Iron Containing Ionic Liquids as Recyclable Catalysts for Aryl Grignard Cross-Coupling of Alkyl Halides

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General. All reaction were performed under air except the cross coupling of phenyl lithium which was done under an atmosphere of dry nitrogen. Diethyl ether was stored over KOH and distilled prior to use. Butylmethylimidazolium chloride (bmim-Cl) was synthesized and recrystallized as reported in literature.ⁱ $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$ and all commercially available alkyl halides were used as received from the supplier, 2-bromooctane was prepared from 2-octanol according to literature.ⁱⁱ 4-Fluorophenylmagnesium bromide and phenyl lithium were purchased from Aldrich as a 2.0 M solution in diethyl ether and as a 1.8 M solution in cyclohexane, resp. p-Tolylmagnesium bromide and (4-phenyl)-phenylmagnesium bromide were prepared from the corresponding bromides following standard procedures and titrated prior to use.ⁱⁱⁱ Flash column chromatography was carried out with silica gel Merck 60.

^1H and ^{13}C NMR spectra were recorded on a Bruker AC 200 in CDCl_3 at 200 and 50 MHz, resp., using the solvent peak as reference. Elemental analysis was carried out at Vienna University, Department of Physicochemistry – Laboratory for Microanalysis, Währinger Str. 42, A-1090 Vienna.

GC–MS analyses were conducted on a VOYAGER Quadrupol (Thermo Finnigan) directly interfaced to a GC 8000 TOP gas chromatograph using a BGB-5 (30m $\times$ 0.32mm i.d., 1.0 μm film thickness) cross-bonded dimethyl polysiloxane capillary column. The electron energy was set to 70 eV and the ion source temperature to 200 °C. The oven program temperature was 80 °C (2 min)//10 °C/min//280 °C (3 min). Source and transfer line temperatures were set at 200 and 280 °C, respectively.

Preparation of butylmethylimidazolium-tetrachloroferrate (bmim- FeCl_4):

Butylmethylimidazolium chloride (5.00g, 28.6 mmol) and $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$ (7.74 g, 28.6 mmol) were mixed in a round bottom flask and stirred for 5 minutes. Almost immediately an endothermic reaction took place and provided bmim- FeCl_4 as a lower layer. The upper aqueous layer was carefully removed and the remaining ionic liquid was dried under stirring for 2d at 80°C and 0.1 mmHg to yield 8.96 g (93 %) of bmim- FeCl_4 as dark brown oil.

The ionic liquid was characterised via Raman spectroscopy and proved to be identical with authentic material reported in literature.^{iv}

Figure 1: Raman-spectra of bmim-FeCl₄

Representing procedure for the bmim-FeCl₄ catalyzed cross coupling - Preparation of 1-fluoro-4-dodecylbenzene 3:

Bmim-FeCl₄ (0.1 mmol), dodecylbromide **1** (500mg, 2.00 mmol) and an exact amount of hexadecane (~0.2 mmol) as internal standard were mixed in a round bottom flask and diluted with 0.5 ml of diethyl ether. A 2M solution of 4-fluorophenylmagnesium bromide **2** in diethyl ether (1.5 ml, 3.00 mmol) was added dropwise under stirring at 0°C. Immediately a colour change to black could be observed. Stirring was continued for 10 minutes at room temperature and the reaction mixture was hydrolyzed carefully with diluted hydrochloric acid. The aqueous layer was extracted with diethyl ether, the combined organic layers were dried over MgSO₄ and the solvent was removed at 40°C/900mbar. GC-MS analysis was done directly from the reaction as well as from the crude product and proved to be identical.

Purification of the crude mixture by flash column chromatography using 100 g silica and light petrol as eluent gave 1-fluoro-4-dodecylbenzene **3** as colourless liquid in 86 % yield.

