Copper(II)-catalyzed coupling reaction: an efficient and regioselective approach to $N',N'$-diaryl acylhydrazines

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1. General information

The solvents were distilled from standard drying agents. Unless otherwise stated, commercial reagents purchased from Alfa Aesar, Acros and Aldrich chemical companies were used without further purification. Reaction products were purified by flash chromatography using Qing Dao Sea Chemical Reagent silica gel (200–300 mesh). \(^1\)H NMR spectra were recorded on a Bruker Avance III 400 (400 MHz) spectrometer and referenced internally to the residual proton resonance in CDCl\(_3\) (\(\delta = 7.26\) ppm), or with tetramethysilane (TMS, \(\delta = 0.00\) ppm) as the internal standard. Chemical shifts were reported as parts per million (ppm) in the \(\delta\) scale downfield from TMS. Multiplicity is indicated as follows: s (singlet), d (doublet), t (triplet), q (quartet), quint (quintet), m (multiplet), dd (doublet of doublet), bs (broad singlet). \(^{13}\)C NMR spectra were recorded on Bruker spectrometer with complete proton decoupling, and chemical shifts were reported in ppm from TMS with the solvent as the internal reference (CDCl\(_3\), \(\delta = 77.0\) ppm). Low-resolution MS spectra were obtained on an Agilent LC-MS 6120 instrument with an ESI mass detector, the data were obtained in the positive or negative ion mode. High resolution mass spectra were recorded on an ESI-ion trap mass spectrometer (Shimadzu, LCMS-IT-TOF). Analytical TLC was performed using EM separations percolated silica gel 0.2 mm layer UV 254 fluorescent sheets.

2. Screening for the optimal conditions of cross-coupling reaction.\(^a\)

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\begin{array}{cccc}
\text{Entry} & 4a \text{ (equiv.)} & \text{Cu(O\text{Ac})}_2 \cdot \text{H}_2\text{O} \text{ (equiv.)} & \text{Solvent} & \text{Yield}^b (%) \\
1 & 1.20 & 0.10 & \text{MeOH} & 81 \\
2 & 0.83 & 0.083 & \text{MeOH} & 45 \\
3 & 0.67 & 0.067 & \text{MeOH} & 67 \\
4 & 1.20 & 0.05 & \text{MeOH} & 43 \\
5 & 1.20 & 0.15 & \text{MeOH} & 80 \\
6 & 1.30 & 0.10 & \text{MeOH} & 47 \\
7 & 1.20 & 0.10 & \text{MeOH} & 72^c \\
8 & 1.20 & 0.10 & \text{MeOH} & 56^d \\
9 & 1.20 & 0.20 & \text{MeOH} & 72 \\
10 & 1.20 & 0.10 & \text{MeCN} & \text{trace} \\
11 & 1.20 & 0.10 & \text{toluene} & 36 \\
12 & 1.20 & 0.10 & \text{DCM} & 35 \\
13 & 1.20 & 0.10 & \text{DCE} & 48 \\
14 & 1.20 & 0.10 & \text{DMSO} & \text{trace} \\
15 & 1.20 & 0.10 & \text{THF} & 60 \\
16 & 1.20 & 0.20 & \text{THF} & 83 \\
17 & 1.20 & 0.10 & \text{dioxane} & 97 \\
18 & 1.20 & 0.05 & \text{dioxane} & 63 \\
\end{array}
\]
3. Preparation of N'-aryl acylhydrazines

1s, 1z, 1aa, 1ab and 1ac were synthesized according to literature methods.\(^1\)\(^\text{3}\)

General procedure for the synthesis of 1a-r, 1t-y:

To a solution of aryl carboxylic acid (4.0 mmol) in DMF (10 mL) was added EDC·HCl (4.4 mmol) and HOBt (4.4 mmol), then arylhydrazine was added and the reaction mixture was stirred at ambient temperature under nitrogen atmosphere for 24-48 h. The reaction mixture was poured into H₂O (150 mL) and extracted with ethyl acetate (30 mL × 3). The organic phases were combined and washed with saturated NaHCO₃ (30 mL × 2) and saturated NaCl (30 mL × 1) respectively, dried over Na₂SO₄. The solution was concentrated in vacuo and purified by column chromatography on silica gel (eluting with 3:1 to 1:1 petroleum ether/ethyl acetate) to give the desired product.

An alternative procedure for the synthesis of 1a

Phenylhydrazine (0.5 g, 4.63 mmol) was added to a solution of benzoic anhydride (1.05 g, 4.63 mmol) in CH₃OH (10 mL) at 0 °C slowly. The mixture was stirred at ambient temperature for 3 h. After removal of the solvent in vacuo, the residue was dissolved in ethyl acetate (100 mL), washed with saturated NaHCO₃ (50 mL × 3) and NaCl (30 mL × 1) respectively. The solution was dried over Na₂SO₄, concentrated in vacuo, and purified by column chromatography on silica gel (eluting with 3:1 to 1:1 petroleum ether/ethyl acetate) to give 1a (0.87 g, 89% yield).

