

Supporting Information for:

**Synergistic Effects in Fe Nanoparticles Doped with *ppm* Levels of Pd and
Ni. A New Catalyst for Nitro Group Reductions under Sustainable
Conditions**

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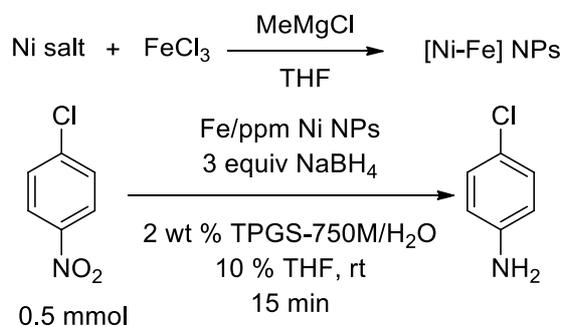
General Remarks

A solution of 2 wt % TPGS-750-M/H₂O solution was prepared by dissolving TPGS-750-M in degassed HPLC grade water, and was stored under argon. TPGS-750-M was made as previously described¹ and is available from Sigma-Aldrich (catalog number 733857). FeCl₃ was purchased from Alfa Aesar. NaBH₄ was purchased from Acros Organics. All commercially available reagents were used without further purification. All reactions were carried out in a sample vial (4 mL) equipped with a Teflon-coated magnetic stir bar. Thin layer chromatography (TLC) was done using Silica Gel 60 F254 plates (0.25 mm thick), purchased from Merck. Column chromatography was done in glass columns using Silica gel 60 (EMD, 40-63 μm) or with pre-packed 25 gram KP-Sil Biotage[®] SNAP Cartridges on the Biotage[®] Isolera Prime autocolumn. GC-MS data were recorded on an Agilent Technologies 7890A GC system coupled with Agilent Technologies 5975C mass spectrometer using HP-5MS column (30 m x 0.250 mm, 0.25 μ) purchased from Agilent Technologies. ¹H and ¹³C NMR spectra were obtained in CDCl₃ or DMSO-d₆ using 400 MHz or 500 MHz Varian NMR spectrometer. Chemical shifts in ¹H NMR spectra are reported in parts per million (ppm) on the δ scale from an internal standard of residual CDCl₃ (7.26 ppm) or the central peak of DMSO-d₆ (2.50 ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, quin = quintet), integration, and coupling constant in Hertz (Hz). Chemical shifts in ¹³C NMR spectra are reported in ppm on the δ scale from the central peak of residual CDCl₃ (77.16 ppm) or the central peak of DMSO-d₆ (39.52 ppm). IR data were collected on a Perkin Elmer Spectrum Tow UATR FT-IR Spectrometer and peaks were described according to relative intensity and resolution as follows: s = strong, m = medium, w = weak, br = broad.

Optimizations

2a Nickel source screening

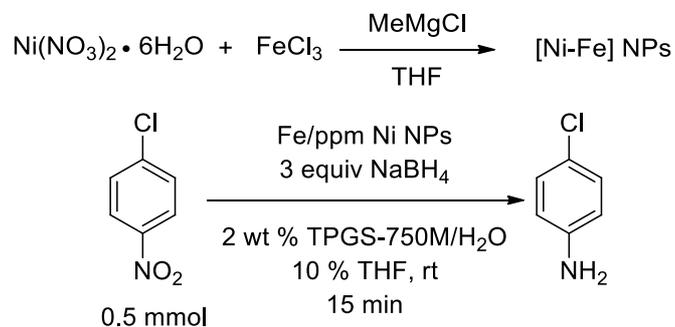
Table S1. Influence of nickel source on reduction of nitroarenes



Entry	Ni source	Ni %	Yield
1	$\text{Ni}(\text{AcO})_2 \cdot 4\text{H}_2\text{O}$	0.16	27 %
2	NiCl_2	0.16	21 %
3	$\text{Ni}(\text{C}_5\text{H}_7\text{O}_2)_2$	0.16	24 %
4	NiBr_2	0.16	41 %
5	$\text{Ni}(\text{NO}_3)_2 \cdot 6\text{H}_2\text{O}$	0.16	43 %

2b Optimal equivalent of MeMgCl

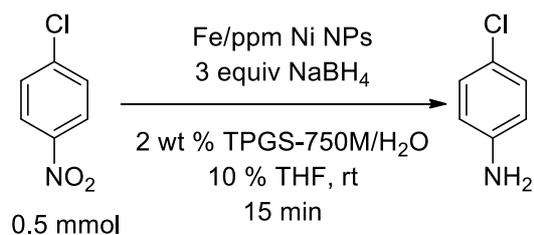
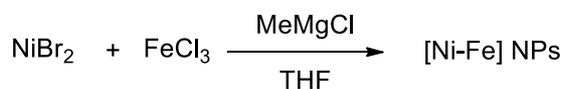
Table S2. Influence of the equivalents of MeMgCl relative to FeCl₃ for making NPs on reduction of nitroarenes with Ni(NO₃)₂·6H₂O as nickel source



Entry	Fe equiv	Ni equiv	Ni %	MeMgCl equiv	Yield
1 ^a	1	0.08	0.16	1.25	44 %
2	1	0.08	0.16	1.27	43 %
3	1	0.08	0.16	1.3	28 %
4	1	0.08	0.16	1.5	26 %
5	1	0.08	0.16	2	7 %

^aIt was difficult to get powder if 1.25 equiv MeMgCl was used to make the nanoparticles.

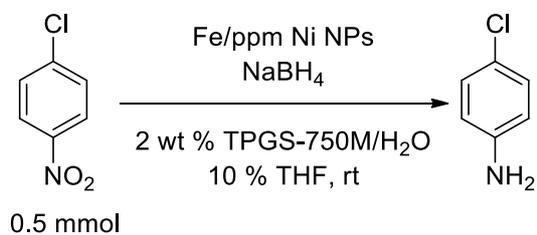
Table S3. Influence of the equivalents of MeMgCl relative to FeCl₃ for making NPs on reduction of nitroarenes with NiBr₂ as nickel source



Entry	Fe equiv	Ni equiv	Ni %	MeMgCl equiv	Yield
1	1	0.08	0.16	1.1	22 %
2	1	0.08	0.16	1.2	26 %
3	1	0.08	0.16	1.25	34 %
4	1	0.08	0.16	1.3	41 %
5	1	0.08	0.16	1.35	60 %
6	1	0.08	0.16	1.4	96 %
7	1	0.08	0.16	1.5	83 %
8	1	0.08	0.16	1.7	77 %
9	1	0.08	0.16	2.0	79 %

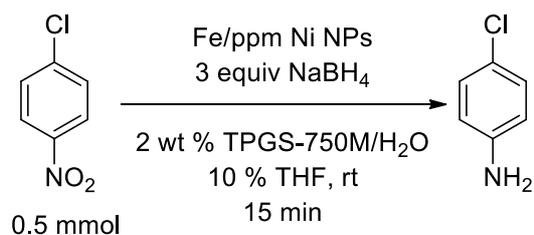
2c Optimal amount of nickel

Table S4. Influence of the amount of nickel on reductions of nitroarenes with $\text{Ni}(\text{NO}_3)_2 \cdot 6\text{H}_2\text{O}$ as nickel source



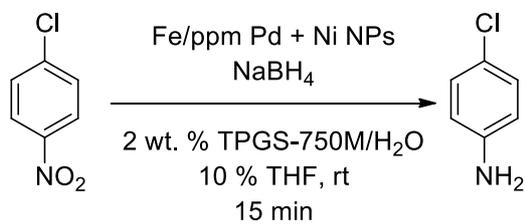
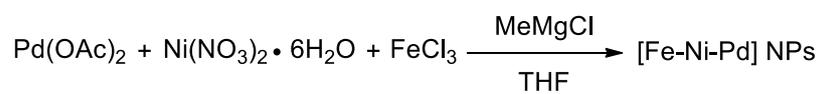
Entry	MeMgCl equiv	Time	Ni %	Yield
1	1.27	15 min	0.04	4 %
2	1.27	15 min	0.08	9 %
3	1.27	15 min	0.12	21 %
4	1.27	15 min	0.16	42 %
5	1.27	15 min	0.20	57 %
6	1.27	12 h	0.16	79 %
7	1.27	15 min	0.32	93 %
8	1.27	15 min	0.64	94 %
9	1.27	15 min	1.28	94 %

Table S5. Influence of the amount of nickel on reductions of nitroarenes with NiBr₂ as nickel source



Entry	MeMgCl equiv	Ni %	Yield
1	1.4	0.04	19 %
2	1.4	0.08	38 %
3	1.4	0.12	61 %
4	1.4	0.16	96 %
5	1.4	0.2	97 %
6	1.5	0.04	5 %
7	1.5	0.08	13 %
8	1.5	0.12	29 %
9	1.5	0.16	83 %
10	1.5	0.2	95 %

2d Table S6. Optimal Amounts of NaBH₄



Entry	NaBH ₄ equiv	Yield ^a
1	1	59 %
2	2	86 %
3	3	96 %
4	4	97 %
5	5	97 %

^aMeMgCl: 1.27 equiv; Ni%: 0.16; Pd%: 0.008

Comparison with Different Reported Catalyst

3a Table S7. Comparison for reductions of the nitro group in 4-chloronitrobenzene to 4-chloroaniline with different reported catalyst

Catalyst	Amount of Catalyst	H source	Reaction condition	Time	Yield (%) ^a	Ref.
Fe/ppm Pd + Ni NPs	0.008% Pd 0.16% Ni 2 mol% Fe	NaBH ₄ (3 equiv)	2% wt. TPGS-750-M, 10 % THF, rt	15 min	>99 (96)	our work
3 wt% Co-L ₁ /C	1 mol%	50 bar H ₂	THF/H ₂ O 110 °C	6 h	95	2
Pd-pol	1.75% Pd	NaBH ₄ (10 equiv)	H ₂ O, rt	5 h	57	3
Pd/ZrP	0.4% Pd	HCOOH	EtOH, 60 °C	16 h	93	4
Fe(OTf) ₃	10 mol% Fe	NaBH ₄ (20 equiv)	EtOH, r.t	4 h	80 (47)	5
Fe-phenanthroline/C	1 mol% Fe	N ₂ H ₄ -H ₂ O (4 equiv)	THF, 100 °C	10 h	96 (96)	6
KOtBu	1.2 equiv	B ₂ pin ₂ (3.1 equiv)	<i>i</i> PrOH, 110 °C	2 h	95 (86)	7
Au/TiO ₂ -VS	1 mol% Au	CO/H ₂ O	EtOH	30 min	99	8
FeBr ₂ -PPh ₃	10 mol% Fe	PhSiH ₃ (2.5 equiv)	toluene 110 °C	16 h	99	9
Pd ⁰ -AmP-MCF	1 mol% Pd	H ₂ (1 atm)	EtOAc, rt	7 h	97	10
[Mo ₃ S ₄ Cl ₃ (dmbpy) ₃](PF ₆)	5 mol%	20 bar H ₂	MeOH, 70 °C	18 h	92 (80)	11
Fe	5 equiv	Fe/HCl	10 equiv HFIP, 2 N HCl, rt	30 min	84	12
Pd(OAc) ₂	1%	N ₂ H ₄ -H ₂ O (5 equiv)	H ₂ O, 50 °C	8 h	97	13
Pd ₉ Ag ₁ -N-doped-MOF-C	0.5 mol%	formic acid	EtOH/H ₂ O, HCOOK, 30 °C	6 h	91	14
NiCl ₂ ·6H ₂ O	0.25 mol%	NaBH ₄	0.01 wt % nanocellulose/H ₂ O, rt	2 h	84	15
Pt-SnO ₂ /Al ₂ O ₃	0.5 wt % Pt	0.1 MPa H ₂	EtOH, 45 °C	1 h	87	16
Co-Mo-S-0.39-180	5 mol% Co, 8 mol% Mo	11 bar H ₂	toluene, 180 °C	7 h	99 (90)	17
PVP-Pd NPs	0.1 mol%	NaBH ₄	EtOH/H ₂ O, rt	1 h	90	18
Ni-MoO ₃ /SBA-15	6 mol%	N ₂ H ₄ -H ₂ O	EtOH, 40 °C	30 min	99	19
0.75-500- γ -Fe ₂ O ₃ /MC	43 wt %	N ₂ H ₄ -H ₂ O	EtOH, 80 °C	1 h	100	20
FeS ₂	0.8 equiv	50 bar H ₂	H ₂ O-THF, 120 °C	18 h	100	21
7 wt% Pd NPs @ POL-2	0.5 mol%	1 atm H ₂	EtOH, 60 °C	3 h	91	22
Co@NC-800	4.2 mol%	3 MPa H ₂	EtOH, 110 °C	6 h	97	23

^aIsolated yield in parentheses.

3b Table S8. Comparison of various reported catalysts for reduction of 1-nitronaphthalene

Catalyst	Amount of Catalyst	H source	Reaction condition	Time	Yield (%) ^a	Ref.
Fe/ppm Pd + Ni NPs	0.008% Pd 0.16% Ni 2 mol% Fe	NaBH₄ (3 equiv)	2% wt. TPGS-750-M, 10 % THF, rt	30 min	99	our work
Pd/ZrP	0.4% Pd	HCOOH	EtOH, 40 °C	16 h	93	4
Fe-phenanthroline/C	1 mol% Fe	N ₂ H ₄ /H ₂ O (4 equiv)	THF, 100 °C	10 h	99	6
Pd ⁰ -AmP-MCF	1 mol% Pd	H ₂ (1 atm)	EtOAc, rt	7 h	97	10
Fe	5 equiv	Fe/HCl	10 equiv HFIP, 2 N HCl, rt	30 min	60	12
Pd ₉ Ag ₁ -N-doped-MOF-C	0.5 mol%	formic acid	EtOH/H ₂ O, HCOOK, 30 °C	6 h	91	14
7 wt% Pd NPs @ POL-2	0.5 mol%	1 atm H ₂	EtOH, rt	1 h	98	22
Ni-PVAm/SBA-15	10 mol% Ni	NaBH ₄ (4 equiv)	H ₂ O, rt	42 min	98	24
Ni NPs	20 mol% Ni			60 min	96	
Co NPs	20 mol% Co	N ₂ H ₄ /H ₂ O	H ₂ O, rt	90 min	97	25
[Pd ₂ (bnp)(β -OH)(CF ₃ CO ₂) ₂](CF ₃ CO ₂) ₂	0.5 mol%	1 atm H ₂	MeOH, 50 °C	12 h	100	26
NAP-Mg-Pd(0)PS	1.98 mol%	PMHS	H ₂ O, Et ₃ N, 80 °C	5 h	91	27
NiS _{2+x} /g-C ₃ N ₄	9 wt %	NaBH ₄	H ₂ O, rt	1 h	94	28
PdNPs@Cell-N-GQD	0.56 mol%	NaBH ₄	H ₂ O/EtOH, rt	2 h	90	29

3c Table S9. Comparison for reduction of morpholino- (4-nitrophenyl)methanone with different reported catalysts

Catalyst	Amount of Catalyst	H source	Reaction condition	Time	Yield (%) ^a	Ref.
Fe/ppm Pd + Ni NPs	0.008% Pd 0.16% Ni 2 mol% Fe	NaBH ₄ (3 equiv)	2% wt. TPGS-750-M, 10 % THF, rt	30 min	99	our work
Fe(OTf) ₃	10 mol% Fe	NaBH ₄ (20 equiv)	EtOH, r.t	4 h	80 (32)	5
KOtBu	1.2 equiv	B ₂ pin ₂ (3.1 equiv)	<i>i</i> PrOH, 110 °C	2 h	93 (80)	7
[Mo ₃ S ₄ Cl ₃ (dnbpy) ₃](PF ₆)	5 mol%	20 bar H ₂	MeOH, 70 °C	18 h	88	11
Fe ₂ O ₃ /NGr@C	5 mol% Fe	HCOOH-Et ₃ N (1.75 equiv)	THF, 120 °C	20-24 h	95	30
Co ₃ O ₄ -NGr/C	2 mol% Co	HCOOH-Et ₃ N (3.5 equiv)	THF, 100 °C	15 h	95	31

^aIsolated yield in parentheses.

Final Optimized Preparation of Fe/ppm Pd + Ni Nanoparticles

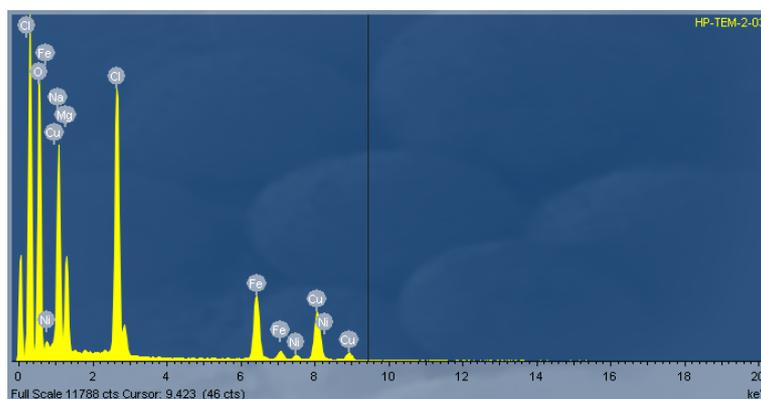
In an oven dried round-bottomed flask, anhydrous 99.99% pure FeCl₃ (162.2 mg, 1 mmol), Pd(OAc)₂ (0.9 mg, 0.004 mmol) and Ni(NO₃)₂·6H₂O (23.2 mg, 0.08 mmol) was added under an atmosphere of dry argon. The flask was covered with a septum, and 5 mL dry THF was added by syringe. The reaction mixture was stirred for 20 min at rt. While maintaining a dry atmosphere at rt, a 1 M solution of MeMgCl in THF was very slowly (1 drop/2 sec) added to the reaction mixture (about 1.2 mL, 1.2 mmol). After addition, a 0.1 M solution of MeMgCl in THF was very slowly (1 drop/2 sec) added to the reaction mixture (about 0.7 mL, 0.07 mmol). After complete addition of the Grignard reagent, the mixture was stirred for an additional 20 min at rt. Appearance of a yellow-brown color was indicative of generation of nanomaterial.

After 20 min, the mixture was quenched with pentane (containing traces of water). THF was then evaporated under reduced pressure at rt. Removal of THF was followed by triturating the mixture with pentane to provide yellow-brown colored nanomaterial as a

powder (trituration was repeated 3-4 times). The Fe nanoparticles obtained were dried under reduced pressure at rt for 10 min yielding 0.6 g Fe/ppm Pd + Ni nanoparticles. The material was used as such for subsequent reactions under micellar conditions.

Characterization of Nanoparticles

EDX for the Fe/ppm Pd + Ni nanoparticles after adding adding NaBH₄



element	atomic%	weight%
Mg K	31	21.7
Cl K	55	55.9
Fe K	13	20.7
Ni K	1	1.7
Totals	100	100

Calculation:

Cl:Mg:Fe:Ni = 55:31:13:1

wt. Fe / wt. Ni = $(13 \times 55.8) / (1 \times 58.7) = 12.3$

Theoretical Ratio:

FeCl₃: 162.2 mg, 1 mmol

Ni(NO₃)₂·6H₂O: 23.2 mg, 0.08 mmol

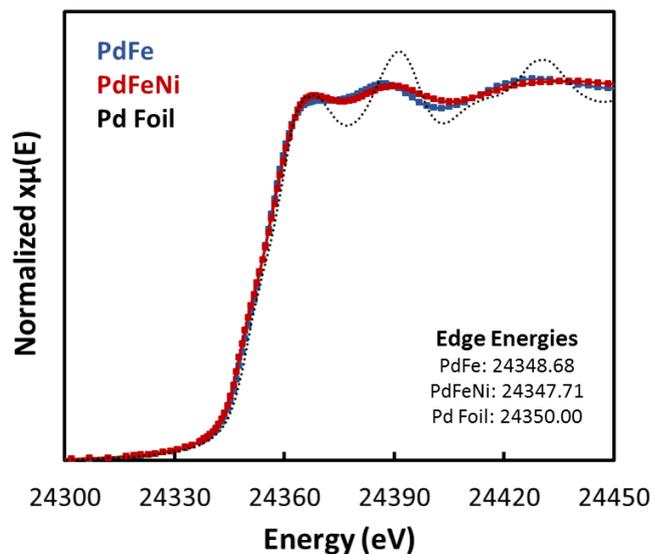
Pd(OAc)₂: 0.9 mg, 0.004 mmol

wt. Fe / wt. Ni = $(1 \times 55.8) / (0.08 \times 58.7) = 11.9$

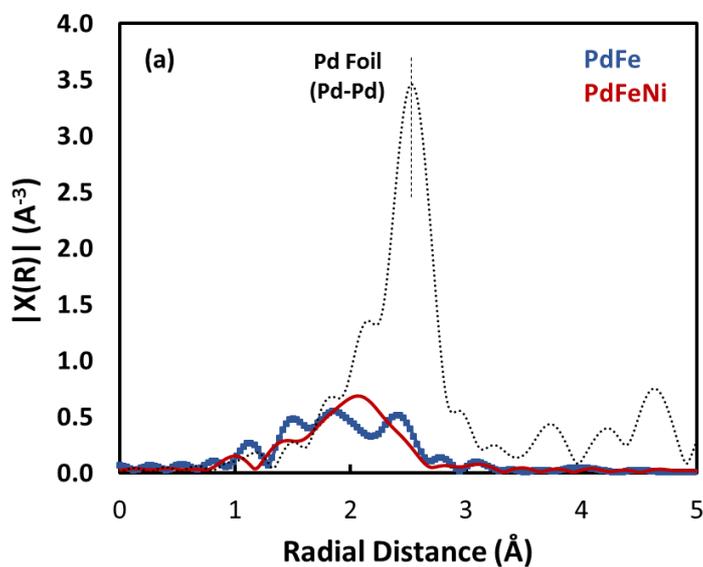
a) The values depend on the location where measurements were made. b) Carbon and oxygen are not included in the table. c) after adding NaBH_4 , the ratio of Fe/Ni is 12.3, which is approximately the theoretical ratio of Fe/Ni which is 11.9. d) Palladium was not observed.

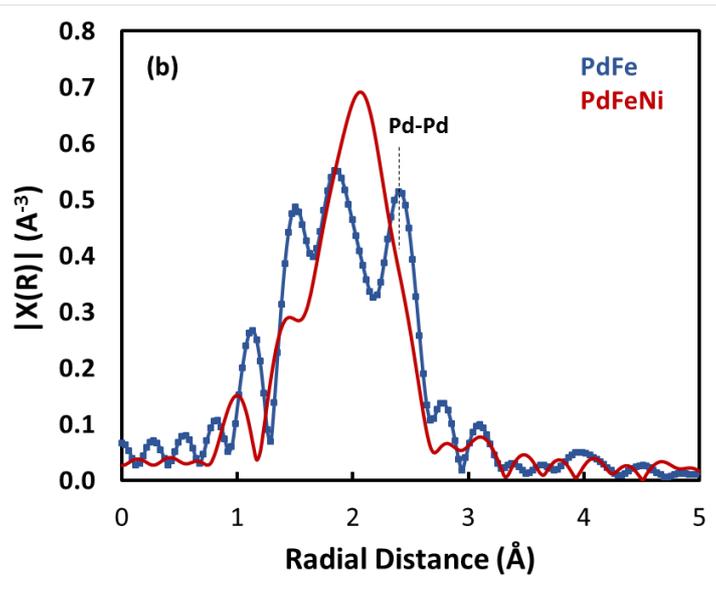
X-ray absorption spectroscopy (XAS)

X-ray absorption spectroscopy (XAS) experiments were performed at the insertion device (Sector 10 ID) of the Materials Research Collaborative Access Team (MR-CAT) at the Advanced Photon Source of Argonne National Laboratory. A Si (111) monochromator with a cryo-cooled first crystal and a 250 mm long second crystal were used to provide Pd K edge energy (24350 eV). Harmonic interference was removed by using a 60cm long flat harmonic rejection mirror with Pt and Rh coatings. Due to the ppm level of Pd loading of the samples, all XAS measurements were done using a 19-element solid-state detector in fluorescence mode. The samples were first finely ground inside an Argon glovebox with/without addition of boron nitride as a diluent to obtain close to an edge step of 1. The mixture was then pressed into a fluorescence sample holder. The sample holder was then transferred to a 10 inch quartz tube (1 in ID) sealed with Kapton windows by two Ultra-Torr fittings attached to three-way valves. The sample tube was then moved to the beamline hutch and flushed with 50 ml/min He prior to the XAS measurement. The beamline was calibrated using a Pd foil and the foil spectrum was collected simultaneously with the samples to correct the edge energies of each sample. Background removal and normalization procedures were carried out using the Athena and Artemis software package to obtain k and r space of the sample spectra.



XANES spectra of the samples (activated by NaBH_4) collected at Pd-K edge. The oxidation state of Pd was determined based on X-ray absorption near-edge structure structures (XANES) data. The Pd edge energies of the PdFe and PdFeNi systems were observed to be close to that of Pd Foil (Pd^0), indicating that all the Pd sites in their most reduced state after activation with NaBH_4 .

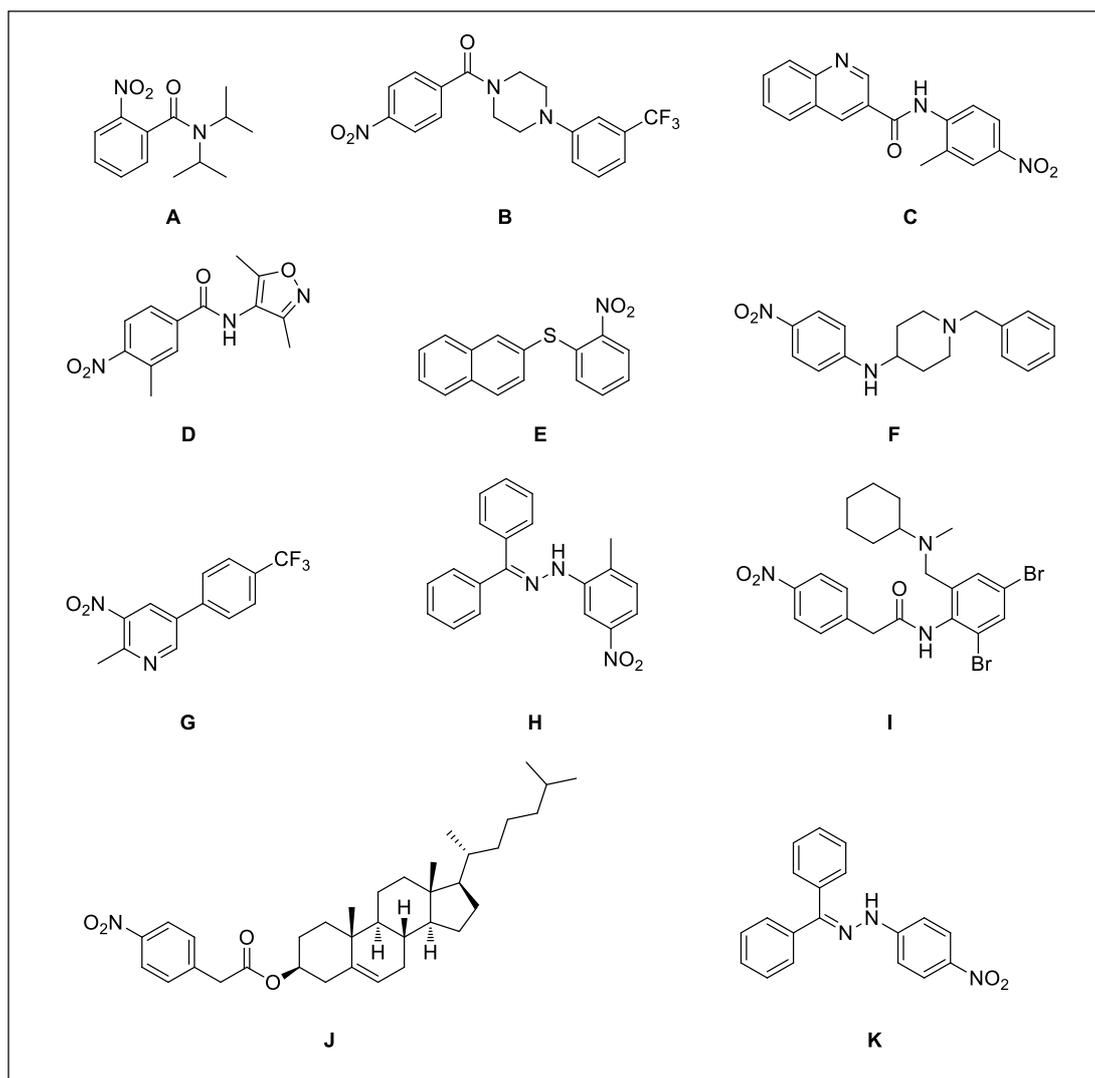




EXAFS spectra of the samples (activated by NaBH_4) collected at Pd-K edge compared to (a) Pd Foil (b) Pd-Pd single scattering at 2.69 \AA . These figures show the presence of Pd-Pd EXAFS feature in PdFe and the absence of this feature in the presence of Ni. This is consistent with the dilution of Pd on the surface due to presence of Ni in the activated Fe/ppm Pd + Ni reagent.

General Details in Experiment

6a Preparation of substrates



Substrates **A** – **D** were synthesized using the general procedure 1 (*vide infra*); Substrates **E** and **F** were synthesized according to the literature;³² Substrate **G** was synthesized using a Suzuki-Miyaura coupling,³³ Substrates **H** and **K** were synthesized using general procedure 2 (*vide infra*); Substrates **I** and **J** was synthesized using general procedure 3 (*vide infra*).

General procedure 1³⁴

In an oven-dried 50 mL round bottom flask containing a PTFE-coated magnetic stir bar, aryl carboxylic acid (5 mmol, 1 equiv), DMF (0.05 mL) and CH₂Cl₂ (10 mL) were added. The mixture was cooled to 0 °C and oxalyl chloride (1.2 equiv) was added in a few portions. The mixture was stirred at rt for 1.5 h. The DCM was then removed via rotary evaporation. Dry CH₂Cl₂ (10 mL), Et₃N (6.6 equiv) and amine (6 mmol) were then added. The mixture was stirred at rt until TLC showed completion. The solution was washed with saturated aqueous

NH₄Cl (2 x 25 mL), NaHCO₃, and brine (2 x 30 mL). The organic layer was separated and dried over anhydrous Na₂SO₄. Volatiles were removed under reduced pressure to obtain crude product that was purified by flash chromatography on silica gel with a gradient elution using hexanes and EtOAc.

General procedure 2

In an oven-dried 25 mL round bottom flask containing a PTFE-coated magnetic stir bar, [Pd(π -allyl)Cl]₂ (0.01 equiv), cBRIDP (0.02 equiv) and dry THF 1 mL were added under an atmosphere of dry argon. The mixture was stirred under argon at 45 °C for 5 min. (Diphenylmethylene)hydrazine (5.25 mmol, 1.05 equiv) and bromonitrobenzene (5 mmol, 1 equiv) and 10 mL aqueous solution of 2 wt % TPGS-750-M were added. The mixture was stirred at 45 °C until the TLC control showed completion. The solution was extracted by CH₂Cl₂. The organic layer was washed with saturated aqueous NH₄Cl (2 x 25 mL), NaHCO₃, and brine (2 x 30 mL). The organic layer was separated and dried over anhydrous Na₂SO₄. Volatiles were removed under reduced pressure to obtain crude product which was purified by flash chromatography on silica gel with a gradient eluent using hexanes and EtOAc.

