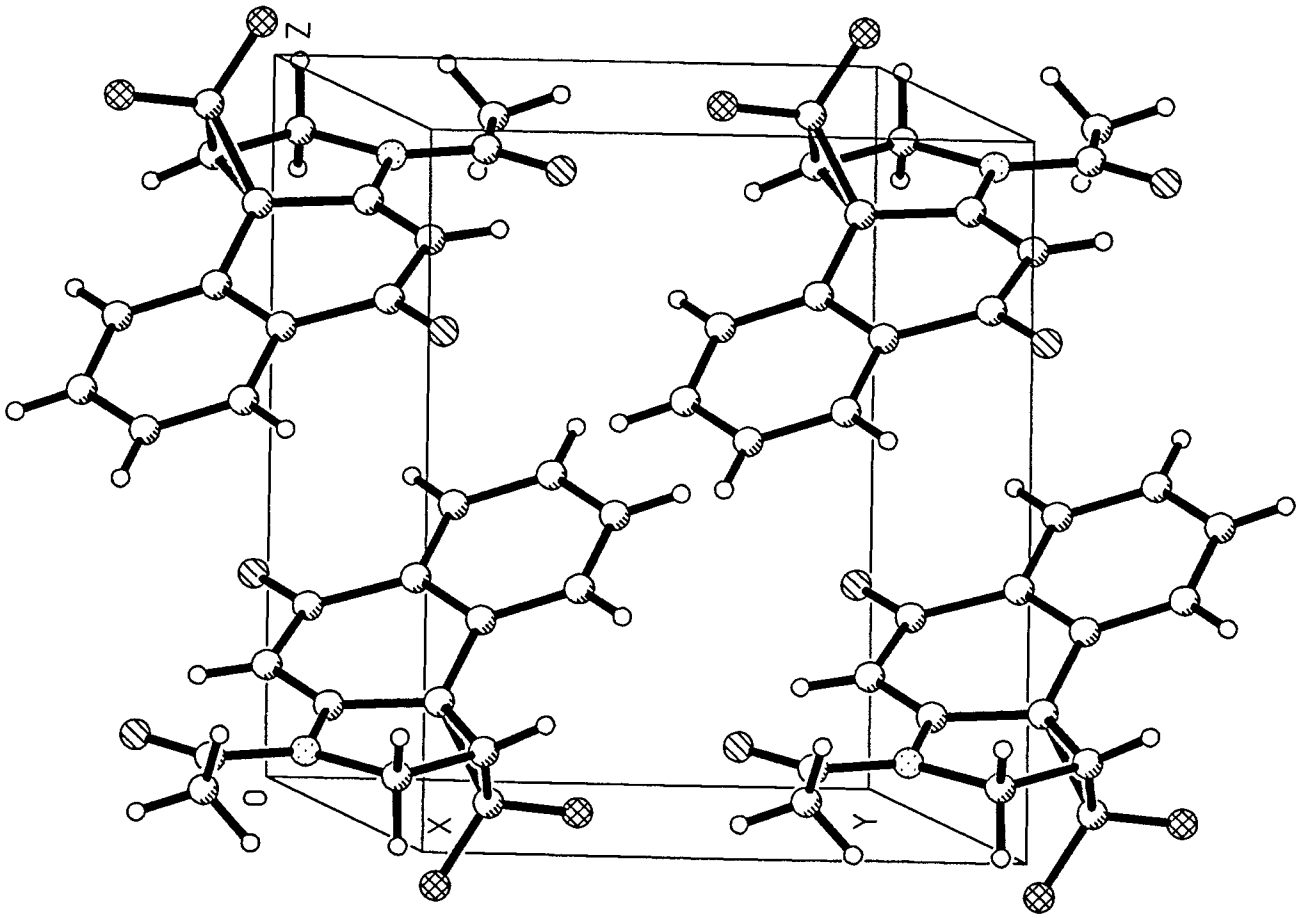
Agent	Configuration	IC_{50} (μM, L1210)
(+)-*N*-BOC-DSA	natural	0.006
(+)-*N*-BOC-CCBI	natural	0.02
(+)-*N*-BOC-CBI	natural	0.08
(+)-*N*-BOC-MCBI	natural	0.09
(+)-*N*-BOC-CPI	natural	0.3
(±)-*N*-BOC-DA	racemic	1
(–)-*N*-BOC-CBQ	natural	2
(+)-*N*-BOC-CI	natural	18
(±)-N-BOC-F_2CBI	racemic	110

