SUPPORTING INFORMATION

Exploration of the nicotinamide-binding site of the tankyrases, identifying 3-aryliso-quinolin-1-ones as potent and selective inhibitors

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Section A: General synthetic methods

Chemical reagents, solvents and starting materials were purchased from Sigma Aldrich, Goss Scientific, Alfa Aesar and Fisher Scientific and were used without further purification. Proton and carbon magnetic resonance spectra were recorded at 400.04 MHz or 500.13 MHz for ^{1}H NMR, at 100.59 MHz or 125.76 MHz for ^{13}C NMR and at 376 MHz for ^{19}F NMR, using CD_3OD, $(CD_3)_2SO$ and $CDCl_3$, containing $SiMe_4$ as an internal standard. Reactions were monitored by thin-layer chromatography (TLC) on silica gel 60Å (particle size 40-63 µm). Most mass spectrometric data were obtained by means of electrospray ionisation using a microTOF instrument from Bruker Daltonics (Bremen, Germany) and calibrated using sodium formate solution. Melting points were obtained using a heated stage microscope (Reichert-Jung). Experiments were conducted at ambient temperature, unless otherwise noted. Solutions in organic solvents were dried with $MgSO_4$. Pd_2dba_3 refers to tris(dibenzyl-ideneacetone)dipalladium, SPhos refers to 2-dicyclohexylphosphino-2',6'-dimethoxybiphenyl, $(Ph_3P)_2PdCl_2$ refers to bis(triphenylphosphine)palladium(II) dichloride. The brine was saturated.

Section B: Experimental methods - chemical synthesis

5-Amino-3-(3-methoxyphenyl)isoquinolin-1-one hydrobromide (12e). Compound **31e** (31 mg, 110 μmol) was stirred with HBr in AcOH (33%, 1.1 mL) at 65°C for 5 h. Evaporation yielded **12e** (29 mg, 73%) as a pale buff solid: mp 202-205°C; ^{1}H NMR (CD_3OD) δ 3.89 (3 H, s, Me), 6.13 (1 H, s, N-H), 6.95 (1 H, s, 4-H), 7.10 (1 H, dt, *J* = 8.2, 0.6 Hz, Ph 4-H), 7.35 (2 H, m, Ph 2,6-H_2), 7.46 (1 H, t, *J* = 7.9 Hz, Ph 5-H), 7.61 (1 H, t, *J* = 7.9 Hz, 7-H), 7.83 (1 H, dd, *J* = 7.7, 1.0 Hz, 6-H), 8.42 (1 H, d, *J* = 8.1 Hz, 8-H); ^{13}C NMR (CD_3OD) (HSQC / HMBC) δ 56.14 (Me), 98.49 (4-C), 113.73 (Ph 2-C), 116.98 (Ph 4-C), 120.39 (Ph 6-C), 127.56 (8a-C), 127.66 (4a-C), 127.82 (7-C), 128.96 (6-C), 129.47 (8-C), 131.60 (Ph 5-C), 134.01 (5-C), 136.68 (Ph 1-C), 144.29 (3-C), 161.82 (Ph 3-C), 164.54 (1-C); MS *m/z* 267.1115 $(M + H)^+$ ($C_{16}H_{13}N_2O_2$ requires 267.1135).

5-Amino-3-(2-trifluoromethylphenyl)isoquinolin-1-one hydrobromide (12g). Compound **31g** (22.4 mg, 70 μmol) was stirred with HBr in AcOH (33%, 1.25 mL) at 65°C for 5 h. Evaporation yielded **12g** (25.2 mg, 94%) as a buff solid: mp >230°C; ^{1}H NMR (CD_3OD) δ 6.65 (1 H, s, 4-H), 7.69 (4 H, m, 7-H + Ph 4,5,6-H_3), 7.85 (1 H, d, *J* = 8.5 Hz, 6-H), 7.88 (1 H, d, *J* = 8.0 Hz, Ph 3-H), 8.45 (1 H, d, *J* = 8.0 Hz, 8-H); ^{13}C NMR ($CDCl_3$) (HSQC / HMBC) δ 100.84 (4-C), 125.24 (q, *J* = 271.3 Hz, CF_3), 127.40 (q, *J* = 5.3 Hz, Ph 1-C), 127.56 (q, *J* = 4.8 Hz, Ph 3-C), 128.21 (7-C), 128.94 (6-C), 129.36 (8-C), 131.44 (Ph 6-C), 130.10 (q, *J* = 30.6 Hz, Ph 2-C), 132.95 (5-C), 133.23 (Ph 4-C), 133.50 (Ph 5-C), 141.90 (3-C), 163.54 (1-C); ^{19}F NMR (CD_3OD) δ -59.36 (s, CF_3); MS *m/z* 305.0872 $(M + H)^+$ ($C_{16}H_{12}F_3N_2O$ requires 305.0904).

5-Amino-3-(3-trifluoromethylphenyl)isoquinolin-1-one hydrobromide (12h). Compound **31h** (70.5 mg, 220 μmol) was stirred with HBr in AcOH (33%, 3.75 mL) at 65°C for 7 h. Evaporation yielded **12h** (82.4 mg, 97%) as a buff solid: mp >230°C; ^{1}H NMR ($(CD_3)_2SO$) δ 7.05 (1 H, d, *J* = 7.7 Hz, 6-H), 7.16 (1 H, s, 4-H), 7.25 (1 H, t, *J* = 7.8 Hz, 7-H), 7.57 (1 H, d, *J* = 7.7 Hz, 8-H), 7.71 (1 H, t, *J* = 7.8 Hz, Ph 5-H), 7.77 (1 H, d, *J* = 7.9 Hz, Ph 4-H), 8.11 (1 H, d, *J* = 8.0 Hz, Ph 6-H), 8.17 (1 H, s, Ph 2-H), 11.56 (1 H, br, NH); ^{13}C NMR ($(CD_3)_2SO$) (HSQC / HMBC) δ 99.07 (4-C), 116.52 (8-C), 119.27 (6-C), 123.26 (q, *J* = 3.9 Hz, Ph 2-C), 125.67 (q, *J* = 3.9 Hz, Ph 4-C), 126.19 (4a-C), 127.27 (7-C), 129.74 (q, *J* = 31.8 Hz, Ph 3-C), 129.89 (Ph 5-C), 130.52 (Ph 6-C), 134.85 (5-C), 136.28 (Ph 1-C), 137.31 (3-C), 162.53 (1-C); ^{19}F NMR ($(CD_3)_2SO$) δ -61.03 (s, CF_3); MS *m/z* 303.0740 $(M - H)^-$ ($C_{16}H_{10}F_3N_2O$ requires 303.0743).

5-Amino-3-(4-trifluoromethylphenyl)isoquinolin-1-one hydrobromide (12i). Compound **31i** (85 mg, 270 μmol) was stirred with HBr in AcOH (33%, 4.0 mL) at 65°C for 7 h. Evaporation yielded **12i** (101 mg, 98%) as a buff solid: mp >230°C (lit.[1] mp 214–215°C for free base); ^{1}H NMR ($(CD_3)_2SO$) δ 7.17 (2 H, m, 4,6-H_2), 7.32 (1 H, t, *J* = 7.5 Hz, 7-H), 7.67 (1 H, d, *J* = 7.5 Hz, 8-H), 7.88 (2 H, d, *J* = 8.0 Hz, Ph 3,5-H_2), 8.04 (2 H, d, *J* = 8.0 Hz, Ph 2,6-H_2), 11.63 (1 H, br, NH); ^{13}C NMR ($(CD_3)_2SO$) (HSQC / HMBC) δ 99.53 (4-C), 117.08 (8-C), 118.87 (6-C), 124.11 (q, *J* = 270.6 Hz, CF_3), 125.64 (q, *J* = 3.5 Hz, Ph 3,5-C_2), 126.28 (4a-C), 127.41 (7-C + Ph 2,6-C_2), 129.20 (q, *J* = 31.8 Hz, Ph 4-C), 136.82 (Ph 1-C), 137.83 (3-C), 139.92 (5-C), 162.46 (1-C); ^{19}F NMR ($(CD_3)_2SO$) δ -61.02 (s, CF_3); MS *m/z* 303.0756 $(M - H)^-$ ($C_{16}H_{10}F_3N_2O$ requires 303.0743).

5-Amino-3-(4-fluorophenyl)isoquinolin-1-one hydrobromide (12j). Compound **31j** (65 mg, 24 μmol) was stirred with HBr in AcOH (33%, 3.5 mL) at 65°C for 5 h. Evaporation yielded **12j** (80 mg, 98%) as a buff solid: mp >230°C; ^{1}H NMR (CD_3OD) δ 6.99 (1 H, s, 4-H), 7.34 (3 H, m, 8-H & Ph 3,5-H_2), 7.39 (1 H, t, *J* = 8.5 Hz, 7-H), 7.45 (1 H, d, *J* = 8.5 Hz, 6-H), 7.89 (2 H, m, Ph 2,6-H_2), 11.71 (1 H, bs, NH); ^{13}C NMR ($(CD_3)_2SO$) (HSQC / HMBC) δ 98.62 (4-C), 115.48 (8-C), 115.68 (d, *J* =6.1 Hz, Ph 3,5-C_2), 124.75 (Ph 1-C), 125.72 (3-C), 126.66 (7-C), 128.99 (d, *J* = 17.2 Hz, Ph 2,6-C_2), 130.11 (6-C), 137.96 (Ph 4-C), 141.34 (5-C), 162.63 (1-C); ^{19}F NMR ($(CD_3)_2SO$) δ -112.47 (m, F); MS *m/z* 253.0756 $(M – H)^-$ ($C_{15}H_{10}FN_2O$ requires 253.0777).

5-Amino-3-(2-chlorophenyl)isoquinolin-1-one hydrobromide (12k). Compound **31k** (40.4 mg, 140 μmol) was stirred with HBr in AcOH (33%, 1.6 mL) at 65°C for 5 h. Evaporation yielded **12k** (47.5 mg, 95%) as a buff solid: mp >230°C; ^{1}H NMR (CD_3OD) δ 6.71 (1 H, s, 4-H), 7.51 (2 H, m, Ph 4,5-H_2), 7.60 (2 H, m, Ph 3,6-H_2), 7.66 (1 H, t, *J* = 8.0 Hz, 7-H), 7.85 (1 H, d, *J* = 7.5 Hz, 6-H), 8.45 (1 H, d, *J* = 8.5 Hz, 8-H); ^{13}C NMR (CD_3OD) (HSQC / HMBC) δ 100.92 (4-C), 127.61 (4a-C), 128.14 (7-C), 128.55 (Ph 5-C), 128.83 (6-C), 129.34 (8-C), 131.22 (Ph 3-C or Ph 6-C), 132.35 (Ph 6-C or Ph 3-C), 132.51 (Ph 4-C), 133.54 (5-C), 134.17 (Ph 2-C), 134.98 (Ph 1-C), 142.26 (3-C), 163.87 (1-C); MS *m/z* 273.0597 (M + H) ($C_{15}H_{12}{}^{37}ClN_2O$ requires 273.0609), 271.0623 $(M + H)^+$ ($C_{15}H_{12}{}^{35}ClN_2O$ requires 271.0638).

5-Amino-3-(3-chlorophenyl)isoquinolin-1-one hydrobromide (12l). Compound **31l** (38.5 mg, 140 μmol) was stirred with HBr in AcOH (33%, 1.5 mL) at 65°C for 5 h. Evaporation yielded **12l** (46.1 mg, 97%) as a buff solid: mp >230°C; ^{1}H NMR (CD_3OD) δ 6.93 (1 H, s, 4-H), 7.55 (2 H, m, Ph 4,6-H_2), 7.63 (1 H, t, *J* = 7.5 Hz, 7-H), 7.71 (1 H, m, Ph 5-H), 7.79 (1 H, d, *J* = 7.5 Hz, 6-H), 7.83 (1 H, s, Ph 2-H), 8.41 (1 H, d, *J* = 8.0 Hz, 8-H); ^{13}C NMR (CD_3OD) (HSQC / HMBC) δ 98.93 (4-C), 126.52 (Ph 5-C),128.09 (7-C), 128.17 (Ph 2-C), 128.47 (6-C), 128.93 (8-C), 131.16 (Ph 4-C or Ph 6-C), 131.84 (Ph 6-C or Ph 4-C), 133.56 (5-C), 136.19 (Ph 1-C), 137.24 (Ph 3-C), 142.63 (3-C), 166.31 (1-C); MS *m/z* 273.0584 $(M + H)^+$ ($C_{15}H_{12}{}^{37}ClN_2O$ requires 273.0609), 271.0616 $(M + H)^+$ ($C_{15}H_{12}{}^{35}ClN_2O$ requires 271.0638).

5-Amino-3-(2,6-dichlorophenyl)isoquinolin-1-one hydrobromide (12n). Compound **31n** (12.7 mg, 40 μmol) was stirred with HBr in AcOH (33%, 1.0 mL) at 65°C for 5 h. Evaporation yielded **12n** (9.0 mg, 58%) as an amber solid: mp 226-228°C; ^{1}H NMR (CD_3OD) δ 6.73 (1 H, s, 4-H), 7.56 (1 H, t, *J* = 6.6 Hz, Ph 4-H), 7.63 (2 H, d, *J* = 7.0 Hz, Ph 3,5-H_2), 7.74 (1 H, t, *J* = 7.9 Hz, 7-H), 7.91 (1 H, d, *J* = 7.5Hz, 6-H), 8.53 (1 H, d, *J* = 8.0 Hz, 8-H); ^{13}C NMR (CD_3OD) (HSQC / HMBC) δ 101.69 (4-C), 128.44 (7-C), 128.98 (6-C), 129.47 (8-C), 129.57 (Ph 3,5-C_2), 133.13 (Ph 4-C), 133.42 (5-C), 133.88 (Ph 1-C), 136.46 (Ph 2,6-C_2), 139.26 (3-C), 164.19 (1-C); MS *m/z* 327.0065 $(M + Na)^+$ ($C_{15}H_{10}{}^{35}Cl_2N_2NaO$ requires 327.0068).

5-Amino-3-(4-hydroxyphenyl)isoquinolin-1-one hydrobromide (12p). Compound **31p** (55 mg, 210 μmol) was stirred with HBr in AcOH (33%, 2.5 mL) at 65°C for 16 h. Evaporation yielded **12p** (68.5 mg, 98%) as a buff solid: mp >230°C; ^{1}H NMR ($(CD_3)_2SO$) δ 6.88 (3 H, m, 4-H + Ph 3,5-H_2), 7.36 (2 H, m, 6,7-H_2), 7.67 (2 H, d, *J* = 9.0 Hz, Ph 2,6-H_2), 7.88 (1 H, d, *J* = 9.0 Hz, 8-H), 11.46 (1 H, br, NH); ^{13}C NMR ($(CD_3)_2SO$) (HSQC / HMBC) δ 96.01 (4-C), 115.55 (Ph 3,5-C_2), 124.59 (7-C), 125.36 (6-C), 125.94 (8-C), 128.09 (Ph 2,6-C_2), 139.99 (3-C), 158.69 (Ph 4-C), 162.45 (1-C); MS *m/z* 253.0958 $(M + H)^+$ ($C_{15}H_{13}N_2O_2$ requires 253.0977).

5-Amino-3-(2-phenylethyl)isoquinolin-1-one hydrobromide (12s). Compound **39** (40 mg, 140 μmol) was stirred with HBr in AcOH (33%, 2.0 mL) at 65°C for 16 h. Evaporation yielded **12s** (35 mg, 70%) as a red-brown solid: mp >230°C; ^{1}H NMR (CD_3OD) δ 2.95 (2 H, t, *J* = 7.0 Hz, ethyl 1-H_2), 3.06 (2 H, t, *J* = 6.0 Hz, ethyl 2-H_2), 6.48 (1 H, s, 4-H), 7.24 (5 H, m, Ph-H_5), 7.56 (1 H, t, *J* = 8.0 Hz, 7-H), 7.75 (1 H, dd, *J* = 8.0, 1.0 Hz, 6-H), 8.38 (1 H, d, *J* = 8.0 Hz, 8-H); ^{13}C NMR (CD_3OD) (HSQC / HMBC) δ 35.83 (ethyl 2-C), 36.51 (ethyl 1-C), 97.82 (4-C), 126.76 (7-C), 127.07 (Ph 3-C), 127.48 (6-C), 129.36 (8-C), 129.43 (Ph 2,6-C_2), 129.62 (Ph 3,5-C_2), 134.04 (5-C), 141.57 (Ph 1-C), 145.88 (3-C), 164.03 (1-C); MS *m/z* 265.1320 $(M + H)^+$ ($C_{17}H_{17}N_2O$ requires 265.1341).

5-Amino-3-(4-aminocarbonylphenyl)isoquinolin-1-one hydrobromide (12u). Compound **31r** (14 mg, 50 μmol) was stirred with HBr in AcOH (33%, 1.0 mL) at 65°C for 16 h. Evaporation yielded **12u** (17.0 mg, 98%) as an amber solid: mp >230°C; ^{1}H NMR ($(CD_3)_2SO$) δ 4.4 (3 H, m, $^+NH_3$), 7.14 (1 H, d, *J* = 7.8 Hz, 6-H), 7.17 (1 H, s, 4-H), 7.30 (1 H, t, *J* = 7.8 Hz, 7-H), 7.46 (1 H, br, CON*H*H), 7.66 (1 H, d, *J* = 7.7 Hz, 8-H), 7.92 (2 H, d, *J* = 8.5 Hz, Ph 2,6-H_2), 7.99 (2 H, d, *J* = 8.5 Hz, Ph 3,5-H_2), 8.08 (1 H, br, CONH*H*), 11.55 (1 H, bs, NH); ^{13}C NMR ($(CD_3)_2SO$) (HSQC / HMBC) δ 98.81 (4-C), 119.83 (8-C), 120.91 (6-C), 126.12 (Ph 4-C), 126.30 (Ph 2,6-C_2), 127.09 (7-C), 127.89 (Ph 3,5-C_2), 134.48 (3-C), 136.30 (Ph 1-C), 138.15 (5-C), 162.50 (1-C), 167.13 ($CONH_2$); MS *m/z* 278.0947 $(M - H)^-$ ($C_{16}H_{12}N_3O_2$ requires 278.0930).

3-(4-(1,1-Dimethylethyl)phenyl)-5-methylisoquinolin-1-one (13c). BuLi (2.5 M in hexanes, 0.46 mL, 1.14 mmol) was added to dry Pr^i_2NH (127.5 mg, 1.3 mmol) in dry THF (2.0 mL) at -78°C and the mixture was stirred at -78°C for 10 min. Compound **41** (200 mg, 1.1 mmol) in dry THF (2.0 mL) was added and the mixture was stirred for 1 h at -78°C. 4-(1,1-Dimethylethyl)benzonitrile (180 mg, 1.1 mmol) in dry THF (2.0 mL) was added and the mixture was stirred for 1 h at -78°C, then at 20°C for 16 h. Water (1.0 mL) was added. The mixture was diluted with CH_2Cl_2, washed thrice with brine and dried. Evaporation and washing (EtOH) gave **13c** (96.5 mg, 29%) as a white solid: mp 204-206°C; IR ν_{max} 3295, 1642 cm^{-1}; ^{1}H NMR ($(CD_3)_2SO$) (COSY) δ 1.33 (9 H, s, CMe_3), 2.55 (3 H, s, 5-Me), 6.82 (1 H, s, 4-H), 7.35 (1 H, t, *J* = 7.6 Hz, 7-H), 7.51 (2 H, d, *J* = 7.6 Hz, Ph 3,5-H_2), 7.54 (1 H, d, *J* = 7.2 Hz, 6-H), 7.75 (2 H, d, *J* = 7.6 Hz, Ph 2,6-H_2), 8.06 (1 H, d, *J* = 8.0 Hz, 8-H), 11.48 (1 H, br, NH); ^{13}C NMR ($(CD_3)_2SO$) (HSQC / HMBC) δ 18.75 (Me), 30.97 (C*Me*$_3$), 34.44 (*C*Me_3), 99.60 (4-C), 124.56 (8-C), 124.86 (8a-C), 125.51 (Ph 3,5-C_2), 125.72 (7-C), 126.56 (Ph 2,6-C_2), 131.44 (Ph 1-C), 133.15 (6-C), 133.60 (4a-C), 136.69 (5-C), 139.84 (3-C), 151.87 (Ph 4-C), 162.97 (1-C); MS *m/z* 292.1686 $(M + H)^+$ ($C_{20}H_{22}NO$ requires 292.1703).

3-(4-Methoxyphenyl)-5-methylisoquinolin-1-one (13d). BuLi (1.6 M in hexanes, 0.7 mL, 1.1 mmol) was added to dry Pr^i_2NH (141 mg, 1.4 mmol) in dry THF (2.0 mL) at -78°C and the mixture was stirred at -78°C for 10 min. Compound **41** (200 mg, 1.1 mmol) in dry THF (2.0 mL) was added and the mixture was stirred for 1 h at -78°C. 4-Methoxybenzonitrile (151 mg, 1.1 mmol) in dry THF (2.0 mL) was added at -78°C and the mixture was stirred for 1 h at -78°C, then at 20°C for 16 h. Water (1.0 mL) was added. The mixture was diluted with CH_2Cl_2, washed thrice with brine and dried. Evaporation and washing (EtOH) gave **13d** (48 mg, 17%) as a white solid: mp 207-208°C; ^{1}H NMR ($(CD_3)_2SO$) (COSY) δ 2.54 (1 H, s, 5-Me), 3.82 (3 H, s, OMe), 6.77 (1 H, s, 4-H), 7.04 (2 H, d, *J* = 8.8 Hz, Ph 3,5-H_2), 7.33 (1 H, t, *J* = 7.6 Hz, 7-H), 7.53 (1 H, d, *J* = 7.1 Hz, 6-H), 7.78 (2 H, d, *J* = 8.8 Hz, Ph 2,6-H_2), 8.05 (1 H, d, *J* = 8.0 Hz, 8-H), 11.45 (1 H, br, NH); ^{13}C NMR ($(CD_3)_2SO$) (HSQC / HMBC) δ 18.81 (5-Me), 55.34 (OMe), 98.87 (4-C), 114.15 (Ph 3,5-C_2), 124.57 (8-C), 124.63 (8a-C), 125.51 (7-C), 126.51 (Ph 1-C), 128.23 (Ph 2,6-C_2), 133.15 (6-C), 133.49 (4a-C), 136.86 (5-C), 139.70 (3-C), 160.14 (Ph 4-C), 163.02 (1-C); MS *m/z* 553.2099 $(2 M + Na)^+$ ($C_{34}H_{30}N_2NaO_4$ requires 553.2104); 288.0994 $(M + Na)^+$ ($C_{17}H_{15}NNaO_2$ requires 288.1000), 266.1179 $(M + H)^+$ ($C_{17}H_{16}NO_2$ requires 266.1181).

5-Methyl-3-(4-trifluoromethylphenyl)isoquinolin-1-one (13e). BuLi (1.6 M in hexanes, 1.1 mL, 1.7 mmol) was added to dry $Pr^i{}_2NH$ (202 mg, 2.0 mmol) in dry THF (2.0 mL) at -78°C and the mixture was stirred at -78°C for 10 min. Compound **41** (300 mg, 1.7 mmol) in dry THF (2.0 mL) was added and the mixture was stirred for 1 h at -78°C. 4-Trifluoromethyl-benzonitrile (289 mg, 1.7 mmol) in dry THF (2.0 mL) was added at -78 °C and the mixture was stirred for 1 h at -78°C, then at 20°C for 16 h. Water (1.0 mL) was added. The mixture was extracted with CH_2Cl_2. The extract was washed thrice with brine and dried. Evaporation and recrystallisation (EtOH) (25 mL) gave **13e** (242 mg, 47%) as white crystals: mp 251-252°C; ^{1}H NMR ($(CD_3)_2SO$) (COSY) δ 2.56 (3 H, s, Me), 6.96 (1 H, s, 4-H), 7.40 (1 H, t, *J* = 7.6 Hz, 7-H), 7.57 (1 H, d, *J* = 7.2 Hz, 6-H), 7.84 (2 H, d, *J* = 8.3 Hz, Ph 3,5-H_2), 8.03 (2 H, d, *J* = 8.2 Hz, Ph 2,6-H_2), 8.08 (1 H, d, *J* = 8.0 Hz, 8-H), 11.75 (1 H, br, N-H); ^{13}C NMR (($(CD_3)_2SO$)) (HSQC / HMBC) δ 18.77 (Me), 101.54 (4-C), 124.62 (8-C), 125.23 (q, *J* = 295.9 Hz, CF_3), 125.51 (8a-C), 125.56 (q, *J* = 3.6 Hz, Ph 3,5-C_2), 126.54 (7-C), 129.25 (q, *J* = 31.6 Hz, Ph 4-C), 133.40 (6-C), 134.21 (4a-C), 136.29 (5-C), 138.10 (Ph 1-C), 138.36 (3-C), 162.91 (1-C); ^{19}F NMR (($(CD_3)_2SO$)) -61.08 (s, CF_3); MS *m/z* 302.0808 $(M - H)^-$ ($C_{17}H_{11}F_3NO$ requires 308.0798).

3-(2-Chlorophenyl)-5-methylisoquinolin-1-one (13f). BuLi (1.6 M in hexanes, 0.7 mL, 1.1 mmol) was added to dry $Pr^i{}_2NH$ (141 mg, 1.4 mmol) in dry THF (2.0 mL) at -78°C and the mixture was stirred at -78°C for 10 min. Compound **41** (200 mg, 1.1 mmol) in dry THF (2.0 mL) was added and the mixture was stirred for 1 h at -78°C. 2-Chlorobenzonitrile (155 mg, 1.1 mmol) in dry THF (2.0 mL) was added at -78°C and the mixture was stirred for 1 h at -78°C, then at 20°C for 16 h. Water (1.0 mL) was added. The mixture was diluted with CH_2Cl_2. This mixture was washed thrice with brine and dried. The evaporation residue was washed (EtOH) to give **13f** (4.9 mg, 2%) as a white solid: mp 178-180°C; ^{1}H NMR ($(CD_3)_2SO$) (COSY) δ 2.53 (3 H, s, Me), 6.58 (1 H, s, 4-H), 7.41 (1 H, t, *J* = 7.7 Hz, 7-H), 7.47 (1 H, td, *J* = 7.5, 1.3 Hz, Ph 4-H), 7.51 (1 H, td, *J* = 7.5, 2.0 Hz, Ph 5-H), 7.59 (3 H, m, 6-H + Ph 3,6-H_2), 8.08 (1 H, d, *J* = 8.0 Hz, 8-H), 11.59 (1 H, br, NH); ^{13}C NMR ($(CD_3)_2SO$) (HSQC / HMBC) δ 18.69 (Me), 102.43 (4-C), 124.61 (8-C), 125.33 (8a-C), 126.25 (7-C), 127.34 (Ph 4-C), 129.70 (Ph 6-C), 130.84 (Ph 5-C), 131.56 (Ph 3-C), 132.29 (Ph 2-C), 133.22 (6-C), 133.69 (4a-C), 134.24 (Ph 1-C), 136.31 (5-C), 138.15 (3-C), 162.24 (1-C); MS *m/z* 292.0514 $(M + Na)^+$ ($C_{16}H_{12}{}^{35}ClNNaO$ requires 292.0505).

3-(3-Chlorophenyl)-5-methylisoquinolin-1-one (13g). BuLi (1.6 M in hexanes, 0.7 mL, 1.1 mmol) was added to dry $Pr^i{}_2NH$ (141 mg, 1.4 mmol) in dry THF (2.0 mL) at -78°C and the mixture was stirred at -78°C for 10 min. Compound **42** (200 mg, 1.1 mmol) in dry THF (2.0 mL) was added and the mixture was stirred for 1 h at -78°C. 3-Chlorobenzonitrile (155 mg, 1.1 mmol) in dry THF (2.0 mL) was added at -78°C and the mixture was stirred for 1 h at -78°C, then at 20°C for 16 h. Water (1.0 mL) was added. The mixture was diluted with CH_2Cl_2, washed thrice with brine and dried. Evaporation and recrystallisation (EtOH) gave **13g** (33 mg, 11%) as a white solid: mp 275-276°C; ^{1}H NMR ($(CD_3)_2SO$) (COSY) δ 2.57 (3 H, s, Me), 6.93 (1 H, s, 4-H), 7.39 (1 H, t, *J* = 7.6 Hz, 7-H), 7.52 (2 H, m, Ph 4,5-H_2), 7.57 (1 H, d, *J* = 7.2 Hz, 6-H), 7.80 (1 H, m, Ph 6-H), 7.93 (1 H, s, Ph 2-H), 8.07 (1 H, d, *J* = 8.0 Hz, 8-H), 11.61 (1 H, br, NH); ^{13}C NMR ($(CD_3)_2SO$) (HSQC / HMBC) δ 18.82 (Me), 100.92 (4-C), 124.57 (8-C), 125.28 (8a-C), 125.64 (Ph 6-C), 126.32 (7-C), 126.74 (Ph 2-C), 129.01 (Ph 4-C), 130.54 (Ph 5-C), 133.33 (6-C), 133.55 (Ph 1-C), 134.14 (4a-C), 136.20 (Ph 3-C), 136.41 (5-C), 138.31 (3-C), 162.87 (1-C); MS *m/z* 292.0453 $(M + Na)^+$ ($C_{16}H_{12}{}^{35}ClNNaO$ requires 292.0506), 270.0661 $(M + H)^+$ ($C_{16}H_{13}{}^{35}ClNO$ requires 270.0686).

3-(4-Chlorophenyl)-5-methylisoquinolin-1-one (13h). BuLi (1.6 M in hexanes, 1.1 mL, 1.7 mmol) was added to dry $Pr^i{}_2NH$ (202 mg, 2.0 mmol) in dry THF (2.0 mL) at -78°C and the mixture was stirred at -78°C for 10 min. Compound **41** (300 mg, 1.7 mmol) in dry THF (2.0 mL) was added and the mixture was stirred for 1 h at -78°C. 4-Chlorobenzonitrile (233 mg, 1.7 mmol) in dry THF (2.0 mL) was added at -78°C and the mixture was stirred for 1 h at -78°C, then at 20°C for 2 h. Water (1.0 mL) was added, followed by CH_2Cl_2 (20 mL). The precipitate was collected by filtration to give **13h** (456 mg, 99%) as a white solid: mp >360°C; ^1H NMR ($(CD_3)_2SO$) (COSY) δ 2.61 (3 H, s, Me), 6.93 (1 H, s, 4-H), 7.44 (1 H, t, J = 7.6 Hz, 7-H), 7.61 (3 H, d, J = 8.5 Hz, 6-H + Ph 2,6-H_3), 7.90 (2 H, d, J = 8.6 Hz, Ph 3,5-H_2), 8.12 (1 H, d, J = 7.8 Hz, 8-H), 11.70 (1 H, s, N-H); ^{13}C NMR ($(CD_3)_2SO$)) (HSQC / HMBC) δ 18.80 (Me), 100.49 (4-C), 124.60 (8-C), 125.11 (8a-C), 126.19 (7-C), 128.73 (Ph 2,6-C_2), 128.78 (Ph 3,5-C_2), 133.01 (4a-C), 133.34 (6-C), 133.96 (Ph 1,4-C_2), 136.49 (5-C), 138.67 (3-C), 162.95 (1-C); MS m/z 270 $(M - H)^-$, 268.0533 $(M - H)^-$ ($C_{16}H_{11}{}^{35}ClNO$ requires 268.0535).

3-(2,6-Dichlorophenyl)-5-methylisoquinolin-1-one (13i). BuLi (1.6 M in hexanes, 0.7 mL, 1.1 mmol) was added to dry $Pr^i{}_2NH$ (141 mg, 1.4 mmol) in dry THF (2.0 mL) at -78°C and the mixture was stirred at -78°C for 10 min. Compound **41** (200 mg, 1.1 mmol) in dry THF (2.0 mL) was added and the mixture was stirred for 1 h at -78°C. 2,6-Dichlorobenzonitrile (194 mg, 1.1 mmol) in dry THF (2.0 mL) was added at -78°C and the mixture was stirred for 1 h at -78°C, then at 20°C for 16 h. Water (1.0 mL) was added. The mixture was diluted with CH_2Cl_2, washed thrice with brine and dried. Evaporation and recrystallisation (EtOH) gave **13i** (35 mg, 10%) as a pale buff solid: mp 202-204°C; ^1H NMR ($(CD_3)_2SO$) (COSY) δ 2.47 (3 H, s, Me), 6.58 (1 H, s, 4-H), 7.43 (1 H, t, J = 7.6 Hz, 7-H), 7.55 (1 H, t, J = 7.2 Hz, Ph 4-H), 7.58 (1 H, d, J = 7.3 Hz, 6-H), 7.59 (2 H, d, J = 7.6 Hz, Ph 3,5-H_2), 8.09 (1 H, d, J = 7.9 Hz, 8-H), 11.62 (1 H, br, NH); ^{13}C NMR ($(CD_3)_2SO$) (HSQC / HMBC) δ 18.66 (Me), 102.81 (4-C), 124.61 (8-C), 125.58 (8a-C), 126.45 (7-C), 128.28 (Ph 3,5-C_2), 131.67 (Ph 4-C), 133.19 (Ph 1-C), 133.29 (6-C), 133.75 (4a-C), 134.69 (Ph 2,6-C_2), 135.20 (3-C), 136.24 (5-C), 162.37 (1-C); MS m/z 326.0991 $(M + Na)^+$ ($C_{16}H_{11}{}^{35}Cl_2NNaO$ requires 326.0115), 304.0286 ($(M + H)^+$ ($C_{16}H_{12}{}^{35}Cl_2NO$ requires 304.0296).

3-(4-Bromophenyl)-5-methylisoquinolin-1-one (13j). BuLi (1.6 M in hexanes, 0.9 mL, 1.4 mmol) was added to dry $Pr^i{}_2NH$ (162 mg, 1.6 mmol) in dry THF (2.0 mL) at -78°C and the mixture was stirred at -78°C for 10 min. Compound **41** (241 mg, 1.4 mmol) in dry THF (2.0 mL) was added and the mixture was stirred for 1 h at -78°C. 4-Bromobenzonitrile (248 mg, 1.4 mmol) in dry THF (2.0 mL) was added at -78°C and the mixture was stirred for 1 h at -78°C, then at 20°C for 16 h. Water (1.0 mL) was added. The mixture was diluted with CH_2Cl_2 (20 mL). The solid was collected by filtration and washed (EtOH) to give **13j** (181 mg, 42%) as a white solid: mp 278-279°C; ^1H NMR ($(CD_3)_2SO$) (COSY) δ 2.55 (3 H, s, Me), 6.88 (1 H, s, 4-H), 7.38 (1 H, t, J = 7.7 Hz, 7-H), 7.56 (1 H, d, J = 7.2 Hz, 6-H), 7.69 (2 H, d, J = 8.5 Hz, Ph 2,6-H_2), 7.78 (2 H, d, J = 8.5 Hz, Ph 3,5-H_2), 8.07 (1 H, d, J = 8.0 Hz, 8-H), 11.59 (1 H, br, NH); ^{13}C NMR ($(CD_3)_2SO$) (HSQC / HMBC) δ 18.81 (Me), 100.47 (4-C),122.66 (Ph 4-C), 124.62 (8-C), 125.13 (8a-C), 126.20 (7-C), 129.03 (Ph 3,5-C_2), 131.66 (Ph 2,6-C_2), 133.34 (6-C), 133.43 (Ph 1-C), 133.97 (4a-C), 136.51 (5-C), 138.81 (3-C), 162.99 (1-C); MS m/z 335.9966 $(M + Na)^+$ ($C_{16}H_{12}{}^{79}BrNNaO$ requires 336.0000)

5-Methyl-3-(4-phenylethynylphenyl)isoquinolin-1-one (13k). BuLi (1.6 M in hexanes, 0.7 mL, 1.1 mmol) was added to dry $Pr^i{}_2NH$ (141 mg, 1.4 mmol) in dry THF (2.0 mL) at -78°C and the mixture was stirred at this temperature for 10 min. Compound **41** (230 mg, 1.1 mmol) in dry THF (2.0 mL) was added and the mixture was stirred for 1 h at -78°C. Compound **43** (194 mg, 1.1 mmol) in dry THF (2.0 mL) was added at -78°C and the mixture was stirred for 1 h at -78°C, then at 20°C for 16 h. Water (1.0 mL) was added. The mixture was diluted with CH_2Cl_2. The solid was collected by filtration and washed (EtOH) to give **13k** (117 mg, 31%) as a white solid: mp 285-287°C; ^{1}H NMR (($(CD_3)_2SO$) (COSY) δ (2.57, s, Me), 6.94 (1 H, s, 4-H), 7.39 (1 H, t, *J* = 7.6 Hz, 7-H), 7.45 (3 H, m, Ph 3,4,5-H_3), 7.56 (1 H, d, *J* = 7.4 Hz, 6-H), 7.59 (2 H, m, Ph 2,6-H_2), 7.67 (2 H, d, *J* = 8.0 Hz, Ar 3,5-H_2), 7.90 (2 H, d, *J* = 8.0 Hz, Ar 2,6-H_2), 8.08 (1 H, d, *J* = 7.9 Hz, 8-H), 11.62 (1 H, br, NH); ^{13}C NMR ($(CD_3)_2SO$) (HSQC / HMBC) δ 18.82 (Me), 88.99 (ethyne 1-C), 90.86 (ethyne 2-C), 100.64 (4-C), 122.09 (Ph 1-C), 122.92 (Ar 4-C), 124.61 (8-C), 125.18 (8a-C), 126.21 (7-C), 126.15 (Ar 2,6-C_2), 128.84 (Ph 3,5-C_2), 129.03 (Ph 10-C), 131.47 (Ph 2,6-C_2), 131.66 (Ar 3,5-C_2), 133.29 (6-C), 134.03 (4a-C), 134.17 (Ar 1-C), 136.50 (5-C), 139.00 (3-C), 163.00 (1-C); MS *m/z* 358.1218 (M + Na)$^+$ ($C_{24}H_{17}NNaO$ requires 358.1208), 336.1402 (M + H)$^+$ ($C_{24}H_{18}NO$ requires 336.1388).

