Supporting information

A versatile, immobilized gold catalyst for the reductive amination of aldehydes in batch and flow

A. I. Carrillo,[a] P. Llanes,[a] Miquel A. Pericàs*[a,b]

[a]*Institute of Chemical Research of Catalonia (ICIQ), The Barcelona Institute of Science and Technology, Avda. Països Catalans, 16, 43007, Tarragona, Spain, and* [b]*Department de Química Inorgànica i Orgànica, Universitat de Barcelona, 080208, Barcelona, Spain*

mapericas@iciq.es

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1. General remarks

All reactions were conducted under air. Synthesis grade solvents were used as received. Tetraethylortholilicate (TEOS, 98%) was used as silica precursor, pluronic (P123) was used as structure-directing agent, hydrochloric acid and APTES were also used in the synthetic protocol to obtain the mesoporous material. Tetrachloroauric acid ($HAuCl_4$) and the photosensitizer Irgacure-2959 were employed in the synthesis and incorporation of gold nanoparticles (AuNPs) into the final hybrid mesoporous material.

AuNPs were obtained by using a Rayonet photochemical chamber reactor model RPR-200. The morphology of the mesoporous silica was determined by transmission electron microscopy (TEM). TEM analyses were carried on a JEOL-1011 microscope (JEOL, 100 Kv). For this purpose, samples were prepared by dipping a sonicated suspension of the material in ethanol on a carbon-coated copper grid. The textural properties of the solids were determined from N_2 adsorption-desorption at 77 K in a Quantachrome Autosorb iQ apparatus. The SBA-15 was previously degassed for 12 h at 523 K at 5 x 10^{-5} bar because of the absence of organic moieties. Au@APTES@SBA was degassed for 12 h at 373 k at 5 x 10^{-5} bar previously to the analysis. The adsorption branch of the obtained isotherms was used to determine the pore size distribution using the Barret-Joyner-Helender (BJH) method. The surface area was calculated using the multipoint BET method in the 0.05-0.30 relative pressure ranges. Mesopore volume was measured at the plateau of the desorption branch of the nitrogen isotherm, P/Po 0 0.8.[1]

XRD measurements were made using a Siemens D5000 diffractometer (Bagg-Brentano parafocusing geometry and vertical θ-θ goniometer) fitted with a curved graphite diffracted-beam monochromator, incident and diffracted- beam Soller slits, at 0.06º receiving slit and scintillation counter as a detector. The angular 2θ diffraction range was between 1 and 5º. Sample was dusted on to a low background Si (510) simple holder. The data was collected with an angular step of 0.03º at 6s per step. Cu kα radiation was obtained from a copper X-ray tube operated at 40 kV and 30mA.

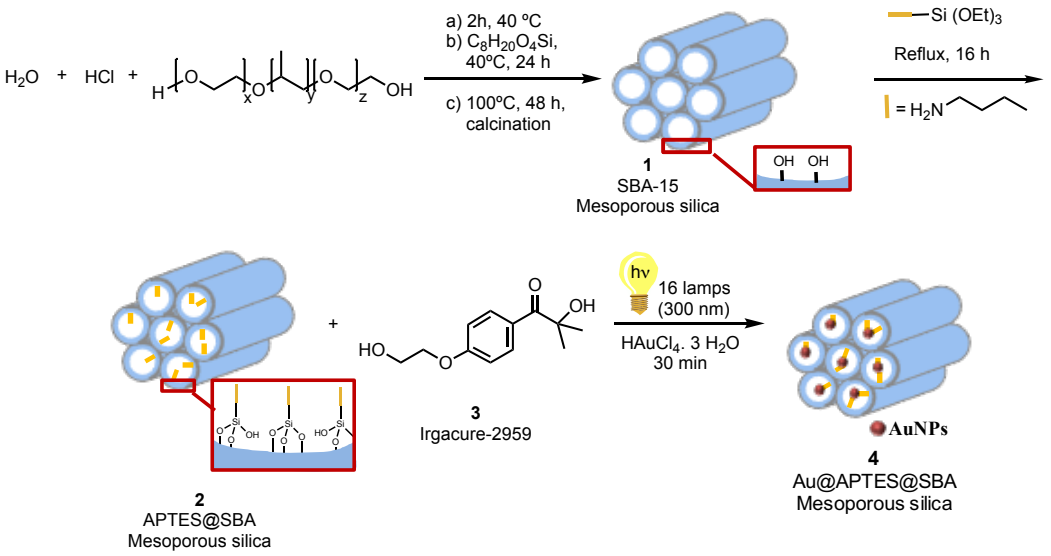
Metal loading in the materials was determined by ICP–OES on a Varian 720ES ICP–OES apparatus. An amount of 25 mg of every sample was digested in 1 mL of HNO_3/HCl during 12 h prior to analysis by ICP–OES.

Flash column chromatography was carried out using 60 mesh silica gel and dry-packed columns with a Teledyne Isco CombiFlash system with UV detector. Thin layer chromatography was carried out using Merck TLC Silicagel 60 F254 aluminium sheets. Components were visualized by UV light (λ = 254 nm) or by staining with phosphomolybdic acid (PMA) solution.

NMR spectra were recorded at 298 K on Bruker Avance 400 Ultrashield or a Bruker Avance 500 Ultrashield apparatus. ^{1}H NMR spectroscopy chemical shifts are quoted in ppm relative to tetramethylsilane (TMS). $CDCl_3$ was used as internal standard for ^{13}C NMR spectra. Chemical shifts are given in δ and coupling constants in Hz.

The continuous flow experiments were carried out using a syringe pump (Legato 200 from KDSCIENTIFIC). The packed-bed reactor consisted in an Omnifit glass chromatography column (10 mm bore size and up to maximal 70 mm of adjustable bed height).

2. Synthesis and characterization of mesoporous materials



Synthesis of SBA-15 (1)[2]

SBA-15 type silica was prepared according to a procedure already described.[2] In a typical synthesis, 20 g of pluronic (P123) were dispersed in 150 mL of water and 600 ml of 2 M HCl solution. Then, 46,6 mL of tetraethyl silicate (TEOS) were added to the solution under stirring. This gel mixture was continuously stirred at 40 ºC for 24 h and finally cured in a Teflon-lined autoclave at 100 ºC for 48 h. Then, the solid was filtered, washed with deionized water, dried in air at room temperature and calcined at 550 ºC under static air conditions for 11 h (1.86 ºC min^{-1}) in order to remove the surfactant.

Synthesis of APTES@SBA (2)[2]

(3-Aminopropyl)triethoxyilane was grafted onto SBA-15 as follows: 5 g of the mesoporous silica were mixed with 300 mL of toluene for 1 h. Then, APTES (2.57 g, 11.62 mmol) was added to the mixture and refluxed for 15 h. Finally, the hot solution was filtered out and the solid sample was washed with fresh toluene and air-dried at 60 ºC, leading to the APTES@SBA.

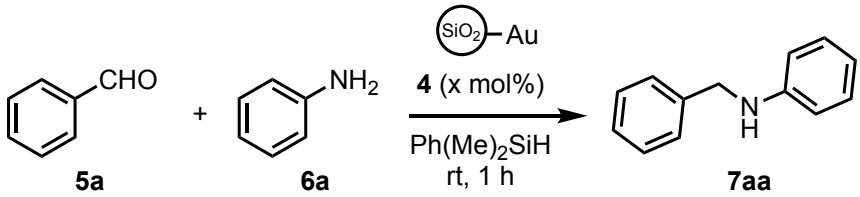
Synthesis of Au@APTES@SBA (4)[1]

$HAuCl_4$. 3 H_2O (0.375 g, 0.952 mmol) was added to an aqueous mixture (285 mL) of the APTES@SBA solid (**2**, 6.25 g). Then, the corresponding amount of Irgacure-2959 (**3**) (0.639 g, 2.85 mmol) was added and the yellow solution was placed into a photo reactor and irradiated with 16 lamps (300 nm) for 30 min. The obtained pink solution was filtered off and washed several times with water in order to remove the

nonreacted salt. Finally, the pink-red solid was dried overnight at 40 ºC. The amount of AuNPs incorporated into the material was determined by ICP analysis (nominal 3 wt %).

3. Studies in batch

3.1. Optimization details of the model reaction in batch



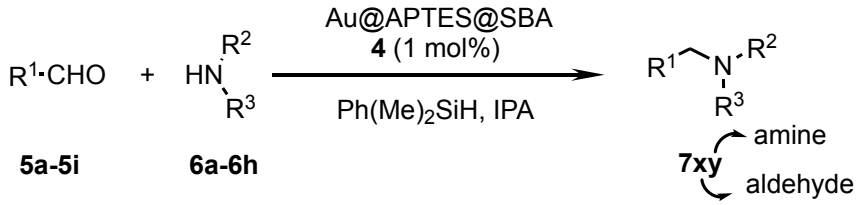
To a solution of benzaldehyde **5a** (0.5 mmol) and aniline **6a** (0.5 mmol) in 1 mL of solvent, phenyldimethylsilane (0.75 mmol) and the hybrid catalyst, Au@APTES@SBA (**4,** 0.5-1 mol%), were added. The reaction mixture was then allowed to stir at room temperature under argon atmosphere for 1 h. After completion of the reaction, the catalyst was removed by filtration and washed three times with CH_2Cl_2 (3 x 5 mL). The filtrate was purified by column chromatography (cyclohexane/ethyl acetate) to give the desired amines.

Table S1[a]: Optimization of the reaction conditions

Entry	Solvent	Catalyst 4 (mol%)	Conv (%)[b]
1	ACN	-	-
2	ACN	0.5	62
3	MeOH	0.5	83
4	IPA	0.5	80
5	IPA	1.0	90
6	Toluene	0.5	94
7	Acetone	0.5	79
8	Methyl THF	0.5	67

[a]Conditions: Benzaldehyde (0.5 mmol), aniline (0.5 mmol), silane (0.75 mmol), Au@APTES@SBA, solvent (1 mL), rt. [b]Conversion (%) was determined by GC by using dodecane as internal standard.

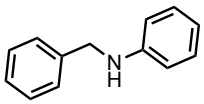
4. Reductive amination reactions in batch catalyzed by 4



To a solution of the corresponding aldehyde (**5a-5i**, 0.5 mmol) and different amines (**6a–6h**, 0.5 mmol) in 1 mL of isopropanol (IPA), phenyldimethylsilane (0.75 mmol) and catalyst, Au@APTES@SBA (**4,** 1 mol%, ICP = 3 wt% Au), were added. Then, the mixture was stirred at room temperature under argon atmosphere for 2 h (**General procedure A**) or at 60 ºC under argon atmosphere for 14 h (**General procedure B**). After completion of the reaction, the catalyst was removed by filtration and washed three times with CH_2Cl_2 (3 x 5 mL). The filtrate was purified by column chromatography (cyclohexane/ethyl acetate) to give the desired amines.

5. Characterization data for compounds 7aa-7ah

Synthesis of *N*-benzylaniline (7aa)[3]



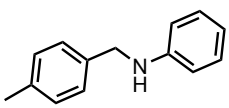
General procedure A was followed with benzaldehyde (**5a**) and aniline (**6a**) as reactants. After purification by flash chromatography with cyclohexane as the eluent the desired product was obtained in 90 % yield (83 mg, 0.45 mmol).

Yellow oil.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.45–7.40 (m, 4H), 7.35–7.33 (m, 1H), 7.27–7.23 (m, 2H), 6.79 (t, *J*= 7.3 Hz, 1H), 6.71 (d, *J*=7.7 Hz, 2H), 4.39 (s, 2H), 4.08 (br s, 1H, NH)

^{13}C NMR ($CDCl_3$, 126 MHz): δ 148.1, 139.4, 129.2 (x2), 128.6 (x2), 127.5 (x2), 127.2, 117.5, 112.8 (x2), 48.3.

Synthesis of *N*-(4-methylbenzyl)aniline (7ba)[3]



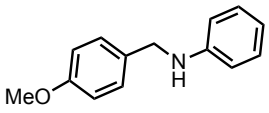
General procedure A was followed with 4-methylbenzaldehyde (**5b**) and aniline (**6a**) as reactants. After purification by flash chromatography with cyclohexane as the eluent the desired product was obtained in 94 % yield (93 mg, 0.47 mmol).

Yellow oil.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.26 (m, 2H), 7.21–7.19 (m, 4H), 6.72–6.68 (m, 1H), 6.64–6.62 (m, 2H), 4.28 (s, 2H), 3.97 (br s, 1H, NH), 2.34 (s, 3H).

^{13}C NMR ($CDCl_3$, 101 MHz): δ 148.2, 136.8, 136.3, 129.2 (x2), 129.3 (x2) 127.5 (x2), 117.5, 112.8 (x2), 48.1, 21.1.

Synthesis of *N*-(4-methoxybenzyl)aniline (7ca)[3]



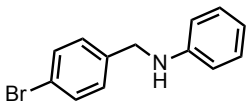
General procedure A was followed with 4-methoxybenzaldehyde (**5c**) and aniline (**6a**) as reactants. After purification by flash chromatography with cyclohexane as the eluent the desired product was obtained in 76 % yield (81 mg, 0.38 mmol).

Yellow oil.

^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.29 (d, *J* = 8.7 Hz, 2H), 7.17 (dd, *J* = 8.6, 7.4 Hz, 2H), 6.88 (d, *J* = 8.7 Hz, 2H), 6.71–6.69 (m, 1H), 6.64–6.63 (m, 2H), 4.25 (s, 2H), 3.93 (br s, 1H, NH), 3.80 (s, 3H).

^{13}C NMR ($CDCl_3$, 126 MHz): δ 158.8, 148.2, 131.4, 129.2 (x2), 128.8 (x2), 117.5, 114.0 (x2), 112.8 (x2), 55.3, 47.8.

Synthesis of *N*-(4-bromobenzyl)aniline (7da)[3]



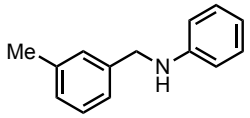
General procedure A was followed with 4-bromobenzaldehyde (**5d**) and aniline (**6a**) as reactants. After purification by flash chromatography with cyclohexane as the eluent the desired product was obtained in 76 % yield (98.3 mg, 0.38 mmol).

Yellow oil.

^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.46 (d, *J* = 8.3 Hz, 2H), 7.24 (d, *J* = 8.3 Hz, 2H), 7.19–7.13 (m, 2H), 6.72 (t, *J* = 7.3 Hz, 1H), 6.60 (d, *J* = 8.1 Hz, 2H), 4.29 (s, 2H), 4.05 (br s, 1H, NH).

^{13}C NMR ($CDCl_3$, 126 MHz): δ 147.8, 138.5, 132.4, 131.7 (x2), 129.3 (x2), 129.0 (x2), 120.9, 117.8, 112.9, 47.7.

Synthesis of *N*-(3-methylbenzyl)aniline (7ea)[4]

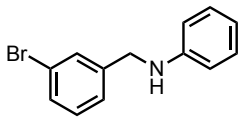


General procedure A was followed with 3-methylbenzaldehyde (**5e**) and aniline (**6a**) as reactants. After purification by flash chromatography with cyclohexane as the eluent the desired product was obtained in 77 % yield (75 mg, 0.38 mmol).

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.25–7.15 (m, 5H), 7.09 (d, *J* = 7.4 Hz, 1H), 6.71 (t, *J* = 7.3 Hz, 1H), 6.64 (d, *J* = 8.3 Hz, 2H), 4,28 (s, 2H), 3.99 (br s, 1H, NH), 2.35 (s, 3H).

^{13}C NMR ($CDCl_3$, 101 MHz): δ 148.2, 139.4, 138.3, 129.2 (x2), 128.5, 128.3, 127.9, 124.6, 117.5, 112.8 (x2), 48.4, 21.4.

Synthesis of *N*-(3-bromobenzyl)aniline (7fa)[4]



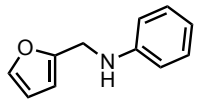
General procedure A was followed with 3-bromobenzaldehyde (**5f**) and aniline (**6a**) as reactants. After purification by flash chromatography with cyclohexane as the eluent the desired product was obtained in 77 % yield (100 mg, 0.38 mmol).

Yellow oil.

^{1}H NMR ($CDCl_3$, 400 MHz):7.46 (s, 1H), 7.32 (d, *J* = 7.9 Hz, 1H), 7.23 (d, *J* = 8.0 Hz, 1H), 7.15–7.08 (m, 3H), 6.65 (t, *J* = 7.3 Hz, 1H), 6.56–6.53 (m, 2H), 4.23 (s, 2H), 4.13 (br s, 1H, NH).

^{13}C NMR ($CDCl_3$, 101 MHz): δ 147.6, 141.9, 130.4, 130.3, 130.2, 129.3 (x2), 125.9, 122.8, 117.9, 112.9 (x2), 47.8.

Synthesis of *N*-(furan-2-ylmethyl)aniline (7ga)[3]



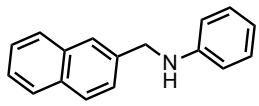
General procedure A was followed with furfural (**5g**) and aniline (**6a**) as reactants. After purification by flash chromatography with cyclohexane as the eluent the desired product was obtained in 76 % yield (66 mg, 0.38 mmol).

Brown oil.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.36 (m, 1H), 7.20–7.16 (m, 2H), 6.75–6.72 (1H), 6.68–6.67 (m, 2H), 6.32–6.31 (m,1H), 6.23 (m, 1H), 4.32 (s, 2H), 4.02 (br s, 1H, NH).

^{13}C NMR ($CDCl_3$, 101 MHz): δ 152.7, 147.6, 141.9 (x2), 129.2 (x2), 118.0, 110.3 (x2), 106.9, 41.4.

Synthesis of *N*-(naphthalen-2-ylmethyl)aniline (7ha)[3]



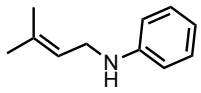
General procedure B was followed with 2-naphtaldehyde (**5h**) and aniline (**6a**) as reactants (0.3 mmol scale, 2 mol% catalyst). After purification by flash chromatography with cyclohexane as the eluent the desired product was obtained in 79 % yield (55 mg, 0.24 mmol).

White solid.

^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.84–7.78 (m, 4H), 7.50–7.44 (m, 3H), 7.20–7.15 (m, 2H), 6.74–6.66 (m, 3H), 4.49 (s, 2H), 4.13 (br s, 1H, NH)

^{13}C NMR ($CDCl_3$, 126 MHz): δ 148.1, 136.9, 133.5, 132.8, 129.3 (x2),128.4, 127.7, 127.7, 126.1, 125.9, 125.7, 125.7, 117.6, 112.9 (x2), 48.5.

Synthesis of *N*-(3-methylbut-2-en-1-yl)aniline (7ia)[5]



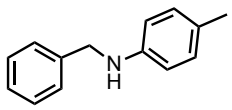
General procedure B was followed with 3-methyl-2-butenal (**5i**) and aniline (**6a**) as reactants. After purification by flash chromatography with cyclohexane as the eluent the desired product was obtained in 80 % yield (65 mg, 0.40 mmol).

Yellow oil.

^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.19–7.16 (m, 2H), 6.72–6.99 (m, 1H), 6.62–6.61 (m, 2H), 5.35–5.32 (m, 1H), 3.69 (d, *J*= 6.7 Hz, 2H), 3.57 (br s, 1H, NH), 1.75 (s, 3H), 1.71 (s, 3H).

