Supporting Information

A Base and Solvent-Free Ruthenium-Catalyzed Alkylation of Amines

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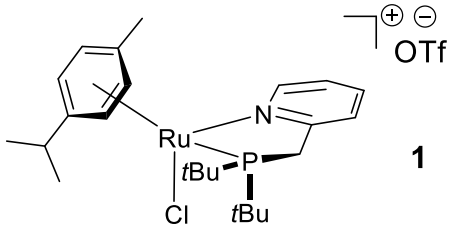
I. General Procedures

All air and water sensitive procedures were carried out either in a Vacuum Atmosphere glove box under nitrogen (2-10 ppm O_2 for all manipulations) or using standard Schlenk techniques under nitrogen. Deuterated NMR solvents were purchased from Cambridge Isotopes Laboratories. Dichloromethane, ethyl ether, and hexanes were purchased from VWR and dried in a J. C. Meyer solvent purification system with alumina/copper(II) oxide columns; toluene was dried using sodium benzophenone ketyl; dichloro(*p*-cymene)ruthenium(II) dimer and (pentamethylcyclopentadienyl)iridium(III) chloride dimer were purchased from strem; 2-((di-*tert*-butylphosphino)methyl)pyridine was synthesized using a published procedure;[1] benzyl alcohol-1-d_1 was synthesized by reduction of benzaldehyde with $NaBD_4$; all other reagents were purchased and used as received.

NMR spectra were recorded on a Varian Mercury 400, Varian VNMRS 500, or VNMRS 600 spectrometer. All chemical shifts are reported in units of ppm and referenced to the residual ^1H or ^{13}C solvent peak and line-listed according to (s) singlet, (bs) broad singlet, (d) doublet, (t) triplet, (dd) double doublet, etc. ^{13}C spectra are delimited by carbon peaks, not carbon count. Air-sensitive NMR spectra were taken in 8" J-Young tubes (Wilmad or Norell) with Teflon valve plugs. X-ray crystallography data were obtained on a Bruker APEX DUO single-crystal diffractometer equipped with an APEX2 CCD detector, Mo fine-focus and Cu micro-focus X-ray sources. High resolution mass spectrometry data were obtained from UC Riverside's High Resolution Mass Spectrometry Facility. GC-MS data were obtained on a Hewlett Packard HP 6890 Series GC System and Agilent Technologies 5973 Inert Mass Selective Detector.

II. Synthesis and Characterization Data for Ruthenium 1 and Iridium 1a

*Complex **1***



1

In the drybox under nitrogen, 2-((di-t-butylphosphino)methyl)pyridine[1] (237 mg, 0.10 mmol) was dissolved in a dry vial in 5 mL of dry dichloromethane. In another vial containing a Teflon stir bar, dichloro(*p*-cymene)ruthenium(II) dimer (310 mg, 0.50 mmol) and sodium trifluoromethanesulfonate (330 mg, 1.90 mmol) were suspended in 10 mL of dry dichloromethane. The suspension was stirred vigorously, and then the phosphinopyridine solution was added slowly dropwise. The phosphinopyridine vial was rinsed with 5 mL of dichloromethane and added to the stirred suspension. After stirring for 1 hour, the solution was filtered to remove the sodium chloride byproduct and the excess sodium triflate. The solvent was evaporated under reduced pressure to yield a glassy solid. Dry diethyl ether (10 mL) was added to the residue, which was then triturated by sonication. The ethyl ether was decanted, and the residue washed with an additional 10 mL of ethyl ether. The pure ruthenium complex was dried under reduced pressure to

give a yellow-orange solid (480 mg, 73%). Recrystallization from dichloromethane and toluene produced crystals suitable for X-ray crystallography.

^{1}H NMR (600 MHz, methylene chloride-d_2) δ 9.21 (d, J = 5.7 Hz, 1H), 7.82 (t, J = 7.6 Hz, 1H), 7.50 – 7.39 (m, 2H), 6.30 (d, J = 6.6 Hz, 1H), 6.20 (d, J = 6.6 Hz, 1H), 6.09 (d, J = 6.0 Hz, 1H), 5.80 (d, J = 6.0 Hz, 1H), 3.76 (dd, J = 16.4, 8.5 Hz, 1H), 3.33 (dd, J = 16.4, 12.8 Hz, 1H), 2.80 (dt, J = 13.8, 6.8 Hz, 1H), 2.17 (s, 3H), 1.53 (d, J = 14.2 Hz, 9H), 1.35 (t, J = 7.0 Hz, 3H), 1.30 (d, J = 6.9 Hz, 3H), 1.22 (d, J = 13.2 Hz, 9H).

^{13}C NMR (126 MHz, methylene chloride-d_2) δ 163.30 (d, J = 3.3 Hz), 157.46, 139.71, 124.96 124.42 (d, J = 9.1 Hz), 107.44, 99.74, 94.43 (d, J = 5.4 Hz), 93.38 (d, J = 6.2 Hz), 39.01 (d, J = 15.7 Hz), 38.37 (d, J = 15.7 Hz), 33.39 (d, J = 22.6 Hz), 31.21, 30.88 (d, J = 2.1 Hz), 29.92 (d, J = 2.7 Hz), 23.47, 21.41, 17.97.

^{31}P NMR (243 MHz, methylene chloride-d_2) δ 87.31.

^{19}F NMR (470 MHz, methylene chloride-d_2) δ -78.84.

HRMS (ASI/EPCI) for $C_{24}H_{38}NPClRu$ $[M]^+$: calc'd 508.1468, found 508.1470.

FT-IR (thin film/cm^{-1}) v = 3062, 2969, 2928, 2876, 2052, 1987, 1605, 1474, 1389, 1373,1265, 1224, 1154, 1107, 1087, 1056, 1031, 874, 830, 807.

NMR Spectra of Ruthenium **1**

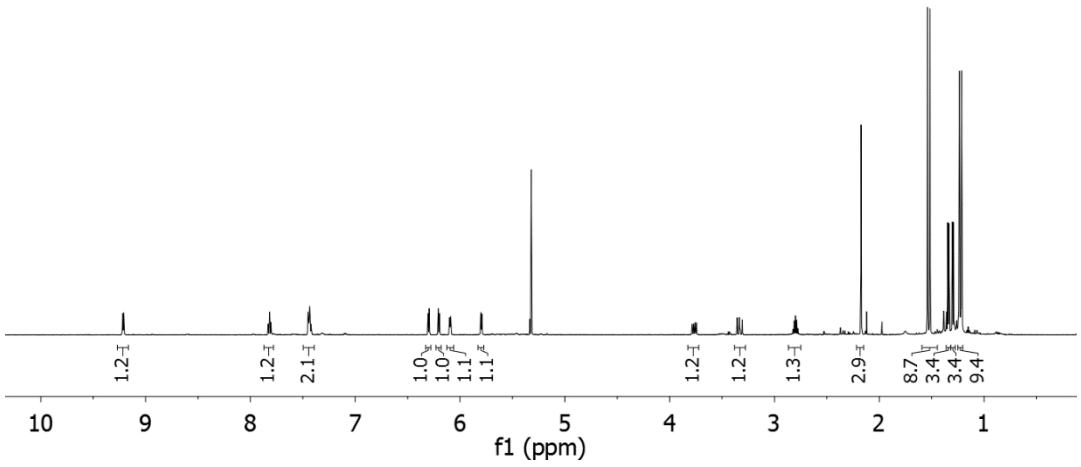


Figure S1. ^{1}H NMR spectrum of complex **1** at 25 °C in CD_2Cl_2.

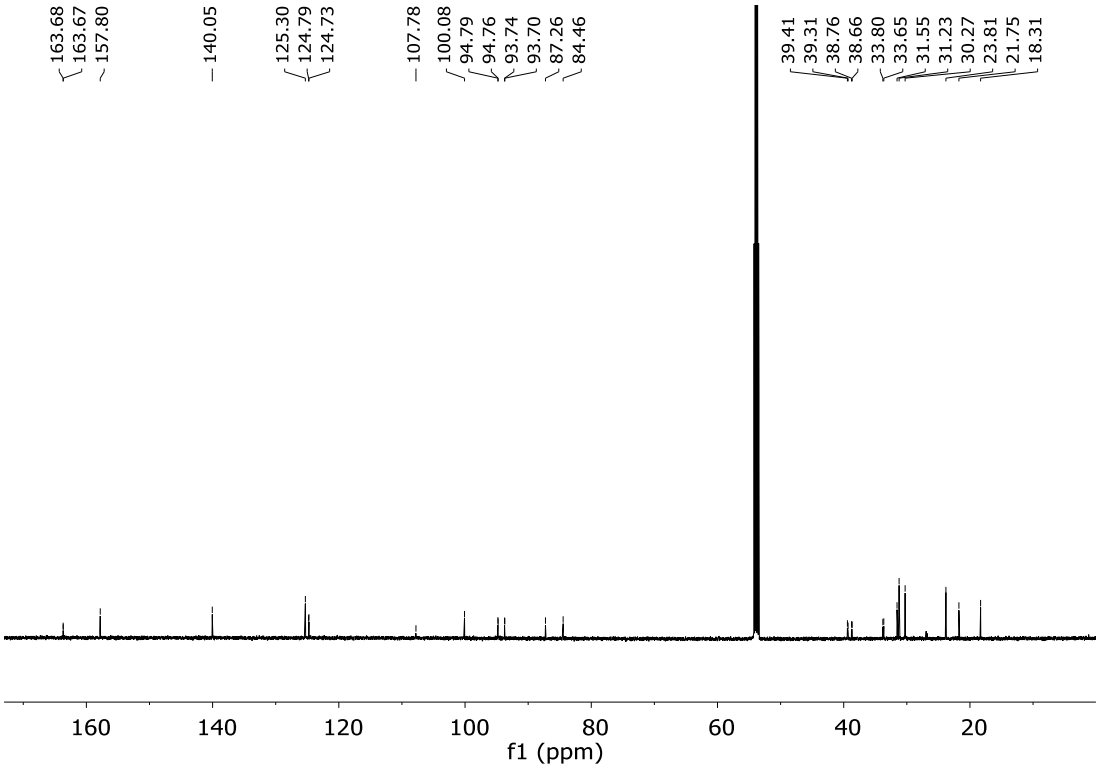


Figure S2. ^{13}C NMR spectrum of complex **1** at 25 °C in CD_2Cl_2.

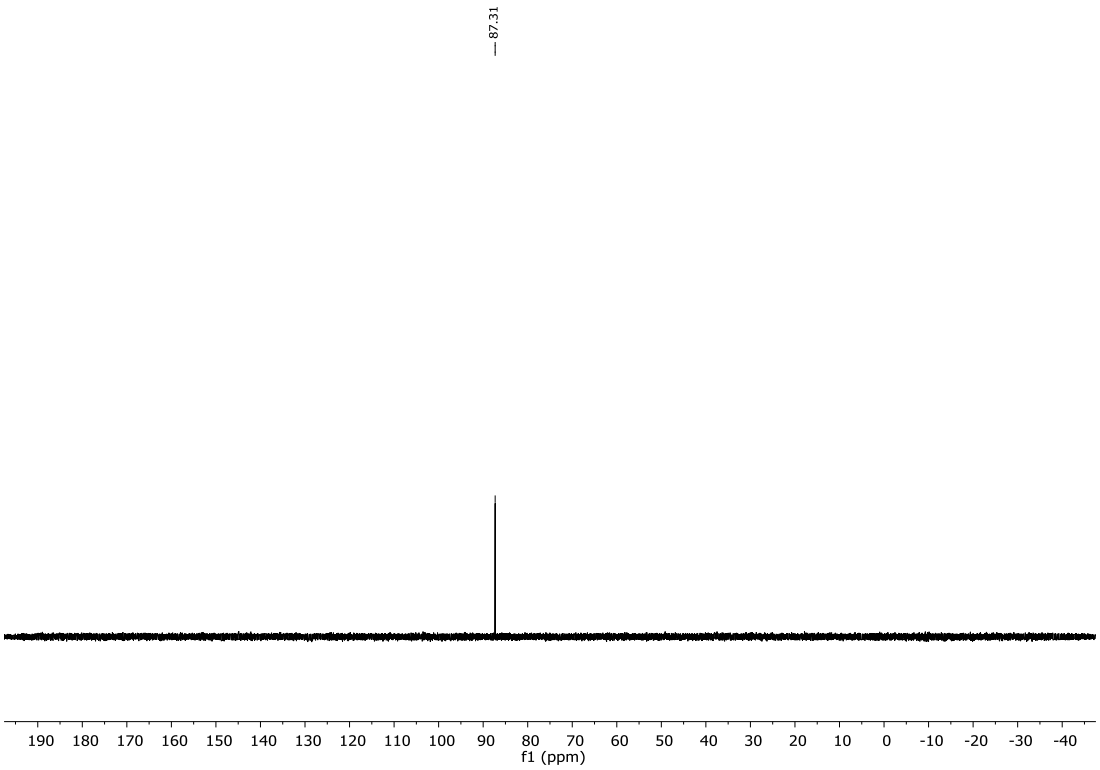
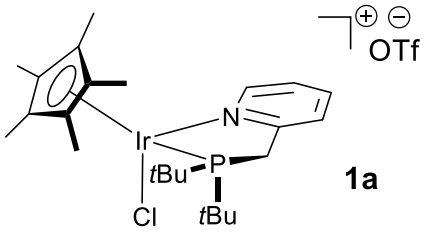


Figure S3. ^{31}P NMR spectrum of complex **1** at 25 °C in CD_2Cl_2.

*Complex **1a***



Complex **1a** was synthesized using the procedure used for the synthesis of complex **1** (see above). 2-((Di-*tert*-butylphosphino)methyl)pyridine[1] (24.0 mg, 93 μmol), pentamethylcyclopentadienyliridium(III) chloride dimer (44.0 mg, 55 μmol), and sodium trifluoromethanesulfonate (33.0 mg, 0.19 mmol) were used. Pure product was isolated as a yellow solid (50 mg, 72% yield). Crystals suitable for X-ray crystallography was obtained from a dichloromethane/ethyl ether solution.

^{1}H NMR (600 MHz, methylene chloride-d_2) δ 8.45 (d, J = 5.9 Hz, 1H), 7.92 (t, J = 7.5 Hz, 1H), 7.70 (d, J = 7.9 Hz, 1H), 7.33 (t, J = 6.7 Hz, 1H), 4.15 (dd, J = 16.4, 9.1 Hz, 1H), 3.92 (dd, J = 16.4, 11.4 Hz, 1H), 1.77 (d, J = 1.8 Hz, 15H), 1.50 (d, J = 14.6 Hz, 9H), 1.14 (d, J = 13.8 Hz, 9H).

^{13}C NMR (151 MHz, methylene chloride-d_2) 164.13, 152.52, 140.31, 125.51, 124.64 (d, J = 7.6 Hz), 94.99 (d, J = 2.2 Hz), 37.90 (d, J = 21.0 Hz), 37.59 (d, J = 19.8 Hz), 35.76 (d, J = 28.5 Hz), 30.71 (d, J = 2.4 Hz), 29.30 (d, J = 3.0 Hz), 10.42.

^{31}P NMR (243 MHz, methylene chloride-d_2) δ 59.86.

HRMS (ESI/APCI): m/z = 600.2148 g/mol, calc'd. for $C_{24}H_{39}ClIrNP^+$ $[M]^+$: 600.2133 g/mol.

FT-IR (thin film/cm^{-1}) ν = 3138, 2970, 2920, 2875, 2428, 2298, 1607, 1565, 1540, 1475, 1375, 1269, 1223, 1150, 1109, 1075, 1031, 940, 896, 827, 810.

NMR Spectra of Iridium **1a**

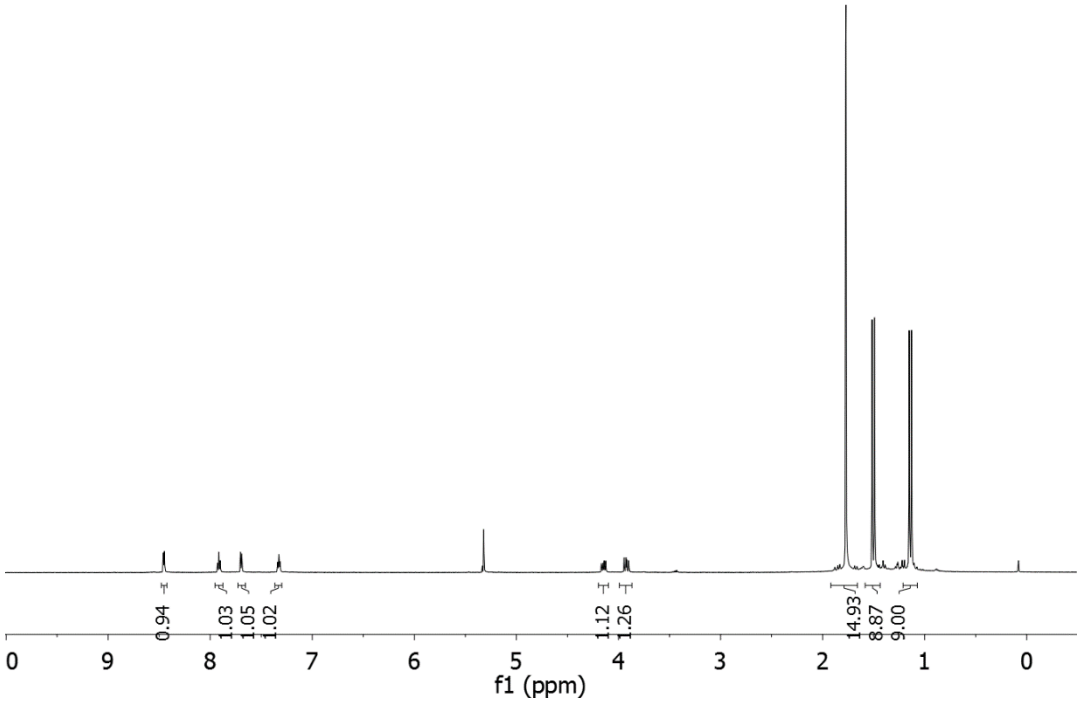


Figure S4. ^{1}H NMR spectrum of complex **1a** at 25 °C in CD_2Cl_2.

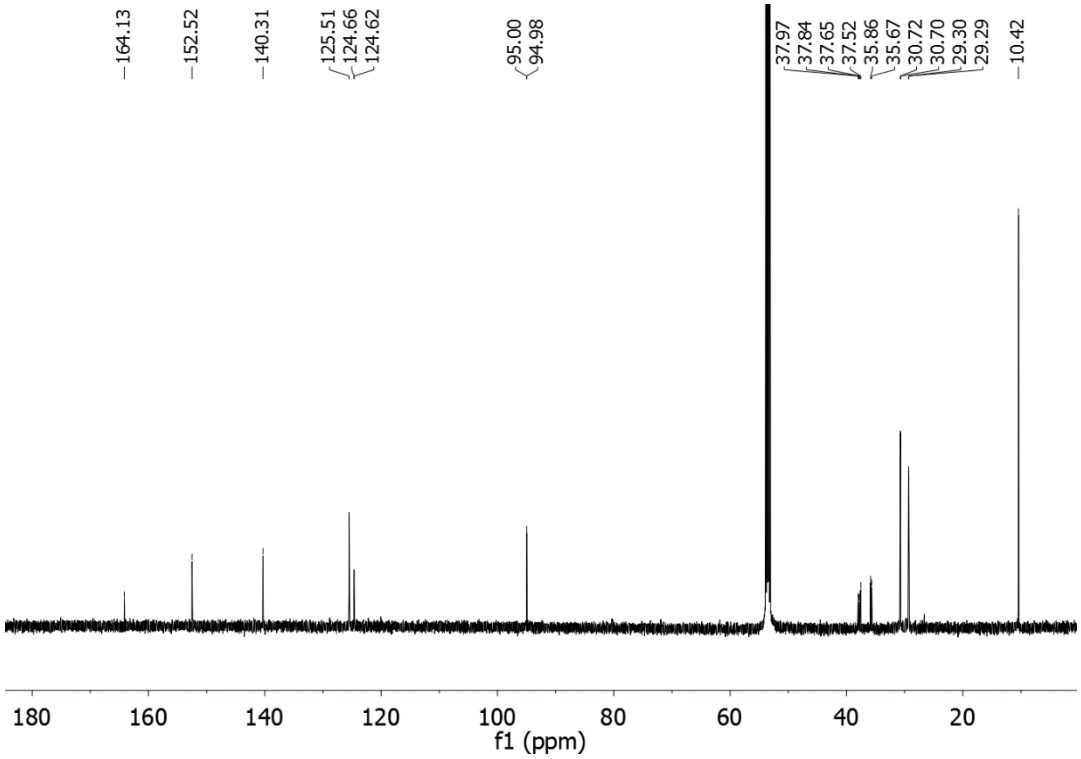


Figure S5. ^{13}C NMR spectrum of complex **1a** at 25 °C in CD_2Cl_2.

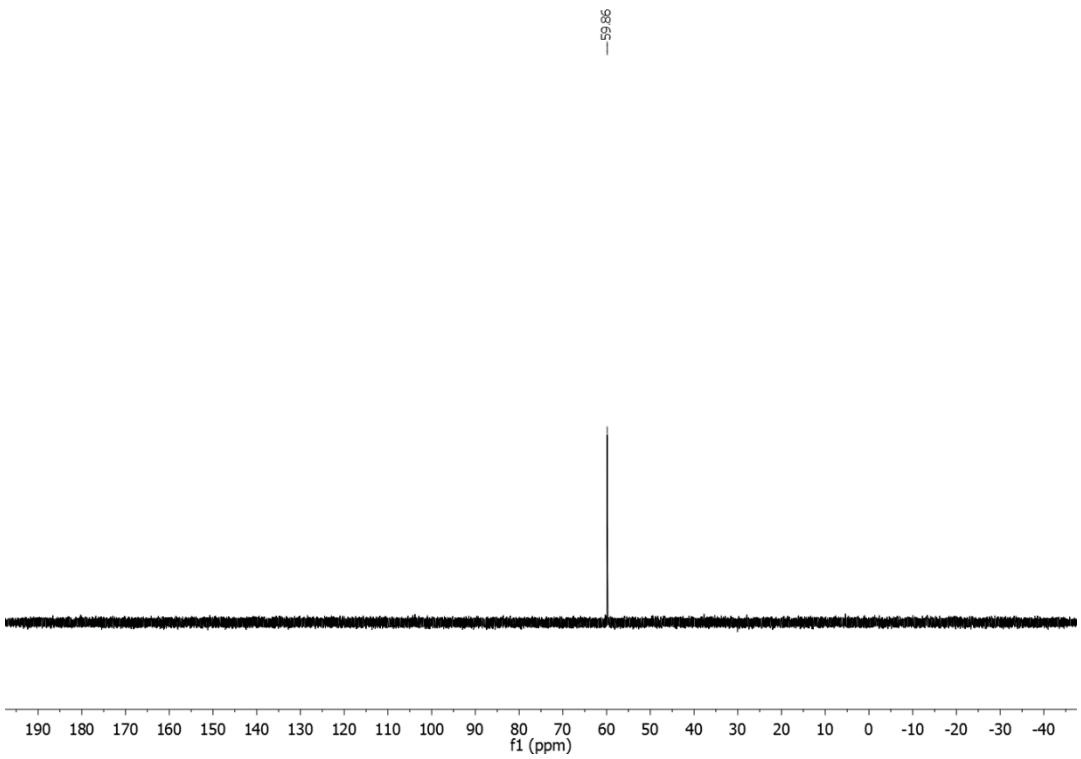


Figure S6. ^{31}P NMR spectrum of complex **1a** at 25 °C in CD_2Cl_2.

III. Reactivity of Ruthenium 1 in the Coupling of Benzylic Alcohols and Amines

Coupling of Benzyl Alcohol and Tryptamine (Open Flask)

In the drybox, a 5 mL Schlenk bomb with a conical bottom was charged with benzyl alcohol **2** (70 µL, 0.67 mmol, 2.2 equiv), tryptamine **4** (48 mg, 0.3 mmol), and 1 mol% ruthenium **1** (2.0 mg, 3.0 µmol). The vessel was taken out of the box and connected to a nitrogen line. Under a slow, steady stream of nitrogen gas, the solution was heated to 110 °C. The solution turns dark brown. After 24 hours, the crude reaction mixture was allowed to cool to room temperature. An aliquot was obtained for ^{1}H NMR analysis in $CDCl_3$. The reaction proceeded with ca. 75% conversion, forming a 3:1 product mixture of **5** and **7**. The spectrum of the crude reaction mixture is shown in Figure S7. The data are consistent with known compounds.[2,3]

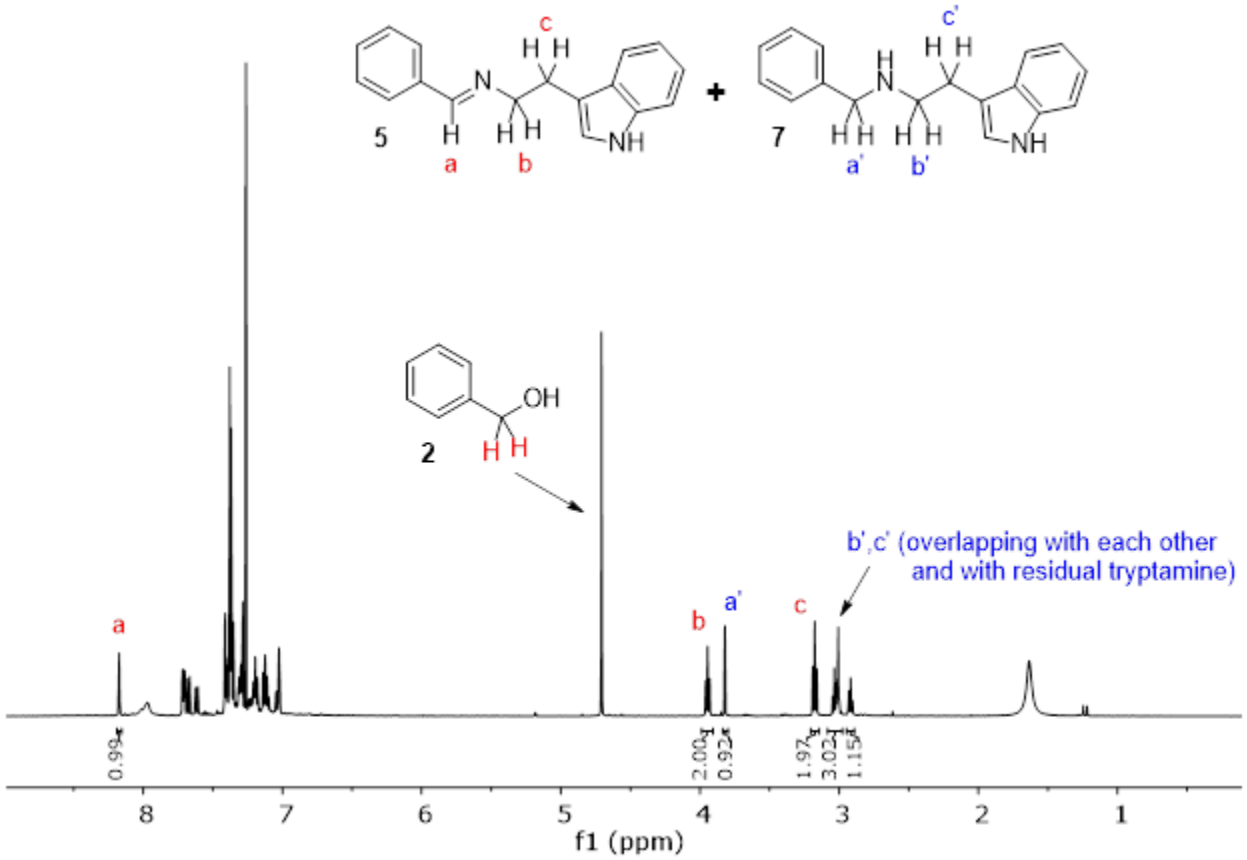


Figure S7. ^{1}H NMR spectrum of the crude reaction mixture for the coupling of benzyl alcohol and tryptamine under a stream of nitrogen gas at 110 °C; **5** and **7** are observed as products.

Coupling of Benzyl Alcohol and Tryptamine (Sealed Flask)

In the drybox, a 5 mL Schlenk bomb with a conical bottom was charged with benzyl alcohol **2** (70 µL, 0.67 mmol, 2.2 equiv), tryptamine **4** (48 mg, 0.3 mmol), and 1 mol% ruthenium **1** (2.0 mg, 3.0 µmol). The vessel was sealed, taken out of the box, and heated to 110 °C. The solution turns dark brown. After 24 hours, the crude reaction mixture was allowed to cool to room temperature. An aliquot was obtained for ^{1}H NMR analysis in $CDCl_3$. The reaction proceeded with ca. 100% conversion, forming **6** as the major product. The spectrum of the crude reaction mixture is shown in Figure S8. The data are consistent with a known compound.[3]

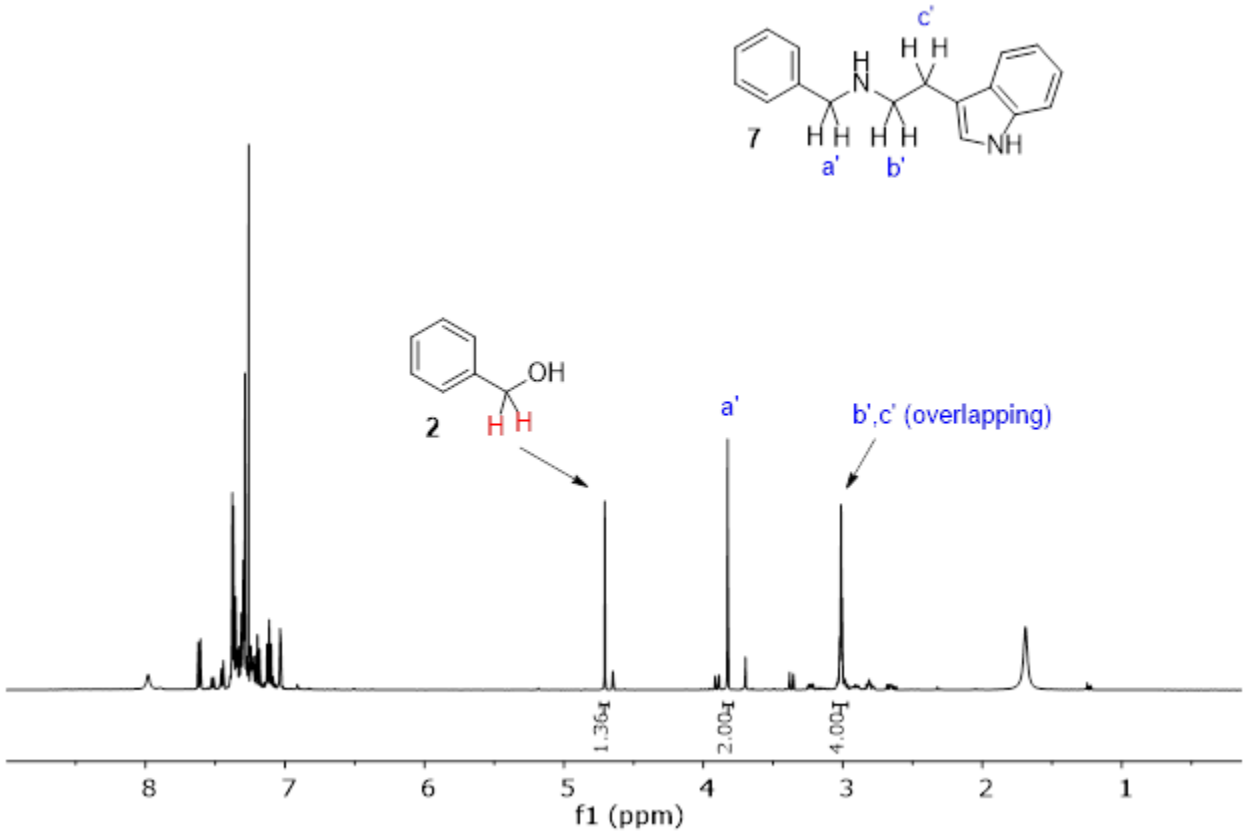


Figure S8. ^{1}H NMR spectrum of the crude reaction mixture for the coupling of benzyl alcohol and tryptamine in a sealed flask at 110 °C; **7** is observed as product.

