A Highly Active and Selective Palladium Pincer Catalyst for the Formation of α-Aryl Ketones via Cross-Coupling

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General Information

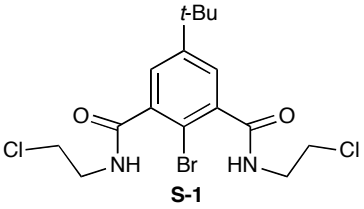
All reactions were carried out under an argon atmosphere in oven-dried glassware with magnetic stirring. All commercially obtained reagents were used as received. Dry 1,4-dioxane was freshly distilled. Dry tetrahydrofuran, dichloromethane, and toluene were obtained from a solvent purification system.

Heating was accomplished by either a heating mantle or silicone oil bath. Purification of reaction products was carried out by flash column chromatography using silica gel 60 (230-400 mesh). TLC visualization was accompanied with UV light. Concentration in vacuo refers to the removal of volatile solvent using a rotary evaporator attached to a dry diaphragm pump (10-15 mm Hg) followed by pumping to a constant weight with an oil pump (<300 mTorr).

^{1}H NMR spectra were recorded at 300 MHz, and are reported relative to $CDCl_3$ (δ 7.27). ^{1}H NMR coupling constants (J) are reported in Hertz (Hz) and multiplicities are indicated as follows: s (singlet), d (doublet), t (triplet), m (multiplet). Proton-decoupled ^{13}C NMR spectra were recorded at 75 MHz and reported relative to $CDCl_3$ (δ 77).

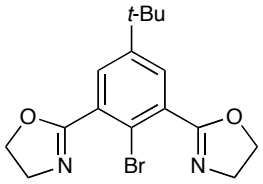
Procedures and Characterization Data for the Pd Complexes

Compounds **1a-b** and **2a-b** are known compounds.[5]



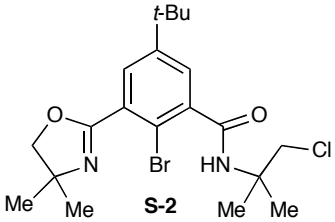
S-1

2-Bromo-5-*tert*-butyl-N^1,N^3-bis(2-chloroethyl)benzene-1,3-dicarbamide (**S-1**): A solution of isophthaloyl dichloride **2a** (0.50 g, 1.48 mmol) in dichloromethane (5 mL) was slowly added to a solution of ethanolamine **3b** (190 mg, 3.12 mmol) in dichloromethane (5 mL), then a solution of triethylamine (1.023 mL, 7.4 mmol) in dichloromethane (5 mL) was added slowly at 0 ºC under argon. The mixture was stirred at room temperature for 5 h. Formation of the intermediate diamide–dialcohol was monitored by TLC. Then, methanesulfonyl chloride (1.69 g, 14.8 mmol) was added at 0 ºC, and the mixture was stirred at room temperature for 16 h. Formation of the product **S-1** was monitored by TLC. At 0 ºC, aqueous potassium carbonate (1 N, ca. 30 mL) was added and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated brine, dried over sodium sulfate, and concentrated under reduce pressure. The crude product was purified by column chromatography (20% EtOAc-Hexanes) to give **S-1** in 76 % yield (473 mg, 1.12 mmol) as a white solid. IR (thin film) ν 3265, 1642 cm^{-1}. ^{1}HNMR (300MHz, $CDCl_3$) δ 7.507 (s, 2H), 6.35 (t, *J* = 5.4 Hz, 2NH), 3.79 (m, 8H), 1.31 (s, 9H). MS (ESI) HRMS calcd for $C_{16}H_{21}BrCl_2N_2O_2$ + H requires *m/z* 423.0163, found 423.0164 and 425.0135.



4a

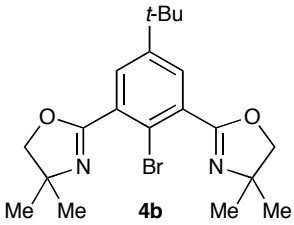
[*t*-BuPheBox-H_2]Br (4a): To a suspension of NaH (60 mg, 2.5 mmol) in THF (5 mL) under argon was added a solution of dichloro carbamide **S-1** (106 mg, 0.25 mmol) in THF (5 mL) at room temperature and stirred for 3 h. The mixture was diluted with dichloromethane (50 mL), and washed with saturated NH_4Cl (10 mL) and brine. The organic phase was separated, and dried with sodium sulfate. Concentration of this solution gave [*t*-BuPhebox-H_2]Br (**4a**), which was purified by column chromatography (20% EtOAc-hexanes) affording a colorless oil, 85 mg (97% yield): IR (thin film) ν 1655 cm^{-1}. ^{1}HNMR (300MHz, $CDCl_3$) δ 7.67 (s, 2H), 4.46 (t, *J* = 9.3 Hz, 4H), 4.09 (t, *J* = 9.3 Hz, 4H), 1.37(s, 9H) ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.4, 150.3, 131.3, 129.9, 117.9, 67.8, 55.2, 34.6, 30.8. MS (ESI) HRMS calcd for $C_{16}H_{19}BrN_2O_2$ + H requires *m/z* 351.0630, found 351.0635 and 353.0639.



S-2

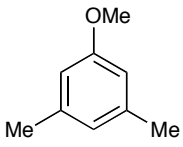
2-Bromo-5-*tert*-butyl-*N*-(1-chloro-2-methylpropan-2-yl)-3-(4,4-dimethyl-4,5-dihydrooxazol-2-yl)benzamide (**S-2**): A solution of isophthaloyl dichloride **2a** (0.50 g, 1.48 mmol) in dichloromethane (5 mL) was slowly added to a solution of 2-amino-2-methyl-1-propanol (291 mg, 3.27 mmol) in dichloromethane (5 mL), then a solution of triethylamine (2.05 mL, 14.8 mmol) in dichloromethane (5 mL) was added slowly at 0 ºC under argon. The mixture was stirred at room temperature for 5 h. Formation of the intermediate diamide–dialcohol was monitored by TLC. Then, methanesulfonyl chloride (1.69 g, 14.8 mmol) was

added at 0 ºC, and the mixture was stirred at room temperature for 16 h. Formation of the product **S-2** was monitored by TLC. At 0 ºC, aqueous potassium carbonate (1 N, ca. 30 mL) was added and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated brine, dried over sodium sulfate, and concentrated under reduce pressure. The crude product was purified by column chromatography (20% EtOAc-Hexanes) to give **S-2** in 73% yield (477.5 mg, 1.08 mmol) as a white solid. IR (thin film) ν 3284, 1651 cm^{-1}. ^{1}HNMR (300MHz, $CDCl_3$) δ 7.51 (d, *J* = 2.7 Hz, 1H), 7.44 (d, *J* = 2.4 Hz, 1H), 5.81 (s, 1NH), 4.09 (s, 2H), 3.86 (s, 2H), 1.45 (s, 6H), 1.36 (s, 6H), 1.26 (s, 9H). MS (ESI) HRMS calcd for $C_{20}H_{28}BrClN_2O_2$ + H requires *m/z* 443.1023, found 443.1017 and 445.0959.



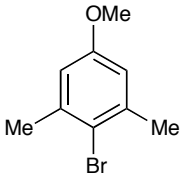
4b

[*t*-BuPheBox-Me$_2$]Br (**4b**): To a suspension of NaH (136 mg, 5.6 mmol) in THF (10 mL) under argon was added a solution of chlorobenzamide **S-2** (250 mg, 0.56 mmol) in THF (5 mL) at room temperature. Then, the mixture was stirred at reflux for 3 h. The mixture was diluted with dichloromethane (50 mL), and washed with saturated NH_4Cl (10 mL) and brine. The organic phase was separated, and dried with sodium sulfate. Concentration of this solution gave [*t*-BuPhebox-Me$_2$]Br (**4b**), which was purified by column chromatography (20% EtOAc-hexanes) affording a light yellow oil, 211.2 mg (92% yield): IR (thin film) ν 1656 cm^{-1}. ^{1}HNMR (300MHz, $CDCl_3$) δ 7.56 (s, 2H), 4.12 (s, 4H), 1.40 (s, 12H), 1.29 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.0, 150.3, 131.6, 129.5, 118.0, 79.3, 68.0, 34.6, 30.9, 28.1. MS (ESI) HRMS calcd for $C_{20}H_{27}BrN_2O_2$ + H requires *m/z* 407.1256, found 407.1257 and 409.1302.



S-3

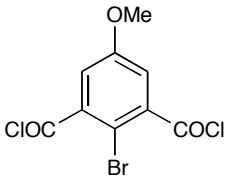
3,5-Dimethylanisol (**S-3**):[1] To a solution of 3,5-dimethylphenol (30.0 g, 246 mmol) in acetone (200 mL) was added anhydrous K_2CO_3 (51.0 g, 369 mmol), and iodomethane (52.4 g, 369 mmol). The mixture was heated at reflux under argon for 24 h. After cooling the reaction to room temperature, was filtrated with celite and washed with acetone, concentrated under reduce pressure. The residue was dissolved in dichloromethane and washed with 2N NaOH. Further simple distillation afforded pure 3,5-dimethylanisol **(S-3)** (31.7 g, 233 mmol) as a colorless liquid in 95% yield. ^{1}HNMR (300MHz, $CDCl_3$) δ 6.99 (s, 1H), 6.63 (s, 2H), 3.85 (s, 3H), 2.38 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.5, 139.9, 122.3, 111.8, 54.9, 21.3. MS (CI) LRMS calcd for $C_9H_{12}O$ + H requires *m/z* 137.09, found 137.10.



S-4

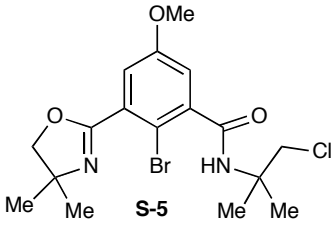
2-Bromo-5-methoxy-1,3-dimethylbenzene (**S-4**):[1] To a stirred solution of 3,5-dimethylanisol (**S-3**)[1] (8.2 g, 60 mmol) in CH_2Cl_2 (100 mL) was added dropwise a 1.0 M solution of bromine in CH_2Cl_2 (9.95 g, 63 mmol) at 0 °C via cannula over a 2-min period under argon. The reaction was stirred at room temperature for 1 h. Progress was monitored by TLC analysis. The product was washed with saturated sodium thiosulfate until the organic phase becomes colorless, dried with sodium sulfate and the solvent was removed under reduce pressure. The residue was purified by simple distillation to give 10.88 g

(66%) of pure 2-bromo-5-methoxy-1,3-dimethylbenzene (**S-4**) as a colorless liquid: ^{1}HNMR (300MHz, $CDCl_3$) δ 6.56 (s, 2H), 3.78 (s, 3H), 2.40(s, 6H), ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.1, 138.8, 118.8, 113.9, 55.6, 24.2. MS (CI) LRMS calcd for $C_9H_{11}BrO$ + H requires *m/z* 215.09, found 215.10 and 217.10.



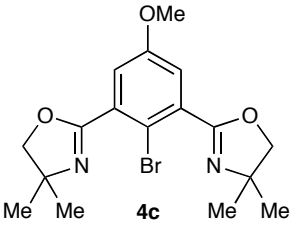
2b

2-Bromo-5-methoxy-isophthaloyl dichloride (**2b**):[1] In a 250 mL three-necked round-bottom flask equipped with a mechanical stirrer and a reflux condenser was added 2-bromo-5-methoxy-1,3-dimethylbenzene (**S-4**)[1] (2.5 g, 11.7 mmol), dissolved in 30 mL of *t*-BuOH–water (1:1) and $KMnO_4$ (3.7 g, 23.4 mmol). The mixture was set to reflux for 2 hours, then cool down to room temperature. More $KMnO_4$ (3.7 g, 23.4 mmol) was added and the reaction mixture was refluxed for another 16 hours. After the mixture was cooled to room temperature, and filtered using vacuum filtration, the *t*-BuOH was removed under reduce pressure. The solution was acidified with concentrated HCl. The resulting white precipitate was collected by vacuum filtration and oven-dried (~80 °C) overnight to give 1.79 g (56% yield) of 2-bromo-5-methoxy-isophthalic acid (**1b**).[1] To a suspension of **1b** (1.0 g, 3.7 mmol) in benzene (50 mL) and a drop of DMF was added $SOCl_2$ (11 mL, 150 mmol) at 0 °C. After the mixture was refluxed for 5 h, excess $SOCl_2$ was removed by distillation to give 1.12 g (99% yield) of the 2-bromo-5-methoxy-isophthaloyl dichloride (**2b**) as a white solid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.55 (s, 2H), 3.98 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.1, 158.9, 139.5, 119.3, 106.8, 56.3. MS (CI, CH_4) LRMS calcd for $C_9H_5BrCl_2O_3$ + H requires *m/z* 310.88, found 310.90 and 312.90.



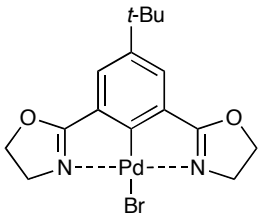
S-5

2-Bromo-*N*-(1-chloro-2-methylpropan-2-yl)-3-(4,4-dimethyl-4,5-dihydrooxazol-2-yl)-5-methoxybenzamide (**S-5**): A solution of 2-bromo-5-methoxy-isophthaloyl dichloride (**2b**) (917 mg, 2.96 mmol) in dichloromethane (10 mL) was slowly added to a solution of 2-amino-2-methyl-1-propanol (580 mg, 6.51 mmol) in dichloromethane (10 mL), then a solution of triethylamine (4.1 mL, 29.6 mmol) in dichloromethane (10 mL) was added slowly at 0 ºC under argon. The mixture was stirred at room temperature for 5 h. Formation of the intermediate diamide–dialcohol was monitored by TLC. Then, methanesulfonyl chloride (3.37 g, 29.6 mmol) was added at 0 ºC, and the mixture was stirred at room temperature for 16 h. Formation of the product **S-5** was monitored by TLC. At 0 ºC, aqueous potassium carbonate (1 N, ca. 50 mL) was added and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated brine, dried over sodium sulfate, and concentrated under reduce pressure. The crude product was purified by column chromatography (20% EtOAc-Hexanes) to give **S-5** in 69% yield (850 mg, 2.04 mmol) as a white solid. IR (thin film) ν 3279, 1657 cm^{-1}. ^{1}HNMR (300MHz, $CDCl_3$) δ 7.14 (d, *J* = 3.0 Hz, 1H), 7.05 (d, *J* = 3.0 Hz, 1H), 5.74 (s, 1NH), 4.15 (s, 2H), 3.91 (s, 2H), 3.82 (s, 3H), 1.51 (s, 6H), 1.41 (s, 6H). MS (ESI) HRMS calcd for $C_{17}H_{22}BrClN_2O_3$ + H requires *m/z* 417.0502, found 417.0508 and 419.0587.



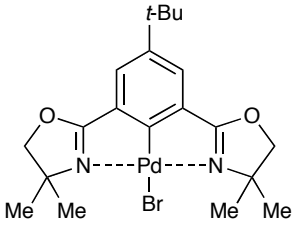
4c

[MeOPheBox-Me$_2$]Br (10): To a suspension of NaH (288 mg, 12 mmol) in THF (10 mL) under argon was added a solution of chloro benzamide **S-5** (500 mg, 1.2 mmol) in THF (10 mL) at room temperature. Then, the mixture was stirred at reflux for 3 h. The mixture was diluted with dichloromethane (50 mL), and washed with saturated NH_4Cl (10 mL) and brine. The organic phase was separated, and dried with sodium sulfate. Concentration of this solution gave [MeOPhebox-Me$_2$]Br (**4c**), which was purified by column chromatography (20% EtOAc-hexanes) affording **4c** in 95% yield (433 mg, 1.14 mmol) as colorless oil, which crystallized to colorless crystals after some period of time. IR (thin film) ν 1665. ^{1}HNMR (300MHz, $CDCl_3$) δ 7.16 (s, 2H), 4.12 (s, 4H), 3.80 (s, 3H), 1.39 (s, 12H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.7, 158.0, 132.8, 118.2, 111.4, 79.5, 68.0, 55.7, 28.1. MS (ESI) HRMS calcd for $C_{17}H_{21}BrN_2O_3$ + H requires *m/z* 381.0736, found 381.0734 and 383.0790.



I

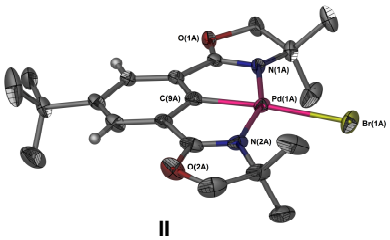
[*t*-BuPheBox-H$_2$]PdBr (I): A mixture of [*t*-BuPheBox-H$_2$]Br (**4a**) (35 mg, 0.1 mmol) and $Pd_2(dba)_3$ (50 mg, 1.1 equiv, 0.055 mmol) were stirred in dry toluene (4 mL) for 3 h at room temperature, by which time the reaction was deemed complete by TLC (60% EtOAc-Hexanes). The reaction mixture was filtered through silica eluting with toluene to remove dba. The silica gel was then washed separated with ethyl acetate to give a reddish solution which was collected and the solvent was removed under reduce pressure to give **I** as a reddish solid (45 mg, 0.10 mmol) in 99% yield. IR (thin film) ν 1640, 1559 cm^{-1}. ^{1}HNMR (300MHz, $CDCl_3$) δ 7.41 (s, 2H), 4.83 (t, *J* = 7.2 Hz, 4H), 4.14 (t, *J* = 7.2 Hz, 4H), 1.32 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.3, 163.8, 143.3, 130.5, 125.3, 82.7, 66.9, 34.9, 31.3. MS (ESI) HRMS calcd for $C_{16}H_{19}BrN_2O_2Pd$ – Br requires *m/z* 377.0481, found 377.0489.



II

[*t*-BuPheBox-Me$_2$]PdBr (II): A mixture of [*t*-BuPheBox-Me$_2$]Br (**4b**) (90 mg, 0.22 mmol) and $Pd_2(dba)_3$ (111 mg, 0.12 mmol) were stirred in dry toluene (6 mL) for 3 h at room temperature, by which time the reaction was deemed complete by TLC (60% EtOAc-Hexanes). The reaction mixture was filtered through silica eluting with toluene to remove dba. The silica gel was then washed separated with ethyl acetate to give a reddish solution which was collected and the solvent was removed under reduce pressure to give **II** as a reddish solid (112 mg, 0.22 mmol) 99% yield. A sample suitable for X-ray analysis was prepared by slow evaporation of a biphasic dichloromethane/ hexanes solution in air to give yellow crystals. IR (thin film) ν 1630, 1558 cm^{-1}. ^{1}HNMR (300MHz, $CDCl_3$) δ 7.33 (s, 2H), 4.44 (s, 4H), 1.65 (s, 12H), 1.29 (s, 9H) ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.6, 163.8, 147.9, 129.4, 124.0, 82.7, 65.9, 34.9, 31.3, 28.1. MS (ESI) HRMS calcd for $C_{16}H_{19}BrN_2O_2Pd$ – Br requires *m/z* 433.1107, found 433.1102.

X-Ray Crystal Structure Data Summary for [*t*-BuPheBox-Me$_2$]PdBr (II):



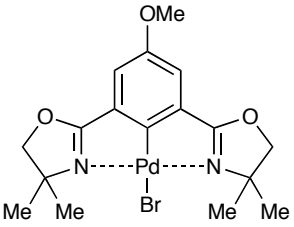
II

Crystal data for complex **II** has been deposited with The Cambridge Crystallographic Data Centre, (http://www.ccdc.cam.ac.uk), deposition number **CCDC 821200**. $C_{20}H_{27}BrN_2O_2Pd$, M = 513.75, yellow needle, 0.26 × 0.12 × 0.01 mm^3, monoclinic, space group $P2_1/n$ (No. 14), a = 12.6447(12), b = 21.628(2), c = 15.6491(15) Å, β = 103.716(6)°, V = 4157.7(7) Å^3, Z = 8, D_c = 1.641 g/cm^3, F_{000} = 2064, MWPC area detector, Cu Kα radiation, λ = 1.54178 Å, T = 110(2)K, $2\theta_{max}$ = 120.0º, 74692 reflections collected, 6004 unique (R_{int} = 0.0634). Final *GooF* = 1.004, *R1* = 0.0311, *wR2* = 0.0690, R indices based on 5333 reflections with I >2sigma(I) (refinement on F^2), 514 parameters, 18 restraints. Lp and absorption corrections applied, μ = 9.576 mm^{-1}. Absolute structure parameter 0.000(4). Displacement ellipsoid plot (50% probability) of **II** is shown above with important atoms numbered. Some hydrogen atoms have been omitted for clarity. Selected bond distances (Å) and angles (deg): Pd(1A)-C(9A) 1.937(4), Pd(1A)-Br(1A) 2.5278(6), Pd(1A)-N(1A) 2.078(3), Pd(1A)-N(2A) 2.074(4), N(1A)-C(3A) 1.291(5), N(2A)-C(10A) 1.293(6), C(9A)-Pd(1A)-Br(1A) 173.96(11), N(1A)-Pd(1A)-N(2A) 157.79(13), C(9A)-Pd(1A)-N(1A) 79.14(115), C(9A)-Pd(1A)-N(2A) 78.69(16), Br(1A)-Pd(1A)-N(1A) 101.43(9), Br(1A)-Pd(1A)-N(2A) 100.47(10).

