PhIO promoted synthesis of nitrile imines and nitrile oxides within micellar core in aqueous media: A regiocontrolled approach to synthesize densely functionalized pyrazole and isoxazoline derivatives

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Content | Page Numbers
---|---
1. Materials and Method | 2
2. General Procedure for the synthesis of pyrazoles and isoxazolines and Physical Characterization data of the synthesized compounds | 3-18
3. $^1$HNMR, $^{13}$CNMR Spectra of the | 19-50
1. Materials and Methods

$^1$H-NMR and $^{13}$C-NMR spectral analysis were carried out on Bruker-Advance Digital 300 MHz and 75 MHz instruments where tetramethylsilane (TMS) was used as internal standard. Infrared spectra were recorded in KBr pallets in reflection mode on a Perkin Elmer RX-1 FTIR spectrophotometer. High Resolution Mass Spectra was obtained using a QTOF MICRO YA263 mass spectrometer. Suitable single crystals of compound 5a and 6f were mounted on a Bruker-AXS SMART APEX II diffractometer equipped with a graphite monochromator. Optical images were obtained using a CARL-ZEISS Axi-Observer optical microscope. DLS study was performed in a MALVERN Zetasizer DLS. All the reactions were monitored by thin layer chromatography carried out on Merck aluminum-blocked silica gel plates coated with silica gel G under UV light and also by exposure to iodine vapor for detection. Melting points were determined on a Köfler Block apparatus and are uncorrected. Synthetic grade chemicals from Sigma-Aldrich, Spectrochem and E-Merck were used for carrying out the organic reactions. For column chromatography Spectrochem 100-200 mesh silica gel was used.
**General Procedure for the synthesis of pyrazoles:**

A mixture of aldehyde (1mmol), phenyl hydrazine (1 mmol) and olefin derivatives (1mmol) were added to a well stirred solution of SDS (10 mol %) in 5 ml H2O at room temperature. Then PhIO (2.5 mmol) was added portion wise to the resulting mixture carefully maintaining the temperature at 0 °C. When the addition was complete, the reaction was allowed to attain room temperature and stirring was continued for the required period of time (monitored by TLC). After completion of the reaction, the mixture was extracted with ethyl acetate (3x10ml). Removal of ethyl acetate under reduced pressure and purification of the crude product by column chromatography (silica gel 100-200 mesh, ethyl acetate-hexane as eluent) provided pure products. All compounds were well characterized by 1H, 13C NMR, FT-IR and HRMS analysis.

3-(4-Methoxy-phenyl)-1-phenyl-1H-pyrazole-4-carboxylic acid methyl ester (4a)

![Chemical structure of 4a](image)

Yield: 85%, (0.261 g); M.p. 91-92 °C (Lit: 94-95 °C); Characteristics: White crystalline solid;

1H NMR (300 MHz, CDCl3): δ 7.99 (s, 1H), 7.68 (d, 3H, J=8.7 Hz), 7.59-7.54(m, 2H), 7.43 (d, 2H, J=8.1 Hz), 7.01-6.98 (m, 2H), 3.89 (s, 3H), 3.83 (s, 3H); 13C NMR (75 MHz, CDCl3): δ 162.3, 160.3, 144.2, 136.4, 129.3, 127.2, 127.1, 121.0, 114.4, 113.3, 55.3, 51.3; HRMS (ESI-TOF) m/z: [M+H]+

Calculated for C18H17N2O3: 309.1239, found: 309.1236; IR (KBr) cm⁻¹: 1133.2, 1240.2, 1500.1, 1598.9, 1730.6, 2967.3, 3024.5; Anal. Calcd for C18H16N2O3: C: 70.12; H: 5.23; N: 9.09%; found: C: 70.10; H: 5.21; N: 9.07%.
**1-Phenyl-3-m-tolyl-1H-pyrazole-4-carboxylic acid methyl ester (4b)**

Yield: 88%, (0.257 g); M.p. 99-100 °C; Characteristics: White amorphous solid;

1H NMR (300 MHz, CDCl3): \(\delta\) 7.65 (s, 1H), 7.58 (d, 1H, \(J=7.5\) Hz), 7.47-7.05 (m, 8H), 3.74 (s, 3H), 3.33 (s, 3H); 13C NMR (75 MHz, CDCl3): \(\delta\) 159.8, 151.7, 140.0, 138.5, 134.0, 132.1, 129.2, 128.6, 126.4, 126.1, 123.1, 118.0, 109.6, 52.1, 21.4; HRMS (ESI-TOF) m/z: [M+H]+ Calculated for C18H17N2O2: 293.1290, found: 293.1288; IR (KBr) cm\(^{-1}\): 1177.0, 1236.2, 1516.3, 1601.3, 1732.3, 2933.2; Anal. Calcd for C18H17N2O2: C: 73.95; H: 5.52; N: 9.58%, found: C: 73.91; H: 5.49; N: 9.54%.

**Methyl 3-(4-fluorophenyl)-1-phenyl-1H-pyrazole-4-carboxylate (4c)**

Yield: 91%, (0.269 g); M.p. 128-129 °C (Lit: 130-131 °C); Characteristics: White crystalline solid;

1H NMR (300 MHz, CDCl3): \(\delta\) 7.80-7.75 (m, 2H), 7.41 (s, 5H), 7.22 (s, 1H), 7.07-7.02 (m, 2H), 3.75 (s, 3H); 13C NMR (75 MHz, CDCl3): \(\delta\) 164.6, 161.3 (C-F), 159.5, 150.7, 140.2, 134.4, 128.8, 128.4, 127.7, 127.3, 115.9, 115.5, 109.3, 52.1; HRMS (ESI-TOF) m/z: [M+H]+ Calculated for C17H13FN2O2: 297.1039, found: 297.1036; IR (KBr) cm\(^{-1}\): 1158.9, 1232.4, 1439.7, 1500.4, 1738.6, 2957.5, 3064.5; Anal. Calcd for C17H13FN2O2: C: 68.91; H: 4.42; N: 9.45%, found: C: 68.90; H: 4.43; N: 9.44%
3-(3-Nitro-phenyl)-1-phenyl-1H-pyrazole-4-carboxylic acid methyl ester (4d)

