

Supplementary Material

Reaction of Tosylmethyl Isocyanide with *N*-Heteroaryl Formamidines: an Alternative Approach to the Synthesis of *N*-Heteroaryl Tosylimidazoles

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General. Melting points were measured on an electrothermal melting point apparatus and are uncorrected. ^1H and ^{13}C NMR spectral data were recorded at 300 and 75 MHz, respectively, using a Varian Mercury 300 MHz NMR spectrometer or at 500 and 125 MHz, respectively, using a Varian NMR System 500 MHz spectrometer. Chemical shifts (δ) are given in parts per million downfield from TMS ($\delta = 0$). Elemental analyses were performed on an EAI EXTERNAL ANALYTICAL, Inc. CE-440 elemental analyzer.

***N,N*-Dimethyl-*N*-pyridylformamide (3a).** In a 25 mL two neck round bottom flask, adapted with a reflux condenser, was placed 2-aminopyridine (0.94 g, 10 mmol) with an excess of *N,N*-dimethylformamide dimethyl acetal (9 mL), and the mixture refluxed for 6 h, until the starting materials (TLC) disappeared. The excess of DMFDMA was removed by adding toluene to the reaction mixture, followed by solvent evaporation under reduced pressure. The compound was further purified by re-crystallization from ethyl alcohol. The amidine was isolated as a yellow semisolid in 71% yield, mp 31–32 °C (lit¹⁴ mp 30–32 °C). ^1H NMR δ 2.3 (3H, s), 3.03 (3H, s), 6.82 (1H, dd, $J = 8.0$ Hz, $J = 4.8$ Hz), 6.93 (1H, d, $J = 7.8$ Hz), 7.49 (1H, dd, $J = 7.8$ Hz, $J = 5.8$ Hz), 8.22 (1H, d, $J = 4.8$ Hz), 8.38 (1H, s). ^{13}C NMR δ 34.7, 40.8, 117.7, 117.9, 137.6, 148.0, 155.1, 162.0.

5-Bromo-*N,N*-dimethyl-*N*-pyridylformamide (3b). Following the previous procedure, 2-amino-5-bromopyridine (1.73 g, 10 mmol) and an excess of *N,N*-dimethylformamide dimethyl acetal (9 mL) gave the title formamide as yellow needles, mp 79–80 °C (lit¹⁴ mp 78–80 °C), in 72% yield. ^1H NMR (CDCl_3) δ 3.07 (3H, s), 3.08 (3H, s), 6.83 (1H, d, $J = 5.1$ Hz), 7.6 (1H, d, $J = 5.1$ Hz), 8.25 (1H, s), 8.38 (1H, s). ^{13}C NMR δ 34.5, 40.6, 112.9, 119.2, 139.9, 148.6, 155.3, 160.7.

5-Chloro-*N,N*-dimethyl-*N*-pyridylformamide (3c). Following the previous procedure, 2-amino-5-chloropyridine (1.28 g, 10 mmol) and an excess of *N,N*-dimethylformamide dimethyl acetal (9 mL) gave the title formamide as brown crystals mp 68–70 °C (lit¹⁴ mp 68–69 °C) in 88% yield. ^1H NMR (CDCl_3) δ 2.95 (3H, s), 2.97 (3H, s), 6.75 (1H, d, $J = 8.7$ Hz), 7.36 (1H, dd, $J = 8.7$ Hz, $J = 2.7$ Hz), 8.05 (1H, d, $J = 2.7$ Hz), 8.25 (1H, s). RMN ^{13}C 34.3, 40.5, 118.4, 124.6, 137.1, 146.2, 155.2, 160.3.

***N,N*-Dimethyl-*N*-pyrimidylformamide (3d).** Following the previous procedure, 2-amino-pyrimidine (0.95 g, 10 mmol) and an excess of *N,N*-dimethylformamide dimethyl acetal (9 mL) gave the title formamide as yellow crystals, mp 103–105 °C in 80% yield. ^1H NMR 3.08 (s, 3H), 3.11 (s, 3H), 6.76 (t, 1H, $J = 8.0$ Hz), 8.43 (d, 2H, $J = 8.0$ Hz), 8.58 (s, 1H). ^{13}C NMR 34.9, 40.9, 114.7, 157.9, 158.1 (2 C), 166.6. Anal Calcd for $\text{C}_7\text{H}_{10}\text{N}_4$: C, 56.0; H, 6.66; N, 37.33. Found: C, 56.39; H, 6.72; N, 37.76.

5-Bromo-*N,N*-dimethyl-*N*-pyrimidylformamide (3e). Following the previous procedure, 2-amino-5-bromopyrimidine (1.74 g, 10 mmol) and an excess of *N,N*-dimethylformamide dimethyl acetal (9 mL) gave the title formamide as dark yellow crystals, mp 153–154 °C in 75% yield. ^1H NMR 3.10 (s, 3H), 3.12 (s, 3H), 8.44 (s, 2H), 8.57 (s, 1H). ^{13}C NMR 35.0, 41.1, 111.9, 158.2, 158.4 (2 C), 165. Anal Calcd for $\text{C}_7\text{H}_{10}\text{N}_4\text{Br}$: C, 36.68; H, 3.93; N, 24.45; Br, 34.93. Found: C, 36.71; H, 3.78; N, 24.64.

