Unexpected Metal-free Fluorination and Oxidation at the C-4 Position of Pyrazoles Promoted by Selectfluor


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General Information

Unless otherwise indicated, all common reagents and solvents were used as obtained from commercial suppliers, without further purification. The melting points were determined using coverslips on a Microquímica MQAPF–302 apparatus. $^1$H and $^{13}$C NMR spectra were acquired on a Bruker DPX 400 spectrometer, using 5 mm sample tubes, 298 K, and a digital resolution of ± 0.01 ppm, in DMSO-$d_6$ or CDCl$_3$, with TMS as the internal reference. The GC was equipped with a split–splitless injector, autosampler, cross-linked HP-5 capillary column (30 m, 0.32 mm of internal diameter), and the helium was used as the carrier gas. The CHN elemental analyses were performed on a Perkin–Elmer 2400 CHN elemental analyzer (University of São Paulo, Brazil) and the high resolution mass spectrometry was performed using an Agilent-QTOF 6530 spectrometer (Santa Maria Federal University, Brazil) and Bruker Daltonics MicrOTOF (University of São Paulo, Brazil). Reagents Selectfluor (95 %) and substrates 1a-c and 2 were purchased from Sigma-Aldrich Brazil. Other arylhydrazones (3a-c) and pyrazoles 4a-c, 5a-c, 6a-c, 7a-c and 10-18 were synthesized according to literature procedures.1-8
Optimization of Reaction Conditions

Table 1. Screening of Selectfluor molar ratio, temperature and time reaction screening in synthesis of compound 8b.

<table>
<thead>
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<th>Entry</th>
<th>Molar Ratio&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Temperature (°C)</th>
<th>Time (h)</th>
<th>Yield&lt;sup&gt;b&lt;/sup&gt;</th>
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<td>25</td>
<td>12</td>
<td>-&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
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<td>1:1.1</td>
<td>82</td>
<td>2</td>
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<tr>
<td>5</td>
<td>1:1.1</td>
<td>82</td>
<td>12</td>
<td>54</td>
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</tbody>
</table>

<sup>a</sup>Starting Material: Selectfluor; <sup>b</sup>Isolated Yields; <sup>c</sup>Isolated starting material

Experimental Procedures and Characterization of Products

General procedure for reactions with Selectfluor: Synthesis of 3-aryl-4-fluoro-1H-pyrazoles (8a-c, 19-20)

To a solution of pyrazole (7, 9-12, 15-18) (1 mmol) in anhydrous acetonitrile (5 mL) was added Selectfluor (1.1 mmol). After the addition, the reaction mixture was stirred at reflux for 2 h and cooled to room temperature. Then destilled water (15 mL) was added under magnetic stirring and extracted with CHCl₃ (2 x 15 mL). The organic layer was washed with destilled water (2 x 20 mL) and brine (1 x 20 mL), dried over Na₂SO₄ and the solvent was evaporated under reduced pressure. Products 8a-c were purified by silica gel chromatography (hexanes:ethyl acetate, 95:5).

General procedures for derivatization reactions from compounds 7:

<table>
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<th>a</th>
<th>b</th>
<th>c</th>
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<td>7, 9</td>
<td>C₆H₅</td>
<td>O₂N-C₆H₅</td>
<td>MeO-C₆H₅</td>
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<tr>
<td>10</td>
<td>-</td>
<td>O₂N-C₆H₅</td>
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Method a – Synthesis of 3-aryl-4-methoxymethyl-1H-1-phenylpyrazoles (9a-c): Accordingly to the literature data to a solution of 7a-c (1 mmol) and sodium hydride (1.8 mmol) stirred in anhydrous DMF (10 mL), pure iodomethane (1.1 mmol) was added at room temperature. After the addition process, the mixture was stirred for a further 24 h at room temperature. After this time, ethyl acetate (15 mL) was added to the reaction and the organic layer was washed with distilled water (3 x 10 mL). Then, the organic layer was dried over Na2SO4, filtered, and the solvent was evaporated under reduced pressure to obtain colourless oil (9a, 75 % yield) or yellow and white solids (9b-c, 83 and 79 % yield, respectively).

