Transition-Metal Free Sonogashira-Type Couplings

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SUPPLEMENTARY INFORMATION

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 ^{1}H and ^{13}C-NMR spectra were recorded at 250 MHz and 293 K and referenced to TMS.

General procedure for transition-metal free Sonogashira-type couplings using microwave heating:[§] In a 10 mL glass tube was placed aryl halide (1.0 mmol), phenylacetylene (122 mg, 0.13 mL, 1.2 mmol), NaOH (80 mg, 2.0 mmol), polyethylene glycol (1 mL), water (1 mL) and a magnetic stir bar. The vessel was sealed with a septum and placed into the microwave cavity. Microwave irradiation of 300 W was used, the temperature being ramped from r.t. to 170 ºC, this taking 30-40 s. Once 170 ºC was reached, the reaction mixture was held at this temperature for 5 min. After allowing the mixture to cool to room temperature, the reaction vessel was opened and the contents poured into a separating funnel, the tube washed with water (2 mL) and diethyl ether (50 mL) and these washings added to separating funnel. The organic material extracted and removed and the aqueous layer washed with further aliquots of ether (50 mL). The organics were then combined, dried over $MgSO_4$ and the ether removed in-vacuuo leaving the crude product. The product was purified and isolated by flash chromatography and its

[§]) **CAUTION**: The water is heated well above its boiling point so all necessary precautions should be taken when performing such experiments. Vessels designed to withhold elevated pressures must be used. The microwave apparatus used here incorporates a protective metal cage around the microwave vessel in case of explosion. After completion of an experiment, the vessel must be allowed to cool to a temperature below the boiling point of the solvent before removal from the microwave cavity and opening to the atmosphere.

identity confirmed by comparison of ^{1}H-and ^{13}C-NMR spectra with those reported in the literature or authentic samples from our laboratories.

Procedure for transition-metal free Sonogashira-type couplings using 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 ºC. 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.

4-(phenylethynyl)acetophenone:[a] ^{1}H NMR ($CDCl_3$): δ 2.45 (s, 3H), 7.23 (m, 3H), 7.42 (m, 2H), 7.47 (d, J = 8.4 Hz, 2H), 7.79 (d, J = 8.4 Hz, 2H); ^{13}C NMR ($CDCl_3$): δ 27.0, 89.1, 93.2, 123.0, 128.6, 128.9, 129.2, 132.1, 132.2, 136.5, 197.6.

4-(phenylethynyl)toluene:[b] ^{1}H NMR ($CDCl_3$): δ 2.22 (s, 3H), 7.01 (d, J =7.8 Hz, 2H), 7.19 (m, 3H), 7.31 (d, J = 8.1 Hz, 2H), 7.40 (dd, J = 7.8 Hz, 1.7 Hz, 2H); ^{13}C NMR ($CDCl_3$): δ 21.9, 89.2, 90.1, 120.5, 124.0, 128.5, 128.8, 129.6, 131.9, 132.1, 138.8.

4-(phenylethynyl)anisole:[c] ^{1}H NMR ($CDCl_3$): δ 3.66 (s, 3H), 6.73 (d, J = 8.7 Hz, 2H), 7.19 (m, 3H), 7.36 (d, J = 8.7 Hz, 2H), 7.40 (dd, J =7.8, 1.8 Hz, 2H); ^{13}C NMR ($CDCl_3$): δ 55.7, 88.5, 89.9, 114.4, 115.8, 124.1, 128.4, 128.8, 131.9, 133.5, 160.1.

Diphenylacetylene:[d] ^{1}H NMR ($CDCl_3$): δ 7.46 (m, 4H), 7.20 (m, 6H); ^{13}C NMR ($CDCl_3$): δ 131.5, 128.3, 128.1, 123.3, 89.4.

Di-*p*-tolylacetylene:[e] ^{1}H NMR ($CDCl_3$): δ 7.37 (d, 4H, *J* = 7.8), 7.11 (d, 4H, *J* = 7.8), 2.37 (s, 6H); ^{13}C NMR ($CDCl_3$): δ 138.15, 132.40, 130.39, 120.34, 88.90, 20.53.

¶ **CAUTION**: A blast shield should be in place and vessels designed to withhold elevated pressures must be used. After completion of an experiment, the vessel must be allowed to cool before opening to the atmosphere.

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c) (a) Arcadi, A.; Cacchi, S.; Fabrizi, G.; Marinelli, F.; Pace, P. *Eur. J. Org. Chem.* **1999**, 3305. (b) Mouries, V.; Waschbuesch, R.; Carran, J.; Savignac, P. *Synthesis* **1998**, 271.

d) Compared with that of an authentic sample in the laboratory from Aldrich.

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Sample Identification	Assay No.	Element	Results	Units
BT 181	89574	Pd	<1	ppm
		Cu	<1	ppm

Analyst Michael Lane