Copper-Catalyzed Aerobic Cascade Cycloamination and Acyloxylation: A Direct Approach to 4-Acyloxy-1H-pyrazoles

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1. General Information

All reagents and metal catalysts were obtained from commercial sources without further purification, and commercially available solvents were purified before use. All new compounds were fully characterized. All melting points were taken on a WRS-1A or a WRS-1B Digital Melting Point Apparatus without correction. Infrared spectra were obtained using an AVATAR 370 FT-IR spectrometer. $^1$H and $^{13}$C NMR spectra were recorded with a Bruker AV-500 spectrometer operating at 500, 125 and 470 MHz, respectively, with chemical shift values being reported in ppm relative to chloroform ($\delta = 7.26$ ppm), dimethyl sulfoxide ($\delta = 2.50$ ppm) or TMS ($\delta = 0.00$ ppm) for $^1$H NMR, and chloroform ($\delta = 77.16$ ppm) or dimethyl sulfoxide ($\delta = 39.52$ ppm) for $^{13}$C NMR. Mass spectra and high resolution mass spectra were recorded with an Agilent 5975N using an Electron impact (EI) or Electrospray ionization (ESI) techniques. Silica gel plate GF254 were used for thin layer chromatography (TLC) and silica gel H or 300-400 mesh were used for flash column chromatography. Yields refer to chromatographically and spectroscopically pure compounds, unless otherwise indicated.
2. Synthesis and Characterization for Hydrazones

2-(1,3-diphenylallylidene)hydrazinyl)phosphonate (1a): A mixture of chalcone (1.04 g, 5.0 mmol) and phosphorohydrazidic acid diethyl ester (1.26 g, 7.5 mmol) in EtOH (20 mL) was stirred overnight at 78 °C. The reaction was cooled to room temperature after complete consumption of chalcone as monitored by TLC analysis. The reaction mixture was evaporated to dry under reduced pressure and the crude product was purified by column chromatography on silica gel (petroleum ether/EtOAc = 2/1) to yield 1a (1.52 g, 85%) as a colorless solid. M.p. 176-178 °C. IR (KBr): 3151, 2978, 2870, 1617, 1544, 1442, 1326, 1235, 1110, 1036, 972, 762 cm⁻¹; ¹H NMR (DMSO-d₆, 500 MHz): δ = 9.35 (d, ²J_P-H = 26.8 Hz, 1H), 7.69-7.65 (m, 3H), 7.45-7.37 (m, 7H), 7.33 (t, J = 7.2 Hz, 1H), 6.69 (d, J = 16.2 Hz, 1H), 4.10-4.01 (m, 4H), 1.25 (t, J = 7.0 Hz, 6H); ¹³C NMR (DMSO-d₆, 125 MHz): δ = 149.7 (d, ³J_P-C = 18.8 Hz), 137.9, 137.5, 136.0, 129.0, 128.7, 128.6, 128.5, 128.3, 127.7, 117.9, 62.3 (d, ²J_P-C = 6.3 Hz), 16.1 (d, ³J_P-C = 6.3 Hz); MS (EI) m/z: 358 (6) [M⁺], 206 (100); HRMS (ESI) m/z: Calcd for C₁₉H₂₄N₂O₃P [M+H⁺]: 359.1519, found: 359.1521.

2-(1-(3-methoxyphenyl)-3-phenylallylidene)hydrazinyl)phosphonate (1b): Following the same procedure used for 1a with 1-(3-methoxyphenyl)-3-phenylprop-2-en-1-one (1.19 g, 5.0 mmol) and phosphorohydrazidic acid diethyl ester (1.26 g, 7.5 mmol) in EtOH (20 mL). The crude product was purified by column chromatography on silica gel (petroleum ether/EtOAc = 1/1) to yield 1b (1.44 g, 74%) as a colorless solid. M.p. 136-138 °C. IR (KBr): 3446, 3166, 2983, 1600, 1464, 1437, 1236, 1030, 978, 888, 767 cm⁻¹; ¹H NMR (DMSO-d₆, 500 MHz): δ = 9.35 (d, ²J_P-H = 26.9 Hz, 1H), 7.69 (d, J = 7.6 Hz, 2H), 7.64 (d, J = 16.2 Hz, 1H), 7.40-7.32 (m, 4H), 7.04-6.98 (m, 3H), 6.72 (d, J = 16.1 Hz, 1H), 4.11-4.02 (m, 4H), 3.77 (s, 3H), 1.26 (t, J = 7.1 Hz, 6H); ¹³C NMR (DMSO-d₆, 125 MHz): δ = 159.0, 149.4 (d, ³J_P-C = 17.6 Hz), 138.9, 137.9, 136.0, 129.3, 129.0, 128.6, 127.7, 121.1, 117.8, 114.2, 114.0, 62.4 (d, ²J_P-C = 5.5 Hz), 55.0, 16.1 (d, ³J_P-C = 6.3 Hz); MS (EI) m/z: 388 (12) [M⁺], 236 (100); HRMS (ESI) m/z: Calcd for C₂₀H₂₆N₂O₄P [M+H⁺]: 389.1625, found: 389.1628.
Diethyl (2-(1-(4-methoxyphenyl)-3-phenylallylidene)hydrazinyl)phosphonate (1c):
Following the same procedure used for 1a with 1-(4-methoxyphenyl)-3-phenylprop-2-en-1-one (1.19 g, 5.0 mmol) and phosphorohydrazidic acid diethyl ester (1.26 g, 7.5 mmol) in EtOH (20 mL). The crude product was purified by column chromatography on silica gel (petroleum ether/EtOAc = 1/1) to yield 1c (1.49 g, 77%) as a colorless solid. M.p. 140-142 °C. IR (KBr): 3445, 3145, 2976, 1607, 1512, 1442, 1302, 1252, 1031, 977, 813, 764 cm\(^{-1}\); \(^1\)H NMR (DMSO-\(d_6\), 500 MHz): \(\delta = 9.22\) (d, \(J_{P-H} = 26.5\) Hz, 1H), 7.68 (d, \(J = 7.5\) Hz, 2H), 7.61 (d, \(J = 16.5\) Hz, 1H), 7.41-7.32 (m, 5H), 6.99 (d, \(J = 8.5\) Hz, 2H), 6.71 (d, \(J = 16.0\) Hz, 1H), 4.10-4.01 (m, 4H), 3.80 (s, 3H), 1.25 (t, \(J = 7.0\) Hz, 6H); 13C NMR (DMSO-\(d_6\), 125 MHz): \(\delta = 159.5, 149.5\) (d, \(J_{P-C} = 17.5\) Hz), 137.9, 136.1, 129.9, 128.9, 128.6, 127.7, 118.2, 113.6, 62.3 (d, \(J_{P-C} = 6.3\) Hz), 55.2, 16.1 (d, \(J_{P-C} = 6.3\) Hz); MS (EI) m/z: 388 (19) [M +], 235 (100); HRMS (ESI) m/z: Calcd for C\(_{20}\)H\(_{26}\)N\(_2\)O\(_4\)P [M+H\(^+\)]: 389.1625, found: 389.1619.

Diethyl (2-(1-(3-chlorophenyl)-3-phenylallylidene)hydrazinyl)phosphonate (1d):
Following the same procedure used for 1a with 1-(3-chlorophenyl)-3-phenylprop-2-en-1-one (1.21 g, 5.0 mmol) and phosphorohydrazidic acid diethyl ester (1.26 g, 7.5 mmol) in EtOH (20 mL). The crude product was purified by column chromatography on silica gel (petroleum ether/EtOAc = 2/1) to yield 1d (1.37 g, 70%) as a colorless solid. M.p. 121-123 °C. IR (KBr): 3442, 3181, 2982, 1443, 1329, 1243, 1127, 1034, 977, 754 cm\(^{-1}\); \(^1\)H NMR (DMSO-\(d_6\), 500 MHz): \(\delta = 9.44\) (d, \(J_{P-H} = 27.0\) Hz, 1H), 7.69 (d, \(J = 7.5\) Hz, 2H), 7.63 (d, \(J = 16.2\) Hz, 1H), 7.49-7.34 (m, 7H), 6.70 (d, \(J = 16.3\) Hz, 1H), 4.10-4.01 (m, 4H), 1.25 (t, \(J = 7.0\) Hz, 6H); 13C NMR (DMSO-\(d_6\), 125 MHz): \(\delta = 148.2\) (d, \(J_{P-C} = 17.5\) Hz), 139.7, 138.0, 135.9, 133.0, 130.2, 129.1, 128.6, 128.4, 128.2, 127.7, 127.4, 117.6, 62.4 (d, \(J_{P-C} = 5.0\) Hz), 16.0 (d, \(J_{P-C} = 6.3\) Hz); MS (EI) m/z: 394 (2) [M\(^+\) \(^{37}\)Cl], 392 (7) [M\(^+\) \(^{35}\)Cl], 240 (100); HRMS (ESI) m/z: Calcd for C\(_{19}\)H\(_{23}\)ClN\(_2\)O\(_3\)P [M+H\(^+\)]: 393.1129, found: 393.1133.

