

Supplementary Information

Switchable Annulation Paths to Diverse *N*-Bridged Bicyclic Scaffolds via Ligand-Directed Dicarbonylation

Yu-Kun Liu^a, Peng Yang^a, Le-Cheng Wang^{a,b}, Zhi-Peng Bao^{a,b}, Xiao-Feng Wu^{a,b*}

^aLeibniz-Institut für Katalyse e. V., Albert-Einstein-Straße 29a, 18059 Rostock, Germany.

^bDalian National Laboratory for Clean Energy, Dalian Institute of Chemical Physics, Chinese Academy of Sciences, Dalian, 116023, Liaoning, China.

* E-mail: xiao-feng.wu@catalysis.de

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1. General information

Reagents and solvents: Unless otherwise noted, reagents were ordered from *Sigma-Aldrich*, *TCI*, *ABCR*, *Alfa Aesar* or *BLD pharm*, and used without purification. Pure solvents were available from *Thermo Fisher*, and degassed (3 times) under argon atmosphere, then store under standard Schlenk technique (anhydrous and under inert atmosphere).

Purification: Analytical thin layer chromatography was performed using *MACHERY-NAGEL Gmbn & Co.* KG silica gel plates (Silica gel 60 UV₂₅₄). Visualization was by ultraviolet fluorescence ($\lambda = 254$ nm) and/or staining with potassium permanganate (KMnO₄). The products were isolated from the reaction mixture by column chromatography on silica gel 60, 0.063-0.2 mm, 70-230 mesh (Merck). Gradient flash chromatography was conducted eluting with PE/EA, PE refers to pentane and EA refers to ethyl acetate, they were listed as volume/volume ratios.

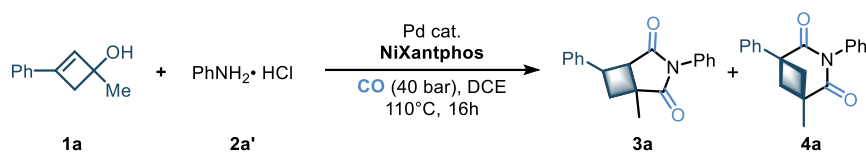
Data collection: GC analysis was performed on an Agilent HP-7890A instrument with FID detector and HP-5 capillary column (polydimethylsiloxane with 5% phenyl groups, 30 m, 0.32 mm i.d., 0.25 μ m film thickness) using argon as carrier gas. Electron impact (EI) mass spectra were recorded on AMD 402 mass spectrometer (70 eV). The data are given as mass units per charge (m/z). High resolution mass spectra (HRMS) were recorded on Agilent 6210. NMR spectra were recorded on Bruker Avance 300 and Bruker ARX 400 spectrometers. Multiplets were assigned as s(singlet), d (doublet), t (triplet), q (quartet), dd (doublet of doublet), m (multiplet) and br (broad). s (singlet). Chemical shifts (ppm) are given relative to solvent: references for CDCl₃ were 7.26 ppm (¹H NMR) and 77.00 ppm (¹³C NMR). All measurements were carried out at room temperature unless otherwise stated.

NOTE: Because of the high toxicity of carbon monoxide, all the reactions should be performed in an autoclave. The laboratory should be well-equipped with a CO detector and alarm system.

2. Optimization of Reaction Conditions

2.1 Optimization of reaction conditions of 3-azabicyclo[3.2.0]heptane scaffolds

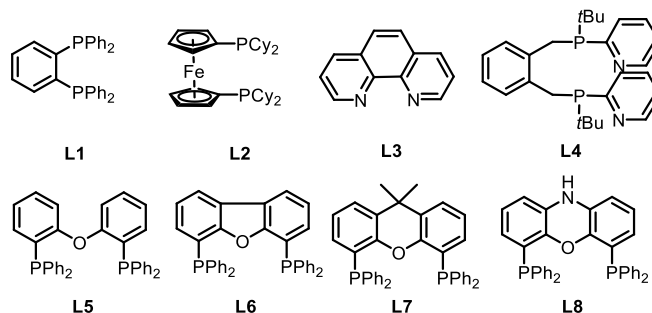
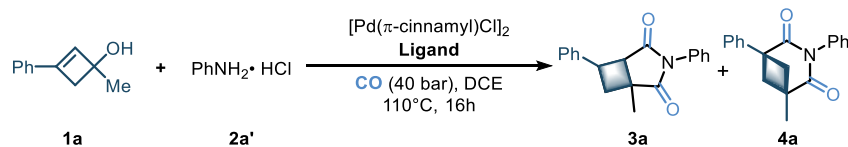
Supplementary Table S1. Optimization of catalyst



Entry	Pd cat.	Yield of 3a ^b (%)	3a:4a (r.r.)
1	Pd(TFA) ₂	27	> 19:1
2 ^c	Pd(TFA) ₂	N.D.	/
3	Pd(OAc) ₂	40	> 19:1
4	Pd(acac) ₂	trace	/
5 ^d	[Pd(π-cinnamyl)Cl] ₂	45	> 19:1
6	Pd(CH ₃ CN)Cl ₂	19	6:1
7	Pd(<i>t</i> -Bu ₃ P) ₂	33	> 19:1
8	Pd ₂ (dBa) ₃	16	> 19:1
9	Pd(dBa) ₂	21	> 19:1
10	PdCl ₂	42	5:1
11	Pd(PPh ₃) ₄	N.D.	/

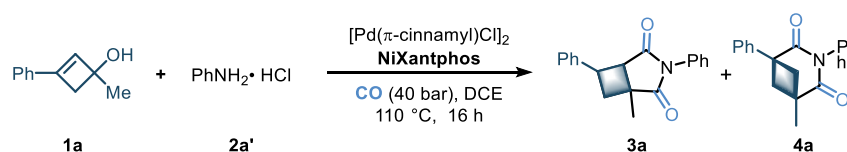
[a] Pd catalyst (2.5 mol%), NiXantphos (5 mol%), **1a** (0.12 mmol), **2a'** (0.1 mmol), CO (40 bar), DCE (1 mL) at 110 °C for 16 h. [b] The yield and r.r. ratio were determined by GC with n-hexadecane as internal standard. [c] PhNH₂ instead of PhNH₂·HCl. [d] 1.25 mol% [Pd(π-cinnamyl)Cl]₂.

Supplementary Table S2. Optimization of ligand



Entry	Ligand	Yield of 3a ^b (%)	3a:4a (r.r.)
1	L1	N.D.	/
2	L2	N.D.	/
3	L3	N.D.	/
4	L4	N.D.	/
5	L5	trace	/
6	L6	trace	/
7	L7	14	14:1
8	L8	45	> 19:1

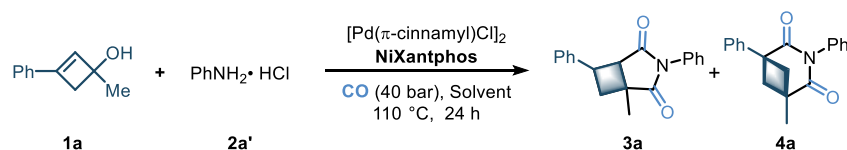
[a] [Pd(π-cinnamyl)Cl]₂ (1.25 mol%), Ligand (5 mol%), **1a** (0.12 mmol), **2a'** (0.1 mmol), CO (40 bar), DCE (1 mL) at 110 °C for 16 h. [b] The yield and r.r. ratio were determined by GC with n-hexadecane as internal standard.

Supplementary Table S3. Optimization of concentration, time and amount of **1a**

Entry	1a (mmol)	2a' (mmol)	DCE	Yield of 3a^b (%)	3a:4a (r.r.)
1	0.12	0.1	1 mL	45	> 19:1
2	0.15	0.1	1 mL	46	> 19:1
3	0.1	0.12	1 mL	37	> 19:1
4	0.1	0.15	1 mL	35	> 19:1
5	0.1	0.2	1 mL	28	> 19:1
6	0.12	0.1	0.5 mL	52	> 19:1
7	0.12	0.1	2.0 mL	23	> 19:1
8 ^c	0.12	0.1	0.5 mL	53 (50)	> 19:1
9 ^c	0.24	0.2	0.7 mL	58 (53)	> 19:1
10 ^d	0.12	0.1	0.5 mL	58	> 19:1
11 ^d	0.2	0.1	0.5 mL	59	> 19:1
12 ^d	0.3	0.1	0.5 mL	45	> 19:1

[a] $[\text{Pd}(\pi\text{-cinnamyl})\text{Cl}]_2$ (1.25 mol%), NiXantphos (5 mol%), **1a**, **2a'**, CO (40 bar), DCE at 110 °C for 16 h. [b] The yield and r.r. ratio were determined by GC with n-hexadecane as internal standard. Isolation yields in parentheses. [c] 24 h. [d] 48 h.

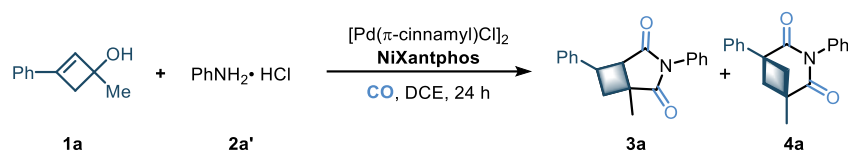
Supplementary Table S4. Optimization of solvent



Entry	Solvent	Yield of 3a^b (%)	3a:4a (r.r.)
1	DCM	47	> 19:1
2	Toluene	29	1:1
3	MeCN	45	7:1
4	THF	26	4:1
5	PhF	38	4:1
6	1,4-dioxane	40	2:1
7	DME	39	2:1
8	HFIP	N.D.	/
9	DMF	N.D.	/
10	DMAc	N.D.	/
11	DCE	58 (53)	> 19:1

[a] $[\text{Pd}(\pi\text{-cinnamyl})\text{Cl}]_2$ (1.25 mol%), NiXantphos (5 mol%), **1a** (0.24 mmol), **2a'** (0.2 mmol), CO (40 bar), Solvent (0.7 mL) at 110 °C for 24 h. [b] The yield and r.r. ratio were determined by GC with n-hexadecane as internal standard. Isolation yields in parentheses.

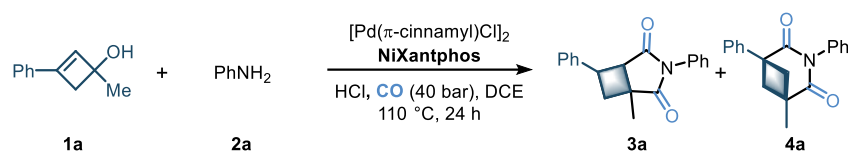
Supplementary Table S5. Optimization of pressure and temperature



Entry	Pressure (bar)	Temperature (°C)	Yield of 3a ^b (%)	3a:4a (r.r.)
1	30	110	46	> 19:1
2	40	100	54	> 19:1
3	60	110	56	> 19:1
4	60	100	54	> 19:1
5	60	90	42	> 19:1
6	40	110	58 (53)	> 19:1

[a] $[\text{Pd}(\pi\text{-cinnamyl})\text{Cl}]_2$ (1.25 mol%), NiXantphos (5 mol%), **1a** (0.24 mmol), **2a'** (0.2 mmol), CO, DCE (0.7 mL) at T °C for 24 h. [b] The yield and r.r. ratio were determined by GC with n-hexadecane as internal standard. Isolation yields in parentheses.

Supplementary Table S6. Optimization of the amount of HCl



Entry	Amount of HCl	Yield of 3a ^b (%)	3a:4a (r.r.)
1	0.2 equiv.	16	> 19:1
2	1.0 equiv.	24	> 19:1
3	1.5 equiv.	46	> 19:1
4	2.0 equiv.	62	> 19:1
5	2.5 equiv.	42	> 19:1
6	3.0 equiv.	43	> 19:1
7 ^c	0.5 equiv.	50	> 19:1
8 ^c	1.0 equiv.	55	> 19:1
9 ^d	2.0 equiv.	68 (64)	> 19:1
10 ^{d,e}	2.0 equiv.	73 (70)	> 19:1

[a] $[\text{Pd}(\pi\text{-cinnamyl})\text{Cl}]_2$ (1.25 mol%), NiXantphos (5 mol%), **1a** (0.24 mmol), **2a** (0.2 mmol), HCl (4 M in 1,4-dioxane), CO (40 bar), DCE (0.7 mL) at 110 °C for 24 h. [b] The yield and r.r. ratio were determined by GC with n-hexadecane as internal standard. Isolation yields in parentheses. [c] $\text{PhNH}_2 \cdot \text{HCl}$ instead of PhNH_2 . [d] 1.5 equiv. of **1a**. [e] Using the preformed 5 mol% NiXantphos Pd G3 complex instead of $[\text{Pd}(\pi\text{-cinnamyl})\text{Cl}]_2$ and NiXantphos.

2.2 Optimization of reaction conditions of 3-azabicyclo[3.1.1]heptane scaffolds

Supplementary Table S7. Optimization of catalyst

Entry	Pd cat.	Yield of 4a ^b (%)	4a/3a (r.r.)
1	(PPh ₃) ₄ Pd	20	3:1
2	Pd ₂ (dBa) ₃	22	4:1
3	Pd(dBa) ₂	14	5:1
4	Pd(OTf) ₂	12	4:1
5	Pd(acac) ₂	14	4:1
6	[Pd(π-cinnamyl)Cl] ₂	15	4:1
7	Pd(COD)Cl ₂	13	4:1
8	Pd(<i>t</i> Bu ₃ P) ₂	29	4:1

[a] Pd(*t*-Bu₃P)₂ (2.5 mol%), MePhos (5 mol%) **1a** (0.12 mmol), **2a'** (0.1 mmol), CO (40 bar), DCE (1 mL) at 110 °C for 16 h. [b] The yield and r.r. ratio were determined by GC with n-hexadecane as internal standard.

Supplementary Table S8. Optimization of the amount of acid

Entry	Acid	Yield of 4a ^b (%)	4a/3a (r.r.)
1	0.5 equiv. HCl	13	5:1
2	1.0 equiv. HCl	25	4:1
3	2.0 equiv. HCl	25	7:1
4	1.0 equiv. CF ₃ COOH	N.D.	/
5	1.0 equiv. PTSA·H ₂ O	N.D.	/

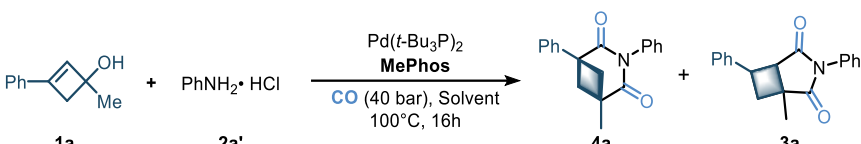
[a] Pd(*t*-Bu₃P)₂ (2.5 mol%), MePhos (5 mol%) **1a** (0.12 mmol), **2a** (0.1 mmol), CO (40 bar), DCE (1 mL) and acid at 110 °C for 16 h. [b] The yield and r.r. ratio were determined by GC with n-hexadecane as internal standard.

Supplementary Table S9. Optimization of the catalyst-ligand ratio, temperature and concentration

Entry	Pd(<i>t</i> -Bu ₃ P) ₂	MePhos	Temperature (°C)	DCE	Yield of 4a ^b (%)	4a/3a (r.r.)
1	2.5 mol%	5 mol%	90	1 mL	19	11:1
2	2.5 mol%	5 mol%	100	1 mL	25	7:1
3	2.5 mol%	5 mol%	110	1 mL	20	4:1
4	2.5 mol%	5 mol%	120	1 mL	13	3:1
5	5 mol%	10 mol%	100	1 mL	35	7:1
6	2.5 mol%	5 mol%	100	0.5 mL	24	7:1
7	2.5 mol%	5 mol%	100	0.7 mL	32	7:1
8	2.5 mol%	5 mol%	100	1.5 mL	28	4:1

[a] Pd(*t*-Bu₃P)₂, ligand, **1a** (0.12 mmol), **2a'** (0.1 mmol), CO (40 bar), DCE for 16 h. [b] The yield and r.r. ratio were determined by GC with n-hexadecane as internal standard.

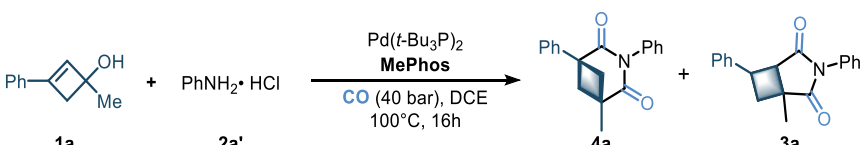
Supplementary Table S10. Optimization of solvent



Entry	Solvent	Yield of 4a ^b (%)	4a/3a (r.r.)
1	THF	11	6:1
2	MeCN	20	>19:1
3	Toluene	4	2:1
4	DCM	39	7:1
5	DCE	40	5:1
5	CHCl ₃	23	3:1
6	PhOMe	16	5:1
7	1,4-dioxane	16	7:1
8	PhCl	16	6:1
9	DMSO	ND	/
10	DMF	12	14:1
11	PhCF ₃	16	3:1
12	DME	15	6:1

[a] Pd(*t*-Bu₃P)₂ (5 mol%), MePhos (10 mol%), **1a** (0.12 mmol), **2a'** (0.1 mmol), CO (40 bar), Solvent (0.7 mL) at 100 °C for 16 h. [b] The yield and r.r. ratio were determined by GC with *n*-hexadecane as internal standard.

Supplementary Table S11. Optimization of the amount of **1a**



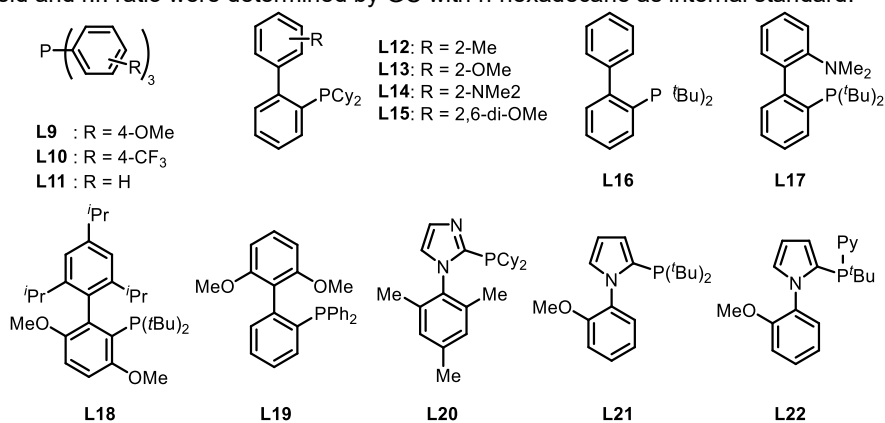
Entry	1a	2a'	Yield of 4a ^b (%)	4a/3a (r.r.)
1	0.12 mmol	0.1 mmol	40	5:1
1	0.15 mmol	0.1 mmol	46	7:1
2	0.2 mmol	0.1 mmol	49	4:1
3 ^c	0.2 mmol	0.1 mmol	53	7:1
4	0.25 mmol	0.1 mmol	32	6:1
5	0.3 mmol	0.1 mmol	34	6:1
6	0.1 mmol	0.12 mmol	26	7:1

[a] Pd(*t*-Bu₃P)₂ (5 mol%), ligand (10 mol%), **1a**, **2a'**, CO (40 bar), DCE (0.7 mL) at 100 °C for 16 h. [b] The yield and r.r. ratio were determined by GC with *n*-hexadecane as internal standard. [c] 24 h.

Supplementary Table S12. Optimization of ligand

Entry	Ligand	Yield of 4a ^b (%)	4a/3a (rr)
1	L9	11	2:1
2	L10	22	1:1
3	L11	25	2:1
10	L12	53	7:1
14	L13	29	7:1
15	L14	35	3:1
12	L15	40	> 19:1
17	L16	7	> 19:1
16	L17	19	> 19:1
11	L18	22	> 19:1
13	L19	38	9:1
18	L20	17	4:1
19	L21	22	> 19:1
20	L22	33	> 19:1
22	Without ligand	7	> 19:1

[a] Pd(*t*-Bu₃P)₂ (5 mol%), ligand (10 mol%) **1a** (0.2 mmol), **2a** (0.1 mmol), CO (40 bar), DCE (0.7 mL) at 110 °C for 24 h. [b] The yield and r.r. ratio were determined by GC with *n*-hexadecane as internal standard.



Supplementary Table S13. Optimization of solvent ratio

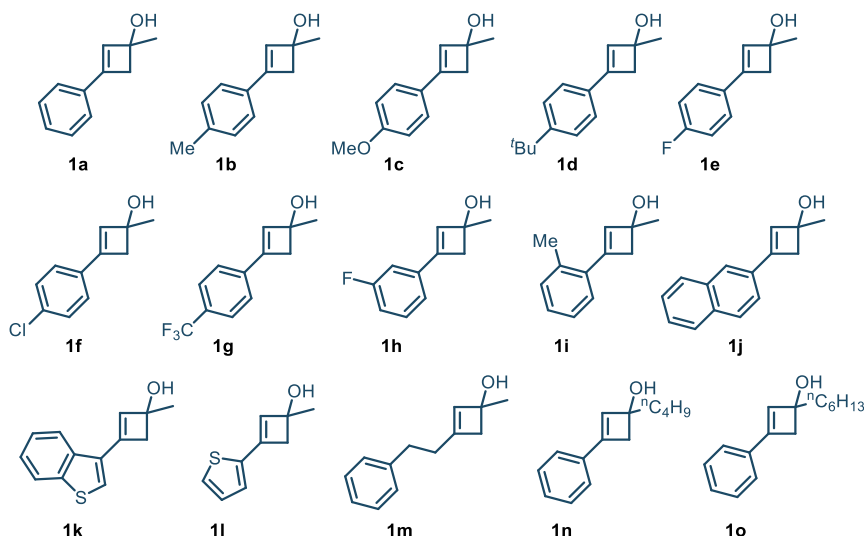
Reaction scheme: **1a** + **2a'** $\xrightarrow[\text{CO (50 bar), DCE/MeCN, 100°C, 24h}]{\text{Pd}(t\text{-Bu}_3\text{P})_2, \text{L12}}$ **4a** + **3a**

Entry	Solvent	Yield of 4a ^b (%)	4a/3a (r.r.)
1	0.65 mL DCE + 0.05 mL MeCN	51	11:1
2	0.6 mL DCE + 0.1 mL MeCN	58	>19:1
3	0.5 mL DCE + 0.2 mL MeCN	64	> 19:1
4 ^c	0.5 mL DCE + 0.2 mL MeCN	60	> 19:1
5 ^d	0.5 mL DCE + 0.2 mL MeCN	74 (71)	> 19:1
6 ^e	0.5 mL DCE + 0.2 mL MeCN	62	> 19:1
7	0.5 mL DCE + 0.3 mL MeCN	59	> 19:1
8	0.45 mL DCE + 0.25 mL MeCN	53	> 19:1
9	0.6 mL DCE + 0.2 mL MeCN	56	> 19:1

[a] Pd(*t*-Bu₃P)₂ (5 mol%), **L12** (10 mol%) **1a** (0.2 mmol), **2a'** (0.1 mmol), CO (50 bar), Solvent at 100 °C. [b] The yield and r.r. ratio were determined by GC with n-hexadecane as internal standard. Isolation yields in parentheses. [c] 40 bar CO. [d] Pd(*t*-Bu₃P)₂ (5 mol%), **L12** (15 mol%). [e] 30 h.

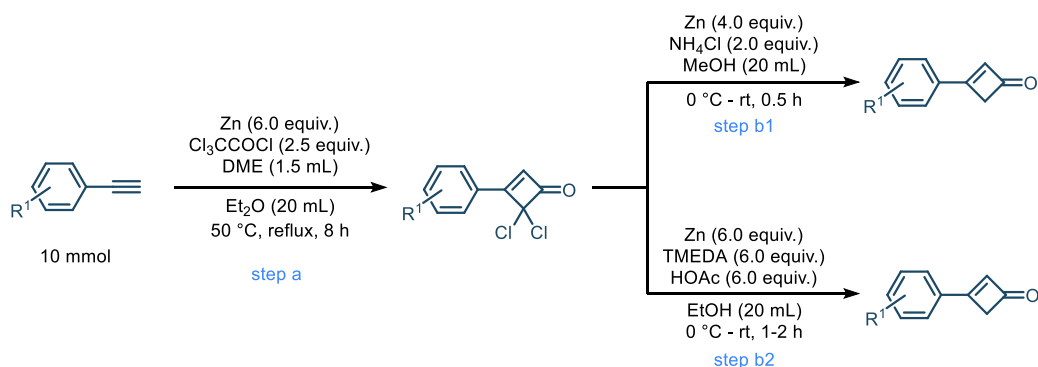
3. General Procedure for the Preparation of Cyclobutenols

3.1 List of tertiary cyclobutenols



All alkenyl cyclobutenols **1a-1o** were prepared according to the reported procedure and their characterization data match the reported data.¹

3.2 Typical procedure of tertiary cyclobutenols

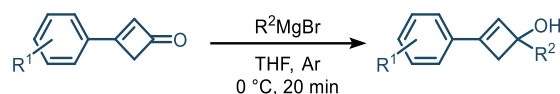


To a flame-dried 100 mL three-necked flask equipped with a magnetic stir bar were charged zinc dust (3.9 g, 60 mmol), Et_2O (20 mL), DME (1.4 g, 1.5 mL, 15 mmol), Cl_3CCOCl (4.5 g, 2.8 mL, 25 mmol), and the corresponding alkyne (10.0 mmol) under a nitrogen atmosphere. The flask was sealed and stirred at 45 °C for 8 h. After cooling to room temperature, the reaction mixture was filtered through Celite and rinsed with Et_2O . The combined organic layers were washed successively with 0.5 M HCl, 5% NaOH solution, and brine, dried over $MgSO_4$, filtered, and concentrated. The crude product was purified by column chromatography on silica gel (PE/EA = 30:1 $\rightarrow$ 20:1) to afford the dichlorocyclobutenone (step a).

To a mixture of zinc dust (2.6 g, 40 mmol), NH_4Cl (1.1 g, 20 mmol), and MeOH (5 mL) at 0 °C was added the indicated dichlorocyclobutenone (10 mmol) in MeOH (15 mL) dropwise. The reaction mixture was stirred at 0 °C for 20 min and then at room temperature for 10 min until full conversion was indicated by TLC. The mixture was filtered through Celite and concentrated. The residue was washed with saturated aqueous $NaHCO_3$ and brine, extracted with DCM, dried over $MgSO_4$, concentrated, and purified by column chromatography (PE/EA = 20:1 $\rightarrow$ 15:1) to give the corresponding cyclobutenones. Precursors **1a-1d**, **1i**, and **1n-1o** were synthesized by this method (step b1).

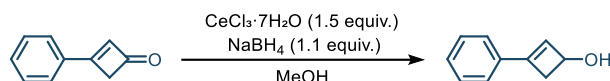
To a mixture of zinc dust (3.9 g, 60 mmol), TMEDA (7.0 g, 9.0 mL, 60 mmol), and EtOH (10 mL) at 0 °C was added HOAc (3.6 g, 3.4 mL, 60 mmol) dropwise. The indicated dichlorocyclobutenone (10 mmol) in EtOH (10 mL) was added dropwise via an addition funnel over 0.5 h. The reaction mixture was stirred at 0 °C for 20 min and then at room temperature for 1–2 h until full conversion was observed by TLC. The mixture was filtered through Celite and

concentrated. The residue was washed with 0.5 M HCl and extracted with MeOtBu. The combined organic layers were washed with saturated aqueous NaHCO₃ and brine, dried over MgSO₄, concentrated, and purified by column chromatography (PE/EA = 15:1 → 10:1) to afford the cyclobutenones. Precursors **1e-1h**, and **1j-1m** were obtained using this method (step b2).

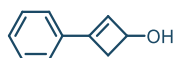


Cyclobutenonols **1a-1o** were prepared according to the following procedure. To a solution of the corresponding cyclobutenone (10 mmol) in THF (30 mL) at 0 °C under a nitrogen atmosphere was added the appropriate Grignard reagent (MeMgBr: 3.0 M in Et₂O, 3.5 mL; ⁿC₄H₉MgBr or ⁿC₆H₁₃MgBr: 1.0 M in THF, 15 mL). The reaction mixture was stirred at 0 °C for 20 min and then quenched with saturated aqueous NH₄Cl. The organic layer was washed with brine, extracted with EA, dried over MgSO₄, filtered, and concentrated. The residue was purified by silica gel column chromatography (PE/EA = 10:1 → 5:1) to afford the corresponding cyclobutenonols.

3.3 Typical procedure of **1p**



Cyclobutenone **1p** were prepared according to a known procedure.² To a solution of 3-phenylcyclobutenone (5 mmol) and CeCl₃·7H₂O (7.5 mmol) in MeOH (15 mL) at room temperature was slowly added NaBH₄ (5.5 mmol) over 15 min. The reaction mixture was stirred at the same temperature for 5 min, then quenched with brine (30 mL) and extracted with Et₂O (3 × 30 mL). The combined organic layers were dried over MgSO₄, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (PE/EA = 10:1 → 5:1) to afford the product **1p**.



3-phenylcyclobut-2-en-1-ol (**1p**)

532.9 mg, 73% yield, pale yellow solid. Eluent: pentane/ethyl acetate = 10:1, R_f = 0.2.

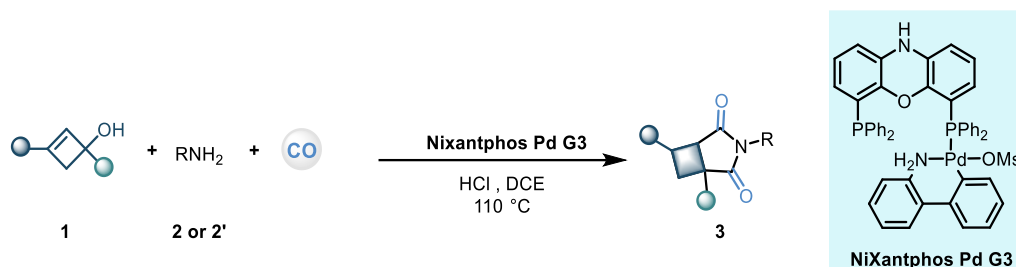
¹H NMR (400 MHz, CDCl₃) δ 7.42 – 7.28 (m, 5H), 6.38 (s, 1H), 4.79 (d, *J* = 3.9 Hz, 1H), 3.19 (dd, *J* = 13.0, 4.0 Hz, 1H), 2.60 (d, *J* = 12.9 Hz, 1H).

¹³C NMR (101 MHz, CDCl₃) δ 147.3, 133.9, 129.4, 128.8, 128.5, 125.5, 67.5, 40.6.

HRMS (ESI) (*m/z*): [M + Na]⁺ Calcd for C₁₀H₁₀ONa 169.0624; Found: 169.0627.

4. General Procedure for the Synthesis of N-Bridged Bicyclic Scaffolds

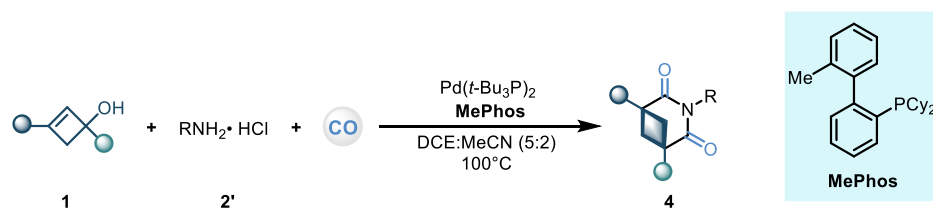
2.1 General procedure for the synthesis of 3-azabicyclo[3.2.0]heptane scaffolds



Condition A: A vial (4 mL) was charged with NiXantphos Pd G3 (5 mol%), cyclobutenol (**1**, 1.5 equiv., 0.3 mmol) and a stirring bar. The vial was closed by PTFE/white rubber septum (Wheaton 13 mm Septa) and phenolic cap and connected with atmosphere with a needle. The vial was evacuated under vacuum and recharged with argon for three times. After that, DCE (0.7 mL), amine (**2**, 0.2 mmol, 1.0 equiv.) and 2 equiv. HCl (4 M in 1,4-dioxane, 100 μL), were added with a syringe under nitrogen atmosphere. Subsequently, the vial (or several vials) was placed in an alloy plate, which was transferred into a 300 mL autoclave of the 4560 series from Parr Instruments. After flushing the autoclave three times with CO, a pressure of 40 bar of CO was adjusted at ambient temperature. Then, the reaction was performed for 24 h at 110 $^\circ\text{C}$. After the reaction was complete, the autoclave was cooled down with ice water to room temperature and the pressure was released carefully. The solution was concentrated in vacuo then purified by silica-gel column chromatography using pentane and ethyl acetate to afford the corresponding product **3a-3w**, **3aa-3ay**.

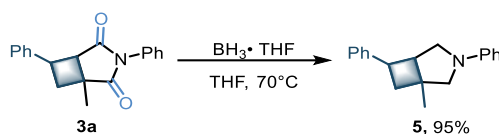
A vial (4 mL) was charged with NiXantphos-Pd G3 (5 mol%), cyclobutenol (**1**, 1.5 equiv., 0.3 mmol), amine hydrochloride (**2'**, 1.0 equiv., 0.2 mmol) and a stirring bar. The vial was closed by PTFE/white rubber septum (Wheaton 13 mm Septa) and phenolic cap and connected with atmosphere with a needle. The vial was evacuated under vacuum and recharged with argon for three times. After that, DCE (0.7 mL) was added with a syringe under nitrogen atmosphere. Subsequently, the vial (or several vials) was placed in an alloy plate, which was transferred into a 300 mL autoclave of the 4560 series from Parr Instruments. After flushing the autoclave three times with CO, a pressure of 40 bar of CO was adjusted at ambient temperature. Then, the reaction was performed for 24 h at 110 $^\circ\text{C}$. After the reaction was complete, the autoclave was cooled down with ice water to room temperature and the pressure was released carefully. The solution was concentrated in vacuo then purified by silica-gel column chromatography using pentane and ethyl acetate to afford the corresponding product **3x-3z**.

2.2 General procedure for the synthesis of 3-azabicyclo[3.1.1]heptane scaffolds

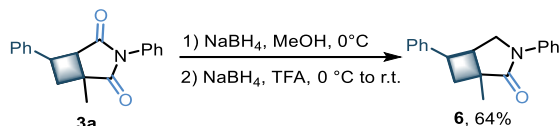


Condition B: A vial (4 mL) was charged with $\text{Pd}(t\text{-Bu}_3\text{P})_2$ (5 mol%), MePhos (15 mol%), cyclobutenol (2 equiv., 0.2 mmol), amine hydrochloride (1.0 equiv., 0.1 mmol) and a stirring bar. The vial was closed by PTFE/white rubber septum (Wheaton 13 mm Septa) and phenolic cap and connected with atmosphere with a needle. The vial was evacuated under vacuum and recharged with argon for three times. After that, DCE (0.5 mL), MeCN (0.2 mL) were added with a syringe under nitrogen atmosphere. Subsequently, the vial (or several vials) was placed in an alloy plate, which was transferred into a 300 mL autoclave of the 4560 series from Parr Instruments. After flushing the autoclave three times with CO, a pressure of 50 bar of CO was adjusted at ambient temperature. Then, the reaction was performed for 24 h at 100 $^\circ\text{C}$. After the reaction was complete, the autoclave was cooled down with ice water to room temperature and the pressure was released carefully. The solution was concentrated in vacuo then purified by silica-gel column chromatography using pentane and ethyl acetate to afford the corresponding product **4**.

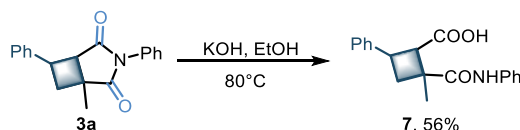
5. Synthetic Applications



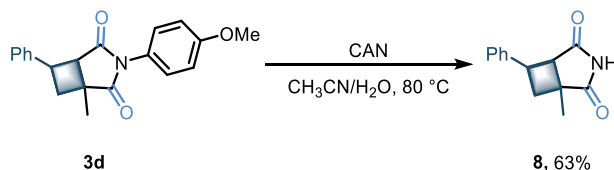
At room temperature, add **3a** (0.1 mmol, 29.1 mg), 0.5 mL THF, an oven-dried stirring bar to a 10 mL Schlenk flask, and slowly add $\text{BH}_3\cdot\text{THF}$ (4 mol/L, 0.4 mL). Then slowly heat it to 70 °C with a nitrogen balloon and keep it for 3 hours. The reaction mixture was then cooled to 0 °C. Add 1.5 mL MeOH quenched the reaction and stirred for 1 hour after returning to room temperature. The crude mixture was filtered and concentrated under vacuum. The crude product was purified by column chromatography (PE/EA =50/1) on silica gel to afford the product **5**.



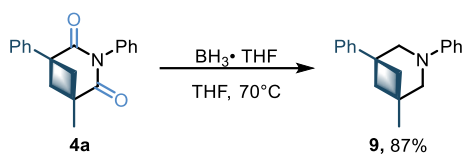
Product **6** was prepared according to a known procedure.³ **3a** (29.1 mg, 0.1 mmol), MeOH (4 mL) and a stirring bar were added into a 25 mL Schlenk tube, then NaBH_4 (18.9 mg, 0.5 mmol) was added in lots at 0 °C and the mixture was stirred at 0 °C for 12 h until this reaction was completed by TLC. Then the reaction was quenched with AcOH and concentrated to remove the solvent. The whole was then dissolved in $\text{CF}_3\text{CO}_2\text{H}$ (1 mL) at 0 °C and treated with NaBH_4 (18.9 mg, 0.5 mmol) in lots (caution: reaction is extremely vigorous!). Then reaction mixture was stirred at 0 °C for 6 h and room temperature for 12 h. When this reaction was completed, H_2O (10 mL) and ethyl acetate (25 mL) were added respectively. After separating the organic layer, the aqueous layer was extracted with ethyl acetate (20 mL x 2). The combined organic layer was washed by saturated NaCl (25 mL) and dried over anhydrous Na_2SO_4 , filtered and concentrated. The residue was purified by column chromatography (petroleum ether/ethyl acetate = 30/1) to give the pure product **6**.



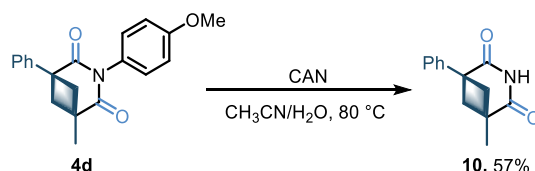
Product **7** was prepared according to a known procedure.⁴ A solution of **3a** (29.1 mg, 0.1 mmol) and KOH (28.0 mg, 0.5 mmol) in ethanol (1 mL) was stirred at 80 °C for 24 h. The solution was neutralized with an aqueous of HCl (1 M) to pH 6. The reaction mixture was concentrated in vacuo and the residue was diluted in ethyl acetate (10 mL) and water (10 mL) and extracted with ethyl acetate (2 × 10 mL). The combined organic phase was dried over Na_2SO_4 , concentrated in vacuo, and the residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 2/3) to afford the pure product **7**.



In an oven-dried 25 mL Schlenk tube, to the solution of **3d** (29.1 mg, 0.1 mmol) in CH_3CN (1.5 mL) was added CAN (265 mg, 0.5 mmol, $(\text{NH}_4)_2\text{Ce}(\text{NO}_3)_6$) in water (2 mL) at 0 °C and the mixture was stirred for 2 h at this temperature. The reaction was then stirred at 80 °C for 16 h. After the reaction was completed, the solution was extracted with ethyl acetate (20 mL x 2), washed with saturated aq. NaCl (20 mL), dried over Na_2SO_4 . The solvent was removed under reduced pressure and the resulting residue was passed through a column of silica gel (petroleum ether/ethyl acetate = 2/1) to remove the impurities and concentrated to give compound **8**.



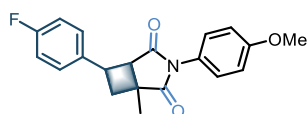
At room temperature, add **4a** (0.1 mmol, 29.1 mg), 0.5 mL THF, an oven-dried stirring bar to a 10 mL Schlenk flask, and slowly add $\text{BH}_3\cdot\text{THF}$ (4 mol/L, 0.4 mL). Then slowly heat it to 70 °C with a nitrogen balloon and keep it for 3 hours. The reaction mixture was then cooled to 0 °C. Add 1.5 mL MeOH quenched the reaction and stirred for 1 hour after returning to room temperature. The crude mixture was filtered and concentrated under vacuum. The crude product was purified by column chromatography (PE/EA = 50/1) on silica gel to afford the product **9**.



In an oven-dried 25 mL Schlenk tube, to the solution of **3d** (29.1 mg, 0.1 mmol) in CH_3CN (1.5 mL) was added CAN (265 mg, 0.5 mmol, $(\text{NH}_4)_2\text{Ce}(\text{NO}_3)_6$) in water (2 mL) at 0 °C and the mixture was stirred for 2 h at this temperature. The reaction was then stirred at 80 °C for 16 h. After the reaction was completed, the solution was extracted with ethyl acetate (20 mL x 2), washed with saturated aq. NaCl (20 mL), dried over Na_2SO_4 . The solvent was removed under reduced pressure and the resulting residue was passed through a column of silica gel (PE/EA = 5/1) to remove the impurities and concentrated to give compound **10**.

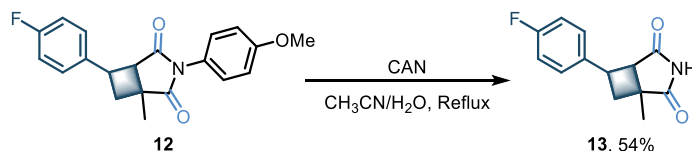
6. Target Synthesis

6.1 Gram-scale synthesis of **11**



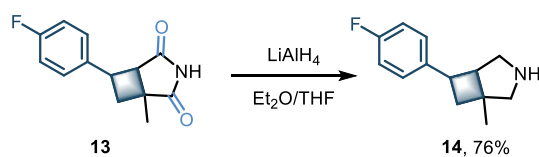
In a glovebox, a beaker was charged with NiXantphos Pd G3 (5 mol%), **1e** (1.5 equiv., 3 mmol), p-anisidine (1.0 equiv., 2 mmol), DCE (7 mL), 2 equiv. HCl (4 M in 1,4-dioxane, 1.0 mL), and a stirring bar. The beaker was transferred into a Parr 4560 series autoclave (300 mL), which was then removed from the glovebox. After flushing the autoclave three times with CO, the pressure was adjusted to 40 bar of CO at ambient temperature. The sealed autoclave was then heated at 110 °C for 24 h. Upon completion, the autoclave was cooled to room temperature using an ice-water bath, and the pressure was carefully released. The reaction mixture was concentrated in vacuo and purified by silica gel column chromatography (PE/EA = 5:1) to afford the corresponding product **11** (427.3 mg, 63% yield).

6.2 synthesis of **12**



In an oven-dried 25 mL Schlenk tube, to the solution of **12** (135.6 mg, 1.0 equiv., 0.4 mmol,) in CH_3CN (4 mL) was added CAN (1.09 g, 5.0 equiv., 2 mmol, $(\text{NH}_4)_2\text{Ce}(\text{NO}_3)_6$) in water (8 mL) at 0 °C and the mixture was stirred for 2 h at this temperature. The reaction was then stirred at 100 °C for 24 h. After the reaction was completed, the solution was extracted with ethyl acetate (20 mL x 2), washed with saturated aq. NaCl (20 mL), dried over Na_2SO_4 . The solvent was removed under reduced pressure and the resulting residue was passed through a column of silica gel (PE/EA = 7/1) to remove the impurities and concentrated to give compound **12**.

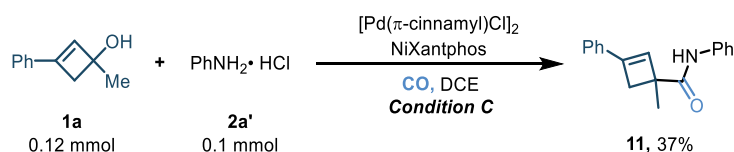
6.2 synthesis of **13**



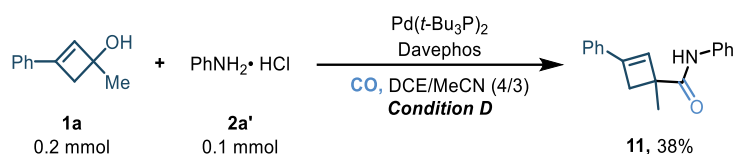
In an oven-dried 25 mL Schlenk tube, to a solution of **13** (46.6 mg, 1.0 equiv., 0.20 mmol) in Et_2O (2 mL) and THF (1.5 mL) was added LiAlH_4 (22.7 mg, 3.0 equiv., 0.6 mmol) at 0 °C. The mixture was then heated to reflux and stirred for 2 h. After cooling to room temperature, water (0.1 mL) was added dropwise, followed by saturated aqueous K_2CO_3 (0.4 mL). The resulting precipitate was filtered off, and the filtrate was extracted with EA, dried over Na_2SO_4 . The solvent was removed under reduced pressure and the resulting residue was passed through a column of silica gel (PE/EA = 1/2) to remove the impurities and concentrated to give compound **13**.

7. Mechanistic Studies

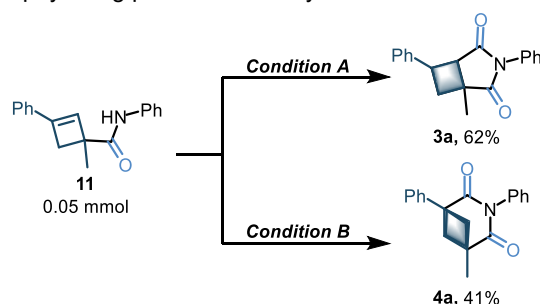
7.1 Intermediate verification experiment



Conditions C: A vial (4 mL) was charged with $[\text{Pd}(\pi\text{-cinnamyl})\text{Cl}]_2$ (1.25 mol%), NiXantphos (5 mol%), cyclobutenol (1.2 equiv., 0.12 mmol), aniline hydrochloride (1.0 equiv., 0.1 mmol) and a stirring bar. The vial was closed by PTFE/white rubber septum (Wheaton 13 mm Septa) and phenolic cap and connected with atmosphere with a needle. The vial was evacuated under vacuum and recharged with argon for three times. After that, DCE (1.0 mL) was added with a syringe under nitrogen atmosphere. Subsequently, the vial (or several vials) was placed in an alloy plate, which was transferred into a 300 mL autoclave of the 4560 series from Parr Instruments. After flushing the autoclave three times with CO, a pressure of 40 bar of CO was adjusted at ambient temperature. Then, the reaction was performed for 16 h at 60 °C. After the reaction was complete, the autoclave was cooled down with ice water to room temperature and the pressure was released carefully. The solution was concentrated in vacuo then purified by silica-gel column chromatography using pentane and ethyl acetate to afford the corresponding product 11.



Conditions D: A vial (4 mL) was charged with $\text{Pd}(t\text{-Bu}_3\text{P})_2$ (1.25 mol%), Davephos (5 mol%), cyclobutenol (2 equiv., 0.2 mmol), aniline hydrochloride (1.0 equiv., 0.1 mmol) and a stirring bar. The vial was closed by PTFE/white rubber septum (Wheaton 13 mm Septa) and phenolic cap and connected with atmosphere with a needle. The vial was evacuated under vacuum and recharged with argon for three times. After that, DCE (0.4 mL), MeCN (0.3 mL) was added with a syringe under nitrogen atmosphere. Subsequently, the vial (or several vials) was placed in an alloy plate, which was transferred into a 300 mL autoclave of the 4560 series from Parr Instruments. After flushing the autoclave three times with CO, a pressure of 40 bar of CO was adjusted at ambient temperature. Then, the reaction was performed for 8 h at 100 °C. After the reaction was complete, the autoclave was cooled down with ice water to room temperature and the pressure was released carefully. The solution was concentrated in vacuo then purified by silica-gel column chromatography using pentane and ethyl acetate to afford the corresponding product 11.

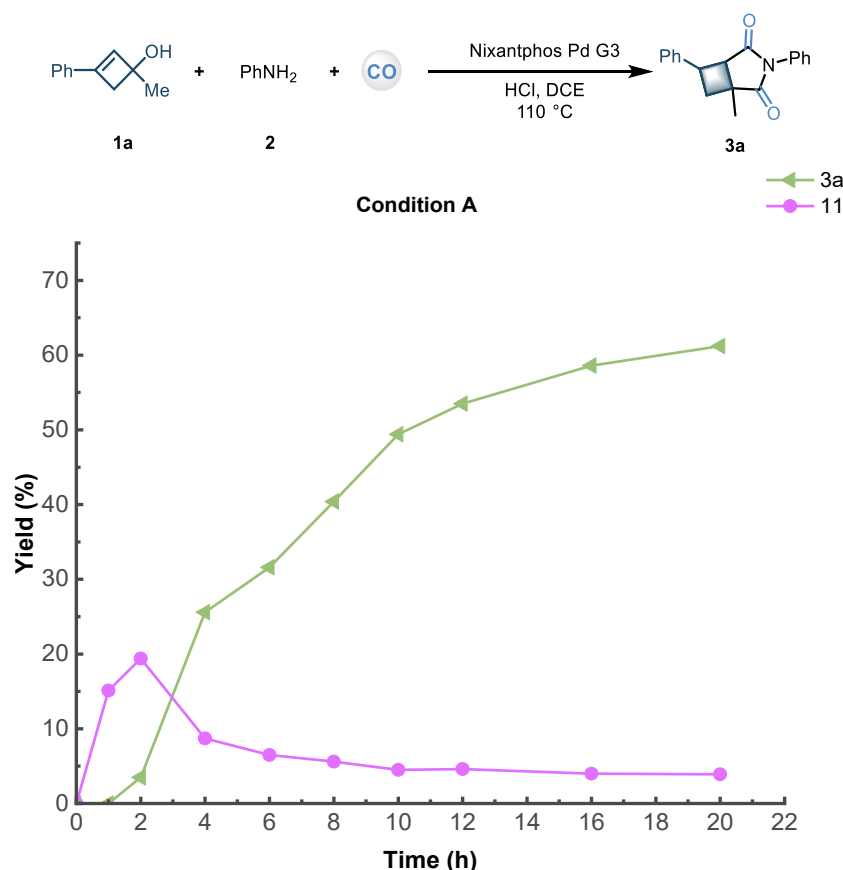


Condition A: A vial (4 mL) was charged with NiXantphos-Pd G3 (5 mol%), 11 (1.0 equiv., 0.05 mmol) and a stirring bar. The vial was closed by PTFE/white rubber septum (Wheaton 13 mm Septa) and phenolic cap and connected with atmosphere with a needle. The vial was evacuated under vacuum and recharged with argon for three times. After that, DCE (0.35 mL) and 2 equiv. HCl (4 M in 1,4-dioxane, 25 μL), were added with a syringe under nitrogen atmosphere. Subsequently, the vial (or several vials) was placed in an alloy plate, which was transferred into a 300 mL autoclave of the 4560 series from Parr Instruments. After flushing the autoclave three times with CO, a pressure of 40 bar of CO was adjusted at ambient temperature. Then, the reaction was performed for 24 h at 110 °C. After the reaction was complete, the autoclave was cooled down with ice water to room temperature and the pressure was released carefully. The solution was concentrated in vacuo then purified by silica-gel column chromatography using pentane and ethyl acetate to afford the corresponding product 3a.

Condition B: A vial (4 mL) was charged with $\text{Pd}(t\text{-Bu}_3\text{P})_2$ (5 mol%), MePhos (15 mol%), 11 (1 equiv., 0.05 mmol), aniline hydrochloride (2a, 1.0 equiv., 0.05 mmol) and a stirring bar. The vial was closed by PTFE/white rubber

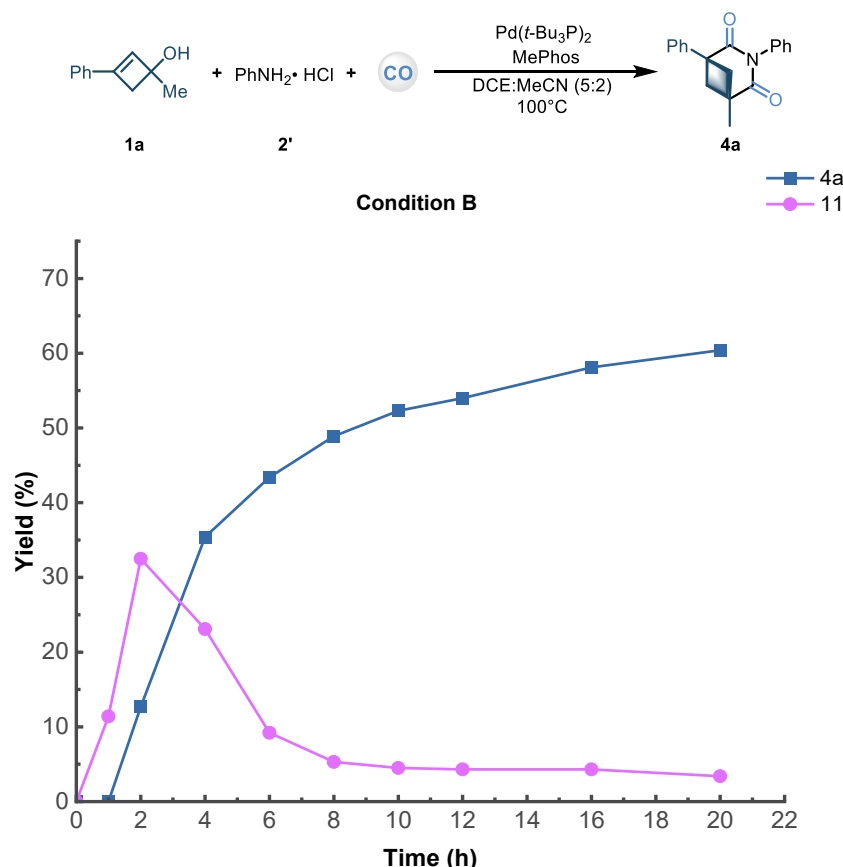
septum (Wheaton 13 mm Septa) and phenolic cap and connected with atmosphere with a needle. The vial was evacuated under vacuum and recharged with argon for three times. After that, DCE (0.25 mL), MeCN (0.1 mL) were added with a syringe under nitrogen atmosphere. Subsequently, the vial (or several vials) was placed in an alloy plate, which was transferred into a 300 mL autoclave of the 4560 series from Parr Instruments. After flushing the autoclave three times with CO, a pressure of 50 bar of CO was adjusted at ambient temperature. Then, the reaction was performed for 24 h at 100 °C. After the reaction was complete, the autoclave was cooled down with ice water to room temperature and the pressure was released carefully. The solution was concentrated in vacuo then purified by silica-gel column chromatography using pentane and ethyl acetate to afford the corresponding product **4a**.

7.2 Kinetic studies



Supplementary Fig. 1. Kinetic studies of 3-azabicyclo[3.2.0]heptane.

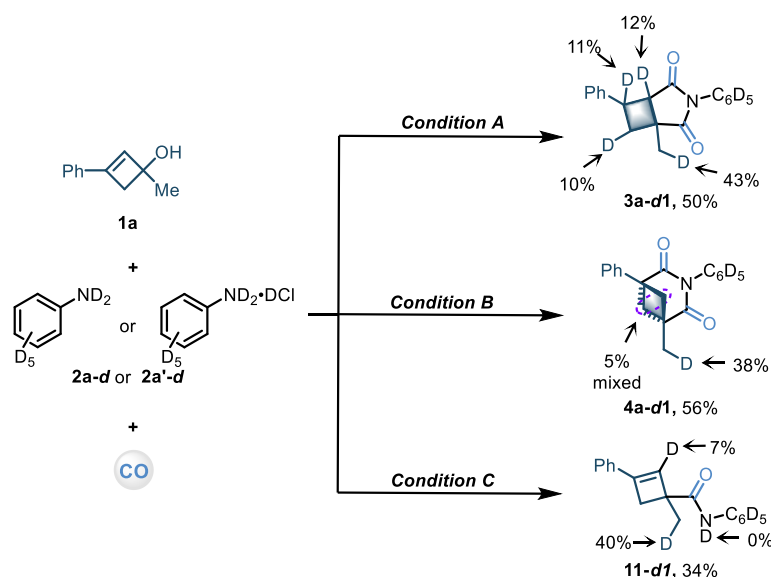
A vial (4 mL) was charged with NiXantphos-Pd G3 (5 mol%), cyclobutenol (**1a**, 1.5 equiv., 0.3 mmol) and a stirring bar. The vial was closed by PTFE/white rubber septum (Wheaton 13 mm Septa) and phenolic cap and connected with atmosphere with a needle. The vial was evacuated under vacuum and recharged with argon for three times. After that, DCE (0.7 mL), aniline (**2a**, 0.2 mmol, 1.0 equiv.) and 2 equiv. HCl (4 M in 1,4-dioxane, 100 μ L), were added with a syringe under nitrogen atmosphere. Subsequently, the vial (or several vials) was placed in an alloy plate, which was transferred into a 300 mL autoclave of the 4560 series from Parr Instruments. After flushing the autoclave three times with CO, a pressure of 40 bar of CO was adjusted at ambient temperature. The reaction mixture was heated to 110 °C. After the reaction was complete, the autoclave was cooled down with ice water to room temperature and the pressure was released carefully. Subsequently, 10 μ L of n-hexadecane was added to the reaction mixture as an internal standard and mixed thoroughly. The yields were determined using GC-FID analysis. The experiments were conducted independently at various reaction times: 1.0 h, 2.0 h, 4.0 h, 6.0 h, 8.0 h, 10.0 h, 12.0 h, 16.0 h, and 20.0h.



Supplementary Fig. 2. Kinetic studies of 3-azabicyclo[3.1.1]heptane.

A vial (4 mL) was charged with $\text{Pd}(t\text{-Bu}_3\text{P})_2$ (5 mol%), MePhos (15 mol%), cyclobutenol (**1a**, 2 equiv., 0.2 mmol), aniline hydrochloride (**2a'**, 1.0 equiv., 0.1 mmol) and a stirring bar. The vial was closed by PTFE/white rubber septum (Wheaton 13 mm Septa) and phenolic cap and connected with atmosphere with a needle. The vial was evacuated under vacuum and recharged with argon for three times. After that, DCE (0.5 mL), MeCN (0.2 mL) were added with a syringe under nitrogen atmosphere. Subsequently, the vial (or several vials) was placed in an alloy plate, which was transferred into a 300 mL autoclave of the 4560 series from Parr Instruments. After flushing the autoclave three times with CO, a pressure of 50 bar of CO was adjusted at ambient temperature. aluminum block. The reaction mixture was heated to 100 °C. After the reaction was complete, the autoclave was cooled down with ice water to room temperature and the pressure was released carefully. Subsequently, 10 μL of *n*-hexadecane was added to the reaction mixture as an internal standard and mixed thoroughly. The yields were determined using GC-FID analysis. The experiments were conducted independently at various reaction times: 1.0 h, 2.0 h, 4.0 h, 6.0 h, 8.0 h, 10.0 h, 12.0 h, 16.0 h, and 20.0 h.

7.3 Isotopic labeling studies

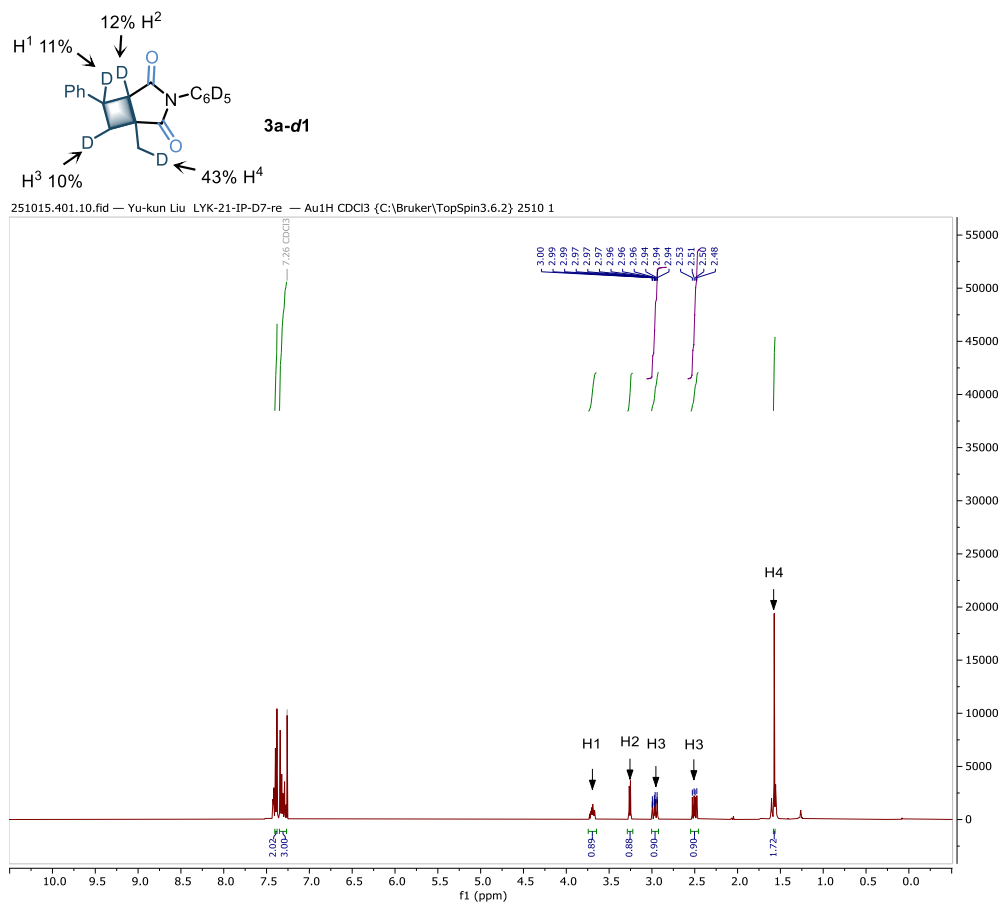


Condition A: A vial (4 mL) was charged with NiXantphos-Pd G3 (5 mol%), cyclobutenol (1.5 equiv., 0.3 mmol) and a stirring bar. The vial was closed by PTFE/white rubber septum (Wheaton 13 mm Septa) and phenolic cap and connected with atmosphere with a needle. The vial was evacuated under vacuum and recharged with argon for three times. After that, DCE (0.7 mL), aniline- d_7 (**2a-d**, 0.2 mmol, 1.0 equiv.) and 2 equiv. HCl (4 M in 1,4-dioxane, 100 μL), were added with a syringe under nitrogen atmosphere. Subsequently, the vial (or several vials) was placed in an alloy plate, which was transferred into a 300 mL autoclave of the 4560 series from Parr Instruments. After flushing the autoclave three times with CO, a pressure of 40 bar of CO was adjusted at ambient temperature. Then, the reaction was performed for 24 h at 110 $^\circ\text{C}$. After the reaction was complete, the autoclave was cooled down with ice water to room temperature and the pressure was released carefully. The solution was concentrated in vacuo then purified by silica-gel column chromatography using pentane and ethyl acetate to afford the corresponding product **3a-d1**.

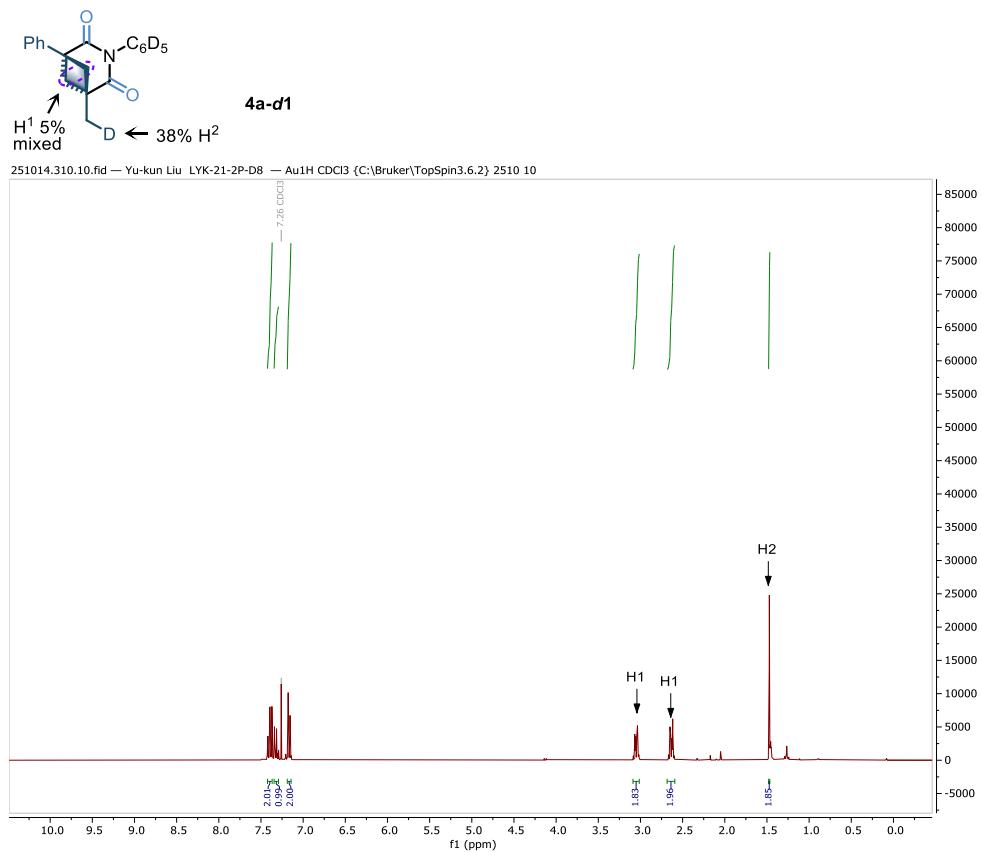
Condition B: A vial (4 mL) was charged with $\text{Pd}(t\text{-Bu}_3\text{P})_2$ (5 mol%), MePhos (15 mol%), cyclobutenol (2 equiv., 0.2 mmol), aniline hydrochloride- d_8 (**2a'-d**, 1.0 equiv., 0.1 mmol) and a stirring bar. The vial was closed by PTFE/white rubber septum (Wheaton 13 mm Septa) and phenolic cap and connected with atmosphere with a needle. The vial was evacuated under vacuum and recharged with argon for three times. After that, DCE (0.5 mL), MeCN (0.2 mL) were added with a syringe under nitrogen atmosphere. Subsequently, the vial (or several vials) was placed in an alloy plate, which was transferred into a 300 mL autoclave of the 4560 series from Parr Instruments. After flushing the autoclave three times with CO, a pressure of 50 bar of CO was adjusted at ambient temperature. Then, the reaction was performed for 24 h at 100 $^\circ\text{C}$. After the reaction was complete, the autoclave was cooled down with ice water to room temperature and the pressure was released carefully. The solution was concentrated in vacuo then purified by silica-gel column chromatography using pentane and ethyl acetate to afford the corresponding product **4a-d1**.

Condition C: A vial (4 mL) was charged with $[\text{Pd}(\pi\text{-cinnamyl})\text{Cl}]_2$ (1.25 mol%), NiXantphos (5 mol%), cyclobutenol (1.2 equiv., 0.12 mmol), aniline hydrochloride- d_8 (**2a'-d**, 1.0 equiv., 0.1 mmol) and a stirring bar. The vial was closed by PTFE/white rubber septum (Wheaton 13 mm Septa) and phenolic cap and connected with atmosphere with a needle. The vial was evacuated under vacuum and recharged with argon for three times. After that, DCE (0.4 mL), MeCN (0.3 mL) were added with a syringe under nitrogen atmosphere. Subsequently, the vial (or several vials) was placed in an alloy plate, which was transferred into a 300 mL autoclave of the 4560 series from Parr Instruments. After flushing the autoclave three times with CO, a pressure of 40 bar of CO was adjusted at ambient temperature. Then, the reaction was performed for 16 h at 60 $^\circ\text{C}$. After the reaction was complete, the autoclave was cooled down with ice water to room temperature and the pressure was released carefully. The solution was concentrated in vacuo then purified by silica-gel column chromatography using pentane and ethyl acetate to afford the corresponding product **11-d1**.

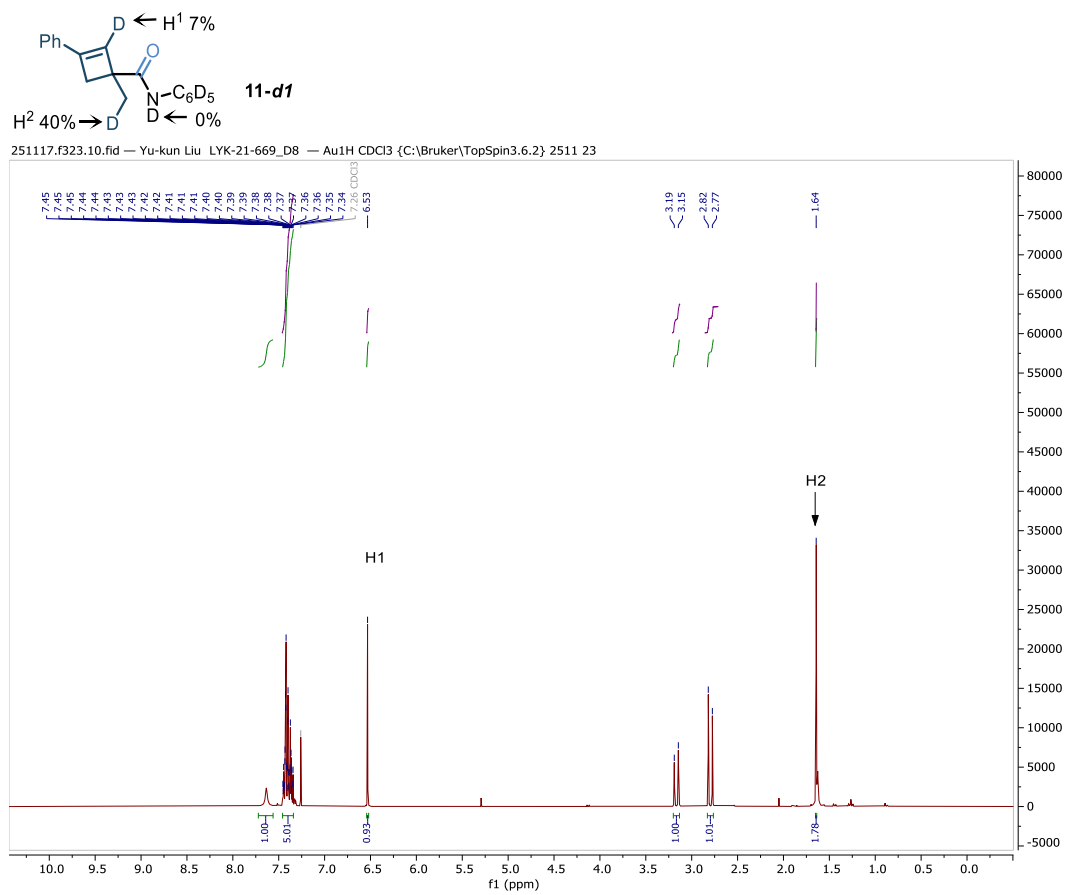
Supplementary Fig. 3. NMR of compound 3a-d1 (400 MHz, CDCl₃).



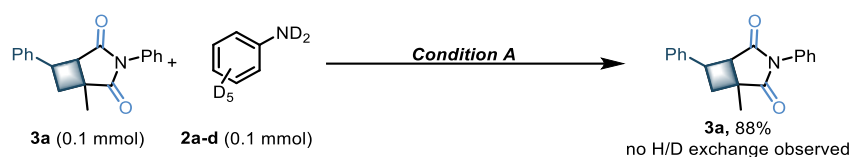
Supplementary Fig. 4. NMR of compound 4a-d1 (300 MHz, CDCl₃).



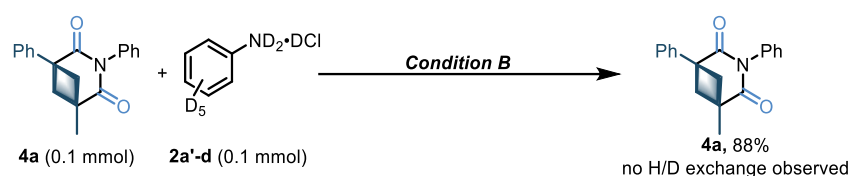
Supplementary Fig. 5. NMR of compound 11-*d*1 (300 MHz, CDCl₃).



7.4 H/D exchange experiments

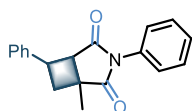


A vial (4 mL) was charged with NiXantphos-Pd G3 (5 mol%), **3a** (1.0 equiv., 0.1 mmol) and a stirring bar. The vial was closed by PTFE/white rubber septum (Wheaton 13 mm Septa) and phenolic cap and connected with atmosphere with a needle. The vial was evacuated under vacuum and recharged with argon for three times. After that, DCE (0.7 mL), aniline-d₇ (**2a-d**, 0.1 mmol, 1.0 equiv.) and 2 equiv. HCl (4 M in 1,4-dioxane, 50 μ L), were added with a syringe under nitrogen atmosphere. Subsequently, the vial (or several vials) was placed in an alloy plate, which was transferred into a 300 mL autoclave of the 4560 series from Parr. Instruments. After flushing the autoclave three times with CO, a pressure of 40 bar of CO was adjusted at ambient temperature. Then, the reaction was performed for 24 h at 110 $^{\circ}$ C. After the reaction was complete, the autoclave was cooled down with ice water to room temperature and the pressure was released carefully. The solution was concentrated in vacuo then purified by silica-gel column chromatography using pentane and ethyl acetate to afford the corresponding product **3a**. The ^1H NMR spectra of product **3a** showed no detectable deuterium incorporation.



A vial (4 mL) was charged with Pd(*t*-Bu₃P)₂ (5 mol%), MePhos (15 mol%), **4a** (1 equiv., 0.1 mmol), aniline hydrochloride-d₈ (**2a'-d**, 1.0 equiv., 0.1 mmol) and a stirring bar. The vial was closed by PTFE/white rubber septum (Wheaton 13 mm Septa) and phenolic cap and connected with atmosphere with a needle. The vial was evacuated under vacuum and recharged with argon for three times. After that, DCE (0.5 mL), MeCN (0.2 mL) were added with a syringe under nitrogen atmosphere. Subsequently, the vial (or several vials) was placed in an alloy plate, which was transferred into a 300 mL autoclave of the 4560 series from Parr. Instruments. After flushing the autoclave three times with CO, a pressure of 50 bar of CO was adjusted at ambient temperature. Then, the reaction was performed for 24 h at 100 $^{\circ}$ C. After the reaction was complete, the autoclave was cooled down with ice water to room temperature and the pressure was released carefully. The solution was concentrated in vacuo then purified by silica-gel column chromatography using pentane and ethyl acetate to afford the corresponding product **4a**. The ^1H NMR spectra of product **4a** showed no detectable deuterium incorporation.

8. Spectroscopic Data of Products



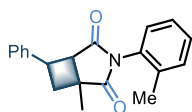
1-methyl-3,6-diphenyl-3-azabicyclo[3.2.0]heptane-2,4-dione (3a)

41.0 mg, 70% yield, white solid. Eluent: pentane/ethyl acetate = 10:1, R_f = 0.3, r.r. > 19:1, d.r. > 20:1.

^1H NMR (300 MHz, CDCl_3) δ 7.47 – 7.40 (m, 2H), 7.37 – 7.34 (m, 1H), 7.33 – 7.31 (m, 2H), 7.30 – 7.20 (m, 5H), 3.62 (td, J = 8.8, 5.5 Hz, 1H), 3.18 (d, J = 5.9 Hz, 1H), 2.89 (dddd, J = 12.8, 9.3, 3.5, 0.9 Hz, 1H), 2.42 (dd, J = 12.8, 8.2 Hz, 1H), 1.49 (s, 3H).

^{13}C NMR (75 MHz, CDCl_3) δ 181.4, 177.2, 142.2, 132.3, 129.3, 129.0, 128.8, 127.2, 126.6, 126.6, 52.1, 41.7, 39.5, 36.9, 21.0.

HRMS (ESI-TOF): m/z calcd. for $[\text{M} + \text{Na}]^+$ $\text{C}_{19}\text{H}_{17}\text{NO}_2\text{Na}^+$ 314.1151; Found: 314.1151.



1-methyl-6-phenyl-3-(o-tolyl)-3-azabicyclo[3.2.0]heptane-2,4-dione (3b)

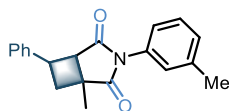
32.4 mg, 53% yield, dr = 1:1.4, white solid. Eluent: pentane/ethyl acetate = 15:1, R_f = 0.3, r.r. > 19:1, d.r. > 20:1.

^1H NMR (300 MHz, CDCl_3) δ 7.46 – 7.31 (m, 8H), 7.24 – 7.13 (m, 1H), 3.76 (td, J = 8.7, 5.5 Hz, 1H), 3.34 – 3.29 (m, 1H), 3.07 – 2.97 (m, 1H), 2.60 – 2.49 (m, 1H), 2.32 (s, 1.75H), 2.19 (s, 1.25H), 1.61 (d, J = 1.8 Hz, 3H).

^{13}C NMR (75 MHz, CDCl_3) δ 181.4, 181.3, 177.2, 177.1, 142.2, 142.1, 135.8, 135.7, 131.4, 131.4, 129.7, 129.0, 128.9, 128.4, 127.8, 127.2, 127.2, 127.2, 126.6, 52.5, 52.2, 42.2, 42.0, 39.6, 39.6, 37.0, 36.6, 21.3, 20.9, 17.8, 17.7.

(Duplicated ^{13}C resonances and minor duplication of certain ^1H signals are attributed to slowly interconverting amide rotamers; no diastereomeric mixture was detected by ^1H NMR)

HRMS (ESI-TOF): m/z calcd. for $[\text{M} + \text{Na}]^+$ $\text{C}_{20}\text{H}_{19}\text{NO}_2\text{Na}^+$ 328.1308; Found: 328.1311.



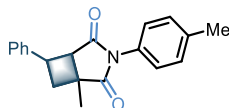
1-methyl-6-phenyl-3-(m-tolyl)-3-azabicyclo[3.2.0]heptane-2,4-dione (3c)

38.3 mg, 63% yield, white solid. Eluent: pentane/ethyl acetate = 30:1, R_f = 0.3, r.r. > 19:1, d.r. > 20:1.

^1H NMR (300 MHz, CDCl_3) δ 7.34 – 7.28 (m, 3H), 7.27 – 7.19 (m, 3H), 7.18 – 7.13 (m, 1H), 7.10 – 7.05 (m, 2H), 3.61 (td, J = 8.5, 5.5 Hz, 1H), 3.16 (d, J = 5.5 Hz, 1H), 2.88 (dddd, J = 12.8, 9.3, 3.5, 0.9 Hz, 1H), 2.41 (dd, J = 12.8, 8.3 Hz, 1H), 2.34 (s, 3H), 1.48 (s, 3H).

^{13}C NMR (75 MHz, CDCl_3) δ 181.5, 177.3, 142.2, 139.4, 132.1, 129.7, 129.2, 129.0, 127.2, 126.6, 123.7, 52.1, 41.7, 39.5, 36.9, 21.5, 21.0.

HRMS (ESI-TOF): m/z calcd. for $[\text{M} + \text{Na}]^+$ $\text{C}_{20}\text{H}_{19}\text{NO}_2\text{Na}^+$ 328.1308; Found: 328.1319.



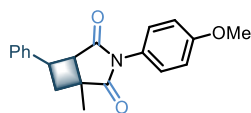
1-methyl-6-phenyl-3-(p-tolyl)-3-azabicyclo[3.2.0]heptane-2,4-dione (3d)

37.7 mg, 62% yield, white solid. Eluent: pentane/ethyl acetate = 15:1, R_f = 0.3, r.r. > 19:1, d.r. > 20:1.

^1H NMR (300 MHz, CDCl_3) δ 7.45 – 7.38 (m, 2H), 7.37 – 7.30 (m, 5H), 7.29 – 7.24 (m, 3H), 3.71 (td, J = 8.7, 5.4 Hz, 1H), 3.27 (dd, J = 5.5, 0.8 Hz, 1H), 2.98 (dddd, J = 12.8, 9.3, 3.5, 0.9 Hz, 1H), 2.51 (dd, J = 12.8, 8.2 Hz, 1H), 2.43 (s, 3H), 1.59 (s, 3H).

^{13}C NMR (75 MHz, CDCl_3) δ 181.5, 177.4, 142.2, 138.8, 130.0, 129.6, 129.0, 127.2, 126.6, 126.4, 52.1, 41.7, 39.5, 36.9, 21.4, 21.1.

HRMS (ESI-TOF): m/z calcd. for $[\text{M} + \text{Na}]^+$ $\text{C}_{20}\text{H}_{19}\text{NO}_2\text{Na}^+$ 328.1308; Found: 328.1307.



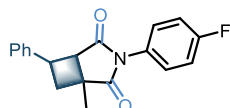
3-(4-methoxyphenyl)-1-methyl-6-phenyl-3-azabicyclo[3.2.0]heptane-2,4-dione (3e)

42.2 mg, 66% yield, white solid. Eluent: pentane/ethyl acetate = 10:1, R_f = 0.2, r.r. > 19:1, d.r. > 20:1.

^1H NMR (400 MHz, CDCl_3) δ 7.45 – 7.39 (m, 2H), 7.37 – 7.34 (m, 2H), 7.33 – 7.28 (m, 3H), 7.06 – 7.02 (m, 2H), 3.87 (s, 3H), 3.70 (td, J = 8.7, 5.6 Hz, 1H), 3.26 (d, J = 5.3 Hz, 1H), 2.98 (dddd, J = 12.8, 9.3, 3.5, 0.9 Hz, 1H), 2.51 (dd, J = 12.8, 8.2 Hz, 1H), 1.58 (s, 3H).

^{13}C NMR (101 MHz, CDCl_3) δ 181.6, 177.5, 159.6, 142.2, 128.9, 127.8, 127.2, 126.6, 124.9, 114.6, 55.6, 52.0, 41.6, 39.5, 36.9, 21.0.

HRMS (ESI-TOF): m/z calcd. for $[\text{M} + \text{Na}]^+$ $\text{C}_{20}\text{H}_{19}\text{NO}_3\text{Na}^+$ 344.1257; Found: 344.1260.



3-(4-fluorophenyl)-1-methyl-6-phenyl-3-azabicyclo[3.2.0]heptane-2,4-dione (3f)

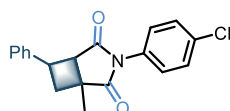
42.4 mg, 68% yield, white solid (95% purity). Eluent: pentane/ethyl acetate = 30:1, R_f = 0.2, r.r. > 19:1, d.r. > 20:1.

^1H NMR (300 MHz, CDCl_3) δ 7.43 – 7.27 (m, 7H), 7.24 – 7.15 (m, 2H), 3.68 (td, J = 8.7, 5.5 Hz, 1H), 3.25 (dd, J = 5.5, 0.8 Hz, 1H), 2.96 (dddd, J = 12.8, 9.3, 3.5, 0.9 Hz, 1H), 2.50 (dd, J = 12.8, 8.2 Hz, 1H), 1.57 (s, 3H).

^{13}C NMR (75 MHz, CDCl_3) δ 181.3, 177.1, 162.3 (d, J = 248.5 Hz), 142.1, 129.0, 128.4 (d, J = 8.8 Hz), 128.2 (d, J = 3.4 Hz), 127.3, 126.6, 116.3 (d, J = 23.0 Hz), 52.0, 41.7, 39.5, 36.9, 21.0.

^{19}F NMR (282 MHz, CDCl_3) δ -112.26 – -112.35 (m).

HRMS (ESI-TOF): m/z calcd. for $[\text{M} + \text{Na}]^+$ $\text{C}_{19}\text{H}_{16}\text{FNO}_2\text{Na}^+$ 332.1057; Found: 332.1059.



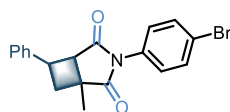
3-(4-chlorophenyl)-1-methyl-6-phenyl-3-azabicyclo[3.2.0]heptane-2,4-dione (3g)

40.6 mg, 62%, white solid. Eluent: pentane/ethyl acetate = 30:1, R_f = 0.3, r.r. > 19:1, d.r. > 20:1.

^1H NMR (300 MHz, CDCl_3) δ 7.38 – 7.33 (m, 2H), 7.30 – 7.23 (m, 3H), 7.22 – 7.13 (m, 4H), 3.55 (td, J = 8.8, 5.5 Hz, 1H), 3.13 (d, J = 5.4 Hz, 0H), 2.83 (dddd, J = 12.8, 9.3, 3.5, 0.9 Hz, 1H), 2.38 (dd, J = 12.8, 8.3 Hz, 1H), 1.44 (s, 3H).

^{13}C NMR (75 MHz, CDCl_3) δ 181.1, 176.9, 142.0, 134.5, 130.7, 129.5, 129.0, 127.8, 127.3, 126.5, 52.0, 41.8, 39.5, 36.9, 21.0.

HRMS (ESI-TOF): m/z calcd. for $[\text{M} + \text{Na}]^+$ $\text{C}_{19}\text{H}_{16}\text{ClNO}_2\text{Na}^+$ 348.0762; Found: 348.0767.



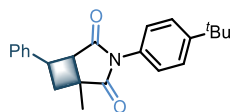
3-(4-bromophenyl)-1-methyl-6-phenyl-3-azabicyclo[3.2.0]heptane-2,4-dione (3h)

46.5 mg, 63% yield, white solid. Eluent: pentane/ethyl acetate = 30:1, R_f = 0.4.

^1H NMR (300 MHz, CDCl_3) δ 7.57 – 7.46 (m, 2H), 7.31 – 7.24 (m, 2H), 7.22 – 7.13 (m, 5H), 3.61 – 3.51 (m, 1H), 3.13 (d, J = 5.5 Hz, 1H), 2.83 (dddd, J = 12.8, 9.3, 3.5, 0.9 Hz, 1H), 2.38 (dd, J = 12.8, 8.2 Hz, 1H), 1.44 (s, 3H).

^{13}C NMR (75 MHz, CDCl_3) δ 181.0, 176.8, 142.0, 132.5, 131.3, 129.0, 128.0, 127.3, 126.5, 122.5, 52.0, 41.8, 39.5, 36.8, 21.0.

HRMS (ESI-TOF): m/z calcd. for $[\text{M} + \text{Na}]^+$ $\text{C}_{19}\text{H}_{16}\text{BrNO}_2\text{Na}^+$ 392.0257; Found: 392.0255.



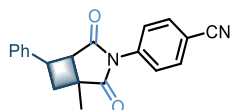
3-(4-(tert-butyl)phenyl)-1-methyl-6-phenyl-3-azabicyclo[3.2.0]heptane-2,4-dione (3i)

44.2 mg, 64% yield, white solid. Eluent: pentane/ethyl acetate = 10:1, R_f = 0.3, r.r. > 19:1, d.r. > 20:1.

^1H NMR (300 MHz, CDCl_3) δ 7.58 – 7.52 (m, 2H), 7.45 – 7.30 (m, 7H), 3.71 (td, J = 8.7, 5.4 Hz, 1H), 3.28 (d, J = 5.4 Hz, 1H), 2.99 (dddd, J = 12.8, 9.3, 3.5, 0.9 Hz, 1H), 2.52 (dd, J = 12.8, 8.2 Hz, 1H), 1.59 (s, 3H), 1.38 (s, 9H).

¹³C NMR (75 MHz, CDCl₃) δ 181.5, 177.4, 151.7, 142.2, 129.5, 128.9, 127.2, 126.6, 126.3, 126.0, 52.0, 41.7, 39.5, 36.9, 34.9, 31.4, 21.0.

HRMS (ESI-TOF): m/z calcd. for [M + Na]⁺ C₂₃H₂₅NO₂Na⁺ 370.1777; Found: 370.1786.



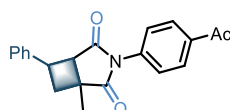
4-(1-methyl-2,4-dioxo-6-phenyl-3-azabicyclo[3.2.0]heptan-3-yl)benzonitrile (3j)

37.9 mg, 60% yield, white solid. Eluent: pentane/ethyl acetate = 10:1, R_f = 0.2, r.r. > 19:1, d.r. > 20:1.

¹H NMR (300 MHz, CDCl₃) δ 7.84 – 7.77 (m, 2H), 7.65 – 7.57 (m, 2H), 7.43 – 7.37 (m, 2H), 7.34 – 7.29 (m, 3H), 3.69 (td, *J* = 8.8, 5.4 Hz, 1H), 3.28 (d, *J* = 5.4 Hz, 1H), 2.97 (dddd, *J* = 12.9, 9.3, 3.5, 0.9 Hz, 1H), 2.53 (dd, *J* = 12.9, 8.3 Hz, 1H), 1.58 (s, 3H).

¹³C NMR (75 MHz, CDCl₃) δ 180.7, 176.4, 141.8, 136.3, 133.1, 129.1, 127.4, 127.0, 126.5, 112.3, 52.0, 41.8, 39.5, 36.9, 21.0.

HRMS (ESI-TOF): m/z calcd. for [M + Na]⁺ C₂₀H₁₆N₂O₂Na⁺ 339.1104; Found: 339.1105.



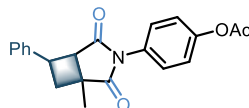
3-(4-acetylphenyl)-1-methyl-6-phenyl-3-azabicyclo[3.2.0]heptane-2,4-dione (3k)

38.5 mg, 50% yield, white solid. Eluent: pentane/ethyl acetate = 10:1, R_f = 0.2, r.r. > 19:1, d.r. > 20:1.

¹H NMR (400 MHz, CDCl₃) δ 8.13 – 8.00 (m, 2H), 7.56 – 7.52 (m, 2H), 7.42 – 7.37 (m, 2H), 7.34 – 7.27 (m, 3H), 3.71 (td, *J* = 8.8, 5.5 Hz, 1H), 3.28 (d, *J* = 5.4 Hz, 1H), 2.97 (dddd, *J* = 12.9, 9.3, 3.5, 0.9 Hz, 1H), 2.64 (s, 3H), 2.55 – 2.49 (m, 1H), 1.58 (s, 3H).

¹³C NMR (101 MHz, CDCl₃) δ 197.2, 180.9, 176.7, 141.9, 136.8, 136.4, 129.3, 129.0, 127.3, 126.5, 126.5, 52.0, 41.8, 39.5, 36.9, 26.8, 21.0.

HRMS (ESI-TOF): m/z calcd. for [M + H]⁺ C₂₁H₂₀NO₃⁺ 334.1438; Found: 334.1445.



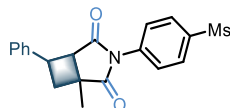
methyl 4-(1-methyl-2,4-dioxo-6-phenyl-3-azabicyclo[3.2.0]heptan-3-yl)benzoate (3l)

35.2 mg, 50% yield, white solid. Eluent: pentane/ethyl acetate = 10:1, R_f = 0.3, r.r. > 19:1, d.r. > 20:1.

¹H NMR (400 MHz, CDCl₃) δ 8.21 – 8.16 (m, 2H), 7.55 – 7.50 (m, 2H), 7.43 – 7.37 (m, 2H), 7.35 – 7.27 (m, 3H), 3.94 (s, 3H), 3.70 (td, *J* = 8.8, 5.5 Hz, 1H), 3.27 (d, *J* = 5.4 Hz, 1H), 2.97 (dddd, *J* = 12.8, 9.3, 3.5, 0.9 Hz, 1H), 2.51 (dd, *J* = 12.8, 8.2 Hz, 1H), 1.57 (s, 3H).

¹³C NMR (101 MHz, CDCl₃) δ 180.9, 176.7, 166.3, 142.0, 136.3, 130.6, 130.1, 129.0, 127.3, 126.5, 126.3, 52.5, 52.0, 41.8, 39.5, 36.9, 21.0.

HRMS (ESI-TOF): m/z calcd. for [M + H]⁺ C₂₁H₁₉NO₄Na⁺ 372.1206; Found: 372.1211.



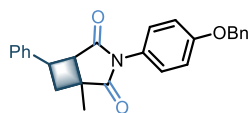
1-methyl-3-(4-(methylsulfonyl)phenyl)-6-phenyl-3-azabicyclo[3.2.0]heptane-2,4-dione (3m)

28.8 mg, 39% yield, white solid. Eluent: pentane/ethyl acetate = 5:3, R_f = 0.3, r.r. > 19:1, d.r. > 20:1.

¹H NMR (300 MHz, CDCl₃) δ 8.12 – 8.07 (m, 2H), 7.71 – 7.66 (m, 2H), 7.44 – 7.37 (m, 2H), 7.35 – 7.29 (m, 3H), 3.71 (td, *J* = 8.7, 5.4 Hz, 1H), 3.30 (d, *J* = 5.5 Hz, 1H), 3.08 (s, 3H), 2.98 (dddd, *J* = 12.9, 9.4, 3.5, 0.9 Hz, 1H), 2.54 (dd, *J* = 12.9, 8.3 Hz, 1H), 1.59 (s, 3H).

¹³C NMR (75 MHz, CDCl₃) δ 180.7, 176.4, 141.8, 140.3, 137.1, 129.1, 128.6, 127.4, 127.2, 126.5, 52.0, 44.7, 41.9, 39.5, 36.9, 21.0.

HRMS (ESI-TOF): m/z calcd. for [M + Na]⁺ C₂₀H₁₉NO₄SN⁺ 392.0927; Found: 392.0925.



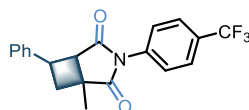
3-(4-(benzyloxy)phenyl)-1-methyl-6-phenyl-3-azabicyclo[3.2.0]heptane-2,4-dione (3n)

37.2 mg, 47% yield, white solid. Eluent: pentane/ethyl acetate = 5:1, R_f = 0.4, r.r. > 19:1, d.r. > 20:1.

^1H NMR (300 MHz, CDCl_3) δ 7.46 – 7.40 (m, 3H), 7.40 – 7.31 (m, 5H), 7.31 – 7.24 (m, 3H), 7.10 – 7.05 (m, 2H), 5.09 (s, 2H), 3.66 (td, J = 8.7, 5.4 Hz, 1H), 3.22 (dd, J = 5.6, 0.8 Hz, 1H), 2.94 (dddd, J = 12.8, 9.3, 3.5, 0.9 Hz, 1H), 2.47 (dd, J = 12.8, 8.2 Hz, 1H), 1.54 (s, 3H).

^{13}C NMR (75 MHz, CDCl_3) δ 181.6, 177.4, 158.8, 142.2, 136.7, 129.0, 128.8, 128.2, 127.8, 127.6, 127.2, 126.6, 125.1, 115.5, 70.4, 52.0, 41.6, 39.5, 36.9, 21.0.

HRMS (ESI-TOF): m/z calcd. for $[\text{M} + \text{Na}]^+ \text{C}_{26}\text{H}_{23}\text{NO}_3\text{Na}^+$ 420.1570; Found: 420.1581.



1-methyl-6-phenyl-3-(4-(trifluoromethyl)phenyl)-3-azabicyclo[3.2.0]heptane-2,4-dione (3o)

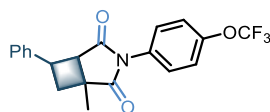
27.4 mg, 38% yield, white solid. Eluent: pentane/ethyl acetate = 50:1, R_f = 0.3, r.r. > 19:1, d.r. > 20:1.

^1H NMR (300 MHz, CDCl_3) δ 7.78 (d, J = 8.3 Hz, 2H), 7.57 (d, J = 8.3 Hz, 2H), 7.45 – 7.37 (m, 2H), 7.35 – 7.27 (m, 3H), 3.71 (td, J = 8.7, 5.5 Hz, 1H), 3.28 (d, J = 5.5 Hz, 1H), 2.98 (dddd, J = 12.9, 9.3, 3.5, 0.9 Hz, 1H), 2.53 (dd, J = 12.8, 8.3 Hz, 1H), 1.58 (s, 3H).

^{13}C NMR (75 MHz, CDCl_3) δ 180.9, 176.7, 141.9, 135.4, 129.0, 127.4, 126.8, 126.5, 126.4 (q, J = 3.7 Hz), 52.0, 41.8, 39.5, 36.9, 21.0.

^{19}F NMR (282 MHz, CDCl_3) δ -62.69 (s).

HRMS (ESI-TOF): m/z calcd. for $[\text{M} + \text{Na}]^+ \text{C}_{20}\text{H}_{16}\text{F}_3\text{NO}_2\text{Na}^+$ 382.1025; Found: 382.1031.



1-methyl-6-phenyl-3-(4-(trifluoromethoxy)phenyl)-3-azabicyclo[3.2.0]heptane-2,4-dione (3p)

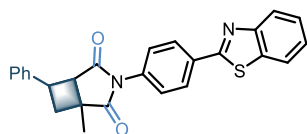
27.6 mg, 37% yield, white solid. Eluent: pentane/ethyl acetate = 30:1, R_f = 0.3, r.r. > 19:1, d.r. > 20:1.

^1H NMR (400 MHz, CDCl_3) δ 7.48 – 7.44 (m, 2H), 7.42 – 7.27 (m, 7H), 3.69 (td, J = 8.8, 5.5 Hz, 1H), 3.28 – 3.25 (m, 1H), 2.96 (dddd, J = 12.8, 9.3, 3.5, 0.9 Hz, 1H), 2.52 (dd, J = 12.8, 8.3 Hz, 1H), 1.57 (s, 3H).

^{13}C NMR (101 MHz, CDCl_3) δ 181.1, 176.9, 148.9 (d, J = 2.1 Hz), 142.0, 130.7, 129.0, 128.0, 127.3, 126.5, 121.8, 52.0, 41.8, 39.5, 36.9, 21.0.

^{19}F NMR (282 MHz, CDCl_3) δ -57.85 (s).

HRMS (ESI-TOF): m/z calcd. for $[\text{M} + \text{Na}]^+ \text{C}_{20}\text{H}_{16}\text{F}_3\text{NO}_3\text{Na}^+$ 398.0974; Found: 398.0977.



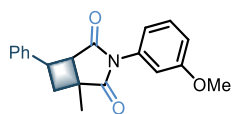
3-(4-(benzo[d]thiazol-2-yl)phenyl)-1-methyl-6-phenyl-3-azabicyclo[3.2.0]heptane-2,4-dione (3q)

35.1 mg, 42% yield, white solid. Eluent: pentane/ethyl acetate = 10:1, R_f = 0.4, r.r. > 19:1, d.r. > 20:1.

^1H NMR (300 MHz, CDCl_3) δ 8.29 – 8.19 (m, 2H), 8.10 (d, J = 8.3 Hz, 1H), 7.93 (d, J = 7.9 Hz, 1H), 7.60 – 7.49 (m, 3H), 7.45 – 7.27 (m, 6H), 3.73 (td, J = 8.7, 5.5 Hz, 1H), 3.29 (d, J = 5.4 Hz, 1H), 2.99 (dddd, J = 12.8, 9.3, 3.5, 0.9 Hz, 1H), 2.53 (dd, J = 12.8, 8.2 Hz, 1H), 1.59 (s, 3H).

^{13}C NMR (75 MHz, CDCl_3) δ 181.1, 176.8, 166.8, 154.3, 142.0, 135.3, 134.5, 133.7, 129.0, 128.3, 127.3, 126.9, 126.6, 126.6, 125.6, 123.6, 121.8, 52.0, 41.8, 39.5, 36.9, 21.1.

HRMS (ESI-TOF): m/z calcd. for $[\text{M} + \text{Na}]^+ \text{C}_{26}\text{H}_{20}\text{N}_2\text{O}_2\text{SNa}^+$ 447.1137; Found: 447.1150.



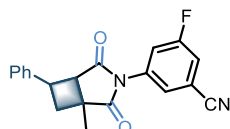
3-(3-methoxyphenyl)-1-methyl-6-phenyl-3-azabicyclo[3.2.0]heptane-2,4-dione (3r)

29.0 mg, 45% yield, white solid. Eluent: pentane/ethyl acetate = 6:1, R_f = 0.3, r.r. > 19:1, d.r. > 20:1.

¹H NMR (300 MHz, CDCl₃) δ 7.44 – 7.37 (m, 3H), 7.35 – 7.28 (m, 3H), 6.99 – 6.94 (m, 2H), 6.92 – 6.89 (m, 1H), 3.84 (s, 3H), 3.70 (td, *J* = 8.8, 5.5 Hz, 1H), 3.25 (d, *J* = 5.4 Hz, 1H), 2.97 (dddd, *J* = 12.8, 9.3, 3.5, 0.9 Hz, 1H), 2.50 (dd, *J* = 12.8, 8.2 Hz, 1H), 1.57 (s, 3H).

¹³C NMR (75 MHz, CDCl₃) δ 181.3, 177.1, 160.3, 142.2, 133.3, 130.0, 129.0, 127.2, 126.6, 118.8, 114.8, 112.3, 55.6, 52.0, 41.7, 39.5, 36.9, 21.0.

HRMS (ESI-TOF): *m/z* calcd. for [M + Na]⁺ C₂₀H₁₉NO₃Na⁺ 344.1257; Found: 344.1267.



3-fluoro-5-(1-methyl-2,4-dioxo-6-phenyl-3-azabicyclo[3.2.0]heptan-3-yl)benzonitrile (3s)

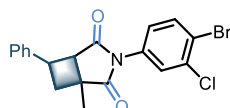
26 mg, 39%, white solid. Eluent: pentane/ethyl acetate = 10:1, *R_f* = 0.3. r.r. > 19:1, d.r. > 20:1.

¹H NMR (300 MHz, CDCl₃) δ 7.67 – 7.65 (m, 1H), 7.54 (ddd, *J* = 9.1, 2.4, 1.8 Hz, 1H), 7.44 – 7.38 (m, 3H), 7.34 – 7.29 (m, 3H), 3.69 (td, *J* = 8.8, 5.5 Hz, 1H), 3.31 – 3.28 (m, 1H), 2.96 (dddd, *J* = 12.9, 9.3, 3.5, 0.9 Hz, 1H), 2.54 (dd, *J* = 12.9, 8.3 Hz, 1H), 1.58 (s, 3H).

¹³C NMR (75 MHz, CDCl₃) δ 180.3, 176.0, 163.9, 160.6, 141.6, 134.8 (d, *J* = 10.6 Hz), 129.1, 127.5, 126.5, 125.8 (d, *J* = 3.7 Hz), 119.0 (d, *J* = 14.3 Hz), 118.7 (d, *J* = 14.2 Hz), 114.4 (d, *J* = 10.5 Hz), 51.8, 41.8, 39.5, 36.9, 21.0.

¹⁹F NMR (282 MHz, CDCl₃) δ -107.25 (t, *J* = 8.4 Hz).

HRMS (ESI-TOF): *m/z* calcd. for [M + Na]⁺ C₂₀H₁₅FN₂O₂Na⁺ 357.1010; Found: 357.1015.



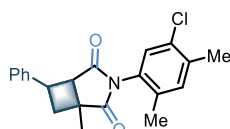
3-(4-bromo-3-chlorophenyl)-1-methyl-6-phenyl-3-azabicyclo[3.2.0]heptane-2,4-dione (3t)

46.9 mg, 56% yield, white solid. Eluent: pentane/ethyl acetate = 10:1, *R_f* = 0.2, r.r. > 19:1, d.r. > 20:1.

¹H NMR (300 MHz, CDCl₃) δ 7.75 (d, *J* = 8.6 Hz, 1H), 7.57 (d, *J* = 2.4 Hz, 1H), 7.43 – 7.36 (m, 2H), 7.33 – 7.29 (m, 2H), 7.22 (dd, *J* = 8.6, 2.4 Hz, 1H), 3.74 – 3.61 (m, 1H), 3.26 (d, *J* = 5.4 Hz, 1H), 2.95 (dddd, *J* = 12.8, 9.3, 3.5, 0.9 Hz, 1H), 2.51 (dd, *J* = 12.8, 8.3 Hz, 1H), 1.56 (s, 3H).

¹³C NMR (75 MHz, CDCl₃) δ 180.7, 176.4, 141.8, 135.2, 134.2, 132.2, 129.0, 128.3, 127.3, 126.5, 125.9, 122.7, 51.9, 41.8, 39.5, 36.8, 21.0.

HRMS (ESI-TOF): *m/z* calcd. for [M + Na]⁺ C₁₉H₁₅BrClNO₂Na⁺ 425.9867; Found: 425.9872.



3-(5-chloro-2,4-dimethylphenyl)-1-methyl-6-phenyl-3-azabicyclo[3.2.0]heptane-2,4-dione (3u)

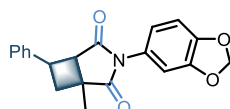
43.0 mg, 61% yield, white solid (95% purity). Eluent: pentane/ethyl acetate = 10:1, *R_f* = 0.2, r.r. > 19:1, d.r. > 20:1.

¹H NMR (400 MHz, CDCl₃) δ 7.48 – 7.41 (m, 2H), 7.41 – 7.30 (m, 4H), 6.67 (d, *J* = 6.0 Hz, 1H), 4.00 (d, *J* = 1.3 Hz, 3H), 3.94 (s, 2H), 3.88 (s, 1H), 3.84 – 3.71 (m, 1H), 3.33 – 3.25 (m, 1H), 3.01 (dddd, *J* = 12.3, 9.2, 2.9, 0.9 Hz, 1H), 2.53 (dt, *J* = 12.8, 8.6 Hz, 1H), 1.60 (d, *J* = 2.7 Hz, 3H).

¹³C NMR (101 MHz, CDCl₃) δ 181.6, 181.4, 177.3, 177.2, 156.8, 154.8, 154.7, 142.4, 142.2, 130.5, 130.0, 128.9, 127.2, 127.1, 126.7, 126.6, 114.2, 113.9, 97.4, 97.4, 56.6, 56.6, 56.6, 56.4, 42.3, 42.0, 39.6, 39.5, 36.9, 36.7, 21.1, 20.9.

(Duplicated ¹³C resonances and minor duplication of certain ¹H signals are attributed to slowly interconverting amide rotamers; no diastereomeric mixture was detected by ¹H NMR)

HRMS (ESI-TOF): *m/z* calcd. for [M + H]⁺ C₂₁H₂₀ClNO₂Na⁺ 376.1075; Found: 376.1077.



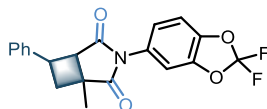
3-(benzo[d][1,3]dioxol-5-yl)-1-methyl-6-phenyl-3-azabicyclo[3.2.0]heptane-2,4-dione (3v)

35.3 mg, 53% yield, white solid. Eluent: pentane/ethyl acetate = 10:3, *R_f* = 0.2, r.r. > 19:1, d.r. > 20:1.

¹H NMR (300 MHz, CDCl₃) δ 7.35 – 7.28 (m, 2H), 7.27 – 7.20 (m, 3H), 6.86 – 6.82 (m, 1H), 6.77 – 6.71 (m, 2H), 5.95 (s, 2H), 3.59 (td, *J* = 8.8, 5.5 Hz, 1H), 3.16 (d, *J* = 5.5 Hz, 1H), 2.87 (dddd, *J* = 12.8, 9.3, 3.5, 0.9 Hz, 1H), 2.47 – 2.37 (m, 1H), 1.48 (s, 3H).

¹³C NMR (75 MHz, CDCl₃) δ 181.5, 177.3, 148.3, 148.0, 142.1, 129.0, 127.2, 126.6, 125.8, 120.5, 108.6, 107.8, 102.0, 51.9, 41.7, 39.5, 36.9, 21.0.

HRMS (ESI-TOF): *m/z* calcd. for [M + Na]⁺ C₂₀H₁₇NO₄Na⁺ 358.1049; Found: 358.1053.



3-(2,2-difluorobenzo[d][1,3]dioxol-5-yl)-1-methyl-6-phenyl-3-azabicyclo[3.2.0]heptane-2,4-dione (3w)

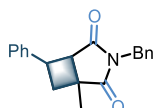
31.0 mg, 42% yield, white solid. Eluent: pentane/ethyl acetate = 10:1, *R_f* = 0.3, r.r. > 19:1, d.r. > 20:1.

¹H NMR (300 MHz, CDCl₃) δ 7.43 – 7.36 (m, 2H), 7.34 – 7.27 (m, 3H), 7.21 – 7.10 (m, 3H), 3.68 (td, *J* = 8.8, 5.5 Hz, 1H), 3.27 (d, *J* = 5.5 Hz, 1H), 2.96 (dddd, *J* = 12.9, 9.3, 3.5, 0.9 Hz, 1H), 2.52 (dd, *J* = 12.9, 8.3 Hz, 1H), 1.57 (s, 3H).

¹³C NMR (75 MHz, CDCl₃) δ 181.1, 176.9, 144.0, 143.6, 141.9, 131.9 (t, *J* = 255.1), 129.0, 127.8, 127.3, 126.5, 122.4, 109.8, 108.9, 51.9, 41.8, 39.5, 36.9, 21.0.

¹⁹F NMR (282 MHz, CDCl₃) δ -49.51 (s).

HRMS (ESI-TOF): *m/z* calcd. for [M + Na]⁺ C₂₀H₁₅NO₄Na⁺ 394.0816; Found: 394.0823.



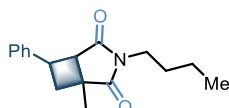
3-benzyl-1-methyl-6-phenyl-3-azabicyclo[3.2.0]heptane-2,4-dione (3x)

18.4 mg, 30% yield, white solid. pentane/ethyl acetate = 30:1, *R_f* = 0.2, r.r. > 19:1, d.r. > 20:1.

¹H NMR (300 MHz, CDCl₃) δ 7.43 – 7.35 (m, 4H), 7.35 – 7.30 (m, 3H), 7.27 (dt, *J* = 1.3, 0.8 Hz, 2H), 7.26 – 7.22 (m, 1H), 4.74 (d, *J* = 2.0 Hz, 2H), 3.43 (td, *J* = 8.7, 5.4 Hz, 1H), 3.13 – 3.07 (m, 1H), 2.79 (ddd, *J* = 12.7, 9.3, 0.9 Hz, 1H), 2.39 (dd, *J* = 12.8, 8.1 Hz, 1H), 1.44 (s, 3H).

¹³C NMR (75 MHz, CDCl₃) δ 182.0, 177.8, 142.3, 136.2, 128.9, 128.6, 128.1, 127.1, 126.5, 51.9, 42.7, 41.7, 39.1, 36.5, 20.8.

HRMS (ESI-TOF): *m/z* calcd. for [M + Na]⁺ C₂₀H₁₉NO₂Na⁺ 328.1308; Found: 328.1315.



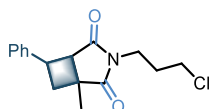
3-butyl-1-methyl-6-phenyl-3-azabicyclo[3.2.0]heptane-2,4-dione (3y)

14.6 mg, 27% yield, colorless oil. pentane/ethyl acetate = 30:1, *R_f* = 0.3, r.r. > 19:1, d.r. > 20:1.

¹H NMR (400 MHz, CDCl₃) δ 7.39 – 7.34 (m, 2H), 7.30 – 7.24 (m, 3H), 3.58 (td, *J* = 7.3, 1.1 Hz, 2H), 3.50 – 3.42 (m, 1H), 3.07 (d, *J* = 5.5 Hz, 1H), 2.80 (dddd, *J* = 12.7, 9.3, 3.5, 0.9 Hz, 1H), 2.39 (dd, *J* = 12.8, 8.1 Hz, 1H), 1.64 – 1.59 (m, 2H), 1.44 (s, 3H), 1.41 – 1.32 (m, 2H), 0.96 (t, *J* = 7.3 Hz, 3H).

¹³C NMR (101 MHz, CDCl₃) δ 182.4, 178.3, 142.4, 128.9, 127.1, 126.6, 51.9, 41.5, 39.3, 38.8, 36.6, 29.9, 20.8, 20.2, 13.8.

HRMS (ESI-TOF): *m/z* calcd. for [M + H]⁺ C₁₇H₂₂NO₂⁺ 272.1645; Found: 272.1647.



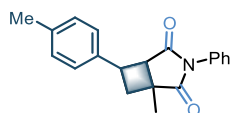
3-(3-chloropropyl)-1-methyl-6-phenyl-3-azabicyclo[3.2.0]heptane-2,4-dione (3z)

17.5 mg, 30% yield, colorless oil. pentane/ethyl acetate = 30:1, *R_f* = 0.3, r.r. > 19:1, d.r. > 20:1.

¹H NMR (300 MHz, CDCl₃) δ 7.38 – 7.31 (m, 2H), 7.27 – 7.20 (m, 3H), 3.75 – 3.68 (m, 2H), 3.55 (t, *J* = 6.5 Hz, 2H), 3.46 (td, *J* = 8.6, 5.3 Hz, 1H), 3.07 (d, *J* = 5.4 Hz, 1H), 2.79 (dddd, *J* = 12.8, 9.3, 3.5, 0.8 Hz, 1H), 2.37 (dd, *J* = 12.8, 8.1 Hz, 1H), 2.11 (p, *J* = 6.7 Hz, 2H), 1.43 (s, 3H).

¹³C NMR (75 MHz, CDCl₃) δ 182.2, 178.1, 142.3, 128.9, 127.1, 126.5, 51.8, 42.3, 41.6, 39.2, 37.0, 36.5, 30.7, 20.8.

HRMS (ESI-TOF): *m/z* calcd. for [M + Na]⁺ C₁₆H₁₅ClNO₂Na⁺ 314.0918; Found: 314.0914.



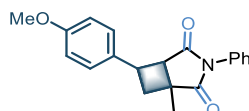
1-methyl-3-phenyl-6-(p-tolyl)-3-azabicyclo[3.2.0]heptane-2,4-dione (3aa)

43.8 mg, 72% yield, white solid. Eluent: pentane/ethyl acetate = 30:1, R_f = 0.3, r.r. > 19:1, d.r. > 20:1.

^1H NMR (300 MHz, CDCl_3) δ 7.55 – 7.48 (m, 2H), 7.45 – 7.36 (m, 3H), 7.25 – 7.15 (m, 4H), 3.66 (td, J = 8.7, 5.4 Hz, 1H), 3.23 (d, J = 5.5 Hz, 1H), 2.95 (dddd, J = 12.8, 9.3, 3.5, 0.9 Hz, 1H), 2.48 (dd, J = 12.8, 8.2 Hz, 1H), 2.37 (s, 3H), 1.57 (s, 3H).

^{13}C NMR (75 MHz, CDCl_3) δ 181.4, 177.2, 139.2, 136.9, 132.3, 129.6, 129.3, 128.7, 126.6, 126.5, 52.2, 41.7, 39.2, 37.0, 21.2, 21.0.

HRMS (ESI-TOF): m/z calcd. for $[\text{M} + \text{Na}]^+$ $\text{C}_{20}\text{H}_{19}\text{NO}_2\text{Na}^+$ 328.1308; Found: 328.1318.



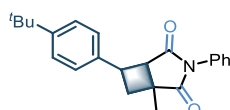
6-(4-methoxyphenyl)-1-methyl-3-phenyl-3-azabicyclo[3.2.0]heptane-2,4-dione (3ab)

37.9 mg, 59% yield, white solid (95% purity). Eluent: pentane/ethyl acetate = 8:1, R_f = 0.2, r.r. > 19:1, d.r. > 20:1.

^1H NMR (400 MHz, CDCl_3) δ 7.54 – 7.48 (m, 2H), 7.44 – 7.39 (m, 1H), 7.39 – 7.35 (m, 2H), 7.26 – 7.22 (m, 2H), 6.94 – 6.90 (m, 2H), 3.82 (s, 3H), 3.67 – 3.60 (m, 1H), 3.21 – 3.18 (m, 1H), 2.94 (dddd, J = 12.8, 9.3, 3.5, 0.9 Hz, 1H), 2.46 (dd, J = 12.8, 8.2 Hz, 1H), 1.57 (s, 3H).

^{13}C NMR (101 MHz, CDCl_3) δ 181.5, 177.3, 158.8, 134.3, 132.3, 129.3, 128.7, 127.7, 126.6, 114.3, 55.5, 52.4, 41.6, 39.1, 37.1, 21.1.

HRMS (ESI-TOF): m/z calcd. for $[\text{M} + \text{Na}]^+$ $\text{C}_{20}\text{H}_{19}\text{NO}_3\text{Na}^+$ 344.1257; Found: 344.1264.



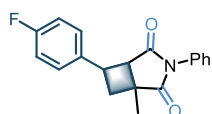
6-(4-(tert-butyl)phenyl)-1-methyl-3-phenyl-3-azabicyclo[3.2.0]heptane-2,4-dione (3ac)

38.1 mg, 55% yield, white solid. Eluent: pentane/ethyl acetate = 15:1, R_f = 0.3, r.r. > 19:1, d.r. > 20:1.

^1H NMR (300 MHz, CDCl_3) δ 7.46 – 7.40 (m, 2H), 7.36 – 7.28 (m, 5H), 7.21 – 7.17 (m, 2H), 3.66 – 3.45 (m, 1H), 3.16 (d, J = 5.4 Hz, 1H), 2.86 (dddd, J = 12.8, 9.3, 3.5, 0.9 Hz, 1H), 2.41 (dd, J = 12.8, 8.2 Hz, 1H), 1.49 (s, 3H), 1.26 (s, 9H).

^{13}C NMR (75 MHz, CDCl_3) δ 181.45, 177.21, 150.23, 139.19, 132.31, 129.30, 128.71, 126.56, 126.33, 125.86, 52.13, 41.69, 39.25, 34.64, 31.47, 21.02.

HRMS (ESI-TOF): m/z calcd. for $[\text{M} + \text{Na}]^+$ $\text{C}_{23}\text{H}_{25}\text{NO}_2\text{Na}^+$ 370.1777; Found: 370.1781.



6-(4-fluorophenyl)-1-methyl-3-phenyl-3-azabicyclo[3.2.0]heptane-2,4-dione (3ad)

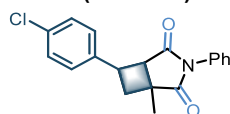
29.2 mg, 47% yield, white solid. Eluent: pentane/ethyl acetate = 10:1, R_f = 0.2, r.r. > 19:1, d.r. > 20:1.

^1H NMR (300 MHz, CDCl_3) δ 7.57 – 7.50 (m, 2H), 7.47 – 7.37 (m, 3H), 7.34 – 7.27 (m, 2H), 7.14 – 7.05 (m, 2H), 3.73 – 3.65 (m, 1H), 3.23 (d, J = 5.5 Hz, 1H), 2.99 (dddd, J = 12.8, 9.3, 3.5, 0.9 Hz, 1H), 2.48 (dd, J = 12.8, 8.3 Hz, 1H), 1.59 (s, 3H).

^{13}C NMR (75 MHz, CDCl_3) δ 181.2, 177.0, 161.9 (d, J = 245.9 Hz), 137.9 (d, J = 3.2 Hz), 132.2, 129.3, 128.8, 128.2 (d, J = 8.1 Hz), 126.5, 115.8 (d, J = 21.5 Hz), 52.2, 41.6, 38.9, 37.0, 21.1.

^{19}F NMR (282 MHz, CDCl_3) δ -104.82 – -123.14 (m).

HRMS (ESI-TOF): m/z calcd. for $[\text{M} + \text{Na}]^+$ $\text{C}_{19}\text{H}_{16}\text{FNO}_2\text{Na}^+$ 332.1057; Found: 332.1067.



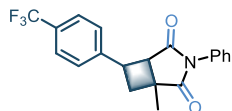
6-(4-chlorophenyl)-1-methyl-3-phenyl-3-azabicyclo[3.2.0]heptane-2,4-dione (3ae)

40.8 mg, 63% yield, white solid. Eluent: pentane/ethyl acetate = 10:1, R_f = 0.2, R_f = 0.2, r.r. > 19:1, d.r. > 20:1.

¹H NMR (400 MHz, CDCl₃) δ 7.56 – 7.51 (m, 2H), 7.47 – 7.42 (m, 1H), 7.41 – 7.36 (m, 4H), 7.31 – 7.26 (m, 2H), 3.69 (td, *J* = 8.7, 5.5 Hz, 1H), 3.23 (d, *J* = 5.5 Hz, 1H), 3.02 – 2.95 (m, 1H), 2.47 (dd, *J* = 12.8, 8.2 Hz, 1H), 1.58 (s, 3H).

¹³C NMR (101 MHz, CDCl₃) δ 181.1, 176.9, 140.6, 133.0, 132.2, 129.3, 129.1, 128.8 (d, *J* = 4.3 Hz), 128.0, 126.5, 52.0, 41.7, 38.9, 36.8, 21.1.

HRMS (ESI-TOF): *m/z* calcd. for [M + Na]⁺ C₁₉H₁₆NO₂Na⁺ 348.0761; Found: 348.0770.



1-methyl-3-phenyl-6-(4-(trifluoromethyl)phenyl)-3-azabicyclo[3.2.0]heptane-2,4-dione (3af)

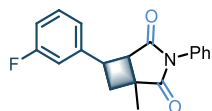
30.2mg, 42%, white solid. Eluent: pentane/ethyl acetate = 10:1, *R_f* = 0.2, r.r. > 19:1, d.r. > 20:1.

¹H NMR (300 MHz, CDCl₃) δ 7.65 (d, *J* = 8.0 Hz, 2H), 7.55 – 7.49 (m, 2H), 7.47 – 7.40 (m, 3H), 7.39 – 7.35 (m, 2H), 3.80 – 3.71 (m, 1H), 3.26 (dt, *J* = 5.6, 0.6 Hz, 1H), 3.01 (dddd, *J* = 12.9, 9.3, 3.5, 0.9 Hz, 1H), 2.50 (dd, *J* = 12.8, 8.3 Hz, 1H), 1.57 (s, 3H).

¹³C NMR (75 MHz, CDCl₃) δ 181.0, 176.8, 146.1, 144.7, 132.1, 129.4, 128.9, 127.0, 126.5, 126.0 (q, *J* = 3.5 Hz), 51.8, 41.8, 39.2, 36.6, 21.1.

¹⁹F NMR (282 MHz, CDCl₃) δ -62.50 (s).

HRMS (ESI-TOF): *m/z* calcd. for [M + Na]⁺ C₂₀H₁₆F₃NO₂Na⁺ 360.1206; Found: 360.1211.



6-(3-fluorophenyl)-1-methyl-3-phenyl-3-azabicyclo[3.2.0]heptane-2,4-dione (3ag)

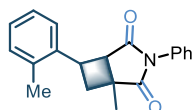
31.7 mg, 51% yield, white solid. Eluent: pentane/ethyl acetate = 10:1, *R_f* = 0.3, r.r. > 19:1, d.r. > 20:1.

¹H NMR (400 MHz, CDCl₃) δ 7.54 – 7.49 (m, 2H), 7.45 – 7.40 (m, 1H), 7.39 – 7.32 (m, 3H), 7.12 – 7.09 (m, 1H), 7.05 – 6.96 (m, 2H), 3.68 (td, *J* = 8.7, 5.4 Hz, 1H), 3.23 (dd, *J* = 5.5, 0.8 Hz, 1H), 2.97 (dddd, *J* = 12.8, 9.3, 3.5, 0.9 Hz, 1H), 2.47 (dd, *J* = 12.8, 8.2 Hz, 1H), 1.57 (s, 3H).

¹³C NMR (101 MHz, CDCl₃) δ 181.1, 176.9, 163.2 (d, *J* = 246.9 Hz), 144.7 (d, *J* = 7.0 Hz), 132.2, 130.6 (d, *J* = 8.3 Hz), 129.3, 128.8, 126.5, 122.3 (d, *J* = 3.0 Hz), 114.2 (d, *J* = 21.0 Hz), 113.6 (d, *J* = 21.7 Hz), 51.9, 41.7, 39.1 (d, *J* = 1.9 Hz), 36.7, 21.0.

¹⁹F NMR (376 MHz, CDCl₃) δ -104.8 – -118.4 (m).

HRMS (ESI-TOF): *m/z* calcd. for [M + Na]⁺ C₁₉H₁₆FNO₂Na⁺ 332.1057; Found: 332.1064.



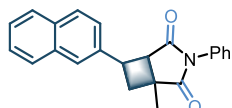
1-methyl-3-phenyl-6-(o-tolyl)-3-azabicyclo[3.2.0]heptane-2,4-dione (3ah)

40.3 mg, 66% yield, white solid. Eluent: pentane/ethyl acetate = 10:1, *R_f* = 0.3, r.r. > 19:1, d.r. > 20:1.

¹H NMR (300 MHz, CDCl₃) δ 7.55 – 7.48 (m, 2H), 7.46 – 7.38 (m, 4H), 7.33 – 7.26 (m, 1H), 7.23 – 7.19 (m, 2H), 3.90 – 3.79 (m, 1H), 3.28 (d, *J* = 5.2 Hz, 1H), 2.96 (dddd, *J* = 12.9, 9.3, 3.5, 0.9 Hz, 1H), 2.50 (dd, *J* = 12.9, 7.8 Hz, 1H), 2.32 (s, 3H), 1.58 (s, 3H).

¹³C NMR (75 MHz, CDCl₃) δ 181.4, 177.3, 139.6, 136.4, 132.3, 130.9, 129.3, 128.7, 127.2, 126.5, 126.5, 124.9, 50.7, 41.4, 36.7, 36.3, 20.9, 20.0.

HRMS (ESI-TOF): *m/z* calcd. for [M + Na]⁺ C₂₀H₁₉NO₂Na⁺ 328.1308; Found: 328.1308.



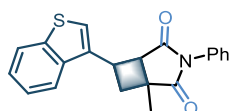
1-methyl-6-(naphthalen-2-yl)-3-phenyl-3-azabicyclo[3.2.0]heptane-2,4-dione (3ai)

43.2 mg, 63% yield, white solid. Eluent: pentane/ethyl acetate = 10:1, *R_f* = 0.3, r.r. > 19:1, d.r. > 20:1.

¹H NMR (300 MHz, CDCl₃) δ 7.83 – 7.74 (m, 3H), 7.66 (dd, *J* = 2.0, 1.0 Hz, 1H), 7.48 – 7.30 (m, 8H), 3.80 (td, *J* = 8.7, 5.8 Hz, 1H), 3.27 (d, *J* = 5.4 Hz, 1H), 2.96 (dddd, *J* = 12.8, 9.3, 3.5, 0.9 Hz, 1H), 2.55 (dd, *J* = 12.8, 8.2 Hz, 1H), 1.52 (s, 3H).

¹³C NMR (75 MHz, CDCl₃) δ 181.4, 177.2, 139.4, 133.4, 132.5, 132.3, 129.4, 129.0, 128.8, 127.9, 127.8, 126.7, 126.6, 126.2, 52.0, 41.8, 39.7, 36.6, 21.1.

HRMS (ESI-TOF): m/z calcd. for $[M + Na]^+ C_{23}H_{19}NO_2Na^+$ 364.1308; Found: 364.1317.



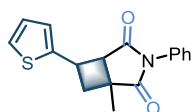
6-(benzo[b]thiophen-3-yl)-1-methyl-3-phenyl-3-azabicyclo[3.2.0]heptane-2,4-dione (3aj)

25.2 mg, 36% yield, white solid. Eluent: pentane/ethyl acetate = 20:1, R_f = 0.2, r.r. > 19:1, d.r. > 20:1.

1H NMR (300 MHz, $CDCl_3$) δ 8.01 – 7.95 (m, 1H), 7.92 – 7.87 (m, 1H), 7.57 – 7.50 (m, 2H), 7.48 – 7.40 (m, 5H), 7.31 (d, J = 1.5 Hz, 1H), 4.00 – 3.92 (m, 1H), 3.26 (d, J = 4.8 Hz, 1H), 3.07 (dddd, J = 13.0, 9.1, 3.8, 0.9 Hz, 1H), 2.70 (dd, J = 12.8, 7.1 Hz, 1H), 1.57 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 181.1, 177.2, 141.0, 137.6, 136.8, 132.2, 129.4, 128.8, 126.5, 125.1, 124.7, 123.1, 122.5, 121.3, 50.5, 42.2, 35.3, 33.9, 21.1.

HRMS (ESI-TOF): m/z calcd. for $[M + Na]^+ C_{21}H_{17}NO_2SNa^+$ 370.0872; Found: 370.0875.



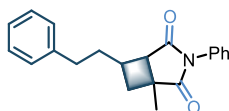
1-methyl-3-phenyl-6-(thiophen-2-yl)-3-azabicyclo[3.2.0]heptane-2,4-dione (3ak)

20.3 mg, 34% yield, white solid (95% purity). Eluent: pentane/ethyl acetate = 10:1, R_f = 0.3, r.r. > 19:1, d.r. > 20:1.

