HETEROCYCLES, Vol. 65, No. 8, 2005, pp. 1975 - 1984
Received, 12th May, 2005, Accepted, 5th July, 2005, Published online, 7th July, 2005

SYNTHESIS OF 2,4-DIARYLIMIDAZOLES THROUGH SUZUKI CROSS-COUPLING REACTIONS OF IMIDAZOLE HALIDES WITH ARYLBORONIC ACIDS

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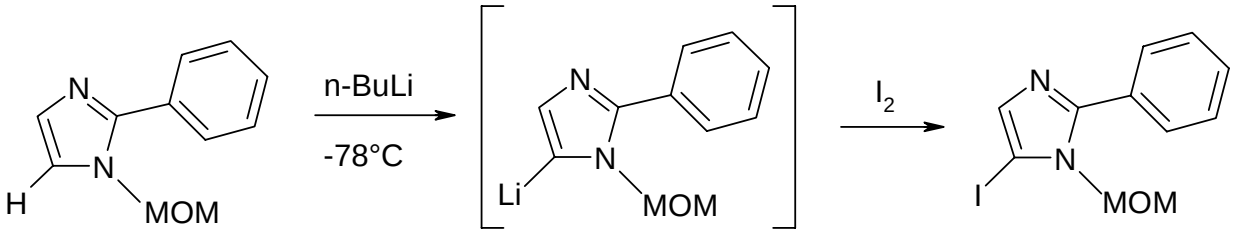
Abstract - The Suzuki coupling, a Pd-catalyzed cross-coupling reaction of a boronic acid with an aryl halide, was used to prepare several 2,4-diarylimidazoles. Iodinated and brominated imidazoles (**3**) and (**9**) proved to be suitable aryl halides for Suzuki coupling. These imidazole halides readily reacted with phenyl-, naphthyl- and biphenylboronic acids under Suzuki conditions to give arylated imidazoles.

INTRODUCTION

Diarylimidazoles have been described as pharmacologically active compounds in several publications over the last twenty years.[1,2] 2,4-Diarylimidazoles for example showed NPY5 receptor antagonist activity[3] as well as antiinflammatory activity.[4] Most of these diarylimidazoles were prepared either by condensating amidines with α-halogenated ketones or by condensating α-amino ketones with KSCN. However, condensation reactions did not always prove to be successful in the preparation of imidazoles and yields in many cases were low.[4] In the nineteen-nineties several chemists successfully introduced cross-coupling reactions such as the Stille reaction,[5] the Negishi reaction[6] or the Suzuki reaction[7] for the arylation of protected imidazoles. Of all these cross-coupling reactions the Suzuki coupling was the most successful in terms of product variety and yield.

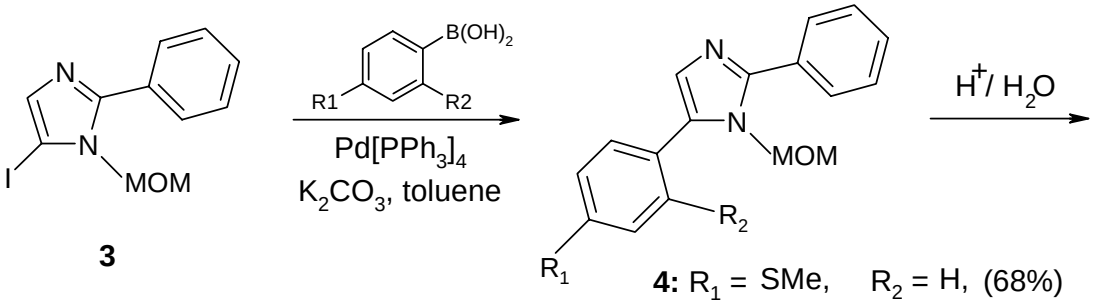
RESULTS

Starting from 1-methoxymethyl-2-phenyl-1*H*-imidazole (**1**)[8] we prepared 4-iodoimidazole (**3**) *via* lithiation of substance (**1**), followed by quenching with iodine.



1 **2** **3**

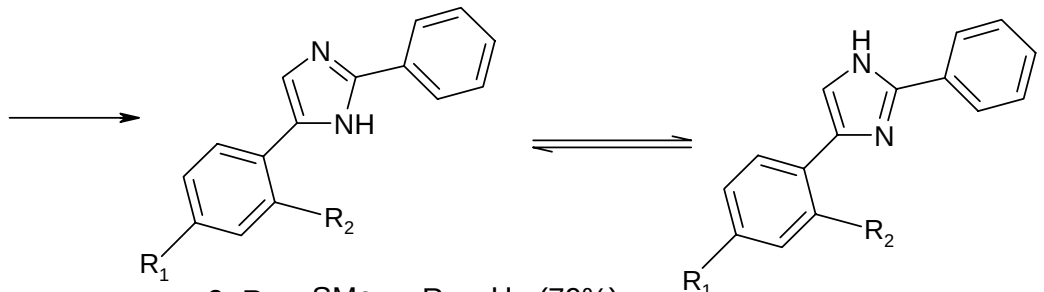
Under Suzuki conditions **3** reacted with 4-methylsulfanylphenylboronic acid and 2-acetylphenylboronic acid to give compounds (**4**) and (**5**) in good yields (68%, 79%). Removal of the MOM protecting group was achieved by refluxing **4** and **5** in a mixture of ethanol and concentrated hydrochloric acid. This yielded **6** in 79% yield and **7** in 22% yield.