General procedure 3³⁵

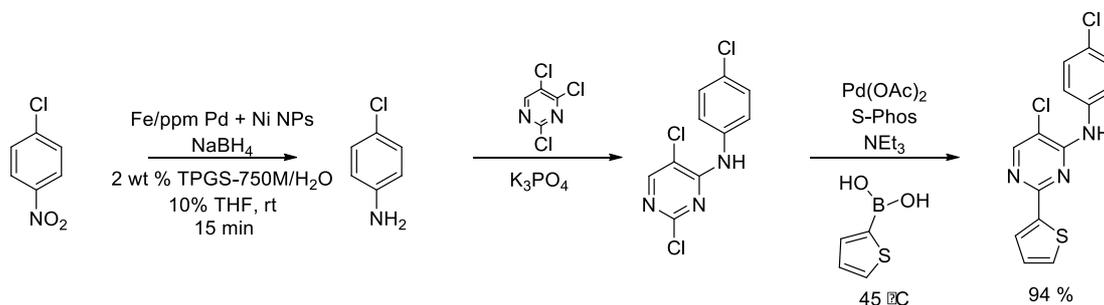
In an oven-dried 50 mL round bottom flask containing a PTFE-coated magnetic stir bar, aryl carboxylic acid (5 mmol, 1 equiv), amine or alcohol (5 mmol, 1 equiv), EDC·HCl (1.1 equiv), DMAP (15 mg) and CH₂Cl₂ (10 mL) were added. The mixture was stirred under reflux until the TLC control showed completion. The solution was washed with saturated aqueous NH₄Cl (2 x 25 mL), NaHCO₃, and brine (2 x 30 mL). The organic layer was separated and dried over anhydrous Na₂SO₄. Volatiles were removed under reduced pressure to obtain crude product which was purified by flash chromatography on silica gel with a gradient eluent using hexanes and EtOAc.

6b General Procedure for Nitro Group Reduction

Fe/ppm Pd + Ni nanoparticle (6 mg, 2 mol % Fe, 80 ppm Pd, 1600 ppm Ni) was added to

reaction vial was covered again and the mixture was vigorously stirred for 16 h until complete consumption of starting material. The resulting mixture was neutralized with 4 M HCl. Benzyl chloroformate (107.3 mg, 0.625 mmol) and Et₃N (76 mg, 3 mmol) were then added. The reaction vial was covered again and the mixture was vigorously stirred overnight. The resulting mixture was neutralized with 4 M HCl. After that, most of the water in the mixture was removed by rotary evaporation. THF (2 mL) was added as solvent, along with 4-methylcyclohexanone (140.2 mg 1.25 mmol) and 4-methylbenzenesulfonic acid (475.6 mg, 2.5 mmol). The reaction vial was covered again and the contents were vigorously stirred at 75 °C for 12 h. After the reaction, the mixture was neutralized by addition of saturated Na₂CO₃ and the mixture was extracted with DCM. The organic extracts were removed by rotary evaporation and purified by flash chromatography over silica gel with Et₂O/hexane (15/85) to obtain pure benzyl (3-methyl-2,3,4,4a,9,9a-hexahydro-1H-carbazol-6-yl) carbamate as a faint yellow semi-solid (58.7 mg, 0.17 mmol, 70%). ¹H NMR (500 MHz, CDCl₃) δ 7.76 (m, 1 H), 7.48 (m, 6 H), 7.34 (m, 1 H), 7.13 (d, *J* = 8.5 Hz, 1 H), 7.03 (m, 1 H), 6.76 (s, 1 H), 5.27 (s, 2 H), 2.80 (dd, *J* = 4.5, 1 H), 2.69 (m, 2 H), 2.23 (m, 1 H), 1.93 (m, 2 H), 1.55 (m, 1 H), 1.14 (d, *J* = 6 Hz, 3 H); ¹³C NMR (125 MHz, CDCl₃) δ 154.2, 136.5, 136.1, 133.2, 129.6, 128.6, 128.24, 128.19, 128.0, 114.3, 110.5, 110.1, 109.0, 66.8, 31.3, 29.6, 29.3, 22.9, 21.7; HRMS(ESI): Calcd. For C₂₁H₂₂O₂N₂Na [M+Na]⁺ 357.1579. Found: 357.1563.

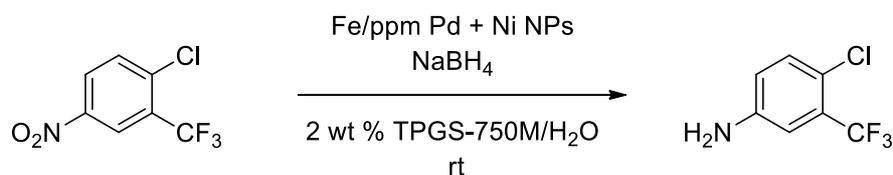
6d 1-Pot 3 step reduction, S_NAr reaction, and Suzuki-Miyaura reaction



Fe/ppm Pd + Ni nanoparticle (5.2 mg, 2 mol % Fe, 80 ppm Pd, 1600 ppm Ni) were placed into an oven dried 4 mL microwave reaction vial containing a PTFE-coated magnetic stir bar. An aqueous solution (2 mL) of 2 wt % TPGS-750-M was added via syringe, and the mixture was stirred at rt for 30 sec. After stirring, NaBH₄ (57 mg, 1.5 mmol) was slowly

added to the reaction mixture. During addition of NaBH₄, the reaction mixture turned black with evolution of hydrogen gas. 4-Chloronitrobenzene (78.8 mg, 0.5 mmol) was then added to the catalyst suspension, and then 0.1 mL THF was added as co-solvent. The reaction vial was covered again and the mixture was vigorously stirred for ca. 15 min until complete consumption of starting material. The resulting mixture was neutralized with 4 M HCl. 2,4,5-Trichloropyrimidine (91.7 mg, 0.5 mmol) and K₃PO₄ (127.3 mg, 0.6 mmol) were then added. The reaction vial was covered again and the mixture was vigorously stirred overnight. After the reaction, thiophen-2-ylboronic acid (96 mg 0.75 mmol), NEt₃ (151.8 mg, 1.5 mmol), Pd(AcO)₂ (2.2 mg, 0.01 mmol) and SPhos (8.2 mg, 0.02) were then added. The reaction vial was covered again and the contents were vigorously stirred at 45 °C for 16 h. After the reaction, the mixture was extracted with EtOAc. The organic extracts were removed by rotary evaporation and purified by flash chromatography over silica gel with Et₂O/hexane (15/85) to obtain pure 5-chloro-N-(4-chlorophenyl)-2-(thiophen-2-yl)pyrimidin-4-amine as white solid (150.6 mg, 0.47 mmol, 94%). ¹H NMR (500 MHz, DMSO-d₆) δ 9.22 (s, 1 H), 8.49 (s, 1 H), 8.21 (d, *J* = 3 Hz, 1 H), 7.82 (d, *J* = 8.5 Hz, 2 H), 7.66 (d, *J* = 5 Hz, 1 H), 7.61 (m, 1 H), 7.46 (d, *J* = 9 Hz, 2 H); ¹³C NMR (125 MHz, DMSO-d₆) δ 158.6, 155.8, 154.9, 141.2, 137.9, 128.69, 128.67, 127.9, 127.50, 127.48, 124.3, 112.5; HRMS(CI): Calcd. For C₁₄H₉Cl₂N₃S [M⁺] 320.9894. Found: 320.9890.

6e E Factor and recycle studies



Procedure for determination of E Factors

Fe/ppm Pd + Ni nanoparticle (11.4 mg, 2 mol % Fe, 80 ppm Pd, 1600 ppm Ni) was placed into an oven dried 5 mL microwave reaction vial containing a PTFE-coated magnetic stir bar. The reaction vial was covered with a rubber septum and 1.0 mL aqueous solution of 2 wt % TPGS-750-M was added via syringe. The mixture was stirred at rt for 10 sec. The septum was opened and NaBH₄ (114 mg, 3 mmol) was added to the reaction mixture. During

addition of NaBH₄ reaction mixture was turned black with evolution of hydrogen gas. 1-Chloro-4-nitro-2-(trifluoromethyl)benzene (225 mg, 1 mmol) was then added and the vial was again covered. The contents were stirred vigorously until complete consumption of the starting material (about 1 h). The resulting mixture was extracted with EtOAc (0.4 mL x 2). The organic layer was then separated (with the aid of centrifuge, if needed) and dried over anhydrous Na₂SO₄, after which the volatiles were removed under reduced pressure and purified by flash chromatography over silica gel with EtOAc/hexanes to obtain 4-chloro-3-(trifluoromethyl)aniline. (186.1 mg, 0.95 mmol, 95%)

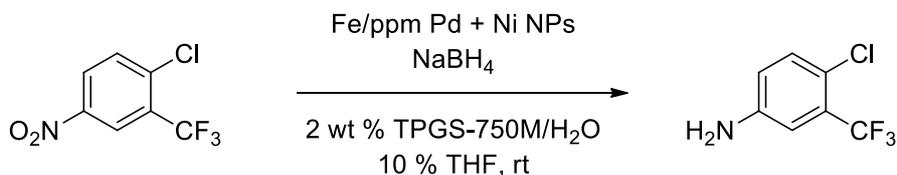
E Factor calculation (without water)

$$\begin{aligned} \text{E Factor} &= (\text{mass organic waste}) / (\text{mass of pure product}) \\ &= (\text{mass EtOAc} / (\text{mass pure product})) \\ &= (721 \text{ mg EtOAc}) / (186.1 \text{ mg pure product}) \\ &= 3.9 \end{aligned}$$

E Factor calculation (with water)

$$\begin{aligned} \text{E Factor} &= (\text{mass organic waste}) / (\text{mass of pure product}) \\ &= (721 \text{ mg EtOAc} + 1000 \text{ mg water}) / (186.1 \text{ mg pure}) \\ &= 9.2 \end{aligned}$$

Procedures for recycle studies



Reaction	Theoretical Yield	Isolated Yield	Percent Yield
A	97.5 mg	95.7 mg	98%
B	97.5 mg	94.8 mg	97%
C	97.5 mg	93.1 mg	95%
D	97.5 mg	93.3 mg	96%
E	97.5 mg	94.5 mg	97%

Reaction A: Fe/ppm Pd + Ni nanoparticle (5.7 mg, 2 mol % Fe, 80 ppm Pd, 1600 ppm Ni) was placed into an oven dried 5 mL microwave reaction vial containing a PTFE-coated magnetic stir bar. The reaction vial was covered with a rubber septum and 1.0 mL aqueous solution of 2 wt % TPGS-750-M was added via syringe. The mixture was stirred at rt for 10 sec. THF (0.1 mL) was added via syringe as co-solvent. The septum was opened and NaBH₄ (57 mg, 3 mmol) was added to the reaction mixture. 1-Chloro-4-nitro-2-(trifluoromethyl)benzene (112.5 mg, 0.5 mmol) was then added and the vial was again covered. The contents were stirred vigorously until complete consumption of the starting material (about 1 h). The resulting mixture was extracted with MTBE (0.4 mL × 3). The organic layer was then separated (with the aid of a centrifuge, if needed) and dried over anhydrous Na₂SO₄, after which the volatiles were removed under reduced pressure and purified by flash chromatography over silica gel with EtOAc/hexanes to obtain 4-chloro-3-(trifluoromethyl)aniline (95.7 mg, 0.49 mmol, 98%).

Reaction B: (1st recycle). Three drops of (4 M) aqueous hydrochloric acid were added to neutralize the aqueous layer. The vial was charged with fresh Fe nanoparticles (2 mg), and THF (0.1 mL). 1-Chloro-4-nitro-2-(trifluoromethyl)benzene (112.5 mg, 0.5 mmol) and NaBH₄ (57 mg, 3 mmol) were then added and the vial was again covered. The contents were stirred vigorously until complete consumption of the starting material (about 1 h). The resulting mixture was extracted with MTBE (0.4 mL × 3). The organic layer was then separated (with the aid of centrifuge, if needed) and dried over anhydrous Na₂SO₄, after which the volatiles were removed under reduced pressure and purified by flash chromatography over silica gel with EtOAc/hexanes to obtain 4-chloro-3-(trifluoromethyl)aniline. (94.8 mg, 0.49 mmol, 97%).

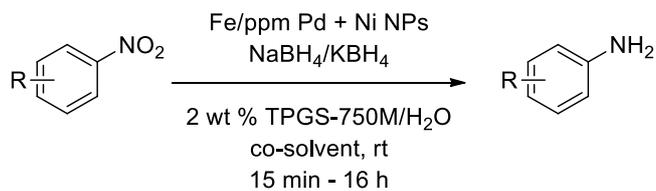
Reaction C: (2nd recycle). Three drops of (4 M) aqueous hydrochloric acid were added to neutralize the aqueous layer. The vial was charged with fresh Fe nanoparticles (2 mg), and THF (0.1 mL). 1-Chloro-4-nitro-2-(trifluoromethyl)benzene (112.5 mg, 0.5 mmol) and NaBH₄ (57 mg, 3 mmol) were then added and the vial was again covered. The contents were stirred vigorously until complete consumption of the starting material (about 1 h). The resulting mixture was extracted with MTBE (0.4 mL × 3). The organic layer was then

separated (with the aid of centrifuge, if needed) and dried over anhydrous Na_2SO_4 , after which the volatiles were removed under reduced pressure and purified by flash chromatography over silica gel with EtOAc/hexanes to obtain 4-chloro-3-(trifluoromethyl)aniline. (93.1 mg, 0.48 mmol, 95%).

Reaction D: (3rd recycle). Three drops of (4 M) aqueous hydrochloric acid solution was added to neutralize the aqueous layer. The vial was charged with fresh Fe nanoparticles (2 mg), and THF (0.1 mL). 1-Chloro-4-nitro-2-(trifluoromethyl)benzene (112.5 mg, 0.5 mmol) and NaBH_4 (57 mg, 3 mmol) were then added and the vial was again covered. The contents were stirred vigorously until complete consumption of the starting material (about 1 h). The resulting mixture was extracted with MTBE (0.4 mL \times 3). The organic layer was then separated (with the aid of centrifuge, if needed) and dried over anhydrous Na_2SO_4 , after which the volatiles were removed under reduced pressure and purified by flash chromatography over silica gel with EtOAc/hexanes to obtain 4-chloro-3-(trifluoromethyl)aniline. (93.3 mg, 0.48 mmol, 96%).

Reaction E: (4th recycle). Three drops of (4 M) aqueous hydrochloric acid solution was added to neutralize the aqueous layer. The vial was charged with fresh Fe nanoparticles (2 mg), and THF (0.1 mL). 1-Chloro-4-nitro-2-(trifluoromethyl)benzene (112.5 mg, 0.5 mmol) and NaBH_4 (57 mg, 3 mmol) were then added and the vial was again covered. The contents were stirred vigorously until complete consumption of the starting material (about 1 h). The resulting mixture was extracted with MTBE (0.4 mL \times 3). The organic layer was then separated (with the aid of centrifuge, if needed) and dried over anhydrous Na_2SO_4 , after which the volatiles were removed under reduced pressure and purified by flash chromatography over silica gel with EtOAc/hexanes to obtain 4-chloro-3-(trifluoromethyl)aniline. (94.5 mg, 0.49 mmol, 97%).

6f Residual palladium, nickel and iron in products



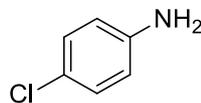
substrate			
Pd Residue	=< 10 ppm	---	---
Ni Residue	=< 1 ppm	1 ppm	1 ppm



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 Cambridge, Massachusetts 02139



CIB001

Sample #: REILLJO3-001-EXP071-001

Test #: 1 Received: 05/06/2016

Completed: 05/09/2016

ICP-OES:

Palladium = < 10 ppm

Nickel = < 1 ppm

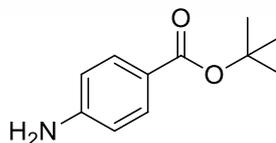
Services
 ICP-OES



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CIB001

Sample #: REILLJO3-001-EXP077-001

Test #: 1 Received: 08/01/2016

Completed: 08/02/2016

ICP-MS: Nickel = 1 ppm

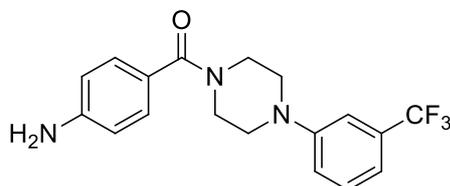
Services
ICP-MS



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CIB001

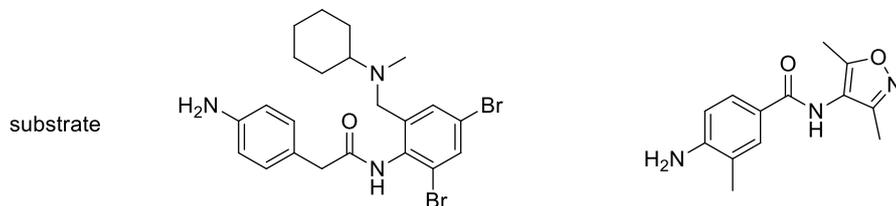
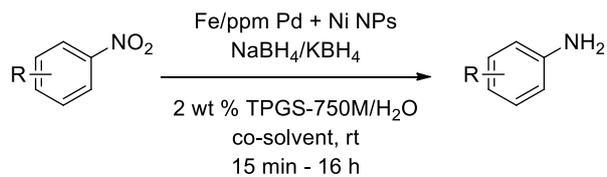
Sample #: REILLJO3-001-EXP076-001

Test #: 1 Received: 08/01/2016

Completed: 08/02/2016

ICP-MS: Nickel = 1 ppm

Services
ICP-MS



Fe Residue

=< 5 ppm

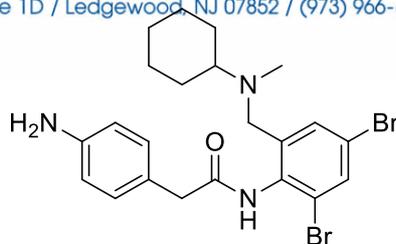
=< 5 ppm



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CIB001

Sample #: REILJO3-001-EXP089

Test #: 1 Received: 05/30/2017

Completed: 06/01/2017

ICP-OES: Iron = < 5 ppm

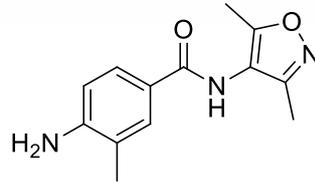
Services
 ICP-OES



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CIB001

Sample #: REILJO3-001-EXP090

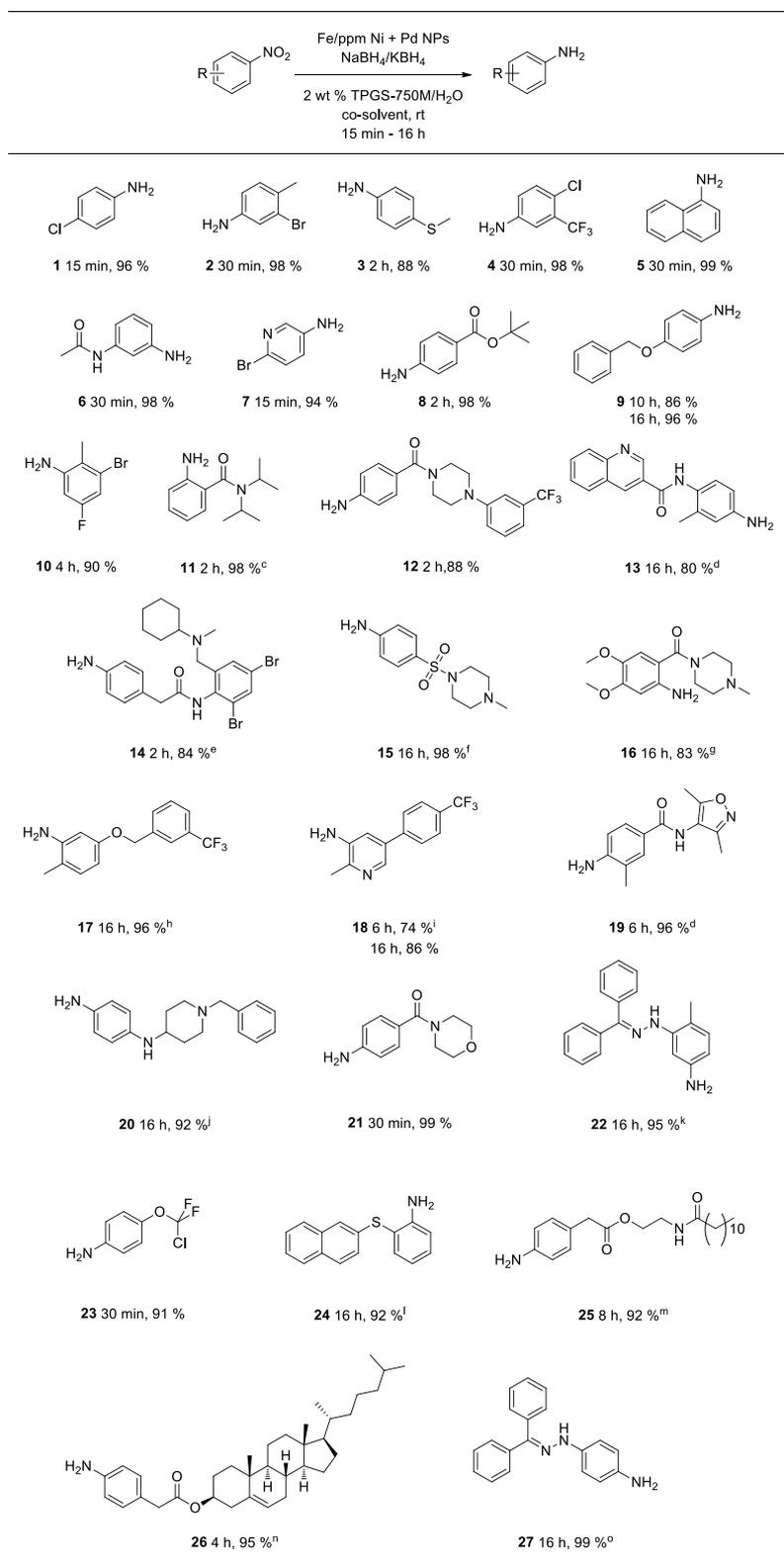
Test #: 1 Received: 05/30/2017

Completed: 06/01/2017

ICP-OES: Iron = < 5 ppm

Services
ICP-OES

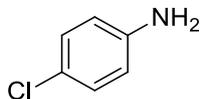
Substrate Scope



^aReaction conditions: nitro compound (0.5 mmol), Fe/ppm Pd + Ni NPs (6 mg, 80 ppm Pd, 1600 ppm Ni), NaBH₄ (1.5 mmol), 2 wt % TPGS-750-M/H₂O (1 mL), THF (0.1 mL); ^bIsolated yield; ^cnitro compound (0.125 mmol), Fe/ppm Pd + Ni NPs (3 mg), NaBH₄ (0.375 mmol), 2 wt % TPGS-750-M/H₂O (1 mL), THF (0.1 mL); ^dDMSO (0.25 mL); ^enitro compound (0.125 mmol), Fe/ppm Pd + Ni NPs (3 mg), NaBH₄ (0.375 mmol), 2 wt % TPGS-750-M/H₂O (1 mL), THF (0.3 mL); ^fnitro compound (0.25 mmol), Fe/ppm Pd + Ni NPs (3 mg), NaBH₄ (0.75 mmol), 2 wt % TPGS-750-M/H₂O (1 mL), CH₃OH (0.25 mL); ^gnitro compound (0.5 mmol), Fe/ppm Pd + Ni NPs (12 mg), NaBH₄ (3 mmol), 2 wt % TPGS-750-M/H₂O (1 mL), THF (0.1 mL); ^hnitro compound (0.25 mmol), Fe/ppm Pd + Ni NPs (3 mg), NaBH₄ (0.75 mmol), TPGS-750-M/H₂O (1 mL); ⁱnitro compound (0.5 mmol), Fe/ppm Pd + Ni NPs (12 mg), NaBH₄ (3 mmol), 2 wt % TPGS-750-M/H₂O (1 mL), DCM (0.1 mL); ^jTHF (0.25 mL); ^knitro compound (0.5 mmol), Fe/ppm Pd + Ni NPs (12 mg), KBH₄ (3 mmol), 2 wt % TPGS-750-M/H₂O (1 mL), THF (0.25 mL); ^lnitro compound (0.125 mmol), Fe/ppm Pd + Ni NPs (1.5 mg), KBH₄ (0.375 mmol), 2 wt % TPGS-750-M/H₂O (1 mL), DMSO (0.25 mL); ^mnitro compound (0.25 mmol), Fe/ppm Pd + Ni NPs (2.5 mg), KBH₄ (0.75 mmol), 2 wt % TPGS-750-M/H₂O (1 mL), THF (0.25 mL); ⁿnitro compound (0.25 mmol), Fe/ppm Pd + Ni NPs (3 mg), NaBH₄ (0.75 mmol), 2 wt % TPGS-750-M/H₂O (1 mL), DCM (0.3 mL); ^onitro compound (0.125 mmol), Fe/ppm Pd + Ni NPs (1.5 mg), KBH₄ (0.75 mmol), 2 wt % TPGS-750-M/H₂O (1 mL), THF (0.25 mL).

Analytical Data

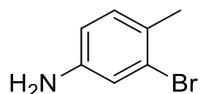
4-Chloroaniline (1) CAS: 106-47-8



1-Chloro-4-nitrobenzene (78.8 mg, 0.5 mmol), Fe nanoparticles (6 mg), and NaBH₄ (57 mg, 1.5 mmol) in 1.0 mL 2 wt % TPGS/H₂O with 0.1 mL THF as co-solvent were reacted at rt for 15 min yielding 61.5 mg (96%) of 4-chloroaniline as a pale yellow solid (hexane/ethyl acetate: 80/20).

Spectral data matched that reported in the literature.³⁶ ¹H NMR (500 MHz, CDCl₃) δ 7.11 (d, *J* = 10 Hz, 2 H), 6.61 (d, *J* = 5 Hz, 2 H), 3.48 (s, br, 2 H); GC-MS, *m/z*: 127 [M⁺].

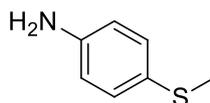
3-Bromo-4-methylaniline (2) CAS: 7745-91-7



2-Bromo-1-methyl-4-nitrobenzene (108 mg, 0.5 mmol), Fe nanoparticles (6 mg), and NaBH₄ (57 mg, 1.5 mmol) in 1.0 mL 2 wt % TPGS/H₂O with 0.1 mL THF as co-solvent were reacted at rt for 30 min yielding 91.2 mg (98%) of 3-bromo-4-methylaniline as a white cristal (hexane/ethyl acetate: 80/20).

Spectral data matched that reported in the literature.³⁷ ¹H NMR (500 MHz, CDCl₃) δ 7.00 (d, *J* = 10 Hz, 1 H), 6.90 (d, *J* = 5 Hz, 1 H), 6.55 (m, 1 H), 3.48 (s, br, 2 H), 2.28 (s, 3 H); GC-MS, *m/z*: 184 [M⁺].

4-(Methylthio)aniline (3) CAS: 104-96-1

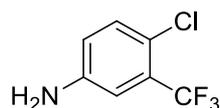


Methyl(4-nitrophenyl)sulfane (84.6 mg, 0.5 mmol), Fe nanoparticles (6 mg), and NaBH₄ (57 mg, 1.5 mmol) in 1.0 mL 2 wt % TPGS/H₂O with 0.1 mL THF as co-solvent were reacted at rt for 2 h yielding 61.1 mg (88%) of 4-(methylthio)aniline as a yellow oil

(hexane/ethyl acetate: 70/30).

Spectral data matched that reported in the literature.³⁸ ¹H NMR (500 MHz, CDCl₃) δ 7.17 (d, *J* = 10 Hz, 2 H), 6.62 (d, *J* = 10 Hz, 2 H), 3.54 (s, br, 2 H), 2.41 (s, 3 H); GC-MS, *m/z*: 139 [M⁺].

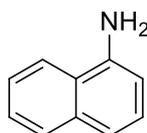
4-Chloro-3-(trifluoromethyl)aniline (4) CAS: 320-51-4



1-Chloro-4-nitro-2-(trifluoromethyl)benzene (112.8 mg, 0.5 mmol), Fe nanoparticles (6 mg), and NaBH₄ (57 mg, 1.5 mmol) in 1.0 mL 2 wt % TPGS/H₂O with 0.1 mL THF as co-solvent were reacted at rt for 30 min yielding 95.9 mg (98%) of 4-chloro-3-(trifluoromethyl)aniline as a yellow oil (hexane/ethyl acetate: 80/20).

Spectral data matched that reported in the literature.³⁹ ¹H NMR (500 MHz, CDCl₃) δ 7.22 (d, *J* = 9 Hz, 1 H), 6.96 (d, *J* = 3 Hz, 1 H), 6.73 (m, 1 H), 3.83 (s, br, 2 H); GC-MS, *m/z*: 195 [M⁺].

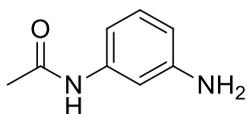
Naphthalen-1-amine (5) CAS: 132-32-7



1-Nitronaphthalene (86.6 mg, 0.5 mmol), Fe nanoparticles (6 mg), and NaBH₄ (57 mg, 1.5 mmol) in 1.0 mL 2 wt % TPGS/H₂O with 0.1 mL THF as co-solvent were reacted at rt for 30 min yielding 71.2 mg (99%) of naphthalen-1-amine as a white cristal (hexane/ethyl acetate: 80/20).

Spectral data matched that reported in the literature.⁴⁰ ¹H NMR (500 MHz, CDCl₃) δ 7.82 (m, 2 H), 7.48 (m, 2 H), 7.31 (m, 2 H), 6.80 (m, 1 H), 4.15 (s, br, 2 H); GC-MS, *m/z*: 143 [M⁺].

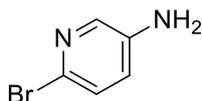
N-(3-Aminophenyl)acetamide (6) CAS: 102-28-3



N-(3-Nitrophenyl)acetamide (90.1 mg, 0.5 mmol), Fe nanoparticles (6 mg), and NaBH₄ (57 mg, 1.5 mmol) in 1.0 mL 2 wt % TPGS/H₂O with 0.1 mL THF as co-solvent were reacted at rt for 30 min yielding 73.8 mg (98%) of *N*-(3-aminophenyl)acetamide as a white oil (DCM/MeOH: 95/5).