\(N'\)-Phenylbenzohydrazide (1a)\(^4\)

White solid; yield: 65%; mp: 173-174 °C; ESI-MS (m/z): 213.2 [M+H]\(^+\). \(^1\)H NMR (400 MHz, CDCl₃) δ: 8.03 (s, 1H), 7.83 (d, \(J = 7.3 \text{ Hz}, 2\text{H}\)), 7.56 (t, \(J = 7.4 \text{ Hz}, 1\text{H}\)), 7.46 (t, \(J = 7.6 \text{ Hz}, 2\text{H}\)), 7.24 (dd, \(J = 11.1, 4.8 \text{ Hz}, 2\text{H}\)), 6.96-6.87 (m, 3H), 6.37 (s, 1H).

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\(a\) 1a (0.2 mmol), solvent (2.0 mL), rt, 24 h.\(^b\) Isolated yield.\(^c\) Proceeded at 50 °C.\(^d\) TEA (1.0 equiv.) was added.\(^e\) dioxane (1.0 mL).\(^f\) dioxane (3.0 mL).
N’-(4-Fluorophenyl)benzohydrazide (1b)

![Structure](image)

Off-white solid; yield: 45%; mp: 173-174 °C; ESI-MS (m/z): 231.1 [M+H]+; 1H NMR (400 MHz, CDCl3) δ: 8.00 (s, 1H), 7.87-7.81 (m, 2H), 7.57 (t, J = 7.4 Hz, 1H), 7.48 (t, J = 7.5 Hz, 2H), 6.92 (m, 4H), 6.35 (s, 1H).

N’-(4-Chlorophenyl)benzohydrazide (1c)

![Structure](image)

White solid; yield: 35%; mp: 149-150 °C; ESI-MS (m/z): 247.2 [M+H]+; 1H NMR (400 MHz, CDCl3) δ: 8.02 (s, 1H), 7.86-7.80 (m, 2H), 7.57 (t, J = 7.4 Hz, 1H), 7.47 (t, J = 7.6 Hz, 2H), 7.19 (d, J = 2.1 Hz, 1H), 7.18 (d, J = 2.1 Hz, 1H), 6.88-6.80 (m, 2H), 6.37 (d, J = 3.1 Hz, 1H); 13C NMR (100 MHz, CDCl3) δ: 167.9, 146.7, 132.4, 132.0, 129.1, 128.8, 127.2, 126.1, 115.0.

N’-(4-Bromophenyl)benzohydrazide (1d)

![Structure](image)

Light yellow solid; yield: 21%; mp: 157-158 °C; ESI-MS (m/z): 291.0 [M+H]+; 1H NMR (400 MHz, CDCl3) δ: 8.00 (s, 1H), 7.83 (d, J = 7.2 Hz, 2H), 7.58 (t, J = 7.4 Hz, 1H), 7.48 (t, J = 7.6 Hz, 2H), 7.35-7.30 (m, 2H), 6.80 (dd, J = 9.3, 2.4 Hz, 2H), 6.37 (s, 1H); 13C NMR (100 MHz, CDCl3) δ: 167.9, 147.1, 132.5, 132.0, 128.9, 127.2, 115.4, 113.4.

N’-(3-Chlorophenyl)benzohydrazide (1e)

![Structure](image)

White solid; yield: 30%; mp: 150-151 °C; GC-MS: 246.1 [M]+; 1H NMR (400 MHz, CDCl3) δ: 7.99 (s, 1H), 7.88-7.80 (m, 2H), 7.58 (t, J = 7.4 Hz, 1H), 7.48 (t, J = 7.6 Hz, 2H), 7.14 (t, J = 8.0 Hz, 1H), 6.93-6.85 (m, 2H), 6.79 (dd, J = 8.2, 1.6 Hz, 1H), 6.40 (d, J = 3.1 Hz, 1H); 13C NMR (100 MHz, CDCl3) δ: 167.9, 149.4, 135.1, 132.5, 131.9, 130.3, 128.9, 127.2, 121.3, 113.7, 112.0.

