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Experimental

General Methods

Pyrimidines were purchased from Aldrich and used as supplied. THF and ether were freshly distilled from sodium-benzophenone. Flash chromatography was carried out using silica gel 200-400 mesh (60 Å). ^{1}H and ^{13}C NMR were recorded at 300 MHz and 75 MHz respectively using a Bruker Avance 300 MHz spectrometer in $CDCl_3$ unless otherwise specified.

GCMS was performed using a Shimadzu GCMS-QP5050A. The instrument uses a quadrupole mass spectrometer and detects samples via electron impact ionization (EI). The University of Wollongong Biomolecular Mass Spectrometry Laboratory analyzed samples for HRMS. The spectra were run on the VG Autospec-oa-tof tandem high resolution mass spectrometer using CI +ve (Chemical ionization), with methane as the carrier gas and PFK (perfluorokerosene) as the reference. We have previously reported the synthesis of compounds A-D, 1-3, 5-7, 20-25, 27-33, 39-40.[1]

4-Chloro-6-ethylamino-2-methylmercaptopyrimidine (4)

4,6-Dichloro-2-methylmercaptopyrimidine (**B**) (500 mg, 2.56 mmol) was added to a pressure vessel with abs. EtOH (10 mL) and ethylamine (1.5 mL, 10 eq). The vessel was sealed and stirred for 24 hrs at 130°C. The product was obtained as a viscous brown oil that was purified by dry column chromatography (silica; 1:3 ethyl acetate/hexane) and then recrystallised twice (hexanes) to afford the product as light brown crystals 123 mg, 20.0%, mp 59-60°C. δ_H 1.18 (t, 3H, J=10.29 Hz), 2.44 (s, 3H), 3.20 (br s, 2H), 5.24 (br s, 1H, -N**H**-), 6.04 (s, 1H). δ_C 13.9, 14.7, 36.2, 97.0 (br), 159.0 (br), 162.5, 172.0. δ_C (DMSO): 13.3, 14.2, 35.0 (rotamer C(6')), 35.7 (rotamer C(6')), 95.3 (rotamer C(5)), 99.1 (rotamer C(5)), 156.3, 162.2, 171.2. δ_C (DMSO, 313K): 13.1, 14.00, 35.0, 98.8, 156.8 (br), 162.3, 171.0. HRMS: $(M + H)^+$ = 204.03539; calcd, 204.03629 (^{35}Cl).

4-Chloro-6-cyclohexylamino-2-methylmercaptopyrimidine (8)

A solution of cyclohexylamine (380 mg, 3.8 mmol) in THF (8 mL) was treated with NaH (300 mg, 60% dispersion in oil, 7.6 mmol) at room temperature, under nitrogen. The yellow suspension was stirred at room temperature for 10 minutes before 4,6-dichloro-2-methylmercaptopyrimidine (**B**) (750 mg, 3.8 mmol) was added and the mixture heated at reflux under nitrogen for 24 hours. The reaction was quenched with ice water (5 mL) and the product was extracted with ethyl acetate (3x30 mL). The combined organic extracts were washed with brine (25 mL), dried ($MgSO_4$), and the solvent removed *in vacuo* to give a brown solid. Recrystallisation (ethyl acetate-hexanes) gave a pale yellow solid, yield 621 mg, 62%. δ_H 1.43 (m, 2H), 1.29 (m, 2H), 1.59 (dt, 2H), 1.65 (dt, 2H), 1.88 (dd, 2H), 2.38 (s,

3H), 3.5 (br s, 1H, -C**H**-NH-), 5.30 (d, 1H, -N**H**-), 5.93 (s, 1H). δ_C 13.7, 24.4, 25.4, 32.4, 49.9, 96.6 (br), 158.5 (br), 161.6, 171.7. HRMS: $(M + H)^+$ = 258.0829; calcd, 258.0832 (^{35}Cl).