Spectral data matched to the reported in literature.⁴¹ ¹H NMR (500 MHz, CDCl₃) δ 8.17 (s, 1 H), 7.03 (t, *J* = 10 Hz, 2 H), 6.77 (d, *J* = 10 Hz, 1 H), 6.37 (d, *J* = 5 Hz, 1 H), 3.68 (s, br, 2 H), 2.06 (s, br, 3 H); ¹³C NMR (100 MHz, CDCl₃) δ 169.1, 147.2, 139.1, 129.6, 111.1, 110.1, 106.9, 24.4.; GC-MS, *m/z*: 150 [M⁺].

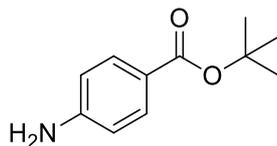
6-Bromopyridin-3-amine (7) CAS: 13534-97-9



2-Bromo-5-nitropyridine (101.5 mg, 0.5 mmol), Fe nanoparticles (6 mg), and NaBH₄ (57 mg, 1.5 mmol) in 1.0 mL 2 wt % TPGS/H₂O with 0.1 mL THF as co-solvent were reacted at rt for 15 min yielding 81.1 mg (94%) of 6-bromopyridin-3-amine as a white cristal (hexane/ethyl acetate: 70/30).

Spectral data matched that reported in the literature.⁴² ¹H NMR (500 MHz, CDCl₃) δ 7.83 (d, *J* = 5 Hz, 1 H), 7.21 (m, 1 H), 6.88 (m, 1 H), 3.49 (s, br, 2 H); GC-MS, *m/z*: 172 [M⁺].

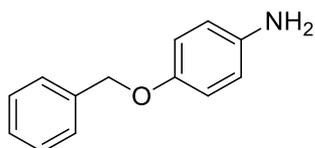
***t*-Butyl 4-aminobenzoate (8) CAS: 18144-47-3**



t-Butyl 4-nitrobenzoate (111.6 mg, 0.5 mmol), Fe nanoparticles (6 mg), and NaBH₄ (57 mg, 1.5 mmol) in 1.0 mL 2 wt % TPGS/H₂O with 0.1 mL THF as co-solvent were reacted at rt for 2 h yielding 94.9 mg (98%) of *t*-butyl 4-aminobenzoate as a white cristal (hexane/ethyl acetate: 80/20).

Spectral data matched that reported in the literature.⁴³ ¹H NMR (500 MHz, DMSO-d₆) δ 7.58 (d, *J* = 10 Hz, 2 H), 6.55 (d, *J* = 5 Hz, 2 H), 5.84 (s, br, 2 H), 1.49 (s, 9 H); ¹³C NMR (125 MHz, DMSO-d₆) δ 165.3, 153.0, 130.9, 117.8, 112.5, 78.8, 28.0. GC-MS, *m/z*: 193 [M⁺].

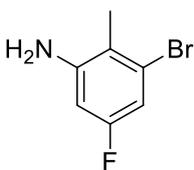
4-(Benzyloxy)aniline (9) CAS: 6373-46-2



1-(Benzyloxy)-4-nitrobenzene (114.6 mg, 0.5 mmol), Fe nanoparticles (6 mg), and NaBH₄ (57 mg, 1.5 mmol) in 1.0 mL 2 wt % TPGS/H₂O with 0.1 mL THF as co-solvent were reacted at rt for 10 h yielding 85.4 mg (86%) of 4-(benzyloxy)aniline as a yellow crystal (hexane/ethyl acetate: 80/20).

Spectral data matched that reported in the literature.⁷ ¹H NMR (500 MHz, CDCl₃) δ 7.47 (m, 2 H), 7.42 (m, 2 H), 7.36 (m, 1 H), 6.86 (d, *J* = 10 Hz, 2 H), 6.66 (d, *J* = 5 Hz, 2 H), 5.03 (s, 2 H), 3.37 (s, br, 2 H); ¹³C NMR (125 MHz, CDCl₃) δ 151.9, 140.3, 137.6, 128.5, 127.8, 127.5, 116.37, 116.1, 70.8. GC-MS, *m/z*: 199 [M⁺].

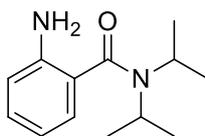
3-Bromo-5-fluoro-2-methylaniline (10) CAS: 502496-36-8



1-Bromo-5-fluoro-2-methyl-3-nitrobenzene (117 mg, 0.5 mmol), Fe nanoparticles (6 mg), and NaBH₄ (57 mg, 1.5 mmol) in 1.0 mL 2 wt % TPGS/H₂O with 0.1 mL THF as co-solvent were reacted at rt for 4 h yielding 92.3 mg (90%) of 3-bromo-5-fluoro-2-methylaniline as a faint yellow liquid (hexane/ethyl acetate: 80/20).

¹H NMR (500 MHz, CDCl₃) δ 6.73 (dd, *J* = 8.5 Hz, *J* = 2.5 Hz, 1 H), 6.35 (dd, *J* = 10 Hz, *J* = 2.5 Hz, 1 H), 3.82 (s, br, 2 H), 2.20 (s, 3 H); ¹³C NMR (100 MHz, CDCl₃) δ 162.5, 160.0, 146.6, 146.5, 125.3, 125.2, 117.6, 109.7, 109.4, 101.2, 100.9, 16.3. ¹⁹F NMR (376 MHz, CDCl₃) δ -115.9; HRMS(CI): Calcd. For C₇H₇BrFN [M⁺] 202.9746. Found: 202.9745.

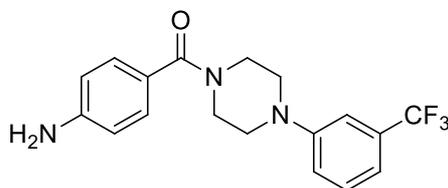
2-Amino-*N,N*-diisopropylbenzamide (11) CAS: 103794-66-7



N,N-Diisopropyl-2-nitrobenzamide (31.3 mg, 0.125 mmol), Fe nanoparticles (3 mg), and NaBH₄ (14.3 mg, 0.375 mmol) in 1.0 mL 2 wt % TPGS/H₂O with 0.1 mL THF as co-solvent were reacted at rt for 2 h yielding 27.0 mg (98%) of 2-amino-*N,N*-diisopropylbenzamide as a colorless oil (hexane/ethyl acetate: 80/20).

Spectral data matched that reported in the literature.⁴⁴ ¹H NMR (500 MHz, CDCl₃) δ 7.12 (m, 1 H), 7.00 (m, 1 H), 6.71 (m, 2 H), 4.03 (s, 2 H), 3.74 (s, br, 2 H), 1.35 (s, 12 H); ¹³C NMR (100 MHz, CDCl₃) δ 170.3, 144.3, 129.4, 125.9, 123.8, 117.6, 116.5, 48.4, 20.9. GC-MS, *m/z*: 220 [M⁺].

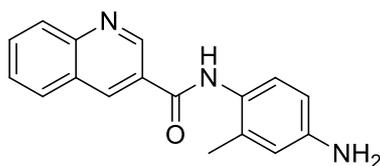
(4-Aminophenyl)(4-(3-(trifluoromethyl)phenyl)piperazin-1-yl)methanone (12) CAS: 747351-56-0



(4-Nitrophenyl)(4-(3-(trifluoromethyl)phenyl)piperazin-1-yl)methanone (189.7 mg, 0.5 mmol), Fe nanoparticles (6 mg), and NaBH₄ (57 mg, 1.5 mmol) in 1.0 mL 2 wt % TPGS/H₂O with 0.1 mL THF as co-solvent were reacted at rt for 2 h yielding 153.4 mg (88%) of (4-aminophenyl)(4-(3-(trifluoromethyl)phenyl) piperazin-1-yl)- methanone as a white solid liquid (DCM/MeOH: 95/5).

Spectral data matched that reported in the literature.⁴⁵ ¹H NMR (500 MHz, DMSO-*d*₆) δ 7.43 (m, 1 H), 7.24 (m, 1 H), 7.18 (m, 3 H), 7.10 (m, 1 H), 6.57 (d, *J* = 5 Hz, 2 H), 5.57 (s, br, 2 H), 3.63 (s, 4 H), 3.26 (s, 4 H). ¹³C NMR (125 MHz, DMSO-*d*₆) δ 170.1, 151.1, 150.6, 130.3 (q, ²*J*_(C-F) = 30 Hz), 128.5, 127.6, 125.5 (q, ¹*J*_(C-F) = 270 Hz), 122.1, 119.5, 115.04 (q, ³*J*_(C-F) = 4 Hz), 112.8, 111.8, 111.4 (q, ³*J*_(C-F) = 4 Hz), 48.3; GC-MS, *m/z*: 349 [M⁺].

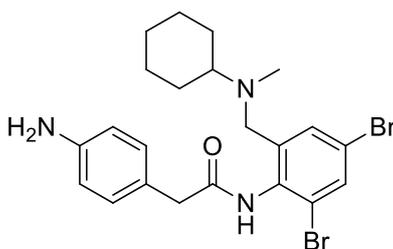
***N*-(4-Amino-2-methylphenyl)quinoline-3-carboxamide (13)**



N-(2-Methyl-4-nitrophenyl)quinoline-3-carboxamide (153.7 mg, 0.5 mmol), Fe nanoparticles (6 mg), and NaBH₄ (57 mg, 1.5 mmol) in 1.0 mL 2 wt % TPGS/H₂O with 0.25 mL DMSO as co-solvent were reacted at rt for 16 h yielding 110.5 mg (80%) of *N*-(4-amino-2-methylphenyl)quinoline-3-carboxamide as a yellow oil (hexane/ethyl acetate: 70/30).

¹H NMR (500 MHz, DMSO-*d*₆) δ 9.92 (s, 1 H), 9.37 (s, 1 H), 8.93 (s, 1 H), 8.13 (t, *J* = 5 Hz, 2 H), 7.90 (t, *J* = 5 Hz, 1 H), 7.72 (t, *J* = 5 Hz, 1 H), 6.99 (d, *J* = 10 Hz, 1 H), 6.49 (s, 1 H), 6.44 (d, *J* = 10 Hz, 1 H), 5.00 (s, br, 2 H), 2.13 (s, 3 H). ¹³C NMR (125 MHz, DMSO-*d*₆) δ 164.0, 149.1, 148.5, 147.2, 136.7, 134.6, 131.1, 129.1, 128.8, 127.7, 127.4, 126.6, 124.5, 115.3, 111.6, 18.1. HRMS(CI): Calcd. For C₁₇H₁₆N₃O [M+H]⁺ 278.1293. Found: 278.1288.

2-(4-Aminophenyl)-*N*-(2,4-dibromo-6-((cyclohexyl(methyl)amino)methyl)phenyl)acetamide (14)

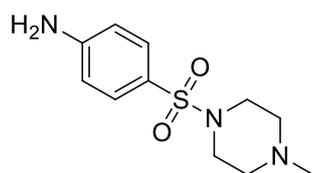


N-(2,4-Bibromo-6-((cyclohexyl(methyl)amino)methyl)phenyl)-2-(4-nitrophenyl)acetamide (67.4 mg, 0.125 mmol), Fe nanoparticles (3 mg), and NaBH₄ (14.3 mg, 0.375 mmol) in 1.0 mL 2 wt % TPGS/H₂O with 0.3 mL THF as co-solvent were reacted at rt for 2 h yielding 53.3 mg (84%) of 2-(4-aminophenyl)-*N*-(2,4-dibromo-6-((cyclohexyl(methyl)amino)methyl)phenyl)acetamide as a pale yellow solid DCM/MeOH: 95/5).

¹H NMR (500 MHz, DMSO-*d*₆) δ 9.58 (s, 1 H), 7.75 (s, 1 H), 7.61 (s, 1 H), 7.03 (d, *J* = 10 Hz, 2 H), 6.51 (d, *J* = 10 Hz, 2 H), 4.91 (s, br, 2 H), 3.44 (s, 2 H), 3.30 (s, 2 H), 2.26 (m, 1 H), 2.00 (s, 3 H), 1.72 (m, 2 H), 1.65 (m, 2 H), 1.55 (m, 1 H), 1.12 (m, 5 H). ¹³C NMR (125

MHz, DMSO- d_6) δ 169.8, 147.3, 142.7, 134.6, 132.3, 130.4, 129.5, 123.7, 122.5, 120.0, 113.8, 62.3, 53.1, 41.7, 37.4, 28.1, 25.9, 25.5. HRMS(CI): Calcd. For $C_{22}H_{28}Br_2ON_3$ $[M+H]^+$ 508.0599. Found: 508.0609.

4-((4-Methylpiperazin-1-yl)sulfonyl)aniline (15) CAS: 21623-68-7



1-Methyl-4-((4-nitrophenyl)sulfonyl)piperazine (71.3 mg, 0.25 mmol), Fe nanoparticles (3 mg), and $NaBH_4$ (28.5 mg, 0.75 mmol) in 1.0 mL 2 wt % TPGS/ H_2O with 0.1 mL THF as co-solvent were reacted at rt for 16 h yielding 62.6 mg (98%) of 4-((4-methylpiperazin-1-yl)sulfonyl)aniline as a white solid (DCM/MeOH: 95/5).

1H NMR (500 MHz, DMSO- d_6) δ 7.29 (d, $J = 5$ Hz, 2 H), 6.61 (d, $J = 10$ Hz, 2 H), 6.01 (s, 2 H), 2.73 (s, 4 H), 2.28 (s, 4 H), 2.07 (s, 3 H). ^{13}C NMR (125 MHz, DMSO- d_6) δ 153.2, 129.6, 119.3, 112.7, 53.6, 45.7, 45.3; HRMS(CI): Calcd. For $C_{11}H_{18}SO_2N_3$ $[M+H]^+$ 256.1120. Found: 256.1118.

(2-Amino-4,5-dimethoxyphenyl)(4-methylpiperazin-1-yl)methanone (16) CAS: 926269-05-8

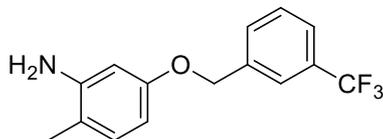


(4,5-Dimethoxy-2-nitrophenyl)(4-methylpiperazin-1-yl)methanone (77.3 mg, 0.25 mmol), Fe nanoparticles (3 mg), and $NaBH_4$ (28.5 mg, 0.75 mmol) in 1.0 mL 2 wt % TPGS/ H_2O with 0.25 mL CH_3OH as co-solvent were reacted at rt for 16 h yielding 57.7 mg (83%) of (2-amino-4,5-dimethoxyphenyl)(4-methylpiperazin-1-yl)methanone as a yellow oil (DCM/MeOH: 90/10).

Spectral data matched that reported in the literature.⁴⁶ 1H NMR (500 MHz, $CDCl_3$) δ 6.63 (s, 1 H), 6.24 (s, 1 H), 4.21 (s, br, 2 H), 3.82 (s, 3 H), 3.77 (s, 3 H), 3.62 (m, 4 H), 2.41 (m, 4 H), 2.29 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.1, 151.6, 141.2, 141.1, 112.4,

110.4, 101.0, 56.9, 55.8, 55.3, 46.1, 45.0 (br); GC-MS, m/z : 279 [M^+].

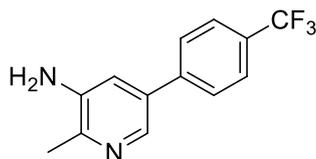
2-Methyl-5-((3-(trifluoromethyl)benzyl)oxy)aniline (17)



1-Methyl-2-nitro-4-((3-(trifluoromethyl)benzyl)oxy)benzene (155.6 mg, 0.5 mmol), Fe nanoparticles (12 mg), and NaBH_4 (114 mg, 3 mmol) in 1.0 mL 2 wt % TPGS/ H_2O with 0.1 mL DCM as co-solvent were reacted at rt for 16 h yielding 135.2mg (96%) of 2-methyl-5-((3-(trifluoromethyl)benzyl)oxy)aniline as a pale yellow crystal (hexane/ethyl acetate: 80/20).

^1H NMR (500 MHz, CDCl_3) δ 7.72 (s, 1 H), 7.61 (m, 2 H), 7.50 (m, 1 H), 6.99 (d, $J = 10$ Hz), 6.36 (m, 2 H) 5.06 (s, 2 H), 3.64 (s, br, 2 H), 2.13 (s, 3 H); ^{13}C NMR (125 MHz, CDCl_3) δ 157.99, 146.7, 138.6, 131.3 (q, $^1J_{\text{C-F}} = 32.5$ Hz), 131.1, 130.6, 129.1, 127.5 (q, $^1J_{\text{C-F}} = 271$ Hz), 124.7 (q, $^1J_{\text{C-F}} = 3.75$ Hz), 124.0 (q, $^1J_{\text{C-F}} = 3.75$ Hz), 115.6, 104.5, 102.0, 69.2, 16.5; ^{19}F NMR (376 MHz, CDCl_3) δ -62.66; HRMS(EI): Calcd. For $\text{C}_{15}\text{H}_{14}\text{NOF}_3$ [M^+] 281.1027. Found: 281.1019.

2-Methyl-5-(4-(trifluoromethyl)phenyl)pyridin-3-amine (18)

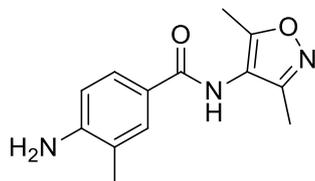


2-Methyl-3-nitro-5-(4-(trifluoromethyl)phenyl)pyridine (141.1 mg, 0.5 mmol), Fe nanoparticles (6 mg), and NaBH_4 (57 mg, 1.5 mmol) in 1.0 mL 2 wt % TPGS/ H_2O with 0.25 mL THF as co-solvent were reacted at rt for 16 h yielding 108 mg (86%) of 2-methyl-5-(4-(trifluoromethyl)phenyl)pyridin-3-amine as a white crystal (hexane/ethyl acetate: 70/30).

^1H NMR (500 MHz, DMSO-d_6) δ 8.02 (s, 1 H), 7.80 (s, 4 H), 7.22 (s, 1 H), 5.23 (s, 2 H), 2.32 (s 3 H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 143.2, 142.5, 142.3, 134.6, 132.5, 128.4 (q, $^1J_{\text{C-F}} = 270.76$ Hz), 128.4 (q, $^1J_{\text{C-F}} = 32$ Hz), 127.2, 125.9 (q, $^1J_{\text{C-F}} = 4$ Hz), 117.5, 20.4; ^{19}F

NMR (376 MHz, DMSO- d_6) δ -61.05; HRMS(EI): Calcd. For $C_{13}H_{11}N_2F_3$ [M^+] 252.0874. Found: 252.0871.

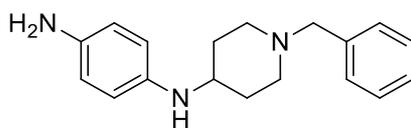
4-Amino-*N*-(3,5-dimethylisoxazol-4-yl)-3-methylbenzamide (19)



N-(3,5-Dimethylisoxazol-4-yl)-3-methyl-4-nitrobenzamide (137.6 mg, 0.5 mmol), Fe nanoparticles (6 mg), and $NaBH_4$ (57 mg, 1.5 mmol) in 1.0 mL 2 wt % TPGS/ H_2O with 0.25 mL DMSO as co-solvent were reacted at rt for 6 h yielding 117.9 mg (96%) of 4-amino-*N*-(3,5-dimethylisoxazol-4-yl)-3-methylbenzamide as a pale yellow solid (hexane/ethyl acetate: 70/30).

1H NMR (500 MHz, DMSO- d_6) δ 10.3 (s, 1 H), 7.63 (s, 1 H), 7.60 (dd, $J = 8$ Hz, $J = 2.5$ Hz, 1 H), 6.64 (d, $J = 10$ Hz, 1 H), 1.92 (s, br, 2 H), 2.16 (s, 3 H), 2.10 (s, 3 H), 1.79 (s, 3 H); ^{13}C NMR (125 MHz, DMSO- d_6) δ 164.7, 161.3, 158.3, 151.1, 130.6, 127.6, 120.0, 119.1, 112.7, 112.7, 113.3, 17.5, 10.4, 6.9; HRMS(EI): Calcd. For $C_{13}H_{15}O_2N_3$ [M^+] 245.1159. Found: 245.1164.

N-1-(1-Benzylpiperidin-4-yl)benzene-1,4-diamine (20) CAS: 1039820-98-8

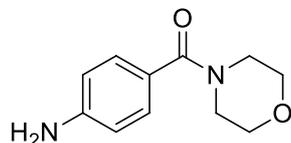


1-Benzyl-*N*-(4-nitrophenyl)piperidin-4-amine (155.7 mg, 0.5 mmol), Fe nanoparticles (12 mg), and KBH_4 (161.8 mg, 3 mmol) in 1.0 mL 2 wt % TPGS/ H_2O with 0.25 mL THF as co-solvent were reacted at rt for 16 h yielding 129.8 mg (92%) of *N*-1-(1-benzylpiperidin-4-yl)benzene-1,4-diamine as a deep red solid (DCM/MeOH: 90/10).

1H NMR (500 MHz, $CDCl_3$) δ 7.34 (m, 4 H), 7.27 (m, 1 H), 6.60 (d, 2 H), 6.51 (d, 2 H), 3.64 (s, 1 H), 3.57 (s, 2 H), 3.19 (m, 3 H), 2.88 (m, 2 H), 2.18 (t, $J = 10$ Hz, 2 H), 2.02 (m, 2 H), 1.50, (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.9, 137.9, 137.4, 129.3, 128.3, 127.3, 116.8, 115.8, 70.5, 62.8, 52.2, 32.3; HRMS(CI): Calcd. For $C_{18}H_{23}N_3$ [M^+] 281.1892.

Found: 281.1899.

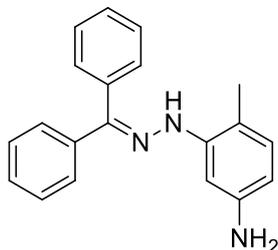
(4-Aminophenyl)(morpholino)methanone (21) CAS: 51207-86-4



Morpholino(4-nitrophenyl)methanone (118.1 mg, 0.5 mmol), Fe nanoparticles (6 mg), and NaBH₄ (57 mg, 1.5 mmol) in 1.0 mL 2 wt % TPGS/H₂O with 0.1 mL THF as co-solvent were reacted at rt for 30 min yielding 102.4 mg (99%) of (4-aminophenyl)(morpholino)methanone as a pale yellow solid (DCM/MeOH: 70/30).

Spectral data matched that reported in the literature.⁷ ¹H NMR (500 MHz, CDCl₃) δ 7.26 (m, 2 H), 6.64 (m, 2 H), 3.92 (s, br, 2 H), 3.68 (m, 8 H); ¹³C NMR (100 MHz, CDCl₃) δ 170.9, 148.7, 129.3, 124.0, 114.0, 66.8; GC-MS, m/z: 206 [M⁺].

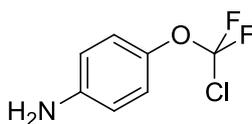
3-(2-(Diphenylmethylene)hydrazinyl)-4-methylaniline (22)



1-(Diphenylmethylene)-2-(2-methyl-5-nitrophenyl)hydrazine (41.4 mg, 0.125 mmol), Fe nanoparticles (1.5 mg), and NaBH₄ (14.3 mg, 0.375 mmol) in 1.0 mL 2 wt % TPGS/H₂O with 0.25 mL DMSO as co-solvent were reacted at rt for 16 h yielding 35.7 mg (95%) of 3-(2-(diphenylmethylene)hydrazinyl)-4-methylaniline as an orange solid (hexane/ethyl acetate: 70/30).

¹H NMR (500 MHz, CDCl₃) δ 7.59 (m, 4 H), 7.52 (m, 1 H), 7.42 (s, 1 H), 7.34 (m, 5 H), 7.29 (d, *J* = 3 Hz, 1 H), 6.79 (d, *J* = 8 Hz, 1 H), 6.17 (dd, *J* = 8 Hz, *J* = 2.5 Hz, 1 H), 3.63 (s, br, 2 H), 1.75 (s, 3 H); ¹³C NMR (125 MHz, CDCl₃) δ 147.0, 145.1, 143.1, 138.5, 133.1, 131.0, 129.8, 129.4, 129.0, 128.3, 128.1, 126.6, 110.9, 116.9, 99.7, 15.7; HRMS(EI): Calcd. For C₂₀H₁₉N₃ [M⁺] 301.1579. Found: 301.1572.

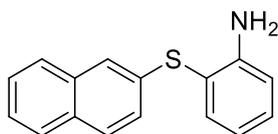
4-(Chlorodifluoromethoxy)aniline (23) CAS: 39065-95-7



1-(Chlorodifluoromethoxy)-4-nitrobenzene (111.8 mg, 0.5 mmol), Fe nanoparticles (6 mg), and NaBH₄ (57 mg, 1.5 mmol) in 1.0 mL 2 wt % TPGS/H₂O with 0.1 mL THF as co-solvent were reacted at rt for 30 min yielding 88.4 mg (91%) of 4-(chlorodifluoromethoxy)aniline as a yellow liquid (hexane/ethyl acetate: 70/30).

¹H NMR (500 MHz, CDCl₃) δ 7.03 (d, *J* = 10 Hz, 2 H), 6.66 (s, 2 H), 3.71 (s, br, 2 H); ¹³C NMR (125 MHz, CDCl₃) δ 146.5, 142.6, 125.8, 122.9, 115.5; ¹⁹F NMR (376 MHz, DMSO-d₆) δ -25.77; HRMS(Cl): Calcd. For C₇H₆ClF₂NO [M⁺] 193.0106. Found: 193.0104.

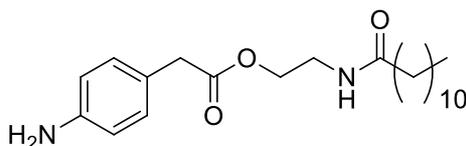
2-(Naphthalen-2-ylthio)aniline (24) CAS: 859330-37-3



Naphthalen-2-yl(2-nitrophenyl)sulfane (35.2 mg, 0.125 mmol), Fe nanoparticles (2.7 mg), and KBH₄ (40.5 mg, 0.75 mmol) in 1.0 mL 2 wt % TPGS/H₂O with 0.25 mL DMSO as co-solvent were reacted at rt for 16 h yielding 28.9 mg (92%) of 2-(naphthalen-2-ylthio)aniline as a yellow solid (hexane/ethyl acetate: 70/30).

Spectral data matched to the reported in literature.⁴⁷ ¹H NMR (500 MHz, CDCl₃) δ 7.77 (d, *J* = 10 Hz, 1 H), 7.72 (d, *J* = 10 Hz, 1 H), 7.66 (d, *J* = 10 Hz, 1 H), 7.53 (m, 2 H), 7.45 (p, *J* = 10 Hz, 2 H), 7.28 (m, 2 H), 6.83 (m, 2 H), 4.31 (s, br, 2 H); ¹³C NMR (125 MHz, CDCl₃) δ 149.0, 137.5, 134.3, 133.9, 131.7, 131.3, 128.8, 127.9, 127.1, 126.7, 125.6, 125.3, 124.5, 118.9, 115.6, 114.5; GC-MS, *m/z*: 251 [M⁺].

2-Dodecanamidoethyl 2-(4-aminophenyl)acetate (25)

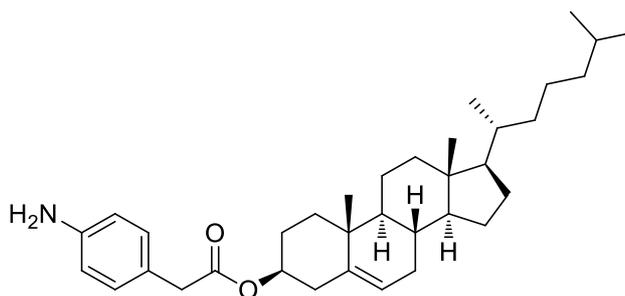


2-Dodecanamidoethyl 2-(4-nitrophenyl)acetate (101.6 mg, 0.25 mmol), Fe nanoparticles (3 mg), and KBH₄ (40.5 mg, 0.75 mmol) in 1.0 mL 2 wt % TPGS/H₂O with 0.25 mL THF as

co-solvent were reacted at rt for 8 h yielding 86.9 mg (92%) of 2-dodecanamidoethyl 2-(4-aminophenyl)acetate as a pale yellow solid (DCM/MeOH: 90/10).

^1H NMR (500 MHz, DMSO- d_6) δ 7.87 (s, 1 H), 6.89(d, J = 5 Hz, 8 H), 6.50 (d, J = 8 Hz, 2 H), 4.95 (s, 2 H), 4.00 (t, J = 5.5 Hz, 2 H), 3.41 (s, 2 H), 3.28 (q, J = 6 Hz, 2 H), 2.07 (t, J = 12.5 Hz, 2 H), 1.47 (m, 2 H), 1.23 (m, 16 H), 0.863 (t, J = 7 Hz, 3 H); ^{13}C NMR (125 MHz, CDCl_3) δ 172.4, 171.7, 147.4, 129.7, 120.9, 113.8, 62.7, 39.5, 37.5, 35.4, 31.3, 29.1, 29.0, 28.9, 28.8, 28.7, 28.6, 25.2, 22.1, 13.9; HRMS(CI): Calcd. For $\text{C}_{22}\text{H}_{37}\text{O}_3\text{N}_2$ $[\text{M}+\text{H}]^+$ 377.2804. Found: 377.2804.

(3S,8S,9S,10R,13R,14S,17R)-10,13-Dimethyl-17-((R)-6-methylheptan-2-yl)-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-3-yl 2-(4-nitrophenyl)acetate (26)

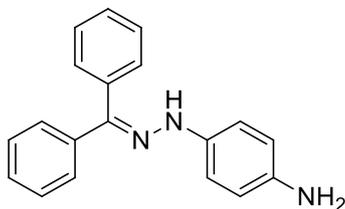


(3S,8S,9S,10R,13R,14S,17R)-10,13-Dimethyl-17-((R)-6-methylheptan-2-yl)-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-3-yl 2-(4-nitrophenyl)acetate (137.4 mg, 0.25 mmol), Fe nanoparticles (3 mg), and NaBH_4 (28.5 mg, 0.75 mmol) in 1.0 mL 2 wt % TPGS/ H_2O with 0.3 mL DCM as co-solvent were reacted at rt for 4 h yielding 123.2 mg (95%) of (3S,8S,9S,10R,13R,14S,17R)-10,13-dimethyl-17-((R)-6-methylheptan-2-yl)-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-3-yl 2-(4-nitrophenyl)acetate as a white solid (hexane/ethyl acetate: 80/20).

^1H NMR (500 MHz, CDCl_3) δ 7.08 (d, J = 10 Hz, 2 H), 6.66 (d, J = 10 Hz, 2 H), 5.35 (d, J = 4 Hz, 1 H), 4.60 (m, 1 H), 3.47 (s, 2 H), 3.16 (s, br, 2 H), 3.29 (m, 2 H), 1.99 (m, 2 H), 1.93 (m, 3 H), 1.12 (m, 20 H), 1.01 (s, 4 H), 0.92 (d, 3 H), 0.87 (dd, J = 7 Hz, J = 2 Hz, 6 H), 0.67 (s, 3 H); ^{13}C NMR (125 MHz, CDCl_3) δ 171.7, 146.3, 139.8, 130.2, 124.4, 122.7, 115.4, 74.4, 56.8, 56.3, 50.1, 42.4, 41.0, 39.9, 39.7, 38.2, 37.1, 36.7, 36.3, 35.9, 32.0, 31.9, 28.3,

28.1, 27.9, 24.4, 24.0, 23.0, 22.7, 21.2, 19.5, 18.9, 12.0; HRMS(EI): Calcd. For $C_{35}H_{53}O_2N$ [M^+] 519.4076. Found: 519.4078.