Diethyl (2-(1-(4-bromophenyl)-3-phenylallylidene)hydrazinyl)phosphonate (1e):
Following the same procedure used for 1a with 1-(4-bromophenyl)-3-phenylprop-2-en-1-one (1.44 g, 5.0 mmol) and phosphorohydrazidic acid diethyl ester (1.26 g, 7.5 mmol) in EtOH (20 mL). The crude product was purified by column chromatography on silica gel (petroleum ether/EtOAc = 2/1) to yield 1e (1.55 g, 71%) as a colorless solid. M.p. 140-142 °C. IR (KBr): 3119, 2979, 2873, 1442, 1251, 1070, 1036, 979, 792 cm\(^{-1}\); \(^1\)H NMR (DMSO-\(d_6\), 500 MHz): \(\delta = 9.40\) (d, \(J_{P-H} = 24.5\) Hz, 1H), 7.69 (d, \(J = 7.5\) Hz, 2H), 7.65-7.62 (m, 3H), 7.42-7.32 (m, 5H), 6.70 (d, \(J = 16.0\) Hz, 1H),
4.10-4.01 (m, 4H), 1.25 (t, J = 7.0 Hz, 6H); 13C NMR (DMSO-d$_6$, 125 MHz): δ = 148.6 (d, 3J$_{P-C}$ = 17.5 Hz), 138.0, 136.7, 135.9, 131.2, 130.7, 129.1, 128.6, 127.7, 121.8, 117.6, 62.4 (d, 2J$_{P-C}$ = 6.3 Hz), 16.1 (d, 3J$_{P-C}$ = 6.3 Hz); MS (EI) m/z: 438 (5) [M$^+$ ($^{81}$Br)], 436 (6) [M$^+$ ($^{79}$Br)], 284 (100); HRMS (ESI) m/z: Calcd for C$_{19}$H$_{23}$BrN$_2$O$_3$P [M+H$^+$]: 437.0624, found: 437.0624.

Diethyl (2-(3-(2-bromophenyl)-1-phenylallylidene)hydrazinyl)phosphonate (1f):
Following the same procedure used for 1a with 3-(2-bromophenyl)-1-phenylprop-2-en-1-one (1.44 g, 5.0 mmol) and phosphorohydrazide acid diethyl ester (1.26 g, 7.5 mmol) in EtOH (20 mL). The crude product was purified by column chromatography on silica gel (petroleum ether/EtOAc = 2/1) to yield 1f (1.75 g, 80%) as a colorless solid. M.p. 192-194 ºC. IR (KBr): 3157, 2981, 2863, 1469, 1437, 1324, 1163, 1110, 1039, 973, 766 cm$^{-1}$; 1H NMR (DMSO-d$_6$, 500 MHz): δ = 9.45 (d, 2J$_{P-H}$ = 27.0 Hz, 1H), 8.16-8.14 (m, 1H), 7.65-7.27 (m, 9H), 7.01 (d, J = 16.0 Hz, 1H), 4.11-4.02 (m, 4H), 1.26 (t, J = 7.3 Hz, 6H); 13C NMR (DMSO-d$_6$, 125 MHz): δ = 149.3 (d, 3J$_{P-C}$ = 18.8 Hz), 137.2, 135.8, 135.4, 132.9, 130.7, 128.7, 128.2, 128.1, 127.9, 124.0, 120.7, 62.4 (d, 2J$_{P-C}$ = 5.0 Hz), 16.1 (d, 3J$_{P-C}$ = 6.3 Hz); MS (EI) m/z: 438 (5) [M$^+$ ($^{81}$Br)], 436 (6) [M$^+$ ($^{79}$Br)], 286 (100); HRMS (ESI) m/z: Calcd for C$_{19}$H$_{23}$BrN$_2$O$_3$P [M+H$^+$]: 437.0624, found: 437.0619.

Diethyl (2-(1,3-bis(4-bromophenyl)allylidene)hydrazinyl)phosphonate (1g):
Following the same procedure used for 1a with 1,3-bis(4-bromophenyl)prop-2-en-1-one (1.83 g, 5.0 mmol) and phosphorohydrazide acid diethyl ester (1.26 g, 7.5 mmol) in EtOH (20 mL). The crude product was purified by column chromatography on silica gel (petroleum ether/EtOAc = 2/1) to yield 1g (1.88 g, 73%) as a colorless solid. M.p. 167-169 ºC. IR (KBr): 3128, 2976, 2900, 1587, 1486, 1436, 1391, 1245, 1072, 1034, 1007, 977, 815, 788 cm$^{-1}$; 1H NMR (DMSO-d$_6$, 500 MHz): δ = 9.42 (d, 2J$_{P-H}$ = 26.8 Hz, 1H), 7.66-7.57 (m, 7H), 7.40 (d, J = 8.5 Hz, 2H), 6.68 (d, J = 16.2 Hz, 1H), 4.09-4.01 (m, 4H), 1.24 (t, J = 7.1 Hz, 6H); 13C NMR (DMSO-d$_6$, 125 MHz): δ = 148.3 (d, 3J$_{P-C}$ = 17.5 Hz), 136.6, 136.5, 135.3, 131.5, 131.2, 130.7, 129.6, 122.2, 121.9, 118.3, 62.4 (d, 2J$_{P-C}$ = 5.0 Hz), 16.1 (d, 3J$_{P-C}$ = 6.3 Hz); MS (EI) m/z: 518 (1) [M$^+$ ($^{81}$Br, $^{79}$Br)], 516 (2) [M$^+$ ($^{2}$×$^{79}$Br)], 408 (54), 406 (100), 404 (53); HRMS (ESI) m/z: Calcd for C$_{19}$H$_{22}$Br$_2$N$_2$O$_3$P [M+H$^+$]: 514.9729, found: 514.9709.
Diethyl (2-(3-(naphthalen-1-yl)-1-phenylallylidene)hydrazinyl)phosphonate (1h):
Following the same procedure used for 1a with 3-(naphthalen-1-yl)-1-phenylprop-2-en-1-one (1.29 g, 5.0 mmol) and phosphorohydrazidic acid diethyl ester (1.26 g, 7.5 mmol) in EtOH (20 mL). The crude product was purified by column chromatography on silica gel (petroleum ether/EtOAc = 2/1) to yield 1h (1.55 g, 76%) as a colorless solid. M.p. 173-175 °C. IR (KBr): 3444, 3143, 2980, 1444, 1390, 1229, 1168, 1115, 1038, 966, 773 cm⁻¹; ¹H NMR (DMSO-dma, 500 MHz): δ = 9.43 (d, 2J_P-H = 26.5 Hz, 1H), 8.21 (d, J = 7.0 Hz, 1H), 7.97-7.83 (m, 3H), 7.70 (d, J = 16.0 Hz, 1H), 7.62-7.47 (m, 9H), 4.12-4.03 (m, 4H), 1.27 (t, J = 7.3 Hz, 6H); ¹³C NMR (DMSO-dma, 125 MHz): δ = 150.1 (d, 3J_P-C = 17.5 Hz), 137.7, 134.3, 133.3, 132.7, 130.7, 129.2, 128.7, 128.6, 128.5, 128.3, 126.8, 126.0, 125.6, 124.7, 122.6, 120.5, 62.4 (d, 2J_P-C = 6.3 Hz), 16.1 (d, 3J_P-C = 6.3 Hz); MS (EI) m/z: 408 (6) [M⁺], 256 (100); HRMS (ESI) m/z: Calcd for C₂₃H₂₆N₂O₃P [M+H]⁺: 409.1676, found: 409.1673.