^{13}C NMR ($CDCl_3$, 126 MHz): δ 148.4, 135.6, 129.2, 121.6, 117.3, 112.9, 41.9, 25.7, 17.9.

Synthesis of N-benzyl-4-methylaniline (7ab)[6]



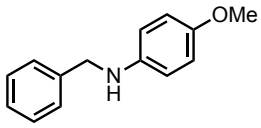
General procedure B was followed with benzaldehyde (**5a**) and 4-methylaniline (**6b**) as reactants. After purification by flash chromatography with cyclohexane as the eluent the desired product was obtained in 81% yield (80 mg, 0.41 mmol).

Yellow oil.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.41–7.35 (m, 4H), 7.31–7.28 (m, 1H), 7.02 (d, *J*= 8.1 Hz, 2H), 6.60 (d, *J*= 8.4 Hz, 2H), 4.34 (s, 2H), 3.94 (br s, 1H, NH), 2.27 (s, 3H).

^{13}C NMR ($CDCl_3$, 101 MHz): δ 145.9, 139.7, 129.7 (x2), 128.6 (x2), 127.5 (x2), 127. 2, 126.8, 113.0 (x2), 48.7, 20.4.

Synthesis of *N*-benzyl-4-methoxyaniline (7ac)[4]



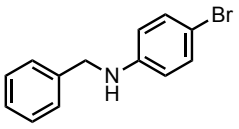
General procedure B was followed with benzaldehyde (**5a**) and 4-methoxyaniline (**6c**) as reactants. After purification by flash chromatography with cyclohexane as the eluent the desired product was obtained in 84% yield (90 mg, 0.42 mmol).

Yellow oil.

^{1}H NMR ($CDCl_3$, 400 MHz): 7.38–7.25 (m, 5H), 6.77 (d, *J* = 9.0 Hz, 2H), 6.60 (d, *J* = 9.0 Hz, 2H), 4.28 (s, 2H), 3.74 (s, 3H).

^{13}C NMR ($CDCl_3$, 101 MHz): 152.2, 142.4, 139.7, 128.6 (x2), 127.5 (x2), 127.2, 114.9 (x2), 114.1 (x2), 55.8, 49.3.

Synthesis of *N*-benzyl-4-bromoaniline (7ad)[7]



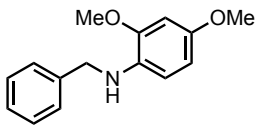
General procedure B was followed with benzaldehyde (**5a**) and 4-bromoaniline (**6d**) as reactants (0.3 mmol scale). After purification by flash chromatography with cyclohexane as the eluent the desired product was obtained in 80 % yield (63 mg, 0.24 mmol).

Yellow oil.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.35–7.28 (m, 5H), 7.23 (d, *J* = 8.9 Hz, 2H), 6.50 (d, *J* = 8.9 Hz, 2H), 4.30 (s, 2H), 4.07 (br s, 1H, NH).

^{13}C NMR ($CDCl_3$, 101 MHz): δ 147.0, 138.8, 131.9 (x2), 128.7 (x2), 127.4 (x3), 114.4 (x2), 109.1, 48.2.

Synthesis of *N*-benzyl-2,4-dimethoxyaniline (7ae)[8]



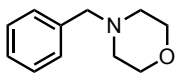
General procedure B (the mixture was heated at 60 ºC for 24 h) was followed with benzaldehyde (**5a**) and butylamine (**6e**) as reactants. After purification by flash chromatography with cyclohexane as the eluent the desired product was obtained in 61 % yield (74 mg, 0.30 mmol).

Yellow oil

^{1}H NMR ($CDCl_3$, 400 MHz): 7.39–7.31 (m, 4H), 7.27–7.26 (m, 1H), 6.50 (d, *J*= 8.5 Hz, 1H), 6.47 (d, *J*= 2.6 Hz,1H), 6.37 (dd, *J*= 8.5, 2.7 Hz, 1H), 4.30 (s, 2H), 4.25 (br s, 1H, NH), 3.82 (s, 3H), 3.74 (s, 3H).

^{13}C NMR ($CDCl_3$, 126 MHz): 151.9, 147.9, 139.8, 132.5, 128.5 (x 2), 127.5 (x2), 127.0, 110.3, 103.7, 99.2, 55.8, 55.5, 48.8.

Synthesis of 4-benzylmorpholine (7af)[9]



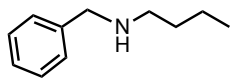
General procedure B was followed with benzaldehyde (**5a**) and morpholine (**6f**) as reactants. After purification by flash chromatography with cyclohexane as the eluent the desired product was obtained in 70 % yield (61 mg, 0.35 mmol).

Yellow oil.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.32–7.25 (m, 5H), 3.72–3.70 (m, 4H), 3.50 (s, 2H), 2.45–2.43 (m, 4H).

^{13}C NMR ($CDCl_3$, 101 MHz): δ 137.9, 129.3 (x2), 128.4 (x2), 127.3, 67.2 (x2), 63.6, 53.8 (x2).

Synthesis of *N*-benzylbutan-1-amine (7ag)[6]



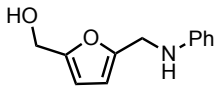
General procedure B was followed with benzaldehyde (**5a**) and butylamine (**6g)** as reactants. After purification by flash chromatography with cyclohexane as the eluent the desired product was obtained in 55 % yield (45 mg, 0.27 mmol).

Yellow oil

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.36–7.34 (m, 4H), 7.30–7.25 (1H), 3.82 (s, 2H), 2.66 (t, *J* = 7.6 Hz, 2H), 1.83 (br s, 1H, NH), 1.53 (dt, *J* = 14.5, 7.1, 2H), 1.38 (dq, *J*= 14.3, 7.2, 2H), 0.94 (t, *J*= 7.3 Hz, 3H).

^{13}C NMR ($CDCl_3$, 101 MHz): δ 140.3, 128.3, 128.1, 126.8, 53.9, 49.1, 32.1, 20.42, 13.93.

Synthesis of (5-(phenylamino)furan-2-yl)metanol (13)[10]



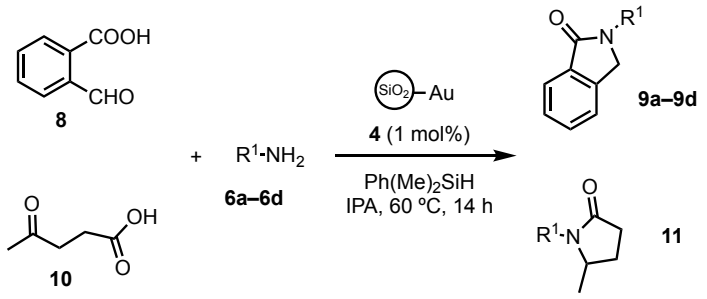
General procedure B was followed with 5-hydroxymethyl-2-furaldehyde (**12**) and aniline (**6a**) as reactants. After purification by flash chromatography with cyclohexane/EtOAc (70:30) as the eluent the desired product was obtained in 66 % yield (67 mg, 0.33 mmol).

Yellow oil.

^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.20–7.17 (m, 2H), 6.76–6.73 (m, 1H), 6.68–6.67 (m, 2H), 6.22 (d, *J* = 3.1 Hz,1H), 6.18 (d, *J* = 3.1 Hz, 1H), 4.58 (s, 2H), 4.31 (s, 2H), 4.03 (br s, 1H, NH).

^{13}C NMR ($CDCl_3$, 126 MHz): δ 153.4, 152.9, 147.5, 129.2 (x2), 118.1, 113.2 (x2), 108.7, 107.8, 57.6, 41.5.

6. General procedure for the synthesis of lactams and cyclic amines in batch catalyzed by 4.



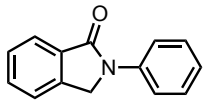
General procedure C for reductive annulation leading to lactams **9a-9d**: To a screw-capped vial, Au@APTES@SBA (**4,** 1 mol%), amine (**6a-6d,** 0.5 mmol), 2-

carboxybenzaldehyde (**8**, 0.5 mmol) in IPA:Me–THF (2 mL, 1:1) and phenyldimethylsilane (1 mmol) were added in this order. The mixture was heated at 60 ºC for 14 h. After completion of the reaction, the catalyst was removed by filtration and washed three times with the solvent (3 x 5 mL). The filtrate was purified by column chromatography (cyclohexane/ethyl acetate mixtures) to give the desired anilines.

General procedure D for reductive annulation leading to lactam **10**: To a screw-capped vial, Au@APTES@SBA (**4,** 1 mol%), amine (**6a-6d,** 0.5 mmol), keto acid (**10**, 0.5 mmol) and phenyldimethylsilane (1.5 mmol) in IPA (1 mL) were added in this order. The mixture was heated at 60 ºC for 14 h. After completion of the reaction, the catalyst was removed by filtration and washed three times with the solvent (3 x 5 mL). The filtrate was purified by column chromatography (cyclohexane/ethyl acetate mixtures) to give the desired anilines.

7. Characterization data for compounds 9a-9d, 11

Synthesis of 2-phenylisoindolin-1-one (9a)[11]



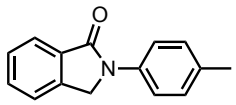
General procedure C was followed with **8** and **6a** as reactants. After purification by flash chromatography with cyclohexane/EtOAc (80:20) as the eluent the desired product was obtained in 90 % yield (100 mg, 0.48 mmol).

White color

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.94 (d, *J* = 7.4 Hz, 1H), 7.88 (d, *J* = 9.8 Hz, 2H), 7.64 –7.58 (m, 1H), 7.53 (d, *J* = 7.9 Hz, 2H), 7.47–7.41 (m, 2H), 7.22–7.16 (m, 1H), 4.88 (s, 2H).

^{13}C NMR ($CDCl_3$, 126 MHz): δ 167.5, 140.1, 139.5, 133.2, 132.0, 129.1 (x2), 128.3, 124.4, 124.1, 122.6, 119.4 (x2), 50.7.

Synthesis of 2-(*p*-tolyl)isoindolin-1-one (9b)[11]



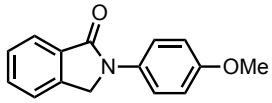
General procedure C was followed with **8** and **6b** as reactants. After purification by flash chromatography with cyclohexane/EtOAc (80:20) as the eluent the desired product was obtained in 87 % yield (98 mg, 0.44 mmol).

White solid

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.93 (d, *J* = 8.4 Hz, 1H), 7.74 (d, *J* = 8.6 Hz, 2H), 7.61–7.57 (m, 1H), 7.52–7.50 (m, 2H), 7.25–7.22 (m, 2H), 4.84 (s, 2H), 2.36 (s, 3H).

^{13}C NMR ($CDCl_3$, 101 MHz): δ 167.4, 140.1, 136.9, 134.2, 133.4, 131.9, 129.7, 128.3 (x2), 124.1, 122.6, 119.7 (x2), 50.9, 20.9.

Synthesis of 2-(4-methoxyphenyl)isoindolin-1-one (9c)[11]



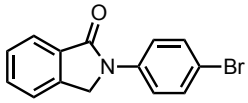
General procedure C was followed with **8** and **6c** as reactants. After purification by flash chromatography with cyclohexane/EtOAc (80:20) as the eluent the desired product was obtained in 90 % yield (105 mg, 0.44 mmol).

Yellow solid

^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.91 (d, *J* = 8.1 Hz, 1H), 7.73 (d, *J* = 9.1 Hz, 2H), 7.59–7.56 (m, 1H), 7.50–7.49 (m, 2H), 6.96 (d, *J* =9.1 Hz, 2H),4.81 (s, 2H), 3.82 (s, 3H).

^{13}C NMR ($CDCl_3$, 126 MHz): δ 167.2, 156.6, 140.1, 133.3, 132.6, 131.8, 128.3, 124.0, 122.5, 121.5 (x2), 114.3 (x2), 55.5, 51.2.

Synthesis of 2-(4-bromophenyl)isoindolin-1-one (9d)[12]



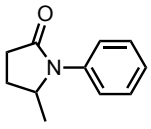
General procedure C was followed with **8** and **6d** as reactants. After purification by flash chromatography with cyclohexane/EtOAc (85:15) as the eluent the desired product was obtained in 80 % yield (115 mg, 0.40 mmol).

White solid

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.93 (d, *J* = 8.3 Hz, 1H), 7.80 (d, *J* = 9.1 Hz, 2H), 7.64 – 7.60 (m, 1H), 7.55 –7.50 (m, 4H), 4.84 (s, 2H),

^{13}C NMR ($CDCl_3$, 101 MHz): δ 167.5, 139.9, 138.6, 133.0, 132.3, 132.1 (x2), 128.5, 124.3, 122.6, 120.7 (x2), 117.2, 50.57.

Synthesis of 5-methyl-1-phenylpyrrolidin-2-one (11)[12]



General procedure D was followed with levulinic acid (**10)** and **6a** as reactants (0.3 mmol scale). After purification by flash chromatography with cyclohexane/EtOAc (45:55) as the eluent the desired product was obtained in 75 % yield (40 mg, 0.23 mmol).

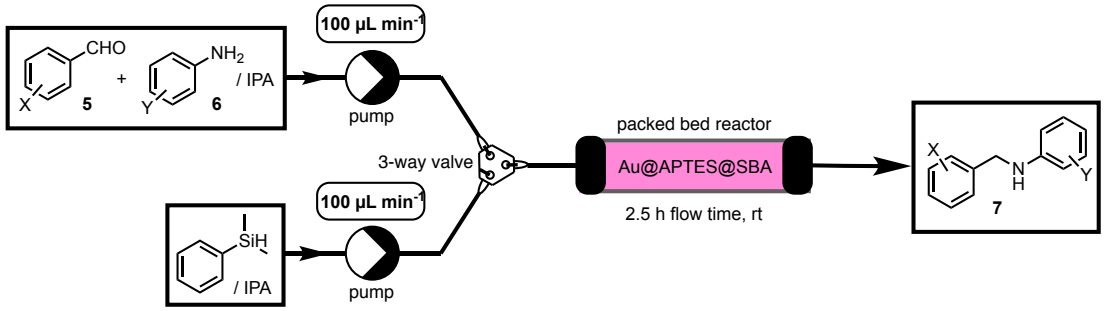
White solid

^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.40 (m, 4H), 7.23 (m, 1H), 4.35–4.31 (m, 1H), 2.70–2.53 (m, 2H), 2.44–2.38 (m, 1H), 1.82–1.75 (m, 1H), 1.24 (d, *J* =6.2 Hz, 3H)

^{13}C NMR ($CDCl_3$, 126 MHz): δ 174.2, 137.6, 128.9 (x2), 125.8, 124.1 (x2), 55.6, 31.4, 26.8, 20.2.

8. Reductive amination in flow

8.1. Description of the set-up and general procedure for flow reductive amination with catalyst 4



The packed bed reactor consisted in a vertically mounted, fritted low-pressure Omnifit column (10 mm bore size and up to maximal 70 mm of adjustable bed height), which was loaded with a mixture of 500 mg of Au@APTES@SBA and 1 mm size glass balls. The column was fed with two independent streams, each connected to a syringe pump:

-Solution A: aldehyde (6.2 mmol, 1 equiv.) and amine (6.2 mmol, 1 equiv.) in isopropanol (15 mL, 0.41 M).

-Solution B: $Ph(Me)_2SiH$ (9.3 mmol, 1.5 equiv.) in isopropanol (15 mL, 0.62 M).

The system was running for 2.5 h at 200 µL min^{-1} flow rate. After this time, the feeding stream was replaced by isopropanol at 200 µL min^{-1} flow rate to rinse the system for 1 h.

Compound **7ab**: the system was running for 5 h 45 min at 100 µL min^{-1} flow rate. After this time, the feeding stream was replaced by isopropanol at 100 µL min^{-1} flow rate to rinse the system for 1 h.

The collected organic phase was concentrated and the residue obtained was purified by flash chromatography with cyclohexane/ethyl acetate mixtures to give the desired anilines.