Table 1. Crystal and Intensity Collection Data for **II**

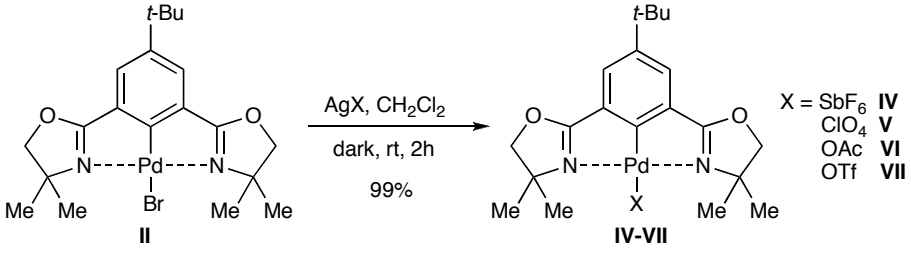
	II
Chemica formula	$C_{20}H_{27}BrN_2O_2Pd$
Formula weight	513.75
Temperature (°K)	110(2)
Wavelength (Å)	1.54178
Crystal system	Monoclinic
Space group	P2(1)/n
a (Å)	12.6447(12)
b (Å)	21.628(2)
c (Å)	15.6494(15)
α (deg)	90
β (deg)	103.716(6)
γ (deg)	90
V (Å^3)	4157.7(7)
Z	8
ρ_{calc} (mg• m^{-3})	1.641
Absorp coeff (mm^{-1})	9.576
F(000)	2060
Crystal size (mm^3)	0.26 x 0.12 x 0.01
Scan rage (deg)	4.14 to 60.00
Index ranges	-14 ≤ *h* ≤ 14 -24 ≤ *k* ≤ 24 -17 ≤ *l* ≤ 17
Reflections collected	74692
No. of unique refins	6004
R(int)	0.0634
Absorption correction	Semi-empirical
Max. and min. transmission	0.9103, 0.1897
Data/restraints/parameters	6004/18/514
Goodness-of-fit on F^2	1.004
R1[a], wR2[a] [I>2σ(I)]	0.0311, 0.0690
R1[a], wR2[a] (all data)	0.0364, 0.0707
Largest diff. peak / hole (e.Å^{-3})	1.114, -0.729

[a] $R1 = [\sum| |F_o| - |F_c|)/\sum|F_o|]$; $wR2 = [\sum(w(F_o^2-F_c^2)^2/\sum(wF_o^4)]^{1/2}$. $S = [\sum(w(F_o^2-F_c^2)^2]/(n-p)^{1/2}$. *n* = number of reflections, *p* = parameters used.



III

[MeOPheBox-Me$_2$]PdBr (**III**): A mixture of [MeOPheBox-Me$_2$]Br (**4c**) (90 mg, 0.22 mmol) and $Pd_2(dba)_3$ (111 mg, 0.12 mmol) were stirred in dry toluene (6 mL) for 3 h at room temperature, by which time the reaction was deemed complete by TLC (60% EtOAc-Hexanes). The reaction mixture was filtered through silica eluting with toluene to remove dba. The silica gel was then washed separated with ethyl acetate to give a reddish solution which was collected and the solvent was removed under reduce pressure to give **III** as a reddish solid (106 mg, 0.22 mmol) 99% yield. IR (thin film) ν 1620, 1559 cm^{-1}. ^{1}HNMR (300MHz, $CDCl_3$) δ 6.89 (s, 2H), 4.44 (s, 4H), 3.79 (s, 3H), 1.66 (s, 12H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.4, 157.0, 130.0, 128.1, 112.8, 82.7, 66.1, 55.9 28.1. MS (ESI) HRMS calcd for $C_{16}H_{19}BrN_2O_2Pd$ – Br requires *m/z* 407.0587, found 407.0589.



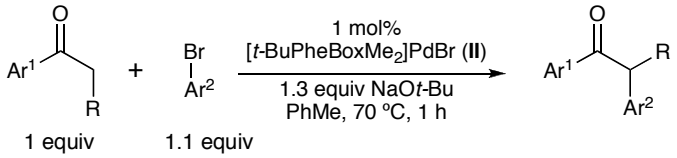
II **IV-VII**

[*t*-BuPheBox-Me$_2$]PdX (**IV-VII**): A mixture of [*t*-BuPheBox-Me$_2$]PdBr **(II)** (5 mg, 0.01 mmol) and AgX (1.5 equiv, 0.015 mmol) under argon was stirred in dry dichloromethane (4 mL) for 2 h at room

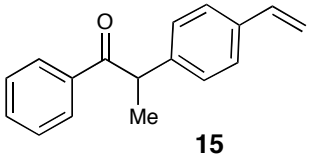
temperature. The mixture was wrapped in aluminum foil to protect the reaction mixture from light during the all reaction time. The reaction mixture was filtered through celite eluting with dichloromethane. The solvent was removed under reduce pressure to give **IV-VII** as yellow solids (0.01 mmol) in quantitative yields. **[*t*-BuPheBox-Me$_2$]PdSbF$_6$ (IV)**: IR (thin film) ν 1642 cm^{-1}. MS (ESI) HRMS calcd for $C_{16}H_{19}F_6N_2O_2PdSb$ – SbF_6 requires *m/z* 433.1107, found 433.1098.

Procedures and Characterization Data for the α-Arylation Products

α-Arylation of Ketones: Compounds **5–14**, **16** and **18-24** are known compounds. Compounds **15** and **17** are new compounds. Full-tabulated data is available below for the new compounds.

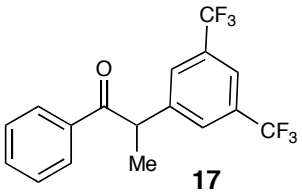


General Procedure for the Selective α-Arylation of Ketones with Aryl Bromides: To an 8 mL glass vial containing a stir bar was added the respective catalyst **I-VII** (0.01 equiv, 0.003 mmol) and capped with a phenolic cap equipped with a teflon/silicone septa. The vial was filled and purged with argon. A solution of sodium tert-butoxide (41 mg, 1.3 equiv, 0.429 mmol) in toluene (1.5 mL) was added via syringe under argon. Then, arylbromide (1.1 equiv, 0.363 mmol) was added via syringe followed by the respective ketone (44 mg, 1.0 equiv, 0.33 mmol) at room temperature. The mixture was stirred for 1 h at 70 ºC under argon. Then, the mixture was cooled down to room temperature. The reaction mixture was quenched with saturated ammonium chloride (4 mL), diluted with Et_2O (20 mL), washed with distilled water (10 mL) and brine (10 mL). Finally, it was dried over sodium sulfate, and concentrated under reduce pressure. The product was purified by flash silica gel column chromatography using either (60% toluene-hexanes) or (50% dichloromethane-hexanes) as the eluents.



15

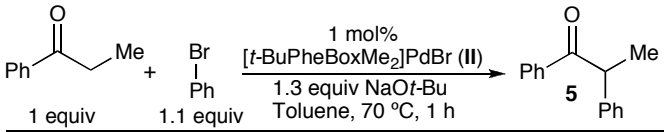
1-phenyl-2-(4-vinylphenyl)propan-1-one (15): To an 8 mL glass vial containing a stir bar was added the catalyst **II** (1.7 mg, 0.01 equiv, 0.0033 mmol) and capped with a phenolic cap equipped with a teflon/silicone septa. The vial was filled and purged with argon. A solution of sodium tert-butoxide (41 mg, 1.3 equiv, 0.429 mmol) in toluene (1.5 mL) was added via syringe under argon. Then, 4-bromostyrene (66 mg, 1.1 equiv, 0.363 mmol) was added via syringe followed by propiophenone (44 mg, 1 equiv, 0.33 mmol) at room temperature. The mixture was stirred for 1 h at 70 ºC under argon. Then, the mixture was cooled down to room temperature. The reaction mixture was quenched with saturated ammonium chloride (4 mL), diluted with Et_2O (20 mL), washed with distilled water (10 mL) and brine (10 mL). Finally, it was dried over sodium sulfate. The solvent was removed under reduced pressure, and the residue was purified by flash silica gel column chromatography (50% dichloromethane-hexanes) to give compound **15** (68 mg, 85%) as a colorless oil (CH_2Cl_2); IR (thin film) ν 3403, 3028, 2920, 1695, 1611, 960 cm^1; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.97 (d, J = 7.6 Hz, 2H), 7.47 (t, J = 7.2 Hz, 1H), 7.47 (m, 4H), 7.26 (d, J = 7.6 Hz, 2H), 6.67 (dd, J = 10.8 Hz, J = 6.4 Hz, 1H), 5.71 (d, J = 17.6 Hz, 1H), 5.22 (d, J = 11.4 Hz, 1H), 4.69 (q, J = 6.8 Hz, 1H), 1.55 (d, J = 6.8 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 200.1, 141.0, 136.4, 136.3, 136.2, 132.7, 128.7, 128.2, 127.9, 126.6, 113.7, 47.5, 19.3. HRMS (ESI) calcd for $C_{17}H_{12}O$ + Li requires m/z 243.1361, found 243.1331.



17

2-(3,5-bis(trifluoromethyl)phenyl)-1-phenylpropan-1-one (**17**): To an 8 mL glass vial containing a stir bar was added the catalyst **II** (1.7 mg, 0.01 equiv, 0.0033 mmol) and capped with a phenolic cap equipped with a teflon/silicone septa. The vial was filled and purged with argon. A solution of sodium tert-butoxide (41 mg, 1.3 equiv, 0.429 mmol) in toluene (1.5 mL) was added via syringe under argon. Then, 1-bromo-3,5-bis(trifluoromethyl)benzene (106 mg, 1.1 equiv, 0.363 mmol) was added via syringe followed by propiophenone (44 mg, 1 equiv, 0.33 mmol) at room temperature. The mixture was stirred for 1 h at 70 ºC under argon. Then, it was cooled down to room temperature. The reaction mixture was quenched with saturated ammonium chloride (4 mL), diluted with Et_2O (20 mL), washed with distilled water (10 mL) and brine (10 mL). It was and dried over sodium sulfate. The solvent was removed under reduced pressure, and the residue was purified by flash silica gel column chromatography (50% dichloromethane-hexanes) to give compound **17** (105 mg, 92%) as a colorless oil; IR (thin film) ν 3400, 3026, 2921, 1691, 1605, 970 cm^{1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.98 (d, J = 7.4 Hz, 2H), 7.79 (s, 2H), 7.76 (s, 1H), 7.59 (t, J = 7.2 Hz, 1H), 7.48 (t, J = 7.6 Hz, 2H), 4.89 (q, J = 11.6 Hz, 1H), 1.62 (d, J = 6.3 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 199.1, 143.5, 135.7, 133.5, 132.05 (q, J = 50.3 Hz, $2CF_3$), 128.8, 128.6, 128.2, 124.9, 121.5, 46.8, 19.6. HRMS (ESI) calcd for $C_{17}H_{12}F_2O$ + Li requires m/z 346.0792, found 346.0792.

Mercury Drop Test Data



1 equiv 1.1 equiv

Entry[a]	Additive	Initial Temp (°C)	HPLC Yield (%)
1	none	rt	93
2	Hg	rt	46
3	Hg	70	17
4[b]	Hg (after 10 min)	70	66
5[c]	Hg	70	9

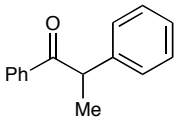
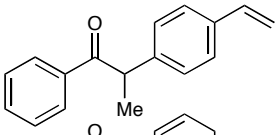
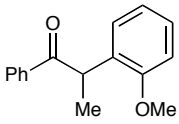
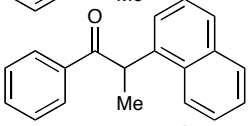
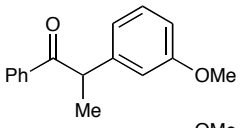
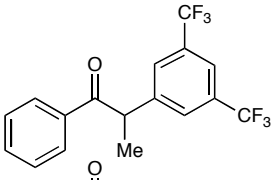
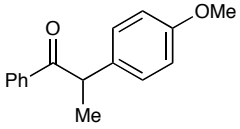
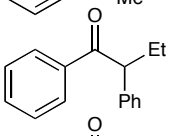
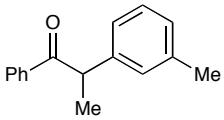
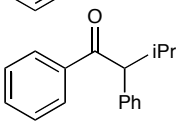
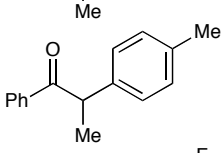
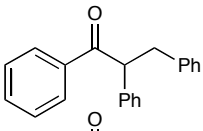
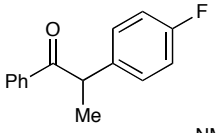
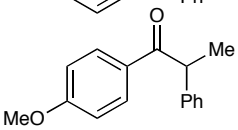
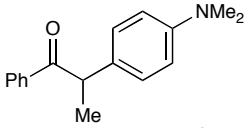
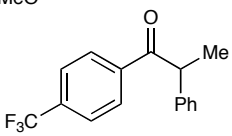
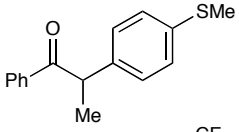
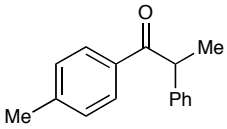
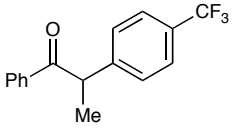
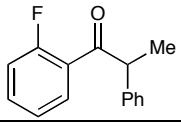
[a]Reaction Details: 0.33 mmol propiophenone in 1.5 mL solvent (0.22 M), Hg^0 (186 mg, 0.93 mmol, 2.8 equiv (280 equiv based on Pd catalyst)); [b]After 10 min of heating, Hg was added to the reaction mixture; [c]After 30 min of heating in the absence of Hg and propiophenone, these reagents were added to the reaction mixture and heating continued for 1 h.

It is possible that pincer complex **II** is serving as an efficient source of heterogeneous Pd which ultimately acts as the active catalyst. If so, addition of a large excess of Hg^0 (relative to catalyst) is expected to completely inhibit product formation by amalgamation of the heterogeneous Pd.[6] Our results show a suppression of product yield, but not complete inhibition of the reaction (Table 4, entry 10). The Hg^0 may be able to react with the homogenous Pd pincer complex, a reaction which has no precedent but has been suggested by Eberhard.[7]

From Eberhard[7]: "*In most cases, Hg(0) will not affect a homogeneous catalyst but forms an amalgam with a heterogeneous catalyst thereby poisoning it. However, it cannot be completely excluded that Hg(0) interferes with catalysis in a way other than killing the true heterogeneous catalyst. Hg(0) would possibly also react with a PCP Pd(0) pincer complex (which to the best of our knowledge is not known yet).*"

The hypothesis by Eberhard that Hg(0) may react with a homogeneous Pd pincer complex deserves further investigation.

References to Known Compounds

Compound No.	Product	Reference	Compound No.	Product	Reference
5		1	**15**		–
6		1	**16**		4
7		1	**17**		–
8		1	**18**		1
9		1	**19**		1
10		3	**20**		1
11		1	**21**		1
12		1	**22**		1
13		1	**23**		2
14		4	**24**		1

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1) P. M. Lundin, J. Esquivias and G. C. Fu, *Angew. Chem. Int. Ed.* 2009, **48**, 154-156.

2) K. Matsubara, K. Ueno, Y. Koga and K. Hara, J, *J. Org. Chem.* 2007, **72**, 5069-5076.

3) a) G. Adjabeng, T. Brenstrum, C. S. Frampton, A. J. Robertson, J. Hillhouse, J. McNulty and A. Capretta, *J. Org. Chem.* 2004, **69**, 5082-5086; b) O. Roy, A. Riahi, F. Hénin and J. Muzart, *Eur. J. Org. Chem.* 2002, 3986-3994.

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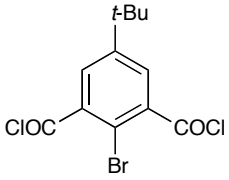
6) (a) D. R. Anton and R. H. Crabtree, *Organometallics* 1983, **2**, 855-859. (b) P. Foley, R. DiCosimo and G. M. Whitesides, *J. Am. Chem. Soc.* 1980, **102**, 6713-6725.

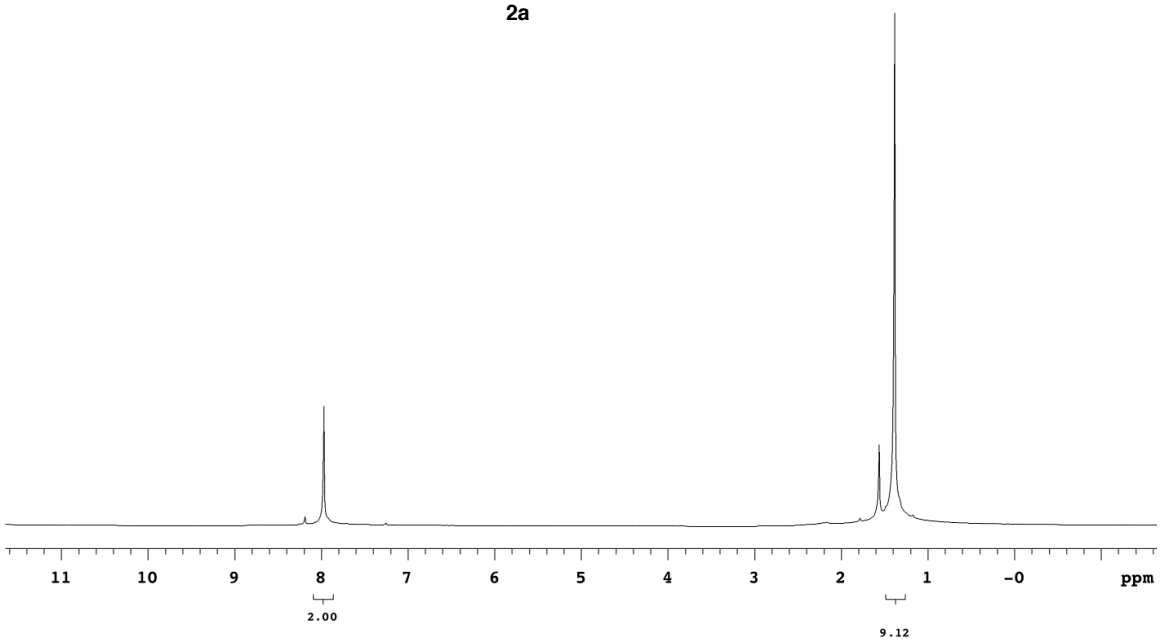
7) M. R. Eberhard, *Org. Lett.* 2004, **6**, 2125-2128.

^{1}H and ^{13}C NMR Spectra

^{1}H NMR ($CDCl_3$, 300 MHz)



2a



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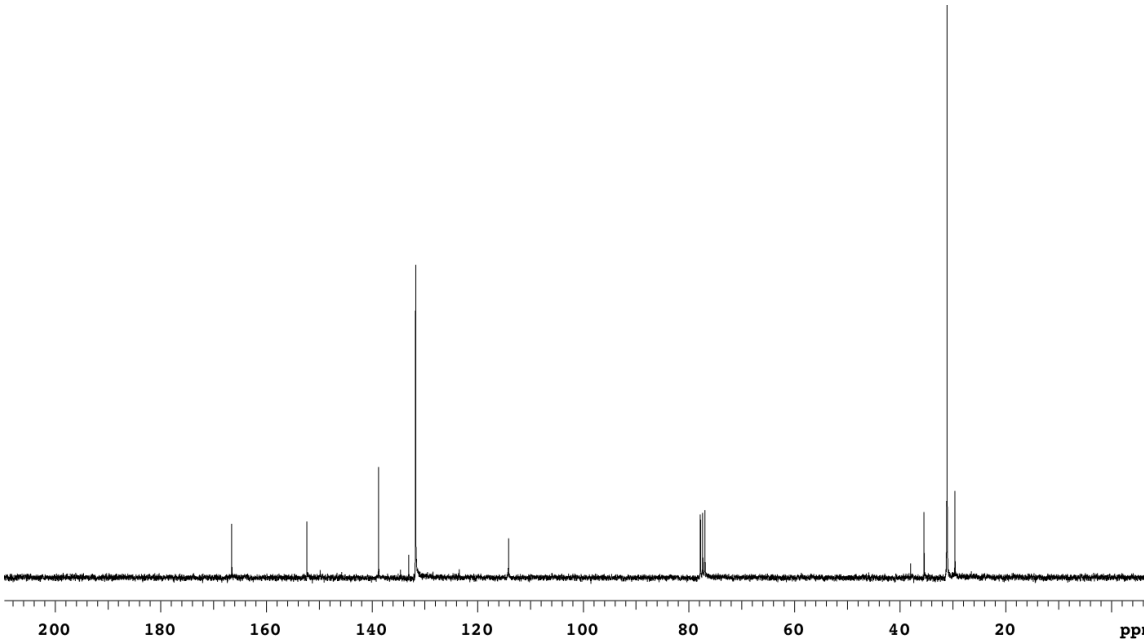

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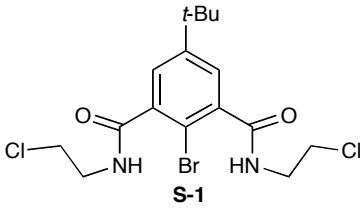

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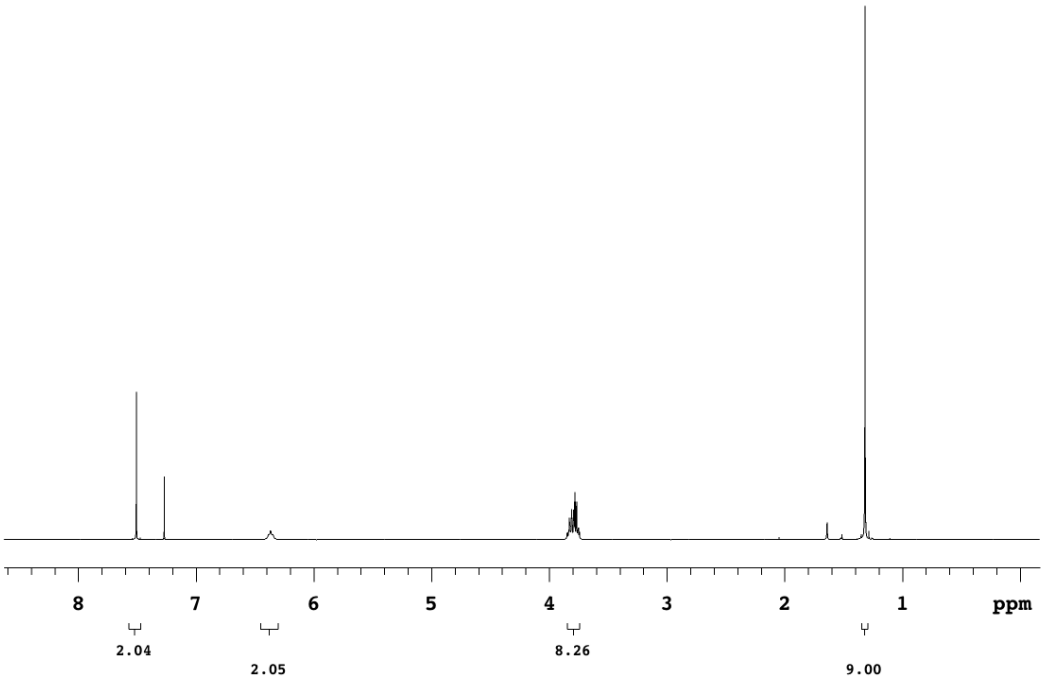

