Transition Metal - Catalysed Arylation of 1-Deazapurines via C-H bond activation.

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(A) Experimental

General notes. All solvents were purified and dried by standard methods. NMR spectra were recorded on a Brucker AV 300 and Brucker AV400. The following abbreviations were used to designate chemical shift multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet. IR spectra were recorded on a Perkin Elmer FT IR 1600 spectrometer (ATR). Mass spectra were obtained on a “Hewlett-Packard” HP GC / MS 5890 / 5972 instrument (EI, 70 eV) by GC inlet or on a MX-1321 instrument (EI, 70 eV) by direct inlet. Column chromatography was performed on silica gel (63 – 200 mesh, Merck). Silica gel Merck 60F254 plates were used for TLC. Satisfactory microanalysis obtained C ± 0.33; H ± 0.45; N ± 0.25.

General Procedure for the Synthesis of Compounds 5a-h; Dichloromethane, primary amine (2a-d), and methyl N-(cyanomethyl)-formimidate (1) were added under an argon atmosphere at r.t. to a Schlenk flask. The reaction mixture was refluxed for 2 h and after that, the mixture was cooled to r.t., and then to 0 °C on an ice bath. Afterwards, 1,3-electrophilic reagent (4a-e) was added, and the mixture continued to stir at the same temperature for 15–20 min and then refluxed for 5 h. The solvent was evaporated to dryness, and the residue was purified by column chromatography (n-Heptane – EtOAc), to give 5a-h as solid products.

General Procedure for the Synthesis of Compounds 6a-n using Cu and Pd catalyst; DMF (8 mL) was added to an argon-purged pressure tube containing 3H-imidazo[4,5-b]pyridine (5a-h) (1 mmol), Pd(OAc)$_2$ (0.05 mmol, 5 mol %), CuI (3 mmol), ArX (2 mmol), and Cs$_2$CO$_3$ (2.5 mmol). Reaction mixture was stirred at 150°C for 30-60 h. After cooling to r.t., the solvent was evaporated under reduced pressure. The products were isolated and purified by column chromatography (gradient elution n-heptane/ethyl acetate, ethyl acetate/isopropanol).

General Procedure for the Synthesis of Compounds 6a-n using Ni catalyst; DMF (8 mL) was added to an argon-purged pressure tube containing 3H-imidazo[4,5-b]pyridine (5a-h) (1 mmol), correspondent NiCl$_2$[PPh$_3$]$_2$ (0.05 mmol, 5 mol %), ArX (2 mmol), and K$_2$CO$_3$ (2.5 mmol). Reaction mixture was stirred at 110°C for 15 h. After cooling to r.t., the solvent was evaporated under reduced pressure. The products were isolated and purified by column chromatography (gradient elution n-heptane/ethyl acetate, ethyl acetate/isopropanol).
(B) Analytical data of all compounds

3-(4-Methoxybenzyl)-5,7-bis(trifluoromethyl)-3H-imidazo[4,5-b]pyridine (5a):
Starting with CH$_2$Cl$_2$ (6 mL), 1 (0.47 mL; 5.33 mmol), 2a (0.68 mL, 5.33 mmol), 4a (0.74 mL, 5.33 mmol), 5a was isolated as yellowish solid (1.018 g, 51%); m.p. 108-110 °C. $^1$H NMR (300.13 MHz, CDCl$_3$): $\delta$ = 3.72 (s, 3H, OCH$_3$), 5.40 (s, 2H, -CH$_2$-), 6.82 (d, $^3$J = 8.7 Hz, 2H, ArH), 7.26 (d, $^3$J = 8.7 Hz, 2H, ArH), 7.80 (s, 1H, 1H). $^{13}$C NMR (62.89 MHz, CDCl$_3$), $\delta$ = 47.6 (-CH$_2$-), 55.3 (OCH$_3$), 111.5 (q, $^3$J$_{CF} = 4.40$ Hz, CH), 114.6 (2CH), 121.8 (q, $^1$J$_{CF} = 274.0$ Hz, CF$_3$), 125.4 (q, $^1$J$_{CF} = 274.0$ Hz, CF$_3$), 126.41 (C), 129.5 (C, q, $^2$J$_{CF} = 35.2$ Hz), 129.9 (2CH), 133.37 (C), 142.8 (q, $^2$J$_{CF} = 35.7$ Hz, C), 148.0 (C), 148.1 (CH), 160.04 (C); $^{19}$F NMR (282.40 MHz, CDCl$_3$): $\delta$ = -66.10 (ArCF$_3$), -62.13 (ArCF$_3$); IR (ATR, cm$^{-1}$): $\nu$ = 3069 (w), 3011 (w), 2958 (w), 2934 (m), 2912 (w), 2839 (w), 1611 (w), 1585 (w), 1513 (m), 1489 (w), 1464 (w), 1455 (w), 1441 (w), 1407 (w), 1390 (w), 1381 (w), 1352 (w), 1327 (w), 1306 (w), 1271 (s), 1255 (s), 1191 (m), 1174 (s), 1129 (s), 1109 (w), 1098 (w), 1033 (m), 964 (w), 940 (w), 940 (w), 921 (w), 903 (w), 880 (s), 842 (w), 833 (w), 804 (w), 759 (w), 748 (w), 728 (w), 709 (w), 681 (w), 666 (w), 655 (m), 632 (w), 597 (w), 564 (w); GC-MS (EI, 70 eV): m/z (%): 375 (M$^+$, 60), 360 (4), 340 (1), 360 (4), 178 (2), 121 (100), 91 (4), 78 (6) 51 (1). HRMS (EI): calcd for C$_{16}$H$_{11}$F$_6$N$_3$O [M$^+$]: 375.08008; found: 375.080093.