9. References

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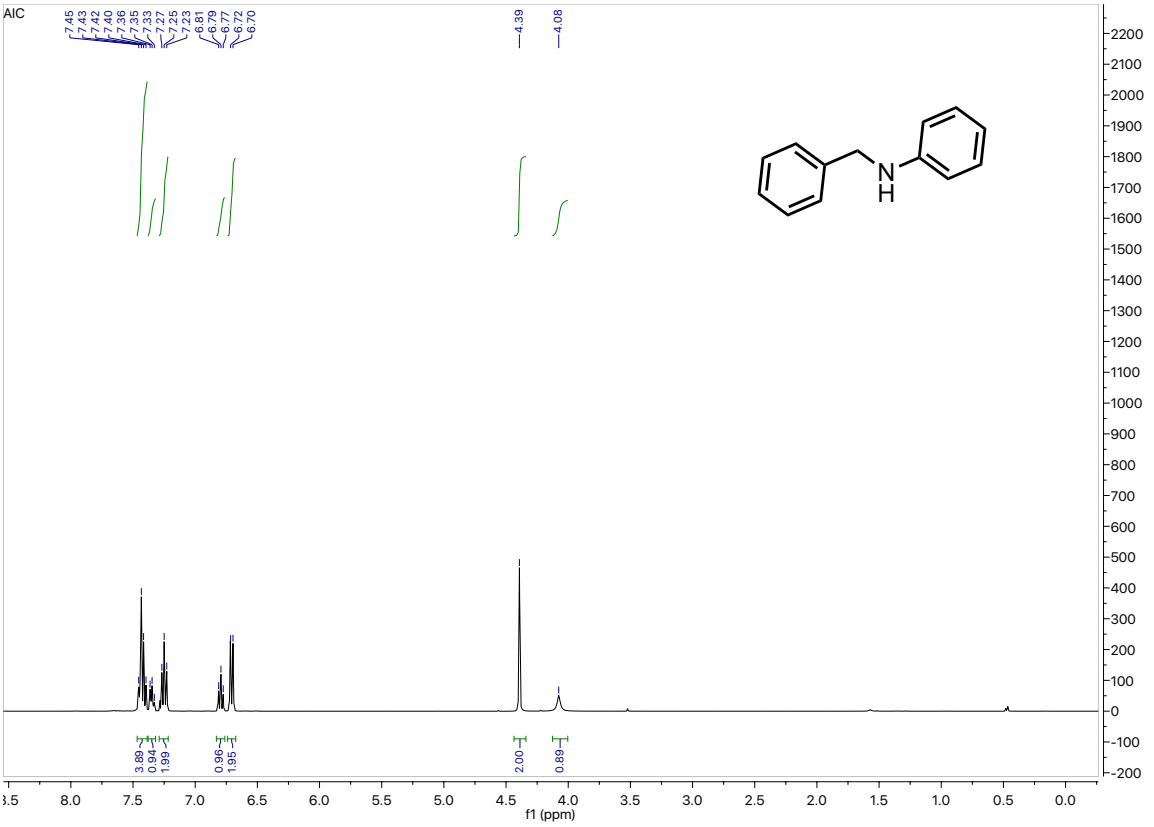
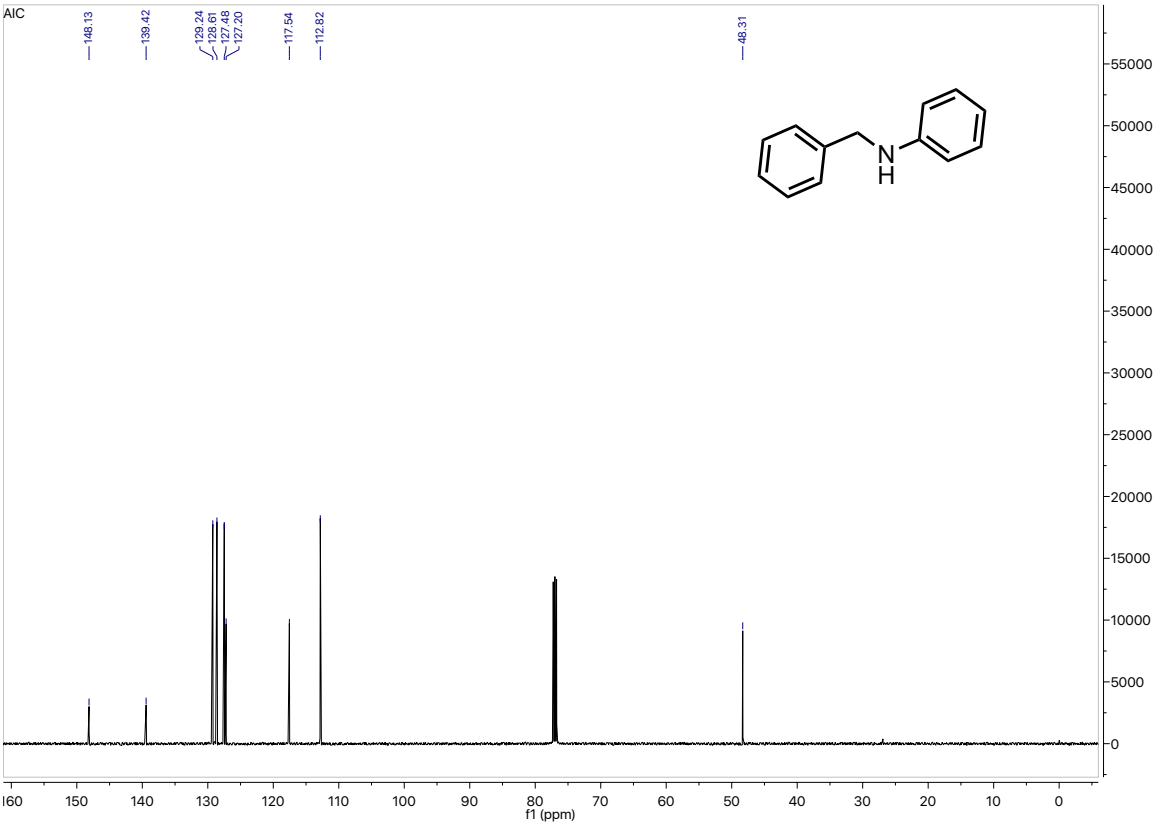
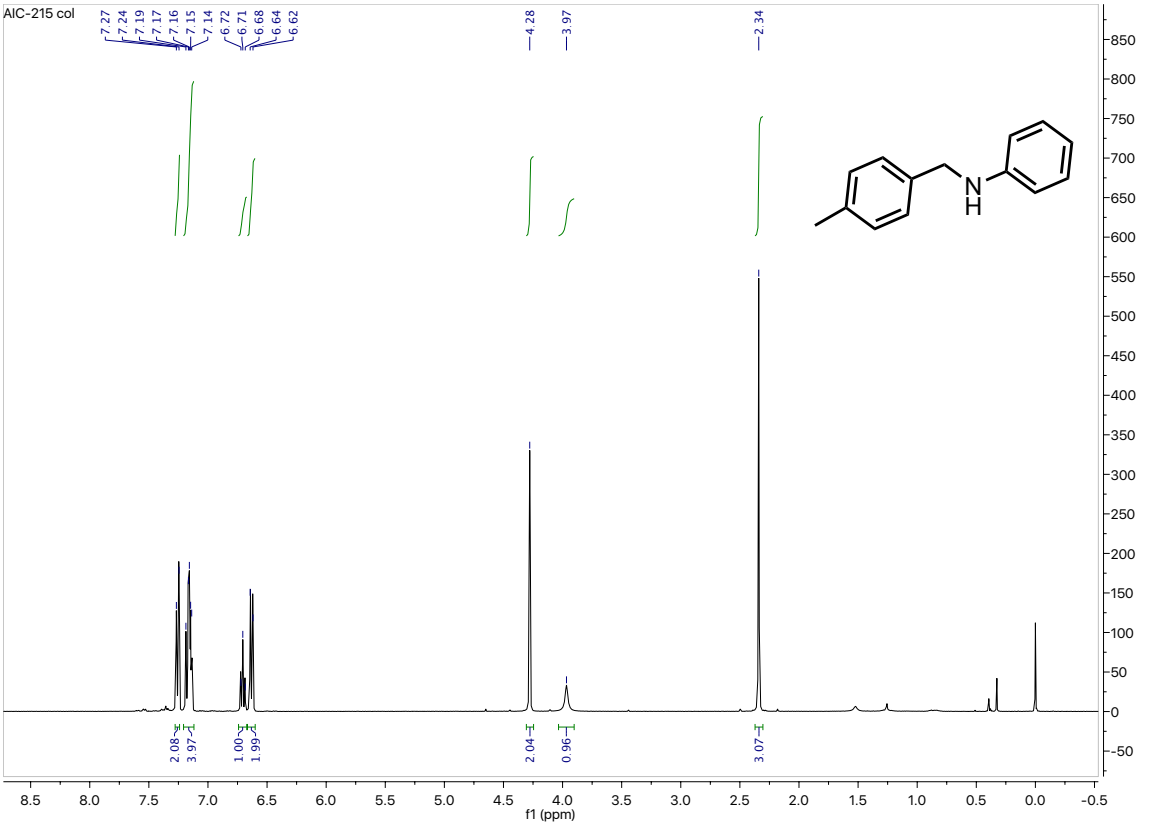
10. NMR spectra for compounds 7aa-7ah, 9a-9d, 11

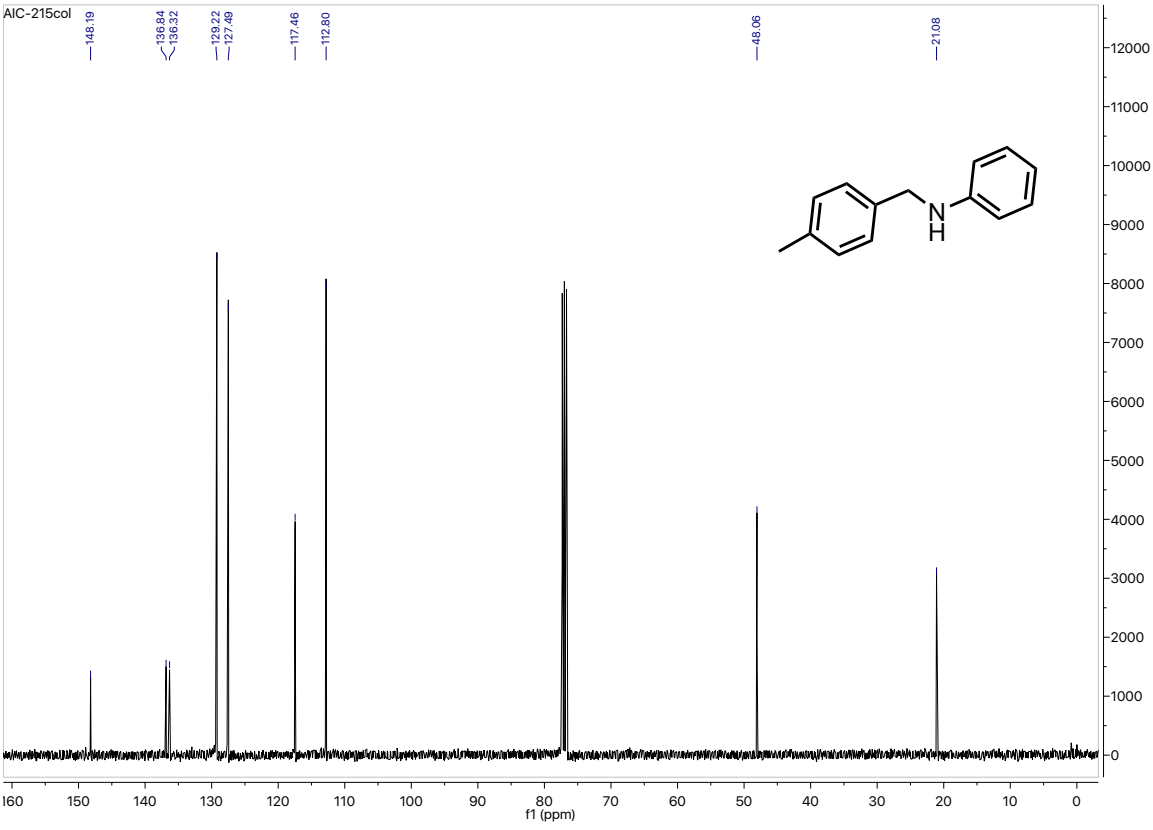
N-benzylaniline (7aa)



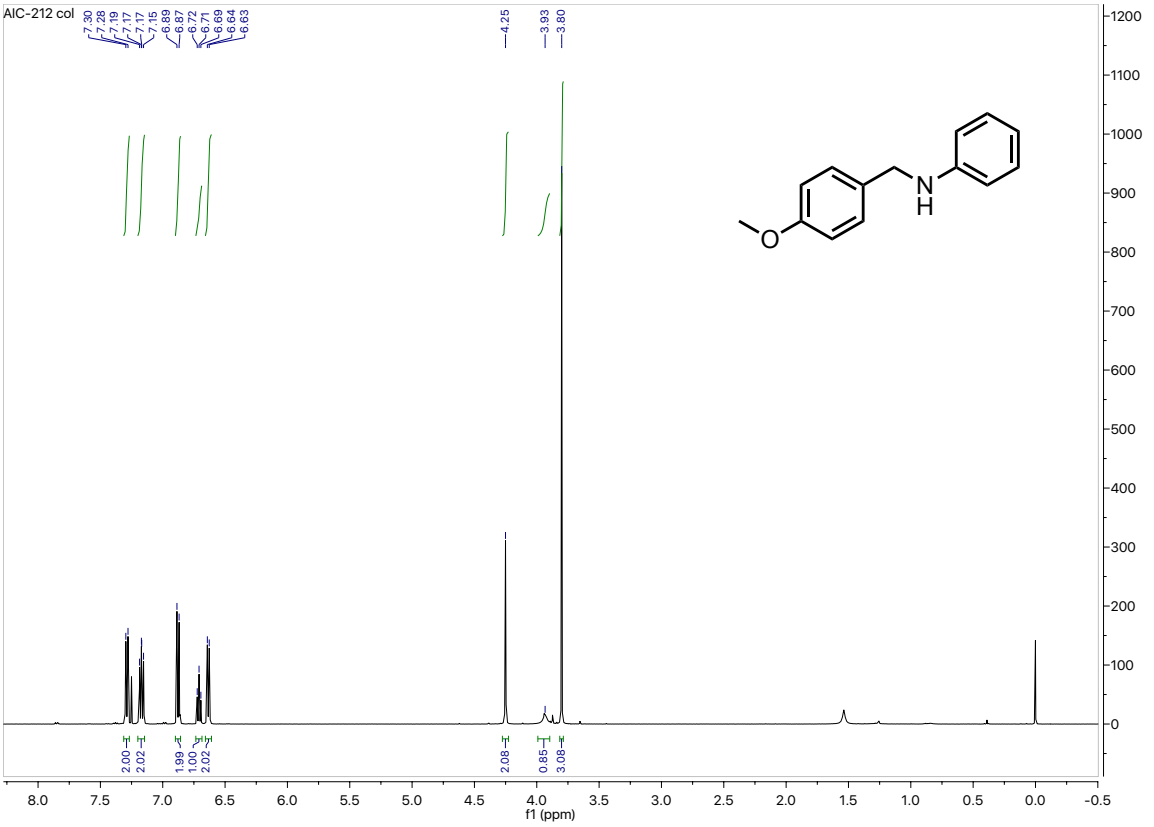


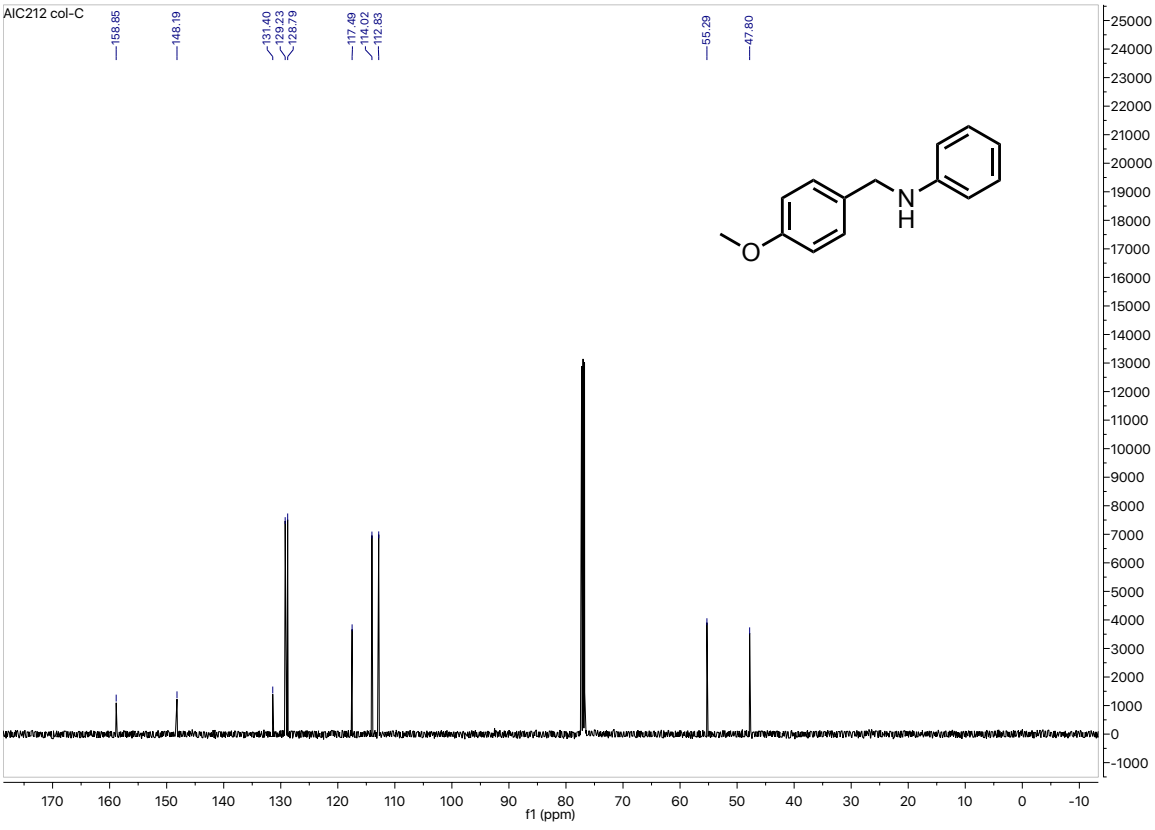
N-(4-methylbenzyl)aniline (7ba)



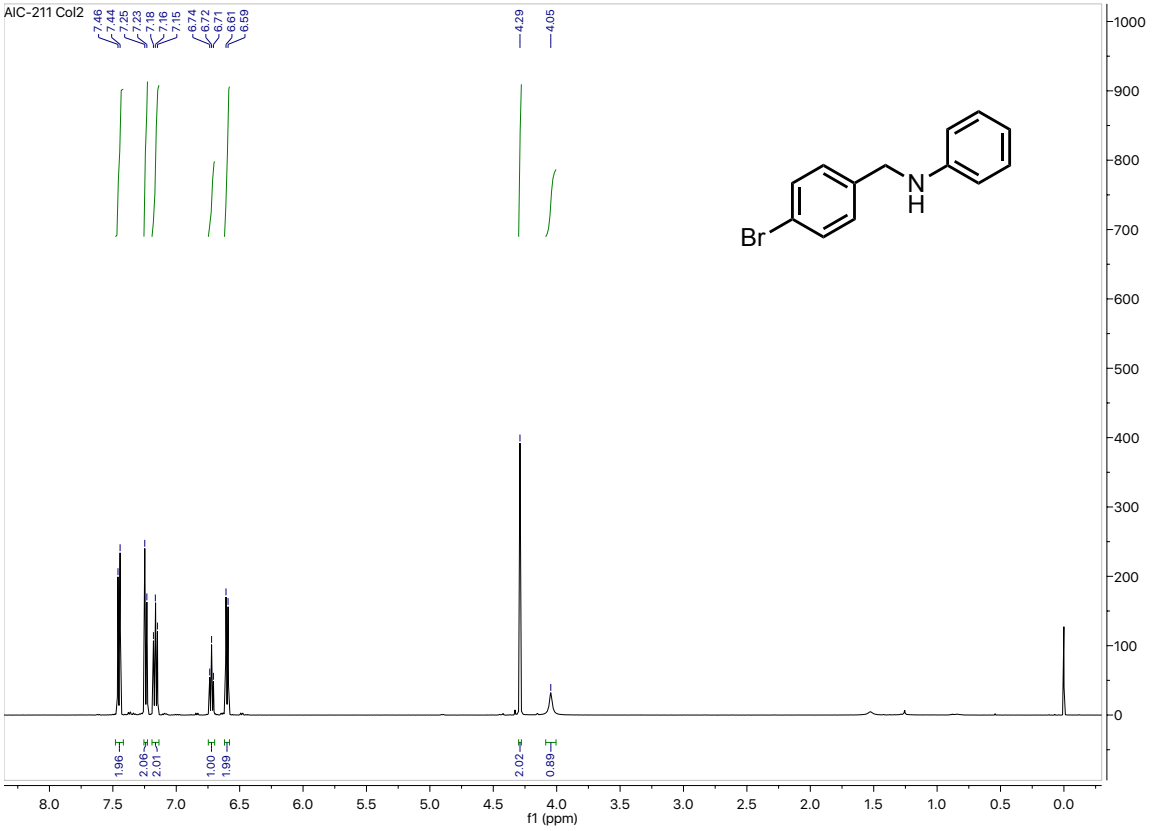


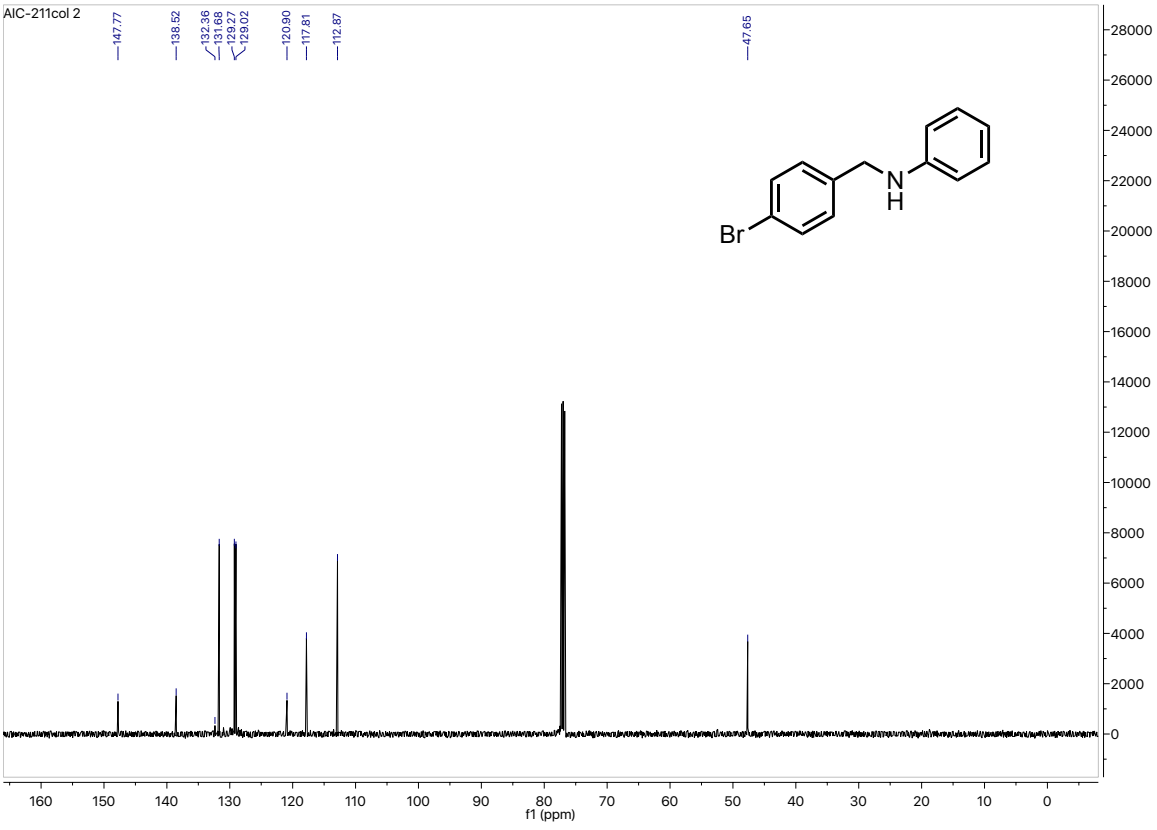
N-(4-methoxybenzyl)aniline (7ca)



