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Supporting Information

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C–H Functionalization/C–N Bond Formation: Copper-Catalyzed Synthesis of Benzimidazoles from Amidines

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Supporting Information

Content

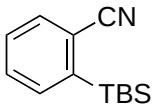
General Considerations

For the synthesis of amidines, all anilines and carbonitriles were commercially available and used as received, except for 2-(*tert*-butyldimethylsilyl)benzonitrile, which was synthesized from 2-iodobenzonitrile and *tert*-butyldimethylsilylchloride (TBSCl). NaH (dry, 95%) was purchased from Sigma-Aldrich and stored in a nitrogen filled glove box. $AlCl_3$ (98.5%, extra pure, anhydrous, powder) was obtained from Acros Organics. DMSO (anhydrous, 99.9+%) was purchased from Sigma-Aldrich in a SureSeal™ bottle. $Cu(OAc)_2$ (anhydrous, 99.999%) was obtained from Sigma-Aldrich and stored in a desiccator with Drierite® as drying agent. Similar results were obtained with $Cu(OAc)_2$ (anhydrous, min. 97%), which was purchased from Strem Chemicals and stored in a desiccator. HOAc (ACS reagent, 99.7+%) was obtained from Sigma-Aldrich. O_2 (extra dry, size 200, minimum purity 99.8%) was obtained from Airgas. *N*-Phenylbenzamidine (97%+) was purchased from Maybridge. All other commercially available materials as solvents and reagents were used as received.

Silica gel chromatography was performed using a Biotage SP4™ EXP Flash Purification System. For the purification of the benzimidazoles, 25+M KP-Sil silica cartridges were used. MeOH or EtOAc was used to transfer the crude reaction material onto the silica gel samplet. The samplet was dried under vacuum prior to usage.

Nuclear magnetic resonance (NMR) spectra were recorded on a Varian Mercury-300 instrument. Chemical shifts (δ) are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard (^{1}H NMR $CDCl_3$: δ 7.27, DMSO-d_6: δ 2.50; ^{13}C NMR $CDCl_3$: δ 77.23, DMSO-d_6: δ 39.51) or fluorobenzene (^{19}F NMR C_6H_5F: δ -113.15) as external standard. ^{13}C NMR spectra were recorded with complete proton decoupling. Due to the existence of tautomers, some ^{13}C NMR signals could not be detected for most of the NH_2 amidines and NH benzimidazoles. Only distinct signals are reported. Infrared (IR) spectra were recorded on a Perkin Elmer System 2000 FT-IR spectrophotometer. Melting points (mp) were taken on a MEL-TEMP® apparatus and are uncorrected. Gas chromatographic (GC) analyses were performed with a Hewlett-Packard 6890 Series GC System with a capillary column with cross-linked methyl siloxane as the stationary phase (25 m × 0.20 mm). GC conversions and GC yields were calculated using dodecane as internal standard. Analytical high performance liquid chromatography (HPLC) was performed on an Agilent 1100/1200 Series HPLC System with an Agilent Eclipse XDB-C18 5 μm stationary phase (150 × 4.6 mm). Microanlyses were carried out by Atlantic Microlab, Inc. (Norcross, GA). In cases where microanalyses were not performed or satisfactory results were not obtained, the ^{1}H NMR and ^{13}C NMR are attached.

Preparation and Analytical Data of Chemical Compounds



2-(*tert*-Butyldimethylsilyl)benzonitrile. Under a positive N_2 pressure, a dry round bottom flask (200 mL in volume) equipped with a stir bar was charged with 2-iodobenzonitrile (4.58 g, 20.0 mmol) and sealed with a rubber septum. Dry THF (60 mL) was added by syringe, and the solution cooled to -78 °C. *t*BuLi (29.4 mL, 50.0 mmol, 2.50 equiv, 1.7 M in pentane) was then slowly added by syringe. After addition was complete, the mixture was stirred for 15 min at -78 °C, before a solution of TBSCl (3.92 g, 26.0 mmol, 1.30 equiv) in THF (10 mL) was added by syringe. After a further 20 min at -78 °C, the cooling bath was removed and the reaction mixture was allowed to warm to room temperature. Water (150 mL) and hexanes (50 mL) were consecutively added. The organic layer was separated and the aqueous layer extracted with hexanes (2 × 100 mL). The combined organic phases were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by silica gel chromatography (Hex/EtOAc, gradient 0% to 4% EtOAc) to give the title compound as a dark oil, yield 1.96 g (45%, GC: 92% purity). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.67 (dq, *J* = 7.5, 0.8 Hz, 1H), 7.58 (dq, *J* = 7.5, 0.8 Hz, 1H), 7.52 (td, *J* = 7.5, 1.5 Hz, 1H), 7.42 (td, *J* = 7.5, 1.5 Hz, 1H), 0.91 (s, 9H), 0.44 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.44, 136.34, 134.18, 131.31, 129.25, 120.91, 118.14, 26.79, 18.10, -4.78. IR (KBr plate, $CDCl_3$) ν 3058, 2955, 2929, 2858, 2223, 1584, 1470, 1429, 1363, 1260, 1126, 1072, 1008, 938, 840, 824, 764, 726, 685, 653, 589, 558, 472, 406.

General Procedures for the Synthesis of Amidines from Anilines and Carbonitriles

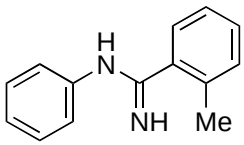
Procedure A. A round bottom flask (100 mL in volume) equipped with a stir bar was charged with NaH (264 mg, 11.0 mmol, 95%, 1.10 equiv) in the glove box. The flask was sealed with a rubber septum and taken out of the glove box. Under a stream of nitrogen, DMSO (5 mL) was added, and the resulting suspension cooled with an ice-water bath prior to the addition of the aniline (12.0 mmol, 1.20 equiv) and the carbonitrile (10.0 mmol). The mixture was kept at 0 °C for 30-60 min and then stirred for the indicated time at room temperature. The septum was removed, and ice-water (50 mL) was added while maintaining vigorous stirring. In the cases, when the amidine precipitated upon

addition of water, the solid was filtered off and dissolved in EtOAc (20 mL). In all other cases, the aqueous layer was extracted with EtOAc (3 × 20 mL). The extracts were combined and washed with water (2 × 50 mL). In both of the aforementioned cases, the organic layer was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was either purified by silica gel chromatography or recrystallization.

Procedure B. Under an air atmosphere, a pressure flask (75 mL in volume) equipped with a stir bar was charged with the aniline (12.0 mmol, 1.20 equiv) and the carbonitrile (10.0 mmol). $AlCl_3$ (1.33 g, 10.0 mmol, 1.00 equiv) was added in one portion while stirring the reaction mixture. The flask was tightly sealed with a screw cap and lowered into a preheated oil bath at 120 °C. The reaction mixture was stirred for the indicated time, and taken out of the oil bath. Ice-water (50 mL) was then added to the hot mixture while maintaining vigorous stirring. If necessary, the mixture was warmed with a heat gun to obtain a homogenous aqueous solution, before it was transferred into a separatory funnel. Concentrated aqueous NaOH was added until a pH of 14 was reached,[a] and the aqueous layer was extracted with $CHCl_3$ (3 × 30 mL). *(Caution: Addition of $CHCl_3$ to base may cause a vigorous reaction. Allow the aqueous layer to cool to room temperature before the extraction with $CHCl_3$.)* The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was either purified by silica gel chromatography or recrystallization.

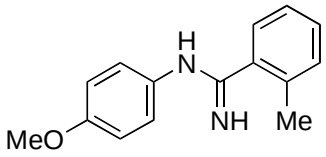
[a] In case of the *tert*-butyl amdines, the aqueous phase was washed with $CHCl_3$ (3 × 30 mL) prior to the addition of concentrated aqueous NaOH.

Analytical Data of the Amidines

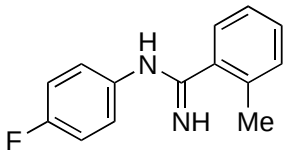


***N*-Phenyl-2-methylbenzamidine.**[1] Following representative procedure A, after 15 h reaction time and recrystallization (Hex/EtOAc), white crystals were obtained, yield 1.82 g (87%, mp 127 °C). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.54-7.14 (m, 6H), 7.00 (s, 3H), 4.77 (s, 2H), 2.50 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 130.86, 130.25, 129.36, 127.99, 125.93, 123.01, 121.88, 19.83. IR (KBr plate, $CDCl_3$) ν 3435, 3288, 3069, 2717, 1637,

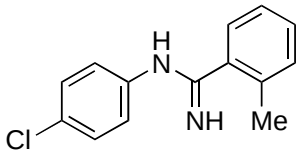
1588, 1484, 1456, 1382, 1279, 1245, 1071, 1039, 1023, 907, 842, 780, 768, 729, 697, 658, 520, 507, 459 cm^{-1}. Anal. Calcd. for $C_{14}H_{14}N_2$: C, 79.97; H, 6.71; Found: C, 80.10; H, 6.70.



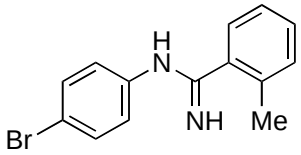
***N*-(4-Methoxyphenyl)-2-methylbenzamidine.** Following representative procedure A, after 15 h reaction time and recrystallization (Hex/EtOAc), a gray powder was obtained, yield 1.84 g (77%, mp 116 °C). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43 (s, 1H), 7.35-7.12 (m, 3H), 7.08-6.52 (m, 4H), 4.78 (s, 2H), 3.78 (s, 3H), 2.49 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 130.82, 129.29, 127.99, 125.92, 122.81, 114.73, 55.59, 19.82. IR (KBr plate, $CDCl_3$) ν 3437, 3287, 3062, 2954, 2834, 1639, 1503, 1455, 1441, 1376, 1286, 1240, 1180, 1103, 1035, 858, 833, 821, 784, 765, 738, 531, 465 cm^{-1}. Anal. Calcd. for $C_{15}H_{16}N_2O$: C, 74.97; H, 6.71; Found: C, 75.10; H, 6.71.



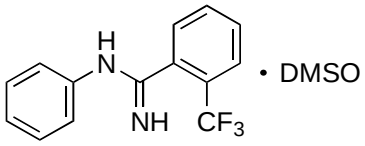
***N*-(4-Fluorophenyl)-2-methylbenzamidine.** Following representative procedure A, after 15 h reaction time and silica gel chromatography (Hex/EtOAc, gradient 12% to 100% EtOAc), a brownish solid was obtained, yield 1.86 g (81%, mp 92 °C). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.58-7.14 (m, 4H), 7.12-6.62 (m, 4H), 4.91 (s, 2H), 2.47 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 130.86, 129.44, 128.01, 125.96, 123.00, 116.18, 19.81. ^{19}F NMR (282 MHz, $CDCl_3$) δ -121.19 (s). IR (KBr plate, $CDCl_3$) ν 3435, 3287, 3104, 1625, 1592, 1497, 1444, 1384, 1212, 1149, 1090, 864, 845, 821, 793, 769, 752, 705, 521, 478 cm^{-1}. Anal. Calcd. for $C_{14}H_{13}FN_2$: C, 73.66; H, 5.74; Found: C, 73.65; H, 5.68.



***N*-(4-Chlorophenyl)-2-methylbenzamidine.** Following representative procedure A, after 15 h reaction time and recrystallization (Hex/EtOAc), an off-white solid was obtained, yield 2.04 g (83%, mp 119 °C). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.64-7.04 (m, 6H), 6.90 (s, 2H), 4.79 (s, 2H), 2.47 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 130.90, 129.52, 127.98, 125.98, 123.34, 19.82. IR (KBr plate, $CDCl_3$) ν 3433, 3285, 3064, 2718, 1623, 1599, 1585, 1484, 1444, 1385, 1245, 1168, 1098, 1043, 10101, 861, 815, 770, 730, 678, 513, 460 cm^{-1}. Anal. Calcd. for $C_{14}H_{13}ClN_2$: C, 68.71; H, 5.35; Found: C, 68.73; H, 5.32.

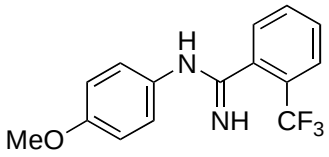


***N*-(4-Bromophenyl)-2-methylbenzamidine.** Following representative procedure A, after 15 h reaction time and recrystallization (Hex/EtOAc), gray crystals were obtained, yield 2.08 g (72%, mp 135 °C). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.64-7.08 (m, 6H), 6.84 (s, 2H), 4.75 (s, 2H), 2.47 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 130.93, 129.57, 128.00, 126.00, 123.80, 19.85. IR (KBr plate, $CDCl_3$) ν 3444, 3288, 3063, 1635, 1580, 1481, 1455, 1377, 1243, 1098, 1070, 1007, 859, 831, 809, 768, 731, 664, 511 cm^{-1}. Anal. Calcd. for $C_{14}H_{13}BrN_2$: C, 58.15; H, 4.53; Found: C, 57.92; H, 4.50.

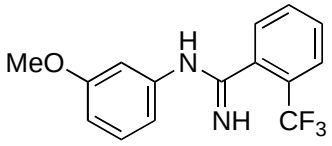


***N*-Phenyl-2-(trifluoromethyl)benzamidine DMSO adduct.** Following representative procedure A, after 16 h reaction time and recrystallization (Hex/EtOAc), orange crystals were obtained, yield 2.99 g (87%, mp 96-99 °C). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.13 (d, *J* = 7.8 Hz, 1H), 7.70-7.47 (m, 3H), 7.42-7.26 (m, 2H), 7.12-6.92 (m, 3H), 2.57 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 132.13, 130.25, 130.11, 129.61, 129.54, 128.25, 127.84, 126.67, 126.60, 126.53, 126.47, 123.37, 121.53, 41.07. ^{19}F NMR (282 MHz, $CDCl_3$) δ -58.32 (s). IR (KBr plate, $CDCl_3$) ν 3303, 1643, 1592, 1486, 1448, 1377, 1316, 1271,

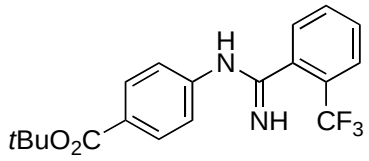
1239, 1175, 1131, 1052, 1035, 953, 909, 837, 774, 700, 669, 646, 599, 524 cm^{-1}. Anal. Calcd. for $C_{16}H_{17}F_3N_2OS$: C, 56.13; H, 5.00; Found: C, 56.26; H, 4.96.