4-(2-(Diphenylmethylene)hydrazinyl)aniline (27) CAS: 1194714-06-1



1-(Diphenylmethylene)-2-(4-nitrophenyl)hydrazine (39.7 mg, 0.125 mmol), Fe nanoparticles (1.5 mg), and KBH_4 (40.5 mg, 0.75 mmol) in 1.0 mL 2 wt % TPGS/ H_2O with 0.25 mL THF as co-solvent were reacted at rt for 16 h yielding 35.5 mg (99%) of 4-(2-(diphenylmethylene)hydrazinyl)aniline as a dark brown solid (hexane/ethyl acetate: 70/30).

1H NMR (500 MHz, $CDCl_3$) δ 7.59 (m, 4 H), 7.52 (m, 1 H), 7.34 (m, 6 H), 6.97 (d, $J = 8.5$ Hz, 2 H), 6.71 (d, $J = 8.5$ Hz, 2 H), 3.83 (s, br, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.0, 138.8, 138.7, 138.2, 133.1, 129.7, 129.3, 129.2, 128.2, 127.7, 126.3, 117.0, 114.3; HRMS(ESI): Calcd. For $C_{19}H_{17}N_3Na$ [$M+Na$] $^+$ 310.1320. Found: 310.1316.

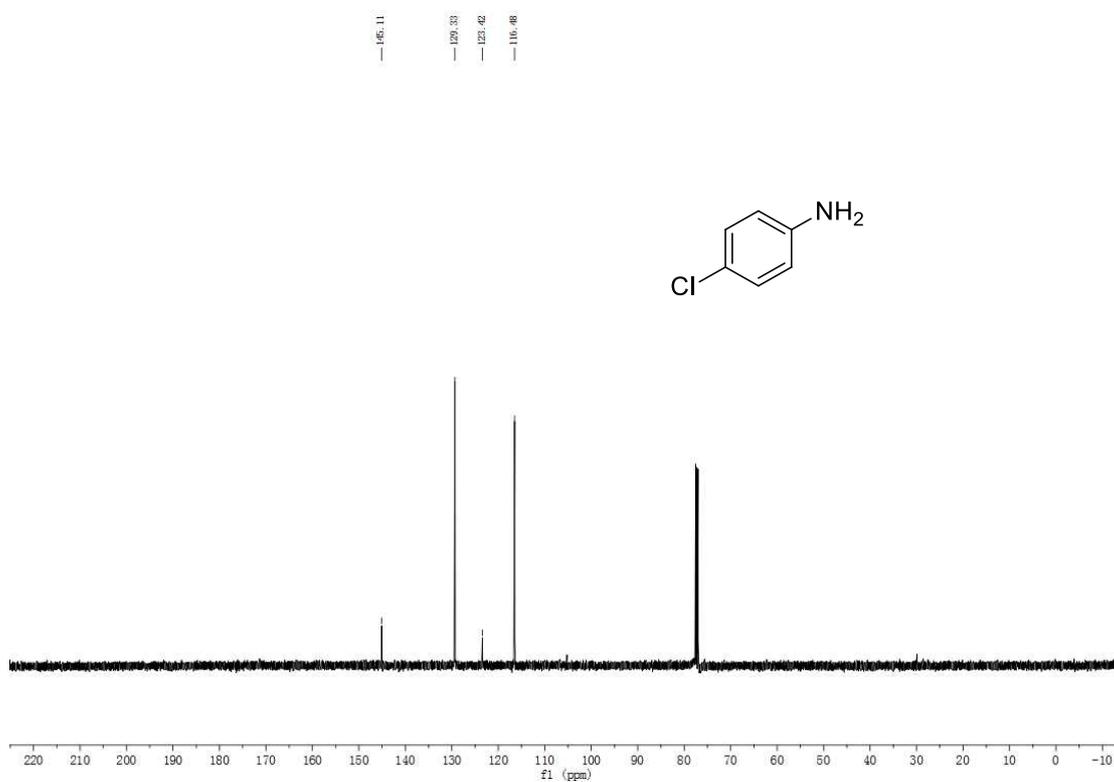
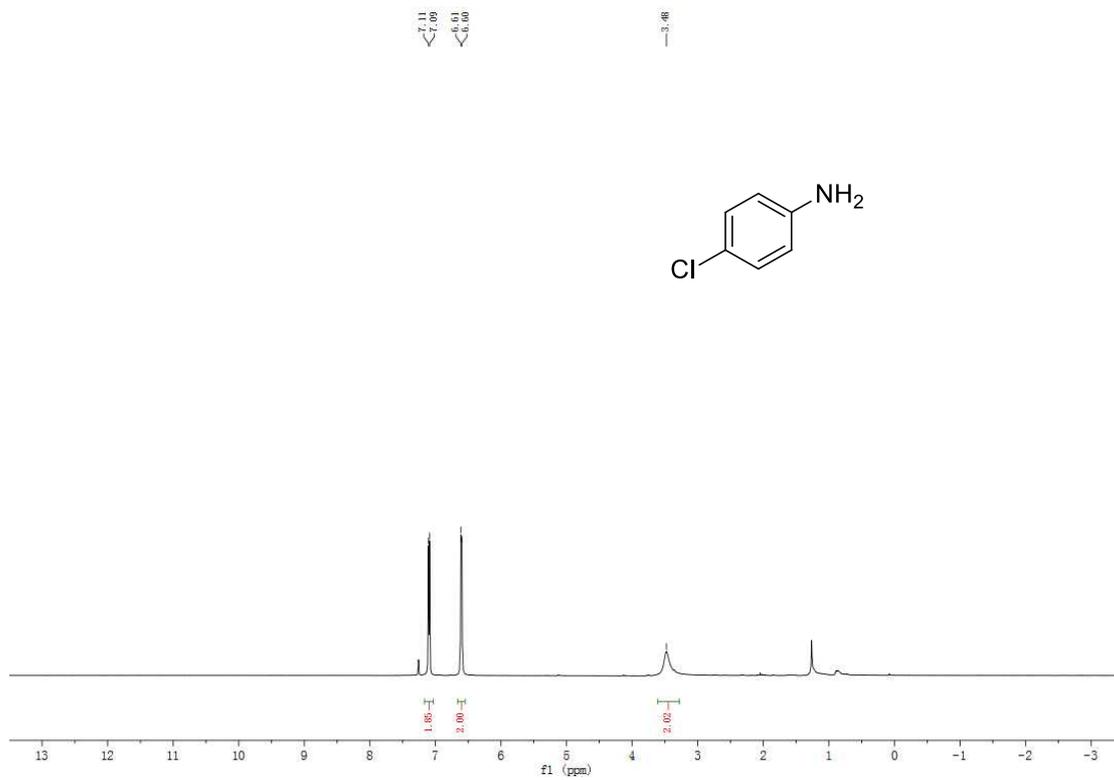
References

1. B. H. Lipshutz, S. Ghorai, A. R. Abela, R. Moser, T. Nishikata, C. Duplais, A. Krasovskiy, R. D. Gaston and R. C. Gadwood, *J. Org. Chem.*, 2011, **76**, 4379-4391.
2. F. A. Westerhaus, R. V. Jagadeesh, G. Wienhöfer, M.-M. Pohl, J. Radnik, A.-E. Surkus, J. Rabeah, K. Junge, H. Junge, M. Nielsen, A. Brückner and M. Beller, *Nat Chem*, 2013, **5**, 537-543.
3. M. M. Dell'Anna, S. Intini, G. Romanazzi, A. Rizzuti, C. Leonelli, F. Piccinni and P. Mastroilli, *J. Mol. Catal. A: Chem.*, 2014, **395**, 307-314.
4. J. Tuteja, S. Nishimura and K. Ebitani, *RSC Adv.*, 2014, **4**, 38241-38249.
5. A. J. MacNair, M.-M. Tran, J. E. Nelson, G. U. Sloan, A. Ironmonger and S. P. Thomas, *Org. Biomol. Chem.*, 2014, **12**, 5082-5088.
6. R. V. Jagadeesh, G. Wienhofer, F. A. Westerhaus, A.-E. Surkus, M.-M. Pohl, H. Junge, K. Junge and M. Beller, *Chem. Commun.*, 2011, **47**, 10972-10974.
7. H. Lu, Z. Geng, J. Li, D. Zou, Y. Wu and Y. Wu, *Org. Lett.*, 2016, **18**, 2774-2776.
8. L. He, L.-C. Wang, H. Sun, J. Ni, Y. Cao, H.-Y. He and K.-N. Fan, *Angew. Chem. Int. Ed.*, 2009, **48**, 9538-9541.
9. K. Junge, B. Wendt, N. Shaikh and M. Beller, *Chem. Commun.*, 2010, **46**, 1769-1771.
10. O. Verho, K. P. J. Gustafson, A. Nagendiran, C.-W. Tai and J.-E. Bäckvall, *ChemCatChem*, 2014, **6**, 3153-3159.
11. E. Pedrajas, I. Sorribes, A. L. Gushchin, Y. A. Laricheva, K. Junge, M. Beller and R. Llusar, *ChemCatChem*, 2017, **9**, 1128-1134.
12. X.-L. Chen, B.-R. Ai, Y. Dong, X.-M. Zhang and J.-Y. Wang, *Tetrahedron Lett.*, 2017, **58**, 3646-3649.
13. Z.-b. Xu, G.-p. Lu and C. Cai, *Catal. Commun.*, 2017, **99**, 57-60.
14. Z. Liu, W. Dong, S. Cheng, S. Guo, N. Shang, S. Gao, C. Feng, C. Wang and Z. Wang, *Catal. Commun.*, 2017, **95**, 50-53.
15. K. J. Prathap, Q. Wu, R. T. Olsson and P. Diner, *Org. Lett.*, 2017, **19**, 4746-4749.
16. M. Liu, W. Tang, Z. Xie, H. Yu, H. Yin, Y. Xu, S. Zhao and S. Zhou, *ACS Catal.*, 2017, **7**, 1583-1591.

17. I. Sorribes, L. Liu and A. Corma, *ACS Catal.*, 2017, **7**, 2698-2708.
18. P. M. Uberman, C. S. García, J. R. Rodríguez and S. E. Martín, *Green Chem.*, 2017, **19**, 739-748.
19. H. Huang, X. Wang, X. Li, C. Chen, X. Zou, W. Ding and X. Lu, *Green Chem.*, 2017, **19**, 809-815.
20. M. Tian, X. Cui, M. Yuan, J. Yang, J. Ma and Z. Dong, *Green Chem.*, 2017, **19**, 1548-1554.
21. J. R. Morse, J. F. Callejas, A. J. Darling and R. E. Schaak, *Chem Commun (Camb)*, 2017, **53**, 4807-4810.
22. Z.-C. Ding, C.-Y. Li, J.-J. Chen, J.-H. Zeng, H.-T. Tang, Y.-J. Ding and Z.-P. Zhan, *Adv. Synth. Catal.*, 2017, **359**, 2280-2287.
23. X. Sun, A. I. Olivos-Suarez, L. Oar-Arteta, E. Rozhko, D. Osadchii, A. Bavykina, F. Kapteijn and J. Gascon, *ChemCatChem*, 2017, **9**, 1854-1862.
24. R. J. Kalbasi, A. A. Nourbakhsh and F. Babaknezhad, *Catal. Commun.*, 2011, **12**, 955-960.
25. R. K. Rai, A. Mahata, S. Mukhopadhyay, S. Gupta, P.-Z. Li, K. T. Nguyen, Y. Zhao, B. Pathak and S. K. Singh, *Inorg. Chem.*, 2014, **53**, 2904-2909.
26. S.-T. Yang, P. Shen, B.-S. Liao, Y.-H. Liu, S.-M. Peng and S.-T. Liu, *Organometallics*, 2017, **36**, 3110-3116.
27. D. Damodara, R. Arundhathi, T. V. Ramesh Babu, M. K. Legan, H. J. Kumpaty and P. R. Likhar, *RSC Adv.*, 2014, **4**, 22567-22574.
28. Y.-N. Zhang, X.-H. Li, Y.-Y. Cai, L.-H. Gong, K.-X. Wang and J.-S. Chen, *RSC Adv.*, 2014, **4**, 60873-60877.
29. S. Keshipour and K. Adak, *RSC Adv.*, 2016, **6**, 89407-89412.
30. R. V. Jagadeesh, K. Natte, H. Junge and M. Beller, *ACS Catal.*, 2015, **5**, 1526-1529.
31. R. V. Jagadeesh, D. Banerjee, P. B. Arockiam, H. Junge, K. Junge, M.-M. Pohl, J. Radnik, A. Bruckner and M. Beller, *Green Chem.*, 2015, **17**, 898-902.
32. N. A. Isley, R. T. H. Linstadt, S. M. Kelly, F. Gallou and B. H. Lipshutz, *Org. Lett.*, 2015, **17**, 4734-4737.
33. S. Handa, Y. Wang, F. Gallou and B. H. Lipshutz, *Science*, 2015, **349**, 1087.

34. J. Wencel-Delord, C. Nimphius, F. W. Patureau and F. Glorius, *Angew. Chem., Int. Ed.*, 2012, **51**, 2247-2251.
35. M. W. Hackl, M. Lakemeyer, M. Dahmen, M. Glaser, A. Pahl, K. Lorenz-Baath, T. Menzel, S. Sievers, T. Böttcher, I. Antes, H. Waldmann and S. A. Sieber, *J. Am. Chem. Soc.*, 2015, **137**, 8475-8483.
36. S. M. Kelly and B. H. Lipshutz, *Org. Lett.*, 2014, **16**, 98-101.
37. S. Chen, G. Lu and C. Cai, *New J. Chem.*, 2015, **39**, 5360-5365.
38. N. Sathitsuksanoh, K. M. Holtman, D. J. Yelle, T. Morgan, V. Stavila, J. Pelton, H. Blanch, B. A. Simmons and A. George, *Green Chem.*, 2014, **16**, 1236-1247.
39. H. Wang, K. Wen, N. Nurahmat, Y. Shao, H. Zhang, C. Wei, Y. Li, Y. Shen and Z. Sun, *Beilstein J. Org. Chem.*, 2012, **8**, 744-748.
40. P. S. Rathore, R. Patidar, T. Shripathi and S. Thakore, *Catal. Sci. Technol.*, 2015, **5**, 286-295.
41. D. Cantillo, M. Baghbanzadeh and C. O. Kappe, *Angew. Chem., Int. Ed.*, 2012, **51**, 10190-10193.
42. A. J. Kasparian, C. Savarin, A. M. Allgeier and S. D. Walker, *J. Org. Chem.*, 2011, **76**, 9841-9844.
43. P. R. Sultane, T. B. Mete and R. G. Bhat, *Org. Biomol. Chem.*, 2014, **12**, 261-264.
44. N. Tezuka, K. Shimojo, K. Hirano, S. Komagawa, K. Yoshida, C. Wang, K. Miyamoto, T. Saito, R. Takita and M. Uchiyama, *J. Am. Chem. Soc.*, 2016, **138**, 9166-9171.
45. J. Feng, S. Handa, F. Gallou and B. H. Lipshutz, *Angew. Chem.*, 2016, **128**, 9125-9129.
46. S. Chakravorty, H. F. Klein, L. E. Hodson, M. Rabillier, Z. Fang, A. Richters, S. C. Pelly and D. Rauh; W. A. L. Van Otterlo, *South Afr. J. Chem.*, 2014, **67**, 71 – 79
47. D. Yang, K. Yan, W. Wei, J. Zhao, M. Zhang, X. Sheng, G. Li, S. Lu and H. Wang, *J. Org. Chem.*, 2015, **80**, 6083-6092.

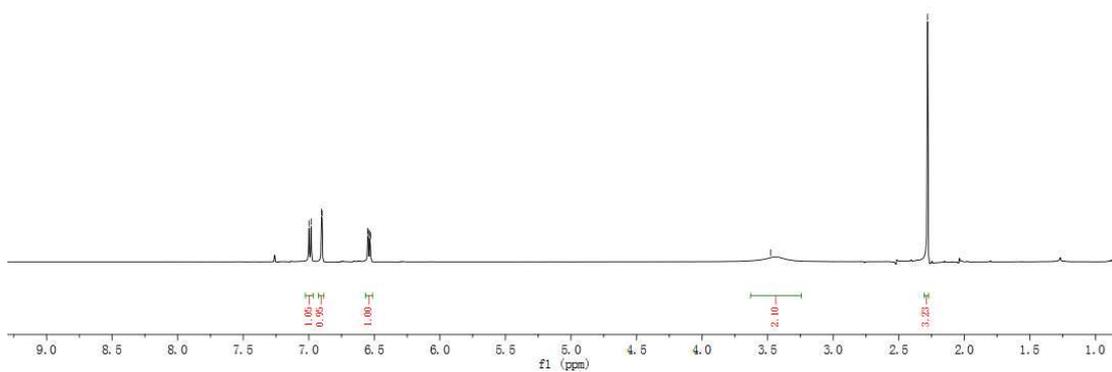
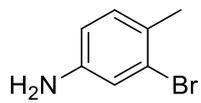
NMR Spectra



7.00
6.96
6.90
6.55
6.53

3.48

2.28



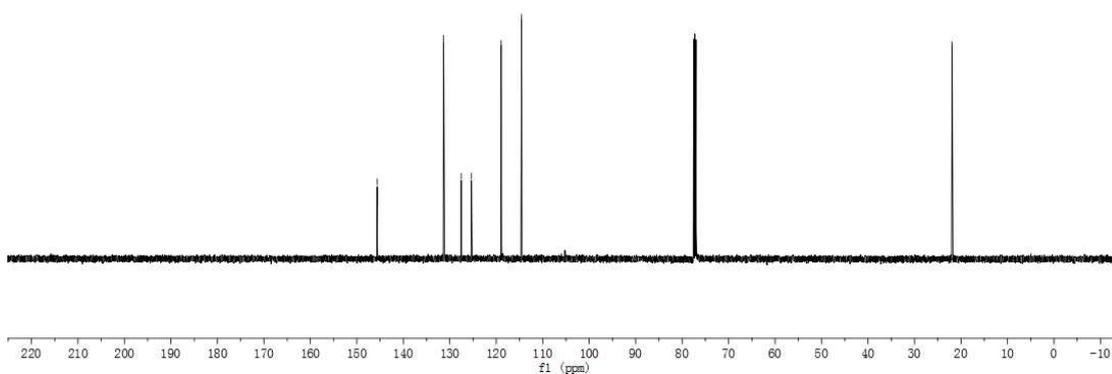
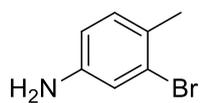
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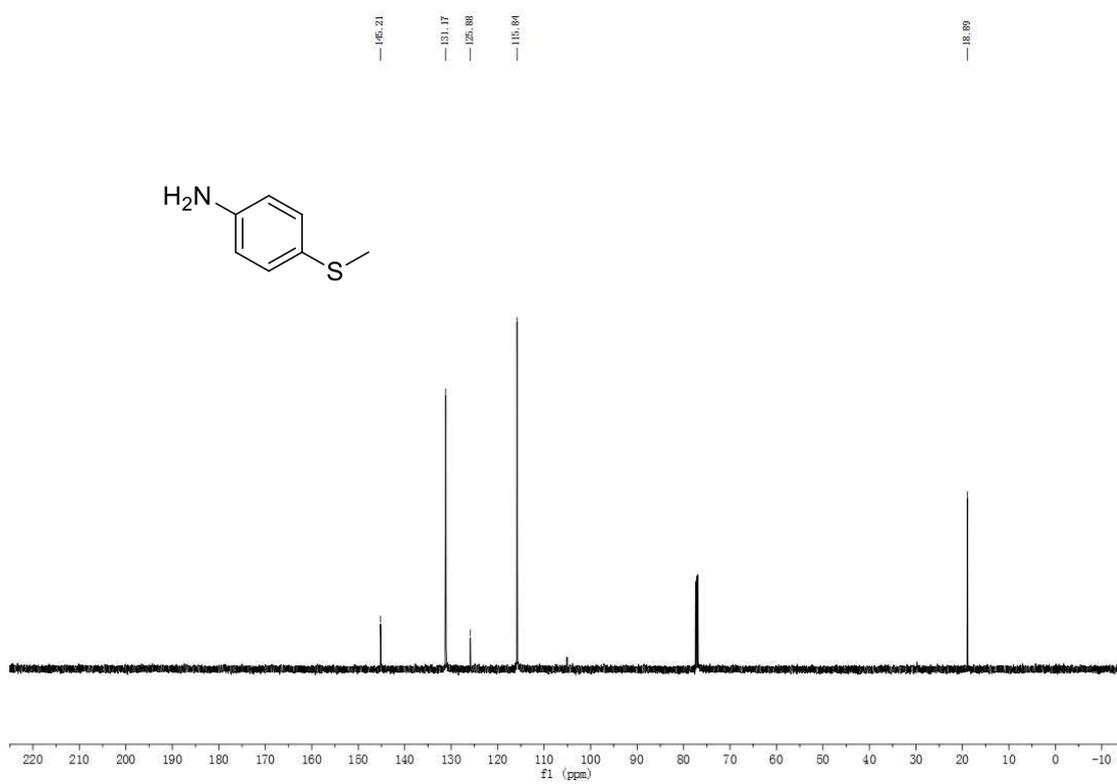
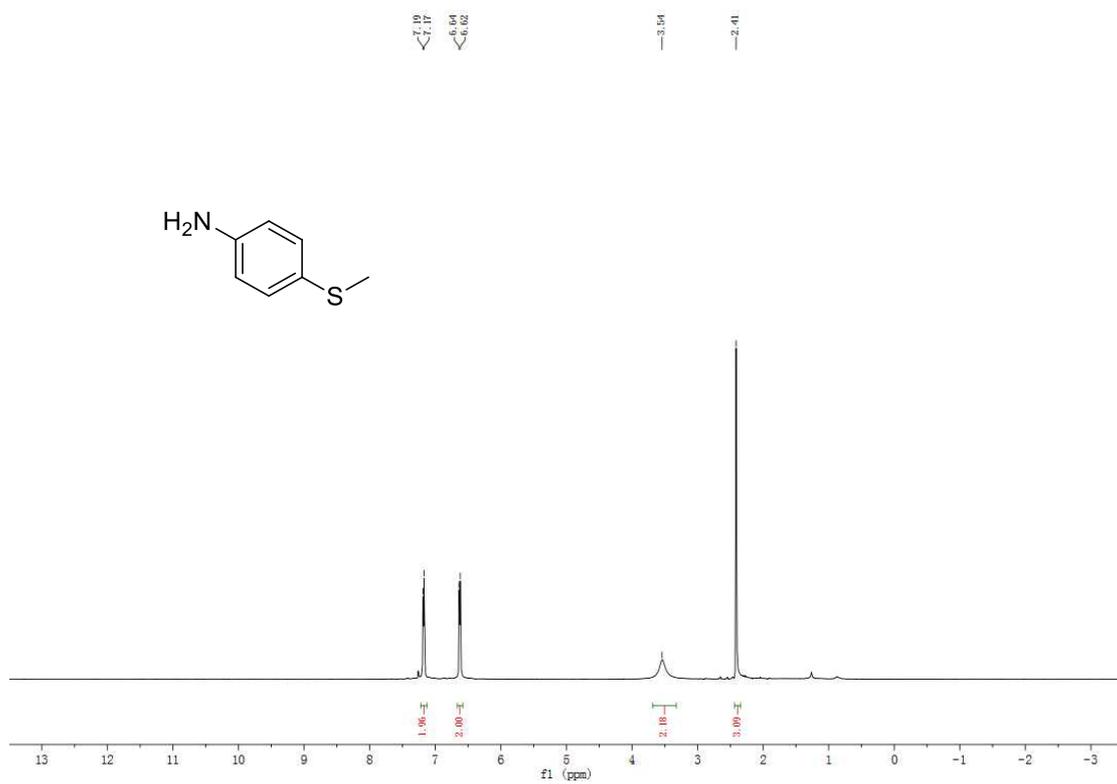
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125.34

