SUPPORTING INFORMATION

Pd-Catalyzed C–N Coupling Reactions Facilitated by Organic Bases: Mechanistic Investigation Leads to Enhanced Reactivity in the Arylation of Weakly Binding Amines

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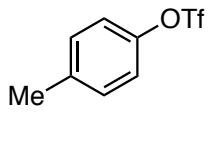
General Information

Unless noted, all chemicals obtained from commercial sources were used as received and all reactions were carried out under an atmosphere of nitrogen. Anhydrous tetrahydrofuran (THF) was purchased from Sigma-Aldrich, stored in J.T. Baker in CYCLE-TAINER® kegs, and was purified via filtration over neutral alumina and copper(II) oxide under an argon atmosphere. Anhydrous 2-methyl tetrahydrofuran (2-MeTHF) was purchased from Sigma-Aldrich in a Sure-Seal™ bottle. $CDCl_3$ and C_6D_6 were purchased from Cambridge Isotope Laboratories. 1,8-Diazabicyclo[5.4.0]undec-7-ene (DBU) was purchased from Chem-Impex International. *N*,*N*-diisopropylethylamine, (DIPEA), 1,5,7- and 7-methyl-1,5,7-triazabicyclo[4.4.0]dec-5-ene (MTBD) were purchased from Sigma-Aldrich. 4-fluoroaniline was purchased from Sigma-Aldrich and was passed through a plug of basic alumina prior to use. $COD(Pd\text{-}AlPhos)_2$ was prepared according to literature procedure using recrystallized AlPhos[1] and was stored in a desiccator on the bench. Other starting materials were either prepared according to referenced literature procedures or were purchased from chemical suppliers (Sigma-Aldrich, Combi-Blocks, Alfa Aesar, or TCI-America) and were used as received. Isolated compounds were purified by flash chromatography using Silicycle SiliaFlashP60 (230-400 mesh) silica gel with the aid of a Biotage SP4 instrument. ^1H, ^{13}C, and ^{19}F spectra were recorded on a Bruker Avance-400 MHz spectrometer. Kinetic data were acquired on a Varian Mercury 300 MHz spectrometer or a Bruker 500 MHz spectrometer. ^1H and ^{13}C spectra were calibrated using residual chloroform or benzene as an internal reference ($CHCl_3$: δ 7.26 ppm and δ 77.36 ppm, respectively. C_6H_6: 7.16 ppm and 128.06 ppm, respectively). ^{19}F NMR spectra were calibrated to an external standard of neat $CFCl_3$ (δ 0.0 ppm). ^{31}P NMR spectra were calibrated to an external standard of H_3PO_4 (δ 0.0 ppm). The following abbreviations were used to explain multiplicities: s = singlet, bs = broad singlet, d = doublet, t = triplet, q = quartet, m = multiplet. HRMS data were recorded on a JEOL Accu-ToF DART (Direct Analysis in Real Time) instrument. Melting points were obtained using a Stanford Research Systems EZ-Melt melting point apparatus.

Standard NMR Parameters

All initial rates measurements were acquired via continuous measurement arrays using a pre-acquisition delay (PAD). The following parameters were used for Varian instruments: steps=20; starting value=0; final value=0; nt=4; gain=20; d1=16; sw=(-100,-140). All spectra were stacked, phased, baseline-corrected, and then analyzed using the MestreNova integrals graph tool.

List of Aryl Triflates (ArOTf)



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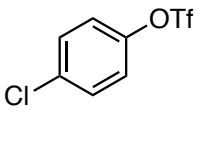

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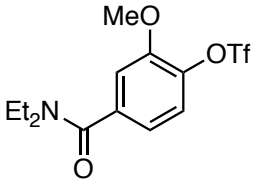

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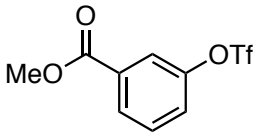

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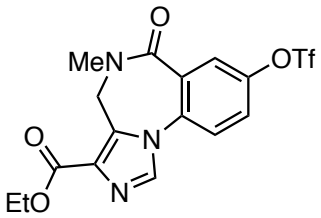

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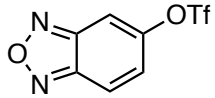

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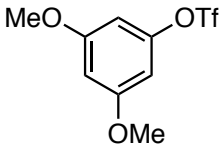

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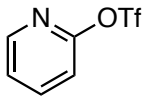

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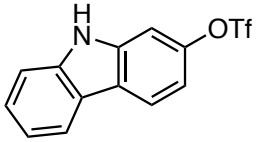

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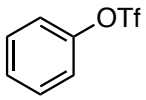

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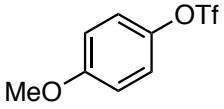

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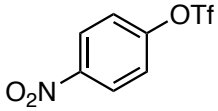

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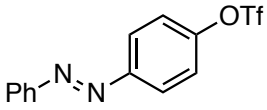

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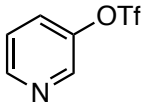

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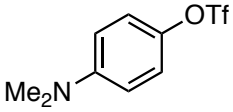
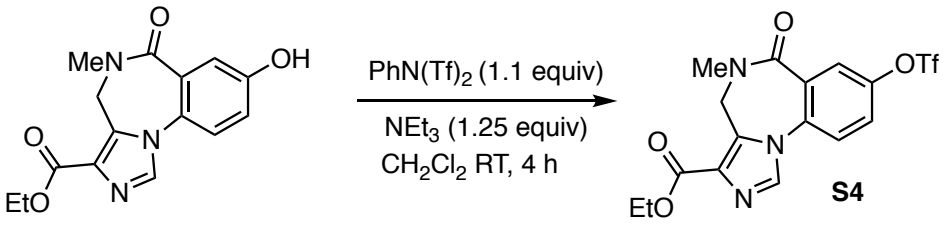


S14

Synthesis of Aryl Triflates

The synthesis of aryl triflates **1**,[2] **S1**,[3] **S2**,[4] **S3**,[5] **S5**,[6] **S11**,[7] **S12**,[8] and **S14**[9] have been previously reported. Triflates **S6**, **S7**, **S8**, **S9**, **S10** and **S13** were purchased from Sigma Aldrich and were used without further purification.



Triflate **S4** was prepared according to the following procedure: A 50 mL round bottom flask was sequentially charged with a stir bar, ethyl 8-hydroxy-5-methyl-6-oxo-5,6-dihydro-4*H*-benzo[*f*]imidazo[1,5-*a*][1,4]diazepine-3-carboxylate[10] (301 mg, 1.0 mmol, 1.0 equiv), and *N*-Phenyl-bis(trifluoromethanesulfonimide) (393 mg, 1.1 mmol, 1.1 equiv). The flask was sealed with a rubber septum and was pierced with a needle connected to a Schlenk line. The flask was evacuated and backfilled with nitrogen (this process was repeated a total of three times), then CH_2Cl_2 (10 mL) was added via syringe. Triethylamine (175 µL, 1.25 mmol, 1.25 equiv) was added to the flask via syringe and the solution was allowed to stir at room temperature. After 4 h, the septum and stir bar were removed from the reaction vessel and the solution was concentrated with the aid of a rotary evaporator. The crude material was purified via silica gel column chromatography (isocratic, 5% MeOH in EtOAc) to afford **S4** as a white, foamy solid (365 mg, 84%) ^{1}H NMR (400 MHz; $CDCl_3$): δ (ppm) 7.99 (s, 1H), 7.90 (s, 1H), 7.55 (m, 2H), 5.24 (v bs, 1H), 4.42 (m, 3H), 3.24 (s, 3H), 1.43 (t, J = 7.1 Hz, 3H). ^{13}C NMR (101 MHz; $CDCl_3$): δ (ppm) 164.8, 163.1, 148.8, 135.5, 135.2, 132.0, 131.6, 129.6, 126.2, 126.1, 124.3, 119.0 (q, J = 321.0 Hz), 61.5, 42.5, 36.4, 14.7. ^{19}F NMR (376 MHz; $CDCl_3$): δ (ppm) 72.6. IR (neat): 2983.3, 1726.1, 1645.2, 1423.4, 1206.9, 960.3, 614.5 cm^{-1}. EA: Calculated for $C_{16}H_{14}F_3N_3O_6S$: C: 44.35; H: 3.26. Found: C: 44.29; H: 3.10.

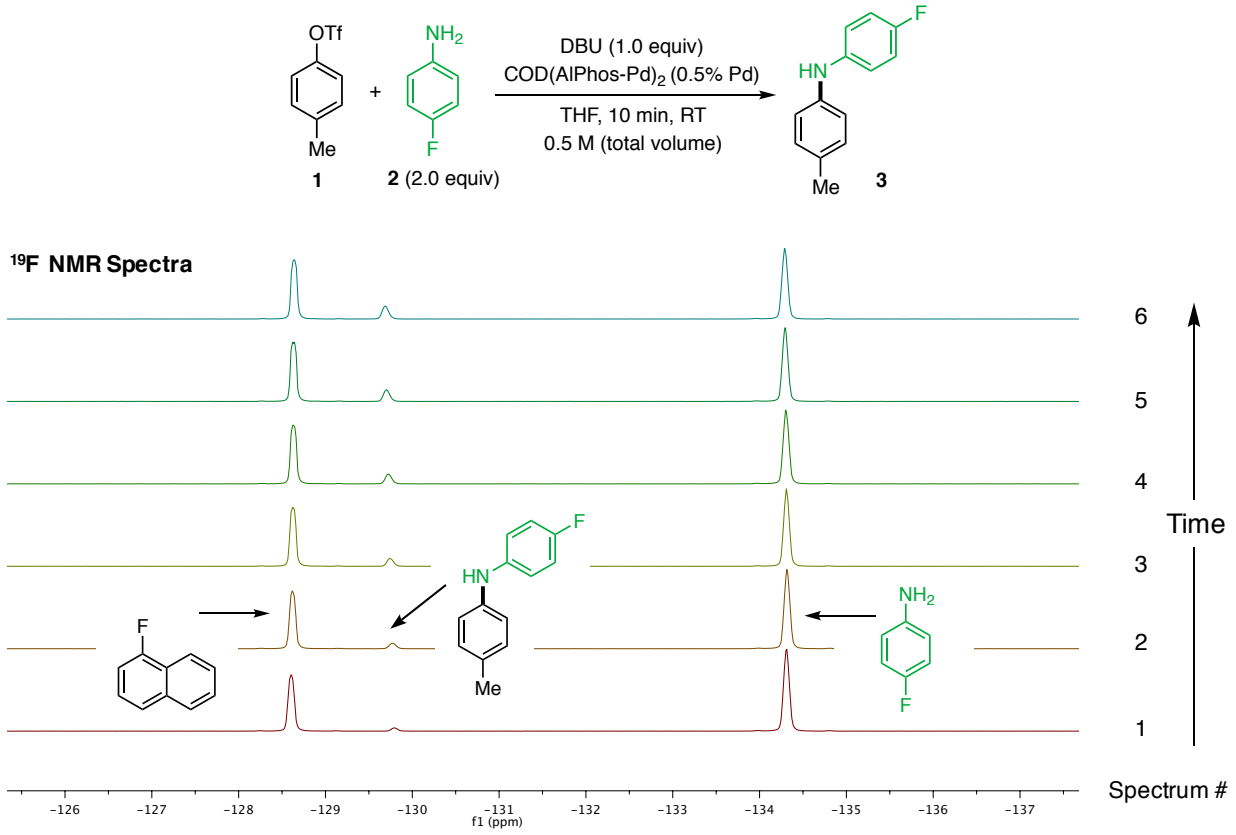
General Procedure for Determining Reaction Orders

In a nitrogen-filled glovebox, a stock solution of reagents was prepared to allow for three x 0.30 mmol scale reactions to be carried out. An oven-dried vial (8 mL) was charged, sequentially, with COD(AlPhos-Pd)$_2$ (4.8 mg, 2.5 μmol, 0.5% Pd), *p*-tolyl triflate (**1**) (177.4 μL, 0.99 mmol, 1.0 equiv), 1-fluoronaphthalene (127.7 μL, 0.99 mmol 1.0 equiv), and THF (684.9 μL) to provide a 1.0 M solution (0.990 mL total volume) relative to *p*-tolyl triflate (*Solution 1*). Liquids were transferred using a calibrated, volumetric pipette and reagent masses were recorded to ensure that the correct amount of material had been added. The vial was sealed with a screw-top cap containing a Teflon septum (Thermo Scientific, catalog number C4015-66A) and the solution was stirred with the aid of a Vortex Mixer for 15 s, which resulted in a dark burgundy-colored, homogenous solution (*Solution 1*). The cap was removed and a calibrated volumetric pipette was used to transfer *Solution 1* (300 μL to each tube, 0.30 mmol relative to ArOTf) to three separate NMR tubes (labeled A-C) to yield three identical, partially-filled NMR tubes. Precision Seal™ rubber septa (Sigma Aldrich, part number: Z554014) were used to cap the three NMR tubes.

Three separate solutions (*Solutions 2A-2C*) were prepared with different concentrations of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) and 4-fluoroaniline (**2**). An oven-dried vial (8 mL) was charged with 4-fluoroaniline (X equiv), DBU (X equiv) and THF (X μL) to prepare a 1.0 M solution (600 μL total volume) relative to one reagent (specific reagent volumes are provided in tables below) (*Solution 2A*). This vial was capped and mixed with the aid of a Vortex Mixer for 5 s. Two additional solutions with different relative concentrations of DBU and **2** were prepared in an analogous manner (*Solutions 2B* and *2C*). A syringe (plastic, 1.0 mL, six inch needle) was used to withdraw 300 μL of *Solution 2A*. This was repeated with separate syringes for *Solutions 2B* and *2C* to yield three syringes each filled with 300 μL. Each needle tip was gently pushed into a soft rubber stopper to prevent leaking, the NMR tubes and syringes were removed from the glovebox, and the reaction materials were transferred to the NMR facility.

After setting up the standard ^{19}F NMR experiment parameters (see General Information), *Solution 2A* was injected into NMR tube A by carefully inserting the needle into the rubber septum. The needle was quickly removed, the NMR tube was vigorously shaken for 2 s, and the tube was inserted into the NMR probe. The experiment was started and the data was collected for

the outlined time. This injection, mixing, and measurement sequence was repeated with NMR tubes B and C with *Solutions 2B* and *2C* respectively. The raw data was then processed in MestreNova and Microsoft® Excel (example shown below) to determine the yield of the reaction, concentration of product, and initial rate of the reaction.



Spectrum #	Time (s)	Standard Area	Product Area
1	0	3792.15	196.197
2	65.2041	3800.18	374.475
3	130.408	3800.67	536.512
4	195.612	3795.16	682.891
5	260.817	3775.81	836.013
6	326.021	3786.1	984.449

(Data obtained from MestreNova)

Time (min)	Yield (%)	Total Concent. (M)	[Product] (M)
0.00	5.17%	0.50	0.02586883
1.09	9.85%	0.50	0.04927069
2.17	14.12%	0.50	0.07058124
3.26	17.99%	0.50	0.08996867
4.35	22.14%	0.50	0.11070644
5.43	26.00%	0.50	0.13000832

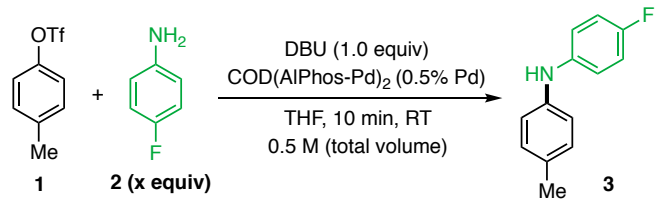
Initial Rate [Product]/Time	0.01905

Figure S1. Representative example of data analysis. Time, Standard Area, and Product area data were extracted from the stacked ^{19}F NMR plots. Yield, [Product], and Initial Rate were determined from this data.

Kinetic Data for the Coupling of Aryl Amines with DBU

Determination of the Reaction Order in 4-Fluoroaniline (2)

The general procedure for determining the reagent dependence was followed. Three solutions of 4-fluoroaniline (*Solution 2B*: 0.50 M; *Solution 2C*: 1.0 M; and *Solution 2C*: 1.5 M) and DBU were prepared according to the following amounts. The procedure was repeated three times with separately prepared stock solutions. The average and standard deviation of the initial rates were determined. The slope of the logarithmic plot of the reaction rate vs [4-fluoroaniline] was used to determine the reaction order.



	Reagent	Amount in Stock Solution	Amount / NMR Tube	mmol / NMR Tube	
1.0 equiv	4-Me ArOTf (µL)	177.4	53.8	0.30	***Solution 1*** Deliver 300 µL to NMR **tubes A-C**
1.0 equiv	1-F naphthalene (µL)	127.7	38.7	0.30	
0.5% Pd	$COD(AlPhos\text{-}Pd)_2$ (mg)	4.8	1.5	0.75 µmol	
	THF (µL)	684.9	207.5	--	
1.0 equiv	DBU (µL)	89.9	45.0	0.30	***Solution 2A*** Dispense 300 µL via syringe to **tube A**
1.0 equiv	4-FAniline (µL)	56.9	28.4	0.30	
	THF (µL)	453.2	226.6	--	
1.0 equiv	DBU (µL)	89.9	45.0	0.60	***Solution 2B*** Dispense 300 µL via syringe to **tube B**
2.0 equiv	4-FAniline (µL)	113.8	56.9	0.30	
	THF (µL)	396.3	198.2	--	
1.0 equiv	DBU (µL)	89.9	45.0	0.90	***Solution 2C*** Dispense 300 µL via syringe to **tube C**
3.0 equiv	4-FAniline (µL)	170.6	85.3	0.30	
	THF (µL)	339.5	169.7	--	

Table S1: Summary of reaction rates determined from formation of product **3** over time by varying the concentration of 4-fluoroaniline.

Equiv.	Rate (slope) (mmol/min)	ln(Rate)	[F-Aniline] (M)	ln([F-Aniline])	Average Rate (mmol/min)	Std Dev
1	0.010761958	-4.5317378	0.5	-0.693147181	-4.6715	0.1352
1	0.008216376	-4.8016261	0.5	-0.693147181		
1	0.009268281	-4.6811573	0.5	-0.693147181		
2	0.01800542	-4.0170825	1	0	-3.9753	0.0368
2	0.01904501	-3.9609502	1	0		
2	0.019297272	-3.9477916	1	0		
3	0.03382912	-3.3864333	1.5	0.405465108	-3.5484	0.1404
3	0.026665789	-3.6243739	1.5	0.405465108		
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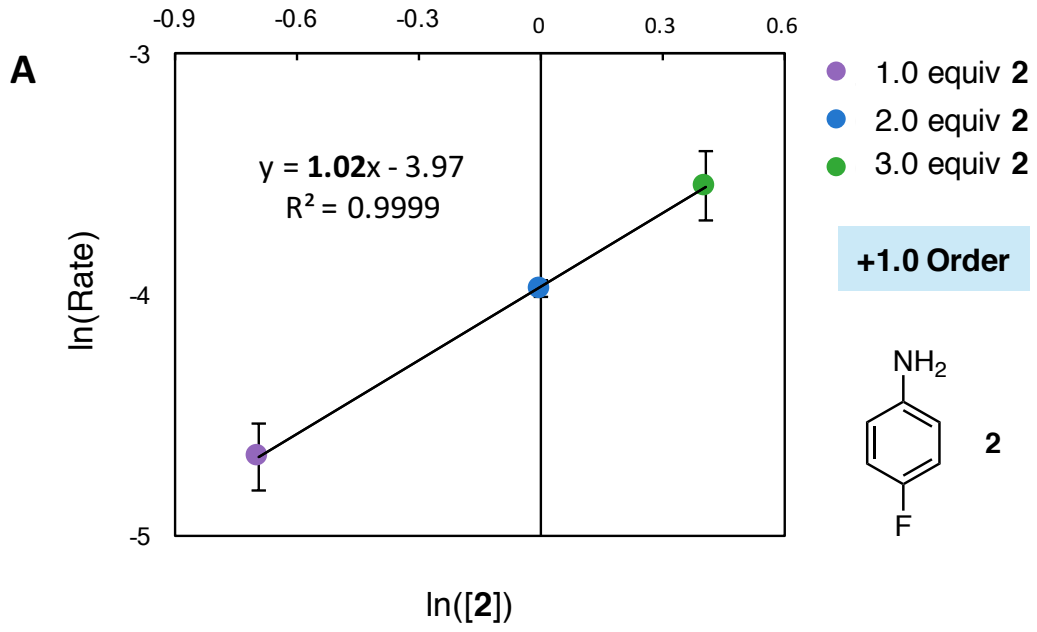
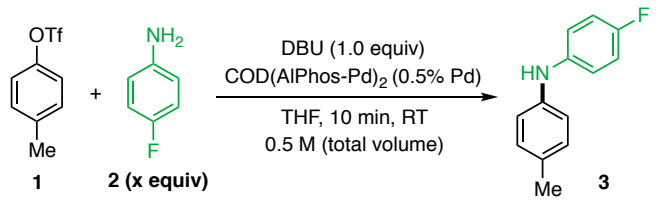


Determination of the Reaction Order in DBU

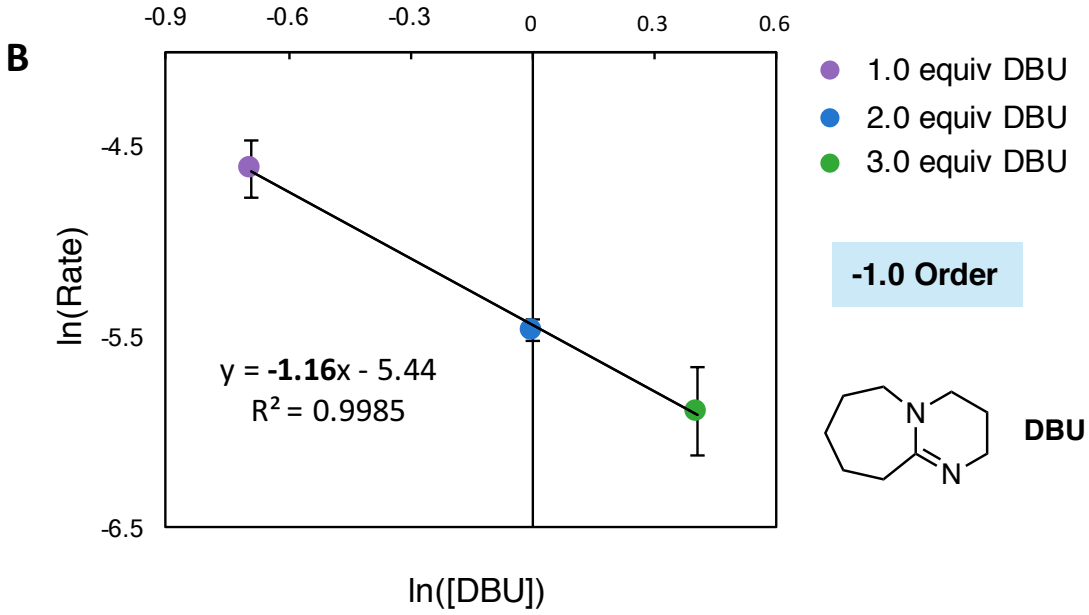
The general procedure for determining the reagent dependence was followed. Three solutions of DBU (*Solution 2B*: 0.50 M; *Solution 2C*: 1.0 M; and *Solution 2C*: 1.5 M) and **2** were prepared according to the following amounts. The procedure was repeated three times with separately prepared stock solutions. The average and standard deviation of the initial rates were determined. The slope of the logarithmic plot of the reaction rate vs [DBU] was used to determine the reaction order.



	Reagent	Amount in Stock Solution	Amount / NMR Tube	mmol / NMR Tube	
1.0 equiv	4-Me ArOTf (µL)	177.4	53.8	0.30	***Solution 1*** Deliver 300 µL to NMR **tubes A-C**
1.0 equiv	1-F naphthalene (µL)	127.7	38.7	0.30	
0.5% Pd	$COD(AlPhos\text{-}Pd)_2$ (mg)	4.8	1.5	0.75 µmol	
	THF (µL)	684.9	207.5	--	
1.0 equiv	DBU (µL)	89.9	45.0	0.30	***Solution 2A*** Dispense 300 µL via syringe to **tube A**
1.0 equiv	4-FAniline (µL)	56.9	28.4	0.30	
	THF (µL)	453.4	226.7	--	
2.0 equiv	DBU (µL)	179.5	89.8	0.60	***Solution 2B*** Dispense 300 µL via syringe to **tube B**
1.0 equiv	4-FAniline (µL)	56.9	28.4	0.30	
	THF (µL)	363.6	181.8	--	
3.0 equiv	DBU (µL)	269.3	134.7	0.90	***Solution 2C*** Dispense 300 µL via syringe to **tube C**
1.0 equiv	4-FAniline (µL)	56.9	28.4	0.30	
	THF (µL)	273.8	136.9	--	

Table S2: Summary of reaction rates determined from formation of product **3** over time by varying the concentration of DBU.

Equiv.	Rate (slope) (mmol/min)	ln(Rate)	[DBU] (M)	ln([DBU])	Average ln(Rate) (mmol/min)	Std Dev
1	0.008973878	-4.7134374	0.5	-0.693147181		
1	0.011753453	-4.4436082	0.5	-0.693147181	-4.8675986	0.15234092
1	0.009085566	-4.7010683	0.5	-0.693147181		
2	0.004261562	-5.4581195	1	0		
2	0.004447986	-5.4153038	1	0	-5.4638291	0.05161754
2	0.00401361	-5.5180641	1	0		
3	0.003491206	-5.6575082	1.5	0.405465108		
3	0.002768811	-5.8893372	1.5	0.405465108	-5.8887373	0.23092971
3	0.002199849	-6.1193664	1.5	0.405465108		



Determination of the Reaction Order in p-tolyl triflate (1)

An adapted general procedure was used to determine the order in **1**.

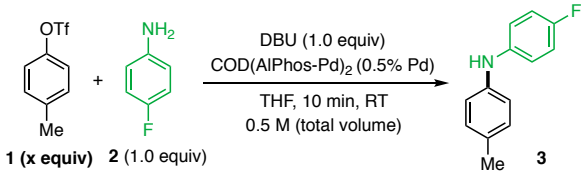
In a nitrogen-filled glovebox, a stock solution of reagents was prepared to allow for three x 0.30 mmol scale reactions to be carried out. An oven-dried vial (8 mL) was charged sequentially with DBU (269.3 μL, 1.8 mmol, 1.0 equiv), 1-fluoronaphthalene (232.2 μL, 1.8 mmol, 1.0 equiv), 4-fluoroaniline (170.6, 1.8 mmol, 1.0 equiv), and THF (1127.9 μL) to prepare a 1.0 M solution (total volume) relative to each reagent (*Solution 1*). Liquids were transferred using a calibrated, volumetric pipette and reagent masses were recorded to ensure that the correct amount of material had been added. The vial was sealed with a screw-top cap containing a Teflon septum (Thermo Scientific, catalog number C4015-66A) and the solution was stirred with the aid of a Vortex Mixer for 5 s (Solution 1). The cap was removed and three syringes (plastic, 1.0 mL, six inch needle) were used to withdraw 300 μL of *Solution 1* (0.30 mmol of DBU, 1-fluoronaphthalene, and 4-fluoroaniline to each syringe), yielding three identical syringes labeled A-C. Each needle tip was gently pushed into a soft rubber stopper to prevent leaking.

A separate oven-dried vial (8 mL) was charged sequentially with COD(AlPhos-Pd)$_2$ (4.8 mg, 2.5 μmol, 0.5% Pd), *p*-tolyl triflate (80.2 μL, 0.495 mmol), and THF (575 μL) to yield a 0.5 M solution relative to ArOTf. The vial was sealed with a screw top cap containing a Teflon septum and the solution was stirred with the aid of a Vortex Mixer for 15 s, which resulted in a dark burgundy-colored, homogenous solution (*Solution 2*). The cap was removed, and a calibrated volumetric pipette was used to transfer *Solution 2* (200 μL, 0.15 mmol each relative to ArOTf) to three separate oven-dried NMR tubes (A-C). This process yielded three identical, partially-filled NMR tubes, each containing *p*-tolyl triflate (0.15 mmol) and precatalyst (1.5 μmol).

To ensure that the NMR tubes contained different concentrations of ArOTf, additional amounts of THF and/or ArOTf were added to NMR tubes A-C such so that the total NMR tube volume was 300 μL (see table below). To NMR tube A, THF (100 μL) was added (0.15 mmol ArOTf total). *Solution 3* was prepared by mixing ArOTf (34.9 μL) and THF (95.1 μL) in a dram vial, and 100 μL of this solution was added to NMR tube B (0.30 mmol ArOTf total). *Solution 4* was prepared by mixing ArOTf (69.9 μL) and THF (60.1) and 100 μL of this solution was added

to NMR tube C (0.45 mmol total). The three NMR tubes were capped with Precision Seal™ rubber septa. The syringes and NMR tubes were then removed from the glovebox and were brought to the NMR facility.

After setting up the standard ^{19}F NMR experiment parameters (see General Information), *Solution 1* (300 µL) was injected into NMR tube A by carefully inserting the needle into the rubber septum. The needle was quickly removed, the NMR tube was vigorously shaken for 2 s, and the tube was inserted into the NMR bore. The experiment was started and the data was collected for the outlined time. This injection of *Solution 1*, mixing, and measurement sequence was repeated with NMR tubes B and C. The raw data was then processed in MestreNova and Microsoft® Excel (example shown below) to determine the yield of the reaction, concentration of product, and initial rate of the reaction.

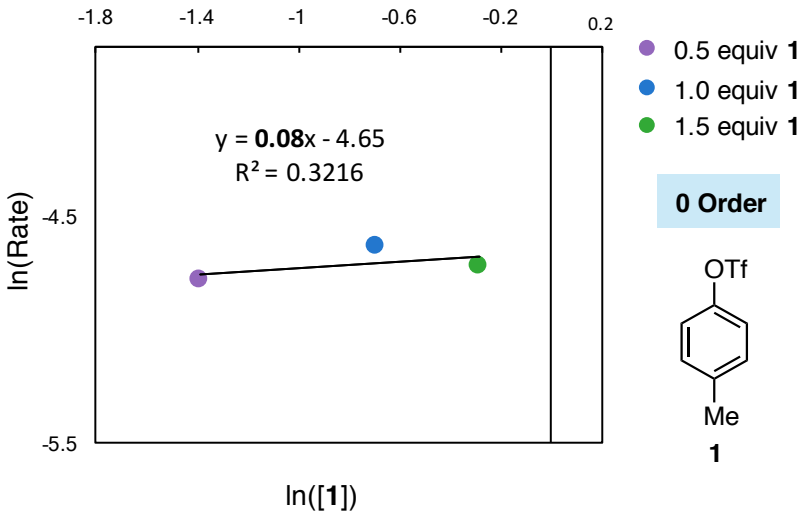


1 (x equiv) **2** (1.0 equiv) **3**

	Reagent	Amount in Stock Solution	Amount / NMR Tube	mmol / NMR Tube	
1.0 equiv	DBU (µL)	269.3	44.9	0.30	***Solution 1*** Dispense 300 µL via syringe to **tubes A-C**
1.0 equiv	1-F naphthalene (µL)	232.2	38.7	0.30	
1.0 equiv	4-FAniline (µL)	170.6	28.4	0.30	
	THF (µL)	1127.9	188.0	--	
0.5 equiv	4-Me ArOTf (µL)	88.7	26.88	0.15	***Solution 2*** Deliver 200 µL to NMR **tubes A-C**
0.5 equiv	COD(AlPhos-Pd)2 (mg)	4.8	1.46	0.75 µmol	
0.5% Pd	THF (µL)	566.5	171.66	--	
0 equiv (0.5 equiv total)	4-Me ArOTf (µL)	0.0	0	0	Deliver 100 µL to NMR **tube A**
	THF (µL)	100.0	100	--	
0.5 equiv (1.0 equiv total)	4-Me ArOTf (µL)	34.9	26.9	0.15	***Solution 3*** Deliver 100 µL to NMR **tube B**
	THF (µL)	95.1	73.1	--	
1.0 equiv (1.5 equiv total)	4-Me ArOTf (µL)	69.9	53.8	0.30	***Solution 4*** Deliver 100 µL to NMR **tube C**
	THF (µL)	60.1	46.2	--	

Table S3: Summary of reaction rates determined from formation of product **3** over time by varying the concentration of *p*-tolyl triflate (**1**).

Equiv	Rate (slope)	ln(Rate)	[ArOTf]	ln(ArOTf])
0.5	0.00838725	-4.7810432	0.25	-1.3862944
1	0.0097299	-4.6325512	0.5	-0.6931472
1.5	0.00895178	-4.7159034	0.75	-0.2876821



Determination of the Reaction Order in total [Pd]

An adapted general procedure was used to determine the order in total [Pd].

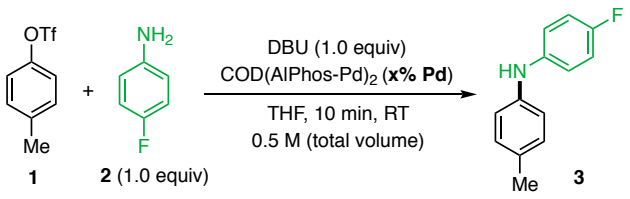
In a nitrogen-filled glovebox, a stock solution of reagents was prepared to allow for three x 0.30 mmol scale reactions to be carried out. An oven-dried vial (8 mL) was charged sequentially with COD(AlPhos-Pd)$_2$ (4.8 mg, 2.5 μmol, 0.5% Pd), *p*-tolyl triflate (174.4 μL, 0.99 mmol, 1.0 equiv), 1-fluoronaphthalene (127.7 μL, 0.99 mmol 1.0 equiv), and and THF (684.9 μL) to prepare a 1.0 M solution (0.990 mL total volume) relative to *p*-tolyl triflate (*Solution 1*). Liquids were transferred using a calibrated, volumetric pipette and reagent masses were recorded to ensure that the correct amount of material had been added. The vial was sealed with a screw top cap containing a Teflon septum (Thermo Scientific, catalog number C4015-66A) and the solution was stirred with the aid of a Vortex Mixer for 15 s, which resulted in a dark burgundy-colored, homogenous solution.

While still in the glovebox, three oven-dried NMR tubes (A-C) were charged with additional COD(AlPhos-Pd)$_2$ (0 mg in tube A; 1.5 mg in tube B; 2.9 mg in C) by carefully weighing the catalyst directly into the NMR tube (see table below). To these NMR tubes, *Solution 1* (300 μL, 0.30 mmol relative to ArOTf) was added via a volumetric pipette. The three NMR tubes were capped with Precision Seal^{TM} rubber septa (Sigma Aldrich, part number: Z554014).

In a separate oven-dried vial (8 mL), DBU (269.3 μL, 1.8 mmol, 1.0 equiv), 4-fluoroaniline (170.6 μL, 1.8 mmol, 1.0 equiv), and THF (1.360 mL) were combined sequentially to prepare a 1.0 M solution relative to each reagent (*Solution 2*). The vial was capped and mixed with the aid of a Vortex Mixer for 2 s. Three separate syringes (plastic, 1.0 mL, six inch needle) were used to withdraw 300 μL of *Solution 2* (0.30 mmol relative to each reagent) each, yielding three identical partially-filled syringes. Each needle tip was gently pushed into a soft rubber stopper to prevent leaking. The syringes and NMR tubes were then removed from the glovebox and were brought to the NMR facility.

After setting up the standard ^{19}F NMR experiment parameters (see General Information), *Solution 2* (300 μL) was injected into NMR tube A by carefully inserting the needle into the rubber septum. The needle was quickly removed, the NMR tube was vigorously shaken for 2 s,

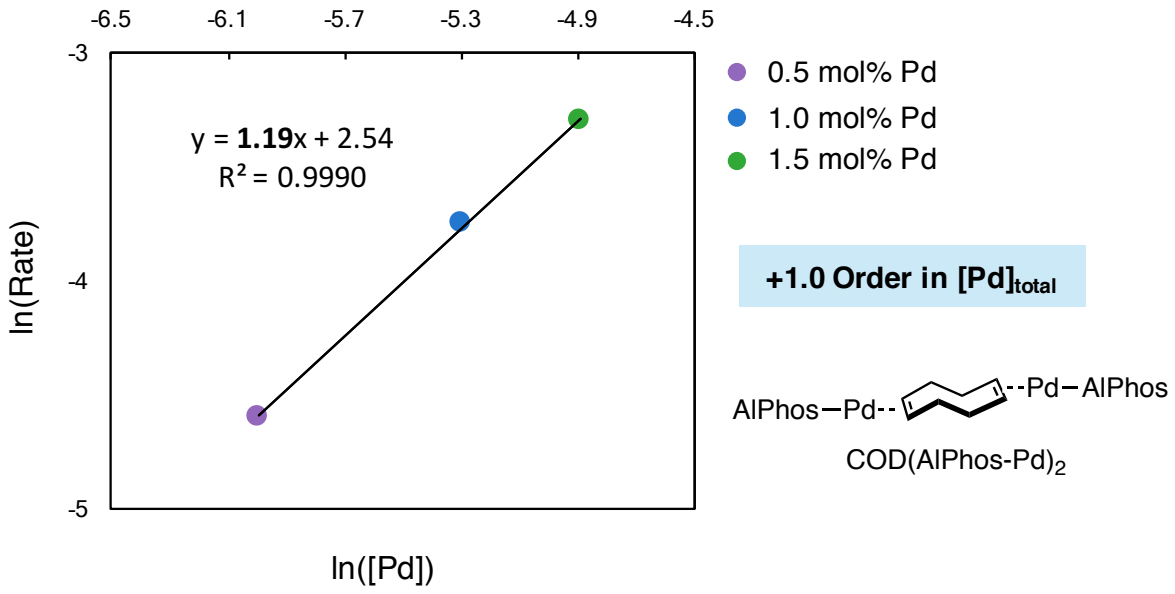
and the tube was inserted into the NMR bore. The experiment was started and the data was collected for the outlined time. This injection of *Solution 2*, mixing, and measurement sequence was repeated with NMR tubes B and C. The raw data was then processed in MestreNova and Microsoft® Excel to determine the yield of the reaction, concentration of product, and initial rate of the reaction.



	Reagent	Amount in Stock Solution	Amount / NMR Tube	mmol / NMR Tube	
1.0 equiv	4-Me ArOTf (µL)	177.4	53.8	0.30	***Solution 1*** Deliver 300 µL to NMR **tubes A-C**
1.0 equiv	1-F naphthalene (µL)	127.7	38.7	0.30	
0.5% Pd	COD(AlPhos-Pd)2 (mg)	4.8	1.5	0.75 µmol	
	THF (µL)	684.9	207.5	--	
1.0 equiv	DBU (µL)	269.3	44.9	0.30	***Solution 2*** Dispense 300 µL via syringe to **tubes A-C**
1.0 equiv	4-FAniline (µL)	170.6	28.4	0.30	
	THF (µL)	1360.1	226.7	--	
0% Pd (0.5% total)	COD(AlPhos-Pd)2 (mg)	0.0	0.0	0	NMR tube A
0.5% Pd (1.0% total)	COD(AlPhos-Pd)2 (mg)	1.5	1.5	0.75 µmol	NMR tube B
1.0% Pd (1.5% total)	COD(AlPhos-Pd)2 (mg)	2.9	2.9	1.5 µmol	NMR tube B
					Weigh directly Into NMR tubes

Table S4: Summary of reaction rates determined from formation of product **3** over time by varying the concentration of Pd.

