

Supporting Information

Nickel-Catalyzed *N*-Arylation of Benzophenone Hydrazone with Bromoarenes

Wei Wu,^[a,b] Xin-Heng Fan,^{*[a]} Li-Peng Zhang,^[a,b] and Lian-Ming Yang^{*[a]}

^[a]Beijing National Laboratory for Molecular Sciences (BNLMS), Key laboratory of Green Printing, Institute of Chemistry, Chinese Academy of Sciences, Beijing 100190, P. R. China

Fax: +8610-62559373; E-mail: yanglm@iccas.ac.cn

^[b]Graduate School of Chinese Academy of Sciences, Beijing 100049, P. R. China

1. General considerations

¹H NMR spectra were recorded on a BRUKER AVANCE 400 or 300 spectrometers. Chemical shifts are reported in ppm from the tetramethylsilane with the solvent resonance as internal standard. Data are reported as follows: chemical shift in ppm (δ), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, and m = multiplet), and coupling constant (Hz). ¹³C NMR spectra were collected on commercial instruments (100 MHz or 75 MHz) with complete proton decoupling. Chemical shifts are reported in ppm from the tetramethylsilane with the solvent resonance as internal standard. Mass spectra were obtained on a Bruker Daltonics Inc. APEXII FT-ICR. Melting points were measured with an X-4 micro melting-point apparatus and uncorrected. Elemental analysis was received with a Carlo Erba-1106 elemental analyzer.

All catalytic reactions were carried out in oven-dried glassware under nitrogen atmosphere and heated in an oil bath. All solvents and reagents were purchased commercially and used without further purification unless otherwise mentioned. Column chromatography was performed on Al₂O₃ (basic, 200–300 mesh). All yields were referred to isolated yields of compounds. The known compounds were partly characterized by melting points (if solid), MS and ¹H NMR, and compared to authentic samples or the literature data. New compounds were characterized by ¹H and ¹³C NMR, MS, and HRMS.

2. Experimental procedures and spectroscopic data

Synthesis of benzophenone hydrazone.^[1] A mixture of benzophenone (1.3 g, 7.3 mmol) and aqueous hydrazine solution (85%, 5 mL) in ethanol (20 mL) was heated to reflux overnight. The solvent was removed in vacuo and the residue was recrystallized from ethanol, affording benzophenone hydrazone (1.2 g, 86%); white solid: 96–97 °C. ¹H NMR (400 MHz, CDCl₃): 7.52–7.41 (m, 5H), 7.28–

7.22 (m, 5H), 5.32 (s, 2H); ^{13}C NMR (100 MHz, CDCl_3): 149.2, 138.5, 133.1, 129.5, 129.0, 128.9, 128.2, 128.1, 126.5.

General procedure for nickel-catalyzed cross-couplings of benzophenone hydrazone with aryl bromines. An oven-dried 25-mL three-necked flask was charged with benzophenone hydrazone (1.3 mmol), $\text{Ni}(\text{PPh}_3)_2\text{Cl}_2$ (0.05 mmol), IPrHCl (0.10 mmol), and $t\text{-BuONa}$ (1.3 mmol). The flask was evacuated and backfilled with nitrogen, with the operation being repeated twice. A solution of the aryl bromine **1** (1.0 mmol) in dioxane (2.5 mL) was added via syringe, and stirred at an oil bath of $50\text{ }^\circ\text{C}$ for 5 h. The reaction mixture was diluted with H_2O (20 mL) and ethyl acetate (30 mL). The organic layer was separated, washed sequentially with brine (40 mL) and water (40 mL), and dried over anhydrous Na_2SO_4 . Concentration under vacuum gave the crude material which was purified by Al_2O_3 column chromatography (petroleum ether/EtOAc, 10:1) to give the desired product **2** with the yields as listed in Table 2 of the text.