4-Chloro-6-cyclopentylamino-2-methylmercaptopyrimidine (9)

Synthesised using the general procedure as for (**8**) using cyclopentylamine. The crude yellow oil was purified by flash chromatography (silica; 1:3 ethyl acetates/hexane) resulting in cream solid, yield 310 mg, 75%. δ_H 1.47 (m, 2H), 1.65 (m, 4H), 2.01 (m, 2H), 3.94 (br s, 1H, -CH-NH-), 5.02 (br s, -NH-), 6.00 (s, 1H). δ_C 14.0, 23.7, 23.7, 33.2, 53.0, 96.7 (br), 159.1, 162.3, 172.1. HRMS: $(M + H)^+$ = 244.06680; calcd, 244.06759 (^{35}Cl).

4-Chloro-6-cyclohexylaminopyrimidine (10)

A suspension of 4,6-dichloropyrimidine (0.50 g, 3.4 mmol) in distilled water (10 ml) was stirred at room temperature for 15 min. To this was added cyclohexylamine (0.4 ml, 3.5 mmol) and the resulting mixture was heated at reflux for 72 hours. The cooled reaction mixture was extracted with CH_2Cl_2 (5 x 20 ml) and the combined organic layers were dried ($MgSO_4$) and concentrated *in vacuo*. The crude residue was subjected to flash chromatography (silica; 15% ethyl acetate/hexane) to obtain **(10)** (0.24 g, 1.1 mmol, 34%) as a white powder, mp 118-120°C. δ_H 1.25 (3H, m), 1.40 (2H, m), 1.65 (1H, m), 1.77 (2H, m), 3.51 (1H, m), 5.38 (1H, br, NH), 6.31 (1H, s), 8.31 (1H, s). δ_C 24.9, 25.6, 33.0, 50.4, 102.3, 158.8, 162.6, 165.5 (br). HRMS: $(M + H)^+$ = 212.0909 ; calcd 212.0905 (^{35}Cl).

6-Cyclohexylamino-4-(*N*-cyclopropylmethyl-*N*-propylamino)pyrimidine (11)

To a solution of 6-chloro-4-cyclohexylaminopyrimidine **(10)** (0.16 g, 0.76 mmol) in dry THF (10 ml) was added *N,N*-propylcyclopropanemethylamine (0.80 ml, 0.56 mmol). The reaction mixture was flushed with nitrogen, and stirred in a sealed tube at 160°C for 66 hours. The reaction mixture was concentrated *in vacuo*. The crude residue was subjected to flash chromatography (silica; 40% ethyl acetate/hexane) gave **(11)** (0.14 g, 0.49 mmol, 64%) as a pale orange solid, mp. 64-67°C. $_H$ 0.27 (2H, m), 0.52 (2H, m), 0.91 (3H, t, J = 7.6 Hz), 1.04 (1H, m), 1.25 (2H, m), 1.26 (3H, m), 1.38 (2H, m), 1.65 (1H, m), 1.76 (2H, m), 2.03 (2H, m), 5.56 (1H, m), 3.39 (4H, m) 4.69 (1H, br), 5.29 (1H, s), 8.12 (1H, s). δ_C 3.8, 9.9, 11.6, 20.7, 24.8, 25.8, 33.1, 49.7, 50.0, 52.2, 79.8, 157.5, 161.5, 161.6 (br). HRMS: $(M + H)^+$ = 289.2390 ; calcd 289.2392 (^{35}Cl).

2,4-*bis*-(*N,N*-dimethylethylenediamino)-6-methylpyrimidine (12)

2,4-dichloro-6-methylpyrimidine **(C)** (0.3g, 1.8 mmol) and N,N-dimethylethylenediamine (0.35g, 4 mmol) were dissolved in THF (15ml). The solution was heated in a sealed tube (160ºC, 24h). Solvent was then removed under reduced pressure. Resulting oil was dissolved in ethyl acetate (100ml) and washed with water (3 x 30ml) removal of ethyl acetate gave product as a light yellow oil 0.34 g

(70%). δ_H 2.15 (3H, s), 2.30 (12H, s), 2.45 (4H, q, *J* = 4.3 Hz), 3.32 (2H, q, *J* = 5.2 Hz), 3.42 (2H, q, *J* = 5.8 Hz), 5.13 (br, 1H), 5.23 (br, 1H), 5.56 (s, 1H). δ_C 23.7, 38.3, 38.8, 57.8, 58.3, 92.7 (br), 162.1, 163.4, 164.2 (br). GCMS: 266.0, calcd 266.0.

