Supporting Information

PTSA-Catalyzed Mannich-type/Cyclization/Oxidation Tandem Reactions: One-Pot Synthesis of 1,3,5-Substituted Pyrazoles from Aldehydes, Hydrazines and Alkynes

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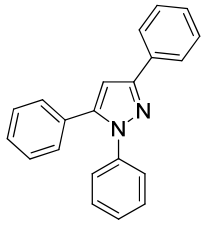
Experimental

General methods and materials. Melting points were uncorrected. NMR spectra were in $CDCl_3$ or DMSO (^1H at 500 MHz and ^{13}C at 125 MHz). Column chromatography was performed on silica gel (300-400 mesh). Unless otherwise noted, all reagents were obtained commercially and used without further purification.

Experimental Section

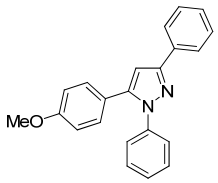
A general experimental procedure for the reaction of aldehyde **1**, hydrazine **2** and alkyne **3** catalyzed by PTSA is described below: To a 5-mL flask, aldehyde **1** (0.5 mmol), hydrazine **2** (0.5 mmol) alkyne **3** (0.6 mmol), dichloromethane (DCM) (2.0 mL) and *p*-toluenesulfonic acid monohydrate (PTSA, 0.1 mmol) were added successively. The reaction mixture was stirred at room temperature, and monitored periodically by TLC. Upon completion (normally 8 h), dichloromethane was removed under reduced pressure by an aspirator, and then the residue was purified by flash chromatography (hexane/ethyl acetate) on silica gel to afford 1,3,5-trisubstituted pyrazoles **4**.



1,3,5-triphenylpyrazole (**4aaa**): pale yellow solid, mp 138-140 ^oC. **^1H NMR** (500 MHz, $CDCl_3$): δ = 7.96-7.91 (m, 2H), 7.46-7.41 (m, 2H), 7.39-7.27 (m, 11H), 6.83 (s, 1H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 152.0, 144.4, 140.2, 133.1, 130.6, 128.9, 128.7, 128.6, 128.5, 128.3, 128.0, 127.4, 125.9, 125.3, 105.2 ppm; **MS**: m/z = 297

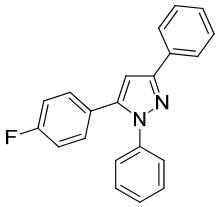
$[M+H^+]$.

The spectral data showed good agreement with the literature data.[1]



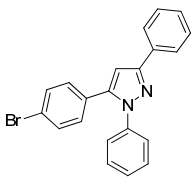
5-(4-Methoxyphenyl)-1,3-diphenyl-pyrazole (**4aac**): pale yellow solid, mp 77-79 °C. **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.83 (d, *J* = 8.9 Hz, 2H), 7.35-7.29 (m, 4H), 7.24-7.09 (m, 6H), 6.84 (d, *J* = 8.9 Hz, 2H), 6.73 (s, 1H), 3.69 (s, 3H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 159.5, 151.8, 144.2, 140.2, 133.1, 129.9, 128.8, 128.6, 127.8, 127.6, 126.1, 125.3, 122.9, 113.9, 105.3, 55.5 ppm; **MS**: m/z = 327 $[M+H^+]$.

The spectral data showed good agreement with the literature data.[1]



5-(4-Fluorophenyl)-1,3-diphenyl-pyrazole (**4aad**): pale yellow solid, mp 141-143 ^{o}C. **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 8.26 (m, 2 H), 7.39-7.27 (m, 5 H), 7.13–6.97 (m, 5 H), 6.72 (s, 1 H), 6.70 (m, 2 H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 160.6, 151.2, 143.8, 140.2, 134.8, 130.7, 128.8, 128.6, 128.4, 127.5, 126.3, 125.2, 124.9, 115.6, 105.0 ppm; **MS**: m/z = 315 $[M+H^+]$.

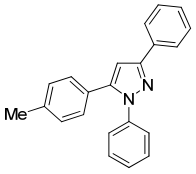
The spectral data showed good agreement with the literature data.[2]



5-(4-Bromoxyphenyl)-1,3-diphenyl-pyrazole (**4aae**): pale yellow solid, mp 126-128

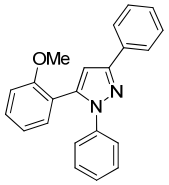
°C. **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.87 (d, 2H, *J* = 8.6 Hz), 7.34-7.21 (m, 12H), 6.76 (s, 1H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 151.9, 144.2, 140.2, 133.7, 131.7, 130.8, 129.2, 128.6, 128.3, 127.1, 126.3, 125.2, 124.9, 123.8, 105.3 ppm; **MS**: m/z = 315 [M+H$^+$].