3

4: R_1 = SMe, R_2 = H, (68%)

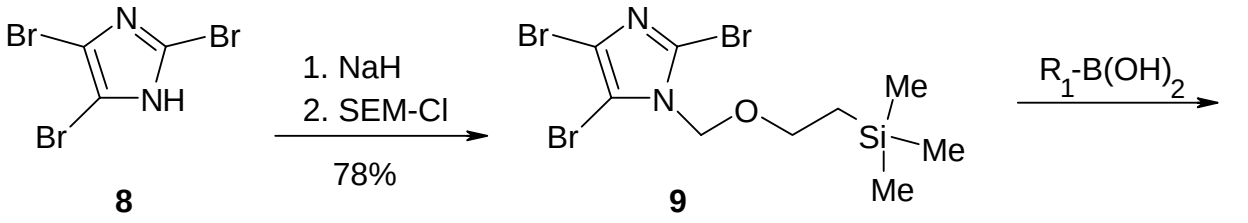
5: R_1 = H, R_2 = COMe, (79%)

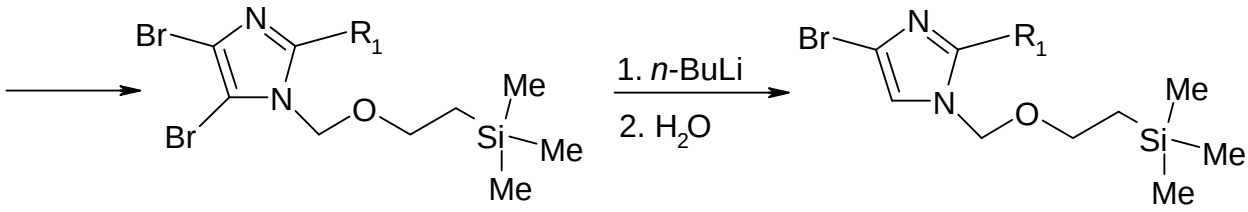


6: R_1 = SMe, R_2 = H, (79%)

7: R_1 = H, R_2 = COMe, (22%)

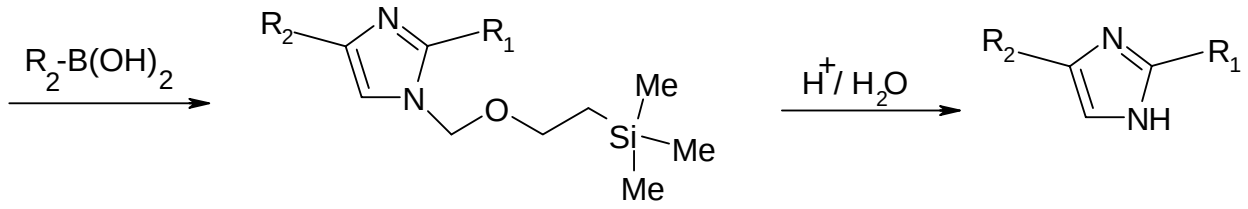
Another suitable halogenated imidazole for Suzuki reactions is 2,4,5-tribromo-1-[[2-trimethylsilylethoxy]methyl]-1*H*-imidazole (**9**).[7] Suzuki coupling with one equivalent of the boronic acids, 2-naphthylboronic acid and 4-biphenylboronic acid, led to selective arylation of position 2 of the imidazole nucleus for compounds (**10**) and (**11**). The products (**10**) and (**11**) were treated with *n*-BuLi, followed by quenching with water to give **12** and **13**. Products (**12**) and (**13**) underwent a second Suzuki coupling with 2-methoxyphenylboronic acid and 4-ethylphenylboronic acid respectively to yield **14** and **15**. Removal of the protecting group through treatment with diluted hydrochloric acid gave product (**16**) in 53% yield and (**17**) in 96% yield.





10: R_1 = 2-naphthyl (81%)
11: R_1 = 4-biphenyl (79%)

12: R_1 = 2-naphthyl (82%)
13: R_1 = 4-biphenyl (45%)



14: R_1 = 2-naphthyl
R_2 = 2-methoxyphenyl (84%) %
15: R_1 = 4-biphenyl
R_2 = 4-ethylphenyl (78%)

16: R_1 = 2-naphthyl
R_2 = 2-methoxyphenyl (53%) %
17: R_1 = 4-biphenyl
R_2 = 4-ethylphenyl (96%)

EXPERIMENTAL

^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance DPx200 spectrometer, using TMS as an internal standard. MS spectra were recorded on a Shimadzu QP 5000. Column chromatography was performed on Merck silica gel 60, 0.063 - 0.200 mm. Melting points were determined with a Kofler melting point apparatus and are uncorrected. Microanalyses were determined by Johannes Theiner at the Institute of Physical Chemistry of the University of Vienna.