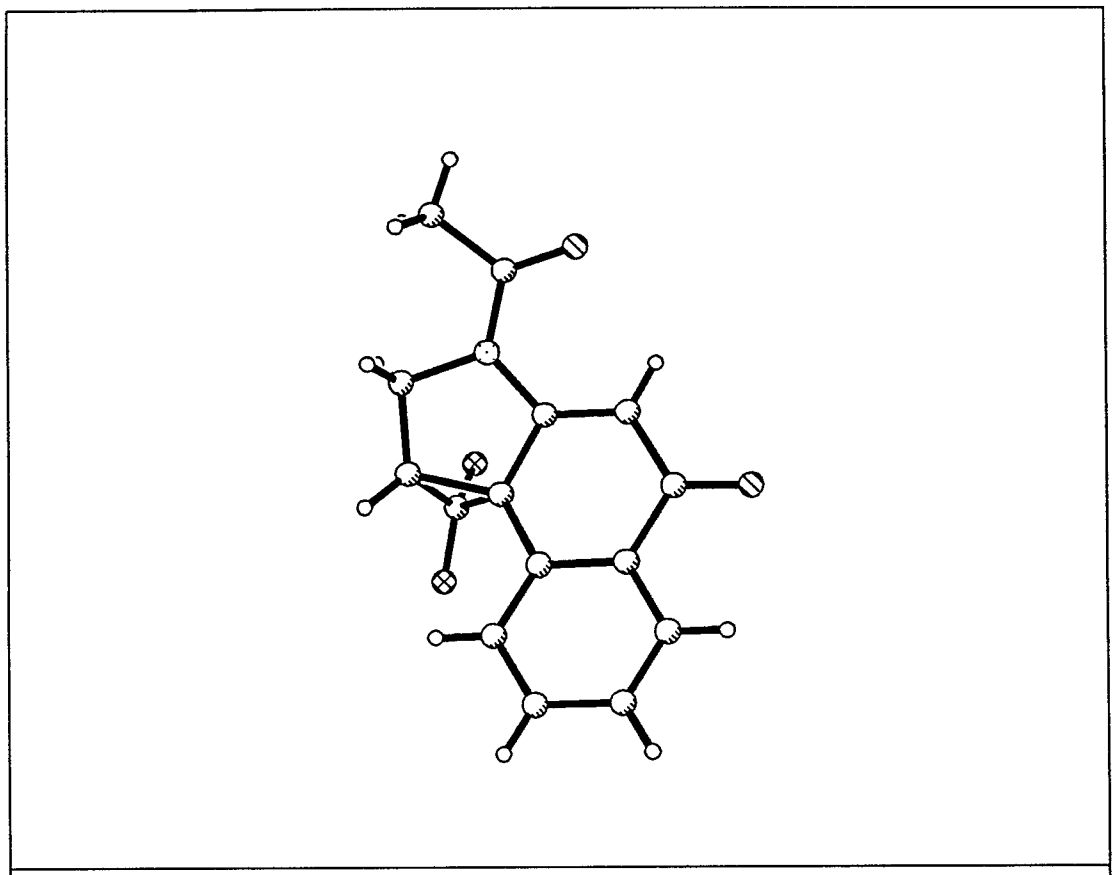
Table 2. In vitro cytotoxic activity of TMI (trimethyloxyindole) derivatives.