1H NMR (300 MHz, $CDCl_3$) δ 7.47 – 7.41 (m, 2H), 7.38 – 7.34 (m, 1H), 7.32 – 7.27 (m, 3H), 7.06 (ddd, J = 3.0, 1.4, 1.0 Hz, 1H), 7.01 (ddd, J = 5.0, 1.4, 0.4 Hz, 1H), 3.68 – 3.60 (m, 1H), 3.12 (d, J = 5.0 Hz, 1H), 2.88 (ddd, J = 12.8, 9.2, 0.9 Hz, 1H), 2.39 (dd, J = 12.6, 8.0 Hz, 1H), 1.50 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 181.3, 177.0, 143.4, 129.3, 128.8, 127.1, 126.6, 126.5, 120.7, 52.0, 41.9, 37.4, 35.2, 21.1.

HRMS (ESI-TOF): m/z calcd. for $[M + Na]^+ C_{17}H_{15}NO_2SNa^+$ 320.0715; Found: 320.0724.



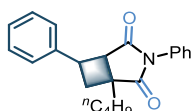
1-methyl-6-phenethyl-3-phenyl-3-azabicyclo[3.2.0]heptane-2,4-dione (3al)

29.7 mg, 46% yield, colorless oil. Eluent: pentane/ethyl acetate = 10:1, R_f = 0.3, r.r. > 19:1, d.r. > 20:1.

1H NMR (400 MHz, $CDCl_3$) δ 7.51 – 7.46 (m, 2H), 7.42 – 7.37 (m, 1H), 7.33 – 7.27 (m, 4H), 7.23 – 7.18 (m, 3H), 2.80 (d, J = 4.4 Hz, 1H), 2.74 – 2.58 (m, 3H), 2.46 – 2.36 (m, 1H), 2.13 – 2.03 (m, 1H), 2.02 – 1.89 (m, 2H), 1.52 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 181.4, 177.5, 141.0, 132.2, 129.2, 128.5, 128.5, 126.4, 126.1, 49.9, 41.8, 38.7, 36.2, 34.6, 32.8, 21.3.

HRMS (ESI-TOF): m/z calcd. for $[M + Na]^+ C_{21}H_{21}NO_2Na^+$ 342.1464; Found: 342.1473.



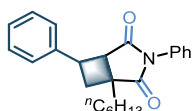
1-butyl-3,6-diphenyl-3-azabicyclo[3.2.0]heptane-2,4-dione (3am)

20.5 mg, 31% yield, white solid. Eluent: pentane/ethyl acetate = 30:1, R_f = 0.3, r.r. > 19:1, d.r. > 20:1.

1H NMR (300 MHz, $CDCl_3$) δ 7.55 – 7.48 (m, 2H), 7.45 – 7.38 (m, 2H), 7.38 – 7.36 (m, 2H), 7.35 – 7.33 (m, 2H), 7.32 – 7.27 (m, 2H), 3.71 (td, J = 8.9, 5.7 Hz, 1H), 3.29 (dd, J = 5.8, 0.8 Hz, 1H), 2.90 (dddd, J = 12.7, 9.2, 3.4, 0.9 Hz, 1H), 2.51 (dd, J = 12.7, 8.5 Hz, 1H), 2.19 – 2.03 (m, 1H), 1.83 – 1.71 (m, 1H), 1.39 – 1.28 (m, 4H), 0.91 (t, J = 7.0 Hz, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 181.1, 177.4, 142.2, 132.3, 129.4, 129.0, 128.8, 127.2, 126.6, 126.6, 50.4, 45.9, 39.9, 35.4, 34.8, 26.3, 22.9, 14.0.

HRMS (ESI-TOF): m/z calcd. for $[M + Na]^+ C_{22}H_{23}NO_2Na^+$ 356.1621; Found: 356.1624.



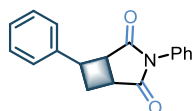
1-hexyl-3,6-diphenyl-3-azabicyclo[3.2.0]heptane-2,4-dione (3an)

24.3 mg, 34% yield, white solid. Eluent: pentane/ethyl acetate = 30:1, R_f = 0.3, r.r. > 19:1, d.r. > 20:1.

^1H NMR (300 MHz, CDCl_3) δ 7.55 – 7.48 (m, 2H), 7.45 – 7.39 (m, 2H), 7.38 – 7.33 (m, 4H), 7.31 – 7.28 (m, 2H), 3.71 (td, J = 8.9, 5.7 Hz, 1H), 3.29 (dd, J = 5.7, 0.8 Hz, 1H), 2.89 (dddd, J = 12.7, 9.3, 3.4, 0.9 Hz, 1H), 2.50 (dd, J = 12.7, 8.5 Hz, 1H), 2.10 (ddd, J = 13.8, 11.2, 4.5 Hz, 1H), 1.82 – 1.71 (m, 1H), 1.30 – 1.25 (m, 8H), 0.92 – 0.73 (m, 3H).

^{13}C NMR (75 MHz, CDCl_3) δ 181.1, 177.4, 142.2, 132.3, 129.4, 129.0, 128.8, 127.2, 126.6, 50.4, 46.0, 39.9, 35.5, 35.1, 31.7, 29.4, 24.2, 22.7, 14.2.

HRMS (ESI-TOF): m/z calcd. for $[\text{M} + \text{Na}]^+ \text{C}_{24}\text{H}_{27}\text{NO}_2\text{Na}^+$ 384.1934; Found: 384.1936.



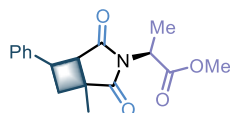
3,6-diphenyl-3-azabicyclo[3.2.0]heptane-2,4-dione (3ao)

24.6 mg, 44% yield, white solid. Eluent: pentane/ethyl acetate = 10:1, R_f = 0.2, r.r. > 19:1, d.r. > 20:1.

^1H NMR (300 MHz, CDCl_3) δ 7.56 – 7.49 (m, 2H), 7.46 – 7.27 (m, 8H), 3.87 (td, J = 8.6, 5.2 Hz, 1H), 3.60 – 3.55 (m, 1H), 3.53 – 3.45 (m, 1H), 2.97 – 2.76 (m, 2H).

^{13}C NMR (101 MHz, CDCl_3) δ 178.7, 177.6, 142.1, 132.2, 129.4, 129.0, 128.9, 127.3, 126.6, 126.5, 46.7, 42.4, 36.1, 30.2.

HRMS (ESI-TOF): m/z calcd. for $[\text{M} + \text{Na}]^+ \text{C}_{18}\text{H}_{15}\text{NO}_2\text{Na}^+$ 300.0995; Found: 300.1001.



From L-Alanine

ethyl (2S)-3-methyl-2-(1-methyl-2,4-dioxo-6-phenyl-3-azabicyclo[3.2.0]heptan-3-yl)butanoate (3ap)

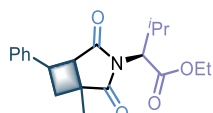
37.5 mg, 55% yield, colorless oil. Eluent: pentane/ethyl acetate = 3:1, R_f = 0.3, r.r. > 19:1, d.r. > 20:1.

^1H NMR (300 MHz, CDCl_3) δ 7.43 – 7.36 (m, 2H), 7.33 – 7.28 (m, 3H), 4.49 – 4.41 (m, 1H), 4.35 – 4.11 (m, 2H), 3.60 (td, J = 8.7, 5.4 Hz, 1H), 3.22 – 3.11 (m, 1H), 2.92 – 2.81 (m, 1H), 2.78 – 2.67 (m, 1H), 2.45 (m, 1H), 1.48 (d, J = 1.3 Hz, 3H), 1.30 – 1.25 (m, 3H), 1.24 – 1.19 (m, 3H), 0.92 (t, J = 6.5 Hz, 3H).

^{13}C NMR (75 MHz, CDCl_3) δ 181.5, 181.4, 177.3, 177.1, 170.0, 170.0, 142.3, 128.9, 127.1, 126.5, 53.0, 52.9, 51.9, 51.9, 48.3, 48.2, 41.7, 41.5, 39.2, 39.0, 36.7, 36.6, 20.7, 20.6, 14.6, 14.3.

(Duplicated ^{13}C resonances and minor duplication of certain ^1H signals are attributed to slowly interconverting amide rotamers; no diastereomeric mixture was detected by ^1H NMR)

HRMS (ESI-TOF): m/z calcd. for $[\text{M} + \text{Na}]^+ \text{C}_{20}\text{H}_{25}\text{NO}_4\text{Na}^+$ 366.1675; Found: 366.1668.



From L-Valine

ethyl (2S)-3-methyl-2-(1-methyl-2,4-dioxo-6-phenyl-3-azabicyclo[3.2.0]heptan-3-yl)butanoate (3aq)

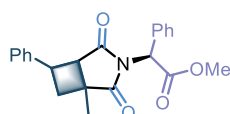
37.5 mg, 55% yield, colorless oil. Eluent: pentane/ethyl acetate = 3:1, R_f = 0.3, r.r. > 19:1, d.r. > 20:1.

^1H NMR (300 MHz, CDCl_3) δ 7.43 – 7.36 (m, 2H), 7.33 – 7.28 (m, 3H), 4.49 – 4.41 (m, 1H), 4.35 – 4.11 (m, 2H), 3.60 (td, J = 8.7, 5.4 Hz, 1H), 3.22 – 3.11 (m, 1H), 2.92 – 2.81 (m, 1H), 2.78 – 2.67 (m, 1H), 2.45 (m, 1H), 1.48 (d, J = 1.3 Hz, 3H), 1.30 – 1.25 (m, 3H), 1.24 – 1.19 (m, 3H), 0.92 (t, J = 6.5 Hz, 3H).

^{13}C NMR (75 MHz, CDCl_3) δ 181.8, 177.4, 168.6, 168.6, 142.2, 128.9, 127.1, 127.1, 126.5, 126.5, 61.6, 58.0, 57.9, 51.9, 51.8, 41.7, 41.4, 39.2, 39.1, 36.5, 36.5, 28.2, 27.7, 21.5, 20.9, 20.8, 19.5, 19.4, 14.3, 14.2.

(Duplicated ^{13}C resonances and minor duplication of certain ^1H signals are attributed to slowly interconverting amide rotamers; no diastereomeric mixture was detected by ^1H NMR)

HRMS (ESI-TOF): m/z calcd. for $[\text{M} + \text{Na}]^+ \text{C}_{20}\text{H}_{25}\text{NO}_4\text{Na}^+$ 366.1675; Found: 366.1668.



From L-2-Phenylglycine

methyl (2S)-2-(1-methyl-2,4-dioxo-6-phenyl-3-azabicyclo[3.2.0]heptan-3-yl)-2-phenylacetate (3ar)

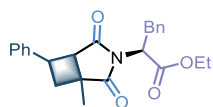
41.4 mg, 57% yield, colorless oil. Eluent: pentane/ethyl acetate = 7:1, R_f = 0.3, r.r. > 19:1, d.r. > 20:1.

^1H NMR (300 MHz, CDCl_3) δ 7.48 – 7.43 (m, 2H), 7.32 – 7.25 (m, 5H), 7.21 – 7.17 (m, 3H), 5.83 (d, J = 6.1 Hz, 1H), 3.75 (d, J = 1.9 Hz, 3H), 3.55 – 3.40 (m, 1H), 3.05 (ddd, J = 10.0, 5.7, 0.8 Hz, 1H), 2.76 (dddd, J = 12.6, 9.3, 7.0, 0.9 Hz, 1H), 2.33 (ddd, J = 12.4, 8.2, 4.0 Hz, 1H), 1.36 (d, J = 3.7 Hz, 3H).

^{13}C NMR (75 MHz, CDCl_3) δ 181.1, 181.1, 176.9, 176.8, 168.3, 168.3, 142.2, 134.0, 129.9, 129.8, 128.9, 128.9, 128.9, 128.7, 128.7, 127.1, 127.1, 126.5, 126.5, 56.7, 56.6, 53.2, 51.8, 51.7, 41.8, 41.6, 39.1, 38.9, 36.6, 20.6, 20.5.

(Duplicated ^{13}C resonances and minor duplication of certain ^1H signals are attributed to slowly interconverting amide rotamers; no diastereomeric mixture was detected by ^1H NMR)

HRMS (ESI-TOF): m/z calcd. for $[\text{M} + \text{Na}]^+ \text{C}_{22}\text{H}_{21}\text{NO}_4\text{Na}^+$ 386.1363; Found: 386.1358.



From L-Phenylalanine

ethyl (2S)-2-(1-methyl-2,4-dioxo-6-phenyl-3-azabicyclo[3.2.0]heptan-3-yl)-3-phenylpropanoate (3as)

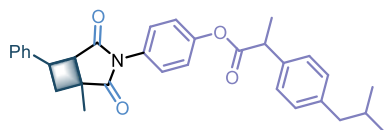
39.3 mg, 50% yield, colorless oil. Eluent: pentane/ethyl acetate = 8:1, R_f = 0.3, r.r. > 19:1, d.r. > 20:1.

^1H NMR (300 MHz, CDCl_3) δ 7.36 – 7.26 (m, 3H), 7.26 – 7.15 (m, 6H), 7.13 – 7.08 (m, 1H), 5.11 (td, J = 8.8, 4.4 Hz, 1H), 4.39 – 4.16 (m, 2H), 3.56 (dd, J = 9.0, 1.7 Hz, 2H), 3.10 (td, J = 8.6, 5.4 Hz, 0.5H), 2.93 – 2.87 (m, 1H), 2.68 (td, J = 8.7, 5.7 Hz, 0.5H), 2.55 (dddd, J = 12.4, 9.2, 3.5, 0.7 Hz, 0.5H), 2.37 (dddd, J = 12.6, 9.3, 3.5, 0.8 Hz, 0.5H), 2.20 (dt, J = 12.6, 7.9 Hz, 1H), 1.33 – 1.27 (m, 4.5H), 1.22 (s, 1.5H).

^{13}C NMR (75 MHz, CDCl_3) δ 181.6, 181.4, 177.2, 177.1, 168.6, 168.6, 142.3, 142.3, 136.7, 136.7, 129.4, 129.3, 128.8, 128.8, 128.7, 128.6, 127.2, 127.0, 126.5, 62.1, 62.1, 52.9, 52.8, 51.9, 51.4, 41.3, 41.1, 38.9, 38.8, 36.5, 36.4, 34.0, 33.6, 20.5, 20.5, 14.3, 14.2.

(Duplicated ^{13}C resonances and minor duplication of certain ^1H signals are attributed to slowly interconverting amide rotamers; no diastereomeric mixture was detected by ^1H NMR)

HRMS (ESI-TOF): m/z calcd. for $[\text{M} + \text{Na}]^+ \text{C}_{24}\text{H}_{25}\text{NO}_4\text{Na}^+$ 414.1675; Found: 414.1669.



From Ibuprofen

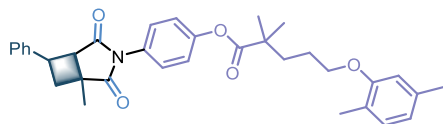
4-(1-methyl-2,4-dioxo-7-phenyl-3-azabicyclo[3.2.0]heptan-3-yl)phenyl 2-(4-isobutylphenyl)propanoate (3at)

54.1 mg, 55%, white solid. Eluent: pentane/ethyl acetate = 10:1, R_f = 0.3, r.r. > 19:1, d.r. > 20:1.

^1H NMR (300 MHz, CDCl_3) δ 7.43 – 7.35 (m, 4H), 7.34 – 7.28 (m, 5H), 7.19 – 7.13 (m, 4H), 3.96 (q, J = 7.1 Hz, 1H), 3.67 (td, J = 8.0, 4.7 Hz, 1H), 3.26 – 3.22 (m, 1H), 3.00 – 2.91 (m, 1H), 2.53 – 2.45 (m, 3H), 1.95 – 1.82 (m, 1H), 1.63 (d, J = 7.1 Hz, 3H), 1.55 (s, 3H), 0.93 (d, J = 6.6 Hz, 6H).

^{13}C NMR (75 MHz, CDCl_3) δ 181.2, 177.0, 172.9, 150.7, 142.1, 141.0, 137.1, 129.7, 129.5, 129.0, 127.4, 127.3, 127.2, 126.5, 122.2, 51.9, 45.4, 45.2, 41.7, 39.5, 36.8, 30.3, 22.5, 21.0, 18.6.

HRMS (ESI-TOF): m/z calcd. for $[\text{M} + \text{Na}]^+ \text{C}_{32}\text{H}_{33}\text{NO}_4\text{Na}^+$ 518.2302; Found: 518.2307.



From Gemfibrozil

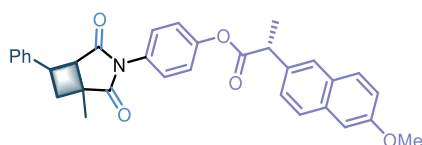
4-(1-methyl-2,4-dioxo-6-phenyl-3-azabicyclo[3.2.0]heptan-3-yl)phenyl 5-(2,5-dimethylphenoxy)-2,2-dimethylpentanoate (3au)

66.1mg, 61%, white solid. Eluent: pentane/ethyl acetate = 10:1, R_f = 0.2, r.r. > 19:1, d.r. > 20:1.

^1H NMR (300 MHz, CDCl_3) δ 7.45 – 7.38 (m, 4H), 7.36 – 7.27 (m, 3H), 7.23 – 7.17 (m, 2H), 7.03 (d, J = 7.4 Hz, 1H), 6.71 – 6.65 (m, 2H), 4.05 – 3.97 (m, 2H), 3.70 (td, J = 8.7, 5.5 Hz, 1H), 3.28 – 3.20 (m, 1H), 2.97 (dddd, J = 12.8, 9.3, 3.5, 0.9 Hz, 1H), 2.51 (dd, J = 12.8, 8.2 Hz, 1H), 2.33 (s, 3H), 2.21 (s, 3H), 1.91 (d, J = 2.3 Hz, 4H), 1.58 (s, 3H), 1.40 (s, 6H).

^{13}C NMR (75 MHz, CDCl_3) δ 181.1, 176.9, 175.9, 156.9, 150.8, 142.0, 136.5, 130.4, 129.5, 128.9, 127.4, 127.1, 126.5, 122.3, 120.8, 112.0, 67.8, 51.9, 42.6, 41.6, 39.4, 37.2, 36.7, 25.3, 25.2, 21.5, 20.9, 15.9.

HRMS (ESI-TOF): m/z calcd. for $[\text{M} + \text{Na}]^+ \text{C}_{34}\text{H}_{37}\text{NO}_5\text{Na}^+$ 562.2563; Found: 562.2578.



From Naproxen

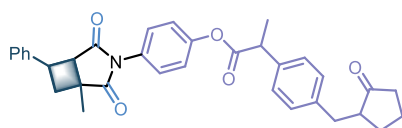
4-(1-methyl-2,4-dioxo-6-phenyl-3-azabicyclo[3.2.0]heptan-3-yl)phenyl (2R)-2-(6-methoxynaphthalen-2-yl)propanoate (3av)

34.9 mg, 34%, white solid. Eluent: pentane/ethyl acetate = 5:1, R_f = 0.3, r.r. > 19:1, d.r. > 20:1.

^1H NMR (300 MHz, CDCl_3) δ 7.79 – 7.72 (m, 3H), 7.50 (dd, J = 8.7, 1.7 Hz, 1H), 7.42 – 7.27 (m, 7H), 7.20 – 7.12 (m, 4H), 4.12 (q, J = 7.1 Hz, 1H), 3.93 (s, 3H), 3.66 (td, J = 8.6, 5.4 Hz, 1H), 3.23 (d, J = 5.0 Hz, 1H), 2.94 (dddd, J = 12.8, 9.3, 3.5, 0.9 Hz, 1H), 2.48 (dd, J = 12.8, 8.2 Hz, 1H), 1.71 (d, J = 7.1 Hz, 3H), 1.55 (s, 3H).

^{13}C NMR (75 MHz, CDCl_3) δ 181.1, 176.9, 172.8, 157.8, 150.6, 142.0, 135.0, 133.9, 129.5, 129.4, 129.0, 128.9, 127.5, 127.3, 127.1, 126.4, 126.2, 122.2, 119.2, 105.6, 55.4, 51.8, 45.6, 41.6, 39.4, 36.7, 20.9, 18.5.

HRMS (ESI-TOF): m/z calcd. for $[\text{M} + \text{Na}]^+$ $\text{C}_{33}\text{H}_{29}\text{NO}_5\text{Na}^+$ 542.1938; Found: 542.1938.



From Loxoprofen

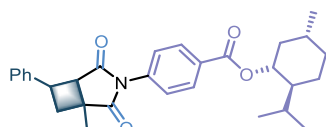
4-(1-methyl-2,4-dioxo-7-phenyl-3-azabicyclo[3.2.0]heptan-3-yl)phenyl 2-(4-((2-oxocyclopentyl)methyl)-phenyl)propanoate (3aw)

64.4 mg, 60%, white solid. Eluent: pentane/ethyl acetate = 10:1, R_f = 0.4, r.r. > 19:1, d.r. > 20:1.

^1H NMR (400 MHz, CDCl_3) δ 7.41 – 7.35 (m, 4H), 7.33 – 7.27 (m, 5H), 7.21 – 7.13 (m, 4H), 3.95 (q, J = 7.1 Hz, 1H), 3.67 (td, J = 8.7, 5.5 Hz, 1H), 3.24 (dd, J = 5.6, 0.7 Hz, 1H), 3.16 (dd, J = 13.9, 4.1 Hz, 1H), 2.94 (dddd, J = 12.8, 9.3, 3.5, 0.9 Hz, 1H), 2.59 – 2.44 (m, 2H), 2.40 – 2.30 (m, 2H), 2.18 – 2.06 (m, 2H), 1.97 (dddd, J = 12.7, 8.8, 6.5, 2.7 Hz, 1H), 1.81 – 1.68 (m, 1H), 1.61 (d, J = 7.1 Hz, 3H), 1.55 – 1.54 (m, 4H).

^{13}C NMR (101 MHz, CDCl_3) δ 220.4, 181.2, 177.0, 172.8, 150.6, 142.1, 139.4, 137.8, 129.6, 129.5, 129.0, 127.7, 127.4, 127.2, 126.5, 122.2, 51.9, 51.1, 45.4, 41.7, 39.2, 38.3, 36.8, 35.3, 29.1, 21.0, 20.7, 18.6.

HRMS (ESI-TOF): m/z calcd. for $[\text{M} + \text{Na}]^+$ $\text{C}_{34}\text{H}_{33}\text{NO}_5\text{Na}^+$ 558.2251; Found: 558.2262.



From L-Menthol

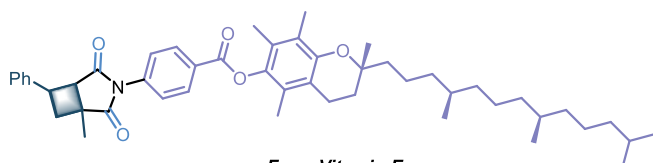
4-(1-methyl-2,4-dioxo-6-phenyl-3-azabicyclo[3.2.0]heptan-3-yl)phenyl (1S,2R,5S)-2-isopropyl-5-methylcyclohexane-1-carboxylate (3ax)

43.0 mg, 47% yield, white solid. Eluent: pentane/ethyl acetate = 30:1, R_f = 0.3, r.r. > 19:1, d.r. > 20:1.

^1H NMR (300 MHz, CDCl_3) δ 8.22 – 8.16 (m, 2H), 7.52 – 7.48 (m, 2H), 7.41 – 7.28 (m, 5H), 4.96 (td, J = 10.8, 4.4 Hz, 1H), 3.77 – 3.64 (m, 1H), 3.27 (d, J = 5.5 Hz, 1H), 3.02 – 2.93 (m, 1H), 2.52 (dd, J = 12.9, 8.3 Hz, 1H), 2.18 – 2.09 (m, 1H), 2.00 – 1.90 (m, 1H), 1.79 – 1.67 (m, 2H), 1.58 (s, 3H), 1.34 – 1.18 (m, 2H), 1.17 – 1.06 (m, 2H), 0.93 (dd, J = 6.8, 5.4 Hz, 7H), 0.80 (d, J = 7.0 Hz, 3H).

^{13}C NMR (75 MHz, CDCl_3) δ 181.0, 176.7, 165.3, 142.0, 136.1, 130.9, 130.6, 129.0, 127.3, 126.5, 126.3, 75.4, 52.0, 47.4, 41.8, 41.1, 39.5, 36.9, 34.4, 31.6, 26.7, 23.8, 22.2, 21.0, 20.9, 16.7.

HRMS (ESI-TOF): m/z calcd. for $[\text{M} + \text{Na}]^+$ $\text{C}_{30}\text{H}_{35}\text{NO}_4\text{Na}^+$ 496.2458; Found: 496.2467.



From Vitamin E

(R)-2,5,7,8-tetramethyl-2-((4R,8R)-4,8,12-trimethyltridecyl)chroman-6-yl 4-(1-methyl-2,4-dioxo-7-phenyl-3-azabicyclo[3.2.0]heptan-3-yl)benzoate (3ay)

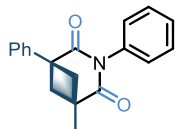
71.6 mg, 48% yield, white solid. Eluent: pentane/ethyl acetate = 10:1, R_f = 0.3, r.r. > 19:1, d.r. > 20:1.

^1H NMR (300 MHz, CDCl_3) δ 8.43 – 8.38 (m, 2H), 7.63 – 7.57 (m, 2H), 7.42 – 7.30 (m, 5H), 3.74 (td, J = 8.6, 5.4 Hz, 1H), 3.31 (d, J = 5.4 Hz, 1H), 3.00 (dddd, J = 12.8, 9.3, 3.5, 0.9 Hz, 1H), 2.63 (t, J = 6.6 Hz, 2H), 2.54 (dd, J =

12.9, 8.3 Hz, 1H), 2.14 (s, 3H), 2.07 (s, 3H), 2.03 (s, 3H), 1.87 – 1.78 (m, 2H), 1.61 (s, 3H), 1.40 – 1.12 (m, 24H), 0.90 – 0.84 (m, 12H).

¹³C NMR (75 MHz, CDCl₃) δ 181.0, 176.7, 164.4, 149.7, 142.0, 140.7, 136.7, 131.2, 129.7, 129.0, 127.3, 127.0, 126.6, 125.2, 123.3, 117.7, 75.3, 52.1, 41.9, 39.51, 39.5, 37.6, 37.4, 36.9, 32.9, 28.1, 25.0, 24.6, 22.9, 22.8, 21.2, 21.1, 20.8, 19.9, 19.8, 13.2, 12.3, 12.0.

HRMS (ESI-TOF): m/z calcd. for [M + Na]⁺ C₄₉H₆₅NO₅Na⁺ 770.4755; Found: 770.4767.



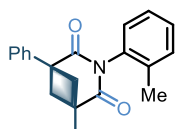
1-methyl-3,5-diphenyl-3-azabicyclo[3.1.1]heptane-2,4-dione (4a)

20.6 mg, 71% yield, white solid. Eluent: pentane/ethyl acetate = 10:1, R_f = 0.2, r.r. > 19:1.

¹H NMR (300 MHz, CDCl₃) δ 7.49 – 7.36 (m, 5H), 7.35 – 7.29 (m, 1H), 7.23 – 7.14 (m, 4H), 3.09 – 3.01 (m, 2H), 2.68 – 2.59 (m, 2H), 1.47 (s, 3H).

¹³C NMR (75 MHz, CDCl₃) δ 177.4, 176.2, 139.2, 133.8, 129.1, 128.6, 128.5, 128.5, 127.6, 126.6, 50.7, 44.6, 43.1, 19.8.

HRMS (ESI-TOF): m/z calcd. for [M + Na]⁺ C₁₉H₁₇NO₂Na⁺ 314.1151; Found: 314.1151.



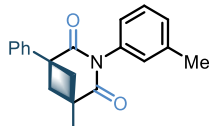
1-methyl-5-phenyl-3-(o-tolyl)-3-azabicyclo[3.1.1]heptane-2,4-dione (4b)

21.3 mg, 70% yield, white solid. Eluent: pentane/ethyl acetate = 10:1, R_f = 0.2, r.r. > 19:1.

¹H NMR (300 MHz, CDCl₃) δ 7.44 – 7.37 (m, 2H), 7.35 – 7.26 (m, 4H), 7.19 – 7.14 (m, 2H), 7.13 – 7.06 (m, 1H), 3.12 – 3.02 (m, 2H), 2.71 – 2.57 (m, 2H), 2.18 (s, 3H), 1.48 (s, 3H).

¹³C NMR (75 MHz, CDCl₃) δ 177.0, 175.7, 139.1, 136.1, 132.9, 131.0, 129.1, 128.6, 128.5, 127.6, 126.9, 126.5, 50.8, 44.8, 44.5, 43.3, 19.7, 17.6.

HRMS (ESI-TOF): m/z calcd. for [M + Na]⁺ C₂₀H₁₉NO₂Na⁺ 328.1308; Found: 328.1315.



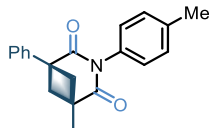
1-methyl-5-phenyl-3-(m-tolyl)-3-azabicyclo[3.1.1]heptane-2,4-dione (4c)

17.3 mg, 56% yield, white solid. Eluent: pentane/ethyl acetate = 10:1, R_f = 0.2, r.r. > 19:1.

¹H NMR (300 MHz, CDCl₃) δ 7.42 – 7.36 (m, 2H), 7.35 – 7.28 (m, 2H), 7.22 – 7.14 (m, 3H), 7.04 – 6.93 (m, 2H), 3.09 – 3.00 (m, 2H), 2.67 – 2.59 (m, 2H), 2.37 (s, 3H), 1.47 (s, 3H).

¹³C NMR (75 MHz, CDCl₃) δ 177.5, 176.3, 139.3, 139.2, 133.7, 129.5, 129.1, 129.0, 128.5, 127.6, 126.6, 125.4, 50.7, 44.7, 43.1, 21.4, 19.8.

HRMS (ESI-TOF): m/z calcd. for [M + Na]⁺ C₂₀H₁₉NO₂Na⁺ 328.1308; Found: 328.1314.



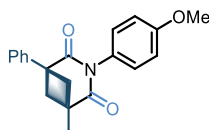
1-methyl-5-phenyl-3-(p-tolyl)-3-azabicyclo[3.1.1]heptane-2,4-dione (4d)

20.6 mg, 67% yield, white solid. Eluent: pentane/ethyl acetate = 10:1, R_f = 0.2, r.r. > 19:1.

¹H NMR (300 MHz, CDCl₃) δ 7.42 – 7.35 (m, 2H), 7.34 – 7.28 (m, 1H), 7.27 – 7.25 (m, 1H), 7.24 (t, J = 0.6 Hz, 1H), 7.18 – 7.13 (m, 2H), 7.10 – 7.05 (m, 2H), 3.10 – 2.97 (m, 2H), 2.66 – 2.57 (m, 2H), 2.38 (s, 3H), 1.46 (s, 3H).

¹³C NMR (75 MHz, CDCl₃) δ 177.6, 176.3, 139.3, 138.5, 131.1, 129.9, 128.6, 128.2, 127.6, 126.7, 50.7, 44.7, 43.1, 21.4, 19.9.

HRMS (ESI-TOF): m/z calcd. for [M + Na]⁺ C₂₀H₁₉NO₂Na⁺ 328.1308; Found: 328.1312.



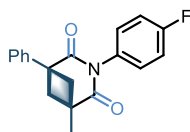
3-(4-methoxyphenyl)-1-methyl-5-phenyl-3-azabicyclo[3.1.1]heptane-2,4-dione (4e)

21.2 mg, 66% yield, white solid. Eluent: pentane/ethyl acetate = 5:1, R_f = 0.2, r.r. > 19:1.

¹H NMR (300 MHz, CDCl₃) δ 7.42 – 7.28 (m, 3H), 7.18 – 7.07 (m, 4H), 6.99 – 6.93 (m, 2H), 3.82 (s, 3H), 3.09 – 2.97 (m, 2H), 2.67 – 2.56 (m, 2H), 1.46 (s, 3H).

¹³C NMR (75 MHz, CDCl₃) δ 177.7, 176.5, 159.5, 139.3, 129.5, 128.6, 127.6, 126.6, 126.4, 114.5, 55.6, 50.7, 44.6, 43.1, 19.9.

HRMS (ESI-TOF): m/z calcd. for [M + Na]⁺ C₂₀H₁₉NO₃Na⁺ 344.1257; Found: 344.1261.



3-(4-fluorophenyl)-1-methyl-5-phenyl-3-azabicyclo[3.1.1]heptane-2,4-dione (4f)

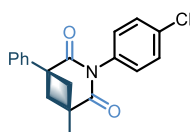
21.1 mg, 68% yield, white solid. Eluent: pentane/ethyl acetate = 10:1, R_f = 0.2, r.r. > 19:1.

¹H NMR (300 MHz, CDCl₃) δ 7.44 – 7.29 (m, 3H), 7.22 – 7.09 (m, 6H), 3.11 – 2.96 (m, 2H), 2.71 – 2.56 (m, 2H), 1.47 (s, 3H).

¹³C NMR (75 MHz, CDCl₃) δ 177.4, 176.3, 164.0, 160.8, 139.1, 130.3 (d, J = 8.9 Hz), 128.6, 127.7, 126.6, 116.2 (d, J = 22.9 Hz), 50.7, 44.5, 43.2, 19.8.

¹⁹F NMR (282 MHz, CDCl₃) δ -113.01 – -113.18 (m).

HRMS (ESI-TOF): m/z calcd. for [M + Na]⁺ C₁₉H₁₆FNO₂Na⁺ 332.1057; Found: 332.1064.



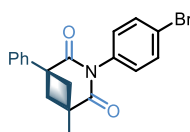
3-(4-chlorophenyl)-1-methyl-5-phenyl-3-azabicyclo[3.1.1]heptane-2,4-dione (4g)

20.6 mg, 64% yield, white solid. Eluent: pentane/ethyl acetate = 10:1, R_f = 0.2, r.r. > 19:1.

¹H NMR (300 MHz, CDCl₃) δ 7.45 – 7.39 (m, 3H), 7.38 – 7.29 (m, 2H), 7.18 – 7.12 (m, 4H), 3.11 – 2.95 (m, 2H), 2.70 – 2.59 (m, 2H), 1.47 (s, 3H).

¹³C NMR (75 MHz, CDCl₃) δ 177.2, 176.1, 139.0, 134.5, 132.2, 129.9, 129.4, 128.6, 127.8, 126.6, 50.7, 44.5, 43.2, 19.8.

HRMS (ESI-TOF): m/z calcd. for [M + Na]⁺ C₁₉H₁₆NO₂Na⁺ 348.0761; Found: 348.0765.



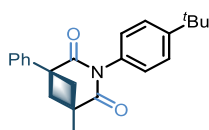
3-(4-bromophenyl)-1-methyl-5-phenyl-3-azabicyclo[3.1.1]heptane-2,4-dione (4h)

20.0 mg, 54% yield, white solid. Eluent: pentane/ethyl acetate = 10:1, R_f = 0.2, r.r. > 19:1.

¹H NMR (300 MHz, CDCl₃) δ 7.61 – 7.55 (m, 2H), 7.43 – 7.29 (m, 3H), 7.17 – 7.06 (m, 4H), 3.08 – 2.97 (m, 2H), 2.68 – 2.58 (m, 2H), 1.46 (s, 3H).

¹³C NMR (75 MHz, CDCl₃) δ 177.1, 176.0, 139.0, 132.8, 132.4, 130.2, 128.6, 127.8, 126.6, 122.6, 50.7, 44.5, 43.2, 19.8.

HRMS (ESI-TOF): m/z calcd. for [M + Na]⁺ C₁₉H₁₆BrNO₂Na⁺ 392.0256; Found: 392.0247.



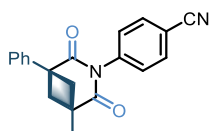
3-(4-(tert-butyl)phenyl)-1-methyl-5-phenyl-3-azabicyclo[3.1.1]heptane-2,4-dione (4i)

22.2 mg, 64% yield, white solid. Eluent: pentane/ethyl acetate = 5:1, R_f = 0.2, r.r. > 19:1.

¹H NMR (300 MHz, CDCl₃) δ 7.48 – 7.43 (m, 2H), 7.42 – 7.35 (m, 2H), 7.34 – 7.28 (m, 1H), 7.18 – 7.14 (m, 2H), 7.14 – 7.09 (m, 2H), 3.08 – 3.00 (m, 1H), 2.66 – 2.58 (m, 1H), 1.47 (s, 1H), 1.33 (s, 3H).

¹³C NMR (75 MHz, CDCl₃) δ 177.5, 176.4, 151.4, 139.3, 131.0, 128.5, 127.8, 127.6, 126.7, 126.2, 50.7, 44.7, 43.1, 34.8, 31.4, 19.8.

HRMS (ESI-TOF): m/z calcd. for [M + Na]⁺ C₂₃H₂₅NO₂Na⁺ 370.1777; Found: 370.1787.



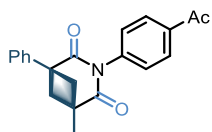
4-(1-methyl-2,4-dioxo-5-phenyl-3-azabicyclo[3.1.1]heptan-3-yl)benzonitrile (4j)

16.8 mg, 53% yield, white solid. Eluent: pentane/ethyl acetate = 5:1, R_f = 0.3, r.r. > 19:1.

¹H NMR (300 MHz, CDCl₃) δ 7.77 – 7.71 (m, 2H), 7.44 – 7.30 (m, 6H), 7.17 – 7.12 (m, 2H), 3.11 – 3.01 (m, 2H), 2.73 – 2.60 (m, 2H), 1.47 (s, 3H).

¹³C NMR (75 MHz, CDCl₃) δ 176.8, 175.7, 138.7, 137.9, 132.9, 129.7, 128.7, 127.9, 126.5, 118.3, 112.5, 50.8, 44.4, 43.3, 19.7.

HRMS (ESI-TOF): m/z calcd. for [M + Na]⁺ C₂₀H₁₆N₂O₂Na⁺ 317.1285; Found: 317.1292.



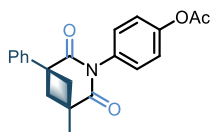
3-(4-acetylphenyl)-1-methyl-5-phenyl-3-azabicyclo[3.1.1]heptane-2,4-dione (4k)

18.3 mg, 55% yield, white solid. Eluent: pentane/ethyl acetate = 8:1, R_f = 0.2, r.r. > 19:1.

¹H NMR (300 MHz, CDCl₃) δ 8.07 – 8.00 (m, 2H), 7.44 – 7.36 (m, 2H), 7.35 – 7.29 (m, 3H), 7.18 – 7.13 (m, 2H), 3.10 – 3.02 (m, 2H), 2.69 – 2.63 (m, 2H), 2.62 (s, 3H), 1.47 (s, 3H).

¹³C NMR (75 MHz, CDCl₃) δ 197.3, 177.0, 175.9, 138.9, 138.1, 137.0, 129.2, 128.9, 128.7, 127.8, 126.6, 50.8, 44.5, 43.3, 26.8, 19.7.

HRMS (ESI-TOF): m/z calcd. for [M + Na]⁺ C₂₁H₁₉NO₃Na⁺ 356.1257; Found: 356.1258.



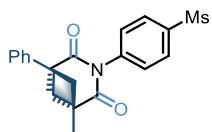
methyl 4-(1-methyl-2,4-dioxo-5-phenyl-3-azabicyclo[3.1.1]heptan-3-yl)benzoate (4l)

16.5 mg, 47% yield, white solid. Eluent: pentane/ethyl acetate = 5:1, R_f = 0.2, r.r. > 19:1.

¹H NMR (300 MHz, CDCl₃) δ 8.15 – 8.10 (m, 2H), 7.43 – 7.36 (m, 2H), 7.35 – 7.28 (m, 3H), 7.18 – 7.13 (m, 2H), 3.92 (s, 3H), 3.12 – 3.00 (m, 2H), 2.73 – 2.58 (m, 2H), 1.47 (s, 3H).

¹³C NMR (75 MHz, CDCl₃) δ 177.0, 175.9, 166.5, 139.0, 138.0, 130.5, 130.3, 128.7, 128.7, 127.8, 126.6, 52.4, 50.8, 44.5, 43.3, 19.7.

HRMS (ESI-TOF): m/z calcd. for [M + Na]⁺ C₂₁H₁₉NO₄Na⁺ 372.1206; Found: 372.1206.



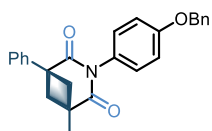
1-methyl-3-(4-(methylsulfonyl)phenyl)-5-phenyl-3-azabicyclo[3.1.1]heptane-2,4-dione (4m)

25.0 mg, 68% yield, white solid. Eluent: pentane/ethyl acetate = 2:1, R_f = 0.3, r.r. > 19:1.

¹H NMR (400 MHz, CDCl₃) δ 8.06 – 8.00 (m, 2H), 7.47 – 7.43 (m, 2H), 7.41 – 7.38 (m, 2H), 7.36 – 7.31 (m, 1H), 7.17 – 7.13 (m, 2H), 3.08 – 3.05 (m, 5H), 2.70 – 2.64 (m, 2H), 1.48 (s, 3H).

¹³C NMR (101 MHz, CDCl₃) δ 176.7, 175.6, 140.2, 138.6, 138.5, 129.7, 128.5, 128.2, 127.8, 126.4, 50.7, 44.5, 44.2, 43.2, 19.5.

HRMS (ESI-TOF): m/z calcd. for [M + Na]⁺ C₂₀H₁₉NO₄SN⁺ 392.0927; Found: 392.0936.



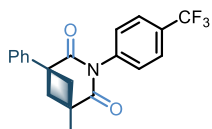
3-(4-(benzyloxy)phenyl)-1-methyl-5-phenyl-3-azabicyclo[3.1.1]heptane-2,4-dione (4n)

29.0 mg, 73% yield, white solid. Eluent: pentane/ethyl acetate = 5:1, R_f = 0.3, r.r. > 19:1.

¹H NMR (400 MHz, CDCl₃) δ 7.45 – 7.37 (m, 6H), 7.35 – 7.29 (m, 2H), 7.19 – 7.10 (m, 4H), 7.06 – 7.02 (m, 2H), 5.08 (s, 2H), 3.08 – 2.97 (m, 2H), 2.69 – 2.57 (m, 2H), 1.47 (s, 3H).

¹³C NMR (101 MHz, CDCl₃) δ 177.7, 176.5, 158.7, 139.3, 136.8, 129.5, 128.7, 128.5, 128.2, 127.6, 126.6, 126.6, 115.4, 70.3, 50.7, 44.6, 43.1, 19.8.

HRMS (ESI-TOF): m/z calcd. for [M + Na]⁺ C₂₆H₂₃NO₃Na⁺ 420.1570; Found: 420.1573.



1-methyl-5-phenyl-3-(4-(trifluoromethyl)phenyl)-3-azabicyclo[3.1.1]heptane-2,4-dione (4o)

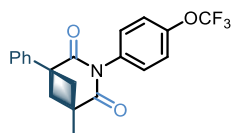
21.4 mg, 60% yield, white solid. Eluent: pentane/ethyl acetate = 15:1, R_f = 0.2, r.r. > 19:1.

¹H NMR (300 MHz, CDCl₃) δ 7.75 – 7.69 (m, 2H), 7.45 – 7.29 (m, 5H), 7.19 – 7.12 (m, 2H), 3.11 – 3.02 (m, 2H), 2.72 – 2.61 (m, 2H), 1.48 (s, 3H).

¹³C NMR (75 MHz, CDCl₃) δ 177.0, 175.9, 138.9, 137.0, 130.7 (d, J = 32.8 Hz), 129.2, 128.7, 127.9, 126.6, 126.2 (q, J = 3.8 Hz), 50.8, 44.5, 43.3, 19.7.

¹⁹F NMR (282 MHz, CDCl₃) δ -62.62 (s).

HRMS (ESI-TOF): m/z calcd. for $[M + Na]^+ C_{20}H_{16}F_3NO_2Na^+$ 382.1025; Found: 382.1032.



1-methyl-5-phenyl-3-(4-(trifluoromethoxy)phenyl)-3-azabicyclo[3.1.1]heptane-2,4-dione (4p)

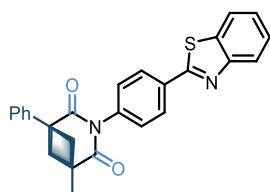
21.8 mg, 58% yield, white solid. Eluent: pentane/ethyl acetate = 10:1, R_f = 0.2, r.r. > 19:1.

1H NMR (300 MHz, $CDCl_3$) δ 7.44 – 7.37 (m, 2H), 7.36 – 7.27 (m, 3H), 7.27 – 7.23 (m, 2H), 7.19 – 7.13 (m, 2H), 3.13 – 2.97 (m, 2H), 2.72 – 2.61 (m, 2H), 1.47 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 177.2, 176.1, 149.0, 139.0, 132.1, 130.1, 128.6, 127.8, 126.6, 121.5, 50.8, 44.5, 43.2, 19.8.

^{19}F NMR (282 MHz, $CDCl_3$) δ -57.85 (s).

HRMS (ESI-TOF): m/z calcd. for $[M + Na]^+ C_{20}H_{16}F_3NO_3Na^+$ 398.0974; Found: 398.0978.



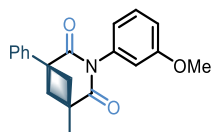
3-(4-(benzo[d]thiazol-2-yl)phenyl)-1-methyl-5-phenyl-3-azabicyclo[3.1.1]heptane-2,4-dione (4q)

25.3 mg, 60% yield, white solid. Eluent: pentane/ethyl acetate = 5:1, R_f = 0.2, r.r. > 19:1.

1H NMR (400 MHz, $CDCl_3$) δ 8.21 – 8.17 (m, 2H), 8.09 (d, J = 7.9 Hz, 1H), 7.94 – 7.88 (m, 1H), 7.51 (ddd, J = 8.3, 7.2, 1.3 Hz, 1H), 7.44 – 7.37 (m, 4H), 7.36 – 7.31 (m, 2H), 7.21 – 7.14 (m, 2H), 3.14 – 3.05 (m, 2H), 2.71 – 2.60 (m, 2H), 1.49 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 177.2, 176.0, 167.1, 154.1, 139.0, 136.1, 135.2, 133.6, 129.3, 128.7, 128.2, 127.8, 126.6, 126.6, 125.6, 123.5, 121.8, 50.8, 44.5, 43.3, 19.8.

HRMS (ESI-TOF): m/z calcd. for $[M + Na]^+ C_{26}H_{20}N_2O_2SNa^+$ 447.1137; Found: 447.1146.



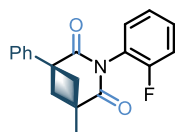
3-(3-methoxyphenyl)-1-methyl-5-phenyl-3-azabicyclo[3.1.1]heptane-2,4-dione (4r)

24.1 mg, 75% yield, white solid. Eluent: pentane/ethyl acetate = 5:1, R_f = 0.3, r.r. > 19:1.

1H NMR (300 MHz, $CDCl_3$) δ 7.43 – 7.28 (m, 4H), 7.19 – 7.14 (m, 2H), 6.94 (ddd, J = 8.4, 2.5, 0.9 Hz, 1H), 6.79 (ddd, J = 7.8, 1.9, 0.9 Hz, 1H), 6.76 – 6.69 (m, 1H), 3.80 (s, 3H), 3.08 – 3.00 (m, 2H), 2.70 – 2.56 (m, 2H), 1.47 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 177.4, 176.2, 160.3, 139.2, 134.9, 129.8, 128.6, 127.7, 126.7, 120.7, 114.9, 114.1, 55.5, 50.7, 44.6, 43.1, 19.8.

HRMS (ESI-TOF): m/z calcd. for $[M + Na]^+ C_{20}H_{19}NO_3Na^+$ 344.1257; Found: 344.1256.



3-(2-fluorophenyl)-1-methyl-5-phenyl-3-azabicyclo[3.1.1]heptane-2,4-dione (4s)

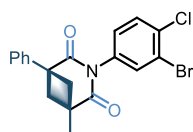
17.7 mg, 57% yield, white solid. Eluent: pentane/ethyl acetate = 10:1, R_f = 0.2, r.r. > 19:1.

1H NMR (400 MHz, $CDCl_3$) δ 7.42 – 7.36 (m, 3H), 7.34 – 7.30 (m, 1H), 7.26 – 7.21 (m, 2H), 7.20 – 7.15 (m, 3H), 3.13 – 3.03 (m, 2H), 2.64 (t, J = 9.0 Hz, 2H), 1.48 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 176.8, 175.6, 158.3 (d, J = 250.4 Hz), 139.0, 130.8, 130.7, 128.6, 127.7, 126.6, 124.5 (d, J = 3.9 Hz), 121.7 (d, J = 13.5 Hz), 116.5 (d, J = 19.9 Hz), 50.9, 44.8, 44.4, 43.3, 19.7.

^{19}F NMR (376 MHz, $CDCl_3$) δ -121.13 – -121.28 (m).

HRMS (ESI-TOF): m/z calcd. for $[M + Na]^+ C_{19}H_{16}FNO_2Na^+$ 332.1057; Found: 332.1057.

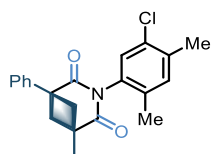


3-(3-bromo-4-chlorophenyl)-1-methyl-5-phenyl-3-azabicyclo[3.1.1]heptane-2,4-dione (4t)

18.1 mg, 45% yield, white solid. Eluent: pentane/ethyl acetate = 10:1, R_f = 0.2, r.r. > 19:1.

¹H NMR (300 MHz, CDCl₃) δ 7.69 (d, *J* = 8.5 Hz, 1H), 7.43 – 7.36 (m, 2H), 7.36 – 7.29 (m, 2H), 7.18 – 7.11 (m, 2H), 7.00 (dd, *J* = 8.5, 2.4 Hz, 1H), 3.07 – 2.97 (m, 2H), 2.69 – 2.59 (m, 2H), 1.46 (s, 3H).
¹³C NMR (75 MHz, CDCl₃) δ 176.9, 175.8, 138.8, 135.1, 134.0, 133.7, 130.7, 128.7, 128.2, 127.9, 126.6, 122.8, 50.8, 44.4, 43.3, 19.7.

HRMS (ESI-TOF): *m/z* calcd. for [M + Na]⁺ C₁₉H₁₅BrClNO₂Na⁺ 425.9867; Found: 425.9855.



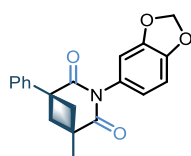
3-(5-chloro-2,4-dimethylphenyl)-1-methyl-5-phenyl-3-azabicyclo[3.1.1]heptane-2,4-dione (4u)

27.8 mg, 79% yield, white solid. Eluent: pentane/ethyl acetate = 5:1, *R_f* = 0.3, r.r. > 19:1.

¹H NMR (300 MHz, CDCl₃) δ 7.42 – 7.34 (m, 2H), 7.33 – 7.27 (m, 1H), 7.19 – 7.13 (m, 3H), 6.56 (s, 1H), 3.92 (s, 3H), 3.80 (s, 3H), 3.11 – 2.98 (m, 2H), 2.59 (dd, *J* = 9.0, 2.8 Hz, 2H), 1.45 (s, 3H).

¹³C NMR (75 MHz, CDCl₃) δ 177.3, 176.1, 156.3, 155.0, 139.3, 131.1, 128.5, 127.6, 126.6, 115.6, 113.7, 97.2, 56.5, 56.4, 50.8, 44.6, 44.5, 43.2, 19.8.

HRMS (ESI-TOF): *m/z* calcd. for [M + Na]⁺ C₂₁H₂₀ClNO₂Na⁺ 376.1075; Found: 376.1077.



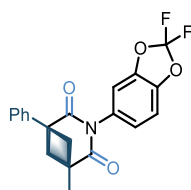
3-(benzo[d][1,3]dioxol-5-yl)-1-methyl-5-phenyl-3-azabicyclo[3.1.1]heptane-2,4-dione (4v)

25.4 mg, 76% yield, white solid. Eluent: pentane/ethyl acetate = 6:1, *R_f* = 0.3, r.r. > 19:1.

¹H NMR (400 MHz, CDCl₃) δ 7.41 – 7.36 (m, 2H), 7.34 – 7.29 (m, 1H), 7.17 – 7.13 (m, 2H), 6.88 – 6.84 (m, 1H), 6.68 – 6.64 (m, 2H), 6.00 (s, 2H), 3.04 – 2.98 (m, 2H), 2.65 – 2.58 (m, 2H), 1.46 (s, 3H).

¹³C NMR (101 MHz, CDCl₃) δ 177.6, 176.4, 148.3, 147.9, 139.2, 128.6, 127.7, 127.3, 126.6, 122.0, 109.5, 108.5, 101.9, 50.7, 44.6, 43.1, 19.8.

HRMS (ESI-TOF): *m/z* calcd. for [M + Na]⁺ C₂₀H₁₇NO₄Na⁺ 358.1049; Found: 358.1054.



3-(2,2-difluorobenzo[d][1,3]dioxol-5-yl)-1-methyl-5-phenyl-3-azabicyclo[3.1.1]heptane-2,4-dione (4w)

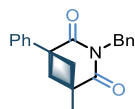
22.4 mg, 60% yield, white solid. Eluent: pentane/ethyl acetate = 10:1, *R_f* = 0.2, r.r. > 19:1.

¹H NMR (400 MHz, CDCl₃) δ 7.43 – 7.38 (m, 2H), 7.36 – 7.30 (m, 1H), 7.18 – 7.10 (m, 3H), 6.98 – 6.89 (m, 2H), 3.09 – 2.99 (m, 2H), 2.71 – 2.59 (m, 2H), 1.47 (s, 3H).

¹³C NMR (101 MHz, CDCl₃) δ 177.3, 176.2, 143.9 (d, *J* = 34.3 Hz), 138.9, 131.9 (t, *J* = 256.7 Hz), 129.3, 128.7, 127.8, 126.6, 124.3, 110.7, 109.6, 50.7, 44.5, 43.2, 19.7.

¹⁹F NMR (376 MHz, CDCl₃) δ -49.37 (s).

HRMS (ESI-TOF): *m/z* calcd. for [M + Na]⁺ C₂₀H₁₅F₂NO₄Na⁺ 394.0861; Found: 394.0862.



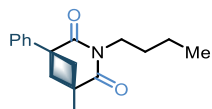
3-benzyl-1-methyl-5-phenyl-3-azabicyclo[3.1.1]heptane-2,4-dione (4x)

21.7 mg, 71% yield, white solid. Eluent: pentane/ethyl acetate = 10:1, *R_f* = 0.2, r.r. > 19:1.

¹H NMR (300 MHz, CDCl₃) δ 7.42 – 7.35 (m, 4H), 7.34 – 7.29 (m, 3H), 7.29 – 7.26 (m, 1H), 7.14 – 7.05 (m, 2H), 4.91 (s, 2H), 2.85 – 2.76 (m, 2H), 2.53 – 2.47 (m, 2H), 1.41 (s, 3H).

¹³C NMR (75 MHz, CDCl₃) δ 177.6, 176.5, 139.4, 137.4, 128.9, 128.6, 128.6, 127.6, 127.6, 126.6, 54.9, 50.5, 44.8, 42.9, 42.6, 19.7.

HRMS (ESI-TOF): *m/z* calcd. for [M + Na]⁺ C₂₀H₁₉NO₂Na⁺ 328.1308; Found: 328.1307.



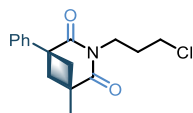
3-butyl-1-methyl-5-phenyl-3-azabicyclo[3.1.1]heptane-2,4-dione (4y)

11.4 mg, 42% yield, colorless oil. Eluent: pentane/ethyl acetate = 15:1, *R_f* = 0.2, r.r. > 19:1.

¹H NMR (400 MHz, CDCl₃) δ 7.42 – 7.36 (m, 2H), 7.34 – 7.29 (m, 1H), 7.13 – 7.08 (m, 2H), 3.79 – 3.66 (m, 2H), 2.83 – 2.77 (m, 2H), 2.52 – 2.45 (m, 2H), 1.56 – 1.51 (m, 2H), 1.40 (s, 3H), 1.38 – 1.28 (m, 2H), 0.92 (t, *J* = 7.3 Hz, 3H).

¹³C NMR (101 MHz, CDCl₃) δ 177.8, 176.7, 139.7, 128.6, 127.6, 126.6, 50.6, 45.1, 43.0, 39.0, 30.3, 20.3, 19.8, 13.9.

HRMS (ESI-TOF): *m/z* calcd. for [M + Na]⁺ C₁₇H₂₁NO₂Na⁺ 294.1464; Found: 294.1469.



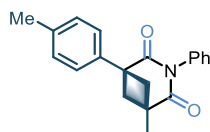
3-(3-chloropropyl)-1-methyl-5-phenyl-3-azabicyclo[3.1.1]heptane-2,4-dione (4z)

12.3 mg, 42% yield, colorless oil. Eluent: pentane/ethyl acetate = 15:1, *R_f* = 0.2, *r.r.* > 19:1.

¹H NMR (400 MHz, CDCl₃) δ 7.42 – 7.37 (m, 2H), 7.35 – 7.30 (m, 1H), 7.12 – 7.08 (m, 2H), 3.90 (t, *J* = 7.0 Hz, 2H), 3.55 (t, *J* = 6.6 Hz, 2H), 2.87 – 2.79 (m, 2H), 2.57 – 2.47 (m, 2H), 2.08 (p, *J* = 6.8 Hz, 2H), 1.41 (s, 3H).

¹³C NMR (101 MHz, CDCl₃) δ 177.7, 176.7, 139.4, 128.6, 127.7, 126.5, 50.6, 44.9, 43.0, 42.6, 37.2, 31.3, 19.7.

HRMS (ESI-TOF): *m/z* calcd. for [M + Na]⁺ C₁₆H₁₈ClNO₂Na⁺ 314.0918; Found: 314.0926.



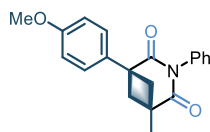
1-methyl-3-phenyl-5-(p-tolyl)-3-azabicyclo[3.1.1]heptane-2,4-dione (4aa)

18.1 mg, 59% yield, white solid. Eluent: pentane/ethyl acetate = 10:1, *R_f* = 0.2, *r.r.* > 19:1.

¹H NMR (300 MHz, CDCl₃) δ 7.49 – 7.35 (m, 3H), 7.23 – 7.17 (m, 4H), 7.08 – 7.02 (m, 2H), 3.09 – 2.92 (m, 2H), 2.65 – 2.53 (m, 2H), 2.36 (s, 3H), 1.46 (s, 3H).

¹³C NMR (75 MHz, CDCl₃) δ 177.5, 176.4, 137.4, 136.3, 133.9, 129.3, 129.1, 128.6, 128.5, 126.5, 50.5, 44.7, 43.1, 21.3, 19.8.

HRMS (ESI-TOF): *m/z* calcd. for [M + Na]⁺ C₂₀H₁₉NO₂Na⁺ 328.1308; Found: 328.1308.



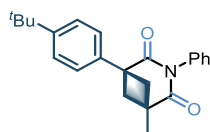
1-(4-methoxyphenyl)-5-methyl-3-phenyl-3-azabicyclo[3.1.1]heptane-2,4-dione (4ab)

20.8 mg, 65% yield, white solid. Eluent: pentane/ethyl acetate = 6:1, *R_f* = 0.2, *r.r.* > 19:1.

¹H NMR (300 MHz, CDCl₃) δ 7.50 – 7.34 (m, 3H), 7.22 – 7.17 (m, 2H), 7.14 – 7.05 (m, 2H), 6.96 – 6.89 (m, 2H), 3.81 (s, 3H), 3.07 – 2.97 (m, 2H), 2.64 – 2.53 (m, 2H), 1.46 (s, 3H).

¹³C NMR (75 MHz, CDCl₃) δ 177.5, 176.5, 159.0, 133.9, 131.4, 129.2, 128.6, 128.5, 127.8, 114.0, 55.4, 50.2, 44.7, 43.1, 19.8.

HRMS (ESI-TOF): *m/z* calcd. for [M + Na]⁺ C₂₀H₁₉NO₃Na⁺ 344.1257; Found: 344.1262.



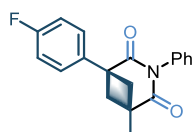
1-(4-(tert-butyl)phenyl)-5-methyl-3-phenyl-3-azabicyclo[3.1.1]heptane-2,4-dione (4ac)

22.4 mg, 65% yield, white solid. Eluent: pentane/ethyl acetate = 10:1, *R_f* = 0.2, *r.r.* > 19:1.

¹H NMR (300 MHz, CDCl₃) δ 7.49 – 7.34 (m, 5H), 7.23 – 7.18 (m, 2H), 7.13 – 7.07 (m, 2H), 3.09 – 2.98 (m, 2H), 2.69 – 2.57 (m, 2H), 1.46 (s, 3H), 1.33 (s, 9H).

¹³C NMR (75 MHz, CDCl₃) δ 177.1, 176.0, 150.1, 135.8, 133.4, 128.7, 128.1, 128.1, 125.9, 125.1, 50.0, 44.2, 42.7, 34.3, 31.0, 19.4.

HRMS (ESI-TOF): *m/z* calcd. for [M + Na]⁺ C₂₃H₂₅NO₂Na⁺ 370.1777; Found: 370.1787.



1-(4-fluorophenyl)-5-methyl-3-phenyl-3-azabicyclo[3.1.1]heptane-2,4-dione (4ad)

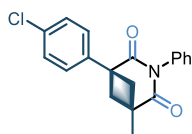
16.8 mg, 54% yield, white solid. Eluent: pentane/ethyl acetate = 10:1, *R_f* = 0.2, *r.r.* > 19:1.

¹H NMR (300 MHz, CDCl₃) δ 7.51 – 7.35 (m, 3H), 7.22 – 7.16 (m, 2H), 7.16 – 7.03 (m, 4H), 3.10 – 2.95 (m, 2H), 2.69 – 2.56 (m, 2H), 1.47 (s, 3H).

¹³C NMR (75 MHz, CDCl₃) δ 177.2, 176.1, 162.2 (d, *J* = 246.2 Hz), 135.1 (d, *J* = 3.1 Hz), 129.2, 128.7, 128.5, 128.5, 128.4, 115.5 (d, *J* = 21.7 Hz), 50.2, 44.7, 43.1, 19.8.

^{19}F NMR (282 MHz, CDCl_3) δ -114.60 – -114.78 (m).

HRMS (ESI-TOF): m/z calcd. for $[\text{M} + \text{Na}]^+ \text{C}_{19}\text{H}_{16}\text{FNO}_2\text{Na}^+$ 332.1057; Found: 332.1062.



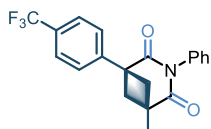
1-(4-chlorophenyl)-5-methyl-3-phenyl-3-azabicyclo[3.1.1]heptane-2,4-dione (4ae)

14.3 mg, 44% yield, white solid. Eluent: pentane/ethyl acetate = 10:1, R_f = 0.2, r.r. > 19:1.

^1H NMR (300 MHz, CDCl_3) δ 7.49 – 7.38 (m, 3H), 7.38 – 7.33 (m, 2H), 7.21 – 7.16 (m, 2H), 7.13 – 7.06 (m, 2H), 3.10 – 2.97 (m, 2H), 2.65 – 2.55 (m, 2H), 1.47 (s, 3H).

^{13}C NMR (75 MHz, CDCl_3) δ 177.1, 175.9, 137.7, 133.7, 133.7, 129.2, 128.7, 128.5, 128.2, 50.3, 44.6, 43.1, 19.8.

HRMS (ESI-TOF): m/z calcd. for $[\text{M} + \text{Na}]^+ \text{C}_{19}\text{H}_{16}\text{ClNO}_2\text{Na}^+$ 348.0761; Found: 348.0767.



1-methyl-3-phenyl-5-(4-(trifluoromethyl)phenyl)-3-azabicyclo[3.1.1]heptane-2,4-dione (4af)

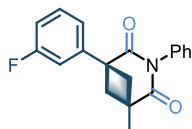
24.0 mg, 67% yield, white solid. Eluent: pentane/ethyl acetate = 10:1, R_f = 0.2, r.r. > 19:1.

^1H NMR (400 MHz, CDCl_3) δ 7.65 (d, J = 8.1 Hz, 2H), 7.49 – 7.44 (m, 2H), 7.43 – 7.38 (m, 1H), 7.30 – 7.27 (m, 2H), 7.22 – 7.18 (m, 2H), 3.13 – 3.02 (m, 2H), 2.68 – 2.58 (m, 2H), 1.49 (s, 3H).

^{13}C NMR (101 MHz, CDCl_3) δ 176.9, 175.6, 143.1, 133.6, 130.0 (q, J = 32.7 Hz), 129.3, 128.8, 128.4, 127.3, 125.6 (q, J = 3.7 Hz), 50.6, 44.5, 43.2, 19.8.

^{19}F NMR (376 MHz, CDCl_3) δ -62.57 (s).

HRMS (ESI-TOF): m/z calcd. for $[\text{M} + \text{Na}]^+ \text{C}_{20}\text{H}_{16}\text{F}_3\text{NO}_2\text{Na}^+$ 382.1025; Found: 382.1027.



1-(3-fluorophenyl)-5-methyl-3-phenyl-3-azabicyclo[3.1.1]heptane-2,4-dione (4ag)

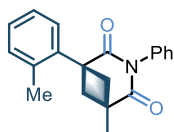
17.4 mg, 56% yield, white solid. Eluent: pentane/ethyl acetate = 10:1, R_f = 0.2, r.r. > 19:1.

^1H NMR (300 MHz, CDCl_3) δ 7.49 – 7.30 (m, 4H), 7.21 – 7.17 (m, 2H), 7.05 – 6.98 (m, 1H), 6.96 – 6.92 (m, 1H), 6.90 – 6.84 (m, 1H), 3.08 – 2.99 (m, 2H), 2.66 – 2.56 (m, 2H), 1.47 (s, 3H).

^{13}C NMR (75 MHz, CDCl_3) δ 177.1, 175.7, 162.9 (d, J = 246.5 Hz), 141.6 (d, J = 7.3 Hz), 133.7, 130.2 (d, J = 8.3 Hz), 129.2, 128.7, 128.5, 122.4 (d, J = 3.1 Hz), 114.7 (d, J = 21.1 Hz), 114.0 (d, J = 22.0 Hz), 50.5, 44.6, 43.1, 19.8.

^{19}F NMR (282 MHz, CDCl_3) δ -108.67 – -117.62 (m).

HRMS (ESI-TOF): m/z calcd. for $[\text{M} + \text{Na}]^+ \text{C}_{19}\text{H}_{16}\text{FNO}_2\text{Na}^+$ 332.1057; Found: 332.1053.



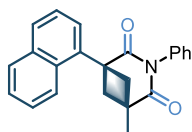
1-methyl-3-phenyl-5-(o-tolyl)-3-azabicyclo[3.1.1]heptane-2,4-dione (4ah)

7.2 mg, 24% yield, white solid. Eluent: pentane/ethyl acetate = 10:1, R_f = 0.2, r.r. = 1:1.

^1H NMR (300 MHz, CDCl_3) δ 7.49 – 7.35 (m, 3H), 7.24 – 7.20 (m, 3H), 7.19 – 7.16 (m, 2H), 7.06 – 7.01 (m, 1H), 3.20 – 3.06 (m, 2H), 2.71 – 2.58 (m, 2H), 2.22 (d, J = 0.5 Hz, 3H), 1.46 (s, 3H).

^{13}C NMR (75 MHz, CDCl_3) δ 177.5, 175.2, 137.4, 137.0, 133.8, 131.1, 129.2, 128.6, 128.5, 128.1, 126.9, 126.1, 51.4, 43.1, 20.5, 19.8.

HRMS (ESI-TOF): m/z calcd. for $[\text{M} + \text{Na}]^+ \text{C}_{20}\text{H}_{19}\text{NO}_2\text{Na}^+$ 328.1308; Found: 328.1313.



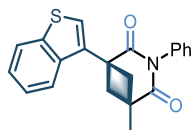
1-methyl-5-(naphthalen-1-yl)-3-phenyl-3-azabicyclo[3.1.1]heptane-2,4-dione (4ai)

21.8 mg, 64% yield, white solid. Eluent: pentane/ethyl acetate = 10:1, R_f = 0.2, r.r. > 19:1.

^1H NMR (300 MHz, CDCl_3) δ 7.80 – 7.70 (m, 3H), 7.52 (d, J = 1.5 Hz, 1H), 7.43 – 7.27 (m, 5H), 7.20 (dd, J = 8.5, 1.8 Hz, 1H), 7.17 – 7.11 (m, 2H), 3.10 – 2.98 (m, 1H), 2.66 – 2.58 (m, 1H), 1.41 (s, 1H).

¹³C NMR (75 MHz, CDCl₃) δ 177.4, 176.2, 136.8, 133.8, 133.3, 132.8, 129.2, 128.6, 128.5, 128.3, 128.0, 127.9, 126.4, 126.3, 125.4, 124.8, 50.9, 44.7, 43.2, 19.8.

HRMS (ESI-TOF): m/z calcd. for [M + Na]⁺ C₂₃H₁₉NO₂Na⁺ 364.1308; Found: 364.1316.



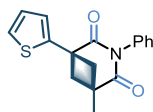
1-(benzo[b]thiophen-3-yl)-5-methyl-3-phenyl-3-azabicyclo[3.1.1]heptane-2,4-dione (4aj)

16.4 mg, 47% yield, white solid. Eluent: pentane/ethyl acetate = 7:1, R_f = 0.3, r.r. > 19:1.

¹H NMR (300 MHz, CDCl₃) δ 7.81 – 7.74 (m, 1H), 7.44 – 7.36 (m, 2H), 7.36 – 7.29 (m, 2H), 7.28 – 7.23 (m, 2H), 7.18 – 7.13 (m, 2H), 7.08 (s, 1H), 3.17 – 3.07 (m, 2H), 2.66 – 2.57 (m, 2H), 1.40 (s, 3H).

¹³C NMR (75 MHz, CDCl₃) δ 177.2, 174.7, 140.6, 137.4, 135.2, 133.6, 129.2, 128.6, 128.5, 124.5, 124.3, 123.7, 123.1, 122.9, 48.0, 44.9, 44.2, 19.8.

HRMS (ESI-TOF): m/z calcd. for [M + Na]⁺ C₂₁H₁₇NO₂Na⁺ 370.0872; Found: 370.0872.



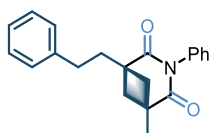
1-methyl-3-phenyl-5-(thiophen-2-yl)-3-azabicyclo[3.1.1]heptane-2,4-dione (4ak)

14.0 mg, 47% yield, white solid. Eluent: pentane/ethyl acetate = 10:1, R_f = 0.2, r.r. > 19:1.

¹H NMR (300 MHz, CDCl₃) δ 7.51 – 7.37 (m, 3H), 7.34 (dd, J = 5.0, 2.9 Hz, 1H), 7.22 – 7.15 (m, 3H), 7.03 (dd, J = 5.0, 1.3 Hz, 1H), 3.03 – 2.91 (m, 2H), 2.70 – 2.59 (m, 2H), 1.47 (s, 3H).

¹³C NMR (75 MHz, CDCl₃) δ 177.3, 175.7, 139.9, 133.8, 129.2, 128.7, 128.5, 126.7, 126.2, 122.1, 47.6, 45.4, 43.4, 19.8.

HRMS (ESI-TOF): m/z calcd. for [M + Na]⁺ C₁₇H₁₅NO₂SNa⁺ 320.0715; Found: 320.0717.



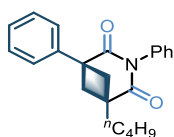
1-methyl-5-phenethyl-3-phenyl-3-azabicyclo[3.1.1]heptane-2,4-dione (4al)

7.7 mg, 24% yield, colorless oil. Eluent: pentane/ethyl acetate = 10:1, R_f = 0.2, r.r. > 19:1.

¹H NMR (400 MHz, CDCl₃) δ 7.52 – 7.45 (m, 2H), 7.43 – 7.37 (m, 1H), 7.32 – 7.27 (m, 4H), 7.22 – 7.17 (m, 3H), 2.80 (d, J = 4.4 Hz, 1H), 2.73 – 2.65 (m, 2H), 2.62 – 2.55 (m, 1H), 2.47 – 2.37 (m, 1H), 2.13 – 2.05 (m, 1H), 2.01 – 1.96 (m, 1H), 1.91 (dd, J = 12.8, 6.8 Hz, 1H), 1.52 (s, 3H).

¹³C NMR (101 MHz, CDCl₃) δ 181.6, 177.6, 141.2, 132.3, 129.3, 128.7, 128.6, 128.4, 126.5, 126.2, 50.0, 41.9, 38.8, 36.3, 34.7, 32.9, 21.4.

HRMS (ESI-TOF): m/z calcd. for [M + Na]⁺ C₂₁H₂₁NO₂Na⁺ 342.1464; Found: 342.1647.



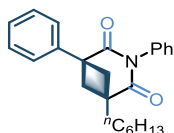
1-butyl-3,5-diphenyl-3-azabicyclo[3.1.1]heptane-2,4-dione (4am)

13.9 mg, 42% yield, white solid. Eluent: pentane/ethyl acetate = 10:1, R_f = 0.2, r.r. > 19:1.

¹H NMR (300 MHz, CDCl₃) δ 7.48 – 7.41 (m, 2H), 7.40 – 7.36 (m, 3H), 7.34 – 7.28 (m, 2H), 7.22 – 7.15 (m, 3H), 3.04 – 2.96 (m, 2H), 2.72 – 2.60 (m, 2H), 1.86 – 1.77 (m, 2H), 1.43 – 1.34 (m, 4H), 0.97 – 0.86 (m, 3H).

¹³C NMR (75 MHz, CDCl₃) δ 177.1, 176.2, 139.4, 133.8, 129.2, 128.6, 128.5, 127.7, 126.6, 50.5, 46.6, 42.9, 33.0, 26.7, 23.2, 14.1.

HRMS (ESI-TOF): m/z calcd. for [M + Na]⁺ C₂₂H₂₃NO₂Na⁺ 356.1621; Found: 356.1627.



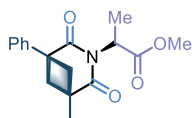
1-hexyl-3,5-diphenyl-3-azabicyclo[3.1.1]heptane-2,4-dione (4an)

12.4 mg, 34% yield, white solid. Eluent: pentane/ethyl acetate = 10:1, R_f = 0.2, r.r. > 19:1.

¹H NMR (300 MHz, CDCl₃) δ 7.48 – 7.42 (m, 2H), 7.41 – 7.36 (m, 3H), 7.35 – 7.28 (m, 2H), 7.23 – 7.15 (m, 3H), 3.05 – 2.95 (m, 2H), 2.69 – 2.59 (m, 2H), 1.87 – 1.76 (m, 2H), 1.39 – 1.24 (m, 8H), 0.91 – 0.85 (m, 3H).

¹³C NMR (75 MHz, CDCl₃) δ 177.0, 176.2, 139.4, 133.8, 129.1, 128.6, 128.5, 127.6, 126.6, 50.5, 46.6, 42.9, 33.2, 31.8, 29.7, 24.4, 22.7, 14.2.

HRMS (ESI-TOF): m/z calcd. for [M + Na]⁺ C₂₄H₂₇NO₂Na⁺ 384.1934; Found: 384.1944.



From L-Alanine

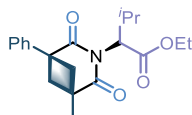
methyl (R)-2-(1-methyl-2,4-dioxo-5-phenyl-3-azabicyclo[3.1.1]heptan-3-yl)-2-phenylacetate (4ap)

14.1 mg, 39% yield, colorless oil. Eluent: pentane/ethyl acetate = 10:1, R_f = 0.2, r.r. > 19:1.

$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.42 – 7.37 (m, 2H), 7.34 – 7.29 (m, 1H), 7.15 – 7.09 (m, 2H), 5.23 (q, J = 7.1 Hz, 1H), 3.72 (s, 3H), 2.96 – 2.83 (m, 2H), 2.61 – 2.44 (m, 2H), 1.57 (d, J = 7.1 Hz, 3H), 1.41 (s, 3H).

$^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 177.0, 175.9, 170.9, 139.2, 128.6, 127.7, 126.6, 52.7, 50.5, 48.1, 44.5, 42.9, 19.6, 14.9.

HRMS (ESI-TOF): m/z calcd. for $[\text{M} + \text{Na}]^+$ $\text{C}_{17}\text{H}_{19}\text{NO}_4\text{Na}^+$ 324.1206; Found: 324.1208.



From L-Valine

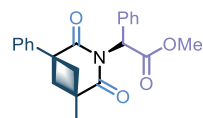
ethyl (R)-3-methyl-2-(1-methyl-2,4-dioxo-5-phenyl-3-azabicyclo[3.1.1]heptan-3-yl)butanoate (4aq)

13.8 mg, 40% yield, colorless oil. Eluent: pentane/ethyl acetate = 10:1, R_f = 0.2, r.r. > 19:1.

$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.42 – 7.36 (m, 2H), 7.35 – 7.29 (m, 1H), 7.12 – 7.08 (m, 2H), 4.75 (d, J = 9.1 Hz, 1H), 4.23 (dq, J = 10.8, 7.1 Hz, 1H), 4.13 – 4.04 (m, 1H), 2.93 – 2.86 (m, 2H), 2.66 (dp, J = 9.1, 6.7 Hz, 1H), 2.55 – 2.50 (m, 2H), 1.42 (s, 3H), 1.25 – 1.18 (m, 6H), 0.84 (d, J = 6.9 Hz, 3H).

$^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 177.1, 176.0, 169.5, 139.1, 128.5, 127.6, 126.4, 61.0, 57.4, 50.4, 44.2, 44.1, 42.8, 27.8, 22.1, 19.6, 19.3, 14.2.

HRMS (ESI-TOF): m/z calcd. for $[\text{M} + \text{Na}]^+$ $\text{C}_{20}\text{H}_{25}\text{NO}_4\text{Na}^+$ 366.1675; Found: 366.1668.



From L-2-Phenylglycine

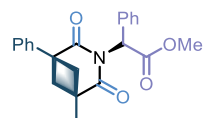
methyl (R)-2-(1-methyl-2,4-dioxo-5-phenyl-3-azabicyclo[3.1.1]heptan-3-yl)-2-phenylacetate (4ar)

13.9 mg, 38% yield, colorless oil. Eluent: pentane/ethyl acetate = 10:1, R_f = 0.2, r.r. > 19:1.

$^1\text{H NMR}$ (300 MHz, CDCl_3) δ 7.54 – 7.49 (m, 2H), 7.39 – 7.36 (m, 2H), 7.34 – 7.31 (m, 4H), 7.12 – 7.08 (m, 2H), 6.30 (s, 1H), 3.78 (s, 3H), 2.94 – 2.76 (m, 2H), 2.55 – 2.44 (m, 2H), 1.41 (s, 3H).

$^{13}\text{C NMR}$ (75 MHz, CDCl_3) δ 176.8, 175.8, 169.0, 139.1, 135.0, 130.2, 128.7, 128.4, 127.8, 126.6, 56.0, 52.9, 50.5, 44.3 (d, J = 2.7 Hz), 42.9, 19.6.

HRMS (ESI-TOF): m/z calcd. for $[\text{M} + \text{Na}]^+$ $\text{C}_{22}\text{H}_{21}\text{NO}_4\text{Na}^+$ 386.1363; Found: 386.1364.



From L-2-Phenylglycine

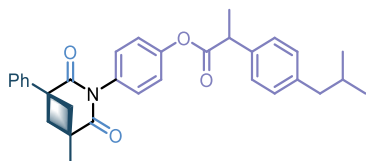
ethyl (R)-2-(1-methyl-2,4-dioxo-5-phenyl-3-azabicyclo[3.1.1]heptan-3-yl)-3-phenylpropanoate (4as)

15.8 mg, 40% yield, colorless oil. Eluent: pentane/ethyl acetate = 10:1, R_f = 0.2, r.r. > 19:1.

$^1\text{H NMR}$ (300 MHz, CDCl_3) δ 7.39 – 7.32 (m, 2H), 7.31 – 7.27 (m, 2H), 7.26 – 7.21 (m, 1H), 7.19 – 7.14 (m, 2H), 6.98 – 6.90 (m, 2H), 5.53 (dd, J = 10.8, 6.6 Hz, 1H), 4.35 – 4.12 (m, 2H), 3.57 – 3.38 (m, 2H), 2.27 (dd, J = 5.4, 3.7 Hz, 3H), 1.57 (s, 3H), 1.34 – 1.20 (m, 5H).

$^{13}\text{C NMR}$ (75 MHz, CDCl_3) δ 176.8, 175.8, 169.5, 139.1, 137.2, 129.4, 128.4, 128.3, 127.5, 126.8, 126.3, 61.6, 52.1, 50.1, 44.0, 42.5, 34.4, 19.4, 14.2.

HRMS (ESI-TOF): m/z calcd. for $[\text{M} + \text{Na}]^+$ $\text{C}_{24}\text{H}_{25}\text{NO}_4\text{Na}^+$ 414.1675; Found: 414.1676.



From Ibuprofen

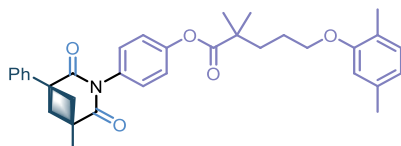
4-(1-methyl-2,4-dioxo-5-phenyl-3-azabicyclo[3.1.1]heptan-3-yl)phenyl 2-(4-isobutylphenyl)propanoate (4at)

21.8 mg, 44% yield, white solid. Eluent: pentane/ethyl acetate = 4:1, R_f = 0.2, r.r. > 19:1.

¹H NMR (400 MHz, CDCl₃) δ 7.49 – 7.44 (m, 2H), 7.40 – 7.34 (m, 2H), 7.31 – 7.28 (m, 2H), 7.26 (d, *J* = 3.6 Hz, 1H), 7.24 (dd, *J* = 4.5, 2.2 Hz, 2H), 7.15 – 7.08 (m, 2H), 6.91 – 6.86 (m, 2H), 3.89 (q, *J* = 7.2 Hz, 1H), 3.00 – 2.93 (m, 2H), 2.75 – 2.68 (m, 2H), 2.46 (d, *J* = 7.2 Hz, 2H), 1.85 (dt, *J* = 13.6, 6.8 Hz, 1H), 1.57 (d, *J* = 7.1 Hz, 3H), 1.32 (s, 3H), 0.90 (d, *J* = 6.6 Hz, 6H).

¹³C NMR (101 MHz, CDCl₃) δ 176.9, 173.2, 147.6, 143.1, 140.9, 137.1, 134.7, 129.5, 129.4, 127.8, 127.3, 127.2, 121.9, 121.0, 69.3, 47.9, 46.7, 45.2, 45.0, 30.2, 28.6, 22.4, 18.5.

HRMS (ESI-TOF): *m/z* calcd. for [M + Na]⁺ C₃₂H₃₃NO₄Na⁺ 518.2302; Found: 518.2309.



From Gemfibrozil

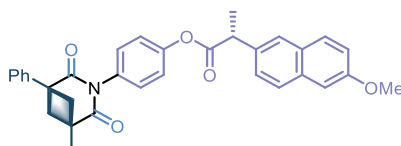
4-(1-methyl-2,4-dioxo-5-phenyl-3-azabicyclo[3.1.1]heptan-3-yl)phenyl 5-(2,5-dimethylphenoxy)-2,2-dimethylpentanoate (4au)

30.9 mg, 57% yield, white solid. Eluent: pentane/ethyl acetate = 7:1, *R_f* = 0.2, r.r. > 19:1.

¹H NMR (300 MHz, CDCl₃) δ 7.44 – 7.37 (m, 2H), 7.36 – 7.29 (m, 1H), 7.24 – 7.19 (m, 2H), 7.19 – 7.12 (m, 4H), 7.01 (d, *J* = 7.4 Hz, 1H), 6.70 – 6.62 (m, 2H), 4.04 – 3.94 (m, 2H), 3.11 – 2.96 (m, 2H), 2.70 – 2.57 (m, 2H), 2.32 (s, 3H), 2.19 (s, 3H), 1.96 – 1.83 (m, 4H), 1.47 (s, 3H), 1.38 (s, 6H).

¹³C NMR (75 MHz, CDCl₃) δ 177.3, 176.1, 175.9, 157.0, 150.9, 139.2, 136.6, 131.0, 130.5, 129.5, 128.6, 127.7, 126.6, 123.7, 122.1, 120.9, 112.1, 67.9, 50.7, 44.5, 43.2, 42.6, 37.3, 25.4, 25.2, 21.5, 19.8, 15.9.

HRMS (ESI-TOF): *m/z* calcd. for [M + Na]⁺ C₃₄H₃₇NO₅Na⁺ 562.2563; Found: 562.2567.



From Naproxen

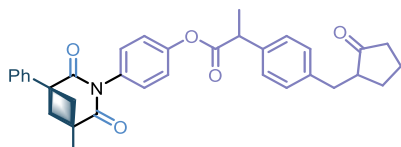
4-(1-methyl-2,4-dioxo-5-phenyl-3-azabicyclo[3.1.1]heptan-3-yl)phenyl (R)-2-(6-methoxynaphthalen-2-yl)propanoate (4av)

37.5 mg, white solid, 63% yield. Eluent: pentane/ethyl acetate = 3:1, *R_f* = 0.3, r.r. > 19:1.

¹H NMR (300 MHz, CDCl₃) δ 7.81 – 7.70 (m, 3H), 7.50 (dd, *J* = 8.5, 1.9 Hz, 1H), 7.42 – 7.35 (m, 2H), 7.34 – 7.28 (m, 1H), 7.19 – 7.08 (m, 8H), 4.22 – 4.03 (m, 1H), 3.92 (s, 3H), 3.07 – 2.95 (m, 2H), 2.68 – 2.54 (m, 2H), 1.70 (d, *J* = 7.1 Hz, 3H), 1.45 (s, 3H).

¹³C NMR (75 MHz, CDCl₃) δ 177.2, 176.1, 172.8, 157.9, 150.7, 139.2, 135.1, 133.9, 131.0, 129.5, 129.4, 129.1, 128.6, 127.7, 127.5, 126.6, 126.3, 126.2, 122.0, 119.2, 105.7, 55.4, 50.7, 45.7, 44.5, 43.1, 19.8, 18.6.

HRMS (ESI-TOF): *m/z* calcd. for [M + Na]⁺ C₃₃H₂₉NO₅Na⁺ 542.1938; Found: 542.1945.



From Loxoprofen

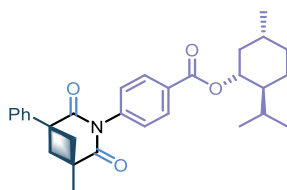
4-(1-methyl-2,4-dioxo-5-phenyl-3-azabicyclo[3.1.1]heptan-3-yl)phenyl 2-(4-((2-oxocyclopentyl)methyl)phenyl)propanoate (4aw)

39.7 mg, 74% yield, white solid. Eluent: pentane/ethyl acetate = 2:1, *R_f* = 0.3, r.r. > 19:1.

¹H NMR (300 MHz, CDCl₃) δ 7.42 – 7.28 (m, 6H), 7.20 – 7.08 (m, 7H), 3.93 (q, *J* = 7.1 Hz, 1H), 3.15 (dd, *J* = 13.8, 4.0 Hz, 1H), 3.06 – 2.98 (m, 2H), 2.67 – 2.46 (m, 3H), 2.41 – 2.29 (m, 2H), 2.18 – 2.03 (m, 2H), 2.02 – 1.91 (m, 1H), 1.81 – 1.67 (m, 1H), 1.60 (d, *J* = 7.2 Hz, 3H), 1.57 – 1.51 (m, 1H), 1.45 (s, 3H).

¹³C NMR (75 MHz, CDCl₃) δ 220.4, 177.3, 176.1, 172.7, 150.7, 139.3, 139.1, 137.8, 131.0, 129.5, 129.4, 128.6, 127.7, 126.6, 122.0, 51.1, 50.7, 45.4, 44.5, 43.1, 38.3, 35.3, 29.3, 20.6, 19.8, 18.5.

HRMS (ESI-TOF): *m/z* calcd. for [M + Na]⁺ C₃₄H₃₃NO₅Na⁺ 558.2251; Found: 558.2258.



From L-Menthol

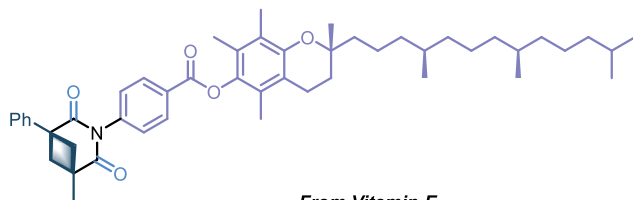
(1R,2S,4R)-4-isopropyl-2-methylcyclohexyl 4-(1-methyl-2,4-dioxo-5-phenyl-3-azabicyclo[3.1.1]heptan-3-yl)benzoate (4ax)

24.3 mg, 51% yield, white solid. Eluent: pentane/ethyl acetate = 10:1, *R_f* = 0.3, r.r. > 19:1.

¹H NMR (300 MHz, CDCl₃) δ 8.16 – 8.11 (m, 2H), 7.44 – 7.37 (m, 2H), 7.35 – 7.27 (m, 3H), 7.18 – 7.13 (m, 2H), 4.94 (td, *J* = 10.8, 4.4 Hz, 1H), 3.11 – 3.01 (m, 2H), 2.70 – 2.60 (m, 2H), 2.18 – 2.08 (m, 1H), 1.94 (qt, *J* = 7.0, 3.5 Hz, 1H), 1.78 – 1.68 (m, 2H), 1.56 (ddt, *J* = 12.4, 11.0, 3.1 Hz, 2H), 1.47 (s, 3H), 1.30 – 1.19 (m, 1H), 1.17 – 1.05 (m, 2H), 0.92 (dd, *J* = 6.8, 5.7 Hz, 6H), 0.79 (d, *J* = 6.9 Hz, 3H).

¹³C NMR (75 MHz, CDCl₃) δ 177.1, 175.9, 165.4, 139.0, 137.8, 131.0, 130.5, 128.6, 128.6, 127.8, 126.6, 75.2, 50.8, 47.4, 44.5, 44.5, 43.2, 41.0, 34.4, 31.6, 26.6, 23.7, 22.2, 20.9, 19.8, 16.6.

HRMS (ESI-TOF): *m/z* calcd. for [M + Na]⁺ C₃₀H₃₅NO₄Na⁺ 496.2458; Found: 496.2469.



From Vitamin E

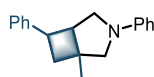
(R)-2,5,7,8-tetramethyl-2-((4R,8R)-4,8,12-trimethyltridecyl)chroman-6-yl 4-(1-methyl-2,4-dioxo-5-phenyl-3-azabicyclo[3.1.1]heptan-3-yl)benzoate (4ay)

34.0 mg, 46% yield, colorless oil. Eluent: pentane/ethyl acetate = 10:1, *R_f* = 0.2, r.r. > 19:1.

¹H NMR (400 MHz, CDCl₃) δ 8.38 – 8.27 (m, 2H), 7.44 – 7.32 (m, 5H), 7.21 – 7.14 (m, 2H), 3.12 – 3.05 (m, 2H), 2.70 – 2.66 (m, 2H), 2.62 (t, *J* = 6.8 Hz, 2H), 2.13 (s, 3H), 2.06 (s, 3H), 2.02 (s, 3H), 1.57 – 1.52 (m, 2H), 1.50 (s, 3H), 1.47 – 1.03 (m, 24H), 0.94 – 0.81 (m, 12H).

¹³C NMR (101 MHz, CDCl₃) δ 177.1, 175.9, 164.5, 149.7, 140.7, 138.9, 138.4, 131.1, 129.8, 128.9, 128.7, 127.8, 127.0, 126.6, 125.2, 123.3, 117.6, 75.2, 50.8, 44.5, 43.3, 39.5, 37.7, 37.6, 37.4, 32.9, 28.1, 25.0, 24.6, 22.9, 22.8, 21.2, 20.8, 19.9, 19.8, 19.8, 13.2, 12.4, 12.0.

HRMS (ESI-TOF): *m/z* calcd. for [M + Na]⁺ C₄₉H₆₅NO₅Na⁺ 770.4755; Found: 770.4758.



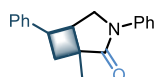
1-methyl-3,6-diphenyl-3-azabicyclo[3.2.0]heptane (5)

25.0 mg, 95% yield, colorless oil. Eluent: pentane/ethyl acetate = 50:1, *R_f* = 0.3, r.r. > 19:1.

¹H NMR (300 MHz, CDCl₃) δ 7.35 – 7.15 (m, 7H), 6.75 (tt, *J* = 7.6, 1.5 Hz, 3H), 3.71 (d, *J* = 9.7 Hz, 1H), 3.61 (d, *J* = 9.9 Hz, 1H), 3.31 – 3.16 (m, 2H), 2.91 (d, *J* = 9.7 Hz, 1H), 2.65 (t, *J* = 6.1 Hz, 1H), 2.55 – 2.43 (m, 1H), 2.10 (dd, *J* = 12.0, 8.6 Hz, 1H), 1.35 (s, 3H).

¹³C NMR (75 MHz, CDCl₃) δ 149.2, 145.7, 129.2, 128.5, 126.6, 126.0, 117.1, 113.6, 62.4, 55.0, 52.0, 40.9, 40.1, 39.7, 25.8.

HRMS (ESI-TOF): *m/z* calcd. for [M + H]⁺ C₁₉H₂₂N⁺ 264.1747; Found: 264.1752.



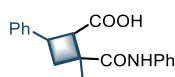
1-methyl-3,6-diphenyl-3-azabicyclo[3.2.0]heptan-2-one (6)

17.7 mg, 64% yield, white solid. Eluent: pentane/ethyl acetate = 30:1, *R_f* = 0.2, r.r. > 19:1.

¹H NMR (400 MHz, CDCl₃) δ 7.76 – 7.73 (m, 2H), 7.45 – 7.39 (m, 2H), 7.38 – 7.32 (m, 3H), 7.25 – 7.23 (m, 2H), 7.22 – 7.17 (m, 1H), 4.10 (dd, *J* = 10.2, 6.5 Hz, 1H), 3.77 (d, *J* = 10.2 Hz, 1H), 3.36 (td, *J* = 9.3, 7.1 Hz, 1H), 2.92 – 2.86 (m, 1H), 2.85 – 2.80 (m, 1H), 2.25 (dd, *J* = 11.9, 9.6 Hz, 1H), 1.44 (s, 3H).

¹³C NMR (101 MHz, CDCl₃) δ 179.0, 143.9, 139.8, 129.1, 128.8, 126.7, 126.6, 125.0, 120.4, 52.7, 44.6, 44.4, 41.2, 39.0, 21.5.

HRMS (ESI-TOF): *m/z* calcd. for [M + Na]⁺ C₁₉H₁₉NONa⁺ 300.1359; Found: 300.1361.

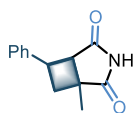


2-methyl-4-phenyl-2-(phenylcarbamoyl)cyclobutane-1-carboxylic acid (7)

17.3 mg, 56% yield, white solid. Eluent: pentane/ethyl acetate = 2:3, *R_f* = 0.2, r.r. > 19:1.

¹H NMR (300 MHz, DMSO) δ 12.04 (s, 1H), 9.32 (s, 1H), 7.86 – 7.58 (m, 2H), 7.35 – 7.26 (m, 6H), 7.23 – 7.16 (m, 1H), 7.09 – 7.01 (m, 1H), 3.79 – 3.63 (m, 1H), 2.99 (d, *J* = 10.0 Hz, 1H), 2.85 – 2.71 (m, 1H), 1.97 (t, *J* = 10.6 Hz, 1H), 1.65 (s, 3H).

¹³C NMR (75 MHz, DMSO) δ 173.4, 173.2, 143.6, 139.2, 128.4, 128.2, 126.6, 126.1, 123.3, 120.4, 54.5, 47.0, 37.2 (d, *J* = 5.7 Hz), 25.4.



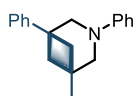
1-methyl-6-phenyl-3-azabicyclo[3.2.0]heptane-2,4-dione (8)

13.6 mg, 63% yield, white solid. Eluent: pentane/ethyl acetate = 2:1, R_f = 0.3, r.r. > 19:1.

$^1\text{H NMR}$ (300 MHz, CDCl_3) δ 8.46 (br, 1H), 7.40 – 7.34 (m, 2H), 7.30 – 7.24 (m, 3H), 3.65 (td, J = 8.7, 5.5 Hz, 1H), 3.11 (d, J = 5.5 Hz, 1H), 2.90 (ddd, J = 12.8, 9.3, 0.9 Hz, 1H), 2.42 (dd, J = 12.8, 8.2 Hz, 1H), 1.47 (s, 3H).

$^{13}\text{C NMR}$ (75 MHz, CDCl_3) δ 182.6, 178.3, 142.2, 129.0, 127.2, 126.5, 53.2, 43.2, 39.2, 36.5, 20.6.

HRMS (ESI-TOF): m/z calcd. for $[\text{M} + \text{Na}]^+$ $\text{C}_{13}\text{H}_{13}\text{NO}_2\text{Na}^+$ 238.0838; Found: 238.0842.

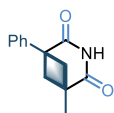


1-methyl-3,5-diphenyl-3-azabicyclo[3.1.1]heptane (9)

23.0 mg, 87% yield, white solid. Eluent: pentane/ethyl acetate = 50:1, R_f = 0.4, r.r. > 19:1.

$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.40 – 7.34 (m, 2H), 7.31 – 7.25 (m, 3H), 7.24 – 7.20 (m, 2H), 6.78 – 6.70 (m, 3H), 3.45 (s, 2H), 3.36 (s, 2H), 2.08 – 2.04 (m, 2H), 2.01 – 1.96 (m, 2H), 1.26 (s, 3H).

$^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 148.4, 146.6, 129.3, 128.5, 126.5, 125.7, 116.1, 110.3, 58.2, 57.2, 41.9, 41.7, 34.7, 24.4.

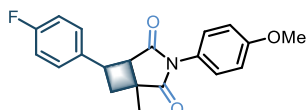


1-methyl-5-phenyl-3-azabicyclo[3.1.1]heptane-2,4-dione (10)

12.2 mg, 57% yield, white solid. Eluent: pentane/ethyl acetate = 5:1, R_f = 0.2.

$^1\text{H NMR}$ (300 MHz, CDCl_3) δ 7.72 (br, 1H), 7.43 – 7.37 (m, 2H), 7.36 – 7.31 (m, 1H), 7.14 – 7.09 (m, 2H), 2.96 – 2.86 (m, 2H), 2.58 – 2.47 (m, 2H), 1.40 (s, 3H).

$^{13}\text{C NMR}$ (75 MHz, CDCl_3) δ 177.4, 176.3, 138.7, 128.7, 127.8, 126.6, 50.7, 45.1, 43.1, 18.9.



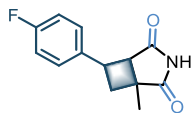
6-(4-fluorophenyl)-3-(4-methoxyphenyl)-1-methyl-3-azabicyclo[3.2.0]heptane-2,4-dione (11)

427.1 mg, 63% yield, white solid. Eluent: pentane/ethyl acetate = 5:1, R_f = 0.3, r.r. > 19:1, d.r. > 20:1.

$^1\text{H NMR}$ (300 MHz, CDCl_3) δ 7.31 – 7.25 (m, 4H), 7.12 – 7.05 (m, 2H), 7.04 – 7.00 (m, 2H), 3.85 (s, 3H), 3.70 – 3.60 (m, 1H), 3.18 (d, J = 5.4 Hz, 1H), 2.95 (dddd, J = 12.8, 9.3, 3.5, 0.9 Hz, 1H), 2.44 (dd, J = 12.8, 8.3 Hz, 1H), 1.56 (s, 3H).

$^{13}\text{C NMR}$ (75 MHz, CDCl_3) δ 181.5, 177.3, 161.9 (d, J = 245.9 Hz), 159.7, 137.9 (d, J = 3.3 Hz), 128.2 (d, J = 8.1 Hz), 127.8, 124.8, 115.8 (d, J = 21.4 Hz), 114.7, 55.7, 52.2, 41.6, 38.9, 37.0, 21.1.

$^{19}\text{F NMR}$ (282 MHz, CDCl_3) δ -115.40 – -115.55 (m).



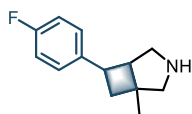
6-(4-fluorophenyl)-1-methyl-3-azabicyclo[3.2.0]heptane-2,4-dione (12)

50.4 mg, 54% yield, brown oil. Eluent: pentane/ethyl acetate = 3:1, R_f = 0.2, d.r. > 20:1.

$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.64 (br, 1H), 7.25 – 7.20 (m, 2H), 7.09 – 7.02 (m, 2H), 3.67 – 3.58 (m, 1H), 3.05 (dd, J = 5.6, 0.9 Hz, 1H), 2.90 (dddd, J = 12.8, 9.3, 3.5, 0.9 Hz, 1H), 2.37 (dd, J = 12.8, 8.2 Hz, 1H), 1.47 (s, 3H).

$^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 182.6, 178.3, 163.1, 160.7, 137.9 (d, J = 3.3 Hz), 128.1, 128.0, 115.9, 115.7, 53.4, 43.1, 38.6, 36.6, 20.7.

$^{19}\text{F NMR}$ (376 MHz, CDCl_3) δ -115.38 – -115.54 (m).



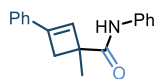
6-(4-fluorophenyl)-1-methyl-3-azabicyclo[3.2.0]heptane (13)

31.2 mg, 76% yield, brown oil. Eluent: pentane/ethyl acetate = 1:2, R_f = 0.3, d.r. > 20:1.

¹H NMR (300 MHz, CDCl₃) δ 7.18 – 7.11 (m, 2H), 7.02 – 6.94 (m, 2H), 4.06 (d, *J* = 10.9 Hz, 1H), 3.90 – 3.72 (m, 2H), 3.53 (dd, *J* = 10.9, 0.8 Hz, 1H), 3.10 (q, *J* = 9.5 Hz, 1H), 2.43 – 2.26 (m, 1H), 2.05 (dddd, *J* = 11.6, 9.2, 3.5, 0.9 Hz, 1H), 1.78 (dd, *J* = 11.5, 9.7 Hz, 1H), 1.28 (s, 3H).

¹³C NMR (75 MHz, CDCl₃) δ 161.5 (d, *J* = 243.9 Hz), 140.1, 128.1 (d, *J* = 7.8 Hz), 115.3 (d, *J* = 21.2 Hz), 67.5, 62.9, 53.0, 38.8, 36.4, 35.9, 26.7.

¹⁹F NMR (282 MHz, CDCl₃) δ -117.07 – -117.35 (m).



1-methyl-N,3-diphenylcyclobut-2-ene-1-carboxamide (14)

Under Conditions D and E, product **11** was obtained as a white solid in 9.3 mg (37% yield) and 10.0 mg (38% yield), respectively.

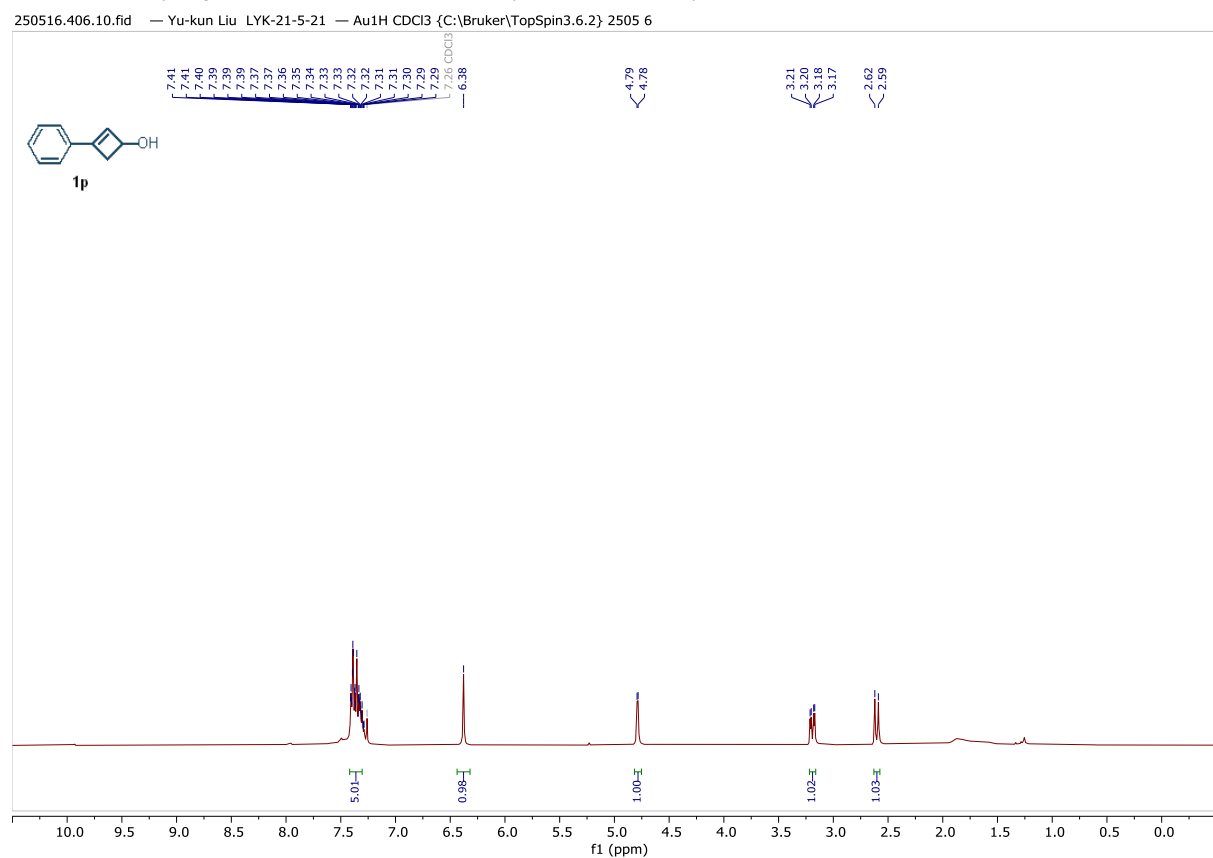
Eluent: pentane/ethyl acetate = 15:1, *R_f* = 0.2.

¹H NMR (300 MHz, CDCl₃) δ 7.63 (br, 1H), 7.55 – 7.49 (m, 2H), 7.46 – 7.34 (m, 5H), 7.33 – 7.27 (m, 2H), 7.13 – 7.04 (m, 1H), 6.53 (s, 1H), 3.17 (d, *J* = 13.4 Hz, 2H), 2.80 (d, *J* = 13.3 Hz, 2H), 1.64 (s, 3H).

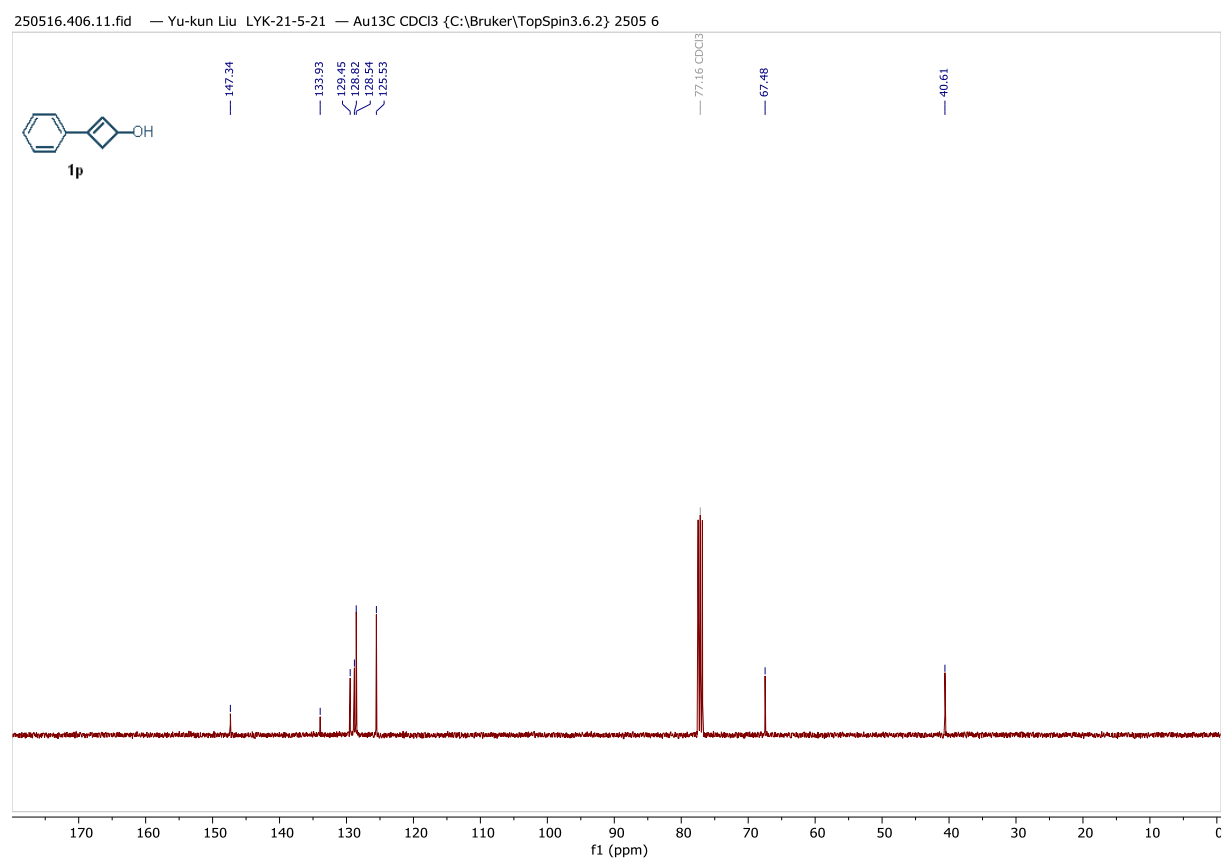
¹³C NMR (75 MHz, CDCl₃) δ 149.4, 138.1, 133.6, 129.4, 129.1, 129.0, 128.7, 125.1, 124.3, 119.9, 48.7, 42.0, 21.6.