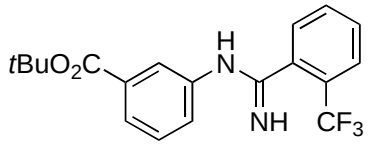
***N*-(4-Methoxyphenyl)-2-(trifluoromethyl)benzamidine.** Following representative procedure A, after 15 h reaction time and recrystallization (Hex/EtOAc), brown needles were obtained, yield 2.50 g (85%, mp 130-131 °C). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.72 (d, *J* = 7.5 Hz, 1H), 7.70-7.48 (m, 3H), 7.06-6.78 (m, 4H), 4.89 (s, 2H), 3.79 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.89, 132.17, 130.16, 129.54, 126.70, 126.63, 126.56, 126.50, 122.53, 114.95, 55.63. ^{19}F NMR (282 MHz, $CDCl_3$) δ -58.36 (s). IR (KBr plate, $CDCl_3$) ν 3291, 3069, 2837, 1643, 1504, 1467, 1379, 1316, 1289, 1272, 1239, 1173, 1130, 1052, 1035, 860, 809, 769, 742, 712, 661, 598, 534 cm^{-1}. Anal. Calcd. for $C_{15}H_{13}F_3N_2O$: C, 61.22; H, 4.45; Found: C, 61.31; H, 4.27.



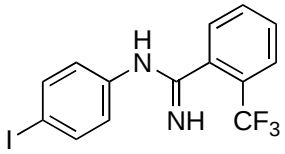
***N*-(3-Methoxyphenyl)-2-(trifluoromethyl)benzamidine.** Following representative procedure A, after 15 h reaction time and silica gel chromatography (Hex/EtOAc, gradient 12% to 100% EtOAc), a red solid was obtained, yield 2.63 g (89%, mp 80-82 °C). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.72 (d, *J* = 7.8 Hz, 1H), 7.70-7.48 (m, 3H), 7.24 (t, *J* = 7.8 Hz, 1H), 6.72-6.48 (m, 3H), 4.91 (m, 2H), 3.80 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 132.18, 130.40, 130.12, 129.64, 128.28, 127.86, 126.71, 126.65, 126.58, 126.52, 113.78, 109.17, 107.16, 55.36. ^{19}F NMR (282 MHz, $CDCl_3$) δ -58.31 (s). IR (KBr plate, $CDCl_3$) ν 3453, 3291, 3071, 2837, 1644, 1594, 1485, 1451, 1435, 1377, 1316, 1283, 1199, 1174, 1130, 1052, 1036, 928, 860, 771, 697, 675, 648, 599, 459 cm^{-1}. Anal. Calcd. for $C_{15}H_{13}F_3N_2O$: C, 61.22; H, 4.45; Found: C, 61.06; H, 4.33.



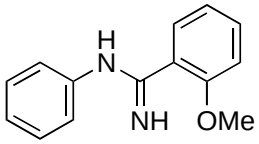
***N*-(4-*tert*-Butoxycarbonylphenyl)-2-(trifluoromethyl)benzamidine.** Following representative procedure A, after 15 h reaction time and recrystallization (Hex/EtOAc), light yellow crystals were obtained, yield 3.02 g (83%, mp 181-182 °C). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.94 (s, 2H), 7.76-7.42 (m, 4H), 6.98 (s, 2H), 4.86 (s, 2H), 1.56 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.93, 132.23, 131.41, 130.05, 129.82, 126.74, 126.68, 121.27, 80.82, 28.41. ^{19}F NMR (282 MHz, $CDCl_3$) δ -58.65 (s). IR (KBr plate, $CDCl_3$) ν 3407, 3192, 2978, 1704, 1648, 1597, 1501, 1368, 1315, 1254, 1162, 1122, 1052, 1035, 871, 852, 768, 707, 650 cm^{-1}. Anal. Calcd. for $C_{19}H_{19}F_3N_2O_2$: C, 62.63; H, 5.26; Found: C, 62.78; H, 5.21.



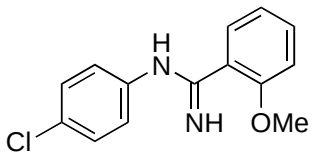
***N*-(3-*tert*-Butoxycarbonylphenyl)-2-(trifluoromethyl)benzamidine.** Following representative procedure A, after 15 h reaction time and silica gel chromatography (Hex/EtOAc, gradient 12% to 60% EtOAc), a glassy solid was obtained, yield 2.20 g (60%, no mp). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.84-7.47 (m, 6H), 7.46-7.32 (m, 1H), 7.22-7.08 (m, 1H), 4.89 (s, 2H), 1.59 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.91, 132.18, 130.09, 129.71, 128.30, 127.88, 126.74, 126.67, 126.61, 126.54, 125.95, 124.48, 122.44, 81.17, 28.32. ^{19}F NMR (282 MHz, $CDCl_3$) δ -58.28 (s). IR (KBr plate, $CDCl_3$) ν 3457, 3353, 3070, 2980, 2934, 1711, 1644, 1594, 1478, 1451, 1431, 1370, 1316, 1273, 1258, 1230, 1173, 1132, 1078, 1052, 1035, 933, 918, 850, 833, 769, 751, 734, 701, 677, 646, 599 cm^{-1}. Anal. Calcd. for $C_{19}H_{19}F_3N_2O_2$: C, 62.63; H, 5.26; Found: C, 62.43; H, 5.16.



***N*-(4-Iodophenyl)-2-(trifluoromethyl)benzamidine.** Following representative procedure A, after 16 h reaction time and recrystallization (Hex/EtOAc), gray needles were obtained, yield 3.20 g (82%, mp 139 °C). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.73 (d, *J* = 7.8 Hz, 1H), 7.70-7.49 (m, 5H), 6.76 (s, 2H), 4.84 (s, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.63, 132.24, 130.05, 129.83, 126.82, 126.75, 126.69, 126.62, 123.93, 86.92. ^{19}F NMR (282 MHz, $CDCl_3$) δ -58.34 (s). IR (KBr plate, $CDCl_3$) ν 3442, 3288, 3065, 1646, 1604, 1576, 1479, 1451, 1383, 1315, 1270, 1241, 1175, 1125, 1051, 1034, 1004, 864, 804, 768, 711, 670, 647, 602, 510 cm^{-1}. Anal. Calcd. for $C_{14}H_{10}F_3IN_2$: C, 43.10; H, 2.58; Found: C, 43.16; H, 2.53.

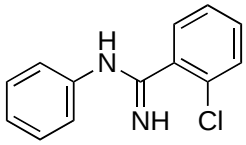


***N*-Phenyl-2-methoxybenzamidine.** Following representative procedure A, after 17 h reaction time and silica gel chromatography (Hex/EtOAc, gradient 12% to 100% EtOAc), a red oil was obtained, which crystallized after a while at room temperature to give a red solid, yield 2.12 g (94%, mp 71-78 °C). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.28-8.15 (m, 1H), 7.48-7.28 (m, 3H), 7.14-6.92 (m, 5H), 5.59 (s, 2H), 3.92 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 131.65, 131.41, 129.64, 123.78, 122.83, 122.04, 111.65, 55.99. IR (KBr plate, $CDCl_3$) ν 3488, 3381, 3074, 2838, 1626, 1587, 1489, 1464, 1437, 1367, 1275, 1240, 1182, 1163, 1100, 1047, 1023, 906, 823, 753, 699, 648, 517 cm^{-1}. Anal. Calcd. for $C_{14}H_{14}N_2O$: C, 74.31; H, 6.24; Found: C, 74.08; H, 6.16.

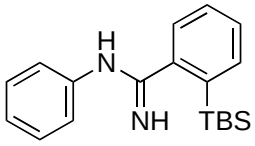


***N*-(4-Chlorophenyl)-2-methoxybenzamidine.** Following representative procedure A, after 14 h reaction time and recrystallization (Hex/EtOAc), red crystals were obtained, yield 2.22 g (85%, mp 94 °C). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.12 (s, 1H), 7.42 (td, *J* =

7.5, 1.8 Hz, 1H), 7.28 (d, *J* = 8.4 Hz, 2H), 7.06 (t, *J* = 7.5 Hz, 1H), 6.97 (d, *J* = 8.4 Hz, 1H), 6.91 (d, *J* = 8.4 Hz, 2H), 5.57 (s, 2H), 3.90 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 131.85, 131.23, 129.59, 127.88, 123.47, 123.32, 121.41, 111.65, 55.97. IR (KBr plate, $CDCl_3$) ν 3490, 3383, 3078, 2940, 2838, 1627, 1484, 1464, 1437, 1369, 1301, 1275, 1241, 1181, 1164, 1091, 1047, 1024, 1010, 859, 832, 804, 753, 675, 514 cm^{-1}. Anal. Calcd. for $C_{14}H_{14}ClN_2O$: C, 64.49; H, 5.03; Found: C, 64.33; H, 4.98.



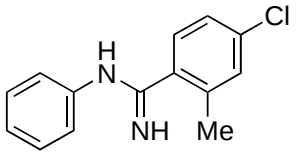
***N*-Phenyl-2-chlorobenzamidine.**[1] Following representative procedure A, after 14 h reaction time and silica gel chromatography (Hex/EtOAc, gradient 12% to 100% EtOAc), a yellow solid was obtained, yield 2.20 g (95%, mp 104-105 °C). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.71 (s, 1H), 7.52-6.78 (m, 8H), 4.94 (s, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 130.75, 130.22, 129.75, 127.22, 123.43, 122.05, 121.72. IR (KBr plate, $CDCl_3$) ν 3449, 3290, 3074, 1639, 1590, 1486, 1434, 1375, 1237, 1070, 1049, 1033, 907, 837, 763, 699, 648, 505 cm^{-1}. Anal. Calcd. for $C_{13}H_{11}ClN_2$: C, 67.68; H, 4.81; Found: C, 67.76; H, 4.94.



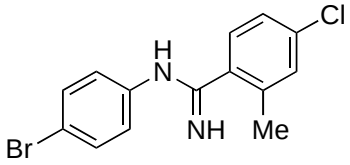
***N*-Phenyl-2-(*tert*-butyldimethylsilyl)benzamidine.** Due to the instability of the amidine containing the TBS group, a modified procedure A was used.

A round bottom flask (100 mL in volume) equipped with a stir bar was charged with NaH (119 mg, 4.95 mmol, 95%, 1.10 equiv) in the glove box. The flask was sealed with a rubber septum and taken out of the glove box. Under a stream of nitrogen, DMSO (5 mL) was added, and the suspension cooled to 0 °C using an immersion cooler. Aniline (492 μL, 5.40 mmol, 1.20 equiv) and 2-(*tert*-butyldimethylsilyl)benzonitrile (978 mg, 4.50 mmol) were added, and the mixture was stirred at 0 °C for 48 h. The septum was removed, and water (50 mL) was added, followed by extraction of the aqueous layer with EtOAc (3 × 30 mL). The combined extracts were washed with water (2 × 30 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by silica gel chromatography (Hex/EtOAc, gradient 12% to 50% EtOAc) to give the

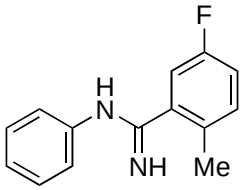
amidine as a brown solid, yield 192 mg (14%, mp 108-112 °C) and 496 mg of reisolated 2-(*tert*-butyldimethylsilyl)benzonitrile. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.69-7.58 (m, 1H), 7.57-7.29 (m, 5H), 7.24-6.98 (m, 3H), 4.96 (bs, 2H), 0.98 (s, 9H), 0.40 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 136.91, 129.58, 129.03, 128.49, 127.90, 123.18, 121.60, 27.54, 17.99, -3.28. IR (KBr plate, $CDCl_3$) ν 3434, 3285, 3054, 2952, 2930, 2857, 1621, 1585, 1558, 1482, 1431, 1380, 1254, 1119, 1072, 906, 837, 826, 813, 774, 735, 701, 670, 525, 511, 469, 417 cm^{-1}.



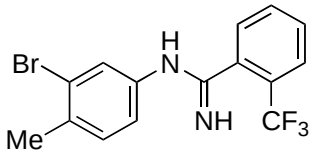
***N*-Phenyl-4-chloro-2-methylbenzamidine.** Following representative procedure A, after 14 h reaction time and silica gel chromatography (Hex/EtOAc, gradient 12% to 100% EtOAc), an off-white solid was obtained, yield 0.82 g (34%, mp 104-105 °C). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.46-7.14 (m, 5H), 7.10-6.84 (m, 3H), 4.88 (s, 2H), 2.45 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 135.04, 130.79, 129.42, 126.12, 123.27, 121.79, 19.78. IR (KBr plate, $CDCl_3$) ν 3437, 3284, 3077, 1636, 1587, 1484, 1448, 1406, 1371, 1237, 1200, 1112, 909, 882, 815, 743, 699, 596, 516 cm^{-1}. Anal. Calcd. for $C_{14}H_{13}ClN_2$: C, 68.71; H, 5.35; Found: C, 68.57; H, 5.36.