The spectral data showed good agreement with the literature data.[3]



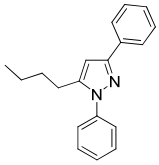
5-(4-Methylphenyl)-1,3-diphenyl-pyrazole (**4aaf**): white solid, mp 115-116 °C. **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.92 (d, *J* = 8.4 Hz, 2H), 7.38-7.33 (m, 12H), 6.79 (s, 1H), 2.36 (s, 3H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 150.9, 143.1, 139.6, 135.6, 134.9, 132.8, 128.9, 127.6, 127.4, 127.1, 126.7, 125.7, 124.8, 124.1, 105.1, 20.2 ppm; **MS**: m/z = 311 [M+H$^+$].

The spectral data showed good agreement with the literature data.[2]



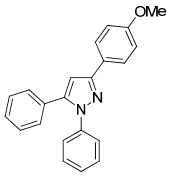
5-(2-Methoxyphenyl)-1,3-diphenylpyrazole (**4aag**): yellow solid, mp 143-144 ºC. **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.87 (d, *J* = 8.8 Hz, 2H), 7.45-7.06 (m, 10H), 7.04-7.01 (m, 2H) 6.83 (s, 1H), 3.45 (s, 3H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 156.5, 152.1, 144.2, 140.2, 133.1, 129.9, 129.6, 128.9, 128.6, 127.8, 127.6, 126.1, 122.9, 121.8, 119.5, 114.6, 105.2, 55.8 ppm; **MS**: m/z = 327 [M+H$^+$].

The spectral data showed good agreement with the literature data.[4]



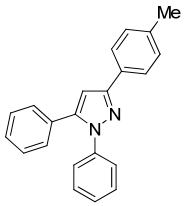
5-Butyl-1,3-diphenylpyrazole (**4aah**): colourless solid, mp 51-52 °C. **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.79 (d, *J* = 7.7 Hz, 2H), 7.37-7.40 (m, 4H), 7.29-7.35 (m, 3H), 7.22 (t, *J* = 7.3 Hz, 1H), 6.46 (s, 1H), 2.59 (t, *J* = 7.6 Hz, 2H), 1.50-1.57 (m, 2H), 1.24-1.29 (m, 2H), 0.83 (t, *J* = 7.5 Hz, 3H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 151.3, 145.7, 139.8, 133.2, 129.1, 128.5, 127.9, 127.7, 125.7, 125.5, 102.7, 30.8, 25.9, 22.3, 13.7 ppm; **MS**: m/z = 277 [$M+H^+$].

The spectral data showed good agreement with the literature data.[5]



3-(4-Methoxyphenyl)-1,5-diphenyl-pyrazole (**4baa**): brown solid, mp 130-132 °C. **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.87 (d, *J* = 8.9 Hz, 2H), 7.39- 7.31 (m, 10H), 6.98 (d, *J* = 8.9 Hz, 2H), 6.77 (s, 1H), 3.86 (s, 3H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 159.6, 151.8, 144.3, 139.8, 130.6, 128.9, 128.7, 128.5, 128.2, 127.3, 127.1, 125.8, 125.2, 113.9, 104.6, 55.2 ppm; **MS**: m/z = 327 [$M+H^+$].

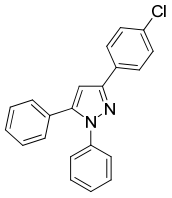
The spectral data showed good agreement with the literature data.[5]



3-(4-Methylphenyl)-1,5-diphenyl-pyrazole (**4caa**): white solid, mp 126-127 °C. **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 8.26 (m, 2 H) 7.43-7.29 (m, 6 H), 7.05-6.95 (m, 6 H),

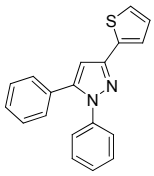
6.85 (s, 1 H), 2.26 (s, 3 H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 151.8, 143.8, 140.6, 137.5, 131.2 131.0, 129.8, 128.8, 128.6, 128.3, 127.6, 126.6, 126.2, 125.5, 105.6, 21.3 ppm; **MS**: m/z = 311 [M+H$^+$].

The spectral data showed good agreement with the literature data.[2]



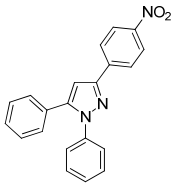
3-(4-Chlorophenyl)-1,5-diphenyl pyrazole(**4daa**): brown solid, mp 144-145 ºC. **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.87 (d, *J* = 8.4 Hz, 2H), 7.38-7.29 (m, 12H), 6.80 (s, 1H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 151.0, 143.5, 139.8, 134.6, 131.9, 131.6, 130.0, 129.1, 128.9, 128.8, 127.9, 127.2, 125.3, 122.1, 105.2 ppm; **MS**: m/z = 332 [M+H$^+$].

