

A Method for the Reductive Scission of Heterocyclic Thioethers

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General Experimental Methods:

10% Palladium on carbon was purchased from Strem Chemical (reduced, dry powder, catalog # 46-1900, lot # 17995300). The use of Pd/C on a dry matrix was imperative. The use of Pd/C on a wet matrix gave lower yields or no reaction.

All other reagents were purchased from commercial suppliers and used without purification.

^1H NMR was conducted at 500 MHz. Spectra were referenced to the residual solvent signal.

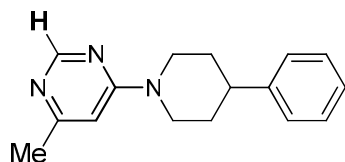
^{13}C NMR was conducted at 126 MHz using a standard ^1H decoupled pulse sequence. Spectra were referenced to the residual solvent signal.

Purification on silica gel refers to column chromatography using an automated MPLC instrument and pre-packed, silica gel columns (25g column for reaction scale ≤ 500 mg; 50g column for reaction scale > 500 mg). The product was eluted using the noted solvent gradient and was monitored at a wavelength of 260 nm.

Analytical TLC was conducted using pre-coated Analtech #21511 silica gel GHLF plates; 250 μM thickness, UV 254 nm indicator.

Substrates are either known compounds or were prepared using known literature procedures and are readily accessible to those skilled in the art of organic synthesis.

General Procedure A:



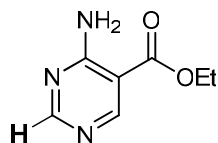
4-Methyl-6-(4-phenylpiperidin-1-yl)pyrimidine (2o). A 21x72 mm vial with a PTFE/silicone septa and a nitrogen-bubbler line was charged with 10% Pd/C (dry powder, 35.5 mg), THF (3 ml) and 4-methyl-2-(methylthio)-6-(4-phenylpiperidin-1-yl)pyrimidine (**1o**) (500 mg, 1.67 mmol). The vial was placed in a 0 $^{\circ}\text{C}$ bath, treated with triethylsilane (800 μl , 5.01 mmol) and stirred at 0 $^{\circ}\text{C}$ for 30 min then at rt for 4.5 h. The crude mixture was filtered through a 45 μM PTFE syringe filter and the filtrate was concentrated to an oil. Purification by chromatography on silica gel (20 to 100% EtOAc/heptane then 0 to 10% MeOH/EtOAc) afforded the title compound (406.7 mg, 1.605 mmol, 96%) as a colorless solid.

^1H NMR (500 MHz, CDCl_3): δ 8.52 (s, 1H); 7.32-7.29 (m, 2H); 7.23-7.20 (m, 3H); 6.42 (s, 1H); 4.56 (bd, $J=13.1$ Hz, 2H); 2.97 (td, $J=13.0$, 2.5 Hz, 2H); 2.80 (tt, $J=12.2$, 3.7 Hz, 1H); 2.36 (s, 3H); 1.95 (d, $J=13.3$ Hz, 2H); 1.70 (dq, $J=12.7$, 4.2, 2H).

^{13}C NMR (126 MHz, CDCl_3): δ 165.3, 162.0, 158.2, 145.5, 128.7, 126.9, 126.7, 101.6, 44.8, 43.1, 33.0, 24.5.

LCMS calc for $\text{C}_{16}\text{H}_{19}\text{N}_3$, 253.16; found 254.14 ($\text{M}+\text{H}^+$).

General Procedure B (for compounds with exchangeable NH protons):



Ethyl 4-aminopyrimidine-5-carboxylate (2a). A 21x72 mm vial with a PTFE/silicone septa and a nitrogen-bubbler line was charged with 10% Pd/C (49.9 mg, 0.047 mmol), THF (3.0 ml) and ethyl 4-amino-2-(methylthio)pyrimidine-5-carboxylate (**1a**) (500 mg, 2.35 mmol). The vial was placed in a 0 °C bath, treated with triethylsilane (1.123 ml, 7.03 mmol) and stirred for 3 h at 0 °C then for 3 h at rt. TLC (20% EtOAc/hexanes, silica gel, UV) indicated the SM (R_f 0.28) was consumed and a major, slightly less polar product (R_f 0.44) was formed. Crude mixture was filtered through a 45 μ m PTFE membrane syringe filter. The flask was rinsed with EtOH (2x3 mL) and the rinse was also passed through the filter. The combined filtrate (pale yellow) was treated with 6N aq HCl (0.5 mL, 3.0 mmol) at rt and the yellow color faded to afford a clear, colorless solution. The mixture was stirred at rt for 4 h and then concentrated. The resulting white, oily solid was diluted in CH_2Cl_2 (2.0 mL), treated with Et_3N (0.5 mL) and directly purified on silica gel (0 to 100 EtOAc/hexanes then 0 to 20% MeOH/EtOAc) to afford the title compound (347.3 mg, 2.078 mmol, 89%) as a colorless solid:

^1H NMR (500 MHz, CDCl_3): δ 8.89 (s, 1H); 8.61 (s, 1H); 7.85 (bs, 1H); 5.77 (bs, 1H); 4.38 (q, $J=7.1$ Hz, 2H); 1.40 (t, $J=7.1$ Hz, 3H).

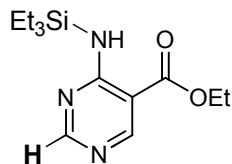
^{13}C NMR (126 MHz, CDCl_3): δ 166.3, 162.6, 161.5, 159.3, 105.5, 61.5, 14.4.

LCMS calc for $\text{C}_7\text{H}_9\text{N}_3\text{O}_2$, 167.07; found 168.12 ($\text{M}+\text{H}^+$).

From 1b: According to general procedure B, a mixture of ethyl 4-amino-2-(ethylthio)pyrimidine-5-carboxylate (**1b**) (500 mg, 2.20 mmol), 10% Pd/C (46.8 mg, 0.044 mmol) and triethylsilane (1.054 ml, 6.60 mmol) in THF (3.0 ml) was allowed to stir for 3 h at 0 °C then for 3 h at rt. Purification on silica gel (0 to 100% EtOAc/hexanes then 0 to 20% MeOH/EtOAc) afforded the title compound (342.4 mg, 93%) as a colorless solid.

From 1c: According to general procedure B, a mixture of ethyl 4-amino-2-(benzylthio)pyrimidine-5-carboxylate (**1c**) (500 mg, 1.73 mmol), 10% Pd/C (36.8 mg, 0.035 mmol) and triethylsilane (0.828 ml, 5.18 mmol) in THF (2.5 ml) was stirred for 3 h at 0 °C then for 3 h at rt. Purification by chromatography on silica gel (0 to 100% EtOAc/hexanes then 0 to 20% MeOH/EtOAc) afforded the title compound (263.8 mg, 91%) as a colorless solid.

Compounds with Analytical Data:



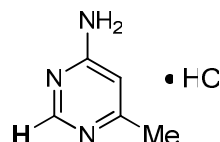
Ethyl 4-((triethylsilyl)amino)pyrimidine-5-carboxylate. According to general procedure A, a mixture of ethyl 4-amino-2-(methylthio)pyrimidine-5-carboxylate (**1a**) (500 mg, 2.35 mmol), 10% Pd/C (49.9 mg, 0.047 mmol) and triethylsilane (1.123 ml, 7.03 mmol) in THF (3.0 ml) was

stirred for 3 h at 0 °C then for 3 h at rt. Purification on silica gel (0 to 40% MTBE/heptane) afforded the title compound (595.5 mg, 90%).

^1H NMR (500 MHz, CDCl_3): δ 8.85 (s, 1H); 8.58 (s, 1H); 7.74 (bs, 1H); 4.35 (q, $J=7.2$ Hz, 2H); 1.38 (t, $J=7.2$ Hz, 3H); 0.97 (t, $J=7.9$ Hz, 9H); 0.84 (q, $J=7.9$ Hz, 6H).

^{13}C NMR (126 MHz, CDCl_3): δ 167.0, 165.5, 160.9, 159.2, 106.8, 61.3, 14.4, 7.2, 4.4.

LCMS calc for $\text{C}_{13}\text{H}_{23}\text{N}_3\text{O}_2\text{Si}$, 281.16; found 282.14 ($\text{M}+\text{H}^+$).

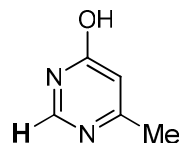


6-Methylpyrimidin-4-amine·HCl (2d). According to general procedure B, a mixture of 2-(ethylthio)-6-methylpyrimidin-4-amine (**1d**) (500 mg, 2.95 mmol), 10% Pd/C (62.9 mg, 0.059 mmol) and triethylsilane (1.416 ml, 8.86 mmol) in THF (4.0 ml) was stirred at rt for 16 h. The concentrated crude mixture from the HCl treatment was diluted with minimal EtOH (0.5 mL) and triturated with heptane and decanted. The solids were dissolved in hot EtOH (1.0 mL) and triturated with heptane (5 mL) with vigorous stirring. The solids were filtered, rinsed with heptane and dried under vacuum to afford the title compound (369.2 mg, 86%) as a colorless solid.