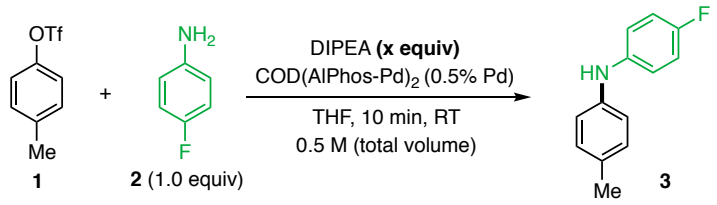
Equiv.	Rate (slope) (mmol/min)	ln(Rate)	[Pd] (M)	ln([Pd])
0.005	0.0099968	-4.6054903	0.0025	-5.9914645
0.01	0.023584404	-3.7471696	0.005	-5.2983174
0.015	0.036783526	-3.3027052	0.0075	-4.8928523



Kinetic Data for the Coupling of Aryl Amines with Other Bases

Determination of the Reaction Order in DIPEA

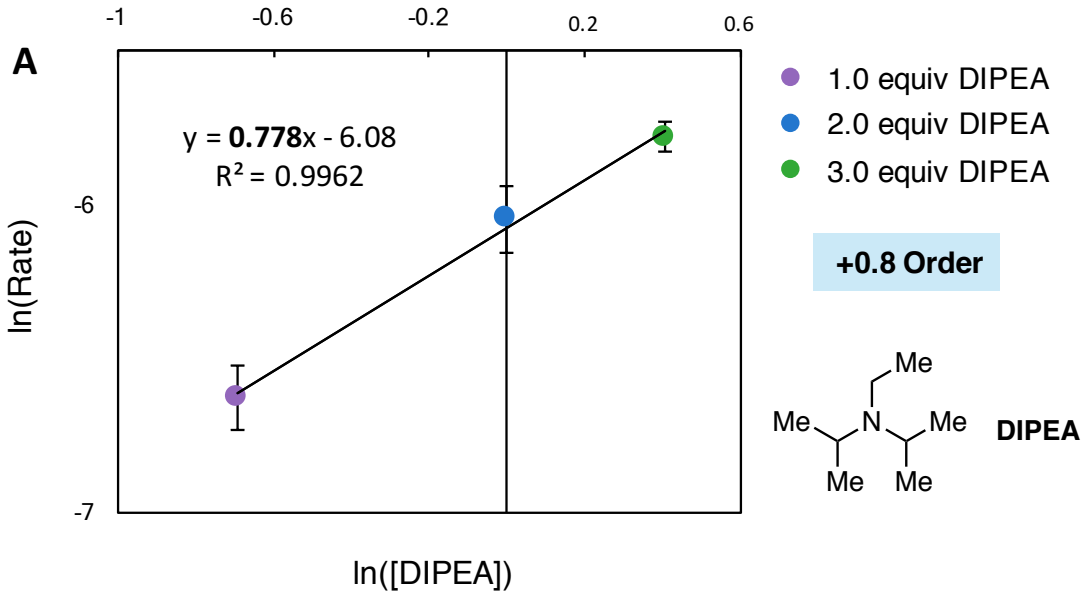
The general procedure for determining the reagent dependence was followed, except *N*,*N*-diisopropyl ethyl amine (DIPEA) was used instead of DBU. Three solutions of DIPEA (*Solution 2B*: 0.50 M; *Solution 2C*: 1.0 M; and *Solution 2C*: 1.5 M) and **2** were prepared according to the following amounts. The procedure was repeated three times with separately prepared stock solutions. The average and standard deviation of the initial rates were determined. The slope of the logarithmic plot of the reaction rate vs [DIPEA] was used to determine the reaction order.



	Reagent	Amount in Stock Solution	Amount / NMR Tube	mmol / NMR Tube	
1.0 equiv	4-Me ArOTf (µL)	177.4	53.8	0.30	***Solution 1*** Deliver 300 µL to NMR **tubes A-C**
1.0 equiv	1-F naphthalene (µL)	127.7	38.7	0.30	
0.5% Pd	$COD(AlPhos\text{-}Pd)_2$ (mg)	4.8	1.5	0.75 µmol	
	THF (µL)	684.9	207.5	--	
1.0 equiv	DIPEA (µL)	107.2	53.6	0.30	***Solution 2A*** Dispense 300 µL via syringe to **tube A**
1.0 equiv	4-FAniline (µL)	56.9	28.4	0.30	
	THF (µL)	435.9	218.0	--	
2.0 equiv	DIPEA (µL)	214.4	107.2	0.60	***Solution 2B*** Dispense 300 µL via syringe to **tube B**
1.0 equiv	4-FAniline (µL)	56.9	28.4	0.30	
	THF (µL)	328.7	164.4	--	
3.0 equiv	DIPEA (µL)	321.6	160.8	0.90	***Solution 2C*** Dispense 300 µL via syringe to **tube C**
1.0 equiv	4-FAniline (µL)	56.9	28.4	0.30	
	THF (µL)	221.5	110.8	--	

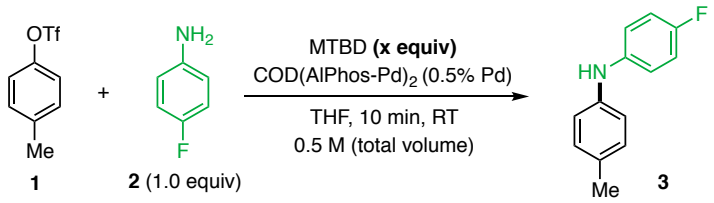
Table S5: Summary of reaction rates determined from formation of product **3** over time by varying the concentration of DIPEA.

Equiv.	Rate (slope) (mmol/min)	ln(Rate)	[DIPEA] (M)	ln([DIPEA])	Average ln(Rate) (mmol/min)	Std Dev
1	0.001228003	-6.7023662	0.5	-0.69314718	-6.627211352	0.10461674
1	0.001266448	-6.6715392	0.5	-0.69314718		
1	0.001491864	-6.5077287	0.5	-0.69314718		
2	0.002678963	-5.9223255	1	0	-6.046473625	0.10825286
2	0.002195903	-6.1211619	1	0		
2	0.002252007	-6.0959334	1	0		
3	0.003265477	-5.7243494	1.5	0.40546511	-5.780263596	0.05065807
3	0.003047787	-5.7933396	1.5	0.40546511		
3	0.002958415	-5.8231017	1.5	0.40546511		



Determination of the Reaction Order in MTBD

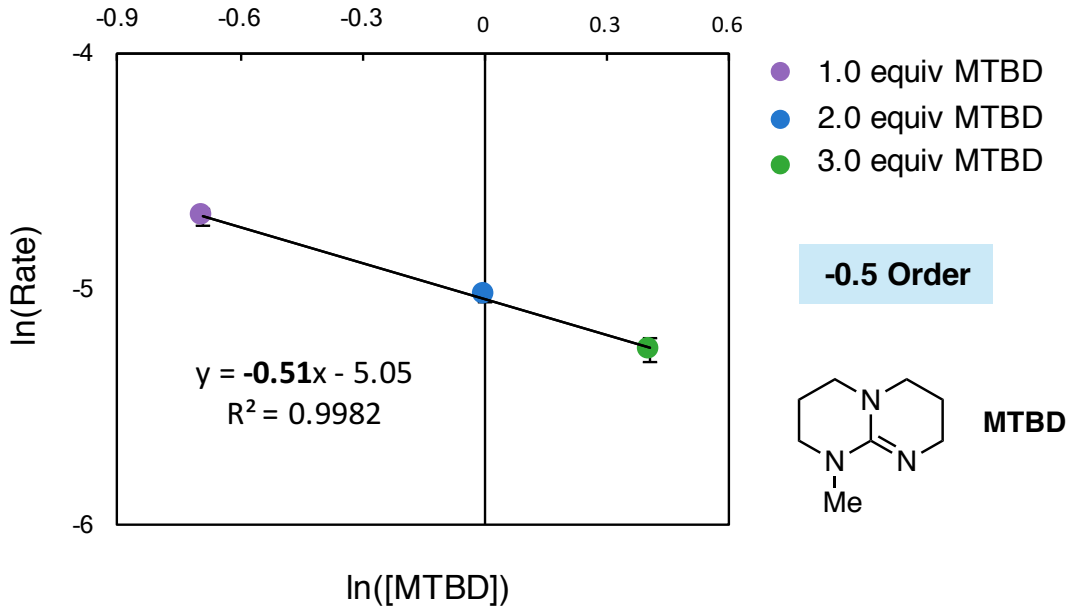
The general procedure for determining the reagent dependence was followed, except 1,3,4,6,7,8-Hexahydro-1-methyl-2*H*-pyrimido[1,2-a]pyrimidine (MTBD) was used instead of DBU. Three solutions of MTBD (*Solution 2B*: 0.50 M; *Solution 2C*: 1.0 M; and *Solution 2C*: 1.5 M) and **2** were prepared according to the following amounts. The procedure was repeated three times with separately prepared stock solutions. The average and standard deviation of the initial rates were determined. The slope of the logarithmic plot of the reaction rate vs [MTBD] was used to determine the reaction order.



	Reagent	Amount in Stock Solution	Amount / NMR Tube	mmol / NMR Tube	
1.0 equiv	4-Me ArOTf (µL)	177.4	53.8	0.30	***Solution 1*** Deliver 300 µL to NMR **tubes A-C**
1.0 equiv	1-F naphthalene (µL)	127.7	38.7	0.30	
0.5% Pd	$COD(AlPhos\text{-}Pd)_2$ (mg)	4.8	1.5	0.75 µmol	
	THF (µL)	684.9	207.5	--	
1.0 equiv	MTBD (µL)	86.2	43.1	0.30	***Solution 2A*** Dispense 300 µL via syringe to **tube A**
1.0 equiv	4-FAniline (µL)	56.9	28.4	0.30	
	THF (µL)	456.9	228.5	--	
2.0 equiv	MTBD (µL)	172.4	86.2	0.60	***Solution 2B*** Dispense 300 µL via syringe to **tube B**
1.0 equiv	4-FAniline (µL)	56.9	28.4	0.30	
	THF (µL)	370.7	185.4	--	
3.0 equiv	MTBD (µL)	258.6	129.3	0.90	***Solution 2C*** Dispense 300 µL via syringe to **tube C**
1.0 equiv	4-FAniline (µL)	56.9	28.4	0.30	
	THF (µL)	284.5	142.3	--	

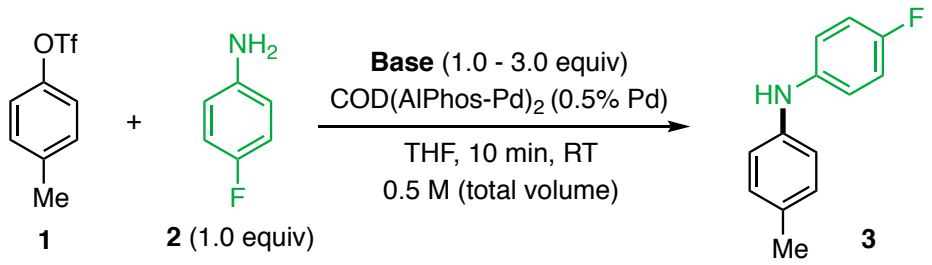
Table S6: Summary of reaction rates determined from formation of product **3** over time by varying the concentration of MTBD.

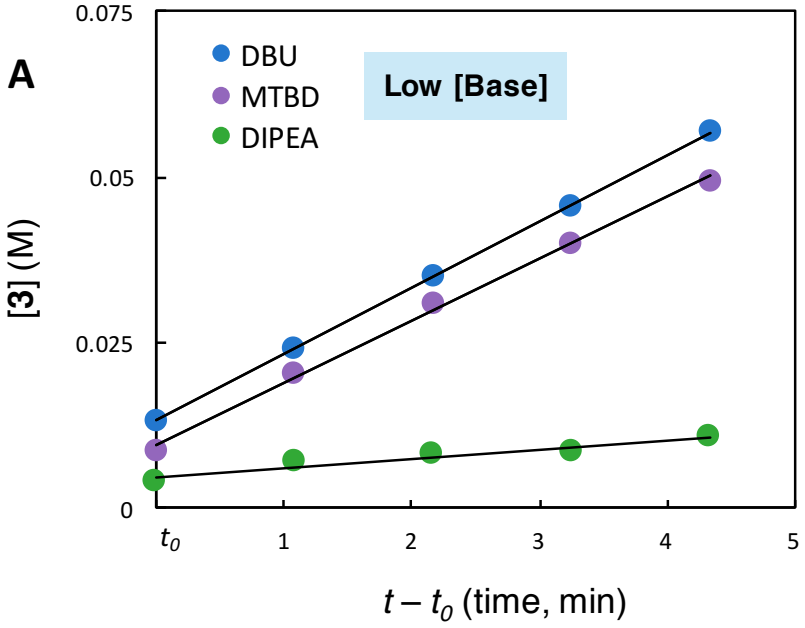
Equiv.	Rate (slope) (mmol/min)	ln(Rate)	[MTBD] (M)	ln([MTBD])	Average ln(Rate) (mmol/min)	Std Dev
1	0.009508	-4.655618	0.5	-0.693147181	-4.6968986	0.035782
1	0.0089237	-4.719047	0.5	-0.693147181		
1	0.0089506	-4.716031	0.5	-0.693147181		
2	0.0063945	-5.052321	1	0	-5.0315487	0.028364
2	0.0067431	-4.999233	1	0		
2	0.0064538	-5.043092	1	0		
3	0.0052345	-5.252478	1.5	0.405465108	-5.2607969	0.048928
3	0.005426	-5.216562	1.5	0.405465108		
3	0.0049254	-5.313351	1.5	0.405465108		



Comparison of Reaction Rates at High and Low [Base]

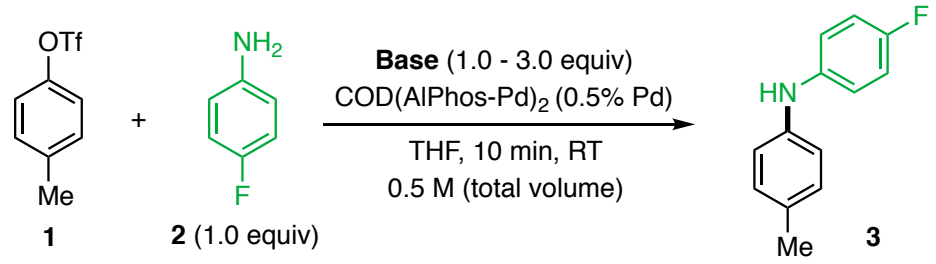
Reaction rates were plotted as the average of three independent runs for identical couplings facilitated by either DBU, DIPEA, or MTBD. The data is taken from kinetic experiments previously outlined. Low base concentration describes the reaction in which 1.0 equivalents (**A**) of base were used, while high base concentration describes 3.0 equivalents were used (**B**).

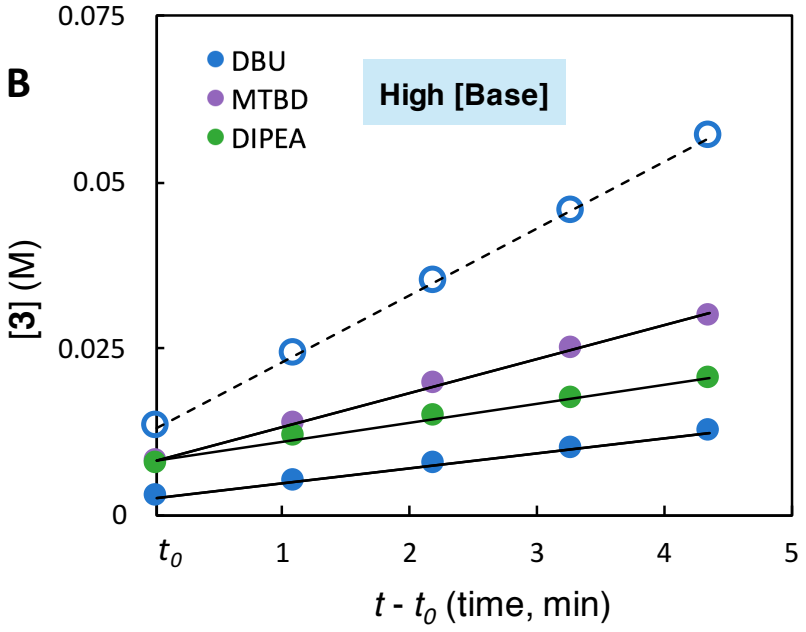




$t - t_0$ Time (min)	[Product] 1.0 eq. DBU	[Product] 1.0 eq. DIPEA	[Product] 1.0 eq. MTBD
t_0	0.013153	0.00393606	0.0099629
1.09	0.024017	0.00707037	0.0202275
2.17	0.035043	0.00796837	0.030694
3.26	0.04555	0.00832167	0.0399992
4.35	0.056757	0.01079708	0.0494319

Comparison of Reaction Rates at High [Base]





t - t_0 Time (min)	[Product] 1.0 eq. DBU	[Product] 1.0 eq. DIPEA	[Product] 1.0 eq. MTBD
t_0	0.002872	0.00762441	0.0078751
1.09	0.004805	0.01163705	0.0136272
2.17	0.007589	0.01488911	0.0195796
3.26	0.01004	0.01746298	0.024831
4.35	0.012512	0.02028529	0.0298574

Note: The blue open circles represent the rate the reaction when performed under the Low [DBU] conditions.

Determination of Resting States

Reactions Facilitated by DBU: p-tolyl triflate (1)

In a nitrogen-filled glovebox, an oven-dried vial (8 mL) was sequentially charged with COD(AlPhos-Pd)$_2$ (9.8 mg, 10.0 μmol, 2% Pd), *p*-tolyl triflate (89.6 μL, 0.50 mmol, 1.0 equiv), and THF (500 μL). The solution was stirred with the aid of a Vortex Mixer for 15 s and the resulting burgundy-colored solution was transferred via pipette to an oven-dried NMR tube. The NMR tube was capped with a Precision Seal^{TM} rubber septum. This process was repeated twice, resulting in two identical NMR tubes containing aryl triflate, precatalyst, and THF (NMR tubes 1 and 2). NMR tube 1 was analyzed by ^{31}P NMR. After the first analysis, DBU (150 μL, 1.0 mmol, 2.0 equiv) was carefully injected into NMR tube 1 via syringe through the septum. The tube was shaken to ensure proper mixing, which resulted in an immediate color change to a light yellow. NMR tube 1 was again analyzed by ^{31}P NMR. To the second, unaltered NMR tube 2, aniline (55 μL, 0.60 mmol, 1.2 equiv) was injected via syringe through the septum, which resulted in a dark burgundy-colored solution. This solution was analyzed via ^{31}P NMR. Finally, DBU (150 μL, 1.0 mmol, 2.0 equiv) was added to NMR tube 2 (containing aryl triflate and aniline) via syringe, and the solution was analyzed by ^{31}P NMR.

The spectrum containing the precatalyst, *p*-tolyl triflate, and THF is labeled **Spectrum A**.
The spectrum containing precatalyst, *p*-tolyl triflate, aniline, and THF is labeled **Spectrum B**.
The spectrum containing precatalyst, *p*-tolyl triflate, DBU, and THF is labeled **Spectrum C**.
The spectrum containing precatalyst, *p*-tolyl triflate, aniline, DBU, and THF is labeled **Spectrum D**.

Quantifcation of Resting State

In a nitrogen-filled glovebox, an oven-dried vial (8 mL) was sequentially charged with COD(AlPhos-Pd)$_2$ (9.8 mg, 10.0 μmol, 2% Pd), *p*-tolyl triflate (89.6 μL, 0.50 mmol, 1.0 equiv), and THF (500 μL). The solution was stirred with the aid of a Vortex Mixer for 15 s and the resulting burgundy-colored solution was transferred via pipette to an oven-dried NMR tube. A sealed capillary tube containing a solution of phosphoric acid in water was added to the NMR tube as an internal reference standard. The NMR tube was capped with a Precision Seal^{TM} rubber

septum. A separate glass vial (8 mL) was charged with DBU (150 μL, 1.0 mmol, 2.0 equiv), aniline (55 μL, 0.60 mmol, 1.2 equiv), and THF (440 μL). The colorless solution was stirred with the aid of a Vortex Mixer for 10 s. A syringe (1.0 mL, plastic) equipped with a needle was used to withdraw the solution from the vial. The needle tip was gently pushed into a rubber stopper to prevent leaking. The NMR tube and the syringe were removed from the glovebox and were transferred to the NMR facility. The contents of the NMR tube were analyzed by ^{31}P NMR (unlocked, no shimming). After analysis, the solution of DBU, aniline, and THF was injected into the NMR tube via syringe by carefully inserting the needle tip into the rubber septum. The tube was shaken (2 s) to ensure proper mixing, which resulted in an immediate color change from burgundy to a light yellow. The tube was then analyzed again by ^{31}P NMR (unlocked, no shimming).

The spectrum containing the precatalyst, *p*-tolyl triflate, THF, and internal standard is labeled **Spectrum E**.

The spectrum containing precatalyst, *p*-tolyl triflate, THF, internal standard, DBU, and aniline is labeled **Spectrum F**. This spectrum shows that the DBU-bound OA complex accounts for 86% of the phosphorus containing material while the remaining 14% is free AlPhos ligand. **Note**: the integral corresponding to phosphoric acid has been doubled to account for the dilution factor.

Reactions Facilitated by DBU: p-nitrophenyl triflate (S11)

An analogous procedure was followed, except *p*-nitrophenyl triflate (**S11**) (135.6 mg, 0.5 mmol, 1.0 equiv) and 4-fluoroaniline (57 μL, 0.60 mmol, 1.2 equiv) were used instead of *p*-tolyl triflate and aniline. The spectrum containing the precatalyst, *p*-nitrophenyl triflate, THF, and 4-fluoroaniline is labeled **Spectrum G**. The spectrum containing *p*-nitrophenyl triflate, THF, and DBU is labeled **Spectrum H**. The spectrum containing *p*-nitrophenyl triflate, THF, DBU, and 4-fluoroaniline is labeled **Spectrum I**.

Determination of Resting States

Reactions Facilitated by DIPEA

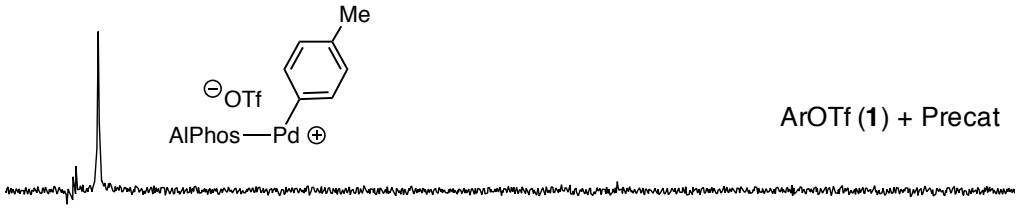
An analogous procedure was followed, except DIPEA (174 μL, 1.0 mmol, 2.0 equiv) and 4-fluoroaniline (57 μL, 0.60 mmol, 1.2 equiv) were used instead of DBU and aniline. The spectrum containing the precatalyst, *p*-tolyl triflate, THF, and DIPEA is labeled **Spectrum J**, while the spectrum containing precatalyst, *p*-tolyl triflate, THF, and DIPEA, 4-fluoroaniline is labeled **Spectrum K**.

Note: **Spectrum J** contains multiple signals that may correspond to a DIPEA bound oxidative addition (OA) complex, including signals that may indicate different isomers. These peaks are also found in **Spectrum K**. Also, free oxidative addition complex is observed in **Spectrum J** which provides further evidence that the DIPEA cannot fully bind to the OA complex and that the aniline binds to the remaining cationic OA complex.

Determination of Resting States: p-tolyl triflate (1) + DBU

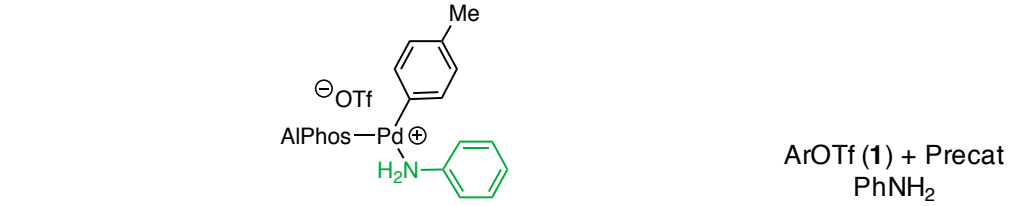
Spectrum A
^{31}P NMR
THF-H_8

A



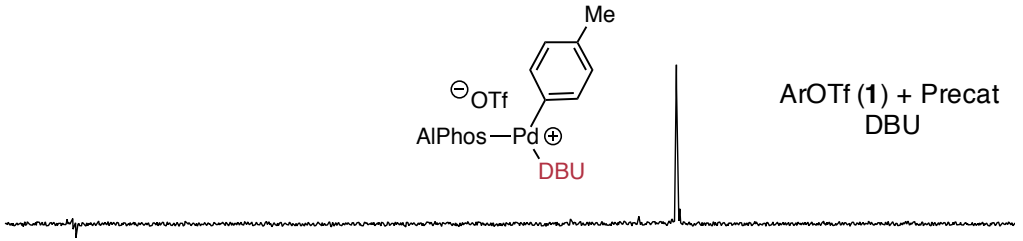
Spectrum B
^{31}P NMR
THF-H_8

B



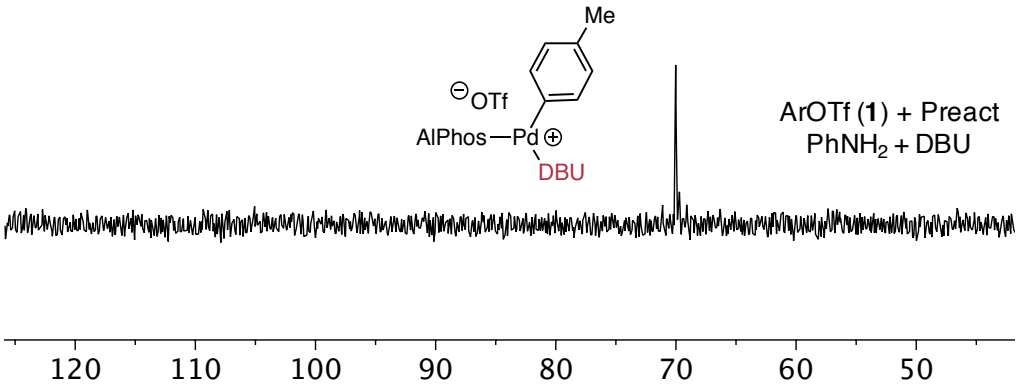
Spectrum C
^{31}P NMR
THF-H_8

C

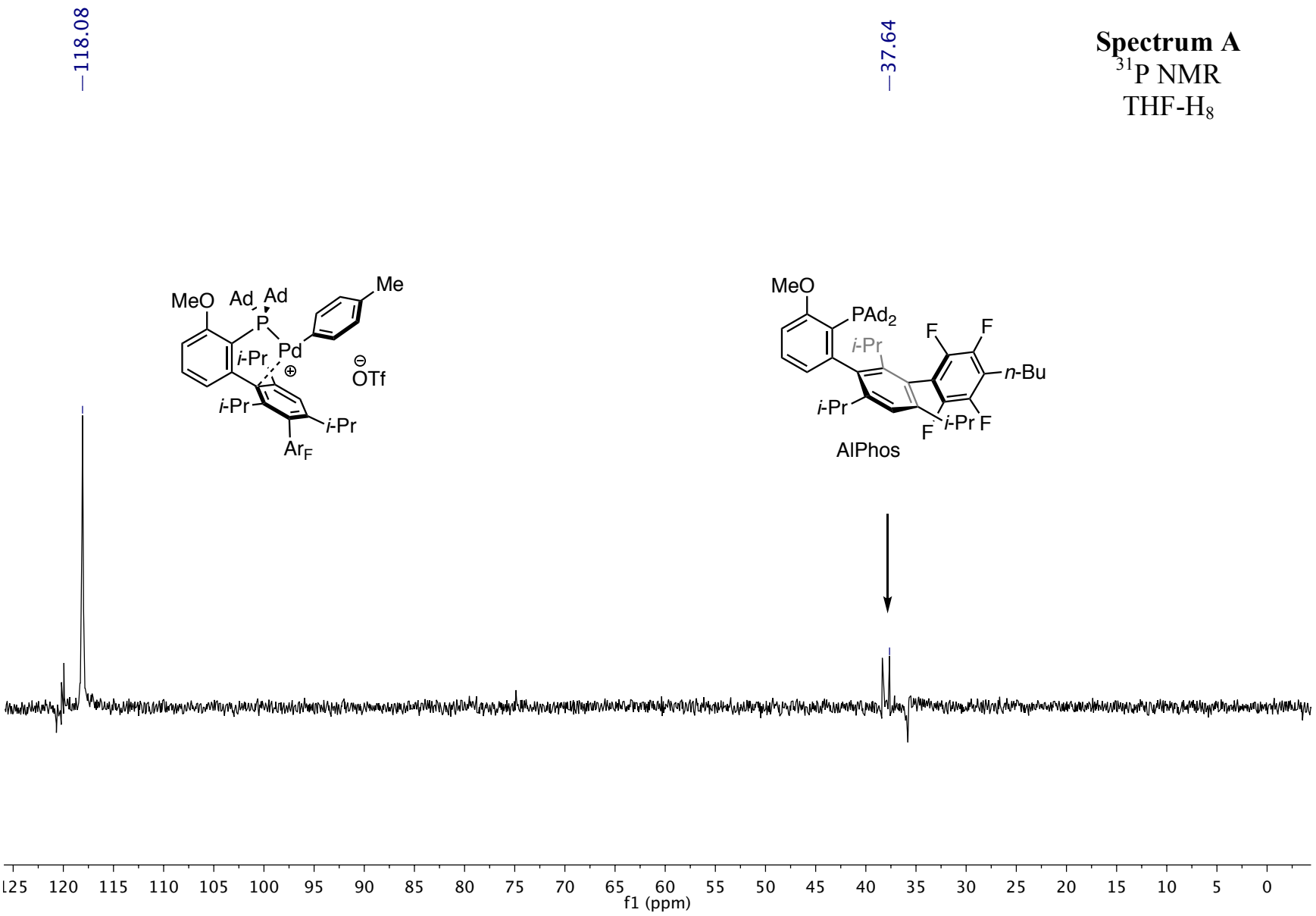


Spectrum D
^{31}P NMR
THF-H_8

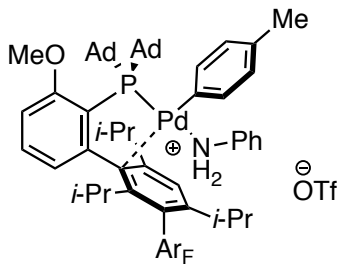
D

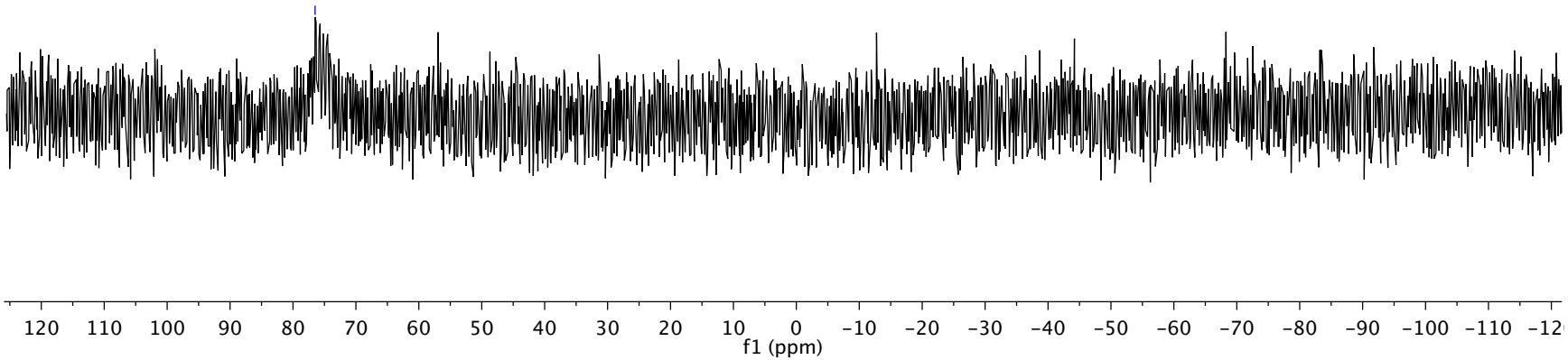


Spectrum A
^{31}P NMR
THF-H_8

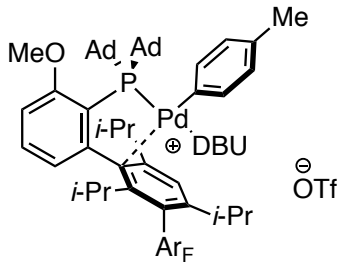


Spectrum B
^{31}P NMR
THF-H_8





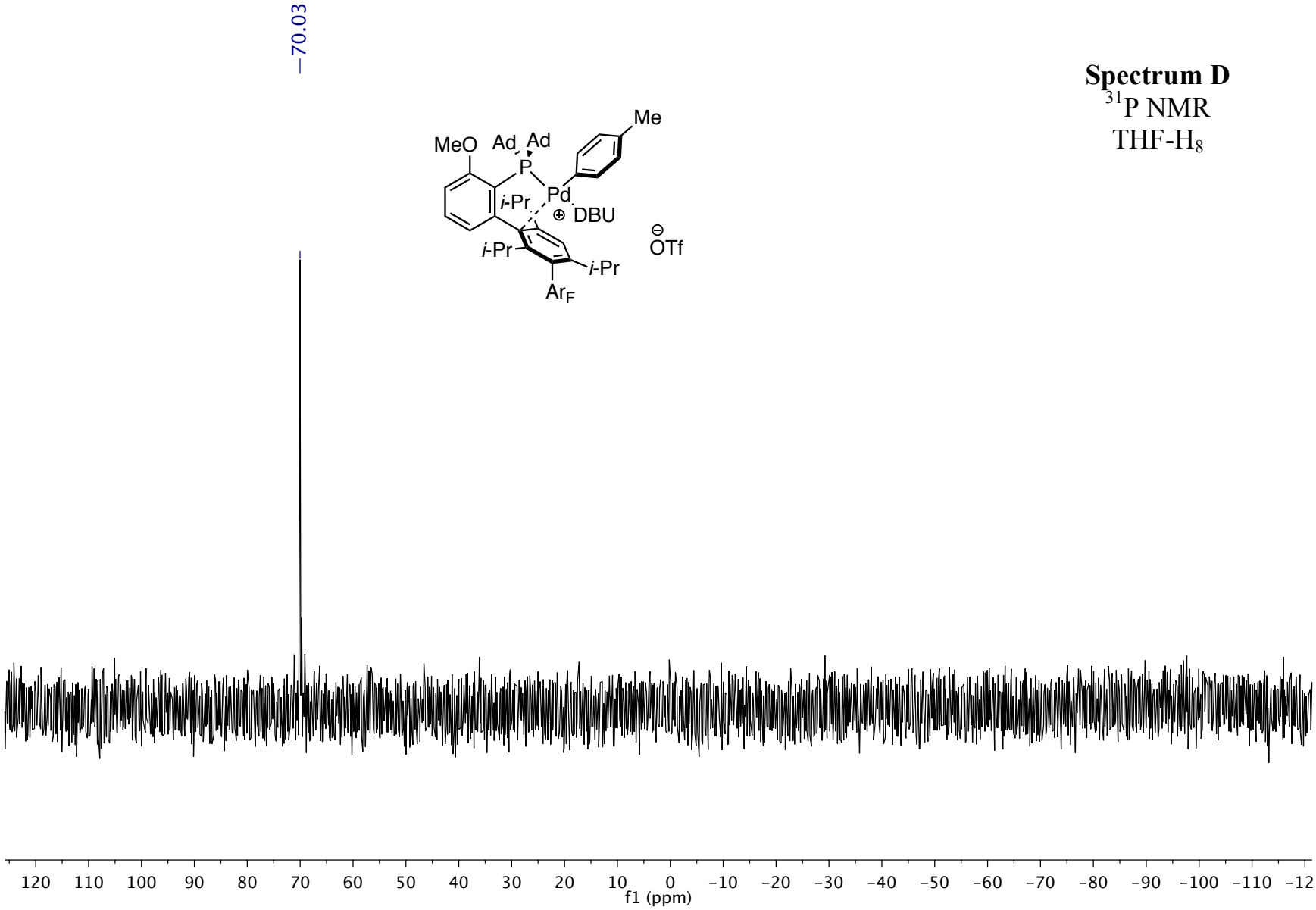
Spectrum C
^{31}P NMR
THF-H_8



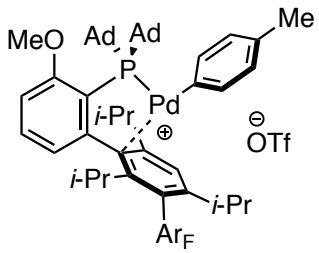
Spectrum D

^{31}P NMR

THF-H_8

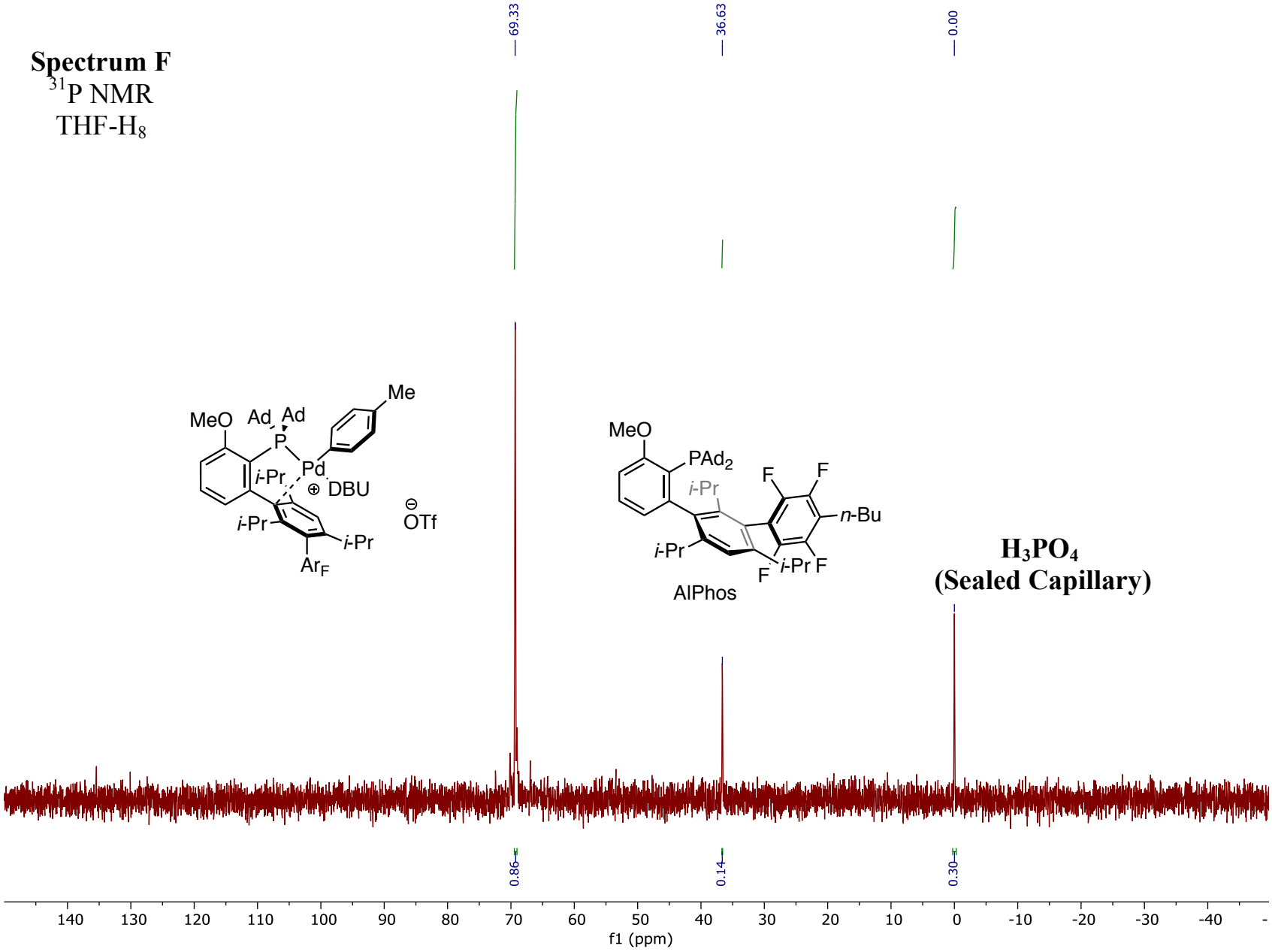


Spectrum E
^{31}P NMR
THF-H_8

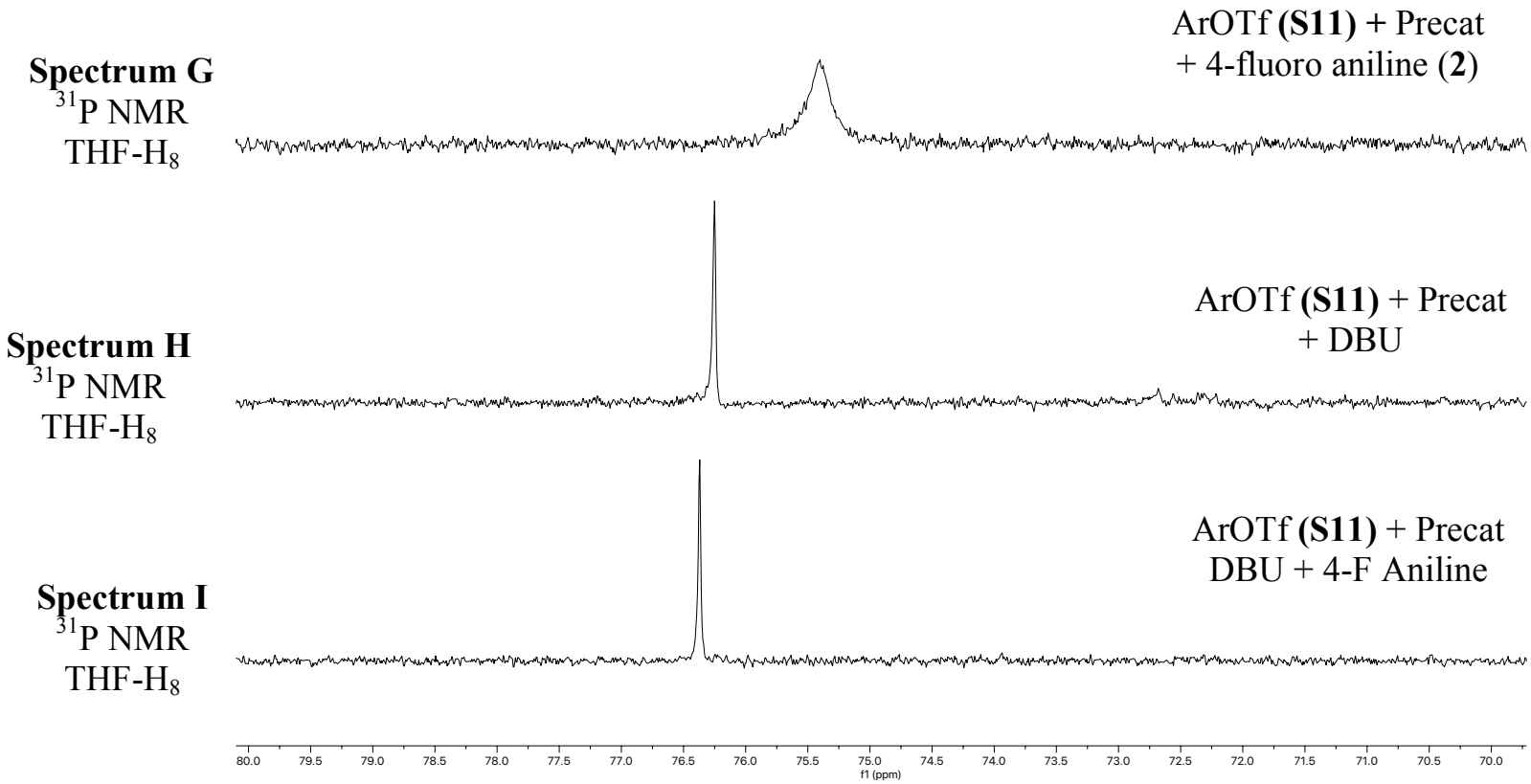


H_3PO_4
(Sealed Capillary)