3-(4-Methoxybenzyl)-5-methyl-7-(trifluoromethyl)-3H-imidazo[4,5-b]pyridine (5b):
Starting with CH$_2$Cl$_2$ (6 mL), 1 (0.56 mL, 6.23 mmol), 2a (0.81 mL, 6.23 mmol), 4b (0.75 mL, 6.23 mmol), 5b was isolated as brown solid (1.3 g, 65%); m.p. 95-97 °C. $^1$H NMR (300.13 MHz, CDCl$_3$): $\delta$ = 2.64 (s, 3H, CH$_3$), 3.69 (s, 3H, OCH$_3$), 5.31 (s, 2H, -CH$_2$-), 6.78 (d, $^3$J = 8.6 Hz, 2H, ArH), 7.18 (d, $^3$J = 8.6 Hz, 2H, ArH), 7.24 (s, 1H), 7.95 (s, 1H). $^{13}$C NMR (75.46 MHz, CDCl$_3$), $\delta$ = 19.2 (CH$_3$), 46.8 (-CH$_2$-), 55.3 (OCH$_3$), 114.3 (q, $^3$J$_{CF} = 4.40$ Hz, CH), 114.4 (2CH), 122.9 (CF$_3$, q, $^1$J$_{CF} = 273.44$ Hz), 127.5 (C), 128.6 (C, q, $^2$J$_{CF} = 34.11$ Hz), 129.1 (C), 129.5 (2CH), 144.6 (CH), 148.0 (C), 154.2 (C), 159.7 (C). $^{19}$F NMR (282.40 MHz, CDCl$_3$): $\delta$ = -62.17 (ArCF$_3$); IR (ATR, cm$^{-1}$):
Starting with CH₂Cl₂ (6 mL), 1 (0.28 mL, 3.12 mmol), 2a (0.41 mL, 3.12 mmol), 4c (0.46 mL, 3.12 mmol), 5c was isolated as yellowish solid (0.992 g, 98); m.p. 144-146 °C. ¹H NMR (300.13 MHz, CDCl₃): δ = 3.71 (s, 3H, OCH₃), 5.36 (s, 2H, -CH₂-), 6.50 (dd,  J = 1.70 Hz,  J = 3.40 Hz, 1H, CH₇ₓfuranyl), 6.80 (d,  J = 8.6 Hz, 2H, ArH), 7.09-7.11 (m, 1H, CH₇ₓfuranyl), 7.25 (d,  J = 8.6 Hz, 2H, ArH), 7.50-7.52 (m, 1H, CH₇ₓfuranyl), 7.85 (s, 1H, ArH), 8.01 (s, 1H, ArH); ¹³C NMR (75.46 MHz, CDCl₃): δ = 47.0 (-CH₂-), 55.3 (OCH₃), 109.3 (CH₇ₓfuranyl), 110.3 (q,  ³JCF = 4.40 Hz, CH), 112.3 (CH₇ₓfuranyl), 114.5 (2CH), 122.7 (CF₃, q,  ¹JC = 273.45 Hz), 127.3 (C), 129.2 (q,  ³JC = 28.11 Hz, C), 129.6 (2CH), 130.1 (C), 143.7 (CH₇ₓfuranyl), 145.5 (CH), 148.2 (C), 153.2 (C), 159.8 (2C); ¹⁹F NMR (282.40 MHz, CDCl₃): δ = -62.32 (ArCF₃); IR (ATR, cm⁻¹):  ν = 3120 (w), 3065 (m), 3013 (w), 2942 (w), 2912 (w), 2838 (w), 1613 (m), 1586 (w), 1513 (s), 1493 (m), 1464 (w), 1454 (w), 1440 (w), 1425 (w), 1396 (m), 1386 (w), 1360 (s), 1313 (w), 1305 (m), 1287 (w), 1261 (w), 1243 (s), 1226 (w), 1201 (m), 1169 (s), 1153 (m), 1127 (s), 1098 (m), 1070 (w), 1031 (s), 1005 (m), 962 (s), 943 (w), 932 (w), 912 (m), 885 (w), 873 (w), 863 (m), 846 (w), 835 (w), 821 (m), 777 (m), 744 (s), 714 (w), 682 (w), 666 (m), 632 (s), 595 (m), 534 (m); GC-MS (EI, 70 eV): m/z (%): 373 (M⁺, 61), 358 (1), 224 (4), 207 (1), 173 (2), 150 (1), 121 (100), 91 (3), 77 (6), 51 (1); HRMS (ESI) calcd for C₁₉H₁₄F₃N₃O₂ [M+H]: 374.11109 found 374.1108.
Starting with CH$_2$Cl$_2$ (6 mL), 1 (0.55 mL, 6.15 mmol), 2b (0.65 mL, 6.15 mmol), 4d (1.37 g, 6.15 equiv.), 5d was isolated as pink solid (1.42 g, 71%); m.p. 143-145 °C. $^1$H NMR (300.13 MHz, DMSO-d$_6$): $\delta$ = 1.83 (s, 9H, 3CH$_3$), 7.20 (dd, $J$ = 3.78 Hz, $J$ = 1.13 Hz, 1H, CH$_{\text{thienyl}}$), 7.69 (d, $^3J$ = 5.0 Hz, 1H, CH$_{\text{thienyl}}$), 7.02 (d, $^3J$ = 3.7 Hz, 1H, CH$_{\text{thienyl}}$), 8.12 (s, 1H, ArH), 8.62 (s, 1H, ArH); $^{13}$C NMR (75.46 MHz, DMSO-d$_6$): $\delta$ = 28.4 (3CH$_3$), 57.5 (C), 109.1 (q, $^3J_{CF}$ = 4.40 Hz, CH), 122.8 (q, $^1J_{CF}$ = 273.99 Hz, CF$_3$), 126.3 (CH), 127.3 (q, $^2J_{CF}$ = 33.56 Hz, C), 128.7 (CH), 130.8 (C), 143.9 (C), 145.4 (CH), 146.2 (2C), 147.9 (C); $^{19}$F NMR (282.40 MHz, DMSO-d$_6$): $\delta$ = -60.85 (ArCF$_3$); IR (ATR, cm$^{-1}$): ~$\nu$ = 3125 (m), 3071 (w), 2976 (m), 2916 (w), 2874 (w), 1597 (s), 1540 (s), 1511 (w), 1482 (s), 1471 (m), 1433 (m), 1409 (w), 1388 (s), 1370 (s), 1350 (m), 1338 (m), 1303 (s), 1281 (w), 1264 (m), 1247 (m), 1224 (s), 1175 (s), 1149 (m), 1132 (s), 1082 (w), 1074 (w), 1063 (w), 1029 (w), 1020 (w), 931 (s), 900 (m), 872 (s), 846 (m), 826 (s), 818 (w), 791 (m), 770 (w), 749 (w), 723 (m), 702 (s), 666 (w), 658 (m), 647 (m), 635 (s), 618 (w), 611 (w), 589 (w), 570 (w), 554 (m), 530 (m); GC-MS (EI, 70 eV): m/z (%): 325 (M$^+$, 31), 269 (100), 250 (2), 224 (2), 205 (1), 146 (1), 57 (1), 41 (2), 29 (1); HRMS (ESI) calcd for C$_{15}$H$_{15}$F$_3$N$_3$ [M+H]$^+$: 326.0933 found 326.0936.

3-tert-Butyl-5-methyl-7-(trifluoromethyl)-3H-imidazo[4,5-b]pyridine (5e):

Starting with CH$_2$Cl$_2$ (6 mL), 1 (0.69 mL, 7.78 mmol), 2b (0.82 mL, 7.78 mmol), 4b (0.94 mL, 7.78 mmol), 5e was isolated as white solid (1.38 g, 69%); m.p. 100-102 °C. $^1$H NMR (300.13 MHz, CDCl$_3$): $\delta$ = 1.77 (s, 9H, 3CH$_3$), 2.64 (s, 3H, CH$_3$), 7.21 (s, 1H, ArH), 8.10 (s, 1H, ArH); $^{13}$C NMR (62.89 MHz, CDCl$_3$): $\delta$ = 24.7 (CH$_3$), 29.1 (3CH$_3$), 57.5 (C), 113.6 (q, $^3J_{CF}$ = 4.12 Hz, CH), 122.9 (q, $^1J_{CF}$ = 273.74 Hz, CF$_3$), 128.1 (q, $^2J_{CF}$ = 33.42 Hz, C), 130.3 (C), 142.9 (CH), 148.4 (C), 152.8 (C); $^{19}$F NMR (282.40 MHz, CDCl$_3$): $\delta$ = -62.23 (ArCF$_3$); IR (ATR, cm$^{-1}$): ~$\nu$ = 3119 (s), 2984 (m), 2922 (s), 2877 (w), 2854 (w), 1813 (w), 1731 (w), 1673 (w), 1596 (s), 1478 (s), 1464 (w), 1435 (w), 1401 (w), 1382 (m), 1371 (m), 1359 (m), 1336 (s), 1302 (w), 1282 (w), 1264 (m), 1228 (s), 1220 (w), 1197 (w), 1164 (m), 1125 (s), 1077 (m), 1031 (m), 997 (w), 968 (m), 934 (w), 910 (m), 892 (s), 863 (s), 834 (w), 809 (m), 758 (w), 724 (s), 680 (m), 669 (m), 638 (s), 627 (w), 563 (m), 547 (w), 533 (w); GC-MS (EI, 70 eV): m/z (%): 257 (M$^+$, 28), 242 (3), 201 (100), 182 (10), 154 (2), 132 (8), 105 (1), 78 (1), 57 (3), 41 (4), 29 (2); HRMS (ESI) calcd for C$_{12}$H$_{15}$F$_3$N$_3$ [M+H]$^+$: 258.12126 found 258.12141.
3-tert-Butyl-5-phenyl-7-(trifluoromethyl)-3H-imidazo[4,5-b]pyridine (5f):