5-Iodo-1-methoxymethyl-2-phenyl-1*H*-imidazole (3)

To 5.647 g (0.030 mol) of **1** in 250 mL of anhydrous THF at -78°C under argon 20 mL of 1.6 M *n*-BuLi in hexane (0.032 mol) were slowly added. After 30 min a solution of 8.630 g (0.034 mol) iodine in 20 mL

of dry THF was added. The reaction mixture was stirred 1 h at -78°C and then allowed to warm to rt. After that a solution of sodium hydrogensulfit (10%) was added until the reaction mixture turned clear. Then the reaction mixture was washed with 150 mL of a saturated aqueous solution of ammonium chloride. The organic layer was dried over anhydrous sodium sulfate and evaporated. The crude product was recrystallized from ethanol to yield 7.351 g (78%) of **3**; mp 83 - 103°C; MS: m/z (rel. int.) 314 (M^+, 13), 284 (2), 187 (2), 77 (4), 45 (100); ^{1}H-NMR ($CDCl_3$): δ = 7.80 - 7.61 (m, 2H, Ar*H*), 7.57 - 7.35 (m, 3H, Ar*H*), 7.24 (s, 1H, Ar*H*), 5.24 (s, 2H, NC*H*$_2$-), 3.42 (s, 3H, -OC*H*$_3$); ^{13}C-NMR ($CDCl_3$): δ = 151.7 (Ar*C*), 136.7 (Ar*C*H), 130.2 (Ar*C*), 129.4 (Ar*C*H), 128.8 (Ar*C*H), 128.6 (Ar*C*H), 76.6 (N*C*H$_2$-), 71.8 (Ar*C*), 56.2 (-O*C*H$_3$); Anal. Calcd for $C_{11}H_{11}N_2OI$: C, 42.06; H, 3.53; N 8.92. Found: C, 42.29; H, 3.40; N 8.72.

1-Methoxymethyl-5-(4-methylsulfanylphenyl)-2-phenyl-1*H*-imidazole (4)

A mixture of **3** (1.571 g, 0.005 mol), 4-methylsulfanylphenylboronic acid (0.924 g, 0.0055 mol), tetrakis(triphenylphosphine)palladium(0) (0.578 g, 0.0005 mol), toluene (90 mL), methanol (18 mL) and 2M potassium carbonate (5.9 mL) was refluxed for 16 h under argon atmosphere. The reaction mixture was cooled to rt and washed with 30 mL of a saturated aqueous solution of ammonium chloride. The organic layer was dried over anhydrous sodium sulfate and evaporated. The residue was subjected to column chromatography with ethyl acetate/*n*-hexane (1:1). The product was recrystallized from acetonitrile to give 1.055g (68%) of **4**; mp 77 - 79°C; MS: m/z (rel. int.) 310 (M+, 44), 279 (12), 265 (24), 69 (77), 45 (100); ^{1}H-NMR ($CDCl_3$): δ = 7.90 - 7.75 (m, 2H, Ar*H*), 7.58 - 7.38 (m, 5H, Ar*H*), 7.38 - 7.27 (m, 2H, Ar*H*), 7.20 (s, 1H, Ar*H*), 5.03 (s, 2H, NC*H*$_2$-), 3.33 (s, 3H, -OC*H*$_3$), 2.53 (s, 3H, -SC*H*$_3$); ^{13}C-NMR ($CDCl_3$): δ = 150.1 (Ar*C*), 138.8 (Ar*C*), 135.0 (Ar*C*), 130.4 (Ar*C*), 129.0 (Ar*C*H), 128.8 (Ar*C*H), 128.7 (Ar*C*H), 128.6 (Ar*C*H), 127.4 (Ar*C*H), 126.4 (Ar*C*H), 126.4 (Ar*C*), 74.9 (N*C*H$_2$-), 55.1 (-O*C*H$_3$), 15.4 (-S*C*H$_3$); Anal. Calcd for $C_{18}H_{18}N_2OS$: C, 69.65; H, 5.84; N 9.02. Found: C, 69.47; H, 5.88; N 8.97.

1-[2-(1-Methoxymethyl-2-phenyl-1*H*-5-imidazolyl)phenyl]-1-ethanone (5)

A mixture of **3** (1.571 g, 0.005 mol), 2-acetylphenylboronic acid (0.902 g, 0.0055 mol), tetrakis(triphenylphosphine)palladium(0) (0.578 g, 0.0005 mol), toluene (90 mL), methanol (18 mL) and 2M potassium carbonate (5.9 mL) was refluxed for 16 h under argon atmosphere. The reaction mixture was cooled to rt and washed with 30 mL of a saturated aqueous solution of ammonium chloride. The organic layer was dried over anhydrous sodium sulfate and evaporated. The residue was subjected to column chromatography with ethyl acetate. This gave 1.210 g (79%) of **5** as a colorless oil; MS: m/z (rel.

