Supporting Information

Copper(II)-Catalyzed Selective Reductive Methylation of Amines with Formic Acid: An Option for Indirect Utilization of CO_2

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1. General information.

The starting materials were commercially available and were used without further purification. Solvents were dried and degassed by standard methods before use. The products were isolated by column chromatography on silica gel (200-300 mesh) using petroleum ether and ethyl acetate mixtures. 1 H NMR and 13 C NMR spectra were recorded on a Bruker Avance 400 spectrometer at ambient temperature. All chemical shifts are reported relative to tetramethylsilane (0.0 ppm for 1 H NMR in CDCl₃) and d-solvent peaks (77.00 ppm for 13 C NMR, CDCl₃), respectively. 1 H NMR peaks are labeled as singlet (s), doublet (d), triplet (t), and multiplet (m). The coupling constants J are reported in Hertz (Hz). GC-MS data were performed on Finnigan HP G1800 A. GC analyses were performed on a Shimadzu GC-2014 equipped with a capillary column (RTX-Wax 30 m × 0.25 μ m) using a flame ionization detector.

2. Experimental Section

General Procedure for reductive methylation of amines (taking secondary amine as an example)

In a 10 mL Schlenk tube, Cu(OAc)₂ (0.025 mmol, 4.6 mg) were dissolved in dry *n*Bu₂O (1.0 mL). After the mixture had been stirred for 5 min, PhSiH₃ (1.5 mmol, 185 μL) was added via a microsyringe, following with amines (0.5 mmol) and HCOOH (0.75 mmol, 28 μL). A bubble gas generation was observed when HCOOH was added. The reaction mixture was stirred for 8 h at 80 °C. After completion, the mixture was diluted with ethyl acetate (5 mL), then quenched with aqueous NaOH (3 M solution; 3 mL) carefully, and stirred for 3 h at room temperature. The mixture was extracted with ethyl acetate (three times) and the combined organic layers were dried over Na₂SO₄ anhydrous. Finally, the organic phase was filtered, concentrated, and purified by silica gel column chromatography (petroleum ether/ethyl acetate mixtures) to give the corresponding methylated amines. All catalytic reactions were performed at least twice to ensure reproducibility.

General Procedure for reductive methylation of *n*-butylamine

In a 10 mL tube with a screw cap, $Cu(OAc)_2$ (0.001 mmol, 1.9 mg) were dissolved in dry nBu_2O (1.0 mL). After the mixture was stirred for 5 min, PhSiH₃ (1.2 mmol, 123 µL) was added via a microsyringe, following with n-butylamine (0.2 mmol, 20 µL) and HCOOH (0.5 mmol, 18 µL). A bubble gas generation was observed when HCOOH was added. The reaction mixture was stirred for 16 h at 80 °C. After completion, the conversion and yield was determined by 1 H NMR using 1,3,5-trimethoxybenzene as internal standard. This reaction was conducted on 10 mmol scale to isolate the product $\bf 3p$ by distillation, and $\bf 3p$ was isolated as a colorless liquid. The byproduct $\bf N$ -methylbutylamine ($\bf 1p$) could be isolated by similar distillation as a colorless liquid.

Procedure for reductive methylation of 1a on a gram-scale

In a 100 mL one-neck flask, $Cu(OAc)_2$ (0.5 mmol, 91 mg) were dissolved in dry nBu_2O (20.0 mL). After the mixture had been stirred for 5 min, $PhSiH_3$ (30.0 mmol) was added, following with **1a** (10.0 mmol) and HCOOH (15.0 mmol). A bubble gas generation was observed when HCOOH was added. After the work-up process (mentioned above), the organic phase was filtered, concentrated, and purified by silica gel column chromatography (petroleum ether/ethyl acetate mixtures) to give the corresponding **3a** in 86% isolated yield (1.0423 g).

3. Investigation of the Key Reaction Parameters

Table S1 Variation of the catalyst loading^a

entry	catalyst loading	conv (%)	yield of 2a (%) ^b	yield of 3a (%) ^b	
1	5%	>99	0	99	
2	3%	99	42	52	
3	1%	92	52	39	

^aReaction conditions: 1a (0.5 mmol), HCOOH (1.5 equiv), PhSiH₃ (3.0 equiv), nBu₂O (1.0 mL), 80°C, 12 h.

Table S2 Variation of the amount of formic acid and phenylsilane^a

entry	HCOOH [equiv]	PhSiH ₃ [equiv]	conv (%)	yield of 2a (%) ^b	yield of 3a (%) ^b
1	1.1	3.0	85	0	83
2	1.3	3.0	96	0	96
3	1.5	3.0	>99	0	99
4	1.5	2.0	>99	13	82

^aReaction conditions: **1a** (0.5 mmol), $Cu(OAc)_2$ (5 mol %, 4.6 mg), nBu_2O (1.0 mL), 80 °C, 12 h. ^bDetermined by GC using 1,3,5-trimethoxybenzene as an internal standard.