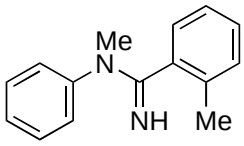
***N*-(4-Bromophenyl)-4-chloro-2-methylbenzamidine.** Following representative procedure A, after 17 h reaction time and silica gel chromatography (Hex/EtOAc, gradient 12% to 100% EtOAc), an off-white solid was obtained, yield 1.76 g (54%, mp 129 °C). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.62-7.06 (m, 5H), 6.80 (s, 2H), 4.91 (s, 2H), 2.44 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 135.23, 132.53, 130.83, 129.34, 126.17, 123.68, 19.76. IR (KBr plate, $CDCl_3$) ν 3432, 3291, 2983, 1639, 1579, 1480, 1446, 1401, 1374, 1242, 1202, 1171, 1111, 1068, 1007, 883, 861, 841, 828, 771, 735, 687, 632, 577, 519 cm^{-1}. Anal. Calcd. for $C_{14}H_{12}BrClN_2$: C, 51.96; H, 3.74; Found: C, 52.19; H, 3.70.



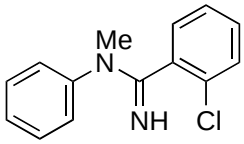
***N*-Phenyl-5-fluoro-2-methylbenzamidine.** Following representative procedure A, after 14 h reaction time and silica gel chromatography (Hex/EtOAc, gradient 12% to 100% EtOAc), a yellow solid was obtained, yield 2.12 g (93%, mp 92 °C). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.48-6.82 (m, 8H), 4.81 (s, 2H), 2.45 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.54, 132.43, 132.33, 129.58, 123.26, 121.77, 116.35, 116.08, 115.14, 114.84, 19.08. ^{19}F NMR (282 MHz, $CDCl_3$) δ -117.24 (s). IR (KBr plate, $CDCl_3$) ν 3447, 3287, 3076, 1591, 1498, 1432, 1361, 1266, 1222, 1185, 1070, 1025, 998, 929, 906, 877, 836, 816, 770, 735, 698, 514, 458 cm^{-1}. Anal. Calcd. for $C_{14}H_{13}FN_2$: C, 73.66; H, 5.74; Found: C, 73.53; H, 5.68.



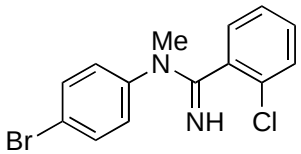
***N*-(3-Bromo-4-methylphenyl)-2-(trifluoromethyl)benzamidine.** Following representative procedure A, after 15 h reaction time and recrystallization (Hex/EtOAc), orange needles were obtained, yield 3.12 g (87%, mp 139 °C). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.72 (d, J = 7.5 Hz, 1H), 7.69-7.48 (m, 3H), 7.18 (s, 2H), 6.93-6.76 (m, 1H), 4.90 (s, 2H), 2.36 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 132.20, 131.69, 130.04, 129.74, 128.27, 127.85, 126.76, 126.70, 126.63, 126.56, 125.10, 120.72, 22.42. ^{19}F NMR (282 MHz, $CDCl_3$) δ -58.34 (s). IR (KBr plate, $CDCl_3$) ν 3485, 3146, 1614, 1597, 1579, 1484, 1367, 1316, 1271, 1234, 1182, 1133, 1111, 1053, 1034, 960, 891, 879, 827, 771, 698, 641, 600, 576, 485, 406, 438 cm^{-1}. Anal. Calcd. for $C_{15}H_{12}BrF_3N_2$: C, 50.44; H, 3.39; Found: C, 50.47; H, 3.34.



***N*-Methyl,*N*-phenyl-2-methylbenzamidine.** Following representative procedure B, after 30 min reaction time and silica gel chromatography (Hex/EtOAc, gradient 12% to 100% EtOAc), a red oil was obtained, yield 1.66 g (74%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.22-6.98 (m, 9H), 6.70-5.80 (bs, 1H), 3.47 (s, 3H), 2.25 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.09, 145.71, 138.73, 134.08, 130.26, 128.72, 128.51, 128.15, 126.49, 125.65, 125.42, 39.05, 19.64. IR (KBr plate) ν 3314, 3062, 2954, 1576, 1496, 1441, 1386, 1321, 1285, 1173, 1115, 1028, 1006, 990, 945, 906, 859, 813, 773, 732, 699, 643, 588, 547, 532, 465 cm^{-1}.

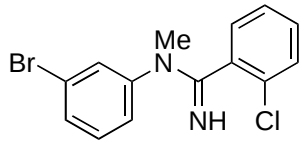


***N*-Methyl,*N*-phenyl-2-chlorobenzamidine.** Following representative procedure B, after 20 min reaction time and silica gel chromatography (Hex/EtOAc, gradient 12% to 100% EtOAc), a purple solid was obtained, yield 1.99 g (81%, mp 75-76 °C). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.23-6.98 (m, 9H), 6.06 (bs, 1H), 3.45 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.05, 145.41, 137.73, 131.03, 129.69, 129.65, 129.57, 128.80, 126.67, 126.57, 125.81, 38.91. IR (KBr plate, $CDCl_3$) ν 3659, 3319, 3059, 2939, 2902, 1950, 1587, 1496, 1436, 1388, 1321, 1262, 1180, 1106, 1056, 1034, 991, 948, 909, 856, 764, 739, 700, 637, 585, 537, 469, 435, 416 cm^{-1}. Anal. Calcd. for $C_{14}H_{13}ClN_2$: C, 68.71; H, 5.35; Found: C, 68.76; H, 5.33.

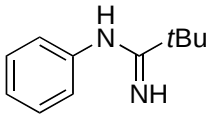


***N*-(4-Bromophenyl),*N*-methyl-2-chlorobenzamidine.** Following representative procedure B, after 30 min reaction time and silica gel chromatography (Hex/EtOAc, gradient 12% to 100% EtOAc), a brownish solid was obtained, yield 2.63 g (81%, mp 88 °C). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.29-7.08 (m, 6H), 6.95 (dt, *J* = 8.7, 2.1 Hz, 2H), 6.74-6.10

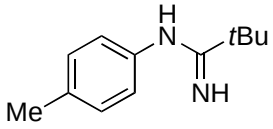
(bs, 1H), 3.42 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.93, 144.61, 137.46, 131.94, 131.00, 130.03, 129.94, 129.56, 128.23, 126.87, 119.11, 38.93. IR (KBr plate, $CDCl_3$) ν 3318, 3058, 1601, 1580, 1491, 1438, 1383, 1322, 1263, 1180, 1104, 1055, 1034, 1010, 995, 855, 831, 766, 743, 714, 695, 644, 584, 538, 440 cm^{-1}. Anal. Calcd. for $C_{14}H_{13}BrClN_2$: C, 51.96; H, 3.74; Found: C, 51.91; H, 3.65.



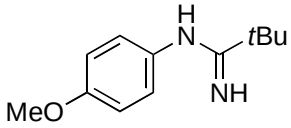
***N*-(3-Bromophenyl),*N*-methyl-2-chlorobenzamidine.** Following representative procedure B, after 30 min reaction time and silica gel chromatography (Hex/EtOAc, gradient 12% to 100% EtOAc), a gray oil was obtained, yield 2.75 g (85%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.30-7.11 (m, 6H), 7.05-6.97 (m, 2H), 6.84-5.92 (bs, 1H), 3.44 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.92, 146.77, 137.32, 131.05, 130.09, 130.00, 129.92, 129.60, 129.53, 128.77, 126.88, 125.25, 122.10, 38.92. IR (KBr plate) ν 3659, 3317, 3060, 2959, 1929, 1599, 1435, 1322, 1263, 1181, 1110, 1056, 1037, 1000, 948, 869, 768, 696, 658, 636, 601, 469, 444, 417 cm^{-1}. Anal. Calcd. for $C_{14}H_{13}BrClN_2$: C, 51.96; H, 3.74; Found: C, 51.93; H, 3.78.



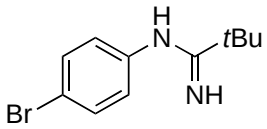
***N*-Phenyl-*tert*-butylamidine.** Following representative procedure B, except that the scale was 20 mmol instead of 10 mmol and the reaction temperature was 140 °C, after 40 min reaction time and recrystallization (Hex), gray needles were obtained, yield 1.98 g (56%, mp 102 °C). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.34-7.26 (m, 2H), 7.03-6.97 (m, 1H), 6.88-6.81 (m, 2H), 4.39 (s, 2H), 1.30 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.44, 150.30, 129.58, 122.68, 121.79, 36.94, 28.70. IR (KBr plate, $CDCl_3$) ν 3500, 3396, 2958, 1630, 1589, 1477, 1398, 1346, 1253, 1217, 1069, 912, 830, 774, 727, 697, 535, 495 cm^{-1}. Anal. Calcd. for $C_{11}H_{16}N_2$: C, 74.96; H, 9.15; Found: C, 74.83; H, 9.14.



***N*-(4-Methylphenyl)-*tert*-butylamidine.** Following representative procedure B, except that the scale was 20 mmol instead of 10 mmol and the reaction temperature was 140 °C, after 40 min reaction time and recrystallization (Hex), yellow crystals were obtained, yield 2.24 g (59%, mp 106-107 °C). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.13-7.07 (m, 2H), 6.72 (dt, *J* = 8.1, 2.1 Hz, 2H), 4.40 (s, 2H), 2.30 (s, 3H), 1.29 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.58, 147.48, 131.87, 130.14, 121.60, 36.92, 28.71, 20.99. IR (KBr plate, $CDCl_3$) ν 3500, 3387, 2961, 1591, 1505, 1478, 1396, 1347, 1256, 1219, 1105, 909, 872, 851, 815, 767, 734, 524, 497 cm^{-1}. Anal. Calcd. for $C_{12}H_{18}N_2$: C, 75.74; H, 9.53; Found: C, 75.85; H, 9.54.



***N*-(4-Methoxyphenyl)-*tert*-butylamidine.** Following representative procedure A, after 15 h reaction time and silica gel chromatography (Hex/EtOAc, gradient 12% to 100% EtOAc), a red solid was obtained, yield 0.77 g (37%, mp 103-104 °C). ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.85 (dt, *J* = 9.0, 2.7 Hz, 2H), 6.75 (dt, *J* = 9.0, 2.7 Hz, 2H), 4.40 (s, 2H), 3.77 (s, 3H), 1.28 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.99, 155.38, 143.21, 122.63, 114.86, 55.59, 36.92, 28.71. IR (KBr plate, $CDCl_3$) ν 3464, 3423, 3321, 2965, 2833, 1598, 1503, 1482, 1464, 1400, 1353, 1287, 1238, 1182, 1163, 1100, 1070, 1037, 909, 878, 857, 818, 777, 735, 712, 522, 464 cm^{-1}. Anal. Calcd. for $C_{12}H_{19}N_2O$: C, 69.87; H, 8.80; Found: C, 69.73; H, 8.81.



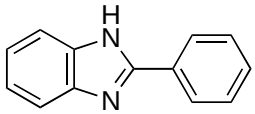
***N*-(4-Bromophenyl)-*tert*-butylamidine.** Following representative procedure B, except that the scale was 20 mmol instead of 10 mmol and the reaction temperature was 140 °C, after 40 min reaction time and recrystallization (Hex), white needles were obtained, yield 2.86 g (56%, mp 123 °C). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.39 (dt, *J* = 8.7, 2.4 Hz, 2H), 6.71 (dt, *J* = 8.7, 2.4 Hz, 2H), 4.39 (s, 2H), 1.28 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ

164.83, 149.47, 132.56, 123.70, 115.42, 37.01, 28.65. IR (KBr plate, $CDCl_3$) ν 3501, 3381, 2960, 1647, 1621, 1595, 1475, 1395, 1365, 1345, 1256, 1215, 1093, 1068, 1005, 871, 848, 804, 644, 543, 504, 466 cm^{-1}. Anal. Calcd. for $C_{11}H_{15}BrN_2$: C, 51.78; H, 5.93; Found: C, 51.77; H, 5.92.

General Procedure for the Synthesis of Benzimidazoles from Amidines

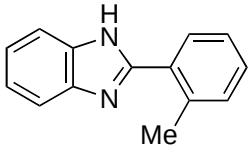
An oven-dried disposable test tube (15 mL in volume) equipped with a stir bar and a rubber septum was cooled to room temperature under vacuum and backfilled with O_2. With the tube open to the air, the amidine (1.00 mmol) and $Cu(OAc)_2$ (27.2 mg, 0.15 mmol, 15 mol%) were added. The tube was evacuated and backfilled with O_2, followed by addition of DMSO (2 mL) by syringe. The reaction mixture was degassed by sonication under vacuum and backfilled with O_2 (this procedure was carried out three times). An O_2-filled balloon was attached to a needle with the aid of a small piece of rubber tubing. The needle was inserted through the rubber septum, and HOAc (286 μL, 5.00 mmol, 5.00 equiv) was added by syringe. The reaction mixture was lowered into a preheated oil bath at 100 °C and stirred for the indicated time. After allowing the reaction mixture to cool to room temperature, the septum was removed and ethyl acetate (8 mL), distilled water (4 mL), and aqueous 30% NH_4OH (4 mL) were added. The aqueous layer was extracted with ethyl acetate (2 × 8 mL). In a round bottom flask (50 mL in volume) equipped with a stir bar, the combined organic layers were stirred with activated charcoal (5-20 mg, NORIT CN1, decolorizing from Acros Organics) for 10-15 min, before being dried over $MgSO_4$, filtered through Celite, and concentrated under reduced pressure. The residue was purified by silica gel chromatography.

Analytical Data of the Benzimidazoles

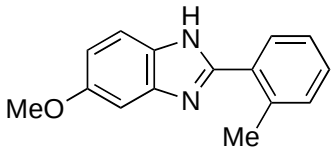


2-Phenylbenzimidazole. Following the representative procedure, after 18 h reaction time and silica gel chromatography (Hex/EtOAc, gradient 12% to 60% EtOAc), a brownish solid was obtained, yield 123 mg (63%, mp 286-289 °C). ^{1}H NMR (300 MHz, DMSO-

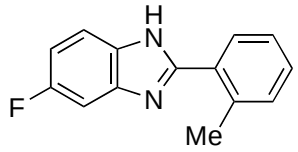
d_6) δ 12.94 (s, 1H), 8.23-8.15 (m, 2H), 7.76-7.44 (m, 5H), 7.26-7.16 (m, 2H). The ^{1}H NMR is identical to a sample of 2-phenylbenzimidazole purchased from Acros Organics.