5-Methyl-3-(4-(piperidin-1-ylmethyl)phenyl)isoquinolin-1-one (13m). BuLi (1.6 M in hexanes, 0.7 mL, 1.1 mmol) was added to dry Pr^i_2NH (142 mg, 1.4 mmol) in dry THF (2.0 mL) at -78°C and the mixture was stirred at -78°C for 10 min. Compound **41** (200 mg, 1.1 mmol) in dry THF (2.0 mL) was added and the mixture was stirred for 1 h at -78°C. Compound **45b** (226 mg, 1.1 mmol) in dry THF (2.0 mL) was added and the mixture was stirred for 1 h at this temperature, then at room temperature for 16 h. Water (1.0 mL) was added. The mixture was diluted with CH_2Cl_2, washed thrice with saturated brine and dried. Evaporation and washing (EtOH) gave **13m** (78 mg, 21%) as a white solid: mp 196-197°C; IR ν_{max} 3440 (NH), 1644 (C=O); ^{1}H NMR ($(CD_3)_2SO$) δ 1.40 (2 H, m, piperidine 4-H_2), 1.50 (4 H, m, piperidine 3,5-H_4), 2.34 (4 H, m, piperidine 2,6-H_4), 2.55 (3 H, s, Me), 3.47 (2 H, s, $PhCH_2$), 6.84 (1 H, s, 4-H), 7.36 (1 H, t, *J* = 7.7 Hz, 7-H), 7.40 (2 H, d, *J* = 8.2 Hz, Ph 3,5-H_2), 7.54 (1 H, d, *J* = 7.1 Hz, 6-H), 7.76 (2 H, d, *J* = 8.2 Hz, Ph 2,6-H_2), 8.06 (1 H, d, *J* = 7.9 Hz, 8-H), 11.48 (1 H, bs, N-H); ^{13}C NMR ($(CD_3)_2SO$) (HSQC / HMBC) δ 18.76 (Me), 23.96 (piperidine 4), 25.55 (piperidine 3,5-C_2), 53.91 (piperidine 2,6-C_2), 62.37 ($PhCH_2$), 99.73 (4-C), 124.56 (8-C), 124.90 (8a-C), 125.79 (7-C), 126.61 (Ph 2,6-C_2), 129.01 (Ph 3,5-C_2), 132.67 (Ph 1-C), 133.18 (6-C), 133.68 (4a-C), 136.66 (5-C), 139.78 (Ph 4-C), 140.06 (3-C), 162.95 (1-C); MS *m/z* 665.3884 (2 M + H)$^+$ ($C_{44}H_{49}N_4O_2$ requires 665.3855), 355.1805 (M + Na)$^+$ ($C_{22}H_{24}N_2NaO$ requires 355.1786).

5-Methyl-3-(4-(pyrrolidin-1-ylmethyl)phenyl)isoquinolin-1-one hydrochloride (13n). BuLi (2.5 M in hexanes, 0.46 mL, 1.14 mmol) was added to dry Pr^i_2NH (127.5 mg, 1.3 mmol) in dry THF (2.0 mL) at -78°C and the mixture was stirred at -78°C for 10 min. Compound **41** (200 mg, 1.13 mmol) in dry THF (2.0 mL) was added and the mixture was stirred for 1 h at -78°C. Compound **45c** (210.5 mg, 1.13 mmol) in dry THF (2.0 mL) was added and the mixture was stirred for 1 h at -78°C, then at 20°C for 16 h. Water (1.0 mL) was added. The mixture was diluted with CH_2Cl_2, washed thrice with brine and dried. Evaporation and washing (EtOH) gave **13n** (32 mg, 9%) as a pale yellow solid: mp >360°C; IR ν_{max} 3413, 1640 cm^{-1}; The solid was then treated for 16 h with aq. HCl (6.0 M, 2.0 mL). Evaporation and drying gave the HCl salt as a white solid: mp >360°C; ^{1}H NMR ($(CD_3)_2SO$) δ 1.70 (4 H, m, pyrrolidine 3,4-H_4), 2.44 (4 H, m, pyrrolidine 2,5-H_4), 2.54 (3 H, s, Me), 3.61 (2 H, s, $PhCH_2$), 6.83 (1 H, s, 4-H), 7.35 (1 H, t, *J* = 7.7 Hz, 7-H), 7.41 (2 H, d, *J* = 8.2 Hz, Ph 3,5-H_2), 7.54 (1 H, d, *J* = 7.2 Hz, 6-H), 7.76 (2 H, d, *J* = 8.2 Hz, Ph 2,6-H_2), 8.05 (1 H, d, *J* = 7.9 Hz, 8-H), 11.52 (1 H, br, NH); ^{13}C NMR ($(CD_3)_2SO$) (HSQC / HMBC) δ 18.77 (Me), 23.12 (pyrrolidine 3,4-C_2), 53.50 (pyrrolidine 2,5-C_2), 59.15 (Ph*C*H_2), 99.72 (4-C), 124.55 (8-C), 124.92 (8a-C), 125.80 (7-C), 126.64 (Ph 2,6-C_2), 128.71 (Ph 3,5-C_2), 132.64 (Ph 1-C), 133.30 (6-C), 133.68 (4a-C), 136.81 (5-C), 139.86 (3-C), 140.96 (Ph 4-C), 163.24 (1-C); MS *m/z* 319.1788 (M + H)$^+$ ($C_{21}H_{23}N_2O$ requires 319.1810).

5-Methyl-3-(4-((4-methylpiperazin-1-yl)methyl)phenyl)isoquinolin-1-one dihydrochloride (13o). BuLi (2.5 M in hexanes, 0.46 mL, 1.14 mmol) was added to dry $Pr^i{}_2NH$ (128 mg, 1.3 mmol) in dry THF (2.0 mL) at -78°C and the mixture was stirred at -78°C for 10 min. Compound **41** (200 mg, 1.13 mmol) in dry THF (2.0 mL) was added and the mixture was stirred for 1 h at -78°C. Compound **45d** (243 mg, 1.13 mmol) in dry THF (2.0 mL) was added and the mixture was stirred for 1 h at -78°C, then at 20°C for 16 h. Water (1.0 mL) was added. The mixture was diluted with CH_2Cl_2, washed thrice with brine and dried. The evaporation residue was washed (EtOH) to give **13o** (8 mg, 2%) as a white solid: mp >360°C. The solid was treated for 16 h with aq. HCl (6 M, 1.0 mL). Evaporation and drying gave the 2.HCl salt: mp >360°C; IR ν_{max} 3419, 1636 cm^{-1}; ^{1}H NMR (($CD_3)_2SO$) δ 2.14 (3 H, s, NMe), 2.35 (8 H, m, piperazine-H_8), 2.54 (3 H, s, 5-Me), 3.49 ($PhCH_2$), 6.83 (1 H, s, 4-H), 7.35 (1 H, t, *J* = 7.7 Hz, 7-H), 7.39 (2 H, d, *J* = 8.2 Hz, Ph 3,5-H_2), 7.54 (1 H, d, *J* = 7.2 Hz, 6-H), 7.76 (2 H, d, *J* = 8.2 Hz, Ph 2,6-H_2), 8.05 (1 H, d, *J* = 7.9 Hz, 8-H), 11.51 (1 H, br, N-H); ^{13}C NMR (($CD_3)_2SO$) (HSQC / HMBC) δ 18.76 (5-Me), 40.08 (NMe), 52.57 (piperazine 2,6-C_2), 54.70 (piperazine 3,5-C_2), 61.57 (Ph*C*H_2), 99.75 (4-C), 124.56 (8-C), 124.92 (8a-C), 125.81 (7-C), 126.65 (Ph 2,6-C_2), 129.65 (Ph 3,5-C_2), 132.79 (Ph 1-C), 133.18 (6-C), 133.69 (4a-C), 136.65 (5-C), 139.67 (Ph 4-C), 139.75 (3-C), 162.94 (1-C); MS *m/z* 348.2076 (M + H)$^+$ ($C_{22}H_{26}N_3O$ requires 348.2076).

5-Methyl-3-(pyridin-4-yl)isoquinolin-1-one (13p). BuLi (1.6 M in hexanes, 0.7 mL, 1.1 mmol) was added to dry $Pr^i{}_2NH$ (142 mg, 1.4 mmol) in dry THF (2.0 mL) at -78°C and the mixture was stirred at -78°C for 10 min. Compound **41** (200 mg, 1.1 mmol) in dry THF (2.0 mL) was added and the mixture was stirred for 1 h at -78°C. 4-Cyanopyridine (118 mg, 1.1 mmol) in dry THF (2.0 mL) was added and the mixture was stirred for 1 h at -78°C, then at 20°C for 16 h. Water (1.0 mL) was added. The mixture was diluted with CH_2Cl_2, washed thrice with brine and dried. Evaporation and recrystallisation (EtOH) gave **13p** (16.5 mg, 6%) as white crystals: mp 268-269°C; IR ν_{max} 3450, 1654 cm^{-1}; ^{1}H NMR (($CD_3)_2SO$) (COSY) δ 2.59 (3 H, s, Me), 7.11 (1 H, s, 4-H), 7.44 (1 H, t, *J* = 7.7 Hz, 7-H), 7.60 (1 H, d, *J* = 7.2 Hz, 6-H), 7.87 (2 H, d, *J* = 6.2 Hz, Ph 3,5-H_2), 8.10 (1 H, d, *J* = 8.0 Hz, 8-H), 8.69 (2 H, d, *J* = 6.2 Hz,, Ph 2,6-H_2), 11.70 (1 H, br, NH); ^{13}C NMR (($CD_3)_2SO$) (HSQC / HMBC) δ 18.76 (Me), 101.87 (4-C), 120.96 (pyridine 3,5-C_2), 124.65 (8-C), 125.83 (8a-C), 126.91 (7-C), 133.49 (6-C), 134.50 (4a-C), 136.06 (5-C), 137.06 (pyridine 4-C), 141.03 (3-C), 150.13 (pyridine 2,6-C_2), 162.85 (1-C); MS *m/z* 235.0864 (M - H)$^-$ ($C_{15}H_{11}N_2O$ requires 235.0871).

3-(Benzo-1,3-dioxol-5-yl)-5-methylisoquinolin-1-one (13q). BuLi (1.6 M in hexanes, 0.70 mL, 1.1 mmol) was added to dry $Pr^i{}_2NH$ (141 mg, 1.4 mmol) in dry THF (2.0 mL) at -78°C and the mixture was stirred at -78°C for 10 min. Compound **41** (200 mg, 1.1 mmol) in dry THF (2.0 mL) was added and the mixture was stirred for 1 h at -78°C. 5-Cyanobenzo-1,3-dioxole (166 mg, 1.1 mmol) in dry THF (2.0 mL) was added at -78°C and the mixture was stirred for 1 h at -78°C, then at 20°C for 16 h. Water (1.0 mL) was added. The mixture was diluted with CH_2Cl_2. The solid was collected by filtration, washed (EtOH) and dried to give **13q** (199 mg, 63%) as a white solid. mp >360°C; ^{1}H NMR (($CD_3)_2SO$) (COSY) δ 2.54 (3 H, s, Me), 6.10 (2 H, s, CH_2), 6.78 (1 H, s, 4-H), 7.02 (1 H, d, *J* = 8.2 Hz, benzodioxole 6-H), 7.33 (1 H, t, *J* = 7.7 Hz, 7-H), 7.34 (1 H, dd, *J* = 8.1, 1.8 Hz, benzodioxole 7-H), 7.43 (1 H, d, *J* = 1.8 Hz, benzodioxole 4-H), 7.52 (1 H, d, *J* = 7.2 Hz, 6-H), 8.04 (1 H, d, *J* = 8.0 Hz, 8-H), 11.44 (1 H, br, NH); ^{13}C NMR (($CD_3)_2SO$) (HSQC / HMBC) δ 18.83 (Me), 99.37 (4-C), 101.52 (CH_2), 107.27 (benzodioxole 4-C), 108.46 (benzodioxole 7-C), 121.07 (benzodioxole

6-C), 124.56 (8-C), 124.72 (8a-C), 125.60 (7-C), 128.40 (benzodioxole 5-C), 133.12 (6-C), 133.62 (4a-C), 136.80 (5-C), 139.77 (3-C), 147.71 (benzodioxole 7a-C), 148.17 (benzodioxole 3a-C), 163.14 (1-C); MS *m/z* 278.0797 $(M - H)^-$ ($C_{17}H_{12}NO_3$ requires 278.0817).

5-Methyl-3-(thiophen-3-yl)isoquinolin-1-one (13r). BuLi (2.5 M in hexanes, 0.46 mL, 1.1 mmol) was added to dry Pr^i_2NH (127.5 mg, 1.3 mmol) in dry THF (2.0 mL) at -78°C and the mixture was stirred at -78°C for 10 min. Compound **41** (200 mg, 1.13 mmol) in dry THF (2.0 mL) was added and the mixture was stirred for 1 h at -78°C. 3-Cyanothiophene (123 mg, 1.1 mmol) in dry THF (2.0 mL) was added and the mixture was stirred for 1 h at -78°C, then at 20°C for 16 h. Water (1.0 mL) was added. The mixture was diluted with CH_2Cl_2 and washed thrice with saturated brine. Drying, evaporation and washing (EtOH) gave **13r** (17 mg, 6%) as a pale buff solid: mp >360°C; IR ν_{max} 3448, 1647 cm^{-1}; ^1H NMR $((CD_3)_2SO)$ (COSY) δ 2.56 (3 H, s, Me), 6.99 (1 H, s, 4-H), 7.34 (1 H, t, *J* = 7.6 Hz, 7-H), 7.54 (1 H, d, *J* = 7.1 Hz, 6-H), 7.70 (1 H, m, thiophene 4-H), 7.78 (1 H, d, *J* = 4.6 Hz, thiophene 5-H), 8.04 (1 H, d, *J* = 8.0 Hz, 8-H), 8.28 (1 H, d, *J* = 1.5 Hz, thiophene 2-H), 11.47 (1 H, br, NH); ^{13}C NMR $((CD_3)_2SO)$ (HSQC / HMBC) δ 18.80 (Me), 99.09 (4-C), 123.46 (thiophene 2-C), 124.58 (8-C), 124.95 (8a-C), 125.74 (7-C), 126.16 (thiophene 5-C), 127.27 (thiophene 4-C), 133.25 (6-C), 133.73 (4a-C), 134.95 (thiophene 1-C), 135.37 (3-C), 136.72 (5-C), 162.80 (1-C); MS *m/z* 264.0454 $(M + Na)^+$ ($C_{14}H_{11}NNaOS$ requires 264.0459).

5-Fluoro-3-(4-methylphenyl)isoquinolin-1-one (14b). BuLi (1.6 M in hexanes, 0.7 mL, 1.1 mmol) was added to dry Pr^i_2NH (142 mg, 1.4 mmol) in dry THF (2.0 mL) at -78°C and the mixture was stirred at -78°C for 10 min. Compound **49** (200 mg, 1.1 mmol) in dry THF (2.0 mL) was added and the mixture was stirred for 1 h at -78°C. 4-Methylbenzonitrile (129 mg, 1.1 mmol) in dry THF (2.0 mL) was added and the mixture was stirred for 1 h at -78°C, then at 20°C for 16 h. Water (1.0 mL) was added. The mixture was diluted with CH_2Cl_2, washed thrice with brine and dried. Evaporation and recrystallisation (EtOH) gave **14b** (50 mg, 18%) as white crystals: mp 232-233°C; IR ν_{max} 3481, 1668, 1235 cm^{-1}; ^1H NMR $((CD_3)_2SO)$ (COSY) δ 2.37 (3 H, s, Me), 6.81 (1 H, s, 4-H), 7.30 (2 H, d, *J* = 8.0 Hz, Ph 3,5-H_2), 7.48 (1 H, m, 7-H), 7.58 (1 H, t, *J* = 8.1 Hz, 6-H), 7.71 (2 H, d, *J* = 8.0 Hz, Ph 2,6-H_2), 8.03 (1 H, d, *J* = 8.0 Hz, 8-H), 11.70 (1 H, br, NH); ^{13}C NMR $((CD_3)_2SO)$ (HSQC / HMBC) δ 20.83 (Me), 94.19 (d, *J* = 5.1 Hz, 4-C), 117.57 (d, *J* = 19.5 Hz, 6-C), 122.77 (d, *J* = 3.3 Hz, 8-C), 126.46 (d, *J* = 3.4 Hz, 8a-C); 126.59 (d, *J* = 7.6 Hz, 7-C), 126.79 (Ph 2,6-C_2), 127.06 (d, *J* = 16.5 Hz, 4a-C), 129.40 (Ph 3,5-H_2), 130.74 (Ph 1-C), 139.38 (Ph 4-C), 141.40 (3-C), 157.26 (d, *J* = 248.1 Hz, 5-C), 161.81 (d, *J* = 2.8 Hz, 1-C); ^{19}F NMR $((CD_3)_2SO)$ δ -122.08 (dd, *J* = 10.4, 5.2 Hz, F); MS *m/z* 252.0807 $(M - H)^-$ ($C_{16}H_{11}FNO$ requires 252.0824).

5-Fluoro-3-(4-methoxyphenyl)isoquinolin-1-one (14c). BuLi (1.6 M in hexanes, 0.7 mL, 1.1 mmol) was added to dry Pr^i_2NH (131 mg, 1.3 mmol) in dry THF (2.0 mL) at -78°C and the mixture was stirred at -78°C for 10 min. Compound **49** (200 mg, 1.1 mmol) in dry THF (2.0 mL) was added and the mixture was stirred for 1 h at -78°C. 4-Methoxybenzonitrile (147 mg, 1.1 mmol) in dry THF (2.0 mL) was added at -78°C and the mixture was stirred for 1 h at -78°C, then at 20°C for 16 h. Water (1.0 mL) was added. The mixture was diluted with CH_2Cl_2, washed thrice with brine and dried. Evaporation and washing (EtOH) gave **14c** (8.1 mg, 3%) as an off-white solid: mp 238-240°C; ^1H NMR $((CD_3)_2SO)$ δ 3.82 (3 H, s, Me), 6.78 (1 H, s, 4-H), 7.05 (2 H, d, *J* = 8.9 Hz, Ph 3,5-H_2), 7.45 (1 H, m, 7-H), 7.57 (1 H, t, *J* = 8.9 Hz, 6-H), 7.77 (2 H, d, *J* = 8.9 Hz, Ph 2,6-H_2), 8.02 (1 H, d, *J* = 8.0 Hz, 8-H), 11.66 (1 H, br, NH); ^{13}C NMR $((CD_3)_2SO)$ (HSQC / HMBC) δ 55.37 (Me), 93.59 (d, *J* = 5.3 Hz, 4-C), 114.23 (Ph 3,5-C_2), 117.52 (d, *J* = 19.6 Hz, 6-C), 122.74 (d, *J* = 3.2 Hz, 8-C), 125.84 (Ph 1-

C), 126.24 (d, J = 3.6 Hz, 8a-C), 126.32 (d, J = 7.6 Hz, 7-C), 129.20 (d, J = 16.5 Hz, 4a-C), 128.35 (Ph 2,6-C_2), 141.19 (3-C), 157.19 (d, J = 247.5 Hz, 5-C), 160.41 (Ph 4-C), 161.82 (1-C); ^{19}F NMR ((CD_3)$_2$SO) δ -122.20 (dd, J = 9.9, 5.2 Hz, F); MS m/z 561.1593 (2 M + Na)$^+$ ($C_{32}H_{24}F_2N_2NaO_4$ requires 561.1602), 292.0747 (M + Na)$^+$ ($C_{16}H_{12}FNNaO_2$ requires 292.0750).

5-Fluoro-3-(4-trifluoromethylphenyl)isoquinolin-1-one (14d). BuLi (1.6 M in hexanes, 0.9 mL, 1.4 mmol) was added to dry $Pr^i{}_2NH$ (170 mg, 1.7 mmol) in dry THF (2.0 mL) at -78°C and the mixture was stirred at -78°C for 10 min. Compound **49** (250 mg, 1.4 mmol) in dry THF (2.0 mL) was added and the mixture was stirred for 1 h at -78°C. 4-Trifluoromethyl-benzonitrile (236 mg, 1.4 mmol) in dry THF (2.0 mL) was added at -78°C and the mixture was stirred for 1 h at -78°C, then at 20°C for 16 h. Water (1.0 mL) was added. The mixture was diluted with CH_2Cl_2 (20 mL). The solid was collected by filtration and washed (EtOH) to give **14d** (424 mg, 99%) as a white solid: mp >360°C; ^{1}H NMR ((CD_3)$_2$SO) (COSY) δ 6.97 (1 H, s, 4-H), 7.55 (1 H, td, J = 7.6, 5.7 Hz, 7-H), 7.63 (1 H, t, J = 8.7 Hz, 6-H), 7.86 (2 H, d, J = 8.1 Hz, Ph 3,5-H_2), 8.05 (3 H, m, Ph 2,6-H_2 + 8-H), 11.92 (1 H, br, NH); ^{13}C NMR ((CD_3)$_2$SO) (HSQC / HMBC) d 96.30 (d, J = 4.9 Hz, 4-C), 117.86 (d, J = 19.5 Hz, 6-C), 122.83 (d, J = 3.4 Hz, 8-C), 124.07 (q, J = 270.1 Hz, CF_3), 125.63 (q, J = 3.5 Hz, Ph 3,5-H_2), 126.59 (d, J = 16.3 Hz, 4a-C), 126.91 (8a-C), 127.52 (d, J = 7.6 Hz, 7-C), 127.99 (Ph 2,6-C_2), 129.58 (q, J = 31.9 Hz, Ph 4-C), 137.47 (1-C), 139.86 (3-C), 157.44 (d, J = 248.5 Hz, 5-C), 161.70 (1-C); ^{19}F NMR (DMSO) δ -61.19 (3 F, s, CF_3), -121.55 (1 F, m, F); MS m/z 306.0559 (M - H)$^-$ ($C_{16}H_8F_4NO$ requires 306.0548)

3-(4-Chlorophenyl)-5-fluoroisoquinolin-1-one (14f). BuLi (1.6 M in hexanes, 0.9 mL, 1.4 mmol) was added to dry $Pr^i{}_2NH$ (170 mg, 1.7 mmol) in dry tetrahydrofuran (2.0 mL) at -78°C and the mixture was stirred at this temperature for 10 min. Compound **49** (250 mg, 1.4 mmol) in dry THF (2.0 mL) was added and the mixture was stirred for 1 h at -78°C. 4-Chlorobenzo-nitrile (190 mg, 1.4 mmol) in dry THF (2.0 mL) was added at -78°C and the mixture was stirred for 1 h at -78°C, then at 20°C for 16 h. Water (1.0 mL) was added. The mixture was diluted with CH_2Cl_2 (20 mL). The solid was collected by filtration and washed (EtOH) to give **14f** (269 mg, 71%) as a white solid: mp 296-297°C; ^{1}H NMR ((CD_3)$_2$SO) (COSY) δ 6.86 (1 H, s, 4-H), 7.49 (1 H, m, 7-H), 7.57 (3 H, m, 6-H + Ph 3,5-H_2), 7.84 (2 H, d, J = 8.6 Hz, Ph 2,6-H_2), 8.05 (1 H, d, J = 7.9 Hz, 8-H), 11.63 (1 H, br, N-H); ^{13}C NMR ((CD_3)$_2$SO) (HSQC / HMBC) δ 94.91 (d, J = 5.4 Hz, 4-C), 117.36 (d, J = 19.6 Hz, 6-C), 122.53 (d, J = 3.5 Hz, 8-C), 126.73 (d, J = 8.0 Hz, 7-C), 126.52 (8a-C), 126.65 (d, J = 16.2 Hz, 4a-C), 128.51 (Ph 3,5-C_2), 128.57 (Ph 2,6-C_2), 132.26 (Ph 1-C), 134.15 (Ph 4-C), 140.00 (3-C), 157.15 (d, J = 248.4 Hz, 5-C), 161.42 (1-C); ^{19}F NMR ((CD_3)$_2$SO) δ -122.79 (m, F); MS m/z 272.0762 (M - H)$^-$ ($C_{15}H_8{}^{35}ClFNO$ requires 272.0784).

3-(4-Bromophenyl)-5-fluoroisoquinolin-1-one (14g). BuLi (1.6 M in hexanes, 0.64 mL, 1.2 mmol) was added to dry $Pr^i{}_2NH$ (121 mg, 1.2 mmol) in dry THF (2.0 mL) at -78°C and the mixture was stirred at -78°C for 10 min. Compound **49** (180 mg, 1.0 mmol) in dry THF (2.0 mL) was added and the mixture was stirred for 1 h at -78°C. 4-Bromobenzonitrile (186 mg, 1.0 mmol) in dry THF (2.0 mL) was added at -78°C and the mixture was stirred for 1 h at -78°C, then at 20°C for 16 h. Water (1.0 mL) was added. The mixture was diluted with CH_2Cl_2 (20 mL). The solid was collected by filtration and washed (EtOH) to give **11g** (238 mg, 61%) as a white solid: mp >360°C; ^{1}H NMR ((CD_3)$_2$SO) (COSY) δ 6.86 (1 H, s, 4-H), 7.47 (1 H, m, 7-H), 7.52 (1 H, t, J = 8.1 Hz, 6-H), 7.67 (2 H, d, J = 8.6 Hz, Ph 2,6-H_2), 7.78 (2 H, d, J = 8.6 Hz, Ph 3,5-H_2), 8.03 (1 H, d, J = 7.9 Hz, 8-H), 11.87 (1 H, bs, N-H); ^{13}C NMR ((CD_3)$_2$SO) δ (HSQC / HMBC) δ 94.61 (d, J = 5.1 Hz, 4-C), 117.08 (d, J = 19.3 Hz, 6-

C), 122.60 (d, *J* = 3.5 Hz, 8-C), 122.66 (Ph 4-C), 126.45 (d, *J* = 7.9 Hz, 7-C), 126.53 (8a-C), 126.80 (d, *J* = 16.3 Hz, 4a-C), 128.85 (Ph 3,5-C_2), 131.45 (Ph 2,6-C_2), 133.27 (Ph 1-C), 140.87 (3-C), 157.20 (d, *J* = 248.3 Hz, 5-C), 162.10 (1-C); ^{19}F NMR ((CD_3)$_2$SO) δ -121.89 (m, F); MS *m/z* 317.9760 (M – H)$^-$ ($C_{15}H_8{}^{81}BrFNO$ requires 317.9753), 315.9773 (M - H)$^-$ ($C_{15}H_8{}^{79}BrFNO$ requires 315.9773).

5-Fluoro-3-(pyridin-4-yl)isoquinolin-1-one (14h). BuLi (1.6 M in hexanes, 0.7 mL, 1.1 mmol) was added to dry $Pr^i{}_2NH$ (131 mg, 1.3 mmol) in dry THF (2.0 mL) at -78°C and the mixture was stirred at -78°C for 10 min. Compound **49** (200 mg, 1.1 mmol) in dry THF (2.0 mL) was added and the mixture was stirred for 1 h at -78°C. 4-Cyanopyridine (114 mg, 1.1 mmol) in dry THF (2.0 mL) was added and the mixture was stirred for 1 h at -78°C, then at 20°C for 16 h. Water (1.0 mL) was added. The mixture was diluted with CH_2Cl_2, washed thrice with brine and dried. Evaporation and washing (EtOH) gave **14h** (264 mg, 99%) as a white solid: mp >360°C; IR ν_{max} 3435, 1675, 1244 cm^{-1}; ^{1}H NMR ((CD_3)$_2$SO) δ 7.10 (1 H, s, 4-H), 7.55 (1 H, m, 7-H), 7.64 (1 H, t, *J* = 8.0 Hz, 6-H), 7.86 (2 H, d, *J* = 6.2 Hz, pyridine 3,5-H_2), 8.06 (1 H, d, *J* = 7.8 Hz, 8-H), 8.70 (2 H, d, *J* = 6.2 Hz, pyridine 2,6-H_2), 11.90 (1 H, br, NH); ^{13}C NMR ((CD_3)$_2$SO) (HSQC / HMBC) δ 96.61 (4-C), 117.89 (d, *J* = 19.8 Hz, 6-C), 121.10 (pyridine 3,5-C_2), 122.86 (8-C), 126.40 (d, *J* = 15.9 Hz, 4a-C), 127.26 (8a-C), 127.86 (d, *J* = 7.9 Hz, 7-C), 138.75 (3-C), 140.57 (pyridine 4-C), 150.19 (pyridine 2,6-C_2), 157.52 (d, *J* = 248.8 Hz, 5-C), 161.79 (1-C); ^{19}F NMR ((CD_3)$_2$SO) δ -121.19 (m, F); MS *m/z* 239.0622 (M - H)$^-$ ($C_{14}H_8FN_2O$ requires 239.0621).

5-Methoxy-3-(4-methylphenyl)isoquinolin-1-one (15b). BuLi (1.6 M in hexanes, 0.8 mL, 1.3 mmol) was added to dry $Pr^i{}_2NH$ (156 mg, 1.55 mmol) in dry THF (2.0 mL) at -78°C and the mixture was stirred at -78°C for 10 min. Compound **51** (250 mg, 1.3 mmol) in dry THF (2.0 mL) was added and the mixture was stirred for 1 h at -78°C. 4-Methylbenzonitrile (151 mg, 1.3 mmol) in dry THF (2.0 mL) was added at -78°C and the mixture was stirred for 1 h at -78°C, then at 20°C for 16 h. Water (1.0 mL) was added. The mixture was diluted with CH_2Cl_2, washed thrice with brine and dried. Evaporation and recrystallisation (EtOH) gave **15b** (16 mg, 5%) as pale yellow crystals: mp 249-251°C; ^{1}H NMR ((CD_3)$_2$SO) (COSY) δ 2.36 (3 H, s, Ph-Me), 3.94 (3 H, s, OMe), 6.92 (1 H, s, 4-H), 7.25 (1 H, dd, *J* = 8.0, 0.9 Hz, 6-H), 7.29 (2 H, d, *J* = 7.9 Hz, Ph 3,5-H_2), 7.41 (1 H, t, *J* = 8.0 Hz, 7-H), 7.66 (2 H, d, *J* = 8.2 Hz, Ph 2,6-H_2), 7.77 (1 H, dt, *J* = 8.0, 0.8 Hz, 8-H), 11.54 (1 H, br, N-H); ^{13}C NMR ((CD_3)$_2$SO) (HSQC / HMBC) δ 20.81 (Me), 55.92 (OMe), 96.35 (4-C), 112.22 (6-C), 118.23 (8-C), 125.66 (4a-C), 126.51 (Ph 2,6-C_2), 126.64 (7-C), 128.52 (8a-C), 129.40 (Ph 3,5-C_2), 131.22 (Ph 1-C), 138.88 (3-C), 139.62 (Ph 4-C), 154.33 (5-C), 162.54 (1-C); MS *m/z* 288.0995 (M + Na)$^+$ ($C_{17}H_{15}NaNO_2$ requires 288.1001).

3-(4-(1,1-Dimethylethyl)phenyl)-5-methoxyisoquinolin-1-one (15c). BuLi (2.5 M in hexanes, 0.42 mL, 1.0 mmol) was added to dry $Pr^i{}_2NH$ (126 mg, 1.2 mmol) in dry THF (2.0 mL) at -78°C and the mixture was stirred at -78°C for 10 min. Compound **51** (200 mg, 1.0 mmol) in dry THF (2.0 mL) was added and the mixture was stirred for 1 h at -78°C. 4-(1,1-Dimethylethyl)benzonitrile (164 mg, 1.0 mmol) in dry THF (2.0 mL) was added at -78°C and the mixture was stirred for 1 h at -78°C, then at 20°C for 16 h. H_2O (1.0 mL) was added and the mixture was diluted with CH_2Cl_2 and washed thrice with brine. Drying, evaporation and washing (EtOH) gave **15c** (72 mg, 23%) as a white solid: mp 249-250°C; IR ν_{max} 3451, 1633 cm^{-1}; ^{1}H NMR ((CD_3)$_2$SO) (COSY) δ 1.33 (9 H, s, Bu^t), 3.96 (3 H, s, OMe), 6.95 (1 H, s, 4-H), 7.27 (1 H, d, *J* = 7.9 Hz, 6-H), 7.44 (1 H, t, *J* = 8.0 Hz, 7-H), 7.52 (2 H, d, *J* = 8.5 Hz, Ph 3,5-H_2), 7.72 (2 H, d, *J* = 8.5 Hz, Ph 2,6-H_2), 7.79 (1 H, d, *J* = 8.0 Hz, 8-H), 11.54 (1 H, br, NH); ^{13}C NMR (($(CD_3)_2SO$) (HSQC / HMBC) δ 30.96 (C(*C*H_3)$_3$), 34.43 (*C*Me_3), 55.90 (OMe), 96.43 (4-C), 112.19 (6-C), 118.19 (8-C), 125.59 (Ph 3,5-C_2), 125.59 (8a-C), 126.30 (Ph 3,5-C_2), 126.63 (7-C), 128.46 (4a-C), 131.19 (Ph 1-C), 139.45 (3-C), 151.85 (Ph 4-C), 154.28 (5-C), 162.47 (1-C); MS *m/z* 308.1639 ($C_{20}H_{22}NO_2$ requires 308.1652).

5-Methoxy-3-(4-trifluoromethylphenyl)isoquinolin-1-one (15d). BuLi (1.6 M in hexanes, 0.8 mL, 1.3 mmol) was added to dry Pr^i_2NH (157 mg, 1.55 mmol) in dry THF (2.0 mL) at -78°C and the mixture was stirred at -78°C for 10 min. Compound **51** (250 mg, 1.3 mmol) in dry THF (2.0 mL) was added and the mixture was stirred for 1 h at -78°C. 4-Trifluoromethyl-benzonitrile (221 mg, 1.3 mmol) in dry THF (2.0 mL) was added at -78°C and the mixture was stirred for 1 h at -78°C, then at 20°C for 16 h. Water (1.0 mL) was added. The mixture was extracted with CH_2Cl_2. The extract was washed thrice with brine and dried. Evaporation and recrystallisation (EtOH) gave **15d** (113 mg, 27%) as white crystals: mp 259-260°C; ^1H NMR (($(CD_3)_2SO$) (COSY) δ 3.95 (3 H, s, Me), 7.04 (1 H, s, 4-H), 7.30 (1 H, d, *J* = 8.0 Hz, 6-H), 7.48 (1 H, t, *J* = 8.0 Hz, 7-H), 7.80 (1 H, d, *J* = 8.0 Hz, 8-H), 7.83 (2 H, d, *J* = 8.3 Hz, Ph3,5-H_2), 7.98 (2 H, d, *J* = 8.2 Hz, Ph 2,6-H_2), 11.75 (1 H, bs, N-H); ^{13}C NMR (($(CD_3)_2SO$) (HSQC / HMBC) δ 55.93 (Me), 98.28 (4-C), 112.46 (6-C), 118.18 (8-C), 124.03 (q, *J* = 270.5 Hz, CF_3), 125.51 (q, *J* = 3.8 Hz, Ph 3,5-C_2), 126.15 (4a-C), 127.40 (7-C), 127.49 (Ph 2,6-C_2), 127.93 (8a-C), 129.14 (q, *J* = 31.9 Hz, Ph 4-C), 137.85 (Ph 1-C), 137.96 (3-C), 154.54 (5-C), 162.30 (1-C); ^{19}F NMR (($(CD_3)_2SO$) δ -61.20 (s, CF_3); MS *m/z* 318.0740 $(M - H)^-$ ($C_{17}H_{11}F_3NO_2$ requires 318.0747).

3-(4-Chlorophenyl)-5-methoxyisoquinolin-1-one (15e). BuLi (1.6 M in hexanes, 0.8 mL, 1.3 mmol) was added to dry Pr^i_2NH (156 mg, 1.55 mmol) in dry THF (2.0 mL) at -78°C and the mixture was stirred at -78°C for 10 min. Compound **51** (250 mg, 1.3 mmol) in dry THF (2.0 mL) was added and the mixture was stirred for 1 h at -78°C. 4-Chlorobenzonitrile (178 mg, 1.3 mmol) in dry THF (2.0 mL) was added -78°C and the mixture was stirred for 1 h at -78°C, then at 20°C for 16 h. Water (1.0 mL) was added. The mixture was diluted with CH_2Cl_2, washed thrice with brine and dried. Evaporation and washing (EtOH) gave **15e** (86 mg, 23%) as an off-white solid: mp 243-245°C; ^1H NMR (($(CD_3)_2SO$) (COSY) δ 4.00 (3 H, s, Me), 7.01 (1 H, s, 4-H), 7.33 (1 H, d, *J* = 7.4 Hz, 6-H), 7.50 (1 H, t, *J* = 8.0 Hz, 7-H), 7.60 (2 H, d, *J* = 6.8 Hz, Ph 3,5-H_2), 7.84 (3 H, m, 8-H + Ph 2,6-H_2), 11.71 (1 H, br, N-H); ^{13}C NMR (($(CD_3)_2SO$) (HSQC / HMBC) δ 55.95 (Me), 97.34 (4-C), 112.39 (6-C), 118.23 (8-C), 125.89 (4a-C), 127.11 (7-C), 128.20 (8a-C), 128.56 (Ph 2,6-C_2), 128.79 (Ph 3,5-C_2), 132.88 (Ph 1-C), 133.91 (Ph 4-C), 138.42 (3-C), 154.44 (5-C), 162.44 (1-C); MS *m/z* 308.0413 $(M + Na)^+$ ($C_{16}H_{12}{}^{35}ClNNaO_2$ requires 308.0449).