^1H NMR (500 MHz, CD_3OD): δ 8.52 (s, 1H); 6.62 (s, 1H); 4.94 (bs, 3H); 2.44 (s, 3H).

^{13}C NMR (126 MHz, CD_3OD): δ 167.0, 155.9, 152.8, 104.7, 18.8.

LCMS calc for $\text{C}_5\text{H}_7\text{N}_3$ 109.06; found 109.98 ($\text{M}+\text{H}^+$).



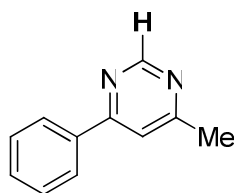
6-Methylpyrimidin-4-ol (2e).¹ According to general procedure A, a mixture of 6-methyl-2-(methylthio)pyrimidin-4-ol (**1e**) (500 mg, 3.20 mmol), 10% Pd/C (170 mg, 0.16 mmol) and triethylsilane (1.534 ml, 9.60 mmol) in THF (4.0 ml) was stirred at rt for 16 h. Purification on silica gel (0 to 10% MeOH/ CH_2Cl_2) afforded the title compound (258.2 mg, 73%) as a colorless solid.

^1H NMR (500 MHz, CDCl_3): δ 8.09 (s, 1H); 6.31 (s, 1H); 2.33 (s, 3H).

^{13}C NMR (126 MHz, CDCl_3): δ 167.0, 164.8, 148.1, 113.6, 24.3.

LCMS calc for $\text{C}_5\text{H}_6\text{N}_2\text{O}$, 110.05; found 110.96 ($\text{M}+\text{H}^+$).

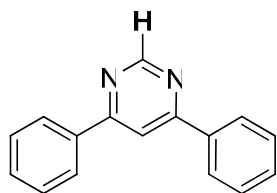
¹ Wang, Z.; Chi, Y.; Harris, A. R.; Gray, D.; Davoren, J. E. *Synthesis* **2011**, 1529–1531.



4-Methyl-6-phenylpyrimidine (2f).² According to general procedure A, a mixture of 4-methyl-2-(methylthio)-6-phenylpyrimidine (**1f**) (500 mg, 2.31 mmol), 10% Pd/C (49.2 mg, 0.046 mmol) and triethylsilane (1.108 ml, 6.93 mmol) in THF (2.5 ml) was stirred for 30 min at 0 °C then for 24 h at rt. Purification on silica gel (0 to 100% EtOAc/heptane) afforded the title compound (383.6 mg, 97%).

¹H NMR (500 MHz, CDCl₃): δ 9.14 (s, 1H); 8.09-8.05 (m, 2H); 7.59 (s, 1H); 7.52-7.49 (m, 3H); 2.60 (s, 3H).

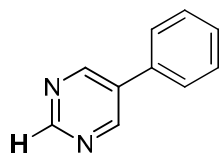
¹³C NMR (126 MHz, CDCl₃): δ 167.6, 163.9, 158.9, 136.9, 131.0, 129.1, 127.3, 116.6, 24.5.
LCMS calc for C₁₁H₁₀N₂, 170.08; found 171.13 (M+H⁺).



4,6-Diphenylpyrimidine (2g).³ According to general procedure A, a mixture of 2-(methylthio)-4,6-diphenylpyrimidine (**1g**) (500 mg, 1.80 mmol), 10% Pd/C (38.2 mg, 0.036 mmol) and triethylsilane (0.861 ml, 5.39 mmol) in THF (4.0 ml) was stirred for 30 min at 0 °C then for 48 h at rt. Purification on silica gel (0 to 40% EtOAc/heptane) afforded the title compound (408.1 mg, 98%) as a colorless solid.

¹H NMR (500 MHz, CDCl₃): δ 9.33 (d, *J*=1.3 Hz, 1H); 8.19-8.14 (m, 4H); 8.11 (d, *J*=1.1 Hz, 1H); 7.58-7.52 (m, 6H).

¹³C NMR (126 MHz, CDCl₃): δ 165.0, 159.4, 137.3, 131.2, 129.3, 127.5, 113.1.
LCMS calc for C₁₆H₁₂N₂, 232.10; found 233.15 (M+H⁺).



5-Phenylpyrimidine (2h).⁴ According to general procedure A, a mixture of 2-(methylthio)-5-phenylpyrimidine (**1h**) (500 mg, 2.47 mmol), 10% Pd/C (52.6 mg, 0.049 mmol) and triethylsilane (1.184 ml, 7.42 mmol) in THF (3.0 ml) was stirred at 0 °C for 1 h then at rt for 4 h. Purification on silica gel (0 to 100% EtOAc/heptane) afforded the title compound (327.5 mg, 85%).

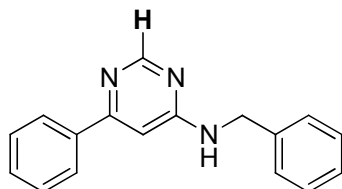
¹H NMR (500 MHz, CDCl₃): δ 9.20 (s, 1H); 8.95 (s, 2H); 7.60-7.56 (m, 2H); 7.55-7.43 (m, 3H).

² Caygill, G. B.; Hartshorn, R. M.; Steel, P. J. *J. Organomet. Chem.* **1990**, 382, 455–469.

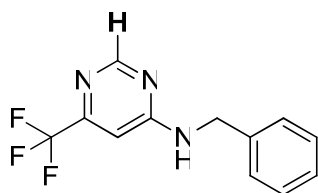
³ Bouilly, L.; Darabantu, M.; Turck, A.; Plé, N. *J. Heterocyclic Chem.* **2005**, 42, 1423–1428.

⁴ Firouzabadi, H.; Iranpoor, N.; Gholinejad, M. *J. Organomet. Chem.* **2010**, 695, 2093–2097.

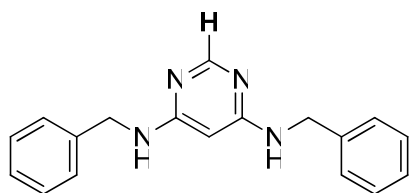
^{13}C NMR (126 MHz, CDCl_3): δ 157.7, 155.1, 134.5, 134.5, 129.6, 129.2, 127.2.
LCMS calc for $\text{C}_{10}\text{H}_8\text{N}_2$, 156.07; found 157.08 ($\text{M}+\text{H}^+$).



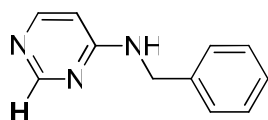
N-Benzyl-6-phenylpyrimidin-4-amine (2i). According to general procedure B, a mixture of *N*-benzyl-2-(methylthio)-6-phenylpyrimidin-4-amine (**1i**) (500 mg, 1.63 mmol), 10% Pd/C (34.6 mg, 0.033 mmol) and triethylsilane (0.779 ml, 4.88 mmol) in THF (2.5 ml) was stirred at 0 °C for 4 hours then at rt for an additional 36 h. Purification on silica gel (0 to 100% EtOAc/heptane) afforded the title compound (354.8 mg, 83%) as a colorless solid.
 ^1H NMR (500 MHz, CDCl_3): δ 8.68 (s, 1H); 7.95-7.91 (m, 2H); 7.47-7.43 (m, 3H); 7.37-7.28 (m, 5H); 6.72 (s, 1H); 5.40 (bs, 1H); 4.63 (d, $J=5.7$ Hz, 2H).
 ^{13}C NMR (126 MHz, CDCl_3): δ 163.2, 158.9, 137.8; 130.4, 129.1 (2C), 128.9 (2C), 127.9, 127.7, 127.1 (2C), 45.8.
LCMS calc for $\text{C}_{17}\text{H}_{15}\text{N}_3$, 261.13; found 262.13 ($\text{M}+\text{H}^+$).