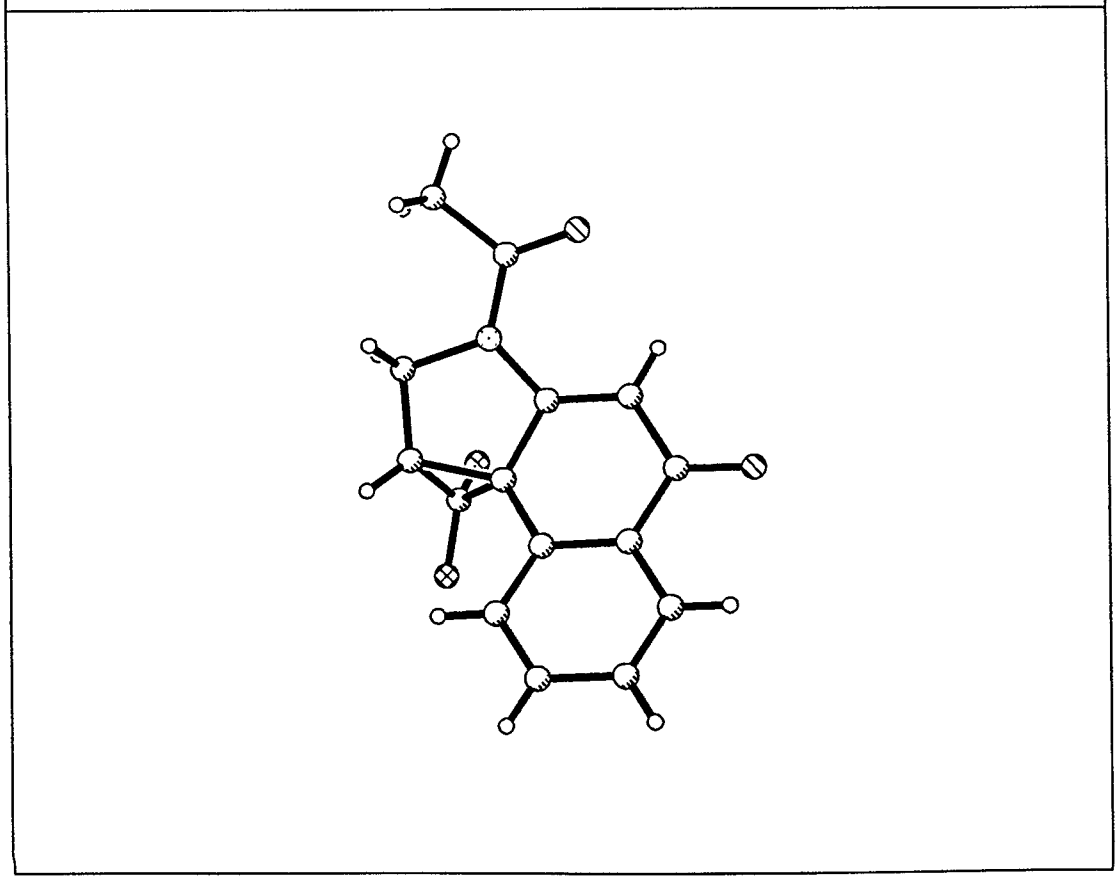
Agent	Configuration	IC_{50} (pM, L1210)
(+)-duocarmycin SA	natural	10
(+)-CCBI-TMI	natural	7
(+)-CBI-TMI	natural	30
(+)-MCBI-TMI	natural	8
(+)-duocarmycin A	natural	500
(–)-CBQ-TMI	natural	4000
(+)-CI-TMI	natural	26000
(±)-F_2CBI-TMI	racemic	36000


C15
C14
O2
N1
C13
C9
C8
F2
C12
C7
O1
C11
C10
F1
C5
C6
C1
C4
C2
C3


C2
C3
C1
C4
C6
O1
C5
C7
F1
C10
C11
C8
F2
C12
C9
C13
N1
C14
O2
C15


Z
O
X
Y





Experimental

A yellow-brown, plate like crystal was sealed in a capillary before mounting and data were collected with a Rigaku AFC6R diffractometer equipped with a copper rotating anode and a highly oriented graphite monochromator. A constant scan speed of 4°/min in ω was used and the weak reflections [$I<5\sigma(I)$] were rescanned to a maximum of 8 times and the counts accumulated to assure good counting statistics. The intensities of three monitor reflections measured after every 200 reflections did not change significantly during 76 hrs of X-ray exposure. Unit cell dimensions and standard deviations were obtained by least squares fit to 25 reflections ($50<2\theta<80^{\circ}$). The data were corrected for Lorentz and polarization effects and not for absorption because of low value of μ. See Table 1 for cell parameters and other relevant data.