Starting with CH₂Cl₂ (6 mL), 1 (0.84 mL, 9.4 mmol), 2b (0.99 mL, 9.4 mmol), 4e (2.03 g, 9.4 equiv.), 5f was isolated as white solid (2.32 g, 77%); m.p. 130-132 °C. ¹H NMR (300.13 MHz, CDCl₃): δ = 1.84 (s, 9H, 3CH₃), 7.35-7.47 (m, 3H, ArH), 7.85 (s, 1H, ArH), 8.03 (d, 3J = 8.3 Hz, 2H, ArH), 8.19 (s, 1H, ArH); ¹³C NMR (62.89 MHz, CDCl₃): δ = 29.2 (3CH₃), 57.8 (C), 111.1 (q, 3JCF = 4.12 Hz, CH), 122.9 (CF₃, q, 1JCF = 274.02 Hz), 127.0 (2CH), 128.8 (q, 2JCF = 33.42 Hz, C), 128.9 (2CH), 129.2 (CH), 131.5 (C), 138.6 (C), 143.9 (CH), 148.8 (C), 151.7 (C); ¹⁹F NMR (282.40 MHz, CDCl₃): δ = -62.24 (ArCF₃); IR (ATR, cm⁻¹): ν = 3117 (m), 3089 (w), 3027 (w), 2979 (m), 2912 (w), 2882 (w), 1812 (w), 1737 (w), 1603 (m), 1580 (w), 1536 (w), 1490 (s), 1476 (s), 1441 (m), 1373 (s), 1339 (m), 1291 (m), 1259 (s), 1228 (s), 1182 (w), 1172 (w), 1163 (w), 1147 (w), 1130 (s), 1085 (w), 1062 (m), 1027 (m), 1001 (w), 969 (w), 943 (s), 910 (w), 869 (s), 835 (w), 821 (m), 790 (w), 767 (s), 726 (s), 687 (s), 672 (w), 665 (m), 647 (m), 635 (m), 620 (s), 555 (m), 531 (w); GC-MS (EI, 70 eV): m/z (%): 319 (M⁺, 22), 300 (1), 264 (17), 263 (100), 242 (2), 215 (1), 193 (2), 158 (1), 140 (2), 57 (1), 41 (1); HRMS (ESI) caleld for C₁₇H₁₇F₃N₃ [M+H]⁺: 320.13691 found 320.13715.

3-Cyclohexyl-5-phenyl-7-(trifluoromethyl)-3H-imidazo[4,5-b]pyridine (5g):

Starting with CH₂Cl₂ (6 mL), 1 (0.52 mL, 5.79 mmol), 2c (0.66 mL, 5.79 mmol), 4e (1.25 g, 5.79 equiv.), 5g was isolated as reddish solid (1.4 g, 70%); m.p. 120-122 °C. ¹H NMR (300.13 MHz, CDCl₃): δ = 1.31-2.04 (m, 8H, 4-CH₂), 2.27-2.33 (m, 2H, -CH₂-), 4.68-4.78 (m, 1H, CH), 7.45-7.58 (m, 3H, ArH), 7.94 (s, 1H, ArH), 8.10-8.14 (m, 2H, ArH), 8.27 (s, 1H, ArH); ¹³C NMR (75.46 MHz, CDCl₃): δ = 25.3 (CH₂), 25.6 (2CH₂), 33.3 (2CH₂), 54.5 (CH), 111.7 (q, 3JCF = 4.40 Hz, CH), 122.9 (q, 1JCF = 273.45 Hz, CF₃), 127.2 (2CH), 128.93 (2CH), 128.94 (q, 2JCF = 34.1 Hz, C), 129.3 (CH), 130.5 (C), 138.6 (C), 143.9 (CH), 148.2 (C), 152.5 (C); ¹⁹F NMR (282.40 MHz, CDCl₃): δ = -62.21 (ArCF₃); IR (ATR, cm⁻¹): ν = 3102 (w), 3089 (w), 3038 (m), 2938 (m), 2922 (m), 2857 (w), 1781 (w), 1748 (w), 1603 (w), 1493 (m), 1478 (m), 1456 (w), 1450 (w), 1399 (w), 1387 (m), 1377 (s), 1346 (w), 1310 (m), 1288 (m), 1265 (s), 1207 (s), 1147 (m), 1140 (w), 1124 (s), 1010 (w), 1084 (w), 1068 (w), 1054 (w), 1029 (w), 1001 (w),
3-Phenethyl-5-(thiophen-2-yl)-7-(trifluoromethyl)-3H-imidazo[4,5-b]pyridine (5h):

Starting with CH₂Cl₂ (6 mL), 1 (0.48 mL, 5.36 mmol), 2d (0.68 mL, 5.36 mmol), 4d (1.2 g, 5.36 equiv.), 5h was isolated as light brown solid (1.5 g, 75%); m.p. 99-101 °C. ¹H NMR (300.13 MHz, CDCl₃): δ = 3.19 (t, J = 7.17, 2H, -CH₂-), 4.51 (t, J = 7.17, 2H, -CH₂-), 7.04-7.09 (m, 3H, ArH), 7.12-7.25 (m, 3H, ArH), 7.37 (d, J = 5.0 Hz, 1H, CHthienyl), 7.61 (d, J = 3.5 Hz, 1H), 7.75 (s, 1H, ArH), 7.81 (s, 1H, ArH); ¹³C NMR (75.46 MHz, CDCl₃): δ = 36.1 (-CH₂-), 45.7 (-CH₂-), 110.5 (q, J = 4.40 Hz, CH), 122.7 (q, J = 273.45 Hz, CF₃), 125.5 (CH), 127.1 (CH), 128.2 (CH), 128.3 (CH) 128.7 (2CH), 128.9 (2CH), 129.6 (q, J = 34.11 Hz, C), 137.3 (C), 144.0 (C), 145.6 (CH), 147.9 (C), 148.3 (2C); ¹⁹F NMR (282.40 MHz, CDCl₃): δ = -62.27 (ArCF₃); IR (ATR, cm⁻¹): ν = 3103 (w), 3084 (w), 3031 (w), 2942 (w), 2869 (w), 1769 (w), 1596 (s), 1538 (m), 1496 (m), 1476 (w), 1454 (w), 1431 (s), 1397 (m), 1375 (s), 1349 (m), 1306 (w), 1298 (w), 1276 (m), 1261 (s), 1202 (s), 1123 (s), 1102 (m), 1027 (m), 1003 (w), 934 (m), 907 (w), 889 (w), 867 (s), 847 (w), 827 (m), 772 (w), 737 (m), 693 (s), 655 (m), 632 (m), 615 (w), 590 (w), 566 (w), 535 (w); GC-MS (EI, 70 eV): m/z (%): 373 (M⁺, 30), 354 (2), 269 (100), 208 (2), 104 (S), 91 (4), 77 (2), 65 (1); HRMS (ESI) calcd for C₁₉H₁₉F₃N₃S [M+H⁺]: 374.09333 found 374.0932.