2-Chloro-4-ethanolamino-6-methylpyrimidine (13)[2] & 4-Chloro-2-ethanolamino-6-methylpyrimidine (14)

2,4-dichloro-6-methylpyrimidine (1 g, 6.1 mmol) was dissolved in THF (20 ml). To this solution was added ethanolamine (0.73g, 12 mmol) in THF 10ml. The combined solution was allowed to stir at 50ºC for 24h. Solvent was removed under reduced pressure yielding yellow oil. Isomers were separated via flash chromatography (silica; 9:1 hexane/ethyl acetate) to give **(13)** (0.33 g, 29%) as a cream solid, mp 120-122°C, and (**14)** (0.56 g, 49%) as a cream solid, mp 94-96°C. **(13)** δ_H 2.29 (s, 3H), 3.57 (2H, q, *J* = 5.5 Hz), 3.8 (2H, t, *J* = 4.7 Hz), 5.91 (1H, br), 6.45 (1H, s). δ_C 23.1, 43.8, 62.2, 108.9, 160.7, 161.9, 169.0. GCMS: 187.0, calcd 187.0. **(14)** δ_H 2.31 (3H, s), 3.53 (2H, br), 3.83 (2H, t, *J* = 5 Hz), 5.5 (1H, br), 6.13 (1H, s). δ_C 23.2, 43.1, 60.9, 100.8 (br), 159.6, 163.7, 166.9 (br). GCMS: 187.0, calcd 187.0.

2,4-*bis*-ethanolamino-6-methylpyrimidine (15)[3]

2,4-dichloro-6-methylpyrimidine (0.3 g, 1.8 mmol), ethanolamine (1 g, 16 mmol) and THF (10 ml) were combined in a pressure vessel. Solution was heated at 160º (24h) and the solvent removed under reduced pressure giving yellow oil. Oil was left open to the air resulting in crystal formation. Recrystalization (ethyl acetate) gave white crystals (0.28 g, 72%), mp 112-114°C. δ_H 1.98 (3H, s), 3.26 (4H, q, *J*= 5.9 Hz), 3.30 (2H, br), 3.46 (4H, t, *J* = 6Hz), 4.67 (1H, br), 5.59 (s, 1H), 6.11 (1H, t, *J* = 5.2 Hz), 6.64 (1H, br). δ_C 23.9, 43.9, 60.4, 61.1, 93.5 (br), 162.5, 163.7, 164.2 (br). GCMS: 212.1, calcd 212.1.

2-Chloro-4-cyclohexylamino-6-methylpyrimidine (16) and 4-chloro-2-cyclohexylamino-6-methylpyrimidine (17)

A suspension of 2,4-dichloro-6-methylpyrimidine (**C**) (2.11 g, 12.9 mmol) in distilled water (15 ml) was stirred at room temperature for 15 minutes. To this was added cyclohexylamine (1.4 ml, 12.7 mmol) and the resulting mixture was heated at reflux for 72 hours. The cooled reaction mixture was extracted with CH_2Cl_2 (4 x 20 ml) and the combined organic layers were dried ($MgSO_4$) and concentrated in vacuo. The crude residue was subjected to flash chromatography (silica; 20% ethyl acetate/hexane) gave 4-chloro-2-cyclohexylamino-6-methylpyrimidine **(16)** (1.44 g, 7.2 mmol, 58%) as a white low melting point solid. Further elution gave 2-chloro-4-cyclohexylamino-6-methylpyrimidine (**17**) (0.61 g, 2.7 mmol, 21%) as a pale yellow oil. **(16)** δ_H 1.26 (3H, m), 1.37 (2H, m), 1.62 (1H, m), 1.76 (2H, m), 1.96 (2H, m), 2.31 (3H, s), 3.51 (1H, m), 5.32 (1H, d), 6.08, (1H, s). δ_C 23.7, 24.5, 25.4, 32.7, 60.3, 100.1 (br), 160.0, 162.9, 166.4. HRMS: $(M + H)^+$ =226.111;