Coupling of 1-Phenylethanol and Tryptamine (Open Flask)

In the drybox, a 5 mL Schlenk bomb with a conical bottom was charged with 1-phenylethanol **3** (100 µL, 0.83 mmol, 1.5 equiv), tryptamine **4** (90 mg, 0.56 mmol, 1 equiv), and 1 mol% ruthenium **1** (3.6 mg, 5.5 µmol). The vessel was taken out of the box and connected to a nitrogen line. Under a slow, steady stream of nitrogen gas, the solution was heated to 110 °C. The solution turns dark brown. After 24 hours, the crude reaction mixture was allowed to cool to room temperature. An aliquot was obtained for ^{1}H NMR analysis in $CDCl_3$. The reaction proceeded with ca. 33% conversion, forming imine **6** as the major product with almost no trace of the amine product. The spectrum of the crude reaction mixture is shown in Figure S9.

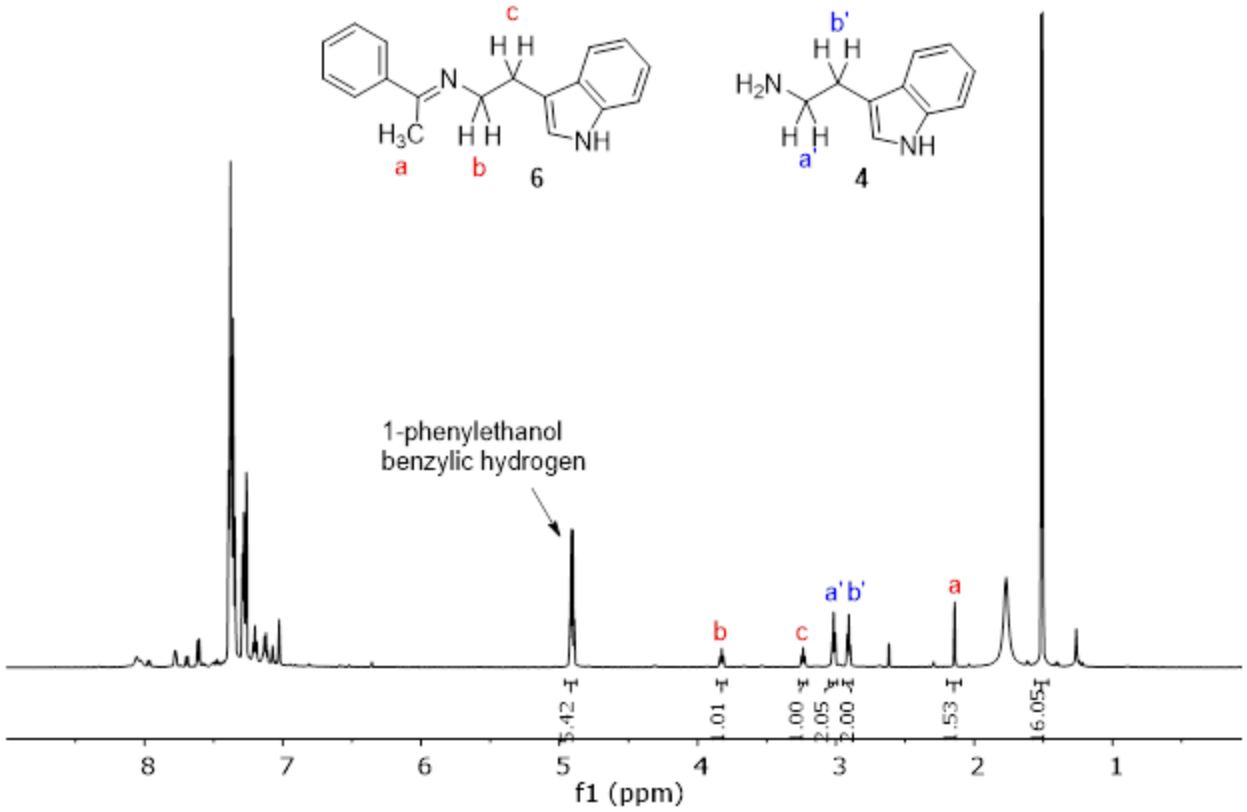


Figure S9. ^{1}H NMR spectrum of the crude reaction mixture for the coupling of 1-phenylethanol and tryptamine under a stream of nitrogen gas at 110 °C; **6** is observed as product.

Coupling of 1-Phenylethanol and Tryptamine (Sealed Flask)

In the drybox, a 5 mL Schlenk bomb with a conical bottom was charged with 1-phenylethanol **3** (100 µL, 0.83 mmol, 7.5 equiv), tryptamine **4** (17.6 mg, 0.11 mmol, 1 equiv), and 5 mol% ruthenium **1** (3.6 mg, 5.5 µmol). The vessel was sealed, taken out of the box, and heated to 130 °C. The solution turns dark brown. After 24 hours, the crude reaction mixture was allowed to cool to room temperature. An aliquot was obtained for ^{1}H NMR analysis in $CDCl_3$. The reaction proceeded with 100% conversion, forming amine **8** as the major product. The spectrum of the crude reaction mixture is shown in Figure S10. The data is consistent with a known compound.[4]

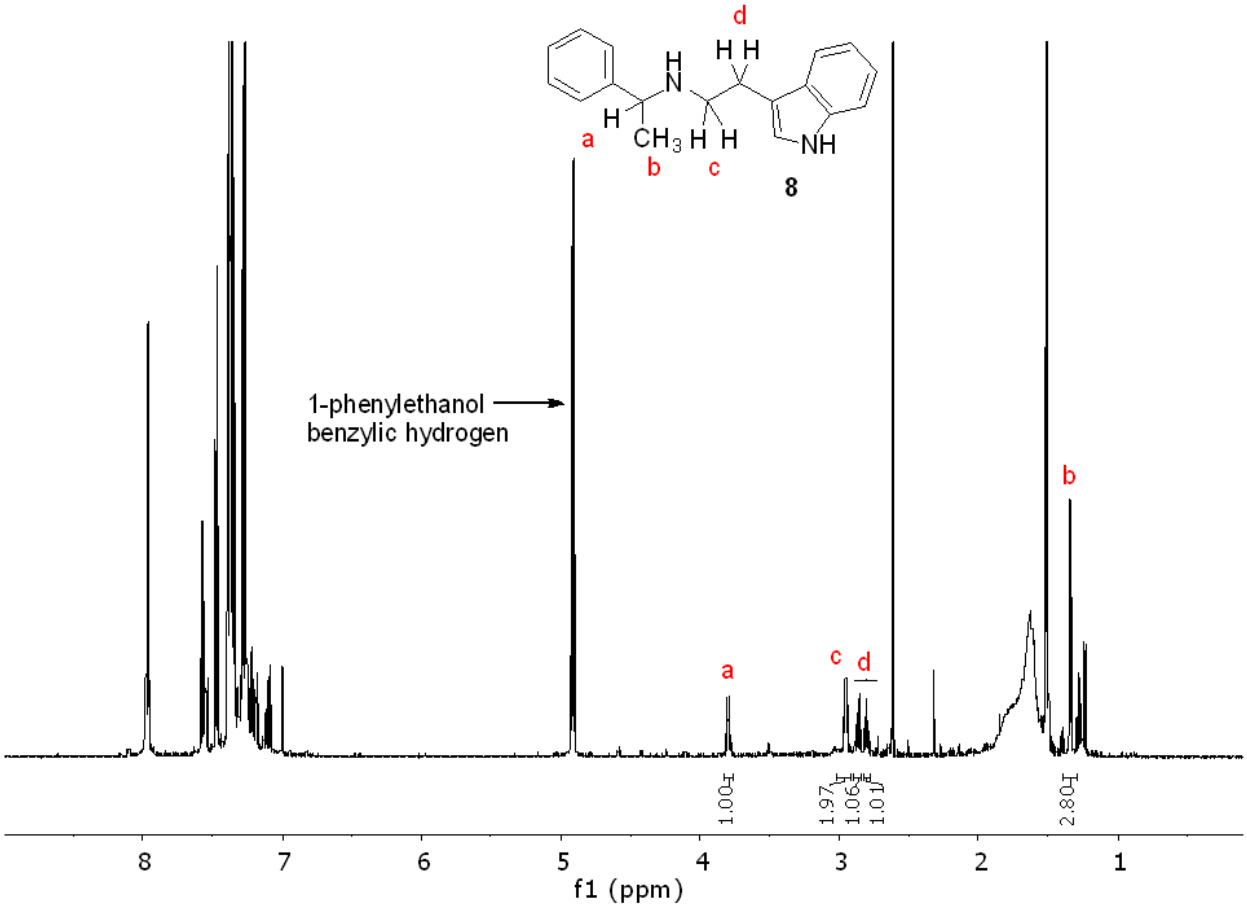
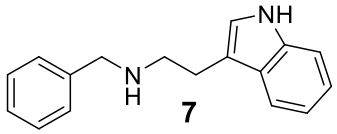


Figure S10. ^{1}H NMR spectrum of the crude reaction mixture for the coupling of 1-phenylethanol and tryptamine in a sealed flask at 130 °C; **8** is the observed product.

IV. Substrate Scope

Coupling of Benzyl Alcohol (and Derivatives) with Various Amines

Amine **7**:



7

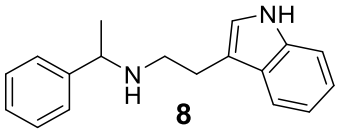
In the drybox, a 5 mL Schlenk bomb with a conical bottom was charged with benzyl alcohol **2** (25 µL, 0.24 mmol, 1.5 equiv), tryptamine **4** (25.6 mg, 0.16 mmol, 1 equiv.), and 1.0 mol% of **1** (1.1 mg, 1.6 µmol). The reaction was sealed, removed from the glove box, and placed into a 110 °C oil bath for 20 hours. After 20 hours, an aliquot from the solution was dissolved in $CDCl_3$ (0.6 mL), and a ^{1}H NMR spectrum was taken to determine conversion. Flash column chromatography (50:50:1 hexanes/ethyl acetate/triethylamine) yielded 28 mg of **7** (72%).

Data are consistent with a known compound.[3]

^{1}H NMR (600 MHz, Methylene Chloride-d_2) δ 8.15 (s, 1H), 7.60 (dd, J = 8.0, 1.0 Hz, 1H), 7.36 (dt, J = 8.1, 1.0 Hz, 1H), 7.34 – 7.25 (m, 4H), 7.25 – 7.19 (m, 1H), 7.16 (ddd, J = 8.2, 7.0, 1.2 Hz, 1H), 7.11 – 7.01 (m, 2H), 3.80 (s, 2H), 2.97 (m, 4H).

^{13}C NMR (151 MHz, Methylene Chloride-d_2) δ 140.95, 136.48, 128.27, 128.10, 127.64, 126.74, 122.01, 121.88, 119.13, 118.85, 114.20, 111.10, 53.76, 49.58, 25.81.

Amine **8**:



8

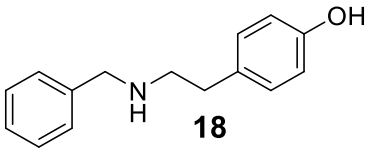
In the drybox, a 5 mL Schlenk bomb with a conical bottom was charged with 1-phenylethanol **3** (100 µL, 0.81 mmol, 7.4 equiv), tryptamine **4** (17.6 mg, 0.11 mmol, 1 equiv.), and 5.0 mol% of **1** (3.6 mg, 5.5 µmol). The reaction was sealed, removed from the glove box, and placed into a 130 °C oil bath for 24 hours. After 24 hours, an aliquot from the solution was dissolved in $CDCl_3$ (0.6 mL), and a ^{1}H NMR spectrum was taken to determine conversion. Flash column chromatography (100% ethyl acetate) yielded 21 mg of **8** (72%).

Data are consistent with a known compound.[4]

^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.12 (br s, 1H), 7.55 (d, J = 7.9 Hz, 1H), 7.39 – 7.34 (m, 1H), 7.34 – 7.22 (m, 5H), 7.22 – 7.17 (m, 1H), 7.10 (td, J = 7.5, 7.0, 0.9 Hz, 1H), 7.00 (s, 1H), 3.85 (q, J = 6.6 Hz, 1H), 2.99 (td, J = 6.4, 5.8, 2.2 Hz, 2H), 2.91 (dt, J = 18.1, 7.0 Hz, 1H), 2.83 (dt, J = 11.3, 7.2 Hz, 1H), 2.74 (br s, 1H), 1.38 (d, J = 6.6 Hz, 3H).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 144.78, 136.56, 128.70, 127.56, 127.30, 126.85, 122.24, 122.20, 119.45, 119.06, 113.76, 111.32, 58.47, 47.64, 25.64, 24.01.

Amine **18**:



18

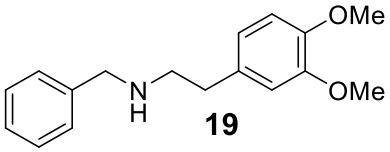
In the drybox, a 5 mL Schlenk bomb with a conical bottom was charged with benzyl alcohol **2** (25 µL, 0.24 mmol, 1.5 equiv), tyramine **12** (22.4 mg, 0.16 mmol, 1 equiv.), and 1.0 mol% of **1** (1.1 mg, 1.6 µmol). The reaction was sealed, removed from the glove box, and placed into a 110 °C oil bath for 5 hours. After 5 hours, an aliquot from the solution was dissolved in $CDCl_3$ (0.6 mL), and a ^{1}H NMR spectrum was taken to determine conversion. Flash column chromatography (1:1 hexanes/ethyl acetate) yielded 25.8 mg of **18** (72%).

Data are consistent with a known compound.[5]

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.37 – 7.19 (m, 5H), 7.03 (d, *J* = 8.4 Hz, 2H), 6.71 (d, *J* = 8.4 Hz, 2H), 3.81 (s, 2H), 2.89 (t, *J* = 7.2 Hz, 2H), 2.76 (t, *J* = 7.2 Hz, 2H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 154.28, 139.63, 131.45, 129.77, 128.45, 128.18, 127.06, 115.42, 53.67, 50.40, 35.09.

Amine **19**:



19

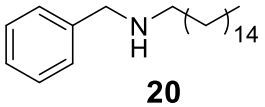
In the drybox, a 5 mL Schlenk bomb with a conical bottom was charged with benzyl alcohol **2** (25 µL, 0.24 mmol, 1.5 equiv), homoveratrylamine **13** (27 µL, 0.16 mmol, 1 equiv.), and 1.0 mol% of **1** (1.1 mg, 1.6 µmol). The reaction was sealed, removed from the glove box, and placed into a 110 °C oil bath for 24 hours. After 24 hours, an aliquot from the solution was dissolved in $CDCl_3$ (0.6 mL), and a ^{1}H NMR spectrum was taken to determine conversion. When complete, the reaction was dissolved in minimal DCM and loaded into a silica column that had been pretreated with 1% triethylamine. Flash column chromatography (1:1 hexanes/ethyl acetate) yielded 38.4 mg of **19** (90%).

Data are consistent with a known compound.[6]

^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.35 – 7.18 (m, 5H), 6.78 (dd, *J* = 8.1, 2.2 Hz, 1H), 6.73 (dt, *J* = 8.1, 2.2 Hz, 1H), 6.71 (s, 1H), 3.84 (m, 6H), 3.79 (d, *J* = 2.2 Hz, 2H), 2.88 (td, *J* = 7.0, 2.0 Hz, 2H), 2.77 (td, *J* = 7.1, 2.1 Hz, 2H).

^{13}C NMR (151 MHz, Chloroform-*d*) δ 148.90, 147.43, 140.17, 132.55, 128.37, 128.08, 126.92, 120.59, 111.92, 111.29, 55.92, 55.81, 53.85, 50.54, 35.85.

Amine **20**:



20

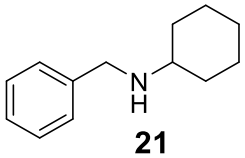
In the drybox, a 5 mL Schlenk bomb with a conical bottom was charged with benzyl alcohol **2** (25 µL, 0.24 mmol, 1.5 equiv), hexadecylamine **14** (38.6 mg, 0.16 mmol, 1 equiv.), and 1.0 mol% of **1** (1.1 mg, 1.6 µmol). The reaction was sealed, removed from the glove box, and placed into a 110 °C oil bath for 20 hours. After 20 hours, an aliquot from the solution was dissolved in $CDCl_3$ (0.6 mL), and a ^1H NMR spectrum was taken to determine conversion. Flash column chromatography (2:1 hexanes/ethyl acetate) yielded 38 mg of **20** (79%). The starting material **14** was only 90% pure.

Data are consistent with a known compound.[7]

^1H NMR (600 MHz, Chloroform-*d*) δ 7.32 (d, *J* = 4.4 Hz, 4H), 7.26 – 7.21 (m, 1H), 3.79 (s, 2H), 2.63 (t, *J* = 7.3 Hz, 2H), 1.51 (p, *J* = 7.3 Hz, 2H), 1.25 (s, 26H), 0.88 (t, *J* = 7.0 Hz, 3H).

^{13}C NMR (151 MHz, $cdcl_3$) δ 140.31, 128.37, 128.15, 126.89, 53.99, 49.43, 31.92, 30.00, 29.69 (br), 29.68, 29.66, 29.66, 29.61, 29.61, 29.56, 29.36, 27.35, 22.69, 14.11.

Amine **21**:



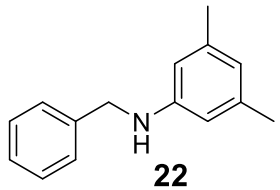
21

In the drybox, a 5 mL Schlenk bomb with a conical bottom was charged with benzyl alcohol **2** (25 µL, 0.24 mmol, 1.5 equiv), cyclohexylamine **15** (19 µL, 0.16 mmol, 1 equiv.), and 1.0 mol% of **1** (1.1 mg, 1.6 µmol). The reaction was sealed, removed from the glove box, and placed into a 110 °C oil bath for 24 hours. After 24 hours, an aliquot from the solution was dissolved in $CDCl_3$ (0.6 mL), and a ^1H NMR spectra was taken to determine conversion. When complete, the crude mixture was purified by flash column chromatography (1:1 hexanes/ethyl acetate) to give 18 mg of **21** (58%).

Data are consistent with a known compound.[8]

^1H NMR (400 MHz, Chloroform-*d*) δ 7.38 – 7.28 (m, 4H), 7.26 – 7.21 (m, 1H), 3.82 (s, 2H), 2.49 (tt, *J* = 10.2, 3.7 Hz, 1H), 1.98 – 1.87 (m, 2H), 1.80 – 1.68 (m, 2H), 1.67 – 1.56 (m, 1H), 1.48 (br s, 1H), 1.30 – 1.09 (m, 5H).

Amine **22**:



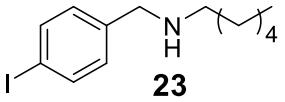
22

In the drybox, a 5 mL Schlenk bomb with a conical bottom was charged with benzyl alcohol **2** (25 µL, 0.24 mmol, 1.5 equiv), 3,5-dimethylaniline **16** (19 µL, 0.16 mmol, 1 equiv.), and 1.0 mol% of **1** (1.1 mg, 1.6 µmol). The reaction was sealed, removed from the glove box, and placed into a 110 °C oil bath for 24 hours. After 24 hours, an aliquot from the solution was dissolved in $CDCl_3$ (0.6 mL), and a ^{1}H NMR spectrum was taken to determine conversion. When complete, the product was purified by flash column chromatography (3:1 hexanes/ethyl acetate) to yield 18.6 mg of **22** (58%).

Data are consistent with a known compound.[9]

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.39 – 7.27 (m, 5H), 6.42 (s, 1H), 6.33 (s, 2H), 4.31 (s, 2H), 2.23 (s, 6H).

Amine **23**:



23

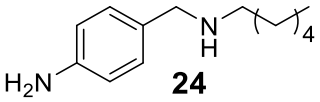
In the drybox, a 5 mL Schlenk bomb with a conical bottom was charged with 4-iodobenzyl alcohol **9** (84 mg, 0.36 mmol, 1.2 equiv), n-hexylamine **17** (39 µL, 0.3 mmol, 1 equiv.), and 1.0 mol% of **1** (2.0 mg, 3.0 µmol). The reaction was sealed, removed from the glove box, and placed into a 110 °C oil bath for 20 hours. After 20 hours, an aliquot from the solution was dissolved in $CDCl_3$ (0.6 mL), and a ^{1}H NMR spectrum was taken to determine conversion. When complete, the product was purified by flash column chromatography (3:1 hexanes/ethyl acetate) to yield 62 mg of **23** (65%) as a yellow-green oil.

23 is a commercial compound (CAS No. 1496214-93-7).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.64 (d, J = 8.0 Hz, 2H), 7.08 (d, J = 8.0 Hz, 2H), 3.73 (s, 2H), 2.59 (t, J = 5.0 Hz, 2H), 1.48 (d, J = 14.7 Hz, 4H), 1.37 – 1.19 (m, 7H), 0.89 (t, J = 5.0 Hz, 3H).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 140.19, 137.38, 130.11, 92.05, 53.41, 49.43, 31.75, 30.02, 27.00, 22.61, 14.04.

Amine **24**:



24

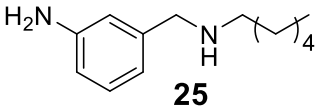
In the drybox, a 5 mL pear-shaped Schlenk bomb was charged with 4-aminobenzyl alcohol **10** (37 mg, 0.30 mmol, 1.0 equiv), hexylamine **17** (48 µL, 0.36 mmol, 1.2 equiv.), and 1.0 mol% of **1** (2.0 mg, 3.0 µmol). The reaction was sealed, removed from the glove box, and placed into a 110 °C oil bath for 12 hours. ^{1}H NMR spectra were taken to determine conversion after 3, 6, and 12 hours. When complete, the reaction was purified by flash column chromatography (95:5:1 dichloromethane/methanol/triethylamine) to yield 51 mg of **24** (77%) as a viscous yellow oil.

24 is a known compound[10] and is commercially available (CAS No. 1502166-32-6).

^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.13 (d, *J* = 12.0 Hz, 2H), 6.65 (d, *J* = 12.0 Hz, 2H), 3.70 (s, 2H), 3.62 (s, 2H), 2.67 – 2.59 (m, 2H), 1.53 (p, *J* = 7.5 Hz, 2H), 1.34 – 1.23 (m, 6H), 0.87 (t, *J* = 6.7 Hz, 3H).

^{13}C NMR (151 MHz, Chloroform-*d*) δ 145.52, 129.61, 128.85, 115.10, 53.13, 48.84, 31.70, 29.41, 26.98, 22.59, 14.03.

Amine **25**:



25

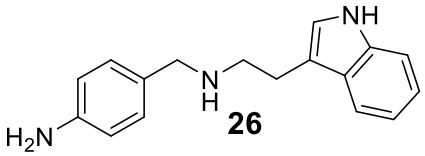
In the drybox, a 5 mL pear-shaped Schlenk bomb was charged with 3-aminobenzyl alcohol **11** (37 mg, 0.30 mmol, 1.0 equiv), hexylamine **17** (48 µL, 0.36 mmol, 1.2 equiv.), and 1.0 mol% of **1** (2.0 mg, 3.0 µmol). The reaction was sealed, removed from the glove box, and placed into a 110 °C oil bath for 3 hours. After 3, an aliquot from the solution was dissolved in $CDCl_3$ (0.6 mL), and a ^{1}H NMR spectrum was taken to determine conversion. The crude reaction mixture was subjected to flash column chromatography (95:5:1 dichloromethane/methanol/triethylamine) to yield 48 mg of **25** (74%) as a viscous yellow oil.

25 is a known compound[11] and is commercially available (CAS No. 1554148-06-9).

^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.10 (t, *J* = 7.9 Hz, 1H), 6.70 (dd, *J* = 4.6, 2.2 Hz, 2H), 6.58 (dd, *J* = 8.0, 2.2 Hz, 1H), 3.72 (s, 2H), 2.64 (t, *J* = 7.4 Hz, 2H), 1.53 (q, *J* = 7.5 Hz, 2H), 1.33 – 1.22 (m, 6H), 0.87 (t, *J* = 6.8 Hz, 3H).

^{13}C NMR (151 MHz, Chloroform-*d*) δ 146.62, 140.14, 129.33, 118.56, 114.97, 114.00, 53.53, 49.02, 31.66, 29.37, 26.91, 22.56, 14.00.

Amine **26**:



26

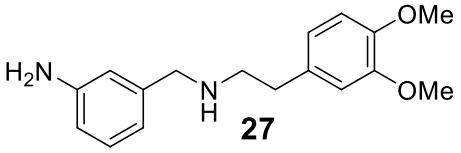
In the drybox, a 5 mL pear-shaped Schlenk bomb was charged with 4-aminobenzyl alcohol **10** (37 mg, 0.30 mmol, 1.0 equiv), tryptamine **4** (58 mg, 0.36 mmol, 1.2 equiv.), and 1.0 mol% of **1** (2.0 mg, 3.0 μmol). The reaction was sealed, removed from the glove box, and placed into a 110 °C oil bath for 12 hours. After 12 hours, an unstirrable gooey solid forms. A ^{1}H NMR spectrum of the crude reaction mixture was taken to determine conversion (70%). The mixture was purified by flash column chromatography (90:10:1 dichloromethane/methanol/triethylamine) to yield 45 mg of **26** (57%) as a brown solid.

26 is a commercial compound (CAS No. 1506350-12-4).

^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.97 (s, 1H), 7.61 (d, *J* = 7.9 Hz, 1H), 7.36 (d, *J* = 8.2 Hz, 1H), 7.19 (t, *J* = 7.6 Hz, 1H), 7.11 (t, *J* = 7.5 Hz, 1H), 7.07 (d, *J* = 7.9 Hz, 2H), 7.02 (s, 1H), 6.62 (d, *J* = 7.8 Hz, 2H), 3.70 (s, 2H), 2.99 (m, 4H).

^{13}C NMR (151 MHz, cdcl$_3$) δ 145.24, 136.35, 130.16, 129.30, 127.47, 121.99, 121.87, 119.25, 118.94, 115.08, 114.08, 111.06, 53.39, 49.17, 25.66.

Amine **27**:



27

In the drybox, a 5 mL pear-shaped Schlenk bomb was charged with 3-aminobenzyl alcohol **11** (37 mg, 0.30 mmol, 1.0 equiv), homoveratrylamine **13** (65 mg, 0.36 mmol, 1.2 equiv.), and 1.0 mol% of **1** (2.0 mg, 3.0 μmol). The reaction was sealed, removed from the glove box, and placed into a 110 °C oil bath for 3 hours. After 3 hours, an aliquot from the solution was dissolved in $CDCl_3$ (0.6 mL), and a ^{1}H NMR spectrum was taken to determine conversion. The crude reaction mixture was subjected to flash column chromatography (95:5:1 dichloromethane/methanol/triethylamine) to yield 62 mg of **27** (72%).

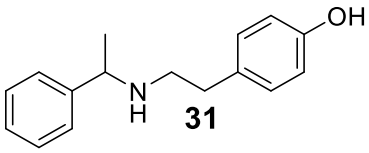
27 is a commercial compound (CAS No. 1556153-38-8).

^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.09 (t, *J* = 7.7 Hz, 1H), 6.80 (d, *J* = 8.1 Hz, 1H), 6.77 – 6.71 (m, 2H), 6.65 (d, *J* = 7.5 Hz, 1H), 6.62 (d, *J* = 2.1 Hz, 1H), 6.59 – 6.55 (m, 1H), 3.86 (s, 6H), 3.73 (s, 2H), 3.63 (br s, 2H), 2.89 (t, *J* = 7.1 Hz, 2H), 2.79 (t, *J* = 7.0 Hz, 2H).

^{13}C NMR (151 MHz, Chloroform-*d*) δ 148.89, 147.43, 146.54, 140.82, 132.35, 129.30, 120.62, 118.39, 114.75, 113.84, 111.93, 111.28, 55.90, 55.81, 53.63, 50.34, 35.59.

Coupling of 1-Phenylethanol (and Derivatives) with Various Amines

Amine **31**:



31

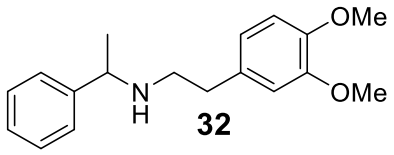
In the drybox, a 5 mL Schlenk bomb with a conical bottom was charged with 1-phenylethanol **3** (100 µL, 0.81 mmol, 7.4 equiv), tyramine **12** (15 mg, 0.16 mmol, 1 equiv.), and 5.0 mol% of **1** (3.6 mg, 5.5 µmol). The reaction was sealed and removed from the glove box and into a 130 °C oil bath for 24 hours. After 24 hours, an aliquot from the solution was dissolved in $CDCl_3$ (0.6 mL), and a ^{1}H NMR spectra was taken to determine conversion. The reaction was purified via flash column chromatography (1:1 hexanes:ethyl acetate) to yield 23 mg of **31** (85%).

31 is a known compound.[12]

^{1}H NMR (600 MHz, Methylene Chloride-d_2) δ 7.44 – 7.17 (m, 5H), 6.94 (d, J = 8.5 Hz, 2H), 6.68 (d, J = 8.4 Hz, 2H), 4.39 (bs, 1H), 3.86 (q, J = 6.7 Hz, 1H), 2.79 – 2.62 (m, 4H), 1.37 (d, J = 6.6 Hz, 3H).