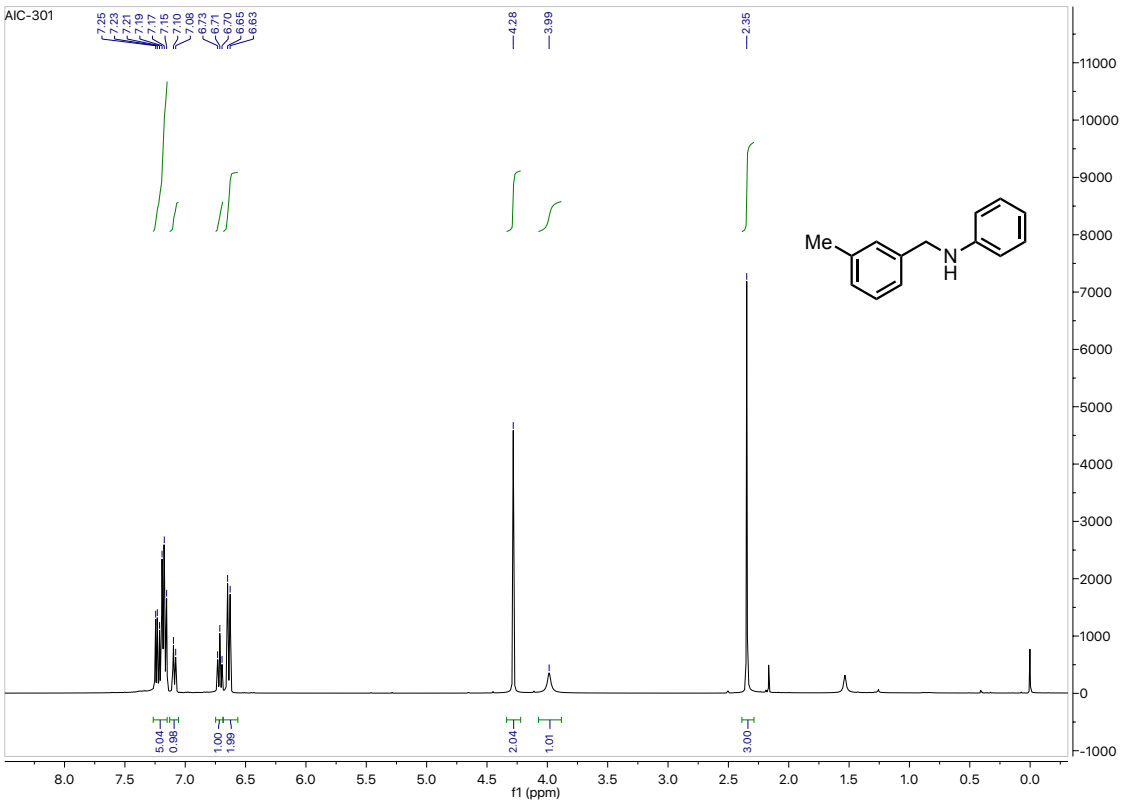


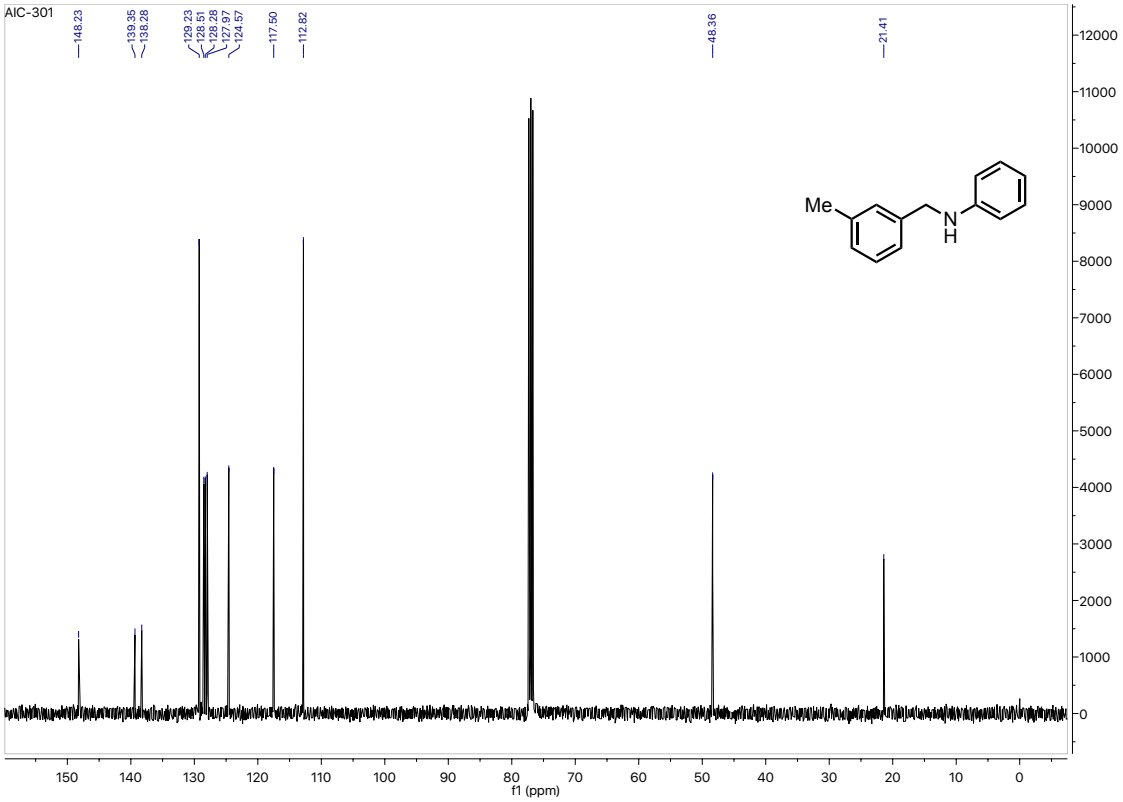
N-(4-bromobenzyl)aniline (7da)



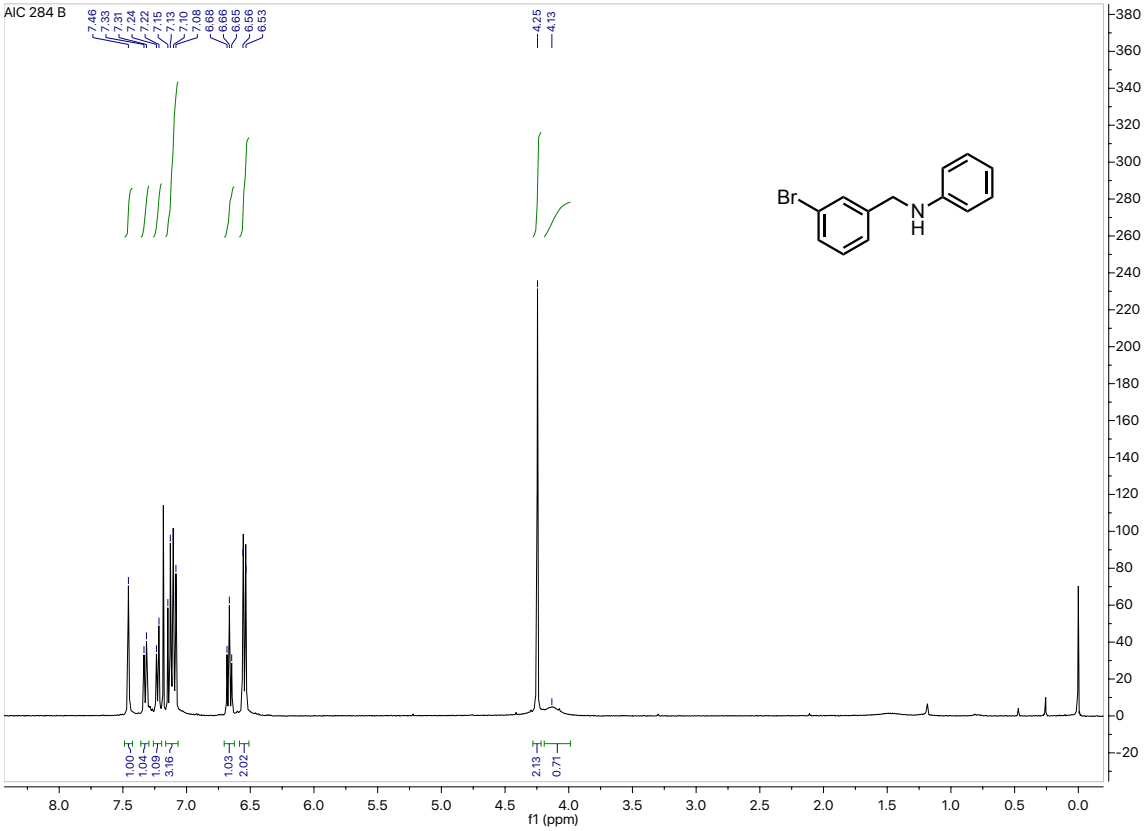


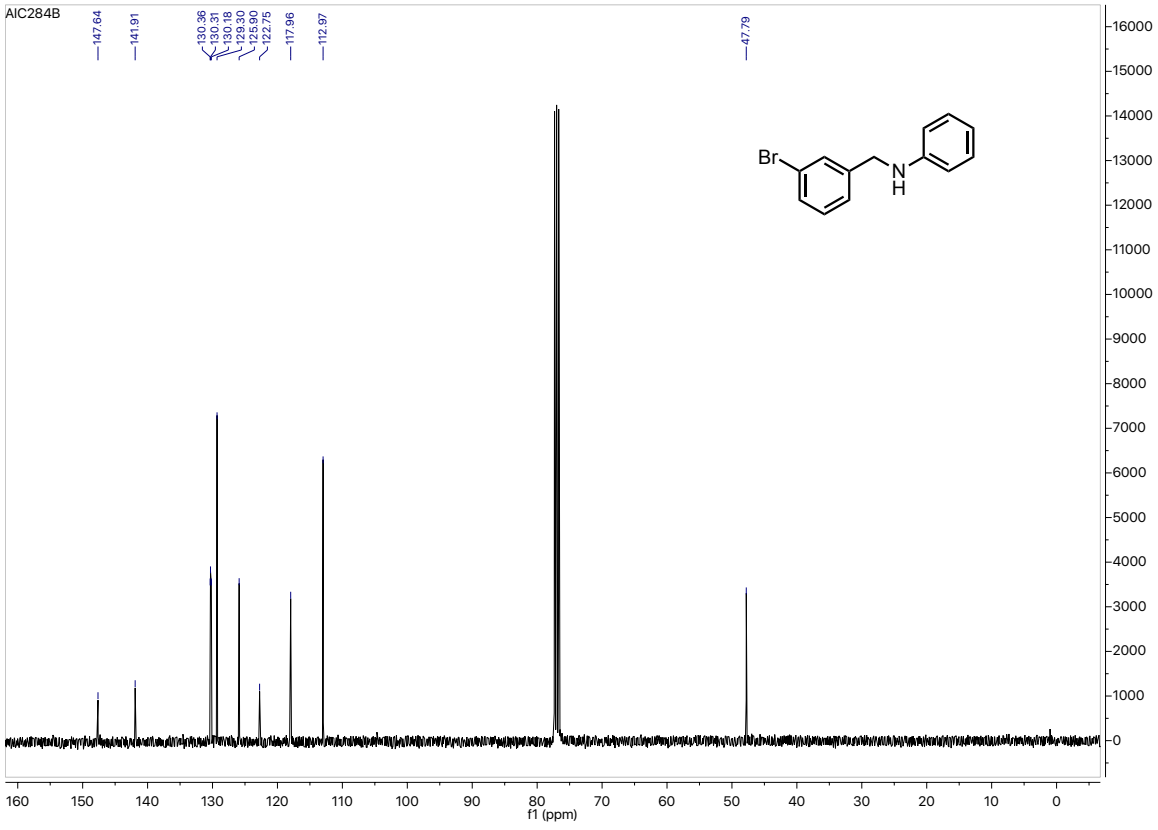
N-(3-methylbenzyl)aniline (7ea)



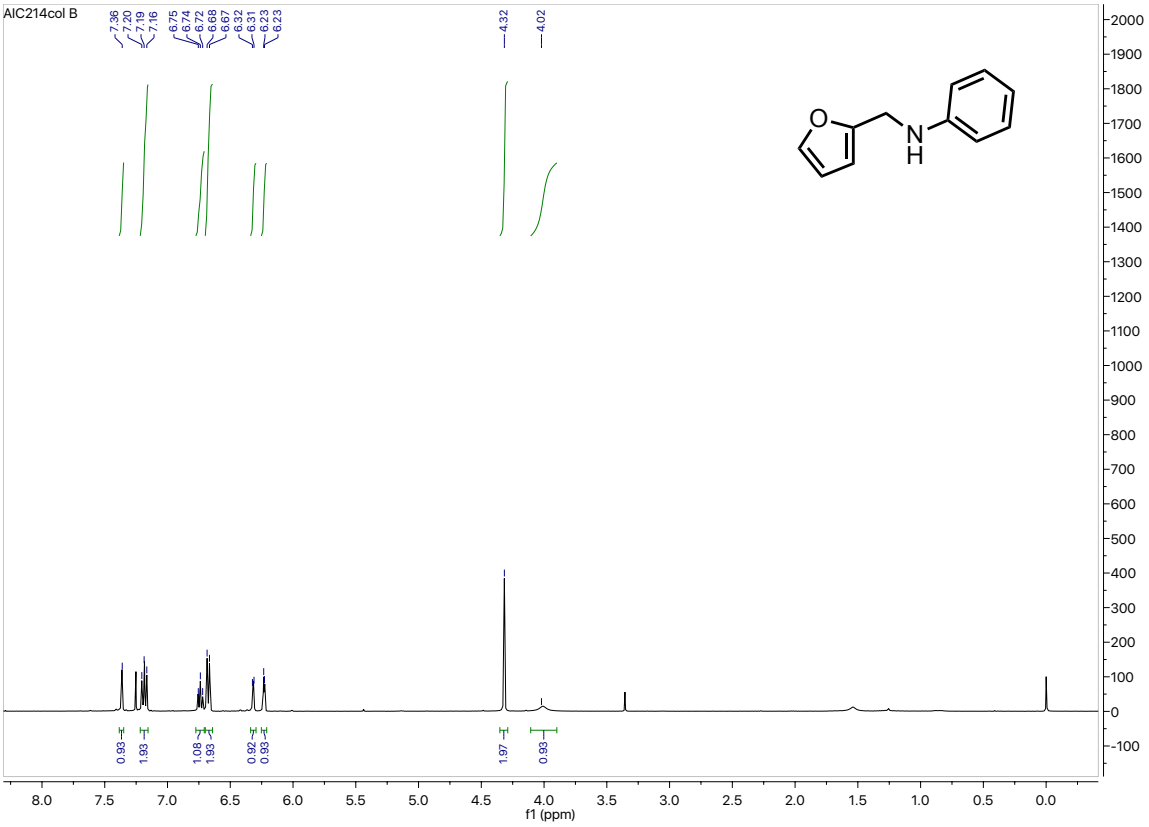


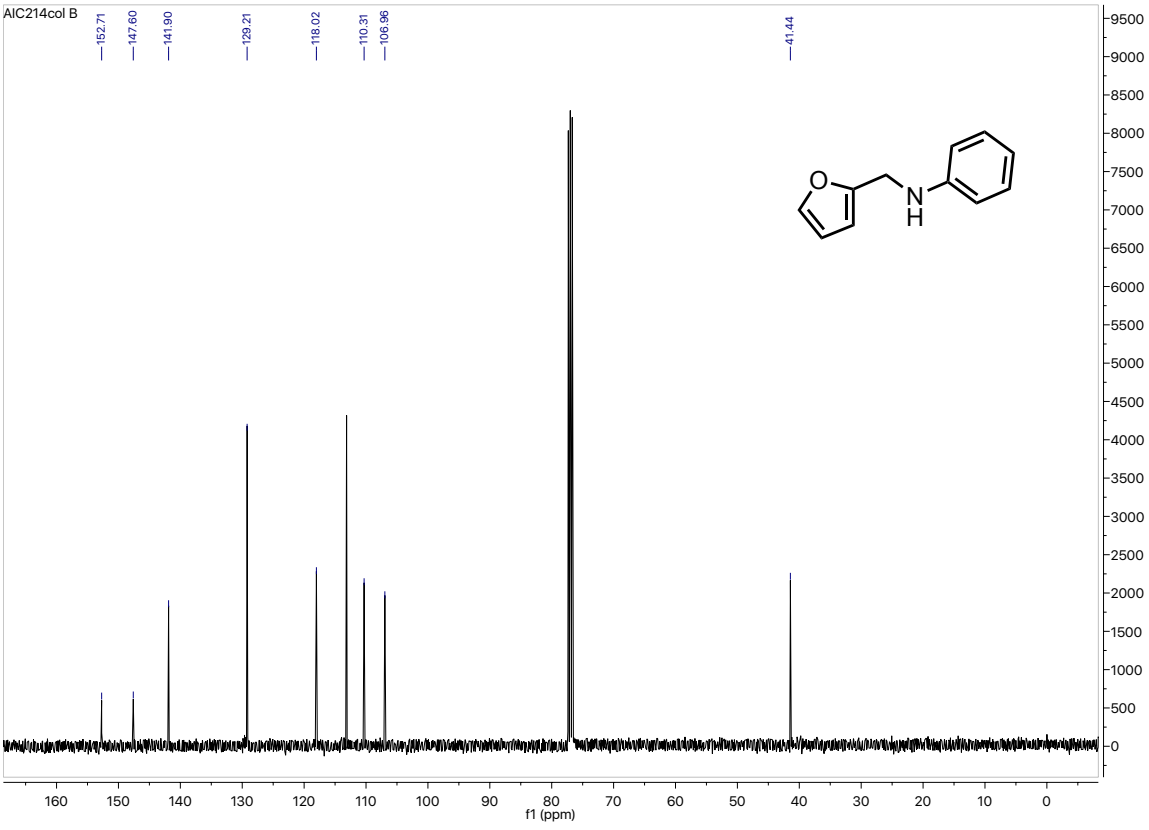
N-(3-bromobenzyl)aniline (7fa)



