Supplementary Material (ESI) for Green Chemistry

Recyclable Copper-Catalyst in Aqueous Media: *O*- and *N*-Arylation Reactions towards the Benzofuroindole Framework.

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Electronic Supplementary Information

General Remarks. All reagents and solvents were purchased and used without further purification. Redistilled water was employed for the copper-catalysed reactions. TLC was carried out on SiO_2 (silica gel 60 F_{254}, Merck), and the spots were located with UV light. Flash chromatography was carried out on SiO_2 (silica gel 60, Merck, 230-400 mesh ASTM). Drying of organic extracts after work-up of reactions was performed over anhydrous Na_2SO_4. ^1H and ^{13}C spectra were recorded in $CDCl_3$ solution in a Bruker AC-300 and chemical shifts are reported in ppm downfield (δ) from Me_4Si. Low and high resolution mass spectra were performed by the Mass Spectroscopy Section of the University of the Basque Country (UPV/EHU). IR spectra were recorded on a Perkin-Elmer 1600-FT infrared spectrophotometer and melting points were determined in a capillary tube and are uncorrected. All the reactions were carried out under argon.

Experimental procedures for compounds 5, 2 and 1.

2-[2'-*N*-(4-Methylbenzenesulfonamido)phenyl]benzo[*b*]furan 5. A schlenk tube was charged with compound **3** (1.82 g, 4.10 mmol), prepared following the procedure described in the literature,[1] CuI (66.6 mg, 0.34 mmol), TMEDA (2.2 ml, 14.35 mmol) and water (50 ml). Then, the tube was sealed under a positive pressure of argon and the so-obtained solution was heated overnight at 120°C. The product was extracted from the aqueous layer with dichloromethane, dried and concentrated *in vacuo*. The product was then isolated from the crude mixture by crystallisation from methanol to afford benzofuran **5** (1.24 g, 83%) as a white solid, mp 126-127 °C (from MeOH); υ_{max} (film)/cm^{-1} 3331, 1161, 1085; δ_H(300 MHz, $CDCl_3$, Me_4Si) 2.23 (3H, s, CH_3), 6.60 (1H, s, H_{arom}), 6.87 (2H, d, *J* 8.10, H_{arom}), 7.22 (1H, dt, *J* 0.90, 7.67, H_{arom}), 7.28 (1H, dd, *J* 7.42, 7.99, H_{arom}), 7.34-7.39 (4H, m, H_{arom}), 7.49 (1H, dd, *J* 1.43, 7.78, H_{arom}), 7.53 (2H, d, *J* 8.69, H_{arom}), 7.70 (1H, d, *J* 8.14, H_{arom}), 7.96 (1H, s, NH); δ_C(75 MHz, $CDCl_3$, Me_4Si) 21.3, 104.7, 111.2, 120.8, 123.0, 123.5, 124.9, 125.2, 125.9, 126.7, 128.0, 128.5,

[1] M. Carril, R. SanMartin, I. Tellitu, E. Domínguez, *Org. Lett*. 2005, **7**, 4787-4789.

129.3, 129.9, 133.7, 135.6, 143.5, 153.7, 154.4; *m/z* (EI) (Found: 363.0929. $C_{21}H_{17}NO_3S$ requires: 363.0929) 363 (M, 15), 208 (100), 180 (64), 152 (31), 91 (36).

