Efficient C7 or C3/C7 Direct Arylation of Tri- or Disubstituted Imidazo[1,2-b]pyrazoles

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Table of contents

I) General information ................................................................................................................................. 2
II) Experimentale procedures .................................................................................................................. 3
   II.1) General procedures ...................................................................................................................... 3
   II.2) C-7 direct arylation of tri-substituted imidazo[1,2-b]pyrazoles 1-5 .............................................. 4
I) General information

All reagents were purchased from commercial suppliers and were used without further purification.

Microwave assisted reactions were carried out in a Biotage Initiator microwave synthesis instrument and temperatures were measured by an IR sensor.

The reactions were monitored by thin-layer chromatography (TLC) analysis using silica gel (60 F254) plates. Compounds were visualized by UV irradiation.

Flash column chromatography was performed on silica gel 60 (230-400 mesh, 0.040-0.063 mm).

Melting points (mp [°C]) were taken on samples in open capillary tubes and are uncorrected.

The infrared spectra of compounds were recorded on a Thermo Scientific Nicolet iS10.

\( ^1 \)H and \( ^{13} \)C NMR spectra were recorded on a spectrometer at 250 MHz (\( ^{13} \)C, 62.9 MHz) or 400 MHz (\( ^{13} \)C, 100 MHz). Chemical shifts are given in parts per million from tetramethylsilane (TMS) as internal standard. The following abbreviations are used for the proton spectra multiplicities: s: singulet, d: doublet, t: triplet, q: quartet, qt: quintuplet, m: multiplet.. Coupling constants (\( J \)) are reported in Hertz (Hz).

CIV is the abbreviation for quaternary carbons. High-resolution mass spectra (HRMS) were performed on a Maxis Bruker 4G.
II) Experimentale procedures

II.1) General procedures

General Procedure A: C-7 direct arylation of the imidazo[1,2-b]pyrazole 1-5

A microwave vial containing a stirring bar was loaded with imidazo[1,2-b]pyrazole 1-5\(^1\) in 1,4-dioxane, (hetero)aryl bromide or chloride (2.0 equiv.), tricyclohexylphosphine tetrafluoroborate (0.20 equiv.) and cesium carbonate (2.0 equiv.). The tube was evacuated and back-filled with dry argon twice. Palladium acetate (0.10 equiv.) was added and the mixture was submitted to microwave irradiation with stirring at 160 °C for 4 hours. It was then cooled to room temperature, and 1,4-dioxane was removed under reduced pressure. The residue was purified by flash chromatography to provide the desired products 1a-5b.

General Procedure B: One pot C-3 and C-7 direct arylation of imidazo[1,2-b]pyrazole 6

A microwave vial containing a stirring bar was loaded with imidazo[1,2-b]pyrazole 6\(^1\) in 1,4-dioxane, (hetero)aryl bromide (3.0 equiv.), tricyclohexylphosphine tetrafluoroborate (0.20 equiv.) and cesium carbonate (4.0 equiv.). The tube was evacuated and back-filled with dry argon twice. Palladium acetate (0.10 equiv.) was added and the mixture was submitted to microwave irradiation with stirring at 160 °C for 4 hours. It was then cooled to room temperature, and 1,4-dioxane was removed under reduced pressure. The residue was purified by flash chromatography to provide the desired products 1a, 6a-b.

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II.2) C-7 direct arylation of tri-substituted imidazo[1,2-b]pyrazoles 1-5

2-(4-methoxyphenyl)-1-methyl-6-phenyl-3,7-di-4-tolyl-1H-imidazo[1,2-b]pyrazole 1a

The reaction was carried out as described

- in general procedure A using imidazo[1,2-b]pyrazole 1 (100 mg, 0.254 mmol), palladium acetate (5.7 mg, 0.0254 mmol), tricyclohexylphosphine tetrafluoroborate (18.7 mg, 0.0508 mmol), caesium carbonate (142 mg, 0.508 mmol) and 4-bromotoluene (89 mg, 63 μL, 0.508 mmol) in 2 mL of 1,4-dioxane. Standard workup followed by flash chromatography (dichloromethane/petroleum ether 6/4) yielded 1a as a beige solid (117 mg, 95%).

- in general procedure B using imidazo[1,2-b]pyrazole 1 (100 mg, 0.329 mmol), palladium acetate (7.4 mg, 0.0329 mmol), tricyclohexylphosphine tetrafluoroborate (24.2 mg, 0.0658 mmol), caesium carbonate (369 mg, 1.32 mmol) and 4-bromotoluene (169 mg, 122 μL, 0.987 mmol) in 2 mL of 1,4-dioxane. Standard workup followed by flash chromatography (dichloromethane/petroleum ether 1/1) yielded 1a as a beige solid (141 mg, 89%).

1H NMR (400 MHz, CDCl3) δ 7.73 (d, J = 8.1 Hz, 2H, HAr), 7.59 (d, J = 6.7 Hz, 2H, HAr), 7.32 (d, J = 8.6 Hz, 2H, HAr), 7.30-7.20 (m, 5H, HAr), 7.14-7.12 (m, 4H, HAr), 6.98 (d, J = 8.6 Hz, 2H, HAr), 3.86 (s, 3H, OCH3), 3.26 (s, 3H, NCH3), 2.38 (s, 3H, CH3), 2.31 (s, 3H, CH3).