Yield: 89%, (0.287 g); M.p. 120-121 °C; Characteristics: Yellow crystalline solid;

$^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 8.62(s, 1H), 8.15-8.05(m, 2H), 7.78 (d, 1H, $J$=8.4 Hz), 7.55-7.41(m, 4H), 7.33 (s, 1H), 7.24 (t, 1H, $J$=8Hz), 3.76 (s, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 164.1, 149.2, 142.8, 139.1, 135.1, 131.1, 129.8, 129.5, 128.6, 128.2, 126.1, 123.7, 123.1, 120.7, 113.5, 109.7, 52.3;
HRMS (ESI-TOF) m/z: [M+H]$^+$ Calculated for C$_{17}$H$_{14}$N$_3$O$_4$: 324.0984, found: 324.0980; IR (KBr) cm$^{-1}$: 1089.7, 1248.8, 1347.1, 1525.1, 1601.8, 1736.9, 2955.3, 3285.9 ; Anal. Caled for C$_{17}$H$_{13}$N$_3$O$_4$: C: 63.16; H: 4.05; N: 13.00%, found: C: 63.11; H: 4.01; N: 13.01%

3-Furan-2-yl-1-phenyl-1H-pyrazole-4-carboxylic acid methyl ester (4e)

Yield: 87%, (0.233 g); M.p. 88-89 °C; Characteristics: Yellow amorphous solid;

$^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.44-7.37(m, 6H), 7.22 (s, 1H), 6.71(s, 1H), 6.42(s, 1H), 3.74(s, 3H);

$^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$159.3, 152.4, 143.6, 142.4, 129.3, 128.6, 126.1, 121.5, 113.6, 111.8, 111.5, 110.1, 109.2, 106.8, 52.1; HRMS (ESI-TOF) m/z: [M+H]$^+$ Calculated for C$_{15}$H$_{13}$N$_2$O$_3$: 269.0926, found:269.0923; IR (KBr) cm$^{-1}$: 1108.7, 1242.1, 1504.4, 1733.1, 2904.2, 3010.2; Anal. Caled for C$_{15}$H$_{12}$N$_2$O$_3$: C: 67.16; H: 4.51; N: 10.44%, found: C: 67.15; H: 4.50; N: 10.46%

1-Phenyl-3-thiophen-2-yl-1H-pyrazole-4-carboxylic acid methyl ester (4f)
Yield: 86%, (0.244 g); M.p. 101-102 °C (Lit: 102-103 °C); Characteristics: Yellow amorphous solid;

$^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.70-7.60 (m, 2H), 7.41-7.33 (m, 3H), 7.27-7.11 (m, 2H), 7.04 -6.98 (m, 2H), 3.73 (s, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 159.4, 147.1, 140.0, 137.5, 135.2, 134.2, 130.2, 128.6, 127.6, 127.5, 126.1, 125.4, 124.7, 109.4, 52.1; HRMS (ESI-TOF) m/z: [M+H]$^+$ Calculated for C$_{15}$H$_{13}$N$_2$O$_2$S: 285.0698, found: 285.0696; IR (KBr) cm$^{-1}$: 1015.4, 1241.8, 1500.6, 1732.8, 2911.3, 3001.6; Anal. Calcd for C$_{15}$H$_{12}$N$_2$O$_2$S: C: 63.36; H: 4.25; N: 9.85%, found: C: 63.39; H: 4.28; N: 9.86%

3-Isopropyl-1-phenyl-1H-pyrazole-4-carboxylic acid ethyl ester (4g)

![Chemical structure of 3-Isopropyl-1-phenyl-1H-pyrazole-4-carboxylic acid ethyl ester (4g)]

Yield: 91%, (0.235 g); Characteristics: Yellow oil;

$^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.63 (s, 1H), 7.36-7.34 (m, 5H), 4.15 (q, 2H, $J=7.2$ Hz), 3.02-2.97(m, 1H), 1.26 (d, 6H, $J=5.4$ Hz), 1.21(t, 3H, $J=7.2$ Hz); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$163.3, 159.4, 136.5, 130.9, 130.0, 128.8, 126.1, 115.4, 109.3, 61.0, 26.6, 23.1, 14.0; HRMS (ESI-TOF) m/z: [M+H]$^+$ Calculated for C$_{15}$H$_{19}$N$_2$O$_2$: 259.1447, found: 259.1444; IR (KBr) cm$^{-1}$: 1242.1, 1357.3, 1502.1, 1578.1, 1601.1, 1736.1, 2922.9; Anal. Calcd for C$_{15}$H$_{18}$N$_2$O$_2$: C: 69.74; H: 7.02; N: 10.84%, found: C: 69.71; H: 7.01; N: 10.83%

1-(4-Nitro-phenyl)-3-phenyl-1H-pyrazole-4-carboxylic acid ethyl ester (4h)

![Chemical structure of 1-(4-Nitro-phenyl)-3-phenyl-1H-pyrazole-4-carboxylic acid ethyl ester (4h)]

Yield: 92%, (0.310 g); M.p. 115-116 °C (Lit118 °C); Characteristics: Yellow crystalline solid;