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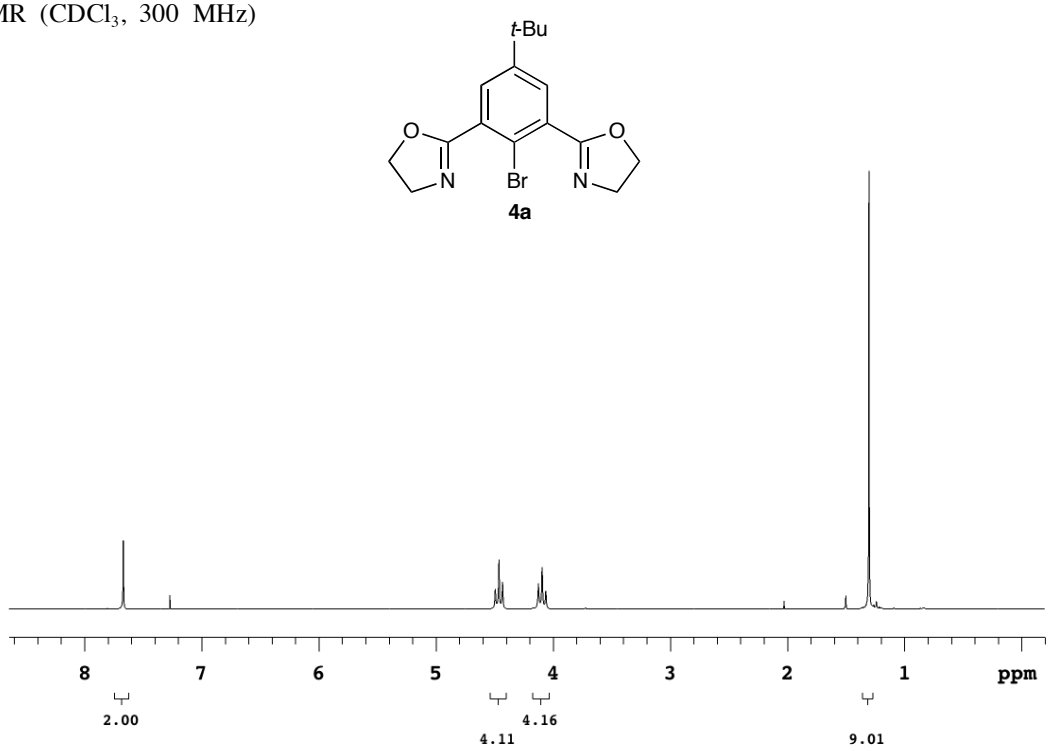

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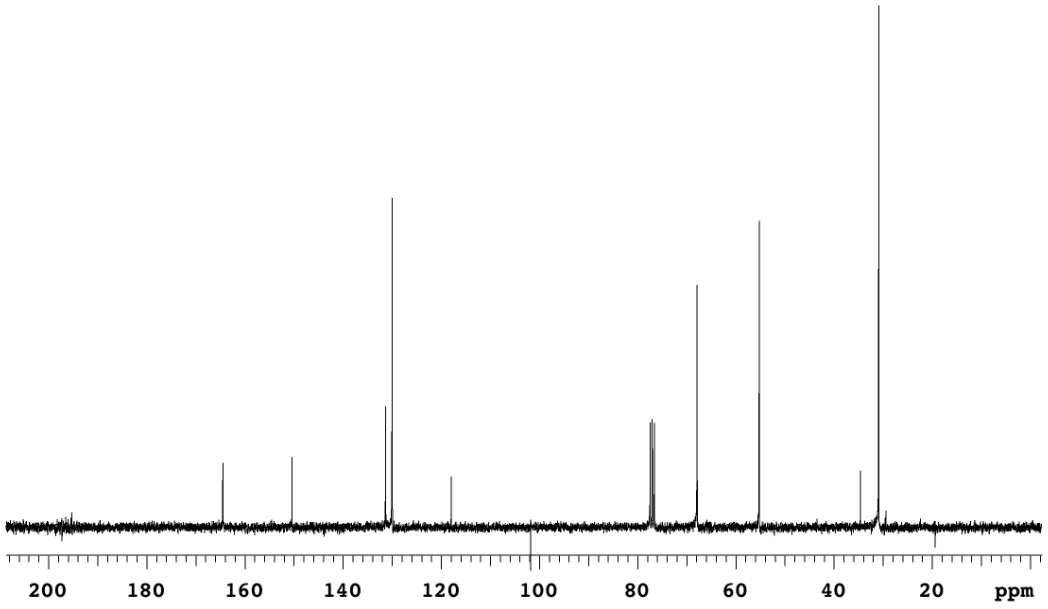

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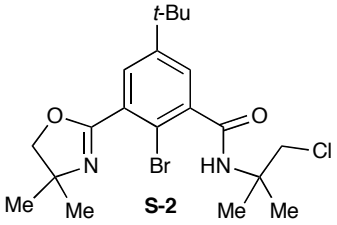
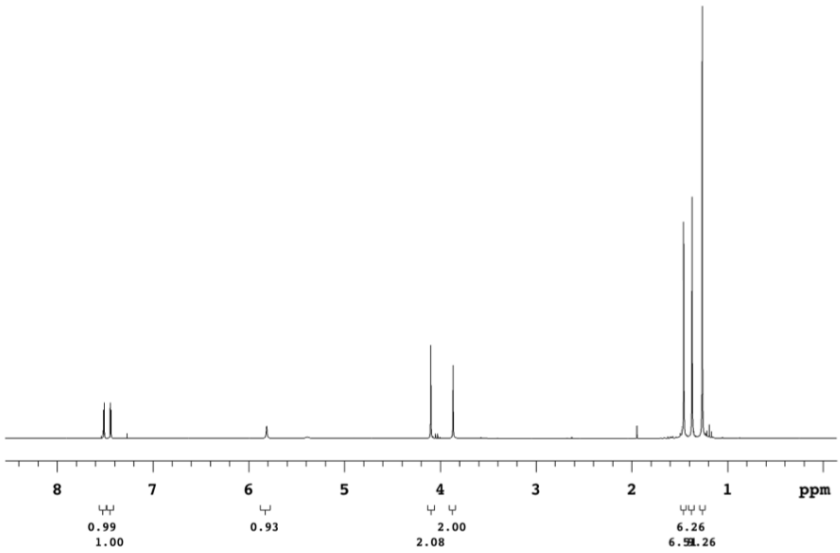


S-2



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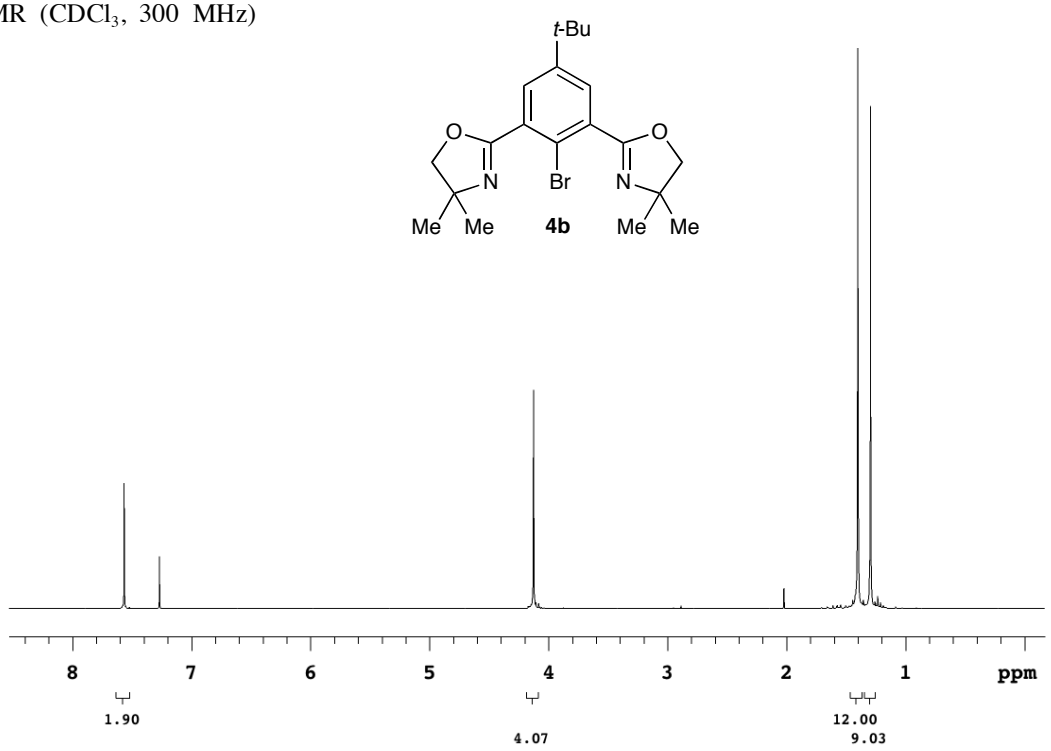

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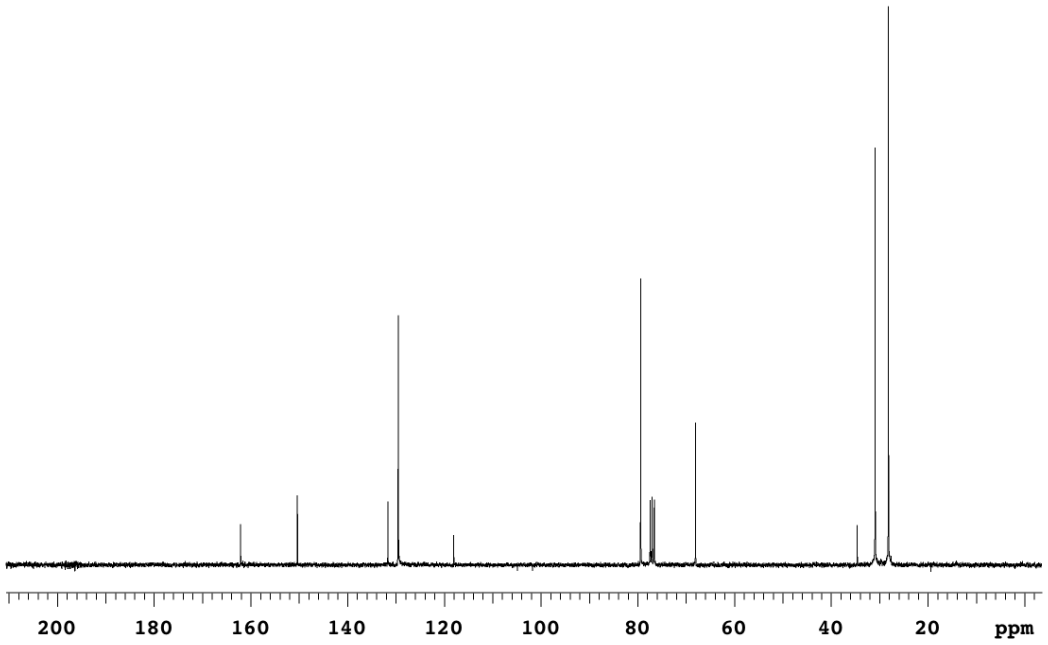
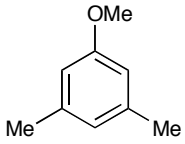
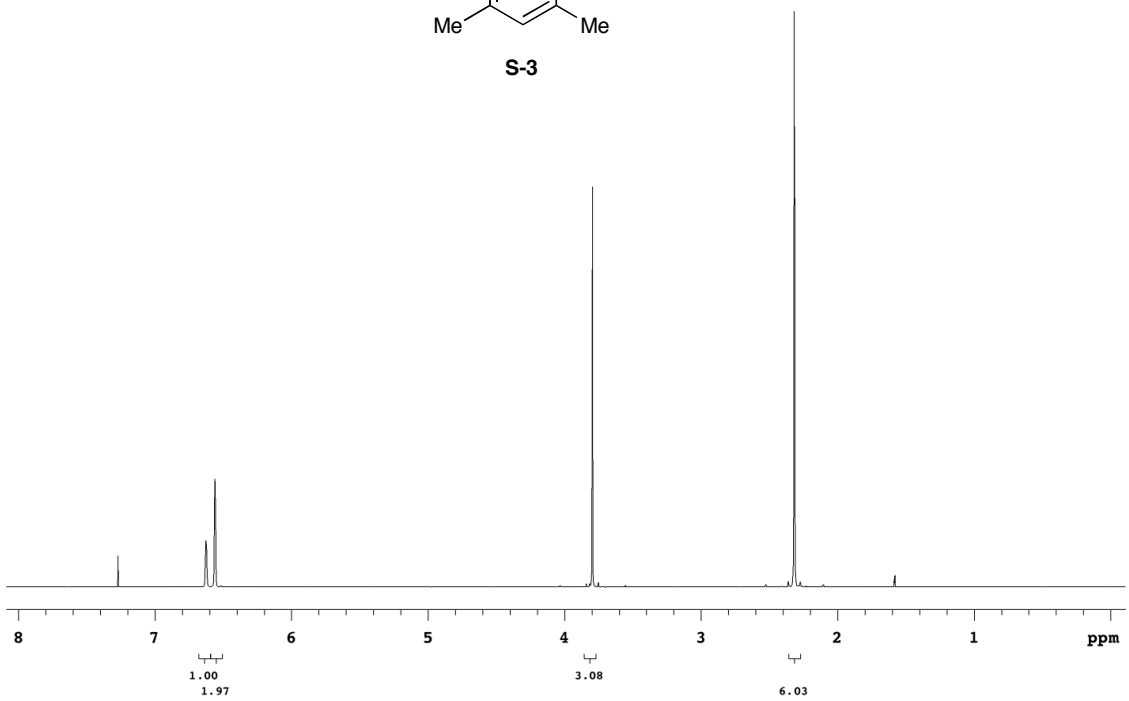


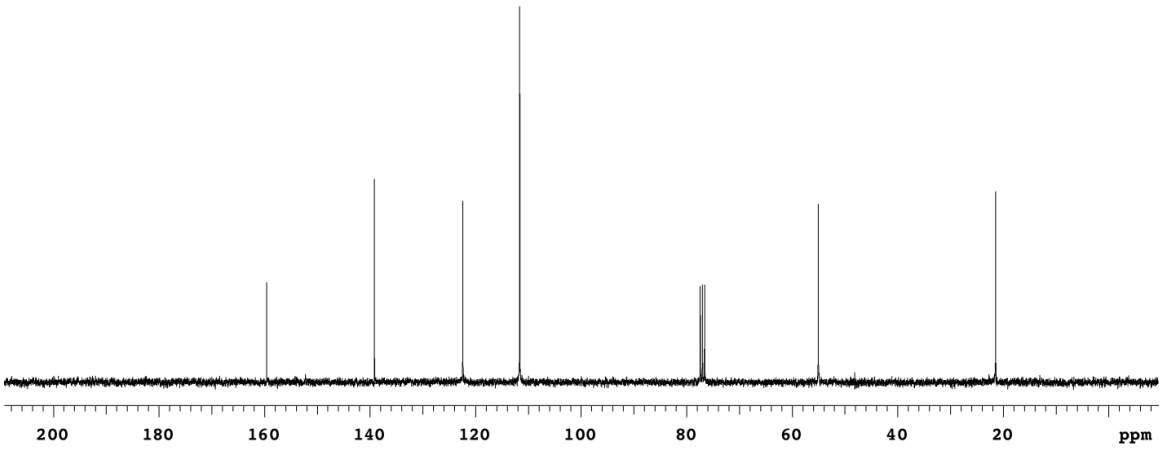
^{1}H NMR ($CDCl_3$, 300 MHz)



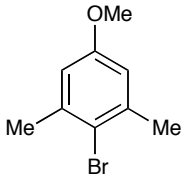
S-3



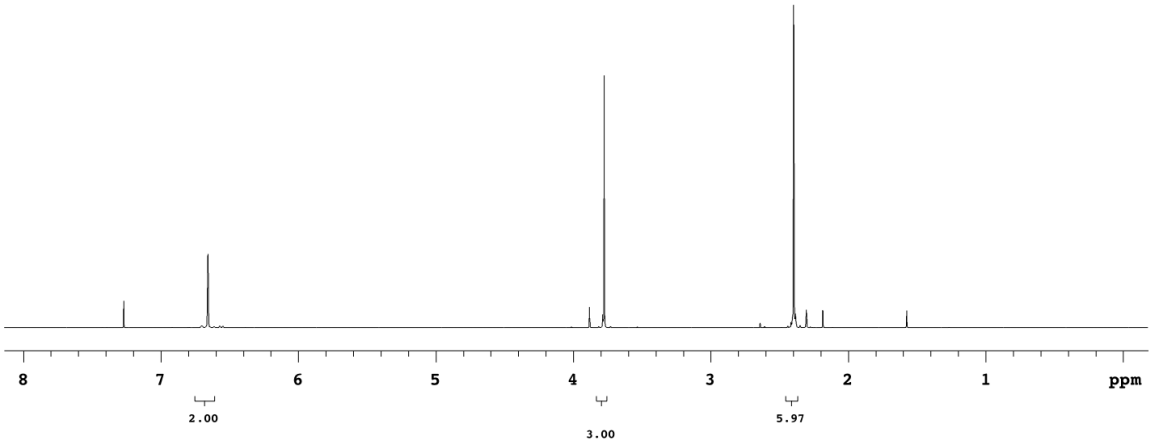
^{13}C NMR ($CDCl_3$, 75 MHz)



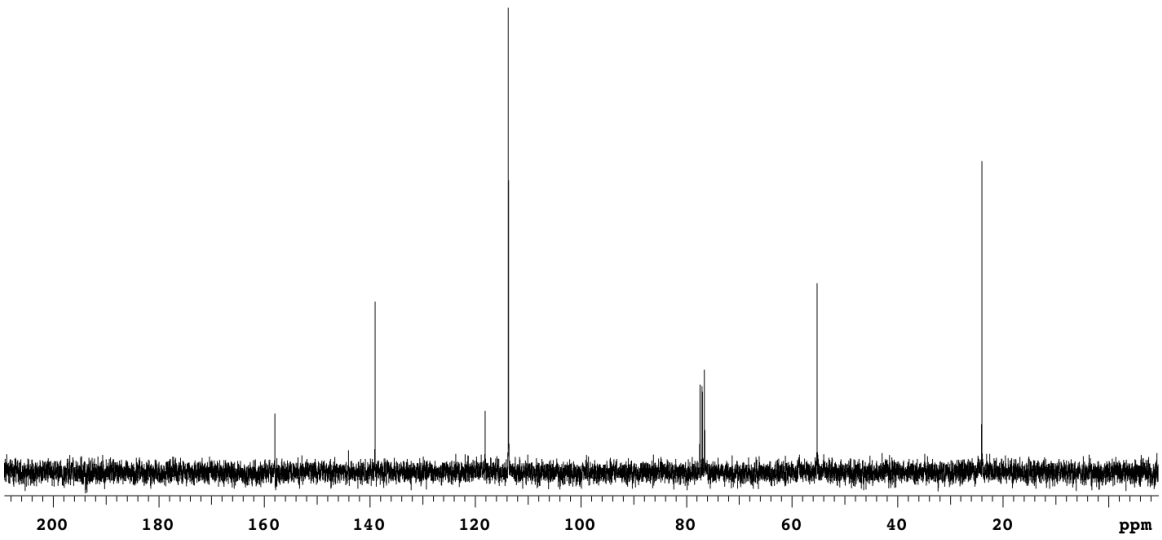
^{1}H NMR ($CDCl_3$, 300 MHz)



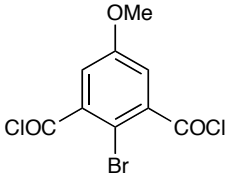
S-4



^{13}C NMR ($CDCl_3$, 75 MHz)



^{1}H NMR ($CDCl_3$, 300 MHz)