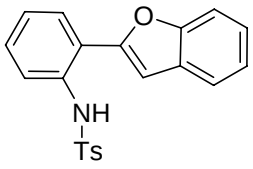
3-Bromo-2-[2'-*N*-(4-methylbenzenesulfonamido)phenyl]benzo[*b*]furan 2. *N*-Bromosuccinimide (259.1 mg, 1.38 mmol) was added in three portions (waiting 1.5 h between each addition) to a solution of benzofuran **5** (457.4 mg, 1.26 mmol) in a mixture of THF (10 ml) and acetonitrile (10 ml) at 0°C. After one hour since the last addition of NBS, water was added and the aqueous layer was extracted with ether. The combined organic phases were dried and concentrated in vacuo and the crude mixture was then purified by flash chromatography (50% hexane/ether) to afford compound **2** (396.5 mg, 71%) as a white solid, mp 138-140°C (from ether); υ_{max} (film)/cm^{-1} 3284, 1161, 1085; δ_H(300 MHz, $CDCl_3$, Me_4Si) 2.22 (3H, s, CH_3), 6.72 (2H, d, *J* 8.03, H_{arom}), 7.15 (2H, d, *J* 8.16, H_{arom}), 7.32 (1H, t, *J* 7.61, H_{arom}), 7.37 (1H, t, *J* 7.41, H_{arom}), 7.43 (1H, t, *J* 7.65, H_{arom}), 7.46-7.51 (3H, m, H_{arom}), 7.59 (1H, s, NH), 7.67 (1H, d, *J* 7.70, H_{arom}), 7.75 (1H, d, *J* 8.11, H_{arom}); δ_C(75 MHz, $CDCl_3$, Me_4Si) 21.4, 96.7, 111.3, 119.7, 122.7, 123.9, 126.2, 126.3, 127.5, 128.2, 129.3, 130.4, 130.7, 134.3, 135.4, 143.5, 148.6, 152.9; *m/z* (EI) (Found: 441.0019. $C_{21}H_{16}NO_3BrS$ requires: 441.0034) 443 (M+2, 7), 441 (M, 7), 207 (100), 179 (16), 152 (15), 91 (32).

10-Tosyl-10*H*-benzo[4,5]furo[3,2-*b*]indole 1. A schlenk tube was charged with compound **2** (75.6 mg, 0.17 mmol), CuI (2.7 mg, 0.014 mmol), DMEDA (78 µl, 0.60 mmol) and water (2.4 ml). Then, the tube was sealed under a positive pressure of argon and the so-obtained solution was heated overnight at 120°C. The product was extracted from the aqueous layer with dichloromethane, dried and concentrated *in vacuo*. The crude mixture was then purified by flash chromatography (50% hexane/dichloromethane) to afford compound **1** (52.5 mg, 85%) as a white solid, mp 172-174°C (from hexane); υ_{max} (film)/cm^{-1} 1590, 1173; δ_H(300 MHz, $CDCl_3$, Me_4Si) 2.24 (3H, s, CH_3), 7.07 (2H, d, *J* 7.99, H_{arom}), 7.32-7.50 (4H, m, H_{arom}), 7.60-7.70 (4H, m, H_{arom}), 8.29 (1H, d, *J* 8.08, H_{arom}), 8.41 (1H, dd, *J* 1.19, 7.43, H_{arom}); δ_C(75 MHz, $CDCl_3$, Me_4Si) 21.5, 112.6, 115.8, 117.5, 118.4, 119.1, 120.6, 123.9, 124.4, 124.9, 125.4, 126.8, 129.7, 129.8, 134.1, 139.4, 144.9, 146.6, 159.2; *m/z* (EI) (Found: 361.0766. $C_{21}H_{15}NO_3S$ requires: 361.0773) 361 (M, 12), 206, (100), 177 (15), 151 (39), 91 (11).

Recycling of the aqueous solution. The procedure described for the synthesis of benzofuran **5** was followed starting from **3** (49.3 mg, 0.111 mmol). After normal work-up the aqueous layer was kept in a schlenk tube under argon. Then, benzofuran **2** (49.2 mg, 0.111 mmol) and TMEDA (0.05 ml, 0.33 mmol) were added and the so-obtained solution was stirred at 120°C overnight. Purification of the crude mixture was accomplished following the procedure described for the synthesis of compound **1**, rendering benzofuroindole **1** in 85% (34 mg).

