Electronic Supplementary Information for

Diastereoselective dearomative cycloaddition of bicyclobutanes with pyridinium ylides: a modular approach to multisubstituted azabicyclo[3.1.1]heptanes

Kushal Dhake,[a,†] Kyla J. Woelk,[a,†] Liam D. N. Krueckl,[a] Faith Alberts,[a] James Mutter,[a] Matthew O. Pohl,[a] Gilian T. Thomas,[a] Muskan Sharma,[a] Jaelyn Bjornerud-Brown,[a] Nahiane Pipaón Fernández,[a] Nathan D. Schley,[b] and David C. Leitch[a,*]

[a]Department of Chemistry, University of Victoria, 3800 Finnerty Rd., Victoria, BC V8P 5C2, Canada.

[b]Department of Chemistry, Vanderbilt University, 2301 Vanderbilt Place Nashville, TN, 37235, United States

*Corresponding author: dcleitch@uvic.ca

Table of Contents

I: General Considerations

Materials. All solvents and common organic reagents were purchased from commercial suppliers and used without further purification. Organic building blocks and starting materials were purchased from Oakwood Chemicals, Sigma Aldrich, or AmBeed and used as received. All Lewis acids were purchased from Strem Chemicals and used as received. All non-commerical compounds were prepared using literature procedures, or syntheses as described in Section V.

Techniques. High-throughput experimentation was performed using 1 mL capacity glass shell vials in sealable aluminum reaction blocks purchased from Analytical Sales. Heating/stirring was achieved using rare-earth magnetic tumble stirrers acquired from V&P Scientific. Photochemistry was performed using a Lumidox® II LED Controller and Lumidox® II LumLamp from Analytical Sales.

Analysis and Spectroscopy. All NMR spectra were acquired on either a Bruker AVANCE 300 MHz spectrometer or a Bruker AVANCE Neo 500 MHz spectrometer. All ^{1}H and ^{13}C NMR chemical shifts are calibrated to residual protio-solvents, and ^{19}F NMR chemical shifts are calibrated to an external standard.

High-resolution electrospray ionization mass spectrometric analysis was performed using a Thermo Scientific Ultimate 3000 ESI-Orbitrap Exactive Plus.

Author contributions

KD, KJW and DCL conceived and designed the project.

KD and KJW equally performed the majority of experiments and data analysis.

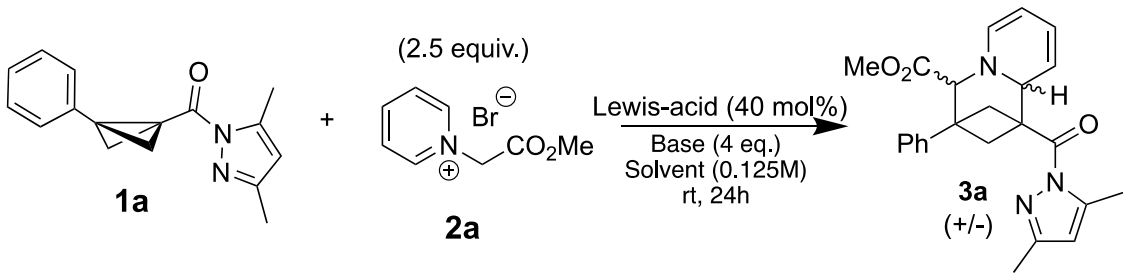
LDNK, FA, JM, MOP, GTT, MS, JBB, and NPF contributed with synthetic experiments and collecting characterization data.

NDS performed X-ray diffraction and data analysis.

KD, KJW, and DCL wrote and edited the manuscript and supplementary information with input from all authors.

II: Reaction Optimization

Catalyst, Base and Solvent Screen 30-well HTE Plate



Procedure (Table S1): For the vials with Lewis acid (A-D): a stock solution for the methyl ester pyridinium **2a** in methanol was prepared and dispensed to 24 x 1 mL glass shell vials (0.063 mmol, 2.5 equiv) followed by solvent evaporation and the addition of micro parylene-coated stir bars to each vial. Two stock solution were prepared for the bicyclobutane **1a**, one in THF and another in MeCN. To two vials was added **1a** (454.2 mg, 1.8 mmol), followed by 7.20 mL of THF or MeCN. The inorganic bases were weighed into the vials containing the pyridinium **2a** using calibrated scoops and triethylamine was added to the remaining vials. To all vials with the base and **2a**, 100 µL of THF or MeCN was added, and the vials were left to stir at rt for 10 minutes. Meanwhile, 24 stock solutions were prepared for the 12 triflate Lewis acids in the two solvents by weighing out the Lewis acid into the vial followed by addition of the bicyclobutane **1a** stock solution (0.48 mL to each vial). The bicyclobutane **1a** and Lewis acids were left to stir for 10 minutes at rt before 100 µL of the mixture was added to each vial (0.125 M concentration). The vials were then sealed and left to stir at rt for 24 hours.

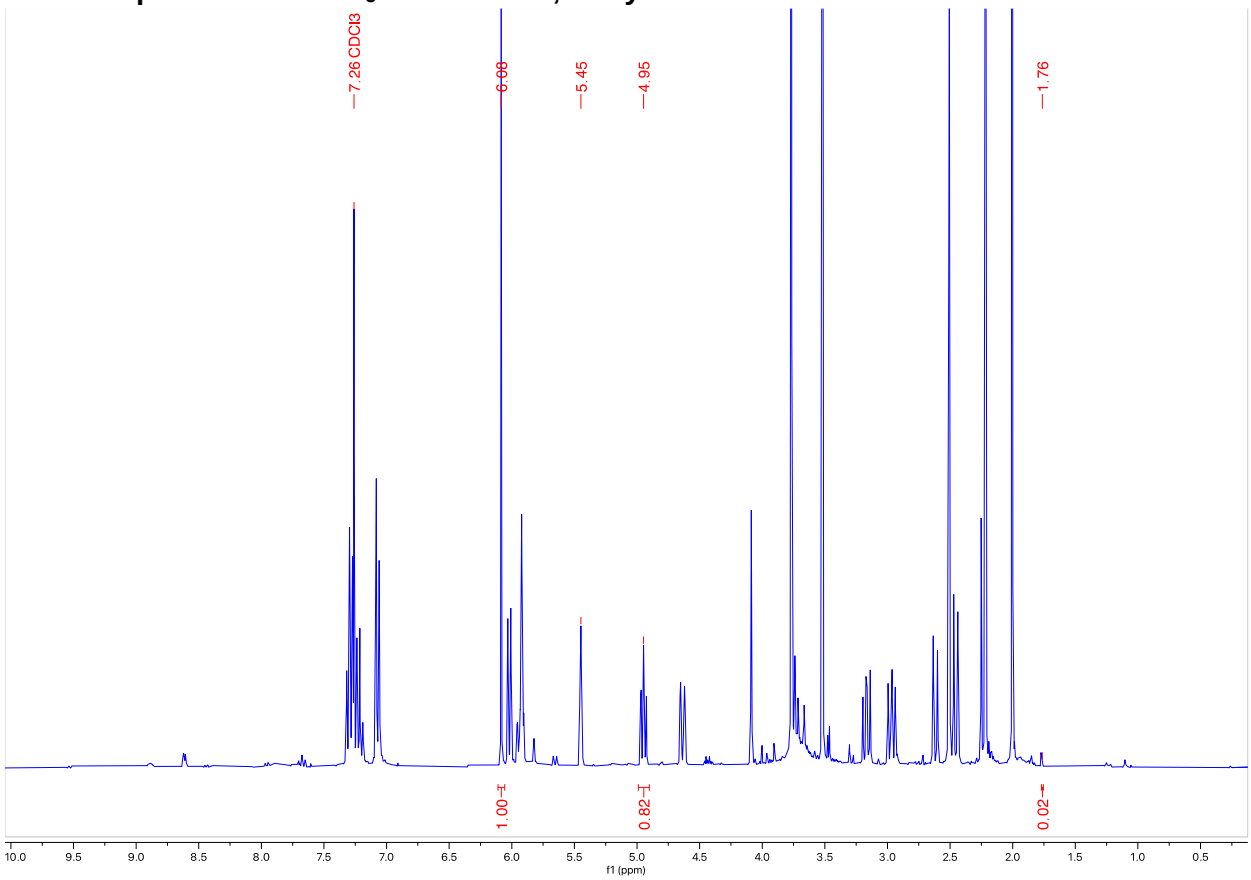
For the vials without Lewis acid (E), pyridinium **2a** (14.5 mg, 0.063 mmol, 2.5 equiv.) and base was weighed into the 1 mL shell vials followed by the addition of stir bars. Half of the acetonitrile solvent (100 µL) was added to all six vials, and they were left to stir for 10 minutes at rt. Two stock solutions of bicyclobutane were made by adding 22.7 mg of **1a** to two vials followed by 0.36 mL of THF and acetonitrile to the vials. The bicyclobutane stock solution was added to each vial (100 µL, 0.125 M) and the reactions were left to stir at rt for 24 hours.

One the reaction time was complete, the solvent was evaporated using a Genevac centrifugal evaporator. A stock solution of 1,3,5-trimethoxybenzene in **$CDCl_3$** (1.4 mg, 0.33 equiv, 0.7 mL) was then added to each vial. The mixtures were stirred for 5 minutes, followed by centrifugation. The supernatant solutions were removed for analysis by NMR spectroscopy. Representative NMR spectra are shown for the conditions in bold.

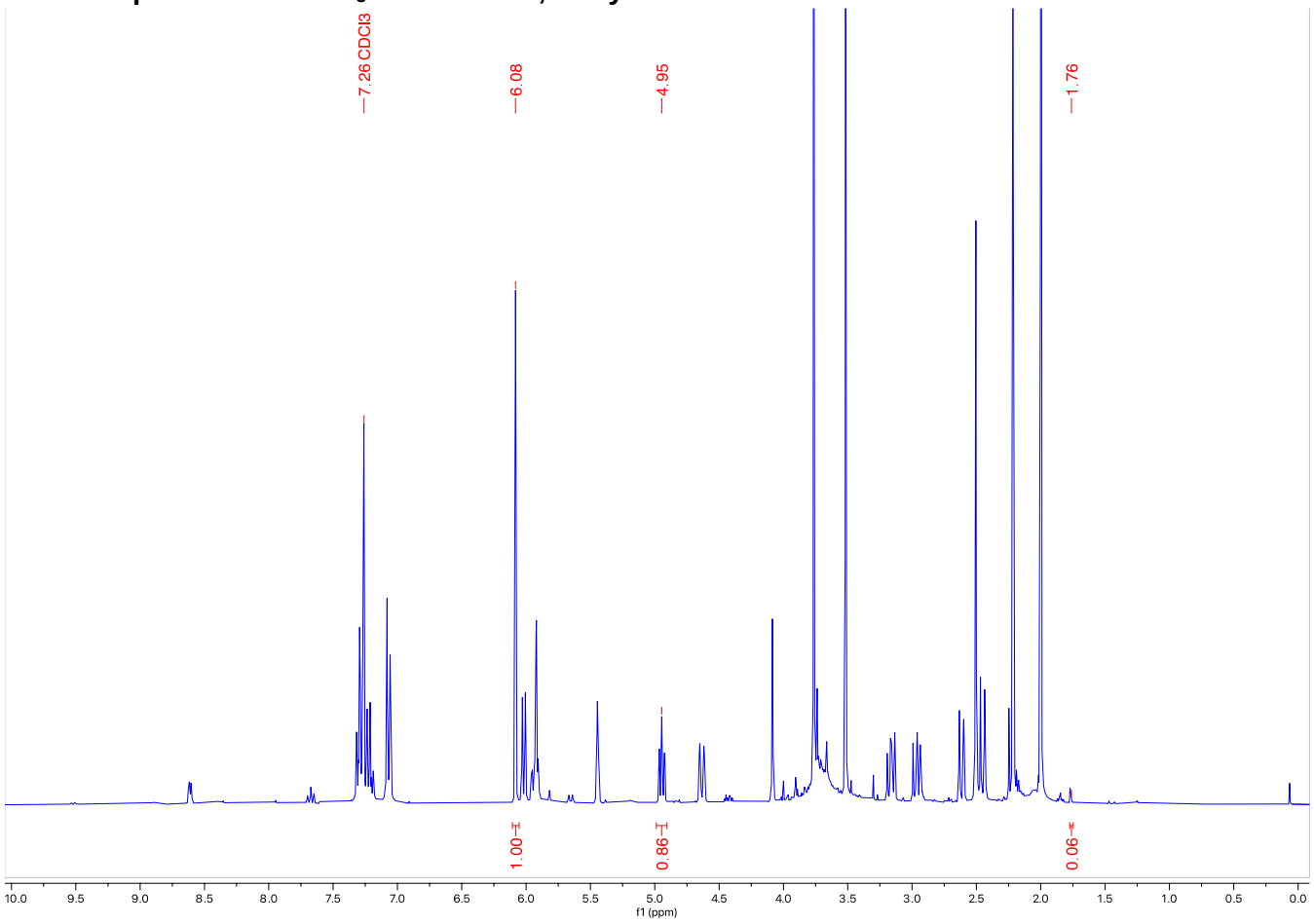
Table S1 – 30-well High-throughput screen at rt

Rxn #	Catalyst	Solvent	Base	% Yield Product	d.r. (major : 1)	% Remaining BCB
A1	LiOTf	THF	Cs_2CO_3	57%	2.4	15%
B1	$Mg(OTf)_2$	THF	Cs_2CO_3	61%	3.1	17%
C1	$Zn(OTf)_2$	THF	Cs_2CO_3	52%	4.8	24%
D1	AgOTf	THF	Cs_2CO_3	31%	3.4	32%
E1	none	THF	Cs_2CO_3	69%	1.1	3%
A2	LiOTf	THF	K_3PO_4	46%	5.6	37%
B2	$Mg(OTf)_2$	THF	K_3PO_4	38%	2.8	50%
C2	$Zn(OTf)_2$	THF	K_3PO_4	25%	4.0	60%
D2	AgOTf	THF	K_3PO_4	68%	8.7	18%
E2	none	MeCN	K_3PO_4	70%	1.6	3%
A3	LiOTf	THF	NEt_3	0%	-	90%
B3	$Mg(OTf)_2$	THF	NEt_3	0%	-	81%
C3	$Zn(OTf)_2$	THF	NEt_3	0%	-	80%
D3	AgOTf	THF	NEt_3	0%	-	94%
E3	none	MeCN	NEt_3	0%	-	100%
A4	LiOTf	MeCN	Cs_2CO_3	57%	>20	15%
B4	$Mg(OTf)_2$	MeCN	Cs_2CO_3	56%	>20	0%
C4	$Zn(OTf)_2$	MeCN	Cs_2CO_3	65%	>20	3%
D4	AgOTf	MeCN	Cs_2CO_3	64%	>20	5%
E4	none	MeCN	Cs_2CO_3	73%	>20	3%
A5	LiOTf	MeCN	K_3PO_4	30%	>20	3%
B5	**$Mg(OTf)_2$**	**MeCN**	**K_3PO_4**	**82%**	**>20**	**1%**
C5	$Zn(OTf)_2$	MeCN	K_3PO_4	50%	>20	6%
D5	AgOTf	MeCN	K_3PO_4	36%	>20	16%
E5	**none**	**MeCN**	**K_3PO_4**	**86%**	**>20**	**3%**
A6	LiOTf	MeCN	NEt_3	0%	-	100%
B6	$Mg(OTf)_2$	MeCN	NEt_3	6%	>20	74%
C6	$Zn(OTf)_2$	MeCN	NEt_3	0%	-	58%
D6	AgOTf	MeCN	NEt_3	0%	-	68%
E6	none	MeCN	NEt_3	0%	-	70%

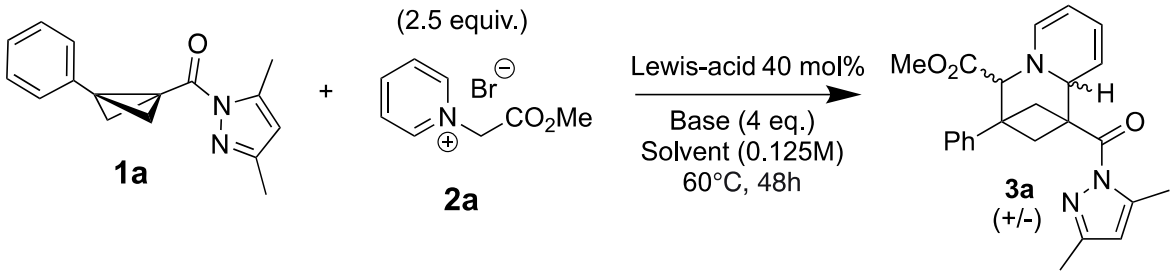
^{1}H NMR spectrum in $CDCl_3$ for Table S1, entry B5



^{1}H NMR spectrum in $CDCl_3$ for Table S1, entry E5



Catalyst, Base and Solvent Screen 96-well HTE Plate



Procedure (Table S2): A stock solution for the methyl ester pyridinium **2a** in methanol was prepared and dispensed to all 96 x 1 mL shell vials (0.063 mmol, 2.5 equiv), followed by solvent evaporation and the addition of micro stir bars to each vial. Two stock solution were prepared for the bicyclobutane **1a**, one in THF and another in MeCN. To two vials was added **1a** (454.2 mg, 1.8 mmol) and then 7.20 mL of THF or MeCN was added to each vial. The inorganic bases were weighed into the reaction vials containing the pyridinium **2a** using calibrated scoops, and triethylamine was added to the remaining vials. To all vials containing the base and **2a**, 100 µL of THF or MeCN was added, and the mixtures were left to stir at rt for 10 minutes. Meanwhile, 24 stock solutions were prepared for the 12 triflate Lewis acids in the two solvents by weighing out the Lewis acid into the vial followed by addition of the bicyclobutane **1a** stock solution (0.48 mL to each vial). The bicyclobutane **1a** and Lewis acid mixtures were left to stir for 10 minutes at rt before 100 µL of the mixture was added to each reaction vial. The vials were then sealed and left to stir at 60 °C for 48 hours. The solvent was then evaporated using a Genevac centrifugal evaporator and then a stock solution of 1,3,5-trimethoxybenzene in $CDCl_3$ (1.4 mg, 0.33 equiv, 0.6 mL) was added to each vial. The mixtures were stirred for 5 minutes, and then the samples were centrifuged before the supernatants were removed for analysis by NMR spectroscopy. Representative NMR spectra are shown for the conditions in bold.

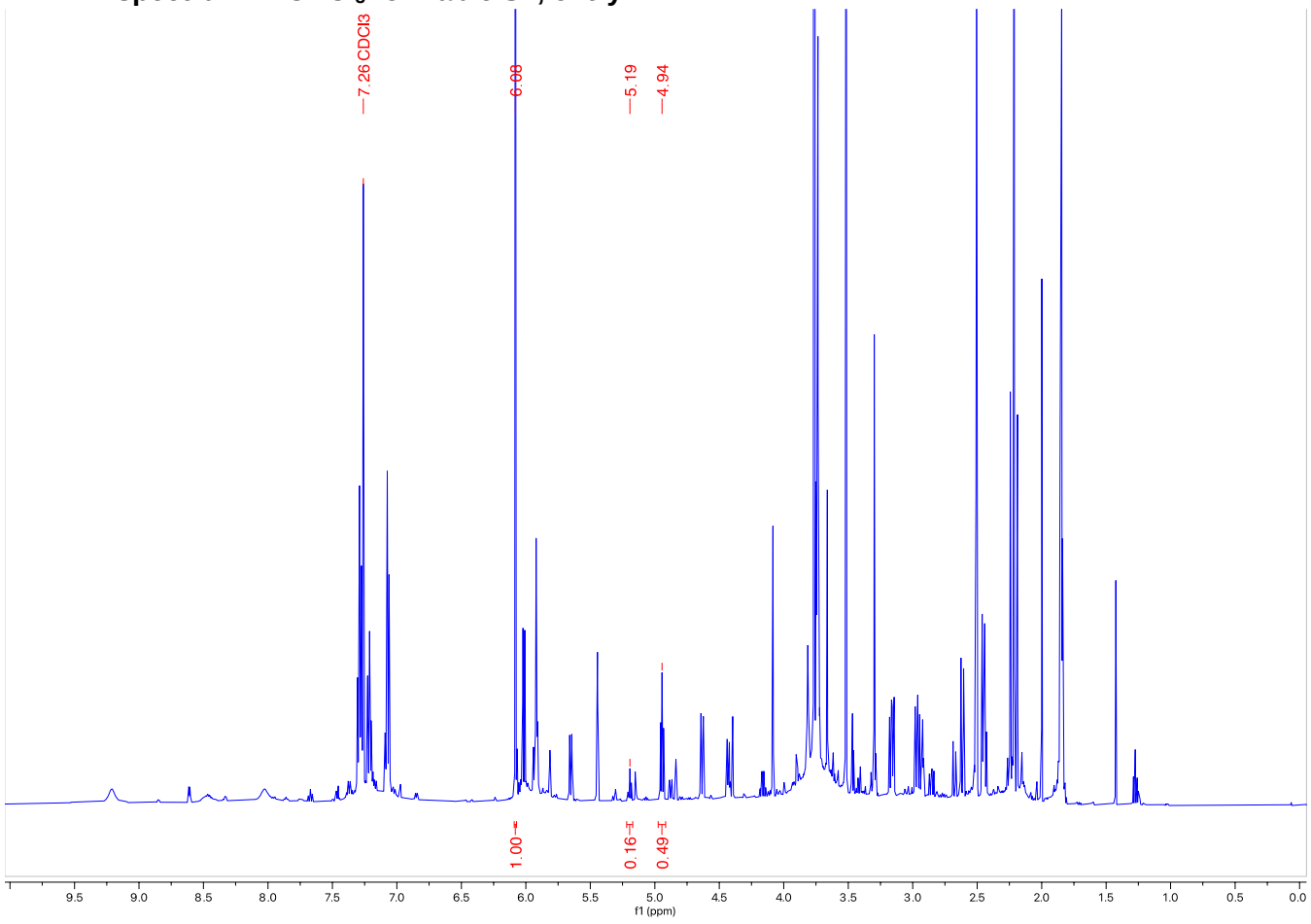
Table S2 – 96-well High-throughput screen at 60°C

Rxn #	Catalyst	Solvent	Base	% Yield Product	d.r. (major : 1)	% Remaining BCB
A1	LiOTf	THF	K_2CO_3	51%	4.1	0%
B1	$Mg(OTf)_2$	THF	K_2CO_3	44%	3.4	0%
C1	$Sc(OTf)_3$	THF	K_2CO_3	2%	-	0%
D1	$Fe(OTf)_3$	THF	K_2CO_3	0%	-	0%
E1	$Zn(OTf)_2$	THF	K_2CO_3	8%	7.0	35%
F1	$Ga(OTf)_3$	THF	K_2CO_3	0%	-	0%
G1	AgOTf	THF	K_2CO_3	31%	3.4	0%
H1	$Sn(OTf)_2$	THF	K_2CO_3	4%	-	0%
I1	$La(OTf)_3$	THF	K_2CO_3	0%	-	3%
J1	$Eu(OTf)_3$	THF	K_2CO_3	0%	-	0%
K1	$Yb(OTf)_3$	THF	K_2CO_3	0%	-	0%
L1	$Bi(OTf)_3$	THF	K_2CO_3	0%	-	0%
A2	**LiOTf**	**THF**	**Cs_2CO_3**	**65%**	**3.1**	**0%**
B2	$Mg(OTf)_2$	THF	Cs_2CO_3	53%	1.2	5%
C2	$Sc(OTf)_3$	THF	Cs_2CO_3	14%	1.3	1%
D2	$Fe(OTf)_3$	THF	Cs_2CO_3	0%	-	0%
E2	$Zn(OTf)_2$	THF	Cs_2CO_3	53%	1.8	7%
F2	$Ga(OTf)_3$	THF	Cs_2CO_3	0%	-	0%
G2	AgOTf	THF	Cs_2CO_3	45%	2.0	21%

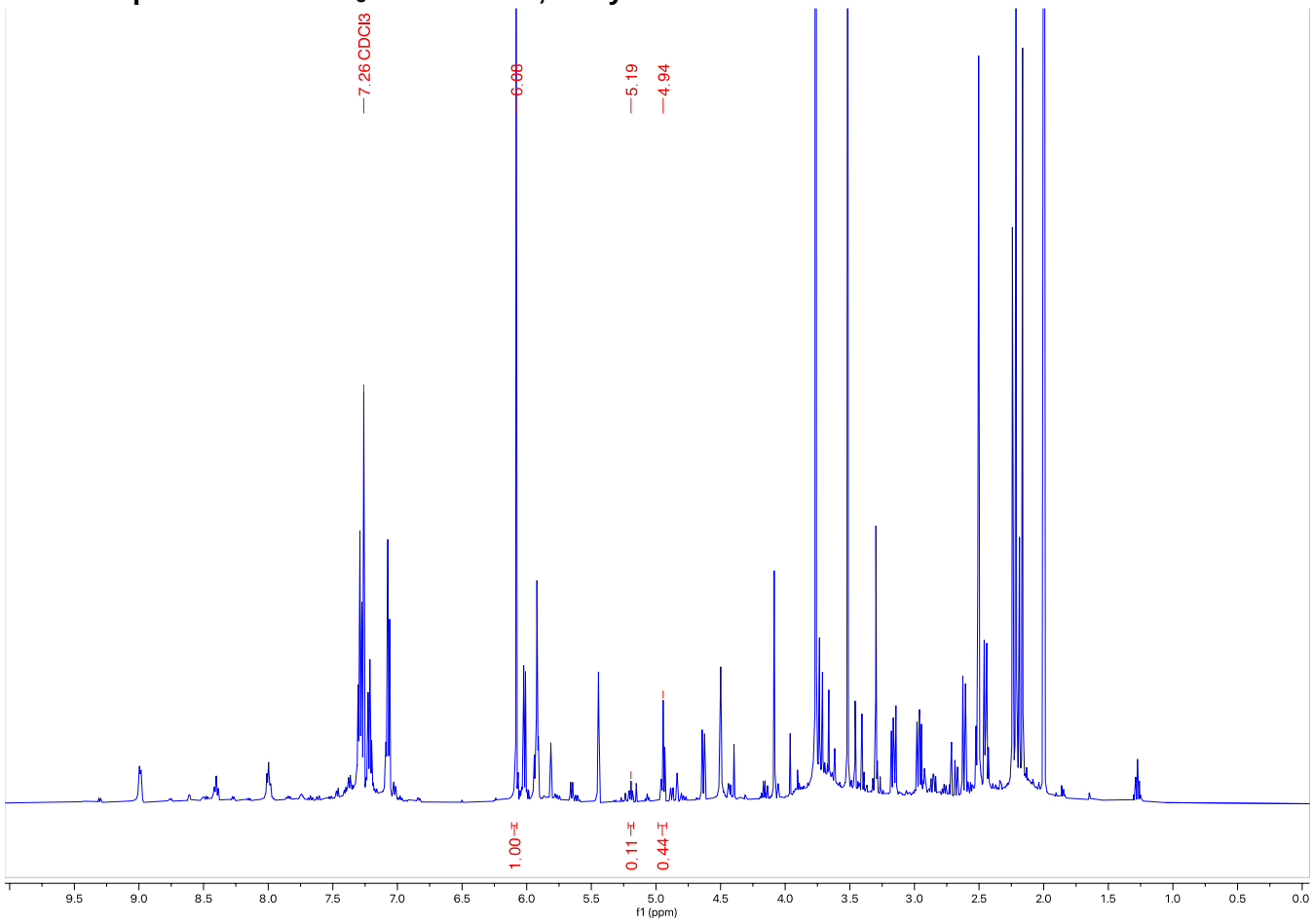
H2	$Sn(OTf)_2$	THF	Cs_2CO_3	5%	-	12%
I2	$La(OTf)_3$	THF	Cs_2CO_3	0%	-	8%
J2	$Eu(OTf)_3$	THF	Cs_2CO_3	4%	-	6%
K2	$Yb(OTf)_3$	THF	Cs_2CO_3	0%	-	3%
L2	$Bi(OTf)_3$	THF	Cs_2CO_3	0%	-	0%
A3	LiOTf	THF	K_3PO_4	56%	4.6	1%
B3	$Mg(OTf)_2$	THF	K_3PO_4	56%	1.7	1%
C3	$Sc(OTf)_3$	THF	K_3PO_4	6%	-	2%
D3	$Fe(OTf)_3$	THF	K_3PO_4	0%	-	0%
E3	$Zn(OTf)_2$	THF	K_3PO_4	51%	2.4	3%
F3	$Ga(OTf)_3$	THF	K_3PO_4	0%	-	0%
G3	AgOTf	THF	K_3PO_4	35%	4.8	0%
H3	$Sn(OTf)_2$	THF	K_3PO_4	0%	-	0%
I3	$La(OTf)_3$	THF	K_3PO_4	2%	-	5%
J3	$Eu(OTf)_3$	THF	K_3PO_4	0%	-	16%
K3	$Yb(OTf)_3$	THF	K_3PO_4	0%	-	5%
L3	$Bi(OTf)_3$	THF	K_3PO_4	0%	-	0%
A4	LiOTf	THF	NEt_3	14%	1.8	50%
B4	$Mg(OTf)_2$	THF	NEt_3	1%	-	0%
C4	$Sc(OTf)_3$	THF	NEt_3	0%	-	25%
D4	$Fe(OTf)_3$	THF	NEt_3	0%	-	0%
E4	$Zn(OTf)_2$	THF	NEt_3	3%	2.0	1%
F4	$Ga(OTf)_3$	THF	NEt_3	0%	-	0%
G4	AgOTf	THF	NEt_3	0%	-	0%
H4	$Sn(OTf)_2$	THF	NEt_3	0%	-	0%
I4	$La(OTf)_3$	THF	NEt_3	0%	-	4%
J4	$Eu(OTf)_3$	THF	NEt_3	0%	-	36%
K4	$Yb(OTf)_3$	THF	NEt_3	0%	-	0%
L4	$Bi(OTf)_3$	THF	NEt_3	0%	-	0%
A5	LiOTf	MeCN	K_2CO_3	34%	3.9	0%
B5	$Mg(OTf)_2$	MeCN	K_2CO_3	0%	-	0%
C5	$Sc(OTf)_3$	MeCN	K_2CO_3	3%	-	0%
D5	$Fe(OTf)_3$	MeCN	K_2CO_3	0%	-	0%
E5	$Zn(OTf)_2$	MeCN	K_2CO_3	15%	2.0	38%
F5	$Ga(OTf)_3$	MeCN	K_2CO_3	0%	-	0%
G5	AgOTf	MeCN	K_2CO_3	23%	1.9	0%
H5	$Sn(OTf)_2$	MeCN	K_2CO_3	0%	-	0%
I5	$La(OTf)_3$	MeCN	K_2CO_3	0%	-	0%
J5	$Eu(OTf)_3$	MeCN	K_2CO_3	0%	-	0%
K5	$Yb(OTf)_3$	MeCN	K_2CO_3	0%	-	0%
L5	$Bi(OTf)_3$	MeCN	K_2CO_3	0%	-	0%
A6	LiOTf	MeCN	Cs_2CO_3	53%	3.4	7%
B6	$Mg(OTf)_2$	MeCN	Cs_2CO_3	53%	3.4	0%
C6	$Sc(OTf)_3$	MeCN	Cs_2CO_3	0%	-	0%
D6	$Fe(OTf)_3$	MeCN	Cs_2CO_3	0%	-	0%
E6	$Zn(OTf)_2$	MeCN	Cs_2CO_3	11%	1.8	13%
F6	$Ga(OTf)_3$	MeCN	Cs_2CO_3	8%	-	0%
G6	AgOTf	MeCN	Cs_2CO_3	30%	2.3	0%
H6	$Sn(OTf)_2$	MeCN	Cs_2CO_3	0%	-	0%
I6	$La(OTf)_3$	MeCN	Cs_2CO_3	0%	-	0%
J6	$Eu(OTf)_3$	MeCN	Cs_2CO_3	0%	-	0%
K6	$Yb(OTf)_3$	MeCN	Cs_2CO_3	0%	-	0%
L6	$Bi(OTf)_3$	MeCN	Cs_2CO_3	0%	-	1%
A7	LiOTf	MeCN	K_3PO_4	45%	3.5	3%
B7	**$Mg(OTf)_2$**	**MeCN**	**K_3PO_4**	**55%**	**4.0**	**0%**
C7	$Sc(OTf)_3$	MeCN	K_3PO_4	0%	-	0%

D7	$Fe(OTf)_3$	MeCN	K_3PO_4	0%	-	0%
E7	$Zn(OTf)_2$	MeCN	K_3PO_4	0%	-	7%
F7	$Ga(OTf)_3$	MeCN	K_3PO_4	0%	-	0%
G7	AgOTf	MeCN	K_3PO_4	28%	2.5	0%
H7	$Sn(OTf)_2$	MeCN	K_3PO_4	0%	-	0%
I7	$La(OTf)_3$	MeCN	K_3PO_4	0%	-	0%
J7	$Eu(OTf)_3$	MeCN	K_3PO_4	0%	-	0%
K7	$Yb(OTf)_3$	MeCN	K_3PO_4	0%	-	0%
L7	$Bi(OTf)_3$	MeCN	K_3PO_4	0%	-	0%
A8	LiOTf	MeCN	NEt_3	0%	-	4%
B8	$Mg(OTf)_2$	MeCN	NEt_3	0%	-	0%
C8	$Sc(OTf)_3$	MeCN	NEt_3	0%	-	0%
D8	$Fe(OTf)_3$	MeCN	NEt_3	0%	-	0%
E8	$Zn(OTf)_2$	MeCN	NEt_3	0%	-	44%
F8	$Ga(OTf)_3$	MeCN	NEt_3	0%	-	0%
G8	AgOTf	MeCN	NEt_3	0%	-	0%
H8	$Sn(OTf)_2$	MeCN	NEt_3	0%	-	0%
I8	$La(OTf)_3$	MeCN	NEt_3	0%	-	4%
J8	$Eu(OTf)_3$	MeCN	NEt_3	0%	-	0%
K8	$Yb(OTf)_3$	MeCN	NEt_3	0%	-	70%
L8	$Bi(OTf)_3$	MeCN	NEt_3	0%	-	0%

^{1}H NMR spectrum in $CDCl_3$ for Table S2, entry A2



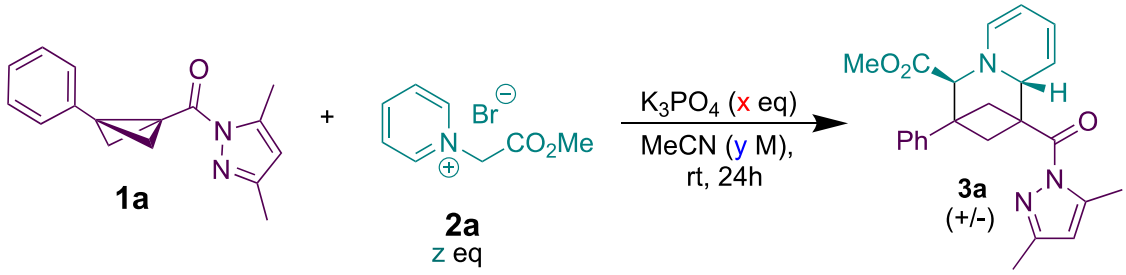
^{1}H NMR spectrum in $CDCl_3$ for Table S2, entry B7



Full Factorial Analysis

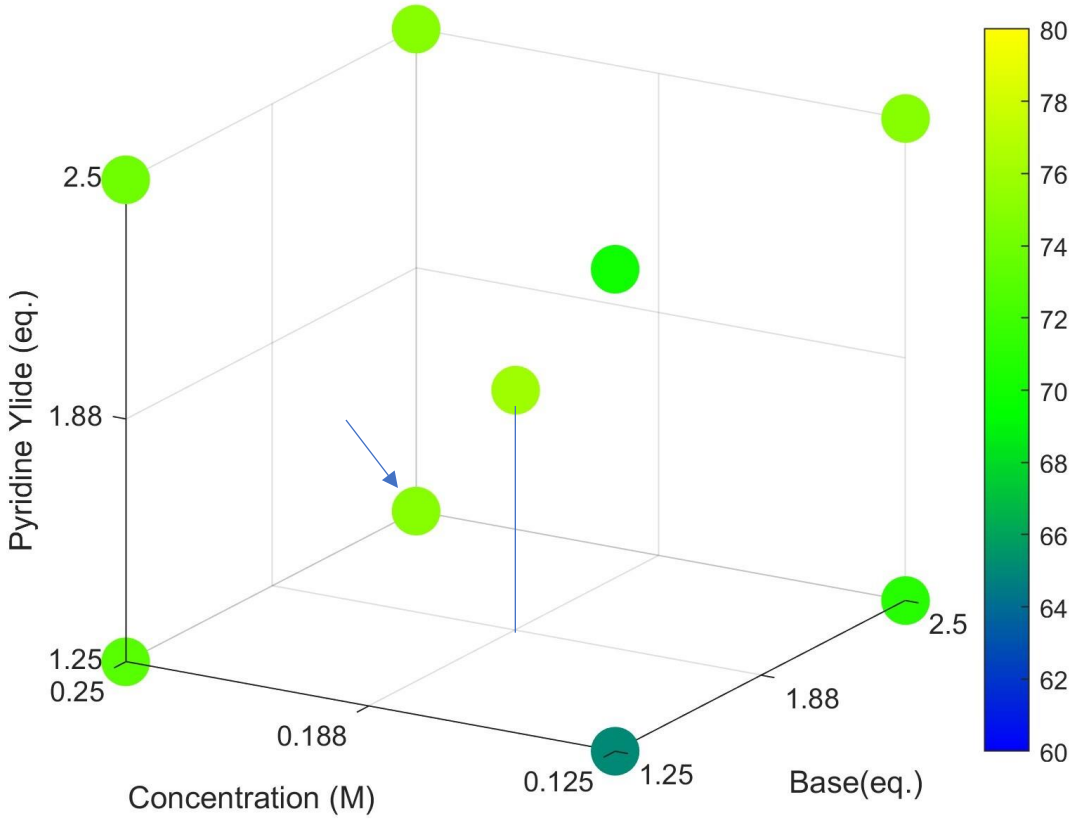
Procedure: For each entry, 25.2 mg (0.1 mmol) of **1a** was weighed in a 1-dram vial (vial A). In another 1-dram vial (vial B), **2a** (**L:** 29.0 mg, 0.125 mmol; **H:** 58.0 mg, 0.250 mmol; **Center**: 43.5 mg, 0.1875 mmol) and K_3PO_4 (**L:** 26.5 mg, 0.125 mmol; **H:** 53.0 mg, 0.250 mmol; **Center:** 39.8 mg, 0.1875 mmol) were added. MeCN (**L:** 0.6 mL; **H:** 0.3 mL; **Center:** 0.4 mL) was added to vial A, and additional MeCN (**L:** 0.2 mL; **H:** 0.1 mL; **Center:** 0.13 mL) was added to vial B. The mixture in vial B was stirred for 5 mins, followed by transfer of the contents of vial A into vial B. The reaction mixtures were stirred at room temperature for 24 hours. After 24 hours, the reaction solvent was evaporated, followed by the addition of a $CDCl_3$ solution of 1,3,5-trimethoxybenzene (0.7 mL, containing 5.6 mg, 0.33 equiv of internal standard). The mixture was shaken vigorously, followed by centrifugation to sediment insoluble solids. The supernatant was removed and analyzed by NMR spectroscopy.

Table S3 – Full factorial screening for reagent loading and concentration

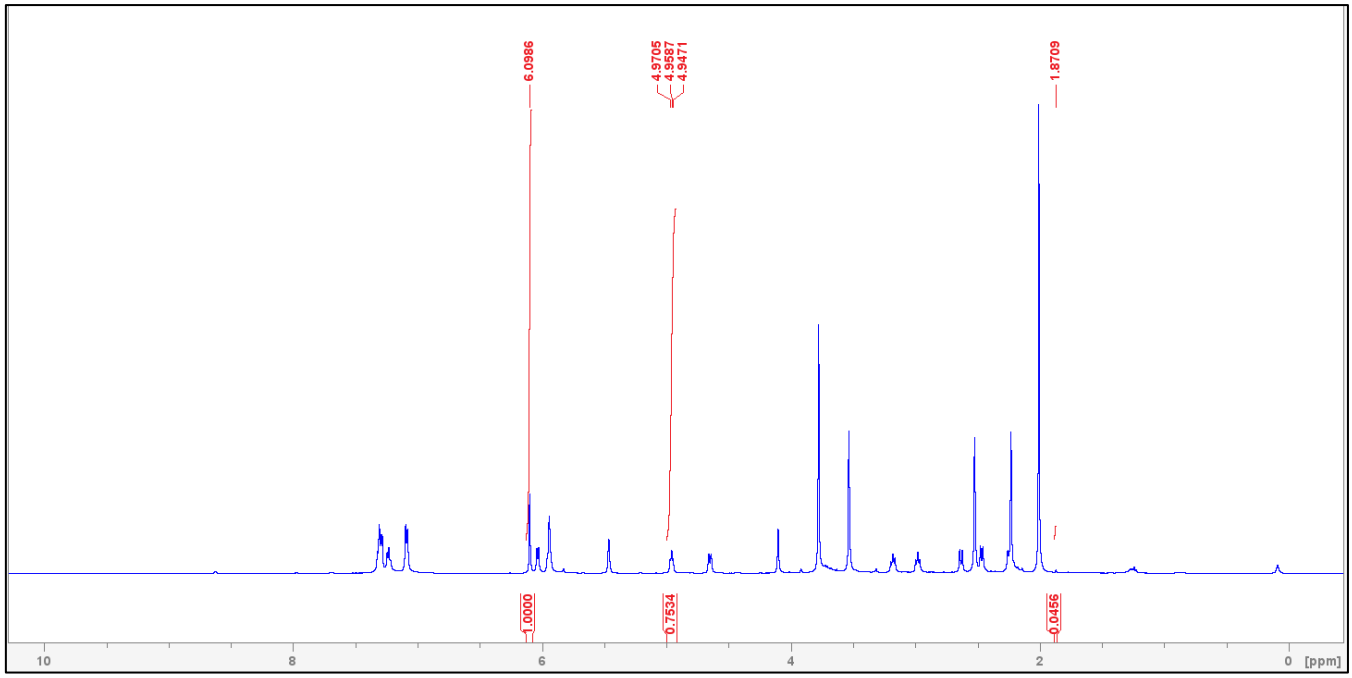


Entry	Base loading capacity (eq)	Concentration of reaction mixture (M)	Pyridine Ylide (eq)	Product Solution yield by ^{1}H NMR (%)	*Unreacted Bicyclobutane (%)
1	1.25 (L)	0.125 (L)	1.25 (L)	65	16
2	2.5 (H)	0.125 (L)	1.25 (L)	71	6
3	1.25 (L)	0.25 (H)	1.25 (L)	73	13
4	**2.5 (H)**	**0.25 (H)**	**1.25 (L)**	**75**	**<5**
5	1.25 (L)	0.125 (L)	2.5 (H)	70	16
6	2.5 (H)	0.125 (L)	2.5 (H)	75	<5
7	1.25 (L)	0.25 (H)	2.5 (H)	74	<5
8	2.5 (H)	0.25 (H)	2.5 (H)	75	<5
9	1.875 (Center-point)	0.1875 (Center-point)	1.875 (Center-point)	76	<5

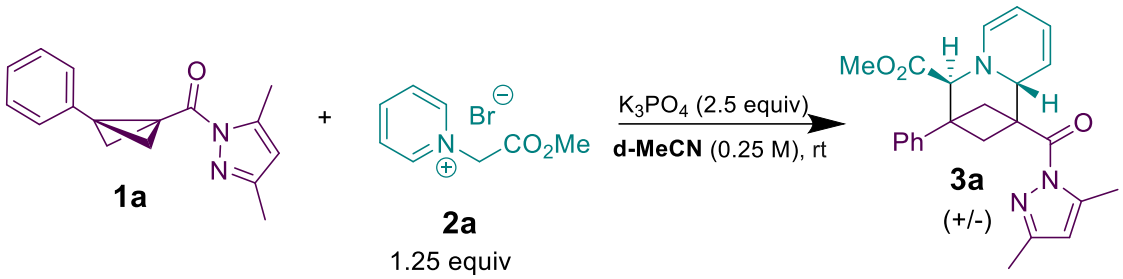
Graphical representation of 3a yield as a function of Design of Experiments settings



^{1}H NMR spectrum in $CDCl_3$ for Table S3, Entry 4:



III: Reaction Progress Monitoring

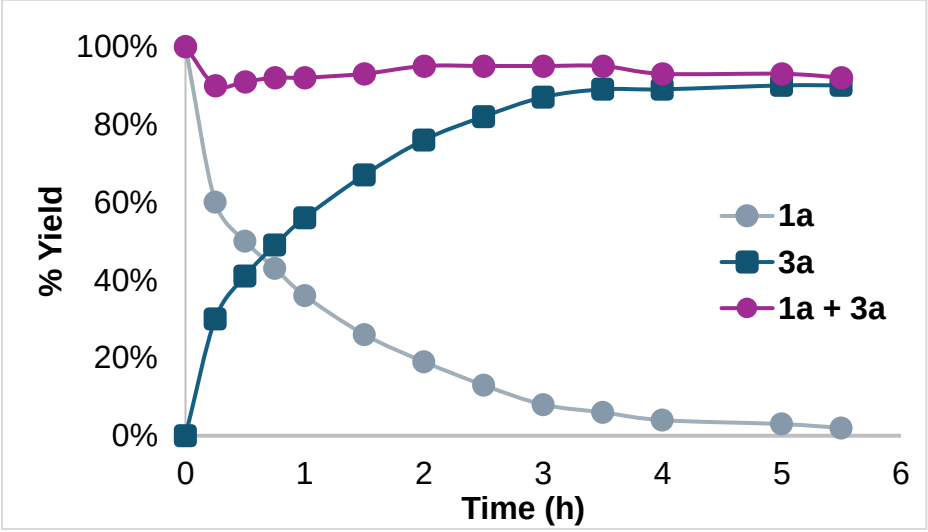


Procedure (Table S4): Pyridinium **2a** (145.0 mg, 0.63 mmol, 1.25 equiv) and K_3PO_4 (265.4 mg, 0.50 mmol, 2.5 equiv) were weighed into a 20 mL vial, followed by the addition of a Teflon-coated stir bar. d-MeCN (1.0 mL) was added to the vial, and the mixture was stirred for 2 minutes at rt. Then, the bicyclobutane **1a** (126.2 mg, 0.50 mmol, 1 equiv) and 1,3,5-trimethoxybenzene internal standard (28.0 mg, 0.17 mmol, 0.33 equiv) were dissolved in d-MeCN (0.50 mL) in a 4 mL vial, and the solution added to the reaction vial. The bicyclobutane vial was washed with another 0.50 mL of d-MeCN, and this was added to the reaction mixture, which represented t = 0.

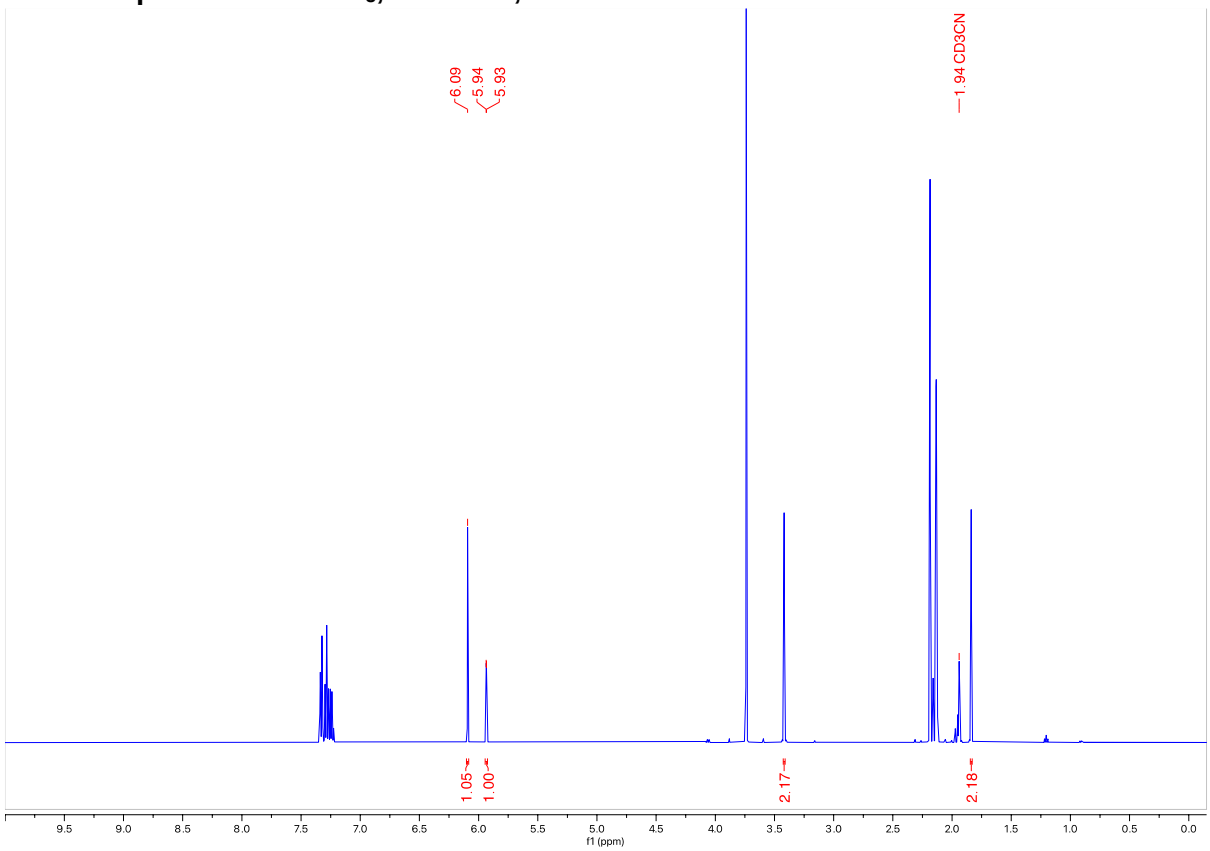
At each time point, a 50 µL sample was withdrawn from the reaction mixture via pipette, diluted with d-MeCN, and passed through a 0.45 µm syringe filter. The filter was washed with an additional 0.3 mL of d-MeCN, and then the sample was analyzed by NMR spectroscopy.

Table S4 – Reaction progress monitoring data:

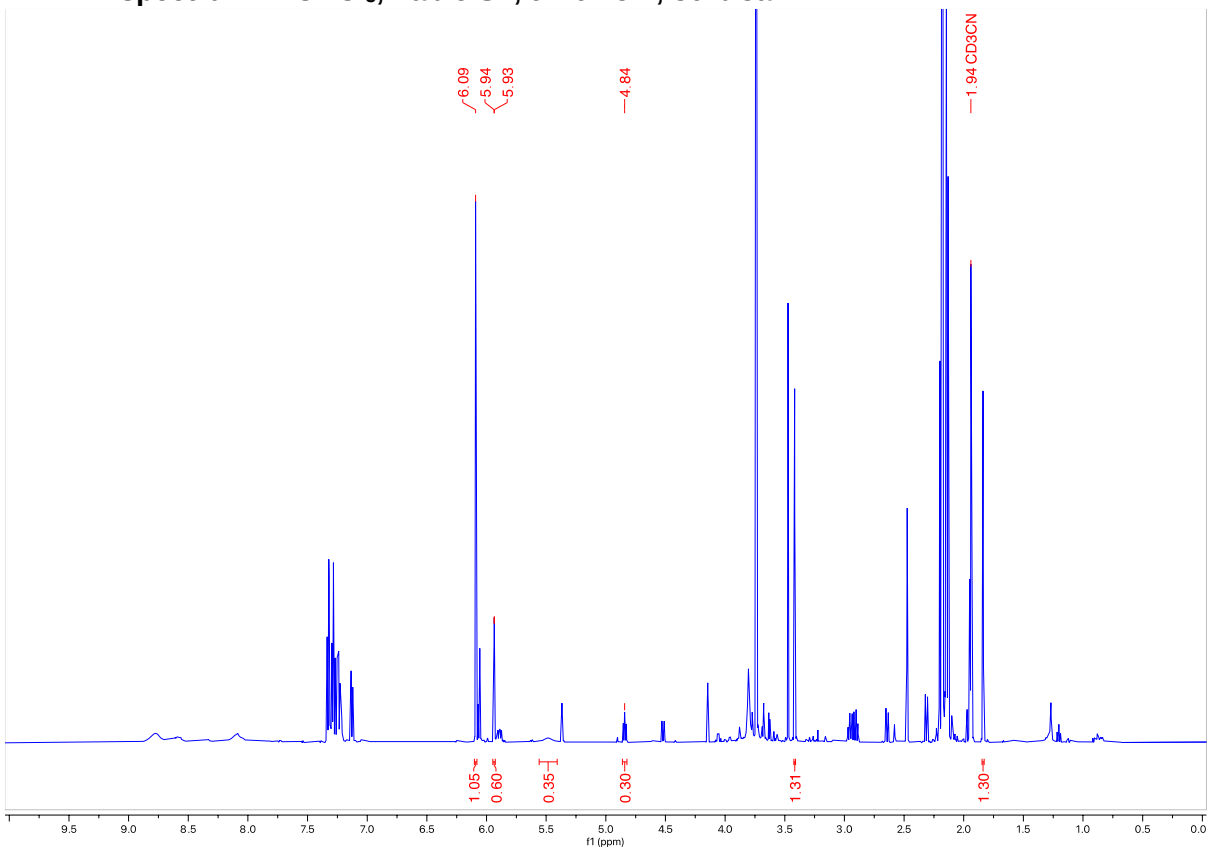
Time (h)	% 1a Remaining	% 3a Yield	%1a + %3a
0.0	100	0	100
0.25	60	30	90
0.5	50	41	91
0.75	43	49	92
1.0	36	56	92
1.5	26	67	93
2.0	19	76	95
2.5	13	82	95
3.0	8	87	95
3.5	6	89	95
4.0	4	89	93
5.0	3	90	93



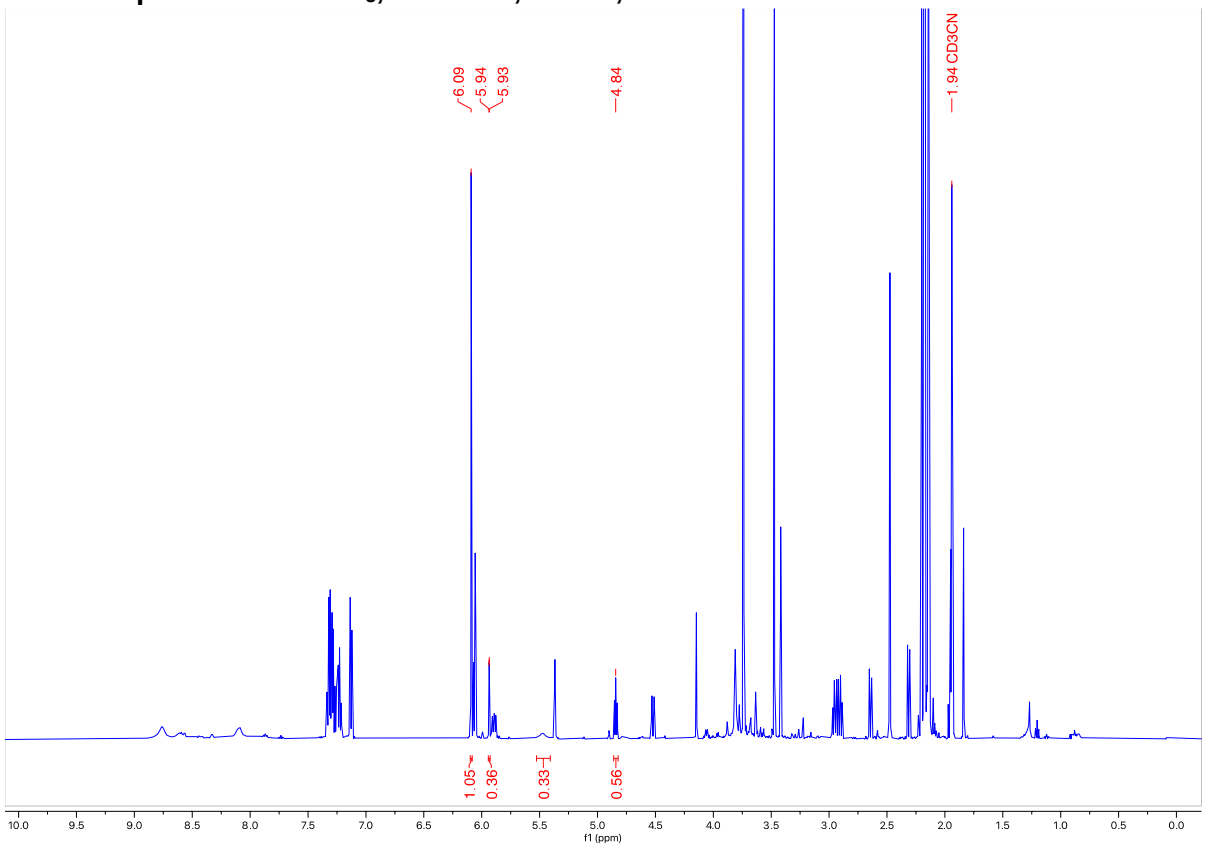
^{1}H NMR spectrum in $CDCl_3$, Table S4, t = 0 h:



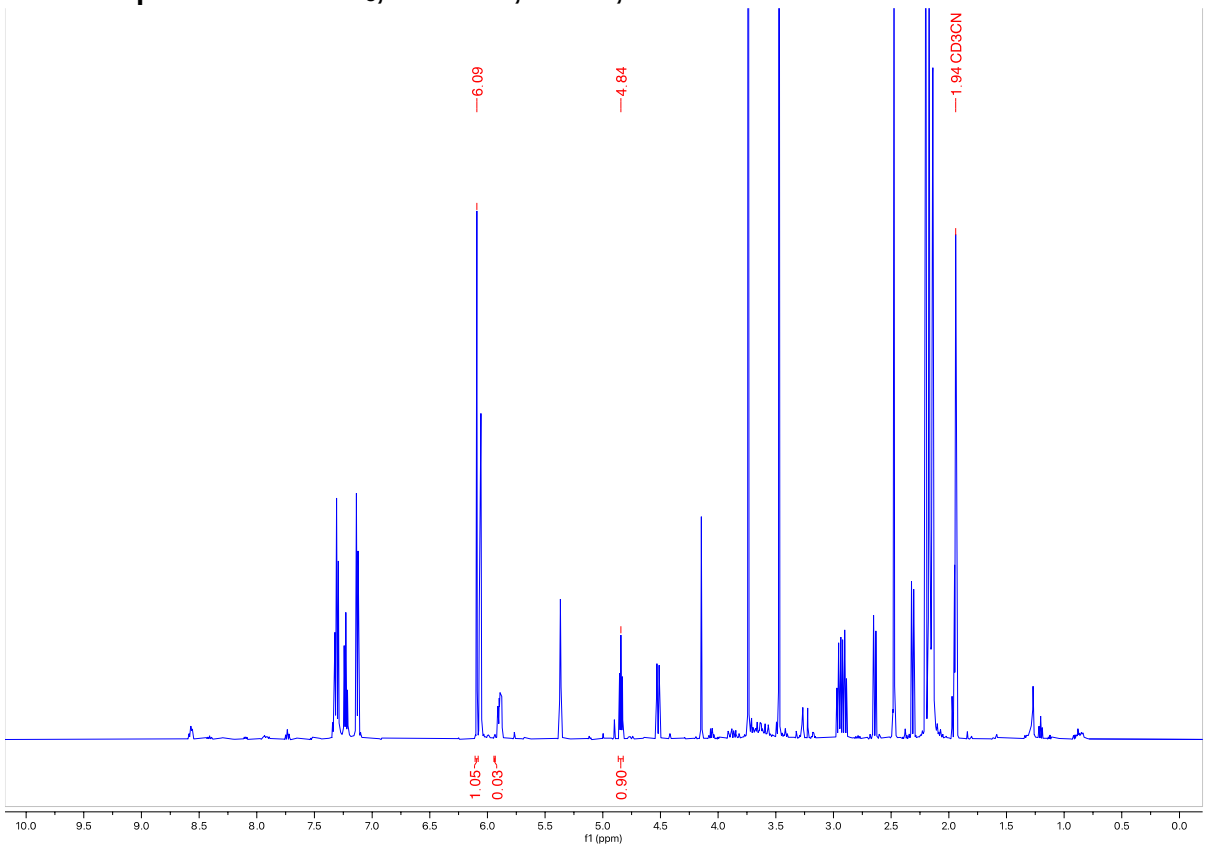
^{1}H NMR spectrum in $CDCl_3$, Table S4, t = 0.15 h, 30% 3a:



^{1}H NMR spectrum in $CDCl_3$, Table S4, t = 1 h, 56% 3a:



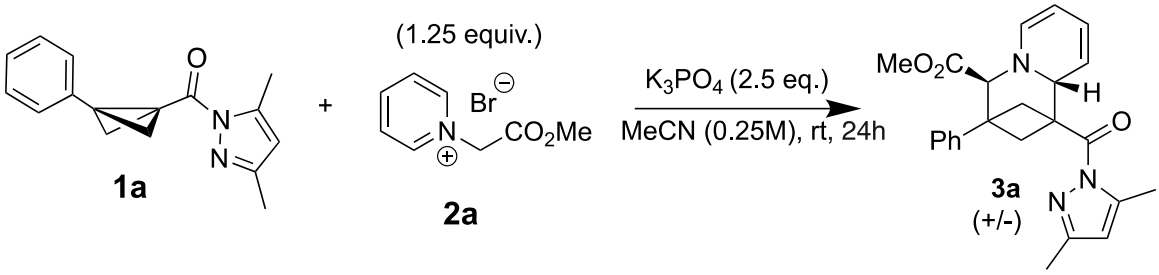
^{1}H NMR spectrum in $CDCl_3$, Table S4, t = 5 h, 90% 3a:



IV: Control Reactions

Reaction Sensitivity

Table S5



Entry	Conditions[a]	3a[b]	1a[b]
1	No K_3PO_4 added	0	84
2	Run at 30°C	81	5
3	Na_2SO_4•$10H_2O$ (1 equiv.)	81	6
4	Molecular Sieves	66	12

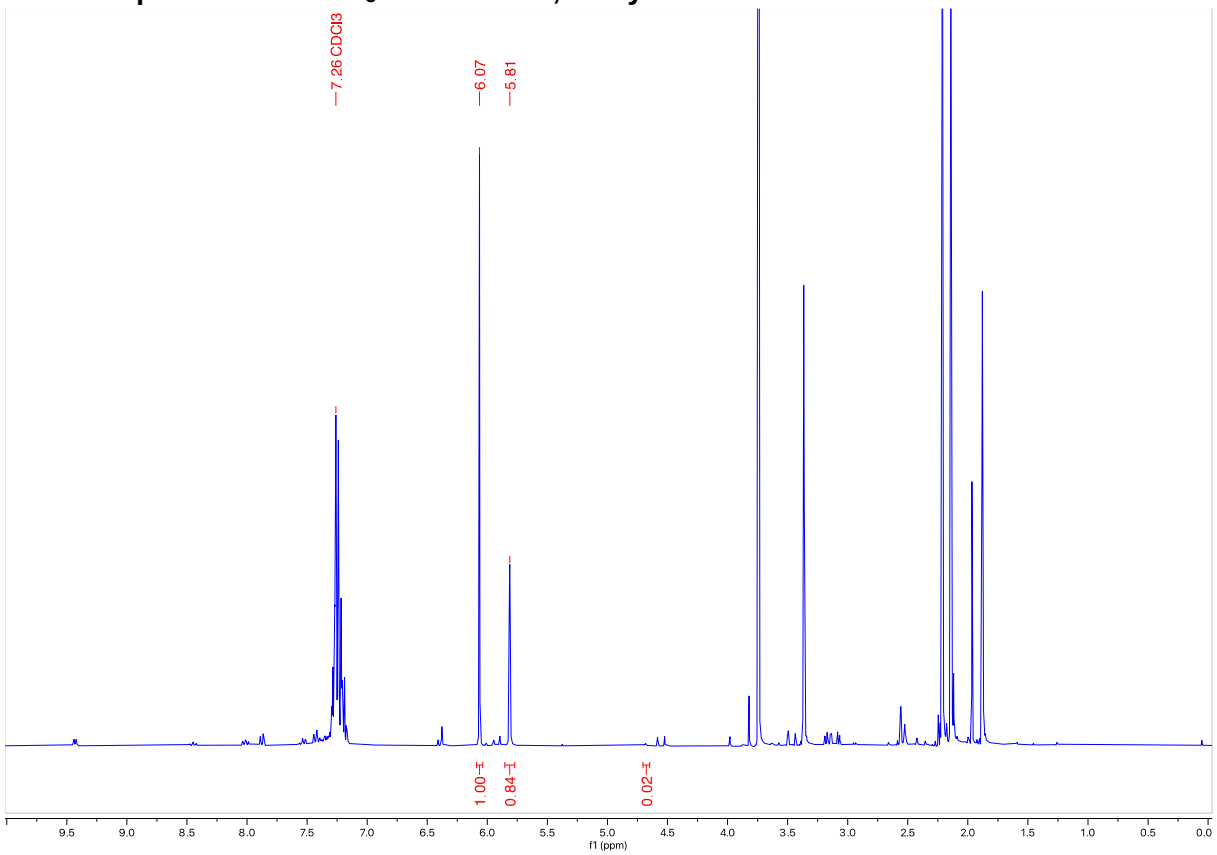
[a]Unless otherwise noted, reactions are performed at room temperature for 24 hours with 0.05 mmol of **1a** and **3a** is formed as a single diastereomer. [b]Amounts of **1a** and **3a** are obtained by ^{1}H NMR spectroscopy by relative integration vs. internal standard, 1,3,5-trimethoxybenzene (TMB).