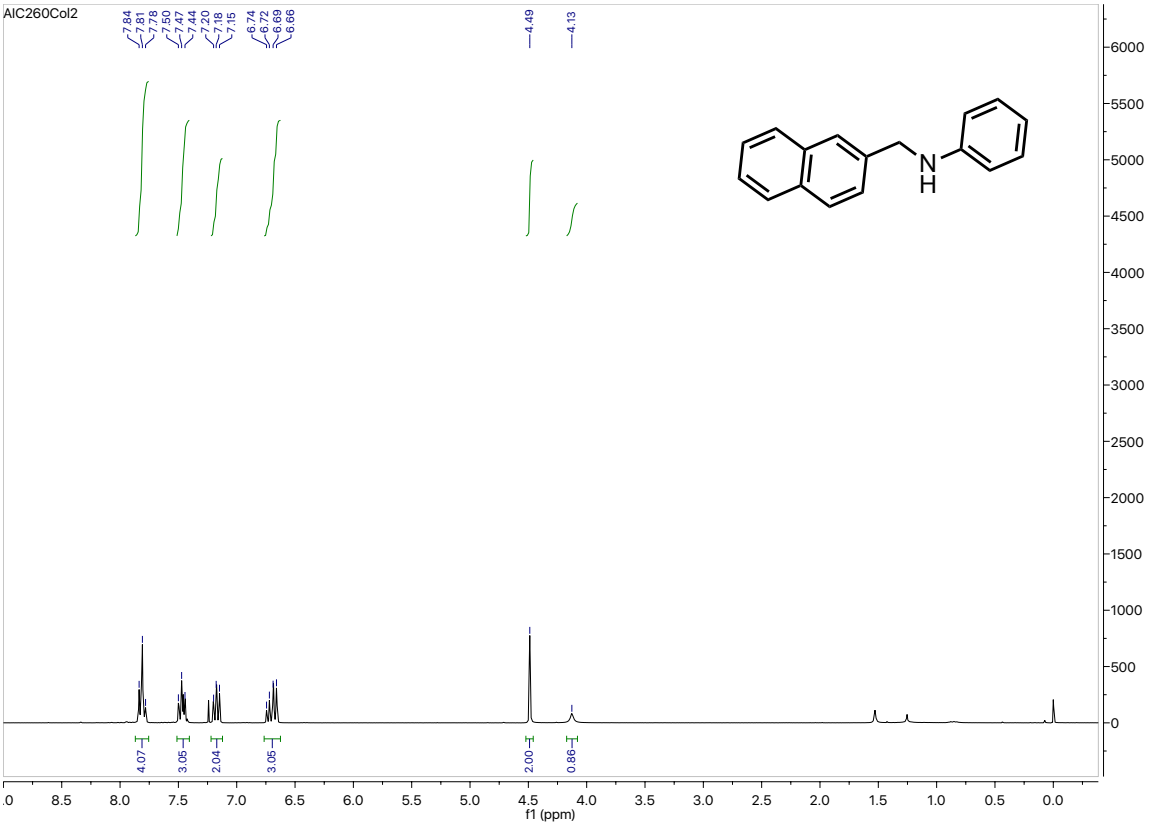


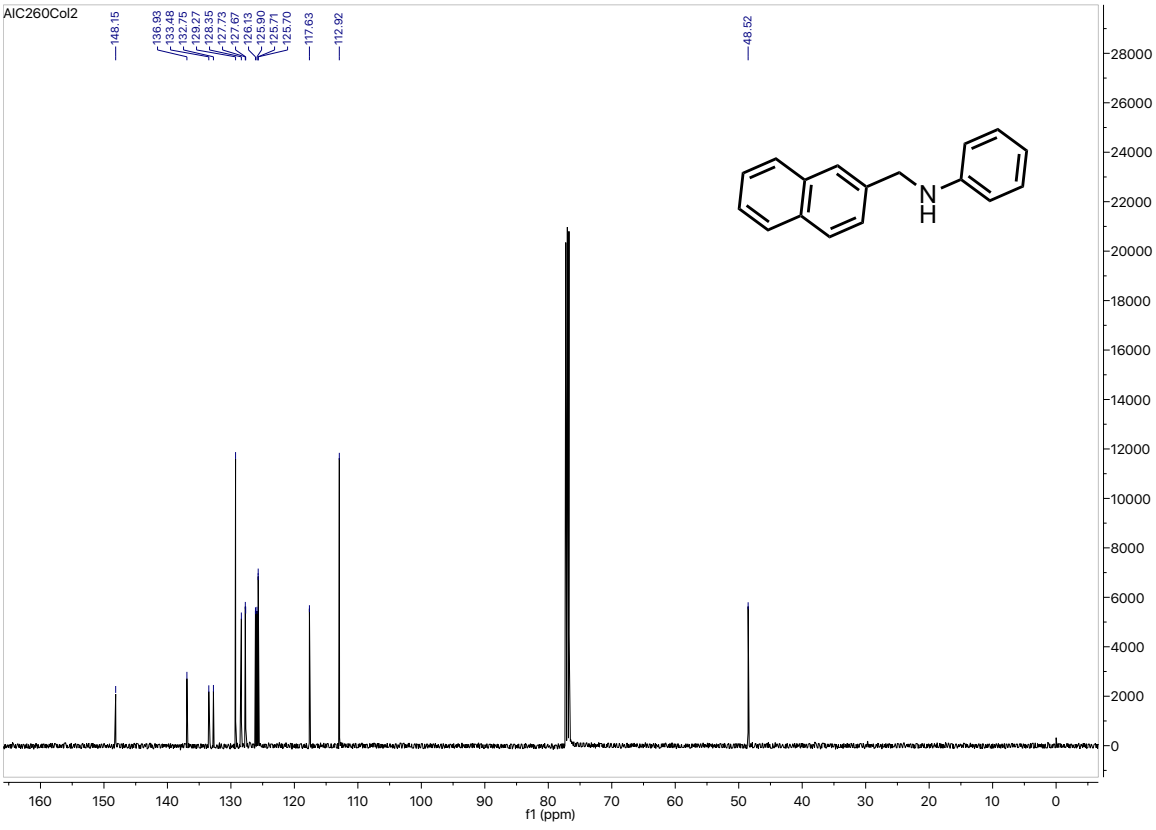
N-(furan-2-ylmethyl)aniline (7ga)



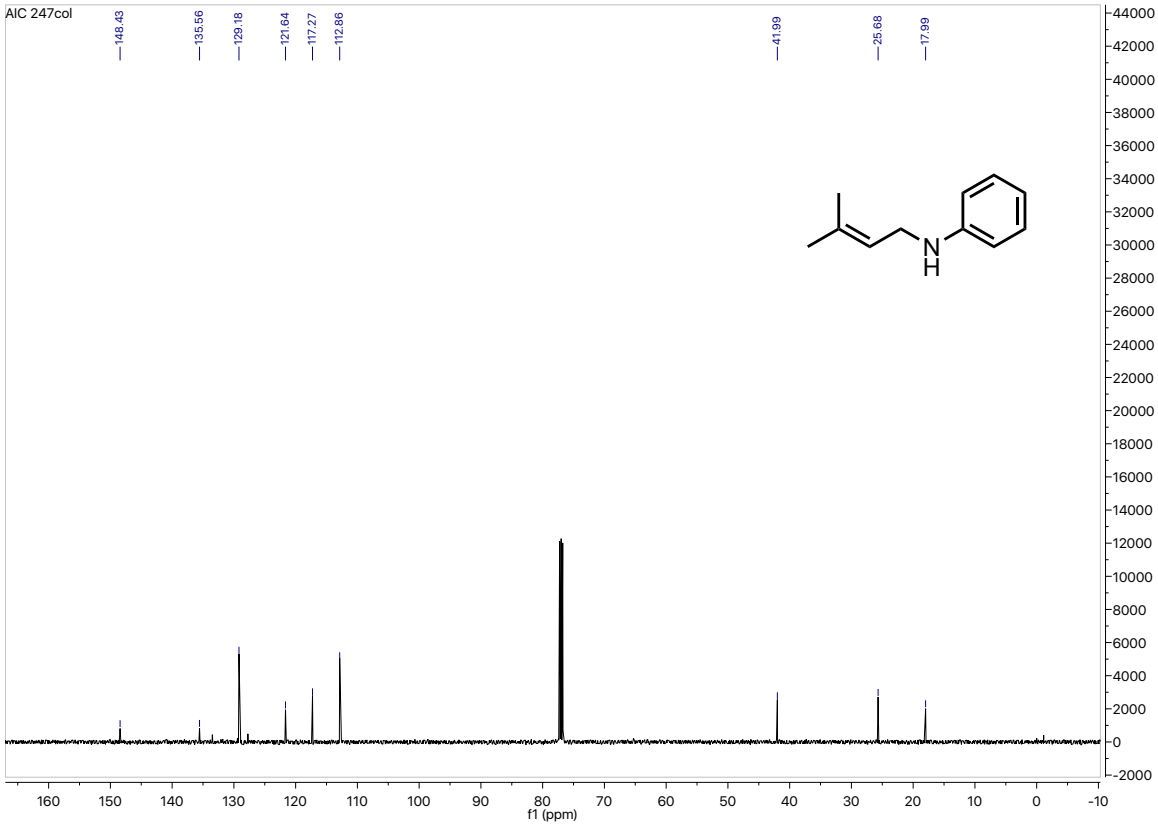


N-(naphthalen-2-ylmethyl)aniline (7ha)

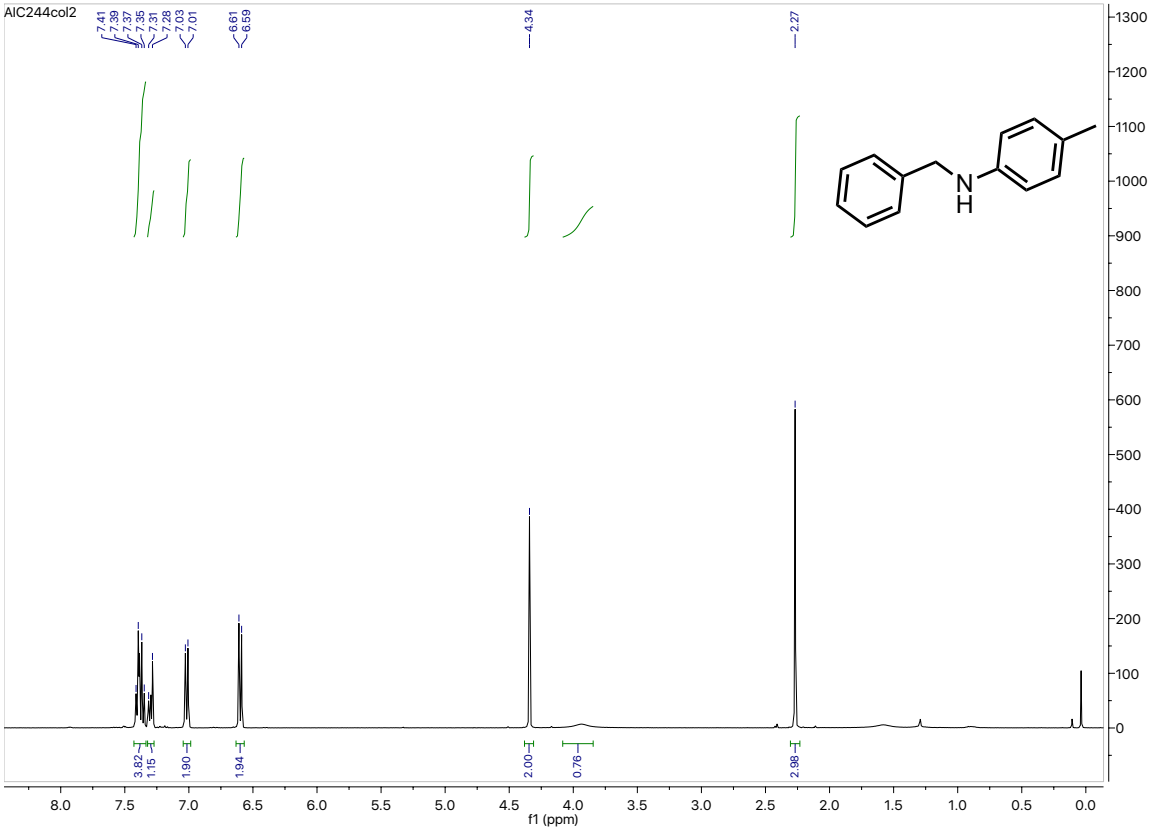


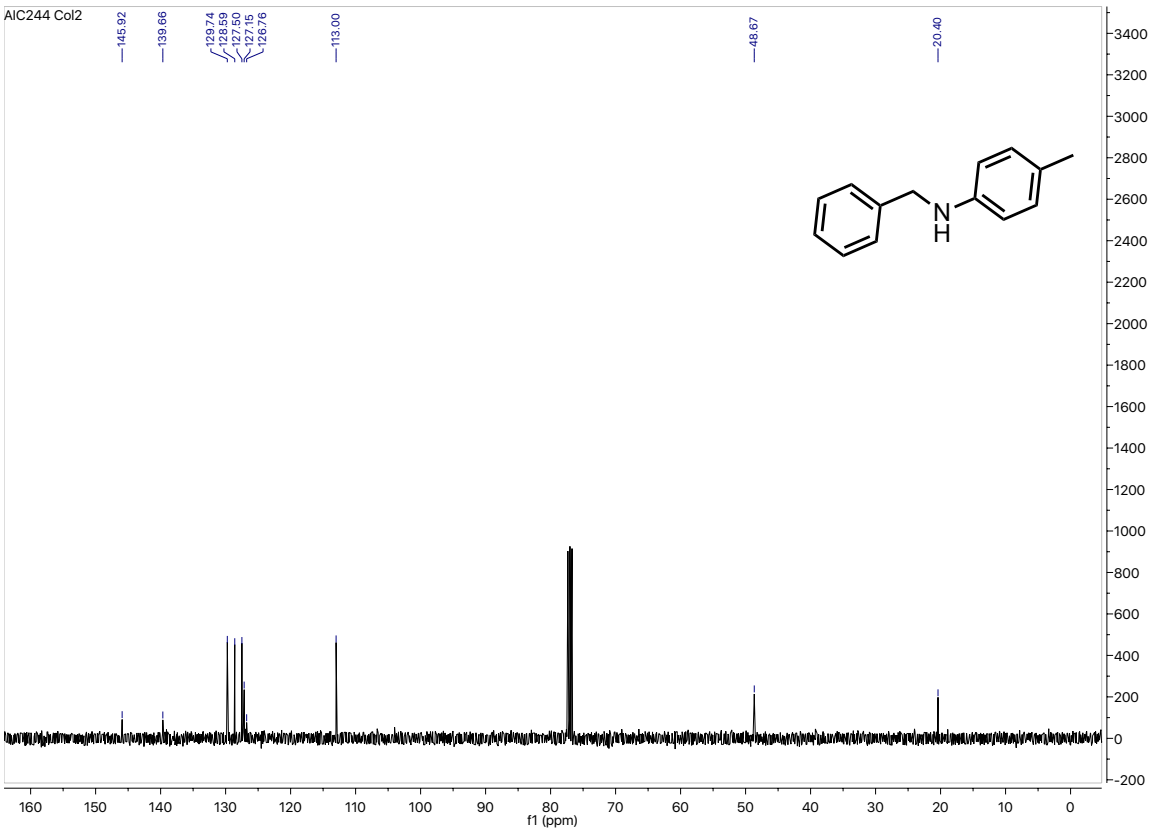


N-(3-methylbut-2-en-1-yl)aniline (7ia)