int.) 306 (M^+, 11), 291 (19), 261 (17), 77 (9), 45 (100); ^{1}H-NMR ($CDCl_3$): δ = 7.89 - 7.37 (m, 9H, Ar*H*), 7.10 (s, 1H, Ar*H*), 4.97 (s, 2H, NCH_2-), 3.11 (s, 3H, -OCH_3), 2.23 (s, 3H, -CO CH_3).; ^{13}C-NMR ($CDCl_3$): δ = 201.8 (-*C*O CH_3), 149.8 (Ar*C*), 141.2 (Ar*C*), 132.8 (Ar*C*), 132.3 (Ar*C*H), 131.0 (Ar*C*H), 130.2 (Ar*C*), 129.1 (Ar*C*H), 128.8 (Ar*C*H), 128.6 (Ar*C*H), 128.4 (Ar*C*H), 127.7 (Ar*C*), 75.0 (NCH_2-), 55.5 (-OCH_3), 29.4 (-CO *C*H_3); two Ar*C*H signals were not detectable; Anal. Calcd for $C_{19}H_{18}N_2O_2$: C, 74.49; H, 5.92; N, 9.14. Found: C, 74.24; H, 5.98; N 9.02.

5-(4-Methylsulfanylphenyl)-2-phenyl-1*H*-imidazole (6)

A solution of 0.310 g (0.001 mol) of **4** in 25 mL of ethanol and 7 mL of concentrated hydrochloric acid was refluxed for 16 h. After cooling to rt the reaction mixture was neutralised with 6M sodium hydroxide. The ethanol was evaporated and the residue was extracted with dichloromethane. The combined organic extracts were dried over anhydrous sodium sulfate and evaporated. The crude product was recrystallized from ethanol to give 0.21 g (79%) of **6**; mp 171 - 174°C; MS: m/z (rel. int.) 266 (M+, 100), 251 (53), 218 (6), 77 (11), 45 (6); ^{1}H-NMR (DMSO-d_6): δ = 12.65 and 12.52 (br s, 1H, N*H*), 8.15 - 7.92 (m, 2H, Ar*H*), 7.90 - 7.62 (m, 3H, Ar*H*), 7.57 - 7.16 (m, 5H, Ar*H*); ^{1}H-NMR (MeOH-d_4): δ = 7.86 - 7.76 (m, 2H, Ar*H*), 7.64 - 7.52 (m, 2H, Ar*H*), 7.41 - 7.11 (m, 6H, Ar*H*), 2.36 (s, 3H, -SCH_3); ^{13}C-NMR (DMSO-d_6): δ = 145.8 (Ar*C*), 140.7 (Ar*C*), 135.4 (Ar*C*), 131.7 (Ar*C*), 130.6 (Ar*C*), 128.7 (Ar*C*H), 128.1 (Ar*C*H), 126.3 (Ar*C*H), 124.9 (Ar*C*H), 114.1 (Ar*C*H), 15.0 (-SCH_3); one Ar*C*H signal was not detectable; Anal. Calcd for $C_{16}H_{14}N_2S$: C, 72.15; H, 5.30; N 10.52. Found: C, 71.88; H, 5.09; N 10.27.

1-[2-(2-Phenyl-1*H*-5-imidazolyl)phenyl]-1-ethanone (7)

A solution of 0.919 g (0.003 mol) of **5** in 45 mL of ethanol and 12 mL of concentrated hydrochloric acid was refluxed for 16 h. After cooling to rt the reaction mixture was neutralised with 6M sodium hydroxide. The ethanol was evaporated and the residue was extracted with dichloromethane. The combined organic extracts were dried over anhydrous sodium sulfate and evaporated. The crude product was recrystallized from ethanol to give 0.173 g (22%) of **7**; mp 172 - 174°C; MS: m/z (rel. int.) 262 (M+, 85), 247 (80), 159 (25), 89 (100), 77 (34); ^{1}H-NMR (DMSO-d_6): δ = 12.89 (br s, 1H, N*H*), 8.03 - 7.87 (m, 2H, Ar*H*), 7.78 - 7.55 (m, 2H, Ar*H*), 7.53 - 7.21 (m, 6H, Ar*H*), 2.31 (s, 3H, -CO CH_3); ^{13}C-NMR (DMSO-d_6): δ = 204.7 (-*C*OCH_3), 145.8 (Ar*C*), 140.1 (Ar*C*), 131.4 (Ar*C*), 130.4 (Ar*C*), 129.7 (Ar*C*H), 128.8 (Ar*C*H), 128.3 (Ar*C*H), 127.3 (Ar*C*H), 126.5 (Ar*C*H), 124.9 (Ar*C*H), 30.9 (-CO *C*H_3); one Ar*C* signal and two Ar*C*H signals were not detectable; Anal. Calcd for $C_{17}H_{14}N_2O$: C, 77.84; H, 5.38; N, 10.68. Found: C, 77.75; H, 5.52; N, 10.44.

