Supporting Information

An Efficient Base Free *N*-arylation of Imidazoles and Amines with Arylboronic Acids Using Copper Exchanged Fluorapatite

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General Consideration	S2
Preparation of Catalysts.....	S2
Experimental procedures for the <i>N</i> -arylation of imidazole and amines	S4
NMR & Mass Data.....	S5-S34
References	S35

General Considerations

All reactions were carried out in glassware that was flame-dried or oven-dried and cooled. Flash column chromatography was performed with Sd Fine silica gel (60-120 mesh). Thin-layer chromatography was carried out with Merck silica gel 60 F₂₅₄ plates. All products are characterized by ¹H NMR, ¹³C NMR, and EI-MS. ¹H NMR spectra were recorded at room temperature on Bruker, Avance 300, and Gemini 200 MHz instrument with respect to TMS. IR spectra were recorded on Nicolet 210 FT-IR (neat or thin film for liquid products, and KBr pellets for solid products). EI-MS spectra were analyzed by VG-7070H Micromass (3 KeV, Xenon). Compounds described in the literature were characterized by comparing their ¹H NMR to the previously reported data.

Preparation and Characterization of Hydroxyapatite Catalysts ¹:

Hydroxyapatite [HAP, Ca₁₀(PO₄)₆(OH)₂]

Ca(NO₃)₂ · 4H₂O (15.576 g, 0.066 mol) dissolved in water (60 mL) was brought to pH 11-12 with concentrated NH₄OH and thereafter diluted to 120 mL. A solution of (NH₄)₂HPO₄ (5.28 g, 0.04 mol) in 100 mL water was brought to pH 11-12 with concentrated NH₄OH and thereafter diluted to 160 mL. The calcium solution was vigorously stirred at room temperature, and the phosphate solution was added dropwise over a period of 30 min to produce a milky, some what gelatinous precipitate which was then stirred and boiled for 10 min. The precipitate was filtered, washed, dried at 80 °C overnight and calcined at 500 °C for 3 h. All the synthetic steps were carried out using doubly distilled water.

Fluorapatite [FAP, $\text{Ca}_{10}(\text{PO}_4)_6(\text{F})_2$]

FAP was obtained by co-precipitation method. A mixture of $(\text{NH}_4)_2\text{HPO}_4$ (7.92 g, 0.06 mol) and NH_4F (1 g, 0.027 mol) in 250 mL of water, maintained at a pH greater than 12 by addition of NH_4OH (15-20 mL), was introduced into 150 mL of a solution of $\text{Ca}(\text{NO}_3)_2 \cdot 4\text{H}_2\text{O}$ (23.6 g, 0.1 mol) under constant stirring. The suspension was refluxed for 4 h. The FAP crystallites were filtered, washed with water, dried overnight at 80 °C and calcined in air at 500 °C for 30 min. All the synthetic steps were carried out using doubly distilled water. (Ca:P:F = 1:0.66:0.16 calculated by XPS)

Copper exchanged HAP and FAP

HAP and FAP (1 g) were stirred with aqueous $\text{Cu}(\text{OAc})_2$ (0.400 g, 2 mmol) each independently in 25 mL water at 60 °C for a period of 10 h. The obtained slurries were filtered, washed with water and dried over night at 80 °C yielding copper exchanged hydroxyapatite (CuHAP), copper exchanged fluorapatite (CuFAP) and copper exchanged *tert*-butoxyapatite (CuTBAP), respectively as a light blue powder (Cu content by means of ICP-MS: CuHAP-0.66 mmol g^{-1} , CuFAP-0.73 mmol g^{-1} , CuTBAP-0.78 mmol g^{-1}).

A typical procedure for *N*-arylation of imidazole with phenylboronic acids:

In a typical experimental procedure, CuFAP(100 mg) was added to a mixture of imidazole (1.2 mmol), phenylboronic acid (1 mmol) in methanol (3 mL) at room temperature, and the mixture was stirred for 6 h. The progress of the reaction was monitored by TLC and on completion of the reaction, the reaction mixture was filtered and the filtrate was concentrated under reduced pressure to give the crude product. The crude product was purified by column chromatography on silica gel (hexane/ethyl acetate, 70/30) to afford the *N*-phenylimidazole.