Method b – Synthesis of 4-chloromethyl-3-(4-nitrophenyl)-1H-1-phenylpyrazole (13): Based on the literature data, to a solution of 7b (1 mmol) in anhydrous CH2Cl2 (10 mL), thionyl chloride (2 mmol) was added slowly at room temperature. After the addition process, the mixture was stirred for a further 3 h at room temperature. After the reaction was completed, distilled water (15 mL) was added to the reaction and the organic layer was washed with more distilled water (3 x 10 mL). Then, the organic layer was dried over Na2SO4, filtered, and the solvent was evaporated under reduced pressure to obtain yellow solid 13 with no further purification.

General procedures for derivatization reactions from compound 13:

Method a – Synthesis of 4-azidomethyl-3-(4-nitrophenyl)-1H-1-phenylpyrazole: Based on the literature data, sodium azide (2 mmol) and pyrazole 13 (1 mmol) were suspended in DMF and stirred at ambient temperature for 6 h. The reaction mixture was given into ice water and was extracted with diethylether. The organic layer was washed with water and dried to give yellow solids 11 with no further purification.
Method b – Synthesis of 4-(N-methyl) methanamine-3-(4-nitrophenyl)-1H-1-phenylpyrazole: Accordingly to the literature data,8 to a stirred solution of pyrazole 13 (1 mmol) in EtOH (1 mL), was added 40% methylamine solution (0.3 mL) and stilted for 3 h at room temperature. The reaction mixture was evaporated, quenched with water (30 mL) and extracted in dichloromethane (2 x 25 mL). The combined organic layer was dried over Na₂SO₄ and concentrated under vacuo to afford dark yellow solid 12.

Method c – Synthesis of 4-(N,N-diethyl)methanamine-3-(4-nitrophenyl)-1H-1-phenylpyrazole: Accordingly to the literature data,8 to a stirred solution of pyrazole 13 (1 mmol) in EtOH (1 mL), was added N,N-diethylamine (2 mmol) and stilted for 3 h at room temperature. The reaction mixture was evaporated, quenched with water (30 mL) and extracted in dichloromethane (2 x 25 mL). The combined organic layer was dried over Na₂SO₄ and concentrated under vacuo to afford yellow solid 15.

Method d – Synthesis of 4-(propylthio)methyl-3-(4-nitrophenyl)-1H-1-phenylpyrazole: To a mixture of prophanethiol (1.2 mmol) and K₂CO₃ (1.2 mmol) in dry acetone (1 mL) under argon atmosphere, was added pyrazole 13 (1 mmol) and stirred for 16 h under reflux. The reaction mixture was evaporated, quenched with water (30 mL) and extracted in dichloromethane (2 x 25 mL). The combined organic layer was dried over Na₂SO₄ and concentrated under vacuo to afford yellow solid 16.

General procedures for derivatization reactions from compound 11 - Synthesis of 4-aminomethyl-3-(4-nitrophenyl)-1H-1-phenylpyrazole:

To the solution of 11 and ammonium chloride (0.07 mmol) in EtOH (8 mL) and water (3 mL), zinc powder (0.04 mmol) was added, the mixture was stirred vigorously at refluxing. After 2 h the reaction is over (monitored by TLC), ethyl acetate (20 mL) and aqueous ammonia (1 mL) was added. The mixture was filtered, and the filtrate was washed with brine, dried over anhydrous sodium sulfate. After removal of solvent under reduced pressure, the residue was purified by recrystallization to give dark yellow solid 14.²
Characterization of all compounds

4-Hydroxymethyl-1H-1,3-diphenylpyrazole (7a): white solid, yield 52%, mp 73 – 75 °C. $^1$H NMR (400.13 MHz, DMSO-$d_6$): δ 8.50 (s, 1H), 7.90 (d, $J =$ 7.4, 4H), 7.53 – 7.46 (m, 4H), 5.18 (s, 1H), 4.59 (s, 2H). $^{13}$C NMR (100.61 MHz, DMSO-$d_6$): δ 151.8, 140.0, 133.5, 138.7, 130.0, 129.0, 128.3, 127.8, 126.5, 118.5, 129.1, 122.5, 54.6. HRMS Calcd. for C$_{16}$H$_{14}$N$_2$O: 251.1179. Found: 251.1151.