3-(4-Bromophenyl)-5-methoxyisoquinolin-1-one (15f). BuLi (1.6 M in hexanes, 0.70 mL, 1.1 mmol) was added to dry Pr^i_2NH (131 mg, 1.3 mmol) in dry THF (2.0 mL) at -78°C and the mixture was stirred at -78°C for 10 min. Compound **51** (200 mg, 1.0 mmol) in dry THF (2.0 mL) was added and the mixture was stirred for 1 h at -78°C. 4-Bromobenzonitrile (188 mg, 1.0 mmol) in dry THF (2.0 mL) was added and the mixture was stirred for 1 h at -78°C, then at 20°C for 16 h. Water (1.0 mL) was added. The mixture was diluted with CH_2Cl_2, washed thrice with brine and dried. Evaporation and washing (EtOH) gave **15f** (48 mg, 14%) as a white solid: mp 263-264°C; IR ν_{max} 3526, 1665, 739 cm^{-1}; ^1H NMR (($(CD_3)_2SO$) δ 3.94 (3 H, s, Me), 6.95 (1 H, s, 4-H), 7.27 (1 H, d, *J* = 7.8 Hz, 6-H), 7.45 (1 H, t, *J* = 8.0 Hz, 7-H), 7.69 (4 H, m, Ph 2,3,5,6-H_4), 7.78 (1 H, d, *J* = 8.0 Hz, 8-H), 11.64 (1 H, br, NH); ^{13}C NMR (($(CD_3)_2SO$) (HSQC / HMBC) δ 55.95 (Me), 97.30 (4-C), 112.39 (6-C), 118.23 (8-C), 122.58 (Ph 4-C), 125.90 (4a-C), 127.11 (7-C), 128.19 (8a-C), 128.79 (Ph 2,6-C_2), 131.70 (Ph 3,5-

C_2), 133.24 (Ph 1-C), 138.49 (3-C), 154.44 (5-C), 162.44 (1-C); MS *m/z* 682.9978 (2 M + Na) ($C_{32}H_{24}{}^{79}Br^{81}BrN_2NaO_4$ requires 682.9981); 661.0145 (2 M + H) ($C_{32}H_{25}{}^{79}Br^{81}BrN_2O_4$ requires 661.0161); 351.9959 (M + Na) ($C_{16}H_{12}{}^{79}BrNNaO_2$ requires 351.9949); 332.0098 (M + H)$^+$ ($C_{16}H_{13}{}^{81}BrNO_2$ requires 332.0110); 330.0113 (M + H)$^+$ ($C_{16}H_{13}{}^{79}BrNO_2$ requires 330.0130).

5-Methoxy-3-(pyridin-4-yl)isoquinolin-1-one (15g). BuLi (1.6 M in hexanes, 0.80 mL, 1.3 mmol) was added to dry $Pr^i{}_2NH$ (157 mg, 1.55 mmol) in dry THF (2.0 mL) at -78°C and the mixture was stirred at -78°C for 10 min. Compound **51** (250 mg, 1.3 mmol) in dry THF (2.0 mL) was added and the mixture was stirred for 1 h at -78°C. 4-Cyanopyridine (135 mg, 1.3 mmol) in dry THF (2.0 mL) was added and the mixture was stirred for 1 h at -78°C, then at 20°C for 16 h. Water (1.0 mL) was added. The mixture was diluted with CH_2Cl_2, washed thrice with brine and dried. Evaporation and washing (EtOH) gave **15g** (284 mg, 87%) as a white solid: mp >360°C; IR ν_{max} 3431, 1673 cm^{-1}; ^{1}H NMR (($CD_3)_2SO$) (COSY) δ 3.96 (3 H, s, Me), 7.16 (1 H, s, 4-H), 7.31 (1 H, d, *J* = 7.9 Hz, 6-H), 7.50 (1 H, t, *J* = 8.0 Hz, 7-H), 7.80 (3 H, m, 8-H + pyridine 3,5-H_2), 8.66 (2 H, d, *J* = 6.1 Hz, pyridine 2,6-H_2), 11.74 (1 H, br, NH); ^{13}C NMR (($CD_3)_2SO$) (HSQC / HMBC) δ 56.04 (Me), 98.74 (4-C), 112.64 (6-C), 118.26 (8-C), 120.76 (pyridine 3,5-C_2), 126.55 (4a-C), 127.70 (8a-C), 127.93 (7-C), 136.82 (pyridine 4-C), 140.86 (3-C), 150.19 (pyridine 2,6-C_2), 154.70 (5-C), 162.39 (1-C); MS *m/z* 253.0972 (M + H) ($C_{15}H_{13}N_2O_2$ requires 253.0977).

3-(Benzo-1,3-dioxol-5-yl)-5-methoxyisoquinolin-1-one (15h). BuLi (1.6 M in hexanes, 0.7 mL, 1.1 mmol) was added to dry $Pr^i{}_2NH$ (125 mg, 1.2 mmol) in dry THF (2.0 mL) at -78°C and the mixture was stirred at -78°C for 10 min. Compound **51** (200 mg, 1.0 mmol) in dry THF (2.0 mL) was added and the mixture was stirred for 1 h at -78°C. 5-Cyanobenzo-1,3-dioxole (152 mg, 1.0 mmol) in dry THF (2.0 mL) was added at -78 °C and the mixture was stirred for 1 h at -78°C, then at 20°C for 16 h. H_2O (1.0 mL) was added. The mixture was diluted with CH_2Cl_2, washed thrice with brine and dried. Evaporation and washing (EtOH) gave **15h** (32 mg, 11%) as an off-white solid: mp 282-284°C; IR ν_{max} 3445, 1631 cm^{-1}; ^{1}H NMR (($CD_3)_2SO$) δ 3.93 (3 H, s, Me), 6.09 (2 H, s, CH_2), 6.86 (1 H, s, 4-C), 7.01 (1 H, d, *J* = 8.1 Hz, Ph 5-H), 7.25 (1 H, d, *J* = 7.2 Hz, 6-H), 7.27 (1 H, dd, *J* = 8.2, 1.9 Hz, Ph 6-H), 7.33 (1 H, d, *J* = 1.8 Hz, Ph 2-H), 7.40 (1 H, t, *J* = 8.0 Hz, 7-H), 7.74 (1 H, d, *J* = 8.0 Hz, 8-H), 11.45 (1 H, br, NH); ^{13}C NMR (($CD_3)_2SO$) (HSQC / HMBC / DEPT) δ 55.91 (OMe), 96.29 (4-C), 101.53 (CH_2), 107.03 (Ph 4-C), 108.54 (Ph 7-C), 112.17 (6-C), 118.21 (8-C), 120.92 (Ph 6-C), 125.54 (4a-C), 126.52 (7-C), 128.20 (Ph 5-C), 128.54 (8a-C), 139.42 (3-C), 147.72 (Ph 7a-C), 148.16 (Ph 3a-C), 154.27 (5-C), 162.51 (1-C); MS *m/z* 613.1595 (2 M + Na) ($C_{34}H_{26}N_2NaO_8$ requires 613.1587); 591.1768 (2 M + H) ($C_{34}H_{27}N_2O_8$ requires 591.1767); 318.0765 (M + Na) ($C_{17}H_{13}NNaO_4$ requires 318.0742); 296.0907 (M + H) ($C_{17}H_{14}NO_4$ requires 296.0923).

5-Methoxy-3-(thiophen-3-yl)isoquinolin-1-one (15i). BuLi (2.5 M in hexanes, 0.42 mL, 1.0 mmol) was added to dry $Pr^i{}_2NH$ (126 mg, 1.24 mmol) in dry THF (2.0 mL) at -78°C and the mixture was stirred at -78°C for 10 min. Compound **51** (200 mg, 1.0 mmol) in dry THF (2.0 mL) was added and the mixture was stirred for 1 h at -78°C. 3-Cyanothiophene (112 mg, 1.0 mmol) in dry THF (2.0 mL) was added at -78°C and the mixture was stirred for 1 h at -78°C, then at 20°C for 16 h. H_2O (1.0 mL) was added. The mixture was diluted with CH_2Cl_2 and washed thrice with brine. Evaporation and washing (EtOH) gave **15i** (37 mg, 14%) as a pale buff solid: mp 286-287°C; IR ν_{max} 3503, 1652, 746 cm^{-1}; ^{1}H NMR (($CD_3)_2SO$) (COSY) δ 3.94 (3 H, s, Me), 7.04 (1 H, s, 4-H), 7.24 (1 H, d, *J* = 7.9 Hz, 6-H), 7.40 (1 H, t, *J* = 8.0 Hz, 7-H), 7.66 (2 H, m, thiophene 4,5-H_2), 7.75 (1 H, d, *J* = 8.0 Hz, 8-H), 8.23 (1 H, d, *J* = 1.2

Hz, thiophene 2-H), 11.48 (1 H, br, NH); ^{13}C NMR (($CD_3)_2SO$) (HSQC / HMBC) δ 55.88 (Me), 95.99 (4-C), 112.28 (6-C), 118.24 (8-C), 123.36 (thiophene 2-C), 125.71 (8a-C), 125.78 (thiophene 5-C), 126.63 (7-C), 127.44 (thiophene 4-C), 128.44 (4a-C), 134.71 (thiophene 1-C), 135.20 (3-C), 154.30 (5-C), 162.29 (1-C); MS *m/z* 280.0399 ($C_{14}H_{11}NNaO_2S$ requires 280.0409).

5-Hydroxy-3-(4-trifluoromethylphenyl)isoquinolin-1-one (16b). Compound **15d** (51 mg, 0.16 mmol) was heated with BBr_3 in CH_2Cl_2 (1.0 M, 4.0 mL) at reflux for 16 h. The evaporation residue was treated with aq. NaOH (2.5 M, 3.5 mL) at 0°C and the mixture was stirred at 20°C for 3 h. The solution was acidified with aq. HCl (2 M). The solid was collected by filtration. Chromatography (EtOAc / petroleum ether 2:3 → 1:1) gave **16b** (3.9 mg, 8%) as a pale buff solid: mp 258-260°C; IR ν_{max} 3399, 3197, 1640, 1329, 1113, 1068 cm^{-1}; ^{1}H NMR (CD_3OD) δ 7.14 (1 H, dd, *J* = 7.8, 1.0 Hz, 6-H), 7.29 (1 H, s, 4-H), 7.37 (1 H, t, *J* = 7.9 Hz, 7-H), 7.81 (3 H, m, 8-H + Ph 3,5-H_2), 7.92 (2 H, d, *J* = 8.2 Hz, Ph 2,6-H_2); ^{13}C NMR (CD_3OD) (HSQC / HMBC) δ 102.03 (4-C), 117.66 (6-C), 118.54 (8-C), 125.54 (q, *J* = 268.9 Hz, CF_3), 126.94 (q, *J* = 3.8 Hz, Ph 3,5-C_2), 127.41 (4a-C), 128.36 (Ph 2,6-C_2), 128.90 (7-C), 129.23 (8a-C), 131.88 (q, *J* = 32.4 Hz, Ph 4-C), 138.33 (3-C), 139.73 (Ph 1-C), 154.84 (5-C), 165.60 (1-C); MS *m/z* 328.0568 $(M + Na)^+$ ($C_{16}H_{10}F_3NNaO_2$ requires 328.0561), 306.0740 $(M + H)^+$ ($C_{16}H_{11}F_3NO_2$ requires 306.0742); MS *m/z* 304.0577 $(M - H)^-$ ($C_{16}H_9F_3NO_2$ requires 304.0585).

5-Nitro-3-(4-trifluoromethylphenyl)isoquinolin-1-one (22i). Compound **30i** (78 mg, 220 μmol) was stirred with HBr in AcOH (33%, 3.5 mL) at 65°C for 7 h. Evaporation yielded **22l** (34.5 mg, 47%) as a yellow solid: mp: 292-294°C; ^{1}H NMR (($CD_3)_2SO$) δ 7.30 (1 H, s, 4-H), 7.70 (1 H, t, *J* = 8.0 Hz, 7-H), 7.89 (2 H, d, *J* = 8.5 Hz, Ph 3,5-H_2), 7.99 (2 H, d, *J* = 8.5 Hz, Ph 2,6-H_2), 8.49 (1 H, d, *J* = 7.5 Hz, 8-H), 8.60 (1 H, d, *J* = 7.5 Hz, 6-H), 12.26 (1 H, br, N-H); ^{13}C NMR (($CD_3)_2SO$) (HSQC / HMBC) δ 98.63 (4-C), 124.01 (q, *J* = 270.8 Hz, CF_3), 125.81 (q, *J* = 3.6 Hz, Ph 3,5-C_2), 126.36 (7-C), 126.89 (8a-C), 128.27 (Ph 2,6-C_2), 129.99 (8-C), 130.04 (q, *J* = 31.8 Hz, Ph 4-C), 130.59 (4a-C), 133.19 (6-C), 137.44 (Ph 1-C), 142.64 (3-C), 144.94 (5-C), 161.33 (1-C); ^{19}F NMR (($CD_3)_2SO$) δ -61.22 (s, CF_3); MS *m/z* 333.0493 $(M - H)^-$ ($C_{16}H_8F_3N_2O_3$ requires 333.0493).

3-(4-Fluorophenyl)-5-nitroisoquinolin-1-one (22j). Compound **30j** (16 mg, 50 μmol) was stirred with HBr in AcOH (33%, 1.0 mL) at 65°C for 7 h. Evaporation yielded **22j** (7.8 mg, 55%) as a yellow solid: mp >360°C; ^{1}H NMR (($CD_3)_2SO$) δ 7.19 (1 H, s, 4-H), 7.36 (2 H, t, *J* = 8.6 Hz, Ph 3,5-H_2), 7.65 (1 H, *J* = 7.9 Hz, 7-H), 7.84 (2 H, dd, *J* = 8.2, 5.3 Hz, Ph 2,6-H_2), 8.46 (1 H, d, *J* = 7.8 Hz, 8-H), 8.59 (1 H, d, *J* = 7.7 Hz, 6-H), 11.95 (1 H, br, NH); ^{13}C NMR (($CD_3)_2SO$) (HSQC / HMBC) δ 96.94 (4-C), 115.56 (d, *J* = 21.8 Hz, Ph 3,5-C_2), 125.41 (7-C), 126.38 (8a-C), 129.36 (8-C), 129.43 (Ph 2,6-C_2), 129.86 (4a-C), 130.63 (Ph 1-C), 132.83 (6-C), 143.07 (3-C), 144.55 (5-C), 160.99 (1-C), 162.94 (d, *J* = 246.6 Hz, Ph 4-C); ^{19}F NMR (($CD_3)_2SO$) δ -110.96 (m, F); MS *m/z* 283.0524 $(M - H)^-$ ($C_{15}H_8FN_2O_3$ requires 283.0524).

1,3-Dichloro-5-nitroisoquinoline (27). Aq. HNO_3 (67%, 430 mg) in conc. H_2SO_4 (3.0 mL) was added dropwise to 1,3-dichloroisoquinoline **26** (1.00 g, 5.1 mmol) in conc. H_2SO_4 (5.0 mL) at 5°C. The mixture was stirred at 0-5°C for 2 h, then poured onto ice. The precipitate was collected, washed (H_2O), dried and recrystallised (EtOAc / petroleum ether) to give **27** (1.12 g, 91%) as a yellow powder: mp 168-170°C (lit.[2] mp 168-170°C); ^{1}H NMR ($CDCl_3$) δ 7.80 (1 H, t, *J* = 7.8 Hz, 7-H), 8.55 (1 H, s, 4-H), 8.62 (1 H, dd, *J* = 7.8, 1.8 Hz, 6-H), 8.72 (1 H, dt, *J* = 8.5, 1.1 Hz, 8-H); ^{13}C NMR ($CDCl_3$) (HSQC / HMBC) δ 115.16 (4-C), 126.00 (4a-

C), 126.64 (7-C), 129.63 (6-C), 131.60 (8a-C), 133.12 (8-C), 144.01 (5-C), 147.08 (3-C), 151.75 (1-C).

1-Methoxy-3-(3-methylphenyl)-5-nitroisoquinoline (30b). Compound **28** (0.84 g, 3.5 mmol), Pd_2dba_3 (0.18 g, 0.35 mmol), SPhos (0.14 g, 0.70 mmol), K_3PO_4 (1.5 g, 7.1 mmol) and 3-methylphenylboronic acid (720 mg 5.3 mmol) were placed in a dry flask. Degassed toluene (20 mL) was added and the mixture was stirred at 100°C for 16 h. Evaporation and chromatography (hexane / EtOAc 15:1) gave **30b** (700 mg, 67%) as yellow crystals: mp 166-169°C; ^{1}H NMR ($CDCl_3$) δ 2.36 (3 H, s, ArMe), 4.11 (3 H, s, OMe), 7.13 (1 H, d, *J* = 7.8 Hz, Ar 4-H), 7.27 (1 H, t, *J* = 7.8 Hz, Ar 5-H), 7.36 (1 H, t, *J* = 7.4 Hz, 7-H), 7.83 (1 H, s, Ar 2-H), 7.85 (1 H, d, *J* = 7.6 Hz Ar 6-H), 8.23-8.26 (2 H, m, 6-H and 4-H), 8.39 (1 H, d, *J* = 7.4 Hz 8-H); ^{13}C NMR (HMBC / HMQC) δ 21.6 (ArMe), 54.0 (OMe), 104.9 (4-C), 124.2 (Ar 6-C), 124.2 (7-C), 127.6 (Ar 2-C) 128.5 (6-C), 128.6 (Ar 5-C), 130.1 (Ar 4-C), 131.1 (8-C), 131.3 (C_q), 138.2 (Ar 1-C), 138.5 (C_q),151.8 (3-C), 151.9 (5-C), 160.3 (1-C); MS *m/z* 295.1076 $(M + H)^+$ ($C_{17}H_{15}N_2O_3$ requires 295.1083).

1-Methoxy-3-(2-methoxyphenyl)-5-nitroisoquinoline (30d). Degassed PhMe (3.0 mL) was added to **28** (102 mg, 430 μmol), Pd_2dba_3 (11.5 mg, 13 μmol), SPhos (23 mg, 56 μmol), 2-methoxybenzeneboronic acid (150 mg, 1.0 mmol) and K_3PO_4 (204 mg, 1.0 mmol) in a dry flask. The mixture was stirred at 100°C for 16 h. The evaporation residue, in $CHCl_3$, was filtered. Chromatography (EtOAc / petroleum ether 1:99) gave **30d** (74 mg, 58%) as a yellow solid: mp 115-117°C; ^{1}H NMR ($CDCl_3$) δ 3.97 (3 H, s, PhOMe), 4.23 (3 H, s, 1-OMe), 7.06 (1 H, d, *J* = 8.3 Hz, Ph 3-H), 7.11 (1 H, td, *J* = 7.6, 1.1 Hz, Ph 4-H), 7.39 (1 H, td, *J* = 7.8, 1.8 Hz, Ph 5-H), 7.55 (1 H, t, *J* = 7.9 Hz, 7-H), 8.15 (1 H, dd, *J* = 7.8, 1.8 Hz, Ph 6-H), 8.43 (1 H, dd, *J* = 7.8, 1.3 Hz, 6-H), 8.59 (1 H, dt, *J* = 8.2, 1.1 Hz, 8-H), 8.78 (1 H, s, 4-H); ^{13}C NMR ($CDCl_3$) (HSQC / HMBC) δ 54.06 (1-OMe), 55.71 (PhOMe), 110.12 (4-C), 111.79 (Ph 3-C), 119.70 (8a-C), 120.87 (Ph 4-C), 124.36 (7-C), 128.18 (6-C), 130.17 (Ph 5-C), 130.91 (8-C), 131.22 (Ph 6-C), 146.81 (5-C), 157.82 (Ph 2-C), 160.04 (1-C); MS *m/z* 333.0858 $(M + Na)^+$ ($C_{17}H_{14}N_2NaO_4$ requires 333.0852), 311.1030 $(M + H)^+$ ($C_{17}H_{15}N_2O_4$ requires 311.1034).

1-Methoxy-3-(3-methoxyphenyl)-5-nitroisoquinoline (30e). Degassed PhMe (3.0 mL) was added to **28** (103 mg, 430 μmol), Pd_2dba_3 (11.6 mg, 13 μmol), SPhos (22 mg, 54 μmol), 3-methoxybenzeneboronic acid (153 mg, 1.0 mmol) and K_3PO_4 (203 mg, 0.96 mmol). The mixture was stirred at 100°C for 16 h. The evaporation residue, in $CHCl_3$, was filtered. Chromatography (EtOAc / petroleum ether 1:99) gave **30e** (81 mg, 81%) as a yellow solid: mp 87-90°C; ^{1}H NMR ($CDCl_3$) δ 3.93 (3 H, s, PhOMe), 4.28 (3 H, s, 1-OMe), 7.00 (1 H, m, Ph 6-H), 7.42 (1 H, t, *J* = 8.0 Hz, Ph 5-H), 7.57 (1 H, t, *J* = 8.0 Hz, 7-H), 7.78 (2 H, m, Ph 2,4-H_2), 8.48 (1 H, dd, *J* = 7.8, 1.3 Hz, 6-H), 8.51 (1 H, s, 4-H), 8.61 (1 H, dt, *J* = 8.2, 1.0 Hz, 8-H); ^{13}C NMR ($CDCl_3$) (HSQC / HMBC) δ 54.16 (PhOMe), 56.00 (1-OMe), 105.38 (4-C), 112.98 (Ph 4-C), 114.79 (Ph 6-C), 119.62 (Ph 2-C), 124.53 (7-C), 128.54 (6-C), 129.76 (Ph 5-C), 131.20 (8-C), 139.72 (Ph 3-C), 144.35 (5-C), 160.26 (1-C); MS *m/z* 311.1030 $(M + H)^+$ ($C_{17}H_{15}N_2O_4$ requires 311.1034).

1-Methoxy-5-nitro-3-(3-trifluoromethylphenyl)isoquinoline (30h). Method A. Degassed PhMe (3.0 mL) was added to **28** (101 mg, 420 μmol), Pd_2dba_3 (41 mg, 45 μmol), SPhos (40 mg, 100 μmol), 3-trifluoromethylbenzeneboronic acid (161 mg, 850 μmol) and K_3PO_4 (179 mg, 840 μmol). The mixture was stirred at 100°C for 16 h. The evaporation residue, in $CHCl_3$, was filtered. Chromatography (Et_2O / petroleum ether 1:199) gave **30h** (80.4 mg, 55%) as a yellow solid: mp 135-137°C; ^{1}H NMR ($CDCl_3$) δ 4.29 (3 H, s, Me), 7.62 (2 H, m, 7-H + Ph 5-H), 7.70 (1 H, d, *J* = 8.0 Hz, Ph 4-H), 8.34 (1 H, d, *J* = 7.9 Hz, Ph 6-H), 8.47 (1

H, s, Ph 2-H), 8.49 (1 H, dd, *J* = 7.7, 1.2 Hz, 6-H), 8.53 (1 H, s, 4-H), 8.62 (1 H, dt, *J* = 7.2, 1.0 Hz, 8-H); ^{13}C NMR ($CDCl_3$) (HSQC / HMBC) δ 54.31 (Me), 105.70 (4-C), 120.30 (8a-C), 123.98 (q, *J* = 3.9 Hz, Ph 2-C), 124.19 (q, *J* = 270.4 Hz, CF_3), 125.08 (7-C), 125.84 (q, *J* = 3.9 Hz, Ph 4-C), 126.89, 128.77 (6-C), 128.78, 29.20 (Ph 5-C), 130.12 (Ph 6-C), 131.27 (8-C), 131.27 (4a-C), 131.30 (q, *J* = 32.3 Hz, Ph 3-C), 139.47 (Ph 1-C), 145.04 (5-C), 150.25 (3-C), 160.75 (1-C); ^{19}F NMR ($CDCl_3$) δ -62.66 (s, CF_3); MS *m/z* 349.0826 $(M + H)^+$ ($C_{17}H_{12}F_3N_2O_3$ requires 349.0802).

1-Methoxy-5-nitro-3-(3-trifluoromethylphenyl)isoquinoline (30h). Method B. Dry DMF (8.0 mL) was added to **37** (300 mg, 1.1 mmol), Pd_2dba_3 (97 mg, 106 μmol), SPhos (99 mg, 0.21 mmol), 3-trifluoromethyl)benzeneboronic acid (403 mg, 2.1 mmol) and K_3PO_4 (675 mg, 3.2 mmol) and the mixture was stirred at 135°C for 16 h. The mixture was filtered (Celite® and the solvent was evaporated. Chromatography (EtOAc / petroleum ether 1:49) gave **30h** (232 mg, 63%) as a yellow solid, with properties as above.

1-Methoxy-5-nitro-3-(4-trifluoromethylphenyl)isoquinoline (30i). To **37** (300 mg, 1.1 mmol) in a dry flask was added Pd_2dba_3 (97 mg, 110 μmol), SPhos (99 mg, 210 μmol), 4-trifluoromethylphenylbenzeneboronic acid (403 mg, 2.1 mmol) and K_3PO_4 (675 mg, 3.2 mmol). Dry DMF (8.0 mL) was added and the mixture was stirred at 135°C for 16 h. The mixture was filtered through Celite® and the solvent was evaporated. Chromatography (EtOAc / petroleum ether 3:197) gave **30i** (209 mg, 57%) as a yellow solid: mp 125-127°C; ^{1}H NMR ($CDCl_3$) δ 4.25 (3 H, s, Me), 7.58 (1 H, t, *J* = 7.9 Hz, 7-H), 7.72 (2 H, d, *J* = 8.2 Hz, Ph 3,5-H_2), 8.25 (2 H, d, *J* = 8.1 Hz, Ph 2,6-H_2), 8.46 (1 H, dd, *J* = 7.8, 1.3 Hz, 6-H), 8.50 (1 H, s, 4-H), 8.58 (1 H, dt, *J* = 8.2, 1.1 Hz, 8-H); ^{13}C NMR ($CDCl_3$) (HSQC / HMBC) δ 54.23 (Me), 105.94 (4-C), 120.18 (4a-C), 125.11 (7-C), 125.57 (q, *J* = 3.6 Hz, Ph 3,5-C_2), 126.42 (q, *J* = 275.0 Hz, CF_3), 127.20 (Ph 2,6-C_2), 128.75 (6-C), 131.17 (8a-C), 131.20 (8-C), 141.79 (Ph 1-C), 144.82 (5-C), 150.01 (3-C), 160.56 (1-C); ^{19}F NMR ($CDCl_3$) δ -62.56 (s, CF_3); MS *m/z* 371.0601 $(M + Na)^+$ ($C_{17}H_{11}F_3N_2O_3Na$ requires 371.0622), 349.0775 $(M + H)^+$ ($C_{17}H_{12}F_3N_2O_3$ requires 349.0780).

3-(4-Fluorophenyl)-1-methoxy-5-nitroisoquinoline (30j). To **37** (200 mg, 710 μmol) in a dry flask was added Pd_2dba_3 (65 mg, 70 μmol), SPhos (66 mg, 140 μmol), 4-fluorobenzeneboronic acid (148 mg, 1.1 mmol) and K_3PO_4 (448 mg, 2.1 mmol). Dry DMF (6.0 mL) was added and the mixture was stirred at 135°C for 16 h. The evaporation residue, in $CHCl_3$, was filtered through Celite®. Chromatography (EtOAc / petroleum ether 1:99 → 1:49) gave **30j** (60 mg, 28%) as a yellow solid: mp 199-200°C; ^{1}H NMR ($CDCl_3$) δ 4.27 (3 H, s, Me), 7.19 (2 H, t, *J* = 8.5 Hz, Ph 3,5-H_2), 7.57 (1 H, t, *J* = 8.0 Hz, 7-H), 8.19 (2 H, m, Ph 2,6-H_2), 8.47 (1 H, s, 4-H), 8.49 (1 H, dd, *J* = 8.0, 1.0 Hz, 6-H), 8.61 (1 H, d, *J* = 8.0 Hz; ^{13}C NMR ($CDCl_3$) (HSQC / HMBC) δ 54.11 (Me), 104.79 (4-C), 115.68 (d, *J* = 21.5 Hz, Ph 3,5-C_2), 119.91 (4a-C), 124.53 (7-C), 128.72 (6-C), 128.97 (d, *J* = 8.3 Hz, Ph 2,6-C_2), 131.26 (8-C), 131.56 (8a-C), 134.81 (Ph 1-C), 144.91 (5-C), 150.93 (3-C), 160.58 (1-C), 163.75 (d, *J* = 248.3 Hz, Ph 4-C); MS *m/z* 299.0808 $(M + H)^+$ ($C_{16}H_{12}FN_2O_3$ requires 299.0834).

3-(2-Chlorophenyl)-1-methoxy-5-nitroisoquinoline (30k). Method A. To **28** (102 mg, 0.43 mmol) were added $Pd_2(dba)_3$ (13 mg, 14 μmol), SPhos (22 mg, 54 μmol), 2-chlorobenzeneboronic acid (202 mg, 1.3 mmol) and K_3PO_4 (202 mg, 0.95 mmol). Degassed PhMe (3.0 mL) was added and the mixture was stirred at 100°C. After 4.5 h, further $Pd_2(dba)_3$ (33.5 mg, 40 μmol) and SPhos (20.5 mg, 40 μmol) were added and the mixture was stirred at 100°C for a further 11.5 h. The evaporation residue, in $CHCl_3$, was filtered. Chromatography (EtOAc / petroleum ether 1:99) gave **30k** (135 mg, 100%) as a yellow solid, with properties as below.

3-(2-Chlorophenyl)-1-methoxy-5-nitroisoquinoline (30k). Method B. To **37** (200 mg, 710 μmol) were added Pd_2dba_3 (65 mg, 70 μmol), SPhos (66 mg, 140 μmol), 2-chlorobenzene-boronic acid (165 mg, 1.1 mmol) and K_3PO_4 (450 mg, 2.1 mmol). Dry DMF (7.5 mL) was added and the mixture was stirred at 135°C for 16 h. The solvent was evaporated. The residue, in $CHCl_3$, was filtered through Celite®. Chromatography (EtOAc / petroleum ether 3:197 → 1:19) gave **30k** (132 mg, 60%) as a yellow solid: mp 122-127°C; ^{1}H NMR ($CDCl_3$) δ 4.21 (3 H, s, Me), 7.39 (1 H, t, *J* = 7.2 Hz, Ph 5-H), 7.40 (1 H, t, *J* = 7.0 Hz, Ph 4-H), 7.53 (1 H, dd, *J* = 7.5, 1.5 Hz, Ph 6-H), 7.63 (1 H, t, *J* = 7.9 Hz, 7-H), 7.73 (1 H, dd, *J* = 7.8, 1.7 Hz, Ph 3-H), 8.37 (1 H, s, 4-H), 8.49 (1 H, dd, *J* = 7.8, 1.3 Hz, 6-H), 8.65 (1 H, dt, *J* = 8.2, 1.1 Hz, 8-H); ^{13}C NMR ($CDCl_3$) (HSQC / HMBC) δ 54.39 (Me), 110.19 (4-C), 119.79 (8a-C), 125.05 (7-C), 126.84 (Ph 4-C), 128.46 (6-C), 129.62 (Ph 5-C), 130.48 (Ph 6-C), 130.74 (4a-C), 131.13 (8-C), 131.67 (Ph 3-C), 144.95 (5-C), 160.29 (1-C); MS *m/z* 315.0533 (M + H)$^+$ ($C_{16}H_{12}{}^{35}ClN_2O_3$ requires 315.0538).

3-(3-Chlorophenyl)-1-methoxy-5-nitroisoquinoline (30l). Method A. To **28** (104 mg, 0.44 mmol) in a dry flask was added $Pd_2(dba)_3$ (44.0 mg, 48 μmol), SPhos (40.3 mg, 98 μmol), 3-chlorobenzeneboronic acid (198 mg, 1.3 mmol) and K_3PO_4 (180 mg, 0.85 mmol). Degassed toluene (3.0 mL) was added and the mixture was stirred at 100°C for 40 h. The evaporation residue, in $CHCl_3$, was filtered. Chromatography (Et_2O / petroleum ether 1: 99) gave **30l** (46 mg, 34%) as a yellow solid, with properties as below.

3-(3-Chlorophenyl)-1-methoxy-5-nitroisoquinoline (30l). Method B. To **37** (200 mg, 710 μmol) were added Pd_2dba_3 (65 mg, 70 μmol), SPhos (66 mg, 140 μmol), 3-chlorobenzene-boronic acid (166 mg, 1.1 mmol) and K_3PO_4 (450 mg, 2.1 mmol). Dry DMF (7.5 mL) was added and the mixture was stirred at 135°C for 16 h. The solvent was evaporated. The residue, in $CHCl_3$, was filtered through Celite®. Chromatography (EtOAc / petroleum ether 3:197 → 1:19) gave **30l** (116 mg, 52%) as a yellow solid: mp 134-141°C; ^{1}H NMR ($CDCl_3$) δ 4.18 (3 H, s, Me), 7.41 (2 H, m, Ph 5,6-H_2), 7.58 (1 H, t, *J* = 8.0 Hz, 7-H), 8.03 (1 H, dt, *J* = 6.9, 1.9 Hz, Ph 4-H), 8.18 (1 H, s, Ph 2-H), 8.47 (1 H, dd, *J* = 7.8, 1.2 Hz, 6-H), 8.48 (1 H, s, 4-H), 8.60 (1 H, dt, *J* = 8.2, 1.1, 8-H); ^{13}C NMR ($CDCl_3$) (HSQC / HMBC) δ 54.29 (Me), 105.53 (4-C), 120.18 (8a-C), 124.90 (7-C), 125.05 (Ph 4-C), 127.21 (Ph 2-C), 128.73 (6-C), 129.24 (Ph 6-C), 129.93 (Ph 5-C), 131.26 (8-C), 131.33 (4a-C), 134.81 (Ph 3-C), 140.43 (3a-C), 144.95 (5-C), 150.30 (3-C), 160.58 (1-C); MS *m/z* 315.0529 (M + H)$^+$ ($C_{16}H_{12}{}^{35}ClN_2O_3$ requires 315.0538).

3-(4-Chlorophenyl)-1-methoxy-5-nitroisoquinoline (30m). Degassed toluene (3.0 mL) was added to **37** (96 mg, 0.34 mmol), $Pd_2(dba)_3$ (31 mg, 34 μmol), SPhos (31.5 mg, 68 μmol), 4-chlorobenzeneboronic acid (79.3 mg, 0.51 mmol) and K_3PO_4 (215 mg, 1.01 mmol). The mixture was stirred at 100°C for 16 h. The evaporation residue, in $CHCl_3$, was filtered (Celite®). Chromatography (EtOAc / petroleum ether 1:39) gave **30m** (104 mg, 98%) as a yellow solid: mp 168-169°C; ^{1}H NMR ($CDCl_3$) δ 4.24 (3 H, s, Me), 7.46 (2 H, dd, *J* = 6.8, 2.0 Hz, Ph 2,6-H_2), 7.56 (1 H, t, *J* = 7.9 Hz, 7-H), 8.13 (2 H, dd, *J* = 6.8, 2.0 Hz, Ph 3,5-H_2), 8.46 (1 H, dd, *J* = 7.7, 1.2 Hz, 6-H), 8.47 (1 H, s, 4-H), 8.59 (1 H, dt, *J* = 8.2, 0.92 Hz, 8-H); ^{13}C NMR ($CDCl_3$) (HSQC / HMBC) δ 54.15 (Me), 105.06 (4-C), 120.04 (4a-C), 124.66 (7-C), 128.31 (Ph 3,5-C_2), 128.65 (6-C), 128.87 (Ph 2,6-C_2), 131.18 (8-C), 131.29 (8a-C), 135.41 (Ph 4-C), 137.07 (3-C), 150.67 (5-C), 160.81 (1-C); MS *m/z* 315.0531 (M + H)$^+$ ($C_{16}H_{11}{}^{35}ClN_2O_3$ requires 315.0536).

3-(2,6-Dichlorophenyl)-1-methoxy-5-nitroisoquinoline (30n). To **37** (240 mg, 850 μmol) was added Pd_2dba_3 (78 mg, 85 μmol), SPhos (79 mg, 170 μmol), 2,6-dichlorobenzeneboronic acid (243 mg, 1.3 mmol) and K_3PO_4 (541 mg, 2.5 mmol). Dry DMF (8.0 mL) was added and the mixture was stirred at 135°C for 16 h. Filtration (Celite®), evaporation and chromatography (EtOAc / petroleum ether 1: 99) gave **30n** (35 mg, 12%) as a yellow solid: mp 122-124°C; ^{1}H NMR ($CDCl_3$) δ 4.17 (3 H, s, Me), 7.30 (1 H, t, *J* = 8.7 Hz, Ph 4-H), 7.44 (2 H, d, *J* = 8.5 Hz, Ph 3,5-H_2), 7.66 (1 H, t, *J* = 8.1 Hz, 7-H), 8.08 (1 H, s, 4-H), 8.52 (1 H, dd, *J* = 7.8, 1.3 Hz, 6-H), 8.67 (1 H, dt, *J* = 8.2, 1.1 Hz, 8-H); ^{13}C NMR ($CDCl_3$) (HSQC / HMBC) δ 54.61 (Me), 111.16 (4-C), 120.08 (4a-C), 125.36 (7-C), 128.24 (Ph 3,5-C_2), 128.56 (6-C), 129.82 (Ph 4-C), 130.75 (8a-C), 131.32 (8-C), 134.86 (Ph 2,6-C_2), 138.19 (Ph 1-C), 144.94 (5-C), 149.95 (3-C), 160.73 (1-C); MS *m/z* 348.9740 (M - H)$^-$ ($C_{16}H_{11}{}^{35}Cl^{37}ClN_2O_3$ requires 348.9961).

3-(3-Cyanophenyl)-1-methoxy-5-nitroisoquinoline (30q). Method A. To **37** (152 mg, 0.64 mmol) in a dry flask was added $Pd_2(dba)_3$ (58.3 mg, 64 μmol), SPhos (60.8 mg, 0.15 mmol), 3-cyanobenzeneboronic acid (147 mg, 1.3 mmol) and K_3PO_4 (270 mg, 1.3 mmol). Degassed toluene (4.5 mL) was added and the mixture was stirred at 100°C for 16 h. The evaporation residue, in $CHCl_3$, was filtered. Chromatography (EtOAc / petroleum ether 1:40) gave **30q** (15.6 mg, 8%) as a yellow solid, with properties as below.