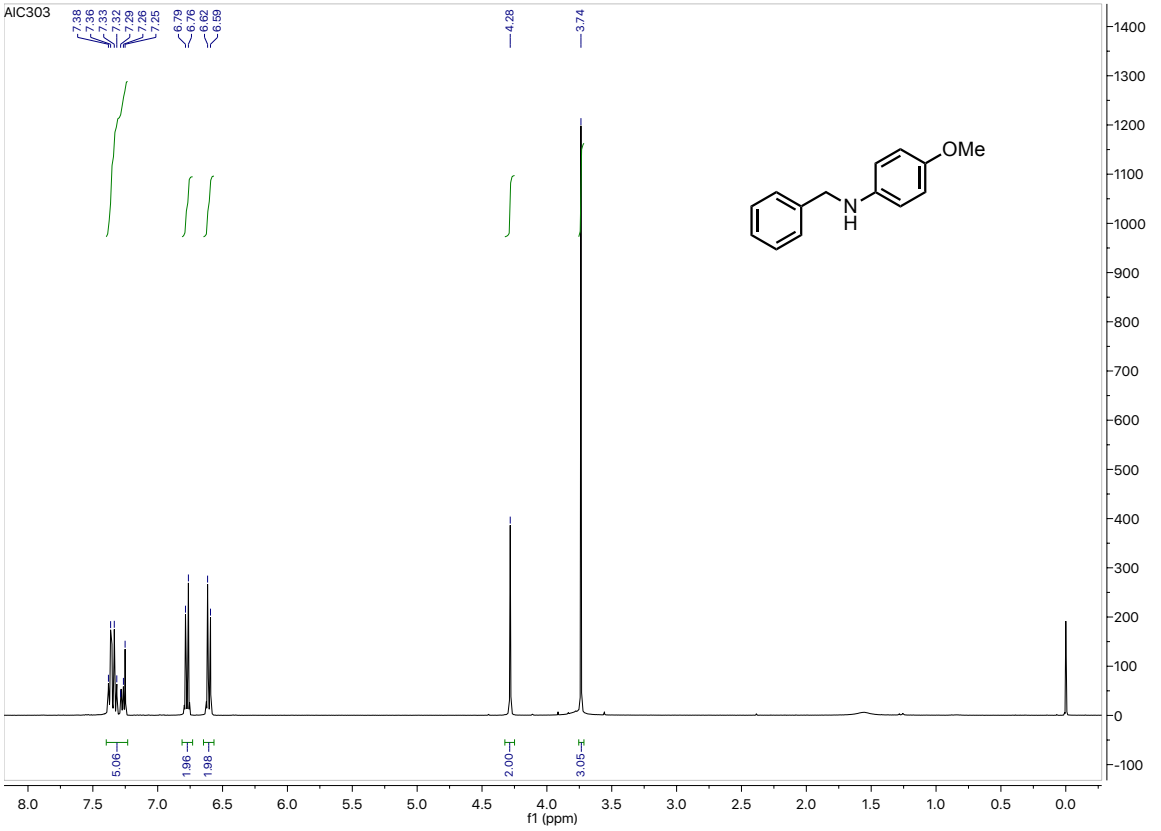


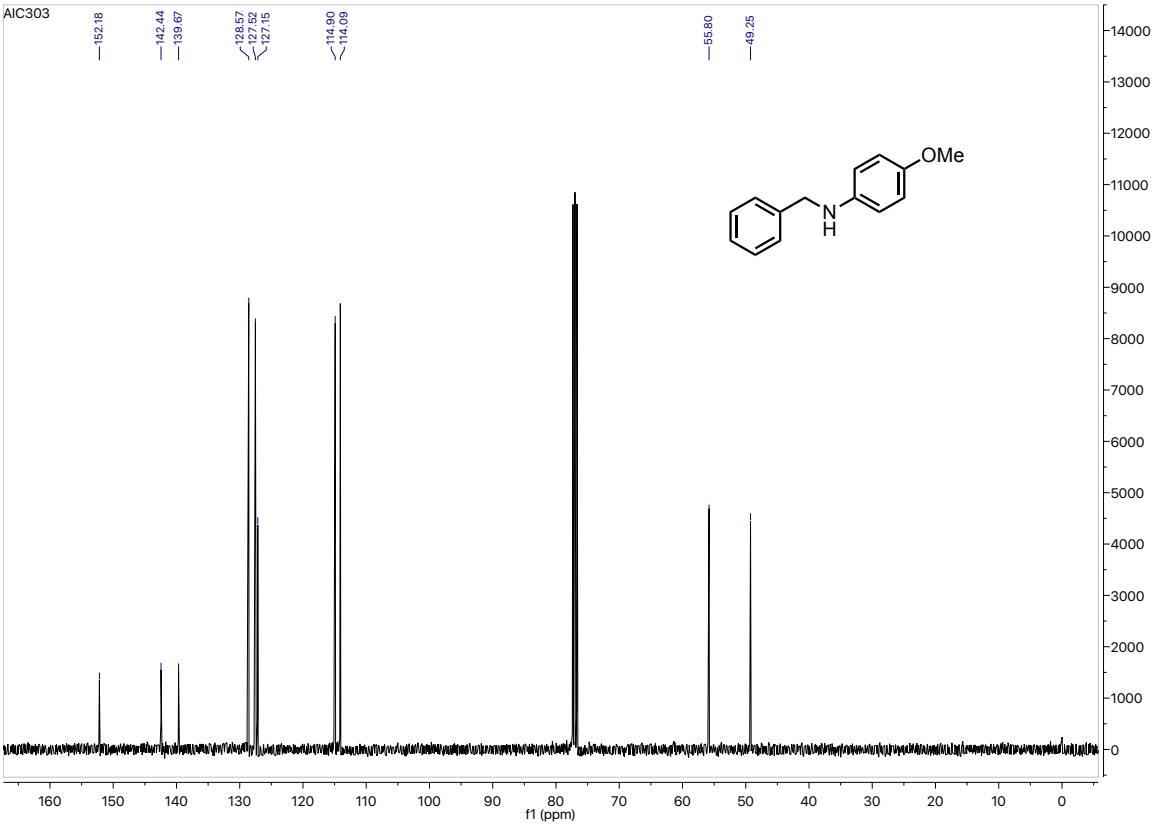
N-benzyl-4-methylaniline (7ab)



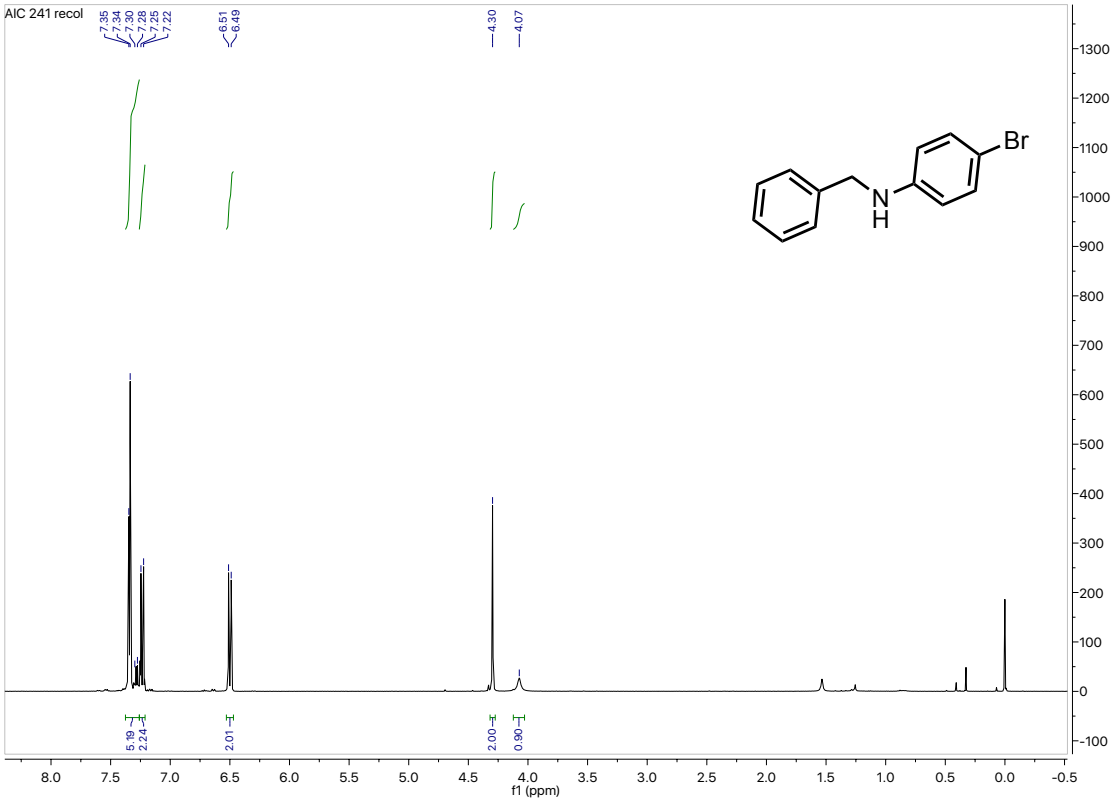


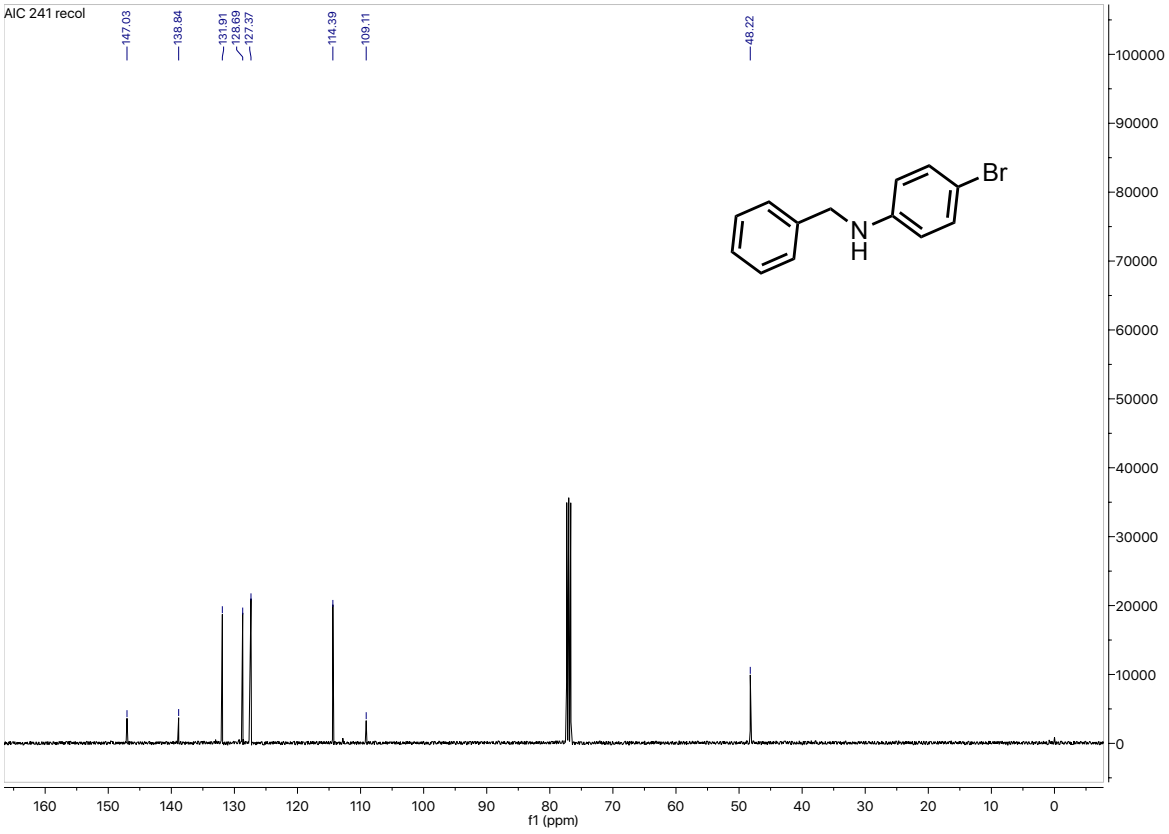
N-benzyl-4-methoxyaniline (7ac)



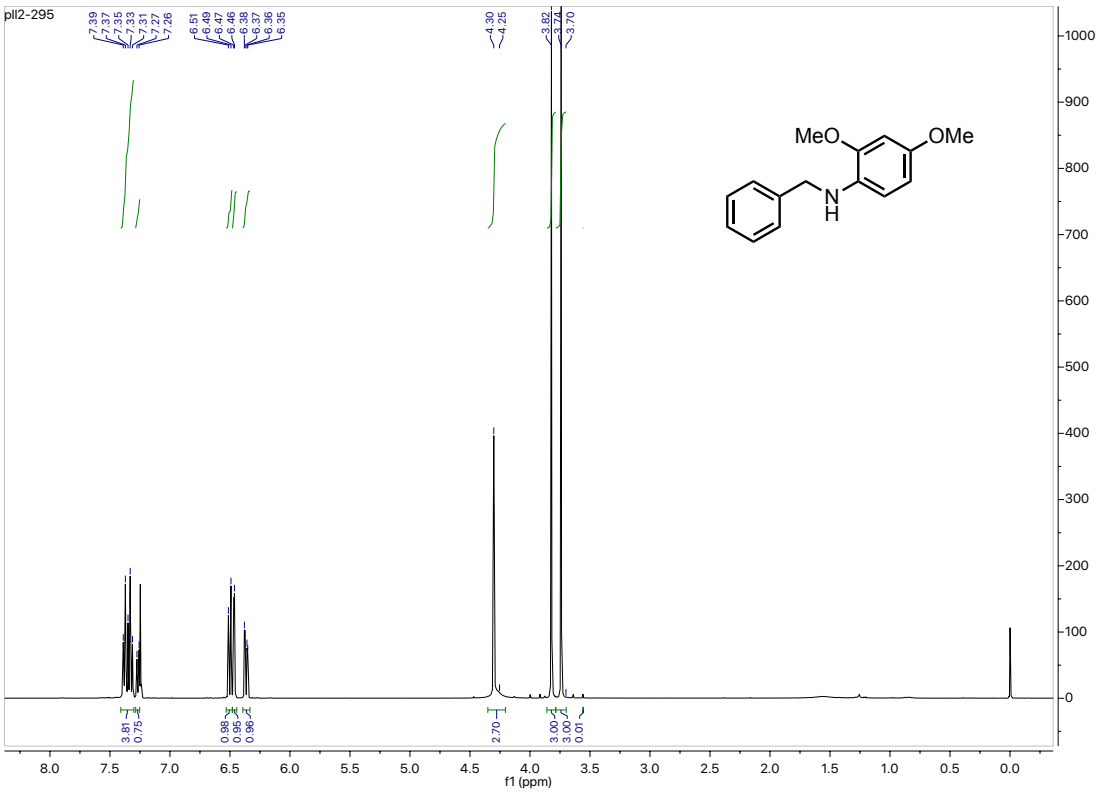


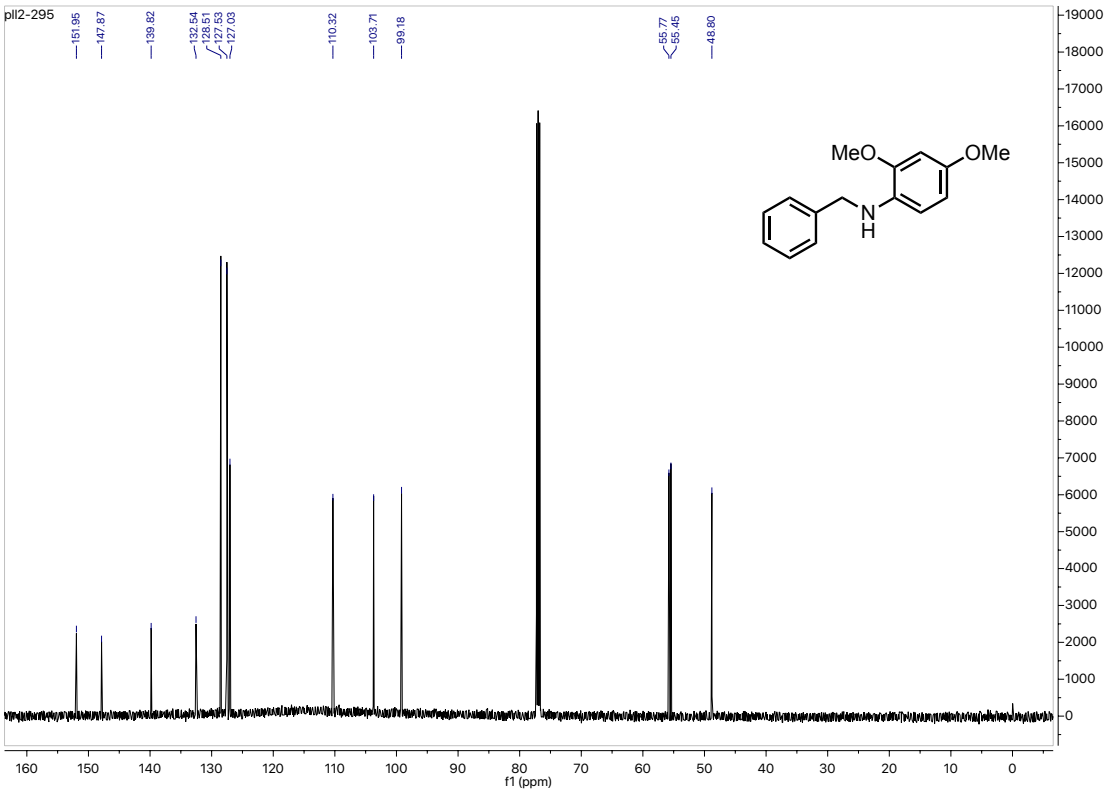
N-benzyl-4-bromoaniline (7ad)



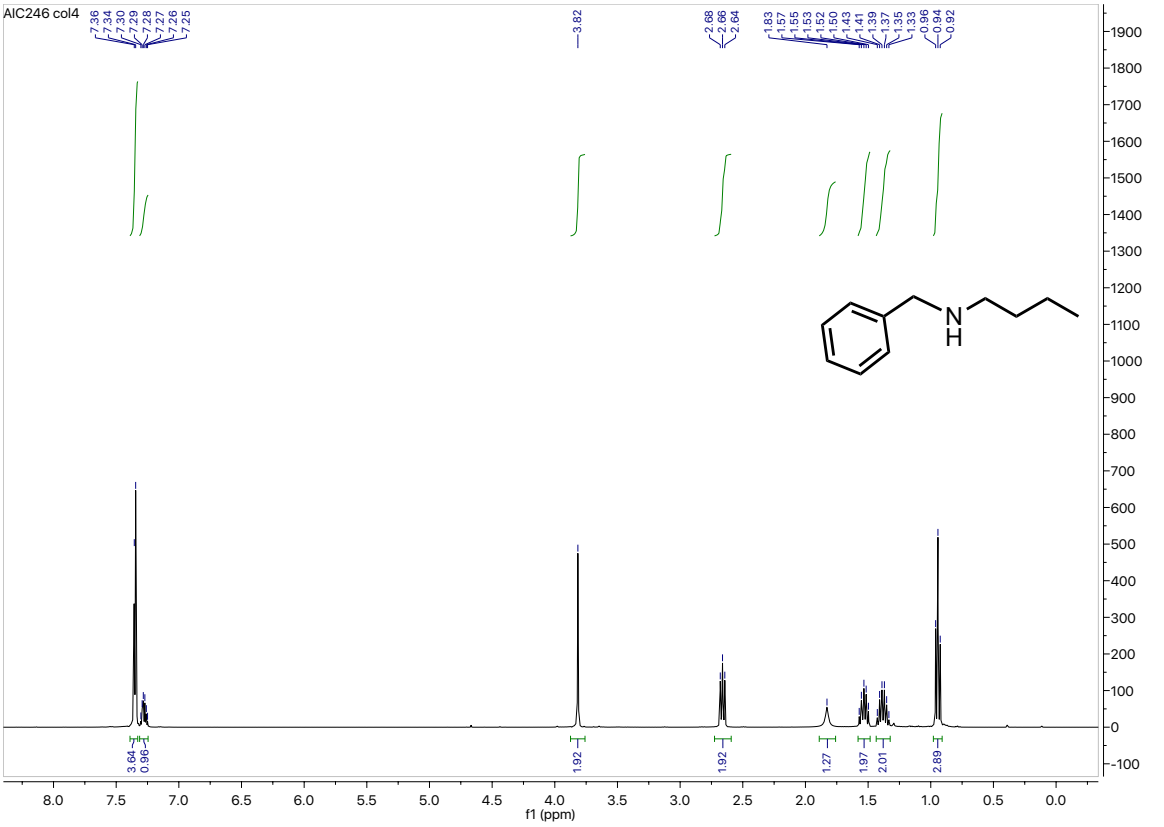


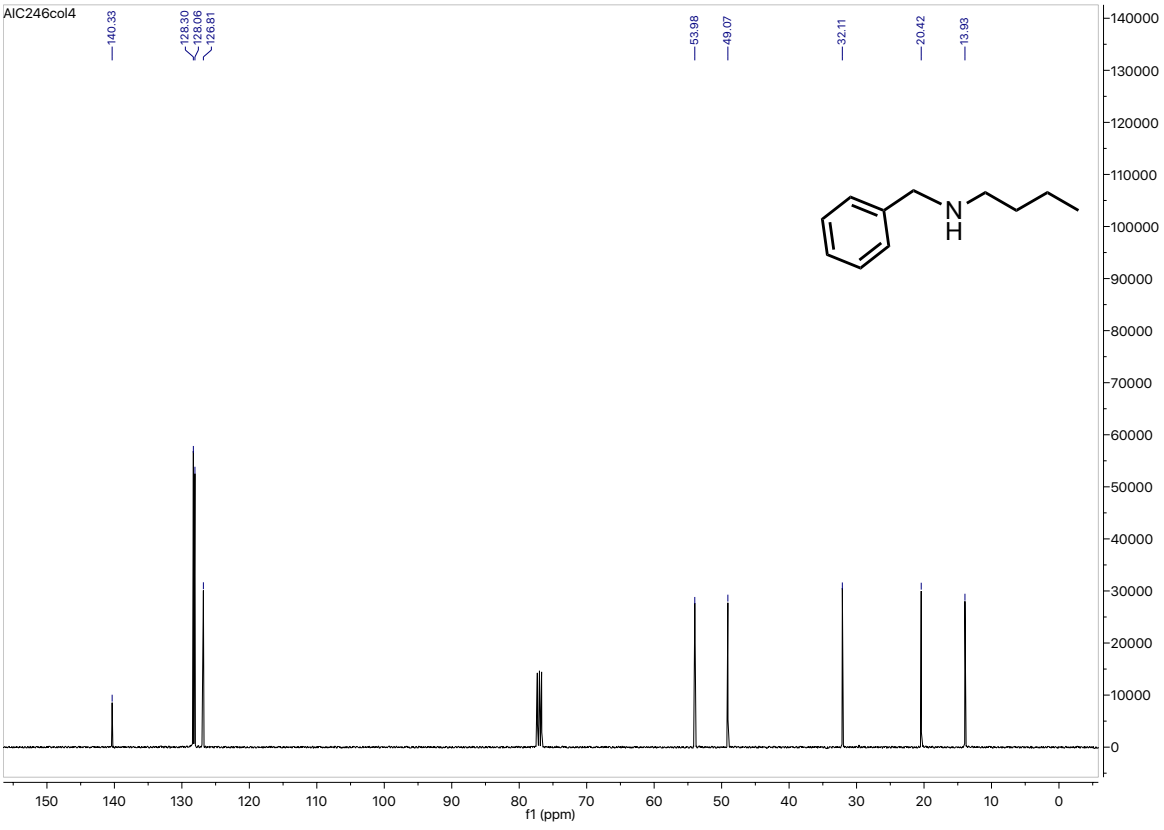
N-benzyl-2,4-dimethoxyaniline (7ae)