Exploration of other synthetic alternatives. 2-(2'-Aminophenyl)benzo[*b*]furan and 2-[2'-*N*-(phenylamino)phenyl]benzo[*b*]furan were prepared by the same procedure employed for the synthesis of benzofuran **5**. Bromination of the former derivatives provided complex mixtures where non-regioselective bromination (bromination at the aryl rings, polybrominated compounds) was observed along with small proportions (<10%) of target 3-bromoderivatives.

On the other hand, in order to study the intramolecular *N*-arylation of a free amine moiety, several experiments were carried out to desulfonylate bromoderivative **2**. Only starting **2** was obtained, and when harsher reaction conditions (higher temperatures and longer reaction times) were employed, decomposition of the latter substrate was observed without detecting the target amino derivative.



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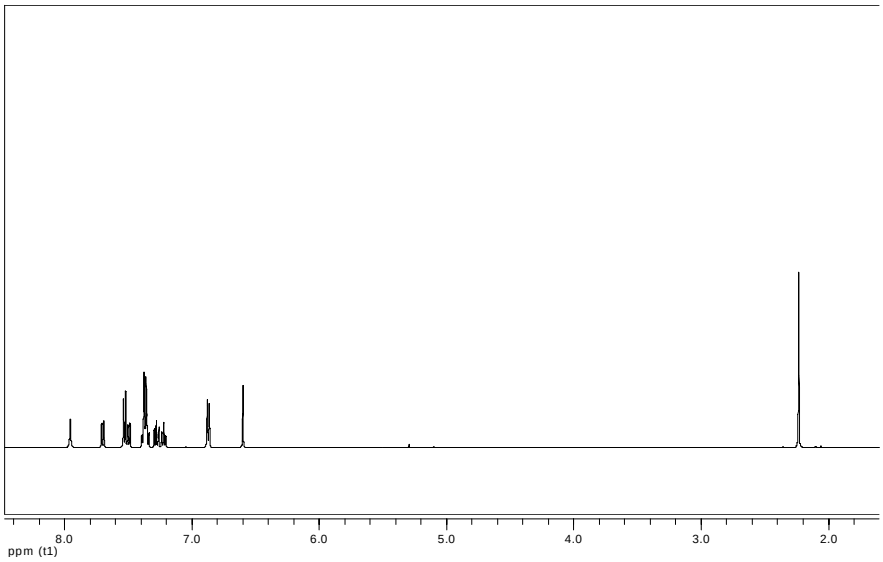