A typical procedure for *N*-arylation of phenylboronic acid with amines:

In a typical experimental procedure, CuFAP (100 mg) was added to a mixture of amine (1.5 mmol), phenylboronic acid (1 mmol) in methanol (3 mL) at room temperature and the mixture was stirred for 3h. The progress of the reaction was monitored by TLC and on completion of the reaction, the reaction mixture is filtered and concentrated under reduced pressure to give the crude product. The crude product was purified by column chromatography on silica gel (hexane/ethyl acetate, 20/1) to afford the diphenylamine.

NMR & Mass Data

The known coupling products are well compared with the reported spectral data.¹

1-Phenyl-1H-imidazole (Table 2, entry 1)

¹H NMR (300MHz, CDCl₃): δ 7.83 (s, 1H), 7.50-7.30 (m, 5H), 7.25 (bs, 1H), 7.18 (bs, 1H); A copy of the ¹H NMR spectra is provided

EI-MS: 144 (100%), 117, 77, 51

IR: (thin film/ neat): cm⁻¹: 3424, 3117, 1600, 1509, 1304, 1253, 1110, 1058, 908, 760, 690, 659, 520.

1-(4-Methylphenyl)-1H-imidazole (Table 2, entry 2).

¹H NMR (300MHz, CDCl₃): δ= 7.76 (s, 1H), 7.24 (m, 4H), 7.19 (bs, 1H), 7.13 (bs, 1H), 2.39 (s, 3H). A copy of the ¹H NMR spectra is provided

EI-MS: 158(100%), 131, 104, 91, 50; IR:(thin film /neat):cm⁻¹; 3391, 3115, 2924, 1612, 1522, 1488, 1304, 1249, 1112, 1058, 964, 908, 816, 735, 661, 616, 523.

1-(4-Methoxyphenyl)-1H-imidazole (Table 2, entry 3)

¹H NMR (300MHz, CDCl₃): δ 7.71 (s, 1H), 7.28 (d, 2H, *J*= 9.0Hz), 7.15 (bs, 1H), 7.11 (bs, 1H), 6.94 (d, 2H, *J* = 9.0 Hz), 3.83 (s, 3H). A copy of the ¹H NMR spectra is provided ¹³C NMR (CDCl₃, 75 MHz): δ = 159.0, 135.8, 130, 130.8, 123 (2C), 118.5, 114.6, (2C), 55.2; EI-MS: 174 (100%), 159, 147, 132, 120, 77; IR: (thin film /neat): cm⁻¹; 3415, 2928, 1675, 1520, 1464, 1302, 1250, 1181, 1113, 1059, 1029, 833, 764, 661, 614, 536

1-(3,4-dimethoxyphenyl)-1H-imidazole (Table 2, entry 4)

¹H NMR (300MHz, CDCl₃): δ 7.77 (s, 1H), 7.16 (br s, 1H), 7.13 (br s, 1H), 6.88 (br s, 2H), 6.86 (br s, 1H), 3.94 (s, 6H). A copy of the ¹H NMR spectra is provided

EI-MS: 169(100 %), 142, 129, 115, 102, 75, 51.

1-(3-nitrophenyl)-1H-imidazole (Table 2, entry 5)

¹H NMR (200MHz, DMSO-d₆): δ 8.36 (s, 1H), 8.24-8.02 (m, 2H), 7.91 (d, 1H, *J* = 9.4 Hz), 7.74 (t, *J* = 8.6 1H), 7.52 (br s, 1H), 7.18 (br s, 1 H). A copy of the ¹H NMR spectra is provided

EI-MS: 189(100%), 132, 116, 89, 76, 63, 50.

1-(4-Fluorophenyl)-1H-imidazole (Table 2, entry 6)

¹H NMR (300 MHz (CDCl₃)): δ 7.79 (br s, 1H), 7.33-7.36 (m, 2H), 7.14-7.21 (m, 4H). A copy of the ¹H NMR spectra is provided

¹³C NMR (CDCl₃, 75 MHz): δ = 163.4, 160, 133.5, 130.4, 123.2 (2C), 118.2, 116.5(2C);
EI-MS: 162 (100%), 141, 135, 129, 108, 95, 83, 71, 57.