Table S3 Influence of reaction time and reaction temperature^a

entry	catalyst	T/℃	t/h	conv (%)	yield of $2a (\%)^b$	yield of $3a (\%)^b$
1	Cu(OAc) ₂	60	12	99	10	84
2	$\operatorname{Cu(OTf)}_2$	60	12	98	86	12
3	CuF ₂	60	12	95	66	27

^aReaction conditions: **1a** (0.5 mmol), catalyst (5 mol %), HCOOH (1.5equiv), PhSiH₃ (3.0 equiv), nBu_2O (1 mL). ^bDetermined by GC using 1,3,5-trimethoxybenzene as an internal standard.

^bDetermined by GC using 1,3,5-trimethoxybenzene as an internal standard.

Table S4 Influence of the solvent in the catalytic methylation of 1a^a

entry	solvent	conv (%)	yield of 2a (%) ^b	yield of 3a (%) ^b
1	toluene	>99	0	99
2	Et_2O	>99	25	74
3	1,4-dioxane	>99	42	54
4	THF	87	34	52
5	DMF	70	27	27
6	CH ₃ CN	>99	92	trace

^aReaction Conditions: **1a** (0.5 mmol), HCOOH (1.5 equiv), PhSiH₃ (3.0 equiv), Cu(OAc)₂ (5 mol %, 4.6 mg), solvent (1.0 mL), 80 °C, 12 h. ^bDetermined by GC using 1,3,5-trimethoxybenzene as an internal standard.

Table S5 Screening of silanes^a

entry	hydrosilane	conv (%)	yield of 2a (%) ^b	yield of 3a (%) ^b
1	-	51	49	0
2	$PhSiH_3$	>99	0	>99
3	Ph_2SiH_2	31	31	0
4	(EtO) ₂ CH ₃ SiH	63	60	0
5	(EtO) ₃ SiH	79	79	0
6	PMHS	31	29	0
7	Et ₃ SiH	27	27	0

^aConditions: **1a** (0.5 mmol), HCOOH (1.5 equiv), hydrosilane (3.0 equiv), Cu(OAc)₂ (5 mol %, 4.6 mg), *n*Bu₂O (1.0 mL), 80 °C, 12 h. ^bDetermined by GC using 1,3,5-trimethoxybenzene as an internal standard.

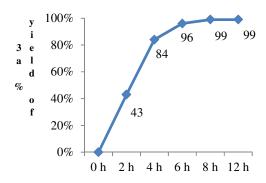


Figure S1. Influence of reaction time.

4. Experimental procedures for control experiment.

In a 10 mL Schlenk tube, Cu(OAc) (5.0 mol%, 4.6 mg) were dissolved in dry *n*Bu₂O (1.0 mL). After the mixture had been stirred for 5 min, PhSiH₃ (1.5 mmol, 185 μL) was added via a microsyringe, following with (1) *N*-methylformanilide (0.5 mmol, 62 μL). (2) *N*-methylaniline (0.5 mmol, 54 μL) and methanol (0.75 mmol). (3) *N*-methylaniline (0.5 mmol, 54 μL), paraformaldehyde (0.75 mmol, 0.0225 g) was added with catalyst. The reaction mixture was stirred at 80 °C, respectively. For control experiment (4), in a 10 mL Schlenk tube, Cu(OAc) (5.0 mol%, 4.6 mg) were dissolved in dry *n*Bu₂O (1.0 mL). After the mixture had been stirred for 5 min, HCOOH (0.75 mmol) and PhSiH₃ (0.5 mmol) were added via microsyringes, and the reaction mixture was stirred at 80 °C.

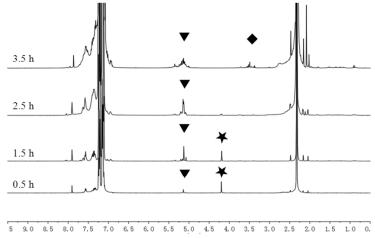


Figure S2. ¹H NMR spectra from the reaction of formic acid (FA), PhSiH₃ (2 equivalent of Si-H) and Cu(OAc)_2 catalyst in toluene. methoxide products \spadesuit , PhSiH₃ \bigstar , bis(silyl)acetal \blacktriangledown .

Scheme S1. The Cu(OAc)₂-catalyzed N-methylation of benzylidene phenylamine with formic acid

Scheme S2 Control experiment to exclude the Eschweiler-Clarke mechanism in the reduction of F to G

5. Characterization Data for the Products.

N,N-dimethylaniline (3a, 3m)¹



Light yellow liquid, 58.7 mg, 97% yield of 3a

¹H NMR (400 MHz, CDCl₃) δ 7.24 (dd, J = 8.8, 7.3 Hz, 2H), 6.85 – 6.62 (m, 3H), 2.94 (s, 6H). ¹³C NMR (101 MHz, CDCl₃) δ 150.6, 129.0, 116.6, 112.6, 40.6. GC-MS (EI, 70 eV) m/z (%) 121.15 (81.29), 120.15 (100.00), 77.05 (29.56).