9. NMR Spectra of the Products

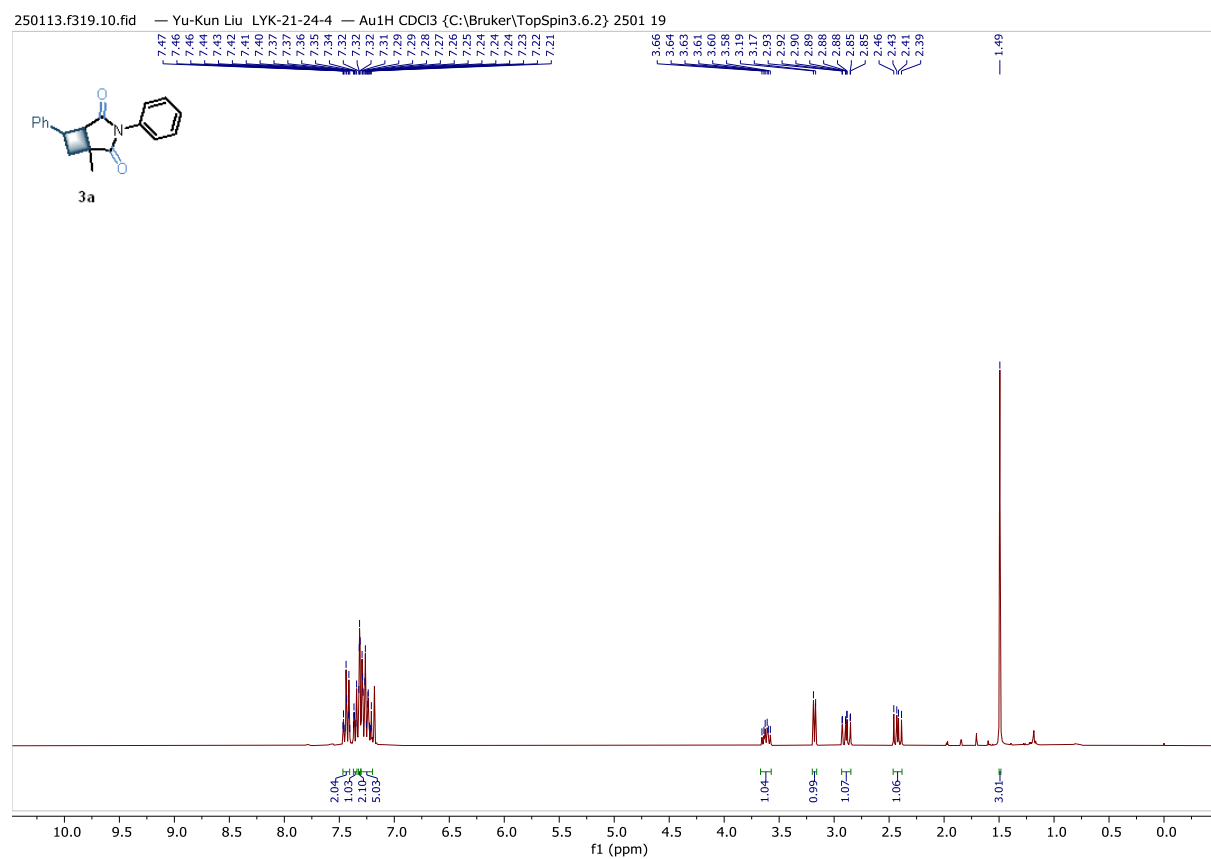
Supplementary Fig. 6. ^1H NMR spectrum of **1p** (400 MHz, CDCl_3)



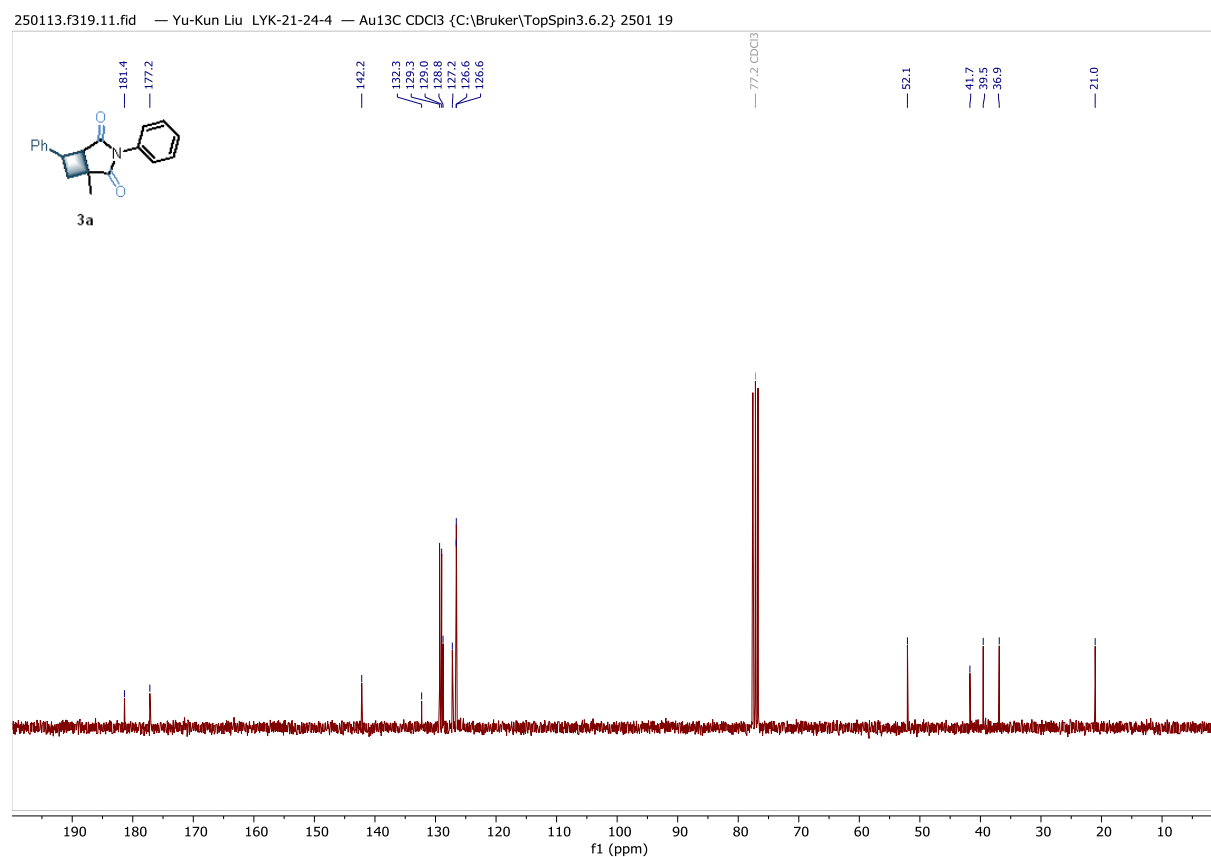
Supplementary Fig. 7. ^{13}C NMR spectrum of **1p** (101 MHz, CDCl_3)



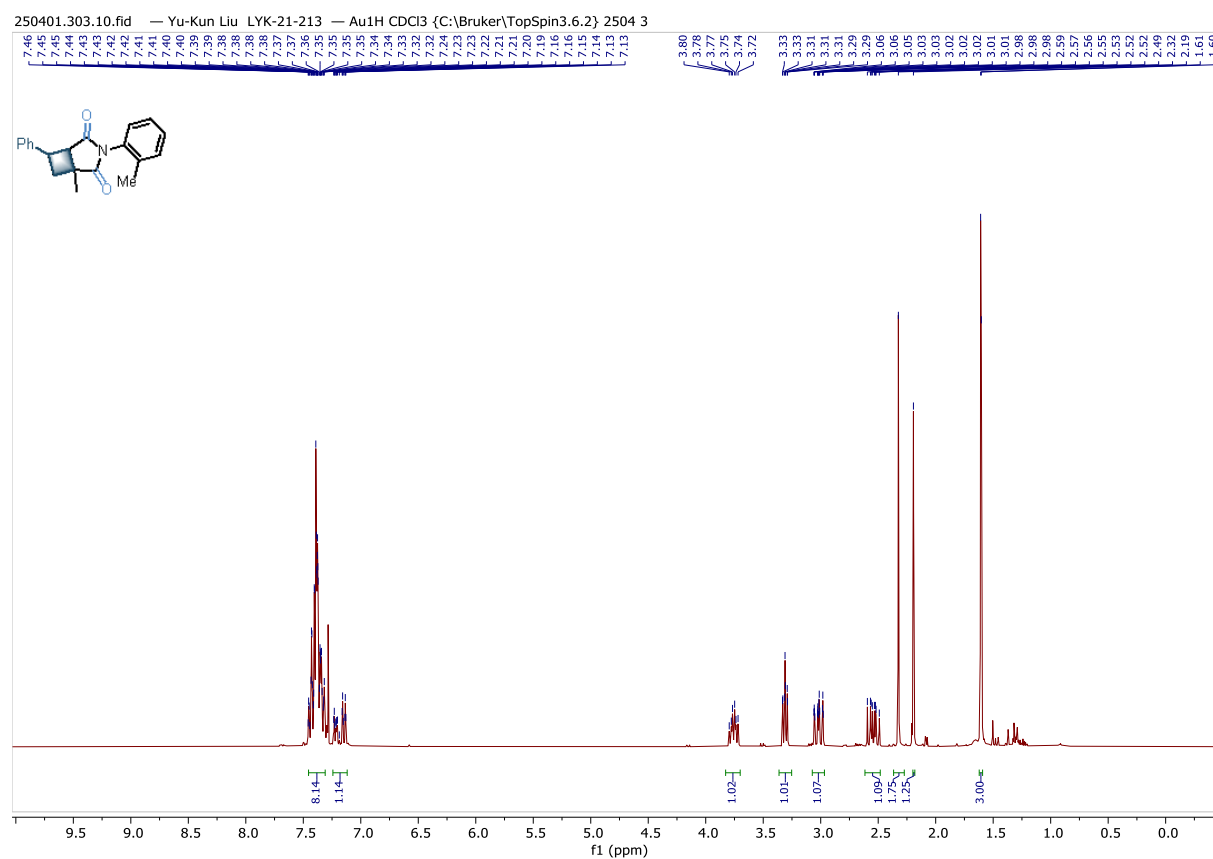
Supplementary Fig. 8. ^1H NMR spectrum of **3a** (300 MHz, CDCl_3)



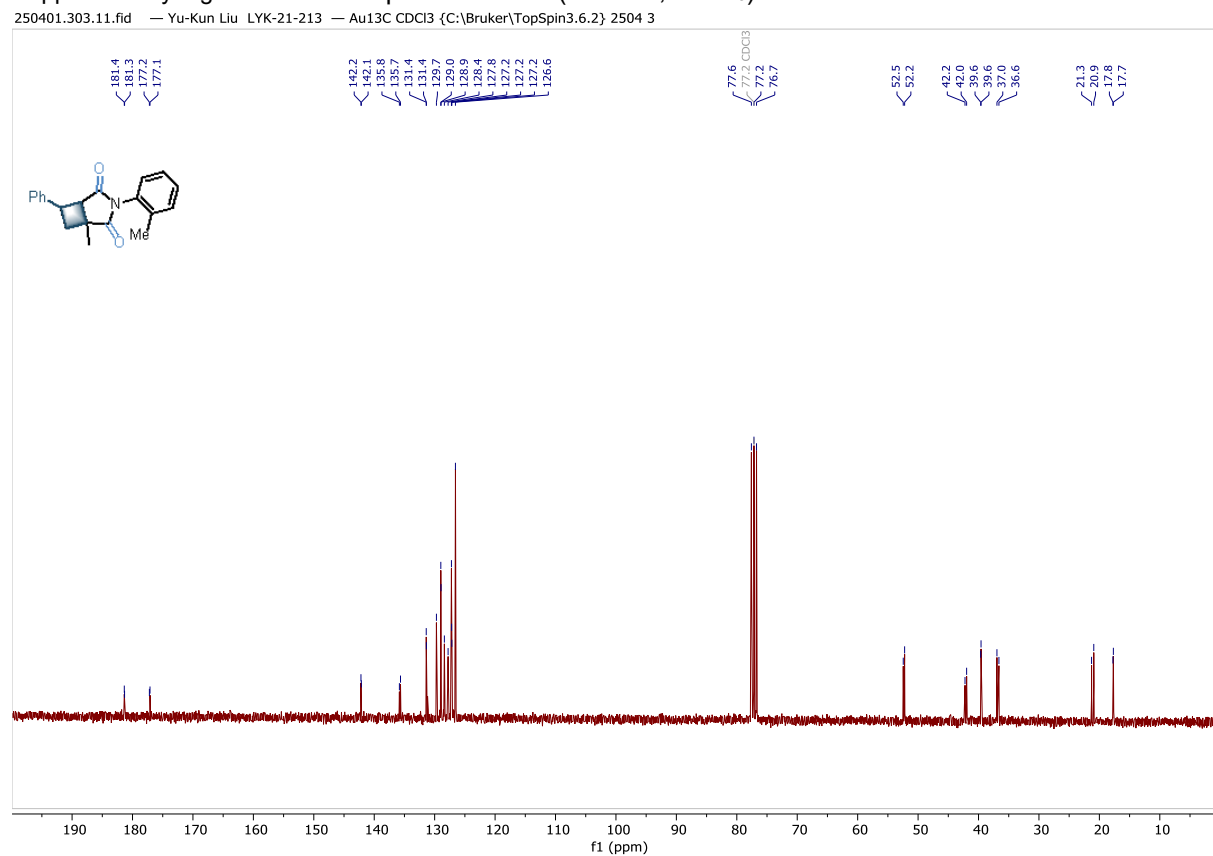
Supplementary Fig. 9. ^{13}C NMR spectrum of **3a** (75 MHz, CDCl_3)



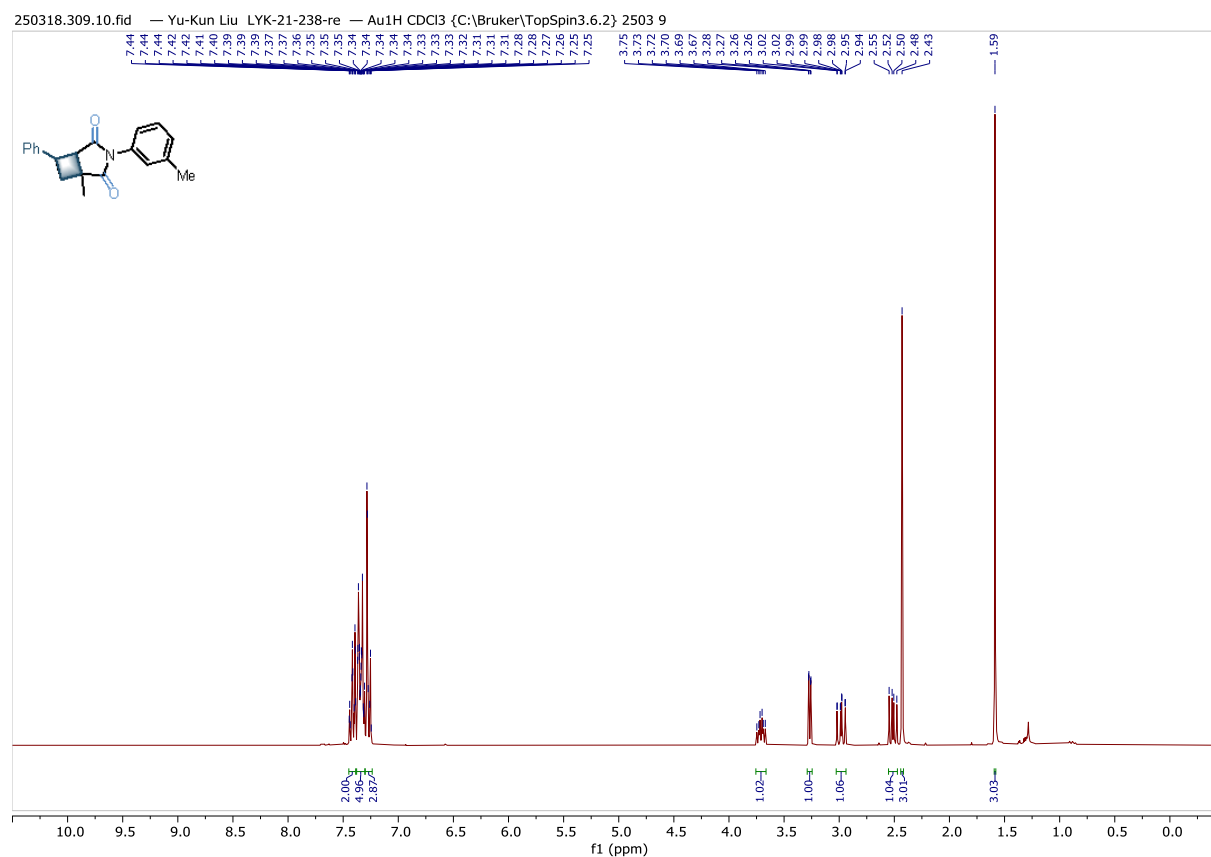
Supplementary Fig. 10. ^1H NMR spectrum of **3b** (300 MHz, CDCl_3)



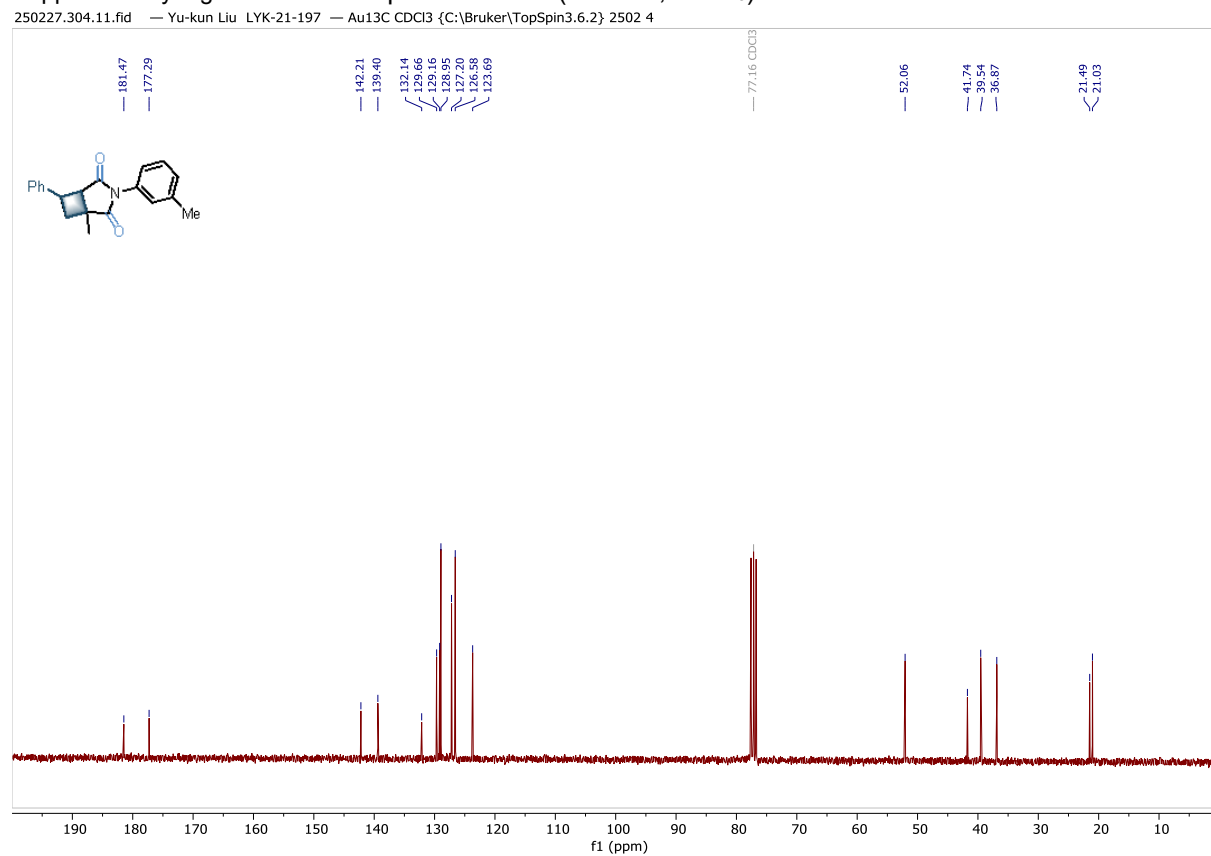
Supplementary Fig. 11. ^{13}C NMR spectrum of **3b** (75 MHz, CDCl_3)



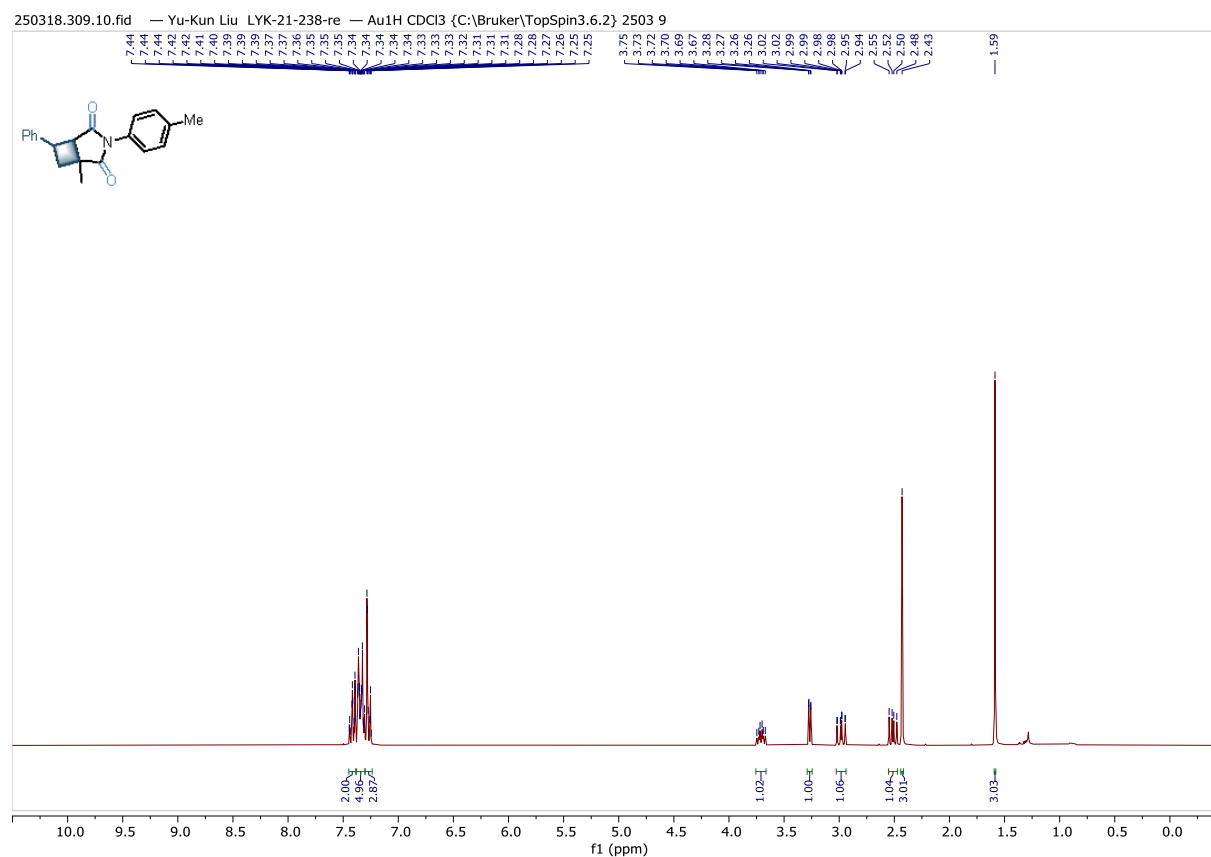
Supplementary Fig. 12. ^1H NMR spectrum of **3c** (300 MHz, CDCl_3)



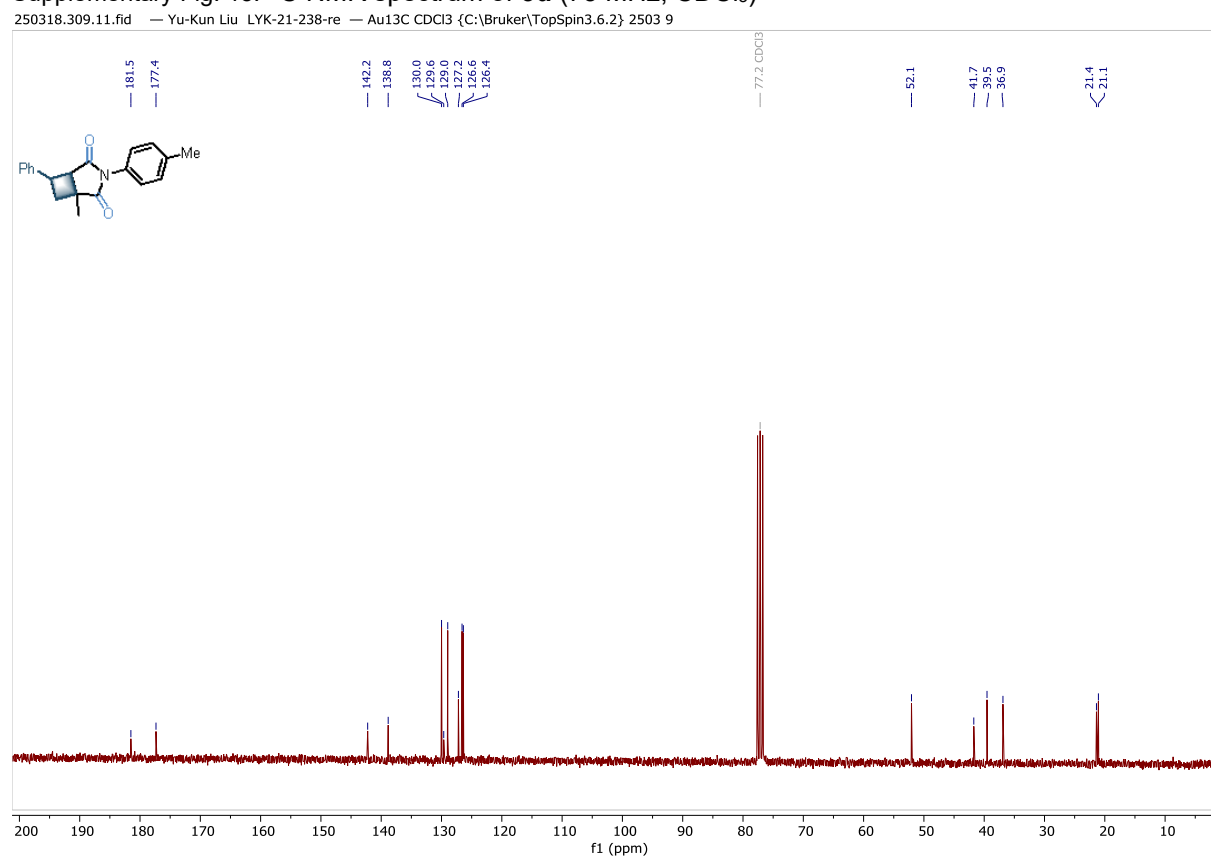
Supplementary Fig. 13. ^{13}C NMR spectrum of **3c** (75 MHz, CDCl_3)



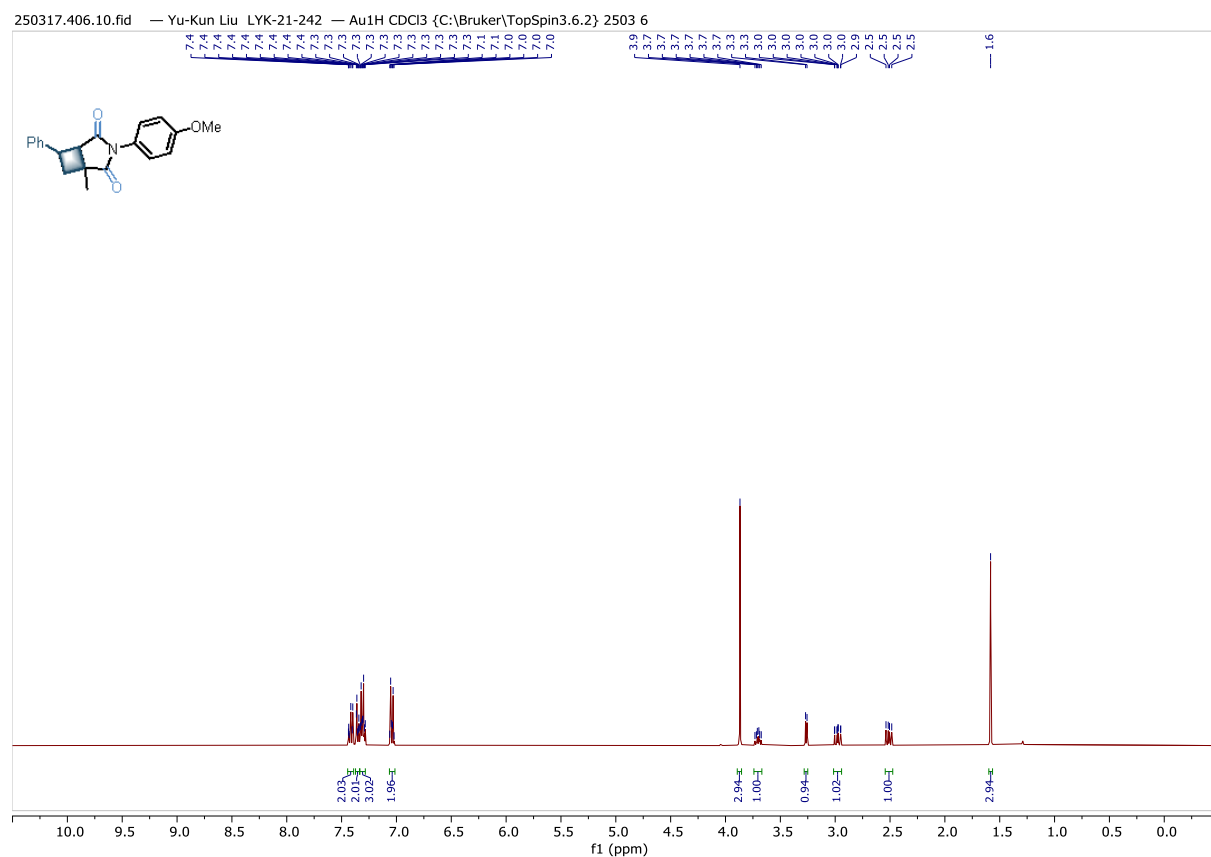
Supplementary Fig. 14. ^1H NMR spectrum of **3d** (300 MHz, CDCl_3)



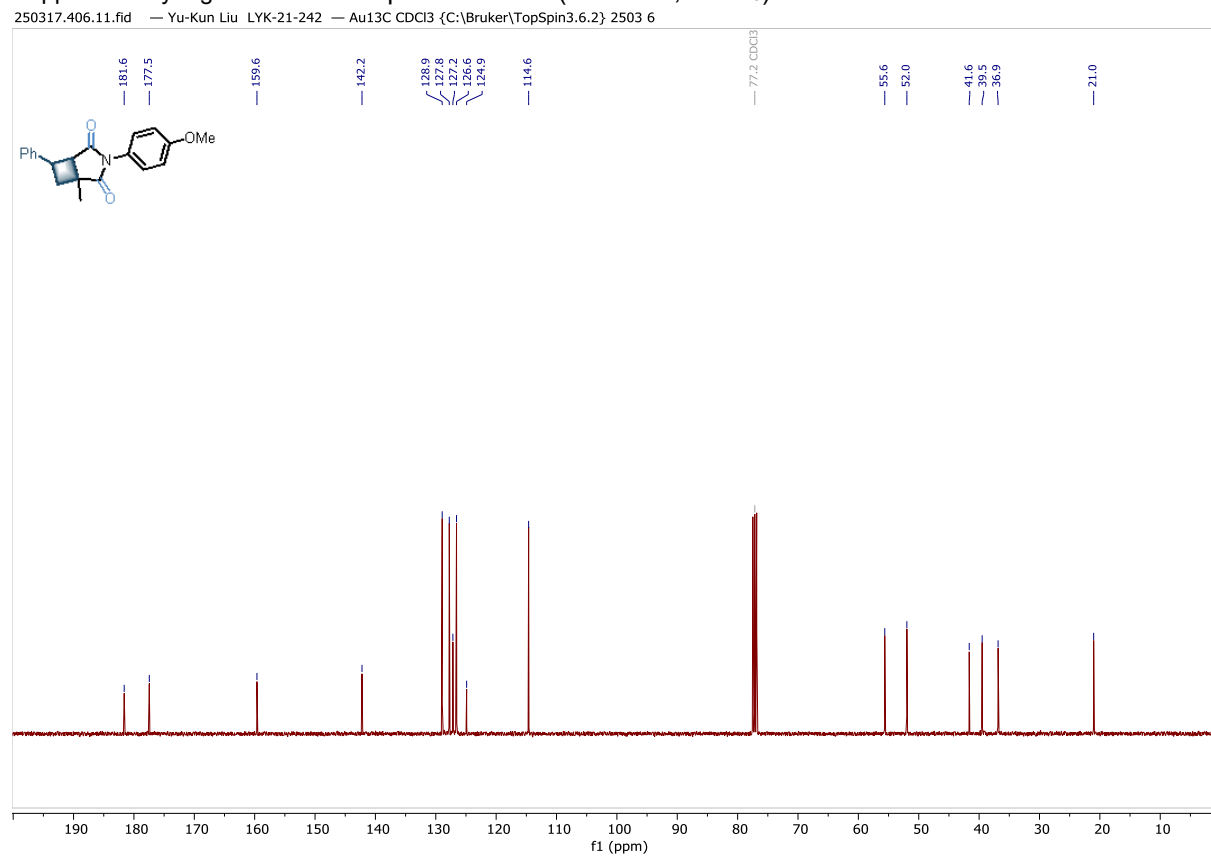
Supplementary Fig. 15. ^{13}C NMR spectrum of **3d** (75 MHz, CDCl_3)



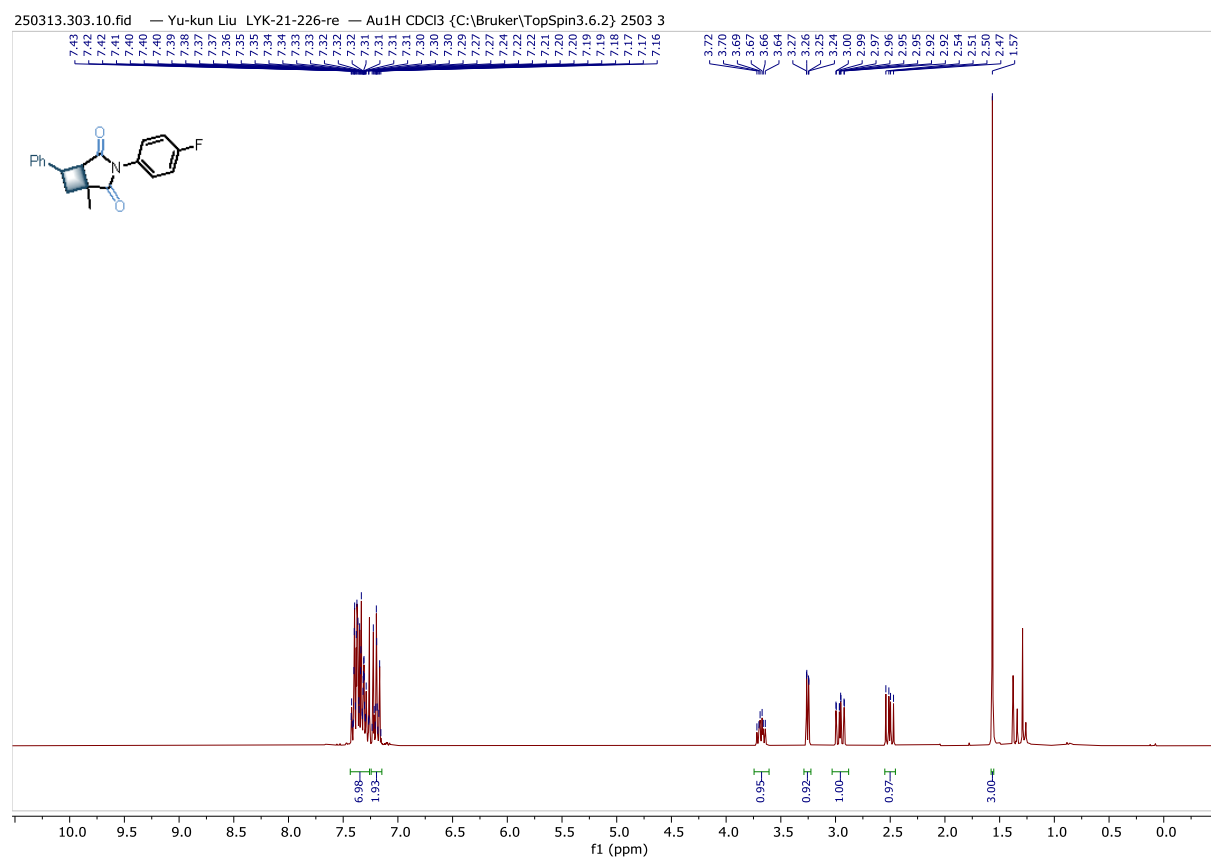
Supplementary Fig. 16. ^1H NMR spectrum of **3e** (400 MHz, CDCl_3)



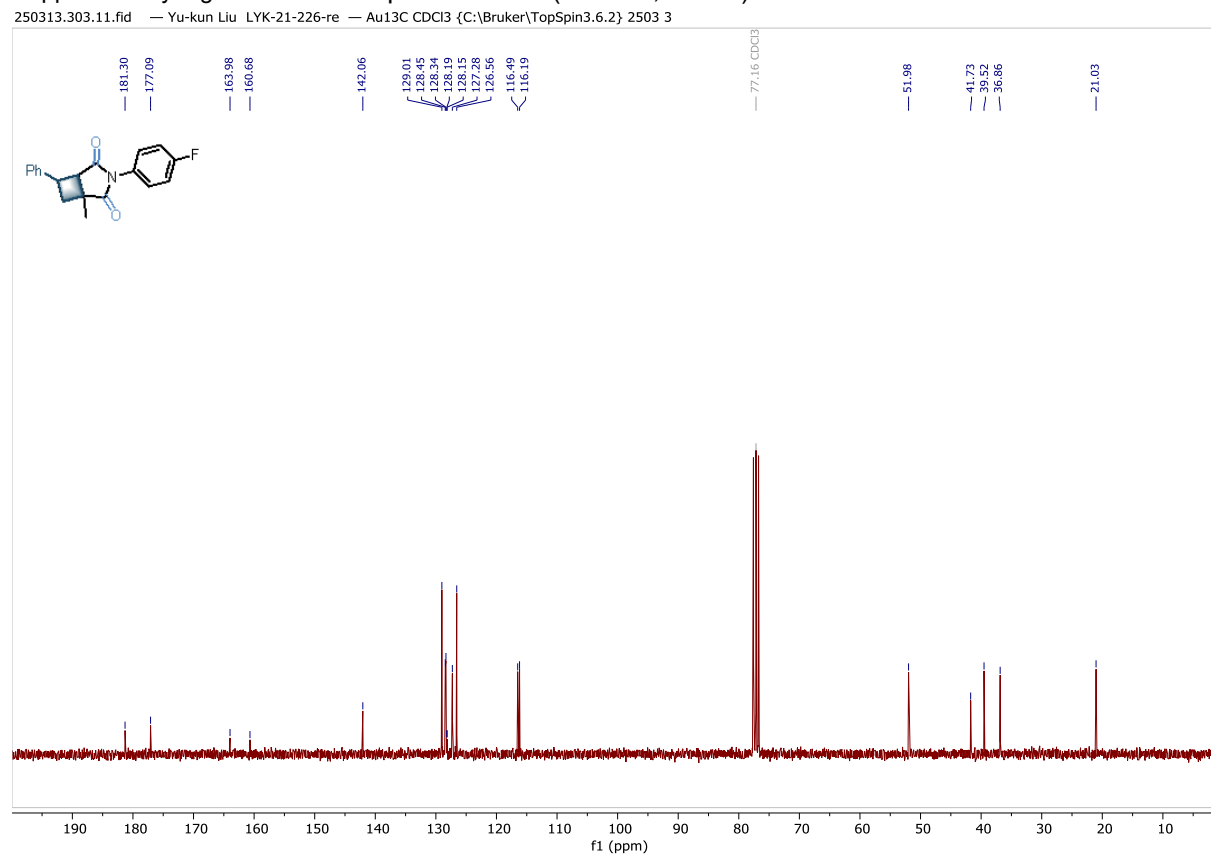
Supplementary Fig. 17. ^{13}C NMR spectrum of **3e** (101 MHz, CDCl_3)



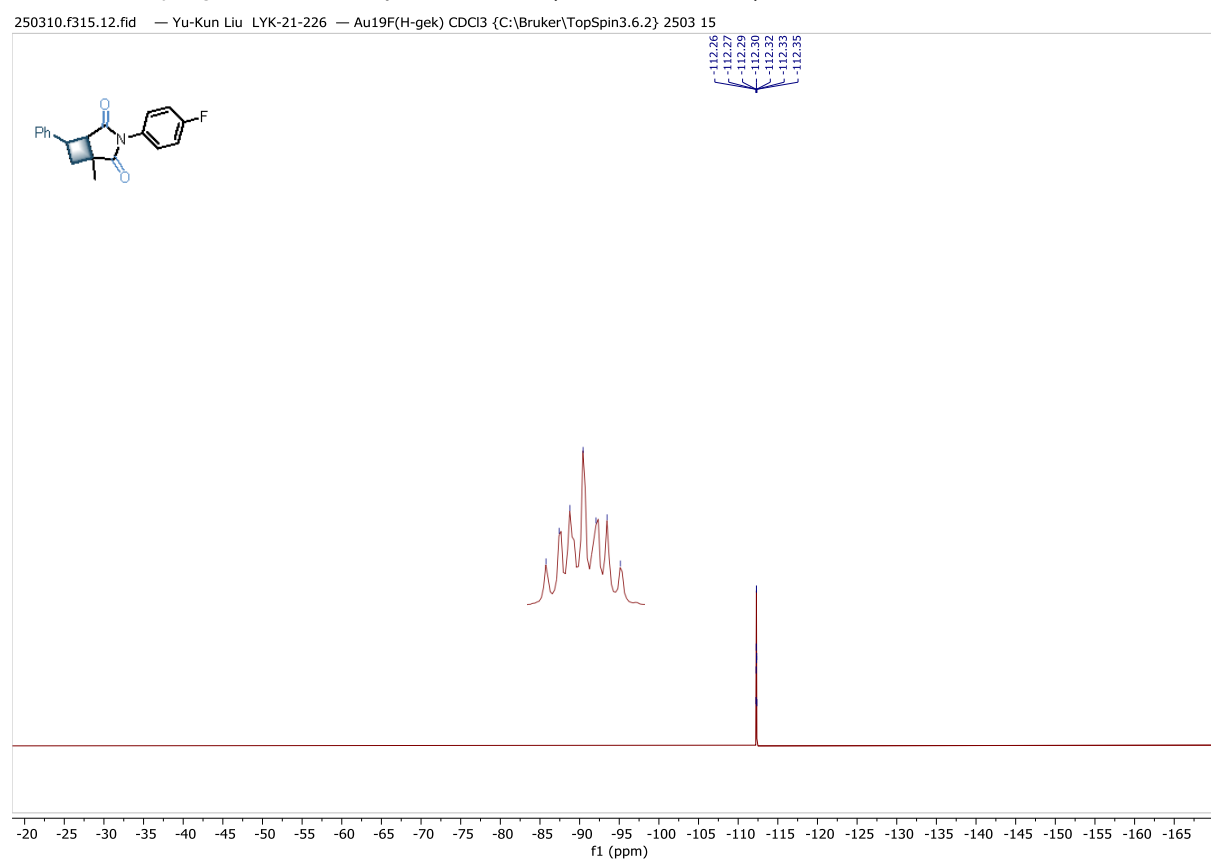
Supplementary Fig. 18. ^1H NMR spectrum of **3f** (300 MHz, CDCl_3)



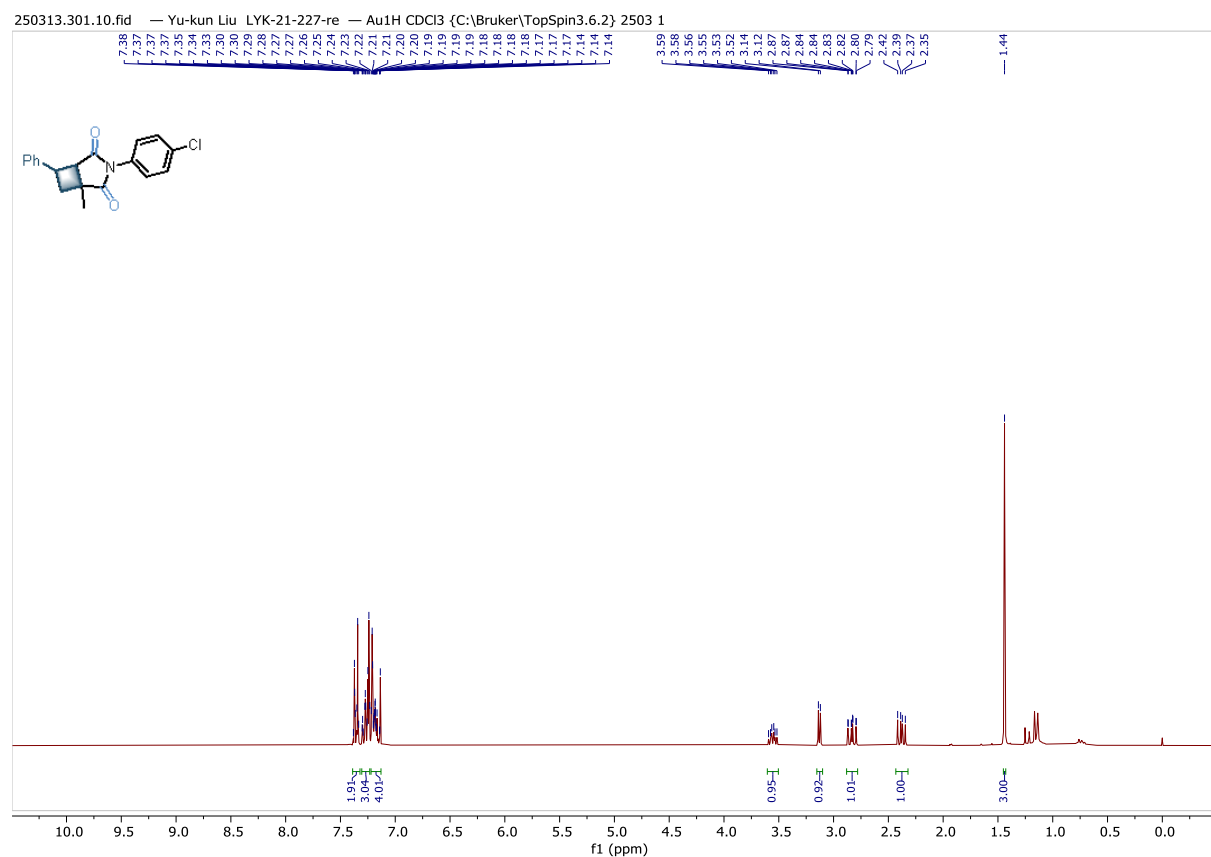
Supplementary Fig. 19. ^{13}C NMR spectrum of **3f** (75 MHz, CDCl_3)



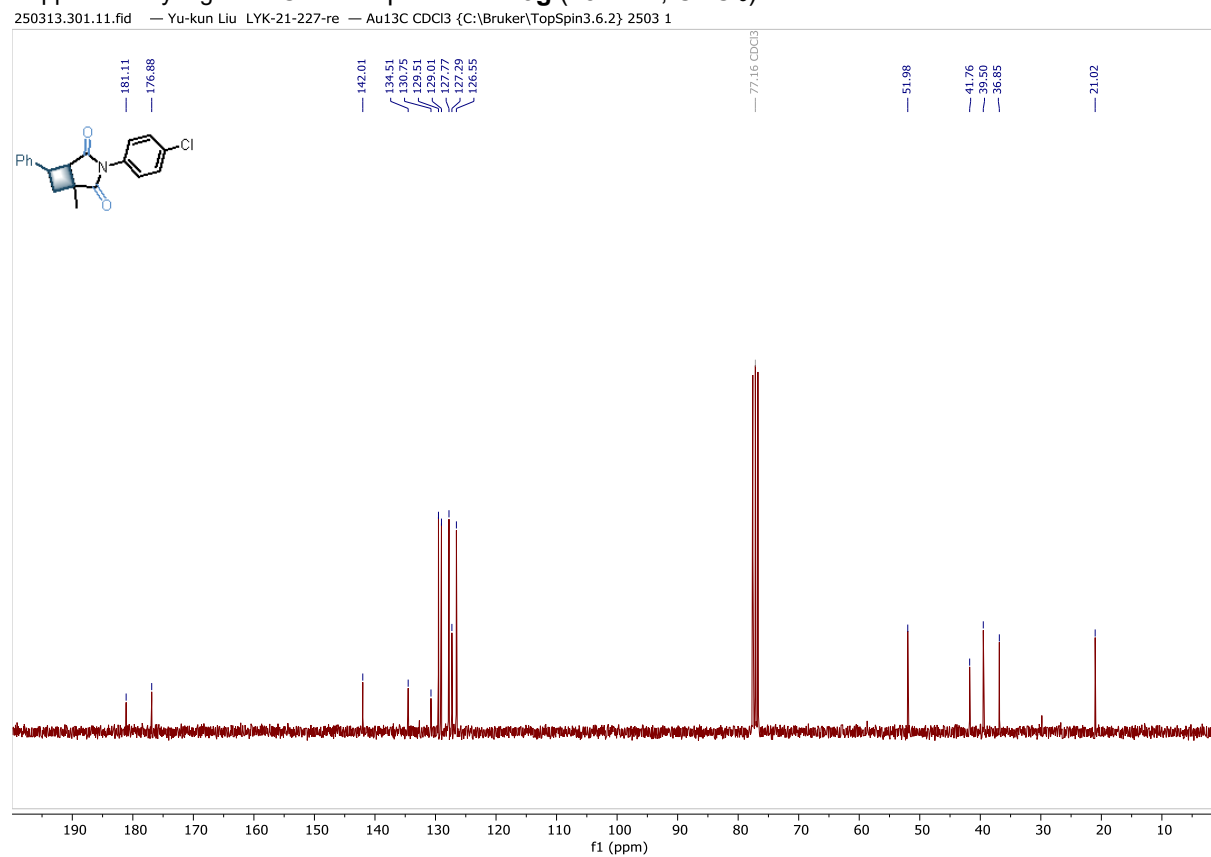
Supplementary Fig. 20. ^{19}F NMR spectrum of **3f** (282 MHz, CDCl_3)



Supplementary Fig. 21. ^1H NMR spectrum of **3g** (300 MHz, CDCl_3)

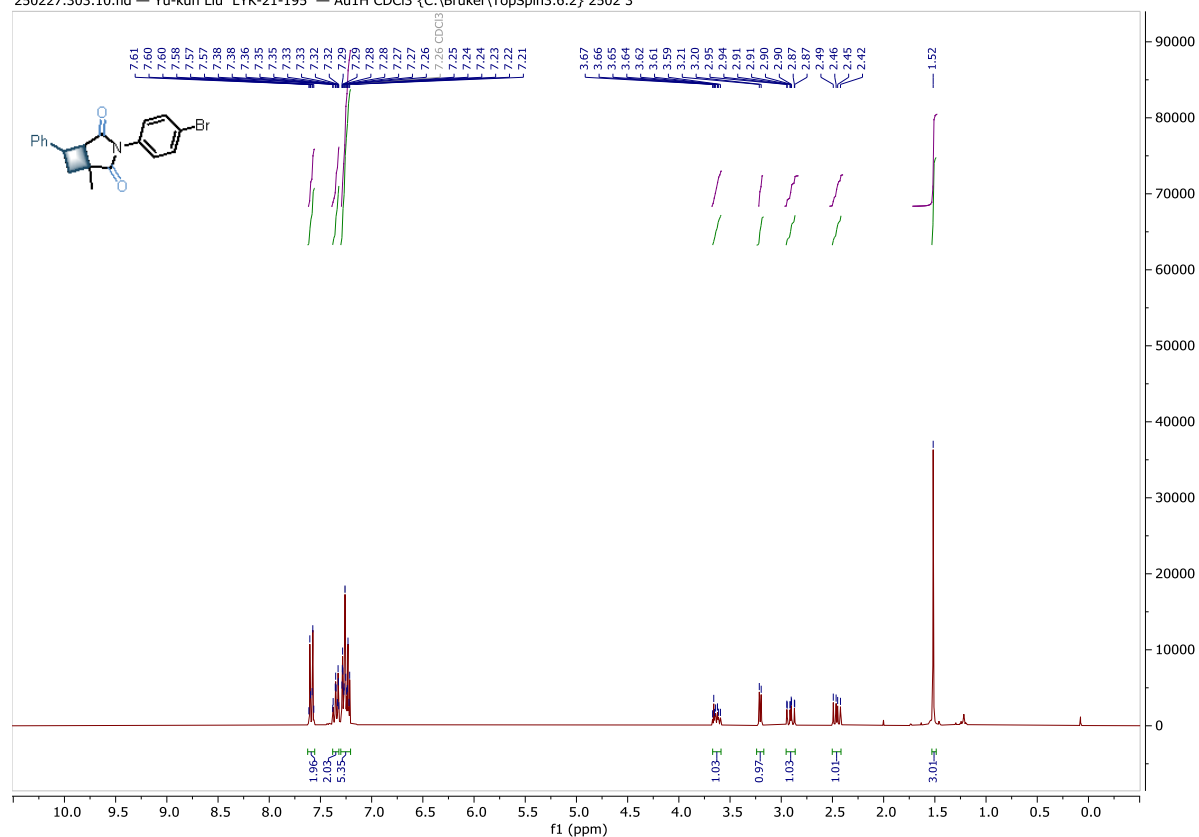


Supplementary Fig. 22. ^{13}C NMR spectrum of **3g** (75 MHz, CDCl_3)



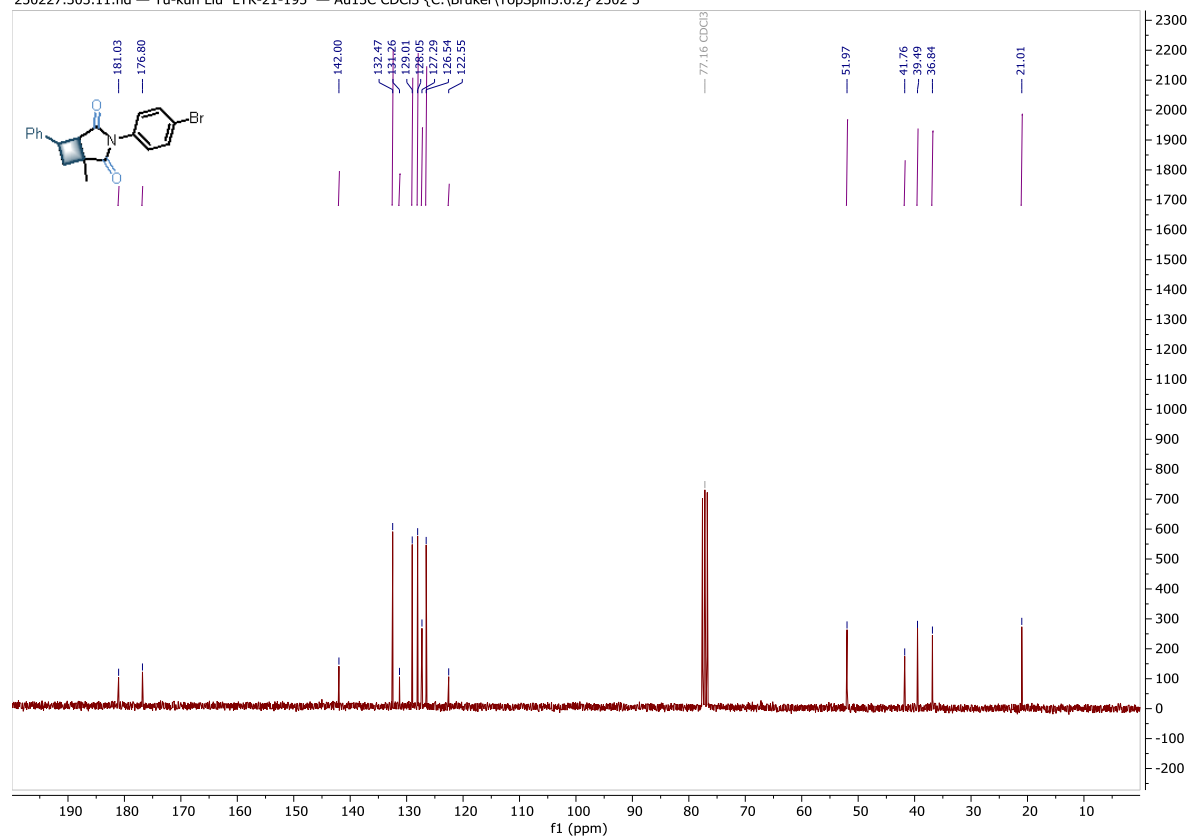
Supplementary Fig. 23. ^1H NMR spectrum of **3h** (300 MHz, CDCl_3)

250227.303.10.fid — Yu-kun Liu LYK-21-195 — Au1H CDCl_3 {C:\Bruker\TopSpin3.6.2} 2502 3



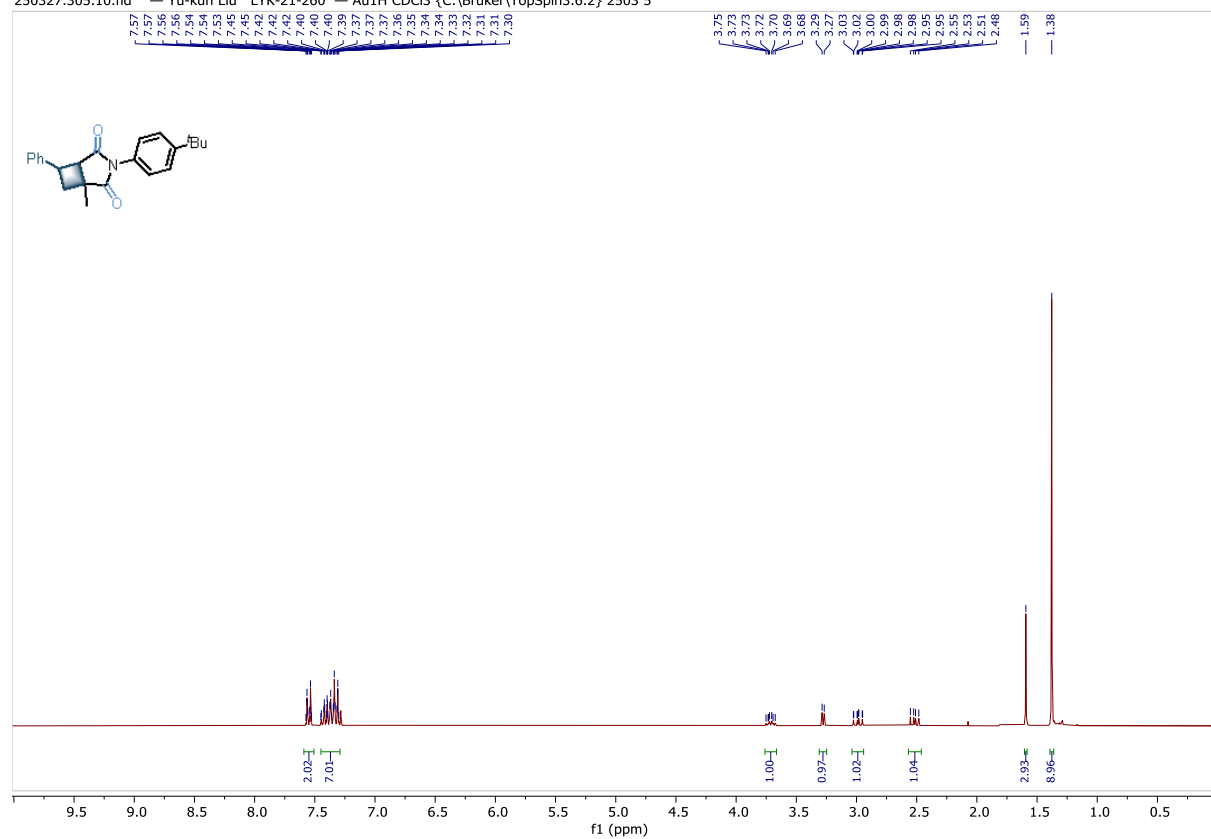
Supplementary Fig. 24. ^{13}C NMR spectrum of **3h** (75 MHz, CDCl_3)

250227.303.11.fid — Yu-kun Liu LYK-21-195 — Au13C CDCl_3 {C:\Bruker\TopSpin3.6.2} 2502 3



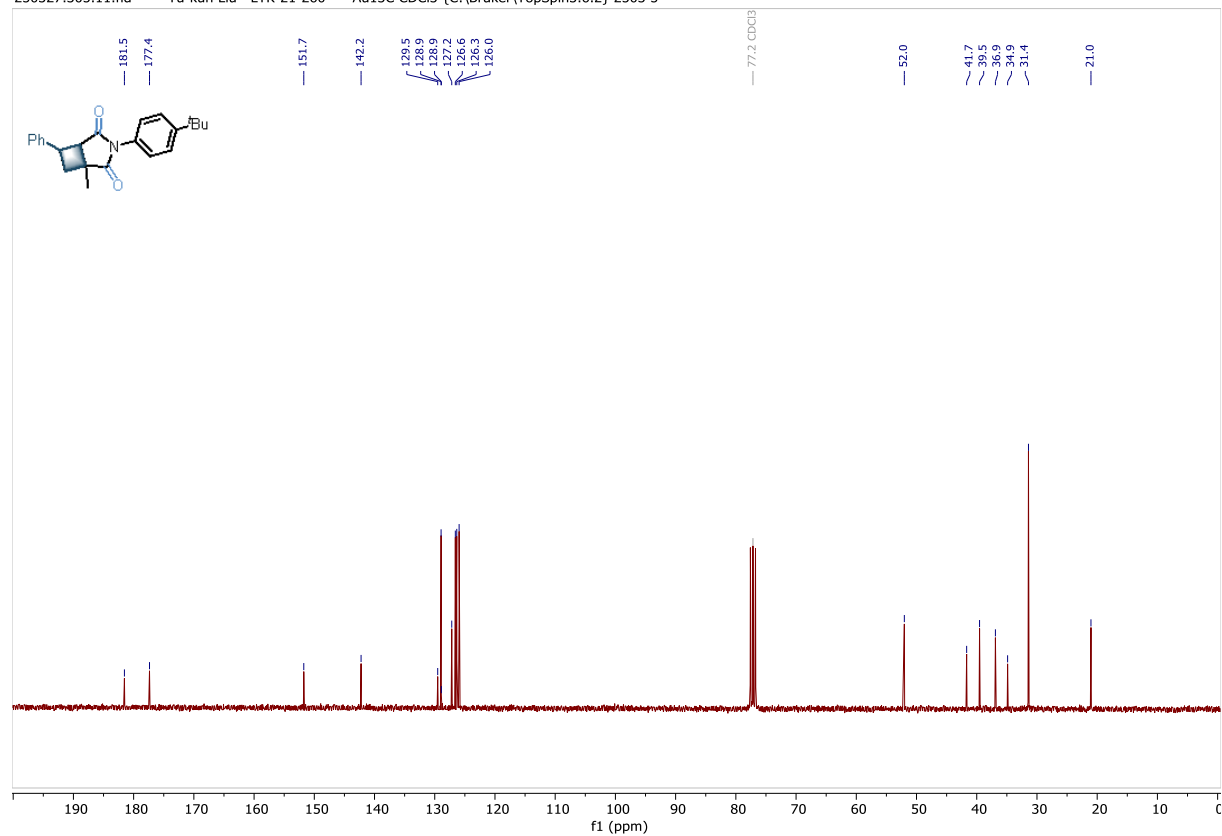
Supplementary Fig. 25. ^1H NMR spectrum of **3i** (300 MHz, CDCl_3)

250327.305.10.fid — Yu-kun Liu LYK-21-260 — Au1H CDCl_3 {C:\Bruker\TopSpin3.6.2} 2503 5



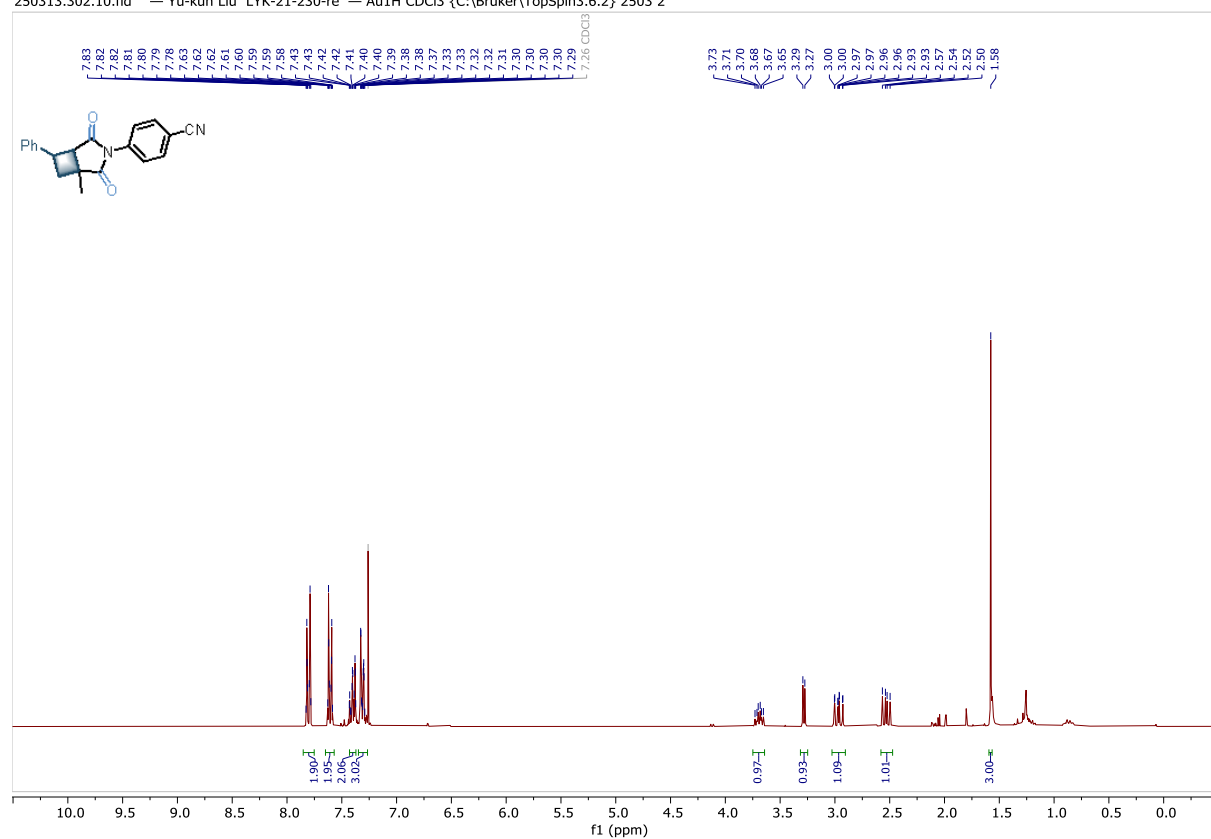
Supplementary Fig. 26. ^{13}C NMR spectrum of **3i** (75 MHz, CDCl_3)

250327.305.11.fid — Yu-kun Liu LYK-21-260 — Au13C CDCl_3 {C:\Bruker\TopSpin3.6.2} 2503 5



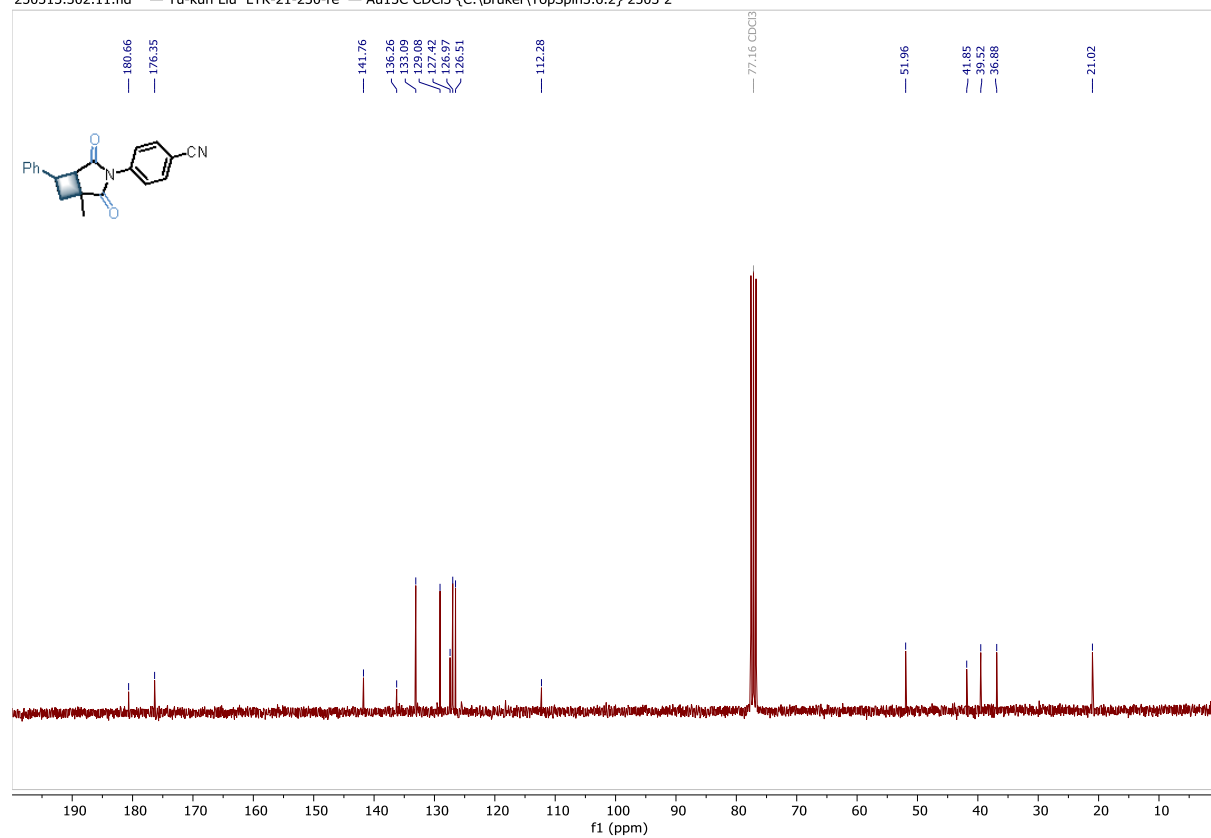
Supplementary Fig. 27. ^1H NMR spectrum of **3j** (300 MHz, CDCl_3)

250313.302.10.fid — Yu-kun Liu LYK-21-230-re — Au1H CDCl_3 {C:\Bruker\TopSpin3.6.2} 2503 2

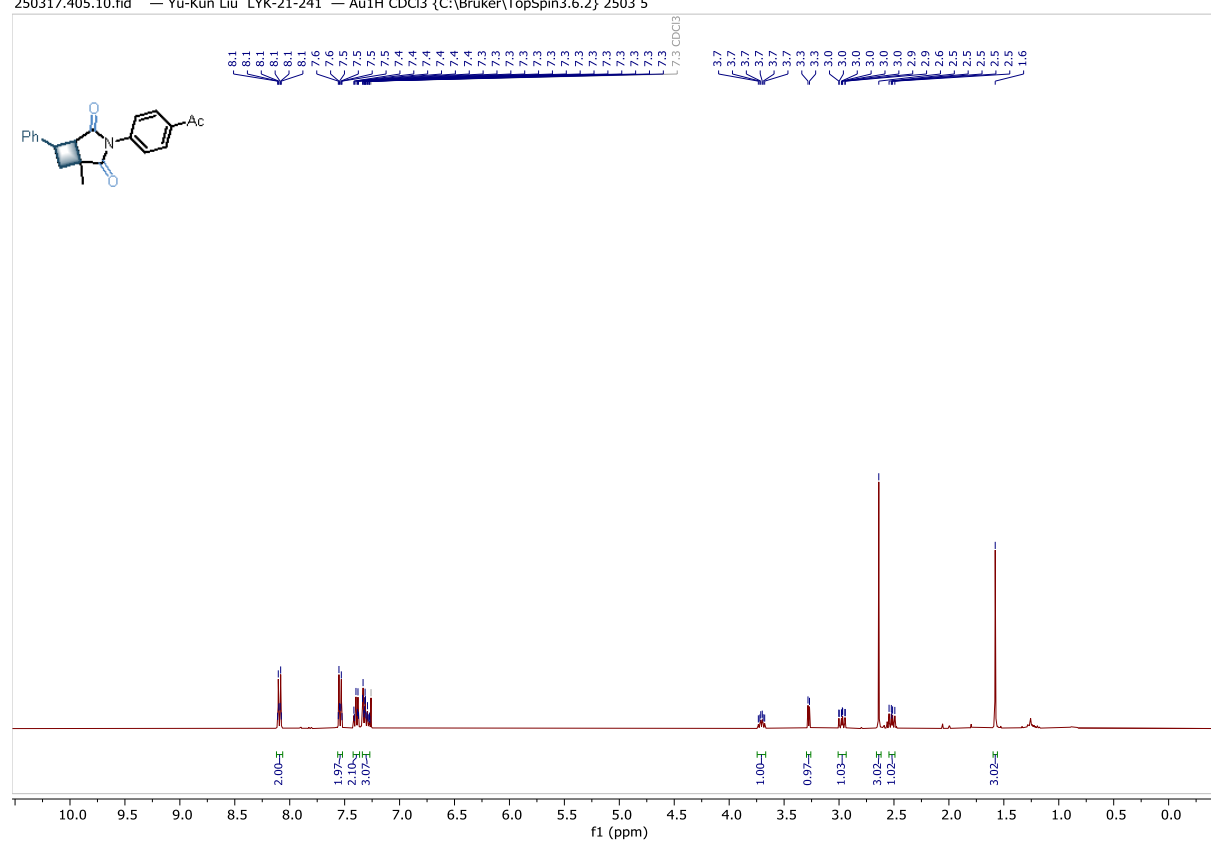


Supplementary Fig. 28. ^{13}C NMR spectrum of **3j** (75 MHz, CDCl_3)

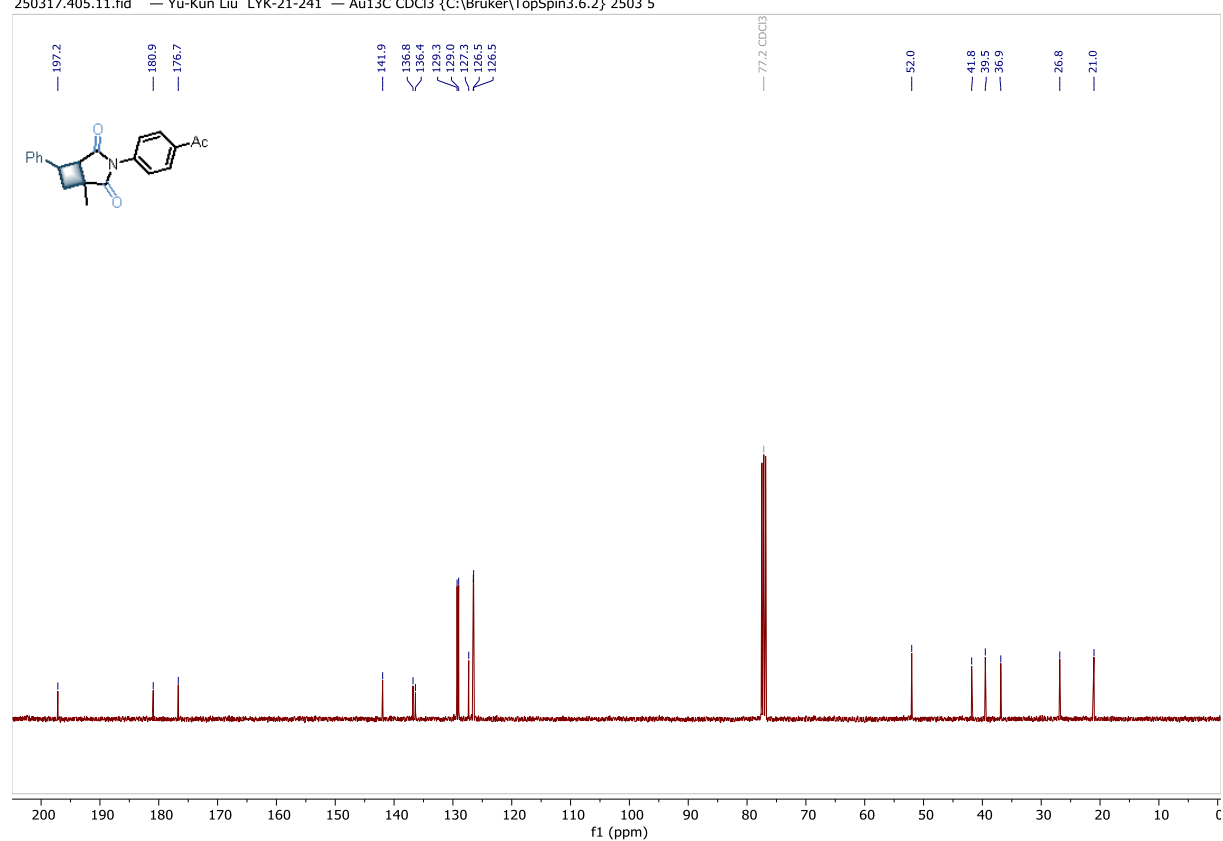
250313.302.11.fid — Yu-kun Liu LYK-21-230-re — Au13C CDCl_3 {C:\Bruker\TopSpin3.6.2} 2503 2



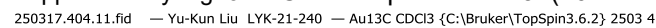
250317.405.10.fid — Yu-Kun Liu LYK-21-241 — Au1H CDCl3 {C:\Bruker\TopSpin3.6.2} 2503 5



250317.405.11.fid — Yu-Kun Liu LYK-21-241 — Au13C CDCl3 {C:\Bruker\TopSpin3.6.2} 2503 5

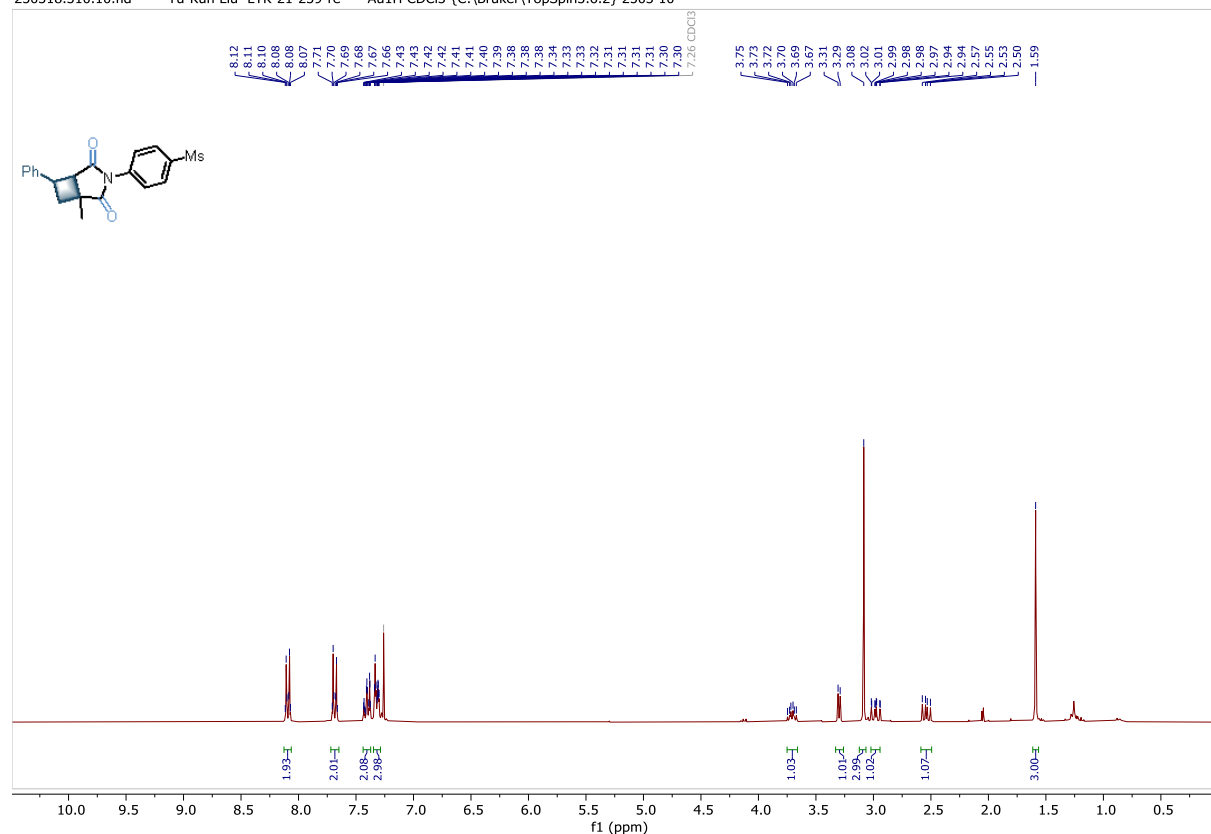


250317.404.10.fid — Yu-Kun Liu LYK-21-240 — Au1H CDCl3 {C:\Bruker\TopSpin3.6.2} 2503 4



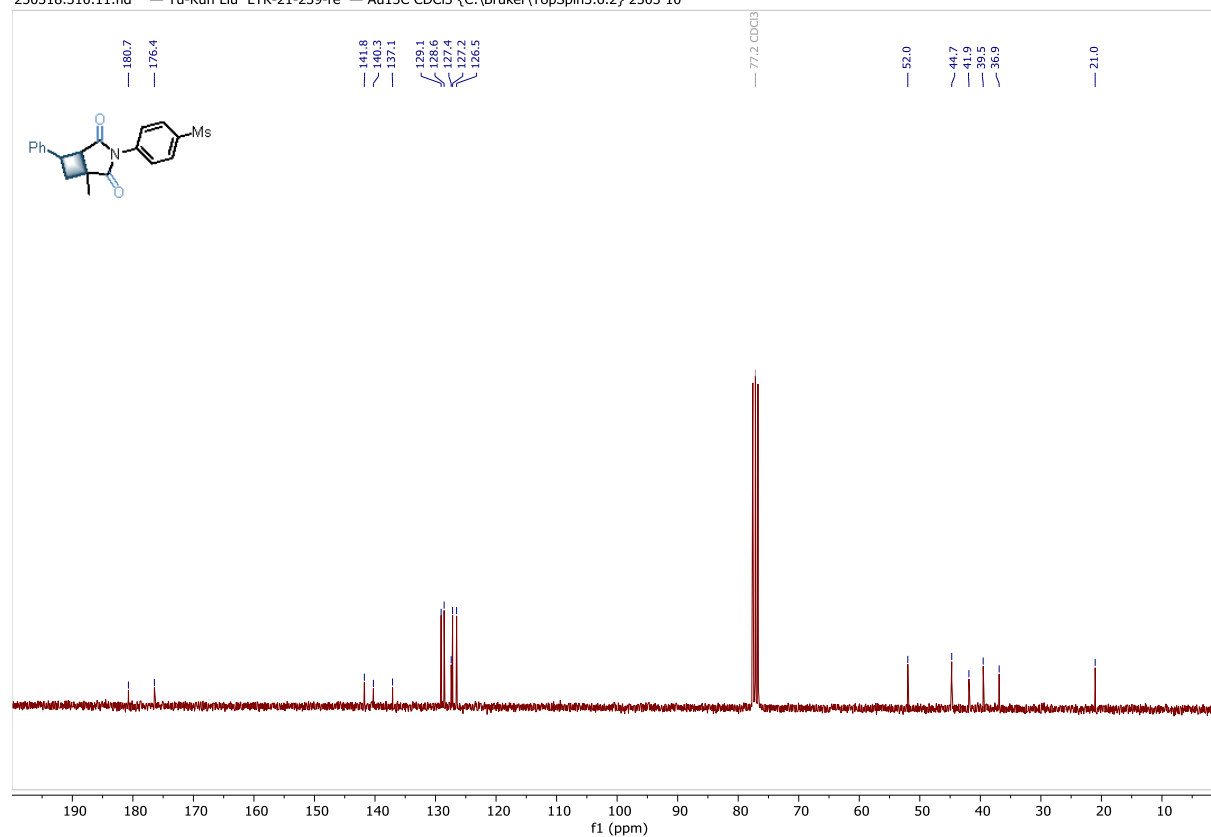
Supplementary Fig. 33. ^1H NMR spectrum of **3m** (300 MHz, CDCl_3)

250318.310.10.fid — Yu-Kun Liu LYK-21-239-re — Au1H CDCl_3 {C:\Bruker\TopSpin3.6.2} 2503 10



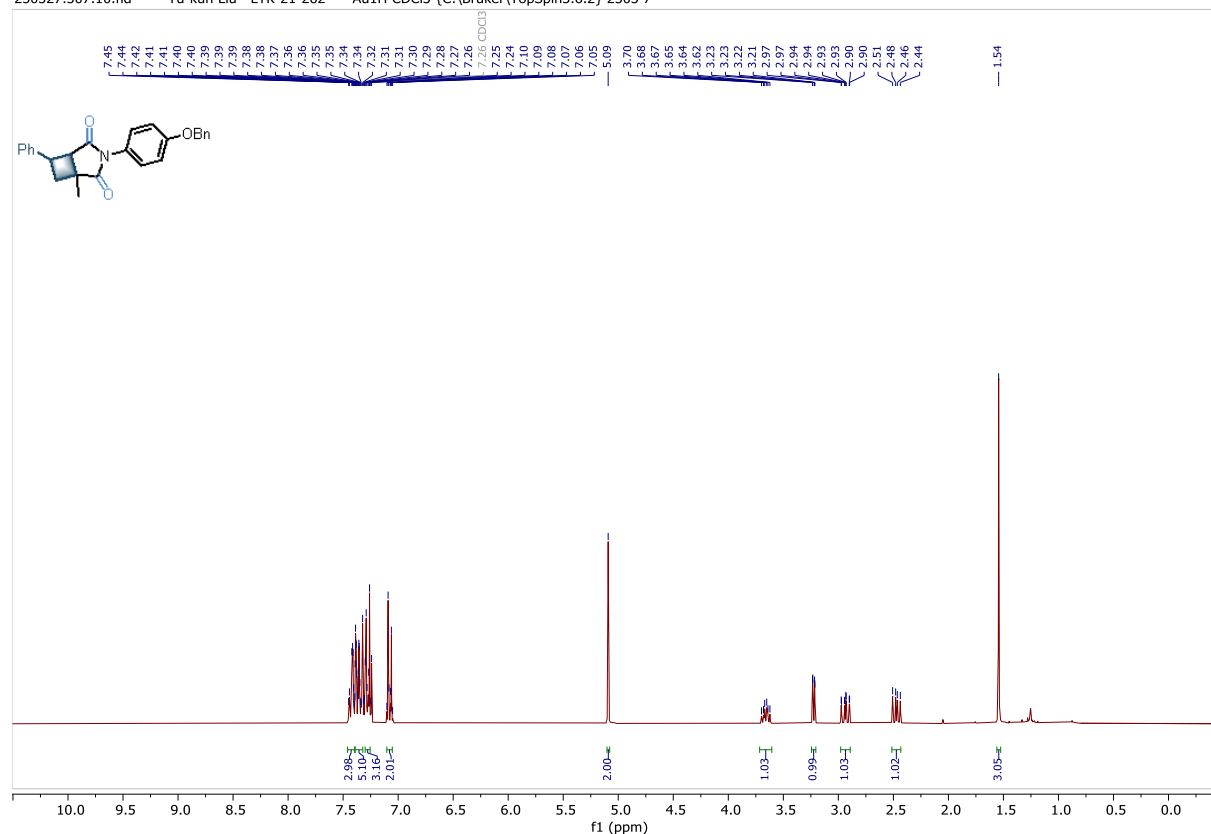
Supplementary Fig. 34. ^{13}C NMR spectrum of **3m** (75 MHz, CDCl_3)

250318.310.11.fid — Yu-Kun Liu LYK-21-239-re — Au13C CDCl_3 {C:\Bruker\TopSpin3.6.2} 2503 10



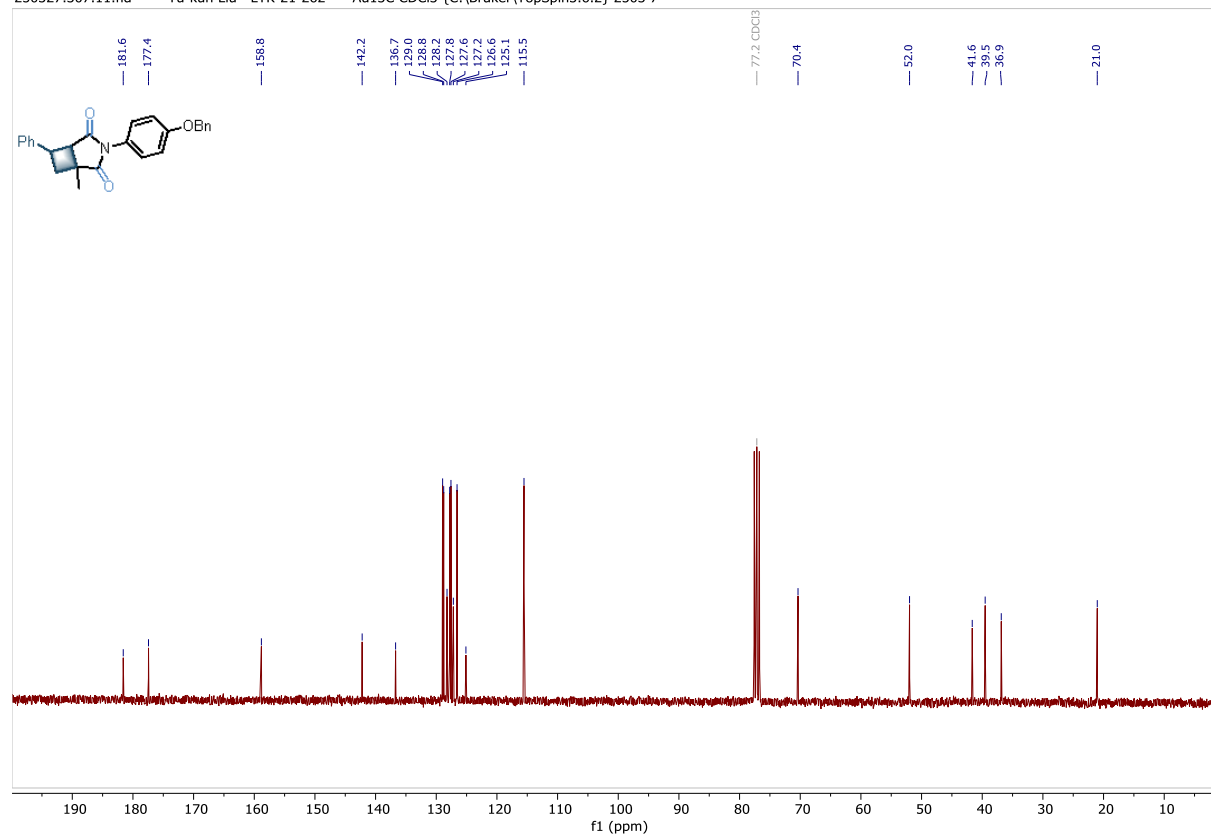
Supplementary Fig. 35. ^1H NMR spectrum of **3n** (300 MHz, CDCl_3)

250327.307.10.fid — Yu-kun Liu LYK-21-262 — Au1H CDCl_3 {C:\Bruker\TopSpin3.6.2} 2503 7



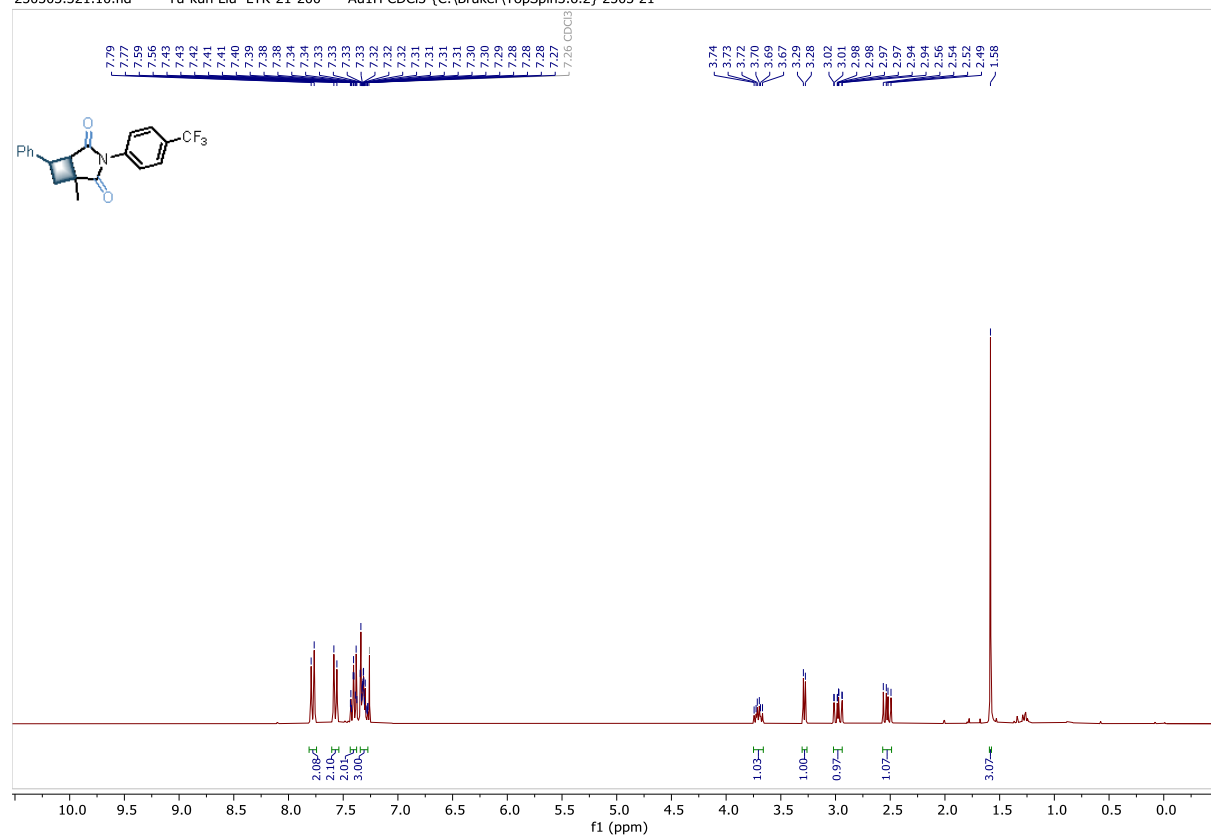
Supplementary Fig. 36. ^{13}C NMR spectrum of **3n** (75 MHz, CDCl_3)

250327.307.11.fid — Yu-kun Liu LYK-21-262 — Au13C CDCl_3 {C:\Bruker\TopSpin3.6.2} 2503 7



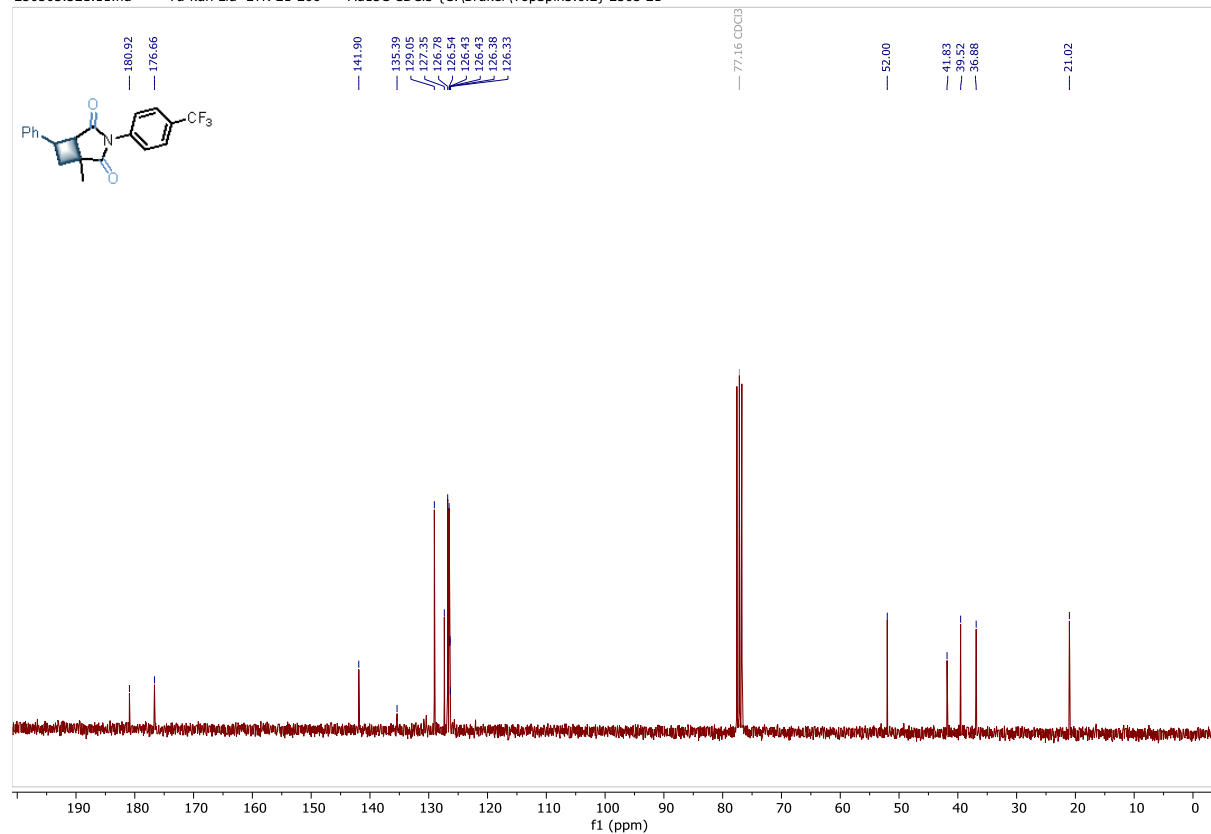
Supplementary Fig. 37. ^1H NMR spectrum of **3o** (300 MHz, CDCl_3)

250303.321.10.fid — Yu-kun Liu LYK-21-200 — Au1H CDCl_3 {C:\Bruker\TopSpin3.6.2} 2503 21



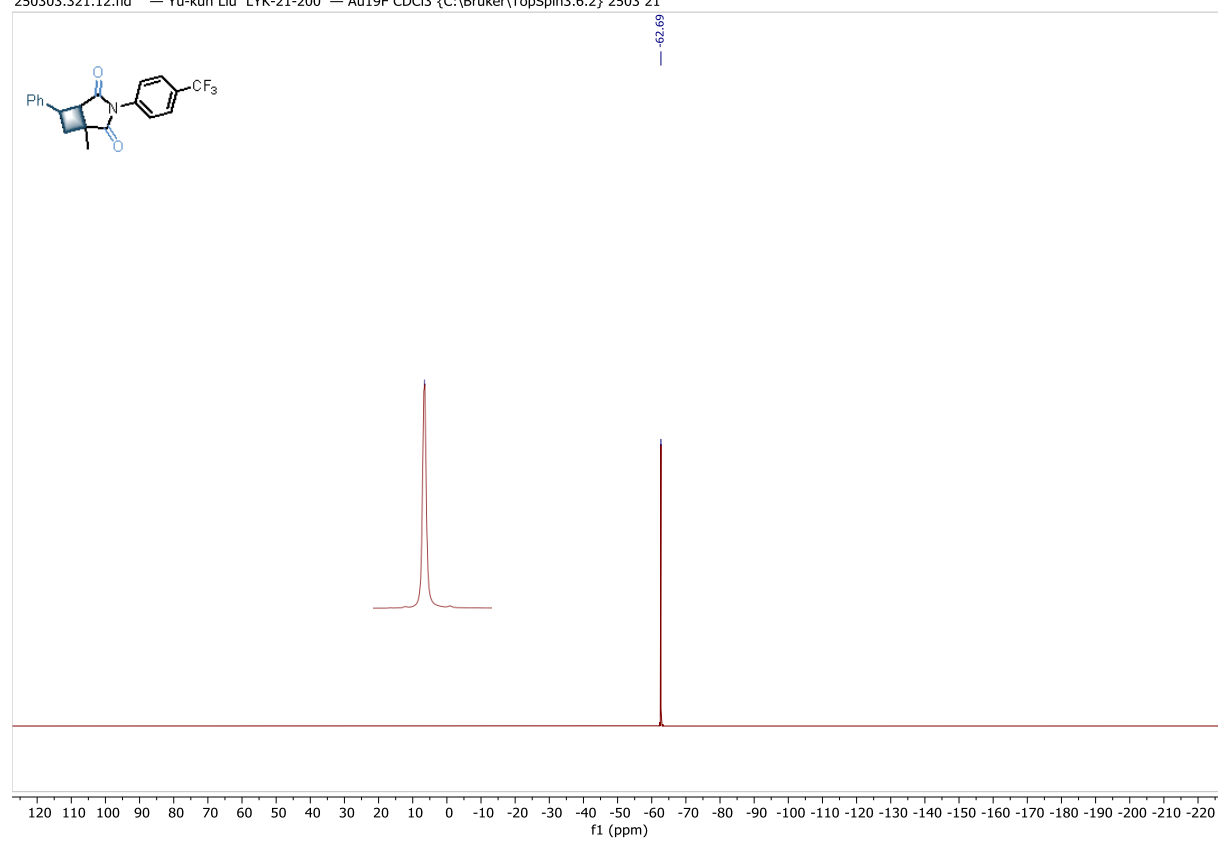
Supplementary Fig. 38. ^{13}C NMR spectrum of **3o** (75 MHz, CDCl_3)

250303.321.11.fid — Yu-kun Liu LYK-21-200 — Au13C CDCl_3 {C:\Bruker\TopSpin3.6.2} 2503 21

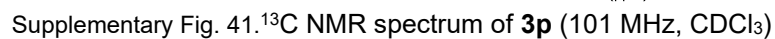


Supplementary Fig. 39. ^{19}F NMR spectrum of **3o** (282 MHz, CDCl_3)

250303.321.12.fid — Yu-kun Liu LYK-21-200 — Au19F CDCl3 {C:\Bruker\TopSpin3.6.2} 2503 21



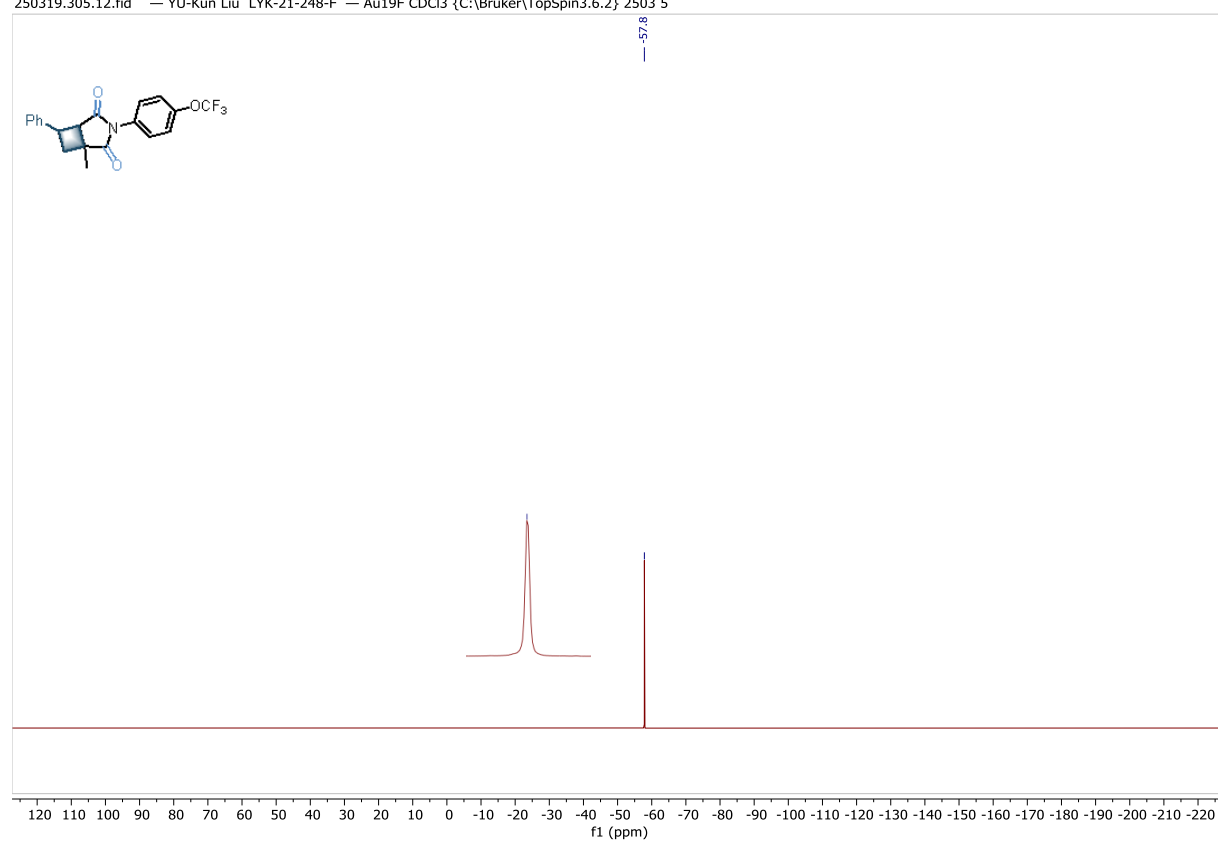
250317.407.10.fid — Yu-Kun Liu LYK-21-248 — Au1H CDCl3 {C:\Bruker\TopSpin3.6.2} 2503 7



250317.407.11.fid — Yu-Kun Liu LYK-21-248 — Au13C CDCl3 {C:\Bruker\TopSpin3.6.2} 2503 7

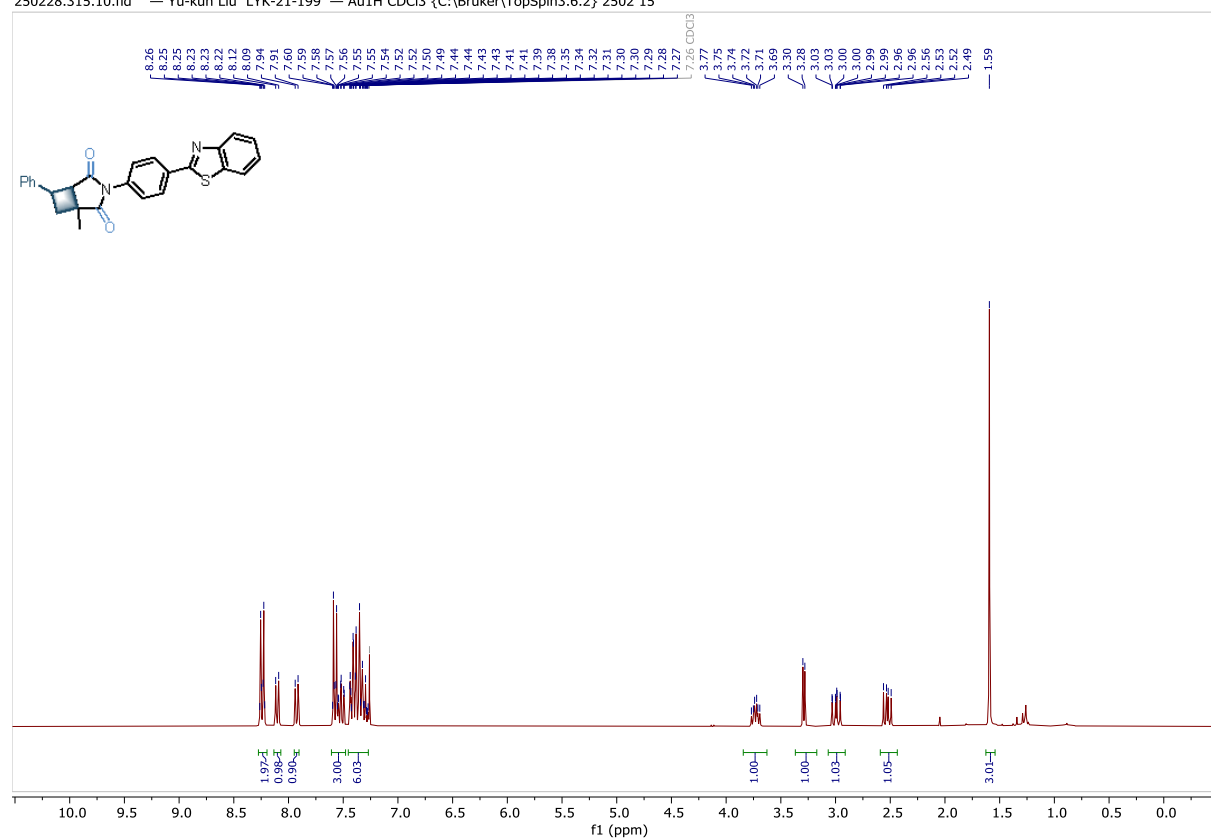
Supplementary Fig. 42. ^{19}F NMR spectrum of **3p** (376 MHz, CDCl_3)

250319.305.12.fid — YU-Kun Liu LYK-21-248-F — Au19F CDCl_3 {C:\Bruker\TopSpin3.6.2} 2503 5



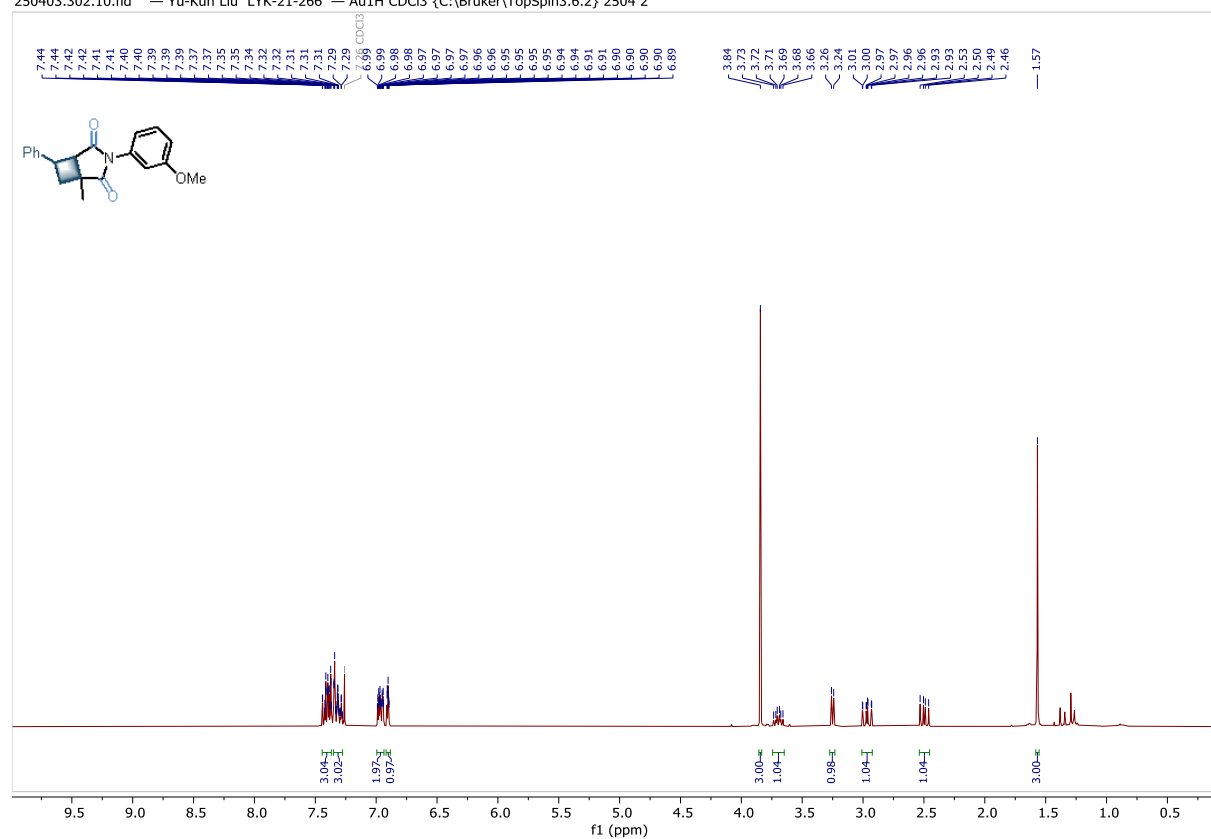
Supplementary Fig. 43. ^1H NMR spectrum of **3q** (300 MHz, CDCl_3)

250228.315.10.fid — Yu-kun Liu LYK-21-199 — Au1H CDCl_3 {C:\Bruker\TopSpin3.6.2} 2502 15



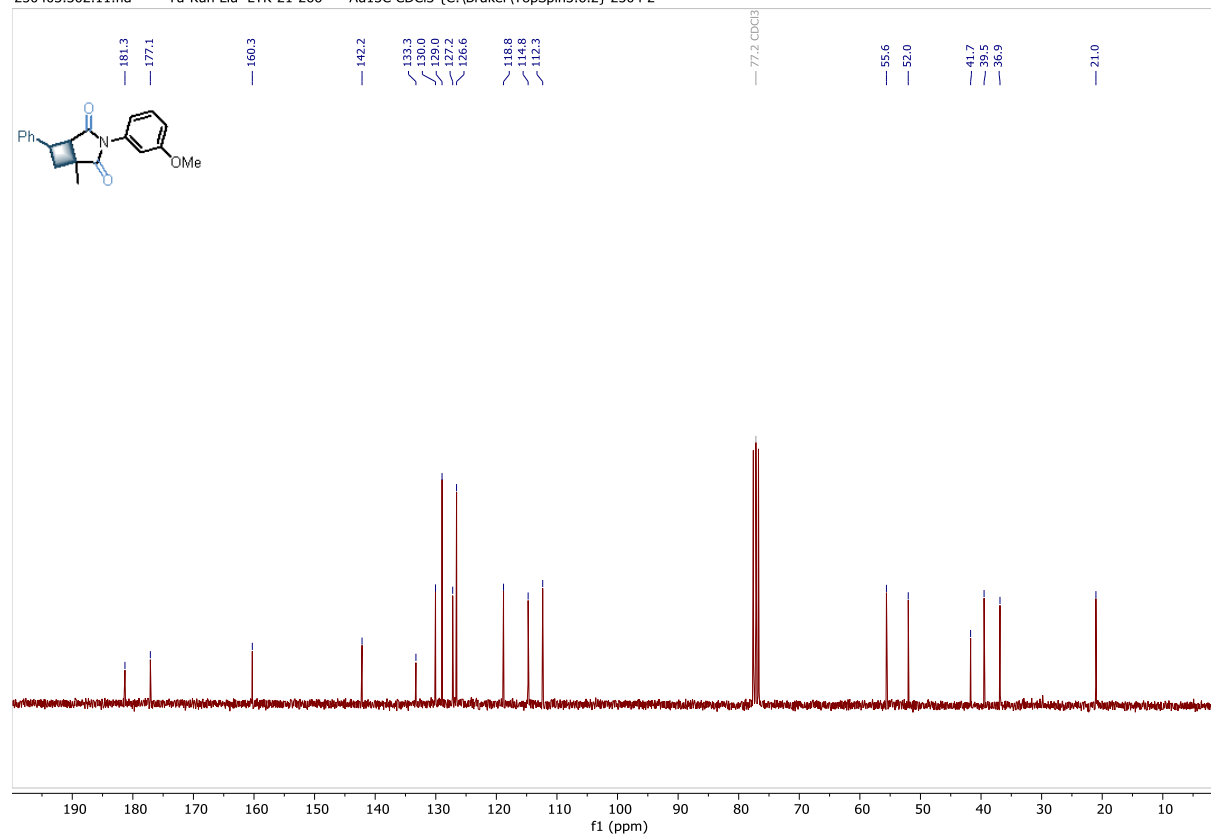
Supplementary Fig. 45. ^1H NMR spectrum of **3r** (300 MHz, CDCl_3)

250403.302.10.fid — Yu-Kun Liu LYK-21-266 — Au1H CDCl_3 {C:\Bruker\TopSpin3.6.2} 2504 2



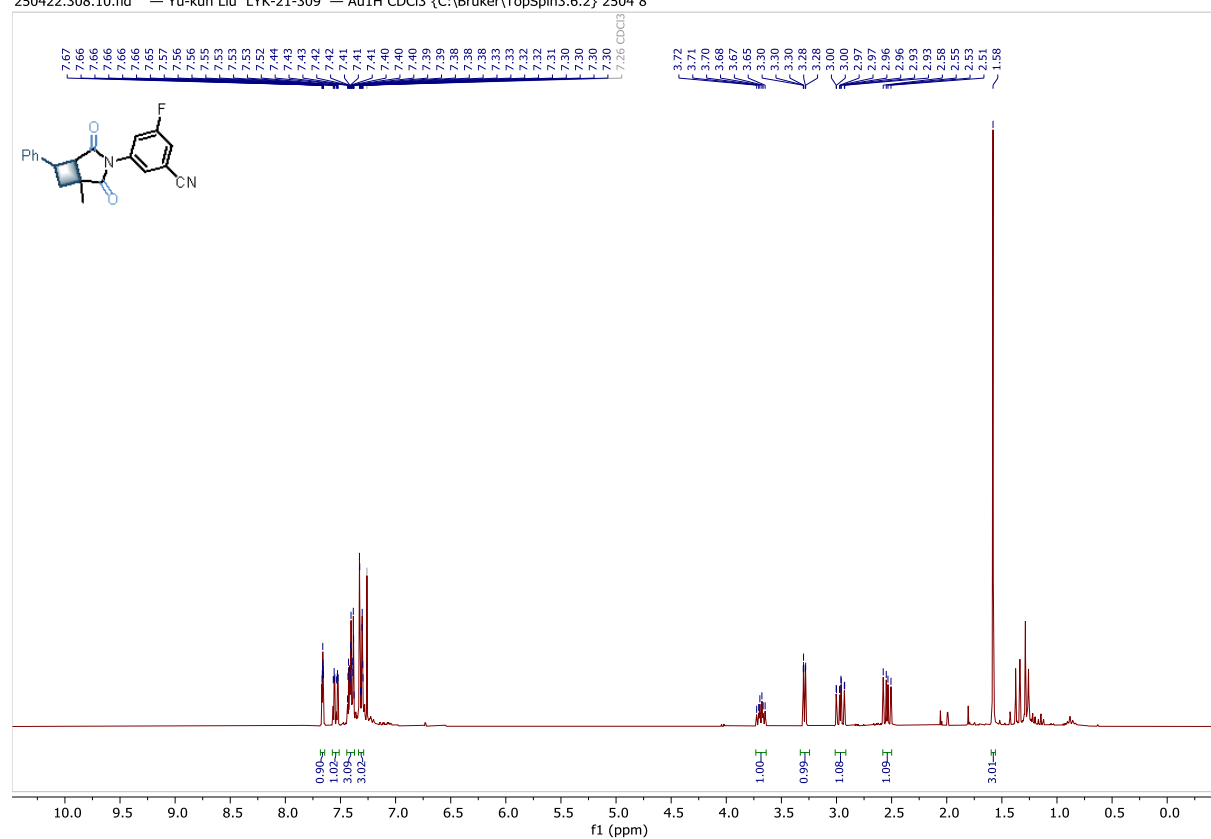
Supplementary Fig. 46. ^{13}C NMR spectrum of **3r** (75 MHz, CDCl_3)

250403.302.11.fid — Yu-Kun Liu LYK-21-266 — Au13C CDCl_3 {C:\Bruker\TopSpin3.6.2} 2504 2



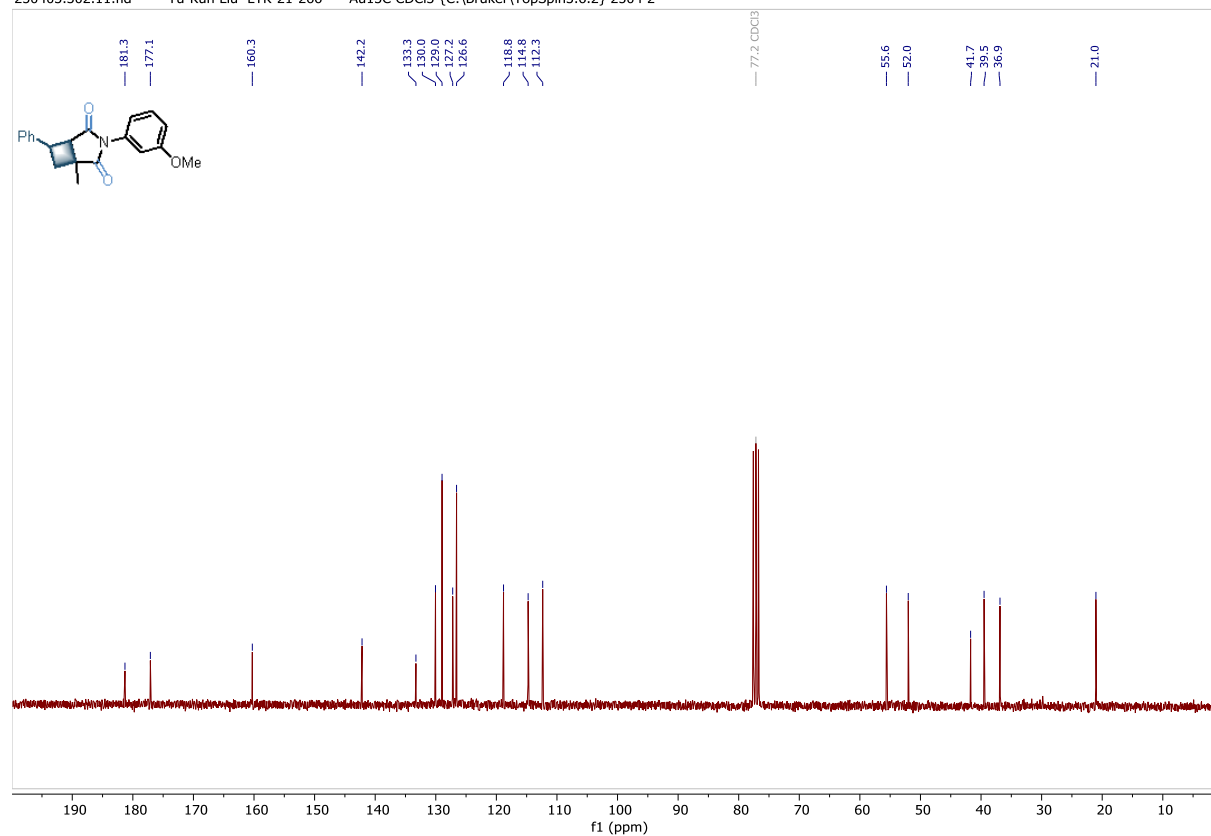
Supplementary Fig. 47. ^1H NMR spectrum of **3s** (300 MHz, CDCl_3)

250422.308.10.fid — Yu-kun Liu LYK-21-309 — Au1H CDCl_3 {C:\Bruker\TopSpin3.6.2} 2504 8



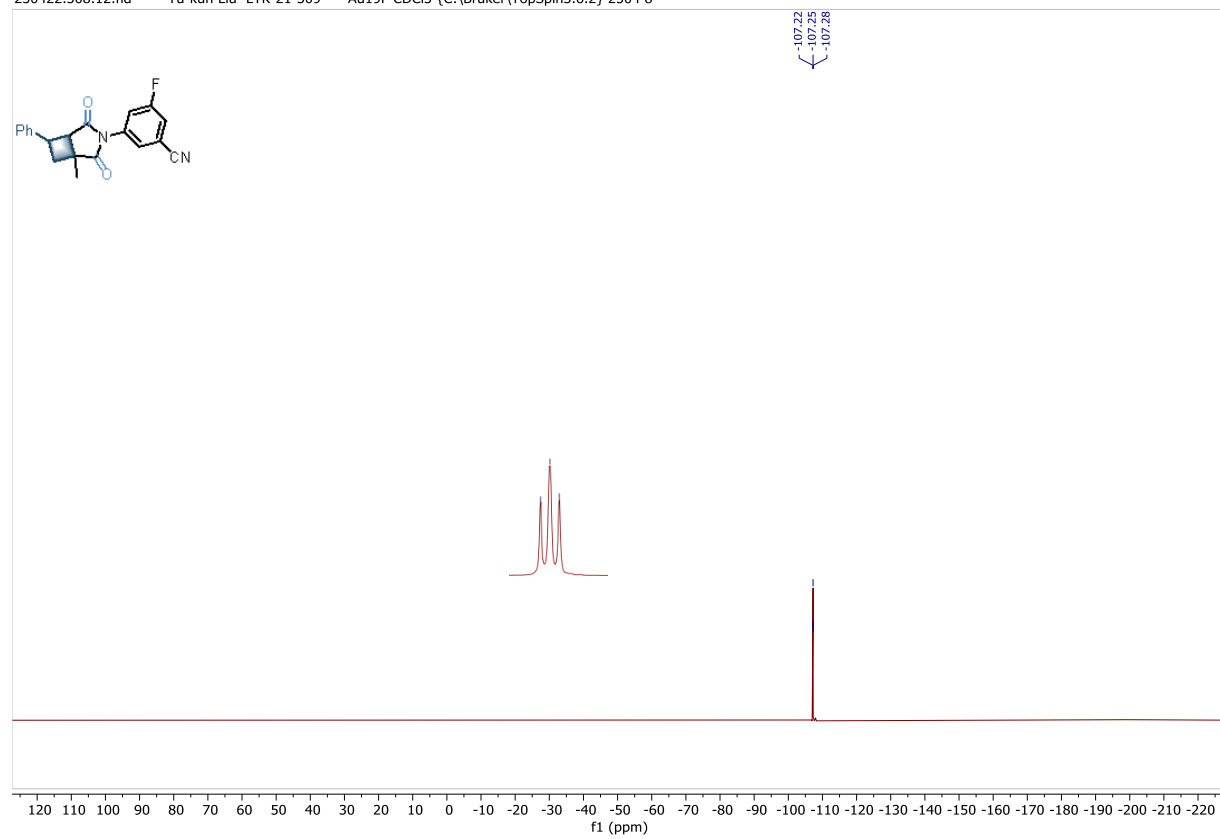
Supplementary Fig. 48. ^{13}C NMR spectrum of **3s** (75 MHz, CDCl_3)

250403.302.11.fid — Yu-Kun Liu LYK-21-266 — Au13C CDCl_3 {C:\Bruker\TopSpin3.6.2} 2504 2



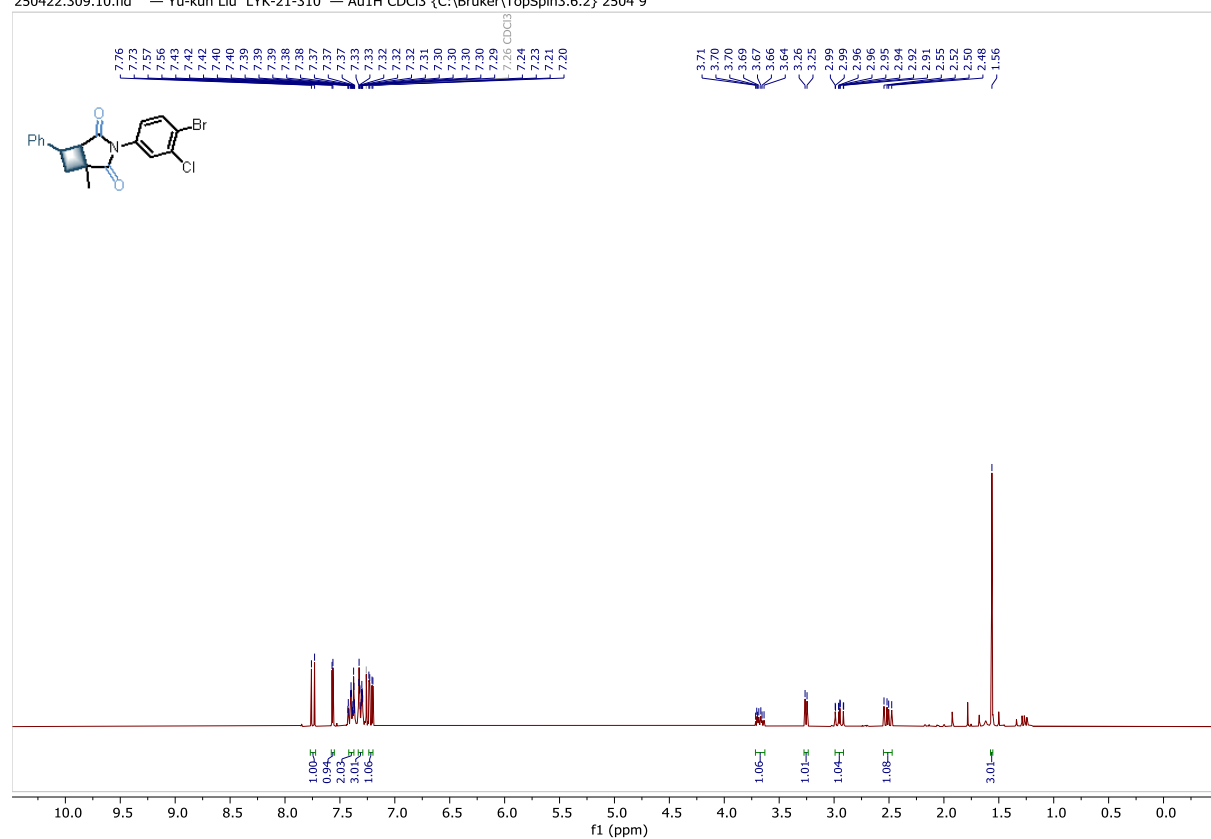
Supplementary Fig. 49. ^{19}F NMR spectrum of **3s** (282 MHz, CDCl_3)

250422.308.12.fid — Yu-kun Liu LYK-21-309 — Au19F CDCl3 {C:\Bruker\TopSpin3.6.2} 2504 8



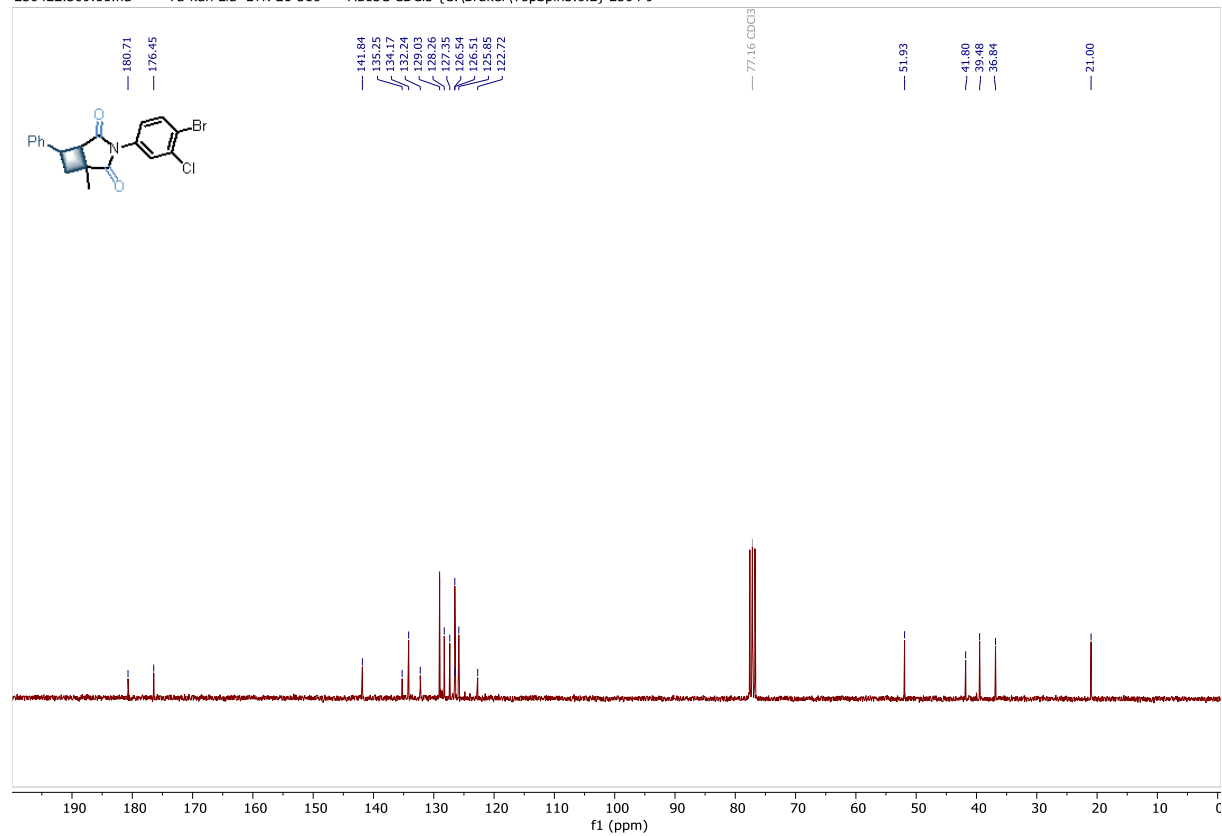
Supplementary Fig. 50. ^1H NMR spectrum of **3t** (300 MHz, CDCl_3)

250422.309.10.fid — Yu-kun Liu LYK-21-310 — Au1H CDCl_3 {C:\Bruker\TopSpin3.6.2} 2504 9

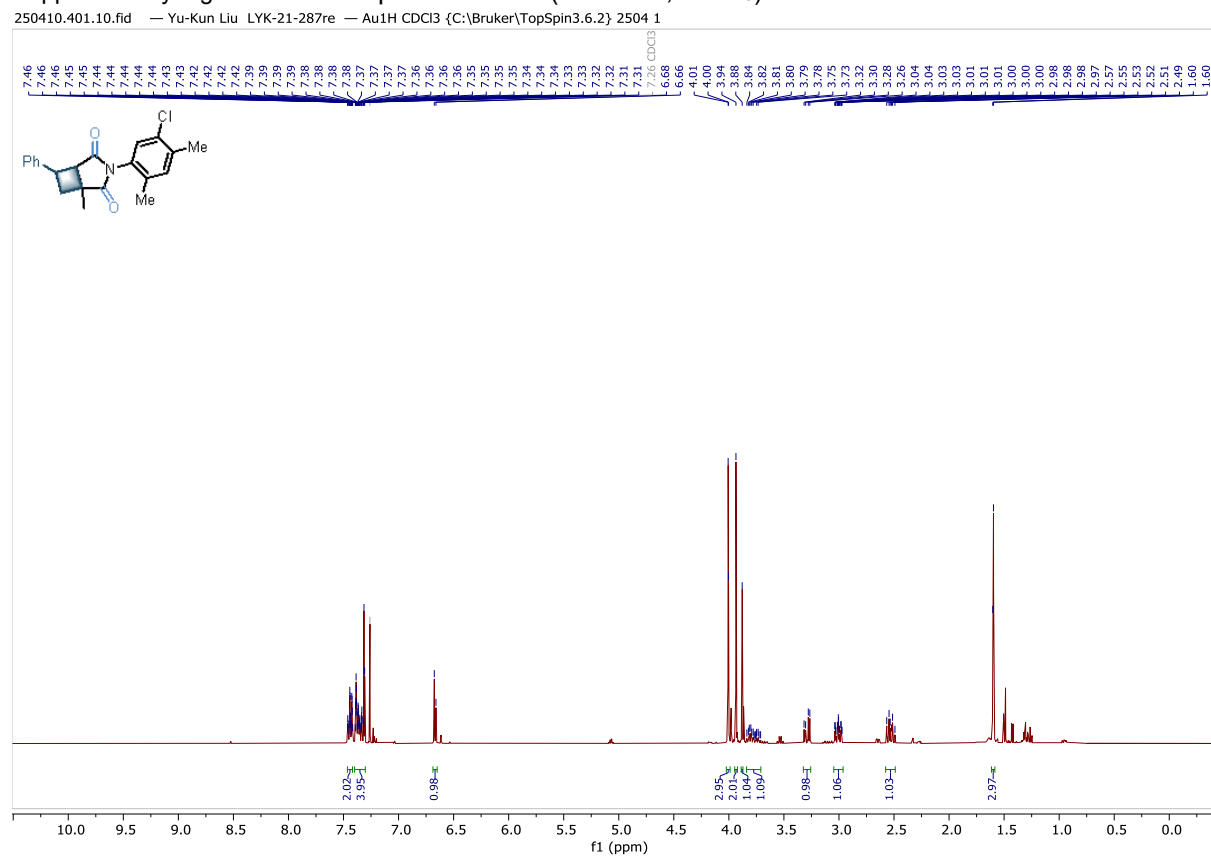


Supplementary Fig. 51. ^{13}C NMR spectrum of **3t** (75 MHz, CDCl_3)

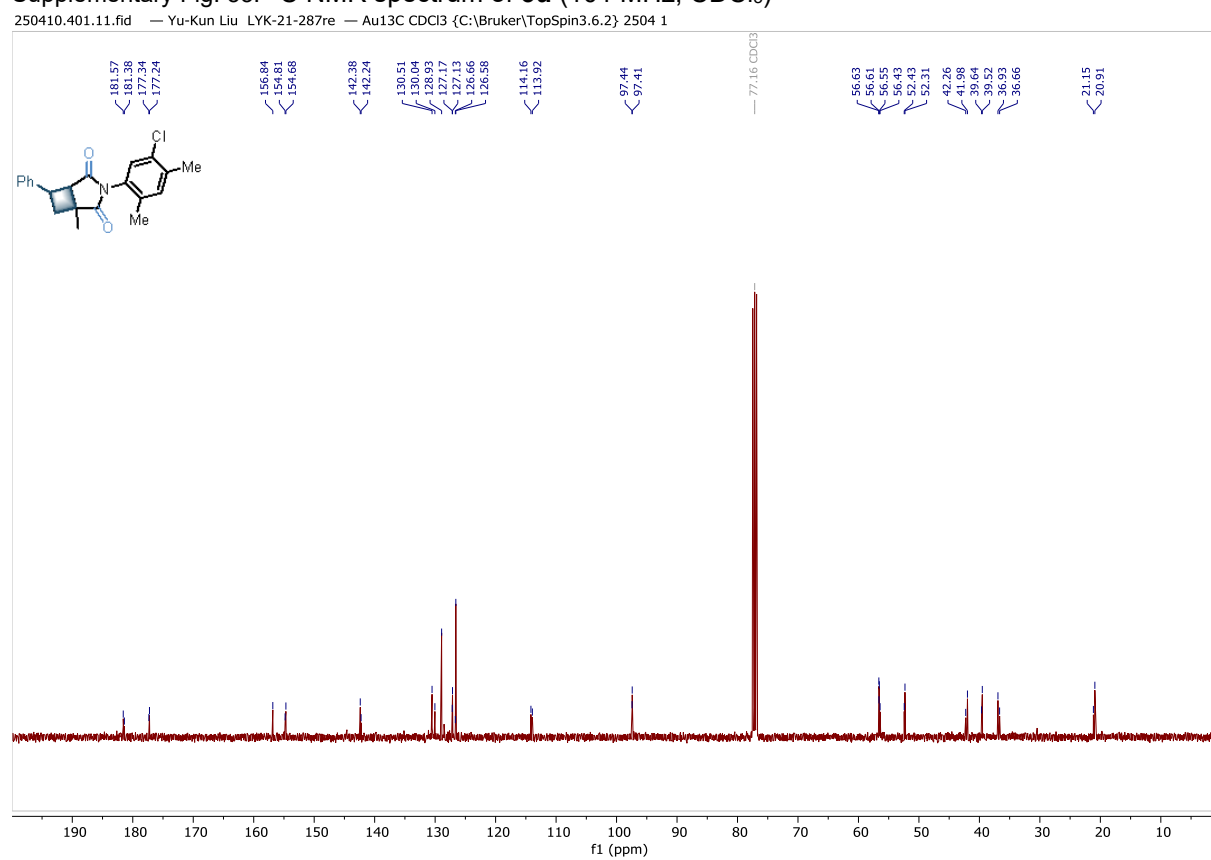
250422.309.11.fid — Yu-kun Liu LYK-21-310 — Au13C CDCl_3 {C:\Bruker\TopSpin3.6.2} 2504 9



Supplementary Fig. 52. ^1H NMR spectrum of **3u** (400 MHz, CDCl_3)

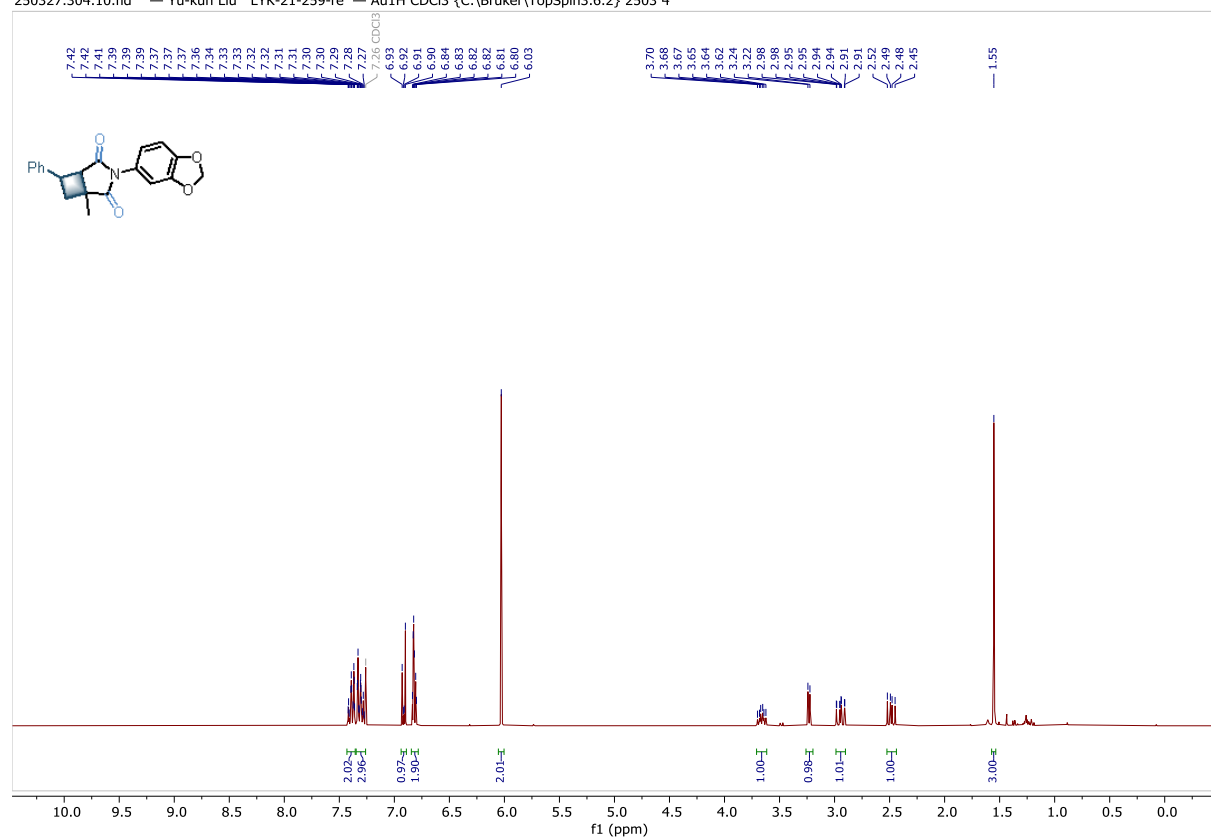


Supplementary Fig. 53. ^{13}C NMR spectrum of **3u** (101 MHz, CDCl_3)



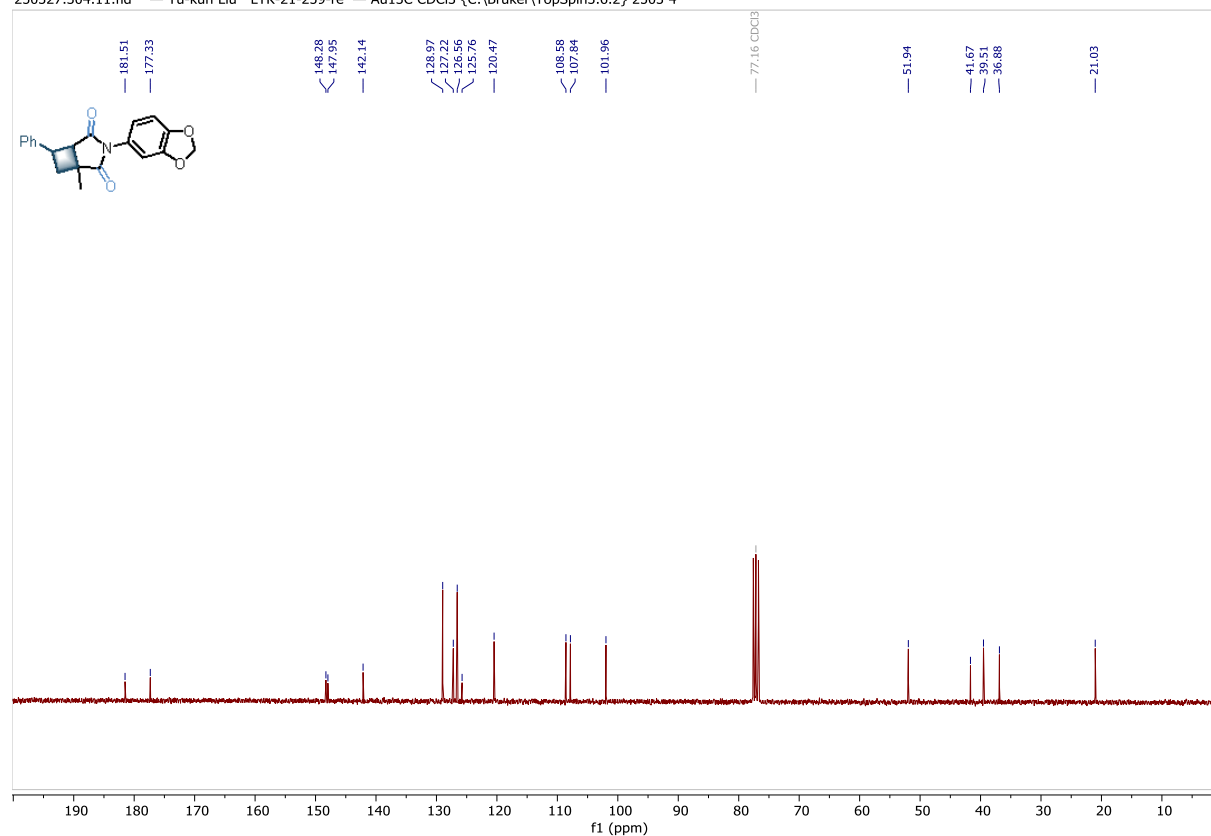
Supplementary Fig. 54. ^1H NMR spectrum of **3v** (300 MHz, CDCl_3)