$^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 8.28 (d, 2H, $J=8.7$ Hz), 7.80 (d, 2H, $J=8.7$ Hz), 7.66 (d, 2H, $J=8.7$ Hz), 7.40-7.29 (m, 4H), 4.26 (q, 2H, $J=7.1$), 1.27 (t, 3H, $J=7.2$); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$
158.9, 152.8, 147.2, 145.0, 134.9, 131.5, 128.9, 126.5, 125.9, 124.0, 123.9, 111.0, 67.7, 14.1; HRMS (ESI-TOF) m/z: [M+H]$^+$ Calculated for C$_{18}$H$_{15}$N$_3$O$_4$: 338.1141, found: 338.1140; IR (KBr) cm$^{-1}$: 1110, 1241.7, 1306.8, 1526.4, 1597.9, 1721.7, 2937.8, 3132.8; Anal. Calcd for C$_{18}$H$_{15}$N$_3$O$_4$: C: 64.09; H: 4.48; N: 12.46%, found: C: 64.09; H: 4.46; N: 12.42%

3-(4-Methoxy-phenyl)-1-(4-nitro-phenyl)-1H-pyrazole-4-carboxylic acid ethyl ester (4i)

![Structure Image]

Yield: 81%, (0.297 g); M.p. 89-90 °C; Characteristics: Yellow crystalline solid;

$^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 8.30 (d, 2H, $J=9$Hz), 7.75 (d, 1H, $J=8.7$ Hz), 7.67 (d, 2H, $J=9$ Hz), 7.27 (s, 1H), 6.98-6.91 (m, 3H), 4.27 (q, 2H, $J=7.1$), 3.81 (s, 3H), 1.29 (t, 3H, $J=7.1$); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 163.3, 160.1, 153.6, 152.2, 140.8, 132.4, 132.1, 129.6, 128.0, 123.9, 122.0, 116.5, 115.6, 113.1, 105.9, 61.7, 56.3, 14.8; HRMS (ESI-TOF) m/z: [M+H]$^+$ Calculated for C$_{19}$H$_{18}$N$_3$O$_5$: 368.1246, found:368.1243; IR (KBr) cm$^{-1}$: 1033.9, 1240.1, 1528.9, 1601.9, 1722.1, 2940.3, 3140.3 ; Anal. Calcd for C$_{19}$H$_{17}$N$_3$O$_5$: C: 62.12; H: 4.66; N: 11.44%, found: C: 62.11; H: 4.62; N: 11.49%

3-(3-Nitro-phenyl)-1-(4-nitro-phenyl)-1H-pyrazole-4-carboxylic acid ethyl ester (4j)

![Structure Image]

Yield: 86%, (0.328 g); M.p. 93-95 °C; Characteristics: Yellow crystalline solid;

$^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 8.69 (s, 1H), 8.37-8.35 (m, 2H), 8.24-8.19 (m, 2H), 7.72 (d, 2H, $J=9$ Hz), 7.62 (t, 1H, $J=8.1$ Hz), 7.46 (s, 1H), 4.33 (q, 2H, $J=7.2$), 1.34 (t, 3H, $J=7.1$Hz); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 167.2, 158.3, 150.3, 148.6, 147.5, 144.6, 141.8, 139.1, 135.4, 134.6, 133.5, 132.2, 129.4, 127.9, 126.3, 124.2, 61.9, 14.1; HRMS (ESI-TOF) m/z: [M+H]$^+$ Calculated for C$_{18}$H$_{13}$N$_4$O$_6$;
383.0992, found: 383.0990; IR (KBr) cm⁻¹: 1078.2, 1238.7, 1310.2, 1530.1, 1607.9, 1730.8, 2960.6, 3149.8; Anal. Calcd for C₁₈H₁₄N₄O₆: C: 56.55; H: 3.69; N: 14.65% found: C: 56.51; H: 3.68; N: 14.61%

3-(4-Bromo-phenyl)-1-(4-nitro-phenyl)-1H-pyrazole-4-carboxylic acid methyl ester (4k)

Yield: 87%, (0.349 g); M.p. 121-122 °C; Characteristics: Yellow crystalline solid;

¹H NMR (300 MHz, CDCl₃): δ 7.89 (d, 2H, J=8.7 Hz), 7.55 (d, 2H, J=9 Hz),7.45-7.14(m, 5H), 3.79(s, 3H); ¹³C NMR (75 MHz, CDCl₃): δ 167.1, 147.7, 145.2, 133.6, 132.9, 130.2, 128.8, 128.5, 127.5, 126.1, 124.6, 124.3, 116.2, 52.5; HRMS (ESI-TOF) m/z: [M+H]⁺ Calculated for C₁₇H₁₃BrN₃O₄: 402.0089, found:402.0085; IR (KBr) cm⁻¹: 1066.7, 1239.1, 1530.0, 1599.1, 1713.1293.9, 3135.6; Anal. Calcd for C₁₇H₁₂BrN₃O₄: C: 50.77; H: 3.01; N: 10.45%, found: C: 50.74; H: 3.00; N: 10.44%

3-(4-Fluoro-phenyl)-1,4-diphenyl-1H-pyrazole (4l)

Yield: 85%, (0.267 g); M.p. 93-95 °C; Characteristics: White crystalline solid;

¹H NMR (300 MHz, CDCl₃): δ 7.84-7.81 (m, 2H), 7.55 (d, 2H, J=8.1Hz), 7.31(t, 2H, J=7.8 Hz), 7.12-7.04 (m, 8H), 6.8 (s, 1H); ¹³C NMR (75 MHz, CDCl₃): δ 163.3 (C-F), 137.8, 132.9, 132.8, 130.2, 129.4, 129.1, 128.9, 128.5, 125.6, 124.8, 120.4, 116.0, 115.9, 115.8, 115.7, 115.6; HRMS (ESI-TOF) m/z: [M+H]⁺ Calculated for C₂₁H₁₆FN₂: 315.1298, found:315.1296; IR (KBr) cm⁻¹: 1159.4, 1294.6, 1431.7, 1604.4, 1655.5, 2850.5 ; Anal. Calcd for C₂₁H₁₅FN₂: C: 80.24; H: 4.81; N: 8.91%, found: C: 80.22; H: 4.80; N: 8.99%
1,4-Diphenyl-3-\textit{m}-tolyl-1\textit{H}-pyrazole (4m)