3-(3-Cyanophenyl)-1-methoxy-5-nitroisoquinoline (30q). Method B. To **37** (200 mg, 710 μmol) were added Pd_2dba_3 (65 mg, 70 μmol), SPhos (66 mg, 140 μmol), 3-cyanobenzeneboronic acid (148 mg, 1.1 mmol) and K_3PO_4 (448 mg, 2.1 mmol). Dry DMF (6.0 mL) was added and the mixture was stirred at 135°C for 16 h. The solvent was evaporated. The residue, in $CHCl_3$, was filtered through Celite®. Chromatography (EtOAc / petroleum ether 1:99 → 1:10) gave **30q** (20 mg, 9%): mp 195-196°C; ^{1}H NMR ($CDCl_3$) δ 4.29 (3 H, s, Me), 7.62 (1 H, t, *J* = 8.0 Hz, Ph 5-H), 7.64 (1 H, t, *J* = 8.0 Hz, 7-H), 7.72 (1 H, dt, *J* = 7.8, 1.3 Hz, Ph 6-H), 8.38 (1 H, dt, *J* = 8.2, 1.2 Hz, Ph 4-H), 8.52 (1 H, dd, *J* = 7.8, 1.3 Hz, 6-H), 8.55 (1 H, s, 4-H), 8.56 (1 H, s, Ph 2-H), 8.65 (1 H, dt, *J* = 8.2, 1.1 Hz, 8-H); ^{13}C NMR ($CDCl_3$) (HSQC / HMBC) δ 54.44 (Me), 105.90 (4-C), 113.31 (Ph 1-C), 121.03 (4a-C), 125.39 (7-C), 128.88 (6-C), 129.55 (Ph 2,5-C_2), 130.98 (Ph 6-C), 131.30 (8-C), 132.45 (Ph 4-C), 140.32 (CN), 145.67 (5-C), 160.92 (1-C).

3-(4-Cyanophenyl)-1-methoxy-5-nitroisoquinoline (30r). To **28** (151 mg, 630 μmol) were added Pd_2dba_3 (58 mg, 63 μmol), SPhos (58 mg, 140 μmol), 4-cyanobenzeneboronic acid (150 mg, 1.3 mmol) and K_3PO_4 (279 mg, 1.3 mmol). Degassed PhMe (4.5 mL) was added and the mixture was stirred at 100°C for 16 h. The evaporation residue, in $CHCl_3$, was filtered. Chromatography (EtOAc / petroleum ether 1:99) gave **30r** (53 mg, 28%) as a yellow solid: mp 206-210°C; ^{1}H NMR ($CDCl_3$) δ 4.30 (3 H, s, Me), 7.66 (1 H, t, *J* = 8.0 Hz, 7-H), 7.81 (2 H, d, *J* = 8.6 Hz, Ph 2,6-H_2), 8.32 (2 H, d, *J* = 8.6 Hz, Ph 3,5-H_2), 8.53 (1 H, dd, *J* = 7.8, 1.2 Hz, 6-H), 8.59 (1 H, s, 4-H), 8.66 (1 H, d, *J* = 8.2 Hz, 8-H); ^{13}C NMR ($CDCl_3$) (HSQC / HMBC) δ 54.36 (Me), 106.64 (4-C), 112.68 (CN), 118.79 (Ph 4-C), 120.80 (8a-C), 125.56 (7-C), 127.58 (Ph 2,6-H_2), 128.85 (6-C), 129.67 (4a-C), 131.26 (8-C), 132.53 (Ph 3,5-H_2), 142.86 (3-C), 145.16 (5-C), 149.59 (Ph 1-C), 160.84 (1-C).

5-Amino-1-methoxy-3-(3-methoxyphenyl)isoquinoline (31e). Compound **30e** (40 mg, 140 μmol) was stirred vigorously with Pd/C (10%, 44 mg) in EtOH (9 mL) under H_2 for 5 h. Filtration (Celite®) and evaporation yielded **31e** (31 mg, 81%) as a pale yellow solid: mp 146-149°C; ^{1}H NMR ($CDCl_3$) δ 3.91 (3 H, s, Ph OMe), 4.21 (3 H, s, 1-OMe), 6.93 (2 H, m, Ph 6-H + 6-H), 7.31 (1 H, t, *J* = 7.8 Hz, 7-H), 7.39 (1 H, t, *J* = 8.0 Hz, Ph 5-H), 7.60 (1 H, s, 4-H), 7.71 (3 H, m, Ph 2,4-H_2 + 8-H); ^{13}C NMR ($CDCl_3$) (HSQC / HMBC) δ 53.60 (1-OMe), 55.31

(Ph-OMe), 104.17 (4-C), 112.39 (Ph 2-C), 113.47 (Ph 6-C), 114.05 (6-C), 114.47 (8-C), 118.94 (Ph 4-C), 119.57 (8a-C), 126.75 (7-C), 128.36 (4a-C), 129.54 (Ph 5-C), 141.22 (Ph 1-C), 141.58 (5-C), 146.53 (3-C), 159.92 (Ph 3-C), 160.68 (1-C); MS *m/z* 303.1110 $(M + Na)^+$ ($C_{17}H_{16}N_2NaO_2$ requires 303.1110), 281.1278 $(M + H)^+$ ($C_{17}H_{17}N_2O_2$ requires 281.1290).

5-Amino-1-methoxy-3-(2-trifluoromethylphenyl)isoquinoline (31g). Compound **30g** (48 mg, 140 μmol) was stirred vigorously with Pt/C (1%, 53 mg) in EtOH (6.0 mL) under H_2 for 4 h. Filtration (Celite®) and evaporation gave **31g** (29 mg, 66%) as a yellow solid: mp 172-174°C; ^{1}H NMR ($CDCl_3$) δ 4.13 (OMe), 6.96 (1 H, dd, *J* = 7.5, 0.5 Hz, 6-H), 7.28 (1 H, s, 4-H), 7.37 (1 H, t, *J* = 7.5 Hz, 7-H), 7.51 (1 H, t, *J* = 7.5 Hz, Ph 5-H), 7.63 (2 H, m, Ph 4,6-H_2), 7.73 (1 H, d, *J* = 8.5 Hz, 8-H), 7.81 (1 H, d, *J* = 8.0 Hz, Ph 3-H); ^{13}C NMR ($CDCl_3$) (HSQC / HMBC) δ 53.85 (Me), 108.10 (4-C), 114.03 (6-C), 114.32 (8-C), 119.34 (8a-C), 124.28 (q, *J* = 272 Hz, CF_3), 126.69 (q, *J* = 5.1 Hz, Ph 3-C), 127.17 (7-C), 127.57 (4a-C), 127.81 (Ph 5-C), 128.54 (q, *J* = 30.1 Hz, Ph 2-C), 131.41 (Ph 6-C), 131.90 (Ph 4-C), 140.55 (Ph 1-C), 141.56 (5-C), 147.56 (3-C), 160.35 (1-C); MS *m/z* 341.0872 $(M + Na)^+$ ($C_{17}H_{13}F_3N_2NaO$ requires 341.0880).

5-Amino-1-methoxy-3-(3-trifluoromethylphenyl)isoquinoline (31h). Compound **30h** (152 mg, 440 μmol) was stirred vigorously with Pd/C (10%, 165 mg) in EtOH (8.0 mL) under H_2 for 5.5 h. Filtration (Celite®) and evaporation gave **31h** (120 mg, 87%) as a pale buff solid: mp 89-91°C; ^{1}H NMR ($CDCl_3$) δ 4.22 (3 H, s, Me), 6.94 (1 H, d, *J* = 7.4 Hz, 6-H), 7.33 (1 H, t, *J* = 7.8 Hz, 7-H), 7.55 (1 H, t, *J* = 7.7 Hz, Ph 5-H), 7.62 (2 H, m, 4-H + Ph 4-H), 7.70 (1 H, d, *J* = 8.2 Hz, 8-H), 8.32 (1 H, d, *J* = 7.6 Hz, Ph 6-H), 8.40 (1 H, s, Ph 2-H); ^{13}C NMR ($CDCl_3$) (HSQC / HMBC) δ 53.70 (Me), 104.50 (4-C), 114.37 (6-C), 114.57 (8-C), 119.87 (4a-C), 123.23 (q, *J* = 3.9 Hz, Ph 2-C), 124.39 (q, *J* = 270.8 Hz, CF_3), 124.63 (q, *J* = 3.9 Hz, Ph 4-C), 127.24 (7-C), 128.22 (8a-C), 129.00 (Ph 5-C), 129.66 (Ph 6-C), 130.95 (q, *J* = 31.8 Hz, Ph 3-C), 140.44 (Ph 1-C), 141.75 (5-C), 145.16 (3-C), 160.97 (1-C); ^{19}F NMR ($CDCl_3$) δ -62.50 (s, CF_3); MS *m/z* 319.1048 $(M + H)^+$ ($C_{17}H_{14}F_3N_2O$ requires 319.1060).

5-Amino-1-methoxy-3-(4-trifluoromethylphenyl)isoquinoline (31i). Compound **30i** (151 mg, 430 μmol) was stirred vigorously with Pd/C (10%, 165 mg) in EtOH (8.0 mL) under H_2 for 5.5 h. Filtration (Celite®) and evaporation gave **31i** (120 mg, 87%) as a buff solid: mp 141-142°C; ^{1}H NMR ($CDCl_3$) δ 4.21 (3 H, s, Me), 6.95 (1 H, dd, *J* = 7.5, 0.8 Hz, 6-H), 7.34 (1 H, t, *J* = 7.7 Hz, 7-H), 7.65 (1 H, s, 4-H), 7.71 (3 H, m, 8-H + Ph 3,5-H_2), 8.25 (2 H, d, *J* = 8.2 Hz, Ph 2,6-H_2); ^{13}C NMR ($CDCl_3$) (HSQC / HMBC) δ 53.70 (Me), 104.97 (4-C), 114.40 (6-C), 114.58 (8-C), 119.96 (4a-C), 123.26 (q, *J* = 269.9 Hz, CF_3), 125.48 (q, *J* = 3.9 Hz, Ph 3,5-C2), 126.68 (Ph 2,6-C_2), 127.37 (7-C), 128.16 (8a-C), 129.86 (q, *J* = 31.9 Hz, Ph 4-C), 141.78 (5-C), 143.06 (Ph 1-C), 145.21 (3-C), 160.97 (1-C); ^{19}F NMR ($CDCl_3$) δ -62.40 (s, CF_3); MS *m/z* 317.0907 $(M - H)^-$ ($C_{17}H_{12}F_3N_2O$ requires 317.0900).

5-Amino-3-(4-fluorophenyl)-1-methoxyisoquinoline (31j). Compound **30j** (108 mg, 360 μmol) was stirred vigorously with Pd/C (10%, 118 mg) in EtOH (8.0 mL) under H_2 for 6 h. Filtration (Celite®) and evaporation gave **31j** (90 mg, 69%) as an off-white solid: mp 154-155°C; ^{1}H NMR ($CDCl_3$) δ 4.21 (3 H, s, Me), 6.94 (1 H, dd, *J* = 7.5, 1.0 Hz, 6-H), 7.15 (2 H, m, Ph 3,5-H_2), 7.31 (1 H, t, *J* = 7.5 Hz, 7-H), 7.54 (1 H, s, 4-H), 7.69 (1 H, dt, *J* = 8.2, 1.0 Hz, 8-H), 8.13 (2 H, m, Ph 2,6-H_2); ^{13}C NMR ($CDCl_3$) (HSQC / HMBC) δ 53.62 (Me), 103.64 (4-C), 114.31 (6-C), 114.67 (8-C), 115.42 (d, *J* = 21.5 Hz, Ph 3,5-C_2), 119.40 (4a-C), 126.72 (7-C), 128.62 (d, *J* = 10.4 Hz, Ph 2,6-C_2), 128.53 (8a-C), 135.85 (d, *J* = 3.3 Hz, Ph 1-C), 141.37 (5-C), 145.98 (3-C), 160.82 (1-C), 163.04 (d, *J* = 246.0 Hz, Ph 4-C); MS *m/z* 269.1074 (M +

H)$^+$ ($C_{16}H_{14}FN_2O$ requires 269.1092); ^{19}F NMR ($CDCl_3$) δ -114.31 (m, F); MS *m/z* 267.0925 (M - H)$^-$ ($C_{16}H_{12}FN_2O$ requires 267.0932).

5-Amino-3-(2-chlorophenyl)-1-methoxyisoquinoline (31k). Compound **30k** (75 mg, 240 μmol) was stirred vigorously with Pt/C (1%, 84 mg) in EtOH (6.0 mL) under H_2 for 5 h. Filtration (Celite®) and evaporation gave **31k** (70 mg, 100%) as a yellow solid: mp 102-103 °C; ^{1}H NMR ($CDCl_3$) δ 4.18 (Me), 6.93 (1 H, dd, *J* = 7.5 Hz, 6-H), 7.35 (3 H, m, 7-H + Ph 4,5-H_2), 7.51 (1 H, dd, *J* = 8.0, 1.0 Hz, Ph 3-H), 7.56 (1 H, s, 4-H), 7.73 (1 H, d, *J* = 8.0 Hz, 8-H), 7.76 (1 H, dd, *J* = 7.5, 1.5 Hz, Ph 6-H); ^{13}C NMR ($CDCl_3$) (HSQC / HMBC) δ 53.78 (Me), 109.13 (4-C), 113.89 (6-C), 114.14 (8-C), 119.29 (4a-C), 126.75 (Ph 4-C), 127.17 (7-C), 127.59 (8a-C), 128.83 (Ph 5-C), 130.27 (Ph 3-C), 131.75 (Ph 6-C), 132.32 (Ph 1-C), 139.34 (Ph 2-C), 141.65 (5-C), 145.86 (3-C), 160.57 (1-C); MS *m/z* 285.0803 (M + H)$^+$ ($C_{16}H_{14}{}^{35}ClN_2O$ requires 285.0796).

5-Amino-3-(3-chlorophenyl)-1-methoxyisoquinoline (31l). Compound **30l** (75 mg, 240 μmol) was stirred vigorously with Pt/C (1%, 84 mg) in EtOH (6.0 mL) under H_2 for 5 h. Filtration (Celite®) and evaporation gave **31l** (62 mg, 91%) as a yellow solid: mp 94-95°C; ^{1}H NMR ($CDCl_3$) 4.20 (Me), 6.93 (1 H, dd, *J* = 7.5, 0.5 Hz, 6-H), 7.33 (3 H, m, 7-H + Ph 5,6-H_2), 7.57 (1 H, s, 4-H), 7.69 (1 H, d, *J* = 8.5 Hz, 8-H), 8.01 (1 H, d, *J* = 7.5 Hz, Ph 3-H), 8.14 (1 H, s, Ph 2-H); ^{13}C NMR ($CDCl_3$) (HSQC / HMBC) 53.69 (Me), 104.39 (4-C), 114.31 (6-C), 114.53 (8-C), 119.72 (4a-C), 124.47 (Ph 4-C), 126.57 (Ph 2-C), 127.07 (7-C), 128.19 (8a-C), 128.01 (Ph 5-C), 129.74 (Ph 6-C), 134.56 (Ph 3-C), 141.47 (5-C), 141.57 (Ph 1-C), 145.18 (3-C), 160.78 (1-C); MS *m/z* 285.0793 (M + H)$^+$ ($C_{16}H_{14}{}^{35}ClN_2O$ requires 285.0796).

5-Amino-3-(2,6-dichlorophenyl)-1-methoxyisoquinoline (31n). Compound **30n** (30 mg, 90 μmol) was stirred vigorously with Pd/C (10%, 33 mg) in EtOH (5.0 mL) under H_2 for 5 h. Filtration (Celite®) and evaporation gave **31n** (27 mg, 94%) as a pale orange solid: mp 103-104°C; ^{1}H NMR ($CDCl_3$) δ 4.12 (3 H, s, Me), 6.95 (1 H, dd, *J* = 7.5, 1.0 Hz, 6-H), 7.19 (1 H, d, *J* = 0.9 Hz, 4-H), 7.25 (1 H, t, *J* = 8.6 Hz, Ph 4-H), 7.36 (1 H, t, *J* = 7.6 Hz, 7-H), 7.42 (2 H, d, *J* = 8.3 Hz, Ph 3,5- H_2), 7.74 (1 H, dt, *J* = 8.2, 1.0 Hz, 8-H); ^{13}C NMR ($CDCl_3$) (HSQC / HMBC) δ 54.02 (Me), 109.70 (4-C), 114.00 (6-C), 114.37 (8-C), 127.36 (7-C), 128.15 (Ph 3,5-C_2), 129.30 (Ph 4-C), 119.69 (4a-C), 127.62 (8a-C), 135.25 (Ph 2,6-C_2), 138.92 (Ph 1-C), 141.65 (5-C), 144.58 (3-C), 160.94 (1-C); MS *m/z* 321.0356 (M + H)$^+$ ($C_{16}H_{13}{}^{35}Cl^{37}ClN_2O$ requires 321.0375), 319.0387 (M + H)$^+$ ($C_{16}H_{13}{}^{35}Cl_2N_2O$ requires 319.0405).

5-Amino-3-(4-hydroxyphenyl)-1-methoxyisoquinoline (31p). Compound **30p** (65 mg, 220 μmol) was stirred vigorously with Pd/C (10%, 71.5 mg) in EtOH (5.0 mL) under H_2 for 6 h. Filtration (Celite®) and evaporation gave **31p** (63 mg, 98%) as a yellow solid: mp >230°C; ^{1}H NMR (CD_3OD) δ 4.17 (3 H, s, Me), 6.87 (2 H, d, *J* = 7.0 Hz, Ph 3,5-H_2), 6.94 (1 H, d, *J* = 7.0 Hz, 6-H), 7.22 (1 H, t, *J* = 8.0 Hz, 7-H), 7.53 (1 H, d, *J* = 8.5 Hz, 8-H), 7.81 (1 H, s, 4-H), 8.07 (2 H, d, *J* = 7.0 Hz, Ph 2,6-H_2); ^{13}C NMR (CD_3OD) (HSQC / HMBC) δ 53.84 (Me), 104.35 (4-C), 114.14 (8-C), 114.63 (6-C), 116.24 (Ph 3,5-C_2), 120.52 (4a-C), 127.40 (7-C), 128.85 (Ph 2,6-C_2), 130.19 (8a-C), 132.74 (Ph 1-C), 144.38 (5-C), 147.73 (3-C), 158.86 (Ph 4-C), 161.74 (1-C); MS *m/z* 267.1123 (M + H)$^+$ ($C_{16}H_{15}N_2O_2$ requires 267.1135).

5-Amino-3-(3-cyanophenyl)-1-methoxyisoquinoline (31q). Compound **30q** (34 mg, 110 μmol) was stirred vigorously with Pd/C (10%, 38 mg) in EtOH (5.0 mL) under H_2 for 6.5 h. Filtration (Celite®), evaporation and chromatography (ethyl acetate / petroleum ether 1:39 → 1:4) gave **31q** (11.2 mg, 37%) as a golden buff solid: mp 183-184°C; ^{1}H NMR ($CDCl_3$) δ 4.22 (3 H, s, Me), 6.96 (1 H, dd, *J* = 7.5, 1.0 Hz, 6-H), 7.35 (1 H, t, *J* = 7.6 Hz, 7-H), 7.56 (1

H, t, J = 7.4 Hz, Ph 5-H), 7.62 (1 H, s, 4-H), 7.63 (1 H, dt, J = 7.9, 1.5 Hz, Ph 6-H), 7.70 (1 H, dt, J = 8.2, 0.9 Hz, 8-H), 8.36 (1 H, dt, J = 7.9, 1.3 Hz, Ph 4-H), 8.46 (1 H, t, J = 1.3 Hz, Ph 2-H); ^{13}C NMR ($CDCl_3$) (HSQC / HMBC) δ 53.80 (Me), 104.72 (4-C), 112.74 (Ph 3-C), 114.52 (6-C), 114.58 (8-C), 119.14 (CN), 120.03 (8a-C), 127.53 (7-C), 128.08 (4a-C), 129.31 (Ph 5-C), 130.26 (Ph 2-C), 130.49 (Ph 4-C), 131.27 (Ph 6-C), 140.84 (Ph 1-C), 141.81 (5-C), 144.22 (3-C), 161.09 (1-C); MS *m/z* 276.1128 $(M + H)^+$ ($C_{17}H_{14}N_3O$ requires 276.1137).

5-Amino-3-(4-cyanophenyl)-1-methoxyisoquinoline (31r). Compound **30r** (37 mg, 120 μmol) was stirred vigorously with Pd/C (10%, 41 mg) in EtOH (5.5 mL) under H_2 for 6.5 h. Filtration (Celite®), evaporation and chromatography (EtOAc / petroleum ether 1:39 → 1:4) gave **31r** (17.3 mg, 52%) as an amber-coloured solid: mp 203-204°C; ^{1}H NMR ($CDCl_3$) δ 4.21 (3 H, s, Me), 6.96 (1 H, dd, J = 7.6, 1.0 Hz, 6-H), 7.36 (1 H, t , J = 7.6 Hz, 7-H), 7.67 (1 H, s, 4-H), 7.70 (1 H, dt, J = 7.3, 0.9 Hz, 8-H), 7.74 (2 H, d, J = 8.7 Hz, Ph 3,5-H_2), 8.25 (2 H, d, J = 8.7 Hz, Ph 2,6-H_2); ^{13}C NMR ($CDCl_3$) (HSQC / HMBC) δ 53.76 (Me), 105.55 (4-C), 111.27 (Ph 4-C), 114.58 (6-C), 114.61 (8-C), 119.17 (CN), 120.18 (4a-C), 126.89 (Ph 2,6-C_2), 127.77 (7-C), 127.98 (8a-C), 132.39 (Ph 3,5-C_2), 141.93 (5-C). 143.93 (Ph 1-C), 144.45 (3-C), 161.04 (1-C); MS *m/z* 276.1124 $(M + H)^+$ ($C_{17}H_{14}N_3O$ requires 276.1137).

Isoquinoline-1,3-dione (33). 2-Carboxyphenylacetic acid **32** (20.0 g, 111 mmol) was heated with finely ground urea (7.33 g, 122 mmol) at 175-185°C for 2 h. Cooling and recrystallisation (MeOH) gave **33** (12.0 g, 67%%) as an off-white solid: mp 220-222°C (lit.[3] mp 236-238°C); ^{1}H NMR ($(CD_3)_2SO$) δ 4.09 (3 H, s, CH_2), 7.44 (1 H, d, J = 7.6 Hz, 5-H), 7.51 (1 H, t, J = 7.6 Hz, 7-H), 7.70 (1 H, td, J = 7.6, 1.2 Hz, 6-H), 8.07 (1 H, dd, J = 7.8, 1.1 Hz, 8-H), 11.36 (1 H, s, N-H); ^{13}C NMR ($(CD_3)_2SO$) (HSQC / HMBC) δ 35.92 (4-C), 124.95 (8a-C), 127.16 (7-C), 127.41 (8-C), 127.87 (5-C), 133.47 (6-C), 136.66 (4a-C), 165.34 (1-C), 170.99 (3-C).

1,3-Dibromoisoquinoline (34). Method A. PBr_3 (10 mL) was added slowly to **33** (1.41 g, 8.7 mmol) and the mixture was heated at reflux for 16 h. The evaporation residue was quenched (sat. aq. $NaHCO_3$) and extracted thrice with $CHCl_3$. Chromatography (EtOAc / petroleum ether 3:17), followed by chromatography (EtOAc / petroleum ether 1:49) gave **34** (358 mg, 14%) as white crystals: mp 148-150°C (lit.[4] mp 147-147.5°C); ^{1}H NMR ($(CD_3)_2SO$) δ 7.93 (1 H, td, J = 6.9, 1.3 Hz, 6-H), 8.00 (1 H, td, J = 6.9, 1.2 Hz, 7-H), 8.10 (1 H, dt, J = 8.1, 0.6 Hz, 5-H), 8.27 (1 H, d, J = 8.4 Hz, 8-H), 8.38 (1 H, s, 4-H); ^{13}C NMR ($(CD_3)_2SO$) (HSQC / HMBC) δ 124.66 (4-C), 126.85 (5-C), 127.13 (8a-C), 127.68 (4a-C), 127.89 (8-C), 130.69 (6-C), 132.69 (7-C), 138.74 (3-C), 143.18 (1-C). Further elution gave **35** (66 mg, 4%) as white crystals: mp 61-63°C (lit.[4] mp 63-64°C; ^{1}H NMR ($(CD_3)_2SO$) (NOE) δ 7.80 (1 H, td, J = 8.0, 1.2 Hz, 6-H), 7.90 (1 H, dt, J = 8.3, 1.2 Hz, 7-H), 8.03 (1 H, d, J = 8.3 Hz, 5-H), 8.23 (1 H, d, J = 8.3 Hz, 8-H), 8.27 (1 H, s, 4-H), 9.24 (1 H, s, 1-H); ^{13}C NMR ($(CD_3)_2SO$) (HSQC / HMBC) δ 123.53 (4-C), 125.76 (5-C), 127.25 (4a-C), 127.80 (8-C), 128.13 (6-C), 131.68 (7-C), 135.19 (3-C), 137.46 (8a-C), 153.19 (1-C).

1,3-Dibromoisoquinoline (34). Method B. Isoquinoline-1,3-dione **33** (3.00 g, 18.6 mmol) was heated under reflux with $POBr_3$ (10.7 g, 37 mmol) in 1,4-dioxane (20 mL) for 22 h. The mixture was quenched with MeOH, then water. The mixture, in water, was extracted thrice with CH_2Cl_2. Drying, evaporation and recrystallisation (PhMe) gave **34** (1.87 g, 35%) as an off-white solid, with properties as above.

4-Phenylethynylbenzonitrile (43). $(Ph_3P)_2PdCl_2$ (96.5 mg, 140 μmol), CuI (52 mg, 300 μmol), sodium ascorbate (33 mg, 160 μmol) and 4-bromobenzonitrile **42** (500 mg, 2.75 mmol) were mixed in a dry flask. Degassed THF (10 mL) and dry $Pr^i{}_2NH$ (5.0 mL) were added and the mixture was stirred at 50 °C for 30 min. Phenylethyne (281 mg, 2.75 mmol) was added and the mixture was stirred for 16 h at 50 °C. The mixture was filtered through Celite®. Evaporation and chromatography (ethyl acetate / petroleum ether 1:199 → 1:99) gave **43** (394 mg, 70%) as an off-white solid: mp 78-79°C (lit.[5] mp 91-92°C); ^{1}H NMR ($CDCl_3$) δ 7.38 (3 H, m, Ph 3,4,5-H_3), 7.55 (2 H, m, Ph 2,6-H_2), 7.60 (4 H, m, NCPh 2,3,5,6-H_4); ^{13}C NMR ($CDCl_3$) (HSQC / HMBC) δ 87.66 (ethyne 1-C), 93.69 ((ethyne 2-C), 111.34 (CN), 118.42 (NCPh 1-C), 122.11 (Ph 1-C), 128.11 (NCPh 4-C), 128.42 (Ph 3,5-C_2), 129.04 (Ph 4-C), 131.69 (Ph 2,6-C_2), 131.93 (NCPh 2,6-C_2), 131.95 (NCPh 3,5-C_2).

4-Dimethylaminomethylbenzonitrile (45a). 4-Bromomethylbenzonitrile (1.00 g, 5.1 mmol) was stirred with aq. Me_2NH (40%, 4.0 mL) for 16 h. The mixture was diluted with water and extracted with CH_2Cl_2. The extract was washed with aqueous citric acid (10%). The combined aqueous solutions were basified by addition of aq. NaOH (15%) and extracted with CH_2Cl_2. The combined solutions in CH_2Cl_2 were dried and the solvent was evaporated to give **45a** (420 mg, 51%) as a colourless oil (lit.[6] oil): ^{1}H NMR ($CDCl_3$) δ 2.24 (6 H, s, NMe_2), 3.47 (2 H, s, CH_2), 7.43 (2 H, d, J = 8.2 Hz, 3,5-H_2), 7.61 (2 H, d, J = 8.2 Hz, 2,6-H_2); ^{13}C NMR ($CDCl_3$) (HSQC / HMBC) δ 45.42 (NMe_2), 63.83 (CH_2), 110.92 (1-C), 118.95 (CN), 129.51 (3,5-C_2), 132.13 (2,6-C_2), 144.62 (4-C).

4-(Piperidin-1-ylmethyl)benzonitrile (45b). 4-Bromomethylbenzonitrile (500 mg, 2.6 mmol) was stirred with K_2CO_3 (388 mg, 2.8 mmol) and piperidine (238 mg, 2.8 mmol) in dry DMF (6.0 mL) at 20°C for 3 h, then at 90°C for 3 d. The mixture was then cooled to 20°C. Water (18 mL) was added and the mixture was stirred for 30 min. This mixture was diluted with EtOAc. The suspension was washed thrice with brine and dried. Evaporation of the solvent gave **45b** (340 mg, 67%) as a pale orange oil (lit.[7] oil): ^{1}H NMR ($CDCl_3$) δ 1.44 (2 H, m, piperidine 4-H_2), 1.57 (4 H, m, piperidine 3,5-H_4), 2.36 (4 H, m, piperidine 2,6-H_4), 3.50 (2 H, s, $PhCH_2$), 7.44 (2 H, d, J = 8.0 Hz, Ph 3,5-H_2), 7.59 (2 H, d, J = 8.3 Hz, Ph 2,6-H_2); ^{13}C NMR ($CDCl_3$) (HSQC / HMBC) δ 24.20 (piperidine 4-C), 25.94 (piperidine 3,5-C_2), 54.60 (piperidine 2,6-C_2), 63.25 ($PhCH_2$), 110.58 (Ph 1-C), 119.07 (CN), 129.46 (Ph 3,5-C_2), 131.99 (Ph 2,6-C_2), 144.84 (Ph 4-C).

4-(Pyrrolidin-1-ylmethyl)benzonitrile (45c). 4-Bromomethylbenzonitrile (1.00 g, 5.1 mmol) in dry THF (15 mL) was stirred with Et_3N (1.08 g, 10.7 mmol) and pyrrolidine (760 mg, 10.7 mmol) for 2 d. This mixture was diluted with EtOAc, washed thrice with water and dried. Evaporation of the solvent gave **45c** (935 mg, 98%) as a pale orange oil (lit.[8] oil): ^{1}H NMR ($CDCl_3$) δ 1.79 (4 H, m, pyrrolidine 2,3-H_4), 2.50 (4 H, m, pyrrolidine 1,4-H_4), 3.65 (2 H, s, $PhCH_2$), 7.44 (2 H, d, J = 8.5 Hz, Ph 3,5-H_2), 7.59 (2 H, d, J = 8.4 Hz, Ph 2,6-H_2); ^{13}C NMR ($CDCl_3$) (HSQC / HMBC) δ 23.53 (pyrrolidine 2,3-C_2), 54.24 (pyrrolidine 1,4-C_2), 60.23 ($PhCH_2$), 110.67 (Ph 1-C), 119.05 (CN), 129.29 (Ph 3,5-C_2), 132.10 (Ph 2,6-C_2), 145.29 (Ph 4-C).

4-((4-Methylpiperazin-1-yl)methyl)benzonitrile (45d). 4-Bromomethylbenzonitrile (1.0 g, 5.1 mmol) was stirred for 24 h with Et_3N (1.03 g, 10.2 mmol) and 1-methylpiperazine (760 mg, 7.6 mmol) in dry CH_2Cl_2 (10 mL). This mixture was diluted with CH_2Cl_2 and washed thrice with sat. aq. $NaHCO_3$ and H_2O. Drying and evaporation gave **45d** (650 mg, 59%) as a white solid: mp 65-67°C (lit.[9] mp 62-64°C): ^{1}H NMR ($CDCl_3$) δ 2.29 (3 H, s, Me), 2.47 (8 H, m, piperazine 2,3,5,6-H_8), 3.54 (2 H, s, $PhCH_2$), 7.43 (2 H, d, J = 8.2 Hz, Ph 3,5-H_2), 7.58 (2

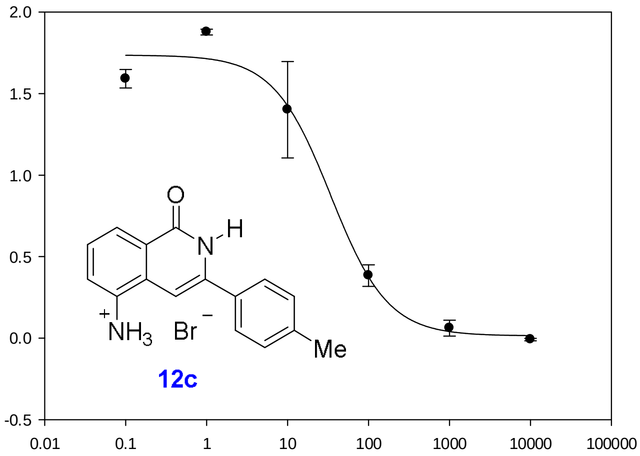
H, d, J = 8.2 Hz, Ph 2,6-H_2); ^{13}C NMR ($CDCl_3$) (HSQC / HMBC) δ 45.98 (Me), 53.08 (piperazine 2,6-C_2), 55.05 (piperazine 3,5-C_2), 62.38 (Ph*C*H_2), 110.85 (Ph 1-C), 118.97 (CN), 129.49 (Ph 3,5-C_2), 132.10 (Ph 2,6-C_2), 144.23 (Ph 4-C).

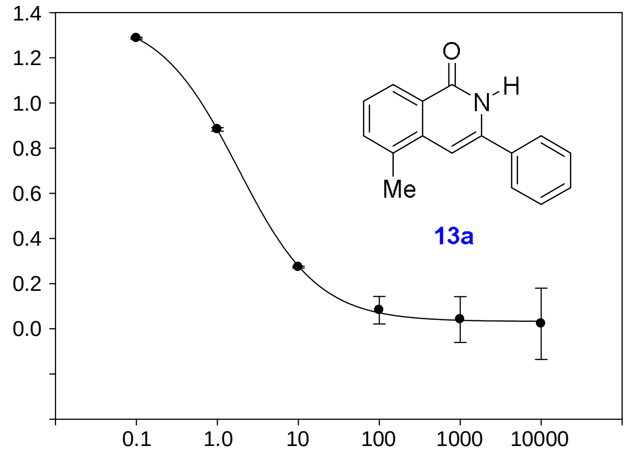
Ferrocenenitrile (47). Ferrocenecarboxylic acid **46** (500 mg, 2.2 mmol) was stirred with oxalyl chloride (634 mg, 5.0 mmol) for 1 h. The evaporation residue, in dry THF (5.0 mL), was added dropwise to saturated NH_3 in Et_2O (25 mL). After 15 min, H_2O (20 mL) was added and organic layer was washed thrice (H_2O). Drying and evaporation gave ferrocene-carboxamide (370 mg, 74%) as a pale orange solid: mp 168-169°C (lit.[10] mp 168-171°C); ^{1}H NMR ($(CD_3)_2SO$) δ 4.15 (5 H, s, Fc'-H_5), 4.32 (2 H, br, Fc 3,4-H_2), 4.74 (2 H, br, Fc 2,5-H_2), 6.91 (1 H, br, NH), 7.28 (1 H, br, NH); ^{13}C NMR ($(CD_3)_2SO$) (HSQC / HMBC) δ 68.49 (Fc 2,5-C_2), 69.31 (Fc'-C_5), 69.91 (Fc 3,4-C_2), 76.42 (Fc 1-C), 171.01 (C=O). This material (352 mg, 1.5 mmol) was stirred with $POCl_3$ (3.5 mL) at 120°C for 2 h, followed by cooling to 0°C and quench with H_2O (1.0 mL). The mixture was diluted with EtOAc and washed thrice with H_2O. Drying and evaporation gave **47** (360 mg, 99%) as a dark orange solid: mp 105-107°C (lit.[11] mp 106-106.5°C); ^{1}H NMR ($(CD_3)_2SO$) δ 4.34 (5 H, s, Fc'-H_5), 4.50 (2 H, s, Fc 3,4-H_2), 4.83 (2 H, s, Fc 2,5-H_2); ^{13}C NMR ($(CD_3)_2SO$) (HSQC / HMBC) δ 51.05 (Fc 1-C), 70.32 (Fc'-C_5), 71.00 (Fc 3,4-C_2), 71.61 (Fc 2,5-C_2), 120.21 (CN).

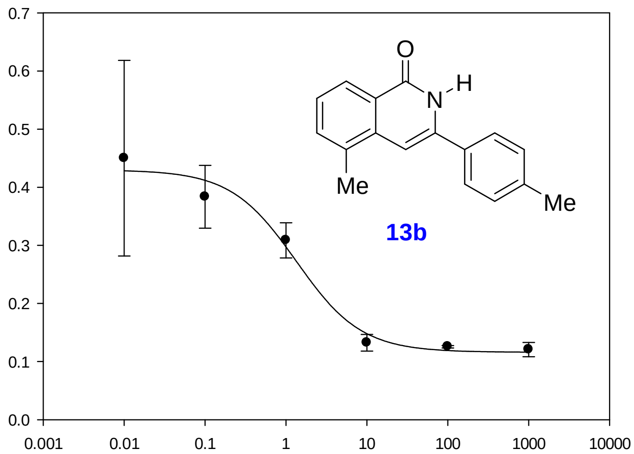
3-Fluoro-2,N,N-trimethylbenzamide (49). $SOCl_2$ (3.0 g, 25 mmol) was added to **48** (1.00 g, 6.5 mmol) at 0°C. The mixture was heated at reflux for 16 h, then the excess $SOCl_2$ was evaporated. The residue, in CH_2Cl_2 (1.0 mL), was added dropwise to a stirred solution of Me_2NH in water (40 %, 3.7 mL) at 10°C. The mixture was then stirred at 20°C for 2.5 h. The mixture was diluted with CH_2Cl_2, then washed thrice with water and dried. Evaporation gave **49** (1.00 g, 85%) as a pale orange oil: ^{1}H NMR ($CDCl_3$) δ 2.19 (3 H, d, J = 2.0 Hz, 2-Me), 2.82 (3 H, s, N-Me), 3.13 (3 H, s, N-Me), 6.96 (1 H, d, J = 7.6 Hz, 6-H), 7.01 (1 H, ddd, J = 7.4, 6.1, 0.8 Hz, 4-H), 7.18 (1 H, m, 5-H); ^{13}C NMR ($CDCl_3$) (HSQC / HMBC) δ 11.20 (d, J = 4.5 Hz, 2-Me), 34.54 (N-Me), 38.28 (N-Me), 115.31 (d, J = 22.5 Hz, 4-C), 121.39 (d, J = 3.6 Hz, 6-C), 121.59 (d, J = 18.3 Hz, 2-C), 127.45 (d, J = 8.6 Hz, 5-C), 138.90 (d, J = 3.9 Hz, 1-C), 161.25 (d, J = 244.5 Hz, 3-C), 169.98 (d, J = 3.3 Hz, C=O); ^{19}F NMR ($CDCl_3$) δ -115.66 (d, J = 6.1 Hz, 3-F); MS *m/z* $(M + H)^+$ 182.0973 ($C_{10}H_{13}FNO$ requires 182.0976).