There were no systematic absences in the data. Therefore space group $P\bar{1}$ was assumed and later confirmed by successful refinement of the structure. The structure was solved by direct methods using SHELXS86. All non-hydrogen atoms were refined anisotropically by the full matrix least-squares method. The function minimized was $\sum w(\|Fo\|-\|Fc\|)^2$. Hydrogen atoms were included in the ideal positions with a fixed isotropic U values of 0.08Å^2. A weighting scheme of the form $w=1/[\sigma^2(Fo^2)+(aP)^2)+bP]$ with a=0.0926 and b=0.18 was used. (P is defined as $Max(Fo^2)+2Fc^2)/3$). An extinction correction was also applied to the data. The refinement converged to the R indices given in the Table 1 which also includes the largest difference peak and the hole in the last cycles of refinement. The final difference map was devoid of significant features.

All calculations were done on a Silicon graphics Personal Iris 4D/35 and an IBM compatible PC using programs TEXSAN (data reduction), SHELXS86 (structure solution), SHELXL-93 (refinement) and SHELXTL-PC (plotting). Final atomic coordinates are listed in Table 2 and bond lengths and bond angles in Table 3.

References

TEXSAN. Structure Analysis Package. Molecular Structure Corporation. The Woodlands, TX 77381. 1992.

SHELXL-93. G.M.Sheldrick, J Appl. Cryst., (1993) in preparation.

Table 1. Crystal data and structure refinement for "BOGF".

Empirical formula	$C_{15}H_{11}F_2NO_2$
Formula weight	275.25
Temperature	296(2) K
Wavelength	1.54178 Å
Crystal system	Triclinic
Space group	$P\bar{1}$
Unit cell dimensions	a = 7.987(1) Å α = 89.25(1)° b = 8.007(1) Å β = 78.82(1)° c = 10.368(1) Å γ = 71.32(1)°
Volume	615.1(1) Å^3
Z and F(000)	2 and 284
Density (calculated)	1.486 Mg/m^3
Absorption coefficient	1.018 mm^{-1}
Crystal size	0.50x0.42 x 0.16 mm
θ range for data collection	4.35 to 60.09°
Scan Type	2θ-θ
Scan width	1.890+0.140tanθ
Scan time/ background time	2:1
Index ranges	$-8 \le h \le 8$, $0 \le k \le 9$, $-11 \le \ell \le 11$
Reflections collected	2025
Independent reflections	1828 (R_{int} = 0.0230)
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	1817 / 0 / 183
Goodness-of-fit on F^2, (S)	1.031
Final R indices [I>2σ(I)]	R1 = 0.0454, wR2 = 0.1354
R indices (all data)	R1 = 0.0567, wR2 = 0.1850
Extinction coefficient	0.005(2)
Largest diff. peak and hole	0.172 and -0.194 eÅ^{-3}

$R1=(\Sigma \| \|F_o\| - \|F_c\| \| / \Sigma |F_o|)$, $wR2=\Sigma w(F_o^2-F_c^2)^2/\Sigma w[(F_o^2)^2]^{\frac{1}{2}}$, $S=[\Sigma w(F_o^2-F_c^2)^2/(n-p)]^{\frac{1}{2}}$

Table 2. Atomic coordinates [x 10^4] and equivalent isotropic displacement parameters [$Å^2$ x 10^3] for "BOGF".

U(eq) is defined as

$$U_{eq}=1/3\sum_i\sum_j U_{ij}a_i^*a_j^*a_i\bullet a_j$$

	x	y	z	U(eq)
F(1)	1098(2)	2276(2)	700(1)	77(1)
F(2)	2221(2)	-369(2)	-241(1)	80(1)
O(1)	-2577(2)	-2176(3)	3534(2)	87(1)
O(2)	3617(3)	-5732(2)	1896(2)	87(1)
N(1)	3635(2)	-2912(2)	1717(2)	61(1)
C(1)	-3047(3)	1260(4)	4494(2)	76(1)
C(2)	-3212(4)	2924(4)	4922(2)	81(1)
C(3)	-1838(4)	3610(3)	4508(2)	77(1)
C(4)	-303(3)	2635(3)	3639(2)	67(1)
C(5)	-125(3)	956(3)	3185(2)	56(1)
C(6)	-1509(3)	242(3)	3623(2)	60(1)
C(7)	-1300(3)	-1597(3)	3222(2)	65(1)
C(8)	448(3)	-2739(3)	2561(2)	63(1)
C(9)	1795(3)	-2063(3)	2161(2)	56(1)
C(10)	1438(3)	-127(3)	2205(2)	55(1)
C(11)	1959(3)	583(3)	889(2)	62(1)
C(12)	3290(3)	149(3)	1726(2)	65(1)
C(13)	4672(3)	-1660(3)	1497(3)	69(1)
C(14)	4488(3)	-4722(3)	1701(2)	67(1)
C(15)	6499(3)	-5334(4)	1444(3)	78(1)