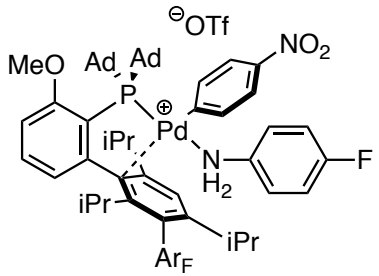
Spectrum F
^{31}P NMR
THF-H_8



Determination of Resting States: p-nitrophenyl triflate (S11) +DBU



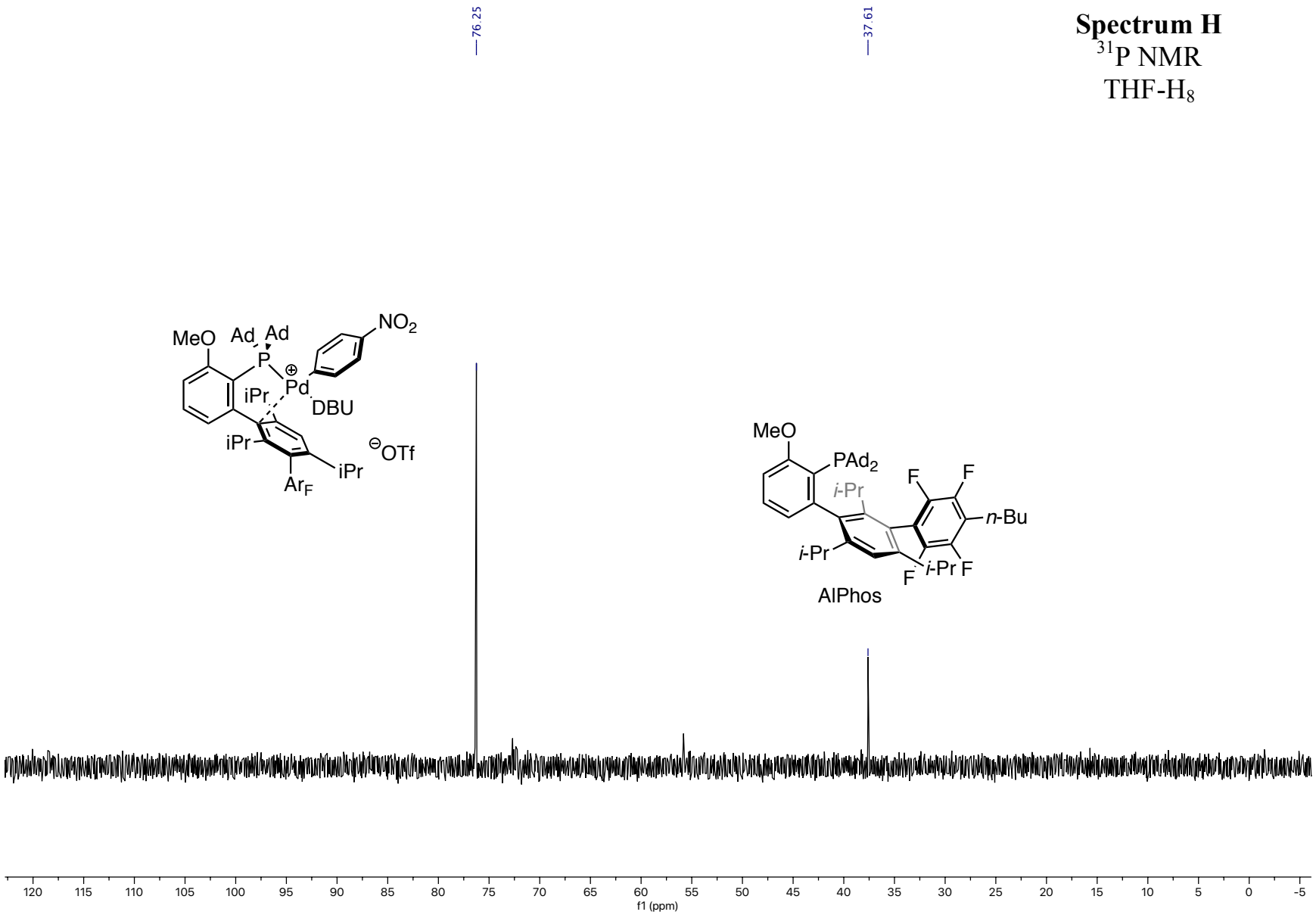
Spectrum G
^{31}P NMR
THF-H_8



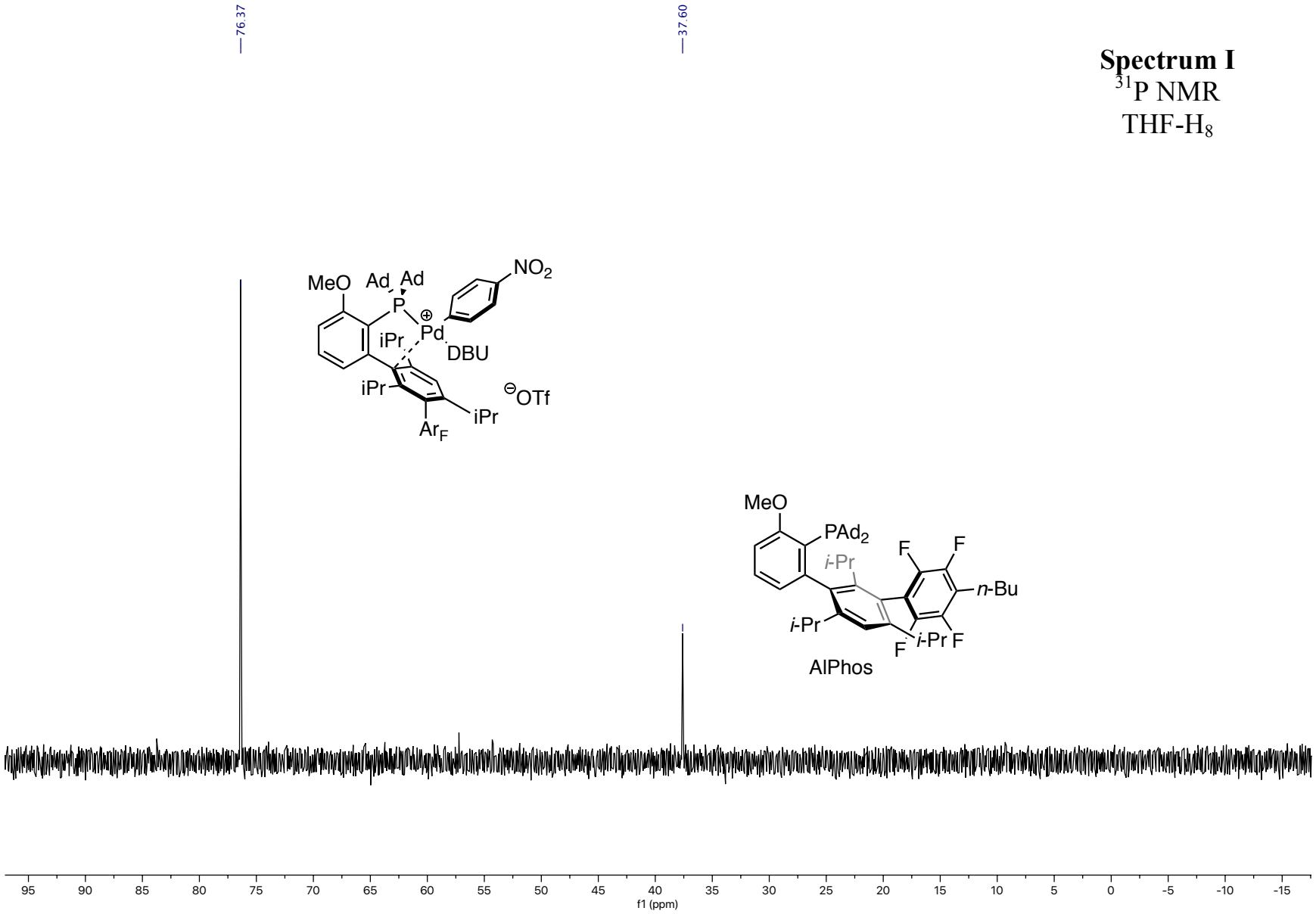
Spectrum H

^{31}P NMR

THF-H_8



Spectrum I
^{31}P NMR
THF-H_8



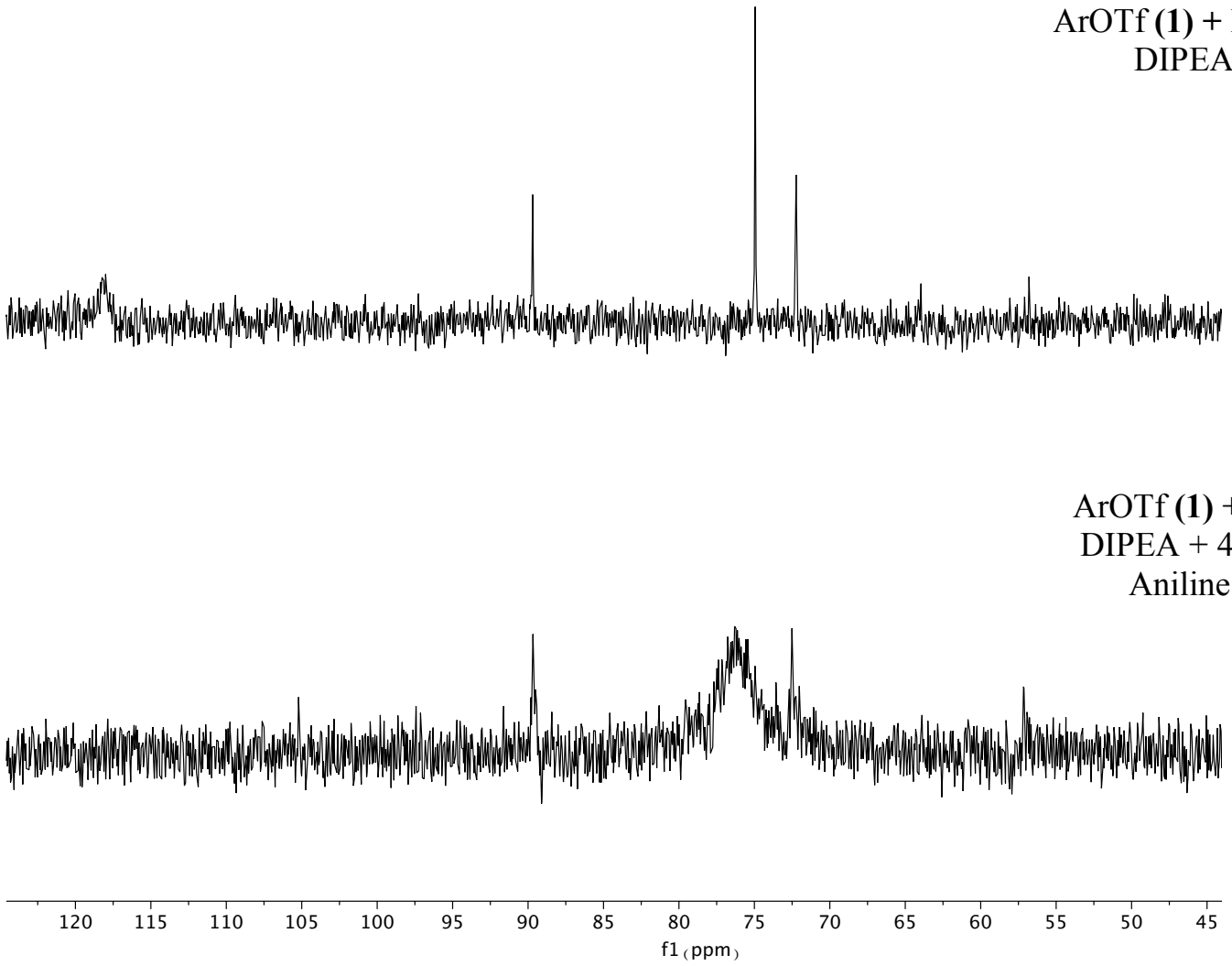
Determination of Resting States: DIPEA

Spectrum J
^{31}P NMR
THF-H_8

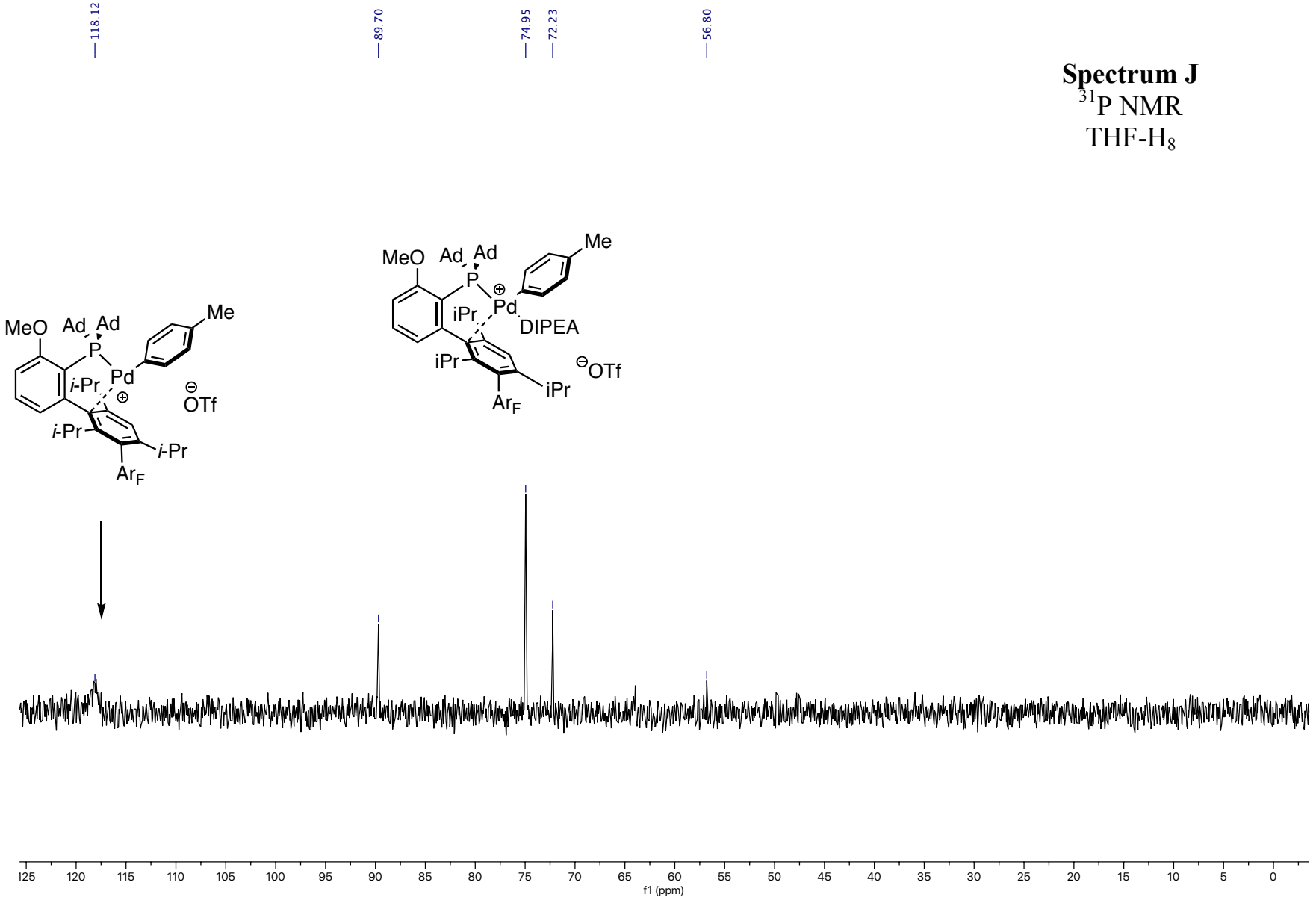
ArOTf **(1)** + Precat
DIPEA

Spectrum K
^{31}P NMR
THF-H_8

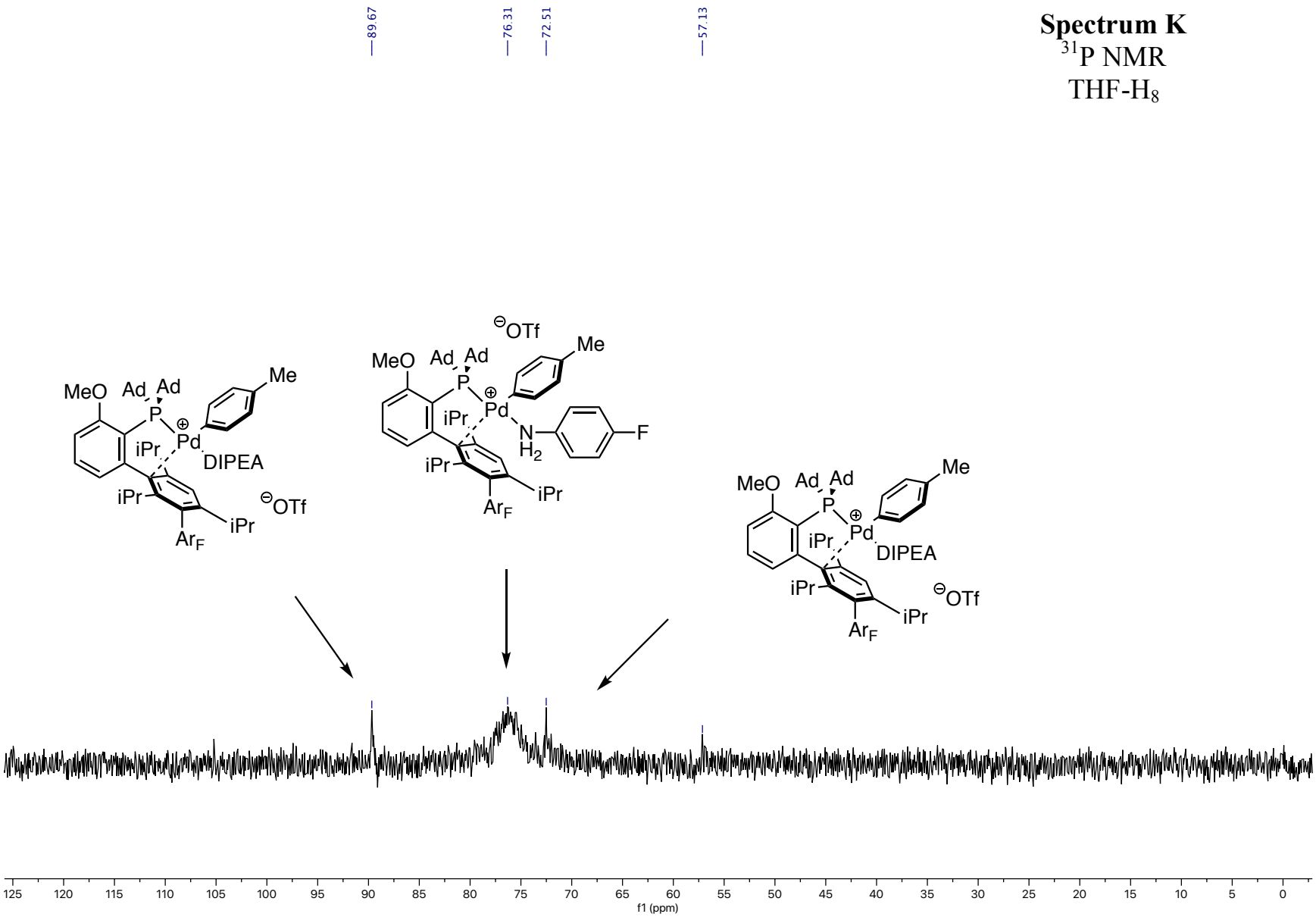
ArOTf **(1)** + Precat
DIPEA + 4-fluoro
Aniline (**2**)



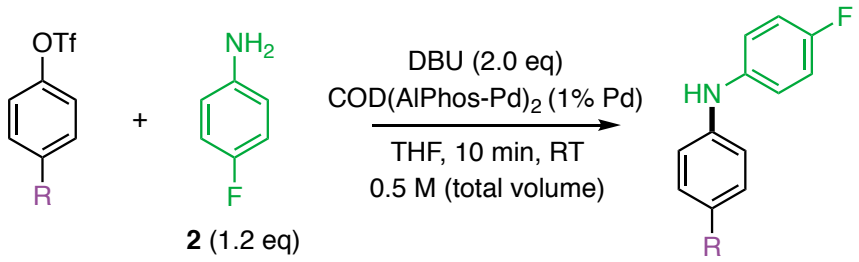
Spectrum J
^{31}P NMR
THF-H_8



Spectrum K
^{31}P NMR
THF-H_8



Hammett Plot: Determination of Reaction Rates



In a nitrogen-filled glovebox, an oven-dried vial (8 mL) was sequentially charged with COD(AlPhos-Pd)$_2$ (3.2 mg, 1.65 μmol 0.005 equiv, 1.0% Pd), an aryl triflate (0.33 mmol, 1.0 equiv), 1-fluoronapthalene (42.6 μL, 0.33 mmol, 1.0 equiv), and THF to prepare a 1.0 M solution relative to aryl triflate (330 μL total volume). This solution (300 μL, 0.30 mmol relative to ArOTf) was transferred to an oven-dried NMR tube via a calibrated microliter pipette. The NMR tube was capped with a Precision Seal^{TM} rubber septa. A THF solution of 4-fluoroaniline (1.2 equiv, 1.2 M total volume) and DBU (2.0 equiv, 2.0 M total volume) was prepared (see table below). A syringe (plastic, 1.0 mL, 6-inch needle) was used to withdraw this solution (300 μL, 0.36 mmol relative to amine and 0.60 mmol relative to DBU). The tip of the needle was carefully pushed into a soft rubber stopper to prevent leaking. The NMR tube and syringe were removed from the glovebox and were transferred to the NMR facility.

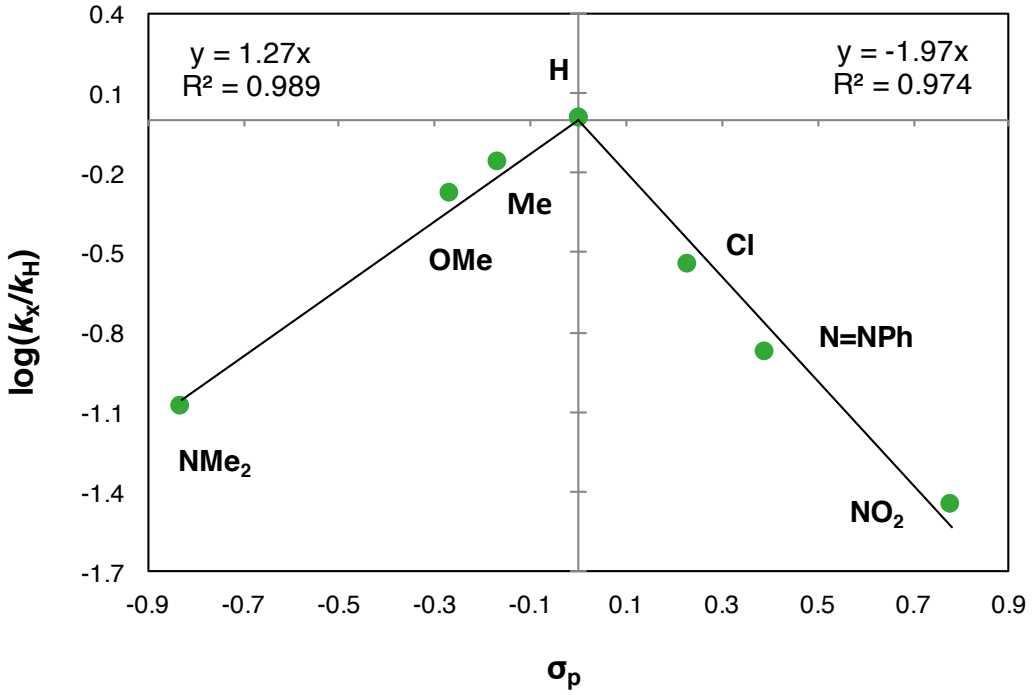
After setting up the standard ^{19}F NMR experiment parameters (see General Information), the DBU and 4-fluoroaniline solution was injected into the NMR tube by carefully inserting the tip of the needle into the septum. The needle was removed, the NMR tube was shaken for 2 s, and the reaction was analyzed by the previously outlined parameters. The initial rate of the reaction was determined. This process was repeated for a total of two runs (three for *p*-H) and the initial rates were averaged. Previously reported Hammett parameters (σ_p)[11] were used to compare reaction rates.

Note: In the coupling of 4-chlorophenyl trifluoromethylsulfonate, fluorobenzene was used as the internal standard due to overlapping product and standard peaks when 1-fluoronaphthalene was used.

Stock Solutions for Initial Rate Determination

Para-Sub.	Equivalents	Reagent	Amount in Stock	Amount / NMR	mmol / NMR	
--	2.0 equiv	DBU (µL)	807.8	89.8	0.60	Dispense 300 µL via syringe
	1.2 equiv	F-Aniline	306.7	34.08	0.36	
		THF Volume (microL)	1585.4	176.2	--	
H	1.0 equiv	Phenyl triflate (µL)	52.9	48.1	0.3	Deliver 300 µL to NMR tube
	1.0 equiv	1-F naphthalene (µL)	42.6	38.7	0.3	
	1.0% Pd	COD(AlPhos-Pd)2 (mg)	3.2	2.94	1.5 µmol	
		THF	231.3	210.3	--	
NMe_2	1.0 equiv	4-NMe2 triflate (mg)	65.7	59.7	0.3	Deliver 300 µL to NMR tube
	1.0 equiv	1-F naphthalene (µL)	42.6	38.7	0.3	
	1.0% Pd	COD(AlPhos-Pd)2 (mg)	3.2	2.94	1.5 µmol	
		THF	218.5	198.7	--	
Me	1.0 equiv	4-Me phenyl triflate (µL)	59.1	53.8	0.3	Deliver 300 µL to NMR tube
	1.0 equiv	1-F naphthalene (µL)	42.6	38.7	0.3	
	1.0% Pd	COD(AlPhos-Pd)2 (mg)	3.2	2.94	1.5 µmol	
		THF	225.1	204.6	--	
Cl	1.0 equiv	4-Cl phenyl triflate (µL)	53.7	48.8	0.3	Deliver 300 µL to NMR tube
	1.0 equiv	**Fluorobenzene** (µL)	31.0	28.2	0.3	
	1.0% Pd	COD(AlPhos-Pd)2 (mg)	3.2	2.94	1.5 µmol	
		THF	242.0	220.0	--	
NO_2	1.0 equiv	NO2 phenyl triflate (mg)	89.5	81.4	0.3	Deliver 300 µL to NMR tube
	1.0 equiv	1-F naphthalene (µL)	31.0	28.2	0.3	
	1.0% Pd	COD(AlPhos-Pd)2 (mg)	3.2	2.94	1.5 µmol	
		THF	206.2	187.5	--	
OMe	1.0 equiv	OMe phenyl triflate (mg)	59.7	54.3	0.3	Deliver 300 µL to NMR tube
	1.0 equiv	1-F naphthalene (µL)	31.0	28.2	0.3	
	1.0% Pd	COD(AlPhos-Pd)2 (mg)	3.2	2.94	1.5 µmol	
		THF	236.0	214.6	--	
N=NPh	1.0 equiv	4-N=NPh triflate (mg)	109.0	99.1	0.3	Deliver 300 µL to NMR tube
	1.0 equiv	1-F naphthalene (µL)	31.0	28.2	0.3	
	1.0% Pd	COD(AlPhos-Pd)2 (mg)	3.2	2.94	1.5 µmol	
		THF	186.7	169.8	--	
NMe_2	1.0 equiv	4-NMe2 triflate (mg)	65.7	59.7	0.3	Deliver 300 µL to NMR tube
	1.0 equiv	1-F naphthalene (µL)	31.0	28.2	0.3	
	1.0% Pd	COD(AlPhos-Pd)2 (mg)	3.2	2.94	1.5 µmol	
		THF	230.1	209.2	--	

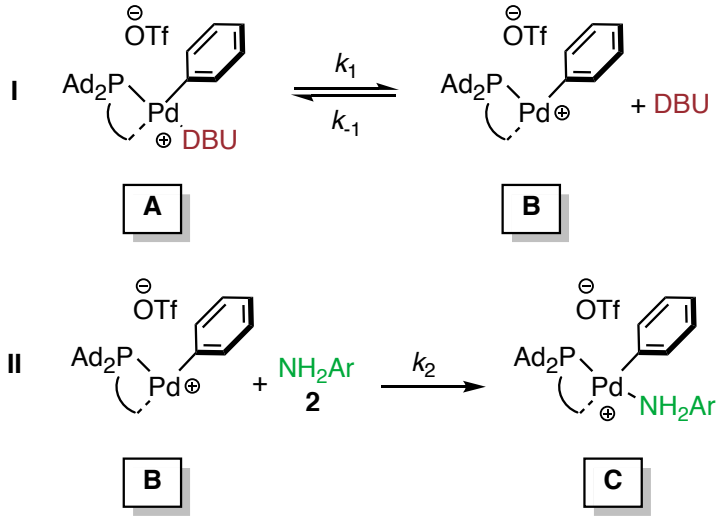
Reaction Rates Compared to Hammett Parameters



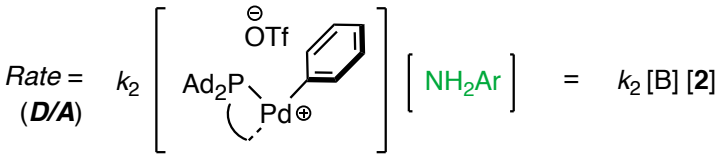
Substituent (x)	Rate (mmol/min)	Average Rate (k_x)	k_x/k_H	log(k_x/k_H)	Hammett Value
H	0.01743179	0.019326	1	0	0
	0.02089282				
	0.01965383				
Me	0.01259969	0.013356	0.691068	-0.160479	-0.17
	0.01411166				
NO_2	0.00065959	0.000683	0.03536	-1.451487	0.78
	0.00070716				
OMe	0.01044717	0.010101	0.522648	-0.281791	-0.01
	0.00975437				
Cl	0.00455625	0.005753	0.448939	-0.347813	0.23
	0.00694916				
N=NPh	0.00237459	0.002546	0.131733	-0.880304	0.39
	0.00271721				
NMe_2	0.00166681	0.001599	0.082732	-1.082325	-0.83
	0.00153098				

Derivation of Dissociative/Associative (D/A) and Associative/Dissociative (A/D) Rate Equations

A. Dissociation/Association (D/A) Mechanism



Assuming that the deprotonation event is fast (see footnote 23 in the manuscript) and the reductive elimination event is non-reversible, the rate of the reaction can be written as:



Applying the pre-equilibrium assumption, the rate can be written in the following way:

$$K_1 = \frac{k_1}{k_{-1}} = \frac{[B]\,[DBU]}{[A]}$$

$$[B] = \frac{K_1\,[A]}{[DBU]}$$

$$Rate_{(D/A)} = \frac{k_2\,K_1\,[A]\,[\mathbf{2}]}{[DBU]}$$

The concentration of intermediate A can be determined by accounting for the total concentration of Pd in solution ($[Pd]_{total}$). Experimentally, the resting state of the reaction was determined to be species A, which should account for most of the concentration of the catalyst. However, we will include the concentration of species B as this species is integral to the pre-equilibrium argument.

$$[Pd]_{total} = [A] + [B]$$

$$[A] = [Pd]_{total} - [B]$$

$$[A] = [Pd]_{total} - \left(\frac{K_1\,[A]}{[DBU]} \right)$$

$$[A] + \left(\frac{K_1\,[A]}{[DBU]} \right) = [Pd]_{total}$$

$$[A] \left(1 + \frac{K_1}{[DBU]} \right) = [Pd]_{total}$$

$$[A] = \frac{[Pd]_{total}}{\left(1 + \frac{K_1}{[DBU]} \right)}$$

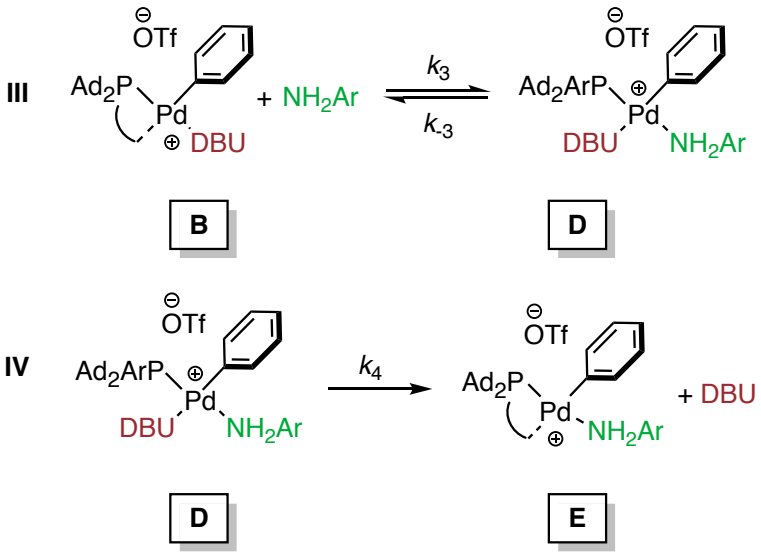
Taking the $[Pd]_{total}$ into account, the rate of the reaction can be simplified to the following equation:

$$Rate = (\boldsymbol{D/A}) \frac{\left(\frac{k_2\,K_1\,[Pd]_{total}\,[\mathbf{2}]}{\left(1 + \frac{K_1}{[DBU]} \right)} \right)}{[DBU]}$$

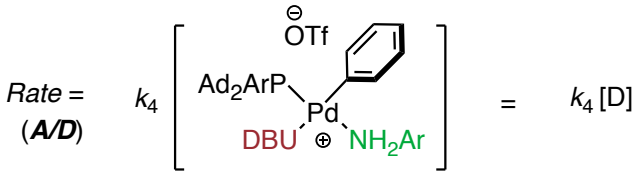
$$Rate = (\boldsymbol{D/A}) \left[\frac{\left(\frac{k_2\,K_1\,[Pd]_{total}\,[\mathbf{2}]}{\left(1 + \frac{K_1}{[DBU]} \right)} \right)}{[DBU]} \right] \left[\frac{\left(\frac{1}{[DBU]} \right)}{\left(\frac{1}{[DBU]} \right)} \right]$$

$$Rate = (\boldsymbol{D/A}) \frac{k_2\,K_1\,[Pd]_{total}\,[\mathbf{2}]}{[DBU] + K_1}$$

B. Association/Dissociation (A/D) Mechanism



Assuming that the deprotonation event is fast (see footnote 23 in the manuscript) and the reductive elimination event is non-reversible, the rate of the reaction can be written as:



Applying the pre-equilibrium assumption, the rate can be written in the following way:

$$K_3 = \frac{k_3}{k_{-3}} = \frac{[D]}{[B]\,[\mathbf{2}]}$$

$$[D] = K_3\,[B]\,[\mathbf{2}]$$

$$\textit{Rate} = k_4\,K_3\,[B]\,[\mathbf{2}] \quad (\textbf{\textit{A/D}})$$

The concentration of intermediate B can be determined by accounting for the total concentration of Pd in solution ($[Pd]_{total}$). Experimentally, the resting state of the reaction was species B, which should account for most of the concentration of the catalyst. However, we will include the concentration of species D as this species is integral to the pre-equilibrium argument.

$$[Pd]_{total} = [B] + [D]$$

$$[B] = [Pd]_{total} - [D]$$

$$[B] = [Pd]_{total} - K_3\,[B]\,[\mathbf{2}]$$

$$[B]\left(1 + K_3\,[\mathbf{2}]\right) = [Pd]_{total}$$

$$[B] = \frac{[Pd]_{total}}{\left(1 + K_3\,[\mathbf{2}]\right)}$$

Taking the $[Pd]_{total}$ into account, the rate of the reaction can be simplified to the following equation:

$$Rate = (\boldsymbol{A/D}) \quad \frac{k_4\,K_3\,[Pd]_{total}\,[\mathbf{2}]}{1 + K_3\,[\mathbf{2}]}$$

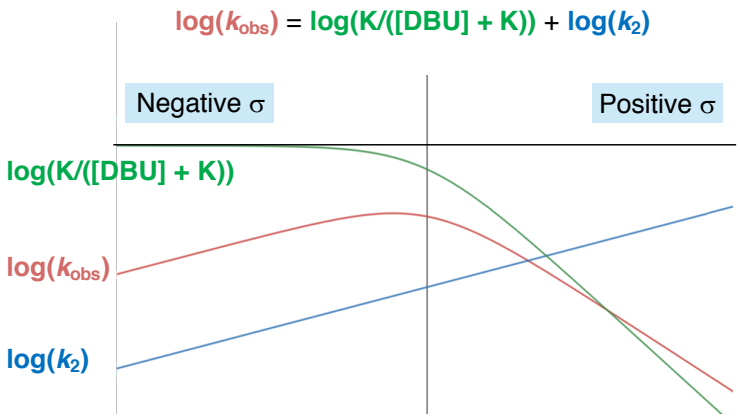
Mathematical Model for Hammett Plot Behavior

As derived above, the observed rate is proportional to a function of two constants:

$$k_{obs} \text{ α } k_2K/(K+[DBU]), \text{ where } K = k_1/k_{-1}.$$

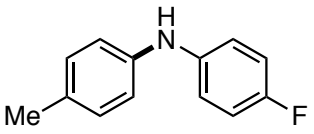
Thus, the logarithm of the rate constant is the sum of two terms plus trivial constant terms that are the same between all reactions: $\log(k_{obs}) = \log(k_2) + \log(K/([DBU]+K))$. We simulated a Hammett plot for this type of rate law using the following procedure:

1. The rate of the irreversible second step is expected to exhibit a small, positive Hammett correlation due to slight ablation of positive charge at palladium in the transition state relative to the preceding ground state. For our model, we assume $\log k_2 = \rho_2\sigma$, and we arbitrarily pick the value $\boldsymbol{\rho_2 = +1/3}$.
2. The equilibrium constant of the first step is assumed to have a large, negative, linear Hammett correlation due to accumulation of charge at palladium in the tricoordinate intermediate relative to the DBU-bound ground state. For our model, we assume $\log K = \rho_1\sigma$, and we arbitrarily pick the value $\boldsymbol{\rho_1 = -1}$.
3. The concentration of DBU is identical at the initiation of all the kinetic experiments in the Hammett series. Thus, we can arbitrarily assign the value **[DBU] = 1** for visualization purposes.
4. Based on these assumptions, the following qualitative behavior is observed. The blue curve was shifted down by a constant for clarity visualization (Green term = $\log(10^{\sigma} / (1 + 10^{\sigma}))$; Blue term = $-2 + \sigma/3$; Red = Green + Blue).