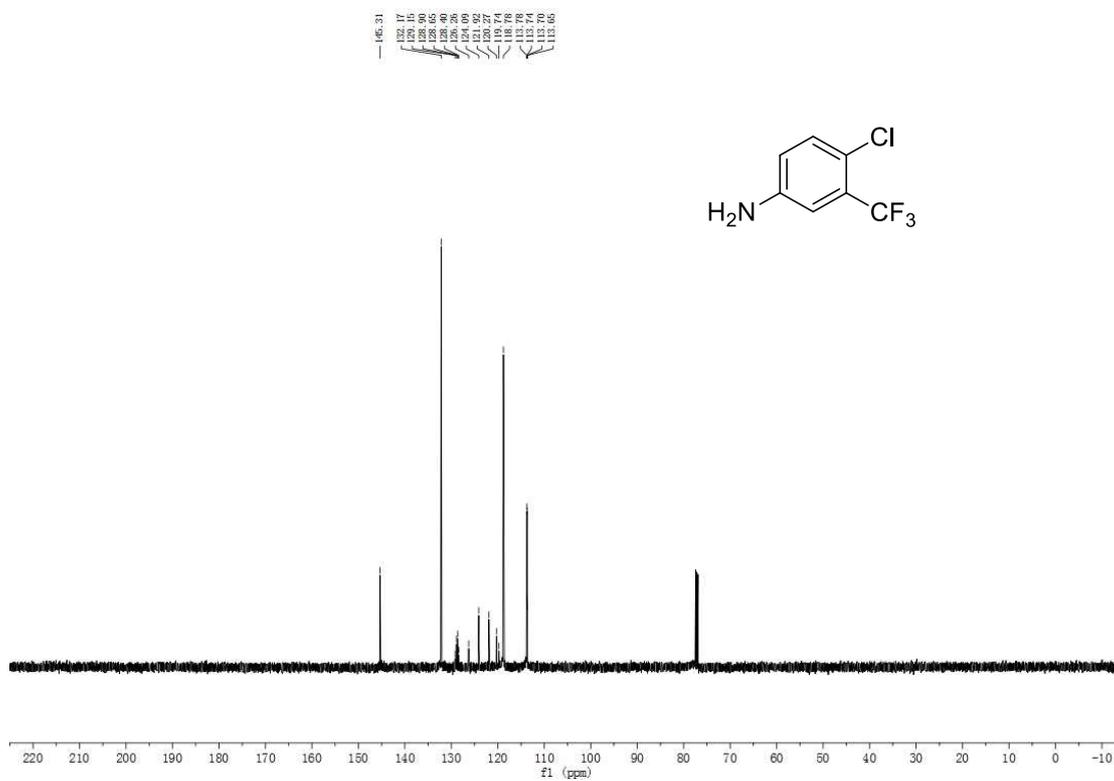
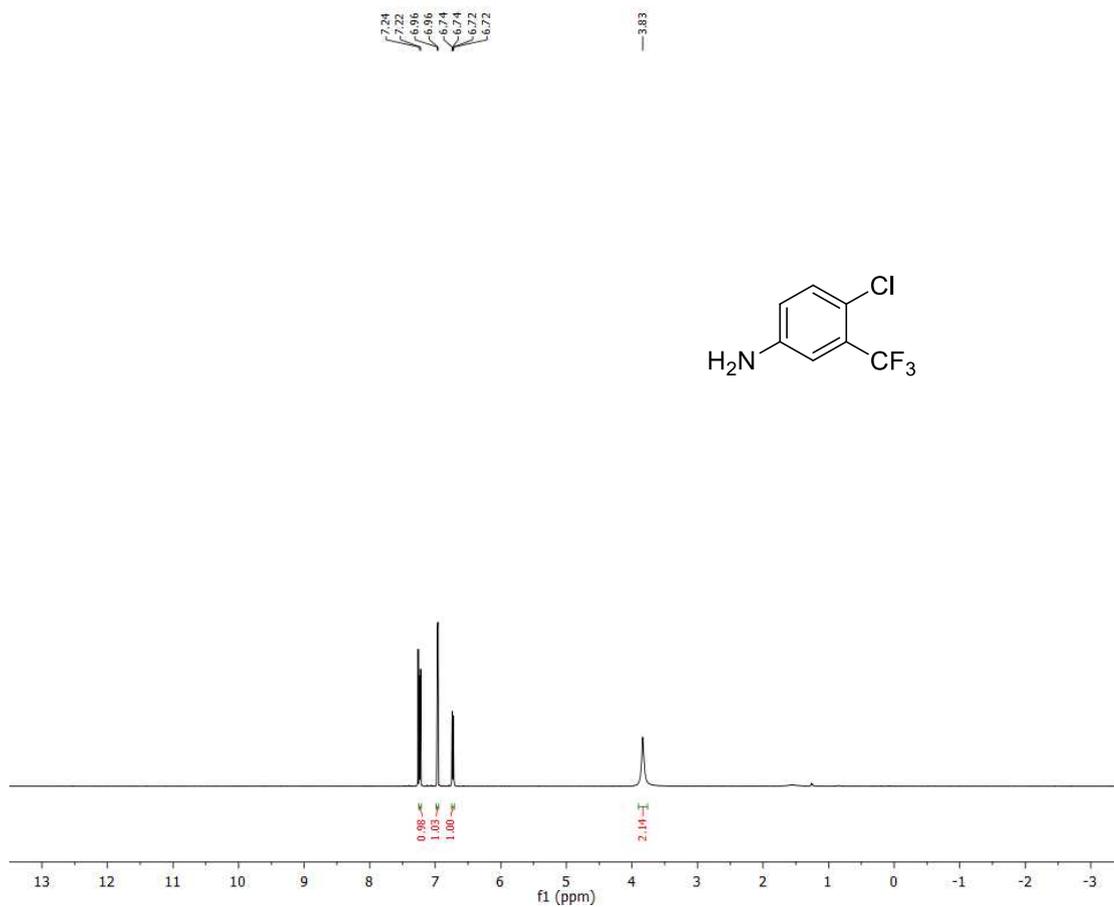
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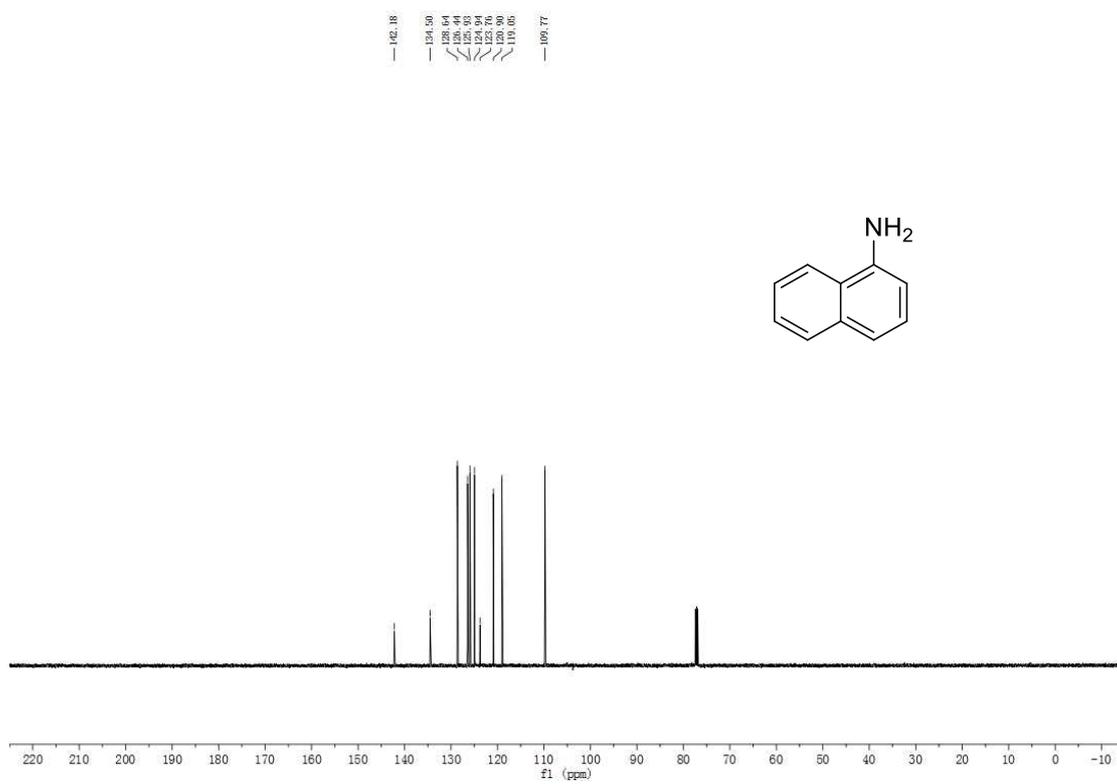
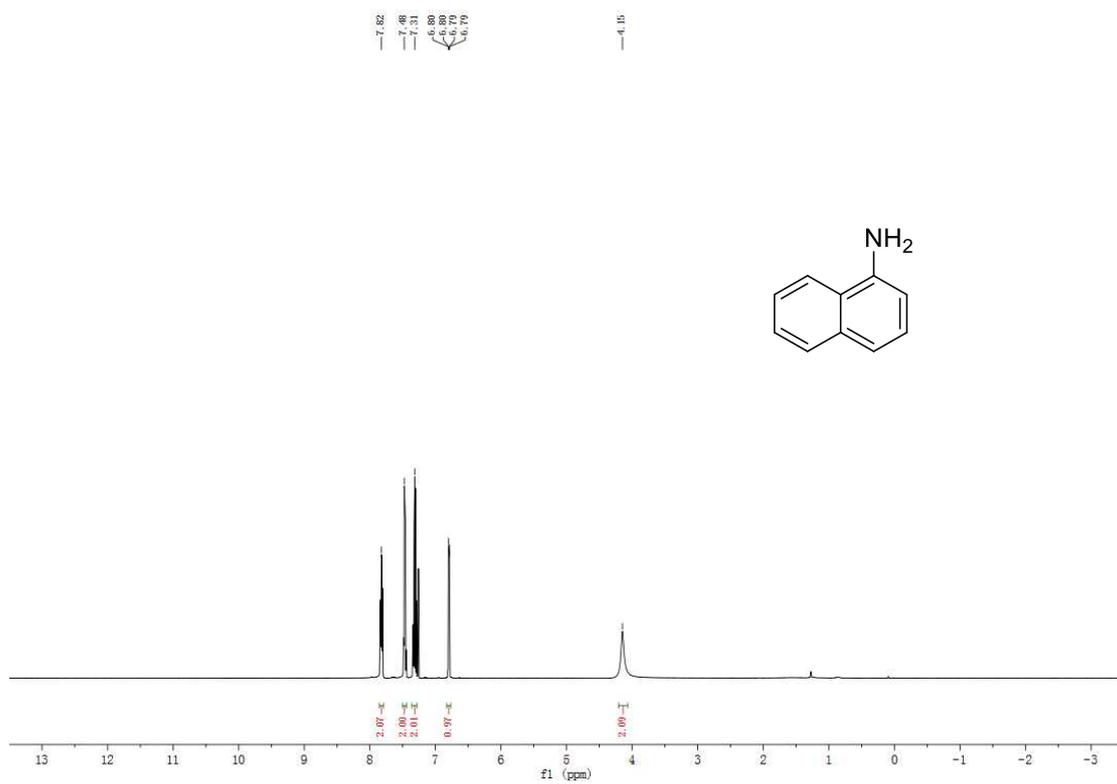
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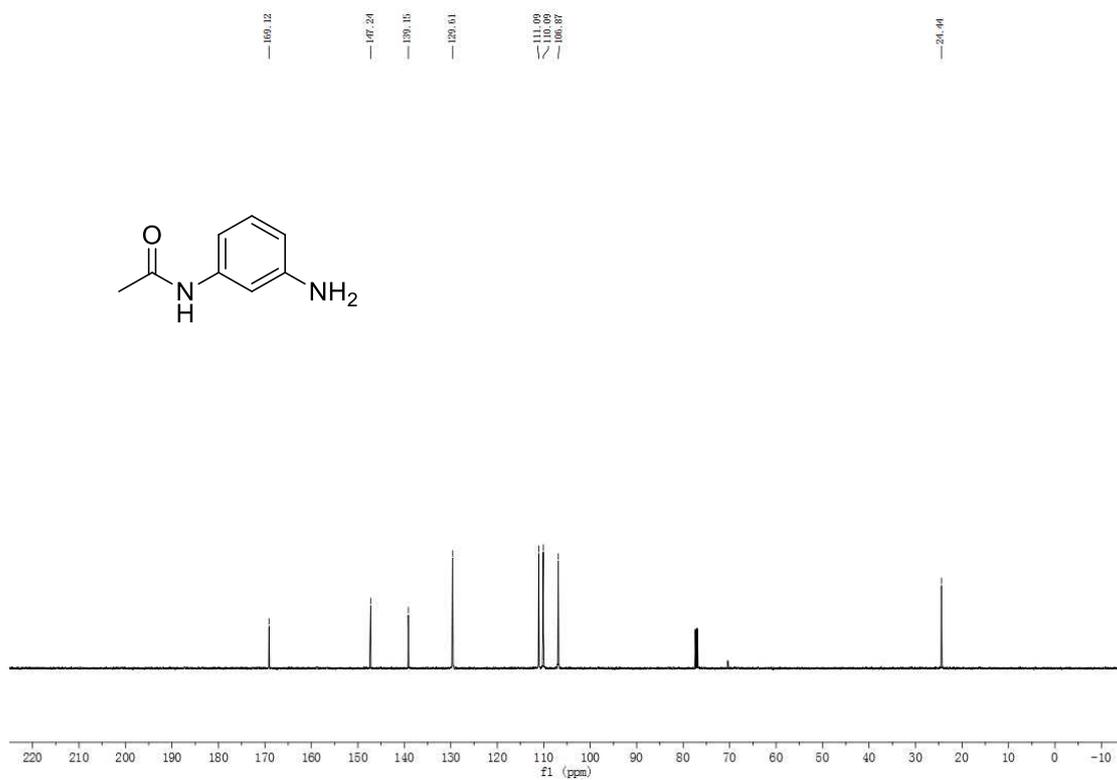
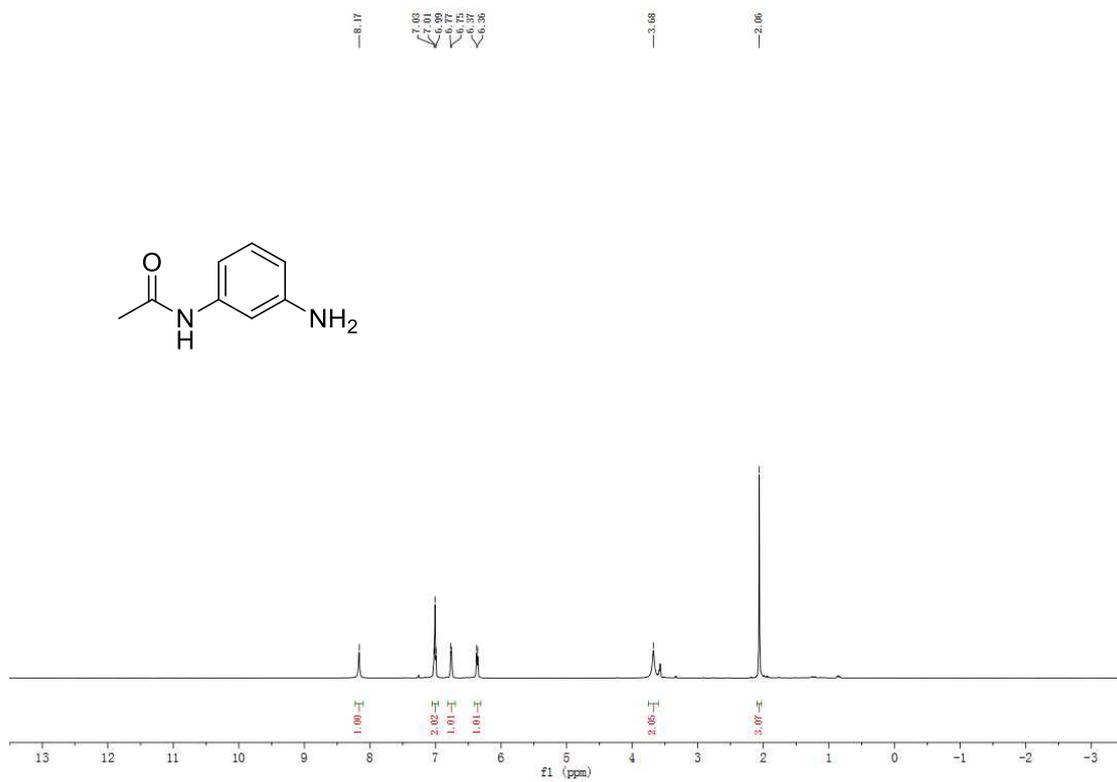
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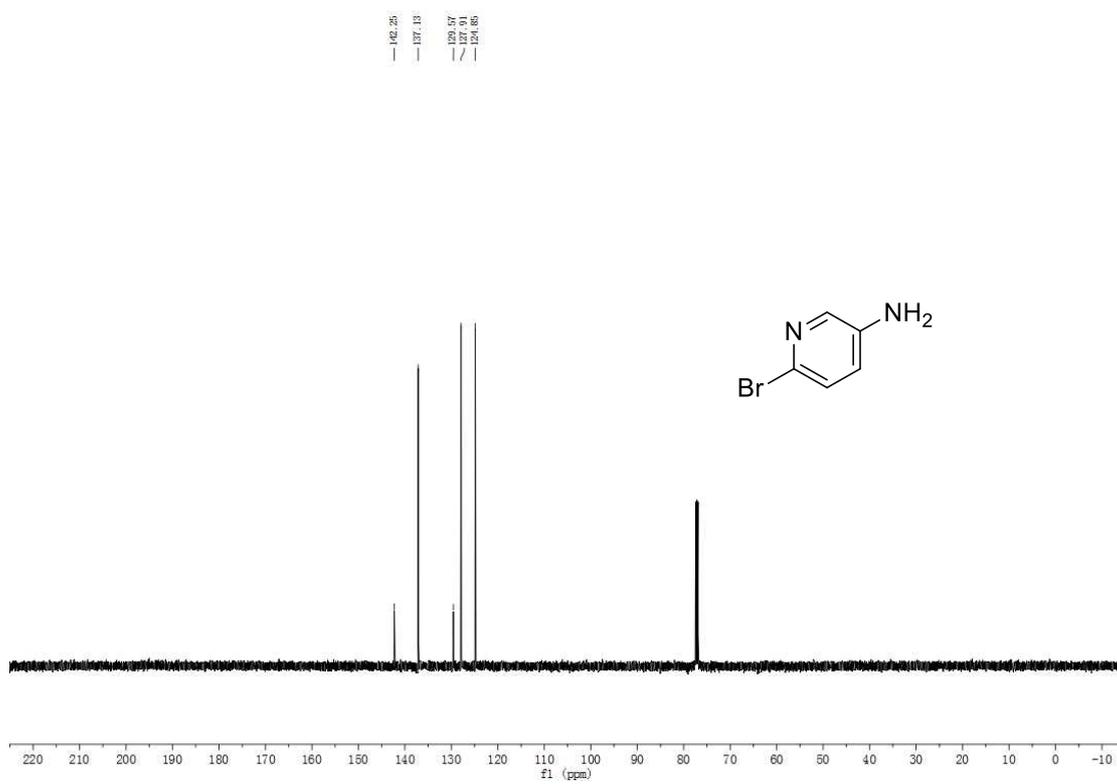
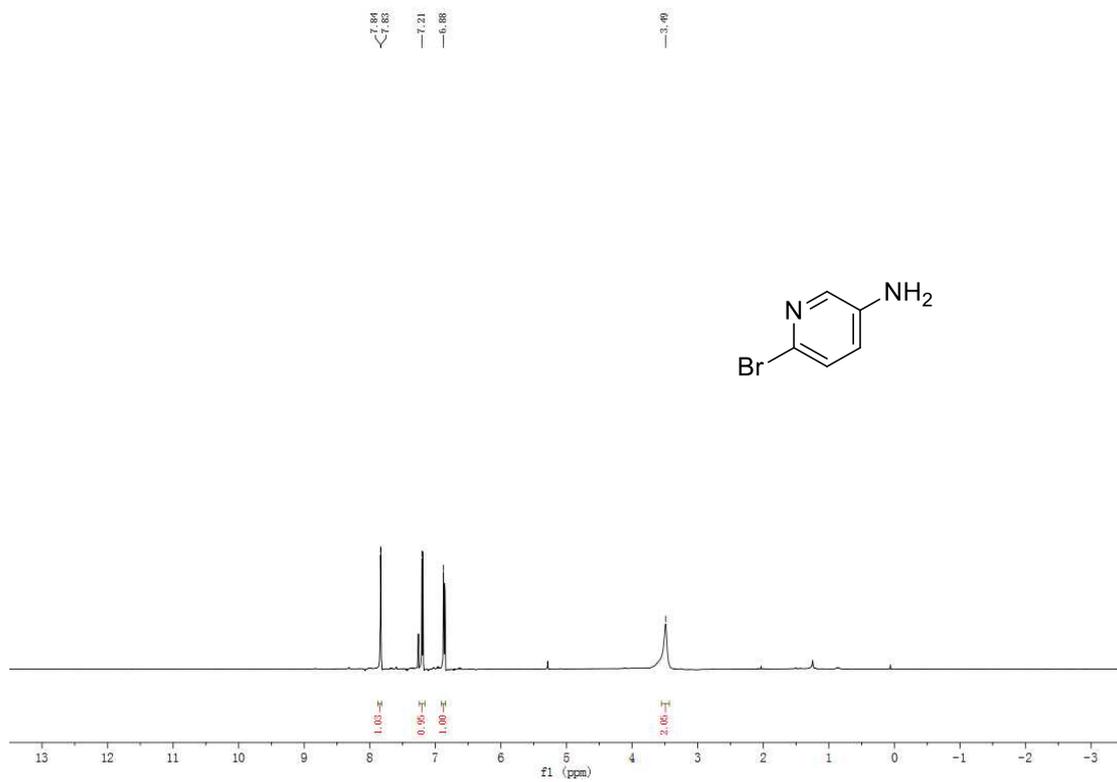


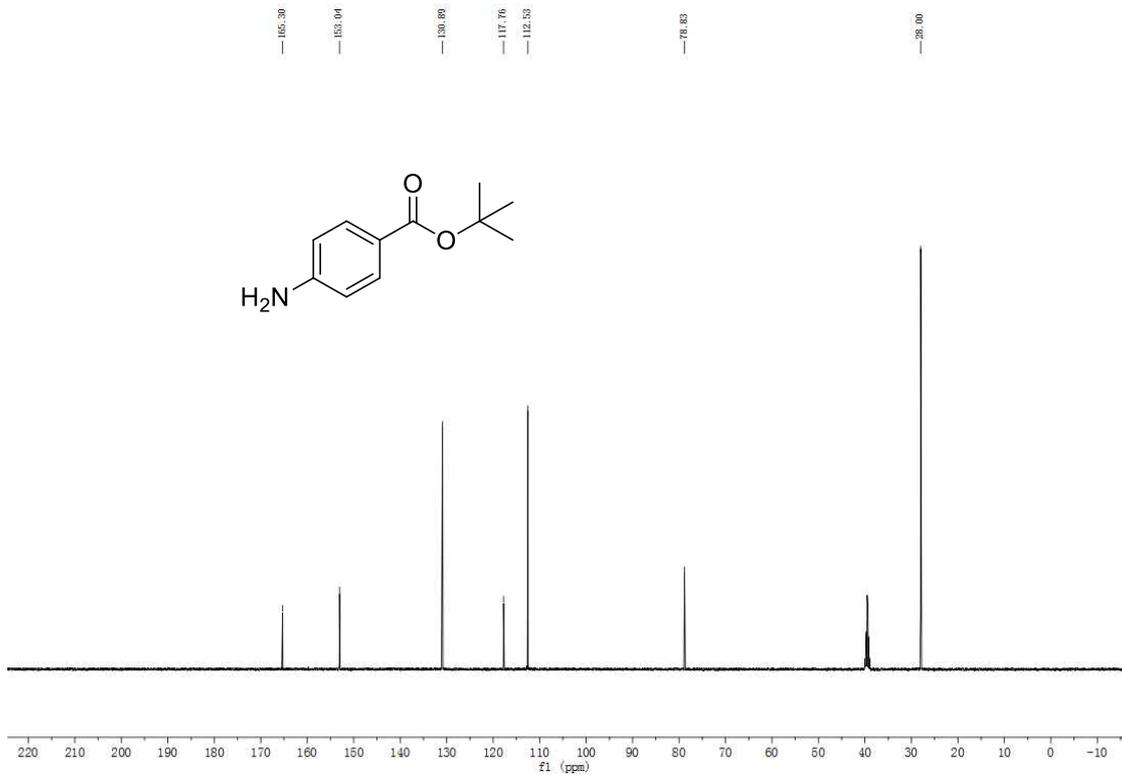
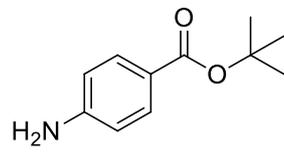
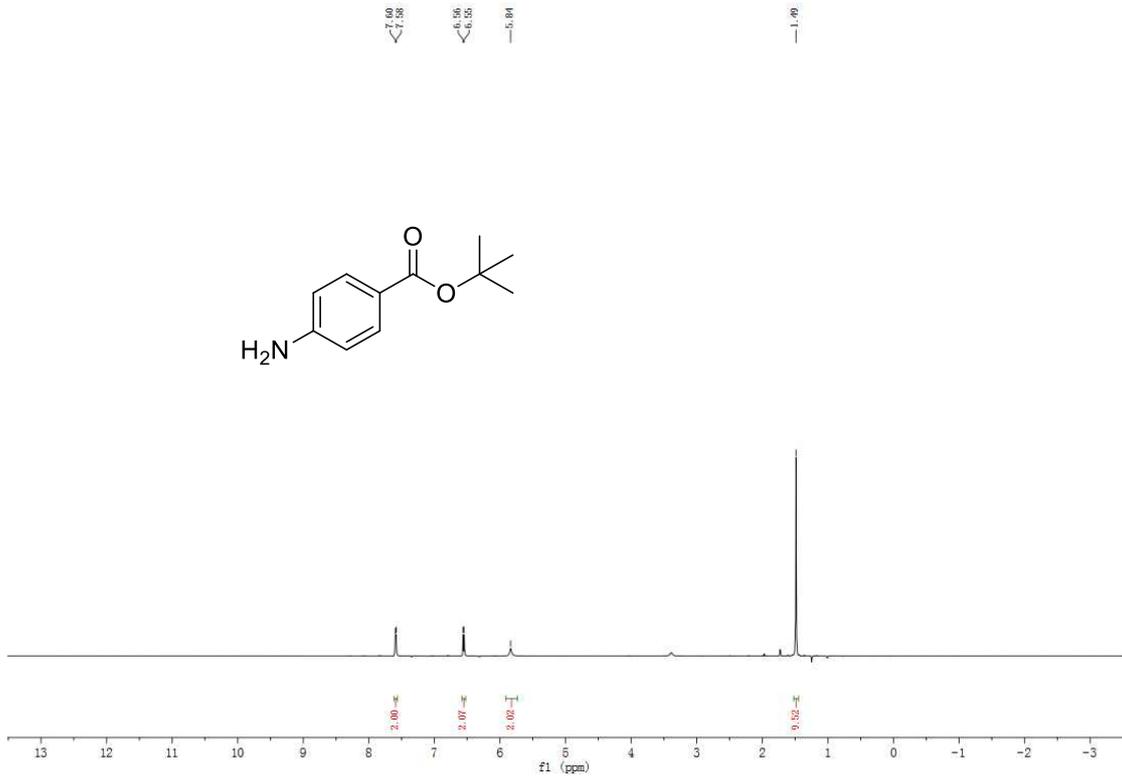
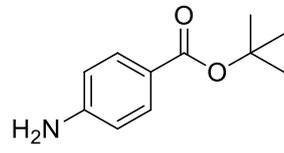


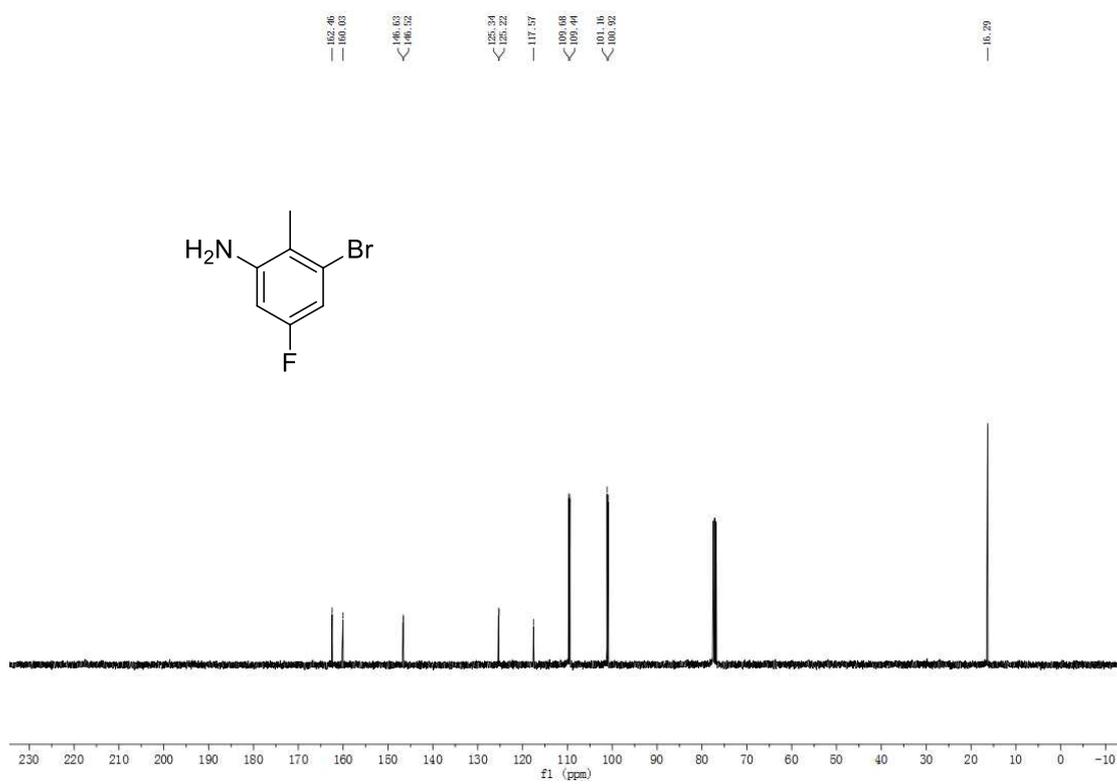
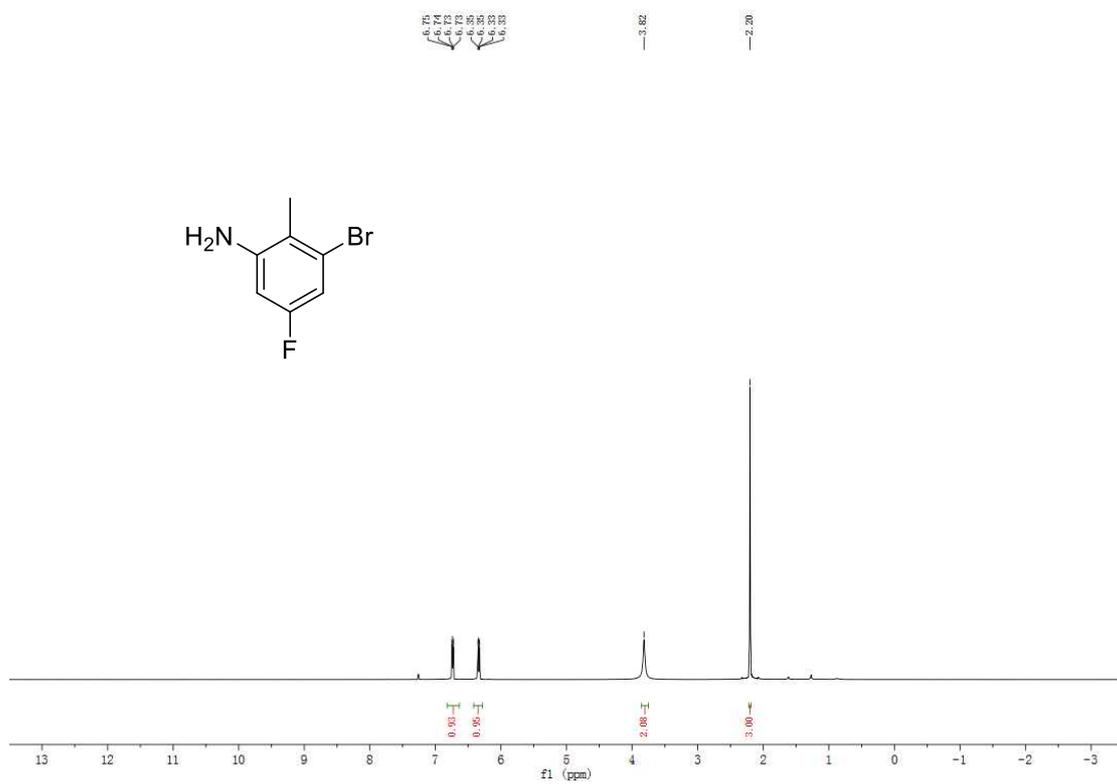


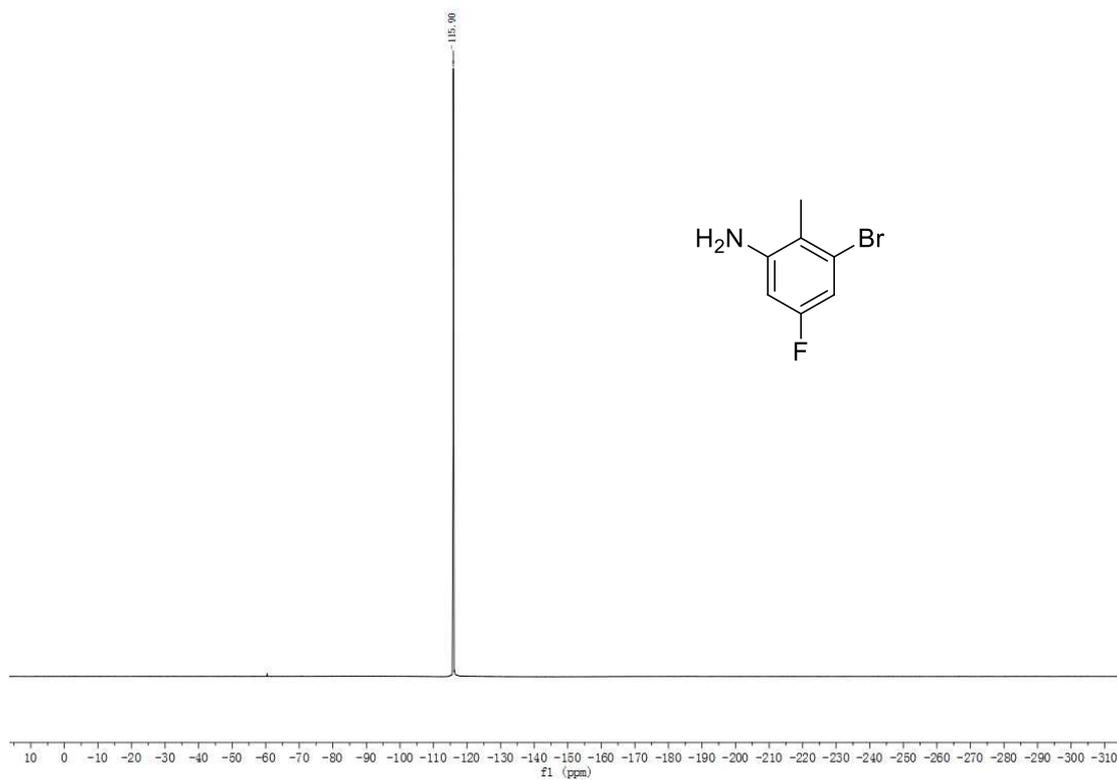




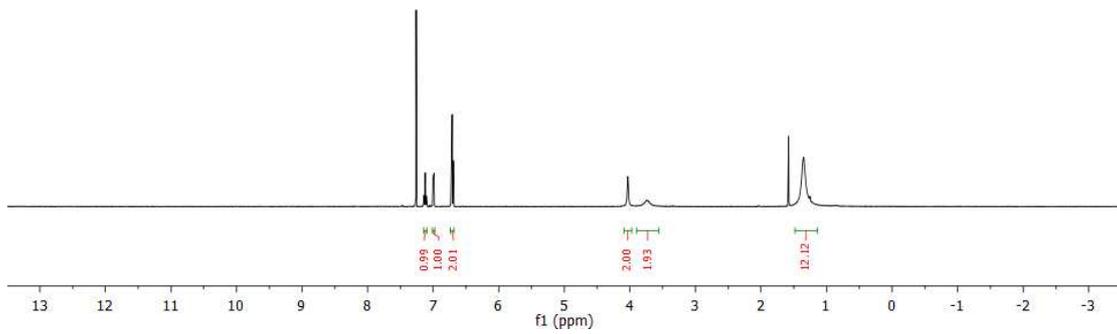
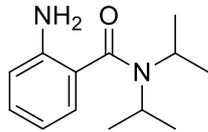