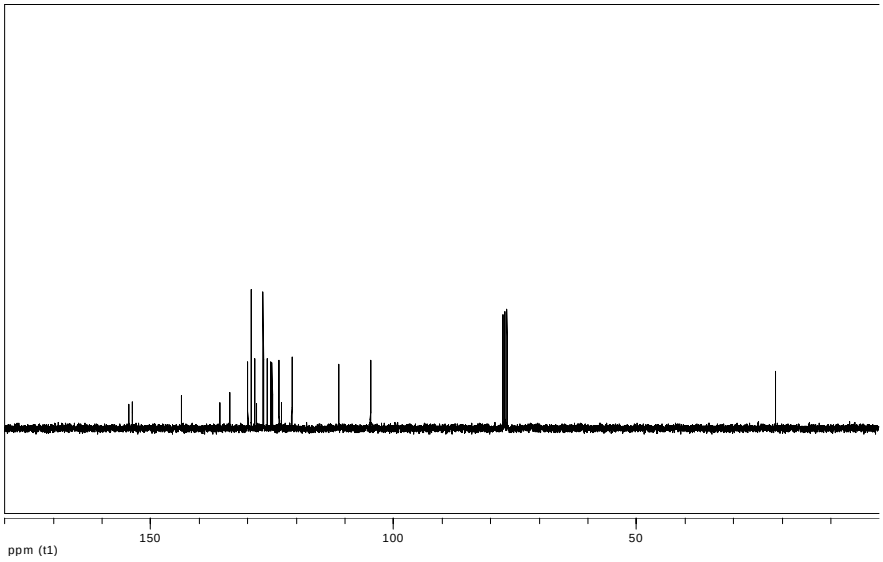

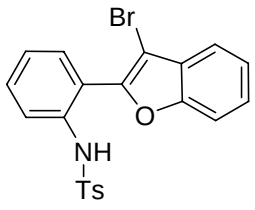

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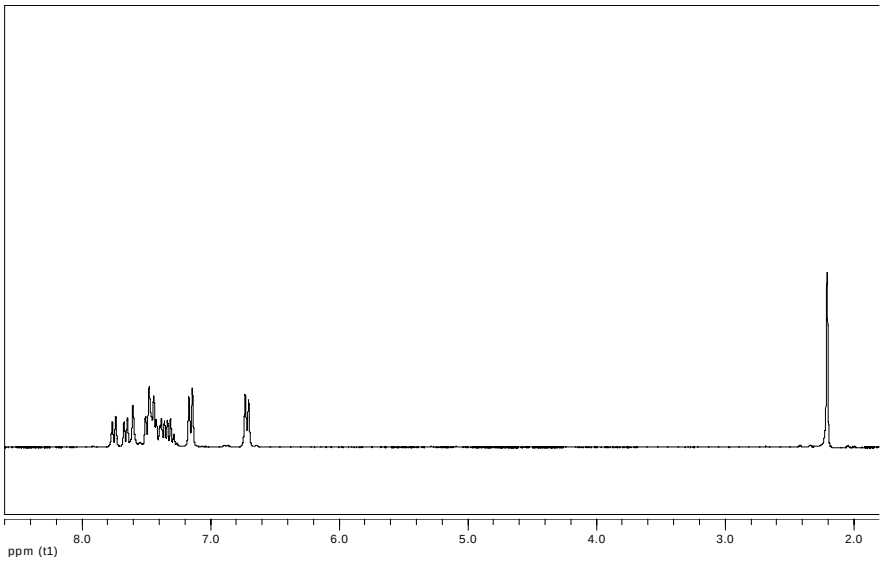

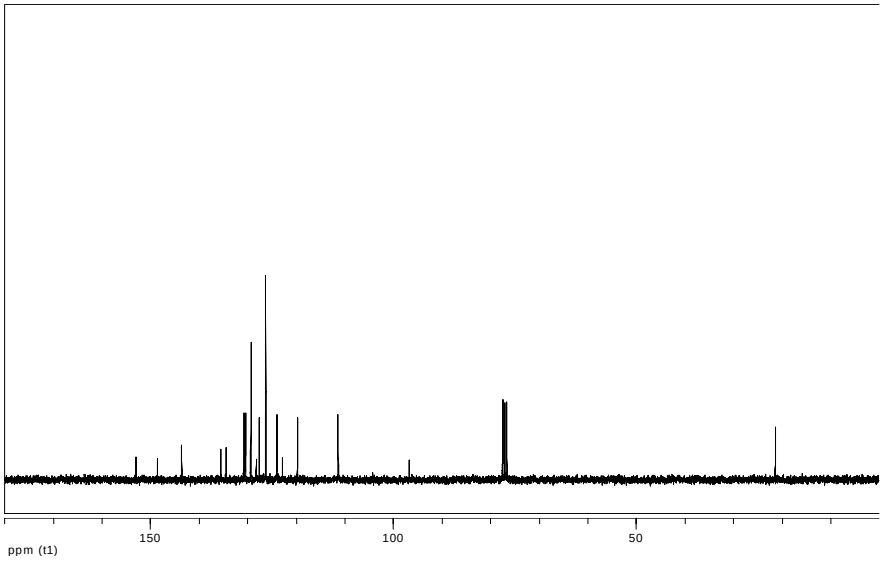

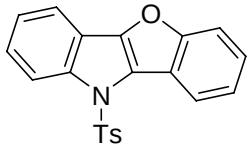

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