Diethyl (2-(1-(naphthalen-2-yl)-3-phenylallylidene)hydrazinyl)phosphonate (1i):
Following the same procedure used for 1a with 1-(naphthalen-2-yl)-3-phenylprop-2-en-1-one (1.29 g, 5.0 mmol) and phosphorohydrazidic acid diethyl ester (1.26 g, 7.5 mmol) in EtOH (20 mL). The crude product was purified by column chromatography on silica gel (petroleum ether/EtOAc = 2/1) to yield 1i (1.72 g, 84%) as a colorless solid. M.p. 144-146 °C. IR (KBr): 3142, 2978, 2866, 1624, 1545, 1438, 1236, 1100, 1037, 974, 815, 764 cm⁻¹; ¹H NMR (DMSO-dma, 500 MHz): δ = 9.41 (d, 2J_P-H = 26.8 Hz, 1H), 7.99-7.94 (m, 4H), 7.75-7.69 (m, 3H), 7.65 (d, J = 8.5 Hz, 1H), 7.55-7.53 (m, 2H), 7.39 (t, J = 7.4 Hz, 2H), 7.34 (t, J = 7.1 Hz, 1H), 6.79 (d, J = 16.2 Hz, 1H), 4.13-4.05 (m, 4H), 1.28 (t, J = 7.0 Hz, 6H); ¹³C NMR (DMSO-dma, 125 MHz): δ = 149.6 (d, 3J_P-C = 18.8 Hz), 138.2, 136.1, 135.0, 132.9, 132.6, 129.0, 128.6, 128.3, 127.9, 127.7, 127.6, 127.5, 126.5, 126.4, 126.3, 118.1, 62.4 (d, 2J_P-C = 5.0 Hz), 16.1 (d, 3J_P-C = 6.3 Hz). MS (EI) m/z: 408 (7) [M⁺], 271 (14), 255 (100); HRMS (ESI) m/z: Calcd for C₂₃H₂₆N₂O₃P [M+H]⁺: 409.1676, found: 409.1673.
Diethyl (2-(1-(furan-2-yl)-3-phenylallylidene)hydrazinyl)phosphonate (1j):
Following the same procedure used for 1a with 1-(furan-2-yl)-3-phenylprop-2-en-1-one (0.99 g, 5.0 mmol) and phosphorohydrazidic acid diethyl ester (1.26 g, 7.5 mmol) in EtOH (20 mL). The crude product was purified by column chromatography on silica gel (petroleum ether/EtOAc = 1/1) to yield 1j (1.36 g, 78%) as a colorless solid. M.p. 137-139 °C. IR (KBr): 3160, 2985, 1621, 1540, 1495, 1436, 1394, 1318, 1235, 1037, 972, 763 cm⁻¹; ¹H NMR (DMSO-d₆, 500 MHz): δ = 9.35 (d, J₂P-H = 26.8 Hz, 1H), 7.77-7.71 (m, 3H), 7.48 (d, J = 16.2 Hz, 1H), 7.41 (t, J = 7.4 Hz, 2H), 7.35 (t, J = 7.2 Hz, 1H), 7.07 (d, J = 16.2 Hz, 1H), 6.65 (d, J = 3.4 Hz, 1H), 6.59-6.58 (m, 1H), 4.11-4.01 (m, 4H), 1.26 (t, J = 7.1 Hz, 6H); ¹³C NMR (DMSO-d₆, 125 MHz): δ = 150.6, 143.4, 140.5 (d, J₃P-C = 18.8 Hz), 137.4, 136.0, 129.1, 128.6, 127.7, 116.6, 111.3, 110.4, 62.5 (d, J₂P-C = 5.0 Hz), 16.0 (d, J₃P-C = 6.3 Hz); MS (EI) m/z: 348 (8) [M+], 196 (100), 195 (90), 152 (30); HRMS (ESI) m/z: Calcd for C₁₇H₂₂N₂O₄P [M+H]+: 349.1312, found: 349.1313.

Diethyl (2-(3-phenyl-1-(pyridin-3-yl)allylidene)hydrazinyl)phosphonate (1k):
Following the same procedure used for 1a with 3-phenyl-1-(pyridin-3-yl)prop-2-en-1-one (1.05 g, 5.0 mmol) and phosphorohydrazidic acid diethyl ester (1.26 g, 7.5 mmol) in EtOH (20 mL). The crude product was purified by column chromatography on silica gel (petroleum ether/EtOAc = 1/2) to yield 1k (1.28 g, 71%) as a colorless solid. M.p. 195-197 °C. IR (KBr): 3184, 2979, 1712, 1621, 1581, 1442, 1328, 1242, 1040, 974, 804, 752 cm⁻¹; ¹H NMR (DMSO-d₆, 500 MHz): δ = 9.53 (d, J₂P-H = 26.9 Hz, 1H), 8.64-8.61 (m, 2H), 7.84 (d, J = 7.9 Hz, 1H), 7.47 (dd, J = 7.8 Hz, 4.8 Hz, 1H), 7.39 (t, J = 7.3 Hz, 2H), 7.34 (t, J = 7.2 Hz, 1H), 6.71 (d, J = 16.2 Hz, 1H), 4.11-4.01 (m, 4H), 1.25 (t, J = 7.1 Hz, 6H); ¹³C NMR (DMSO-d₆, 125 MHz): δ = 149.4, 149.3, 147.2 (d, J₃P-C = 18.8 Hz), 138.0, 136.2, 135.9, 133.3, 129.1, 128.6, 127.8, 123.4, 117.6, 62.4 (d, J₂P-C = 5.0 Hz), 16.1 (d, J₃P-C = 6.3 Hz); MS (EI) m/z: 359 (3) [M⁺], 222 (14), 207 (100); HRMS (ESI) m/z: Calcd for C₁₈H₂₃N₃O₃P [M+H]+: 360.1472, found: 360.1481.

Diethyl (2-(1,5-diphenylpenta-1,4-dien-3-ylidene)hydrazinyl)phosphonate (1l):
Following the same procedure used for 1a with 1,5-diphenylpenta-1,4-dien-3-one (1.17 g, 5.0 mmol) and phosphorohydrazidic acid diethyl ester (1.26 g, 7.5 mmol) in EtOH (20 mL). The crude product was purified by column chromatography on silica gel (petroleum ether/EtOAc = 2/1) to yield 1l (1.65 g, 86%) as a colorless solid. M.p. 112-114 °C. IR (KBr): 3166, 3022, 2979, 1625, 1540, 1492, 1440, 1333, 1236, 1093,
1032, 980, 801, 754 cm\(^{-1}\); \(^1\)H NMR (DMSO-\(d_6\), 500 MHz): \(\delta = 9.20\) (d, \(^2\)\(J_{P-H} = 27.0\) Hz, 1H), 7.76 (d, \(J = 7.4\) Hz, 2H), 7.62 (d, \(J = 7.4\) Hz, 2H), 7.44-7.35 (m, 6H), 7.29 (t, \(J = 7.3\) Hz, 1H), 7.17 (d, \(J = 16.4\) Hz, 1H), 7.12 (d, \(J = 16.1\) Hz, 1H), 7.03 (d, \(J = 16.1\) Hz, 1H), 4.12-4.02 (m, 4H), 1.27 (t, \(J = 7.1\) Hz, 6H); \(^{13}\)C NMR (DMSO-\(d_6\), 125 MHz): \(\delta = 147.0\) (d, \(^3\)\(J_{P-C} = 18.8\) Hz), 136.5, 136.3, 132.1, 128.8, 128.7, 128.6, 128.1, 127.6, 126.9, 125.1, 117.5, 62.4 (d, \(^2\)\(J_{P-C} = 5.0\) Hz), 16.1 (d, \(^3\)\(J_{P-C} = 6.3\) Hz); MS (EI) m/z: 384 (5) [M\(^+\)], 233 (33), 230 (100), 103 (25), 91 (20); HRMS (ESI) m/z: Calcd for C\(_{21}\)H\(_{26}\)N\(_2\)O\(_3\)P [M+H\(^+\)\(^+\)]: 385.1676, found: 385.1672.

Diisopropyl (2-(1,3-diphenylallylidene)hydrazinyl)phosphonate (1a’): Following the same procedure used for 1a with chalcone (1.04 g, 5.0 mmol) and phosphorohydrazidic acid diisopropyl ester (1.47 g, 7.5 mmol) in EtOH (20 mL). The crude product was purified by column chromatography on silica gel (petroleum ether/EtOAc = 2/1) to yield 1a’ (1.58 g, 82%) as a colorless solid. M.p. 172-174 °C. IR (KBr): 3176, 2979, 1617, 1443, 1328, 1256, 1213, 1011, 763 cm\(^{-1}\); \(^1\)H NMR (DMSO-\(d_6\), 500 MHz): \(\delta = 9.27\) (d, \(^2\)\(J_{P-H} = 26.7\) Hz, 1H), 7.69-7.65 (m, 3H), 7.45-7.33 (m, 8H), 6.67 (d, \(J = 16.1\) Hz, 1H), 4.61-4.53 (m, 2H), 1.27 (d, \(J = 6.2\) Hz, 6H), 1.24 (d, \(J = 6.2\) Hz, 6H); \(^{13}\)C NMR (DMSO-\(d_6\), 125 MHz): \(\delta = 149.3\) (d, \(^3\)\(J_{P-C} = 18.8\) Hz), 137.8, 137.7, 136.0, 129.0, 128.6, 128.5, 128.4, 128.2, 127.6, 118.0, 70.6 (d, \(^2\)\(J_{P-C} = 5.0\) Hz), 23.6 (d, \(^3\)\(J_{P-C} = 5.0\) Hz), 23.4 (d, \(^3\)\(J_{P-C} = 5.0\) Hz); MS (EI) m/z: 386 (7) [M\(^+\)], 206 (100); HRMS (ESI) m/z: Calcd for C\(_{21}\)H\(_{28}\)N\(_2\)O\(_3\)P [M+H\(^+\)\(^+\)]: 387.1832, found: 387.1830.