250327.304.10.fid — Yu-kun Liu LYK-21-259-re — Au1H CDCl_3 {C:\Bruker\TopSpin3.6.2} 2503 4



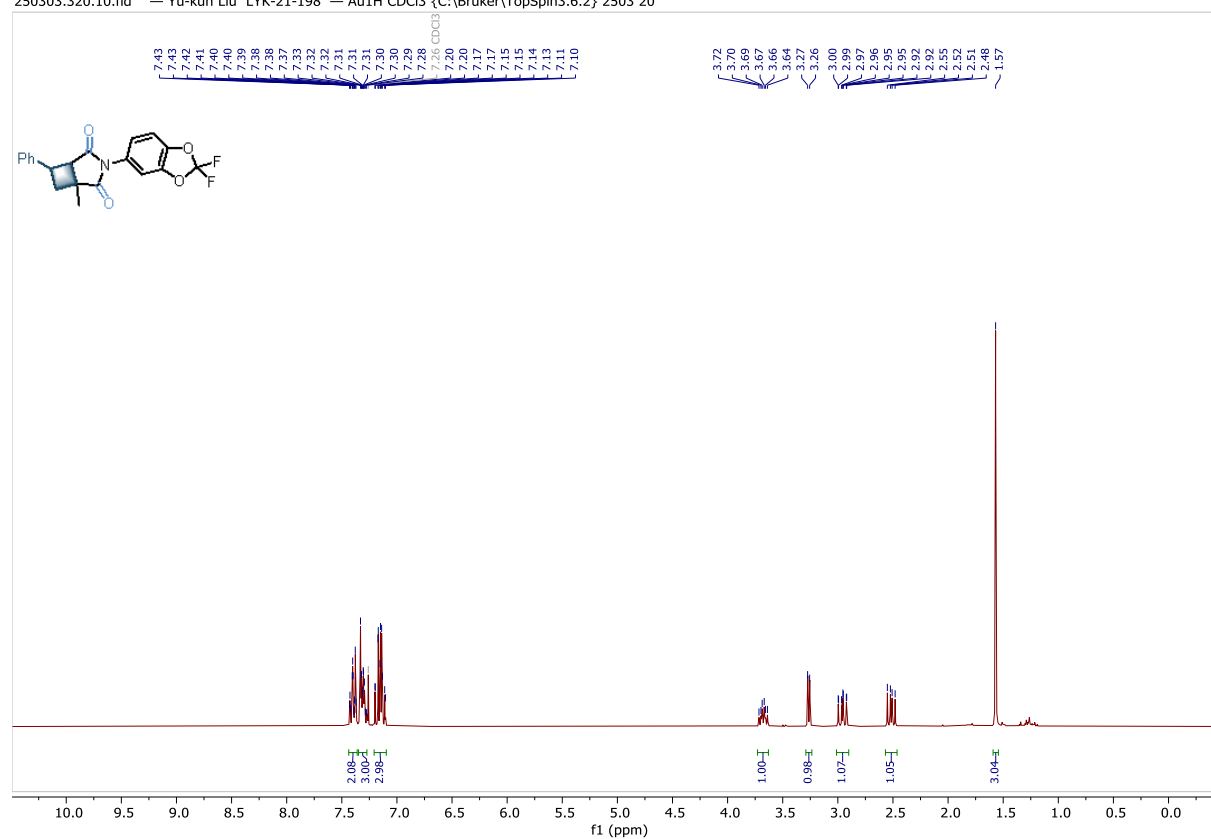
Supplementary Fig. 55. ^{13}C NMR spectrum of **3v** (75 MHz, CDCl_3)

250327.304.11.fid — Yu-kun Liu LYK-21-259-re — Au13C CDCl_3 {C:\Bruker\TopSpin3.6.2} 2503 4



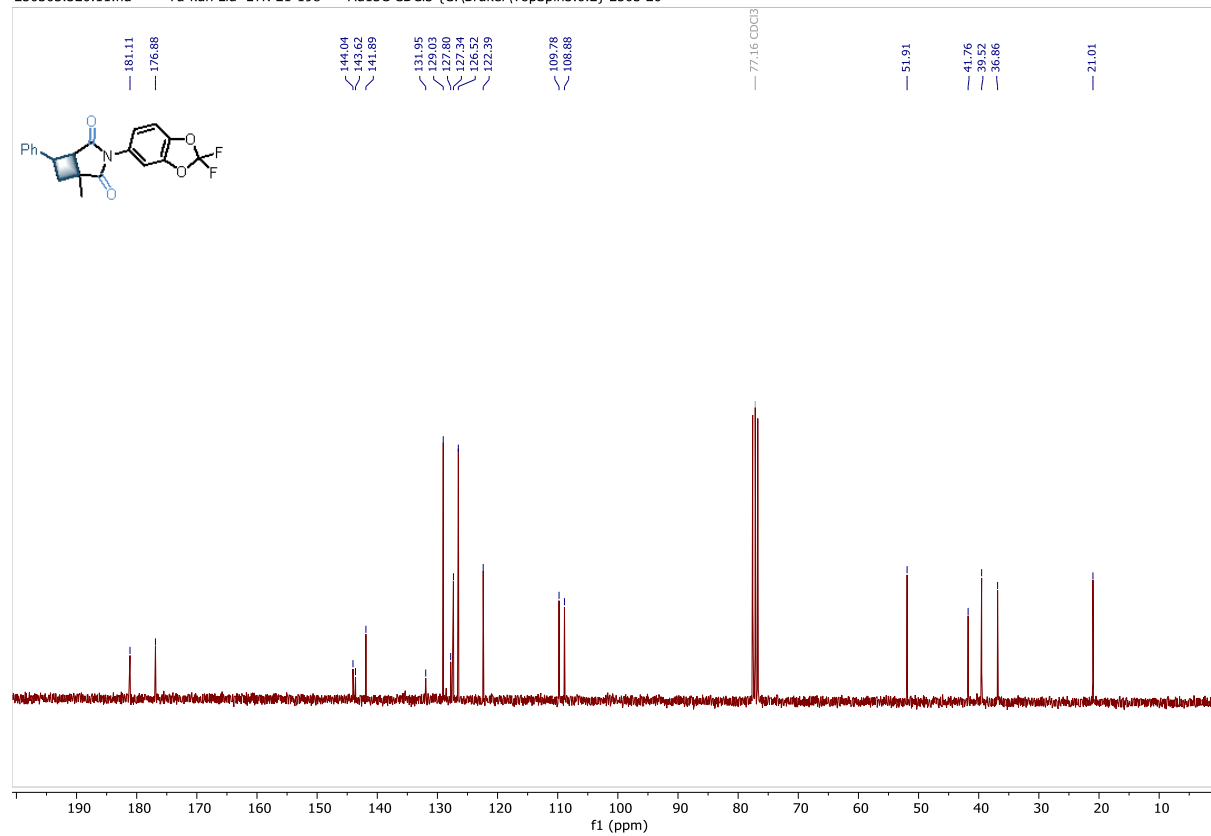
Supplementary Fig. 56. ^1H NMR spectrum of **3w** (300 MHz, CDCl_3)

250303.320.10.fid — Yu-kun Liu LYK-21-198 — Au1H CDCl_3 {C:\Bruker\TopSpin3.6.2} 2503 20



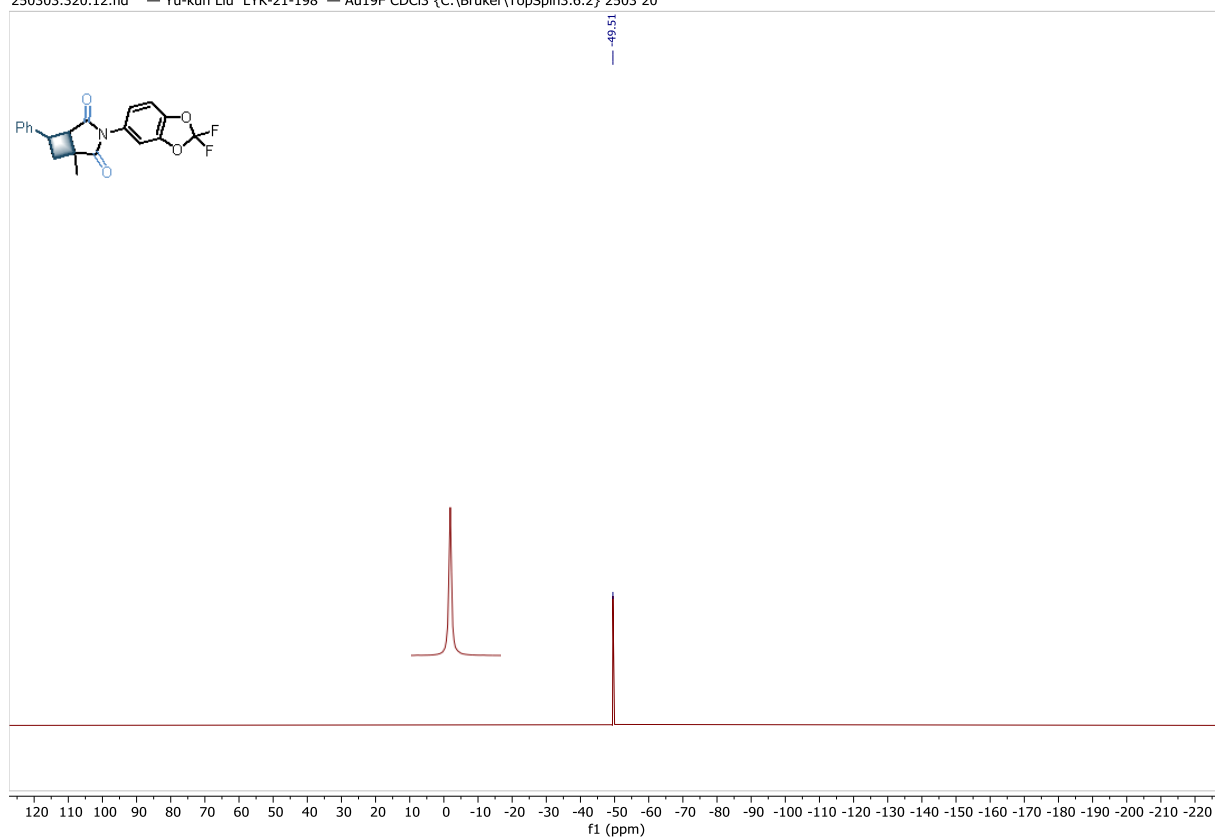
Supplementary Fig. 57. ^{13}C NMR spectrum of **3w** (75 MHz, CDCl_3)

250303.320.11.fid — Yu-kun Liu LYK-21-198 — Au13C CDCl_3 {C:\Bruker\TopSpin3.6.2} 2503 20



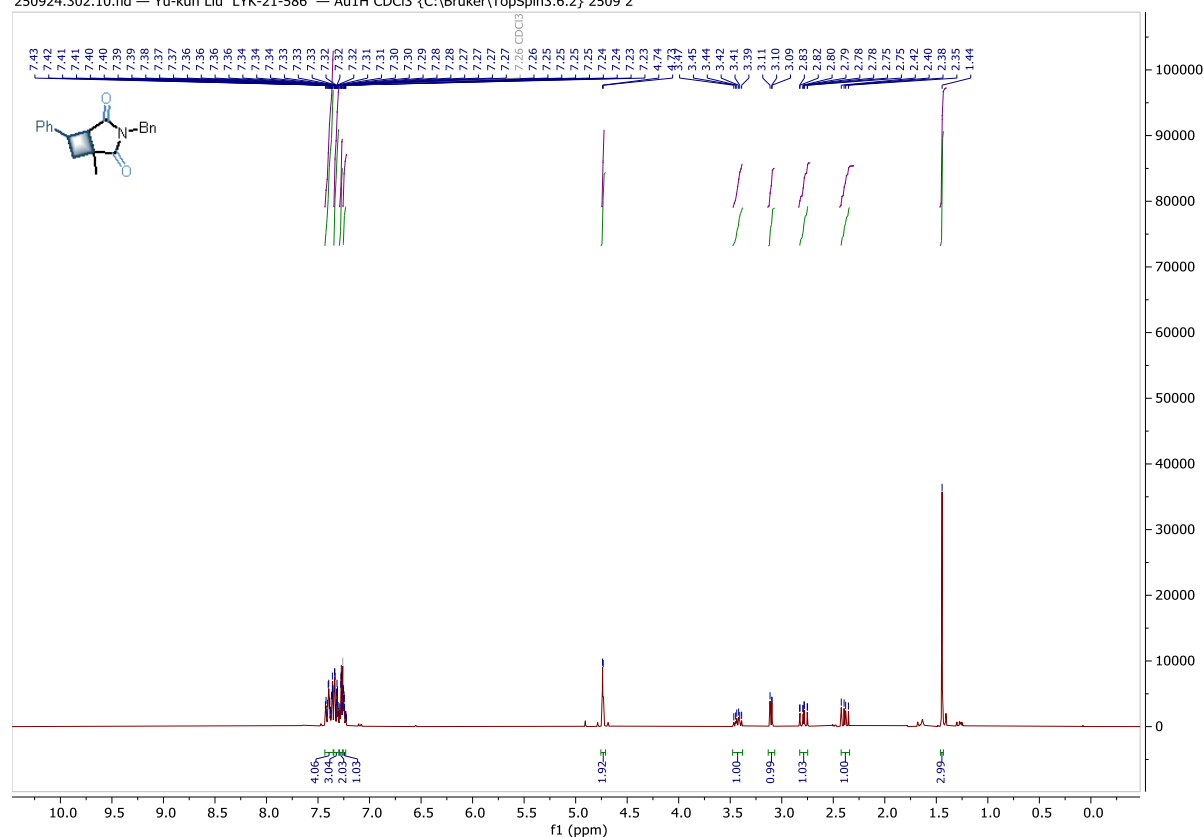
Supplementary Fig. 58. ^{19}F NMR spectrum of **3w** (282 MHz, CDCl_3)

250303.320.12.fid — Yu-kun Liu LYK-21-198 — Au19F CDCl_3 {C:\Bruker\TopSpin3.6.2} 2503 20



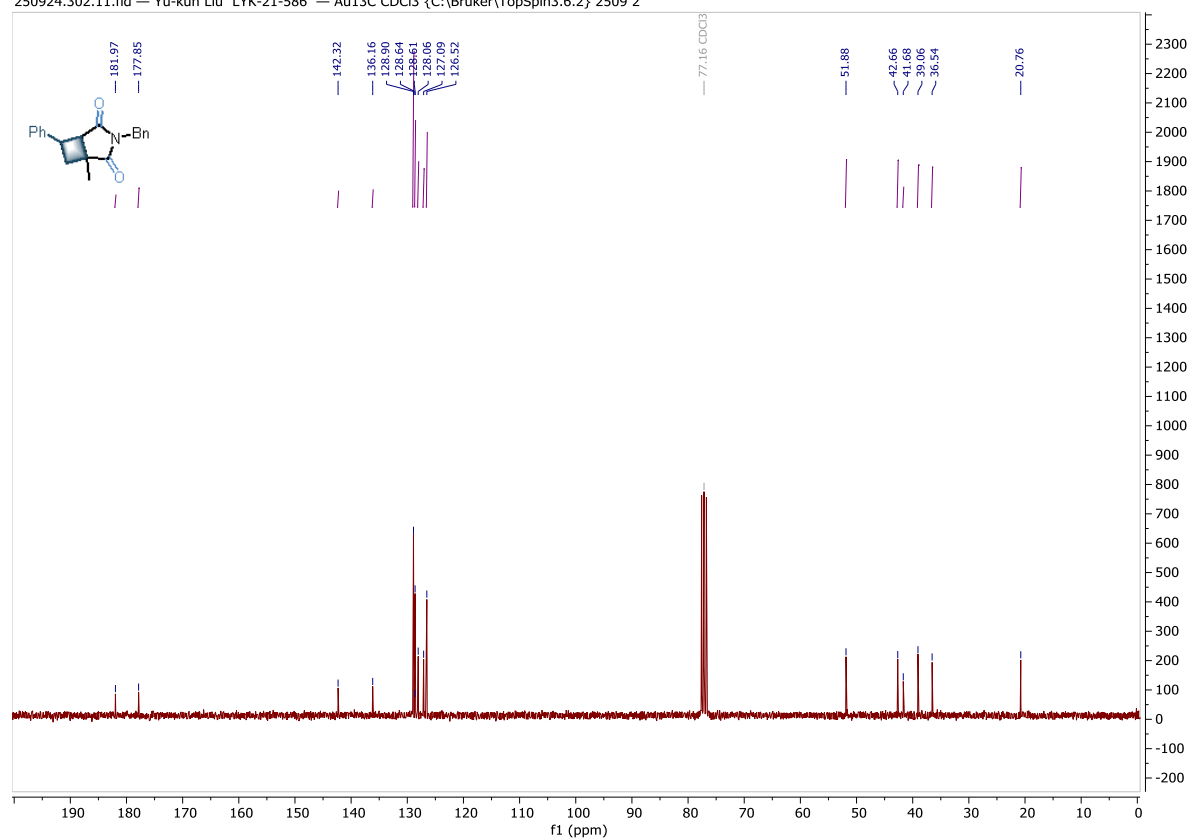
Supplementary Fig. 59. ^1H NMR spectrum of **3x** (300 MHz, CDCl_3)

250924.302.10.fid — Yu-kun Liu LYK-21-586 — Au1H CDCl_3 {C:\Bruker\TopSpin3.6.2} 2509 2



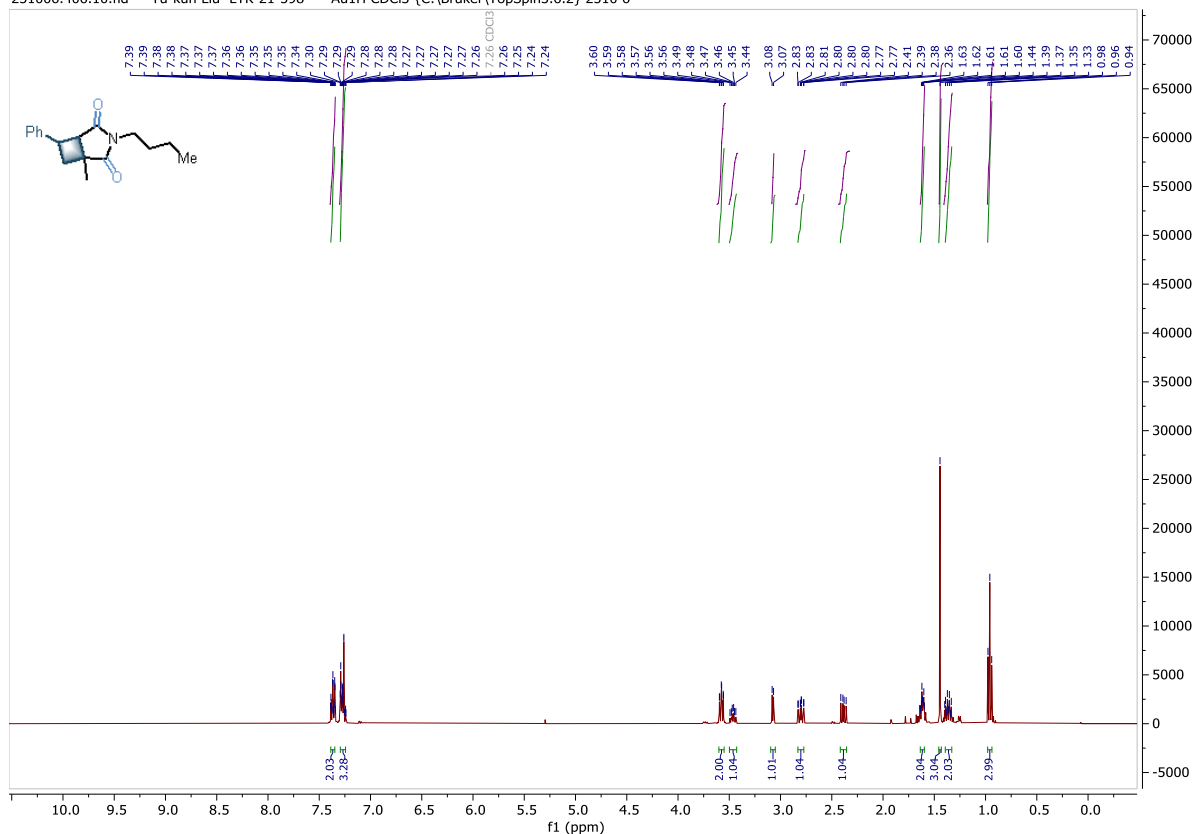
Supplementary Fig. 60. ^{13}C NMR spectrum of **3x** (75 MHz, CDCl_3)

250924.302.11.fid — Yu-kun Liu LYK-21-586 — Au13C CDCl_3 {C:\Bruker\TopSpin3.6.2} 2509 2



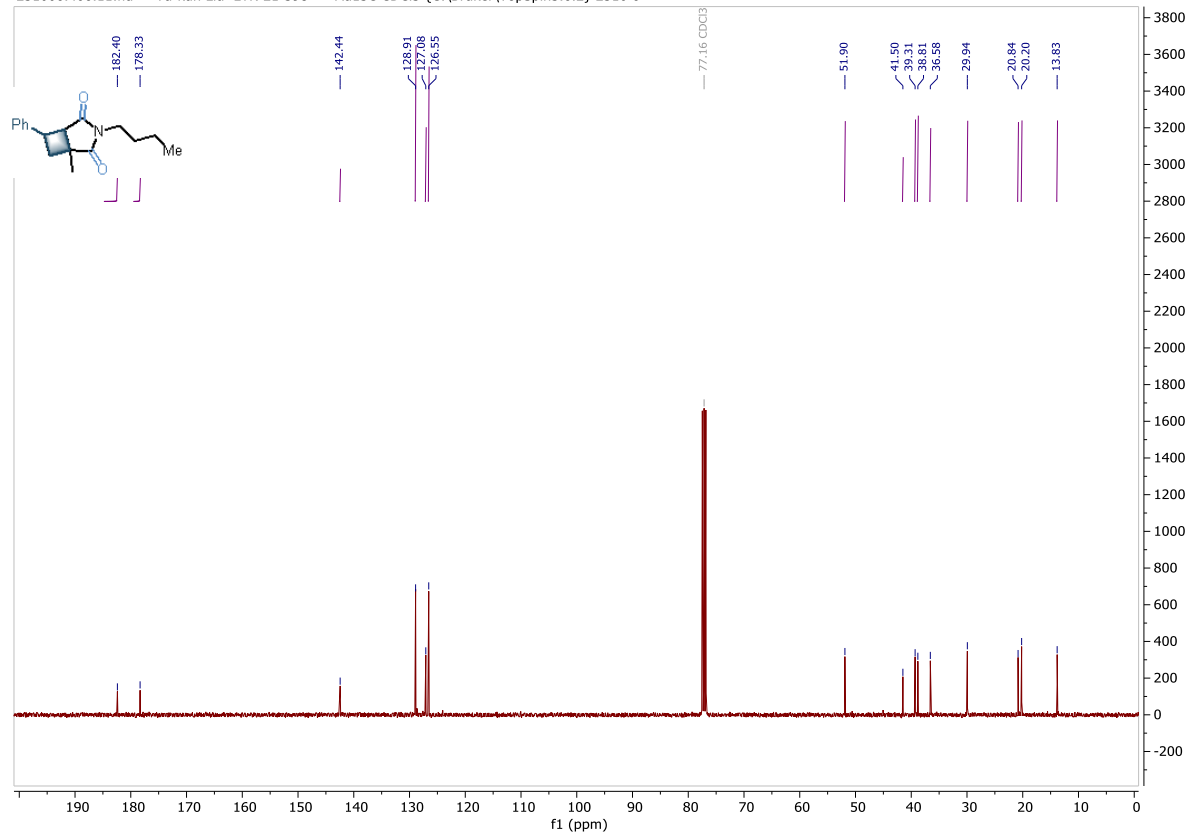
Supplementary Fig. 61. ^1H NMR spectrum of **3y** (400 MHz, CDCl_3)

251006.406.10.fid — Yu-kun Liu LYK-21-598 — Au1H CDCl_3 {C:\Bruker\TopSpin3.6.2} 2510 6



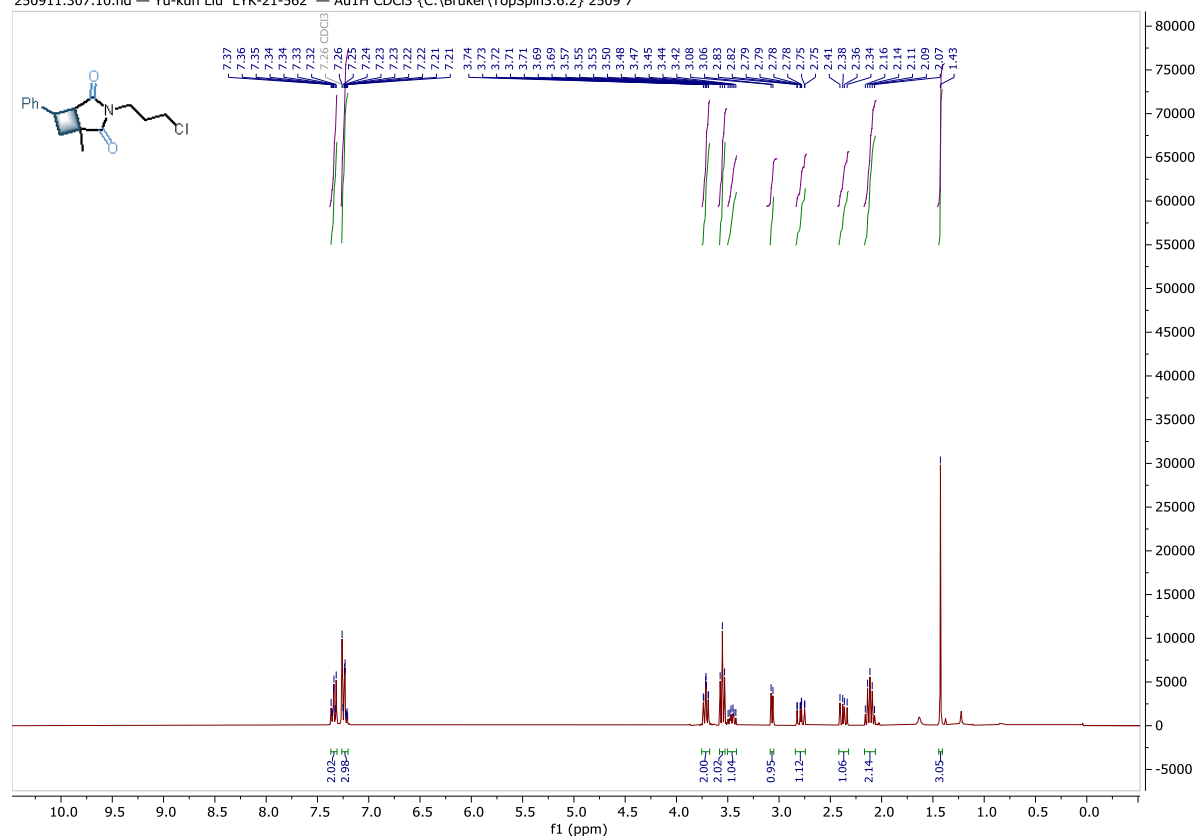
Supplementary Fig. 62. ^{13}C NMR spectrum of **3y** (75 MHz, CDCl_3)

251006.406.11.fid — Yu-kun Liu LYK-21-598 — Au13C CDCl_3 {C:\Bruker\TopSpin3.6.2} 2510 6



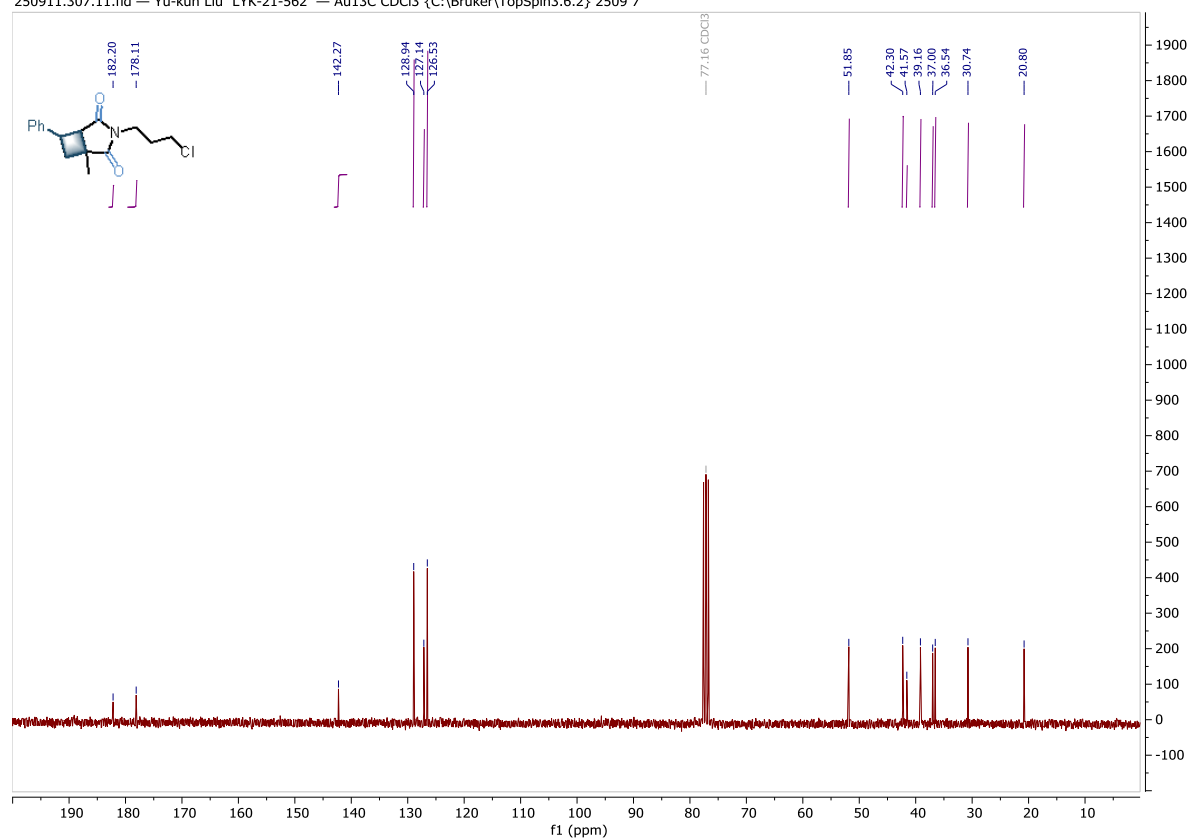
Supplementary Fig. 63. ^1H NMR spectrum of **3z** (300 MHz, CDCl_3)

250911.307.10.fid — Yu-kun Liu LYK-21-562 — Au1H CDCl_3 {C:\Bruker\TopSpin3.6.2} 2509 7



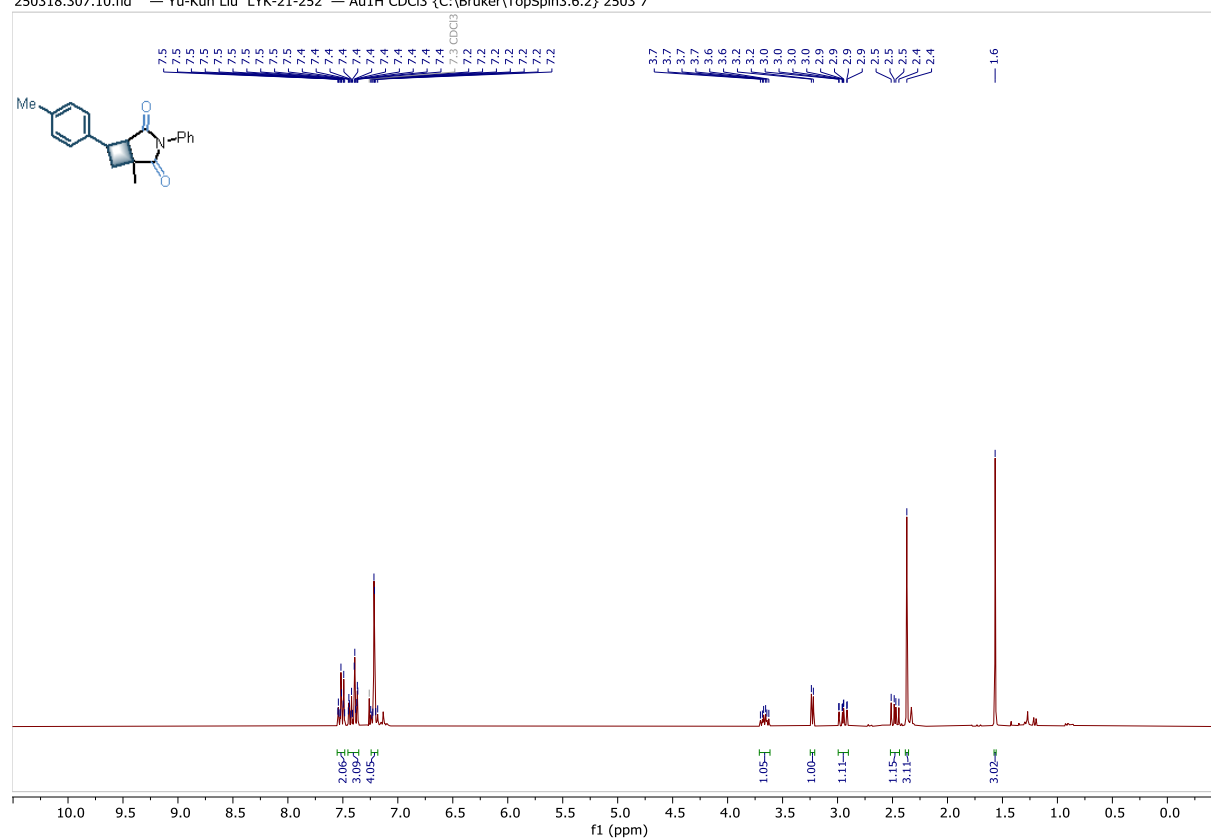
Supplementary Fig. 64. ^{13}C NMR spectrum of **3z** (75 MHz, CDCl_3)

250911.307.11.fid — Yu-kun Liu LYK-21-562 — Au13C CDCl_3 {C:\Bruker\TopSpin3.6.2} 2509 7



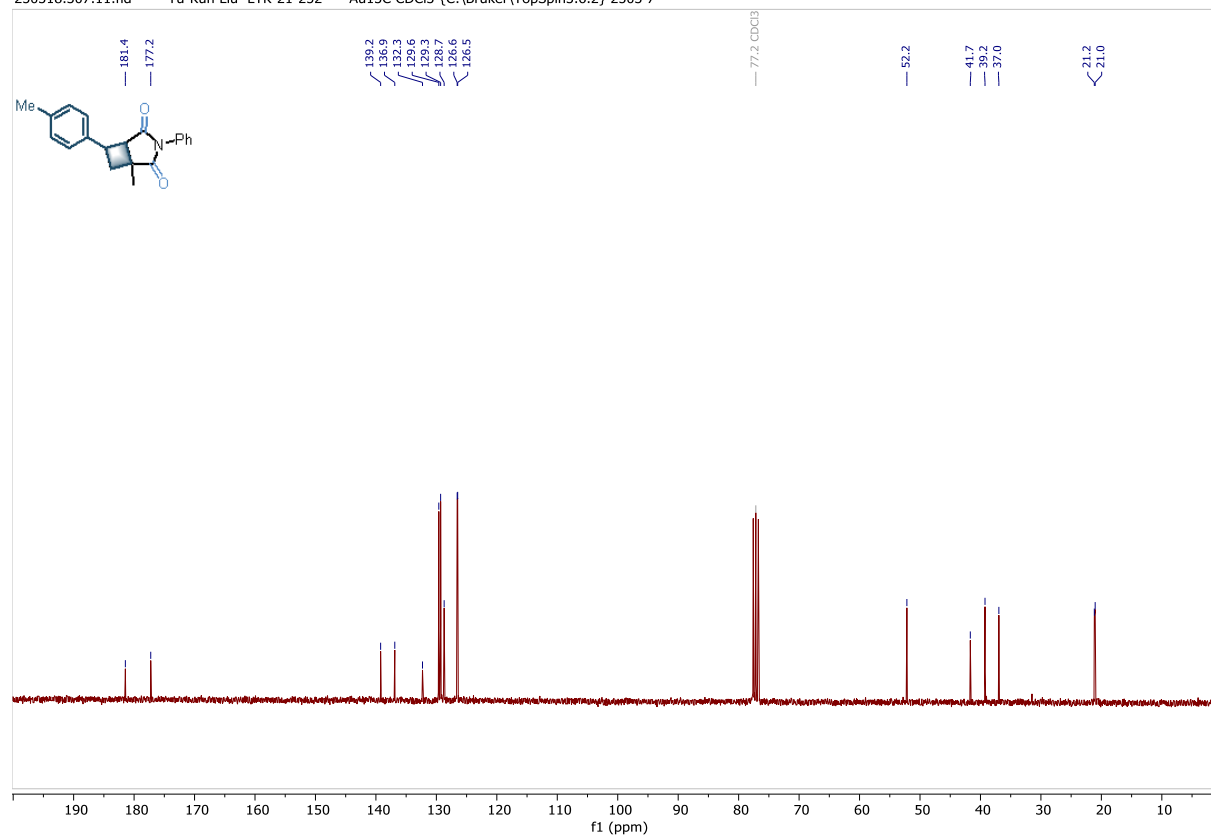
Supplementary Fig. 65. ^1H NMR spectrum of **3aa** (300 MHz, CDCl_3)

250318.307.10.fid — Yu-Kun Liu LYK-21-252 — Au1H CDCl_3 {C:\Bruker\TopSpin3.6.2} 2503 7



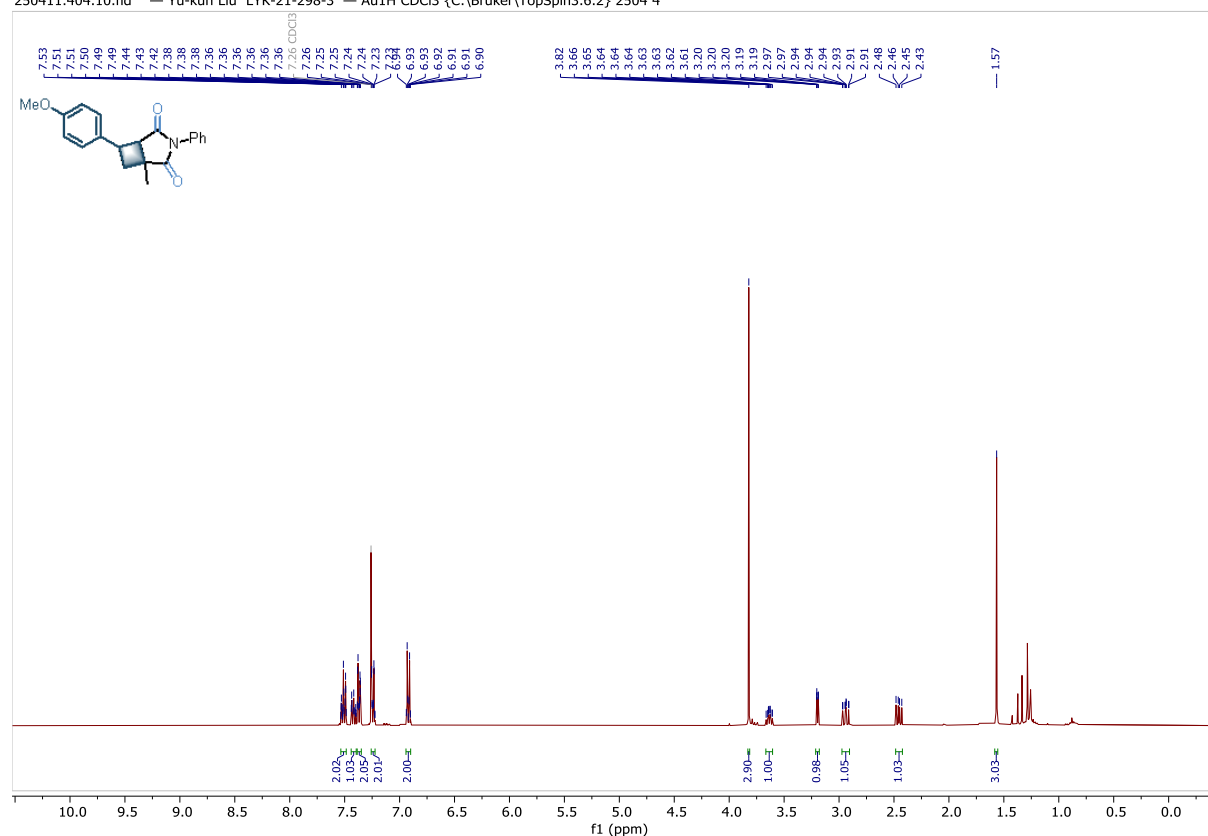
Supplementary Fig. 66. ^{13}C NMR spectrum of **3aa** (75 MHz, CDCl_3)

250318.307.11.fid — Yu-Kun Liu LYK-21-252 — Au13C CDCl_3 {C:\Bruker\TopSpin3.6.2} 2503 7



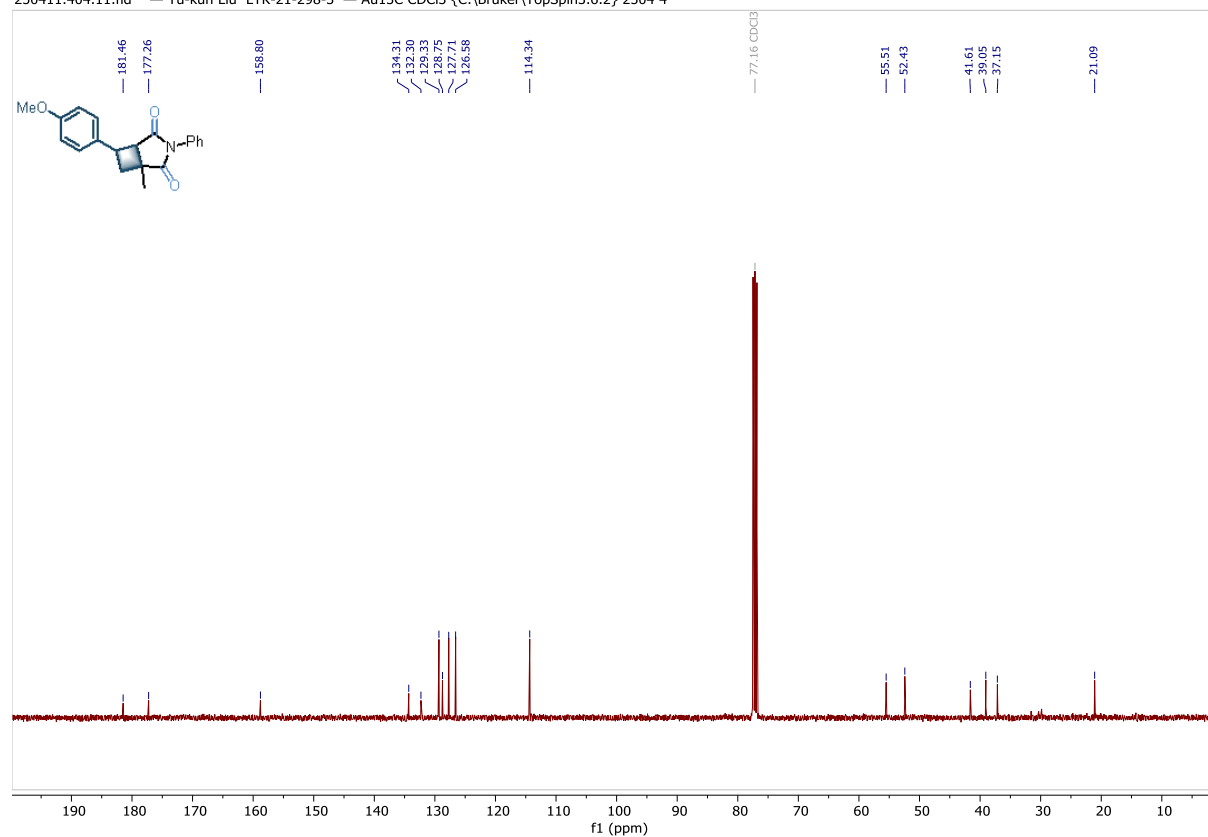
Supplementary Fig. 67. ^1H NMR spectrum of **3ab** (400 MHz, CDCl_3)

250411.404.10.fid — Yu-kun Liu LYK-21-298-3 — Au1H CDCl_3 {C:\Bruker\TopSpin3.6.2} 2504 4

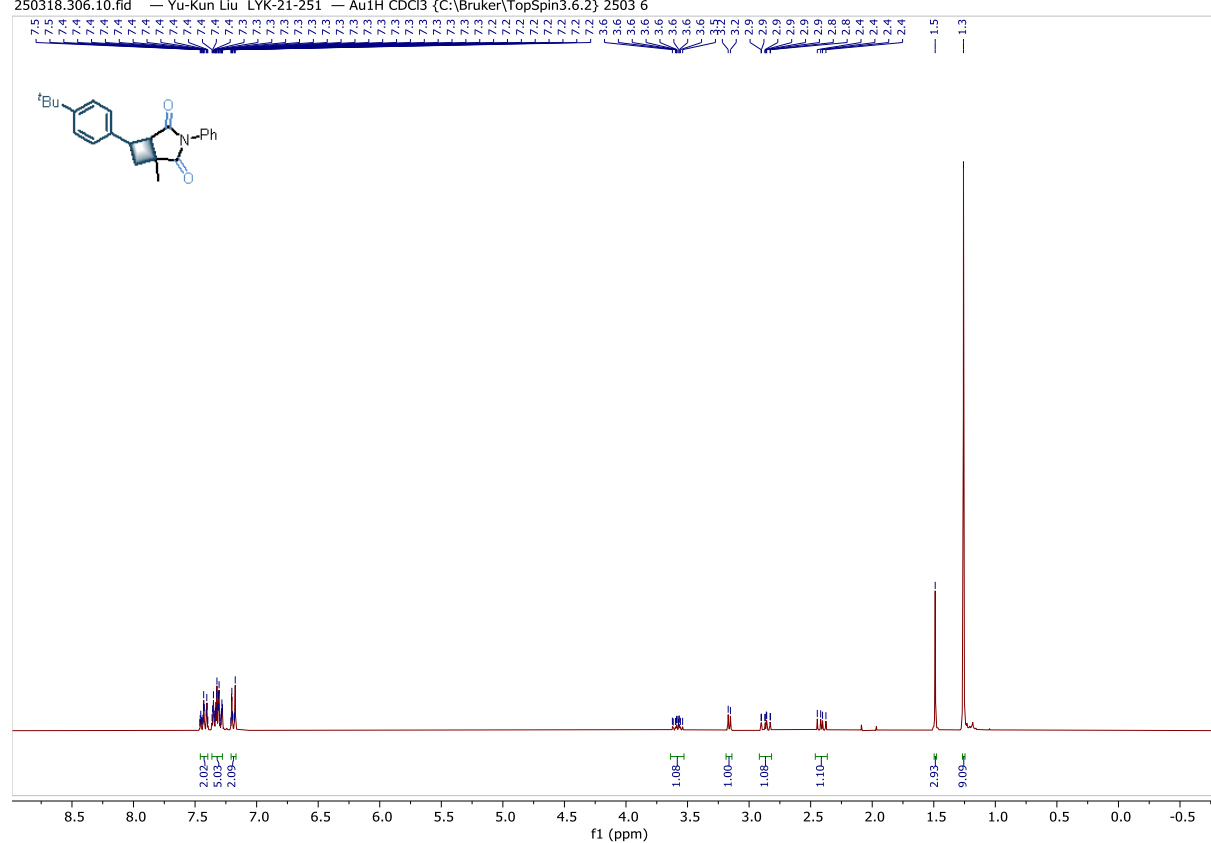


Supplementary Fig. 68. ^{13}C NMR spectrum of **3ab** (101 MHz, CDCl_3)

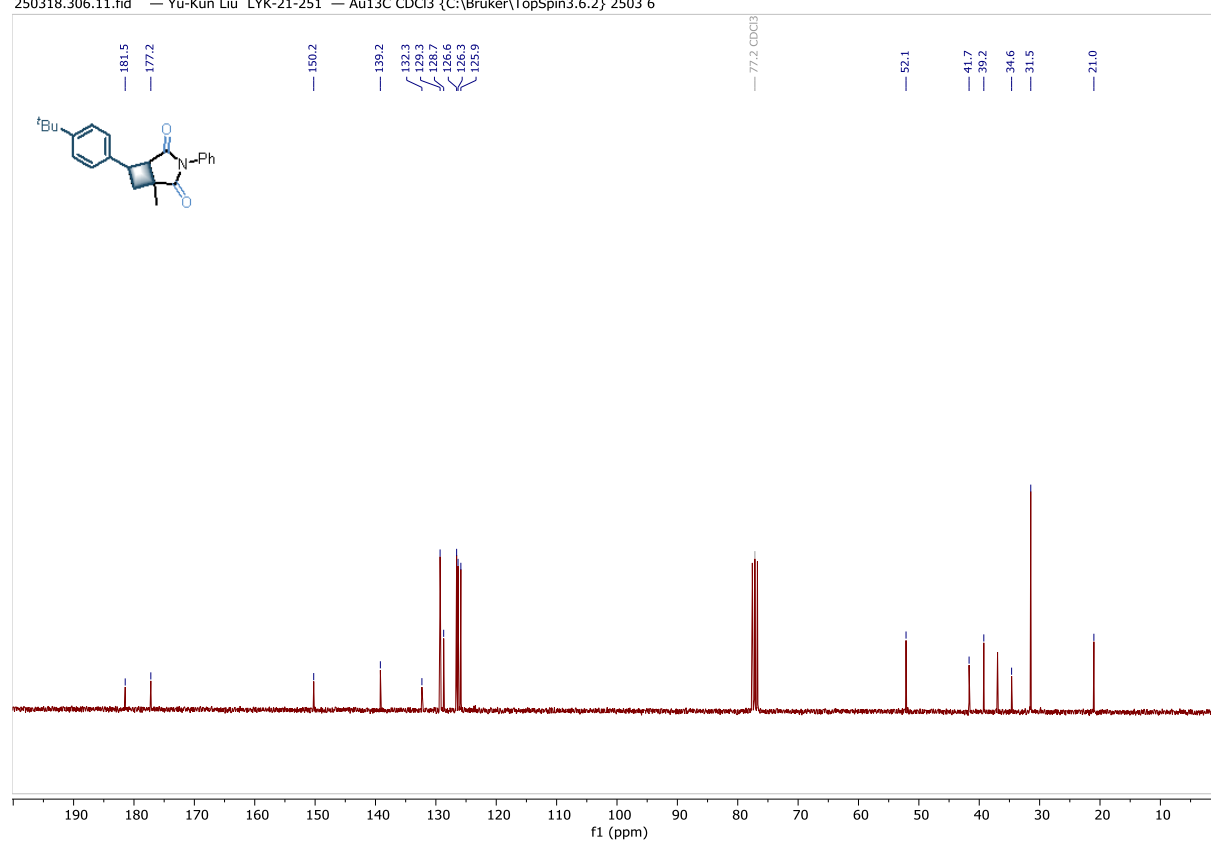
250411.404.11.fid — Yu-kun Liu LYK-21-298-3 — Au13C CDCl_3 {C:\Bruker\TopSpin3.6.2} 2504 4



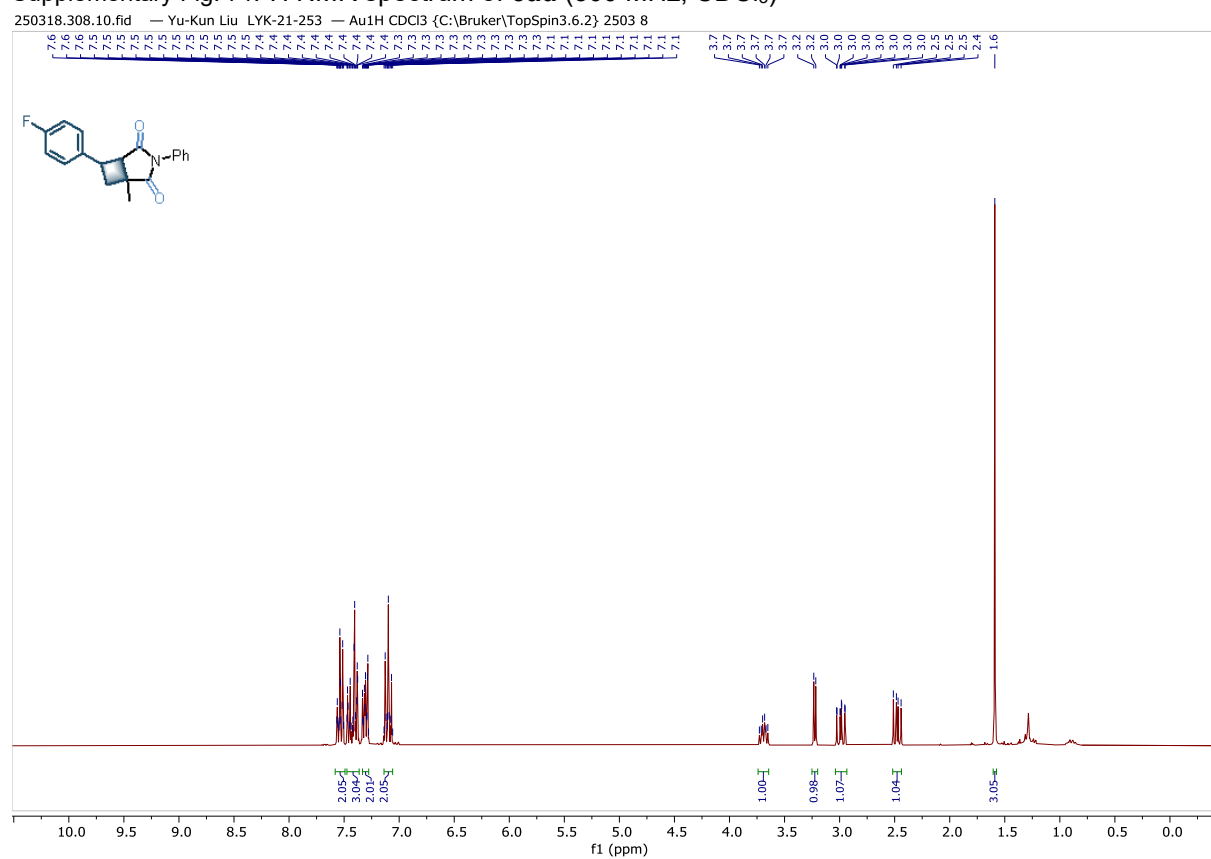
250318.306.10.fid — Yu-Kun Liu LYK-21-251 — Au1H CDCl3 {C:\Bruker\TopSpin3.6.2} 2503 6



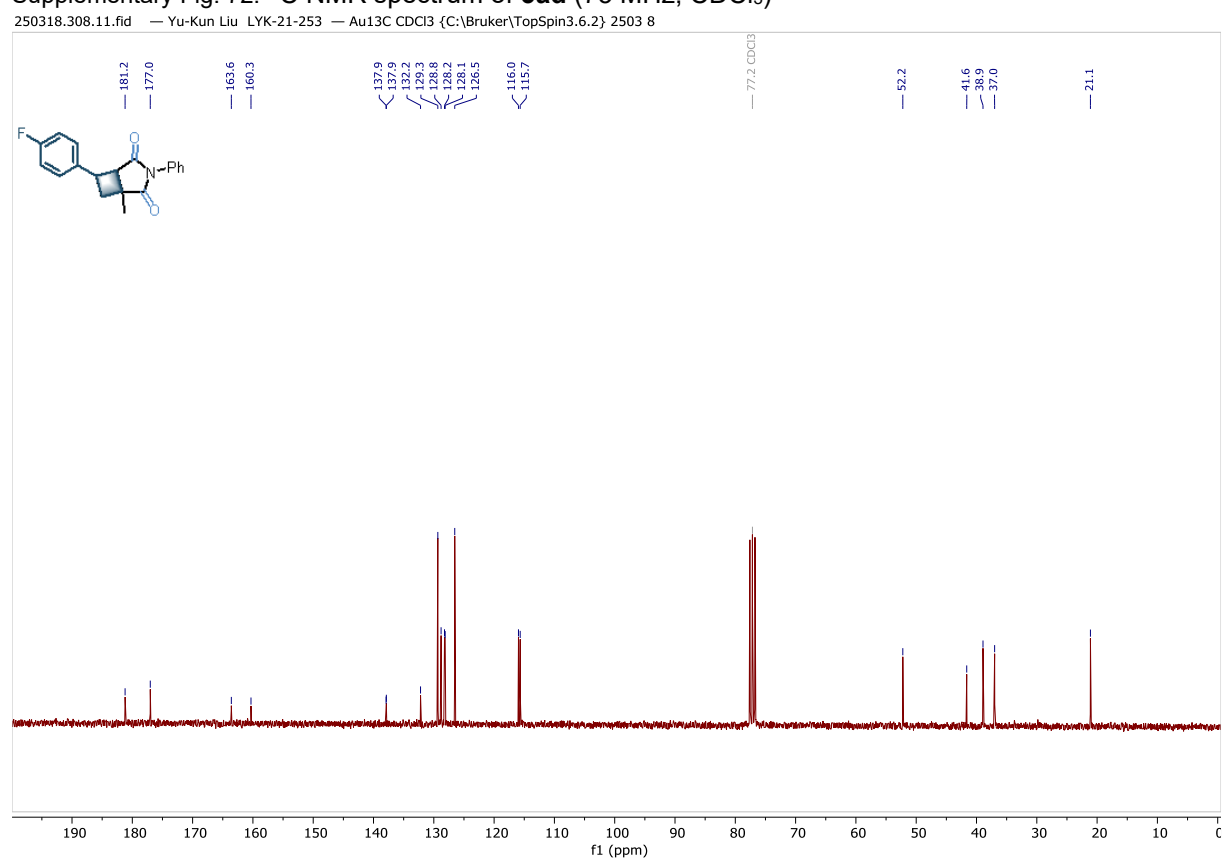
250318.306.11.fid — Yu-Kun Liu LYK-21-251 — Au13C CDCl3 {C:\Bruker\TopSpin3.6.2} 2503 6



Supplementary Fig. 71. ^1H NMR spectrum of **3ad** (300 MHz, CDCl_3)

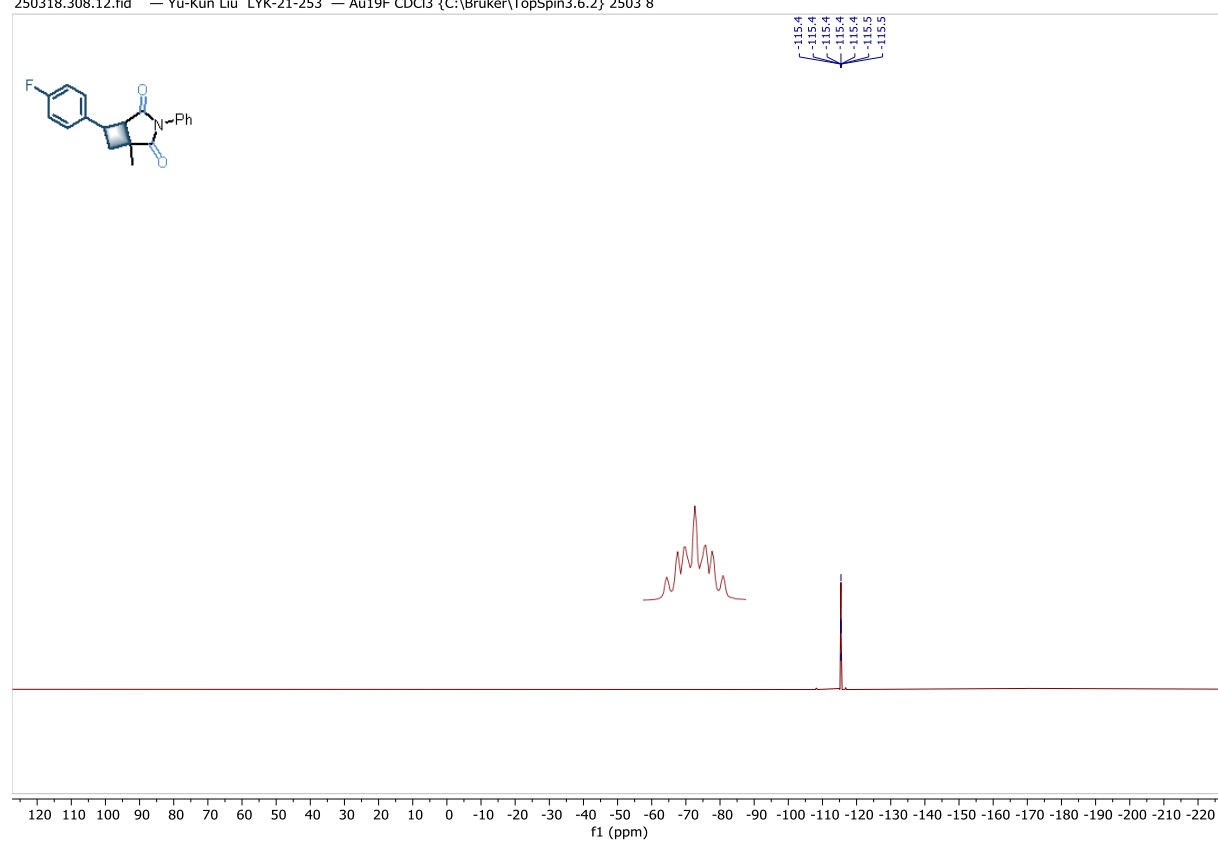


Supplementary Fig. 72. ^{13}C NMR spectrum of **3ad** (75 MHz, CDCl_3)

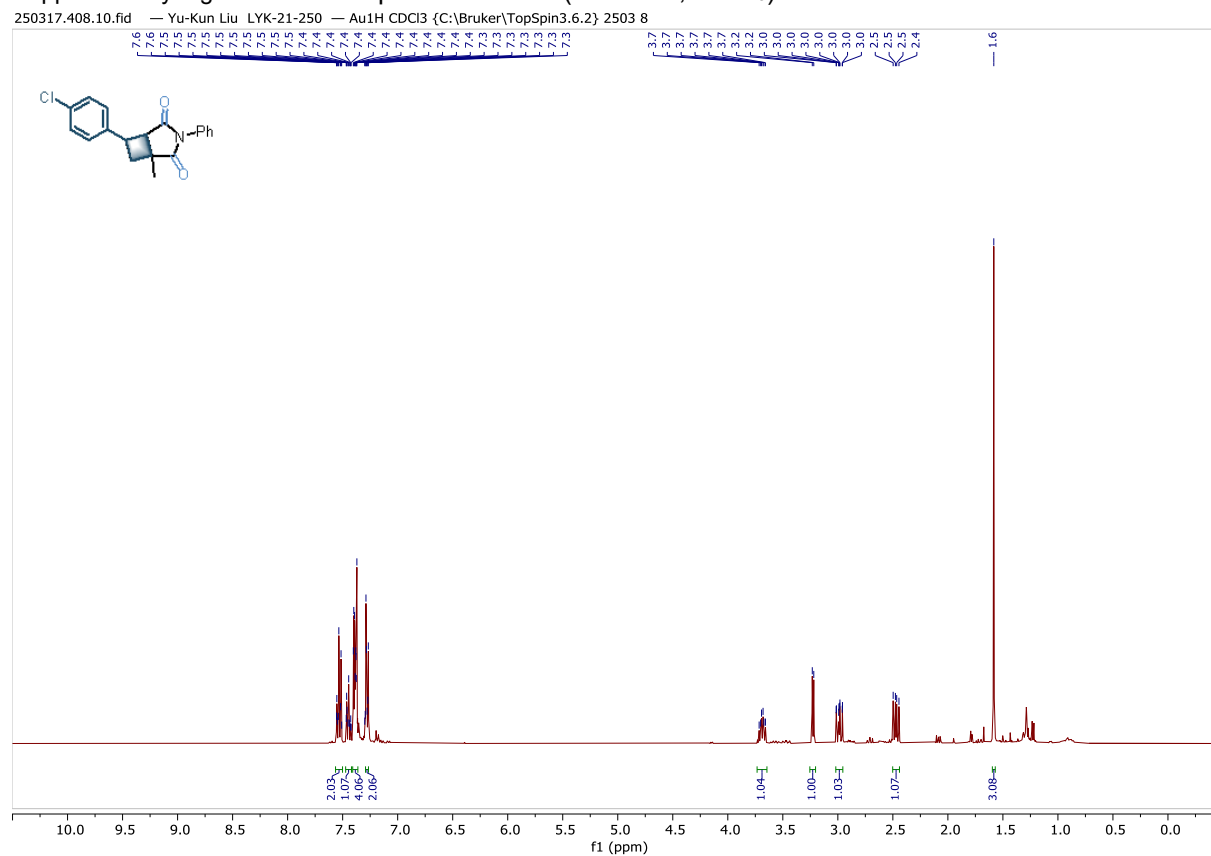


Supplementary Fig. 73. ^{19}F NMR spectrum of **3w** (282 MHz, CDCl_3)

250318.308.12.fid — Yu-Kun Liu LYK-21-253 — Au19F CDCl_3 {C:\Bruker\TopSpin3.6.2} 2503 8

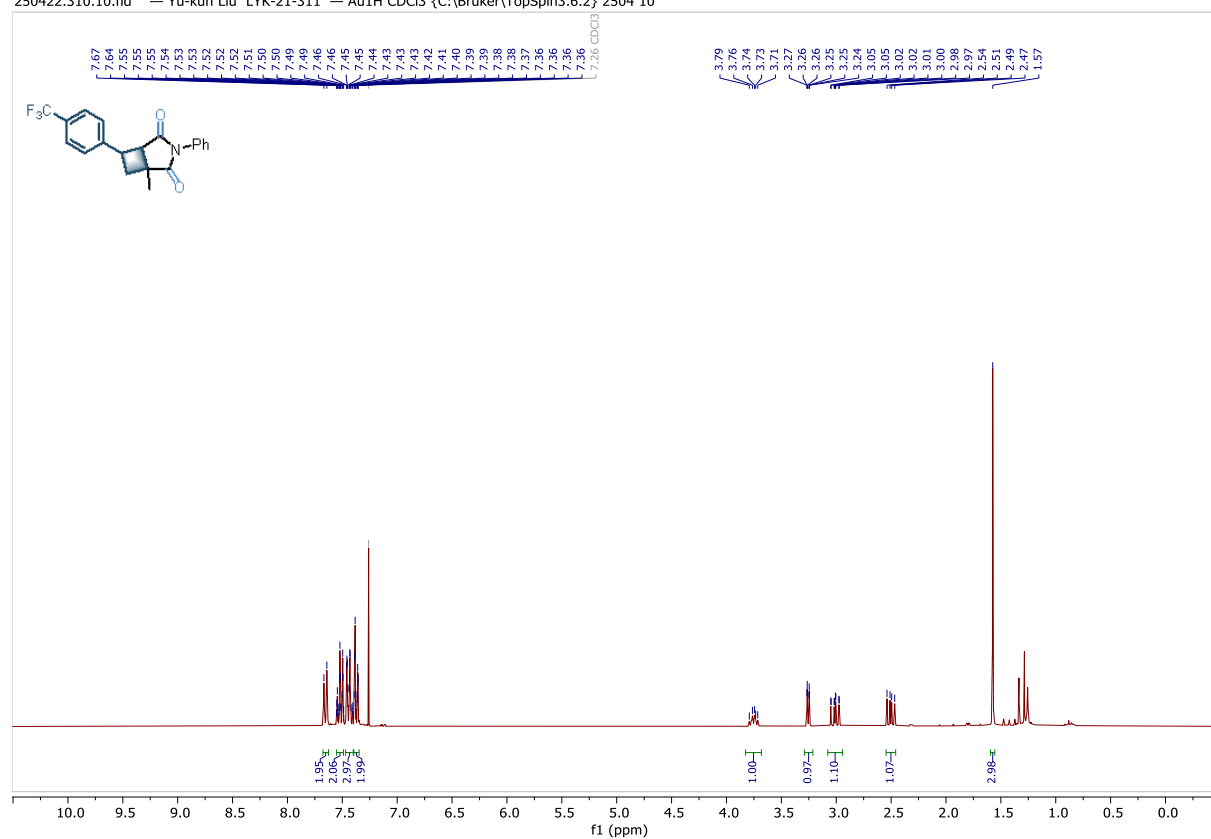


Supplementary Fig. 74. ^1H NMR spectrum of **3ae** (400 MHz, CDCl_3)



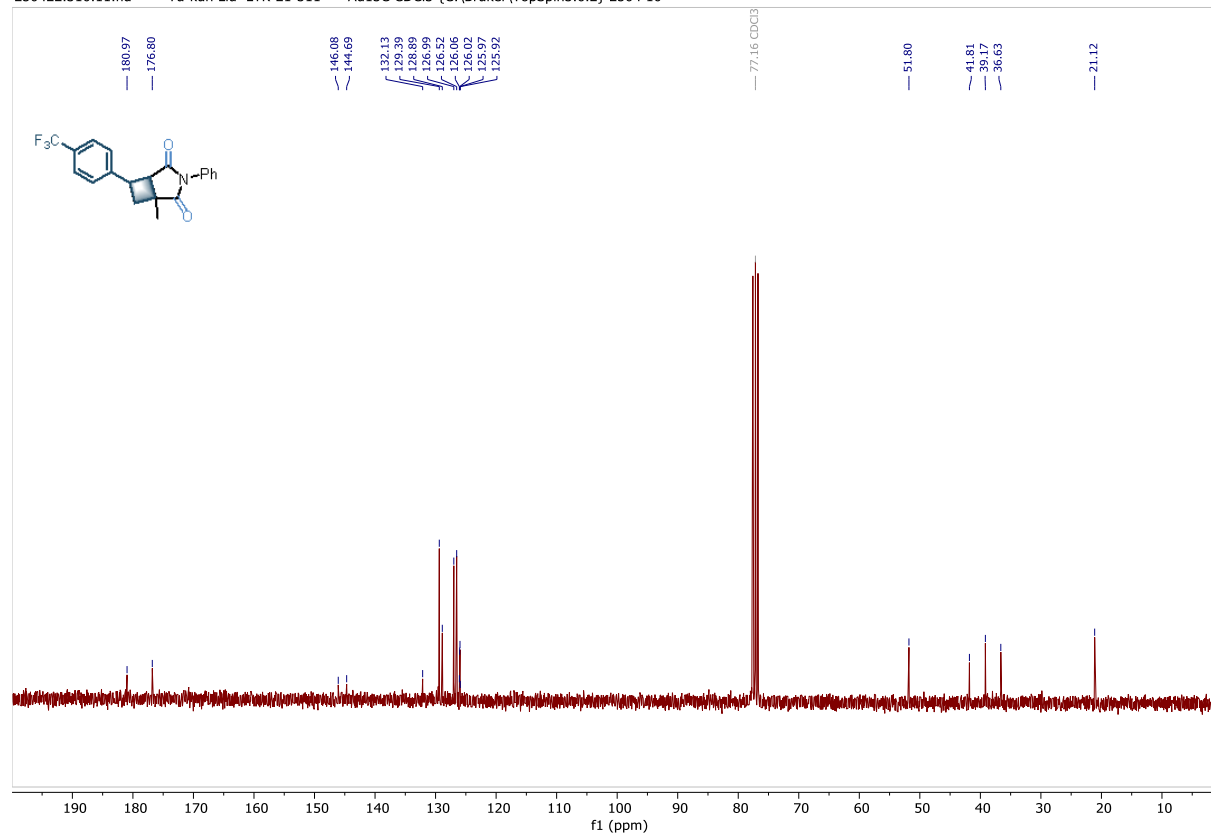
Supplementary Fig. 76. ^1H NMR spectrum of **3af** (300 MHz, CDCl_3)

250422.310.10.fid — Yu-kun Liu LYK-21-311 — Au1H CDCl_3 {C:\Bruker\TopSpin3.6.2} 2504 10



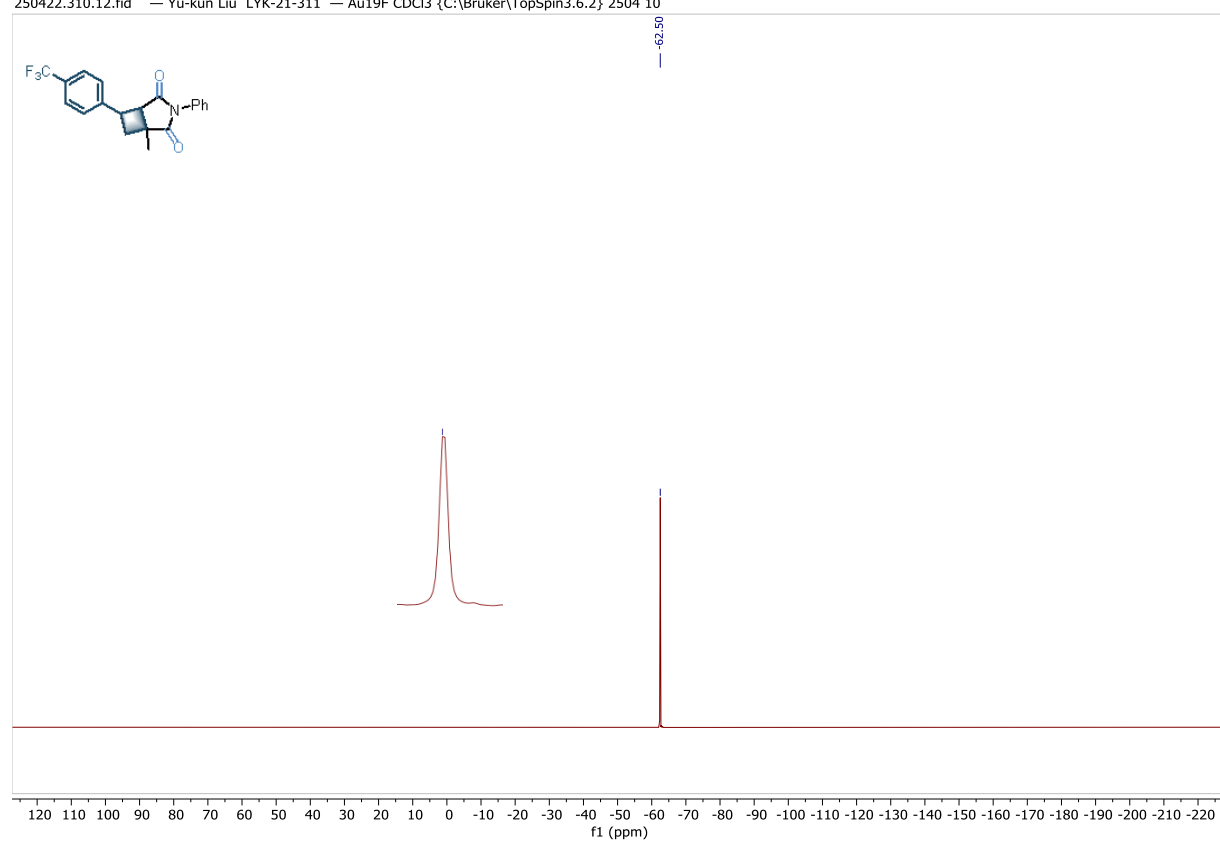
Supplementary Fig. 77. ^{13}C NMR spectrum of **3af** (75 MHz, CDCl_3)

250422.310.11.fid — Yu-kun Liu LYK-21-311 — Au13C CDCl_3 {C:\Bruker\TopSpin3.6.2} 2504 10



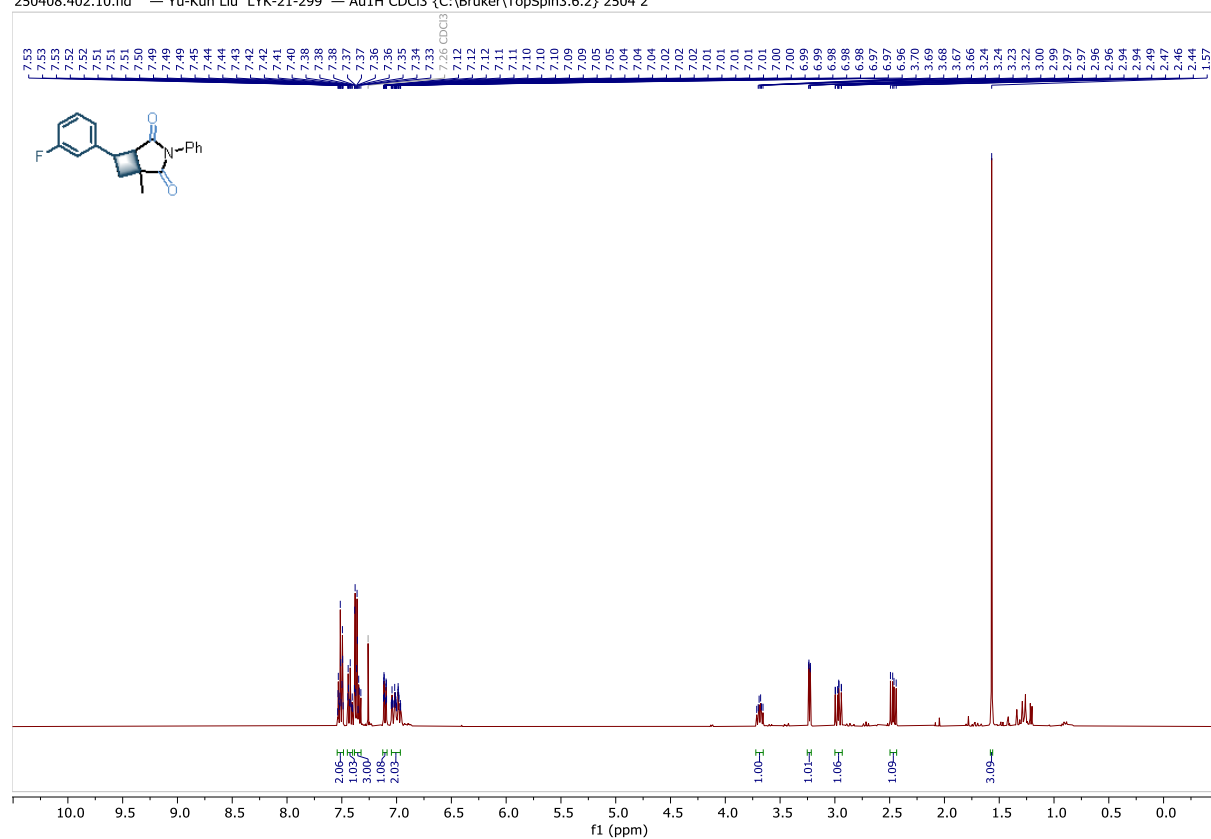
Supplementary Fig. 78. ^{19}F NMR spectrum of **3af** (282 MHz, CDCl_3)

250422.310.12.fid — Yu-kun Liu LYK-21-311 — Au19F CDCl3 {C:\Bruker\TopSpin3.6.2} 2504 10



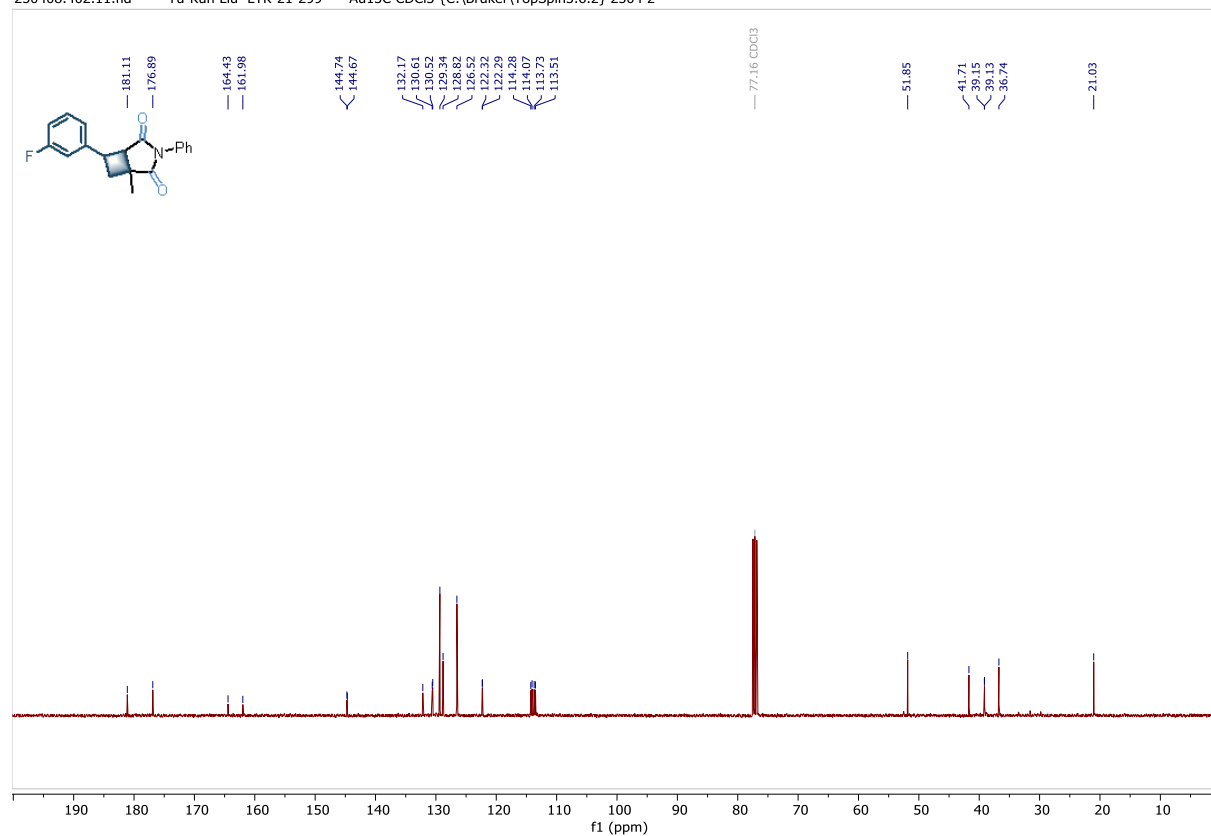
Supplementary Fig. 79. ^1H NMR spectrum of **3ag** (400 MHz, CDCl_3)

250408.402.10.fid — Yu-Kun Liu LYK-21-299 — Au1H CDCl_3 {C:\Bruker\TopSpin3.6.2} 2504 2



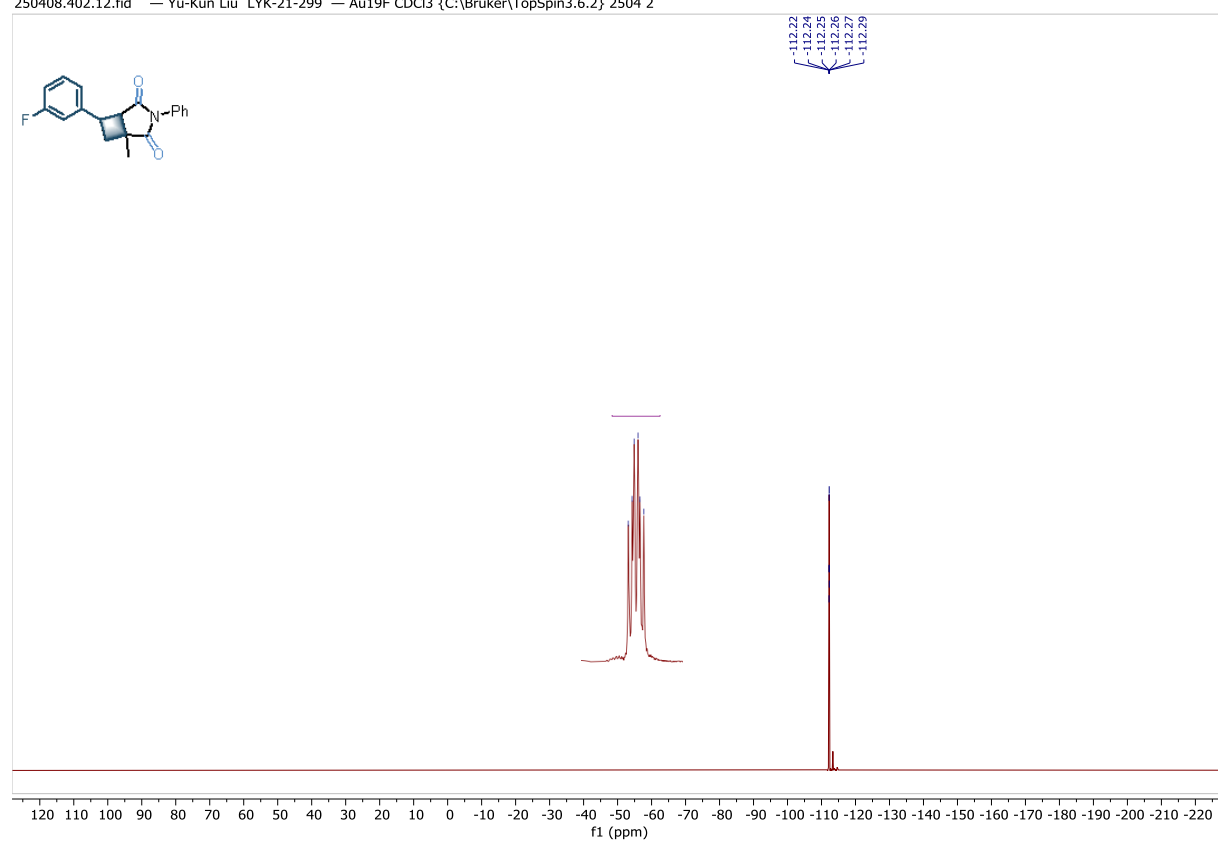
Supplementary Fig. 80. ^{13}C NMR spectrum of **3ag** (101 MHz, CDCl_3)

250408.402.11.fid — Yu-Kun Liu LYK-21-299 — Au13C CDCl_3 {C:\Bruker\TopSpin3.6.2} 2504 2



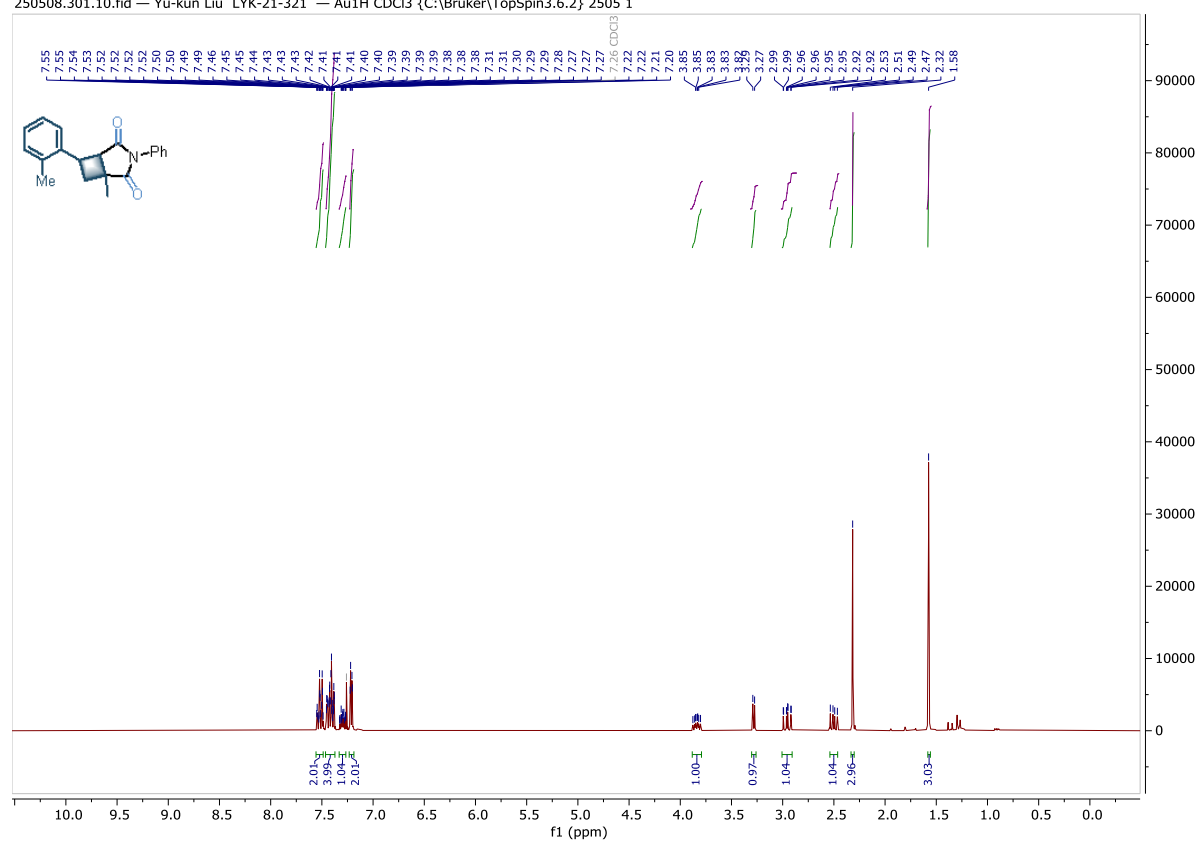
Supplementary Fig. 81. ^{19}F NMR spectrum of **3ag** (376 MHz, CDCl_3)

250408.402.12.fid — Yu-Kun Liu LYK-21-299 — Au19F CDCl3 {C:\Bruker\TopSpin3.6.2} 2504 2



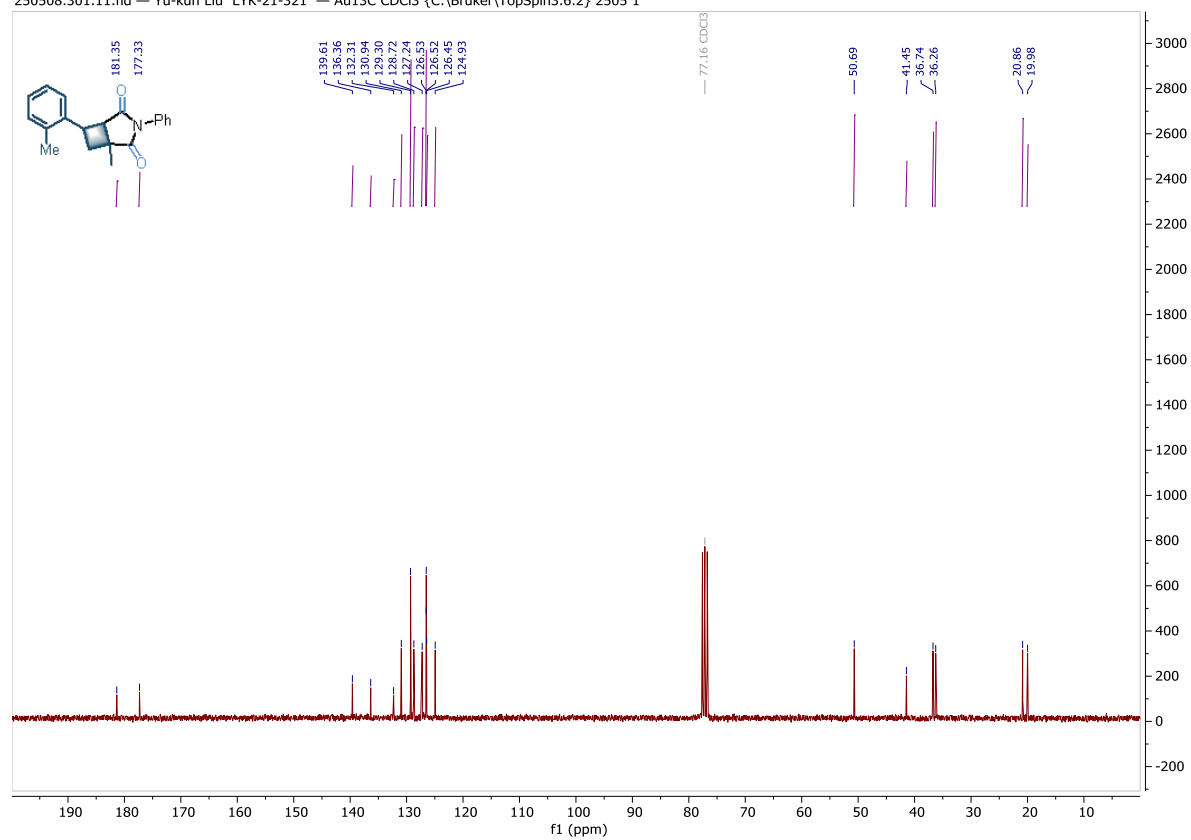
Supplementary Fig. 82. ^1H NMR spectrum of **3ah** (400 MHz, CDCl_3)

250508.301.10.fid — Yu-kun Liu LYK-21-321 — Au1H CDCl_3 {C:\Bruker\TopSpin3.6.2} 2505 1

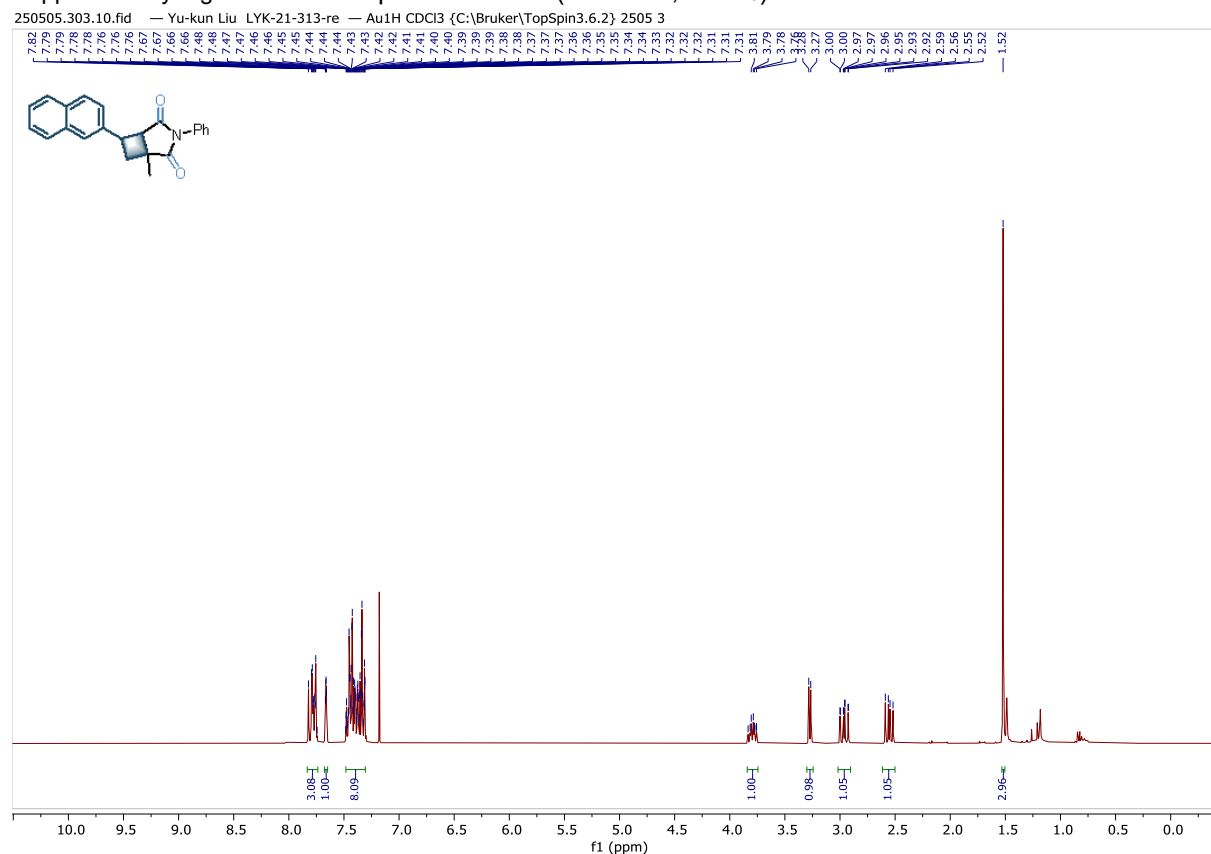


Supplementary Fig. 83. ^{13}C NMR spectrum of **3ah** (101 MHz, CDCl_3)

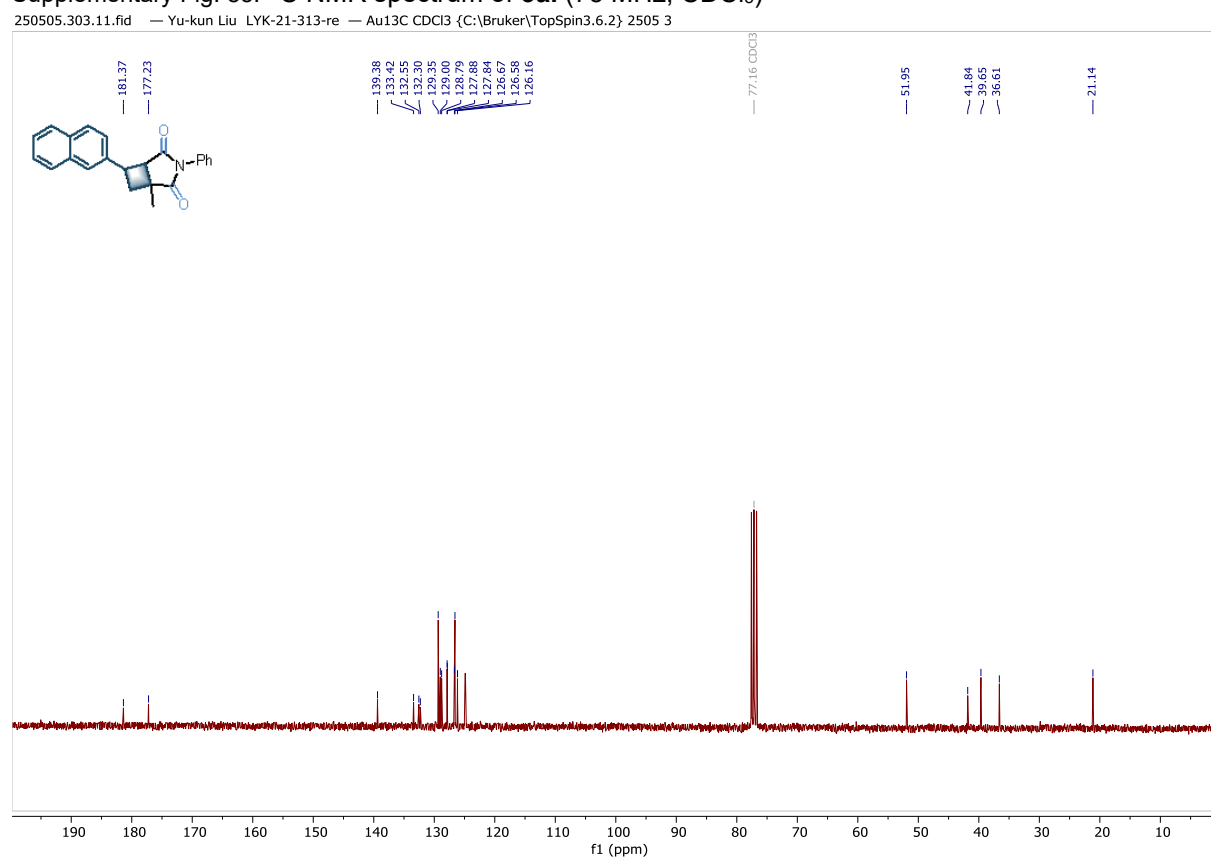
250508.301.11.fid — Yu-kun Liu LYK-21-321 — Au13C CDCl_3 {C:\Bruker\TopSpin3.6.2} 2505 1



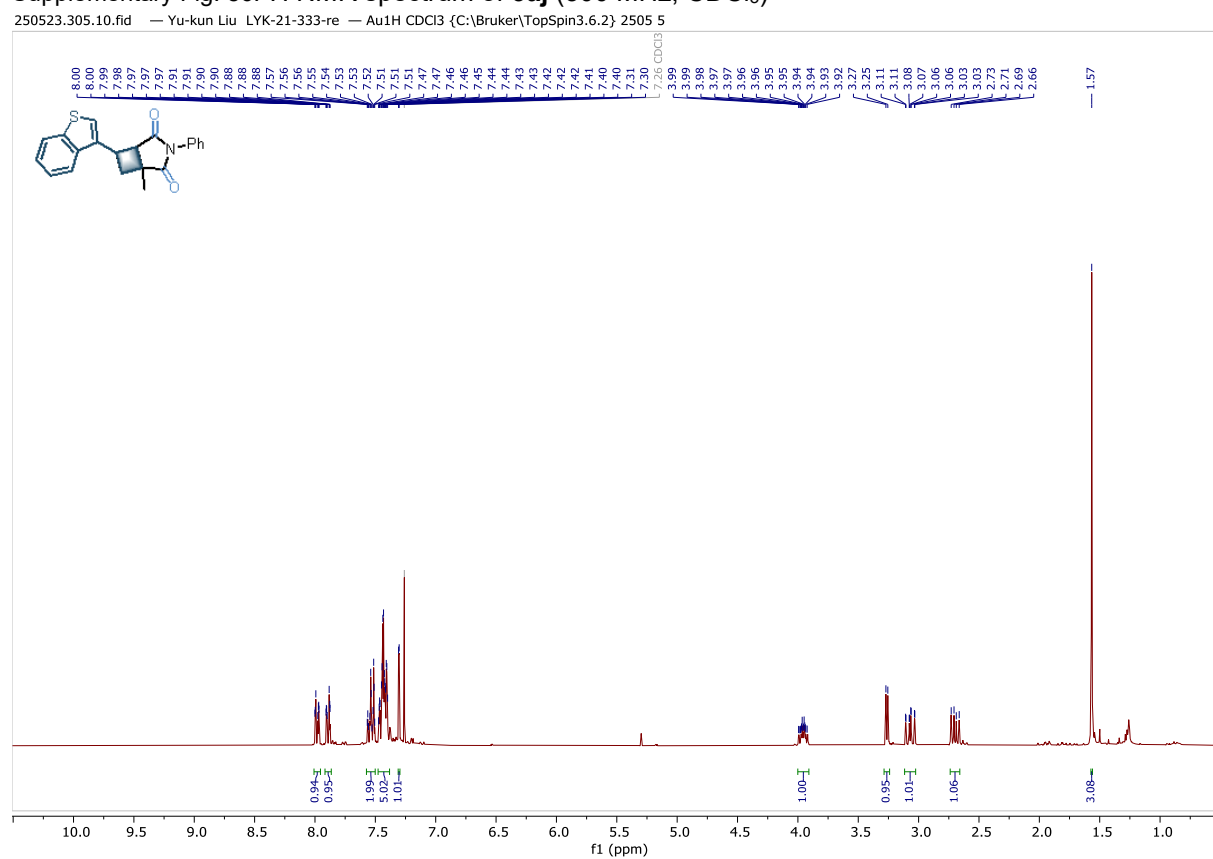
Supplementary Fig. 84. ^1H NMR spectrum of **3ai** (300 MHz, CDCl_3)



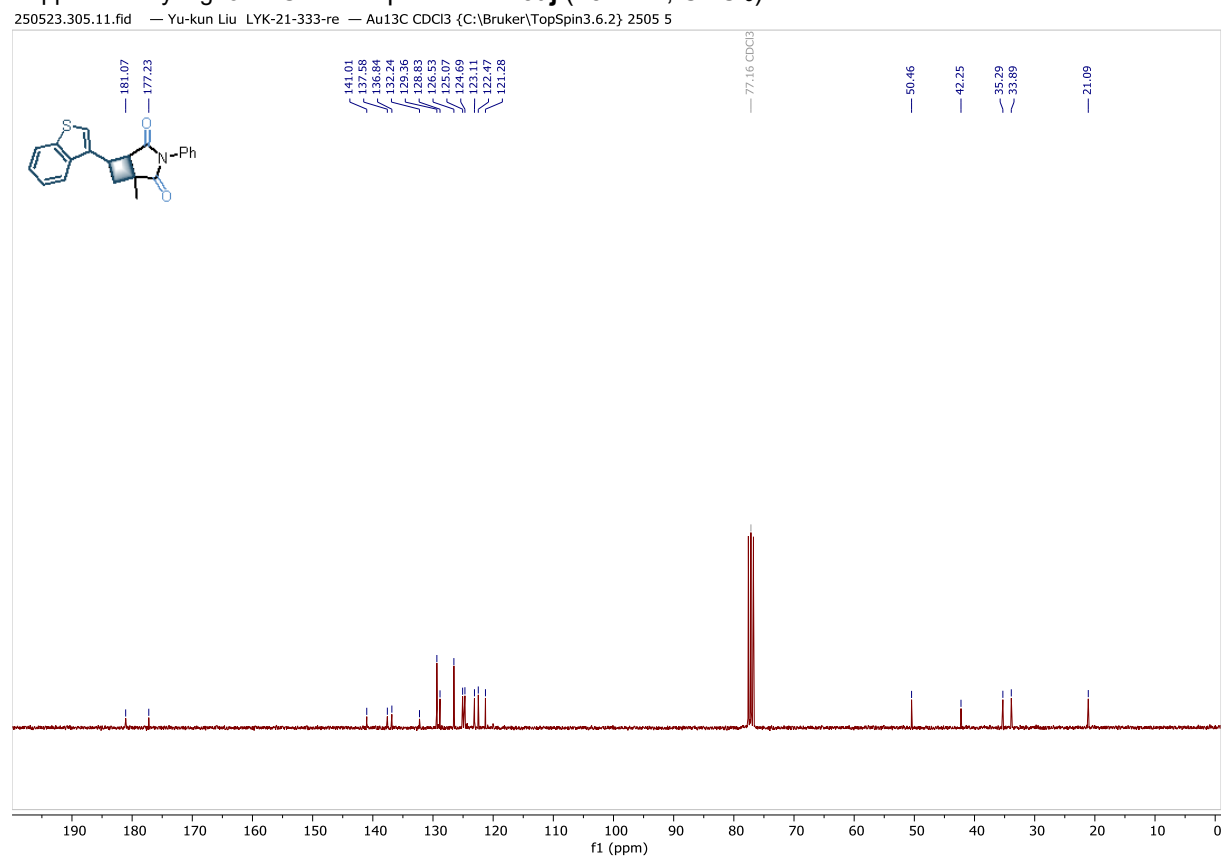
Supplementary Fig. 85. ^{13}C NMR spectrum of **3ai** (75 MHz, CDCl_3)



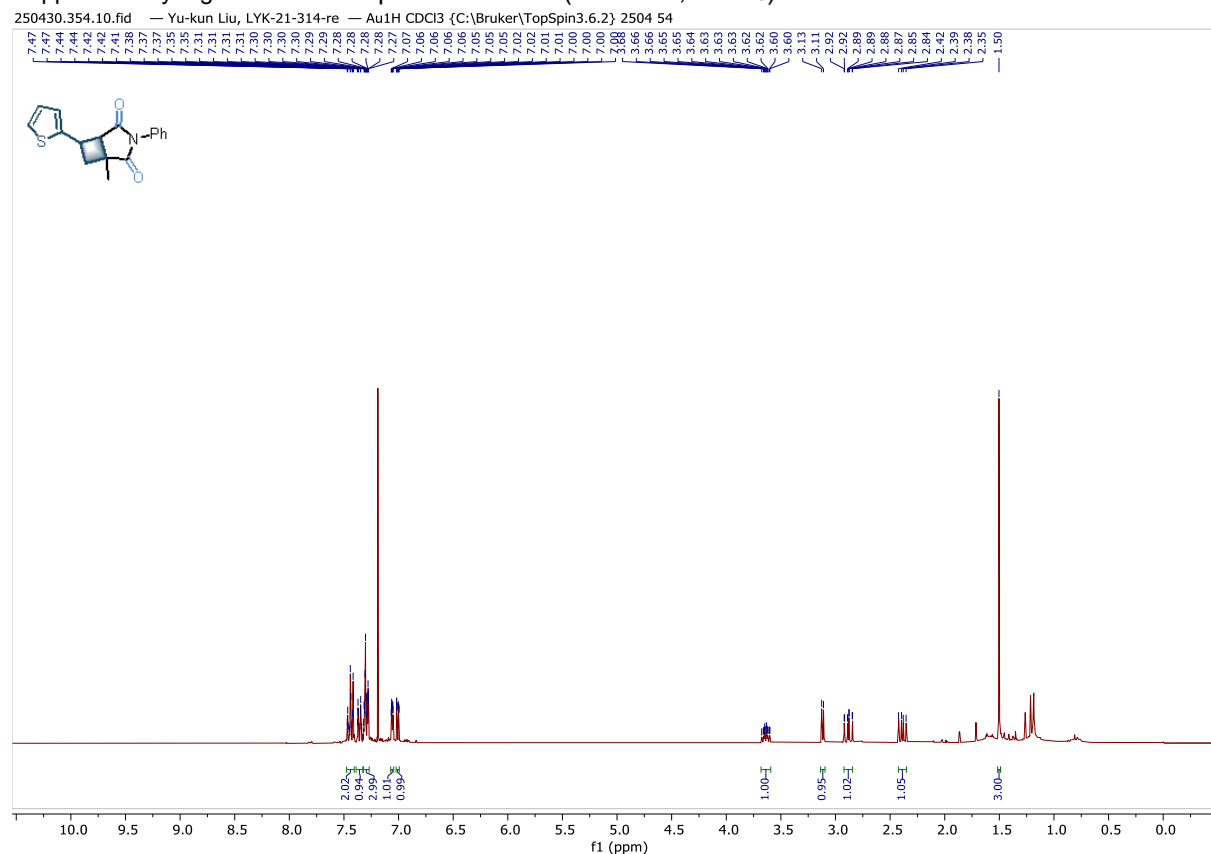
Supplementary Fig. 86. ^1H NMR spectrum of **3aj** (300 MHz, CDCl_3)



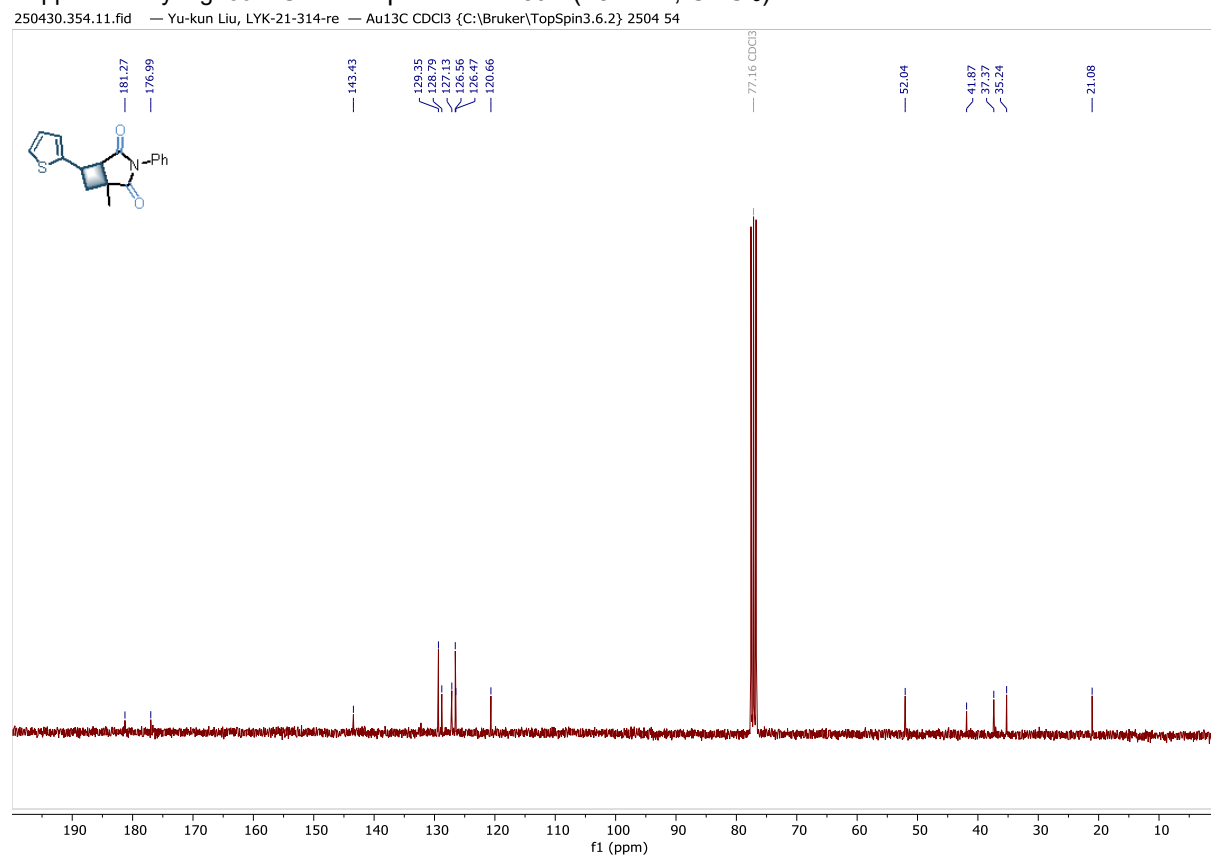
Supplementary Fig. 87. ^{13}C NMR spectrum of **3aj** (75 MHz, CDCl_3)



Supplementary Fig. 88. ^1H NMR spectrum of **3ak** (300 MHz, CDCl_3)

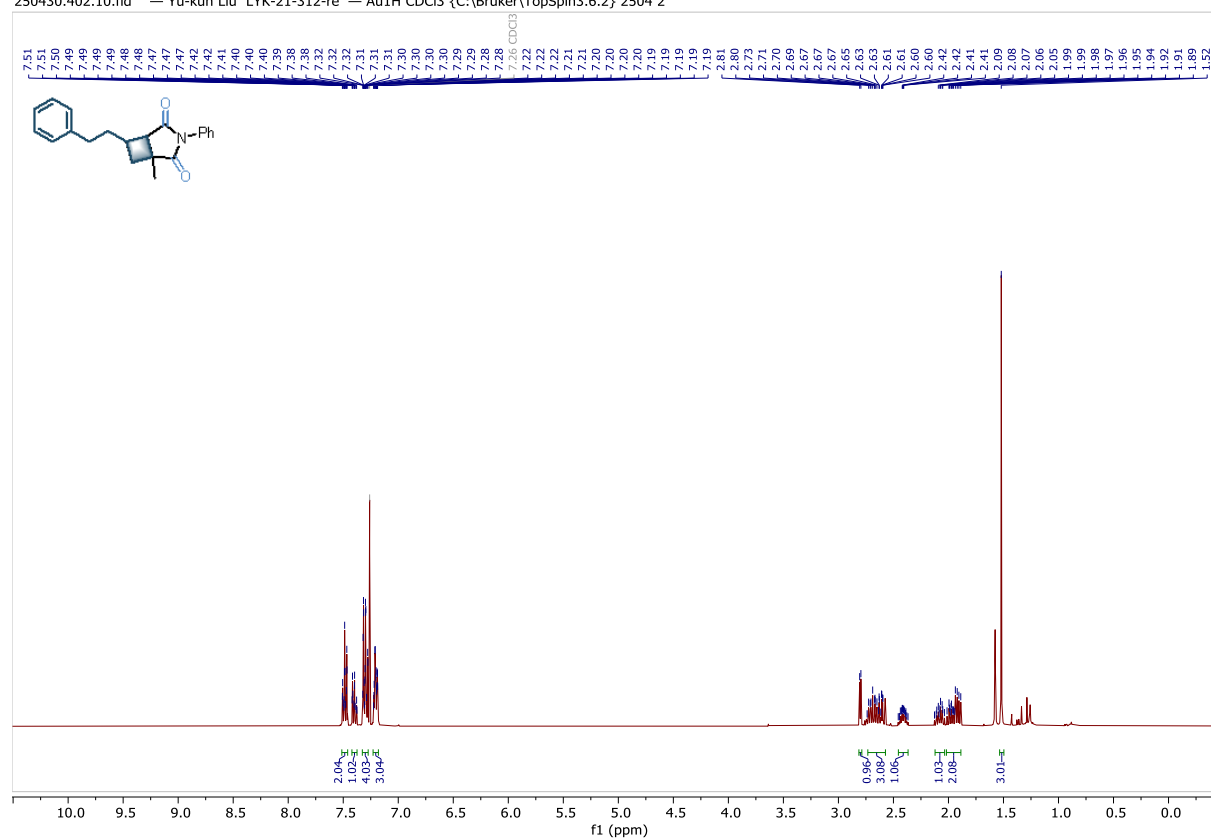


Supplementary Fig. 89. ^{13}C NMR spectrum of **3ak** (75 MHz, CDCl_3)



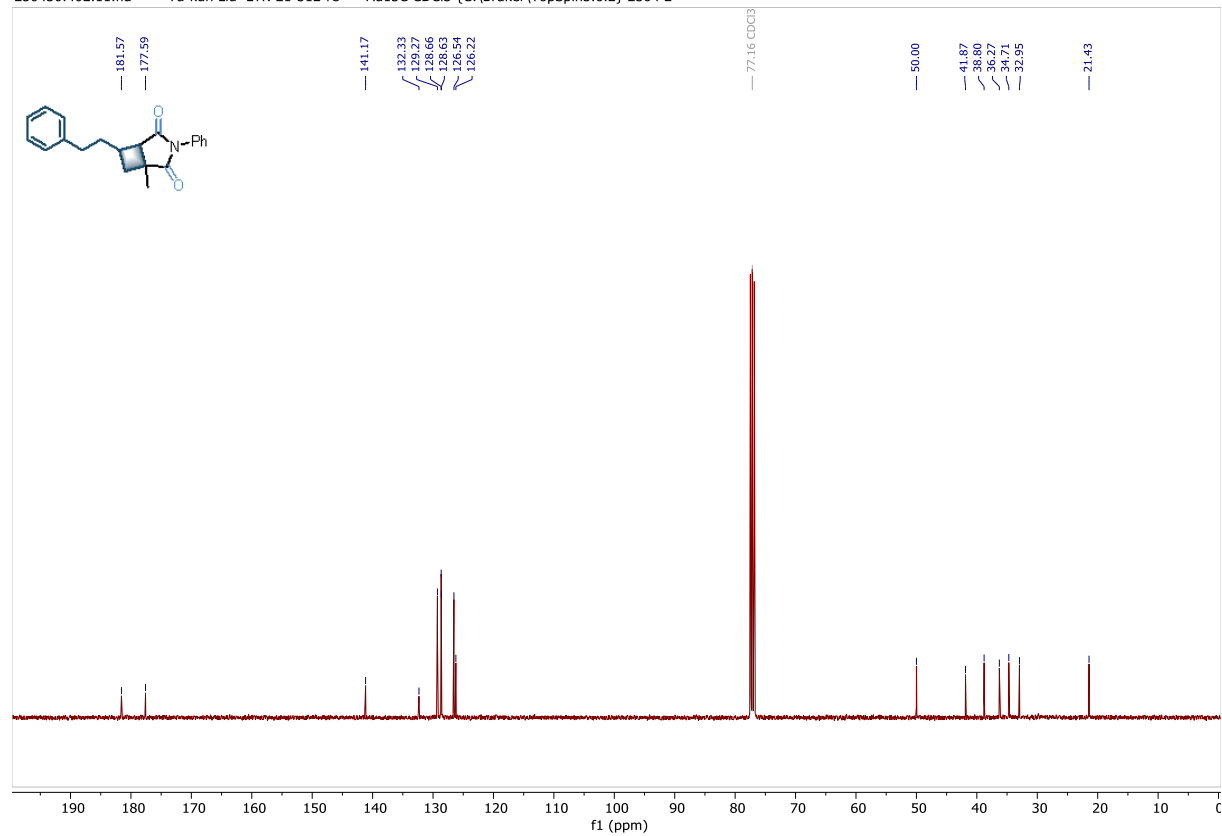
Supplementary Fig. 90. ^1H NMR spectrum of **3al** (400 MHz, CDCl_3)

250430.402.10.fid — Yu-kun Liu LYK-21-312-re — Au1H CDCl_3 {C:\Bruker\TopSpin3.6.2} 2504 2



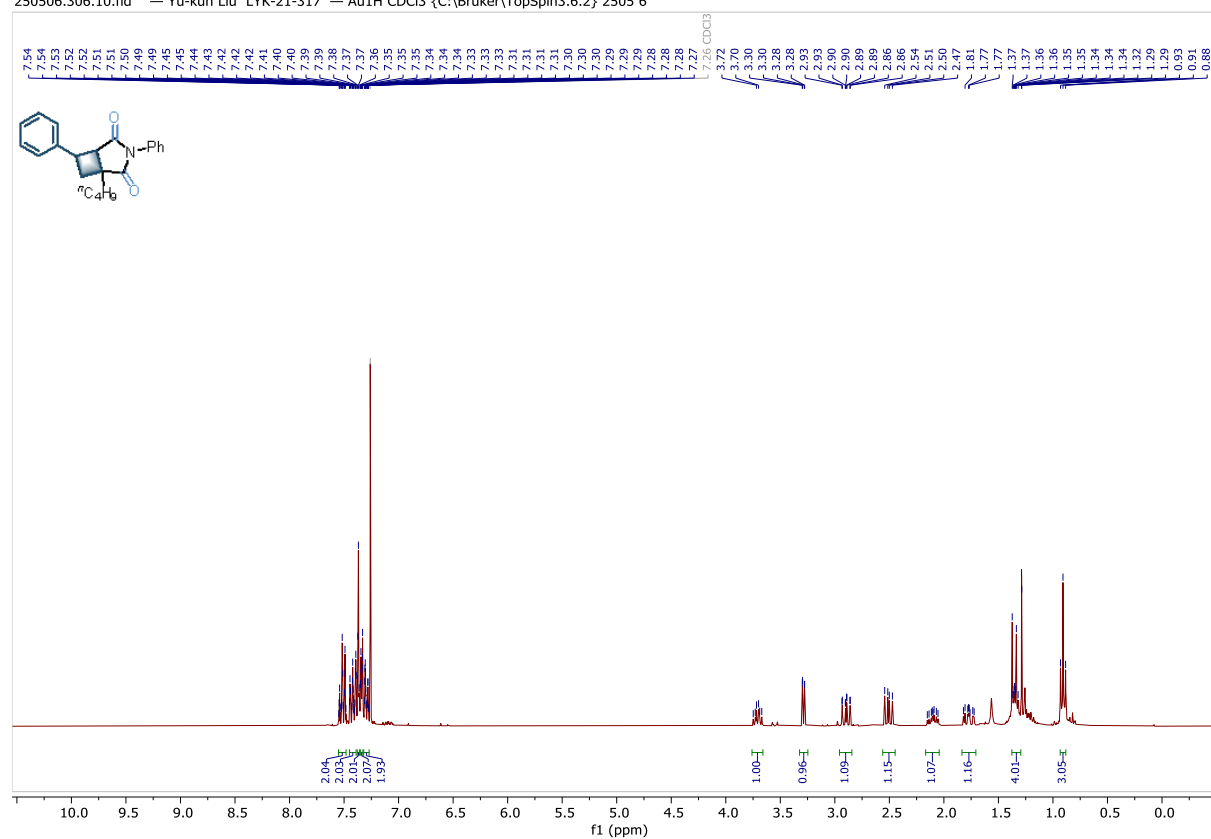
Supplementary Fig. 91. ^{13}C NMR spectrum of **3al** (101 MHz, CDCl_3)

250430.402.11.fid — Yu-kun Liu LYK-21-312-re — Au13C CDCl_3 {C:\Bruker\TopSpin3.6.2} 2504 2

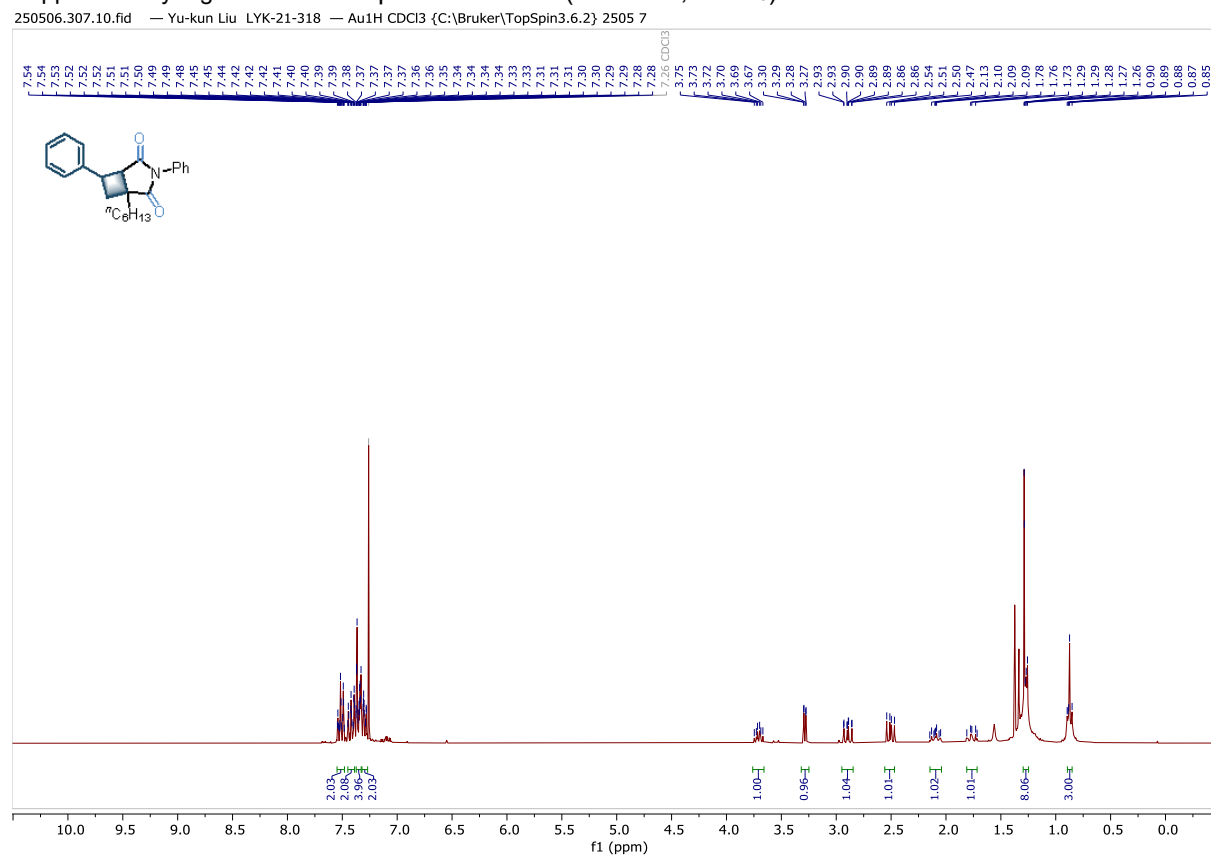


Supplementary Fig. 92. ^1H NMR spectrum of **3am** (300 MHz, CDCl_3)