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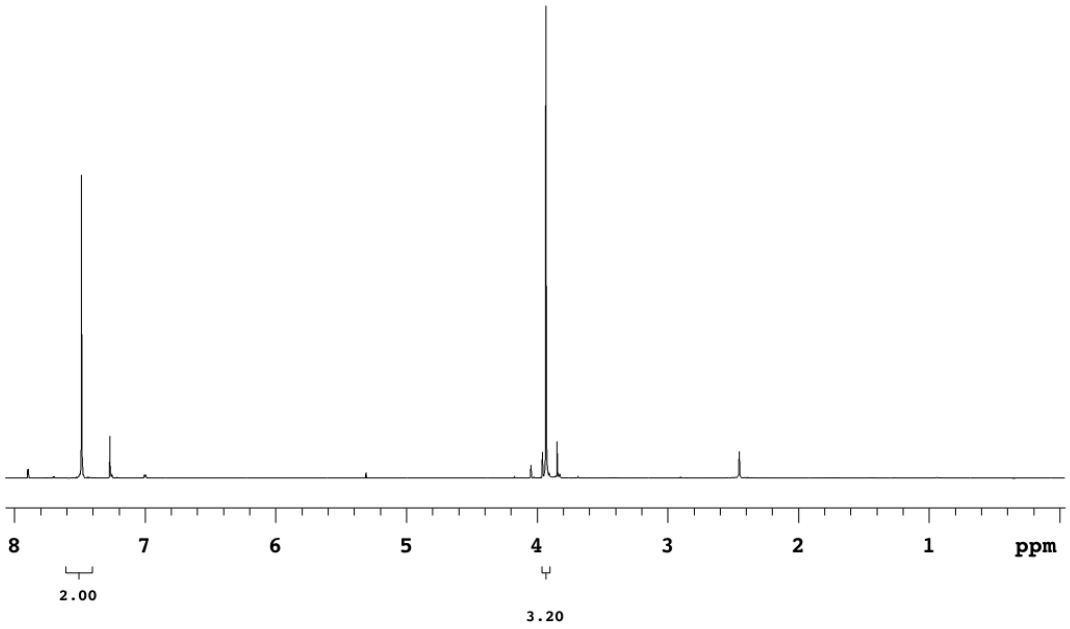
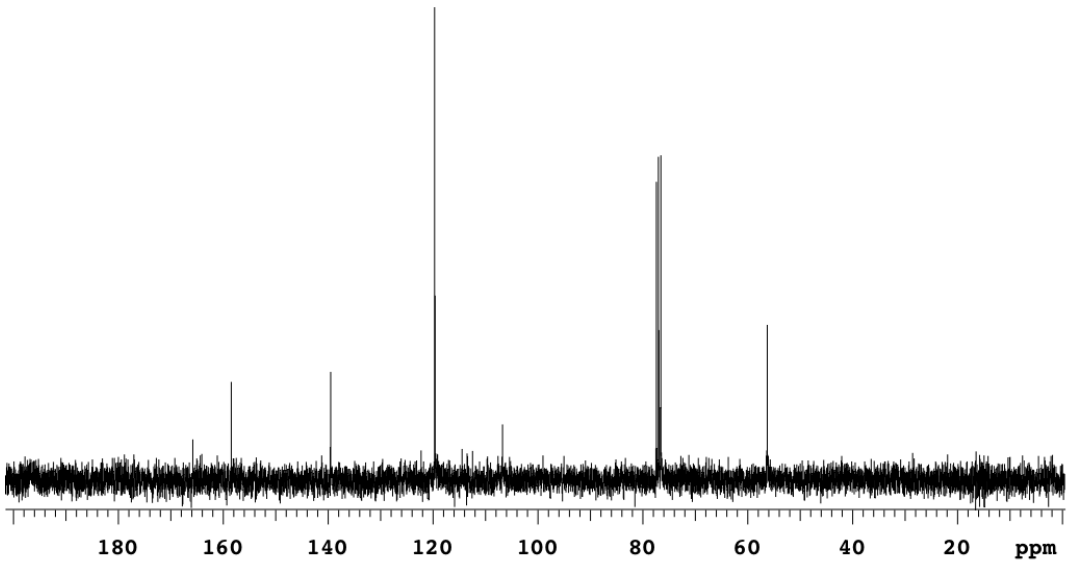
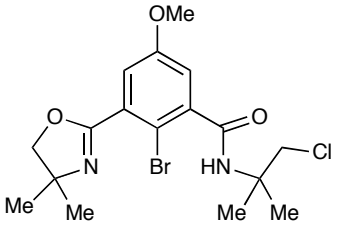


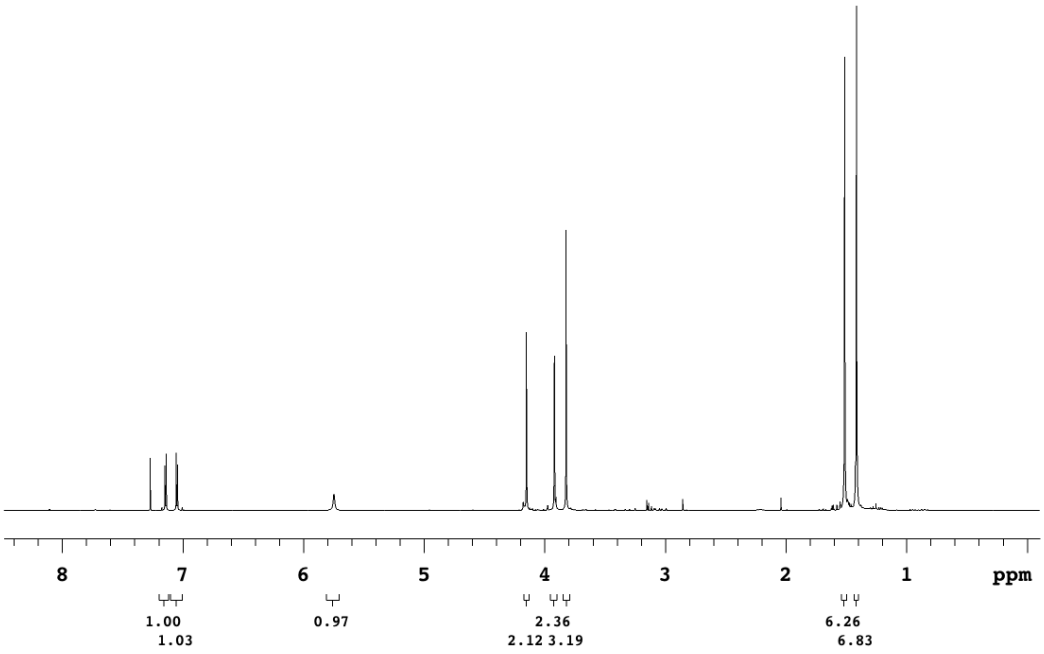
^{13}C NMR ($CDCl_3$, 75 MHz)



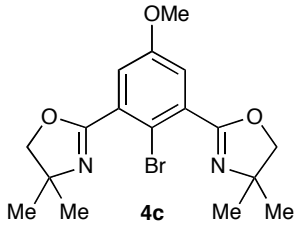
^{1}H NMR ($CDCl_3$, 300 MHz)



S-5

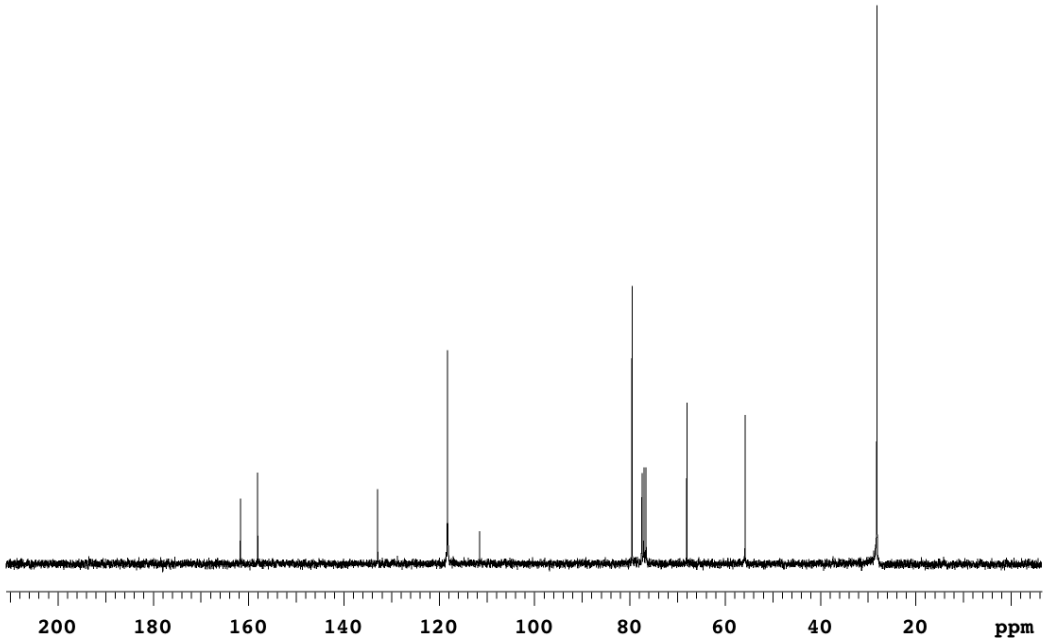


^{1}H NMR ($CDCl_3$, 300 MHz)

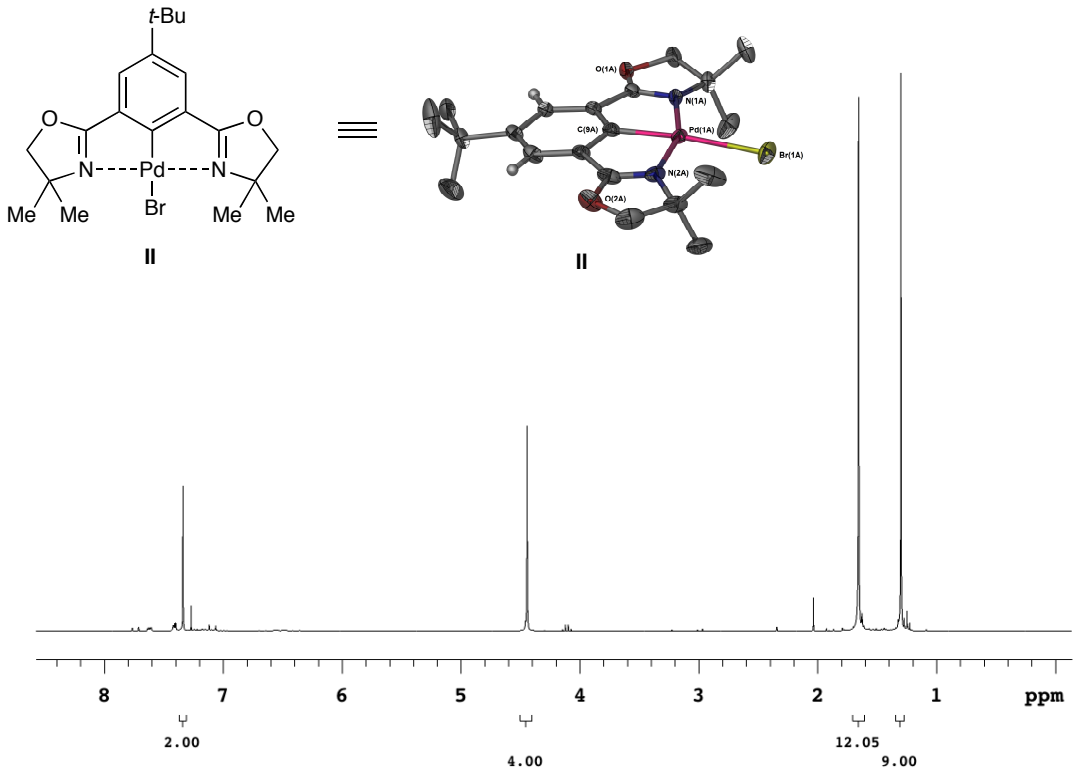


4c

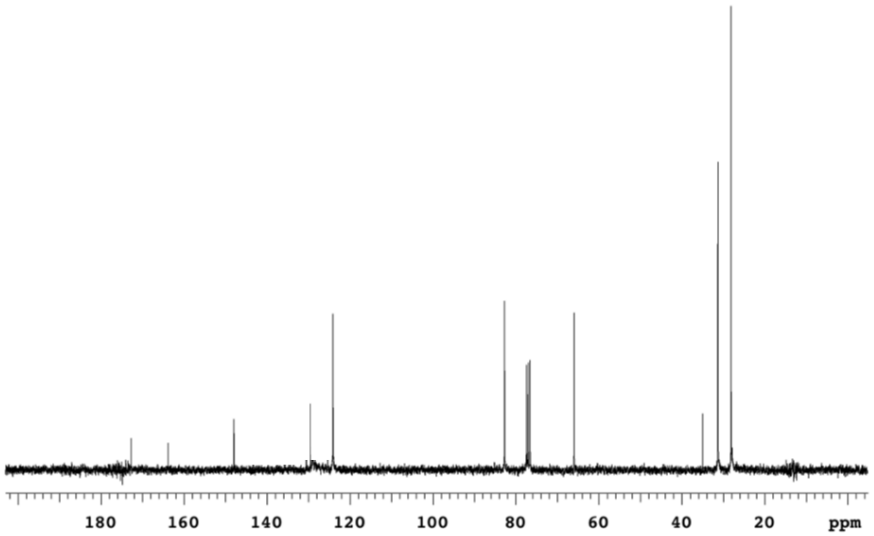
^{13}C NMR ($CDCl_3$, 75 MHz)



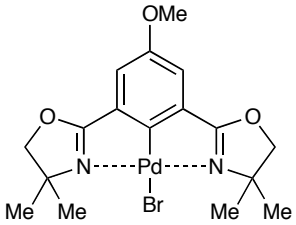
^{1}H NMR ($CDCl_3$, 300 MHz)



^{13}C NMR ($CDCl_3$, 75 MHz)



^{1}H NMR ($CDCl_3$, 300 MHz)



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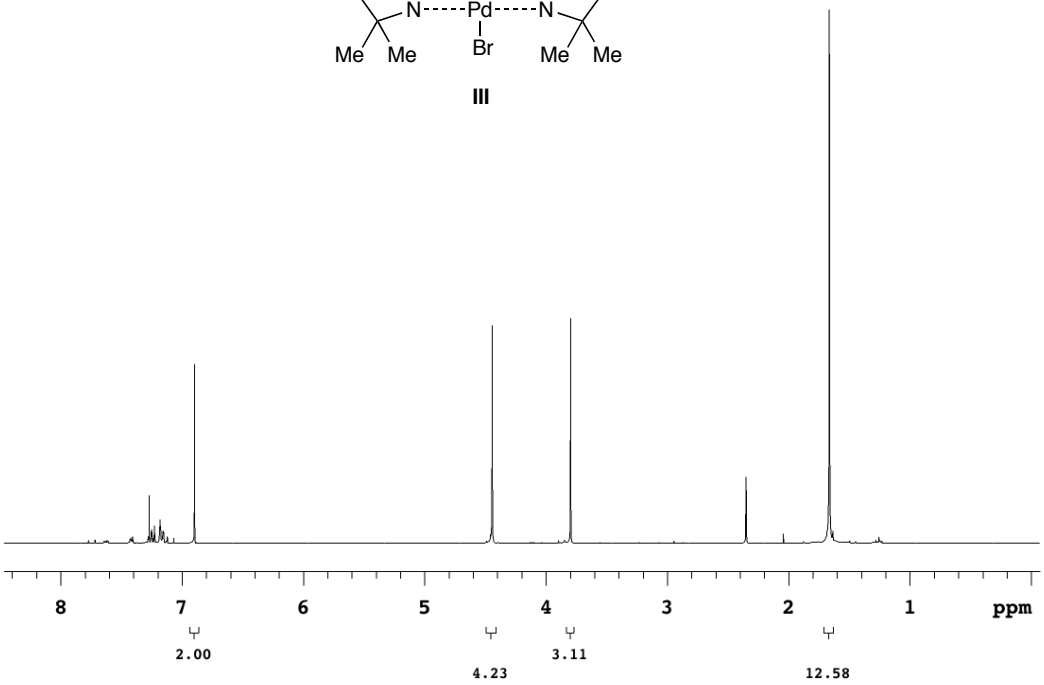
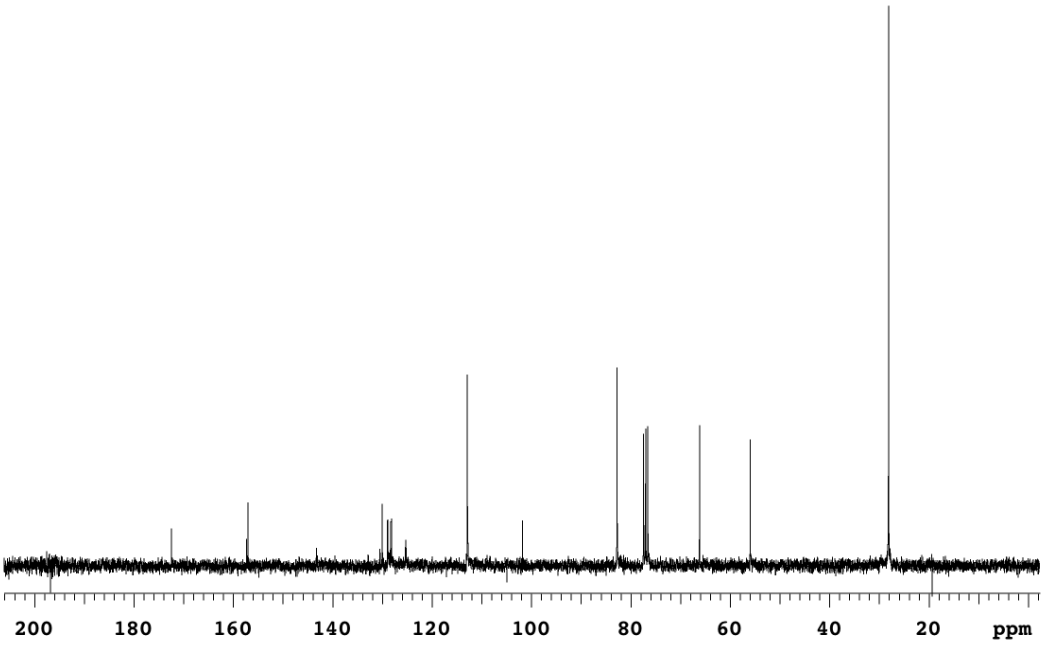


^{13}C NMR ($CDCl_3$, 75 MHz)



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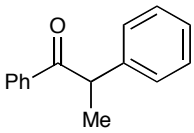

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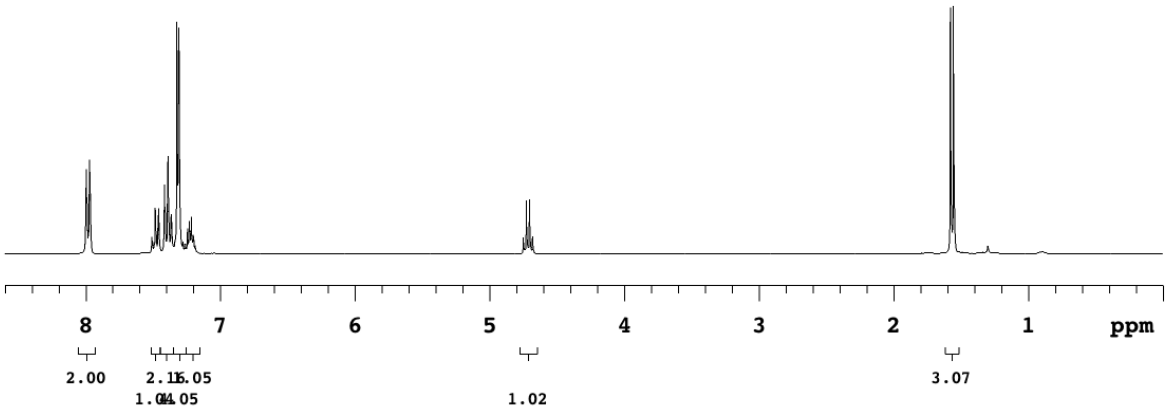
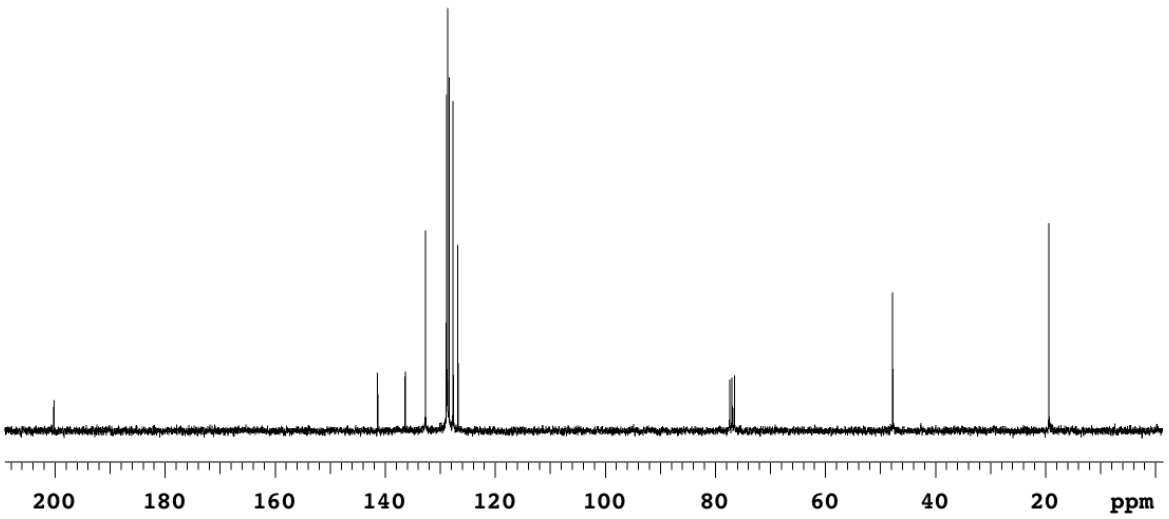
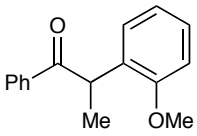


^{13}C NMR ($CDCl_3$, 75 MHz)



^{1}H NMR ($CDCl_3$, 300 MHz)