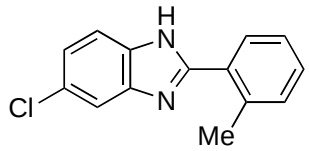
2-(2-Methylphenyl)benzimidazole.[2] Following the representative procedure, after 18 h reaction time and silica gel chromatography (Hex/EtOAc, gradient 12% to 60% EtOAc), a white solid was obtained, yield 185 mg (89%, mp 223-224 °C). ^{1}H NMR (300 MHz, DMSO-d_6) δ 12.67 (s, 1H), 7.79-7.72 (m, 1H), 7.72-7.44 (m, 2H), 7.43-7.31 (m, 3H), 7.26-7.16 (m, 2H), 2.62 (s, 3H). ^{13}C NMR (75 MHz, DMSO-d_6) δ 151.99, 137.05, 131.30, 130.11, 129.48, 129.34, 125.99, 21.11. IR (KBr pellet) ν 2872, 1592, 1542, 1449, 1407, 1370, 1315, 1275, 1229, 1099, 972, 765, 742, 726, 454 cm^{-1}. Anal. Calcd. for $C_{14}H_{12}N_2$: C, 80.74; H, 5.81; Found: C, 80.68; H, 5.81.



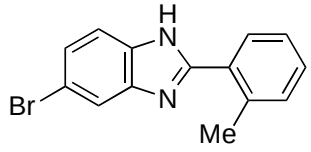
5-Methoxy-2-(2-methylphenyl)benzimidazole. Following the representative procedure, after 18 h reaction time and silica gel chromatography (Hex/EtOAc, gradient 12% to 60% EtOAc), an orange solid was obtained, yield 166 mg (70%, mp 135 °C). ^{1}H NMR (300 MHz, DMSO-d_6) δ 12.49 (s, 1H), 7.77-6.78 (m, 7H), 3.80 (s, 3H), 2.61 (s, 3H). ^{13}C NMR (75 MHz, DMSO-d_6) δ 136.85, 131.31, 130.19, 129.26, 129.10, 125.98, 55.46, 21.19. IR (KBr pellet) ν 2959, 1630, 1592, 1542, 1459, 1404, 1322, 1267, 1199, 1158, 1115, 1095, 1029, 972, 826, 771, 728, 671, 629, 569, 454 cm^{-1}. Anal. Calcd. for $C_{14}H_{15}N_2O$: C, 75.61; H, 5.92; Found: C, 75.37; H, 5.93.



5-Fluoro-2-(2-methylphenyl)benzimidazole. Following the representative procedure, after 18 h reaction time and silica gel chromatography (Hex/EtOAc, gradient 12% to 80% EtOAc), a white powder was obtained, yield 194 mg (86%, mp 198 °C). ^{1}H NMR (300 MHz, DMSO-d_6) δ 12.78 (s, 1H), 7.78-7.28 (m, 6H), 7.14-7.00 (m, 1H), 2.60 (s, 3H). ^{13}C NMR (75 MHz, DMSO-d_6) δ 137.06, 131.35, 129.78, 129.51, 129.45, 126.04, 21.08. ^{19}F NMR (282 MHz, DMSO-d_6) δ -119.21 (s), -121.11 (s). IR (KBr pellet) ν 2667, 1631, 1602, 1491, 1448, 1410, 1363, 1309, 1258, 1220, 1144, 1112, 963, 842, 801, 744, 759, 731, 614, 569, 495, 454, 431 cm^{-1}. Anal. Calcd. for $C_{14}H_{11}FN_2$: C, 74.32; H, 4.90; Found: C, 74.02; H, 4.93.

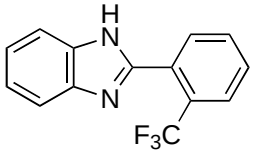


5-Chloro-2-(2-methylphenyl)benzimidazole. Following the representative procedure, after 18 h reaction time and silica gel chromatography (Hex/EtOAc, gradient 12% to 80% EtOAc), a white powder was obtained, yield 216 mg (89%, mp 178 °C). ^{1}H NMR (300 MHz, DMSO-d_6) δ 12.85 (s, 1H), 7.80-7.33 (m, 6H), 7.23 (d, J = 8.4 Hz, 1H), 2.60 (s, 3H). ^{13}C NMR (75 MHz, DMSO-d_6) δ 137.16, 131.38, 129.66, 129.59, 129.52, 126.06, 21.06. IR (KBr pellet) ν 2963, 1618, 1584, 1543, 1441, 1397, 1304, 1275, 1223, 1096, 1059, 969, 925, 856, 804, 770, 731, 600, 455 cm^{-1}. Anal. Calcd. for $C_{14}H_{11}ClN_2$: C, 69.28; H, 4.57; Found: C, 69.21; H, 4.57.

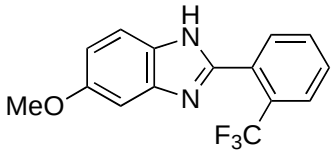


5-Bromo-2-(2-methylphenyl)benzimidazole. Following the representative procedure, after 18 h reaction time and silica gel chromatography (Hex/EtOAc, gradient 12% to 50% EtOAc), an off-white solid was obtained, yield 256 mg (89%, mp 184-185 °C). ^{1}H NMR (300 MHz, DMSO-d_6) δ 12.85 (s, 1H), 7.80 (s, 1H), 7.78-7.72 (m, 1H), 7.57 (d, J = 8.4

Hz, 1H), 7.45-7.32 (m, 4H), 2.60 (s, 3H). ^{13}C NMR (75 MHz, DMSO-d_6) δ 153.21, 137.17, 131.37, 129.66, 129.54, 129.53, 126.05, 124.79, 114.07, 21.06. IR (KBr pellet) ν 2698, 1581, 1543, 1487, 1438, 1394, 1305, 1275, 1223, 1097, 1045, 971, 915, 854, 806, 768, 754, 731, 681, 593, 569485, 454, 418 cm^{-1}. Anal. Calcd. for $C_{14}H_{11}BrN_2$: C, 58.56; H, 3.86; Found: C, 58.49; H, 3.82.



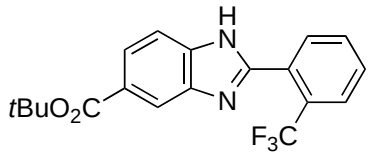
2-(2-(Trifluoromethyl)phenyl)benzimidazole. Following the representative procedure, after 18 h reaction time and silica gel chromatography (Hex/EtOAc, gradient 12% to 80% EtOAc), an off-white solid was obtained, yield 227 mg (87%, mp 270-273 °C). ^{1}H NMR (300 MHz, DMSO-d_6) δ 12.81 (s, 1H), 7.98-7.90 (m, 1H), 7.89-7.72 (m, 3H), 7.63 (s, 2H), 7.29-7.20 (m, 2H). ^{13}C NMR (75 MHz, DMSO-d_6) δ 149.44, 132.45, 132.25, 130.35, 130.33, 130.30, 130.27, 130.24, 128.49, 128.08, 127.67, 127.27, 126.75, 126.68, 126.61, 126.54, 125.59, 121.96. ^{19}F NMR (282 MHz, DMSO-d_6) δ -56.43 (s). IR (KBr pellet) ν 3047, 2788, 1591, 1544, 1493, 1479, 1456, 1441, 1407, 1374, 1311, 1281, 1269, 1223, 1182, 1121, 1057, 1035, 1007, 972, 766, 751, 692, 647, 597, 567, 430, 421 cm^{-1}. Anal. Calcd. for $C_{14}H_9F_3N_2$: C, 64.12; H, 3.46; Found: C, 64.21; H, 3.45.



5-Methoxy-2-(2-(trifluoromethyl)phenyl)benzimidazole. Following the representative procedure using the *para* substituted amidine, after 18 h reaction time and silica gel chromatography (Hex/EtOAc, gradient 12% to 70% EtOAc), a light orange foam was obtained, yield 213 mg (73%, mp 168 °C). ^{1}H NMR (300 MHz, DMSO-d_6) δ 12.64 (s, 1H), 7.93 (d, J = 7.5 Hz, 1H), 7.87-7.70 (m, 3H), 7.60-7.44 (m, 1H), 7.10 (s, 1H), 6.87 (dd, J = 8.7, 2.4 Hz, 1H), 3.81 (s, 3H). ^{13}C NMR (75 MHz, DMSO-d_6) δ 132.41, 132.19, 130.44, 130.41, 130.05, 127.97, 127.57, 126.75, 126.68, 126.61, 126.54, 125.54, 121.99, 55.47. ^{19}F NMR (282 MHz, DMSO-d_6) δ -56.45 (s). IR (KBr pellet) ν 2932, 1634, 1594, 1405,

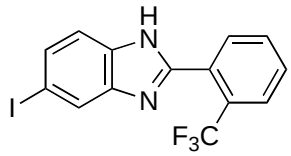
1359, 1315, 1268, 1121, 1056, 1034, 974, 835, 814, 773, 694, 648, 597, 563, 435 cm^{-1}. Anal. Calcd. for $C_{15}H_{11}F_3N_2O$: C, 61.64; H, 3.79; Found: C, 61.73; H, 3.84.

The reaction was also conducted with the *meta* substituted amidine to give 5-methoxy-2-(2-(trifluoromethyl)phenyl)benzimidazole as the main product. Following the representative procedure, after 18 h reaction time and silica gel chromatography (Hex/EtOAc, gradient 12% to 70% EtOAc), a light yellow foam was obtained, yield 216 mg (74%, mp 161 °C; GC: 19:1 mixture of regioisomers in favor of the isomer shown above; the yield corresponds to the mixture of compounds).

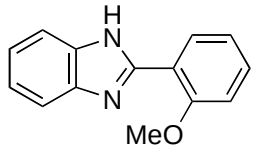


5-*tert*-Butoxycarbonyl-2-(2-(trifluoromethyl)phenyl)benzimidazole. Following the representative procedure using the *para* substituted amidine, after 36 h reaction time and silica gel chromatography (Hex/EtOAc, gradient 12% to 50% EtOAc), a white foam was obtained, yield 318 mg (88%, no mp). ^{1}H NMR (300 MHz, DMSO-d_6) δ 13.13 (s, 1H), 8.20 (s, 1H), 7.96 (d, J = 7.5 Hz, 1H), 7.91-7.75 (m, 4H), 7.69 (d, J = 8.7 Hz, 1H), 1.57 (s, 9H). ^{13}C NMR (75 MHz, DMSO-d_6) δ 165.46, 151.83, 132.56, 132.20, 130.62, 129.67, 129.65, 128.52, 128.11, 127.71, 127.30, 126.86, 126.79, 126.72, 126.66, 125.52, 125.40, 123.33, 121.89, 80.35, 27.91. ^{19}F NMR (282 MHz, DMSO-d_6) δ -56.52 (s). IR (KBr pellet) ν 2979, 1710, 1626, 1585, 1549, 1478, 1445, 1408, 1370, 1315, 1167, 1055, 1036, 951, 845, 771, 695, 647, 598, 565, 426 cm^{-1}. Anal. Calcd. for $C_{19}H_{17}F_3N_2O_2$: C, 62.98; H, 4.73; Found: C, 62.74; H, 4.90.

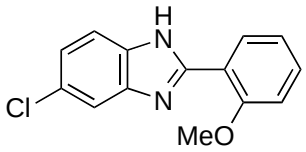
The reaction was also conducted with the *meta* substituted amidine to give 5-*tert*-butoxycarbonyl-2-(2-(trifluoromethyl)phenyl)benzimidazole as product. After 36 h reaction time and silica gel chromatography (Hex/EtOAc, gradient 12% to 60% EtOAc), a white foam was obtained, yield 251 mg (69%, no mp; GC: 90% conversion of the starting material; no regioisomer detected by GC and HPLC).



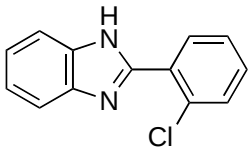
5-Iodo-2-(2-(trifluoromethyl)phenyl)benzimidazole. Following the representative procedure, after 18 h reaction time and silica gel chromatography (Hex/EtOAc, gradient 12% to 50% EtOAc), a white solid was obtained, yield 345 mg (89%, mp 191-193 °C). ^{1}H NMR (300 MHz, DMSO-d_6) δ 12.99 (s, 1H), 7.99 (s, 1H), 7.95 (d, J = 7.5 Hz, 1H), 7.89-7.74 (m, 3H), 7.54 (dd, J = 8.4 Hz, 1H), 7.47 (d, J = 8.4 Hz, 1H). ^{13}C NMR (75 MHz, DMSO-d_6) δ 150.20, 132.48, 132.23, 130.68, 130.48, 129.71, 129.68, 129.65, 129.62, 128.48, 128.08, 127.67, 127.26, 126.79, 126.72, 126.65, 126.58, 125.50, 121.87. ^{19}F NMR (282 MHz, DMSO-d_6) δ -56.49 (s). IR (KBr pellet) ν 2783, 1608, 1582, 1547, 1488, 1449, 1429, 1314, 1268, 1215, 1178, 1133, 1057, 1034, 972, 907, 808, 770, 693, 669, 647, 596, 562, 421 cm^{-1}. Anal. Calcd. for $C_{14}H_{19}F_3IN_2$: C, 43.32; H, 2.08; Found: C, 43.33; H, 2.05.