![Structure of 1,4-Diphenyl-3-\textit{m}-tolyl-1\textit{H}-pyrazole (4m)]

Yield: 81%, (0.251 g); M.p. 81-82 °C; Characteristics: Yellow amorphous solid;

$^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.46-7.41 (m, 3H), 7.33-7.27 (m, 4H), 7.23-7.20 (m, 3H), 7.10 (t, 2H, $J$=7.5 Hz), 6.95 (d, 2H, $J$=7.5 Hz), 6.84 (s, 1H), 2.22 (s, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 152.0, 139.9, 139.1, 137.6, 137.1, 131.0, 130.4, 129.5, 129.1, 127.9, 126.6, 126.9, 124.4, 123.5, 120.9, 21.0;

HRMS (ESI-TOF) m/z: [M+H]$^+$ Calculated for C$_{22}$H$_{19}$N$_2$: 311.1548, found:311.1545;

IR (KBr) cm$^{-1}$: 1129.9, 1291.6, 1430.5, 1600.5, 1651.3, 2890.6; Anal. Calcd for C$_{22}$H$_{18}$N$_2$: C: 85.13; H: 5.85; N: 9.03; found: C: 85.15; H: 5.88; N: 9.07%

3-Furan-2-yl-1,4-diphenyl-1\textit{H}-pyrazole (4n)

![Structure of 3-Furan-2-yl-1,4-diphenyl-1\textit{H}-pyrazole (4n)]

Yield: 84%, (0.240 g); M.p. 73-74 °C; Characteristics: Yellow amorphous solid;

$^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.77 (d, 2H, $J$=7.5 Hz), 7.48-7.26 (m, 6H), 7.14-7.07 (m, 4H), 6.61-6.40 (m, 2H); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 152.0, 147.2, 141.9, 139.3, 130.4, 130.3, 129.1, 126.4, 121.4, 118.8, 115.2, 114.9, 110.7, 108.2; HRMS (ESI-TOF) m/z: [M+H]$^+$ Calculated for C$_{19}$H$_{15}$N$_2$O: 287.1184, found: 287.1181; IR (KBr) cm$^{-1}$: 1094.5, 1240.6, 1430.6, 1500.9, 1699.1, 2698.7; Anal. Calcd for C$_{19}$H$_{14}$N$_2$O: C: 79.70; H: 4.93; N: 9.78%; found: C: 79.71; H: 4.91; N: 9.74%
1-(4-Nitro-phenyl)-3,4-diphenyl-1H-pyrazole (4o)

Yield: 83%, (0.283 g); M.p. 99-101 °C (Lit: 102-103 °C); Characteristics: Yellow amorphous solid;

\(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta\) 8.16-8.07 (m, 2H), 7.68 (d, 1H, \(J=7.5\) Hz), 7.60-7.31 (m, 11H), 7.23 (s, 1H); \(^{13}\)C NMR (75 MHz, CDCl\(_3\)): \(\delta\) 153.9, 152.0, 139.1, 133.5, 132.2, 132.1, 129.4, 127.9, 126.3, 124.2, 122.4, 116.2, 113.9; HRMS (ESI-TOF) m/z: [M+H]**+** Calculated for C\(_{21}\)H\(_{16}\)N\(_3\)O\(_2\), found: 342.1239; IR (KBr) cm\(^{-1}\): 1136.5, 1255.0, 1550.4, 1607.4, 1728.5, 2960.2, 3148.3; Anal. Caled for C\(_{21}\)H\(_{15}\)N\(_3\)O\(_2\): C: 73.89; H: 4.43; N: 12.31%, found: C: 73.87; H: 4.45; N: 12.30%

4-(4-Fluoro-phenyl)-3-isopropyl-1-phenyl-1H-pyrazole (5a)

Yield: 94%, (0.263 g); M.p. 80-81 °C; Characteristics: Yellow crystalline solid;

\(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta\) 7.76 (s, 1H), 7.62 (d, 2H, \(J=7.8\) Hz), 7.40-7.14 (m, 5H), 7.06-6.97 (m, 2H), 3.13 (m, 1H), 1.25 (d, 6H, \(J=6.9\) Hz); \(^{13}\)C NMR (75 MHz, CDCl\(_3\)): \(\delta\) 157.2 (C-F), 140.2, 137.5, 130.1, 129.9, 129.4, 127.5, 126.5, 126.1, 125.4, 121.6, 118.8, 115.6, 115.3, 114.9, 26.5, 22.6; HRMS (ESI-TOF) m/z: [M+H]**+** Calculated for C\(_{18}\)H\(_{18}\)FN\(_2\), found: 281.1450; IR (KBr) cm\(^{-1}\): 1174.8, 1241.2, 1504.3, 1575.5, 1608.9, 2850.8; Anal. Caled for C\(_{18}\)H\(_{17}\)FN\(_2\): C: 77.12; H: 6.11; N: 9.99%, found: C: 77.10; H: 6.10; N: 9.98%

4-(4-fluorophenyl)-1-phenyl-3-(\(p\)-tolyl)-1H-pyrazole (5b)
Yield: 87%, (0.285 g); M.p. 83-84°C; Characteristics: Yellow amorphous solid;  

$^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.63 (d, 3H, $J=8.1$ Hz), 7.54-7.34 (m, 3H), 7.28-6.94 (m, 8H), 2.37 (s, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 162.0 (C-F), 154.8, 150.5, 137.8, 137.5, 132.6, 131.4, 130.2, 129.3, 129.2, 128.9, 125.4, 116.9, 116.6, 116.1, 115.8, 21.5; HRMS (ESI-TOF) m/z: [M+H]$^+$  
Calculated for C$_{22}$H$_{18}$FN$_2$: 329.1454, found: 329.1450; IR (KBr) cm$^{-1}$: 1098.6, 1244.2, 1446.5, 1520.1, 1605.5, 2866.3; Anal. Calcd for C$_{22}$H$_{17}$FN$_2$: C: 80.47; H: 5.22; N: 8.53%, found: C: 80.47; H: 5.23; N: 8.52%  