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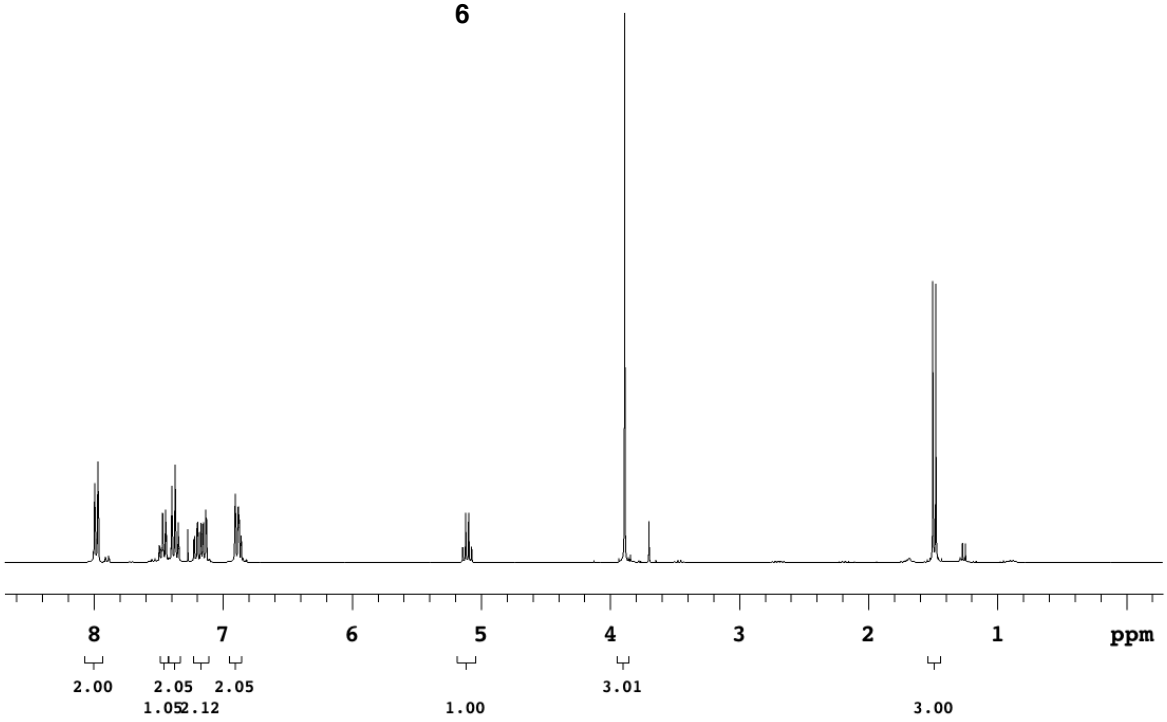
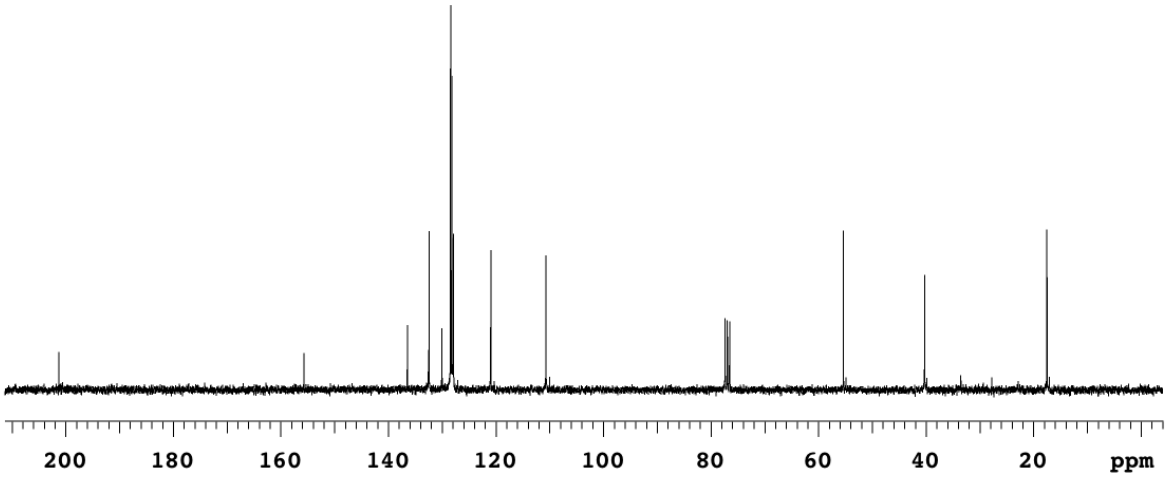


^{13}C NMR ($CDCl_3$, 75 MHz)



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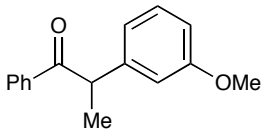

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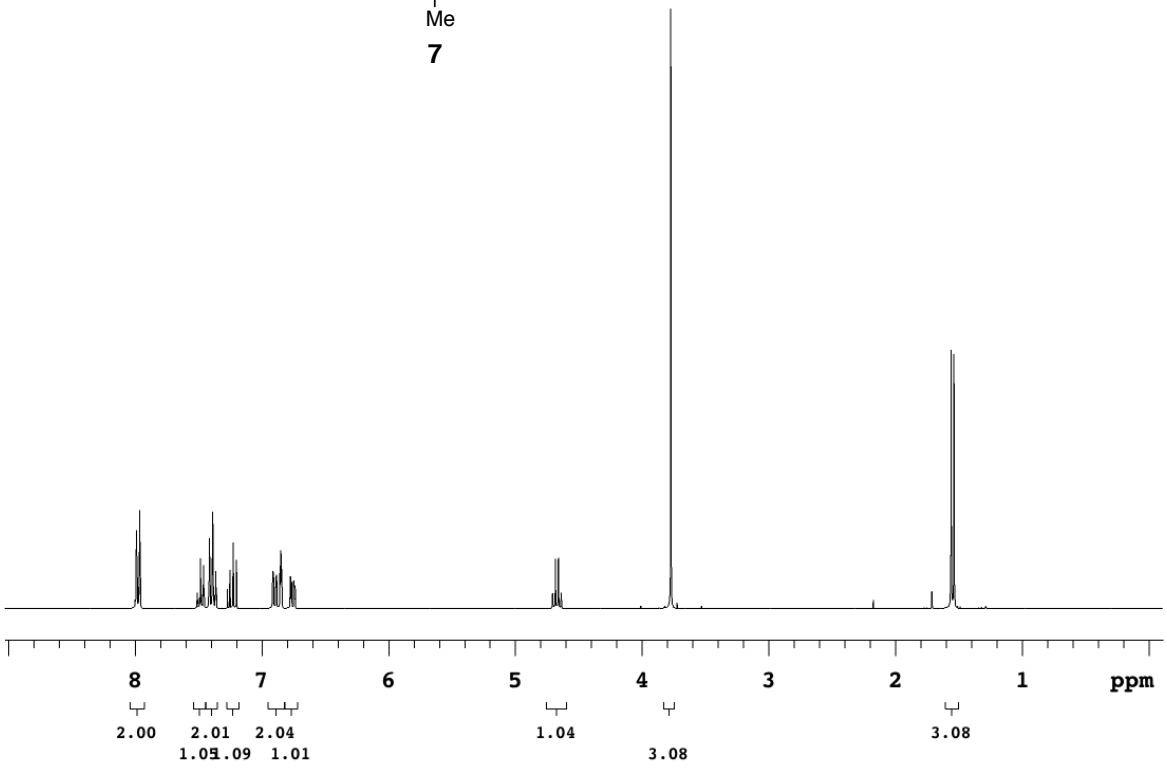
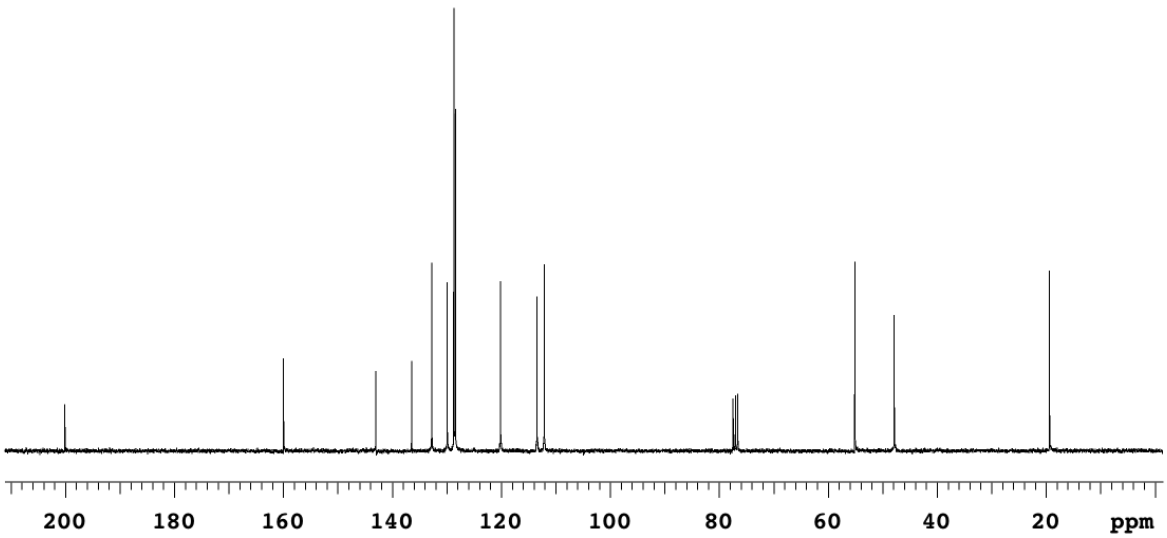


^{13}C NMR ($CDCl_3$, 75 MHz)



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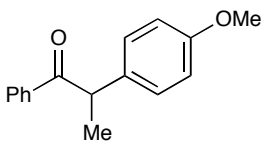

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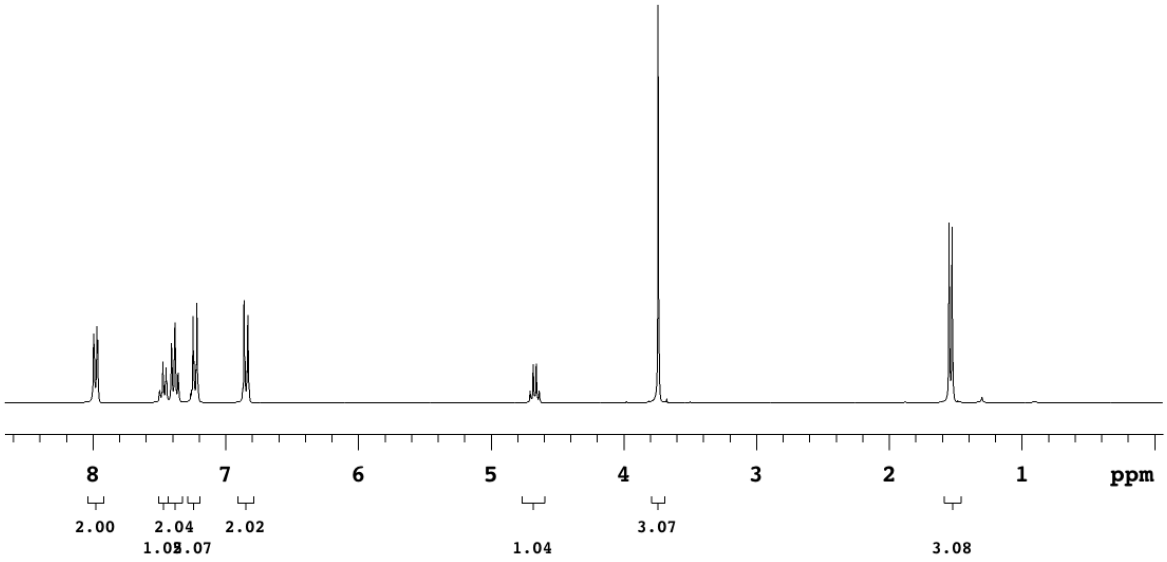
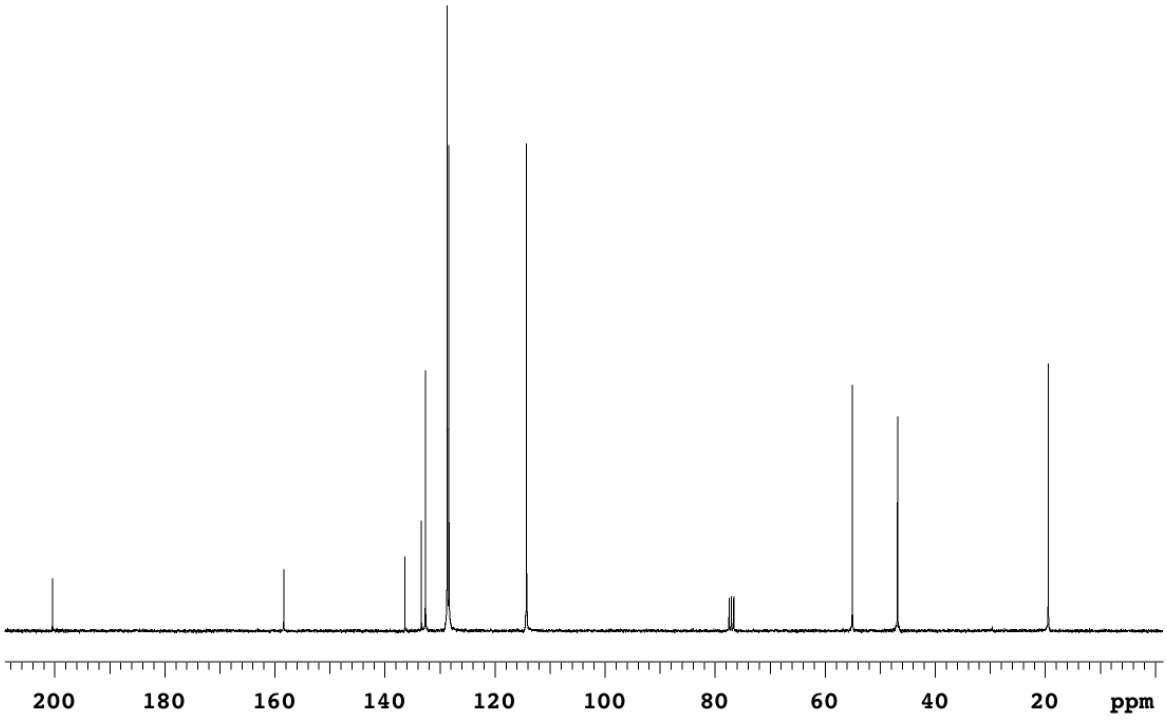
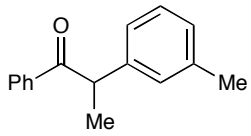


^{13}C NMR ($CDCl_3$, 75 MHz)



^{1}H NMR ($CDCl_3$, 300 MHz)



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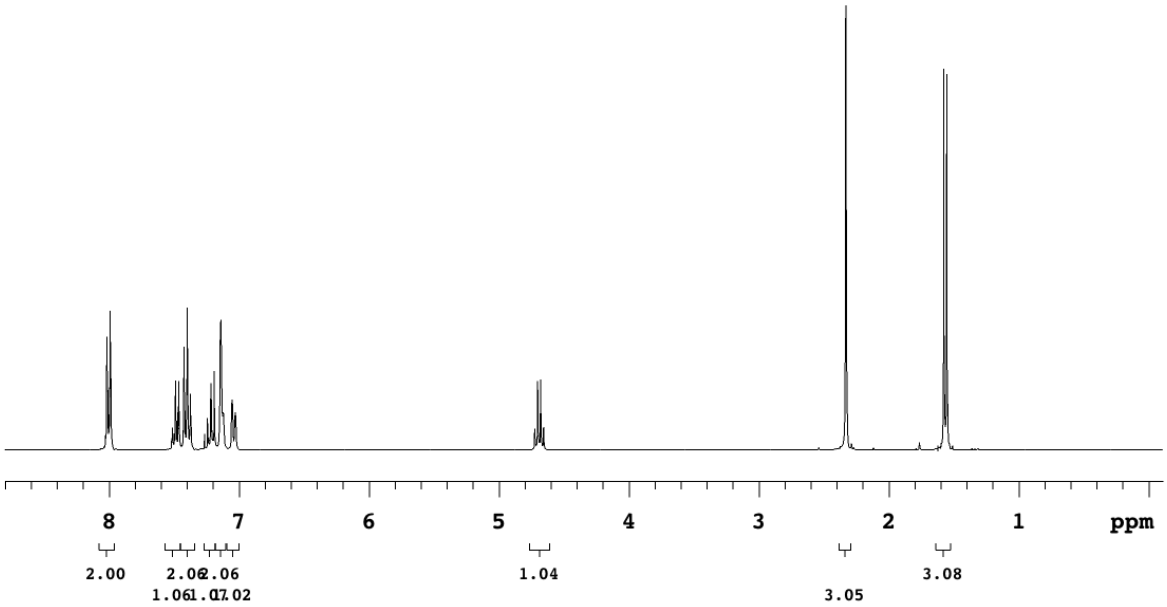
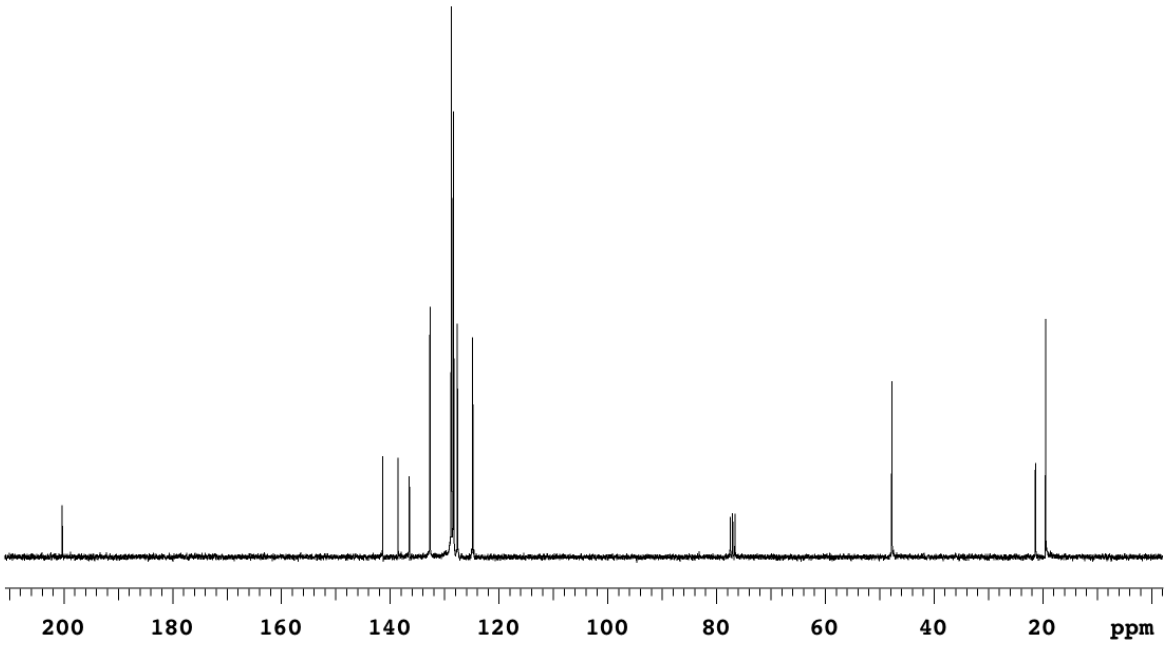


^{13}C NMR ($CDCl_3$, 75 MHz)



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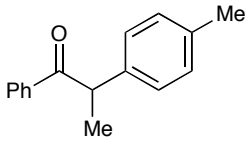

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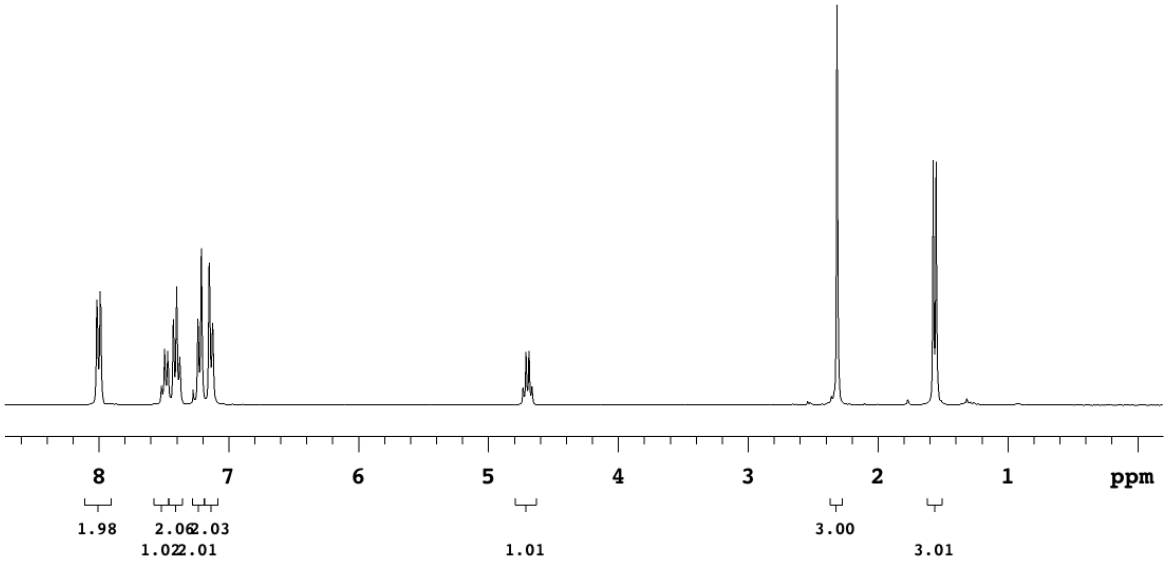
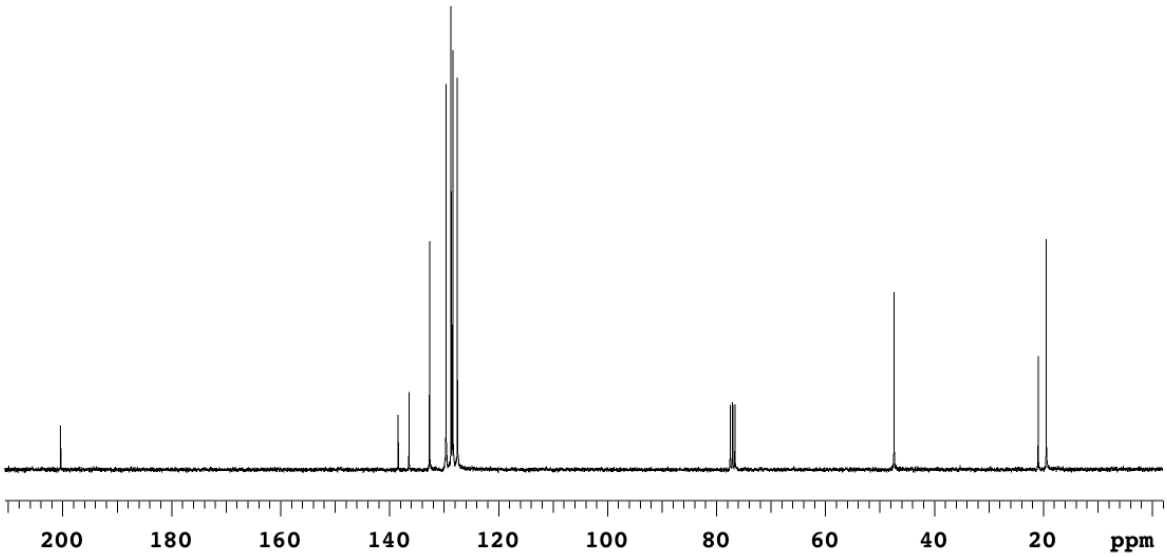


^{13}C NMR ($CDCl_3$, 75 MHz)



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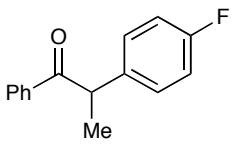