R_f = 0.8 (light petrol); ¹H-NMR (CDCl₃, 200 MHz) δ(ppm) = 7.14 (dd, J_{HH} = 8.51 Hz, ⁴J_{HF} = 5.58 Hz, 2H, H-2), 6.97 (dd, J_{HH} = 8.70 Hz, ³J_{HF} = 8.70 Hz, 2H, H-3), 2.59 (t, J = 7.73 Hz,

2H, -CH₂Ph), 1.61 (quin, J = 7.14 Hz, 2H, -CH₂CH₂Ph) 1.29 (m, 18H, -CH₂-), 0.91 (t, J = 6.75 Hz, 3 H, CH₃-). ¹³C-NMR (CDCl₃, 50 MHz) δ (ppm) = 161.13(s, ¹J_{CF} = 243.0 Hz, C-4), 138.46 (s, ⁴J_{CF} = 3.18 Hz, C-1), 129.61 (d, ³J_{CF} = 7.7 Hz, C-2), 114.87 (d, ²J_{CF} = 21.2 Hz, C-3), 35.14 (t, -CH₂Ph), 31.95 (t), 31.65 (t), 31.63 (t), 29.7 (m), 29.6 (t), 29.5 (t), 29.4 (t), 29.2 (t), 22.7 (t, -CH₂CH₃), 14.11 (q, -CH₃). Anal. Calcd. for C₁₈H₂₉F: C, 81.76; H, 11.05. Found: C, 81.59; H, 11.32. GC/ EI-MS: R_t = 18.0 min; m/z = 264.3 (M⁺, 14), 122.1 (4), 110.2 (33), 119.1 (100), 96.1(2), 83.1 (4), 71.2 (4), 55.2 (4).

Figure 2: GC-MS-spectra of crude reaction mixture

R _t = 9.15 min:	1-dodecene
R _t = 9.27 min:	dodecane
R _t = 12.04 min:	4,4'-fluorobiphenyl
R _t = 14.71 min:	n-hexadecane (internal standard)
R _t = 18.05 min:	4-fluorophenyldodecane

Figure 3: GC-spectra of purified product 3

Figure 4: NMR-spectra of pure product **3**

All other cross coupling products are already known to literature. After purification via flash column chromatography ¹H-NMR and ¹³C-NMR spectra of all products **4** (CAS: 104-41-6), **5** (2474-41-1), **6** (92298-94-7), **7** (738614-96-5), **8**(90734-22-8), **9** (4501-36-4) and **12** (665288-6) correspond to data reported in literature. GC-MS analysis for the volatile products **3**, **6**, **7**, **8**, **9** and **12** proved a purity >98%.

Procedure for the recycling of bmim-FeCl₄ catalyzed cross coupling of Grignard reagents with alkyl halides:

Bmim-FeCl₄ (0.1 mmol), dodecylbromide **1** (500mg, 2.00 mmol) and an exact amount of hexadecane (~0.2 mmol) as internal standard were mixed in a round bottom flask and diluted with 0.5 ml of diethyl ether. A solution of 4-fluorophenylmagnesium bromide **2** in diethyl ether (1.5 ml, 3.00 mmol) was added dropwise under stirring at 0°C. Immediately a colour change to black could be observed. Stirring was continued for 10 minutes at room temperature and the reaction was left to settle down. The upper ethereal layer was carefully decanted and

the remaining bmim-FeCl₄/ MgBr₂-layer was washed twice with 0.5 ml of diethyl ether each. The combined organic layers were concentrated without hydrolysis and subjected directly to flash column chromatography.

Fresh bmim-FeCl₄ (0.1 mmol), dodecylbromide **1** (500mg, 2.00 mmol) and an exact amount of hexadecane (~0.2 mmol) were added again to the orange bmim-FeCl₄/ MgBr₂-slurry and diluted with 0.5 ml of diethyl ether. Subsequent addition of 4-fluorophenylmagnesium bromide (1.5 ml, 3.00 mmol) at 0°C gave a colour change to black again and the reaction procedure was repeated like described above.

ⁱ Dupont, J.; Consort, C.; Suarez, P.; de Souza, R. *Org. Synth.* **2003**, 79, 236.

ⁱⁱ Alnajja, M. S.; Kuivila, H. G. *J. Am. Chem. Soc.* **1985**, 107, 416.

ⁱⁱⁱ Watson, S. C.; Eastham, J. F. *J. Organomet. Chem.* **1967**, 9, 165-168.

^{iv} (a) Hayashi, S.; Hamaguchi, H. *Chem. Lett.* **2004**, 33, 1590. (b) Sitze, M. S.; Schreiter, E. R.; Patterson, E. V.; Freeman, R. G. *Inorg. Chem.* **2001**, 40, 2298.