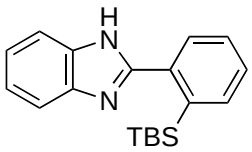
2-(2-Methoxyphenyl)benzimidazole.[2] Following the representative procedure, after 18 h reaction time and silica gel chromatography (Hex/EtOAc, gradient 12% to 70% EtOAc), an off-white solid was obtained, yield 153 mg (68%, mp 175-178 °C). ^{1}H NMR (300 MHz, DMSO-d_6) δ 12.16 (s, 1H), 8.36 (dd, J = 7.8, 1.8 Hz, 1H), 7.69-7.57 (m, 2H), 7.52-7.43 (m, 1H), 7.27-7.08 (m, 4H), 4.02 (s, 3H). ^{13}C NMR (75 MHz, DMSO-d_6) δ 156.78, 148.98, 142.75, 134.77, 131.29, 129.77, 122.10, 121.55, 120.90, 118.46, 118.12, 112.10, 111.97, 55.77 cm^{-1}. IR (KBr pellet) ν 3045, 1603, 1585, 1523, 1489, 1475, 1438, 1394, 1305, 1283, 1247, 1181, 1164, 1091, 1027, 746, 693, 561, 478. Anal. Calcd. for $C_{14}H_{12}N_2O$: C, 74.98; H, 5.39; Found: C, 74.69; H, 5.36.



5-Chloro-2-(2-methoxyphenyl)benzimidazole.[3] Following the representative procedure, after 18 h reaction time and silica gel chromatography (Hex/EtOAc, gradient 12% to 50% EtOAc), an off-white powder was obtained, yield 194 mg (75%, mp 200-201 °C). ^{1}H NMR (300 MHz, DMSO-d_6) δ 12.30 (s) 12.24 (s) (1H), 8.33 (dd, J = 7.8, 1.8 Hz, 1H), 7.74-7.57 (m, 2H), 7.54-7.45 (m, 1H), 7.24 (d, J = 8.1 Hz, 1H), 7.28-7.17 (m, 1H), 7.12 (td, J = 7.5, 0.6 Hz, 1H), 4.02 (s, 3H). ^{13}C NMR (75 MHz, DMSO-d_6) δ 156.87, 150.51, 150.17, 143.67, 141.55, 135.49, 133.60, 131.71, 129.84, 126.28, 126.02, 122.23, 121.93, 120.98, 119.72, 117.80, 117.59, 113.29, 112.19, 111.64, 55.85. IR (KBr pellet) ν 2958, 1604, 1584, 1480, 1438, 1424, 1390, 1300, 1250, 1250, 1163, 1126, 1096, 1058, 1021, 967, 929, 865, 799, 749, 707, 673, 600, 488, 427, 406 cm^{-1}. Anal. Calcd. for $C_{14}H_{11}ClN_2O$: C, 65.00; H, 4.29; Found: C, 64.90; H, 4.32.

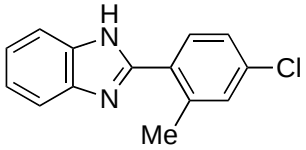


2-(2-Chlorophenyl)benzimidazole.[4] Following the representative procedure, after 18 h reaction time and silica gel chromatography (Hex/EtOAc, gradient 12% to 60% EtOAc), an off-white solid was obtained, yield 185 mg (81%, mp 217-219 °C). ^{1}H NMR (300 MHz, DMSO-d_6) δ 12.76 (s, 1H), 7.95-7.88 (m, 1H), 7.74-7.48 (m, 5H), 7.29-7.20 (m, 2H). ^{13}C NMR (75 MHz, DMSO-d_6) δ 149.13, 132.13, 131.66, 131.24, 130.38, 130.00, 127.47. IR (KBr pellet) ν 2772, 1591, 1570, 1491, 1464, 1443, 1405, 1374, 1317, 1275, 1232, 1122, 1054, 1036, 974, 761, 751, 743, 731, 653, 618 cm^{-1}. Anal. Calcd. for $C_{13}H_9ClN_2$: C, 68.28; H, 3.97; Found: C, 68.22; H, 3.93.

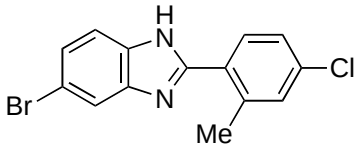


2-(2-(*tert*-Butyldimethylsilyl)phenyl)benzimidazole. Following the representative procedure, except that the reaction was conducted on a 0.5 mmol scale, after 18 h reaction

time and silica gel chromatography (Hex/EtOAc, gradient 12% to 40% EtOAc), a light brown solid was obtained, yield 124 mg (80%, mp 230-239 °C). ^{1}H NMR (300 MHz, DMSO-d_6) δ 12.58 (s, 1H), 7.74-7.67 (m, 1H), 7.63 (d, J = 6.6 Hz, 1H), 7.57-7.44 (m, 4H), 7.25-7.13 (m, 2H), 0.90 (s, 9H), -0.08 (s, 6H). ^{13}C NMR (75 MHz, DMSO-d_6) δ 153.54, 143.28, 138.06, 137.63, 136.31, 134.50, 129.71, 128.54, 128.09, 122.28, 121.35, 118.78, 111.19, 27.73, 17.30, -3.46. IR (KBr pellet) ν 2925, 1623, 1549, 1469, 1420, 1368, 1314, 1265, 1215, 1131, 1119, 1069, 1007, 972, 933, 907, 838, 822, 765, 752, 736, 717, 676, 648, 569, 474, 406 cm^{-1}. Anal. Calcd. for $C_{19}H_{24}N_2Si$: C, 73.97; H, 7.84; Found: C, 73.87; H, 7.69.

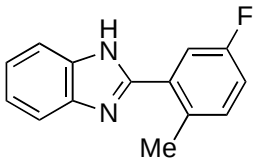


2-(4-Chloro-2-methylphenyl)benzimidazole. Following the representative procedure, after 18 h reaction time and silica gel chromatography (Hex/EtOAc, gradient 12% to 80% EtOAc), a light brown solid was obtained, yield 207 mg (85%, mp 258-260 °C). ^{1}H NMR (300 MHz, DMSO-d_6) δ 12.72 (s, 1H), 7.78 (d, J = 8.1 Hz, 1H), 7.69 (d, J = 6.9 Hz, 1H) 7.54 (d, J = 6.9 Hz, 1H), 7.50 (d, J = 2.1 Hz, 1H), 7.45 (dd, J = 8.4, 2.4 Hz, 1H), 7.29-7.15 (m, 1H), 2.63 (s, 3H). ^{13}C NMR (75 MHz, DMSO-d_6) δ 150.88, 143.69, 139.58, 134.43, 133.83, 131.14, 130.93, 128.94, 126.01, 122.61, 121.60, 119.04, 111.37, 20.93. IR (KBr pellet) ν 2663, 1596, 1474, 1451, 1416, 1320, 1273, 1230, 1199, 1108, 968, 874, 820, 767, 750, 574, 456 cm^{-1}. Anal. Calcd. for $C_{14}H_{11}ClN_2$: C, 69.28; H, 4.57; Found: C, 68.98; H, 4.51.

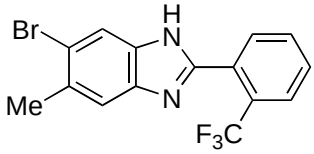


5-Bromo-2-(4-chloro-2-methylphenyl)benzimidazole. Following the representative procedure, after 18 h reaction time and silica gel chromatography (Hex/EtOAc, gradient 12% to 40% EtOAc), a light yellow foam was obtained, yield 284 mg (88%, mp 165-168 °C). ^{1}H NMR (300 MHz, DMSO-d_6) δ 12.90 (s, 1H), 7.80 (s, 1H), 7.77 (d, J = 8.4 Hz, 1H), 7.57 (d, J = 8.7 Hz, 1H), 7.51-7.47 (m, 1H), 7.44 (dd, J = 8.4, 2.1 Hz, 1H), 7.35 (dd, J = 8.7, 1.8 Hz, 1H), 2.61 (s, 3H). ^{13}C (75 MHz, DMSO-d_6) δ 152.10, 139.70, 134.17,

131.19, 130.99, 128.37, 126.06, 124.99, 20.87. IR (KBr pellet) ν 2975, 1599, 1479, 1438, 1407, 1302, 1276, 1200, 1110, 1047, 968, 915, 875, 810, 593, 578, 458, 421 cm^{-1}. Anal. Calcd. for $C_{14}H_{10}BrClN_2$: C, 52.29; H, 3.13; Found: C, 52.07; H, 3.05.

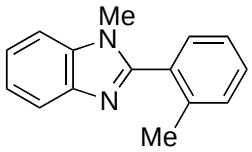


2-(5-Fluoro-2-methylphenyl)benzimidazole. Following the representative procedure, after 18 h reaction time and silica gel chromatography (Hex/EtOAc, gradient 12% to 80% EtOAc), an off-white solid was obtained, yield 201 mg (89%, mp 202-203 °C). ^{1}H NMR (300 MHz, DMSO-d_6) δ 12.72 (s, 1H), 7.73-7.67 (m, 1H), 7.60 (dd, J = 10.2, 2.7 Hz, 1H), 7.57-7.51 (m, 1H), 7.43 (dd, J = 8.4, 5.7 Hz, 1H), 7.30-7.17 (m, 3H), 2.60 (s, 3H). ^{13}C NMR (75 MHz, DMSO-d_6) δ 161.88, 158.69, 150.76, 150.72, 143.57, 134.41, 133.26, 133.25, 133.20, 133.16, 131.51, 131.41, 122.78, 121.63, 119.16, 116.16, 115.98, 155.88, 115.67, 111.46, 20.49. ^{19}F NMR (282 MHz, DMSO-d_6) δ -116.79 (q, J = 8.3 Hz). IR (KBr pellet) ν 2775, 1589, 1500, 1450, 1421, 1394, 1320, 1267, 1216, 1083, 1014, 989, 870, 818, 753, 743, 468 cm^{-1}. Anal. Calcd. for $C_{14}H_{11}FN_2$: C, 74.32; H, 4.90; Found: C, 74.11; H, 4.89.

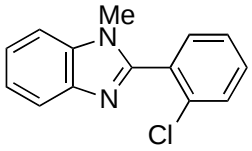


6-Bromo-5-methyl-2-(2-(trifluoromethyl)phenyl)benzimidazole. Following the representative procedure, after 36 h reaction time and silica gel chromatography (Hex/EtOAc, gradient 12% to 50% EtOAc), a white solid was obtained, yield 283 mg (80%, mp 232-234 °C; HPLC: 14:1, GC: 15:1 mixture of regioisomers in favor of the isomer shown; yield corresponds to the mixture of compounds). ^{1}H NMR (300 MHz, DMSO-d_6) δ 12.88 (s, 1H), 7.94 (d, J = 8.1 Hz, 1H), 7.91-7.73 (m, 4H), 7.61 (s, 1H), 2.46 (s, 3H). ^{13}C NMR (75 MHz, DMSO-d_6) δ 150.36, 132.47, 132.19, 130.69, 130.42, 129.86, 129.83, 128.07, 127.66, 126.77, 126.72, 126.65, 126.58, 125.52, 121.89, 117.52, 23.02. ^{19}F NMR (282 MHz, DMSO-d_6) δ -56.51 (s). IR (KBr pellet) ν 2954, 1583, 1549, 1438, 1396, 1314,

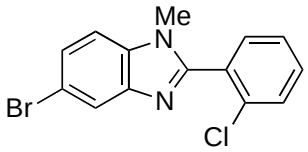
1269, 1177, 1133, 1056, 1035, 983, 857, 773, 694, 668, 646, 598, 426 cm^{-1}. Anal. Calcd. for $C_{15}H_{10}BrF_3N_2$: C, 50.73; H, 2.84; Found: C, 50.45; H, 2.74.



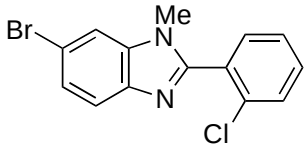
***N*-Methyl-2-(2-methylphenyl)benzimidazole.** Following the representative procedure, exept that 2.00 eq. HOAc were used instead of 5.00 eq., after 48 h reaction time and silica gel chromatography (Hex/EtOAc, gradient 12% to 50% EtOAc), an off-white solid was obtained, yield 151 mg (68%, mp 118-120 °C). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.88-7.80 (m, 1H), 7.46-7.28 (m, 7H), 3.63 (s, 3H), 2.27 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.92, 143.07, 138.15, 135.68, 130.59, 130.42, 130.05, 130.02, 125.91, 122.76, 122.40, 119.99, 109.68, 30.79, 19.86. IR (KBr plate, $CDCl_3$) ν 3053, 1942, 1615, 1526, 1473, 1458, 1430, 1383, 1326, 1278, 1242, 1152, 1133, 1052, 1036, 1005, 931, 828, 783, 755, 733, 669, 599, 555, 463, 442, 414 cm^{-1}. Anal. Calcd. for $C_{15}H_{14}N_2$: C, 81.05; H, 6.35; Found: C, 81.04; H, 6.37.



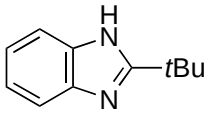
***N*-Methyl-2-(2-chlorophenyl)benzimidazole.** Following the representative procedure, exept that 2.00 eq. HOAc were used instead of 5.00 eq., after 48 h reaction time and silica gel chromatography (Hex/EtOAc, gradient 12% to 50% EtOAc), an off-white solid was obtained, yield 167 mg (69%, mp 122-124 °C). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.89-7.81 (m, 1H), 7.62-7.30 (m, 7H), 3.68 (s, 3H), ^{13}C NMR (75 MHz, $CDCl_3$) δ 151.62, 143.01, 135.80, 134.38, 132.59, 131.50, 130.12, 129.86, 127.19, 123.13, 122.54, 120.24, 109.82, 30.98. IR (KBr plate, $CDCl_3$) ν 3404, 3061, 2946, 2361, 1615, 1602, 1569, 1525, 1456, 1440, 1386, 1328, 1284, 1244, 1152, 1127, 1083, 1037, 1006, 822, 767, 745, 730, 656, 595, 545, 471, 431 cm^{-1}. Anal. Calcd. for $C_{14}H_{11}ClN_2$: C, 69.28; H, 4.57; Found: C, 69.07; H, 4.51.