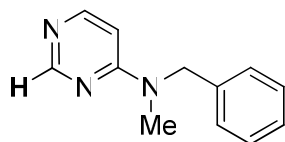
N-Benzyl-6-(trifluoromethyl)pyrimidin-4-amine (2j). According to general procedure A, a mixture of *N*-benzyl-2-(methylthio)-6-(trifluoromethyl)pyrimidin-4-amine (**1j**) (250 mg, 0.835 mmol), 10% Pd/C (17.8 mg, 0.017 mmol) and triethylsilane (0.400 ml, 2.506 mmol) in THF (1.5 ml) was stirred at 0 °C for 4 hours then at rt for an additional 20 h. Purification on silica gel (0 to 30% EtOAc/heptane) afforded the title compound (203.3 mg, 96%) as a colorless solid.
 ^1H NMR (500 MHz, CD_3OD): δ 8.51 (s, 1H); 7.33-7.25 (m, 5H); 6.86 (s, 1H); 4.65 (s, 2H).
 ^{13}C NMR (126 MHz, CD_3OD): δ 164.2, 160.2, 153.3 (q, $J_{\text{C-F}}=34.8$ Hz), 139.6, 129.6, 128.7, 128.4, 122.4 (q, $J_{\text{C-F}}=272.4$ Hz), 103.8, 45.4.
LCMS calc for $\text{C}_{12}\text{H}_{10}\text{F}_3\text{N}_3$, 253.08; found 254.08 ($\text{M}+\text{H}^+$).



N,N'-Dibenzylpyrimidine-4,6-diamine (2k).⁵ According to general procedure B, a mixture of *N,N'*-dibenzyl-2-(methylsulfanyl)pyrimidine-4,6-diamine (**1k**) (500 mg, 1.49 mmol), 10% Pd/C (79.0 mg, 0.074 mmol) and triethylsilane (0.949 ml, 5.94 mmol) in DMA (3.0 ml) was stirred at 0 °C for 30 min then at rt for 24 h. The concentrated crude residue, after treatment with HCl, was dissolved in minimal EtOH (2 mL) and poured into saturated, aqueous NaHCO₃ (10 mL). The resulting precipitate was filtered. The filter cake was washed with EtOAc and heptane and then dried under vacuum to afford the title compound (415 mg, 96%) as a colorless solid. ¹H NMR (500 MHz, DMSO-d₆): δ 7.90 (s, 1H); 7.30-7.24 (m, 8H); 7.19 (t, *J*=7.0 Hz, 2H); 7.11 (t, *J*=6.2 Hz, 2H); 5.38 (bs, 1H); 4.35 (bs, 4H). ¹³C NMR (126 MHz, DMSO-d₆): δ 162.4, 157.5, 140.1, 128.2, 127.0, 126.5, 43.7. LCMS calc for C₁₈H₁₈N₄, 290.15; found 291.12 (M+H⁺).



N-Benzylpyrimidin-4-amine (2l). According to general procedure B, a mixture of *N*-benzyl-2-(methylthio)pyrimidin-4-amine (**1l**) (1000 mg, 4.32 mmol), 10% Pd/C (46.0 mg, 0.043 mmol) and triethylsilane (2.071 ml, 12.97 mmol) in THF (5 ml) was stirred at rt for 16 h. Purification on silica gel (20 to 100% EtOAc/heptane then 0 to 10% MeOH/EtOAc) afforded the title compound (718 mg, 94%) as a colorless solid. ¹H NMR (500 MHz, CDCl₃): δ 8.56 (s, 1H); 8.17 (d, *J*=6.0 Hz, 1H); 7.37-7.28 (m, 5H); 6.32 (dd, *J*=6.0, 1.2 Hz, 1H); 5.39 (bs, 1H); 4.54 (s, 2H). ¹³C NMR (126 MHz, CDCl₃): δ 162.2, 158.7, 155.6, 137.8, 129.0, 127.8, 127.6, 104.0, 45.5. LCMS calc for C₁₁H₁₁N₃, 185.10; found 186.16 (M+H⁺).

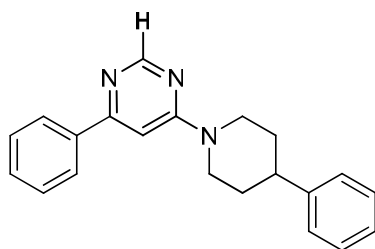


N-Benzyl-N-methylpyrimidin-4-amine (2m). According to general procedure A, a mixture of *N*-benzyl-*N*-methyl-2-(methylthio)pyrimidin-4-amine (**1m**) (500 mg, 2.04 mmol), 10% Pd/C (43.4 mg, 0.041 mmol) and triethylsilane (0.977 ml, 6.11 mmol) in THF (2.5 ml) was stirred for 1 h at 0 °C then for 5 h at rt. Purification on silica gel (50 to 100% EtOAc/heptane then 0 to 10% MeOH/EtOAc) afforded the title compound (272.2 mg, 67.0%) as a colorless oil which solidified on standing to a colorless solid. ¹H NMR (500 MHz, CDCl₃): δ 8.61 (s, 1H); 8.16 (d, *J*=6.2 Hz, 1H); 7.32-7.29 (m, 2H); 7.26-7.23 (m, 1H); 7.18 (d, *J*=7.5 Hz, 2H); 6.41 (dd, *J*=6.2, 1.2 Hz, 1H); 4.79 (s, 2H); 3.04 (s, 3H).

⁵ Wang, L.-X.; Wang, D.-X.; Huang, Z.-T.; Wang, M.-X. *J. Org. Chem.* **2010**, *75*, 741–747.

^{13}C NMR (126 MHz, CDCl_3): δ 161.8, 158.4, 155.5, 137.2, 128.9, 127.5, 127.2, 102.8, 52.4, 35.4.

LCMS calc for $\text{C}_{12}\text{H}_{13}\text{N}_3$, 199.11; found 200.22 ($\text{M}+\text{H}^+$).

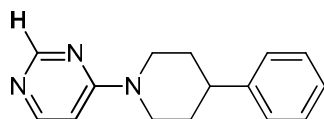


4-Phenyl-6-(4-phenylpiperidin-1-yl)pyrimidine (2n). According to general procedure A, a slurry of 2-(methylthio)-4-phenyl-6-(4-phenylpiperidin-1-yl)pyrimidine (**1n**) (500 mg, 1.38 mmol), 10% Pd/C (29.4 mg, 0.028 mmol) and triethylsilane (0.663 ml, 4.15 mmol) in THF (3.0 ml) was stirred at 0 °C for 2 h then rt for 16 h. Purification on silica gel (0 to 100% EtOAc/heptane) afforded the title compound (401.4 mg, 92%) as a colorless solid.

^1H NMR (500 MHz, CDCl_3): δ 8.72 (s, 1H); 8.00-7.97 (m, 2H); 7.50-7.44 (m, 3H); 7.32 (t, $J=7.6$ Hz, 2H); 7.24-7.21 (m, 3H); 6.95 (s, 1H); 4.68 (bd, $J=13.1$ Hz, 2H); 3.05 (td, $J=13.0$, 2.5 Hz, 2H); 2.85 (tt, $J=12.3$, 3.5, 1H); 2.00 (bd, $J=13.3$ Hz, 2H); 1.76 (qd, $J=12.7$, 4.2 Hz, 2H).

^{13}C NMR (126 MHz, CDCl_3): δ 163.5, 162.5, 158.8, 145.5, 138.5, 130.2, 129.0, 128.8, 127.2, 127.0, 126.8, 98.8, 45.1, 43.2, 33.2.

LCMS calc for $\text{C}_{21}\text{H}_{21}\text{N}_3$, 315.17; found 316.12 ($\text{M}+\text{H}^+$).

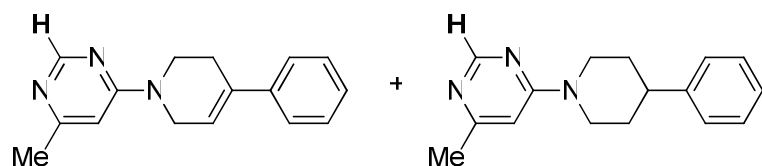


4-(4-Phenylpiperidin-1-yl)pyrimidine (2p). According to general procedure A, a mixture of 2-(methylthio)-4-(4-phenylpiperidin-1-yl)pyrimidine (**1p**) (520 mg, 1.82 mmol), 10% Pd/C (38.8 mg, 0.036 mmol) and triethylsilane (0.873 ml, 5.47 mmol) in THF (3.0 ml) was stirred at 0 °C for 1 h then at rt for 29 h. Purification on silica gel (20 to 100% EtOAc/heptane then 0 to 10% MeOH/EtOAc) afforded the title compound (267.5 mg, 61%) as a colorless solid.

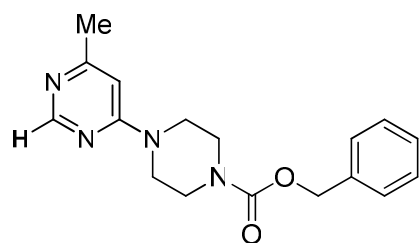
^1H NMR (500 MHz, CDCl_3): δ 8.61 (s, 1H); 8.19 (d, $J=6.3$ Hz, 1H); 7.32 (t, $J=7.5$ Hz, 2H); 7.24-7.20 (m, 3H); 6.55 (d, $J=6.3$ Hz, 1H); 4.57 (bd, $J=13.0$ Hz, 2H); 2.99 (td, $J=13.0$, 2.5 Hz, 2H); 2.82 (tt, $J=12.2$, 3.7 Hz, 1H); 1.97 (bd, $J=13.3$ Hz, 2H); 1.71 (qd, $J=12.8$, 4.2 Hz, 2H).