^{13}C NMR (151 MHz, Methylene Chloride-d_2) δ 155.26, 144.22, 131.09, 130.08, 128.94, 127.71, 127.15, 115.83, 58.59, 48.92, 34.87, 23.42.

Amine **32**:



32

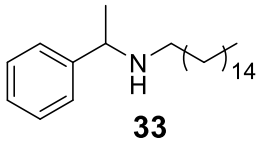
In the drybox, a 5 mL Schlenk bomb with a conical bottom was charged with 1-phenylethanol **3** (100 µL, 0.81 mmol, 7.4 equiv), homoveratrylamine **13** (19 µL, 0.11 mmol, 1 equiv.), and 5.0 mol% of **1** (3.6 mg, 5.5 µmol). The reaction was sealed, removed from the glove box, and into a 130 °C oil bath for 24 hours. After 24 hours, an aliquot from the solution was dissolved in $CDCl_3$ (0.6 mL), and a ^{1}H NMR spectra was taken to determine conversion. When complete, the reaction was dissolved in minimal DCM and loaded into a silica column. The reaction was purified via flash column chromatography (3:1 hexanes:ethyl acetate) to yield 21 mg **32** (67%) as a clear oil.

Data are consistent with a known compound.[13]

^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.32 – 7.28 (m, 2H), 7.27 – 7.20 (m, 3H), 6.76 (d, J = 8.1 Hz, 1H), 6.68 (dd, J = 8.1, 2.0 Hz, 1H), 6.65 (d, J = 1.9 Hz, 1H), 3.86 – 3.77 (m, 7H, including benzylic CH), 2.81 – 2.63 (m, 4H), 1.36 (d, J = 6.6 Hz, 3H).

^{13}C NMR (151 MHz, Chloroform-*d*) δ 148.87, 147.44, 144.47, 132.16, 128.48, 127.12, 126.61, 120.58, 111.85, 111.23, 58.22, 55.89, 55.78, 48.63, 35.37, 23.75.

Amine **33**:



33

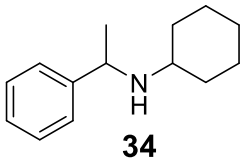
In the drybox, a 5 mL Schlenk bomb with a conical bottom was charged with 1-phenylethanol **3** (100 µL, 0.81 mmol, 7.4 equiv), hexadecylamine **14** (26.5 mg, 0.11 mmol, 1 equiv.), and 5.0 mol% of **1** (3.6 mg, 5.5 µmol). The reaction was sealed, removed from the glove box, and placed into a 130 °C oil bath for 24 hours. After 24 hours, an aliquot from the solution was dissolved in $CDCl_3$ (0.6 mL), and a ^{1}H NMR spectra was taken to determine conversion. Flash column chromatography (4:1 hexanes:ethyl acetate) yielded 24.4 mg of **33** (79%). The starting material **14** was only 90% pure.

33 is a known compound.[14]

^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.35 – 7.28 (m, 3H), 7.27 – 7.21 (m, 2H), 3.76 (q, *J* = 6.5, 6.0 Hz, 1H), 2.55 – 2.45 (m, 1H), 2.46 – 2.36 (m, 1H), 1.46 (d, *J* = 7.2 Hz, 4H), 1.39 – 1.33 (m, 3H), 1.33 – 1.10 (m, 24H), 0.92 – 0.86 (m, 3H).

^{13}C NMR (151 MHz, cdcl$_3$) δ 145.95, 128.61, 127.05, 126.79, 58.63, 48.09, 32.15, 30.43, 29.92 (br), 29.90, 29.88, 29.83, 29.81, 29.77, 29.59, 27.59, 24.50, 22.92, 14.34.

Amine **34**:



34

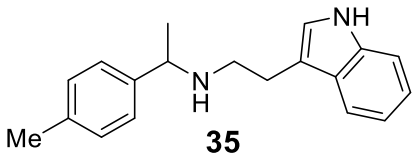
In the drybox, a 5 mL Schlenk bomb with a conical bottom was charged with 1-phenylethanol **3** (100 µL, 0.81 mmol, 7.4 equiv), cyclohexylamine **15** (26.5 mg, 0.11 mmol, 1 equiv.), and 5.0 mol% of **1** (3.6 mg, 5.5 µmol). The reaction was sealed, removed from the glove box, and placed into a 130 °C oil bath for 19 hours. After 19 hours, an aliquot from the solution was dissolved in $CDCl_3$ (0.6 mL), and a ^{1}H NMR spectra was taken to determine conversion. Flash column chromatography (2:1 hexanes/ethyl acetate) yielded 15 mg of **34** (66%).

Data are consistent with a known compound.[15]

^{1}H NMR (500 MHz, Methylene Chloride-d_2) δ 7.39 – 7.26 (m, 4H), 7.21 (m, 1H), 3.95 (qd, *J* = 6.6, 0.8 Hz, 1H), 2.26 (tt, *J* = 10.2, 3.8 Hz, 1H), 2.01 – 1.91 (m, 1H), 1.66 (tdt, *J* = 19.8, 10.0, 4.0 Hz, 3H), 1.54 (m, 1H), 1.28 (d, *J* = 6.6 Hz, 4H, including *NH*), 1.19 – 1.09 (m, 3H), 1.09 – 0.95 (m, 2H).

^{13}C NMR (126 MHz, Methylene Chloride-d_2) δ 147.32, 128.78, 127.08, 127.07, 54.94, 35.08, 33.81, 26.81, 25.79, 25.53, 25.39.

Amine **35**:



35

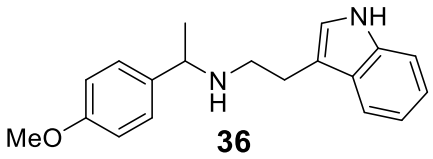
In the drybox, a 5 mL Schlenk bomb with a conical bottom was charged with 1-(4-methylphenyl)ethanol **28** (100 µL, 0.72 mmol, 6.5 equiv), tryptamine **4** (17.6 mg, 0.11 mmol, 1 equiv.), and 5.0 mol% of **1** (3.6 mg, 5.5 µmol). The reaction was sealed, removed from the glove box, and placed into a 130 °C oil bath for 24 hours. Flash column chromatography (100% ethyl acetate) yielded 21 mg of **35** (69%).

35 is a known compound.[16]

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.05 (br s, 1H), 7.54 (d, *J* = 7.9 Hz, 1H), 7.35 (d, *J* = 8.1 Hz, 1H), 7.22 – 7.14 (m, 3H), 7.14 – 7.05 (m, 3H), 7.00 (d, *J* = 2.2 Hz, 1H), 3.79 (q, *J* = 6.6 Hz, 1H), 2.97 (dd, *J* = 8.6, 6.5 Hz, 2H), 2.92 – 2.78 (m, 2H), 2.33 (s, 4H, including *NH*), 1.34 (d, *J* = 6.6 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 141.88, 136.55, 136.34, 129.11, 127.38, 126.50, 121.96, 121.93, 119.20, 118.88, 113.76, 111.06, 57.97, 47.52, 25.58, 24.00, 21.03.

Amine **36**:



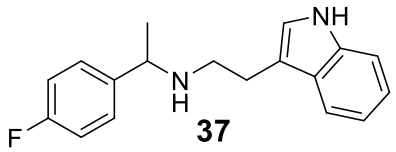
36

In the drybox, a 5 mL Schlenk bomb with a conical bottom was charged with 1-(4-methoxyphenyl)ethanol **29** (100 µL, 0.71 mmol, 6.5 equiv), tryptamine **4** (17.6 mg, 0.11 mmol, 1 equiv.), and 5.0 mol% of **1** (3.6 mg, 5.5 µmol). The reaction was sealed, removed from the glove box, and placed into a 130 °C oil bath for 24 hours. Flash column chromatography (100% ethyl acetate) yielded 23 mg of **36** (72%).

^{1}H NMR (600 MHz, Chloroform-*d*) δ 8.13 (br s, 1H), 7.53 (d, *J* = 7.9 Hz, 1H), 7.35 (dd, *J* = 8.2, 1.8 Hz, 1H), 7.23 – 7.17 (m, 2H), 7.18 – 7.12 (m, 1H), 7.05 (ddd, *J* = 8.7, 7.2, 1.8 Hz, 1H), 7.02 (d, *J* = 2.3 Hz, 1H), 6.82 (dd, *J* = 8.7, 2.1 Hz, 2H), 3.83 – 3.69 (m, 4H, including *OCH$_3$* and benzylic *CH*), 2.95 – 2.86 (m, 2H), 2.85 – 2.79 (m, 1H), 2.77 – 2.72 (m, 1H), 1.28 – 1.26 (m, 3H).

^{13}C NMR (151 MHz, Chloroform-*d*) δ 159.10, 138.60, 136.96, 128.15, 128.11, 122.43, 122.35, 119.59, 119.34, 114.72, 114.15, 111.57, 58.00, 55.74, 48.27, 26.35, 24.72.

Amine **37**:



37

In the drybox, a 5 mL Schlenk bomb with a conical bottom was charged with 1-(4-fluorophenyl)ethanol **30** (100 µL, 0.80 mmol, 7.3 equiv), tryptamine **4** (17.6 mg, 0.11 mmol, 1 equiv.), and 5.0 mol% of **1** (3.6 mg, 5.5 µmol). The reaction was sealed, removed from the glove box, and placed into a 130 °C oil bath for 24 hours. Flash column chromatography (100% ethyl acetate) yielded 24 mg of **37** (77%).

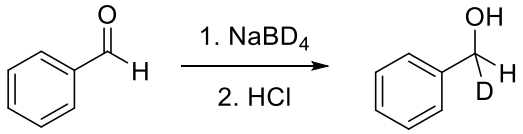
37 is a known compound.[16]

^{1}H NMR (500 MHz, Methylene Chloride-d_2) δ 8.17 (br s, 1H), 7.51 (d, J = 7.9 Hz, 1H), 7.35 (dd, J = 8.2, 1.0 Hz, 1H), 7.30 – 7.23 (m, 2H), 7.18 – 7.12 (m, 1H), 7.09 – 7.01 (m, 2H), 7.01 – 6.94 (m, 2H), 3.84 (q, J = 6.6 Hz, 1H), 2.98 – 2.91 (m, 2H), 2.86 (m, 1H), 2.76 (m, 3H, including *NH*), 1.32 (d, J = 6.6 Hz, 3H).

^{13}C NMR (126 MHz, Methylene Chloride-d_2) δ 162.45 (d, J = 244.6 Hz), 141.05, 136.97, 128.87 (d, J = 7.9 Hz), 127.93, 122.68, 122.46, 119.70, 119.22, 115.60 (d, J = 21.2 Hz), 113.97, 111.65, 58.11, 47.99, 25.85, 24.20.

V. NMR Studies to Probe the Mechanism of Coupling

*Synthesis of **2**-1-d_1*



2-1-d_1

Benzyl alcohol **2**-1-d_1 was synthesized by reduction of benzaldehyde using sodium borodeuteride (98% D, Sigma-Aldrich). To an ice-water bath cooled solution of benzaldehyde (2 mL, 19.6 mmol) dissolved in 1:1 ethanol/dichloromethane was added $NaBD_4$ (0.6 g, 14.3 mmol). The solution was stirred for 30 minutes at 0 °C then at room temperature for 15 minutes. The solution was again cooled to 0 °C then 6 M HCl was added slowly until effervescence stopped. The mixture was filtered and the filtrate extracted with dichloromethane (3 x 25 mL). The organic layer was washed with saturated aqueous $NaHCO_3$ (25 mL), water (25 mL), and brine (25 mL). The solvent was evaporated in vacuo. Flash column chromatography (9:1 hexanes/ethyl acetate) yielded 1.2 g of pure product (57%). ^{1}H NMR (16 scans, 10 second delay) analysis shows 93% deuterium incorporation (Figure S11).

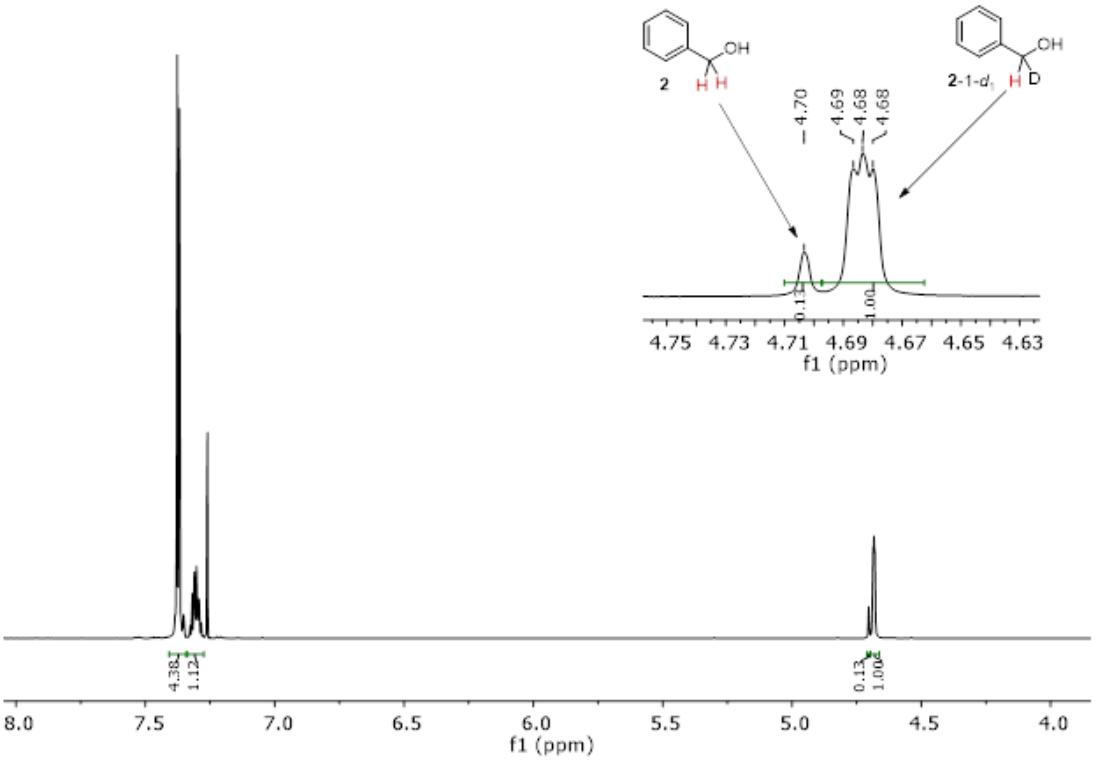


Figure S11. ^{1}H NMR spectrum of benzyl alcohol **2**-1-d_1.

*^{13}C NMR Studies of the Coupling of Benzyl Alcohol **2**-1-d_1 and n-Hexylamine*

In the drybox, a J-Young NMR tube was charged with **2**-1-d_1 (350 μL, 3.15 mmol, 1.1 equiv.), *n*-hexylamine (400 μL, 3.0 mmol, 1.0 equiv.), and ruthenium **1** (20.0 mg, 30 μmol, 1 mol%). The J-Young tube was sealed, taken out of the drybox, and heated to 110 °C in an oil bath. After 2 hours, the reaction mixture was allowed to cool to room temperature and a ^{13}C NMR spectrum was taken (a separate NMR tube containing a deuterated solvent was used to lock and shim the NMR). The reaction mixture was again heated. ^{13}C NMR spectra were taken at 0, 2, 8, and 24 hours of heating, which are shown in Figures S12 (stacked spectra) and S13A-D. Disappearance of the starting materials, **2**-1-d_1 and hexylamine, and formation of the benzylated amine is observed. Figures S13A-D are zoomed in views of the region of the ^{13}C NMR spectra showing in more detail the changes described in the main text that occur as the starting materials react to form the coupled secondary amine product. The figures clearly show the ^{13}C-^{2}H three-line coupling pattern for the deuterated carbons. Figure S13A shows the deuterated benzylic carbon of **2**-1-d_1 (centered at 63.48 ppm), which is located to the right of a very small peak for the non-deuterated benzylic carbon of **2** (centered at 63.82 ppm). After 2 hours of heating (Figure S13B), the peak for the deuterated carbon decreases and the peak for the non-deuterated carbon increases. This indicates the presence of a rapid redox equilibrium between benzyl alcohol and benzaldehyde. The peak of the non-deuterated carbon increases because a rapid equilibrium between *n*-hexylamine and its corresponding imine also exists (Figure S13B; deuterium is incorporated into the α-carbon leading to the peak with a three-line pattern at 41.72 ppm), confirming that *n*-hexylamine is the proton donor that causes the increase in the non-deuterated carbon peak of benzyl alcohol. Figure S13D show that the benzylic carbon and alkyl α-carbon of the product BnHexNH both contain deuterium (peaks with three-line patterns at 53.20 and 49.14 ppm, respectively). Also, figure S12 shows formation of small amounts of the imine intermediate (161.0 ppm); the benzaldehyde carbon, which is expected to appear at ca. 190 ppm, was not observed. Moreover, after 24 hours of heating, we analyzed the side products—Hex_2NH, Bn_2O, $BnN(Hex)_2$ and Bn_2Hex—present in the crude reaction mixture by GC-MS (see next section for GC-MS data). We also confirmed the presence of dihexylamine in the ^{13}C NMR spectrum (seen clearly in Figure S13B), which appears soon after heating to 110 °C, by spiking the crude reaction mixture with an authentic dihexylamine sample.

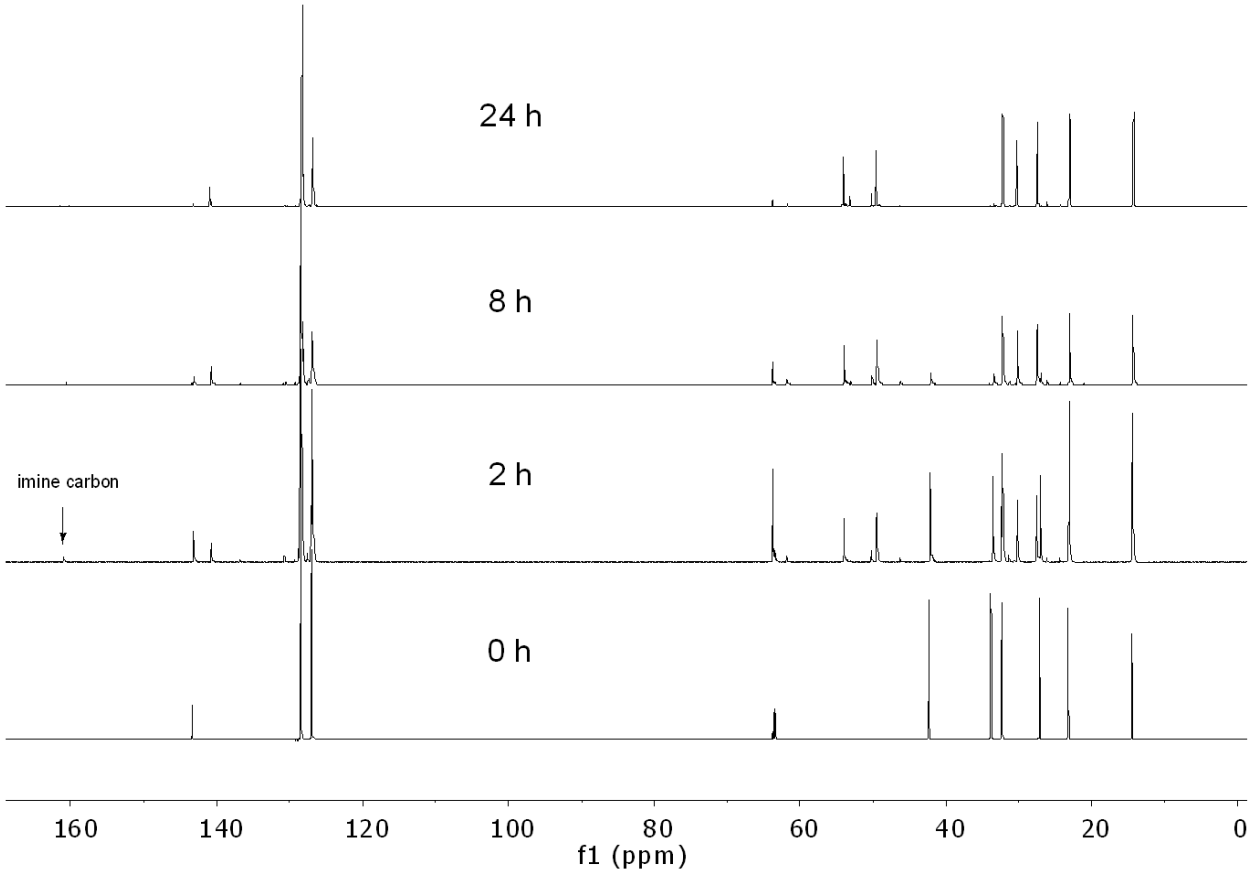


Figure S12. ^{13}C NMR stacked spectra of the crude reaction mixture after 0, 2, 8, and 24 hours of heating at 110 °C.

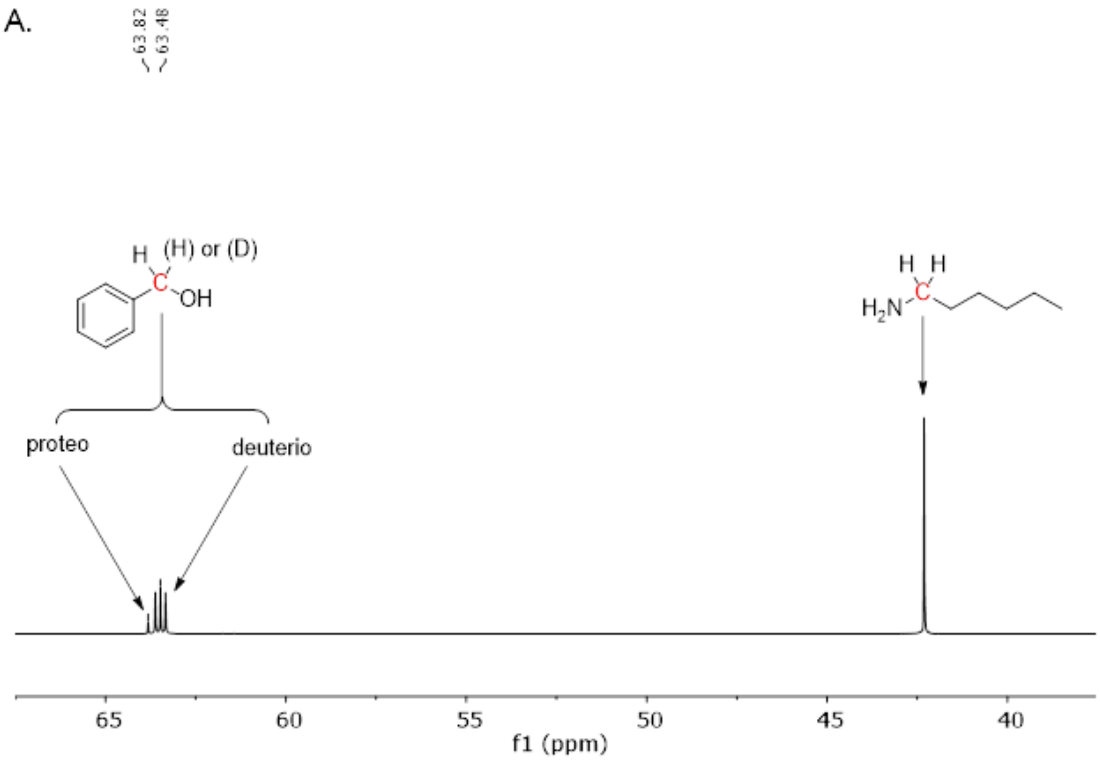


Figure S13A. ^{13}C NMR spectrum of the crude reaction mixture prior to heating to 110 °C.

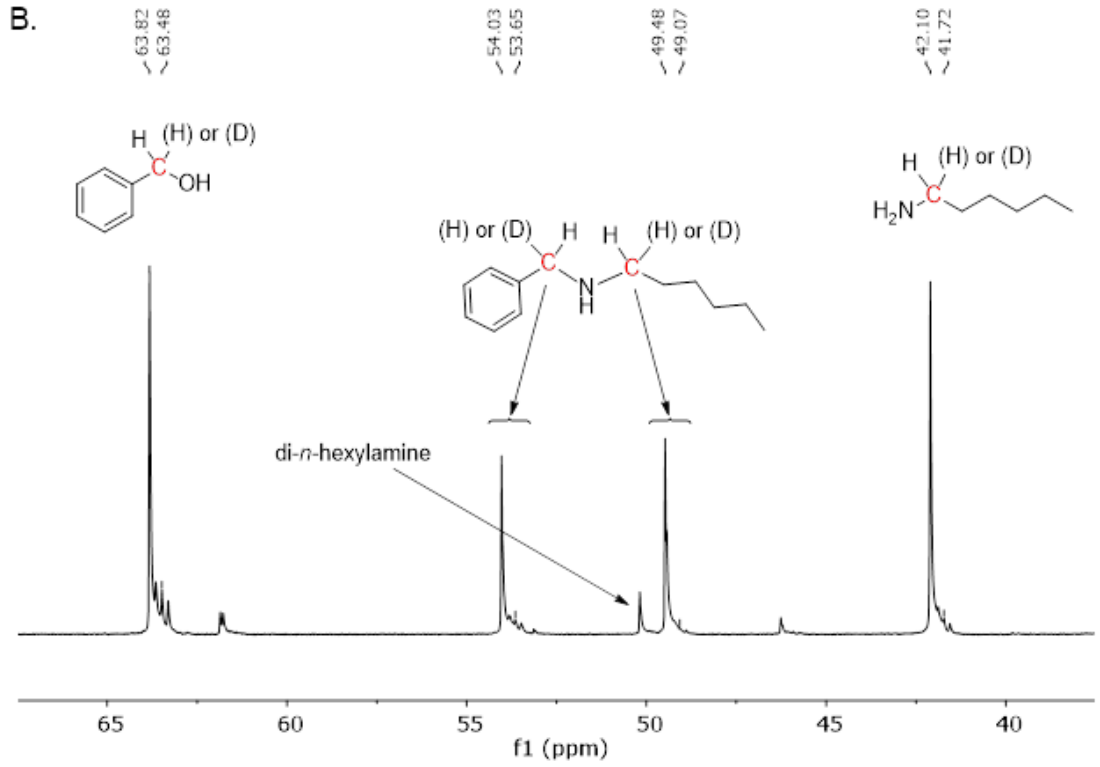


Figure S13B. ^{13}C NMR spectrum of the crude reaction mixture after 2 h of heating at 110 °C.

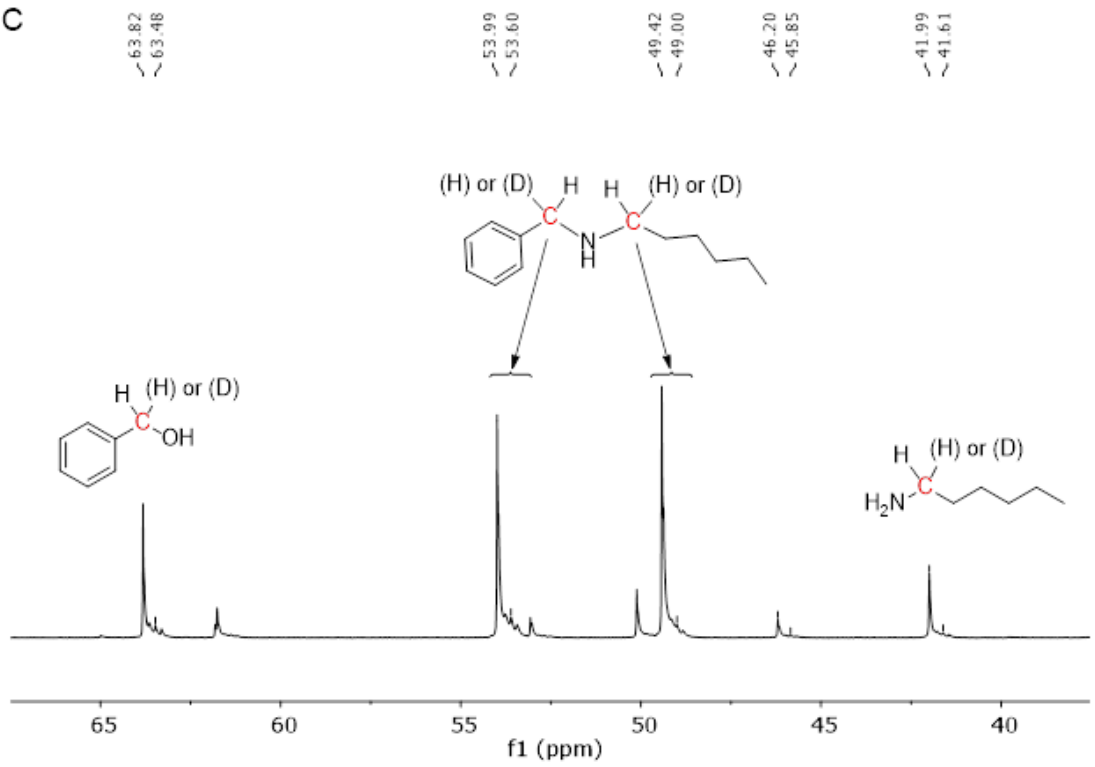


Figure S13C. ^{13}C NMR spectrum of the crude reaction mixture after 8 h of heating at 110 °C.

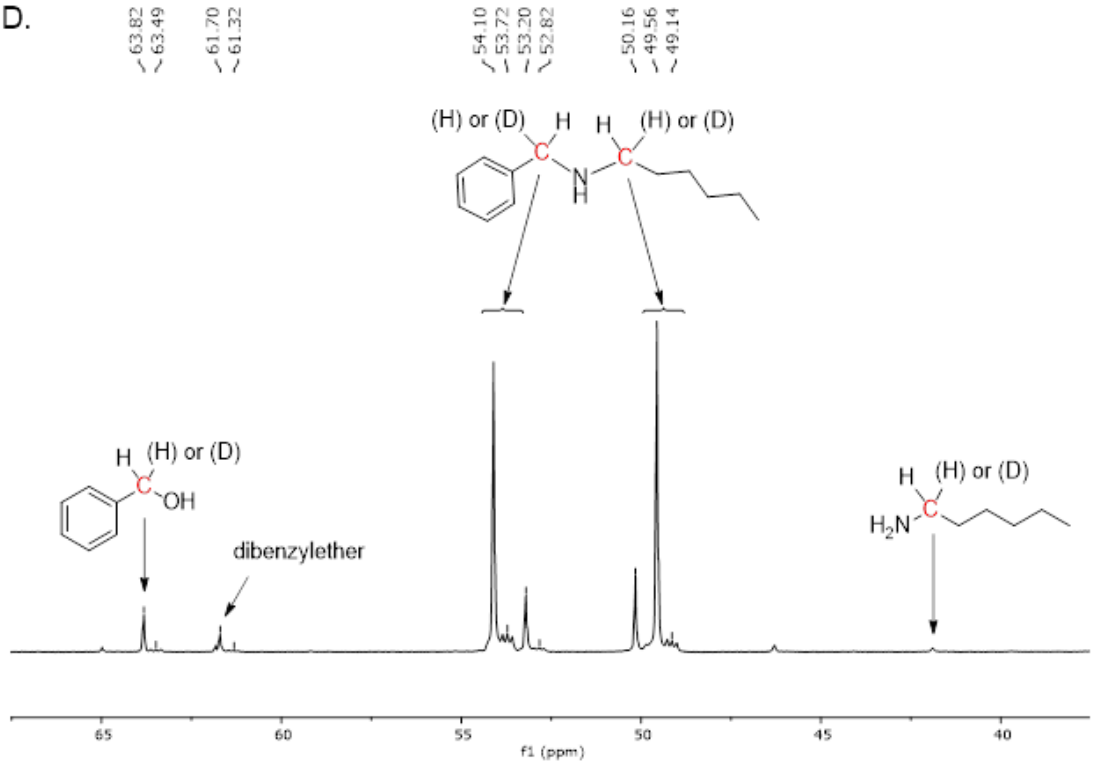


Figure S13D. ^{13}C NMR spectrum of the crude reaction mixture after 24 h of heating at 110 °C.