Dimethyl (2-(1,3-diphenylallylidene)hydrazinyl)phosphonate (1a’’): Following the same procedure used for 1a with chalcone (1.04 g, 5.0 mmol) and phosphorohydrazidic acid dimethyl ester (1.05 g, 7.5 mmol) in EtOH (20 mL). The crude product was purified by column chromatography on silica gel (petroleum ether/EtOAc = 2/1) to yield 1a’’ (1.42 g, 86%) as a colorless solid. M.p. 172-174 °C. IR (KBr): 3154, 3016, 1621, 1442, 1328, 1256, 1213, 1011, 763 cm\(^{-1}\); \(^1\)H NMR (DMSO-\(d_6\), 500 MHz): \(\delta = 9.41\) (d, \(^2\)\(J_{P-H} = 26.8\) Hz, 1H), 7.69-7.64 (m, 3H), 7.47-7.42 (m, 5H), 7.39 (t, \(J = 7.3\) Hz, 2H), 7.34 (t, \(J = 7.2\) Hz, 1H), 6.70 (d, \(J = 16.1\) Hz, 1H), 3.70 (d, \(^3\)\(J_{P-H} = 11.2\) Hz, 6H); \(^{13}\)C NMR (DMSO-\(d_6\), 125 MHz): \(\delta = 150.2\) (d, \(^3\)\(J_{P-C} = 17.5\) Hz), 138.1, 137.4, 136.0, 129.0, 128.7, 128.6, 128.5, 128.2, 127.7, 117.9, 53.3 (d, \(^2\)\(J_{P-C} = 5.0\) Hz); MS (EI) m/z: 330 (15) [M\(^+\)], 206 (100); HRMS (ESI) m/z: Calcd for C\(_{17}\)H\(_{20}\)N\(_2\)O\(_3\)P [M+H\(^+\)\(^+\)]: 331.1206, found: 331.1198.
3. Synthesis and Characterization for Pyrazoles

3.5-Diphenyl-1H-pyrazol-4-yl acetate (3aa)\(^1\): A mixture of compound 1a (107.5 mg, 0.3 mmol), CuCl\(_2\) (4.0 mg, 0.03 mmol), HOAc (21.6 mg, 0.36 mmol), K\(_2\)CO\(_3\) (49.8 mg, 0.36 mmol) and H\(_2\)O (50 \(\mu\)L) in DMSO (1.5 mL) was stirred at 50 °C for 5 h under oxygen atmosphere. The reaction was cooled to room temperature after complete consumption of 1a as monitored by TLC analysis. Upon completion, the reaction was diluted by EtOAc (10 mL) and H\(_2\)O (30 mL). The aqueous layer was extracted with EtOAc (3\(\times\)10 mL) and the combined organic layer was dried over Na\(_2\)SO\(_4\), then filtered and concentrated in vacuo. The given residue was purified by column chromatography on silica gel (petroleum ether/EtOAc = 7/1) to give 3aa (57.6 mg, 69%) as a white solid. M.p. 188-190 °C. IR (KBr): 3422, 3227, 1761, 1492, 1448, 1370, 1197, 1145, 955, 760, 693 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\), 500 MHz): \(\delta\) = 9.19 (br, NH), 7.60-7.59 (m, 4H), 7.36-7.32 (m, 6H), 2.28 (s, 3H); \(^{13}\)C NMR (CDCl\(_3\), 125 MHz): \(\delta\) = 169.2, 139.6, 129.7, 129.0, 128.9, 128.6, 126.4, 20.9; MS (EI) m/z: 278 (10) [M\(^+\)], 237 (18), 236 (100).

3-(3-Methoxyphenyl)-5-phenyl-1H-pyrazol-4-yl acetate (3ba): Following the same procedure used for 3aa with compound 1b (116.5 mg, 0.3 mmol), CuCl\(_2\) (4.0 mg, 0.03 mmol), HOAc (21.6 mg, 0.36 mmol), K\(_2\)CO\(_3\) (49.8 mg, 0.36 mmol) and H\(_2\)O (50 \(\mu\)L) in DMSO (1.5 mL). After 6 h at 50 °C, purification by column chromatography on silica gel (petroleum ether/EtOAc = 5/1) to yield 3ba (64.6 mg, 70%) as a yellow oil. IR (KBr): 3321, 2933, 1762, 1709, 1594, 1465, 1368, 1270, 1195, 1036, 971 cm\(^{-1}\); \(^1\)H NMR (DMSO-\(d_6\), 500 MHz): \(\delta\) = 7.70 (d, \(J = 7.5\) Hz, 2H), 7.48 (t, \(J = 7.5\) Hz, 2H), 7.41-7.26 (m, 4H), 6.96 (d, \(J = 6.7\) Hz, 1H), 3.81 (s, 3H), 2.36 (s, 3H); \(^{13}\)C NMR (DMSO-\(d_6\), 125 MHz): \(\delta\) = 169.2, 159.6, 141.6, 130.2, 129.0, 128.8, 128.4, 128.1, 125.5, 125.1, 117.8, 113.9, 110.8, 110.5, 55.1, 20.6; MS (MALDI/DHB) m/z: 309 (100) [M\(^+\)]; HRMS (MALDI/DHB) m/z: Calcd for C\(_{18}\)H\(_{17}\)N\(_2\)O\(_3\) [M+H]\(^+\): 309.1234, found: 309.1234.

3-(3-Chlorophenyl)-5-phenyl-1H-pyrazol-4-yl acetate (3ca): Following the same procedure used for 3aa with compound 1c (117.8 mg, 0.3 mmol), CuCl\(_2\) (4.0 mg, 0.03 mmol), HOAc (21.6 mg, 0.36 mmol), K\(_2\)CO\(_3\) (49.8 mg, 0.36 mmol) and H\(_2\)O (50 \(\mu\)L) in DMSO (1.5 mL). After 4 h at 50 °C, purification by column chromatography on silica gel (petroleum ether/EtOAc = 7/1) to yield 3da (62.8 mg, 67%) as a white solid.
M.p. 163-165 °C. IR (KBr): 3240, 3079, 2924, 1760, 1590, 1371, 1204, 1150, 1006, 961, 890, 764, 692 cm⁻¹; ¹H NMR (CDCl₃, 500 MHz): δ = 11.00 (br, NH), 7.61 (s, 1H), 7.55 (d, J = 7.8 Hz, 2H), 7.48 (d, J = 7.2 Hz, 1H), 7.38-7.33 (m, 3H), 7.29-7.22 (m, 2H), 2.30 (s, 3H); ¹³C NMR (CDCl₃, 125 MHz): δ = 168.9, 139.9, 138.4, 134.8, 131.9, 130.2, 129.1, 128.9, 128.7, 128.6, 126.5, 126.3, 124.5, 20.9; MS (MALDI/DHB) m/z: 315 (33) [M⁺H (³⁵Cl)], 313 (100) [M⁺H (³⁷Cl)]; HRMS (ESI) m/z: (MALDI/DHB) m/z: Calcd for C₁₇H₁₄N₂O₂Cl [M⁺H]⁺: 313.0738, found: 313.0738.

3-(4-Methoxyphenyl)-5-phenyl-1H-pyrazol-4-yl acetate (3da): Following the same procedure used for 3aa with compound 1d (116.5 mg, 0.3 mmol), CuCl₂ (4.0 mg, 0.03 mmol), HOAc (21.6 mg, 0.36 mmol), K₂CO₃ (49.8 mg, 0.36 mmol) and H₂O (50 μL) in DMSO (1.5 mL). After 4 h at 50 °C, purification by column chromatography on silica gel (petroleum ether/EtOAc = 5/1) to yield 3da (55.5 mg, 60%) as a white solid. M.p. 174-176 °C. IR (KBr): 3228, 2861, 1759, 1615, 1537, 1511, 1368, 1251, 1030, 958, 834, 696 cm⁻¹; ¹H NMR (CDCl₃, 500 MHz): δ = 11.11 (br, NH), 7.59 (d, J = 6.6 Hz, 2H), 7.50 (d, J = 8.8 Hz, 2H), 7.36-7.29 (m, 3H), 3.80 (s, 3H), 2.27 (s, 3H); ¹³C NMR (CDCl₃, 125 MHz): δ = 169.2, 159.9, 139.8, 139.2, 129.8, 128.9, 128.5, 128.4, 127.8, 126.5, 121.9, 114.4, 55.4, 20.9; MS (MALDI/DHB) m/z: 309 [M⁺H]; HRMS (MALDI/DHB) m/z: (ESI) m/z: Calcd for C₁₈H₁₇N₂O₃ [M⁺H]⁺: 309.1234, found: 309.1234.