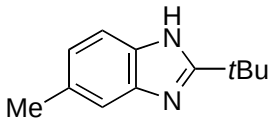
***N*-Methyl-5-bromo-2-(2-chlorophenyl)benzimidazole.** Following the representative procedure, exept that 2.00 eq. HOAc were used instead of 5.00 eq., after 48 h reaction time and silica gel chromatography (Hex/EtOAc, gradient 12% to 50% EtOAc), a white solid was obtained, yield 269 mg (84%, mp 114-116 °C). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.95 (dd, *J* = 1.8, 0.6 Hz, 1H), 7.59-7.51 (m, 2H), 7.50 (dd, *J* = 6.9, 1.8 Hz, 1H), 7.47-7.38 (m, 2H), 7.31-7.25 (m, 2H), 3.65 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.66, 144.21, 134.78, 134.33, 132.50, 131.80, 129.97, 129.58, 127.32, 126.21, 123.03, 115.59, 111.13, 31.18. IR (KBr plate, $CDCl_3$) ν 3063, 2947, 1602, 1523, 1469, 1422, 1385, 1319, 1143, 1085, 1044, 912, 866, 839, 795, 767, 750, 733, 660, 593, 567, 433 cm^{-1}. Anal. Calcd. for $C_{14}H_{10}BrClN_2$: C, 52.29; H, 3.13; Found: C, 52.15; H, 3.02.



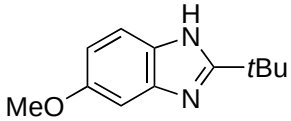
***N*-Methyl-6-bromo-2-(2-chlorophenyl)benzimidazole.** Following the representative procedure, exept that 2.00 eq. HOAc were used instead of 5.00 eq., after 48 h reaction time and silica gel chromatography (Hex/EtOAc, gradient 12% to 40% EtOAc), a highly viscous yellow oil was obtained, yield 173 mg (54%; HPLC: 5:1, GC: 7.6:1 mixture of regioisomers in favor of the isomer shown; yield corresponds to the isomer shown; minor isomer not isolated in pure form). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.69 (d, *J* = 8.7 Hz, 1H), 7.62-7.39 (m, 6H), 3.65 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.30, 141.88, 136.87, 134.33, 132.50, 131.79, 129.97, 129.54, 127.32, 125.94, 121.52, 116.40, 113.04, 31.16. IR (KBr plate, $CDCl_3$) ν 3398, 3063, 2946, 1611, 1524, 1466, 1448, 1381, 1327, 1315, 1271, 1237, 1127, 1105, 1083, 1038, 910, 810, 773, 757, 733, 719, 662, 593, 562, 471, 432 cm^{-1}. Anal. Calcd. for $C_{14}H_{10}BrClN_2$: C, 52.29; H, 3.13; Found: C, 52.21; H, 3.23.



2-*tert*-Butylbenzimidazole.[5] Following the representative procedure, after 18 h reaction time and silica gel chromatography (Hex/EtOAc, gradient 12% to 100% EtOAc), a white powder was obtained, yield 150 mg (86%, complete sublimation at 310 °C). ^{1}H NMR (300 MHz, DMSO-d_6) δ 12.09 (s, 1H), 7.56-7.49 (m, 1H), 7.42-7.37 (m, 1H), 7.16-7.05 (m, 2H), 1.39 (s, 9H). ^{13}C NMR (75 MHz, DMSO-d_6) δ 162.15, 142.79, 134.65, 121.44, 120.73, 118.32, 110.77, 33.19, 29.28. IR (KBr pellet) ν 3050, 2965, 2873, 2773, 1621, 1592, 1533, 1486, 1452, 1410, 1362, 1309, 1277, 1222, 1184, 1015, 994, 937, 791, 749, 731, 618, 540, 463, 412 cm^{-1}. Anal. Calcd. for $C_{11}H_{14}N_2$: C, 75.82; H, 8.10; Found: C, 75.90; H, 8.12.

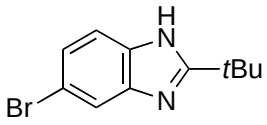


5-Methyl-2-*tert*-butylbenzimidazole.[6] Following the representative procedure, an off-white solid was obtained after 18 h reaction time and silica gel chromatography (Hex/EtOAc, gradient 12% to 70% EtOAc), yield 162 mg (86%, mp 252 °C). ^{1}H NMR (300 MHz, DMSO-d_6) δ 11.96 (s), 11.94 (s) (1H), 7.39 (d, J = 8.1 Hz), 7.27 (d, J = 8.1 Hz) (1H), 7.32 (s), 7.19 (s) (1H), 6.97-6.87 (m, 1H), 2.39 (s), 2.37 (s) (3H), 1.38 (s, 9H). ^{13}C NMR (75 MHz, DMSO-d_6) δ 162.09, 161.60, 143.19, 140.88, 134.95, 132.68, 130.49, 129.44, 122.72, 122.16, 118.17, 117.89, 110.59, 110.29, 33.17, 33.15, 29.30, 21.36, 21.32. IR (KBr pellet) ν 2970, 1633, 1541, 1490, 1456, 1401, 1365, 1309, 1284, 1266, 1233, 1217, 1180, 1000, 861, 805, 761, 737, 603, 417 cm^{-1}. Anal. Calcd. for $C_{12}H_{16}N_2$: C, 76.55; H, 8.57; Found: C, 76.54; H, 8.55.



5-Methoxy-2-*tert*-butylbenzimidazole. Following the representative procedure, after 18 h reaction time and silica gel chromatography (Hex/EtOAc, gradient 12% to 70% EtOAc), an off-white solid was obtained, yield 170 mg (83%, mp 209 °C). ^{1}H NMR (300 MHz, DMSO-d_6) δ 11.94 (s, 1H), 7.40 (d, J = 8.7 Hz), 7.27 (d, J = 8.7 Hz) (1H), 7.10 (d, J =

1.8 Hz), 6.89 (d, *J* = 2.1 Hz) (1H), 6.75 (dd, *J* = 9.3, 2.0 Hz) 6.72 (dd, *J* = 9.0, 2.1 Hz) (1H), 3.76 (s), 3.74 (s) (3H), 1.37 (s, 9H). ^{13}C NMR (75 MHz, DMSO-d_6) δ 162.54, 161.20, 155.30, 154.81, 143.63, 137.19, 135.24, 129.05, 118.70, 110.94, 110.69, 109.73, 101.36, 94.37, 55.42, 55.39, 33.19, 33.14, 29.29. IR (KBr pellet) ν 2968, 2831, 1633, 1598, 1523, 1490, 1455, 1436, 1404, 1365, 1313, 1264, 1219, 1199, 1034, 997, 952, 815, 725, 632, 579, 549, 429 cm^{-1}. Anal. Calcd. for $C_{12}H_{16}N_2O$: C, 70.56; H, 7.90; Found: C, 70.33; H, 7.87.

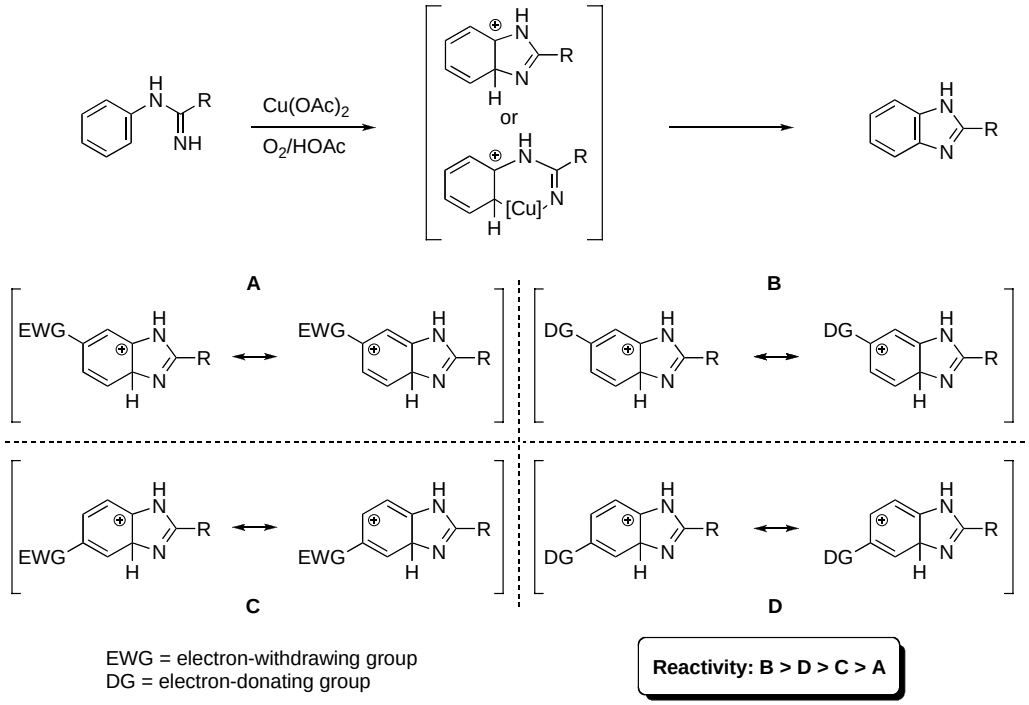


5-Bromo-2-*tert*-butylbenzimidazole. Following the representative procedure, after 18 h reaction time and silica gel chromatography (Hex/EtOAc, gradient 12% to 70% EtOAc), a white powder was obtained, yield 229 mg (89%, mp 293 °C). ^{1}H NMR (300 MHz, DMSO-d_6) δ 12.30 (s, 1H), 7.80-7.32 (m, 2H), 7.25 (dd, *J* = 8.4, 2.0 Hz, 1H), 1.38 (s, 9H). ^{13}C NMR (75 MHz, DMSO-d_6) δ 33.28, 29.15. IR (KBr pellet) ν 3074, 2970, 1617, 1532, 1478, 1447, 1393, 1364, 1298, 1278, 1243, 1217, 1175, 1052, 996, 915, 864, 807, 739, 682, 595, 414 cm^{-1}. Anal. Calcd. for $C_{12}H_{16}BrN_2$: C, 52.19; H, 5.18; Found: C, 52.26; H, 5.12.

Reactivity Study of Electron-rich and Electron-poor Amidines

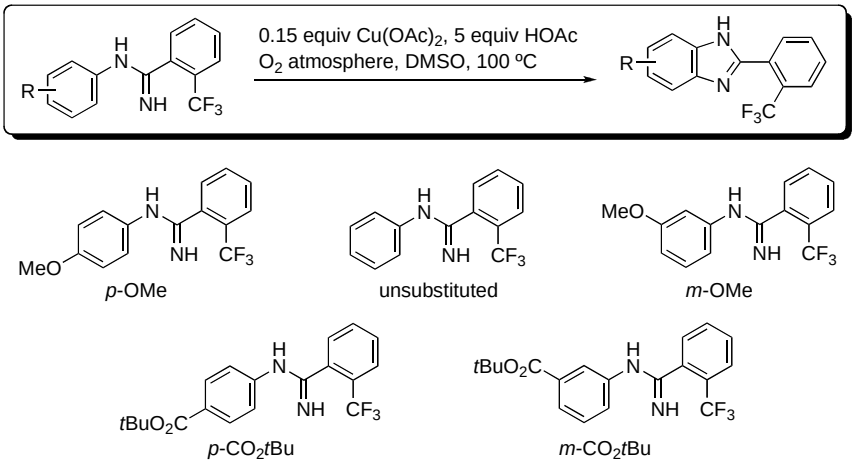
To probe the action of an electrophilic aromatic substitution mechanism, we reacted an unsubstituted amidine and amidines substituted with either an electron-donating (OMe) or electron-withdrawing group (CO_2tBu) in the *para* or *meta* position of the aniline-derived part of the amidine. The reactions were stopped after 2, 4, 6, and 8 h and the conversion of the starting material as well as the yield of the formed benzimidazole were assigned based on the GC data (Table 1).

If an electrophilic aromatic substitution mechanism operates, a considerable difference in reactivity should be found for the differently substituted amidines; the highest reactivity should be observed for the amidine with an OMe in the *meta* position, the lowest for the amidine with a CO_2tBu group in the same position. This would be in accordance with the ability of these substituents to stabilize the carbocation in the intermediate of the electrophilic aromatic substitution process (Scheme 1). In our study we observed the highest reactivity for the amidine with an OMe in the *meta* position, the lowest for the amidine with a CO_2tBu group in the same position. This result is consistent in direction, but the difference in reactivity is too small to be certain that an electrophilic aromatic substitution mechanism operates in this transformation.



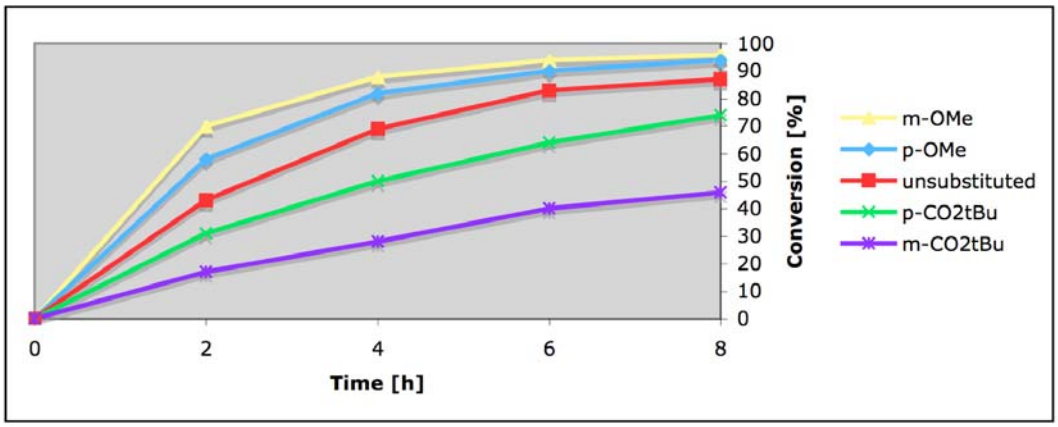
Scheme 1. Influence of the Substituent and the Substitution Pattern on the Reactivity.