1-(*p*-Tolyl)-2-(diphenylmethylene)hydrazine (2a).^[2] Yellow sticky. ^1H NMR (400 MHz, CDCl_3): 7.64–7.50 (m, 5H), 7.48 (s, 1H), 7.38–7.26 (m, 5H), 7.08 (d, $J = 8.0$ Hz, 2H), 7.01 (d, $J = 8.0$ Hz, 2H), 2.30 (s, 3H). MS (EI, m/z , rel.%): 77 (26%), 105 (100%), 182 (44%), 286 (M^+ , 3%).

1-(*m*-Tolyl)-2-(diphenylmethylene)hydrazine (2b). Yellow sticky. ^1H NMR (300 MHz, CDCl_3): 7.60–7.48 (m, 5H), 7.45 (s, 1H), 7.34–7.30, (m, 5H), 7.13 (t, $J = 7.7$ Hz, 1H), 6.91 (s, 1H), 6.88 (d, $J = 7.8$ Hz, 1H), 6.67 (d, $J = 7.3$ Hz, 1H), 2.31 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3): 144.6, 144.0, 139.1, 138.5, 132.9, 129.7, 129.3, 129.2, 129.1, 128.2, 128.0, 126.5, 120.1, 113.5, 110.2, 21.6; MS (EI, m/z , rel.%): 44 (53%), 77 (28%), 180 (100%), 286 (M^+ , 68%). HRMS calcd for $\text{C}_{21}\text{H}_{20}\text{N}_2\text{O}_2$: 286.1470; Found: 286.1473.

1-(*o*-Tolyl)-2-(diphenylmethylene)hydrazine (2c).^[3] Yellow solid: mp $84\text{--}85\text{ }^\circ\text{C}$. ^1H NMR (400 MHz, CDCl_3): 7.71 (d, $J = 8.0$ Hz, 1H), 7.64 (t, $J = 6.0$ Hz, 2H), 7.60 (d, $J = 8.0$ Hz, 2H), 7.53 (t, $J = 6.0$ Hz, 1H), 7.47 (s, 1H), 7.39–7.31 (m, 5H), 7.25 (t, $J = 8.0$ Hz, 1H), 7.02 (d, $J = 8.0$ Hz, 1H), 6.80 (t, $J = 8.0$ Hz, 1H). MS (EI, m/z , rel.%): 77 (42%), 106 (57%), 180 (100%), 286 (M^+ , 68%).

1-Phenyl-2-(diphenylmethylene)hydrazine (2d). [CAS: 574-61-8] Yellow solid: mp $134\text{--}135\text{ }^\circ\text{C}$ (lit ⁽⁴⁾. mp $134\text{--}136\text{ }^\circ\text{C}$). ^1H NMR (300 MHz, CDCl_3): 7.65–7.50 (m, 5H), 7.49 (s, 1H), 7.32 (t, $J = 7.8$ Hz, 5H), 7.25 (t, $J = 7.5$ Hz, 2H), 7.11 (d, $J = 7.8$ Hz, 2H), 6.88 (t, $J = 7.4$ Hz, 1H); ^{13}C NMR (75 MHz, CDCl_3): 144.7, 144.2, 138.4, 132.8, 129.8, 129.3, 129.2, 128.3, 128.1, 126.5, 120.1, 113.0, MS (EI, m/z , rel.%): 77 (21%), 180 (79%), 272 (M^+ , 100%).

1-(4-Anisyl)-2-(diphenylmethylene)hydrazine (2e).^[5] Yellow sticky. ^1H NMR (400 MHz, CDCl_3): 7.59 (t, $J = 8.0$ Hz, 4H), 7.52 (t, $J = 8.0$ Hz, 1H), 7.39 (s, 1H), 7.36–7.28 (m, 5H), 7.05 (d, $J = 8.0$ Hz, 2H), 6.85 (d, $J = 8.0$ Hz, 2H), 3.79 (s, 3H). MS (EI, m/z , rel.%): 122 (67%), 180 (75%), 300 (100%), 302 (M^+ , 58%).