3-(4-Bromophenyl)-5-phenyl-1H-pyrazol-4-yl acetate (3ea): Following the same procedure used for 3aa with compound 1e (131.2 mg, 0.3 mmol), CuCl₂ (4.0 mg, 0.03 mmol), HOAc (21.6 mg, 0.36 mmol), K₂CO₃ (49.8 mg, 0.36 mmol) and H₂O (50 μL) in DMSO (1.5 mL). After 5 h at 50 °C, purification by column chromatography on silica gel (petroleum ether/EtOAc = 7/1) to yield 3da (70.7 mg, 66%) as a white solid. M.p. 239-241 °C. IR (KBr): 3220, 1775, 1753, 1491, 1450, 1369, 1193, 1149, 958, 884, 824, 760, 683 cm⁻¹; H NMR (DMSO-d₆, 500 MHz): δ = 13.59-13.57 (m, NH), 7.73 (d, J = 8.4 Hz, 1.5H), 7.68 (d, J = 8.5 Hz, 1.3H), 7.65 (d, J = 8.2 Hz), 7.60 (d, J = 8.3 Hz, 0.8H), 7.51 (t, J = 7.7 Hz, 1.3H), 7.45 (t, J = 7.6 Hz, 0.8H), 7.41 (t, J = 7.4 Hz, 0.6H), 7.35 (t, J = 7.3 Hz, 0.4H), 2.37 (s, 3H); ¹³C NMR (DMSO-d₆, 125 MHz): δ = 169.1, 142.4, 141.3, 133.5, 132.3, 132.2, 131.8, 131.2, 129.2, 128.8, 128.5, 128.3, 128.2, 127.8, 127.6, 127.5, 127.3, 125.6, 125.4, 121.6, 120.9, 20.6; MS (MALDI/DHB) m/z: 359 (98) [M⁺H (¹⁸Br)], 357 (100) [M⁺H (²³Br)]; HRMS (MALDI/DHB) m/z: Calcd for C₁₇H₁₄N₂O₃Br [M⁺H]⁺: 357.0233, found: 357.0233.
5-(2-Bromophenyl)-3-phenyl-1H-pyrazol-4-yl acetate (3fa): Following the same procedure used for 3aa with compound 1f (131.2 mg, 0.3 mmol), CuCl₂ (4.0 mg, 0.03 mmol), HOAc (21.6 mg, 0.36 mmol), K₂CO₃ (49.8 mg, 0.36 mmol) and H₂O (50 μL) in DMSO (1.5 mL). After 8 h at 50 °C, purification by column chromatography on silica gel (petroleum ether/EtOAc = 7/1) to yield 3fa (65.6 mg, 61%) as a yellow oil. IR (KBr): 3219, 3070, 2927, 1767, 1607, 1442, 1367, 1251, 1190, 1145, 1019, 883, 760 cm⁻¹; ^1H NMR (DMSO-d₆, 500 MHz): δ = 13.59-13.34 (m, NH), 7.74-7.37 (m, 9H), 2.19 (s, 3H); ^13C NMR (DMSO-d₆, 125 MHz): δ = 168.6, 143.5, 133.0, 132.3, 131.8, 129.0, 128.8, 128.3, 127.7, 125.5, 122.6, 20.4; MS (EI) m/z: 358 (4) [M + (81Br)], 356 (5) [M + (79Br)], 104 (100); HRMS (ESI) m/z: Calcd for C₁₇H₁₄N₂O₂Br [M+H]^+: 357.0233, found: 357.0223.

3,5-bis(4-Bromophenyl)-1H-pyrazol-4-yl acetate (3ga): Following the same procedure used for 3aa with compound 1g (154.9 mg, 0.3 mmol), CuCl₂ (4.0 mg, 0.03 mmol), HOAc (21.6 mg, 0.36 mmol), K₂CO₃ (49.8 mg, 0.36 mmol) and H₂O (50 μL) in DMSO (1.5 mL). After 4 h at 50 °C, purification by column chromatography on silica gel (petroleum ether/EtOAc = 7/1) to yield 3ga (61.5 mg, 47%) as a white solid. M.p. 245-247 °C. IR (KBr): 3220, 1776, 1759, 1702, 1486, 1372, 1197, 1147, 1010, 956, 825, 746 cm⁻¹; ^1H NMR (DMSO-d₆, 500 MHz): δ = 13.66 (br, NH), 7.72-7.59 (m, 8H), 2.37 (s, 3H); ^13C NMR (DMSO-d₆, 125 MHz): δ = 169.0, 141.4, 132.2, 131.8, 128.4, 127.6, 127.4, 20.6; MS (MALDI/DHB) m/z: 439 (50) [M +H (2×^{81}Br)], 437 (100) [M +H (^{81}Br, {^{79}Br})], 435 (50) [M +H (2×^{79}Br)]; HRMS (MALDI/DHB) m/z: Calcd for C₁₇H₁₃N₂O₂Br₂ [M+H]^+: 434.9338, found: 434.9338.

5-(Naphthalen-1-yl)-3-phenyl-1H-pyrazol-4-yl acetate (3ha): Following the same procedure used for 3aa with compound 1h (122.5 mg, 0.3 mmol), CuCl₂ (4.0 mg, 0.03 mmol), HOAc (21.6 mg, 0.36 mmol), K₂CO₃ (49.8 mg, 0.36 mmol) and H₂O (50 μL) in DMSO (1.5 mL). After 4 h at 50 °C, purification by column chromatography on silica gel (petroleum ether/EtOAc = 7/1) to yield 3ha (62.2 mg, 63%) as a colorless oil. IR (KBr): 3241, 2919, 1764, 1709, 1446, 1367, 1199, 1100, 1010, 988, 776 cm⁻¹; ^1H NMR (DMSO-d₆, 500 MHz): δ = 13.75-13.35 (m, NH), 8.32-7.71 (m, 5H), 7.64-7.37 (m, 7H), 2.14-2.01 (m, 3H); ^13C NMR (DMSO-d₆, 125 MHz): δ = 168.8, 133.3, 132.6, 132.2, 131.0, 129.4, 129.2, 128.8, 128.4, 128.2, 127.8, 126.9, 126.4, 126.2, 126.0, 125.7, 125.4, 125.1, 20.3; MS (MALDI/DHB) m/z: 329 (100)
3-(Naphthalen-2-yl)-5-phenyl-1H-pyrazol-4-yl acetate (3ia): Following the same procedure used for 3aa with compound 1i (122.5 mg, 0.3 mmol), CuCl₂ (4.0 mg, 0.03 mmol), HOAc (21.6 mg, 0.36 mmol), K₂CO₃ (49.8 mg, 0.36 mmol) and H₂O (50 μL) in DMSO (1.5 mL). After 4 h at 50 °C, purification by column chromatography on silica gel (petroleum ether/EtOAc = 7/1) to yield 3ia (63.9 mg, 65%) as a white solid. M.p. 206-208 °C. IR (KBr): 3430, 3244, 3056, 1766, 1636, 1447, 1364, 1192, 1135, 754 cm⁻¹; ¹H NMR (DMSO-d₆, 500 MHz): δ = 13.65-13.59 (m, NH), 8.22-7.69 (m, 7H), 7.57-7.36 (m, 5H), 2.43 (s, 3H); ¹³C NMR (DMSO-d₆, 125 MHz): δ = 169.3, 142.4, 142.2, 133.5, 133.4, 133.1, 132.4, 132.0, 129.6, 129.2, 128.9, 128.5, 128.2, 127.8, 127.6, 127.5, 126.9, 126.8, 126.4, 126.2, 125.6, 125.4, 124.3, 124.1, 123.9, 123.1, 20.6; MS (EI) m/z: 328 (13) [M⁺], 286 (100); HRMS (ESI) m/z: Calcd for C₂₁H₁₇N₂O₂ [M+H]+: 329.1285, found: 329.1274.