The spectral data showed good agreement with the literature data.[2]



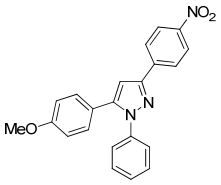
3-(2-Thienyl)-1,5-Diphenyl-pyrazole (**4eaa**): yellow solid, mp 119-121 ºC. **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.08-7.89 (m, 13H), 6.86 (s, 1H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 150.6, 144.4, 140.2, 133.1, 130.6, 128.9, 128.7, 128.6, 128.5, 128.3, 127.4, 126.2, 125.9, 123.9, 108.2 ppm; **MS**: m/z = 303 [M+H$^+$].

The spectral data showed good agreement with the literature data.[6]



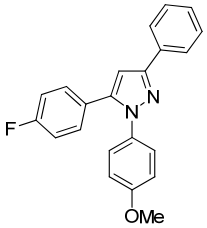
3-(4-Nitrophenyl)-1,5-Diphenyl-phenylpyrazole (**4faa**): yellow solid, mp 161-163 ^{o}C. **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.98-7.95 (m, 2 H), 7.78-7.74 (m, 3 H), 7.25-7.13 (m, 4 H), 7.05-6.91 (m, 5 H), 6.49 (s, 1 H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 154.5, 149.8, 147.5, 144.6, 140.8, 139.1, 132.6, 130.2, 128.9, 128.5, 127.6, 125.9, 125.6, 124.3, 105.2 ppm; **MS**: m/z = 342 [M+H^{+}].

The spectral data showed good agreement with the literature data.[2]



1-Phenyl-3-(4-nitrophenyl)-5-(4-methoxyphenyl)pyrazole (**4fac**): yellow solid, mp 176-178 ^{o}C. **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 8.12-8.10 (m, 2 H), 7.91-7.90 (m, 2 H), 7.44-7.28 (m, 2 H), 7.23-7.19 (m, 2 H), 7.10–7.07 (m, 3 H), 6.73 (m, 2 H), 6.65 (s, 1 H), 3.66 (s, 3H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 160.5, 148.9, 147.6, 145.0, 140.8, 139.1, 130.2, 128.8, 127.5, 125.8, 125.5, 124.2, 123.0, 114.6, 105.2, 54.3 ppm; **MS**: m/z = 372 [M+H^{+}].

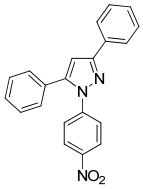
The spectral data showed good agreement with the literature data.[2]



1-(4-Methoxyphenyl)-3-phenyl-5-(4-fluorophenyl)pyrazole (**4abd**): pale brown solid, mp 132-135 ^{o}C. **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 8.26 (m, 2 H,), 7.45 (m, 2 H), 7.29(m, 3 H), 7.10 (m, 2 H), 6.76 (s, 1 H), 6.75-6.66 (m, 4 H), 3.77 (s, 3 H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 162.7, 158.9, 151.8, 143.1, 133.9, 133.6, 130.7, 128.8,

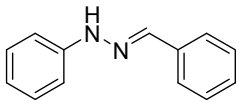
126.7, 125.9, 124.4, 123.1, 115.4, 114.0, 105.3, 54.7 ppm; **MS**: m/z = 345 [M+H$^+$].

The spectral data showed good agreement with the literature data.[2]



1-(4-Nitrophenyl)-3,5-diphenylpyrazole (**4aca**): brown solid, mp 120-123 ^{o}C. **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 8.32 (d, *J* = 9.0 Hz, 2H), 7.76-7.74 (m, 2H), 7.58-7.25 (m, 10H), 6.84 (s, 1H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 153.8, 146.5, 145.9, 144.5, 134.1, 133.6, 129.8, 129.1, 128.9, 128.7, 127.6, 126.3, 125.6, 125.3, 105.4 ppm; **MS**: m/z = 342 [M+H$^+$].

The spectral data showed good agreement with the literature data.[7]



N-Benzylidene-N'-phenylhydrazine (**5aa**): light yellow solid, mp 156-157 ^{o}C. **^{1}H NMR** (500 MHz, DMSO): δ = 10.35 (s, 1H), 7.88 (s, 1H), 7.62-7.66 (m, 2H), 7.35-7.40 (m, 2H), 7.29 (tt, *J* = 1.3, 7.3 Hz, 1H), 7.20-7.25 (m, 2H), 7.04-7.09 (m, 2H), 6.74 (tt, *J* = 1.1, 7.3 Hz, 1H) ppm; **^{13}C NMR** (125 MHz, DMSO): δ = 145.5, 136.8, 135.9, 129.4, 128.7, 128.2, 125.8, 119.0, 112.3 ppm; **MS**: m/z = 197 [M+H$^+$].

The spectral data showed good agreement with the literature data.[8]

References

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