^{13}C NMR (126 MHz, CDCl_3): 161.3, 158.7, 155.8, 145.4, 128.8, 126.9, 126.7, 103.2, 44.8, 43.0, 33.0.

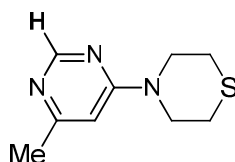
LCMS calc for $\text{C}_{15}\text{H}_{17}\text{N}_3$, 239.14; found 240.17 ($\text{M}+\text{H}^+$).



4-Methyl-6-(4-phenyl-5,6-dihydropyridin-1(2H)-yl)pyrimidine (2q). According to general procedure A, a mixture of 4-methyl-2-(methylthio)-6-(4-phenyl-5,6-dihydropyridin-1(2H)-yl)pyrimidine (**1q**) (500 mg, 1.68 mmol), 10% Pd/C (35.8 mg, 0.034 mmol), triethylsilane (0.806 ml, 5.04 mmol) in THF (2.5 ml) was stirred at 0 °C for 1 h then at rt for 12 h. Purification on silica gel (40 to 100% EtOAc/heptane then 0 to 10% MeOH/EtOAc) afforded a mixture of the title compound (374.3 mg, 89%) and 4-methyl-6-(4-phenylpiperidin-1-yl)pyrimidine (**2o**) in a 7:1 ratio (¹H NMR) as a colorless solid.
¹H NMR (500 MHz, CDCl₃): δ 8.55 (s, 1H); 7.41-7.26 (m, 5H); 6.39 (s, 1H); 6.15-6.12 (m, 1H); 4.18 (d, *J*=3.3 Hz, 2H); 3.94 (app t, *J*=5.6 Hz, 2H); 2.67-2.63 (m, 2H); 2.38 (s, 3H).
¹³C NMR (126 MHz, CDCl₃): δ 165.2, 161.9, 158.0, 140.5, 136.3, 128.7, 127.6, 125.1, 120.3, 101.7, 44.5, 40.5, 27.4, 24.5.
 LCMS calc for C₁₆H₁₇N₃, 251.14; found 252.15 (M+H⁺).



Benzyl 4-(6-methylpyrimidin-4-yl)piperazine-1-carboxylate (2r). According to general procedure A, a mixture of benzyl 4-(6-methyl-2-(methylthio)pyrimidin-4-yl)piperazine-1-carboxylate (**1r**) (500 mg, 1.400 mmol), 10% Pd/C (29.7 mg, 0.028 mmol) and triethylsilane (0.668 ml, 4.18 mmol) in THF (2.5 ml) was stirred at 0 °C for 6 h then at rt for 2 h. Purification on silica gel (20 to 100% EtOAc/heptane then 0 to 10% MeOH/EtOAc) afforded the title compound (399.3 mg, 92%) as a colorless syrup which solidified to a colorless solid on standing under vacuum.
¹H NMR (500 MHz, CDCl₃): δ 8.52 (s, 1H); 7.37-7.30 (m, 5H); 6.36 (s, 1H); 5.17 (s, 2H); 3.67-3.58 (m, 8H); 2.37 (s, 3H).
¹³C NMR (126 MHz, CDCl₃): δ 165.8, 162.2, 158.1, 155.4, 136.6, 128.8, 128.4, 128.2, 101.8, 67.6, 43.6 (2C), 24.5.
 LCMS calc for C₁₇H₂₀N₄O₂, 312.16; found 313.13 (M+H⁺).

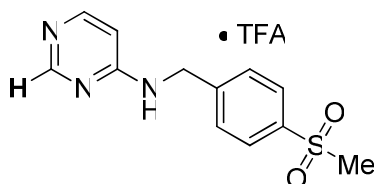


4-(6-Methylpyrimidin-4-yl)thiomorpholine (2s). According to general procedure A, a mixture of 4-(6-methyl-2-(methylthio)pyrimidin-4-yl)thiomorpholine (**1s**) (250 mg, 1.04 mmol), 10% Pd/C (55.1 mg, 0.052 mmol) and triethylsilane (0.496 ml, 3.11 mmol) in THF (1.5 ml) was stirred at 0 °C for 30 min then heated at 60 °C (hot plate temperature) for 72 h. Purification on silica gel (20 to 100% EtOAc/heptane then 0 to 10% MeOH/EtOAc) afforded the title compound (175.0 mg, 87%).

¹H NMR (500 MHz, CDCl₃): δ 8.50 (s, 1H); 6.33 (s, 1H); 3.98 (bs, 4H); 2.64 (bs, 4H); 2.35 (s, 3H).

¹³C NMR (126 MHz, CDCl₃): δ 165.7, 161.6, 158.3, 101.8, 47.0, 26.7, 24.5.

LCMS calc for C₉H₁₃N₃S, 195.08; found 196.14 (M+H⁺).

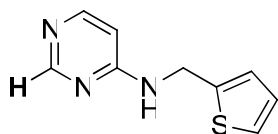


N-(4-(Methylsulfonyl)benzyl)pyrimidin-4-amine·TFA (2t). According to general procedure A, a mixture of *N*-(4-(methylsulfonyl)benzyl)-2-(methylthio)pyrimidin-4-amine (**1t**) (500 mg, 1.62 mmol), 10% Pd/C (34.4 mg, 0.032 mmol) and triethylsilane (0.774 ml, 4.85 mmol) in DMA (2.5 ml) was stirred for 3 h at 0 °C then for 12 h at rt. Purification by preparative RP-LC (60g–C18, 5% to 30% ACN/water+0.05% TFA) afforded the title compound as a colorless solid (560.6 mg, 92%).

¹H NMR (500 MHz, DMSO-*d*₆): δ 9.85 (bs, 1H); 8.79 (s, 1H); 8.22 (d, *J*=6.9 Hz, 1H); 7.90 (d, *J*=8.0 Hz, 2H); 7.59 (d, *J*=8.0 Hz, 2H); 6.87 (d, *J*=6.8 Hz, 1H); 4.80 (bs, 2H); 3.19 (s, 3H).

¹³C NMR (126 MHz, DMSO-*d*₆): δ 162.5, 153.0, 143.5, 143.4, 139.8, 128.2, 127.3, 116.9 (q, *J*_{C-F}=298.8 Hz), 106.3, 43.5.

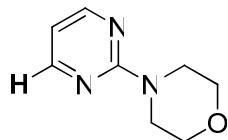
LCMS calc for C₁₂H₁₃N₃O₂S, 263.07; found 264.07 (M+H⁺).



N-(Thiophen-2-ylmethyl)pyrimidin-4-amine (2u). According to general procedure B, a mixture of 2-(methylthio)-*N*-(thiophen-2-ylmethyl)pyrimidin-4-amine (**1u**) (500 mg, 2.11 mmol), 10% Pd/C (44.8 mg, 0.042 mmol) and triethylsilane (1.009 ml, 6.32 mmol) in THF (2.5 ml) was stirred at 0 °C for 1 h then at rt for 16 h. Purification on silica gel (50 to 100% EtOAc/hexanes then 0 to 10% MeOH/EtOAc) afforded the title compound (365 mg, 91%) as a colorless solid.

¹H NMR (500 MHz, CDCl₃): δ 8.61 (s, 1H); 8.19 (d, *J*=6.0 Hz, 1H); 7.24 (d, *J*=5.1 Hz, 1H); 7.02 (d, *J*=3.4 Hz, 1H); 6.97 (dd, *J*=5.1, 3.5 Hz, 1H); 6.37 (d, *J*=6.0 Hz, 1H); 5.28 (bs, 1H); 4.74 (d, *J*=5.7 Hz, 2H).

^{13}C NMR (126 MHz, CDCl_3): δ 161.8, 158.7, 155.4, 140.9, 127.1, 126.0, 125.3, 104.5, 40.3.
LCMS calc for $\text{C}_9\text{H}_9\text{N}_3\text{S}$, 191.05; found 192.08 ($\text{M}+\text{H}^+$).

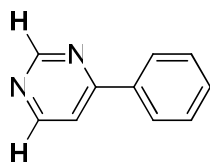


4-(Pyrimidin-2-yl)morpholine (4a). According to general procedure A, a mixture of 4-(4-(methylthio)pyrimidin-2-yl)morpholine (**3a**) (500 mg, 2.37 mmol), 10% Pd/C (50.4 mg, 0.047 mmol) and triethylsilane (1.134 ml, 7.10 mmol) in THF (2.5 ml) was stirred at 0 °C for 1 h then at rt for 1 h. Purification on silica gel (0 to 100% EtOAc/heptane) afforded the title compound (369.8 mg, 95%) as a colorless oil which solidified to a low-melting solid on standing under vacuum.