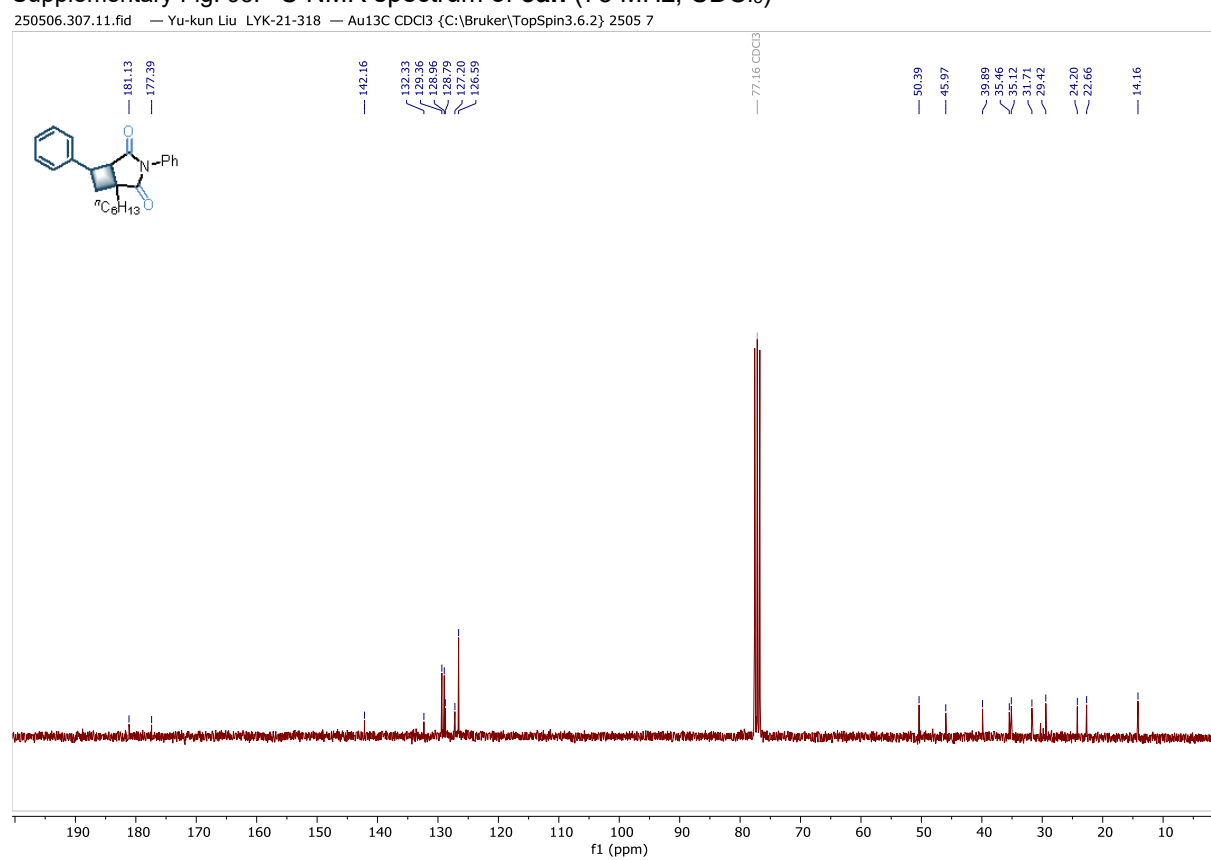
250506.306.10.fid — Yu-kun Liu LYK-21-317 — Au1H CDCl_3 {C:\Bruker\TopSpin3.6.2} 2505 6



Supplementary Fig. 94. ^1H NMR spectrum of **3an** (300 MHz, CDCl_3)

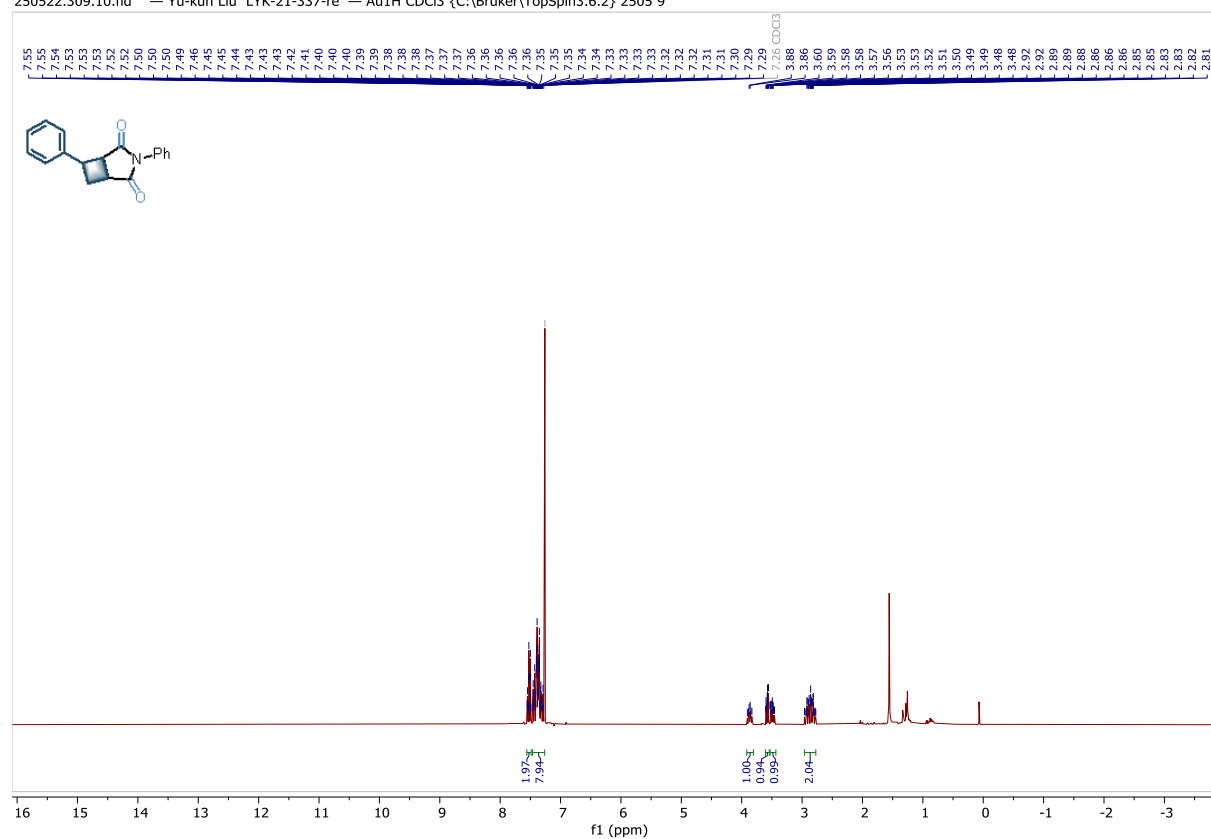


Supplementary Fig. 95. ^{13}C NMR spectrum of **3an** (75 MHz, CDCl_3)



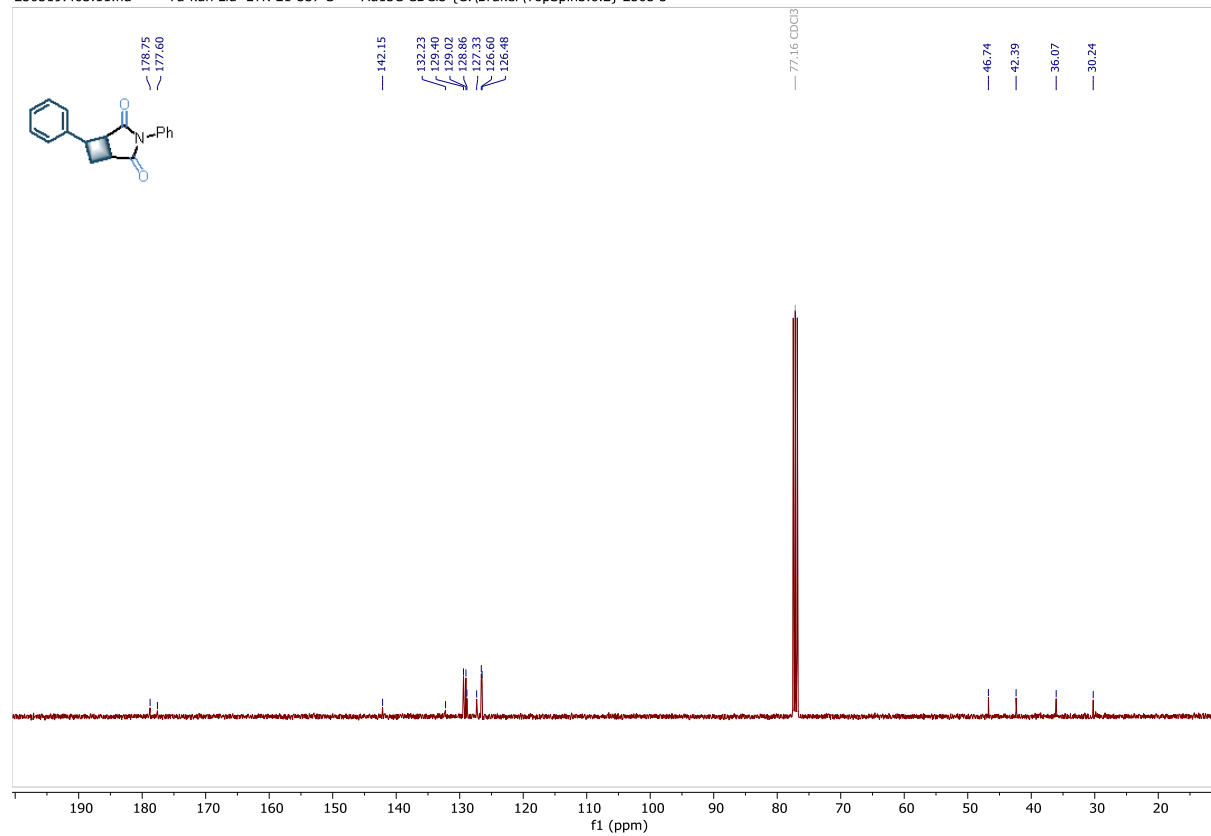
Supplementary Fig. 96. ^1H NMR spectrum of **3ao** (300 MHz, CDCl_3)

250522.309.10.fid — Yu-kun Liu LYK-21-337-re — Au1H CDCl_3 {C:\Bruker\TopSpin3.6.2} 2505 9

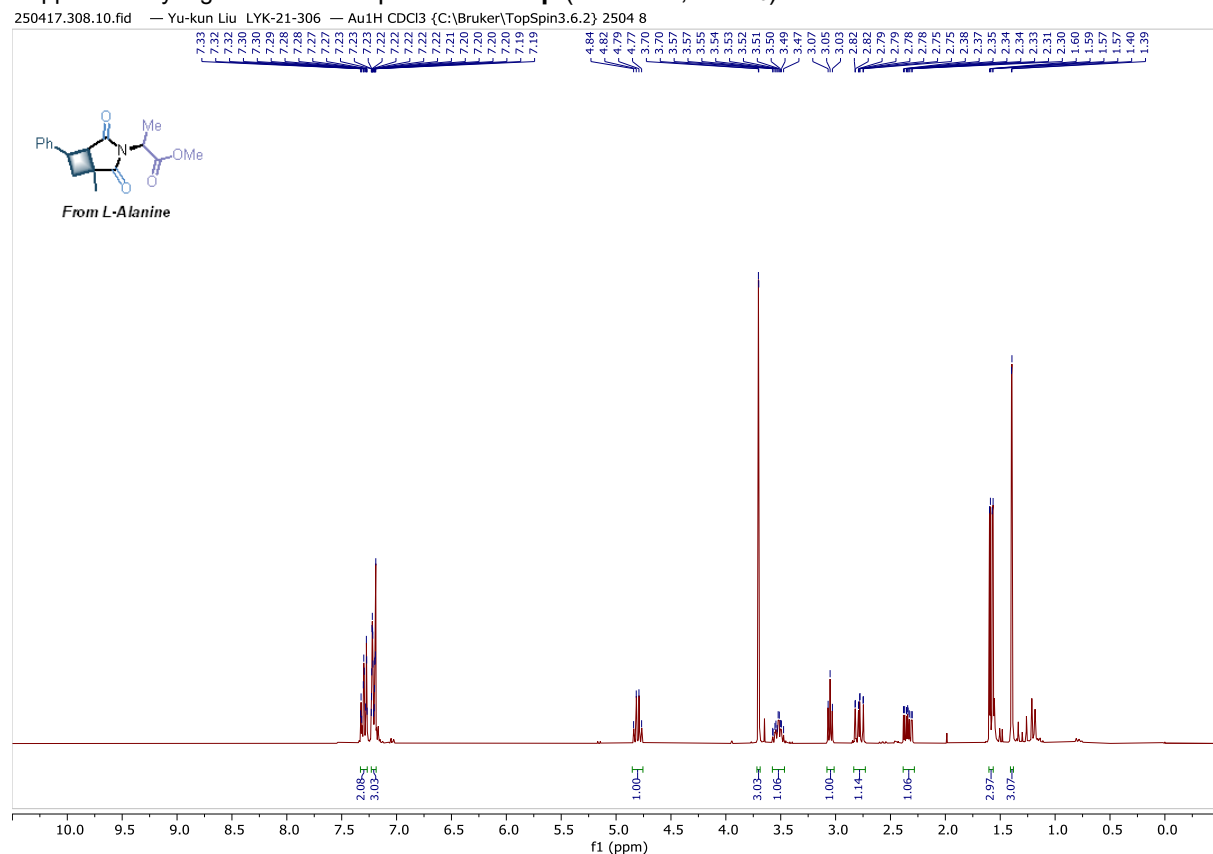


Supplementary Fig. 97. ^{13}C NMR spectrum of **3ao** (75 MHz, CDCl_3)

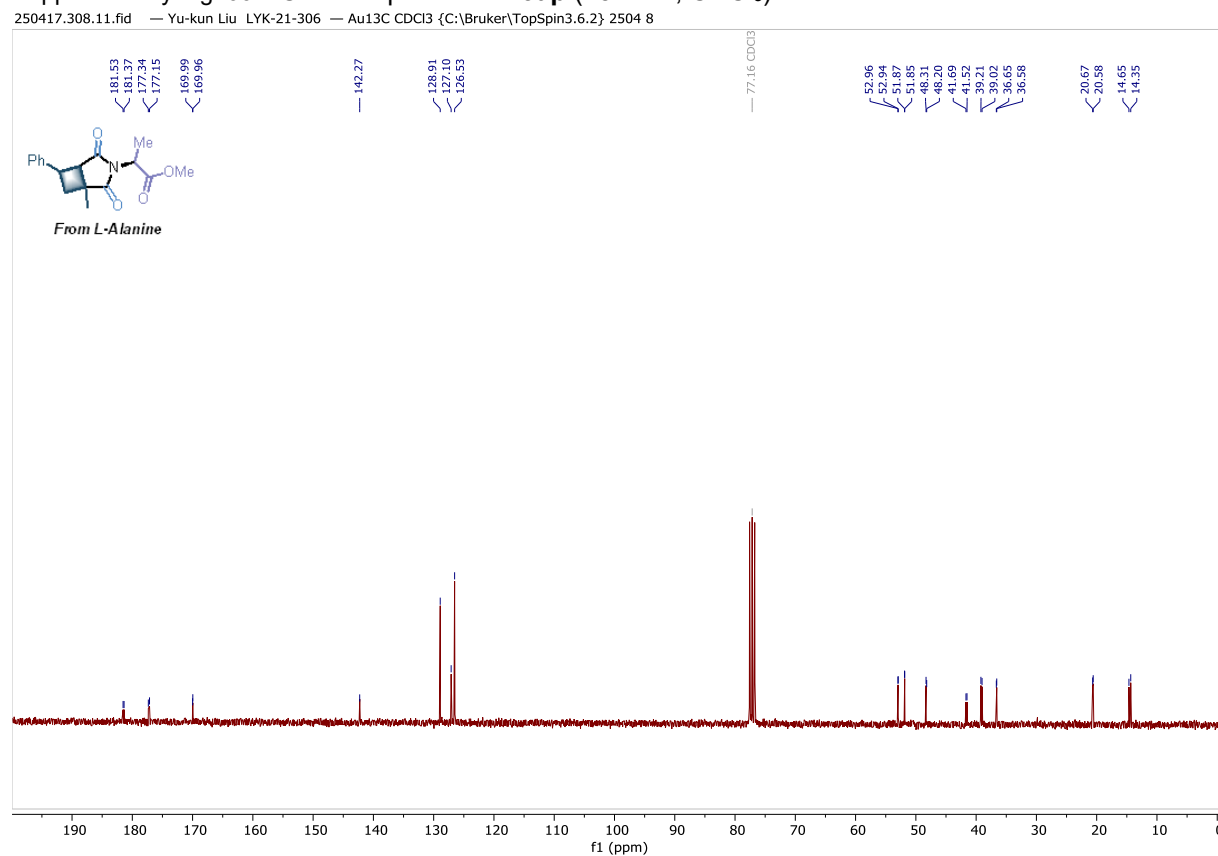
250519.403.11.fid — Yu-kun Liu LYK-21-337-S — Au13C CDCl_3 {C:\Bruker\TopSpin3.6.2} 2505 3



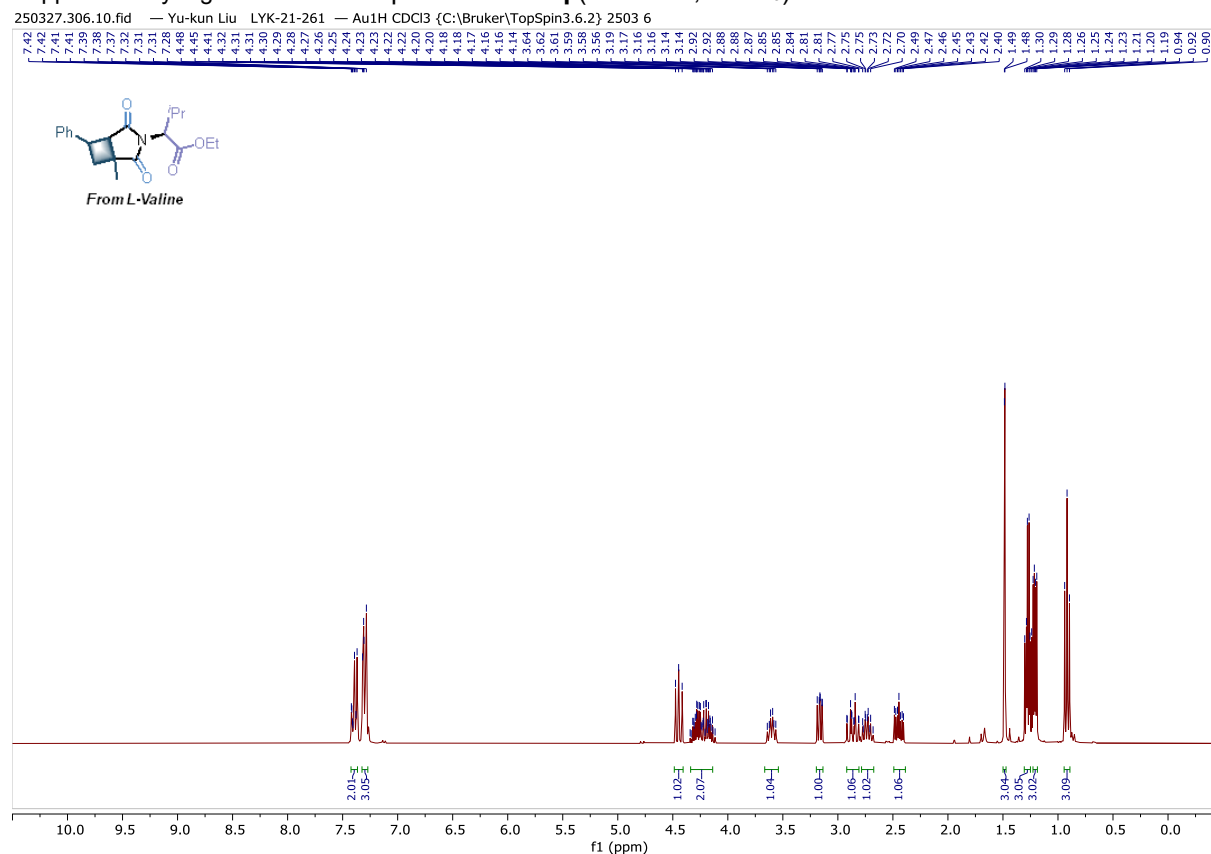
Supplementary Fig. 98. ^1H NMR spectrum of **3ap** (300 MHz, CDCl_3)



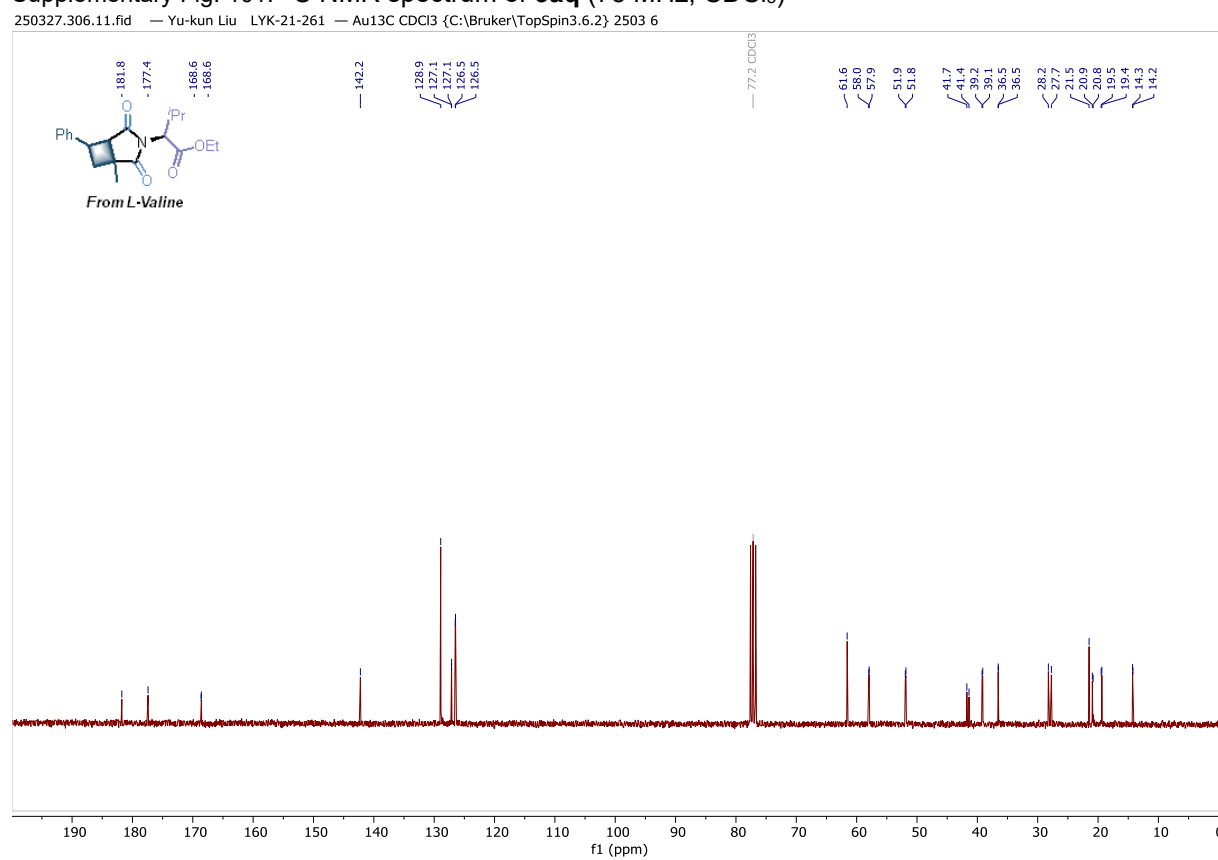
Supplementary Fig. 99. ^{13}C NMR spectrum of **3ap** (75 MHz, CDCl_3)



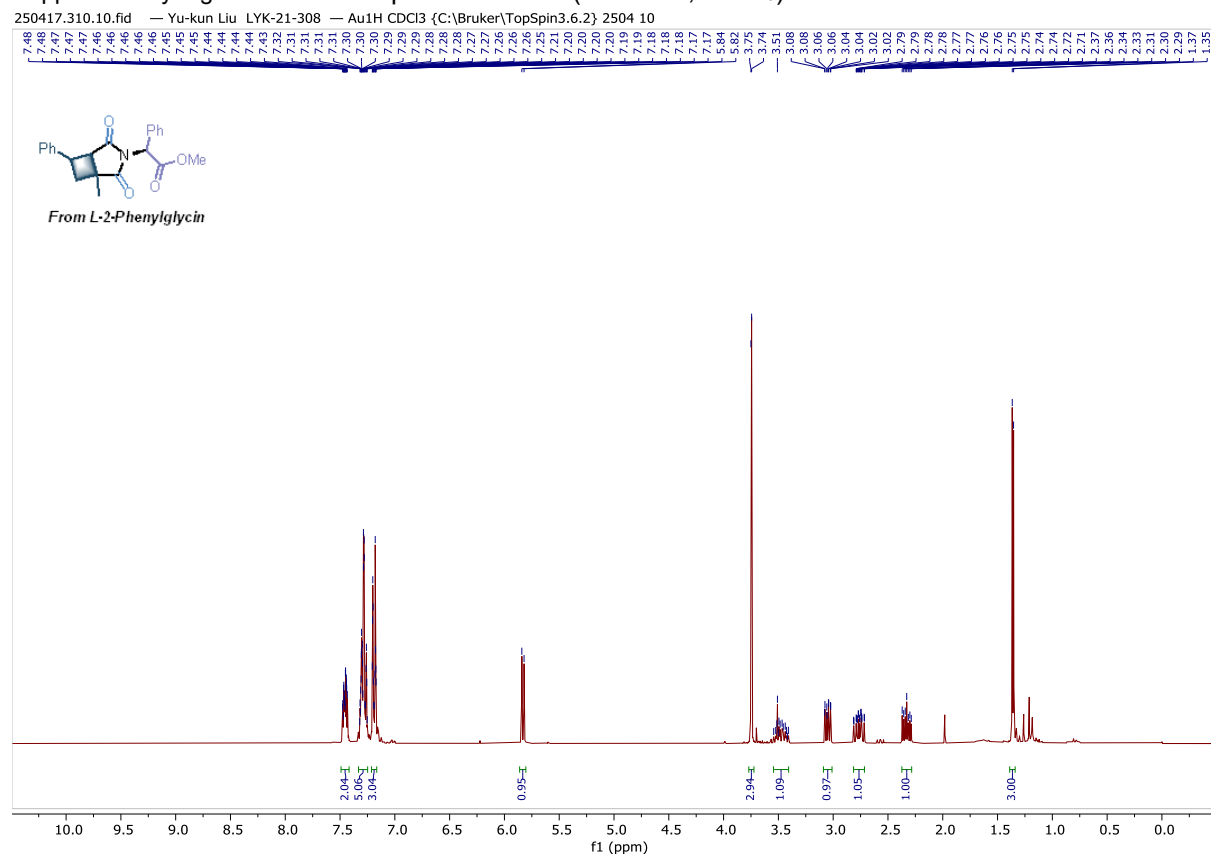
Supplementary Fig. 100. ^1H NMR spectrum of **3aq** (300 MHz, CDCl_3)



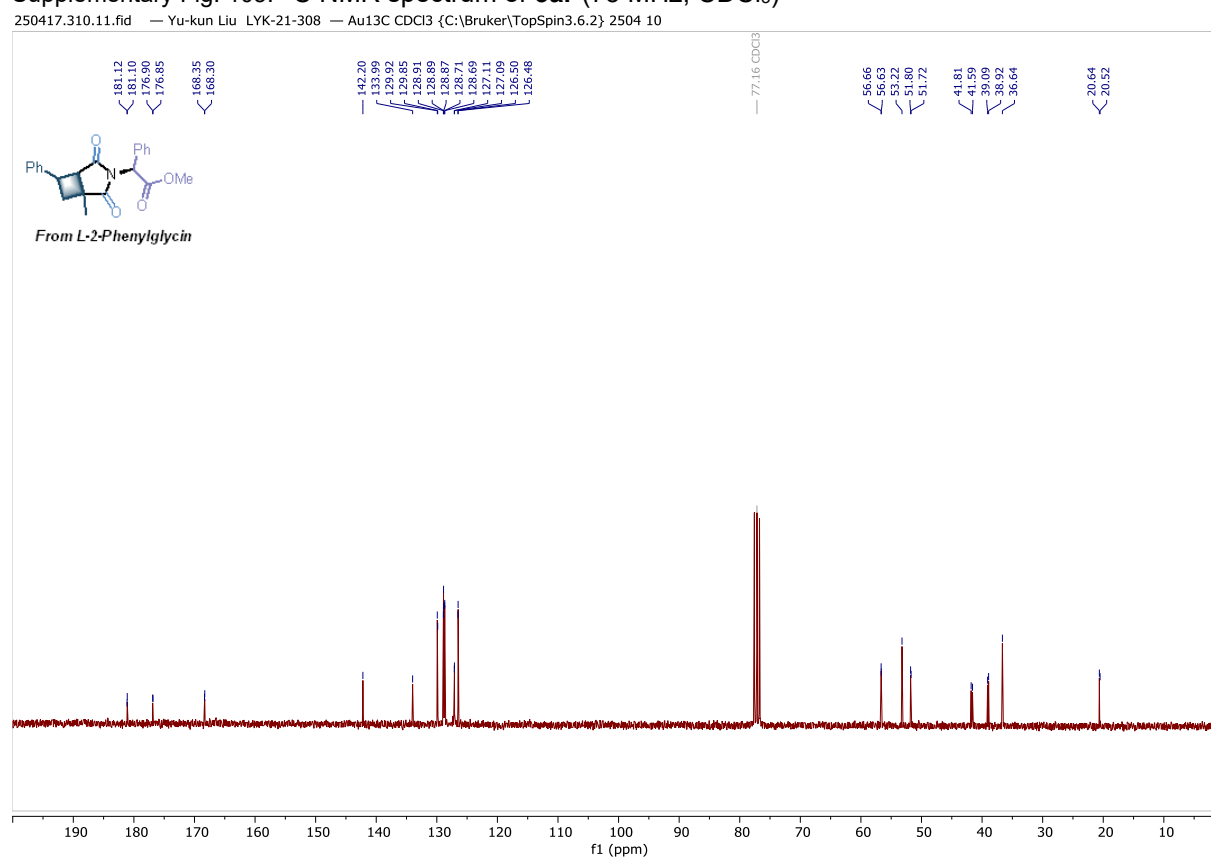
Supplementary Fig. 101. ^{13}C NMR spectrum of **3aq** (75 MHz, CDCl_3)



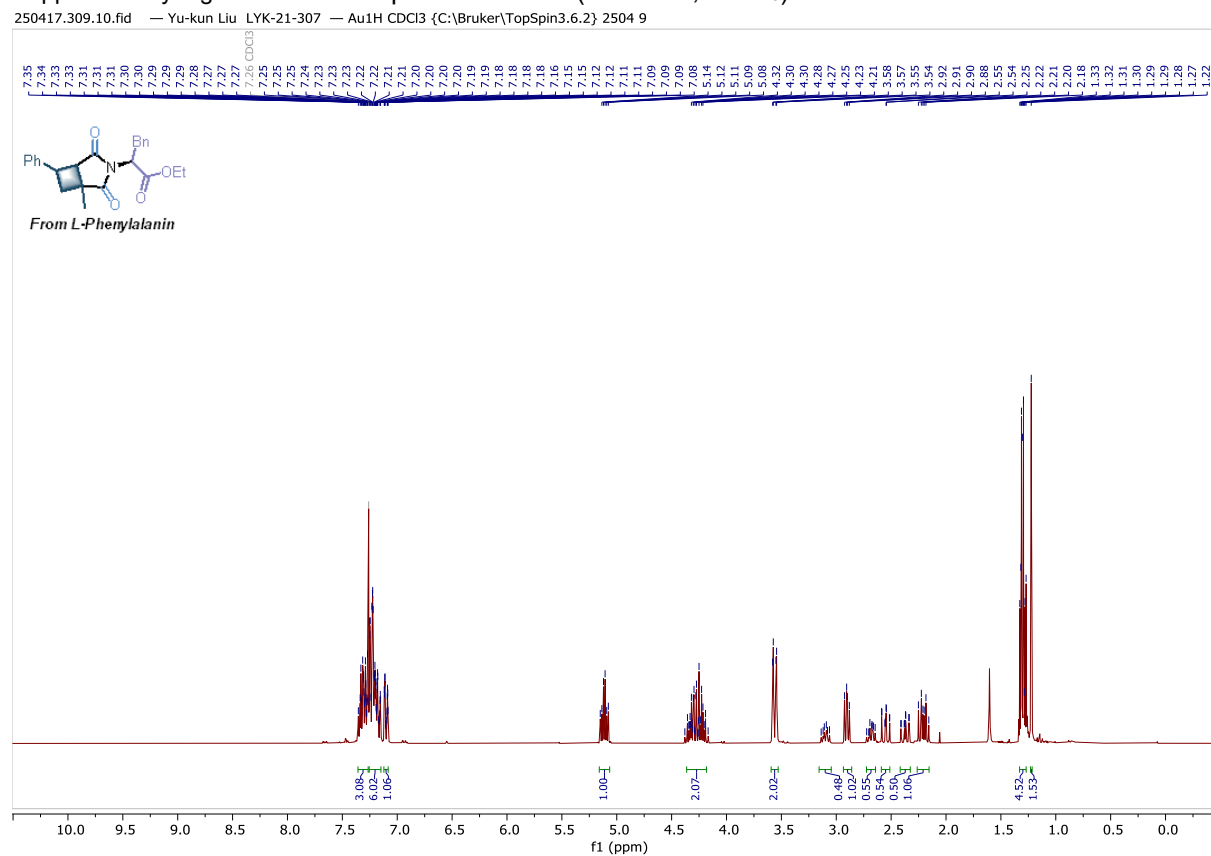
Supplementary Fig. 102. ^1H NMR spectrum of **3ar** (300 MHz, CDCl_3)



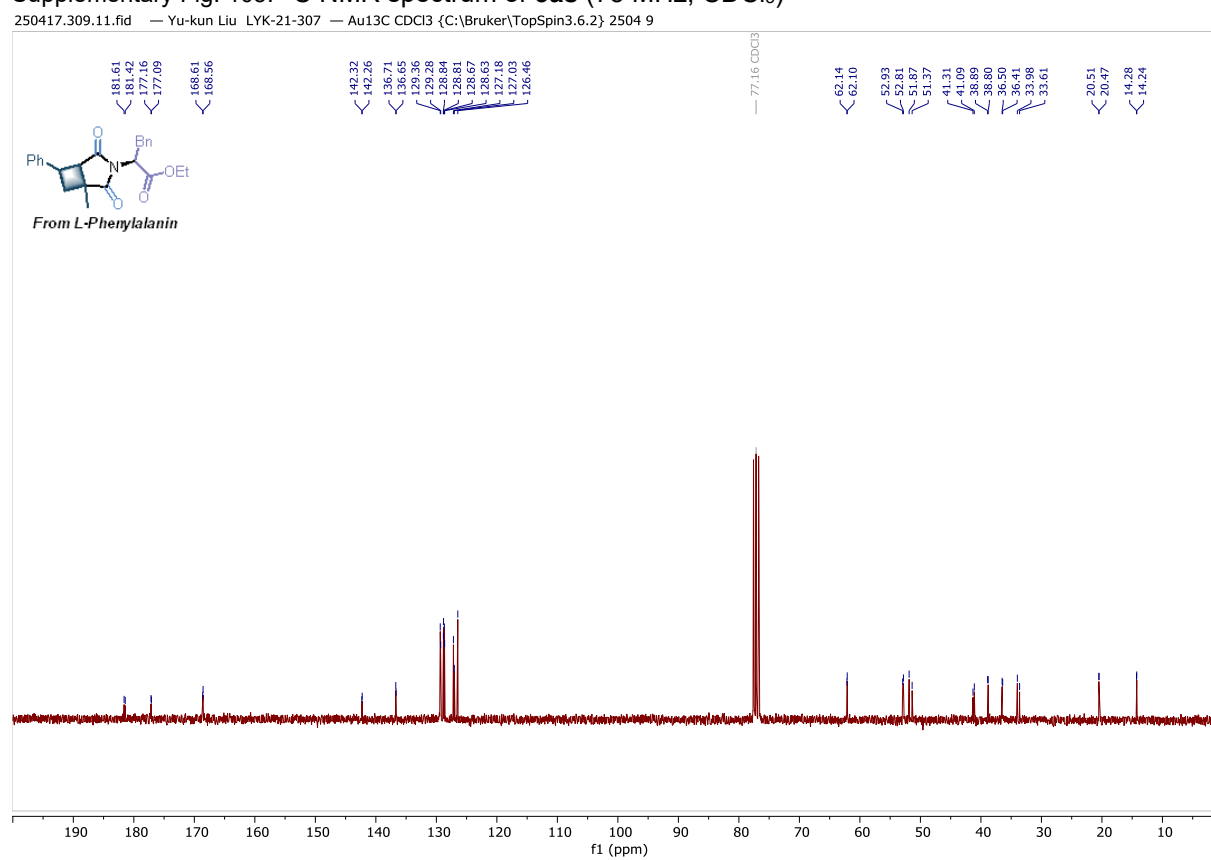
Supplementary Fig. 103. ^{13}C NMR spectrum of **3ar** (75 MHz, CDCl_3)



Supplementary Fig. 104. ^1H NMR spectrum of **3as** (300 MHz, CDCl_3)

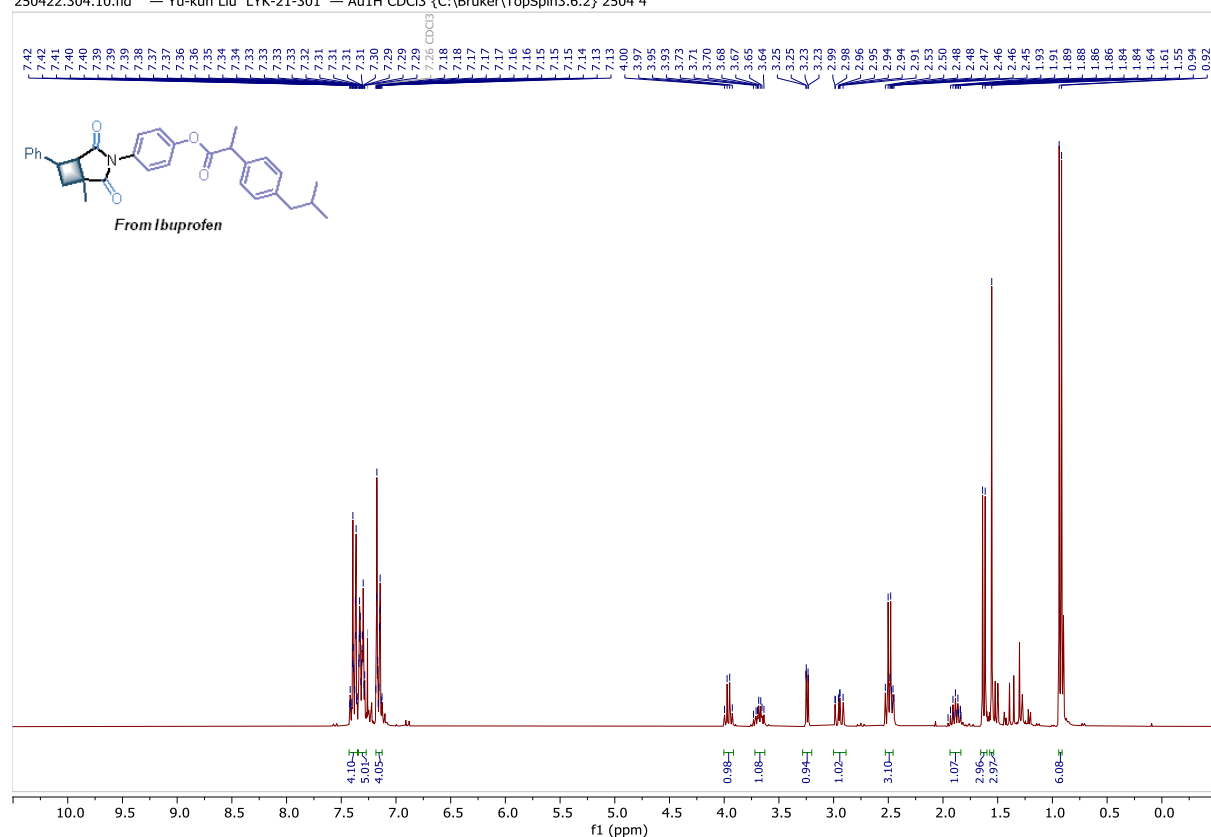


Supplementary Fig. 105. ^{13}C NMR spectrum of **3as** (75 MHz, CDCl_3)



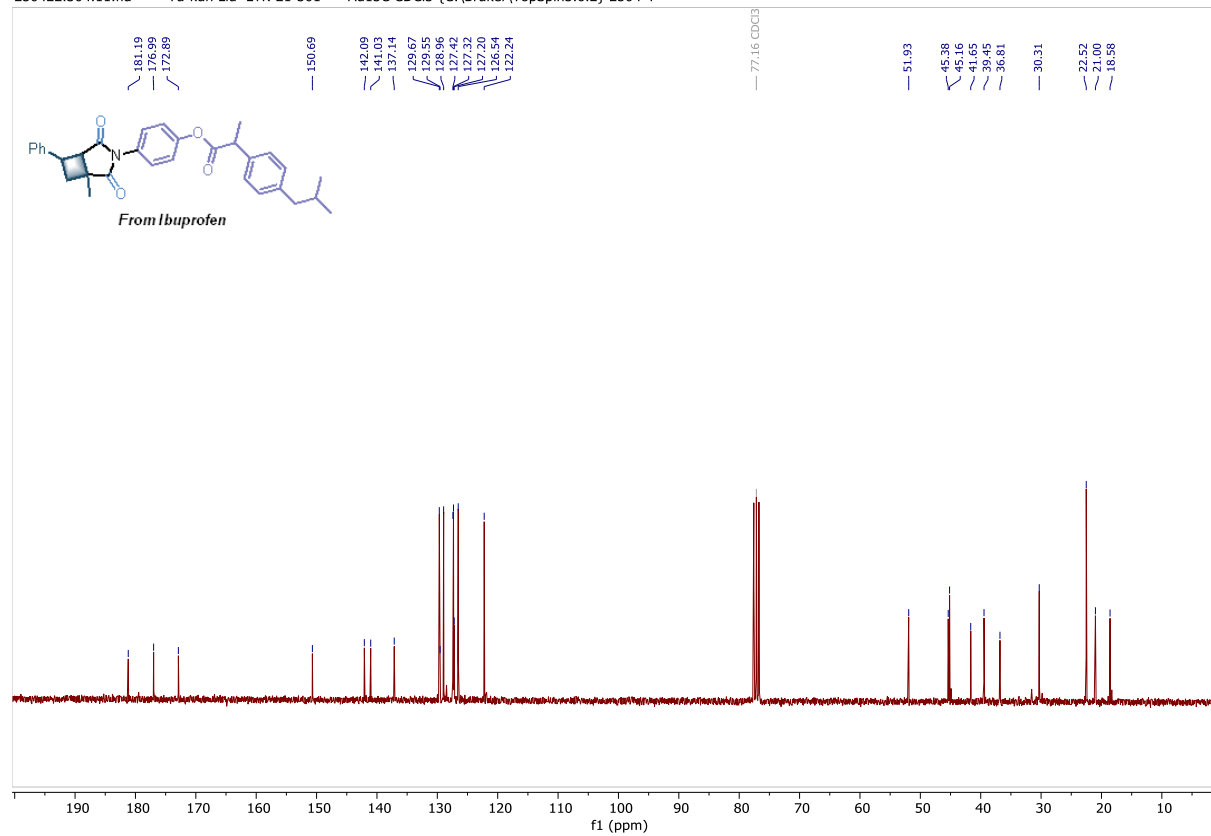
Supplementary Fig. 106. ^1H NMR spectrum of **3at** (300 MHz, CDCl_3)

250422.304.10.fid — Yu-kun Liu LYK-21-301 — Au1H CDCl_3 {C:\Bruker\TopSpin3.6.2} 2504 4



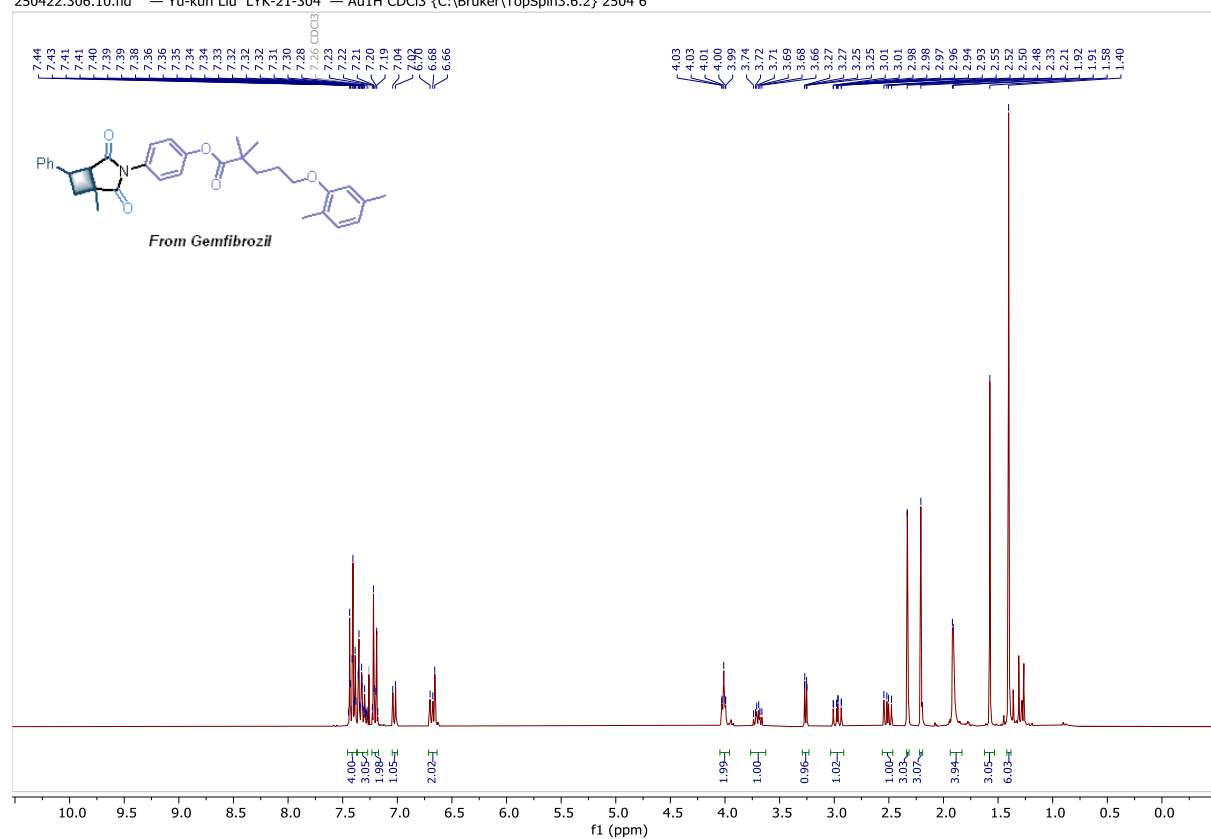
Supplementary Fig. 107. ^{13}C NMR spectrum of **3at** (75 MHz, CDCl_3)

250422.304.11.fid — Yu-kun Liu LYK-21-301 — Au13C CDCl_3 {C:\Bruker\TopSpin3.6.2} 2504 4



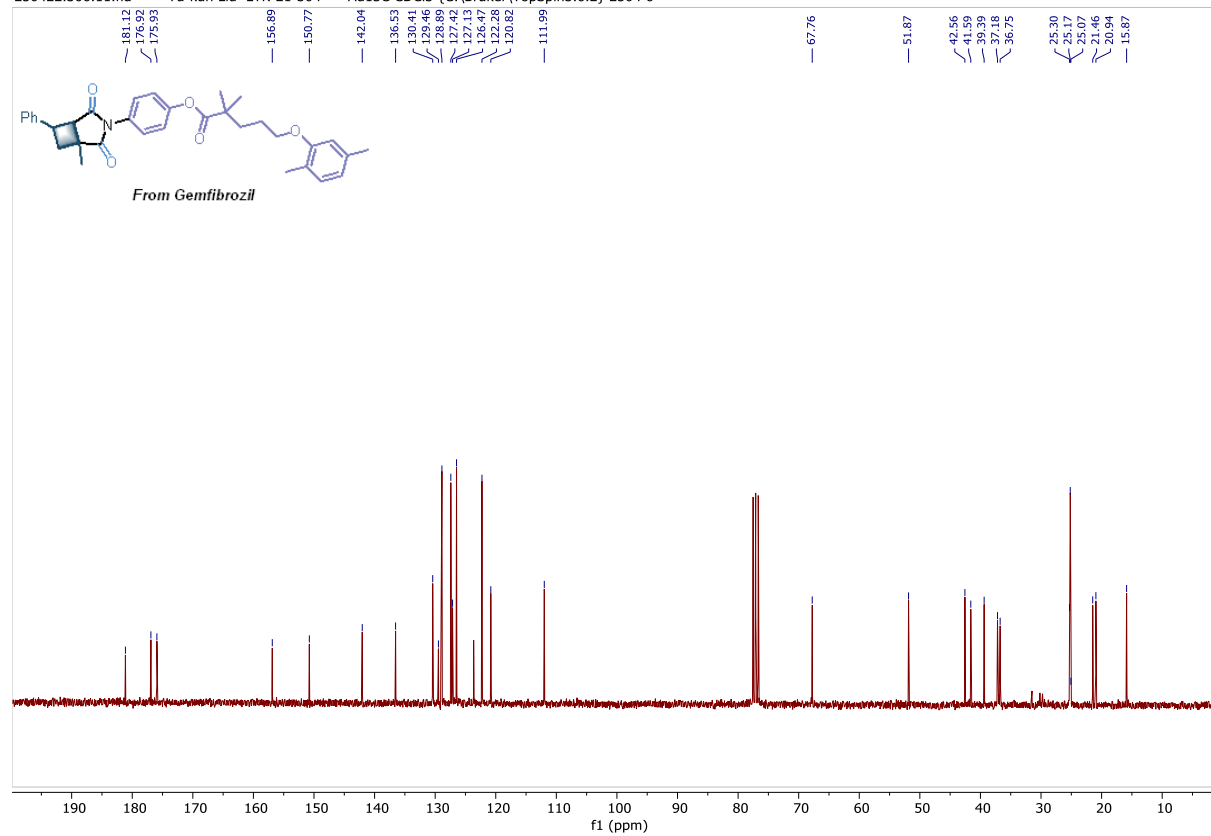
Supplementary Fig. 108. ^1H NMR spectrum of **3au** (300 MHz, CDCl_3)

250422.306.10.fid — Yu-kun Liu LYK-21-304 — Au1H CDCl_3 {C:\Bruker\TopSpin3.6.2} 2504 6



Supplementary Fig. 109. ^{13}C NMR spectrum of **3au** (75 MHz, CDCl_3)

250422.306.11.fid — Yu-kun Liu LYK-21-304 — Au13C CDCl_3 {C:\Bruker\TopSpin3.6.2} 2504 6



250512.307.10.fid — Yu-kun Liu LYK-21-320 — Au1H CDCl3 {C:\Bruker\TopSpin3.6.2} 2505 7

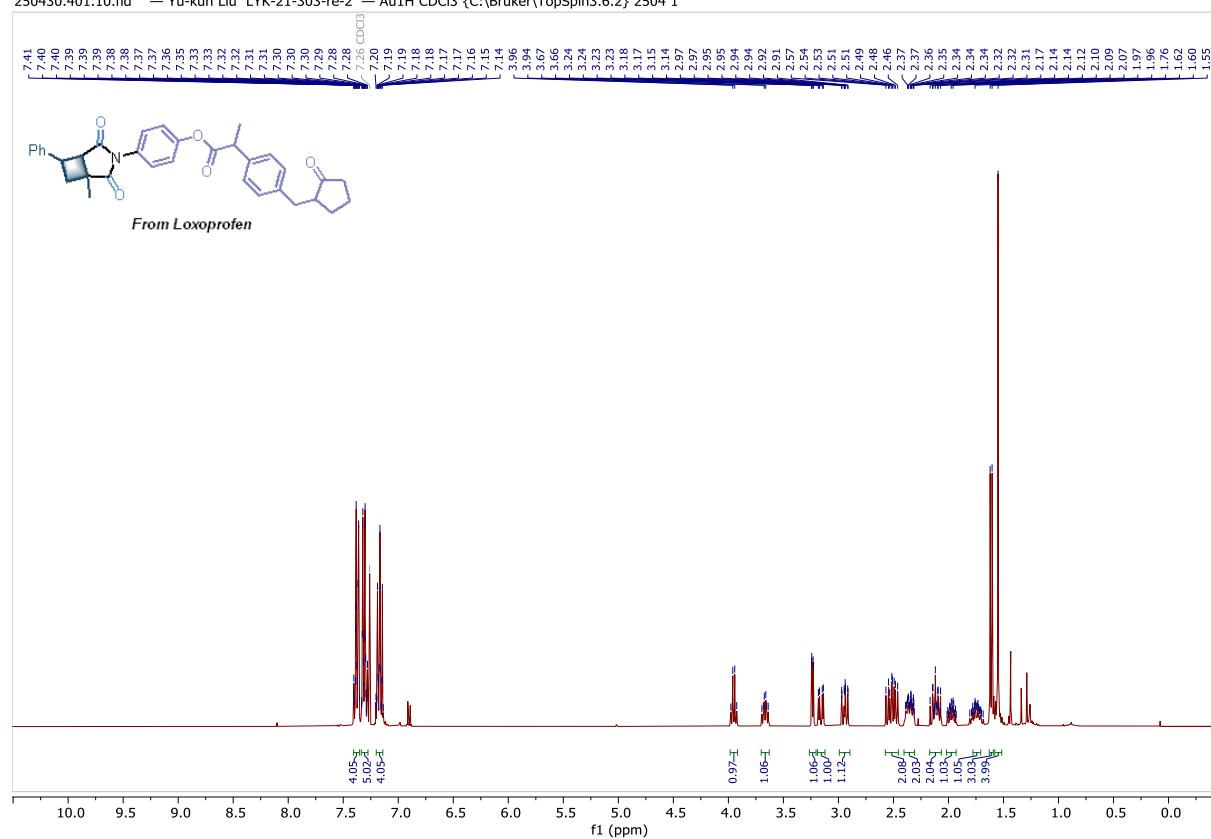


250512.307.11.fid — Yu-kun Liu LYK-21-320 — Au13C CDCl3 {C:\Bruker\TopSpin3.6.2} 2505 7

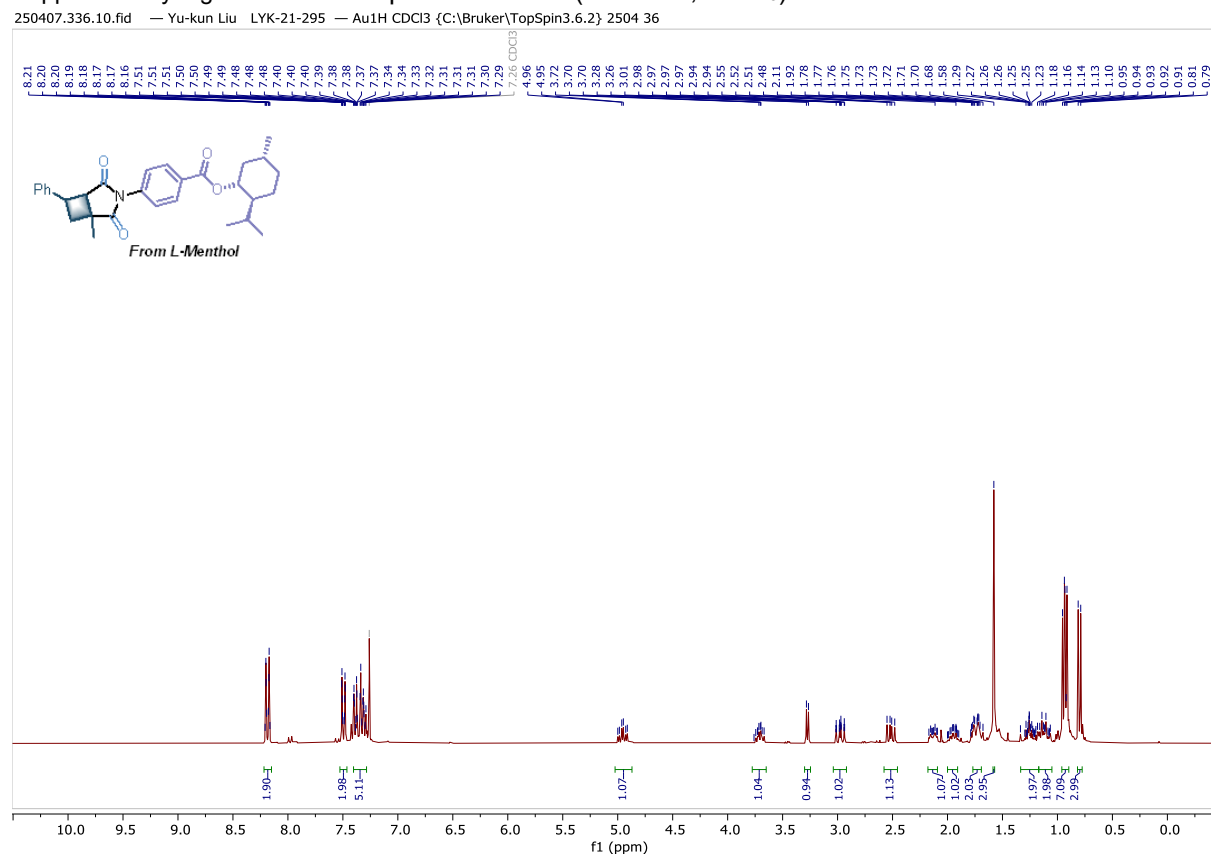


Supplementary Fig. 112. ^1H NMR spectrum of **3aw** (400 MHz, CDCl_3)

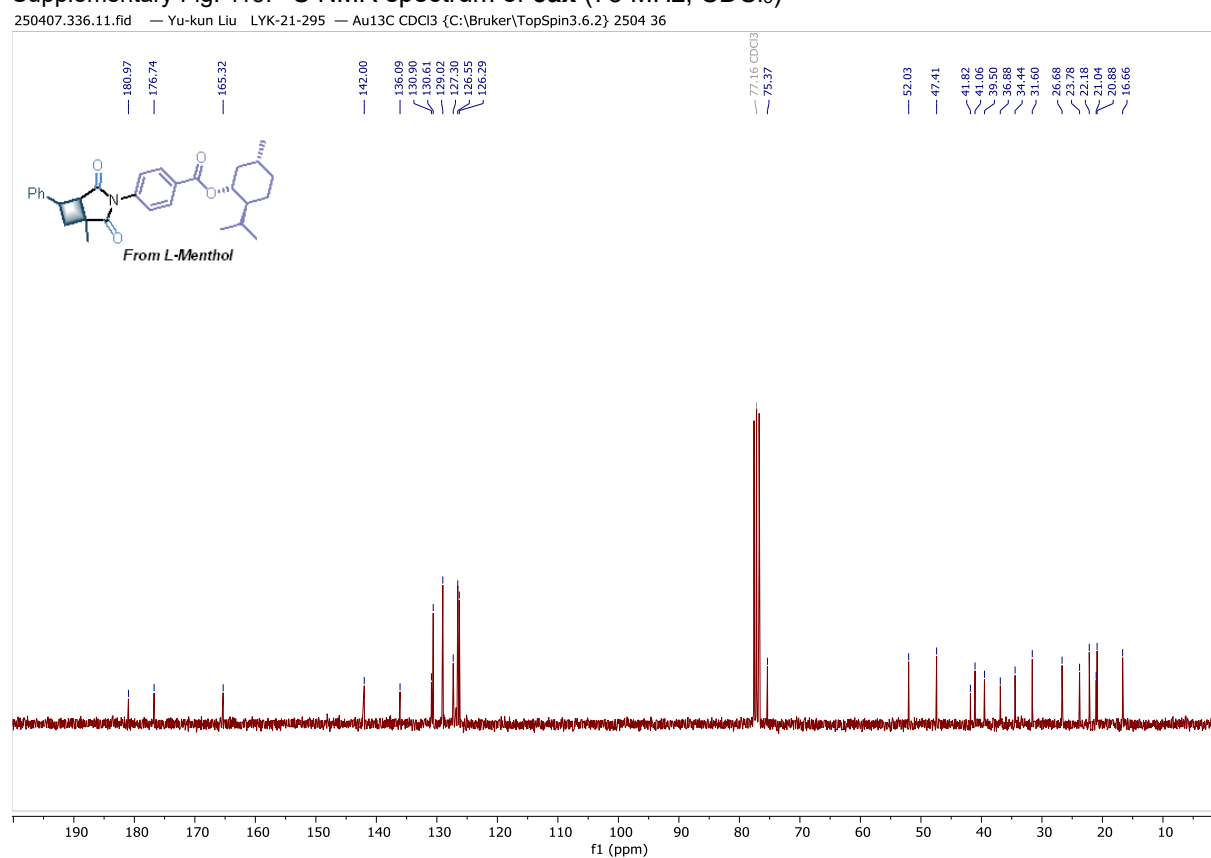
250430.401.10.fid — Yu-kun Liu LYK-21-303-re-2 — Au1H CDCl_3 {C:\Bruker\TopSpin3.6.2} 2504 1



Supplementary Fig. 114. ^1H NMR spectrum of **3ax** (300 MHz, CDCl_3)



Supplementary Fig. 115. ^{13}C NMR spectrum of **3ax** (75 MHz, CDCl_3)



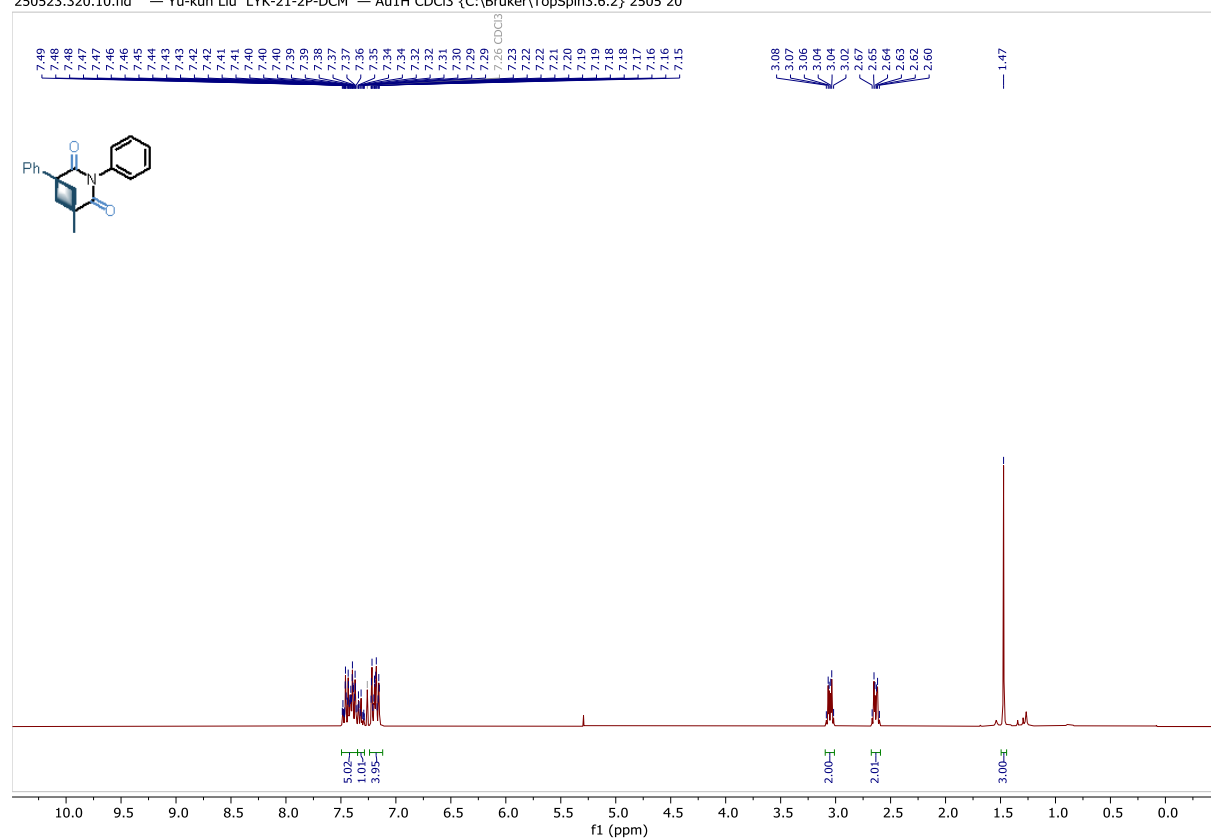
250407.335.10.fid — Yu-kun Liu LYK-21-294 — Au1H CDCl3 {C:\Bruker\TopSpin3.6.2} 2504 35



250407.335.11.fid — Yu-kun Liu LYK-21-294 — Au13C CDCl3 {C:\Bruker\TopSpin3.6.2} 2504 35

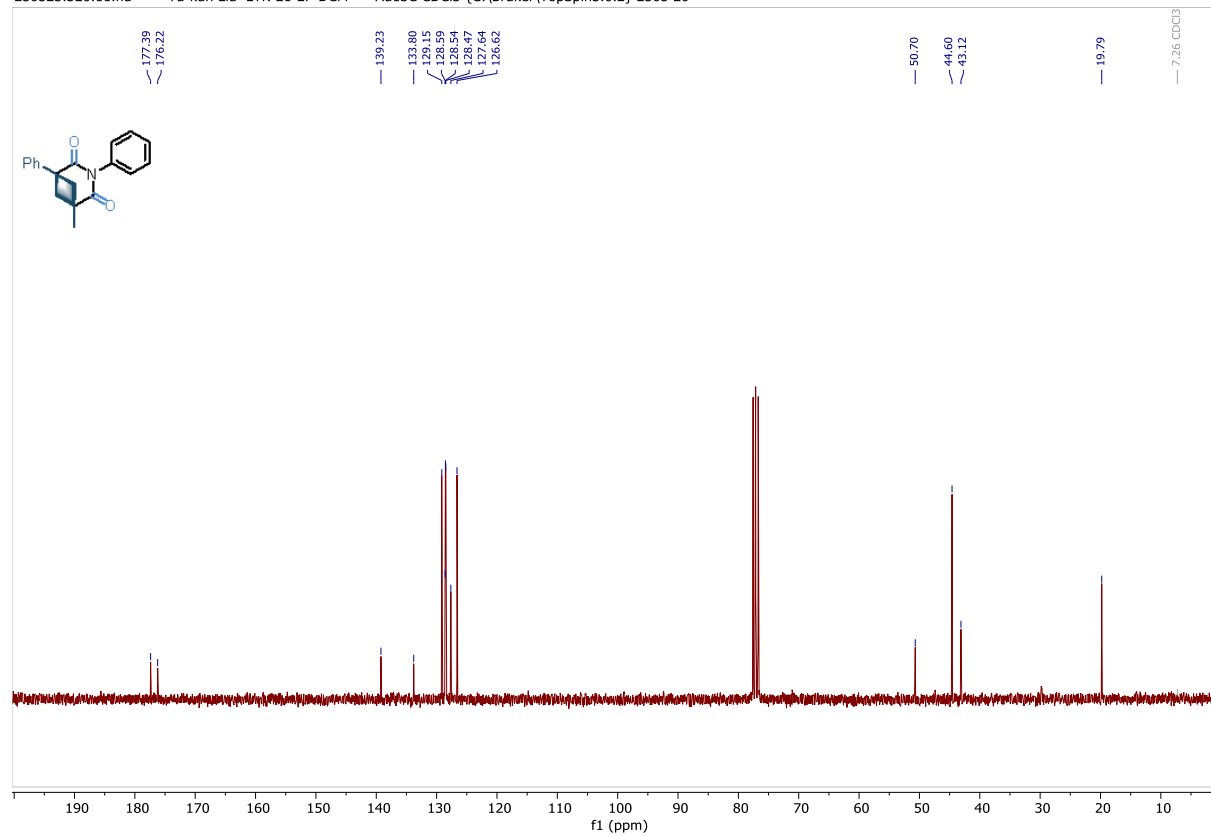
Supplementary Fig. 118. ^1H NMR spectrum of **4a** (300 MHz, CDCl_3)

250523.320.10.fid — Yu-kun Liu LYK-21-2P-DCM — Au1H CDCl_3 {C:\Bruker\TopSpin3.6.2} 2505 20



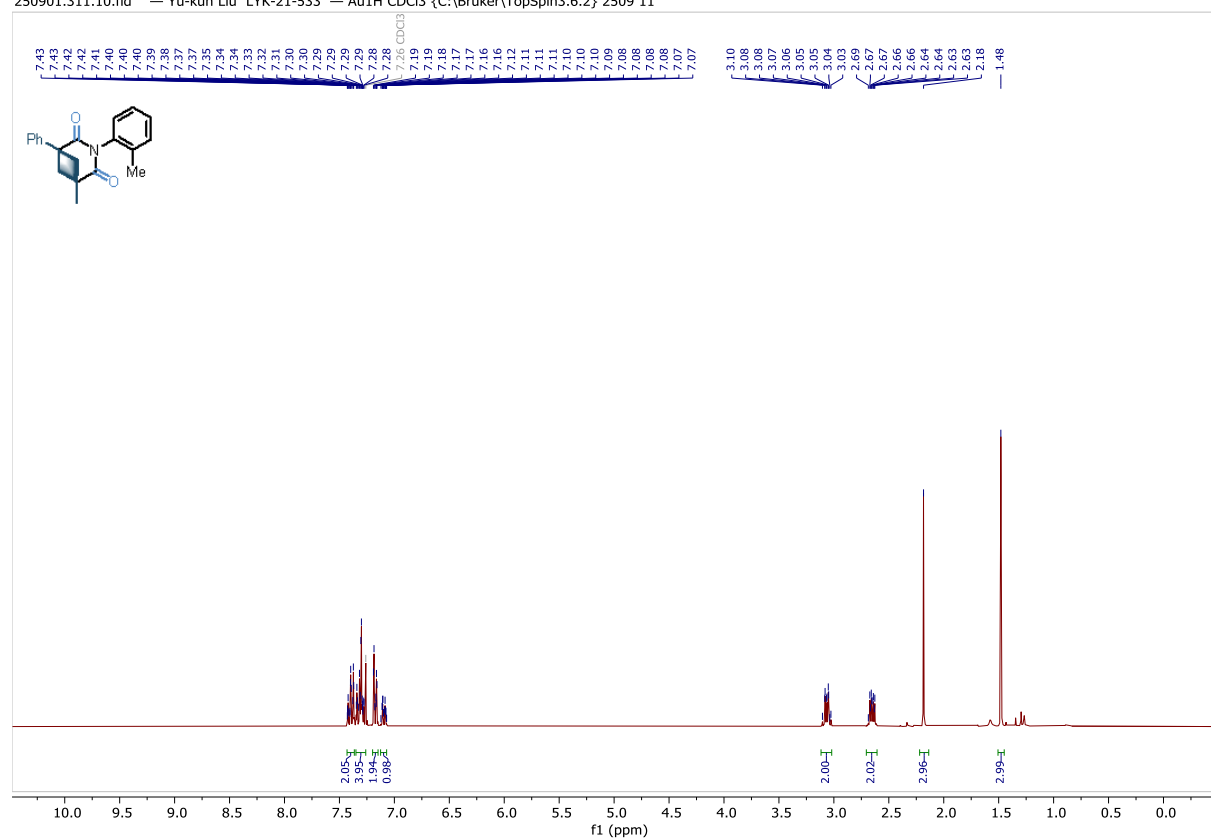
Supplementary Fig. 119. ^{13}C NMR spectrum of **4a** (75 MHz, CDCl_3)

250523.320.11.fid — Yu-kun Liu LYK-21-2P-DCM — Au13C CDCl_3 {C:\Bruker\TopSpin3.6.2} 2505 20



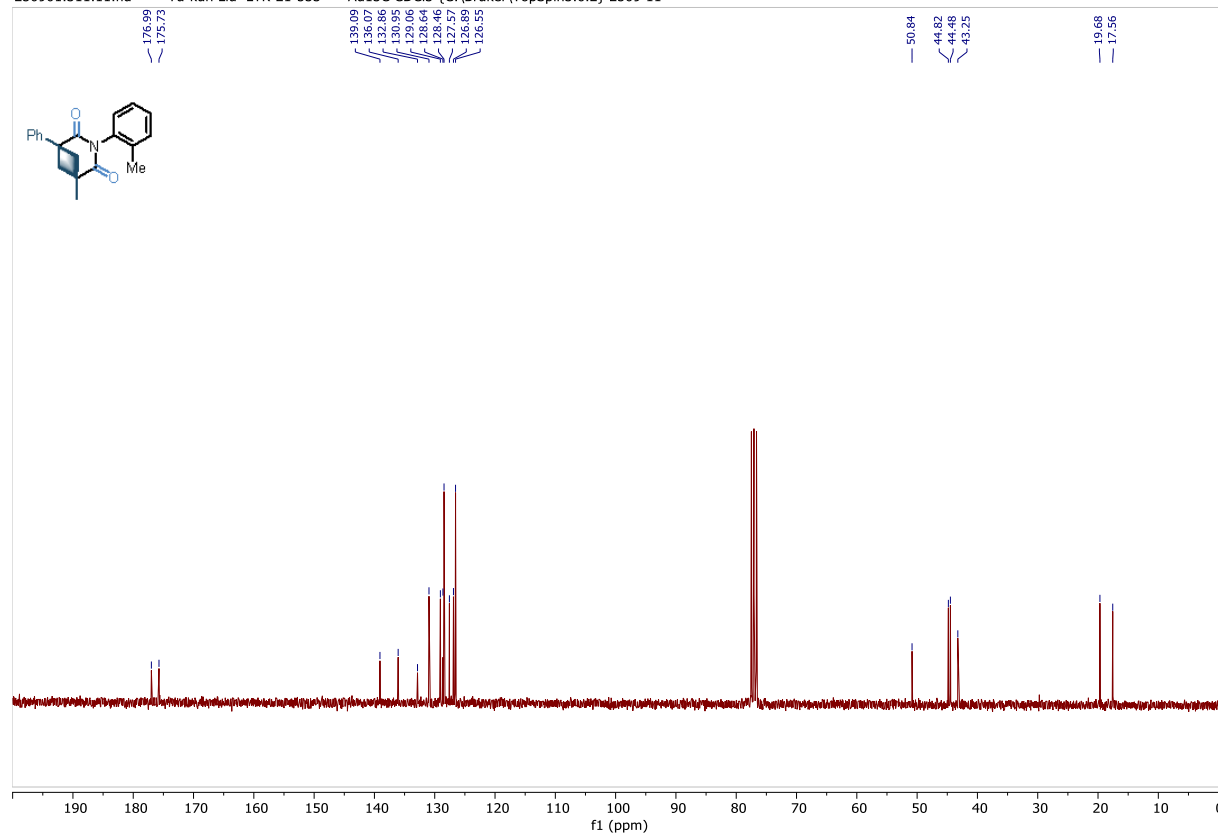
Supplementary Fig. 120. ^1H NMR spectrum of **4b** (300 MHz, CDCl_3)

250901.311.10.fid — Yu-kun Liu LYK-21-533 — Au1H CDCl_3 {C:\Bruker\TopSpin3.6.2} 2509 11



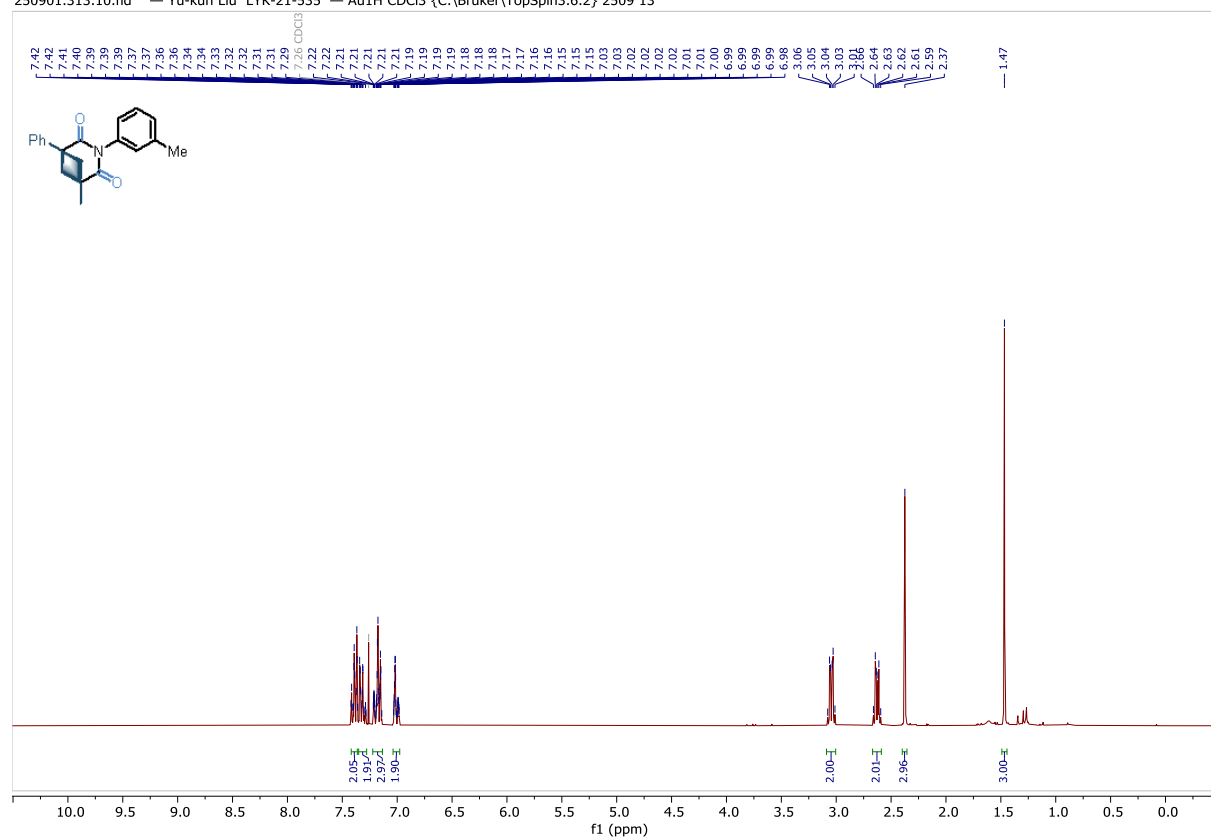
Supplementary Fig. 121. ^{13}C NMR spectrum of **4a** (75 MHz, CDCl_3)

250901.311.11.fid — Yu-kun Liu LYK-21-533 — Au13C CDCl_3 {C:\Bruker\TopSpin3.6.2} 2509 11



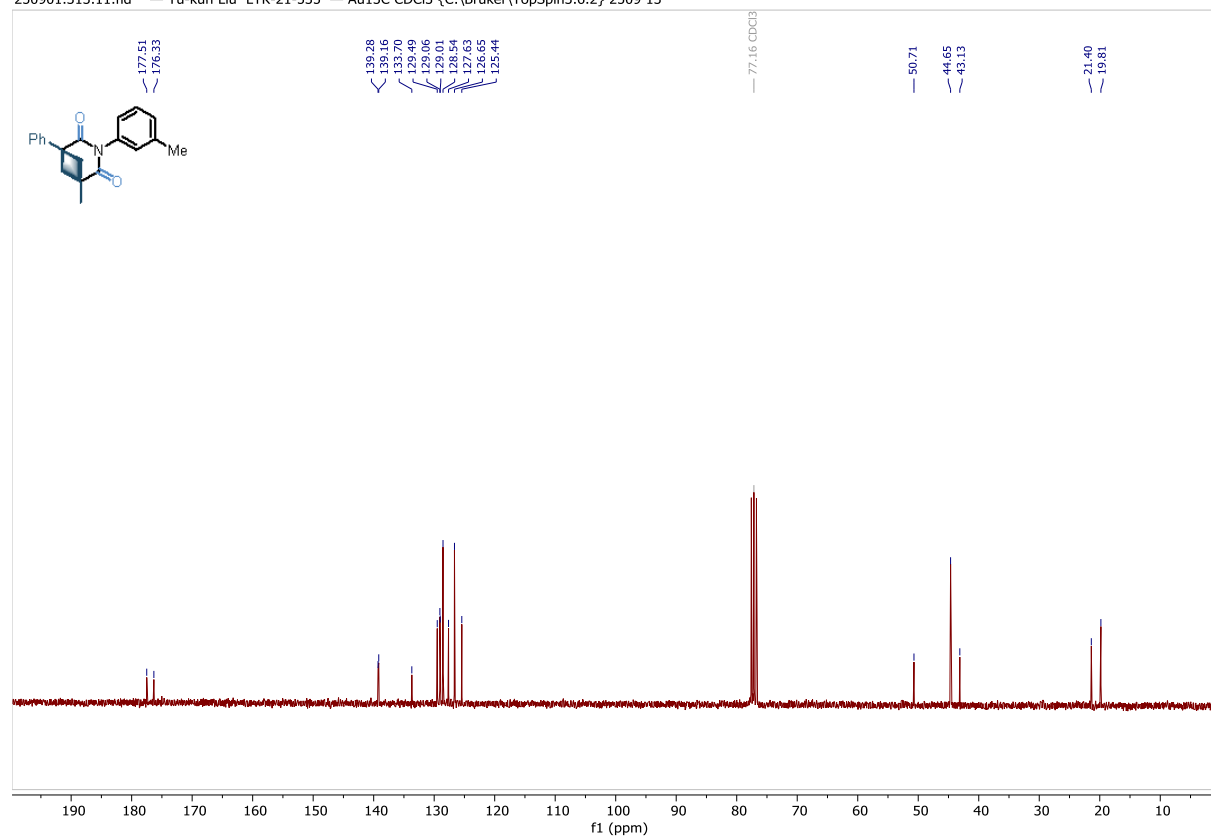
Supplementary Fig. 122. ^1H NMR spectrum of **4c** (300 MHz, CDCl_3)

250901.313.10.fid — Yu-kun Liu LYK-21-535 — Au1H CDCl_3 {C:\Bruker\TopSpin3.6.2} 2509 13



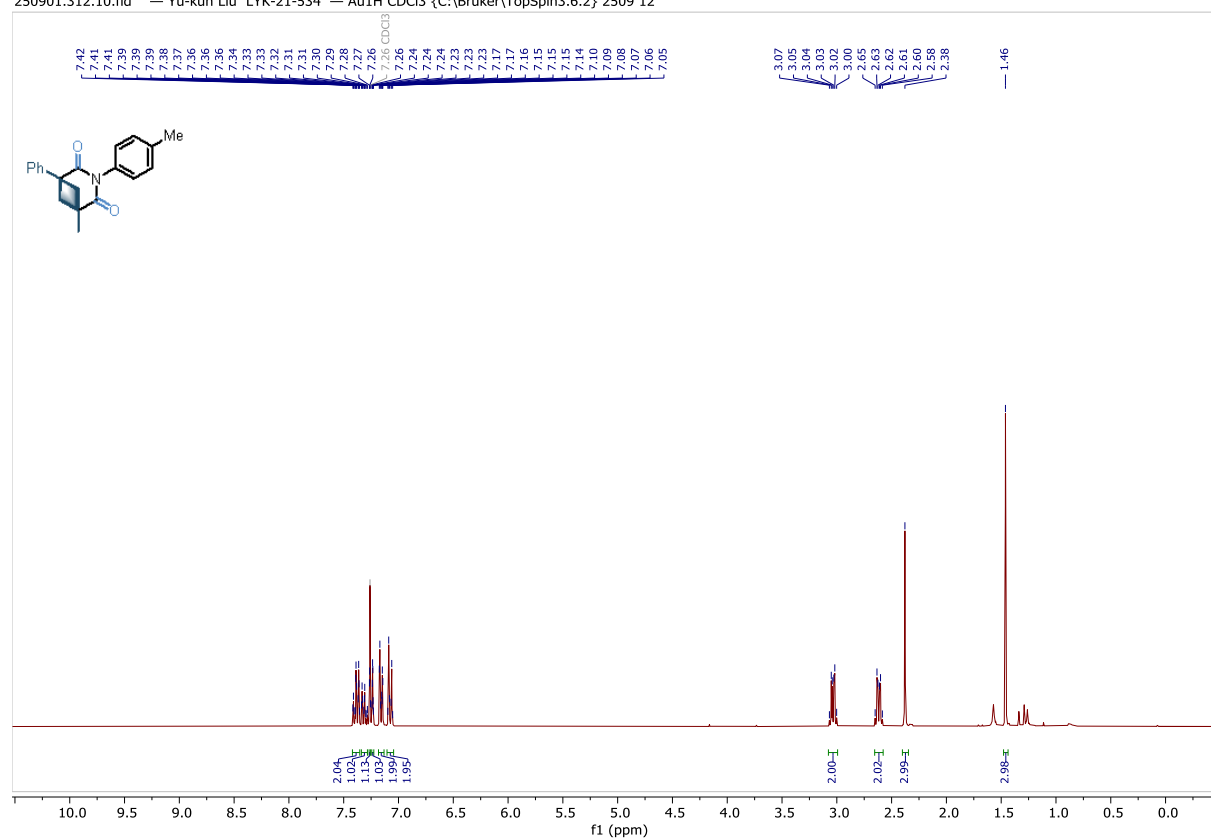
Supplementary Fig. 123. ^{13}C NMR spectrum of **4c** (75 MHz, CDCl_3)

250901.313.11.fid — Yu-kun Liu LYK-21-535 — Au13C CDCl_3 {C:\Bruker\TopSpin3.6.2} 2509 13



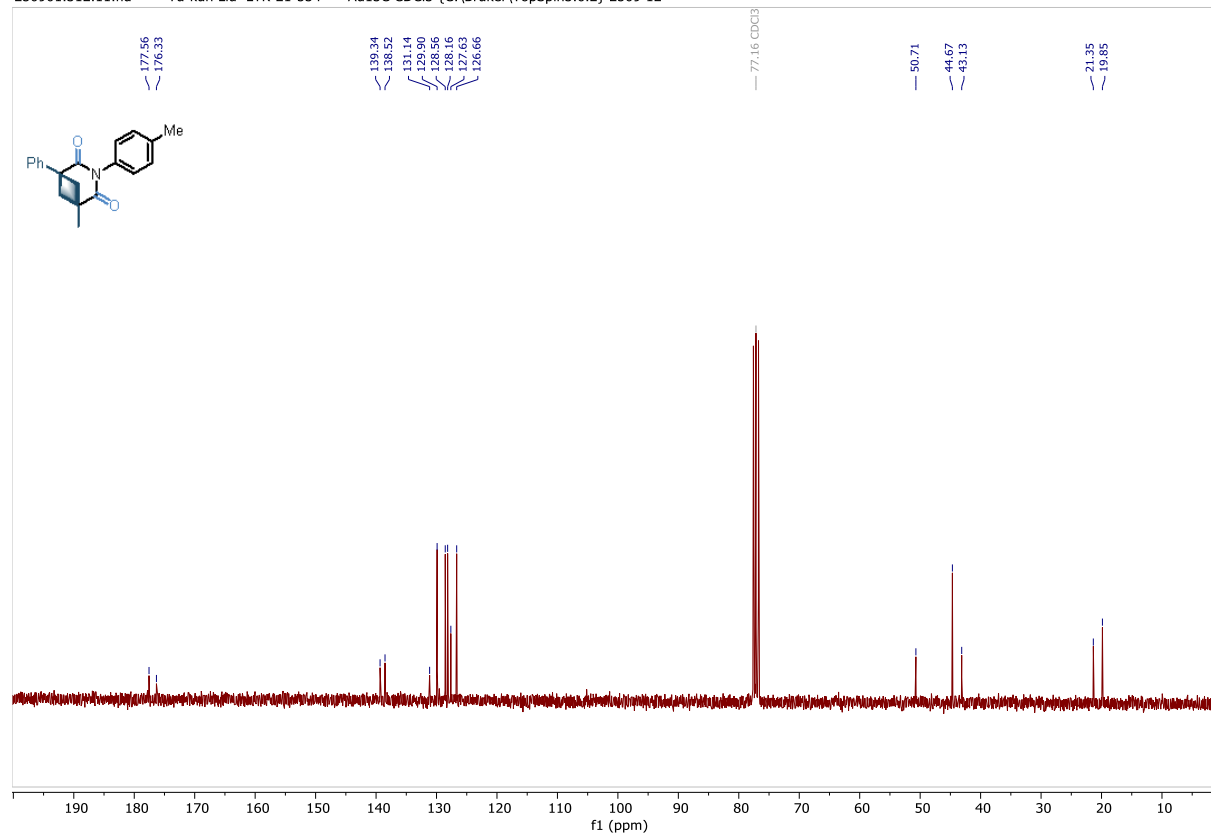
Supplementary Fig. 124. ^1H NMR spectrum of **4d** (300 MHz, CDCl_3)

250901.312.10.fid — Yu-kun Liu LYK-21-534 — Au1H CDCl_3 {C:\Bruker\TopSpin3.6.2} 2509 12

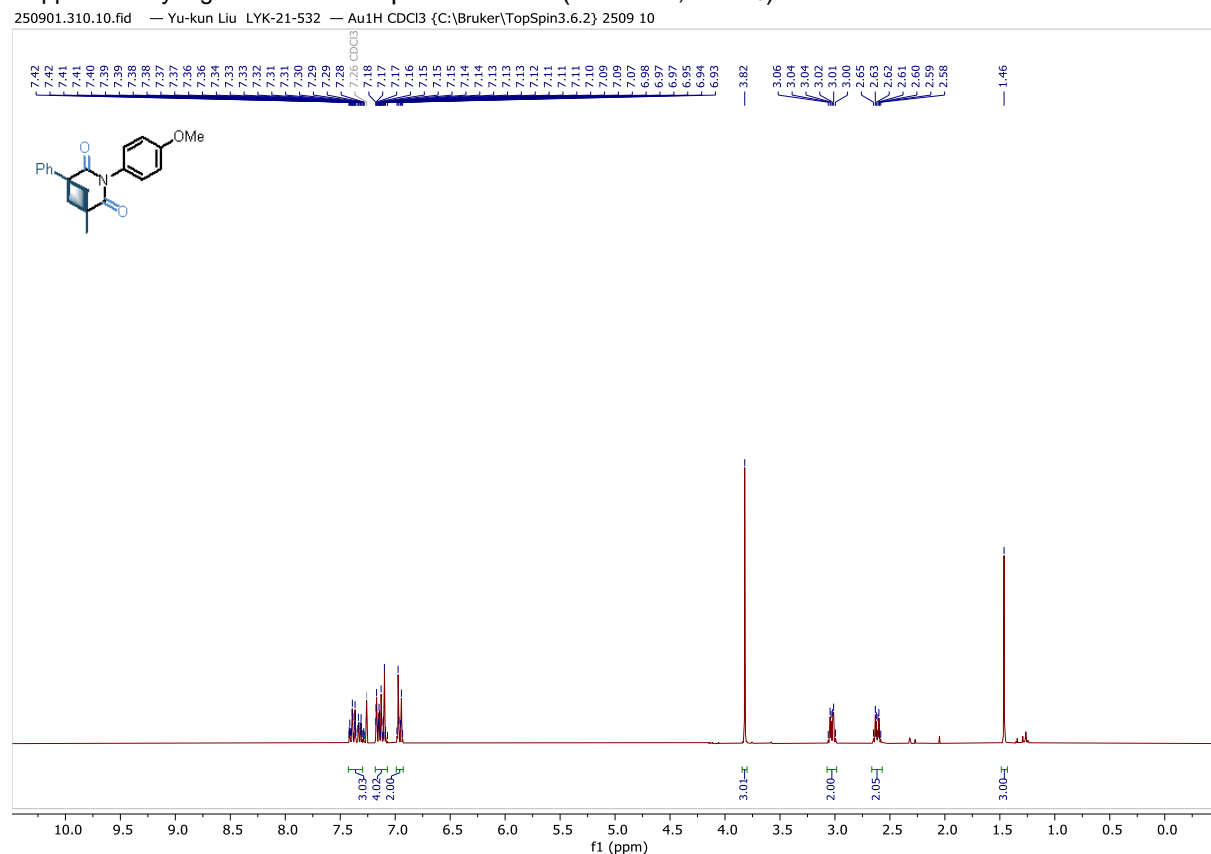


Supplementary Fig. 125. ^{13}C NMR spectrum of **4d** (75 MHz, CDCl_3)

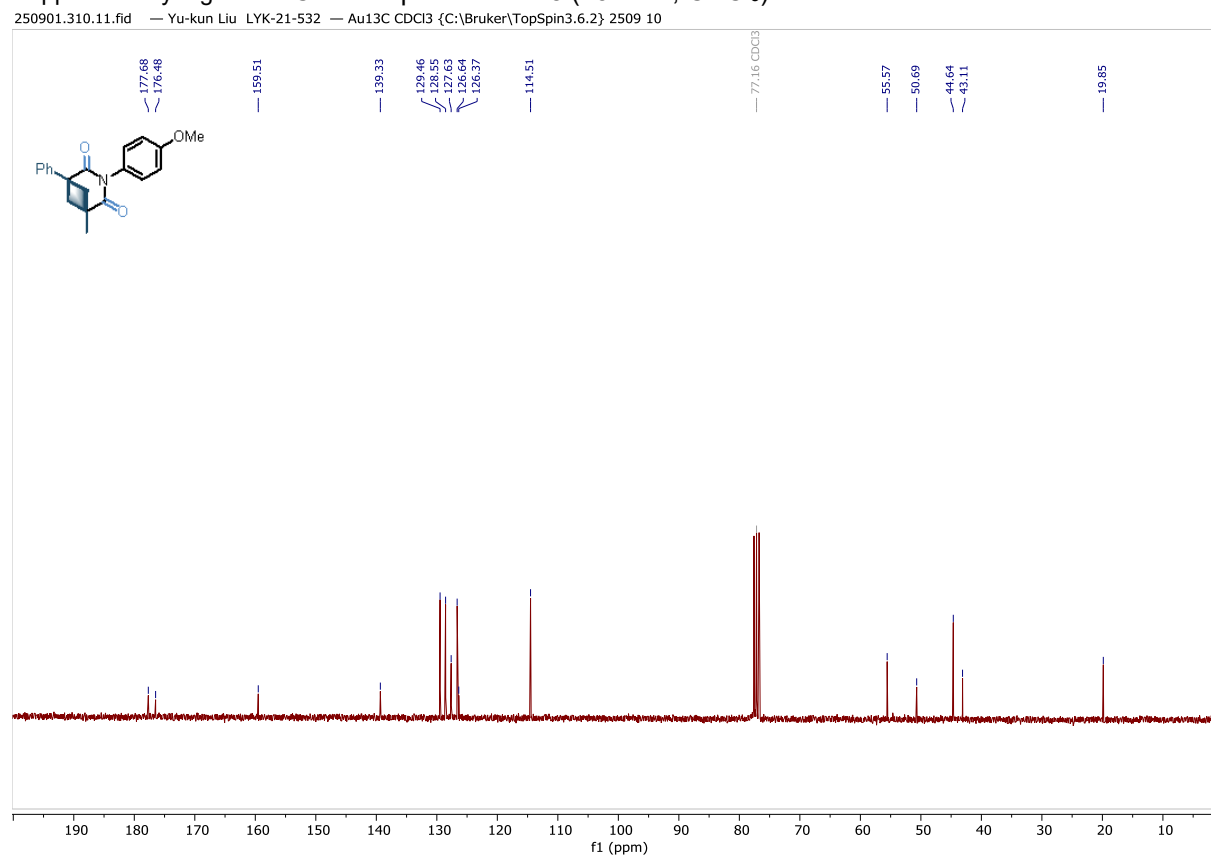
250901.312.11.fid — Yu-kun Liu LYK-21-534 — Au13C CDCl_3 {C:\Bruker\TopSpin3.6.2} 2509 12



Supplementary Fig. 126. ^1H NMR spectrum of **4e** (300 MHz, CDCl_3)

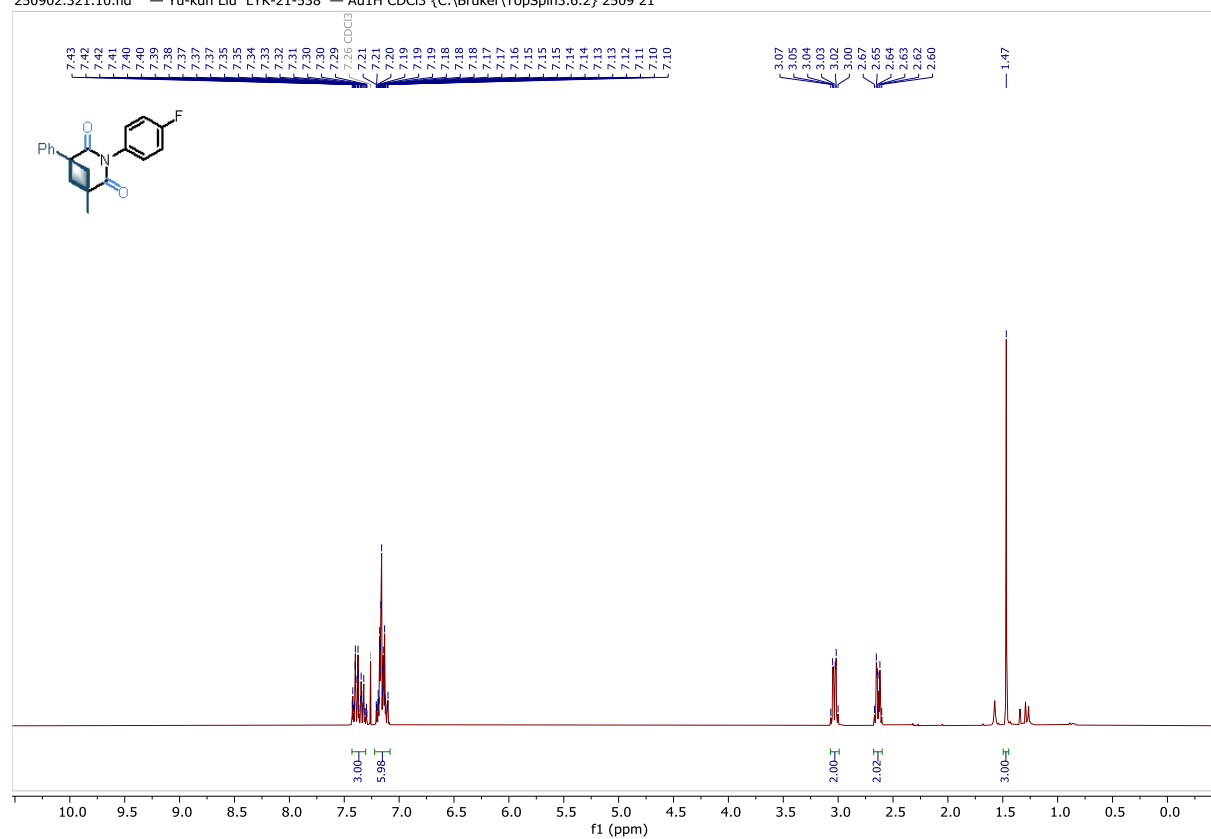


Supplementary Fig. 127. ^{13}C NMR spectrum of **4e** (75 MHz, CDCl_3)



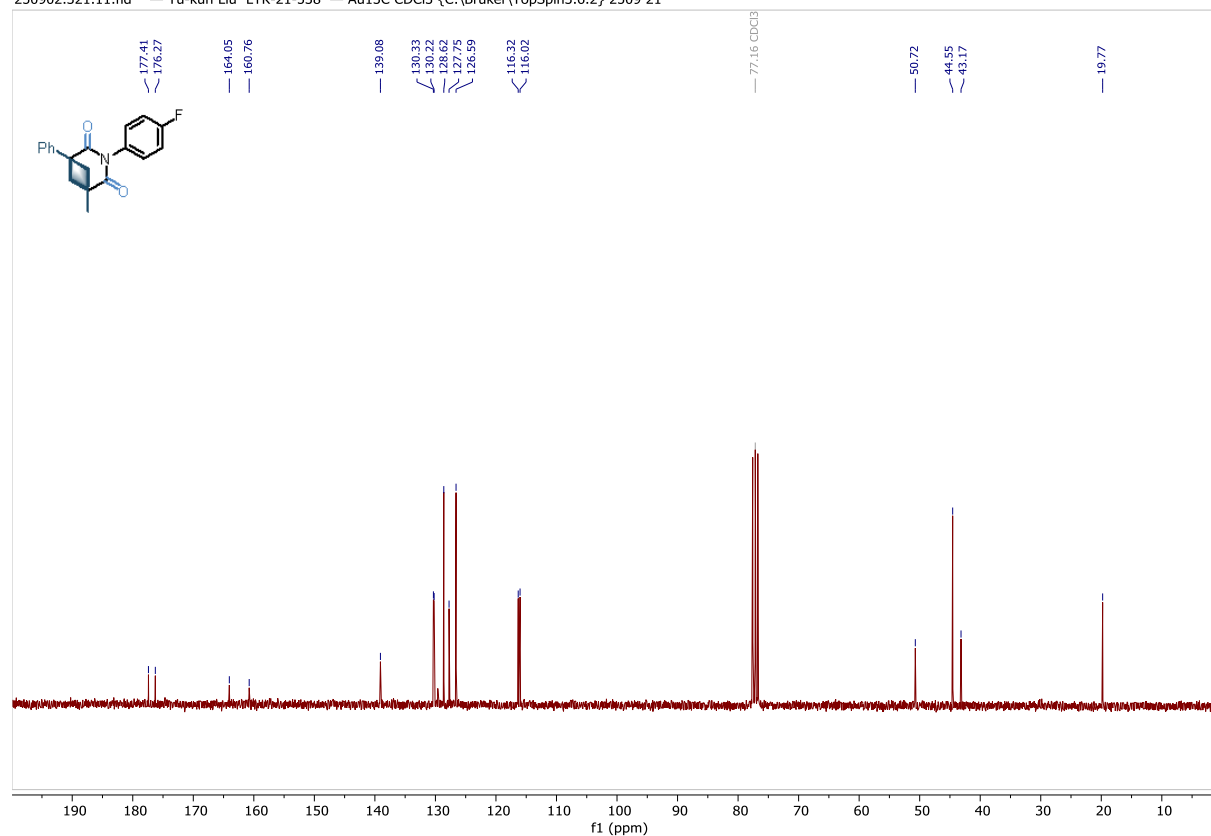
Supplementary Fig. 128. ^1H NMR spectrum of **4f** (300 MHz, CDCl_3)

250902.321.10.fid — Yu-kun Liu LYK-21-538 — Au1H CDCl_3 {C:\Bruker\TopSpin3.6.2} 2509 21



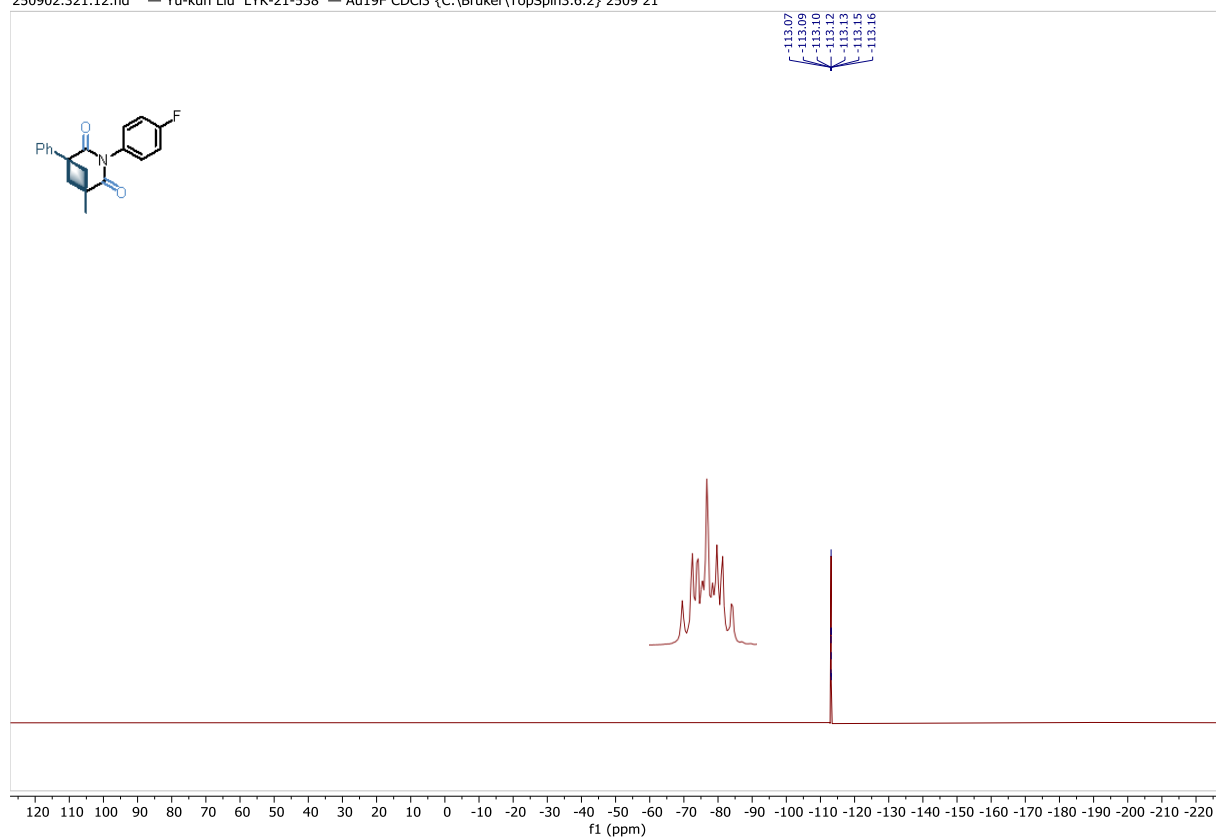
Supplementary Fig. 129. ^{13}C NMR spectrum of **4f** (75 MHz, CDCl_3)

250902.321.11.fid — Yu-kun Liu LYK-21-538 — Au13C CDCl_3 {C:\Bruker\TopSpin3.6.2} 2509 21



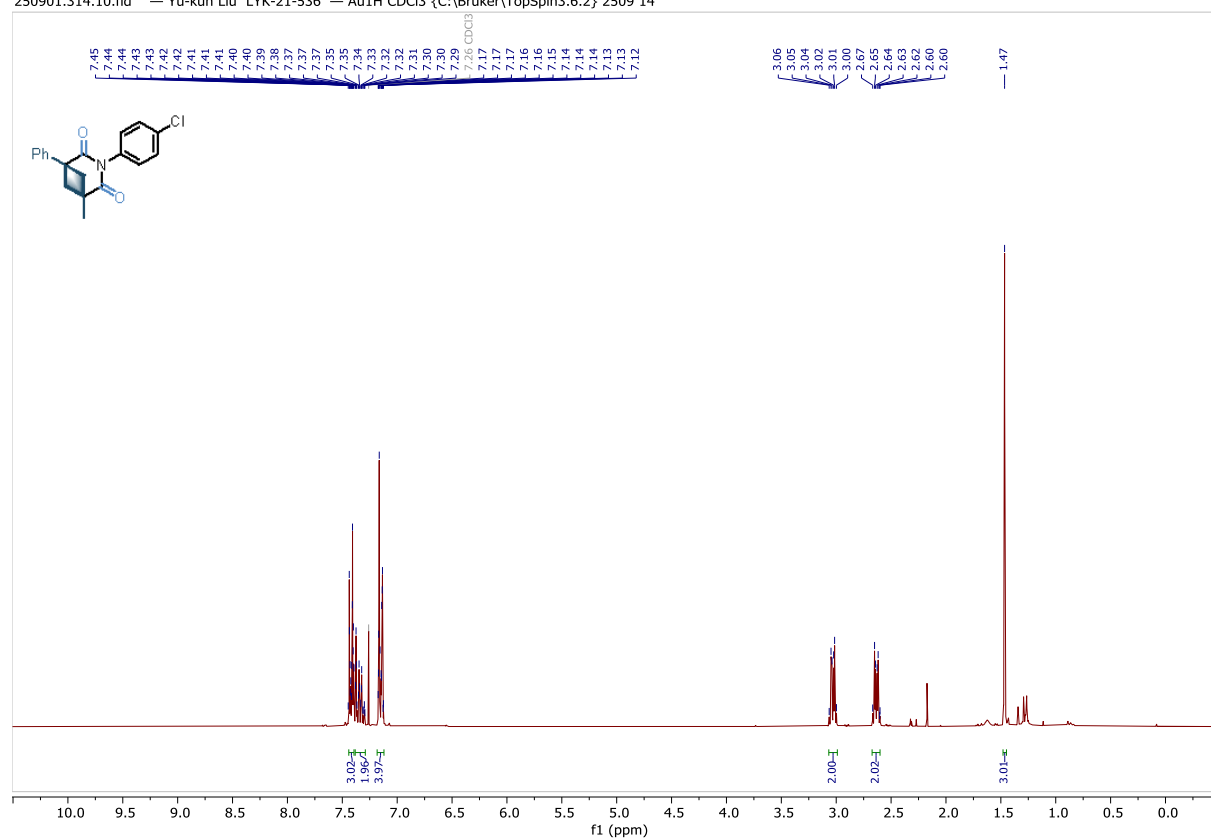
Supplementary Fig. 130. ^{19}F NMR spectrum of **4f** (282 MHz, CDCl_3)

250902.321.12.fid — Yu-kun Liu LYK-21-538 — Au19F CDCl_3 {C:\Bruker\TopSpin3.6.2} 2509 21



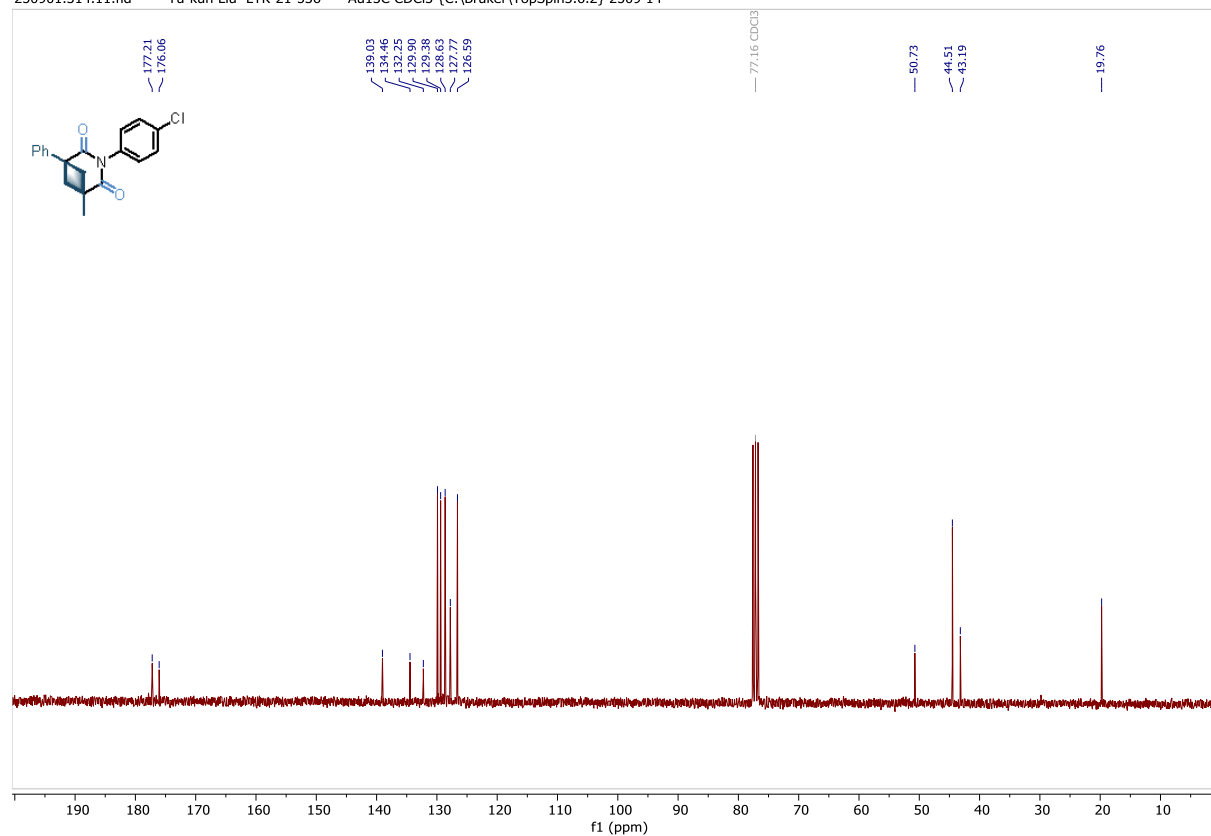
Supplementary Fig. 131. ^1H NMR spectrum of **4g** (300 MHz, CDCl_3)

250901.314.10.fid — Yu-kun Liu LYK-21-536 — Au1H CDCl_3 {C:\Bruker\TopSpin3.6.2} 2509 14



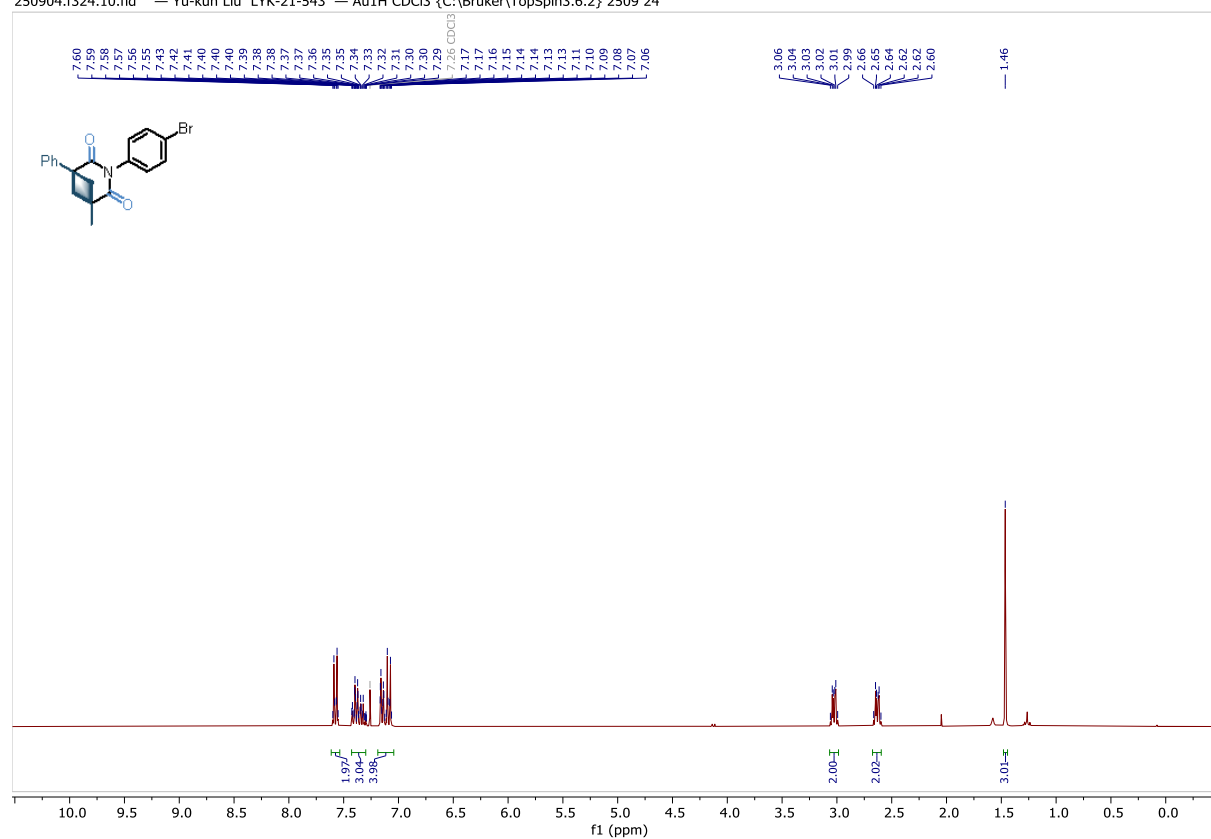
Supplementary Fig. 132. ^{13}C NMR spectrum of **4g** (75 MHz, CDCl_3)

250901.314.11.fid — Yu-kun Liu LYK-21-536 — Au13C CDCl_3 {C:\Bruker\TopSpin3.6.2} 2509 14



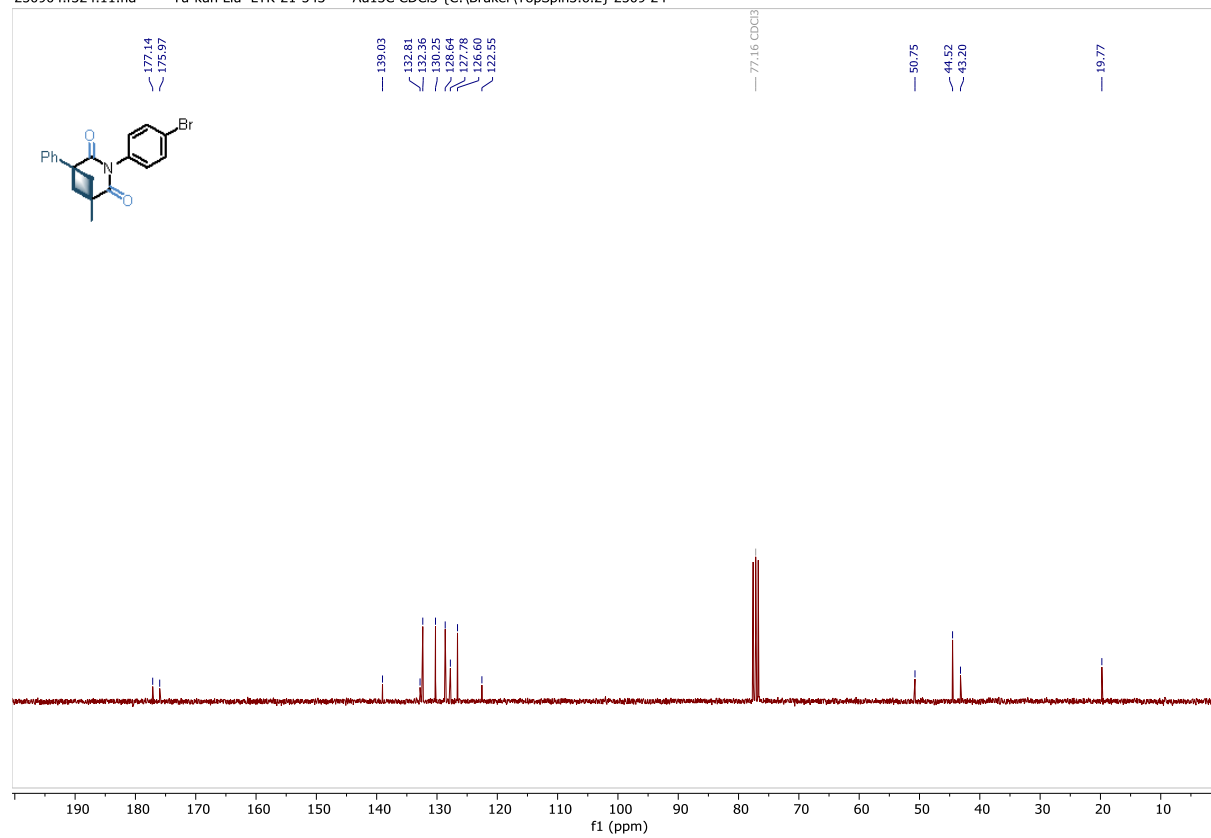
Supplementary Fig. 133. ^1H NMR spectrum of **4h** (300 MHz, CDCl_3)

250904.f324.10.fid — Yu-kun Liu LYK-21-543 — Au1H CDCl_3 {C:\Bruker\TopSpin3.6.2} 2509 24



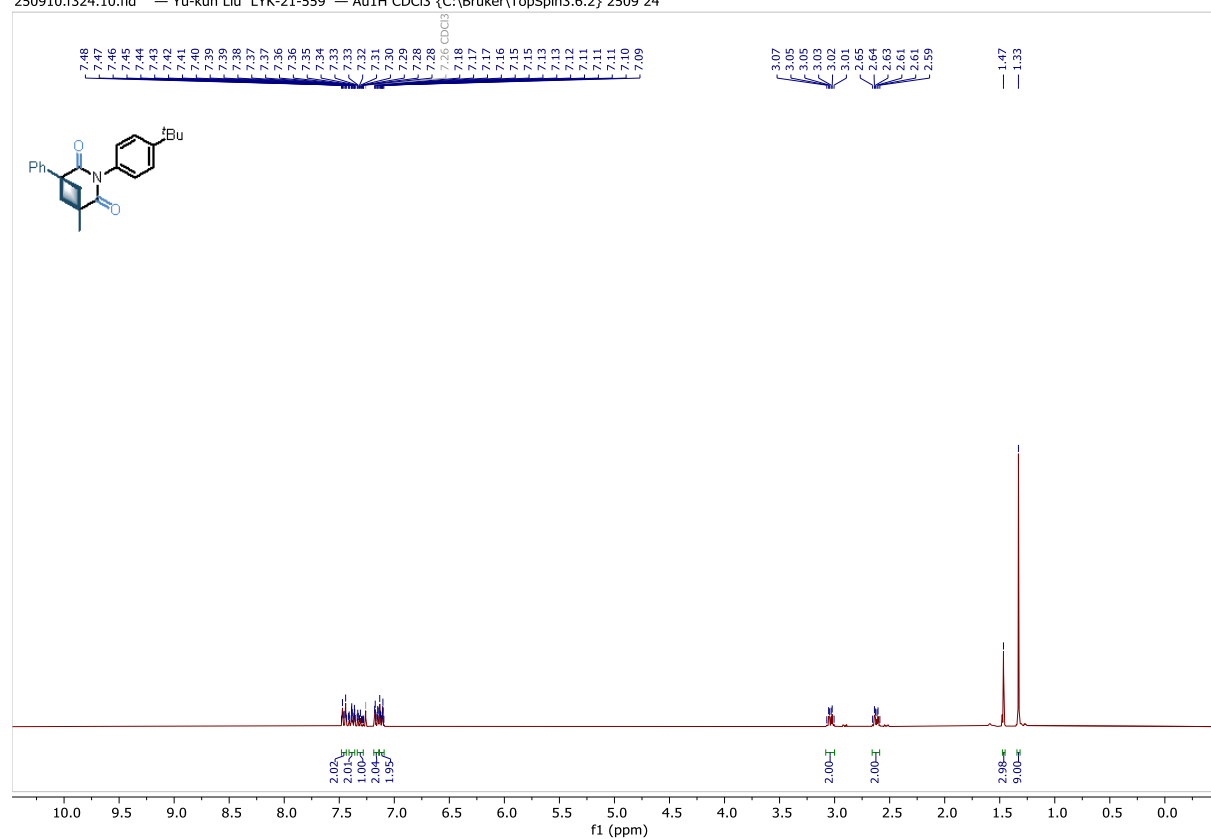
Supplementary Fig. 134. ^{13}C NMR spectrum of **4h** (75 MHz, CDCl_3)

250904.f324.11.fid — Yu-kun Liu LYK-21-543 — Au13C CDCl_3 {C:\Bruker\TopSpin3.6.2} 2509 24



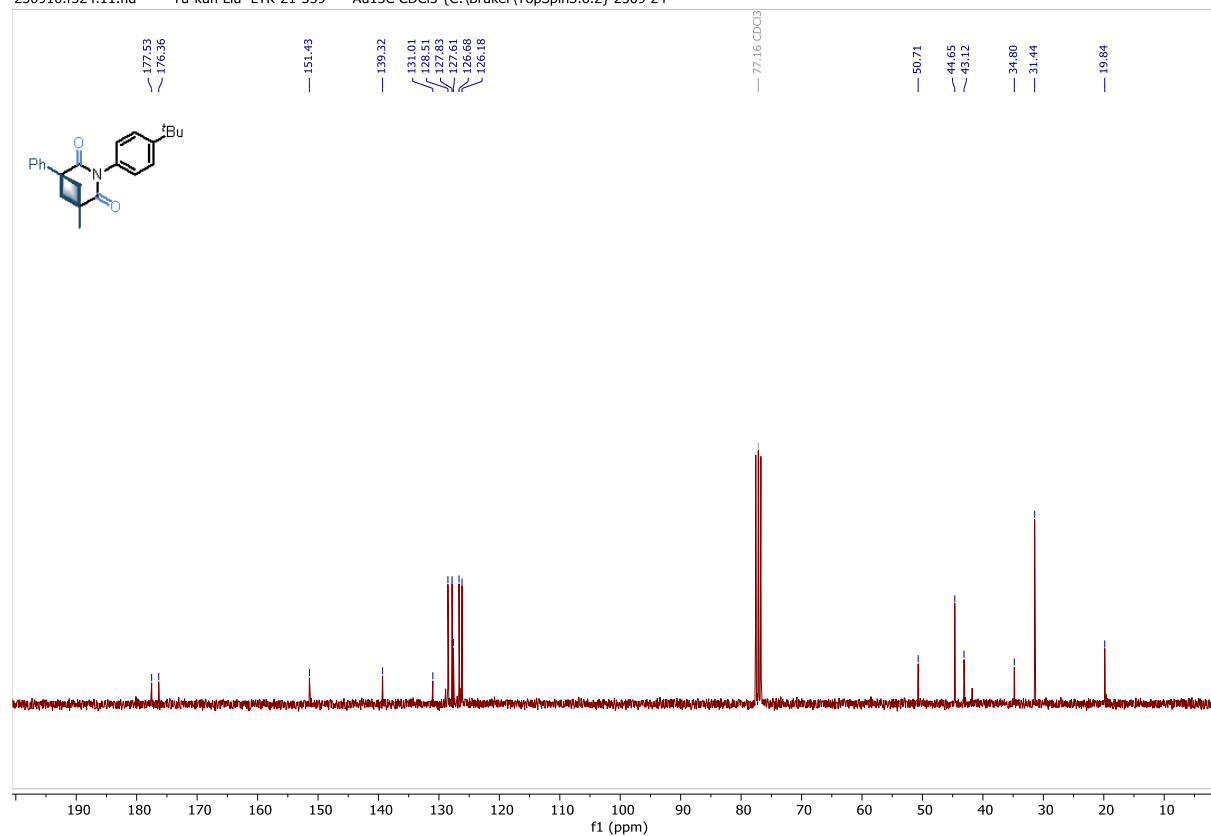
Supplementary Fig. 135. ^1H NMR spectrum of **4i** (300 MHz, CDCl_3)

250910.f324.10.fid — Yu-kun Liu LYK-21-559 — Au1H CDCl_3 {C:\Bruker\TopSpin3.6.2} 2509 24



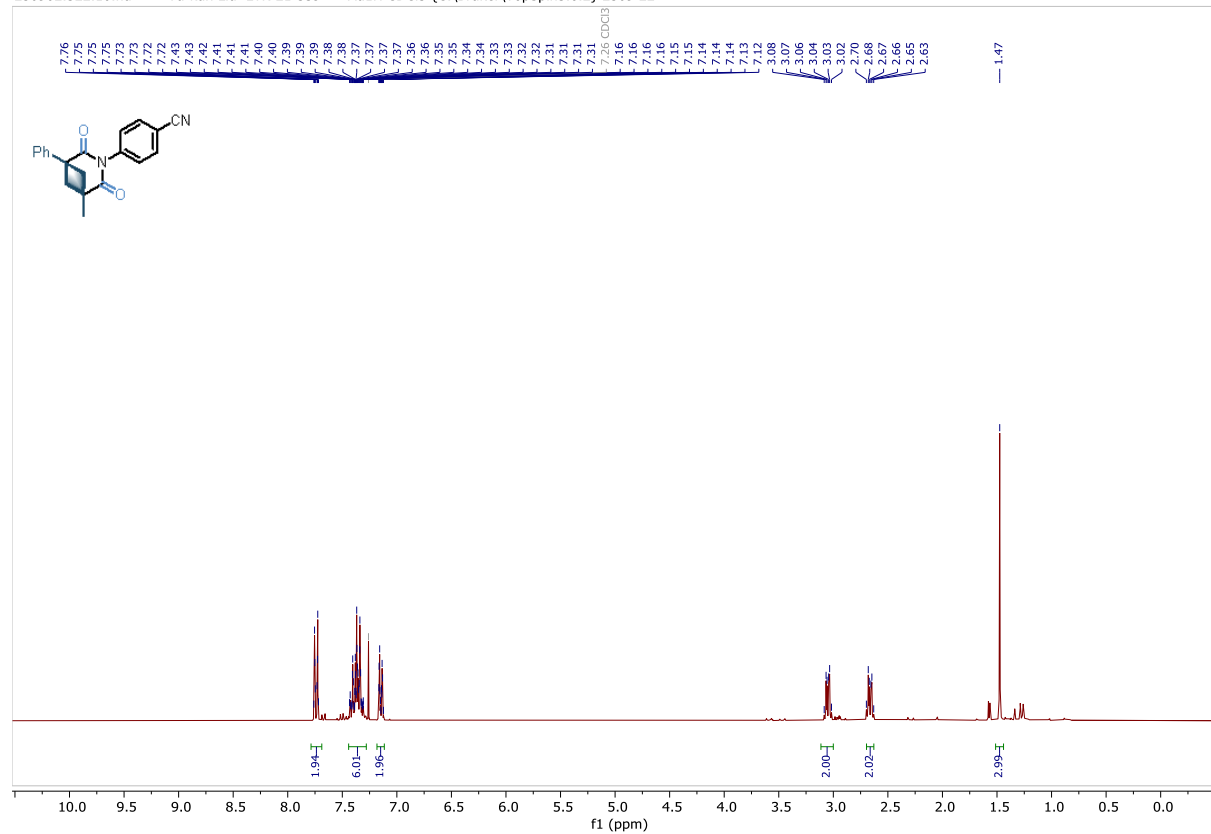
Supplementary Fig. 136. ^{13}C NMR spectrum of **4i** (75 MHz, CDCl_3)