1-(3-Anisyl)-2-(diphenylmethylene)hydrazine (2f).^[2] Yellow solid: mp 102–103 °C. ¹H NMR (400 MHz, CDCl₃): 7.63–7.56 (m, 4H), 7.53 (d, *J* = 8.0 Hz, 1H), 7.48 (s, 1H), 7.34–7.28 (m, 5H), 7.13 (t, *J* = 8.0 Hz, 1H), 6.78 (t, *J* = 2.0 Hz, 1H), 6.56 (d, *J* = 8.0 Hz, 1H), 6.41 (dd, *J* = 8.0, 2.0 Hz, 1H), 3.82 (s, 3H). MS (EI, *m/z*, rel.%): 77 (37%), 180 (100%), 302 (M⁺, 59%).

1-(2-Anisyl)-2-(diphenylmethylene)hydrazine (2g).^[3] Yellow solid: mp 155–156 °C. ¹H NMR (300 MHz, CDCl₃): 7.99 (s, 1H), 7.68 (d, *J* = 9.0 Hz, 1H), 7.63–7.47 (m, 5H), 7.36–7.25 (m, 5H), 6.98 (t, *J* = 6.0 Hz, 1H), 6.83–6.72 (m, 2H), 3.67 (s, 3H); ¹³C NMR (75 MHz, CDCl₃): 145.4, 144.9, 138.6, 134.3, 133.1, 129.6, 129.1, 128.1, 127.9, 126.6, 121.6, 119.2, 112.4, 110.1, 55.6; MS (ESI, *m/z*, rel.%): 77 (100%), 180 (19%), 302 (M⁺, 16%).

1-(2,4-Dimethoxyphenyl)-2-(diphenylmethylene)hydrazine (2h). Yellow solid: mp 115–117 °C. ¹H NMR (300 MHz, CDCl₃): 7.77 (s, 1H), 7.60–7.54 (m, 5H), 7.50 (d, *J* = 6.0 Hz, 1H), 7.35 (d, *J* = 7.5 Hz, 2H), 7.28 (t, *J* = 7.9 Hz, 3H), 6.53 (d, *J* = 9.0 Hz, 1H), 6.41 (s, 1H), 3.78 (s, 3H), 3.66 (s, 3H); ¹³C NMR (75 MHz, CDCl₃): 153.8, 146.5, 144.1, 138.8, 133.3, 129.6, 129.2, 129.1, 128.7, 128.2, 127.8, 126.5, 112.8, 104.7, 99.1, 55.9, 55.7; MS (EI, *m/z*, rel.%): 180 (100%), 332 (M⁺, 18%). HRMS calcd for C₂₁H₂₀N₂O₂: 332.1525; Found: 332.1528.

1-(4-Fluorophenyl)-2-(diphenylmethylene)hydrazine (2i).^[5] Yellow sticky. ¹H NMR (400 MHz, CDCl₃): 7.61–7.57 (m, 4H), 7.54–7.51 (m, 1H), 7.42 (s, 1H), 7.35–7.29 (m, 5H), 7.05–7.00 (m, 2H), 6.96 (t, *J* = 8.0 Hz, 2H). MS (EI, *m/z*, rel.%): 77 (24%), 180 (100%), 290 (M⁺, 75%).

1-(4-Chlorophenyl)-2-(diphenylmethylene)hydrazine (2j).^[2] Yellow solid: mp 116–117 °C. ¹H NMR (400 MHz, CDCl₃): 7.62–7.49 (m, 5H), 7.46 (s, 1H), 7.35–7.27 (m, 5H), 7.19 (d, *J* = 8.0 Hz, 2H), 7.01 (d, *J* = 8.0 Hz, 2H). MS (EI, *m/z*, rel.%): 77 (28%), 180 (100%), 306 (M⁺, 58%), 308 ([M+2]⁺, 10%).