Side Products from the Coupling of 2-1-d_1 and Hexylamine

The crude reaction mixture for the coupling of **2**-1-d_1 and *n*-hexylamine after 24 hours of heating at 110 °C was analyzed by GC-MS. The chromatogram of the crude mixture is shown in Figure S14. The desired product and four coupling side products—Hex_2NH, Bn_2O, $BnN(Hex)_2$ and Bn_2Hex—are observed in the chromatogram. These were identified by their corresponding mass spectra (Figure S15 – S19). Small amounts of other side products, which are not analyzed here, can also be observed.

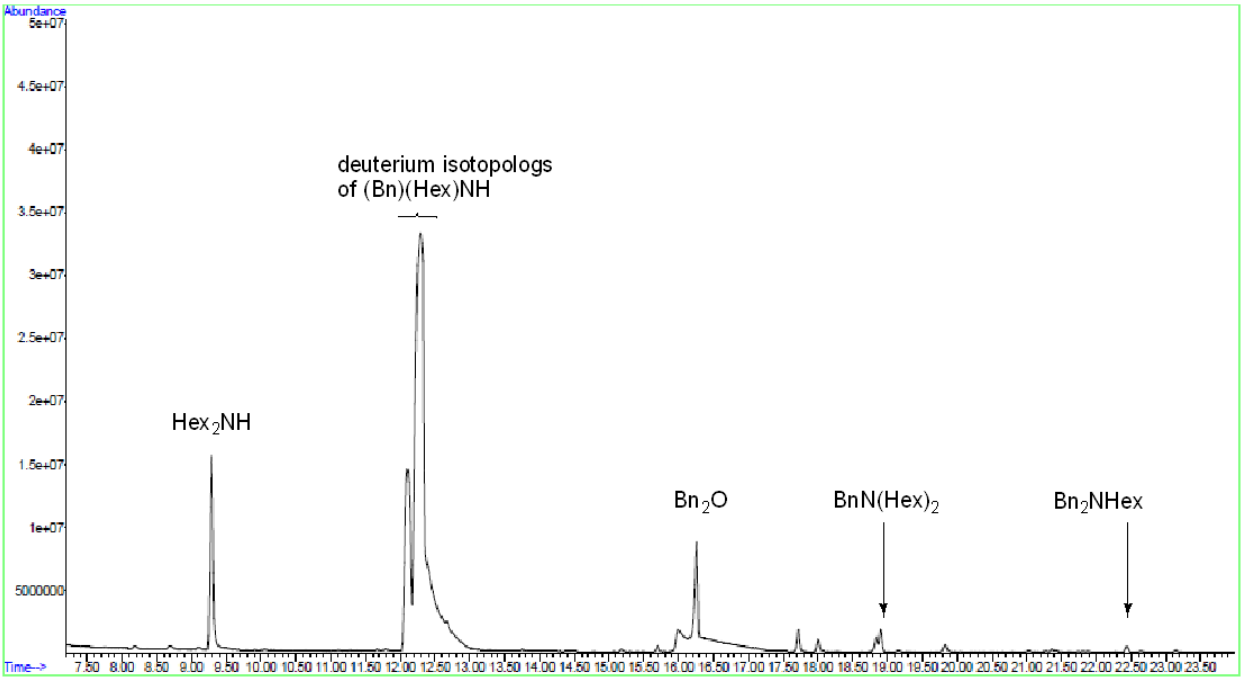


Figure S14. GC chromatogram of the crude reaction mixture for the coupling of benzyl alcohol-1-d_1 and *n*-hexylamine after 24 h of heating at 110 °C.

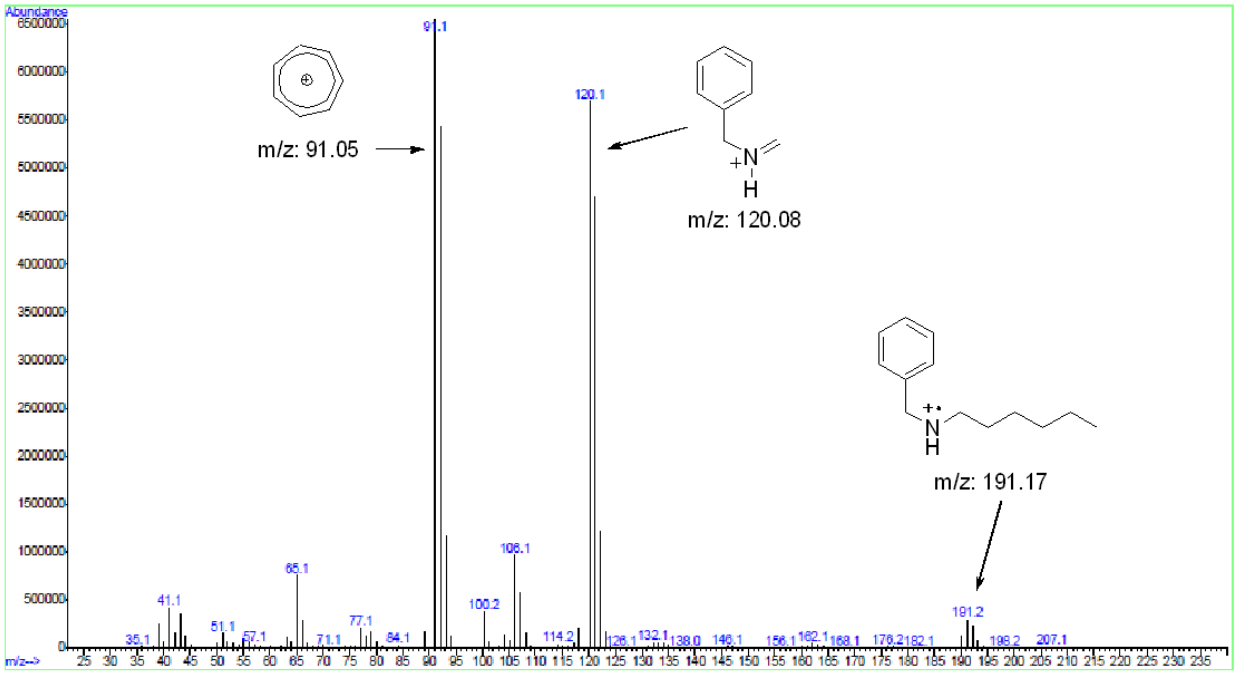


Figure S15. Mass spectrum of the GC peak at 12.1 min (the desired benzyl(hexyl)amine product) observed in Figure S11.

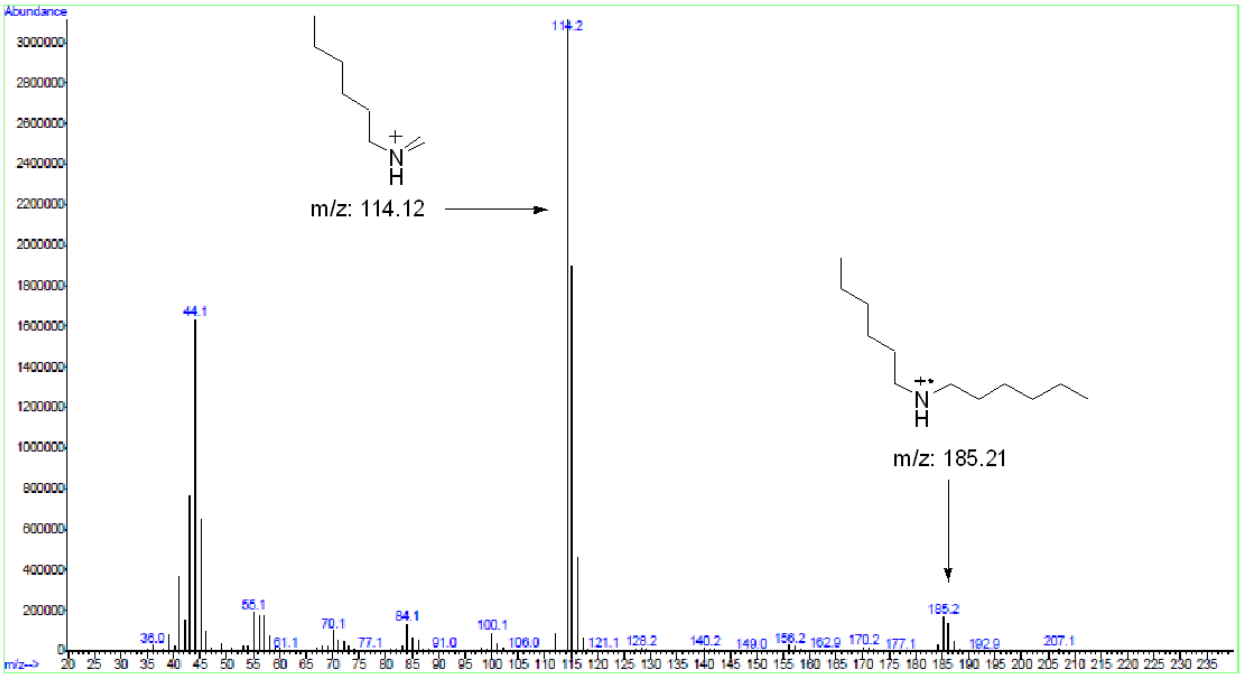


Figure S16. Mass spectrum of the GC peak at 9.3 min (the dihexylamine side product) observed in Figure S11.

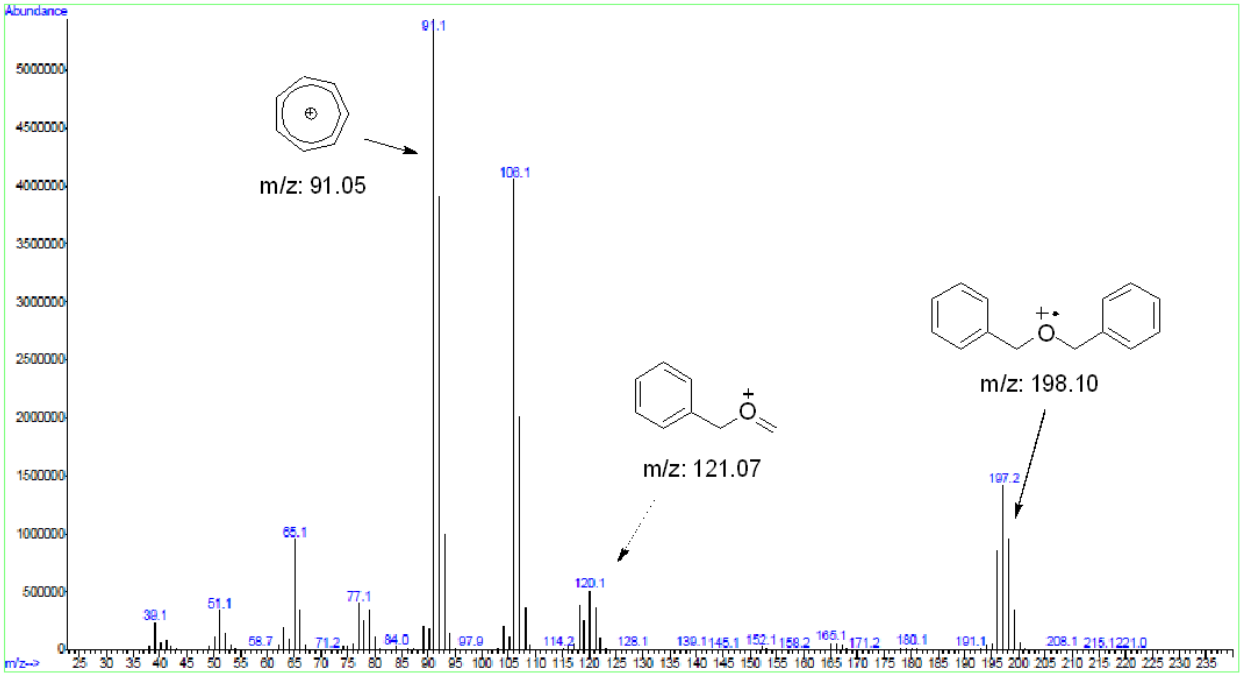


Figure S17. Mass spectrum of the GC peak at 16.2 min (the dibenzyl ether side product) observed in Figure S11.

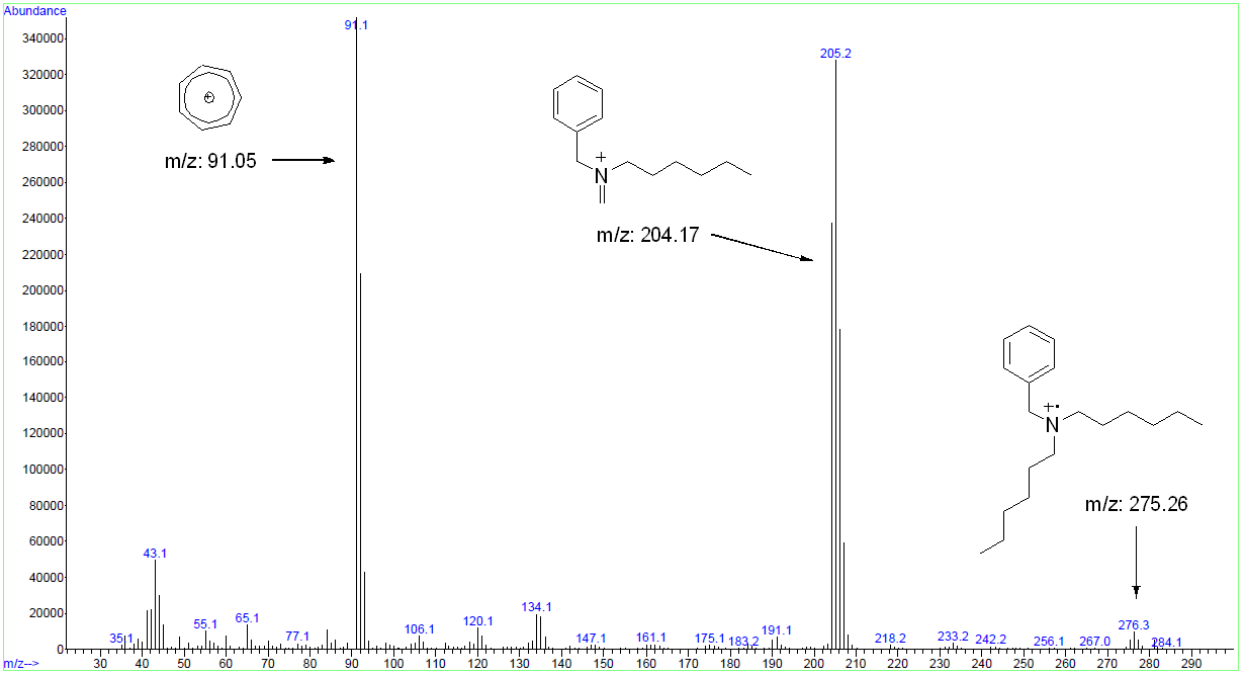


Figure S18. Mass spectrum of the GC peak at 18.9 min (the benzyl(dihexyl)amine side product) observed in Figure S11.

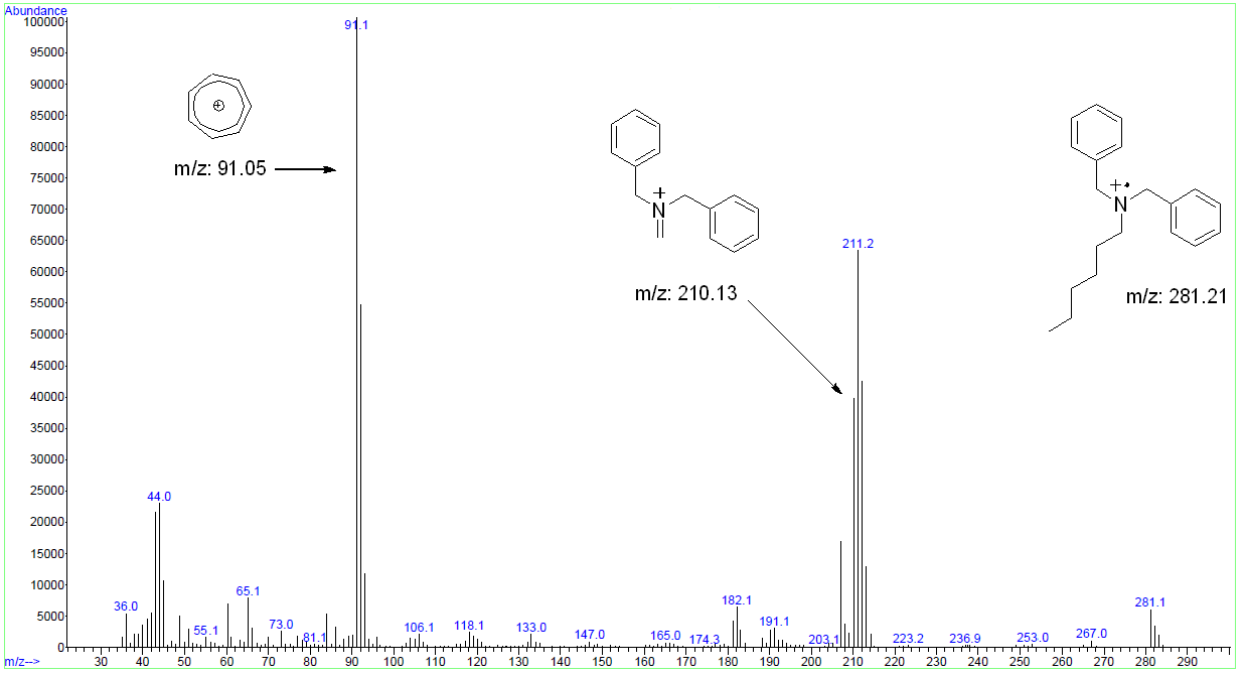


Figure S19. Mass spectrum of the GC peak at 22.4 min (the dibenzyl(hexyl)amine side product) observed in Figure S11.

^{31}P NMR Showing Bound PN Ligand After 48 h of Heating

A ^{31}P NMR spectrum (Figure S20) of the crude reaction mixture from the ^{13}C NMR studies above was taken after 24 hours of heating. The spectrum does not show a peak corresponding to the free phosphinopyridine ligand, which appears at 36.0 ppm. Thus, we believe that the PN ligand remains bound to the catalyst. The ^{31}P spectrum shows five peaks: the major species is a broad triplet at 92.1 ppm, consistent with a protonated (uncharged), metal-bound ligand, but four singlets at 97.9, 84.0, 65.5, and 60.5 ppm are also present.

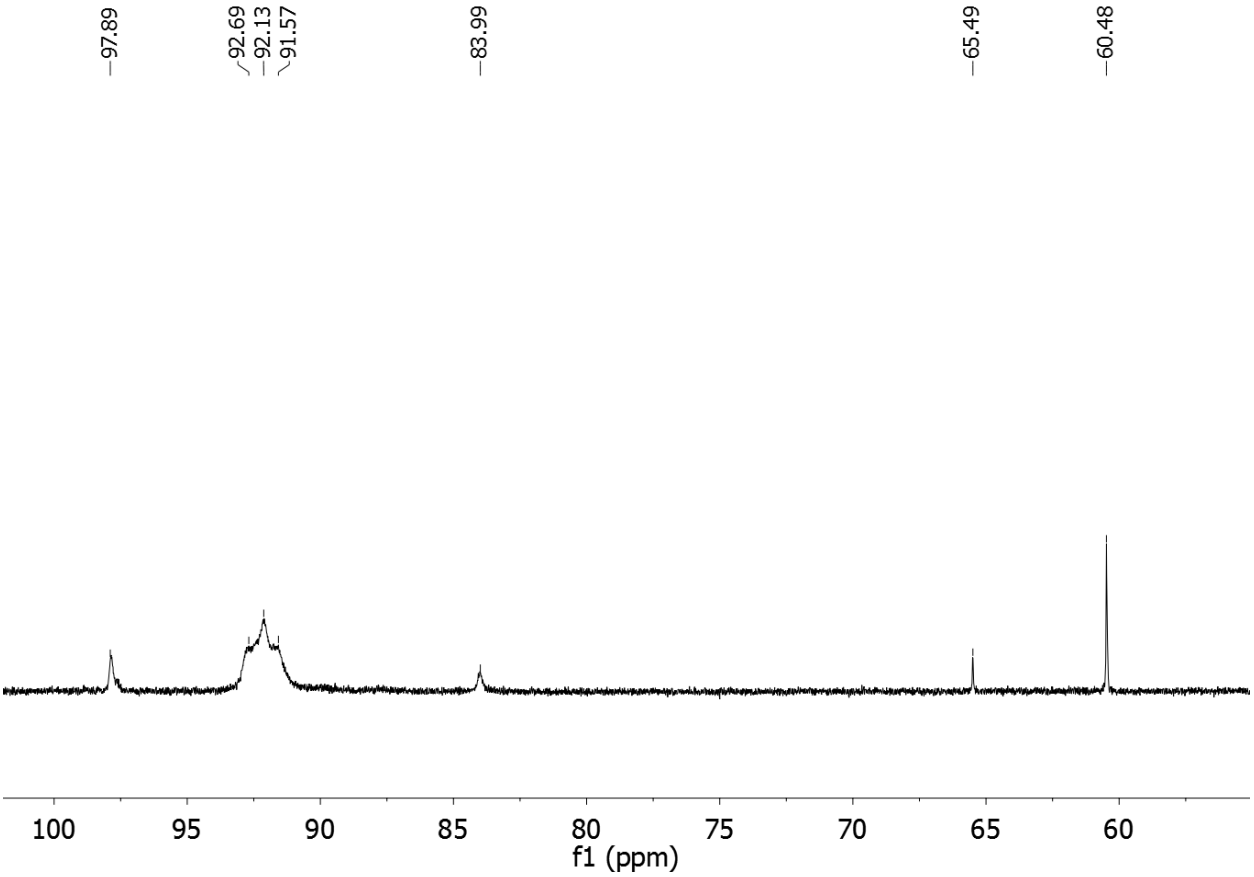


Figure S20. ^{31}P NMR spectrum of the crude reaction mixture after 24 h of heating at 110 °C.

^{1}H NMR Studies in 1,2-Dichlorobenzene-d_4

In the dry box, a J-Young tube was charged with a 10:1 mixture of benzyl alcohol **2**-1-d_1 (ca. 93% D, 8 μL, 77 μmol) and ruthenium **1** (5 mg, 7.6 μmol) dissolved in 0.6 mL of 1,2-dichlorobenzene-d_4. The J-Young tube was sealed, removed from the drybox, and heated to 110 °C in an oil bath. After 15 min, heating was stopped and a ^{1}H NMR spectrum of the crude reaction mixture (Figure S21) was taken. Heating was continued and NMR spectra were taken after 2, 6, 8, 24, and 48 hours of heating (Figures S22 A-B show the stacked spectra). Figure S22A shows the disappearance of benzyl alcohol **2**-1-d_1 and formation of the coupled dibenzyl ether product. It also shows formation of low concentrations of the benzaldehyde intermediate, which appears soon after heating and remains present during the duration of the experiment. Figure S22B shows formation of a doublet (J_{HP} = 40 Hz) at δ = -8.90 ppm which is consistent with a transient ruthenium hydride species. This species forms slowly upon heating and disappears over time. We believe this is not the active catalyst because this peak disappears (Figure S22B, 24 h) while catalysis is ongoing. Figure S22B also shows the slow disappearance of the cymene hydrogens that is coordinated to ruthenium (best observed through its four differentiated aromatic hydrogens). Interestingly, much of the starting benzyl alcohol remains when all the cymene become dissociated from ruthenium (Figure S22A, 24 h). Continued heating leads to almost complete conversion of **2**-1-d_1 to the coupled benzyl ether product (Figure S22A, 48 h). Thus, the active ruthenium catalyst does not have a coordinated cymene. Figure S23A more clearly shows the free cymene present in the crude reaction mixture. Interestingly, analysis of the peaks corresponding to the remaining starting benzyl alcohol (Figure S23B) reveals that the ratio of the deuterated (-CHDOH) and non-deuterated (-CH_2OH) starting material is ca. 9:1. Likewise, the ratio of the deuterated and non-deuterated dibenzyl ether product is also ca. 9:1. This data is consistent with a mechanism where catalysis occurs with β-hydride elimination in the dehydrogenation step (see main text, Scheme 1). Since all the hydrides that are utilized to reduce the imine intermediate in the hydrogenation step (Scheme 1) come from the benzylic hydrogens/deuteriums, the D:H ratio in the starting benzyl alcohol is unchanged in the product. This observation is consistent with a ruthenium monohydride active catalyst.[17]

We also performed this reaction under neat conditions by heating **2**-1-d_1 (47 μL, 0.46 mmol) and precatalyst **1** (3 mg, 4.6 μmmol) in a J-Young tube 110 °C for 12 hours. Analysis of the crude reaction mixture by ^{1}H NMR in $CDCl_3$ shows that the deuterium content in the benzyl ether product and in the starting material remaining are both ca. 90% (Figure S24). This indicates that the mechanism of catalysis under neat conditions is also proceeding through a ruthenium monohydride active catalyst and that the reaction performed in 1,2-dichlorobenzene-d_4 is a valid experiment which can be compared to reactions performed under neat conditions.

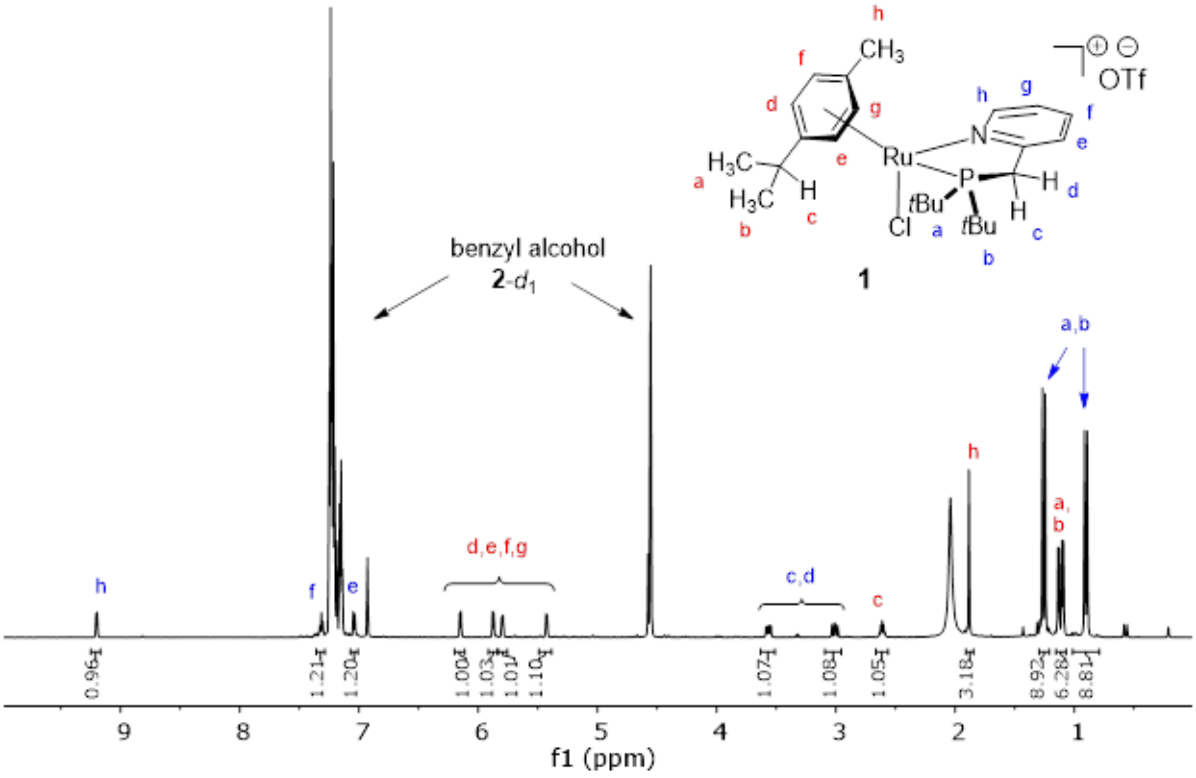


Figure S21. ^{1}H NMR spectrum of the crude reaction mixture after 15 min of heating at 110 °C in 1,2-dichlorobenzene-d_4.