3-(4-Methoxybenzyl)-2-p-tolyl-5,7-bis(trifluoromethyl)-3H-imidazo[4,5-b]pyridine (6a):

brownish solid; mp 106–108 °C; ¹H NMR (250.12 MHz, DMSO-d₆): δ = 2.40 (s, 3H, CH₃), 3.67 (s, 3H, OCH₃), 5.65 (s, 2H, -CH₂-), 6.80 (d, J = 8.82 Hz, 2H, ArH), 6.96 (d, J = 8.82 Hz, 2H, ArH), 7.37 (d, J = 8.19 Hz, 2H, ArH), 7.73 (d, J = 8.19 Hz, 2H, ArH), 8.11 (s, 1H, ArH); ¹³C NMR (62.89 MHz, CDCl₃): δ = 21.5 (CH₃), 47.1 (-CH₂-), 55.2 (OCH₃), 111.6 (CH), 114.2 (2CH), 121.9 (q, J = 274.2 Hz, CF₃), 125.8 (C), 126.3 (q, J = 274.2 Hz,
3-(4-Methoxybenzyl)-5-methyl-2-p-tolyl-7-(trifluoromethyl)-3H-imidazo[4,5-b]pyridine (6b):

[Chemical structure]

Deep brown solid; mp 114–116 °C; $^1$H NMR (250.13 MHz, DMSO-d$_6$): $\delta$ = 2.36 (s, 3H, CH$_3$), 2.66 (s, 3H, CH$_3$), 3.65 (s, 3H, OCH$_3$), 5.57 (s, 2H, -CH$_2$-), 6.79 (d, $^3$J = 8.75 Hz, 2H, ArH), 6.92 (d, $^3$J = 8.75 Hz, 2H, ArH), 7.32 (d, $^3$J = 8.00 Hz, 2H, ArH), 7.54 (s, 1H, ArH), 7.66 (d, $^3$J = 8.12 Hz, 2H, ArH); $^{13}$C NMR (62.89 MHz, CDCl$_3$): $\delta$ = 21.4 (CH$_3$), 24.5 (CH$_3$), 46.3 (-CH$_2$-), 55.2 (OCH$_3$), 114.2 (2CH), 114.4 (q, $^3$J$_{CF}$ = 4.12 Hz, CH), 123.0 (q, $^1$J$_{CF}$ = 273.74 Hz, CF$_3$), 126.7 (C), 127.7 (q, $^2$J$_{CF}$ = 33.42 Hz, C), 128.3 (2CH), 128.8 (C), 129.1 (C), 129.4 (2CH), 129.5 (2CH), 140.7 (C), 149.9 (C), 153.3 (C), 156.1 (C), 159.1 (C); $^{19}$F NMR (300.13 MHz, CDCl$_3$): $\delta$ = -61.83 (ArCF$_3$); IR (ATR, cm$^{-1}$): $\tilde{\nu}$ = 3066 (w), 3038 (w), 3009 (w), 2957 (w), 2921 (m), 2839 (w), 1613 (m), 1597 (w), 1584 (w), 1511 (s), 1468 (m), 1449 (m), 1426 (w), 1407 (m), 1388 (m), 1372 (w), 1362 (w), 1300 (m), 1279 (m), 1261 (w), 1245 (s), 1225 (w), 1190 (w), 1175 (w), 1162 (m), 1124 (s), 1097 (m), 1031 (s), 961 (w), 927 (w), 896 (s), 871 (s), 834 (w), 820 (s), 802 (w), 776 (m), 749 (w), 730 (s), 719 (s), 708 (w), 695 (w), 679 (s), 665 (w), 648 (m), 638 (w), 629 (w), 621 (w), 592 (s), 555 (m), 535 (w); GC-MS (EI, 70 eV): m/z (%): 411 (M$^+$, 49), 392 (1), 290 (2), 270 (1), 206 (1), 161 (1), 121 (100), 77 (4); HRMS (ESI) calcd for C$_{23}$H$_{20}$F$_3$N$_3$O $[M + H]^+$: 412.16312 found 412.16302.

5-(Furan-2-yl)-3-(4-methoxybenzyl)-2-p-tolyl-7-(trifluoromethyl)-3H-imidazo[4,5-b]pyridine (6c):

GC-MS (EI, 70 eV): m/z (%): 465 (M$^+$, 31), 446 (1), 232 (1), 121 (100), 77 (4); HRMS (EI) calcd for C$_{23}$H$_17$F$_6$N$_3$O $[M^+]$: 466.13486 found 466.13458.
brown solid; mp 98–100 °C; $^1$H NMR (300.13 MHz, CDCl$_3$): $\delta$ = 2.36 (s, 3H, CH$_3$), 3.68 (s, 3H, OCH$_3$), 5.48 (s, 2H, -CH$_2$-), 6.49 (dd, $J = 1.70$ Hz, $J = 3.40$ Hz, 1H, CH$_{furyl}$), 6.71 (d, $J = 8.87$ Hz, 2H, ArH), 7.01 (d, $J = 8.87$ Hz, 2H, ArH), 7.04-7.06 (m, 1H, CH$_{furyl}$), 7.21 (d, $J = 8.31$ Hz, 2H, ArH), 7.48-7.50 (m, 1H, CH$_{furyl}$), 7.54 (d, $J = 8.31$ Hz, 2H, ArH), 7.85 (s, 1H, ArH); $^{13}$C NMR (62.89 MHz, CDCl$_3$): $\delta$ = 21.5 (CH$_3$), 46.6 (-CH$_2$-), 55.2 (OCH$_3$), 108.9 (CH$_{furyl}$), 112.3 (CH$_{furyl}$), 114.1 (2CH), 122.9 (CF$_3$, q, $^1$J$_{CF} = 272.37$ Hz), 124.0 (CH), 126.6 (C), 128.3 (q, $^2$J$_{CF} = 34.33$ Hz, C), 128.6 (CH), 128.7 (2CH), 129.4 (CH), 129.5 (2CH), 137.9 (C), 140.9 (CH$_{furyl}$), 143.5 (C), 144.1 (C), 150.2 (C), 152.4 (C), 153.5 (C), 155.2 (C), 159.2 (C); $^{19}$F NMR (282.40 MHz, CDCl$_3$): $\delta$ = -61.97 (ArCF$_3$); IR (ATR, cm$^{-1}$): $\tilde{\nu}$ = 3033 (w), 2998 (w), 2956 (w), 2929 (w), 2873 (w), 2837 (w), 1809 (w), 1731 (w), 1698 (m), 1612 (s), 1586 (w), 1513 (s), 1496 (w), 1463 (s), 1455 (s), 1416 (m), 1406 (m), 1371 (m), 1270 (w), 1246 (s), 1165 (m), 1134 (s), 1095 (w), 1030 (w), 1019 (w), 944 (w), 912 (w), 878 (w), 821 (s), 767 (w), 732 (m), 677 (w), 664 (m), 638 (w), 622 (w), 590 (w), 561 (w), 533 (w); GC-MS (EI, 70 eV): m/z (%): 463 (M$^+$, 50), 444 (1), 342 (3), 121 (100), 116 (2), 91 (2), 77 (4); HRMS (EI) calcd for C$_{26}$H$_{20}$F$_3$N$_3$O$_2$ [M$^+$]: 463.15021 found 463.151076.

3-tert-Butyl-5-(thiophen-2-yl)-2-p-tolyl-7-(trifluoromethyl)-3H-imidazo[4,5-b]pyridine (6d):

light brown solid; mp 190–192 °C; $^1$H NMR (300.13 MHz, CDCl$_3$): $\delta$ = 1.66 (s, 9H, 3CH$_3$), 2.35 (s, 3H, CH$_3$), 7.06-7.09 (d, $^3$J = 3.59 Hz, 1H, CH$_{thienyl}$), 7.14-7.19 (m, 2H, ArH), 7.31-7.35 (m, 2H, ArH), 7.54 (d, $^3$J = 3.78 Hz, 1H, CH$_{thienyl}$), 7.58 (dd, $J = 3.78$ Hz, $J = 1.13$ Hz, 1H, CH$_{thienyl}$), 7.74 (s, 1H, ArH); $^{13}$C NMR (75.46 MHz, CDCl$_3$): $\delta$ = 21.5 (CH$_3$), 31.0 (3CH$_3$), 61.2 (C), 109.8 (q, $^3$J$_{CF} = 4.40$ Hz, CH), 122.9 (q, $^1$J$_{CF} = 273.99$ Hz, CF$_3$), 125.7 (CH), 127.7 (CH), 128.0 (q, $^2$J$_{CF} = 34.11$ Hz, C), 128.3 (CH), 128.6 (2CH), 129.7 (2CH), 131.4 (C), 139.8 (C), 143.5 (C), 145.0 (C), 146.1 (C), 146.7 (C), 150.1 (C); $^{19}$F NMR (282.40 MHz, CDCl$_3$): $\delta$ = -61.98 (ArCF$_3$); IR (ATR, cm$^{-1}$): $\tilde{\nu}$ = 3094 (w), 3069 (w), 3022 (w), 2980 (w), 2960 (w), 2919 (w), 2871 (w), 1618 (w), 1606 (w), 1589 (m), 1548 (w), 1536 (w), 1510 (w), 1504 (w), 1467 (s), 1429 (m), 1390 (w), 1381 (s), 1351 (m), 1334 (w), 1304 (w), 1276 (m), 1257 (m), 1248 (w), 1226 (w), 1218 (w), 1183 (w), 1170 (w), 1155 (w), 1137 (s), 1126 (m), 1072 (w), 1063 (w), 1053 (m), 1026 (w), 1015 (w), 950 (w), 945 (w), 906 (w), 875 (w), 864 (m), 849 (w), 827 (w), 817 (m),
3-tert-Butyl-5-phenyl-2-p-tolyl-7-(trifluoromethyl)-3H-imidazo[4,5-b]pyridine (6e):