^1H NMR (500 MHz, CDCl_3): δ 8.31 (d, $J=4.7$ Hz, 2H); 6.50 (t, $J=4.7$, 1H); 3.81-3.74 (m, 8H).

^{13}C NMR (126 MHz, CDCl_3): δ 162.0, 157.9, 110.5, 67.0, 44.4.

LCMS calc for $\text{C}_8\text{H}_{11}\text{N}_3\text{O}$, 165.09; found 166.10 ($\text{M}+\text{H}^+$).

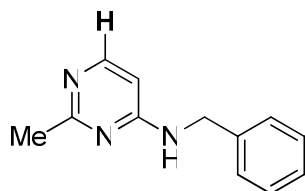


4-Phenylpyrimidine (4b).⁶ According to general procedure A, a mixture of 2,4-bis(ethylthio)-6-phenylpyrimidine (**3b**) (500 mg, 1.81 mmol), 10% Pd/C (38.5 mg, 0.036 mmol) and triethylsilane (0.867 ml, 5.43 mmol) in THF (2.5 ml) was stirred at 0 °C for 3 h then at rt for 2 h. Purification on silica gel (0 to 100% EtOAc/heptane) afforded the title compound (249.1 mg, 88%) as a colorless solid.

^1H NMR (500 MHz, CDCl_3): δ 9.28 (d, $J=1.4$ Hz, 1H); 8.77 (d, $J=5.4$ Hz, 1H); 8.12-8.07 (m, 2H); 7.73 (dd, $J=5.4$, 1.4 Hz, 1H); 7.54-7.51 (m, 3H).

^{13}C NMR (126 MHz, CDCl_3): δ 164.2, 159.3, 157.7, 136.7, 131.3, 129.3, 127.4, 117.2.

LCMS calc for $\text{C}_{10}\text{H}_8\text{N}_2$, 156.07; found 157.08 ($\text{M}+\text{H}^+$).



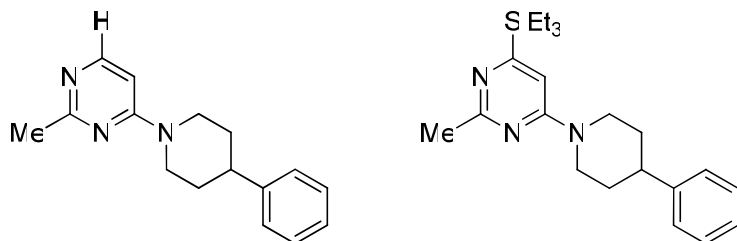
N-Benzyl-2-methylpyrimidin-4-amine (4c). According to general procedure A, a mixture of *N*-benzyl-6-(ethylthio)-2-methylpyrimidin-4-amine (**3c**) (500 mg, 1.93 mmol), 10% Pd/C (41.0 mg, 0.039 mmol) and triethylsilane (0.924 ml, 5.78 mmol) in THF (3.0 ml) was stirred at 0 °C for 3 h. Purification on silica gel (20 to 100% EtOAc/heptane then 0 to 10% MeOH) afforded the title compound (371.1 mg, 97%) as a colorless solid.

⁶ Sasada, T.; Kobayashi, F.; Sakai, N.; Konakahara, T. *Org. Lett.* **2009**, *11*, 2161–2164.

^1H NMR (500 MHz, CDCl_3): δ 8.09 (d, $J=5.9$ Hz, 1H); 7.36-7.26 (m, 5H); 6.13 (d, $J=6.0$ Hz, 1H); 5.42 (bs, 1H); 4.51 (bs, 2H); 2.50 (s, 3 H).

^{13}C NMR (126 MHz, CDCl_3): δ 167.8, 162.5, 156.0, 138.1, 129.0, 127.8, 127.6, 100.7, 45.6, 26.2.

LCMS calc for $\text{C}_{12}\text{H}_{13}\text{N}_3$, 199.11; found 200.16 ($\text{M}+\text{H}^+$).



2-Methyl-4-(4-phenylpiperidin-1-yl)pyrimidine (4d) and 2-methyl-4-(4-phenylpiperidin-1-yl)-6-(triethylsilyl)pyrimidine (15). According to general procedure A, a mixture of 4-(ethylthio)-2-methyl-6-(4-phenylpiperidin-1-yl)pyrimidine (**3d**) (250 mg, 0.798 mmol), 10% Pd/C (16.98 mg, 0.016 mmol) and triethylsilane (0.382 ml, 2.393 mmol) in THF (1.5 ml) was stirred at 0 °C for 3 h. Purification on silica gel (40 to 100% EtOAc/heptane then 0 to 10% MeOH/EtOAc) afforded 2-methyl-4-(4-phenylpiperidin-1-yl)pyrimidine (**4d**) (198.1 mg, 98%) as a colorless solid and 2-methyl-4-(4-phenylpiperidin-1-yl)-6-(triethylsilyl)pyrimidine (**15**) (5.0 mg, 1.7%).

4d: ^1H NMR (500 MHz, CDCl_3): δ 8.12 (d, $J=6.2$ Hz, 1H); 7.34-7.28 (m, 2H); 6.36 (d, $J=6.3$ Hz, 1H); 4.59 (d, $J=13.0$ Hz, 2H); 2.95 (td, $J=12.9$, 2.5 Hz, 2H); 2.80 (tt, $J=12.2$, 3.7 Hz, 1H); 2.51 (s, 3H); 1.95 (d, $J=13.3$ Hz, 2H).

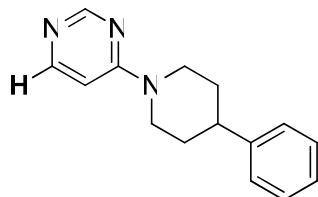
^{13}C NMR (126 MHz, CDCl_3): δ 167.6, 161.7, 155.9, 145.6, 128.8, 126.9, 126.7, 100.0, 44.7, 43.1, 33.1, 26.5.

LCMS calc for $\text{C}_{16}\text{H}_{19}\text{N}_3$, 253.16; found 254.14 ($\text{M}+\text{H}^+$).

15: ^1H NMR (500 MHz, CDCl_3): δ 7.32 (t, $J=7.5$ Hz, 2H); 7.23 (d, $J=7.3$ Hz, 3H); 6.57 (s, 1H); 4.60 (d, $J=13.1$ Hz, 2H); 2.92 (t, $J=12.9$ Hz, 2H); 2.79 (tt, $J=12.3$, 3.3, 1H); 2.52 (s, 3H); 1.96 (d, $J=13.2$ Hz, 2H); 1.71 (qd, $J=12.7$, 4.2 Hz, 2H); 1.43-1.12 (m, 1H); 0.99 (t, $J=7.8$ Hz, 9H); 0.83 (q, $J=7.9$ Hz, 6H).

^{13}C NMR (126 MHz, CDCl_3): δ 172.8, 166.5, 160.4, 145.8, 128.7, 127.0, 126.6, 106.8, 44.5, 43.2, 33.1, 26.7, 7.6, 2.8.

LCMS calc for $\text{C}_{22}\text{H}_{33}\text{N}_3\text{Si}$, 367.24; found 368.19 ($\text{M}+\text{H}^+$).

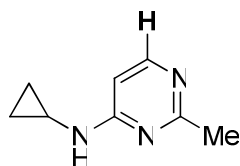


4-(4-Phenylpiperidin-1-yl)pyrimidine (4e). According to general procedure A, a mixture of 4-(ethylthio)-6-(4-phenylpiperidin-1-yl)pyrimidine (**3e**) (500 mg, 1.67 mmol), 10% Pd/C (35.5 mg, 0.033 mmol) and triethylsilane (0.800 ml, 5.01 mmol) in THF (2.5 ml) was stirred at 0 °C for 3 h. Purification on silica gel (40 to 100% EtOAc/heptane then 0 to 10% MeOH/EtOAc) afforded the title compound (357.3 mg, 89%) as a colorless solid.

^1H NMR (500 MHz, CDCl_3): δ 8.61 (s, 1H); 8.19 (d, $J=6.3$ Hz, 1H); 7.32 (app t, $J=7.5$ Hz, 2H); 7.22 (app t, $J=8.0$ Hz, 3H); 6.55 (d, $J=6.3$ Hz, 1H); 4.57 (d, $J=13.0$ Hz, 2H); 2.99 (td, $J=13.0$, 2.5 Hz, 2H); 2.82 (tt, $J=12.2$, 3.7 Hz, 1H); 1.97 (d, $J=13.3$ Hz, 2H); 1.71 (qd, $J=12.8$, 4.2 Hz, 2H).