13C NMR (101 MHz, CDCl3) δ 160.19 (CIV), 151.76 (CIV), 140.28 (CIV), 136.51 (CIV), 135.75 (CIV), 134.92 (CIV), 132.46 (CHAr), 131.09 (CHAr), 130.02 (CIV), 128.98 (2 x CHAr), 128.59 (CHAr), 127.96 (CHAr), 127.06 (CHAr), 126.96 (CHAr), 125.99 (CIV), 121.50 (CIV), 118.13 (CIV), 114.56 (CHAr), 95.24 (CIV), 55.33 (OCH3), 31.45 (NCH3), 21.30 (CH3), 21.24 (CH3). IR (neat, cm⁻¹): 1600, 1520, 1248, 840, 820. HRMS (ESI): Exact mass calcd. for C33H30N3O: 484.23834 [M+H]+, 506.22028 [M+Na]+ found: 484.23842 [M+H]+, 506.21974 [M+Na]+. Mp: 186-188 °C.
The reaction was carried out as described in general procedure A using imidazo[1,2-b]pyrazole 1 (100 mg, 0.254 mmol), palladium acetate (5.7 mg, 0.0254 mmol), tricyclohexylphosphine tetrafluoroborate (18.7 mg, 0.0508 mmol), caesium carbonate (142 mg, 0.508 mmol) and 4-bromobenzotrifluoride (114 mg, 72 μL, 0.508 mmol) in 2 mL of 1,4-dioxane. Standard workup followed by flash chromatography (dichloromethane/petroleum ether 1/1) yielded 1b as a pale yellow solid (123 mg, 90%). $^1$H NMR (400 MHz, CDCl₃) $\delta$ 7.71 (d, $J = 8.1$ Hz, 2H, H₆), 7.58 (d, $J = 8.4$ Hz, 2H, H₆), 7.53 (d, $J = 7.9$ Hz, 2H, H₆), 7.47 (d, $J = 8.1$ Hz, 2H, H₆), 7.33 (d, $J = 8.5$ Hz, 2H, H₆), 7.29 – 7.25 (m, 3H, H₆), 7.12 (d, $J = 8.1$ Hz, 2H, H₆), 7.00 (d, $J = 8.5$ Hz, 2H, H₆), 3.88 (s, 3H, OCH₃), 3.30 (s, 3H, NCH₃), 2.32 (s, 3H, CH₃). $^{13}$C NMR (101 MHz, CDCl₃) $\delta$ 160.31 (CⅣ), 152.26 (CⅣ), 140.07 (CⅣ), 137.17 (CⅣ), 136.82 (CⅣ), 134.27 (CⅣ), 132.46 (CH₆), 130.97 (CH₆), 129.19 (CⅣ), 129.03 (CH₆), 128.87 (CH₆), 128.18 (CH₆), 128.07 ($^2J_{C,F} = 33.0$ Hz, CⅣ), 127.42 (CH₆), 127.14 (CH₆), 125.63 (CⅣ), 125.14 ($^2J_{C,F} = 3.72$ Hz, CH₆), 124.41 ($^1J_{C,F} = 273$ Hz, CⅣ), 121.13 (CⅣ), 118.42 (CⅣ), 114.64 (CH₆), 94.33 (CⅣ), 55.34 (OCH₃), 31.73 (NCH₃), 21.29 (CH₃). IR (neat, cm⁻¹): 1603, 1322, 1118, 1066, 838, 697. HRMS (ESI): Exact mass calcd. for C₃₃H₂₇F₃N₃O: 538.2107 [M+H]⁺, 560.19202 [M+Na]⁺ found: 538.21007 [M+H]⁺, 560.19113 [M+Na]⁺. Mp: 226-228 °C.
2,7-bis(4-methoxyphenyl)-1-methyl-6-phenyl-3-(4-tolyl)-1H-imidazo[1,2-b]pyrazole 1c

The reaction was carried out as described in general procedure A using imidazo[1,2-b]pyrazole 1 (150 mg, 0.382 mmol), palladium acetate (8.8 mg, 0.0382 mmol), tricyclohexylphosphine tetrafluoroborate (28.0 mg, 0.0763 mmol), caesium carbonate (213 mg, 0.763 mmol) and 4-bromoanisole (142 mg, 95 μL, 0.763 mmol) in 2 mL of 1,4-dioxane. Standard workup followed by flash chromatography (dichloromethane/petroleum ether) yielded 1c as a white solid (122 mg, 64%, 25% of starting material was recovered). ¹H NMR (400 MHz, CDCl₃) δ 7.73 (d, J = 8.2 Hz, 2H, H₄), 7.60 (d, J = 7.7 Hz, 2H, H₄), 7.35-7.28 (m, 4H, H₄), 7.28-7.18 (m, 3H, H₄), 7.11 (d, J = 8.2 Hz, 2H, H₄), 6.97 (d, J = 8.6 Hz, 2H, H₄), 6.90 (d, J = 8.6 Hz, 2H, H₄), 3.86 (s, 3H, OCH₃), 3.83 (s, 3H, OCH₃), 3.24 (s, 3H, NCH₃), 2.31 (s, 3H, CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 160.20 (CIV), 158.24 (CIV), 151.70 (CIV), 140.36 (CIV), 136.51 (CIV), 134.93 (CIV), 132.47 (CH₄), 132.37 (CH₄), 128.98 (CH₄), 128.95 (CIV), 128.48 (CH₄), 127.99 (CH₄), 127.04 (CH₄), 126.94 (CH₄), 126.02 (CIV), 125.35 (CIV), 121.50 (CIV), 118.13 (CIV), 114.57 (CH₄), 113.74 (CH₄), 94.78 (CIV), 55.34 (OCH₃), 55.23 (OCH₃), 31.36 (NCH₃), 21.31 (CH₃). IR (neat, cm⁻¹): 1597, 1519, 1503, 1244, 1171, 835, 822. HRMS (ESI): Exact mass calcd. for C₃₃H₃₀N₃O₂: 500.23325 [M+H]⁺, found: 500.233465 [M+H]⁺. Mp: 207-209 °C.
The reaction was carried out as described in general procedure A using imidazo[1,2-b]pyrazole 1 (100 mg, 0.254 mmol), palladium acetate (5.7 mg, 0.0254 mmol), tricyclohexylphosphine tetrafluoroborate (18.7 mg, 0.0508 mmol), caesium carbonate (143 mg, 0.508 mmol) and 4-bromopyridine (80.3 mg, 0.508 mmol) in 2 mL of 1,4-dioxane. Standard workup followed by flash chromatography (dichloromethane/petroleum ether 1/1 to dichloromethane/ethyl acetate 9/1) yielded 1d as a beige solid (49 mg, 41%, 49% of the starting material were recovered). \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.52 (d, \(J = 3.3\) Hz, 2H, H\(_{Ar}\)), 7.69 (d, \(J = 8.2\) Hz, 2H, H\(_{Ar}\)), 7.53-7.50 (m, 2H, H\(_{Ar}\)), 7.36 – 7.25 (m, 7H, H\(_{Ar}\)), 7.11 (d, \(J = 8.2\) Hz, 2H, H\(_{Ar}\)), 7.01 (d, \(J = 3.3\) Hz, 2H, H\(_{Ar}\)), 3.88 (s, 3H, OCH\(_3\)), 3.36 (s, 3H, NH\(_3\)), 2.32 (s, 3H, CH\(_3\)). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 160.38 (C\(_{IV}\)), 152.68 (C\(_{IV}\)), 149.57 (CH\(_{Ar}\)), 141.60 (C\(_{IV}\)), 139.96 (C\(_{IV}\)), 136.97 (C\(_{IV}\)), 134.03 (C\(_{IV}\)), 132.48 (CH\(_{Ar}\)), 129.34 (C\(_{IV}\)), 129.07 (CH\(_{Ar}\)), 129.05 (CH\(_{Ar}\)), 128.26 (CH\(_{Ar}\)), 127.70 (CH\(_{Ar}\)), 127.20 (CH\(_{Ar}\)), 125.47 (C\(_{IV}\)), 125.39 (C\(_{IV}\)), 120.97 (C\(_{IV}\)), 118.59 (CH\(_{Ar}\)), 114.68 (CH\(_{Ar}\)), 93.33 (C\(_{IV}\)), 55.37 (OCH\(_3\)), 31.96 (NCH\(_3\)), 21.31 (CH\(_3\)). IR (neat, cm\(^{-1}\)): 1602, 1590, 1504, 1250, 1170, 1023, 827. HRMS (ESI): Exact mass calcd. for C\(_{31}\)H\(_{27}\)N\(_4\)O: 471.21794 [M+H]\(^+\), found: 471.21777 [M+H]\(^+\). Mp: 237-239°C.
2,3-bis(4-methoxyphenyl)-1-methyl-6-phenyl-7-(4-tolyl)-1H-imidazo[1,2-b]pyrazole 2a