250910.f324.11.fid — Yu-kun Liu LYK-21-559 — Au13C CDCl_3 {C:\Bruker\TopSpin3.6.2} 2509 24



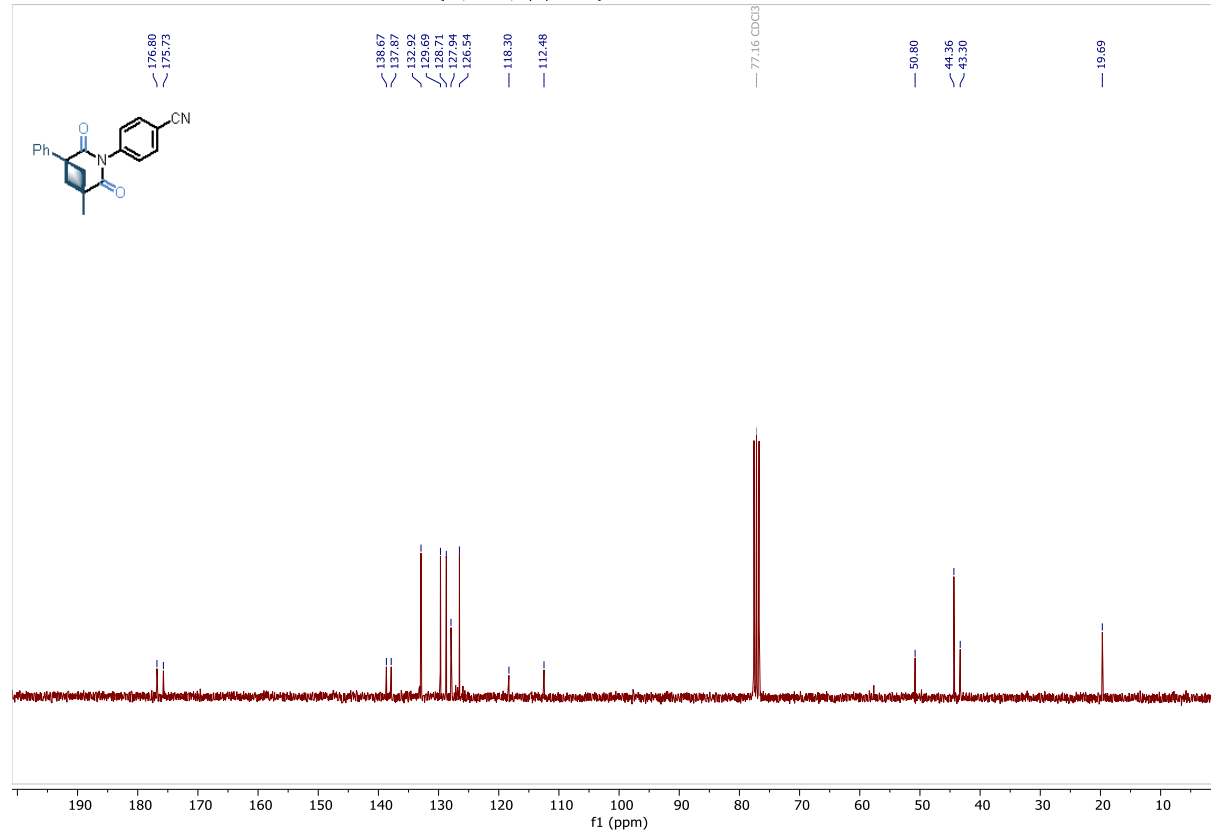
Supplementary Fig. 137. ^1H NMR spectrum of **4j** (300 MHz, CDCl_3)

250902.322:10.fid — Yu-kun Liu LYK-21-539 — Au1H CDCl3 {C:\Bruker\TopSpin3.6.2} 2509 22



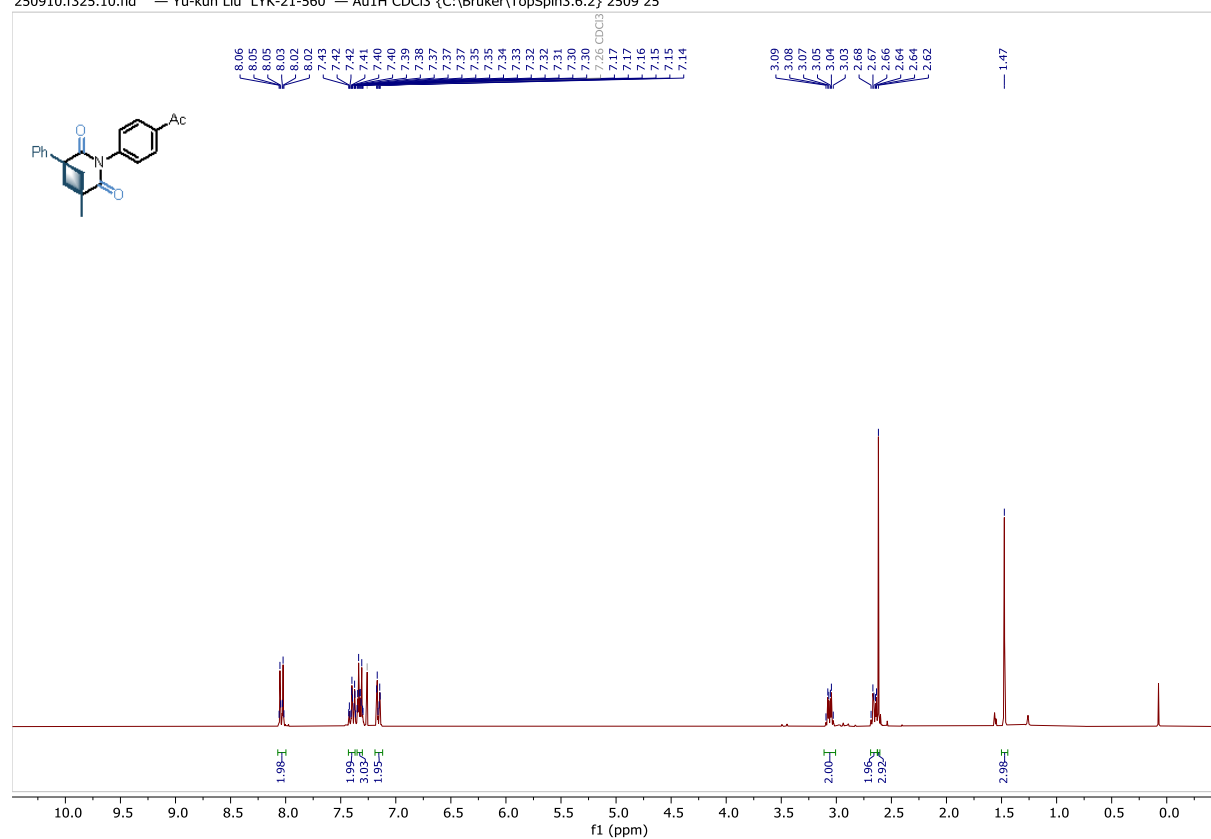
Supplementary Fig. 138. ^{13}C NMR spectrum of **4j** (75 MHz, CDCl_3)

250902.322.11.fid — Yu-kun Liu LYK-21-539 — Au13C CDCl3 {C:\Bruker\TopSpin3.6.2} 2509 22



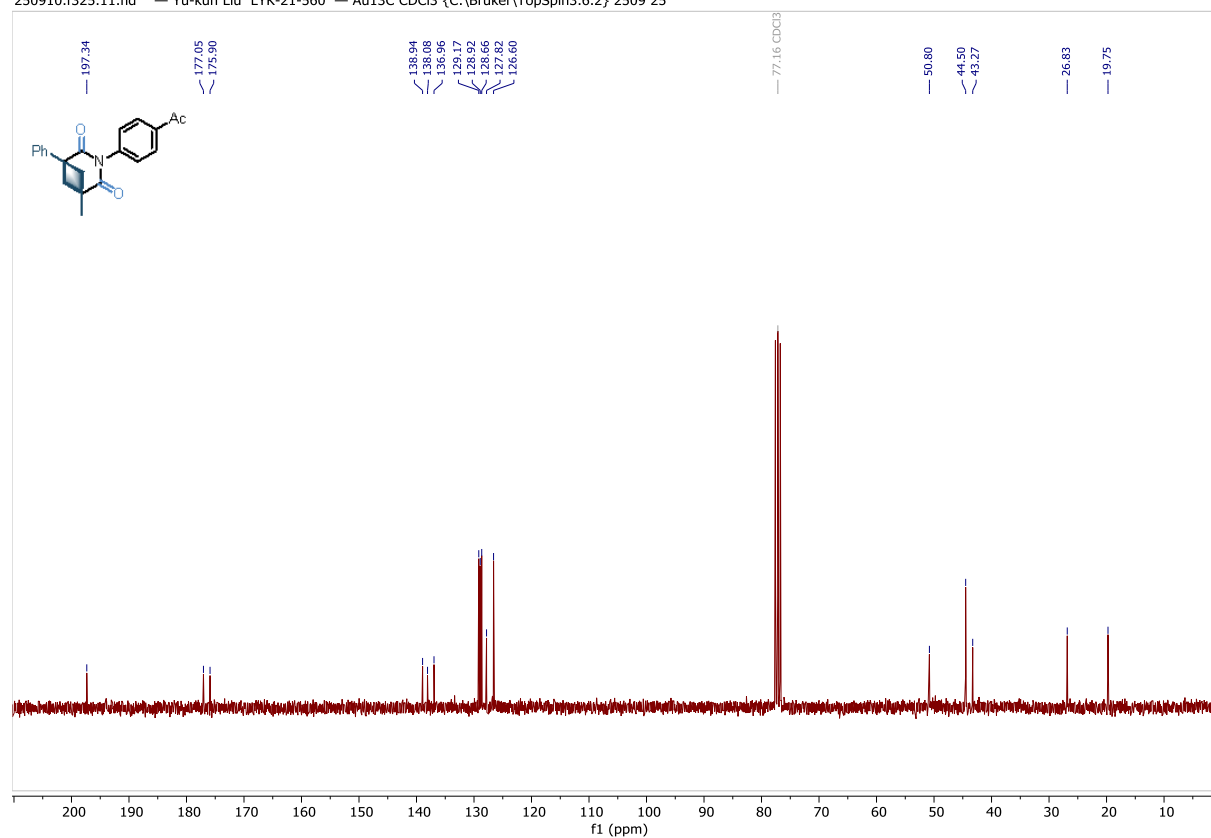
Supplementary Fig. 139. ^1H NMR spectrum of **4k** (300 MHz, CDCl_3)

250910.f325.10.fid — Yu-kun Liu LYK-21-560 — Au1H CDCl_3 {C:\Bruker\TopSpin3.6.2} 2509 25



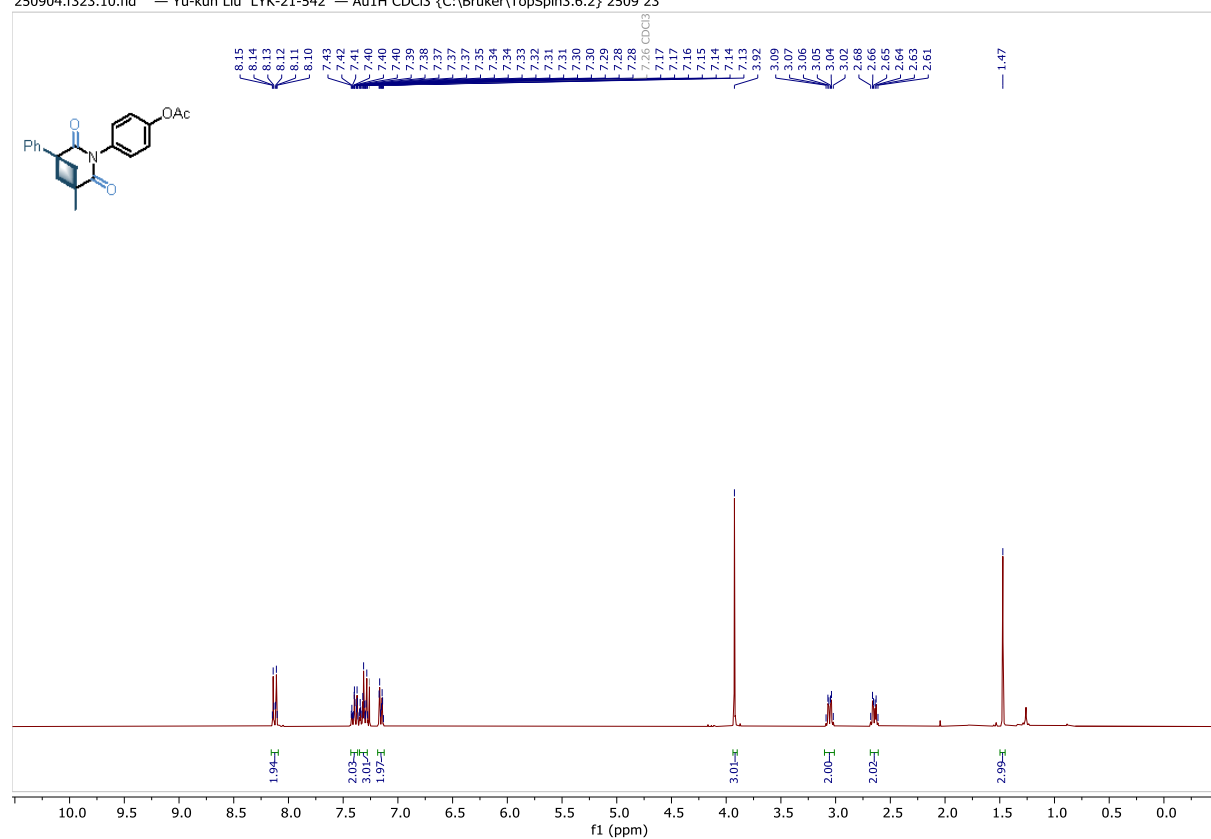
Supplementary Fig. 140. ^{13}C NMR spectrum of **4k** (75 MHz, CDCl_3)

250910.f325.11.fid — Yu-kun Liu LYK-21-560 — Au13C CDCl_3 {C:\Bruker\TopSpin3.6.2} 2509 25



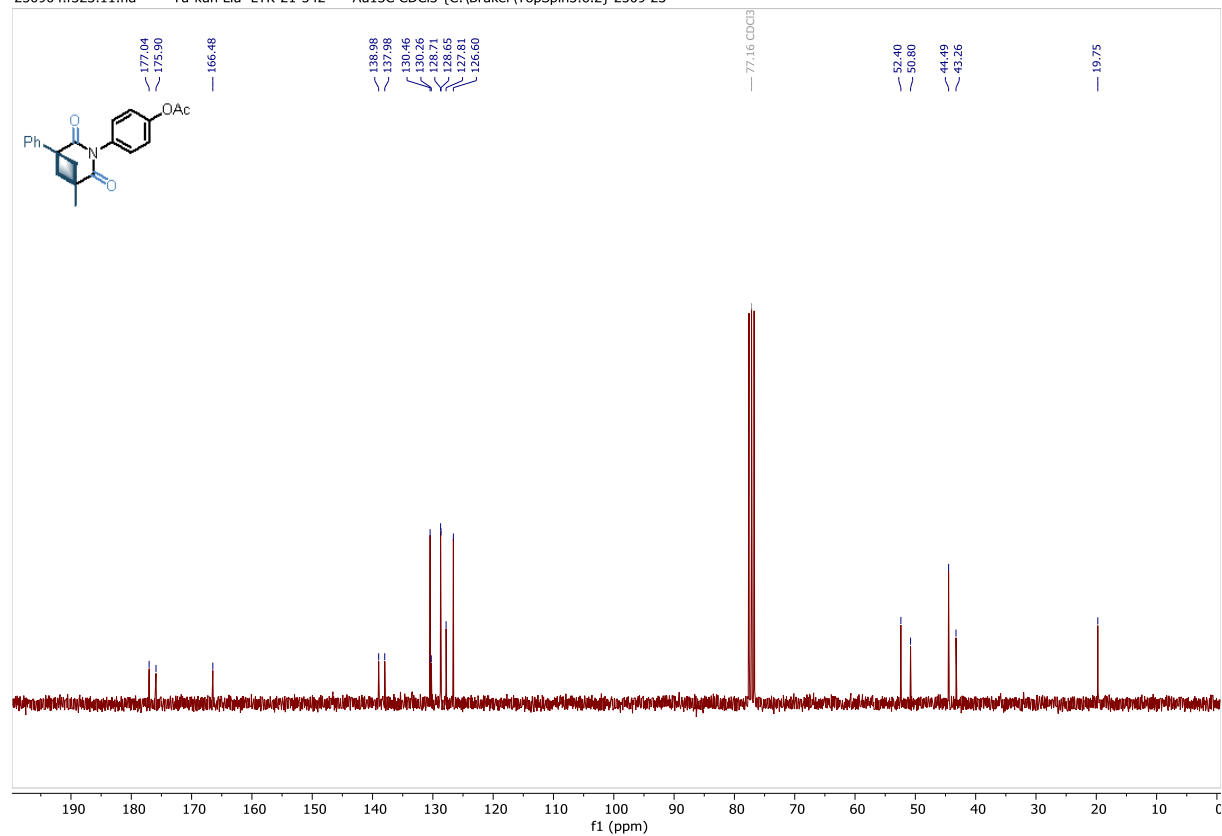
Supplementary Fig. 141. ^1H NMR spectrum of **4I** (300 MHz, CDCl_3)

250904.f323.10.fid — Yu-kun Liu LYK-21-542 — Au1H CDCl_3 {C:\Bruker\TopSpin3.6.2} 2509 23



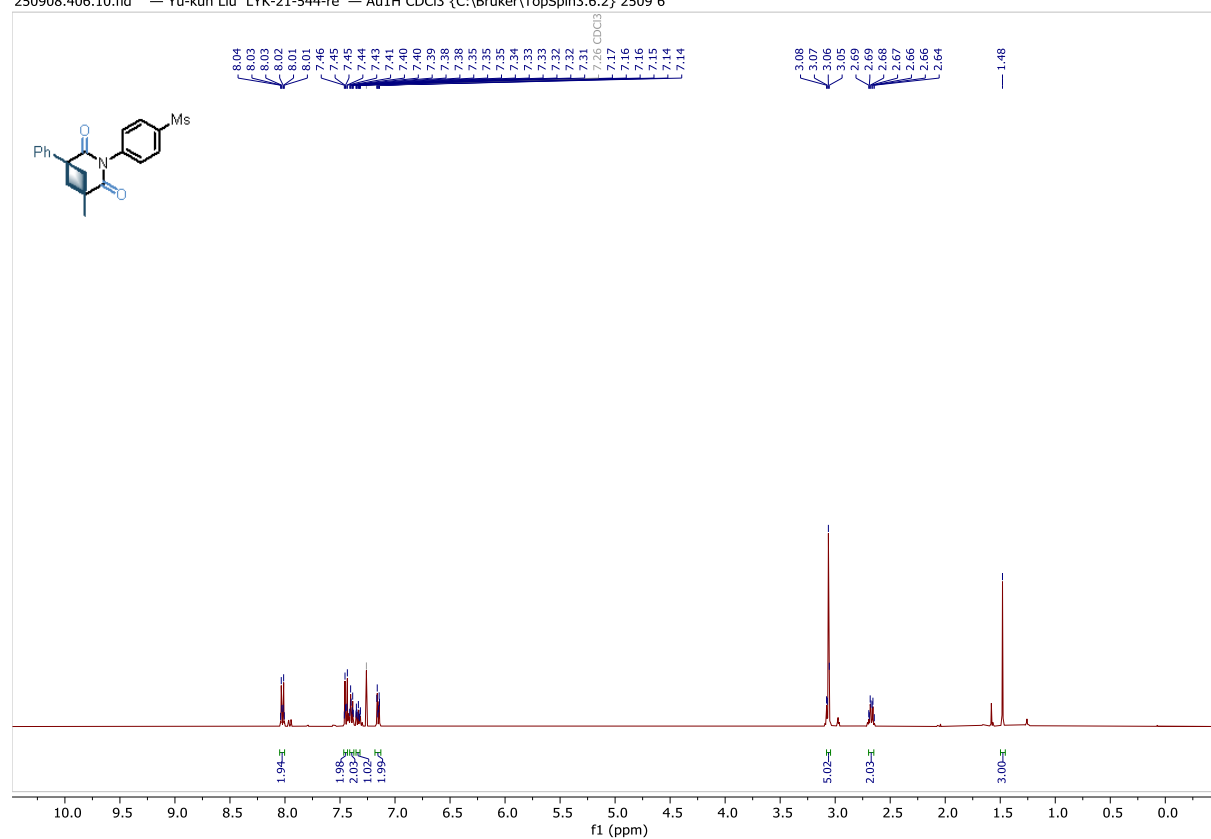
Supplementary Fig. 142. ^{13}C NMR spectrum of **4I** (75 MHz, CDCl_3)

250904.f323.11.fid — Yu-kun Liu LYK-21-542 — Au13C CDCl_3 {C:\Bruker\TopSpin3.6.2} 2509 23



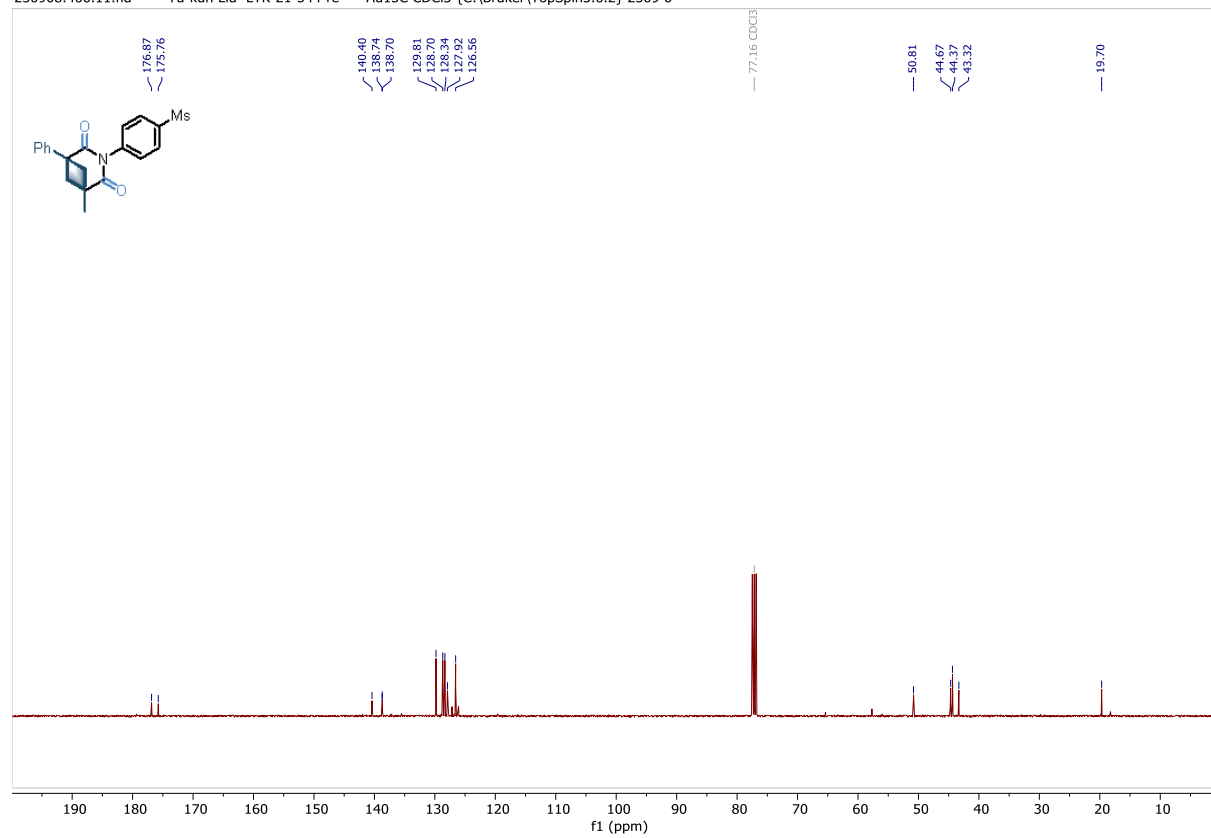
Supplementary Fig. 143. ^1H NMR spectrum of **4m** (400 MHz, CDCl_3)

250908.406.10.fid — Yu-kun Liu LYK-21-544-re — Au1H CDCl_3 {C:\Bruker\TopSpin3.6.2} 2509 6



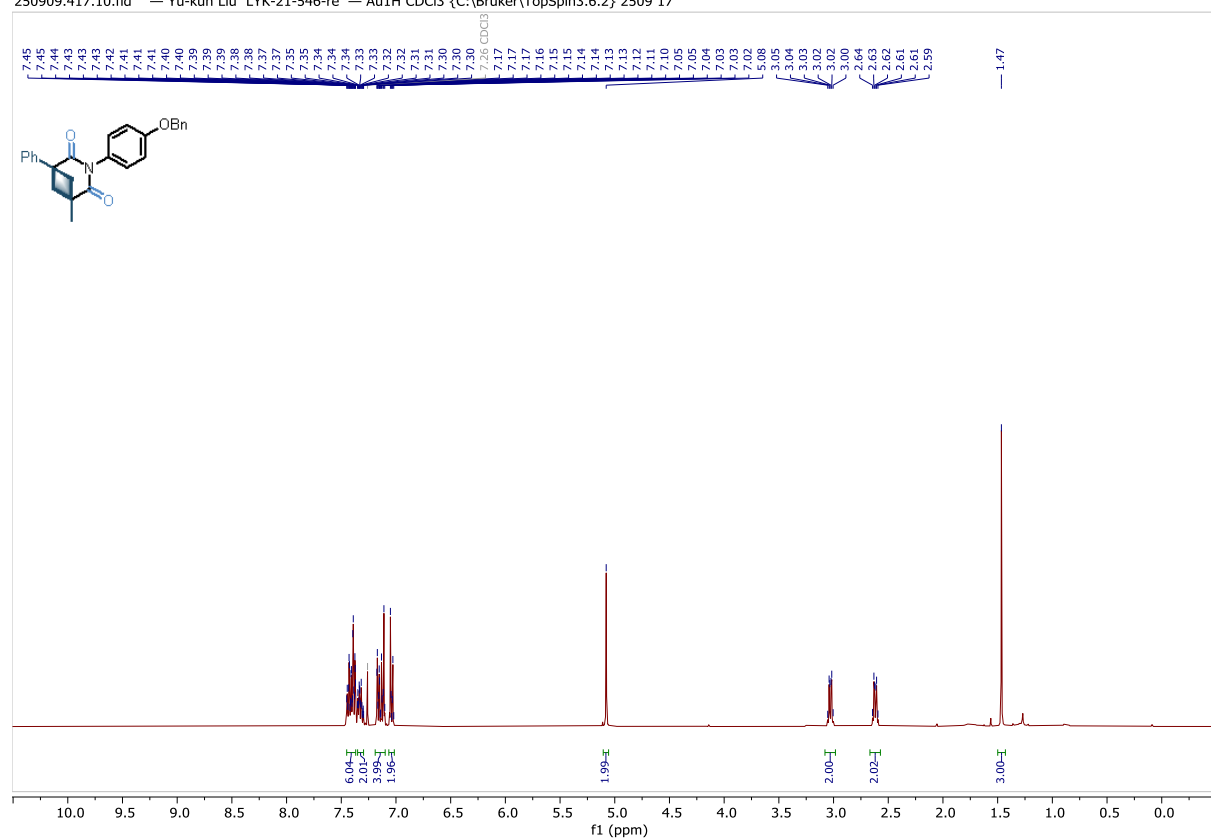
Supplementary Fig. 144. ^{13}C NMR spectrum of **4m** (101 MHz, CDCl_3)

250908.406.11.fid — Yu-kun Liu LYK-21-544-re — Au13C CDCl_3 {C:\Bruker\TopSpin3.6.2} 2509 6



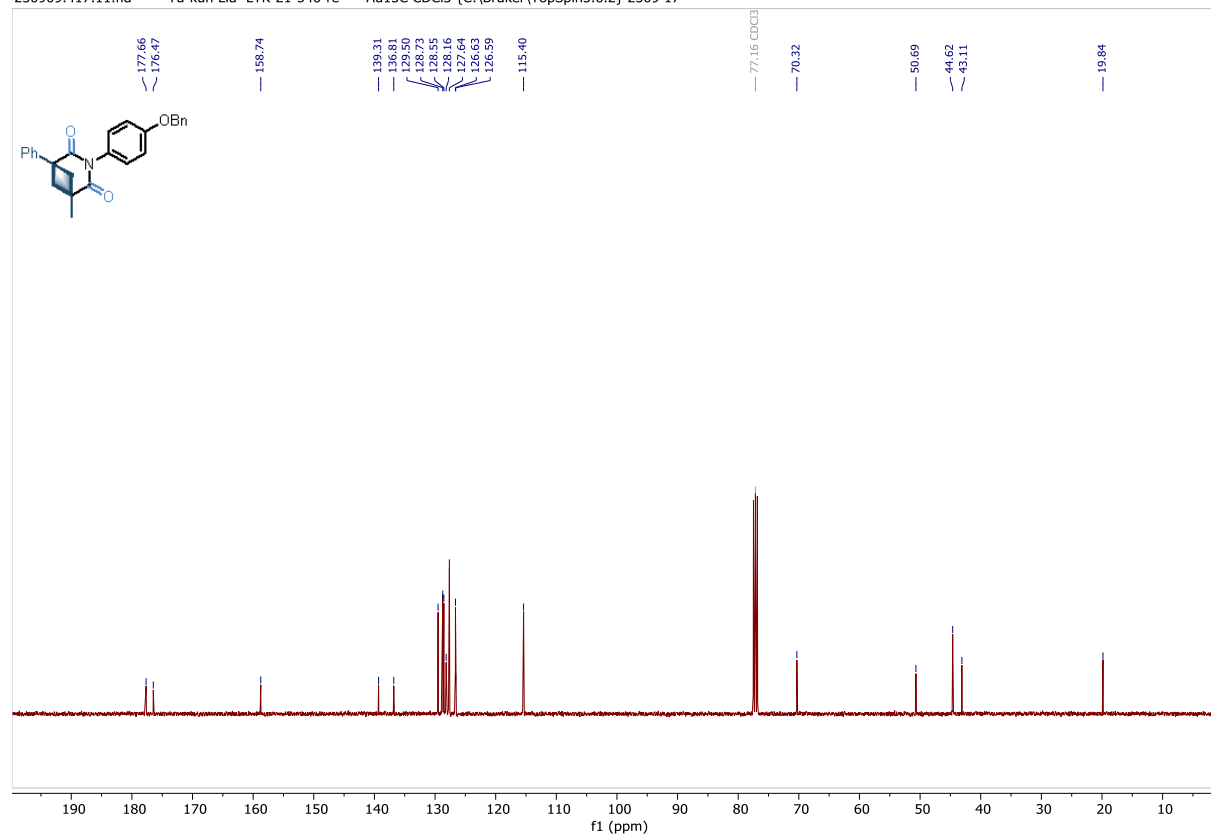
Supplementary Fig. 145. ^1H NMR spectrum of **4n** (400 MHz, CDCl_3)

250909.417.10.fid — Yu-kun Liu LYK-21-546-re — Au1H CDCl_3 {C:\Bruker\TopSpin3.6.2} 2509 17



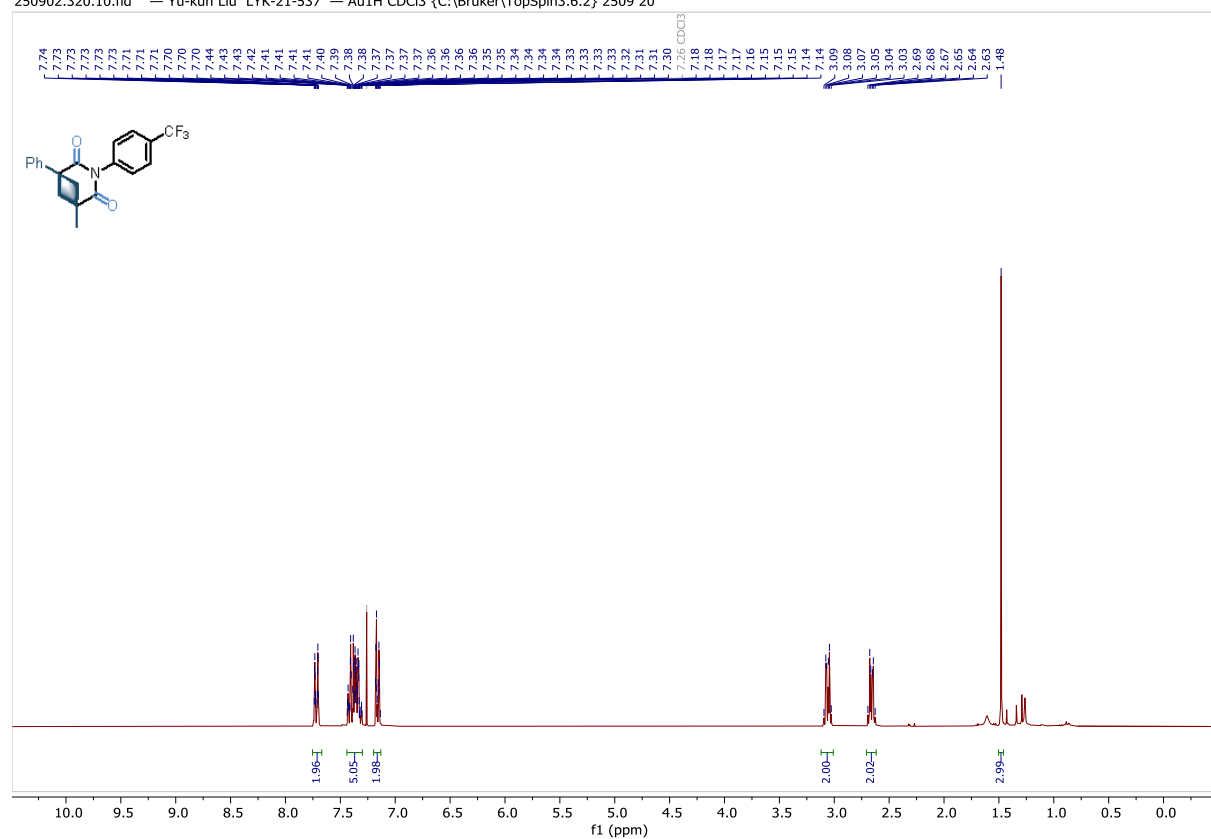
Supplementary Fig. 146. ^{13}C NMR spectrum of **4n** (101 MHz, CDCl_3)

250909.417.11.fid — Yu-kun Liu LYK-21-546-re — Au13C CDCl_3 {C:\Bruker\TopSpin3.6.2} 2509 17



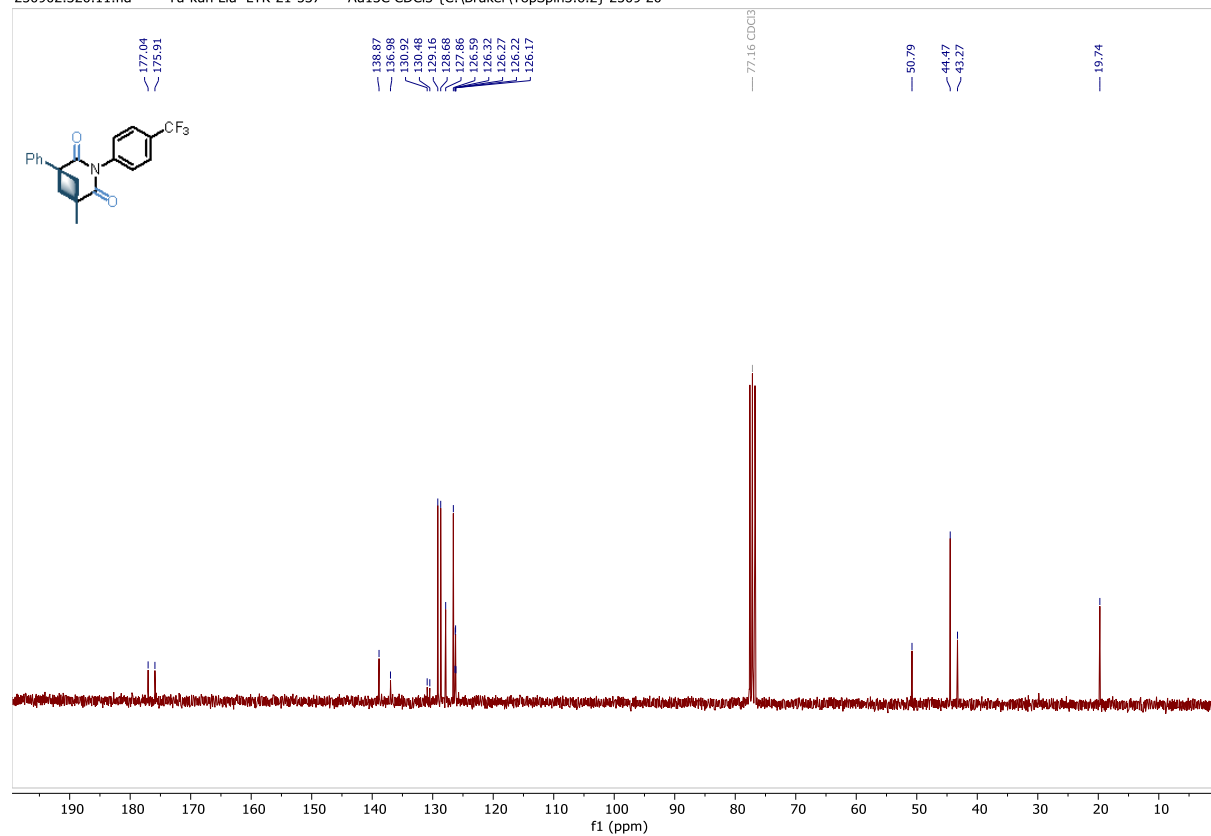
Supplementary Fig. 147. ^1H NMR spectrum of **4o** (300 MHz, CDCl_3)

250902.320.10.fid — Yu-kun Liu LYK-21-537 — Au1H CDCl_3 {C:\Bruker\TopSpin3.6.2} 2509 20



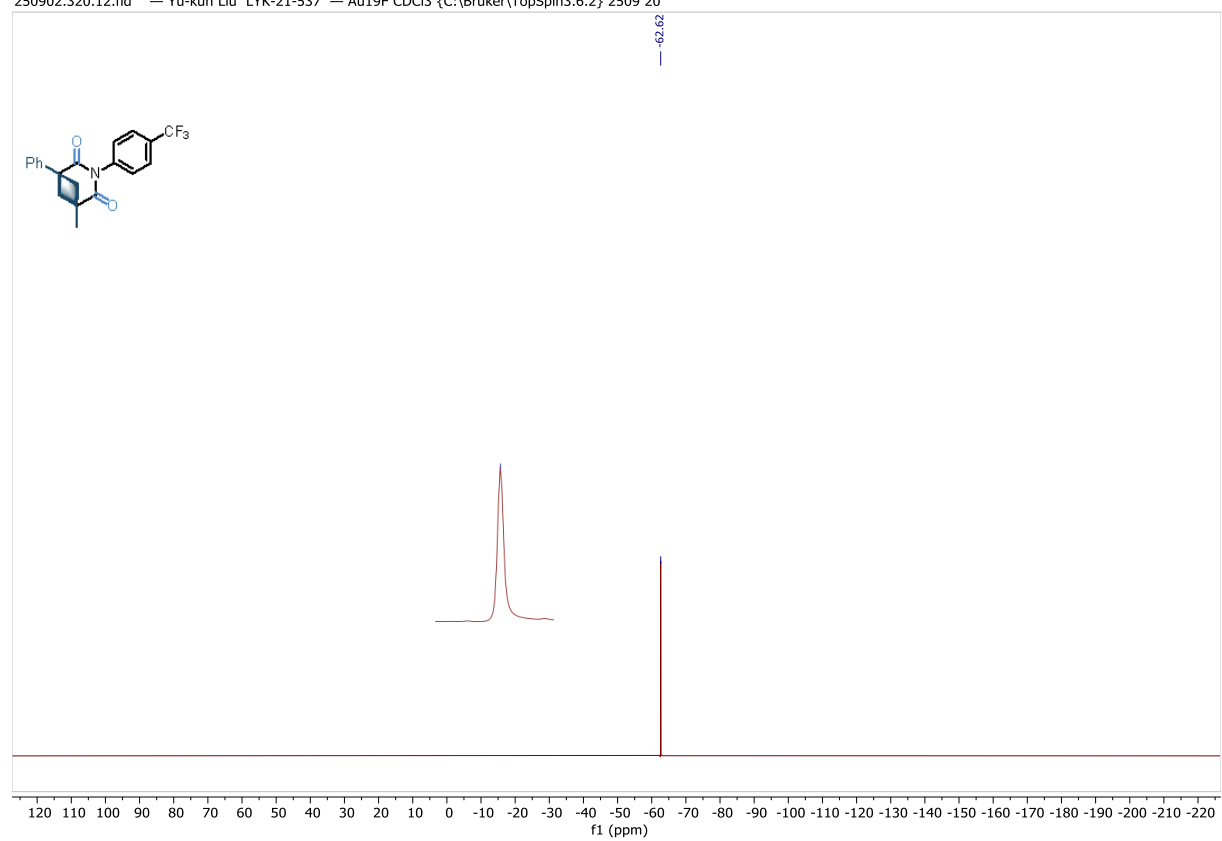
Supplementary Fig. 148. ^{13}C NMR spectrum of **4o** (75 MHz, CDCl_3)

250902.320.11.fid — Yu-kun Liu LYK-21-537 — Au13C CDCl_3 {C:\Bruker\TopSpin3.6.2} 2509 20



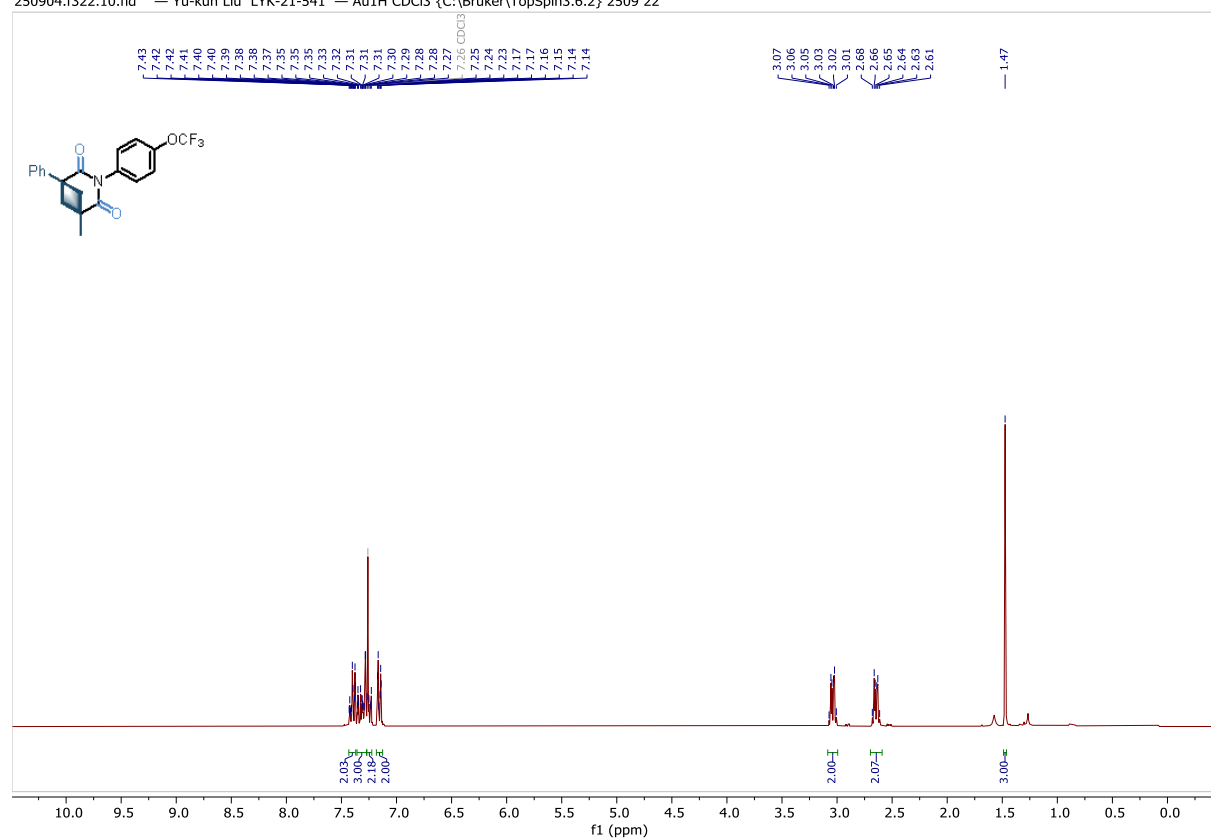
Supplementary Fig. 149. ^{19}F NMR spectrum of **4o** (282 MHz, CDCl_3)

250902.320.12.fid — Yu-kun Liu LYK-21-537 — Au19F CDCl3 {C:\Bruker\TopSpin3.6.2} 2509 20



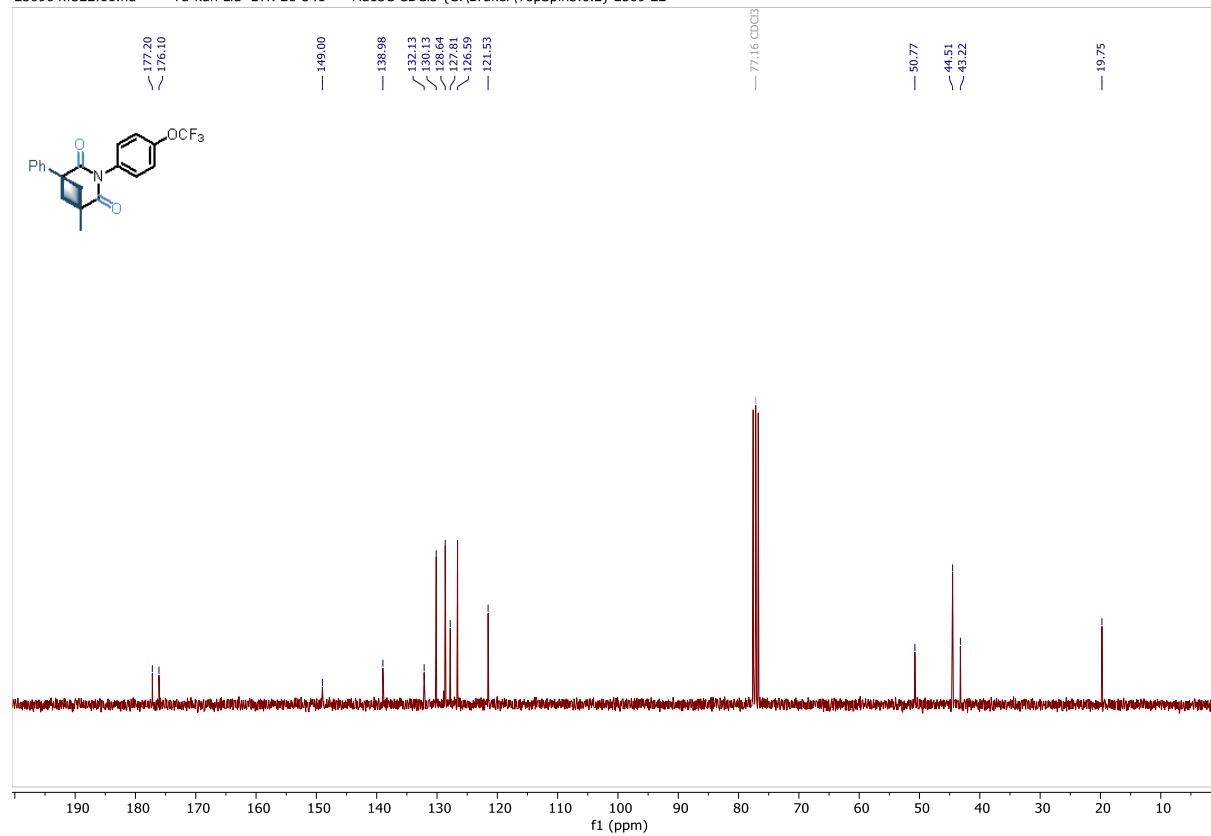
Supplementary Fig. 150. ^1H NMR spectrum of **4p** (300 MHz, CDCl_3)

250904.f322.10.fid — Yu-kun Liu LYK-21-541 — Au1H CDCl_3 {C:\Bruker\TopSpin3.6.2} 2509 22



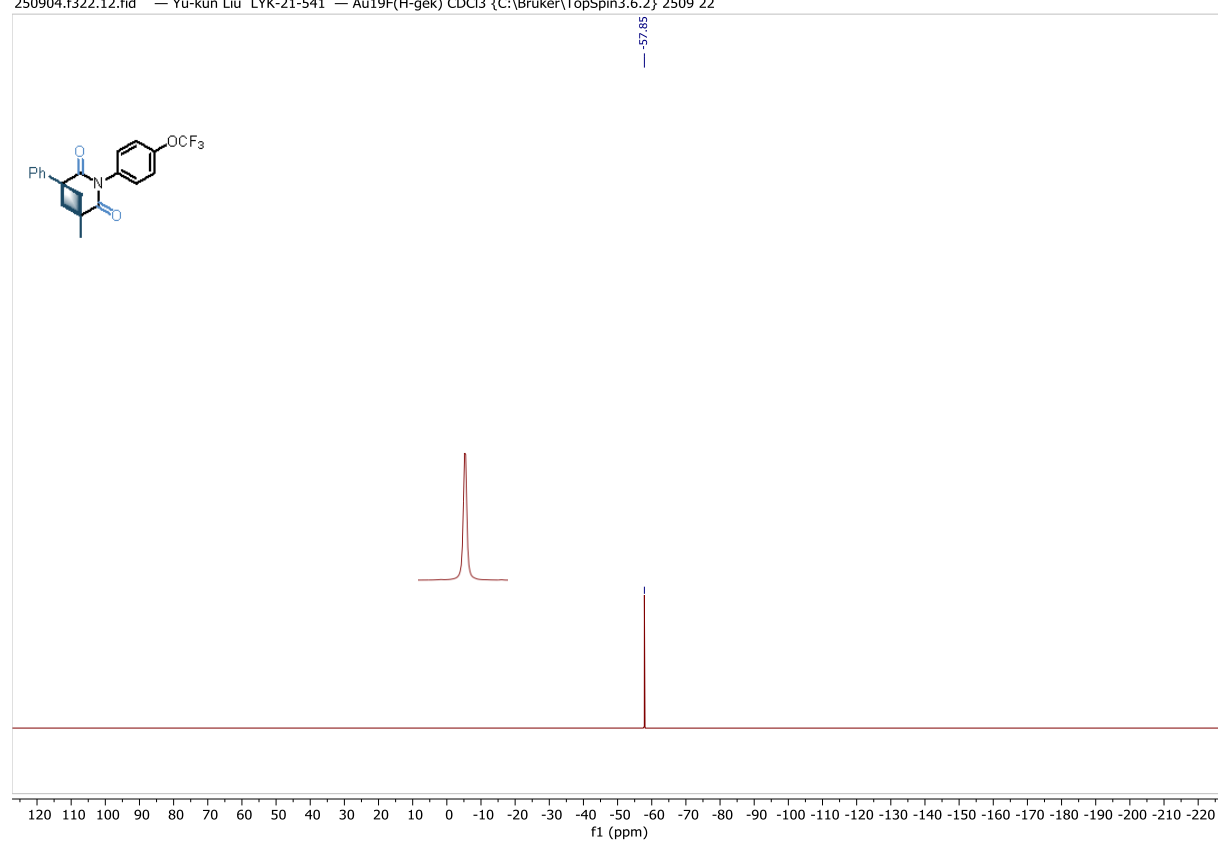
Supplementary Fig. 151. ^{13}C NMR spectrum of **4p** (75 MHz, CDCl_3)

250904.f322.11.fid — Yu-kun Liu LYK-21-541 — Au13C CDCl_3 {C:\Bruker\TopSpin3.6.2} 2509 22

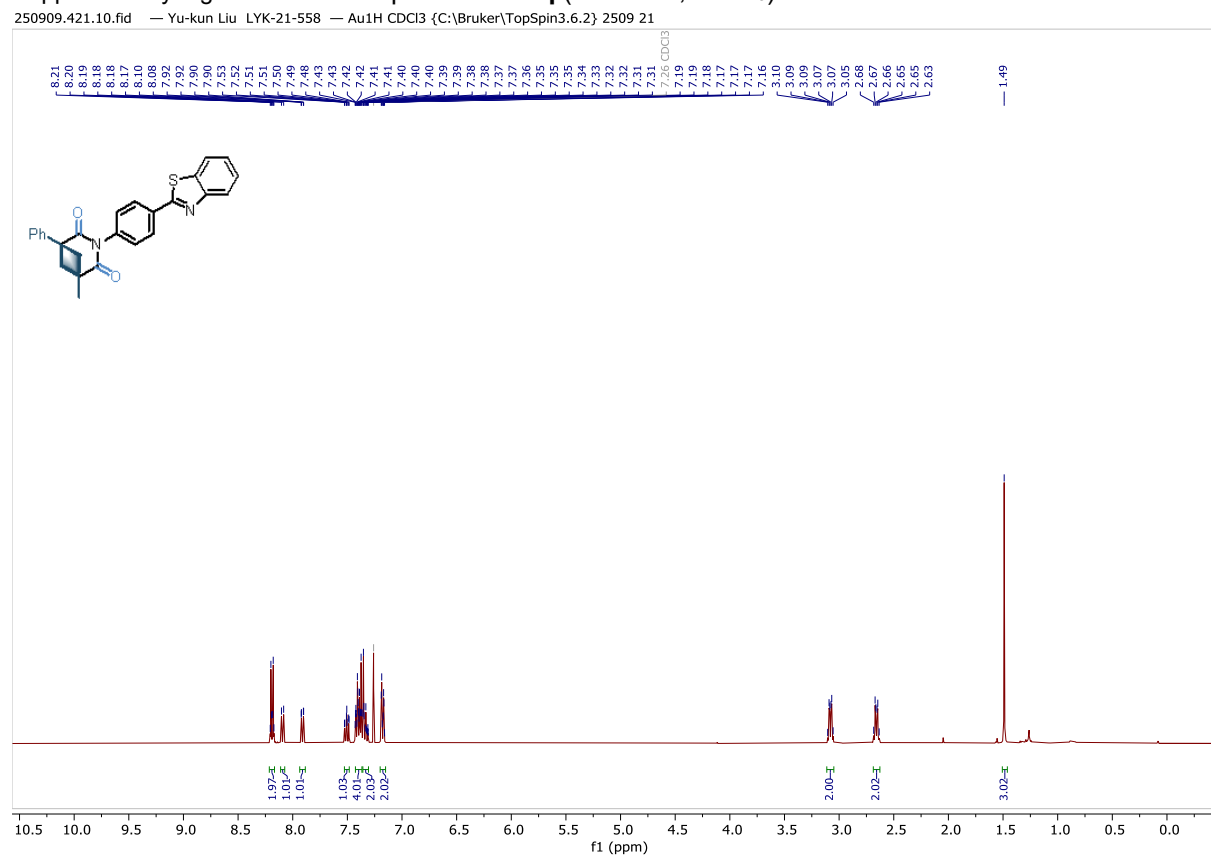


Supplementary Fig. 152. ^{19}F NMR spectrum of **4p** (282 MHz, CDCl_3)

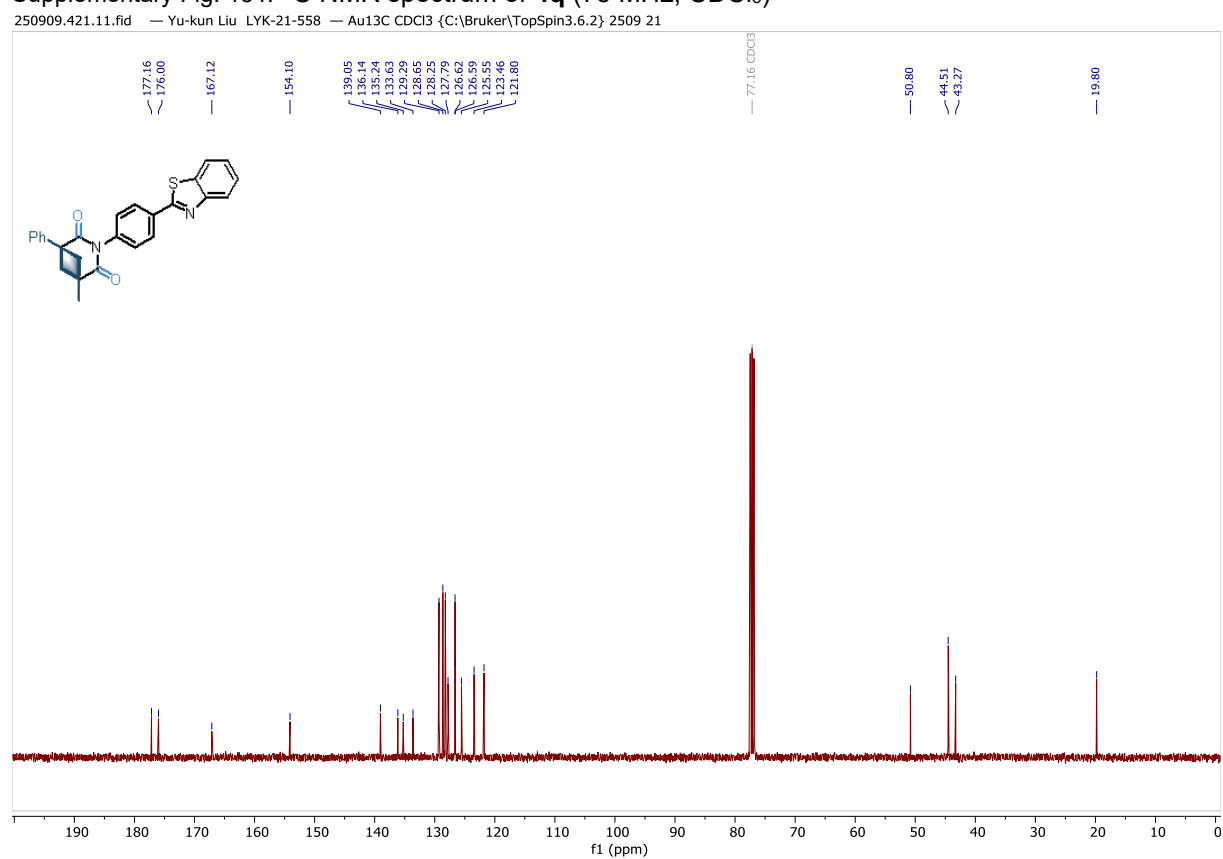
250904.f322.12.fid — Yu-kun Liu LYK-21-541 — Au19F(H-gek) CDCl_3 {C:\Bruker\TopSpin3.6.2} 2509 22



Supplementary Fig. 153. ^1H NMR spectrum of **4q** (300 MHz, CDCl_3)

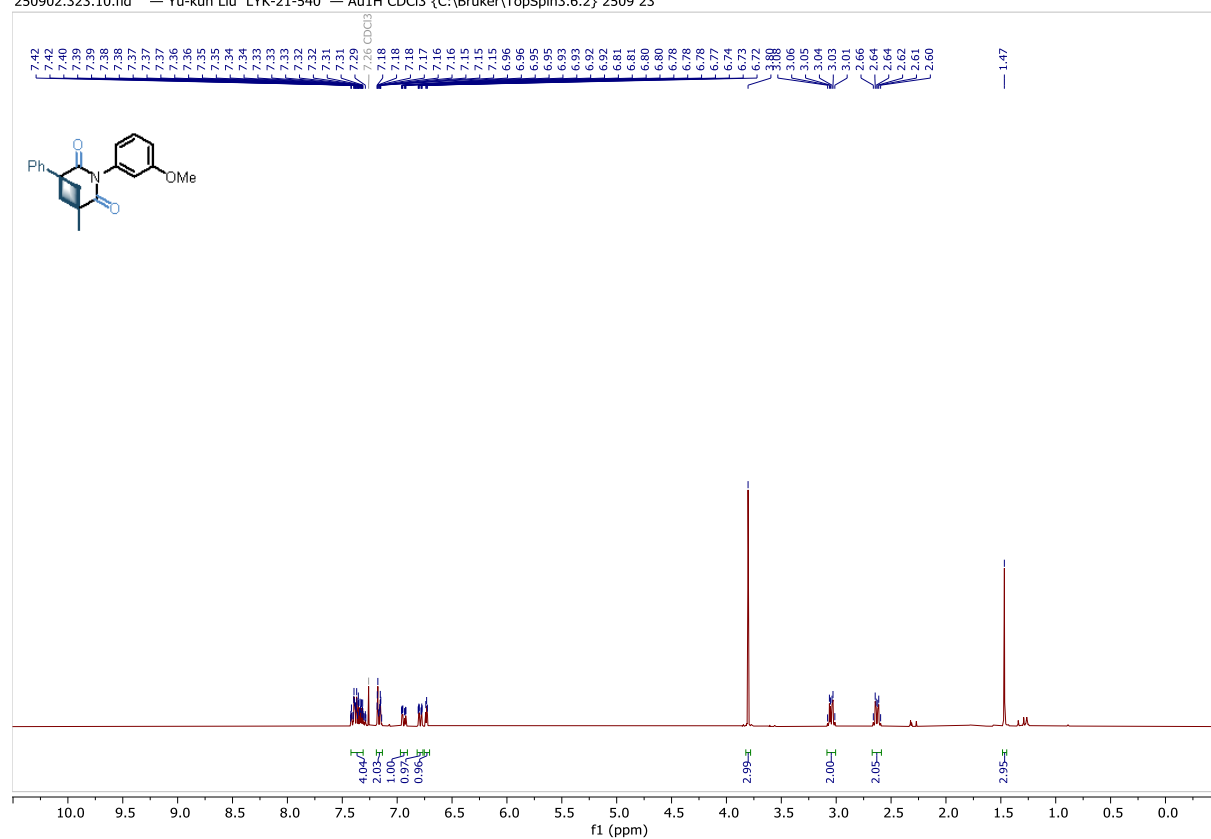


Supplementary Fig. 154. ^{13}C NMR spectrum of **4q** (75 MHz, CDCl_3)



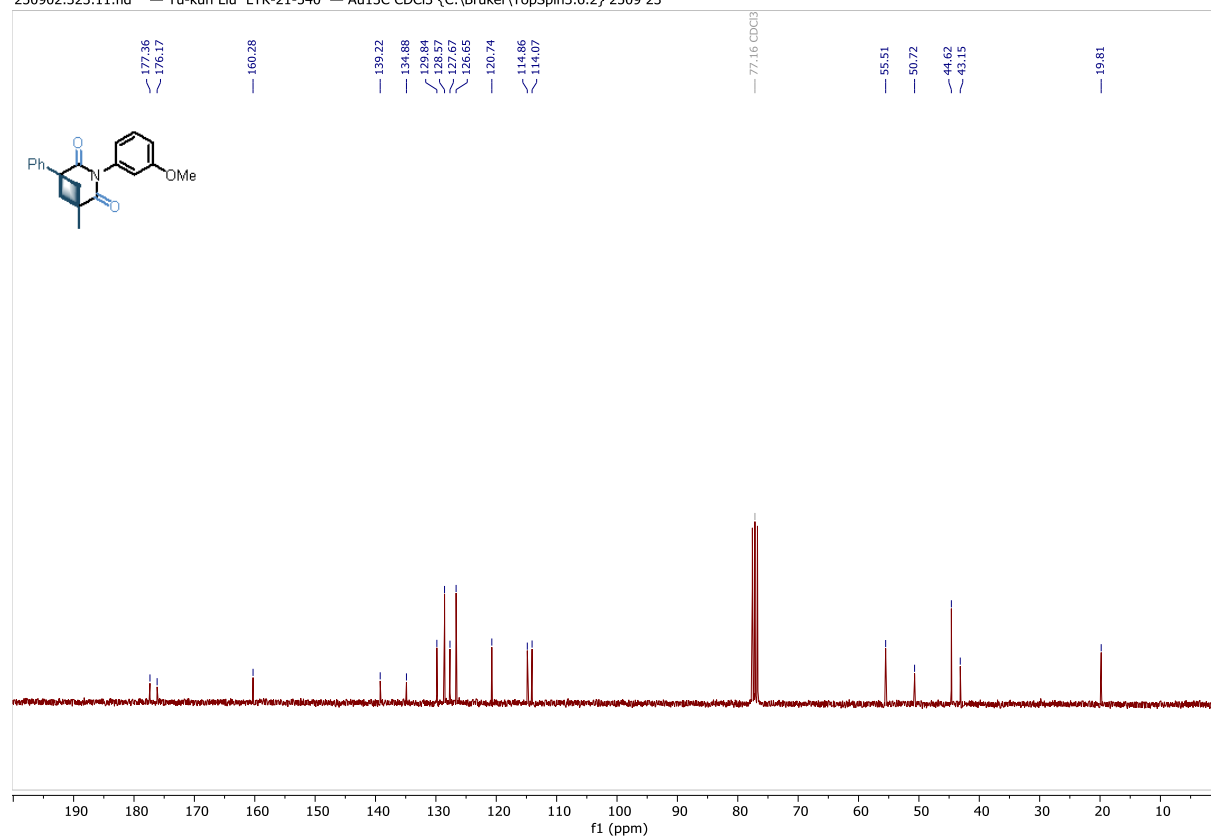
Supplementary Fig. 155. ^1H NMR spectrum of **4r** (300 MHz, CDCl_3)

250902.323.10.fid — Yu-kun Liu LYK-21-540 — Au1H CDCl_3 {C:\Bruker\TopSpin3.6.2} 2509 23

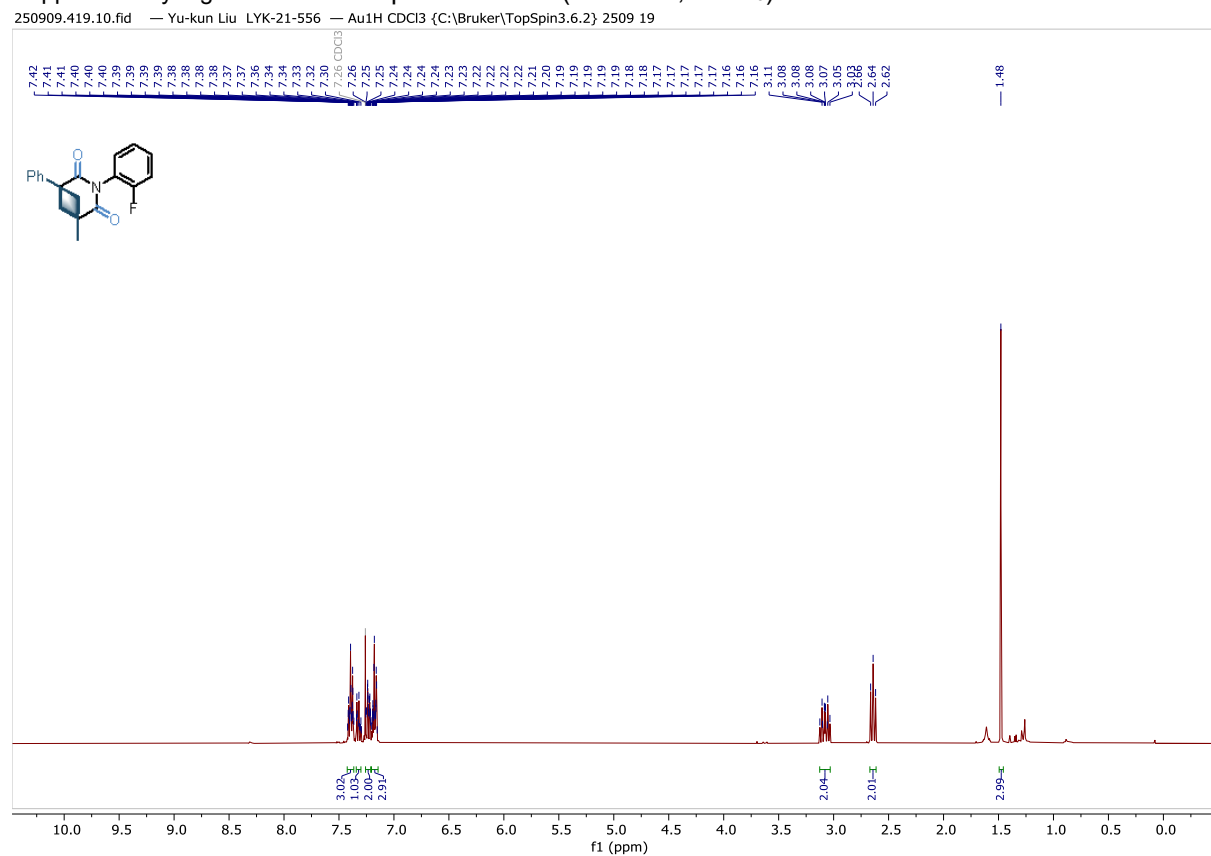


Supplementary Fig. 156. ^{13}C NMR spectrum of **4r** (75 MHz, CDCl_3)

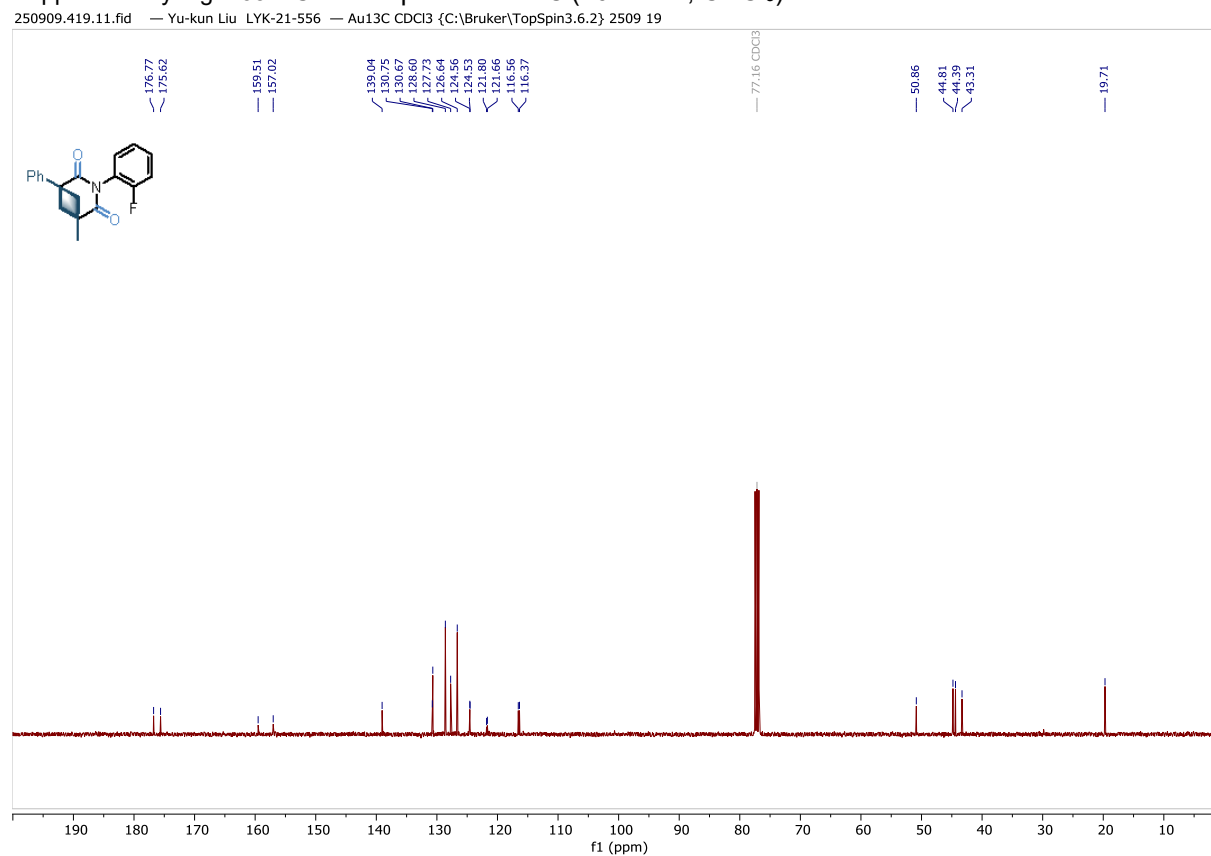
250902.323.11.fid — Yu-kun Liu LYK-21-540 — Au13C CDCl_3 {C:\Bruker\TopSpin3.6.2} 2509 23



Supplementary Fig. 157. ^1H NMR spectrum of **4s** (400 MHz, CDCl_3)

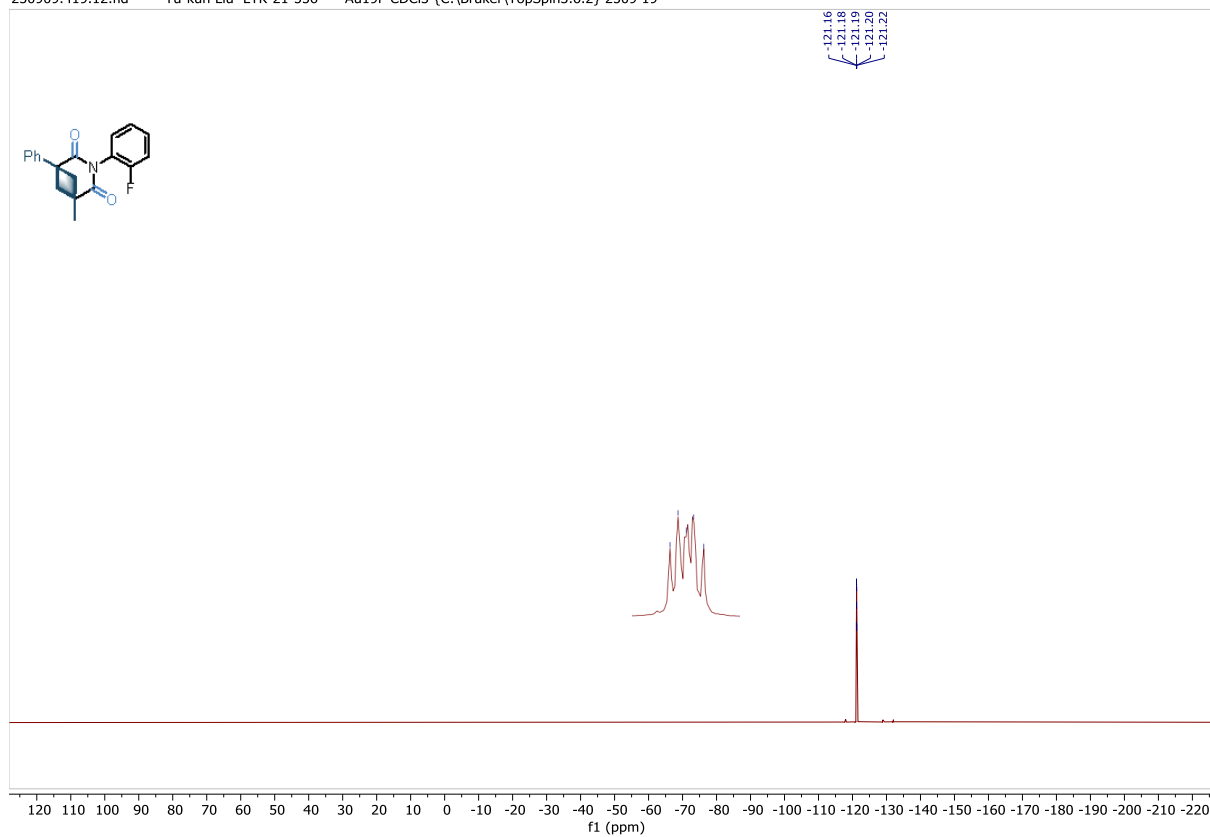


Supplementary Fig. 158. ^{13}C NMR spectrum of **4s** (101 MHz, CDCl_3)



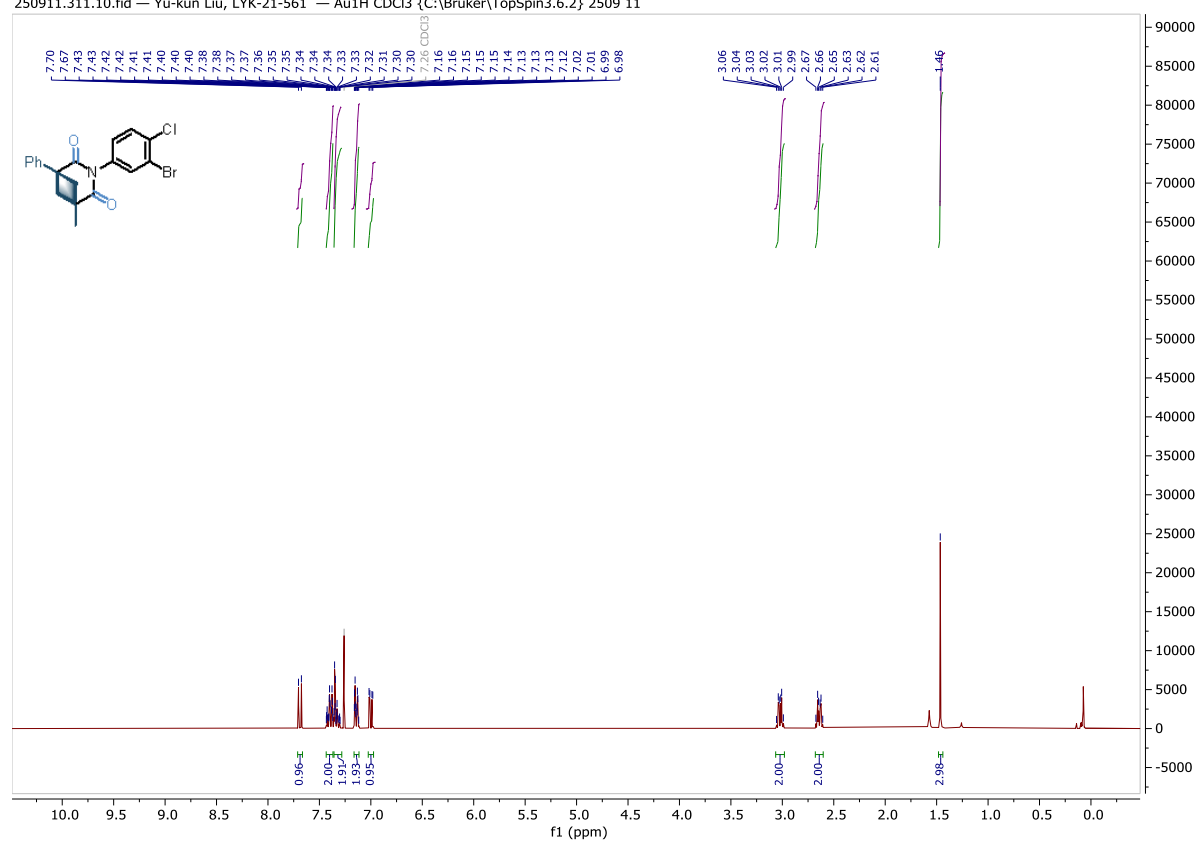
Supplementary Fig. 159. ^{19}F NMR spectrum of **4s** (376 MHz, CDCl_3)

250909.419.12.fid — Yu-kun Liu LYK-21-556 — Au19F CDCl_3 {C:\Bruker\TopSpin3.6.2} 2509 19



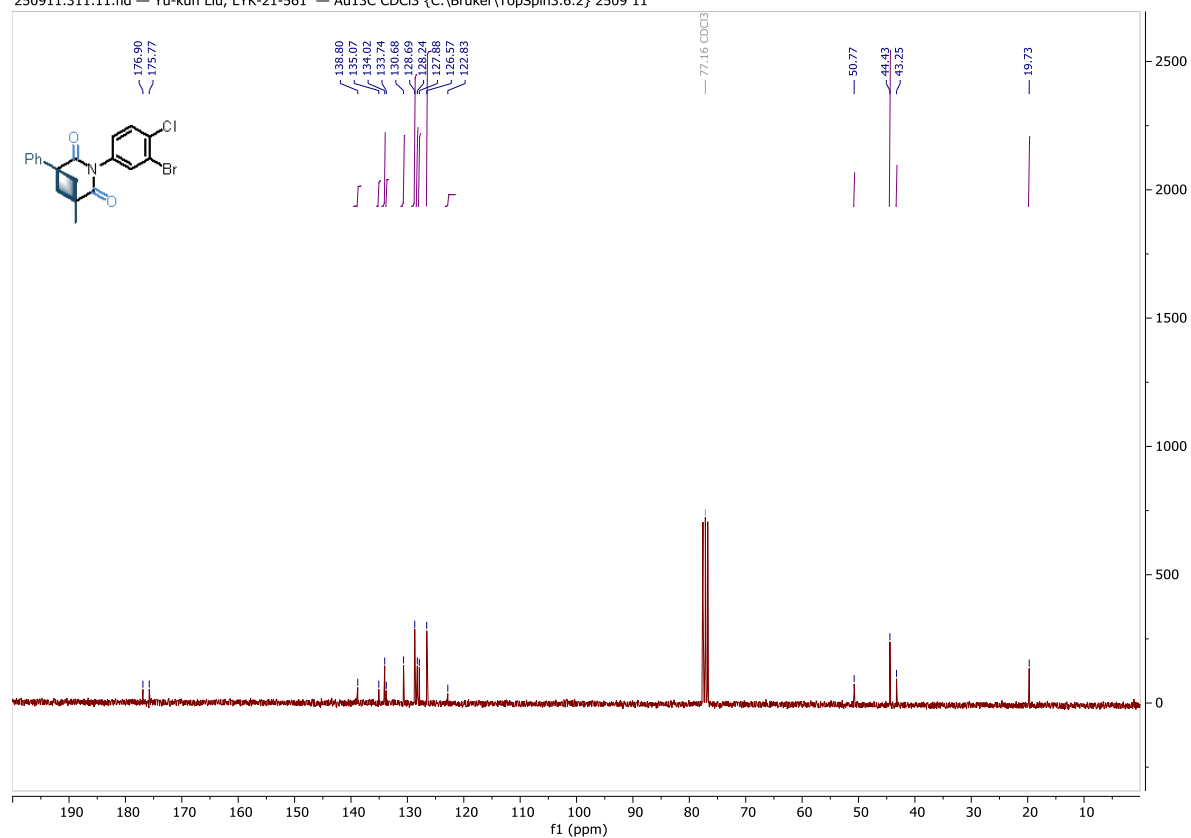
Supplementary Fig. 160. ^1H NMR spectrum of **4t** (300 MHz, CDCl_3)

250911.311.10.fid — Yu-kun Liu, LYK-21-561 — Au1H CDCl_3 {C:\Bruker\TopSpin3.6.2} 2509 11



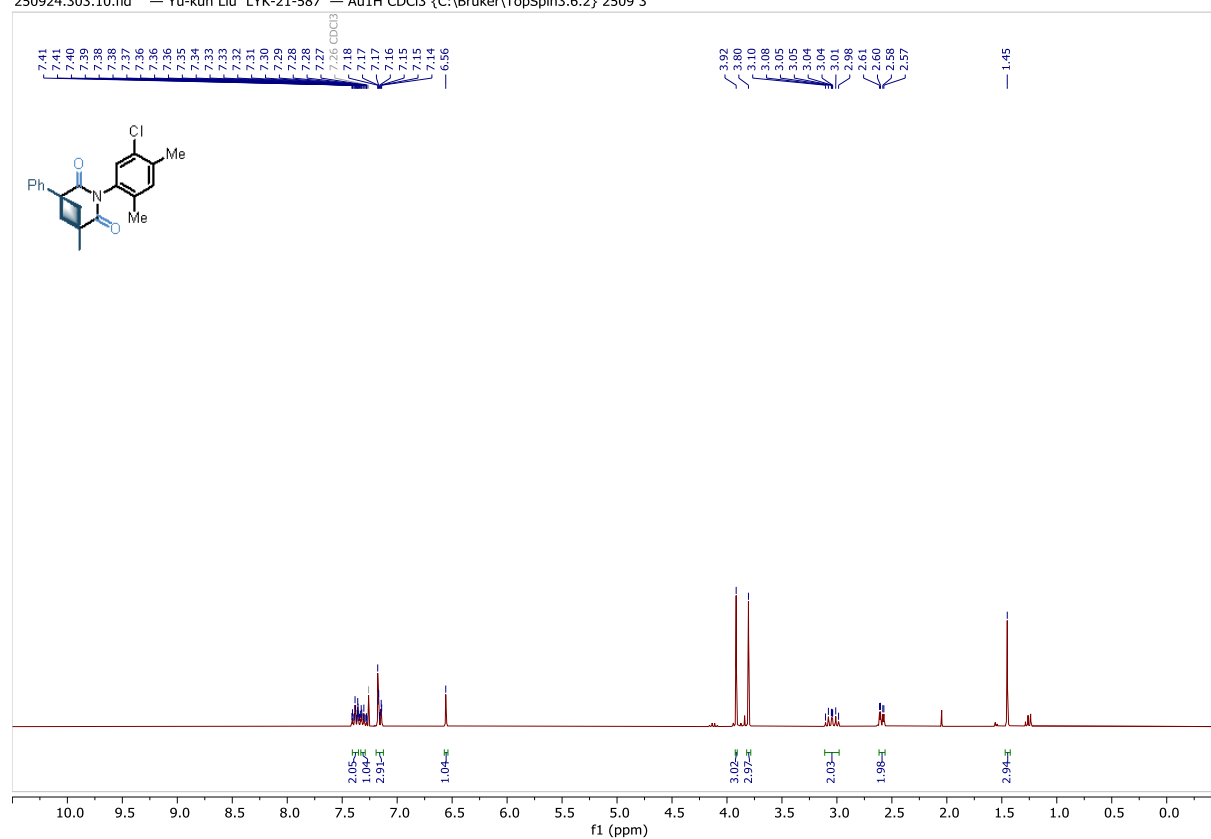
Supplementary Fig. 161. ^{13}C NMR spectrum of **4t** (75 MHz, CDCl_3)

250911.311.11.fid — Yu-kun Liu, LYK-21-561 — Au13C CDCl_3 {C:\Bruker\TopSpin3.6.2} 2509 11



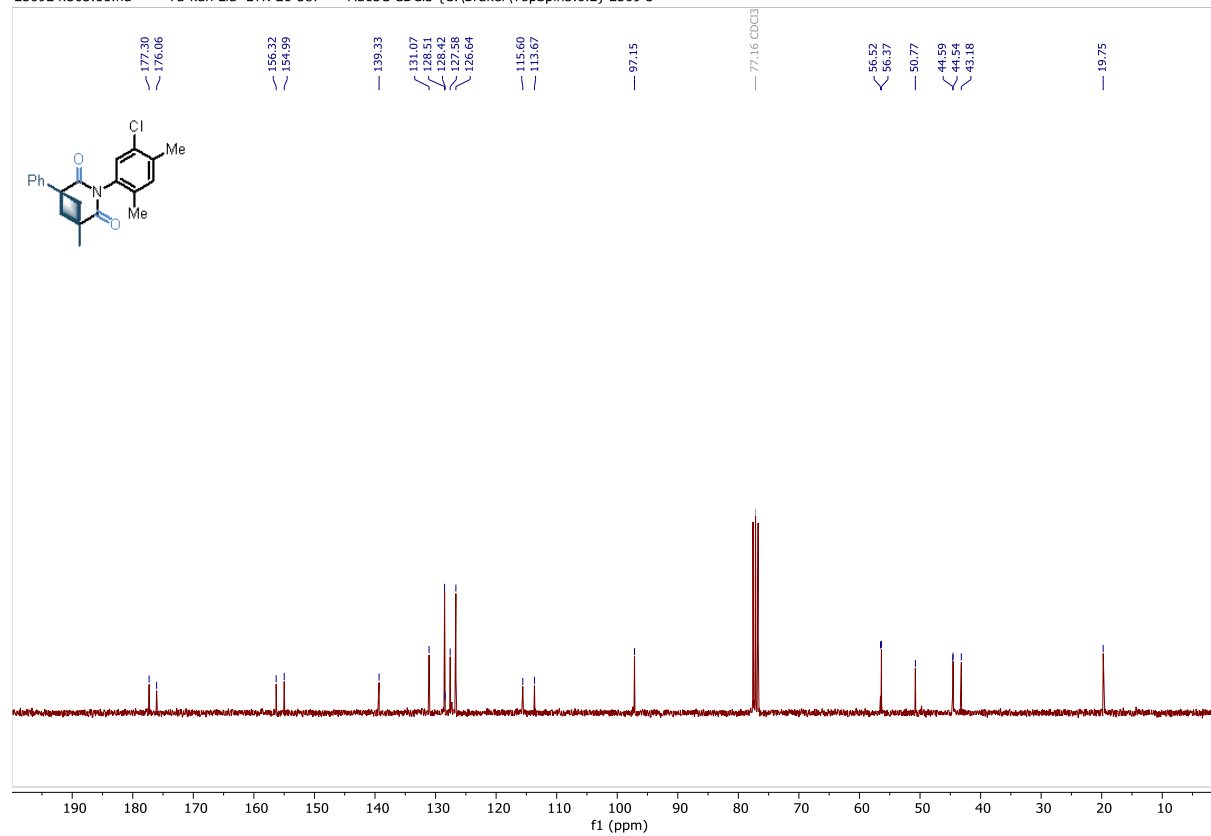
Supplementary Fig. 162. ^1H NMR spectrum of **4u** (300 MHz, CDCl_3)

250924.303.10.fid — Yu-kun Liu LYK-21-587 — Au1H CDCl_3 {C:\Bruker\TopSpin3.6.2} 2509 3



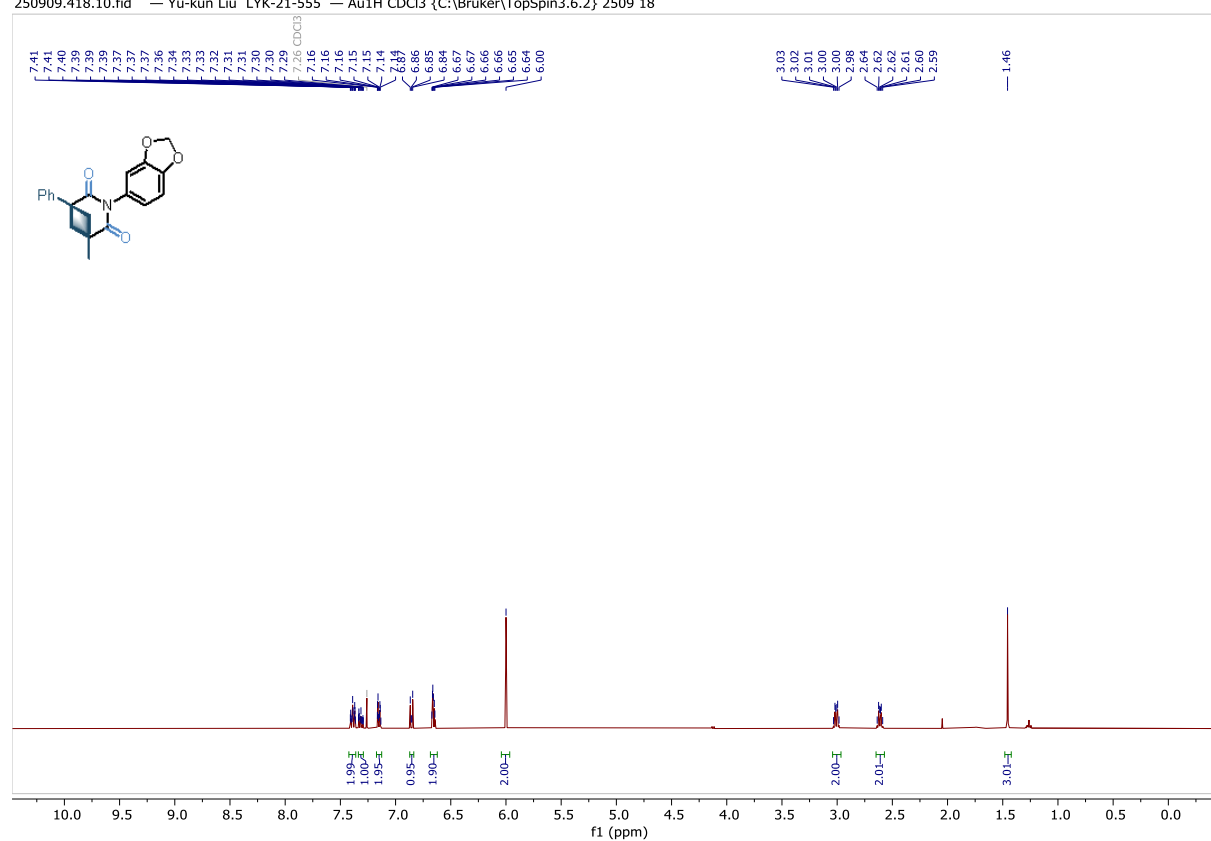
Supplementary Fig. 163. ^{13}C NMR spectrum of **4u** (75 MHz, CDCl_3)

250924.303.11.fid — Yu-kun Liu LYK-21-587 — Au13C CDCl_3 {C:\Bruker\TopSpin3.6.2} 2509 3



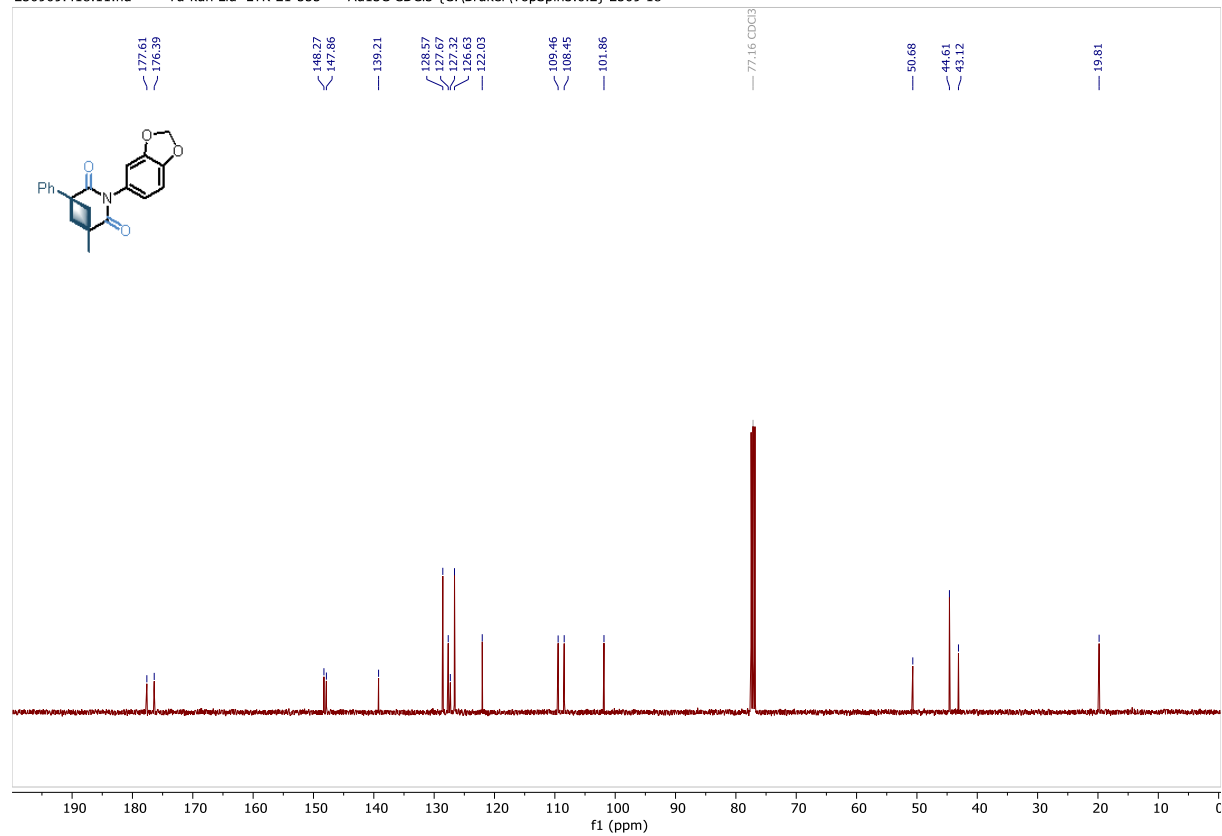
Supplementary Fig. 164. ^1H NMR spectrum of **4v** (300 MHz, CDCl_3)

250909.418.10.fid — Yu-kun Liu LYK-21-555 — Au1H CDCl_3 {C:\Bruker\TopSpin3.6.2} 2509 18



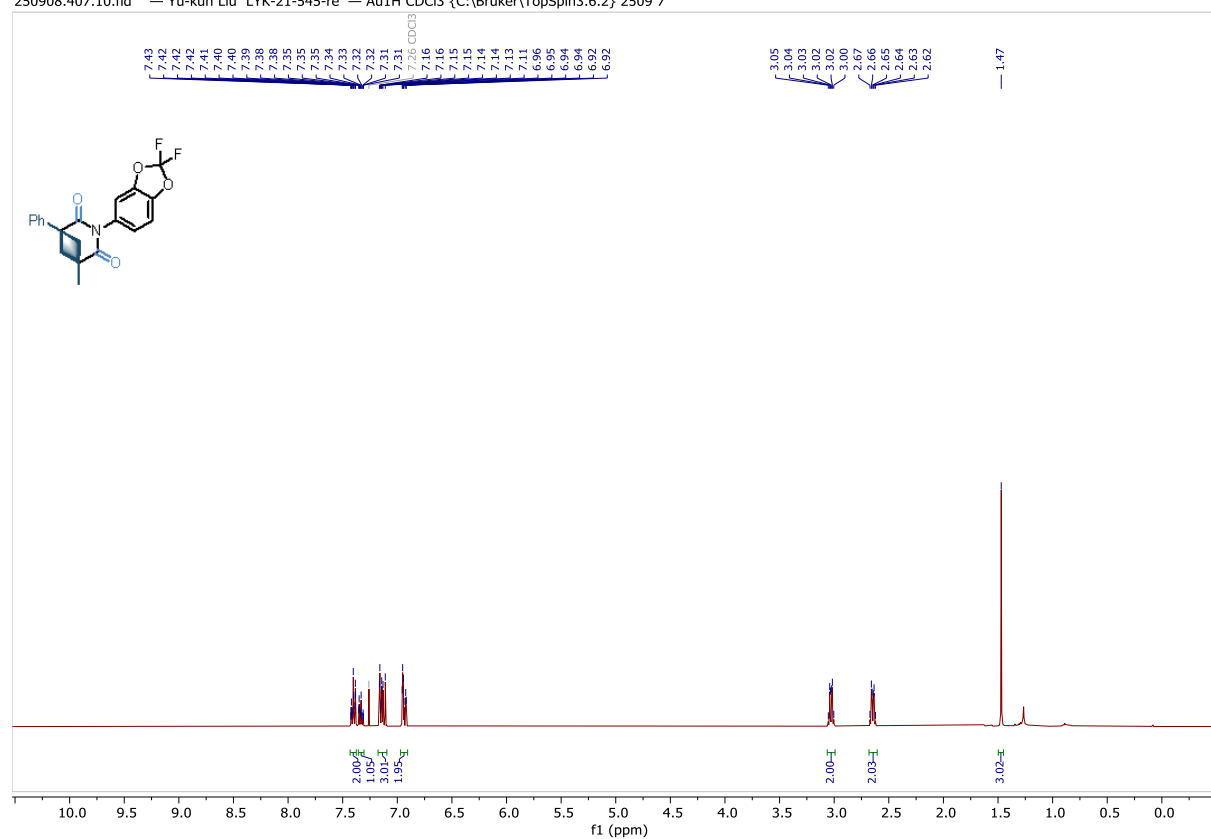
Supplementary Fig. 165. ^{13}C NMR spectrum of **4v** (75 MHz, CDCl_3)

250909.418.11.fid — Yu-kun Liu LYK-21-555 — Au13C CDCl_3 {C:\Bruker\TopSpin3.6.2} 2509 18



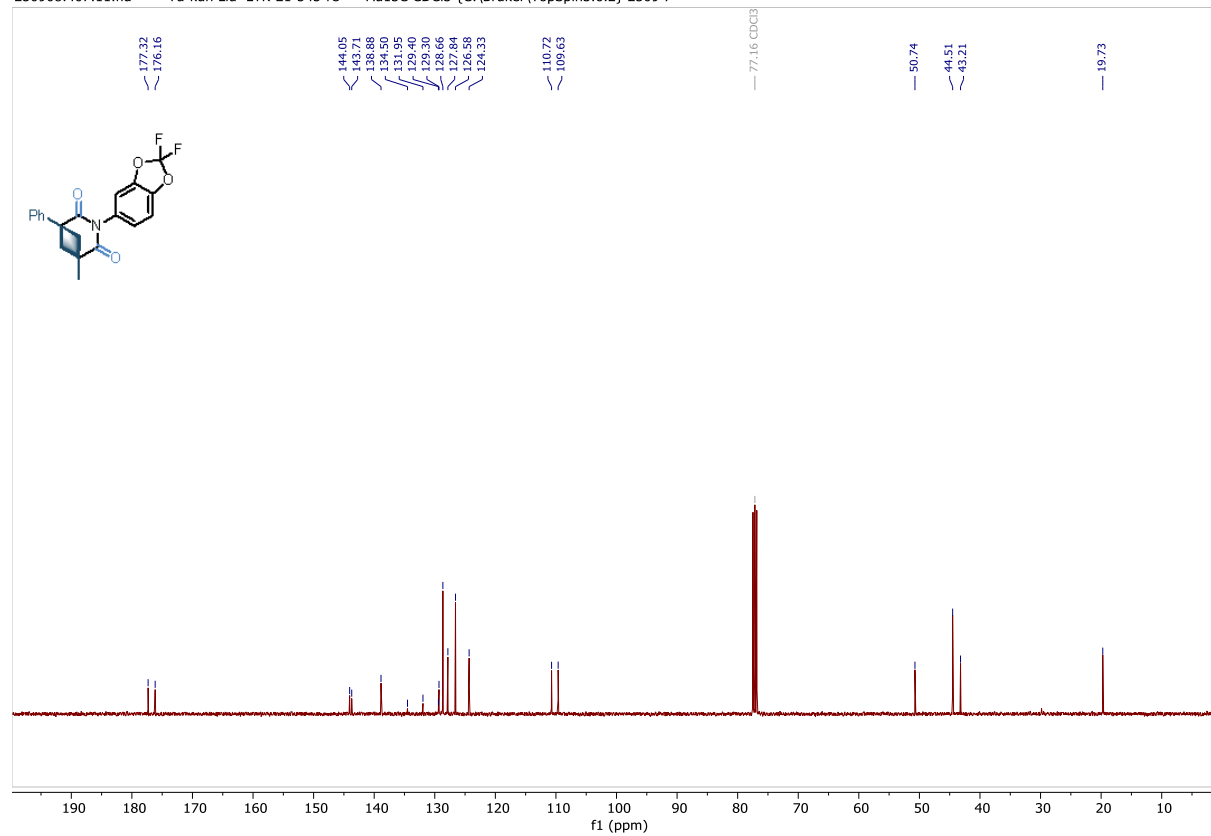
Supplementary Fig. 166. ^1H NMR spectrum of **4w** (400 MHz, CDCl_3)

250908.407.10.fid — Yu-kun Liu LYK-21-545-re — Au1H CDCl_3 {C:\Bruker\TopSpin3.6.2} 2509 7



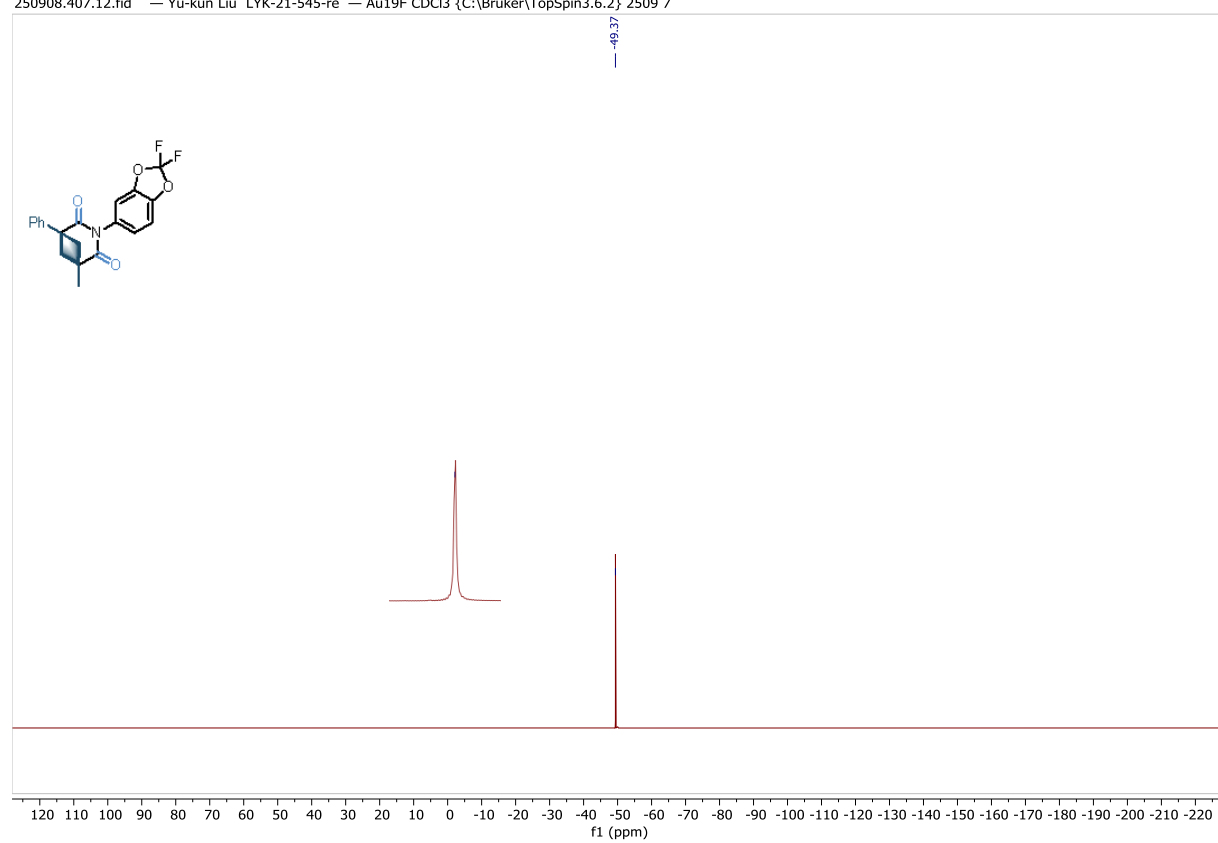
Supplementary Fig. 167. ^{13}C NMR spectrum of **4w** (101 MHz, CDCl_3)

250908.407.11.fid — Yu-kun Liu LYK-21-545-re — Au13C CDCl_3 {C:\Bruker\TopSpin3.6.2} 2509 7



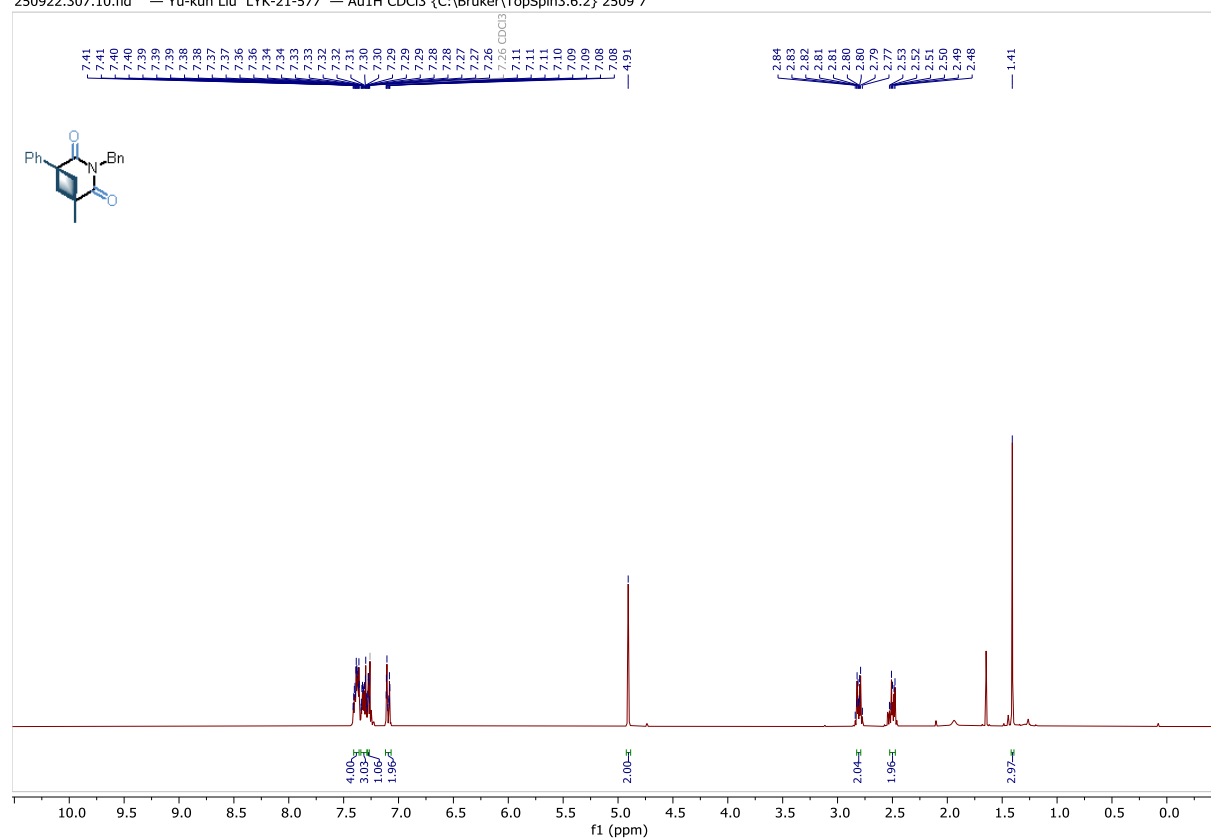
Supplementary Fig. 168. ^{19}F NMR spectrum of **4w** (376 MHz, CDCl_3)

250908.407.12.fid — Yu-kun Liu LYK-21-545-re — Au19F CDCl_3 {C:\Bruker\TopSpin3.6.2} 2509 7



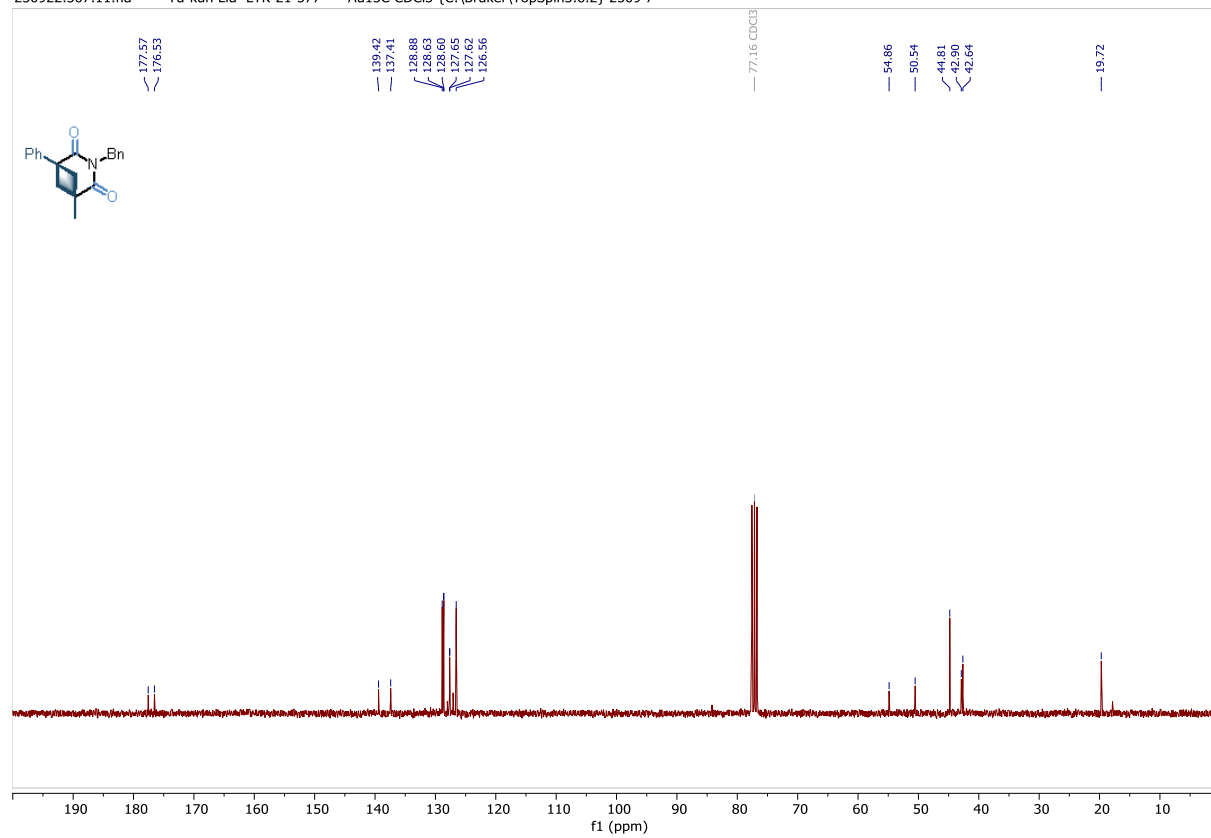
Supplementary Fig. 169. ^1H NMR spectrum of **4x** (300 MHz, CDCl_3)

250922.307.10.fid — Yu-kun Liu LYK-21-577 — Au1H CDCl_3 {C:\Bruker\TopSpin3.6.2} 2509 7



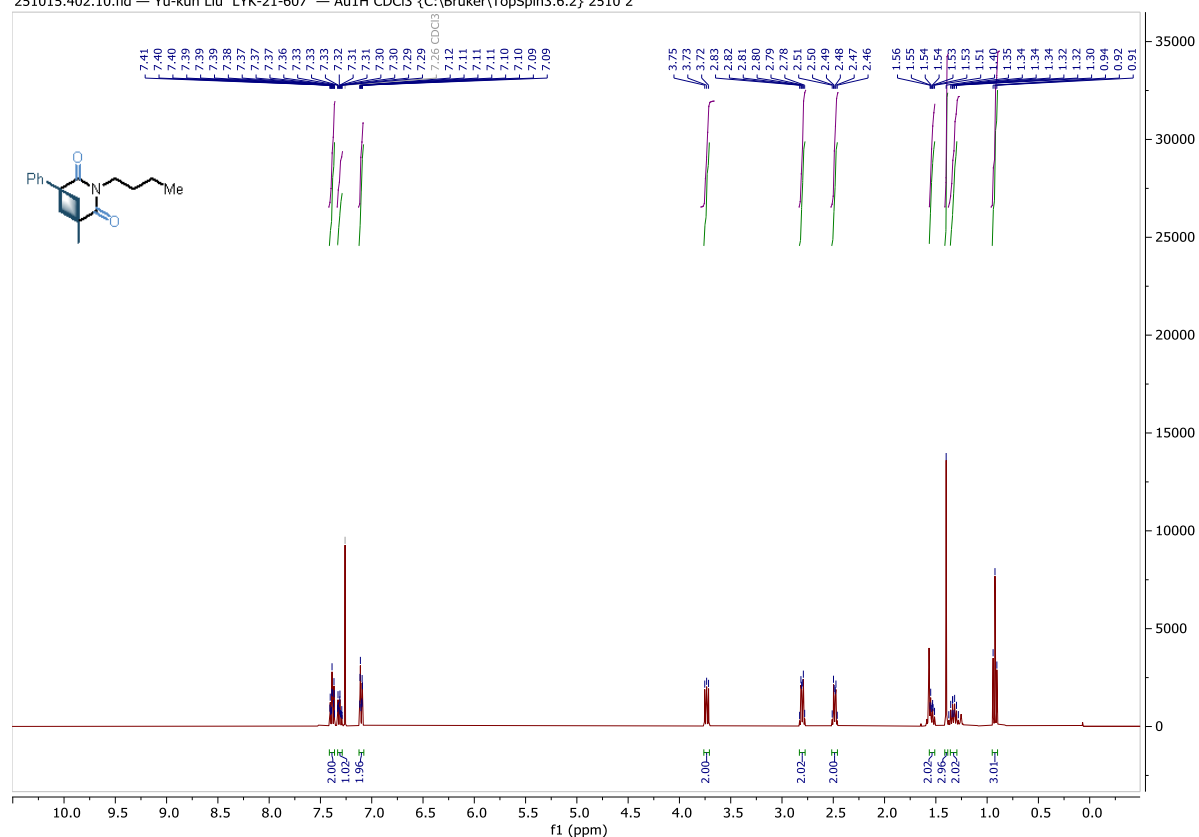
Supplementary Fig. 170. ^{13}C NMR spectrum of **4x** (75 MHz, CDCl_3)

250922.307.11.fid — Yu-kun Liu LYK-21-577 — Au13C CDCl_3 {C:\Bruker\TopSpin3.6.2} 2509 7



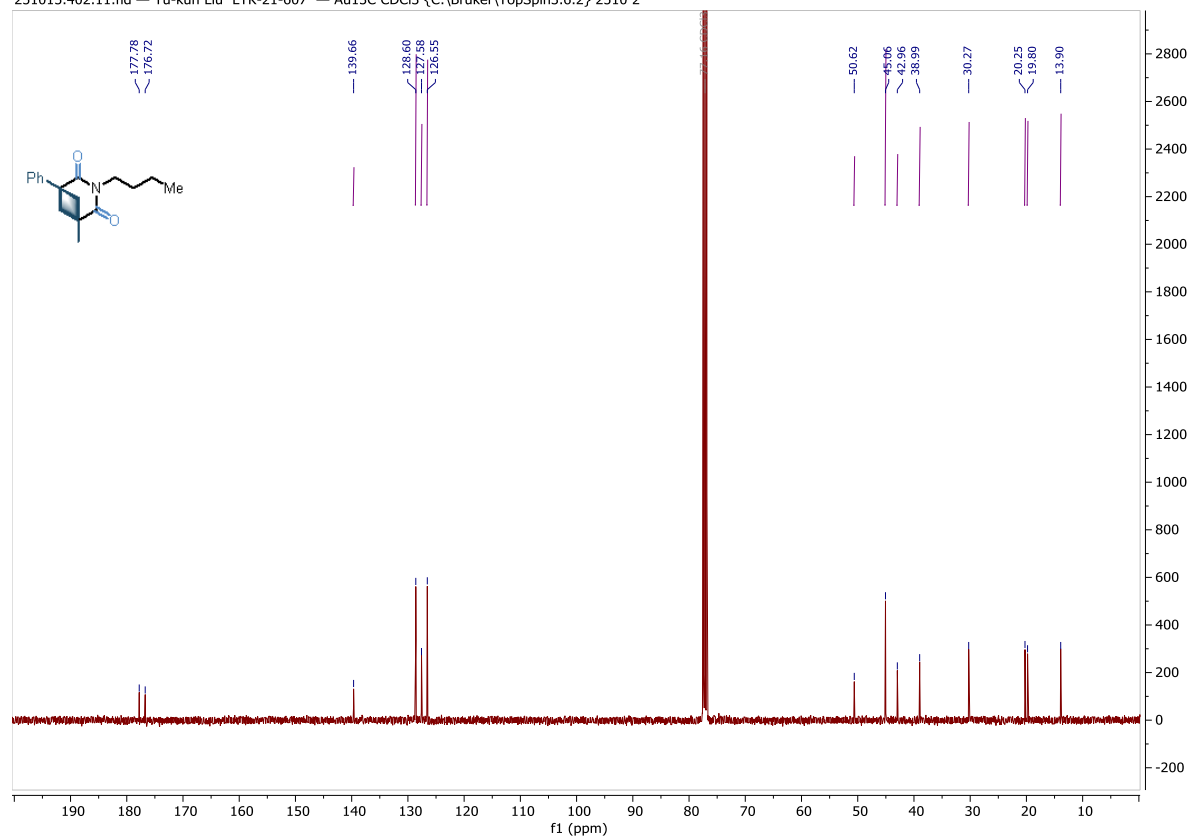
Supplementary Fig. 171. ^1H NMR spectrum of **4y** (400 MHz, CDCl_3)

251015.402.10.fid — Yu-kun Liu LYK-21-607 — Au1H CDCl_3 {C:\Bruker\TopSpin3.6.2} 2510 2



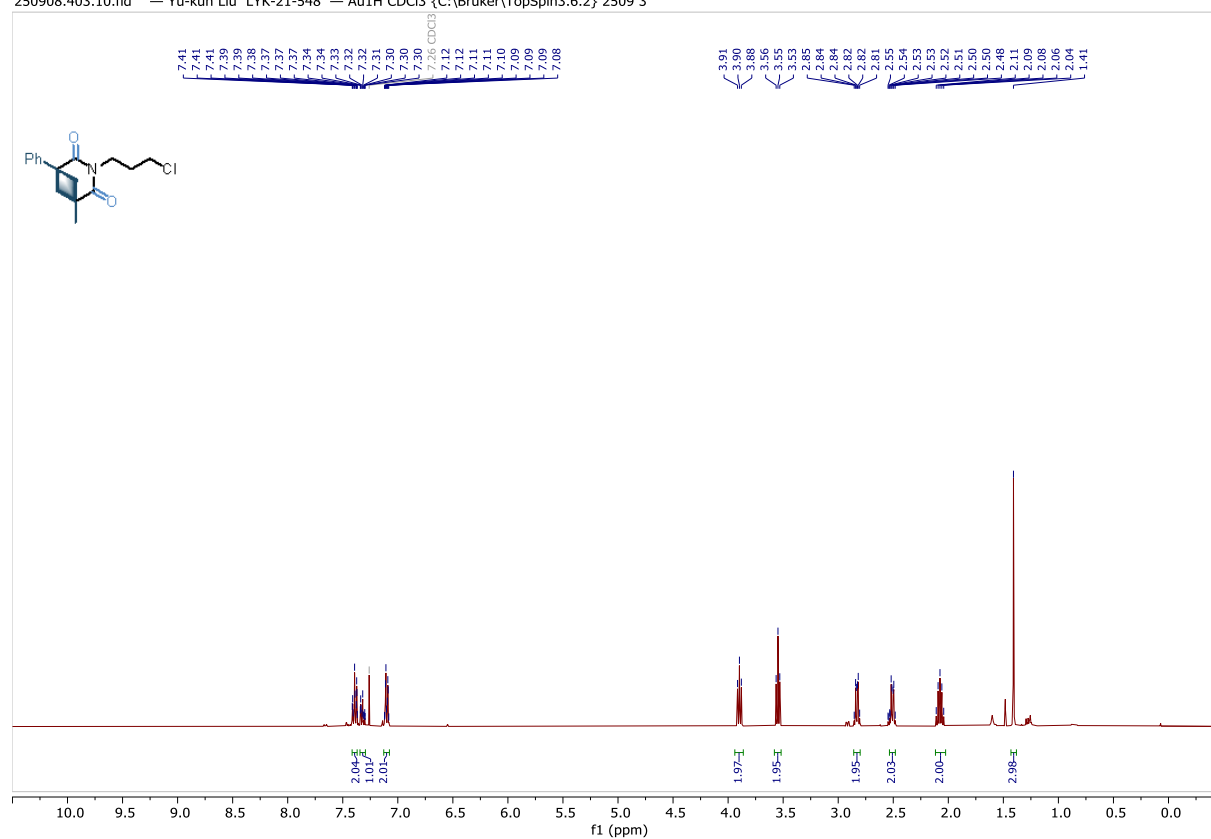
Supplementary Fig. 172. ^{13}C NMR spectrum of **4y** (101 MHz, CDCl_3)

251015.402.11.fid — Yu-kun Liu LYK-21-607 — Au13C CDCl_3 {C:\Bruker\TopSpin3.6.2} 2510 2



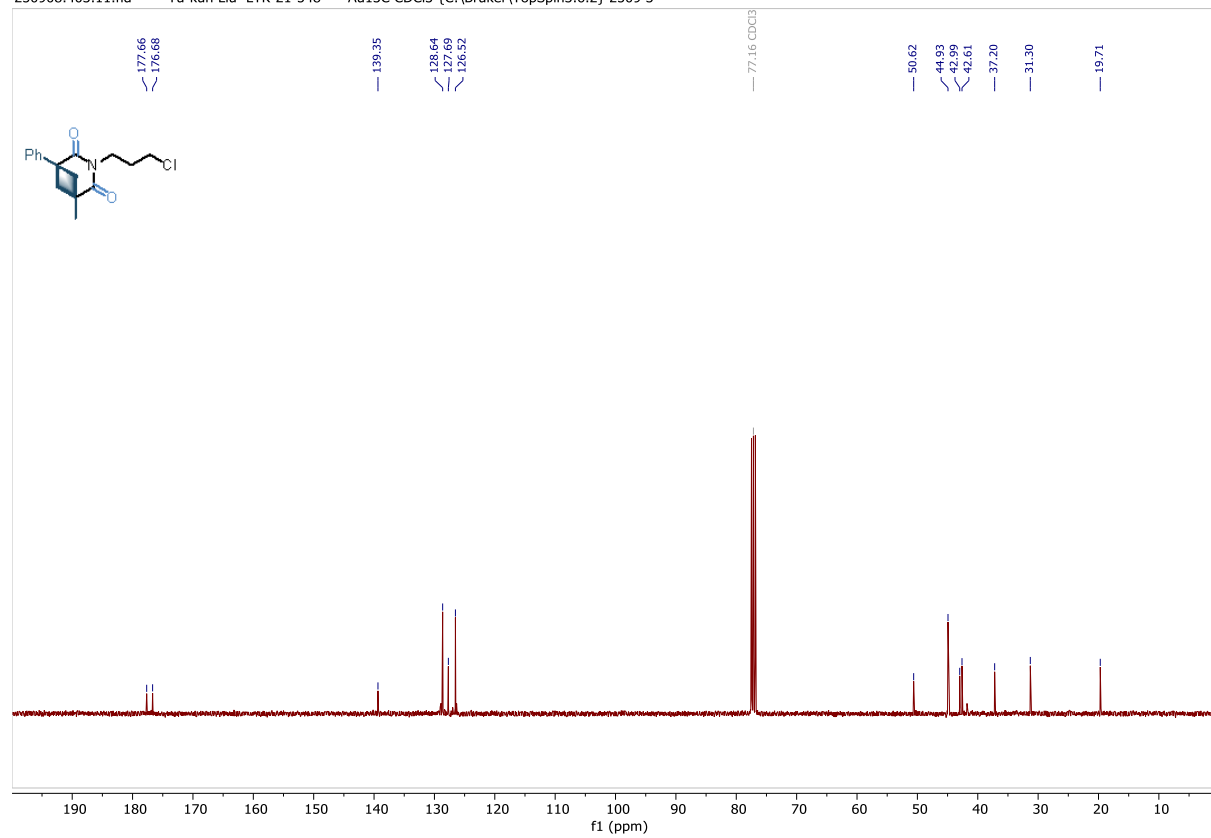
Supplementary Fig. 173. ^1H NMR spectrum of **4z** (400 MHz, CDCl_3)

250908.403.10.fid — Yu-kun Liu LYK-21-548 — Au1H CDCl_3 {C:\Bruker\TopSpin3.6.2} 2509 3