4,5-Dibromo-2-(2-naphthyl)-1-{[2-(1,1,1-trimethylsilyl)ethoxy]methyl}-1*H*-imidazole (10)

A mixture of **9** (2.175 g, 0.005 mol), 2-naphthylboronic acid (0.894 g, 0.0052 mol), tetrakis(triphenylphosphine)palladium(0) (0.578 g, 0.0005 mol), toluene (90 mL), methanol (18 mL) and 2M potassium carbonate (5.6 mL) was refluxed for 16 h under argon atmosphere. The reaction mixture was cooled to rt and washed with 30 mL of a saturated aqueous solution of ammonium chloride. The organic layer was dried over anhydrous sodium sulfate and evaporated. The residue was subjected to column chromatography with ethyl acetate/*n*-hexane (1+9). The fractions with the desired product were united and evaporated under reduced pressure. The product was recrystallized from ethanol to give 1.953 g (81%) of **10**; mp 84 - 86°C; MS: m/z (rel. int.) 480 / 482 / 484 (M+, 0.42 / 0.83 / 0.41), 424 (3), 103 (11), 73 (100), 45 (6); ^{1}H-NMR ($CDCl_3$): δ = 8.30 (s, 1H, Ar*H*), 7.97 - 7.78 (m, 4H, Ar*H*), 7.60 - 7.44 (m, 2H, Ar*H*), 5.35 (s, 2H, NCH_2-), 3.70 (t, *J* = 8.2 Hz, 2H, -OC$\underline{H_2}$$CH_2$-), 0.98 (t, *J* = 8.2 Hz, 2H, -$OCH_2C\underline{H_2}$-), 0.01 (s, 9H, -Si(CH_3)$_3$); ^{13}C-NMR ($CDCl_3$): δ = 149.8 (Ar*C*), 133.8 (Ar*C*), 132.9 (Ar*C*), 128.6 (Ar*C*H), 128.6 (Ar*C*H), 127.7 (Ar*C*H), 127.2 (Ar*C*H), 126.7 (Ar*C*H), 126.5 (Ar*C*), 125.9 (Ar*C*H), 118.0 (Ar*C*), 105.4 (Ar*C*), 74.7 (NCH_2-), 67.0 (-O$\underline{C}H_2CH_2$-), 18.0 (-$OCH_2\underline{C}H_2$-), -1.4 (-Si(CH_3)$_3$); one Ar*C*H signal was not detectable; Anal. Calcd for $C_{19}H_{22}N_2OBr_2Si$: C, 47.32; H, 4.60; N, 5.81. Found: C, 47.11; H, 4.52; N, 5.77.

2-(4-Biphenyl)-4,5-dibromo-1-{[2-(1,1,1-trimethylsilyl)ethoxy]methyl}-1*H*-imidazole (11)

A mixture of **9** (2.175 g, 0.005 mol), biphenyl-4-boronic acid (1.030 g, 0.0052 mol), tetrakis(triphenylphosphine)palladium(0) (0.578 g, 0.0005 mol), toluene (90 mL), methanol (18 mL) and 2M potassium carbonate (5.6 mL) was refluxed for 16 h under argon atmosphere. The reaction mixture was cooled to rt and washed with 30 mL of a saturated aqueous solution of ammonium chloride. The organic layer was dried over anhydrous sodium sulfate and evaporated under reduced pressure. The residue was subjected to column chromatography with ethyl acetate/*n*-hexane (1+9). The fractions with the desired product were united and evaporated under reduced pressure. The product was recrystallized from ethanol/ethyl acetate to give 2.008 g (79%) of **11**; mp 88 - 90°C; MS: m/z (rel. int.) 506 / 508 / 510 (M+, 0.48 / 0.99 / 0.52), 450 (4), 103 (15), 73 (100), 45 (7); ^{1}H-NMR ($CDCl_3$): δ = 7.92 - 7.78 (m, 2H, Ar*H*), 7.73 - 7.54 (m, 4H, Ar*H*), 7.51 - 7.31 (m, 3H, Ar*H*), 5.33 (s, 2H, NCH_2-), 3.69 (t, *J* = 8.2 Hz, 2H, -OC$\underline{H_2}$$CH_2$-), 0.96 (t, *J* = 8.2 Hz, 2H, -$OCH_2C\underline{H_2}$-), 0.01 (s, 9H, -Si(CH_3)$_3$); ^{13}C-NMR ($CDCl_3$): δ = 149.5 (Ar*C*), 142.4 (Ar*C*), 140.0 (Ar*C*), 129.2 (Ar*C*H), 128.9 (Ar*C*H), 128.1 (Ar*C*), 127.8 (Ar*C*H), 127.3 (Ar*C*H), 127.1 (Ar*C*H), 117.9 (Ar*C*), 105.3 (Ar*C*), 74.6 (NCH_2-), 67.0 (-O$\underline{C}H_2CH_2$-), 18.0 (-$OCH_2\underline{C}H_2$-),

-1.4 (-Si(*C*H_3)$_3$); Anal. Calcd for $C_{21}H_{24}N_2OBr_2Si$: C, 49.62; H, 4.76; N, 5.51. Found: C, 49.66; H, 4.70; N, 5.34.