Table 3. Bond lengths [Å] and angles [°] for "BOGF".

F(1)-C(11)	1.341(2)	F(2)-C(11)	1.350(3)
O(1)-C(7)	1.238(3)	O(2)-C(14)	1.217(3)
N(1)-C(14)	1.388(3)	N(1)-C(9)	1.393(3)
N(1)-C(13)	1.482(3)	C(1)-C(2)	1.367(4)
C(1)-C(6)	1.392(3)	C(2)-C(3)	1.375(4)
C(3)-C(4)	1.379(3)	C(4)-C(5)	1.385(3)
C(5)-C(6)	1.399(3)	C(5)-C(10)	1.477(3)
C(6)-C(7)	1.483(3)	C(7)-C(8)	1.443(3)
C(8)-C(9)	1.348(3)	C(9)-C(10)	1.483(3)
C(10)-C(11)	1.507(3)	C(10)-C(12)	1.551(3)
C(11)-C(12)	1.456(3)	C(12)-C(13)	1.502(3)
C(14)-C(15)	1.491(3)		

C(14)-N(1)-C(9)	124.9(2)	C(14)-N(1)-C(13)	121.6(2)
C(9)-N(1)-C(13)	112.5(2)	C(2)-C(1)-C(6)	121.1(2)
C(1)-C(2)-C(3)	120.1(2)	C(2)-C(3)-C(4)	120.0(2)
C(3)-C(4)-C(5)	120.5(2)	C(4)-C(5)-C(6)	119.6(2)
C(4)-C(5)-C(10)	123.4(2)	C(6)-C(5)-C(10)	117.0(2)
C(1)-C(6)-C(5)	118.7(2)	C(1)-C(6)-C(7)	120.6(2)
C(5)-C(6)-C(7)	120.6(2)	O(1)-C(7)-C(8)	120.5(2)
O(1)-C(7)-C(6)	120.2(2)	C(8)-C(7)-C(6)	119.1(2)
C(9)-C(8)-C(7)	119.6(2)	C(8)-C(9)-N(1)	130.1(2)
C(8)-C(9)-C(10)	120.8(2)	N(1)-C(9)-C(10)	109.0(2)
C(5)-C(10)-C(9)	117.2(2)	C(5)-C(10)-C(11)	120.2(2)
C(9)-C(10)-C(11)	113.9(2)	C(5)-C(10)-C(12)	128.6(2)
C(9)-C(10)-C(12)	106.2(2)	C(11)-C(10)-C(12)	56.84(14)
F(1)-C(11)-F(2)	108.0(2)	F(1)-C(11)-C(12)	119.9(2)
F(2)-C(11)-C(12)	121.3(2)	F(1)-C(11)-C(10)	118.0(2)
F(2)-C(11)-C(10)	120.9(2)	C(12)-C(11)-C(10)	63.11(14)
C(11)-C(12)-C(13)	116.6(2)	C(11)-C(12)-C(10)	60.05(14)
C(13)-C(12)-C(10)	106.4(2)	N(1)-C(13)-C(12)	105.6(2)
O(2)-C(14)-N(1)	120.9(2)	O(2)-C(14)-C(15)	122.7(2)
N(1)-C(14)-C(15)	116.4(2)		

Table 4. Anisotropic displacement parameters [$Å^2 \times 10^3$] for "BOGF".

