

Rapid, easy cyanation of aryl bromides and chlorides using nickel salts in conjunction with microwave promotion

Riina K. Arvela and Nicholas E. Leadbeater*

*Department of Chemistry, King's College London, Strand, London, WC2R 2LS
United Kingdom*

nicholas.leadbeater@kcl.ac.uk

SUPPLEMENTARY INFORMATION

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Experimental Section

General: Microwave experiments were conducted using a CEM Discover Synthesis Unit (CEM Corp., Matthews, NC).¹ The machine consists of a continuous focused microwave power delivery system with operator selectable power output from 0-300 W. Reactions were performed in glass vessels (capacity 10 mL) sealed with a septum. The pressure is controlled by a load cell connected to the vessel *via* a 14-gauge needle which penetrates just below the septum surface. The temperature of the contents of the vessel was monitored using a calibrated infrared temperature control mounted under the reaction vessel. All experiments were performed using a stirring option whereby the contents of the vessel are stirred by means of a rotating magnetic plate located below the floor of the microwave cavity and a Teflon-coated magnetic stir bar in the vessel. All chemicals were reagent grade and used as purchased. The ¹H and ¹³C-NMR spectra were recorded at 250 MHz and 293 K and referenced to TMS.

General procedure for cyanation of aryl bromides using nickel cyanide and microwave heating: In a 10 mL glass tube was placed aryl bromide (1.0 mmol), Ni(CN)₂•4H₂O (110 mg, 0.6 mmol), 1.0 mL NMP and a magnetic stir bar. The vessel was sealed with a septum and placed into the microwave cavity. Microwave irradiation of 120 W was used, the temperature being ramped from r.t. to 200 °C. Once this temperature was reached, the reaction mixture was held at this temperature for 10 min. After allowing the mixture to cool to room temperature, the reaction vessel was opened and the contents poured into a separating funnel and the tube washed with water and then with ether, these washings being added to the separating funnel. Further water and diethyl ether (20 mL of each) were added and the organic material extracted and removed. After further extraction of the aqueous layer with ether, the organic layers were combined and washed 3 times with water (40 mL) to remove remaining traces of NMP. The organic washings were then dried over MgSO₄ and the ether removed in-vacuo leaving the crude product. Products were characterized by comparison of ¹H- and ¹³C-NMR spectra with those of authentic samples or in the literature² and yields determined by NMR with reference to a known quantity of an internal standard.

General procedure for cyanation of aryl bromides using sodium cyanide and nickel bromide and microwave heating: In a 10 mL glass tube was placed aryl bromide (1.0 mmol), NaCN (98 mg, 2 mmol), NiBr₂ (219 mg, 1 mmol) 1.0 mL NMP and a magnetic stir bar. The reactions were run and purified using the same protocols as for the case of those using Ni(CN)₂.

General procedure for cyanation of aryl bromides using sodium cyanide and nickel bromide and conventional heating: The reaction protocol was as in the case of the microwave methodology except that the tube containing the reagents, after sealing, was placed into a pre-heated oil bath at 170 °C. It was held there and stirred for the allotted time before being removed from the oil and allowed to cool. The work-up procedure was as with the microwave methodology.

General procedure for cyanation of aryl chlorides: In a 10 mL glass tube was placed aryl chloride (1.0 mmol), NaCN (98 mg, 2 mmol), NiBr₂ (219 mg, 1 mmol), 1.0 mL NMP and a magnetic stir bar. The reactions were run and purified using the same protocols as for the case of those using aryl bromides.

4-Methylbenzonitrile:² ¹H NMR (CDCl₃): δ 7.44 (d, 2H, J = 8.1 Hz), 7.18 (d, 2H, J = 8.1 Hz), 2.33 (s, 3H); ¹³C NMR (CDCl₃): δ 142.7, 131.0, 128.8, 118.1, 108.2, 20.8.

Benzonitrile:³ ¹H NMR (CDCl₃): δ 7.54 – 7.58 (m, 2H), 7.50 – 7.53 (m, 1H), 7.37 – 7.41 (m, 2H); ¹³C NMR (CDCl₃): δ 133.2, 132.5, 129.5, 119.2, 112.8.