1-(4-Trifluoromethylphenyl)-1H-imidazole (Table 2, entry 7)

¹H NMR (300 MHz, CDCl₃): δ=7.84 (br s, 1H), 7.69 (d, 2H, *J*= 8.91Hz), 7.46 (d, 2H, *J*= 8.91Hz), 7.23 (br s, 1H), 7.14(br s, 1H). A copy of the ¹H NMR spectra is provided
EI-MS: 212 (100%), 186, 158, 146, 42.

1-phenyl-1H-benzimidazole² (Table 2, entry 8)

¹H NMR (300MHz, CDCl₃): δ=8.09 (s, 1H), 7.81-7.87 (m, 1H), 7.43-7.60 (m, 6H), 7.5-7.3 (m, 2H). A copy of the ¹H NMR spectra is provided
¹³C NMR (CDCl₃, 75 MHz): δ=144, 142.2, 136.5, 133.7, 130, 127.9, 124, 123.5, 122.8 (2C), 120.6, 110.5,(2C); EI MS: 194 (100%), 165, 138, 77, 50.

1-(4-Methylphenyl)-1H-benzimidazole² (Table 2, entry 9)

¹H NMR (300MHz, CDCl₃) δ 8.01 (br s, 1H), 7.78 - 7.84 (m, 1H), 7.39-7.45 (m, 1H), 7.20 –7.31 (m, 6H), 2.42 (s, 3H). A copy of the ¹H NMR spectra is provided
¹³C NMR (CDCl₃, 75 MHz): δ=144, 142, 138, 134 (2C), 130.5, 124, 123.6, 122.8 (2C), 120.3, 110.1(2C), 21; EI-MS: 209 (M⁺+1); 208(M⁺), 192, 179, 151, 91, 65.

1-(4-Methoxyphenyl)-1H-benzimidazole² (Table 2, entry 10)

¹H NMR (300 MHz (CDCl₃)): δ 8.06 (br s, 1H), 7.86-7.88 (m, 1H), 7.45-7.47(m, 1H), 7.41 (d, 2H, J = 9.0Hz), 7.30-7.33 (m, 2H), 7.06 (d, 2H, J=9.0Hz), 3.88(s, 3H); EI-MS: 224(100%), 209, 192, 181, 141, 121, 117, 82, 77, 55, 47.

Diphenylamine³ (Table 3, entry 1)

¹H NMR (300 MHz (CDCl₃)): δ 7.23-7.16 (m, 4H), 7.02-6.97 (m, 4H), 6.89-6.82 (m, 2H), 5.56 (br s, 1H); EI-MS: 168, 96, 81, 67, 54, 45; A copy of the ¹H NMR spectra is provided.

N-Phenyl-4-methylaniline⁴ (Table 3, entry 2)

¹H NMR (200 MHz (CDCl₃)): δ 7.26-7.12 (m, 2H), 7.08-6.76 (m, 7H), 5.52 (br s, 1H), 2.29 (s, 3H); EI-MS: 184 (M⁺, 100), 168, 155, 116, 92, 77; A copy of the ¹H NMR spectra is provided.

***N*-(4-methoxyphenyl)aniline ⁵ (Table 3, entry 3)**

¹H NMR (300 MHz (CDCl₃)): δ 7.20-7.11 (m, 2H), 7.07-6.99 (m, 2H), 6.88-6.73 (m, 5H), 5.39 (br s, 1H), 3.77 (s, 3H); EI-MS: 199, 184(100), 154, 128, 103, 77; A copy of the ¹H NMR spectra is provided.

***N*-(4-chlorophenyl) aniline (Table 3, entry 4)**

¹H NMR (200MHz, CDCl₃) δ 7.24-7.15 (m, 3H), 7.0-6.95(m, 4H), 6.90-6.81 (t, 2H *J*=7.03 Hz), 5.58 (br s, 1H); EI-MS: 203, 140, 134, 96, 84, 76, 51; A copy of the ¹H NMR spectra is provided.