3-(Furan-2-yl)-5-phenyl-1H-pyrazol-4-yl acetate (3ja): Following the same procedure used for 3aa with compound 1j (104.5 mg, 0.3 mmol), CuCl₂ (4.0 mg, 0.03 mmol), HOAc (21.6 mg, 0.36 mmol), K₂CO₃ (49.8 mg, 0.36 mmol) and H₂O (50 μL) in DMSO (1.5 mL). After 6 h at 50 °C, purification by column chromatography on silica gel (petroleum ether/EtOAc = 7/1) to yield 3ja (44.4 mg, 55%) as a gray solid. M.p. 152-155 °C. IR (KBr): 3221, 2928, 1764, 1710, 1631, 1452, 1368, 1195, 1008, 892, 737 cm⁻¹; ¹H NMR (DMSO-d₆, 500 MHz): δ = 7.78 (s, 1H), 7.69 (d, J = 7.4 Hz, 2H), 7.48 (t, J = 7.7 Hz, 2H), 7.38 (t, J = 7.3 Hz, 1H), 6.69 (s, 1H), 6.61 (s, 1H), 2.40 (s, 3H); ¹³C NMR (DMSO-d₆, 125 MHz): δ = 169.2, 142.9, 129.3, 129.1, 128.6, 128.3, 127.8, 127.3, 125.5, 111.6, 106.9, 20.5; MS (EI) m/z: 268 (8) [M⁺], 105 (100); HRMS (ESI) m/z: Calcd for C₁₅H₁₃N₂O₃ [M+H]+: 269.0921, found: 269.0909.

5-Phenyl-3-(pyridin-3-yl)-1H-pyrazol-4-yl acetate (3ka): Following the same procedure used for 3aa with compound 1k (107.8 mg, 0.3 mmol), CuCl₂ (4.0 mg, 0.03 mmol), HOAc (21.6 mg, 0.36 mmol), K₂CO₃ (49.8 mg, 0.36 mmol) and H₂O (50 μL) in DMSO (1.5 mL). After 6 h at 50 °C, purification by column chromatography on silica gel (petroleum ether/EtOAc = 5/1) to yield 3ka (43.5 mg, 52%) as a white solid. M.p. 153-155 °C. IR (KBr): 3433, 3038, 2817, 1752, 1644, 1380, 1209, 1021, 947, 701 cm⁻¹; ¹H NMR (DMSO-d₆, 500 MHz): δ = 13.69 (br, NH), 8.91-7.39 (m, 9H), 2.38 (s, 3H); ¹³C NMR (DMSO-d₆, 125 MHz): δ = 169.2, 149.0, 146.4, 132.9, 129.2, 128.7, 125.6, 125.2, 124.9, 124.1, 20.6; MS (EI) m/z: 279 (27) [M⁺], 105 (100);
5-Phenyl-3-styryl-1H-pyrazol-4-yl acetate (3la): Following the same procedure used for 3aa with compound 1l (115.3 mg, 0.3 mmol), CuCl₂ (4.0 mg, 0.03 mmol), HOAc (21.6 mg, 0.36 mmol), K₂CO₃ (49.8 mg, 0.36 mmol) and H₂O (50 µL) in DMSO (1.5 mL). After 8 h at 50 °C, purification by column chromatography on silica gel (petroleum ether/EtOAc = 7/1) to yield 3la (42.9 mg, 47%) as a red solid. M.p. 138-142 °C. IR (KBr): 3247, 3030, 2925, 1757, 1595, 1446, 1370, 1204, 1016, 952, 751 cm⁻¹; ¹H NMR (DMSO-d₆, 500 MHz): δ = 13.33 (br, NH), 7.69 (d, J = 7.1 Hz, 2H), 7.60 (d, J = 7.4 Hz, 2H), 7.46 (t, J = 7.5 Hz, 2H), 7.40 (m, 3H), 7.30 (t, J = 7.4 Hz, 1H), 7.16 (d, J = 16.7 Hz, 1H), 6.98 (d, J = 16.6 Hz, 1H), 2.42 (s, 3H); ¹³C NMR (DMSO-d₆, 125 MHz): δ = 169.2, 139.2, 136.4, 129.3, 129.2, 129.1, 128.9, 128.8, 128.7, 128.1, 126.5, 126.3, 125.4, 125.1, 20.6; MS (EI) m/z: 304 (32) [M⁺], 262 (100); HRMS (ESI) m/z: Calcd for C₁₉H₁₇N₂O₂ [M+H]⁺: 305.1285, found: 305.1279.

3,5-Diphenyl-1H-pyrazol-4-yl butyrate (3ab): Following the same procedure used for 3aa with compound 1a (107.5 mg, 0.3 mmol), CuCl₂ (4.0 mg, 0.03 mmol), n-butyric acid (31.7 mg, 0.36 mmol), K₂CO₃ (49.8 mg, 0.36 mmol) and H₂O (50 µL) in DMSO (1.5 mL). After 4 h at 50 °C, purification by column chromatography on silica gel (petroleum ether/EtOAc = 7/1) to yield 3ab (60.7 mg, 66%) as a pale yellow solid. M.p. 110-113 °C. IR (KBr): 3234, 2961, 1765, 1589, 1459, 1439, 1262, 1148, 957, 767 cm⁻¹; ¹H NMR (DMSO-d₆, 500 MHz): δ = 7.69 (d, J = 7.3 Hz, 4H), 7.47 (t, J = 7.4 Hz, 3H), 7.37 (t, J = 7.4 Hz, 2H), 2.65 (t, J = 7.2 Hz, 2H), 1.63 (m, 2H), 0.88 (t, J = 7.4 Hz, 3H); ¹³C NMR (DMSO-d₆, 125 MHz): δ = 171.6, 140.0, 128.9, 128.8, 128.3, 128.1, 125.6, 125.1, 35.2, 17.8, 13.4; MS (MALDI/DHB) m/z: 307 (100) [M⁺H]; HRMS (MALDI/DHB) m/z: Calcd for C₁₉H₁₉N₂O₂ [M+H]⁺: 307.1441, found: 307.1441.

3,5-Diphenyl-1H-pyrazol-4-yl pivalate (3ac): Following the same procedure used for 3aa with compound 1a (107.5 mg, 0.3 mmol), CuCl₂ (4.0 mg, 0.03 mmol), pivalic acid (36.8 mg, 0.36 mmol), K₂CO₃ (49.8 mg, 0.36 mmol) and H₂O (50 µL) in DMSO (1.5 mL). After 10 h at 50 °C, purification by column chromatography on silica gel (petroleum ether/EtOAc = 7/1) to yield 3ac (54.8 mg, 57%) as a white solid. M.p.
213-215 °C; IR (KBr): 3371, 2969, 1753, 1589, 1477, 1256, 1110, 958, 771, 707, 693 cm⁻¹; ¹H NMR (CDCl₃, 500 MHz): δ = 10.81-10.37 (m, 1H), 7.60 (d, J = 6.7 Hz), 7.37-7.31 (m, 6H), 1.32 (s, 9H); ¹³C NMR (CDCl₃, 125 MHz): δ = 176.2, 139.8, 129.6, 129.1, 128.8, 128.6, 126.8, 39.0, 27.3; MS (MALDI/DHB) m/z: 321 (100) [M⁺H]; HRMS (MALDI/DHB) m/z: Calcd for C₂₀H₂₁N₂O₂ [M+H]+: 321.1598, found: 321.1598.

3,5-Diphenyl-1H-pyrazol-4-yl cyclohexanecarboxylate (3ad): Following the same procedure used for 3aa with compound 1a (107.5 mg, 0.3 mmol), CuCl₂ (4.0 mg, 0.03 mmol), cyclohexanecarboxylic acid (46.2 mg, 0.36 mmol), K₂CO₃ (49.8 mg, 0.36 mmol) and H₂O (50 µL) in DMSO (1.5 mL). After 3 h at 50 °C, purification by column chromatography on silica gel (petroleum ether/EtOAc = 7/1) to yield 3ad (61.2 mg, 59%) as a white solid. M.p. 201-203 °C; IR (KBr): 3217, 2929, 2856, 2348, 1755, 1590, 1490, 1446, 1244, 1149, 956, 764, 691 cm⁻¹; ¹H NMR (CDCl₃, 500 MHz): δ = 11.03-10.73 (br, 1H), 7.60 (d, J = 7.1 Hz, 4H), 7.38-7.31 (m, 6H), 2.61-2.50 (m, 1H), 2.01 (d, J = 11.2 Hz, 2H), 1.83-1.76 (m, 2H), 1.68 (d, J = 12.0 Hz, 1H), 1.57-1.49 (m, 2H), 1.40-1.23 (m, 3H); ¹³C NMR (CDCl₃, 125 MHz): δ = 173.9, 139.7, 129.7, 128.9, 128.6, 126.6, 43.2, 29.0, 25.7, 25.5; MS (MALDI/DHB) m/z: 347 (100) [M⁺H]; HRMS (MALDI/DHB) m/z: Calcd for C₂₂H₂₃N₂O₂ [M+H]+: 347.1754, found: 347.1754.