2,6-Dimethylbenzonitrile:⁴ ¹H NMR (CDCl₃): δ 7.25 (t, 1H, J = 7.7 Hz), 7.03 (d, 2H, J = 7.7 Hz), 2.43 (s, 6H); ¹³C NMR (CDCl₃): δ 142.5, 132.5, 127.7, 117.6, 113.7, 21.1.

4-Acetylbenzonitrile:⁵ ¹H NMR (CDCl₃): δ 7.97 (d, 2H, J = 8.4 Hz), 7.70 (d, 2H, J = 8.4 Hz), 2.57 (s, 3H); ¹³C NMR (CDCl₃): δ 196.9, 140.3, 132.9, 129.1, 118.3, 116.7, 27.1.

4-Methoxybenzonitrile:⁶ ¹H NMR (CDCl₃): δ 7.50 (d, 2H, J = 8.9 Hz), 6.87 (d, 2H, J = 8.9 Hz), 3.77 (s, 3H); ¹³C NMR (CDCl₃): δ 163.3, 134.3, 119.6, 115.2, 104.1, 56.0.

2-Methoxybenzonitrile:⁷ ¹H NMR (CDCl₃): δ 7.42 – 7.47 (m, 2H), 6.88 – 6.94 (m, 2H), 3.83 (s, 3H); ¹³C NMR (CDCl₃): δ 160.2, 133.5, 132.7, 119.8, 115.5, 110.4, 100.6, 55.0.

4-Aminobenzonitrile:⁸ ¹H NMR (CDCl₃): δ 7.31 (d, 2H, J = 8.7), 6.56 (d, 2H, J = 8.7), 4.2 (br s, 1H); ¹³C NMR (CDCl₃): δ 151.2, 134.2, 120.8, 114.8, 100.0.

4-Formylbenzonitrile:⁹ ¹H NMR (CDCl₃): δ 10.02 (s, 1H), 7.93 (d, 2H, J = 8.3), 7.78 (d, 2H, J = 8.3); ¹³C NMR (CDCl₃): δ 191.1, 139.1, 133.3, 130.3, 118.1, 117.9.

4-Cyanobenzoic acid:¹⁰ ¹H NMR (d₆-DMSO): δ 13.5 (br s, 1H), 8.07 (d, 2H, J = 8.4 Hz), 7.93 (d, 2H, J = 8.4 Hz); ¹³C NMR (d₆-DMSO): δ 166.6, 135.1, 133.0, 130.3, 118.6, 115.3.

4-Nitrobenzonitrile:¹¹ ¹H NMR (CDCl₃): δ 8.28 (d, 2H, J = 8.9 Hz), 7.82 (d, 2H, J = 8.9 Hz); ¹³C NMR (CDCl₃): δ 150.4, 133.9, 124.7, 118.7, 117.3.

Pyridine-2-carbonitrile:¹² ¹H NMR (CDCl₃): δ 8.66 (d, 1H, J = 4.9 Hz), 7.79 (t, 1H, J = 7.8 Hz), 7.64 (d, 1H, J = 7.8 Hz), 7.45 – 7.49 (m, 1H); ¹³C NMR (CDCl₃): δ 151.5, 137.4, 134.4, 128.9, 127.3, 117.6.

Thiophene-2-carbonitrile:¹³ ¹H NMR (CDCl₃): δ 7.53 – 7.56 (m, 2H), 7.05 (dd, 1H, J = 5.0, 3.7 Hz); ¹³C NMR (CDCl₃): δ 136.4, 131.6, 126.6, 113.2, 108.8.

4-Hydroxybenzonitrile:¹⁴ ¹H NMR (d₆-DMSO): δ 10.6 (br s, 1H), 7.61 (d, 2H, J = 8.8 Hz), 6.90 (d, 2H, J = 8.8 Hz); ¹³C NMR (d₆-DMSO): δ 161.9, 134.5, 119.8, 116.7, 101.3.

References

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