1-(3-Chlorophenyl)-2-(diphenylmethylene)hydrazine (2k). Yellow sticky. ¹H NMR (400 MHz, CDCl₃): 7.63–7.51 (m, 5H), 7.48 (s, 1H), 7.36–7.28 (m, 5H), 7.16 (s, 1H), 7.12 (d, *J* = 8.0 Hz, 1H), 6.87 (dd, *J* = 8.0, 1.1 Hz, 2H), 6.80 (dd, *J* = 8.0, 1.1 Hz, 2H); ¹³C NMR (100 MHz, CDCl₃): 145.8, 145.5, 138.1, 135.2, 132.6, 130.2, 129.8, 129.5, 129.1, 128.5, 128.3, 128.2, 126.7, 119.9, 113.0, 111.2. MS (EI, *m/z*, rel.%): 77 (31%), 180 (100%), 306 (M⁺, 69%), 308 ([M+2]⁺, 15%). HRMS calcd for C₁₉H₁₅ClN₂: 306.0924; Found: 306.0927.

1-(4-Bromophenyl)-2-(diphenylmethylene)hydrazine (2l).^[2] Yellow sticky. ¹H NMR (300 MHz, CDCl₃): 7.63–7.53 (m, 5H), 7.47 (s, 1H), 7.37–7.28 (m, 7H), 6.97 (d, *J* = 8.7 Hz, 2H). MS (EI, *m/z*, rel.%): 77 (30%), 180 (100%), 350 (M⁺, 50%), 352 ([M+2]⁺, 37%).

1-{4-[*N,N*-Di(*p*-tolyl)amino]phenyl}-2-(diphenylmethylene)hydrazine (2m). [CAS: 1020717-64-9] Yellow solid: mp 152–155 °C. ¹H NMR (400 MHz, CDCl₃): 7.62–7.49 (m, 5H), 7.44 (s, 1H), 7.34–7.28 (m, 5H), 7.08–6.83 (m, 12H), 2.28 (s, 6H); ¹³C NMR (75 MHz, CDCl₃): 146.1, 144.1, 141.0, 140.8, 138.6, 133.0, 131.2, 129.8, 129.3, 128.4, 128.1, 126.8, 126.6, 123.1, 114.0, 20.9. MS (EI, *m/z*, rel.%):

180 (27%), 288 (34%), 465 (100%), 467(M^+ , 5%). HRMS calcd for $C_{33}H_{29}N_3$: 467.2361; Found: 467.2368.

1-(1-Naphthyl)-2-(diphenylmethylene)hydrazine (2n).^[2] Yellow solid: mp 105–106 °C. 1H NMR (400 MHz, $CDCl_3$): 8.19 (s, 1H), 7.78 (t, $J = 8.0$ Hz, 2H), 7.72–7.55 (m, 5H), 7.51–7.44 (m, 3H), 7.42–7.36 (m, 3H), 7.34–7.29 (m, 3H), 7.24 (d, $J = 8.0$ Hz, 1H). MS (EI, m/z, rel.%): 77 (34%), 115 (51%), 180 (100%), 322 (M^+ , 49%).

1-(2-Naphthyl)-2-(diphenylmethylene)hydrazine (2o). [CAS: 265099-34-1]. Yellow solid: mp 154–155 °C. 1H NMR (400 MHz, $CDCl_3$): 7.71 (t, $J = 8.0$ Hz, 3H), 7.67 (s, 1H), 7.66–7.58 (m, 4H), 7.57–7.52 (m, 1H), 7.45 (d, $J = 4.0$ Hz, 1H), 7.42–7.35 (m, 4H), 7.34–7.23 (m, 4H). MS (EI, m/z, rel.%): 77 (23%), 115 (43%), 180 (100%), 322 (M^+ , 90%).

1-(3-Thienyl)-2-(diphenylmethylene)hydrazine (2p). Yellow solid: mp 205–207 °C. 1H NMR (400 MHz, $CDCl_3$): 7.60–7.45 (m, 6H), 7.34–7.26 (m, 5H), 7.19 (dd, $J = 8.0, 4.0$ Hz, 1H), 6.85 (d, $J = 4.0$ Hz, 1H); 6.59 (d, $J = 4.0$ Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): 145.1, 144.7, 138.4, 132.9, 129.8, 129.4, 129.2, 128.3, 128.1, 126.6, 125.5, 118.3, 99.2. MS (EI, m/z, rel.%): 77 (22%), 180 (100%), 278 (M^+ , 62%). HRMS calcd for $C_{17}H_{14}N_2S$: 278.0878; Found: 278.0881.