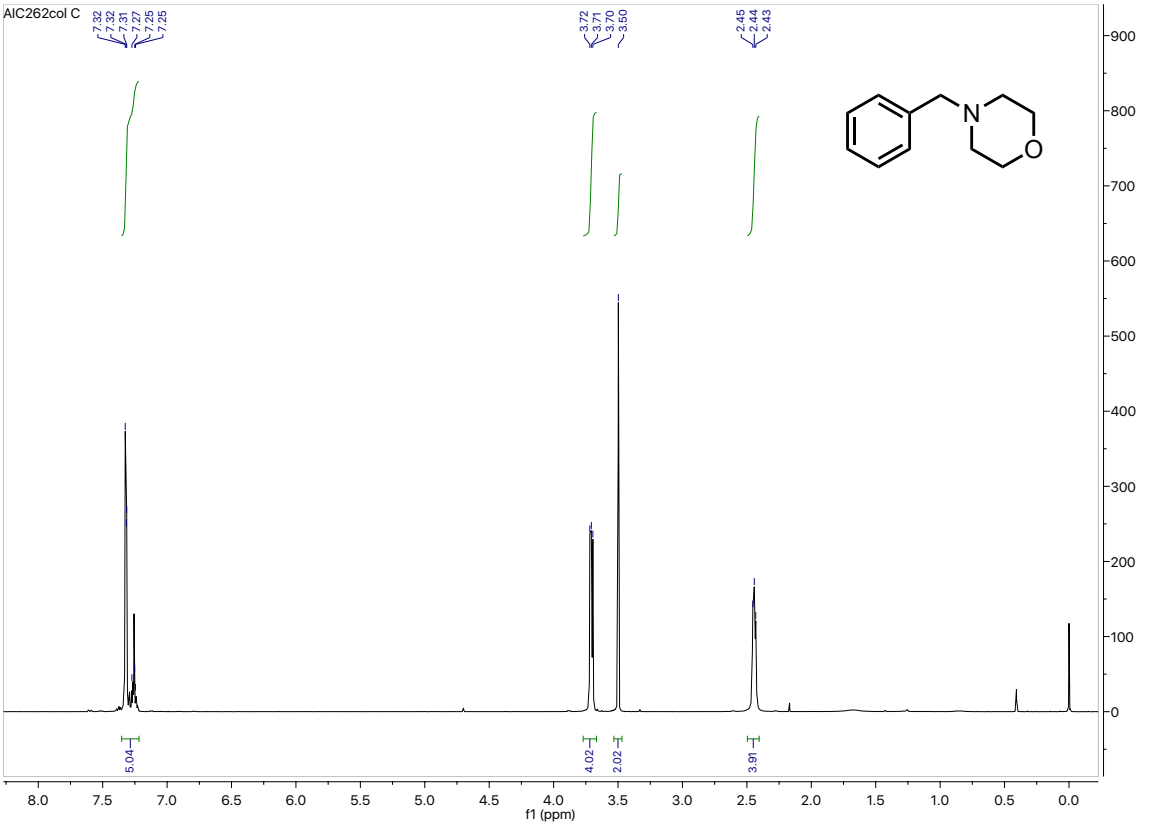


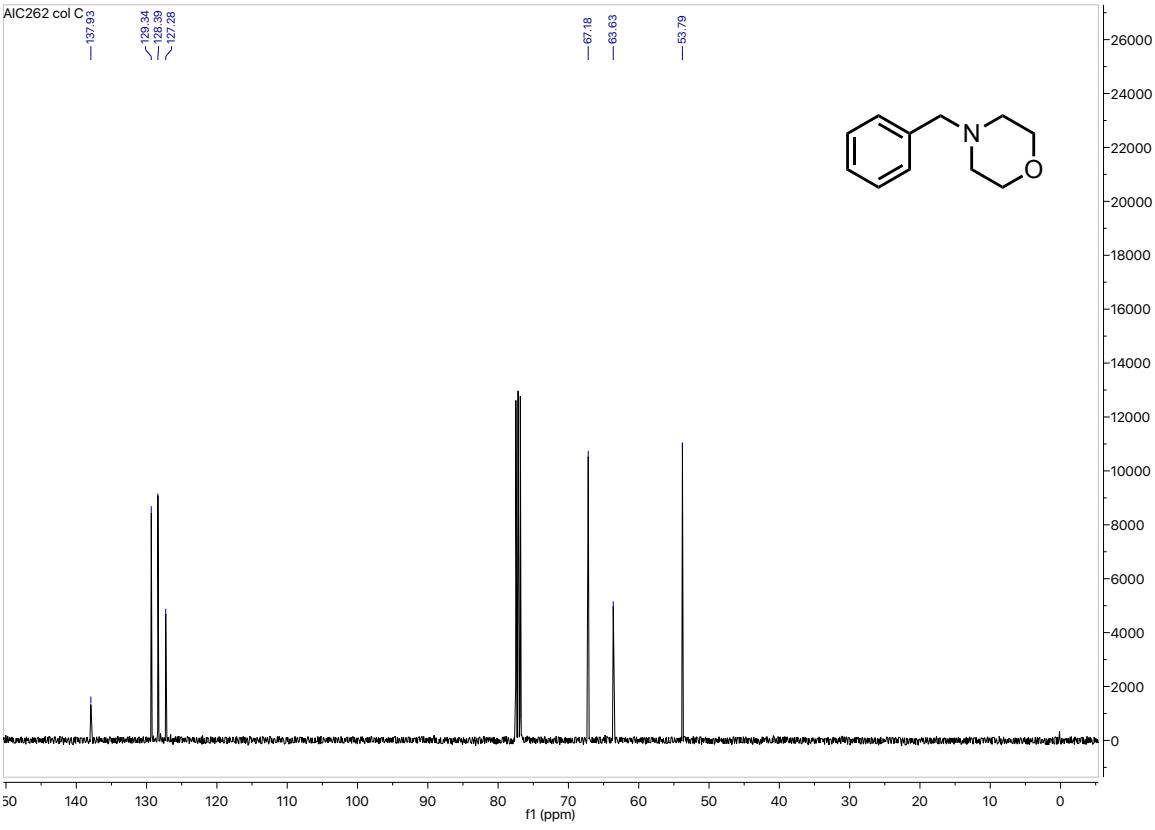
N-benzylbutan-1-amine (7ag)



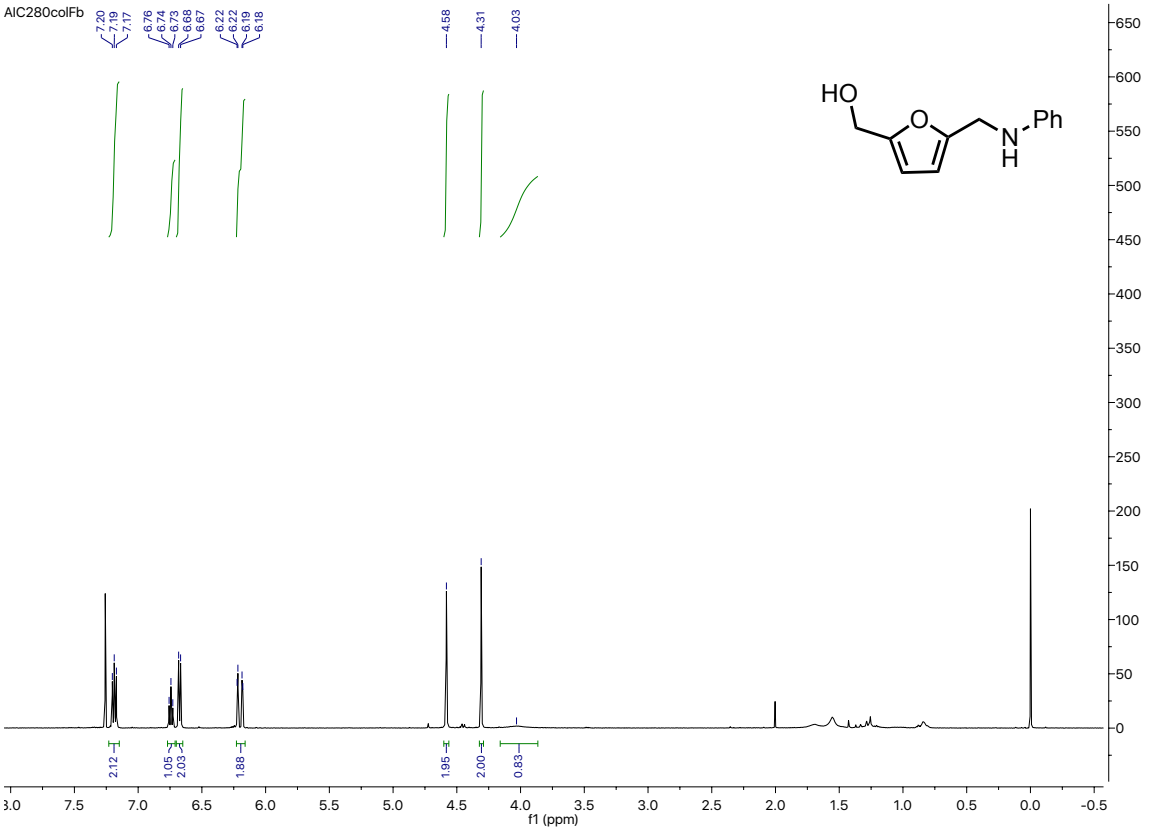


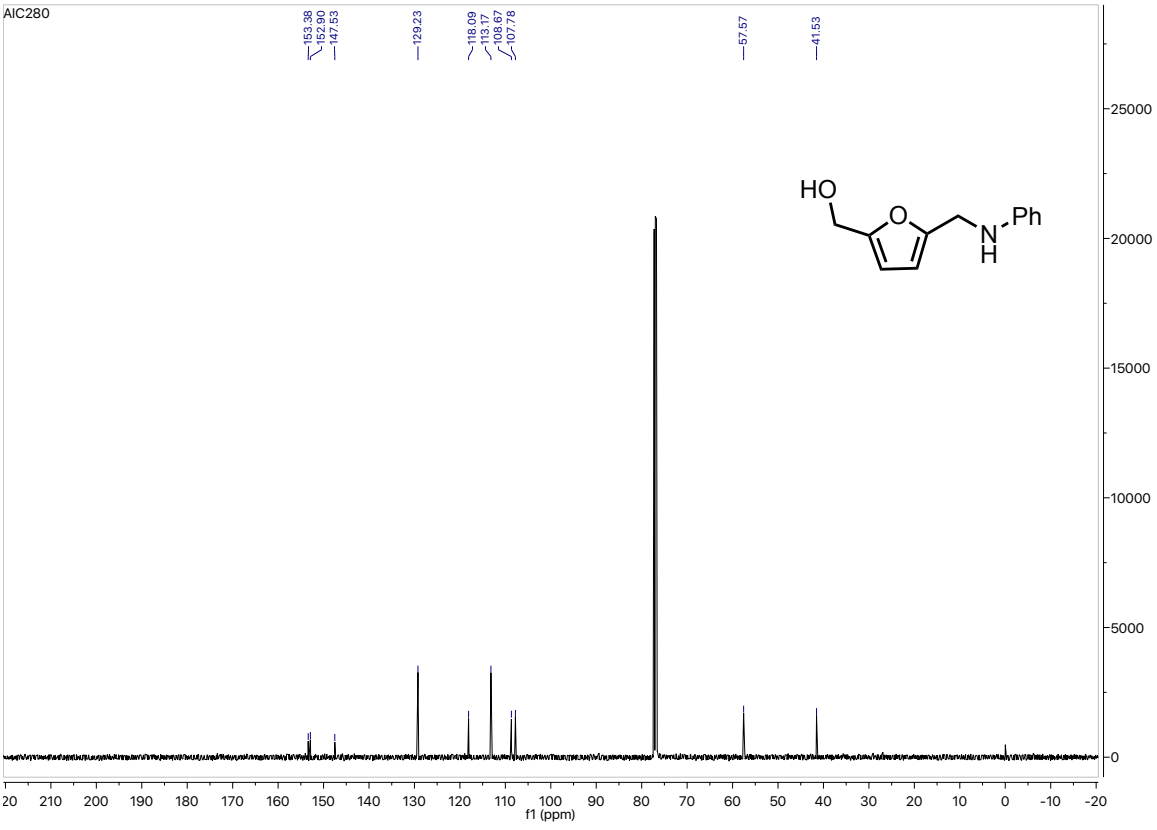
4-benzylmorpholine (7af)



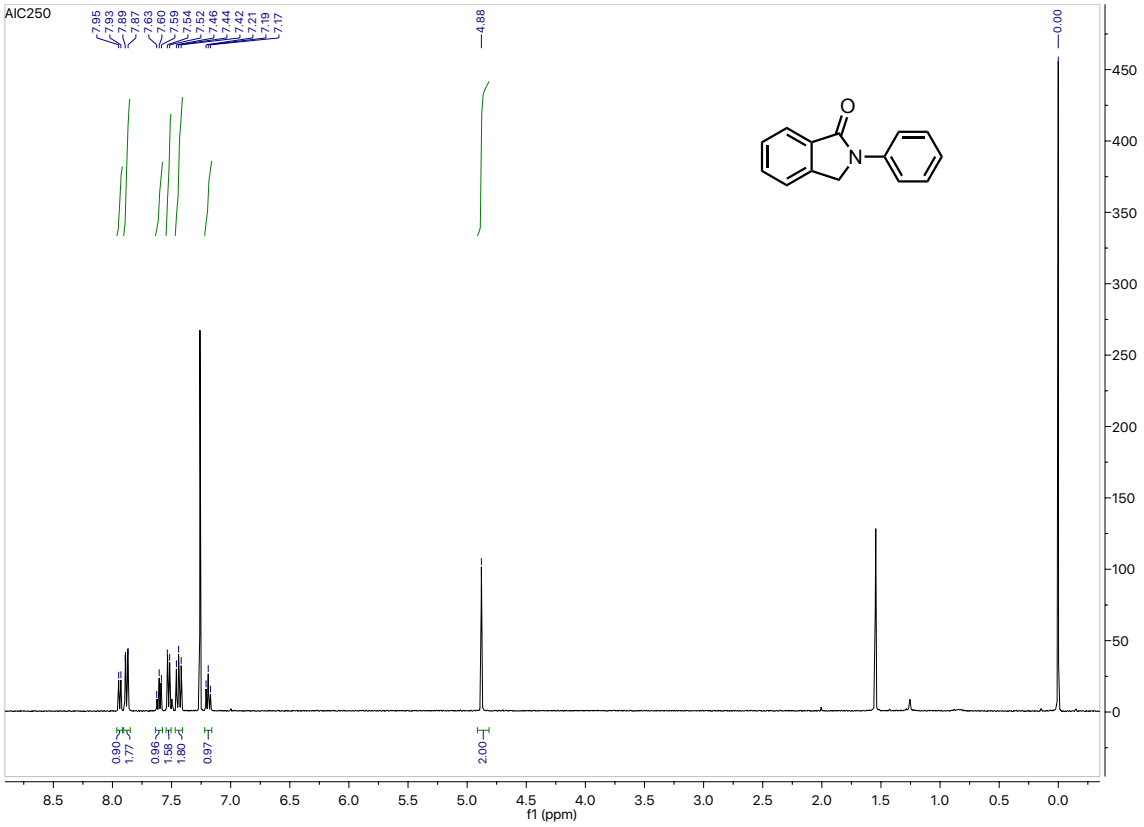


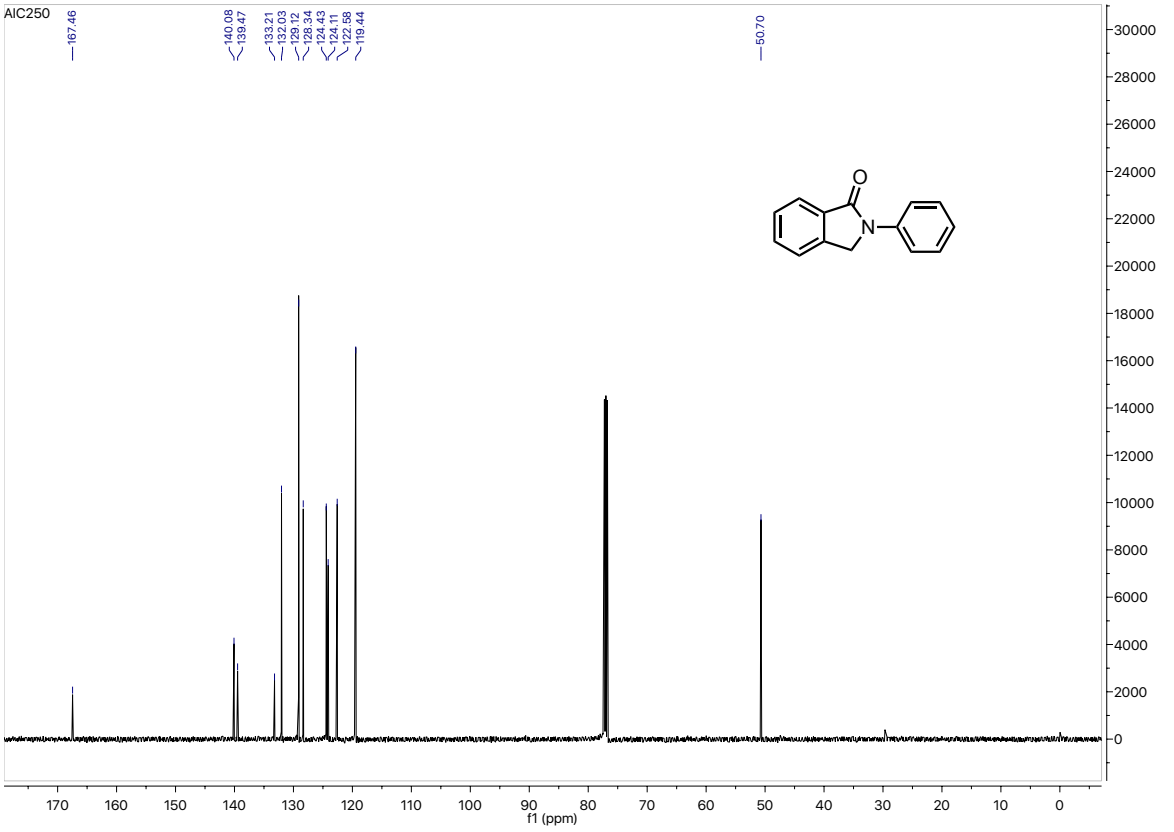
(5-(phenylamino)furan-2-yl)metanol (13)