The reaction was carried out as described in general procedure A using imidazo[1,2-b]pyrazole 2 (100 mg, 0.244 mmol), palladium acetate (5.5 mg, 0.0244 mmol), tricyclohexylphosphine tetrafluoroborate (18.0 mg, 0.0488 mmol), caesium carbonate (137 mg, 0.488 mmol) and 4-bromotoluene (83.4 mg, 60 μL, 0.488 mmol) in 2 mL of 1,4-dioxane. Standard workup followed by flash chromatography (dichloromethane/petroleum ether 1/1) yielded 2a as a beige solid (105 mg, 86%). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.76 (d, $J$ = 8.9 Hz, 2H, H$_{Ar}$), 7.58 (d, $J$ = 8.0 Hz, 2H, H$_{Ar}$), 7.31 (d, $J$ = 8.8 Hz, 2H, H$_{Ar}$), 7.29 – 7.23 (m, 5H, H$_{Ar}$), 7.15 (d, $J$ = 7.8 Hz, 2H, H$_{Ar}$), 6.99 (d, $J$ = 8.8 Hz, 2H, H$_{Ar}$), 6.85 (d, $J$ = 8.9 Hz, 2H, H$_{Ar}$), 3.87 (s, 3H, OCH$_3$), 3.79 (s, 3H, OCH$_3$), 3.26 (s, 3H, NCH$_3$), 2.37 (s, 3H, CH$_3$). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 160.15 (C IV), 158.41 (C IV), 151.76 (C IV), 140.25 (C IV), 135.74 (C IV), 134.92 (C IV), 132.48 (CH$_{Ar}$), 131.08 (CH$_{Ar}$), 130.03 (C IV), 128.99 (CH$_{Ar}$), 128.60 (CH$_{Ar}$), 128.55 (CH$_{Ar}$), 128.45 (C IV), 127.97 (CH$_{Ar}$), 126.97 (CH$_{Ar}$), 121.51 (C IV), 117.90 (C IV), 114.57 (CH$_{Ar}$), 113.80 (CH$_{Ar}$), 95.25 (C IV), 55.34 (OCH$_3$), 55.22 (OCH$_3$), 31.46 (NCH$_3$), 21.24 (CH$_3$). IR (neat, cm$^{-1}$): 1592, 1519, 1501, 1247, 1171, 1028, 842, 823, 793. HRMS (ESI): Exact mass calcd. for C$_{33}$H$_{30}$N$_{3}$O$_{2}$: 500.23325 [M+H]$^+$, found: 500.23325 [M+H]$^+$. Mp: 192-194°C.
The reaction was carried out as described in general procedure A using imidazo[1,2-b]pyrazole 2 (100 mg, 0.244 mmol), palladium acetate (5.50 mg, 0.0244 mmol), tricyclohexylphosphine tetrafluoroborate (18.0 mg, 0.0488 mmol), caesium carbonate (137 mg, 0.488 mmol) and 4-bromobenzotrifluoride (110 mg, 68 μL, 0.488 mmol) in 2 mL of 1,4-dioxane. Standard workup followed by flash chromatography (dichloromethane/petroleum ether 1/1) yielded 2b as a white solid (116 mg, 86%).

$\text{H NMR (400 MHz, CDCl}_3\text{): } \delta 7.75 \text{(d, } J = 8.9 \text{ Hz, 2H, H}_{\text{Ar}}), 7.57 \text{(d, } J = 8.2 \text{ Hz, 2H, H}_{\text{Ar}}), 7.52 \text{(d, } J = 7.6 \text{ Hz, 2H, H}_{\text{Ar}}), 7.47 \text{(d, } J = 8.1 \text{ Hz, 2H, H}_{\text{Ar}}), 7.32 \text{(d, } J = 8.7 \text{ Hz, 2H, H}_{\text{Ar}}), 7.29-7.23 \text{ (m, 3H, H}_{\text{Ar}}), 7.00 \text{(d, } J = 8.7 \text{ Hz, 2H, H}_{\text{Ar}}), 6.85 \text{(d, } J = 8.9 \text{ Hz, 2H, H}_{\text{Ar}}), 3.87 \text{(s, 3H, OCH}_3\text{)}, 3.78 \text{(s, 3H, NH}_3\text{)}, 3.29 \text{(s, 3H, CH}_3\text{).}$

$\text{C NMR (101 MHz, CDCl}_3\text{): } 160.29 \text{ (C}_{\text{IV}}), 158.60 \text{ (C}_{\text{IV}}), 152.27 \text{ (C}_{\text{IV}}), 140.05 \text{ (C}_{\text{IV}}), 137.23 \text{ (C}_{\text{IV}}), 134.31 \text{ (C}_{\text{IV}}), 132.50 \text{ (CH}_{\text{Ar}}), 130.98 \text{ (CH}_{\text{Ar}}), 128.88 \text{ (CH}_{\text{Ar}}), 128.68 \text{ (C}_{\text{IV}}), 128.65 \text{ (CH}_{\text{Ar}}), 128.20 \text{ (CH}_{\text{Ar}}), 127.86 \text{(2}_{J_{C-F}} = 32.5 \text{ Hz, C}_{\text{IV}}), 127.44 \text{(CH}_{\text{Ar}}), 125.16 \text{(2}_{J_{C-F}} = 3.80 \text{ Hz, CH}_{\text{Ar}}), 124.44 \text{(3}_{J_{C-F}} = 273 \text{ Hz, C}_{\text{IV}}), 121.15 \text{ (C}_{\text{IV}}), 121.14 \text{ (C}_{\text{IV}}), 118.19 \text{(C}_{\text{IV}}), 114.66 \text{(CH}_{\text{Ar}}), 113.87 \text{(CH}_{\text{Ar}}), 94.35 \text{(C}_{\text{IV}}), 55.35 \text{(OCH}_3\text{)}, 55.23 \text{(NH}_3\text{)}, 31.74 \text{(CH}_3\text{).}$

$\text{IR (neat, cm}^{-1}\text{): 1603, 1505, 1261, 1245, 1176, 1112, 836. HRMS (ESI): Exact mass calcd. for C}_{33}\text{H}_{28}\text{F}_3\text{N}_3\text{O}_2: 554.20499 \text{ [M+H]}^+, \text{found: 554.20472 [M+H]}^+. \text{Mp: 193-195 °C.}$
2,3-bis(4-methoxyphenyl)-1-methyl-6-phenyl-7-(pyridin-4-yl)-1\textit{H}-imidazo[1,2-\textit{b}]pyrazole 2c

\[ \text{C}_{31}\text{H}_{26}\text{N}_{4}\text{O}_{2} \]