4-(4-Fluoro-phenyl)-3-(3-nitro-phenyl)-1-phenyl-$^{1}$H-pyrazole (5c)  

Yield: 89%, (0.319 g); M.p. 101-103°C; Characteristics: Yellow crystalline solid;  

$^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 8.45 (s, 1H), 8.10-8.07 (m, 1H), 7.94-7.88 (m, 2H), 7.78-7.71 (m, 3H), 7.46-7.20 (m, 7H); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$158.8 (C-F), 155.5, 143.3, 142.6, 134.4, 129.6, 128.8, 125.3, 125.2, 124.8, 124.4, 124.0, 122.9, 122.1, 117.8, 117.4, 117.1, 113.8, 110.8, 110.6; HRMS (ESI-TOF) m/z: [M+H]$^+$  
Calculated for C$_{21}$H$_{15}$FN$_3$O$_2$: 360.1148, found:360.1144; IR (KBr) cm$^{-1}$: 1130.8, 1249.3, 1327.6, 1529.5, 1611.0, 2950.1, 3026.5; Anal. Calcd for C$_{21}$H$_{14}$FN$_3$O$_2$: C: 70.19; H: 3.93; 11.69%, found: C: 70.20; H: 3.92; N: 11.68%
4-(4-Fluoro-phenyl)-3-isopropyl-1-(4-nitro-phenyl)-1H-pyrazole (5d)

Yield: 86%, (0.279 g); M.p. 85-86 °C; Characteristics: Yellow crystalline solid;

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\begin{align*}
\text{\textsuperscript{1}H NMR (300 MHz, CDCl}_3\text{):} & \; \delta \; 8.36 \; (s, \; 1H), \; 8.19 \; (d, \; 2H, \; J= 9 \; Hz), \; 8.04 \; (d, \; 2H, \; J= 8.6 \; Hz), \; 7.64-7.61 \; (m, \; 2H), \; 7.37-7.24 \; (m, \; 2H), \; 3.13 \; (m, \; 1H), \; 1.23 \; (d, \; 6H, \; J=6.6 \; Hz); \\
\text{\textsuperscript{13}C NMR (75 MHz, CDCl}_3\text{):} & \; \delta \; 161.2 \; (C-F), \; 147.2, \; 137.5, \; 130.5, \; 130.2, \; 127.5, \; 125.9, \; 124.9, \; 123.8, \; 123.6, \; 123.4, \; 116.1, \; 115.6, \; 114.3, \; 26.6, \; 22.2; \\
\text{HRMS (ESI-TOF) m/z:} & [M+H]^+ \; \text{Calculated for C}_{18}\text{H}_{17}\text{FN}_3\text{O}_2: \; 326.1305, \; \text{found: 326.1301;} \\
\text{IR (KBr) cm}^{-1}: & 1025.6, \; 1246.6, \; 1509.4, \; 1598.5, \; 1631.2, \; 2896.3, \; 3010.2; \text{Anal. Caled for C}_{18}\text{H}_{16}\text{FN}_3\text{O}_2: C: 66.45; \; H: 4.96; \; N: 12.92%, \; \text{found: C: 66.44; H: 4.94; N: 12.95%}
\end{align*}
\]

2-Phenyl-2,4-dihydro-chromeno[4,3-c]pyrazole (7a)

Yield: 91%, (0.226 g); M.p. 79-80 °C (Lit: 81-82 °C); Characteristics: Yellow crystalline solid;

\[
\begin{align*}
\text{\textsuperscript{1}H NMR (300 MHz, CDCl}_3\text{):} & \; \delta \; 7.80 \; (dd, \; 1H, \; J=7.5 \; Hz, \; 1.8 \; Hz), \; 7.65-7.60 \; (m, \; 2H), \; 7.41-7.34 \; (m, \; 3H), \; 7.24-7.12 \; (m, \; 1H), \; 6.98-6.87 \; (m, \; 3H), \; 5.27 \; (s, \; 2H); \\
\text{\textsuperscript{13}C NMR (75 MHz, CDCl}_3\text{):} & \; \delta \; 156.4, \; 154.1, \; 135.8, \; 133.1, \; 130.0, \; 129.6, \; 129.1, \; 126.3, \; 122.7, \; 122.3, \; 122.1, \; 119.2, \; 117.4, \; 63.3; \\
\text{HRMS (ESI-TOF) m/z:} & [M+H]^+ \; \text{Calculated for C}_{16}\text{H}_{13}\text{N}_2\text{O:} \; 249.1028, \; \text{found:249.1025;} \text{ IR (KBr) cm}^{-1}: 1089.6, \; 1229.8, \; 1471.3, \; 1502.8, \; 1599.3, \; 1689.9, \; 2800.3; \text{Anal. Caled for C}_{16}\text{H}_{12}\text{N}_2\text{O:} \; C: 77.40; \; H: 4.87; \; N: 11.28%, \; \text{found: C: 77.45; H: 4.84; N: 11.25%}
\end{align*}
\]

**General Procedure for the synthesis of isoxazolines**

The reaction was performed via the same method for pyrazoles. A mixture of aldehyde (1 mmol), hydroxyl amine hydrochloride (1 mmol), sodium acetate (1 mmol), and olefin derivatives (1 mmol)
were added to a well stirred solution of SDS (10 mol %) in 5 ml H₂O at room temperature. Then PhIO (1.5 mmol) was added portion wise to the resulting mixture carefully maintaining the temperature at 0 °C. When the addition was complete the reaction was allowed to attain room temperature and stirring was continued for the required period of time (monitored by TLC). After completion of the reaction, the mixture was extracted with ethyl acetate (3x10ml). Removal of ethyl acetate under reduced pressure and purification of the crude product by column chromatography (silica gel 100-200 mesh, ethyl acetate-hexane as eluent) provided pure products. All compounds were well characterized by ¹H, ¹³C NMR, FT-IR and HRMS analysis.