N’-(2-Chlorophenyl)benzohydrazide (1f)

![Structure](image)

White solid; yield: 33%; mp: 154-155 °C; GC-MS: 246.1 [M]+; 1H NMR (400 MHz, CDCl3) δ: 7.95 (s, 1H), 7.85 (d, J = 7.2 Hz, 2H), 7.58 (t, J = 7.4 Hz, 1H), 7.48 (t, J = 7.6 Hz, 2H), 7.31 (dd, J = 7.9, 1.3 Hz, 1H), 7.19-7.12 (m, 1H), 7.01-6.96 (m, 1H), 6.85 (td, J = 7.8, 1.5 Hz, 1H), 6.66 (d, J = 2.4 Hz, 1H); 13C NMR (100 MHz, CDCl3) δ: 167.6, 143.9, 132.4, 132.0, 129.6, 128.8, 127.7, 127.2, 121.6, 119.9, 113.8.
$N'-(4$-Methoxyphenyl)$benzohydrazide$\,(1g)$

Off-white solid; yield: 37%; mp: 139-140 °C; ESI-MS (m/z): 243.1 [M+H]$^+$; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$: 7.97 (s, 1H), 7.86-7.79 (m, 2H), 7.56 (t, $J = 7.4$ Hz, 1H), 7.47 (t, $J = 7.5$ Hz, 2H), 6.91 (d, $J = 8.9$ Hz, 2H), 6.85-6.78 (m, 2H), 6.28 (d, $J = 3.4$ Hz, 1H), 3.75 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$: 167.9, 155.0, 141.4, 132.2, 132.1, 128.7, 127.3, 116.0, 114.6, 55.6.

$N'-(3$-Methoxyphenyl)$benzohydrazide$\,(1h)$

White solid; yield: 55%; mp: 141-142 °C; ESI-MS (m/z): 243.2 [M+H]$^+$; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$: 8.01 (s, 1H), 7.83 (d, $J = 7.3$ Hz, 2H), 7.56 (t, $J = 7.4$ Hz, 1H), 7.46 (t, $J = 7.6$ Hz, 2H), 7.14 (t, $J = 8.3$ Hz, 1H), 6.52 (d, $J = 8.8$ Hz, 1H), 6.47 (dd, $J = 8.2$, 1.6 Hz, 2H), 6.37 (d, $J = 3.6$ Hz, 1H), 3.75 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$: 167.8, 160.7, 149.5, 132.3, 132.0, 130.11, 128.8, 127.2, 106.6, 106.4, 100.0, 55.2.

$N'-(2$-Methoxyphenyl)$benzohydrazide$\,(1i)$

Off-white solid; yield: 50%; mp: 143-144 °C; ESI-MS (m/z): 243.1 [M+H]$^+$; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$: 7.96 (s, 1H), 7.84 (d, $J = 7.2$ Hz, 2H), 7.55 (t, $J = 7.4$ Hz, 1H), 7.47 (t, $J = 7.5$ Hz, 2H), 6.95-6.91 (m, 1H), 6.89-6.83 (m, 3H), 6.75 (s, 1H), 3.90 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$: 167.4, 147.6, 137.3, 132.6, 132.1, 128.7, 127.1, 121.1, 121.0, 112.9, 110.4, 55.6.

$N'-(4$-$(\text{tri}$-\text{Fluoromethoxy})$phenyl)$benzohydrazide$\,(1j)$

Light yellow solid; yield: 25%; mp: 157-158 °C; ESI-MS (m/z): 297.1 [M+H]$^+$; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$: 8.02 (s, 1H), 7.88-7.80 (m, 2H), 7.58 (t, $J = 7.4$ Hz, 1H), 7.48 (t, $J = 7.6$ Hz, 2H), 7.09 (d, $J = 8.4$ Hz, 2H), 6.91 (dd, $J = 9.5$, 2.6 Hz, 2H), 6.42 (d, $J = 3.3$ Hz, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$: 167.9, 161.1, 146.8, 143.5, 132.5, 132.0, 128.9, 127.1, 122.3, 114.6.

$N'-(4$-$(\text{Methylsulfonyl})$phenyl)$benzohydrazide$\,(1k)$
Light yellow solid; yield: 16%; mp: 201-203 °C; ESI-MS (m/z): 291.1 [M+H]+; 1H NMR (400 MHz, DMSO-d6) δ: 10.53 (s, 1H), 8.78 (s, 1H), 7.94 (d, J = 7.2 Hz, 2H), 7.67 (d, J = 8.7 Hz, 2H), 7.61 (t, J = 7.0 Hz, 1H), 7.53 (t, J = 7.4 Hz, 2H), 6.89 (d, J = 8.7 Hz, 2H), 3.08 (s, 3H); 13C NMR (100 MHz, DMSO-d6) δ: 166.8, 154.1, 133.1, 132.4, 129.8, 129.1, 129.0, 127.9, 111.8, 44.8.