MW: 486.56 g/mol

The reaction was carried out as described in general procedure A using imidazo[1,2-\textit{b}]pyrazole 2 (100 mg, 0.244 mmol), palladium acetate (5.50 mg, 0.0244 mmol), tricyclohexylphosphine tetrafluoroborate (18.0 mg, 0.0488 mmol), caesium carbonate (137 mg, 0.488 mmol) and 4-bromopyridine (77 mg, 0.488 mmol) in 2 mL of 1,4-dioxane. Standard workup followed by flash chromatography (dichloromethane to dichloromethane/ethyl acetate 1/1) yielded 2c as a beige solid (83 mg, 70%, 23% of starting material were recovered). \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}) \( \delta \) 8.50 (d, \( J = 6.0 \) Hz, 2H, H\textsubscript{Ar}), 7.73 (d, \( J = 8.6 \) Hz, 2H, H\textsubscript{Ar}), 7.51 (d, \( J = 7.6 \) Hz, 2H, H\textsubscript{Ar}), 7.34-7.24 (m, 7H, H\textsubscript{Ar}), 7.00 (d, \( J = 8.1 \) Hz, 2H, H\textsubscript{Ar}), 6.84 (d, \( J = 8.6 \) Hz, 2H, H\textsubscript{Ar}), 3.87 (s, 3H, OCH\textsubscript{3}), 3.78 (s, 3H, OCH\textsubscript{3}), 3.35 (s, 3H, NCH\textsubscript{3}). \textsuperscript{13}C NMR (101 MHz, CDCl\textsubscript{3}) \( \delta \) 160.35 (C\textsubscript{IV}), 158.67 (C\textsubscript{IV}), 152.69 (C\textsubscript{IV}), 149.53 (CH\textsubscript{Ar}), 141.70 (C\textsubscript{IV}), 139.93 (C\textsubscript{IV}), 134.04 (C\textsubscript{IV}), 132.50 (CH\textsubscript{Ar}), 129.05 (CH\textsubscript{Ar}), 128.82 (C\textsubscript{IV}), 128.70 (CH\textsubscript{Ar}), 128.28 (CH\textsubscript{Ar}), 127.72 (CH\textsubscript{Ar}), 125.36 (CH\textsubscript{Ar}), 120.97 (C\textsubscript{IV}), 120.92 (C\textsubscript{IV}), 118.35 (C\textsubscript{IV}), 114.70 (CH\textsubscript{Ar}), 113.89 (CH\textsubscript{Ar}), 93.33 (C\textsubscript{IV}), 55.37 (OCH\textsubscript{3}), 55.23 (OCH\textsubscript{3}), 31.98 (NCH\textsubscript{3}). IR (neat, cm\textsuperscript{-1}): 1593, 1520, 1499, 1245, 1174, 1029, 828, 695. HRMS (ESI): Exact mass calcd. for C\textsubscript{31}H\textsubscript{27}N\textsubscript{4}O\textsubscript{2}: 487.21285 [M+H]\textsuperscript{+}, found: 487.21267 [M+H]\textsuperscript{+}. Melting Point: 248-250 °C.
2-(4-methoxyphenyl)-1-methyl-6-phenyl-7-(4-tolyl)-3-(4-(trifluoromethyl)phenyl)-IH-imidazo[1,2-b]pyrazole 3a

The reaction was carried out as described in general procedure A using imidazo[1,2-b]pyrazole 3 (100 mg, 0.224 mmol), palladium acetate (5.0 mg, 0.0224 mmol), tricyclohexylphosphine tetrafluoroborate (16.5 mg, 0.0447 mmol), caesium carbonate (125 mg, 0.447 mmol) and 4-bromotoluene (76 mg, 55 μL, 0.447 mmol) in 2 mL of 1,4-dioxane. Standard workup followed by flash chromatography (dichloromethane/petroleum ether 2/3) yielded 3a as a white solid (109 mg, 91 %). 

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.00 (d, $J = 8.7$ Hz, 2H, H$_{Ar}$), 7.59 (d, $J = 7.7$ Hz, 2H, H$_{Ar}$), 7.53 (d, $J = 8.7$ Hz, 2H, H$_{Ar}$), 7.33 (d, $J = 8.8$ Hz, 2H, H$_{Ar}$), 7.30 – 7.22 (m, 5H, H$_{Ar}$), 7.16 (d, $J = 7.9$ Hz, 2H, H$_{Ar}$), 7.03 (d, $J = 8.8$ Hz, 2H, H$_{Ar}$), 3.89 (s, 3H, OCH$_3$), 3.27 (s, 3H, NCH$_3$), 2.39 (s, 3H, CH$_3$). 

$^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 160.64 (C$_{IV}$), 152.00 (C$_{IV}$), 140.28 (C$_{IV}$), 136.07 (C$_{IV}$), 134.60 (C$_{IV}$), 132.61 (C$_{IV}$), 132.34 (CH$_{Ar}$), 131.09 (CH$_{Ar}$), 130.90 (C$_{IV}$), 129.61 (C$_{IV}$), 129.07 (CH$_{Ar}$), 128.51 (CH$_{Ar}$), 128.08 ($^2$J$_{C-F}$ = 31.8 Hz C$_{IV}$), 128.06 (CH$_{Ar}$), 127.19 (CH$_{Ar}$), 126.58 (CH$_{Ar}$), 125.20 ($^2$J$_{C-F}$ = 3.82 Hz, CH$_{Ar}$), 124.25 ($^2$J$_{C-F}$ = 273 Hz, C$_{IV}$), 120.77 (C$_{IV}$), 116.78 (C$_{IV}$), 114.90 (CH$_{Ar}$), 95.61 (C$_{IV}$), 55.39 (OCH$_3$), 31.48 (NCH$_3$), 21.25 (CH$_3$). 

IR (neat, cm$^{-1}$): 1613, 1591, 1320, 1112, 841. 