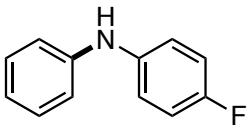


5. Although adjustments of the numerical values used above can shift the slopes and alter the width of the intermediate region, the shape of the red trace is preserved: an upward sloping linear region on the left, with slope approximating ρ_2, the Hammett constant of the irreversible step; an intermediate central region of downward curvature; and a downward sloping linear region on the right, with slope approximating $(\rho_1 + \rho_2)$, the sum of Hammett constants of the two steps.

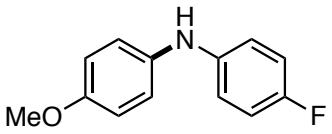
Hammett Plot: Product Synthesis and Characterization Data



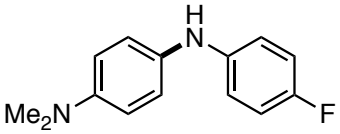
3



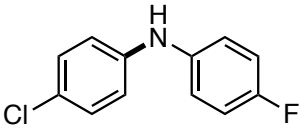
S15



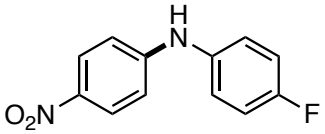
S16



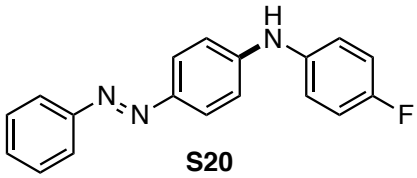
S17



S18



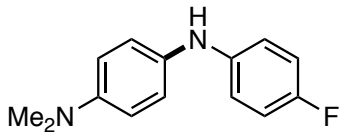
S19



S20

Products **3,**[12] **S15**,[13] and **S16**[14] have been previously reported and fully characterized. Products **S17**[15] and **S18**[16] have been previously reported but without ^{19}F NMR data. These products were independently synthesized to verify ^{19}F NMR product signals. Products **S19** and **S20** were prepared according to the following procedures.

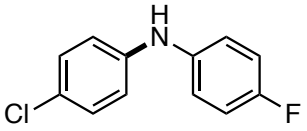
N^1-(4-fluorophenyl)-N^4,N^4-dimethylbenzene-1,4-diamine (S17)



S17 was prepared according to the general procedure for measuring initial rates for the Hammett Plot. Two identical reactions were set up utilizing 4-(dimethylamino)phenyl trifluoromethanesulfonate (59.7 μL, 80.8 mg, 0.30 mmol), 4-fluoroaniline (34 μL 0.36 mmol, 1.2 equiv), DBU (90 μL, 0.60 mmol, 2.0 equiv), COD(AlPhos-Pd)$_2$ (2.9 mg, 1.5 μmmol, 1.0 mol% Pd), and THF (0.35 mL, 1.0 M total volume). 1-fluoronaphthalene (39 μL, 0.30 mmol) was also added as an internal standard. Following the NMR analysis, the following was done: The NMR tubes were placed in a 60 °C oil bath for 16 h. After cooling to room temperature, the two reaction mixtures were diluted with CH_2Cl_2, combined in a round bottom flask (0.60 mmol scale total), and concentrated with the aid of a rotary evaporator. The crude material was purified by automated silica gel column chromatography (10-30% EtOAc in hexanes, 50 g silica gel, 14 column volumes) to afford a slightly off-white crystalline solid (115 mg, 95% averaged yield). **^{1}H NMR** (400 MHz; C_6D_6): δ (ppm) 6.95 – 6.86 (m, 2H), 6.83 – 6.74 (m, 2H), 6.63 – 6.51 (m, 4H), 4.69 (s, 1H), 2.55 (s, 6H). **^{13}C NMR** (101 MHz; C_6D_6): δ (ppm) ^{13}C NMR (101 MHz, C_6D_6) δ 157.11 (d, J = 236.5 Hz), 147.56, 142.93, 133.31, 123.24, 116.73 (d, J = 7.3 Hz), 116.04, 115.93 (d, J = 22.4 Hz), 40.92 **^{19}F NMR** (376 MHz, C_6D_6): δ (ppm) -125.9. **M.P.**: 104.8-105.6 °C. **IR** (neat): 3296.3, 2850.9, 1511.3, 1305.0, 1053.6, 936.0, 812.6 cm^{-1}.

Characterization data of **S17** is consistent with that previously reported though the ^{19}F NMR was not previously reported.[15]

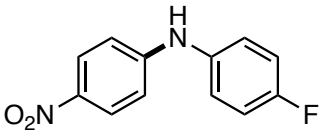
4-chloro-*N*-(4-fluorophenyl)aniline (S18)



S18 was prepared according to an adapted procedure for Pd-Catalyzed C–N coupling using DBU[17] using 4-chlorophenyl trifluoromethanesulfonate (130 mg, 0.50 mmol), 4-fluoroaniline (47 μL, 0.60 mmol, 1.0 equiv), DBU (150 μL, 1.0 mmol, 2.0 equiv), COD(AlPhos-Pd)$_2$ (4.8 mg, 2.5 μmmol, 1.0 mol% Pd), and THF (0.50 mL). The reaction was heated in a 60 °C oil bath for 16 h. After cooling to room temperature, the crude material was purified by automated silica gel column chromatography (10-30% EtOAc in hexanes, 50 g silica gel, 14 column volumes) to afford a colorless oil (92 mg, 87% yield). **^{1}H NMR** (400 MHz; $CDCl_3$): δ (ppm) 7.30 – 7.12 (m, 2H), 7.11 – 6.95 (m, 4H), 6.95 – 6.84 (m, 2H), 5.56 (bs, 1H) **^{13}C NMR** (101 MHz; $CDCl_3$): δ (ppm) 158.6 (d, J = 240.9 Hz), 143.0, 138.8 (d, J = 2.6 Hz), 129.6, 125.3, 121.2 (d, J = 7.8 Hz), 118.1, 116.4 (d, J = 22.6 Hz). **^{19}F NMR** (376 MHz, $CDCl_3$): δ (ppm). -121.1 (s). **IR** (neat): 3409.2, 1593.6, 1504.9, 1311.4, 1211.6, 1090.9, 812.4 cm^{-1}.

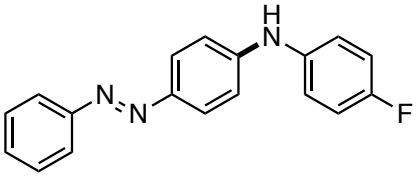
Characterization data of **S18** is consistent with that previously reported though the ^{19}F NMR was not previously reported.[16]

4-fluoro-*N*-(4-nitrophenyl)aniline (S19)



S19 was prepared according to an adapted procedure for Pd-catalyzed C–N coupling using DBU[17] using 4-nitrophenyl trifluoromethanesulfonate (136 mg, 0.50 mmol), 4-fluoroaniline (57 µL, 0.60 mmol, 1.2 equiv), DBU (150 µL, 1.0 mmol, 2.0 equiv), COD(AlPhos-Pd)$_2$ (4.8 mg, 2.5 µmmol, 1.0 mol% Pd), and THF (0.50 mL). The reaction was heated in a 60 °C oil bath for 16 h. After cooling to room temperature, the crude material was purified by automated silica gel column chromatography (10-40% EtOAc in hexanes, 50 g silica gel, 14 column volumes) to afford a crystalline, orange solid (82 mg, 71% yield). **^{1}H NMR** (400 MHz; $CDCl_3$): δ (ppm) 8.18 – 8.09 (m, 2H), 7.25 – 7.18 (m, 2H), 7.16 – 7.08 (m, 2H), 6.89 – 6.83 (m, 2H), 6.18 (s, 1H). **^{13}C NMR** (101 MHz; $CDCl_3$) 160.4 (d, J = 245.1 Hz),151.1, 140.1, 135.7, 125.2 (d, J = 8.3 Hz), 117.0 (d, J = 22.7 Hz), 113.5. **^{19}F NMR** (376 MHz, $CDCl_3$): δ (ppm) -116.6 (s). **M.P.**: 187.9-190.2. **IR** (neat): 3391.7, 1596.0, 1505.0, 1223.7, 1136.4, 819.1, 690.0 cm^{-1}. **HRMS** (DART) m/z calcd. for $C_{12}H_9FN_2O_2$ ($[M+H]^+$): 233.0726. Found: 233.0739.

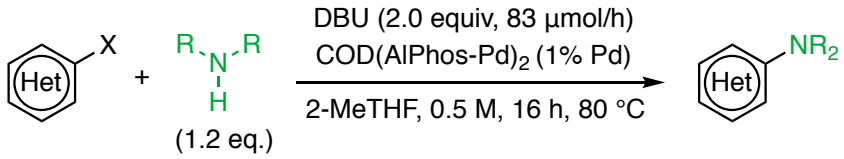
***E*)-4-fluoro-*N*-(4-(phenyldiazenyl)phenyl)aniline (S20)**



S20 was prepared according to the general procedure for measuring initial rates for the Hammett Plot. Two identical reactions were set up utilizing (*E*)-4-(phenyldiazenyl)phenyl trifluoromethanesulfonate (99.1 mg, 0.30 mmol), 4-fluoroaniline (34 μL 0.36 mmol, 1.2 equiv), DBU (90 μL, 0.60 mmol, 2.0 equiv), COD(AlPhos-Pd)$_2$ (2.9 mg, 1.5 μmmol, 1.0 mol% Pd), and THF (0.35 mL, 1.0 M total volume). 1-fluoronaphthalene (39 μL, 0.30 mmol) was also added as an internal standard. Following the initial rate measurement, the NMR tubes were placed in a 60 °C oil bath for 16 h. After cooling to room temperature, the two reaction mixtures were diluted with CH_2Cl_2, transferred to a round bottom flask (0.60 mmol scale total), and concentrated with the aid of a rotary evaporator. The crude material was purified by automated silica gel column chromatography (10-40% EtOAc in hexanes, 50 g silica gel, 14 column volumes) to afford a bright orange solid (161 mg, 92% averaged yield). **^{1}H NMR** (400 MHz; $CDCl_3$): δ (ppm) 8.24 (d, *J* = 8.26 Hz, 4 H), 7.86 (t, *J* =7.5 Hz, 2 H), 7.78 (t, *J* =7.3 Hz, 1 H), 7.54-7.51 (m, 2 H), 7.44-7.39 (m, 2H), 7.38-7.34 (m, 2H), 6.29 (bs, 1H). **^{13}C NMR** (101 MHz; $CDCl_3$): δ (ppm) 159.2 (d, *J* = 242.6 Hz), 158.13, 153.27, 147.55, 146.69, 137.43, 137.40, 130.36, 129.35, 125.34, 123.15 (d, *J* = 7.9 Hz), 122.77, 116.56 (d, *J* = 22.5 Hz), 115.35. **^{19}F NMR** (376 MHz, $CDCl_3$): δ (ppm) -119.3 (s). **M.P.:** 187.9-190.2 °C. **IR** (neat): 3391.7, 1596.0, 1505.0, 1223.7, 1136.4, 819.1, 690.0. **HRMS** (DART) m/z calcd. for $C_{18}H_{15}FN_3$ ($[M+H]^+$): 292.1250. Found: 292.1264.

General Procedure for the Pd-Catalyzed C-N Coupling Using DBU

This general procedure was adapted from the original report of this system.[17]



An oven-dried reaction tube (Fisher 16 x 125 mm tubes – Cat. No. 1495935A) equipped with a stir bar was sequentially charged with solid reagents, including precatalyst (4.8 mg, 2.5 µmmol, 1.0 mol% Pd), aryl triflate (0.5 mmol, 1.0 equiv), and amine (0.60 mmol, 1.2 equiv). The reaction tube was sealed with a screw cap (Kimble Chase, Open Top S/T, Part No. 73804-15425) containing a Teflon septum (Thermo Scientific, 10/90 Teflon/Sil, Cat. No. B7995-15) and was pierced with a needle connected to a Schlenk line. The tube was evacuated and backfilled with nitrogen (this process was repeated a total of three times), then 2-MeTHF (0.5 mL) was added via syringe. If reagents were liquid, solvent was added to the nitrogen-filled tube containing precatalyst, followed by the addition of aryl triflate and/or amine. The top of the reaction tube was covered in parafilm, the tube was placed in an oil bath heated to 80 °C. Depending on the reaction conditions used, one of the following methods was performed:

General Procedure I: Slow Addition of DBU

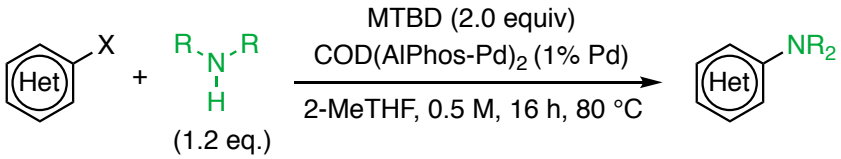
A syringe (1.0 mL Norm-Ject, plastic, 4.726 mm diameter) charged with DBU (200 µL) was fixed to a syringe pump (Harvard Apparatus, PHD ULTRA) and the needle (6 inch, Air-Tight disposable) was inserted into the septum of the reaction tube. The DBU was added to the reaction tube (150 µL, 1.0 mmol, 12.5 µL/h, 12 h) via syring pump and the reaction tube was heated at 80 °C during this addition process. After 16 h, the reaction mixture was cooled to room temperature, diluted with CH_2Cl_2, transferred to a round bottom flask, and concentrated with the aid of a rotary evaporator. The crude material was purified by automated silica gel column chromatography.

General Procedure II: Normal Addition of DBU

DBU (150 µL, 1.0 mmol) was added to the reaction tube in one portion via syringe and the reaction tube was heated at 80 °C. After 16 h, the reaction mixture was allowed to cool to room temperature and then was diluted with CH_2Cl_2, transferred to a round bottom flask, and concentrated with the aid of a rotary evaporator. The crude material was purified by automated silica gel column chromatography.

General Procedure for the Pd-Catalyzed C-N Coupling Utilizing MTBD

A procedure analogous to the procedure employing slow addition of DBU was used.

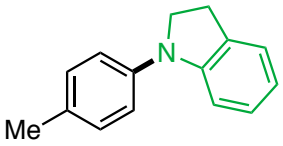


General Procedure III:

An oven-dried reaction tube (Fisher 16 x 125 mm tubes – Cat. No. 1495935A) equipped with a stir bar was sequentially charged with solid reagents, including precatalyst (4.8 mg, 2.5 µmmol, 1.0 mol% Pd), aryl triflate (0.5 mmol, 1.0 equiv), and amine (0.60 mmol, 1.2 equiv). The reaction tube was sealed with a screw cap (Kimble Chase, Open Top S/T, Part No. 73804-15425) containing a Teflon septum (Thermo Scientific, 10/90 Teflon/Sil, Cat. No. B7995-15) and was pierced with a needle connected to a Schlenk line. The tube was evacuated and backfilled with nitrogen (this process was repeated a total of three times), then 2-MeTHF (0.5 mL) and MTBD (144 µL, 1.0 mmol) were added sequentially via syringe. If reagents were liquid, solvent was added to the nitrogen-filled tube containing precatalyst, followed by the addition of aryl triflate, amine, and MTBD. The top of the reaction tube was covered in parafilm and the tube was placed in a pre-heated 80 °C oil bath. After 16 h, the reaction mixture was cooled to room temperature, diluted with CH_2Cl_2, transferred to a round bottom flask, and concentrated with the aid of a rotary evaporator. The crude material was purified by automated silica gel column chromatography.

Characterization Data for Products 1a-9a

1-(*p*-tolyl)indoline (1a)



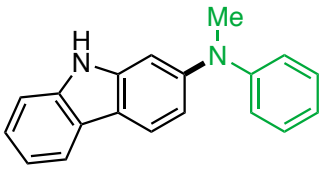
1a was prepared according to **General Procedures I** and **II** using using *p*-tolyl trifluoromethanesulfonate (120 mg, 90 µL, 0.50 mmol), indoline (67 µL 0.60 mmol, 1.2 equiv), DBU (150 µL, 1.0 mmol, 2.0 equiv), COD(AlPhos-Pd)$_2$ (4.8 mg, 2.5 µmmol, 1.0 mol% Pd), and 2-MeTHF (0.5 mL). The reaction was also performed on the same scale using MTBD (144 µL, 1.0 mmol, 2.0 equiv) instead of DBU. The product was purified by automated flash column chromatography (1-7% EtOAc in hexanes, 100 g silica gel, 22 column volumes) to afford a white crystalline solid. **^{1}H NMR** (400 MHz; $CDCl_3$): δ 7.21 (m, 5H), 7.11 (m, 2H), 6.79 (dd, *J* = 7.4 Hz, 3.9 Hz, 1 H), 3.97 (t, *J* = 8.5 Hz, 2H), 3.16 (t, *J* = 8.5 Hz, 2H) 2.39 (s, 3H) (ppm). **^{13}C NMR** (101 MHz; $CDCl_3$): δ 142.131.3, 130.9, 130.0, 127.4, 125.2, 118.7, 118.4, 108.1, 52.6, 28.5, 21.1 (ppm). **M.P.:** 68.1-70.5 °C. **IR** (neat): 3025.2, 2918.1, 2850.6, 1596.4, 1384.4, 1224.8, 741.8 cm^{-1}.

Characterization data is consistent with that of previously reported.[18]

Procedure I: Slow addition of DBU (2.0 equiv) : 1st run: 103 mg, 98% yield; 2nd run: 104 mg, 99% yield ^{1}H NMR yield: 99% relative to hexamethylbenzene internal standard.
Procedure I: Slow addition of DBU (1.2 equiv): ^{1}H NMR yield: 68% relative to hexamethylbenzene internal standard.
Procedure II: Normal addition of DBU: ^{1}H NMR yield: 10% relative to hexamethylbenzene internal standard.

The reaction was also performed according to **General Procedure III** on the same scale using MTBD (144 µL, 1.0 mmol, 2.0 equiv) instead of DBU to afford **1a (**98 mg, 94% yield).

***N*-methyl-*N*-phenyl-9*H*-carbazol-2-amine (2a)**



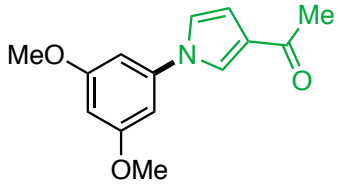
2a was prepared according to **General Procedures I** and **II** using 9*H*-carbazol-2-yl trifluoromethanesulfonate (158 mg, 0.50 mmol), *N*-methyl aniline (65 µL 0.60 mmol, 1.2 equiv), DBU (150 µL, 1.0 mmol, 2.0 equiv), COD(AlPhos-Pd)$_2$ (4.8 mg, 2.5 µmmol, 1.0 mol% Pd), and 2-MeTHF (0.5 mL). The product was purified by automated flash column chromatography (1-10% EtOAc in hexanes (10 column volumes) followed by 10-60% EtOAc in hexanes (8 column volumes), 50 g silica gel) to afford a white powder. **^{1}H NMR** (400 MHz; C_6D_6): δ (ppm) 7.93 (d, *J* = 7.7 Hz, 1H), 7.83 (d, *J* = 8.4 Hz, 1H), 7.33 (ddd, *J* = 8.1, 7.1, 1.1 Hz, 1H), 7.26 – 7.17 (m, 2H), 7.07 – 7.01 (m, 3H), 6.96 (dd, *J* = 8.4, 2.0 Hz, 1H), 6.90 (tt, *J* = 7.2, 1.2 Hz, 1H), 6.80 (d, *J* = 2.0 Hz, 1H), 6.47 (s, 1H), 3.12 (s, 2H). **^{13}C NMR** (101 MHz; C_6D_6): δ (ppm) 150.3, 148.2, 141.1, 140.2, 129.5, 125.1, 124.0, 121.4, 120.8, 120.1, 119.8, 119.6, 119.1, 115.3, 110.6, 104.2, 40.7. **IR** (neat): 3403.9, 3055.7, 2923.0, 1592.4, 1459.9, 1323.8, 906.6 cm^{-1}. **HRMS** (ESI) m/z calcd. for $C_{19}H_{17}N_2$ ($[M+H]^+$): 273.1392. Found: 273.1399.

I: Slow addition of DBU: 1st run: 121 mg, 90%, 2nd run: 124 mg, 91%.

II: Normal addition of DBU: 12% ^{1}H NMR yield (dimethyl sulfone internal standard). Note: product could not be isolated due to incomplete conversion of the aryl triflate and co-elution of the product and starting material during the purification.

The reaction was also performed according to **General Procedure III** on the same scale using MTBD (144 µL, 1.0 mmol, 2.0 equiv) instead of DBU to afford **2a (**65 mg, 48%).

1-(1-(3,5-dimethoxyphenyl)-1*H*-pyrrol-3-yl)ethan-1-one (3a)

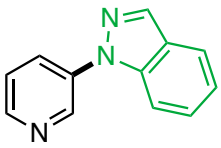


3a was prepared according to **General Procedures I** and **II** using 3,5-dimethoxyphenyl trifluoromethanesulfonate (154 mg, 0.50 mmol), 3-acetylpyrrole (70.5 mg, 0.60 mmol, 1.2 equiv), DBU (150 µL, 1.0 mmol, 2.0 equiv), COD(AlPhos-Pd)$_2$ (4.8 mg, 2.5 µmmol, 1.0 mol% Pd), and 2-MeTHF (0.5 mL). The product was purified by automated flash column chromatography (20-50% EtOAc in hexanes, 50 g silica gel, 14 column volumes) to afford a light yellow oil. **^{1}H NMR** (400 MHz; $CDCl_3$): δ (ppm) 7.61 (t, *J* = 2.0 Hz, 1H), 6.98 (dd, *J* = 3.1, 2.1 Hz, 1H), 6.70 (dd, *J* = 3.1, 1.7 Hz, 1H), 6.51 (d, *J* = 2.3 Hz, 2H), 6.38 (t, *J* = 2.2 Hz, 1H), 3.79 (s, 6H), 2.42 (s, 3H). **^{13}C NMR** (101 MHz; $CDCl_3$): δ (ppm) ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.8, 161.8, 141.6, 127.7, 124.3, 121.5, 110.8, 99.9, 98.8, 55.8, 55.8, 27.4.
IR (neat): 2938.8, 2844.7, 1656.9, 1597.4, 1202.7, 1062.8, 731.9 cm^{-1}. **EA:** Calculated for $C_{14}H_{15}NO_3$: C: 68.56; H: 6.16. Found: C: 68.31; H: 6.24.

I: Slow addition of DBU: 1st run: 120 mg, 98% yield; 2nd run: 114 mg, 93% yield.
II: Normal addition of DBU: 50 mg, 41% yield.

The reaction was also performed according to **General Procedure III** on the same scale using MTBD (144 µL, 1.0 mmol, 2.0 equiv) instead of DBU to afford **3a (**118 mg, 96% yield).

1-(pyridin-3-yl)-1*H*-indazole (4a)



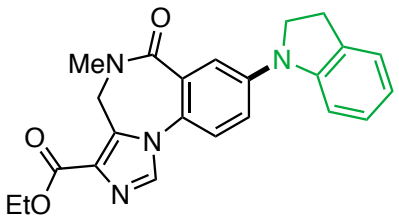
4a was prepared according to **General Procedures I** and **II** using 3-pyridyl triflate (79 µL, 0.50 mmol) 1-*H*-indazole (70.9 mg, 0.60 mmol, 1.2 equiv), DBU (150 µL, 1.0 mmol, 2.0 equiv), COD(AlPhos-Pd)$_2$ (4.8 mg, 2.5 µmmol, 1.0 mol% Pd), and 2-MeTHF (0.5 mL). The product was purified by automated flash column chromatography (5-40% EtOAc in hexanes, 50 g silica gel, 14 column volumes) to afford a white solid. **^{1}H NMR** (400 MHz; $CDCl_3$): δ ppm 9.06 (d, *J* = 2.6 Hz, 1H), 8.57 (d, *J* = 4.8 Hz, 1H), 8.21 (s, 1H), 8.08 – 7.95 (m, 1H), 7.77 (d, *J* = 8.1 Hz), 7.71 (d, *J* = 8.5 Hz, 1H), 7.48 – 7.37 (m, 2H), 7.22 (t, *J* = 7.5 Hz, 1H). **^{13}C NMR** (101 MHz; $CDCl_3$): δ ppm 147.7, 143.8, 139.0, 137.1, 136.8, 129.8, 127.9, 125.8, 124.2, 122.2, 121.8. **M.P.:** 59.1-61.5 °C. **IR** (neat): 3049.3, 2922.1, 2359.1, 1581.5, 1485.6, 1202.0, 750.0.

I: Slow addition of DBU: 1st run: 96 mg, 98% yield; 2nd run: 95 mg, 97% yield.
II: Normal addition of DBU: 45 mg, 46% yield.

The reaction was also performed according to **General Procedure III** on the same scale using MTBD (144 µL, 1.0 mmol, 2.0 equiv) instead of DBU to afford **4a (**25 mg, 26% yield).

Characterization data is consistent with that previously reported and is consistent with *N*-1 arylation.[19] GC/MS analysis of the crude reaction mixture showed only one isomer.

ethyl 8-(indolin-1-yl)-5-methyl-6-oxo-5,6-dihydro-4*H*-benzo[*f*]imidazo[1,5-*a*][1,4]diazepine-3-carboxylate (5a)



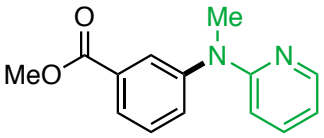
5a was prepared according to **General Procedures I** and **II** using ethyl 5-methyl-6-oxo-8-(((trifluoromethyl)sulfonyl)oxy)-5,6-dihydro-4*H*-benzo[*f*]imidazo[1,5-*a*][1,4]diazepine-3 carboxylate (217 mg, 0.50 mmol), indoline (67 µL, 0.60 mmol, 1.2 equiv), DBU (150 µL, 1.0 mmol, 2.0 equiv), COD(AlPhos-Pd)$_2$ (4.8 mg, 2.5 µmmol, 1.0 mol% Pd), and 2-MeTHF (0.5 mL). The product was purified by automated flash column chromatography (0-4% MeOH in CH_2Cl_2, 100 g silica gel, 20 column volumes) to afford an off-white solid powder that was judged to be >95% pure by ^{1}H NMR spectroscopy. White, crystalline material was obtained via crystallization in $CHCl_3$. **^{1}H NMR** (400 MHz; $CDCl_3$): δ (ppm) 7.85 (s, 1H), 7.78 (d, *J* = 2.8 Hz, 1H), 7.46 (dd, *J* = 8.7, 2.8 Hz, 1H), 7.35 (d, *J* = 8.8 Hz, 1H), 7.22 (m, 2H), 7.11 (m, 2H), 6.82 (t, *J* = 7.3 Hz, 1H), 5.16 (bs, 1H), 4.42 (bs, 3H), 4.02 (bs, 2H), 3.24 (s, 3H), 3.17 (t, *J* = 8.3 Hz, 2H), 1.44 (t, *J* = 7.1 Hz, 4H). **^{13}C NMR** (101 MHz; $CDCl_3$): δ (ppm) 166.9, 163.5, 145.6, 144.7, 135.7, 135.0, 131.9, 130.31, 128.6, 127.5, 125. 124.5, 123.1, 120.6, 120.4, 119.5, 109.1, 61.2, 52.2, 42.8, 36.1, 28.3, 14.7. **M.P.:** 257.3-259.1 °C. **IR** (neat): 2925.4, 2358.6, 1725.5, 1489.5, 1375.0, 1216.8, 1063.3. **HRMS** (DART) m/z calcd. for $C_{23}H_{22}N_4O_3$ ($[M+H]^+$): 403.1770. Found: 403.1756.

I: Slow addition of DBU: 1st run: 143 mg, 71% yield; 2nd run: 136 mg, 68% yield.

II: Normal addition of DBU: 12% ^{1}H NMR yield (hexamethylbenzene internal standard). Note: product could not be isolated due to incomplete conversion of the aryl triflate and co-elution of the product and starting material during the purification.

The reaction was also performed according to **General Procedure III** on the same scale using MTBD (144 µL, 1.0 mmol, 2.0 equiv) instead of DBU to afford **5a (**133 mg, 66% yield.).

methyl 3-(methyl(pyridin-2-yl)amino)benzoate (6a)

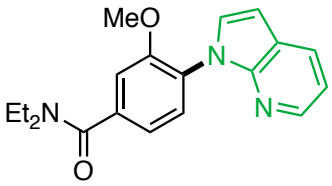


6a was prepared according to **General Procedures I** and **II** using methyl 3-(((trifluoromethyl)sulfonyl)oxy)benzoate (142 mg, 0.50 mmol), 2-(Methylamino)pyridine (62 µL, 0.60 mmol, 1.2 equiv), DBU (150 µL, 1.0 mmol, 2.0 equiv), COD(AlPhos-Pd)$_2$ (4.8 mg, 2.5 µmmol, 1.0 mol% Pd), and 2-MeTHF (0.5 mL). The product was purified by automated flash column chromatography (0-20% EtOAc in hexanes, 50 g silica gel, 14 column volumes) to afford a colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) 8.23 (d, *J* = 4.4 Hz, 1H), 7.93 (s, 1H), 7.84 (d, *J* = 6.7 Hz, 1H), 7.49 – 7.39 (m, 2H), 7.37 – 7.30 (m, 1H), 6.68 – 6.60 (m, 1H), 6.56 (d, *J* = 8.6 Hz, 1H), 3.89 (s, 3H), 3.48 (s, 3H). **^{13}C NMR** (101 MHz; $CDCl_3$): δ (ppm) 167.0, 158.9, 148.3, 147.5, 137.2, 132.1, 130.8, 130.0, 127.2, 126.5, 114.2, 109.7, 52.6, 38.7. **IR** (neat): 3001.7, 2951.1, 2357.2, 1719.9, 1435.9, 1237.0, 758.7. **HRMS** (DART) m/z calcd. for $C_{14}H_{14}N_2O_2$ ($[M+H]^+$): 243.1134. Found: 243.1126.

Slow addition of DBU: 1st run: 85 mg, 70% yield; 2nd run: 82 mg, 68% yield.
Normal addition of DBU: 13 mg, 11% yield.

The reaction was also performed according to **General Procedure III** on the same scale using MTBD (144 µL, 1.0 mmol, 2.0 equiv) instead of DBU to afford **6a** (76 mg, 63% yield).

***N*,*N*-diethyl-3-methoxy-4-(1*H*-pyrrolo[2,3-*b*]pyridin-1-yl)benzamide (7a)**

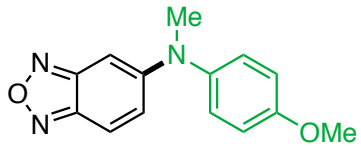


7a was prepared according to **General Procedures I** and **II** using 4-(diethylcarbamoyl)-2-methoxyphenyl trifluoromethanesulfonate (178 mg, 0.50 mmol), 7-azaindole (70.9 mg, 0.60 mmol, 1.2 equiv), DBU (150 µL, 1.0 mmol, 2.0 equiv), COD(AlPhos-Pd)$_2$ (4.8 mg, 2.5 µmmol, 1.0 mol% Pd), and 2-MeTHF (0.5 mL). The product was purified by automated flash column chromatography (30-75% EtOAc in hexanes, 50 g silica gel, 16 column volumes) to afford an opaque, white oil. **^{1}H NMR** (400 MHz; $CDCl_3$): δ 8.30 (d, *J* = 4.7 Hz, 1H), 7.92 (d, J = 7.7 Hz, 1H), 7.59 (d, *J* = 7.9 Hz, 1H), 7.38 (d, *J* = 3.6 Hz, 1H), 7.38 (m, 3H), 6.57 (d, *J* = 3.7 Hz, 1H), 3.77 (s, 3H), 3.46 (overlapping bs, 4H), 1.20 (m, 6H) (ppm) **^{13}C NMR** (101 MHz; $CDCl_3$): δ 170.6, 154.4, 148.2, 143.5, 137.6, 130.3, 129.1, 128.5, 127.7, 121.0, 118.7, 116.6, 111.2, 100.9, 56.1, 43.5, 39.5, 14.6, 13.1 (ppm) **IR** (neat): 2970.5, 2934.0, 1622.8, 1423.5, 1252.4, 1030.5, 722.1. **Elemental Analysis:** Calculated for $C_{19}H_{21}N_3O_2$: C: 70.57; H: 6.55. Found: C: 70.20; H: 6.72.

I: Slow addition of DBU: 1st run: 146 mg, 90%, 2nd run: 155 mg, 96% yield.
II: Normal addition of DBU: 147 mg, 91% yield.

The reaction was also performed according to **General Procedure III** on the same scale using MTBD (144 µL, 1.0 mmol, 2.0 equiv) instead of DBU to afford **7a (**140 mg, 87% yield).

***N*-(4-methoxyphenyl)-*N*-methylbenzo[*c*][1,2,5]oxadiazol-5-amine (8a)**

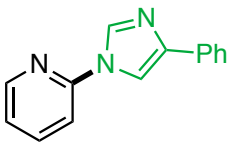


8a was prepared according to **General Procedures I** and **II** using benzo[*c*][1,2,5]oxadiazol-5-yl trifluoromethanesulfonate (134 mg, 0.50 mmol), 4-methoxy-*N*-methylaniline (82 mg, 0.60 mmol, 1.2 equiv), DBU (150 µL, 1.0 mmol, 2.0 equiv), COD(AlPhos-Pd)$_2$ (4.8 mg, 2.5 µmmol, 1.0 mol% Pd), and 2-MeTHF (0.5 mL). The product was purified by automated flash column chromatography (0-30% EtOAc in hexanes, 100 g silica gel, 16 column volumes) to afford an orange-red oil. **^{1}H NMR** (400 MHz; $CDCl_3$): δ (ppm) 7.44 (d, *J* = 9.9 Hz, 1H), 7.14 – 7.07 (m, 2H), 6.97 – 6.89 (m, 3H), 6.60 (d, *J* = 2.2 Hz, 1H), 3.83 (s, 3H), 3.32 (s, 3H). **^{13}C NMR** (101 MHz; $CDCl_3$): δ (ppm) ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.4, 151.1, 150.4, 146.9, 140.1, 128.7, 128.3, 116.0, 115.5, 88.6, 55.9, 41.7. **IR** (neat): 2931.9, 2835.9, 2360.0, 1739.2, 1485.7, 1003.7, 803.5. **HRMS** (DART) m/z calcd. for $C_{14}H_{13}N_3O_2$ ($[M+H]^+$): 256.1086. Found: 256.1090.

I: Slow addition of DBU: 1st run: 54 mg, 42% yield; 2nd run: 47 mg, 46% yield (reaction performed on 0.40 mmol scale due to limited material).
II: Normal addition of DBU: 4% NMR yield (hexamethylbenzene internal standard).

The reaction was also performed according to **General Procedure III** on the same scale using MTBD (144 µL, 1.0 mmol, 2.0 equiv) instead of DBU to afford **8a** (20 mg, 16% yield).