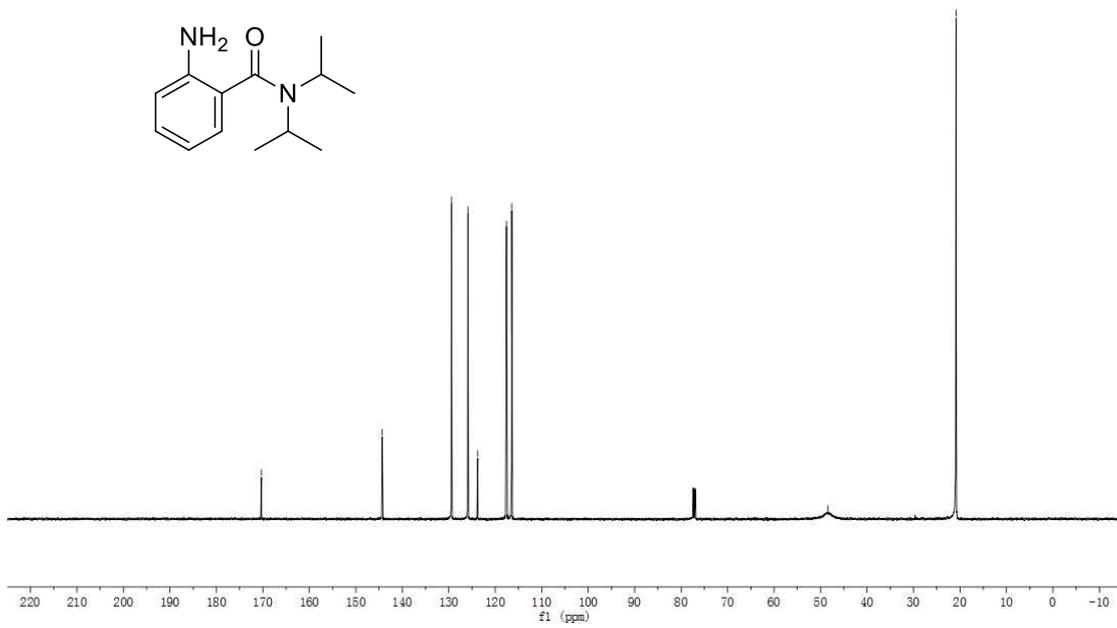
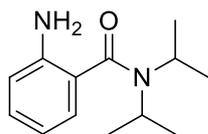


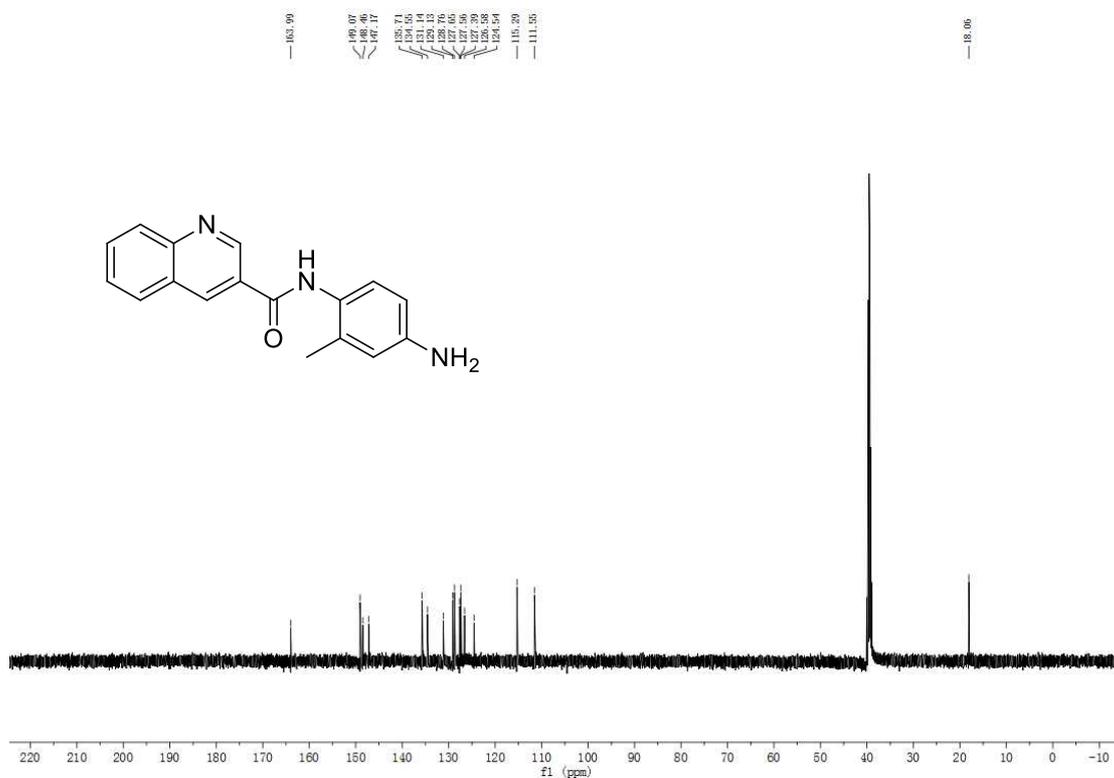
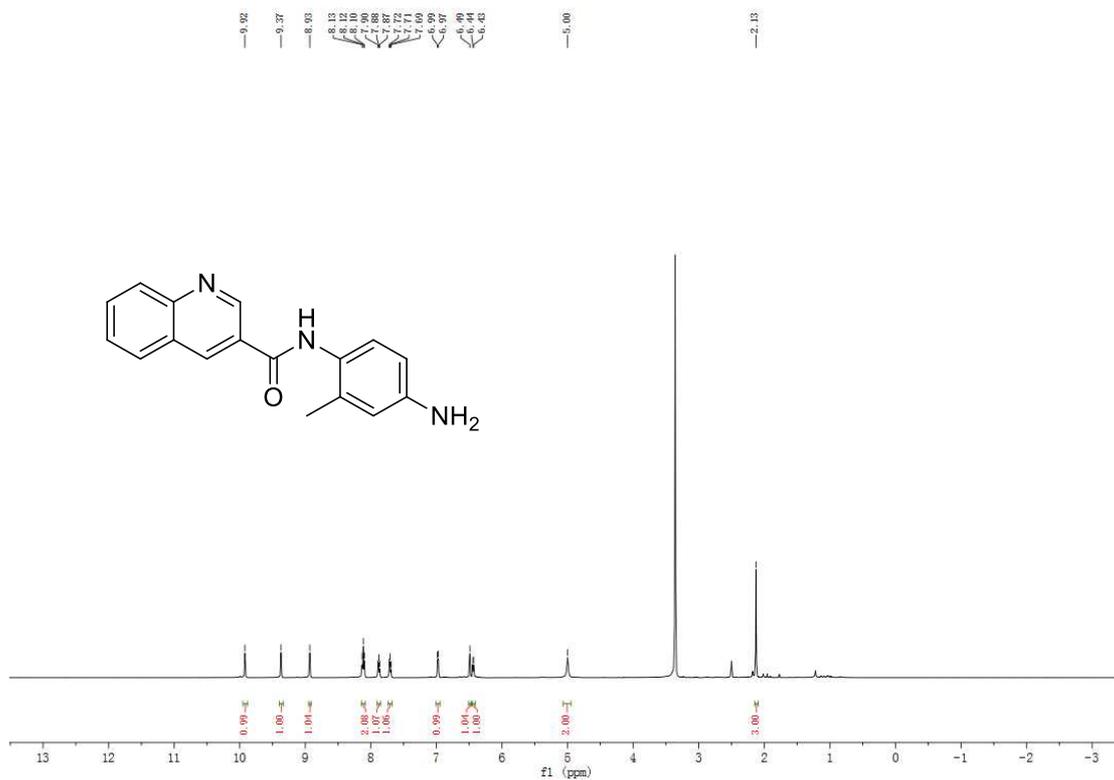


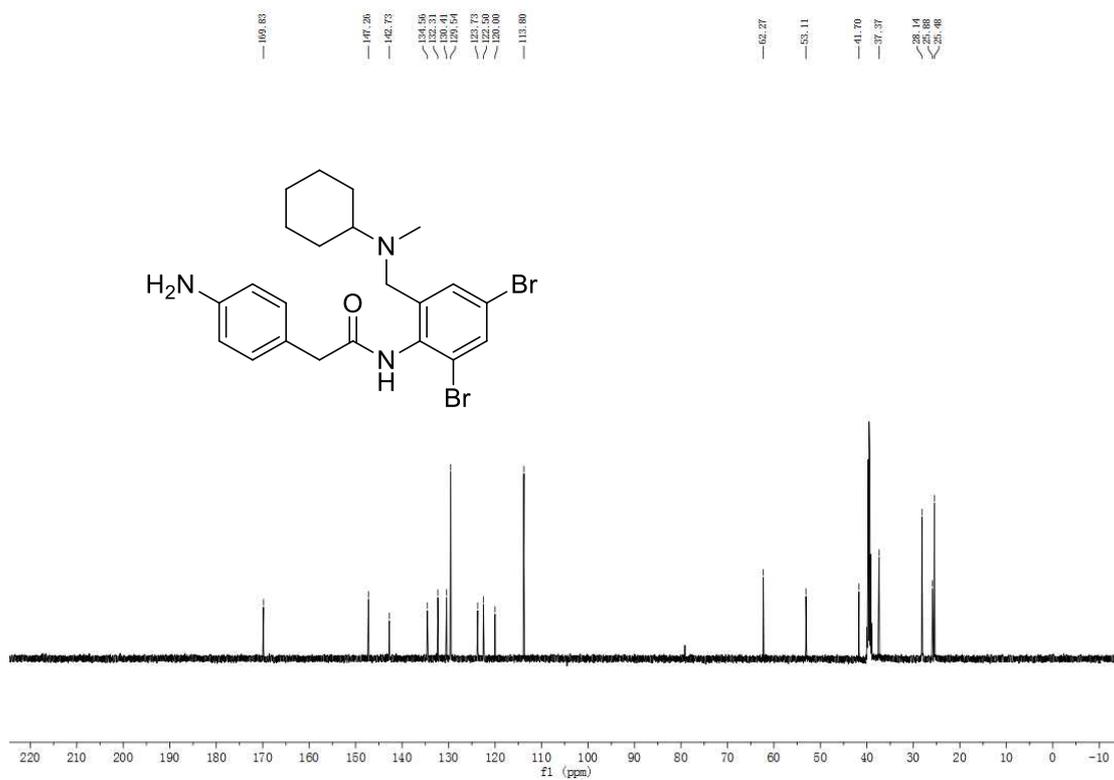
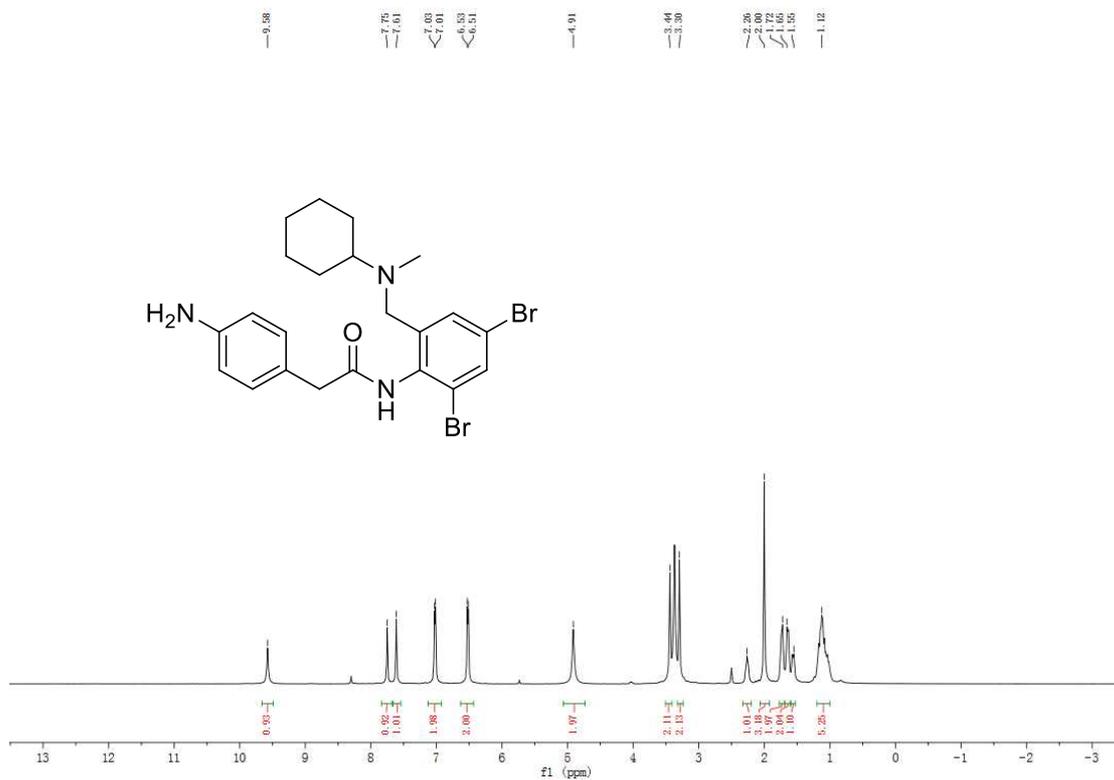
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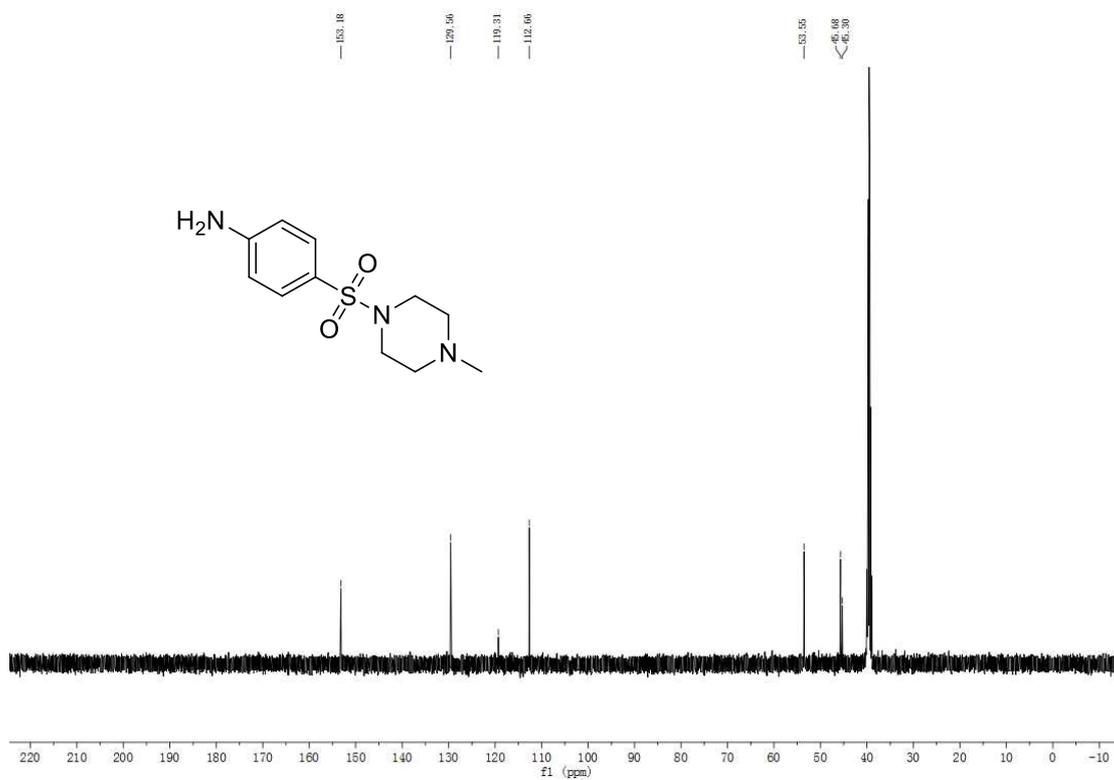
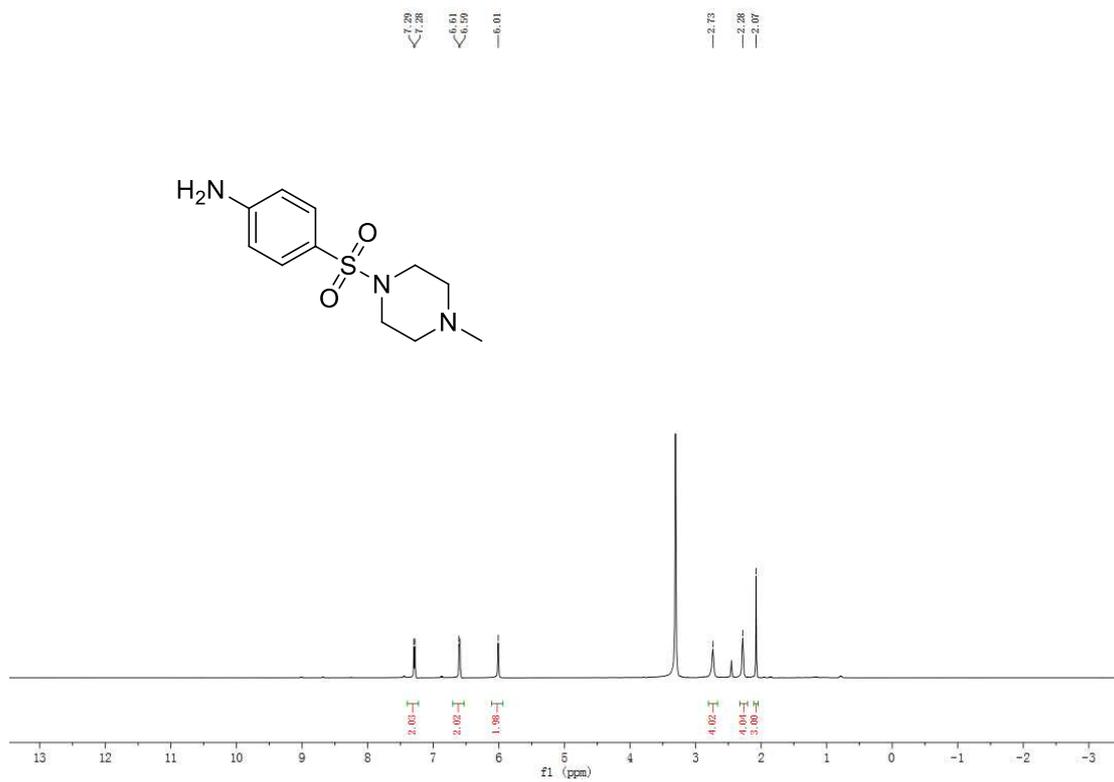


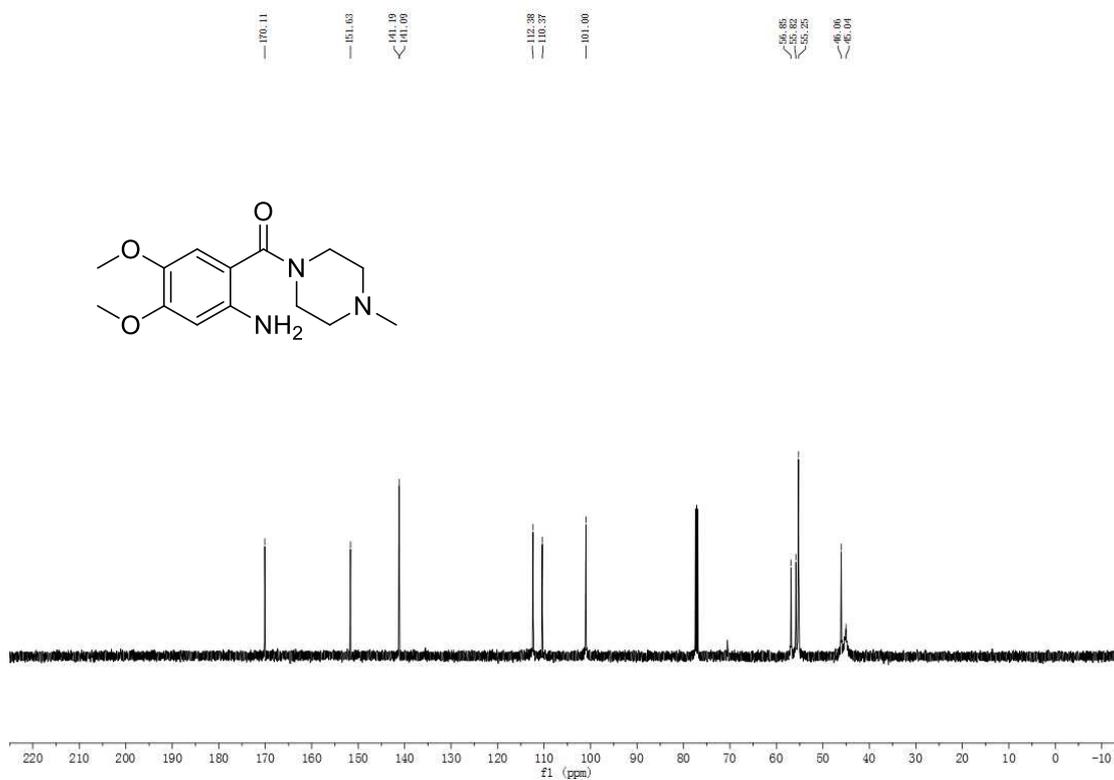
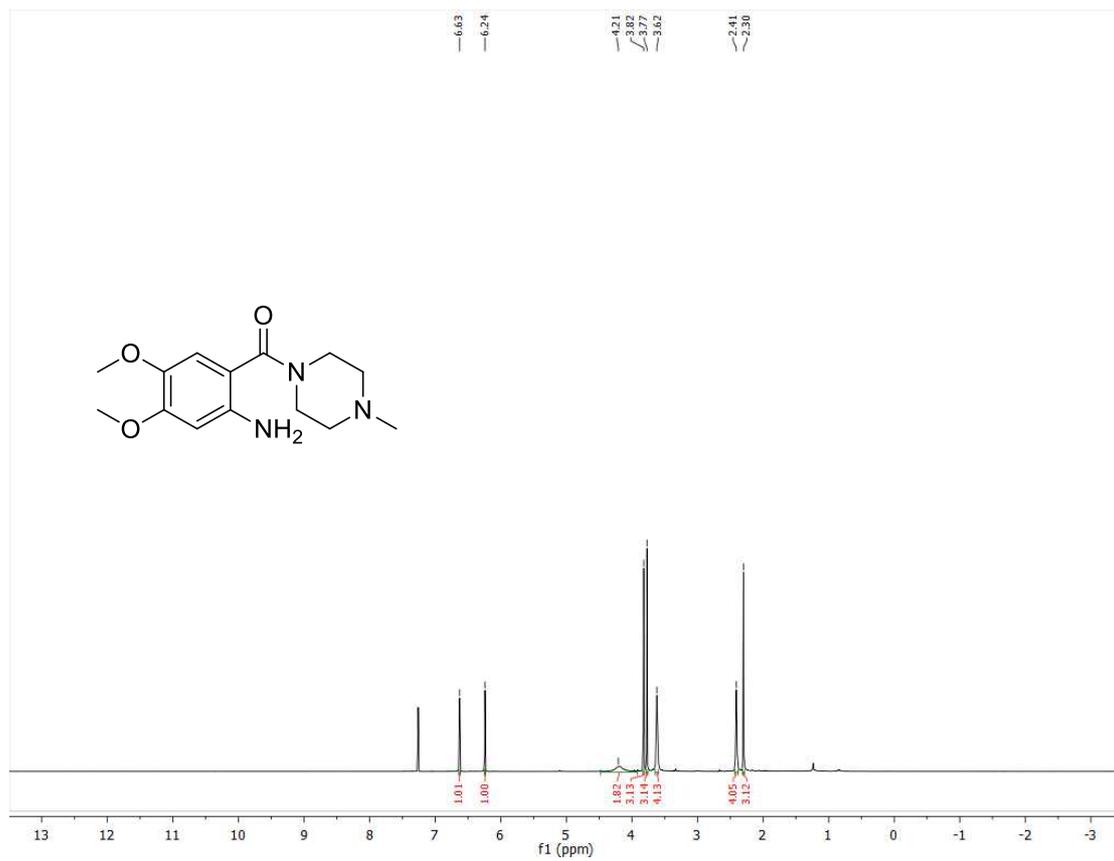
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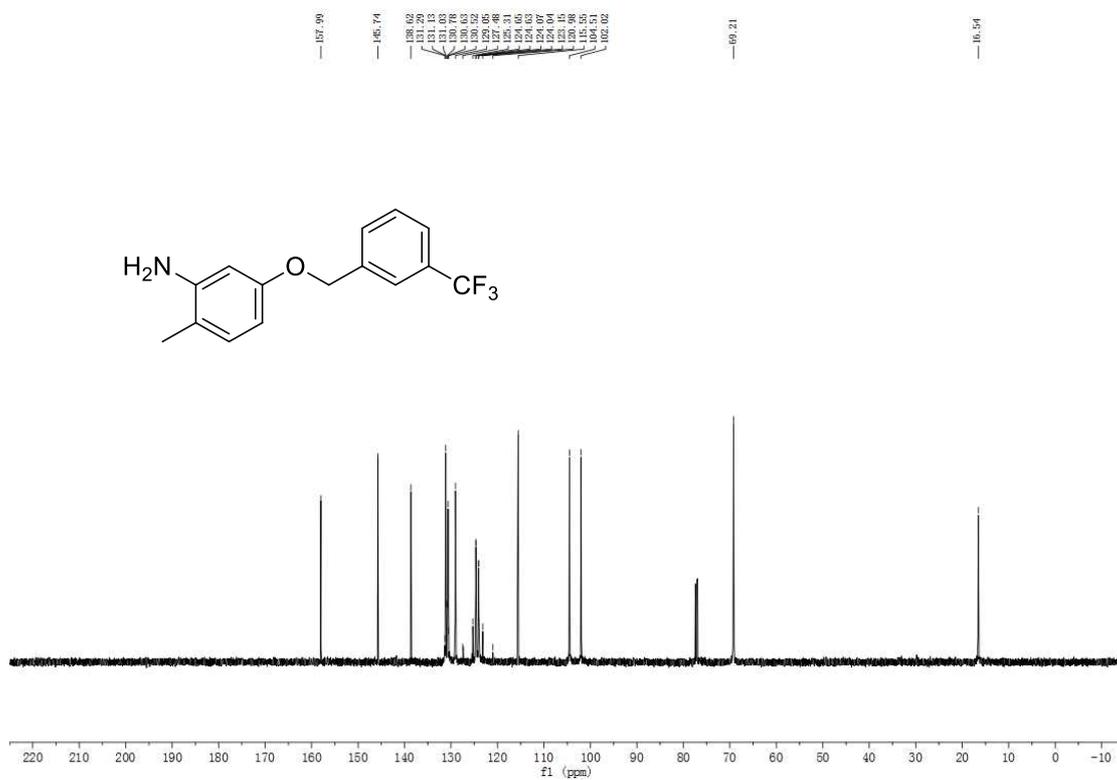
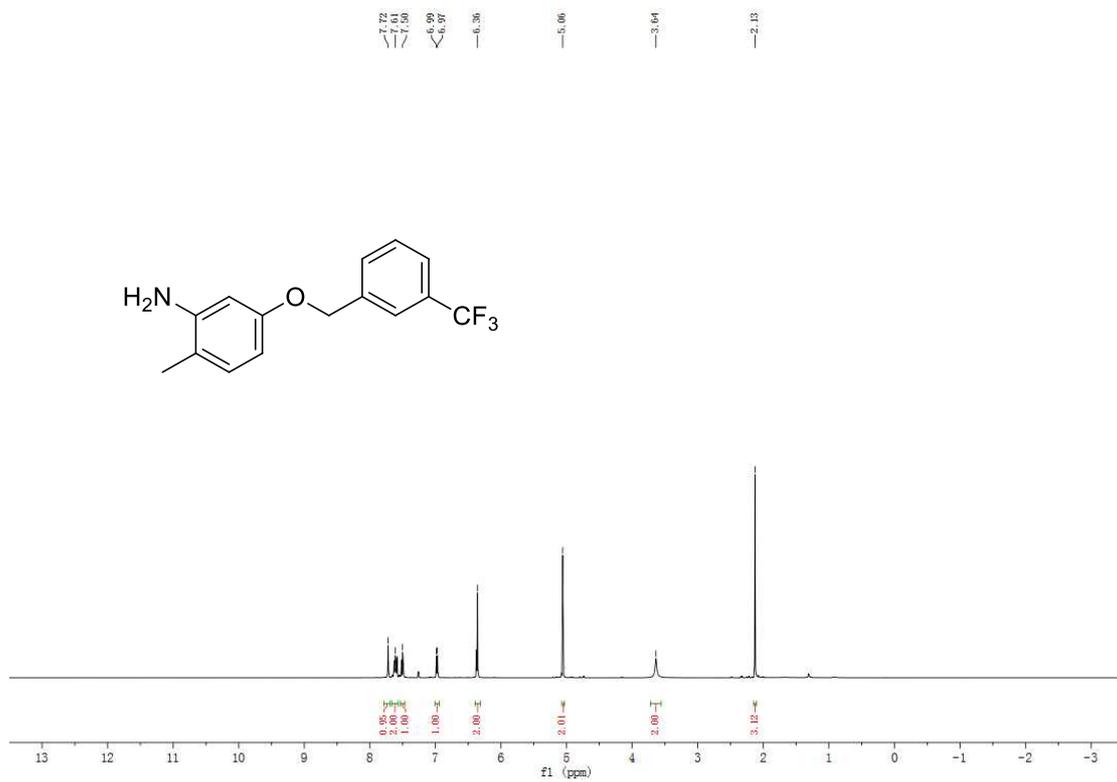