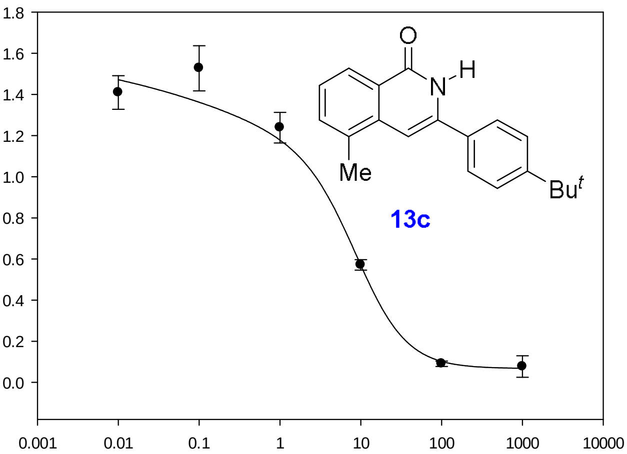
3-Methoxy-2,N,N-trimethylbenzamide (51). $SOCl_2$ (2.74 g, 23 mmol) was added to **50** (1.00 g, 6.0 mmol) at 0°C. The mixture was heated at reflux for 16 h, then the excess $SOCl_2$ was evaporated. The residue, in CH_2Cl_2 (3.0 mL), was added dropwise to a stirred solution of Me_2NH in water (40 %, 3.7 mL) at 10°C. The mixture was then stirred at 20°C for 3.5 h. The mixture was diluted with CH_2Cl_2, then washed thrice with water and dried. The solvent was evaporated to give **51** (980 mg, 85%) as a pale yellow oil: ^{1}H NMR ($CDCl_3$) δ 2.12 (3 H, s, 2-Me), 2.81 (3 H, s, N-Me), 3.12 (3 H, s, N-Me), 3.82 (3 H, s, OMe), 6.76 (1 H, dd, J = 7.6, 0.8 Hz, 4-H), 6.81 (1 H, d, J = 8.2 Hz, 6-H), 7.18 (1 H, t, J = 7.6 Hz, 5-H); ^{13}C NMR ($CDCl_3$) (HSQC / HMBC) δ 12.42 (Me), 34.44 (N-Me), 38.24 (N-Me), 55.44 (OMe), 110.10 (6-C), 117.73 (4-C), 122.69 (2-C), 126.97 (5-C), 137.99 (1-C), 157.76 (3-C), 171.23 (C=O); MS *m/z* 216.0988 $(M + Na)^+$ ($C_{11}H_{15}NNaO_2$ requires 216.0995).

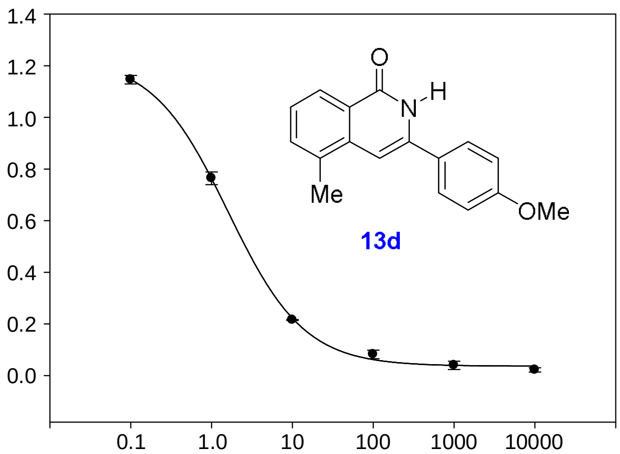
Section C: Examples of graphs of enzyme activity *vs.* concentration for inhibition of tankyrase-2 by isoquinolin-1-ones. X-Axes – concentration of inhibitor (nM); Y-axes – optical density (490 nm).

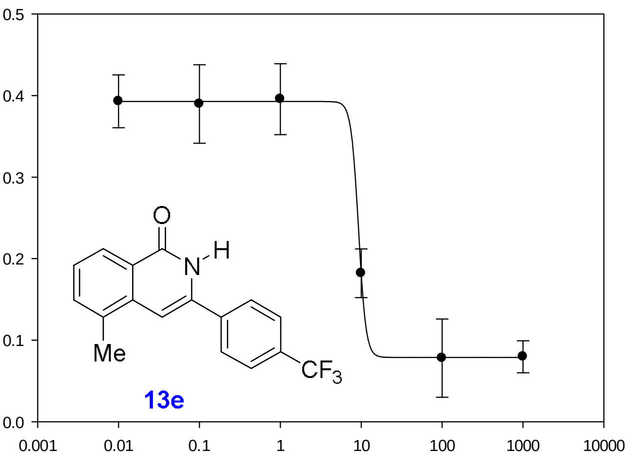


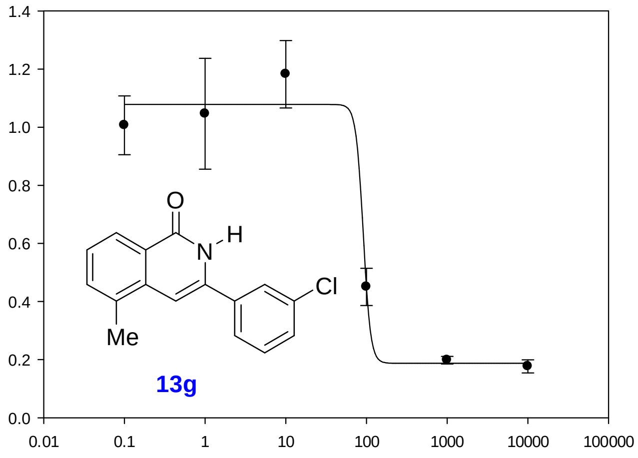








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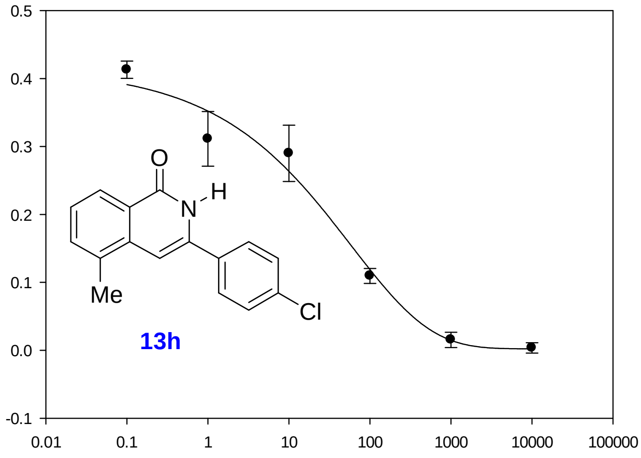
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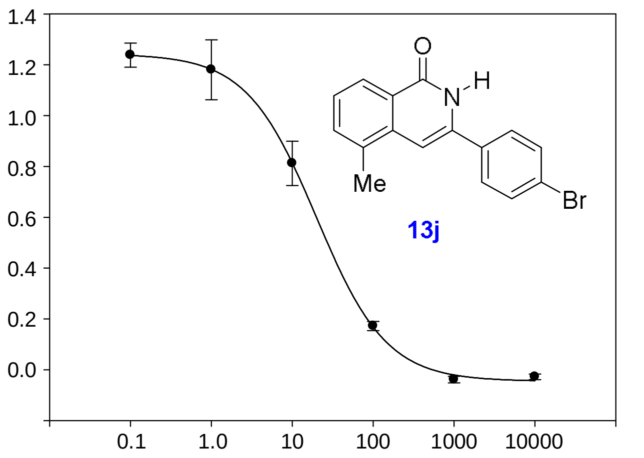
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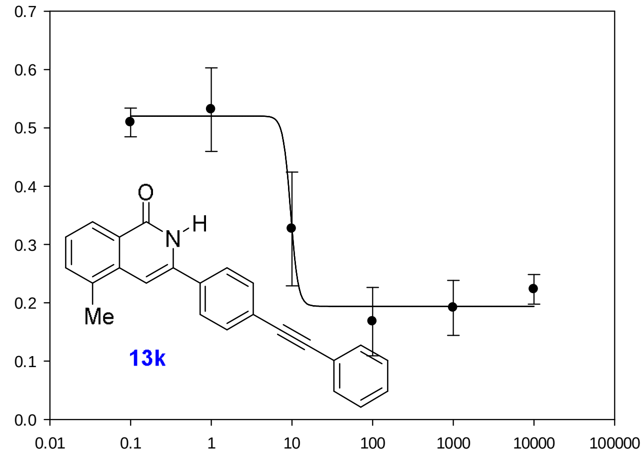
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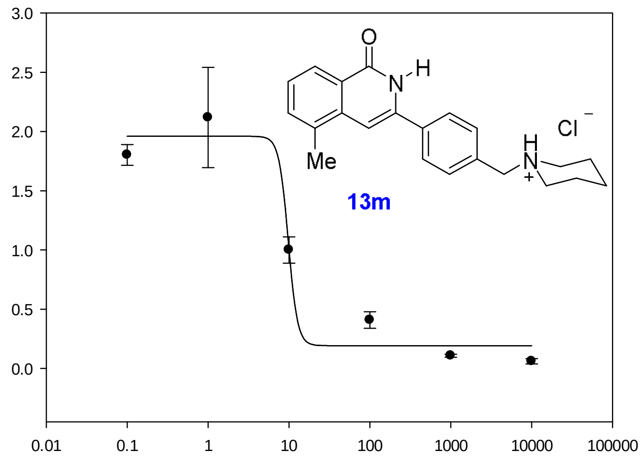
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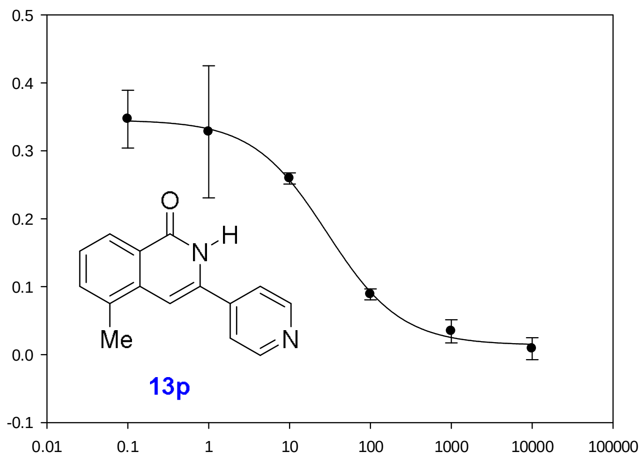
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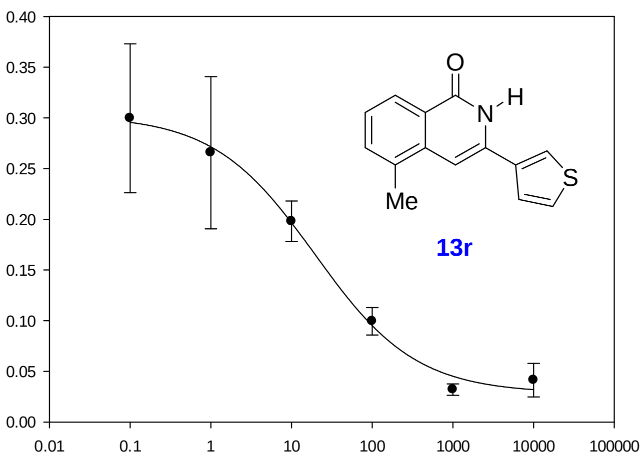
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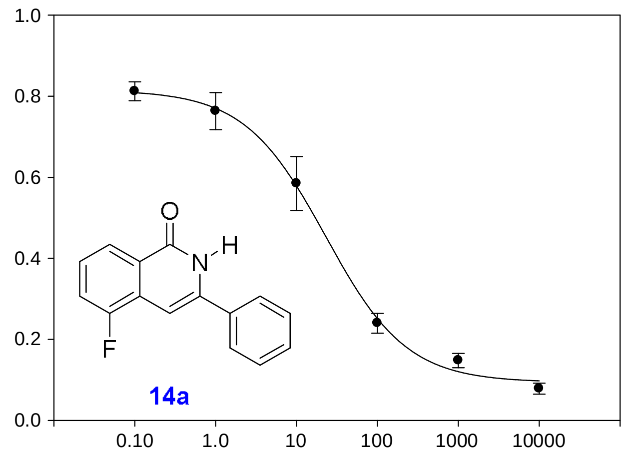
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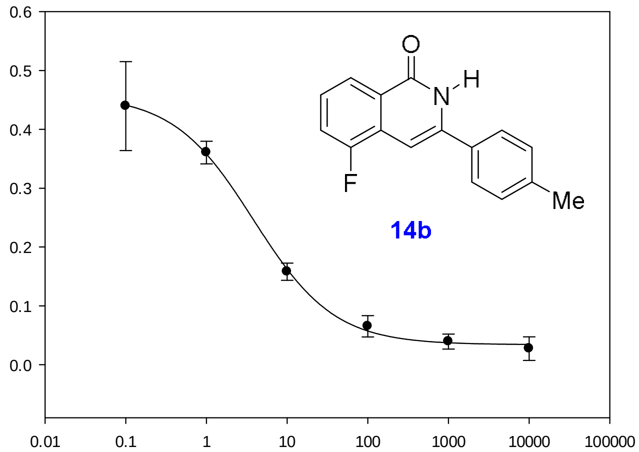
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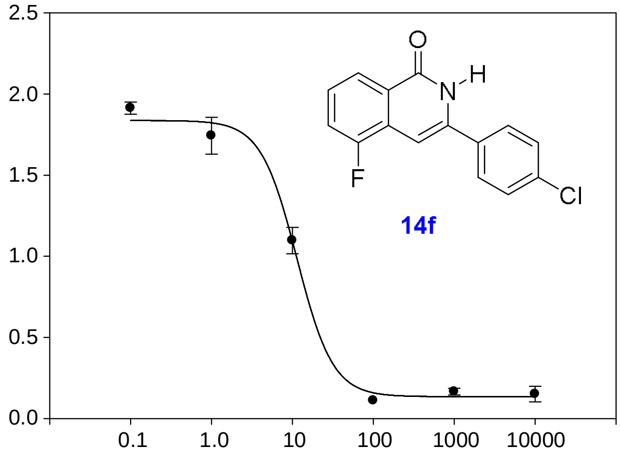
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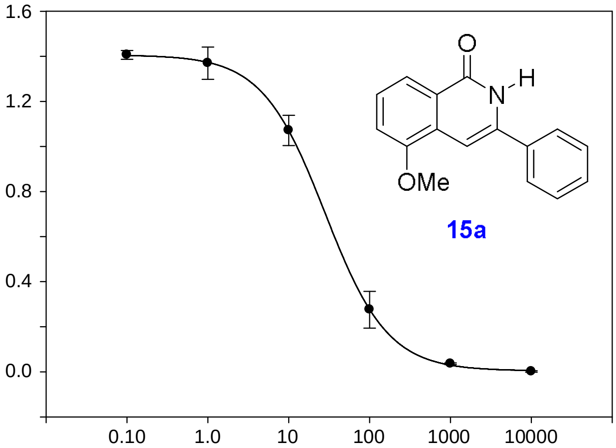
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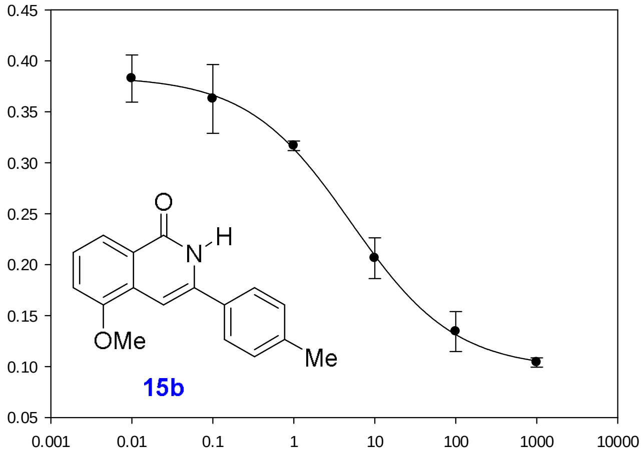
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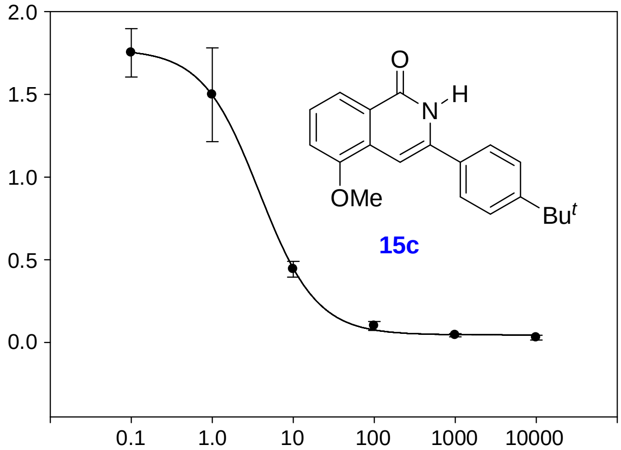
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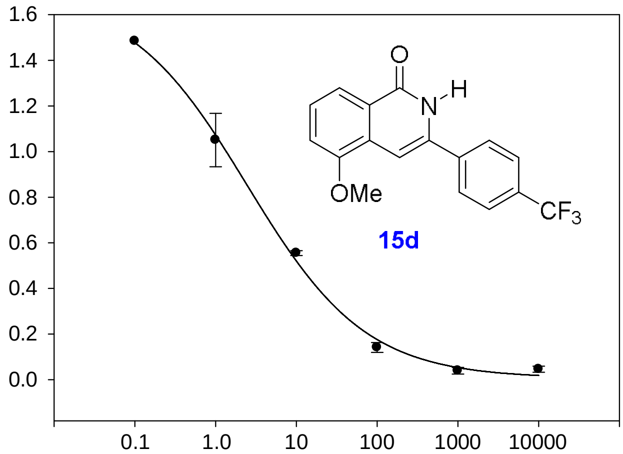
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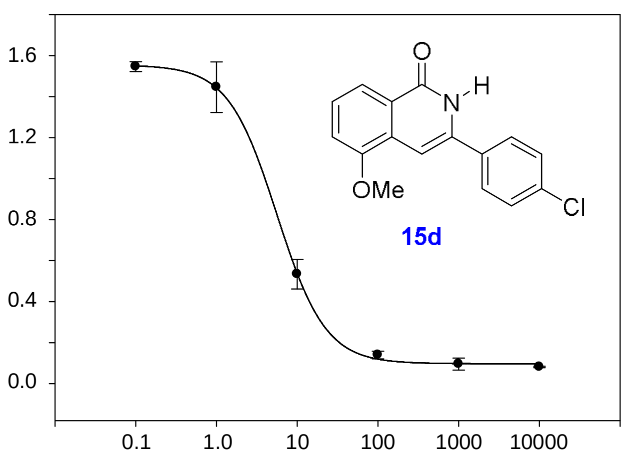
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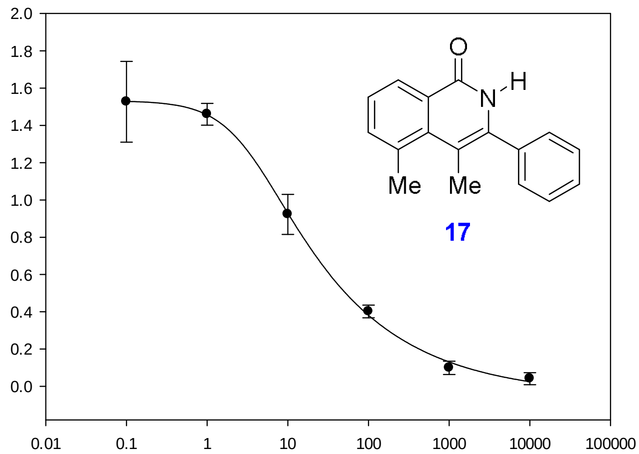
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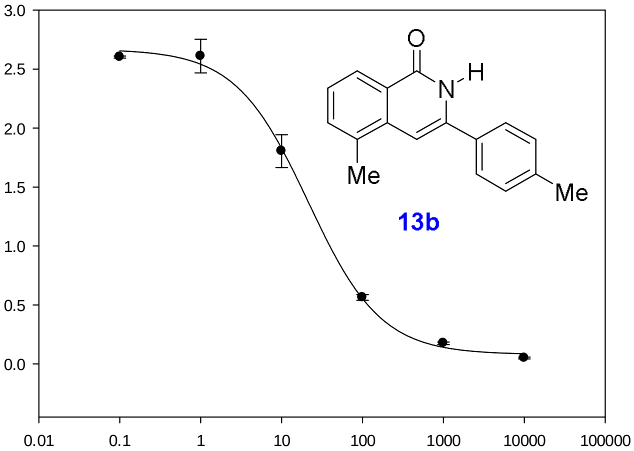
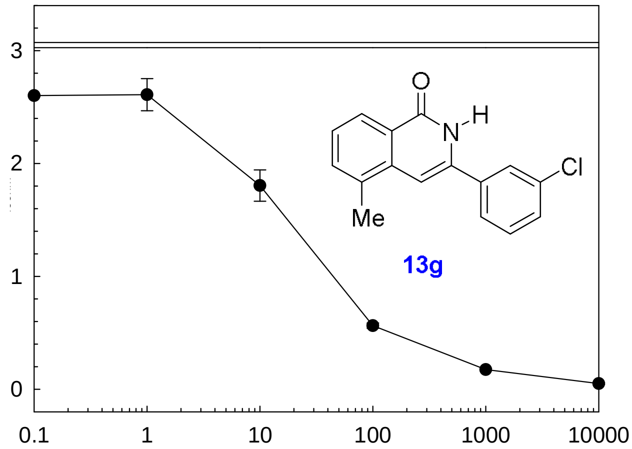
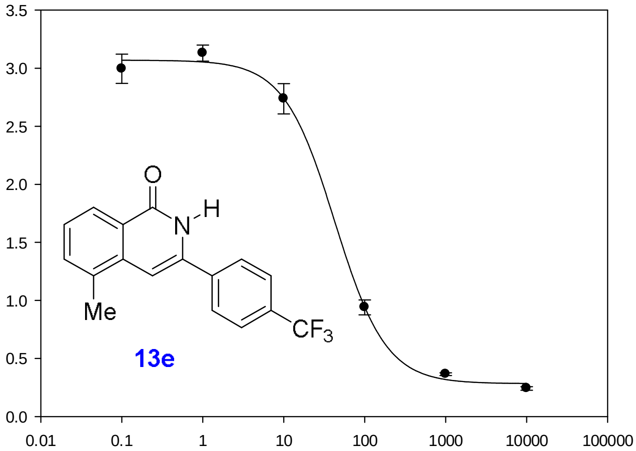
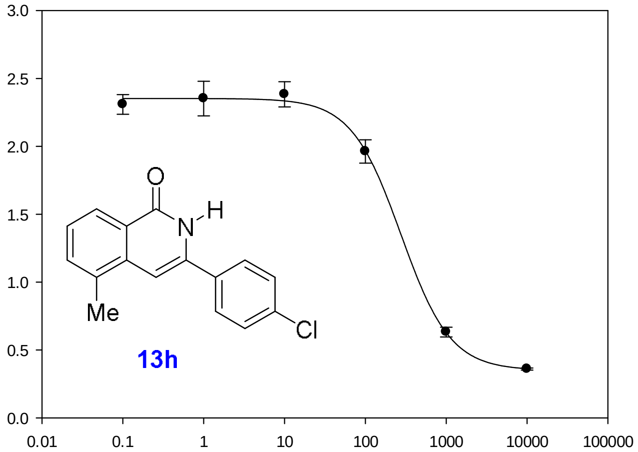
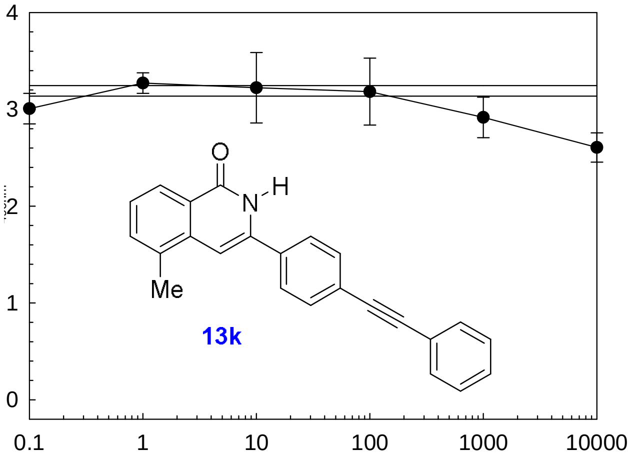
Section D: Examples of graphs of enzyme activity *vs.* concentration for inhibition of tankyrase-1 by isoquinolin-1-ones. X-Axes – concentration of inhibitor (nM); Y-axes – optical density (490 nm).

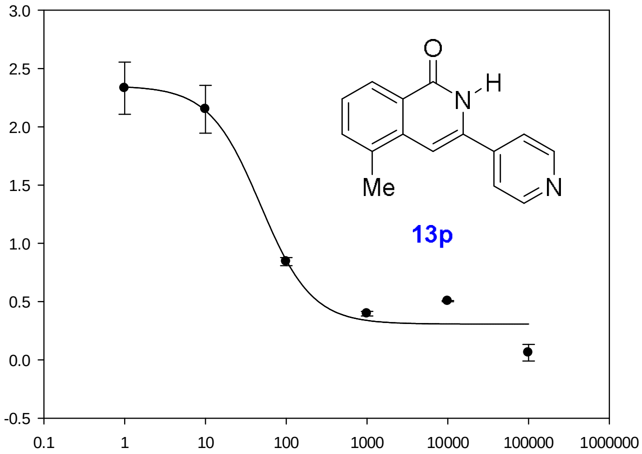


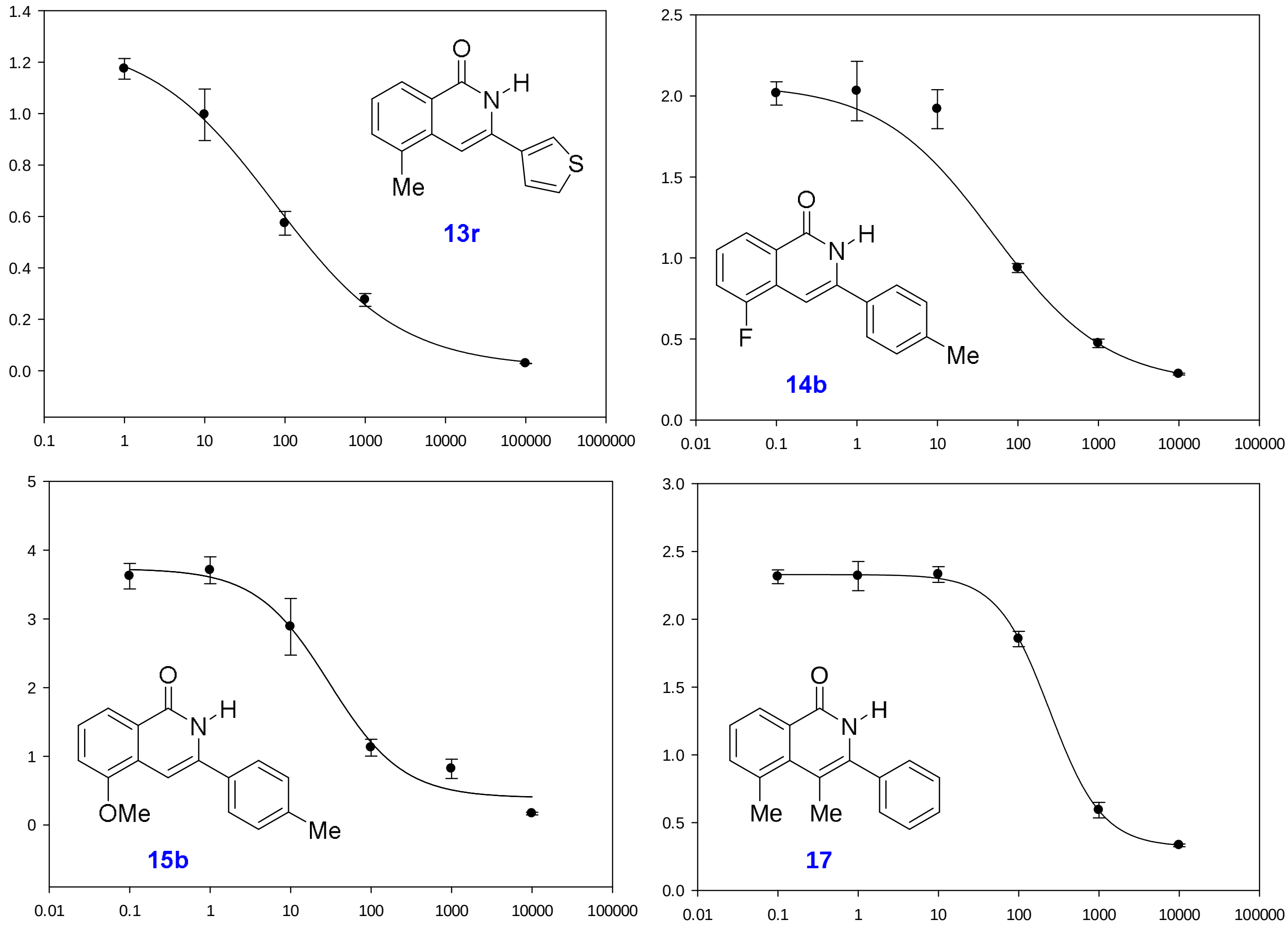








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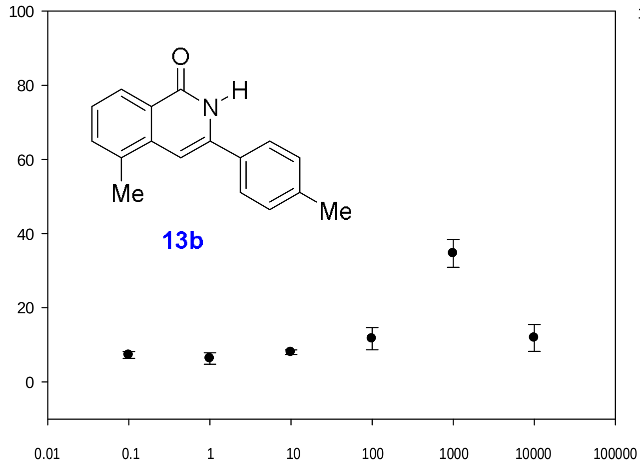
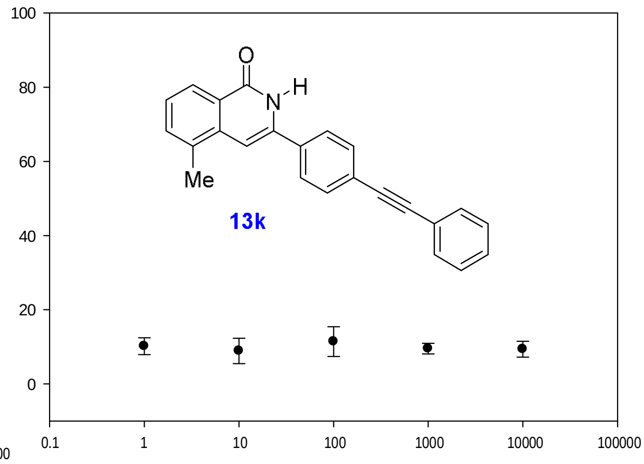
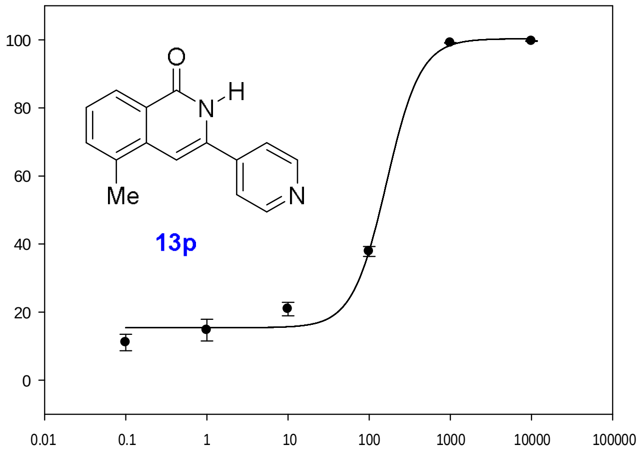
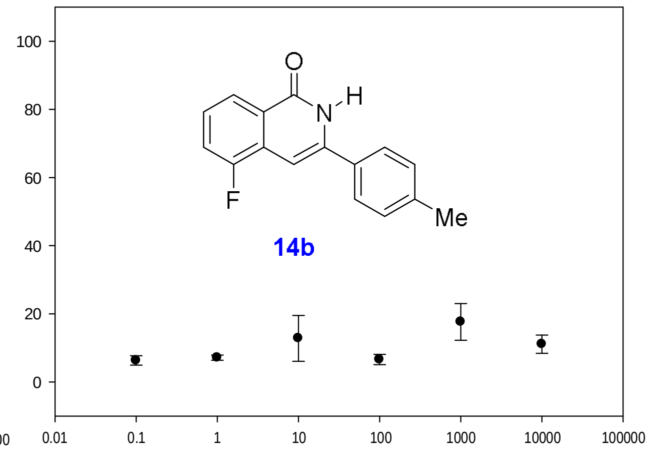
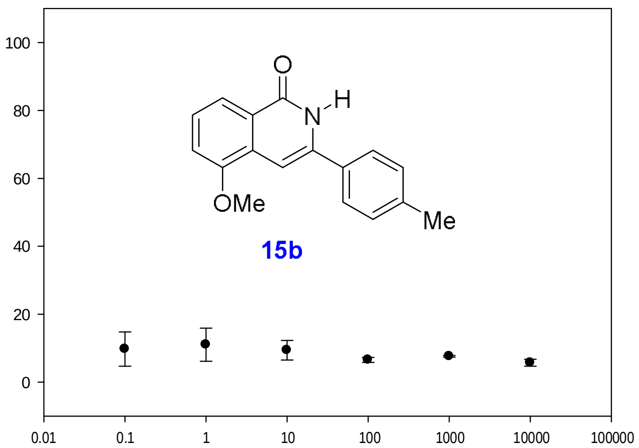
Section E: Graphs of enzyme activity *vs.* concentration for inhibition of human PARP-2 by isoquinolin-1-ones. X-Axes – concentration of inhibitor (nM); Y-axes – % Inhibition.