***N*-(4-fluorophenyl) aniline (Table 3, entry 5)**

¹H NMR (200MHz, CDCl₃) δ 7.26-7.15 (m, 3H), 7.05-6.95(m, 4H), 6.90-6.81 (t, 2H *J*=7.03 Hz), 5.58 (br s, 1H); EI-MS: 187, 140, 134, 96, 84, 76, 51; A copy of the ¹H NMR spectra is provided.

***N*-(2-methylphenyl) aniline.⁵ (Table 3, entry 6)**

¹H NMR (200MHz, CDCl₃) δ 7.27-7.16 (m, 4H), 7.12 (dd J = 7.86, 6.88 Hz 1H), 7.0-6.88 (m, 4H), 5.41 (br s, 1H), 2.30 (s, 3H); EI-MS: 183, 167, 149, 106, 83, 71, 51(100). HRMS For C₁₃H₁₄N (M⁺) calcd 184.1126, found 184.1189.

***N*-(4-trifluoromethylphenyl) aniline. (Table 3, entry 7)**

¹H NMR (300MHz, CDCl₃) δ 7.53-6.91 (m, 9H); EI-MS: 237 (100), 167, 155, 141, 106, 84, 66, 57.

***N*-(2-bromophenyl) aniline (Table 3, entry 8)**

¹H NMR (300MHz, CDCl₃) δ 7.48 (dd, 1H J=1.5, 1.8 Hz), 7.31-7.10(m, 6H), 7.0 (t, 1H J=7.3 Hz), 6.69 (dt, 1H J=1.7, 8.1Hz), 6.03 (bs, 1H); EI-MS: 248, 168(100%), 84, 77, 51, 43. HRMS For C₁₂H₁₁BrN (M⁺) calcd 248.0074, found 248.0049 A copy of the ¹H NMR spectra is provided.

***N*-(3-nitrophenyl) aniline.⁶ (Table 3, entry 9)**

¹H NMR (200MHz, CDCl₃) δ 7.82 (s, 1H), 7.67 (d, 1H *J*=7.63Hz), 7.4-7.22 (m, 4H), 7.16-7.0 (m, 3H), 5.9 (br, s 1H); EI-MS: 214(100%), 167, 149, 119, 105, 91, 71, 57, 43; A copy of the ¹H NMR spectra is provided.

***N*-(Butyl) aniline⁶ (Table 4, entry 1).**

¹H NMR (300MHz, CDCl₃) δ 7.10 (t, 1H *J*= 7.55 Hz), 6.61 (t, 1H *J*=7.55 Hz), 6.55-6.48 (m, 2H), 3.10 (t, 3H *J*= 6.79 Hz), 1.67-1.55 (m, 2H), 1.51-1.37 (m, 2H), 0.97 (t, 3H *J*= 7.55 Hz); EI-MS: 149, 119, 106 (100), 77, 51, 43; A copy of the ¹H NMR spectra is provided.

***N*-(Hexyl) aniline (Table 4, entry 2)**

¹H NMR (300MHz, CDCl₃) δ 7.09 (t, 2H *J*=7.55 Hz), 6.61 (t, 1H *J*=7.55), 6.54-6.48 (m, 2H), 3.4 (br s, 1H), 3.07 (t, 2H *J*= 6.78 Hz), 1.60-1.55 (m, 2H), 1.45-1.24 (m, 6H), 0.91 (t, 3H *J*= 6.79) EI-MS: 177,106 (100%),97, 85, 69, 57, 43; A copy of the ¹H NMR spectra is provided.