^{13}C NMR (126 MHz, CDCl_3): δ 161.3, 158.7, 155.8, 145.4, 128.8, 126.9, 126.7, 103.1, 44.8, 43.0, 33.0.

LCMS calc for $\text{C}_{15}\text{H}_{17}\text{N}_3$, 239.14; found 240.14 ($\text{M}+\text{H}^+$).

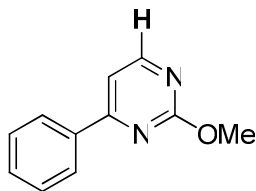


N-Cyclopropyl-2-methylpyrimidin-4-amine (4f). According to general procedure A, a mixture of *N*-cyclopropyl-6-(ethylthio)-2-methylpyrimidin-4-amine (**3f**) (500 mg, 2.39 mmol), 10% Pd/C (50.8 mg, 0.048 mmol) and triethylsilane (1.145 ml, 7.17 mmol) in THF (3.0 ml) was stirred at 0 °C for 2 h. Purification on silica gel (40 to 100% EtOAc/heptane then 0 to 10% MeOH/EtOAc) afforded the title compound (345.5 mg, 97%) as a colorless solid.

^1H NMR (500 MHz, CDCl_3): δ 8.18 (d, $J=5.9$ Hz, 1H); 6.49 (d, $J=5.9$ Hz, 1H); 5.65 (bs, 1H); 2.52-2.47 (m, 1H); 2.46 (s, 3H); 0.83-0.77 (m, 2H); 0.57-0.52 (m, 2H).

^{13}C NMR (126 MHz, CDCl_3): δ 167.5, 164.0, 156.4, 100.3, 26.0, 23.4, 7.8.

LCMS calc for $\text{C}_8\text{H}_{11}\text{N}_3$, 149.10; found 150.09 ($\text{M}+\text{H}^+$).

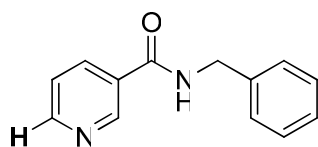


2-Methoxy-4-phenylpyrimidine (4g). According to general procedure A, a mixture of 4-(ethylthio)-2-methoxy-6-phenylpyrimidine (**3g**) (250 mg, 1.02 mmol), 10% Pd/C (21.60 mg, 0.020 mmol) and triethylsilane (0.486 ml, 3.04 mmol) in THF (1.5 ml) was stirred at 0 °C for 1 h then at rt for 1 h. Purification on silica gel (40 to 100% EtOAc/heptane then 0 to 10% MeOH/EtOAc) afforded the title compound (184.3 mg, 98%) as a pale yellow oil.

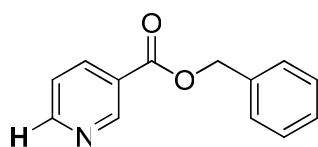
^1H NMR (500 MHz, CDCl_3): δ 8.56 (d, $J=5.1$ Hz, 1H); 8.12-8.10 (m, 2H); 7.51-7.48 (m, 3H); 7.37 (d, $J=5.2$ Hz, 1H); 4.10 (s, 3H).

^{13}C NMR (126 MHz, CDCl_3): δ 166.6, 166.1, 160.0, 136.6, 131.4, 129.1, 127.4, 110.7, 55.0.

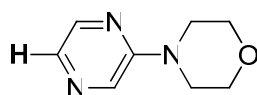
LCMS calc for $\text{C}_{11}\text{H}_{10}\text{N}_2\text{O}$, 186.08; found 187.16 ($\text{M}+\text{H}^+$).



N-Benzylnicotinamide.⁷ According to general procedure A, a mixture of *N*-benzyl-6-(ethylthio)nicotinamide (**5a**) (500 mg, 1.84 mmol), 10% Pd/C (39.1 mg, 0.037 mmol) and triethylsilane (0.880 ml, 5.51 mmol) in THF (2.5 ml) was stirred at 0 °C for 1 h then at rt for 4 h. Purification on silica gel (40 to 100% EtOAc/heptane then 0 to 10% MeOH/EtOAc) afforded *N*-benzylnicotinamide (357.8 mg, 92%) as a pale yellow syrup which solidified on standing. ¹H NMR (500 MHz, CDCl₃): δ 8.97 (s, 1H); 8.70 (d, *J*=4.8 Hz, 1H); 8.13 (dt, *J*=8.0, 2.0 Hz, 1H); 7.39-7.35 (m, 5H); 7.33-7.29 (m, 1H); 6.59 (bs, 1H); 4.66 (d, *J*=5.7 Hz, 2H). ¹³C NMR (126 MHz, CDCl₃): δ 165.7, 152.5, 148.1, 137.9, 135.4, 130.3, 129.1, 128.2, 128.0, 123.7, 44.4. LCMS calc for C₁₃H₁₂N₂O, 212.09; found 213.09 (M+H⁺).



Benzyl nicotinate.⁸ According to general procedure A, a mixture of benzyl 6-(ethylthio)nicotinate (**5b**) (500 mg, 1.83 mmol), 10% Pd/C (38.9 mg, 0.037 mmol) and triethylsilane (0.876 ml, 5.49 mmol) in THF (2.5 ml) was stirred at 0 °C for 1 h then at rt for 4 h. Purification on silica gel (0 to 100% MTBE/heptane) afforded benzyl nicotinate (319.1 mg, 82%) as a pale yellow oil. ¹H NMR (500 MHz, CDCl₃): δ 9.27 (d, *J*=2.1 Hz, 1H); 8.78 (dd, *J*=4.9, 1.7 Hz, 1H); 8.32 (app dt, *J*=7.9, 2.0 Hz, 1H); 7.46-7.33 (m, 6H); 5.40 (s, 2H). ¹³C NMR (126 MHz, CDCl₃): δ 165.3, 153.8, 151.3, 137.4, 135.7, 128.9, 128.7, 128.5, 126.3, 123.5, 67.3. LCMS calc for C₁₃H₁₁NO₂, 213.08; found 214.10 (M+H⁺).



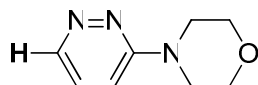
4-(Pyrazin-2-yl)morpholine.⁹ According to general procedure A, a mixture of 4-(5-(ethylthio)pyrazin-2-yl)morpholine (**6**) (500 mg, 2.22 mmol), 10% Pd/C (47.2 mg, 0.044 mmol) and triethylsilane (1.063 ml, 6.66 mmol) in THF (2.5 ml) was stirred at 0 °C for 30 min then at rt for 2.5 h. Purification on silica gel (20 to 100% EtOAc/heptane) afforded 4-(pyrazin-2-yl)morpholine (337.0 mg, 92%) as a colorless solid. ¹H NMR (500 MHz, CDCl₃): δ 8.12 (s, 1H); 8.07 (s, 1H); 7.89 (d, *J*=2.5 Hz, 1H); 3.83 (app t, *J*=4.8, 4H); 3.55 (app t, *J*=4.9, 4H). ¹³C NMR (126 MHz, CDCl₃): δ 155.3, 141.9, 133.8, 131.1, 66.7, 45.0.

⁷ Cui, X.; Zhang, Y.; Shi, F.; Deng, Y. *Chem-Eur. J.* **2011**, *17*, 1021–1028.

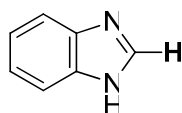
⁸ Khan, K. M.; Maharvi, G. M.; Hayat, S.; Zia-Ullah; Choudhary, M. I.; Atta-ur-Rahman *Tetrahedron* **2003**, *59*, 5549–5554.

⁹ Organ, M.; Abdel-Hadi, M.; Avola, S.; Dubovyk, I.; Hadei, N.; Kantchev, E.; O'Brien, C.; Sayah, M.; Valente, C. *Chem-Eur. J.* **2008**, *14*, 2443–2452.

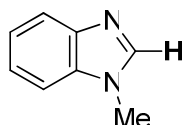
LCMS calc for C₈H₁₁N₃O, 165.09; found 166.16 (M+H⁺).