General procedure for sensitivity reactions (Table S5): Pyridinium **2a** (29.0 mg, 0.13 mmol, 1.25 equiv) and K_3PO_4 (53.1 mg, 0.25 mmol, 2.5 equiv) were weighed into four 4 mL vials, followed by the addition of stir bars. MeCN (0.2 mL) was added to all four vials, and they were left to stir for 5 minutes at rt. A stock solution of **1a** was made from 121.1 mg of **1a** and 0.96 mL of MeCN. The bicyclobutane stock solution was then added to each vial (0.2 mL, 0.25 M) and the reaction mixtures were left to stir at rt for 24 hours. The solvent was then evaporated using a Genevac centrifugal evaporator, followed by dilution with a stock solution of 1,3,5-trimethoxybenzene in $CDCl_3$ (0.7 mL, containing 5.6 mg, 0.33 equiv of internal standard). The mixtures were stirred for 5 minutes, centrifuged, and the supernatant removed for analysis by NMR spectroscopy.

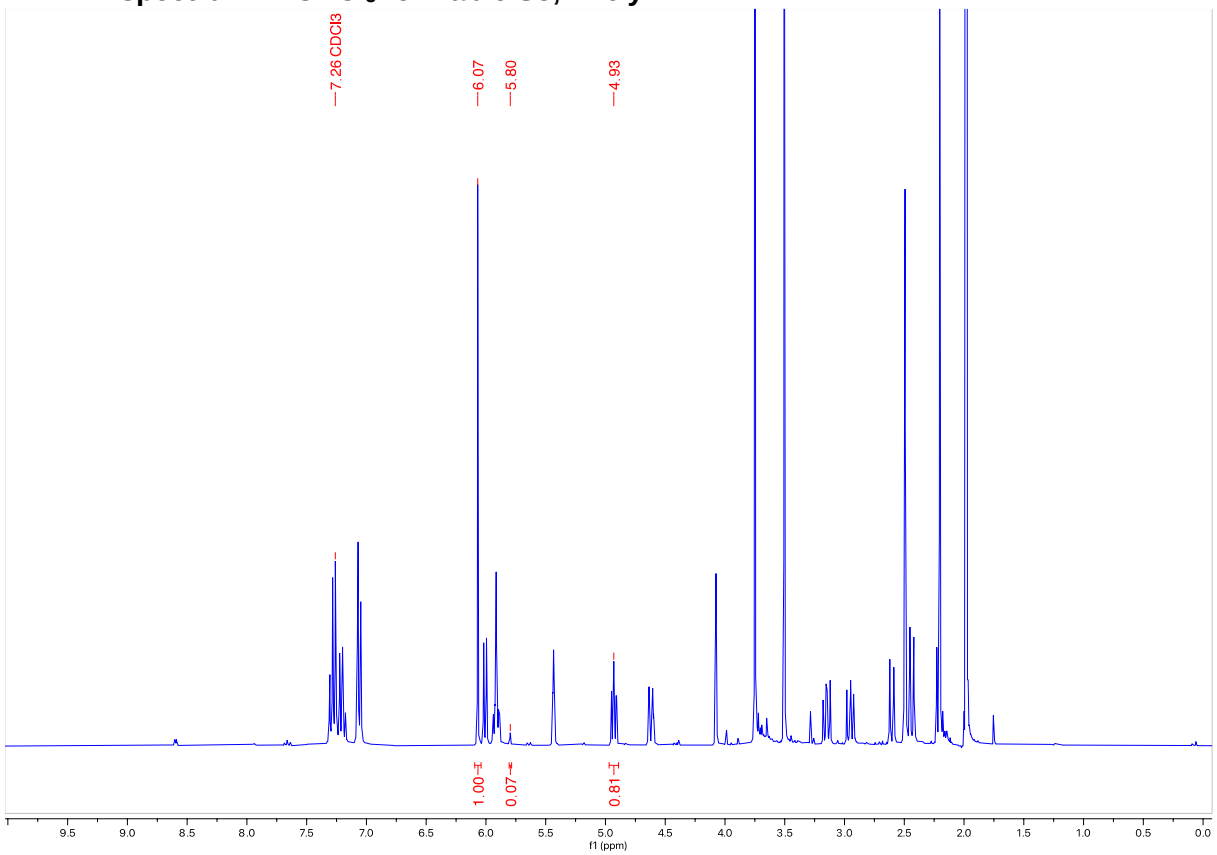
Deviations from the general procedure:

Entry 1: No base was added to the reaction.
Entry 2: The reaction mixture was stirred at 30 °C.
Entry 3: Na_2SO_4•$10H_2O$ (32.2 mg, 0.10 mmol, 1 equiv) was added to the pyridinium/base vial before solvent was added.
Entry 4: 4Å molecular sieves (100 mg) was added to the pyridinium/base vial before solvent was added.

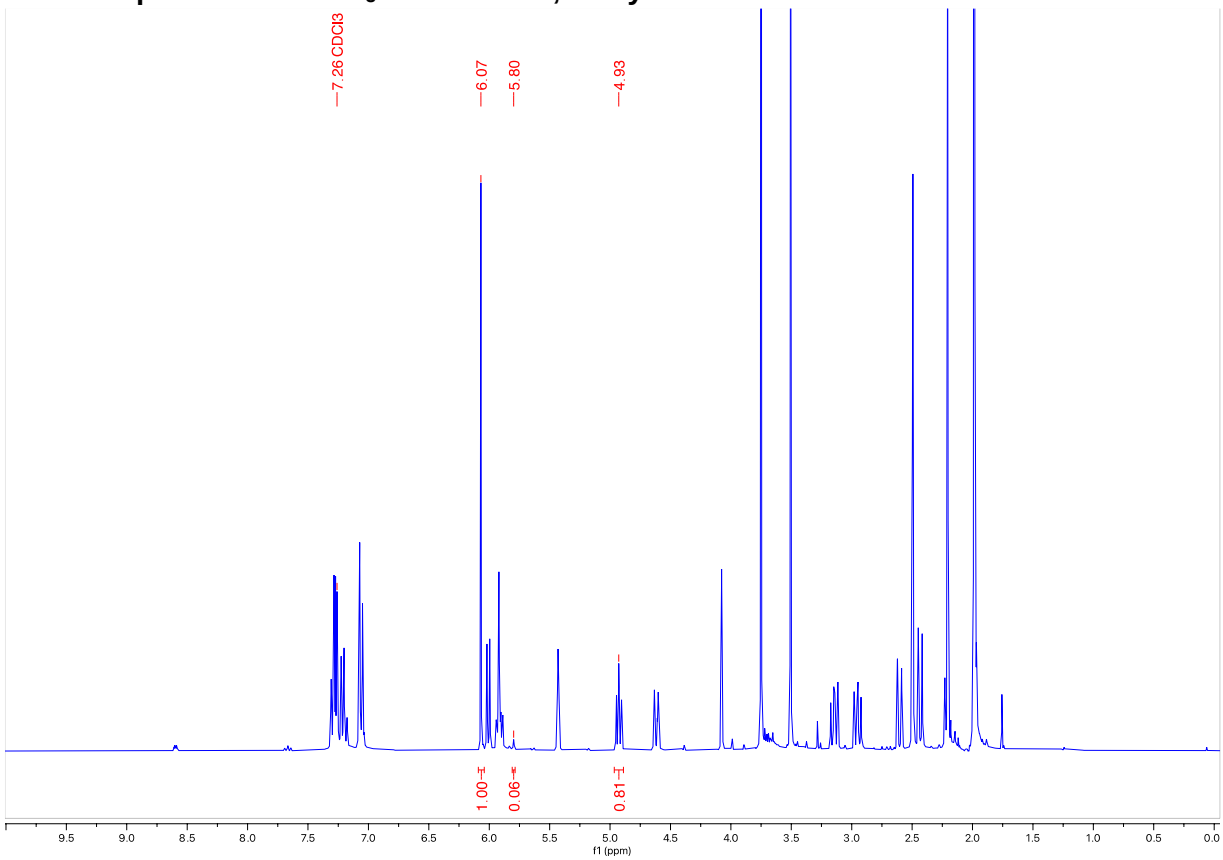
^{1}H NMR spectrum in $CDCl_3$ for Table S5, Entry 1:



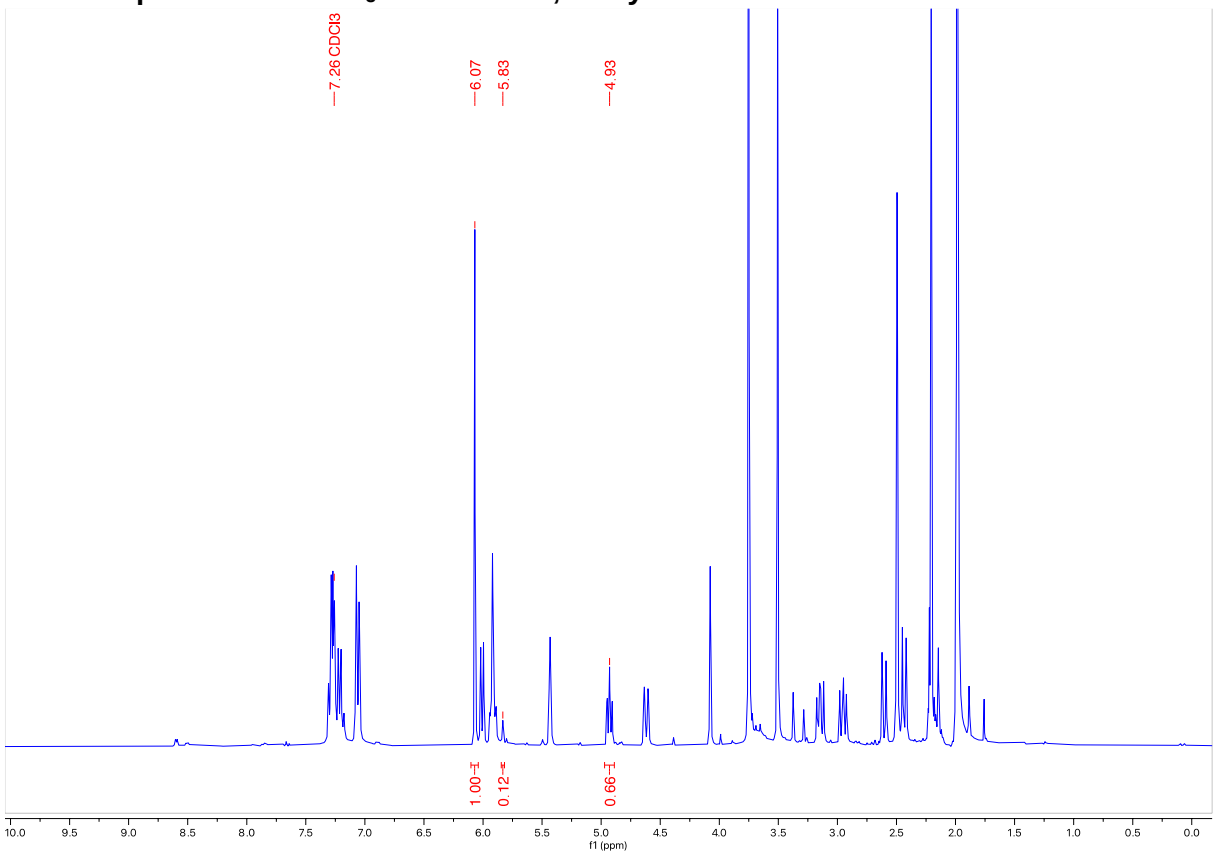
^{1}H NMR spectrum in $CDCl_3$ for Table S5, Entry 2:



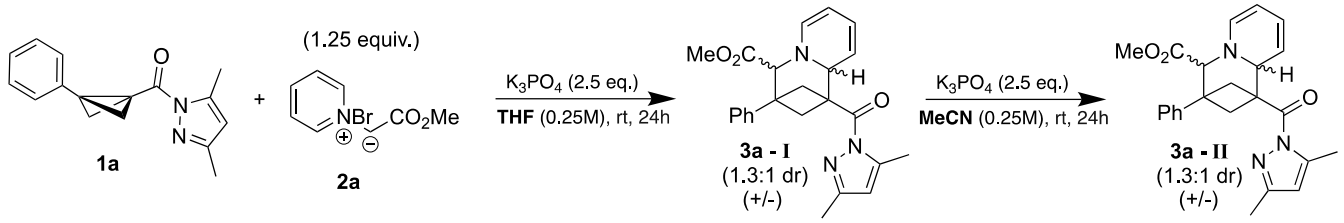
^{1}H NMR spectrum in $CDCl_3$ for Table S5, Entry 3:



^{1}H NMR spectrum in $CDCl_3$ for Table S5, Entry 4:

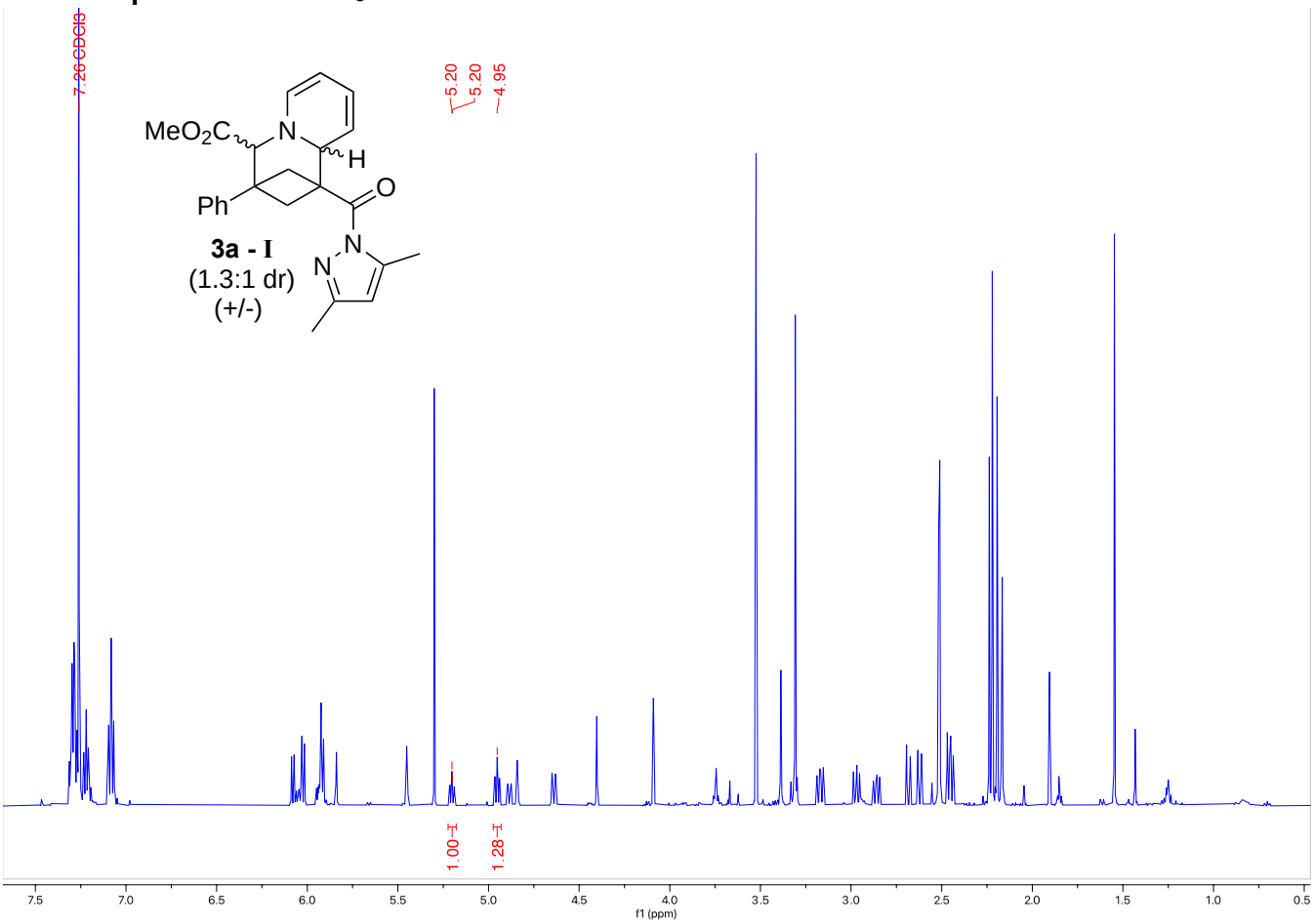


Epimerization Test

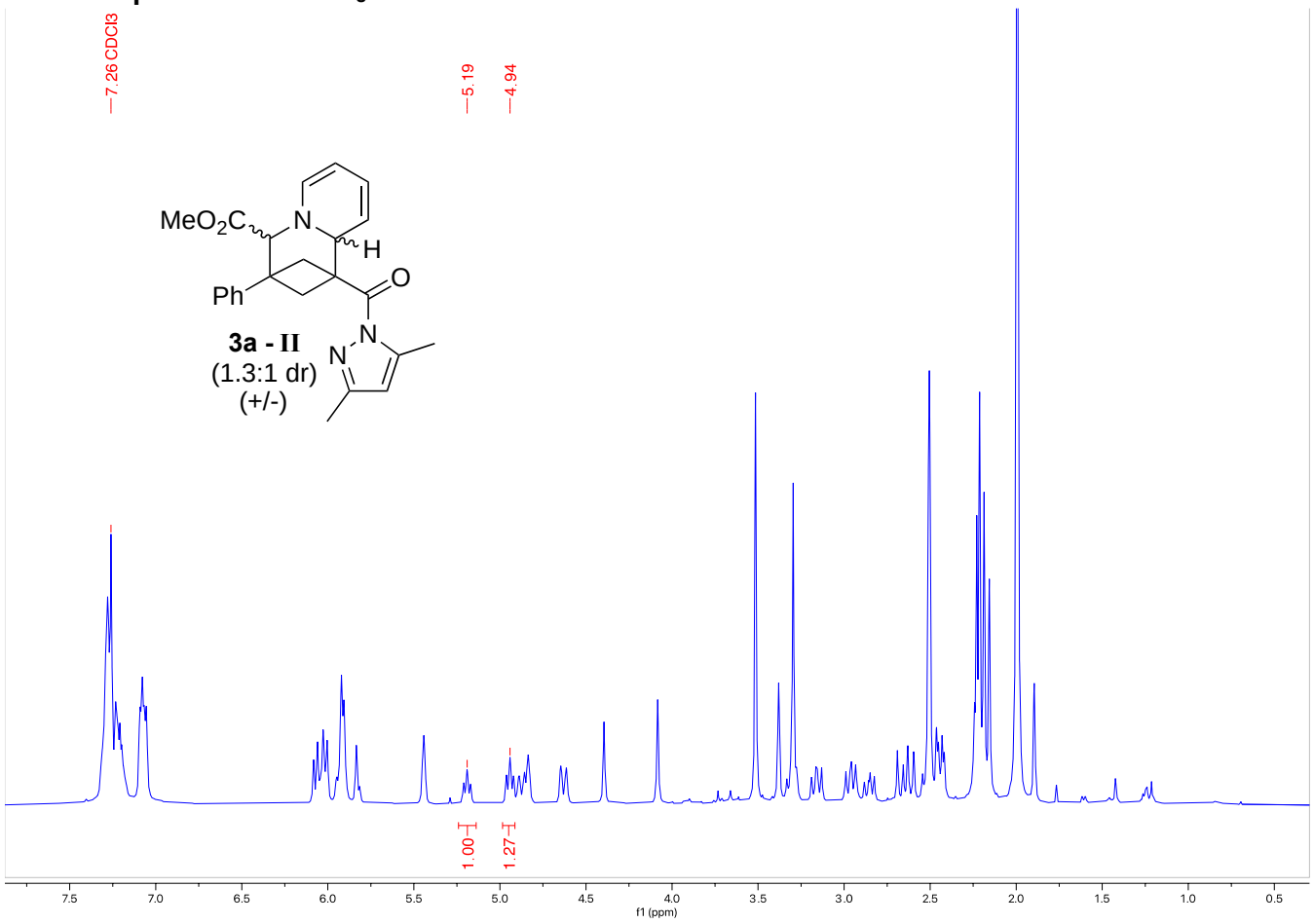


Procedure: Pyridinium **2a** (58.0 mg, 0.25 mmol, 1.25 equiv) and K_3PO_4 (106.1 mg, 0.50 mmol, 2.5 equiv) were weighed into a 4 mL vial, followed by the addition of a stir bar. **THF** (0.4 mL) was added to the vial, and the mixture stirred for 5 minutes at rt. After 5 minutes, **1a** (50.5 mg, 0.20 mmol) was dissolved in THF (0.4 mL) and added to the reaction mixture. The reaction mixture was stirred at rt for 24 hours. The solvent was then evaporated using a Genevac centrifugal evaporator. The crude **3a** – **I** obtained was dissolved in dichloromethane and eluted through a plug of basic alumina. Solvent evaporation provided **3a** – **I** as a mixture of diastereomers as determined by NMR spectroscopy (1.3:1 dr). This compound was then dissolved in MeCN (0.8 mL, 0.25 M), and K_3PO_4 (106.1 mg, 0.50 mmol, 2.5 equiv) was added to the vial. The reaction mixture was stirred for 24 hours at rt. The solvent was then evaporated using a Genevac centrifugal evaporator. Analysis by NMR spectroscopy revealed the diastereomeric ratio was unchanged (1.3:1 dr).

^{1}H NMR spectrum in $CDCl_3$ for 3a - I:

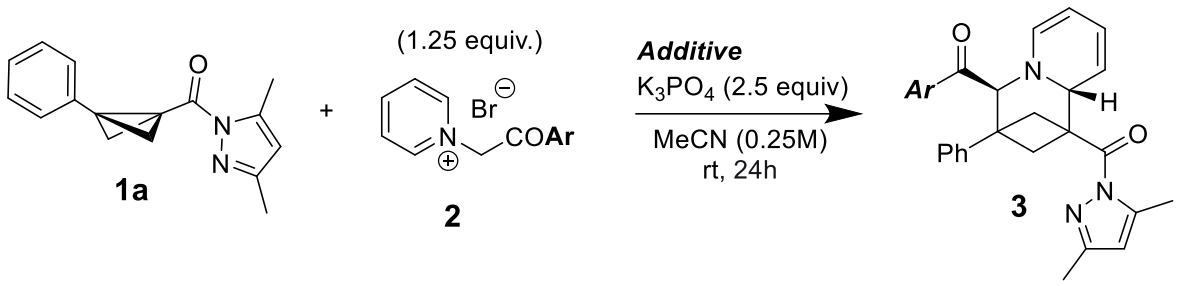


^{1}H NMR spectrum in $CDCl_3$ for 3a - II:



Counter Anion / Additive Effects

Table S6



Entry[a]	*Ar*	% Yield 3[b]		
		No additive	$Mg(OTf)_2$ (0.4 equiv)	$NaPF_6$ (1.3 equiv)
1	Ph (**3m**)	25	82	85
2	*p*-tolyl (**3x**)	25	43	52
3	*p*-Cl Ph (**3y**)	24	48	74

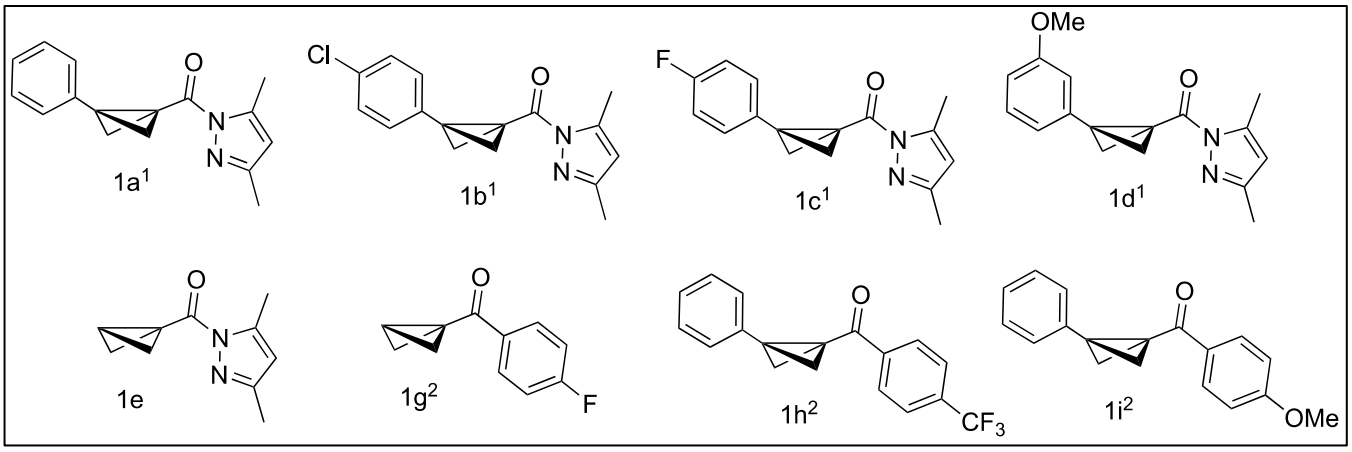
[a]Unless otherwise noted, reactions are performed at room temperature for 24 hours with 0.05 mmol of **1a**. Products **3** are formed as a single diastereomer, (>20:1 dr by ^{1}H NMR spectroscopy). [b]Yields of products **3** are obtained by ^{1}H NMR spectroscopy by relative integration vs. internal standard, 1,3,5-trimethoxybenzene (TMB).

General procedure (no additive or $Mg(OTf)_2$) (Table S6): To a 1 mL vial was added the appropriate pyridinium **2** (0.06 mmol, 1.25 equiv)**,** K_3PO_4 base (26.5 mg, 0.13 mmol, 2.5 equiv), and a stir bar. Half of the acetonitrile solvent (0.1 mL) was added to the vial, and the mixture stirred for 2 minutes at room temperature. The bicyclobutane **1a** (12.6 mg, 0.05 mmol, 1 equiv) was weighed into another 1 mL vial, and quantitatively transferred to the vial containing pyridinium/base using the other half of the acetonitrile reaction solvent (0.10 mL). If required, $Mg(OTf)_2$ (6.5 mg, 0.02 mmol, 0.4 equiv) was then added as a solid. The reaction mixture was stirred for 24 hours at room temperature. The solvent was then evaporated using a Genevac centrifugal evaporator, followed by dilution with a stock solution of 1,3,5-trimethoxybenzene in $CDCl_3$ (0.7 mL, containing 5.6 mg, 0.33 equiv of internal standard). The mixtures were stirred for 5 minutes, centrifuged, and the supernatant removed for analysis by NMR spectroscopy.

General procedure <u>with</u> $NaPF_6$ (Table S6): To a 1 mL vial was added the appropriate pyridinium **2** (0.06 mmol, 1.25 equiv)**,** $NaPF_6$, and a stir bar. Half of the acetonitrile solvent (0.1 mL) was added to the vial, and the mixture stirred for 2 hours at room temperature. The K_3PO_4 base (26.5 mg, 0.13 mmol, 2.5 equiv) was then added to the reaction vial, and the mixture stirred for 2 minutes at room temperature. The bicyclobutane **1a** (12.6 mg, 0.05 mmol, 1 equiv) was weighed into another 1 mL vial, and quantitatively transferred to the vial containing pyridinium/base using the other half of the acetonitrile reaction solvent (0.10 mL). The reaction mixture was stirred for 24 hours at room temperature. The solvent was then evaporated using a Genevac centrifugal evaporator, followed by dilution with a stock solution of 1,3,5-trimethoxybenzene in $CDCl_3$ (0.7 mL, containing 5.6 mg, 0.33 equiv of internal standard). The mixtures were stirred for 5 minutes, centrifuged, and the supernatant removed for analysis by NMR spectroscopy.

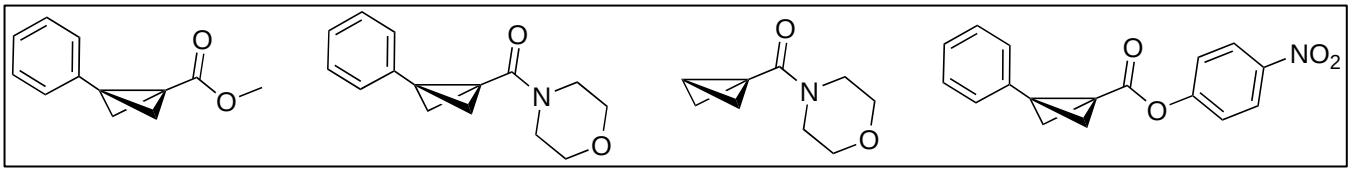
V: Substrate Synthesis

Bicyclobutane Synthesis

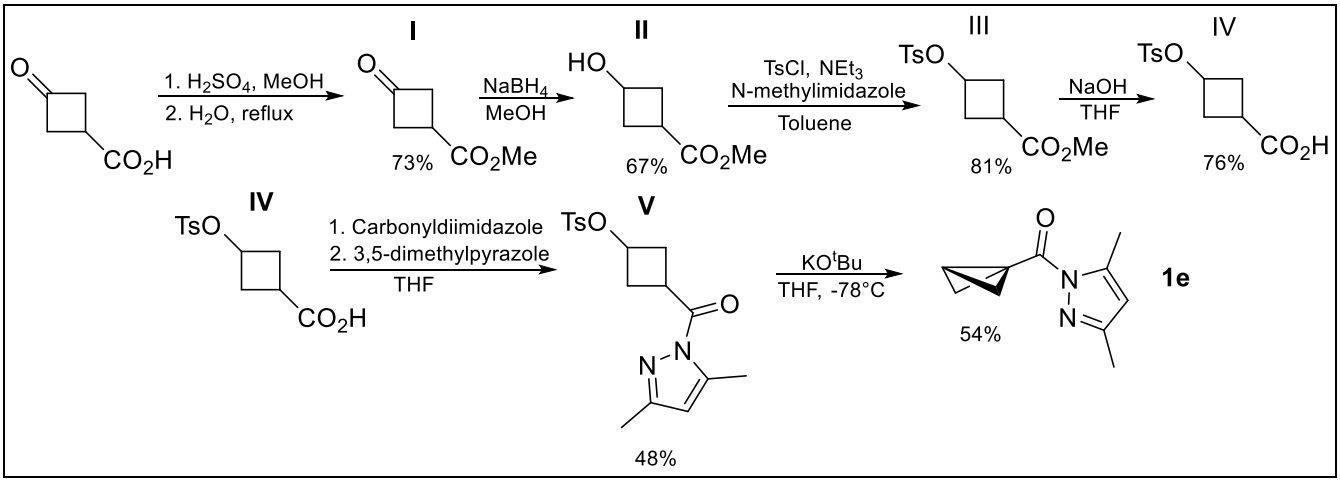


Bicyclobutane substrates **1a-1d**[1]**, 1g-h**[2], have been reported and were prepared according to the literature procedures.

Unsuccessful bicyclobutanes in the cycloaddition reaction are listed below:



Synthesis of bicyclo[1.1.0]butan-1-yl(3,5-dimethyl-1H-pyrazol-1-yl)methanone (1e):



Methyl 3-oxocyclobutane-1-carboxylate (I) synthesis:

3-Oxocyclobutanecarboxylic acid (10.0 g, 87.6 mmol) was dissolved in methanol (100 mL, 0.88 M) and then concentrated sulfuric acid was added dropwise (0.47 mL, 10 mol%). The reaction mixture was left to stir at rt for 4 hours, followed by the addition of water (100 mL). The mixture was then stirred at 90 °C

overnight. The acidic mixture was quenched with saturated sodium bicarbonate until the pH was basic (pH > 9), and then the aqueous solution was extracted with DCM (5 x 50 mL). The organic layers were combined, dried with Mg_2SO_4, filtered, and the solvent evaporated to give compound **I** without further purification (8.16 g, 73% yield).

Methyl 3-hydroxycyclobutane-1-carboxylate (II) synthesis:

Compound **I** (8.16 g, 63.7 mmol) was dissolved in methanol (80 mL, 0.8 M). The mixture was cooled to 0 °C followed by the portionwise addition of solid $NaBH_4$ (1.20 g, 0.5 equiv, 31.8 mmol). The mixture was warmed to rt and left to stir overnight. The reaction was quenched with saturated ammonium chloride (80 mL) and then extracted with DCM (3 x 80 mL). The organic layers were combined, dried with Mg_2SO_4, filtered and then the solvent was evaporated to give compound **II** without further purification (5.53 g, 67% yield).

Methyl 3-(tosyloxy)cyclobutane-1-carboxylate (III) synthesis:

Compound **II** (5.53 g, 42.5 mmol) was dissolved in toluene (80 mL, 0.53 M) followed by the addition of *N*-methylimidazole (3.4 mL, 1.0 equiv, 42.5 mmol). 4-Toluenesulfonyl chloride (12.2 g, 1.5 equiv, 63.7 mmol) was then added, followed by triethylamine (8.9 mL, 1.5 equiv, 63.7 mmol), and the mixture stirred at 60 °C overnight. The reaction was quenched with saturated ammonium chloride (80 mL) and then extracted with toluene (3 x 80 mL). The organic layers were combined, dried with Mg_2SO_4, filtered and then the solvent was evaporated to give compound **III** without further purification (9.8 g, 81% yield).

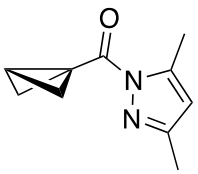
3-(Tosyloxy)cyclobutane-1-carboxylic acid (IV) synthesis:

Compound **III** (9.8 g, 34.5 mmol) was dissolved in THF (40 mL, 0.86 M) and then 1 M NaOH (40 mL) was added to the mixture, which was stirred at rt overnight. The reaction mixture was acidified with 1 M HCl (pH < 3) and then extracted with DCM (3 x 40 mL). The organic layers were combined, dried with Mg_2SO_4, filtered and then the solvent was evaporated to give compound **IV** without further purification (7.11 g, 76% yield).

3-(3,5-dimethyl-1H-pyrazole-1-carbonyl)cyclobutyl 4-methylbenzenesulfonate (VI) synthesis:

Compound **IV** (7.11 g, 26.3 mmol) was dissolved in THF (50 mL, 0.53 mmol) and then the solution was cooled to 0 °C before addition of carbonyldiimidazole (4.48 g, 1.05 equiv, 27.6 mmol). The mixture was stirred at rt for 1 hour, followed by the addition of 3,5-dimethylpyrazole (2.65 g, 1.05 equiv, 27.6 mmol). The mixture was then stirred at rt overnight. The reaction was quenched with saturated ammonium chloride (50 mL) and then extracted with ethyl acetate (3 x 50 mL). The organic layers were combined, dried with Mg_2SO_4, filtered and then the solvent was evaporated. The product was purified by column chromatography (Biotage® Sfär 100g Column, 0-100% EtOAc/hexanes, eluted at 20% EtOAc) to give compound **IV** as a white solid (4.39 g, 48% yield).

Bicyclo[1.1.0]butan-1-yl(3,5-dimethyl-1H-pyrazol-1-yl)methanone (1e) synthesis:

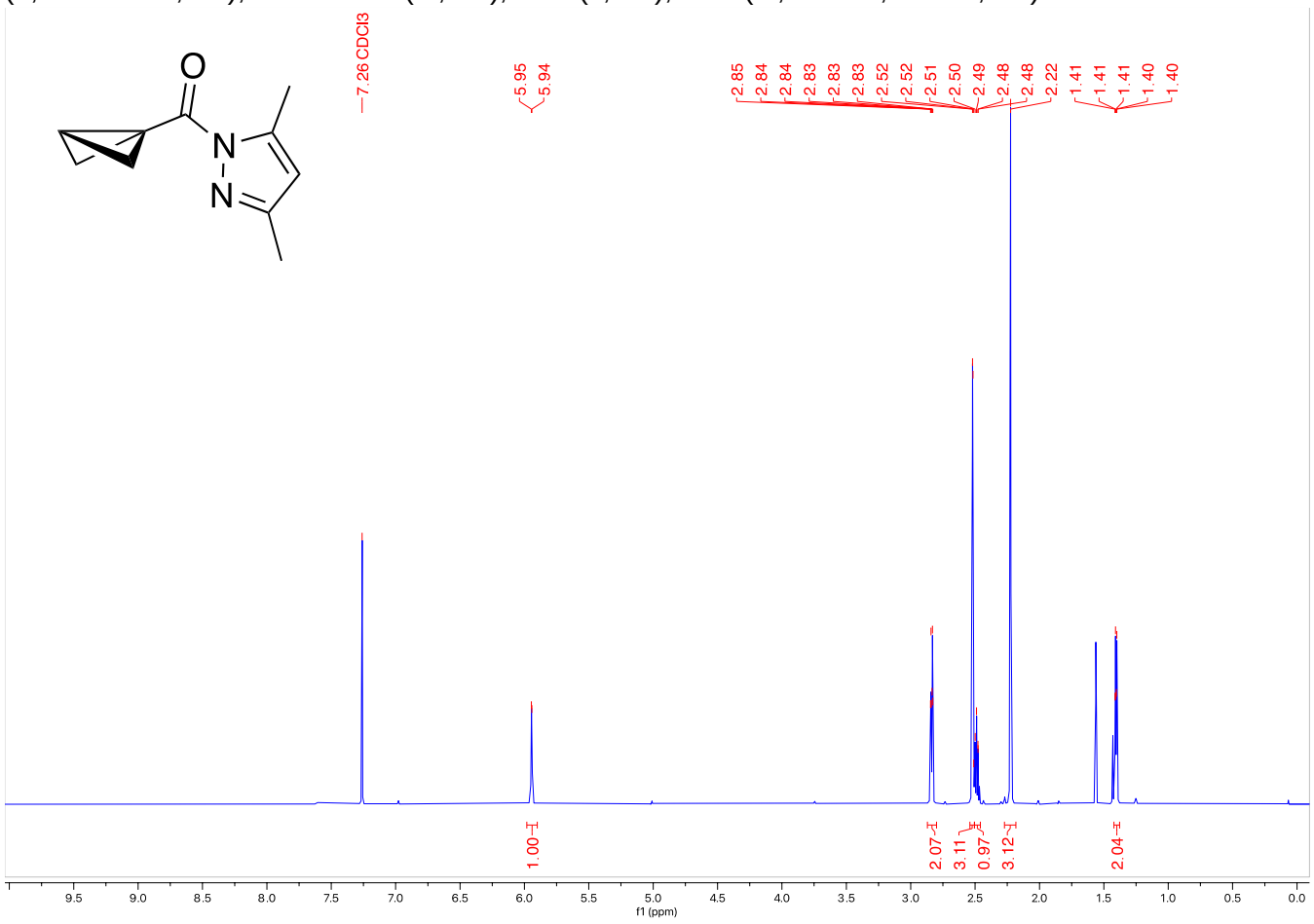


Compound **VI** (209.5 mg, 0.60 mmol) was dissolved in anhydrous THF containing 250 ppm BHT as inhibitor (12.0 mL, 0.05 M) in a 40 mL vial. The solution was cooled to -78 °C. Potassium *tert*-butoxide (74.1 mg, 1.1 equiv, 0.66 mmol) was added as a solid, and the reaction was stirred at -78 °C for 2 hours. While keeping the mixture as cold as possible, the reaction was quenched with cold (~2-4°C) ammonium

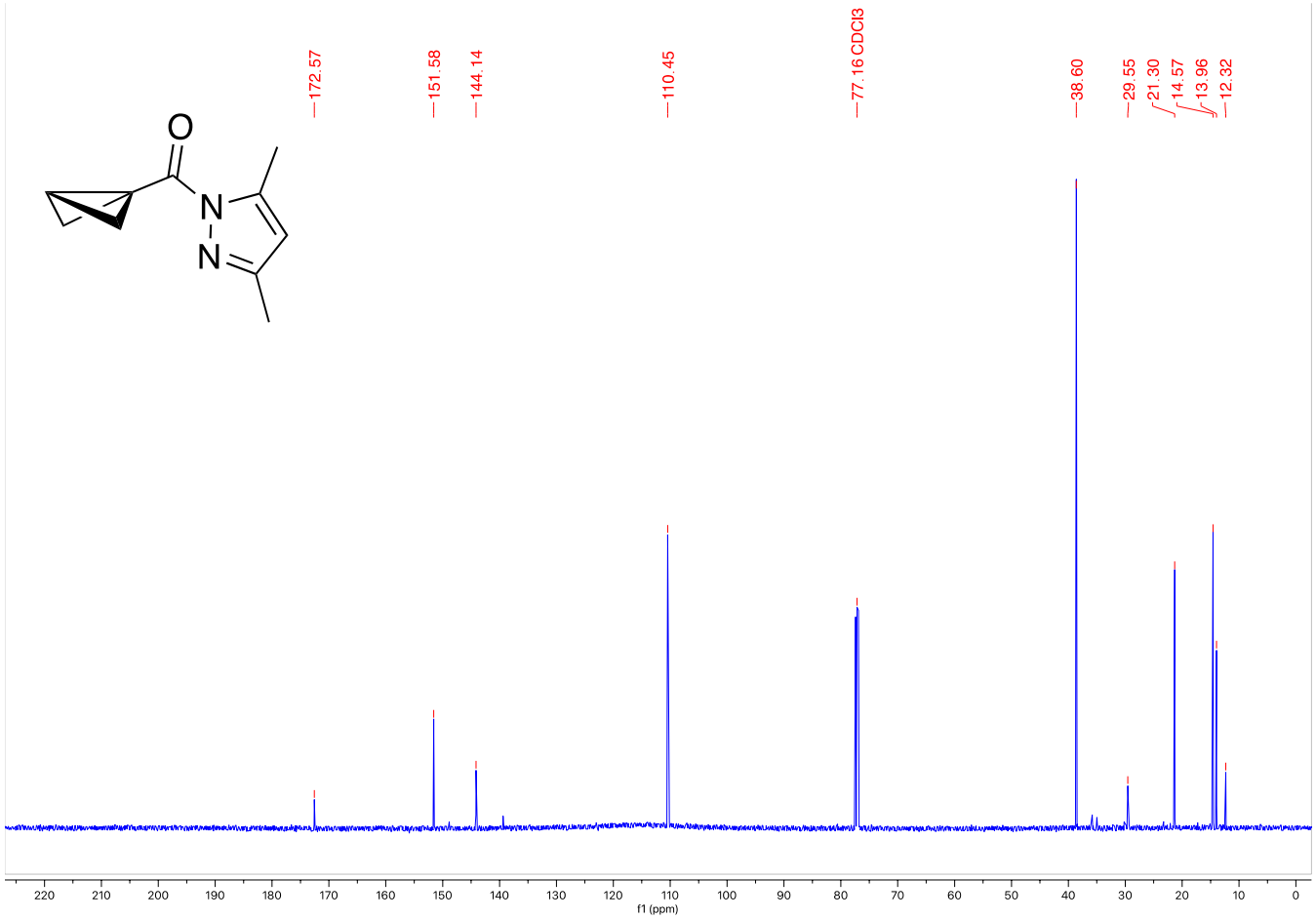
chloride (10 mL), and the aqueous layer extracted with cold (~2-4°C) THF (containing 250 ppm BHT as inhibitor, 3 x 10 mL). The THF layers were combined and dried with Mg_2SO_4 (being cautious that the solution remained cold AT ALL TIMES), filtered, and then concentrated on a rotary evaporator using a water bath that remained at ~10-15°C. The crude product was purified using column chromatography, with the crude material loaded using cold hexanes (Biotage® Sfär 10g Column, 0-100% EtOAc/hexanes, eluted at 10% EtOAc). The product **1e** was obtained as a clear colourless oil (57.0 mg, 54% yield). **NOTE:** The neat product is prone to rapid polymerization at ambient temperature. For short term storage, we stored neat **1e** in a -20 °C freezer; for long term storage, we stored **1e** as a 0.5 M stock solution in frozen acetonitrile in a -80 °C freezer.

HRMS(ESI): calc'd for [$C_{10}H_{12}N_3O + H^+$], 177.10224; found: 177.10216.

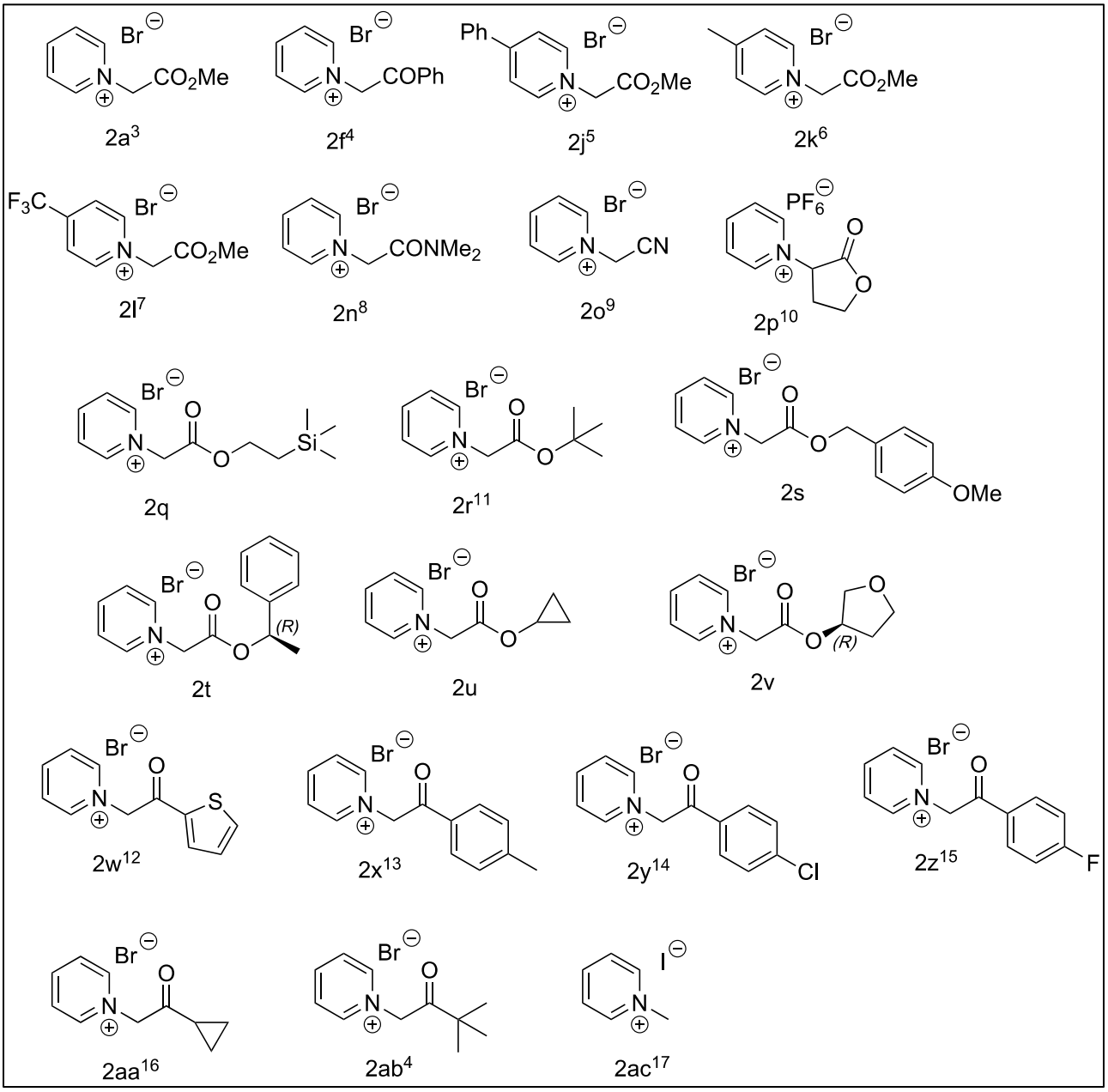
^{1}H NMR (500 MHz, $CDCl_3$, 292 K, ppm): δ 5.94 (d, J = 1.1 Hz, 1H), 2.84 (dt, J = 3.4, 0.9 Hz, 2H), 2.52 (d, J = 1.0 Hz, 3H), 2.50 – 2.46 (m, 1H), 2.22 (s, 3H), 1.40 (dt, J = 3.1, 0.9 Hz, 2H).



^{13}C NMR (126 MHz, $CDCl_3$, 292 K, ppm): δ 172.57, 151.58, 144.14, 110.45, 38.60, 29.55, 21.30, 14.57, 13.96, 12.32.

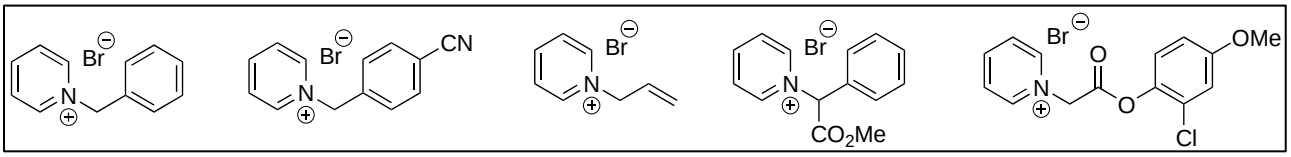


Pyridinium Synthesis



Pyridinium substrates **2a-p, 2r, and 2w-ac** have been reported and were prepared according to the literature procedures.[3-17] Pyridiniums **2q, and 2s-2v** are not reported previously and were prepared according to the general procedure outlined below.

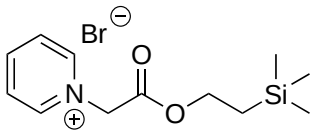
Unsuccessful pyridiniums in the cycloaddition reaction:



General procedure for pyridinium synthesis: To a 40 mL vial containing a stir bar was added the appropriate bromoester (2.00 mmol, 1 equiv) and ethyl acetate (10 mL, 0.20 M). The reaction mixture was stirred at room temperature for 2 minutes before adding pyridine (158 mg, 161 µL, 2.00 mmol, 1 equiv). The reaction mixture was stirred for 12 h at room temperature. Then, the solvent was evaporated to give the desired pyridinium salt. If required, the crude product was stirred in excess diethyl ether for 1 h, collected by filtration, and dried *in vacuo* to remove soluble impurities.

Characterization data for new pyridinium salts:

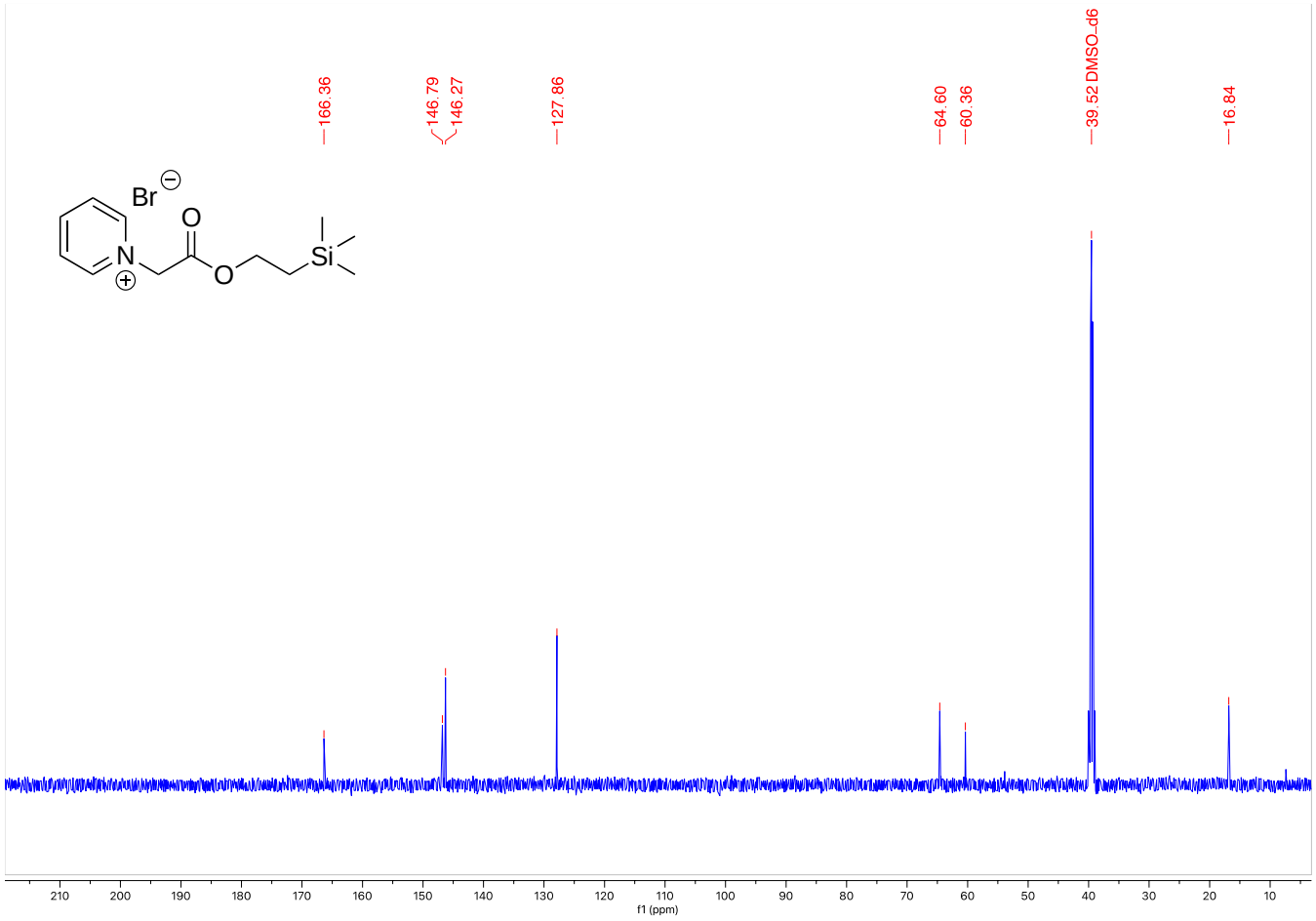
1-(2-oxo-2-(2-(trimethylsilyl)ethoxy)ethyl)pyridin-1-ium bromide (2q)



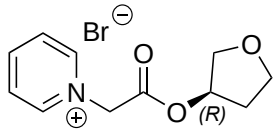
HRMS(ESI): calc'd for [$C_{12}H_{20}BrNO_2Si^+$ - Br^-], 238.12578; found: 238.12605.

^{1}H NMR (500 MHz, DMSO-d$_6$, 292 K, ppm): δ 9.05 – 9.00 (m, 2H), 8.71 – 8.65 (m, 1H), 8.21 (dd, J = 7.9, 6.6 Hz, 2H), 5.63 (s, 2H), 4.29 – 4.20 (m, 2H), 1.03 – 0.92 (m, 2H), 0.00 (s, 9H).

^{13}C NMR (126 MHz, DMSO-d_6, 292 K, ppm): δ 166.36, 146.79, 146.27, 127.86, 64.60, 60.36, 16.84.