eluent: petroleum ether/ ethyl acetate = 50/1

4-Methyl-*N*,*N*-dimethylaniline (3b)¹

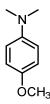


Light yellow liquid, 66.1 mg, 98% yield

¹H NMR (400 MHz, CDCl₃) δ 7.05 (d, J = 8.1 Hz, 2H), 6.69 (d, J = 8.2 Hz, 2H), 2.89 (s, 6H), 2.25 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 148.8, 129.5, 126.1, 113.2, 41.1, 20.2. GC-MS (EI, 70 eV) m/z (%) 35.20 (77.14), 134.15 (100.00), 91.10 (22.96).

eluent: petroleum ether/ ethyl acetate = 50/1

4-Methoxy-N,N-dimethylaniline (3c, 3o)²

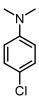


White solid, mp=46–48 °C, 69.5 mg, 92% yield of 3c

¹H NMR (400 MHz, CDCl₃) δ 6.88 – 6.81 (m, 2H), 6.79 – 6.72 (m, 2H), 3.76 (s, 3H), 2.86 (s, 6H). ¹³C NMR (101 MHz, CDCl₃) δ 152.1, 145.5, 115.0, 114.6, 55.7, 41.9. GC-MS (EI, 70 eV) m/z (%) 151.25 (59.49), 136.20 (100.00).

eluent: petroleum ether/ ethyl acetate = 50/1

4-Chloro-*N*,*N*-dimethylaniline (3d)¹



Yellow liquid, 67.4 mg, 87% yield

¹H NMR (400 MHz, CDCl₃) δ 7.17 (d, J = 8.9 Hz, 2H), 6.64 (d, J = 8.7 Hz, 2H), 2.92 (s, 6H). ¹³C NMR (101 MHz, CDCl₃) δ 149.1, 128.8, 121.4, 113.6, 40.6. GC-MS (EI, 70 eV) m/z (%) 157.10 (25.27), 156.10 (39.00), 155.10 (82.99), 154.10 (100.00).

eluent: petroleum ether/ ethyl acetate = 50/1

N-ethyl-N-methylaniline $(3f)^2$



Yellow liquid, 62.1 mg, 92% yield

¹H NMR (400 MHz, CDCl₃) δ 7.22 (t, J = 7.7 Hz, 2H), 6.84 – 6.52 (m, 3H), 3.39 (q, J = 7.0 Hz, 2H), 2.89 (s, 3H), 1.10 (t, J = 7.1 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 149.1, 129.1, 116.0, 112.3, 46.8, 37.4, 11.1. GC-MS (EI, 70 eV) m/z (%) 135.15 (31.98), 120.15 (100.00), 77.05 (33.12).

eluent: petroleum ether/ ethyl acetate = 50/1

N-Isopropyl-N-methylaniline $(3g)^2$



Yellow liquid, 34.3 mg, 46% yield

¹H NMR (400 MHz, CDCl₃) δ 7.22 (t, J = 7.9 Hz, 2H), 6.79 (d, J = 8.2 Hz, 2H), 6.69 (t, J = 7.2 Hz, 1H), 4.18 – 3.96 (m, 1H), 2.72 (s, 3H), 1.15 (d, J = 6.6 Hz, 6H). ¹³C NMR (101 MHz, CDCl₃) δ 150.1, 129.1, 116.4, 113.3, 48.9, 29.8, 19.3. GC-MS (EI, 70 eV) m/z (%) 149.20 (19.30), 134.15 (100.00), 77.05 (20.49).

eluent: petroleum ether/ ethyl acetate = 100/1 to 50/1

N-benzyl-N-methylaniline $(3h)^2$



Yellow liquid, 84.7 mg, 86% yield

¹H NMR (400 MHz, CDCl₃) δ 7.38 – 7.27 (m, 2H), 7.27 – 7.15 (m, 5H), 6.79 – 6.64 (m, 3H), 4.53 (s, 2H), 3.01 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 149.7, 139.0, 129.1, 128.52, 126.8, 126.7, 116.5, 112.3, 56.6, 38.5. GC-MS (EI, 70 eV) m/z (%) 197.15 (79.61), 196.10 (25.26), 120.10 (71.12), 91.10 (100.00), 77.05 (27.50).

eluent: petroleum ether/ ethyl acetate = 100/1 to 50/1

N-allyl-N-methylaniline $(3i)^2$



Yellow liquid, 56.6 mg, 77% yield

¹H NMR (400 MHz, CDCl₃) δ 7.22 (t, J = 7.8 Hz, 2H), 6.87 – 6.54 (m, 1H), 6.84 – 6.59 (m, 3H), 5.84 (ddd, J = 22.1, 10.2, 5.1 Hz, 1H), 5.24 – 5.05 (m, 2H), 3.91 (d, J = 5.0 Hz, 2H), 2.93 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 149.4, 133.8, 129.1, 116.4, 116.1, 112.4, 55.2, 38.0. GC-MS (EI, 70 eV) m/z (%) 148.08 (70.11), 147.15 (100.00), 146.26 (25.67), 120.28 (34.38).