4-(Pyridazin-3-yl)morpholine. According to general procedure A, a mixture of 4-(6-(ethylthio)pyridazin-3-yl)morpholine (**7**) (500 mg, 2.27 mmol), 10% Pd/C (47.2 mg, 0.044 mmol) and triethylsilane (1.063 ml, 6.66 mmol) in THF (2.5 ml) was stirred at 0 °C for 1 h then at rt for 2 days. Purification on silica gel (20 to 100% EtOAc/ heptane then 0 to 10% MeOH/EtOAc) afforded 4-(pyridazin-3-yl)morpholine (110 mg, 30%) as a yellow solid. ¹H NMR (500 MHz, CDCl₃): δ 8.61 (d, *J*=4.3 Hz, 1H); 7.22 (dd, *J*=9.3, 4.5 Hz, 1H); 6.88 (d, *J*=9.3 Hz, 1H); 3.84 (app t, *J*=4.7 Hz, 4H); 3.62 (app t, *J*=4.7 Hz, 4 H). ¹³C NMR (126 MHz, CDCl₃): δ 160.4, 144.1, 127.5, 112.4, 66.8, 45.4. LCMS calc for C₈H₁₁N₃O, 165.09; found 166.13 (M+H⁺).



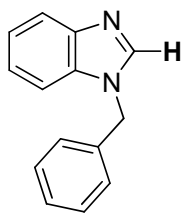
Benzimidazole.¹⁰ According to general procedure A, a mixture of 2-(methylthio)benzimidazole (**8a**) (1000 mg, 6.09 mmol), 10% Pd/C (130 mg, 0.122 mmol) and triethylsilane (2.92 ml, 18.27 mmol) in THF (6.0 ml) was stirred at 0 °C for 30 min then at rt for 24 h. Purification on silica gel (20 to 100% EtOAc/heptane then 0 to 10% MeOH/EtOAc) afforded benzimidazole (712.4 mg, 99%) as a colorless solid. Analytical data were in agreement with a commercially available sample. ¹H NMR (500 MHz, DMSO-d₆): δ 12.42 (bs, 1H); 8.19 (s, 1H); 7.57 (bs, 2H); 7.17 (s, 2H). LCMS calc for C₇H₆N₂, 118.05; found 119.26 (M+H⁺).



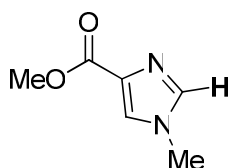
1-Methyl-1H-benzo[d]imidazole.¹¹ According to general procedure A, a mixture of 1-methyl-2-(methylthio)-1H-benzo[d]imidazole (**8b**) (500 mg, 2.80 mmol), 10% Pd/C (59.7 mg, 0.056 mmol) and triethylsilane (1.344 ml, 8.41 mmol) in THF (3.0 ml) was stirred at 0 °C for 1 h then at rt for 2 h. Purification on silica gel (40 to 100% EtOAc/heptane then 0 to 10% MeOH/EtOAc) afforded 1-methyl-1H-benzo[d]imidazole (362.6 mg, 98%) as a colorless solid. Analytical data were in agreement with a commercially available sample. ¹H NMR (500 MHz, CDCl₃): δ 7.83 (s, 1H); 7.80 (d, *J*=8.5 Hz, 1H); 7.37 (d, *J*=7.8 Hz, 1H); 7.32-7.26 (m, 2H); 3.80 (s, 3H). ¹³C NMR (126 MHz, CDCl₃): δ 143.9, 143.7, 134.7, 123.1, 122.2, 120.4, 109.5, 31.1. LCMS calc for C₈H₈N₂, 132.07; found 133.07 (M+H⁺).

¹⁰ Selvam, K.; Annadhasan, M.; Velmurugan, R.; Swaminathan, M. *Bull. Chem. Soc. Jpn.* **2010**, *83*, 831–837.

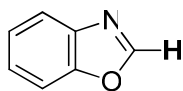
¹¹ van den Berg, D.; Zoellner, K. R.; Ogunrombi, M. O.; Malan, S. F.; Terre'Blanche, G.; Castagnoli, Jr., N.; Bergh, J. J.; Petzer, J. P. *Bioorgan. Med. Chem.* **2007**, *15*, 3692–3702.



1-Benzyl-1H-benzo[d]imidazole. According to general procedure A, a mixture of 1-benzyl-2-(methylthio)-1H-benzo[d]imidazole (**8c**) (500 mg, 1.97 mmol), 10% Pd/C (41.8 mg, 0.039 mmol) and triethylsilane (0.942 ml, 5.90 mmol) in THF (3.0 ml) was stirred at 0 °C for 8 h. Purification on silica gel (40 to 100% EtOAc/heptane then 0 to 10% MeOH/EtOAc) afforded 1-benzyl-1H-benzo[d]imidazole (355.3 mg, 87%) and benzimidazole (26.4 mg, 11%). Analytical data were in agreement with a commercially available sample.
¹H NMR (500 MHz, CDCl₃): δ 7.95 (s, 1H); 7.83 (d, *J*=7.7 Hz, 1 H); 7.36-7.24 (m, 6H); 7.19 (d, *J*=7.2 Hz, 2H); 5.37 (s, 2H).
¹³C NMR (126 MHz, CDCl₃): δ 144.2, 143.4, 135.7, 134.1, 129.3, 128.5, 127.3, 123.3, 122.5, 120.7, 110.2, 49.1.
 LCMS calc for C₁₄H₁₂N₂, 208.10; found 209.12 (M+H⁺).



Methyl 1-methyl-1H-imidazole-4-carboxylate.¹² According to general procedure A, a mixture of methyl 1-methyl-2-(methylthio)-1H-imidazole-4-carboxylate (**9**) (250 mg, 1.34 mmol), 10% Pd/C (28.6 mg, 0.027 mmol) and triethylsilane (0.643 ml, 4.03 mmol) in THF (2.0 ml) was stirred at 0 °C for 1 h then at rt for 1 h. Purification on silica gel (40 to 100% EtOAc/heptane then 0 to 10% MeOH/EtOAc) afforded methyl 1-methyl-1H-imidazole-4-carboxylate (185.3 mg, 98%). Analytical data were in agreement with a commercially available sample.
¹H NMR (500 MHz, CDCl₃): δ 7.70 (s, 1H); 7.52 (s, 1H); 3.89 (s, 3H); 3.84 (s, 3H).
¹³C NMR (126 MHz, CDCl₃): δ 161.1, 142.7, 137.9, 123.2, 51.7, 34.3.
 LCMS calc for C₆H₈N₂O₂, 140.06; found 141.10 (M+H⁺).



Benzo[d]oxazole.¹³ According to general procedure A, a mixture of 2-(methylthio)benzo[d]oxazole (**10**) (500 mg, 3.03 mmol), 10% Pd/C (64.4 mg, 0.061 mmol) and triethylsilane (1.450 ml, 9.08 mmol) in THF (3.0 ml) was stirred at 0 °C for 30 min then at rt for 12 h. Purification on silica gel (0 to 100% CH₂Cl₂/heptane) afforded a clear, colorless oil (294.5 mg). ¹H NMR indicated 18 mol% triethylsilane; therefore, the corrected yield of

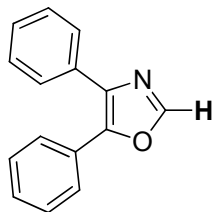
¹² O'Connell, J. F.; Parquette, J.; Yelle, W. E.; Wang, W.; Rapoport, H. *Synthesis* **1988**, 767–771.

¹³ Lee, J. J.; Kim, J.; Jun, Y. M.; Lee, B. M.; Kim, B. H. *Tetrahedron* **2009**, 65, 8821–8831.

benzo[d]oxazole was 67%. Analytical data were in agreement with a sample of commercially available benzoxazole.

^1H NMR (500 MHz, CDCl_3): δ 8.10 (s, 1H); 7.80 (dd, $J=7.0, 2.0$ Hz, 1H); 7.60-7.57 (m, 1H); 7.42-7.35 (m, 2H).

LCMS calc for $\text{C}_7\text{H}_5\text{NO}$, 119.04; found 119.97 ($\text{M}+\text{H}^+$).

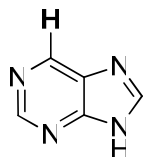


4,5-Diphenyloxazole.¹⁴ According to general procedure A, a mixture of 2-(methylthio)-4,5-diphenyloxazole (**11**) (500 mg, 1.87 mmol), 10% Pd/C (39.8 mg, 0.037 mmol) and triethylsilane (0.896 ml, 5.61 mmol) in THF (2.5 ml) was stirred at 0 °C for 15 min then at 60 °C (hot plate temperature) for 20 h. Purification on silica gel (0 to 25% MTBE/heptane) afforded a colorless solid (376.0 mg). ^1H NMR indicated 3 mol% triethylsilane; therefore, the corrected yield of 4,5-diphenyloxazole was 88%.

^1H NMR (500 MHz, CDCl_3): δ 7.96 (s, 1H); 7.68-7.66 (m, 2H); 7.63-7.60 (m, 2H); 7.41-7.33 (m, 6H).

^{13}C NMR (126 MHz, CDCl_3): δ 149.9, 146.0, 135.0, 132.4, 129.0, 128.9 (2C), 128.8, 128.4, 128.1, 127.0.