4-Hydroxymethyl-3-(4-nitrophenyl)-1H-1-phenylpyrazole (7b): orange solid, yield 87%, mp 143 – 144 °C. $^1$H NMR (400.13 MHz, DMSO-$d_6$): δ 8.58 (s, 1H), 8.33 (d, $J =$ 8.3, 2H), 8.20 (d, $J =$ 8.5, 2H), 7.92 (d, $J =$ 8.0, 2H), 7.55 (t, $J =$ 8.0, 2H), 7.36 (t, $J =$ 4.9, 1H), 4.64 (d, $J =$ 4.9, 2H). $^{13}$C NMR (100.61 MHz, DMSO-$d_6$): δ 148.5, 147.1, 139.9, 139.7, 130.0, 128.4, 127.0, 124.2, 118.8, 129.8, 123.4, 54.4. Anal. Calcd. for C$_{16}$H$_{13}$N$_3$O$_3$ (295.10): C, 65.08; H, 4.44; N, 14.23. Found: C, 64.78; H, 4.48; N, 14.17.

4-Hydroxymethyl-3-(4-methoxyphenyl)-1H-1-phenylpyrazole (7c): white solid, yield 60%, mp 125 – 127 °C. $^1$H NMR (400.13 MHz, DMSO-$d_6$): δ 8.45 (s, 1H), 7.89 – 7.84 (m, 4H), 7.50 (t, $J =$ 7.8, 2H), 7.29 (t, $J =$ 7.6, 1H), 7.04 (d, $J =$ 8.8, 2H), 5.18 (s, 1H), 4.56 (d, $J =$ 2.4, 2H), 3.81 (s, 3H). $^{13}$C NMR (100.61 MHz, DMSO-$d_6$): δ 159.6, 150.7, 140.0, 129.9, 126.3, 126.0, 118.4, 114.4, 128.9, 114.4, 128.9, 123.4, 54.6. Calcd. for C$_{17}$H$_{16}$N$_2$O$_2$ (280.12): C, 72.84; H, 5.75; N, 9.99. Found: C, 72.79; H, 5.51; N, 10.01.

4-Fluoro-1H-1,3-diphenylpyrazole (8a): yellow oil, yield 63%. $^1$H NMR (400.13 MHz, CDCl$_3$): δ 8.01 (d, $J =$ 9.0, 2H), 7.89 (d, $J =$ 4.7, 1H), 7.73 (d, $J =$ 8.8, 2H), 7.49 (t, $J =$ 7.8, 4H), 7.39 (t, $J =$ 7.3, 1H), 7.32 (t, $J =$ 7.3, 1H). $^{13}$C NMR (100.61 MHz, CDCl$_3$): δ 150.3 (d, $J =$ 252), 140.0, 138.9 (d, $^2J =$ 6.4), 130.8 (d, $^3J =$ 3,7), 129.4, 128.7, 128.3, 126.3, 126.3 (d, $^4J =$ 3,7), 118.4, 114.4 (d, $^2J =$ 30). $^{19}$F NMR (376.3 MHz, CDCl$_3$): δ -172.6 (d, $J =$ 3.1). HRMS Calcd. for C$_{15}$H$_{12}$FN$_2$: 239.0979. Found: 239.0977.

4-Fluoro-3-(4-nitrophenyl)-1H-1-phenylpyrazole (8b): yellow solid, yield 65%, m.p. 135 – 137 °C. $^1$H NMR (400.13 MHz, CDCl$_3$): δ 8.28 (d, $J =$ 9.0, 2H), 8.10 (d, $J =$ 8.8, 2H), 7.90 (d, $^2J =$ 4.4, 1H), 7.69 (d, $J =$ 7.8, 2H), 7.48 (t, $J =$ 8.3, 2H), 7.34 (t, $J =$ 7.3, 1H). $^{13}$C NMR (100.61 MHz, CDCl$_3$): δ 150.6 (d, $J =$ 254), 147.2, 139.6, 137.0 (d, $^3J =$ 3,8), 136.6 (d, $^2J =$ 6.1), 129.6, 127.2, 126.5 (d, $^4J =$ 4,4), 124.0, 118.7, 114.7 (d, $^2J =$ 4,4), 71.3, 118.9, 114.7 (d, $^2J =$ 4,4).
30. $^{19}$F NMR (376.3 MHz, CDCl$_3$): δ -169.9 (d, $J = 4.2$). Anal. Calcd. for C$_{15}$H$_{10}$FN$_3$O$_2$ (283.07): C, 63.60; H, 3.56; N, 14.83. Found: C, 63.60; H, 3.29; N, 14.83.