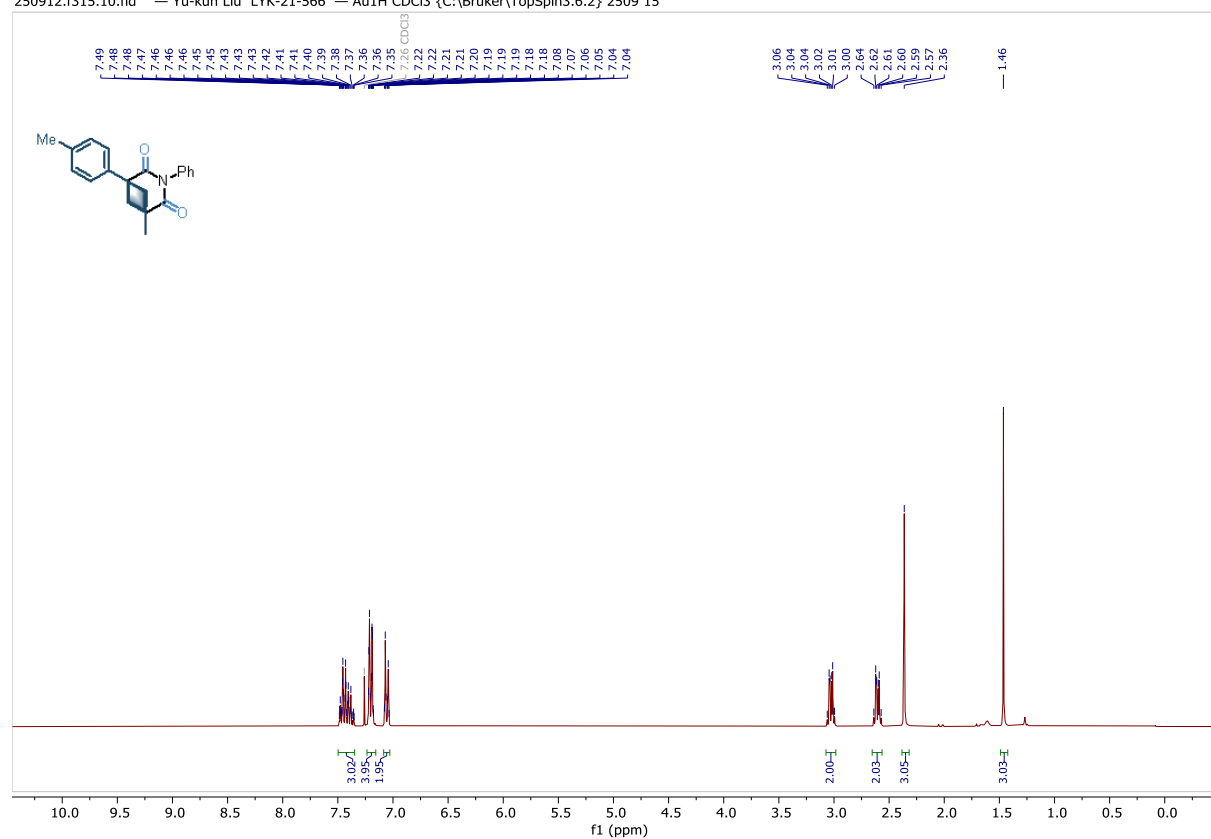
Supplementary Fig. 174. ^{13}C NMR spectrum of **4y** (101 MHz, CDCl_3)

250908.403.11.fid — Yu-kun Liu LYK-21-548 — Au13C CDCl_3 {C:\Bruker\TopSpin3.6.2} 2509 3



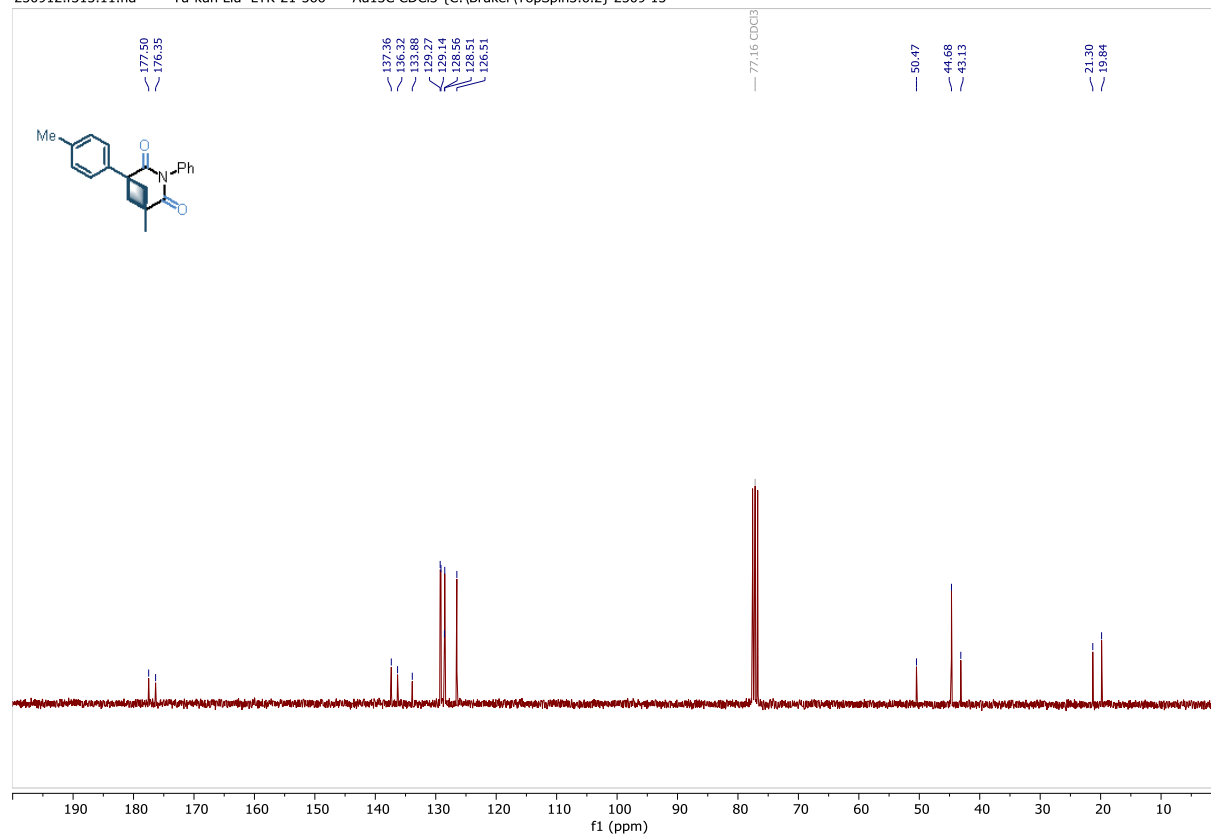
Supplementary Fig. 175. ^1H NMR spectrum of **4aa** (300 MHz, CDCl_3)

250912.f315.10.fid — Yu-kun Liu LYK-21-566 — Au1H CDCl_3 {C:\Bruker\TopSpin3.6.2} 2509 15



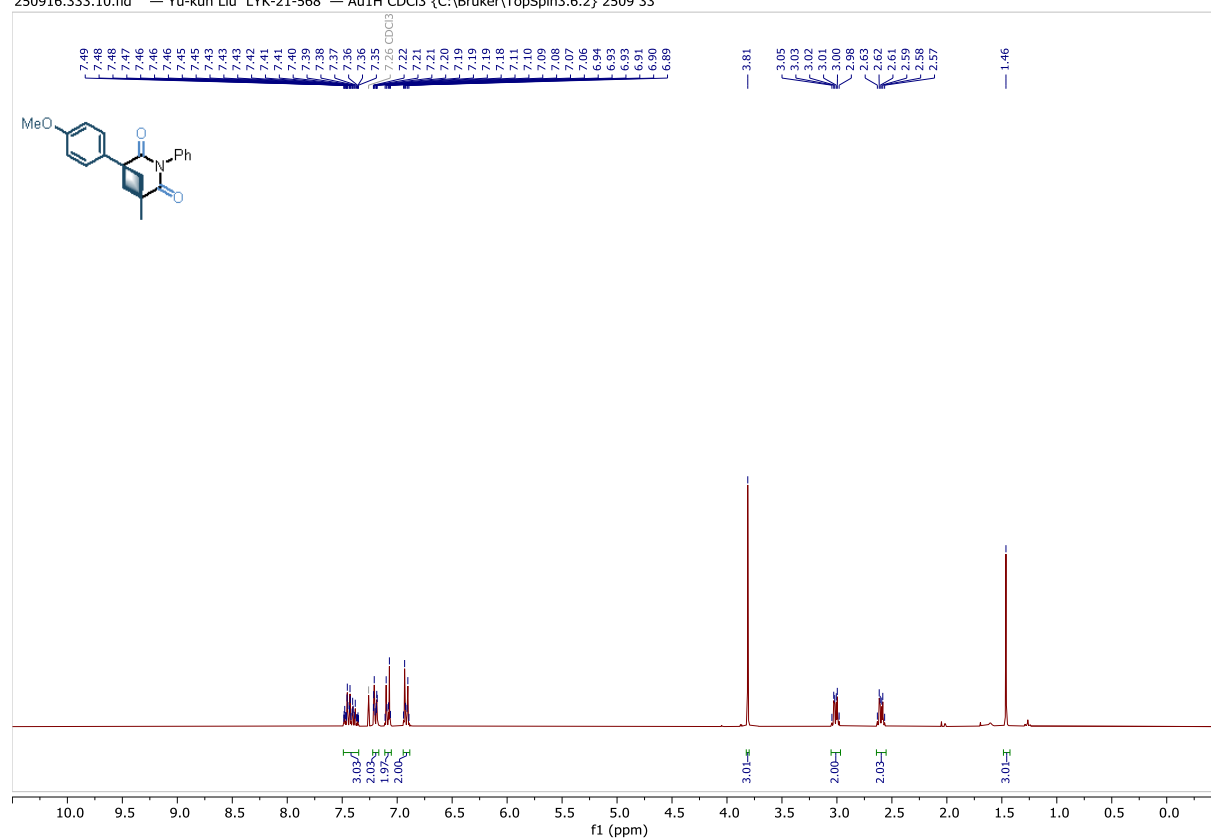
Supplementary Fig. 176. ^{13}C NMR spectrum of **4aa** (75 MHz, CDCl_3)

250912.f315.11.fid — Yu-kun Liu LYK-21-566 — Au13C CDCl_3 {C:\Bruker\TopSpin3.6.2} 2509 15



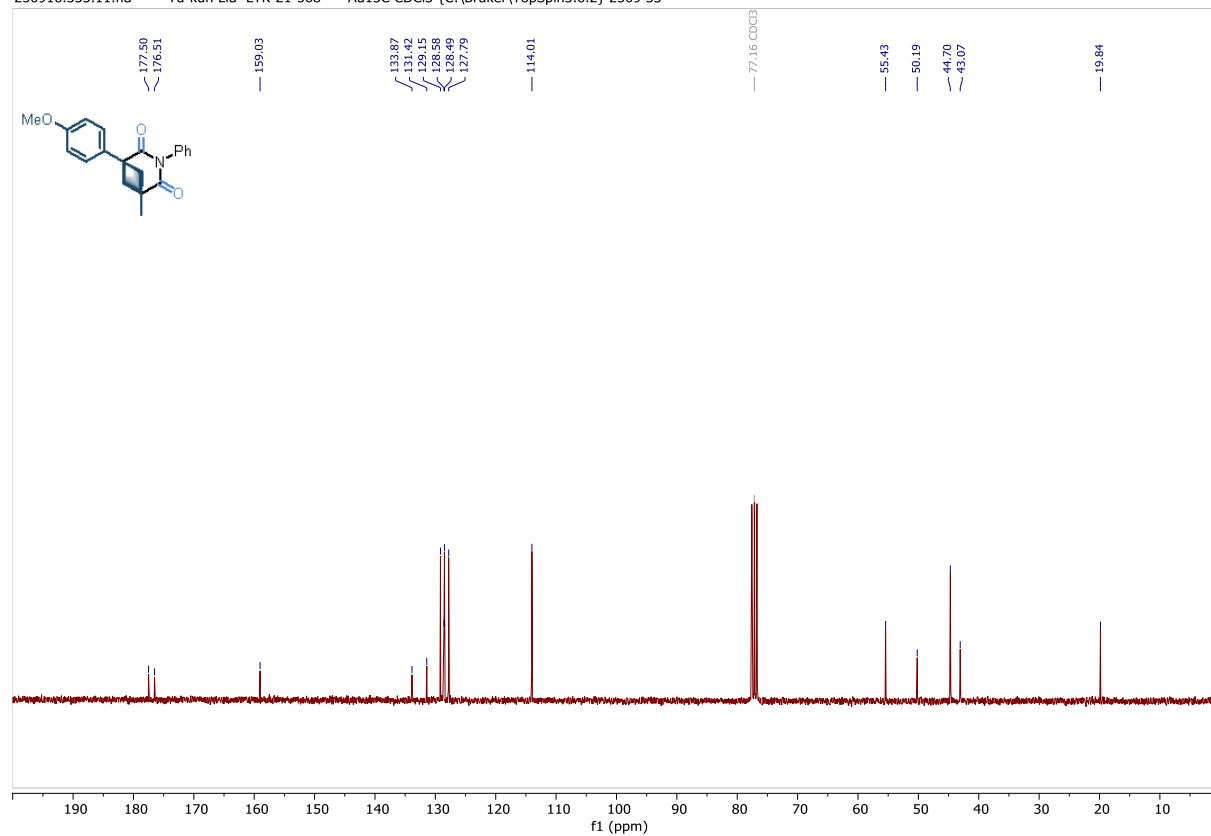
Supplementary Fig. 177. ^1H NMR spectrum of **4ab** (300 MHz, CDCl_3)

250916.333.10.fid — Yu-kun Liu LYK-21-568 — Au1H CDCl_3 {C:\Bruker\TopSpin3.6.2} 2509 33



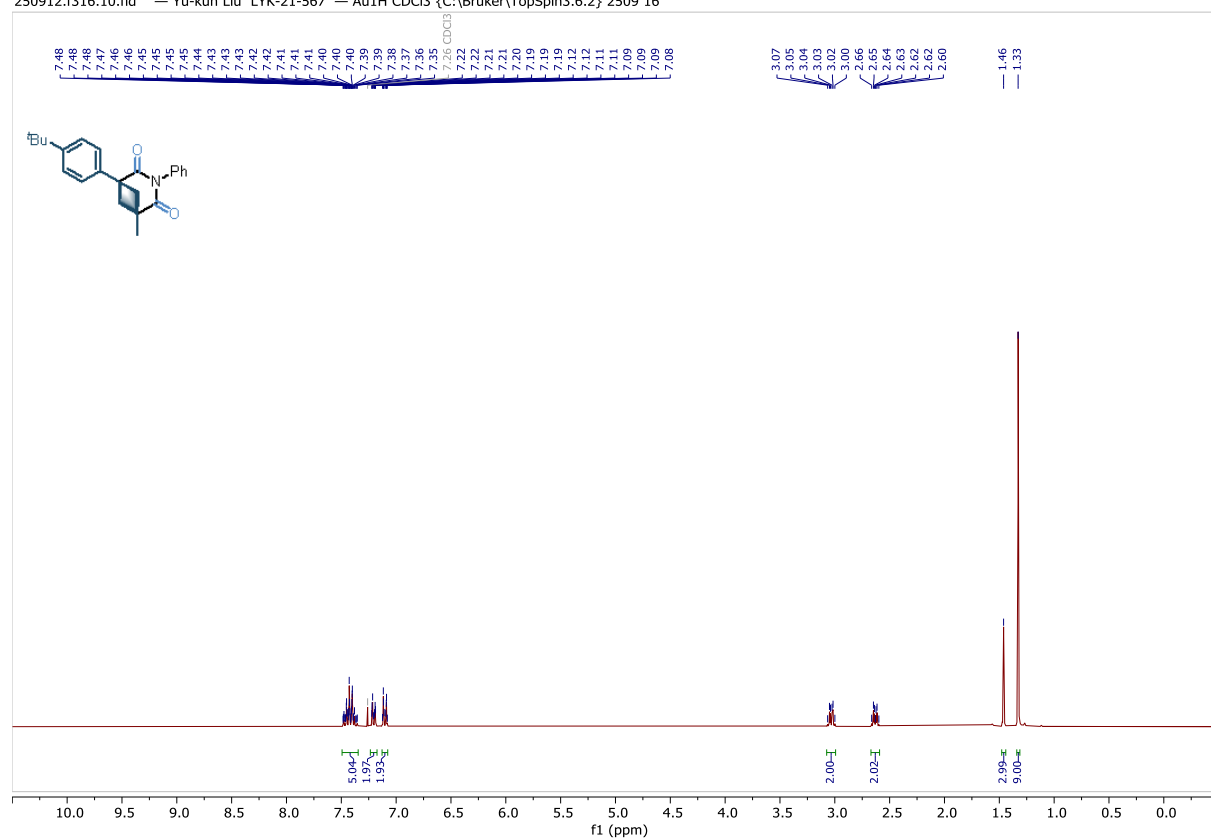
Supplementary Fig. 178. ^{13}C NMR spectrum of **4ab** (75 MHz, CDCl_3)

250916.333.11.fid — Yu-kun Liu LYK-21-568 — Au13C CDCl_3 {C:\Bruker\TopSpin3.6.2} 2509 33



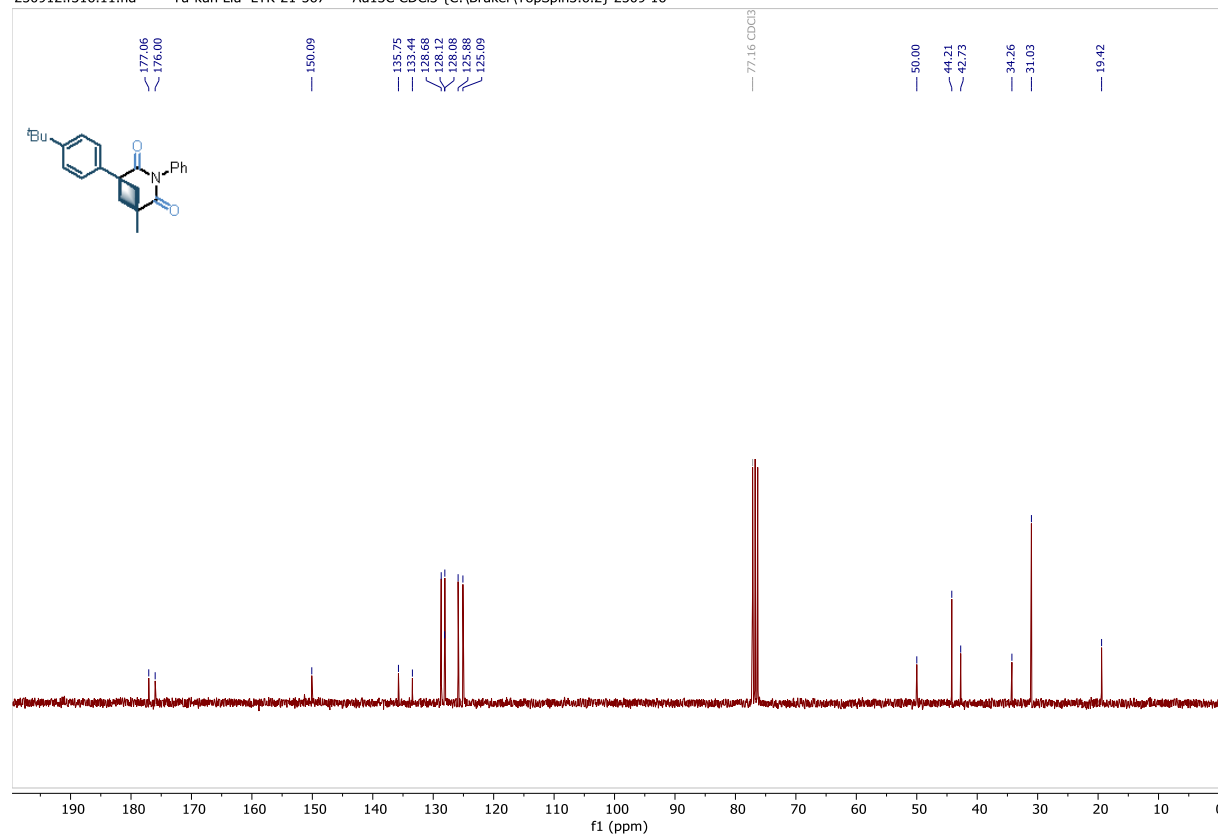
Supplementary Fig. 179. ^1H NMR spectrum of **4ac** (300 MHz, CDCl_3)

250912.f316.10.fid — Yu-kun Liu LYK-21-567 — Au1H CDCl_3 {C:\Bruker\TopSpin3.6.2} 2509 16



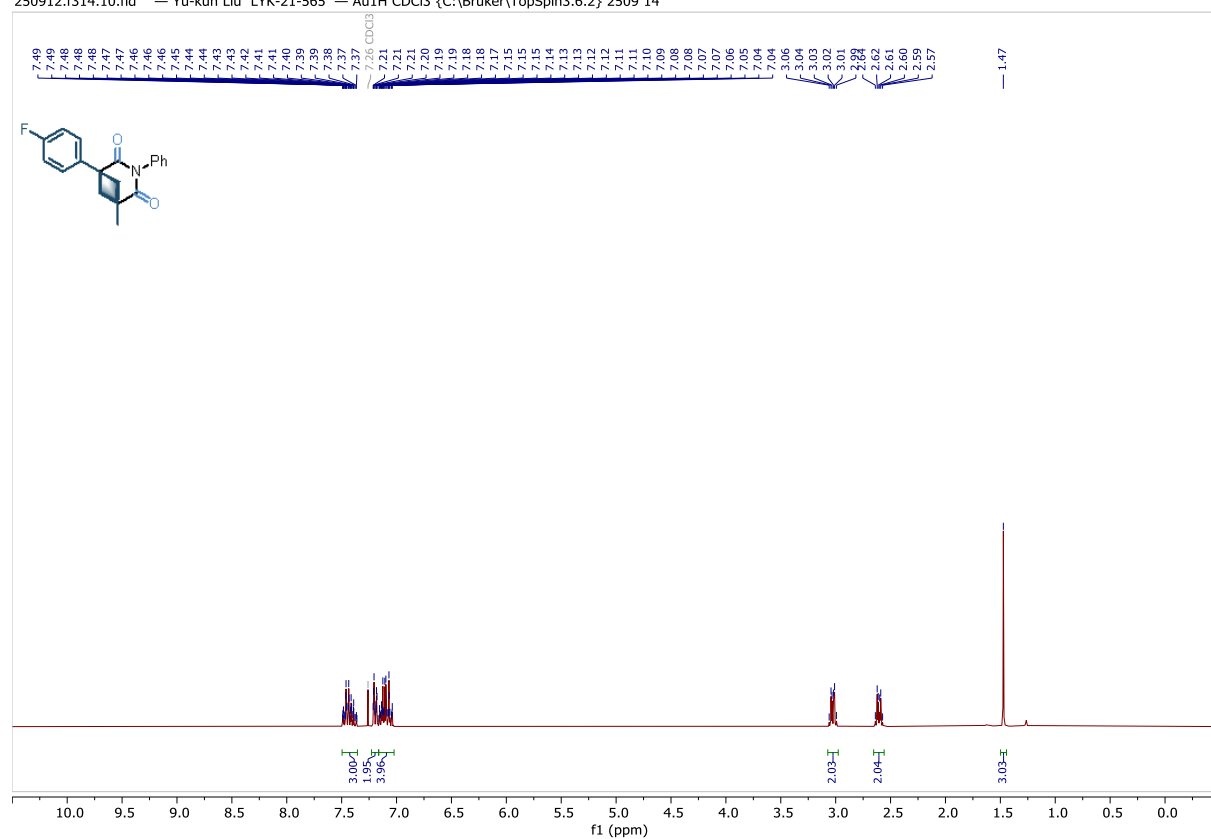
Supplementary Fig. 180. ^{13}C NMR spectrum of **4ab** (75 MHz, CDCl_3)

250912.f316.11.fid — Yu-kun Liu LYK-21-567 — Au13C CDCl_3 {C:\Bruker\TopSpin3.6.2} 2509 16



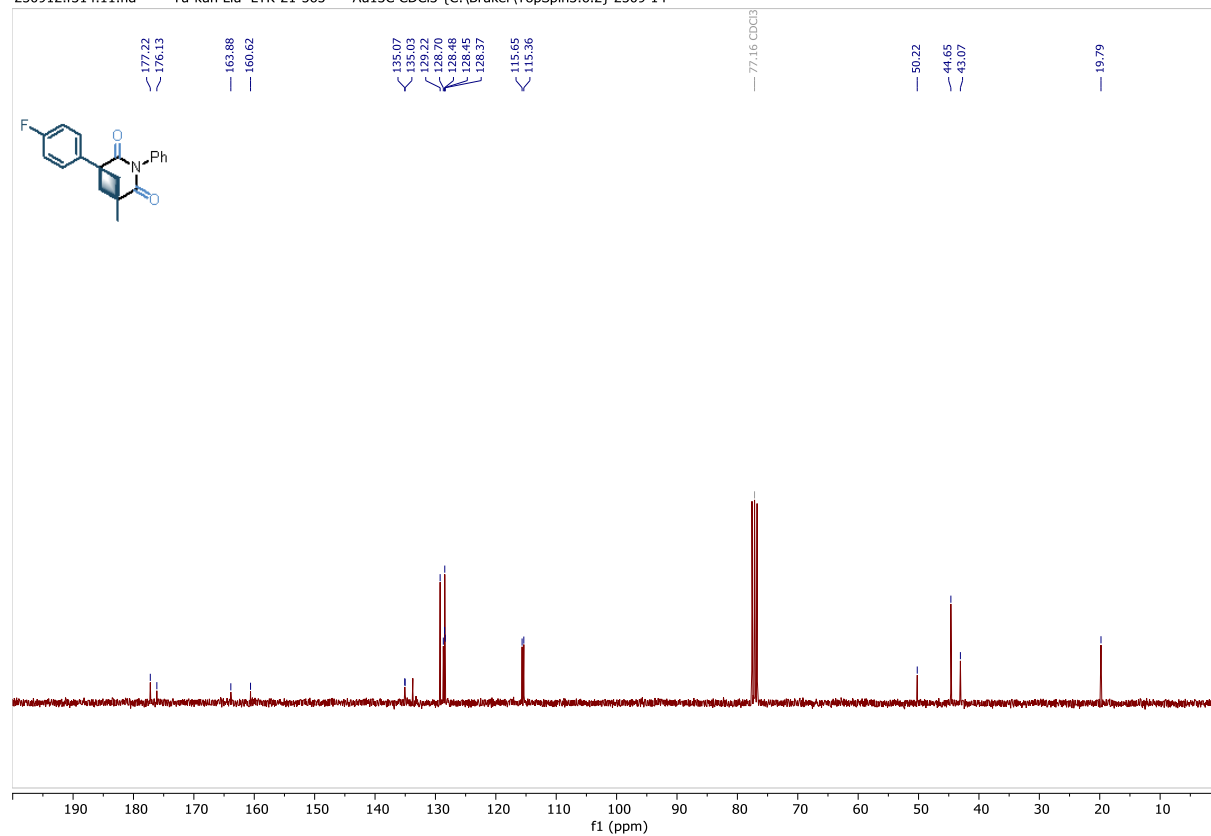
Supplementary Fig. 181. ^1H NMR spectrum of **4ad** (300 MHz, CDCl_3)

250912.f314.10.fid — Yu-kun Liu LYK-21-565 — Au1H CDCl_3 {C:\Bruker\TopSpin3.6.2} 2509 14



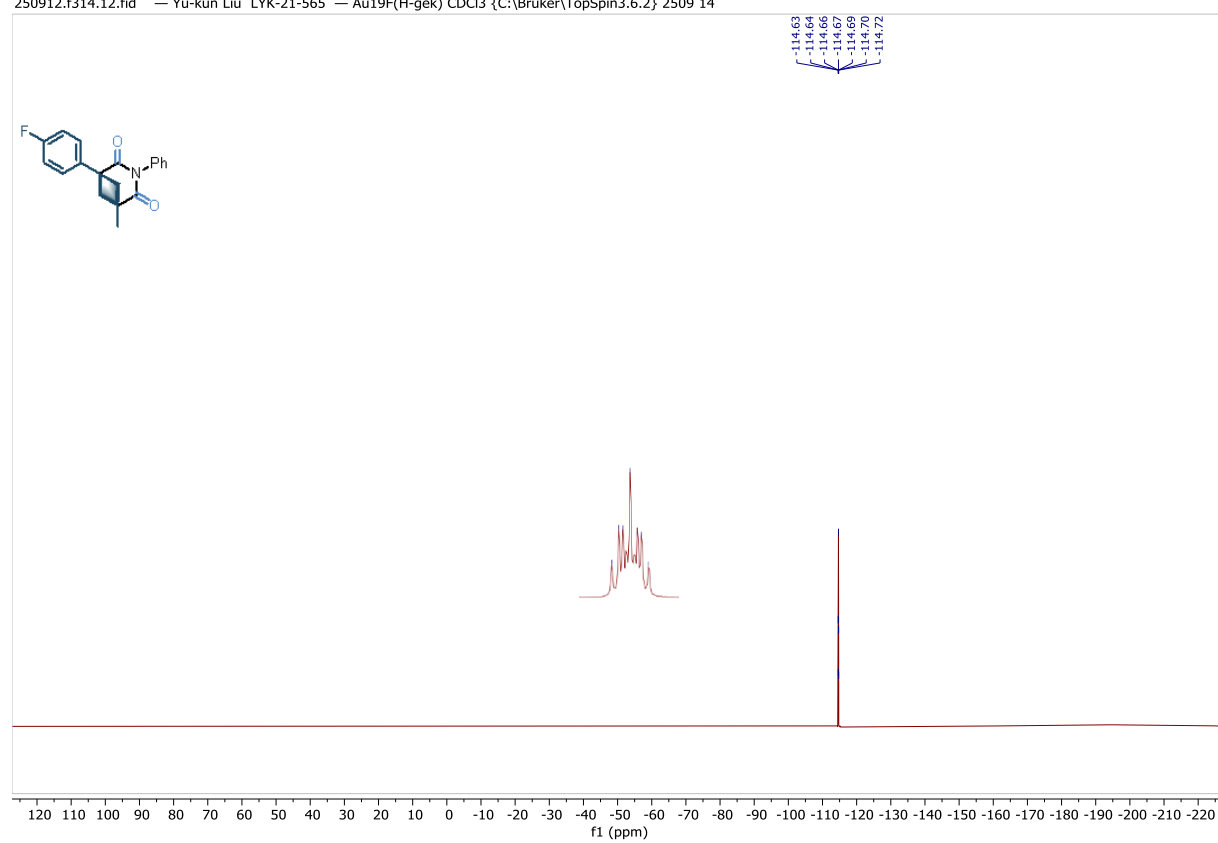
Supplementary Fig. 182. ^{13}C NMR spectrum of **4ad** (75 MHz, CDCl_3)

250912.f314.11.fid — Yu-kun Liu LYK-21-565 — Au13C CDCl_3 {C:\Bruker\TopSpin3.6.2} 2509 14



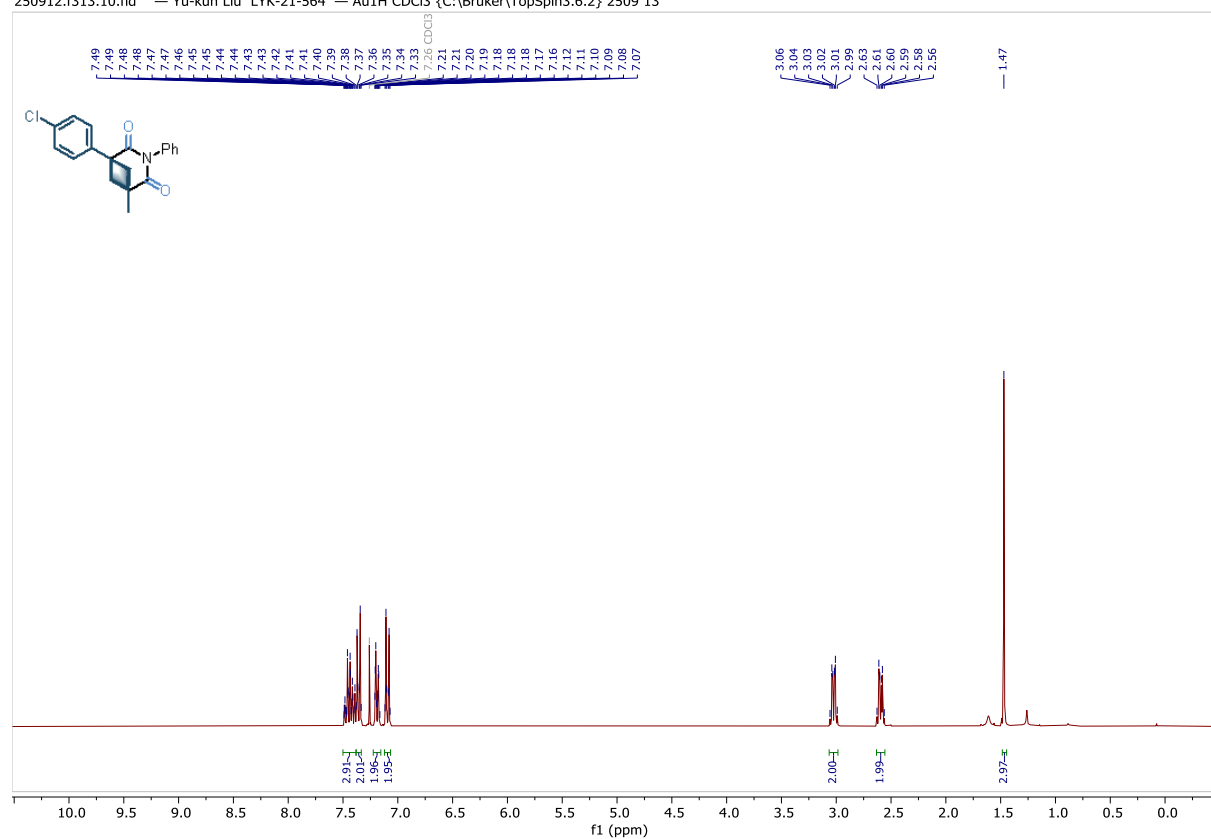
Supplementary Fig. 183. ^{19}F NMR spectrum of **4ad** (282 MHz, CDCl_3)

250912.f314.12.fid — Yu-kun Liu LYK-21-565 — Au19F(H-gek) CDCl_3 {C:\Bruker\TopSpin3.6.2} 2509 14



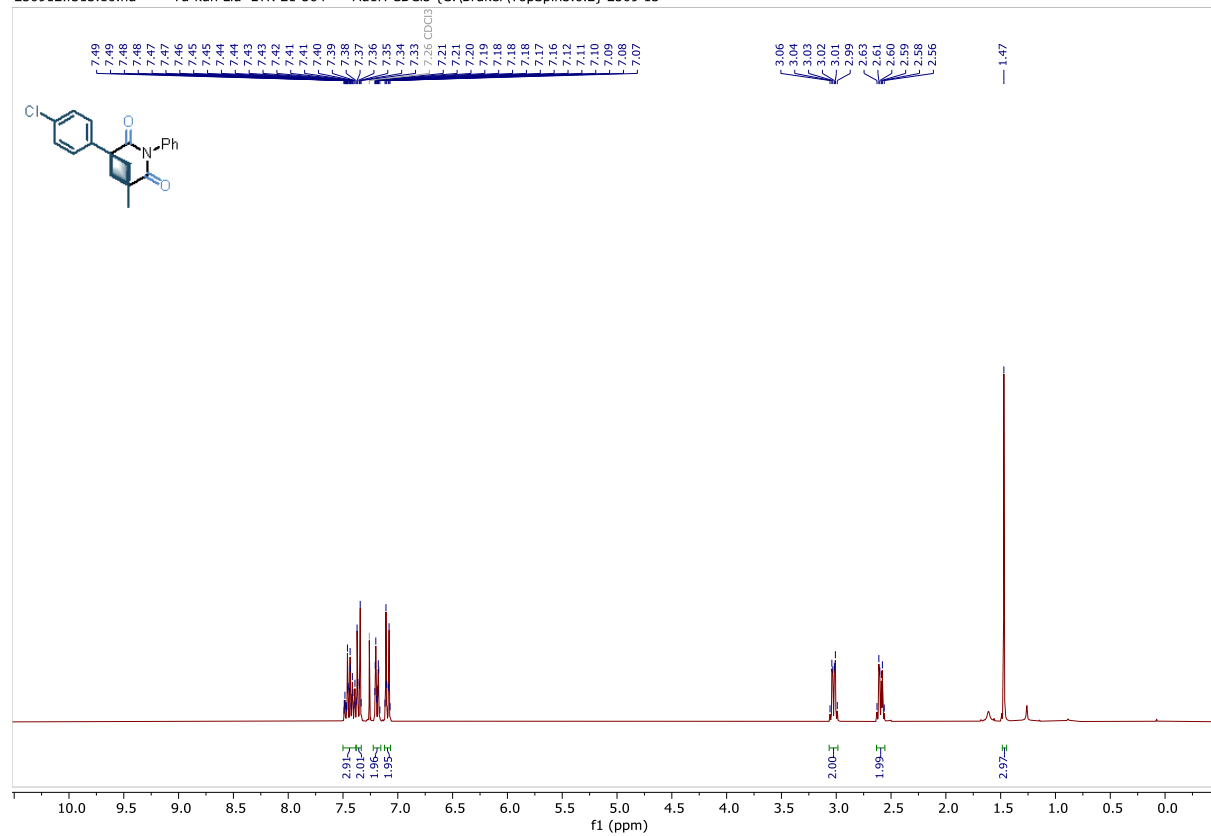
Supplementary Fig. 184. ^1H NMR spectrum of **4ae** (300 MHz, CDCl_3)

250912.f313.10.fid — Yu-kun Liu LYK-21-564 — Au1H CDCl_3 {C:\Bruker\TopSpin3.6.2} 2509 13



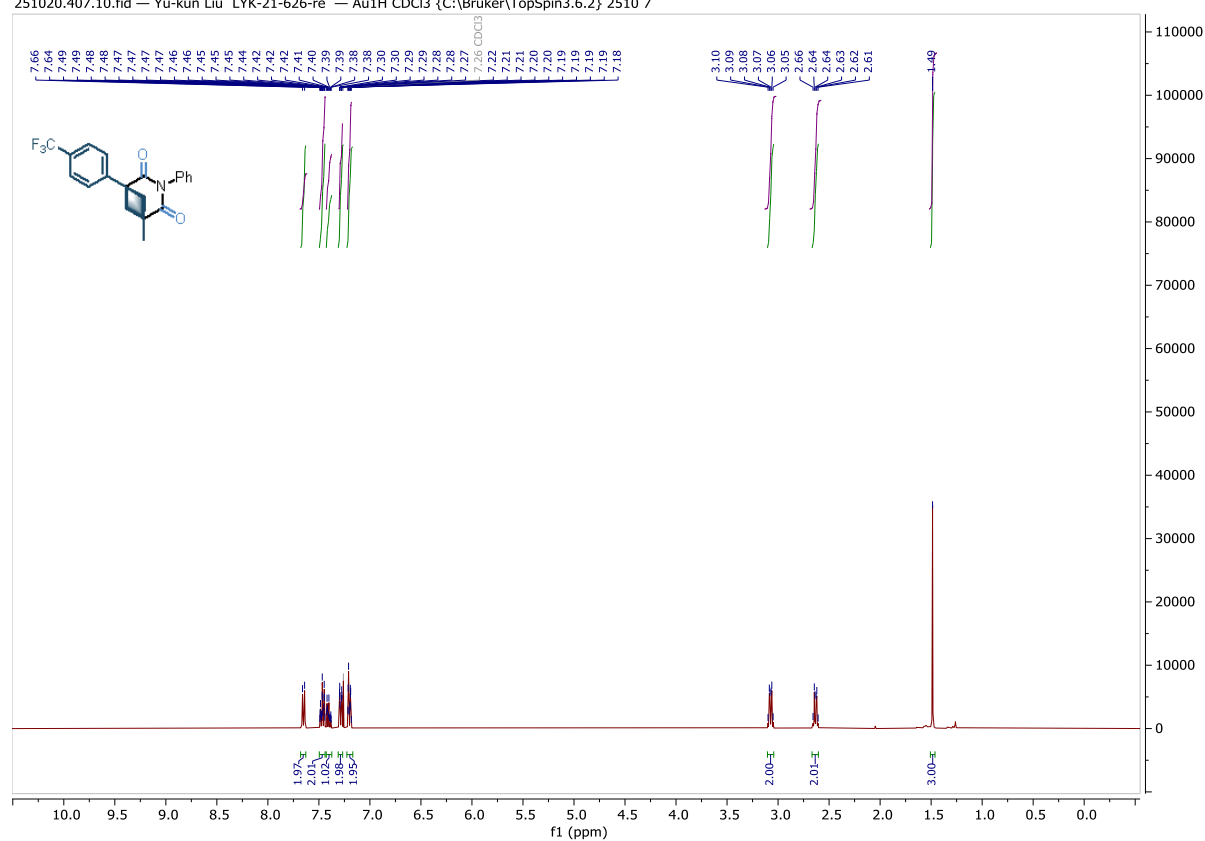
Supplementary Fig. 185. ^{13}C NMR spectrum of **4ae** (75 MHz, CDCl_3)

250912.f313.10.fid — Yu-kun Liu LYK-21-564 — Au1H CDCl_3 {C:\Bruker\TopSpin3.6.2} 2509 13



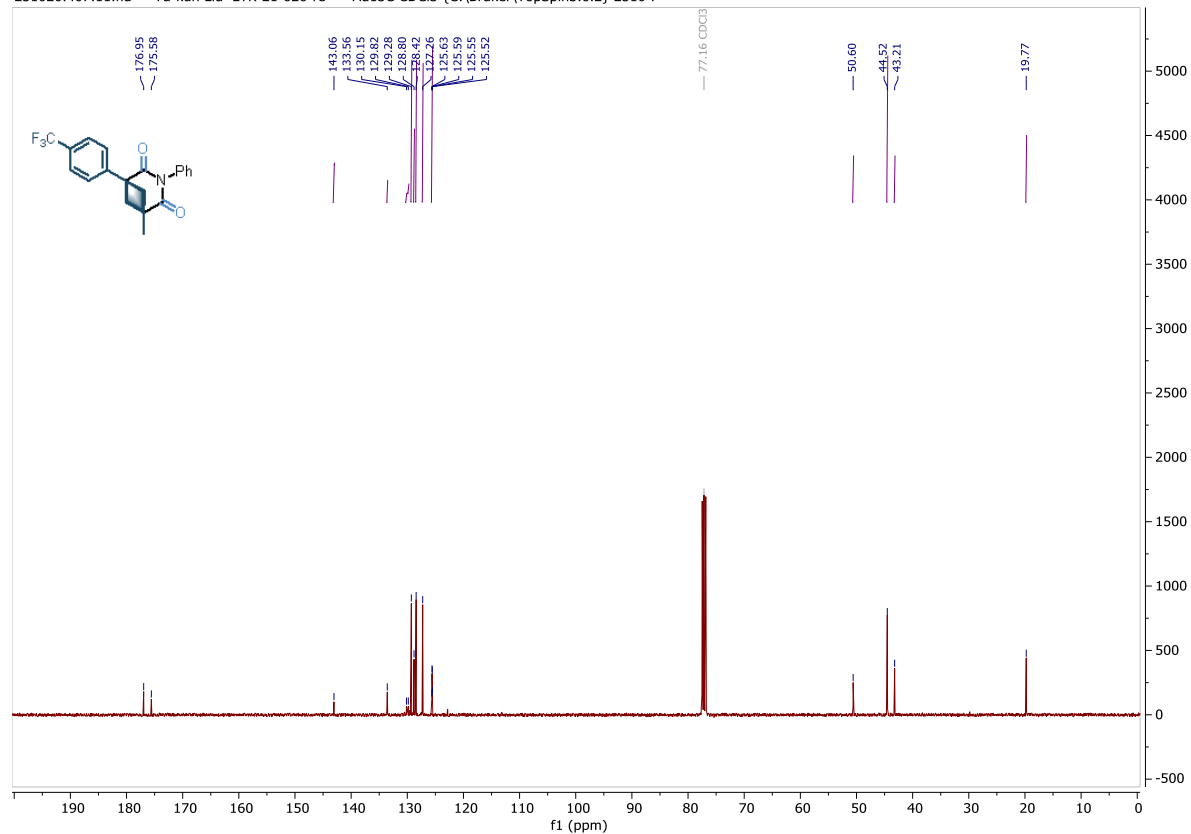
Supplementary Fig. 186. ^1H NMR spectrum of **4af** (400 MHz, CDCl_3)

251020.407.10.fid — Yu-kun Liu LYK-21-626-re — Au1H CDCl_3 {C:\Bruker\TopSpin3.6.2} 2510 7



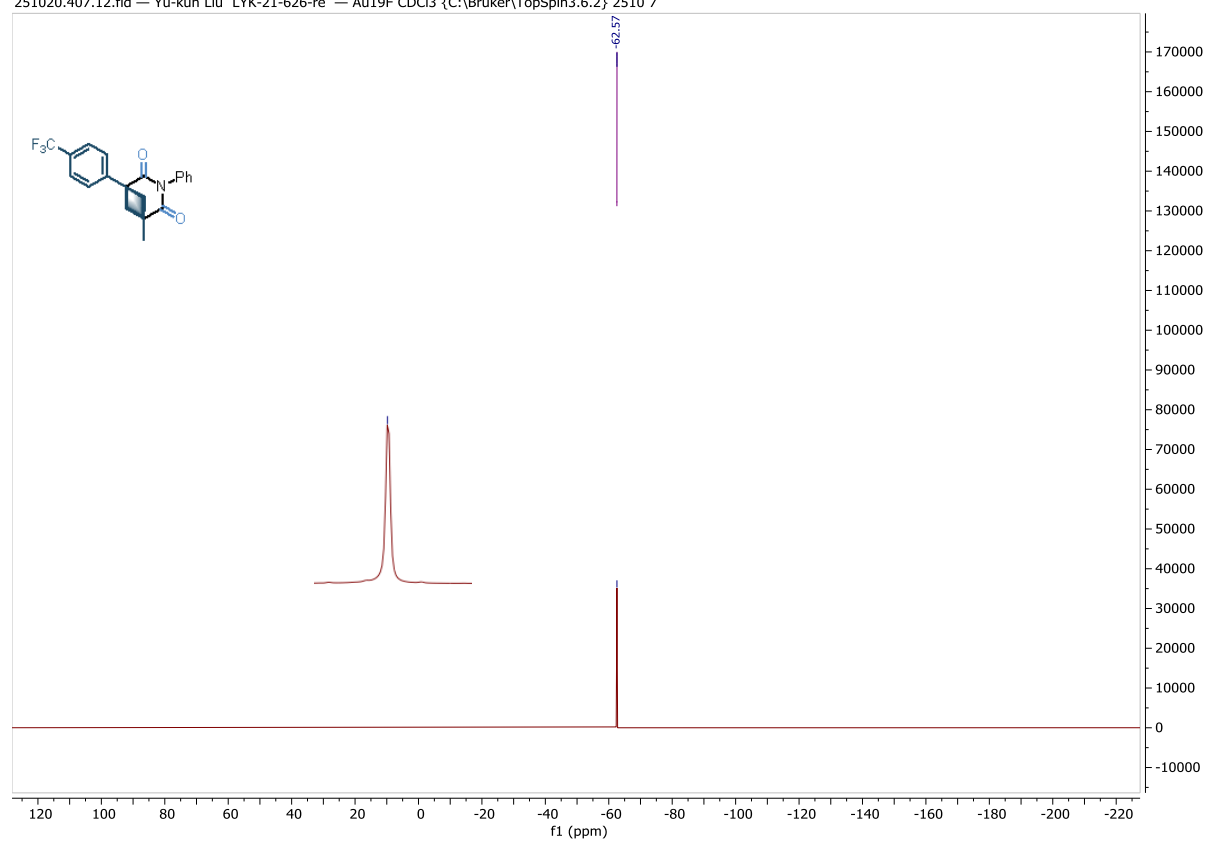
Supplementary Fig. 187. ^{13}C NMR spectrum of **4af** (101 MHz, CDCl_3)

251020.407.11.fid — Yu-kun Liu LYK-21-626-re — Au13C CDCl_3 {C:\Bruker\TopSpin3.6.2} 2510 7



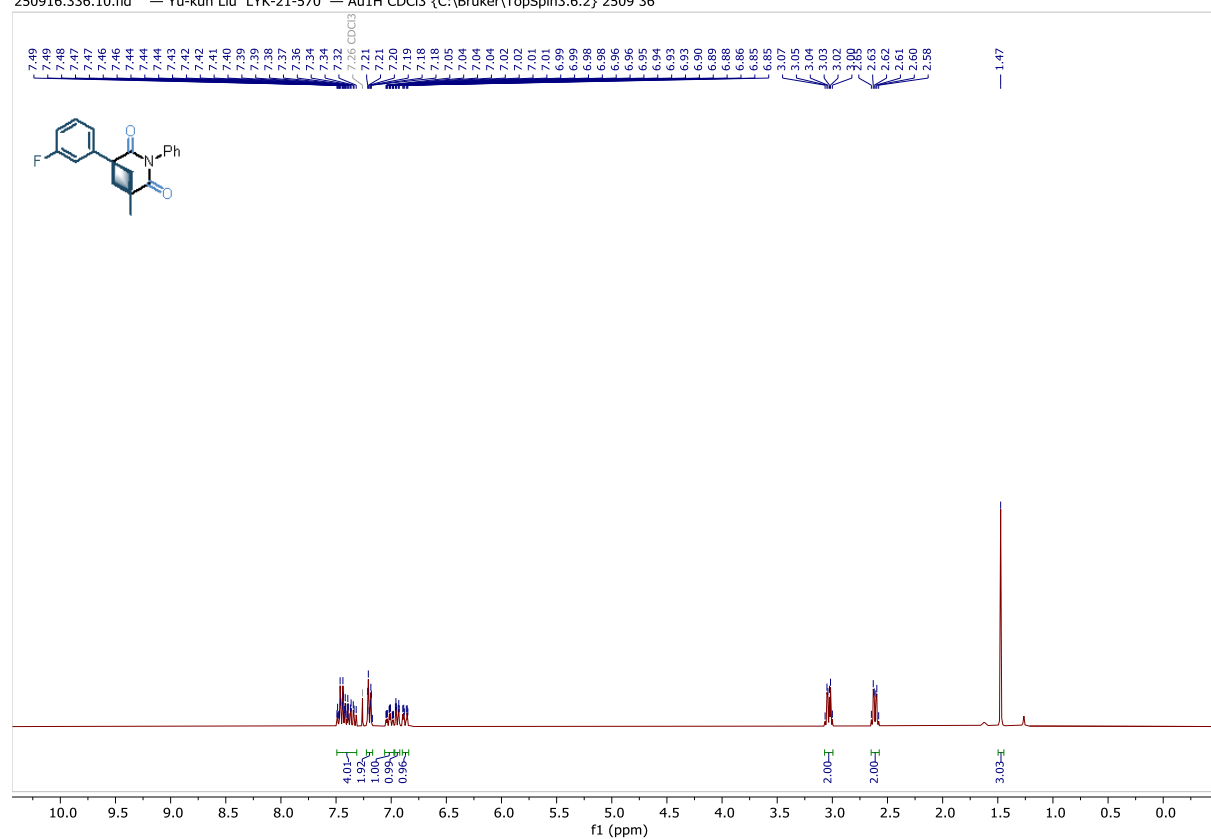
Supplementary Fig. 188. ^{19}F NMR spectrum of **4af** (376 MHz, CDCl_3)

251020.407.12.fid — Yu-kun Liu LYK-21-626-re — Au19F CDCl_3 {C:\Bruker\TopSpin3.6.2} 2510 7



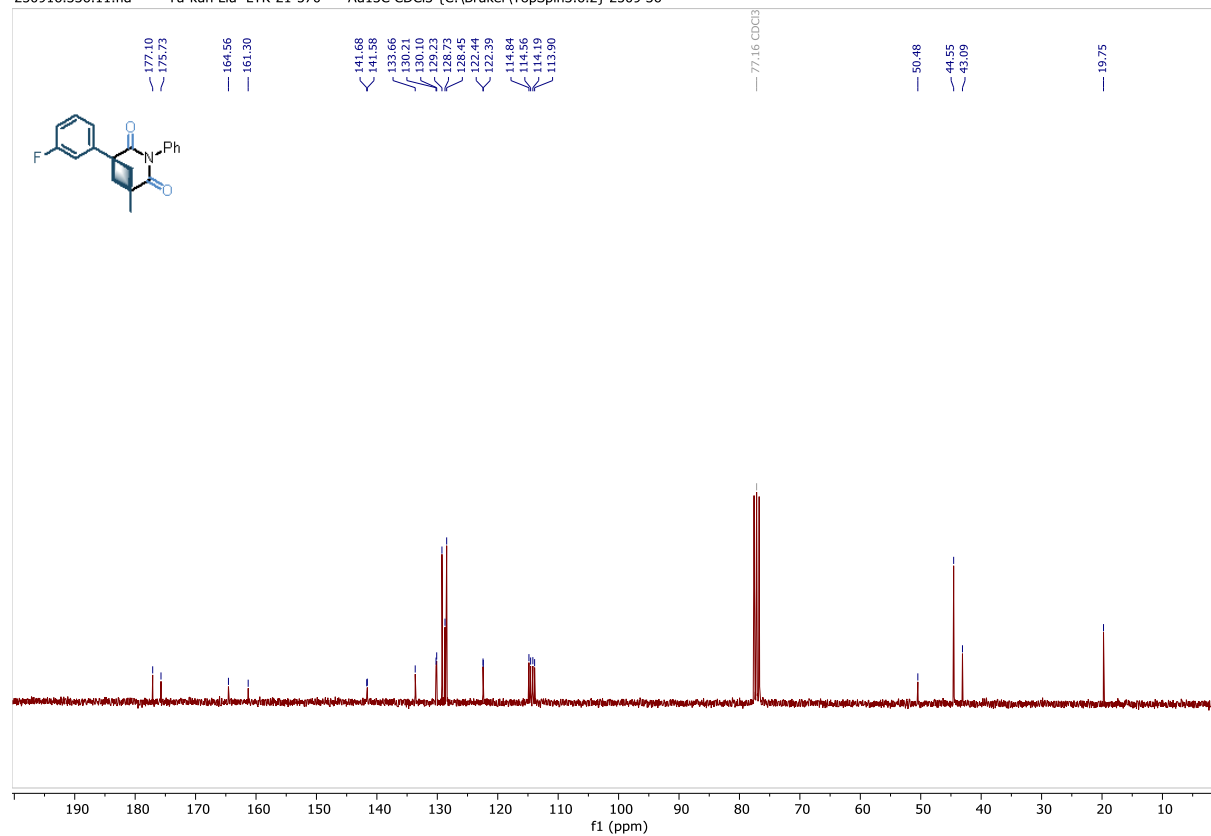
Supplementary Fig. 189. ^1H NMR spectrum of **4ag** (300 MHz, CDCl_3)

250916.336.10.fid — Yu-kun Liu LYK-21-570 — Au1H CDCl_3 {C:\Bruker\TopSpin3.6.2} 2509 36



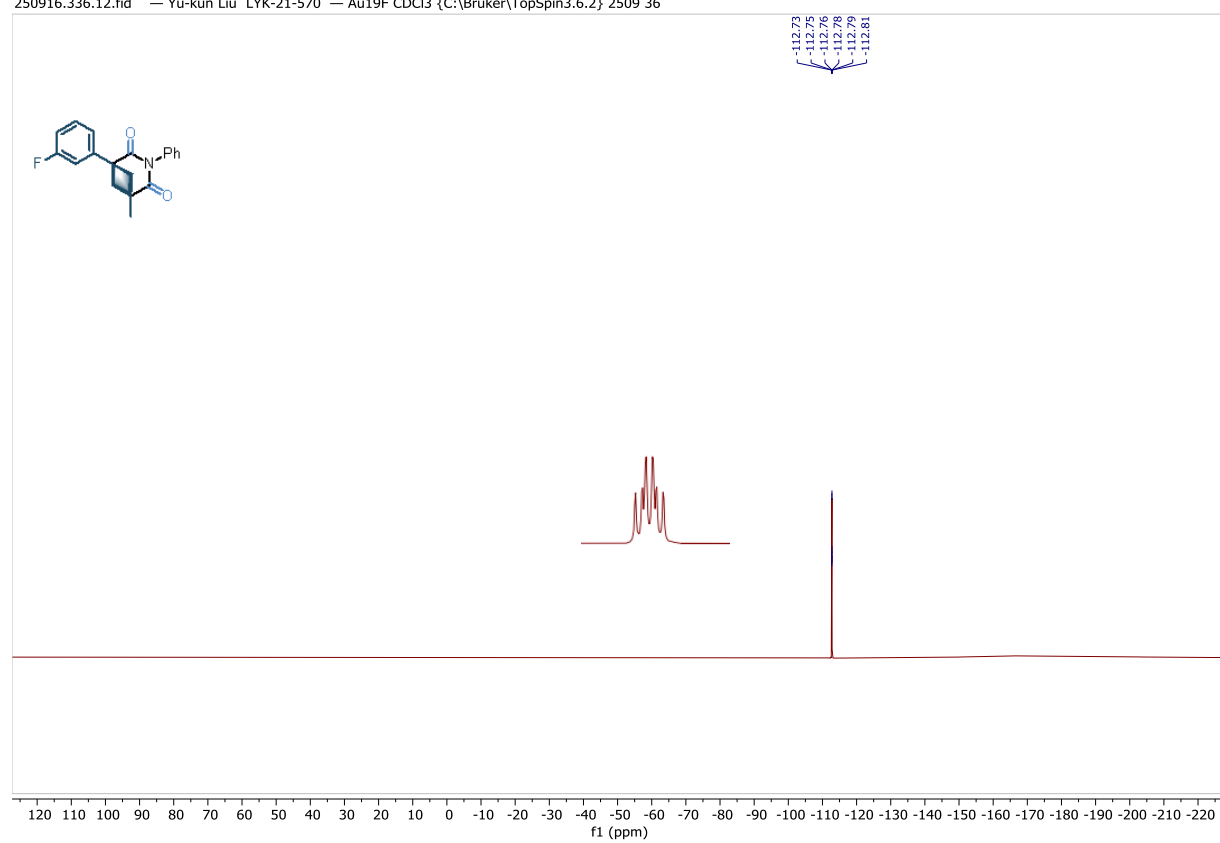
Supplementary Fig. 190. ^{13}C NMR spectrum of **4ag** (75 MHz, CDCl_3)

250916.336.11.fid — Yu-kun Liu LYK-21-570 — Au13C CDCl_3 {C:\Bruker\TopSpin3.6.2} 2509 36



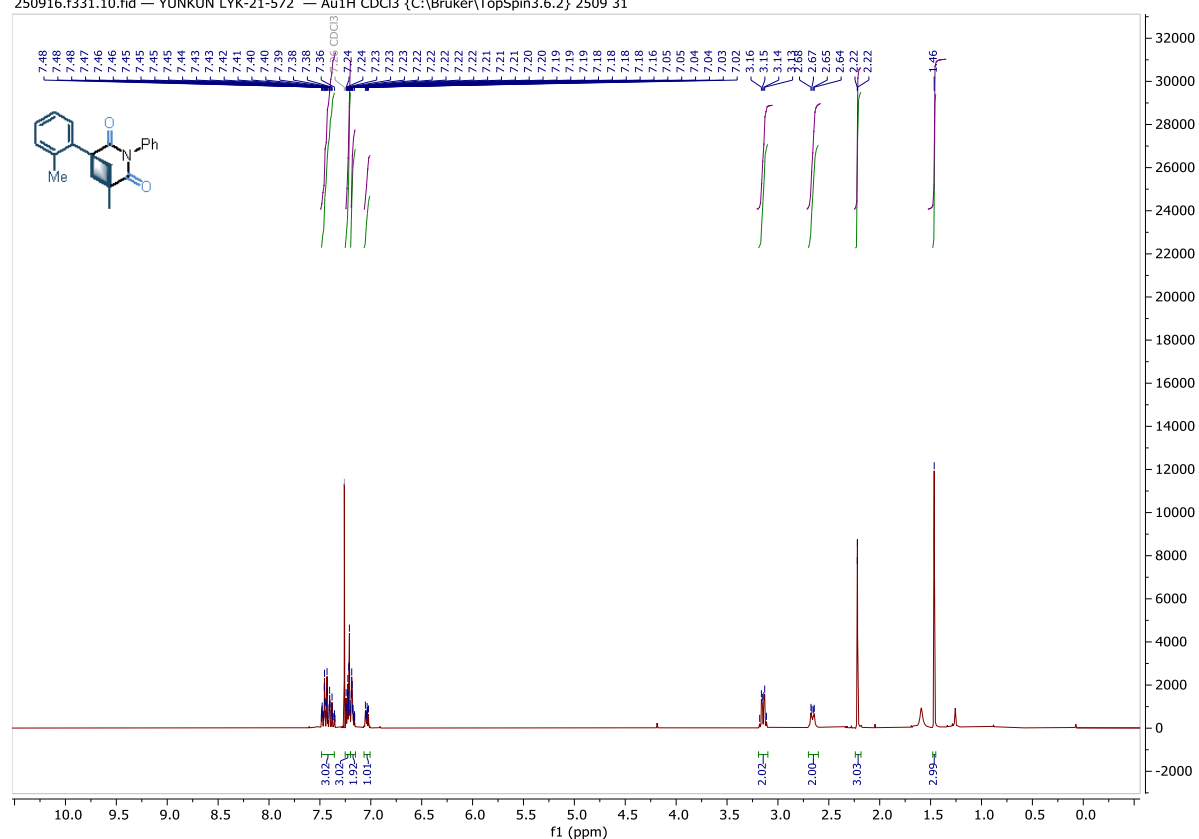
Supplementary Fig. 191. ^{19}F NMR spectrum of **4ag** (282 MHz, CDCl_3)

250916.336.12.fid — Yu-kun Liu LYK-21-570 — Au19F CDCl_3 {C:\Bruker\TopSpin3.6.2} 2509 36



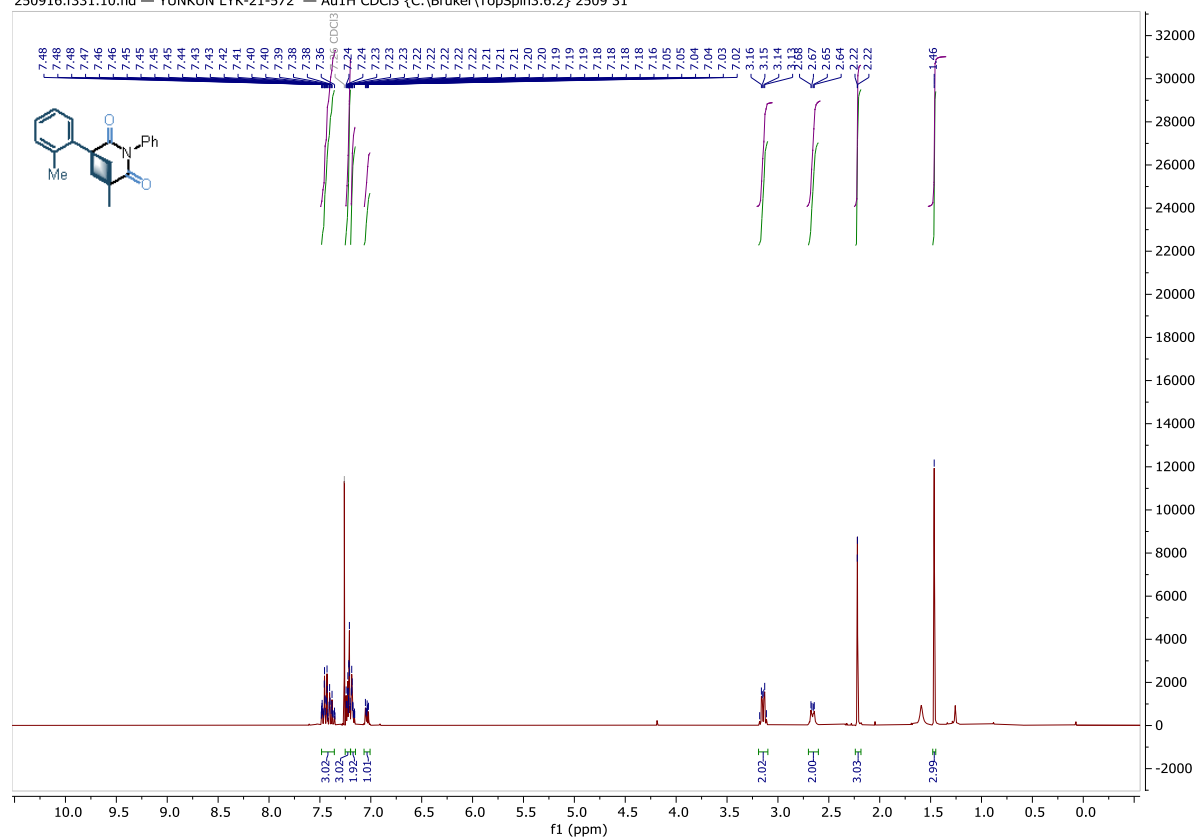
Supplementary Fig. 192. ^1H NMR spectrum of **4ah** (300 MHz, CDCl_3)

250916.f331.10.fid — YUNKUN LYK-21-572 — Au1H CDCl_3 {C:\Bruker\TopSpin3.6.2} 2509 31

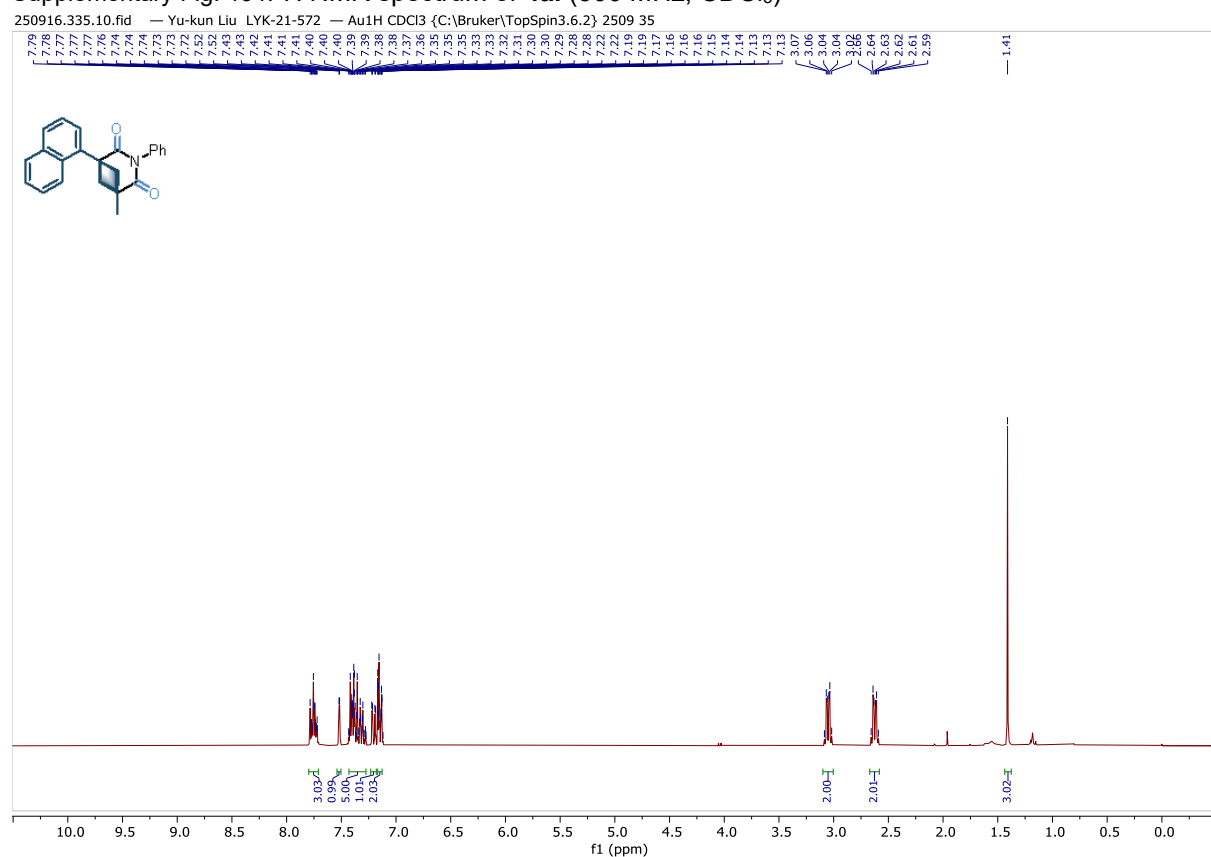


Supplementary Fig. 193. ^{13}C NMR spectrum of **4ah** (75 MHz, CDCl_3)

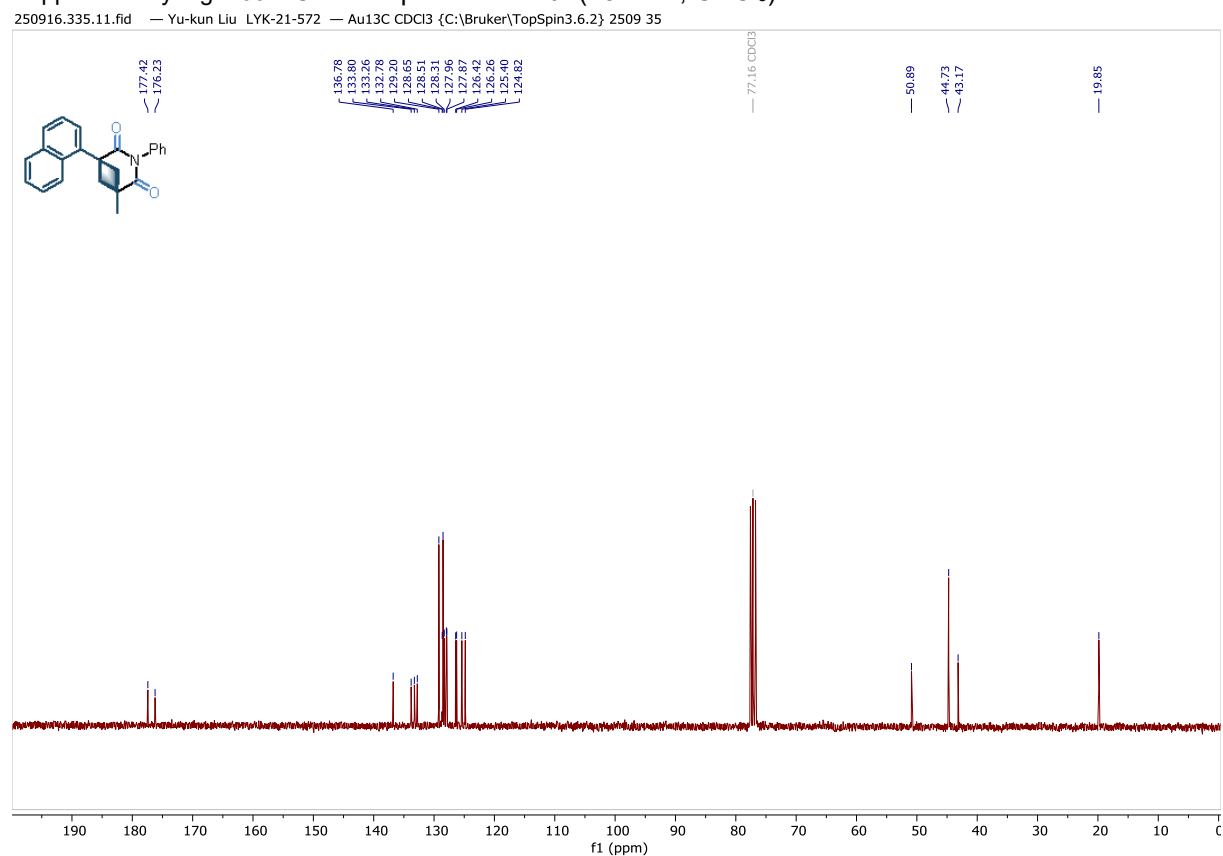
250916.f331.10.fid — YUNKUN LYK-21-572 — Au1H CDCl_3 {C:\Bruker\TopSpin3.6.2} 2509 31



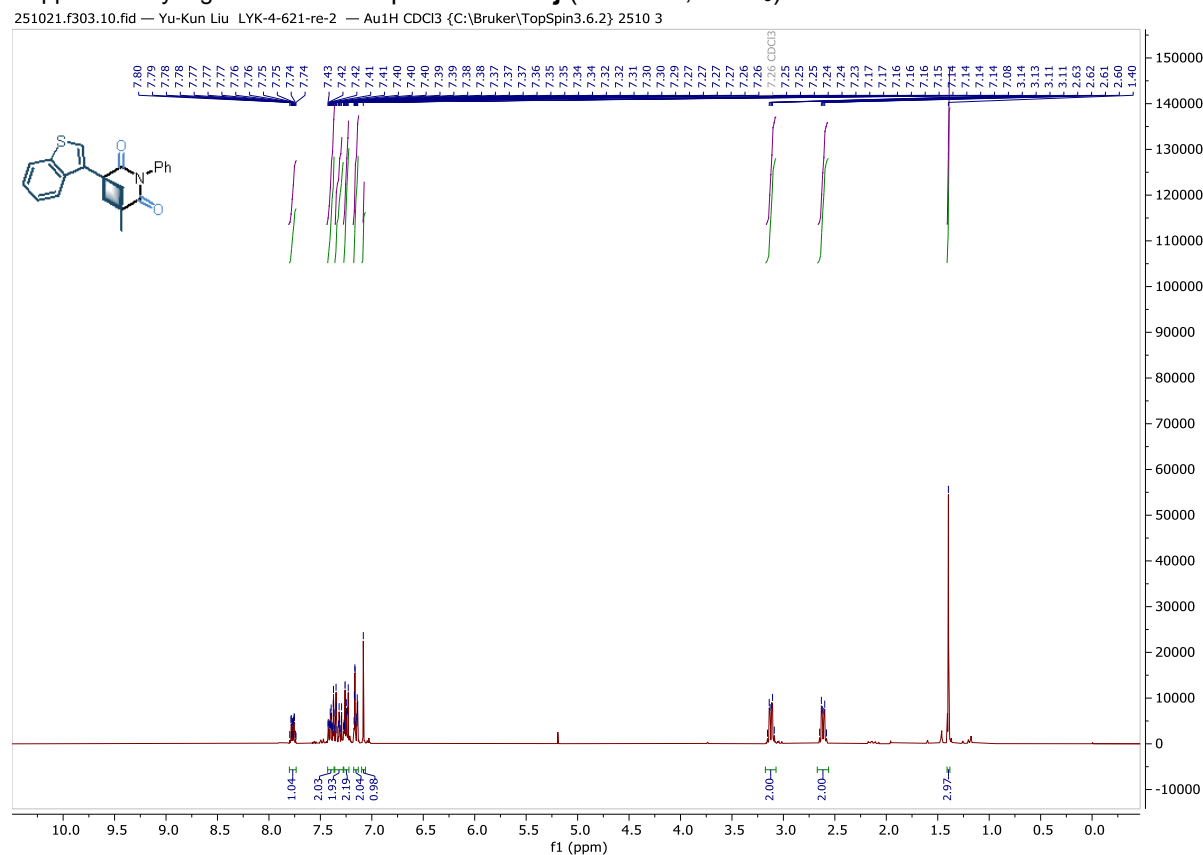
Supplementary Fig. 194. ^1H NMR spectrum of **4ai** (300 MHz, CDCl_3)



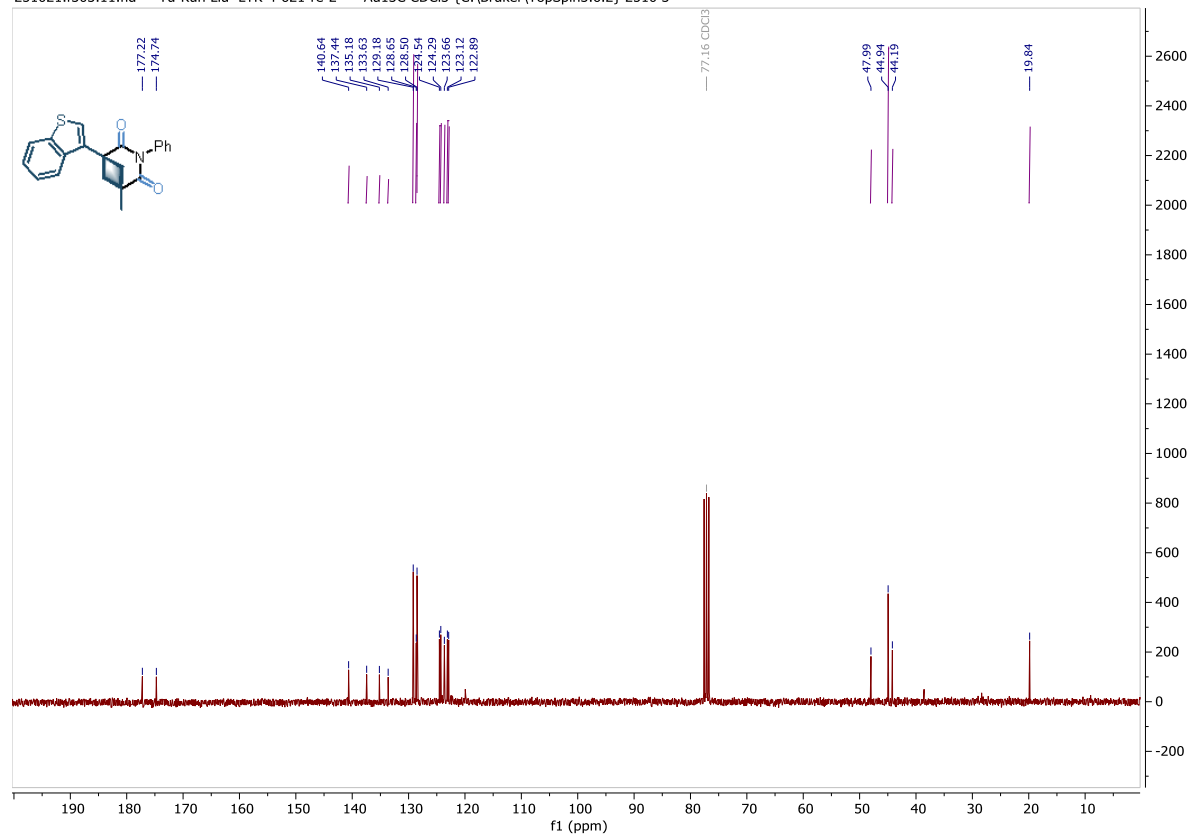
Supplementary Fig. 195. ^{13}C NMR spectrum of **4ai** (75 MHz, CDCl_3)



251021.f303.10.fid — Yu-Kun Liu LYK-4-621-re-2 — Au1H CDCl3 {C:\Bruker\TopSpin3.6.2} 2510 3

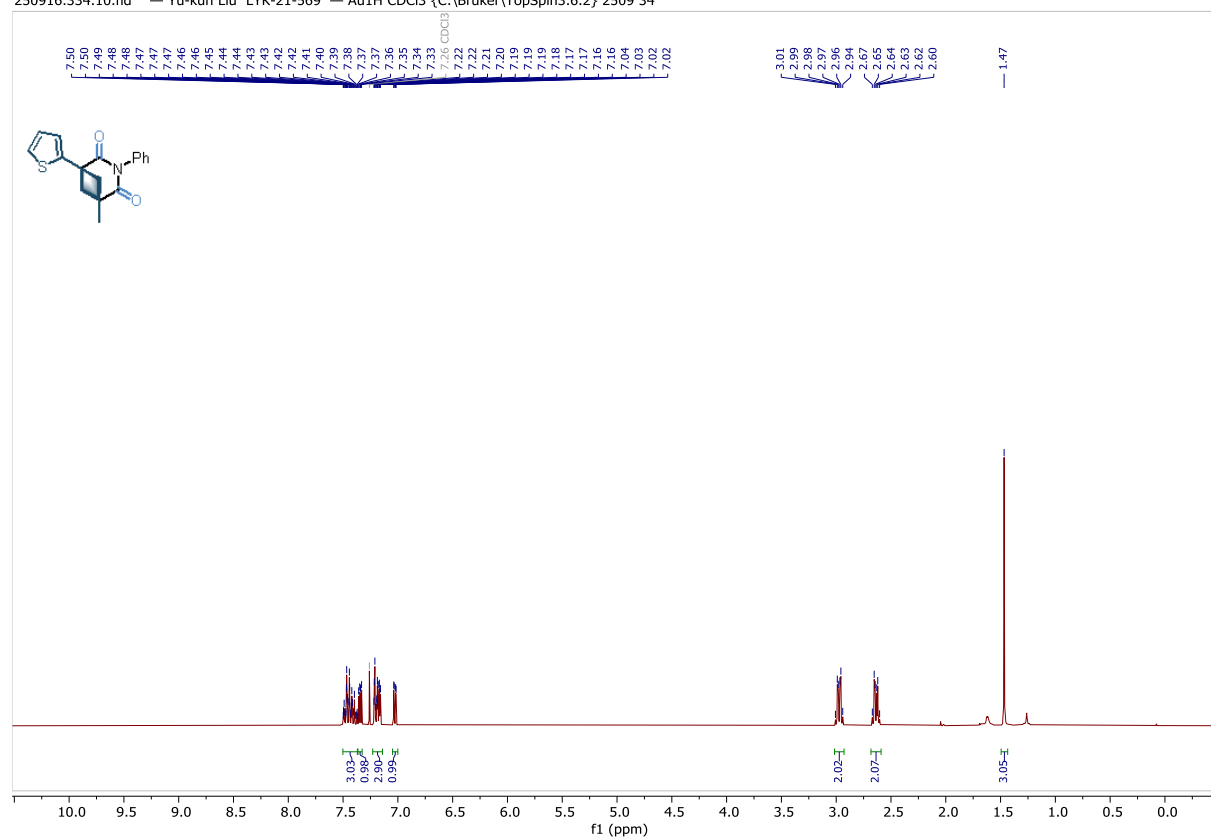


251021.f303.11.fid — Yu-Kun Liu LYK-4-621-re-2 — Au13C CDCl3 {C:\Bruker\TopSpin3.6.2} 2510 3



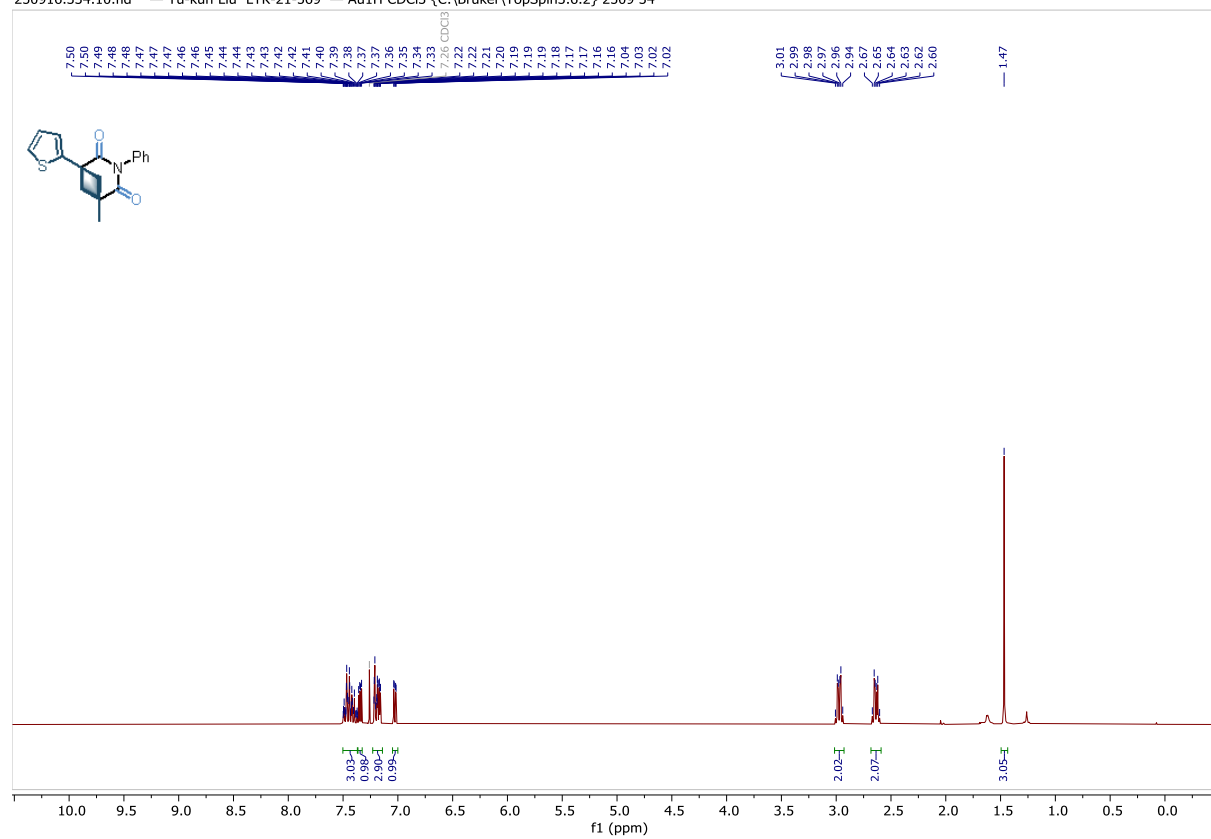
Supplementary Fig. 198. ^1H NMR spectrum of **4ak** (300 MHz, CDCl_3)

250916.334.10.fid — Yu-kun Liu LYK-21-569 — Au1H CDCl_3 {C:\Bruker\TopSpin3.6.2} 2509 34

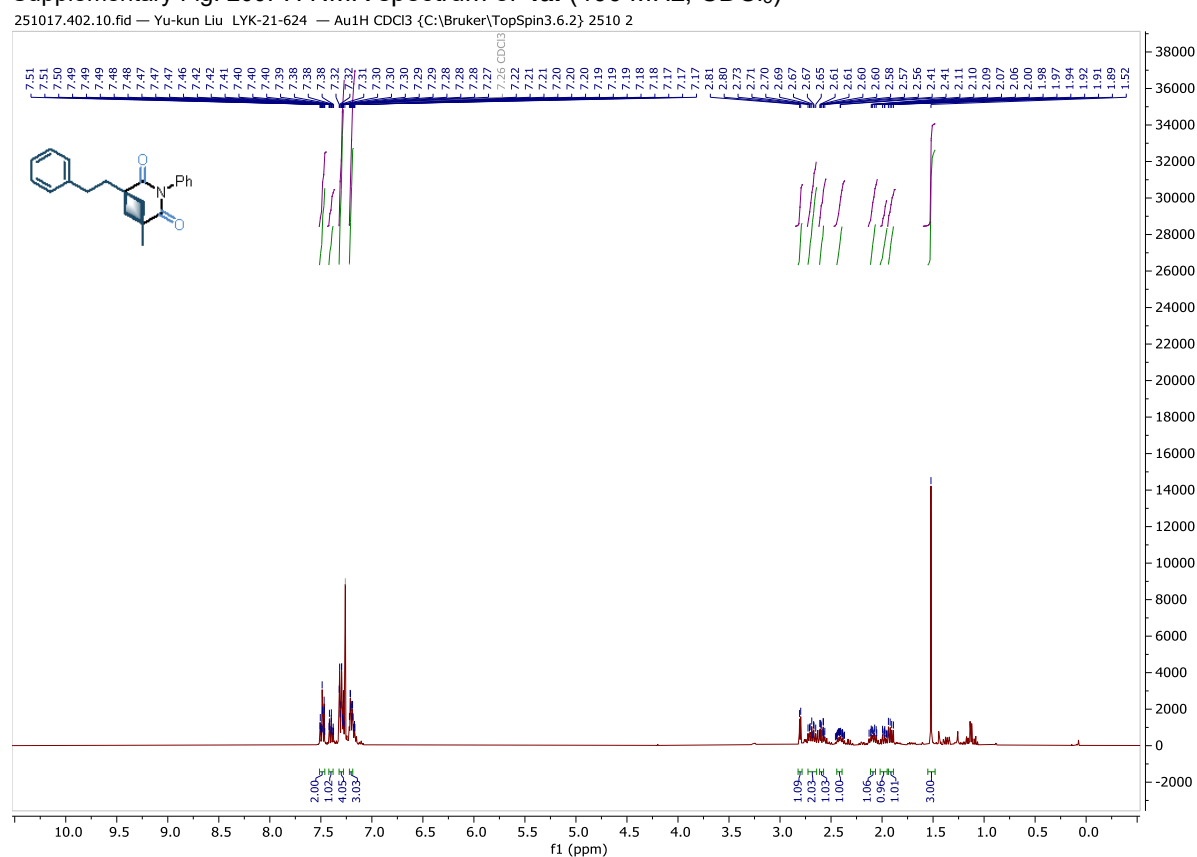


Supplementary Fig. 199. ^{13}C NMR spectrum of **4ak** (75 MHz, CDCl_3)

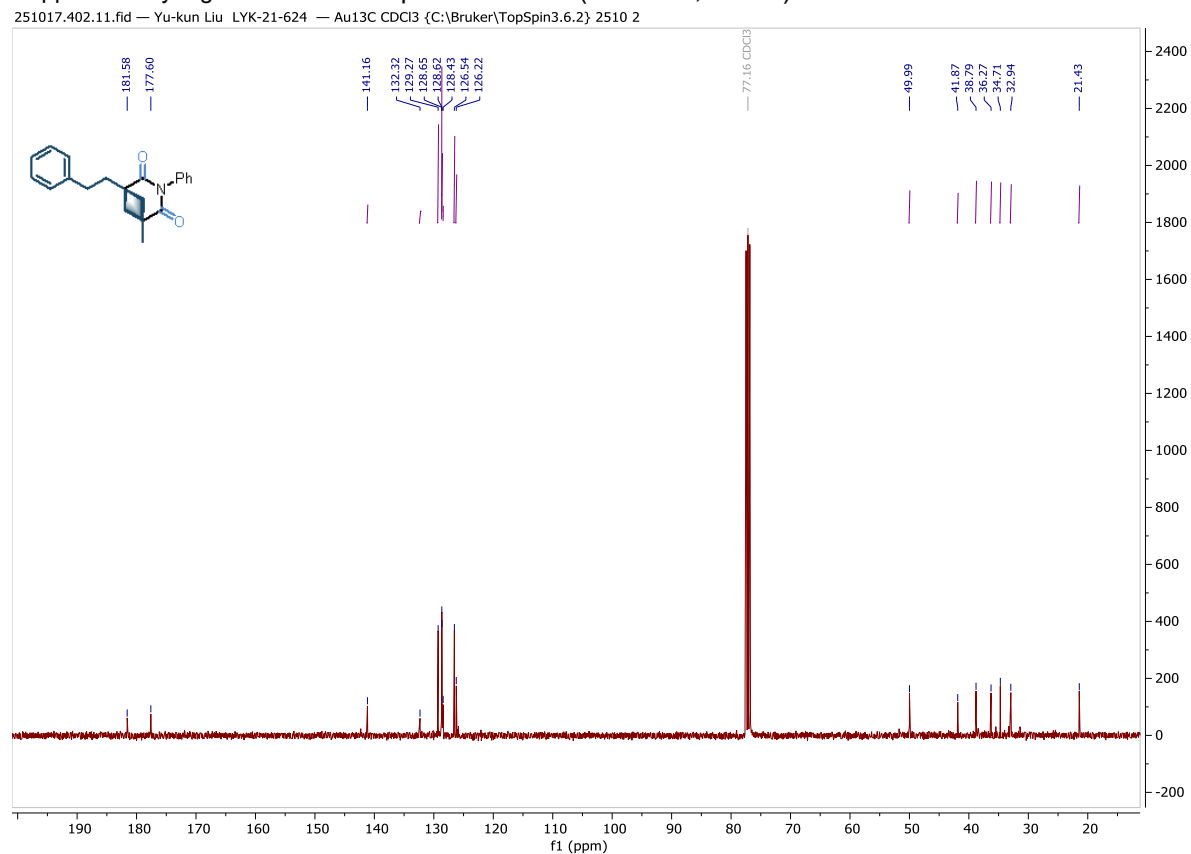
250916.334.10.fid — Yu-kun Liu LYK-21-569 — Au1H CDCl_3 {C:\Bruker\TopSpin3.6.2} 2509 34



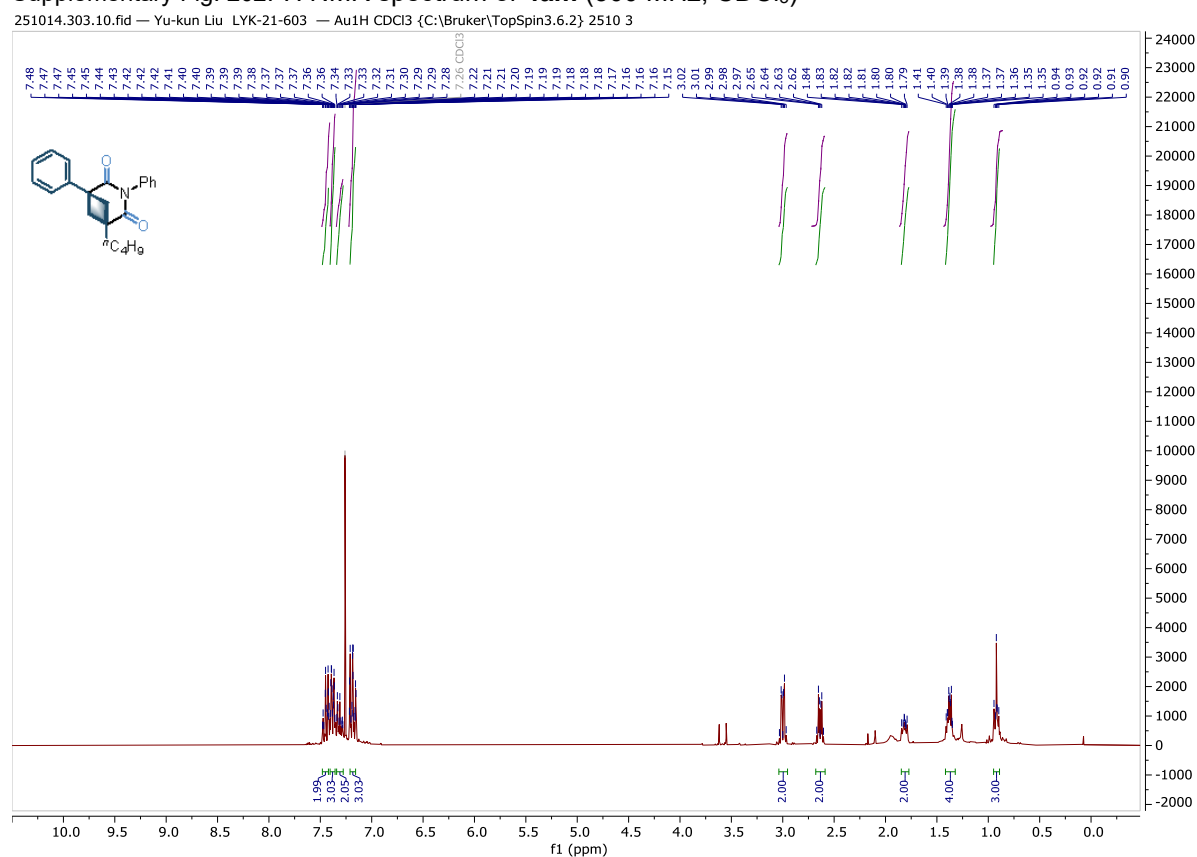
Supplementary Fig. 200. ^1H NMR spectrum of **4al** (400 MHz, CDCl_3)



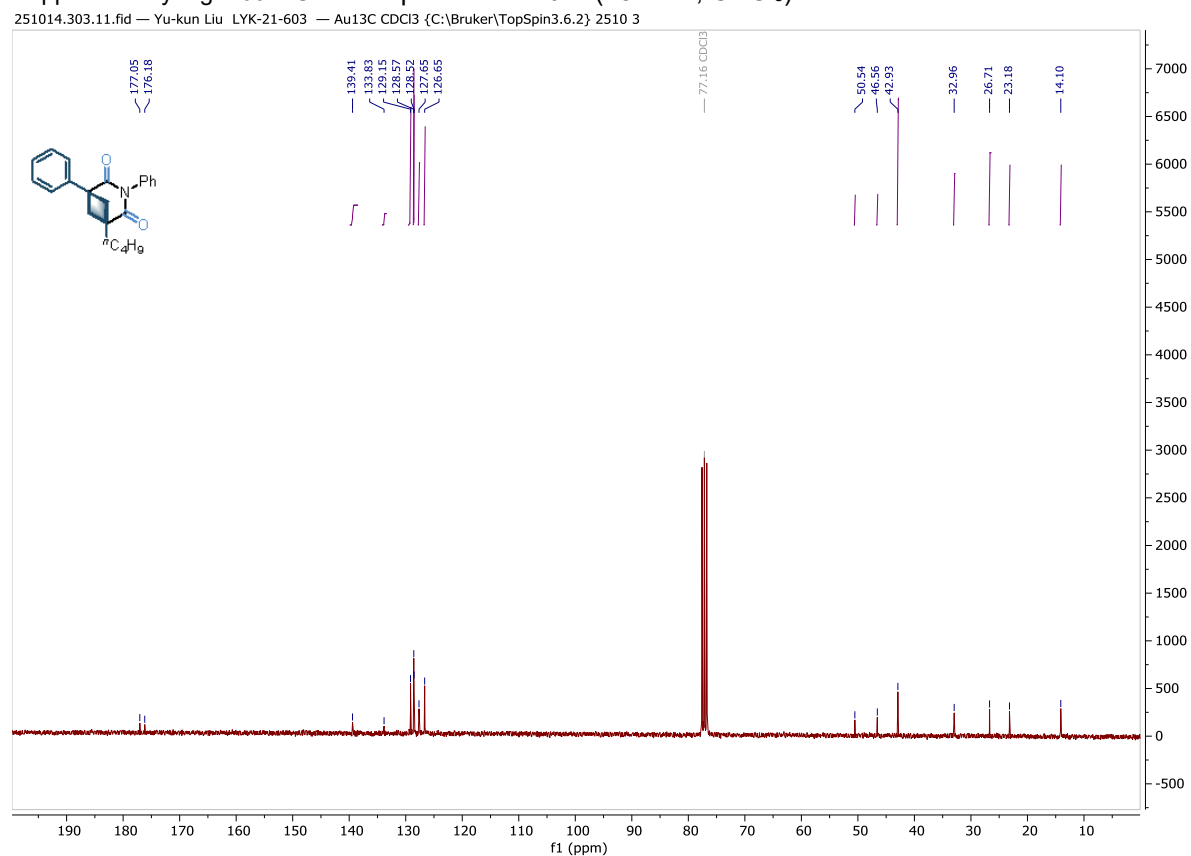
Supplementary Fig. 201. ^{13}C NMR spectrum of **4al** (101 MHz, CDCl_3)



Supplementary Fig. 202. ^1H NMR spectrum of **4am** (300 MHz, CDCl_3)

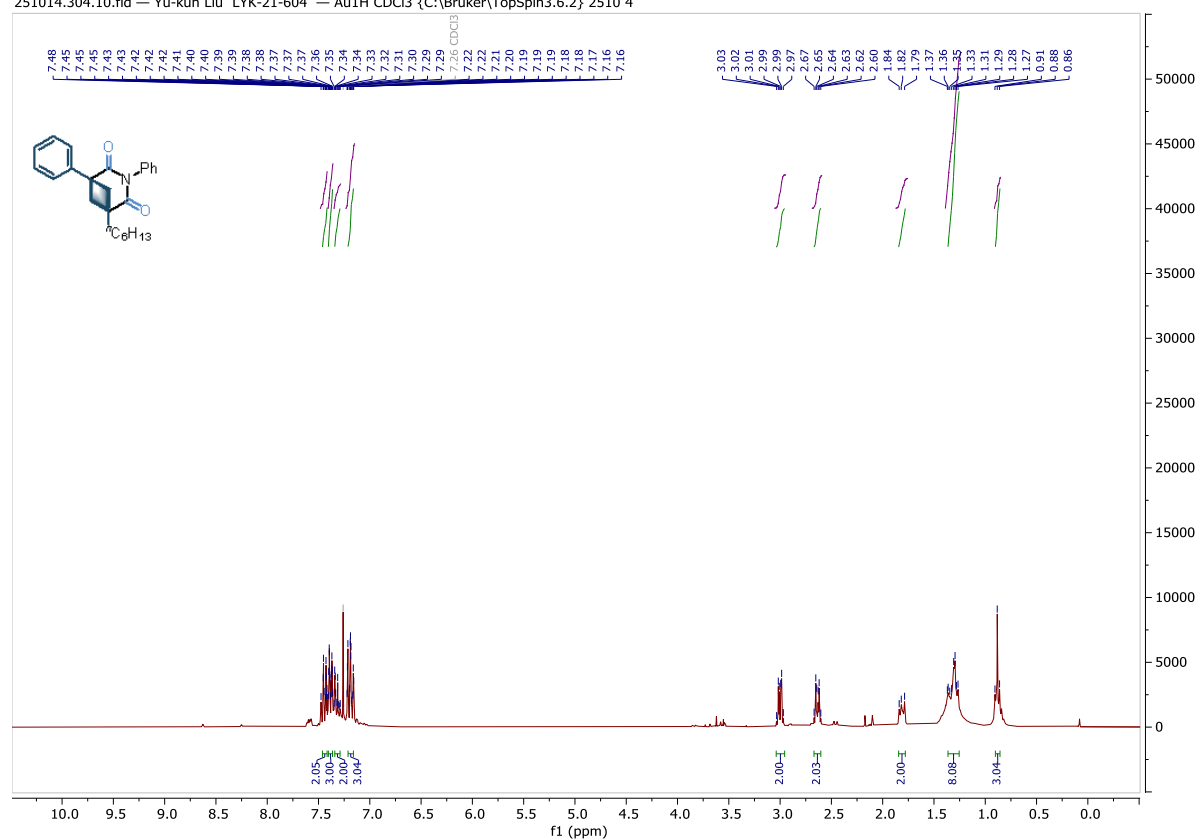


Supplementary Fig. 203. ^{13}C NMR spectrum of **4am** (75 MHz, CDCl_3)



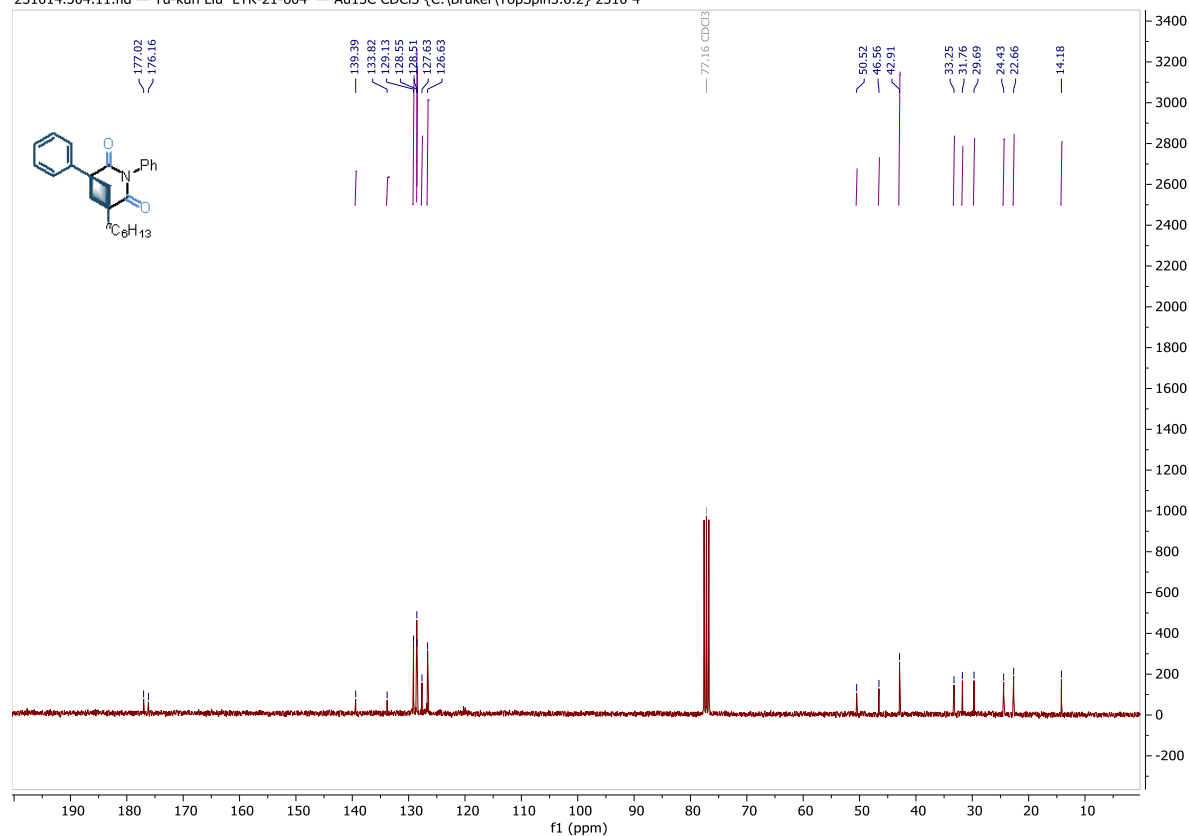
Supplementary Fig. 204. ^1H NMR spectrum of **4an** (300 MHz, CDCl_3)

251014.304.10.fid — Yu-kun Liu LYK-21-604 — Au1H CDCl_3 {C:\Bruker\TopSpin3.6.2} 2510 4



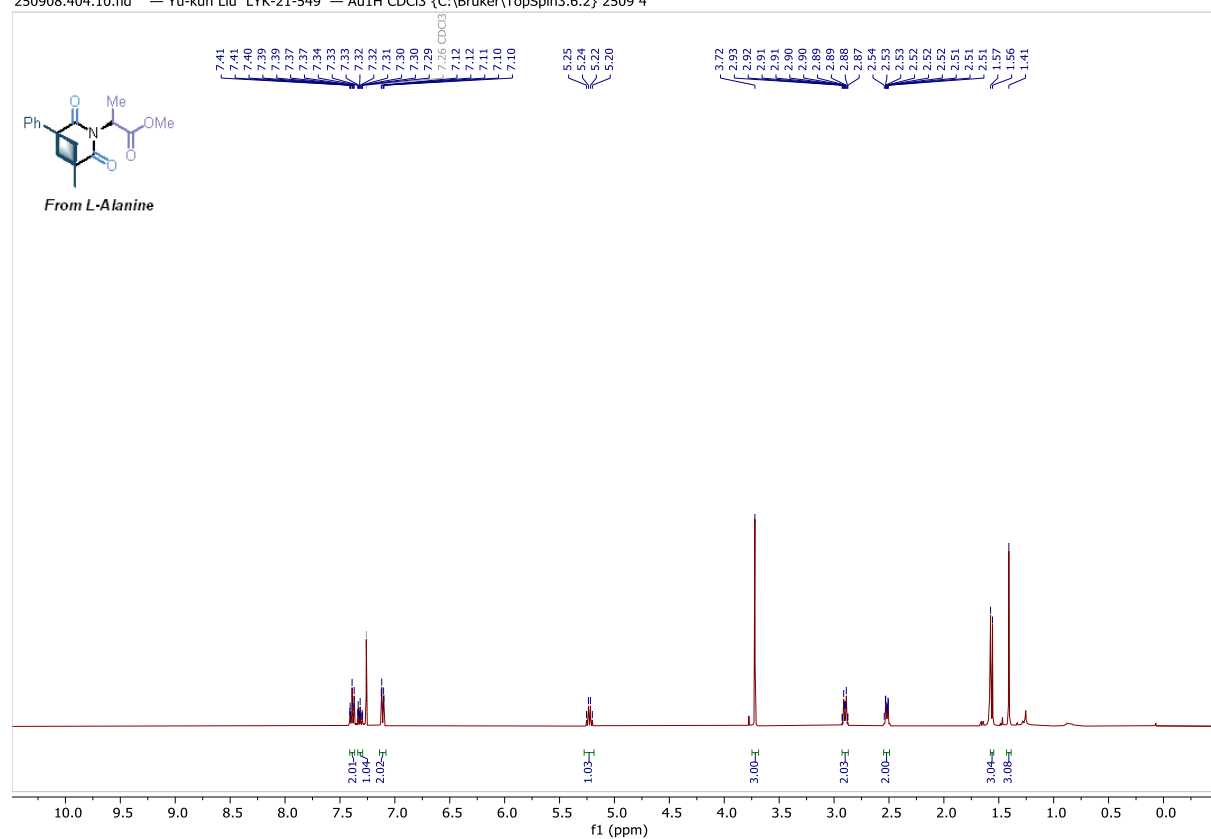
Supplementary Fig. 205. ^{13}C NMR spectrum of **4an** (75 MHz, CDCl_3)

251014.304.11.fid — Yu-kun Liu LYK-21-604 — Au13C CDCl_3 {C:\Bruker\TopSpin3.6.2} 2510 4



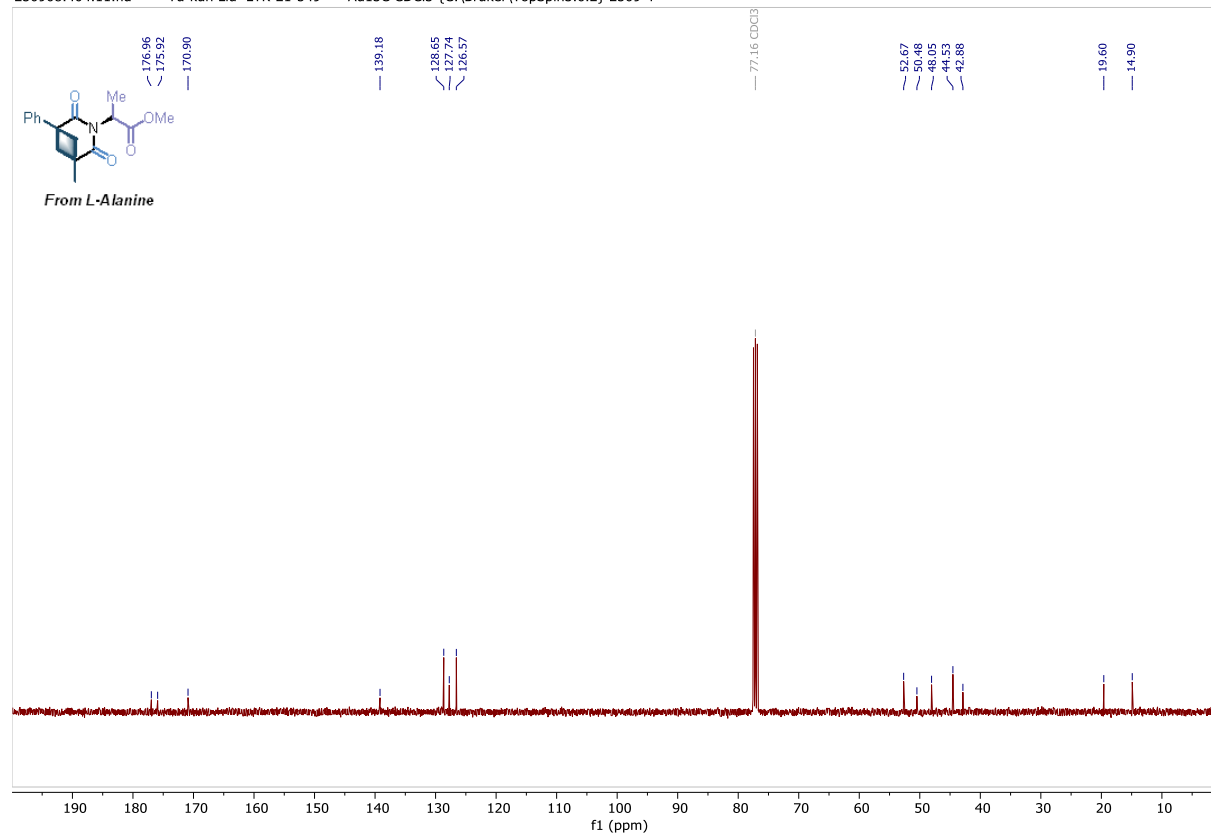
Supplementary Fig. 206. ^1H NMR spectrum of **4ap** (400 MHz, CDCl_3)

250908.404.10.fid — Yu-kun Liu LYK-21-549 — Au1H CDCl_3 {C:\Bruker\TopSpin3.6.2} 2509 4



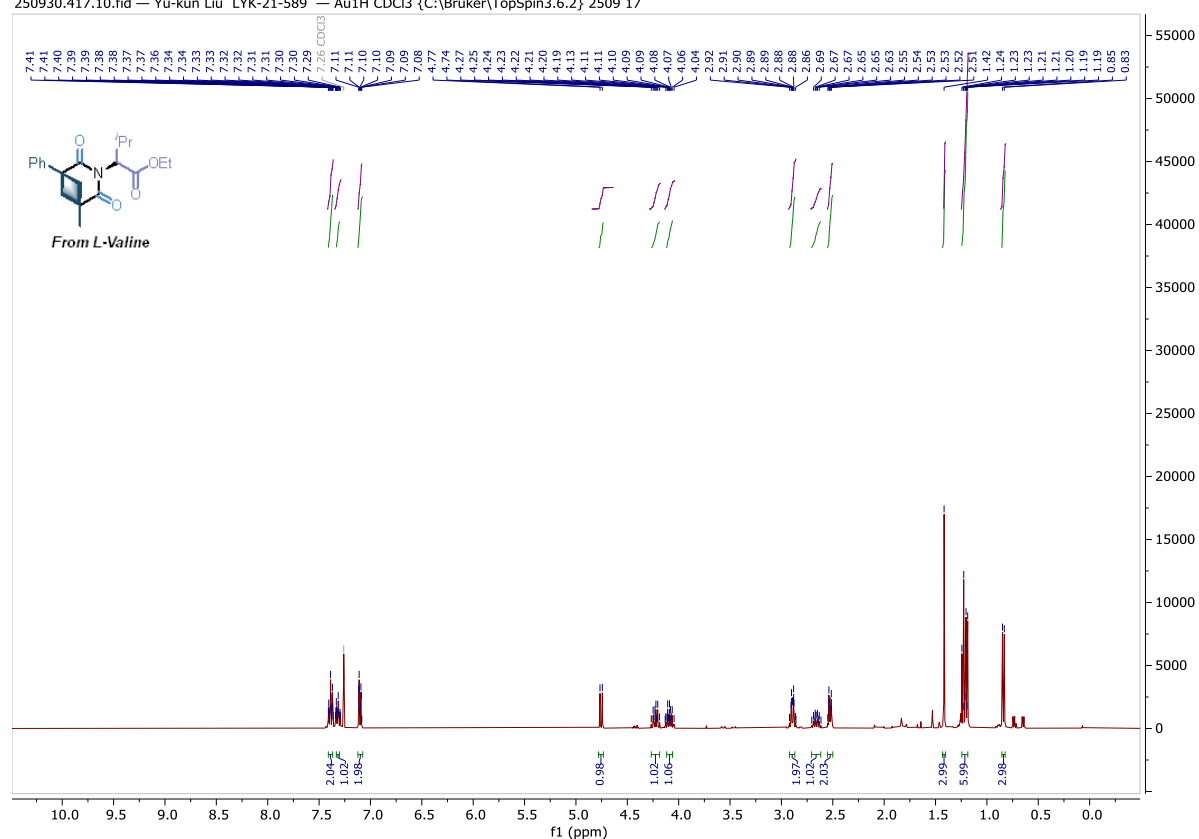
Supplementary Fig. 207. ^{13}C NMR spectrum of **4ap** (101 MHz, CDCl_3)

250908.404.11.fid — Yu-kun Liu LYK-21-549 — Au13C CDCl_3 {C:\Bruker\TopSpin3.6.2} 2509 4



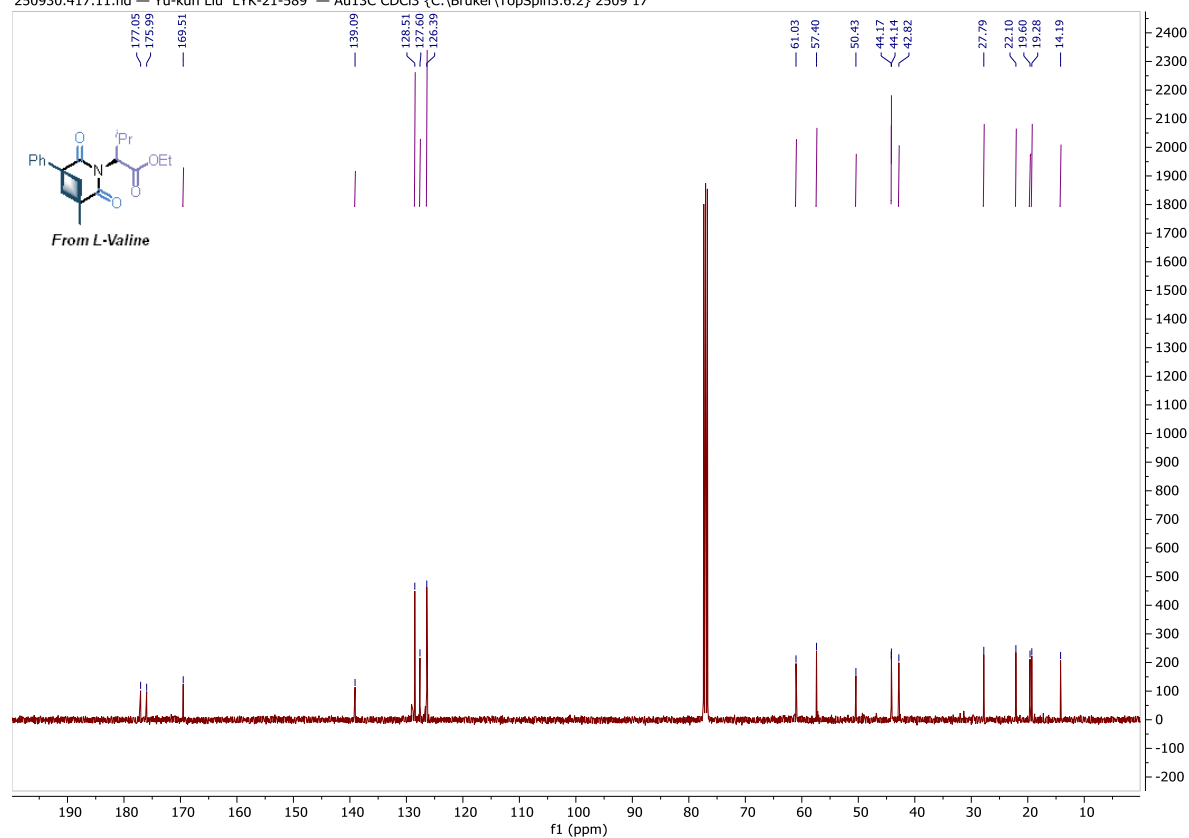
Supplementary Fig. 208. ^1H NMR spectrum of **4aq** (400 MHz, CDCl_3)

250930.417.10.fid — Yu-kun Liu LYK-21-589 — Au1H CDCl_3 {C:\Bruker\TopSpin3.6.2} 2509 17



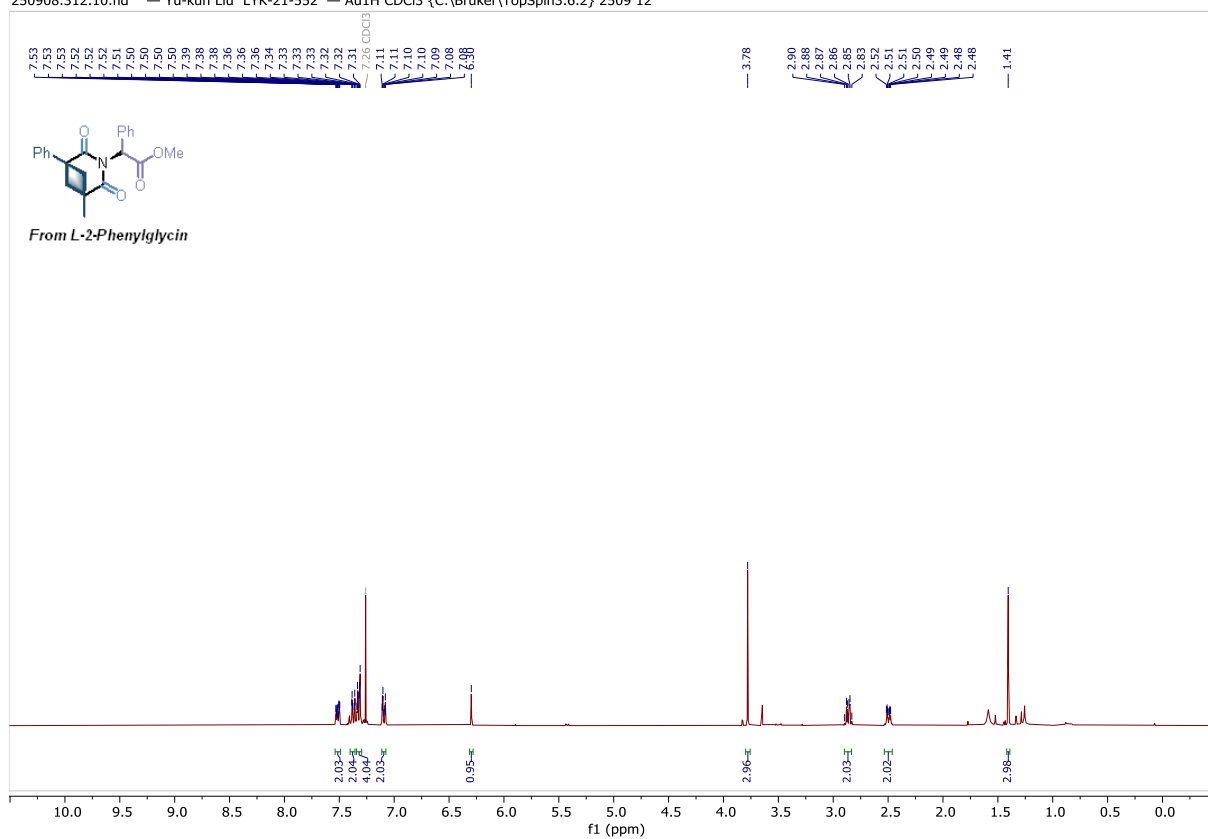
Supplementary Fig. 209. ^{13}C NMR spectrum of **4aq** (101 MHz, CDCl_3)

250930.417.11.fid — Yu-kun Liu LYK-21-589 — Au13C CDCl_3 {C:\Bruker\TopSpin3.6.2} 2509 17



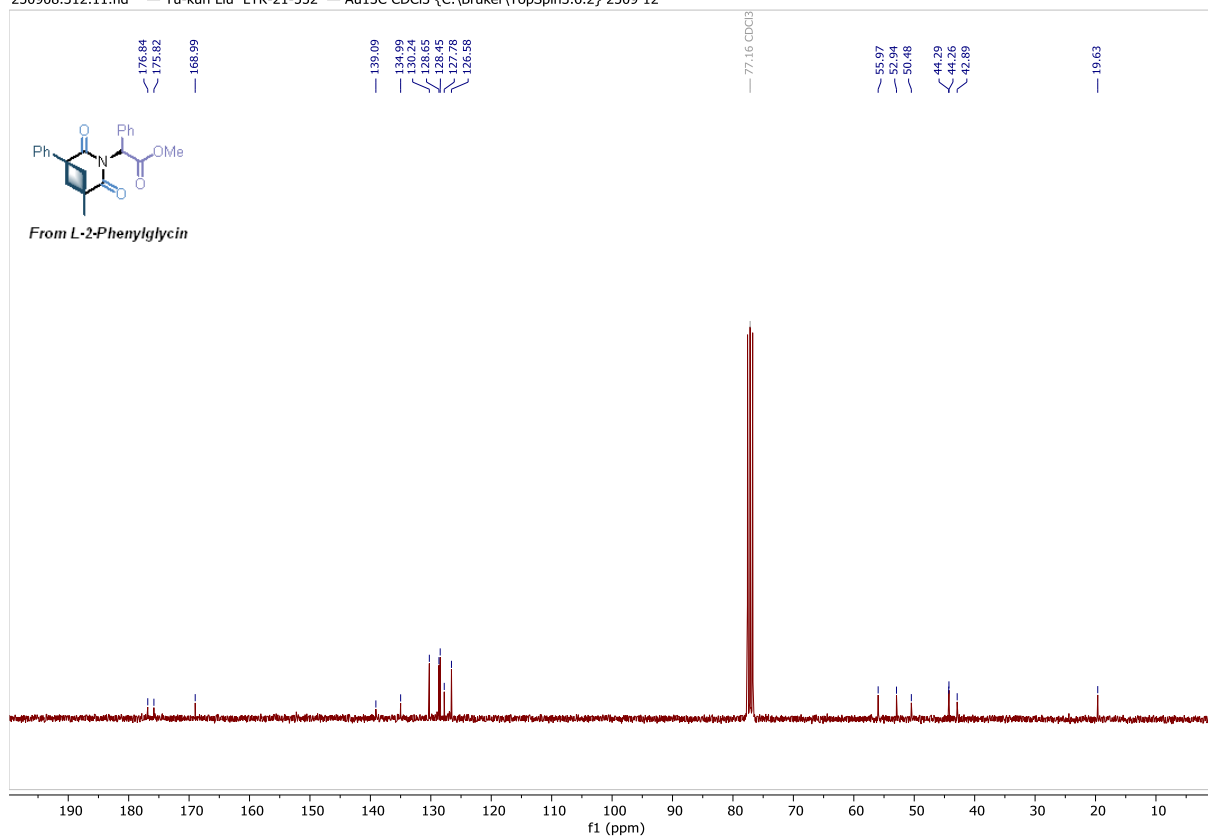
Supplementary Fig. 210. ^1H NMR spectrum of **4ar** (300 MHz, CDCl_3)

250908.312.10.fid — Yu-kun Liu LYK-21-552 — Au ^1H CDCl_3 {C:\Bruker\TopSpin3.6.2} 2509 12



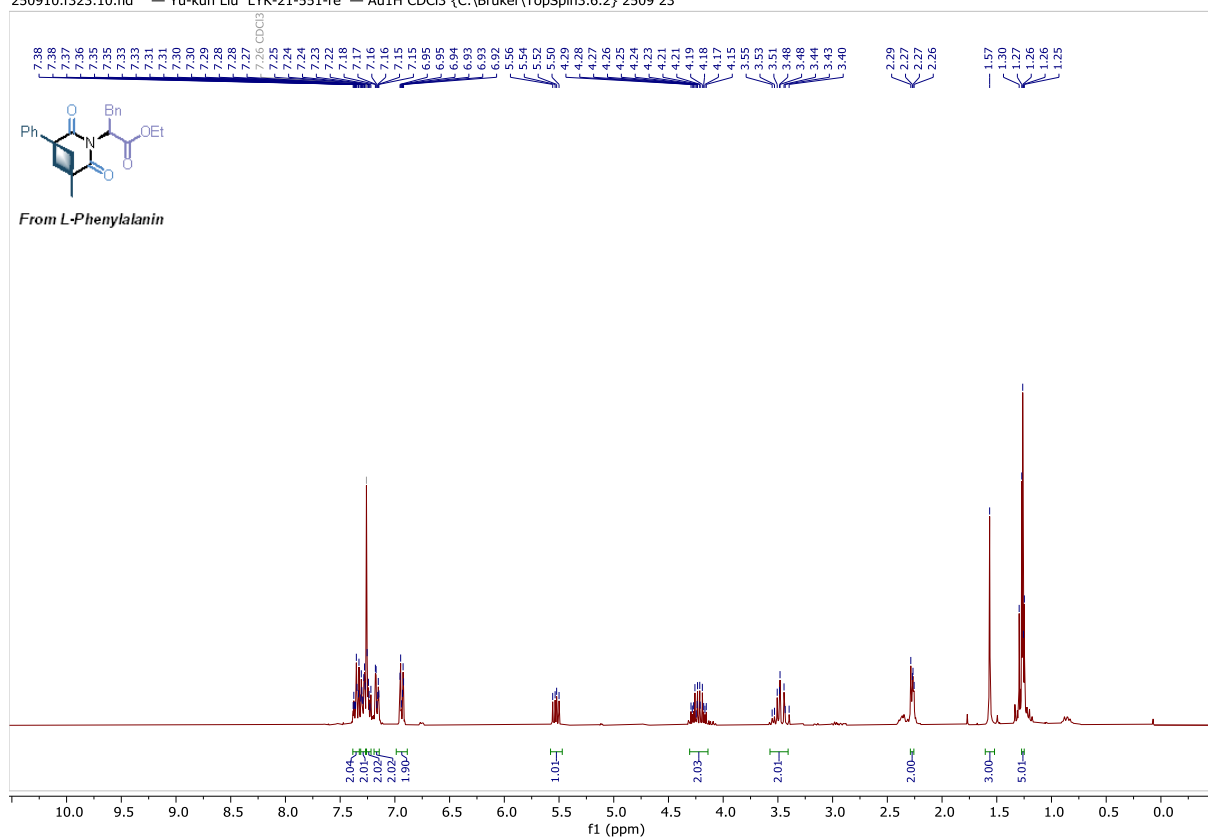
Supplementary Fig. 211. ^{13}C NMR spectrum of **4ar** (75 MHz, CDCl_3)