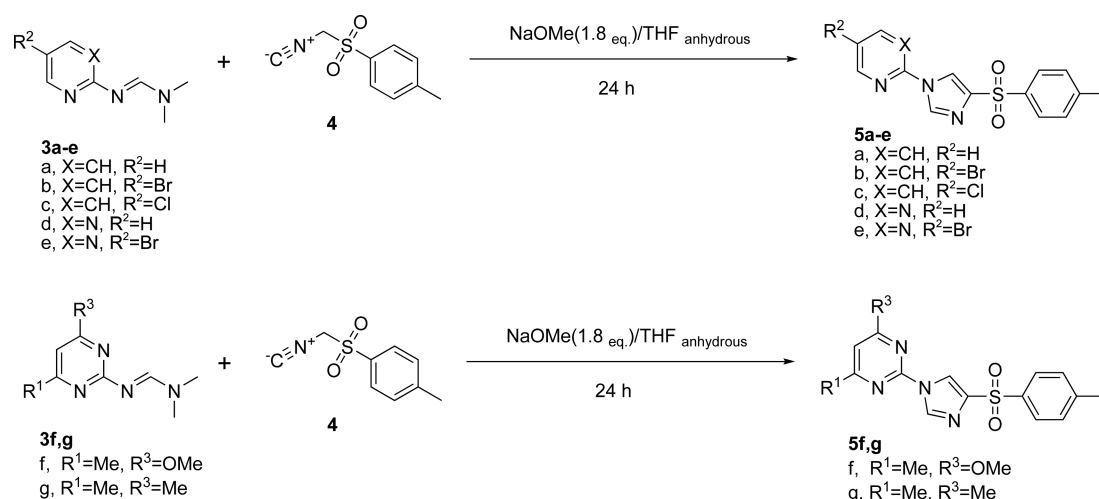
4-Methoxy-6-methyl-*N,N*-dimethyl-*N*-pyrimidylformamide (3f). Following the previous procedure, 2-amino-4-methoxy-6-methylpyrimidine (1.39 g, 10 mmol) and an excess of *N,N*-dimethylformamide dimethyl acetal (9 mL) gave the title formamide as yellow crystals, mp 117–119 °C in 82% yield. ^1H NMR 2.38 (s, 3H), 3.11 (s, 3H), 3.14 (s, 3H), 3.95 (s, 3H), 6.28 (s, 1H), 8.61 (s, 1H). ^{13}C NMR 23.5, 35.0, 41, 53.8, 102.3, 158.3, 163.2, 168.7, 170.7. Anal Calcd for $\text{C}_9\text{H}_{10}\text{N}_4\text{O}$: C, 55.67; H, 7.21; N, 28.86. Found: C, 55.49; H, 7.45; N, 29.01.

4,6-Dimethyl-*N,N*-dimethyl-*N*-pyrimidylformamide (3g). Following the previous procedure, 2-amino-4,6-dimethylpyrimidine (1.23 g, 10 mmol) and an excess of *N,N*-dimethylformamide dimethyl acetal (9 mL) gave the title formamide as yellow crystals in 90% yield, mp 138–139 °C. ^1H NMR 2.33 (s, 6H), 3.07 (s, 3H), 3.09 (s, 3H), 6.56 (s, 1H), 8.55 (s, 1H). ^{13}C NMR 23.3 (2C), 34.3, 40.3, 113.2, 157.3, 165.8 (2 C), 167.9. Anal Calcd for $\text{C}_9\text{H}_{14}\text{N}_4$: C, 60.67; H, 7.86; N, 31.46. Found: C, 60.28; H, 8.09; N, 31.64.

2-Ethoxy Pyrimidine (7). Sodium (0.10 g, 4.6 mmol) was placed in a 25 mL two neck-round bottom flask adapted with a condenser and under nitrogen atmosphere. Then, the flask was immersed in an ice bath, absolute ethyl alcohol (10 mL) was carefully poured from the top of condenser, and the

mixture stirred until all sodium was dissolved. 2-pyrimidyl formamidine (0.1 g, 0.33 mmol) was added and the mixture heated at 70 °C for 6 h. Solvent was removed, by evaporation under reduced pressure. Then water (10 mL) was added and the extraction was carried out with CHCl_3 (3×10

mL). Organic extracts were combined and dried (anhydrous Na_2SO_4), the solvent was removed under reduced pressure to yield 2-ethoxypyrimidine as a colorless oil in 20% yield, ^1H NMR. CDCl_3 δ 1.42 (t, $J=7.1$ Hz, 3H), 4.40 (q, $J=7.1$ Hz, 2H), 6.91 (t, $J=4.9$ Hz, 1H), 8.50 (d, $J=4.9$ Hz, 2H).



Scheme 2. The synthesis of 2-(4-tosylimidazo-1-yl)pyrimidines and pyridines.