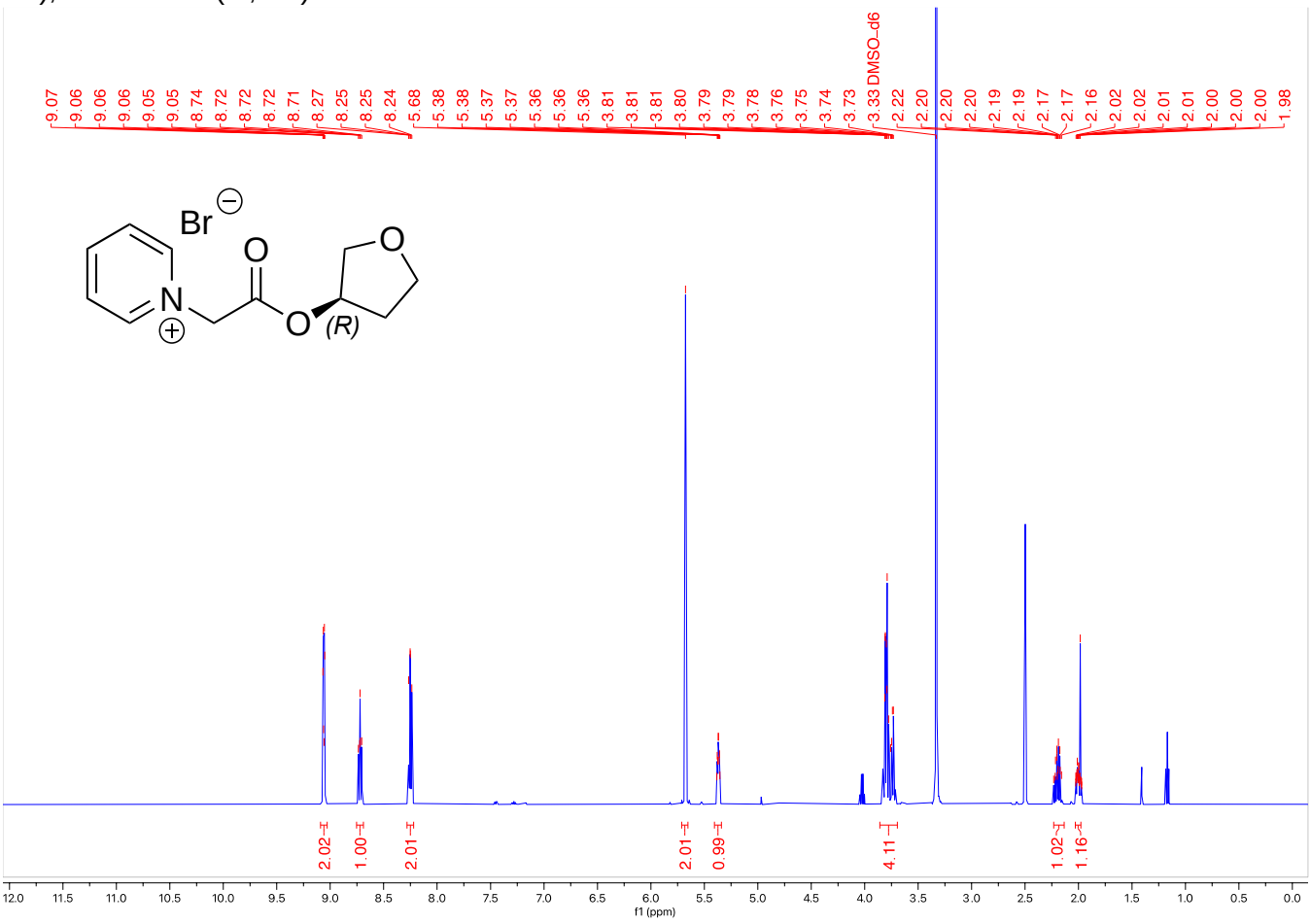


(*R*)-1-(2-oxo-2-((tetrahydrofuran-3-yl)oxy)ethyl)pyridin-1-ium bromide (2v)

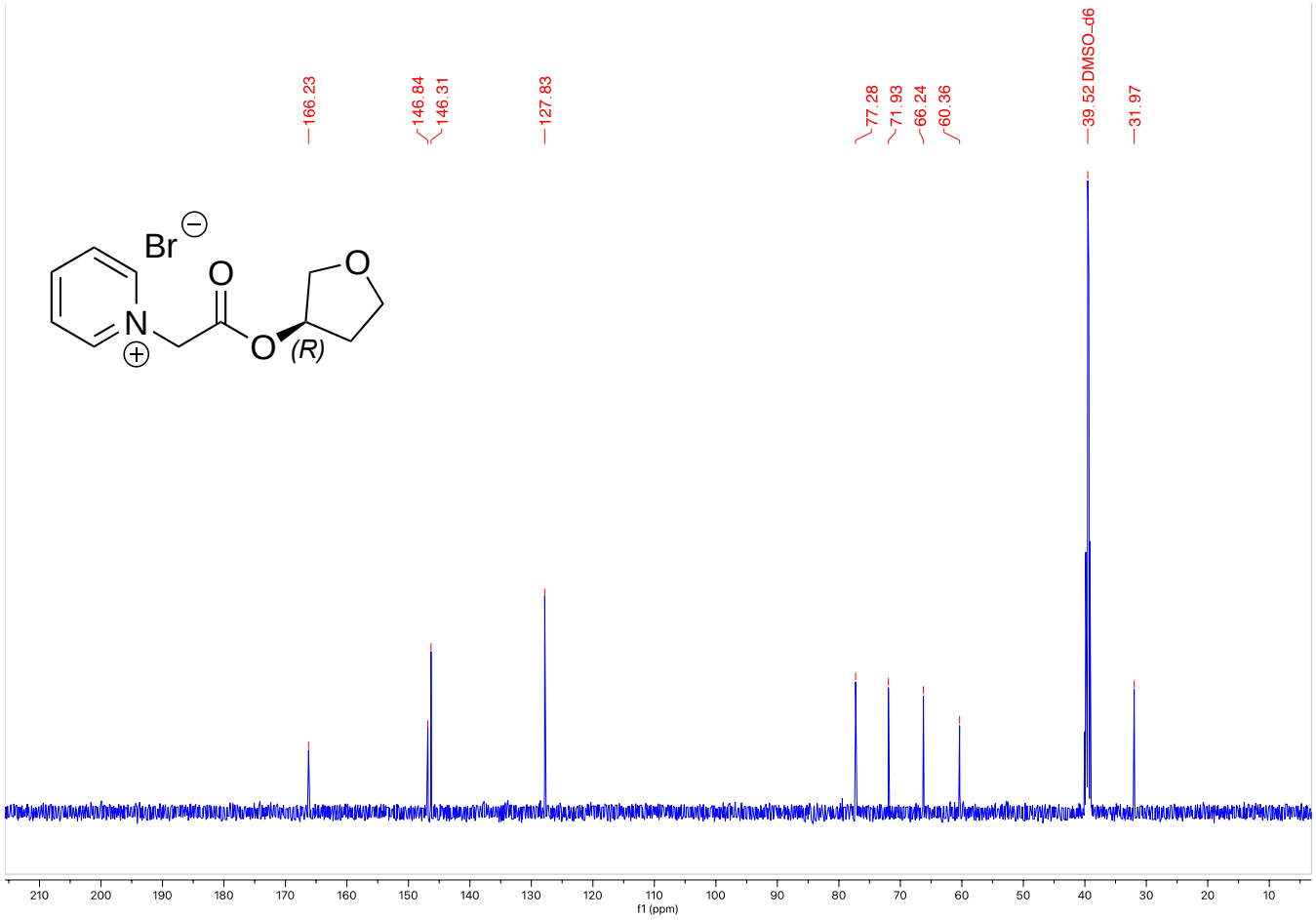


HRMS(ESI): calc'd for [$C_{11}H_{14}BrNO_3^+$ - Br^-], 208.09682; found: 208.09693.

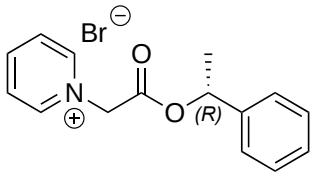
^{1}H NMR (500 MHz, DMSO-d$_6$, 292 K, ppm): δ 9.09 – 9.03 (m, 2H), 8.75 – 8.69 (m, 1H), 8.25 (dd, J = 8.0, 6.7 Hz, 2H), 5.68 (s, 2H), 5.37 (ddt, J = 6.0, 3.6, 1.7 Hz, 1H), 3.86 – 3.69 (m, 4H), 2.23 – 2.13 (m, 1H), 2.03 – 1.98 (m, 1H).



^{13}C NMR (126 MHz, DMSO-d_6, 292 K, ppm): δ 166.23, 146.84, 146.31, 127.83, 77.28, 71.93, 66.24, 60.36, 31.97.

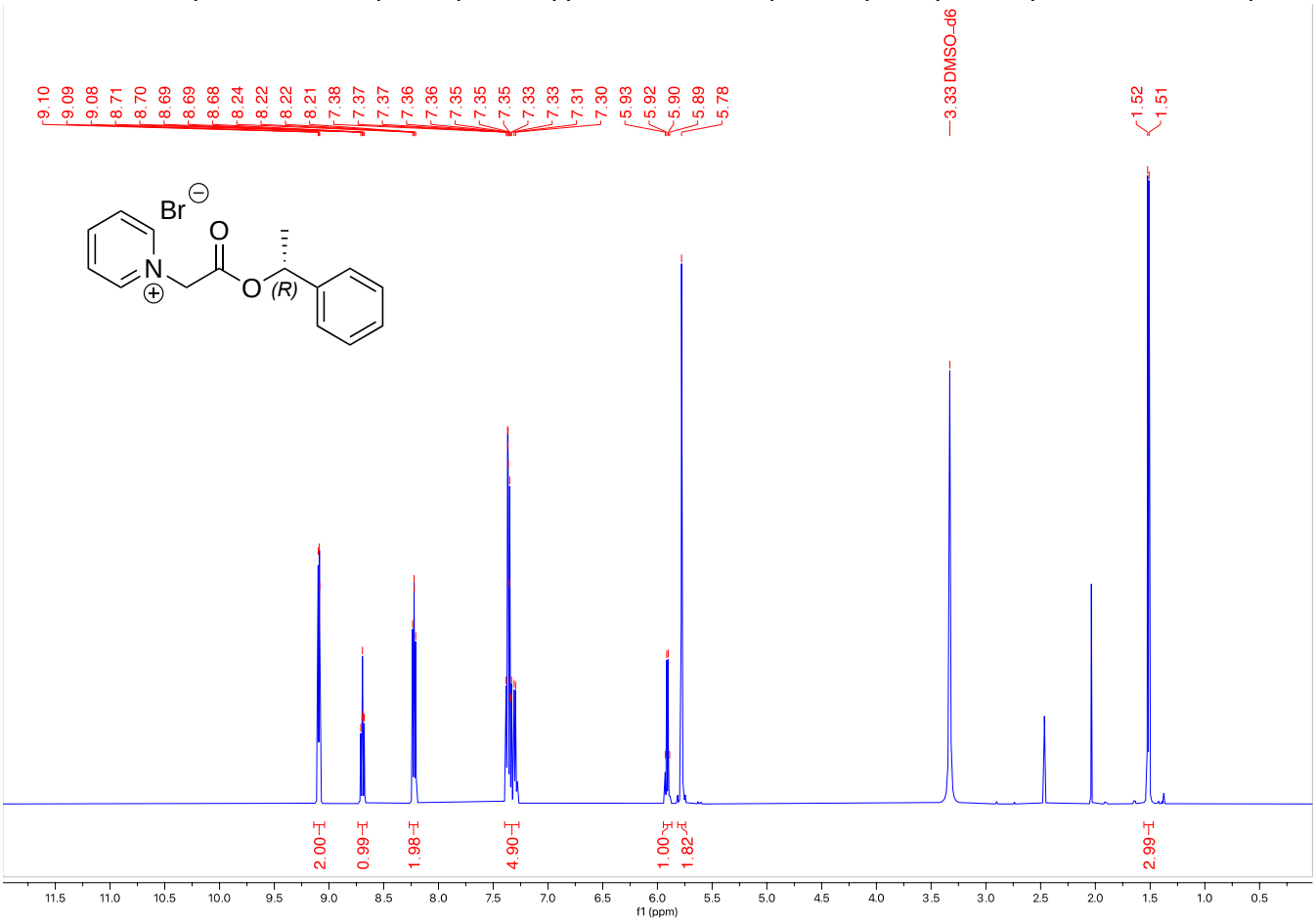


(*R*)-1-(2-oxo-2-(1-phenylethoxy)ethyl)pyridin-1-ium bromide (2t)

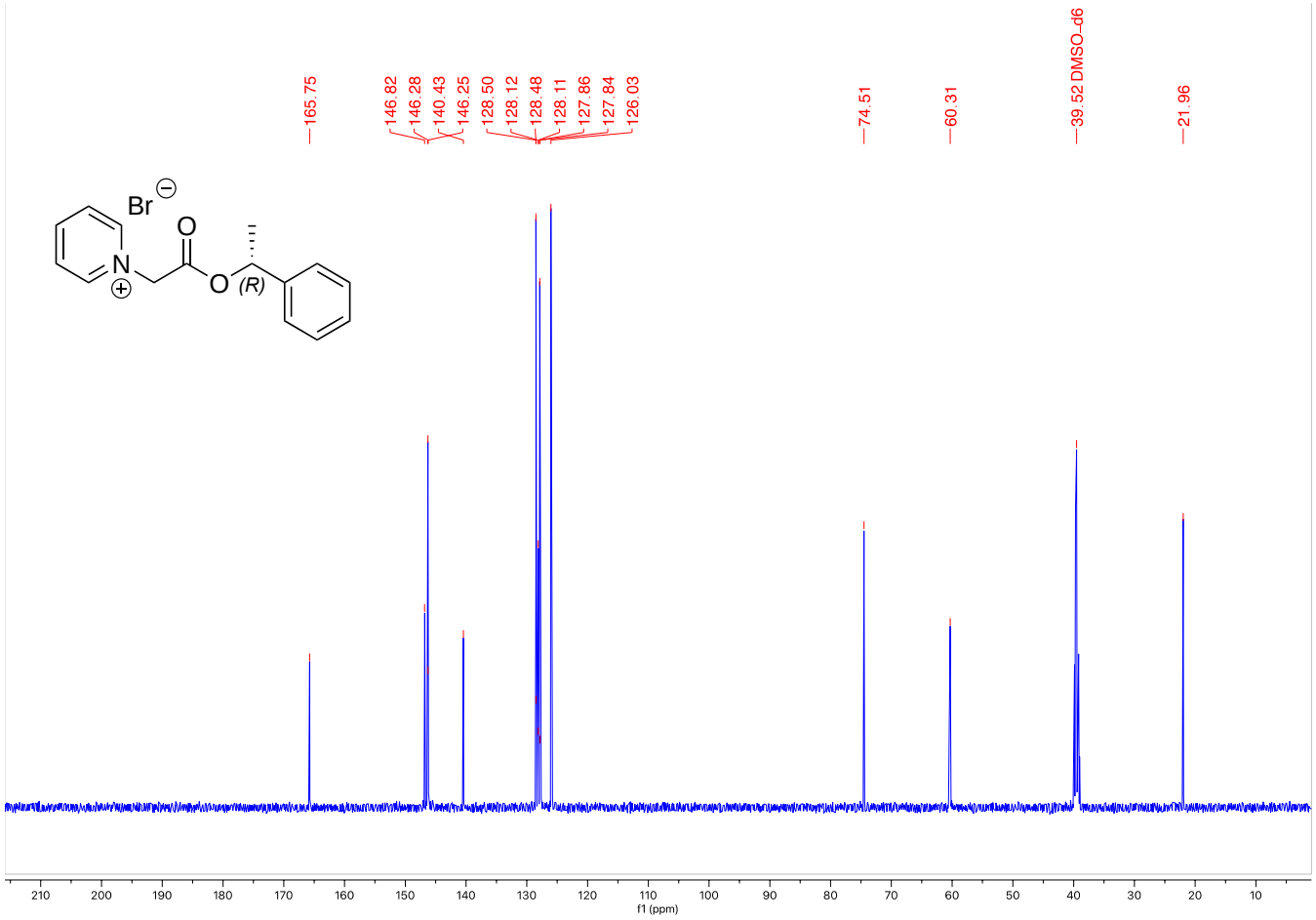


HRMS(ESI): calc'd for [$C_{15}H_{16}BrNO_2^+$ - Br^-], 242.11755; found: 242.11738.

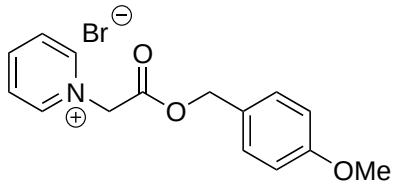
^{1}H NMR (500 MHz, DMSO-d$_6$, 292 K, ppm): δ 9.14 – 9.04 (m, 2H), 8.74 – 8.65 (m, 1H), 8.22 (dd, J = 7.9, 6.6 Hz, 2H), 7.39 – 7.26 (m, 5H), 5.91 (q, J = 6.5 Hz, 1H), 5.78 (s, 2H), 1.52 (d, J = 6.6 Hz, 3H).



^{13}C NMR (126 MHz, DMSO-d$_6$, 292 K, ppm): δ 165.75, 146.82, 146.28, 146.25, 140.43, 128.50, 128.48, 128.12, 128.11, 127.86, 127.84, 126.03, 74.51, 60.31, 21.96.

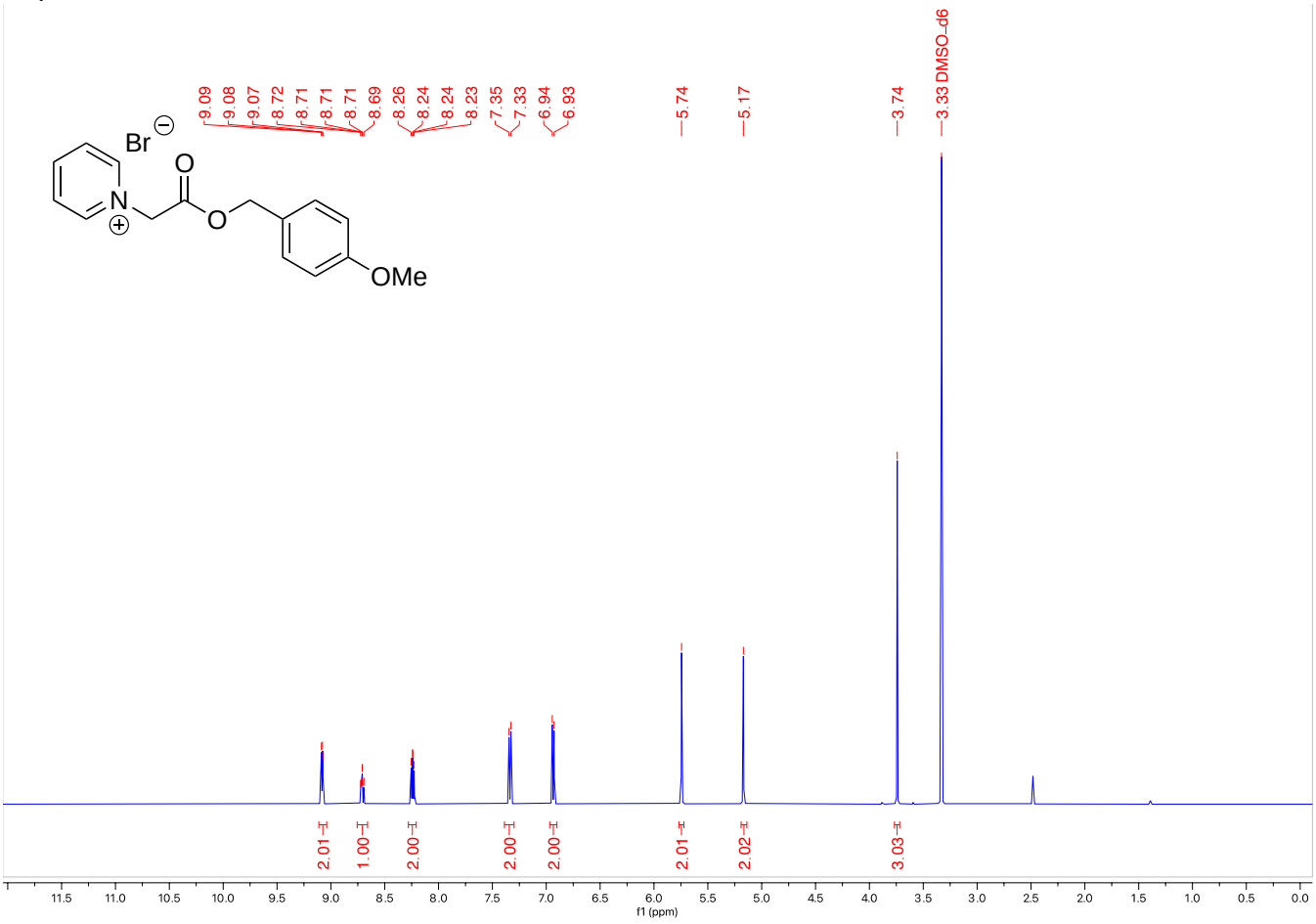


1-(2-((4-methoxybenzyl)oxy)-2-oxoethyl)pyridin-1-ium bromide (2s)

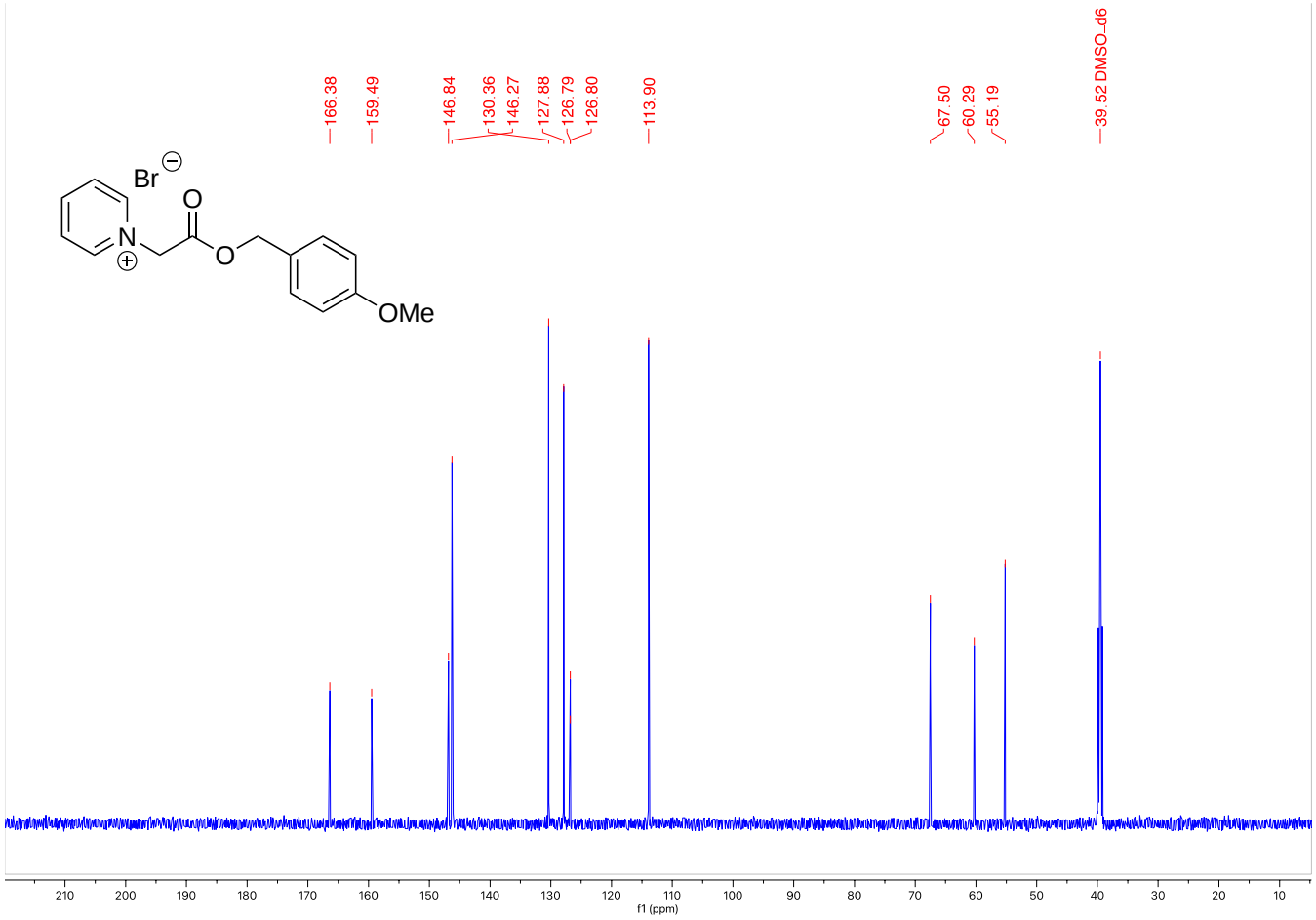


HRMS(ESI): calc'd for [$C_{15}H_{16}BrNO_3^+$ - Br^-], 258.11247; found: 258.11294.

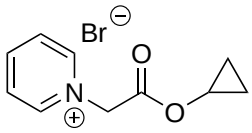
^{1}H NMR (500 MHz, DMSO-d_6, 292 K, ppm): δ 9.11 – 9.04 (m, 2H), 8.76 – 8.66 (m, 1H), 8.24 (dd, J = 7.8, 6.5 Hz, 2H), 7.34 (d, J = 8.7 Hz, 2H), 6.94 (d, J = 8.7 Hz, 2H), 5.74 (s, 2H), 5.17 (s, 2H), 3.74 (s, 3H).



^{13}C NMR (126 MHz, DMSO-d$_6$, 292 K, ppm): δ 166.38, 159.49, 146.84, 146.27, 130.36, 127.88, 126.80, 126.79, 113.90, 67.50, 60.29, 55.19.

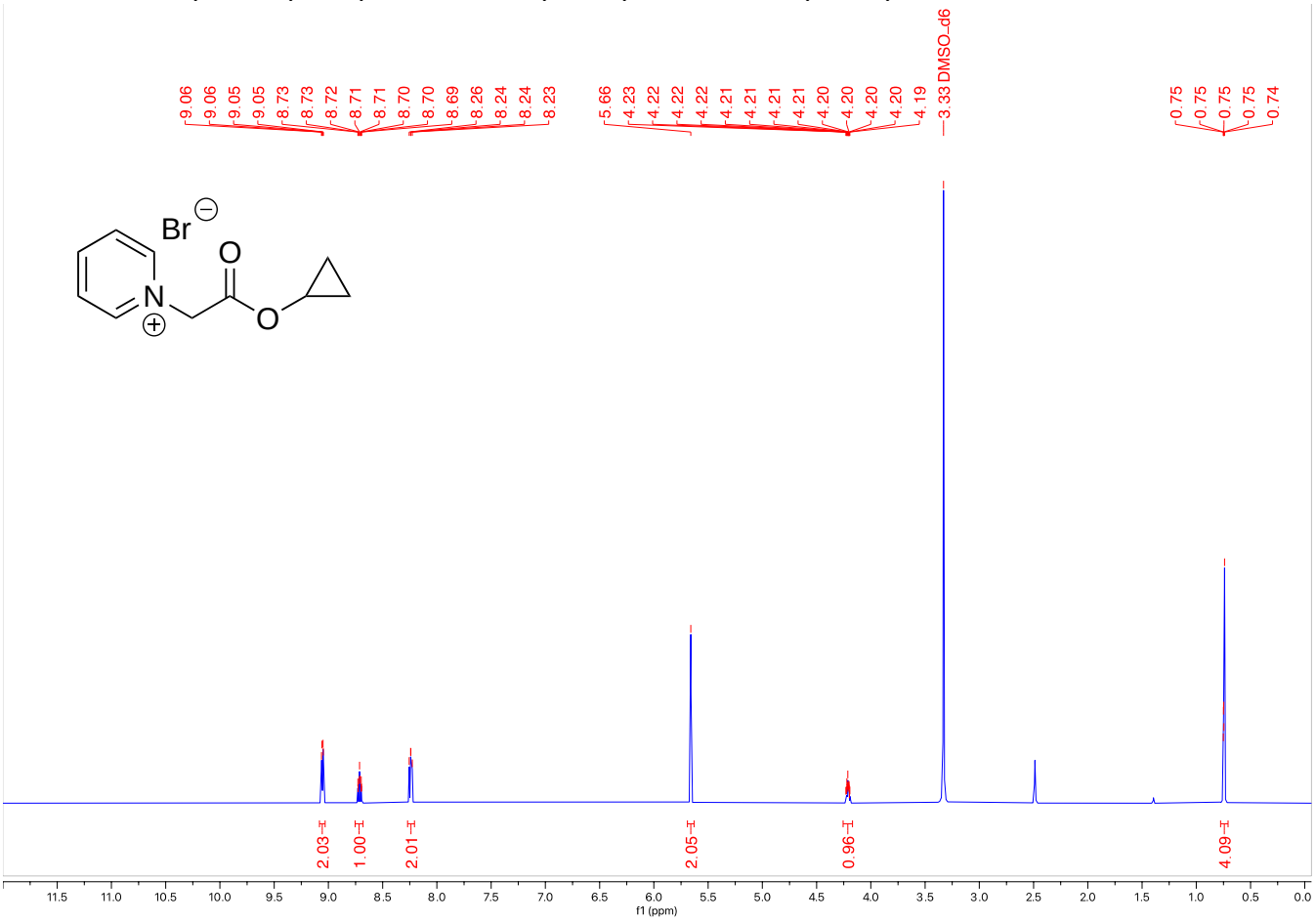


1-(2-cyclopropoxy-2-oxoethyl)pyridin-1-ium bromide (2u)

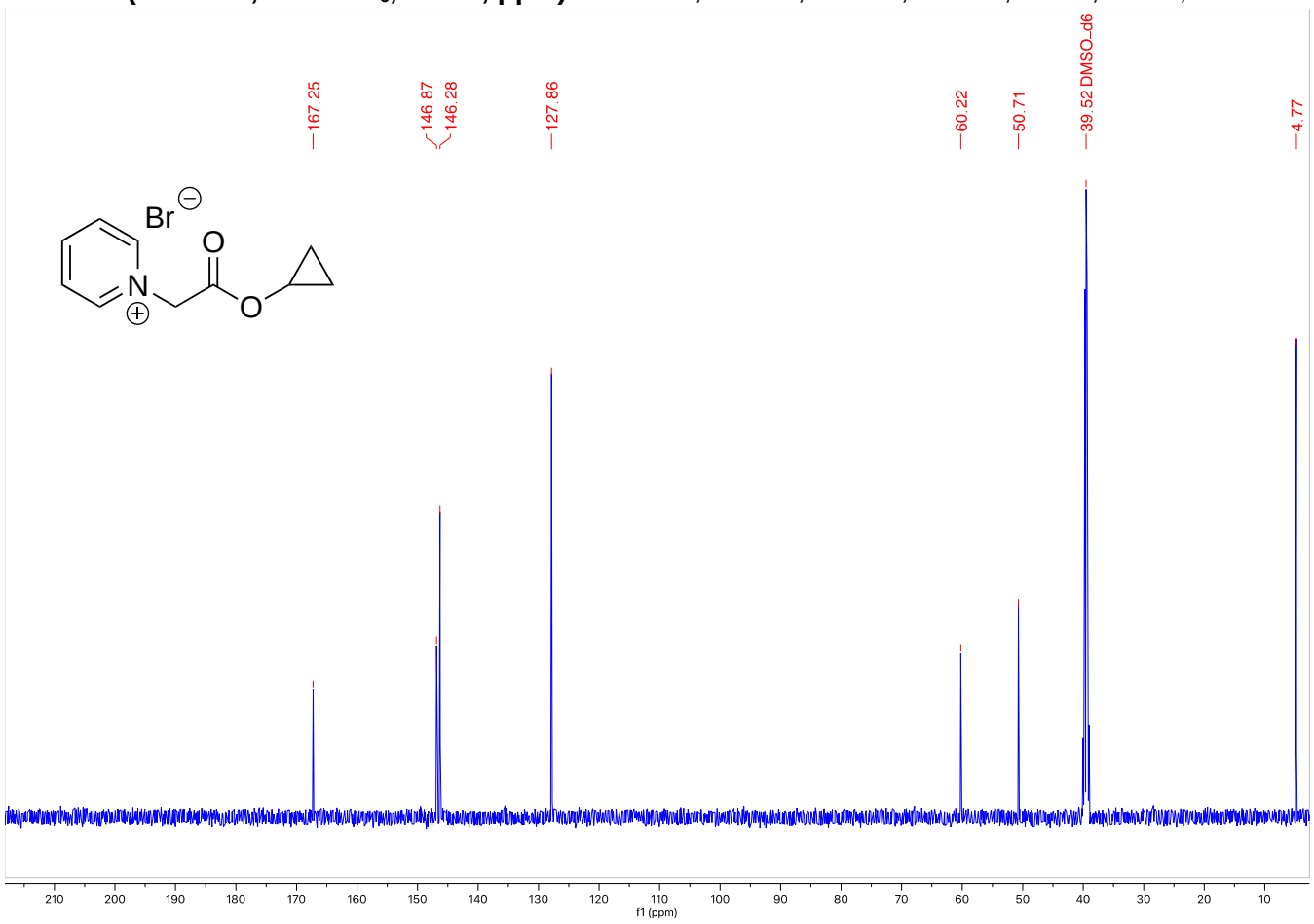


HRMS(ESI): calc'd for [$C_{10}H_{12}BrNO_2^+$ - Br^-], 178.08625; found: 178.08637.

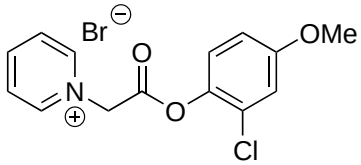
^{1}H NMR (500 MHz, DMSO-d_6, 292 K, ppm): δ 9.08 – 9.03 (m, 2H), 8.75 – 8.68 (m, 1H), 8.24 (dd, J = 7.9, 6.6 Hz, 2H), 5.66 (s, 2H), 4.26 – 4.17 (m, 1H), 0.78 – 0.71 (m, 4H).



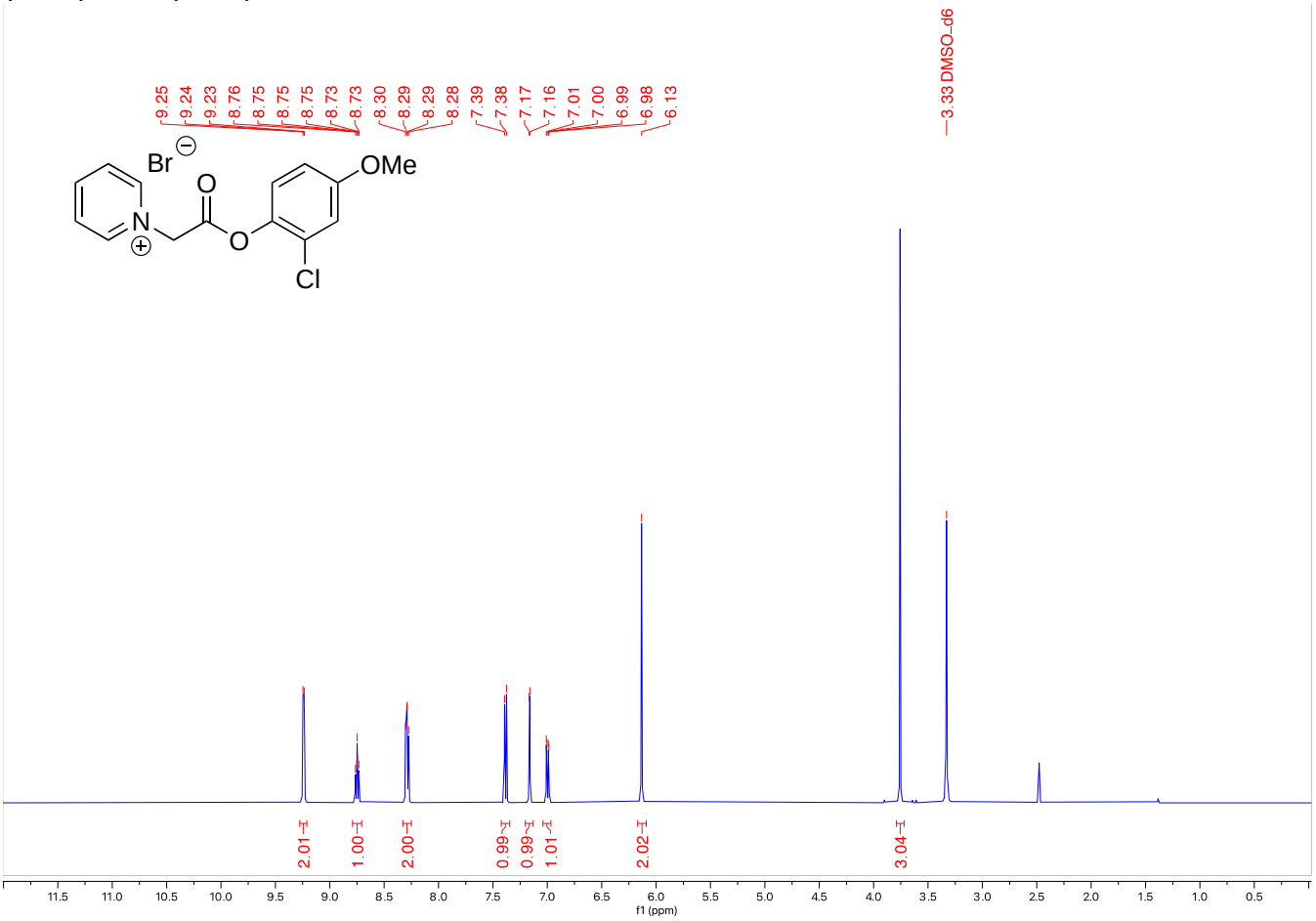
^{13}C NMR (126 MHz, DMSO-d$_6$, 292 K, ppm): δ 167.25, 146.87, 146.28, 127.86, 60.22, 50.71, 4.77.



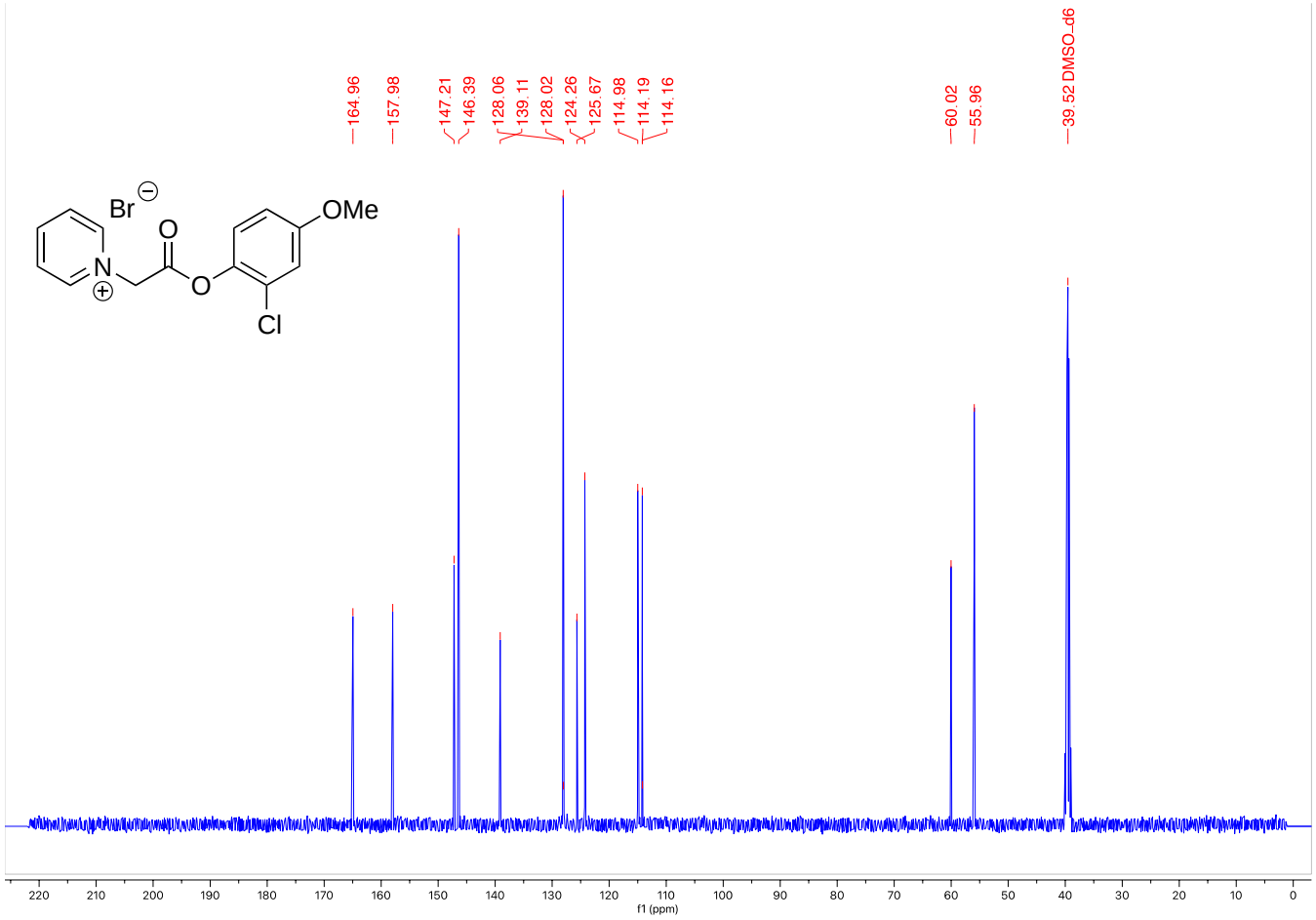
1-(2-(2-chloro-4-methoxyphenyl)-2-oxoethyl)pyridin-1-ium bromide



^{1}H NMR (500 MHz, DMSO-d$_6$, 292 K, ppm): δ 9.28 – 9.21 (m, 2H), 8.79 – 8.71 (m, 1H), 8.29 (dd, J = 8.0, 6.5 Hz, 2H), 7.38 (d, J = 9.0 Hz, 1H), 7.16 (d, J = 3.0 Hz, 1H), 7.00 (dd, J = 9.0, 2.9 Hz, 1H), 6.13 (s, 2H), 3.76 (s, 3H).



^{13}C NMR (126 MHz, DMSO-d_6, 292 K, ppm): δ 164.96, 157.98, 147.21, 146.39, 139.11, 128.06, 128.02, 125.67, 124.26, 114.98, 114.19, 114.16, 60.02, 55.96.



VII: Azabicyclo[3.1.1]heptane Synthesis

Two general procedures are given below (A and B). Specific amounts of reactants, reagents, and solvents are given for each example.

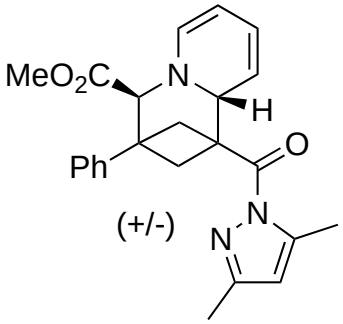
General Procedure A:

To a 4 mL vial was added the appropriate pyridinium salt **2,** K_3PO_4, and a stir bar. Half of the total acetonitrile solvent was added to this vial, and the mixture stirred for 2 minutes at room temperature. The appropriate bicyclobutane **1** was weighed into another 4 mL vial, and quantitatively transferred to the vial containing pyridinium/base using the other half of the acetonitrile reaction solvent. The reaction mixture was stirred for 24 hours at room temperature. The solvent was then evaporated, the residue dissolved in dichloromethane, and the resulting solution passed through a plug of basic alumina, using excess dichloromethane to elute. Evaporation of the eluent provided the products **3**.

General Procedure B (ketone-based pyridinium salts):

To a 4 mL vial was added the appropriate pyridinium **2,** $NaPF_6$, and a stir bar. Half of the total acetonitrile solvent was added to the vial, and the mixture stirred for 2 hours at room temperature. The K_3PO_4 base was then added to the reaction vial, and the mixture stirred for 2 minutes at room temperature. The appropriate bicyclobutane **1** was weighed into another 4 mL vial, and quantitatively transferred to the vial containing pyridinium/base using the other half of the acetonitrile reaction solvent. The reaction mixture was stirred for 24 hours at room temperature. The solvent was then evaporated, the residue dissolved in dichloromethane, and the resulting solution passed through a plug of basic alumina, using excess dichloromethane to elute. Evaporation of the eluent provided the products **3**.

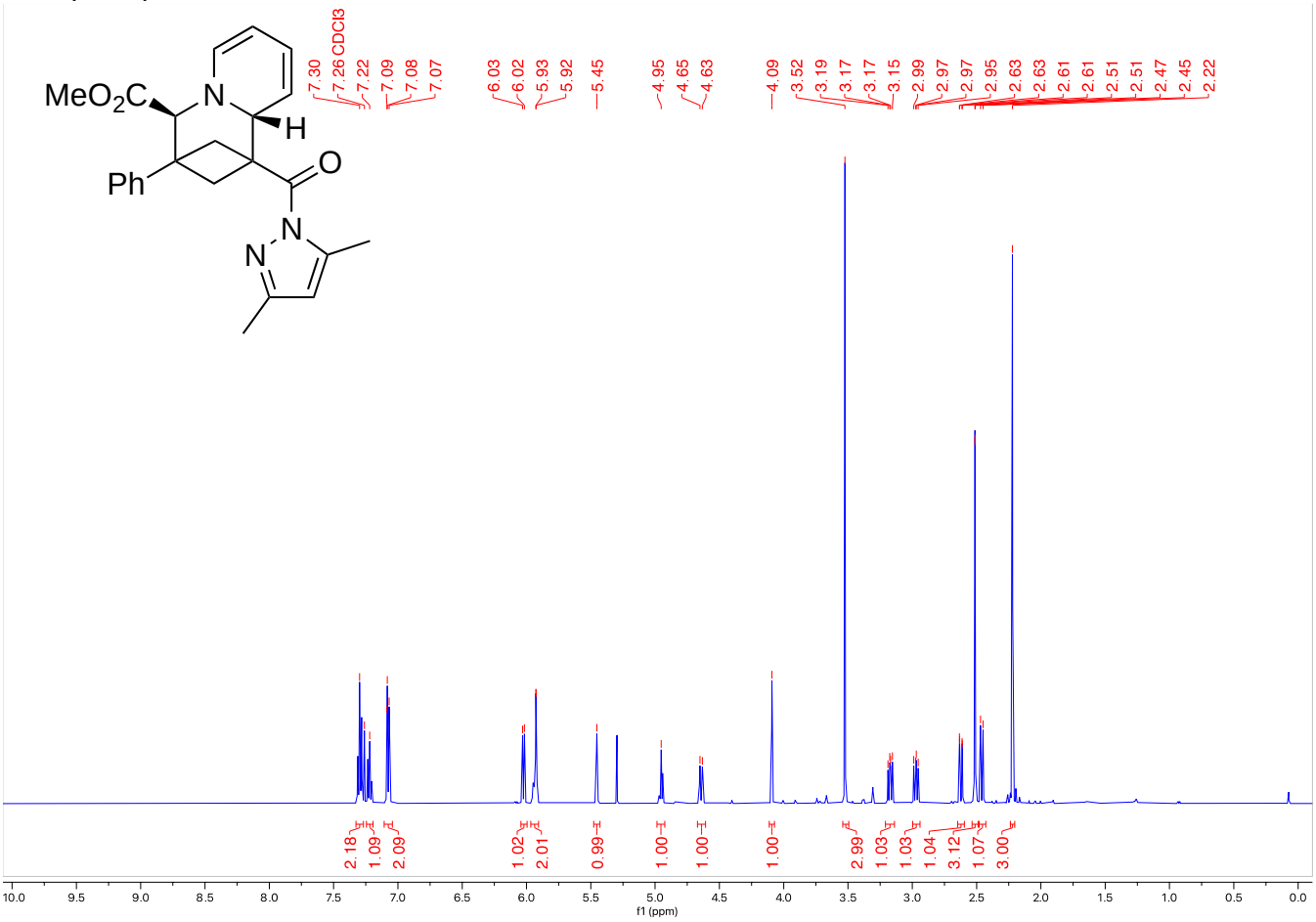
Methyl 1-(3,5-dimethyl-1H-pyrazole-1-carbonyl)-3-phenyl-1,3,4,9a-tetrahydro-2H-1,3-methanoquinolizine-4-carboxylate (3a)



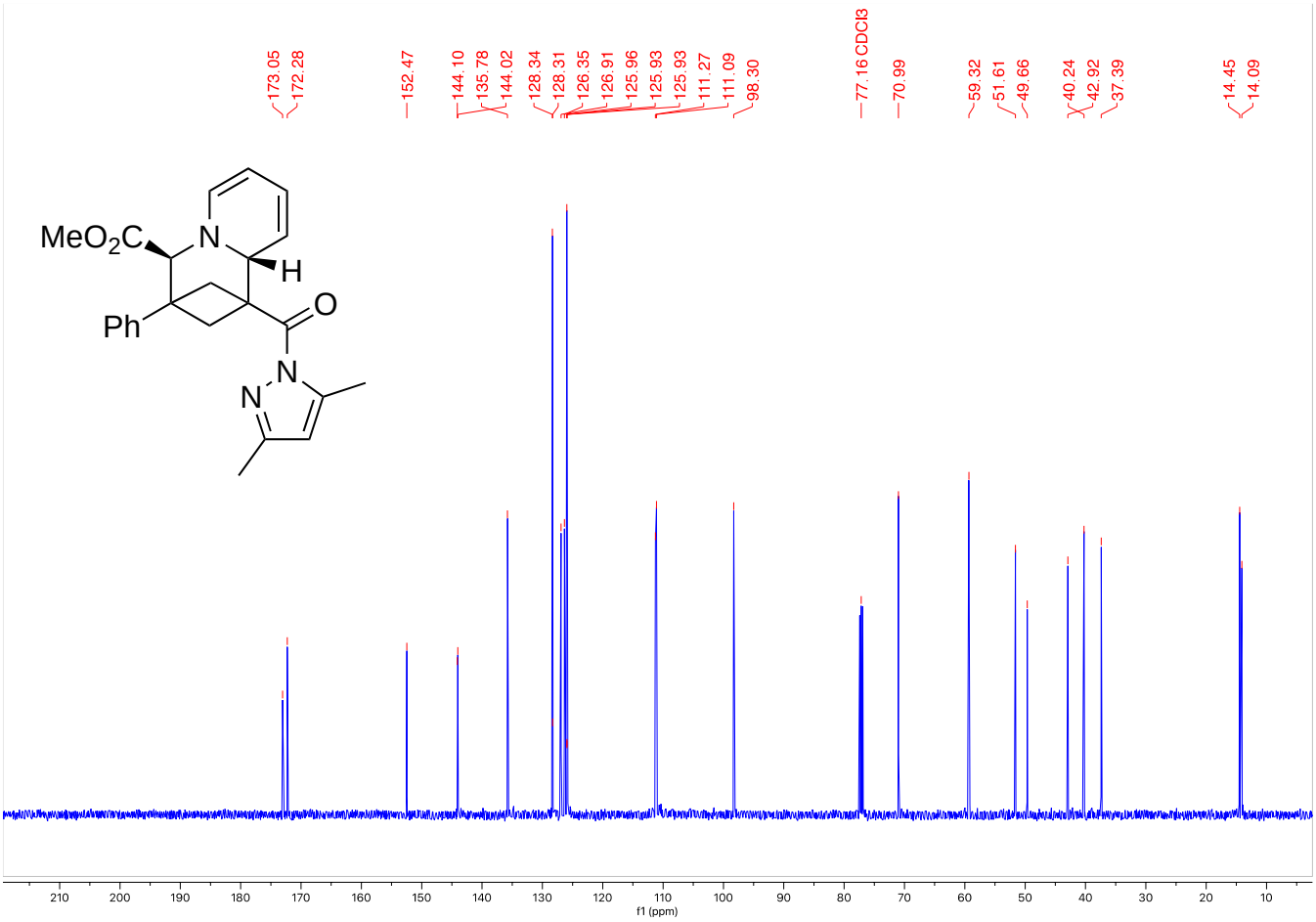
Product was synthesized following general procedure A on a 0.30 mmol scale. Reagent amounts used: bicyclobutane **1a** (75.7 mg, 0.30 mmol), pyridinium **2a** (1.25 equiv, 87.0 mg, 0.38 mmol), and K_3PO_4 (2.5 equiv, 159.2 mg, 0.75 mmol) in 1.2 mL acetonitrile (0.25 M). Isolated 106.4 mg of an orange solid (**88% yield**).

HRMS(ESI): calc'd for [$C_{31}H_{31}N_3O_4$ + H^+], 404.19687; found: 404.19668.

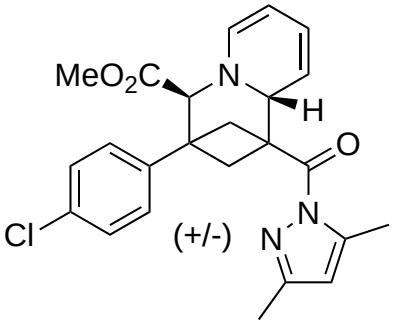
^{1}H NMR (500 MHz, $CDCl_3$, 292 K, ppm): δ 7.30 (m, 2H), 7.24 – 7.19 (m, 1H), 7.11 – 7.04 (m, 2H), 6.02 (dt, J = 7.1, 0.9 Hz, 1H), 5.97 – 5.91 (m, 2H), 5.48 – 5.43 (m, 1H), 4.95 (ddd, J = 7.0, 5.4, 1.3 Hz, 1H), 4.64 (ddt, J = 9.4, 2.3, 1.1 Hz, 1H), 4.09 (s, 1H), 3.52 (s, 3H), 3.17 (dd, J = 10.2, 7.4 Hz, 1H), 2.97 (dd, J = 9.7, 7.4 Hz, 1H), 2.62 (dd, J = 10.2, 0.9 Hz, 1H), 2.51 (d, J = 1.1 Hz, 3H), 2.46 (d, J = 9.7 Hz, 1H), 2.22 (s, 3H).



^{13}C NMR (126 MHz, $CDCl_3$, 292 K, ppm): δ 173.05, 172.28, 152.47, 144.10, 144.02, 135.78, 128.34, 128.31, 126.91, 126.35, 125.96, 125.93, 125.93, 111.27, 111.09, 98.30, 70.99, 59.32, 51.61, 49.66, 42.92, 40.24, 37.39, 14.45, 14.09.



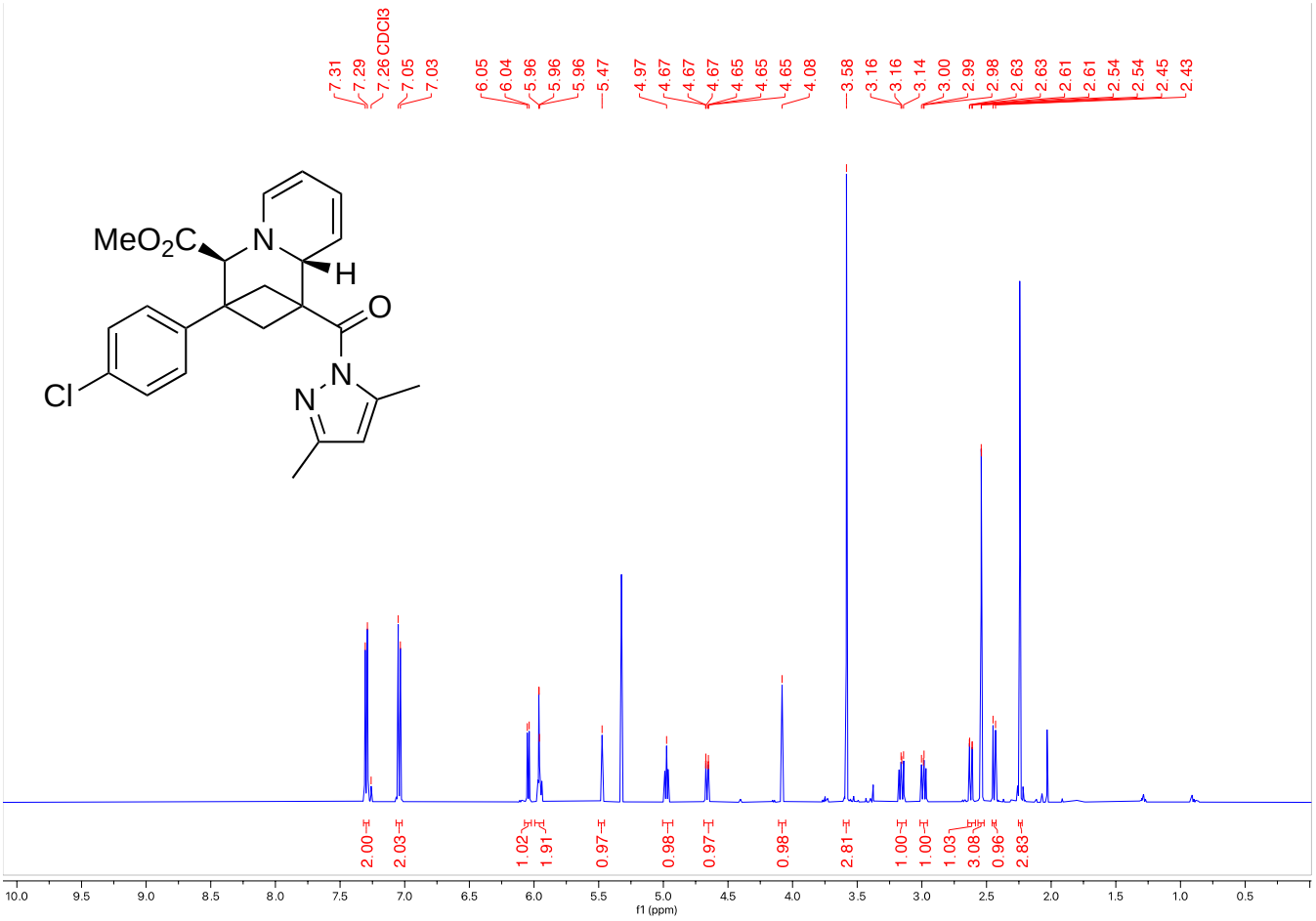
Methyl 3-(4-chlorophenyl)-1-(3,5-dimethyl-1H-pyrazole-1-carbonyl)-1,3,4,9a-tetrahydro-2H-1,3-methanoquinolizine-4-carboxylate (3b)



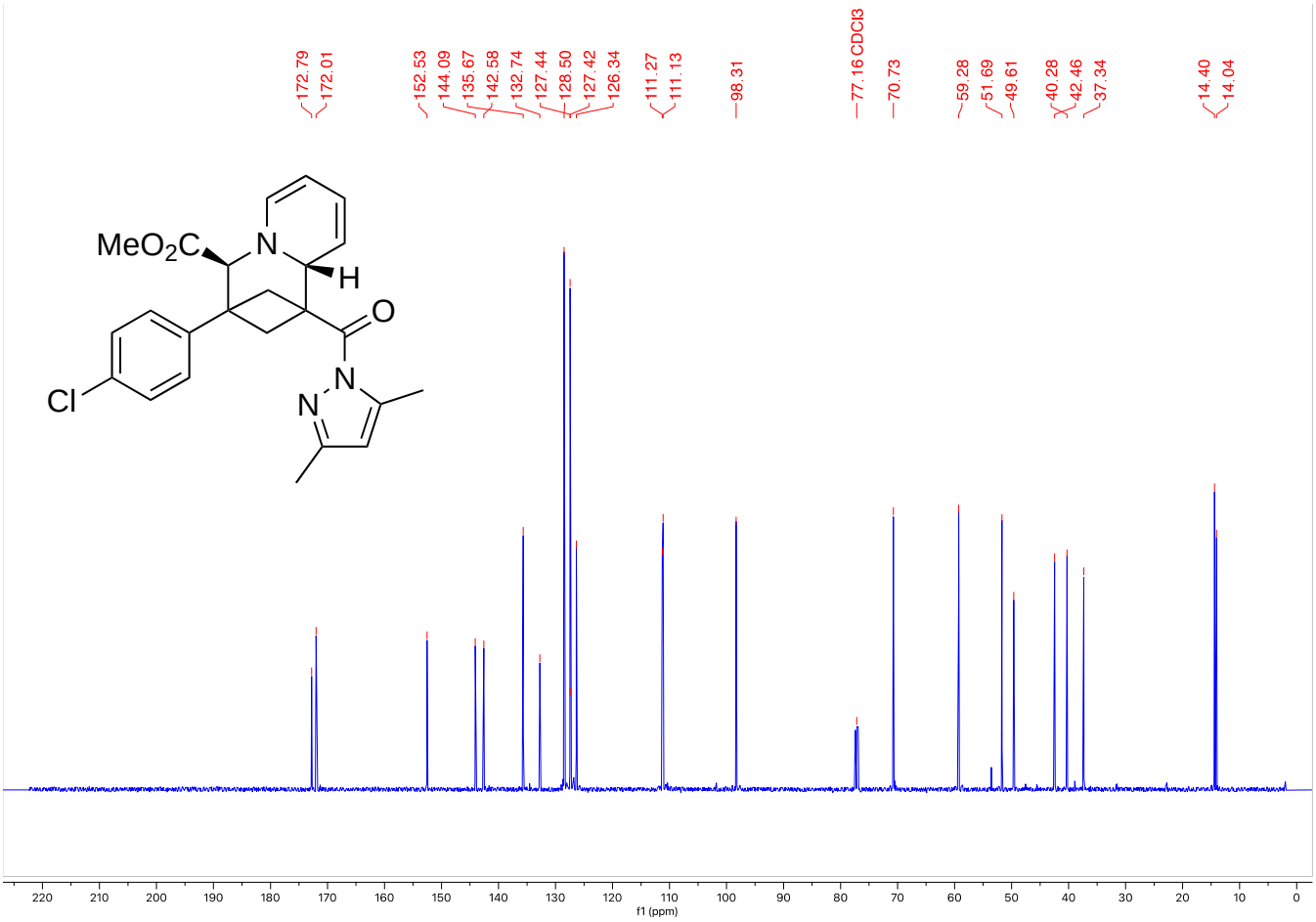
Product was synthesized following general procedure A on a 0.20 mmol scale. Reagent amounts used: bicyclobutane **1b** (57.4 mg, 0.20 mmol), pyridinium **2a** (1.25 equiv, 57.8 mg, 0.25 mmol), and K_3PO_4 (2.5 equiv, 106.1 mg, 0.50 mmol) in 0.8 mL acetonitrile (0.25 M). Isolated 77.9 mg of a yellow oil (**71% yield**).

HRMS(ESI): calc'd for [$C_{24}H_{24}ClN_3O_3$ + H^+], 438.15790; found: 438.15843.

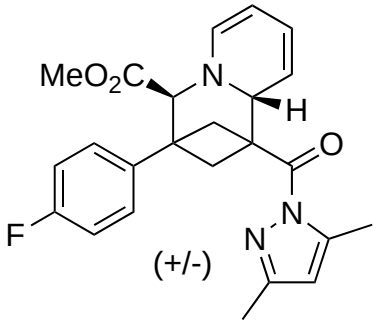
^{1}H NMR (500 MHz, $CDCl_3$, 292 K, ppm): δ 7.32 – 7.28 (m, 2H), 7.07 – 7.02 (m, 2H), 6.04 (d, J = 7.1 Hz, 1H), 5.99 – 5.92 (m, 2H), 5.47 (s, 1H), 4.97 (ddd, J = 7.0, 5.4, 1.3 Hz, 1H), 4.66 (ddt, J = 9.4, 2.2, 1.1 Hz, 1H), 4.08 (s, 1H), 3.58 (s, 3H), 3.16 (dd, J = 10.2, 7.4 Hz, 1H), 2.99 (dd, J = 9.7, 7.4 Hz, 1H), 2.62 (dd, J = 10.2, 1.0 Hz, 1H), 2.54 (d, J = 1.1 Hz, 3H), 2.44 (d, J = 9.7 Hz, 1H), 2.24 (s, 3H).



^{13}C NMR (126 MHz, $CDCl_3$, 292 K, ppm): δ 172.79, 172.01, 152.53, 144.09, 142.58, 135.67, 132.74, 128.50, 127.44, 127.42, 126.34, 111.27, 111.13, 98.31, 70.73, 59.28, 51.69, 49.61, 42.46, 40.28, 37.34, 14.40, 14.04.