Light brown solid; mp 239–240 °C; \(^1\)H NMR (300 MHz, CDCl₃): δ = 1.68 (s, 9H, 3CH₃), 2.35 (s, 3H, CH₃), 7.16-7.19 (m, 2H, ArH), 7.32-7.40 (m, 3H, ArH), 7.43-7.48 (m, 2H, ArH), 7.86 (s, 1H, ArH); 13C NMR (75.46 MHz, CDCl₃): δ = 21.5 (CH₃), 31.1 (3CH₃), 60.9 (C), 111.1 (q, \(^3\)J_CF = 4.40 Hz, CH), 123.1 (q, \(^1\)J_CF = 273.45 Hz, CF₃), 126.9 (2CH), 127.9 (q, \(^2\)J_CF = 33.56 Hz, C), 128.6 (2CH), 128.9 (2CH), 129.1 (CH), 129.6 (2CH), 131.6 (2C), 138.9 (2C), 139.8 (2C), 150.7 (C); \(^1^9\)F NMR (282.40 MHz, CDCl₃): δ = -61.63 (ArCF₃); IR (ATR, cm⁻¹): \(\tilde{\nu}\) = 3054 (w), 3028 (w), 2982 (w), 2922 (m), 2853 (w), 1698 (w), 1658 (m), 1619 (w), 1593 (m), 1498 (w), 1469 (m), 1461 (m), 1381 (s), 1331 (w), 1318 (w), 1302 (w), 1276 (m), 1247 (s), 1184 (w), 1175 (w), 1147 (w), 1128 (s), 1113 (w), 1082 (w), 1070 (w), 1056 (w), 1017 (w), 973 (w), 959 (m), 947 (w), 923 (w), 907 (w), 877 (s), 853 (w), 828 (w), 819 (m), 794 (w), 777 (m), 733 (m), 727 (w), 701 (m), 694 (w), 680 (w), 666 (w), 635 (w), 626 (s), 604 (w), 575 (w), 534 (w); GC-MS (EI, 70 eV): m/z (%): 415 (M⁺, 8), 359 (100), 338 (3), 196 (1), 146 (2), 118 (2), 91 (1), 57 (1), 41 (2), 29 (1); HRMS (ESI) calcd for C₂₂H₂₁F₃N₃S [M+H]⁺: 416.14028 found 416.14085.

3-tert-Butyl-2-(2,4-dimethylphenyl)-5-methyl-7-(trifluoromethyl)-3H-imidazo[4,5-b]pyridine (6f):

Light grey gummy solid; \(^1\)H NMR (300.13 MHz, CDCl₃): δ = 1.60 (s, 9H, 3CH₃), 2.26 (s, 6H, 2CH₃), 2.64 (s, 3H, CH₃), 7.00-7.02 (m, 3H, ArH), 7.20 (s, 1H, ArH); 13C NMR (75.46 MHz, CDCl₃): δ = 21.2 (2CH₃), 24.7 (CH₃), 30.8 (3CH₃), 60.6 (C), 113.4 (q, \(^3\)J_CF = 4.40 Hz, CH), 123.1 (q, \(^1\)J_CF = 273.45 Hz, CF₃), 127.3 (q, \(^2\)J_CF = 33.01 Hz, C), 127.6 (CH), 129.2 (C), 131.0 (CH), 134.7 (2C), 137.4 (CH), 150.3 (C), 151.7 (2C), 156.2 (C); \(^1^9\)F NMR (282.40 MHz, CDCl₃): δ = -61.78 (ArCF₃); IR (ATR, cm⁻¹): \(\tilde{\nu}\) = 2968 (w), 2922 (m), 2861 (w), 1737 (w), 1604 (w), 1589 (m), 1495 (w), 1476 (w), 1457 (m), 1386 (s),
3-tert-Butyl-2-(4-ethylphenyl)-5-methyl-7-(trifluoromethyl)-3H-imidazo[4,5-b]pyridine (6g):

Light brown gummy solid; \(^1\)H NMR (300.13 MHz, CDCl\(_3\)): \(\delta = 1.17\) (t, 3H, CH\(_3\)), \(1.58\) (s, 9H, 3CH\(_3\)), \(2.55\) (m, 2H, -CH\(_2\)-), \(2.62\) (s, 3H, CH\(_3\)), \(7.05\) (d, \(3^J = 8.68\) Hz, 2H, ArH), \(7.19\) (s, 1H, ArH), \(7.31\) (d, \(3^J = 8.10\) Hz, 2H, ArH); \(^13\)C NMR (62.89 MHz, CDCl\(_3\)): \(\delta = 15.6\) (CH\(_3\)), \(24.8\) (CH\(_3\)), \(28.6\) (-CH\(_2\)-), \(30.9\) (3CH\(_3\)), \(60.7\) (C), \(113.5\) (q, \(3^J_{CF} = 4.58\) Hz, CH), \(123.2\) (q, \(1^J_{CF} = 273.74\) Hz, CF\(_3\)), \(126.9\) (2CH), \(128.3\) (2CH), \(132.3\) (C), \(138.6\) (C), \(143.1\) (C), \(145.9\) (C), \(150.4\) (C), \(151.8\) (C), \(155.8\) (q, \(2^J_{CF} = 34.33\) Hz, C); \(^19\)F NMR (282.40 MHz, CDCl\(_3\)): \(\delta = -61.74\) (ArCF\(_3\)); IR (ATR, cm\(^{-1}\)): \(\tilde{\nu} = 3023\) (w), \(2964\) (s), \(2929\) (m), \(2872\) (w), \(2725\) (w), \(2632\) (w), \(2300\) (w), \(2228\) (w), \(1905\) (w), \(1788\) (w), \(1737\) (w), \(1659\) (w), \(1592\) (m), \(1499\) (s), \(1462\) (s), \(1410\) (w), \(1386\) (s), \(1365\) (s), \(1306\) (m), \(1268\) (w), \(1228\) (s), \(1169\) (w), \(1158\) (w), \(1136\) (s), \(1072\) (m), \(1049\) (w), \(1019\) (m), \(1006\) (w), \(979\) (w), \(965\) (w), \(933\) (w), \(898\) (s), \(871\) (m), \(846\) (w), \(831\) (w), \(819\) (s), \(783\) (w), \(765\) (w), \(732\) (m), \(703\) (w), \(685\) (m), \(669\) (w), \(646\) (w), \(634\) (w), \(615\) (w), \(690\) (m), \(554\) (w); GC-MS (EI, 70 eV): m/z (%): 361 (M\(^+\), 11), 305 (100), 285 (4), 270 (1), 132 (2), 116 (3), 77 (1), 57 (1), 41 (1); HRMS (ESI) calcd for C\(_{20}\)H\(_{23}\)F\(_3\)N\(_3\) [M+H]\(^+\): 362.18386 found 362.18417.