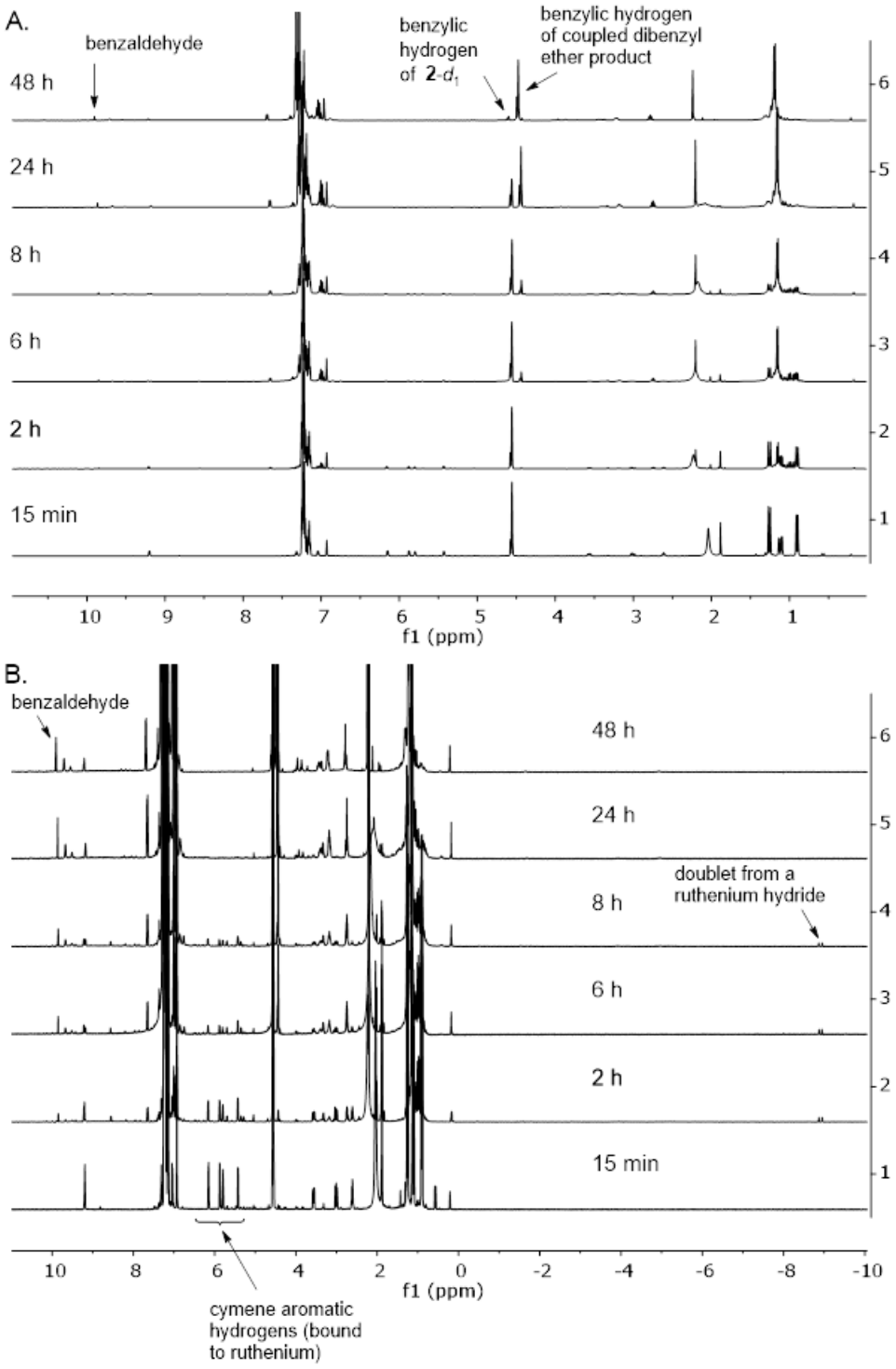


Figure S22. ^{1}H NMR stacked spectra of a time-course experiment for the homocoupling of benzyl alcohol **2**-1-d_1 in 1,2-dichlorobenzene-d_4. (A)The figure shows the disappearance of the starting material and formation of the coupled benzyl ether product. The figure also shows formation of a benzaldehyde intermediate. B) The figure shows formation of a transient ruthenium hydride species as well as the disappearance of ruthenium-bound cymene.

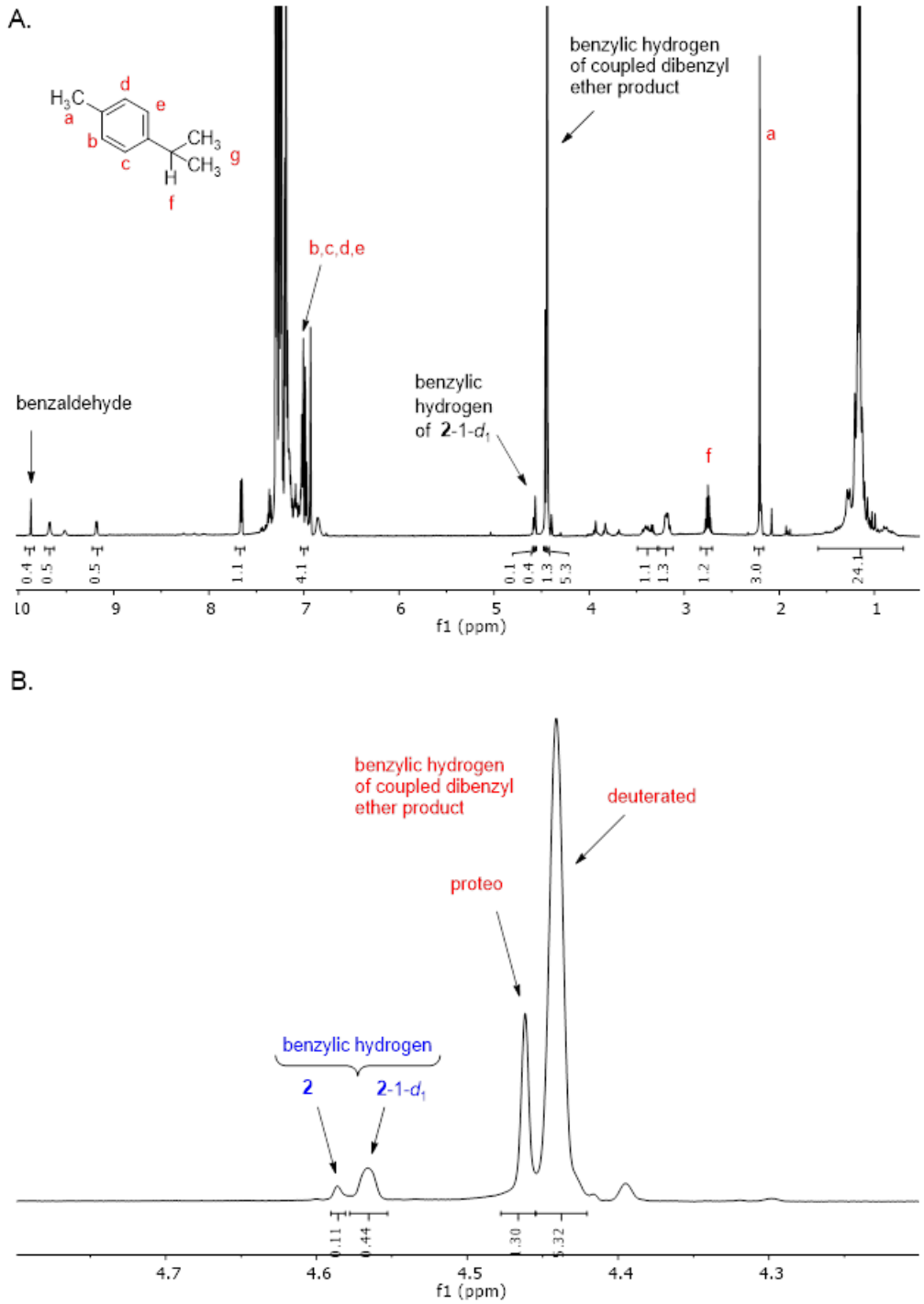


Figure S23. ^{1}H NMR of the crude reaction mixture after 48 h of heating at 110 °C in 1,2-dichlorobenzene-d_4. A) The spectrum clearly shows free cymene. B) The spectrum shows that the ratio of deuterated:non-deuterated starting material remaining and the ratio of deuterated:non-deuterated product are ca. 90%.

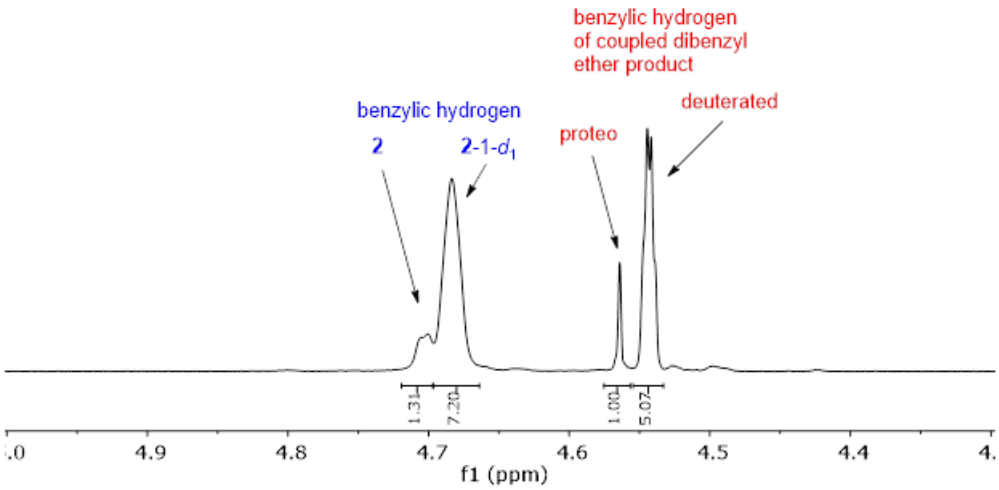
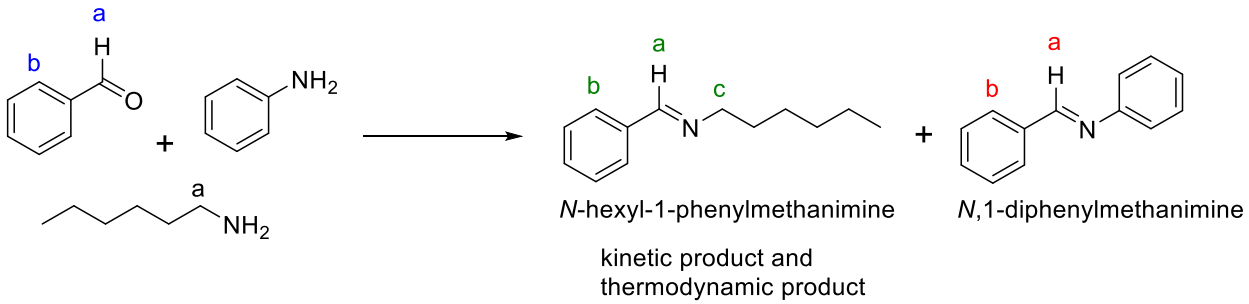


Figure S24. ^{1}H NMR spectrum of an aliquot of the crude reaction mixture after 12 h of heating at 110 °C under neat conditions (solvent: $CDCl_3$). The spectrum shows that the ratio of deuterated:non-deuterated starting material remaining and the ratio of deuterated:non-deuterated product are ca. 90%.

VI. Studies on the Selectivity of Coupling in the Presence of Unprotected Anilines

To probe the selectivity of amine coupling in the presence of unprotected anilines, we determined whether condensation of benzaldehyde with *n*-hexylamine (to form *N*-hexyl-1-phenylmethanimine) is kinetically and/or thermodynamically preferred over the condensation of benzaldehyde with aniline (to form *N*,1-diphenylmethanimine). Thus, benzaldehyde (25 µL, 0.24 mmol), *n*-hexylamine (34 µL, 0.26 mmol, 1.05 equiv), and aniline (24 µL, 0.26 mmol, 1.05 equiv) were mixed in 0.6 mL of benzene-d_6 in an NMR tube. ^{1}H NMR spectra were taken immediately after mixing and after 1 hour of heating at 80 °C (Figure S25). *N*-hexyl-1-phenylmethanimine is both the kinetic and the thermodynamic product. We also performed an experiment wherein the *N*,1-diphenylmethanimine is first pre-formed. Addition of *n*-hexylamine and heating to 80 °C for 1 hour gives *N*-hexyl-1-phenylmethanimine as the major product in a ratio similar to that observed in Figure S25 B.



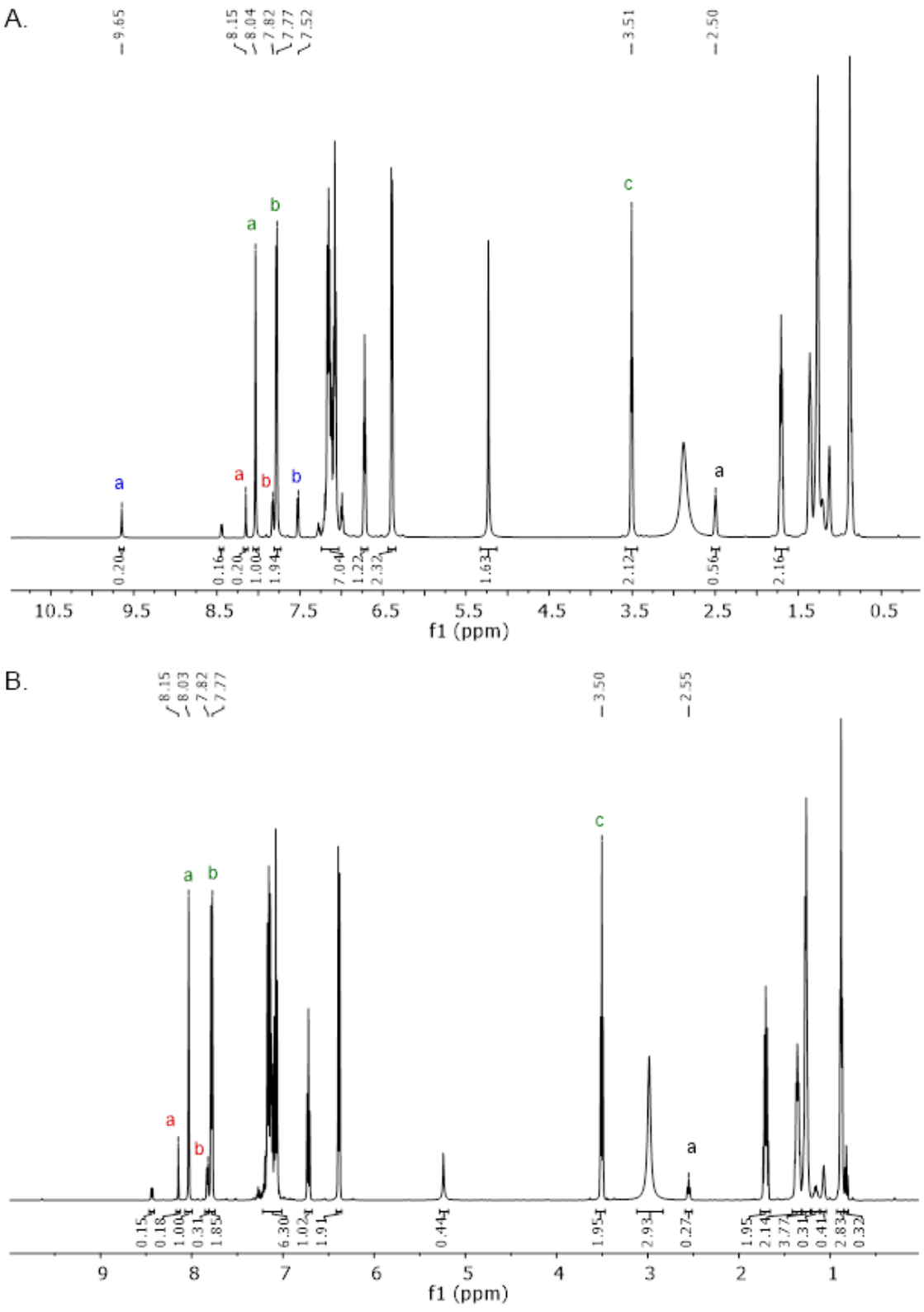


Figure S25. ^{1}H NMR spectra of a mixture of benzaldehyde, *n*-hexylamine, and aniline. A) Spectrum ca. 10 minutes after mixing. B) Spectrum after heating to 80 °C for 1 h.

Rate Constants of Aniline vs. Hexylamine Condensation to Benzaldehyde

To gain more insight into the rate-determining step of the coupling reaction, we measured rate constants to compare the rates of condensation of aniline and hexylamine to benzaldehyde. Thus, NMR kinetics data were obtained: condensation of hexylamine to benzaldehyde (k_{obs} = 2.5(1) × 10^{-3} s^{-1}) is ca. 7 times faster than the condensation of aniline to benzaldehyde (k_{obs} = 3.53(1) × 10^{-4} s^{-1}).

Because condensation of *n*-hexylamine to benzaldehyde is rapid, we used a procedure wherein *n*-hexylamine is added right before NMR kinetics data are obtained. A 0.1 M benzaldehyde solution in benzene (10.0 μL, 0.1 mmol benzaldehyde in 1.00 mL solution) was prepared using a volumetric flask and the solution transferred into an NMR tube. A ^{1}H NMR spectrum was taken. Then *n*-hexylamine (13.1 μL, 0.1 mmol, 1 equiv) was added and the kinetics data obtained (8 scans, 5 sec delay) at room temperature. 16 data points were obtained over a period of ca. 16 minutes (68% conversion). The integration as a function of time for 6 peaks (2 decaying peaks from starting material and 2 rising peaks from the product) were plotted. Fitting the data in kaleidagraph gave an average pseudo first order rate constant of 2.5(1) × 10^{-3} s^{-1}.

The rate constant for the condensation of aniline to benzaldehyde was performed using the same procedure. A 0.1 M benzaldehyde solution was prepared and a ^{1}H NMR spectrum taken. Then aniline (9.1 μL, 0.1 mmol, 1 equiv) was added and the kinetics data obtained (16 scans, 10 sec delay) every 10 minutes over a period of 3 hours (77% conversion). The integration as a function of time for five peaks (3 decaying peaks from starting material and 2 rising peaks from the product) were plotted. Fitting the data in kaleidagraph gave an average pseudo first order rate constant of 2.53(1) × 10^{-4} s^{-1}.

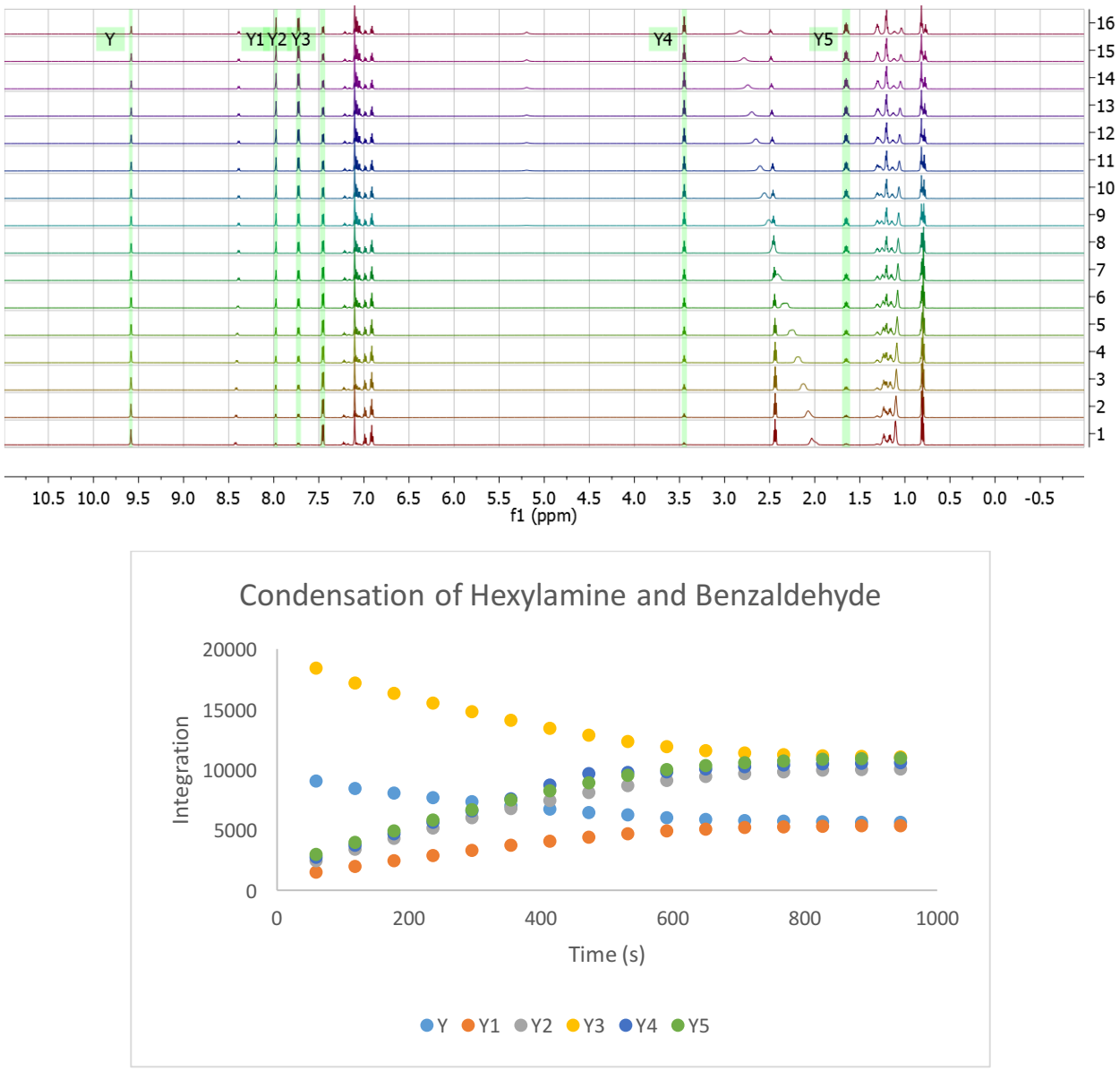


Figure S26. ^{1}H NMR kinetics experiment on the condensation of *n*-hexylamine and benzaldehyde at room temperature. Top: ^{1}H NMR stacked spectra obtained at time intervals of 59 seconds. Bottom: Plots of integration vs time for peaks Y – Y5 in the stacked spectra. Data were fitted in Kaleidagraph. Average $k_{obs} = 2.5(1) \times 10^{-3}$ s^{-1}.

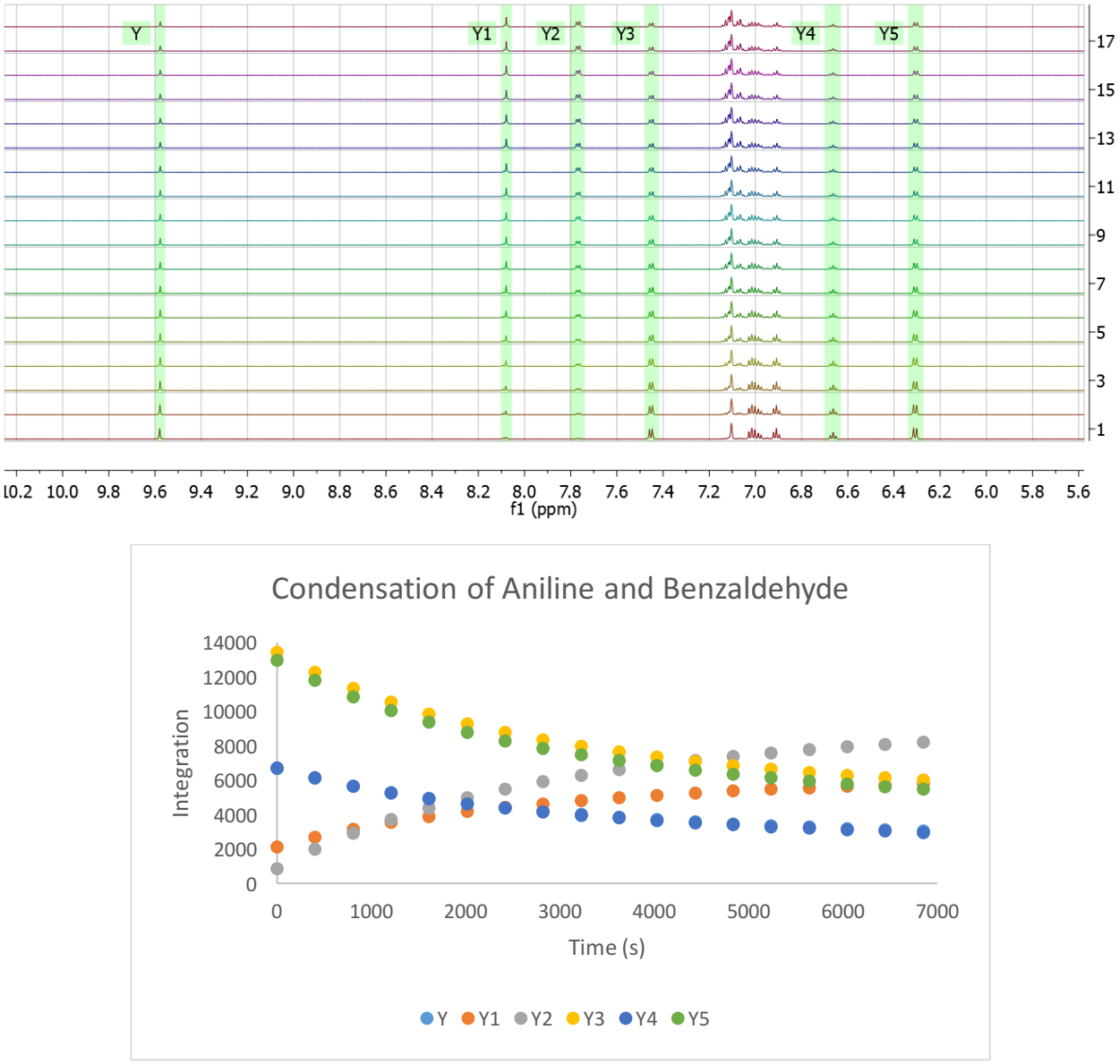


Figure S27. ^{1}H NMR kinetics experiment on the condensation of aniline and benzaldehyde at room temperature. Top: ^{1}H NMR stacked spectra obtained at time intervals of 10 minutes. Bottom: Plots of integration vs time for peaks Y – Y5 in the stacked spectra. Data were fitted in Kaleidagraph. Average $k_{obs} = 2.53(1) \times 10^{-4}$ s^{-1}.

VII. Deuterium Exchange between Benzyl Alcohol 2-1-d_1 and Di-*n*-hexylamine

To probe reversible dehydrogenatioin of di-*n*-hexylamine, we examined deuterium exchange between **2**-1-d_1 and di-*n*-hexylamine. Thus, a J-Young NMR tube was charged, in the drybox, with **2**-1-d_1 (ca. 93% D, 47 µL, 0.45 mmol), di-*n*-hexylamine (106 µL, 0.46 mmol), and precatalyst **1** (3.0 mg, 4.5 µmol). The J-Young tube was sealed and heated to 110 °C in an oil bath for 8 hours. Benzene-d_6 (0.5 ml) was then added and a ^{13}C NMR spectrum was obtained. Although deuterium incorporation into the di-*n*-hexylamine is not apparent (Figure S26), the peak for the non-deuterated benzylic carbon at 64.42 ppm slightly increases in integration. By contrast, heating **2**-1-d_1 and *n*-hexylamine for 2 hours leads to significantly more increase in the integration of the non-deuterated carbon (cf. Figure S13B). This indicates that dehydrogenation of the di-*n*-hexylamine is much slower than dehydrogenation of *n*-hexylamine. Thus, formation of the secondary amine product is favored.

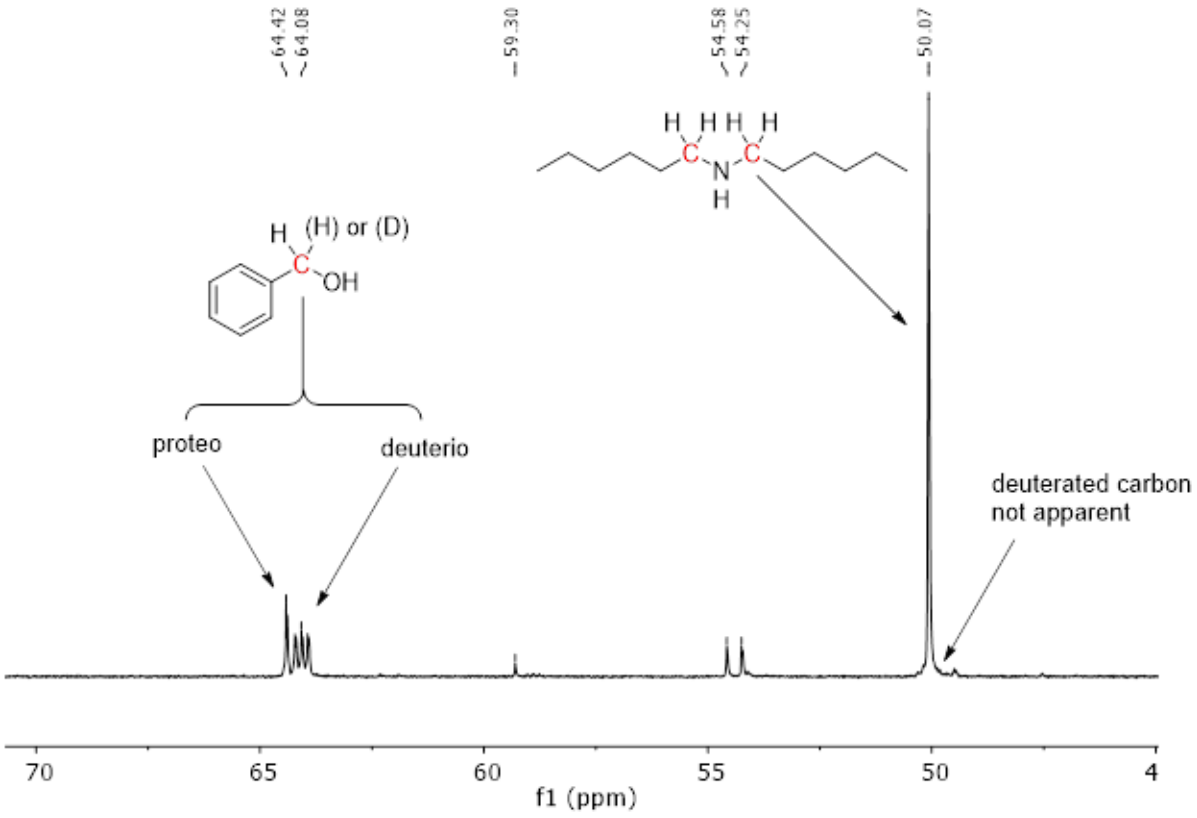


Figure S28. ^{13}C NMR (zoomed in) of a crude mixture of **2**-1-d_1 and di-n-hexylamine heated to 110 °C for 8 h in the presence of 1 mol% of precatalyst **1**.

VIII. Rates of Homocoupling of Benzyl Alcohol and *n*-Hexylamine

To gain more insight into the rate determining step of the reaction, we studied the rates of the homocoupling of benzyl alcohol into dibenzyl ether and the homocoupling of *n*-hexylamine into di-*n*-hexylamine. The kinetics of homocoupling were observed to be zero order in both benzyl alcohol and *n*-hexylamine with the homocoupling of benzyl alcohol being ca. 3 times faster ($3.5(7) \times 10^{-4}$ mMs^{-1} vs $1.0(6) \times 10^{-4}$ mMs^{-1}).

A stock solution of precatalyst **1** was used to keep catalyst concentration constant.

The rate of benzyl alcohol homocoupling was obtained by preparing a 5.0 mM stock solution of **1** (6.6 mg, 10 μmol in 2.00 mL) in 1,2-dichlorobenzene. A 550 μL (2.75 μmol, 5% catalyst loading) aliquot was transferred to a J-Young tube and benzyl alcohol (5.2 μL, 50 μmol, 90 mM) was added. A ^{1}H NMR kinetics experiment was performed at 109.4 °C (tempcal) over a period of 43 hours (Figure S29AB). A linear plot is observed for the disappearance of the starting material as well as the appearance of the product (Figure S29C) indicating zero order kinetics.