2-(4-phenyl-1H-imidazol-1-yl)pyridine (9a)

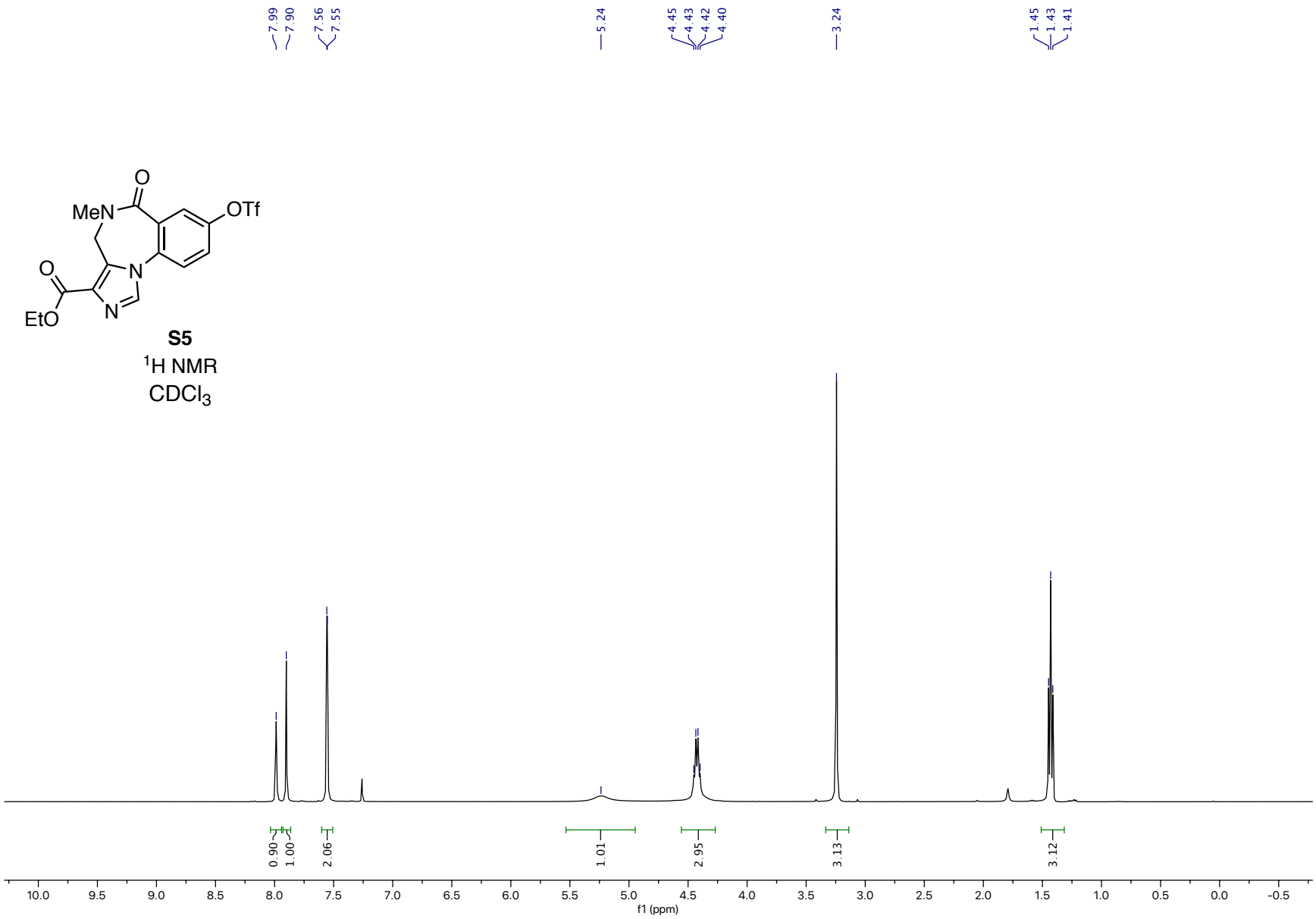


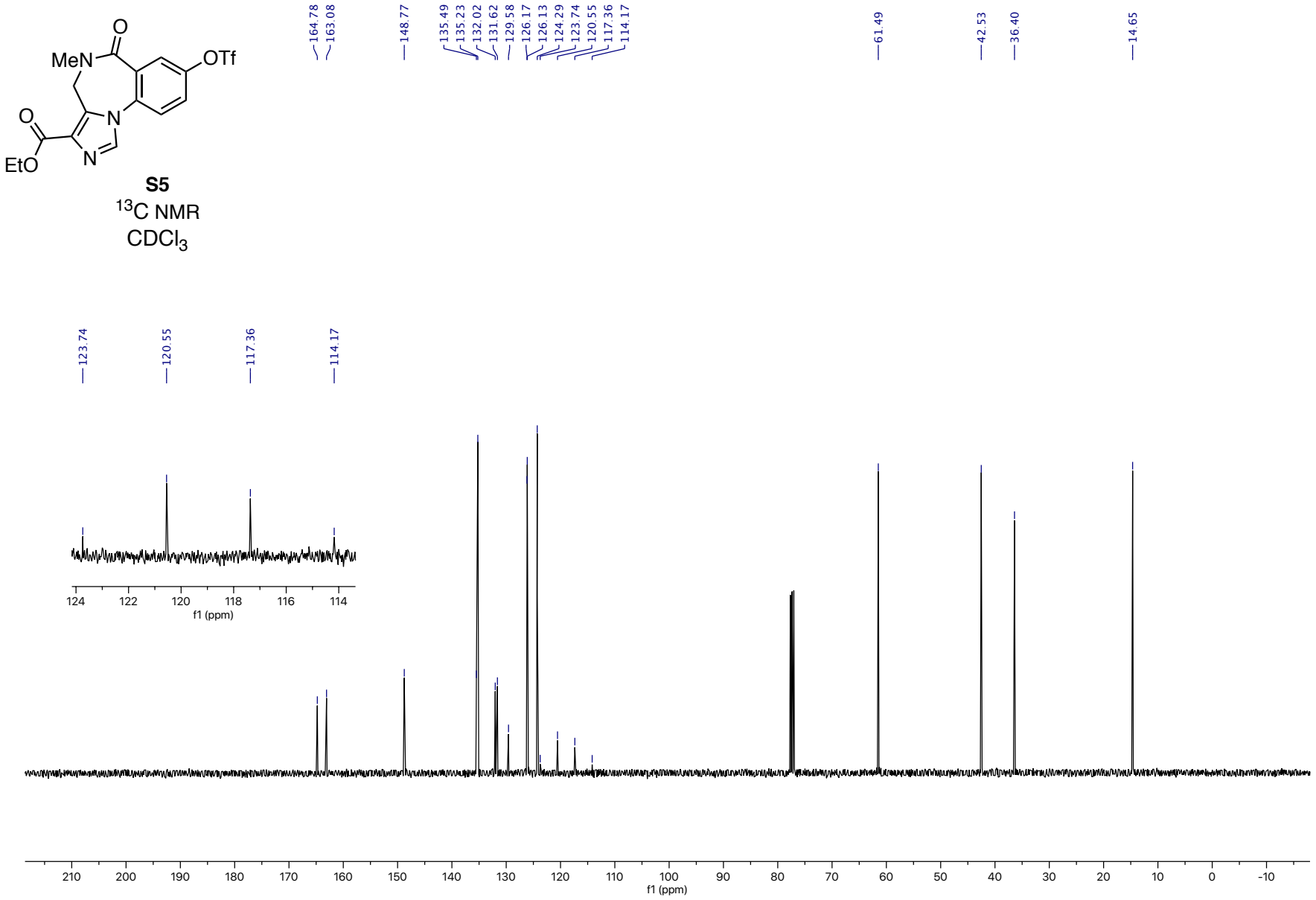
9a was prepared according to **General Procedures I** and **II** using 2-pyridyl trifluoromethanesulfonate (76.9 μL, 0.50 mmol), 4-phenyl-1*H*-imidazole (86.5 mg, 0.60 mmol, 1.2 equiv), DBU (150 μL, 1.0 mmol, 2.0 equiv), COD(AlPhos-Pd)$_2$ (9.6 mg, 5.0 μmmol, 2.0 mol% Pd), and 2-MeTHF (0.5 mL). The product was purified by automated flash column chromatography (20-70% EtOAc in hexanes, 50 g silica gel, 14 column volumes) to afford a white solid. **^{1}H NMR** (400 MHz; $CDCl_3$): δ (ppm) 8.33 (d, *J* = 3.2 Hz, 1H), 8.26 (s, 1H), 7.80 (s, 1H), 7.75 (d, *J* = 7.1 Hz), 7.63 (td, *J* = 7.8, 1.9 Hz, 1H), 7.29 (t, *J* = 7.6 Hz, 2H), 7.19 (m, 2H), 7.07 (dd, *J* = 7.4, 4.9 Hz, 1H). **^{13}C NMR** (101 MHz; $CDCl_3$): δ (ppm) 149.3, 149.0, 143.5, 139.2, 135.2, 133.8, 128.8, 127.4, 125.2, 122.2, 112.3, 111.6 **M.P.:** 135.6-137.8 °C. **IR** (neat): 2931.9, 2835.9, 2360.0, 1739.2, 1485.7, 1003.7, 803.5.

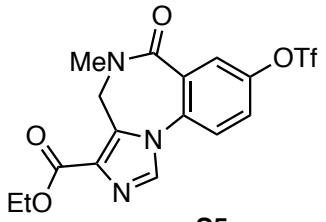
Characterization data is consistent with that previously reported.[20] We note that we saw concentration and shift dependence on whether new or old $CDCl_3$ was used (attributed to acidity) that resulted in shifting of the peaks.

I: Slow addition of DBU (2% Pd): 1st run: 90 mg, 81% yield; 2nd run: 84 mg, 76% yield.
I: Slow addition of DBU (1% Pd): 48 mg, 43% yield.
II: Normal addition of DBU: 35 mg, 32% yield.

The reaction was also performed according to **General Procedure III** on the same scale using MTBD (144 μL, 1.0 mmol, 2.0 equiv) instead of DBU to afford **9a (**24 mg, 22% yield).


7.99
7.90
7.56
7.55
5.24
4.45
4.43
4.42
4.40
3.24
1.45
1.43
1.41
MeN
O
OTf
O
N
EtO
N
S5
1H NMR
CDCl3
0.90
1.00
2.06
1.01
2.95
3.13
3.12
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

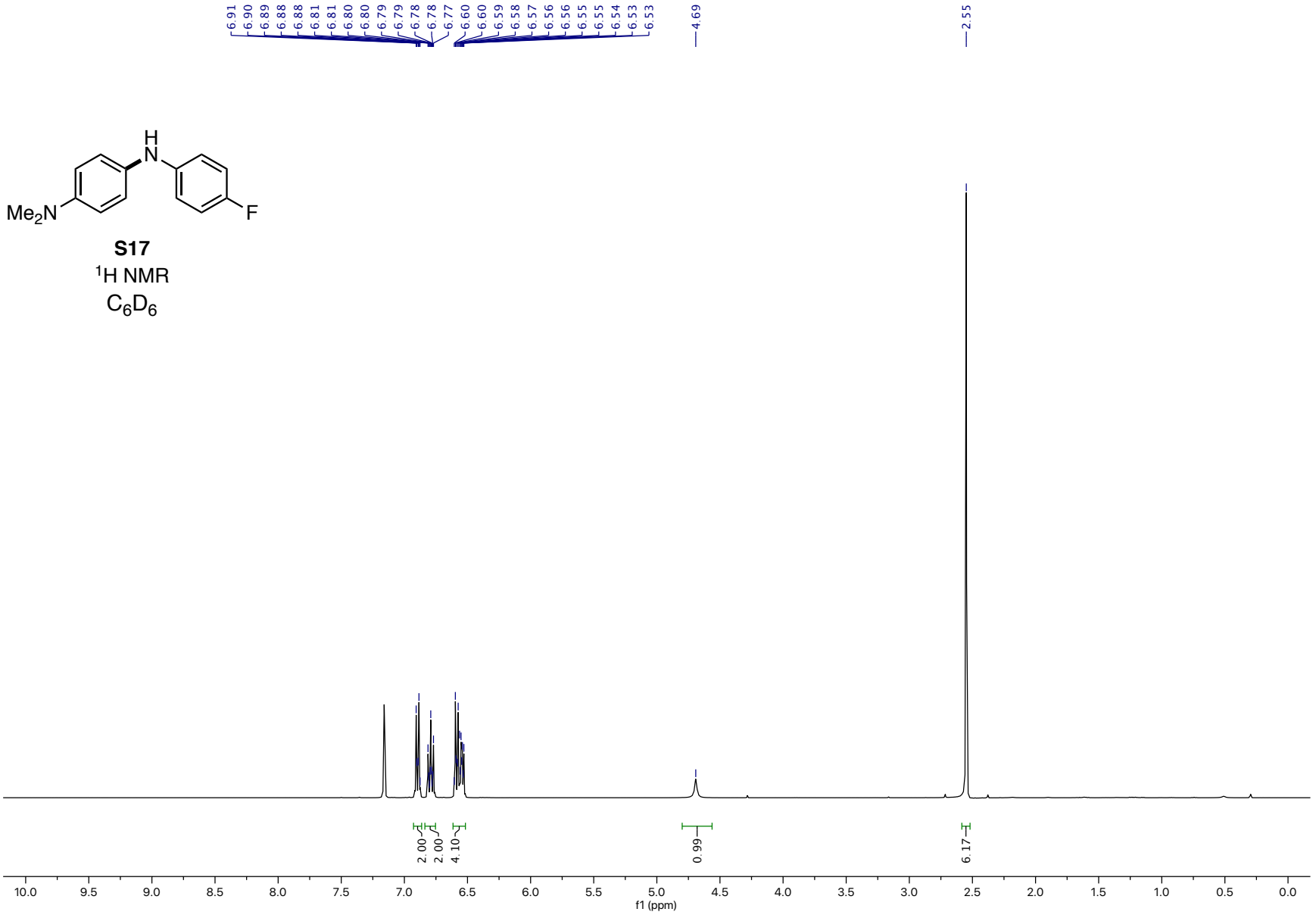

MeN
OTf
O
O
EtO
N
N
S5
13C NMR
CDCl3
164.78
163.08
148.77
135.49
135.23
132.02
131.62
129.58
126.17
126.13
124.29
123.74
120.55
117.36
114.17
61.49
42.53
36.40
14.65
f1 (ppm)
f1 (ppm)

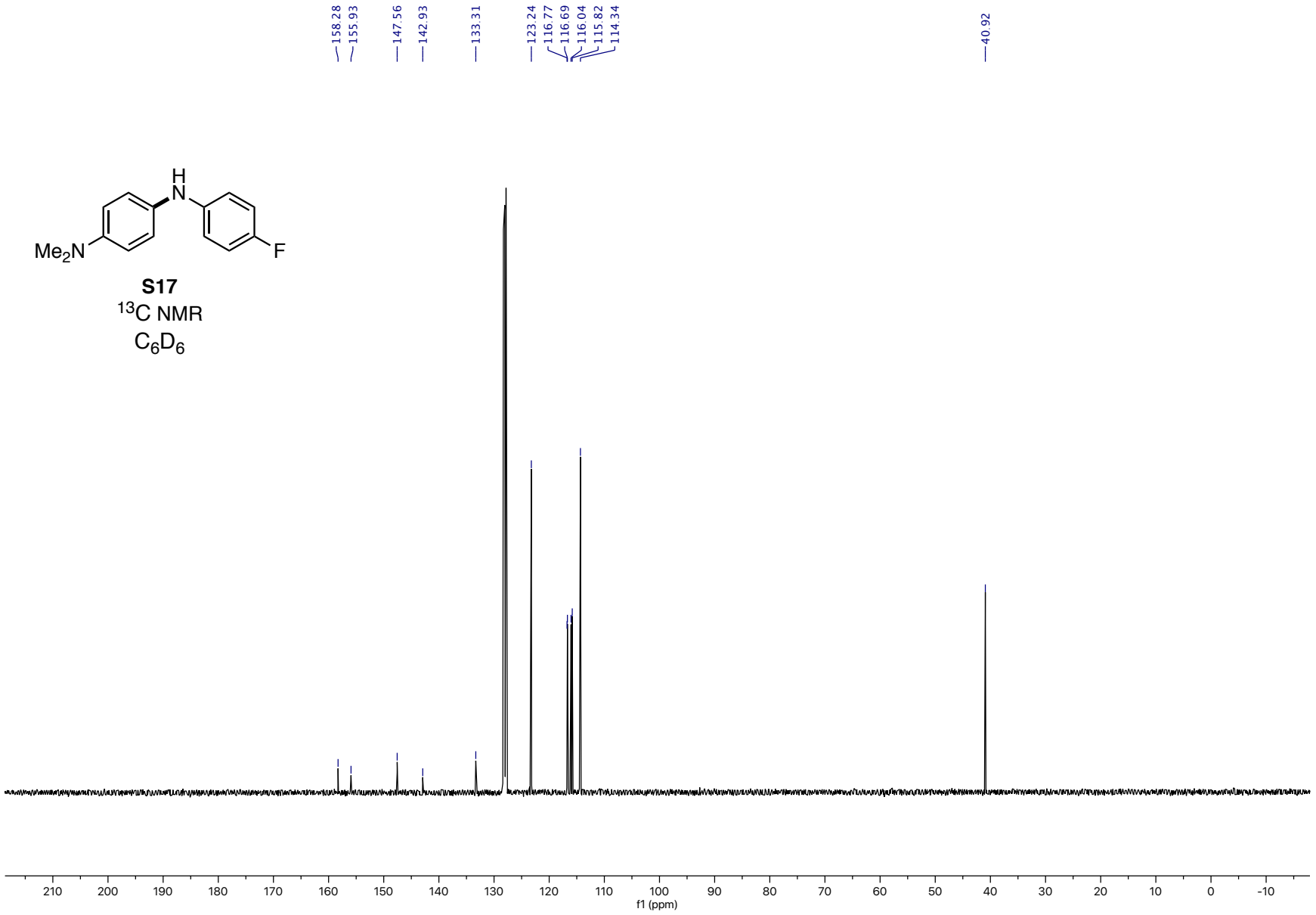


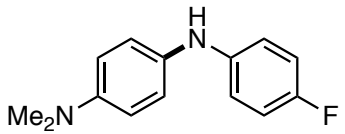
S5

^{19}F NMR

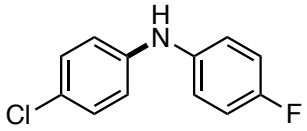
$CDCl_3$


6.91
6.90
6.89
6.88
6.88
6.81
6.81
6.80
6.80
6.79
6.79
6.78
6.78
6.77
6.60
6.60
6.59
6.58
6.57
6.56
6.56
6.55
6.55
6.54
6.53
6.53
4.69
2.55
H
N
Me2N
F
S17
1H NMR
C6D6
2.00
2.00
4.10
0.99
6.17
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


158.28
155.93
147.56
142.93
133.31
123.24
116.77
116.69
116.04
115.82
114.34
40.92
H
N
Me2N
F
S17
13C NMR
C6D6
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)



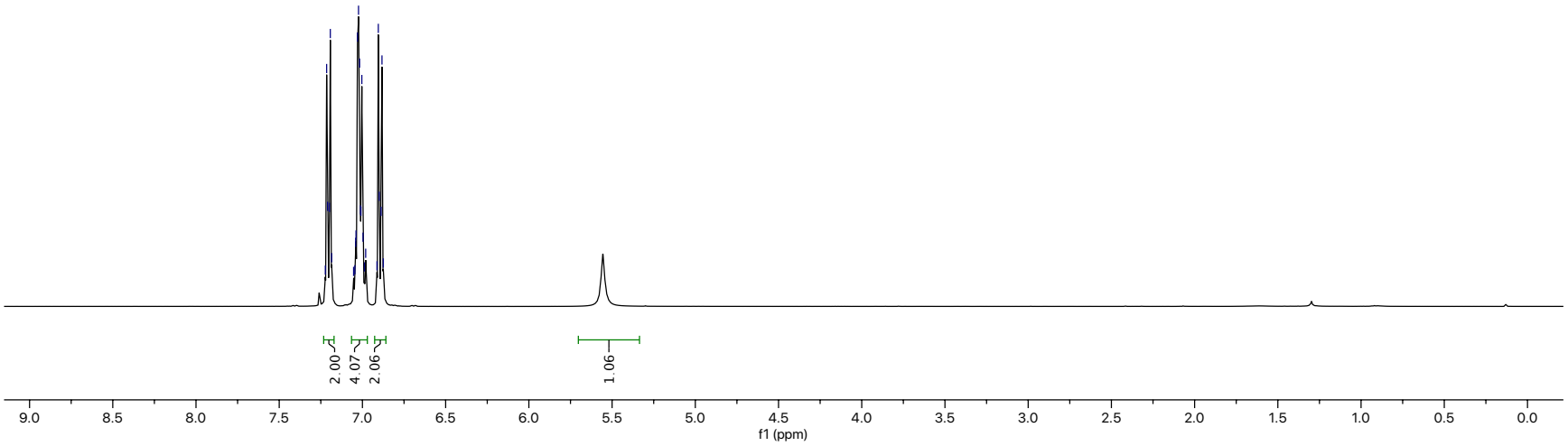
S17
^{19}F NMR
C_6D_6

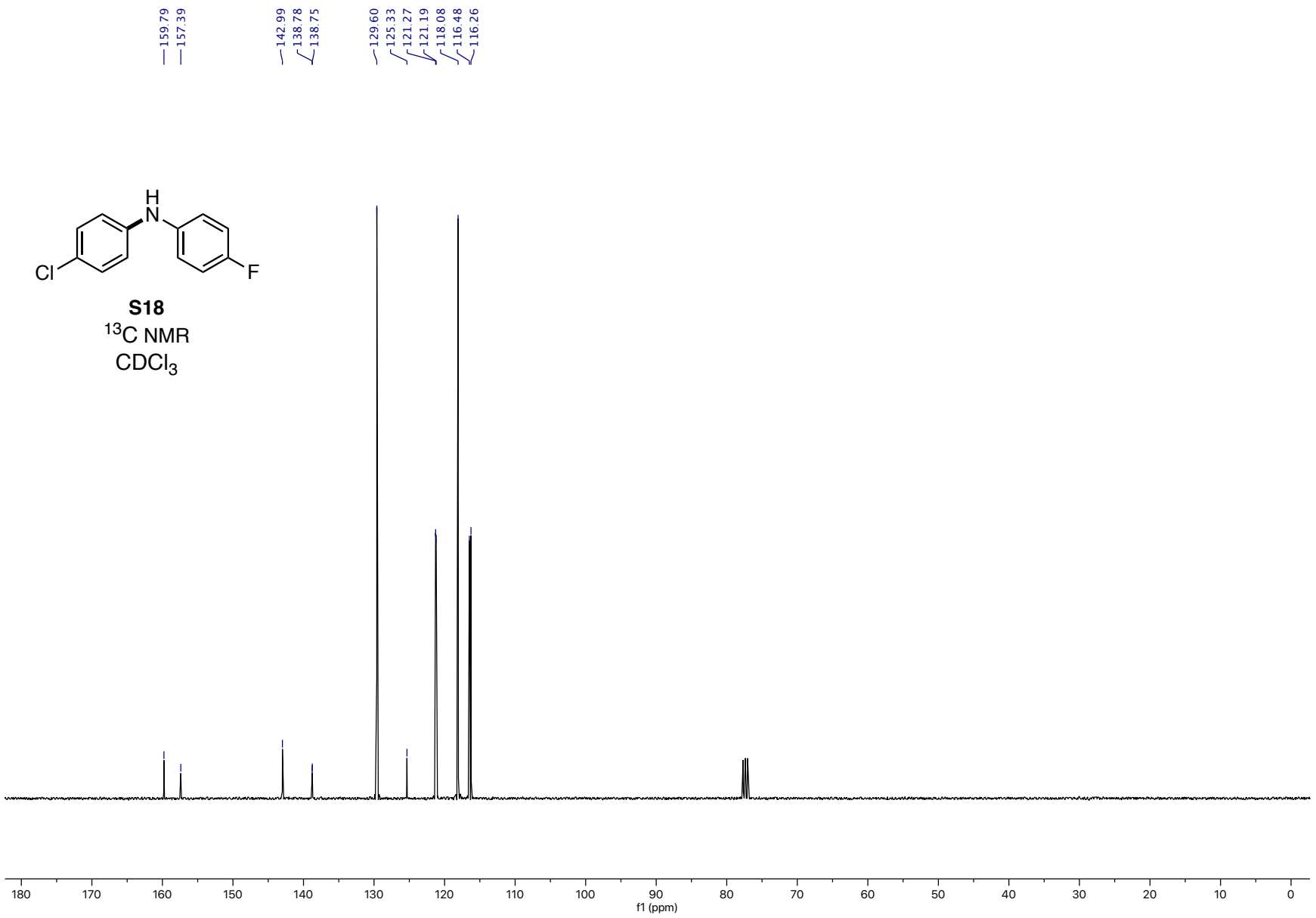


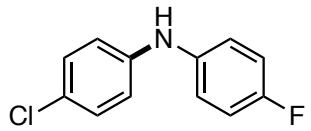
S18

^{1}H NMR

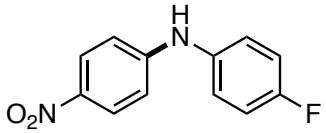
$CDCl_3$




159.79
157.39
142.99
138.78
138.75
129.60
125.33
121.27
121.19
118.08
116.48
116.26
H
N
Cl
F
S18
13C NMR
CDCl3
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



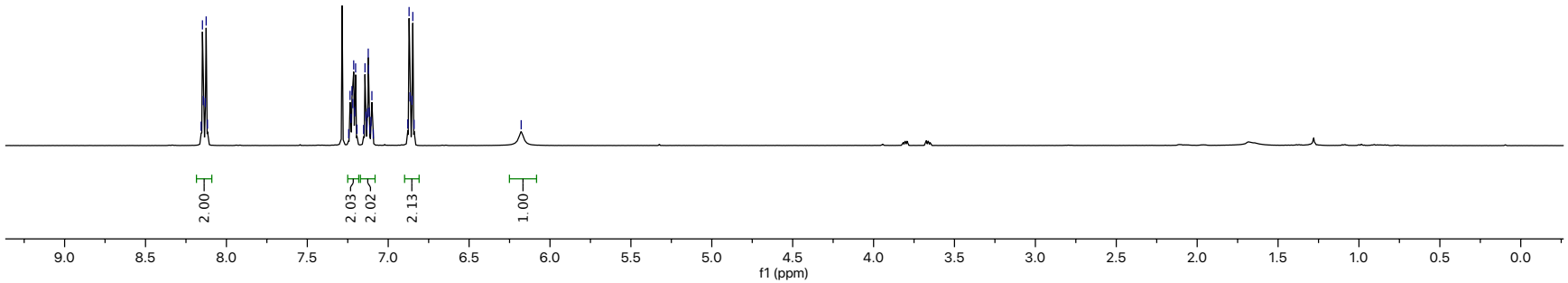
S18
^{19}F NMR
$CDCl_3$

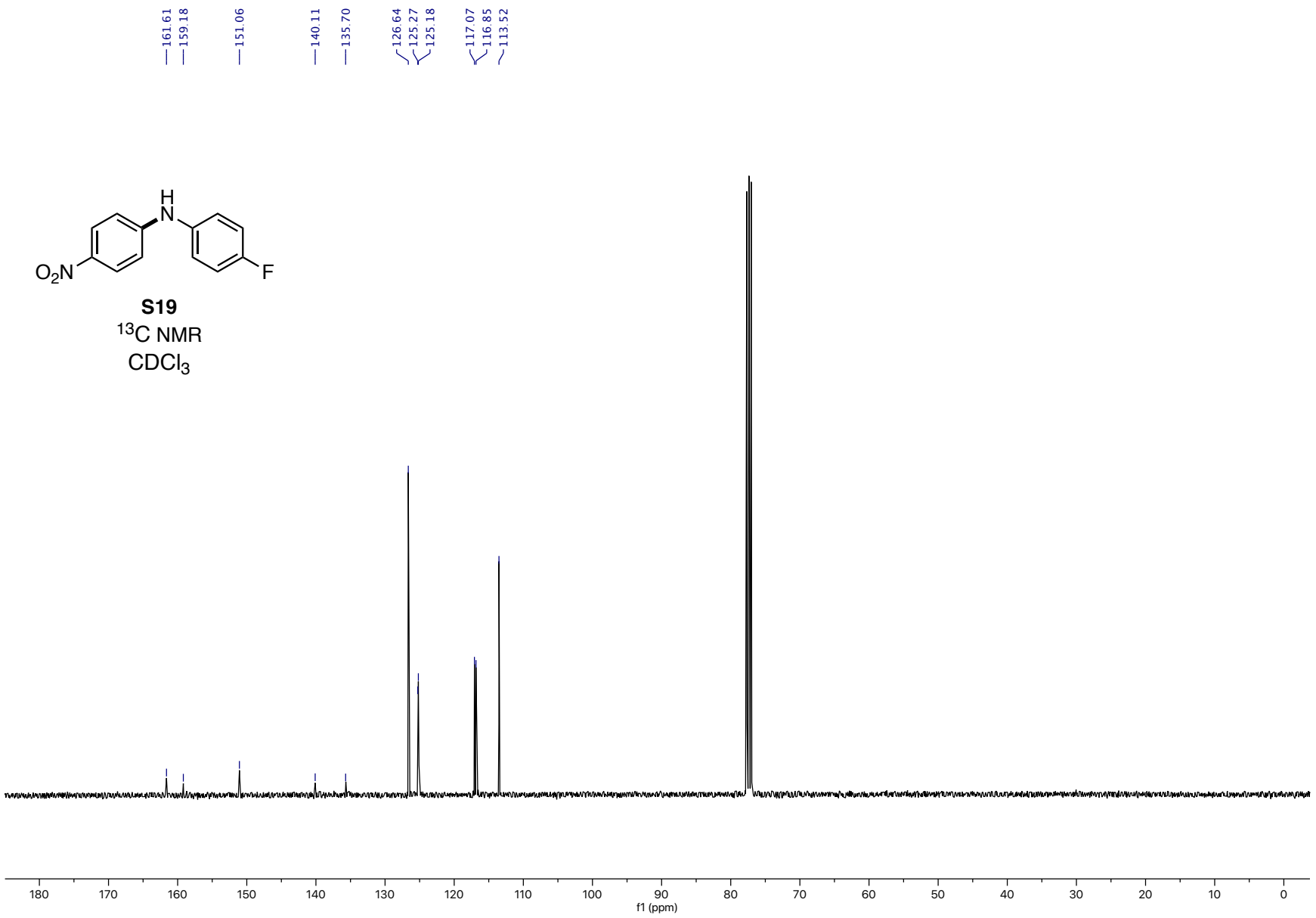


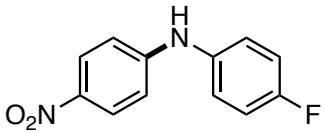
S19

^{1}H NMR

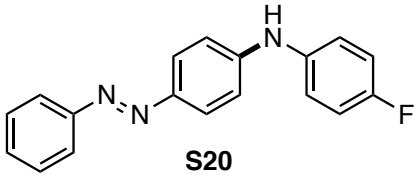
$CDCl_3$




161.61
159.18
151.06
140.11
135.70
126.64
125.27
125.18
117.07
116.85
113.52
H
N
O2N
F
S19
13C NMR
CDCl3
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



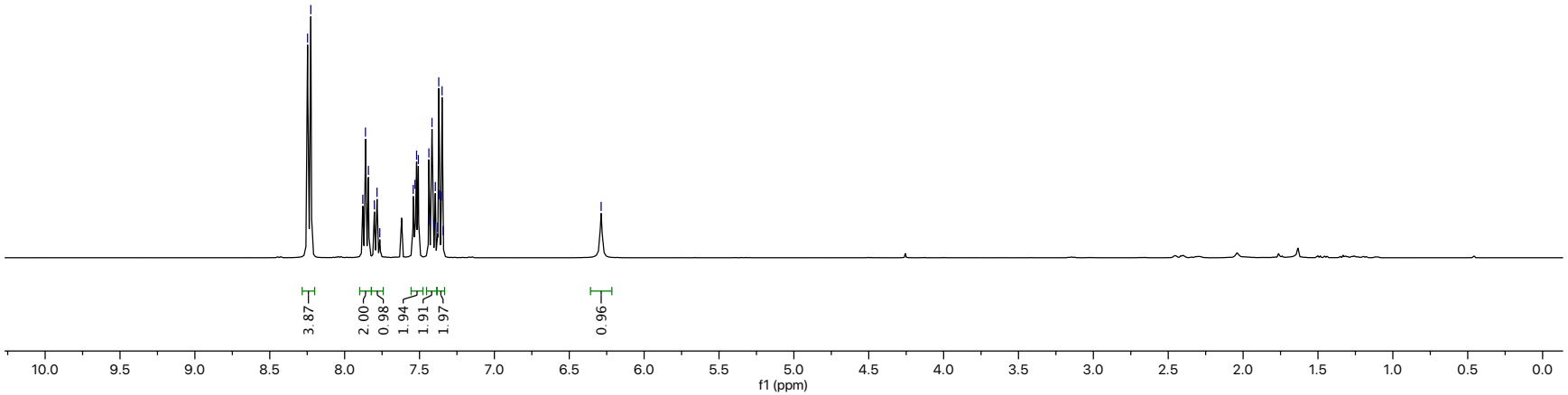
S19
^{19}F NMR
$CDCl_3$

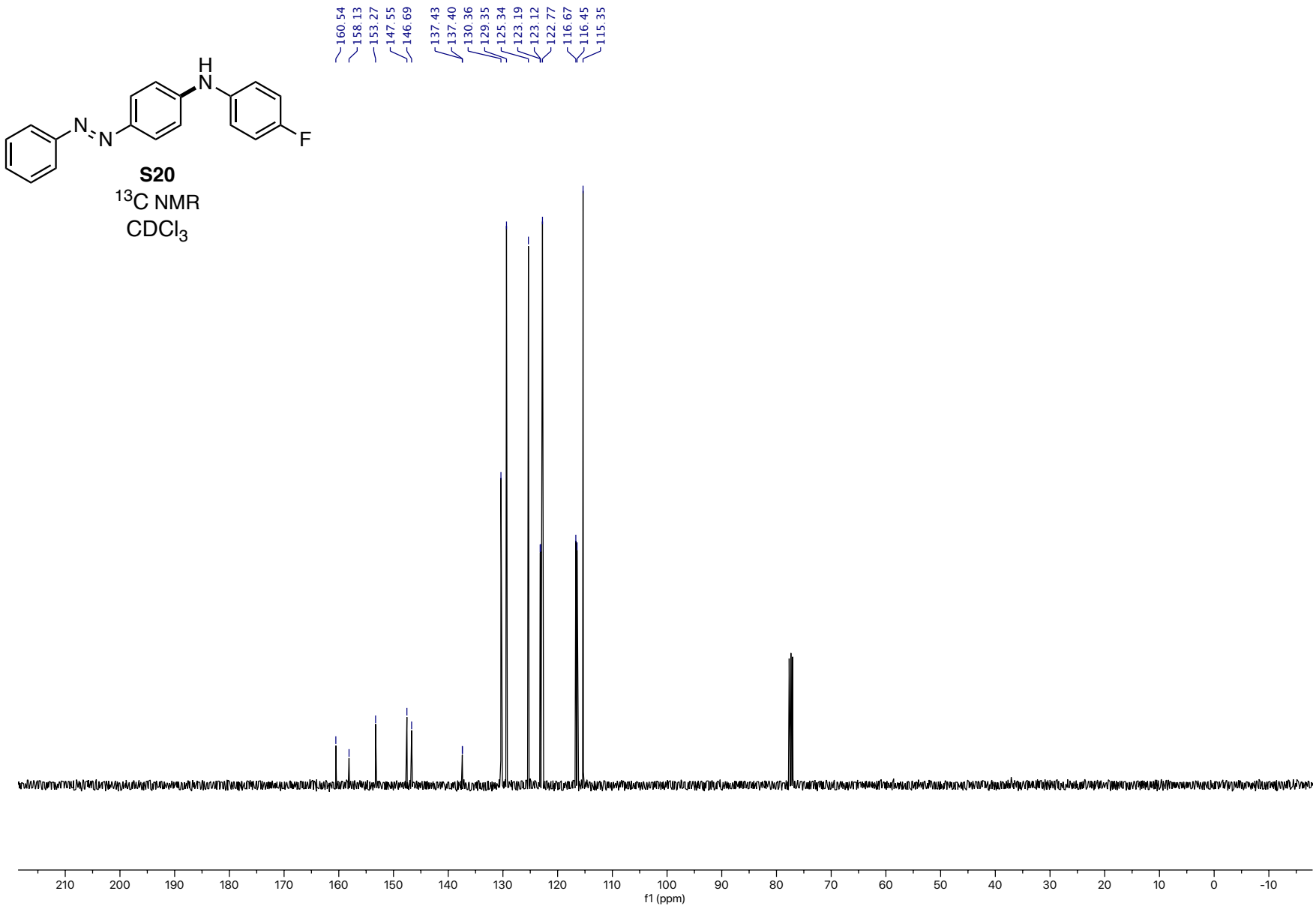


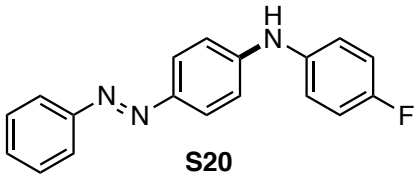
S20

^{1}H NMR

$CDCl_3$



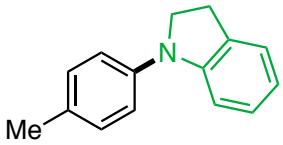

160.54
158.13
153.27
147.55
146.69
137.43
137.40
130.36
129.35
125.34
123.19
123.12
122.77
116.67
116.45
115.35
H
N
N
N
F
S20
13C NMR
CDCl3
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)