4-(2-(4-methoxyphenyl)-1-methyl-6-phenyl-3-(4-(trifluoromethyl)phenyl)-1H-imidazo[1,2-b]pyrazol-7-yl)benzonitrile 3b

\[
\text{C}_{33}\text{H}_{23}\text{F}_{3}\text{N}_{4}\text{O}
\]
MW: 548.55 g/mol

The reaction was carried out as described in general procedure A using imidazo[1,2-b]pyrazole 3 (100 mg, 0.224 mmol), palladium acetate (5.1 mg, 0.0224 mmol), tricyclohexylphosphine tetrafluoroborate (14.7 mg, 0.0448 mmol), caesium carbonate (126 mg, 0.448 mmol) and 4-bromobenzonitrile (82 mg, 0.448 mmol) in 2 mL of 1,4-dioxane. Standard workup followed by flash chromatography (dichloromethane/petroleum ether 1/1) yielded 3b as a white solid (101 mg, 82%).

\[
\text{H NMR (400 MHz, CDCl}_3) \delta 7.96 (d, J = 8.1 \text{ Hz}, 2\text{H, H}_{Ar}), 7.61 (d, J = 8.1 \text{ Hz}, 2\text{H, H}_{Ar}), 7.54 (d, J = 8.1 \text{ Hz}, 2\text{H, H}_{Ar}), 7.48-7.44 (m, 4\text{H, H}_{Ar}), 7.35-7.30 (m, 5\text{H, H}_{Ar}), 7.05 (d, J = 8.4 \text{ Hz}, 2\text{H, H}_{Ar}), 3.90 (s, 3\text{H, OCH}_3), 3.33 (s, 3\text{H, NCH}_3).
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\text{13C NMR (101 MHz, CDCl}_3) \delta 160.84 (\text{C}_{IV}), 152.67 (\text{C}_{IV}), 139.93 (\text{C}_{IV}), 138.06 (\text{C}_{IV}), 133.62 (\text{C}_{IV}), 132.35 (\text{CH}_{Ar}), 132.11 (\text{CH}_{Ar}), 131.23 (\text{C}_{IV}), 131.20 (\text{CH}_{Ar}), 128.91 (\text{CH}_{Ar}), 128.85 (J_{C,F} = 32.4 \text{ Hz}, \text{C}_{IV}), 128.38 (\text{CH}_{Ar}), 127.90 (\text{CH}_{Ar}), 126.83 (\text{CH}_{Ar}), 125.30 (J_{C,F} = 3.81 \text{ Hz} \text{CH}_{Ar}), 124.14 (J_{C,F} = 273 \text{ Hz}, \text{C}_{IV}) 120.19 (\text{C}_{IV}), 119.10 (\text{C}_{IV}), 117.22 (\text{C}_{IV}), 115.04 (\text{CH}_{Ar}), 109.48 (\text{C}_{IV}), 94.74 (\text{C}_{IV}), 55.42 (\text{OCH}_3), 31.90 (\text{NCH}_3).
\]

IR (neat, cm\(^{-1}\)): 2223, 1592, 1302, 1287, 1252, 1125, 1077, 902, 771. HRMS (ESI): Exact mass calcd. for C\(_{33}\)H\(_{24}\)F\(_3\)N\(_4\)O: 549.18967 [M+H]\(^+\), 571.17162 [M+Na]\(^+\), found: 549.18975 [M+H]\(^+\), 571.17105 [M+Na]\(^+\). Mp: 246-248 °C.
2-(4-methoxyphenyl)-1-methyl-6-phenyl-7-(pyridin-4-yl)-3-(4-(trifluoromethyl)phenyl)-1H-imidazo[1,2-b]pyrazole 3c

![Chemical Structure](image.png)

The reaction was carried out as described in general procedure A using imidazo[1,2-b]pyrazole 3 (100 mg, 0.223 mmol), palladium acetate (5.0 mg, 0.0223 mmol), tricyclohexylphosphine tetrafluoroborate (16.4 mg, 0.0447 mmol), caesium carbonate (125 mg, 0.447 mmol) and 4-bromopyridine (71 mg, 0.447 mmol) in 2 mL of 1,4-dioxane. Standard workup followed by flash chromatography (dichloromethane to dichloromethane/ethyl acetate 1/1) yielded 3c as a beige solid (77 mg, 66%, 25% of starting material were recovered).

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.54 (d, $J = 6.2$ Hz, 2H, H$_{Ar}$), 7.96 (d, $J = 8.3$ Hz, 2H, H$_{Ar}$), 7.57 – 7.49 (m, 4H, H$_{Ar}$), 7.38 – 7.30 (m, 5H, H$_{Ar}$), 7.27 (d, $J = 6.2$ Hz, 2H, H$_{Ar}$), 7.05 (d, $J = 8.7$ Hz, 2H, H$_{Ar}$), 3.90 (s, 3H, OCH$_3$), 3.38 (s, 3H, NCH$_3$).

$^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 160.83 (C$_{IV}$), 152.89 (C$_{IV}$), 149.64 (CH$_{Ar}$), 141.34 (C$_{IV}$), 139.98 (C$_{IV}$), 133.71 (C$_{IV}$), 132.36 (CH$_{Ar}$), 132.11 (C$_{IV}$), 131.22, (C$_{IV}$), 128.96 (CH$_{Ar}$), 128.51 ($^2$J$_{C-F} = 31.3$ Hz, C$_{IV}$), 128.36 (CH$_{Ar}$), 128.12 (CH$_{Ar}$), 126.81 (CH$_{Ar}$), 125.44 (CH$_{Ar}$), 125.34 ($^1$J$_{C-F} = 3.78$ Hz CH$_{Ar}$), 124.15 ($^1$J$_{C-F} = 273$ Hz, C$_{IV}$), 120.23 (C$_{IV}$), 117.19 (C$_{IV}$), 115.03 (CH$_{Ar}$), 93.64 (C$_{IV}$), 55.42 (OCH$_3$), 31.99 (NCH$_3$).

IR (neat, cm$^{-1}$): 1592, 1323, 1162, 843, 709.

2-(4-methoxyphenyl)-1-methyl-6-phenyl-7-(3-tolyl)-3-(4-(trifluoromethyl)phenyl)-1H-imidazo[1,2-b]pyrazole 3d

\[
\text{C}_{33}\text{H}_{26}\text{F}_{3}\text{N}_{3}\text{O}
\]