4-Bromo-2-(2-naphthyl)-1-{[2-(1,1,1-trimethylsilyl)ethoxy]methyl}-1*H*-imidazole (12)

A solution of *n*-BuLi in *n*-hexane (1.6 M, 0.63 mL, 0.001 mol) was added dropwise under argon at -78°C to a solution of **10** (0.482 g, 0.001 mol) in dry THF (15 mL). After stirring the reaction mixture for 1 min at -78°C water (1 mL) was added. The reaction mixture was allowed to warm to rt, and after that was washed with 30 mL of a saturated aqueous solution of ammonium chloride. The organic layer was dried over anhydrous sodium sulfate and evaporated. The product was recrystallized from ethanol to give 0.331 g (82%) of **12**; mp 80 - 83°C; MS: m/z (rel. int.) 404 / 402 (M+, 1.71 / 1.71), 265 (13), 103 (8), 73 (100), 43 (12); ^{1}H-NMR ($CDCl_3$): δ = 8.25 (s, 1H, Ar*H*), 7.95 - 7.76 (m, 4H, Ar*H*), 7.58 - 7.42 (m, 2H, Ar*H*), 7.12 (s, 1H, Ar*H*), 5.28 (s, 2H, NC*H*$_2$-), 3.62 (t, *J* = 8.1 Hz, 2H, -OC*H*$_2$CH$_2$-), 0.95 (t, *J* = 8.1 Hz, 2H, -OCH$_2$C*H*$_2$-), 0.00 (s, 9H, -Si(C*H*$_3$)$_3$); ^{13}C-NMR ($CDCl_3$): δ = 148.5 (Ar*C*), 133.4 (Ar*C*), 132.9 (Ar*C*), 128.5 (Ar*C*H), 128.4 (Ar*C*H), 128.4 (Ar*C*H), 127.7 (Ar*C*H), 127.0 (Ar*C*H), 126.6 (Ar*C*H), 126.3 (Ar*C*), 126.1 (Ar*C*H), 120.5 (Ar*C*H), 115.6 (Ar*C*), 75.7 (N*C*H$_2$-), 66.8 (-O*C*H$_2$CH$_2$-), 17.8 (-OCH$_2$*C*H$_2$-), -1.4 (-Si(*C*H$_3$)$_3$); Anal. Calcd for $C_{19}H_{23}N_2OBrSi$: C, 56.57; H, 5.75; N, 6.94. Found: C, 56.86; H, 5.48; N, 6.87.

2-(4-Biphenyl)-4-bromo-1-{[2-(1,1,1-trimethylsilyl)ethoxy]methyl}-1*H*-imidazole (13)

A solution of *n*-BuLi in *n*-hexane (1.6 M, 0.63 mL, 0.001 mol) was added dropwise under argon at -78°C to a solution of **11** (0.508 g, 0.001 mol) in dry THF (15 mL). After stirring the reaction mixture for 1 min at -78°C water (1 mL) was added. The reaction mixture was allowed to warm to rt, and after that was washed with 30 mL of a saturated aqueous solution of ammonium chloride. The organic layer was dried over anhydrous sodium sulfate and evaporated. The product was recrystallized from ethanol to give 0.193 g (45%) of **13**; mp 94 - 96°C; MS: m/z (rel. int.) 430 / 428 (M+, 1 / 1), 291 (8), 103 (8), 73 (100), 44 (10); ^{1}H-NMR ($CDCl_3$): δ = 7.92 - 7.80 (m, 2H, Ar*H*), 7.76 - 7.58 (m, 4H, Ar*H*), 7.53 - 7.32 (m, 3H, Ar*H*), 7.11 (s, 1H, Ar*H*), 5.28 (s, 2H, NC*H*$_2$-), 3.63 (t, *J* = 8.1 Hz, 2H, -OC*H*$_2$CH$_2$-), 0.96 (t, *J* = 8.2 Hz, 2H, -OCH$_2$C*H*$_2$-), 0.02 (s, 9H, -Si(C*H*$_3$)$_3$); ^{13}C-NMR ($CDCl_3$): δ = 148.2 (Ar*C*), 142.0 (Ar*C*), 140.1 (Ar*C*), 129.2 (Ar*C*H), 128.8 (Ar*C*H), 127.9 (Ar*C*), 127.7 (Ar*C*H), 127.2 (Ar*C*H), 127.0 (Ar*C*H), 120.4 (Ar*C*H), 115.6 (Ar*C*), 75.6 (N*C*H$_2$-), 66.8 (-O*C*H$_2$CH$_2$-), 17.8 (-OCH$_2$*C*H$_2$-), -1.4 (-Si(*C*H$_3$)$_3$); Anal. Calcd for $C_{21}H_{25}N_2OBrSi$: C, 58.74; H, 5.87; N, 6.52. Found: C, 58.90; H, 5.58; N, 6.57.