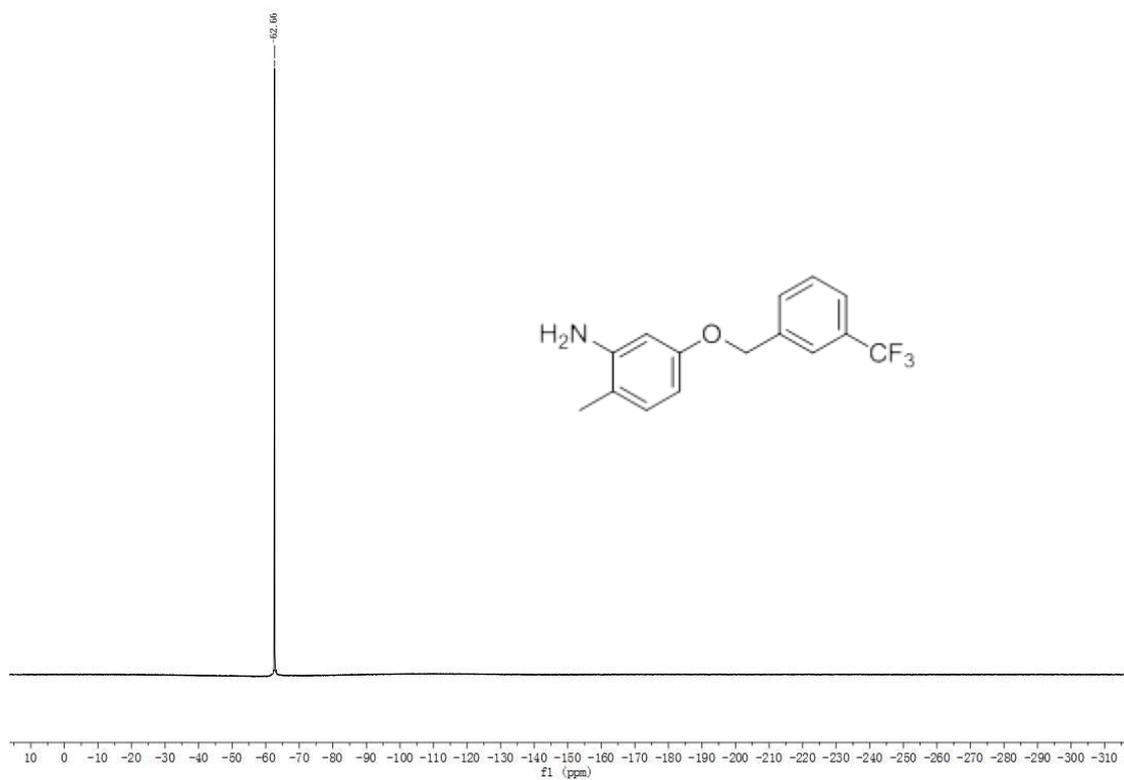


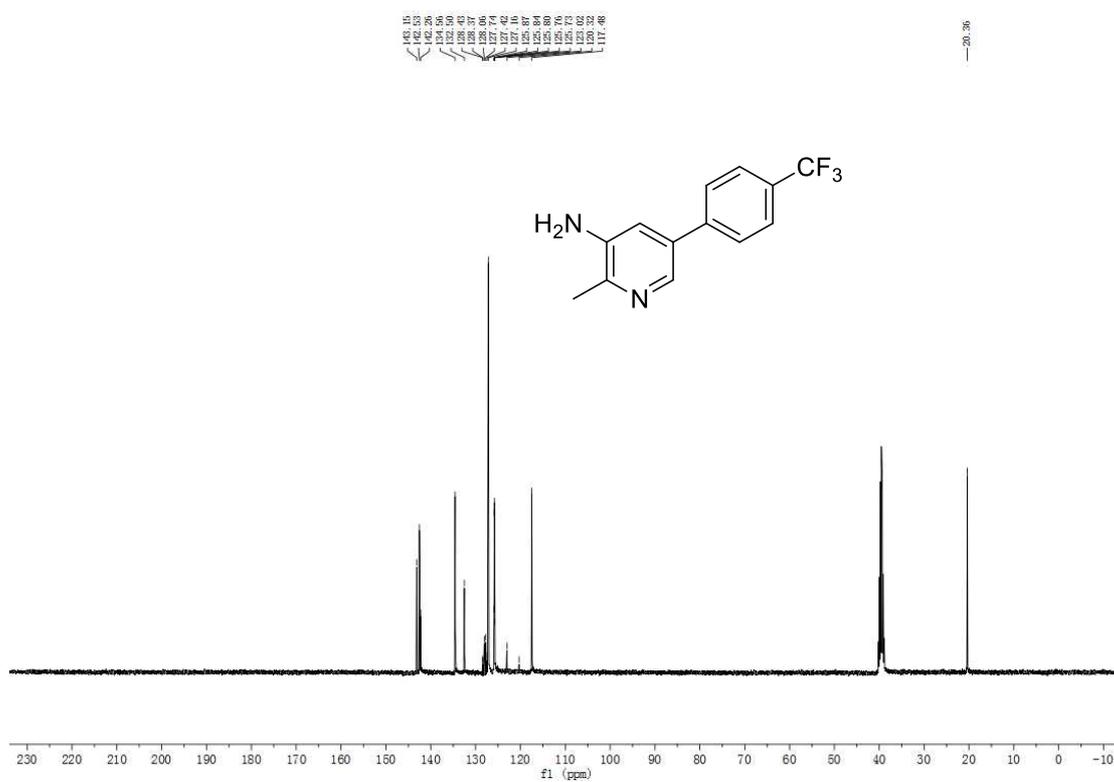
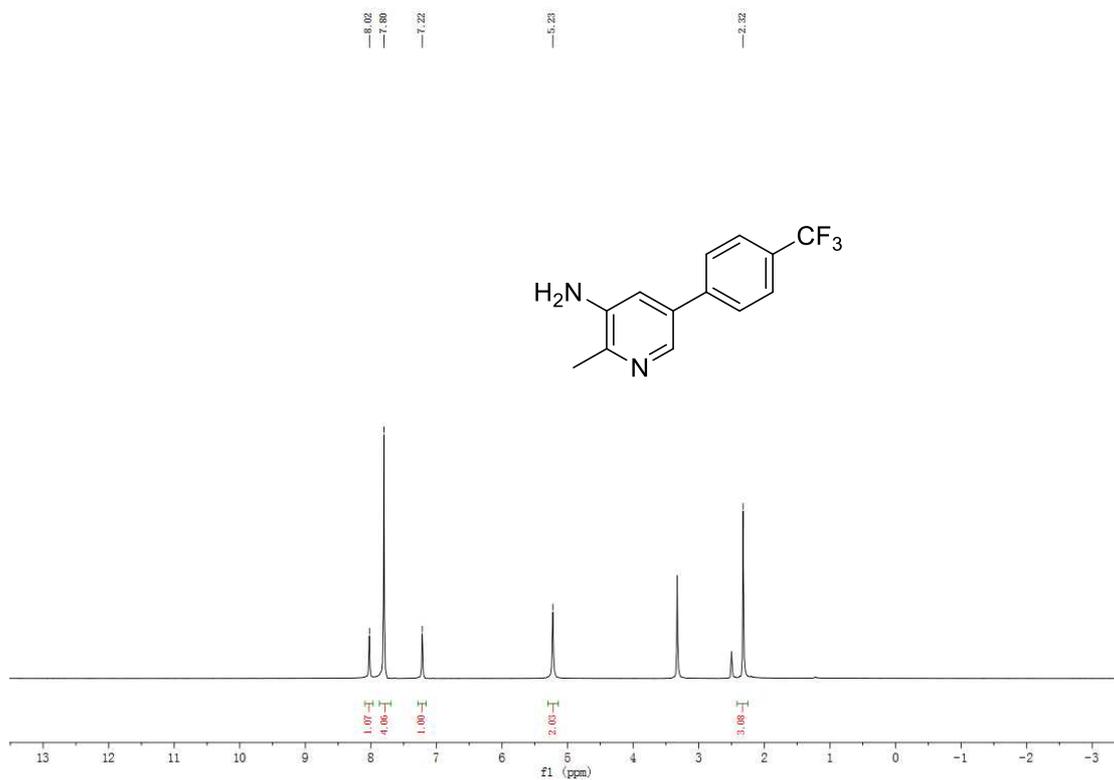


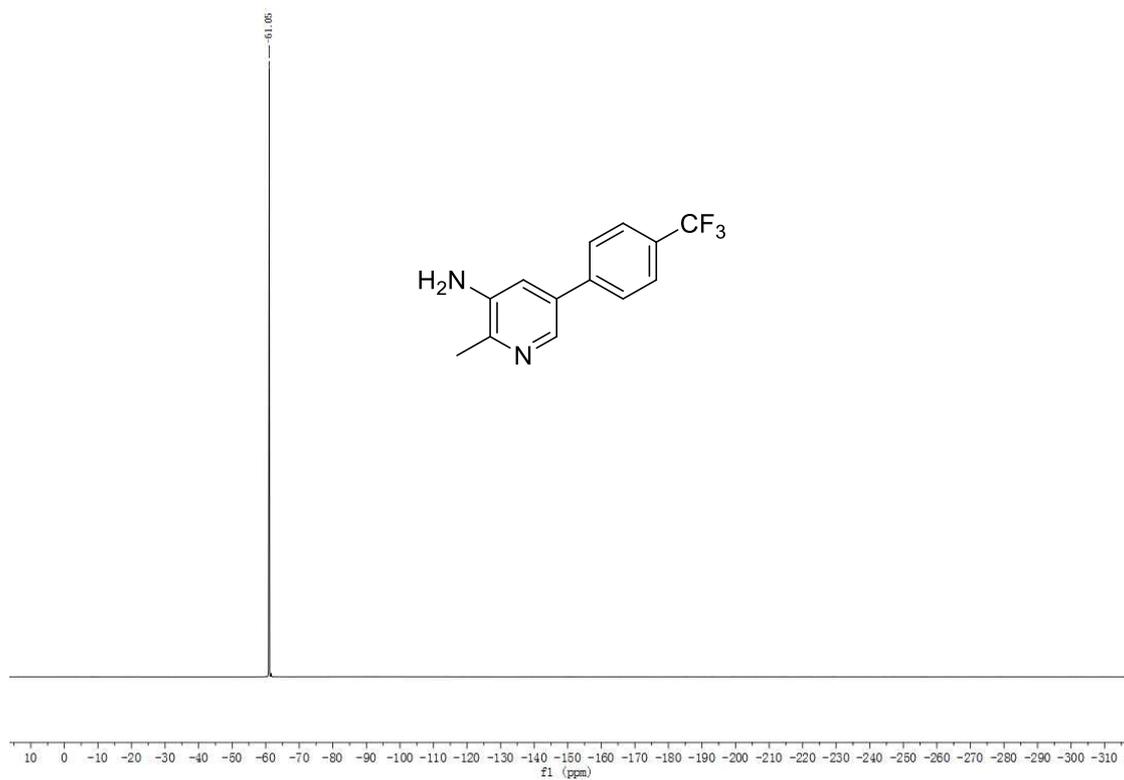


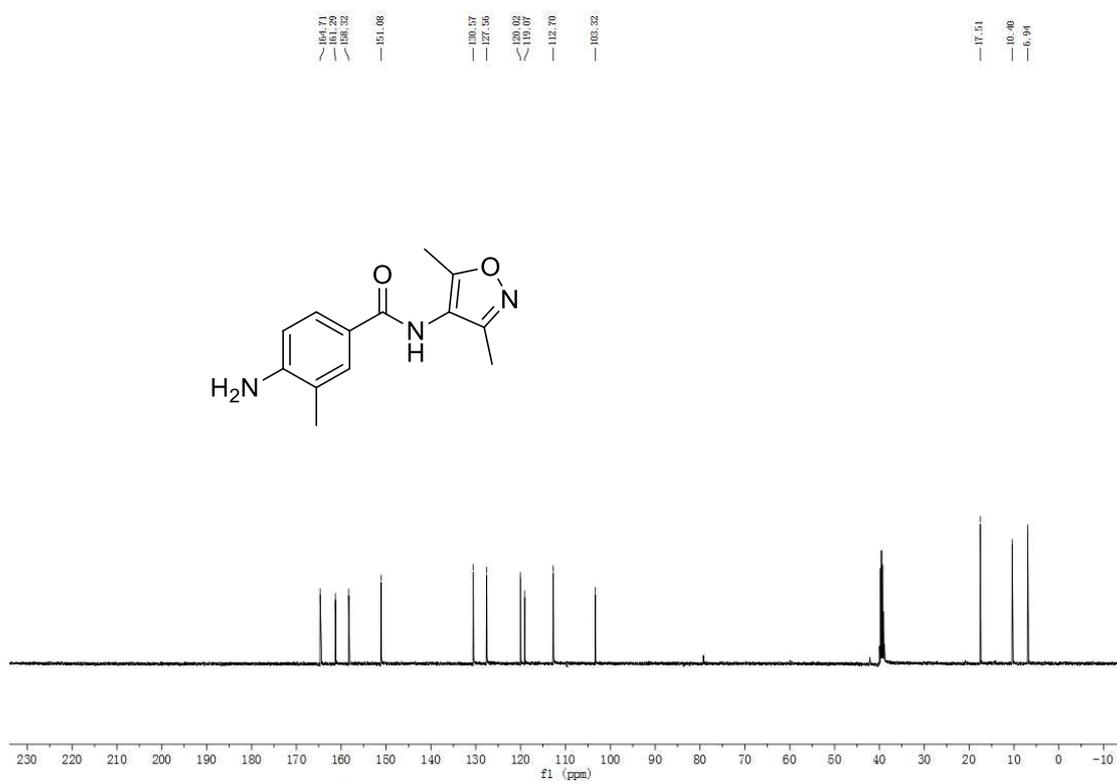
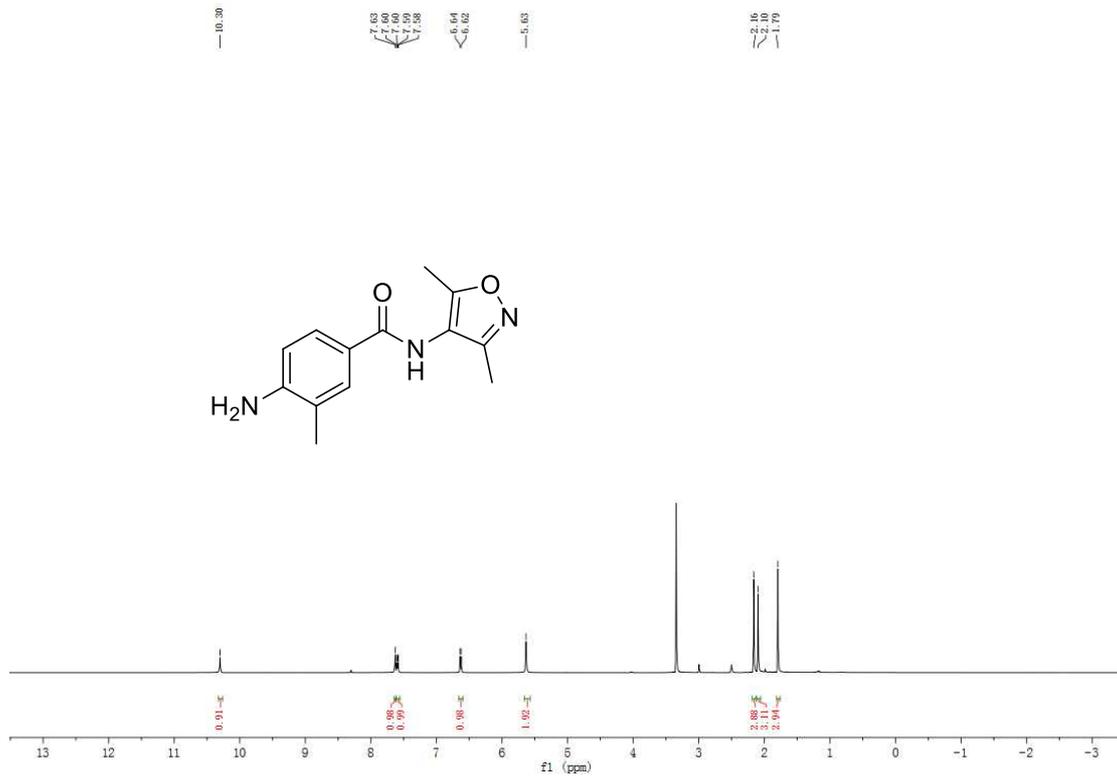


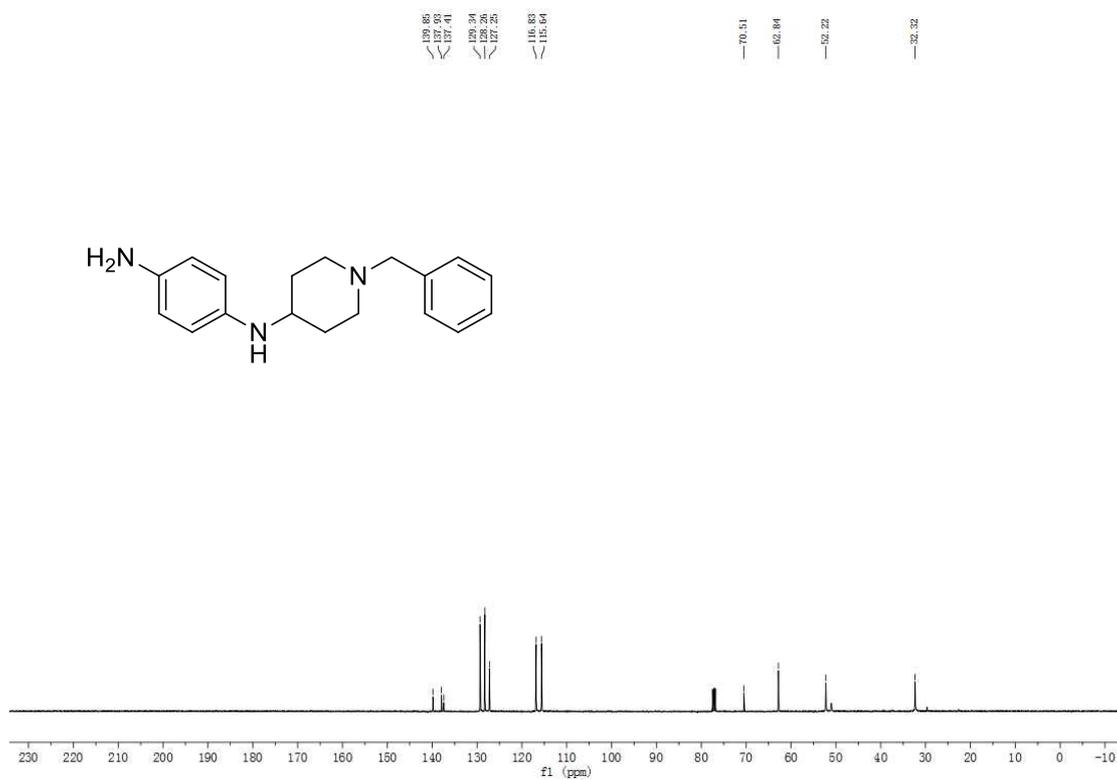
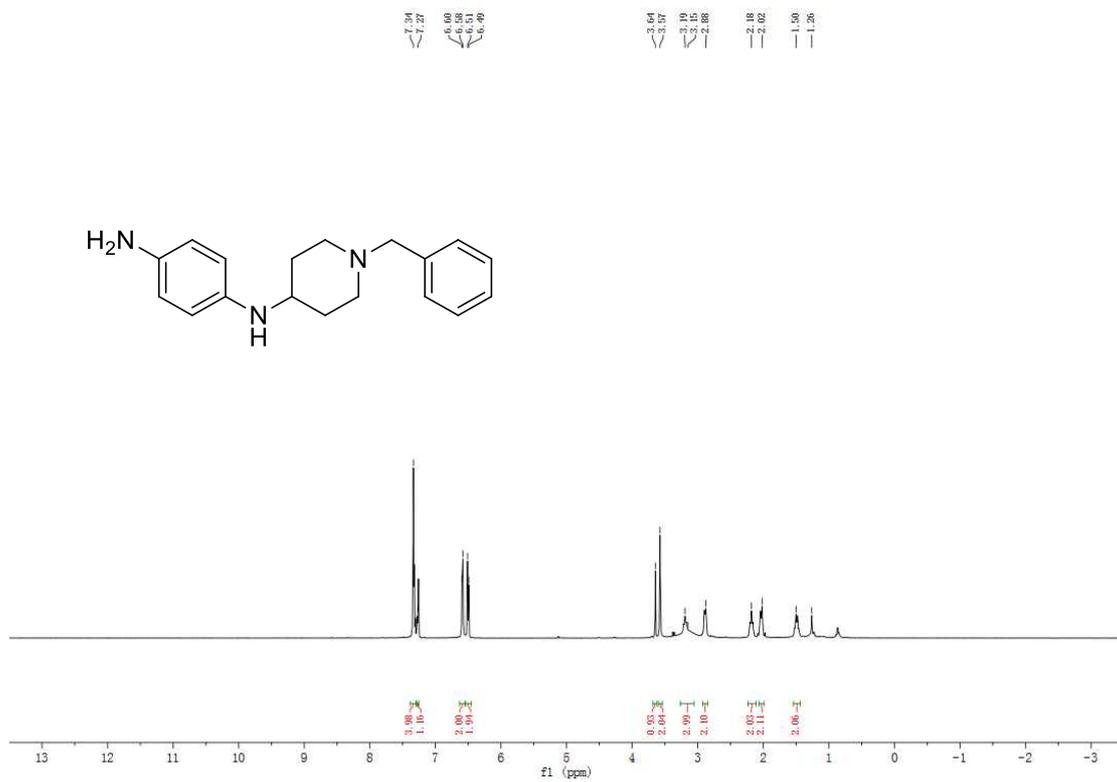


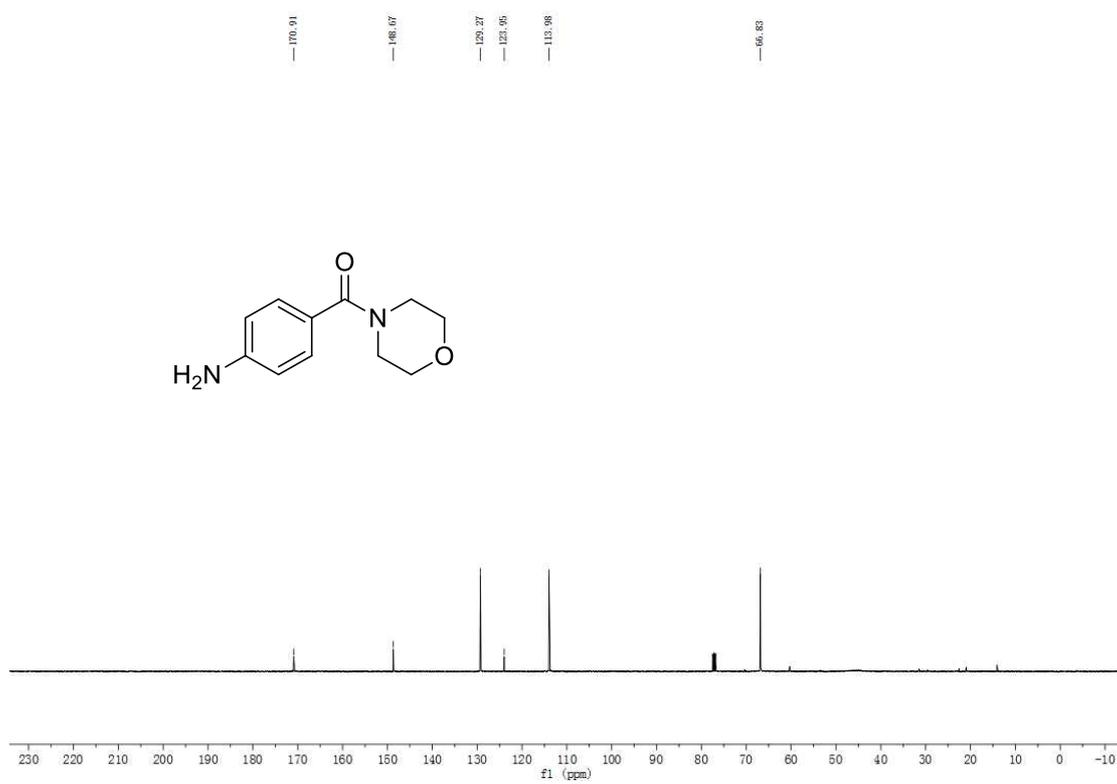
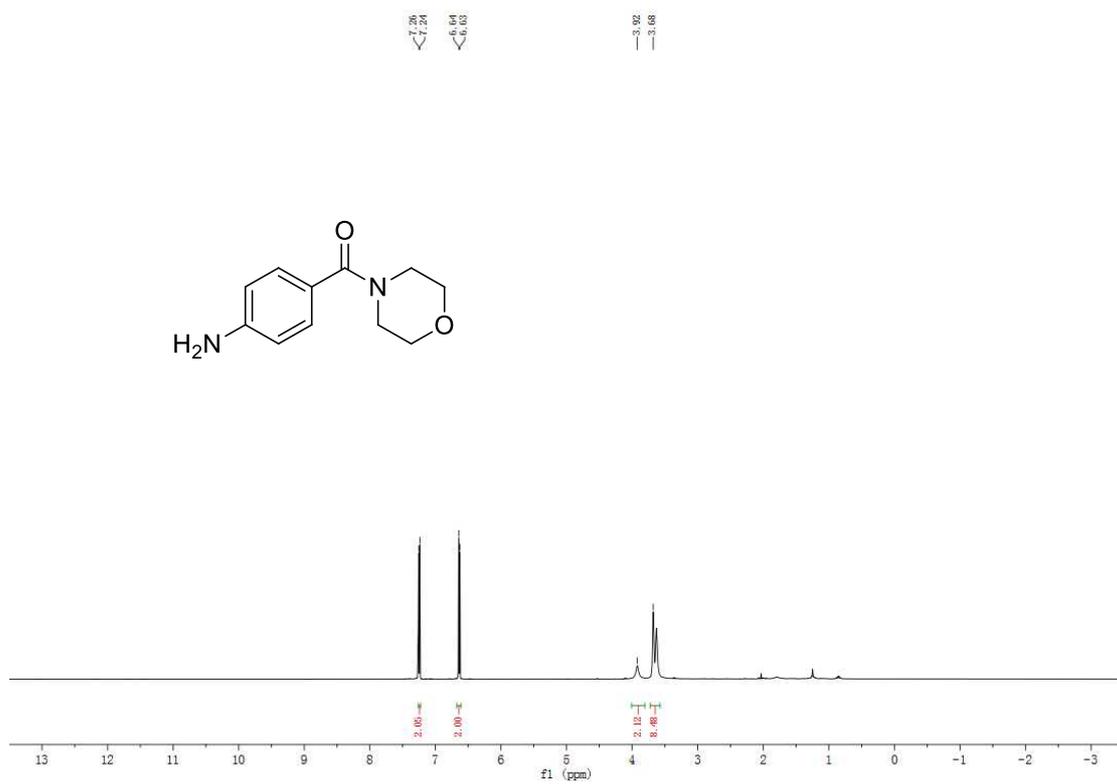


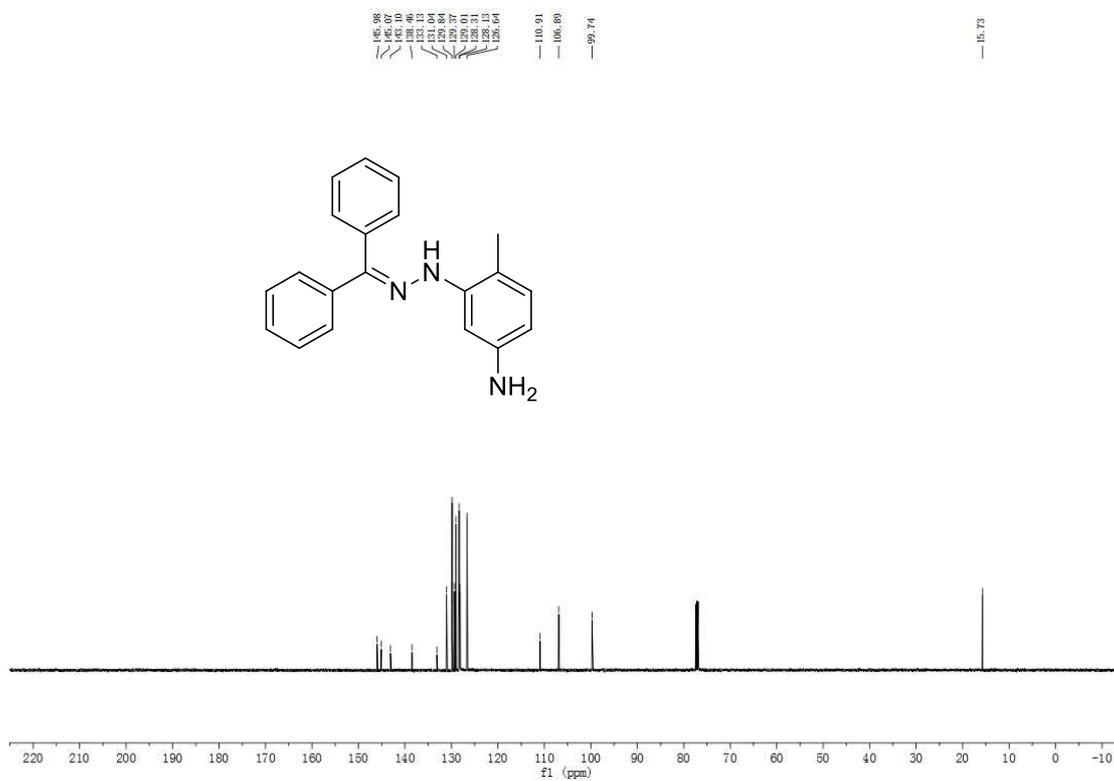
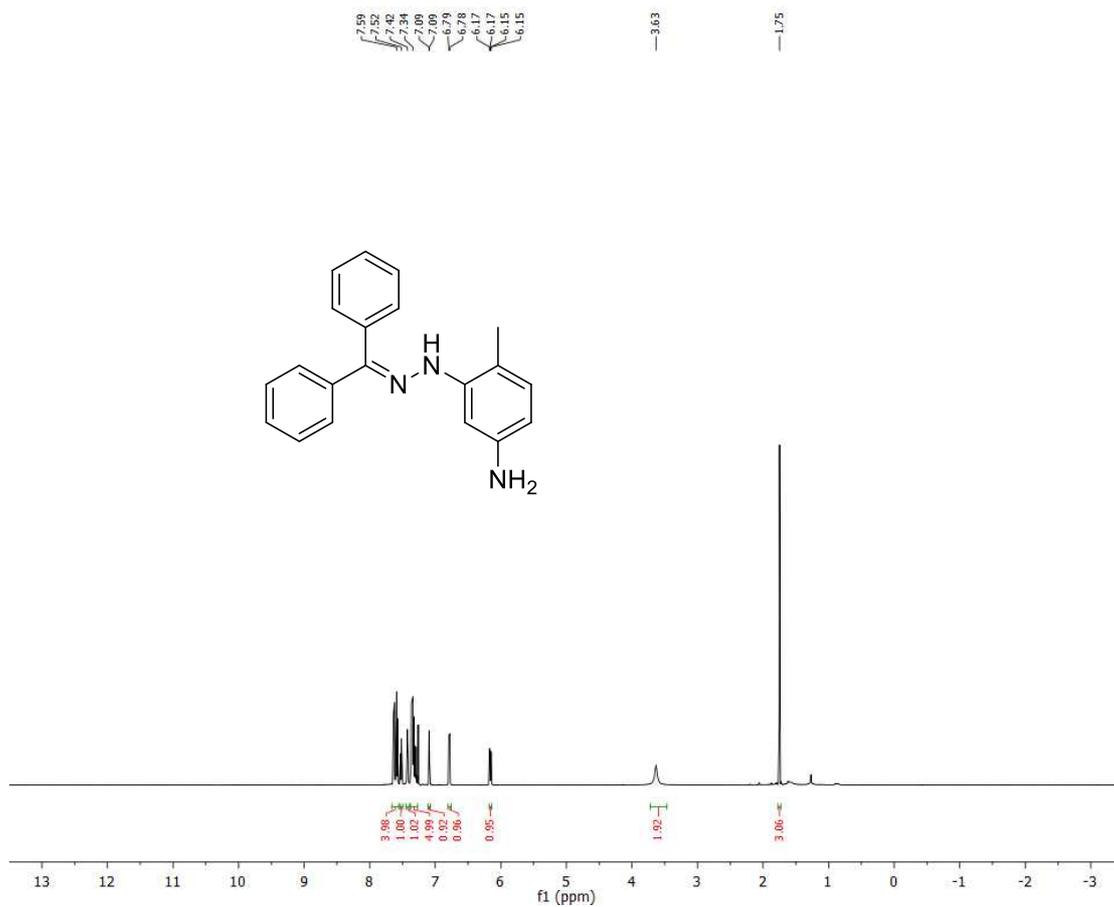