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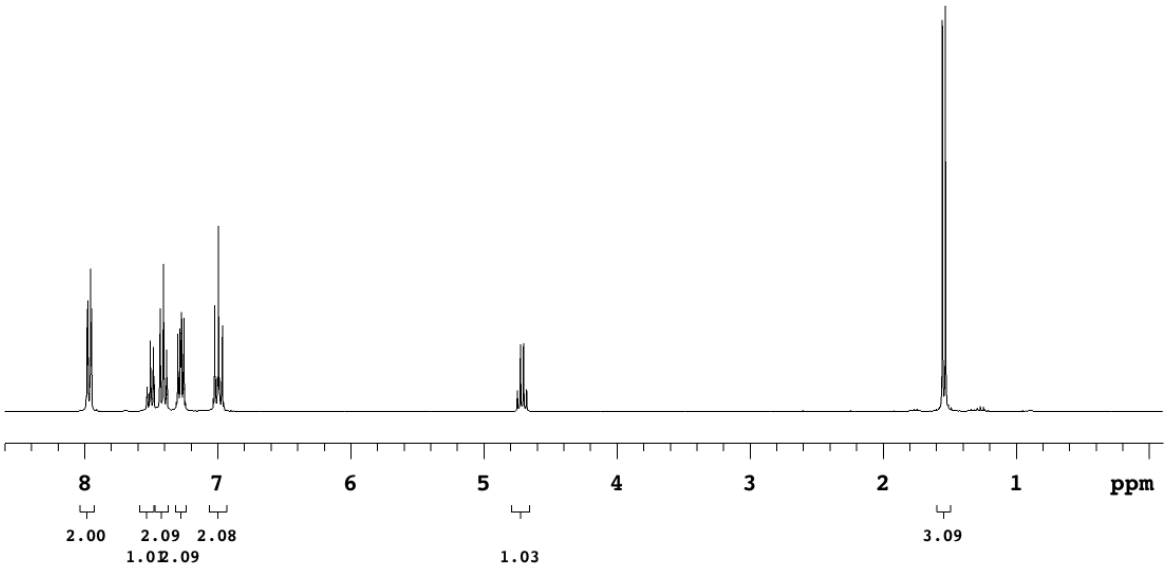
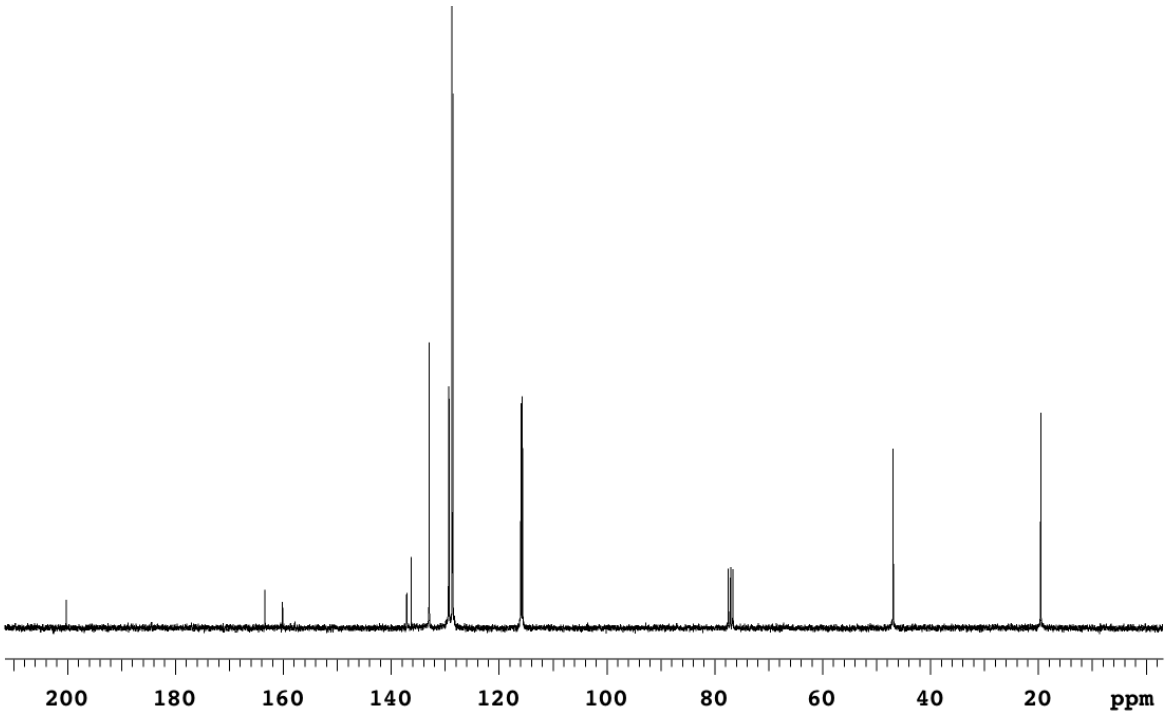
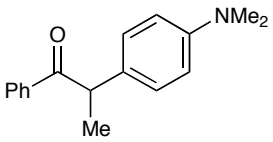


^{13}C NMR ($CDCl_3$, 75 MHz)



^{1}H NMR ($CDCl_3$, 300 MHz)



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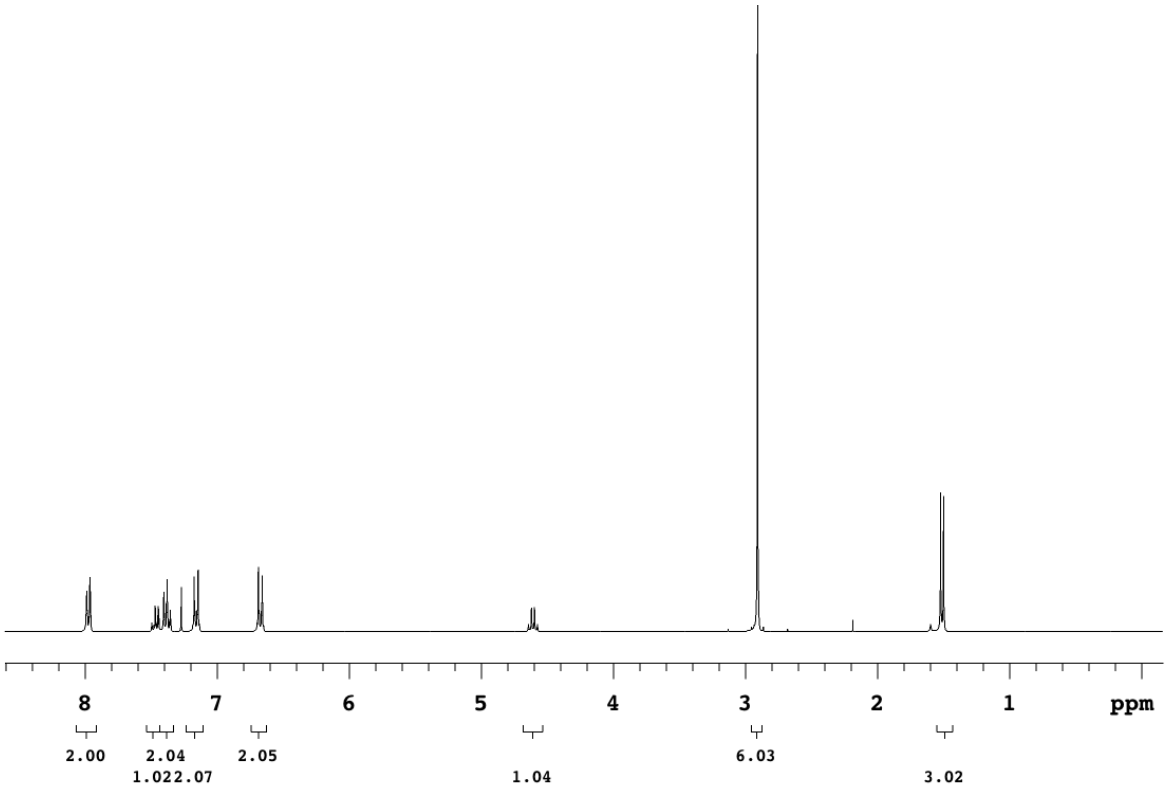
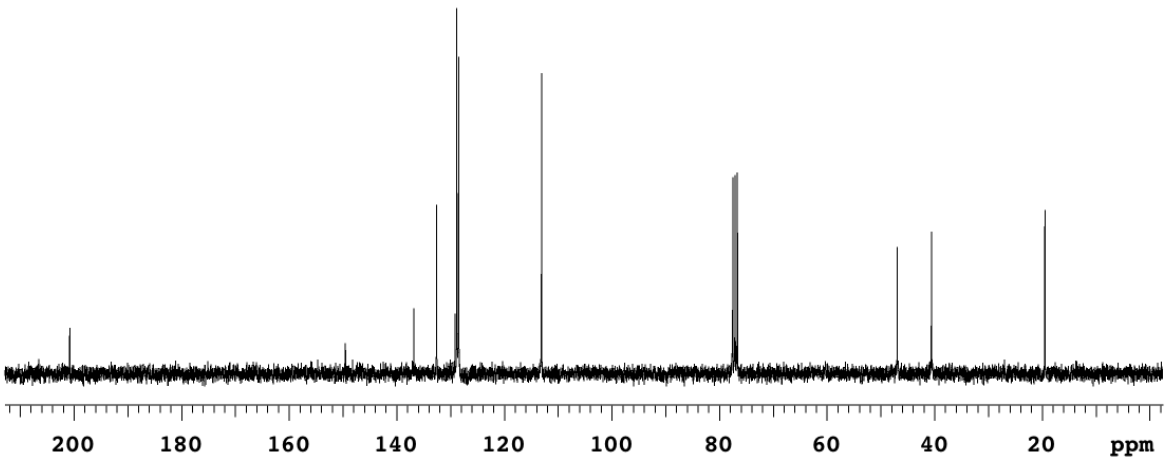
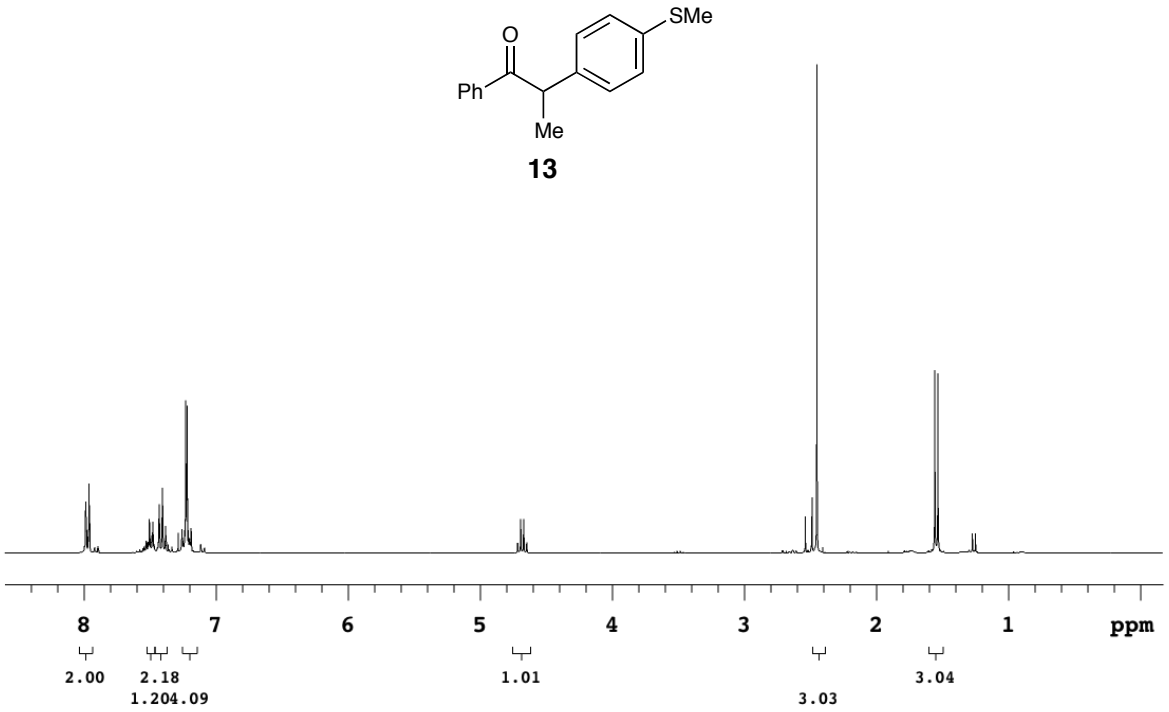


^{13}C NMR ($CDCl_3$, 75 MHz)



^{1}H NMR ($CDCl_3$, 300 MHz)



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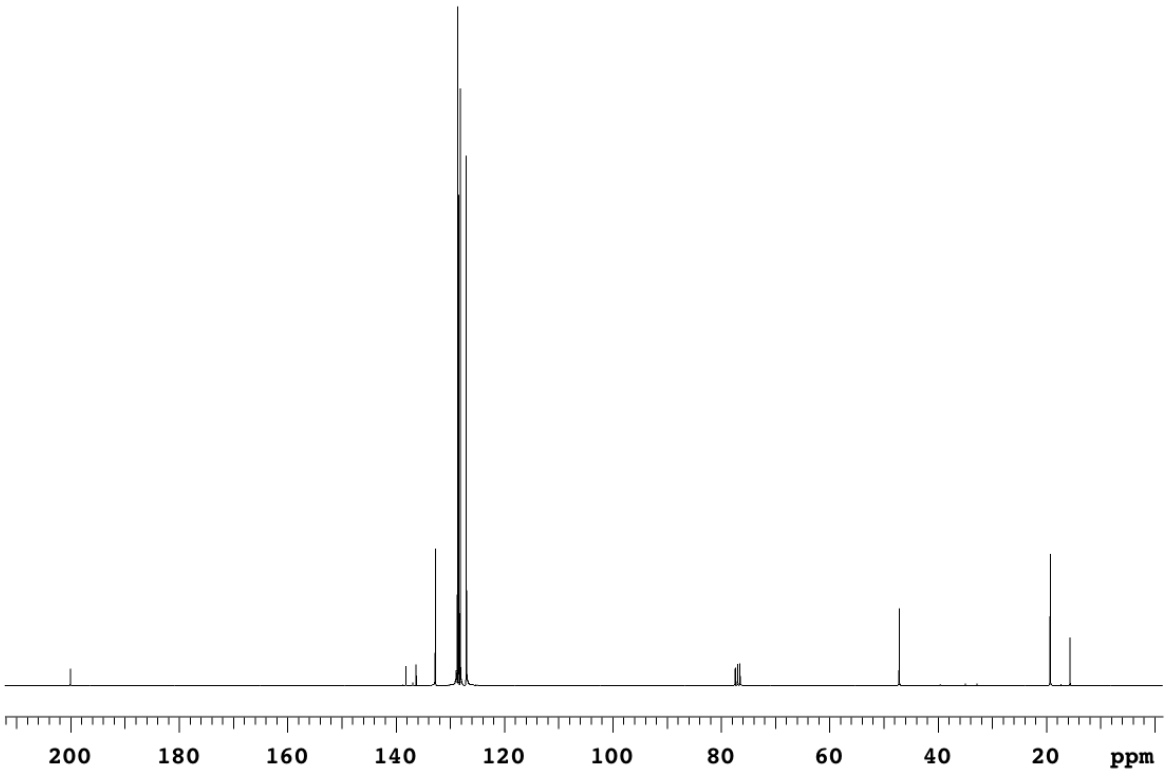

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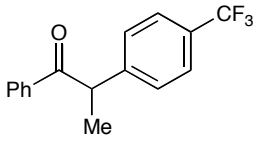

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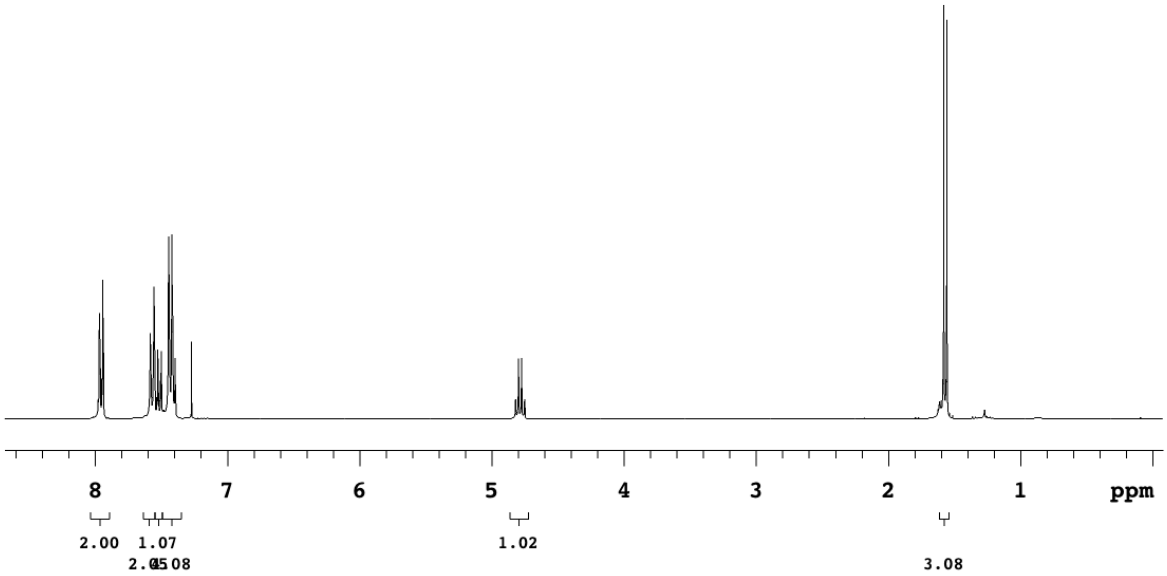

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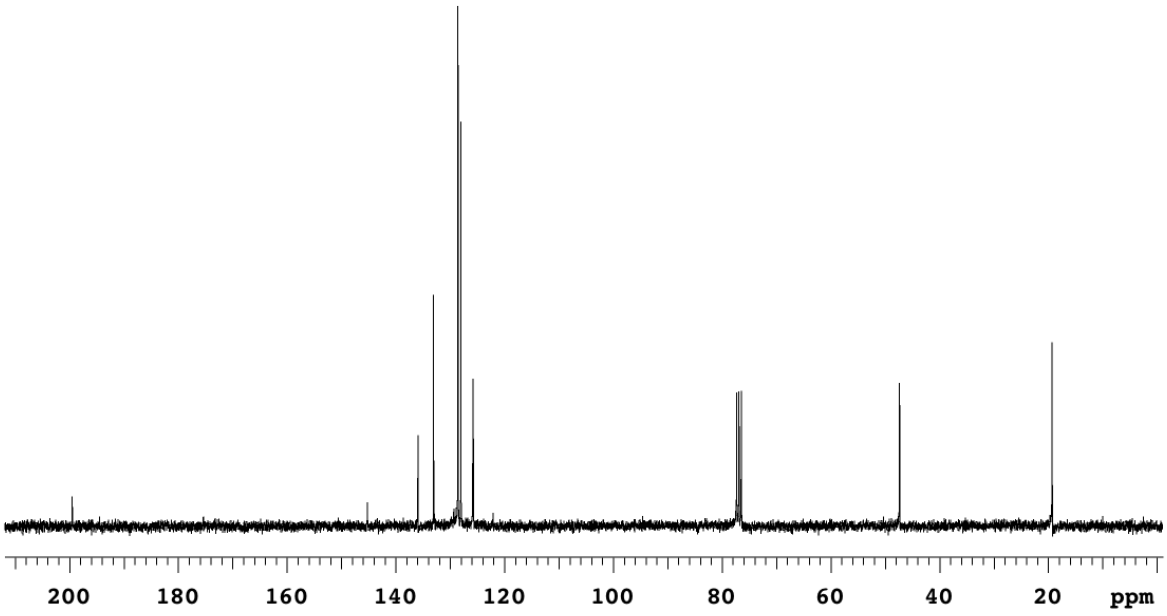
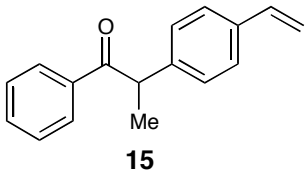


^{1}H NMR ($CDCl_3$, 300 MHz)