N’-(4-Nitrophenyl)benzohydrazide (1l)

Brown solid; yield: 42%; mp: 192-193 °C; ESI-MS (m/z): 256.1 [M-H]-; 1H NMR (400 MHz, DMSO-d6) δ: 10.65 (s, 1H), 9.24 (s, 1H), 8.09 (d, J = 9.2 Hz, 2H), 7.97-7.90 (m, 2H), 7.62 (t, J = 7.4 Hz, 1H), 7.54 (t, J = 7.5 Hz, 2H), 6.84 (d, J = 9.2 Hz, 2H); 13C NMR (100 MHz, DMSO-d6) δ: 166.2, 155.0, 138.1, 132.3, 132.0, 128.5, 127.4, 125.9, 110.7.

N’-p-Tolylbenzohydrazide (1m)

White solid; yield: 55%; ESI-MS (m/z): 225.1 [M-H]-; 1H NMR (400 MHz, CDCl3) δ: 7.94 (s, 1H), 7.83 (d, J = 7.2 Hz, 2H), 7.56 (t, J = 7.4 Hz, 1H), 7.47 (t, J = 7.5 Hz, 2H), 7.05 (d, J = 8.1 Hz, 2H), 6.85 (d, J = 8.3 Hz, 2H), 6.30 (d, J = 3.6 Hz, 1H), 2.27 (s, 3H).

N’-m-Tolylbenzohydrazide (1n)

White solid; yield: 40%; mp: 152-153 ℃; ESI-MS (m/z): 225.2 [M-H]-; 1H NMR (400 MHz, CDCl3) δ: 8.03 (s, 1H), 7.84 (d, J = 7.5 Hz, 2H), 7.56 (t, J = 7.3 Hz, 1H), 7.46 (t, J = 7.6 Hz, 2H), 7.13 (dd, J = 10.8, 5.3 Hz, 1H), 6.74 (d, J = 6.8 Hz, 3H), 6.34 (s, 1H), 2.28 (s, 3H); 13C NMR (100 MHz, CDCl3) δ: 167.8, 148.0, 139.1, 132.4, 132.2, 129.1, 128.7, 127.2, 122.3, 114.6, 111.0, 21.5.

N’-o-Tolylbenzohydrazide (1o)

White solid; yield: 32%; mp: 159-160 ℃; ESI-MS (m/z): 225.2 [M-H]-; 1H NMR (400 MHz, CDCl3) δ: 7.97 (s, 1H), 7.84 (d, J = 7.2 Hz, 2H), 7.56 (t, J = 7.4 Hz, 1H), 7.47 (t, J = 7.6 Hz, 2H), 7.12 (t, J = 7.2 Hz, 2H), 6.94 (d, J = 7.8 Hz, 1H), 6.90-6.82 (m, 1H), 6.27 (d, J = 3.8 Hz, 1H), 2.31 (s, 3H); 13C NMR (100 MHz, CDCl3) δ: 167.5, 145.7, 132.4, 132.2, 130.6, 128.8, 127.1, 126.9, 121.2, 112.4, 100.0, 17.0.

N’-(3,5-diMethylphenyl)benzohydrazide (1p)
White solid; yield: 43%; mp: 181-182 °C; ESI-MS (m/z): 241.1 [M+H]+; 1H NMR (400 MHz, CDCl3) δ: 7.97 (s, 1H), 7.85 (d, J = 7.3 Hz, 2H), 7.56 (t, J = 7.3 Hz, 1H), 7.48 (t, J = 7.5 Hz, 2H), 6.56 (d, J = 8.3 Hz, 3H), 6.30 (s, 1H), 2.25 (s, 6H); 13C NMR (100 MHz, CDCl3) δ: 167.6, 148.0, 139.0, 132.4, 132.2, 128.8, 127.2, 123.4, 111.7, 21.4.

\(N'-(3,4\text{-dMethylphenyl})\text{benzohydrazide (1q)}\)

Brown solid; yield: 41%; mp: 147-148 °C; ESI-MS (m/z): 241.1 [M+H]+; 1H NMR (400 MHz, CDCl3) δ: 8.22 (s, 1H), 7.86-7.79 (m, 2H), 7.54 (d, J = 7.4 Hz, 1H), 7.45 (t, J = 7.6 Hz, 2H), 6.99 (d, J = 8.0 Hz, 1H), 6.69 (dd, J = 9.7, 7.6 Hz, 2H), 6.31 (s, 1H), 2.18 (d, J = 6.9 Hz, 6H); 13C NMR (100 MHz, CDCl3) δ: 167.7, 145.9, 137.4, 132.1, 130.2, 129.7, 128.7, 128.4, 127.2, 115.7, 111.5, 20.0, 18.9.