3,5-Diphenyl-1H-pyrazol-4-yl acetylprolinate (3ae): Following the same procedure used for 3aa with compound 1a (107.5 mg, 0.3 mmol), CuCl₂ (4.0 mg, 0.03 mmol), acetylproline (56.6 mg, 0.36 mmol), K₂CO₃ (49.8 mg, 0.36 mmol) and H₂O (50 µL) in DMSO (1.5 mL). After 5 h at 50 °C, purification by column chromatography on silica gel (petroleum ether/EtOAc = 2/1) to yield 3ae (67.5 mg, 60%) as a yellow oil. IR (KBr): 3395, 3036, 2926, 1771, 1623, 1448, 1363, 1248, 1140, 1027, 767 cm⁻¹; ¹H NMR (CDCl₃, 500 MHz): δ = 7.73 (d, J = 7.3 Hz, 4H), 7.46 (t, J = 7.6 Hz, 4H), 7.38 (t, J = 7.4 Hz, 2H), 4.67 (dd, J = 8.7, 3.8 Hz, 1H), 3.57-3.52 (m, 2H), 2.33-2.28 (m, 1H), 2.02 (s, 3H), 1.92-1.84 (m, 3H); ¹³C NMR (CDCl₃, 125 MHz): δ = 170.8, 168.7, 140.5, 128.9, 128.8, 128.2, 127.9, 126.1, 58.0, 47.3, 28.9, 24.5, 22.0; MS (ESI) m/z: 376 (100) [M⁺H]; HRMS (ESI) m/z: Calcd for C₂₂H₂₃N₃O₃ [M+H]+: 376.1656, found: 376.1652.
3,5-Diphenyl-1H-pyrazol-4-yl benzoate (3af): Following the same procedure used for 3aa with compound 1a (107.5 mg, 0.3 mmol), CuCl2 (4.0 mg, 0.03 mmol), benzoic acid (44.0 mg, 0.36 mmol), K2CO3 (49.8 mg, 0.36 mmol) and H2O (50 µL) in DMSO (1.5 mL). After 5 h at 50 °C, purification by column chromatography on silica gel (petroleum ether/EtOAc = 7/1) to yield 3af (56.2 mg, 55%) as a white solid. M.p. 233-235 oC. IR (KBr): 3434, 3220, 3057, 1743, 1593, 1492, 1449, 1246, 1148, 1060, 957, 765, 699 cm⁻¹; ¹H NMR (DMSO-d6, 500 MHz): δ = 13.63 (br, NH), 8.22-8.20 (m, 2H), 7.80-7.66 (m, 5H), 7.64 (t, J = 7.9 Hz, 2H), 7.46-7.28 (m, 6H); ¹³C NMR (DMSO-d6, 125 MHz): δ = 164.4, 142.5, 134.6, 133.7, 132.0, 129.9, 129.3, 129.2, 128.7, 128.5, 128.2, 128.0, 127.8, 127.7, 125.6, 125.4; MS (EI) m/z: 340 (18) [M⁺], 105 (100).

3,5-Diphenyl-1H-pyrazol-4-yl 2-methylbenzoate (3ag): Following the same procedure used for 3aa with compound 1a (107.5 mg, 0.3 mmol), CuCl2 (4.0 mg, 0.03 mmol), 2-methylbenzoic acid (49.0 mg, 0.36 mmol), K2CO3 (49.8 mg, 0.36 mmol) and H2O (50 µL) in DMSO (1.5 mL). After 3 h at 50 °C, purification by column chromatography on silica gel (petroleum ether/EtOAc = 7/1) to yield 3ag (62.7 mg, 59%) as a white solid. M.p. 288-290 °C; IR (KBr): 3212, 1744, 1607, 1589, 1485, 1256, 1182, 1150, 1082, 960, 769, 692 cm⁻¹; ¹H NMR (DMSO-d6, 500 MHz): δ = 13.64-13.56 (br, 1H), 8.03-7.98 (m, 2H), 7.73 (d, J = 7.4 Hz, 2H), 7.65 (d, J = 7.5 Hz, 2H), 7.60 (d, J = 7.7 Hz, 1H), 7.53 (t, J = 7.7 Hz, 1H), 7.45 (t, J = 7.4 Hz, 2H), 7.39-7.35 (m, 3H), 7.29 (t, J = 6.9 Hz, 1H), 2.42 (s, 3H); ¹³C NMR (DMSO-d6, 125 MHz): δ = 164.4, 142.5, 138.9, 135.2, 133.6, 131.9, 130.2, 129.2, 129.1, 128.7, 128.5, 128.2, 128.0, 127.8, 127.7, 127.1, 125.6, 125.4, 20.7; MS (MALDI/DHB) m/z: 355 (100) [M⁺H]; HRMS (MALDI/DHB) m/z: Calcd for C23H19N2O2 [M+H]+: 355.1441, found: 355.1441.

3,5-Diphenyl-1H-pyrazol-4-yl 3-methylbenzoate (3ah): Following the same procedure used for 3aa with compound 1a (107.5 mg, 0.3 mmol), CuCl2 (4.0 mg, 0.03 mmol), 3-methylbenzoic acid (49.0 mg, 0.36 mmol), K2CO3 (49.8 mg, 0.36 mmol)
and H₂O (50 μL) in DMSO (1.5 mL). After 4 h at 50 °C, purification by column chromatography on silica gel (petroleum ether/EtOAc = 7/1) to yield 3ah (59.5 mg, 56%) as a white solid. M.p. 206-209 °C. IR (KBr): 3225, 3037, 2927, 1740, 1595, 1487, 1447, 1229, 1143, 1033, 953, 730 cm⁻¹; ¹H NMR (DMSO-d₆, 500 MHz): δ = 8.24 (d, J = 7.5 Hz, 1H), 7.71 (d, J = 7.6 Hz, 4H), 7.60 (t, J = 7.1 Hz, 1H), 7.46-7.40 (m, 6H), 7.34 (t, J = 7.3 Hz, 2H), 2.43 (s, 3H); ¹³C NMR (DMSO-d₆, 125 MHz): δ = 164.8, 140.5, 133.4, 132.1, 130.7, 128.9, 128.2, 128.1, 127.4, 125.6, 125.5, 125.5, 21.1; MS (EI) m/z: 354 (6) [M +], 119 (100); HRMS (ESI) m/z: Calcd for C₂₃H₁₉N₂O₂ [M+H]+: 355.1441, found: 355.1434.

3,5-Diphenyl-1H-pyrazol-4-yl 4-methoxybenzoate (3ai): Following the same procedure used for 3aa with compound 1a (107.5 mg, 0.3 mmol), CuCl₂ (4.0 mg, 0.03 mmol), 4-methoxybenzoic acid (54.8 mg, 0.36 mmol), K₂CO₃ (49.8 mg, 0.36 mmol) and H₂O (50 μL) in DMSO (1.5 mL). After 4 h at 50 °C, purification by column chromatography on silica gel (petroleum ether/EtOAc = 5/1) to yield 3ai (53.3 mg, 48%) as a white solid. M.p. 226-228 °C. IR (KBr): 3223, 1739, 1604, 1509, 1243, 1168, 1058, 1021, 957, 763 cm⁻¹; ¹H NMR (CDCl₃, 500 MHz): δ = 9.66 (br, NH), 8.18 (d, J = 8.8 Hz, 2H), 7.68 (d, J = 7.2 Hz, 4H), 7.35-7.28 (m, 6H), 7.01 (d, J = 8.8 Hz, 2H), 3.90 (s, 3H); ¹³C NMR (CDCl₃, 125 MHz): δ = 164.4, 164.3, 139.8, 132.7, 129.8, 129.1, 129.0, 128.6, 126.4, 121.2, 114.2, 55.7; MS (ESI) m/z: 371 (100) [M+H]; HRMS (ESI) m/z: Calcd for C₂₃H₁₉N₂O₃ [M+H]+: 371.1390, found: 371.1390.