General procedure for the preparation of arylhydrazine hydrochlorides 3 from the hydrolysis of *N*-aryl benzophenone hydrazones 2. *N*-aryl benzophenone hydrazone (0.5 mmol) was stirred at room temperature in HCl/ethanol (6 mL, 10:1 v/v) for 24 h. The reaction mixture was extracted with CH_2Cl_2 (15 mL \times 3), and the combined CH_2Cl_2 solutions was concentrated to afford the crude product, which was further washed with dichloromethane to give the purified product 3.

***p*-Tolyldiazine hydrochloride (3a).** [CAS: 637-60-5] White solid: 98–100 °C, 48% yield. 1H NMR (300 MHz, DMSO): 10.23 (br. s, 3H), 7.09 (d, $J = 9.0$ Hz, 2H), 6.92 (d, $J = 9.0$ Hz, 2H), 2.22 (s, 3H). MS (ESI, m/z, rel.%): 106 (42%), 123 ($[M+1]^+$, 100%).

Phenyldiazine hydrochloride (3b). [CAS: 61929-58-6] White solid: 222–224 °C, 56% yield. 1H NMR (400 MHz, $CDCl_3$): 10.37 (s, 3H), 7.27 (t, $J = 8.0$ Hz, 2H), 7.02 (d, $J = 8.0$ Hz, 2H), 4.09 (t, $J = 8.0$ Hz, 1H). MS (ESI, m/z, rel.%): 109 ($[M+1]^+$, 100%).

(4-Fluorophenyl)diazine hydrochloride (3c). [CAS: 823-85-8] Brown liquid, 35% yield. 1H NMR (300 MHz, DMSO): 10.31 (br. s, 3H), 7.14 (t, $J = 9.0$ Hz, 2H), 7.06 (d, $J = 9.0$ Hz, 1H), 7.05 (d, $J = 9.0$ Hz, 1H), MS (ESI, m/z, rel.%): 127 ($[M+1]^+$, 100%).

General procedure for the preparation of *N*-aryl pyridine-2-aldehyde hydrazones 4 from *N*-aryl benzophenone hydrazones 2. A mixture of *N*-aryl benzophenone hydrazone (1 mmol) and picolinaldehyde (1.5 mmol) in ethanol (5 mL) containing hydrochloric acid (concd., 0.5 mL) was stirred at room temperature for 24 h. Purification of the crude product by flash chromatography (10% EtOAc/hexanes) afforded the desired products 4.

(E)-1-(4-Anisyl)-2-(pyridin-2-ylmethylene)hydrazine (4a). [CAS: 78893-15-9] Yellow solid: 97% yield. ^1H NMR (400 MHz, CDCl_3): 8.51 (d, $J = 4.0$ Hz, 1H), 8.11 (br. s, 1H), 7.95 (d, $J = 8.0$ Hz, 1H), 7.81 (s, 1H); 7.69 (t, $J = 8.0$ Hz, 1H), 7.16 (t, $J = 8.0$ Hz, 1H), 7.09 (d, $J = 8.0$ Hz, 2H), 6.85 (d, $J = 8.0$ Hz, 2H), 3.77 (s, 3H). MS (EI, m/z , rel.%): 122 (83%), 227 (M^+ , 100%).

(E)-1-(4-Fluorophenyl)-2-(pyridin-2-ylmethylene)hydrazine (4b). [CAS: 518342-23-9] Yellow solid: 86% yield. ^1H NMR (400 MHz, CDCl_3): 8.52 (d, $J = 8.0$ Hz, 1H), 8.14 (s, 1H), 7.95 (d, $J = 8.0$ Hz, 1H), 7.81 (s, 1H), 7.69 (t, $J = 8.0$ Hz, 1H), 7.17 (t, $J = 8.0$ Hz, 1H), 7.12–7.05 (m, 2H), 6.97 (t, $J = 8.0$ Hz, 2H). MS (EI, m/z , rel.%): 92 (28%), 215 (M^+ , 100%).