LCMS calc for $\text{C}_{15}\text{H}_{11}\text{NO}$, 221.08; found 222.13 ($\text{M}+\text{H}^+$).

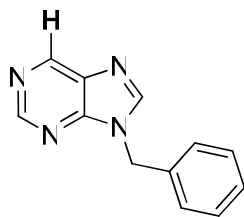


9H-Purine. According to general procedure A, a mixture of 6-(propylthio)-9H-purine (**12a**) (1000 mg, 5.15 mmol), 10% Pd/C (110 mg, 0.103 mmol) and triethylsilane (2.467 ml, 15.44 mmol) in THF (5.0 ml) was stirred at 0 °C for 1 h then at rt for 10 h. Purification on silica gel (0 to 10% MeOH/ CH_2Cl_2) afforded 9H-purine (555.0 mg, 90%) as a colorless solid. Analytical data were in agreement with a sample of commercially available purine.

^1H NMR (500 MHz, $\text{DMSO}-d_6$): δ 9.11 (s, 1H); 8.90 (s, 1H); 8.61 (s, 1H).

LCMS calc for $\text{C}_5\text{H}_4\text{N}_4$, 120.04; found 121.00 ($\text{M}+\text{H}^+$).

¹⁴ Davies, J. R.; Kane, P. D.; Moody, C. J. *Tetrahedron* **2004**, 60, 3967–3977.

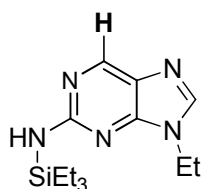


9-Benzyl-9H-purine.¹⁵ According to general procedure A, a mixture of 9-benzyl-6-(propylthio)-9H-purine (**12b**) (500 mg, 1.76 mmol), 10% Pd/C (37.4 mg, 0.035 mmol) and triethylsilane (0.842 ml, 5.27 mmol) in THF (2.5 ml) was stirred 0 °C for 15 min then at rt for 90 min. Purification on silica gel (0 to 100% EtOAc/heptane then 0 to 10% MeOH/EtOAc) afforded the title compound (327.5 mg, 89%) as a colorless solid.

¹H NMR (500 MHz, CDCl₃): δ 9.16 (s, 1H); 9.02 (s, 1H); 8.06 (s, 1H); 7.39-7.29 (m, 5H); 5.46 (s, 2H).

¹³C NMR (126 MHz, CDCl₃): δ 153.1, 151.6, 148.9, 145.2, 135.1, 134.2, 129.4, 128.9, 128.1, 47.4.

LCMS calc for C₁₂H₁₀N₄, 210.09; found 211.14 (M+H⁺).



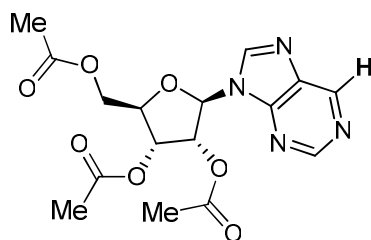
9-Ethyl-N-(triethylsilyl)-9H-purin-2-amine. According to general procedure A, a mixture of 9-ethyl-6-(methylthio)-9H-purin-2-amine (**13**) (500 mg, 2.389 mmol), 10% Pd/C (50.9 mg, 0.048 mmol) and triethylsilane (1.145 ml, 7.17 mmol) in THF (3.0 ml) was stirred for 3 h at 0 °C then for 3 h at rt. Purification on silica gel (0 to 20% MeOH/EtOAc) afforded a clear, colorless syrup. Drying under vacuum (0.01 torr) for 12 h afforded the title compound (633.0 mg, 95%) as a colorless solid.

¹H NMR (500 MHz, CDCl₃): δ 8.65 (s, 1H); 7.72 (s, 1H); 4.72 (bs, 1H); 4.13 (q, *J*=7.3 Hz, 2H); 1.37 (t, *J*=7.3 Hz, 3H); 0.99 (t, *J*=7.8 Hz, 9H); 0.83 (q, *J*=7.9 Hz, 6H).

¹³C NMR (126 MHz, CDCl₃): δ 161.5, 153.2, 149.8, 141.7, 128.3, 38.5, 15.5, 7.3, 4.5.

LCMS calc for C₁₃H₂₃N₅Si, 277.17; found 164.09 (M-SiEt₃+2H⁺).

¹⁵ Nair, V.; Chi, G.; Uchil, V. R. Patent Application US2006/172973 A1.

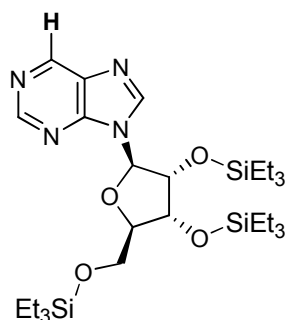


(2*R*,3*R*,4*R*,5*R*)-2-(Acetoxymethyl)-5-(9*H*-purin-9-yl)tetrahydrofuran-3,4-diyl diacetate.¹⁶

According to general procedure A, a mixture of (2*R*,3*R*,4*R*,5*R*)-2-(acetoxymethyl)-5-(6-(methylthio)-9*H*-purin-9-yl)tetrahydrofuran-3,4-diyl diacetate (**14a**) (500 mg, 1.18 mmol), 10% Pd/C (25.07 mg, 0.024 mmol) and triethylsilane (0.564 ml, 3.53 mmol) in THF (2.0 ml) was stirred at 0 °C for 2 h then at rt for 10 h. Purification on silica gel (40 to 100% EtOAc/heptane then 0 to 10% MeOH/EtOAc) afforded the title compound (417.2 mg, 94%) as a colorless wax. ¹H NMR (500 MHz, CDCl₃): δ 9.16 (s, 1H); 9.00 (s, 1H); 8.24 (s, 1H); 6.25 (d, *J*=5.2 Hz, 1H); 5.98 (app t, *J*=5.4 Hz, 1H); 5.68 (app t, *J*=5.3 Hz, 1H); 4.49-4.44 (m, 2H); 4.39-4.36 (m, 1H); 2.15 (s, 3H); 2.11 (s, 3H); 2.07 (s, 3H).

¹³C NMR (126 MHz, CDCl₃): δ 170.5, 169.8, 169.6, 153.1, 151.1, 149.4, 143.8, 134.9, 86.6, 80.6, 73.2, 70.7, 63.2, 20.9, 20.7, 20.6.

LCMS calc for C₁₆H₁₈N₄O₇, 378.12; found 379.10 (M+H⁺).



9-(((2*R*,3*R*,4*R*,5*R*)-3,4-Bis((triethylsilyl)oxy)-5-(((triethylsilyl)oxy)methyl)tetrahydrofuran-2-yl))-9*H*-purine.

According to general procedure A, a slurry of (2*R*,3*S*,4*R*,5*R*)-2-(hydroxymethyl)-5-(6-(methylthio)-9*H*-purin-9-yl)tetrahydrofuran-3,4-diol (**14b**) (500 mg, 1.68 mmol), 10% Pd/C (35.7 mg, 0.034 mmol) and triethylsilane (1.606 ml, 10.06 mmol) in THF (3.0 ml) was stirred at 0 °C for 20 min then at rt for 24 h. The slurry slowly became homogenous during the first 2 h. Purification on silica gel (0 to 100% EtOAc/heptane) afforded the title compound (876.8 mg, 88%) as a clear, colorless syrup.

¹H NMR (500 MHz, CDCl₃): δ 9.13 (s, 1H); 8.96 (s, 1H); 8.53 (s, 1H); 6.14 (d, *J*=4.9 Hz, 1H); 4.70 (t, *J*=4.6 Hz, 1H); 4.36 (t, *J*=4.1 Hz, 1H); 4.14 (q, *J*=3.3 Hz, 1H); 3.99 (dd, *J*=11.3, 3.8 Hz, 1H); 3.78 (dd, *J*=11.3, 2.6 Hz, 1H); 0.98 (dt, *J*=10.7, 7.9 Hz, 18H); 0.80 (t, *J*=7.9 Hz, 9H); 0.70-0.59 (m, 12H); 0.52-0.34 (m, 6H).

¹³C NMR (126 MHz, CDCl₃): δ 152.8, 151.4, 148.8, 144.5, 134.8, 88.4, 85.5, 76.3, 72.1, 62.0, 7.0, 6.9, 6.7, 5.1, 4.8, 4.4.

LCMS calc for C₂₈H₅₄N₄O₄Si₃, 594.35; found 595.36 (M+H⁺).

¹⁶ Patching, S. G.; Baldwin, S. A.; Baldwin, A. D.; Young, J. D.; Gallagher, M. P.; Henderson, P. J. F.; Herbert, R. B. *Org. Biomol. Chem.* **2005**, *3*, 462–470.