eluent: petroleum ether/ ethyl acetate = 100/1

N-(2-hydroxyethyl)-N-methylaminobenzene (3j)²



Brown liquid, 61.2 mg, 81% yield

¹H NMR (400 MHz, CDCl₃) δ 7.23 (t, J = 7.6 Hz, 2H), 6.81 – 6.70 (m, 3H), 3.77 (t, J = 5.6 Hz, 2H), 3.44 (t, J = 5.6 Hz, 2H), 2.93 (s, 3H), 2.15 (br, 1H). ¹³C NMR (101 MHz, CDCl₃) δ 149.9, 129.1, 117.1, 112.9, 59.9, 55.3, 38.7. GC-MS (EI, 70 eV) m/z (%) 151.20 (16.32), 120.10 (100.00), 77.05 (25.60).

eluent: petroleum ether/ ethyl acetate = 5/1

N-methylpiperidine $(3k)^3$



Less colour liquid

¹H NMR (400 MHz, CDCl₃) δ 2.33 (s, 4H), 2.24 (s, 3H), 1.68 – 1.51 (m, 4H), 1.41 (s, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 56.5, 46.9, 26.0, 23.7. GC-MS (EI, 70 eV) m/z (%) 99.15 (42.36), 98.15 (100.00), 71.10 (22.54).

N-methylmorpholine $(3l)^4$



Less colour liquid

¹H NMR (400 MHz, CDCl₃) δ 3.71 (t, J = 4.6 Hz, 4H), 2.41 (s, 4H), 2.29 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 66.7, 55.2, 46.2. GC-MS (EI, 70 eV) m/z (%) 101.15 (100.00), 100.15 (36.36), 71.10 (60.10).

4-Chloro-N,N-dimethylaniline (3n)¹



White solid, mp=55-57 °C

¹H NMR (400 MHz, CDCl₃) δ 7.30 (d, J = 9.1 Hz, 2H), 6.59 (d, J = 8.8 Hz, 2H), 2.92 (s, 6H). ¹³C NMR (101 MHz, CDCl₃) δ 149.5, 131.6, 114.1, 108.5, 40.5. GC-MS (EI, 70 eV) m/z (%) 201.00 (93.41), 200.00 (100.00), 199.00 (99.32), 198.00 (97.76), 118.15 (45.22), 77.10 (20.98).

eluent: petroleum ether/ ethyl acetate = 50/1

N,N-dimethylbutylamine $(3p)^4$



Colourless liquid.

¹H NMR (400 MHz, CDCl₃) δ 2.30 – 2.16 (m, 8H), 1.48 – 1.41 (m, 2H), 1.37-1.28 (m, 2H), 0.92 (t, J = 7.3 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 59.6, 45.5, 29.9, 20.6, 14.0. GC-MS (EI, 70 eV) 101.15 (100.00), 71.10 (12.15).

N-methylbutylamine $(4p)^5$



Colourless liquid

¹H NMR (400 MHz, CDCl₃) δ 2.57 (t, J = 7.0 Hz, 2H), 2.43 (s, 3H), 1.47 (m, 2H), 1.35 (m, 2H), 1.03 (s, 1H), 0.92 (t, J = 7.3 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ51.78, 36.42, 31.98, 20.30, 13.84. GC-MS (EI, 70 eV) 87.12 (100.00), 84.07 (25.46), 70.06 (21.72), 57.09 (64.71), 56.08 (49.95), 55.10 (22.88).