Section F: Data from NCI 60-cell-line evaluations of selected isoquinolinones

Developmental Therapeutics Program

One Dose Mean Graph

NSC: D-776981 / 1 | **Conc:** 1.00E-5 Molar | **Test Date:** Sep 03, 2013

Experiment ID: 1309OS63 | **Report Date:** Mar 09, 2014

Panel/Cell Line	Growth Percent
Leukemia	
CCRF-CEM	11.74
HL-60(TB)	-15.76
K-562	16.70
MOLT-4	29.65
RPMI-8226	13.56
SR	10.58
Non-Small Cell Lung Cancer	
A549/ATCC	30.68
HOP-62	26.14
HOP-92	17.79
NCI-H226	41.37
NCI-H23	44.64
NCI-H322M	36.56
NCI-H460	15.37
NCI-H522	12.26
Colon Cancer	
COLO 205	2.19
HCC-2998	42.78
HCT-116	24.97
HCT-15	29.33
HT29	2.46
KM12	28.81
SW-620	23.07
CNS Cancer	
SF-268	43.62
SF-295	10.74
SF-539	-32.54
SNB-19	18.99
SNB-75	-4.05
U251	16.39
Melanoma	
LOX IMVI	44.92
MALME-3M	21.77
M14	3.63
MDA-MB-435	-67.48
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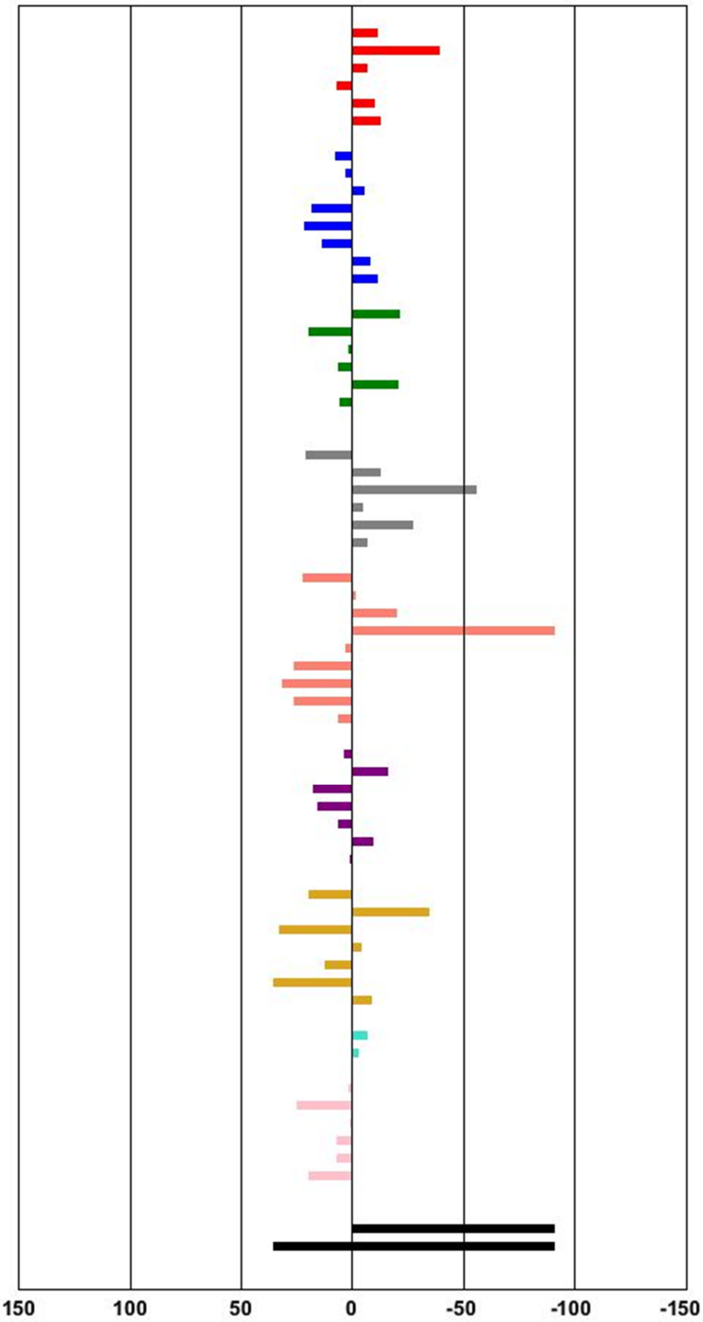
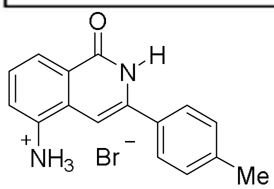
SK-MEL-5	54.72
UACC-257	49.14
UACC-62	29.29
Ovarian Cancer	
IGROV1	26.40
OVCAR-3	7.21
OVCAR-4	40.65
OVCAR-5	38.48
OVCAR-8	29.33
NCI/ADR-RES	14.21
SK-OV-3	24.13
Renal Cancer	
786-0	42.29
A498	-11.43
ACHN	55.68
RXF 393	19.56
SN12C	35.12
TK-10	58.35
UO-31	14.73
Prostate Cancer	
PC-3	16.95
DU-145	20.51
Breast Cancer	
MCF7	24.96
MDA-MB-231/ATCC	47.77
HS 578T	23.96
BT-549	29.99
T-47D	29.98
MDA-MB-468	42.25
Mean	23.11
Delta	90.59
Range	125.83

Mean Growth Percent - Growth Percent





12c

Single concentration 10 μM

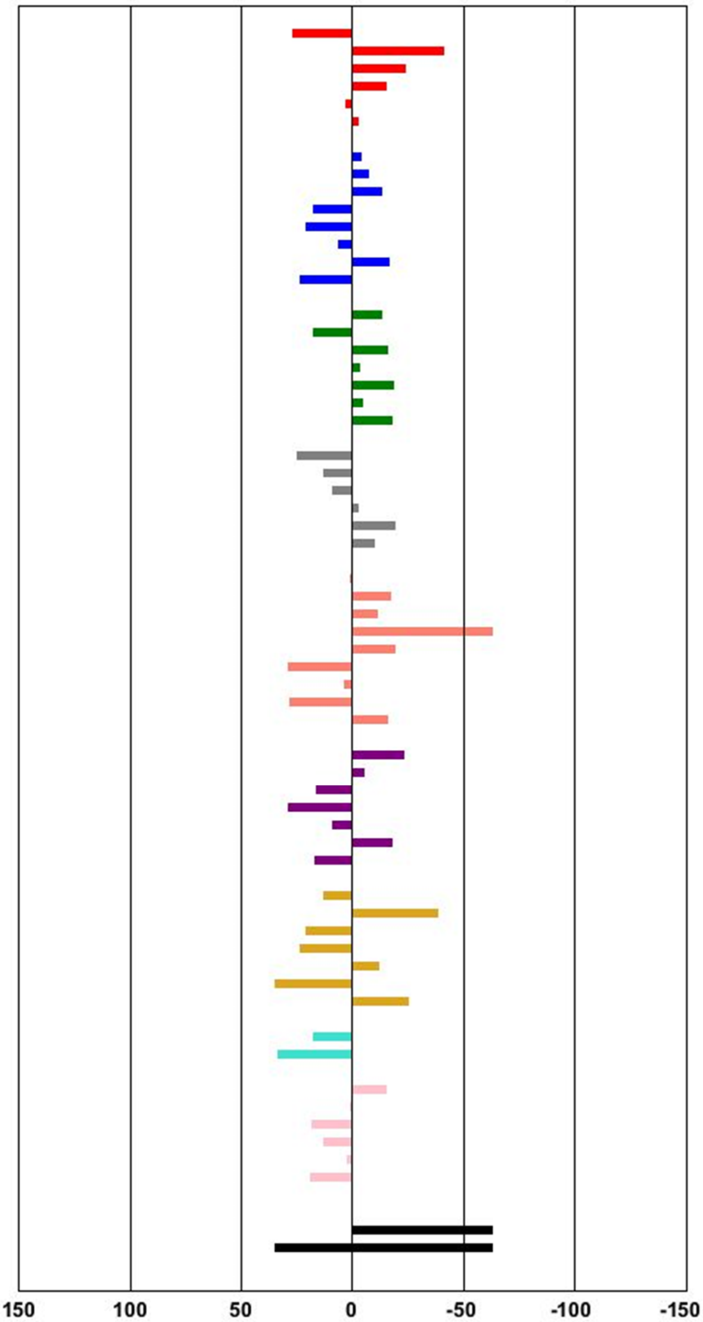
Developmental Therapeutics Program

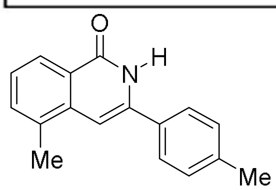
One Dose Mean Graph

NSC: D-776983 / 1	Conc: 1.00E-5 Molar	Test Date: Sep 03, 2013
Experiment ID: 1309OS63		Report Date: Mar 09, 2014

Panel/Cell Line	Growth Percent
Leukemia	
CCRF-CEM	59.93
HL-60(TB)	-7.60
K-562	9.76
MOLT-4	18.16
RPMI-8226	36.07
SR	30.75
Non-Small Cell Lung Cancer	
A549/ATCC	29.40
HOP-62	26.50
HOP-92	20.23
NCI-H226	50.99
NCI-H23	54.18
NCI-H322M	39.54
NCI-H460	16.79
NCI-H522	56.60
Colon Cancer	
COLO 205	20.17
HCC-2998	50.88
HCT-116	17.62
HCT-15	30.23
HT29	15.26
KM12	28.69
SW-620	15.89
CNS Cancer	
SF-268	57.93
SF-295	45.78
SF-539	42.04
SNB-19	30.64
SNB-75	14.27
U251	23.83
Melanoma	
LOX IMVI	33.91
MALME-3M	16.18
M14	22.20
MDA-MB-435	-29.61
SK-MEL-2	14.33
SK-MEL-28	61.87
SK-MEL-5	36.73
UACC-257	61.64
UACC-62	17.76
Ovarian Cancer	
IGROV1	10.20
OVCAR-3	28.40
OVCAR-4	49.10
OVCAR-5	61.71
OVCAR-8	41.95
NCI/ADR-RES	15.52
SK-OV-3	50.25
Renal Cancer	
786-0	45.79
A498	-4.86
ACHN	54.07
RXF 393	56.56
SN12C	21.78
TK-10	68.27
UO-31	8.37
Prostate Cancer	
PC-3	50.68
DU-145	66.41
Breast Cancer	
MCF7	18.22
MDA-MB-231/ATCC	34.29
HS 578T	51.38
BT-549	46.20
T-47D	35.31
MDA-MB-468	52.19
Mean	33.30
Delta	62.91
Range	97.88

Mean Growth Percent - Growth Percent





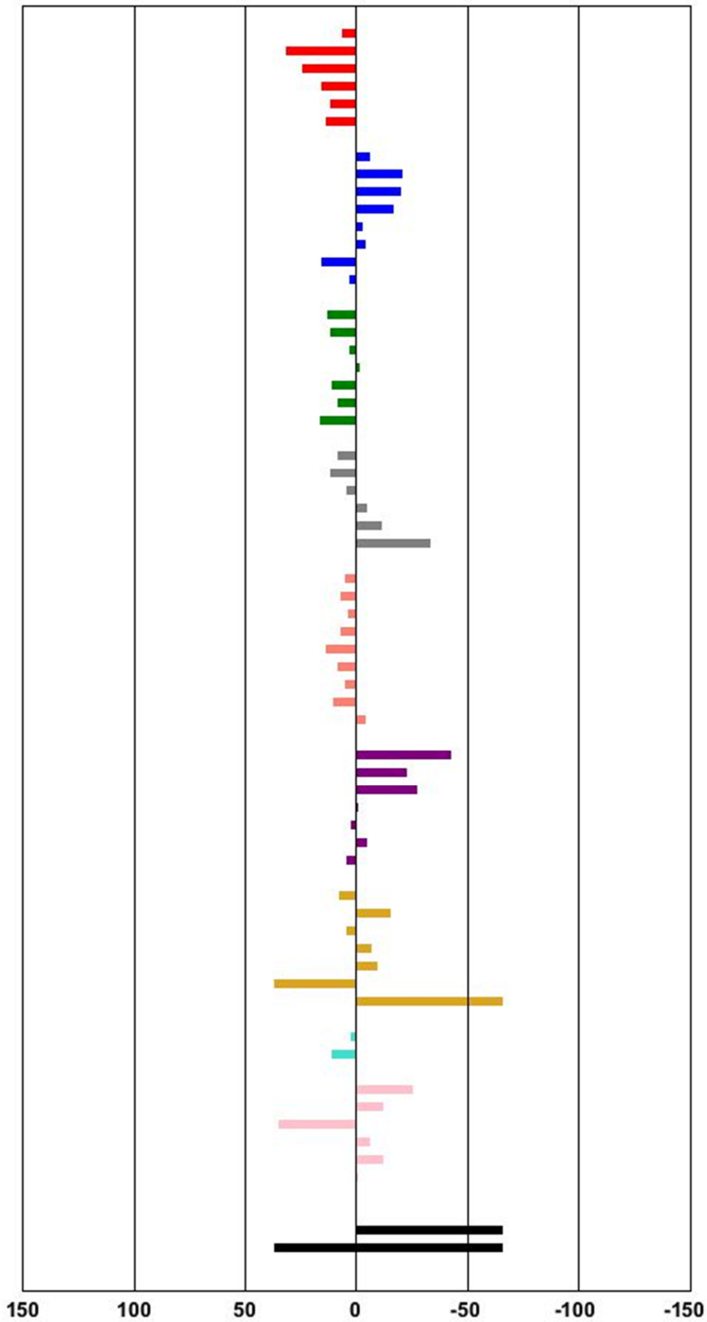
13b

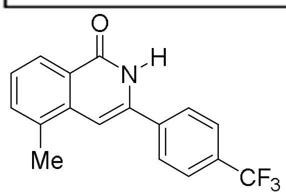
Single concentration 10 μM

Developmental Therapeutics Program One Dose Mean Graph	NSC: D-776982 / 1	Conc: 1.00E-5 Molar	Test Date: Sep 03, 2013
	Experiment ID: 1309OS63		Report Date: Mar 09, 2014

Panel/Cell Line	Growth Percent
Leukemia	
CCRF-CEM	94.16
HL-60(TB)	119.72
K-562	112.32
MOLT-4	103.64
RPMI-8226	99.44
SR	101.76
Non-Small Cell Lung Cancer	
A549/ATCC	82.43
HOP-62	67.40
HOP-92	68.40
NCI-H226	71.70
NCI-H23	85.76
NCI-H322M	84.34
NCI-H460	103.32
NCI-H522	90.82
Colon Cancer	
COLO 205	100.92
HCC-2998	99.60
HCT-116	90.84
HCT-15	86.78
HT29	98.86
KM12	96.37
SW-620	104.26
CNS Cancer	
SF-268	96.02
SF-295	99.45
SF-539	92.43
SNB-19	83.92
SNB-75	77.28
U251	54.91
Melanoma	
LOX IMVI	92.86
MALME-3M	95.13
M14	91.86
MDA-MB-435	94.87
SK-MEL-2	101.59
SK-MEL-28	96.15
SK-MEL-5	92.75
UACC-257	98.41
UACC-62	84.48
Ovarian Cancer	
IGROV1	45.70
OVCAR-3	65.78
OVCAR-4	60.91
OVCAR-5	87.84
OVCAR-8	90.13
NCI/ADR-RES	83.84
SK-OV-3	92.54
Renal Cancer	
786-0	95.67
A498	73.11
ACHN	92.16
RXF 393	81.39
SN12C	79.22
TK-10	124.75
UO-31	22.35
Prostate Cancer	
PC-3	90.17
DU-145	98.77
Breast Cancer	
MCF7	63.22
MDA-MB-231/ATCC	76.66
HS 578T	122.81
BT-549	82.45
T-47D	76.59
MDA-MB-468	87.33
Mean	88.08
Delta	65.73
Range	102.40

Mean Growth Percent - Growth Percent





13e

Single concentration 10 μM

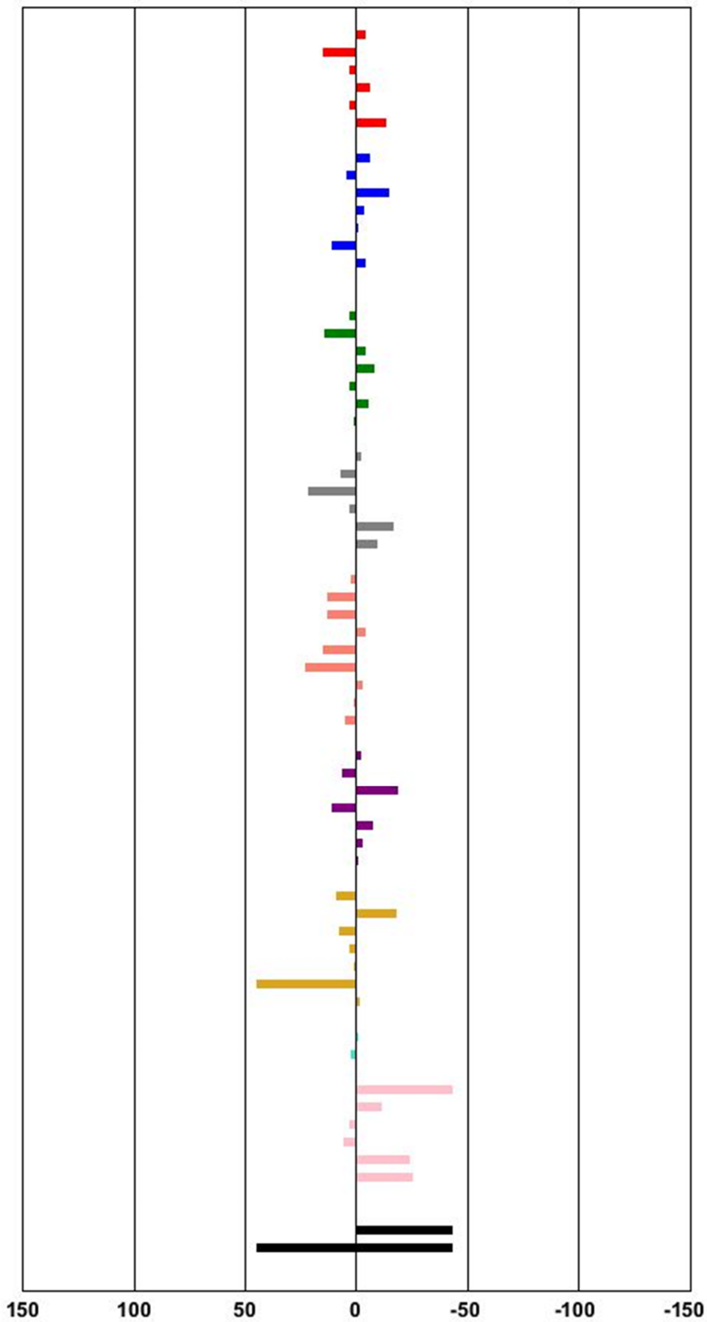
Developmental Therapeutics Program

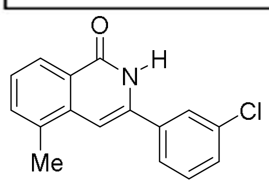
One Dose Mean Graph

NSC: D-776986 / 1	**Conc:** 1.00E-5 Molar	**Test Date:** Sep 03, 2013
Experiment ID: 1309OS63		**Report Date:** Mar 09, 2014

Panel/Cell Line	Growth Percent
Leukemia	
CCRF-CEM	96.41
HL-60(TB)	114.45
K-562	102.69
MOLT-4	94.28
RPMI-8226	102.56
SR	86.93
Non-Small Cell Lung Cancer	
A549/ATCC	93.90
HOP-62	104.34
HOP-92	85.55
NCI-H226	96.89
NCI-H23	99.36
NCI-H322M	110.79
NCI-H460	95.89
NCI-H522	100.04
Colon Cancer	
COLO 205	103.00
HCC-2998	114.19
HCT-116	96.41
HCT-15	91.94
HT29	102.75
KM12	94.86
SW-620	100.91
CNS Cancer	
SF-268	98.01
SF-295	106.97
SF-539	121.50
SNB-19	102.73
SNB-75	83.63
U251	90.83
Melanoma	
LOX IMVI	102.25
MALME-3M	112.57
M14	112.44
MDA-MB-435	95.79
SK-MEL-2	114.59
SK-MEL-28	122.79
SK-MEL-5	97.45
UACC-257	100.65
UACC-62	104.94
Ovarian Cancer	
IGROV1	98.09
OVCAR-3	106.11
OVCAR-4	81.45
OVCAR-5	110.94
OVCAR-8	92.87
NCI/ADR-RES	97.11
SK-OV-3	99.33
Renal Cancer	
786-0	108.36
A498	82.22
ACHN	107.49
RXF 393	102.74
SN12C	100.83
TK-10	144.66
UO-31	98.67
Prostate Cancer	
PC-3	99.64
DU-145	102.35
Breast Cancer	
MCF7	56.70
MDA-MB-231/ATCC	88.58
HS 578T	102.57
BT-549	105.42
T-47D	76.14
MDA-MB-468	74.54
Mean	99.86
Delta	43.16
Range	87.96

Mean Growth Percent - Growth Percent





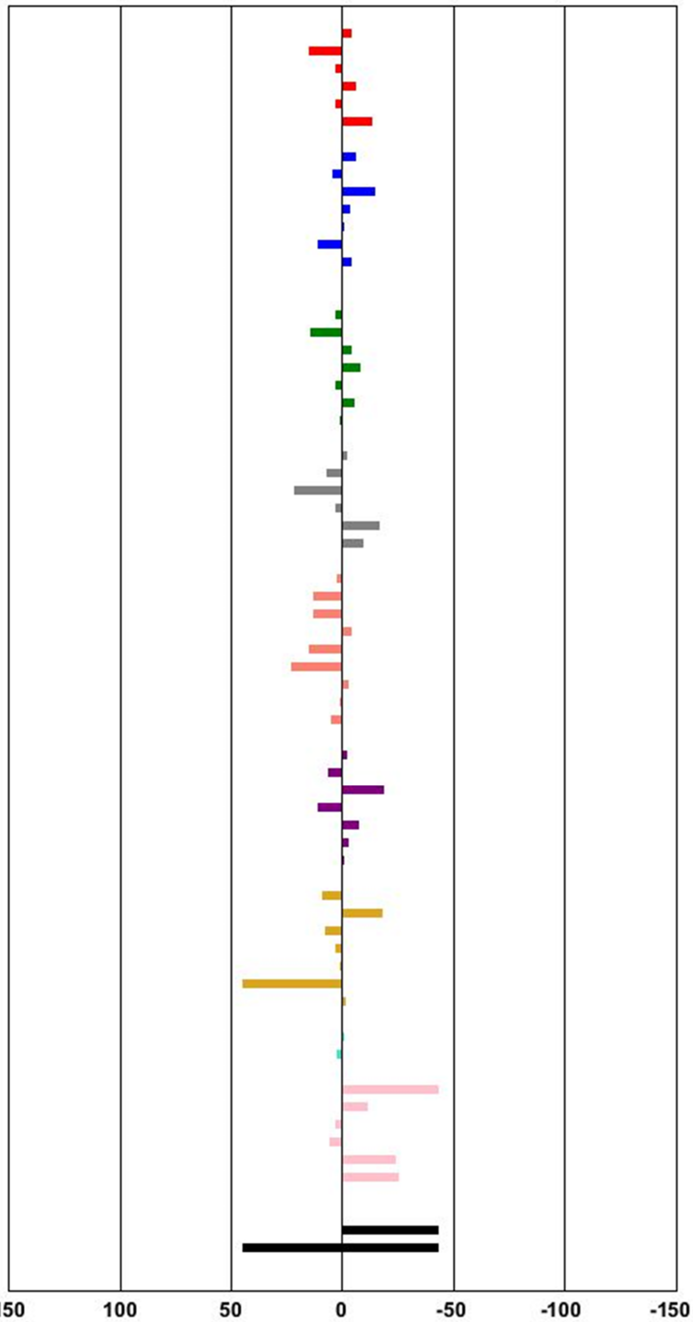
13g

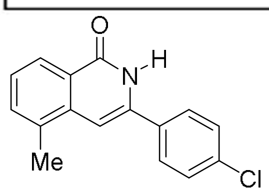
Single concentration 10 μM

Developmental Therapeutics Program	NSC: D-776986 / 1	Conc: 1.00E-5 Molar	Test Date: Sep 03, 2013
One Dose Mean Graph	Experiment ID: 1309OS63		Report Date: Mar 09, 2014

Panel/Cell Line	Growth Percent
Leukemia	
CCRF-CEM	96.41
HL-60(TB)	114.45
K-562	102.69
MOLT-4	94.28
RPMI-8226	102.56
SR	86.93
Non-Small Cell Lung Cancer	
A549/ATCC	93.90
HOP-62	104.34
HOP-92	85.55
NCI-H226	96.89
NCI-H23	99.36
NCI-H322M	110.79
NCI-H460	95.89
NCI-H522	100.04
Colon Cancer	
COLO 205	103.00
HCC-2998	114.19
HCT-116	96.41
HCT-15	91.94
HT29	102.75
KM12	94.86
SW-620	100.91
CNS Cancer	
SF-268	98.01
SF-295	106.97
SF-539	121.50
SNB-19	102.73
SNB-75	83.63
U251	90.83
Melanoma	
LOX IMVI	102.25
MALME-3M	112.57
M14	112.44
MDA-MB-435	95.79
SK-MEL-2	114.59
SK-MEL-28	122.79
SK-MEL-5	97.45
UACC-257	100.65
UACC-62	104.94
Ovarian Cancer	
IGROV1	98.09
OVCAR-3	106.11
OVCAR-4	81.45
OVCAR-5	110.94
OVCAR-8	92.87
NCI/ADR-RES	97.11
SK-OV-3	99.33
Renal Cancer	
786-0	108.36
A498	82.22
ACHN	107.49
RXF 393	102.74
SN12C	100.83
TK-10	144.66
UO-31	98.67
Prostate Cancer	
PC-3	99.64
DU-145	102.35
Breast Cancer	
MCF7	56.70
MDA-MB-231/ATCC	88.58
HS 578T	102.57
BT-549	105.42
T-47D	76.14
MDA-MB-468	74.54
Mean	99.86
Delta	43.16
Range	87.96

Mean Growth Percent - Growth Percent





13h

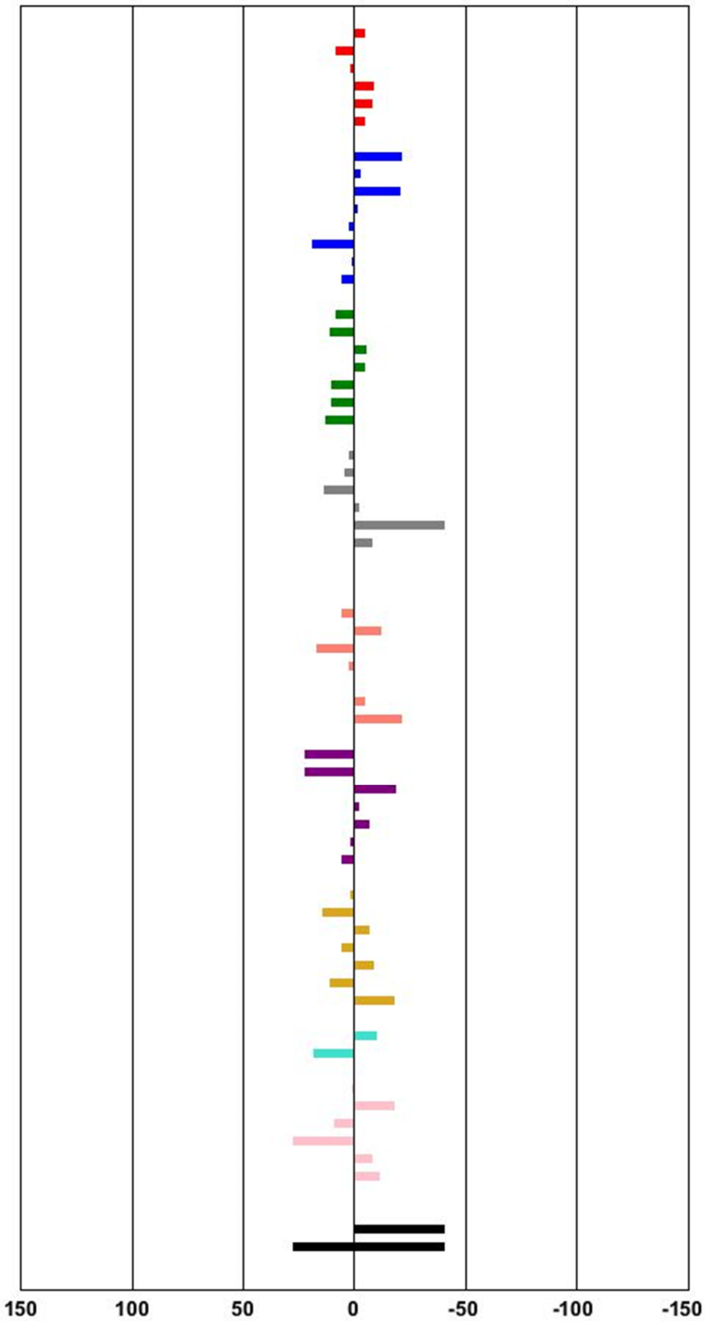
Single concentration 10 μM

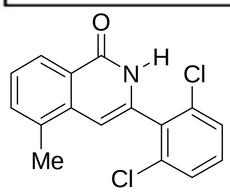
Developmental Therapeutics Program — One Dose Mean Graph

NSC: D-776987 / 1	Conc: 1.00E-5 Molar	Test Date: Sep 03, 2013
Experiment ID: 1309OS63		Report Date: Mar 09, 2014

Panel/Cell Line	Growth Percent
Leukemia	
CCRF-CEM	97.16
HL-60(TB)	110.10
K-562	103.57
MOLT-4	93.09
RPMI-8226	93.85
SR	97.62
Non-Small Cell Lung Cancer	
A549/ATCC	80.47
HOP-62	99.32
HOP-92	81.54
NCI-H226	100.48
NCI-H23	103.90
NCI-H322M	120.90
NCI-H460	102.81
NCI-H522	107.58
Colon Cancer	
COLO 205	110.10
HCC-2998	112.40
HCT-116	96.39
HCT-15	97.42
HT29	111.97
KM12	112.13
SW-620	114.61
CNS Cancer	
SF-268	103.83
SF-295	105.81
SF-539	115.41
SNB-19	100.18
SNB-75	61.59
U251	93.97
Melanoma	
LOX IMVI	102.34
MALME-3M	102.23
M14	107.49
MDA-MB-435	90.05
SK-MEL-2	118.34
SK-MEL-28	103.95
SK-MEL-5	101.70
UACC-257	97.49
UACC-62	80.84
Ovarian Cancer	
IGROV1	124.23
OVCAR-3	123.96
OVCAR-4	83.31
OVCAR-5	99.74
OVCAR-8	95.21
NCI/ADR-RES	103.39
SK-OV-3	107.54
Renal Cancer	
786-0	103.56
A498	115.86
ACHN	95.26
RXF 393	107.32
SN12C	93.57
TK-10	112.31
UO-31	83.95
Prostate Cancer	
PC-3	91.83
DU-145	120.18
Breast Cancer	
MCF7	102.99
MDA-MB-231/ATCC	84.14
HS 578T	110.94
BT-549	129.00
T-47D	94.21
MDA-MB-468	90.53
Mean	101.82
Delta	40.23
Range	67.41

Mean Growth Percent - Growth Percent



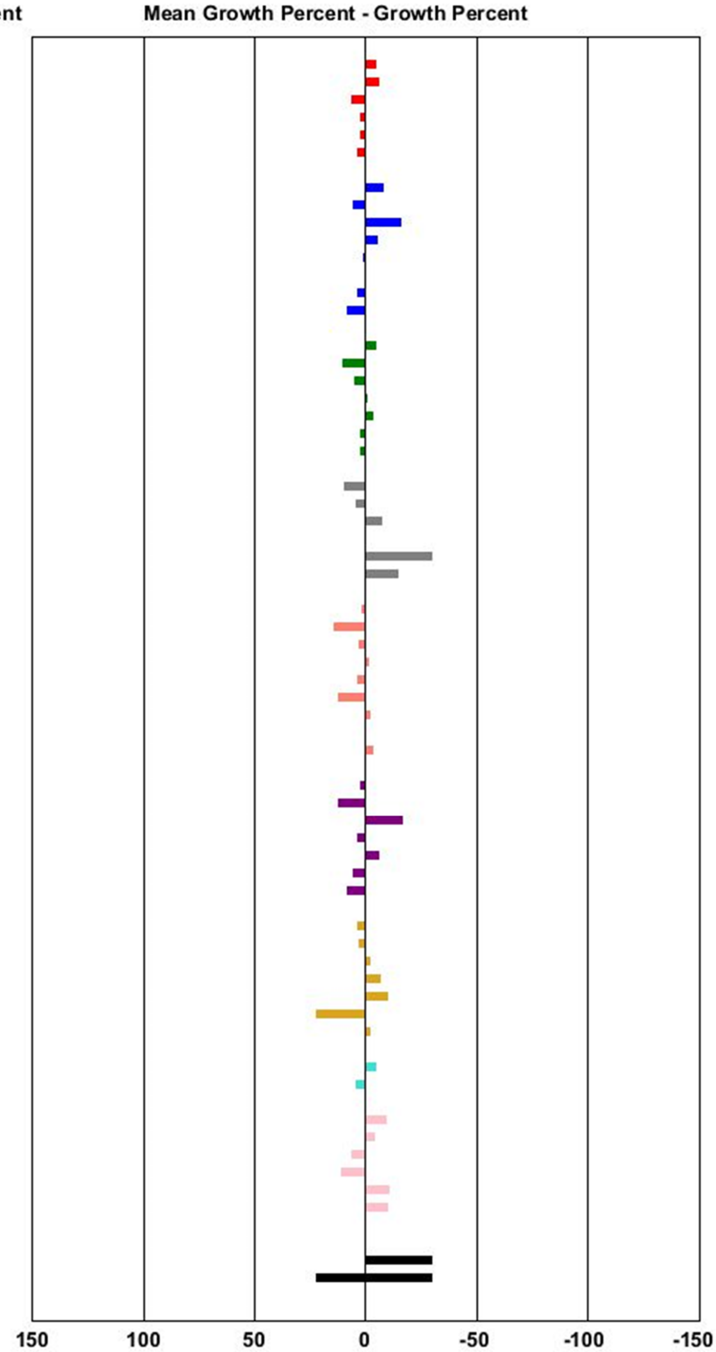


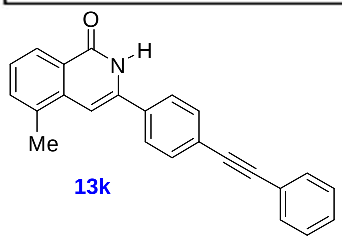
13i

Single concentration 10 μM

Developmental Therapeutics Program	**NSC:** D-776988 / 1	**Conc:** 1.00E-5 Molar	**Test Date:** Sep 03, 2013
One Dose Mean Graph	**Experiment ID:** 1309OS63		**Report Date:** Mar 09, 2014

Panel/Cell Line	Growth Percent
Leukemia	
CCRF-CEM	97.92
HL-60(TB)	96.57
K-562	108.28
MOLT-4	104.34
RPMI-8226	104.44
SR	105.51
Non-Small Cell Lung Cancer	
A549/ATCC	94.30
HOP-62	107.95
HOP-92	86.51
NCI-H226	96.83
NCI-H23	103.08
NCI-H322M	102.65
NCI-H460	105.77
NCI-H522	110.42
Colon Cancer	
COLO 205	97.43
HCC-2998	112.52
HCT-116	107.29
HCT-15	101.88
HT29	99.27
KM12	104.64
SW-620	104.65
CNS Cancer	
SF-268	111.49
SF-295	106.59
SF-539	94.94
SNB-19	102.28
SNB-75	72.31
U251	87.49
Melanoma	
LOX IMVI	103.85
MALME-3M	116.37
M14	105.22
MDA-MB-435	100.95
SK-MEL-2	105.79
SK-MEL-28	114.49
SK-MEL-5	100.18
UACC-257	102.58
UACC-62	99.26
Ovarian Cancer	
IGROV1	104.27
OVCAR-3	114.50
OVCAR-4	85.60
OVCAR-5	105.59
OVCAR-8	96.23
NCI/ADR-RES	107.84
SK-OV-3	110.50
Renal Cancer	
786-0	105.95
A498	105.15
ACHN	100.32
RXF 393	96.06
SN12C	92.50
TK-10	124.37
UO-31	100.64
Prostate Cancer	
PC-3	97.89
DU-145	106.16
Breast Cancer	
MCF7	93.41
MDA-MB-231/ATCC	98.49
HS 578T	108.55
BT-549	112.74
T-47D	91.46
MDA-MB-468	92.34
Mean	102.18
Delta	29.87
Range	52.06





13k

Single concentration 10 μM

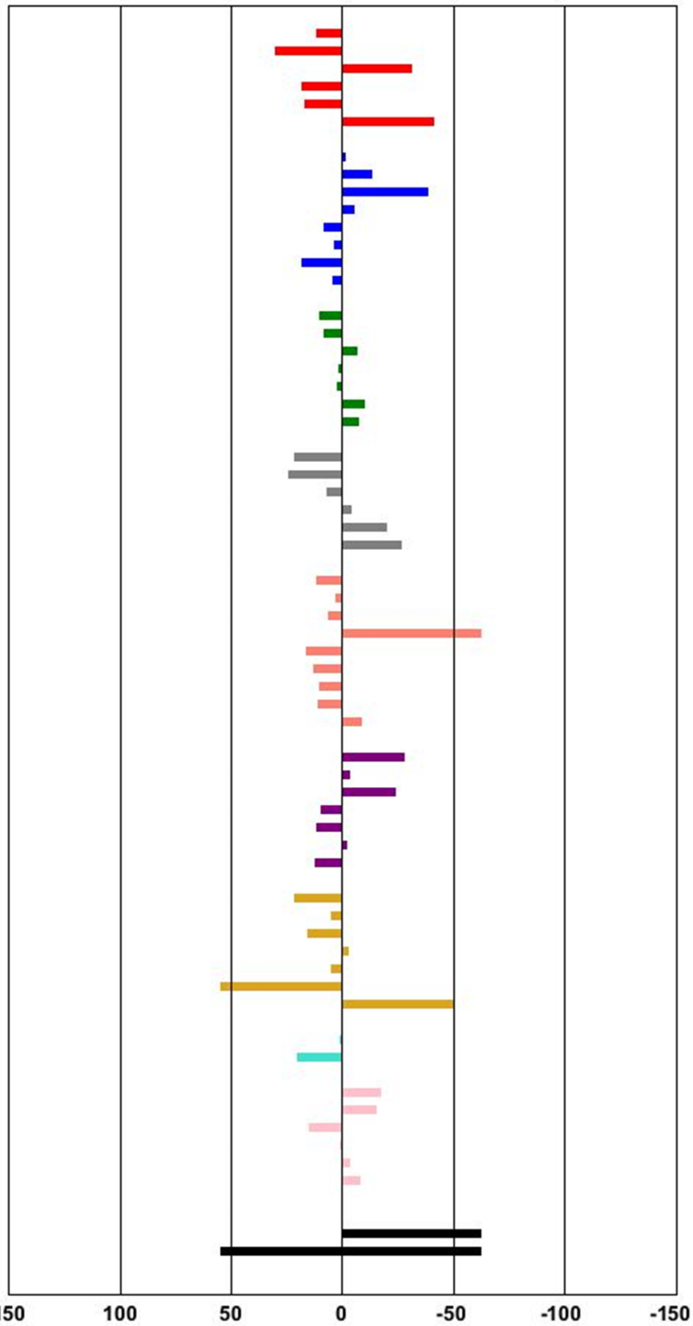
Developmental Therapeutics Program

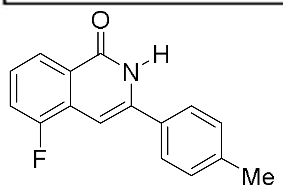
One Dose Mean Graph

NSC: D-776989 / 1	**Conc:** 1.00E-5 Molar	**Test Date:** Sep 03, 2013
Experiment ID: 1309OS63		**Report Date:** Mar 09, 2014

Panel/Cell Line	Growth Percent
Leukemia	
CCRF-CEM	88.63
HL-60(TB)	106.90
K-562	46.09
MOLT-4	94.96
RPMI-8226	93.77
SR	36.38
Non-Small Cell Lung Cancer	
A549/ATCC	75.78
HOP-62	64.19
HOP-92	38.81
NCI-H226	72.04
NCI-H23	85.41
NCI-H322M	80.58
NCI-H460	95.35
NCI-H522	81.06
Colon Cancer	
COLO 205	87.23
HCC-2998	84.89
HCT-116	70.45
HCT-15	78.49
HT29	79.13
KM12	67.03
SW-620	69.89
CNS Cancer	
SF-268	98.17
SF-295	100.91
SF-539	83.96
SNB-19	73.11
SNB-75	57.08
U251	50.91
Melanoma	
LOX IMVI	88.51
MALME-3M	79.80
M14	83.09
MDA-MB-435	14.55
SK-MEL-2	92.92
SK-MEL-28	89.53
SK-MEL-5	87.15
UACC-257	87.56
UACC-62	68.28
Ovarian Cancer	
IGROV1	49.32
OVCAR-3	73.72
OVCAR-4	53.19
OVCAR-5	86.44
OVCAR-8	88.22
NCI/ADR-RES	75.31
SK-OV-3	89.22
Renal Cancer	
786-0	98.59
A498	81.60
ACHN	92.61
RXF 393	74.44
SN12C	81.92
TK-10	131.55
UO-31	27.66
Prostate Cancer	
PC-3	77.96
DU-145	96.82
Breast Cancer	
MCF7	59.88
MDA-MB-231/ATCC	61.91
HS 578T	91.62
BT-549	78.08
T-47D	73.69
MDA-MB-468	69.08
Mean	76.99
Delta	62.44
Range	117.00