\(N'-(6\text{-Chloropyridin-2-yl})\text{benzohydrazide (1r)}\)

Grey solid; yield: 87%; mp: 217-218 °C; ESI-MS (m/z): 248.0 [M+H]+; 1H NMR (400 MHz, DMSO-d6) δ: 10.48 (s, 1H), 8.89 (s, 1H), 7.95-7.90 (m, 2H), 7.55 (dd, J = 16.1, 8.1 Hz, 4H), 6.76 (d, J = 7.4 Hz, 1H), 6.59 (d, J = 8.2 Hz, 1H); 13C NMR (100 MHz, DMSO-d6) δ: 166.8, 160.8, 148.8, 141.0, 133.2, 132.3, 129.0, 127.9, 113.7, 105.3.

\(N'\text{-Benzylbenzohydrazide (1s)}\)

White solid; yield: 87%; mp: 118-119 °C; ESI-MS (m/z): 227.1 [M+H]+; 1H NMR (400 MHz, DMSO-d6) δ: 10.05 (d, J = 6.2 Hz, 1H), 7.79 (dd, J = 5.2, 3.3 Hz, 2H), 7.54-7.48 (m, 1H), 7.47-7.41 (m, 2H), 7.41-7.36 (m, 2H), 7.35-7.30 (m, 2H), 7.26 (ddd, J = 7.2, 3.8, 1.3 Hz, 1H), 5.42 (q, J = 5.8 Hz, 1H), 3.99 (d, J = 5.6 Hz, 2H); 13C NMR (100 MHz, DMSO-d6) δ: 165.6, 138.5, 133.2, 131.2, 128.5, 128.3, 128.1, 127.0, 127.0, 54.8.

\(4\text{-Methoxy-}N'\text{-phenylbenzohydrazide (1t)}\)

Brown solid; yield: 55%; mp: 179-180 °C; ESI-MS (m/z): 243.1 [M+H]+; 1H NMR (400 MHz, CDCl3) δ: 7.82 (d, J = 1.9 Hz, 2H), 7.80 (s, 1H), 7.24 (dd, J = 8.3, 7.0 Hz, 2H), 6.98-6.88 (m, 5H),
6.33 (s, 1H), 3.87 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ: 171.0, 167.1, 154.9, 134.4, 133.9, 130.4, 123.8, 118.9, 117.6, 60.6.

4-Hydroxy-$N'$-phenylbenzohydrazide (1u)

![Image](image1)

White solid; yield: 53%; mp: 222-223 °C; ESI-MS (m/z): 229.1 [M+H]$^+$; $^1$H NMR (400 MHz, DMSO-d$_6$) δ: 10.11 (d, $J$ = 2.8 Hz, 1H), 10.06 (s, 1H), 7.79 (t, $J$ = 5.7 Hz, 3H), 7.14 (dd, $J$ = 8.3, 7.4 Hz, 2H), 6.84 (d, $J$ = 8.7 Hz, 2H), 6.77 (d, $J$ = 7.6 Hz, 2H), 6.97 (t, $J$ = 7.3 Hz, 1H); $^{13}$C NMR (100 MHz, DMSO-d$_6$) δ: 166.5, 161.0, 150.2, 129.7, 129.1, 124.1, 119.0, 115.5, 112.8.

4-Bromo-$N'$-phenylbenzohydrazide (1v)

![Image](image2)

White solid; yield: 76%; mp: 195-196 °C; ESI-MS (m/z): 292.1 [M+H]$^+$; $^1$H NMR (400 MHz, DMSO-d$_6$) δ: 10.43 (d, $J$ = 2.8 Hz, 1H), 7.91 (d, $J$ = 2.8 Hz, 1H), 7.88-7.83 (m, 2H), 7.75-7.69 (m, 2H), 7.15 (t, $J$ = 7.9 Hz, 2H), 6.78 (d, $J$ = 7.7 Hz, 2H), 6.72 (t, $J$ = 7.3 Hz, 1H); $^{13}$C NMR (100 MHz, DMSO-d$_6$) δ: 165.9, 149.8, 132.6, 132.0, 129.9, 129.2, 125.8, 119.2, 112.8.

4-Amino-$N'$-phenylbenzohydrazide (1w)

![Image](image3)

Off-white solid; yield: 42%; mp: 201-202 °C; GC-MS (m/z): 227.0 [M]$^+$; $^1$H NMR (400 MHz, DMSO-d$_6$) δ: 9.88 (d, $J$ = 2.7 Hz, 1H), 7.69 (d, $J$ = 2.7 Hz, 1H), 7.64 (d, $J$ = 8.6 Hz, 2H), 7.12 (dd, $J$ = 8.3, 7.5 Hz, 2H), 6.75 (d, $J$ = 7.7 Hz, 2H), 6.69 (t, $J$ = 7.3 Hz, 1H), 6.57 (d, $J$ = 8.6 Hz, 2H), 5.67 (s, 2H); $^{13}$C NMR (100 MHz, DMSO-d$_6$) δ: 166.4, 152.0, 150.0, 128.8, 128.6, 119.5, 118.3, 112.6, 112.3.