The anisotropic displacement factor exponent takes the form:

$-2\pi^2(h^2a^{*2}U_{11}+k^2b^{*2}U_{22}+l^2c^{*2}U_{33}+2hka^*b^*U_{12}+2hla^*c^*U_{13}+2klb^*c^*U_{23})$

	U11	U22	U33	U23	U13	U12
F(1)	77(1)	67(1)	79(1)	26(1)	-10(1)	-18(1)
F(2)	87(1)	85(1)	57(1)	10(1)	-6(1)	-20(1)
O(1)	68(1)	100(1)	104(1)	17(1)	-12(1)	-45(1)
O(2)	90(1)	61(1)	108(2)	7(1)	-25(1)	-20(1)
N(1)	54(1)	61(1)	62(1)	10(1)	-10(1)	-14(1)
C(1)	55(1)	96(2)	67(2)	19(1)	-3(1)	-17(1)
C(2)	77(2)	84(2)	59(1)	5(1)	-3(1)	0(1)
C(3)	93(2)	67(2)	62(1)	3(1)	-19(1)	-10(1)
C(4)	72(1)	63(1)	63(1)	10(1)	-14(1)	-17(1)
C(5)	54(1)	60(1)	52(1)	12(1)	-13(1)	-14(1)
C(6)	53(1)	71(1)	55(1)	15(1)	-11(1)	-17(1)
C(7)	55(1)	81(2)	67(1)	22(1)	-18(1)	-30(1)
C(8)	65(1)	60(1)	69(1)	11(1)	-18(1)	-25(1)
C(9)	55(1)	60(1)	53(1)	12(1)	-14(1)	-19(1)
C(10)	48(1)	60(1)	56(1)	13(1)	-10(1)	-18(1)
C(11)	61(1)	61(1)	60(1)	14(1)	-6(1)	-17(1)
C(12)	55(1)	67(1)	72(1)	13(1)	-7(1)	-23(1)
C(13)	52(1)	75(2)	82(2)	16(1)	-12(1)	-22(1)
C(14)	73(2)	64(1)	56(1)	4(1)	-17(1)	-10(1)
C(15)	71(2)	75(2)	72(2)	-2(1)	-18(1)	-1(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$ x 10^3) for "BOGF".

	x	y	z	U(eq)
H(1A)	-3978(3)	802(4)	4789(2)	80
H(2A)	-4257(4)	3592(4)	5494(2)	80
H(3A)	-1943(4)	4733(3)	4814(2)	80
H(4A)	620(3)	3108(3)	3356(2)	80
H(8A)	643(3)	-3936(3)	2411(2)	80
H(12A)	3561(3)	1100(3)	2139(2)	80
H(13A)	5373(3)	-1821(3)	605(3)	80
H(13B)	5485(3)	-1834(3)	2108(3)	80
H(15A)	6952(3)	-4974(17)	598(7)	80
H(15B)	6944(3)	-6598(4)	1457(15)	80
H(15C)	6895(3)	-4825(16)	2113(9)	80