4-Fluoro-3-(4-methoxyphenyl)-1H-1-phenylpyrazole (8c): yellow solid, yield 40%, m.p. 92 – 93 °C. $^1$H NMR (400.13 MHz, CDCl$_3$): δ 7.89 (d, $J = 8.3$, 2H), 7.81 (d, $^2J = 4.8$, 1H), 7.66 (d, $J = 8.8$, 2H), 7.43 (t, $J = 7.6$, 2H), 7.26 (t, $J = 7.6$, 1H), 6.97 (d, $J = 8.6$, 2H), 3.83 (s, 3H). $^{13}$C NMR (100.61 MHz, CDCl$_3$): δ 159.7, 148.7 (d, $^2J = 252$), 140.1, 138.8 (d, $^2J = 6.7$), 129.4, 127.5 (d, $^4J = 3.7$), 126.3, 123.4 (d, $^3J = 3.8$), 118.3, 114.1, 113.9 (d, $^2J = 30$), 55.0. $^{19}$F NMR (376.3 MHz, CDCl$_3$): δ -172.8 (d, $^2J = 3.4$).

Anal. Calcd. for C$_{16}$H$_{13}$FN$_2$O (268.10): C, 71.63; H, 4.88; N, 10.44. Found: C, 71.81; H, 4.88; N, 10.51.

4-Methoxymethyl-1H-1,3-diphenylpyrazole (9a): colourless oil, yield 75%. $^1$H NMR (400.13 MHz, DMSO-d$_6$): δ 7.97 (s, 1H), 7.84 (d, $J = 7.2$, 2H, Ar), 7.74 (d, $J = 7.7$, 2H), 7.46 – 7.41 (m, 4H), 7.34 (t, $J = 7.4$, 1H), 7.24 (t, $J = 7.4$, 1H), 4.48 (s, 2H), 3.43 (s, 3H). $^{13}$C NMR (100.61 MHz, DMSO-d$_6$): δ 152.1, 140.0, 133.1, 128.5, 128.3, 128.0, 127.9, 126.3, 119.0, 129.4 , 117.9, 65.3, 57.7. HRMS Calcd. for C$_{17}$H$_{17}$N$_2$O: 265.1335, Found: 265.1317.

4-Methoxymethyl-3-(4-nitrophenyl)-1H-1-phenylpyrazole (9b): yellow solid, yield 52%, mp 129 – 130 °C. $^1$H NMR (400.13 MHz, DMSO-d$_6$): δ 8.68 (s, 1H), 8.34 (d, $J = 8.3$, 2H), 8.11 (d, $J = 8.5$, 2H), 7.93 (d, $J = 8.0$, 2H), 7.53 (t, $J = 8.0$, 2H), 7.37 (t, $J = 7.3$, 1H), 4.51 (s, 2H), 3.37 (s, 3H). $^{13}$C NMR (100.61 MHz, DMSO-d$_6$): δ 149.1, 147.2, 139.6, 131.0, 128.5, 127.2, 119.1, 119.0, 130.0, 124.4, 64.6, 54.4. Anal. Calcd. for C$_{17}$H$_{15}$N$_3$O$_3$: 309.11: C, 66.01; H, 4.89; N, 13.58. Found: C, 65.81; H, 4.65; N, 13.75.

4-Methoxymethyl-3-(4-methoxyphenyl)-1H-1-phenylpyrazole (9c): white solid, yield 66%, mp 121 – 122 °C. $^1$H NMR (400.13 MHz, DMSO-d$_6$): δ 8.55 (s, 1H), 7.89 (d, $J = 7.6$, 2H), 7.77 (d, $J = 8.9$, 2H), 7.51 (t, $J = 8.5$, 2H), 7.31 (t, $J = 7.3$, 1H), 7.05 (d, $J = 8.9$, 2H), 4.43 (s, 2H), 3.81 (s, 3H), 3.34 (s, 3H). $^{13}$C NMR (100.61 MHz, DMSO-d$_6$): δ 159.7, 151.3, 140.0, 130.0, 129.9, 126.5, 125.7, 118.6, 114.5, 129.1, 117.6, 64.9, 57.4, 55.6. HRMS Calcd. for C$_{18}$H$_{18}$N$_2$O$_2$: 295.1441. Found: 295.1403.