4-Nitro-$N'$-phenylbenzohydrazide (1x)

![Image](image4)

Brown solid; yield: 51%; mp: 190-191 °C; ESI-MS (m/z): 258.1 [M+H]$^+$; $^1$H NMR (400 MHz, DMSO-d$_6$) δ: 10.67 (d, $J$ = 2.1 Hz, 1H), 8.40-8.32 (m, 2H), 8.20-8.12 (m, 2H), 8.01 (d, $J$ = 2.1 Hz, 1H), 7.21-7.12 (m, 2H), 6.84-6.78 (m, 2H), 6.74 (t, $J$ = 7.3 Hz, 1H); $^{13}$C NMR (100 MHz, DMSO-d$_6$) δ: 164.8, 149.3, 149.1, 138.7, 128.8, 128.8, 123.6, 118.9, 112.4.

3-Nitro-$N'$-phenylbenzohydrazide (1y)

![Image](image5)
Yellow solid; yield: 93%; mp: 160-161 °C; GC-MS (m/z): 257.1 [M]+; ¹H NMR (400 MHz, DMSO-d₆) δ: 10.73 (d, J = 2.6 Hz, 1H), 8.77-8.70 (m, 1H), 8.47-8.40 (m, 1H), 8.37 (dd, J = 6.6, 1.2 Hz, 1H), 8.02 (d, J = 2.6 Hz, 1H), 7.83 (t, J = 8.0 Hz, 1H), 7.23-7.12 (m, 2H), 6.82 (d, J = 7.7 Hz, 2H), 6.74 (t, J = 7.3 Hz, 1H); ¹³C NMR (100 MHz, DMSO-d₆) δ: 164.3, 149.1, 147.8, 134.4, 133.6, 130.3, 128.8, 126.2, 122.1, 118.8, 112.4.

N¹-Phenylacetohydrazide (1z)

White solid; yield: 89%; mp: 131-132 °C; ESI-MS (m/z): 151.1 [M+H]+; ¹H NMR (400 MHz, DMSO-d₆) δ: 9.57 (s, 0.91H), 8.89 (s, 0.13H), 7.93 (s, 0.13H), 7.61 (d, J = 1.7 Hz, 0.88H), 7.20-7.16 (m, 0.29H), 7.14-7.10 (m, 1.77H), 6.75-6.74 (m, 0.11H), 6.66-6.72 (m, 2.84H), 1.89 (s, 2.53H), 1.85 (s, 0.41H); ¹³C NMR (100 MHz, DMSO-d₆) δ: 175.2, 169.0, 149.4, 148.8, 129.0, 128.6, 118.8, 118.4, 112.1, 111.8, 20.6, 19.2.

2,2,2-triFluoro-N¹-phenylacetohydrazide (1aa)

White solid; yield: 33%; mp: 124-125 °C; ESI-MS (m/z): 227.2 [M+Na]+; ¹H NMR (400 MHz, CDCl₃) δ: 8.18 (s, 1H), 7.33-7.22 (m, 2H), 6.99 (t, J = 7.4 Hz, 1H), 6.83 (dd, J = 8.5, 0.9 Hz, 2H), 6.05 (s, 1H); ¹³C NMR (100 MHz, CDCl₃) δ: 157.7, 157.4, 145.8, 129.4, 122.4, 117.2, 114.3, 113.8.

tert-Butyl 2-phenylhydrazinecarboxylate (1ab)¹c

White solid; yield: 76%; mp: 93-94 °C; ESI-MS (m/z): 231.1 [M+Na]+; ¹H NMR (400 MHz, CDCl₃) δ: 7.27-7.20 (m, 2H), 6.88 (t, J = 7.4 Hz, 1H), 6.82 (d, J = 7.8 Hz, 2H), 6.38 (s, 1H), 5.74 (s, 1H), 1.46 (s, 9H).

tert-Butyl 2-(4-chlorophenyl)hydrazinecarboxylate (1ac)

White solid; yield: 58%; mp: 124-125 °C; ESI-MS (m/z): 241.0 [M-H]-; ¹H NMR (400 MHz, CDCl₃) δ: 7.19 (d, J = 2.2 Hz, 1H), 7.17 (d, J = 2.2 Hz, 1H), 6.75 (d, J = 8.8 Hz, 2H), 6.38 (s, 1H), 5.75 (s, 1H), 1.45 (s, 9H); ¹³C NMR (100 MHz, CDCl₃) δ: 156.1, 147.1, 129.1, 125.5, 114.2, 81.5, 28.2.