The rate of *n*-hexylamine homocoupling was obtained by transferring 550 μL (2.75 μmol, 5% catalyst loading) of the 5.0 mM stock solution of precatalyst **1** into a J-Young tube. *n*-Hexylamine (6.6 μL, 50 μmol, 90 mM) was then added. A ^{1}H NMR kinetics experiment was performed at 109.4 °C (tempcal) over a period of 43 hours (Figure S30A). A linear plot is observed (Figure S30B) for the disappearance of the starting material as well as the appearance of the product indicating zero order kinetics. Because the peaks of the starting material and product were overlapping, we deleted kinetics data wherein peaks overlapped.

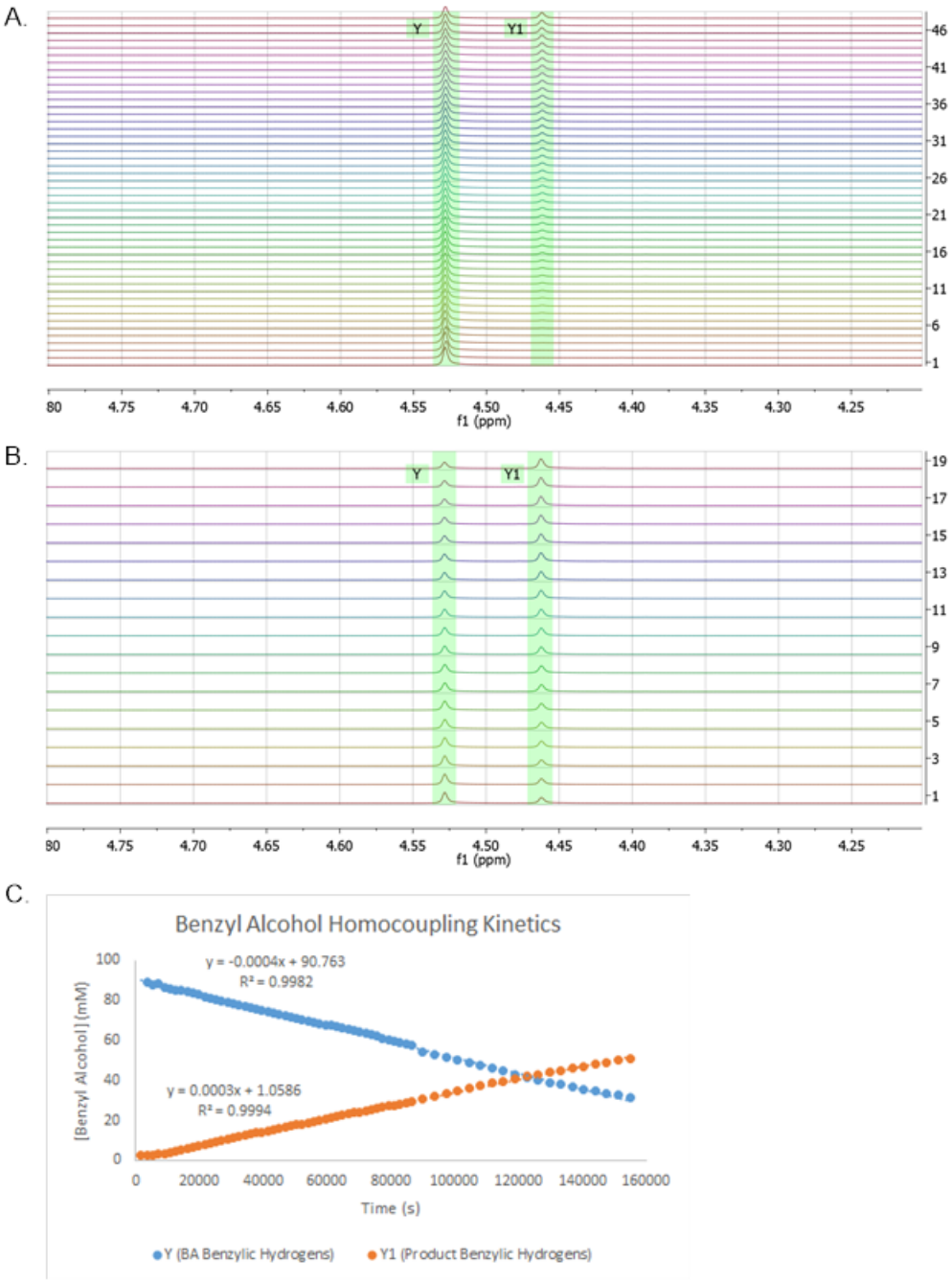
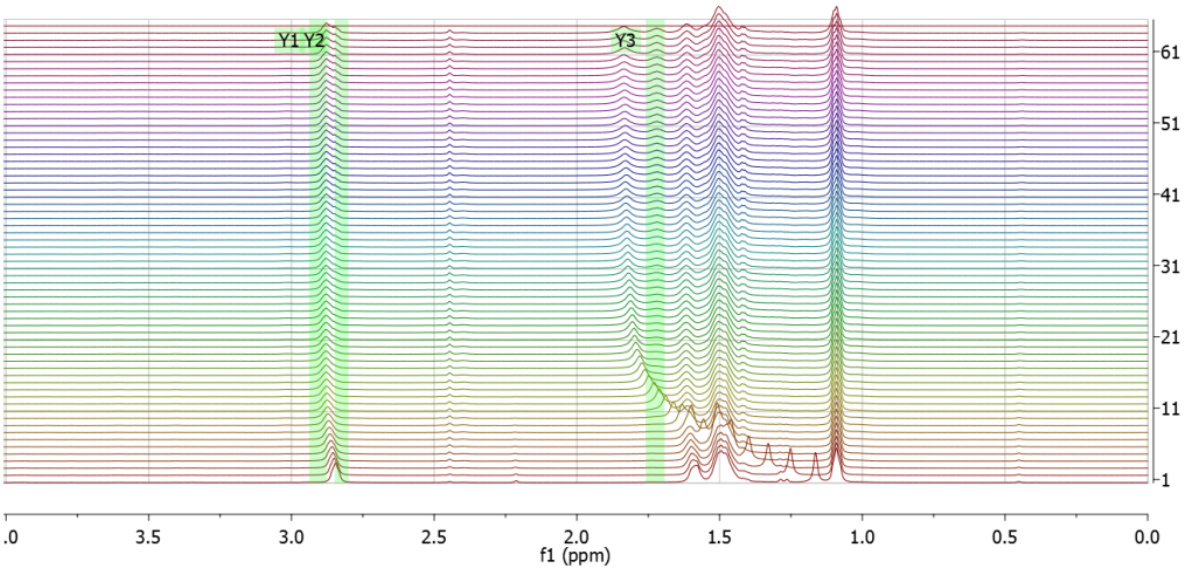


Figure S29. ^{1}H NMR kinetics experiment on the homocoupling of benzyl alcohol into dibenzyl ether at 109.4 °C (tempcal) over a total reaction time of 43 hours. A. ^{1}H NMR stacked spectra obtained over the first 24 hours at 30-minute time intervals. B. ^{1}H NMR stacked spectra obtained over the next 19 hours at 60-minute time intervals. C. Plots of integration vs time for peaks Y and Y1 in the stacked spectra which correspond to the benzylic hydrogens of the starting material and product, respectively. Average $k_{obs} = 3.5(7) \times 10^{-4}$ mM s^{-1}.

A.



B.

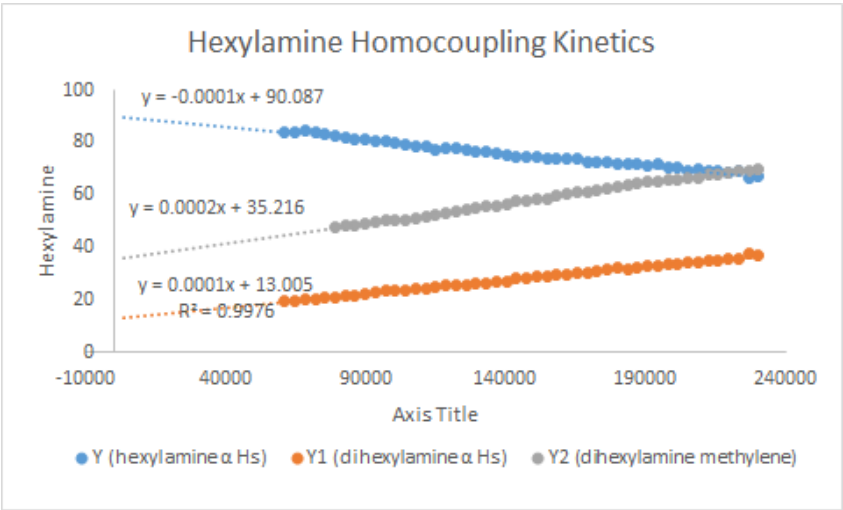
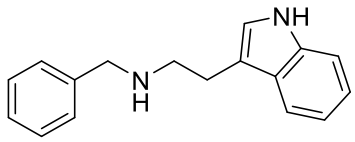


Figure S30. ^{1}H NMR kinetics experiment on the homocoupling of *n*-hexylamine into di-*n*-hexylamine at 109.4 °C (tempcal) over a total reaction time of 64 hours. A. ^{1}H NMR stacked spectra obtained at 60-minute time intervals. Because peaks overlapped over the 16 hours, the data for these times were omitted. B. Plots of concentration vs time for peaks Y (hexylamine α hydrogens), Y1 (dihexylamine α hydrogens) and Y2 (dihexylamine methylene hydrogens) in the stacked spectra. Average $k_{obs} = 1.0(6) \times 10^{-4}$ mM s^{-1}.

IX. NMR Spectra



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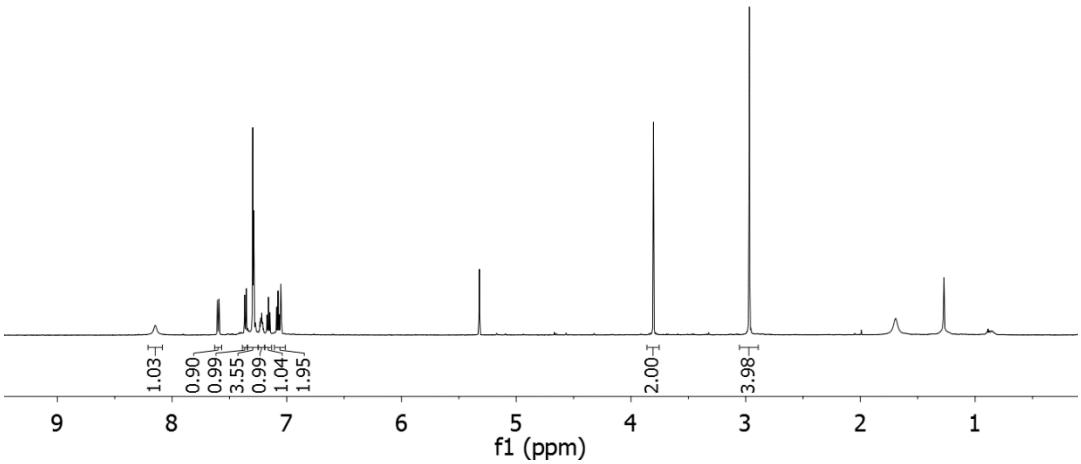
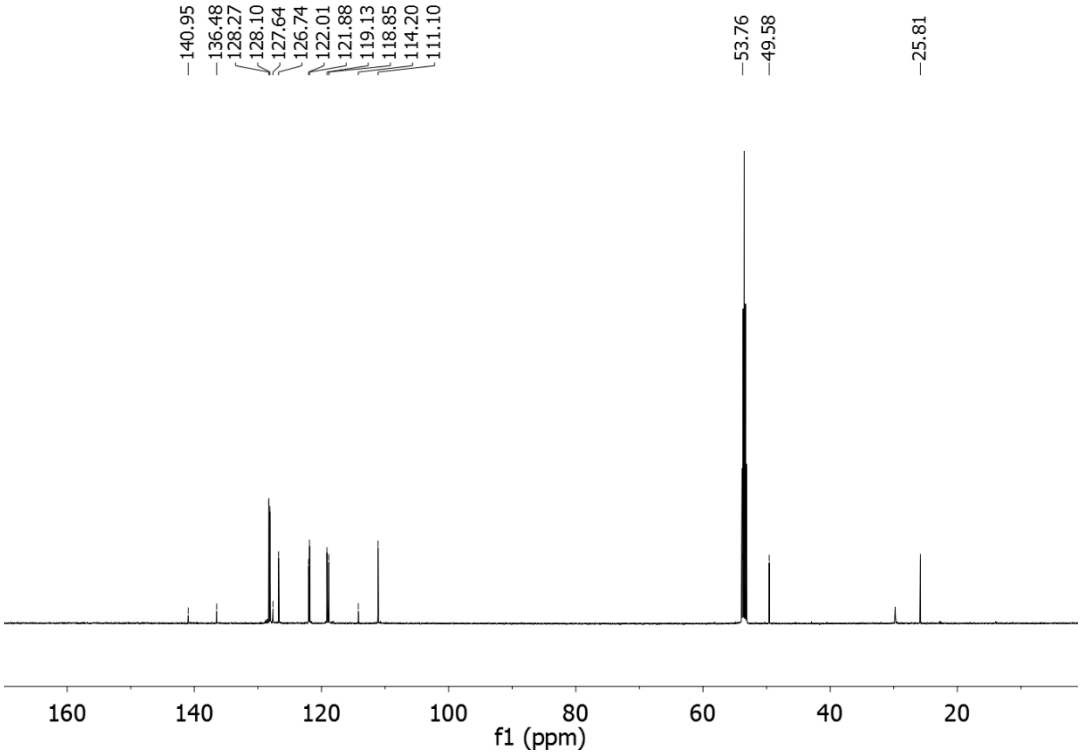
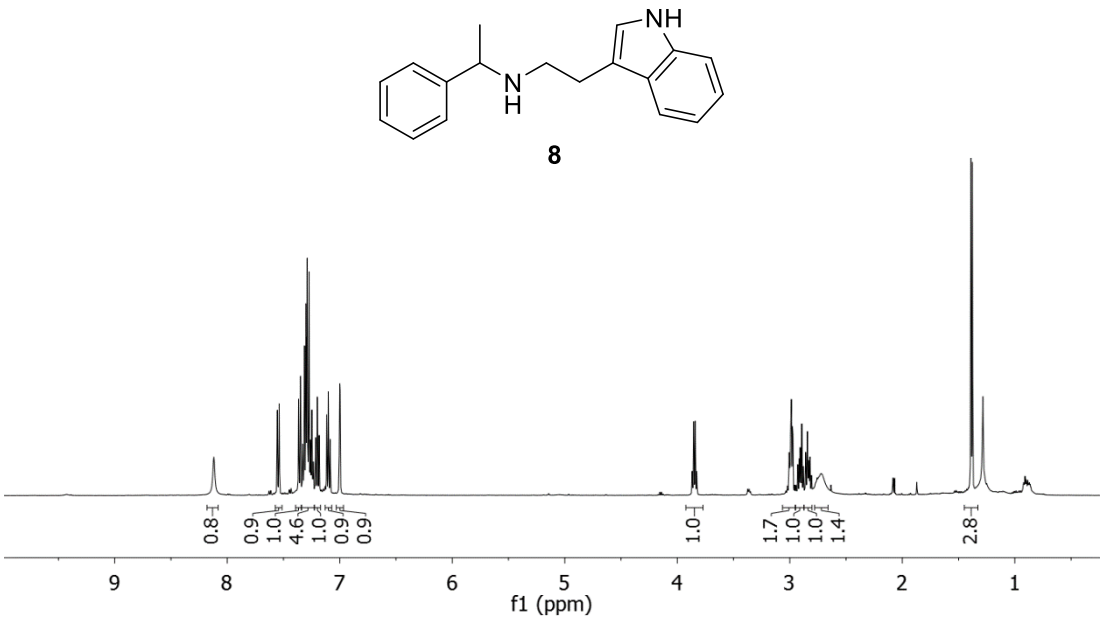


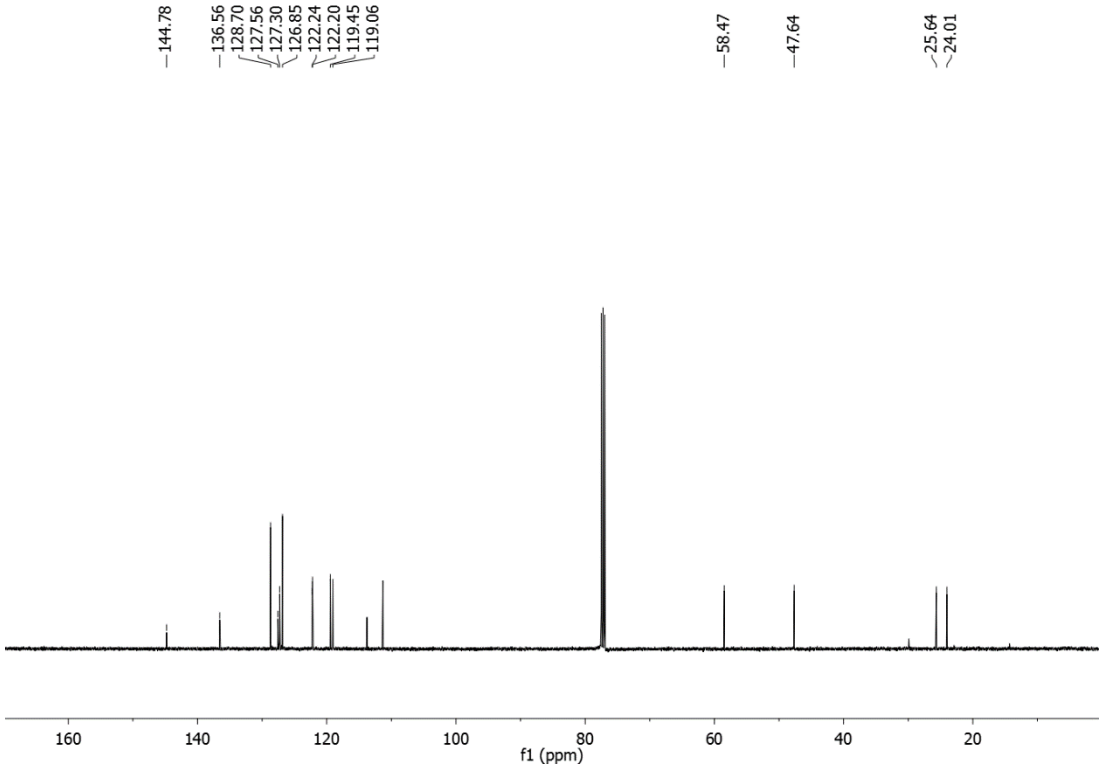
^{1}H NMR spectrum of compound **7** at 25 °C in CD_2Cl_2.



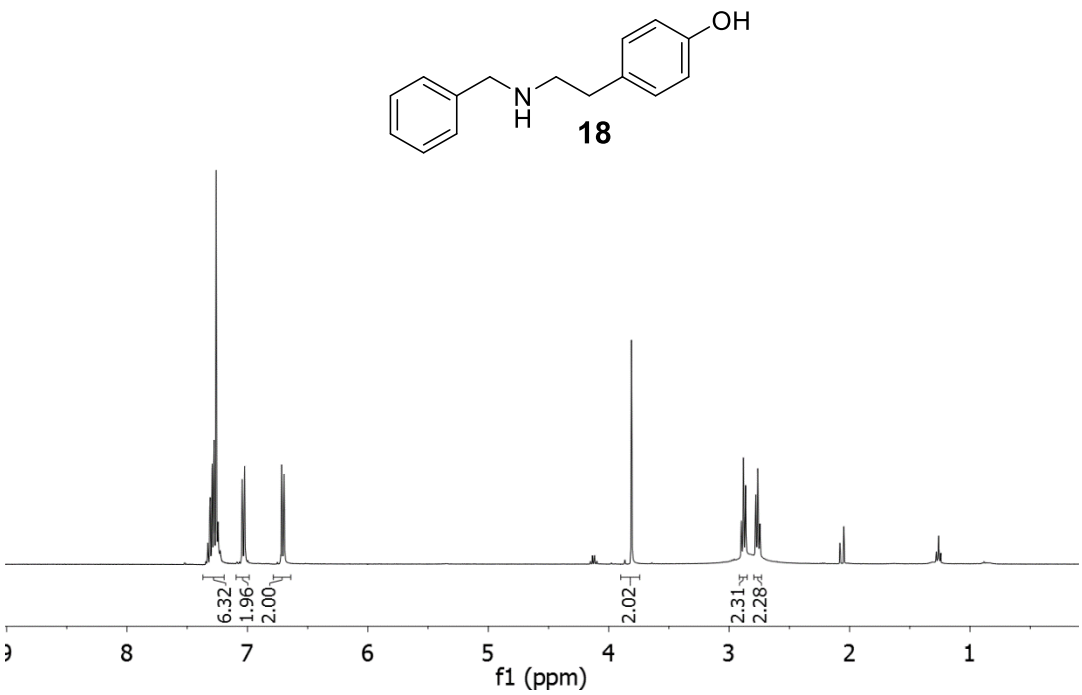
^{13}C NMR spectrum of compound **7** at 25 °C in CD_2Cl_2.



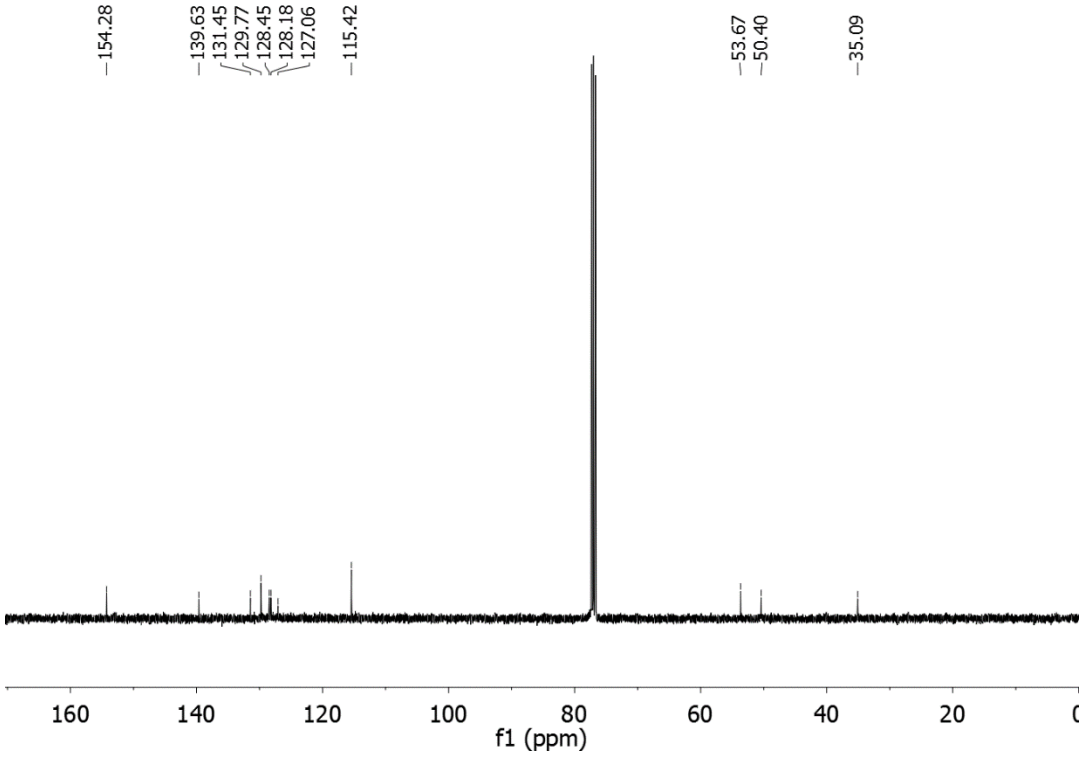
^{1}H NMR spectrum of compound **8** at 25 °C in $CDCl_3$.



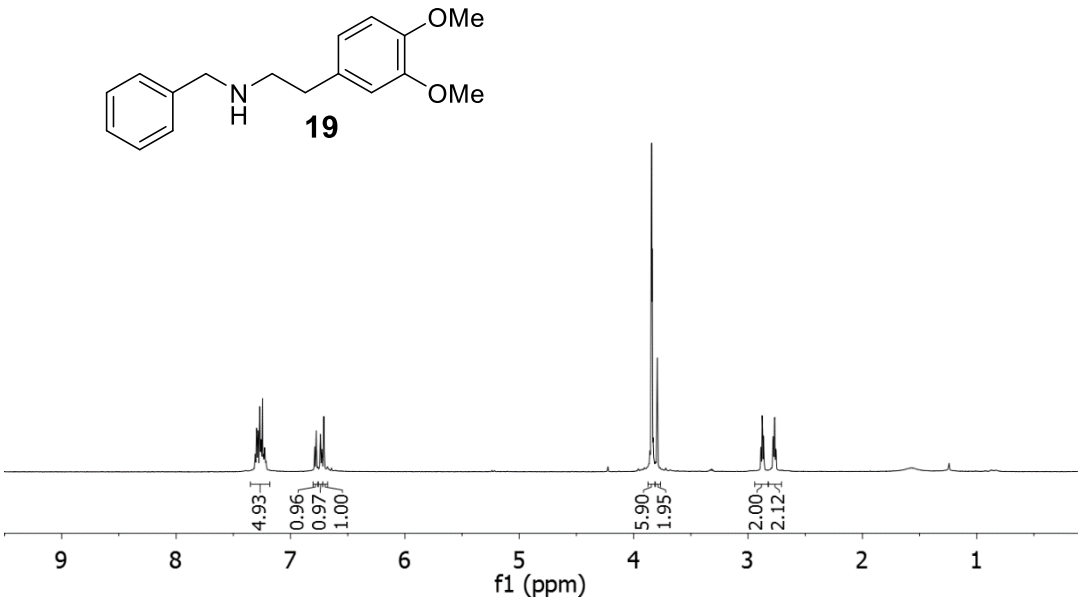
^{13}C NMR spectrum of compound **8** at 25 °C in $CDCl_3$.



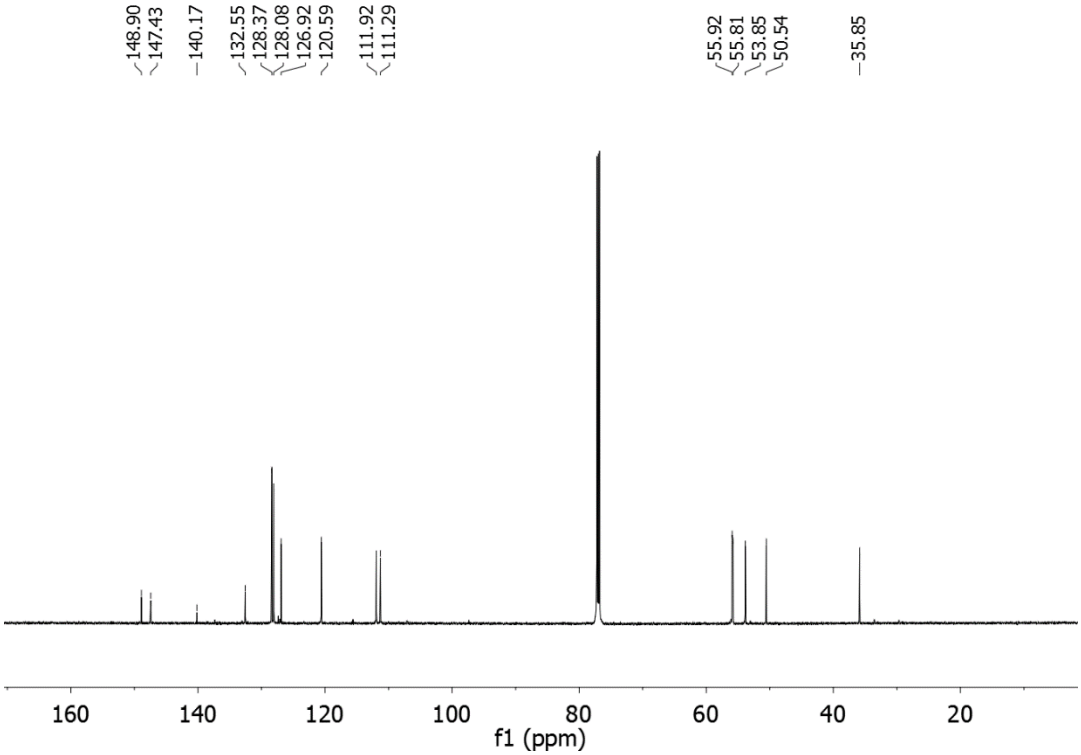
^{1}H NMR spectrum of compound **18** at 25 °C in $CDCl_3$.



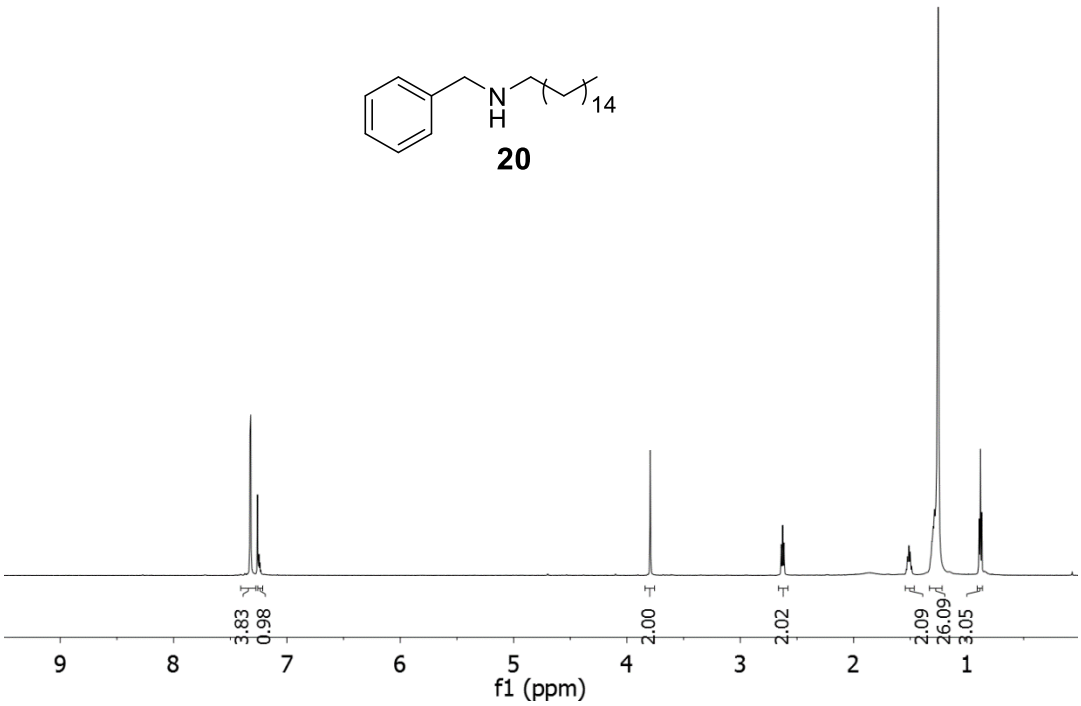
^{13}C NMR spectrum of compound **18** at 25 °C in $CDCl_3$.