calcd,226.111 (^{35}Cl). **(17)** δ_H 1.18 (3H, m), 1.37, (2H, m), 1.57 (1H, m), 1.67 (2H, m), 1.96 (2H, m), 2.24 (3H, s), 3.81 (1H, m), 5.09 (1H, br), 6.36 (1H, s). δ_C 23.9, 24.7, 25.7, 33.0, 49.4, 108.6, 161.1, 161.3, 169.2. HRMS: $(M + H)^+$ = 226.1094; calcd, 226.1111 (^{35}Cl).

4-Chloro-2-*n*hexylamino-6-methylpyrimidine (18) & 2-chloro-4-*n*hexylamino-6-methylpyrimidine (19)

2,4-dichloro-6-methylpyrimidine (0.5 g, 3 mmol) was dissolved in 5M lithium perchlorate in ethyl ether (10 ml). Hexyl amine (3.04 g, 30 mmol) was added and the sealed vessel stirred at RT 24h. Water (20 ml) was added and the solution extracted with ether (3 x 40 ml). Solvent was removed under reduced pressure to give a yellow oil. Isomers were separated by preparative TLC (silica; 7:3 hexane/ethyl acetate) to give **(18)** as an off white solid (0.118 g, 17%), mp 36-38°C, and (**19)** as a yellow oil (0.09 g, 13.2%). **(18)** δ_H 0.89 (3H, t, *J* = 6.6 Hz), 1.32 (6H, m), 1.58 (2H, quin, *J* = 7.1 Hz), 2.3 (1H, s), 3.4 (2H, q, *J* = 6 Hz), 5.13 (1H, br), 6.4 (1H, s). δ_C 14.7, 23.3, 24.5, 28.8, 30.9, 40.9, 109.6, 161.8, 162.9, 170.1. GCMS: 227.0, calcd 227.0. **(19)** δ_H 0.88 (3H, t, *J* = 6.4 Hz), 1.35 (6H, m), 1.59 (2H, quin, *J* = 7 Hz), 2.32 (3H, s), 3.25 (2H, br), 5.29 (1H, br), 6.06 (1H, s). δ_C 13.4, 21.9, 23.2, 25.9, 28.5, 30.8, 41.0, 99.2 (br), 159.6, 163.6, 167.1 (br). GCMS: 227.0, calcd 227.0.

2,4-Dimorpholino-6-methylpyrimidine (26)

2,4-dichloro-6-methylpyrimidine (0.3 g, 1.8 mmol) and morpholine (5 ml) were allowed to stir at room temp (24h). Water (10ml) was added and the solution chilled. Resulting white solid was collected by filtration. Recrystalization (ethanol) gave 0.43 g (89%) as white solid, mp 126-128°C (lit.[x] y°C). δ_H 2.23 (3H, s), 3.54 (4H, m), 3.75 (4H, m), 5.76 (1H, s). δ_C 24.4, 44.2, 44.3, 66.5, 66.9, 91.8, 163.3, 166.5, 166.5. GCMS: 264.2, calcd 264.2.

4-Cyclohexylamino-2-(*N*-cyclopropylmethyl-*N*-propylamino)-6-methylpyrimidine (34)