MW: 537.57 g/mol

The reaction was carried out as described in general procedure A using imidazo[1,2-b]pyrazole 3 (100 mg, 0.224 mmol), palladium acetate (5.0 mg, 0.0224 mmol), tricyclohexylphosphine tetrafluoroborate (16.5 mg, 0.0447 mmol), caesium carbonate (125 mg, 0.447 mmol) and 3-bromotoluene (76 mg, 54 μL, 0.447 mmol) in 2 mL of 1,4-dioxane. Standard workup followed by flash chromatography (dichloromethane/petroleum ether 1/1) yielded 3d as a white solid (94 mg, 78%). \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) \(\delta\) 8.00 (d, \(J = 7.6\) Hz, 2H, H\(_{Ar}\)), 7.60 (d, \(J = 6.3\) Hz, 2H, H\(_{Ar}\)), 7.54 (d, \(J = 7.6\) Hz, 2H, H\(_{Ar}\)), 7.34 (d, \(J = 7.7\) Hz, 2H, H\(_{Ar}\)), 7.27-7.19 (m, 6H, H\(_{Ar}\)), 7.11 (d, \(J = 6.8\) Hz, 1H, H\(_{Ar}\)), 7.03 (d, \(J = 7.7\) Hz, 2H, H\(_{Ar}\)), 3.89 (s, 3H, OCH\(_3\)), 3.27 (s, 3H, NCH\(_3\)), 2.34 (s, 3H, CH\(_3\)). \(^1\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) \(\delta\) 160.66 (C\(_{IV}\)), 151.93 (C\(_{IV}\)), 140.28 (C\(_{IV}\)), 137.83 (C\(_{IV}\)), 134.57 (C\(_{IV}\)), 132.63 (C\(_{IV}\)), 132.35 (CH\(_{Ar}\)), 131.92 (CH\(_{Ar}\)), 130.94 (C\(_{IV}\)), 128.58 (C\(_{IV}\)), 128.48 (CH\(_{Ar}\)), 128.26 (CH\(_{Ar}\)), 128.10 \((^2\)\(J_{C-F} = 32.5\) Hz, C\(_{IV}\)), 128.16 (CH\(_{Ar}\)), 128.05 (CH\(_{Ar}\)), 127.24 (CH\(_{Ar}\)), 127.21 (CH\(_{Ar}\)), 126.60 (CH\(_{Ar}\)), 125.20 \((^3\)\(J_{C-F} = 3.82\) Hz, CH\(_{Ar}\)), 124.26 \((^1\)\(J_{C-F} = 273\) Hz, C\(_{IV}\)), 120.76 (C\(_{IV}\)), 116.79 (C\(_{IV}\)), 114.91 (CH\(_{Ar}\)), 95.83 (C\(_{IV}\)), 55.39 (OCH\(_3\)), 31.51 (NCH\(_3\)), 21.50 (CH\(_3\)). IR (neat, cm\(^{-1}\)): 1610, 1321, 1163, 1111, 840. HRMS (ESI): Exact mass calcld. for C\(_{33}\)H\(_{27}\)F\(_3\)N\(_3\)O: 538.21007 [M+H]\(^+\), found: 538.21010 [M+H]\(^+\). Mp: 199-201 °C.
2-(4-methoxyphenyl)-1-methyl-6-phenyl-7-(2-tolyl)-3-(4-(trifluoromethyl)phenyl)-1H-imidazo[1,2-b]pyrazole 3e

The reaction was carried out as described in general procedure A using imidazo[1,2-b]pyrazole 3 (100 mg, 0.224 mmol), palladium acetate (5.0 mg, 0.0224 mmol), tricyclohexylphosphine tetrafluoroborate (16.5 mg, 0.0448 mmol), caesium carbonate (125 mg, 0.448 mmol) and 2-bromotoluene (76 mg, 54 μL, 0.448 mmol) in 2 mL of 1,4-dioxane. Standard workup followed by flash chromatography (dichloromethane/petroleum ether 3/2) yielded 3e as a white solid (85 mg, 71%). $^1$H NMR (400 MHz, CDCl₃) δ 8.03 (d, J = 8.2 Hz, 2H, H Ar), 7.57-7.53 (m, 4H, H Ar), 7.38 (t, J = 7.0 Hz, 1H, H Ar), 7.34 (d, J = 8.7 Hz, 2H, H Ar), 7.28-7.20 (m, 6H, H Ar), 7.03 (d, J = 8.7 Hz, 2H, H Ar), 3.88 (s, 3H, OCH 3), 3.12 (s, 3H, NCH 3), 2.14 (s, 3H, CH 3). $^{13}$C NMR (101 MHz, CDCl₃) δ 160.64 (C IV), 151.63 (C IV), 140.40 (C IV), 138.83 (C IV), 135.03 (C IV), 132.67 (C IV), 132.49 (CH Ar), 132.30 (CH Ar), 132.23 (C IV), 130.81 (C IV), 130.13 (CH Ar), 128.17 (CH Ar), 128.06 ($^3$J C-F = 32.4 Hz, C IV), 127.58 (CH Ar), 127.25 (CH Ar), 127.14 (CH Ar), 126.54 (CH Ar), 125.78 (CH Ar), 125.20 ($^3$J C-F = 3.74 Hz, CH Ar), 124.28 ($^3$J C-F = 273 Hz, C IV) 120.76 (C IV), 116.79 (C IV), 114.91 (CH Ar), 93.98 (C IV), 55.38 (OCH 3), 30.89 (NCH 3), 20.63 (CH 3). IR (neat, cm⁻¹): 1610, 1323, 1298, 1104, 838. HRMS (ESI): Exact mass calcd. for C₃₃H₂₆F₃N₅O: 538.21007 [M+H]⁺, found: 538.21002 [M+H]⁺. Mp: 238-238 °C.
The reaction was carried out as described in general procedure A using imidazo[1,2-b]pyrazole 4 (100 mg, 0.224 mmol), palladium acetate (5.10 mg, 0.0224 mmol), tricyclohexylphosphine tetrafluoroborate (14.7 mg, 0.0447 mmol), caesium carbonate (126 mg, 0.447 mmol) and 4-bromotoluene (76.4 mg, 0.447 mmol) in 2 mL of 1,4-dioxane. Standard workup followed by flash chromatography (dichloromethane/petroleum ether 1/1) yielded 4a as a white solid (85 mg, 71%). \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.74 – 7.65 (m, 4H, H\(_{Ar}\)), 7.60 – 7.51 (m, 4H, H\(_{Ar}\)), 7.31 – 7.22 (m, 5H, H\(_{Ar}\)), 7.16 (d, \(J = 7.7\) Hz, 2H, H\(_{Ar}\)), 6.87 (d, \(J = 8.9\) Hz, 2H, H\(_{Ar}\)), 3.80 (s, 3H, OCH\(_3\)), 3.30 (s, 3H, NCH\(_3\)), 2.39 (s, 3H, CH\(_3\)). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 159.00 (C\(_{IV}\)), 152.48 (C\(_{IV}\)), 140.80 (C\(_{IV}\)), 135.99 (C\(_{IV}\)), 134.65 (C\(_{IV}\)), 133.21 (C\(_{IV}\)), 131.39 (CH\(_{Ar}\)), 131.03 (CH\(_{Ar}\)), 129.83 (\(^2\)J\(_{C:F}\) = 32.8 Hz, C\(_{IV}\)), 129.70 (C\(_{IV}\)), 129.21 (CH\(_{Ar}\)), 129.08 (CH\(_{Ar}\)), 128.58 (CH\(_{Ar}\)), 128.01 (CH\(_{Ar}\)), 127.17 (CH\(_{Ar}\)), 127.11 (C\(_{IV}\)), 126.02 (\(^3\)J\(_{C:F}\) = 3.79 Hz CH\(_{Ar}\)), 123.90 (\(^4\)J\(_{C:F}\) = 273 Hz, C\(_{IV}\)), 120.45 (C\(_{IV}\)), 119.03 (C\(_{IV}\)), 114.08 (CH\(_{Ar}\)), 95.57 (C\(_{IV}\)), 55.26 (OCH\(_3\)), 31.89 (NCH\(_3\)), 21.25 (CH\(_3\)). IR (neat, cm\(^{-1}\)): 1325, 1248, 1160, 1125, 1106, 1070, 834. HRMS (ESI): Exact mass calcd. for C\(_{33}\)H\(_{26}\)F\(_3\)N\(_3\)O: 538.21007 [M+H]\(^+\), found: 538.20987 [M+H]\(^+\). Melting Point: 224-226 °C.
4-(3-(4-methoxyphenyl)-1-methyl-6-phenyl-2-(4-(trifluoromethyl)phenyl)-1H-imidazo[1,2-b]pyrazol-7-yl)benzonitrile 4b