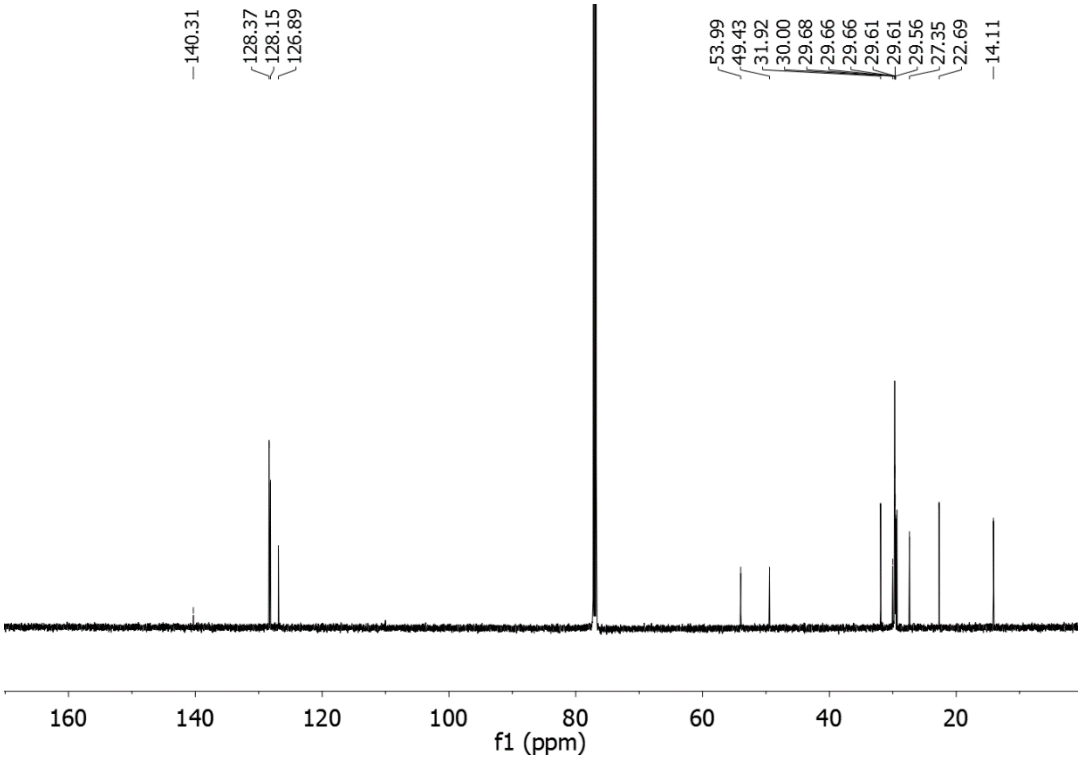
^{1}H NMR spectrum of compound **19** at 25 °C in $CDCl_3$.



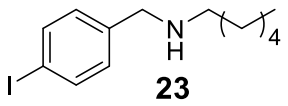
^{13}C NMR spectrum of compound **19** at 25 °C in $CDCl_3$.



^{1}H NMR spectrum of compound **20** at 25 °C in $CDCl_3$.



^{13}C NMR spectrum of compound **20** at 25 °C in $CDCl_3$.



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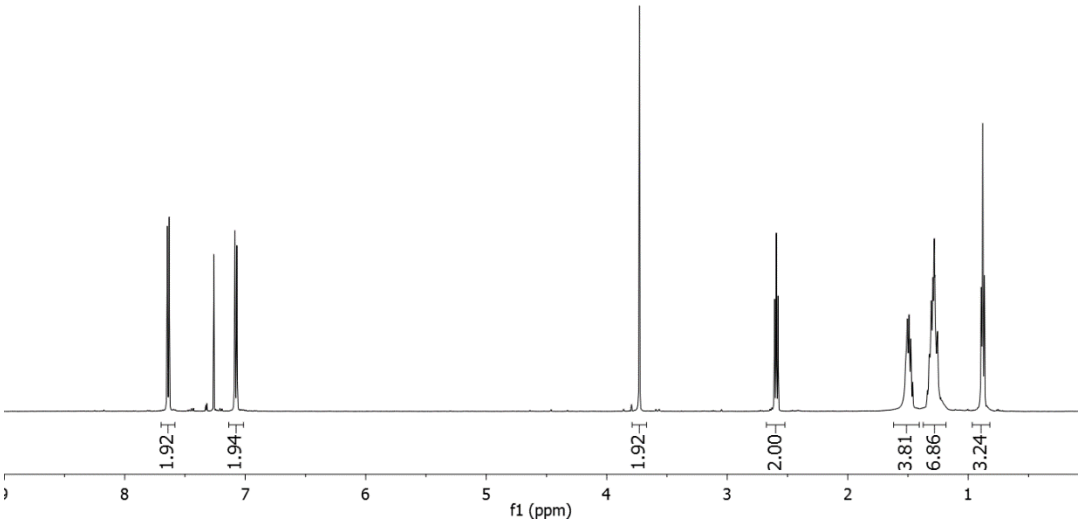
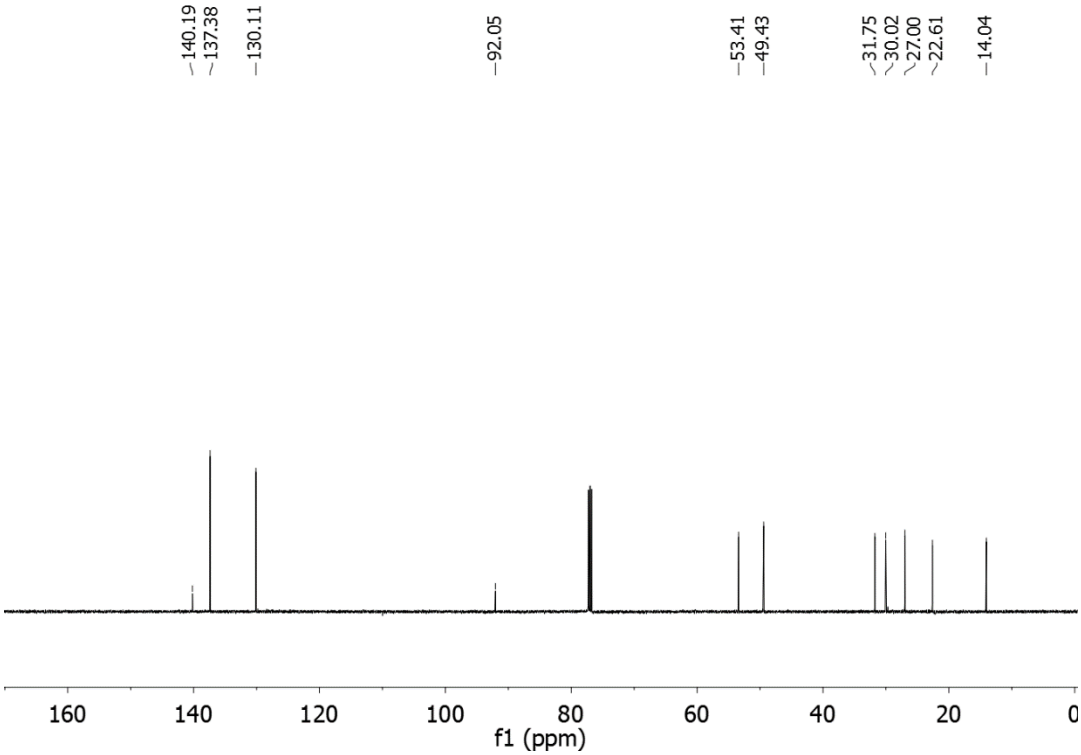
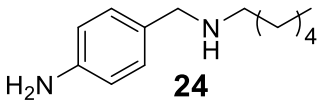


^{1}H NMR spectrum of compound **23** at 25 °C in $CDCl_3$.



^{13}C NMR spectrum of compound **23** at 25 °C in $CDCl_3$.



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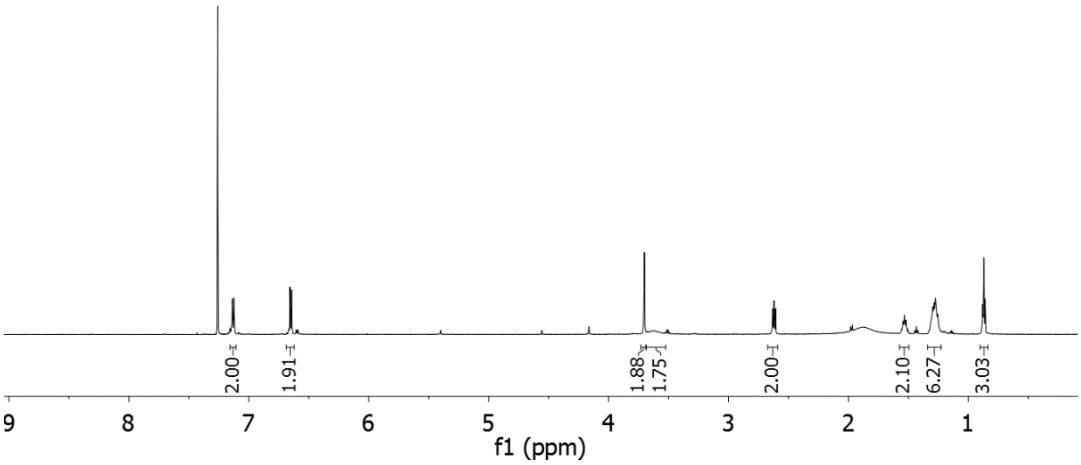
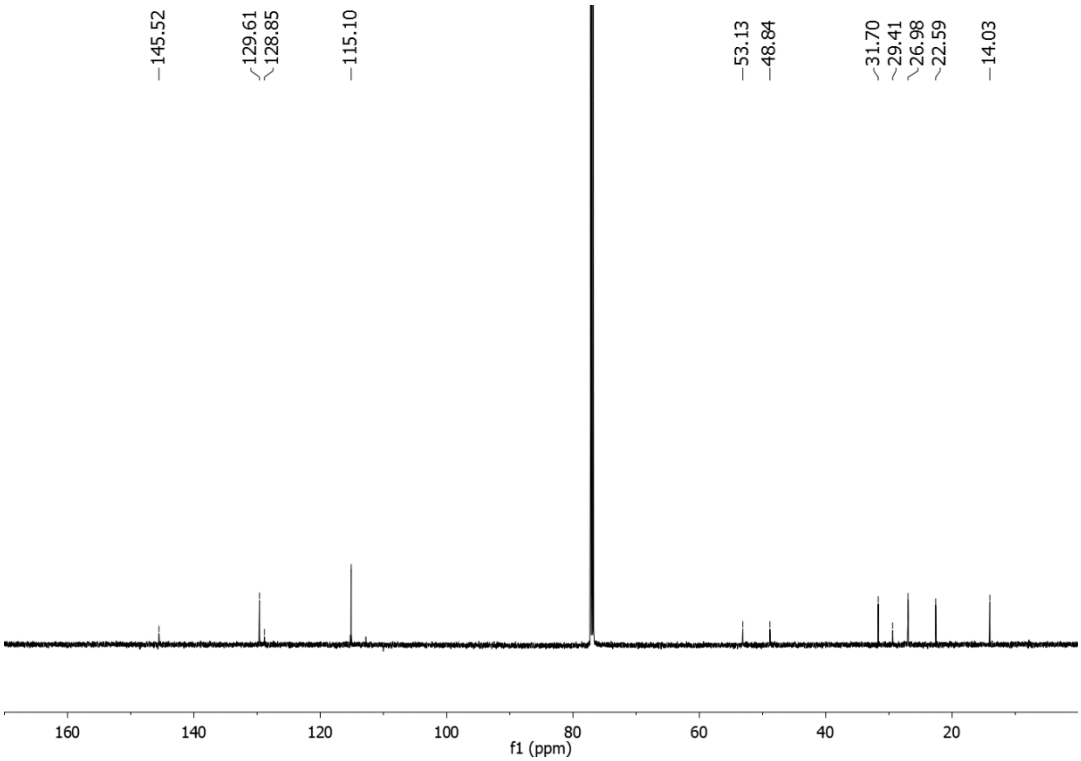
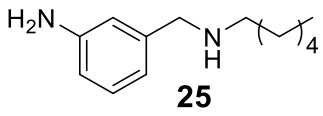


^{1}H NMR spectrum of compound **24** at 25 °C in $CDCl_3$.



^{13}C NMR spectrum of compound **24** at 25 °C in $CDCl_3$.



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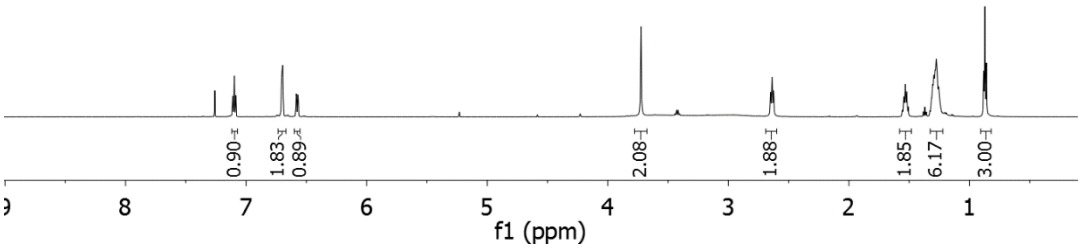
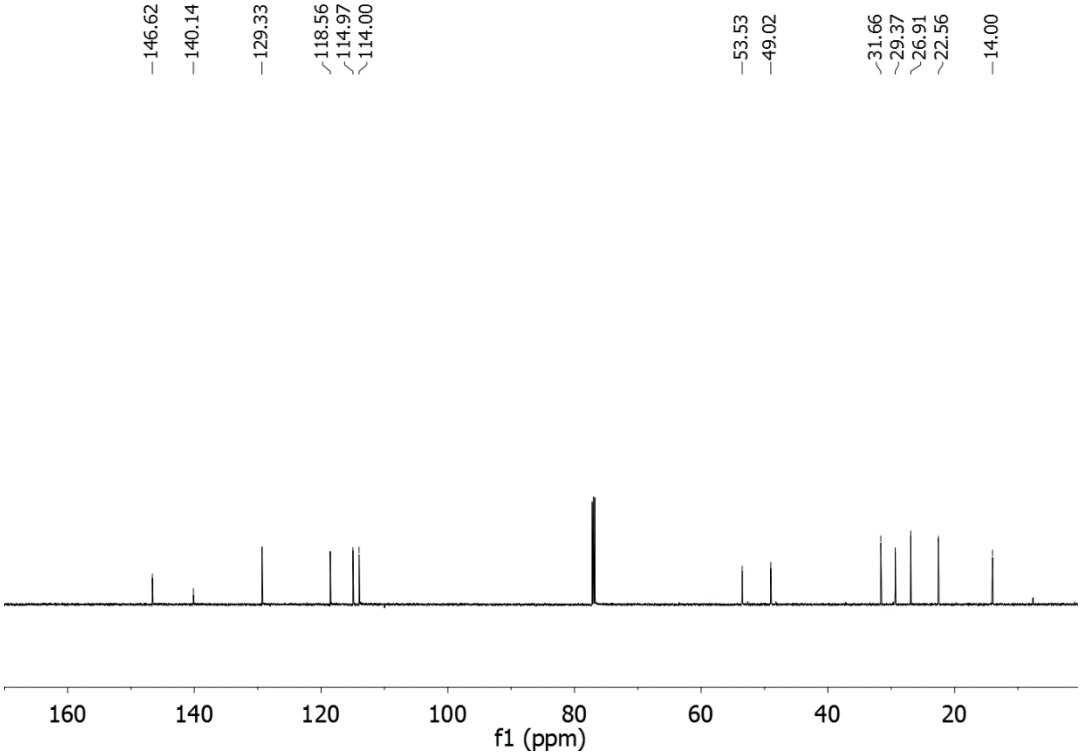
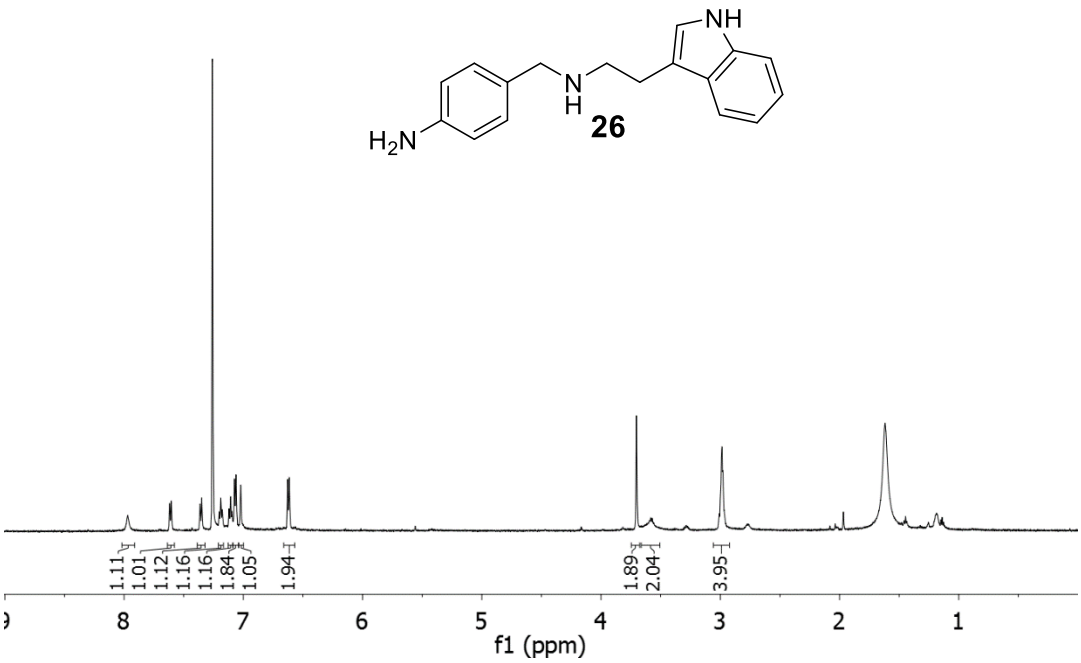


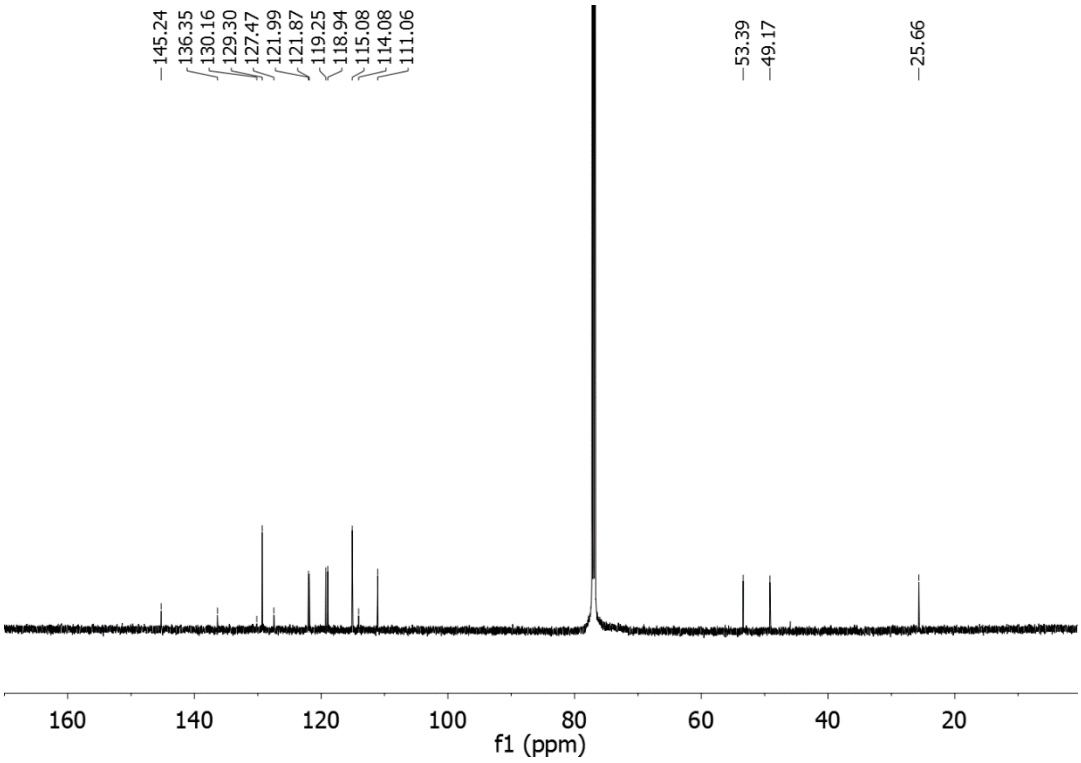
^{1}H NMR spectrum of compound **25** at 25 °C in $CDCl_3$.



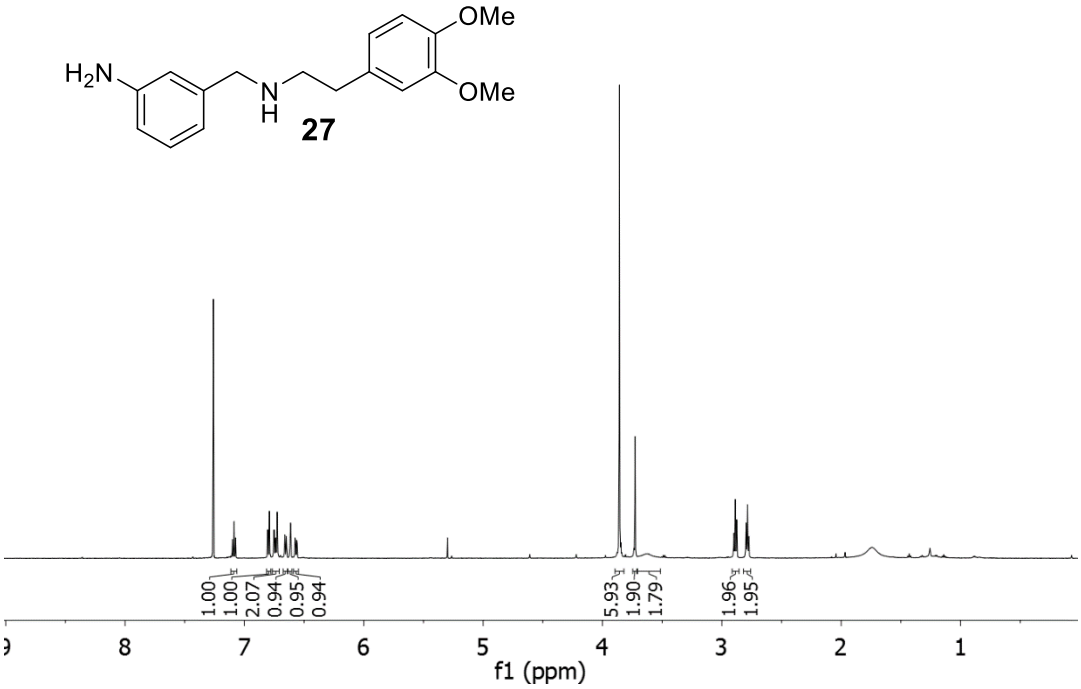
^{13}C NMR spectrum of compound **25** at 25 °C in $CDCl_3$.



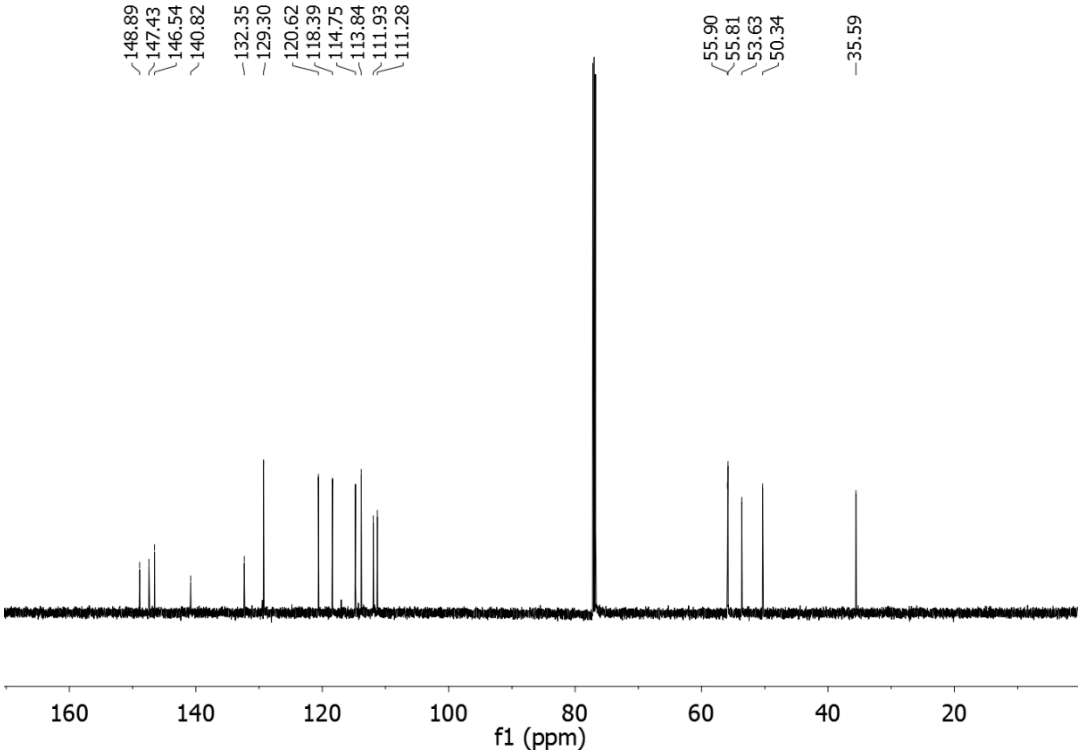
^{1}H NMR spectrum of compound **26** at 25 °C in $CDCl_3$.



^{13}C NMR spectrum of compound **26** at 25 °C in $CDCl_3$.



^{1}H NMR spectrum of compound **27** at 25 °C in $CDCl_3$.