Mean Growth Percent - Growth Percent





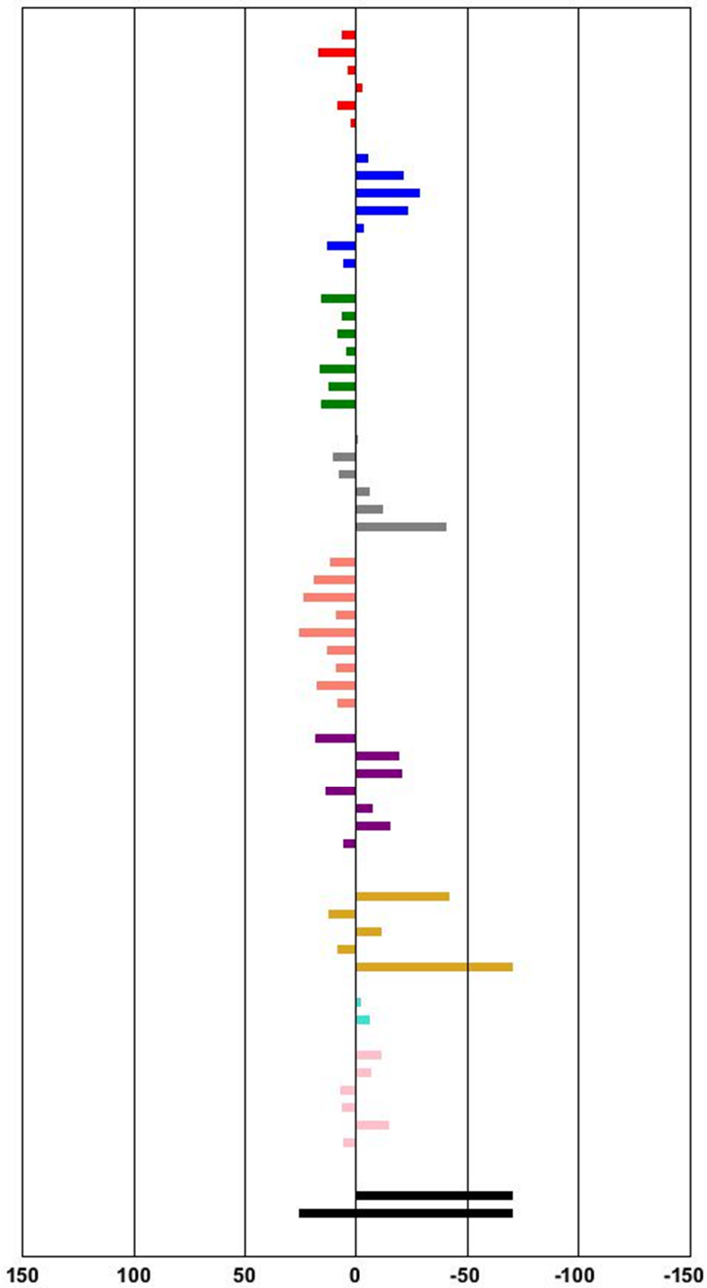
14b

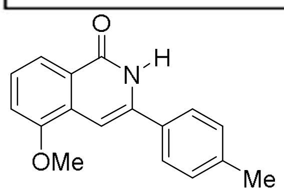
Single concentration 10 μM

Developmental Therapeutics Program One Dose Mean Graph	NSC: D-776984 / 1	Conc: 1.00E-5 Molar	Test Date: Sep 03, 2013
	Experiment ID: 1309OS63		Report Date: Mar 09, 2014

Panel/Cell Line	Growth Percent
Leukemia	
CCRF-CEM	93.71
HL-60(TB)	104.54
K-562	91.43
MOLT-4	85.54
RPMI-8226	95.63
SR	89.86
Non-Small Cell Lung Cancer	
A549/ATCC	82.82
HOP-62	66.72
HOP-92	59.53
NCI-H226	64.83
NCI-H23	84.77
NCI-H460	100.74
NCI-H522	93.38
Colon Cancer	
COLO 205	103.39
HCC-2998	93.89
HCT-116	95.92
HCT-15	92.07
HT29	103.95
KM12	99.67
SW-620	103.52
CNS Cancer	
SF-268	87.61
SF-295	98.05
SF-539	95.51
SNB-19	81.86
SNB-75	75.81
U251	47.75
Melanoma	
LOX IMVI	99.21
MALME-3M	106.58
M14	111.16
MDA-MB-435	96.47
SK-MEL-2	113.15
SK-MEL-28	100.48
SK-MEL-5	96.43
UACC-257	105.40
UACC-62	95.74
Ovarian Cancer	
IGROV1	106.10
OVCAR-3	68.57
OVCAR-4	67.37
OVCAR-5	101.34
OVCAR-8	80.58
NCI/ADR-RES	72.73
SK-OV-3	92.99
Renal Cancer	
786-0	88.27
A498	46.14
ACHN	100.14
RXF 393	76.95
TK-10	95.63
UO-31	17.97
Prostate Cancer	
PC-3	86.26
DU-145	82.25
Breast Cancer	
MCF7	76.90
MDA-MB-231/ATCC	81.44
HS 578T	94.70
BT-549	94.15
T-47D	73.55
MDA-MB-468	93.51
Mean	87.76
Delta	69.79
Range	95.18

Mean Growth Percent - Growth Percent





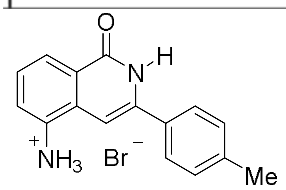
15b

Single concentration 10 μM

National Cancer Institute Developmental Therapeutics Program
In-Vitro Testing Results

NSC : D - 776981 / 1	Experiment ID : 1312NS05	Test Type : 08	Units : Molar
Report Date : February 14, 2014	Test Date : December 30, 2013	QNS :	MC :
COMI : HAP2-135 (132198)	Stain Reagent : SRB Dual-Pass Related	SSPL : 0FMB	

			Log10 Concentration												
	Time		Mean Optical Densities					Percent Growth							
Panel/Cell Line	Zero	Ctrl	-8.0	-7.0	-6.0	-5.0	-4.0	-8.0	-7.0	-6.0	-5.0	-4.0	GI50	TGI	LC50
Leukemia															
CCRF-CEM	0.377	2.216	2.104	2.122	1.585	0.448	0.450	94	95	66	4	4	1.79E-6	> 1.00E-4	> 1.00E-4
HL-60(TB)	1.300	3.338	3.277	3.345	2.685	1.015	1.352	97	100	68	-22	3	1.58E-6	.	> 1.00E-4
K-562	0.373	2.432	2.425	2.172	1.438	0.537	0.550	100	87	52	8	9	1.09E-6	> 1.00E-4	> 1.00E-4
MOLT-4	0.716	2.636	2.669	2.624	2.359	0.846	0.756	102	99	86	7	2	2.83E-6	> 1.00E-4	> 1.00E-4
RPMI-8226	0.995	2.946	2.921	2.901	2.664	1.292	1.086	99	98	86	15	5	3.20E-6	> 1.00E-4	> 1.00E-4
SR	0.498	2.418	2.273	2.201	1.129	0.485	0.415	92	89	33	-3	-17	4.93E-7	8.39E-6	> 1.00E-4
Non-Small Cell Lung Cancer															
A549/ATCC	0.440	2.251	2.221	2.221	1.993	0.709	0.589	98	98	86	15	8	3.19E-6	> 1.00E-4	> 1.00E-4
HOP-62	0.520	1.813	1.808	1.736	1.480	0.829	0.738	100	94	74	24	17	3.03E-6	> 1.00E-4	> 1.00E-4
HOP-92	1.452	2.004	1.936	1.938	1.796	1.523	1.547	88	88	62	13	17	1.78E-6	> 1.00E-4	> 1.00E-4
NCI-H226	1.160	2.706	2.657	2.660	2.464	1.885	1.713	97	97	84	46	36	7.47E-6	> 1.00E-4	> 1.00E-4
NCI-H23	0.564	1.604	1.590	1.599	1.533	0.988	0.905	99	99	93	41	33	6.65E-6	> 1.00E-4	> 1.00E-4
NCI-H322M	0.827	1.928	1.859	1.839	1.749	1.418	1.538	94	92	84	54	65	> 1.00E-4	> 1.00E-4	> 1.00E-4
NCI-H460	0.266	2.653	2.703	2.774	2.587	0.494	0.327	102	105	97	10	3	3.46E-6	> 1.00E-4	> 1.00E-4
NCI-H522	0.891	2.260	2.210	2.232	1.991	1.007	0.848	96	98	80	8	-5	2.65E-6	4.31E-5	> 1.00E-4
Colon Cancer															
COLO 205	0.459	1.607	1.665	1.582	1.456	0.408	0.309	105	98	87	-11	-33	2.38E-6	7.70E-6	> 1.00E-4
HCC-2998	0.590	1.837	1.693	1.802	1.525	0.759	0.659	88	97	75	14	6	2.55E-6	> 1.00E-4	> 1.00E-4
HCT-116	0.267	2.274	2.263	2.129	1.438	0.437	0.448	99	93	58	8	9	1.47E-6	> 1.00E-4	> 1.00E-4
HCT-15	0.370	2.036	1.893	1.882	1.251	0.618	0.567	91	91	53	15	11	1.19E-6	> 1.00E-4	> 1.00E-4
HT29	0.306	1.664	1.675	1.768	1.653	0.358	0.384	101	108	99	4	6	3.28E-6	> 1.00E-4	> 1.00E-4
KM12	0.476	2.457	2.382	2.411	1.648	0.862	0.743	96	98	59	19	13	1.70E-6	> 1.00E-4	> 1.00E-4
SW-620	0.255	1.888	1.858	1.815	1.248	0.596	0.617	98	96	61	21	22	1.87E-6	> 1.00E-4	> 1.00E-4
CNS Cancer															
SF-268	0.609	2.010	1.962	1.911	1.727	1.211	0.940	97	93	80	43	24	6.44E-6	> 1.00E-4	> 1.00E-4
SF-295	0.613	2.796	2.637	2.500	2.164	0.567	0.594	93	86	71	-8	-3	1.86E-6	8.01E-6	> 1.00E-4
SNB-19	0.742	2.514	2.398	2.442	2.178	1.285	1.367	93	96	81	31	35	4.13E-6	> 1.00E-4	> 1.00E-4
SNB-75	0.848	1.764	1.687	1.572	1.465	0.819	0.783	92	79	67	-3	-8	1.76E-6	8.96E-6	> 1.00E-4
U251	0.460	2.289	2.237	2.226	1.596	0.751	0.845	97	97	62	16	21	1.83E-6	> 1.00E-4	> 1.00E-4
Melanoma															
LOX IMVI	0.291	1.682	1.602	1.664	1.425	0.787	0.580	94	99	82	36	21	4.86E-6	> 1.00E-4	> 1.00E-4
MALME-3M	0.814	1.392	1.346	1.342	1.274	1.138	1.241	92	91	80	56	74	> 1.00E-4	> 1.00E-4	> 1.00E-4
M14	0.488	2.148	2.052	1.982	1.420	0.761	0.941	94	90	56	16	27	1.43E-6	> 1.00E-4	> 1.00E-4
MDA-MB-435	0.558	2.683	2.593	2.482	0.614	0.315	0.573	96	91	3	-44	1	2.89E-7	.	> 1.00E-4
SK-MEL-5	0.646	3.060	3.125	3.129	1.836	1.164	0.311	102	102	49	21	-52	9.52E-7	1.96E-5	9.41E-5
UACC-257	0.994	2.402	2.286	2.356	2.123	1.835	1.790	92	97	80	60	57	> 1.00E-4	> 1.00E-4	> 1.00E-4
UACC-62	1.154	2.780	2.720	2.713	2.252	1.770	1.778	96	96	68	38	38	3.90E-6	> 1.00E-4	> 1.00E-4
Ovarian Cancer															
IGROV1	0.774	2.252	2.222	2.238	1.968	1.250	1.049	98	99	81	32	19	4.30E-6	> 1.00E-4	> 1.00E-4
OVCAR-3	0.462	1.647	1.630	1.607	1.353	0.571	0.692	99	97	75	9	19	2.41E-6	> 1.00E-4	> 1.00E-4
OVCAR-4	0.678	1.324	1.289	1.223	1.170	0.920	0.793	95	84	76	37	18	4.72E-6	> 1.00E-4	> 1.00E-4
OVCAR-8	0.560	2.518	2.476	2.493	2.292	1.061	0.914	98	99	88	26	18	4.09E-6	> 1.00E-4	> 1.00E-4
NCI/ADR-RES	0.847	2.346	2.263	2.297	1.870	0.963	1.017	94	97	68	8	11	2.00E-6	> 1.00E-4	> 1.00E-4
SK-OV-3	0.967	2.295	2.183	2.036	2.001	1.261	1.253	92	80	78	22	22	3.16E-6	> 1.00E-4	> 1.00E-4
Renal Cancer															
786-0	0.857	2.819	2.811	2.769	2.692	1.811	1.442	100	97	94	49	30	9.32E-6	> 1.00E-4	> 1.00E-4
A498	1.760	2.429	2.248	2.252	2.075	1.554	1.531	73	74	47	-12	-13	7.71E-7	6.31E-6	> 1.00E-4
CAKI-1	0.562	2.678	2.591	2.458	1.944	1.152	1.036	96	90	65	28	22	2.56E-6	> 1.00E-4	> 1.00E-4
RXF 393	0.716	1.437	1.460	1.415	1.284	0.681	0.859	103	97	79	-5	20	2.21E-6	.	> 1.00E-4
SN12C	0.705	2.821	2.681	2.674	2.262	1.425	1.180	93	93	74	34	22	3.95E-6	> 1.00E-4	> 1.00E-4
TK-10	0.892	1.833	1.847	1.921	1.923	1.297	1.086	101	109	110	43	21	7.86E-6	> 1.00E-4	> 1.00E-4
UO-31	0.759	2.020	1.847	1.790	1.494	0.967	0.888	86	82	58	16	10	1.58E-6	> 1.00E-4	> 1.00E-4
Prostate Cancer															
PC-3	0.648	2.476	2.389	2.353	1.857	1.067	1.093	95	93	66	23	24	2.36E-6	> 1.00E-4	> 1.00E-4
DU-145	0.290	1.340	1.336	1.356	1.260	0.568	0.516	100	101	92	26	21	4.40E-6	> 1.00E-4	> 1.00E-4
Breast Cancer															
MCF7	0.321	1.749	1.600	1.550	1.218	0.512	0.479	90	86	63	13	11	1.81E-6	> 1.00E-4	> 1.00E-4
MDA-MB-231/ATCC	0.735	1.844	1.837	1.726	1.413	0.950	0.902	99	89	61	19	15	1.86E-6	> 1.00E-4	> 1.00E-4
HS 578T	1.382	2.490	2.434	2.402	2.217	1.532	1.527	95	92	75	14	13	2.57E-6	> 1.00E-4	> 1.00E-4
BT-549	1.098	2.011	2.009	1.891	1.669	1.145	1.101	100	87	63	5	.	1.66E-6	> 1.00E-4	> 1.00E-4
T-47D	0.813	1.822	1.746	1.654	1.649	1.220	1.156	92	83	83	40	34	5.91E-6	> 1.00E-4	> 1.00E-4
MDA-MB-468	0.800	1.509	1.480	1.470	1.399	0.863	0.895	96	94	84	9	13	2.86E-6	> 1.00E-4	> 1.00E-4



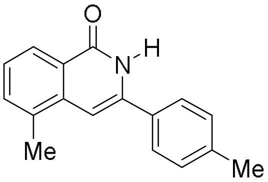
12c

Five concentrations:
10 nM, 100 nM, 1.0 μM, 10 μM, 100 μM

National Cancer Institute Developmental Therapeutics Program
In-Vitro Testing Results

NSC : D - 776983 / 1	Experiment ID : 1401NS08	Test Type : 08	Units : Molar
Report Date : February 14, 2014	Test Date : January 06, 2014	QNS :	MC :
COMI : HAP4-093 (132200)	Stain Reagent : SRB Dual-Pass Related	SSPL : 0FMB	

	Time		Log10 Concentration													
			Mean Optical Densities					Percent Growth								
Panel/Cell Line	Zero	Ctrl	-8.0	-7.0	-6.0	-5.0	-4.0	-8.0	-7.0	-6.0	-5.0	-4.0	GI50	TGI	LC50
Leukemia															
CCRF-CEM	0.703	3.042	3.040	3.040	2.963	1.520	1.260	100	100	97	35	24	5.69E-6	> 1.00E-4	> 1.00E-4
K-562	0.162	1.747	1.909	1.823	0.895	0.458	0.356	110	105	46	19	12	8.62E-7	> 1.00E-4	> 1.00E-4
MOLT-4	0.554	2.595	2.700	2.650	2.607	1.150	1.066	105	103	101	29	25	5.11E-6	> 1.00E-4	> 1.00E-4
RPMI-8226	1.058	2.893	2.826	2.888	2.746	1.548	1.344	96	100	92	27	16	4.40E-6	> 1.00E-4	> 1.00E-4
SR	0.412	1.396	1.436	1.439	1.089	0.440	0.379	104	104	69	3	-8	1.92E-6	1.81E-5	> 1.00E-4
Non-Small Cell Lung Cancer															
A549/ATCC	0.432	2.110	2.094	2.111	1.793	0.999	0.968	99	100	81	34	32	4.54E-6	> 1.00E-4	> 1.00E-4
HOP-62	0.733	1.490	1.340	1.289	1.129	0.936	0.926	80	73	52	27	26	1.23E-6	> 1.00E-4	> 1.00E-4
HOP-92	1.618	2.015	1.970	1.864	1.749	1.489	1.535	89	62	33	-8	-5	2.58E-7	6.39E-6	> 1.00E-4
NCI-H226	1.070	2.779	2.704	2.506	2.353	1.805	1.874	96	84	75	43	47	6.04E-6	> 1.00E-4	> 1.00E-4
NCI-H23	0.510	1.509	1.532	1.508	1.411	0.939	0.886	102	100	90	43	38	7.09E-6	> 1.00E-4	> 1.00E-4
NCI-H322M	1.060	2.250	2.230	2.180	1.982	1.721	1.688	98	94	77	56	53	> 1.00E-4	> 1.00E-4	> 1.00E-4
NCI-H460	0.336	2.886	2.970	2.896	2.687	0.742	0.741	104	101	93	16	16	3.62E-6	> 1.00E-4	> 1.00E-4
NCI-H522	0.934	2.467	2.408	2.350	2.203	0.825	0.796	96	92	83	-12	-15	2.22E-6	7.51E-6	> 1.00E-4
Colon Cancer															
COLO 205	0.405	1.465	1.336	1.363	1.251	0.507	0.484	88	90	80	10	7	2.66E-6	> 1.00E-4	> 1.00E-4
HCC-2998	0.432	1.282	1.296	1.278	1.252	0.928	1.047	102	100	97	58	72	> 1.00E-4	> 1.00E-4	> 1.00E-4
HCT-116	0.300	2.488	2.335	2.342	1.973	0.800	0.760	93	93	76	23	21	3.12E-6	> 1.00E-4	> 1.00E-4
HCT-15	0.322	1.919	1.804	1.736	1.468	0.586	0.622	93	88	72	17	19	2.47E-6	> 1.00E-4	> 1.00E-4
HT29	0.247	1.329	1.414	1.307	1.248	0.418	0.339	108	98	92	16	9	3.58E-6	> 1.00E-4	> 1.00E-4
KM12	0.610	2.780	2.777	2.809	2.165	1.317	1.163	100	101	72	33	25	3.58E-6	> 1.00E-4	> 1.00E-4
SW-620	0.380	2.193	2.163	2.110	1.578	0.686	0.602	98	95	66	17	12	2.12E-6	> 1.00E-4	> 1.00E-4
CNS Cancer															
SF-268	0.589	1.857	1.805	1.776	1.694	1.077	1.037	96	94	87	38	35	5.80E-6	> 1.00E-4	> 1.00E-4
SF-295	0.517	2.498	2.260	2.277	2.069	0.790	0.740	88	89	78	14	11	2.75E-6	> 1.00E-4	> 1.00E-4
SF-539	1.021	2.713	2.550	2.586	2.486	1.000	0.974	90	92	87	-2	-5	2.59E-6	9.48E-6	> 1.00E-4
SNB-19	0.787	2.462	2.419	2.220	1.869	1.368	1.454	97	86	65	35	40	3.07E-6	> 1.00E-4	> 1.00E-4
SNB-75	0.649	1.398	1.246	1.258	1.155	0.500	0.519	80	81	68	-23	-20	1.56E-6	5.57E-6	> 1.00E-4
U251	0.564	2.326	2.278	1.790	1.464	1.004	1.043	97	70	51	25	27	1.10E-6	> 1.00E-4	> 1.00E-4
Melanoma															
LOX IMVI	0.231	1.442	1.476	1.420	1.323	0.684	0.679	103	98	90	37	37	5.77E-6	> 1.00E-4	> 1.00E-4
MALME-3M	0.686	1.212	1.252	1.215	1.177	0.939	0.869	108	101	93	48	35	9.06E-6	> 1.00E-4	> 1.00E-4
M14	0.584	2.260	2.115	2.125	1.793	0.775	0.794	91	92	72	11	13	2.32E-6	> 1.00E-4	> 1.00E-4
MDA-MB-435	0.538	2.411	2.295	2.256	0.692	0.297	0.295	94	92	8	-45	-45	3.16E-7	1.43E-6	> 1.00E-4
SK-MEL-2	1.009	1.896	1.996	1.947	1.862	1.120	1.051	111	106	96	13	5	3.56E-6	> 1.00E-4	> 1.00E-4
SK-MEL-28	0.537	1.610	1.556	1.583	1.410	0.968	1.015	95	97	81	40	45	5.76E-6	> 1.00E-4	> 1.00E-4
SK-MEL-5	0.681	2.460	2.393	2.284	1.911	0.982	0.992	96	90	69	17	17	2.32E-6	> 1.00E-4	> 1.00E-4
UACC-257	0.944	1.982	1.982	1.924	1.766	1.393	1.443	100	94	79	43	48	6.48E-6	> 1.00E-4	> 1.00E-4
UACC-62	0.904	2.587	2.436	2.278	2.023	1.504	1.567	91	82	67	36	39	3.43E-6	> 1.00E-4	> 1.00E-4
Ovarian Cancer															
IGROV1	0.882	2.466	2.487	2.391	2.011	1.418	1.379	101	95	71	34	31	3.70E-6	> 1.00E-4	> 1.00E-4
OVCAR-3	0.579	1.730	1.757	1.566	1.385	0.549	0.482	102	86	70	-5	-17	1.84E-6	8.51E-6	> 1.00E-4
OVCAR-4	0.641	1.431	1.344	1.302	1.101	0.949	0.976	89	84	58	39	42	2.68E-6	> 1.00E-4	> 1.00E-4
OVCAR-5	0.765	1.718	1.623	1.658	1.505	1.193	1.254	90	94	78	45	51	.	> 1.00E-4	> 1.00E-4
OVCAR-8	0.643	2.494	2.465	2.252	2.145	1.154	1.230	98	87	81	28	32	3.82E-6	> 1.00E-4	> 1.00E-4
NCI/ADR-RES	0.567	1.760	1.762	1.608	1.472	0.672	0.689	100	87	76	9	10	2.43E-6	> 1.00E-4	> 1.00E-4
SK-OV-3	0.918	2.147	2.028	1.998	1.738	1.148	1.220	90	88	67	19	25	2.23E-6	> 1.00E-4	> 1.00E-4
Renal Cancer															
786-0	0.719	2.668	2.664	2.644	2.440	1.466	1.526	100	99	88	38	41	5.84E-6	> 1.00E-4	> 1.00E-4
A498	1.649	2.239	2.214	2.178	2.022	1.389	1.425	96	90	63	-16	-14	1.47E-6	6.31E-6	> 1.00E-4
ACHN	0.425	2.005	1.900	1.950	1.876	1.049	1.048	93	97	92	39	39	6.29E-6	> 1.00E-4	> 1.00E-4
CAKI-1	0.684	2.825	2.554	2.406	2.129	1.026	1.061	87	80	67	16	18	2.18E-6	> 1.00E-4	> 1.00E-4
RXF 393	0.911	1.877	1.842	1.697	1.592	1.147	1.105	96	81	70	24	20	2.78E-6	> 1.00E-4	> 1.00E-4
SN12C	0.794	2.676	2.494	2.261	2.094	1.377	1.465	90	78	69	31	36	3.16E-6	> 1.00E-4	> 1.00E-4
TK-10	0.637	1.442	1.474	1.503	1.373	0.885	0.874	104	108	91	31	29	4.82E-6	> 1.00E-4	> 1.00E-4
UO-31	0.907	2.242	2.003	1.786	1.390	1.097	0.986	82	66	36	14	6	3.41E-7	> 1.00E-4	> 1.00E-4
Prostate Cancer															
PC-3	0.770	2.695	2.515	2.442	2.265	1.320	1.335	91	87	78	29	29	3.66E-6	> 1.00E-4	> 1.00E-4
DU-145	0.365	1.440	1.496	1.406	1.292	0.662	0.584	105	97	86	28	20	4.15E-6	> 1.00E-4	> 1.00E-4
Breast Cancer															
MCF7	0.469	2.510	2.236	2.331	1.993	0.739	0.789	87	91	75	13	16	2.52E-6	> 1.00E-4	> 1.00E-4
MDA-MB-231/ATCC	0.764	1.986	2.013	1.726	1.414	1.250	1.247	102	79	53	40	40	1.75E-6	> 1.00E-4	> 1.00E-4
HS 578T	1.546	2.453	2.288	2.283	2.271	1.626	1.544	82	81	80	9	.	2.64E-6	9.59E-5	> 1.00E-4
BT-549	0.596	1.451	1.361	1.338	1.227	0.778	0.745	89	87	74	21	17	2.84E-6	> 1.00E-4	> 1.00E-4
T-47D	0.529	1.116	1.036	1.075	0.969	0.725	0.748	86	93	75	33	37	3.99E-6	> 1.00E-4	> 1.00E-4
MDA-MB-468	0.648	1.331	1.268	1.252	1.178	0.803	0.758	91	88	78	23	16	3.18E-6	> 1.00E-4	> 1.00E-4



13b

Five concentrations:
10 nM, 100 nM, 1.0 µM, 10 µM, 100 µM

Section G: Crystal data for small-molecule X-ray crystallography

Table 1. Crystal data and structure refinement for **13i.**

Identification code	k12farm8
Empirical formula	C34 H28 Cl4 N2 O3
Formula weight	654.38
Temperature	150(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	P21/n
Unit cell dimensions	a = 14.1190(3)Å α = 90°
	b = 13.6440(3)Å β = 96.302(1)°
	c = 15.7740(4)Å γ = 90°
Volume	3020.33(12) $Å^3$
Z	4
Density (calculated)	1.439 Mg m^{-3}
Absorption coefficient	0.431 mm^{-1}
F(000)	1352
Crystal size	0.25 × 0.15 × 0.08 mm
θ range for data collection	3.62 to 26.37°
Index ranges	-17<=h<=17; -17<=k<=17; -19<=l<=19
Reflections collected	56157
Independent reflections	6157 [R(int) = 0.0932]
Reflections observed (>2σ)	4274
Data Completeness	0.997
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.928 and 0.832
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	6157 / 0 / 391
Goodness-of-fit on F^2	1.034
Final R indices [I>2σ(I)]	R1 = 0.0502 *wR*2 = 0.1070
R indices (all data)	R1 = 0.0868 *wR*2 = 0.1250
Largest diff. peak and hole	0.382 and -0.377 e$Å^{-3}$

Notes:

Small crystal – poor diffraction at higher Bragg angles, hence data truncated at θ = 26.4°. Two molecules in the asymmetric unit plus one solvent entity (ethanol). Hydrogen-bonding present. Methyl hydrogen atoms attached to C16 and C16A are disordered.

D-H	d(D-H)	d(H..A)	<DHA	d(D..A)	A
O2-H2	0.840	1.988	174.03	2.825	O1A
N1-H1	0.880	1.947	170.53	2.819	O1A
N1A-H1A	0.880	2.030	160.14	2.874	O1

Table 2. Atomic coordinates (× 10^4) and equivalent isotropic displacement parameters (Å^2 × 10^3) for 1.U(eq) is defined as one third of the trace of the orthogonallised Uij tensor for **13i**.

Atom	x	y	z	U(eq)
Cl(1)	6739(1)	6508(1)	5251(1)	43(1)
Cl(2)	6779(1)	3145(1)	7104(1)	35(1)
O(1)	8901(1)	2703(1)	5088(1)	30(1)
O(2)	6729(2)	3007(2)	3249(2)	51(1)
N(1)	7908(2)	3810(2)	5586(1)	26(1)
C(1)	6168(2)	5613(2)	5800(2)	31(1)
C(2)	5211(2)	5739(2)	5874(2)	34(1)
C(3)	4733(2)	5046(2)	6300(2)	38(1)
C(4)	5216(2)	4233(2)	6660(2)	36(1)
C(5)	6181(2)	4132(2)	6585(2)	29(1)
C(6)	6690(2)	4804(2)	6142(2)	26(1)
C(7)	7708(2)	4650(2)	6035(2)	25(1)
C(8)	8425(2)	5243(2)	6344(2)	26(1)
C(9)	9396(2)	5012(2)	6224(2)	24(1)
C(10)	9587(2)	4125(2)	5812(2)	25(1)
C(11)	8802(2)	3491(2)	5473(2)	26(1)
C(12)	10522(2)	3860(2)	5709(2)	30(1)
C(13)	11260(2)	4467(2)	6004(2)	33(1)
C(14)	11076(2)	5357(2)	6393(2)	32(1)
C(15)	10161(2)	5644(2)	6503(2)	26(1)
C(16)	9966(2)	6627(2)	6895(2)	34(1)
C(17)	7352(2)	2287(2)	2980(2)	47(1)
C(18)	7566(3)	2559(3)	2092(2)	51(1)
Cl(1A)	8342(1)	-1484(1)	5145(1)	38(1)
Cl(2A)	8970(1)	1794(1)	7072(1)	38(1)
O(1A)	6463(1)	2497(1)	4942(1)	29(1)
N(1A)	7483(2)	1314(2)	5481(1)	25(1)
C(1A)	9101(2)	-663(2)	5728(2)	26(1)
C(2A)	10060(2)	-884(2)	5836(2)	30(1)
C(3A)	10687(2)	-241(2)	6291(2)	34(1)
C(4A)	10352(2)	597(2)	6654(2)	33(1)
C(5A)	9385(2)	789(2)	6545(2)	28(1)
C(6A)	8723(2)	187(2)	6066(2)	25(1)
C(7A)	7699(2)	449(2)	5932(2)	25(1)
C(8A)	6993(2)	-75(2)	6225(2)	25(1)
C(9A)	6024(2)	259(2)	6099(2)	24(1)

C(10A)	5826(2)	1162(2)	5674(2)	24(1)
C(11A)	6594(2)	1704(2)	5340(2)	25(1)
C(12A)	4902(2)	1535(2)	5562(2)	29(1)
C(13A)	4173(2)	1015(2)	5849(2)	31(1)
C(14A)	4353(2)	114(2)	6253(2)	32(1)
C(15A)	5261(2)	-279(2)	6385(2)	27(1)
C(16A)	5426(2)	-1265(2)	6805(2)	35(1)

Table 3. Bond lengths [Å] and angles [°] for **13i**.

Cl(1)-C(1)	1.745(3)	Cl(2)-C(5)	1.744(3)
O(1)-C(11)	1.250(3)	O(2)-C(17)	1.414(4)
N(1)-C(11)	1.366(3	N(1)-C(7)	1.392(3)
C(1)-C(2)	1.380(4)	C(1)-C(6)	1.402(4)
C(2)-C(3)	1.378(4)	C(3)-C(4)	1.391(4)
C(4)-C(5)	1.388(4)	C(5)-C(6)	1.398(4)
C(6)-C(7)	1.481(4)	C(7)-C(8)	1.345(4)
C(8)-C(9)	1.439(4)	C(9)-C(10)	1.414(4)
C(9)-C(15)	1.414(4)	C(10)-C(12)	1.396(4)
C(10)-C(11)	1.461(4)	C(12)-C(13)	1.371(4)
C(13)-C(14)	1.398(4)	C(14)-C(15)	1.379(4)
C(15)-C(16)	1.514(4)	C(17)-C(18)	1.511(5)
Cl(1A)-C(1A)	1.741(3)	Cl(2A)-C(5A)	1.737(3)
O(1A)-C(11A)	1.254(3)	N(1A)-C(11A)	1.360(3)
N(1A)-C(7A)	1.394(3)	C(1A)-C(2A)	1.381(4)
C(1A)-C(6A)	1.405(4)	C(2A)-C(3A)	1.388(4)
C(3A)-C(4A)	1.384(4)	C(4A)-C(5A)	1.384(4)
C(5A)-C(6A)	1.401(4)	C(6A)-C(7A)	1.482(4)
C(7A)-C(8A)	1.349(4)	C(8A)-C(9A)	1.435(4)
C(9A)-C(15A)	1.417(4)	C(9A)-C(10A)	1.416(4)
C(10A)-C(12A)	1.394(4)	C(10A)-C(11A)	1.457(4)
C(12A)-C(13A)	1.367(4)	C(13A)-C(14A)	1.394(4)
C(14A)-C(15A)	1.385(4)	C(15A)-C(16A)	1.506(4)
C(11)-N(1)-C(7)	124.8(2)	C(2)-C(1)-C(6)	122.9(3)
C(2)-C(1)-Cl(1)	117.7(2)	C(6)-C(1)-Cl(1)	119.4(2)
C(3)-C(2)-C(1)	119.5(3)	C(2)-C(3)-C(4)	120.1(3)
C(5)-C(4)-C(3)	119.1(3)	C(4)-C(5)-C(6)	122.7(3)
C(4)-C(5)-Cl(2)	117.7(2)	C(6)-C(5)-Cl(2)	119.5(2)
C(5)-C(6)-C(1)	115.6(3)	C(5)-C(6)-C(7)	121.5(2)
C(1)-C(6)-C(7)	122.9(2)	C(8)-C(7)-N(1)	119.6(2)
C(8)-C(7)-C(6)	125.0(2)	N(1)-C(7)-C(6)	115.3(2)
C(7)-C(8)-C(9)	120.6(2)	C(10)-C(9)-C(15)	119.1(2)
C(10)-C(9)-C(8)	118.8(2)	C(15)-C(9)-C(8)	122.1(2)
C(12)-C(10)-C(9)	120.5(3)	C(12)-C(10)-C(11)	119.6(2)
C(9)-C(10)-C(11)	119.9(2)	O(1)-C(11)-N(1)	119.5(2)
O(1)-C(11)-C(10)	124.5(2)	N(1)-C(11)-C(10)	116.0(2)
C(13)-C(12)-C(10)	119.8(3)	C(12)-C(13)-C(14)	120.2(3)
C(15)-C(14)-C(13)	121.6(3)	C(14)-C(15)-C(9)	118.8(2)

C(14)-C(15)-C(16)	121.2(3)	C(9)-C(15)-C(16)	120.0(2)
O(2)-C(17)-C(18)	107.6(3)	C(11A)-N(1A)-C(7A)	124.1(2)
C(2A)-C(1A)-C(6A)	122.8(3)	C(2A)-C(1A)-Cl(1A)	117.6(2)
C(6A)-C(1A)-Cl(1A)	119.6(2)	C(1A)-C(2A)-C(3A)	119.1(3)
C(4A)-C(3A)-C(2A)	120.6(3)	C(3A)-C(4A)-C(5A)	118.8(3)
C(4A)-C(5A)-C(6A)	123.1(3)	C(4A)-C(5A)-Cl(2A)	118.0(2)
C(6A)-C(5A)-Cl(2A)	118.8(2)	C(5A)-C(6A)-C(1A)	115.5(2)
C(5A)-C(6A)-C(7A)	121.2(2)	C(1A)-C(6A)-C(7A)	123.4(2)
C(8A)-C(7A)-N(1A)	119.7(2)	C(8A)-C(7A)-C(6A)	124.7(2)
N(1A)-C(7A)-C(6A)	115.6(2)	C(7A)-C(8A)-C(9A)	121.0(2)
C(15A)-C(9A)-C(10A)	119.0(2)	C(15A)-C(9A)-C(8A)	122.6(2)
C(10A)-C(9A)-C(8A)	118.5(2)	C(12A)-C(10A)-C(9A)	120.7(3)
C(12A)-C(10A)-C(11A)	119.4(2)	C(9A)-C(10A)-C(11A)	119.8(2)
O(1A)-C(11A)-N(1A)	120.2(2)	O(1A)-C(11A)-C(10A)	123.0(2)
N(1A)-C(11A)-C(10A)	116.9(2)	C(13A)-C(12A)-C(10A)	119.7(3)
C(12A)-C(13A)-C(14A)	120.2(3)	C(15A)-C(14A)-C(13A)	122.0(3)
C(14A)-C(15A)-C(9A)	118.4(3)	C(14A)-C(15A)-C(16A)	120.6(3)
C(9A)-C(15A)-C(16A)	121.1(3)		

Table 4. Anisotropic displacement parameters (Å^2 × 10^3) for **13i**. The anisotropic displacement factor exponent takes the form: -2 gpi^2 [h^2 a*^{2} U11 + ... + 2 h k a* b* U

Atom	U11	U22	U33	U23	U13	U12
Cl(1)	36(1)	30(1)	64(1)	15(1)	9(1)	7(1)
Cl(2)	43(1)	27(1)	34(1)	4(1)	7(1)	-2(1)
O(1)	36(1)	20(1)	34(1)	-4(1)	9(1)	2(1)
O(2)	54(2)	55(2)	44(2)	11(1)	14(1)	15(1)
N(1)	28(1)	19(1)	32(1)	-1(1)	4(1)	1(1)
C(1)	34(2)	25(2)	33(2)	-2(1)	4(1)	0(1)
C(2)	30(2)	35(2)	39(2)	-5(1)	4(1)	6(1)
C(3)	28(2)	47(2)	40(2)	-9(2)	7(1)	2(1)
C(4)	36(2)	39(2)	36(2)	-6(1)	9(1)	-9(1)
C(5)	33(2)	24(1)	30(2)	-6(1)	3(1)	-1(1)
C(6)	28(2)	20(1)	29(1)	-5(1)	6(1)	0(1)
C(7)	30(2)	19(1)	26(1)	2(1)	6(1)	3(1)
C(8)	31(2)	20(1)	28(1)	0(1)	4(1)	3(1)
C(9)	28(1)	22(1)	23(1)	4(1)	4(1)	2(1)
C(10)	31(2)	21(1)	24(1)	4(1)	4(1)	1(1)
C(11)	31(2)	20(1)	26(1)	5(1)	5(1)	5(1)
C(12)	33(2)	28(2)	30(2)	2(1)	8(1)	7(1)
C(13)	27(2)	37(2)	35(2)	3(1)	7(1)	5(1)
C(14)	33(2)	33(2)	29(2)	2(1)	1(1)	-2(1)
C(15)	30(2)	25(1)	24(1)	3(1)	1(1)	2(1)
C(16)	32(2)	27(2)	41(2)	-3(1)	0(1)	-3(1)
C(17)	40(2)	40(2)	61(2)	4(2)	10(2)	-1(2)
C(18)	50(2)	61(2)	44(2)	-9(2)	10(2)	-11(2)
Cl(1A)	35(1)	27(1)	53(1)	-13(1)	1(1)	1(1)
Cl(2A)	50(1)	25(1)	35(1)	-7(1)	-3(1)	5(1)
O(1A)	34(1)	20(1)	32(1)	6(1)	2(1)	4(1)
N(1A)	28(1)	19(1)	28(1)	2(1)	4(1)	3(1)
C(1A)	30(2)	20(1)	29(2)	1(1)	2(1)	0(1)
C(2A)	35(2)	22(1)	34(2)	2(1)	7(1)	7(1)
C(3A)	30(2)	35(2)	37(2)	8(1)	2(1)	3(1)
C(4A)	35(2)	30(2)	33(2)	1(1)	-2(1)	-5(1)
C(5A)	34(2)	20(1)	28(2)	3(1)	2(1)	2(1)
C(6A)	30(2)	22(1)	24(1)	3(1)	2(1)	2(1)
C(7A)	32(2)	18(1)	23(1)	-2(1)	2(1)	3(1)
C(8A)	32(2)	17(1)	27(1)	1(1)	3(1)	4(1)
C(9A)	29(2)	21(1)	22(1)	-3(1)	4(1)	0(1)

C(10A)	30(2)	21(1)	22(1)	-4(1)	4(1)	2(1)
C(11A)	32(2)	21(1)	21(1)	-3(1)	0(1)	3(1)
C(12A)	30(2)	29(2)	27(1)	-3(1)	-1(1)	6(1)
C(13A)	26(2)	34(2)	33(2)	-4(1)	2(1)	4(1)
C(14A)	31(2)	36(2)	29(2)	-5(1)	5(1)	-6(1)
C(15A)	32(2)	23(1)	26(1)	-4(1)	2(1)	1(1)
C(16A)	39(2)	31(2)	36(2)	4(1)	7(1)	-5(1)

Table 5. Hydrogen coordinates (× 10^4) and isotropic displacement parameters (Å^2 × 10^3) for **13i**.