The reaction was carried out as described in general procedure A using imidazo[1,2-b]pyrazole 4 (100 mg, 0.224 mmol), palladium acetate (5.10 mg, 0.0224 mmol), tricyclohexylphosphine tetrafluoroborate (14.7 mg, 0.0447 mmol), caesium carbonate (126 mg, 0.447 mmol) and 4-bromobenzonitrile (82 mg, 0.447 mmol) in 2 mL of 1,4-dioxane. Standard workup followed by flash chromatography (dichloromethane/petroleum ether 1/1) yielded 4b as a beige solid (91 mg, 74%).

\[
\begin{align*}
\text{C}_{33}\text{H}_{23}\text{F}_{3}\text{N}_{4}\text{O} \\
\text{MW: 548.55 g/mol}
\end{align*}
\]

\[\begin{align*}
\text{1H NMR (400 MHz, CDCl}_3\text{)} & \delta 7.77 (d, J = 8.0 \text{ Hz, 2H, H}_\text{Ar}), 7.68 (d, J = 8.7 \text{ Hz, 2H, H}_\text{Ar}), 7.64 (d, J = 7.7 \text{ Hz, 2H, H}_\text{Ar}), 7.58 (d, J = 8.0 \text{ Hz, 2H, H}_\text{Ar}), 7.51-7.56 (m, 4H, H}_\text{Ar}), 7.33-7.31 (m, 3H, H}_\text{Ar}), 6.91 (d, J = 8.8 \text{ Hz, 2H, H}_\text{Ar}), 3.83 (s, 3H, OCH}_3), 3.39 (s, 3H, NH}_3). \\
\text{13C NMR (101 MHz, CDCl}_3\text{)} & \delta 159.25 (CIV), 153.18 (CIV), 140.43 (CIV), 138.20 (CIV), 133.77 (CIV), 132.73 (CIV), 132.10 (CH}_\text{Ar}), 131.41 (CH}_\text{Ar}), 131.15 (CH}_\text{Ar}), 129.31 (CH}_\text{Ar}), 128.96 (CH}_\text{Ar}), 128.32 (CH}_\text{Ar}), 127.85 (CH}_\text{Ar}), 127.43 (CIV), 126.15 (CH}_\text{Ar}), 123.82 (CH}_\text{Ar}), 119.87 (CIV), 119.48 (CIV), 119.13 (CIV), 114.17 (CH}_\text{Ar}), 109.34 (CIV), 94.60 (CIV), 55.28 (OCH}_3), 32.31 (NCH}_3). \\
\text{IR (neat, cm}^{-1}) & \text{: 2223, 1602, 1523, 1322, 1250, 1069, 1017, 830. \\
\text{HRMS (ESI):} & \text{Exact mass calcd. for C}_{33}\text{H}_{24}\text{F}_{3}\text{N}_{4}\text{O: 549.18967 [M+H]}^+, \text{found: 549.18935 [M+H]}^+. \\
\text{Mp: 246-248 ºC.}
\end{align*}
\]
The reaction was carried out as described in general procedure A using imidazo[1,2-b]pyrazole 5 (100 mg, 0.0263 mmol), palladium acetate (5.90 mg, 0.0263 mmol), tricyclohexylphosphine tetrafluoroborate (19.3 mg, 0.0526 mmol), caesium carbonate (147 mg, 0.526 mmol) and 4-bromotoluene (89.9 mg, 65 μL, 0.526 mmol) in 2 mL of 1,4-dioxane. Standard workup followed by flash chromatography (dichloromethane to dichloromethane/ethyl acetate 1/1) yielded 5a as a yellow solid (89.0 mg, 72%). 1H NMR (400 MHz, CDCl₃) δ 8.51 (d, J = 5.6 Hz, 2H, H Ar), 7.86 (d, J = 5.6 Hz, 2H, H Ar), 7.63 (d, J = 6.9 Hz, 2H, H Ar), 7.38 (d, J = 7.7 Hz, 2H, H Ar), 7.33-7.27 (m, 5H, H Ar), 7.19 (d, J = 7.7 Hz, 2H, H Ar), 7.09 (d, J = 8.6 Hz, 2H, H Ar), 3.94 (s, 3H, OCH₃), 3.28 (s, 3H, NCH₃), 2.42 (s, 3H, CH₃). 13C NMR (101 MHz, CDCl₃) δ 160.93 (C IV), 152.16 (C IV), 149.43 (CH Ar), 140.25 (C IV), 136.85 (C IV), 136.23 (C IV), 134.45 (C IV), 132.63 (C IV), 132.19 (CH Ar), 131.10 (CH Ar), 129.36 (C IV), 129.12 (CH Ar), 128.48 (CH Ar), 128.10 (CH Ar), 127.29 (CH Ar), 120.40 (C IV), 119.85 (CH Ar), 115.40 (C IV), 115.08 (CH Ar), 95.78 (C IV), 55.44 (OCH₃), 31.45 (NCH₃), 21.26 (CH₃). IR (neat, cm⁻¹): 1591, 1513, 1248, 1169, 989, 840, 819. HRMS (ESI): Exact mass calcd. for C₃₁H₂₇N₄O: 471.21794 [M+H]⁺, found: 471.021797 [M+H]⁺. Melting Point: 271-273 °C.
2-(4-methoxyphenyl)-1-methyl-6-phenyl-3-(pyridin-4-yl)-7-(4-(trifluoromethyl)phenyl)-
1H-imidazo[1,2-b]pyrazole 5b

\[
\text{C}_{31}\text{H}_{23}\text{F}_{3}\text{N}_{4}\text{O} \\
\text{MW: } 524.53\text{g/mol}
\]