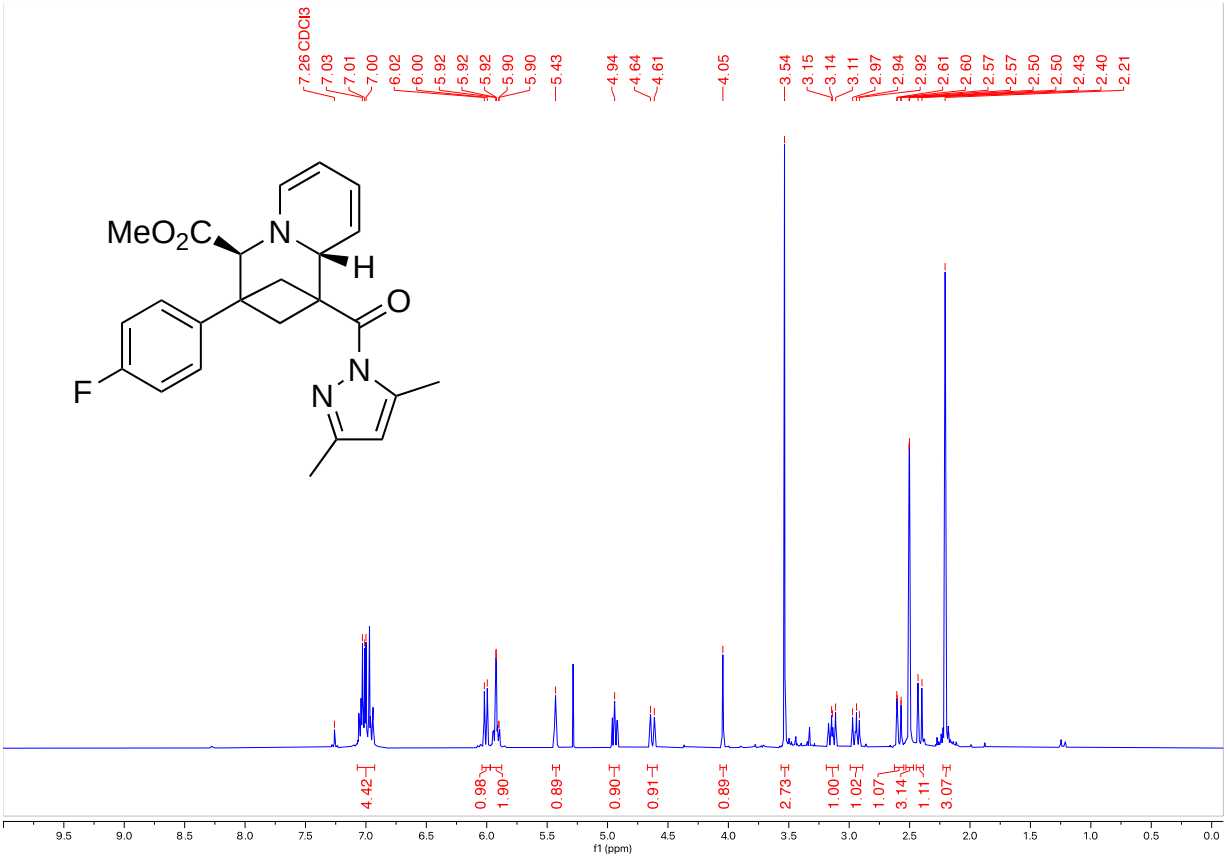
Methyl (3,5-dimethyl-1H-pyrazole-1-carbonyl)-3-(4-fluorophenyl)-1,3,4,9a-tetrahydro-2H-1,3-methanoquinolizine-4-carboxylate (3c)



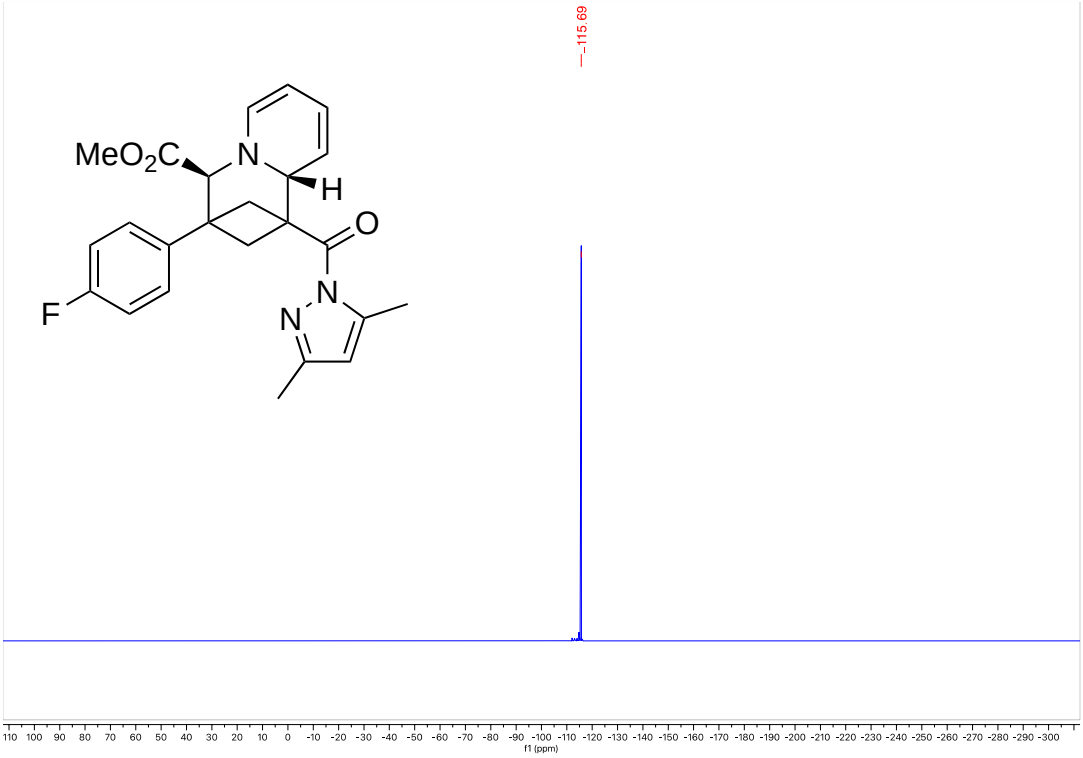
Product was synthesized following general procedure A on a 0.30 mmol scale. Reagent amounts used: bicyclobutane **1c** (81.1 mg, 0.30 mmol), pyridinium **2a** (1.25 equiv, 87.0 mg, 0.38 mmol), and K_3PO_4 (2.5 equiv, 159.2 mg, 0.75 mmol) in 1.2 mL acetonitrile (0.25 M). Isolated 89.0 mg of an orange solid (**57% yield**). Single crystals for X-ray diffraction were grown from a supersaturated solution of **3c** in dichloromethane at -20 °C.

HRMS(ESI): calc'd for [$C_{24}H_{24}FN_3O_3$ + H^+], 422.18745; found: 422.18770

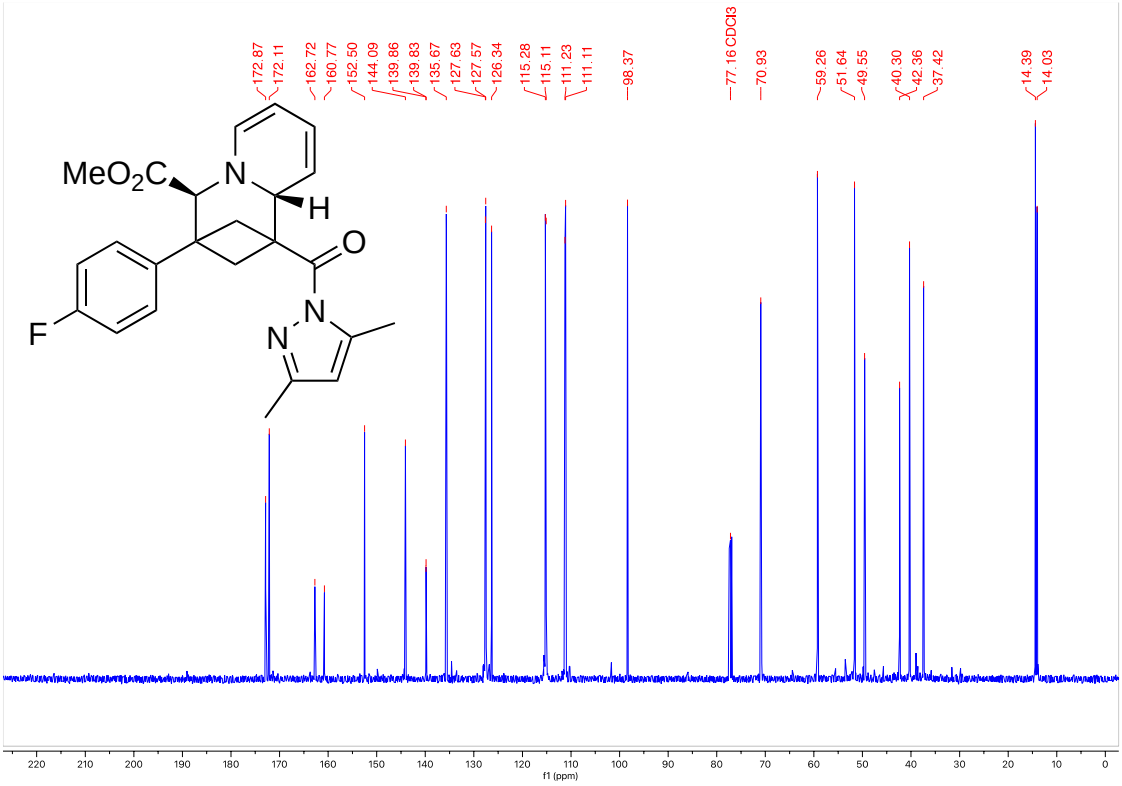
^{1}H NMR (300 MHz, $CDCl_3$, 292 K, ppm): δ 7.07 – 6.93 (m, 4H), 6.01 (d, J = 7.1 Hz, 1H), 5.92 (m, 2H), 5.46 – 5.40 (m, 1H), 4.94 (ddd, J = 6.9, 5.4, 1.3 Hz, 1H), 4.67 – 4.59 (m, 1H), 4.05 (s, 1H), 3.54 (s, 3H), 3.14 (dd, J = 10.2, 7.4 Hz, 1H), 2.94 (dd, J = 9.7, 7.4 Hz, 1H), 2.59 (d, J = 10.2, 1H), 2.50 (d, J = 1.0 Hz, 3H), 2.41 (d, J = 9.7 Hz, 1H), 2.21 (s, 3H).



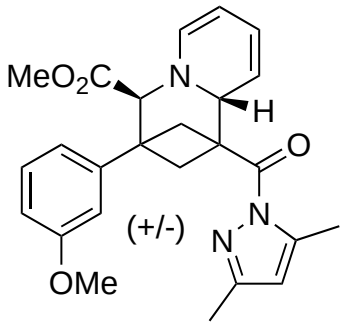
^{19}F NMR (300 MHz, $CDCl_3$, 292 K, ppm): δ 115.69.



^{13}C NMR (300 MHz, $CDCl_3$, 292 K, ppm): δ 172.87, 172.11, 162.72, 160.77, 152.50, 144.09, 139.86, 139.83, 135.67, 127.63, 127.57, 126.34, 115.28, 115.11, 111.23, 111.11, 98.37, 70.93, 59.26, 51.64, 49.55, 42.36, 40.30, 37.42, 14.39, 14.03.



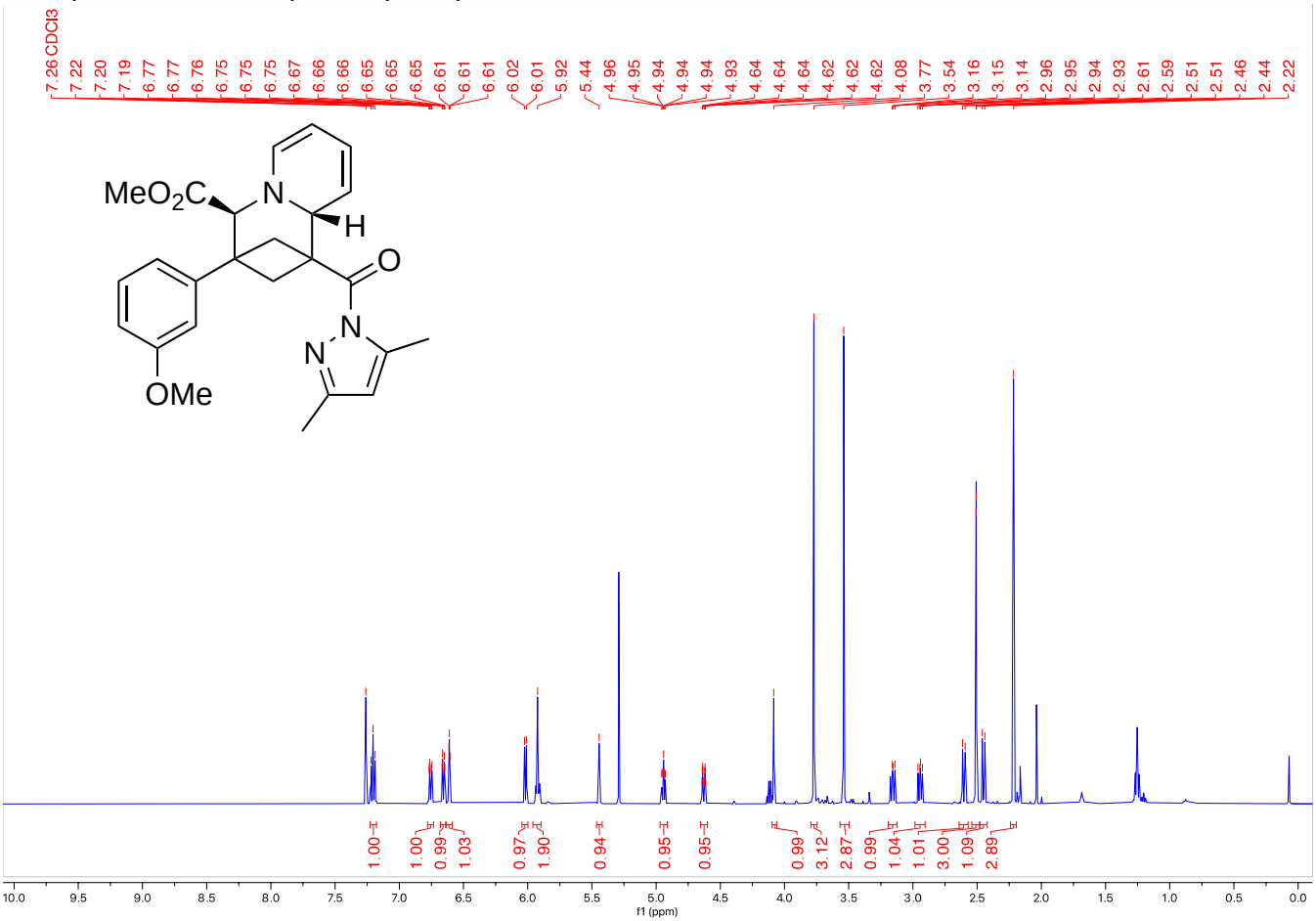
Methyl 1-(3,5-dimethyl-1*H*-pyrazole-1-carbonyl)-3-(3-methoxyphenyl)-1,3,4,9a-tetrahydro-2*H*-1,3-methanoquinolizine-4-carboxylate (3d)



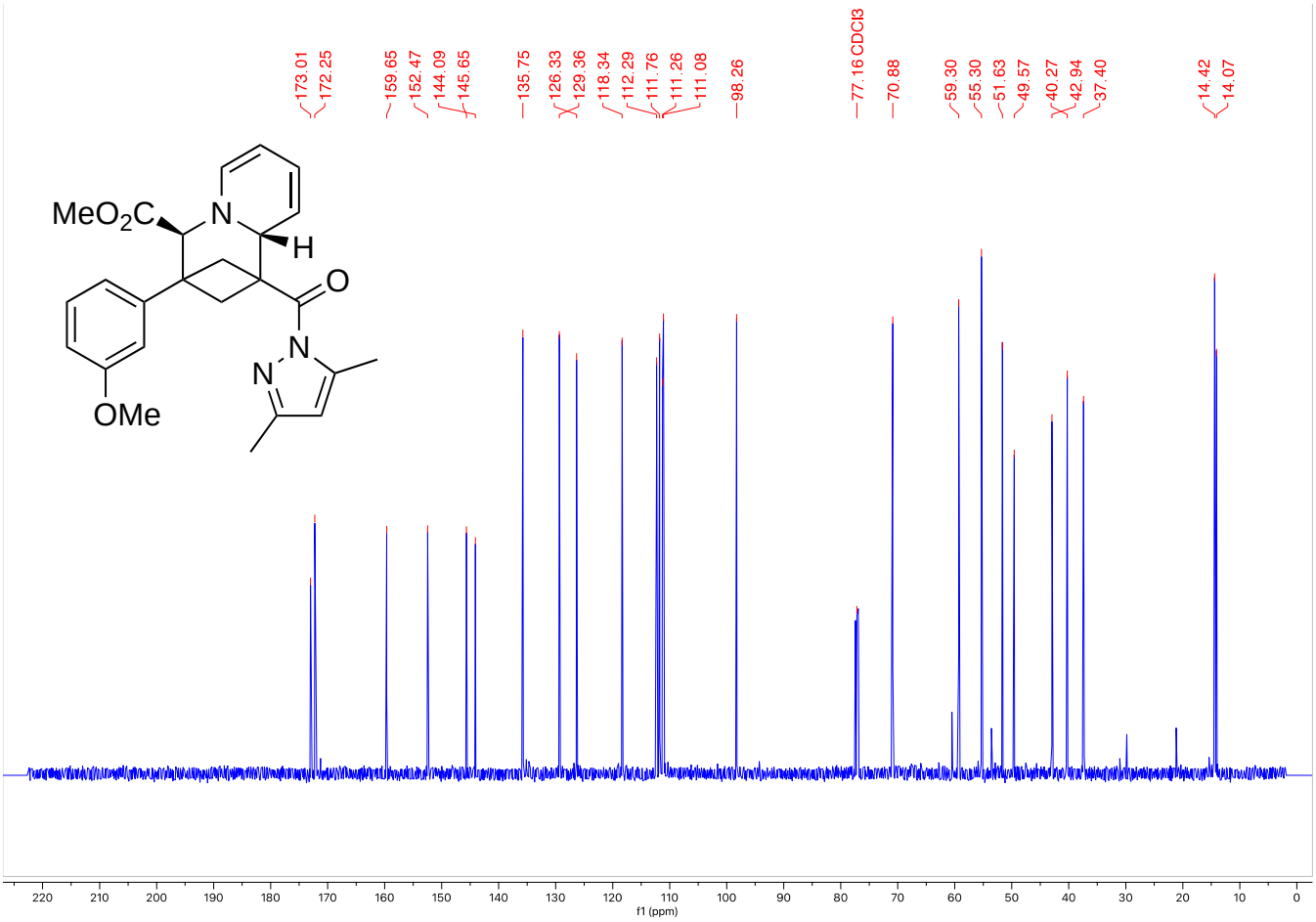
Product was synthesized following general procedure on a 0.30 mmol scale. Reagent amounts used: bicyclobutane **1d** (81.1 mg, 0.30 mmol), pyridinium **2a** (1.25 equiv, 86.7 mg, 0.38 mmol), and K_3PO_4 (2.5 equiv, 159.2 mg, 0.75 mmol) in 1.2 mL acetonitrile (0.25 M). Isolated 51.9 mg of an orange solid (**32% yield**).

HRMS(ESI): calc'd for [$C_{25}H_{27}N_3O_4$ + H^+], 434.20744; found: 434.20746.

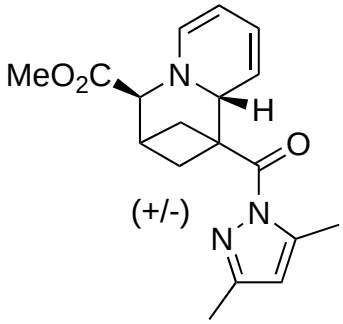
^{1}H NMR (500 MHz, $CDCl_3$, 292 K, ppm): δ 7.20 (t, J = 7.9 Hz, 1H), 6.76 (dd, J = 8.1, 2.4 Hz, 1H), 6.66 (d, J = 7.7 Hz, 1H), 6.61 (m, 1H), 6.02 (d, J = 7.1 Hz, 1H), 5.96 – 5.90 (m, 2H), 5.44 (s, 1H), 4.94 (ddd, J = 6.9, 5.4, 1.3 Hz, 1H), 4.65 – 4.60 (m, 1H), 4.08 (s, 1H), 3.77 (s, 3H), 3.54 (s, 3H), 3.16 (dd, J = 10.2, 7.4 Hz, 1H), 2.94 (dd, J = 9.7, 7.4 Hz, 1H), 2.60 (d, J = 10.2 Hz, 1H), 2.51 (d, J = 1.1 Hz, 3H), 2.45 (d, J = 9.7 Hz, 1H), 2.22 (s, 3H).



^{13}C NMR (126 MHz, $CDCl_3$, 292 K, ppm): δ 173.01, 172.25, 159.65, 152.47, 145.65, 144.09, 135.75, 129.36, 126.33, 118.34, 112.29, 111.76, 111.26, 111.08, 98.26, 70.88, 59.30, 55.30, 51.63, 49.57, 42.94, 40.27, 37.40, 14.42, 14.07.



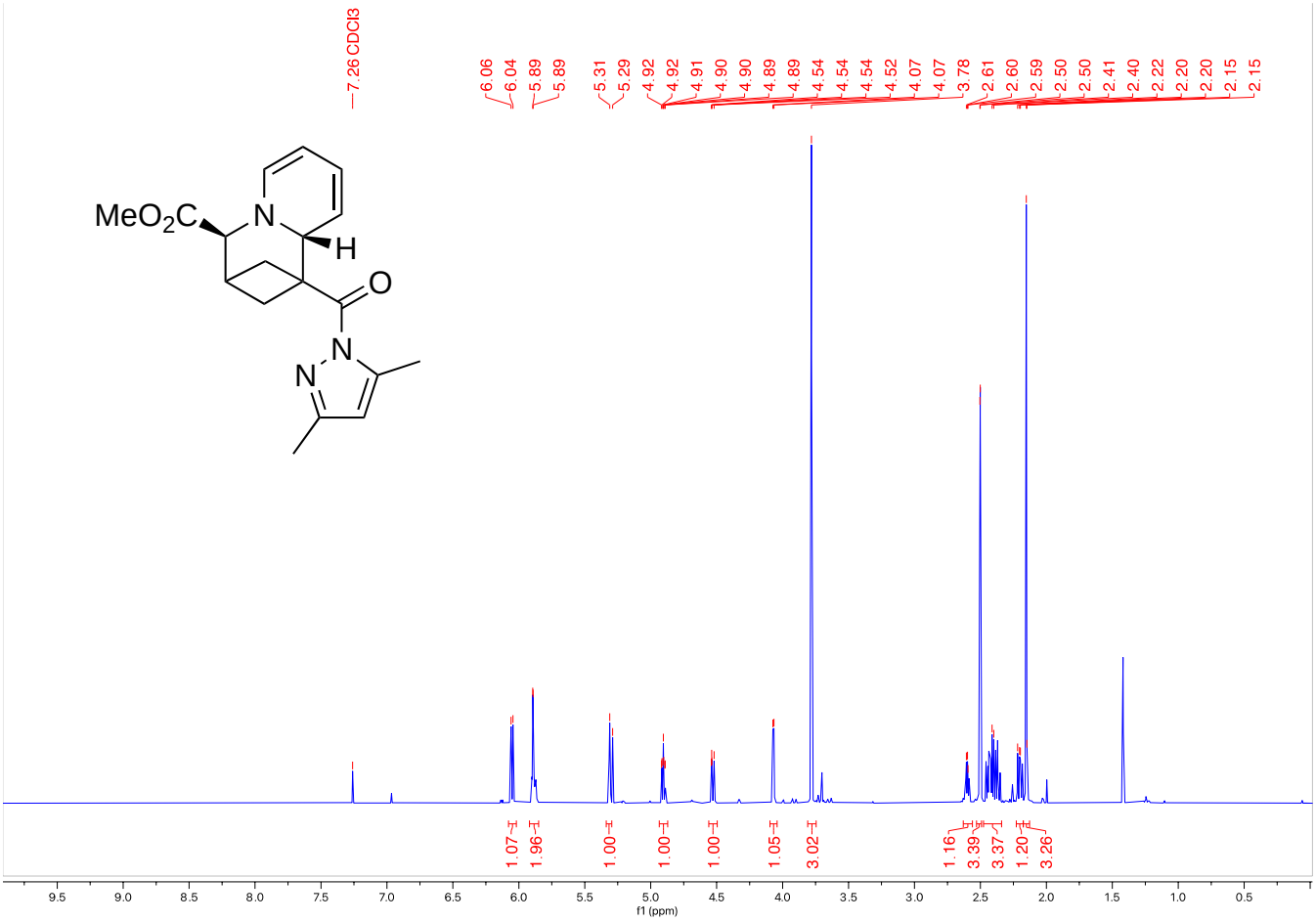
Methyl 1-(3,5-dimethyl-1H-pyrazole-1-carbonyl)-1,3,4,9a-tetrahydro-2H-1,3-methanoquinolizine-4-carboxylate (3e)



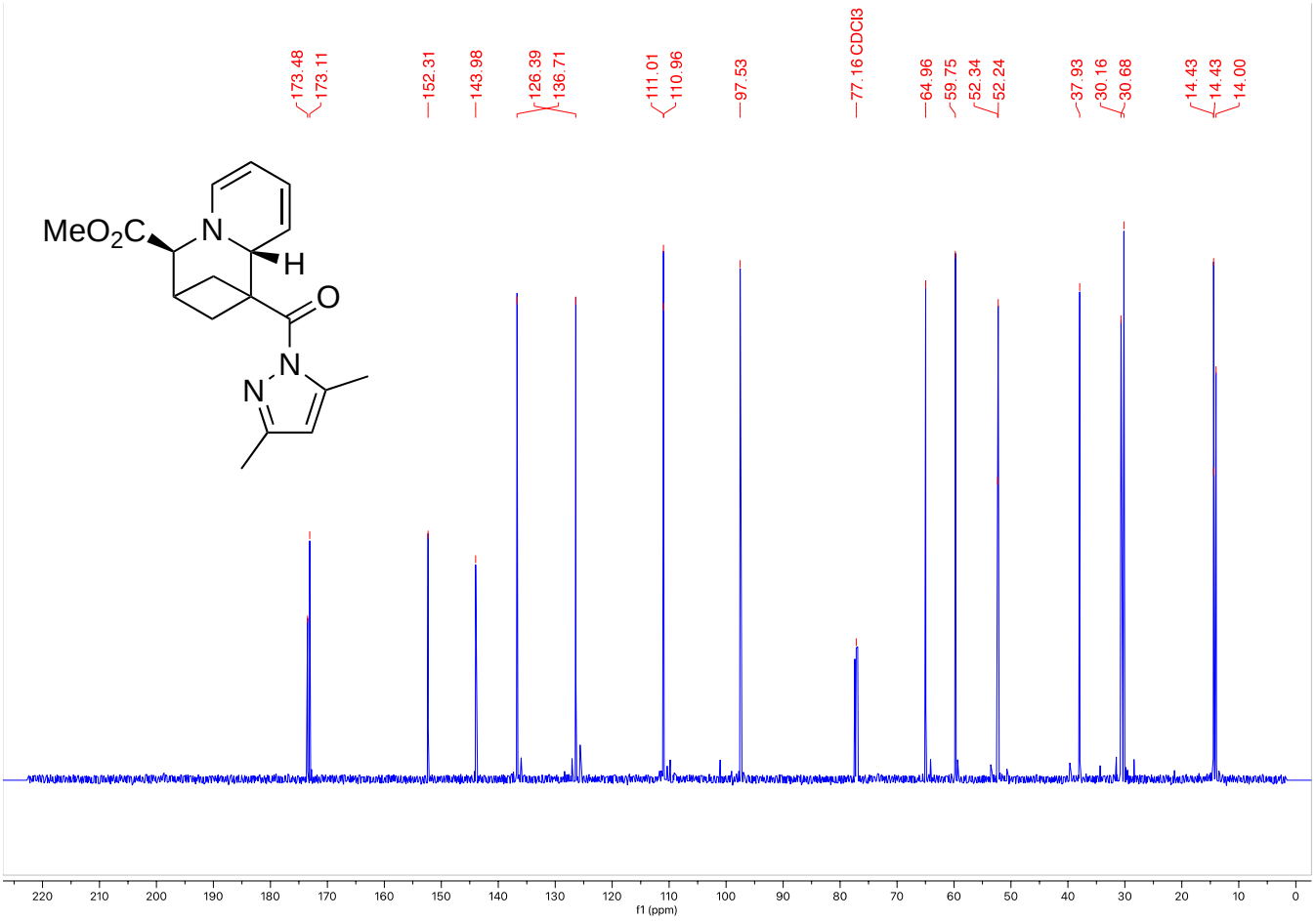
Product was synthesized following general procedure A on a 0.30 mmol scale. Reagent amounts used: bicyclobutane **1e** (52.9 mg, 0.30 mmol), pyridinium **2a** (1.25 equiv, 87.0 mg, 0.38 mmol), and K_3PO_4 (2.5 equiv, 159.2 mg, 0.75 mmol) in 1.20 mL acetonitrile (0.25 M). Isolated 43.0 mg of an orange oil (**35% yield**)

HRMS(ESI): calc'd for [$C_{18}H_{21}N_3O_3$ + H^+], 328.16557; found: 328.16540

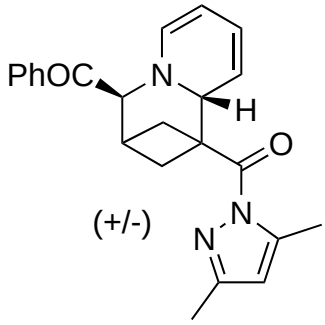
^{1}H NMR (500 MHz, $CDCl_3$, 292 K, ppm): δ 6.08 – 6.03 (m, 1H), 5.93 – 5.84 (m, 2H), 5.31 (t, J = 2.1 Hz, 1H), 4.90 (ddd, J = 6.9, 5.4, 1.3 Hz, 1H), 4.53 (dddd, J = 9.4, 2.2, 1.3, 0.8 Hz, 1H), 4.07 (d, J = 4.1 Hz, 1H), 3.78 (s, 3H), 2.64 – 2.56 (m, 1H), 2.50 (d, J = 1.1 Hz, 3H), 2.48 – 2.33 (m, 3H), 2.24 – 2.17 (m, 1H), 2.15 (s, 3H).



^{13}C NMR (300 MHz, $CDCl_3$, 292 K, ppm): δ 173.48, 173.11, 152.31, 143.98, 136.71, 126.39, 111.01, 110.96, 97.53, 64.96, 59.75, 52.34, 52.24, 37.93, 30.68, 30.16, 14.43, 14.43, 14.00.



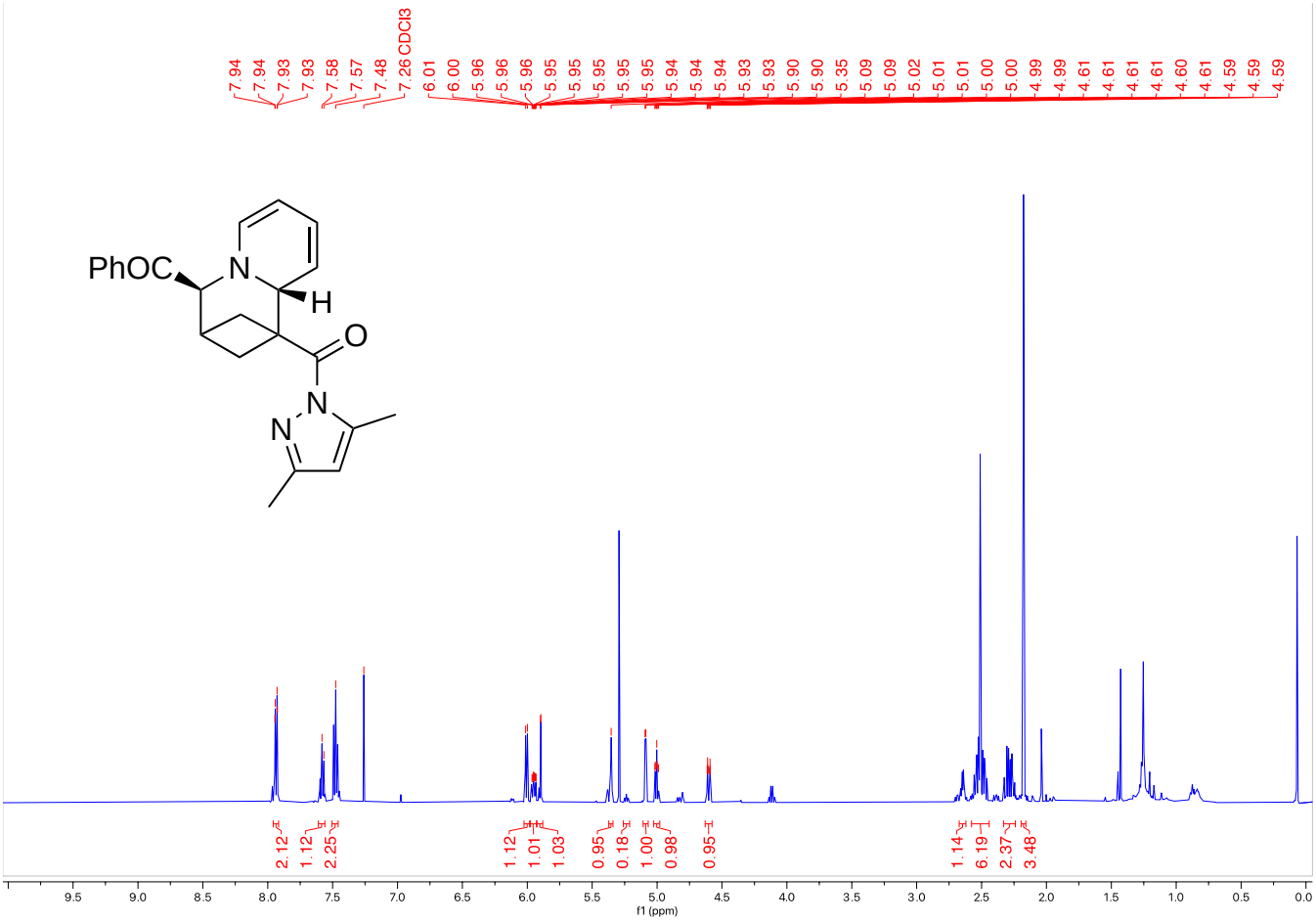
(4-benzoyl-3,4-dihydro-2H-1,3-methanoquinolizin-1(9aH)-yl)(3,5-dimethyl-1H-pyrazol-1-yl)methanone (3f)



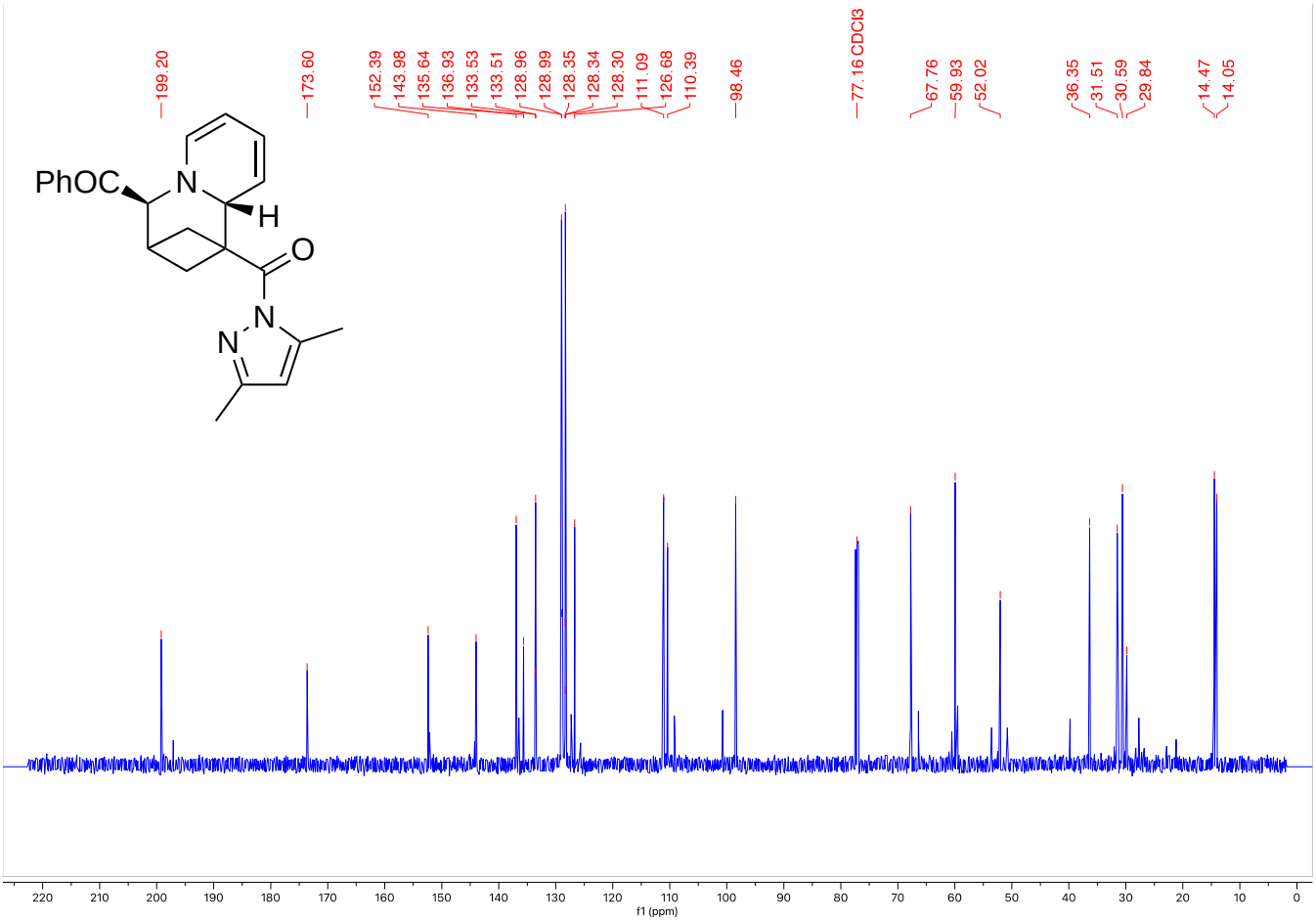
Product was synthesized following general procedure B on a 0.30 mmol scale. Reagent amounts used: bicyclobutane **1e** (52.9 mg, 0.30 mmol), pyridinium **2f** (1.25 equiv, 103.9 mg, 0.38 mmol), $NaPF_6$ (1.3 equiv, 65.5 mg), and K_3PO_4 (2.5 equiv, 159.2 mg, 0.75 mmol) in 1.2 mL acetonitrile (0.25 M). Isolated 27.8 mg of an orange solid as a mixture of diastereomers (**25% yield, 6:1 dr**).

HRMS(ESI): calc'd for [$C_{23}H_{23}N_3O_2$ + H^+], 374.18631; found: 374.18672.

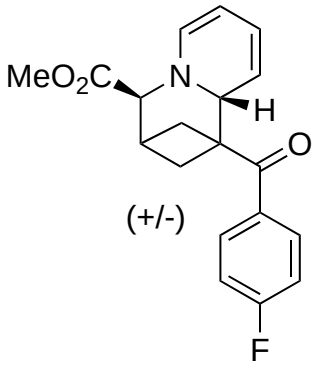
^{1}H NMR (300 MHz, $CDCl_3$, 292 K, ppm): δ 7.96 – 7.92 (m, 2H), 7.61 – 7.56 (m, 1H), 7.50 – 7.46 (m, 2H), 6.01 (d, J = 7.0 Hz, 1H), 5.95 (dddd, J = 9.3, 5.4, 2.2, 0.8 Hz, 1H), 5.90 (d, J = 1.2 Hz, 1H), 5.35 (t, J = 2.4 Hz, 1H), 5.09 (d, J = 3.6 Hz, 1H), 5.00 (ddd, J = 6.9, 5.4, 1.4 Hz, 1H), 4.63 – 4.58 (m, 1H), 2.67 – 2.62 (m, 1H), 2.58 – 2.44 (m, 5H), 2.33 – 2.24 (m, 2H), 2.18 (s, 3H).



^{13}C NMR (76 MHz, $CDCl_3$, 292 K, ppm): δ 199.20, 173.60, 152.39, 143.98, 136.93, 135.64, 133.53, 133.51, 128.99, 128.96, 128.35, 128.34, 128.30, 126.68, 111.09, 110.39, 98.46, 67.76, 59.93, 52.02, 36.35, 31.51, 30.59, 29.84, 14.47, 14.05.



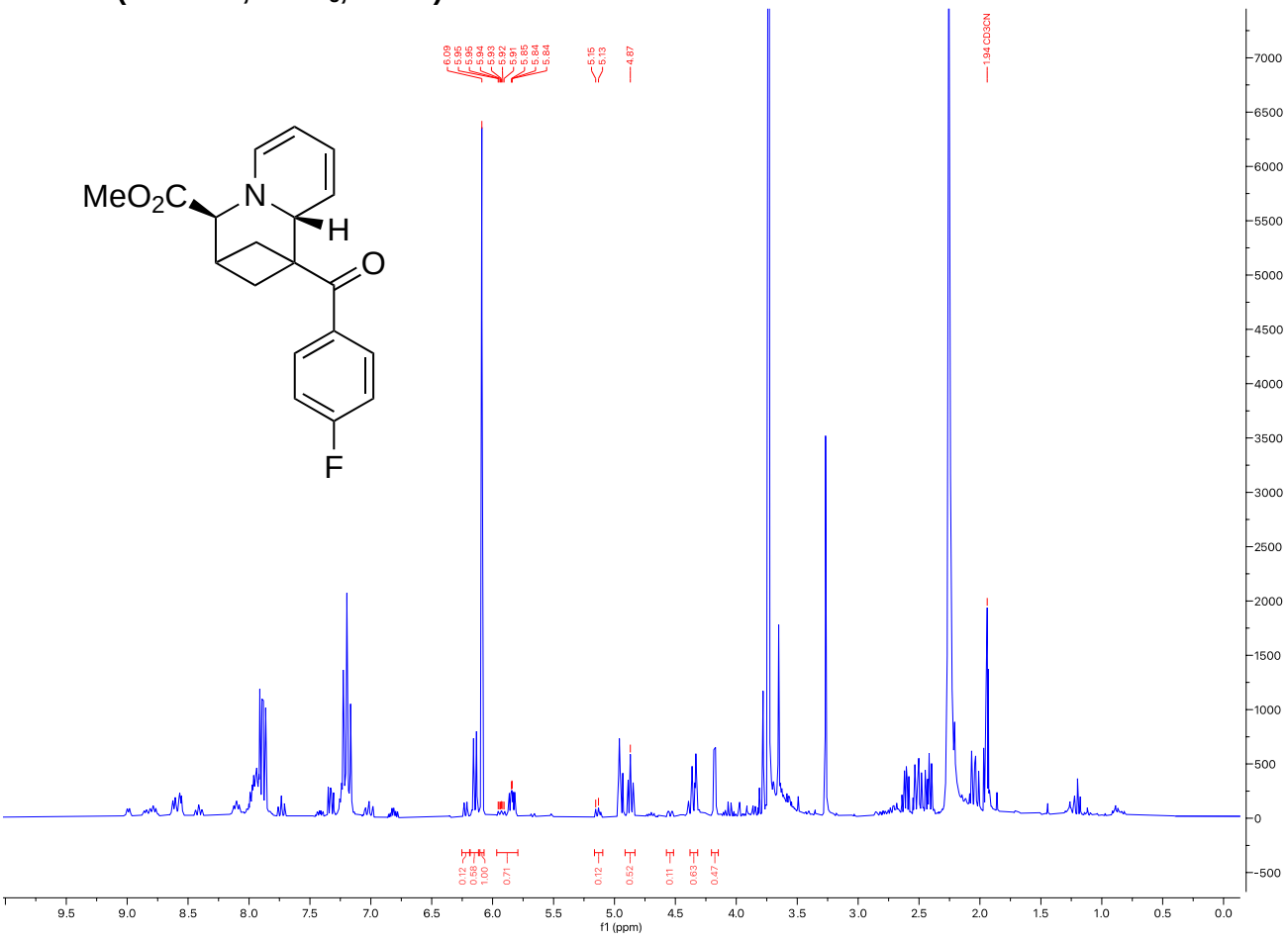
Methyl 1-(4-fluorobenzoyl)-1,3,4,9a-tetrahydro-2H-1,3-methanoquinolizine-4-carboxylate (3g)



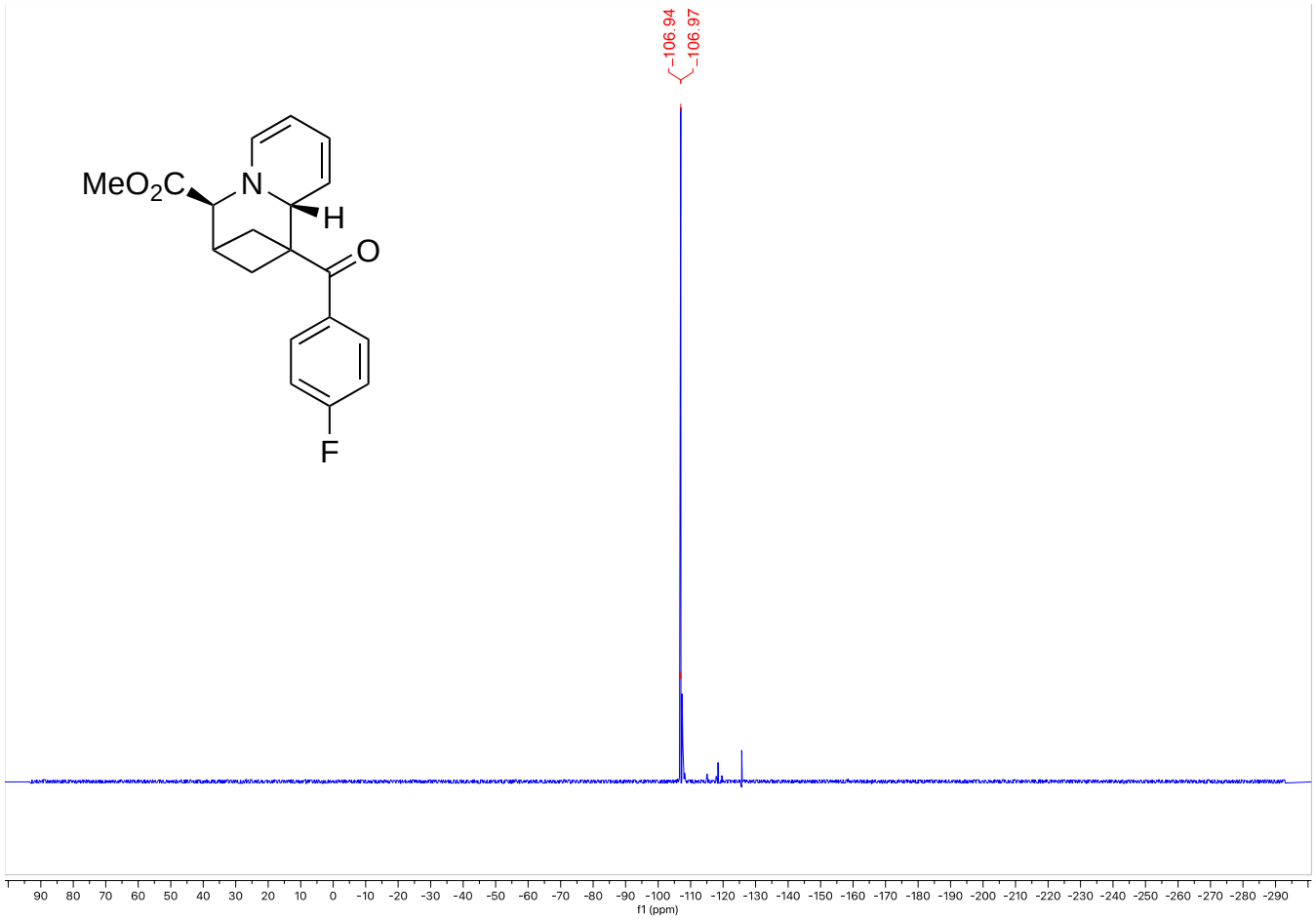
Product was synthesized following general procedure A on a 0.05 mmol scale. Reagent amounts used: bicyclobutane **1g** (8.8 mg, 0.05 mmol), pyridinium **2a** (1.25 equiv, 14.5 mg, 0.06 mmol), and K_3PO_4 (2.5 equiv, 26.5 mg, 0.13 mmol) in 0.2 mL d-MeCN (0.25 M). Solution yield determined by NMR spectroscopy using 1,3,5-trimethoxybenzene internal standard (**72% solution yield, 5:1 dr**). Note: this product is not stable on basic alumina.

HRMS(ESI): calc'd for [$C_{19}H_{18}FNO_3$ + H^+], 328.13435; found: 328.13393.

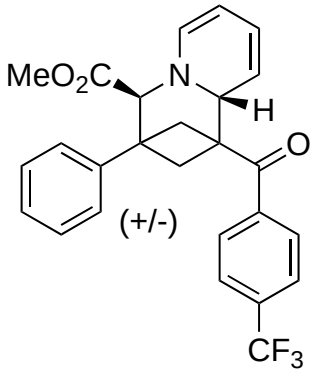
^{1}H NMR (500 MHz, $CDCl_3$, 292 K)



^{19}F NMR (300 MHz, $CDCl_3$, 292 K, ppm): δ 106.94, 106.97.



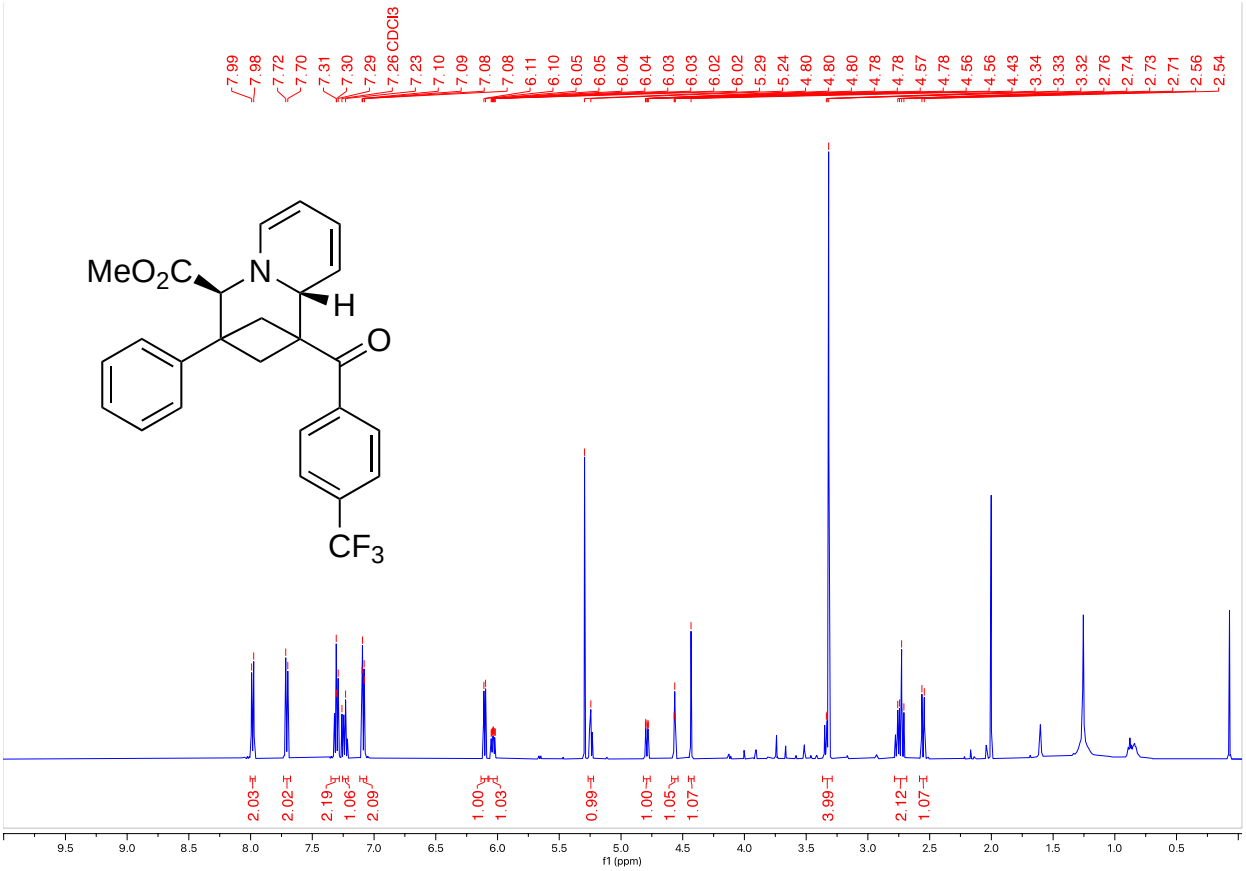
Methyl 3-phenyl-1-(4-(trifluoromethyl)benzoyl)-1,3,4,9a-tetrahydro-2H-1,3-methanoquinolizine-4-carboxylate (3h)



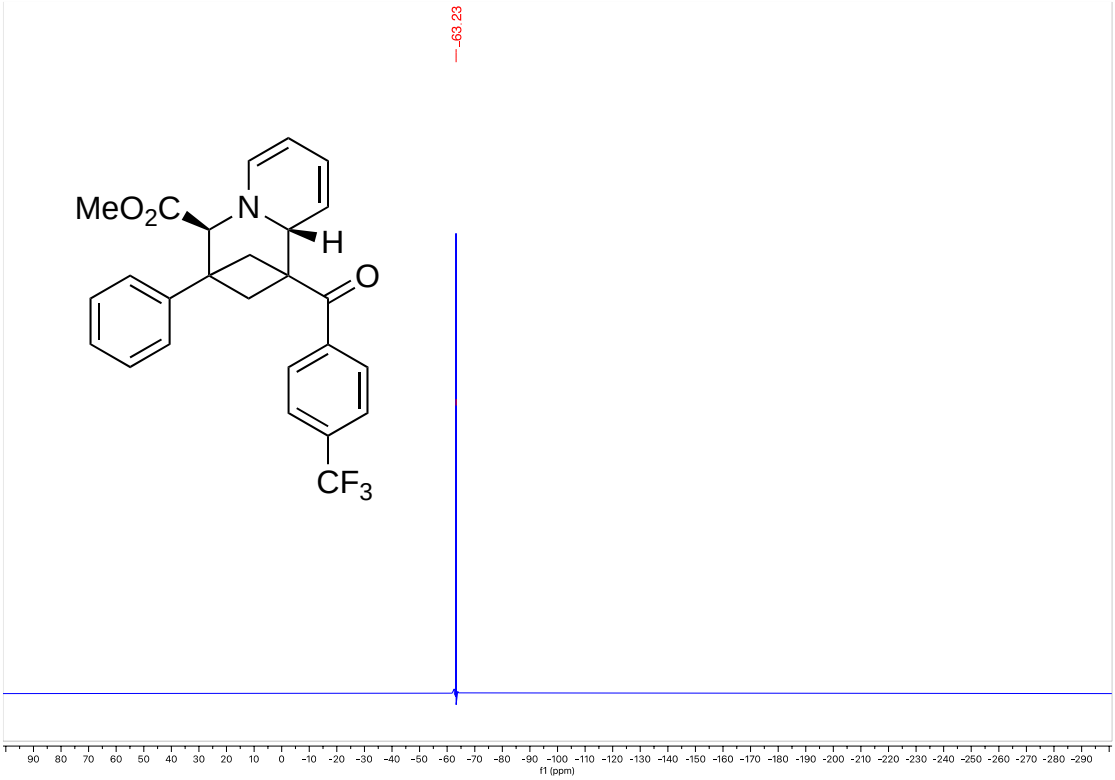
Product was synthesized following general procedure A on a 0.30 mmol scale. Reagent amounts used: bicyclobutane **1h** (90.7 mg, 0.30 mmol), pyridinium **2a** (1.25 equiv, 86.7 mg, 0.38 mmol), and K_3PO_4 (2.5 equiv, 159.2 mg, 0.75 mmol) in 1.8 mL acetonitrile (0.17 M). Isolated 32.1 mg of an orange oil (**24% yield**).

HRMS(ESI): calc'd for [$C_{26}H_{22}FNO_3$ + H^+], 454.16246; found: 454.16208.

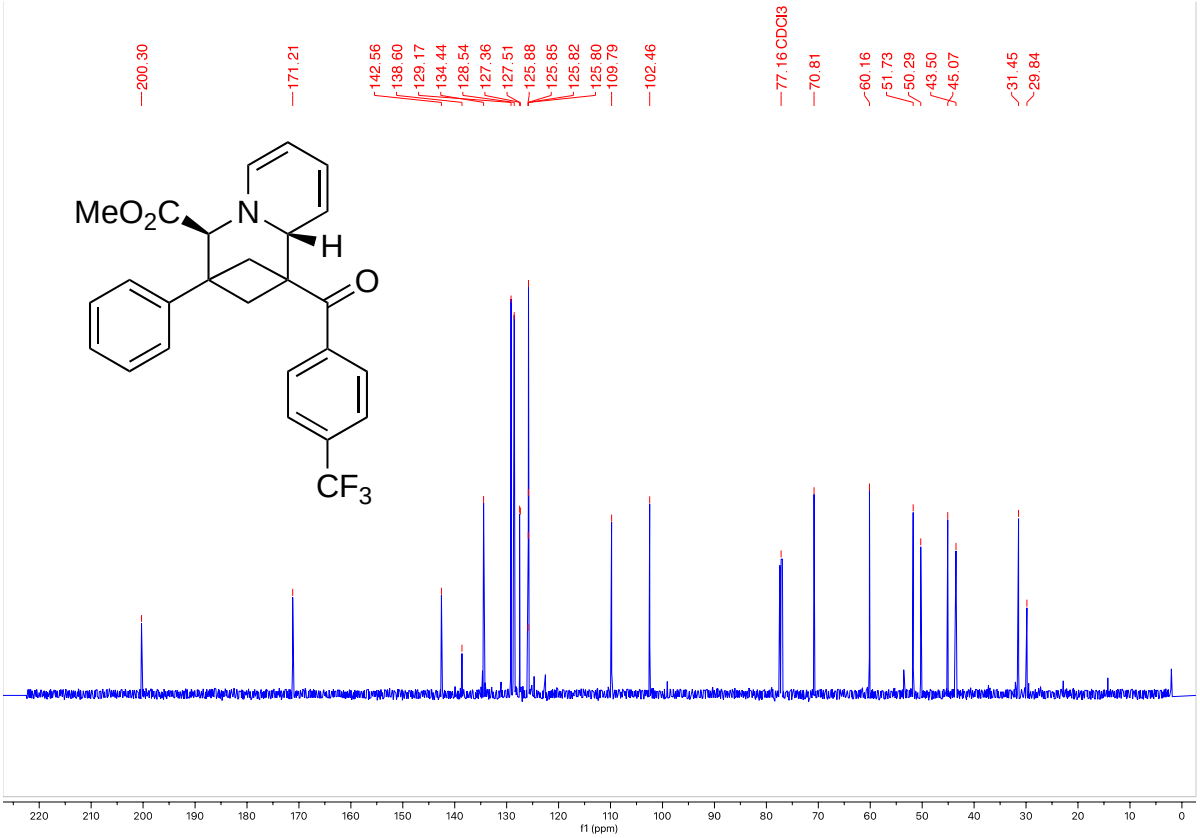
^{1}H NMR (500 MHz, $CDCl_3$, 292 K, ppm): δ 7.98 (d, J = 8.2 Hz, 1H), 7.71 (d, J = 8.2 Hz, 2H), 7.35 – 7.28 (m, 2H), 7.25 – 7.21 (m, 1H), 7.12 – 7.06 (m, 2H), 6.10 (dt, J = 7.0, 0.8 Hz, 1H), 6.03 (ddd, J = 9.0, 5.2, 2.2 Hz, 1H), 5.24 (ddd, J = 6.8, 5.3, 1.3 Hz, 1H), 4.79 (ddd, J = 8.9, 2.5, 1.2 Hz, 1H), 4.56 (t, J = 2.5 Hz, 1H), 4.43 (s, 1H), 3.32 (m, 4H), 2.79 – 2.69 (m, 2H), 2.55 (d, J = 10.0 Hz, 1H).



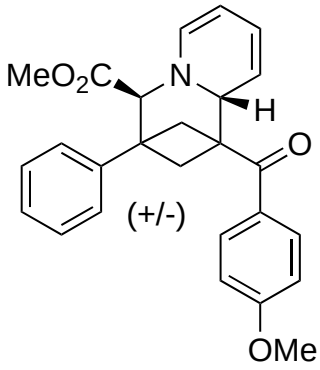
^{19}F NMR (300 MHz, $CDCl_3$, 292 K, ppm): δ 63.23.



^{13}C NMR (126 MHz, $CDCl_3$, 292 K, ppm): δ 200.30, 171.21, 142.56, 138.60, 134.44, 129.17, 128.54, 127.51, 127.36, 125.88, 125.85, 125.82, 125.80, 109.79, 102.46, 70.81, 60.16, 51.73, 50.29, 45.07, 43.50, 31.45, 29.84.