5-(Furan-2-yl)-3-(4-methoxybenzyl)-2-phenyl-7-(trifluoromethyl)-3H-imidazo[4,5-b]pyridine (6h):

Brown solid; mp 103–105 °C; \(^1\)H NMR (300.13 MHz, CDCl\(_3\)): \(\delta = 3.67\) (s, 3H, OCH\(_3\)), \(5.48\) (s, 2H, -CH\(_2\)-), \(6.49\) (dd, \(J = 1.89\) Hz, \(J = 3.40\) Hz, 1H, CH\(_{furyl}\)), \(6.72\) (d, \(3^J = 8.69\) Hz, 2H, ArH), \(7.03\) (d, \(3^J = 8.88\) Hz, 1H, CH\(_{furyl}\)), \(7.26\) (d, \(3^J = 8.69\) Hz, 1H, CH\(_{furyl}\)), \(7.37\) (d, \(3^J = 8.69\) Hz, 2H, ArH), \(7.44\) (m, 1H, ArH), \(7.61-7.66\) (m, 2H, ArH), \(7.73\) (d, \(3^J = 8.50\) Hz, 2H, ArH), \(7.86\) (s, 1H, ArH); \(^13\)C NMR (75.46 MHz, CDCl\(_3\)): \(\delta = 46.7\) (-CH\(_2\)-), \(55.2\) (OCH\(_3\)), \(107.8\) (CH\(_{furyl}\)), \(111.4\) (CH\(_{furyl}\)), \(114.3\) (2CH), \(121.7\) (q, \(1^J_{CF} = 274.55\) Hz, CF\(_3\)), \(124.1\) (CH), \(126.4\) (C), \(127.9\) (2CH), \(128.6\) (q, \(3^J_{CF} = 34.33\) Hz, C); IR (ATR, cm\(^{-1}\)): \(\tilde{\nu} = 3 023\) (w), \(2964\) (s), \(2929\) (m), \(2872\) (w), \(2725\) (w), \(2632\) (w), \(2300\) (w), \(2228\) (w), \(1905\) (w), \(1788\) (w), \(1737\) (w), \(1659\) (w), \(1592\) (m), \(1499\) (s), \(1462\) (s), \(1410\) (w), \(1386\) (s), \(1365\) (s), \(1306\) (m), \(1268\) (w), \(1228\) (s), \(1169\) (w), \(1158\) (w), \(1136\) (s), \(1072\) (m), \(1049\) (w), \(1019\) (m), \(1006\) (w), \(979\) (w), \(965\) (w), \(933\) (w), \(898\) (s), \(871\) (m), \(846\) (w), \(831\) (w), \(819\) (s), \(783\) (w), \(765\) (w), \(732\) (m), \(703\) (w), \(685\) (m), \(669\) (w), \(646\) (w), \(634\) (w), \(615\) (w), \(690\) (m), \(554\) (w)); GC-MS (EI, 70 eV): m/z (%): 361 (M\(^+\), 11), 305 (100), 290 (58), 284 (5), 270 (3), 250 (1), 132 (1), 102 (1), 89 (2), 77 (1), 57 (2), 41 (2), 29 (1); HRMS calcd for C\(_{20}\)H\(_{23}\)F\(_3\)N\(_3\) [M+H]\(^+\): 362.18386 found 362.18395.
3-Phenethyl-2-phenyl-5-(thiophen-2-yl)-7-(trifluoromethyl)-3H-imidazo[4,5-b]pyridine (6i):

Bright yellow solid; mp 137–139 °C; \(^1H\) NMR (300.13 MHz, CDCl\(_3\)): \(\delta = 3.14 (t, J = 6.99, 2H, -CH\textsubscript{2}-), 4.57 (t, J = 7.55, 2H, -CH\textsubscript{2}-), 6.99 (d, J = 8.12 Hz, 2H, ArH), 7.12-7.16 (m, 2H, ArH), 7.28-7.44 (m, 5H, ArH), 7.51-7.59 (m, 2H, ArH), 7.63 (d, J = 7.18 Hz, 2H, ArH), 7.76 (s, 1H, ArH); \(^13C\) NMR (62.89 MHz, CDCl\(_3\)): \(\delta = 35.6 (-\text{CH}\textsubscript{2}-), 45.6 (-\text{CH}\textsubscript{2}-), 110.3 (q, J\textsubscript{CF} = 4.12 Hz, CH), 122.8 (q, J\textsubscript{CF} = 274.00 Hz, CF\textsubscript{3}), 124.2 (CH), 125.8 (2CH), 126.0 (CH), 126.9 (CH), 127.9 (CH), 128.3 (q, J\textsubscript{CF} = 33.88 Hz, C), 128.7 (CH), 128.8 (3CH), 129.0 (CH), 129.3 (CH), 129.5 (C), 130.4 (CH), 134.2 (C), 134.3 (C), 146.6 (C), 149.8 (C), 156.5 (C); \(^19F\) NMR (282.40 MHz, CDCl\(_3\)): \(\delta = -61.99 (\text{ArCF}_3); IR (\text{ATR}, \text{cm}^{-1}): \tilde{\nu} = 3025 (w), 2960 (s), 2927 (m), 2868 (w), 1907 (w), 1732 (w), 1600 (m), 1544 (m), 1496 (m), 1467 (w), 1453 (w), 1443 (w), 1418 (w), 1384 (s), 1367 (w), 1339 (w), 1329 (w), 1309 (w), 1271 (m), 1250 (m), 1228 (w), 1155 (w), 1125 (s), 1099 (w), 1073 (w), 1049 (w), 1029 (w), 1020 (w), 1004 (w), 959 (w), 942 (w), 929 (w), 898 (w), 868 (m), 846 (w), 833 (w), 809 (s), 779 (w), 755 (m), 739 (w), 696 (w), 684 (m), 666 (w), 618 (w), 609 (w), 586 (w), 558 (m), 532 (w); GC-MS (EI, 70 eV): m/z (%): 449 (M\(^+\), 39), 328 (3), 121 (100), 105 (17), 77 (13), 39 (1); HRMS (ESI) calcd for C\(_{25}\)H\(_{19}\)F\(_3\)N\(_3\)O\(_2\) [M+H\(^+\)]: 450.10370 found 450.10288.

3-Cyclohexyl-2-(2-fluorophenyl)-5-phenyl-7-(trifluoromethyl)-3H-imidazo[4,5-b]pyridine (6j):