The reaction was carried out as described in general procedure A using imidazo[1,2-b]pyrazole 5 (100 mg, 0.263 mmol), palladium acetate (5.9 mg, 0.0263 mmol), tricyclohexylphosphine tetrafluoroborate (19.3 mg, 0.0526 mmol), caesium carbonate (147 mg, 0.526 mmol) and 4-bromobenzotrifluoride (118 mg, 74 \( \mu \)L, 0.526 mmol) in 2 mL of 1,4-dioxane. Standard workup followed by flash chromatography (dichloromethane to dichloromethane/ethyl acetate 1/1) yielded 5b as a yellow solid (102 mg, 74%). \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 8.49 (d, \( J = 6.0 \) Hz, 2H, H\(_{Ar}\)), 7.80 (d, \( J = 6.0 \) Hz, 2H, H\(_{Ar}\)), 7.60 (d, \( J = 8.1 \) Hz, 2H, H\(_{Ar}\)), 7.55 – 7.50 (m, 2H, H\(_{Ar}\)), 7.48 (d, \( J = 8.1 \) Hz, 2H, H\(_{Ar}\)), 7.37 (d, \( J = 8.2 \) Hz, 2H, H\(_{Ar}\)), 7.33-7.28 (m, 3H, H\(_{Ar}\)), 7.08 (d, \( J = 8.2 \) Hz, 2H, H\(_{Ar}\)), 3.92 (s, 3H, OCH\(_3\)), 3.29 (s, 3H, NCH\(_3\)). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \( \delta \) 161.05 (C IV), 152.62 (C IV), 149.63 (CH\(_{Ar}\)), 140.08 (C IV), 136.61 (C IV), 136.50 (C IV), 133.83 (C IV), 132.73 (C IV), 132.20 (CH\(_{Ar}\)), 131.10 (CH\(_{Ar}\)), 128.76 (CH\(_{Ar}\)), 128.37 (\(^2\)J\(_{C-F} = 32.4 \) Hz C IV), 128.32 (CH\(_{Ar}\)), 127.73 (CH\(_{Ar}\)), 125.28 (\(^2\)J\(_{C-F} = 3.84 \) Hz CH\(_{Ar}\)), 124.32 (\(^2\)J\(_{C-F} = 273 \) Hz, C IV), 120.06 (C IV), 119.96 (CH\(_{Ar}\)), 115.67 (C IV), 115.16 (CH\(_{Ar}\)), 94.77 (C IV), 55.46 (OCH\(_3\)), 31.72 (NCH\(_3\)). IR (neat, cm\(^{-1}\)): 1592, 1512, 1324, 1161, 1104, 1065, 674. HRMS (ESI): Exact mass calcd. for C\(_{31}\)H\(_{24}\)F\(_3\)N\(_4\)O: 525.18967 [M+H]\(^+\), found: 525.18964 [M+H]\(^+\). Mp: 251-253 °C.
The reaction was carried out as described in general procedure B using imidazo[1,2-b]pyrazole 6 (100 mg, 0.329 mmol), palladium acetate (8.04 mg, 0.0329 mmol), tricyclohexylphosphine tetrafluoroborate (24.0 mg, 0.0658 mmol), caesium carbonate (369 mg, 1.32 mmol) and 4-bromobenzotrifluoride (222 mg, 138 μL, 0.987 mmol) in 2 mL of 1,4-dioxane. Standard workup followed by flash chromatography (dichloromethane/petroleum ether 3/7) yielded 6a as a white solid (151 mg, 78%). 

\[ ^1H \text{ NMR (400 MHz, CDCl}_3 \text{)} \delta 8.01 (d, J = 8.4 \text{ Hz, } 2H, H_{Ar}), 7.64 - 7.47 (m, 8H, H_{Ar}), 7.41 - 7.29 (m, 5H, H_{Ar}), 7.07 (d, J = 8.4 \text{ Hz, } 2H, H_{Ar}), 3.92 (s, 3H, OCH}_3), 3.33 (s, 3H, NH}_3). \]

\[ ^13C \text{ NMR (101 MHz, CDCl}_3 \text{)} \delta 160.76 (C_{IV}), 152.49 (C_{IV}), 140.08 (C_{IV}), 136.81 (C_{IV}), 133.96 (C_{IV}), 132.34 (CH_{Ar}), 132.28 (C_{IV}), 131.09 (C_{IV}), 131.05 (CH_{Ar}), 128.78 (CH_{Ar}), 128.37 (J_{C-F} = 32.6 \text{ Hz, } C_{IV}), 128.27 (CH_{Ar}), 128.20 (J_{C-F} = 32.8 \text{ Hz, } C_{IV}), 127.64 (CH_{Ar}), 126.73 (CH_{Ar}), 125.25 (J_{C-F} = 3.70 \text{ Hz, } 2xCH_{Ar}), 124.36 (J_{C-F} = 273 \text{ Hz, } C_{IV}), 124.18 (J_{C-F} = 273 \text{ Hz, } C_{IV}), 120.39 (C_{IV}), 117.03 (C_{IV}), 114.99 (CH_{Ar}), 94.65 (C_{IV}), 55.39 (OCH}_3), 31.74 (NCH}_3). \]

IR (neat, cm\(^{-1}\)):
- 1613, 1320, 1249, 1162, 1103, 1076, 1064, 1016, 834.

HRMS (ESI): Exact mass calcd. for C\(_{33}\)H\(_{23}\)F\(_6\)N\(_3\)O: 592.18181 [M+H]\(^+\), found: 592.18163 [M+H]\(^+\). Mp: 220-222°C.
3,3’-(2-(4-methoxyphenyl)-1-methyl-6-phenyl-1H-imidazo[1,2-b]pyrazole-3,7-diyl)dibenzonitrile 6b

C₃₃H₂₃N₅O
MW: 505.57 g/mol

The reaction was carried out as described in general procedure B using imidazo[1,2-b]pyrazole 6 (100 mg, 0.329 mmol), palladium acetate (8.04 mg, 0.0329 mmol), tricyclohexylphosphine tetrafluoroborate (24.0 mg, 0.0638 mmol), caesium carbonate (369 mg, 1.32 mmol) and 3-bromobenzonitrile (180 mg, 0.987 mmol) in 2 mL of 1,4-dioxane. Standard workup followed by flash chromatography (dichloromethane/petroleum ether 1/1) yielded 6b as a beige solid (131 mg, 79%). ¹H NMR (400 MHz, CDCl₃) δ 8.19 (s 1H), 8.13 (d, J = 8.1 Hz, 1H), 7.71 (s, 1H), 7.60 (t, J = 6.7 Hz, 2H), 7.55 – 7.30 (m, 10H), 7.09 (t, J = 6.7 Hz, 2H), 3.94 (s, 3H, OCH₃), 3.32 (s, 3H, NCH₃). ¹³C NMR (101 MHz, CDCl₃) δ 160.95 (CIV), 152.53 (CIV), 139.99 (CIV), 135.48 (CH₅), 134.46 (CIV), 134.00 (CH₅), 133.53 (CIV), 132.22 (CH₅), 131.11 (CIV), 130.71 (CH₅), 130.20 (CH₅), 130.12 (CIV), 129.96 (CH₅), 129.93 (CH₅), 129.25 (CH₅), 129.19 (CH₅), 128.68 (CH₅), 128.40 (CH₅), 127.88 (CH₅), 119.84 (CIV), 118.87 (CIV), 118.77 (CIV), 116.16 (CIV), 115.17 (CH₅), 112.58 (2 x CIV), 93.78 (CIV), 55.44 (OCH₃), 31.73 (NCH₃). IR (neat, cm⁻¹): 2228, 1594, 1573, 1512, 1254, 1175, 1030, 843. HRMS (ESI): Exact mass calcd. for C₃₃H₂₄N₅O: 506.19754 [M+H]⁺, found: 506.19752 [M+H]⁺. Mp: 234-236°C.