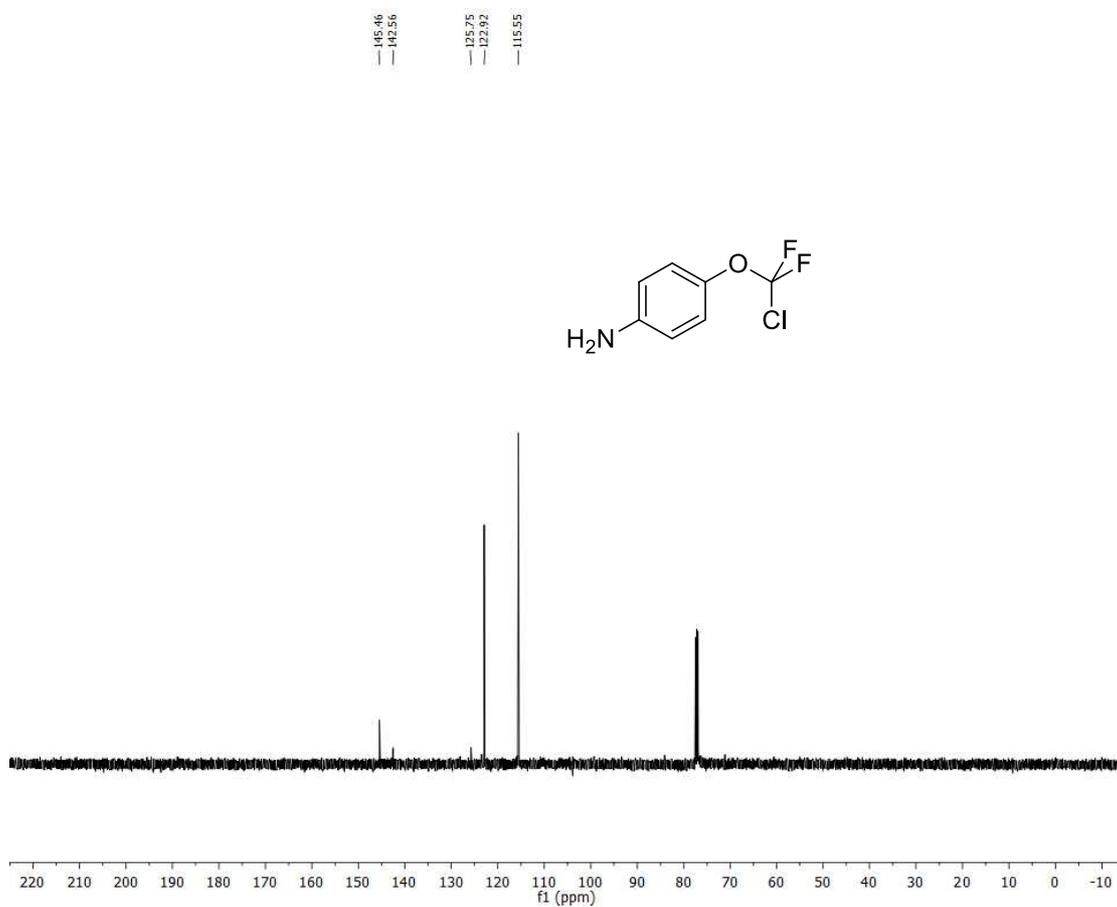
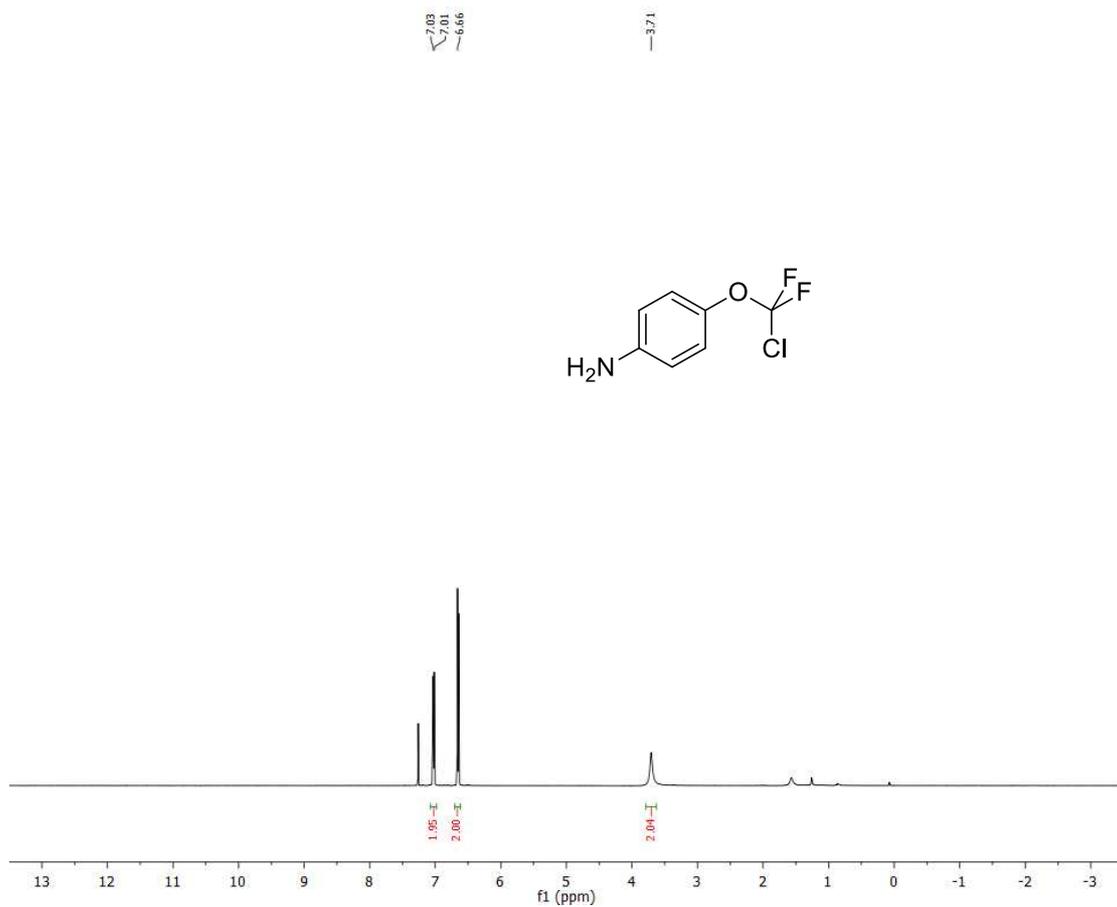


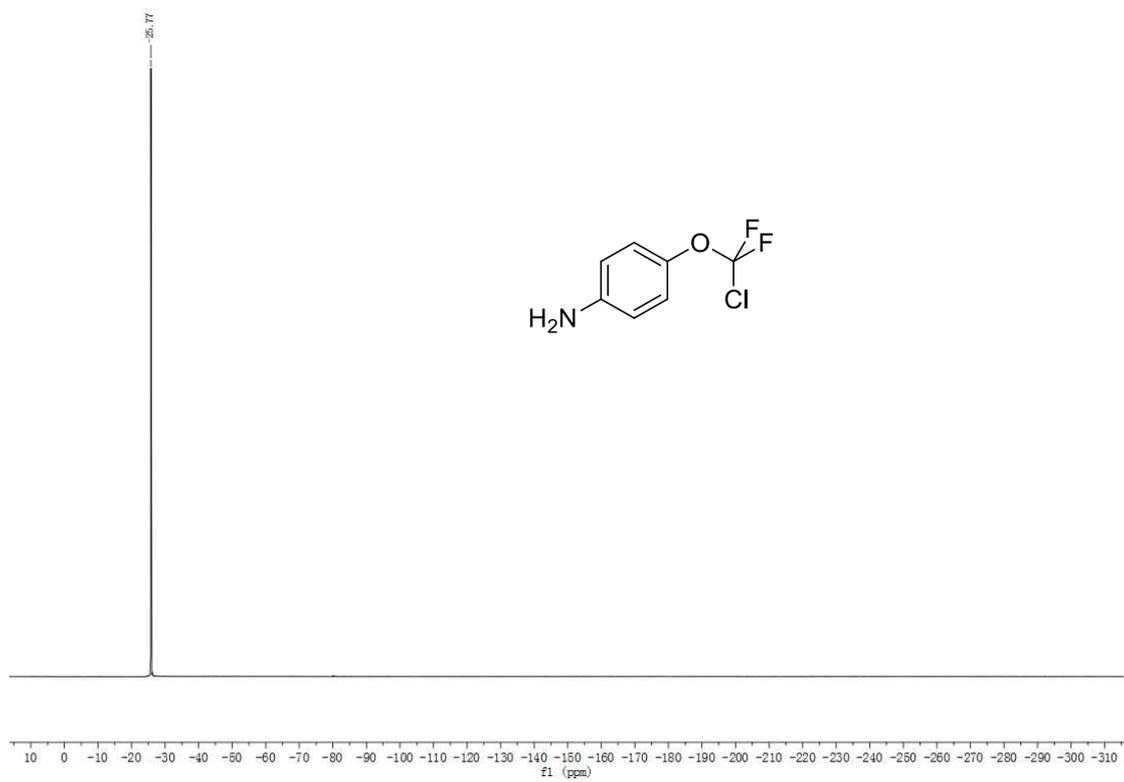






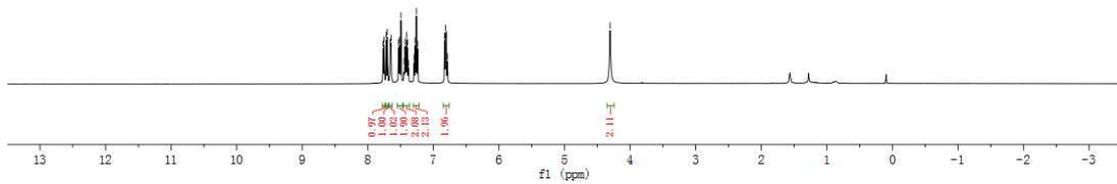
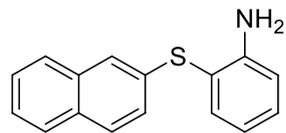




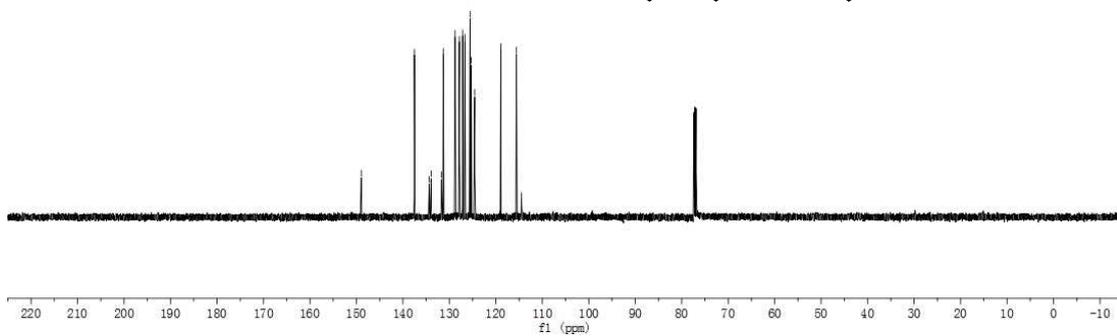
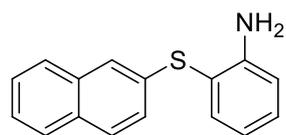


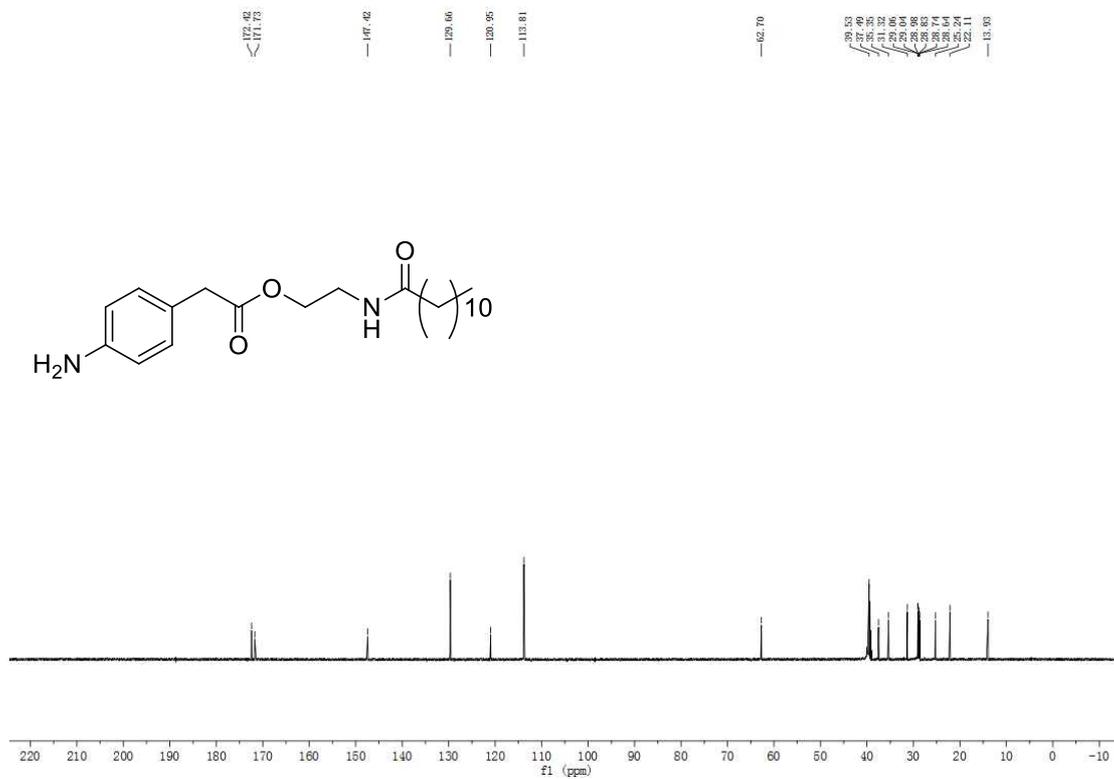
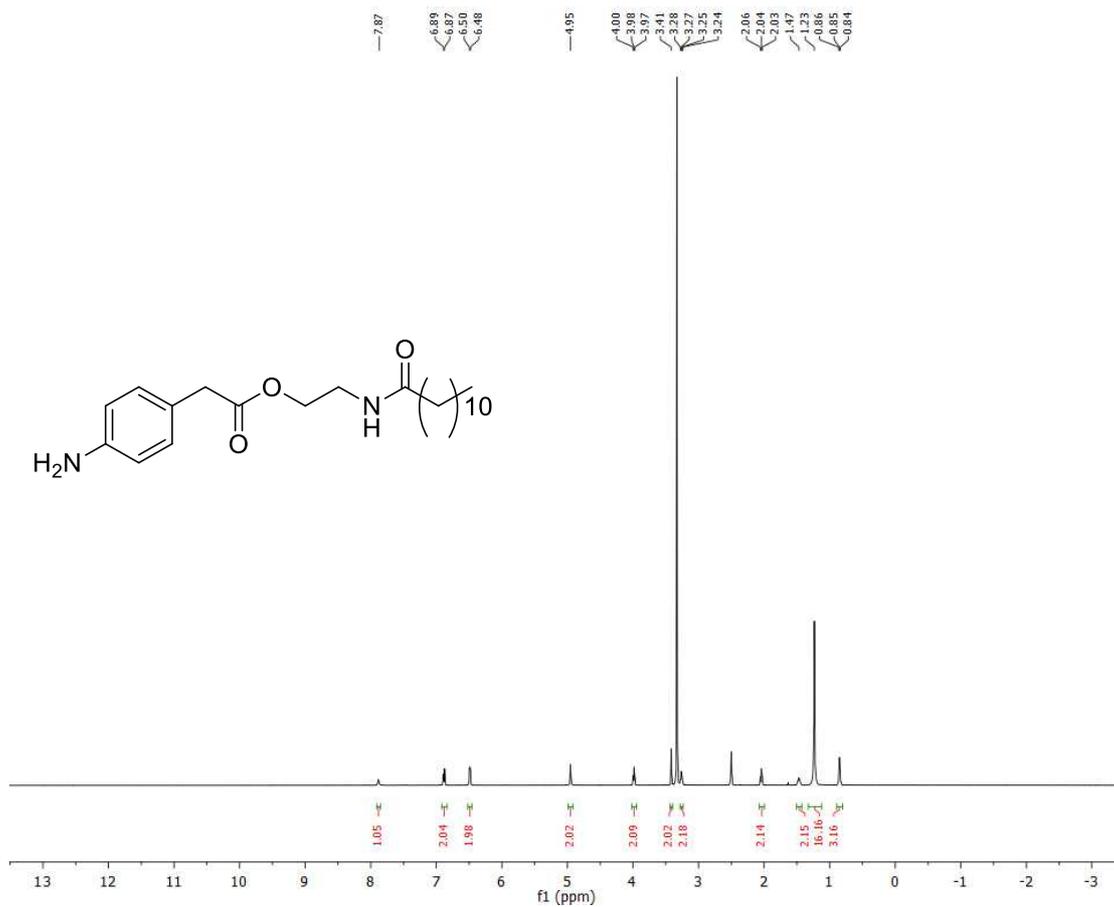
7.77
7.75
7.70
7.66
7.55
7.52
7.49
7.43
7.40
7.38
7.39
7.29
7.20
6.84
6.81
6.79

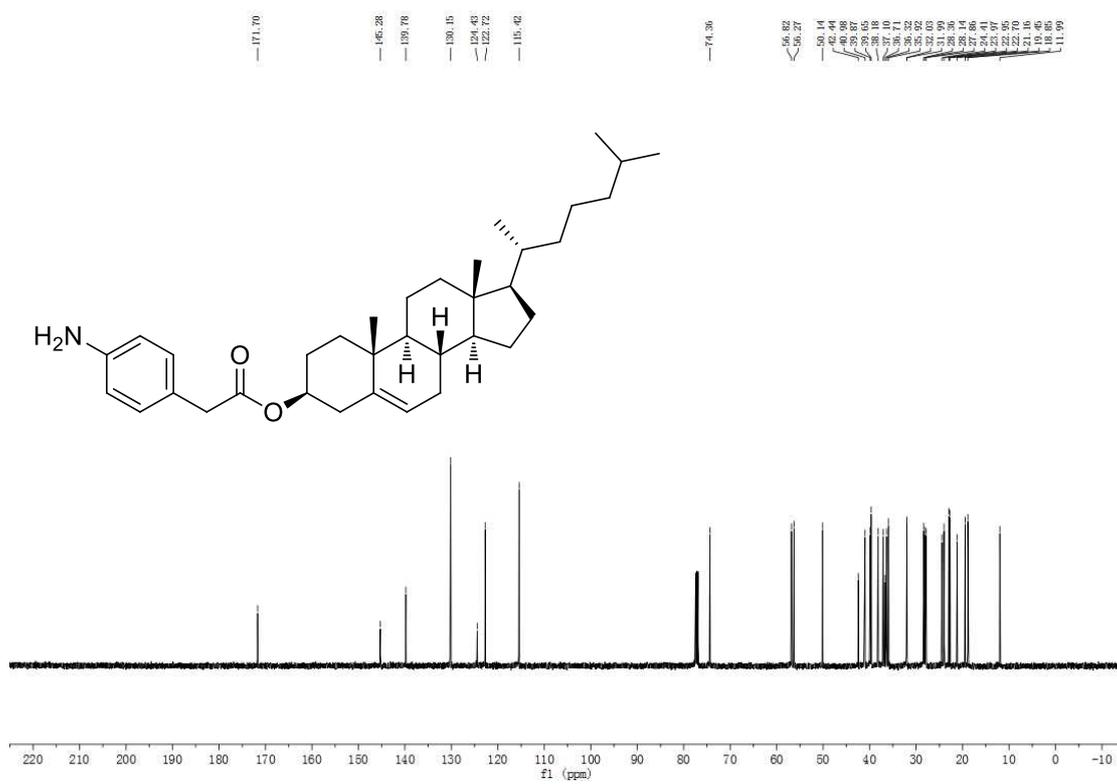
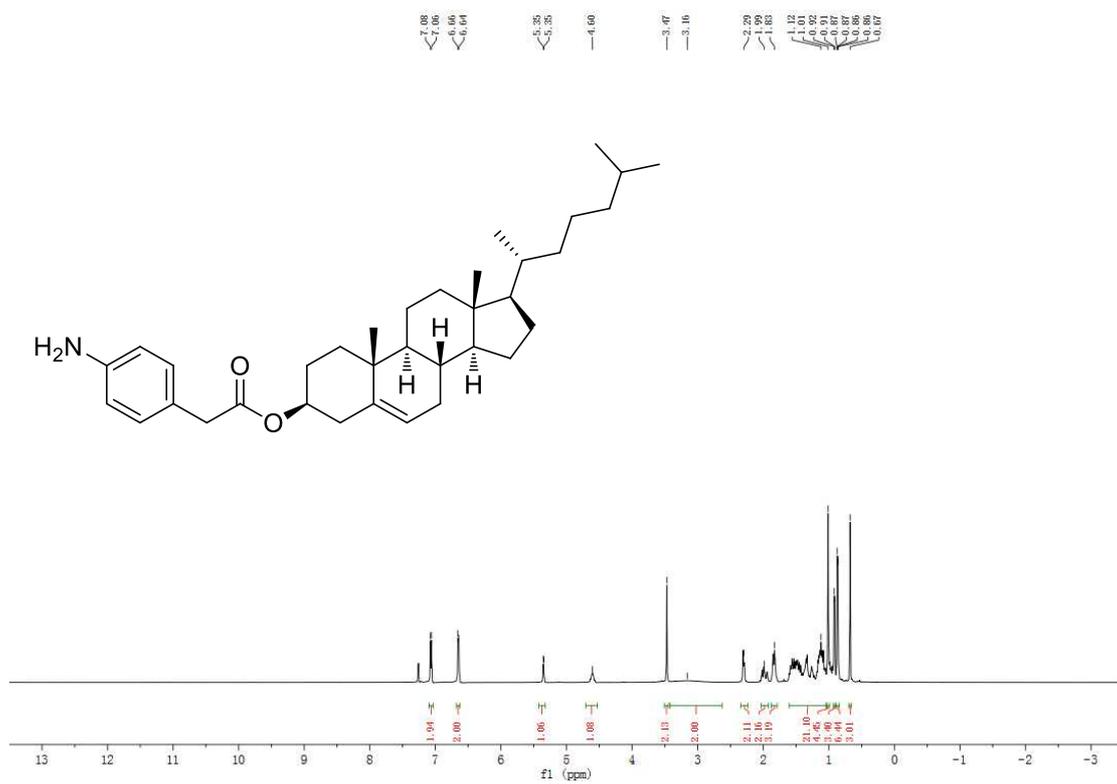
4.31

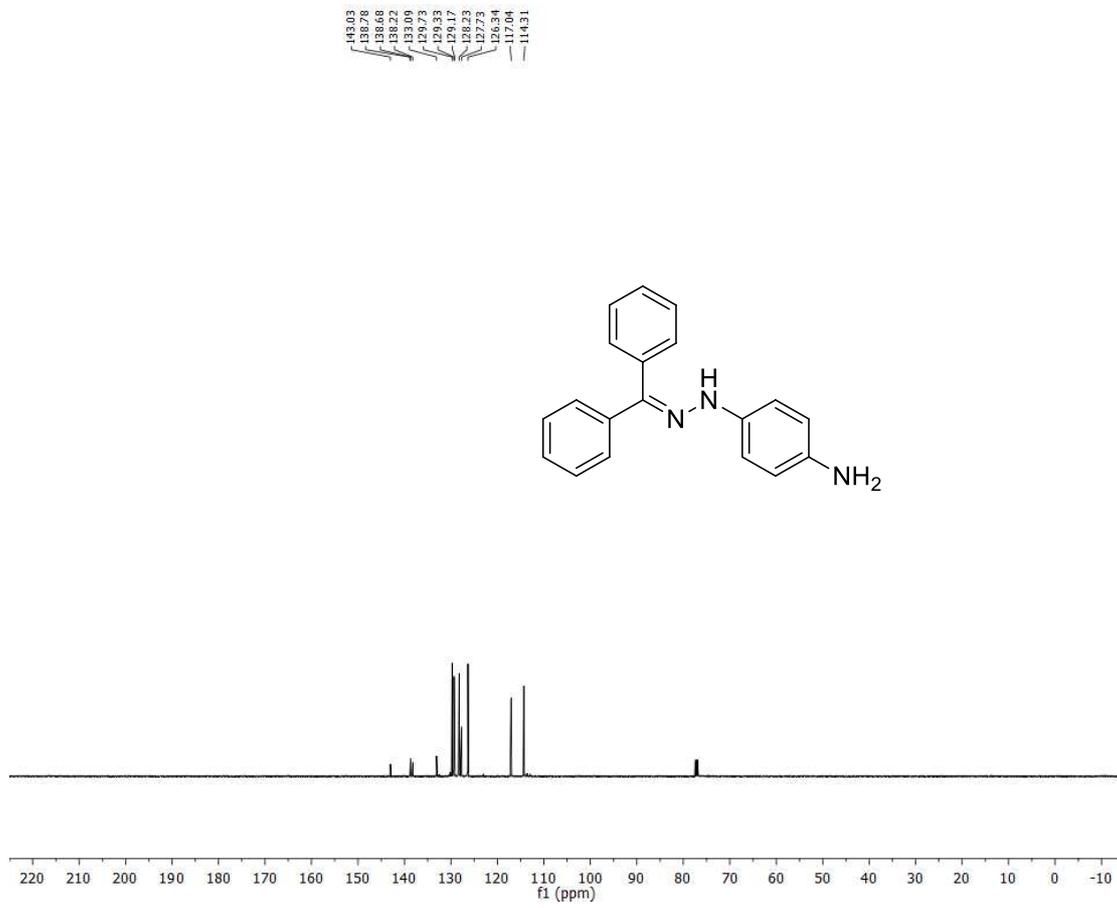
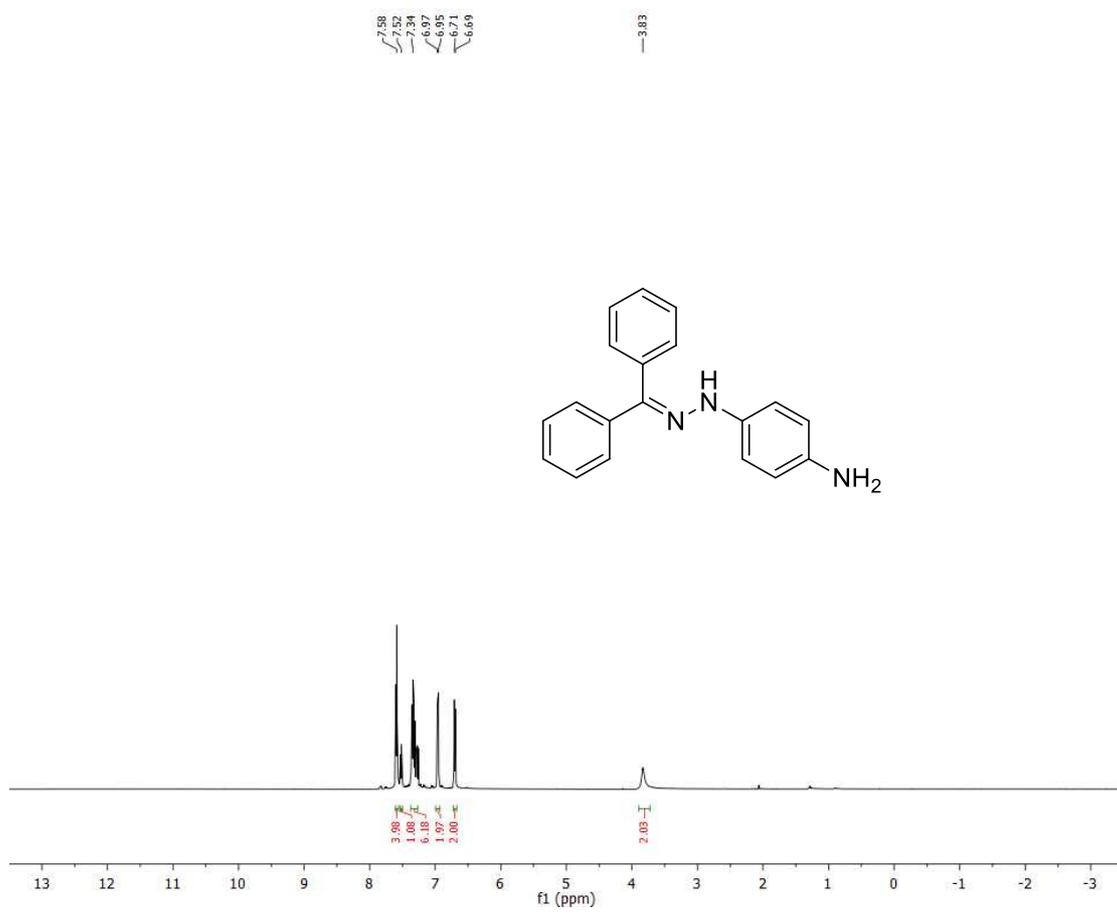


148.96
137.53
135.94
133.79
131.79
129.79
128.76
127.85
126.65
125.55
124.94
118.92
115.57
114.50

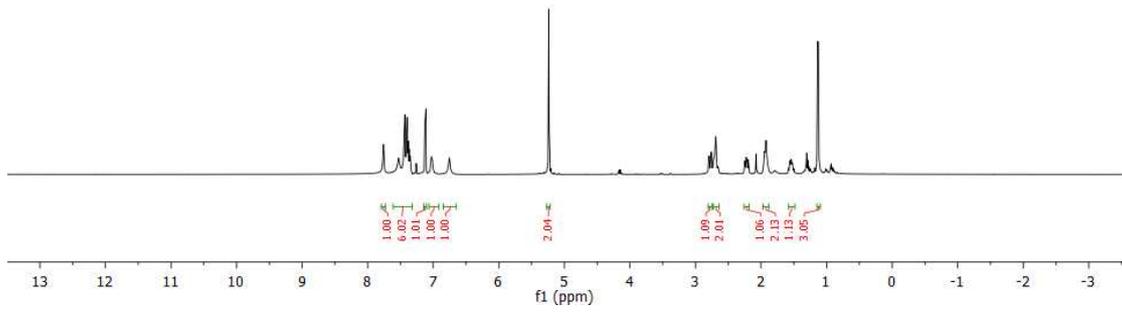
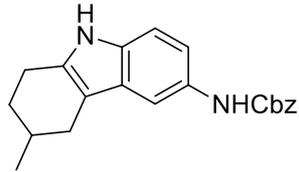








7.76
7.49
7.13
7.01
6.75
5.24
2.80
2.79
2.76
2.69
2.23
1.92
1.55
1.14
1.13



154.17
136.50
135.14
133.18
129.59
128.58
128.24
128.19
127.99
114.26
110.49
110.12
108.99
66.78
31.35
29.58
29.34
22.87
21.70