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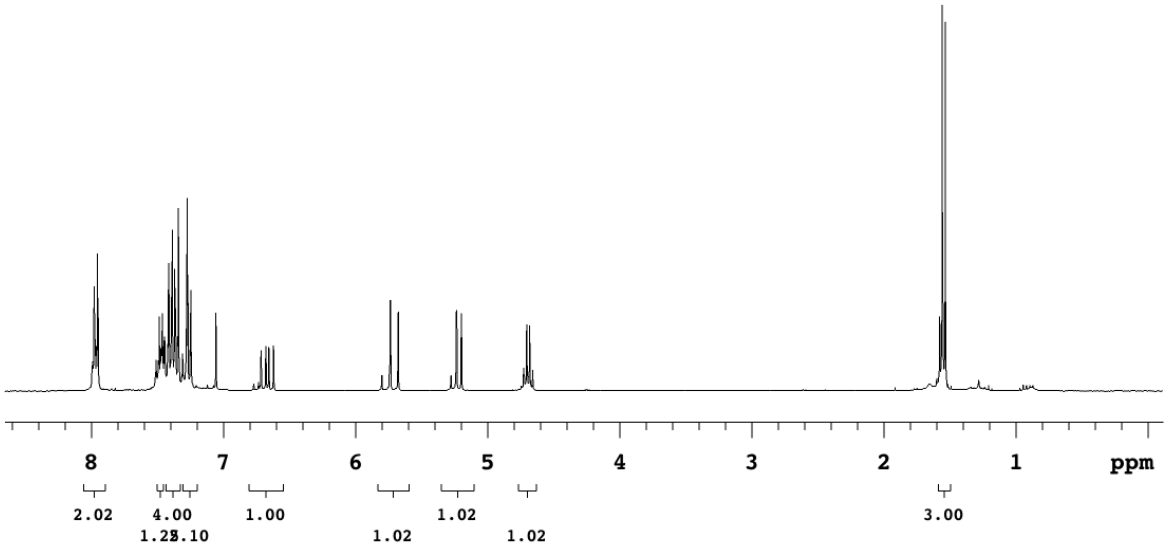
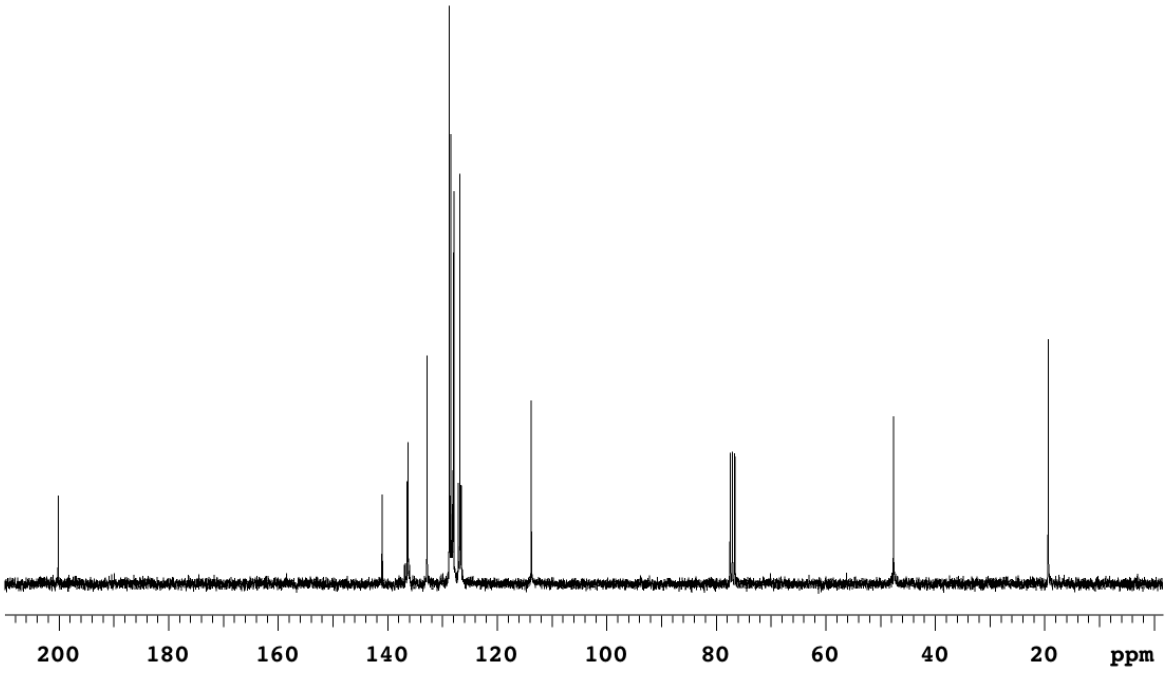
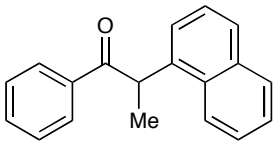


^{13}C NMR ($CDCl_3$, 75 MHz)



^{1}H NMR ($CDCl_3$, 300 MHz)



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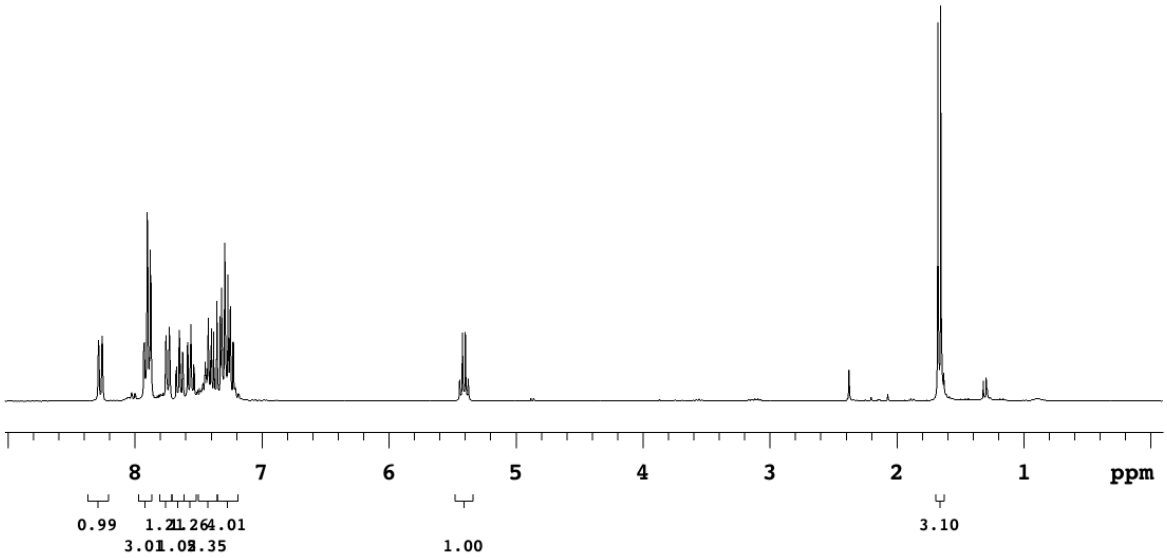
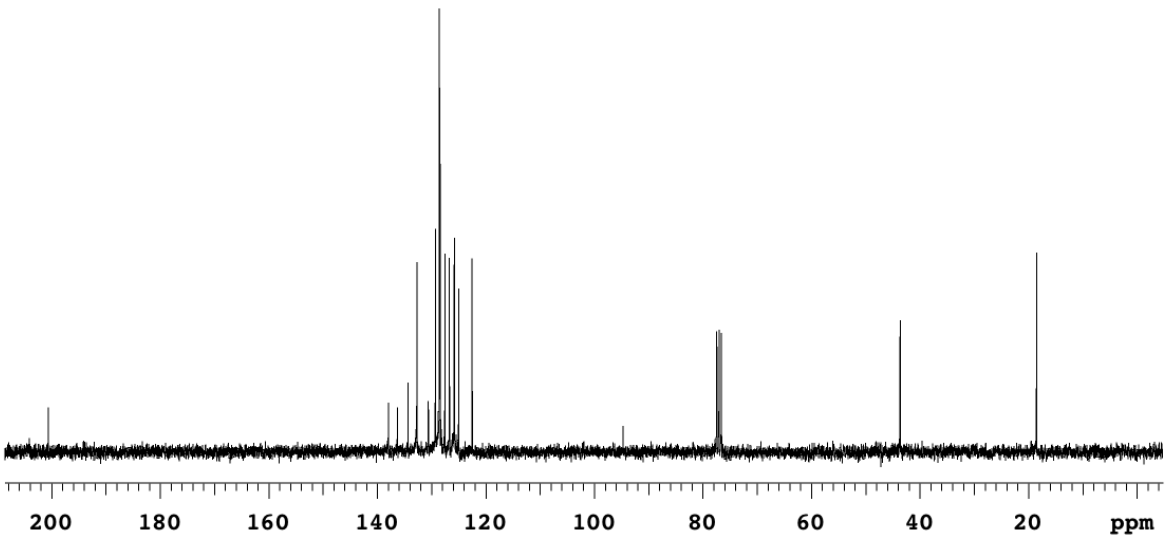


^{13}C NMR ($CDCl_3$, 75 MHz)



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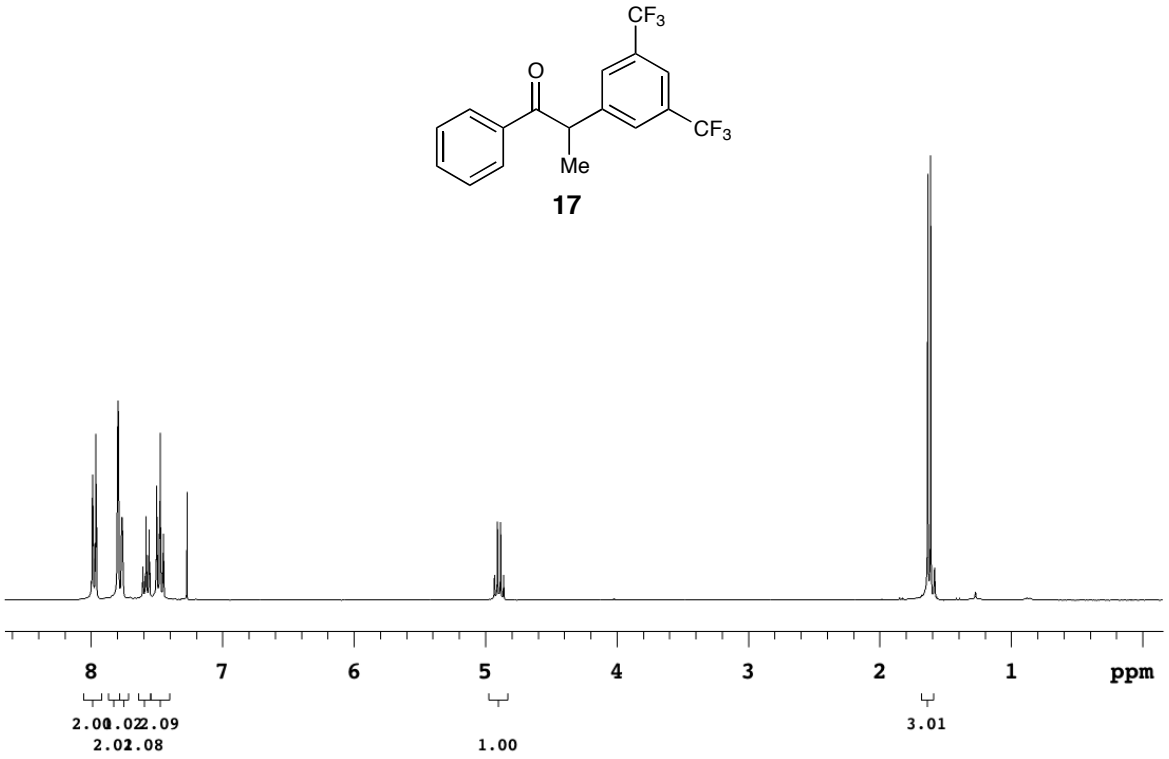

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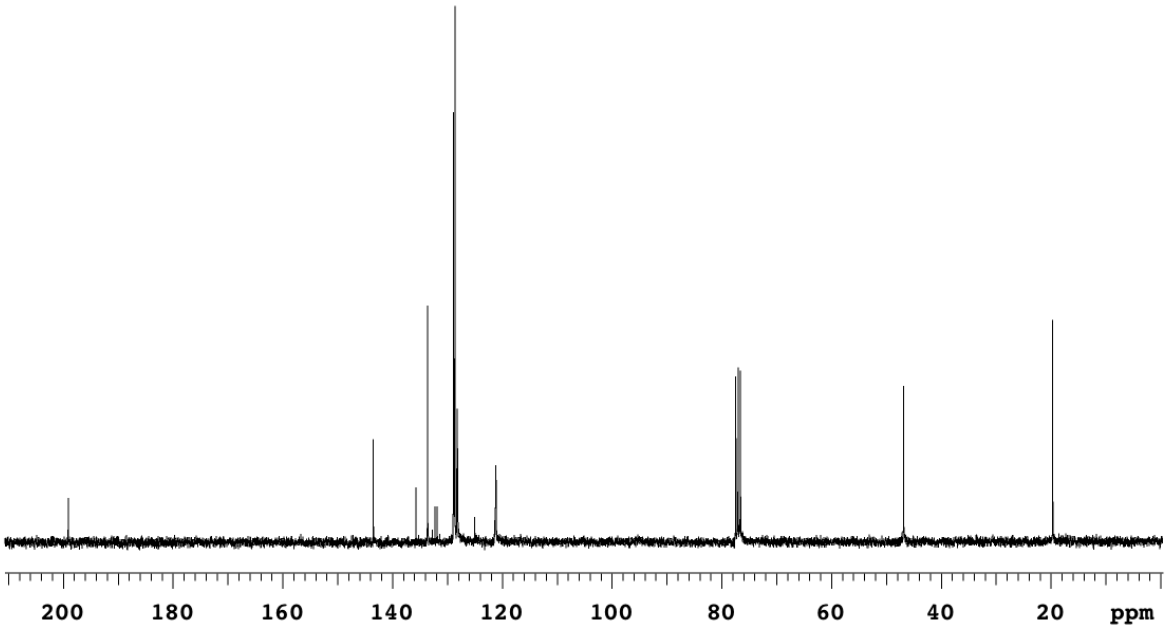
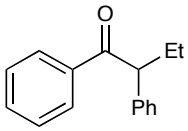


^{1}H NMR ($CDCl_3$, 300 MHz)



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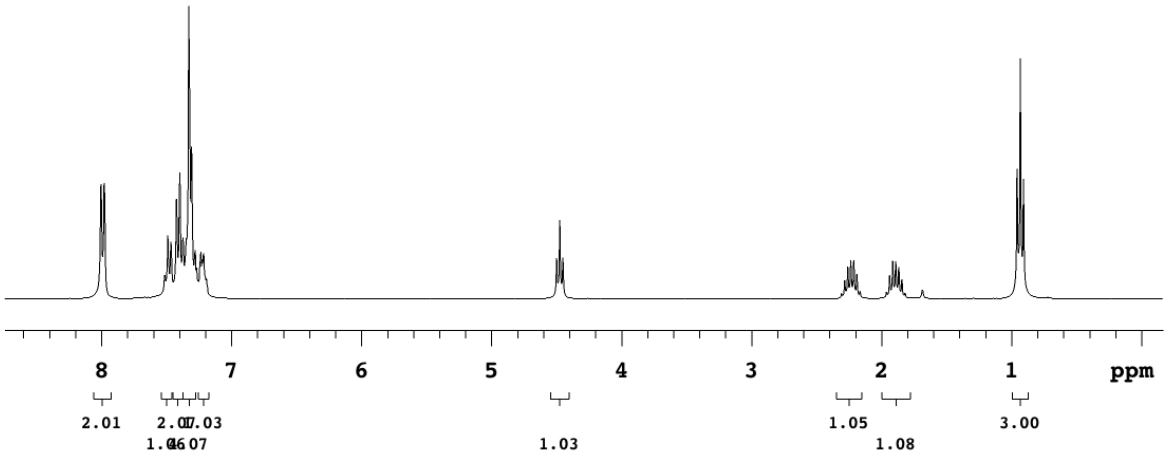
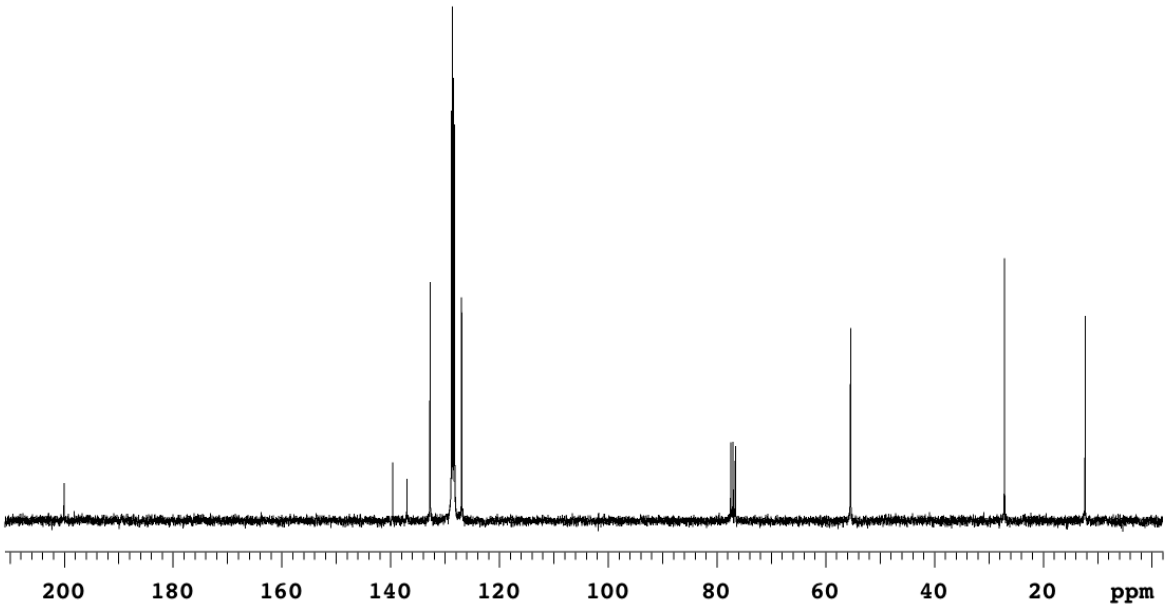
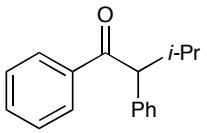


^{13}C NMR ($CDCl_3$, 75 MHz)



^{1}H NMR ($CDCl_3$, 300 MHz)



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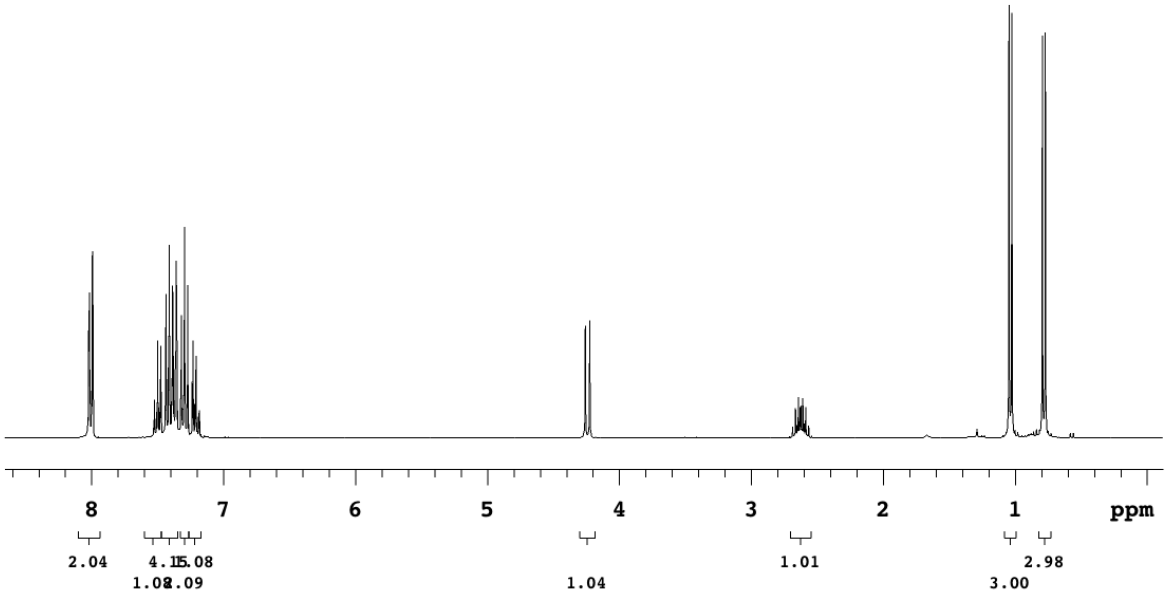
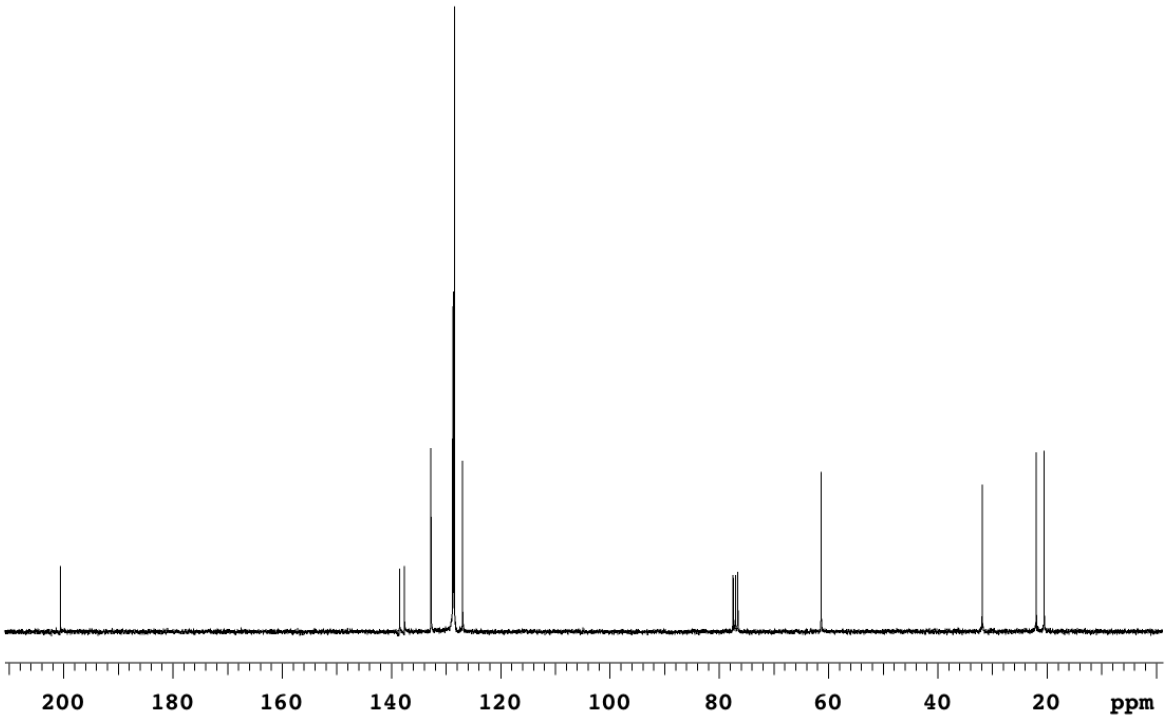
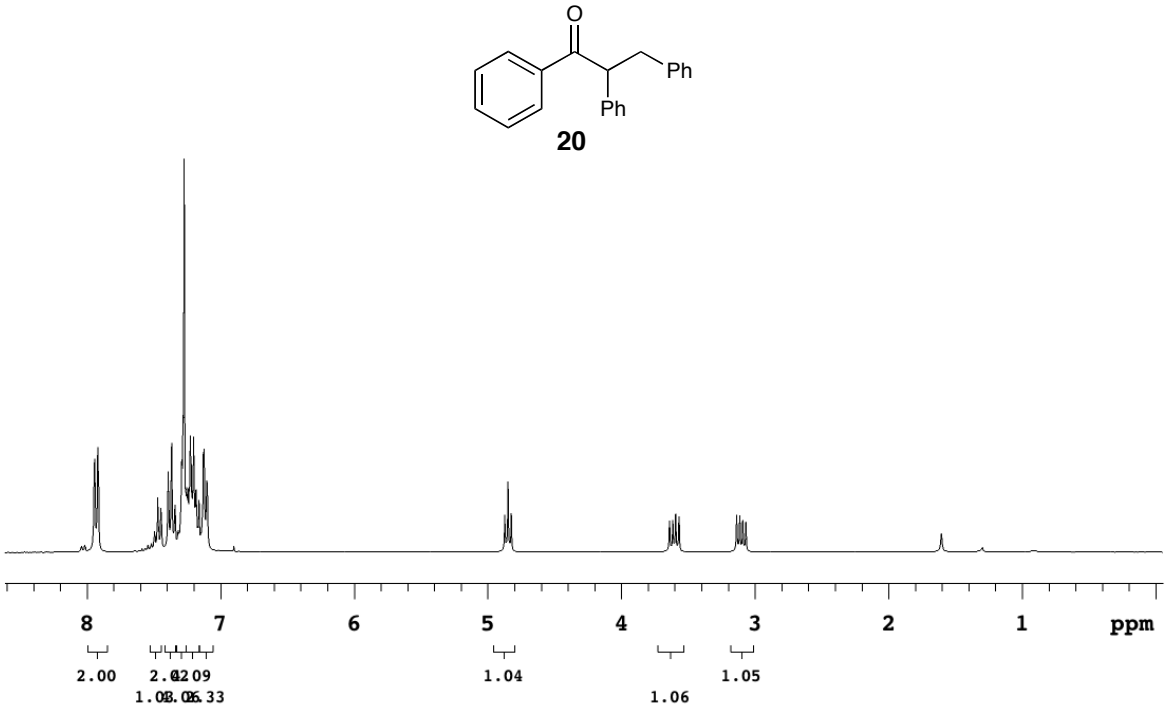