N-methylformanilide (2a)⁴



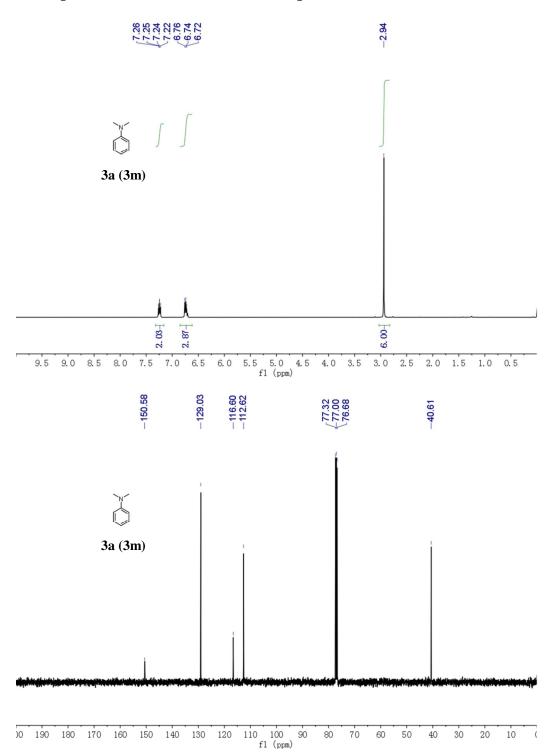
Yellow liquid

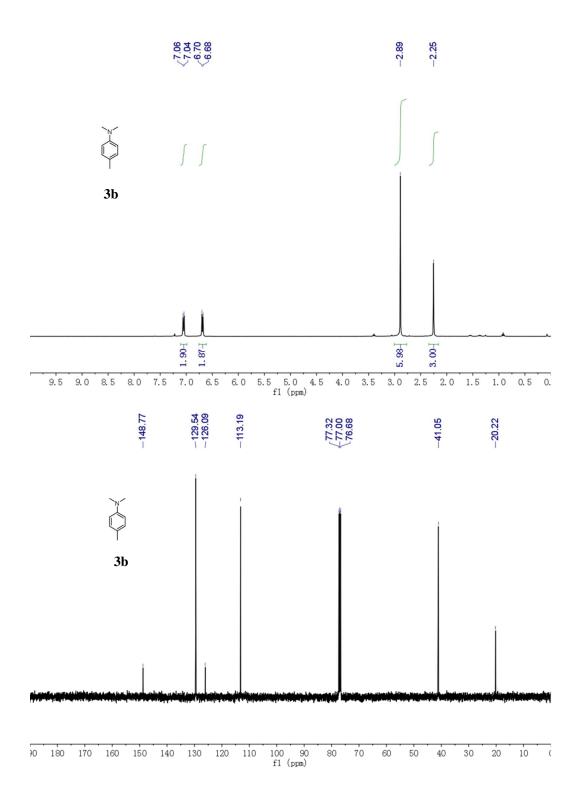
¹H NMR (400 MHz, CDCl₃) δ 8.46 (s, 1H), 7.40 (t, J = 7.8 Hz, 2H), 7.26 (dd, J = 10.0, 4.8 Hz, 1H), 7.16 (d, J = 7.5 Hz, 2H), 3.31 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 162.3, 142.1, 129.6, 126.4, 122.3, 32.0. GC-MS (EI, 70 eV) m/z (%) 135.15 (70.68), 106.10 (100.00), 94.10 (30.45), 79.10 (20.54), 77.10 (42.48), 66.05 (21.05).

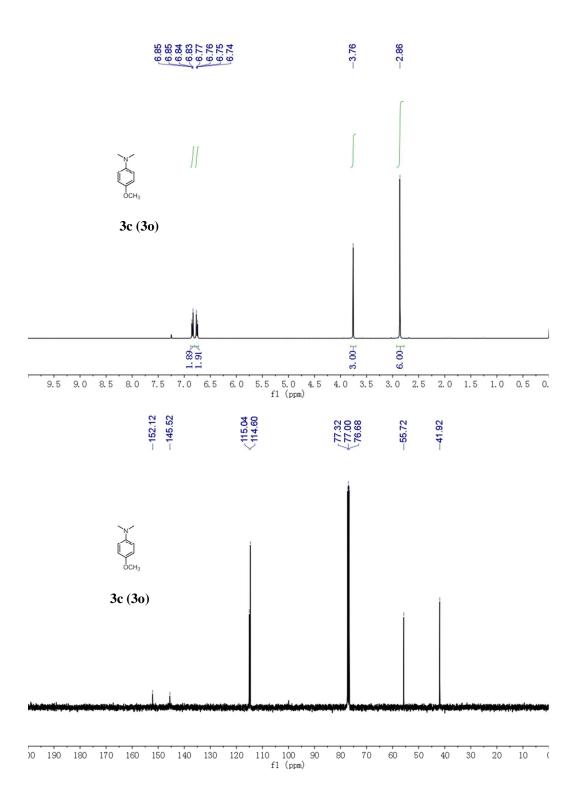
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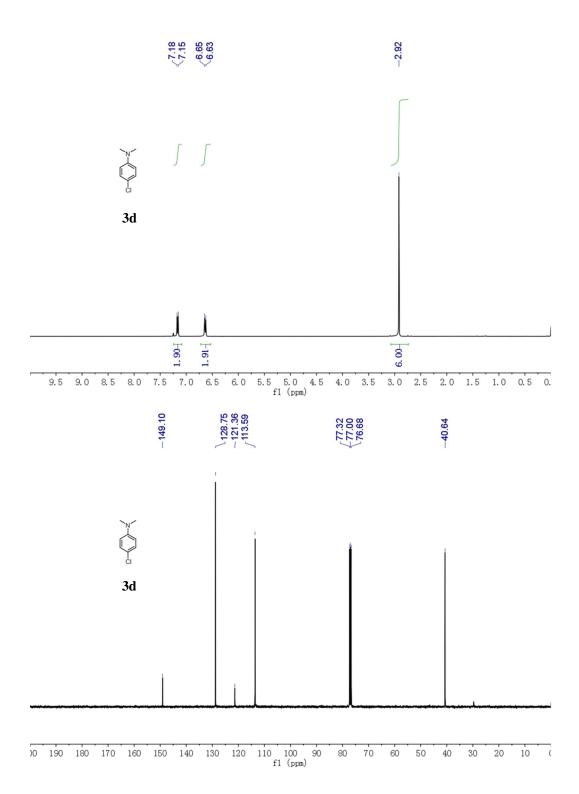
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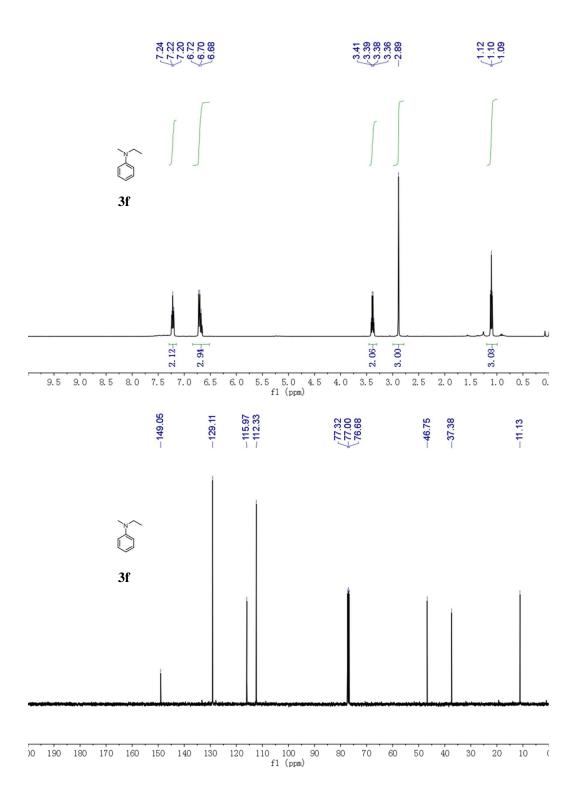
6. Copies of ¹H NMR and ¹³C NMR spectra of the isolated amines.