Bright yellow solid; mp 137–139 °C; \(^1H\) NMR (300.13 MHz, CDCl\(_3\)): \(\delta = 3.14 (t, J = 6.99, 2H, -CH\textsubscript{2}-), 4.57 (t, J = 7.55, 2H, -CH\textsubscript{2}-), 6.99 (d, J = 8.12 Hz, 2H, ArH), 7.12-7.16 (m, 2H, ArH), 7.28-7.44 (m, 5H, ArH), 7.51-7.59 (m, 2H, ArH), 7.63 (d, J = 7.18 Hz, 2H, ArH), 7.76 (s, 1H, ArH); \(^13C\) NMR (62.89 MHz, CDCl\(_3\)): \(\delta = 35.6 (-\text{CH}\textsubscript{2}-), 45.6 (-\text{CH}\textsubscript{2}-), 110.3 (q, J\textsubscript{CF} = 4.12 Hz, CH), 122.8 (q, J\textsubscript{CF} = 274.00 Hz, CF\textsubscript{3}), 124.2 (CH), 125.8 (2CH), 126.0 (CH), 126.9 (CH), 127.9 (CH), 128.3 (q, J\textsubscript{CF} = 33.88 Hz, C), 128.7 (CH), 128.8 (3CH), 129.0 (CH), 129.3 (CH), 129.5 (C), 130.4 (CH), 134.2 (C), 134.3 (C), 146.6 (C), 149.8 (C), 156.5 (C); \(^19F\) NMR (282.40 MHz, CDCl\(_3\)): \(\delta = -61.99 (\text{ArCF}_3); IR (\text{ATR}, \text{cm}^{-1}): \tilde{\nu} = 3025 (w), 2960 (s), 2927 (m), 2868 (w), 1907 (w), 1732 (w), 1600 (m), 1544 (m), 1496 (m), 1467 (w), 1453 (w), 1443 (w), 1418 (w), 1384 (s), 1367 (w), 1339 (w), 1329 (w), 1309 (w), 1271 (m), 1250 (m), 1228 (w), 1155 (w), 1125 (s), 1099 (w), 1073 (w), 1049 (w), 1029 (w), 1020 (w), 1004 (w), 959 (w), 942 (w), 929 (w), 898 (w), 868 (m), 846 (w), 833 (w), 809 (s), 779 (w), 755 (m), 739 (w), 696 (w), 684 (m), 666 (w), 618 (w), 609 (w), 586 (w), 558 (m), 532 (w); GC-MS (EI, 70 eV): m/z (%): 449 (M\(^+\), 39), 328 (3), 121 (100), 105 (17), 77 (13), 39 (1); HRMS (ESI) calcd for C\(_{25}\)H\(_{19}\)F\(_3\)N\(_3\)S [M+H\(^+\)]: 450.12463 found 450.12452.
light brown solid; mp 188–190 °C. \(^1\)H NMR (300.13 MHz, CDCl\(_3\)): \(\delta = 1.17-1.39 \text{ (m, 4H, 2-CH}_2\text{-)}, 1.66-1.86 \text{ (m, 4H, 2-CH}_2\text{-)}, 2.70-2.82 \text{ (m, 2H, -CH}_2\text{-)}, 3.97-4.05 \text{ (m, 1H, CH), 7.13-7.19 \text{ (m, 1H, ArH), 7.23-7.28 \text{ (m, 1H, ArH), 7.33-7.51 \text{ (m, 4H, ArH), 7.57-7.63 \text{ (m, 1H, ArH), 7.85 (s, 1H, ArH), 8.01-8.05 \text{ (m, 2H, ArH); 13C NMR (62.89 MHz, CDCl}_3\text{:} \delta = 25.3 \text{ (-CH}_2\text{-), 26.1 (2-CH}_2\text{-), 30.9 (2-CH}_2\text{-), 58.4 (CH), 111.2 (q, ^3\text{J}_{CF} = 4.58 \text{ Hz, CH), 115.9 (d, ^2\text{J}_{CF} = 21.06 \text{ Hz, CH), 118.5 (d, ^2\text{J}_{CF} = 15.11 \text{ Hz, C), 123.1 (q, ^1\text{J}_{CF} = 274.20 \text{ Hz, CF}_3\text{), 124.9 (d, ^3\text{J}_{CF} = 3.66 \text{ Hz, CH), 127.0 (2CH), 128.5 (q, ^2\text{J}_{CF} = 33.87 \text{ Hz, C), 128.9 (2CH), 129.2 (CH), 130.8 (q, ^3\text{J}_{CF} = 1.83 \text{ Hz, C), 132.6 (q, ^3\text{J}_{CF} = 2.29 \text{ Hz, CH), 138.8 (C), 149.6 (C), 151.6 (C), 151.9 (C), 158.3 (C), 162.3 (C); ^19\text{F NMR (282.40 MHz, CDCl}_3\text{:} \delta = -112.63 \text{ (ArF), -61.96 (ArCF}_3\text{); IR (ATR, cm}^{-1}\text{:} \nu = 3054 \text{ (w), 2922 (m), 2850 (m), 1616 (w), 1606 (w), 1591 (w), 1506 (w), 1480 (m), 1446 (s), 1416 (m), 1386 (s), 1355 (w), 1319 (m), 1281 (s), 1252 (s), 1224 (w), 1211 (m), 1194 (w), 1187 (w), 1154 (s), 1137 (s), 1124 (s), 1109 (w), 1097 (w), 1076 (m), 1028 (w), 962 (m), 923 (w), 883 (m), 876 (s), 851 (w), 834 (m), 798 (m), 772 (s), 740 (m), 710 (w), 695 (s), 675 (w), 661 (m), 617 (m), 562 (w), 537 (w); GC-MS (EI, 70 eV): m/z (%): 439 (M\(^+\), 20), 420 (4), 370 (5), 357 (100), 336 (3), 158 (1), 140 (1), 102 (1), 41 (1); HRMS (ESI) calcd for C\(_{25}\)H\(_{22}\)F\(_4\)N\(_3\) [M+H]+: 440.17444 found 440.17533.

3-tert-Butyl-2-(2-fluorophenyl)-5-phenyl-7-(trifluoromethyl)-3H-imidazo[4,5-b]pyridine (6k):
yellow solid; mp 156–158 °C. \(^1\)H NMR (300.13 MHz, CDCl\(_3\)): \(\delta = 1.71 \text{ (s, 9H, CH}_3\text{), 7.06-7.22 \text{ (m, 3H, ArH), 7.37-7.49 \text{ (m, 4H, ArH), 7.88 \text{ (s, 1H, ArH), 8.06 \text{ (d, ^3\text{J} = 8.49 \text{ Hz, 2H, ArH); 13C NMR (62.89 MHz, CDCl}_3\text{:} \delta = 30.1 (3CH}_3\text{), 61.1 (C), 111.2 (q, ^3\text{J}_{CF} = 4.58 \text{ Hz, CH), 115.5 (d, ^2\text{J}_{CF} = 21.06 \text{ Hz, CH), 123.0 (q, ^1\text{J}_{CF} = 274.20 \text{ Hz, CF}_3\text{), 123.2 (d, ^2\text{J}_{CF} = 16.02 \text{ Hz, C), 124.1 (d, ^3\text{J}_{CF} = 3.66 \text{ Hz, CH), 127.0 (2CH), 128.5 (q, ^2\text{J}_{CF} = 33.88 \text{ Hz, C), 128.9 (2CH), 129.1 (CH), 130.5 (q, ^3\text{J}_{CF} = 1.83 \text{ Hz, C), 131.6 (d, ^3\text{J}_{CF} = 2.29 \text{ Hz, CH), 131.9 (d, ^3\text{J}_{CF} = 7.78 \text{ Hz, CH), 138.8 (C), 150.5 (C), 150.9 (C), 151.1 (C), 158.5 (C), 162.5 (C); ^19\text{F NMR (282.40 MHz, CDCl}_3\text{:} \delta = -111.97 \text{ (ArF), -61.90 (ArCF}_3\text{); IR (ATR, cm}^{-1}\text{:} \nu = 3466 \text{ (w), 3057 \text{ (w), 2980 (w), 1737 (w), 1621 (w), 1580 (w), 1513 (w), 1474 (w), 1455 (m), 1448 (w), 1379 (s), 1366 (w), 1337 (w), 1320 (w), 1273 (w), 1255 (m), 1169 (s), 1153 (m), 1136 (w), 1113 (m), 1102 (w), 1067 (w), 1053 (m), 1035 (w), 1022 (w), 1000 (w), 983 (w), 960 (m), 948 (w), 933 (w), 919 (w), 883 (m), 867 (m), 818 (w), 798 (w), 768 (s), 747 (m), 732 (w), 687 (s), 672 (w), 620 (m), 602 (w), 591 (w), 529 (w); GC-MS (EI, 70
eV): m/z (%): 413 (M⁺, 13), 357 (100), 336 (4), 236 (1), 215 (1), 189 (3), 140 (2), 121 (1), 57 (1), 41 (1); HRMS (ESI) calcd for C_{23}H_{20}F_{4}N_{3} [M+H]^+: 414.15879 found 414.15857.