3-Phenyl-4,5-dihydro-isoxazole-5-carboxylic acid ethyl ester (6a)

Yield: 92%, (0.201 g); M.p. 28-29 °C (Lit: 31-33 °C); Characteristics: Yellow amorphous solid;

¹H NMR (300 MHz, CDCl₃): δ 7.68-7.63 (m, 2H), 7.45-7.41 (m, 3H), 5.16 (dd, 1H, J=10.4, 7.8 Hz), 4.26 (q, 2H, J=7.1Hz), 3.65-3.62 (m, 2H), 1.32 (t, 3H, J=7.1 Hz); ¹³C NMR (75 MHz, CDCl₃): δ 170.3, 156.1, 133.7, 130.5, 128.8, 128.5, 126.9, 126.8, 78.1, 62.0, 38.9, 14.1; HRMS (ESI-TOF) m/z: [M+H]⁺ Calculated for C₁₂H₁₄NO₃: 220.0974, found: 220.0971; IR (KBr) cm⁻¹: 1032.6, 1210.1, 1449.1, 1736.1, 2963.7, 3471.2 ; Anal. Calcd for C₁₂H₁₃NO₃: C: 65.74; H: 5.98; N: 6.39%, found: C: 65.71; H: 5.96; N: 6.36%

3-(3-Nitro-phenyl)-4,5-dihydro-isoxazole-5-carboxylic acid ethyl ester (6b)

Yield: 89%, (0.235 g); M.p. 66-67 °C (Lit: 65-67 °C); Characteristics: White crystalline solid;
\( ^1H\) NMR (300 MHz, CDCl\(_3\)): \( \delta \) 8.30 (s, 1H), 8.17 (d, 1H, \( J=8.4\) Hz), 7.98 (d, 1H, \( J=7.8\) Hz), 7.56-7.51 (m, 1H), 5.22 (dd, 1H, \( J=10.2, 7.8\) Hz), 4.20 (q, 2H, \( J=7.1\) Hz), 3.70-3.63 (m, 2H,), 1.25 (t, 3H, \( J=7.2\) Hz); \( ^{13}C\) NMR (75 MHz, CDCl\(_3\)): \( \delta \) 169.8, 154.6, 148.3, 132.4, 130.1, 129.8, 124.9, 121.9, 78.8, 62.4, 38.4, 14.1; HRMS (ESI-TOF) m/z: \([M+H]^+\) Calculated for C\(_{12}\)H\(_{13}\)N\(_2\)O\(_5\): 265.0824, found: 265.0820; IR (KBr) cm\(^{-1}\): 1145.7, 1210.9, 1463.7, 1548.1, 1720.6, 2863.3, 2933.4, 3012.3, 3548.5; Anal. Calcd for C\(_{12}\)H\(_{13}\)N\(_2\)O\(_5\): C: 54.55; H: 4.58; N: 10.60%, found: C: 54.54; H: 4.56; N: 10.62% 

3-Thiophen-2-yl-4,5-dihydro-isoxazole-5-carboxylic acid ethyl ester (6c)

Yield: 84%, (0.189 g); Characteristics: Yellow oil;

\( ^1H\) NMR (300 MHz, CDCl\(_3\)): \( \delta \) 7.59-7.57 (m, 1H), 7.37-7.34 (m, 1H), 7.19-7.17 (m, 1H), 5.09 (dd, 1H, \( J=10.2, 7.8\) Hz), 4.18 (q, 2H, \( J=6.9\) Hz), 3.60-3.57 (m, 2H,), 1.24 (t, 3H, \( J=7.1\) Hz); \( ^{13}C\) NMR (75 MHz, CDCl\(_3\)): \( \delta \) 170.5, 163.1, 134.8, 129.0, 129.1, 127.4, 78.2, 62.1, 38.9, 14.1; HRMS (ESI-TOF) m/z: \([M+H]^+\) Calculated for C\(_{10}\)H\(_{12}\)NO\(_3\)S: 226.0538, found: 226.0536; IR (KBr) cm\(^{-1}\): 1156.3, 1216.2, 1440.4, 1608.2, 1730.1, 2866.3, 2998.3, 3263.6; Anal. Calcd for C\(_{10}\)H\(_{11}\)NO\(_3\)S: C: 53.32; H: 4.92; N: 6.22%, found: C: 53.35; H: 4.90; N: 6.21%

3-(4-Methoxy-phenyl)-4,5-dihydro-isoxazole-5-carboxylic acid ethyl ester (6d)

Yield: 85%, (0.209 g); Characteristics: Yellow oil;

\( ^1H\) NMR (300 MHz, CDCl\(_3\)): \( \delta \) 7.55-7.51 (m, 2H), 6.88-6.82 (m, 2H), 5.05 (dd, 1H, \( J=10.2, 7.8\) Hz), 4.18 (q, 2H, \( J=7.2\) Hz), 3.76 (s, 3H), 3.55-3.51 (m, 2H,), 1.24 (t, 3H, \( J=7.2\) Hz); \( ^{13}C\) NMR (75 MHz, CDCl\(_3\)): \( \delta \) 170.4, 161.3, 155.6, 128.6, 121.8, 114.4, 113.7, 78.1, 62.1, 55.6, 39.2, 14.2; HRMS (ESI-TOF) m/z: \([M+H]^+\) Calculated for C\(_{10}\)H\(_{11}\)NO\(_3\): 218.0350, found: 218.0350; IR (KBr) cm\(^{-1}\): 1145.7, 1210.9, 1463.7, 1548.1, 1720.6, 2863.3, 2933.4, 3012.3, 3548.5; Anal. Calcd for C\(_{10}\)H\(_{11}\)NO\(_3\): C: 53.32; H: 4.92; N: 6.22%, found: C: 53.35; H: 4.90; N: 6.21%
3,5-Diphenyl-4,5-dihydro-isoxazole (6e)