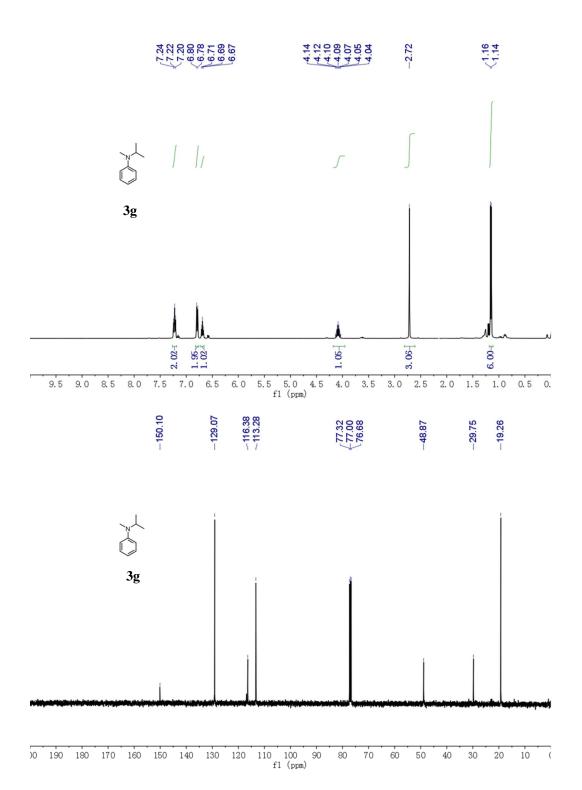


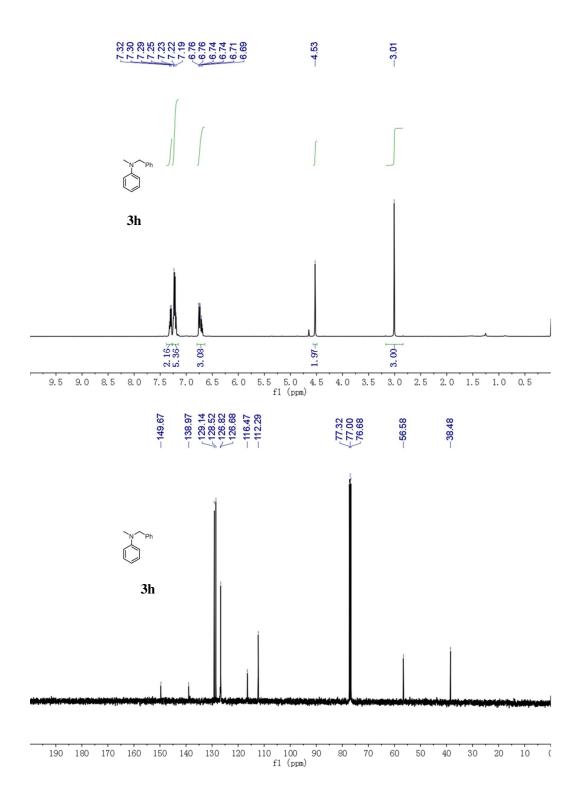


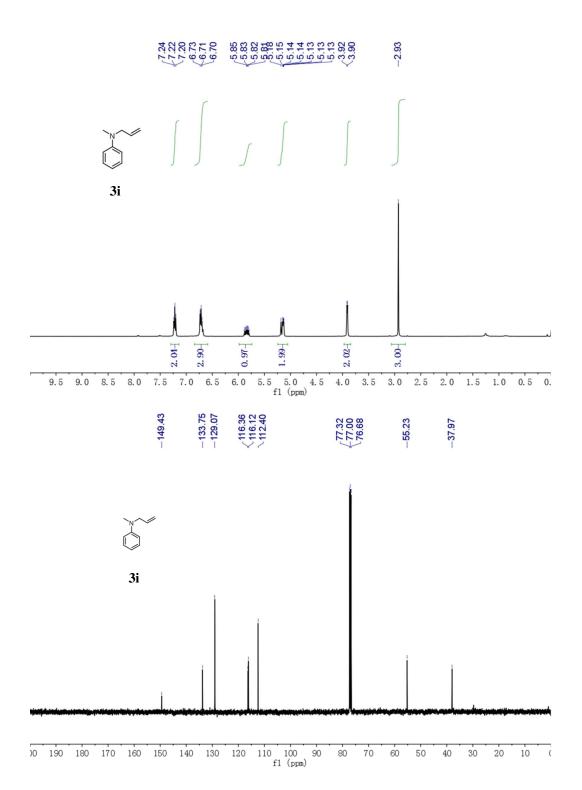


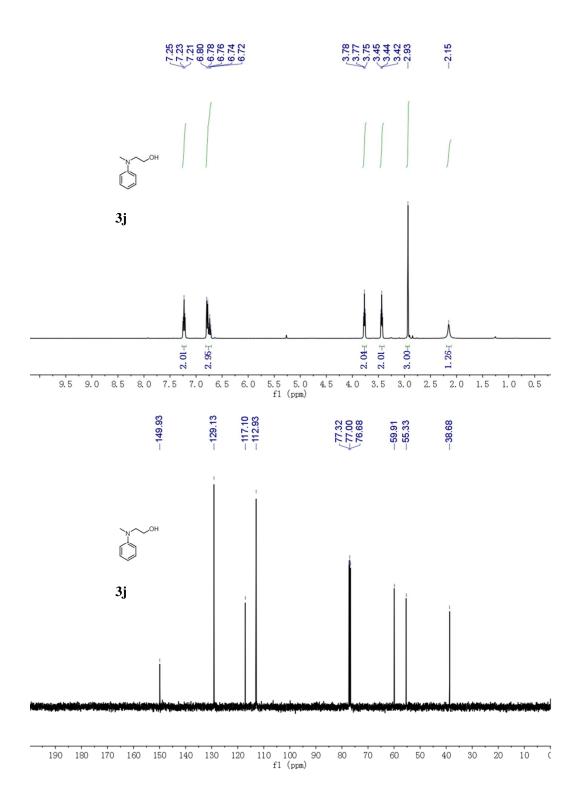