3-tert-Butyl-5-methyl-7-(trifluoromethyl)-2-(3-(trifluoromethyl)phenyl)-3H-imidazo[4,5-b]pyridine (6l): deep brown gummy solid; ¹H NMR (300.13 MHz, CDCl₃): δ = 1.60 (s, 9H, 3CH₃), 2.67 (s, 3H, CH₃), 7.26 (s, 1H, ArH), 7.48-7.75 (m, 4H, ArH); ¹³C NMR (75.46 MHz, CDCl₃): δ = 24.8 (CH₃), 31.0 (3CH₃), 60.9 (C), 113.9 (q, ³J_{CF} = 4.40 Hz, CH), 122.9 (q, ¹J_{CF} = 273.45 Hz, CF₃), 123.7 (q, ¹J_{CF} = 272.35 Hz, CF₃), 126.4 (q, ³J_{CF} = 3.85 Hz, CH), 126.8 (q, ³J_{CF} = 3.85 Hz, CH), 127.8 (q, ²J_{CF} = 32.56 Hz, C), 128.6 (CH), 129.5 (C), 130.5 (q, ²J_{CF} = 32.46 Hz, C), 133.2 (CH), 135.7 (C), 150.1 (C), 152.6 (C), 153.7 (C); ¹⁹F NMR (282.40 MHz, CDCl₃): δ = -62.77 (ArCF₃), -62.01 (ArCF₃); IR (ATR, cm⁻¹): ν = 2961 (w), 2926 (m), 2855 (w), 1728 (w), 1591 (w), 1477 (w), 1468 (w), 1433 (w), 1389 (m), 1368 (m), 1335 (w), 1318 (m), 1304 (m), 1274 (m), 1229 (m), 1162 (m), 1127 (s), 1094 (w), 1072 (m), 1032 (w), 1003 (w), 984 (w), 933 (w), 901 (m), 853 (w), 808 (m), 742 (w), 729 (w), 706 (s), 697 (w), 666 (w), 651 (w), 628 (w), 586 (w), 536 (w); GC-MS (EI, 70 eV): m/z (%): 401 (M⁺, 3), 382 (2), 345 (100), 326 (4), 172 (3), 152 (1), 145 (1), 146 (1), 57 (2), 41 (2), 29 (1); HRMS (ESI) calcd for C_{19}H_{17}F_{6}N_{3} [M+H]^+: 402.13994 found 402.1395.

3-Cyclohexyl-5-phenyl-7-(trifluoromethyl)-2-(4-(trifluoromethyl)phenyl)-3H-imidazo[4,5-b]pyridine (6m): light yellow solid; mp 225–227 °C; ¹H NMR (300.13 MHz, CDCl₃): δ = 1.15-1.40 (m, 4H, 2-CH₂-), 1.86-1.96 (m, 4H, 2-CH₂-), 2.75-2.93 (m, 2H, -CH₂-), 4.22-4.33 (m, 1H, CH), 7.35-7.41 (m, 1H, ArH), 7.43-7.51 (m, 2H, ArH), 7.73-7.79 (m, 4H, ArH), 7.87 (s, 1H, ArH), 8.02-8.10 (m, 2H, ArH); ¹³C NMR (62.89 MHz, CDCl₃): δ = 25.2 (-CH₂-), 26.00 (2-CH₂-), 31.12 (2-CH₂-), 58.05 (CH), 111.54 (q, ³J_{CF} = 4.58 Hz, CH), 123.4 (q, ¹J_{CF} = 274.20 Hz, 2CF₃), 125.87 (q, ³J_{CF} = 4.12 Hz, 2CH), 126.9 (2CH), 128.9 (2CH), 129.3 (CH), 130.1 (2CH), 132.3 (q, ²J_{CF} = 32.96 Hz, 2C), 133.7 (C), 1386 (2C), 151.8 (C), 153.1 (C), 155.0 (C); ¹⁹F NMR (282.40 MHz, CDCl₃): δ = -62.87 (ArCF₃), -62.06 (ArCF₃); IR (ATR, cm⁻¹): ν = 3068 (w), 2945 (m), 2858 (m), 1621 (w), 1592 (w), 1469 (w), 1446 (w), 1426 (m), 1406 (w), 1385 (s), 1381 (s), 1351 (w), 1317 (s), 1276
(m), 1255 (m), 1227 (w), 1173 (m), 1153 (m), 1129 (s), 1104 (m), 1078 (w), 1062 (m), 1029 (w), 1015 (m), 994 (w), 962 (m), 922 (w), 891 (w), 881 (s), 854 (s), 822 (w), 785 (w), 770 (s), 754 (w), 742 (w), 713 (m), 692 (s), 675 (w), 666 (w), 620 (s), 596 (m), 556 (w); GC-MS (EI, 70 eV): m/z (%): 489 (M+, 16), 470 (3), 434 (2), 408 (24), 407 (100), 344 (1), 236 (1), 140 (1), 55 (2), 41 (2); HRMS (EI) calcd for C_{26}H_{21}F_{6}N_{3} [M+]: 489.16342 found 489.163581.

3-tert-Butyl-2-(4-ethylphenyl)-5-phenyl-7-(trifluoromethyl)-3H-imidazo[4,5-b]pyridine (6n):
brown solid (0.168 g, 63%); mp 227–229 °C; $^1$H NMR (300.13 MHz, CDCl$_3$): $\delta = 1.20$ (t, $J = 7.55$ Hz, 3H, CH$_3$), 1.69 (s, 9H, 3CH$_3$), 2.65 (q, $J = 15.11$, $J = 7.55$ Hz, 2H, -CH$_2$-), 7.20 (d, $^3J = 8.31$ Hz, 2H, ArH), 7.36 (d, $^3J = 8.12$ Hz, 2H, ArH), 7.39-7.49 (m, 3H, ArH), 7.86 (s, 1H, ArH), 8.05 (d, $^3J = 8.12$ Hz, 2H, ArH); $^{13}$C NMR (75.46 MHz, CDCl$_3$): $\delta =$ 15.6 (CH$_3$), 28.9 (-CH$_2$-), 31.1 (3CH$_3$), 60.9 (C), 110.9 (q, $^3J_{CF} = 4.40$ Hz, CH), 121.3 (q, $^1J_{CF} = 273.99$ Hz, CF$_3$), 126.9 (2CH), 127.5 (2CH), 127.5 (q, $^2J_{CF} = 33.56$ Hz, C), 128.9 (2CH), 129.0 (CH), 129.7 (2CH), 131.9 (C), 139.0 (C), 146.1 (C), 150.6 (2C), 150.7 (C), 157.3 (C); $^{19}$F NMR (282.40 MHz, CDCl$_3$): $\delta =$ -61.83 (ArCF$_3$); IR (ATR, cm$^{-1}$): $\tilde{\nu} =$ 3086 (w), 2967 (s), 2872 (w), 1915 (w), 1737 (w), 1619 (w), 1598 (w), 1500 (w), 1463 (m), 1378 (s), 1316 (w), 1285 (w), 1255 (m), 1204 (w), 1176 (m), 1153 (s), 1127 (s), 1083 (w), 1055 (w), 1016 (w), 1000 (w), 958 (m), 930 (w), 877 (m), 839 (m), 794 (w), 773 (m), 729 (w), 691 (s), 666 (w), 626 (m), 579 (w), 547 (w); GC-MS (EI, 70 eV): m/z (%): 423 (M$^+$, 9), 368 (23), 367 (100), 352 (34), 331 (3), 282 (1), 189 (2), 140 (2), 116 (8), 89 (2), 77 (2), 57 (8), 41 (8), 29 (4); HRMS (ESI) calcd for C$_{25}$H$_{23}$F$_3$N$_3$ [M+H$^+$]: 424.19951 found 424.19997.
(C) Copies of 2D-NMR correlations (HMBC, HSQC and NOESY) of 6a.