Yield: 90%, (0.200 g); M.p. 70-72 °C (Lit: 75-76 °C); Characteristics: Yellow crystalline solid;

$^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.65-7.51 (m, 2H), 7.31-7.21 (m, 8H), 5.61 (dd, 1H, $J$=10.2, 8.1Hz), 3.65 (dd, 1H, $J$=16.6,10.8 Hz), 3.21 (dd, 1H, $J$=16.8, 8.4Hz); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$156.0, 140.8, 137.4, 130.2, 129.1, 129.0, 128.1, 128.0, 126.1, 125.9, 82.5, 43.1; HRMS (ESI-TOF) m/z: [M+H]$^+$ Calculated for C$_{13}$H$_{15}$NO: 224.1075, found: 224.1072; IR (KBr) cm$^{-1}$: 1059.3, 1212.7, 1453.0, 1599.6, 2830, 3030.2, 3532.2 ; Anal. Calcd for C$_{13}$H$_{13}$NO: C: 80.69; H: 5.87; N: 6.27%, found: C: 80.66; H: 5.89; N: 6.29%

3-(4-bromophenyl)-5-phenyl-4,5-dihydroisoxazole (6f)

Yield: 90%, (0.272 g); M.p. 140-141 °C (Lit: 141-142 °C); Characteristics: White crystalline solid;

$^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.53-7.46 (m, 5H), 7.37-7.29 (m, 4H), 5.73 (dd, 1H, $J$=10.8, 8.4Hz), 3.73 (dd, 1H, $J$=16.7,10.8 Hz), 3.33 (dd, 1H, $J$=16.5, 8.4Hz); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 150.3, 140.7, 132.7, 132.1, 129.0, 128.4, 128.3, 126.1, 82.9, 42.9; HRMS (ESI-TOF) m/z: [M+H]$^+$ Calculated for C$_{15}$H$_{13}$BrNO: 302.0181, found: 302.0179; IR (KBr) cm$^{-1}$: 1101.4, 1439.6, 1598.2,
3-isopropyl-5-phenyl-4,5-dihydroisoxazole (6g)

Yield: 91%, (0.172 g); Characteristics: Yellow oil;

\[
\begin{align*}
\text{\textsuperscript{1}H NMR} (300 \text{ MHz, CDCl}_3): & \delta 7.27-7.17 (m, 5H), 5.44 (dd, 1H, J=10.5, 8.1 \text{ Hz}), 3.28 (dd, 1H, J=17.1, 10.8 \text{ Hz}), 2.81(dd, 1H, J=16.8, 8.1 \text{ Hz}), 2.65 (m, 1H), 1.11 (d, 6H, J=6.9 \text{ Hz}); \\
\text{\textsuperscript{13}C NMR} (75 \text{ MHz, CDCl}_3): & \delta 157.1, 135.4, 131.5, 126.0, 123.1, 122.1, 121.9, 120.0, 75.4, 37.3, 21.9, 14.3; \\
\text{HRMS (ESI-TOF) m/z: [M+H]}^+ & \text{ Calculated for C}_{12}\text{H}_{16}\text{NO: 190.1232, found: 190.1230; IR (KBr) cm}^{-1}: 1010.6, 1310.9, 1567.1, 2900.6, 3028.9, 3412.9; \\
\text{Anal. Calcd for C}_{12}\text{H}_{16}\text{NO: C: 76.16; H: 7.99; N: 7.40%}, \text{ found: C: 76.18; H: 7.97; N: 7.42%}
\end{align*}
\]

3-Phenyl-3a,4,5,6,7,7a-hexahydro-benzo[d]isoxazole (6h)

Yield: 92%, (0.185 g); M.p. 80-81 °C (Lit: 79-81 °C); Characteristics: White crystalline solid;

\[
\begin{align*}
\text{\textsuperscript{1}H NMR} (300 \text{ MHz, CDCl}_3): & \delta 7.59-7.56 (m, 2H), 7.35-7.30 (m, 3H), 4.83-4.75 (m, 1H), 3.68-3.63(m, 1H), 2.01-1018 (m, 8H); \\
\text{\textsuperscript{13}C NMR} (75 \text{ MHz, CDCl}_3): & \delta 160.2, 129.5, 128.7, 127.0, 84.9, 51.4, 31.1, 30.1, 27.0, 23.7; \\
\text{HRMS (ESI-TOF) m/z: [M+H]}^+ & \text{ Calculated for C}_{13}\text{H}_{16}\text{NO: 202.1232, found: 202.1230; IR (KBr) cm}^{-1}: 1310.4, 1400.6, 1558.3, 1701.8, 2904.5, 3010.5, 3396.3; \\
\text{Anal. Calcd for C}_{13}\text{H}_{16}\text{NO: C: 77.58; H: 7.51; N: 6.96%}, \text{ found: C: 77.55; H: 7.50; N: 6.92%}
\end{align*}
\]
3,5-Diphenyl-isoxazole (6i)

Yield: 86%, (0.190 g); M.p. 139-140 °C (Lit: 140-142 °C); Characteristics: white crystalline solid;

\[ ^1H \text{ NMR (300 MHz, CDCl}_3\text{): } \delta \text{ 7.98-7.94(m, 2H), 7.54-7.48(m, 8H), 6.98 (s, 1H);} \]
\[ ^{13}C \text{ NMR (75 MHz, CDCl}_3\text{): } \delta \text{ 172.1, 161.8, 137.4, 133.7, 130.0, 129.9, 129.2, 128.8, 128.6, 128.5, 128.3, 128.2, 128.1, 127.6, 97.5;} \]