250908.312.11.fid — Yu-kun Liu LYK-21-552 — Au ^{13}C CDCl_3 {C:\Bruker\TopSpin3.6.2} 2509 12



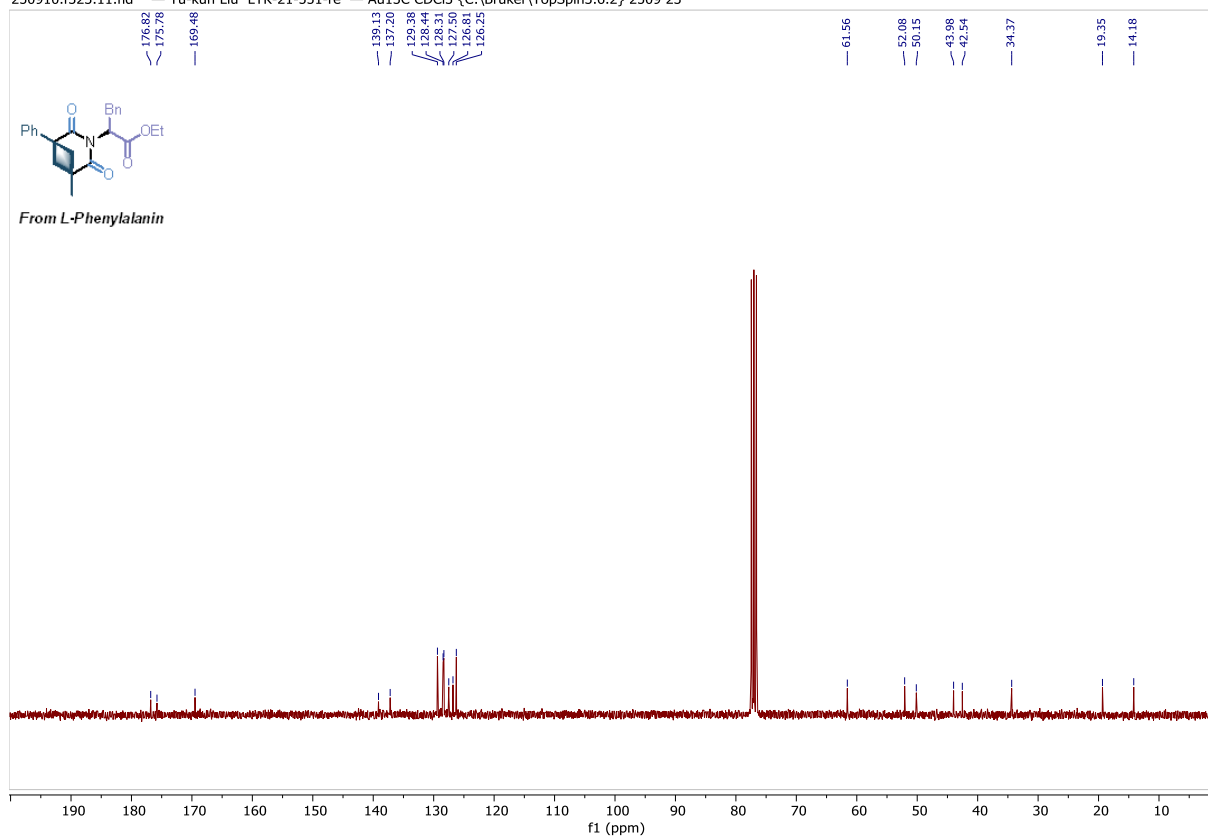
Supplementary Fig. 212. ^1H NMR spectrum of **4as** (300 MHz, CDCl_3)

250910.f323.10.fid — Yu-kun Liu LYK-21-551-re — Au1H CDCl_3 {C:\Bruker\TopSpin3.6.2} 2509 23



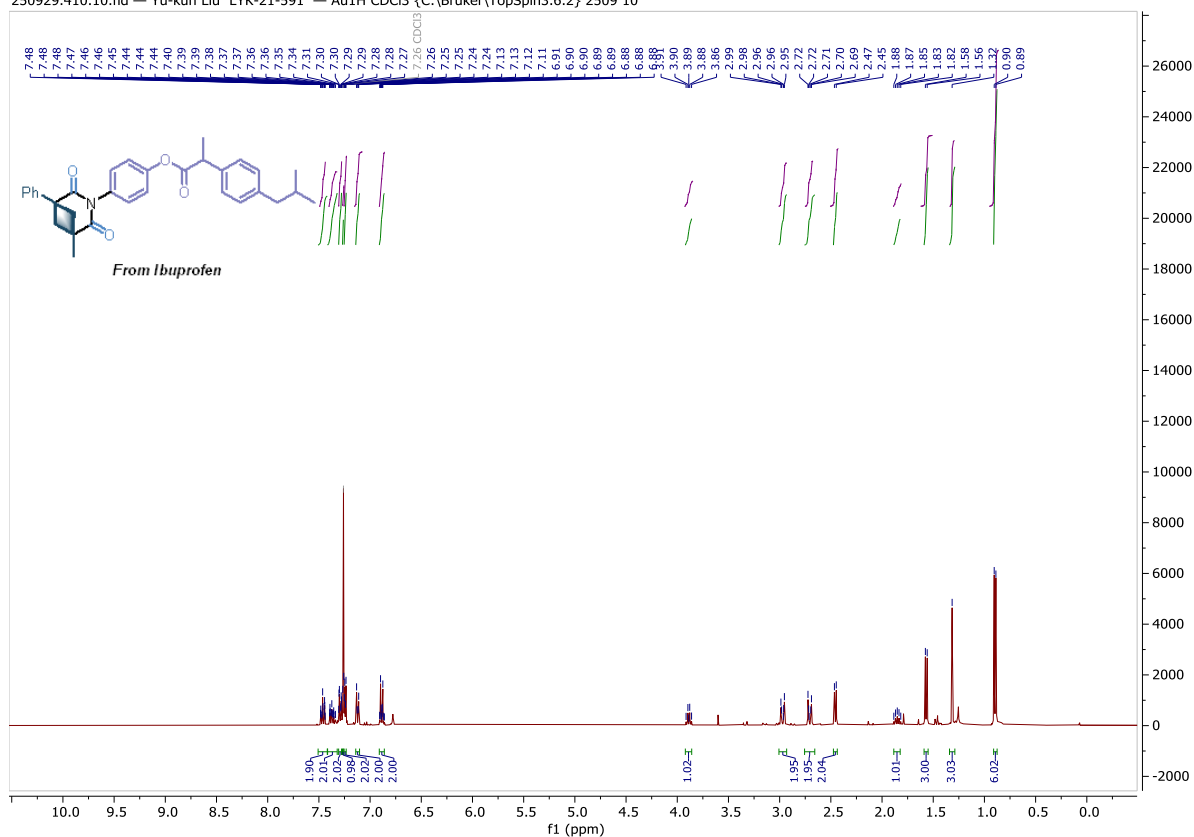
Supplementary Fig. 213. ^{13}C NMR spectrum of **4as** (75 MHz, CDCl_3)

250910.f323.11.fid — Yu-kun Liu LYK-21-551-re — Au13C CDCl_3 {C:\Bruker\TopSpin3.6.2} 2509 23



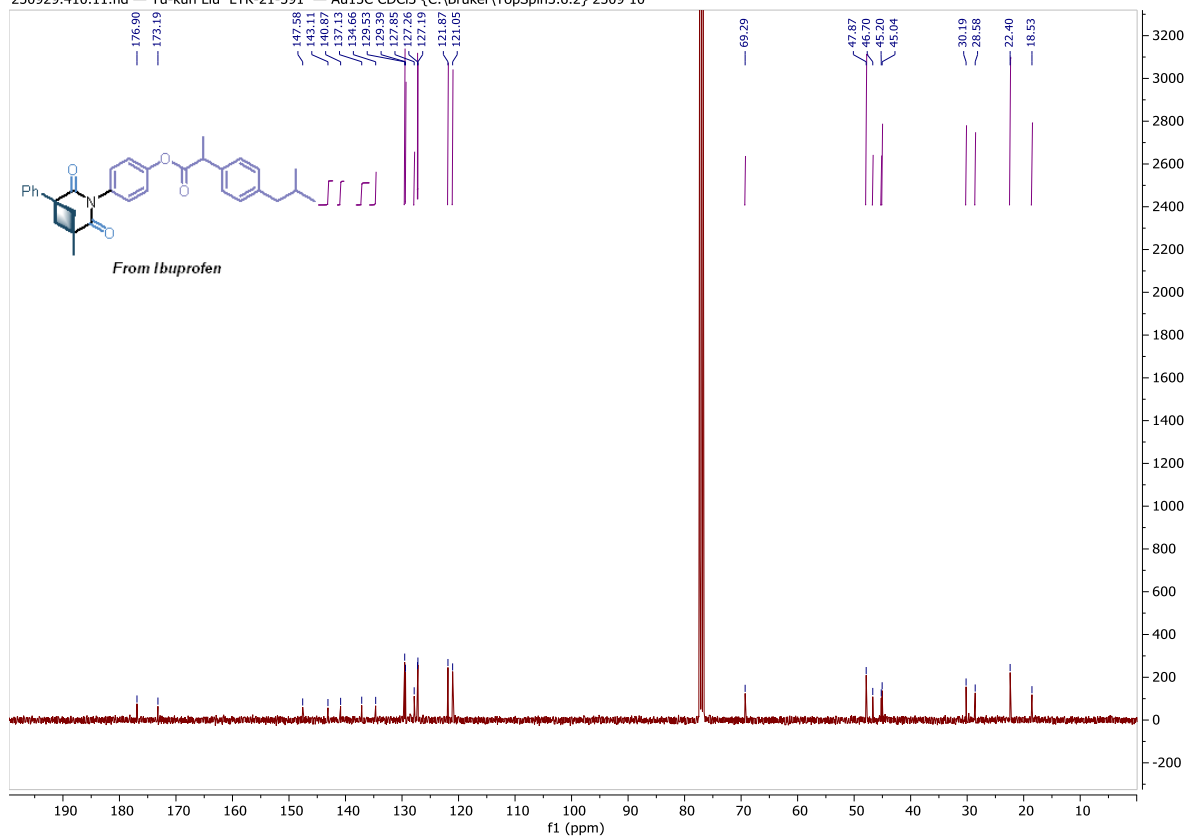
Supplementary Fig. 214. ^1H NMR spectrum of **4at** (400 MHz, CDCl_3)

250929.410.10.fid — Yu-kun Liu LYK-21-591 — Au1H CDCl_3 {C:\Bruker\TopSpin3.6.2} 2509 10



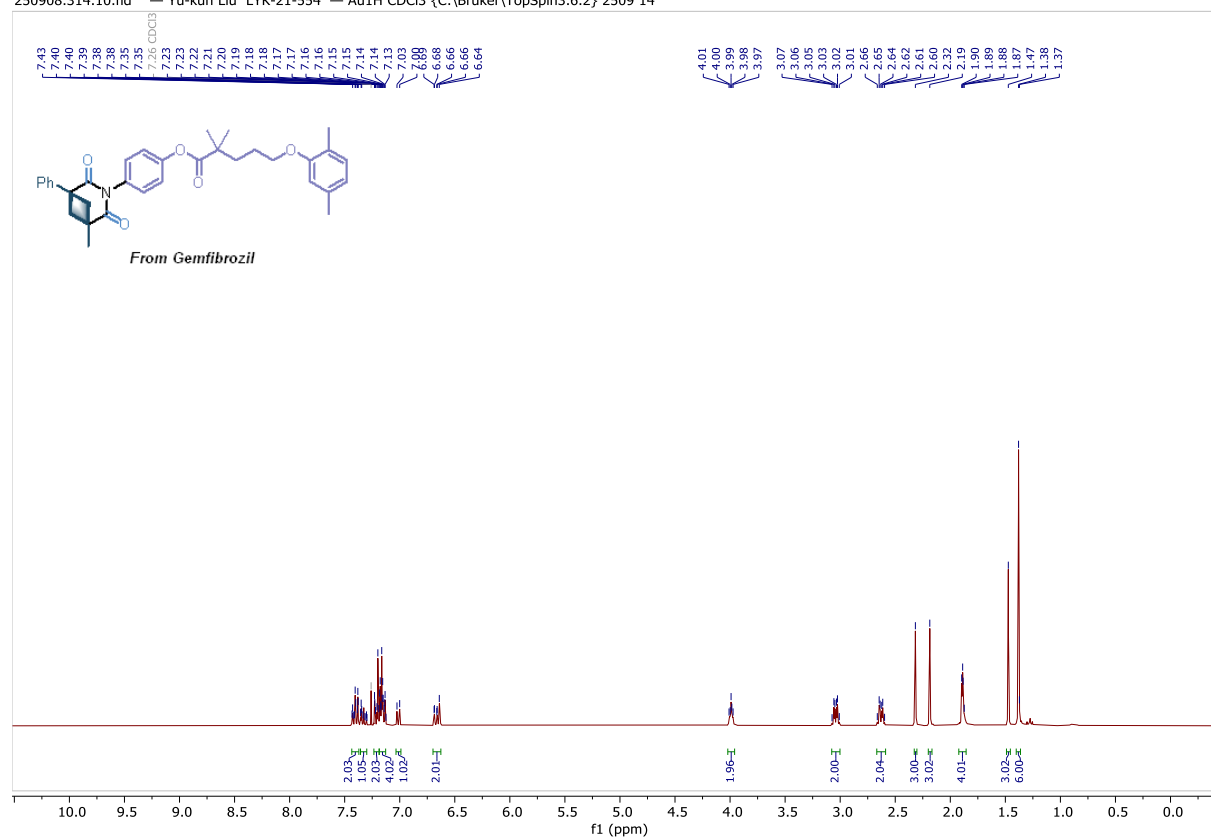
Supplementary Fig. 215. ^{13}C NMR spectrum of **4at** (101 MHz, CDCl_3)

250929.410.11.fid — Yu-kun Liu LYK-21-591 — Au13C CDCl_3 {C:\Bruker\TopSpin3.6.2} 2509 10



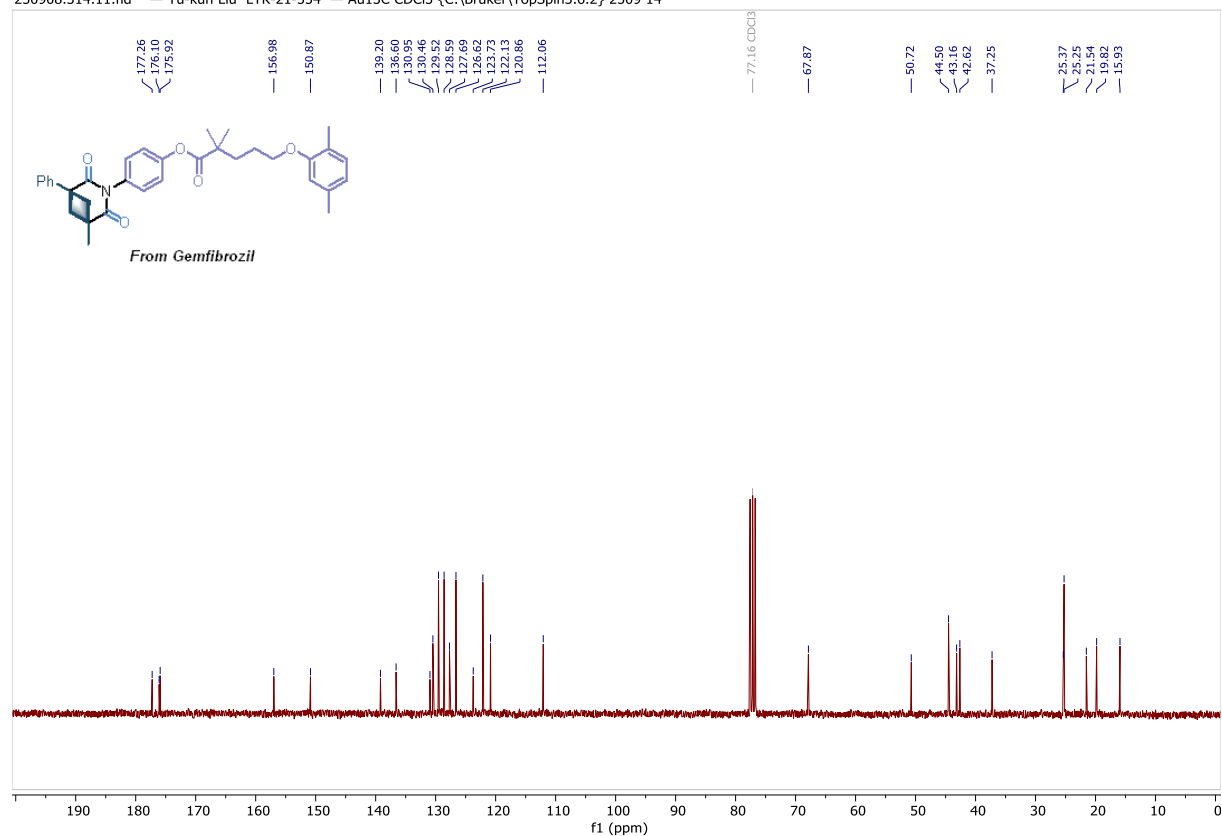
Supplementary Fig. 216. ^1H NMR spectrum of **4au** (300 MHz, CDCl_3)

250908.314.10.fid — Yu-kun Liu LYK-21-554 — Au1H CDCl_3 {C:\Bruker\TopSpin3.6.2} 2509 14



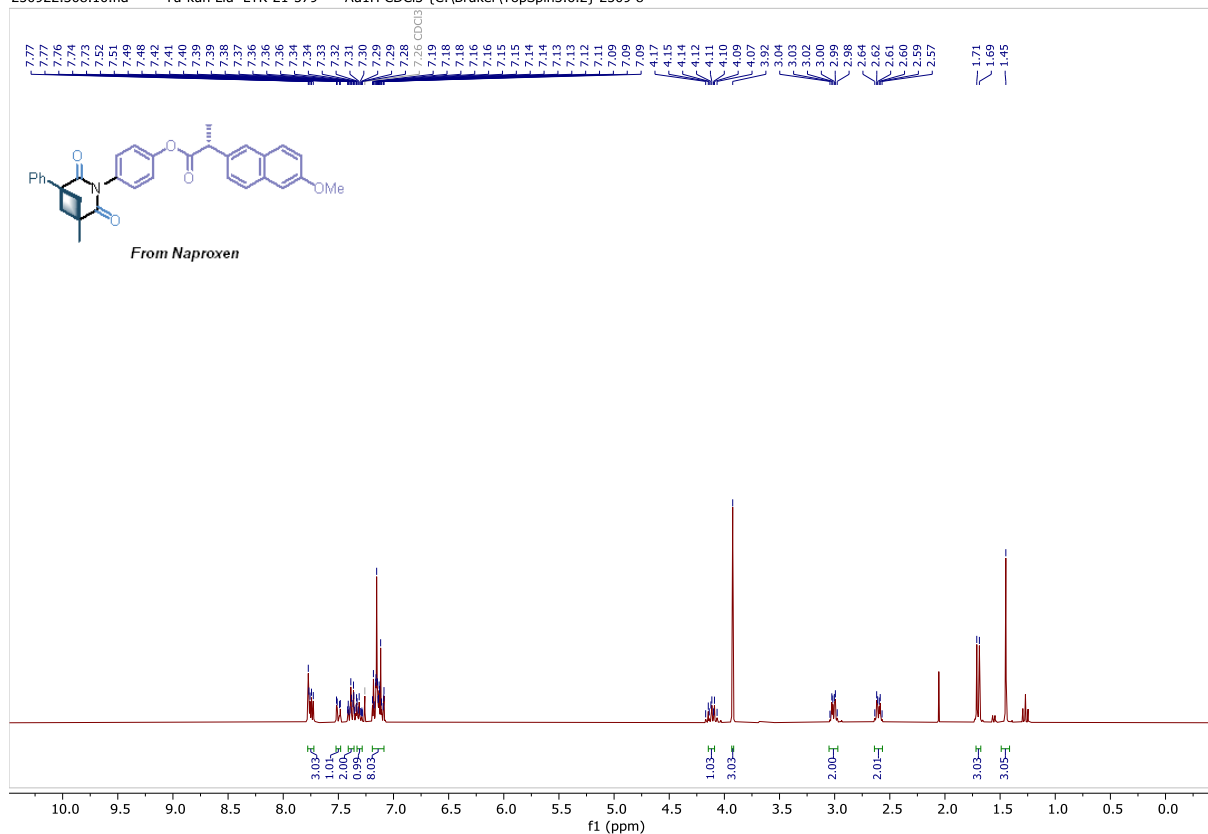
Supplementary Fig. 217. ^{13}C NMR spectrum of **4au** (75 MHz, CDCl_3)

250908.314.11.fid — Yu-kun Liu LYK-21-554 — Au13C CDCl_3 {C:\Bruker\TopSpin3.6.2} 2509 14



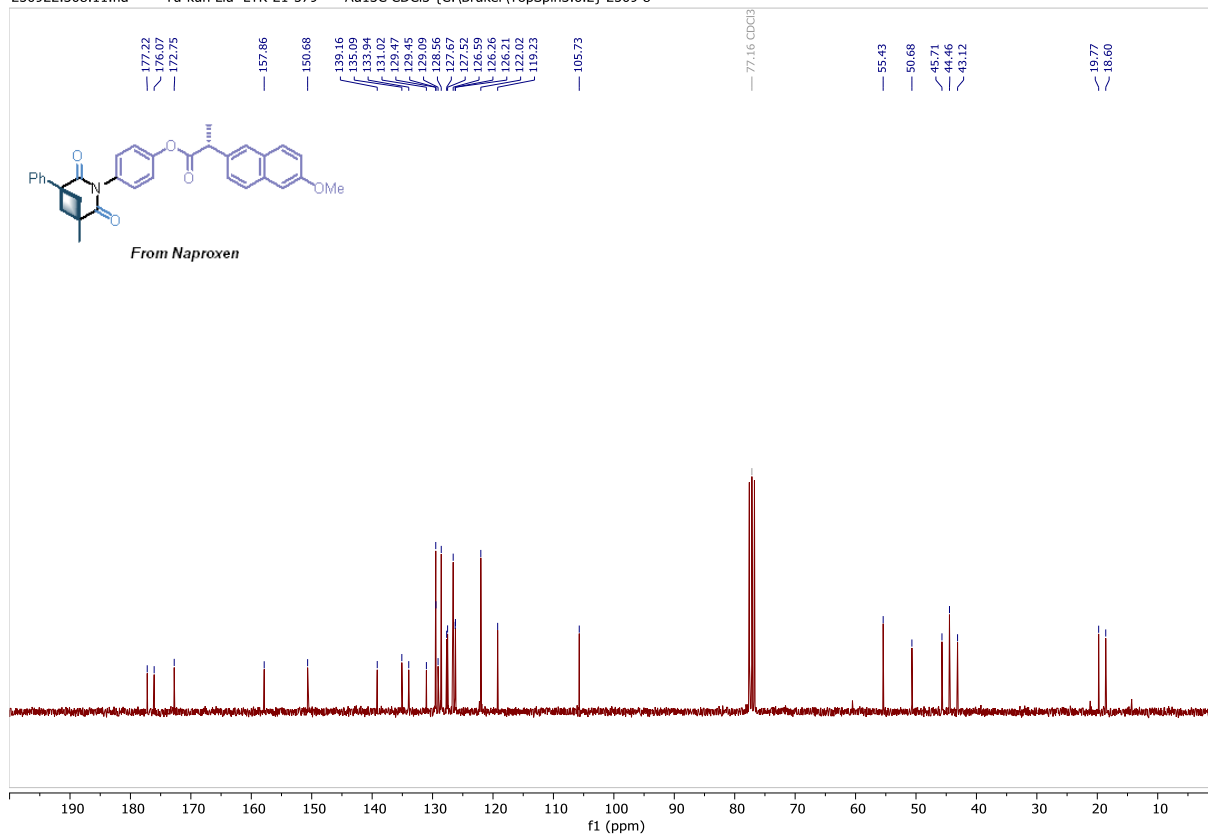
Supplementary Fig. 218. ^1H NMR spectrum of **4av** (300 MHz, CDCl_3)

250922.308.10.fid — Yu-kun Liu LYK-21-579 — Au1H CDCl_3 {C:\Bruker\TopSpin3.6.2} 2509 8

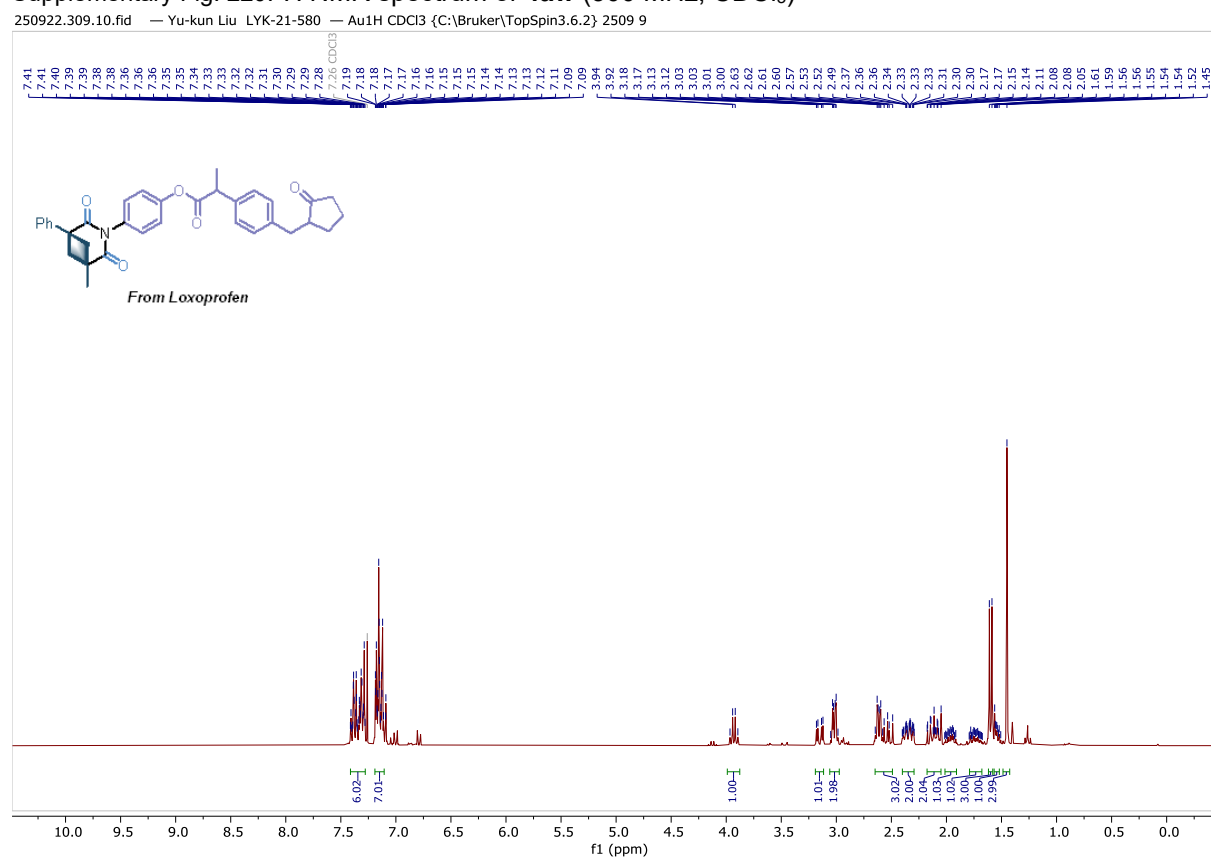


Supplementary Fig. 219. ^{13}C NMR spectrum of **4av** (75 MHz, CDCl_3)

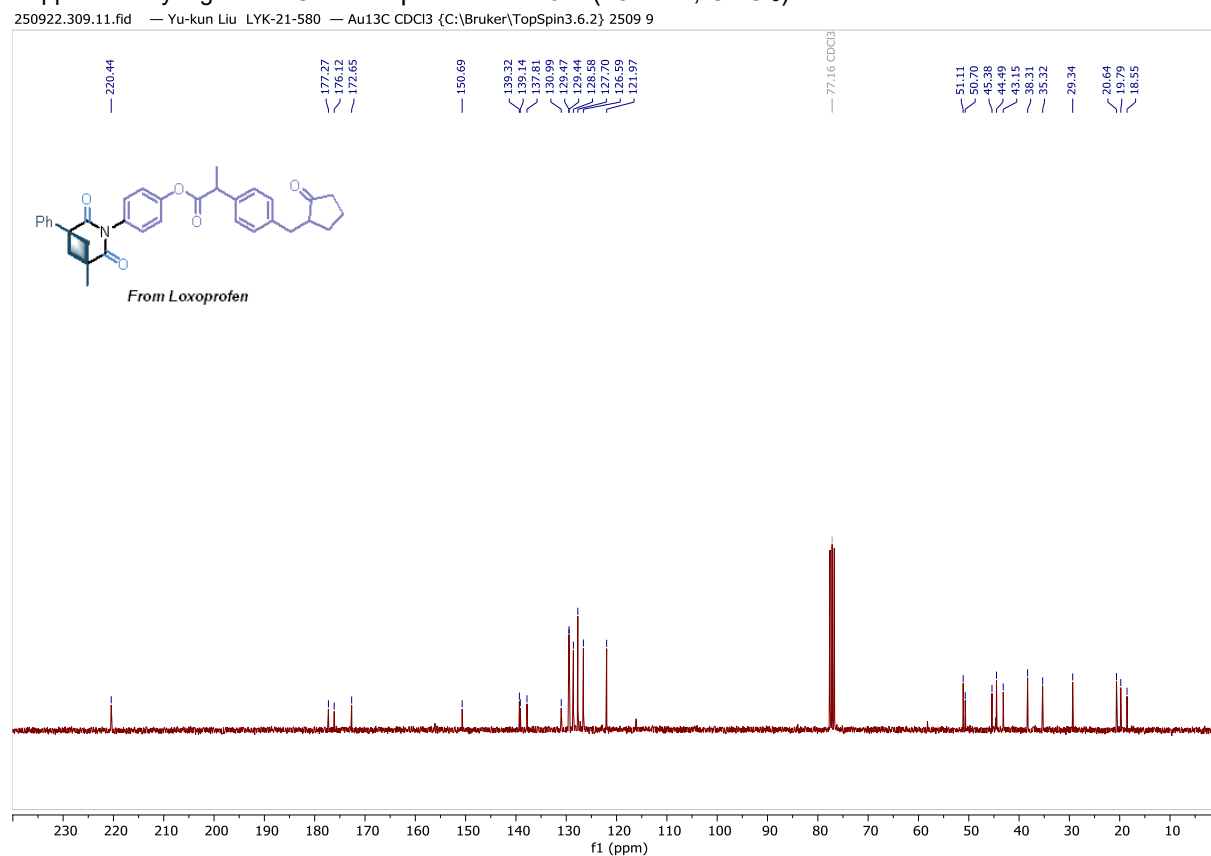
250922.308.11.fid — Yu-kun Liu LYK-21-579 — Au13C CDCl_3 {C:\Bruker\TopSpin3.6.2} 2509 8



Supplementary Fig. 220. ^1H NMR spectrum of **4aw** (300 MHz, CDCl_3)

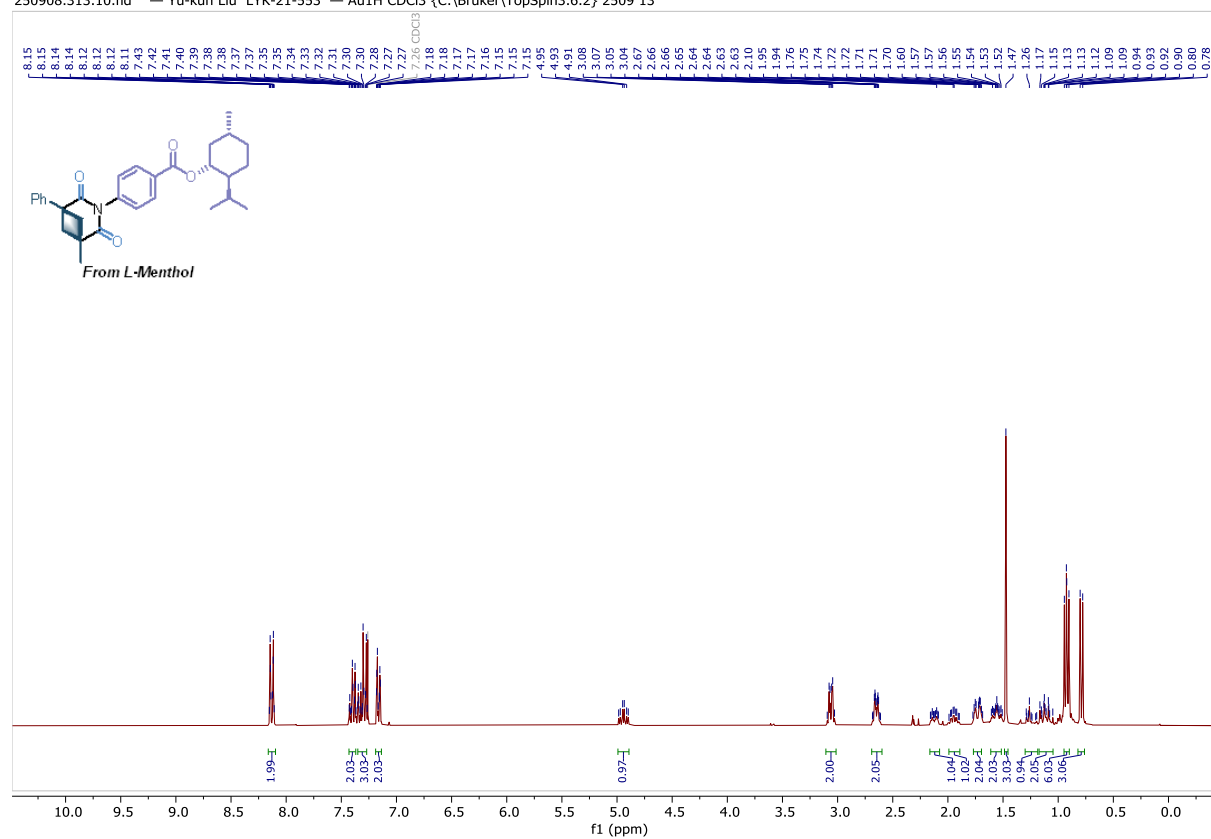


Supplementary Fig. 221. ^{13}C NMR spectrum of **4aw** (75 MHz, CDCl_3)



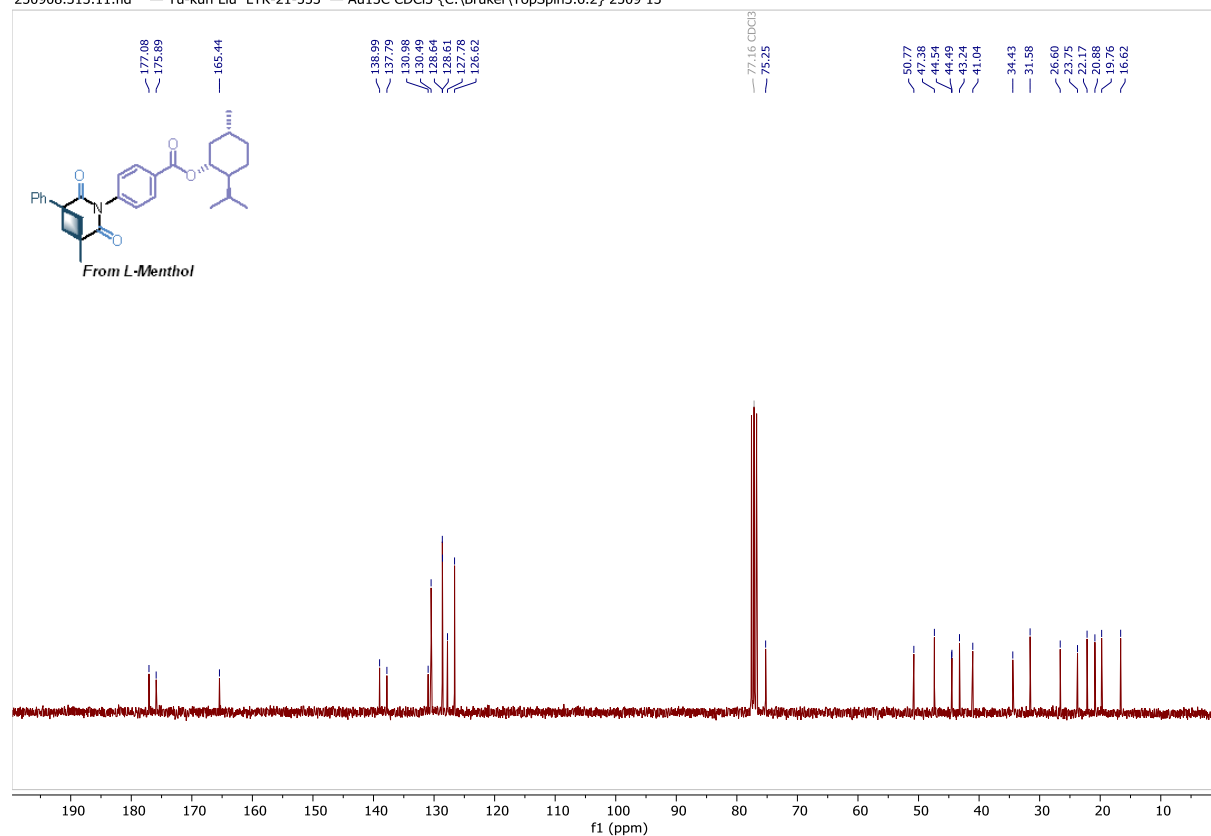
Supplementary Fig. 222. ^1H NMR spectrum of **4ax** (300 MHz, CDCl_3)

250908.313.10.fid — Yu-kun Liu LYK-21-553 — Au1H CDCl_3 {C:\Bruker\TopSpin3.6.2} 2509 13

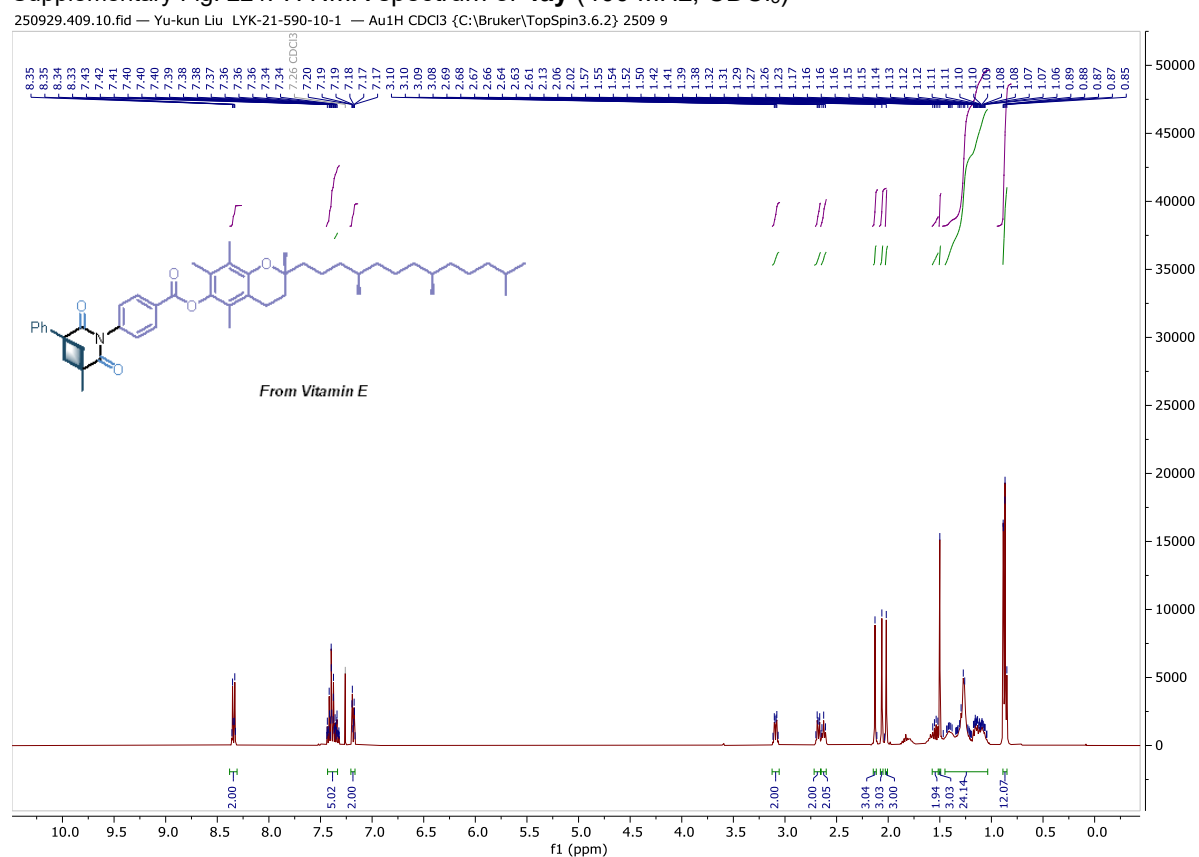


Supplementary Fig. 223. ^{13}C NMR spectrum of **4ax** (75 MHz, CDCl_3)

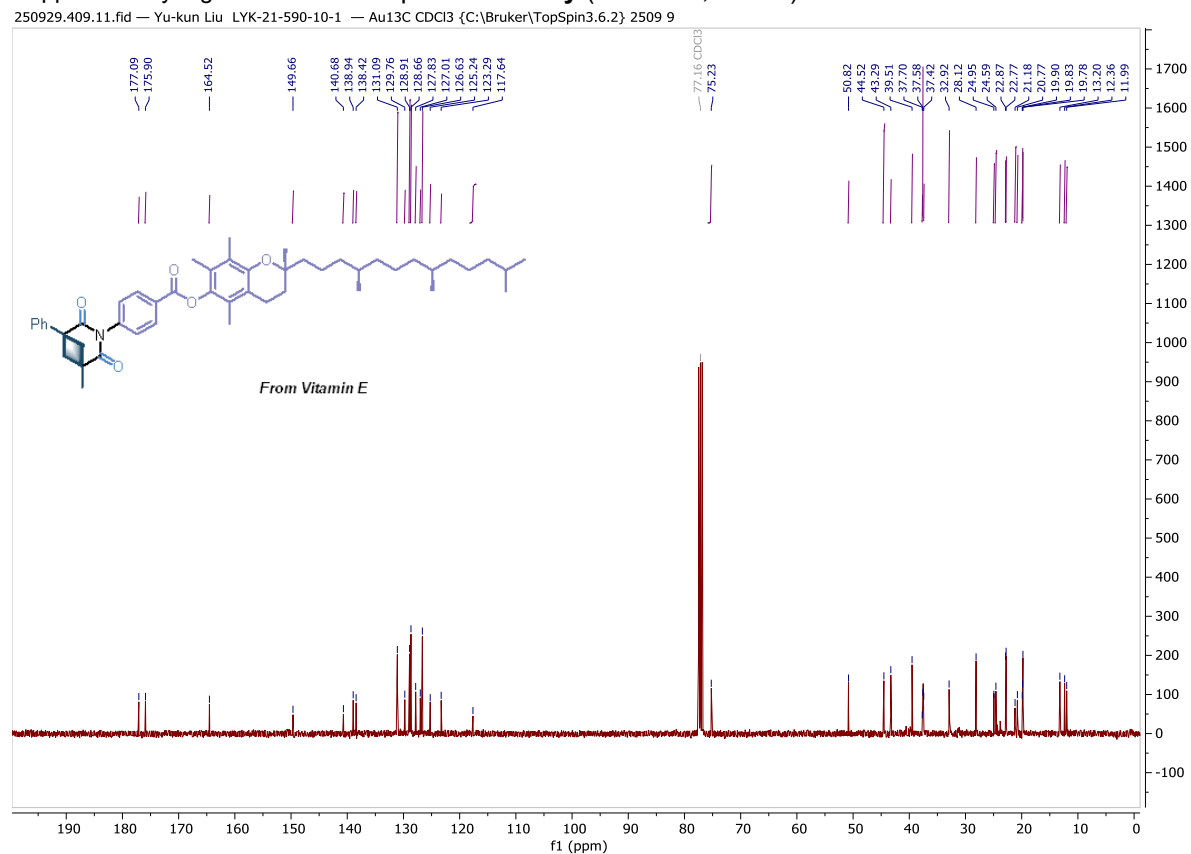
250908.313.11.fid — Yu-kun Liu LYK-21-553 — Au13C CDCl_3 {C:\Bruker\TopSpin3.6.2} 2509 13



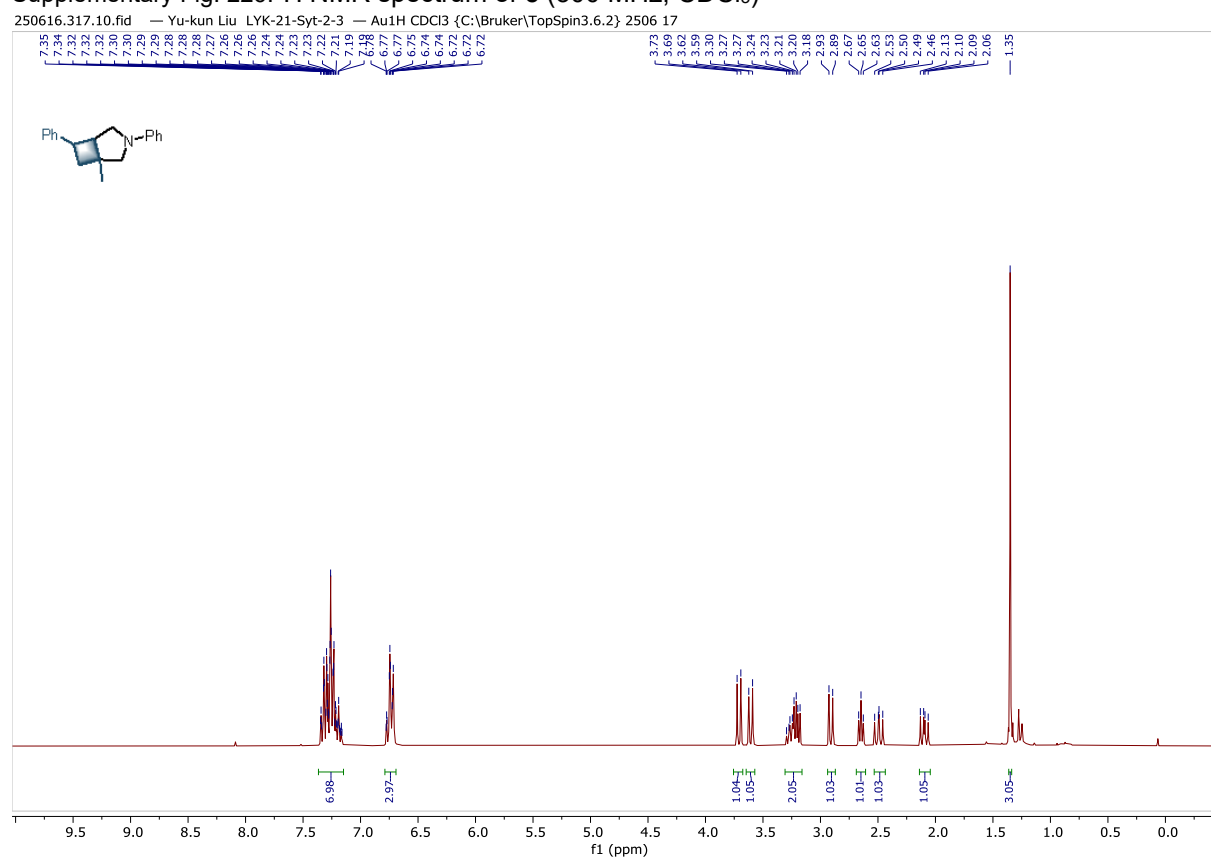
Supplementary Fig. 224. ^1H NMR spectrum of **4ay** (400 MHz, CDCl_3)



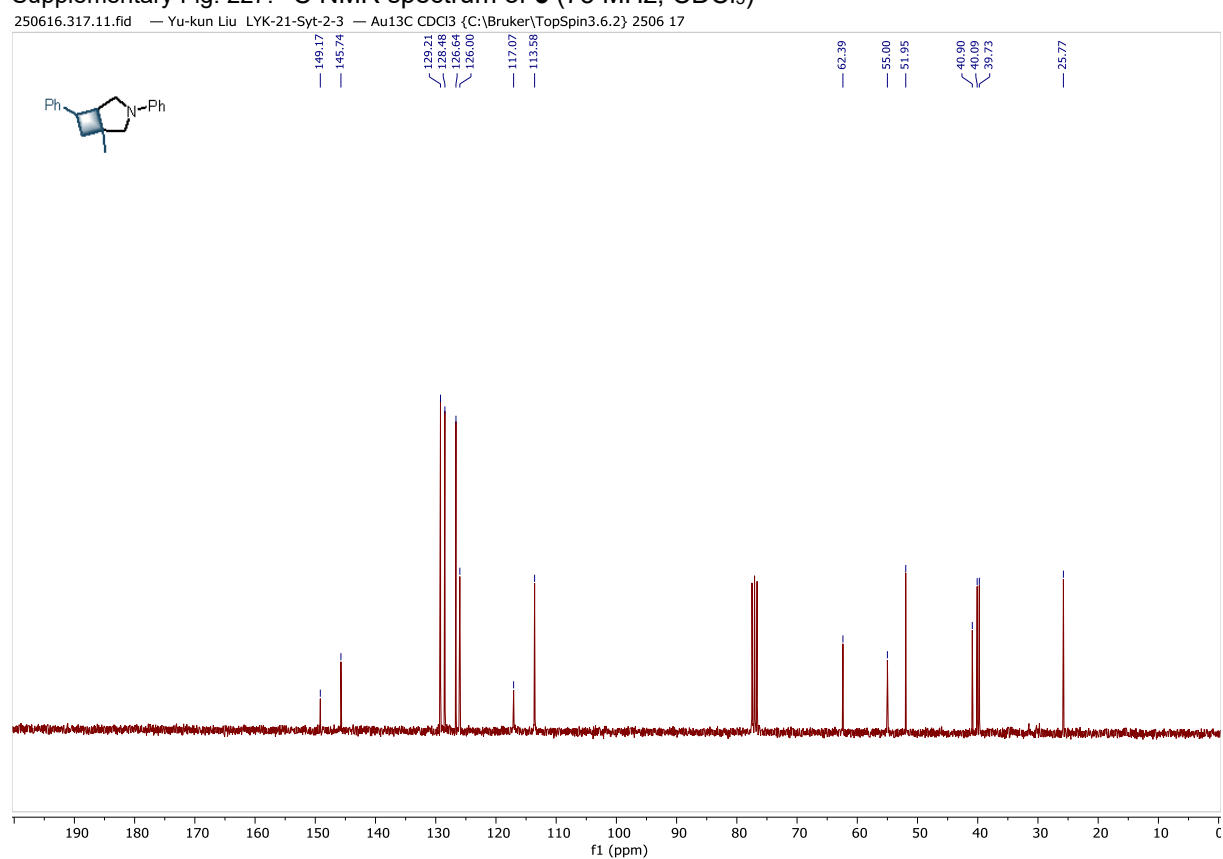
Supplementary Fig. 225. ^{13}C NMR spectrum of **4ay** (101 MHz, CDCl_3)



Supplementary Fig. 226. ^1H NMR spectrum of **5** (300 MHz, CDCl_3)

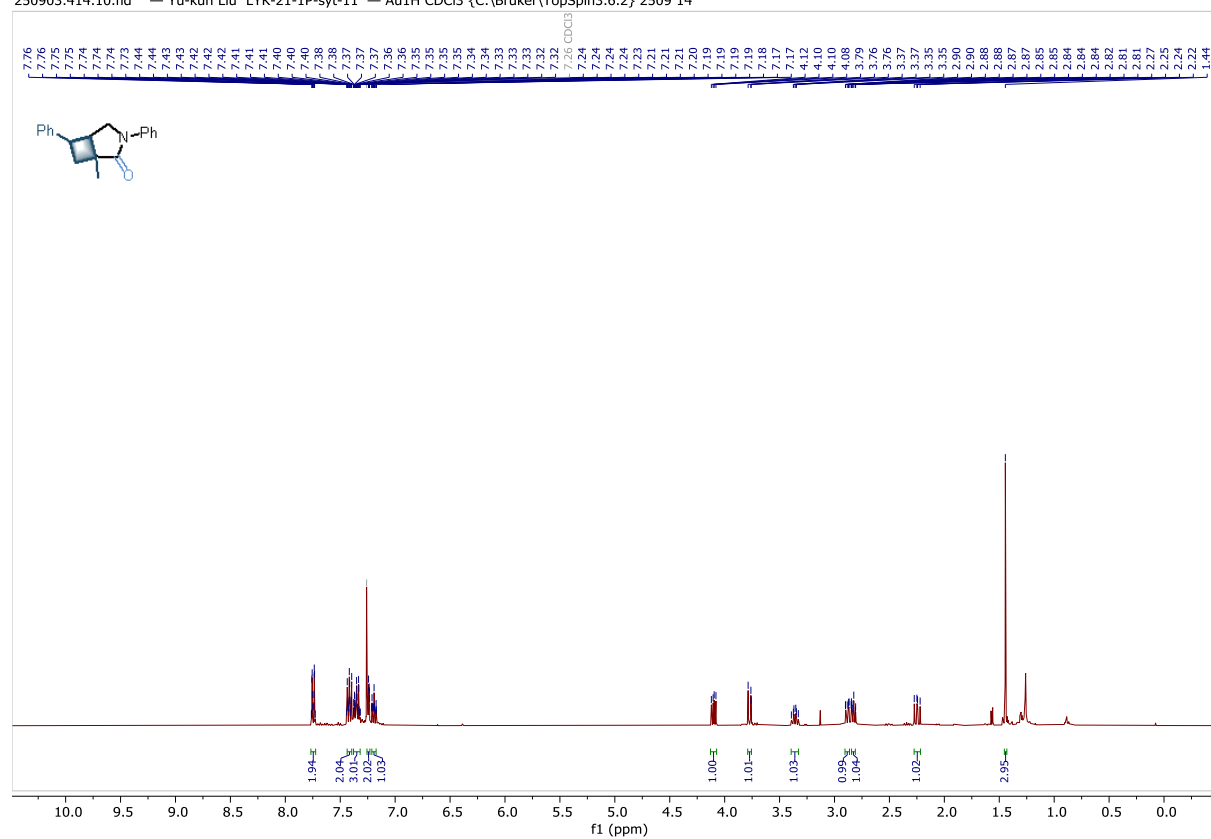


Supplementary Fig. 227. ^{13}C NMR spectrum of **5** (75 MHz, CDCl_3)



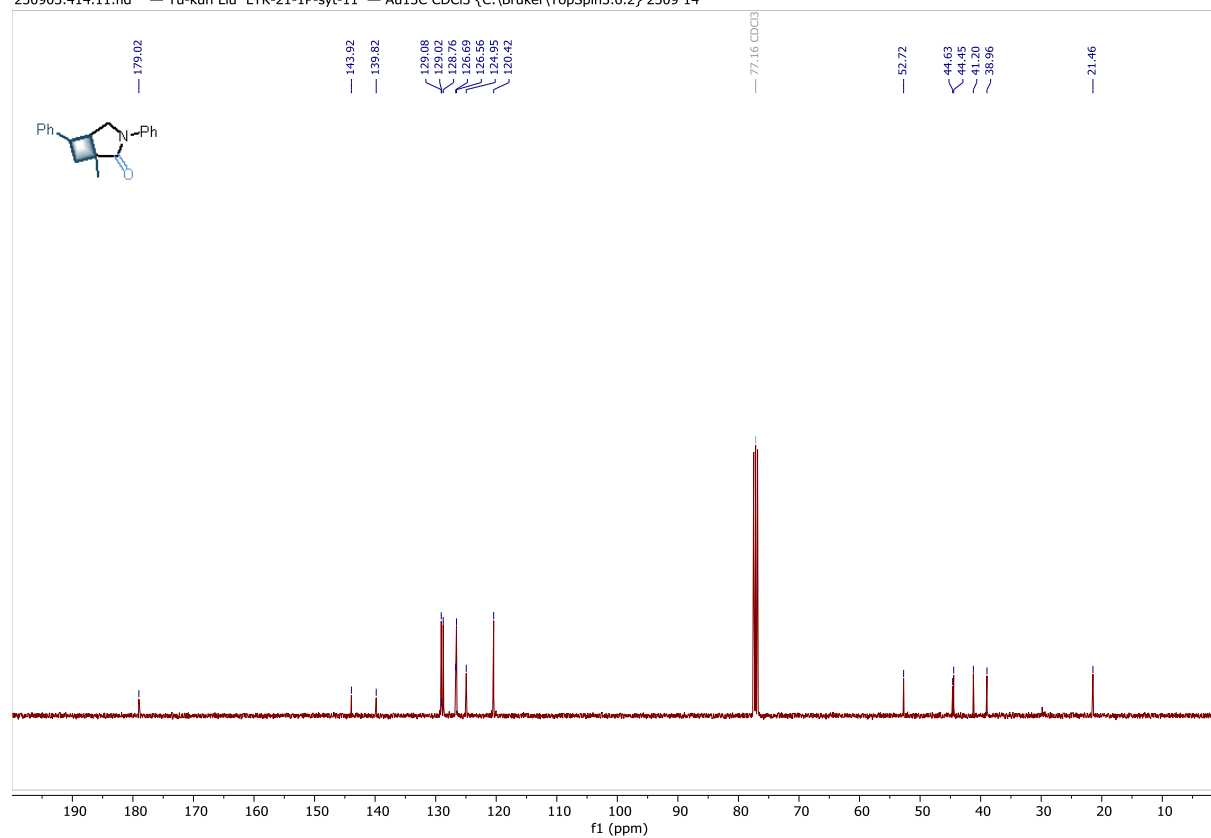
Supplementary Fig. 228. ^1H NMR spectrum of **6** (400 MHz, CDCl_3)

250903.414.10.fid — Yu-kun Liu LYK-21-1P-syt-11 — Au1H CDCl_3 {C:\Bruker\TopSpin3.6.2} 2509 14



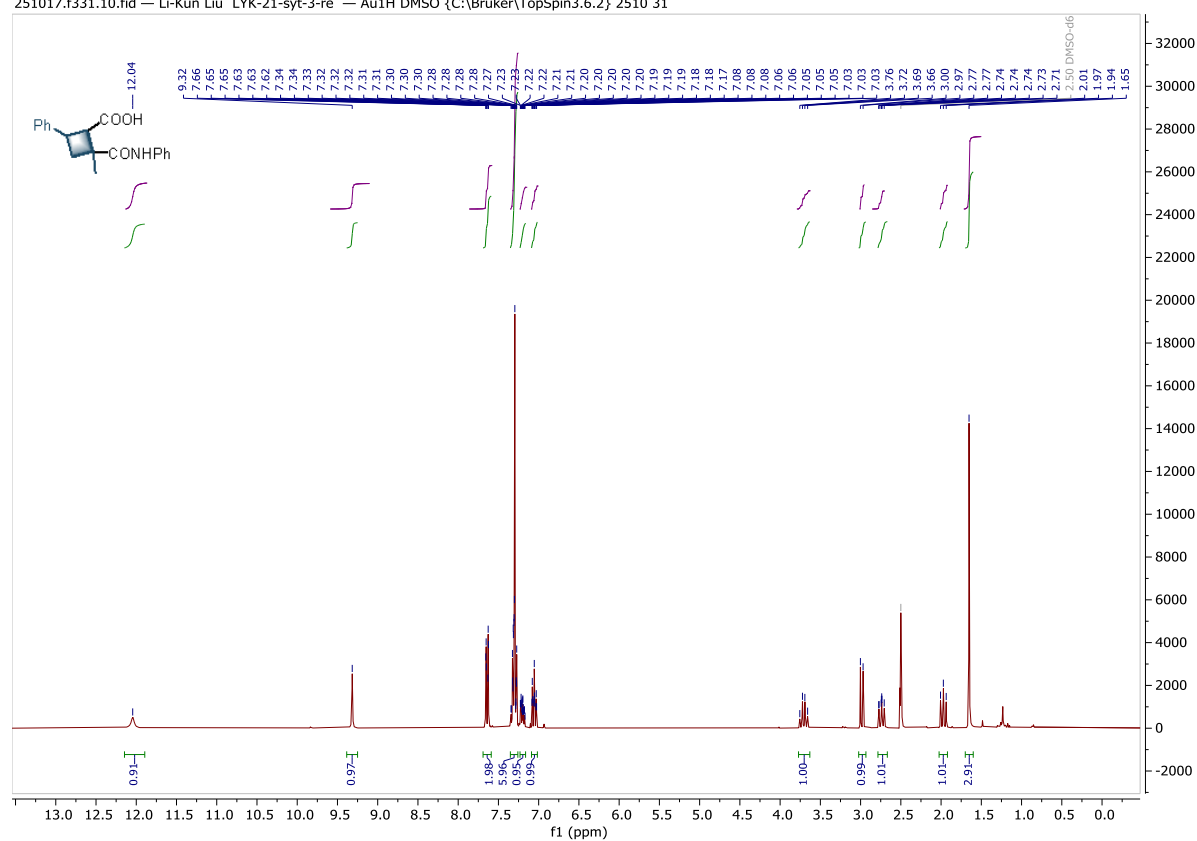
Supplementary Fig. 229. ^{13}C NMR spectrum of **6** 101 MHz, CDCl_3)

250903.414.11.fid — Yu-kun Liu LYK-21-1P-syt-11 — Au13C CDCl_3 {C:\Bruker\TopSpin3.6.2} 2509 14



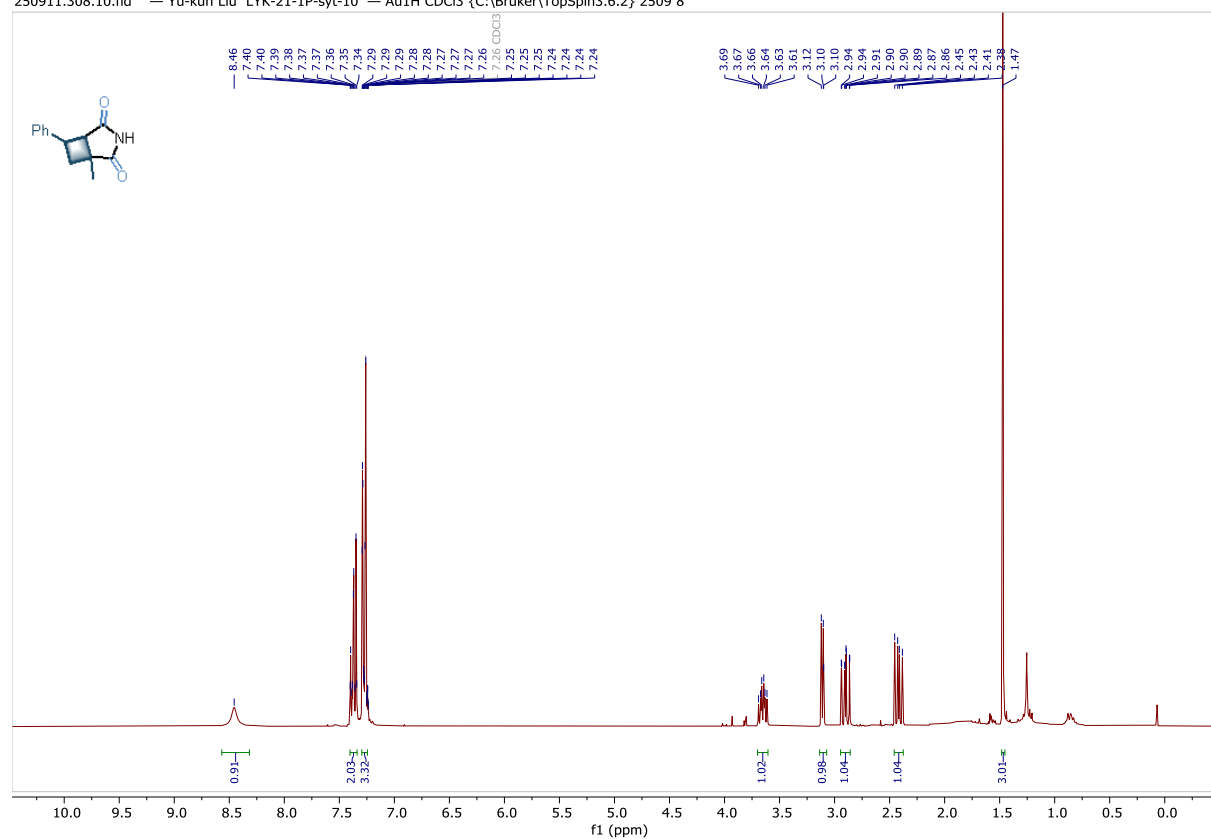
Supplementary Fig. 230. ^1H NMR spectrum of **7** (300 MHz, $\text{DMSO-}d_6$)

251017.f331.10.fid — Li-Kun Liu LYK-21-syt-3-re — Au1H DMSO {C:\Bruker\TopSpin3.6.2} 2510 31



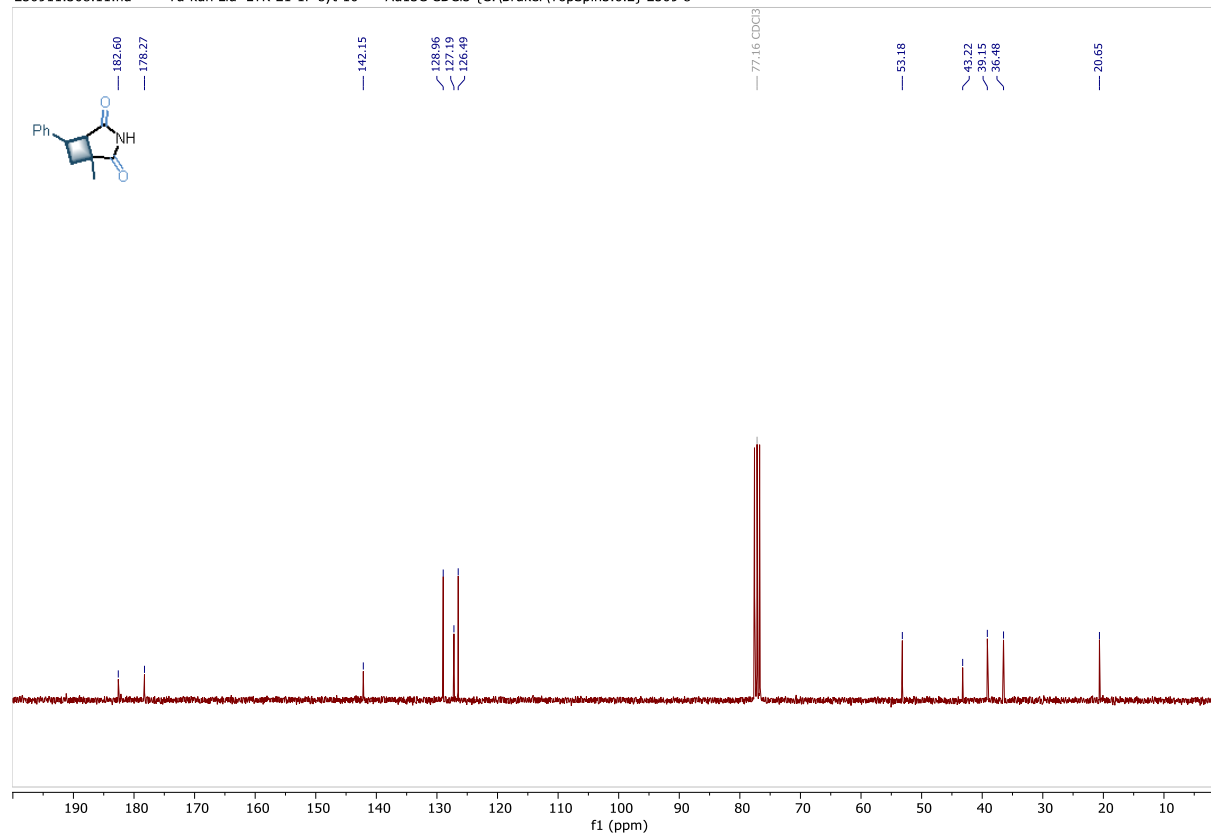
Supplementary Fig. 232. ^1H NMR spectrum of **8** (300 MHz, CDCl_3)

250911.308.10.fid — Yu-kun Liu LYK-21-1P-syt-10 — Au1H CDCl_3 {C:\Bruker\TopSpin3.6.2} 2509 8



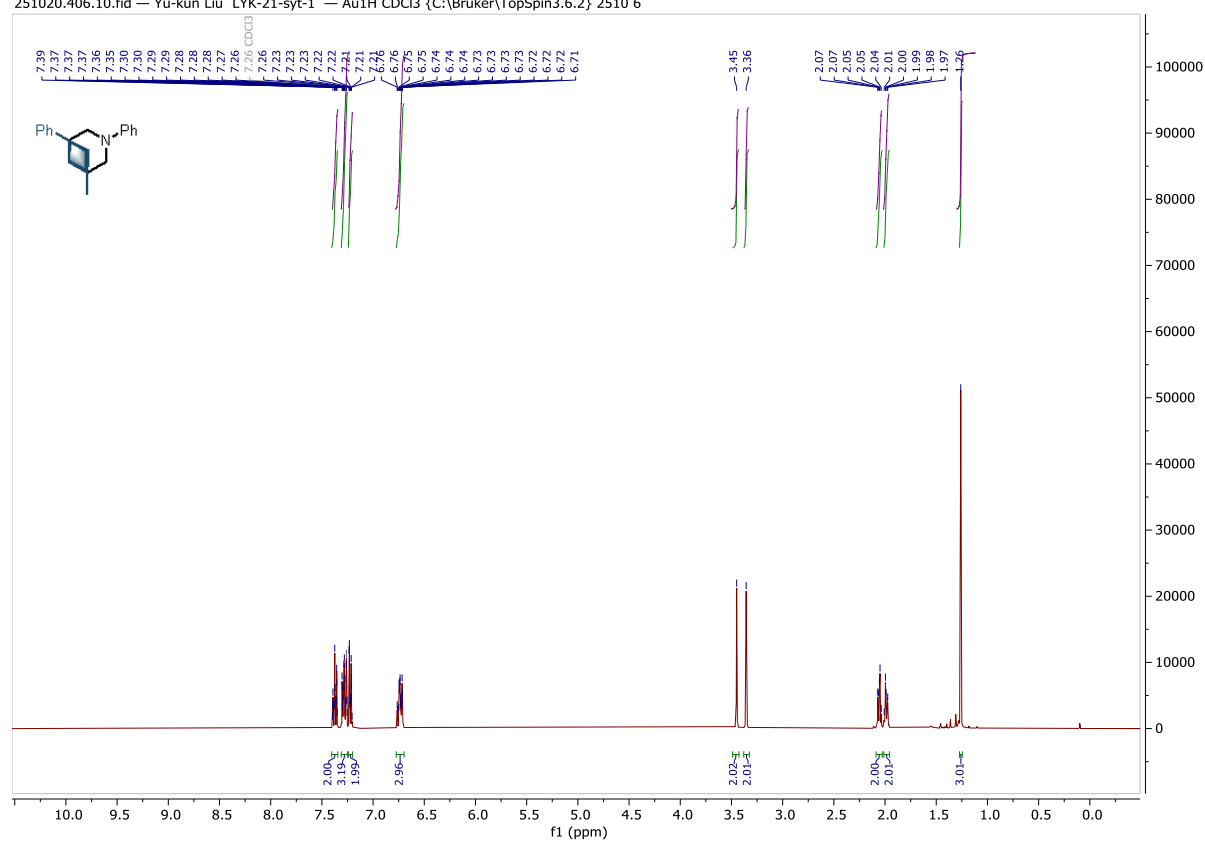
Supplementary Fig. 233. ^{13}C NMR spectrum of **8** (75 MHz, CDCl_3)

250911.308.11.fid — Yu-kun Liu LYK-21-1P-syt-10 — Au13C CDCl_3 {C:\Bruker\TopSpin3.6.2} 2509 8



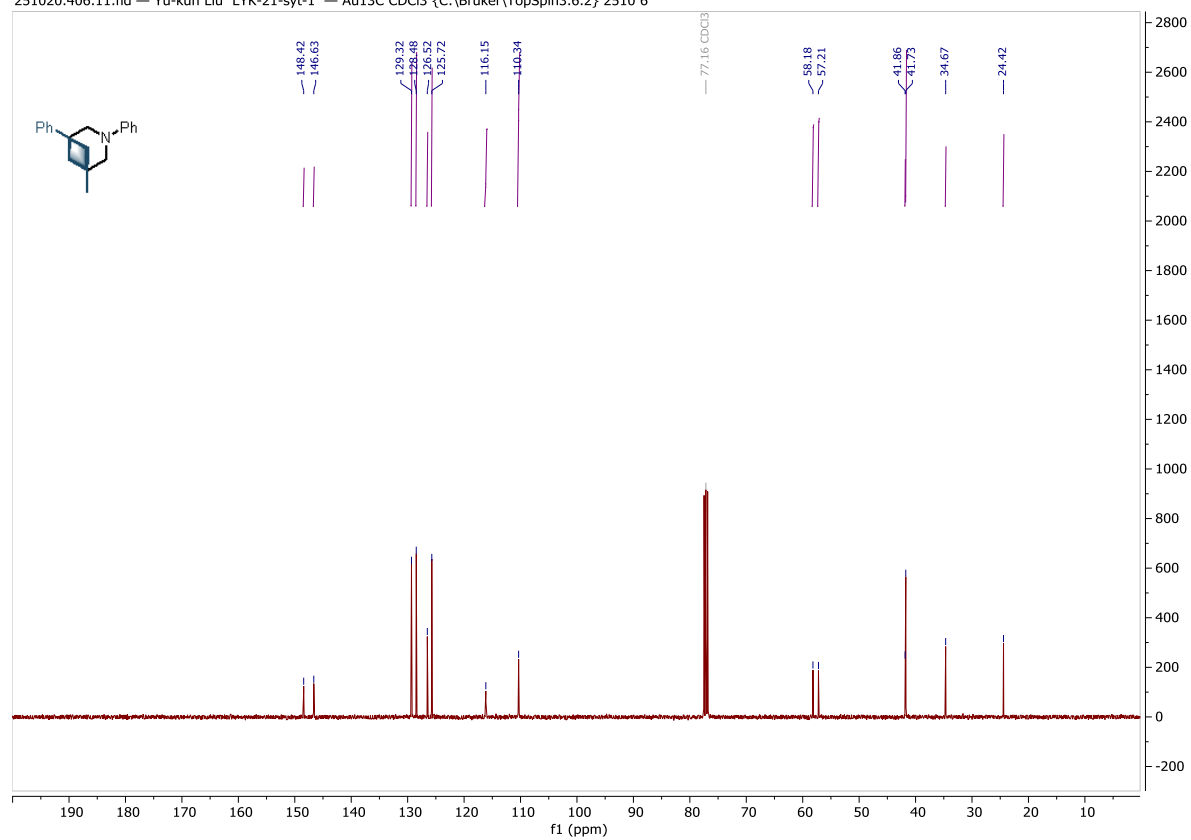
Supplementary Fig. 234. ^1H NMR spectrum of **9** (400 MHz, CDCl_3)

251020.406.10.fid — Yu-kun Liu LYK-21-syt-1 — Au1H CDCl_3 {C:\Bruker\TopSpin3.6.2} 2510 6



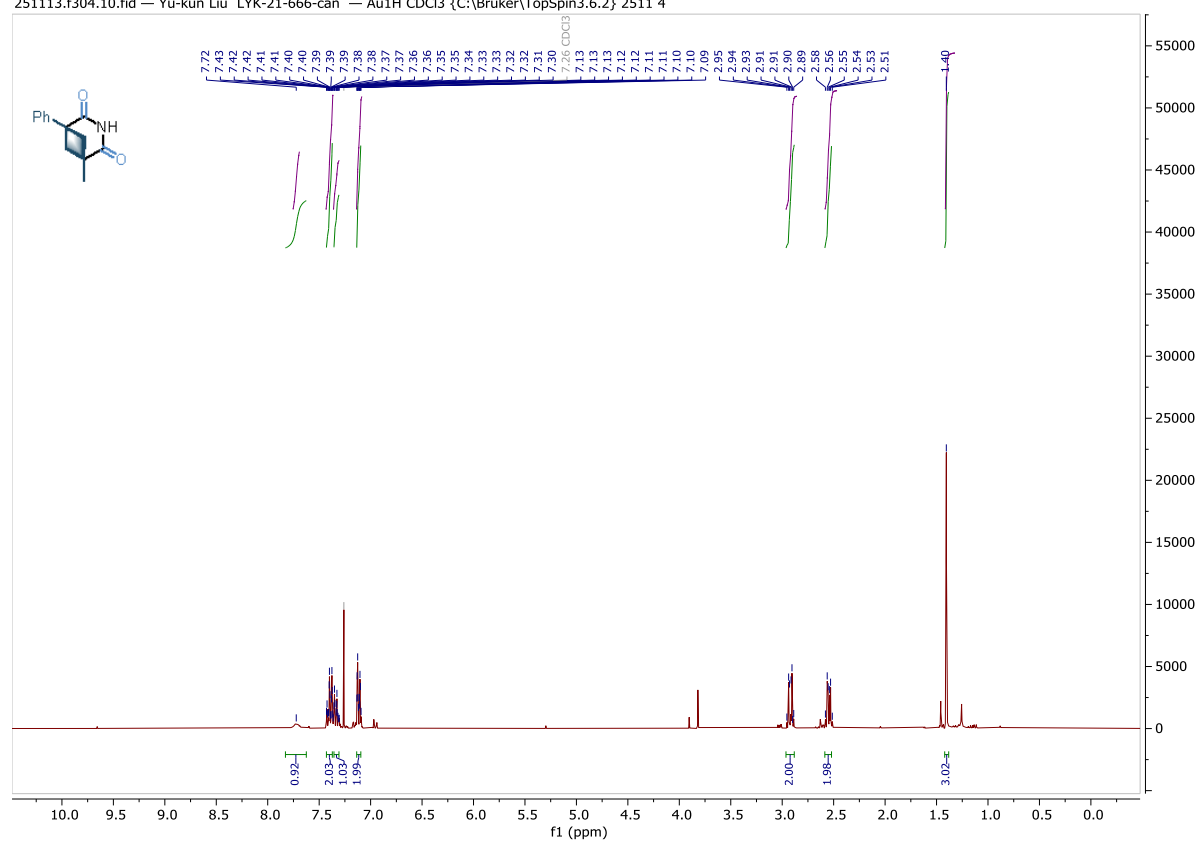
Supplementary Fig. 235. ^{13}C NMR spectrum of **9** (101 MHz, CDCl_3)

251020.406.11.fid — Yu-kun Liu LYK-21-syt-1 — Au13C CDCl_3 {C:\Bruker\TopSpin3.6.2} 2510 6



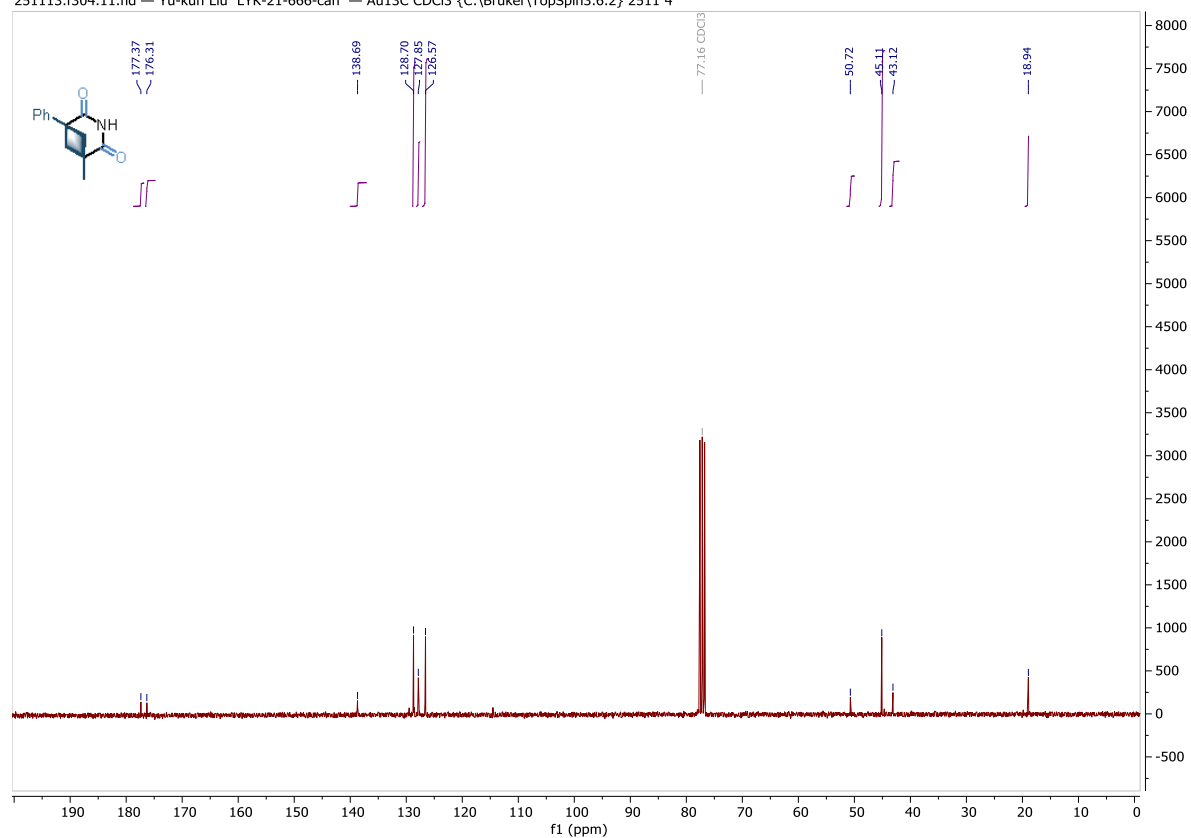
Supplementary Fig. 236. ^1H NMR spectrum of **10** (300 MHz, CDCl_3)

251113.f304.10.fid — Yu-kun Liu LYK-21-666-can — Au1H CDCl_3 {C:\Bruker\TopSpin3.6.2} 2511 4

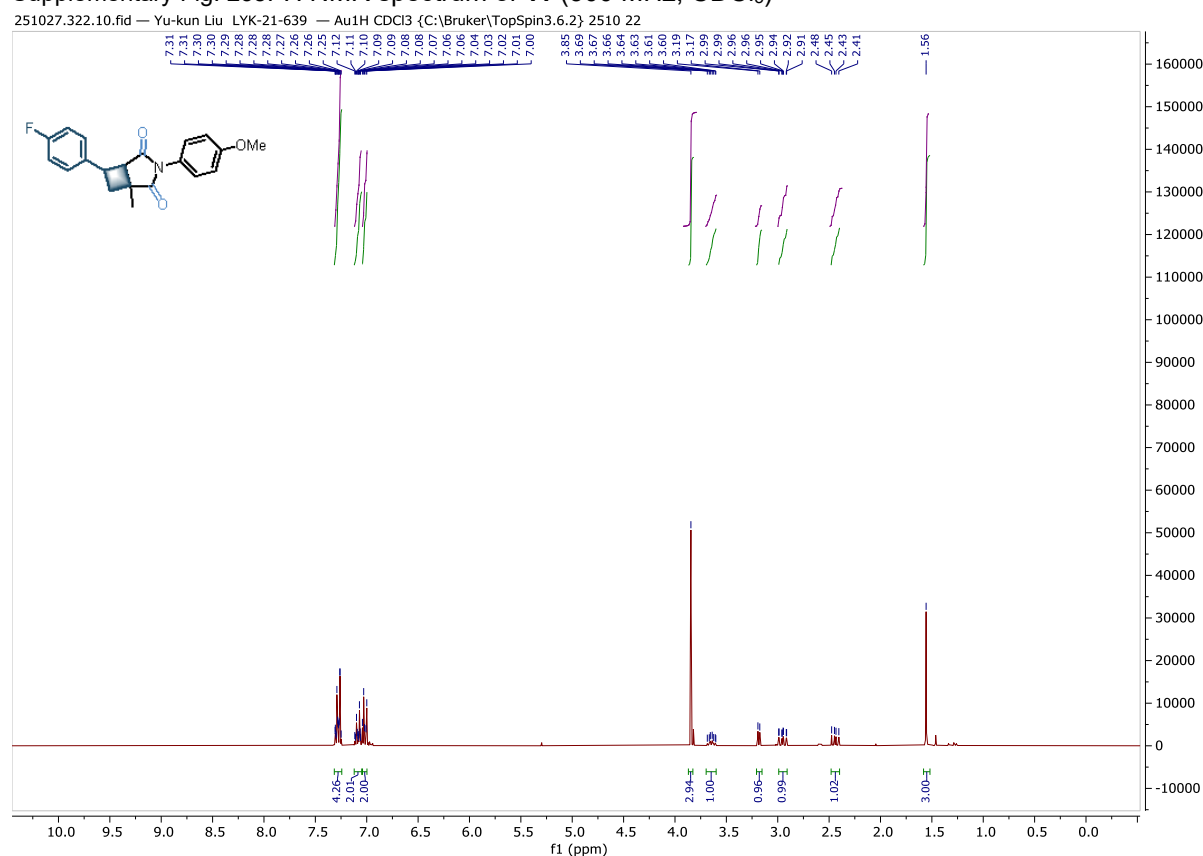


Supplementary Fig. 237. ^{13}C NMR spectrum of **10** (75 MHz, CDCl_3)

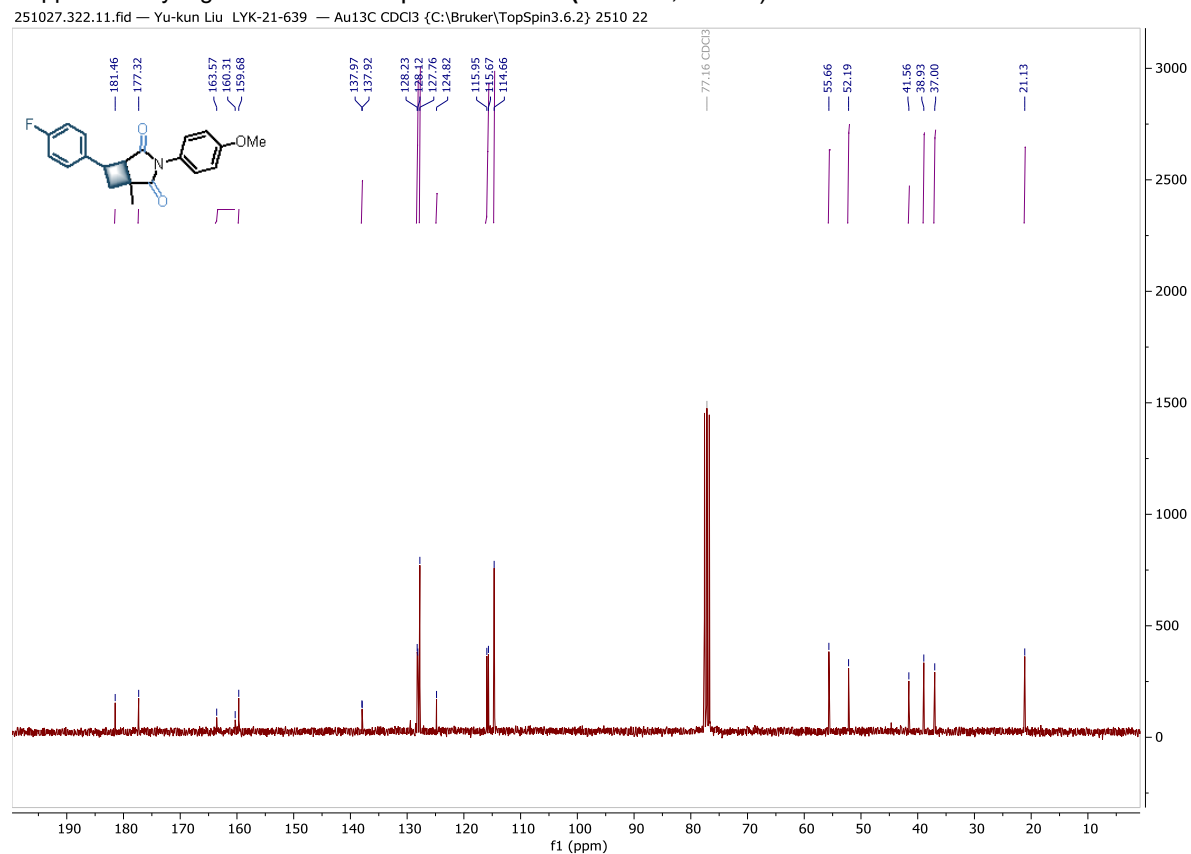
251113.f304.11.fid — Yu-kun Liu LYK-21-666-can — Au13C CDCl_3 {C:\Bruker\TopSpin3.6.2} 2511 4



Supplementary Fig. 238. ^1H NMR spectrum of **11** (300 MHz, CDCl_3)

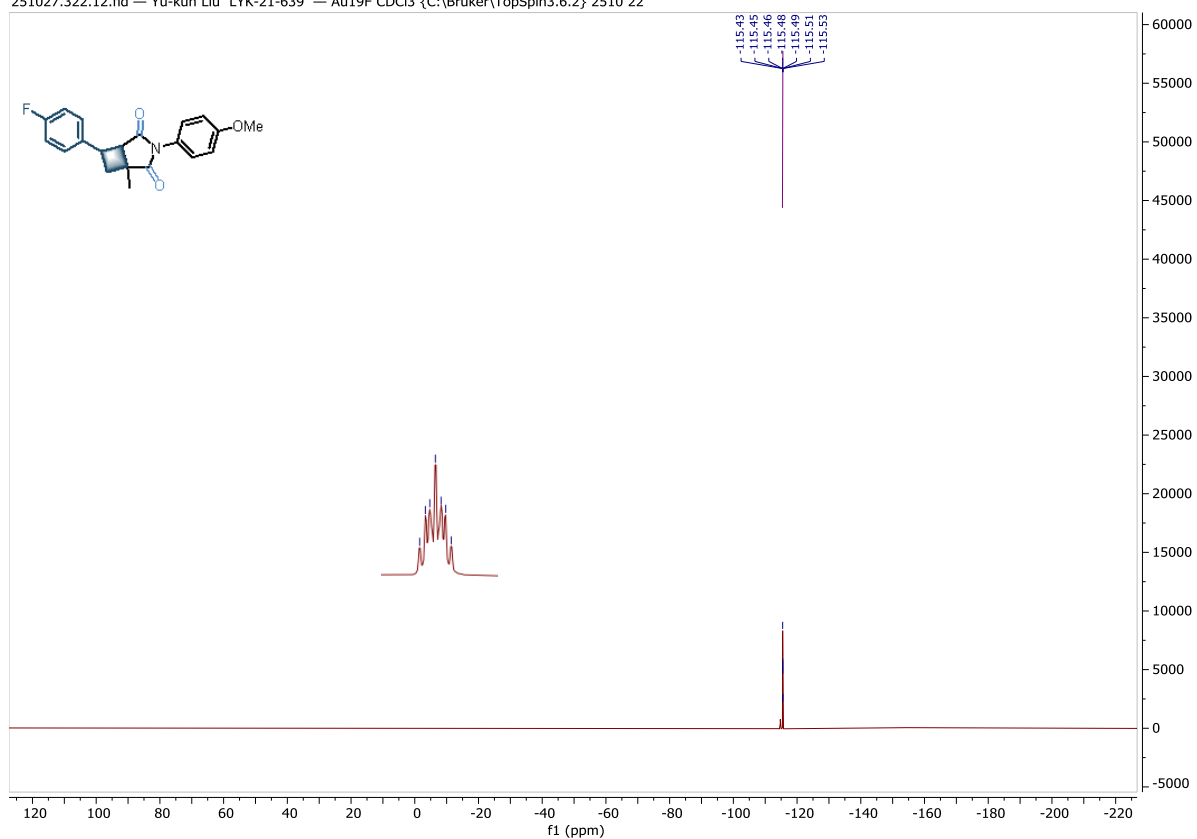


Supplementary Fig. 239. ^{13}C NMR spectrum of **11** (75 MHz, CDCl_3)



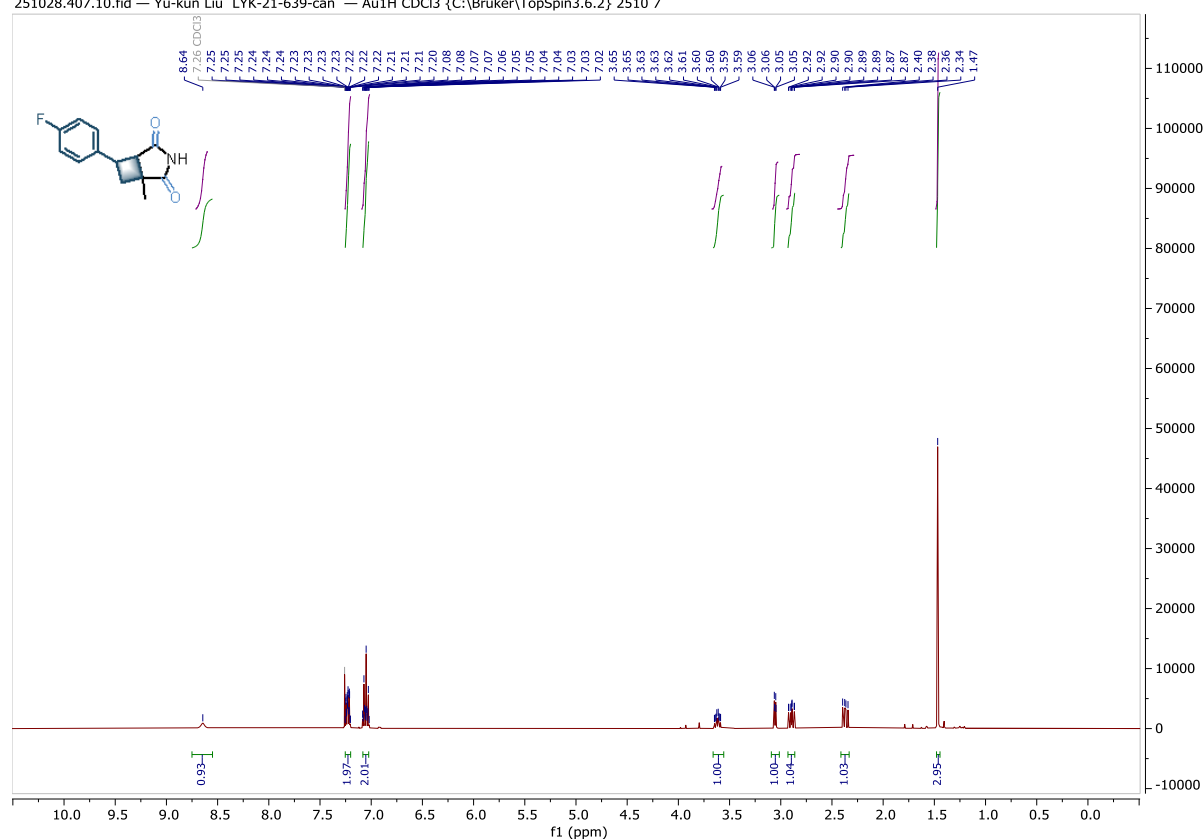
Supplementary Fig. 240. ^{19}F NMR spectrum of **11** (282 MHz, CDCl_3)

251027.322.12.fid — Yu-kun Liu LYK-21-639 — Au ^{19}F CDCl_3 {C:\Bruker\TopSpin3.6.2} 2510 22



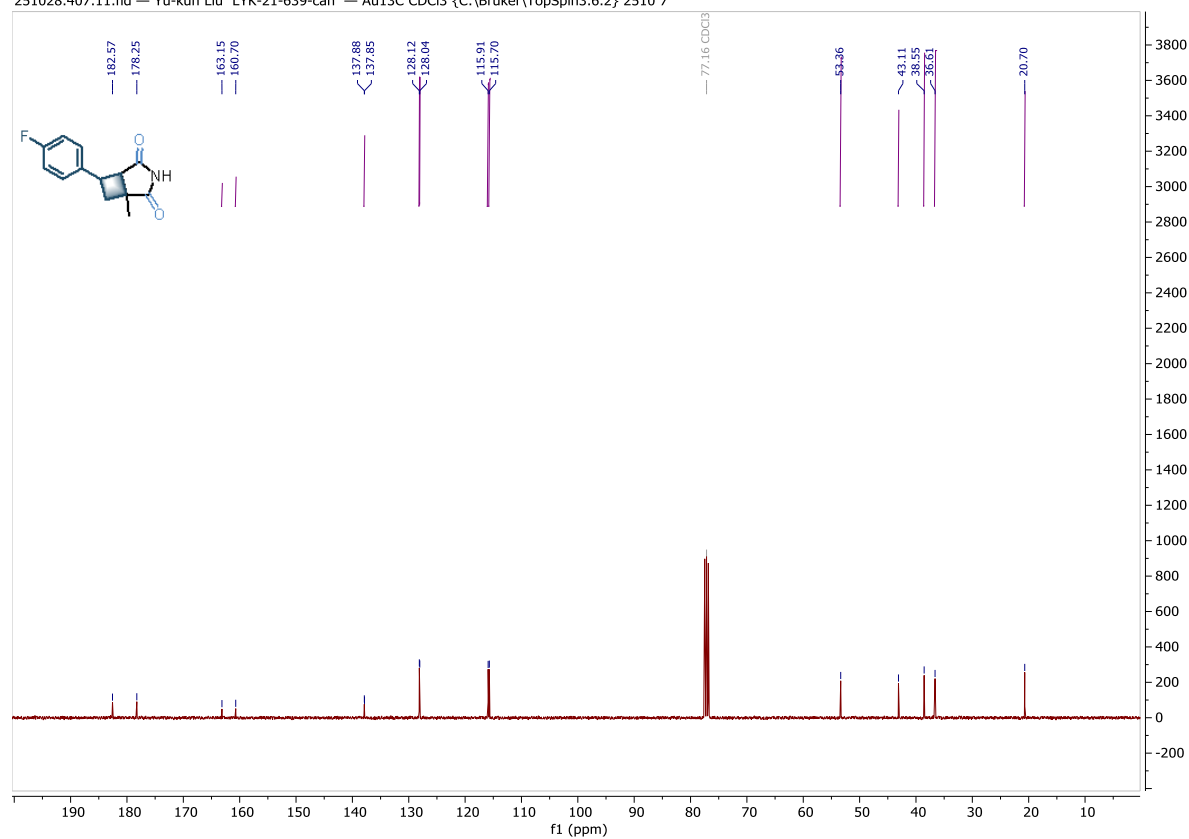
Supplementary Fig. 241. ^1H NMR spectrum of **12** (400 MHz, CDCl_3)

251028.407.10.fid — Yu-kun Liu LYK-21-639-can — Au1H CDCl_3 {C:\Bruker\TopSpin3.6.2} 2510 7



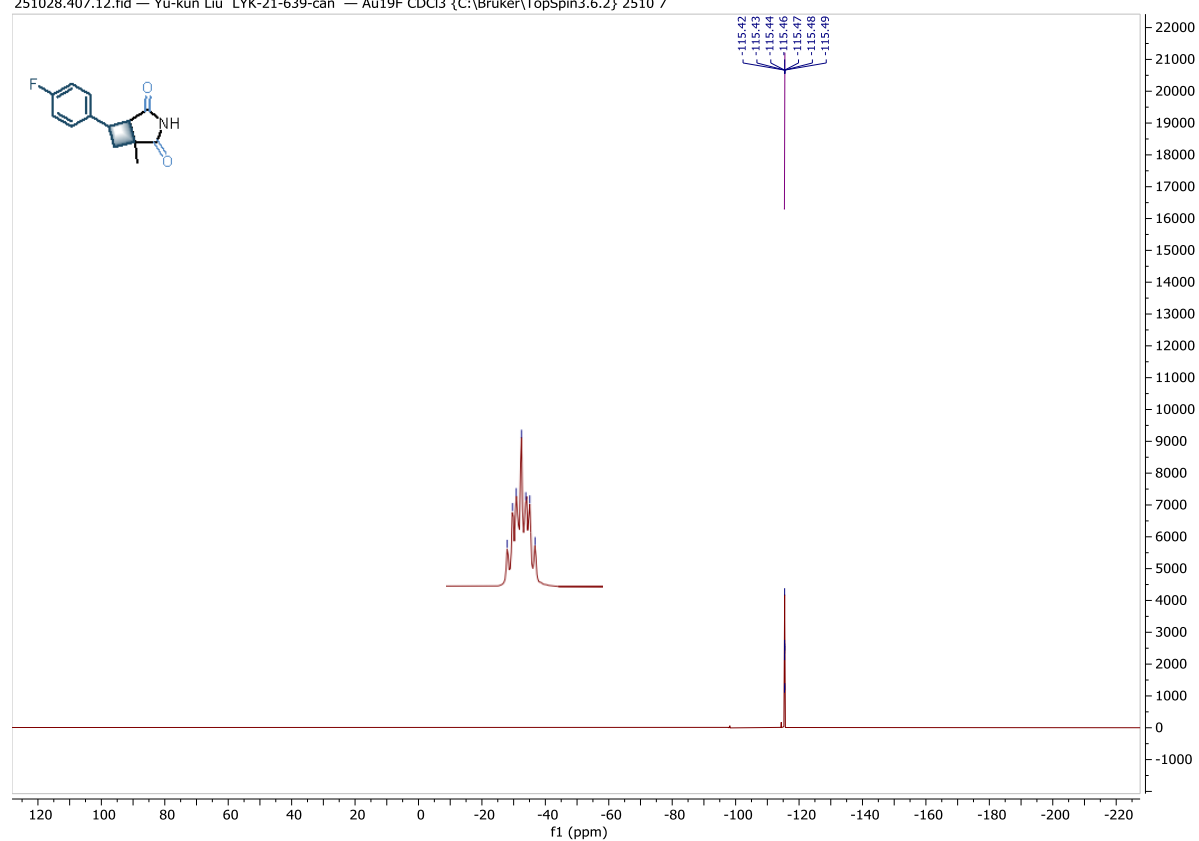
Supplementary Fig. 242. ^{13}C NMR spectrum of **12** (101 MHz, CDCl_3)

251028.407.11.fid — Yu-kun Liu LYK-21-639-can — Au13C CDCl_3 {C:\Bruker\TopSpin3.6.2} 2510 7



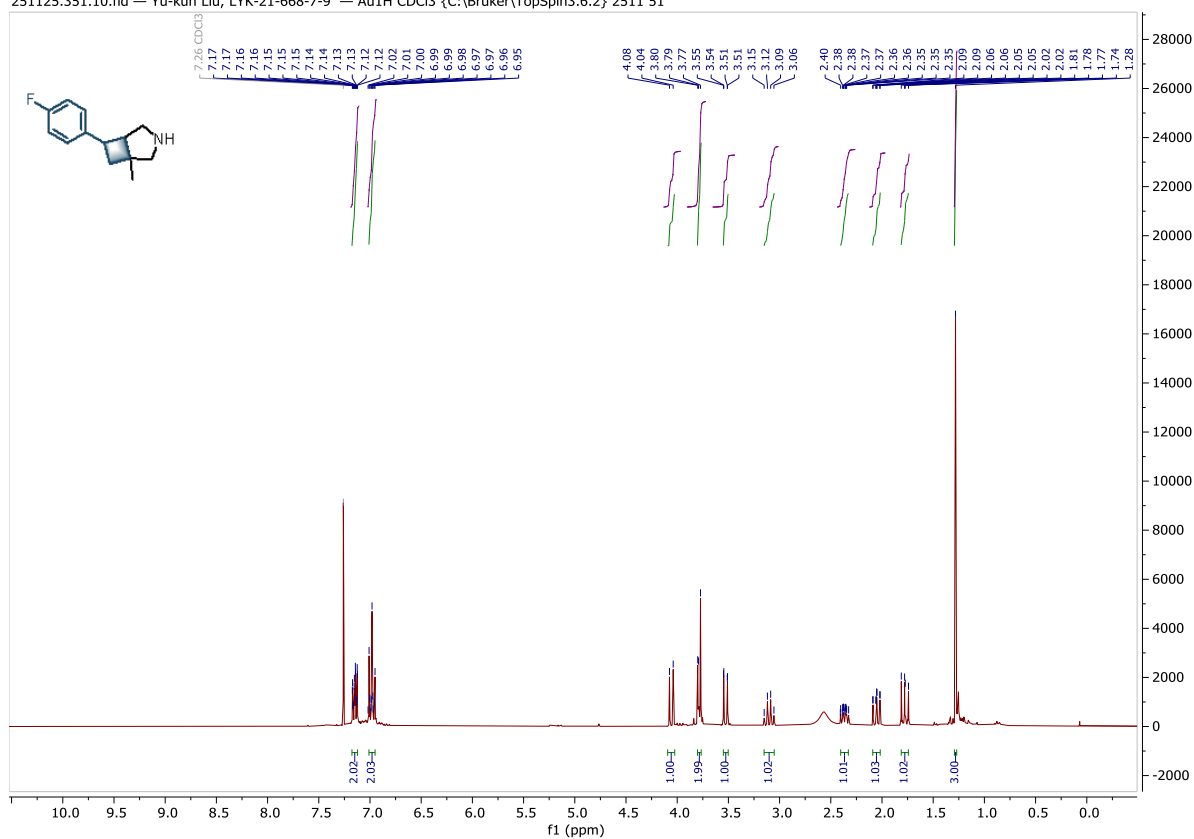
Supplementary Fig. 243. ^{19}F NMR spectrum of **12** (376 MHz, CDCl_3)

251028.407.12.fid — Yu-kun Liu LYK-21-639-can — Au19F CDCl_3 {C:\Bruker\TopSpin3.6.2} 2510 7



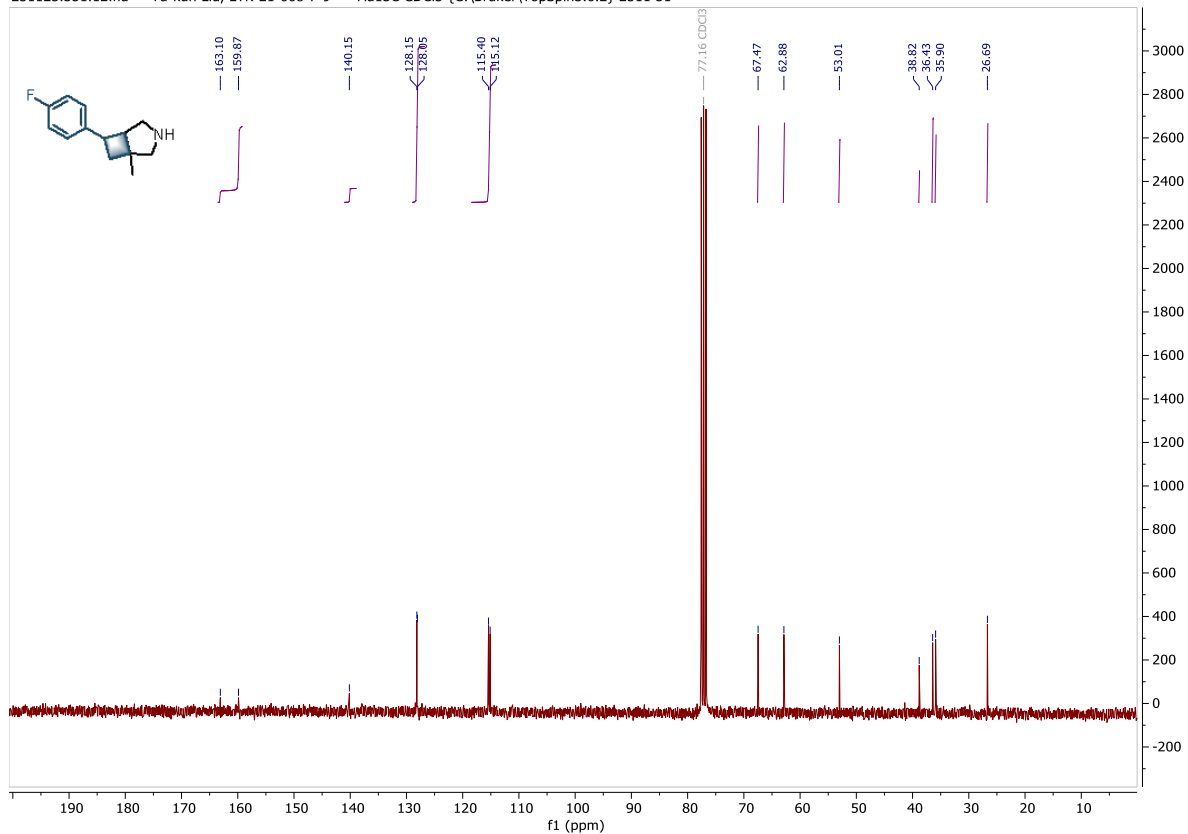
Supplementary Fig. 244. ^1H NMR spectrum of **13** (300 MHz, CDCl_3)

251125.351.10.fid — Yu-kun Liu, LYK-21-668-7-9 — Au1H CDCl_3 {C:\Bruker\TopSpin3.6.2} 2511 51



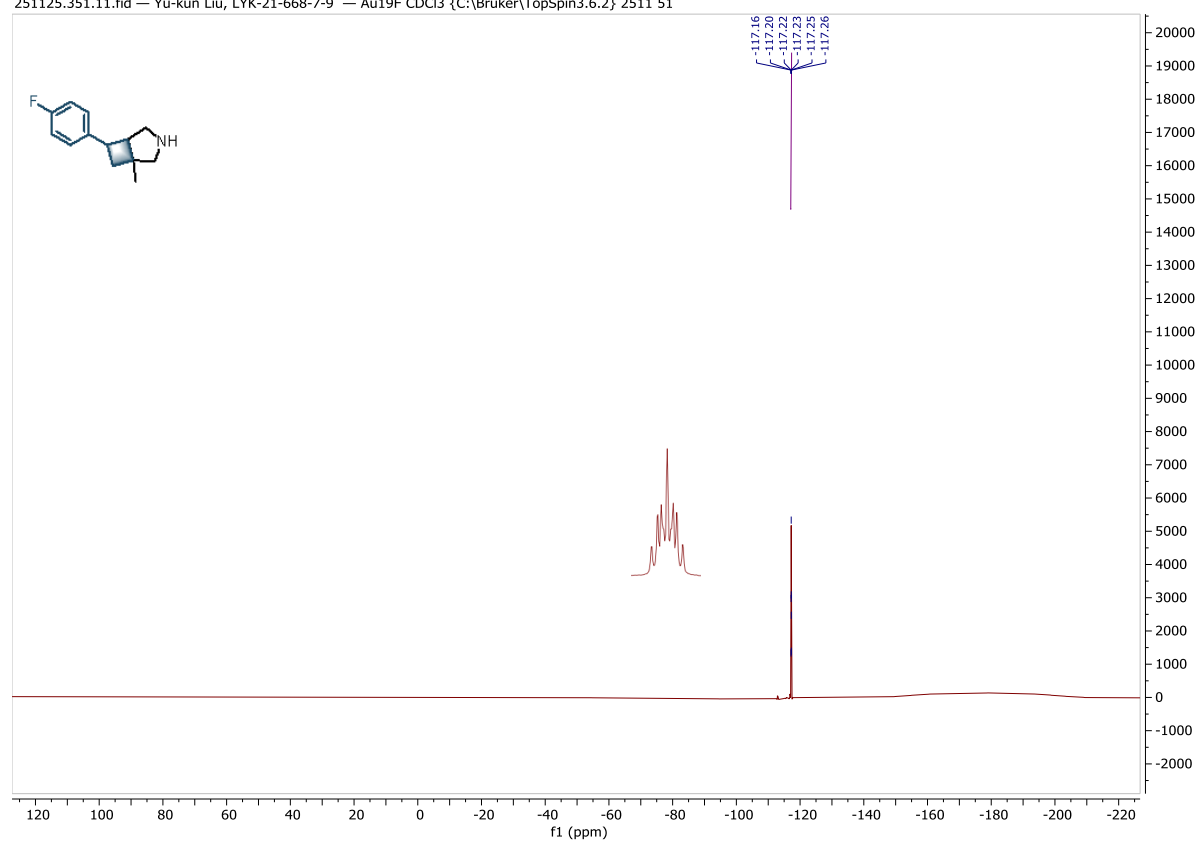
Supplementary Fig. 245. ^{13}C NMR spectrum of **13** (75 MHz, CDCl_3)

251125.351.12.fid — Yu-kun Liu, LYK-21-668-7-9 — Au13C CDCl_3 {C:\Bruker\TopSpin3.6.2} 2511 51

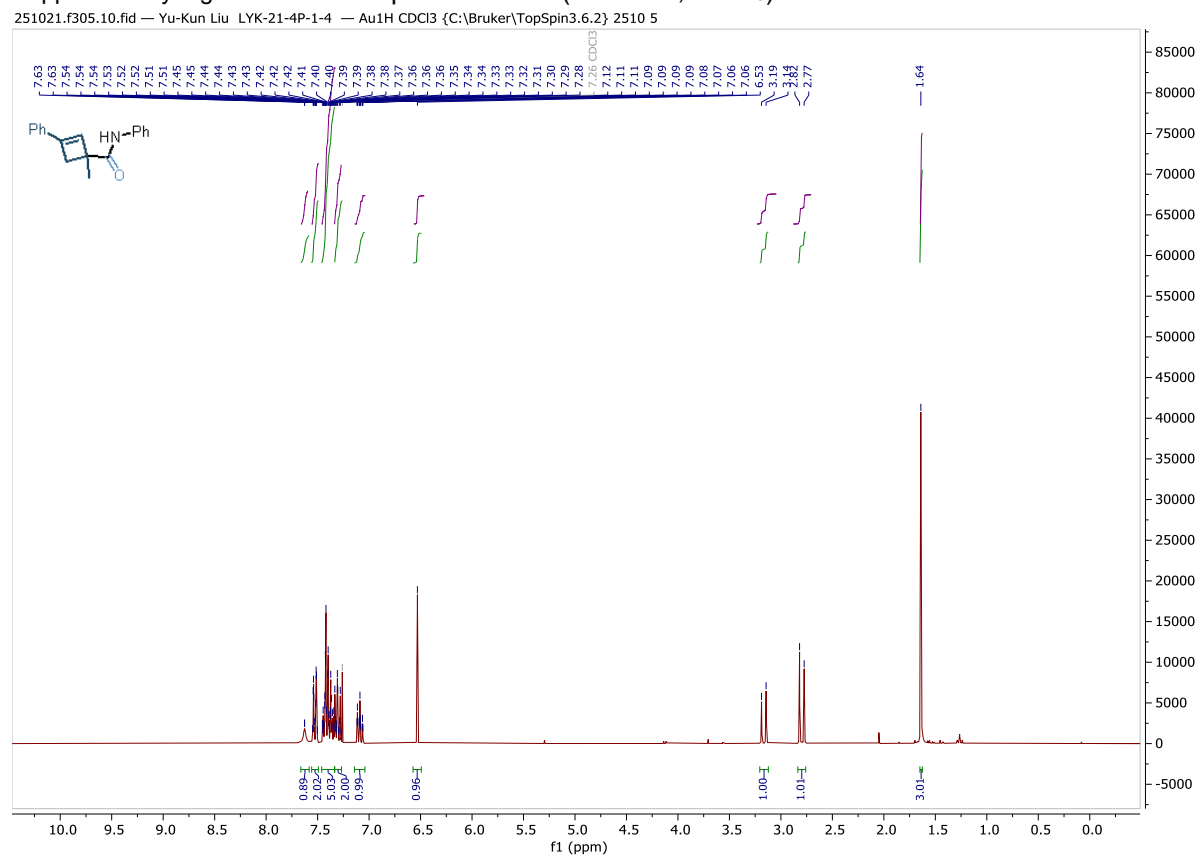


Supplementary Fig. 246. ^{19}F NMR spectrum of **13** (282 MHz, CDCl_3)

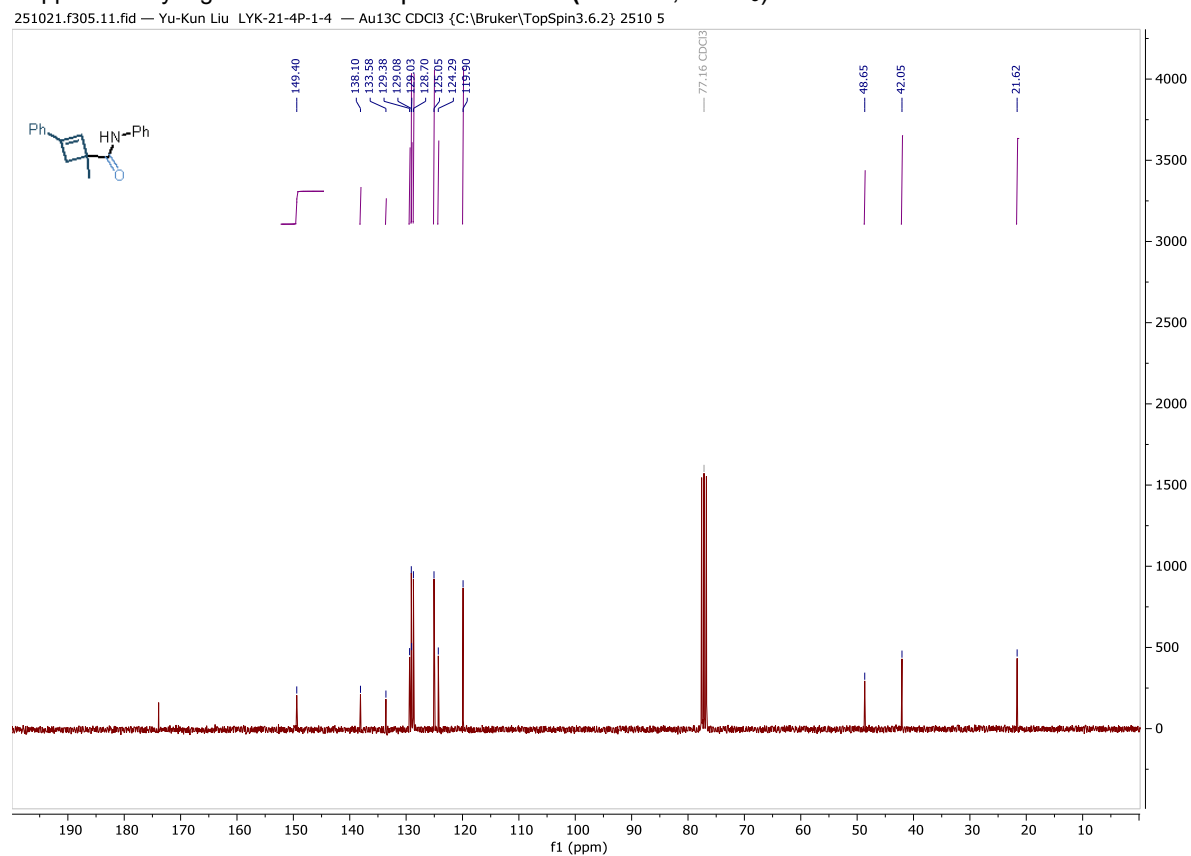
251125.351.11.fid — Yu-kun Liu, LYK-21-668-7-9 — Au19F CDCl_3 {C:\Bruker\TopSpin3.6.2} 2511 51



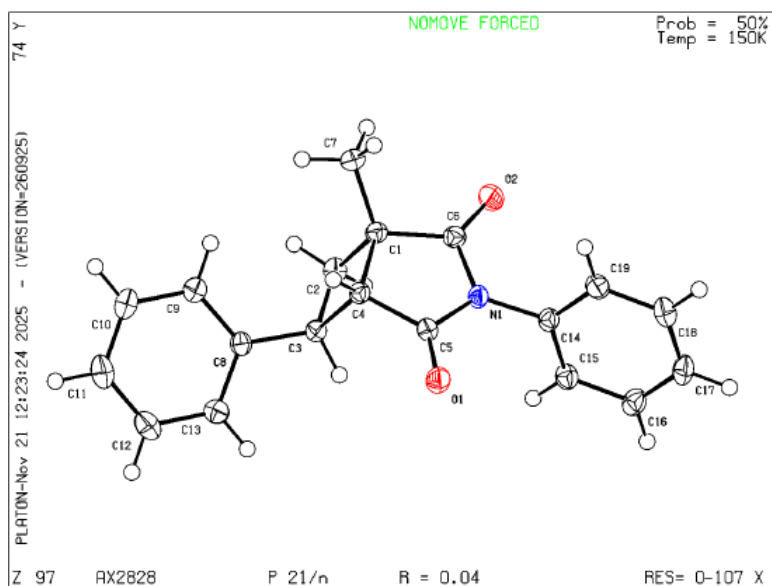
Supplementary Fig. 247. ^1H NMR spectrum of **14** (300 MHz, CDCl_3)



Supplementary Fig. 248. ^{13}C NMR spectrum of **14** (75 MHz, CDCl_3)



10. X-ray Crystallographic Data



Supplementary Fig. 249 ORTEP drawing of product **3a** (CCDC 2440434)

Bond precision: C-C = 0.0016 Å Wavelength=0.71073
 Cell: a=9.2101(10) b=6.7056(8) c=23.590(3)
 alpha=90 beta=95.856(3) gamma=90

Temperature: 150 K

	Calculated	Reported
Volume	1449.3(3)	1449.3(3)
Space group	P 21/n	P 21/n
Hall group	-P 2yn	-P 2yn
Moiety formula	C ₁₉ H ₁₇ N O ₂	?
Sum formula	C ₁₉ H ₁₇ N O ₂	C ₁₉ H ₁₇ N O ₂
Mr	291.34	291.33
Dx, g cm ⁻³	1.335	1.335
Z	4	4
Mu (mm ⁻¹)	0.087	0.087
F ₀₀₀	616.0	616.0
F ₀₀₀ '	616.27	
h,k,lmax	12,9,32	12,9,32
Nref	3937	3935
Tmin,Tmax	0.977,0.996	0.960,0.990
Tmin'	0.963	

Cor.r.ection method= # Reported T Limits: Tmin=0.960 Tmax=0.990

AbsCor.r. = MULTI-SCAN

Data completeness= 0.999

Theta(max)= 29.202

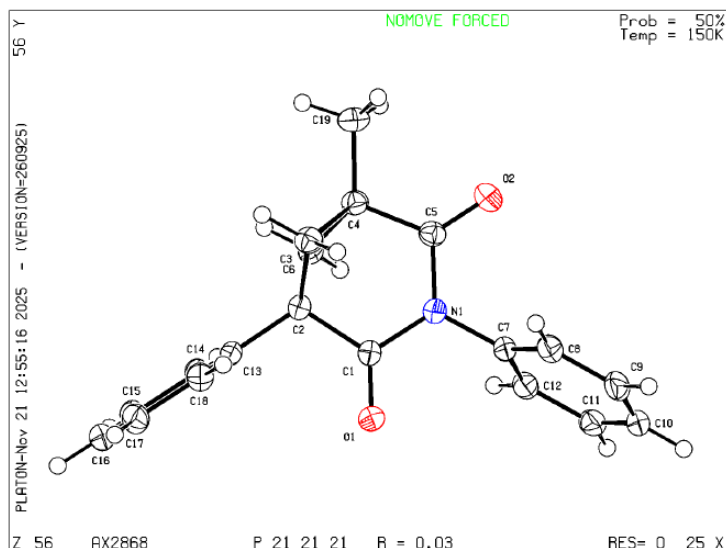
R(reflections)= 0.0392(3347)

wR2(reflections)= 0.1102(3935)

S = 1.031

Npar= 200

The crystal was grown from pentane at low temperature.



Supplementary Fig. 250. ORTEP drawing of product **4a** (CCDC 2463827)

Bond precision:	C-C = 0.0021 Å	Wavelength=0.71073
Cell:	a=5.6627(9) alpha=90	b=11.8497(18) beta=90
Temperature:	150 K	c=21.731(3) gamma=90
	Calculated	Reported
Volume	1458.2(4)	1458.2(4)
Space group	P 21 21 21	P 21 21 21
Hall group	P 2ac 2ab	P 2ac 2ab
Moiety formula	C19 H17 N O2	?
Sum formula	C19 H17 N O2	C19 H17 N O2
Mr	291.34	291.33
Dx,g cm-3	1.327	1.327
Z	4	4
Mu (mm-1)	0.086	0.086
F000	616.0	616.0
F000'	616.27	
h,k,lmax	7,16,29	7,16,29
Nref	3945[2289]	3941
Tmin,Tmax	0.979,0.985	0.980,0.990
Tmin'	0.979	

Cor.r.ection method= # Reported T Limits: Tmin=0.980 Tmax=0.990

AbsCor.r. = MULTI-SCAN

Data completeness= 1.72/1.00

Theta(max)= 29.217

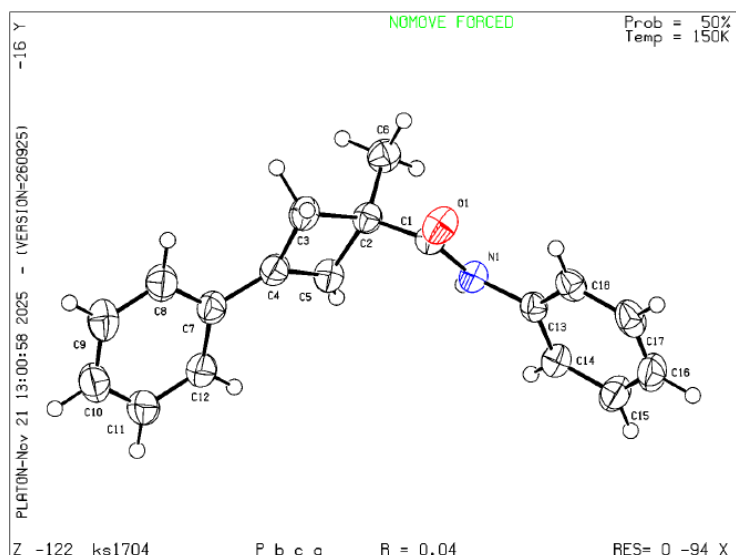
R(reflections)= 0.0320(3738)

wR2(reflections)= 0.0865(3941)

S = 1.042

Npar= 200

The crystal was grown from pentane at low temperature.



Supplementary Fig. 251. ORTEP drawing of product **11** (CCDC 2501737)

Bond precision:	C-C = 0.0017 Å	Wavelength=0.71073
Cell:	a=9.7630(2) alpha=90	b=9.9422(2) beta=90 c=29.7893(6) gamma=90
Temperature:	150 K	
	Calculated	Reported
Volume	2891.52(10)	2891.52(10)
Space group	P b c a	P b c a
Hall group	-P 2ac 2ab	-P 2ac 2ab
Moiety formula	C ₁₈ H ₁₇ N O	?
Sum formula	C ₁₈ H ₁₇ N O	C ₁₈ H ₁₇ N O
Mr	263.33	263.32
Dx, g cm ⁻³	1.210	1.210
Z	8	8
Mu (mm ⁻¹)	0.075	0.075
F ₀₀₀	1120.0	1120.0
F ₀₀₀ '	1120.44	
h,k,lmax	12,13,39	12,13,39
Nref	3490	3488
Tmin,Tmax	0.987,0.993	0.980,0.990
Tmin'	0.983	
Cor.r.ection method= # Reported T Limits: Tmin=0.980 Tmax=0.990		
AbsCor.r. = MULTI-SCAN		
Data completeness= 0.999	Theta(max)= 28.000	
R(reflections)= 0.0409(3049)	wR2(reflections)= 0.1158(3488)	
S = 1.040	Npar= 195	

The crystal was grown from pentane at low temperature.

11. Supplementary References

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- 3 Wang, Z., Shen, C. & Dong, K. Palladium-Catalyzed Enantioselective Migratory Hydroamidocarbonylation of Amide-Linked Alkenes to Access Chiral α -Alkyl Succinimides. *Angew. Chem. Int. Ed.* **136**, e202410967 (2024).
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