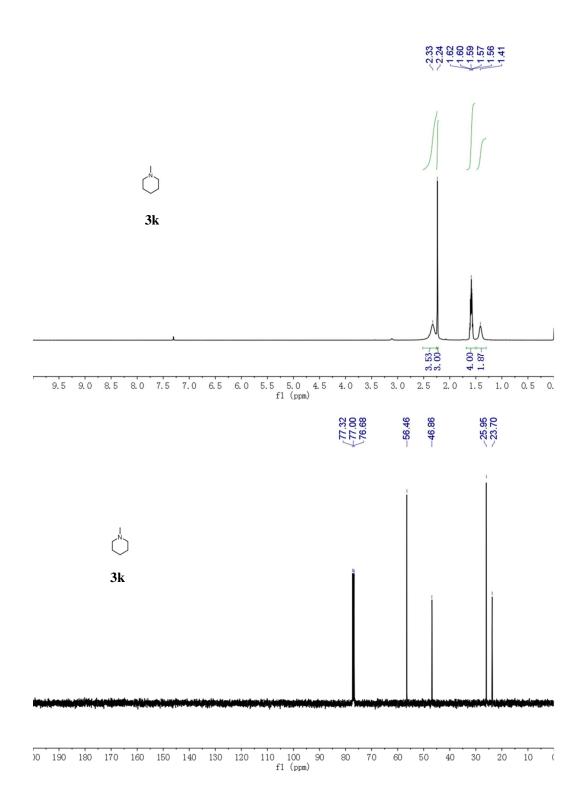


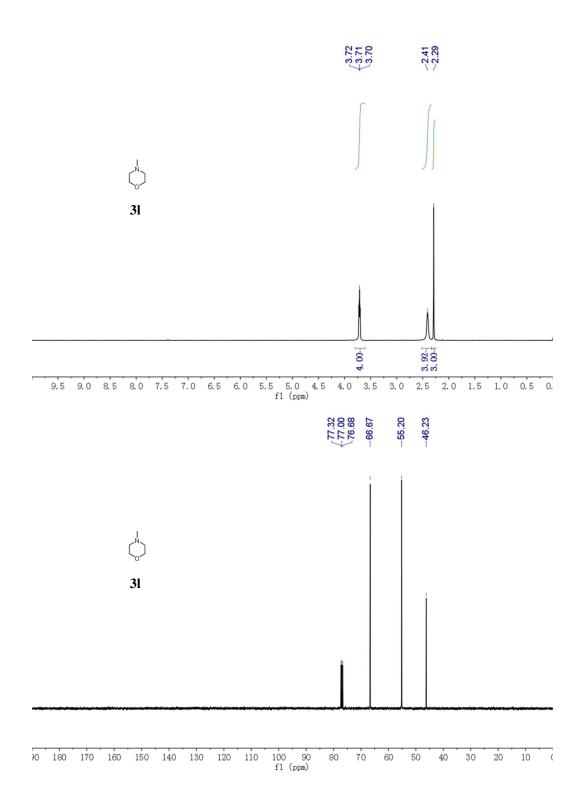


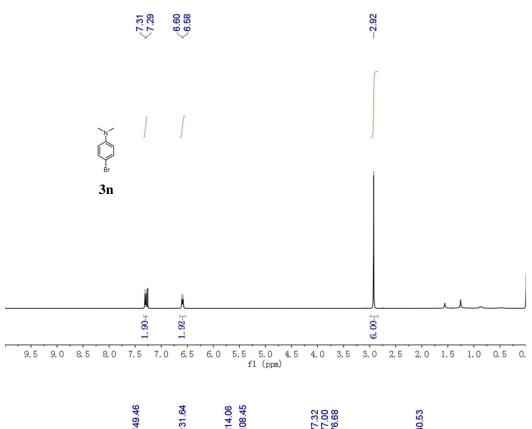


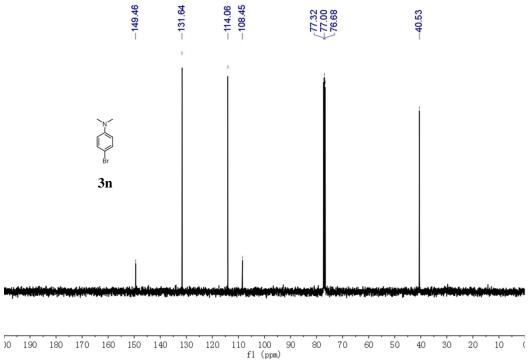