(E)-tert-Butyl 2-phenylidiazene carboxylate (4)⁷
Brown oil; $^1$H NMR (400 MHz, CDCl$_3$) δ: 7.92-7.90 (m, 1H), 7.89 (t, $J = 1.9$ Hz, 1H), 7.56-7.53 (m, 1H), 7.53 (t, $J = 1.0$ Hz, 1H), 7.51 (dd, $J = 3.1$, 1.7 Hz, 1H), 1.66 (s, 9H); HRMS (ESI) calcd. for C$_{11}$H$_{14}$N$_2$O$_2$Na [M+Na]$^+$: 229.0947, found: 229.0955.

Methyl 4-methoxybenzoate (5t)

$^1$H NMR (400 MHz, CDCl$_3$) δ: 8.02-7.96 (m, 2H), 6.95-6.88 (m, 2H), 3.88 (s, 3H), 3.86 (s, 3H).

4. One-pot synthesis of $N'$,$N'$-diarylacylhydrazide

Phenylhydrazine (0.22 g, 2.0 mmol) was added to a solution of benzoic anhydride (0.45 g, 2.0 mmol) in CH$_3$OH (15 mL) dropwise at 0 °C. The reaction mixture was stirred at ambient temperature for 3 h. Then Cu(OAc)$_2$·H$_2$O (80 mg, 0.4 mmol), 1,10-phen·H$_2$O (160 mg, 0.8 mmol) and TEA (1.13 mL, 8.0 mmol) were added sequentially. The mixture was stirred at room temperature for additional 24 h, then quenched by saturated NaCl solution (30 mL), extracted with EtOAc (30 mL ×3), and dried over Na$_2$SO$_4$. The crude product was purified by flash column chromatography (eluting with 10:1 petroleum ether/ethyl acetate) to provide 2a (230 mg, 80% yield).

5. Control synthesis of tert-butyl 2,2-diphenylhydrazinecarboxylate

Cu(OAc)$_2$·H$_2$O (20 mg, 0.1 mmol), 1,10-phen·H$_2$O (160 mg, 0.2 mmol) and TEA (0.28 mL, 2.0 mmol) were added sequentially to a solution of 1ab (0.10 g, 0.5 mmol) in CH$_3$OH (6.0 mL). The mixture was stirred at -40 °C for 2 h, then quenched by saturated NaCl solution (20 mL), extracted with EtOAc (20 mL ×3), and dried over Na$_2$SO$_4$. The crude product was purified by flash column chromatography (eluting with 50:1 petroleum ether/ethyl acetate) to provide 4 (81 mg, 79% yield). $^1$H NMR (400 MHz, CDCl$_3$) δ: 7.92-7.90 (m, 1H), 7.89 (t, $J = 1.9$ Hz, 1H), 7.56-7.53 (m, 1H), 7.53 (t, $J = 1.0$ Hz, 1H), 7.51 (dd, $J = 3.1$, 1.7 Hz, 1H), 1.66 (s, 9H); HRMS (ESI) calcd. for C$_{11}$H$_{14}$N$_2$O$_2$Na [M+Na]$^+$: 229.0947, found: 229.0955.

Intermediate 4 was converted to 2ab following a similar procedure for 2a in 85% yield.
6. References