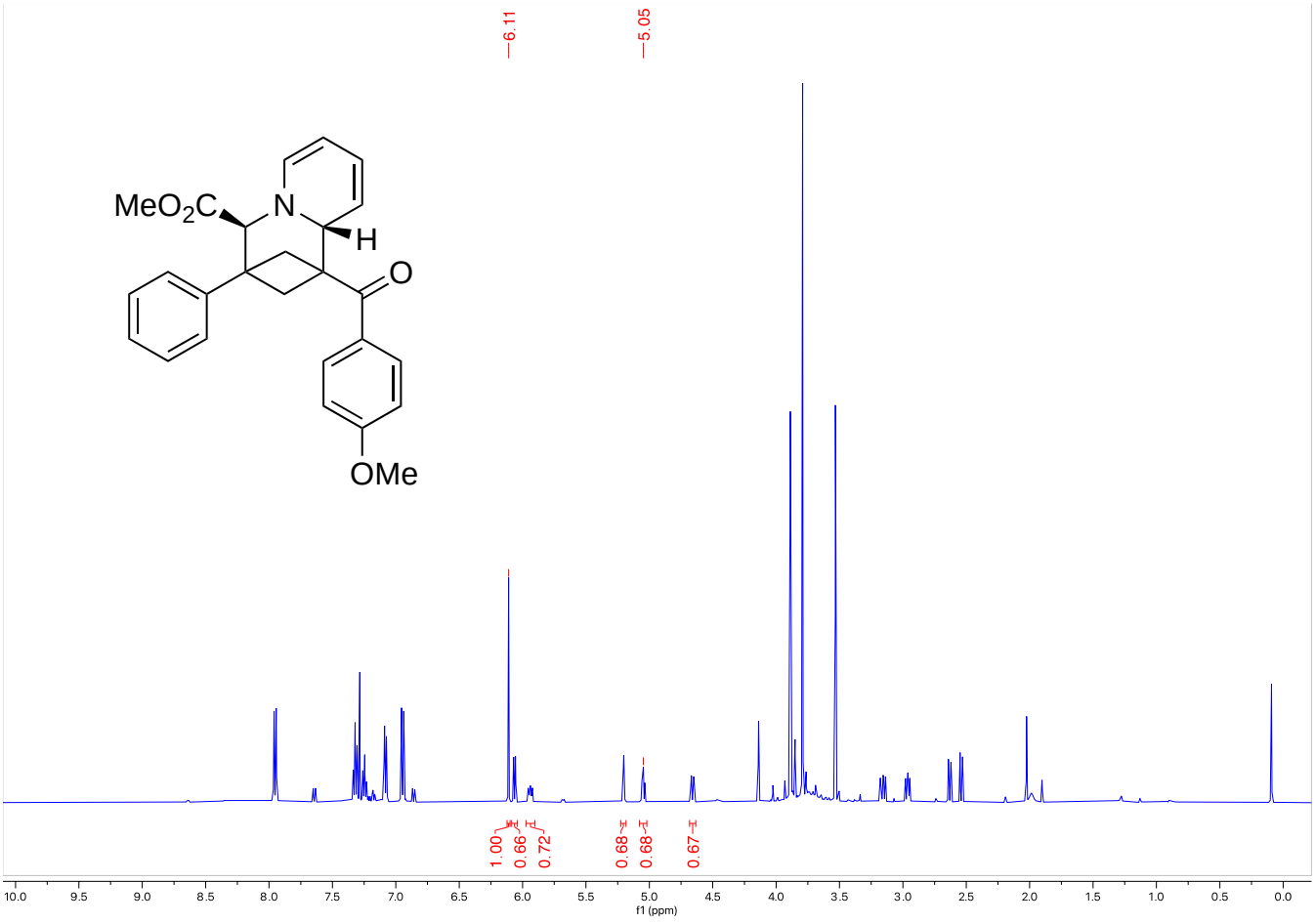
Methyl 1-(4-methoxybenzoyl)-3-phenyl-1,3,4,9a-tetrahydro-2H-1,3-methanoquinolizine-4-carboxylate (3i)



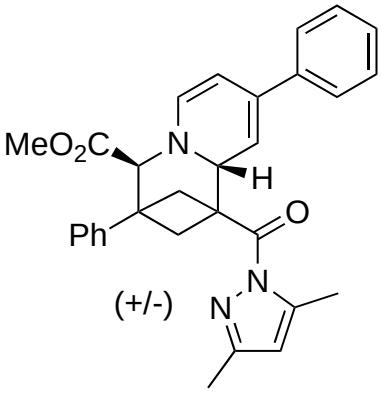
Product was synthesized following general procedure A on a 0.025 mmol scale. Reagent amounts used: bicyclobutane **1a** (6.6 mg, 0.025 mmol), pyridinium **2a** (1.25 equiv, 7.3 mg, 0.031 mmol), and K_3PO_4 (2.5 equiv, 13.3 mg, 0.063 mmol) in 0.1 mL acetonitrile (0.25 M). Solution yield determined by NMR spectroscopy using 1,3,5-trimethoxybenzene internal standard (**65% solution yield**).

HRMS(ESI): calc'd for [$C_{26}H_{25}NO_4$ + H^+], 416.18564; found: 416.18549.

^{1}H NMR (500 MHz, $CDCl_3$, 292 K):



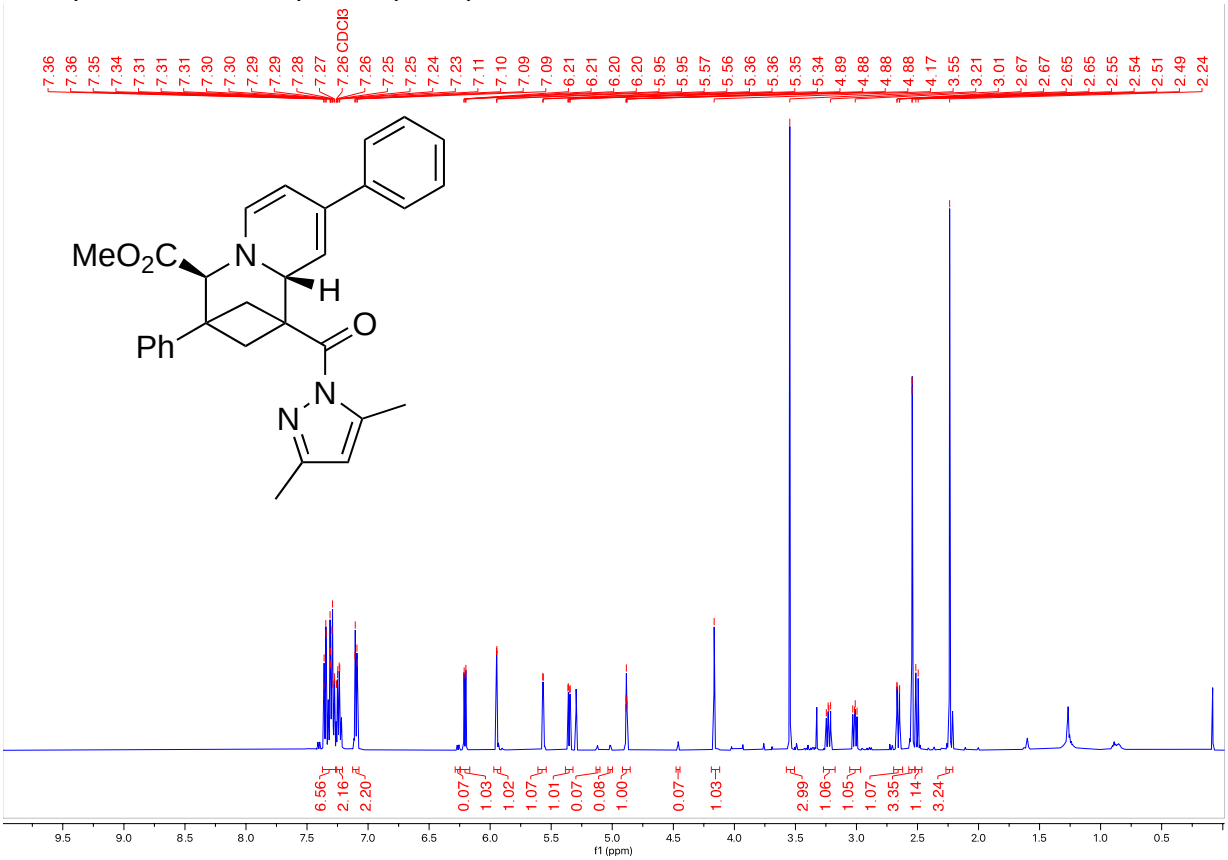
Methyl 1-(3,5-dimethyl-1H-pyrazole-1-carbonyl)-3,8-diphenyl-1,3,4,9a-tetrahydro-2H-1,3-methanoquinolizine-4-carboxylate (3j)



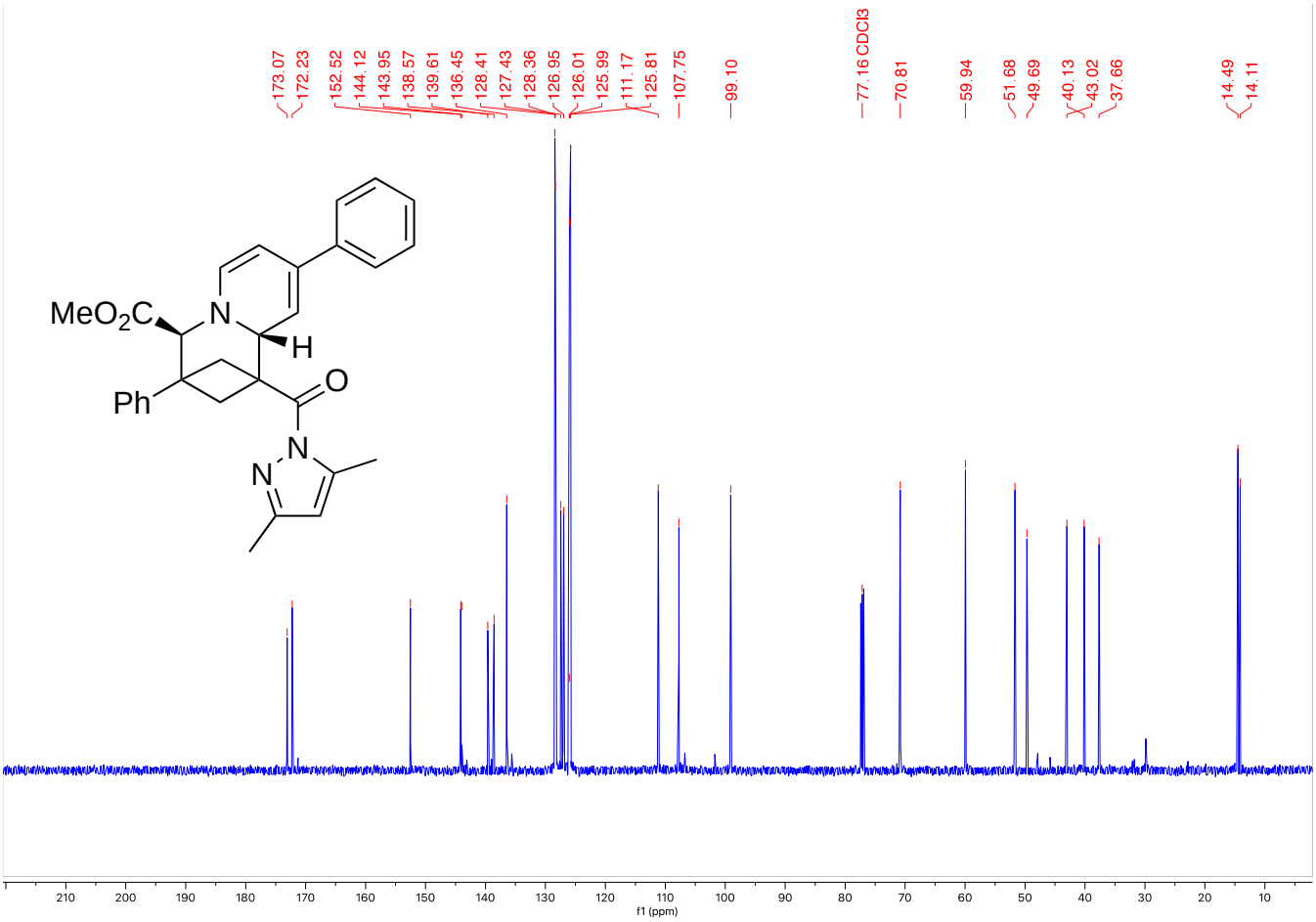
Product was synthesized following general procedure **A** on a 0.30 mmol scale. Reagent amounts used: bicyclobutane **1a** (75.7 mg, 0.30 mmol), pyridinium **2j** (1.25 equiv, 115.6 mg, 0.38 mmol), and K_3PO_4 (2.5 equiv, 159.2 mg, 0.75 mmol) in 1.2 mL acetonitrile (0.25 M). Isolated 94.4 mg of an orange solid (**66% yield, 15:1 dr**).

HRMS(ESI): calc'd for [$C_{30}H_{29}N_3O_3$ + H^+], 480.22817; found: 480.22797.

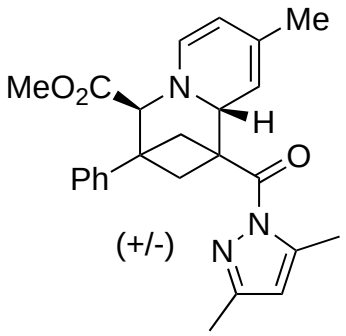
^{1}H NMR (500 MHz, $CDCl_3$, 292 K, ppm): δ 7.37 – 7.27 (m, 6H), 7.24 (dd, J = 7.3, 1.7 Hz, 2H), 7.10 (dd, J = 8.2, 1.3 Hz, 2H), 6.21 (dd, J = 7.2, 0.8 Hz, 1H), 5.95 (d, J = 1.2 Hz, 1H), 5.57 (d, J = 2.6 Hz, 1H), 5.35 (dd, J = 7.3, 1.9 Hz, 1H), 4.92 – 4.85 (m, 1H), 4.17 (s, 1H), 3.55 (s, 3H), 3.23 (dd, J = 10.2, 7.4 Hz, 1H), 3.01 (dd, J = 9.8, 7.4 Hz, 1H), 2.66 (dd, J = 10.2, 0.9 Hz, 1H), 2.54 (d, J = 1.0 Hz, 3H), 2.50 (d, J = 9.8 Hz, 1H), 2.24 (s, 3H).



^{13}C NMR (126 MHz, $CDCl_3$, 292 K, ppm): δ 173.07, 172.23, 152.52, 144.12, 143.95, 139.61, 138.57, 136.45, 128.41, 128.36, 127.43, 126.95, 126.01, 125.99, 125.81, 111.17, 107.75, 99.10, 70.81, 59.94, 51.68, 49.69, 43.02, 40.13, 37.66, 14.49, 14.11.



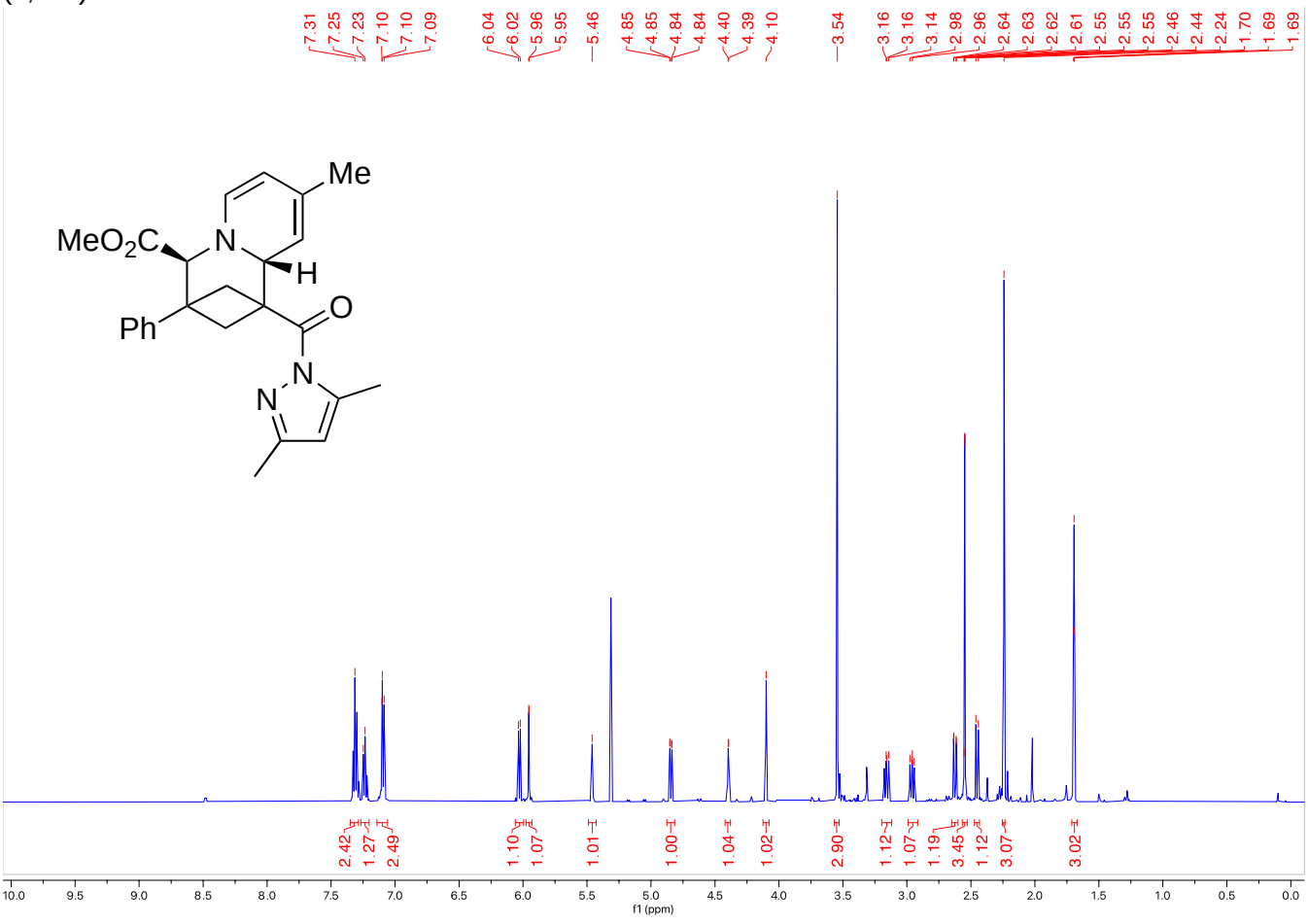
Methyl 1-(3,5-dimethyl-1H-pyrazole-1-carbonyl)-8-methyl-3-phenyl-1,3,4,9a-tetrahydro-2H-1,3-methanoquinolizine-4-carboxylate (3k)



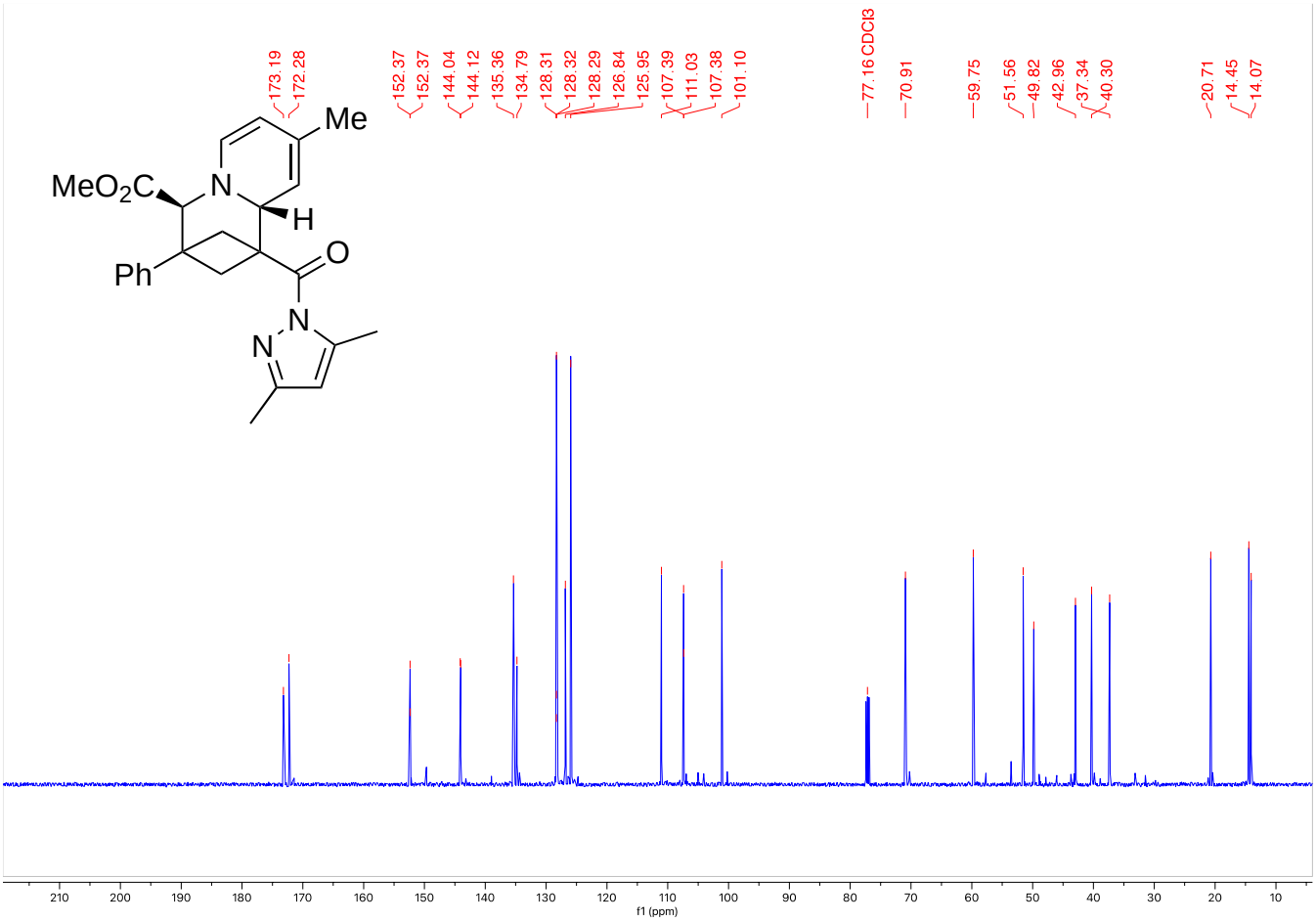
Product was synthesized following general procedure **A** on a 0.30 mmol scale. Reagent amounts used: bicyclobutane **1a** (75.7 mg, 0.30 mmol), pyridinium **2k** (1.25 equiv, 92.3 mg, 0.38 mmol), and K_3PO_4 (2.5 equiv, 159.2 mg, 0.75 mmol) in 1.2 mL acetonitrile (0.25 M). Isolated 72.0 mg of an orange solid (**58% yield**).

HRMS(ESI): calc'd for [$C_{25}H_{27}N_3O_3$ + H^+], 418.21252; found: 418.21251.

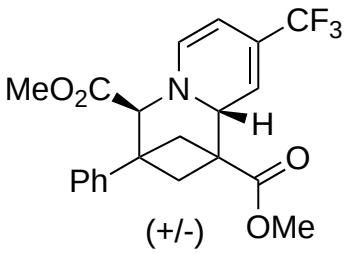
^{1}H NMR (500 MHz, $CDCl_3$, 292 K, ppm): δ 7.35 – 7.27 (m, 2H), 7.27 – 7.20 (m, 1H), 7.12 – 7.07 (m, 2H), 6.03 (d, J = 7.2 Hz, 1H), 5.95 (d, J = 1.2 Hz, 1H), 5.46 (t, J = 2.1 Hz, 1H), 4.84 (dd, J = 7.2, 1.8 Hz, 1H), 4.39 (q, J = 1.5 Hz, 1H), 4.10 (s, 1H), 3.54 (s, 3H), 3.16 (dd, J = 10.2, 7.4 Hz, 1H), 2.96 (dd, J = 9.7, 7.4 Hz, 1H), 2.62 (dd, J = 10.2, 0.9 Hz, 1H), 2.55 (d, J = 1.1 Hz, 3H), 2.45 (d, J = 9.7 Hz, 1H), 2.24 (s, 3H).



^{13}C NMR (126 MHz, $CDCl_3$, 292 K, ppm): δ 173.19, 172.28, 152.37, 152.37, 144.12, 144.04, 135.36, 134.79, 128.32, 128.31, 128.29, 126.84, 125.95, 111.03, 107.39, 107.38, 101.10, 70.91, 59.75, 51.56, 49.82, 42.96, 40.30, 37.34, 20.71, 14.45, 14.07.



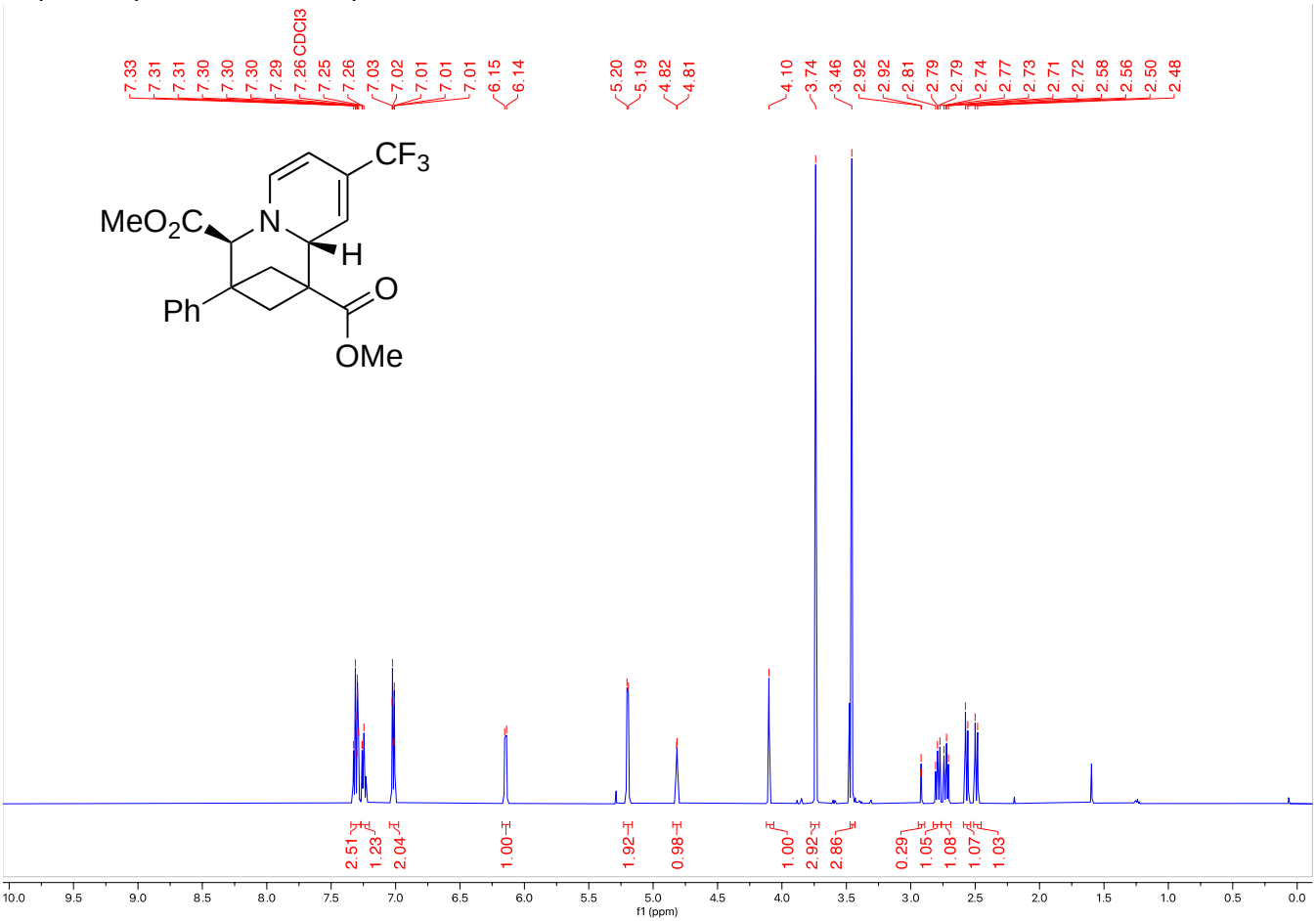
Dimethyl 3-phenyl-8-(trifluoromethyl)-3,4-dihydro-2H-1,3-methanoquinolizine-1,4(9aH)-dicarboxylate (3l)



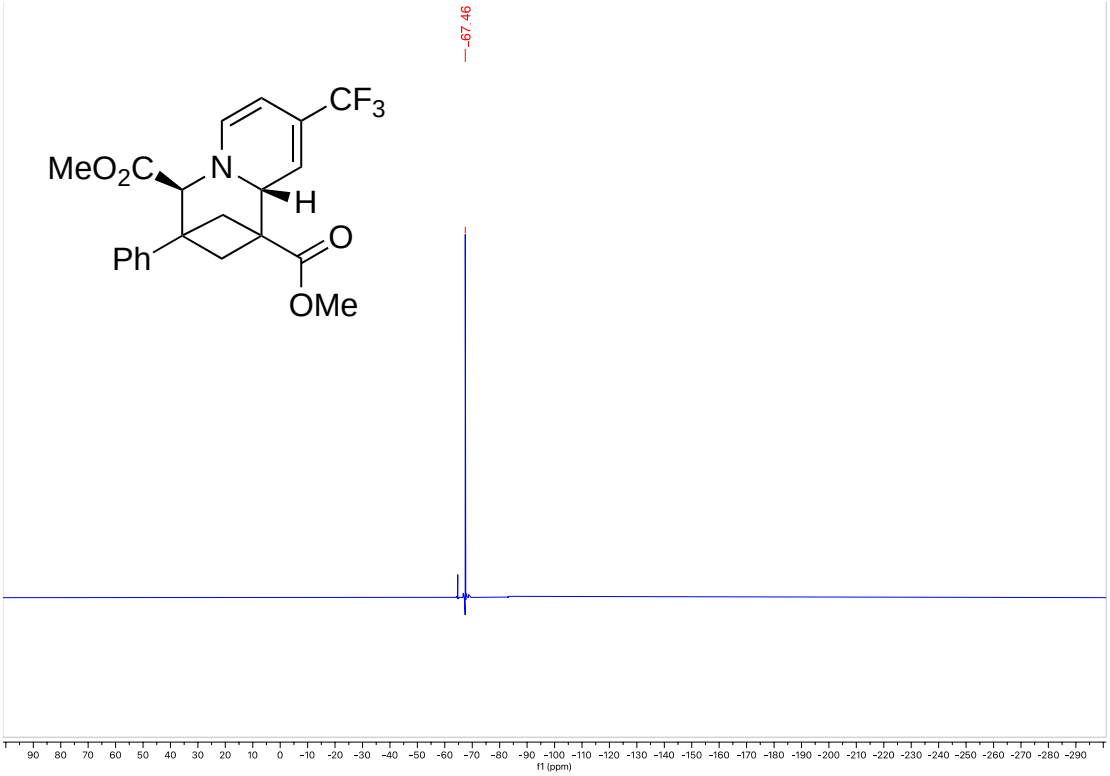
Product was synthesized following general procedure **A** on a 0.50 mmol scale. Reagent amounts used: bicyclobutane **1a** (126.2 mg, 0.30 mmol), pyridinium **2l** (1.25 equiv, 187.5 mg, 0.63 mmol), and K_3PO_4 (2.5 equiv, 265.3 mg, 1.25 mmol) in 2.0 mL **methanol** (0.25 M) and the reaction was cooled to 5 °C for the bicyclobutane addition to pyridnium/base. Isolated 122.0 mg of a light yellow solid (**60% yield,** additional 15% methyl ester bicyclobutane).

HRMS(ESI): calc'd for [$C_{21}H_{20}F_3NO_4$ + H^+], 408.14172; found: 408.14150.

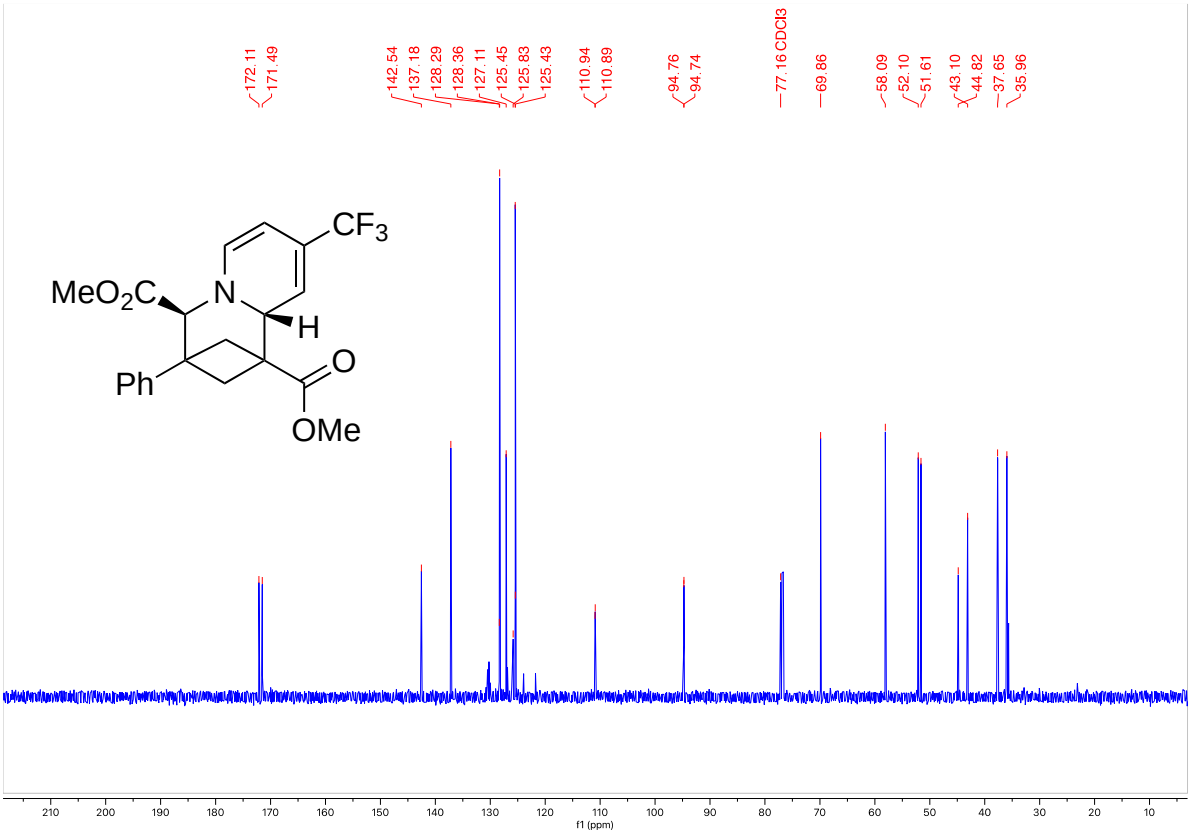
^{1}H NMR (500 MHz, $CDCl_3$, 292 K, ppm): δ 7.35 – 7.27 (m, 2H), 7.25 (d, J = 7.3 Hz, 1H), 7.05 – 6.98 (m, 2H), 6.15 (d, J = 7.7 Hz, 1H), 5.20 (d, J = 5.9 Hz, 2H), 4.82 (d, J = 1.9 Hz, 1H), 4.10 (s, 1H), 3.74 (s, 3H), 3.46 (s, 3H), 2.79 (dd, J = 9.7, 7.5 Hz, 1H), 2.72 (dd, J = 9.7, 7.5 Hz, 1H), 2.57 (d, J = 9.7 Hz, 1H), 2.49 (d, J = 9.6 Hz, 1H).



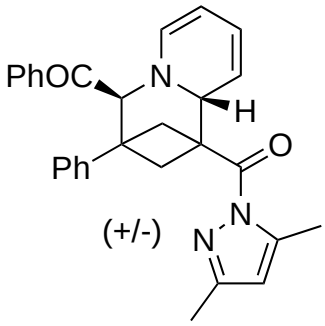
^{19}F NMR (300 MHz, $CDCl_3$, 292 K, ppm): δ 67.46



^{13}C NMR (126 MHz, $CDCl_3$, 292 K, ppm): δ 172.11, 171.49, 142.54, 137.18, 128.36, 128.29, 127.11, 125.83, 125.45, 125.43, 110.94, 110.89, 94.76, 94.74, 69.86, 58.09, 52.10, 51.61, 44.82, 43.10, 37.65, 35.96.



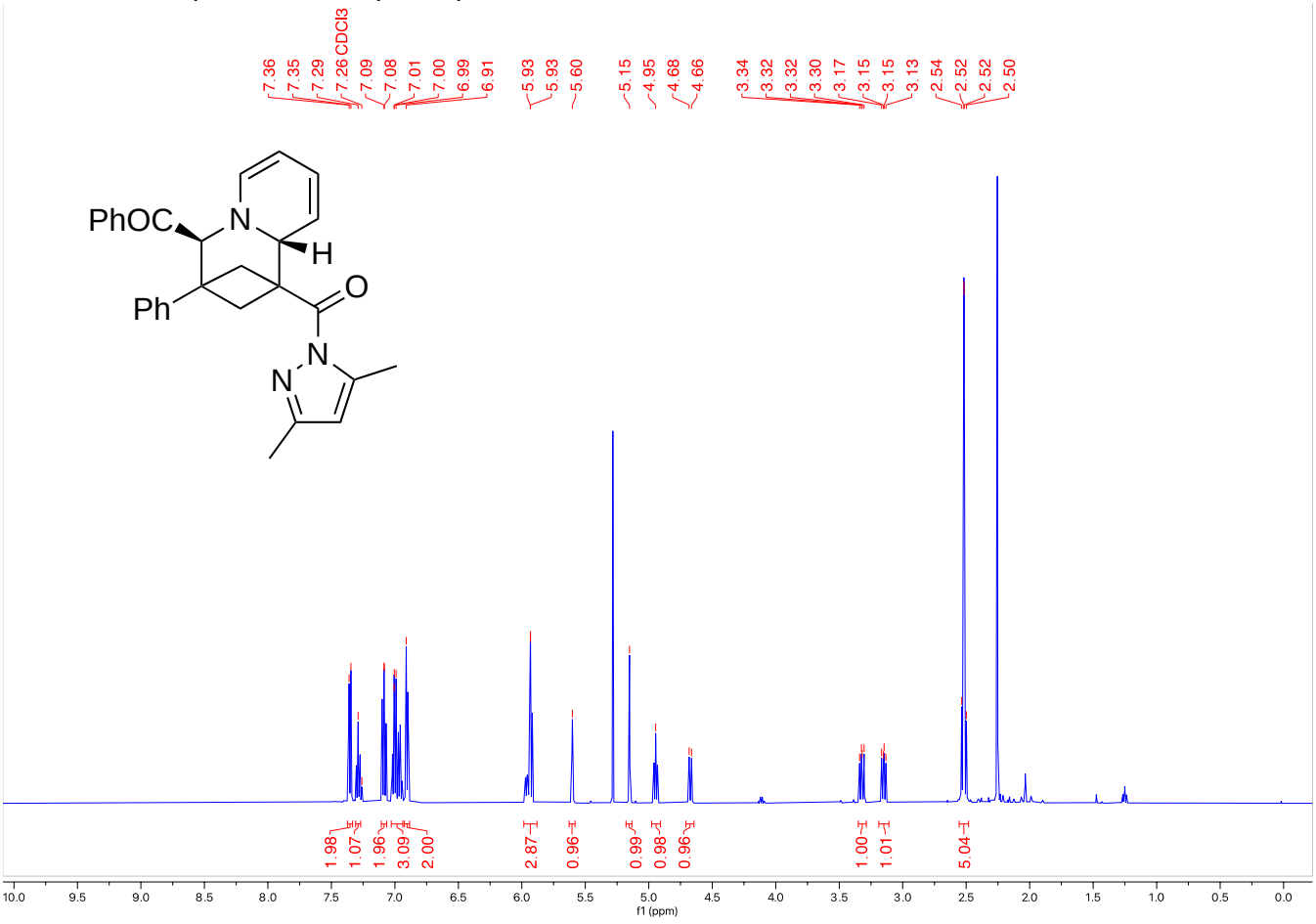
4-Benzoyl-3-phenyl-3,4-dihydro-2H-1,3-methanoquinolizin-1(9aH)-yl)(3,5-dimethyl-1H-pyrazol-1-yl)methanone (3m)



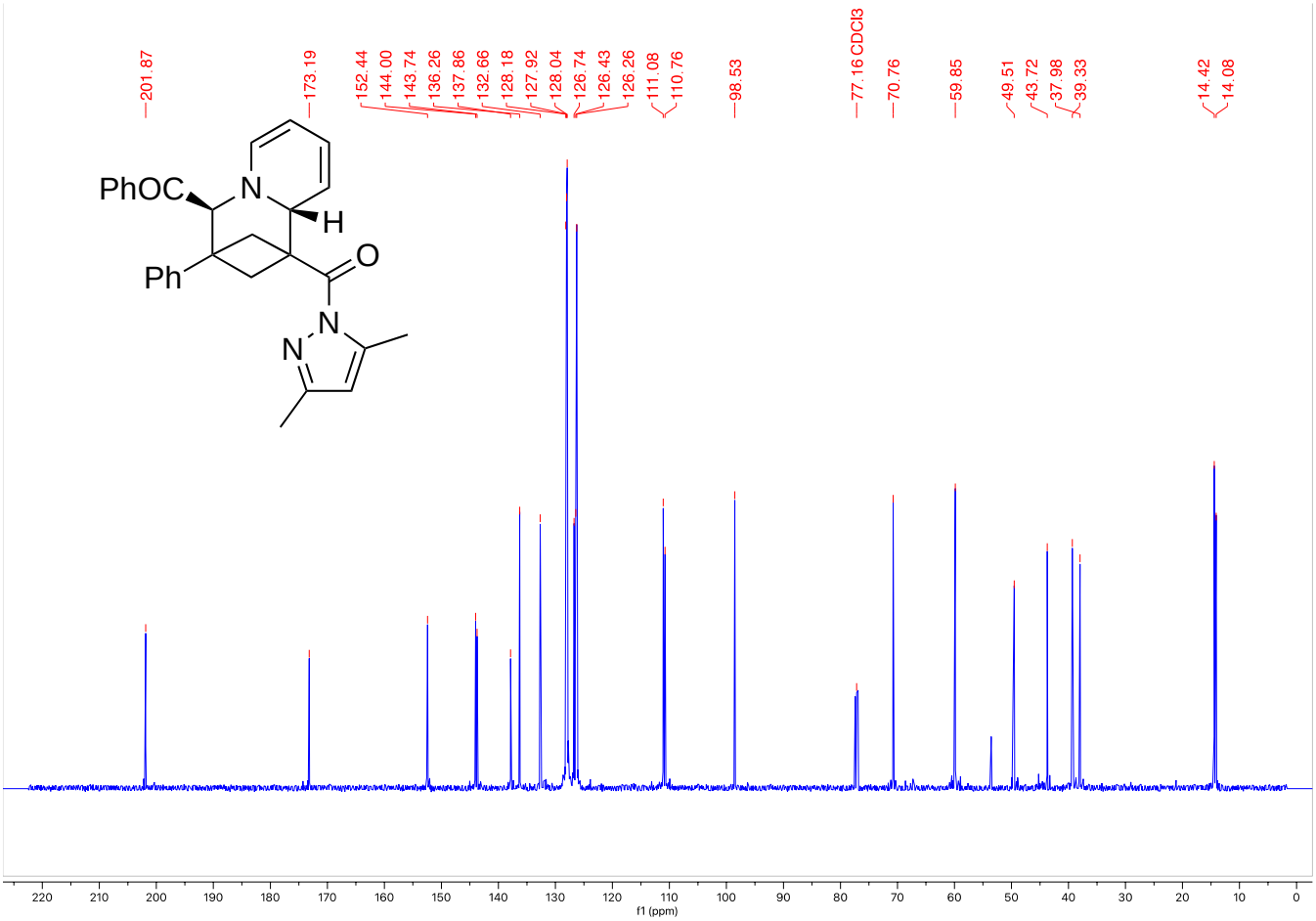
Product was synthesized following general procedure **B** on a 1.0 mmol scale. Reagent amounts used: bicyclobutane **1a** (252.3 mg, 1.0 mmol), pyridinium **2f** (1.25 equiv, 318.7 mg, 1.15 mmol), $NaPF_6$ (1.3 equiv, 218.3 mg, 1.30 mmol) and K_3PO_4 (2.5 equiv, 530.7 mg, 2.5 mmol) in 4.0 mL acetonitrile (0.25 M). Isolated 338.7 mg of an orange solid (**75% yield**).

HRMS(ESI): calc'd for [$C_{29}H_{27}N_3O_2$ + H^+], 450.21761; found: 450.21745.

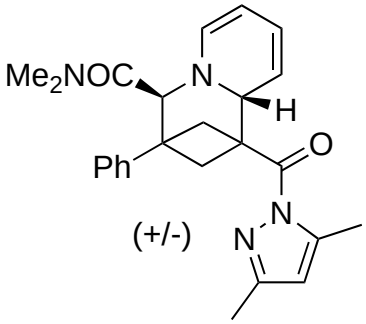
^{1}H NMR (300 MHz, $CDCl_3$, 292 K, ppm): δ 7.35 (m, 2H), 7.29 (m, 1H), 7.11 – 7.06 (m, 2H), 7.03 – 6.94 (m, 3H), 6.92 – 6.88 (m, 2H), 5.98 – 5.88 (m, 3H), 5.60 (t, J = 2.3 Hz, 1H), 5.15 (s, 1H), 4.95 (ddd, J = 6.9, 5.4, 1.4 Hz, 1H), 4.67 (ddt, J = 9.3, 2.2, 1.1 Hz, 1H), 3.32 (dd, J = 10.1, 7.4 Hz, 1H), 3.15 (dd, J = 9.5, 7.4 Hz, 1H), 2.55 – 2.48 (m, 5H).



^{13}C NMR (300 MHz, $CDCl_3$, 292 K, ppm): δ 201.87, 173.19, 152.44, 144.00, 143.74, 137.86, 136.26, 132.66, 128.18, 128.04, 127.92, 126.74, 126.43, 126.26, 111.08, 110.76, 98.53, 70.76, 59.85, 49.51, 43.72, 39.33, 37.98, 14.42, 14.08.



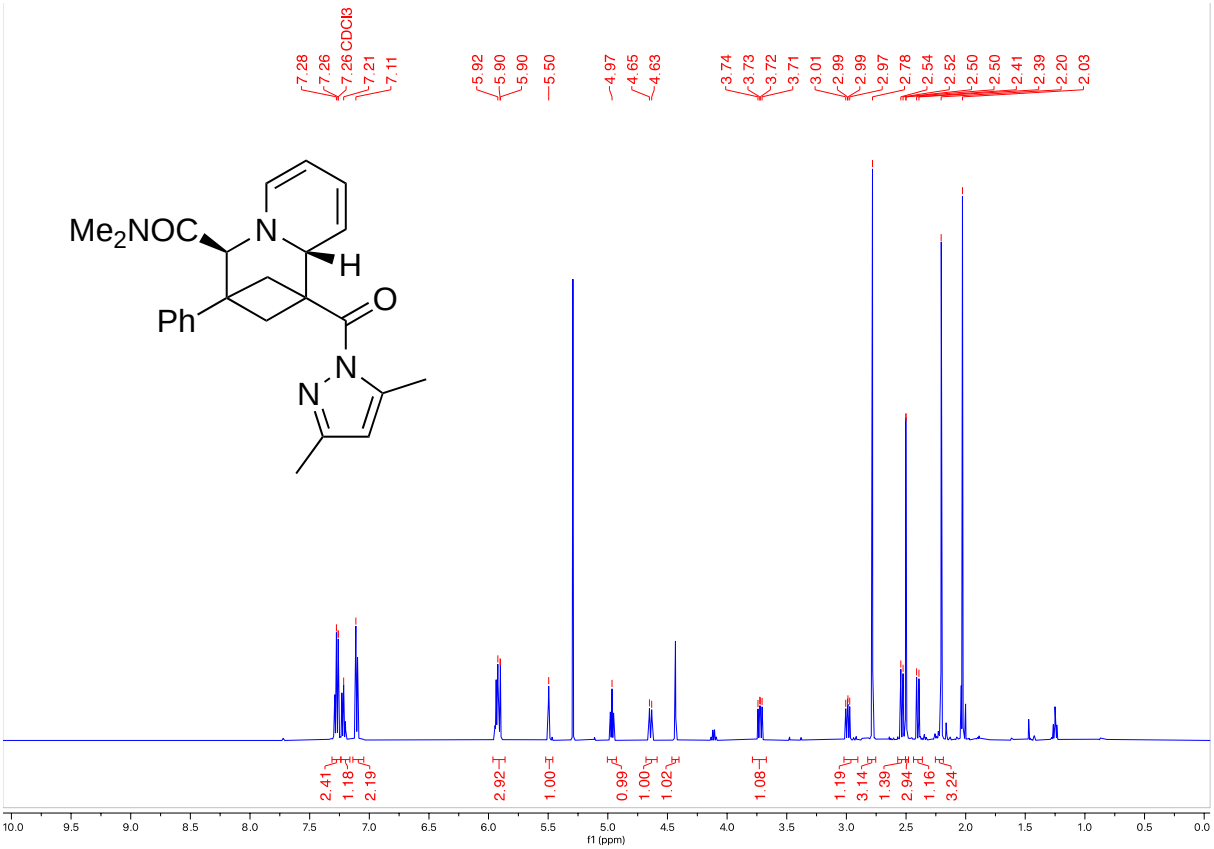
1-(3,5-Dimethyl-1H-pyrazole-1-carbonyl)-N,N-dimethyl-3-phenyl-1,3,4,9a-tetrahydro-2H-1,3-methanoquinolizine-4-carboxamide (3n)



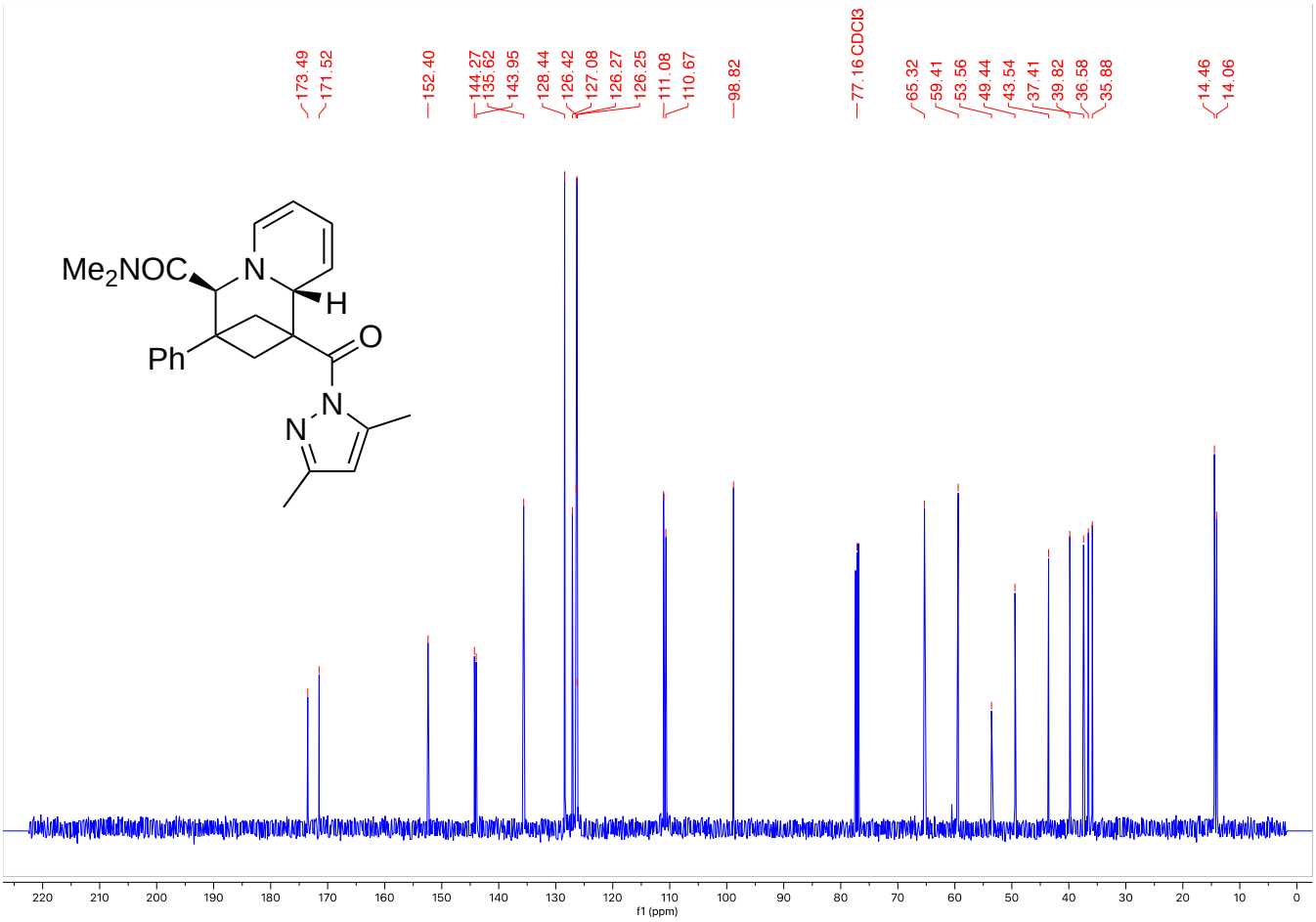
Product was synthesized following general procedure A on a 0.30 mmol scale. The reaction was conducted for 24 hours before a second charge of pyridinium and base was added, and stirred for another 24 hours. Reagent amounts used: bicyclobutane **1a** (75.7 mg, 0.30 mmol), pyridinium **2n** (2.5 equiv, 183.1 mg, 0.75 mmol, two portions), and K_3PO_4 (4 equiv, 254.7 mg, 1.20 mmol, two portions) in 1.2 mL acetonitrile (0.25 M). Product was purified by two successive elutions through a basic alumina plug. Isolated 42.3 mg of an orange oil (**34% yield**)

HRMS(ESI): calc'd for [$C_{25}H_{28}N_4O_2$ + H^+], 417.22851; found: 417.22821.

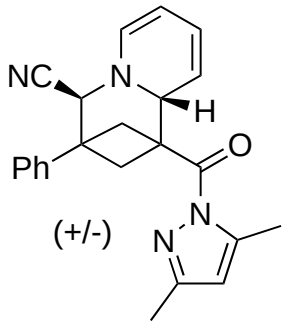
^{1}H NMR (500 MHz, $CDCl_3$, 292 K, ppm): δ 7.31 – 7.24 (m, 2H), 7.24 – 7.16 (m, 1H), 7.14 – 7.05 (m, 2H), 5.96 – 5.86 (m, 3H), 5.50 (t, J = 2.5 Hz, 1H), 4.97 (ddd, J = 6.8, 5.3, 1.3 Hz, 1H), 4.68 – 4.59 (m, 1H), 4.43 (s, 1H), 3.72 (dd, J = 9.9, 7.4 Hz, 1H), 2.99 (dd, J = 9.5, 7.4 Hz, 1H), 2.78 (s, 3H), 2.53 (d, J = 9.5 Hz, 1H), 2.50 (d, J = 1.1 Hz, 3H), 2.40 (d, J = 9.9 Hz, 1H), 2.21 (s, 3H).



^{13}C NMR (126 MHz, $CDCl_3$, 292 K, ppm): δ 173.49, 171.52, 152.40, 144.27, 143.95, 135.62, 128.44, 127.08, 126.42, 126.27, 126.25, 111.08, 110.67, 98.82, 65.32, 59.41, 53.56, 49.44, 43.54, 39.82, 37.41, 36.58, 35.88, 14.46, 14.06.



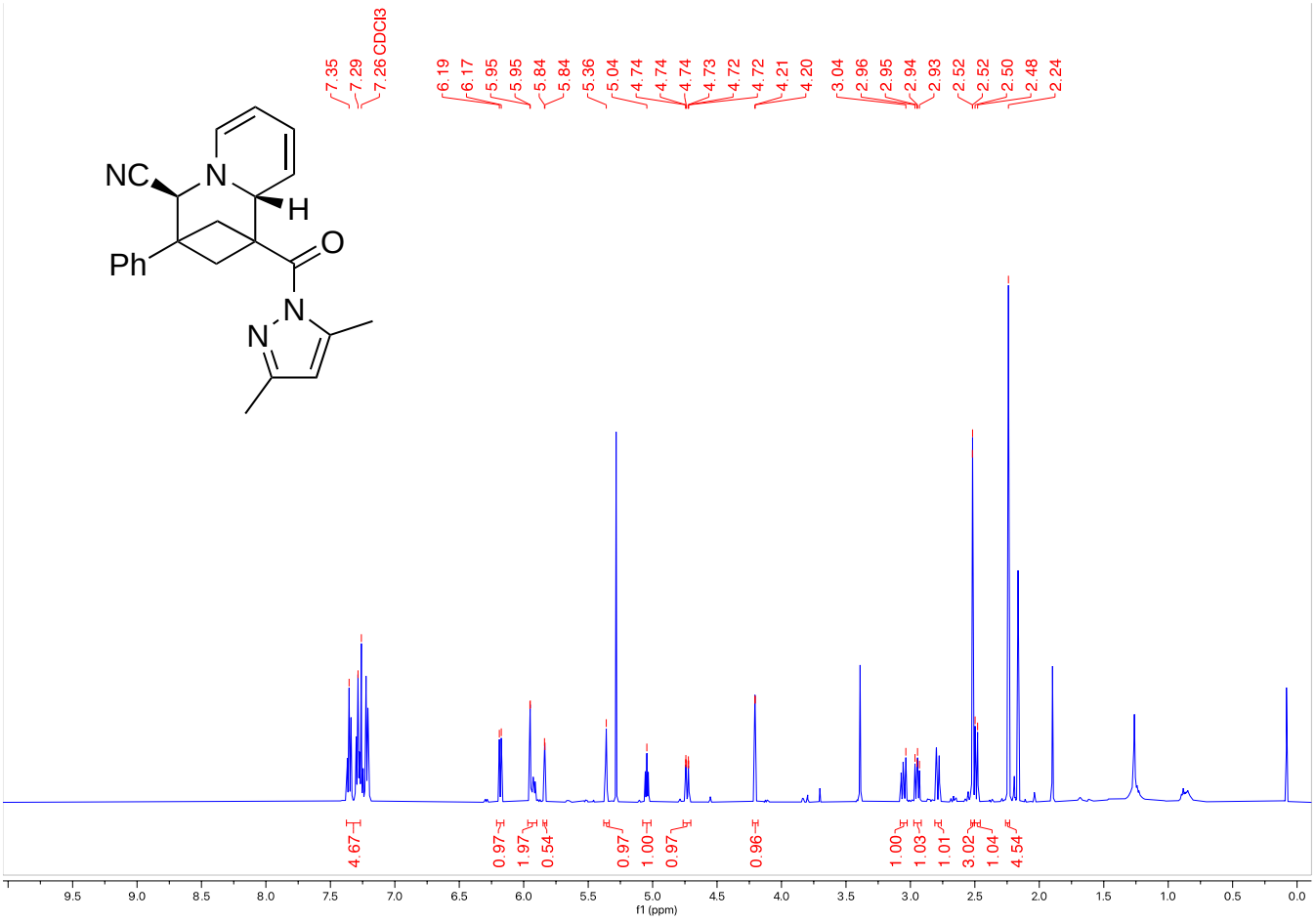
1-(3,5-dimethyl-1H-pyrazole-1-carbonyl)-3-phenyl-1,3,4,9a-tetrahydro-2H-1,3-methanoquinolizine-4-carbonitrile (3o)



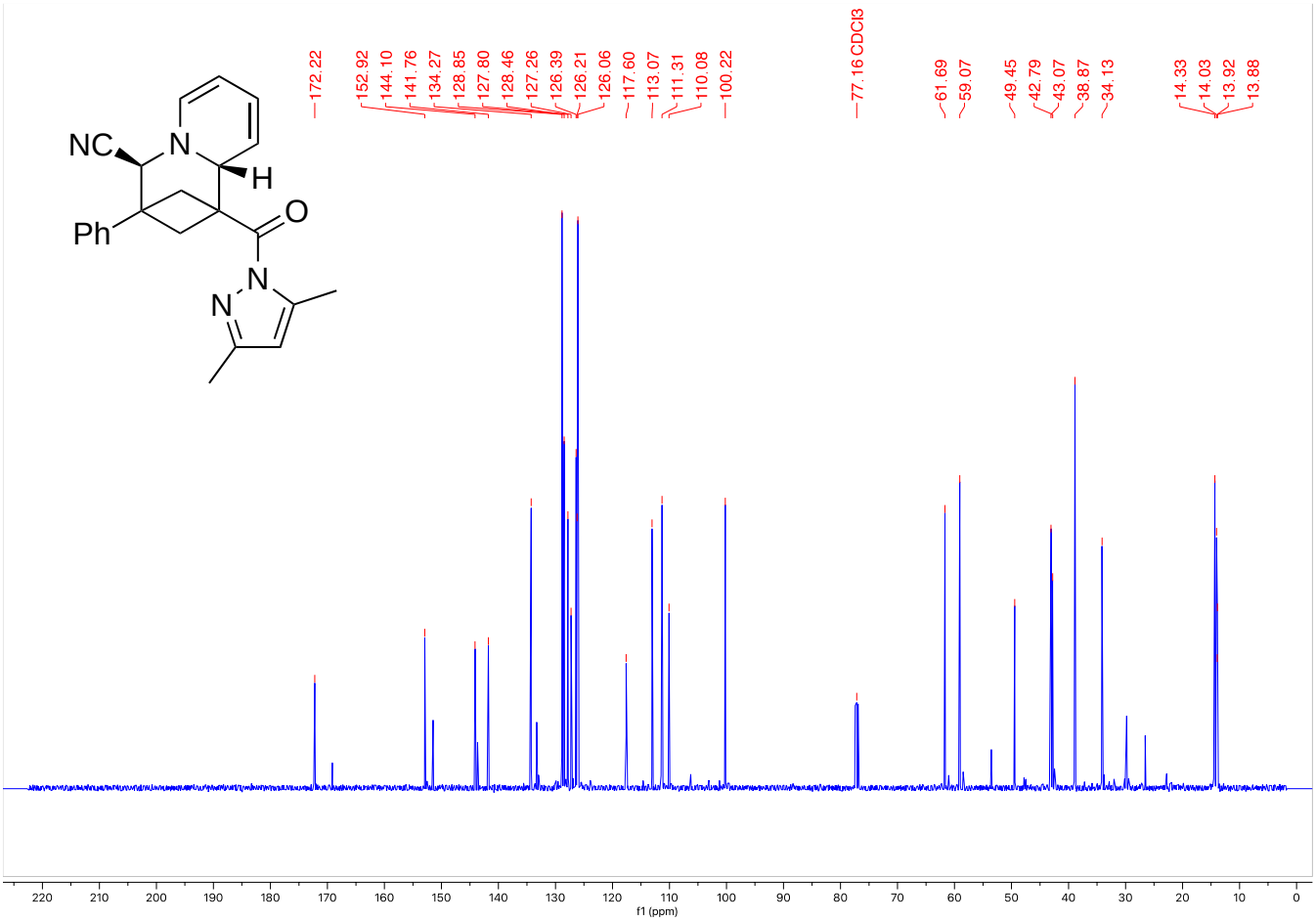
Product was synthesized following general procedure **B** on a 0.30 mmol scale with a 72 h reaction time. Reagent amounts used: bicyclobutane **1a** (75.7 mg, 0.30 mmol), pyridinium **2o** (1.25 equiv, 74.3 mg, 0.38 mmol), $NaPF_6$ (1.3 equiv, 65.5 mg, 0.39 mmol) and K_3PO_4 (2.5 equiv, 159.2 mg, 0.75 mmol) in 1.2 mL acetonitrile (0.25 M). Isolated 78.3 mg of a pale yellow oil (**46% yield,** additional 25% unreacted **1a**).