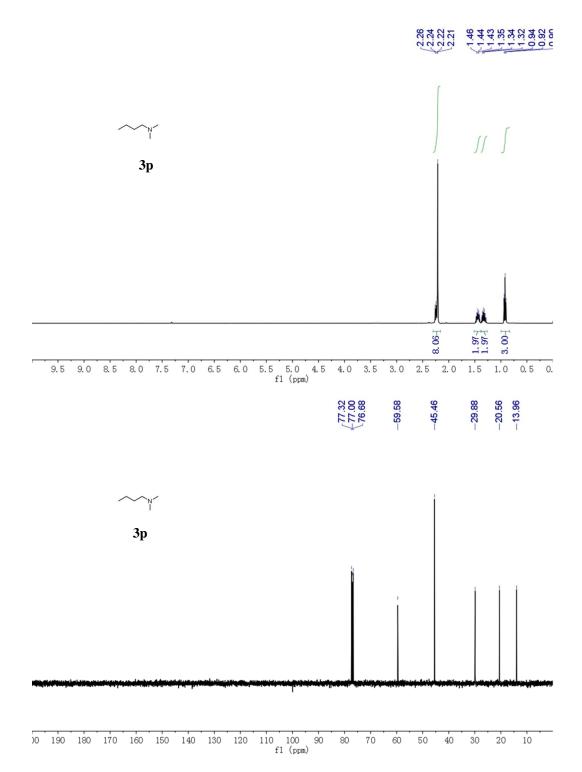


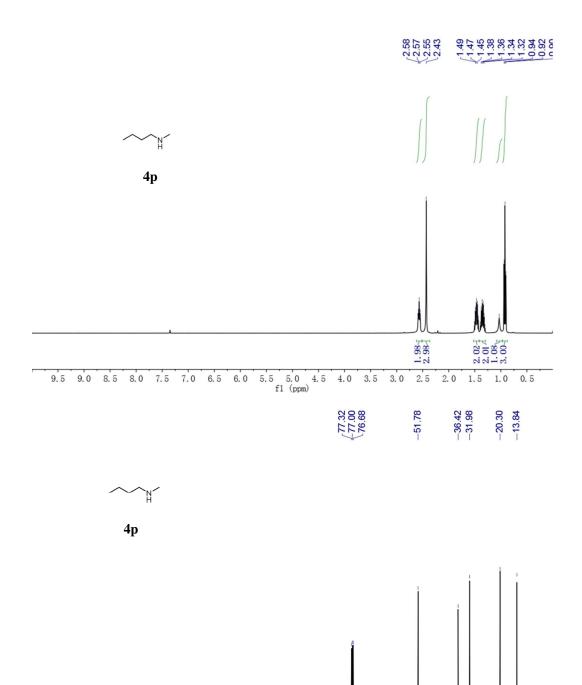












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