To a solution of 2-chloro-4-cyclohexylamino-6-methylpyrimidine (0.15 g, 0.66 mmol) in dry THF (10 ml) was added *N*,*N*-propylcyclopropanemethylamine (1.00 ml, 7.00 mmol). The reaction mixture was flushed with nitrogen, and stirred in a sealed tube at 160°C for 18 hours. The reaction mixture was concentrated *in vacuo*. The crude residue was subjected to flash chromatography (silica; 10% ethyl acetate/hexane) gave **(34)** (0.12 g, 0.40 mmol, 61%) as a brown oil. δ_H 0.27 (2H, m), 0.45 (2H, m), 0.89 (3H, t, *J* = 7.4 Hz), 1.21 (3H, m), 1.38 (2H, m), 1.63 (2H, m), 1.70 (1H, m), 1.75 (2H, m), 2.01 (2H, m), 2.03 (1H, m), 2.16 (3H, s), 3.46 (2H, d, *J* = 6.6 Hz), 3.51 (1H, m), 3.53 (2H, t, *J* = 7.4 Hz), 4.32 (1H, br), 5.44 (1H, s). δ_C 3.5, 10.2 11.5, 21.0, 24.4, 24.9, 25.7, 33.3, 49.2, 49.8, 51.5, 91.5 (br), 161.6, 163.2, 171.2 (br). HRMS: $(M + H)^+$ = 303.2533; calcd, 303.2549 (^{35}Cl).

4-Cyclohexylamino-2-diethylamino-6-methylpyrimidine (35)

To a solution of 2-chloro-4-cyclohexylamino-6-methylpyrimidine (0.13 g, 0.60 mmol) in dry THF (10 ml) was added diethylamine (0.70 ml, 6.74 mmol). The reaction mixture was flushed with nitrogen, and stirred in a sealed tube at 160 °C for 48 hours. The reaction mixture was concentrated *in vacuo*. The crude residue was subjected to flash chromatography (silica; 10% ethyl acetate/hexane) gave **(35)** (0.05 g, 0.20 mmol, 33%) as beige crystals, mp. 64-66 °C. δ_H 1.14 (6H, t, *J* = 7.2 Hz), 1.21 (3H, m), 1.38 (2H, m), 1.63 (1H, m), 1.72 (2H ,m), 2.00 (2H, m), 2.17 (3H, s), 3.51 (1H, m), 3.59 (4H, q, *J* = 7.2 Hz), 4.39 (1H, br), 5.47 (1H, s). δ_C 13.5, 24.5, 25.0, 25.8, 33.4, 41.1, 49.6, 91.1 (br), 161.1, 162.4, 165.3 (br). HRMS: $(M + H)^+$ = 262.223; calcd, 263.224 (^{35}Cl).

2-Chloro-6-methyl-4-(2,3-dimethylcyclohexylamino)pyrimidine (36)

A suspension of 2,4-dichloro-6-methylpyrimidine **(C)** (1.96 g, 12.0 mmol) in distilled water (15 ml) was stirred at room temperature for 15 minutes to promote solubilisation. To this, 2,3-dimethylcyclohexylamine (1.85 ml, 12.2 mmol) was added and the resulting mixture was heated at reflux for 72 hours. The cooled reaction mixture was extracted with CH_2Cl_2 (4 x 20 ml) and the combined organic layers were dried ($MgSO_4$) and concentrated *in vacuo*. The crude residue was subjected to flash chromatography (silica; 10% ethyl acetate/hexane) gave **(36)** (1.13 g, 4.5 mmol, 37%) as a white low melting point solid. δ_H 0.89, 0.91, 0.93, 0.94, 0.95, 0.96, 0.97 (6H, s, 2'-CH_3, 3'-CH_3, diastereomers), 1.21 (2H, m), 1.42 (3H, m), 1.67 (2H, m), 1.84 (1H, m), 2.03 (1H, m), 2.32 (3H, s), 5.24 (1H, br), 6.06, 6.07, 6.09, 6.11 (1H ,s, diastereomers). HRMS: $(M + H)^+$ = 254.1405; calcd, 254.1424 (^{35}Cl).