S20

^{19}F NMR

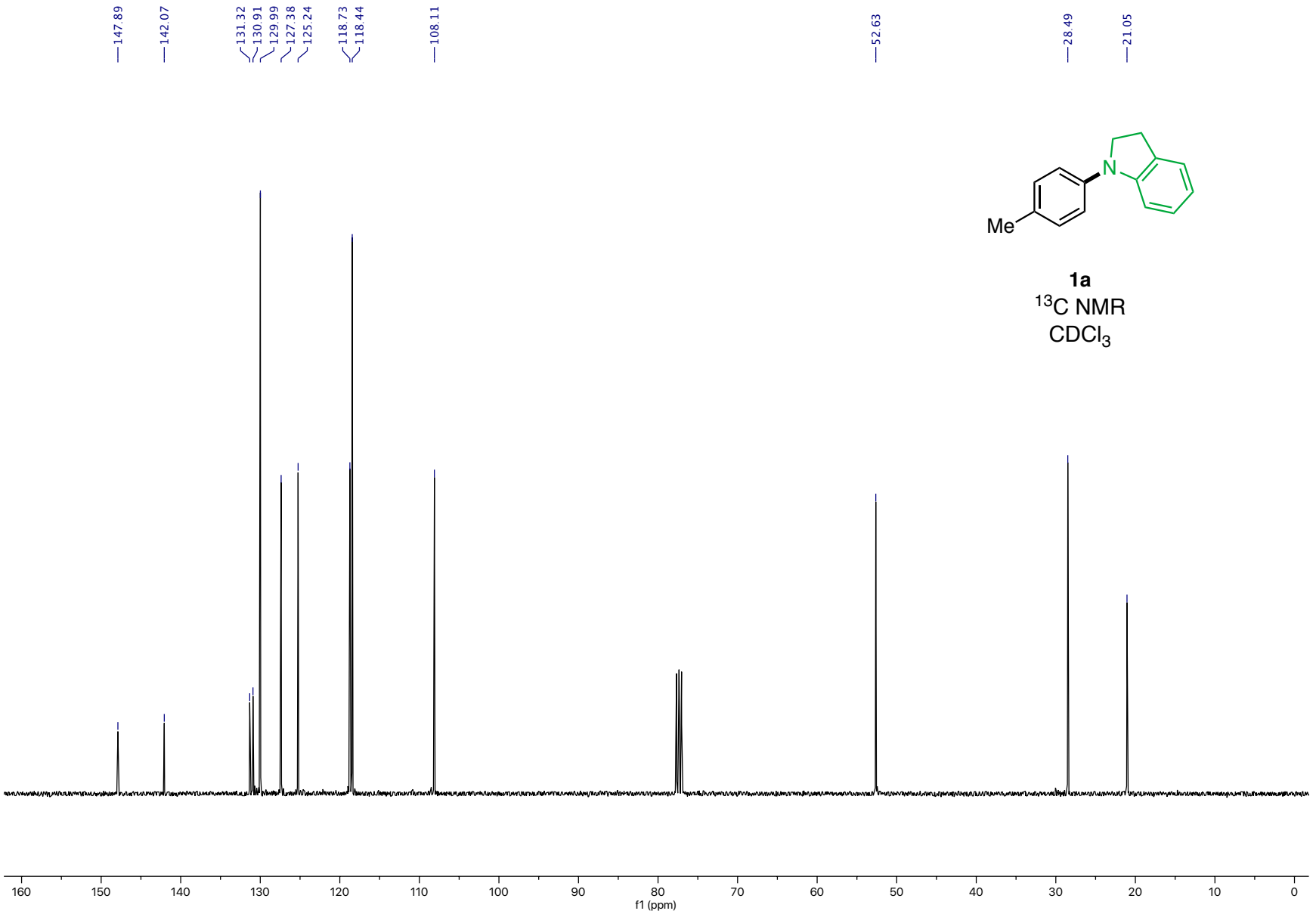
$CDCl_3$



1a

^{1}H NMR

$CDCl_3$


147.89
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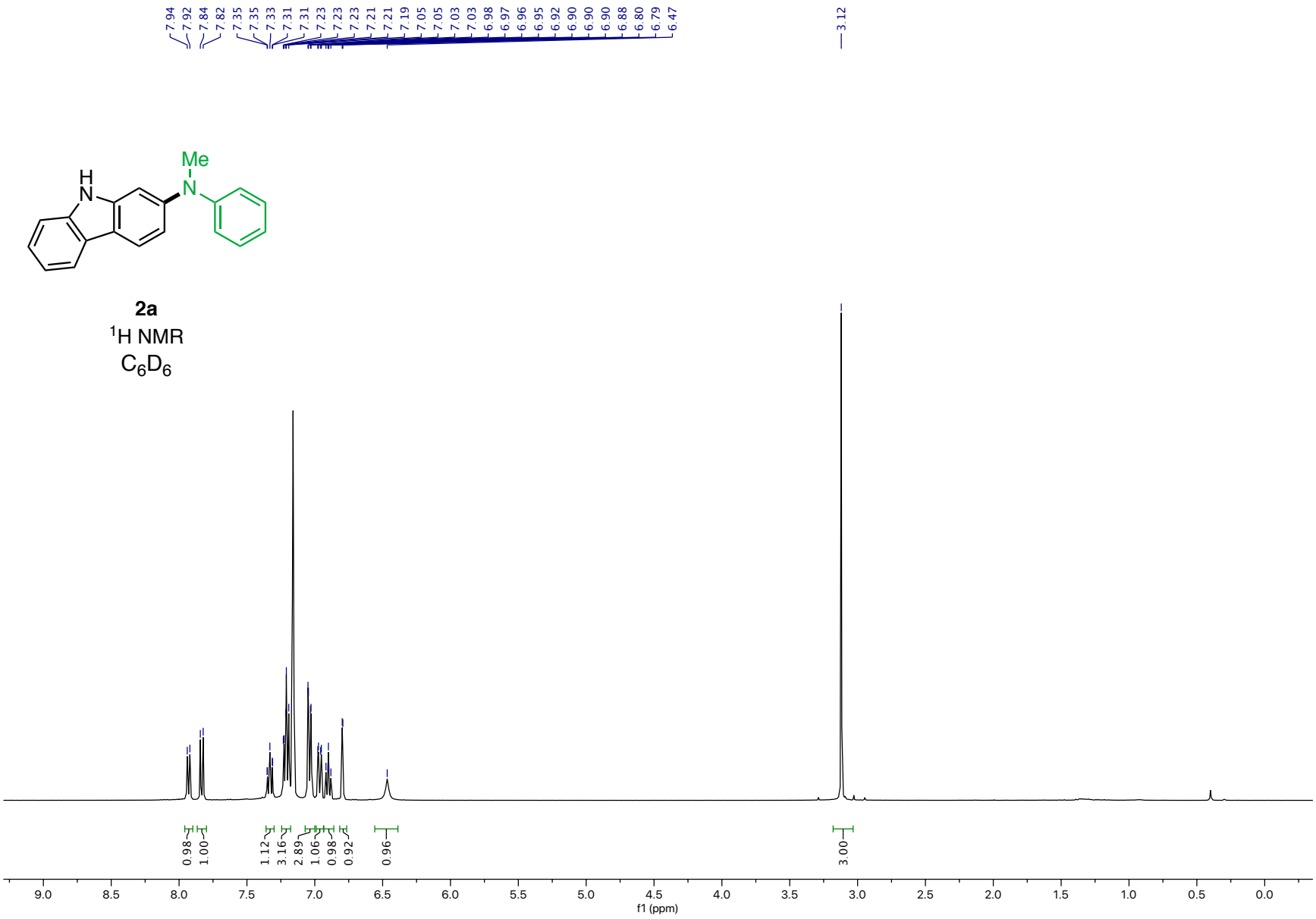
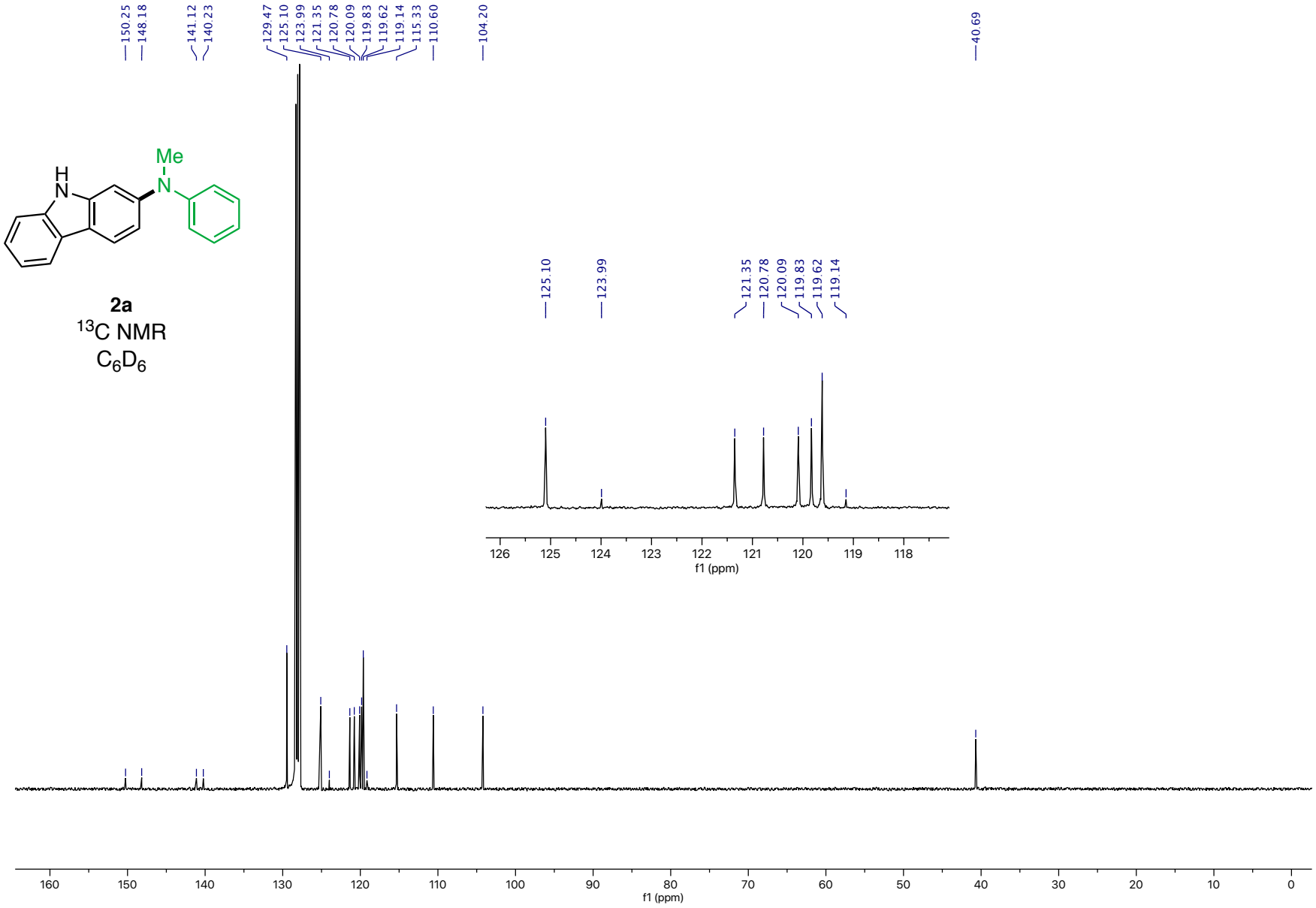
129.99
127.38
125.24
118.73
118.44
108.11
52.63
28.49
21.05
Me
N
1a
13C NMR
CDCl3
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.94
7.92
7.84
7.82
7.35
7.35
7.33
7.31
7.31
7.23
7.23
7.23
7.21
7.21
7.19
7.05
7.05
7.03
7.03
6.98
6.97
6.96
6.95
6.92
6.90
6.90
6.90
6.88
6.80
6.79
6.47
3.12
Me
N
H
N
2a
1H NMR
C6D6
0.98
1.00
1.12
3.16
2.89
1.06
0.98
0.92
0.96
3.00
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


150.25
148.18
141.12
140.23
129.47
125.10
123.99
121.35
120.78
120.09
119.83
119.62
119.14
115.33
110.60
104.20
40.69
Me
N
H
N
2a
13C NMR
C6D6
125.10
123.99
121.35
120.78
120.09
119.83
119.62
119.14
126
125
124
123
122
121
120
119
118
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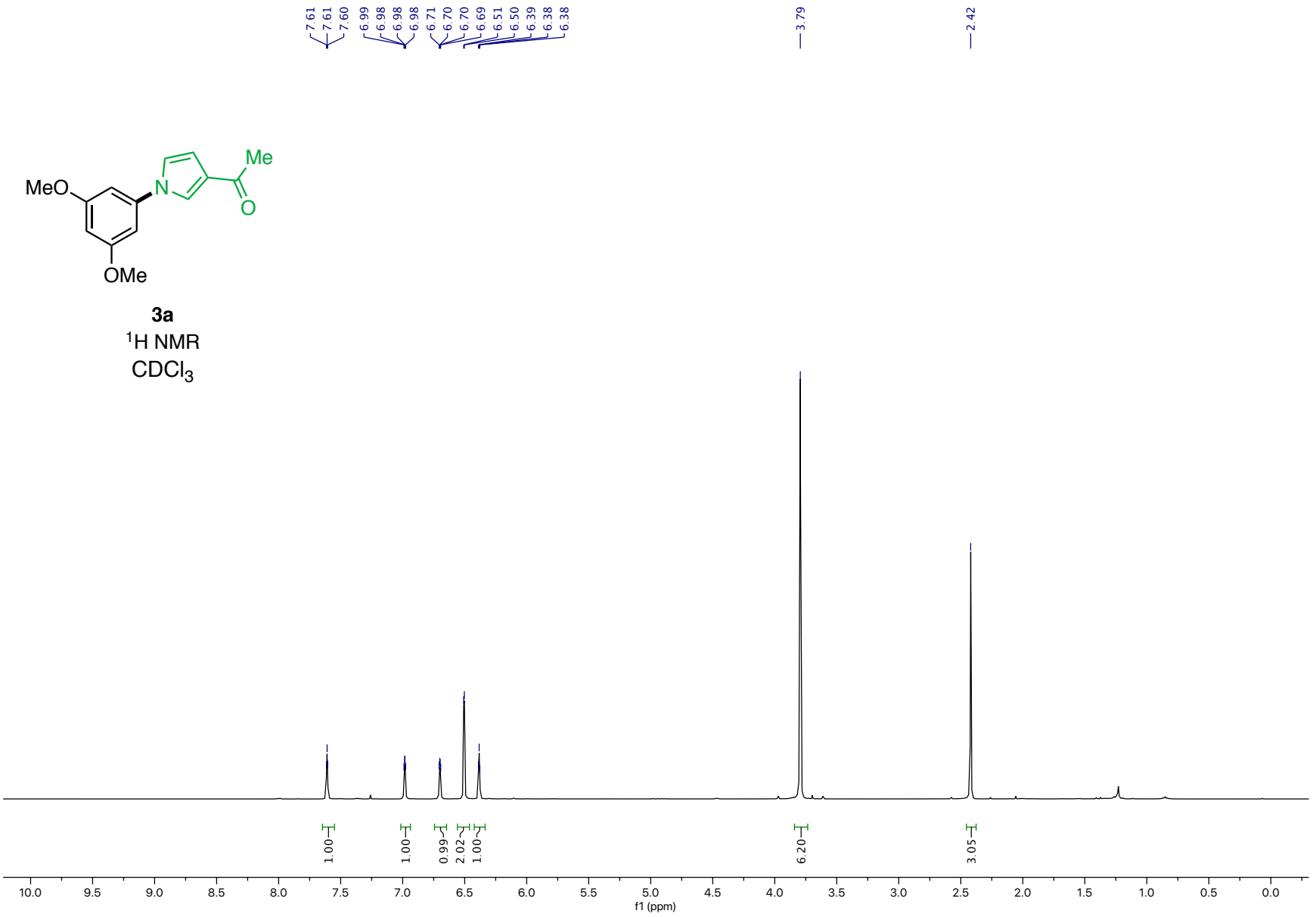
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1H NMR
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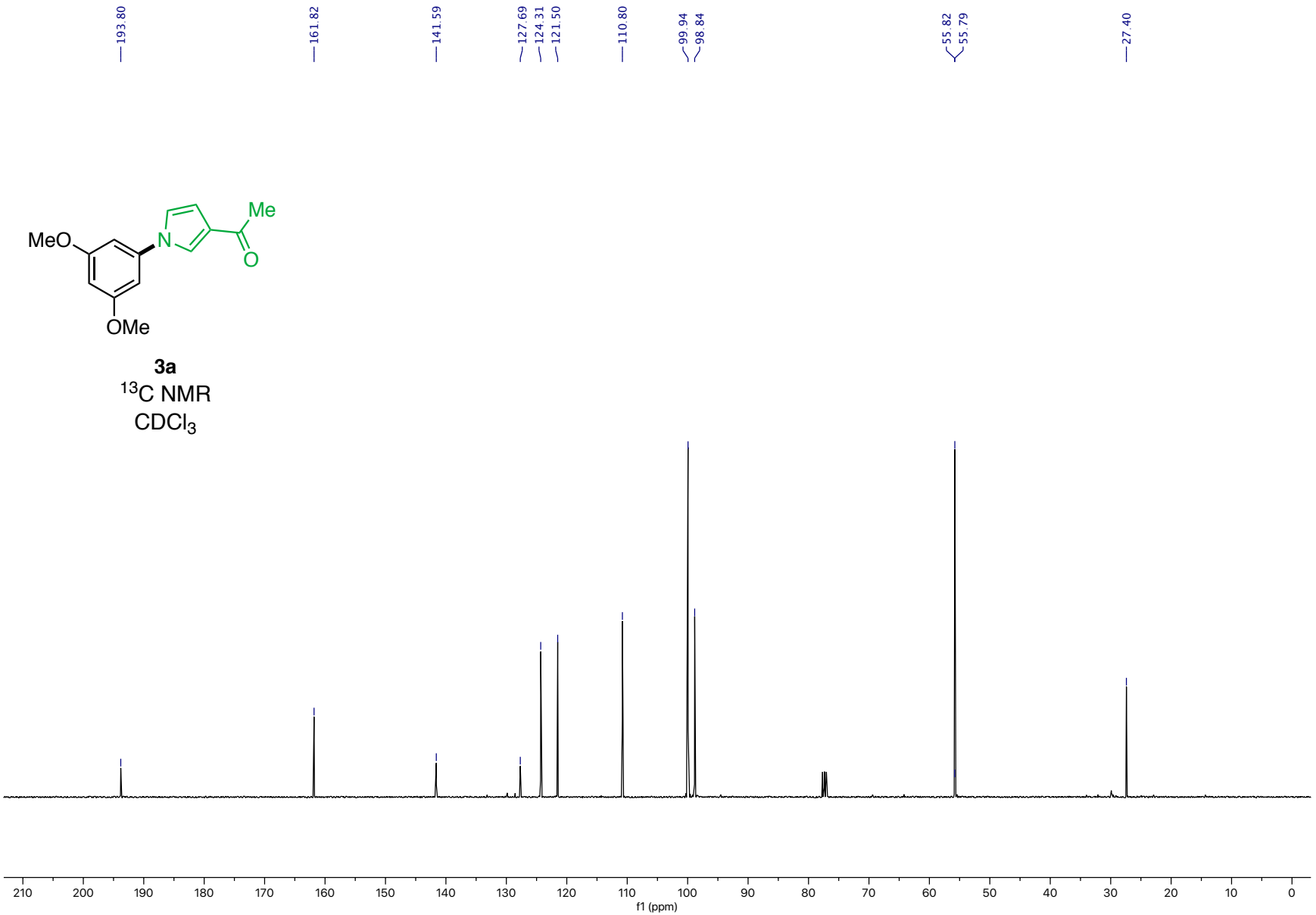
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OMe
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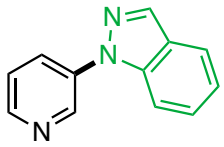

4a
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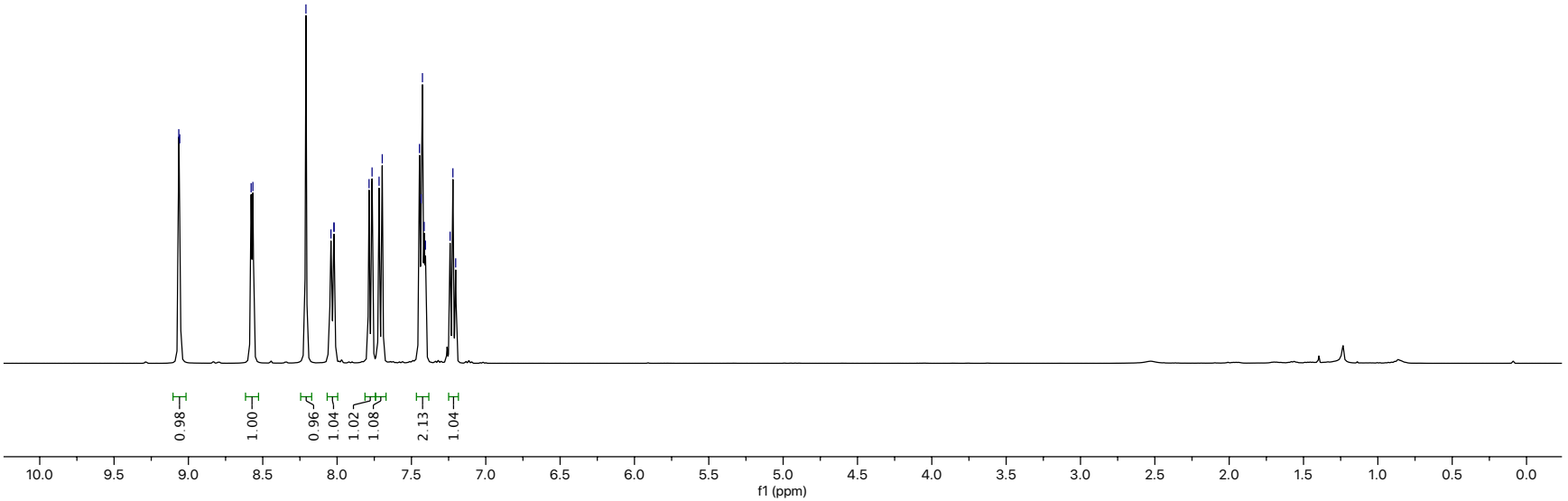

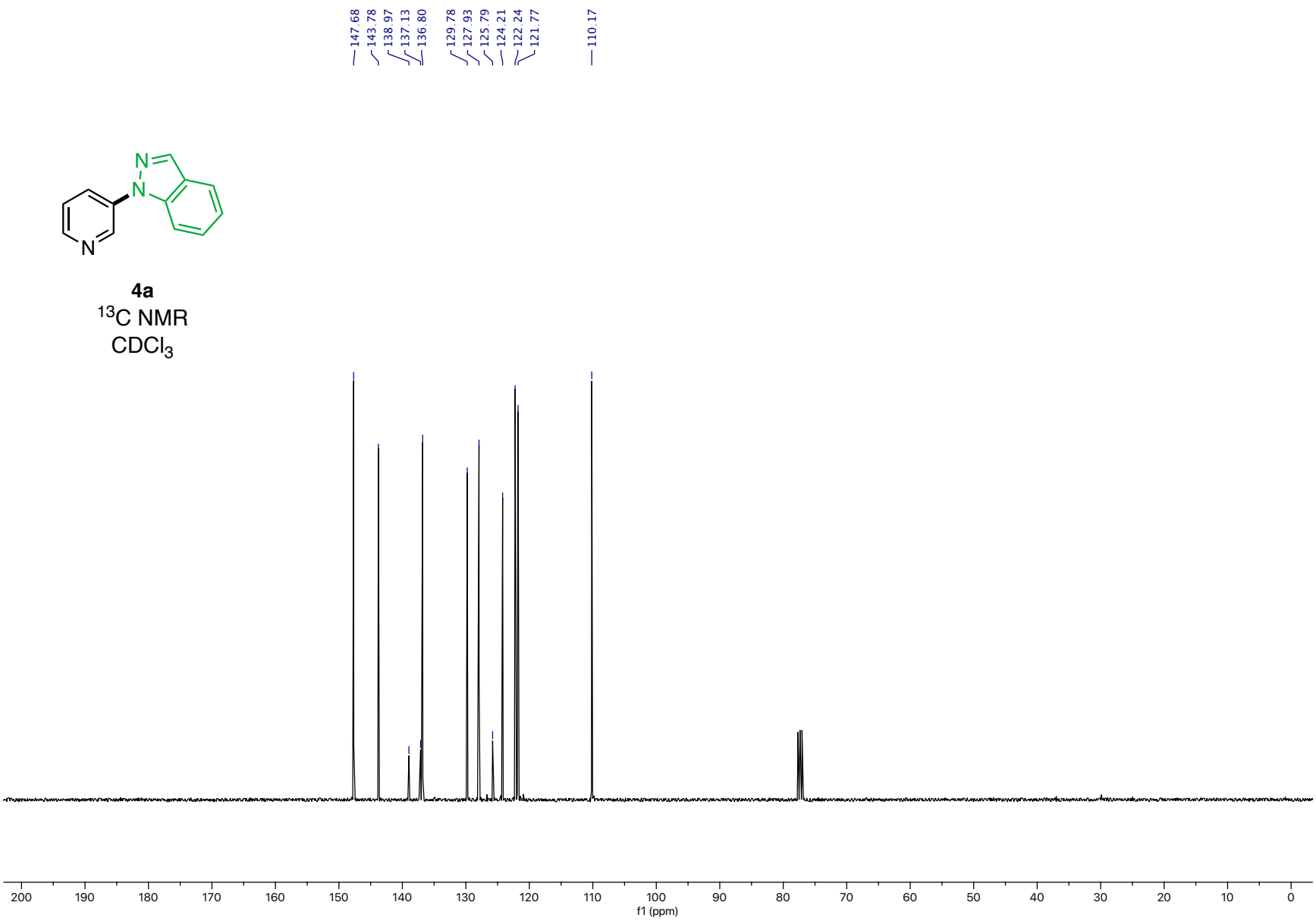
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N
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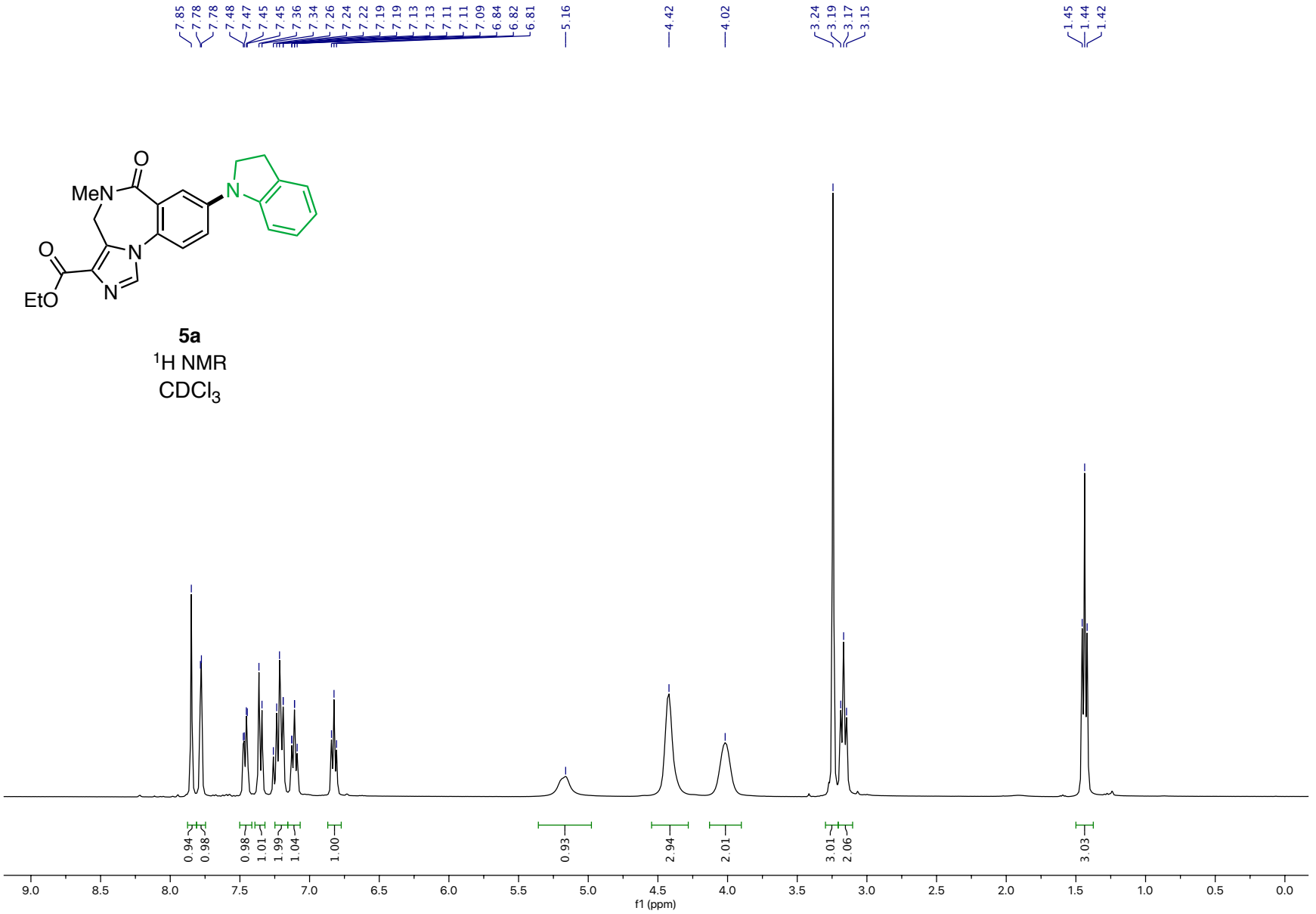

5a

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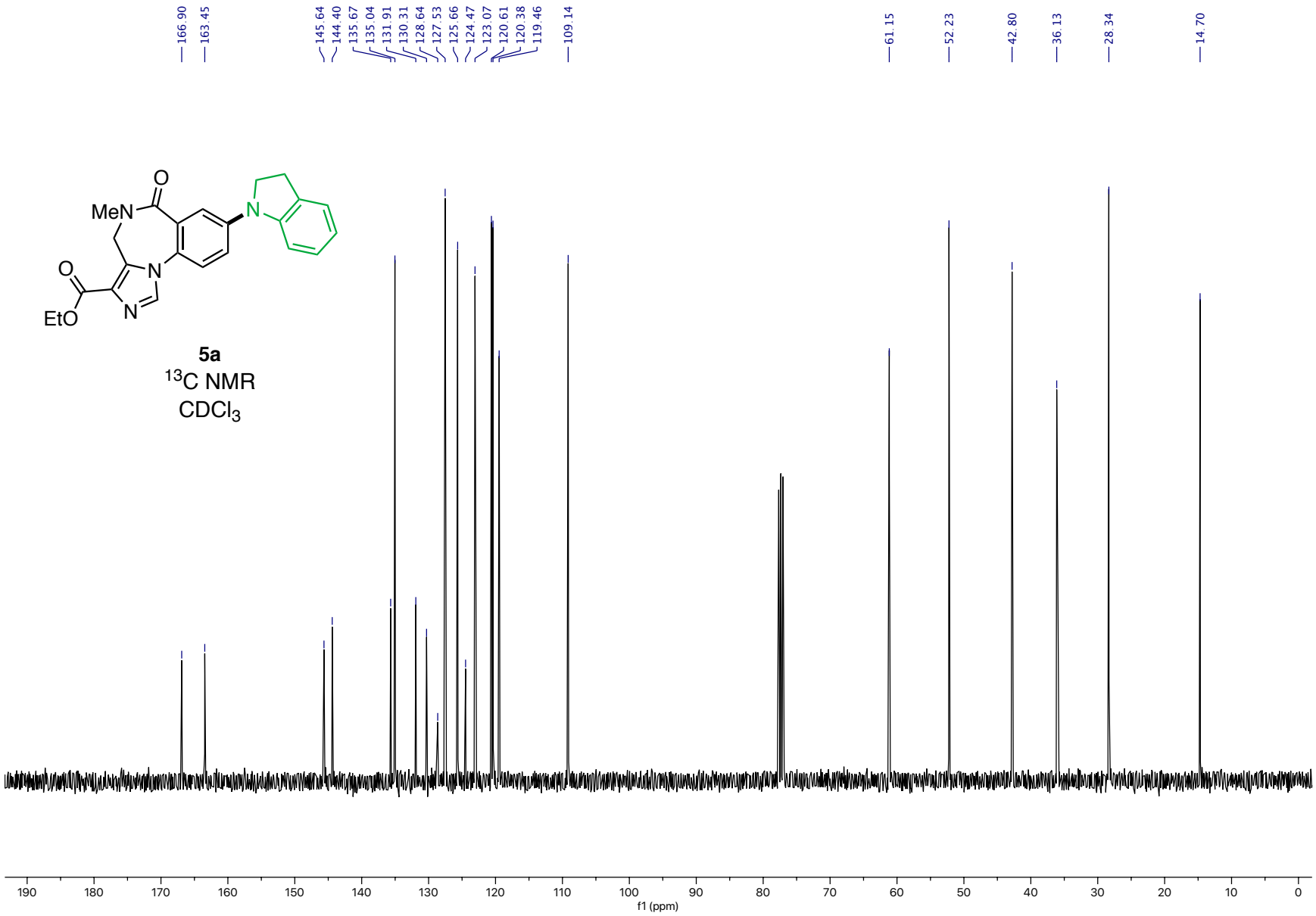
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EtO
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5a
13C NMR
CDCl3
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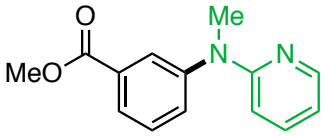
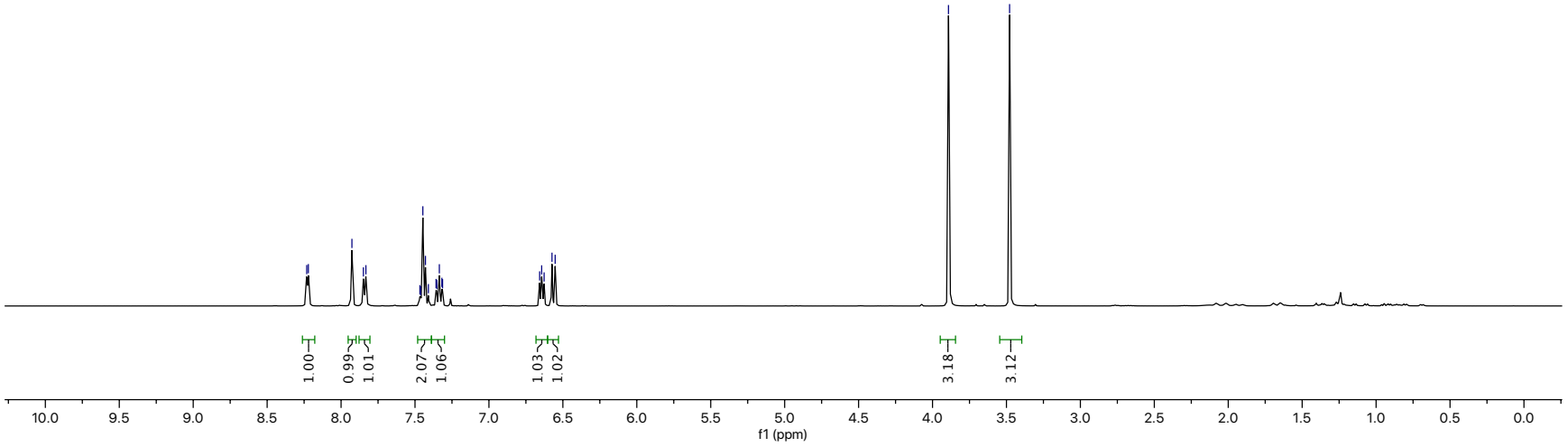
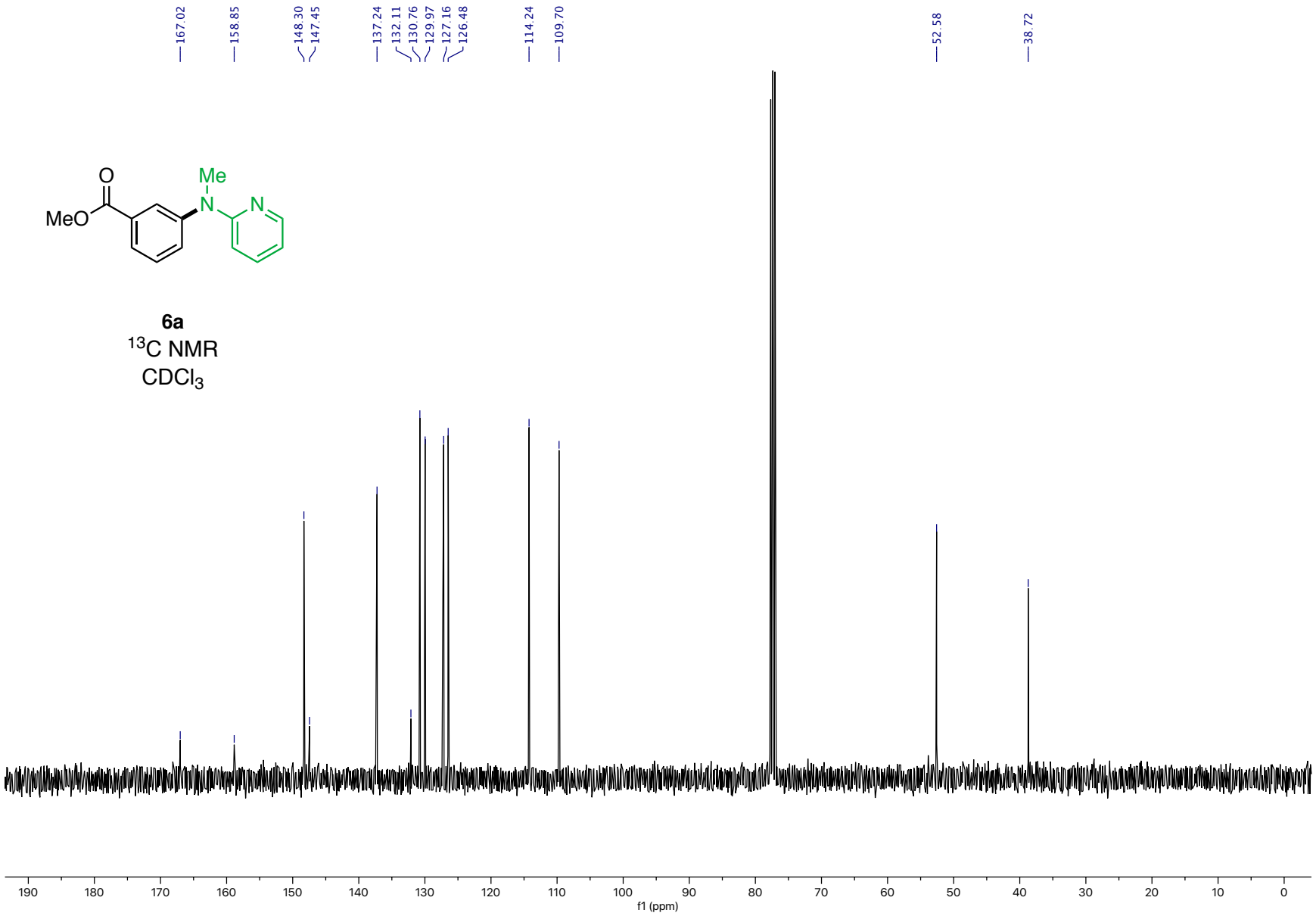