Selected torsion angles

-0.90	(0.38)	C6 - C1 - C2 - C3
1.26	(0.37)	C1 - C2 - C3 - C4
-0.51	(0.36)	C2 - C3 - C4 - C5
-0.61	(0.33)	C3 - C4 - C5 - C6
176.86	(0.20)	C3 - C4 - C5 - C10
-0.21	(0.34)	C2 - C1 - C6 - C5
176.58	(0.21)	C2 - C1 - C6 - C7
0.96	(0.31)	C4 - C5 - C6 - C1
-176.67	(0.19)	C10 - C5 - C6 - C1
-175.84	(0.19)	C4 - C5 - C6 - C7
6.54	(0.28)	C10 - C5 - C6 - C7
8.55	(0.33)	C1 - C6 - C7 - O1
-174.73	(0.20)	C5 - C6 - C7 - O1
-166.47	(0.20)	C1 - C6 - C7 - C8
10.26	(0.31)	C5 - C6 - C7 - C8
176.17	(0.20)	O1 - C7 - C8 - C9
-8.84	(0.32)	C6 - C7 - C8 - C9
167.74	(0.21)	C7 - C8 - C9 - N1
-9.44	(0.31)	C7 - C8 - C9 - C10
-5.51	(0.36)	C14 - N1 - C9 - C8
-174.41	(0.22)	C13 - N1 - C9 - C8
171.93	(0.19)	C14 - N1 - C9 - C10
3.03	(0.24)	C13 - N1 - C9 - C10
158.50	(0.19)	C4 - C5 - C10 - C9
-23.97	(0.26)	C6 - C5 - C10 - C9
-55.67	(0.29)	C4 - C5 - C10 - C11
121.86	(0.22)	C6 - C5 - C10 - C11
14.16	(0.33)	C4 - C5 - C10 - C12
-168.31	(0.19)	C6 - C5 - C10 - C12
26.30	(0.28)	C8 - C9 - C10 - C5
-151.42	(0.18)	N1 - C9 - C10 - C5
-121.63	(0.22)	C8 - C9 - C10 - C11
60.65	(0.22)	N1 - C9 - C10 - C11
177.98	(0.19)	C8 - C9 - C10 - C12
0.25	(0.22)	N1 - C9 - C10 - C12
7.45	(0.30)	C5 - C10 - C11 - F1
154.32	(0.19)	C9 - C10 - C11 - F1
-111.36	(0.24)	C12 - C10 - C11 - F1
-129.12	(0.22)	C5 - C10 - C11 - F2
17.74	(0.27)	C9 - C10 - C11 - F2
112.06	(0.23)	C12 - C10 - C11 - F2
118.81	(0.22)	C5 - C10 - C11 - C12
-94.32	(0.20)	C9 - C10 - C11 - C12
-157.25	(0.19)	F1 - C11 - C12 - C13
-17.04	(0.29)	F2 - C11 - C12 - C13
94.37	(0.20)	C10 - C11 - C12 - C13
108.38	(0.22)	F1 - C11 - C12 - C10
-111.41	(0.22)	F2 - C11 - C12 - C10
-104.36	(0.24)	C5 - C10 - C12 - C11
108.33	(0.19)	C9 - C10 - C12 - C11
0.00		C11 - C10 - C12 - C11
144.03	(0.22)	C5 - C10 - C12 - C13
-3.28	(0.23)	C9 - C10 - C12 - C13
-111.62	(0.22)	C11 - C10 - C12 - C13
-174.39	(0.19)	C14 - N1 - C13 - C12
-5.08	(0.25)	C9 - N1 - C13 - C12
-59.34	(0.25)	C11 - C12 - C13 - N1
4.90	(0.24)	C10 - C12 - C13 - N1
11.37	(0.34)	C9 - N1 - C14 - O2
179.30	(0.21)	C13 - N1 - C14 - O2
-168.20	(0.20)	C9 - N1 - C14 - C15
-0.26	(0.31)	C13 - N1 - C14 - C15

Least-squares planes (x,y,z in crystal coordinates) and deviations from them (indicates atom used to define plane)*

- 0.071 (0.017) x + 6.886 (0.008) y + 3.686 (0.021) z = 0.715 (0.006)

*	0.000 (0.000)	C10
*	0.000 (0.000)	C12
*	0.000 (0.000)	C11

Rms deviation of fitted atoms = 0.000

2.424 (0.009) x + 0.240 (0.008) y + 10.299 (0.002) z = 2.604 (0.002)

Angle to previous plane (with approximate esd) = 71.04 (0.14)

*	-0.024 (0.001)	N1
*	0.007 (0.001)	C9
*	0.012 (0.001)	C10
*	-0.026 (0.001)	C12
*	0.030 (0.001)	C13

Rms deviation of fitted atoms = 0.022

- 0.071 (0.017) x + 6.886 (0.008) y + 3.686 (0.021) z = 0.715 (0.006)

Angle to previous plane (with approximate esd) = 71.04 (0.14)

*	0.000 (0.000)	C10
*	0.000 (0.000)	C12
*	0.000 (0.000)	C11

Rms deviation of fitted atoms = 0.000

3.817 (0.006) x - 0.871 (0.007) y + 9.578 (0.004) z = 2.832 (0.001)

Angle to previous plane (with approximate esd) = 84.94 (0.13)

*	0.088 (0.001)	C5
*	0.041 (0.001)	C6
*	-0.102 (0.002)	C7
*	0.030 (0.002)	C8
*	0.103 (0.001)	C9
*	-0.160 (0.001)	C10

Rms deviation of fitted atoms = 0.097