4-Fluoromethyl-3-(4-nitrophenyl)-1H-1-phenylpyrazole (10): yellow solid, yield 43%, mp 143-144 °C. $^1$H NMR (400.13 MHz, CDCl$_3$): δ 8.32 (d, $J = 8.5$, 2H), 8.13 (d, $J = 3.2$, 1H), 8.04 (d, 2H, $J = 8.5$), 7.76 (d, 2H, $J = 8.0$), 7.51 (t, 2H, $J = 7.5$), 7.37 (t, 1H, $J = 7.0$), 5.46 (d, 2H, $J = 49.4$). $^{13}$C NMR (100.61 MHz, DMSO-d$_6$): δ 150.4, 147.6, 139.4, 138.7, 129.6, 127.5, 124.0, 119.4, 130.5 (d, $^5J = 5.1$), 128.4 (d, $^5J = 2.5$), 116.7 (d, ...
$J = 21.3$), 74.9 (d, $J = 162.9$). $^{19}$F NMR (376.3 MHz, CDCl$_3$): δ -194.3 (t, $J = 49.4$).

HRMS Calcd. for C$_{16}$H$_{12}$FN$_3$O$_2$: 298.0986. Found: 298.0951.

4-Azidomethyl-3-(4-nitrophenyl)-1H-1-phenylpyrazole (11): yellow solid, yield 70%, mp 105 – 106 °C. $^1$H NMR (400.13 MHz, CDCl$_3$): δ 8.33 (d, $J = 9.0$, 2H), 8.09 (s, 1H), 8.01 (d, $J = 9.0$, 2H), 7.78 (d, $J = 7.5$, 2H), 7.52 (t, $J = 7.4$, 2H), 7.38 (t, $J = 7.4$, 1H), 4.48 (s, 2H). $^{13}$C NMR (100.61 MHz, CDCl$_3$): δ 149.2, 147.5, 139.5, 138.9, 129.6, 128.3, 127.4, 124.0, 119.3, 128.4, 115.7, 45.2. Anal. Calcd. for C$_{16}$H$_{12}$N$_6$O$_2$ (320.30): C, 60.00; H, 3.78; N, 26.24. Found: C, 60.08; H, 3.82; N, 25.89.

4-($N$-methyl)methanamine-3-(4-nitrophenyl)-1H-1-phenylpyrazole (12): yellow solid, yield 86%, mp 81 – 82 °C. $^1$H NMR (400.13 MHz, DMSO-d$_6$): δ 8.54 (s, 1H), 8.31 (d, $J = 8.9$, 2H), 8.21 (d, $J = 8.9$, 2H), 8.03 (s, 1H), 7.90 (d, $J = 7.8$, 2H), 7.53 (t, $J = 7.6$, 2H), 7.35 (t, $J = 7.4$, 1H), 3.74 (s, 2H), 2.39 (s, 3H). $^{13}$C NMR (100.61 MHz, CDCl$_3$): δ 148.7, 147.1, 140.2, 139.8, 130.1, 129.9, 128.7, 124.2, 118.8, 127.0, 121.8, 46.0, 36.3. Anal. Calcd. for C$_{17}$H$_{16}$N$_4$O$_2$ (308.13): C, 66.22; H, 5.23; N, 18.17. Found: C, 66.60; H, 5.34; N, 18.11.

4-Chloromethyl-3-(4-nitrophenyl)-1H-1-phenylpyrazole (13): yellow solid, yield 90%, mp 156 – 157 °C. $^1$H NMR (400.13 MHz, DMSO-d$_6$): δ 8.75 (s, 1H), 8.34 (d, $J = 8.9$, 2H), 8.12 (d, $J = 8.9$, 2H), 7.65 (d, $J = 7.6$, 2H), 7.55 (t, $J = 7.4$, 2H), 7.38 (t, $J = 7.4$, 1H), 4.97 (s, 2H). $^{13}$C NMR (100.61 MHz, DMSO-d$_6$): δ 148.5, 147.4, 139.4, 139.0, 130.1, 128.6, 127.5, 124.4, 119.1, 131.3, 119.0, 37.7. Anal. Calcd. for C$_{16}$H$_{12}$ClN$_3$O$_2$ (313.74): C, 61.25; H, 3.86; N, 13.39. Found: C, 61.01; H, 4.02; N, 13.60.