HRMS(ESI): calc'd for [$C_{31}H_{31}N_3O_4$ + H^+], 371.18664; found: 371.18638.

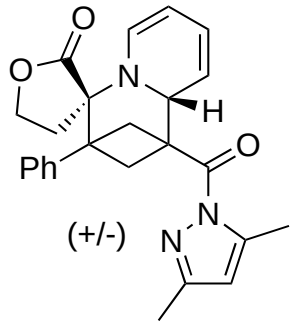
^{1}H NMR (500 MHz, $CDCl_3$, 292 K, ppm): δ 7.38 – 7.27 (m, 5H), 6.18 (dd, J = 7.2, 1.0 Hz, 1H), 5.97 – 5.90 (m, 2H), 5.84 (d, J = 1.3 Hz, 1H), 5.36 (t, J = 2.3 Hz, 1H), 5.04 (ddd, J = 6.9, 5.4, 1.3 Hz, 1H), 4.73 (ddt, J = 9.5, 2.2, 1.1 Hz, 1H), 4.21 (s, 1H), 3.05 (dd, J = 10.6, 7.5 Hz, 1H), 2.95 (dd, J = 9.9, 7.5 Hz, 1H), 2.79 (dd, J = 10.6, 1.3 Hz, 1H), 2.52 (d, J = 1.1 Hz, 3H), 2.49 (d, J = 10.0 Hz, 1H), 2.24 (s, 3H).



^{13}C NMR (126 MHz, $CDCl_3$, 292 K, ppm): δ 172.22, 152.92, 144.10, 141.76, 134.27, 128.85, 128.46, 127.80, 127.26, 126.39, 126.21, 126.06, 117.60, 113.07, 111.31, 110.08, 100.22, 61.69, 59.07, 49.45, 43.07, 42.79, 38.87, 34.13, 14.33, 14.03, 13.92, 13.88.



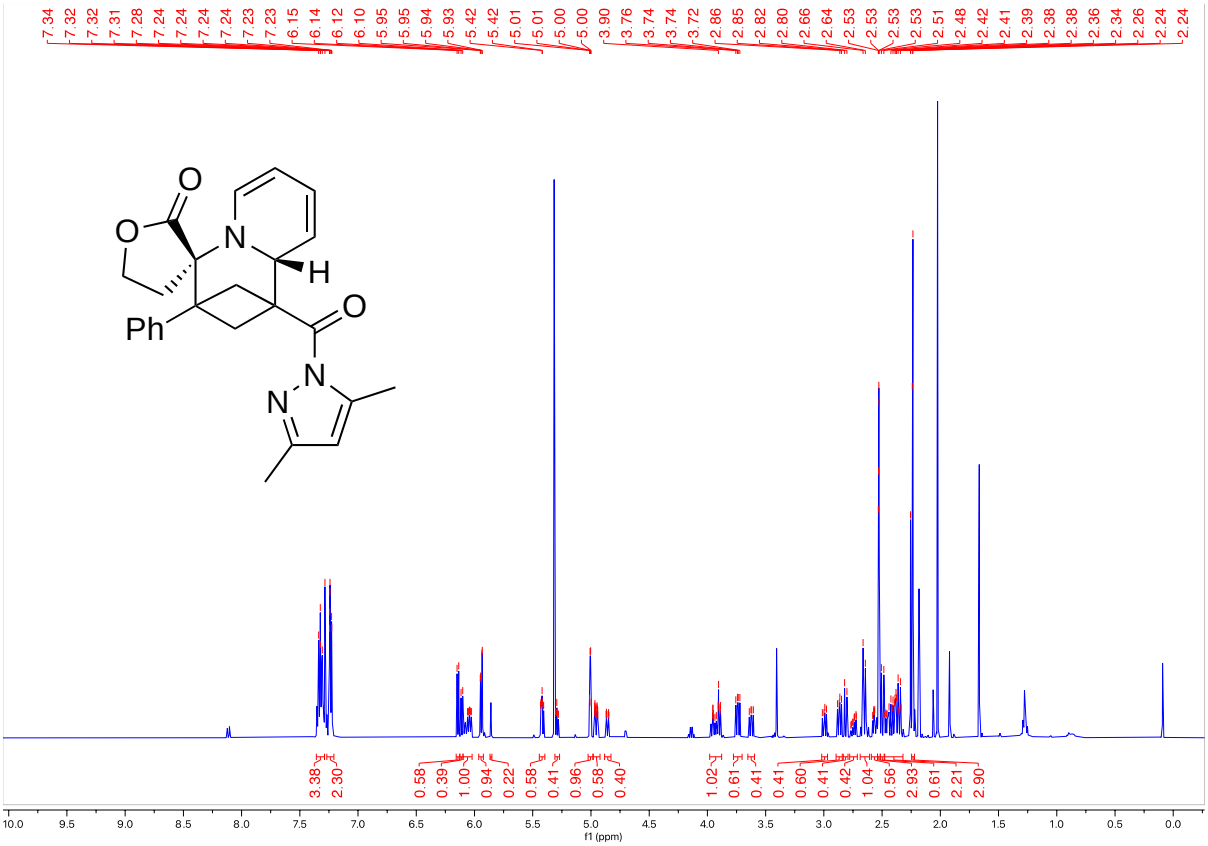
1'-(3,5-dimethyl-1H-pyrazole-1-carbonyl)-3'-phenyl-1',2',3',4,5,9a'-hexahydro-2H-spiro[furan-3,4'-[1,3]methanoquinolizin]-2-one (3p)



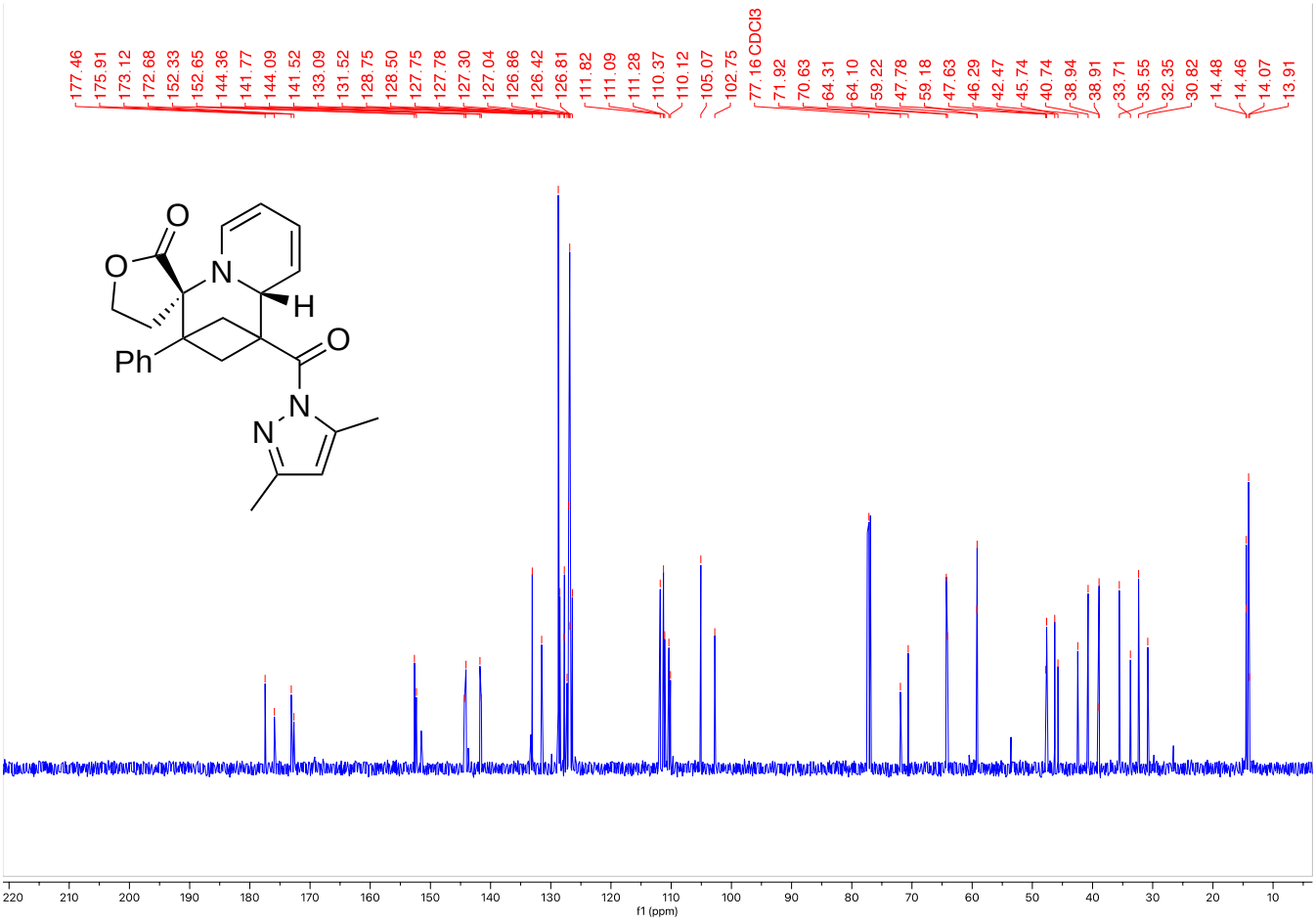
Product was synthesized following general procedure **A** on a 0.30 mmol scale with a reaction time of 72 h. Reagent amounts used: bicyclobutane **1a** (75.7 mg, 0.30 mmol), pyridinium **2p** (1.25 equiv, 91.5 mg, 0.38 mmol), and K_3PO_4 (2.5 equiv, 159.2 mg, 0.75 mmol) in 1.2 mL acetonitrile (0.25 M). Isolated 87.9 mg of an orange solid as a mixture of diastereomers (**59% yield, 1.5:1 dr,** additional 13% unreacted **1a**).

HRMS(ESI): calc'd for [$C_{25}H_{25}N_3O_3$ + H^+], 416.19687; found: 416.19723.

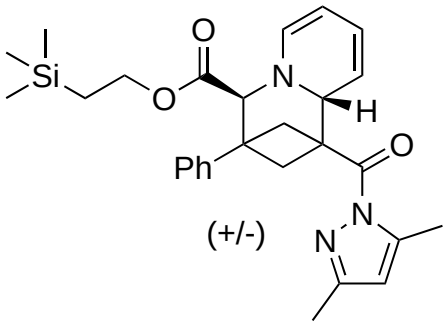
^{1}H NMR (500 MHz, $CDCl_3$, 292 K, ppm): δ 7.32 (dd, J = 8.4, 7.6 Hz, 3H), 7.27 – 7.21 (m, 2H), 6.14 (d, J = 7.0 Hz, 0.6H), 6.04 (ddd, J = 9.0, 5.1, 2.2 Hz, 0.4H), 5.94 (m, 1H), 5.42 (ddd, J = 6.7, 5.1, 1.3 Hz, 0.6H), 5.31 – 5.27 (m, 0.4H), 5.01 (m, 1H), 4.95 (dddd, J = 8.9, 2.9, 1.3, 0.7 Hz, 0.6H), 4.88 – 4.81 (m, 0.4H), 3.98 – 3.88 (m, 1H), 3.74 (dd, J = 10.4, 7.2 Hz, 0.6H), 3.62 (dd, J = 10.2, 7.2 Hz, 0.4H), 3.00 (dd, J = 10.4, 7.2 Hz, 0.4H), 2.87 (dd, J = 10.1, 7.2 Hz, 0.6H), 2.81 (d, J = 10.3 Hz, 0.4H), 2.74 (ddd, J = 13.7, 7.7, 2.0 Hz, 0.4H), 2.65 (d, J = 10.1 Hz, 1H), 2.59 – 2.54 (m, 0.6H), 2.53 (dd, J = 2.4, 1.0 Hz, 3H), 2.50 (d, J = 10.4 Hz, 0.6H), 2.48 – 2.32 (m, 2H), 2.24 (d, J = 3.0 Hz, 3H).



^{13}C NMR (126 MHz, $CDCl_3$, 292 K, ppm): δ 177.46, 175.91, 173.12, 172.68, 152.65, 152.33, 144.36, 144.09, 141.77, 141.52, 133.09, 131.52, 128.75, 128.50, 127.78, 127.75, 127.30, 127.04, 126.86, 126.81, 126.42, 111.82, 111.28, 111.09, 110.37, 110.12, 105.07, 102.75, 71.92, 70.63, 64.31, 64.10, 59.22, 59.18, 47.78, 47.63, 46.29, 45.74, 42.47, 40.74, 38.94, 38.91, 35.55, 33.71, 32.35, 30.82, 14.48, 14.46, 14.07, 13.91.



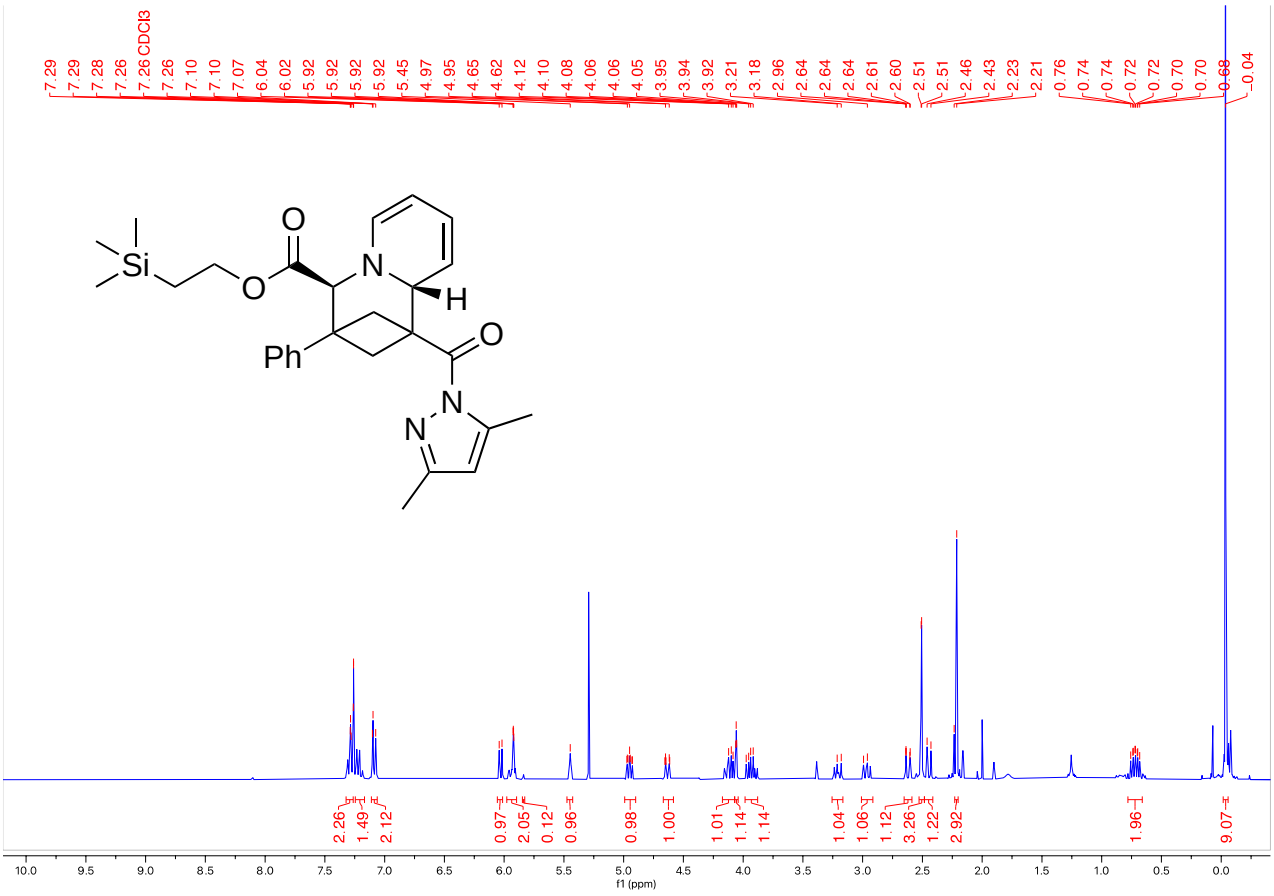
2-(Trimethylsilyl)ethyl 1-(3,5-dimethyl-1H-pyrazole-1-carbonyl)-3-phenyl-1,3,4,9a-tetrahydro-2H-1,3-methanoquinolizine-4-carboxylate (3q)



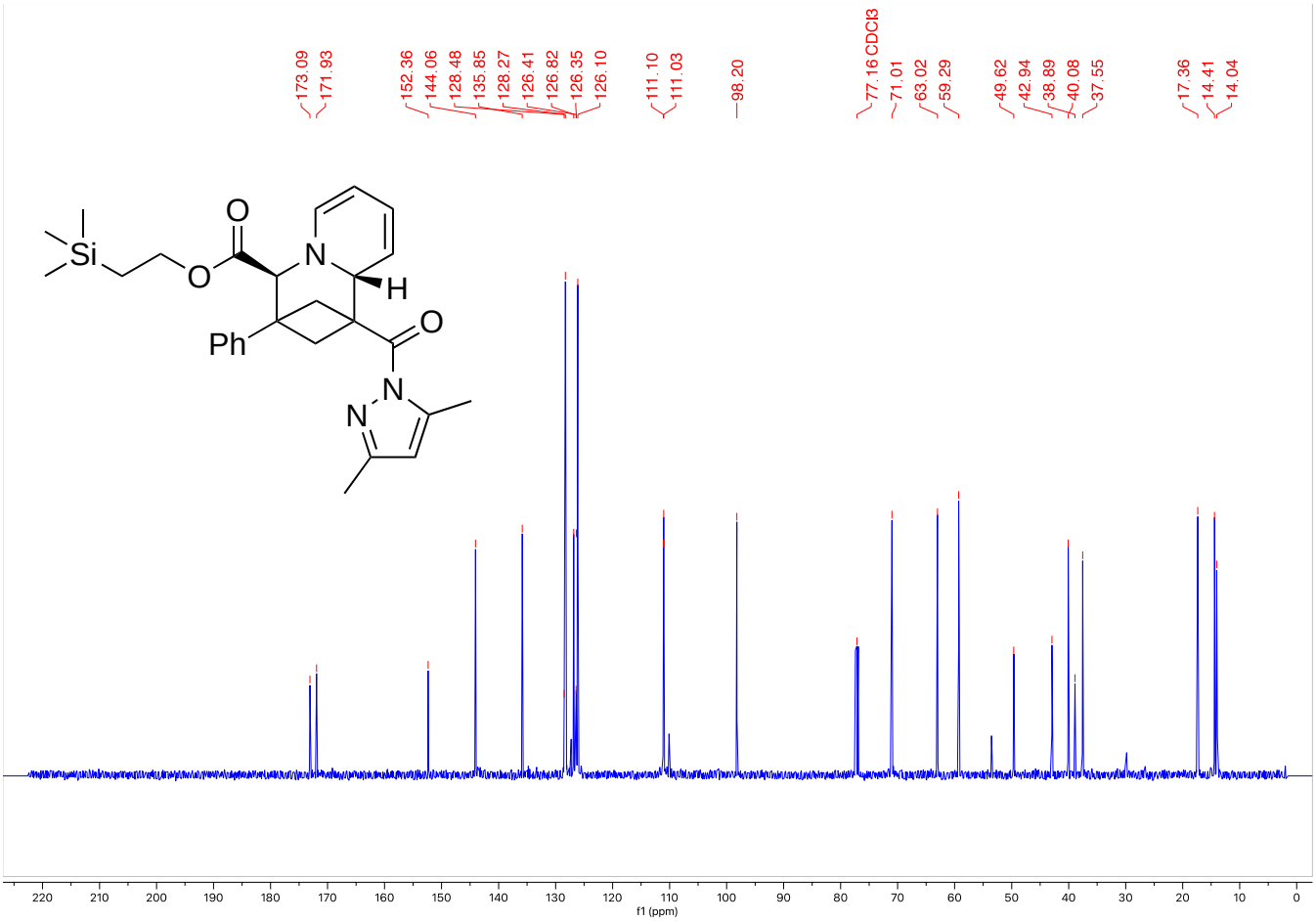
Product was synthesized following general procedure **A** on a 0.30 mmol scale. Reagent amounts used: bicyclobutane **1a** (75.7 mg, 0.30 mmol), pyridinium **2q** (1.25 equiv, 119.4 mg, 0.38 mmol), and K_3PO_4 (2.5 equiv, 159.2 mg, 0.75 mmol) in 1.2 mL acetonitrile (0.25 M). Isolated 124.0 mg of an orange oil (**75% yield,** additional 9% unreacted **1a**).

HRMS(ESI): calc'd for [$C_{28}H_{35}N_3O_3Si$ + H^+], 490.25205; found: 490.25209.

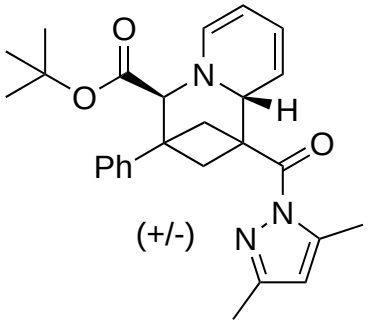
H NMR (500 MHz, $CDCl_3$, 292 K, ppm): δ 7.32 – 7.26 (m, 2H), 7.25 – 7.17 (m, 1H), 7.11 – 7.06 (m, 2H), 6.03 (dt, J = 7.0, 0.9 Hz, 1H), 5.98 – 5.90 (m, 2H), 5.44 (d, J = 2.3 Hz, 1H), 4.95 (ddd, J = 6.9, 5.4, 1.3 Hz, 1H), 4.63 (dddd, J = 9.4, 2.3, 1.3, 0.9 Hz, 1H), 4.17 – 4.07 (m, 1H), 4.06 (d, J = 1.4 Hz, 1H), 3.93 (td, J = 10.9, 6.5 Hz, 1H), 3.21 (dd, J = 10.2, 7.4 Hz, 1H), 2.96 (dd, J = 9.7, 7.4 Hz, 1H), 2.65 – 2.59 (m, 1H), 2.51 (d, J = 1.1 Hz, 3H), 2.44 (d, J = 9.7 Hz, 1H), 2.21 (s, 3H), 0.78 – 0.66 (m, 2H), -0.04 (s, 9H).



^{13}C NMR (126 MHz, $CDCl_3$, 292 K, ppm): δ 173.09, 171.93, 152.36, 144.06, 135.85, 128.48, 128.27, 126.82, 126.41, 126.35, 126.10, 111.10, 111.03, 98.20, 71.01, 63.02, 59.29, 49.62, 42.94, 40.08, 38.89, 37.55, 17.36, 14.41, 14.04.



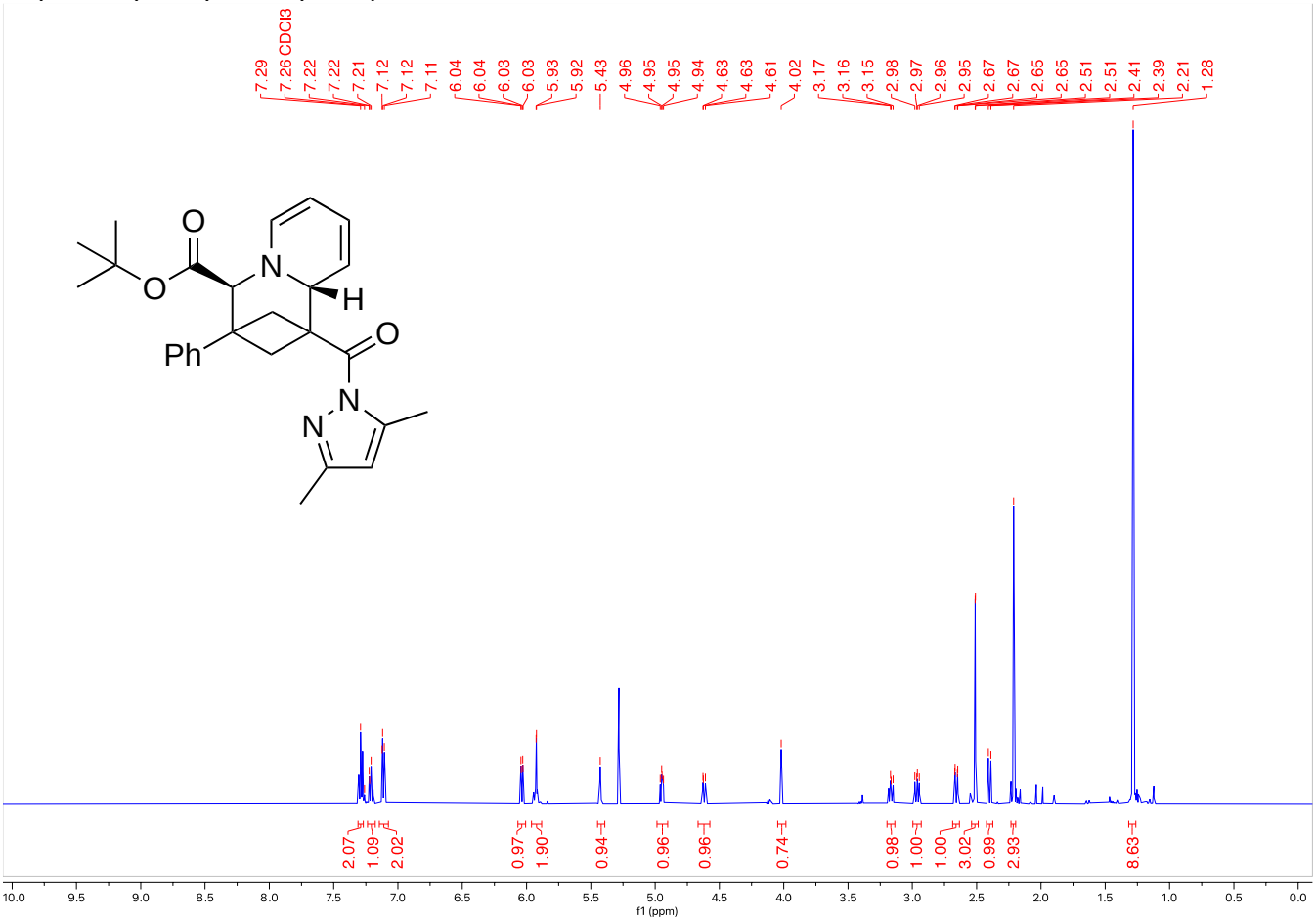
***Tert*-butyl 1-(3,5-dimethyl-1H-pyrazole-1-carbonyl)-3-phenyl-1,3,4,9a-tetrahydro-2H-1,3-methanoquinolizine-4-carboxylate (3r)**



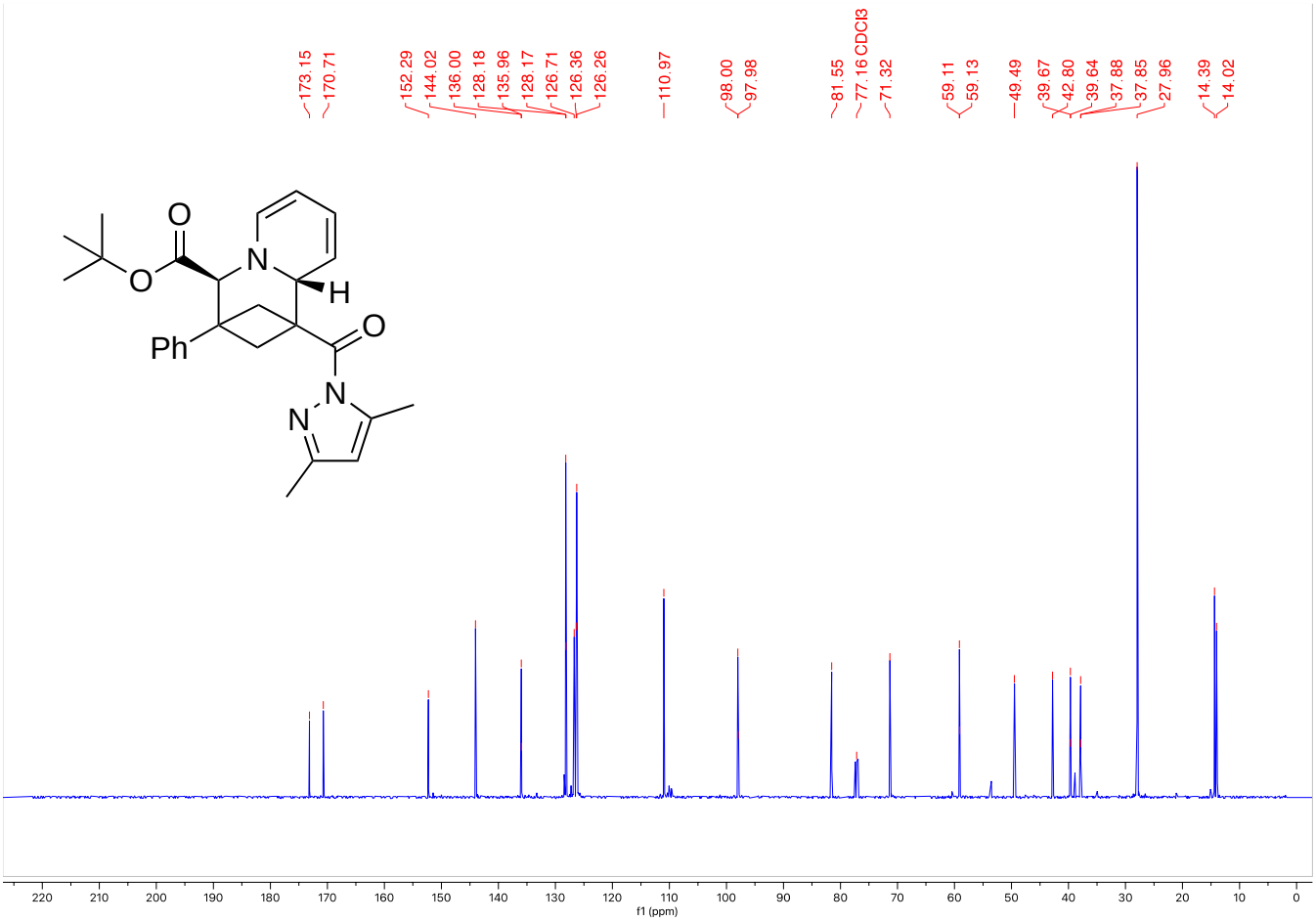
Product was synthesized following general procedure A on a 0.30 mmol scale. Reagent amounts used: bicyclobutane **1a** (81.1 mg, 0.30 mmol), pyridinium **2r** (1.25 equiv, 102.4 mg, 0.38 mmol), and K_3PO_4 (2.5 equiv, 159.2 mg, 0.75 mmol) in 1.2 mL acetonitrile (0.25 M). Isolated 101.7 mg of an orange oil (**61% yield**).

HRMS(ESI): calc'd for [$C_{27}H_{31}N_3O_3$ + H^+], 446.24382; found: 446.24392

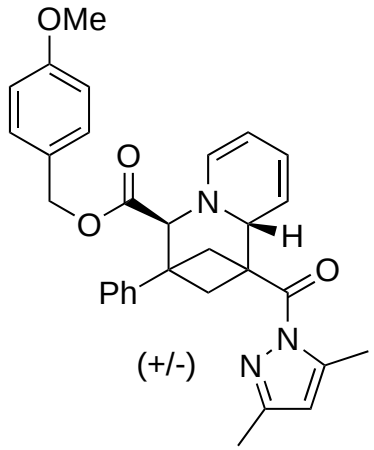
^{1}H NMR (500 MHz, $CDCl_3$, 292 K, ppm): δ 7.31 – 7.27 (m, 2H), 7.24 – 7.18 (m, 1H), 7.14 – 7.07 (m, 2H), 6.04 (dd, J = 7.1, 0.9 Hz, 1H), 5.96 – 5.88 (m, 2H), 5.43 (t, J = 2.4 Hz, 1H), 4.95 (ddt, J = 6.7, 5.4, 1.2 Hz, 1H), 4.62 (ddt, J = 9.4, 2.3, 1.1 Hz, 1H), 4.02 (s, 1H), 3.17 (ddd, J = 10.2, 7.5, 2.9 Hz, 1H), 2.96 (dd, J = 9.6, 7.4 Hz, 1H), 2.66 (dd, J = 10.1, 1.2 Hz, 1H), 2.51 (d, J = 1.0 Hz, 3H), 2.40 (d, J = 9.6 Hz, 1H), 2.21 (s, 3H), 1.28 (s, 9H).



^{13}C NMR (126 MHz, $CDCl_3$, 292 K, ppm): δ 173.15, 170.71, 152.29, 144.02, 136.00, 135.96, 128.18, 128.17, 126.71, 126.36, 126.26, 110.97, 98.00, 97.98, 81.55, 71.32, 59.13, 59.11, 49.49, 42.80, 39.67, 39.64, 37.88, 37.85, 27.96, 14.39, 14.02.



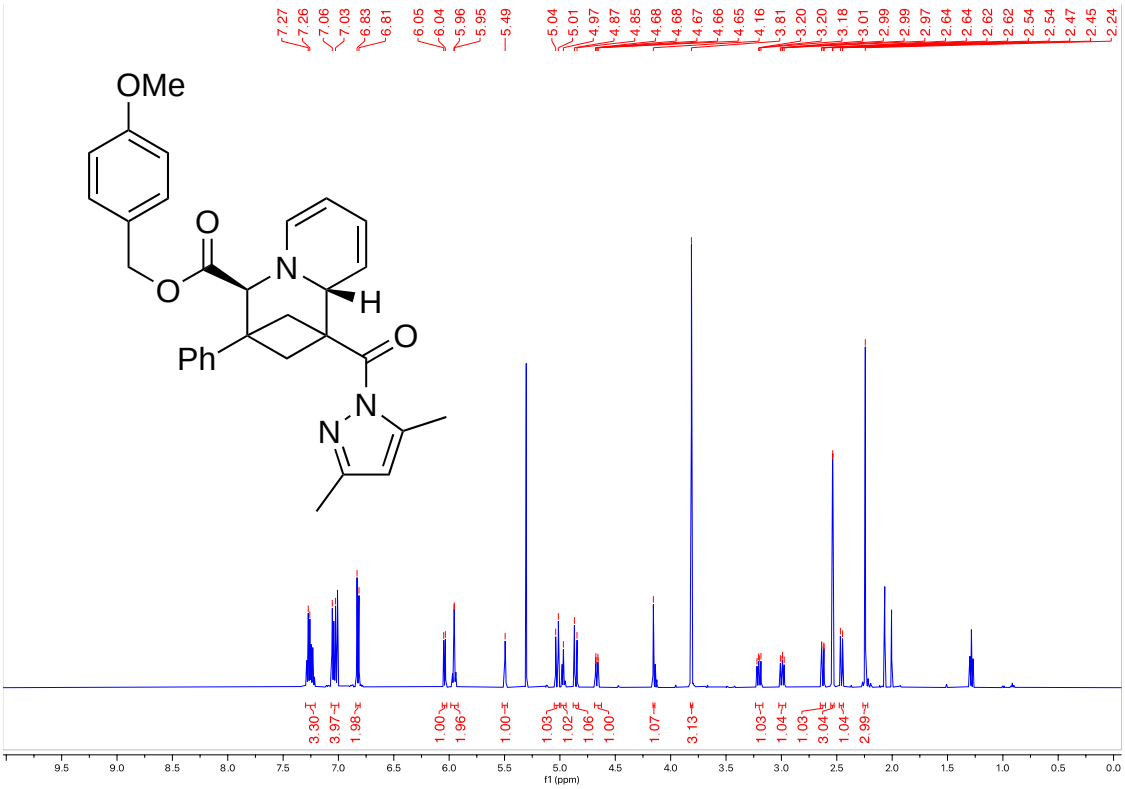
4-Methoxybenzyl (1r,3r)-1-(3,5-dimethyl-1H-pyrazole-1-carbonyl)-3-phenyl-1,3,4,9a-tetrahydro-2H-1,3-methanoquinolizine-4-carboxylate (3s)



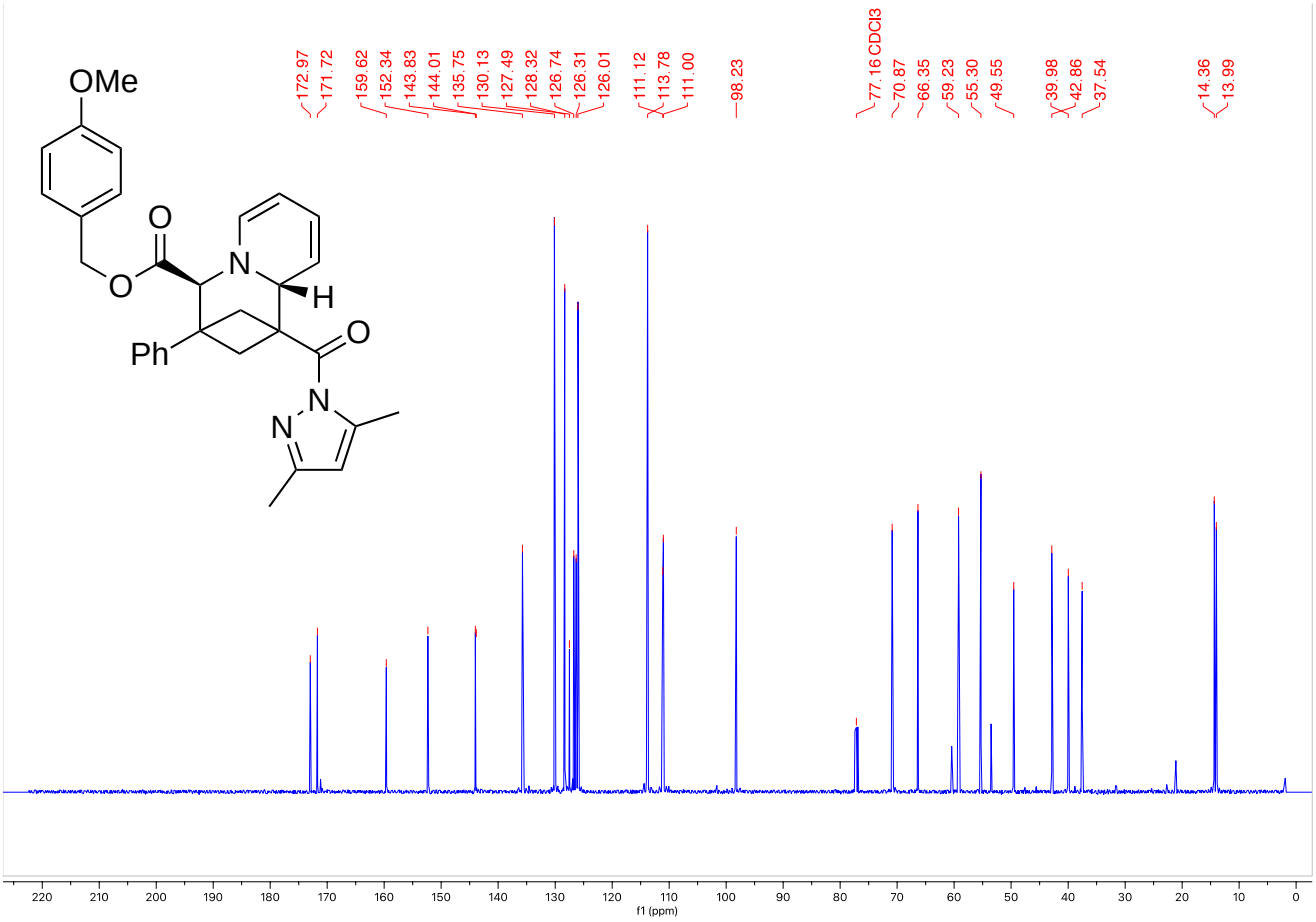
Product was synthesized following general procedure A on a 0.30 mmol scale. Reagent amounts used: bicyclobutane **1a** (81.1 mg, 0.30 mmol), pyridinium **2s** (1.25 equiv, 126.4 mg, 0.38 mmol), and K_3PO_4 (2.5 equiv, 159.2 mg, 0.75 mmol) in 1.2 mL acetonitrile (0.25 M). Isolated 136.2 mg of an orange oil (**71% yield**).

HRMS(ESI): calc'd for [$C_{31}H_{31}N_3O_4$ + H^+], 510.23874; found: 510.24009.

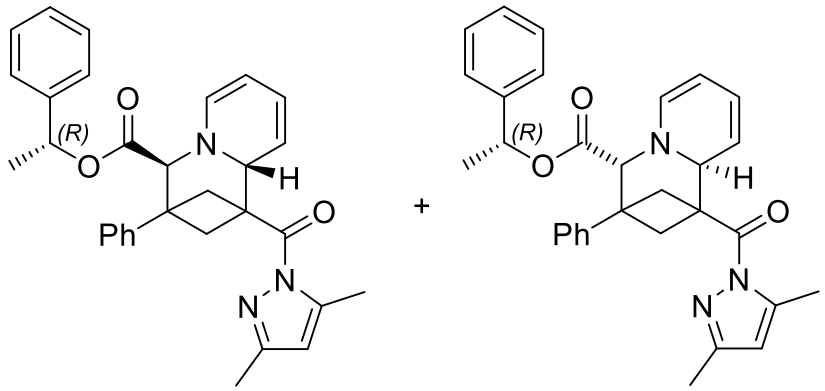
^{1}H NMR (500 MHz, $CDCl_3$, 292 K, ppm): δ 7.30 – 7.21 (m, 3H), 7.07 – 7.00 (m, 4H), 6.84 – 6.80 (m, 2H), 6.04 (d, J = 7.0,1H), 5.99 – 5.92 (m, 2H), 5.52 – 5.47 (m, 1H), 5.03 (d, J = 12.0 Hz, 1H), 4.97 (ddd, J = 6.9, 5.4, 1.3 Hz, 1H), 4.86 (d, J = 12.0 Hz, 1H), 4.67 (ddt, J = 9.4, 2.2, 1.1 Hz, 1H), 4.16 (s, 1H), 3.81 (s, 3H), 3.20 (dd, J = 10.2, 7.4 Hz, 1H), 2.99 (dd, J = 9.7, 7.4 Hz, 1H), 2.63 (d, J = 10.3, 1H), 2.54 (d, J = 1.1 Hz, 3H), 2.46 (d, J = 9.7 Hz, 1H), 2.24 (s, 3H).



^{13}C NMR (126 MHz, $CDCl_3$, 292 K, ppm): 172.97, 171.72, 159.62, 152.34, 144.01, 143.83, 135.75, 130.13, 128.32, 127.49, 126.74, 126.31, 126.01, 113.78, 111.12, 111.00, 98.23, 70.87, 66.35, 59.23, 55.30, 49.55, 42.86, 39.98, 37.54, 14.36, 13.99.



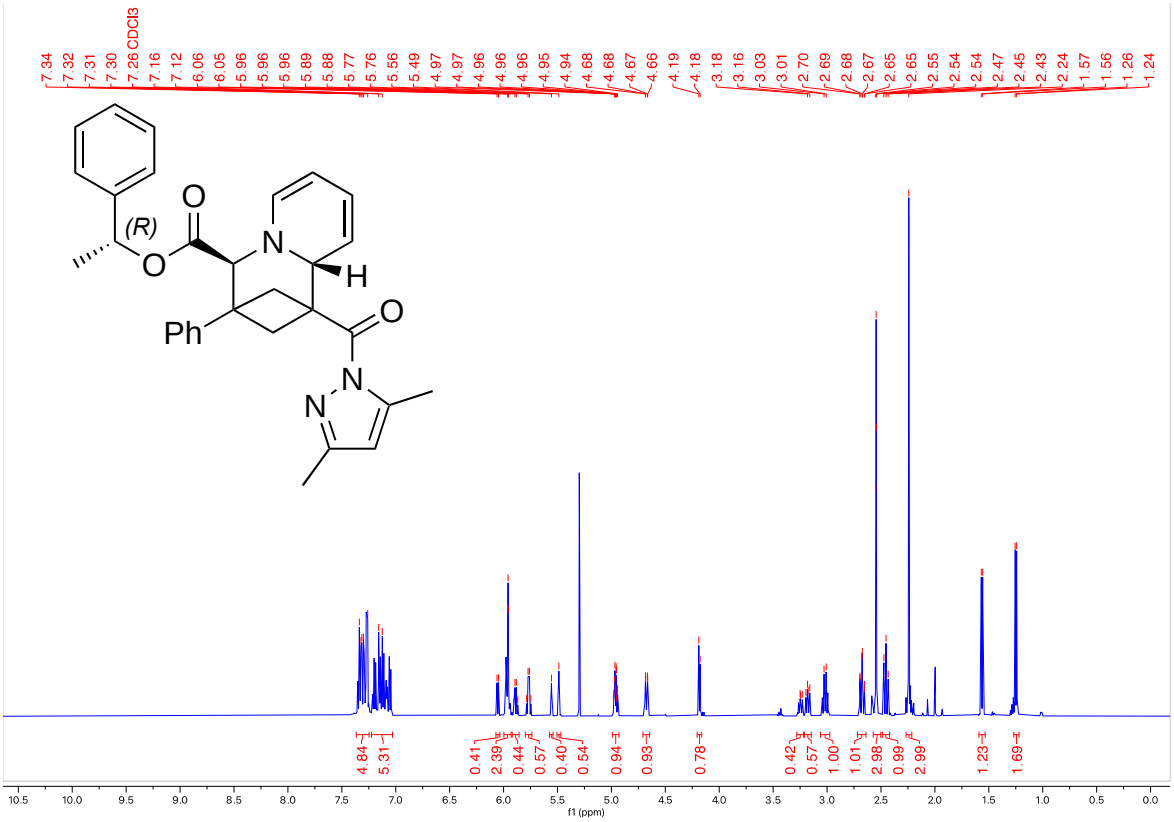
(*R*)-1-phenylethyl 1-(3,5-dimethyl-1H-pyrazole-1-carbonyl)-3-phenyl-1,3,4,9a-tetrahydro-2H-1,3-methanoquinolizine-4-carboxylate (3t)



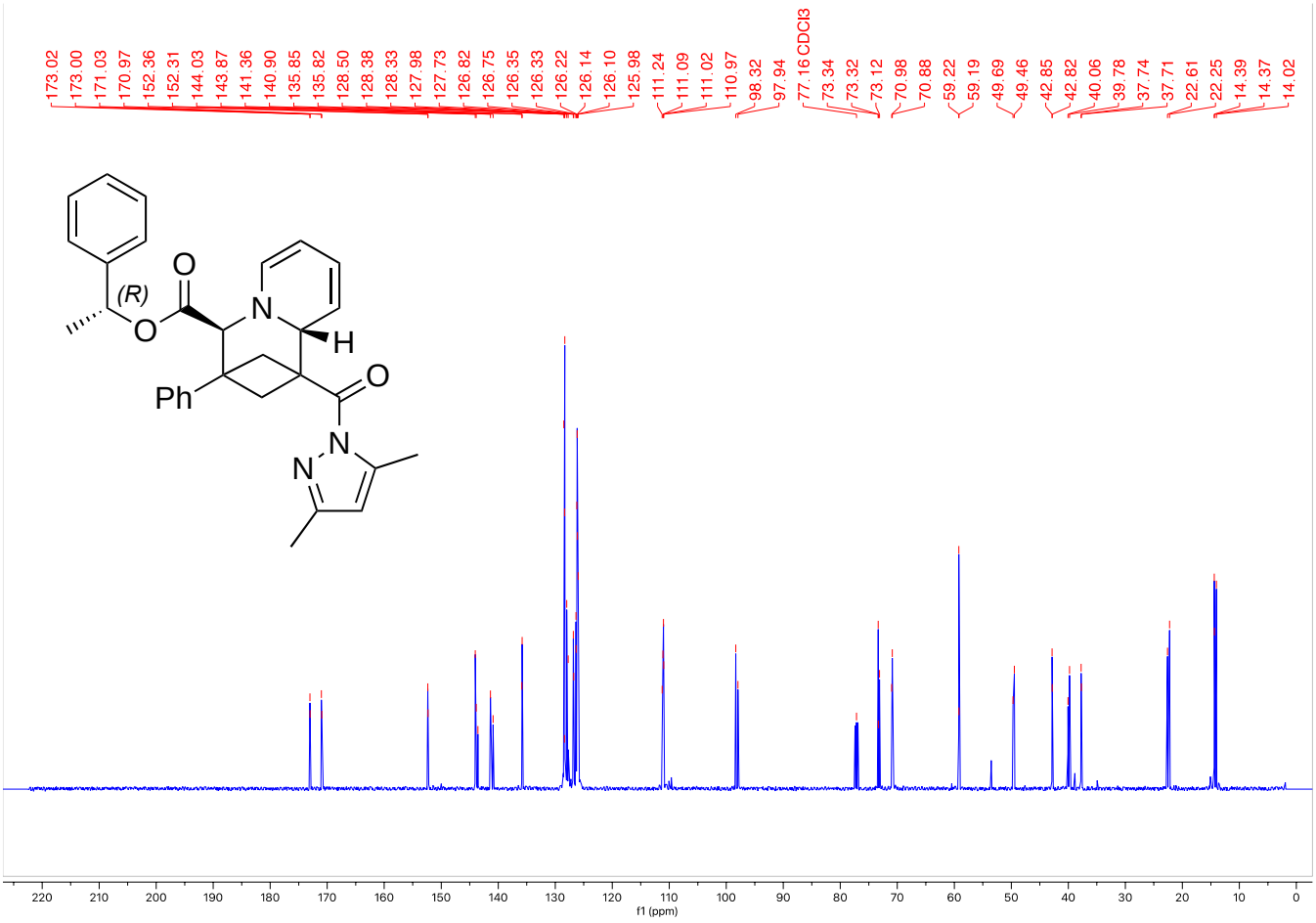
Product was synthesized following general procedure A on a 0.30 mmol scale. Reagent amounts used: bicyclobutane **1a** (81.1 mg, 0.30 mmol), pyridinium **2t** (1.25 equiv, 120.4 mg, 0.38 mmol), and K_3PO_4 (2.5 equiv, 159.2 mg, 0.75 mmol) in 1.2 mL acetonitrile (0.25 M). Isolated 120.2 mg of an orange oil (**65% yield, 1:1.4 d.r.**).

HRMS(ESI): calc'd for [$C_{31}H_{31}N_3O_3$ + H^+], 494.24382; found: 494.24426.

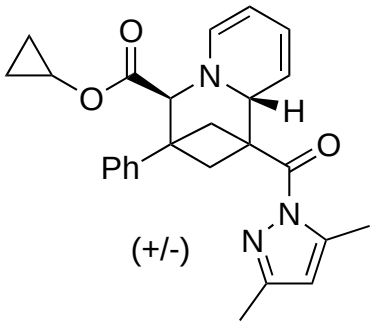
^{1}H NMR (500 MHz, $CDCl_3$, 292 K, ppm): δ 7.37 – 7.25 (m, 5H), 7.23 – 7.03 (m, 5H), 6.05 (d, J = 7.0 Hz, 0.4H), 6.00 – 5.93 (m, 2.6H), 5.89 (q, J = 6.5 Hz, 0.4H), 5.77 (q, J = 6.6 Hz, 0.6H), 5.56 (s, 0.4H), 5.49 (s, 0.6H), 4.96 (dtd, J = 6.9, 5.3, 1.3 Hz, 1H), 4.67 (ddq, J = 9.1, 2.3, 1.3 Hz, 1H), 4.18 (d, J = 6.2 Hz, 1H), 3.25 (dd, J = 10.2, 7.5 Hz, 0.4H), 3.18 (dd, J = 10.2, 7.4 Hz, 0.6H), 3.02 (dt, J = 9.7, 7.7 Hz, 1H), 2.67 (td, J = 10.3, 1.1 Hz, 1H), 2.54 (d, J = 1.1 Hz, 3H), 2.45 (t, J = 10.1 Hz, 1H), 2.24 (s, 3H), 1.56 (d, J = 6.6 Hz, 1H), 1.25 (dd, J = 6.6, 2H).



^{13}C NMR (126 MHz, $CDCl_3$, 292 K, ppm): δ 173.02, 173.00, 171.03, 170.97, 152.36, 152.31, 144.03, 143.87, 143.56, 141.36, 140.90, 135.85, 135.82, 128.50, 128.40, 128.38, 128.33, 127.98, 127.73, 126.82, 126.75, 126.35, 126.33, 126.22, 126.14, 126.10, 125.98, 111.24, 111.09, 111.02, 110.97, 98.32, 97.94, 73.34, 73.32, 73.12, 70.98, 70.88, 59.22, 59.19, 49.69, 49.46, 42.85, 42.82, 40.06, 39.78, 37.74, 37.71, 22.61, 22.25, 14.39, 14.37, 14.02.



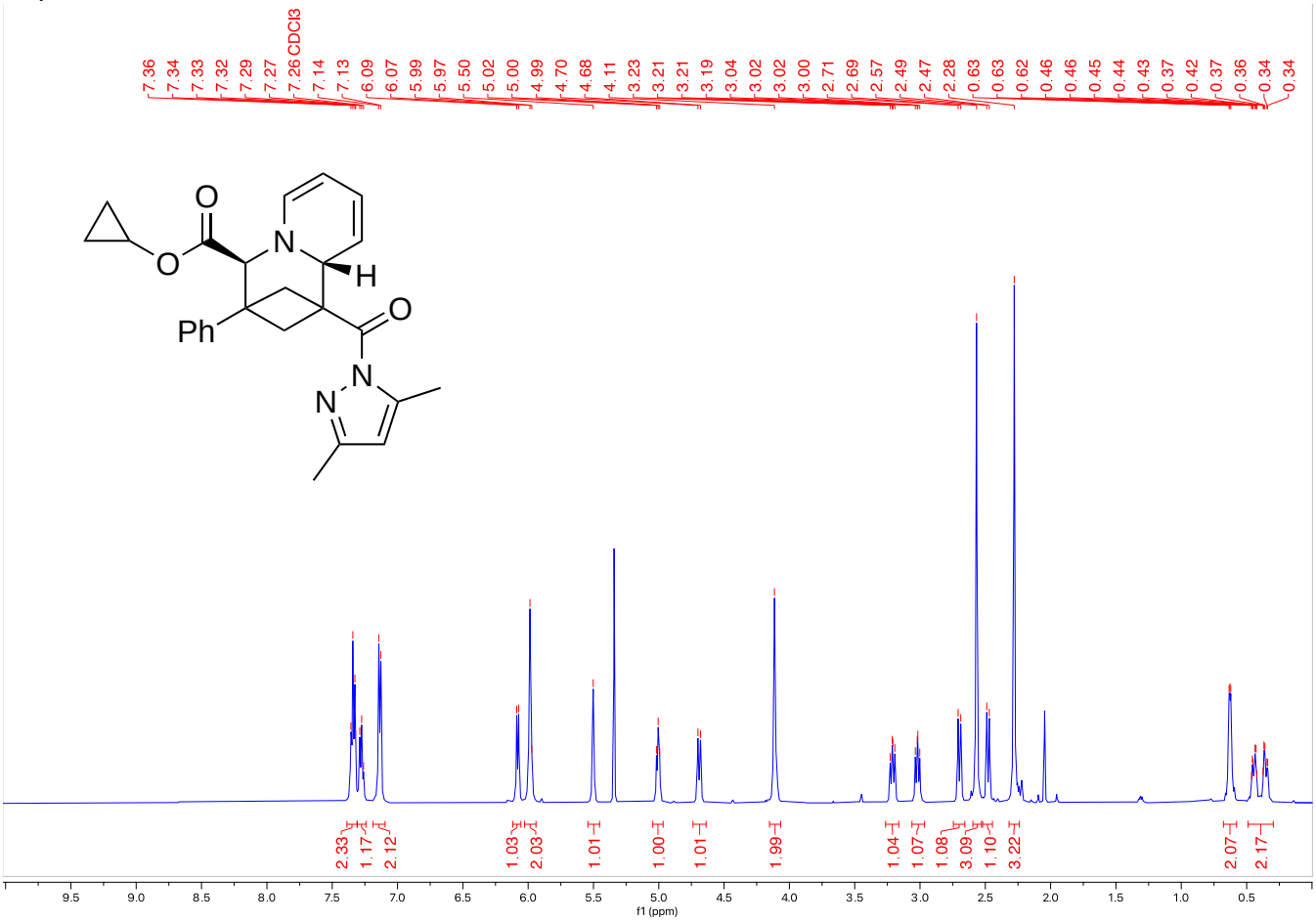
Cyclopropyl 1-(3,5-dimethyl-1H-pyrazole-1-carbonyl)-3-phenyl-1,3,4,9a-tetrahydro-2H-1,3-methanoquinolizine-4-carboxylate (3u)



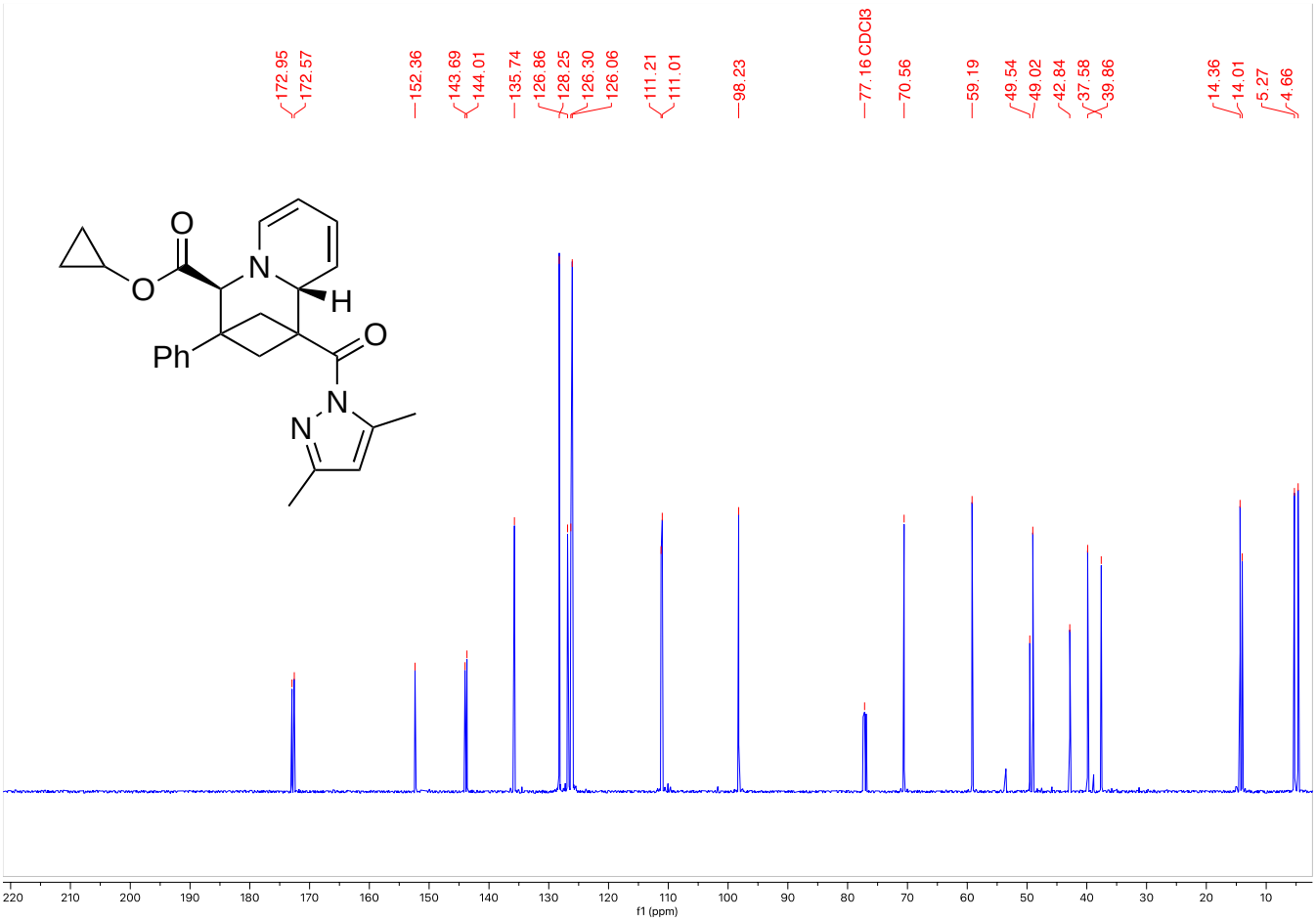
Product was synthesized following general procedure **A** on a 0.30 mmol scale. Reagent amounts used: bicyclobutane **1a** (75.7 mg, 0.30 mmol), pyridinium **2u** (1.25 equiv, 96.8 mg, 0.38 mmol), and K_3PO_4 (2.5 equiv, 159.2 mg, 0.75 mmol) in 1.2 mL acetonitrile (0.25 M). Isolated 109 mg of an orange solid (**85% yield**).