4-(2-Methoxyphenyl)-2-(2-naphthyl)-1-{[2-(1,1,1-trimethylsilyl)ethoxy]methyl}-1*H*-imidazole (14)

A mixture of **12** (0.403 g, 0.001 mol), 2-methoxyphenylboronic acid (0.182 g, 0.0012 mol), tetrakis(triphenylphosphine)palladium(0) (0.116 g, 0.0001 mol), toluene (18 mL), methanol (3.6 mL) and 2M potassium carbonate (1 mL) was refluxed for 16 h under argon atmosphere. The reaction mixture was cooled to rt and washed with 10 mL of a saturated aqueous solution of ammonium chloride. The organic layer was dried over anhydrous sodium sulfate and evaporated. The residue was subjected to column chromatography with ethyl acetate/*n*-hexane (2+8). The product was recrystallized from ethanol to give 0.362 g (84%) of **14**; mp 88 - 93°C; MS: m/z (rel. int.) 430 (M+, 13), 371 (13), 314 (17), 226 (22), 73 (100); ^{1}H-NMR ($CDCl_3$): δ = 8.47 - 8.29 (m, 2H, Ar*H*), 8.07 - 7.82 (m, 4H, Ar*H*), 7.78 (s, 1H, Ar*H*), 7.61 - 7.44 (m, 2H, Ar*H*), 7.33 - 7.18 (m, 1H, Ar*H*), 7.16 - 6.93 (m, 2H, Ar*H*), 5.39 (s, 2H, NCH_2-), 3.99 (s, 3H, -OCH_3), 3.69 (t, *J* = 8.1 Hz, 2H, -OC$\underline{H_2}$$CH_2$-), 0.99 (t, *J* = 8.1 Hz, 2H, -$OCH_2C\underline{H_2}$-), 0.02 (s, 9H, -Si(CH_3)$_3$); ^{13}C-NMR ($CDCl_3$): δ = 156.0 (Ar*C*), 147.5 (Ar*C*), 136.7 (Ar*C*), 133.2 (Ar*C*), 133.1 (Ar*C*), 128.5 (Ar*C*H), 128.3 (Ar*C*H), 128.2 (Ar*C*H), 127.7 (Ar*C*), 127.7 (Ar*C*H), 127.7 (Ar*C*H), 127.4 (Ar*C*H), 126.6 (Ar*C*H), 126.6 (Ar*C*H), 126.3 (Ar*C*H), 122.6 (Ar*C*), 121.7 (Ar*C*H), 120.9 (Ar*C*H), 110.5 (Ar*C*H), 75.5 (N*C*H_2-), 66.3 (-O$\underline{C}$$H_2CH_2$-), 55.2 (-O*C*$H_3$), 17.7 (-$OCH_2\underline{C}H_2$-), -1.4 (-Si(*C*$H_3$)$_3$); Anal. Calcd for $C_{26}H_{30}N_2O_2Si$: C, 72.52; H, 7.02; N, 6.51. Found: C, 72.73; H, 6.78; N, 6.28.

2-(4-Biphenyl)-4-(4-ethylphenyl)-1-{[2-(1,1,1-trimethylsilyl)ethoxy]methyl}-1*H*-imidazole (15)

A mixture of **13** (0.429 g, 0.001 mol), 4-ethylphenylboronic acid (0.180 g, 0.0012 mol), tetrakis(triphenylphosphine)palladium(0) (0.116 g, 0.0001 mol), toluene (18 mL), methanol (3.6 mL) and 2M potassium carbonate (1 mL) was refluxed for 16 h under argon atmosphere. The reaction mixture was cooled to rt and washed with 10 mL of a saturated aqueous solution of ammonium chloride. The organic layer was dried over anhydrous sodium sulfate and evaporated. The residue was subjected to column chromatography with ethyl acetate/*n*-hexane (2+8). The product was recrystallized from isopropanol to give 0.355 g (78%) of **15**; mp 135 - 141°C; MS: m/z (rel. int.) 454 (4), 396 (14), 337 (7), 73 (100), 45 (8); ^{1}H-NMR ($CDCl_3$): δ = 7.99 - 7.18 (m, 14H, Ar*H*), 5.34 (s, 2H, NCH_2-), 3.65 (t, *J* = 8.2 Hz, 2H, -OC$\underline{H_2}$$CH_2$-), 2.68 (q, *J* = 7.6 Hz, 2H, $CH_3C\underline{H_2}$-), 1.27 (t, *J* = 7.6 Hz, 3H, C$\underline{H_3}$$CH_2$-), 0.97 (t, *J* = 8.2 Hz, 2H, -$OCH_2C\underline{H_2}$-), 0.02 (s, 9H, -Si(CH_3)$_3$); ^{13}C-NMR ($CDCl_3$): δ = 148.4 (Ar*C*), 143.0 (Ar*C*), 141.6 (Ar*C*), 141.5 (Ar*C*), 140.4 (Ar*C*), 131.4 (Ar*C*), 129.4 (Ar*C*H), 129.1 (Ar*C*), 128.8 (Ar*C*H), 128.0 (Ar*C*H), 127.6 (Ar*C*H), 127.2 (Ar*C*H), 127.1 (Ar*C*H), 125.0 (Ar*C*H), 116.7 (Ar*C*H), 75.6 (N*C*H_2-), 66.4 (-O$\underline{C}$$H_2CH_2$-), 28.6 ($CH_3\underline{C}H_2$-), 17.8 (-$OCH_2\underline{C}H_2$-), 15.6 ($\underline{C}H_3CH_2$-), -1.4 (-Si(*C*$H_3$)$_3$); Anal. Calcd for $C_{29}H_{34}N_2OSi$: C, 76.61; H, 7.54; N, 6.16. Found: C, 76.36; H, 7.64; N, 6.11.