N- (Heptyl) aniline. (Table 4, entry 3)

^1H NMR (300MHz, CDCl_3) δ 7.09 (t, 2H $J=7.6$ Hz), 6.61 (t, 1H $J=7.6$ Hz), 6.51 (d, 2H $J=8.3$ Hz), 3.4 (br s, 1H), 3.08 (t, 2H $J=7.6$ Hz), 1.68-1.53 (m, 2H), 1.44-1.2 (m, 8H), 0.89 (t, 3H $J=6.04$ Hz). HRMS For $\text{C}_{13}\text{H}_{22}\text{N}$ (M^+) calcd 192.1752, found 192.1765. A copy of the ^1H NMR spectra is provided

N- (Octyl) aniline (Table 4, entry 4)

^1H NMR (300MHz, CDCl_3) δ 7.09 (t, 2H $J=7.6$ Hz), 6.61 (t, 1H $J=7.6$ Hz), 6.51 (d, 2H $J=8.3$ Hz), 3.4 (br s, 1H), 3.08 (t, 2H $J=7.6$ Hz), 1.68-1.53 (m, 2H), 1.44-1.2 (m, 10H), 0.89 (t, 3H $J=6.04$ Hz) EI-MS: 205,106 (100%),93, 77,55. HRMS For $\text{C}_{14}\text{H}_{24}\text{N}$ (M^+) calcd 206.1908, found 206.1959. A copy of the ^1H NMR spectra is provided.

N-(Phenyl) benzylamine⁶ (Table 4, entry 5)?

^1H NMR (300MHz, CDCl_3) δ 7.37-7.16 (m, 5H), 7.27-7.20 (m, 1H), 7.15-7.04 (m, 1H), 6.70-6.60 (m, 1H), 6.55 (d, 2H $J=7.81$ Hz), 4.29 (s, 2H), 3.90 (br s, 1H); EI-MS: 183,135, 91(100%), 77,55.

***N*-Cyclohexylaniline⁶ (Table 4, entry 6)**

¹H NMR (300MHz, CDCl₃) δ 7.07 (t, 2H *J*=8.3 Hz), 6.58 (t, 1H *J*=7.55 Hz), 6.5 (d, 2H *J*=7.5 Hz), 3.28-3.18 (m, 1H), 2.11-2.02 (m, 2H), 1.82-1.71 (m, 2H), 1.70-1.60 (m, 1H), 1.45-1.06 (m, 5H); EI-MS: 174 (100%), 148, 132, 119, 97, 83, 71, 57. A copy of the ¹H NMR spectra is provided.

***N*- Phenyl furfurylamine (Table 4, entry 8)**

¹H NMR (300MHz, CDCl₃) δ 7.32 (s, 1H), 7.12 (t, 2H *J*=8.3 Hz), 6.68 (t, 1H *J*=7.6 Hz), 6.60 (d, 2H *J*=7.6 Hz), 6.28 (br s, 1H), 6.19 (br s, 1H), 4.3 (s, 2H) EI-MS: 173, 81 (100%), 77, 53, 40. HRMS For C₁₁H₁₂N (M⁺) calcd 174.0918, found 174.0916 A copy of the ¹H NMR spectra is provided.

Table 2, entry 3.

Table 2, entry 4

Table 2, entry 5.

Table 2, entry 6,

Table 2. entry 7

Table 3, entry 1

Table 3, entry 2

Table 3, entry 3

Table 3, entry 4.

Table 3, entry 5.

Table 3, entry 8.

Table 4. entry 1

Table 4, entry 2

Table 4, entry 3.

Table 4, entry 4.

Table 4, entry 6.

Table. 4, Entry 8

References

- (1) Choudary, B. M.; Sridhar, C.; Kantam, M. L.; Venkanna, G. T.; Sreedhar, B. *J. Am. Chem. Soc.* **2005**, 127, 9948.
- 2) Collman, J. P.; Zhong, M. *Org. Lett.* **2000**, 2, 1233.
- 3) Hartwig, J. F.; Kawatsura, M.; Hauck, S. I.; Shaughnessy, K. H.; Alcazar-Roman, L. *M. J. Org. Chem.* **1999**, 64, 5575.
- 4) Wolfe, J. P.; Buchwald, S. L. *J. Org. Chem.* **1997**, 62, 6066.
- 5) Louie, J.; Driver, M. S.; Hamann, B. C.; Hartwig, J. F. *J. Org. Chem.* **1997**, 62, 1268.
- 6) Zhang, Z.; Mao, J.; Zhu, D.; Wu, F.; Chen, H.; Wan, B. *Tetrahedron.* **2006**, 62, 4443.