HRMS(ESI): calc'd for [$C_{31}H_{31}N_3O_4$ + H^+], 430.21252; found: 430.21299.

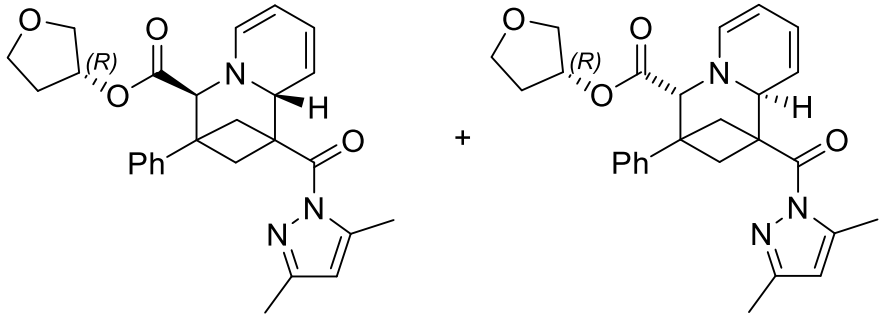
^{1}H NMR (500 MHz, $CDCl_3$, 292 K, ppm): δ 7.34 (t, J = 7.5 Hz, 2H), 7.28 (d, J = 7.2 Hz, 1H), 7.14 (d, J = 7.5 Hz, 2H), 6.08 (d, J = 7.1 Hz, 1H), 5.99 (m, 2H), 5.50 (s, 1H), 5.00 (t, J = 6.3 Hz, 1H), 4.69 (d, J = 9.4 Hz, 1H), 4.11 (s, 2H), 3.21 (dd, J = 10.2, 7.4 Hz, 1H), 3.02 (dd, J = 9.7, 7.4 Hz, 1H), 2.70 (d, J = 10.2 Hz, 1H), 2.57 (s, 3H), 2.48 (d, J = 9.7 Hz, 1H), 2.28 (s, 3H), 0.68 – 0.58 (m, 2H), 0.49 – 0.30 (m, 2H).



^{13}C NMR (126 MHz, $CDCl_3$, 292 K, ppm): δ 172.95, 172.57, 152.36, 144.01, 143.69, 135.74, 128.25, 126.86, 126.30, 126.06, 111.21, 111.01, 98.23, 70.56, 59.19, 49.54, 49.02, 42.84, 39.86, 37.58, 14.36, 14.01, 5.27, 4.66.



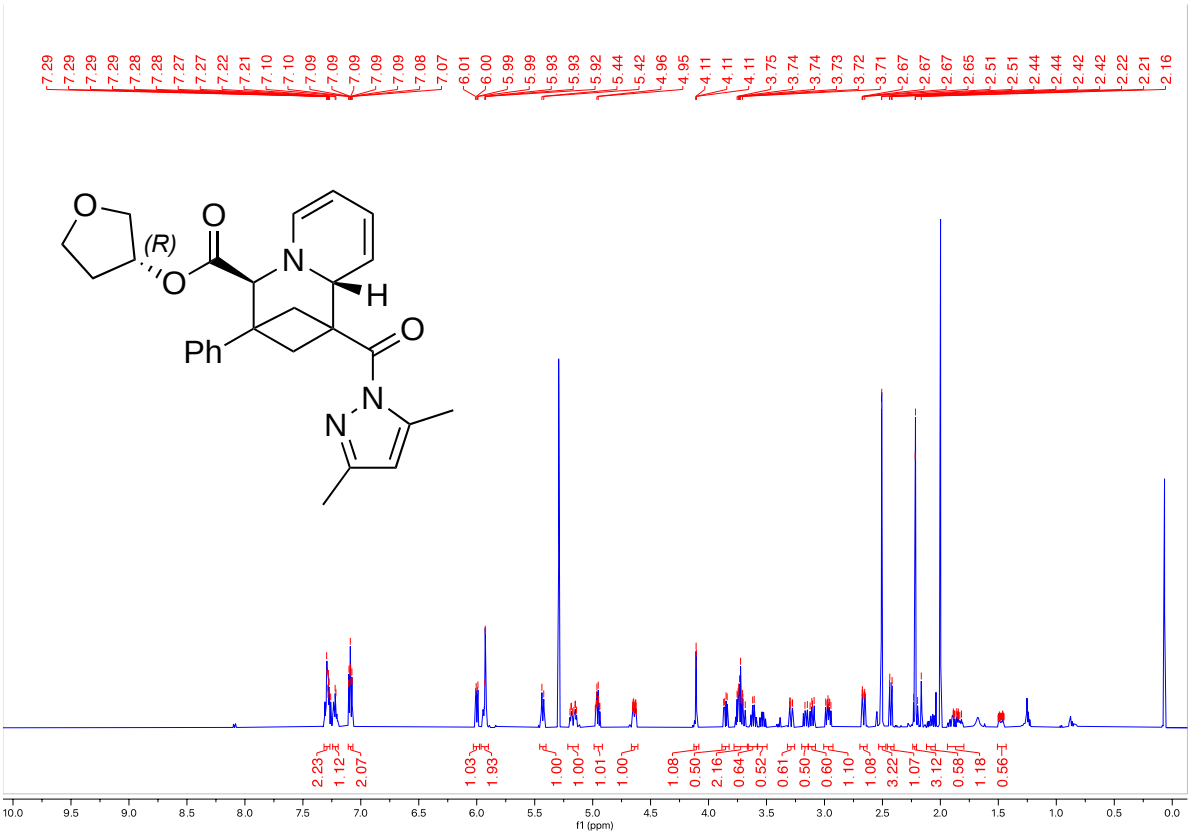
(*R*)-tetrahydrofuran-3-yl 1-(3,5-dimethyl-1H-pyrazole-1-carbonyl)-3-phenyl-1,3,4,9a-tetrahydro-2H-1,3-methanoquinolizine-4-carboxylate (3v)



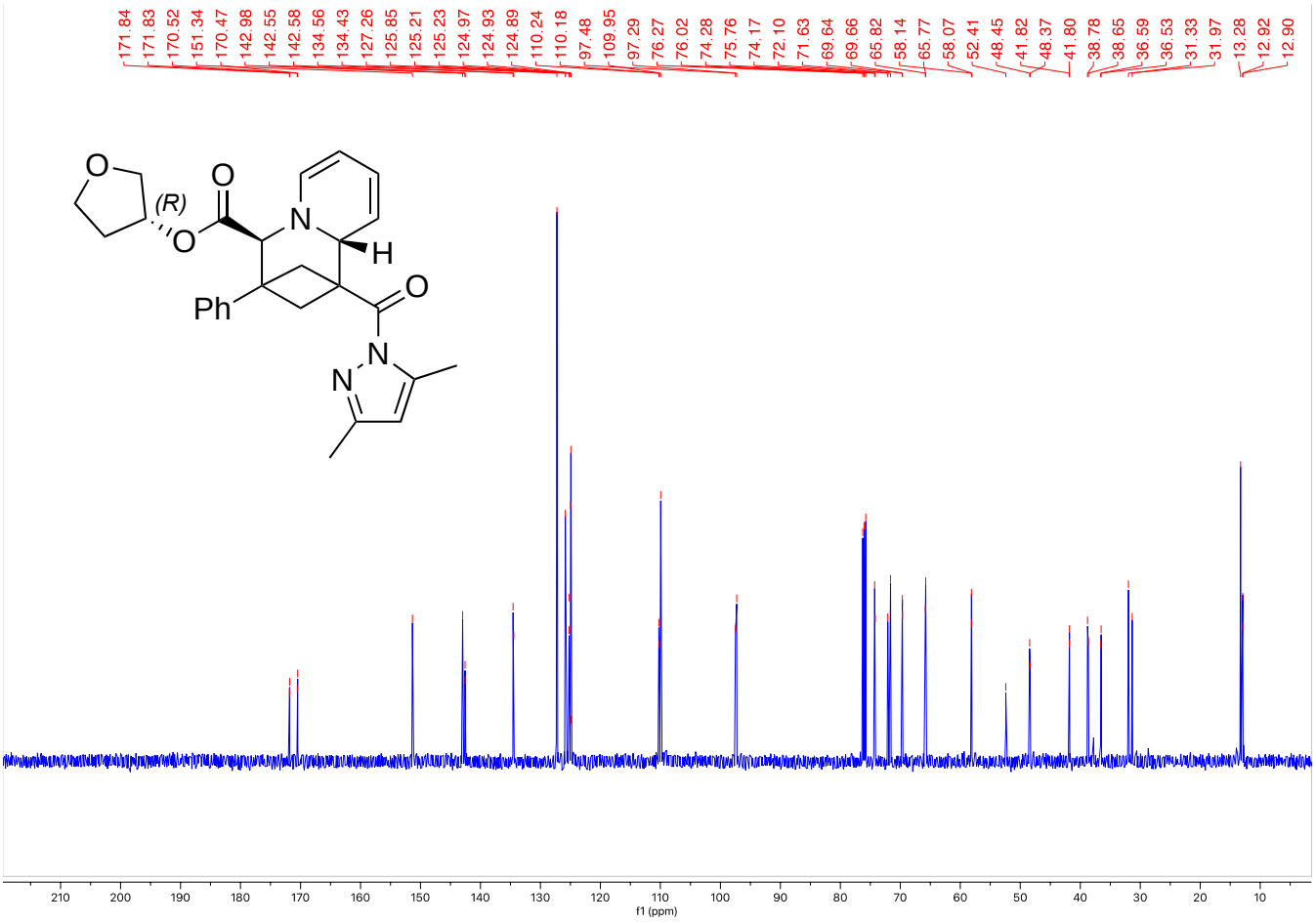
Product was synthesized following general procedure **A** on a 0.30 mmol scale. Reagent amounts used: bicyclobutane **1a** (75.7 mg, 0.30 mmol), pyridinium **2v** (1.25 equiv, 108.1 mg, 0.38 mmol), and K_3PO_4 (2.5 equiv, 159.2 mg, 0.75 mmol) in 1.2 mL acetonitrile (0.25 M). Isolated 67.2 mg of an orange oil as a mixture of diastereomers (**70% yield, 1.2:1 dr**).

HRMS(ESI): calc'd for [$C_{27}H_{29}N_3O_4$ + H^+], 460.22309; found: 460.22293.

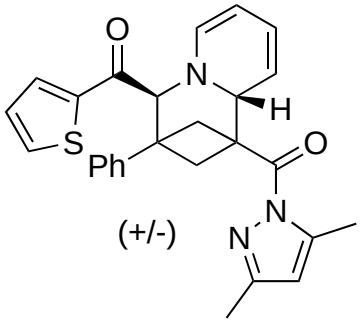
^{1}H NMR (500 MHz, $CDCl_3$, 292 K, ppm): δ 7.29 (m, 2H), 7.22 (m, 1H), 7.13 – 7.06 (m, 2H), 6.00 (dd, J = 7.1, 2.6 Hz, 1H), 5.93 (s, 2H), 5.43 (d, J = 7.3 Hz, 1H), 5.17 (d, J = 17.0 Hz, 1H), 4.96 (q, J = 6.2 Hz, 1H), 4.65 (d, J = 9.6 Hz, 1H), 4.11 (s, 1H), 3.86 (dd, J = 10.6, 4.6 Hz, 0.5H), 3.79 – 3.67 (m, 2H), 3.62 (td, J = 8.7, 6.5 Hz, 0.5H), 3.54 (td, J = 8.7, 6.5 Hz, 0.5H), 3.33 – 3.26 (m, 0.5H), 3.14 (ddd, J = 29.3, 10.2, 7.4 Hz, 1H), 2.97 (ddd, J = 9.7, 7.4, 5.4 Hz, 1H), 2.66 (dd, J = 10.2, 2.7 Hz, 1H), 2.51 (s, 3H), 2.43 (dd, J = 9.7, 1.7 Hz, 1H), 2.22 (d, J = 1.5 Hz, 3H), 2.06 (dd, J = 14.1, 7.9 Hz, 0.5H), 1.96 – 1.79 (m, 1H), 1.48 (d, J = 13.4 Hz, 0.5H).



^{13}C NMR (126 MHz, $CDCl_3$, 292 K, ppm): δ 171.84, 171.83, 170.52, 170.47, 151.34, 142.98, 142.58, 142.55, 134.56, 134.43, 127.26, 125.85, 125.23, 125.21, 124.97, 124.93, 124.89, 110.24, 110.18, 109.95, 97.48, 97.29, 76.27, 76.02, 75.76, 74.28, 74.17, 72.10, 71.63, 69.66, 69.64, 65.82, 65.77, 58.14, 58.07, 52.41, 48.45, 48.37, 41.82, 41.80, 38.78, 38.65, 36.59, 36.53, 31.97, 31.33, 13.28, 12.92, 12.90.



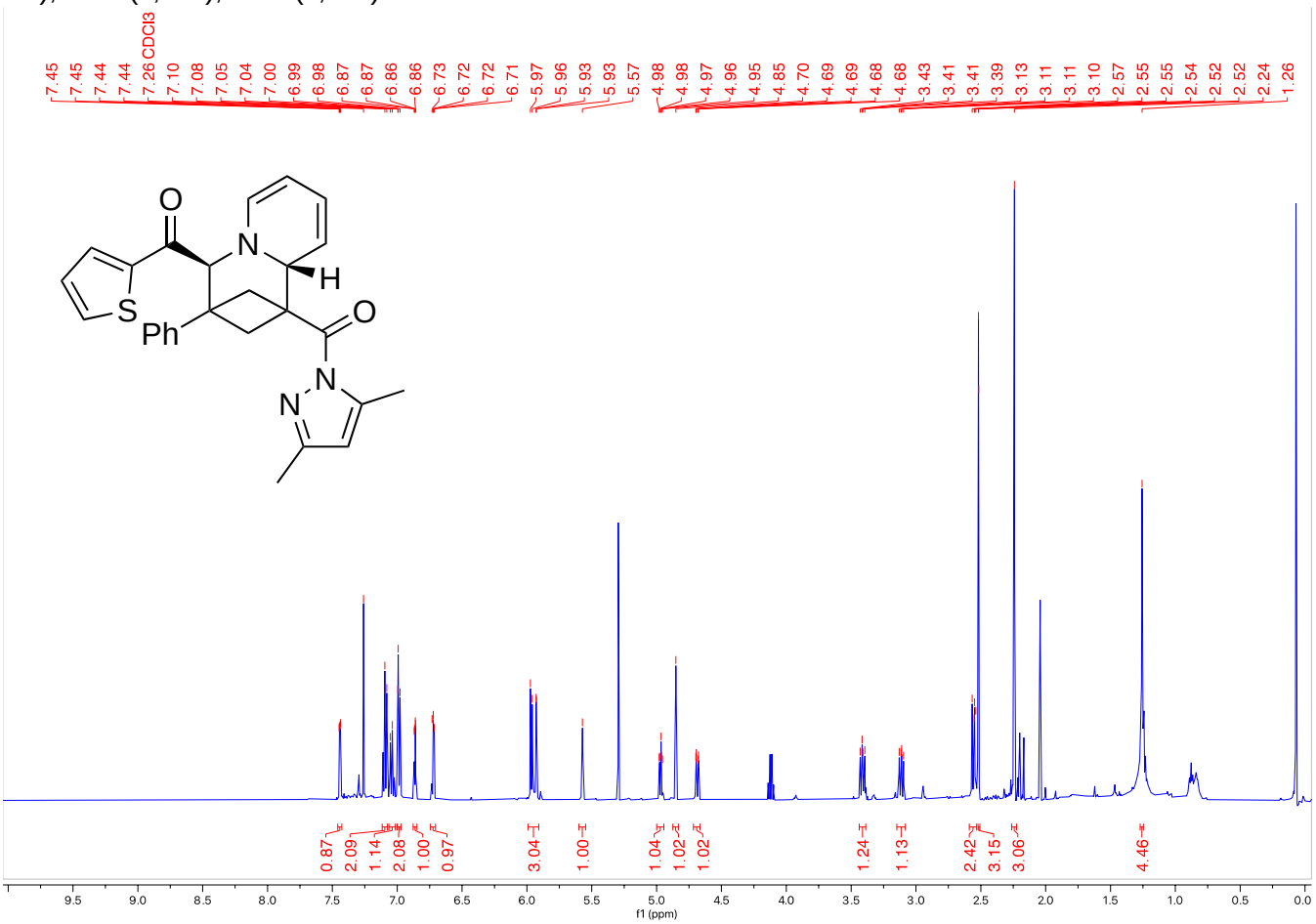
(3,5-dimethyl-1H-pyrazol-1-yl)(3-phenyl-4-(thiophene-2-carbonyl)-3,4-dihydro-2H-1,3-methanoquinolizin-1(9aH)-yl)methanone (3w)



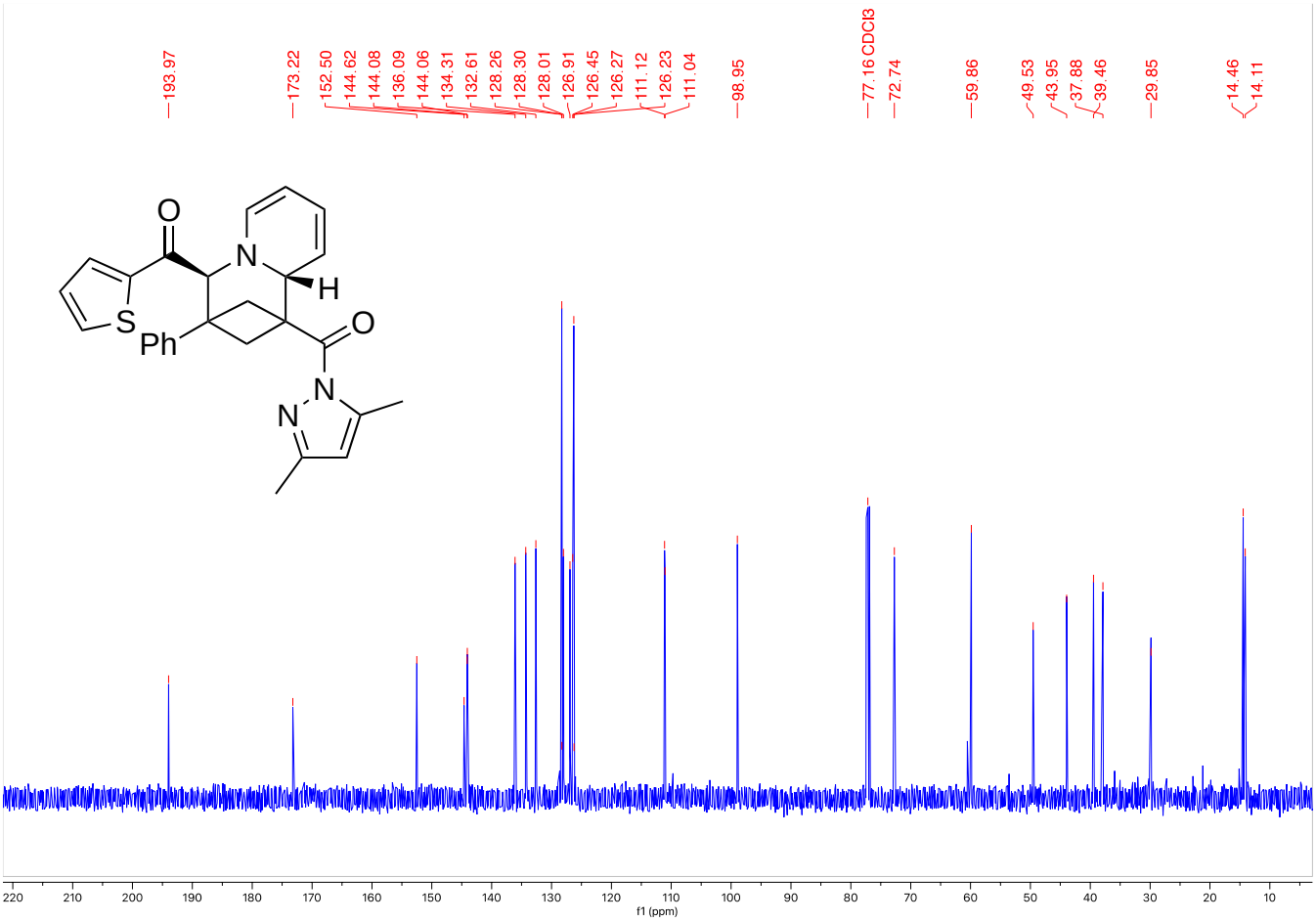
Product was synthesized following general procedure B on a 0.30 mmol scale. Reagent amounts used: bicyclobutane **1a** (75.7 mg, 0.30 mmol), pyridinium **2w** (1.25 equiv, 106.6 mg, 0.38 mmol), $NaPF_6$ (1.3 equiv, 65.5 mg), and K_3PO_4 (2.5 equiv, 159.2 mg, 0.75 mmol) in 1.2 mL acetonitrile (0.25 M). Isolated 21.7 mg of an orange solid (**16% yield**).

HRMS(ESI): calc'd for [$C_{31}H_{31}N_3O_4$ + H^+], 456.17403; found: 456.17402.

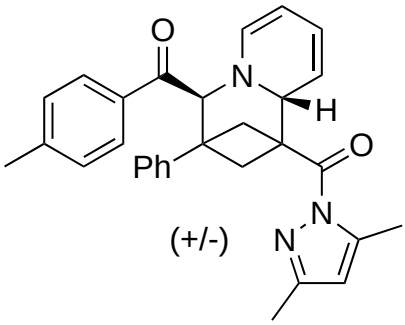
^{1}H NMR (500 MHz, $CDCl_3$, 292 K, ppm): δ 7.44 (dd, J = 4.9, 1.1 Hz, 1H), 7.12 – 7.07 (m, 2H), 7.06 – 7.01 (m, 1H), 7.00 – 6.97 (m, 2H), 6.86 (dd, J = 3.9, 1.1 Hz, 1H), 6.72 (dd, J = 4.9, 3.9 Hz, 1H), 5.99 – 5.91 (m, 3H), 5.57 (s, 1H), 4.97 (ddd, J = 7.0, 5.5, 1.4 Hz, 1H), 4.85 (s, 1H), 4.69 (ddt, J = 9.5, 2.2, 1.1 Hz, 1H), 3.41 (dd, J = 10.3, 7.4 Hz, 1H), 3.11 (dd, J = 9.6, 7.4 Hz, 1H), 2.59 – 2.53 (m, 2H), 2.52 (s, 3H), 2.24 (s, 3H), 1.26 (s, 3H).



^{13}C NMR (126 MHz, $CDCl_3$, 292 K, ppm): δ 193.97, 173.22, 152.50, 144.62, 144.08, 144.06, 136.09, 134.31, 132.61, 128.30, 128.26, 128.01, 126.91, 126.45, 126.27, 126.23, 111.12, 111.04, 98.95, 72.74, 59.86, 49.53, 43.95, 39.46, 37.88, 29.85, 14.46, 14.11.



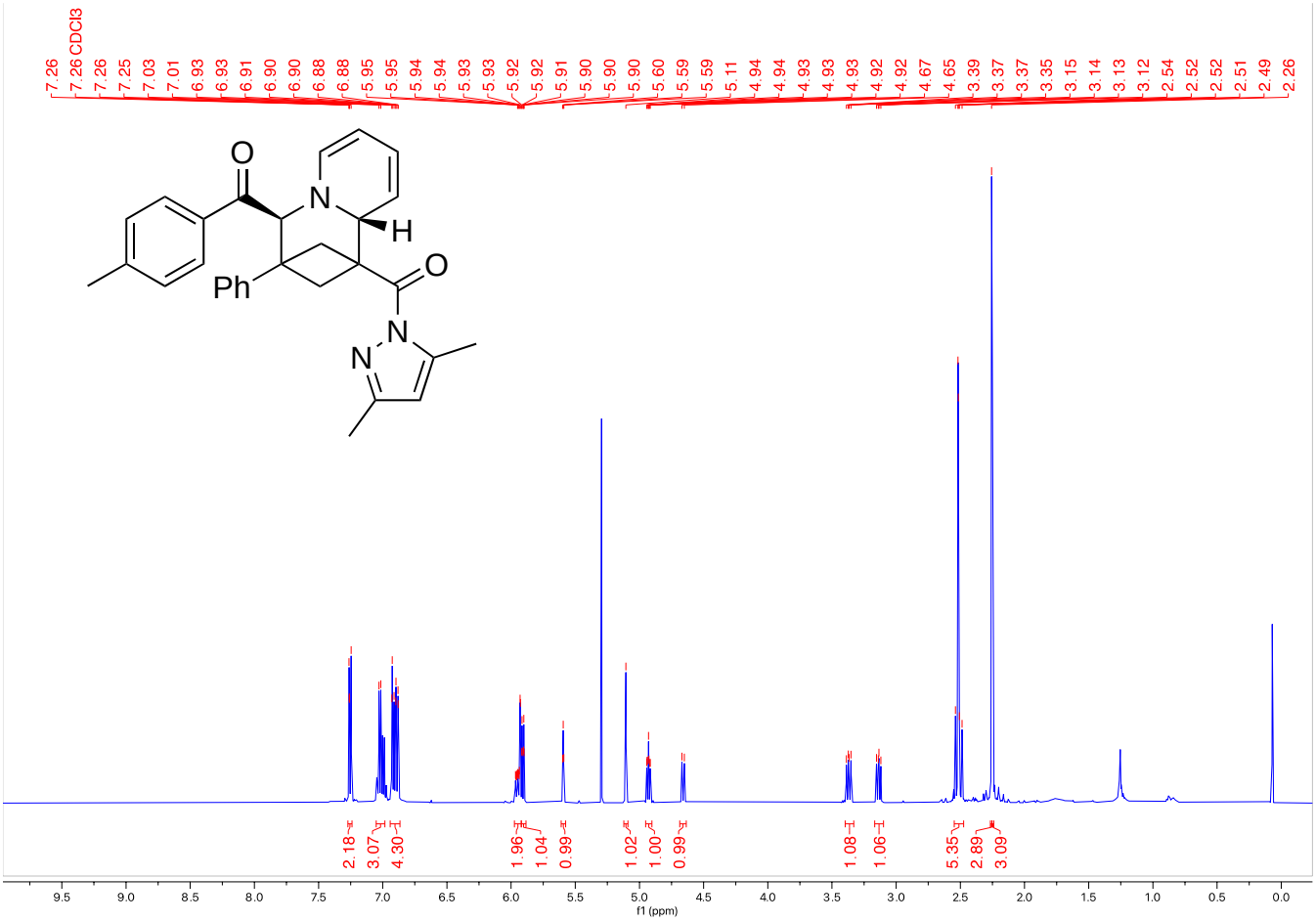
(3,5-dimethyl-1H-pyrazol-1-yl)(-4-(4-methylbenzoyl)-3-phenyl-3,4-dihydro-2H-1,3-methanoquinolizin-1(9aH)-yl)methanone (3x)



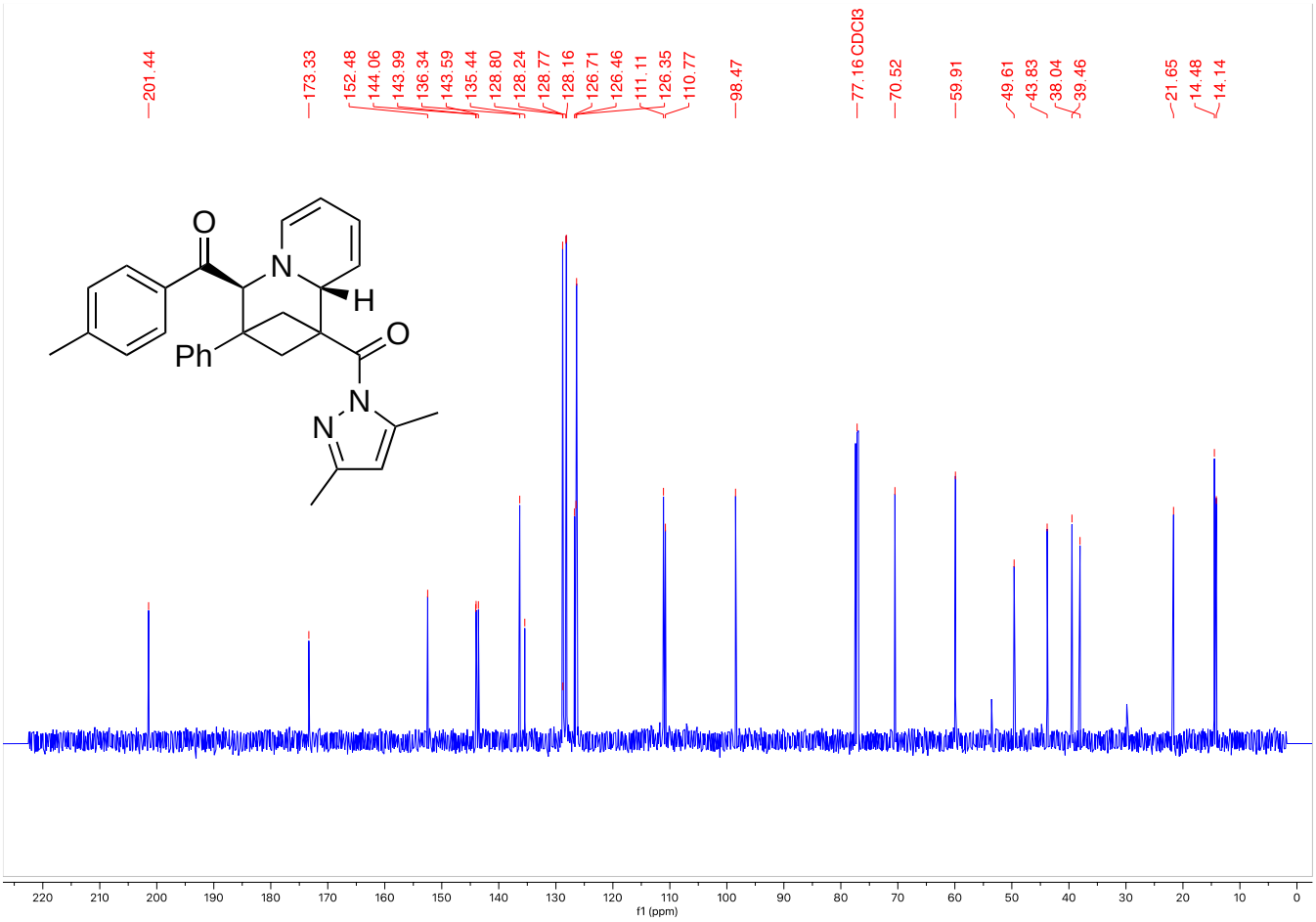
Product was synthesized following general procedure **B** on a 0.30 mmol scale. Reagent amounts used: bicyclobutane **1a** (75.7 mg, 0.30 mmol), pyridinium **2x** (1.25 equiv, 109.2 mg, 0.38 mmol), $NaPF_6$ (1.3 equiv, 65.5 mg, 0.39 mmol) and K_3PO_4 (2.5 equiv, 159.2 mg, 0.75 mmol) in 1.2 mL acetonitrile (0.25 M). Isolated 109.1 mg of an orange solid (**78% yield**).

HRMS(ESI): calc'd for [$C_{30}H_{29}N_3O_2$ + H^+], 464.23326; found: 464.23339.

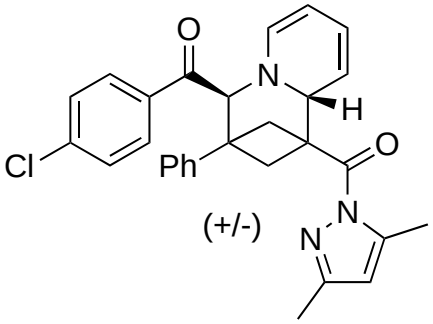
^{1}H NMR (500 MHz, $CDCl_3$, 292 K, ppm): δ 7.27 – 7.24 (m, 2H), 7.05 – 6.98 (m, 3H), 6.94 – 6.87 (m, 4H), 5.97 – 5.92 (m, 2H), 5.91 (d, J = 7.0 Hz, 1H), 5.59 (t, J = 2.4 Hz, 1H), 5.11 (s, 1H), 4.93 (ddd, J = 6.9, 5.4, 1.3 Hz, 1H), 4.66 (ddt, J = 9.2, 2.2, 1.0 Hz, 1H), 3.37 (dd, J = 10.1, 7.4 Hz, 1H), 3.14 (dd, J = 9.5, 7.4 Hz, 1H), 2.55 – 2.47 (m, 5H), 2.26 (s, 3H), 2.25 (s, 3H).



^{13}C NMR (126 MHz, $CDCl_3$, 292 K, ppm): δ 201.44, 173.33, 152.48, 144.06, 143.99, 143.59, 136.34, 135.44, 128.80, 128.77, 128.24, 128.16, 126.71, 126.46, 126.35, 111.11, 110.77, 98.47, 70.52, 59.91, 49.61, 43.83, 39.46, 38.04, 21.65, 14.48, 14.14.



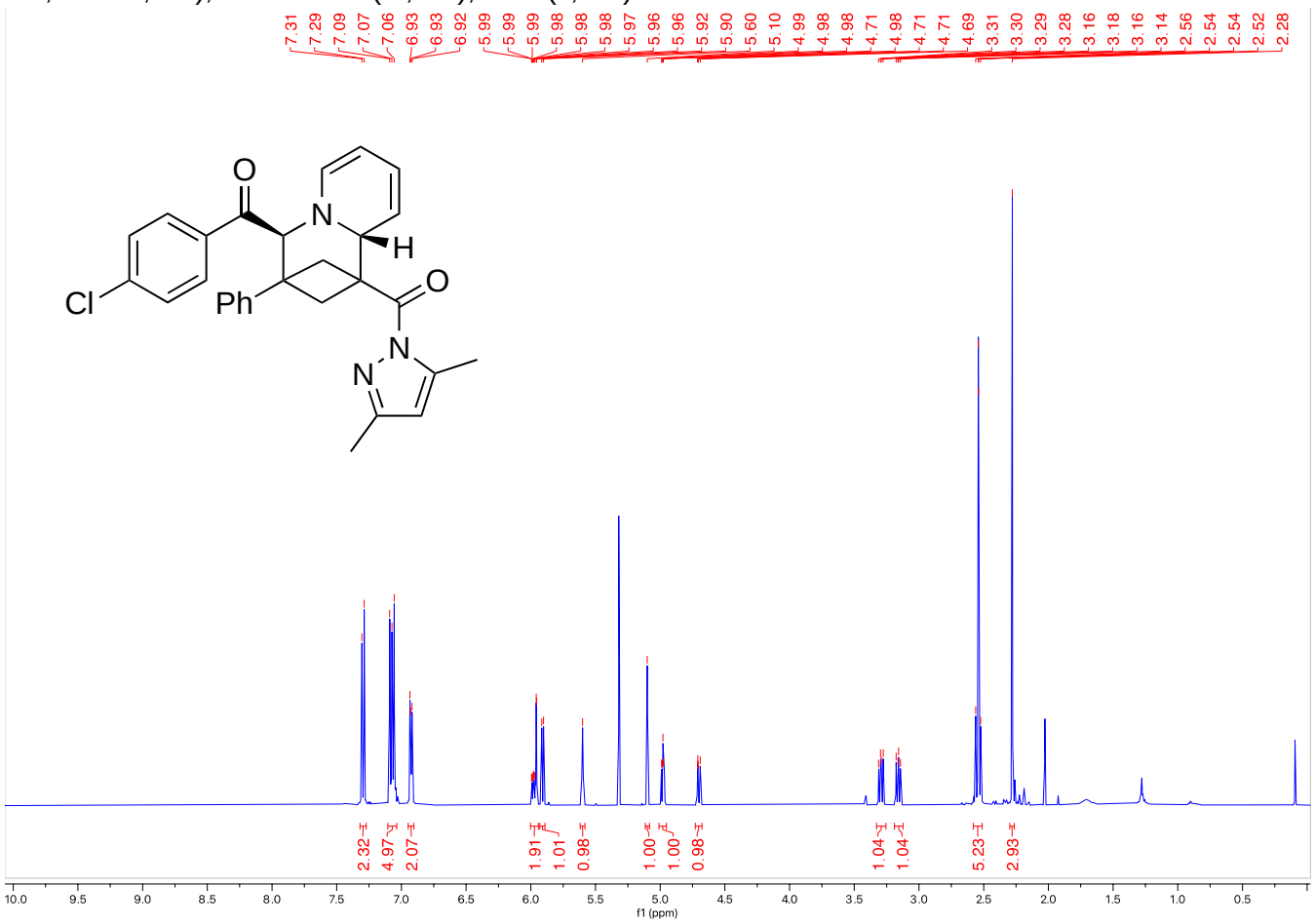
(4-(4-chlorobenzoyl)-3-phenyl-3,4-dihydro-2H-1,3-methanoquinolizin-1(9aH)-yl)(3,5-dimethyl-1H-pyrazol-1-yl)methanone (3y)



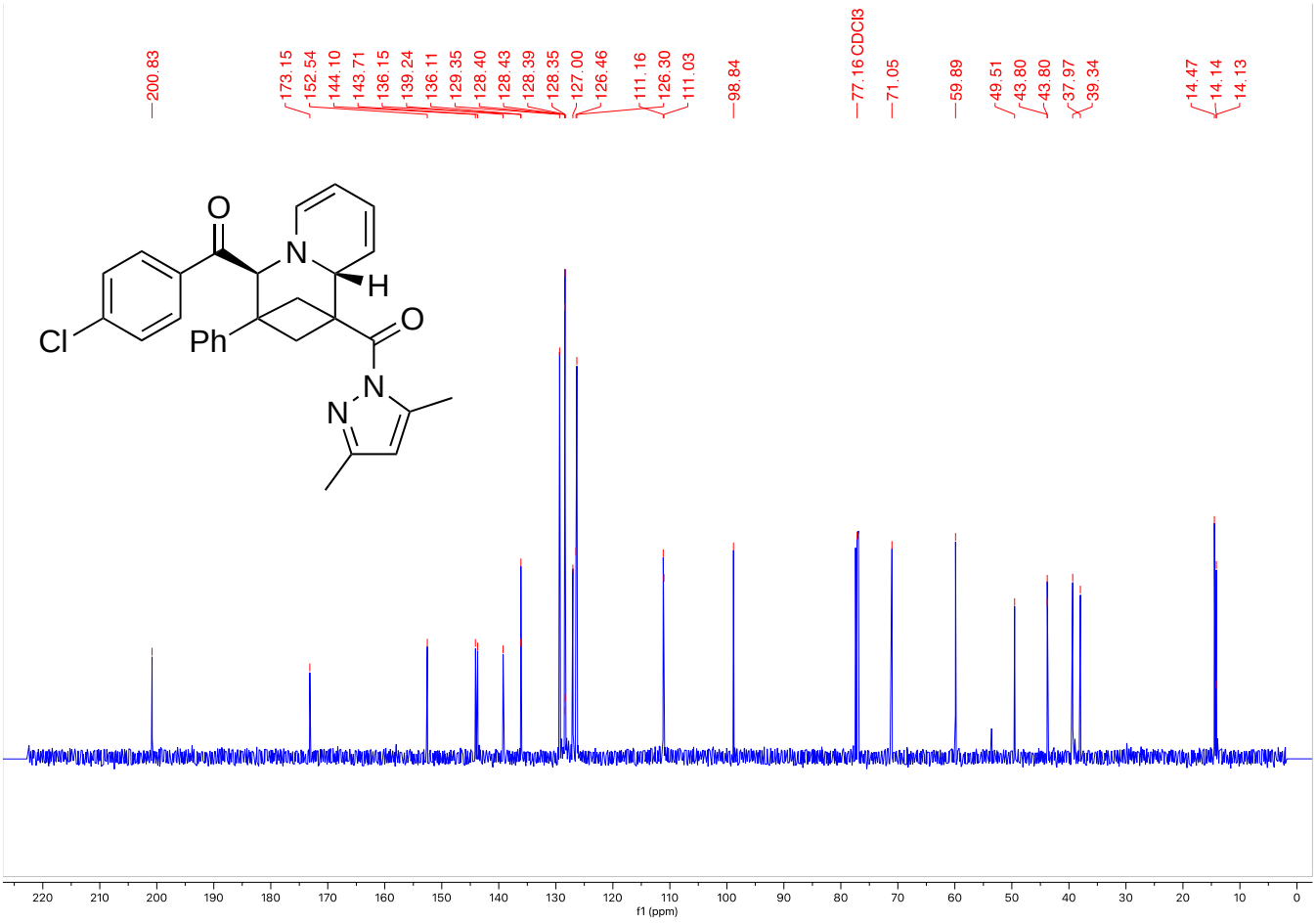
Product was synthesized following general procedure **B** on a 0.30 mmol scale. Reagent amounts used: bicyclobutane **1a** (75.7 mg, 0.30 mmol), pyridinium **2y** (1.25 equiv, 116.8 mg, 0.38 mmol), $NaPF_6$ (1.3 equiv, 65.5 mg, 0.39 mmol) and K_3PO_4 (2.5 equiv, 159.2 mg, 0.75 mmol) in 1.2 mL acetonitrile (0.25 M). Isolated 122.5 mg of an orange solid (**84% yield**).

HRMS(ESI): calc'd for [$C_{29}H_{26}ClN_3O_2$ + H^+], 484.17863; found: 484.17963.

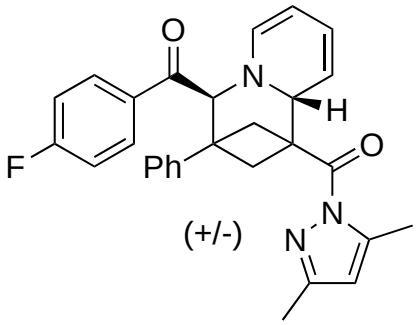
^{1}H NMR (500 MHz, $CDCl_3$, 292 K, ppm): δ 7.29 (dd, J = 8.7, 2.0 Hz, 2H), 7.10 – 7.04 (m, 5H), 6.95 – 6.90 (m, 2H), 6.00 – 5.94 (m, 2H), 5.91 (d, J = 7.0 Hz, 1H), 5.60 (s, 1H), 5.10 (s, 1H), 4.98 (ddd, J = 6.9, 5.4, 1.4 Hz, 1H), 4.70 (ddd, J = 9.4, 2.3, 1.1 Hz, 1H), 3.29 (dd, J = 10.2, 7.4 Hz, 1H), 3.16 (dd, J = 9.5, 7.4 Hz, 1H), 2.58 – 2.51 (m, 5H), 2.28 (s, 3H).



^{13}C NMR (126 MHz, $CDCl_3$, 292 K, ppm): δ 200.83, 173.15, 152.54, 144.10, 143.71, 139.24, 136.15, 136.11, 129.35, 128.43, 128.40, 128.39, 128.35, 127.00, 126.46, 126.30, 111.16, 111.03, 98.84, 71.05, 59.89, 49.51, 43.80, 43.80, 39.34, 37.97, 14.47, 14.14, 14.13.



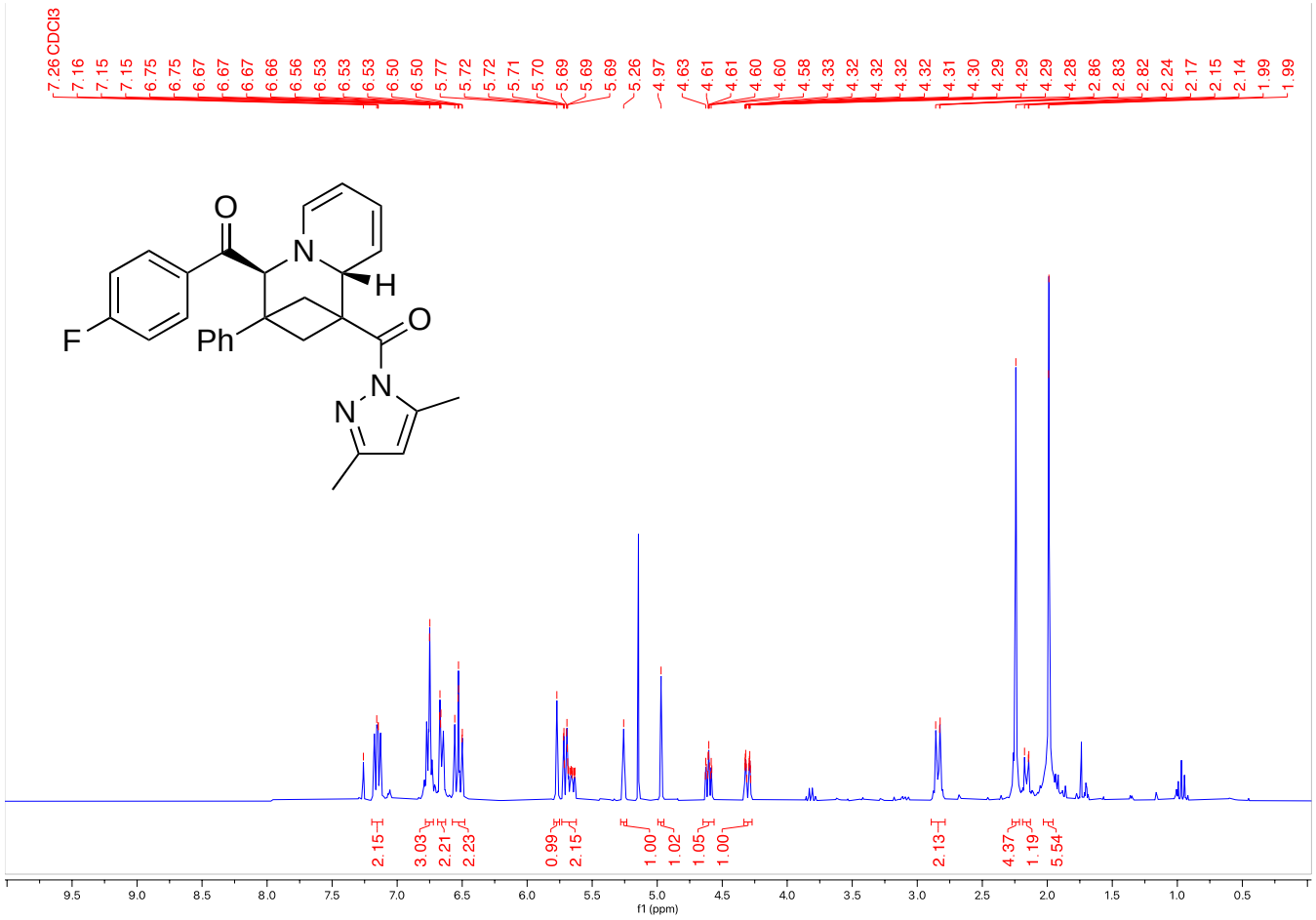
(3,5-dimethyl-1H-pyrazol-1-yl)(4-(4-fluorobenzoyl)-3-phenyl-3,4-dihydro-2H-1,3-methanoquinolizin-1(9aH)-yl)methanone (3z)



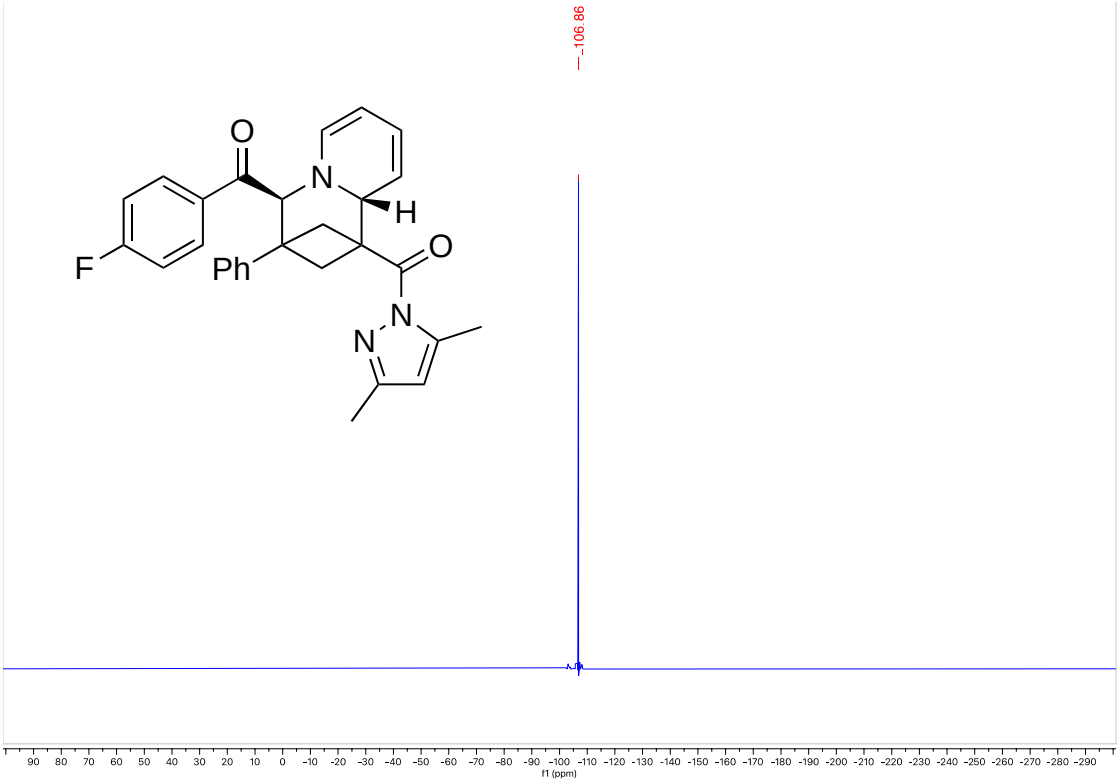
Product was synthesized following general procedure B on a 0.30 mmol scale. Reagent amounts used: bicyclobutane **1a** (75.7 mg, 0.30 mmol), pyridinium **2z** (1.25 equiv, 111.1 mg, 0.38 mmol), $NaPF_6$ (1.3 equiv, 65.5 mg), and K_3PO_4 (2.5 equiv, 159.2 mg, 0.75 mmol) in 1.2 mL acetonitrile (0.25 M). Isolated 101.7 mg of an orange oil (**61% yield**).

HRMS(ESI): calc'd for [$C_{31}H_{31}N_3O_4$ + H^+], 468.20819; found: 468.20805.

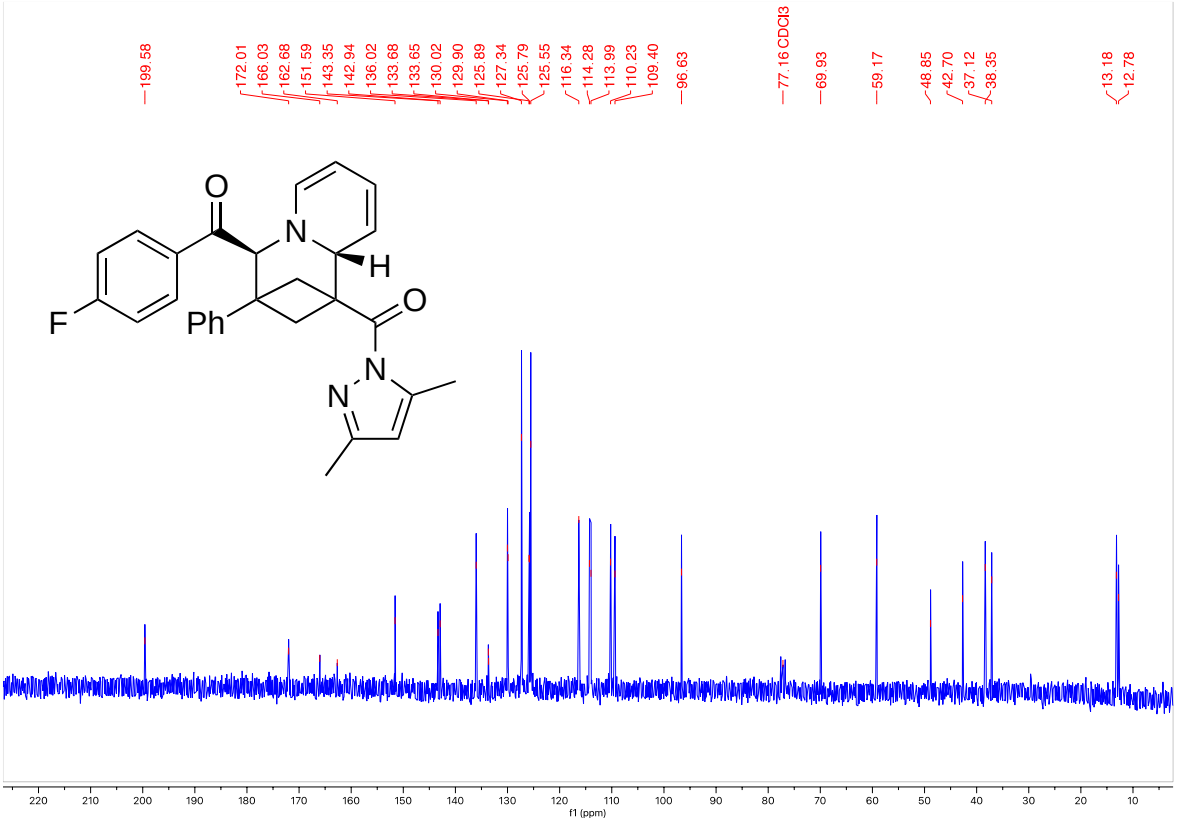
^{1}H NMR (300 MHz, $CDCl_3$, 292 K, ppm): δ 7.20 – 7.11 (m, 2H), 6.75 (m, 3H), 6.67 (m, 2H), 6.58 – 6.48 (m, 2H), 5.77 (s, 1H), 5.73 – 5.62 (m, 2H), 5.26 (s, 1H), 4.97 (s, 1H), 4.61 (ddt, J = 7.7, 5.4, 1.1 Hz, 1H), 4.30 (dddd, J = 9.4, 2.3, 1.4, 0.8 Hz, 1H), 2.89 – 2.79 (m, 2H), 2.24 (m, 4H), 2.19 – 2.13 (m, 1H), 1.99 (d, J = 0.9 Hz, 3H).



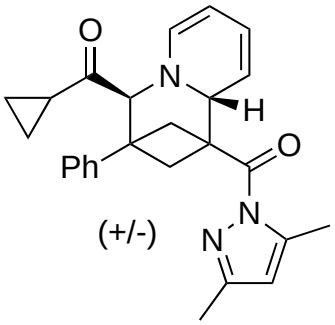
^{19}F NMR (300 MHz, $CDCl_3$, 292 K, ppm): δ 106.86.



^{13}C NMR (76 MHz, $CDCl_3$, 292 K, ppm): δ 199.58, 172.01, 166.03, 162.68, 151.59, 143.35, 142.94, 136.02, 133.68, 133.65, 130.02, 129.90, 127.34, 125.89, 125.79, 125.55, 116.34, 114.28, 113.99, 110.23, 109.40, 96.63, 69.93, 59.17, 48.85, 42.70, 38.35, 37.12, 13.18, 12.78.



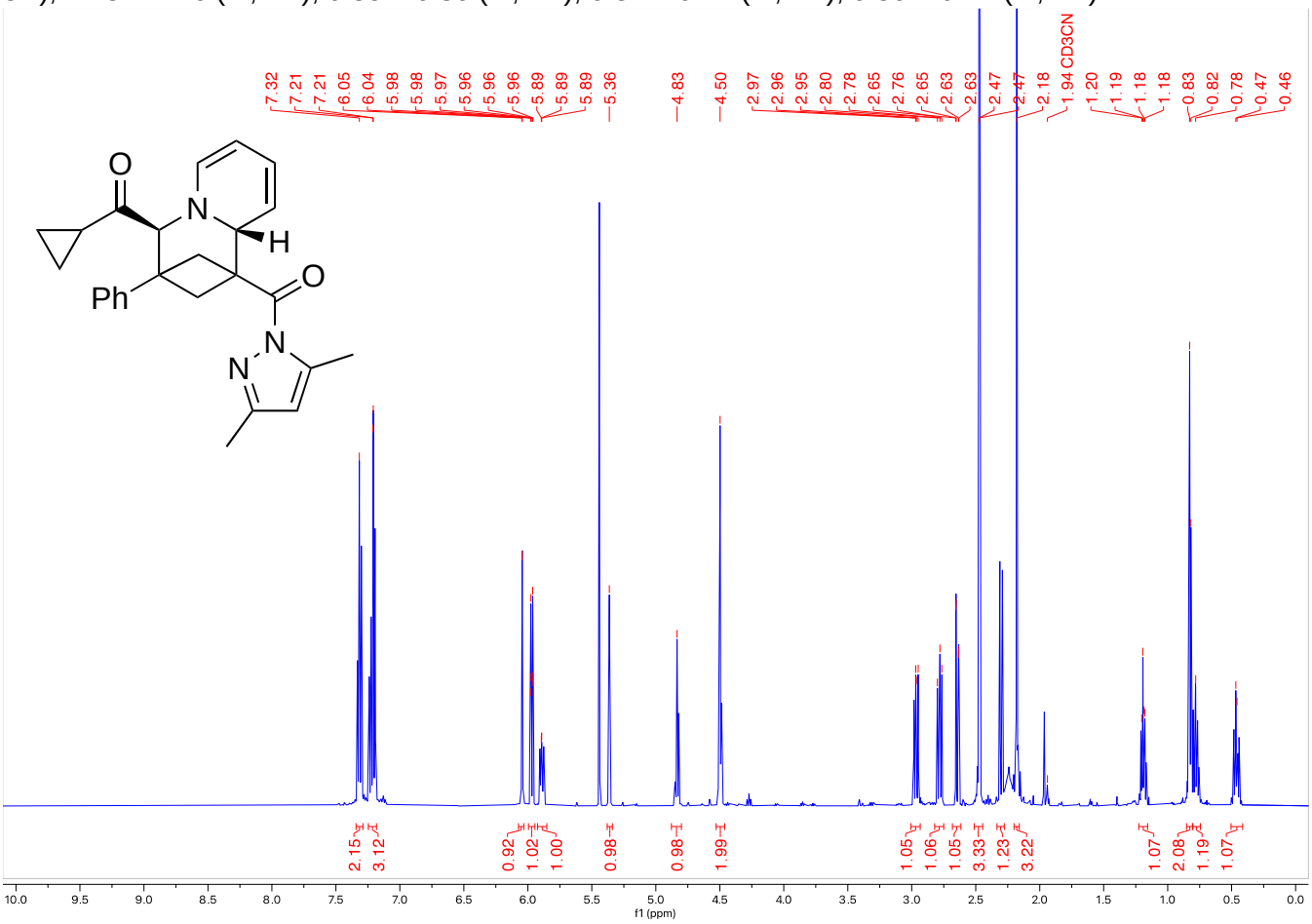
4-(cyclopropanecarbonyl)-3-phenyl-3,4-dihydro-2H-1,3-methanoquinolizin-1(9aH)-yl)(3,5-dimethyl-1H-pyrazol-1-yl)methanone (3aa)



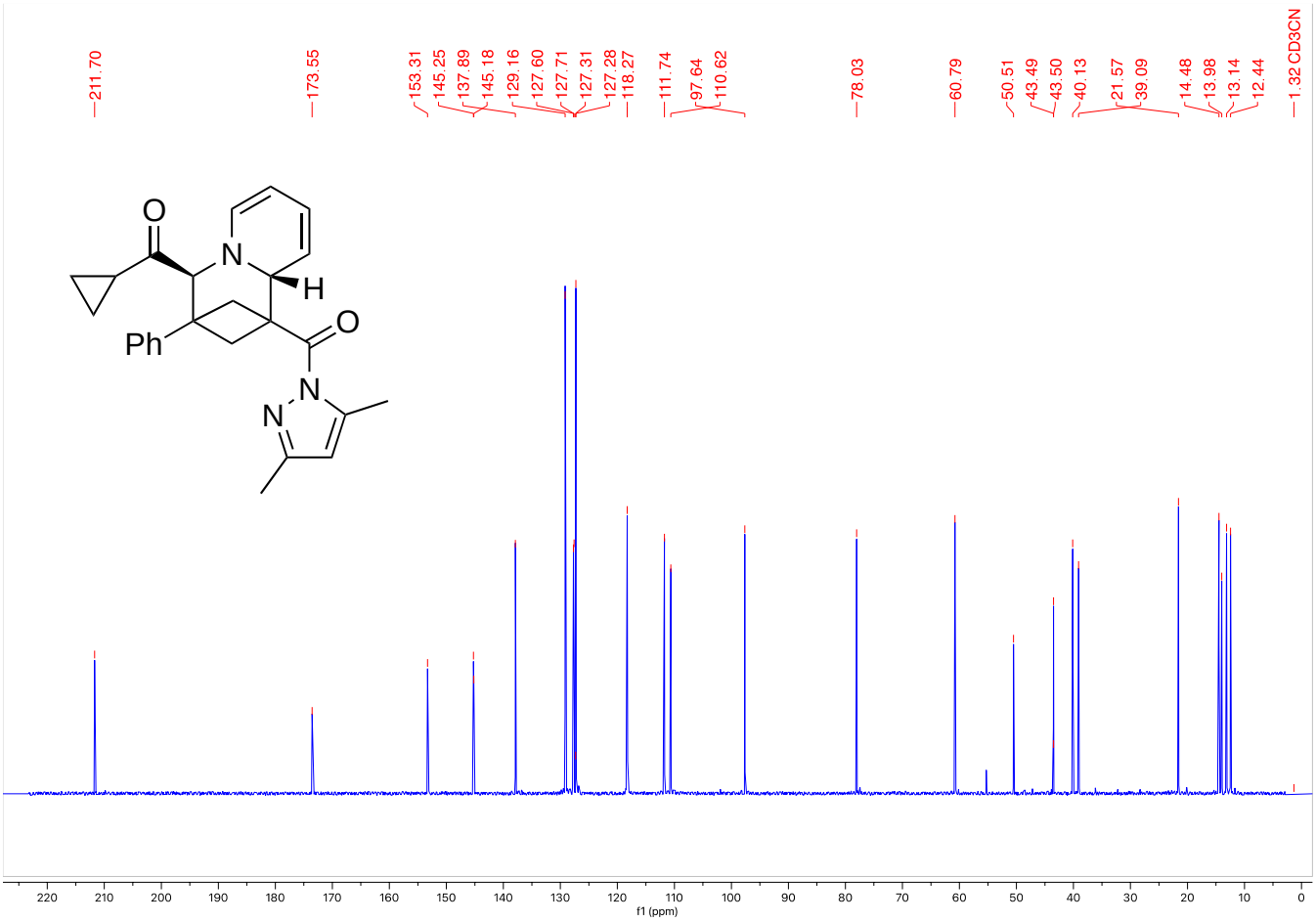
Product was synthesized following general procedure B on a 0.30 mmol scale. Reagent amounts used: bicyclobutane **1a** (75.7 mg, 0.30 mmol), pyridinium **2aa** (1.25 equiv, 90.8 mg, 0.38 mmol), $NaPF_6$ (1.3 equiv, 65.5 mg), and K_3PO_4 (2.5 equiv, 159.2 mg, 0.75 mmol) in 1.2 mL acetonitrile (0.25 M). Isolated 92.8 mg of an orange solid (**75% yield**).