2-(*N*-Cyclopropanemethyl-*N*-propylamino)-6-methyl-4-(2,3-dimethylcyclohexyl-amino)pyrimidine (37)

To a solution of 2-chloro-6-methyl-4-(2,3-dimethylcyclohexyl-amino)pyrimidine (0.17 g, 0.67 mmol) in dry THF (10 ml) was added *N,N*-propylcyclopropanemethylamine (1.00 ml, 7.00 mmol). The reaction mixture was flushed with nitrogen, and stirred in a sealed tube at 160°C for 64 hours. The reaction mixture was concentrated *in vacuo*. The crude residue was subjected to flash chromatography (silica; 15% ethyl acetate/hexane) gave the title compound (0.15 g, 0.46 mmol, 68%) as a yellow oil. δ_H 0.26 (2H, m), 0.49 (2H, m), 0.87 (3H, t, *J* = 7.6 Hz), 0.89, 0.91, 0.92, 0.94, 0.96, 0.99 (6H, 7 x s, diastereomers), 1.21 (2H, m), 1.23 (1H, m), 1.38 (3H, m), 1.61 (2H, m), 1.64 (2H, m), 1.72 (1H, m), 1.89 (1H, m), 2.18 (3H, s), 3.37 (2H, m), 3.52 (2H, m), 4.88 (1H, br), 5.63, 5.64, 5.65 (1H, s, diastereomers). HRMS: $(M + H)^+$ = 331.2867; calcd, 331.2862 (^{35}Cl).

2-Diethylamino-6-methyl-4-(2,3-dimethylcyclohexylamino)pyrimidine (38)

To a solution of 2-chloro-6-methyl-4-(2,3-dimethylcyclohexyl-amino)pyrimidine (0.14 g, 0.57 mmol) in dry THF (10 ml) was added diethylamine (0.70 ml, 6.74 mmol). The reaction mixture was flushed with nitrogen, and stirred in a sealed tube at 160 °C for 64 hours. The reaction mixture was concentrated *in vacuo*. The crude residue was subjected to flash chromatography (silica; 15% ethyl acetate/hexane) gave (**38)** (0.09 g, 0.44 mmol, 54%) as a pale yellow oil. δ_H 0.88, 0.89, 0.90, 0.91, 0.94, 0.96, 0.99 (6H, 7 x s, diastereomers) 1.16 (6H, t, *J* = 7.2 Hz), 1.21 (2H, m), 1.25 (2H, m), 1.38 (1H, m), 1.61 (2H, m), 1.72 (1H, m), 1.89 (1H, m), 2.18 (3H, s), 3.45, (4H, m), 5.02 (1H, br), 5.59, 5.60, 5.61 (1H, 3 x s, diastereomers). HRMS: $(M + H)^+$ = 291.2551; calcd, 291.2549 (^{35}Cl).

Refernces for Supplementary Information

[1] A. McCluskey, P. A. Keller, J. Morgan,J. Garner, *Org. Biomol. Chem.* **2003**, *1*, 3353.

[2] M. Yanai, S. Takeda, T. Baba,K. Kitagawa, *Yakugaku Zasshi* **1974**, *94*, 1503.

[3] A. M. Buzueva, Khim. Geterotsikl. Soedin., Sb. 1: Azotsoderzhashchie Geterotsikly **1967**, 367.

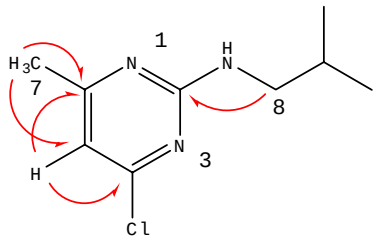
Typical Example of Identification of Regioisomers *via* 2D NMR

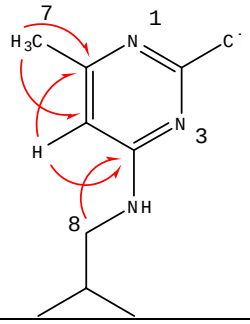
Assignment of C(2) or C(4) substitutions were confirmed by HMBC and HMQC experiments, and in all instances confirmed the above assignments based on line broadening effects. Figures 2 and 3 show the 1H and 13C NMR spectra for regioisomers 24 and 25 respectively, and are typical of spectra recorded. Table 2 shows the tabulated data of chemical shifts for each regioisomer including HMBC correlations. Due to the line broadening observed in 25, its spectra was recorded at 40ºC so that the line width of the C(5) signal was narrow enough to record strong correlations. At 17ºC (standard temperature of NMR laboratory) the line width at half height (w0) of the C(5) signal was 4 ppm. DEPT 90, 135 and HMQC were used to assign appropriate carbon-hydrogens correlations. HMBC correlations were consistent for the alkyl chain in both isomers with carbons C(8)-(10) showing connections to each other.