6a

^{1}H NMR

$CDCl_3$

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N
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6a
13C NMR
CDCl3
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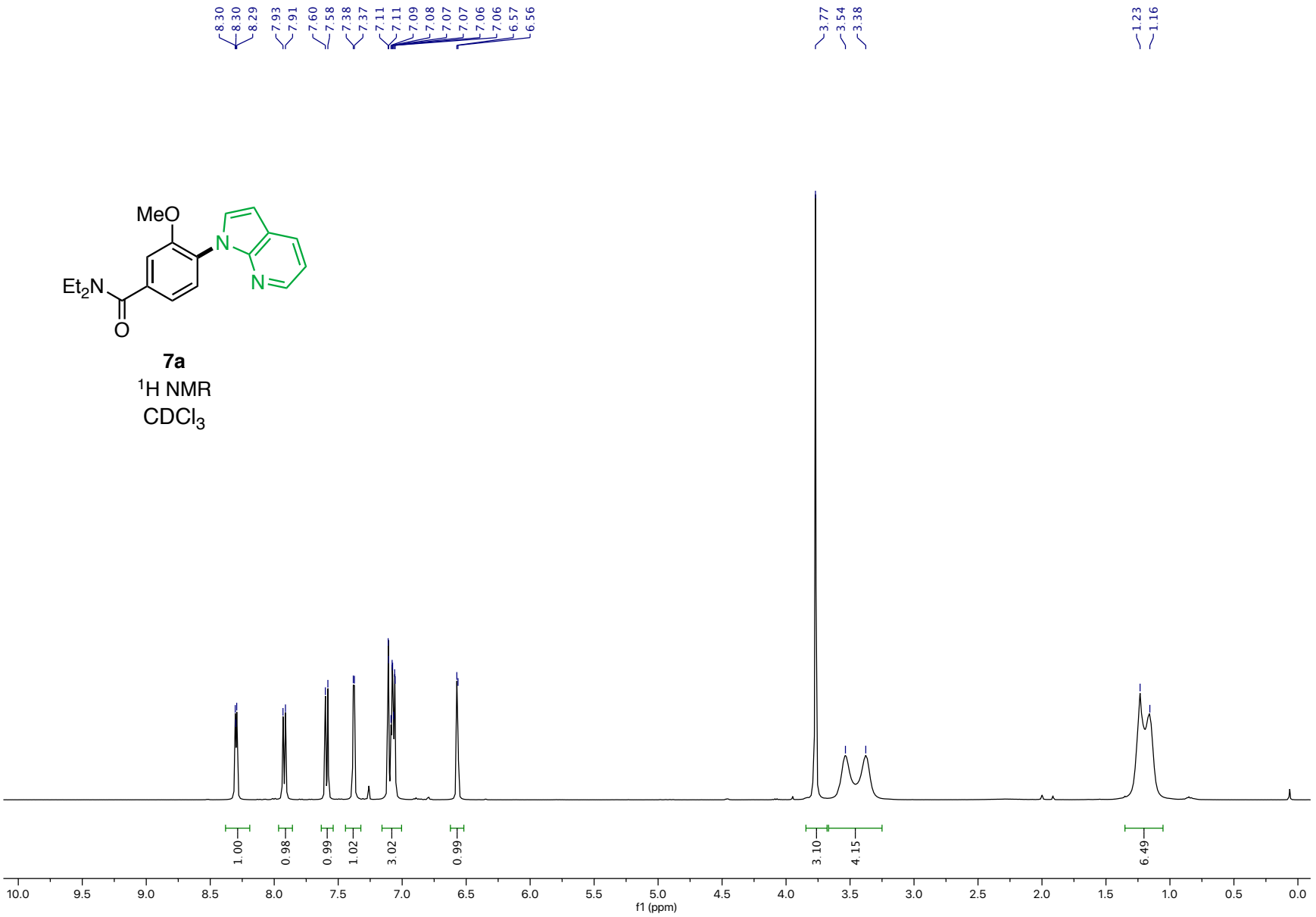
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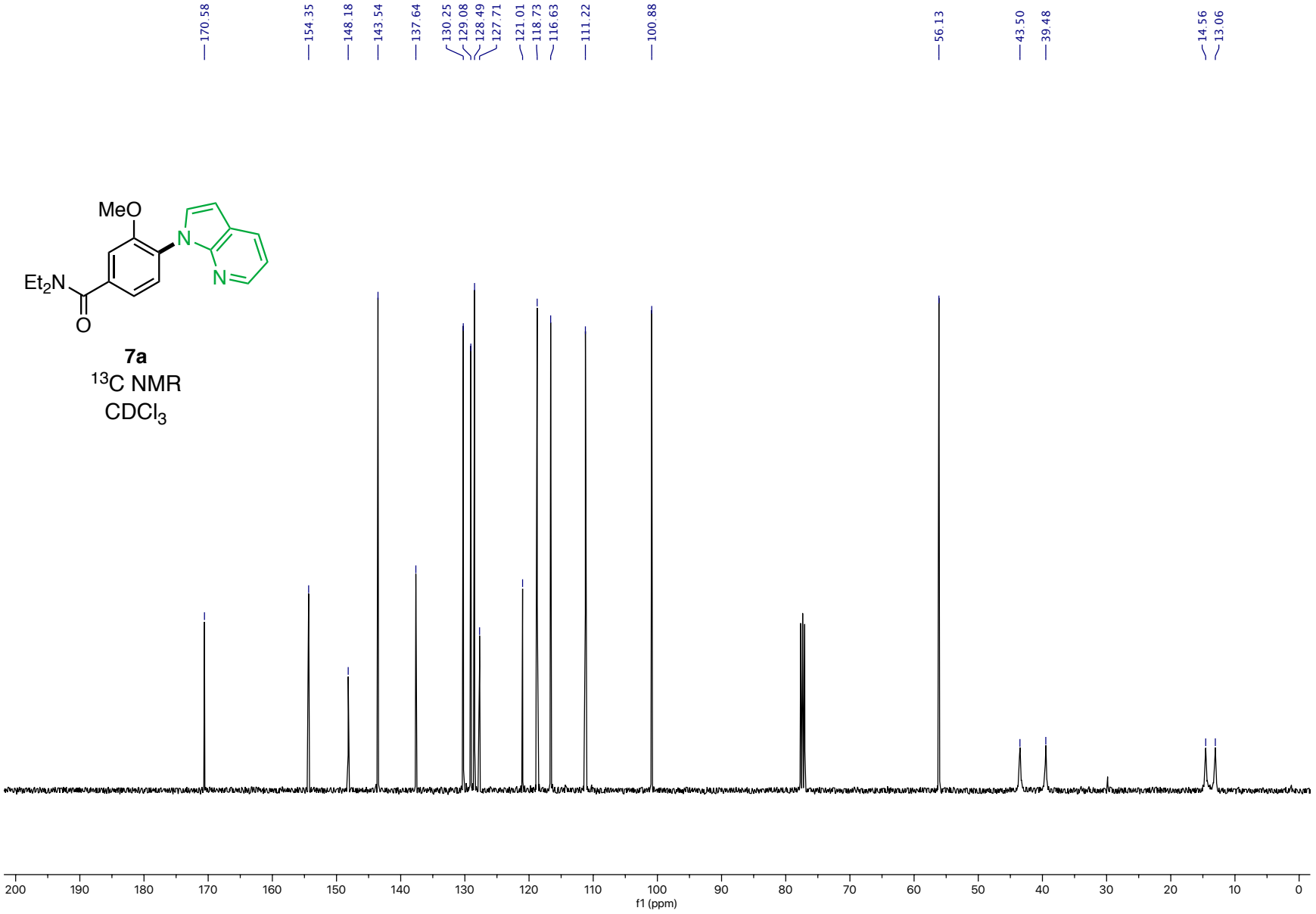
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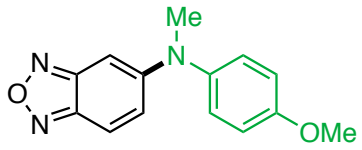
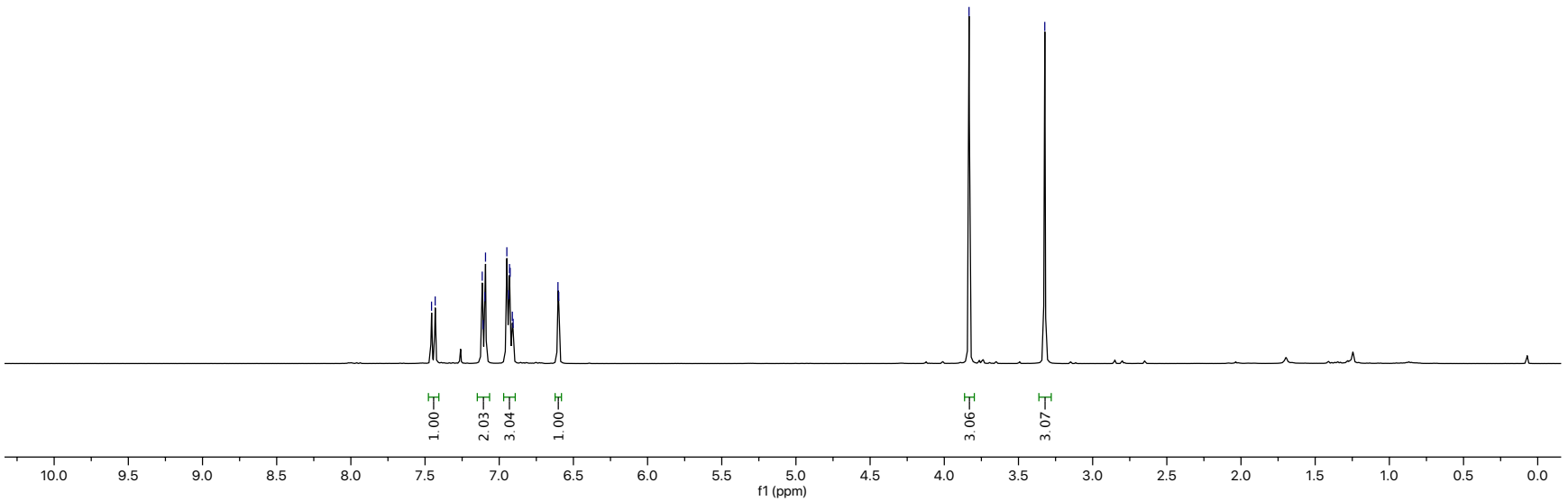
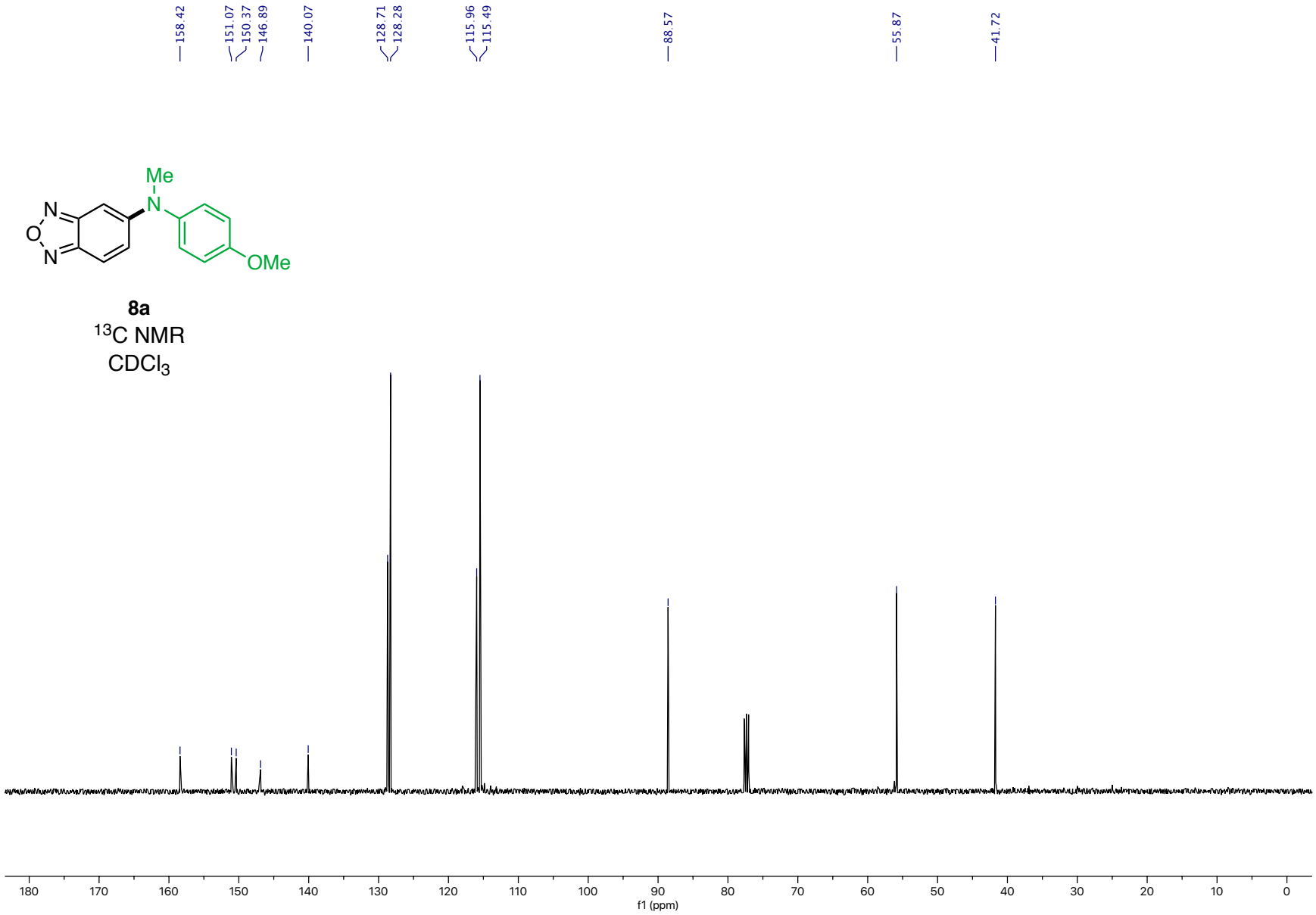


8a

^{1}H NMR

$CDCl_3$

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8a
13C NMR
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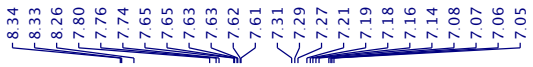
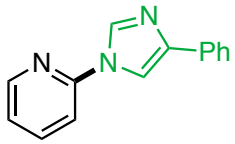
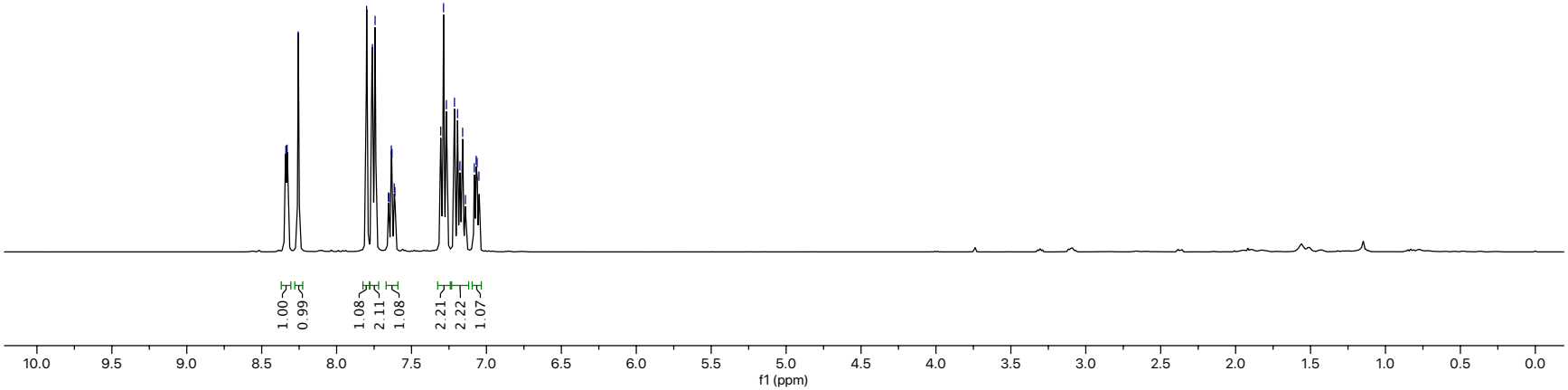
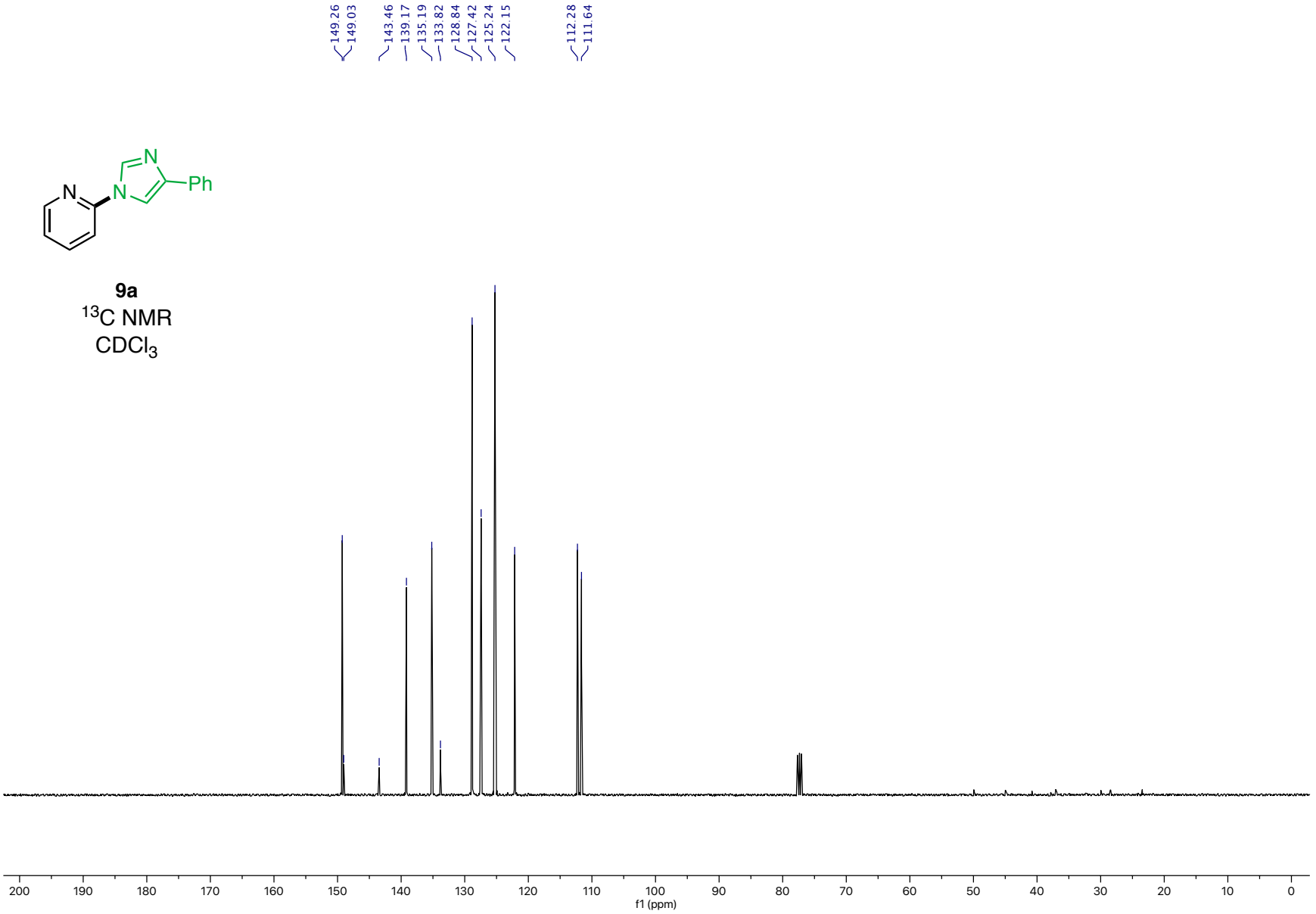




9a
^{1}H NMR
$CDCl_3$

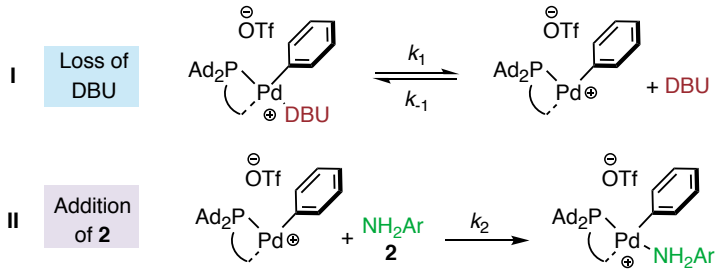




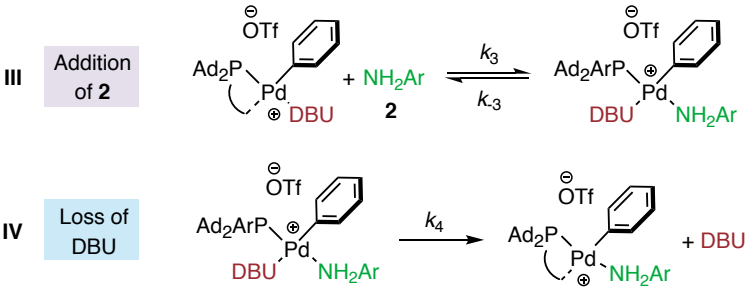
9a
^{13}C NMR
$CDCl_3$

Discussion on Dissociation/Association vs Association/Dissociation Mechanisms

A. Dissociation/Association (D/A) Mechanism



B. Association/Dissociation (A/D) Mechanism



Our experimentally determined reagent dependences match the rate law derived from the D/A mechanism (**A**) (pages S44-S47), providing evidence that this mechanism is at play. While a first order dependence on **2** is predicted for both mechanisms, only the rate of mechanism **A** is inversely dependent on DBU concentration, which was observed experimentally. Additionally, these mechanisms differ in that the D/A mechanism (**A**) invokes the formation of a pseudo-3-coordinate palladium center whereas the A/D mechanism (**B**) invokes the formation of a 4-coordinate species. Based on our hypothesis that only one amine can bind the AlPhos-bound Pd center, we performed the following experiments. We believe that these conclusions provide additional evidence that mechanism **A** is more likely at play.

Computational studies of palladium-catalyzed C–N couplings facilitated by dialkyl monophosphine ligands have provided insight on the ability for amines to bind to Pd.[21] The studies showed that the geometry of the oxidative addition (OA) complex influences the amine binding event. Specifically, rotation of Ar(Pd)X around the C_{aryl}-P bond of the ligand allows the OA complex to adopt a geometry that minimizes steric interactions at the Pd center. (Figure S2).

This rotation lets the amine to bind to a sterically accessible Pd center (Figure S2, **II**) instead of a sterically congested Pd center (Figure S2, **I**).

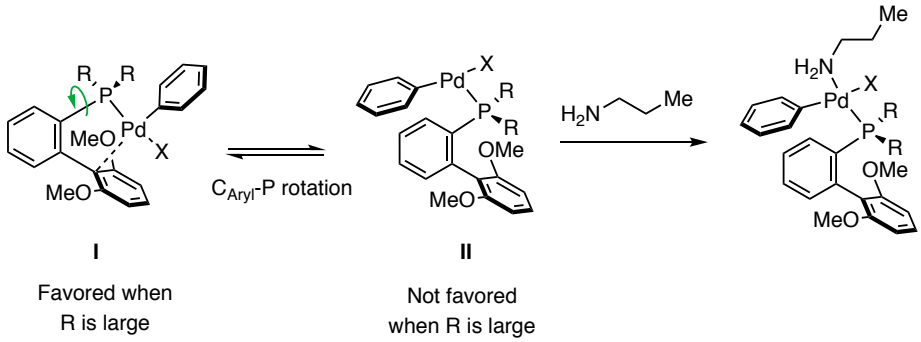


Figure S2: C_{aryl}-P bond rotation of an SPhos OA complexes and the preferred geometry for amine binding.

Because the size of the alkyl groups on the phosphorus atom of the ligand influences the rotation of the C_{aryl}-P bond, these groups affect the ability of the OA complex to adopt the preferred geometry for amine binding. Ligands bearing smaller cyclcohexyl groups readily convert to conformation **II** while ligands bearing large adamantyl groups (such as AlPhos) do not. Instead, OA complexes derived from ligands with adamantyl groups adopt conformation **I** due to the high energetic penalty associated with C_{aryl}-P bond rotation. Because conformation **I** has a congested coordination sphere, the OA complex cannot easily accept multiple amine ligands (Figure S3).

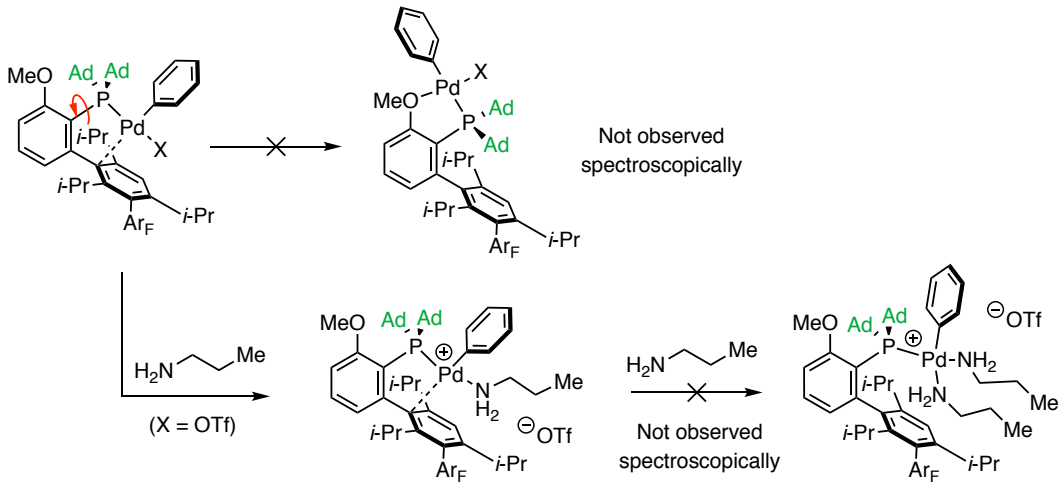


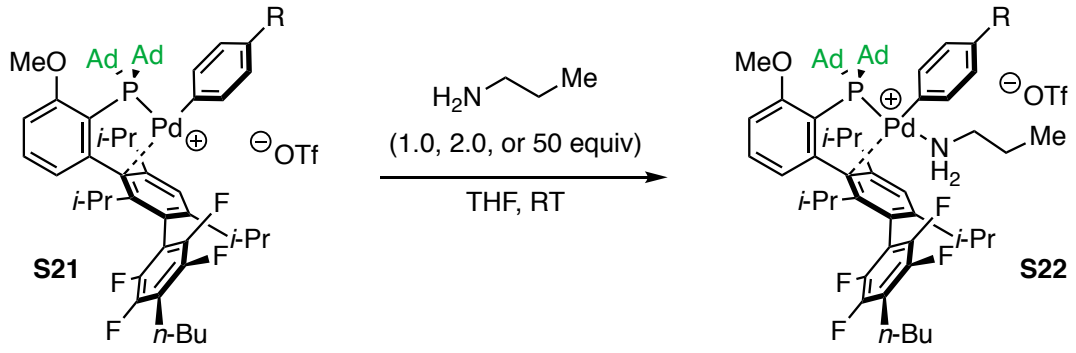
Figure S3: Limited C_{aryl}-P bond rotation of an AlPhos OA complex and its effect on amine binding.

This effect was observed in the coupling of *p*-tolyl triflate with *n*-propyl amine facilitated by an AlPhos-supported catalyst and DBU. Only one aliphatic amine was found to bind to the Pd center of the OA complex. Even with a non-coordinating triflate anion, the sterically congested AlPhos-bound Pd center does not accept a second molecule of *n*-propyl amine. This *n*-propyl amine-bound AlPhos-supported OA complex (**S22**) has been characterized and analyzed via X-ray diffraction.[17] Because *n*-propyl amine is both smaller and more nucleophilic than aniline, one would expect that if two *n*-propyl amine molecules cannot bind to the Pd center, then it is unlikely for both a molecule of aniline and one of DBU to bind to the Pd center.

To ensure that only one molecule of *n*-propyl amine was binding to the AlPhos-supported Pd center in the solution phase, we used ^{31}P NMR to analyze the AlPhos-supported OA complex (**S21**) in the presence of excess *n*-propyl amine (50 equiv, Figure S4). We then conducted the same study with a CyAlPhos-bound OA complex[17] (previously reported, **S23**) and compared the results. (Figure S5). Because the size of the alkyl groups on the phosphorus atom of AlPhos and CyAlPhos differ, the OA complexes derived from these ligands differ in their ability to adopt the preferred geometry for amine binding. In the case of the AlPhos-supported OA complex, only one resonance was observed when 1.0, 2.0, and 50 equivalents of amine were added. This suggests that only one amine binds to the Pd center as the 2-amine bound OA complex should have a unique ^{31}P NMR shift. In contrast, when 2.0 equivalents of *n*-propyl amine were added to the CyAlPhos-supported OA complex, two unique peaks were observed in the ^{31}P NMR spectrum. These data suggest that there is a mixture of complexes differing in whether one or two equivalents of amine were bound. When additional *n*-propyl amine was added to the CyAlPhos-supported OA complex, the species with two amines bound dominated. This CyAlPhos-supported *n*-propyl amine-bound complex (**S24**) was crystallized and characterized by X-ray diffraction.

We believe that these results show that the addition of the second amine to the Pd center of the OA complex is only possible when ligands bearing smaller alkyl groups (cyclohexyl instead of adamantyl) are employed. This effect has been observed in both solution and solid states. Moreover, we believe that these results show the reluctance for more than one amine or base molecule to bind to the AlPhos-supported OA complex, which provides strong evidence against mechanism **B**.

Figure S4: Addition of propyl amine to an AlPhos supported OA complex, **S21**.



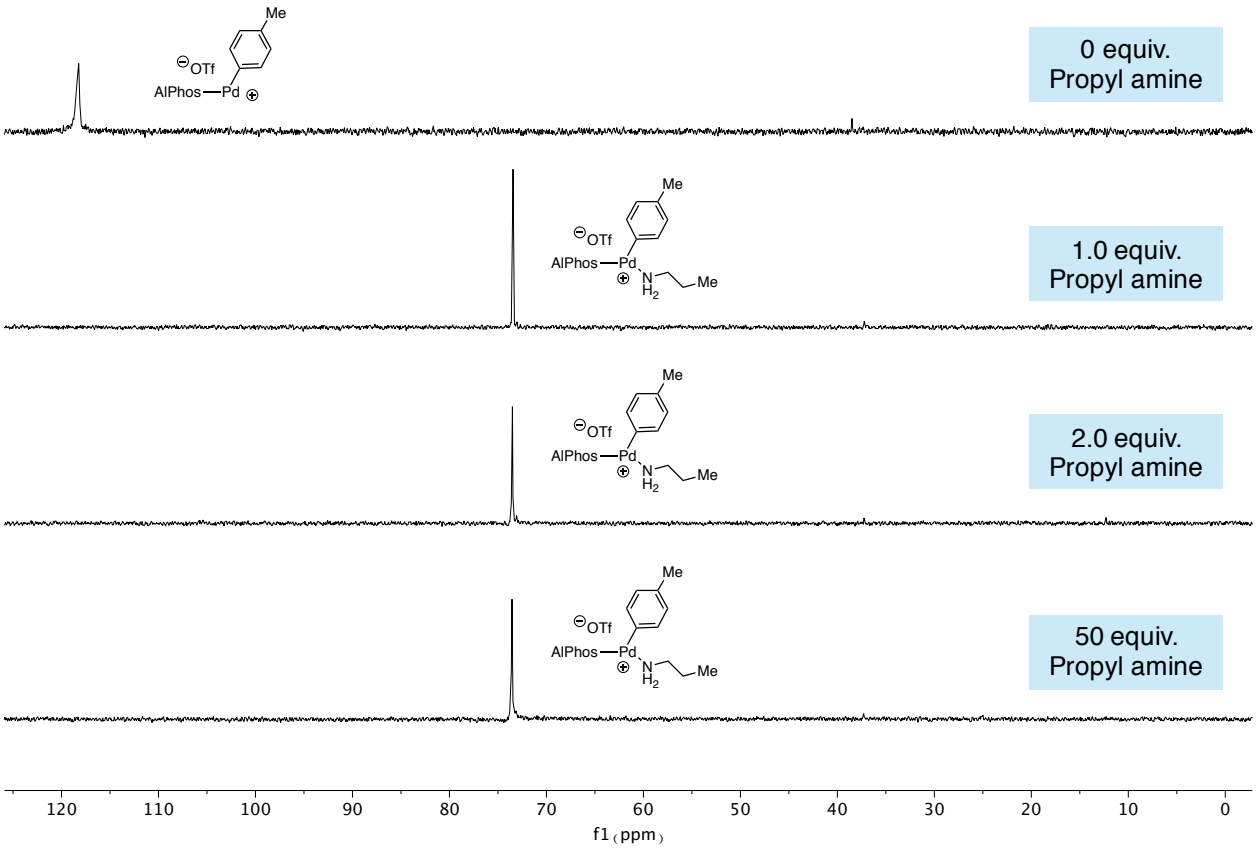
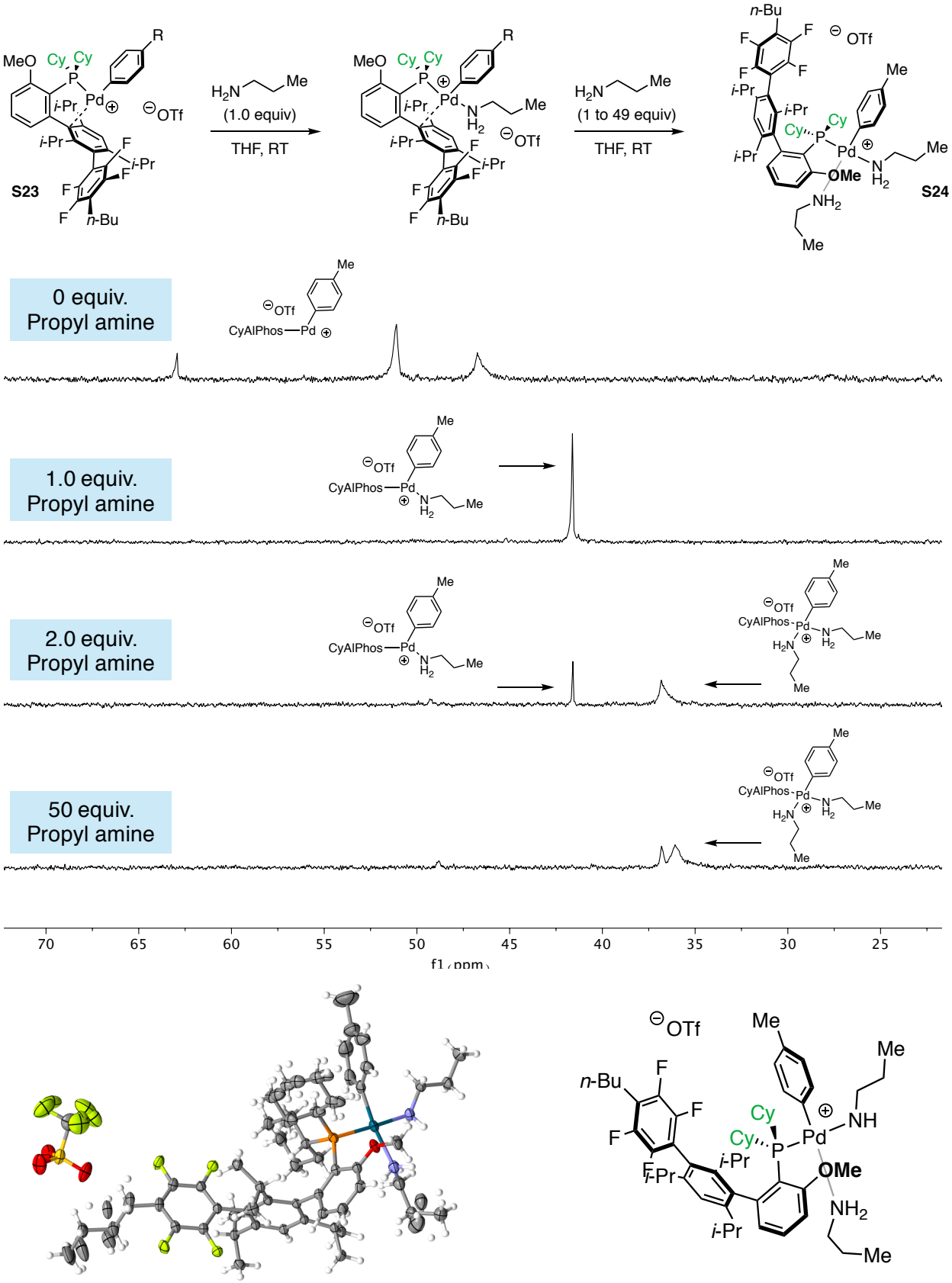


Figure S5: Addition of propyl amine to a CyAlPhos supported OA complex, **S22**.

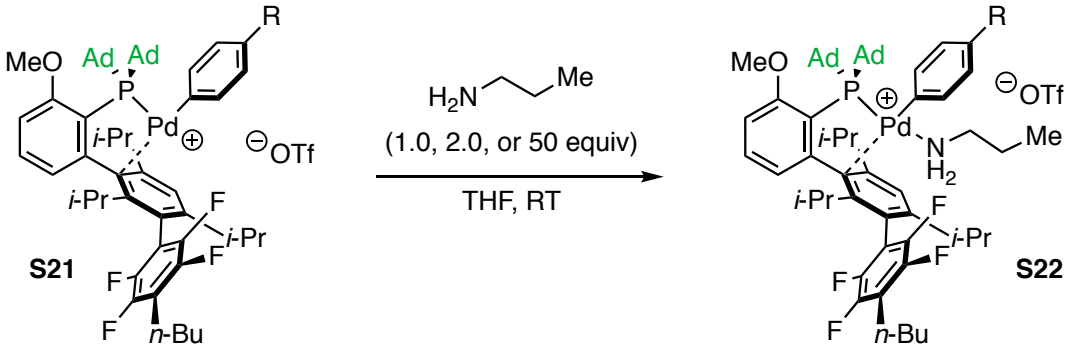


General Procedure for Measuring Amine Addition to OA Complexes

In a nitrogen-filled glovebox, an oven-dried NMR tube was charged with oxidative addition complex (8.6 μmol, 1.0 equiv) and tetrahydrofuran (THF, 0.40 mL). The NMR tube was sealed with a septum cap and the tube was shaken for 5 s to afford a homogenous, orange-colored solution. While still in the glovebox, a stock solution of *n*-propyl amine (28.4 μL) in THF (4.00 mL) was prepared in an oven-dried vial (8 mL). A Hamilton® syringe was used to withdraw 200 μL (17.2 μmol propyl amine, 2.0 equiv) of this stock solution and the tip of the needle was gently pushed into a soft rubber stopper to prevent leaking. A second Hamilton® syringe was used to withdraw neat *n*-propyl amine (34.0 μL, 413 μmol, 48 equiv), after which the needle tip was gently pushed into the rubber stopper. The NMR tube and syringes were removed from the glovebox and were transferred to the NMR facility.

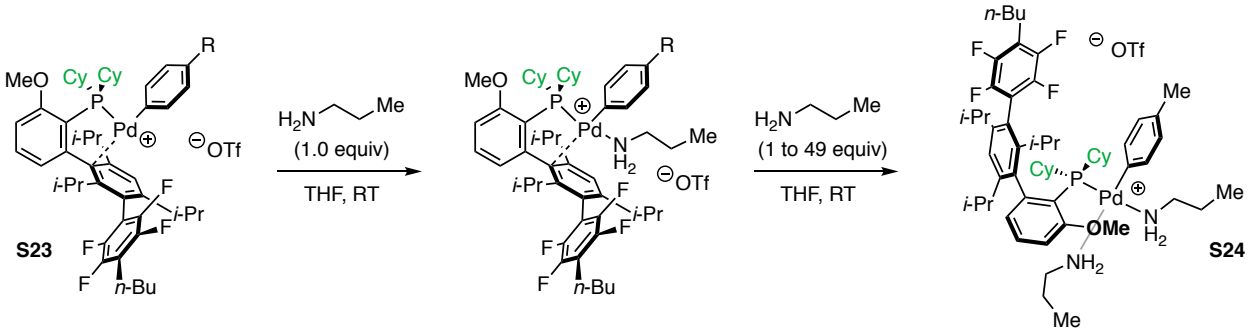
The NMR tube was inserted into the instrument bore and a ^{31}P spectrum of the oxidative addition complex was acquired (0 equiv *n*-propyl amine). Afterward, the NMR tube was removed from the instrument and 100 μL (8.6 μmol *n*-propyl amine, 1.0 equiv) of the stock solution (half of the volume of solution in the Hamilton® syringe) was added to the NMR tube by carefully inserting the tip of the needle through the septum of the NMR tube. The needle was removed and the NMR tube was shaken for 2 s, which resulted in a color change to a pale-yellow-colored, homogenous solution. A second ^{31}P NMR spectrum was acquired (1.0 equiv *n*-propyl amine). This process was repeated and another 100 μL (8.6 μmol *n*-propyl amine, 1.0 equiv) of the stock solution was added via syringe (2.0 equiv *n*-propyl amine total). After the third ^{31}P NMR spectrum was acquired, the tube was removed from the instrument and neat *n*-propyl amine (34.0 μL, 413 μmol, 48 equiv) was added to the NMR tube via syringe. The final NMR spectrum (with 50 equiv *n*-propyl amine total added) was acquired.

Procedure Measuring Amine Addition to an AlPhos-Supported OA Complex



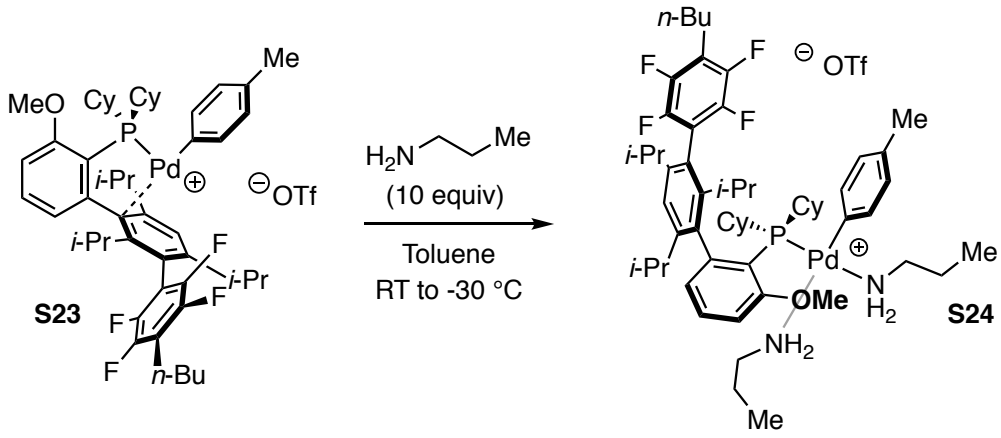
The general procedure was followed using **S21**[17] (10.0 mg, 8.6 μmol, 1.0 equiv). The following NMR spectra were collected: **Spectrum L** (0 equiv propyl amine); **Spectrum M** (1.0 equiv propyl amine); **Spectrum N** (2.0 equiv propyl amine); **Spectrum O** (50 equiv propyl amine).