(E)-1-(2-Naphthyl)-2-(pyridin-2-ylmethylene)hydrazine (4c). [CAS: 385408-14-0] Yellow solid: mp 163–165 $^\circ\text{C}$, 94% yield. ^1H NMR (300 MHz, CDCl_3): 8.56 (d, $J = 6.0$ Hz, 1H), 8.35 (br. s, 1H), 8.03 (d, $J = 6.0$ Hz, 1H), 7.90 (s, 1H), 7.80–7.68 (m, 4H), 7.52 (s, 1H), 7.45–7.35 (m, 2H), 7.30 (t, $J = 6.0$ Hz, 1H), 7.20 (t, $J = 6.0$ Hz, 1H). MS (EI, m/z , rel.%): 115 (93%), 143 (77%), 169 (50%), 218 (44%), 247 (M^+ , 100%).

General procedure for the Fischer Cyclization of *N*-aryl benzophenone hydrazones **2 to Indoles **5**.** *N*-aryl benzophenone hydrazone (1 mmol) was refluxed with a ketone (1.5 mmol) and *p*-TsOH·H₂O (2.0 mmol) or concd. hydrochloric acid (0.2 mL) in ethanol (5 mL) for 24 h until complete conversion (monitored by TLC). Purification of the crude product by flash chromatography (70% EtOAc/hexanes) afforded the desired product **5**.

6-Methoxy-2,3-dimethyl-1H-indole (5a).^[2] Brown solid: 68–70 $^\circ\text{C}$, 53% yield. ^1H NMR (400 MHz, CDCl_3): 7.60 (s, 1H), 7.36 (d, $J = 8.0$ Hz, 1H), 6.79 (s, 1H), 6.77 (dd, $J = 8.0, 4.0$ Hz, 1H), 3.84 (s, 3H), 2.71 (q, $J = 7.6$ Hz, 2H), 2.22 (s, 3H), 1.25 (t, $J = 8.0$ Hz, 3H). MS (EI, m/z , rel.%): 174 (100%), 189 (M^+ , 27%).

3-Fluoro-6,7,8,9-tetrahydro-5H-carbazole (5b). [CAS: 2367-17-1]. Yellow solid: 134–136 $^\circ\text{C}$, 66% yield. ^1H NMR (400 MHz, CDCl_3): 9.64 (s, 1H), 7.33 (dd, $J = 8.0, 4.0$ Hz, 1H), 7.08 (dd, $J = 8.0, 4.0$ Hz, 2H), 6.99 (dt, $J = 8.0, 4.0$ Hz, 1H), 2.80–2.65 (m, 2H), 2.52 (dd, $J = 8.0, 4.0$ Hz, 1H), 2.20–2.10 (m, 1H), 1.91–1.80 (m, 1H), 1.66–1.56 (m, 1H), 1.45–1.34 (m, 1H), 1.28 (dt, $J = 8.0, 4.0$ Hz, 1H). MS (EI, m/z , rel.%): 189 [M^+].

2-Ethyl-3-methyl-1H-indole (5c). [CAS: 19013-49-1]. White solid: 132–134 $^\circ\text{C}$, 60% yield. ^1H NMR (300 MHz, $\text{DMSO}-d_6$): 11.6 (s, 1H), 7.39 (t, $J = 6.3$ Hz, 2H), 7.32 (t, $J = 6.9$ Hz, 1H), 7.19 (t, $J = 7.2$ Hz, 1H), 2.69–2.52 (m, 2H), 1.35 (s, 3H), 1.24 (t, $J = 7.2$ Hz, 3H). MS (EI, m/z , rel.%): 159 (M^+ , 100%).

3. Reference

- [1] H. B. Wang, L. Sun, X. N. Li, J. L. Duan, W. Pei, *Synth. Commun.* **2011**, *41*, 3223–3227.
- [2] S. Wagaw, B. H. Yang, S. L. Buchwald, *J. Am. Chem. Soc.* **1999**, *121*, 10251–10263.