Atom	x	y	z	U(eq)
H(2)	6631	2896	3756	104(19)
H(1)	7422	3459	5359	31
H(2B)	4883	6299	5633	41
H(3)	4072	5124	6347	46
H(4)	4890	3753	6953	44
H(8)	8289	5821	6646	32
H(12)	10648	3260	5436	36
H(13)	11897	4282	5943	39
H(14)	11594	5774	6586	38
H(16A)	9279	6701	6921	50
H(16B)	10192	7153	6544	50
H(16C)	10301	6663	7472	50
H(16D)	10568	6977	7037	50
H(16E)	9656	6525	7414	50
H(16F)	9547	7015	6486	50
H(17A)	7049	1633	2975	56
H(17B)	7949	2267	3373	56
H(18A)	6976	2542	1702	77
H(18B)	8024	2092	1899	77
H(18C)	7837	3221	2099	77
H(1A)	7952	1627	5276	30
H(2A)	10290	-1468	5602	36
H(3A)	11350	-377	6354	41
H(4A)	10780	1032	6972	40
H(8A)	7139	-673	6519	30
H(12A)	4779	2148	5287	35
H(13A)	3543	1267	5772	38
H(14A)	3837	-239	6443	38
H(16G)	6106	-1427	6845	53
H(16H)	5059	-1765	6464	53
H(16I)	5220	-1245	7378	53
H(16J)	4818	-1530	6946	53
H(16K)	5864	-1193	7327	53
H(16L)	5703	-1713	6414	53

Table 6. Dihedral angles [°] for **13i**.

Atom1 - Atom2 - Atom3 - Atom4	Dihedral
C(6) - C(1) - C(2) - C(3)	-0.1(4)
Cl(1) - C(1) - C(2) - C(3)	179.8(2)
C(1) - C(2) - C(3) - C(4)	0.7(4)
C(2) - C(3) - C(4) - C(5)	0.1(4)
C(3) - C(4) - C(5) - C(6)	-1.6(4)
C(3) - C(4) - C(5) - Cl(2)	175.9(2)
C(4) - C(5) - C(6) - C(1)	2.1(4)
Cl(2) - C(5) - C(6) - C(1)	-175.4(2)
C(4) - C(5) - C(6) - C(7)	-176.8(3)
Cl(2) - C(5) - C(6) - C(7)	5.8(4)
C(2) - C(1) - C(6) - C(5)	-1.2(4)
Cl(1) - C(1) - C(6) - C(5)	178.9(2)
C(2) - C(1) - C(6) - C(7)	177.6(3)
Cl(1) - C(1) - C(6) - C(7)	-2.3(4)
C(11) - N(1) - C(7) - C(8)	4.3(4)
C(11) - N(1) - C(7) - C(6)	-174.6(2)
C(5) - C(6) - C(7) - C(8)	-117.3(3)
C(1) - C(6) - C(7) - C(8)	63.9(4)
C(5) - C(6) - C(7) - N(1)	61.6(3)
C(1) - C(6) - C(7) - N(1)	-117.2(3)
N(1) - C(7) - C(8) - C(9)	-0.7(4)
C(6) - C(7) - C(8) - C(9)	178.2(2)
C(7) - C(8) - C(9) - C(10)	-3.1(4)
C(7) - C(8) - C(9) - C(15)	176.7(2)
C(15) - C(9) - C(10) - C(12)	2.4(4)
C(8) - C(9) - C(10) - C(12)	-177.8(2)
C(15) - C(9) - C(10) - C(11)	-176.3(2)
C(8) - C(9) - C(10) - C(11)	3.5(4)
C(7) - N(1) - C(11) - O(1)	177.1(2)
C(7) - N(1) - C(11) - C(10)	-3.8(4)
C(12) - C(10) - C(11) - O(1)	0.2(4)
C(9) - C(10) - C(11) - O(1)	178.9(2)
C(12) - C(10) - C(11) - N(1)	-178.9(2)
C(9) - C(10) - C(11) - N(1)	-0.3(4)
C(9) - C(10) - C(12) - C(13)	-0.6(4)
C(11) - C(10) - C(12) - C(13)	178.1(2)

C(10) - C(12) - C(13) - C(14)	-1.1(4)
C(12) - C(13) - C(14) - C(15)	1.0(4)
C(13) - C(14) - C(15) - C(9)	0.9(4)
C(13) - C(14) - C(15) - C(16)	-177.6(3)
C(10) - C(9) - C(15) - C(14)	-2.5(4)
C(8) - C(9) - C(15) - C(14)	177.7(2)
C(10) - C(9) - C(15) - C(16)	176.0(2)
C(8) - C(9) - C(15) - C(16)	-3.8(4)
C(6A) - C(1A) - C(2A) - C(3A)	-0.4(4)
Cl(1A) - C(1A) - C(2A) - C(3A)	179.4(2)
C(1A) - C(2A) - C(3A) - C(4A)	1.8(4)
C(2A) - C(3A) - C(4A) - C(5A)	-0.9(4)
C(3A) - C(4A) - C(5A) - C(6A)	-1.4(4)
C(3A) - C(4A) - C(5A) - Cl(2A)	175.2(2)
C(4A) - C(5A) - C(6A) - C(1A)	2.7(4)
Cl(2A) - C(5A) - C(6A) - C(1A)	-173.95(19)
C(4A) - C(5A) - C(6A) - C(7A)	-177.0(3)
Cl(2A) - C(5A) - C(6A) - C(7A)	6.4(3)
C(2A) - C(1A) - C(6A) - C(5A)	-1.7(4)
Cl(1A) - C(1A) - C(6A) - C(5A)	178.4(2)
C(2A) - C(1A) - C(6A) - C(7A)	177.9(3)
Cl(1A) - C(1A) - C(6A) - C(7A)	-1.9(4)
C(11A) - N(1A) - C(7A) - C(8A)	2.9(4)
C(11A) - N(1A) - C(7A) - C(6A)	-175.9(2)
C(5A) - C(6A) - C(7A) - C(8A)	-115.8(3)
C(1A) - C(6A) - C(7A) - C(8A)	64.6(4)
C(5A) - C(6A) - C(7A) - N(1A)	63.0(3)
C(1A) - C(6A) - C(7A) - N(1A)	-116.7(3)
N(1A) - C(7A) - C(8A) - C(9A)	-1.7(4)
C(6A) - C(7A) - C(8A) - C(9A)	177.0(2)
C(7A) - C(8A) - C(9A) - C(15A)	178.9(2)
C(7A) - C(8A) - C(9A) - C(10A)	-1.2(4)
C(15A) - C(9A) - C(10A) - C(12A)	2.1(4)
C(8A) - C(9A) - C(10A) - C(12A)	-177.8(2)
C(15A) - C(9A) - C(10A) - C(11A)	-177.0(2)
C(8A) - C(9A) - C(10A) - C(11A)	3.0(4)
C(7A) - N(1A) - C(11A) - O(1A)	178.5(2)
C(7A) - N(1A) - C(11A) - C(10A)	-1.0(4)
C(12A) - C(10A) - C(11A) - O(1A)	-0.7(4)

C(9A) - C(10A) - C(11A) - O(1A)	178.5(2)
C(12A) - C(10A) - C(11A) - N(1A)	178.9(2)
C(9A) - C(10A) - C(11A) - N(1A)	-1.9(4)
C(9A) - C(10A) - C(12A) - C(13A)	-1.4(4)
C(11A) - C(10A) - C(12A) - C(13A)	177.8(2)
C(10A) - C(12A) - C(13A) - C(14A)	0.0(4)
C(12A) - C(13A) - C(14A) - C(15A)	0.5(4)
C(13A) - C(14A) - C(15A) - C(9A)	0.2(4)
C(13A) - C(14A) - C(15A) - C(16A)	-178.5(3)
C(10A) - C(9A) - C(15A) - C(14A)	-1.5(4)
C(8A) - C(9A) - C(15A) - C(14A)	178.4(2)
C(10A) - C(9A) - C(15A) - C(16A)	177.2(2)
C(8A) - C(9A) - C(15A) - C(16A)	-2.8(4)

Table 7. Crystal data and structure refinement for **15b**.

Identification code	k12farm10
Formula weight	265.30
Temperature	150(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	P21/n
Unit cell dimensions	a = 12.5690(8)Å α = 90°
	b = 17.0250(11)Å β = 104.837(2)°
	c = 13.3300(11)Å γ = 90°
Volume	2757.3(3) $Å^3$
Z	8
Density (calculated)	1.278 Mg m^{-3}
Absorption coefficient	0.084 mm^{-1}
F(000)	1120
Crystal size	0.30 × 0.08 × 0.08 mm
θ range for data collection	3.52 to 25.03°
Index ranges	-14<=h<=14; -20<=k<=20; -11<=l<=15
Reflections collected	12394
Independent reflections	4788 [R(int) = 0.1450]
Reflections observed (>2σ)	1941
Data Completeness	0.982
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	1.000 and 0.710
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4788 / 0 / 365
Goodness-of-fit on F^2	0.895
Final R indices [I>2σ(I)]	*R*1 = 0.0717 *wR*2 = 0.1299
R indices (all data)	*R*1 = 0.2113 *wR*2 = 0.1699
Largest diff. peak and hole	0.259 and -0.241 e$Å^{-3}$

Notes:

Two independent molecules in the asymmetric unit, which form hydrogen-bonded dimers.

Crystal quality poor - small fragment taken from a non-merohedrally twinned needle. Unit cell parameters reflect the sample quality. However, the structure is unambiguous. Data truncated to 25 degree Bragg angle.

Hydrogen bonds with H..A < r(A) + 2.000 Angstroms and <DHA > 110 deg.

D-H	d(D-H)	d(H..A)	<DHA	d(D..A)	A
N1-H1	0.880	1.917	168.55	2.785	O1A
N1A-H1A	0.880	2.095	163.52	2.950	O1

Table 8. Atomic coordinates (× 10^4) and equivalent isotropic displacement parameters ($Å^2 \times 10^3$) for 1.U(eq) is defined as one third of the trace of the orthogonallised Uij tensor for **15b**.

Atom	**x**	**y**	**z**	**U(eq)**
O(1)	4518(2)	1373(1)	-78(2)	50(1)
O(2)	701(2)	3499(1)	-299(3)	76(1)
N(1)	3249(2)	1302(2)	854(2)	42(1)
C(1)	3670(3)	1634(2)	109(3)	46(1)
C(2)	3060(3)	2313(2)	-435(3)	44(1)
C(3)	3416(3)	2679(2)	-1231(3)	53(1)
C(4)	2872(3)	3325(2)	-1706(4)	65(1)
C(5)	1944(4)	3608(2)	-1412(4)	72(1)
C(6)	1590(3)	3260(2)	-636(4)	62(1)
C(7)	2139(3)	2589(2)	-126(3)	48(1)
C(8)	1785(3)	2199(2)	675(3)	53(1)
C(9)	2328(3)	1560(2)	1161(3)	44(1)
C(10)	2011(3)	1117(2)	1975(3)	48(1)
C(11)	1408(3)	1453(2)	2609(4)	68(1)
C(12)	1129(4)	1037(3)	3386(4)	83(2)
C(13)	1447(4)	257(3)	3583(4)	71(1)
C(14)	2019(3)	-74(2)	2953(4)	69(1)
C(15)	2300(3)	331(2)	2160(4)	59(1)
C(16)	1147(4)	-195(3)	4464(5)	117(2)
C(17)	19(4)	4110(3)	-875(4)	103(2)
O(1A)	4580(2)	54(1)	1769(2)	59(1)
O(2A)	8876(2)	-1580(1)	3110(2)	68(1)
N(1A)	6113(2)	279(2)	1218(2)	44(1)
C(1A)	5547(3)	-119(2)	1807(3)	45(1)
C(2A)	6148(3)	-725(2)	2490(3)	48(1)
C(3A)	5629(3)	-1157(2)	3129(3)	54(1)
C(4A)	6200(3)	-1722(2)	3751(4)	59(1)
C(5A)	7298(3)	-1886(2)	3788(3)	59(1)
C(6A)	7818(3)	-1469(2)	3165(3)	56(1)
C(7A)	7252(3)	-868(2)	2501(3)	43(1)
C(8A)	7758(3)	-417(2)	1841(3)	49(1)
C(9A)	7206(3)	148(2)	1208(3)	40(1)
C(10A)	7670(3)	638(2)	512(3)	42(1)
C(11A)	8796(3)	628(2)	582(4)	63(1)
C(12A)	9240(3)	1053(2)	-91(4)	66(1)
C(13A)	8608(3)	1518(2)	-851(4)	58(1)

C(14A)	7495(3)	1542(2)	-908(3)	56(1)
C(15A)	7029(3)	1111(2)	-254(3)	50(1)
C(16A)	9095(3)	1960(2)	-1614(4)	77(1)
C(17A)	9459(3)	-2218(2)	3716(4)	82(2)

Table 9. Bond lengths [Å] and angles [°] for **15b**.

O(1)-C(1)	1.238(4)	O(2)-C(6)	1.369(4)
O(2)-C(17)	1.438(5	N(1)-C(1)	1.360(4)
N(1)-C(9)	1.395(4)	C(1)-C(2)	1.472(5)
C(2)-C(3)	1.399(5)	C(2)-C(7)	1.405(4)
C(3)-C(4)	1.364(5)	C(4)-C(5)	1.406(5)
C(5)-C(6)	1.363(5)	C(6)-C(7)	1.416(5)
C(7)-C(8)	1.423(5)	C(8)-C(9)	1.357(5)
C(9)-C(10)	1.459(5)	C(10)-C(15)	1.392(5)
C(10)-C(11)	1.394(5)	C(11)-C(12)	1.373(6)
C(12)-C(13)	1.394(6)	C(13)-C(14)	1.360(5)
C(13)-C(16)	1.529(6)	C(14)-C(15)	1.382(5)
O(1A)-C(1A)	1.239(4)	O(2A)-C(6A)	1.364(4)
O(2A)-C(17A)	1.438(4	N(1A)-C(1A)	1.367(4)
N(1A)-C(9A)	1.394(4)	C(1A)-C(2A)	1.453(5)
C(2A)-C(7A)	1.404(4)	C(2A)-C(3A)	1.406(5)
C(3A)-C(4A)	1.350(5)	C(4A)-C(5A)	1.397(5)
C(5A)-C(6A)	1.377(5)	C(6A)-C(7A)	1.420(5)
C(7A)-C(8A)	1.434(5)	C(8A)-C(9A)	1.348(5)
C(9A)-C(10A)	1.476(5)	C(10A)-C(15A)	1.385(5)
C(10A)-C(11A)	1.395(5)	C(11A)-C(12A)	1.377(5)
C(12A)-C(13A)	1.369(6)	C(13A)-C(14A)	1.382(5)
C(13A)-C(16A)	1.514(5)	C(14A)-C(15A)	1.380(5)
C(6)-O(2)-C(17)	117.7(4)	C(1)-N(1)-C(9)	126.2(3)
O(1)-C(1)-N(1)	121.0(3)	O(1)-C(1)-C(2)	123.2(4)
N(1)-C(1)-C(2)	115.8(3)	C(3)-C(2)-C(7)	121.4(3)
C(3)-C(2)-C(1)	119.8(3)	C(7)-C(2)-C(1)	118.8(4)
C(4)-C(3)-C(2)	119.5(4)	C(3)-C(4)-C(5)	120.0(4)
C(6)-C(5)-C(4)	121.2(4)	C(5)-C(6)-O(2)	125.0(4)
C(5)-C(6)-C(7)	120.1(4)	O(2)-C(6)-C(7)	114.9(4)
C(2)-C(7)-C(6)	117.8(4)	C(2)-C(7)-C(8)	120.3(3)
C(6)-C(7)-C(8)	122.0(4)	C(9)-C(8)-C(7)	121.1(3)
C(8)-C(9)-N(1)	117.8(3)	C(8)-C(9)-C(10)	124.8(3)
N(1)-C(9)-C(10)	117.4(3)	C(15)-C(10)-C(11)	116.5(4)
C(15)-C(10)-C(9)	121.4(3)	C(11)-C(10)-C(9)	122.1(3)
C(12)-C(11)-C(10)	121.9(4)	C(11)-C(12)-C(13)	121.2(4)
C(14)-C(13)-C(12)	116.7(4)	C(14)-C(13)-C(16)	122.7(4)
C(12)-C(13)-C(16)	120.6(4)	C(13)-C(14)-C(15)	123.1(4)
C(14)-C(15)-C(10)	120.5(4)	C(6A)-O(2A)-C(17A)	116.0(3)

C(1A)-N(1A)-C(9A)	125.8(3)	O(1A)-C(1A)-N(1A)	120.5(3)
O(1A)-C(1A)-C(2A)	122.8(3)	N(1A)-C(1A)-C(2A)	116.6(3)
C(7A)-C(2A)-C(3A)	120.9(3)	C(7A)-C(2A)-C(1A)	118.9(3)
C(3A)-C(2A)-C(1A)	120.2(3)	C(4A)-C(3A)-C(2A)	119.3(4)
C(3A)-C(4A)-C(5A)	122.0(4)	C(6A)-C(5A)-C(4A)	119.5(4)
O(2A)-C(6A)-C(5A)	125.5(4)	O(2A)-C(6A)-C(7A)	114.0(3)
C(5A)-C(6A)-C(7A)	120.6(3)	C(2A)-C(7A)-C(6A)	117.8(3)
C(2A)-C(7A)-C(8A)	119.6(3)	C(6A)-C(7A)-C(8A)	122.6(3)
C(9A)-C(8A)-C(7A)	121.8(3)	C(8A)-C(9A)-N(1A)	117.4(3)
C(8A)-C(9A)-C(10A)	125.0(3)	N(1A)-C(9A)-C(10A)	117.6(3)
C(15A)-C(10A)-C(11A)	116.5(3)	C(15A)-C(10A)-C(9A)	122.9(3)
C(11A)-C(10A)-C(9A)	120.6(4)	C(12A)-C(11A)-C(10A)	121.5(4)
C(13A)-C(12A)-C(11A)	122.1(4)	C(12A)-C(13A)-C(14A)	116.4(4)
C(12A)-C(13A)-C(16A)	121.8(4)	C(14A)-C(13A)-C(16A)	121.8(4)
C(15A)-C(14A)-C(13A)	122.5(4)	C(14A)-C(15A)-C(10A)	120.9(3)

Table 10. Anisotropic displacement parameters ($Å^2 \times 10^3$) for **15b**. The anisotropic displacement factor exponent takes the form: -2 gpi^2 [h^2 a*^{2} U11 + ... + 2 h k a* b* U

Atom	U11	U22	U33	U23	U13	U12
O(1)	43(2)	49(2)	58(2)	2(1)	12(1)	3(1)
O(2)	82(2)	59(2)	93(3)	16(2)	30(2)	29(2)
N(1)	39(2)	35(2)	49(2)	6(2)	4(2)	2(1)
C(1)	44(2)	41(2)	52(3)	-5(2)	10(2)	-8(2)
C(2)	42(2)	39(2)	47(3)	-4(2)	3(2)	-1(2)
C(3)	61(2)	44(2)	50(3)	5(2)	8(2)	0(2)
C(4)	80(3)	53(3)	62(4)	5(2)	19(3)	3(2)
C(5)	92(3)	56(3)	65(4)	12(2)	17(3)	20(2)
C(6)	70(3)	48(2)	67(4)	0(2)	17(3)	9(2)
C(7)	48(2)	36(2)	55(3)	1(2)	2(2)	3(2)
C(8)	50(2)	47(2)	62(3)	-3(2)	12(2)	5(2)
C(9)	39(2)	45(2)	48(3)	-3(2)	9(2)	-1(2)
C(10)	40(2)	45(2)	59(3)	-6(2)	10(2)	2(2)
C(11)	83(3)	62(3)	62(4)	-2(3)	26(3)	15(2)
C(12)	86(3)	105(4)	68(4)	-2(3)	39(3)	19(3)
C(13)	77(3)	81(3)	64(4)	9(3)	35(3)	6(3)
C(14)	73(3)	64(3)	80(4)	13(3)	39(3)	8(2)
C(15)	57(2)	50(2)	80(4)	2(2)	38(2)	2(2)
C(16)	133(4)	135(5)	112(6)	43(4)	86(4)	29(4)
C(17)	117(4)	91(4)	102(5)	35(3)	30(4)	69(3)
O(1A)	43(2)	59(2)	77(2)	20(2)	19(1)	10(1)
O(2A)	56(2)	73(2)	71(2)	30(2)	10(2)	20(1)
N(1A)	44(2)	35(2)	51(2)	5(2)	11(2)	4(1)
C(1A)	45(2)	40(2)	50(3)	-3(2)	13(2)	-4(2)
C(2A)	50(2)	35(2)	62(3)	2(2)	19(2)	2(2)
C(3A)	58(2)	52(2)	55(3)	4(2)	17(2)	4(2)
C(4A)	70(3)	50(2)	60(3)	11(2)	21(2)	-4(2)
C(5A)	76(3)	48(2)	53(3)	8(2)	16(2)	4(2)
C(6A)	54(2)	51(2)	63(3)	7(2)	16(2)	7(2)
C(7A)	48(2)	38(2)	36(3)	0(2)	-1(2)	4(2)
C(8A)	41(2)	48(2)	57(3)	1(2)	9(2)	0(2)
C(9A)	39(2)	45(2)	32(3)	-8(2)	2(2)	3(2)
C(10A)	41(2)	41(2)	46(3)	-2(2)	12(2)	1(2)
C(11A)	50(2)	63(3)	73(4)	24(2)	11(2)	-4(2)
C(12A)	44(2)	75(3)	74(4)	10(3)	6(2)	-9(2)
C(13A)	57(3)	52(2)	64(3)	9(2)	16(2)	-4(2)

C(14A)	62(3)	55(2)	53(3)	11(2)	18(2)	9(2)
C(15A)	47(2)	50(2)	55(3)	5(2)	15(2)	9(2)
C(16A)	74(3)	87(3)	70(4)	18(3)	20(3)	-10(2)
C(17A)	75(3)	85(3)	84(4)	46(3)	17(3)	35(3)

Table 5. Hydrogen coordinates ($\times 10^4$) and isotropic displacement parameters ($Å^2 \times 10^3$) for **15b**.

Atom	x	y	z	U(eq)
H(1)	3591	886	1172	51
H(3)	4032	2478	-1439	63
H(4)	3119	3585	-2236	78
H(5)	1558	4050	-1761	86
H(8)	1157	2389	873	64
H(11)	1183	1986	2499	81
H(12)	712	1286	3798	99
H(14)	2235	-608	3063	83
H(15)	2695	70	1737	71
H(16A)	374	-358	4245	175
H(16B)	1257	144	5076	175
H(16C)	1618	-660	4636	175
H(17A)	436	4602	-799	155
H(17B)	-632	4180	-609	155
H(17C)	-210	3964	-1610	155
H(1A)	5757	651	808	53
H(3A)	4885	-1053	3123	65
H(4A)	5844	-2017	4175	71
H(5A)	7684	-2282	4239	71
H(8A)	8504	-518	1850	59
H(11A)	9268	320	1107	75
H(12A)	10010	1022	-26	79
H(14A)	7033	1868	-1417	67
H(15A)	6257	1139	-330	60
H(16D)	9513	1596	-1935	115
H(16E)	9586	2374	-1247	115
H(16F)	8502	2197	-2152	115
H(17D)	9103	-2716	3453	123
H(17E)	9449	-2151	4443	123
H(17F)	10222	-2223	3662	123

Table 6. Dihedral angles [°] for **15b**.

Atom1 - Atom2 - Atom3 - Atom4	Dihedral
C(9) - N(1) - C(1) - O(1)	177.4(3)
C(9) - N(1) - C(1) - C(2)	-2.0(5)
O(1) - C(1) - C(2) - C(3)	2.2(5)
N(1) - C(1) - C(2) - C(3)	-178.4(3)
O(1) - C(1) - C(2) - C(7)	-176.6(3)
N(1) - C(1) - C(2) - C(7)	2.8(5)
C(7) - C(2) - C(3) - C(4)	1.2(6)
C(1) - C(2) - C(3) - C(4)	-177.6(3)
C(2) - C(3) - C(4) - C(5)	-1.5(6)
C(3) - C(4) - C(5) - C(6)	1.8(7)
C(4) - C(5) - C(6) - O(2)	179.7(4)
C(4) - C(5) - C(6) - C(7)	-1.6(7)
C(17) - O(2) - C(6) - C(5)	7.0(6)
C(17) - O(2) - C(6) - C(7)	-171.8(4)
C(3) - C(2) - C(7) - C(6)	-1.0(5)
C(1) - C(2) - C(7) - C(6)	177.8(3)
C(3) - C(2) - C(7) - C(8)	179.1(4)
C(1) - C(2) - C(7) - C(8)	-2.2(5)
C(5) - C(6) - C(7) - C(2)	1.2(6)
O(2) - C(6) - C(7) - C(2)	-179.9(3)
C(5) - C(6) - C(7) - C(8)	-178.9(4)
O(2) - C(6) - C(7) - C(8)	0.0(6)
C(2) - C(7) - C(8) - C(9)	0.5(6)
C(6) - C(7) - C(8) - C(9)	-179.4(4)
C(7) - C(8) - C(9) - N(1)	0.4(5)
C(7) - C(8) - C(9) - C(10)	-178.8(4)
C(1) - N(1) - C(9) - C(8)	0.4(5)
C(1) - N(1) - C(9) - C(10)	179.8(3)
C(8) - C(9) - C(10) - C(15)	154.8(4)
N(1) - C(9) - C(10) - C(15)	-24.5(5)
C(8) - C(9) - C(10) - C(11)	-25.3(6)
N(1) - C(9) - C(10) - C(11)	155.4(4)
C(15) - C(10) - C(11) - C(12)	1.1(7)
C(9) - C(10) - C(11) - C(12)	-178.8(4)
C(10) - C(11) - C(12) - C(13)	0.5(8)
C(11) - C(12) - C(13) - C(14)	-1.6(7)

C(11) - C(12) - C(13) - C(16)	178.9(5)
C(12) - C(13) - C(14) - C(15)	1.0(7)
C(16) - C(13) - C(14) - C(15)	-179.5(5)
C(13) - C(14) - C(15) - C(10)	0.6(7)
C(11) - C(10) - C(15) - C(14)	-1.7(6)
C(9) - C(10) - C(15) - C(14)	178.3(4)
C(9A) - N(1A) - C(1A) - O(1A)	178.8(3)
C(9A) - N(1A) - C(1A) - C(2A)	0.7(5)
O(1A) - C(1A) - C(2A) - C(7A)	-178.4(3)
N(1A) - C(1A) - C(2A) - C(7A)	-0.4(5)
O(1A) - C(1A) - C(2A) - C(3A)	1.4(6)
N(1A) - C(1A) - C(2A) - C(3A)	179.5(3)
C(7A) - C(2A) - C(3A) - C(4A)	-0.7(6)
C(1A) - C(2A) - C(3A) - C(4A)	179.4(4)
C(2A) - C(3A) - C(4A) - C(5A)	0.7(6)
C(3A) - C(4A) - C(5A) - C(6A)	-0.9(6)
C(17A) - O(2A) - C(6A) - C(5A)	3.8(6)
C(17A) - O(2A) - C(6A) - C(7A)	-175.9(4)
C(4A) - C(5A) - C(6A) - O(2A)	-178.7(4)
C(4A) - C(5A) - C(6A) - C(7A)	1.0(6)
C(3A) - C(2A) - C(7A) - C(6A)	0.9(6)
C(1A) - C(2A) - C(7A) - C(6A)	-179.3(4)
C(3A) - C(2A) - C(7A) - C(8A)	-180.0(4)
C(1A) - C(2A) - C(7A) - C(8A)	-0.1(5)
O(2A) - C(6A) - C(7A) - C(2A)	178.7(3)
C(5A) - C(6A) - C(7A) - C(2A)	-1.1(6)
O(2A) - C(6A) - C(7A) - C(8A)	-0.4(6)
C(5A) - C(6A) - C(7A) - C(8A)	179.8(4)
C(2A) - C(7A) - C(8A) - C(9A)	0.3(6)
C(6A) - C(7A) - C(8A) - C(9A)	179.4(4)
C(7A) - C(8A) - C(9A) - N(1A)	0.0(5)
C(7A) - C(8A) - C(9A) - C(10A)	179.7(3)
C(1A) - N(1A) - C(9A) - C(8A)	-0.6(5)
C(1A) - N(1A) - C(9A) - C(10A)	179.8(3)
C(8A) - C(9A) - C(10A) - C(15A)	168.2(4)
N(1A) - C(9A) - C(10A) - C(15A)	-12.2(5)
C(8A) - C(9A) - C(10A) - C(11A)	-10.0(6)
N(1A) - C(9A) - C(10A) - C(11A)	169.7(3)
C(15A) - C(10A) - C(11A) - C(12A)	-1.4(6)

C(9A) - C(10A) - C(11A) - C(12A)	176.9(4)
C(10A) - C(11A) - C(12A) - C(13A)	1.2(7)
C(11A) - C(12A) - C(13A) - C(14A)	0.1(7)
C(11A) - C(12A) - C(13A) - C(16A)	-177.7(4)
C(12A) - C(13A) - C(14A) - C(15A)	-1.3(6)
C(16A) - C(13A) - C(14A) - C(15A)	176.5(4)
C(13A) - C(14A) - C(15A) - C(10A)	1.2(6)
C(11A) - C(10A) - C(15A) - C(14A)	0.2(6)
C(9A) - C(10A) - C(15A) - C(14A)	-178.0(3)

Section H: Details of the diffraction data and refinement of the structures of complexes of selected isoquinolin-1-ones with tankyrase-2.

Compound	**11a**	**11b**	**11c**	**11d**	**12a**	**12f**
PDB code	4UVL	4UVP	4UVS	4UVT	4UVZ	4UVO
Data						
Beam line	ESRF ID23-1	ESRF ID23-1	ESRF ID14-1	ESRF ID23-1	ESRF ID23-1	ESRF ID23-2
Wavelength (Å)	1.07227	1.07227	0.93340	1.07227	1.07227	0.87260
Space group	$C222_1$	$C222_1$	$C222_1$	$C222_1$	$C222_1$	$C222_1$
Cell dimensions						
a, b, c (Å)	91.30, 97.78, 118.88	91.16, 97.70, 118.69	91.45, 98.68, 119.21	91.54, 97.62, 118.07	91.03, 98.06, 118.03	91.31, 98.25, 119.11
Resolution (Å)	50-2.0 (2.05-2.00)	50-1.75 (1.80-1.75)	50-2.0 (2.05-2.00)	50-1.95 (2.00-1.95)	50-1.60 (1.64-1.60)	50-1.85 (1.90-1.85)
R_{merge}	0.090 (0.706)	0.049 (0.463)	0.080 (0.522)	0.070 (0.597)	0.057 (0.702)	0.071 (0.671)
I / σI	15.50 (2.85)	16.29 (2.19)	14.48 (2.60)	18.62 (3.37)	20.38 (2.78)	17.10 (2.53)
Completeness (%)	100 (100)	98.4 (85.8)	99.7 (99.9)	99.3 (98.9)	98.4 (97.2)	99.8 (99.9)
Redundancy	7.2 (7.3)	3.5 (2.7)	3.7 (3.7)	7.2 (7.4)	7.3 (7.4)	5.6 (5.6)
Refinement						
R_{work} / R_{free}	0.17253 / 0.21402	0.16841 / 0.20541	0.18164 / 0.21424	0.16868 / 0.21306	0.16365 / 0.18851	0.16633 / 0.19735
B-factors						
Protein	26.6065	21.283	19.9235	26.6735	19.3375	21.6805
Inhibitor	32.4065	19.976	18.473	30.7105	14.0475	26.6415
R.m.s.d.						
Bond lengths (Å)	0.014	0.015	0.013	0.013	0.014	0.015
Bond angles (°)	1.389	1.491	1.305	1.370	1.431	1.441
Ramachandran plot (%)						
Favoured regions	98.53	99.27	98.78	98.78	99.02	99.27
Additionally allowed regions	-	0.57	0.28	0.85	1.13	1.13

Compound	**12m**	**13h**	**13n**	**14f**	**15e**	**17**
PDB code	4UVN	4UVV	4UVU	4UVX	4UVY	4UVW
Data						
Beam line	ESRF ID14-1	Diamond I038	Diamond I038	Diamond I038	Diamond I04-1	ESRF ID23-2
Wavelength (Å)	0.93340	0.976250	0.976250	0.976250	0.92000	0.87260
Space group	$C222_1$	$C222_1$	$C222_1$	$C222_1$	$C222_1$	$C222_1$

Cell dimensions						91.23 97.72 117.81
a, b, c (Å)	90.69, 98.15, 118.0	91.23, 97.72, 117.81	90.23, 98.56, 118.94	90.58, 98.51, 118.50	91.38, 98.36, 119.51	93.56, 96.73, 117.09
Resolution (Å)	50-2.20 (2.26-2.20)	50-1.90 (1.95-1.90)	30-1.95 (2.00-1.95)	30-1.95 (2.00-1.95)	30-1.95 (2.00-1.95)	50-2.10 (2.15-2.10)
R_{merge}	0.095 (0.592)	5.7 (70.8)	8.9 (77.3)	8.2 (78.7)	12.3 (94.4)	9.0 (92.6)
I / σI	12.85 (2.27)	18.59 (2.45)	12.54 (2.38)	13.60 (2.27)	12.59 (2.07)	17.42 (2.87)
Completeness (%)	97.1 (99.3)	99.9 (100)	99.9 (100)	99.9 (100)	99.9 (99.9)	99.9 (100)
Redundancy	3.8 (3.7)	6.7 (6.7)	6.6 (6.6)	6.6 (6.6)	6.7 (6.9)	7.4 (7.5)
Refinement						
R_{work} / R_{free}	0.18423 / 0.23870	0.16623 / 0.19803	0.1711 / 0.1918	0.1693 / 0.2112	0.1730 / 0.2126	0.1709 / 0.2098
B-factors						
Protein	20.947	34.8	35.2	36.6	25.6	38.0
Inhibitor	16.717	27.9	37.0	31.8	33.8	32.2
R.m.s.d.						
Bond lengths (Å)	0.013	0.011	0.009	0.011	0.009	0.012
Bond angles (°)	1.354	1.4	1.4	1.4	1.2	1.5
Ramachandran plot (%)						
Favoured regions	99.02	99.27	98.29	98.53	98.80	98.04
Additionally allowed regions	0.85	0.73	1.71	1.47	1.20	1.96

Section I: References for Supporting Information

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