3,5-Diphenyl-1H-pyrazol-4-yl nicotinate (3aj): Following the same procedure used for 3aa with compound 1a (107.5 mg, 0.3 mmol), CuCl₂ (4.0 mg, 0.03 mmol), nicotinic acid (44.3 mg, 0.36 mmol), K₂CO₃ (49.8 mg, 0.36 mmol) and H₂O (50 μL) in DMSO (1.5 mL). After 27 h at 50 °C, purification by column chromatography on silica gel (petroleum ether/EtOAc = 3/1) to yield 3aj (45.1 mg, 44%) as a white solid. M.p. 173-175 °C. IR (KBr): 3442, 2922, 2855, 1744, 1594, 1456, 1264, 1154, 1082, 1029, 948, 695 cm⁻¹; ¹H NMR (DMSO-d₆, 500 MHz): δ = 13.65 (br, NH), 9.37 (s, 1H), 8.95-8.56 (m, 2H), 7.71-7.34 (m, 11H); ¹³C NMR (DMSO-d₆, 125 MHz): δ = 170.3, 163.5, 154.8, 150.7, 137.7, 129.2, 128.9, 127.9, 125.6, 124.4, 124.2; MS (EI) m/z: 341 (48) [M⁺], 106 (100); HRMS (ESI) m/z: Calcd for C₂₁H₁₆N₃O₂ [M+H]⁺: 342.1237, found: 342.1227.
3,5-Diphenyl-1H-pyrazol-4-yl cinnamate (3ak)\[^1\]: Following the same procedure used for 3aa with compound 1a (107.5 mg, 0.3 mmol), CuCl\(_2\) (4.0 mg, 0.03 mmol), cinnamic acid (53.4 mg, 0.36 mmol), K\(_2\)CO\(_3\) (49.8 mg, 0.36 mmol) and H\(_2\)O (50 \(\mu\)L) in DMSO (1.5 mL). After 8 h at 50 °C, purification by column chromatography on silica gel (petroleum ether/EtOAc = 7/1) to yield 3ak (55.2 mg, 50%) as a white solid. M.p. 210-213 °C. IR (KBr): 3434, 3227, 2922, 1730, 1631, 1446, 1314, 1228, 1189, 1122, 954, 764, 688 cm\(^{-1}\); \(^1\)H NMR (DMSO-\(d_6\), 500 MHz): \(\delta = 13.55\) (br, NH), 7.95 (d, \(J = 16.1\) Hz, 1H), 7.86-7.33 (m, 15H), 7.04 (d, \(J = 16.1\) Hz, 1H); \(^13\)C NMR (DMSO-\(d_6\), 125 MHz): \(\delta = 164.9, 147.6, 133.7, 131.2, 129.2, 129.0, 128.9, 128.8, 128.3, 127.8, 125.6, 125.4, 116.3\); MS (EI) m/z: 366 (2) [M\(^+\)], 220 (100).

4. Mechanistic Studies

A mixture of 1a (107.5 mg, 0.3 mmol), CuCl\(_2\) (4.0 mg, 0.03 mmol), AcOH (21.6 mg, 0.36 mmol), K\(_2\)CO\(_3\) (49.8 mg, 0.36 mmol), TEMPO (46.9 mg, 0.3 mmol) and H\(_2\)O (50 \(\mu\)L) in DMSO (1.5 mL) was stirred at 50 °C for 6 h under O\(_2\). The reaction was cooled to room temperature after complete consumption of 1a as monitored by TLC analysis, diluted by EtOAc (10 mL) and H\(_2\)O (30 mL). The aqueous layer was extracted with EtOAc (3 \(\times\) 10 mL) and the combined organic layer was dried over Na\(_2\)SO\(_4\), filtered and concentrated in vacuum. The residue was purified by column chromatography on silica gel (petroleum ether/ EtOAc = 7:1) to give 3aa (7.5 mg, 9%) and 4 (44.3 mg, 67%).

3,5-Diphenyl-1H-pyrazole (4)\[^2\]: White solid. M.p. 202-204 °C. IR (KBr): 3425, 3096, 3001, 2856, 1606, 1570, 1495, 1461, 1294, 1272, 1180, 1074, 1056, 975, 915, 752, 686 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\), 500 MHz): \(\delta = 8.24\) (br, NH), 7.74-7.72 (m, 4H), 7.40-7.32 (m, 6H), 6.84 (s, 1H); \(^13\)C NMR (CDCl\(_3\), 125 MHz): \(\delta = 148.8, 131.2, 129.2, 129.0, 128.9, 128.8, 128.3, 127.8, 125.6, 125.4, 116.3\).
A mixture of $1 \alpha'$ (115.9 mg, 0.3 mmol), CuCl$_2$ (4.0 mg, 0.03 mmol), HOAc (21.6 mg, 0.36 mmol), K$_2$CO$_3$ (49.8 mg, 0.36 mmol) and H$_2$O (50 µL) in DMSO (1.5 mL) was stirred at 50 °C for 4 h under O$_2$. The reaction was cooled to room temperature after complete consumption of $1 \alpha'$ as monitored by TLC analysis. Upon completion, the reaction was diluted by EtOAc (10 mL) and H$_2$O (30 mL). The aqueous layer was extracted with EtOAc (3×10 mL) and the combined organic layer was dried over Na$_2$SO$_4$, then filtered and concentrated in vacuo. The residue was purified by column chromatography on silica gel (petroleum ether/EtOAc = 5/1) to give 5 (49.3 mg, 41%) and 3aa (10.8 mg, 13%).

**Diisopropyl (4-hydroxy-3,5-diphenyl-1H-pyrazol-1-yl)phosphonate (5):** A pale yellow solid. M.p. 118-121 °C. IR (KBr): 3125, 2979, 1456, 1237, 1140, 1007, 803, 690 cm$^{-1}$; $^1$H NMR (DMSO-$d_6$, 500 MHz): $\delta$ = 8.65 (s, 1H), 8.03-8.01 (m, 2H), 7.54-7.52 (m, 2H), 7.50-7.49 (m, 2H), 7.40-7.32 (m, 8H), 4.64-4.57 (m, 2H), 1.22 (d, $J$ = 6.9 Hz, 6H), 1.15 (d, $J$ = 6.2 Hz, 6H); $^{13}$C NMR (DMSO-$d_6$, 125 MHz): $\delta$ = 145.0 (d, $^{2}J_{P,C} = 11.3$ Hz), 138.3 (d, $^{3}J_{P,C} = 8.8$ Hz), 135.3 (d, $^{3}J_{P,C} = 11.3$ Hz), 134.0, 130.3, 128.9, 128.2, 128.1, 127.8, 126.4, 73.9 (d, $^{2}J_{P,C} = 6.3$ Hz), 23.3 (d, $^{3}J_{P,C} = 3.8$ Hz), 22.8 (d, $^{3}J_{P,C} = 6.3$ Hz); MS (EI) m/z: 400 (10) [M$^+$], 236 (100). HRMS (ESI) m/z: Calcd for C$_{21}$H$_{26}$N$_2$O$_4$P [M+H$^+$]: 401.1625, found: 401.1622.

A mixture of 5 (40.0 mg, 0.1 mmol), AcOH (7.2 mg, 0.12 mmol), K$_2$CO$_3$ (16.6 mg, 0.12 mmol), and H$_2$O (17 µL) in DMSO (0.5 mL) was stirred at 50 °C for 53 h under O$_2$. The reaction was cooled to room temperature after complete consumption of 5 as monitored by TLC analysis, diluted by EtOAc (10 mL) and H$_2$O (30 mL). The aqueous layer was extracted with EtOAc (3×10 mL) and the combined organic layer
was dried over Na$_2$SO$_4$, filtered and concentrated in vacuum. The residue was purified by column chromatography on silica gel (petroleum ether/ EtOAc = 7:1) to give 3aa (23.8 mg, 86%).

5. X-Ray Crystal Structure for Compound 3aa

Crystallographic data for 3aa: C$_{17}$H$_{14}$N$_2$O$_2$, M = 278.30, triclinic, P-1 (No. 2), a = 5.834 (16) Å, b = 12.53 (4) Å, c = 19.70 (5) Å, $\alpha$ = 87.16 (4)$^\circ$, $\beta$ = 86.36 (4)$^\circ$, $\gamma$ = 88.79 (4)$^\circ$, V = 1436 (7) Å$^3$, Z = 4, Crystal size: 0.10 × 0.06 × 0.03 mm, T = 295 K, $\rho_{\text{calc}}$ = 1.287 g·cm$^{-3}$, $R_1$ = 0.0849 (I>4$\sigma$(I)), wR$_2$ = 0.3048 (all data), GOF = 1.088, reflections collected/unique: 4973 / 2892 (Rint = 0.0213, Data: 4973, restraints: 0, parameters: 370. CCDC 1032969 contains the supplementary crystallographic data for this paper. The data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

6. References


7. Copies of $^1$H and $^{13}$C NMR Spectra for All Compounds