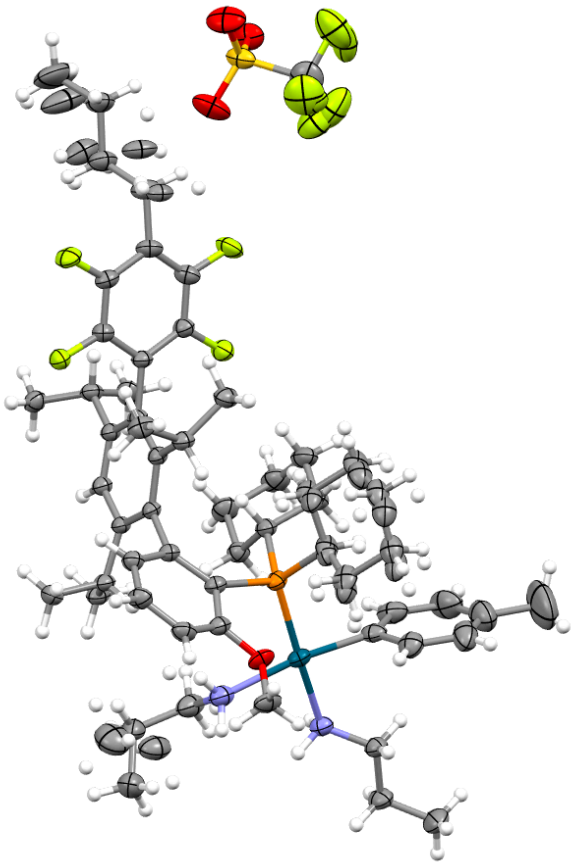
Procedure Measuring Amine Addition to an CyAlPhos-Supported OA Complex



The general procedure was followed using **S22**[17] (9.1 mg, 8.6 μmol, 1.0 equiv). The following NMR spectra were collected: **Spectrum P** (0 equiv propyl amine); **Spectrum Q** (1.0 equiv propyl amine); **Spectrum R** (2.0 equiv propyl amine); **Spectrum S** (50 equiv propyl amine).

Crystallization Procedure and Crystal Data





In a nitrogen-filled glovebox, **S23**[17] (5.0 mg, 4.7 µmol) was weighed into an oven-dried vial (8 mL). Toluene (0.50 mL) was added via syringe, and the solution was stirred with the aid of a Vortex mixer for 5 s to afford a faint yellow solution. Afterward, *n*-propyl amine (3.9 µL, 47 µmol, 10.0 eq) was added via Hamilton® syringe. The solution was stirred for an additional 5 s, which resulted in a colorless solution. The 8 mL vial was uncapped and placed into a 20 mL vial containing pentane (2.0 mL). The larger vial was capped and was left undisturbed in a -30 °C glovebox freezer to allow for crystallization via vapor diffusion (pentane into toluene) to take place for ~2 weeks. After decanting the solvent, this process afforded small, colorless crystals of **S24** that were analyzed by X-ray diffraction.

Crystal Data

Table S7: Crystal data and structure refinement for X17162_sq.

Identification code	X17162_sq	
Empirical formula	C58 H84 F7 N2 O4 P Pd S	
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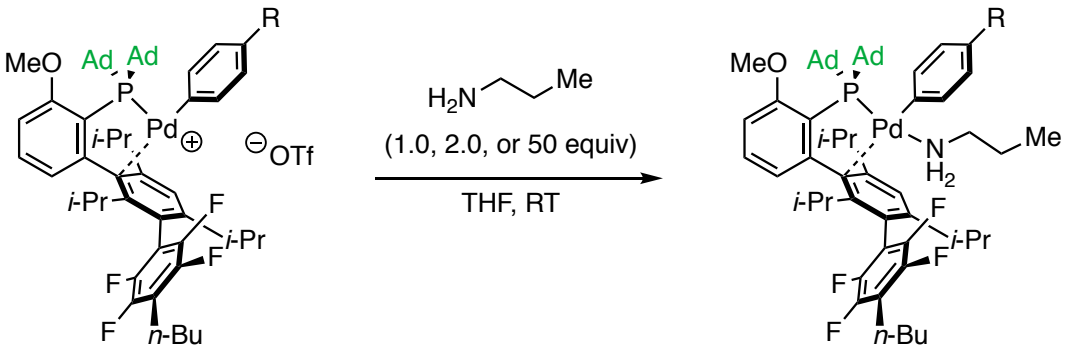
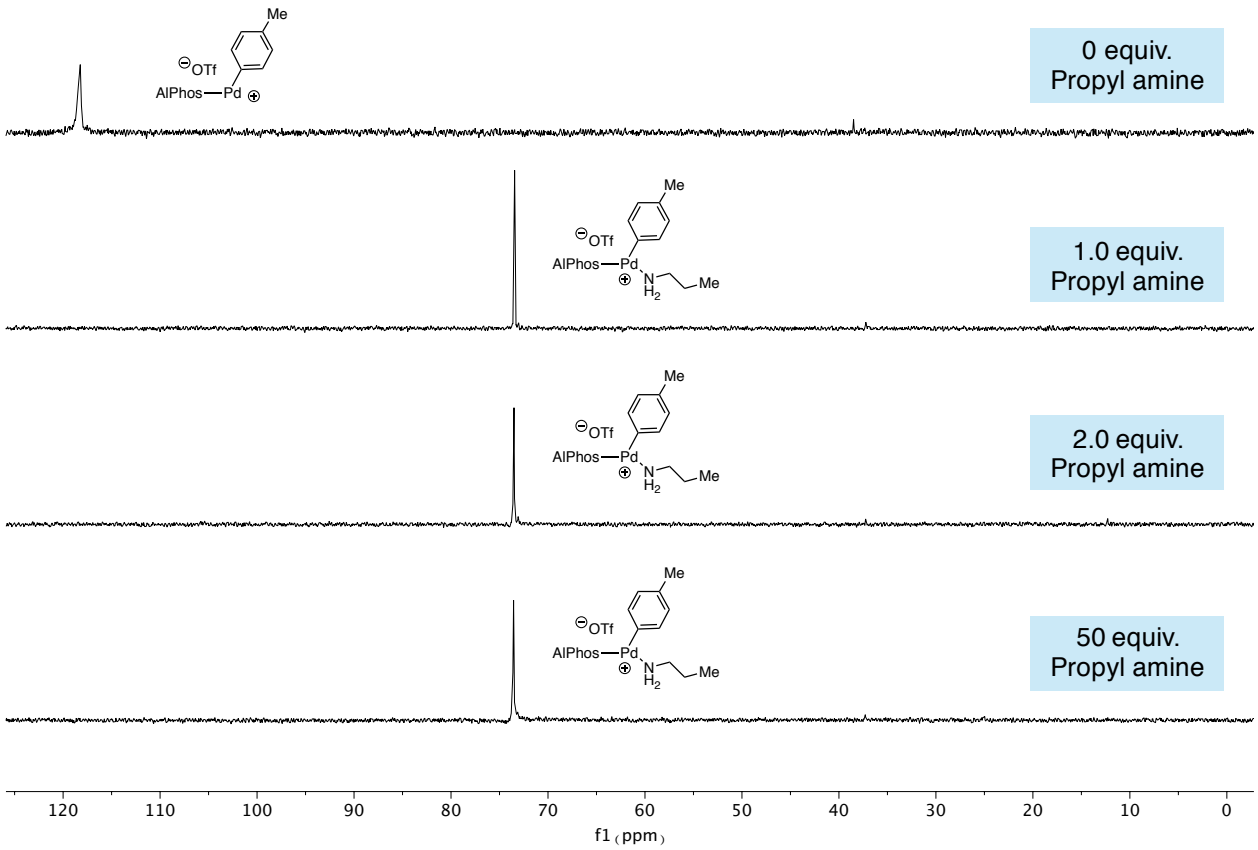
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P2$_1$/c	
Unit cell dimensions	a = 20.138(2) Å	⟨ = 90°.
	b = 13.1828(13) Å	® = 106.9117(16)°.
	c = 24.998(2) Å	© = 90°.
Volume	6349.3(11) Å^3	
Z	4	
Density (calculated)	1.230 Mg/m^3	
Absorption coefficient	0.413 mm^{-1}	
F(000)	2472	
Crystal size	0.130 x 0.085 x 0.070 mm^3	
Theta range for data collection	1.057 to 30.033°.	
Index ranges	-28<=h<=28, -18<=k<=18, -35<=l<=35	
Reflections collected	257135	
Independent reflections	18594 [R(int) = 0.0732]	
Completeness to theta = 25.242°	100.0 %	
Absorption correction	Semi-empirical from equivalents	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	18594 / 756 / 828	
Goodness-of-fit on F^2	1.028	
Final R indices [I>2sigma(I)]	R1 = 0.0562, wR2 = 0.1448	
R indices (all data)	R1 = 0.0793, wR2 = 0.1609	
Extinction coefficient	n/a	
Largest diff. peak and hole	3.623 and -1.905 e.Å^{-3}	





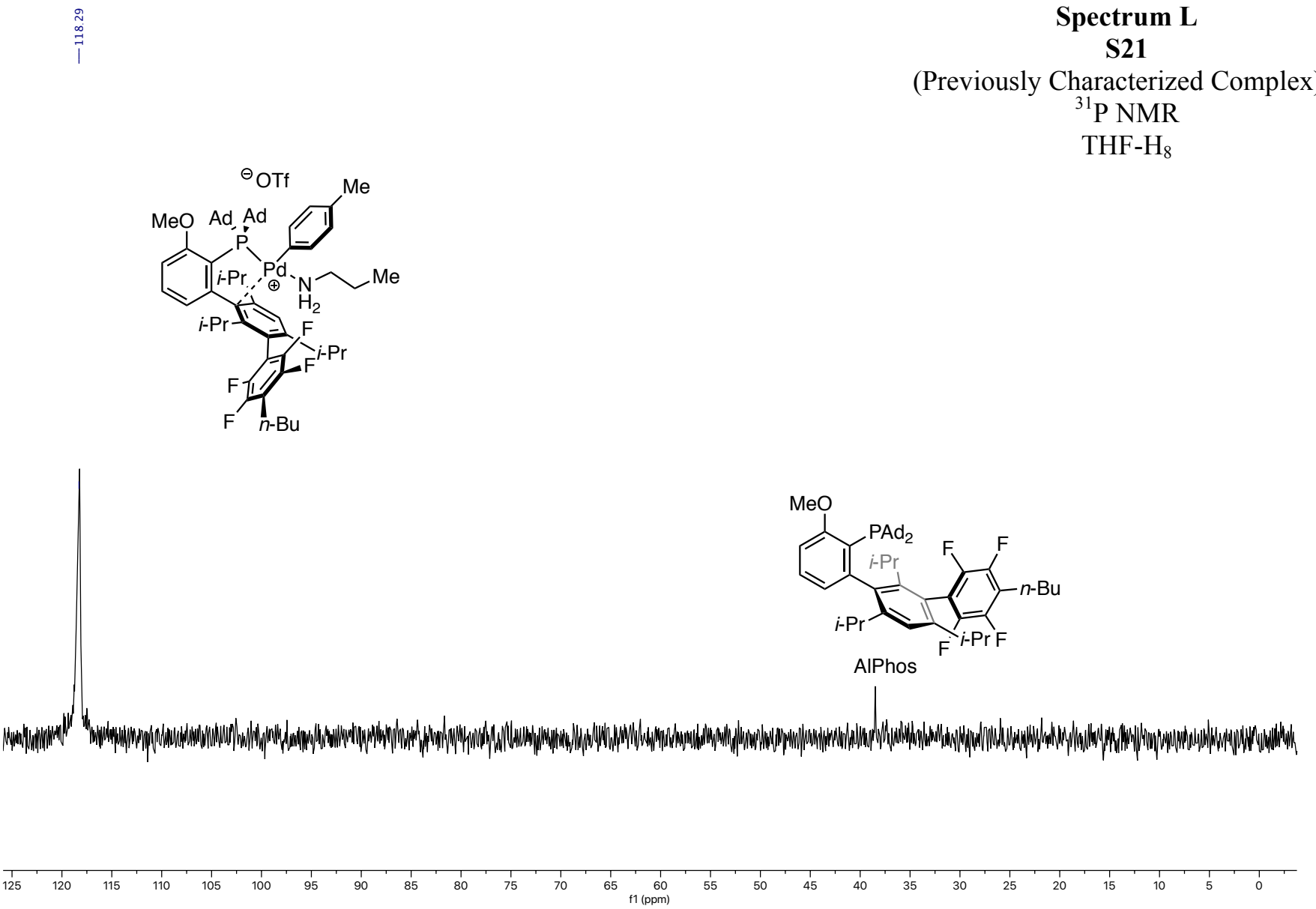
Spectrum L
S21
^{31}P NMR
THF-H_8

Spectrum M
^{31}P NMR
THF-H_8

Spectrum N
^{31}P NMR
THF-H_8

Spectrum O
^{31}P NMR
THF-H_8

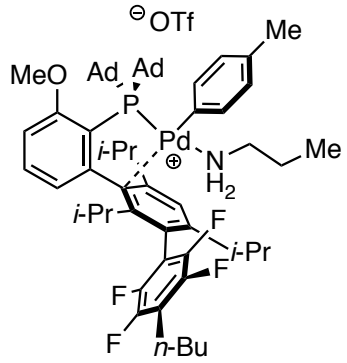
Spectrum L
S21
(Previously Characterized Complex)[17]
^{31}P NMR
THF-H_8



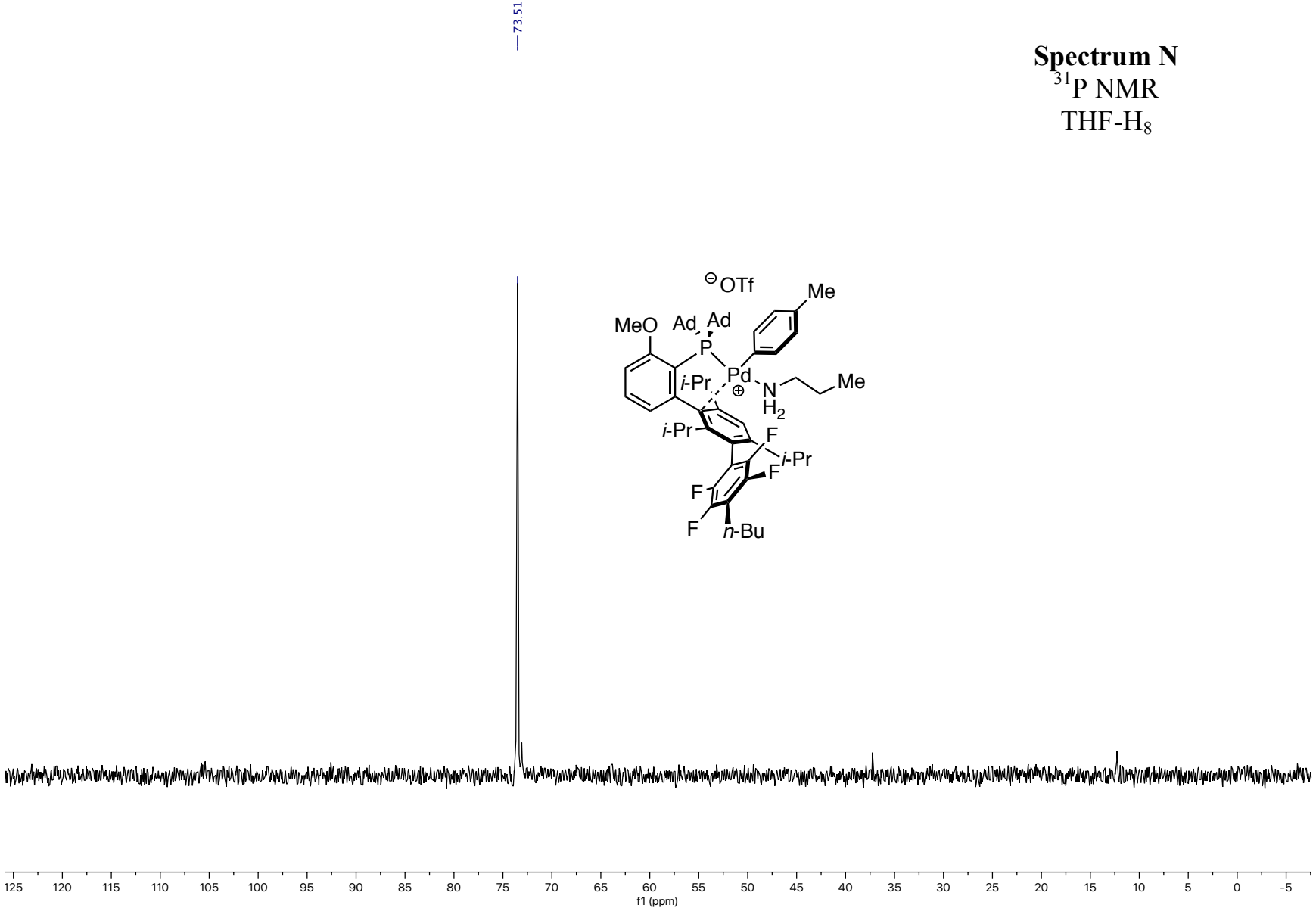
Spectrum M

^{31}P NMR

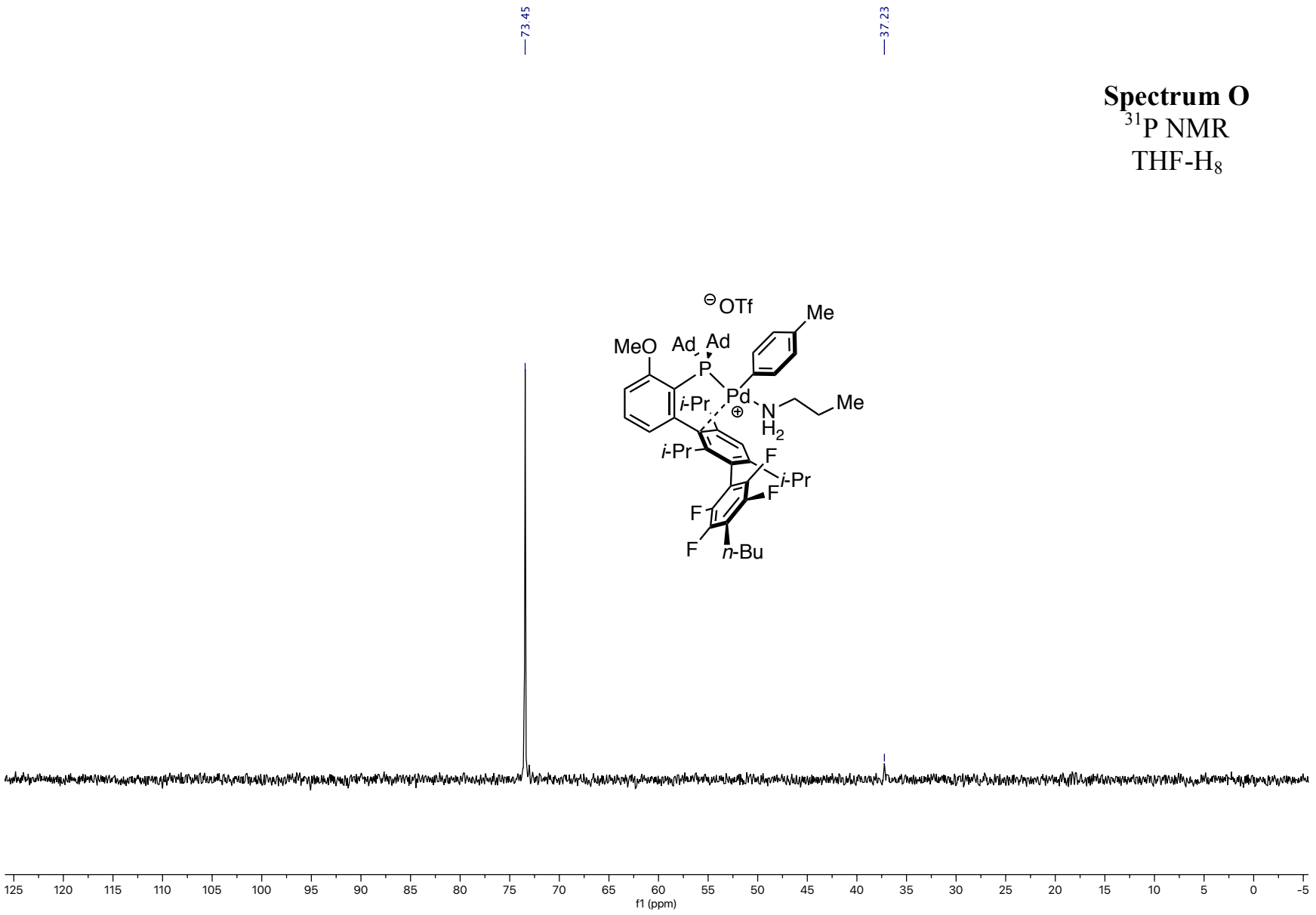
THF-H_8

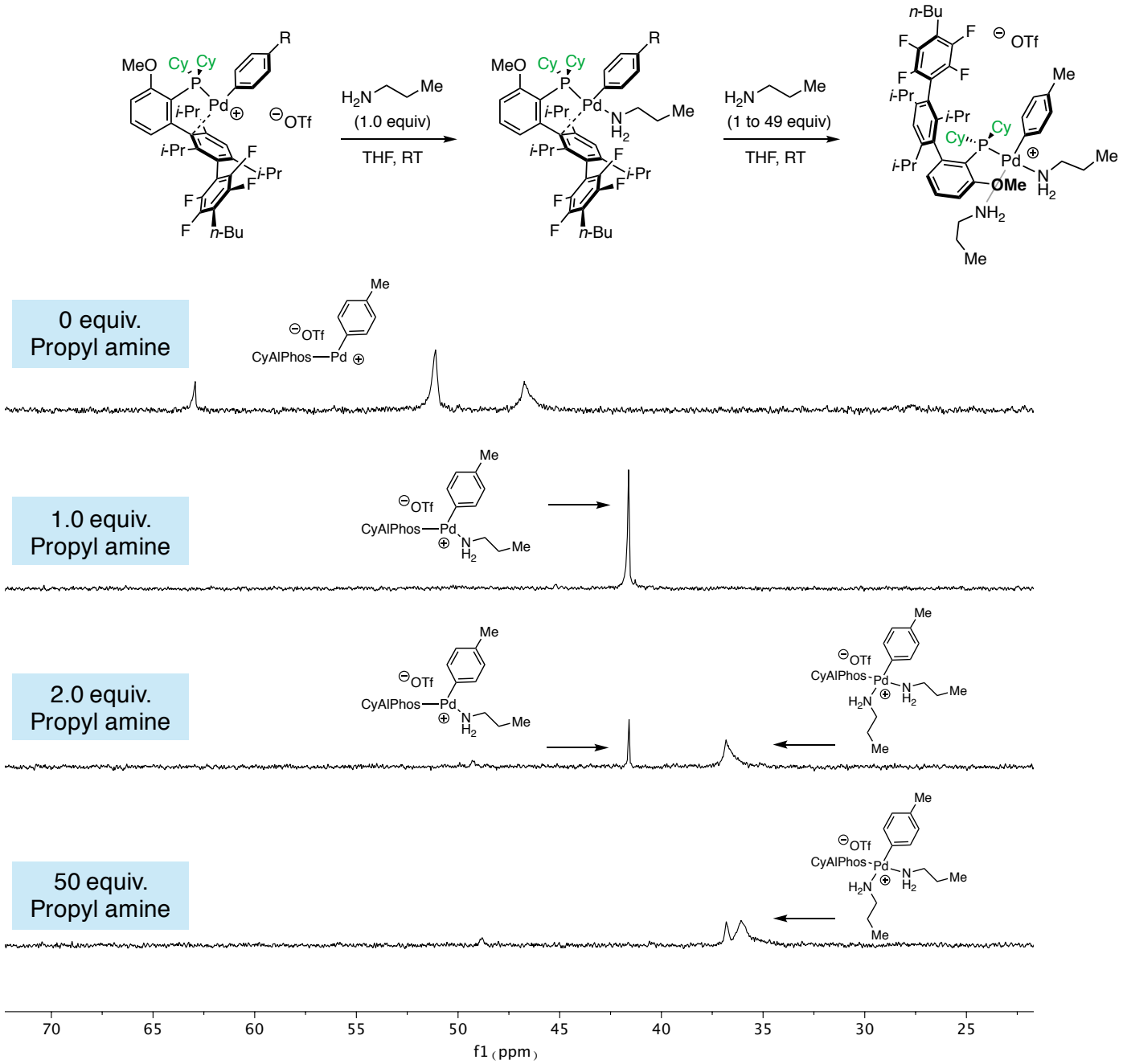


Spectrum N
^{31}P NMR
THF-H_8



Spectrum O
^{31}P NMR
THF-H_8





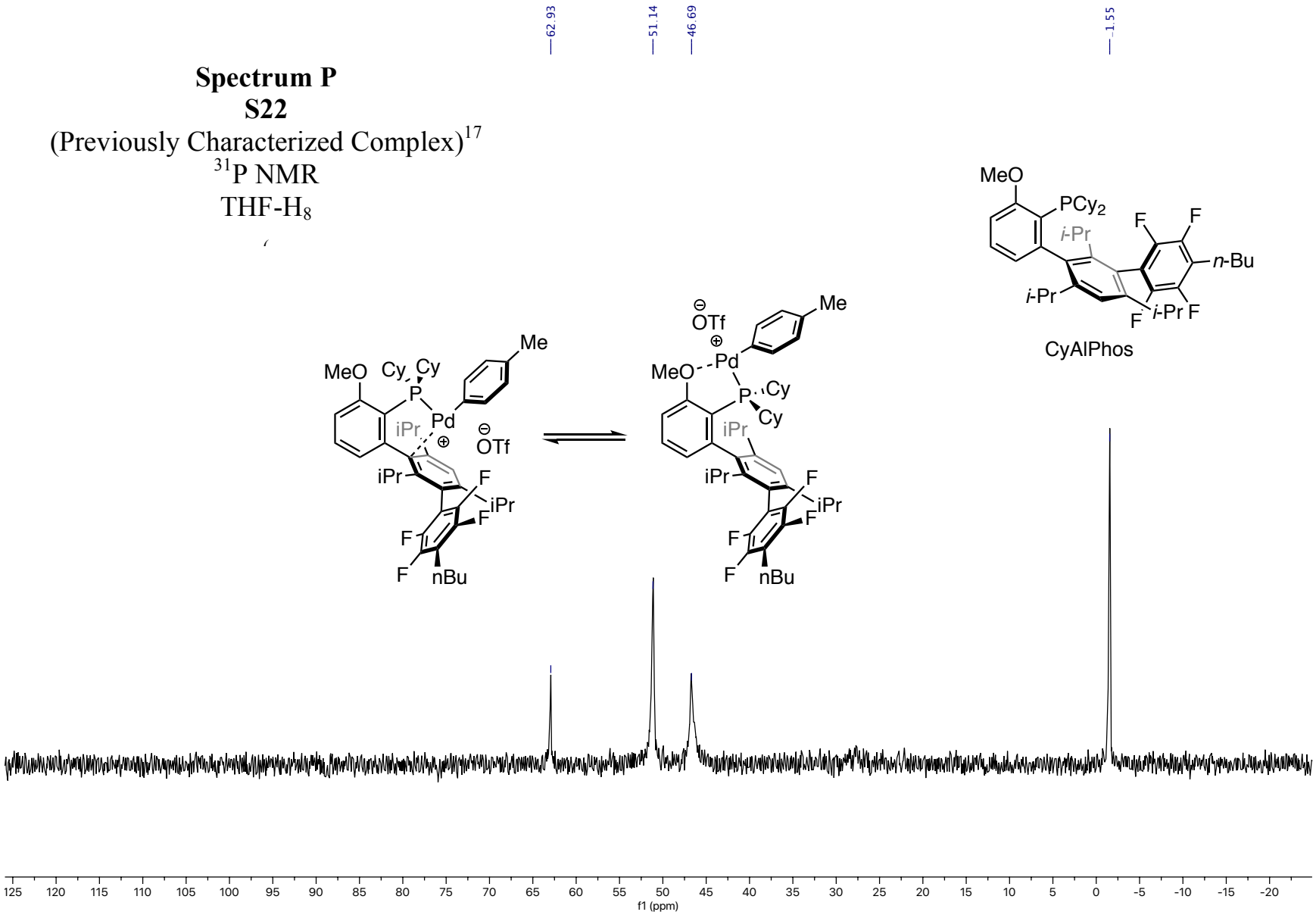
Spectrum P
S22
^{31}P NMR
THF-H_8

Spectrum Q
^{31}P NMR
THF-H_8

Spectrum R
^{31}P NMR
THF-H_8

Spectrum S
^{31}P NMR
THF-H_8

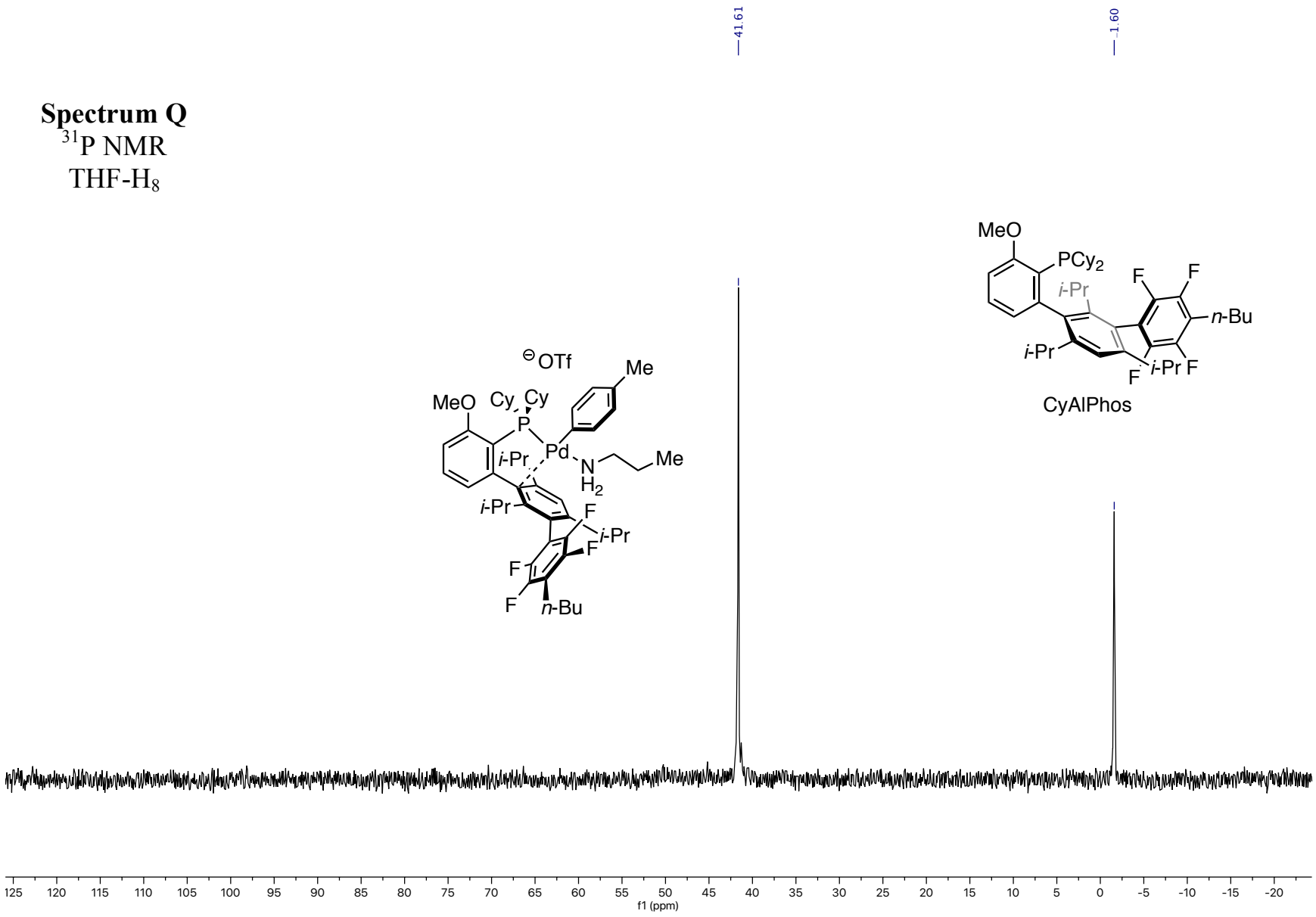
Spectrum P
S22
(Previously Characterized Complex)[17]
^{31}P NMR
THF-H_8



Spectrum Q

^{31}P NMR

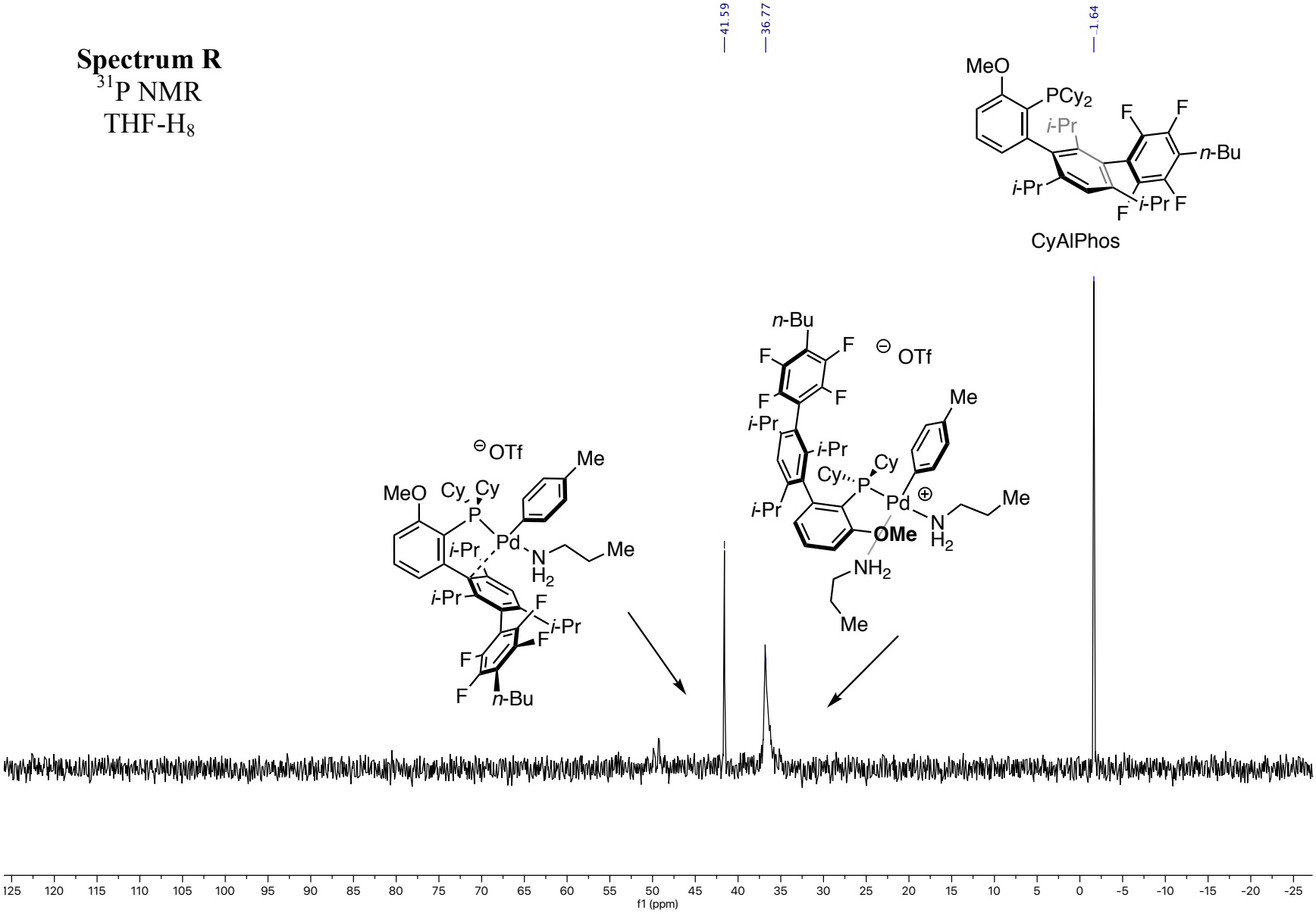
THF-H_8



Spectrum R

^{31}P NMR

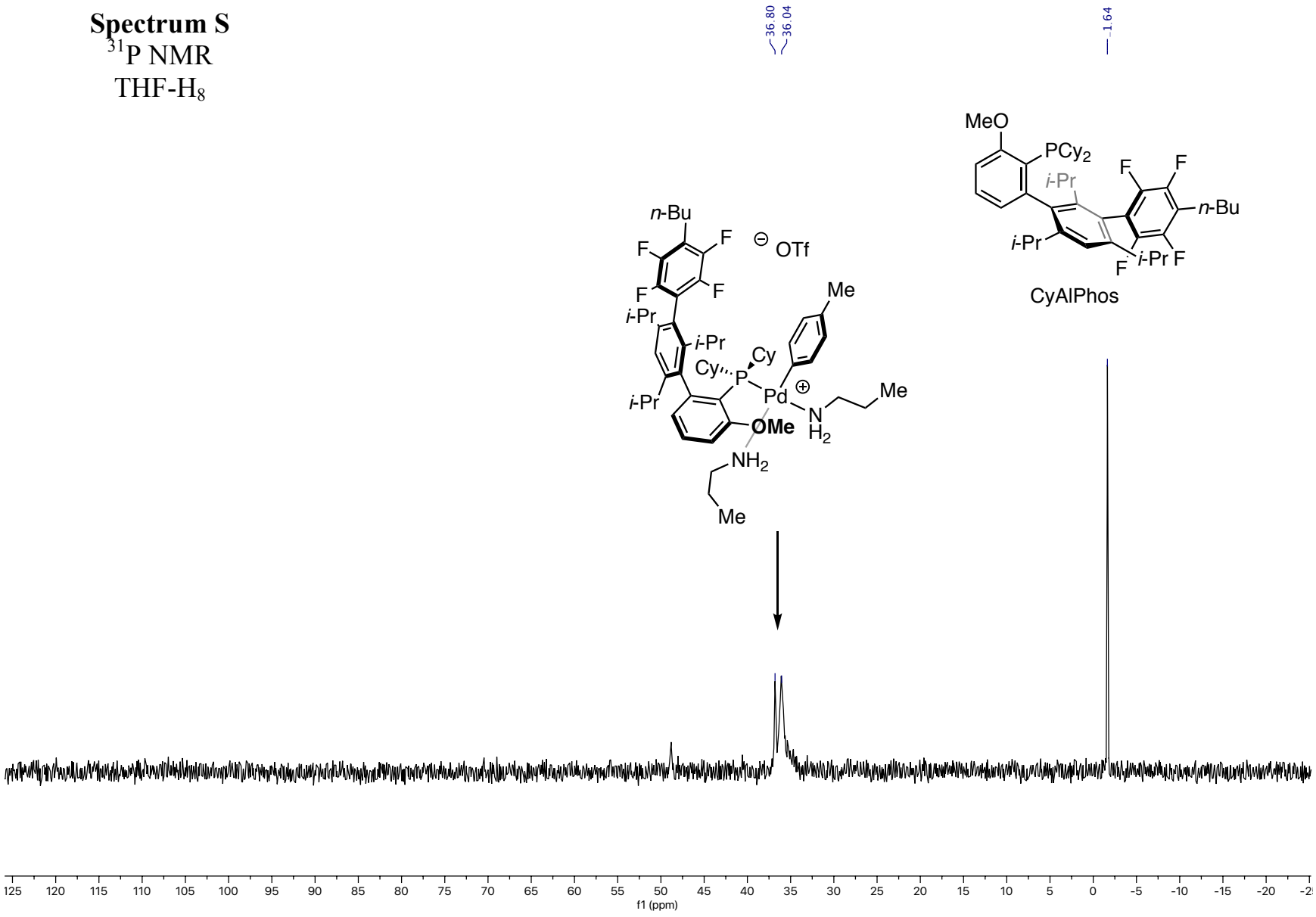
THF-H_8



Spectrum S

^{31}P NMR

THF-H_8



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