Table 1. Results of the Reactivity Study of Electron-rich and Electron-poor Amidines.

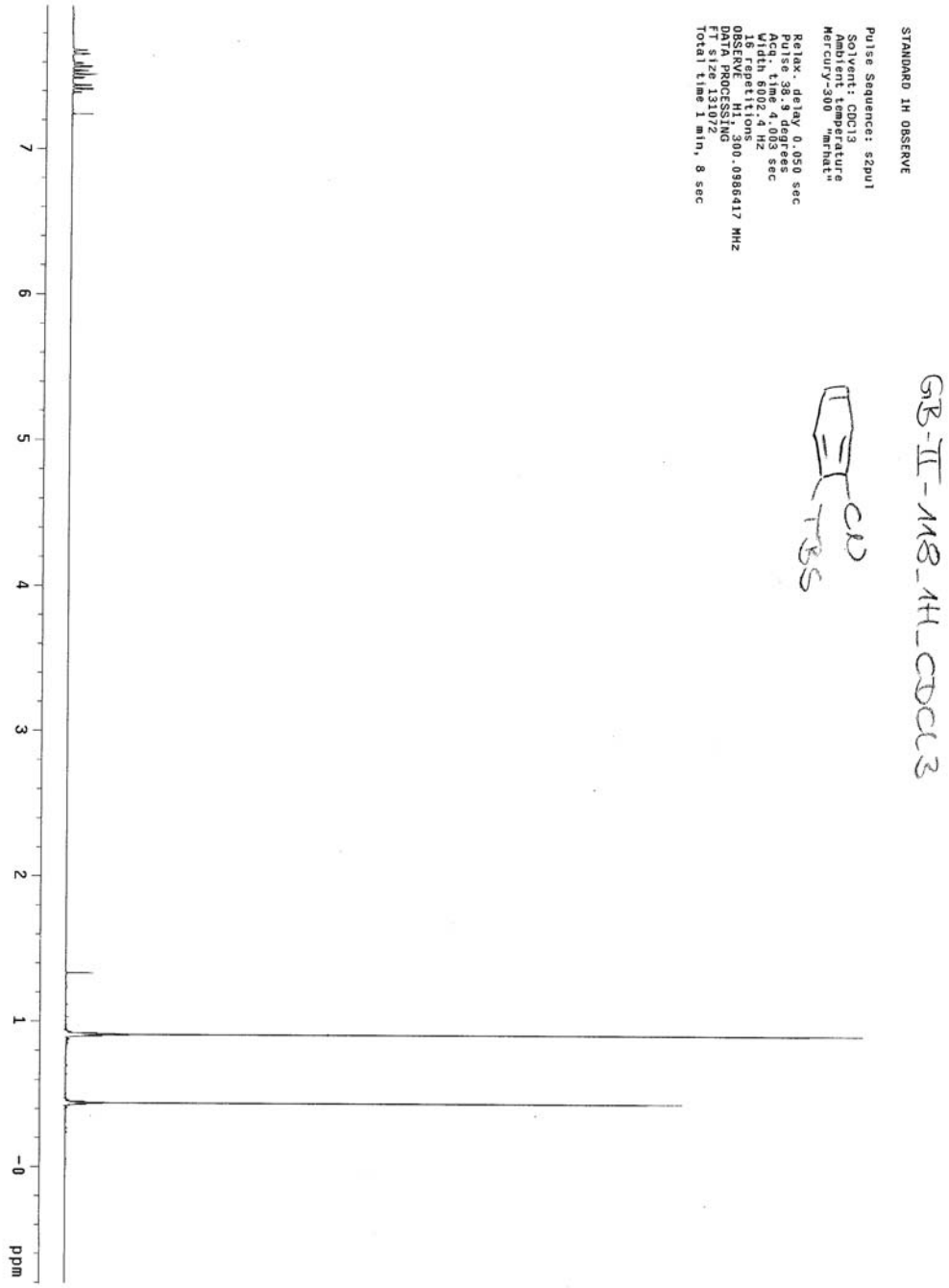


Time	unsubstituted		*p*-OMe		*m*-OMe		*p*-CO_2tBu		*m*-CO_2tBu	
	Conv.	Yield	**Conv.**	Yield	**Conv.**	Yield	**Conv.**	Yield	**Conv.**	Yield
2 h	**43%**	40%	**58%**	43%	**70%**	47%	**31%**	25%	**17%**	11%
4 h	**69%**	62%	**82%**	56%	**88%**	65%	**50%**	35%	**28%**	21%
6 h	**83%**	73%	**90%**	68%	**94%**	68%	**64%**	54%	**40%**	31%
8 h	**87%**	80%	**94%**	70%	**96%**	71%	**74%**	63%	**46%**	41%

Reactions were carried out with 0.5 mmol of the corresponding amidine in 1 mL DMSO. Conversions (Conv.) and yields are based on GC analyses. The data is corrected. Dodecane was used as internal standard.



Spectra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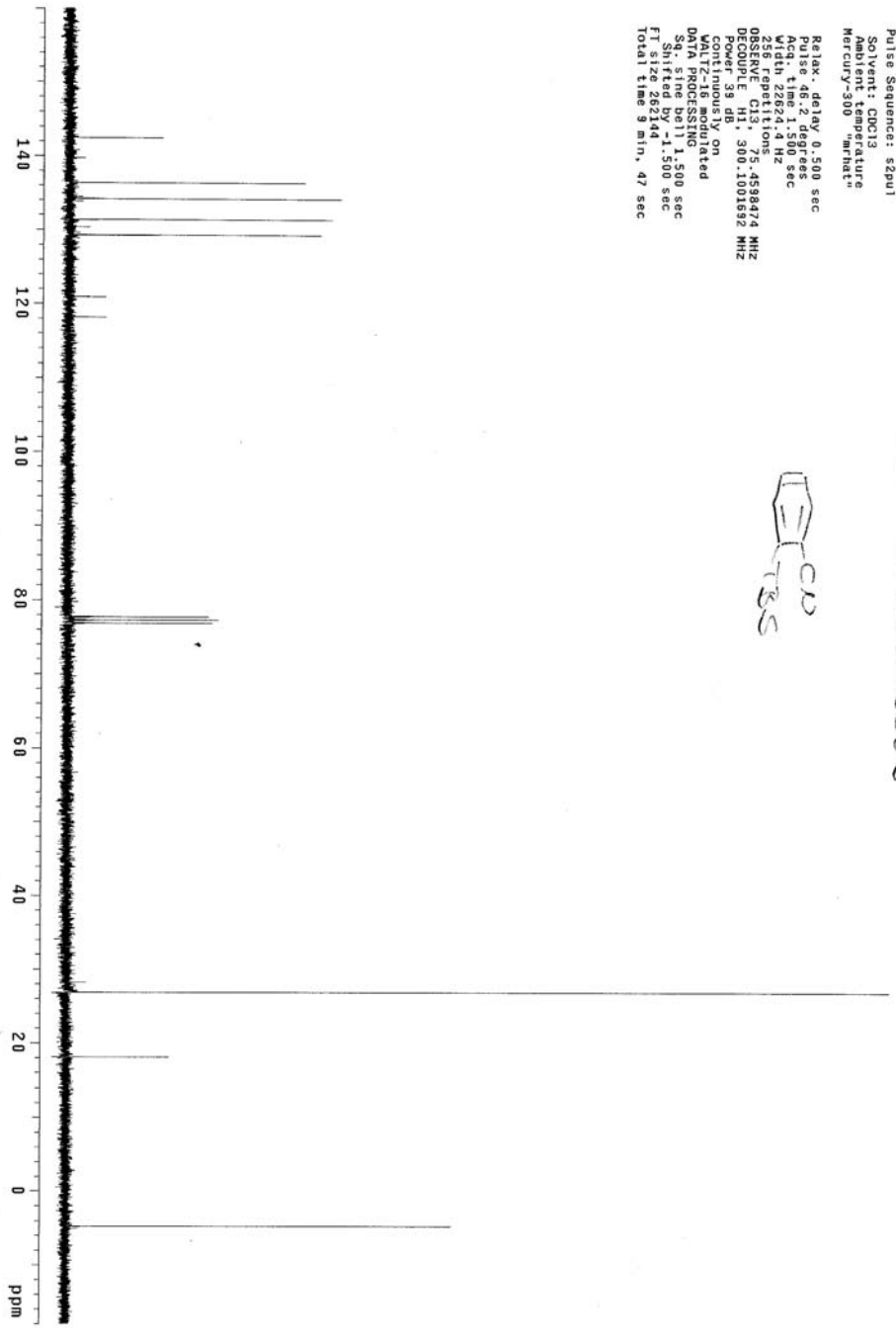
Mercury-300 "mrhat"
Relax. delay 0.050 sec
Pulse 38.9 degrees
Acq. time 4.003 sec
Width 6002.4 Hz
16 repetitions
OBSERVE H1, 300.0986417 MHz
DATA PROCESSING
FT size 131072
Total time 1 min, 8 sec
GB-II-MB_1H_CDCl3
CO
TBS
7
6
5
4
3
2
1
-0
ppm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Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
Mercury-300 "mrhat"
Relax. delay 0.500 sec
Pulse 46.2 degrees
Acq. time 1.500 sec
Width 22624.4 Hz
256 repetitions
OBSERVE C13, 75.4598474 MHz
DECOUPLE H1, 300.1001692 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Sp, sine bell 1.500 sec
Shifted by -1.500 sec
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GB-II-112_13C_CDCl3
CO
TBS
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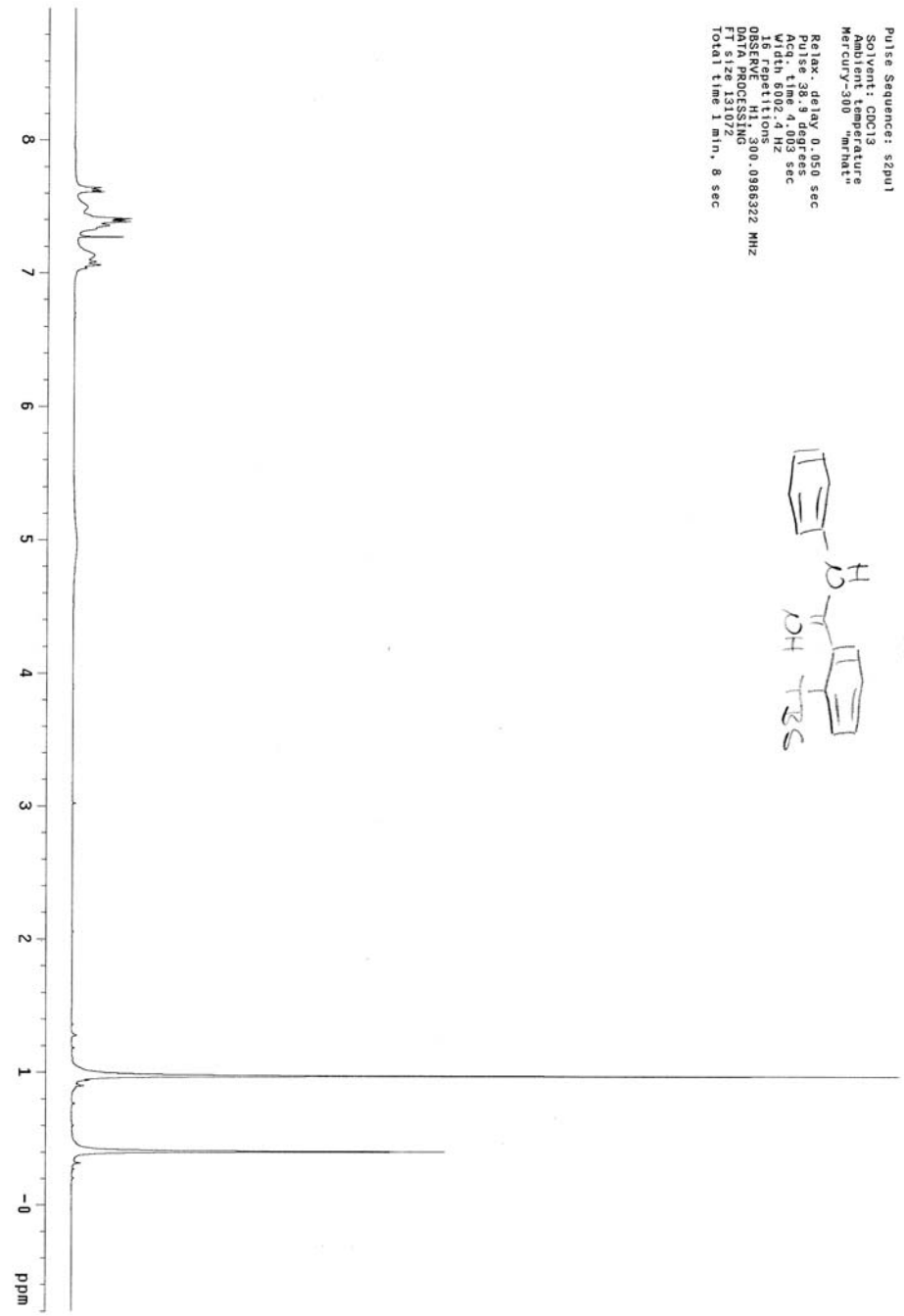
120
100
80
60
40
20
0
ppm