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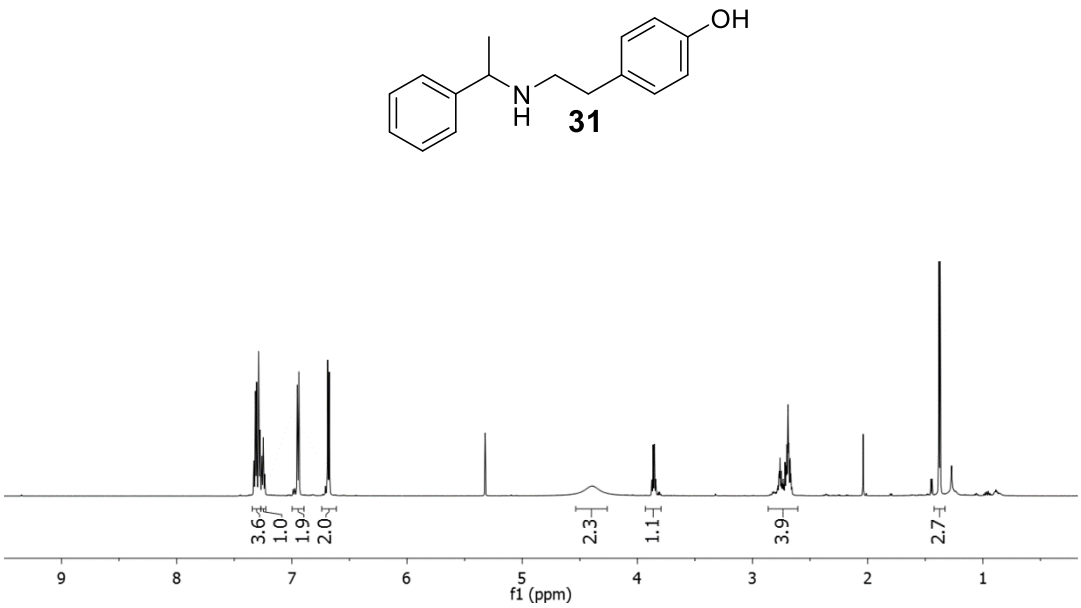
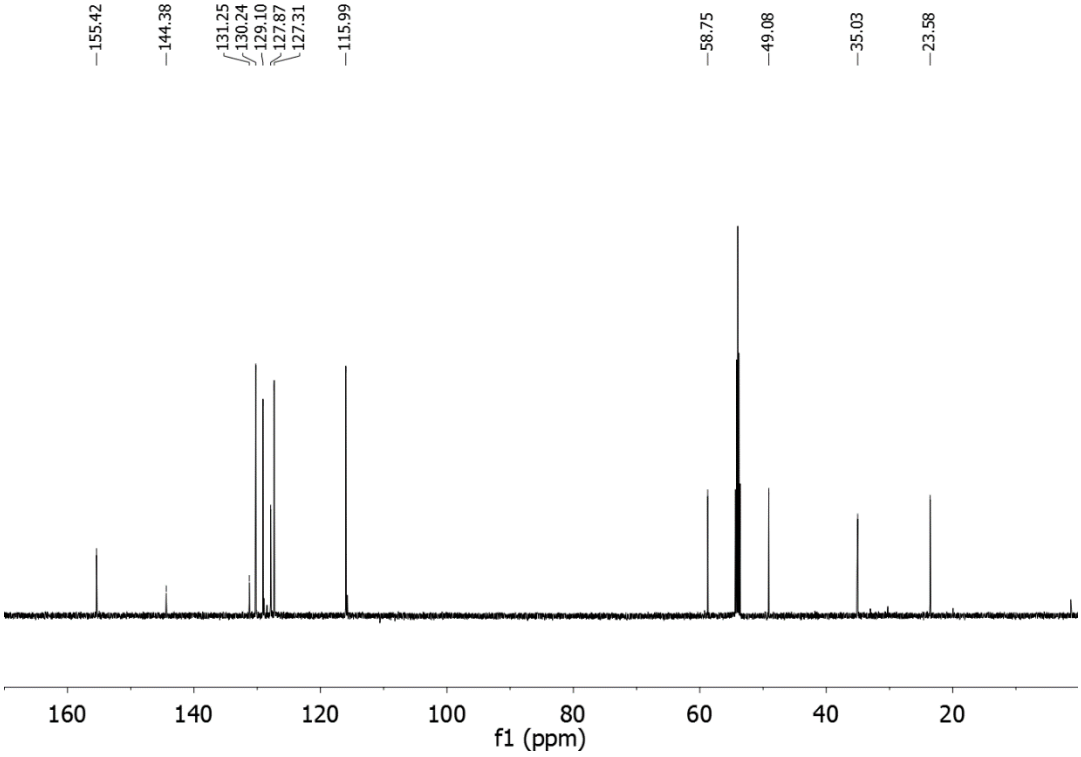
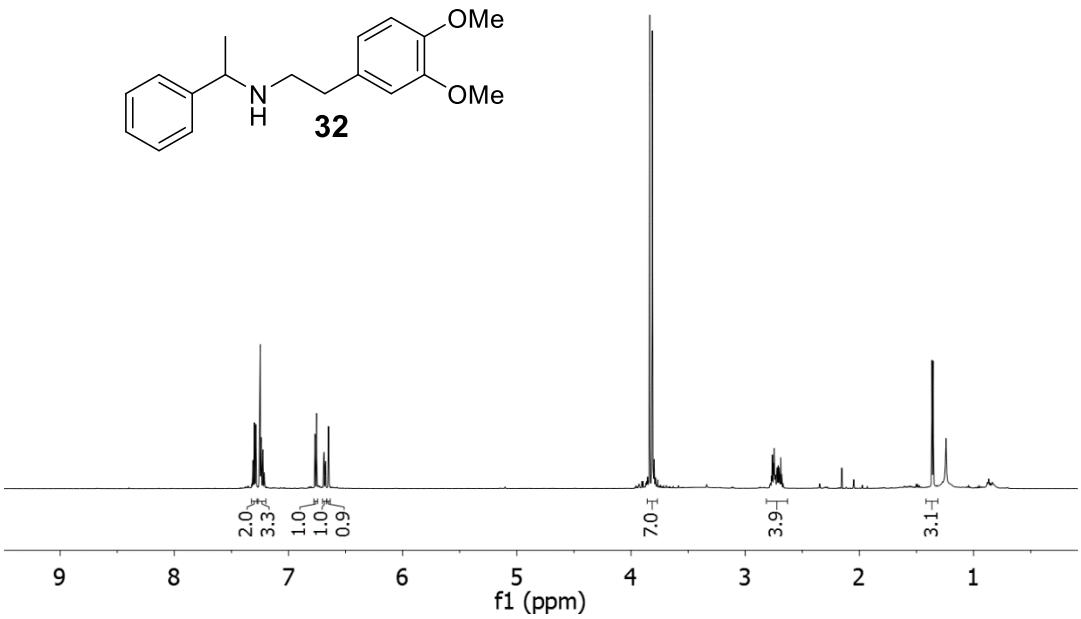


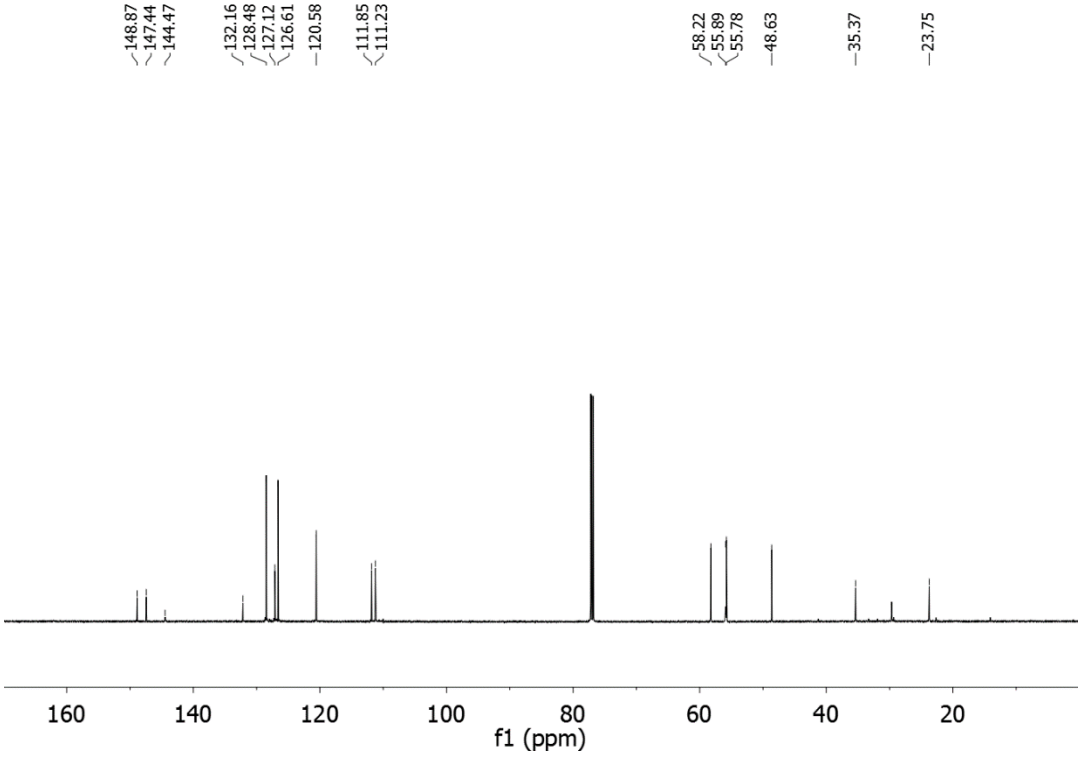
^{1}H NMR spectrum of compound **31** at 25 °C in CD_2Cl_2.



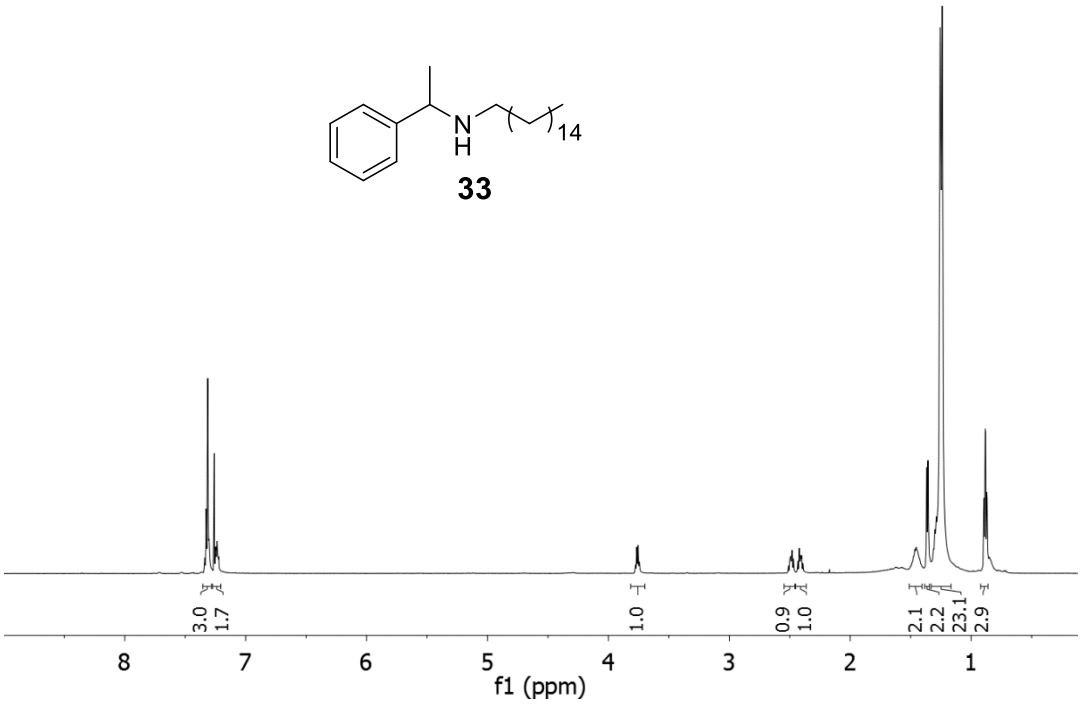
^{13}C NMR spectrum of compound **31** at 25 °C in CD_2Cl_2.



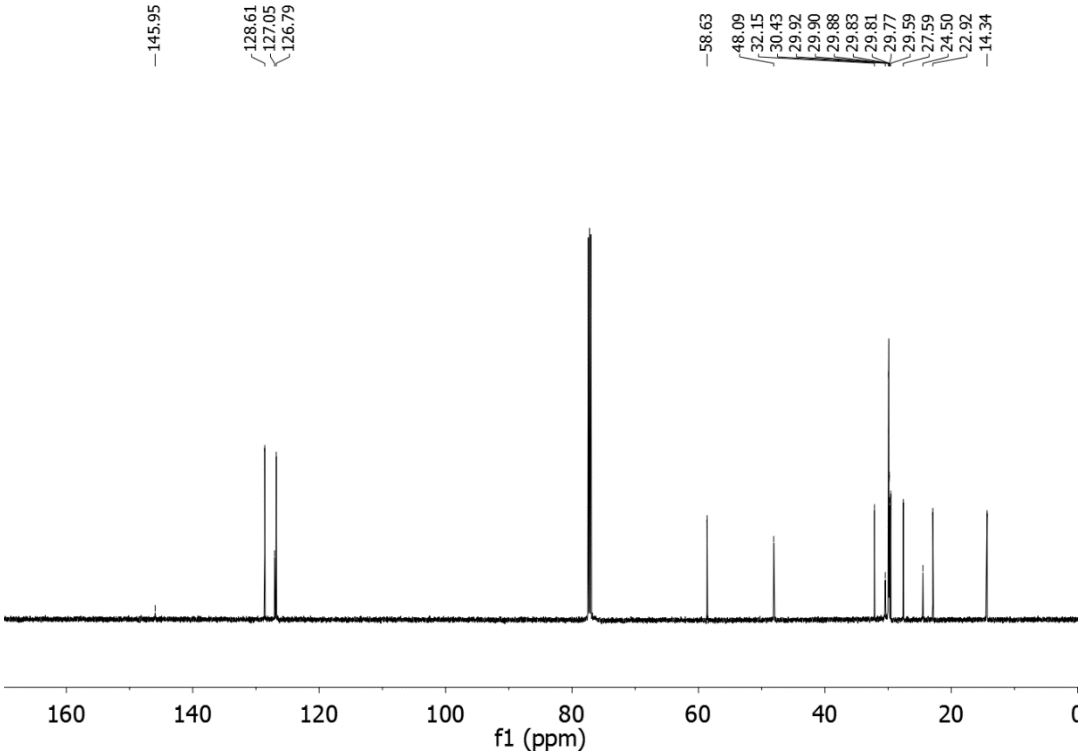
^{1}H NMR spectrum of compound **32** at 25 °C in $CDCl_3$.



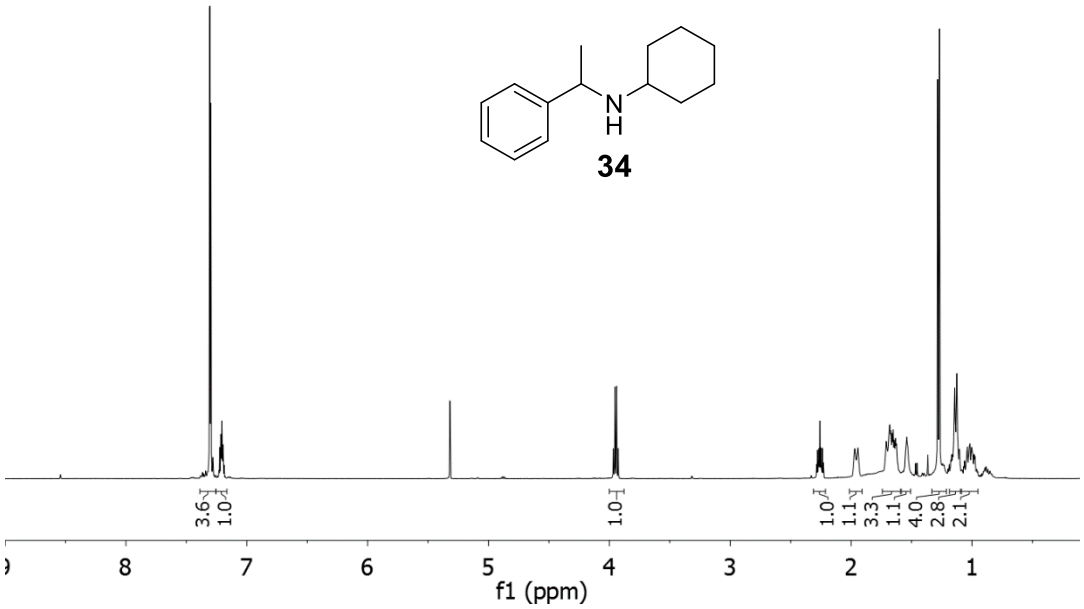
^{13}C NMR spectrum of compound **32** at 25 °C in $CDCl_3$.



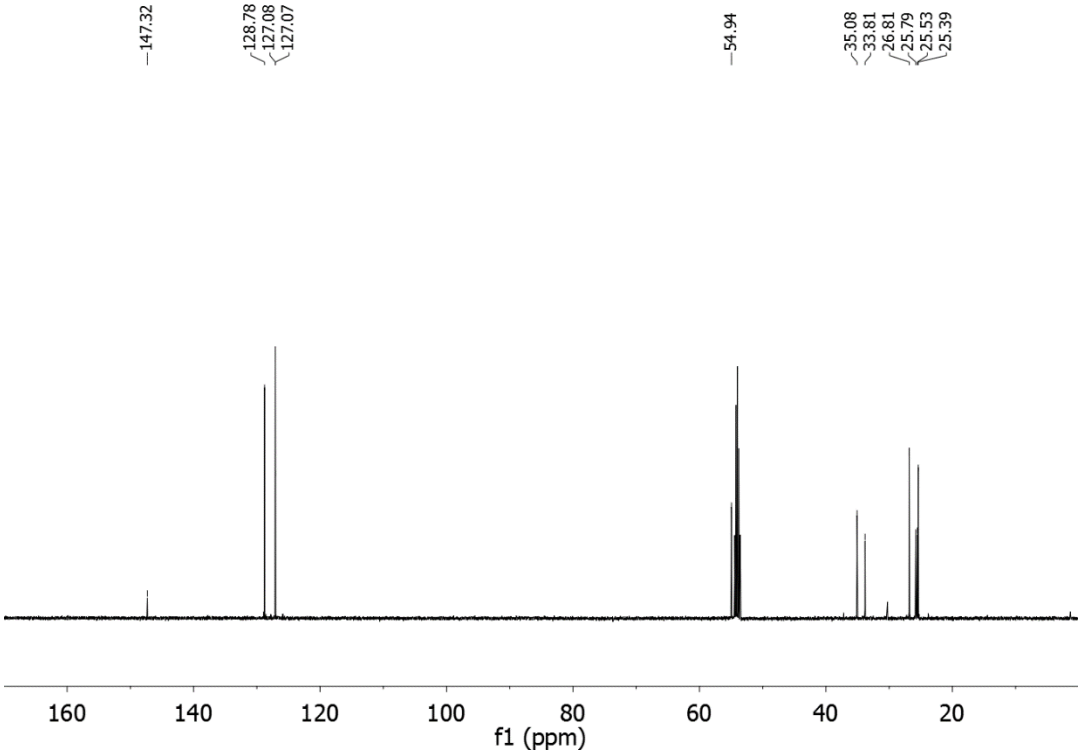
^{1}H NMR spectrum of compound **33** at 25 °C in $CDCl_3$.



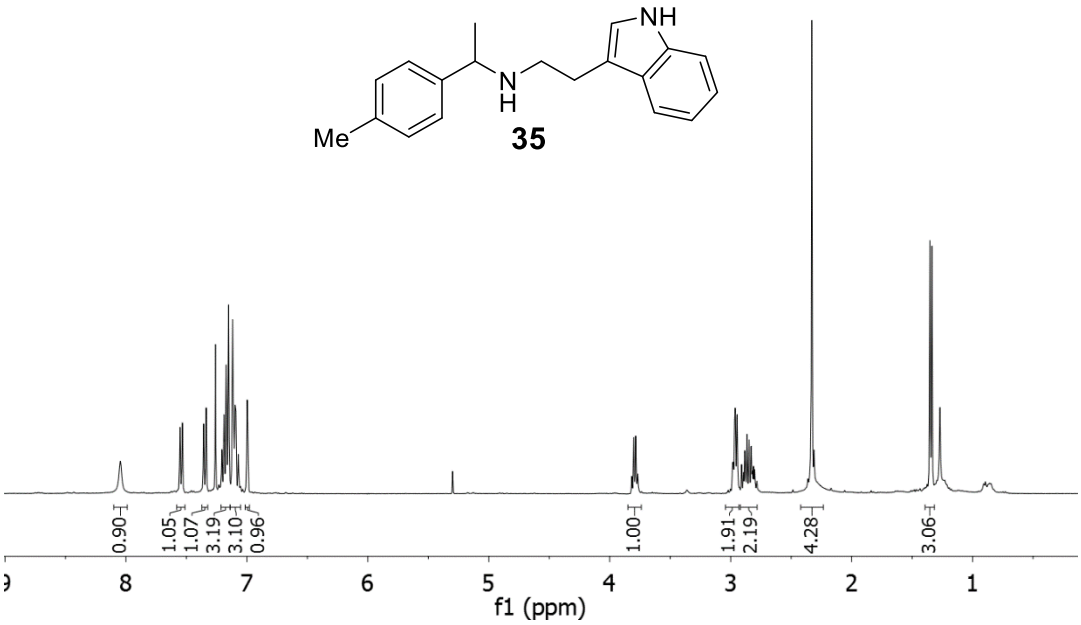
^{13}C NMR spectrum of compound **33** at 25 °C in $CDCl_3$.



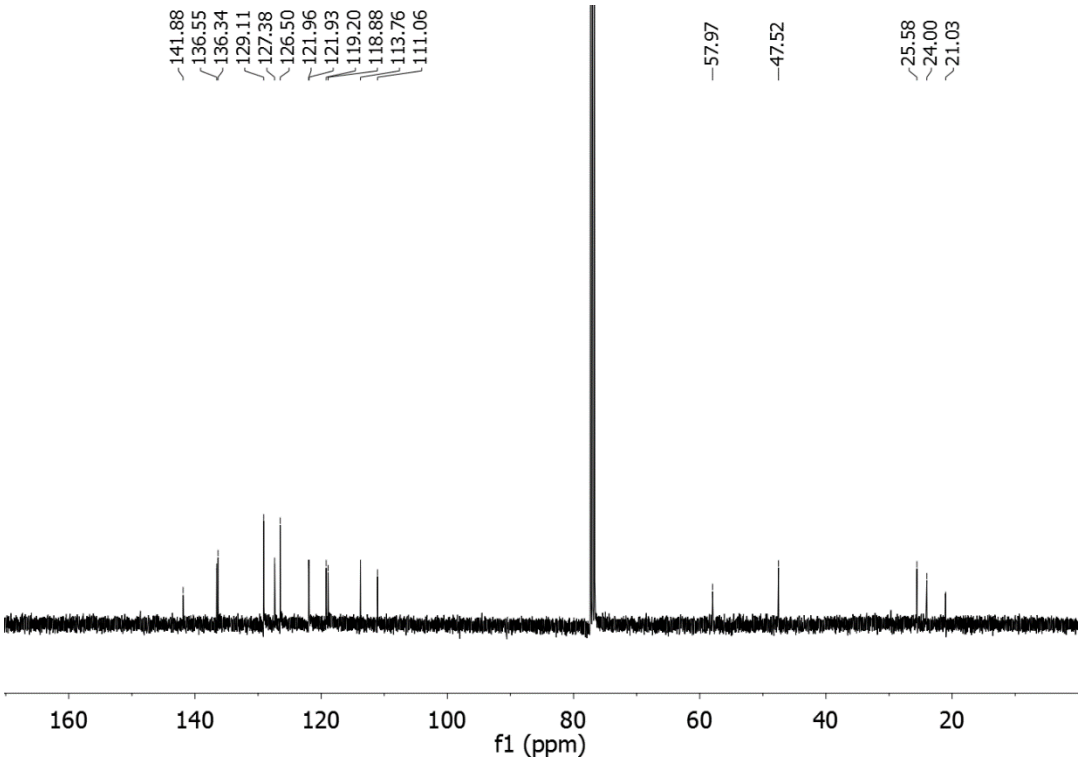
^{1}H NMR spectrum of compound **34** at 25 °C in CD_2Cl_2.



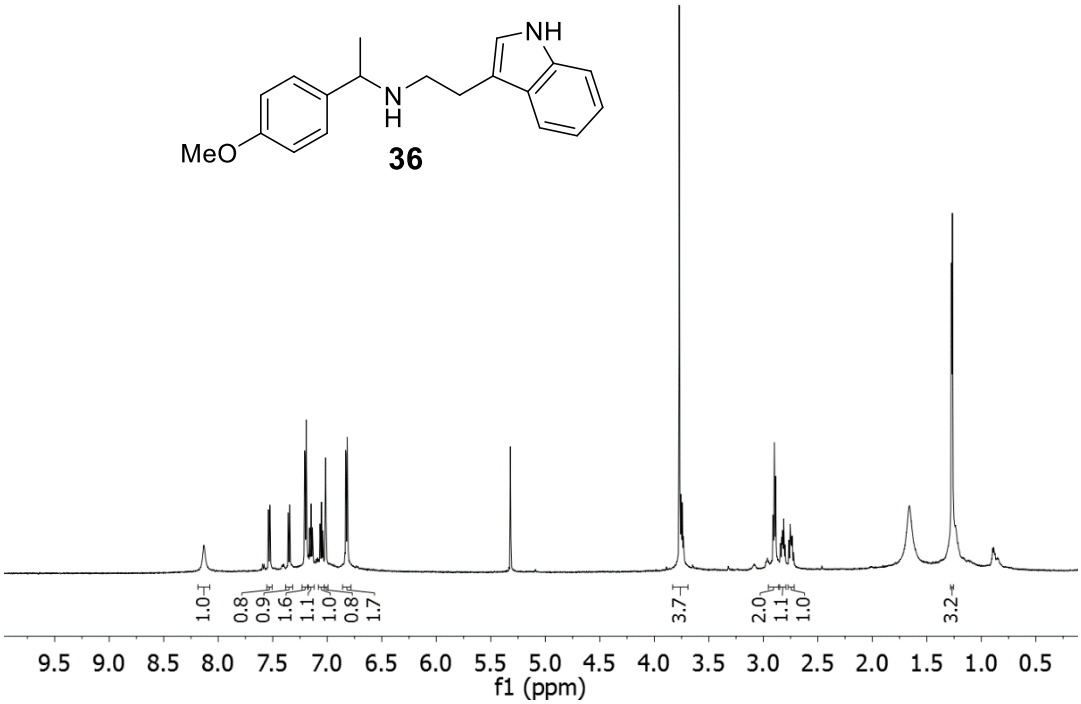
^{13}H NMR spectrum of compound **34** at 25 °C in CD_2Cl_2.



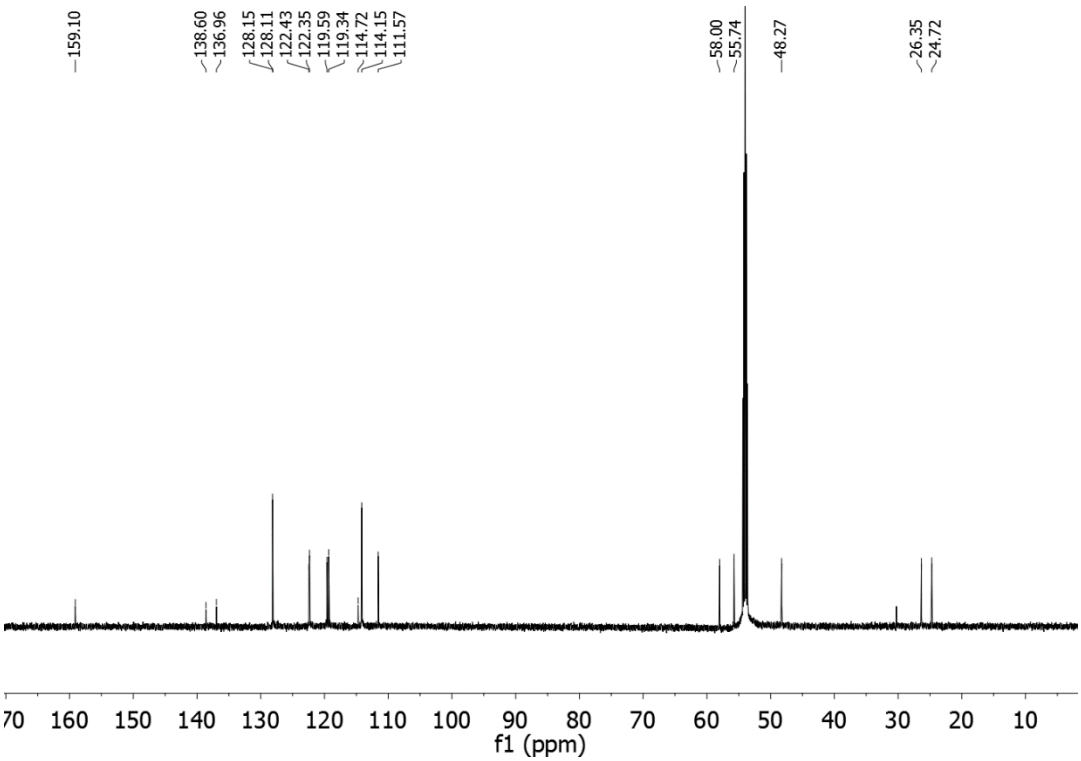
^{1}H NMR spectrum of compound **35** at 25 °C in $CDCl_3$.



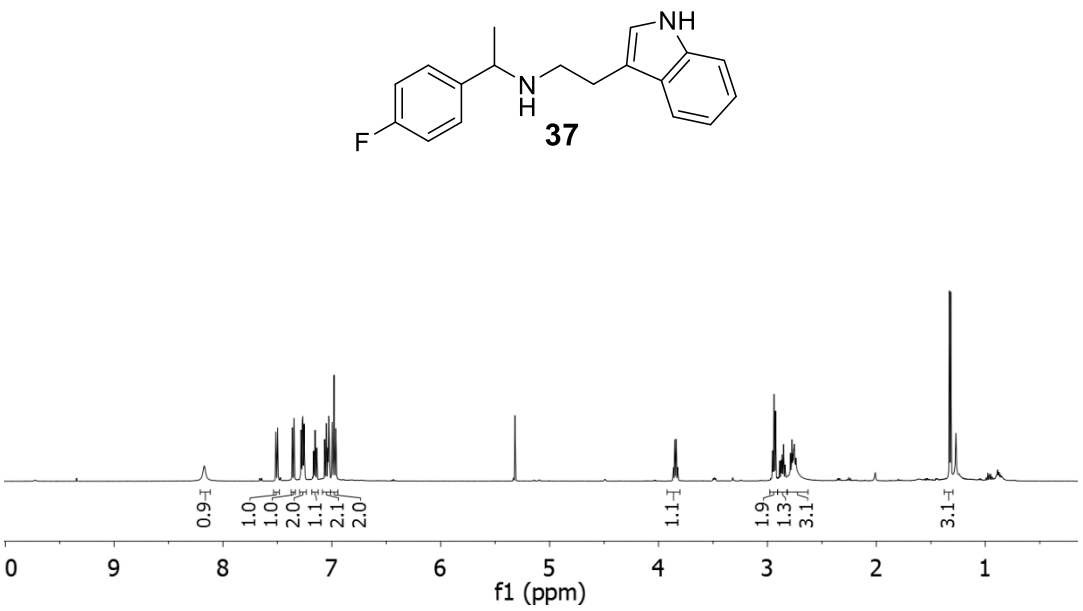
^{13}C NMR spectrum of compound **35** at 25 °C in $CDCl_3$.



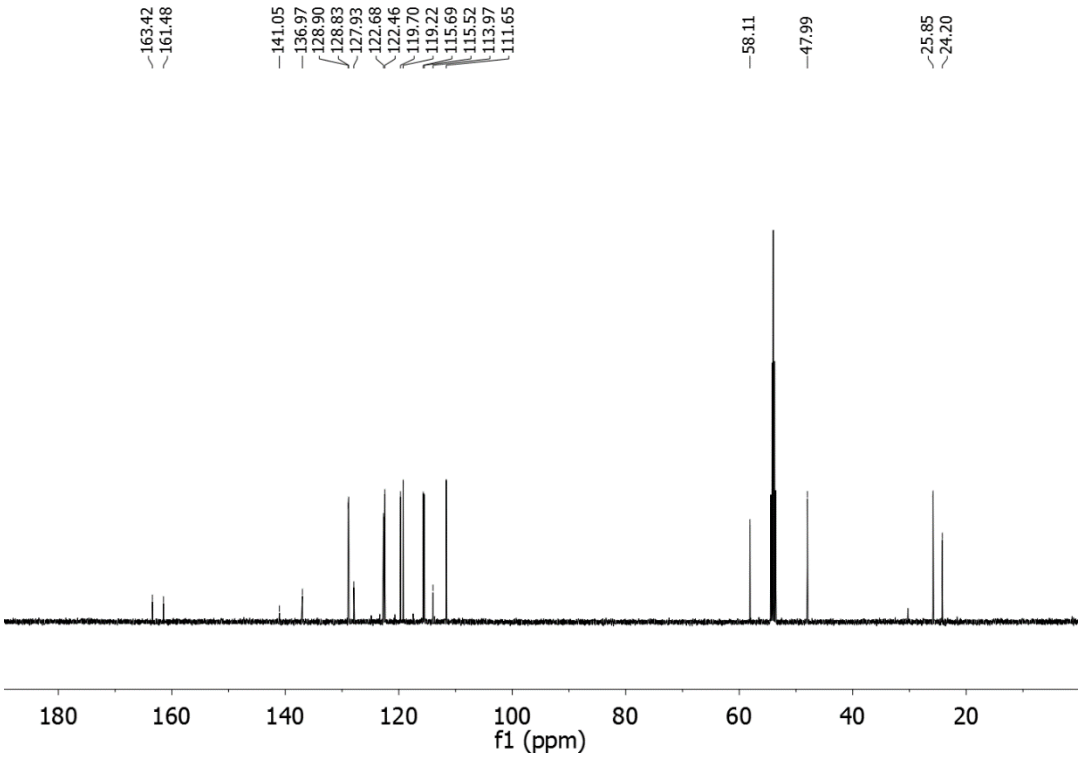
^{1}H NMR spectrum of compound **36** at 25 °C in CD_2Cl_2.



^{13}C NMR spectrum of compound **36** at 25 °C in CD_2Cl_2.



^{1}H NMR spectrum of compound **37** at 25 °C in CD_2Cl_2.



^{13}C NMR spectrum of compound **37** at 25 °C in CD_2Cl_2.

IX. References

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