4-Aminomethyl-3-(4-nitrophenyl)-1H-1-phenylpyrazole (14): dark yellow solid, yield 61%, mp 88 – 90 °C. $^1$H NMR (400.13 MHz, DMSO-d$_6$): δ 8.77 (s, 1H), 8.32 (d, $J = 8.9$, 2H), 8.05 (d, $J = 8.9$, 2H), 7.91 (d, $J = 7.8$, 2H), 7.55 (t, $J = 7.6$, 2H), 7.37 (t, $J = 7.4$, 1H), 4.64 (s, 2H). $^{13}$C NMR (100.61 MHz, DMSO-d$_6$): δ 148.6, 147.4, 139.4, 139.2, 130.1, 128.5, 124.5, 119.0, 131.0, 116.4, 44.9. Anal. Calcd. for C$_{16}$H$_{14}$N$_4$O$_2$ (294.31): C, 65.30; H, 4.79; N, 19.04. Found: C, 65.47; H, 4.80; N, 19.51.

4-($N$,$N$-diethyl)methanamine-3-(4-nitrophenyl)-1H-1-phenylpyrazole (15): yellow solid, yield 65%, mp 92 – 94 °C. $^1$H NMR (400.13 MHz, DMSO-d$_6$): δ 8.32 – 8.26 (m, 4H), 7.97 (s, 1H), 7.78 (d, $J = 7.8$, 2H), 7.49 (t, $J = 7.6$, 2H), 7.32 (t, $J = 7.4$, 1H), 3.61 (s, 2H), 2.62 (q, 4H), 1.07 (t, $J = 7.1$, 6H). $^{13}$C NMR (100.61 MHz, CDCl$_3$): δ 150.0, 147.1, 140.2, 139.8, 129.5, 129.1, 128.9, 126.7, 123.5, 126.7, 120.3, 47.8, 46.4, 11.5.

4-(Propylthio)methyl-3-(4-nitrophenyl)-1H-1-phenylpyrazole (16): yellow solid, yield 36%, mp 96 – 98 °C. $^1$H NMR (400.13 MHz, CDCl3): $\delta$ 8.31 (d, $J = 8.9$, 2H), 8.08 (d, $J = 8.9$, 2H), 8.01 (s, 1H), 7.76 (d, $J = 7.8$, 2H), 7.49 (t, $J = 7.6$, 2H), 7.34 (t, $J = 7.4$, 1H), 3.82 (s, 2H), 2.58 (t, $J = 7.1$, 2H), 1.66 (sext., 2H), 1.02 (t, $J = 7.3$, 3H). $^{13}$C NMR (100.61 MHz, CDCl3): $\delta$ 148.9, 147.2, 139.7, 139.6, 129.5, 128.5, 128.3, 123.8, 119.0, 126.9, 118.6, 34.5, 25.9, 22.6, 13.5. Anal. Calcd. for C19H19N3O2S (353.12): C, 64.57; H, 5.42; N, 11.89. Found: C, 64.32; H, 5.37; N, 11.71.

4-Hydroxymethyl-3-(4-nitrophenyl)-1H-1-tert-butylpyrazole (17): yellow oil, yield 58%. $^1$H NMR (400.13 MHz, DMSO-d$_6$): $\delta$ 8.28 (d, $J = 8.3$, 2H), 8.09 (d, $J = 8.5$, 2H), 7.92 (s, 1H), 5.16 (t, $J = 4.9$, 1H), 4.52 (s, 2H), 1.58 (s, 9H). $^{13}$C NMR (100.61 MHz, DMSO-d$_6$): $\delta$ 146.6, 145.8, 141.1, 128.0, 124.3, 129.2, 124.3, 59.0, 54.5. Anal. Calcd. for C14H17N3O3 (275.13): C, 61.08; H, 6.22; N, 15.26. Found: C, 60.81; H, 6.65; N, 14.75.