7. $^1$H and $^{13}$C NMR spectra

$N'\text{-Phenylbenzohydrazide (1a)}$

$N'\text{-}(4\text{-Fluorophenyl)benzohydrazide (1b)}$
\textit{N'-(4-Chlorophenyl)benzohydrazide (1c)}
N’-(4-Bromophenyl)benzohydrazide (1d)
$N'$-(3-Chlorophenyl)benzohydrazide (1e)
$N'-(2\text{-Chlorophenyl})\text{benzohydrazide (1f)}$
$N'$-(4-Methoxyphenyl)benzohydrazide (1g)
N′-(3-Methoxyphenyl)benzohydrazide (1h)
$N^\prime$-(2-Methoxyphenyl)benzohydrazide (Ii)
$N'-(4-(trifluoromethoxy)phenyl)benzohydrazide (1j)$
$N'\text{-}(4\text{-}(\text{Methylsulfonyl})\text{phenyl})\text{benzohydrazide \ (1k)}}$
N'-{(4-Nitrophenyl)benzohydrazide (11)}
N'-p-Tolylbenzohydrazide (1m)
N'-m-Tolylbenzohydrazide (1n)
$N'\text{-}o\text{-}\text{Tolylbenzohydrazide (1o)}$
$N'$-(3,5-diMethylphenyl)benzohydrazide (1p)
$N'$-(3,4-diMethylphenyl)benzohydrazide (1q)
$N'-(6$-Chloropyridin-2-yl)benzohydrazide (1r)$
$N'$-Benzylnitrosohydrazide (1s)
4-Methoxy-\(N'\)-phenylbenzohydrazide (1t)
4-Hydroxy-\(N'\)-phenylbenzohydrazide (1u)
4-Bromo-\textsuperscript{N'}-phenylbenzohydrazide (1v)
4-Amino-N'-phenylbenzohydrazide (1w)
4-Nitro-N' phenylbenzohydrazide (1x)
3-Nitro-\(N'\)-phenylbenzohydrazide (1y)
$N'$-Phenylacetohydrazide (1z)
2,2,2-triFluoro-N'-phenylacetohydrazide (1aa)
*tert*-Butyl 2-phenylhydrazinecarboxylate (1ab)
*tert*-Butyl 2-(4-chlorophenyl)hydrazinecarboxylate (1ac)
$N',N'$-diphenylbenzohydrazide (2a)
$N',N'$-bis(4-fluorophenyl)benzohydrazide (2b)
$N',N'-\text{bis(4-chlorophenyl)benzohydrazide (2c)}$
$N',N'$-bis(4-bromophenyl)benzohydrazide (2d)
N',N'-bis(3-chlorophenyl)benzohydrazide (2e)
$N',N'$-bis(2-chlorophenyl)benzohydrazide (2f)
$N',N'$-bis(4-methoxyphenyl)benzohydrazide (2g)
$N',N'$-bis(3-methoxyphenyl)benzohydrazide (2h)
$N',N'$-bis(2-methoxyphenyl)benzohydrazide (2i)
$N',N'$-bis(4-(trifluoromethoxy)phenyl)benzohydrazide (2j)
$N',N'$-bis(4-(methylsulfonyl)phenyl)benzohydrazide (2k)
$N',N'$-bis(4-nitrophenyl)benzohydrazide (2l)
$N',N'-di(p$-tolyl)benzohydrazide (2m)$
$N',N'-di(m\text{-}tolyl)$benzohydrazide (2n)
$N',N'\text{-di(o-tolyl)benzohydrazide (2o)}$
$N',N'$-bis(3,5-dimethylphenyl)benzohydrazide (2p)
$N',N'$-bis(3,4-dimethylphenyl)benzohydrazide (2q)
$N',N'$-bis(6-chloropyridin-2-yl)benzohydrazide (2r)
4-methoxy-\(N',N'\)-diphenylbenzohydrazide (2t)
4-hydroxy-\(N',N'-\text{diphenylbenzohydrazide}\) (2u)
4-bromo-\(N',N'-diphenylbenzohydrazide\) (2v)
4-amino-\(N',N'\)-diphenylbenzohydrazide (2w)
4-nitro-$N'$,$N'$-diphenylbenzohydrazide (2x)
3-nitro-$N'$,$N'$-diphenylbenzohydrazide (2y)
$N',N'$-diphenylacetohydrazide (2z)
2,2,2-trifluoro-N',N'-diphenylacetohydrazide (2aa)
*tert*-butyl 2,2-diphenylhydrazinecarboxylate (2ab)
*tert*-butyl 2,2-bis(4-chlorophenyl)hydrazinecarboxylate (2ac)
(E)-tert-butyl 2-phenyldiazenecarboxylate (4)

Methyl 4-methoxybenzoate (5t)
$N'(4\text{-methoxyphenyl})-N'\text{-phenylbenzohydrazide (7a)}$
$N'$-phenyl-$N'$-$p$-tolylbenzohydrazide (7b)
$N^\prime$-(4-chlorophenyl)-$N^\prime$-phenylbenzohydrazide (7c)
$N'$-phenyl-$N'$-m-tolyldihydrazide (7d)
$N'\text{-}(3\text{-chlorophenyl})-N'\text{-phenylbenzohydrazide (7e)}$
$N'$(naphthalen-2-yl)-$N'$-phenylbenzohydrazide (7f)
$N'(4\text{-bromophenyl})$-$N'(4\text{-methoxyphenyl})$benzohydrazide (7g)
$N'-(4$-methoxyphenyl)-$N'-p$-tolylbenzohydrazide (7h)$
$N'(4$-methoxyphenyl)$-N'(4$-nitrophenyl)$benzohydrazide$ (7i)
$N'-(2$-methoxyphenyl)$-N'-(4$-methoxyphenyl)$benzohydrazide$ (7j)$
4-bromo-N'(4-methoxyphenyl)-N'phenylbenzohydrazide (7k)
tert-butyl 2-(4-methoxyphenyl)-2-phenylhydrazinecarboxylate (7l)