STANDARD 1H OBSERVE
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
Mercury-300 "mrhat"
Relax. delay 0.050 sec
Pulse 38.0 degrees
Acq. time 4.085 sec
Width 6002.4 Hz
16 repetitions
OBSERVE H1, 300.0986322 MHz
DATA PROCESSING
FT size 131072
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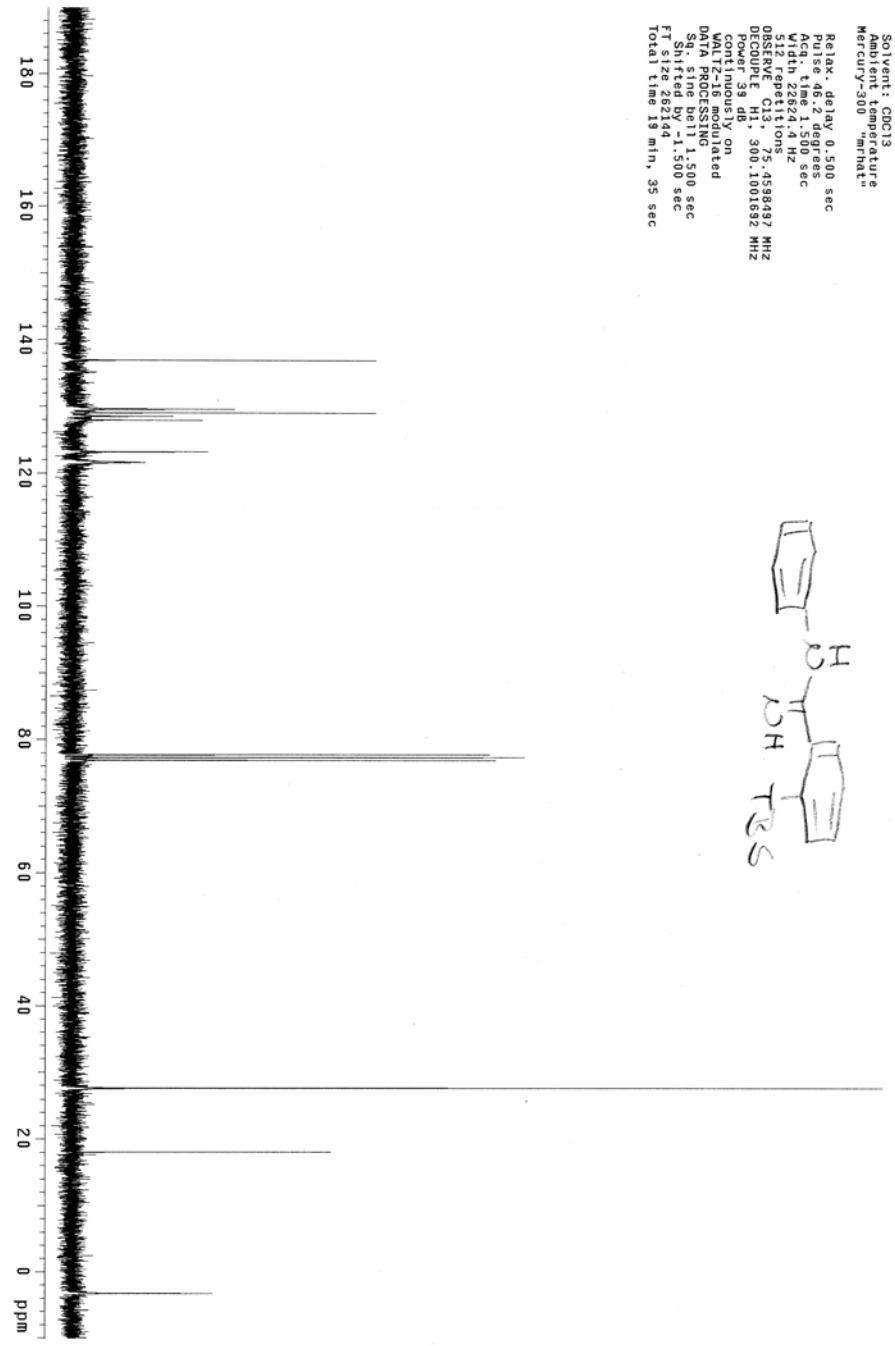
TBS
8
7
6
5
4
3
2
1
-0
ppm


13C OBSERVE
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
Mercury-300 "mrhat"
Relax. delay 0.500 sec
Pulse 46.2 degrees
Acq. time 1.500 sec
Width 20242.7 Hz
512 repetitions
OBSERVE C13, 75.4598497 MHz
DECOUPLE H1, 300.1001692 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Sq. sine bell 1.500 sec
FT Shifted by -1.500 sec
FT size 262144
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TBS
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160
140
120
100
80
60
40
20
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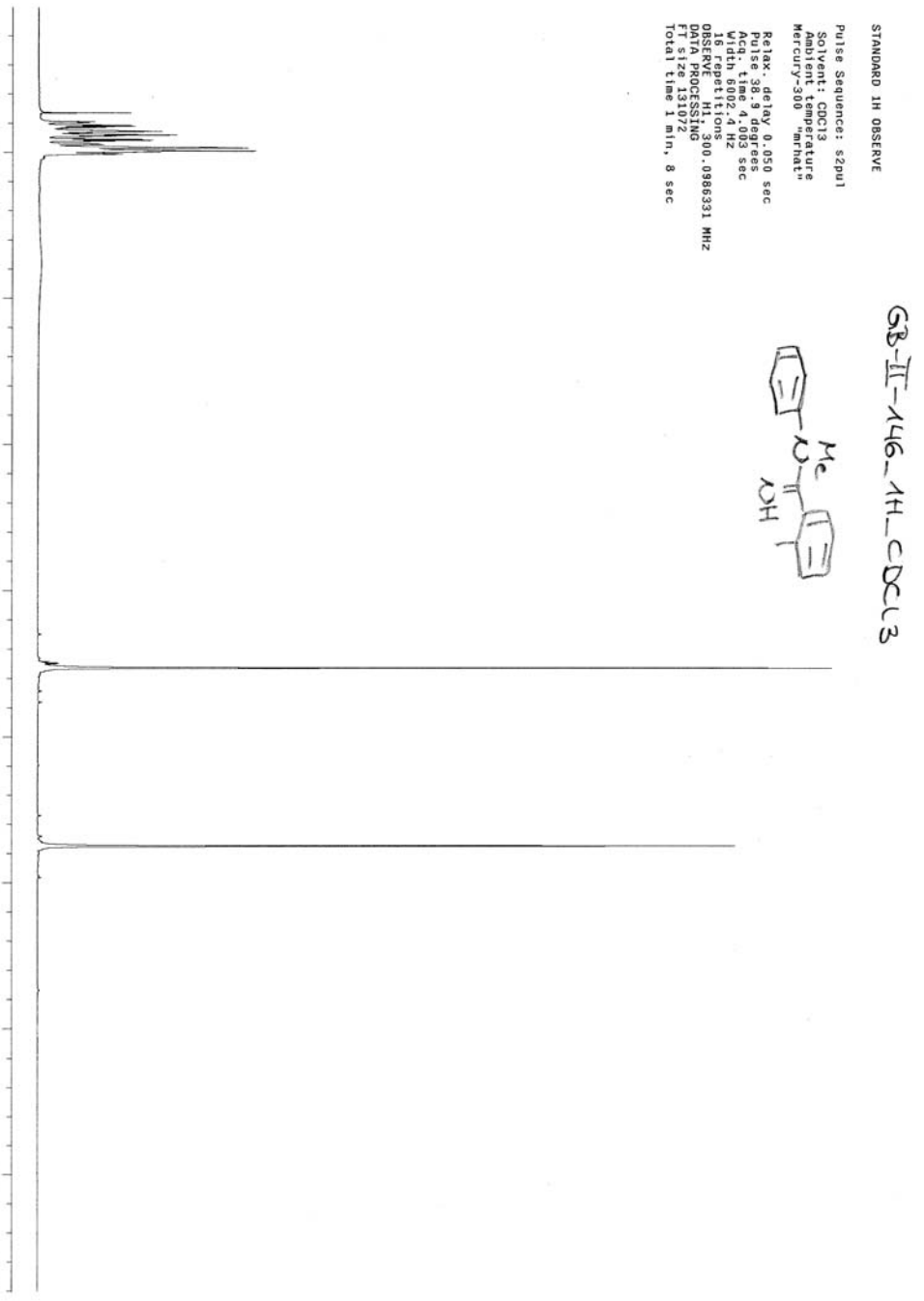
ppm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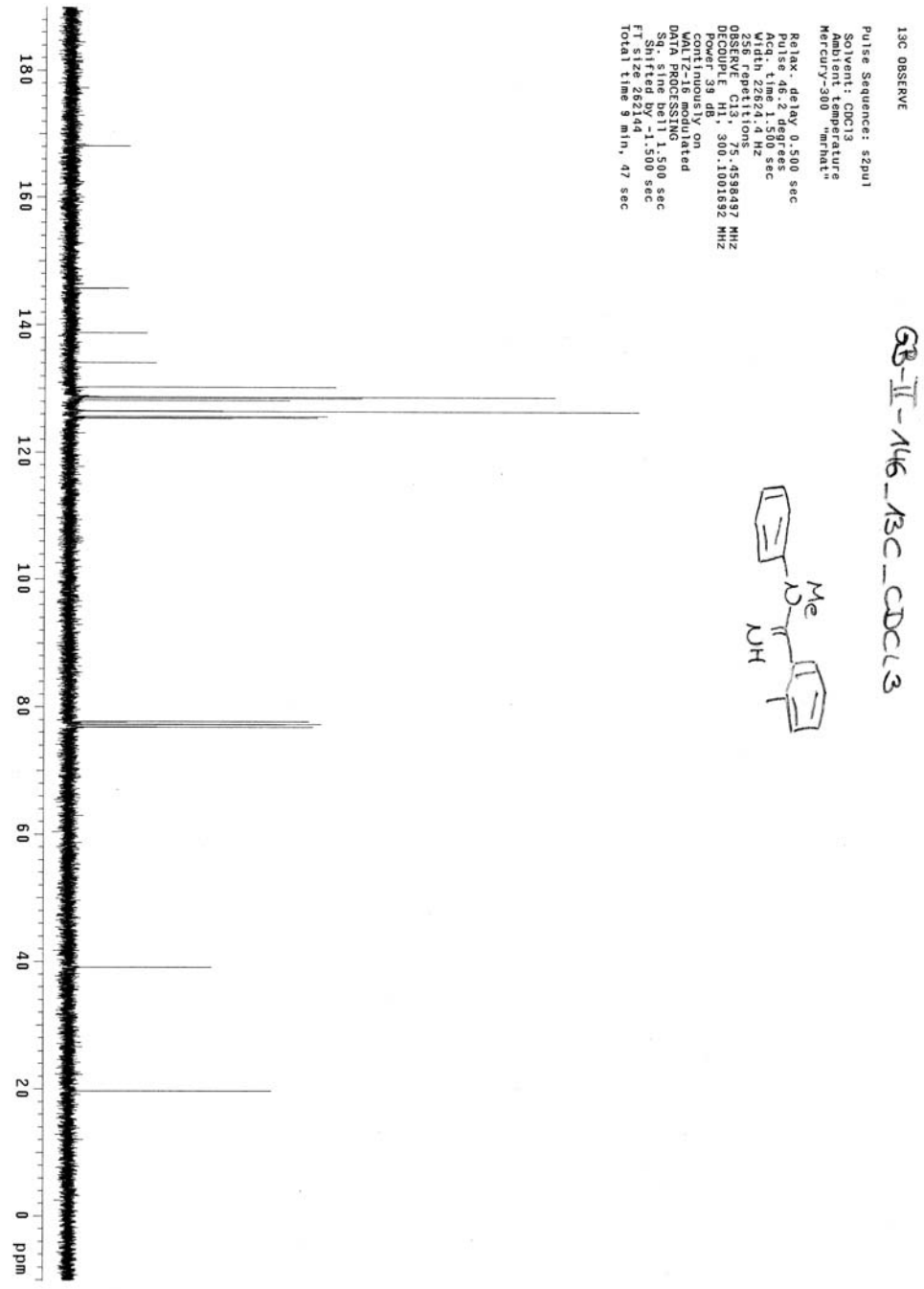
STANDARD 1H OBSERVE
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
Mercury-300 "mrhat"
Relax. delay 0.050 sec
Pulse 38.9 degrees
Acq. time 4.003 sec
Width 6002.4 Hz
1 repetitions
OBSERVE H1, 300.0986331 MHz
DATA PROCESSING
FT size 131072
Total time 1 min, 8 sec
Me
OH
7
6
5
4
3
2
1
-0
ppm


13C OBSERVE
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Solvent: CDCl3
Ambient temperature
Mercury-300 "mrhal"
Relax. delay 0.500 sec
Pulse 46.2 degrees
Acq. time 1.500 sec
Width 22624.7 Hz
256 repetitions
OBSERVE C13, 75.4598497 MHz
DECOUPLE H1, 300.1001692 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Sq. sine bell 1.500 sec
FT Shifted by -1.500 sec
Total time 9 min, 47 sec
GB-II-146_13C_CDCl3
Me
NH
180
160
140
120
100
80
60
40
20
0
ppm

References

[1] a) B. Singh, J. C. Collins, *J. Chem. Soc., Chem. Commun.* **1971**, 498–499; b) F. C. Cooper, M. W. Partridge, *J. Chem. Soc.* **1953**, 255–260.

[2] a) L.-H. Du, Y.-G. Wang, *Synthesis* **2007**, 675–678; b) G. Speier, L. Párkányi, *J. Org. Chem.* **1986**, *51*, 218–221.

[3] D. Yang, D. Fokas, J. Li, L. Yu, C. M. Baldino, *Synthesis* **2005**, 47–56.

[4] R. P. Giani, M. Borsa, E. Parini, G. C. Tonon, *Synthesis* **1985**, 550–552.

[5] J. Charton, S. Girault-Mizzi, C. Sergheraert, *Chem. Pharm. Bull.* **2005**, *53*, 492–497.

[6] G. A. Russel, L. Wang, R. Rajaratnam, *J. Org. Chem.* **1996**, *61*, 8988–8991.