4-Hydroxymethyl-3-(4-nitrophenyl)-1H-pyrazole (18): yellow solid, yield 63%, mp 179 – 181 °C. $^1$H NMR (400.13 MHz, DMSO-d$_6$): $\delta$ 13.08 (s, 1H), 8.27 (d, $J = 8.2$, 2H), 8.10 (d, $J = 8.6$, 2H), 7.82 (s, 1H), 5.13 (t, $J = 4.9$, 1H), 4.55 (s, 2H). $^{13}$C NMR (100.61 MHz, DMSO-d$_6$): $\delta$ 146.8, 146.7, 141.2, 128.1, 120.2, 130.8, 124.2, 54.5. Anal. Calcd. for C10H9N3O3 (219.06): C, 54.79; H, 4.14; N, 19.17. Found: C, 54.69; H, 4.17; N, 19.05.

4-Fluoro-3-(4-nitrophenyl)-1H-1-tert-butylpyrazole (19): yellow solid, yield 35%, mp 107 – 108 °C. $^1$H NMR (400.13 MHz, CDCl3): $\delta$ 8.24 (d, $J = 9.0$, 2H), 8.03 (d, $J = 9.0$, 2H), 7.50 (d, $J = 4.7$), 1.61 (s, 9H). $^{13}$C NMR (100.61 MHz, CDCl3): $\delta$ 147.6 (d, $J = 251.8$), 146.6, 138.1 (d, $^2J = 4.2$), 133.5 (d, $^2J = 5.8$), 126.1 (d, $^2J = 46.6$), 123.9, 114.0 (d, $^2J = 29.0$), 59.8, 29.4. $^{19}$F NMR (376.3 MHz, CDCl3): $\delta$ -162.6, (s). Anal. Calcd. for C13H14FN3O2 (263.27): C, 59.31; H, 5.36; N, 15.96. Found: C, 59.47; H, 5.26; N, 16.29.

4-Fluoro-3-(4-nitrophenyl)-1H-pyrazole (20): yellow solid, yield 34%, mp 185 – 187 °C. $^1$H NMR (400.13 MHz, DMSO-d$_6$): $\delta$ 13.2 (s, 1H), 8.40-8.31 (m, 2H), 8.09-8.02 (m, 3H). $^{13}$C NMR (100.61 MHz, DMSO-d$_6$): $\delta$ 148.1 (d, $J = 247.8$), 148.8, 138.1, 134.1 (d, $^2J = 6.9$), 126.5 (d, $^4J = 3.4$), 124.7, 117.5 (d, $^2J = 28.9$). $^{19}$F NMR (376.3 MHz, CDCl3): $\delta$ -174.3 (s). Anal. Calcd. for C9H6FN3O2 (207.04): C, 52.18; H, 2.92; N, 20.28. Found: C, 52.45; H, 2.96; N, 20.29.
References


$^{13}$C NMR

Chemical Shifts:
- 146.538
- 147.068
- 139.863
- 139.888
- 129.861
- 129.819
- 128.415
- 127.010
- 124.225
- 123.395
- 118.786

Chemical Structure:

$^{7b}$
$^1$H NMR
\[^{13}\text{C} \text{NMR}\]

![NMR spectrum image]
$^{13}$C NMR (expansion)
$^1$H NMR
$^1$H NMR (expansion)

$^{1}$H NMR (expansion)
$^{13}$C NMR (expansion)
$^{19}$F NMR

$\text{ppm (t1)}$ -169.900 -169.950 -170.000 -170.050

$\text{ppm (t1)}$ -25 -50 -75 -100 -125 -150 -175 -200 -225 -250 -275

$4.229$
$^1$H NMR (expansion)

S28
$^{13}$C NMR (expansion)
$^1{H} \text{NMR}$
1H NMR
$^1$H NMR
$^1$H NMR (expansion)
$^{13}$C NMR (expansion)
$^{13}$C NMR
$\text{H}_2\text{O}$

DMSO-$d_6$

$\text{H}^1$ NMR
$^1$H NMR
$^1$H NMR
$^1$H NMR
$^{13}$C NMR
$^{13}$C NMR
$^{13}$C NMR (expansion)