Compound **23** was assigned as the C(4) substituted regioisomer through a number of correlations. Firstly C(5) was identified at 99.8 ppm as the only aromatic carbon with an attached hydrogen (DEPT 90). H(5) exhibited correlations for the aromatic carbons at 164.4 and 167.9 ppm and no correlation for the aromatic carbon at 160.4 ppm. H(8), the methylene group of the alkyl chain correlated to the carbon at 164.4 ppm identifying which ring carbon the amine substituent was attached. C(6) was assigned to 167.9 ppm because of the correlation to the methyl group hydrogens H(7). Therefore C(4) could be assigned to the peak at 164.4 ppm as C(5)'s other neighbour. The lack of H(5) correlations to C(2) were typical of both regioisomers. An additional indicator of C(4) substitution was that H(8) typically appeared as a broad singlet, rather than exhibiting usual coupling to its neighbours.

For the assignment of compound **22**, C-H(5) was assigned to 108.85 (DEPT 90) and exhibited correlations to the aromatic carbons at 161.0 and 169.4 but not 162.3 ppm. The methyl hydrogens H(7) showed strong correlations to C(5) and at 169.37 ppm, which was therefore assigned as C(6). The methylene group of the alkyl chain H(8) was connected to the pyrimidine ring through a correlation to 162.3 ppm. Because C-H(5) correlated to different carbons than C(8), and based on the logical connections observed with C(4) substitution, we concluded that 161.0 could be assigned to C(4). Therefore C(2) was assigned to 162.3 ppm, as the amine bonded aromatic carbon.

Table 2: Tabulated NMR data for compounds 22 and 23. Important HMBC correlations are indicated by red arrows.





Compound 22				Compound 23			
Atom	^{13}C	^{1}H	HMBC	Atom	^{13}C	^{1}H	HMBC
2	162.34	-	-	2	160.33	-	-
4	160.97	-	-	4	164.40	-	-
5	108.85	6.37 (s, 1H)	4, 6	5	99.80	6.03 (s, 1H)	4, 6
6	169.37	-	-	6	167.87	-	-
7	23.77	2.23 (s, 3H)	5, 6	7	23.74	2.27 (s, 3H)	5, 6,
8	48.82	3.20 (t, 2H)	2, 9, 10	8	49.19	3.04 (br s, 2H)	4, 9, 10
9	28.30	1.82 (m, 1H)	8, 10	9	28.28	1.81 (m, 1H)	8, 10
10,10′	20.08	0.90 (d, 6H)	8, 9, 10	10,10′	20.07	0.90 (d, 6H)	8, 9, 10
NH	-	5.35 (br s, 1H)	-	NH	-	5.32 (br s, 1H)	-

* We have previously reported the experimental for compounds A-D, 1-3, 5-7, 20-25, 27-33, 39-40. The experimental for all other compounds may be found in the supplementary information.

† Assignment of C-2 or C-4 substituents were confirmed by HMBC and HMQC experiments, and in all instances confirmed the above assignments based on line broadening effects.

‡ Coalescence temperature (Tc) for the purpose of qualitative analysis is reported as the temperature at which coalescence is actually observed; that is, a very low, broad baseline hump is observed, or Tc is estimated by extrapolating between the two measurements at which it occurred.

‡ Compounds were geometry optimized using the Moller Plesset function at MP2 level of theory. Conformer distributions were calculated using molecular mechanics at the MMFF level of theory. Compounds were rotated by 30° increments for all available torsion points C(aryl)-N bond of the amine substituent. The program allowed for a maximum of 20,000 conformations and a maximum DE = 100 kJ mol^{-1} difference. Conformations that had similar energies and van der Waals overlap were treated as identical by the program, reducing the set of 'unique' conformers reported. Each conformer can be regarded as representative of a number of conformations with the same energy and similar structural space.