HRMS (ESI-TOF) m/z: [M+H]^+ Calculated for C\textsubscript{15}H\textsubscript{12}NO: 222.0919, found: 222.0914;

IR (KBr) cm\textsuperscript{-1}: 1201.4, 1455.4, 1540.2, 1604.4, 21910.5, 3042.5, 3112.2, 3564.8 ;

Anal. Calcd for C\textsubscript{15}H\textsubscript{11}NO: C: 81.43; H: 5.01; N: 6.33%, found: C: 81.41; H: 5.05; N: 6.35%

3a,4-Dihydro-3H-chromeno[4,3-c]isoxazole (7b)

Yield: 92%, (0.161 g); M.p. 60-62 °C (Lit: 62-64 °C); Characteristics: White crystalline solid;

\[ ^1H \text{ NMR (300 MHz, CDCl}_3\text{): } \delta \text{ 7.68 (d, 1H, J=7.5 Hz), 7.26-7.18 (m, 1H), 6.92-6.83(m, 2H,), 4.60-} \]
\[ 4.53(m, 2H), 4.01-3.94 (m, 1H), 3.89-3.75 (m, 2H);} \]
\[ ^{13}C \text{ NMR (75 MHz, CDCl}_3\text{): } \delta \text{ 155.6, 152.8,} \]
\[ 132.5, 125.6, 121.8, 117.4, 113.0, 70.6, 69.2, 45.9;} \]

HRMS (ESI-TOF) m/z: [M+H]^+ Calculated for C\textsubscript{10}H\textsubscript{10}NO\textsubscript{2}:176.0712, found:176.0710;

IR (KBr) cm\textsuperscript{-1}: 1026.3, 1209.2, 1410.4, 1560.3, 1710.1, 2896.3, 3010.5, 3566.9; Anal. Calcd for C\textsubscript{10}H\textsubscript{9}NO\textsubscript{2}: C: 68.56; H: 5.01; N: 8.00%, found: C: 68.58; H: 5.16; N: 8.01%

4H-Chromeno[4,3-c]isoxazole (7c)
Yield: 90%, (0.155 g); M.p. 42-43 °C (Lit: 42 °C); Characteristics: White crystalline solid;

$^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 8.24 (s, 1H), 7.91 (dd, 1H, $J=7.6$, 1.5 Hz), 7.42-7.36 (m, 1H), 7.16-7.04 (m, 2H), 5.27 (s, 2H); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 154.8, 153.6, 150.6, 132.1, 124.5, 122.4, 117.9, 113.9, 111.1, 61.3; HRMS (ESI-TOF) m/z: [M+H]$^+$ Calculated for C$_{10}$H$_7$NO$_2$: 174.0555, found: 174.0553; IR (KBr) cm$^{-1}$: 1045.6, 1211.8, 1496.8, 1501.1, 1705.1, 2988.9, 3112.5, 3496.9; Anal. Calcd for C$_{10}$H$_7$NO$_2$: C: 69.36; H: 4.07; N: 8.09%, found: C: 69.38; H: 4.09; N: 8.07%
2. $^1$HNMR and $^{13}$CNMR Spectra of the Compounds (4a-4o, 5a-5d, 6a-6i, 7a-7c):

$^1$H NMR of Compound 4a
$^{13}$C NMR of Compound 4a
$^1$H NMR of Compound 4b
$^{13}$C NMR of Compound 4b
$^1$H NMR of Compound 4c
$^{13}$C NMR of Compound 4c
$^1$H NMR of Compound 4d
$^{13}$C NMR of Compound 4d
$^1$H NMR of Compound 4e
$^{13}$C NMR of Compound 4e
$^1$H NMR of Compound 4f
$^{13}$C NMR of Compound 4f
$^1$H NMR of Compound 4g
$^{13}$C NMR of Compound 4g
$^1$H NMR of Compound 4h
$^{13}$C NMR of Compound 4h
$^1$H NMR of Compound 4i
$^{13}$C NMR of Compound 4i
$^1$H NMR of Compound 4j
$^{13}$C NMR of Compound 4j
$^{13}$C NMR of Compound 4k
$^{13}$C NMR of Compound 4k
$^1$H NMR of Compound 4l
$^{13}$C NMR of Compound 41
$^1$H NMR of Compound 4m
$^{13}$C NMR of Compound 4m
$^1$H NMR of Compound 4n
$^{13}$C NMR of Compound 4n
$^{1}\text{H NMR of Compound 4o}$
$^{13}$C NMR of Compound 4o
$^1$H NMR of Compound 5a
$^{13}$C NMR of Compound 5a
$^1$H NMR of Compound 5b
$^{13}$C NMR of Compound 5b
$^{1}$H NMR of Compound 5c
$^{13}$C NMR of Compound 5c
$^1$H NMR of Compound 5d
$^{13}$C NMR of Compound 5d
$^1$H NMR of Compound 6a
$^{13}$C NMR of Compound 6a
$^1$H NMR of Compound 6b
$^{13}$C NMR of Compound 6b
$^1$H NMR of Compound 6c
$^{13}$C NMR of Compound 6c
$^1$H NMR of Compound 6d
$^{13}$C NMR of Compound 6d
$^1$H NMR of Compound 6e
$^{13}$C NMR of Compound 6e
$^1$H NMR of Compound 6f
$^{13}$C NMR of Compound 6f
$^1$H NMR of Compound 6g
$^{13}$C NMR of Compound 6g
$^1$H NMR of Compound 6h
$^{13}$C NMR of Compound 6h
$^1$H NMR of Compound 6i
$^{13}$C NMR of Compound 6i
$^1$H NMR of Compound 7a
\[ ^{13}C \text{NMR of Compound 7a} \]
$^1$H NMR of Compound 7b
$^{13}$C NMR of Compound 7b
$^1$H NMR of Compound 7c
$^{13}$C NMR of Compound 7c