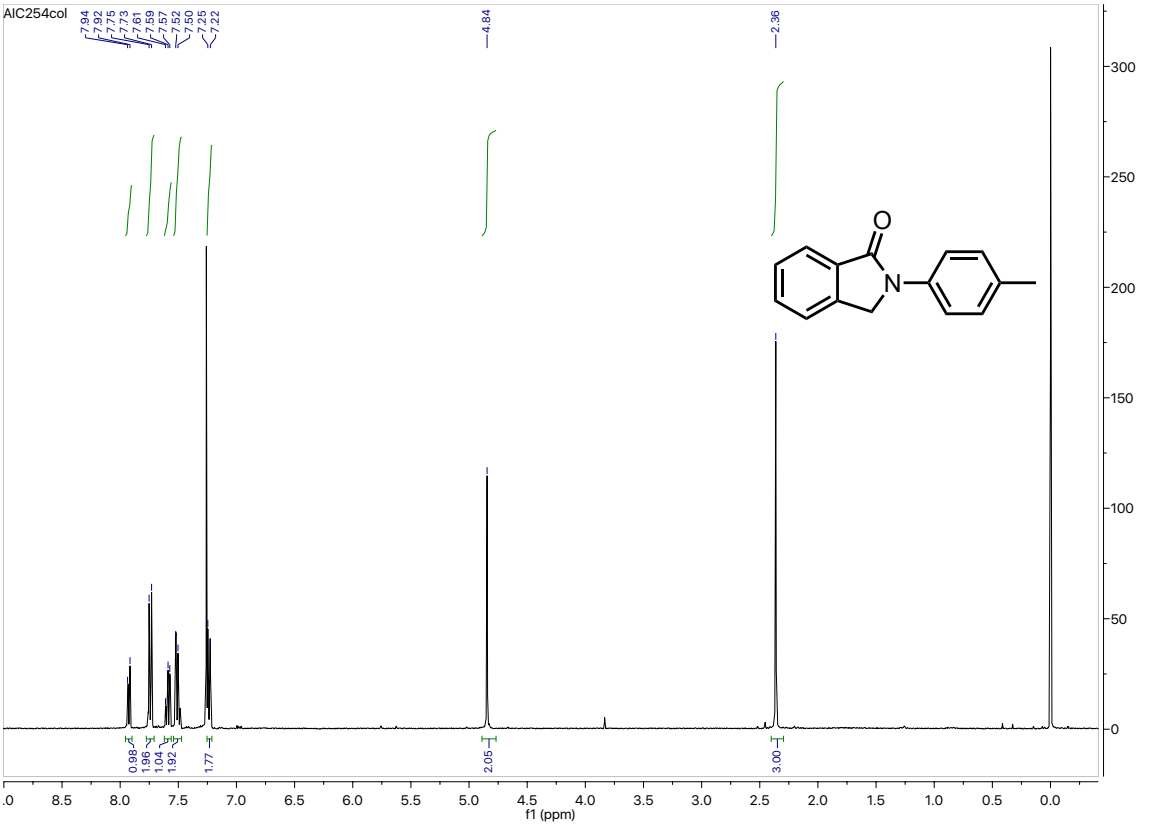


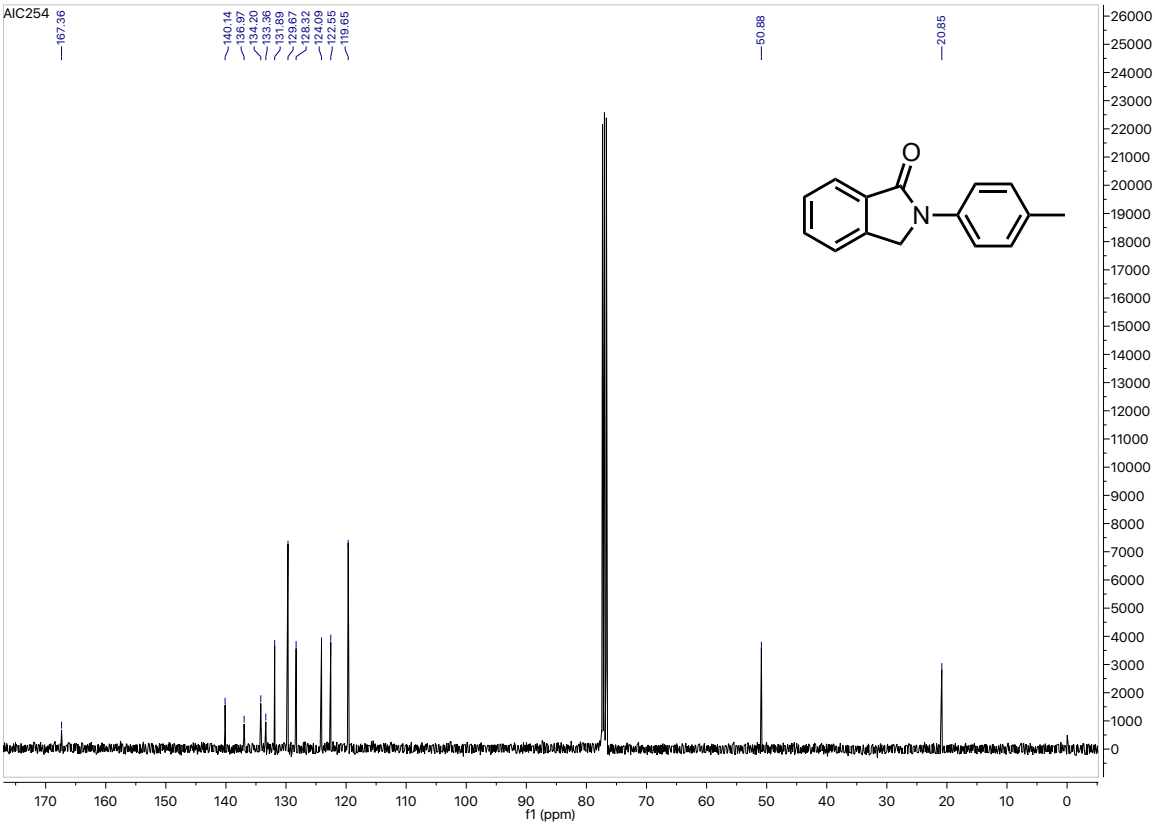
2-phenylisoindolin-1-one (9a)



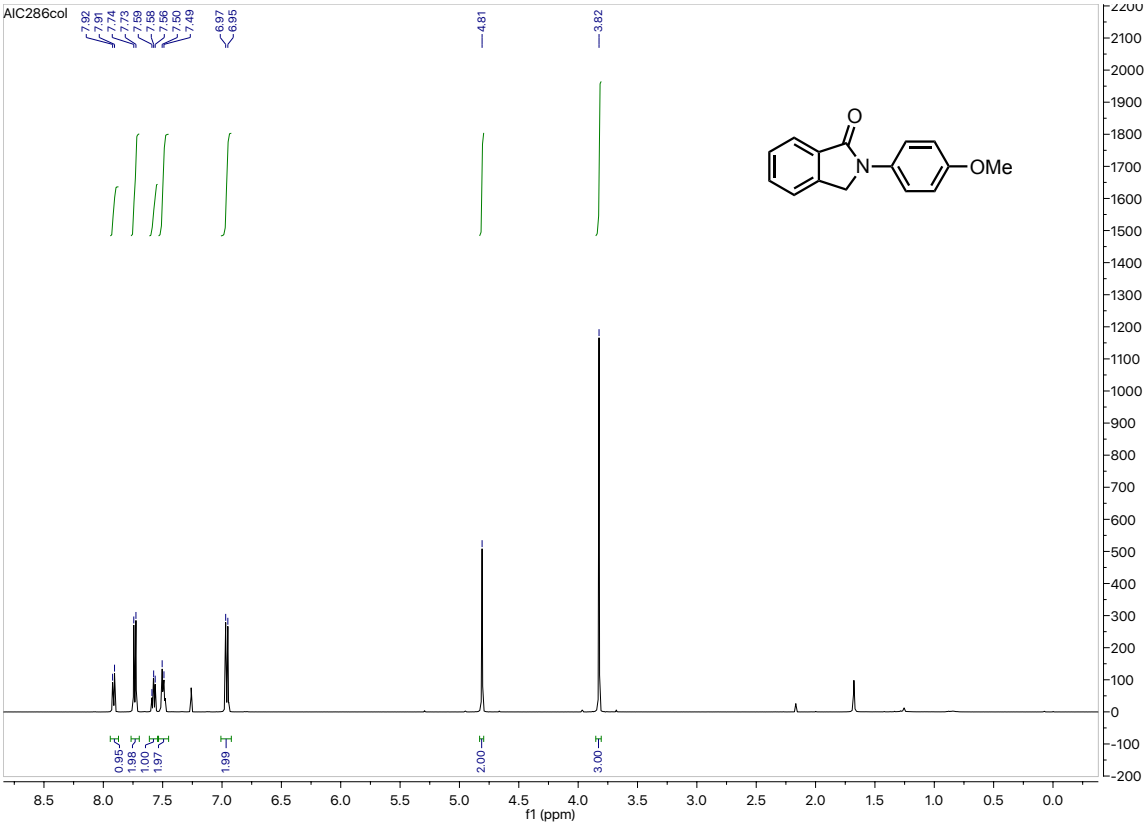


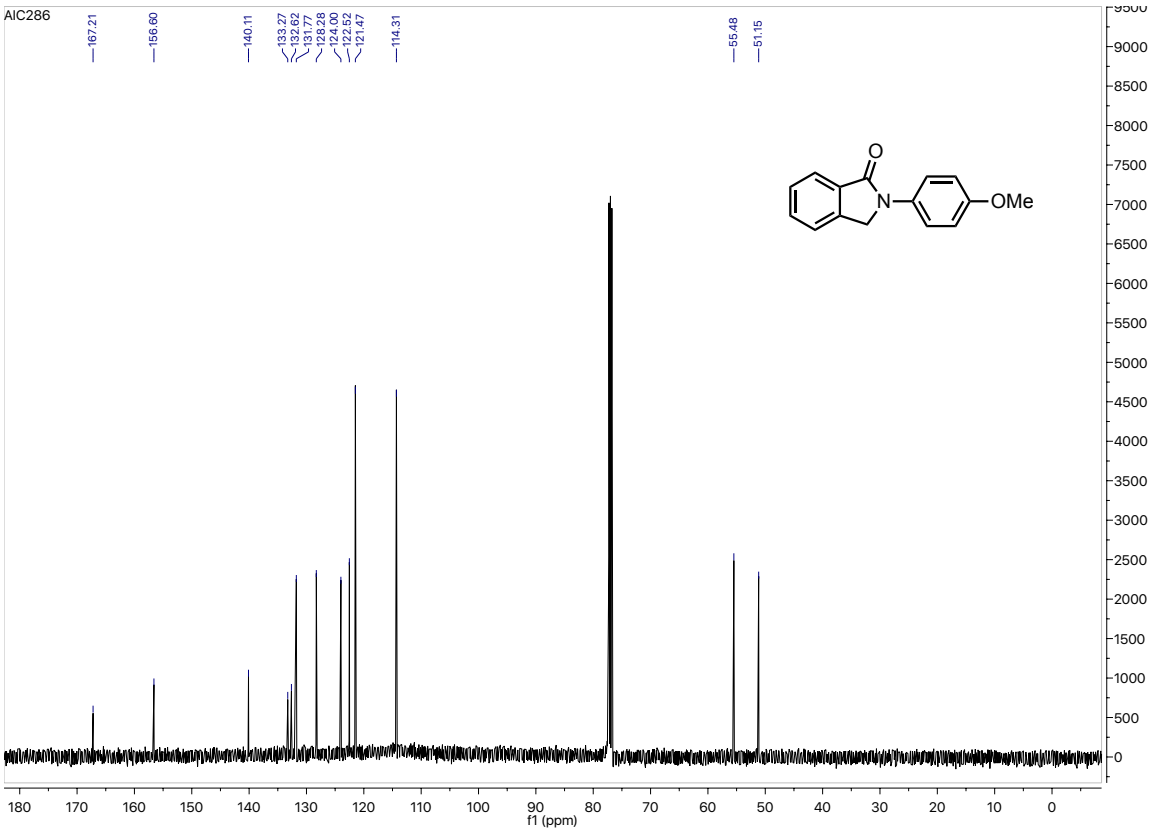
2-(*p*-tolyl)isoindolin-1-one (9b)



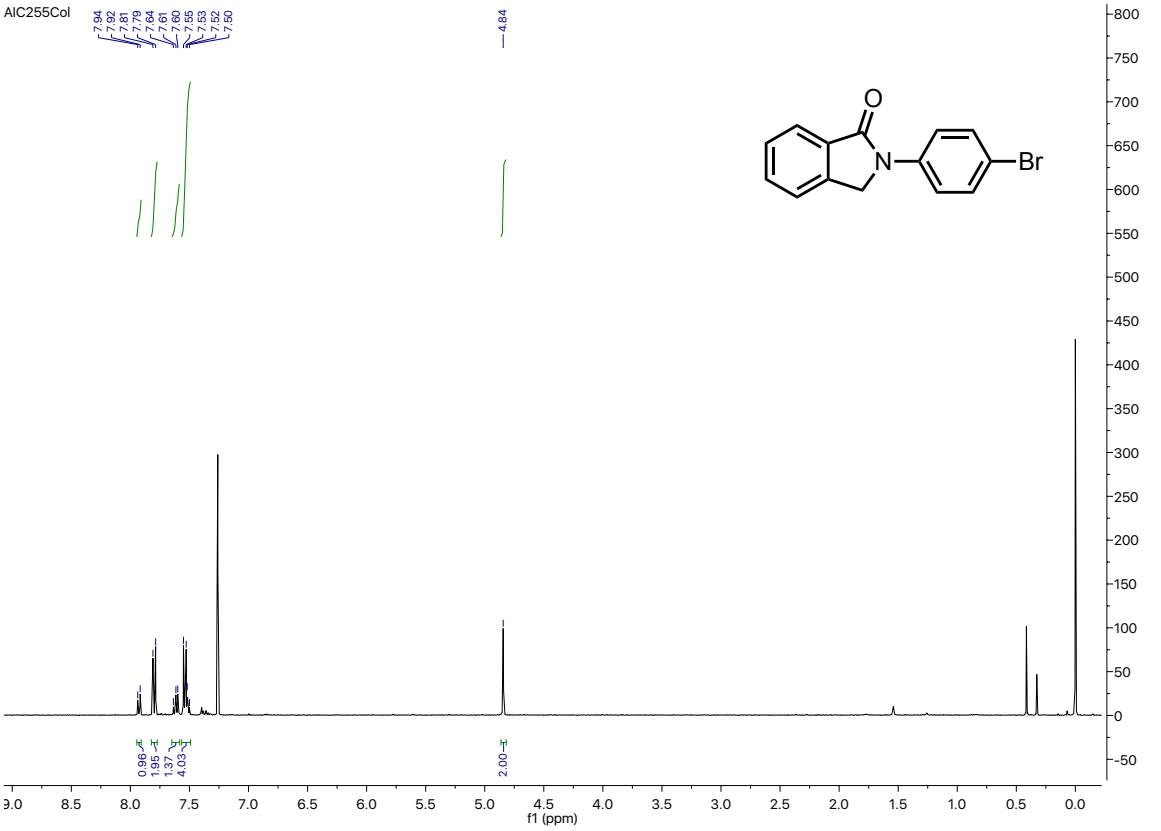


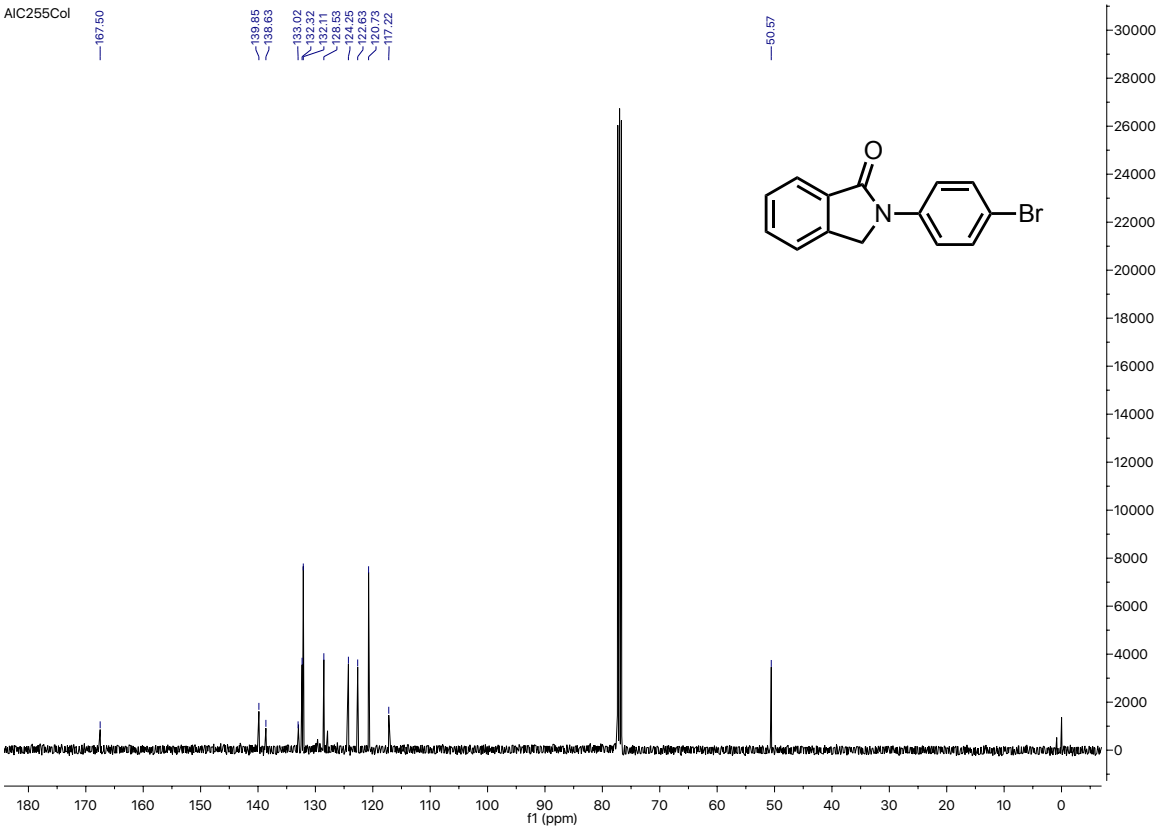
2-(4-methoxyphenyl)isoindolin-1-one (9c)





2-(4-bromophenyl)isoindolin-1-one (9d)





5-methyl-1-phenylpyrrolidin-2-one (11)