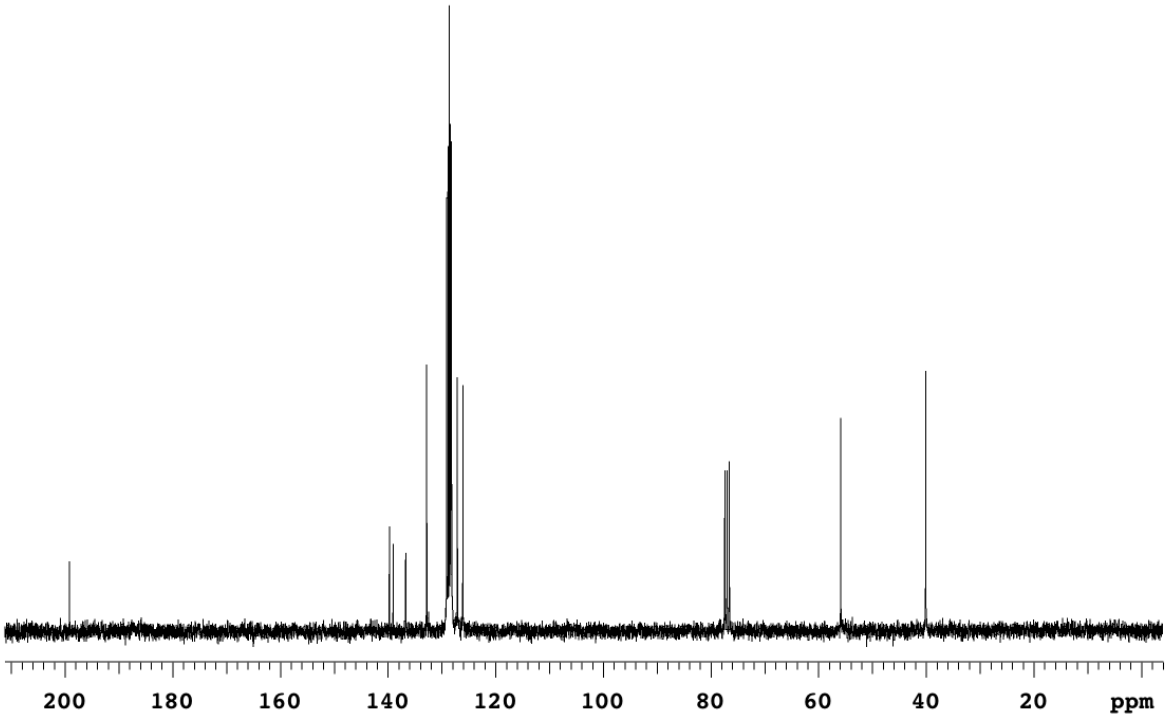
^{13}C NMR ($CDCl_3$, 75 MHz) ^{1}H NMR ($CDCl_3$, 300 MHz)



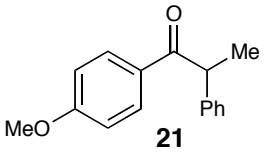
^{1}H NMR ($CDCl_3$, 300 MHz)



^{13}C NMR ($CDCl_3$, 75 MHz) ^{1}H NMR ($CDCl_3$, 300 MHz)



^{1}H NMR ($CDCl_3$, 300 MHz)



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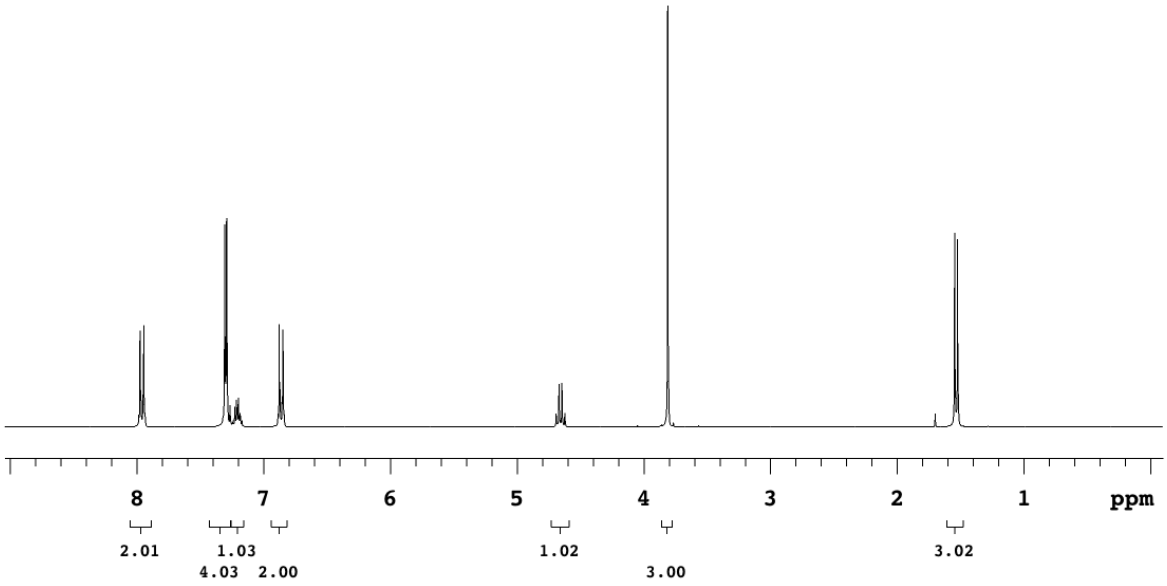
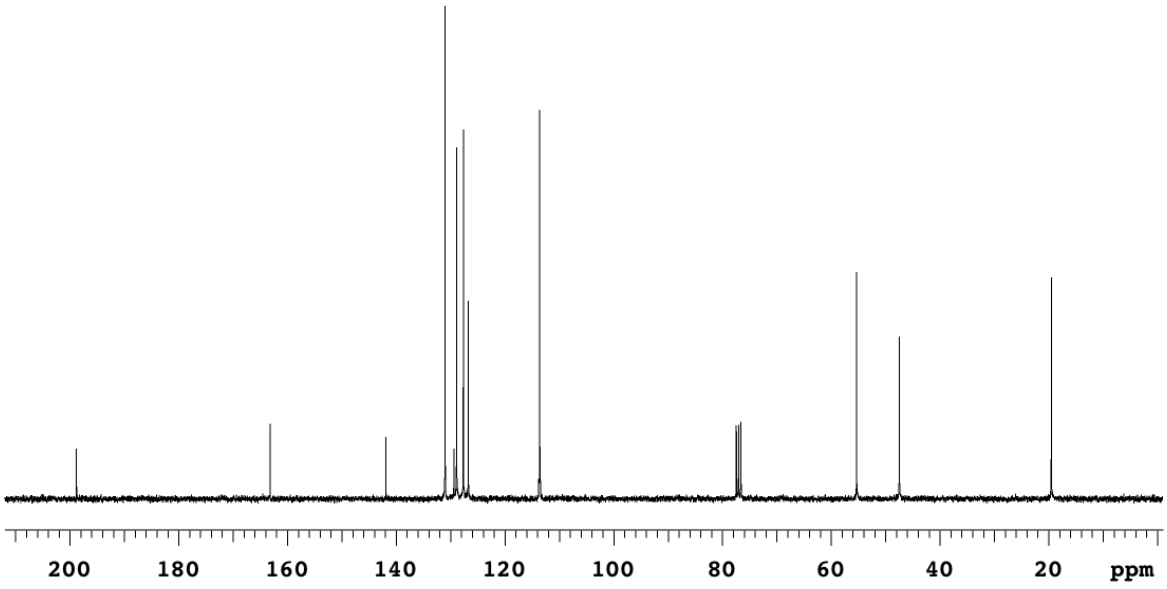
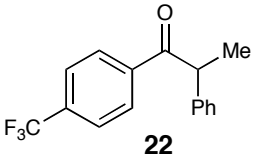


^{13}C NMR ($CDCl_3$, 75 MHz)



^{1}H NMR ($CDCl_3$, 300 MHz)



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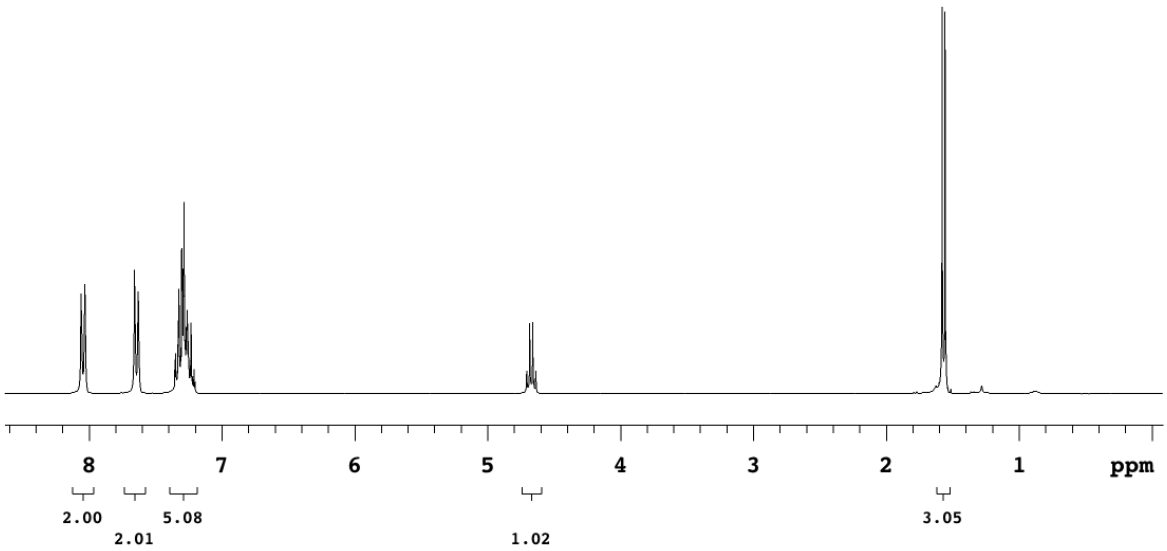
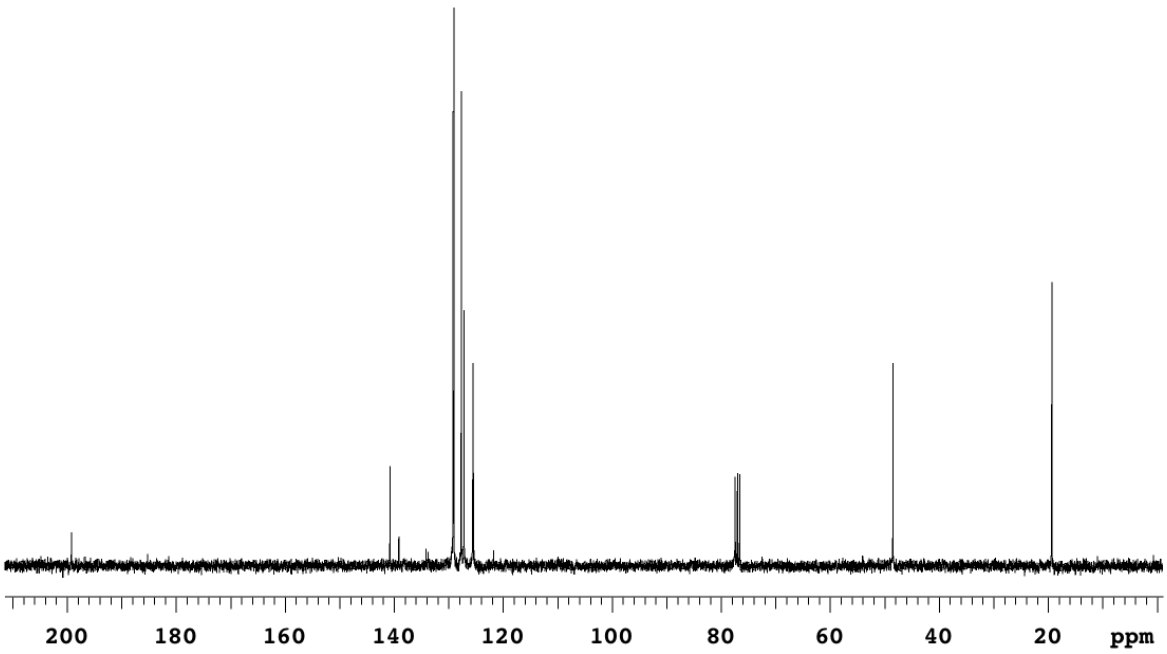
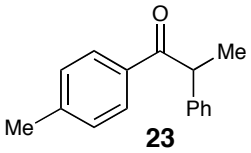


^{13}C NMR ($CDCl_3$, 75 MHz)



^{1}H NMR ($CDCl_3$, 300 MHz)



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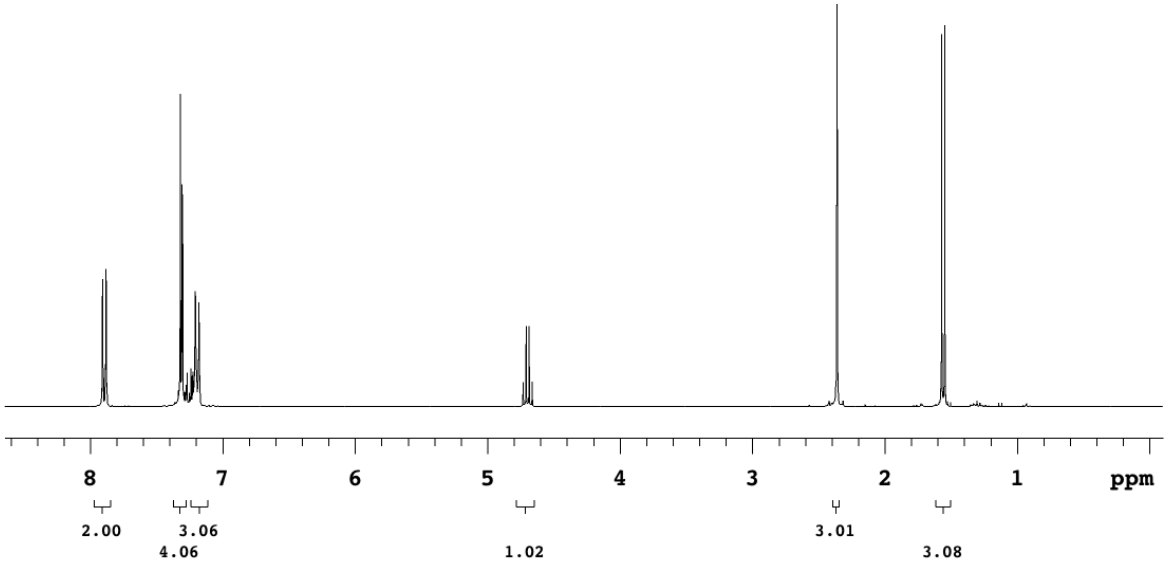
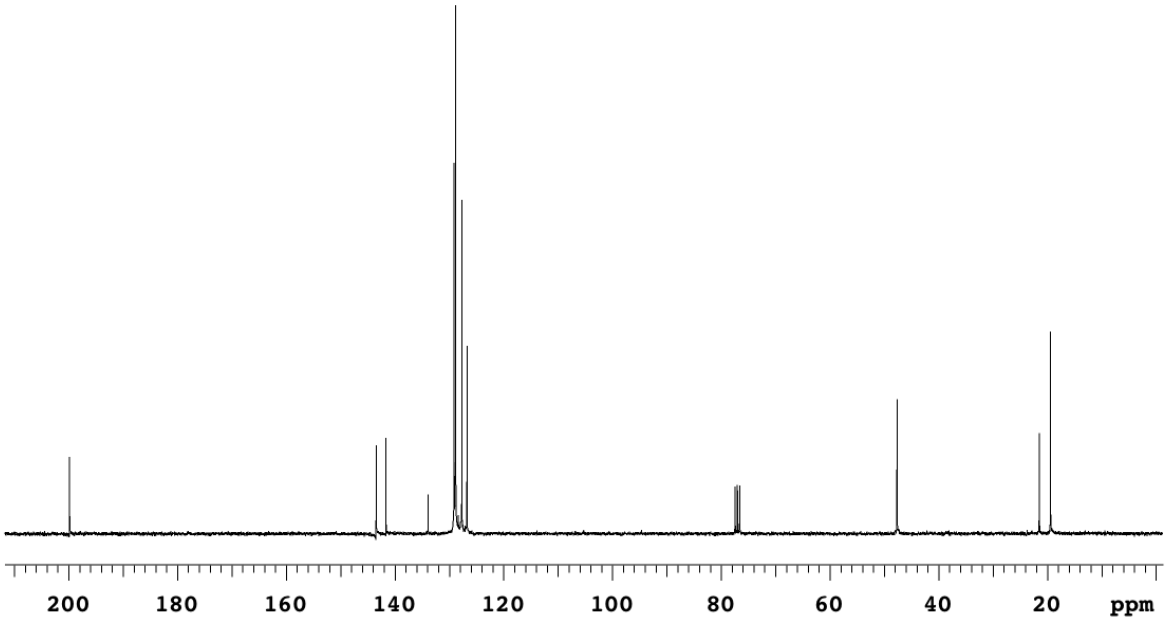
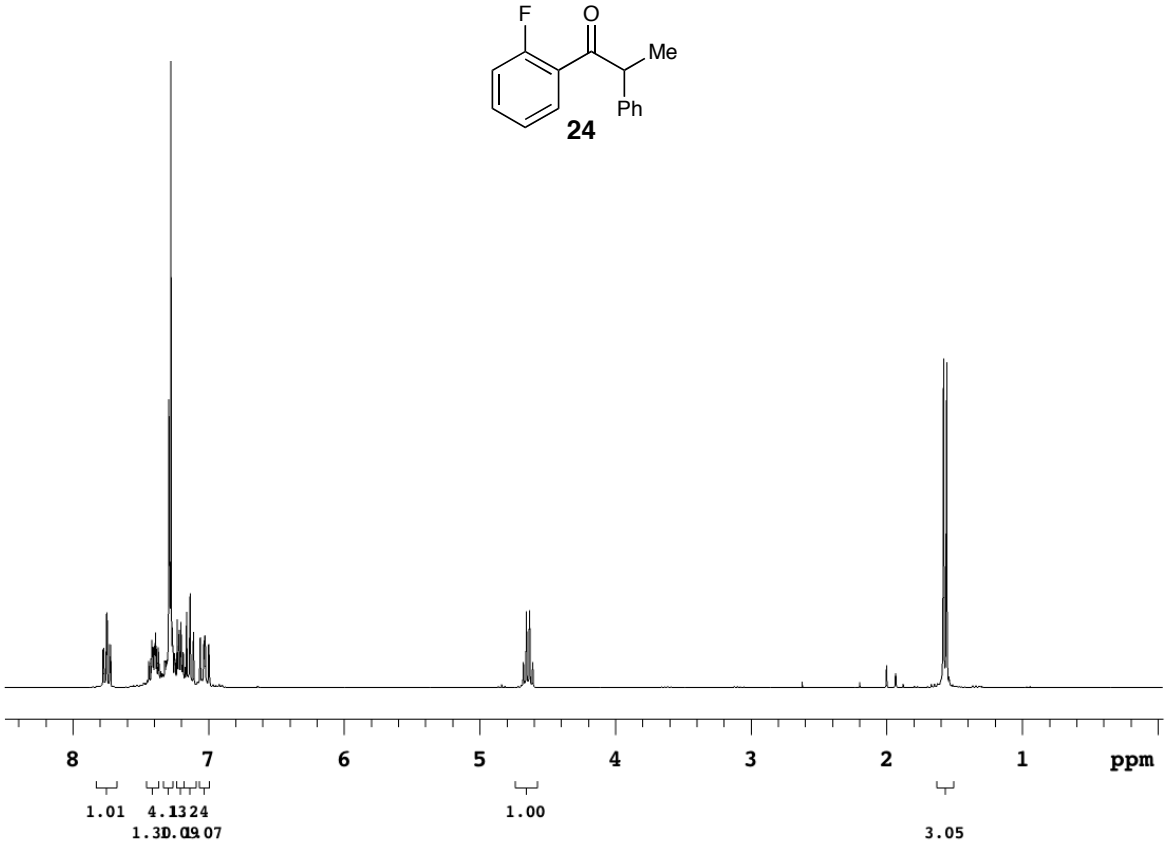


^{13}C NMR ($CDCl_3$, 75 MHz) ^{1}H NMR ($CDCl_3$, 300 MHz)



^{1}H NMR ($CDCl_3$, 300 MHz)



^{13}C NMR ($CDCl_3$, 75 MHz)