4-(2-Methoxyphenyl)-2-(2-naphthyl)-1*H*-imidazole (16)

A solution of 0.431 g (0.001 mol) of **14** in 25 mL of ethanol and 7 mL of concentrated hydrochloric acid was refluxed for 16 h. After cooling to rt the reaction mixture was neutralised with 6M sodium hydroxide. The ethanol was evaporated and the residue was extracted with dichloromethane. The combined organic extracts were dried over anhydrous sodium sulfate and evaporated. The crude product was recrystallized from ethanol to give 0.190 g of a mixed crystal of **16** with ethanol in the ratio 1 : 1. This is equal to 0.165 g (55%) of pure **16**; mp 80 - 83°C; MS: m/z (rel. int.) 300 (M+, 55), 150 (18), 132 (84), 77 (18), 45 (100); ^{1}H-NMR ($CDCl_3$): δ = 10.74 (br s, 1H, N*H*), 8.31 (s, 1H, Ar*H*), 8.12 - 7.74 (m, 5H, Ar*H*), 7.64 (s, 1H, Ar*H*), 7.56 - 7.40 (m, 2H, Ar*H*), 7.33 - 7.18 (m, 1H, Ar*H*), 7.13 - 6.94 (m, 2H, Ar*H*), 4.01 (s, 3H, -OC*H*$_3$), 3.72 (q, *J* = 7.0 Hz, 2H, $CH_3C\underline{H_2}OH$), 1.23 (t, *J* = 7.0 Hz, 3H, $C\underline{H_3}CH_2OH$); ^{13}C-NMR ($CDCl_3$): δ = 155.0 (Ar*C*), 146.0 (Ar*C*), 133.2 (Ar*C*), 133.1 (Ar*C*), 128.5 (Ar*C*H), 128.1 (Ar*C*H), 127.9 (Ar*C*H), 127.6 (Ar*C*H), 127.5 (Ar*C*), 126.8 (Ar*C*H), 126.4 (Ar*C*H), 126.2 (Ar*C*H), 123.9 (Ar*C*H), 123.1 (Ar*C*H), 121.2 (Ar*C*H), 111.2 (Ar*C*H), 58.1 ($CH_3\underline{C}H_2OH$), 55.6 (-O$\underline{C}H_3$), 18.3 ($\underline{C}H_3CH_2OH$); one ArCH signal and two ArC signals were not detectable; Anal. Calcd for $C_{20}H_{16}N_2O$. C_2H_6O: C, 76.28; H, 6.40; N, 8.09. Found: C, 76.13; H, 5.99; N, 7.98.

2-(4-Biphenylyl)-4-(4-ethylphenyl)-1*H*-imidazole (17)

A solution of 0.455 g (0.001 mol) of **15** in 30 mL of acetone, 7 mL of concentrated hydrochloric acid and 5 mL of water was refluxed for 16 h. After cooling to rt the reaction mixture was neutralised with 6M sodium hydroxide. The ethanol was evaporated and the residue was extracted with dichloromethane. The combined organic extracts were dried over anhydrous sodium sulfate and evaporated. The residue was subjected to column chromatography with ethyl acetate/*n*-hexane (2+8). The product was recrystallized from ethanol/ethyl acetate to give 0.311 g (96%) of **17**; mp 200 - 215°C; MS: m/z (rel. int.) 324 (100), 309 (52), 162 (27), 154 (73), 77 (12); ^{1}H-NMR (DMSO-d_6): δ = 12.65 (br s, 1H, N*H*), 8.21 - 8.03 (m, 2H, Ar*H*), 7.88 - 7.58 (m, 7H, Ar*H*), 7.55 - 7.30 (m, 3H, Ar*H*), 7.29 - 7.14 (m, 2H, Ar*H*), 2.60 (q, *J* = 7.6 Hz, 2H, $CH_3C\underline{H_2}$-), 1.19 (t, *J* = 7.5 Hz, 3H, $C\underline{H_3}CH_2$-); ^{13}C-NMR (DMSO-d_6): δ = 145.6 (Ar*C*), 141.9 (Ar*C*), 139.5 (Ar*C*), 139.5 (Ar*C*), 129.7 (Ar*C*), 129.0 (Ar*C*H), 127.9 (Ar*C*H), 127.6 (Ar*C*H), 126.9 (Ar*C*H), 126.5 (Ar*C*H), 125.5 (Ar*C*H), 124.5 (Ar*C*H), 27.9 ($CH_3\underline{C}H_2$-), 15.6 ($\underline{C}H_3CH_2$-); one Ar*C*H signal and two Ar*C* signals were not detectable; Anal. Calcd for $C_{23}H_{20}N_2$: C, 85.15; H, 6.21; N, 8.63. Found: C, 84.85; H, 6.08; N, 8.35.

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