HRMS(ESI): calc'd for [$C_{31}H_{31}N_3O_4$ + H^+], 414.21761; found: 414.21722.

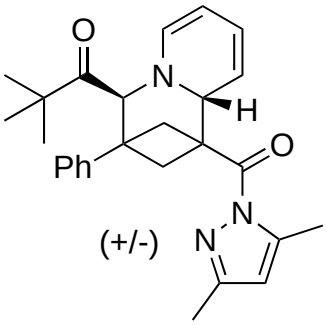
^{1}H NMR (500 MHz, CD3CN, 292 K, ppm): δ 7.34 – 7.29 (m, 2H), 7.25 – 7.18 (m, 3H), 6.05 (d, J = 1.2 Hz, 1H), 5.97 (d, J = 7.0, 1H), 5.89 (dddd, J = 9.4, 5.5, 2.2, 0.9 Hz, 1H), 5.36 (t, J = 2.3 Hz, 1H), 4.83 (ddd, J = 6.9, 5.4, 1.3 Hz, 1H), 4.53 – 4.46 (m, 2H), 2.97 (dd, J = 9.5, 7.3 Hz, 1H), 2.78 (dd, J = 10.1, 7.3 Hz, 1H), 2.64 (dd, J = 10.1, 0.9 Hz, 1H), 2.47 (d, J = 1.1 Hz, 3H), 2.30 (d, J = 9.5 Hz, 1H), 2.18 (s, 3H), 1.23 – 1.16 (m, 1H), 0.85 – 0.80 (m, 2H), 0.81 – 0.74 (m, 1H), 0.50 – 0.41 (m, 1H).



^{13}C NMR (126 MHz, CD3CN, 292 K, ppm): δ 211.70, 173.55, 153.31, 145.25, 145.18, 137.89, 129.16, 127.71, 127.60, 127.31, 127.28, 118.27, 111.74, 110.62, 97.64, 78.03, 60.79, 50.51, 43.50, 43.49, 40.13, 39.09, 21.57, 14.48, 13.98, 13.14, 12.44.



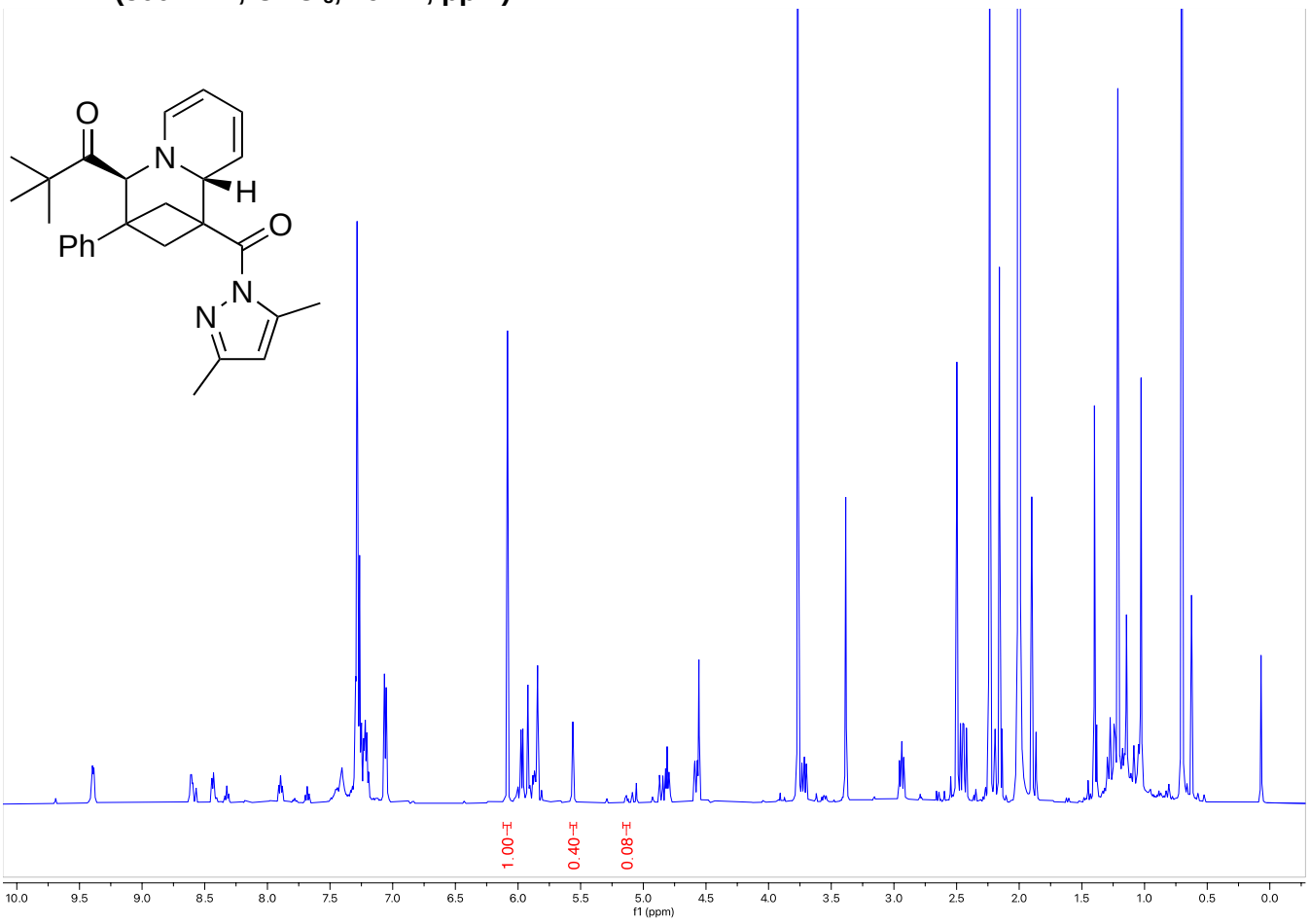
1-(1-(3,5-dimethyl-1H-pyrazole-1-carbonyl)-3-phenyl-1,3,4,9a-tetrahydro-2H-1,3-methanoquinolizin-4-yl)-2,2-dimethylpropan-1-one (3ab)



Product was synthesized following general procedure B on a 0.05 mmol scale. Reagent amounts used: bicyclobutane **1a** (12.6 mg, 0.05 mmol), pyridinium **2ab** (1.25 equiv, 16.1 mg, 0.06 mmol), $NaPF_6$ (1.3 equiv, 10.9 mg, 0.06 mmol) and K_3PO_4 (2.5 equiv, 26.4 mg, 0.13 mmol) in 0.2 mL acetonitrile (0.25 M). Solution yield determined by NMR spectroscopy using 1,3,5-trimethoxybenzene internal standard (**48% solution yield, 5:1 dr**).

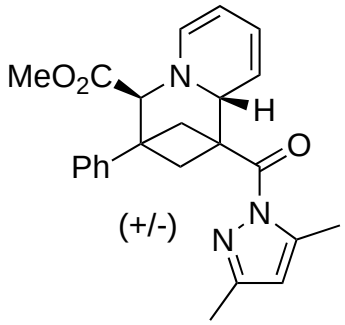
HRMS(ESI): calc'd for [$C_{27}H_{31}N_3O_2$ + H^+], 430.24891; found: 430.24905.

^{1}H NMR (500 MHz, $CDCl_3$, 292 K, ppm):



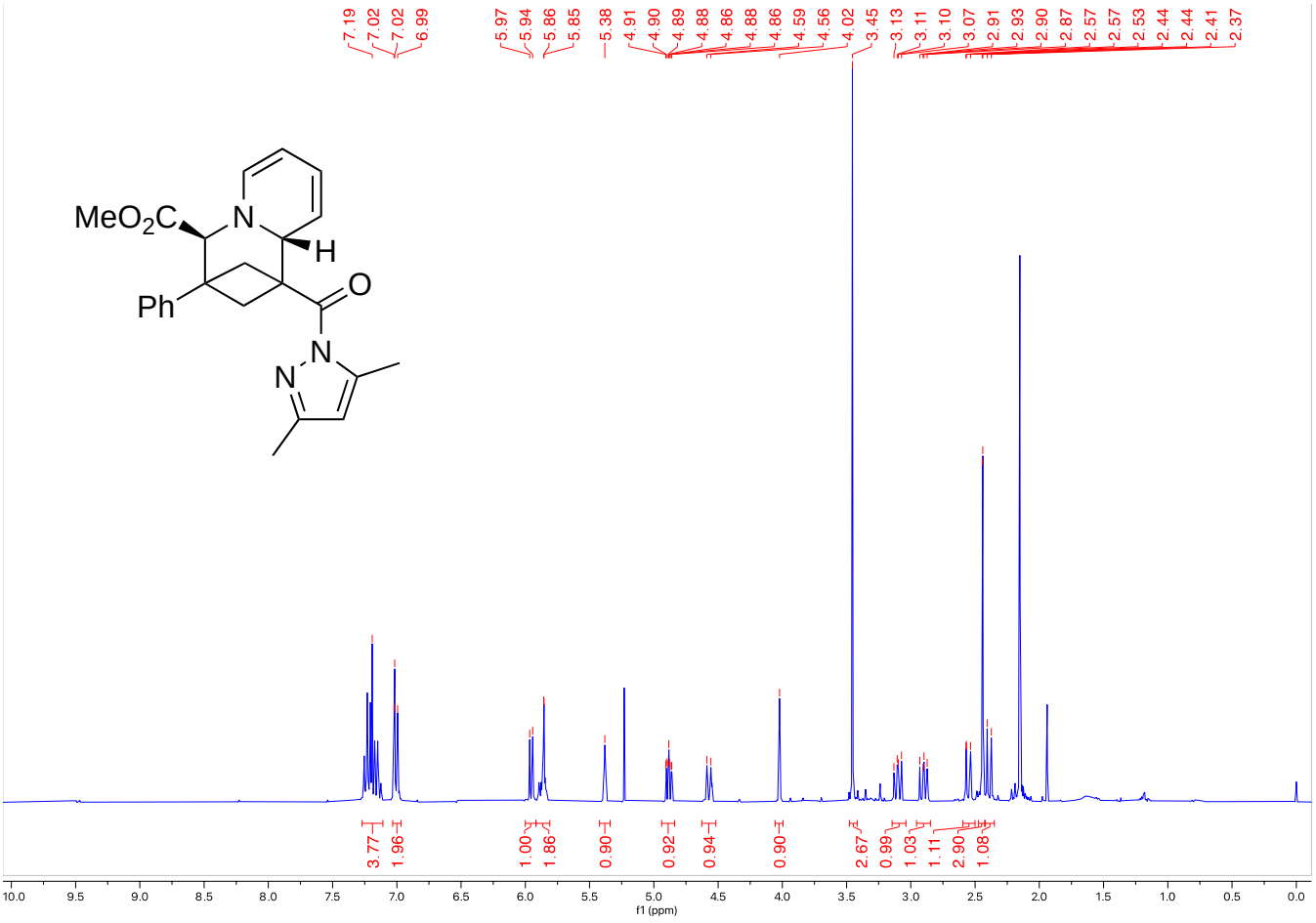
VIII: Larger Scale Synthesis

Methyl 1-(3,5-dimethyl-1H-pyrazole-1-carbonyl)-3-phenyl-1,3,4,9a-tetrahydro-2H-1,3-methanoquinolizine-4-carboxylate (3a)



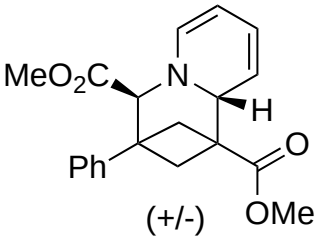
Product was synthesized following general procedure **A** on a 2.0 mmol scale. Reagent amounts used: bicyclobutane **1a** (504.6 mg, 2.0 mmol), pyridinium **2a** (1.25 equiv, 580.2 mg, 2.5 mmol), and K_3PO_4 (2.5 equiv, 1.0614 g, 5.0 mmol) in 8.0 mL acetonitrile (0.25 M). Isolated 655.0 mg of an orange solid (**65% yield**).

^{1}H NMR (500 MHz, $CDCl_3$, 292 K, ppm):



IX: Diversification Reactions

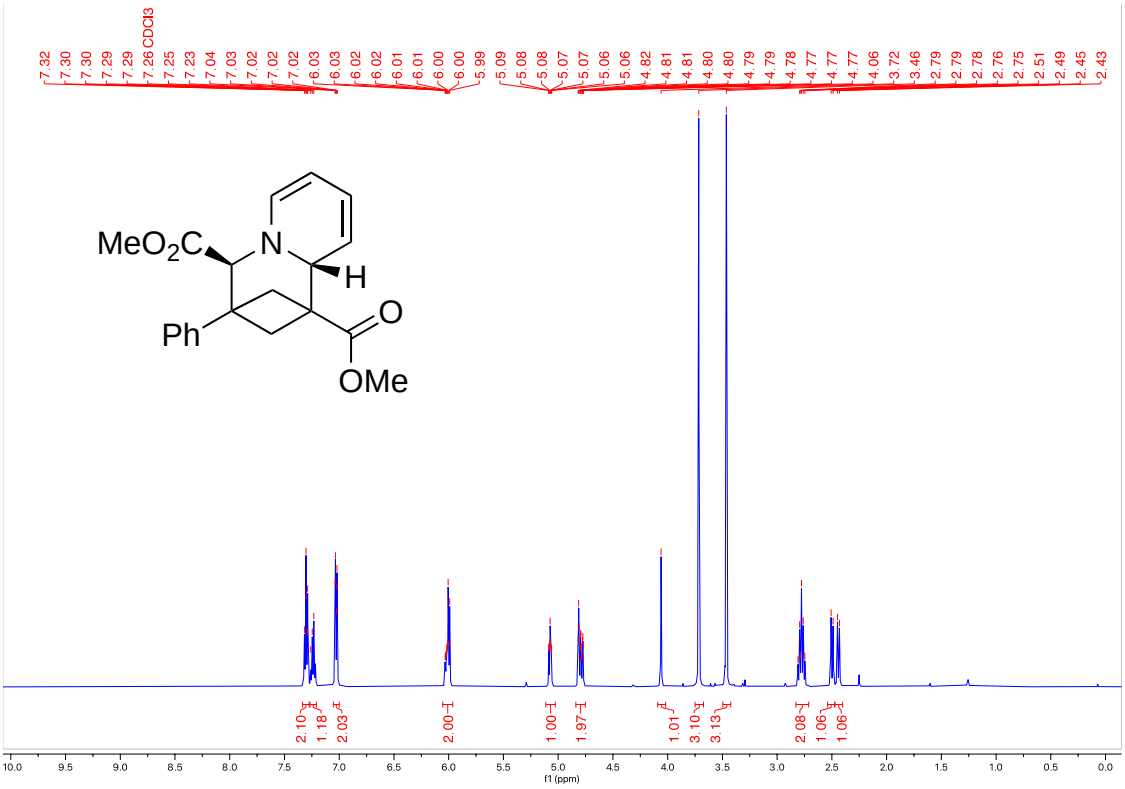
Dimethyl 3-phenyl-3,4-dihydro-2*H*-1,3-methanoquinolizine-1,4(9a*H*)-dicarboxylate (4a)



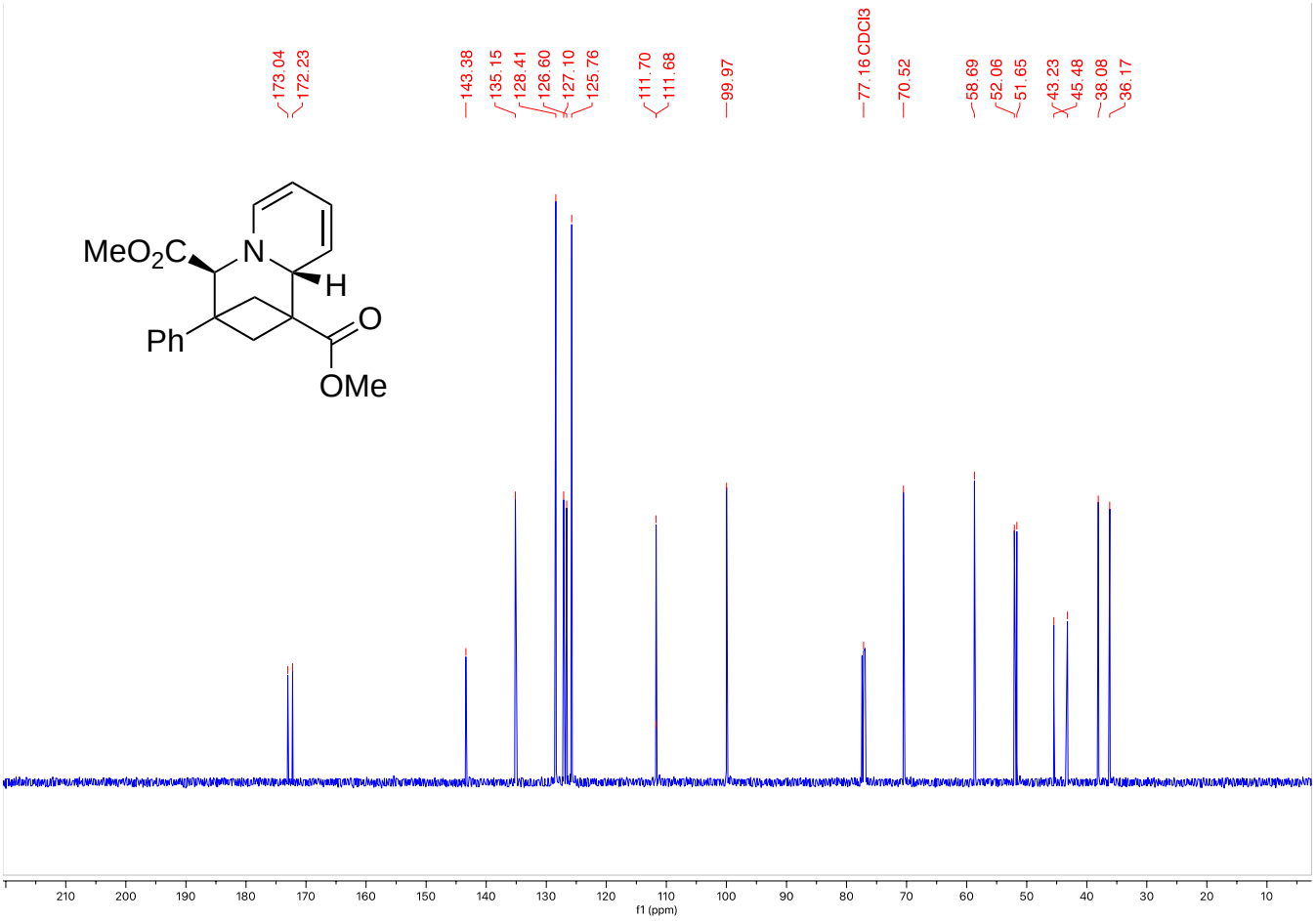
To a 250 mL round bottom flask was added pyridinium **2a** (1.25 equiv, 1.1497 g, 4.95 mmol) and K_3PO_4 (2.5 equiv, 2.1032 g, 9.91 mmol) as well as a stir bar. Acetonitrile (4 mL) was added, and the mixture stirred for 5 minutes at room temperature. Then, bicyclobutane **1a** (1 equiv, 1.00 g, 3.96 mmol) was weighed into a 20 mL vial. Using acetonitrile (12 mL), **1a** was quantitatively transferred to the reaction flask. The mixture was stirred for 36 hours at room temperature. Then, an equal volume of methanol (16 mL) and additional K_3PO_4 (1.0 equiv, 0.8413 g, 3.96 mmol) were added to the reaction mixture, which was stirred at rt for 24 hours. Then, the solvent was evaporated *in vacuo*, the residue extracted into dichloromethane (30 mL), and the solution passed through a plug of basic alumina plug using excess dichlormethane to elute. Evaporation of the solvent yielded 948.9 mg of a light orange solid (**71% yield**).

HRMS(ESI): calc'd for [$C_{20}H_{21}NO_4$ + H^+], 340.15434; found: 340.15427.

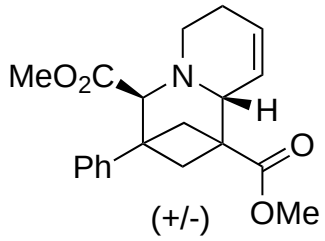
^{1}H NMR (500 MHz, $CDCl_3$, 292 K, ppm): δ 7.30 (t, J = 7.4 Hz, 2H), 7.24 (d, J = 7.4 Hz, 1H), 7.05 – 7.00 (m, 2H), 6.05 – 5.96 (m, 2H), 5.07 (ddd, J = 6.9, 5.3, 1.3 Hz, 1H), 4.84 – 4.75 (m, 2H), 4.06 (s, 1H), 3.72 (s, 3H), 3.46 (s, 3H), 2.78 (p, J = 7.5 Hz, 2H), 2.50 (d, J = 9.0 Hz, 1H), 2.44 (d, J = 8.9 Hz, 1H).



^{13}C NMR (126 MHz, $CDCl_3$, 292 K, ppm): δ 173.04, 172.23, 143.38, 135.15, 128.41, 127.10, 126.60, 125.76, 111.70, 111.68, 99.97, 70.52, 58.69, 52.06, 51.65, 45.48, 43.23, 38.08, 36.17.



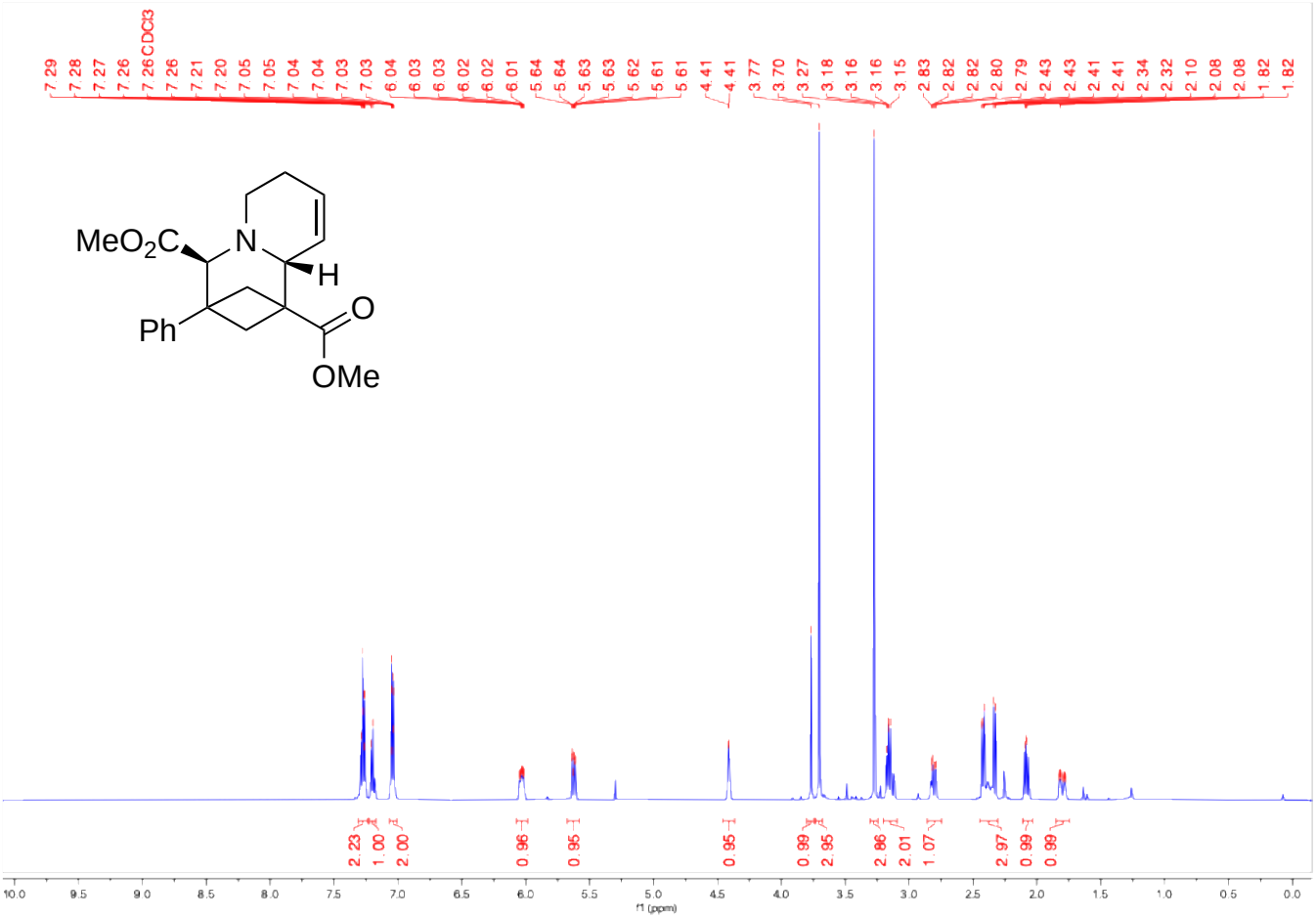
Dimethyl 3-phenyl-3,4,7,9a-tetrahydro-2H-1,3-methanoquinolizine-1,4(6H)-dicarboxylate (4b):



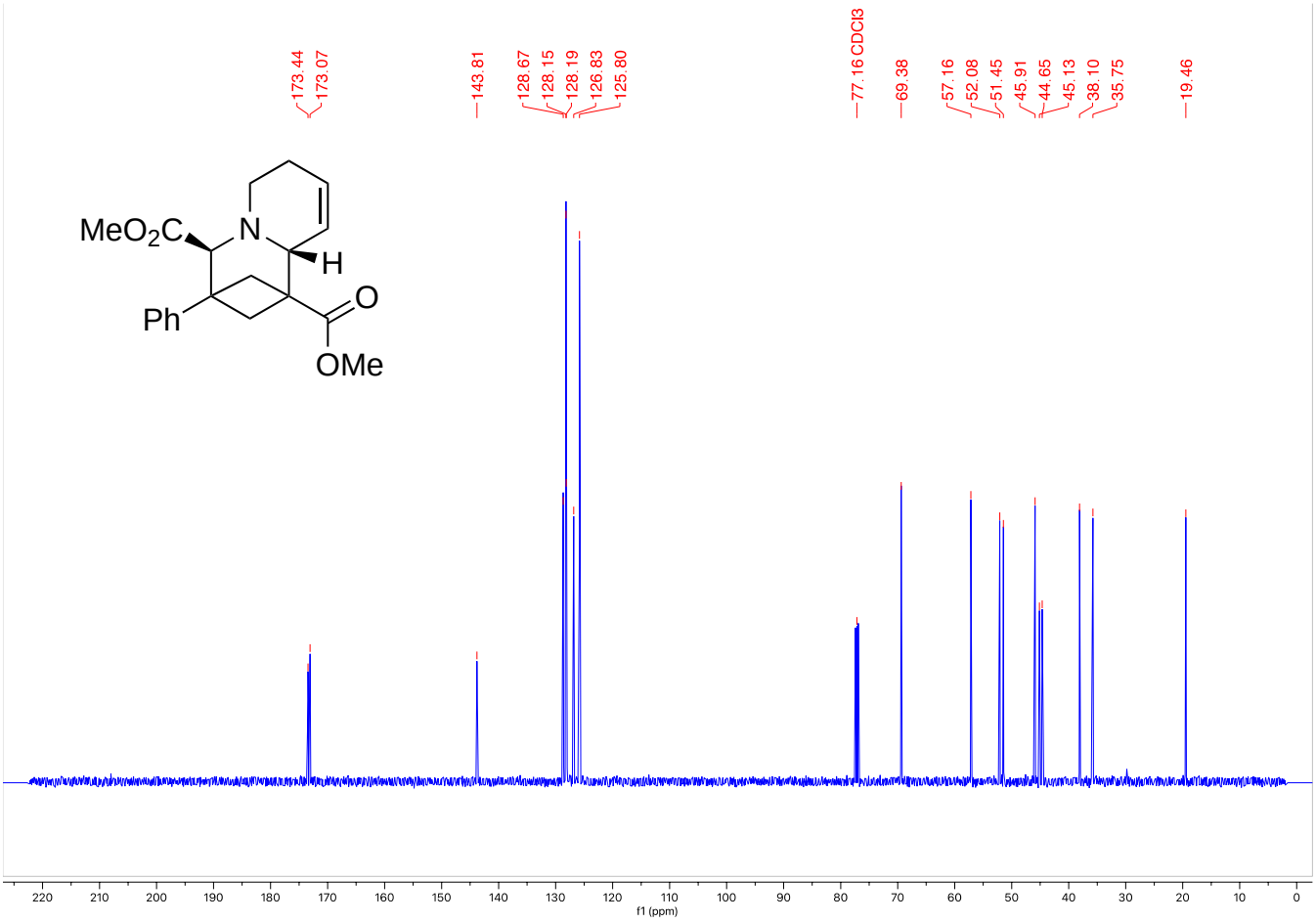
To a 40 mL vial containing a stir bar was added dimethyl 3-phenyl-3,4-dihydro-2H-1,3-methanoquinolizine-1,4(9aH)-dicarboxylate (**4a**) (339.4 mg, 1.00 mmol) and sodium cyanoborohydride (2.5 equiv, 157.1 mg, 2.5 mmol). The mixture of solids was cooled to 0 °C, followed by the addition of cold (~0 °C) methanol (10 mL, 0.1 M) with stirring. The reaction mixture was stirred for 5 minutes at 0 °C, followed by removal of the ice bath. The mixture was then stirred for 4 hours. The reaction was quenched with saturated sodium bicarbonate solution (10 mL) and extracted with DCM (3 x 10 mL). The organic layers were combined, washed with brine, then dried with Mg_2SO_4. The solution was filtered, and the solvent evaporated. Crude **4b** was obtained as a light yellow crystalline solid (263.0 mg, 77% yield, NMR spectrum below). The product was purified further by column chromatography (Biotage® Sfär 10g Column, 0-100% EtOAc/hexanes, eluted at 26% EtOAc) to obtain a white crystalline solid (198.0 mg, 58% Yield). Single crystals for X-ray diffraction were grown from an ethyl acetate/hexanes solution of **4b**.

HRMS(ESI): calc'd for [$C_{20}H_{23}NO_4$ + H^+], 342.16999; found: 342.16998.

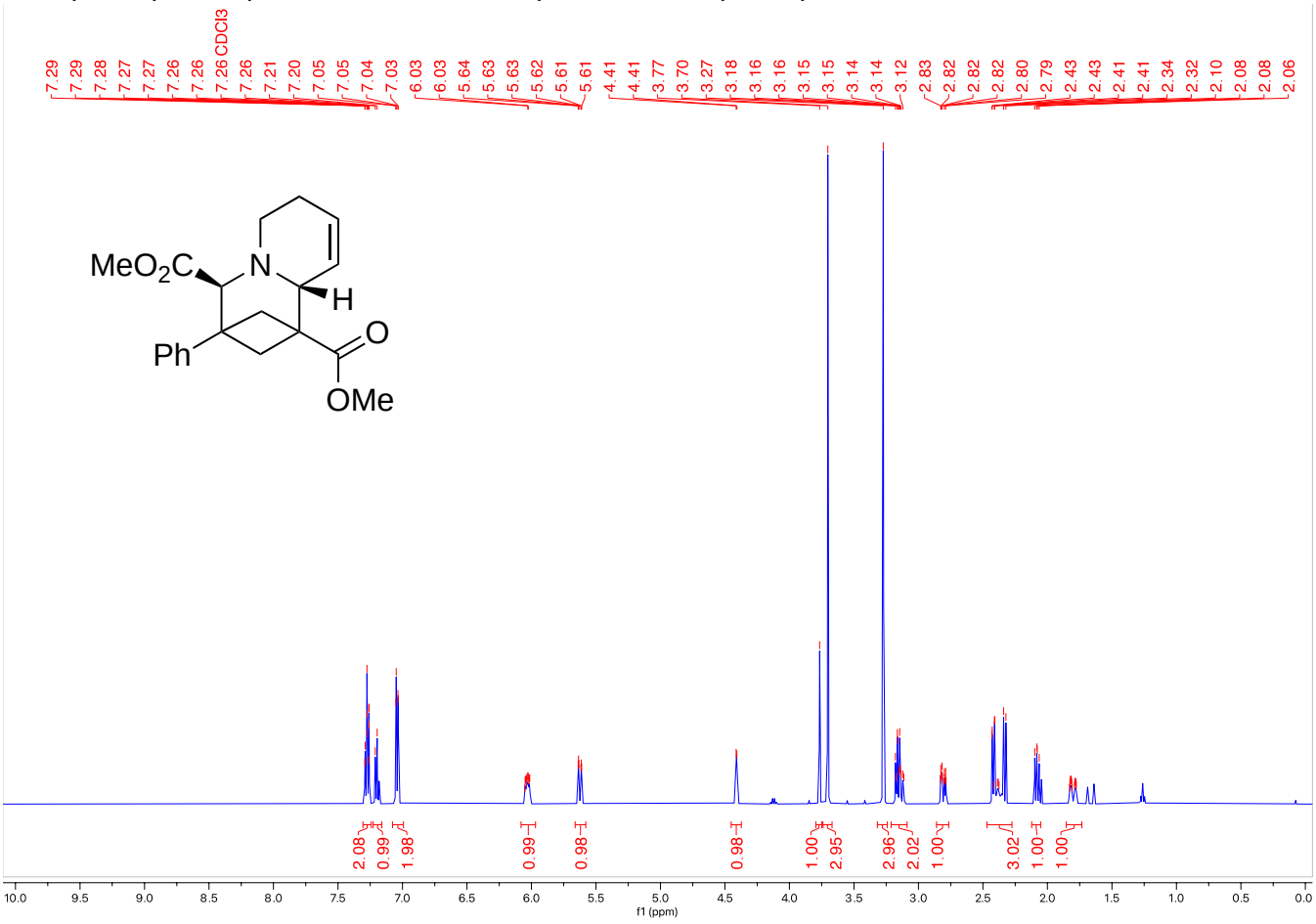
^{1}H NMR (500 MHz, $CDCl_3$, 292 K, ppm) crude, prior to chromatography:



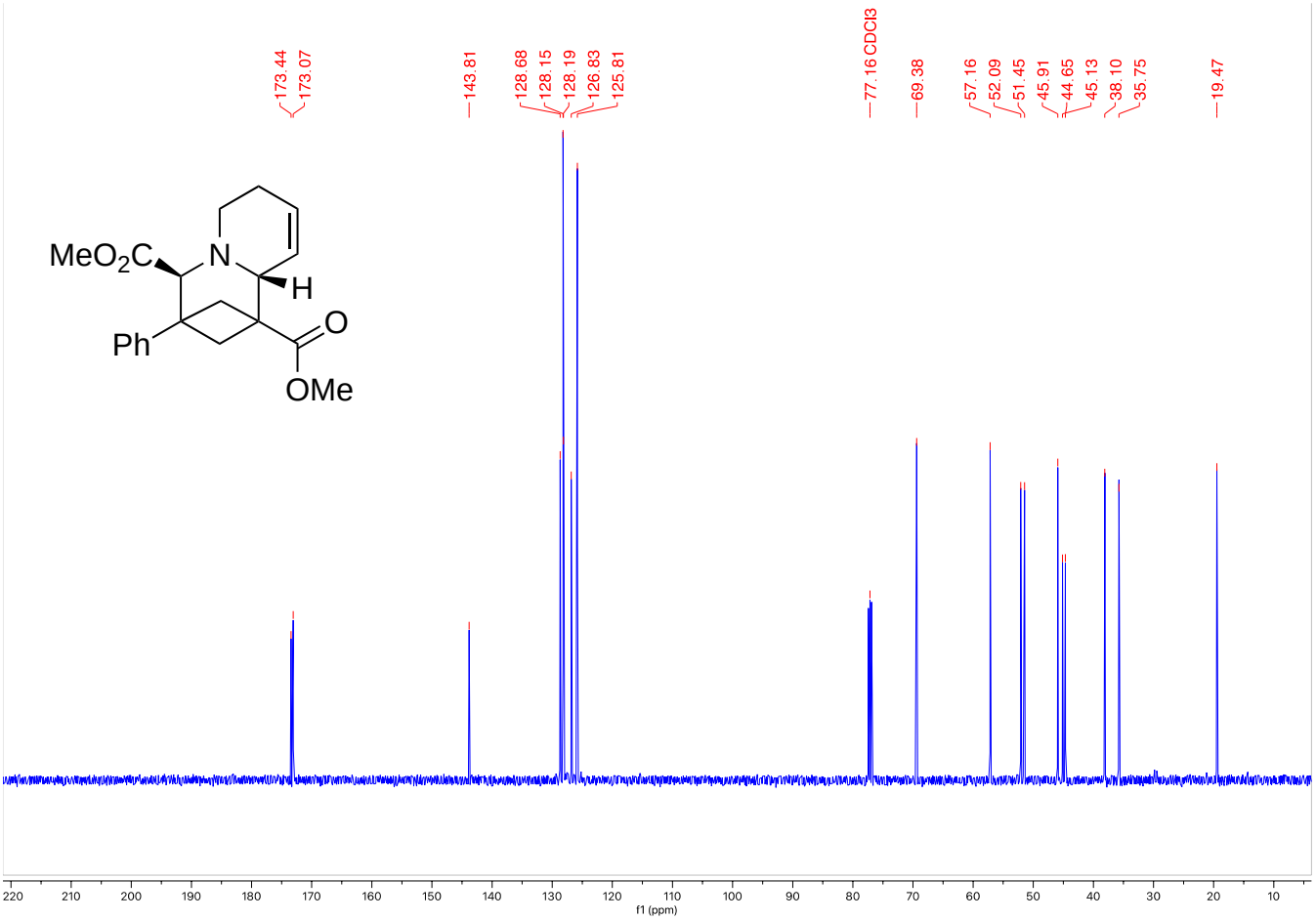
^{13}C NMR (126 MHz, $CDCl_3$, 292 K, ppm) crude, prior to chromatography:



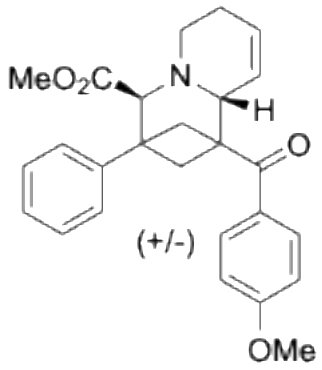
^{1}H NMR (500 MHz, $CDCl_3$, 292 K, ppm) after column: δ 7.31 – 7.24 (m, 2H), 7.20 (d, J = 7.4 Hz, 1H), 7.08 – 6.99 (m, 2H), 6.03 (ddt, J = 10.0, 5.7, 1.6 Hz, 1H), 5.66 – 5.58 (m, 1H), 4.41 (d, J = 3.0 Hz, 1H), 3.77 (s, 1H), 3.70 (s, 3H), 3.27 (s, 3H), 3.21 – 3.09 (m, 2H), 2.81 (ddt, J = 14.1, 5.4, 1.2 Hz, 1H), 2.47 – 2.28 (m, 3H), 2.08 (dd, J = 9.4, 7.6 Hz, 1H), 1.85 – 1.73 (m, 1H).



^{13}C NMR (126 MHz, $CDCl_3$, 292 K, ppm) after column: δ 173.44, 173.07, 143.81, 128.68, 128.19, 128.15, 126.83, 125.81, 69.38, 57.16, 52.09, 51.45, 45.91, 45.13, 44.65, 38.10, 35.75, 19.47.



Methyl 1-(4-methoxybenzoyl)-3-phenyl-1,3,4,6,7,9a-hexahydro-2H-1,3-methanoquinolizine-4-carboxylate (4i)

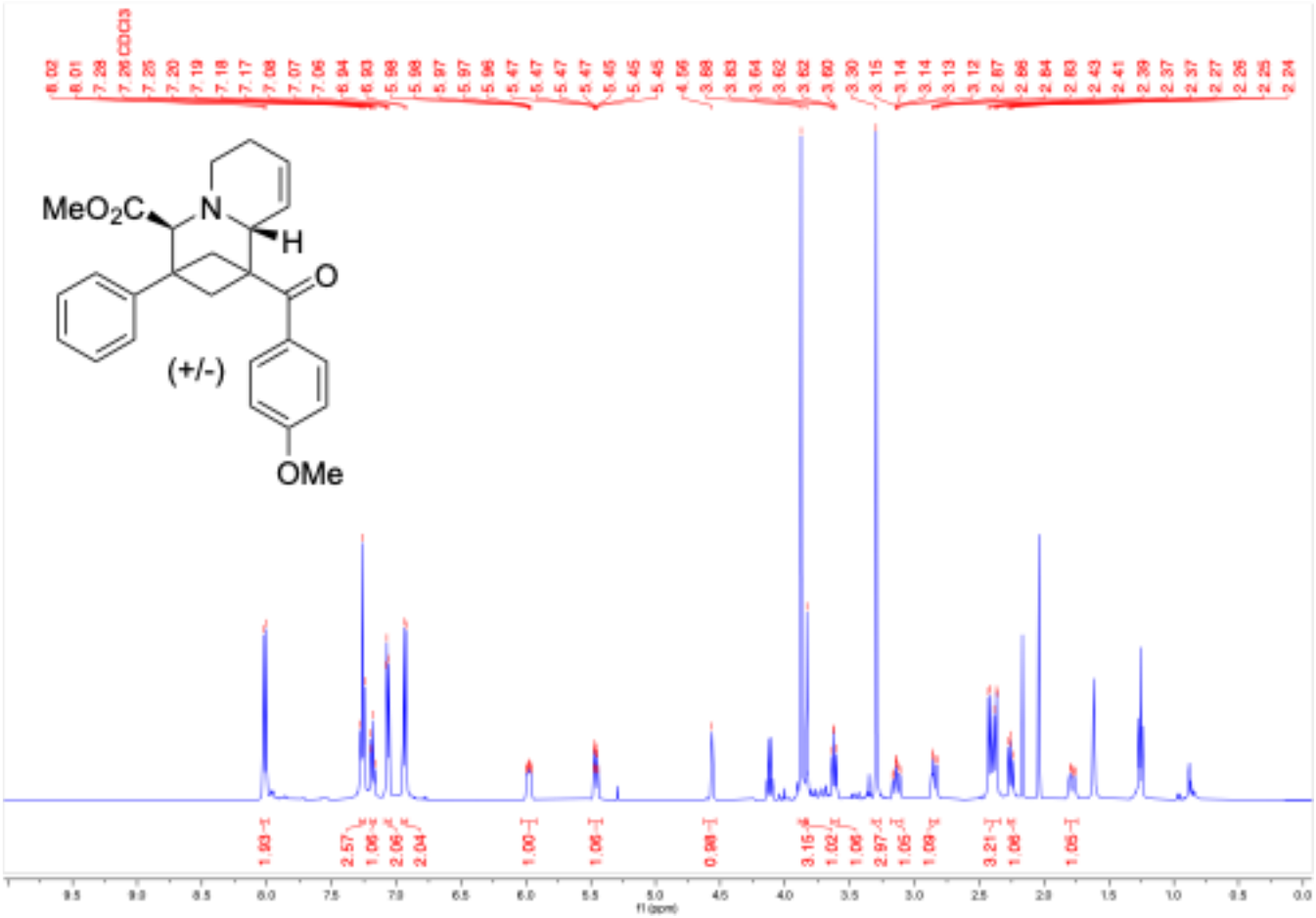


To a 4 mL vial was added the pyridinium salt **2i** (1.25 equiv., 46.2 mg, 0.20 mmol)**,** K_3PO_4, (2.5 equiv., 84.9 mg, 0.40 mmol), bicyclobutane **1i** (1 equiv., 42.3 mg, 0.16 mmol) and a stir bar. Acetonitrile was added to the vial (0.64 mL, 0.25 M) and the reaction mixture was stirred for 24 hours at room temperature. The solvent was then evaporated, the residue redissolved in methanol and cooled down to 0°C. Then $NaBH_3CN$ (25.1 mg, 2.5 equiv., 0.40 mmol) and acetic acid (9.2 µL, 1 equiv., 0.16 mmol) was added to the cooled solution and it was allowed to warm to room temperature and left to stir overnight. The reaction

mixture was quenched with $NaHCO_3$ (5 mL) and then extracted DCM (3 x 5 mL). The organic layers were combined then dried with Mg_2SO_4. The solution was filtered and the solvent was evaporated to give the crude product. The product was purified further by column chromatography (Biotage® Sfär 5g Column, 0-100% EtOAc/hexanes, eluted at 35% EtOAc) to obtain a white solid (16.5 mg, 25% Yield).

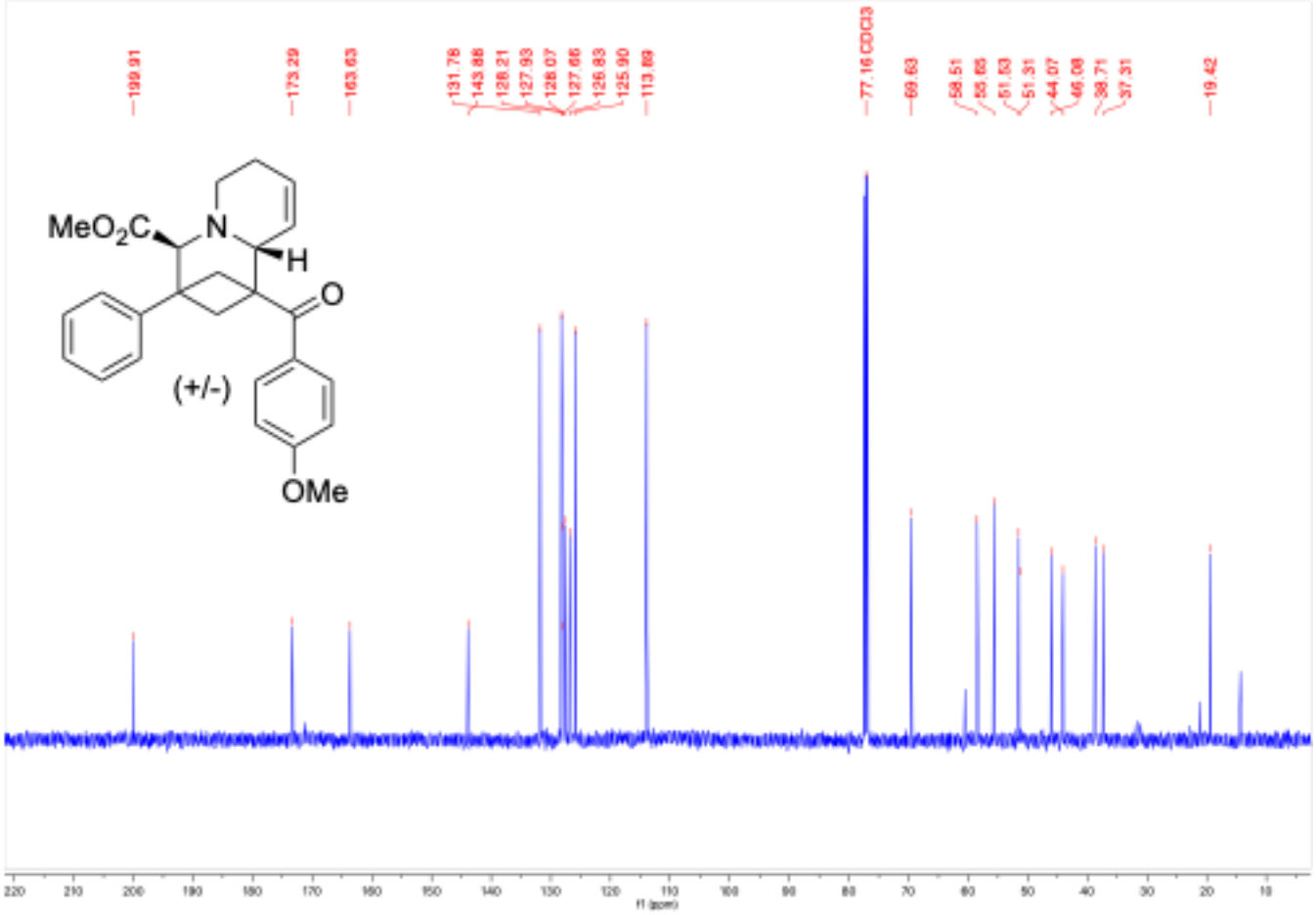
HRMS(ESI): calc'd for [$C_{26}H_{27}NO_4$ + H^+], 418.20129; found: 418.20115.

^{1}H NMR (500 MHz, $CDCl_3$, 292 K, ppm): δ 8.01 (d, J = 8.9 Hz, 2H), 7.26 (d, J = 15.0 Hz, 2H), 7.20 – 7.15 (m, 1H), 7.09 – 7.05 (m, 2H), 6.94 (d, J = 8.9 Hz, 2H), 5.97 (ddd, J = 7.1, 4.8, 2.8 Hz, 1H), 5.46 (ddt, J = 10.4, 2.9, 1.4 Hz, 1H), 4.56 (s, 1H), 3.88 (s, 3H), 3.83 (s, 1H), 3.64 – 3.59 (m, 1H), 3.30 (s, 3H), 3.14 (ddd, J = 14.0, 11.9, 4.1 Hz, 1H), 2.85 (dd, J = 14.1, 5.2 Hz, 1H), 2.45 – 2.34 (m, 3H), 2.26 (dd, J = 9.7, 7.4 Hz, 1H), 1.84 – 1.74 (m, 1H).

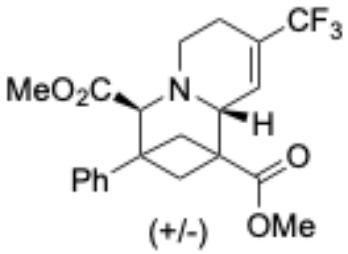


^{13}C NMR (126 MHz, $CDCl_3$, 292 K, ppm): δ 199.91, 173.29, 163.63, 143.88, 131.78, 128.21, 128.07, 127.93, 127.66, 126.83, 125.90, 113.89, 69.63, 58.51, 55.65, 51.53, 51.31, 46.08, 44.07, 38.71, 37.31,

19.42.



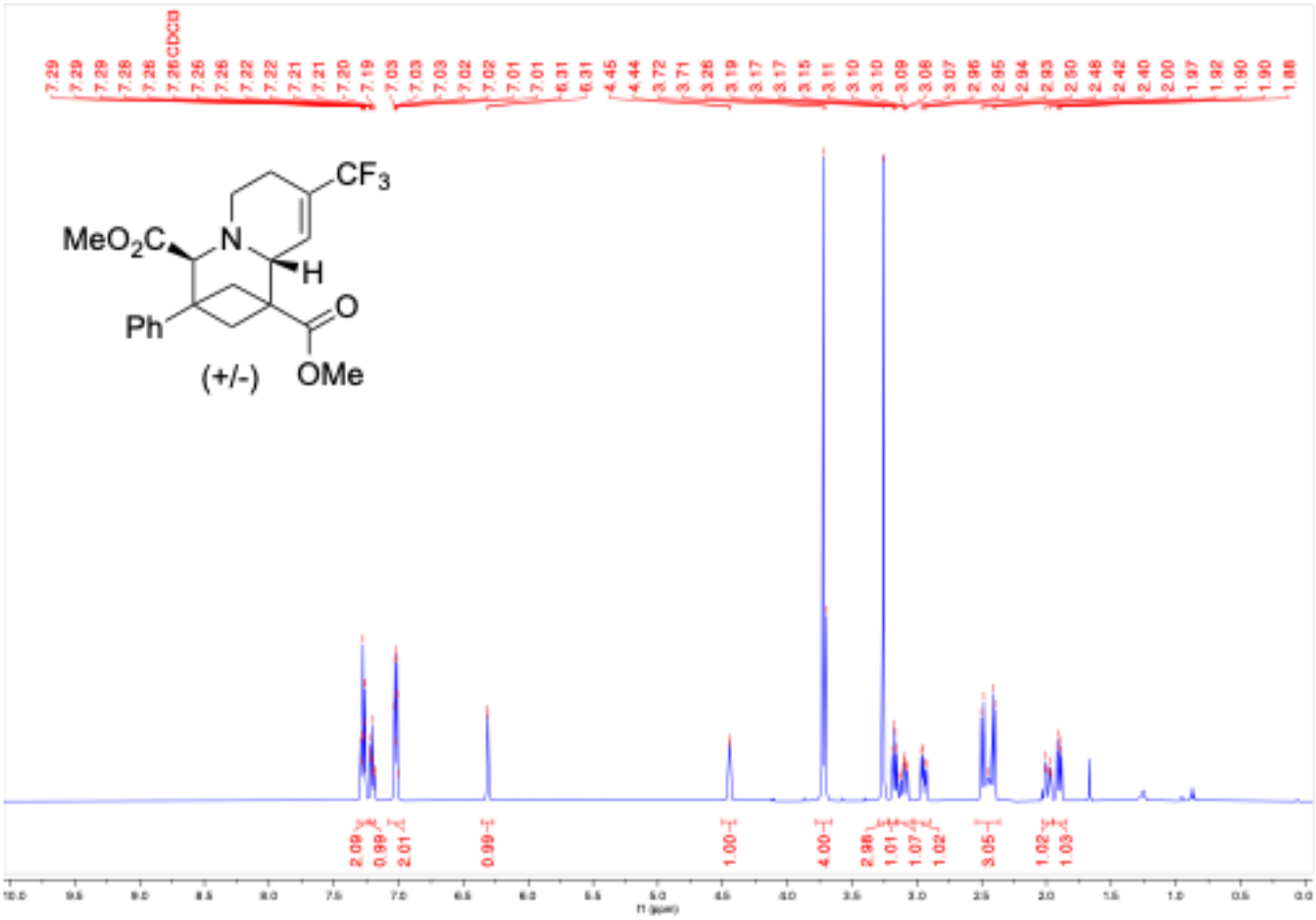
Dimethyl 3-phenyl-8-(trifluoromethyl)-3,4,7,9a-tetrahydro-2*H*-1,3-methanoquinolizine-1,4(6*H*)-dicarboxylate (4l)



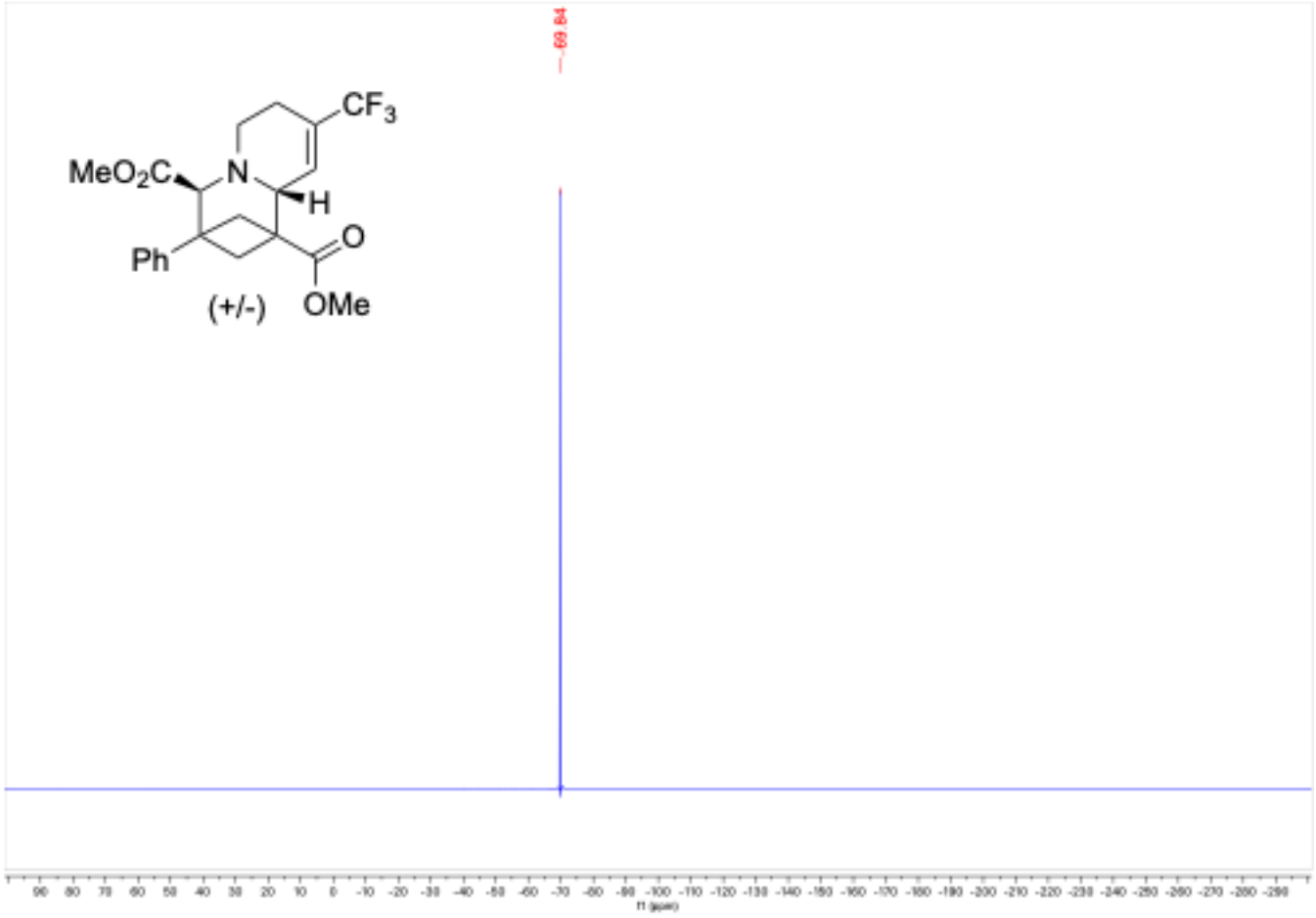
To an 8 mL vial was containing a stir bar was added compound **3l-OMe** (1.0 equiv., 122.4 mg, 0.30 mmol) and sodium cyanoborohydride (2.5 equiv, 47.2 mg, 2.5 mmol). The mixture of solids was cooled to 0 °C, followed by the addition of cold (~0 °C) methanol (3.5 mL, 0.1 M) and acetic acid (0.353 mL) with stirring. The reaction mixture was warmed gradually to room temperature and then stirred for 4 hours. The reaction was quenched with saturated sodium bicarbonate solution (10 mL) and extracted with DCM (2 x 14 mL). The organic layers were combined, washed with brine, then dried with Mg_2SO_4. The solution was filtered, and the solvent evaporated to give the crude product. The product was purified further by column chromatography (Biotage® Sfär 5g Column, 0-100% EtOAc/hexanes, eluted at 11% EtOAc) to obtain a white solid (42.0 mg, 34% Yield).

HRMS(ESI): calc'd for [$C_{21}H_{22}F_3NO_4$ + H^+], 410.15737; found: 410.15698.

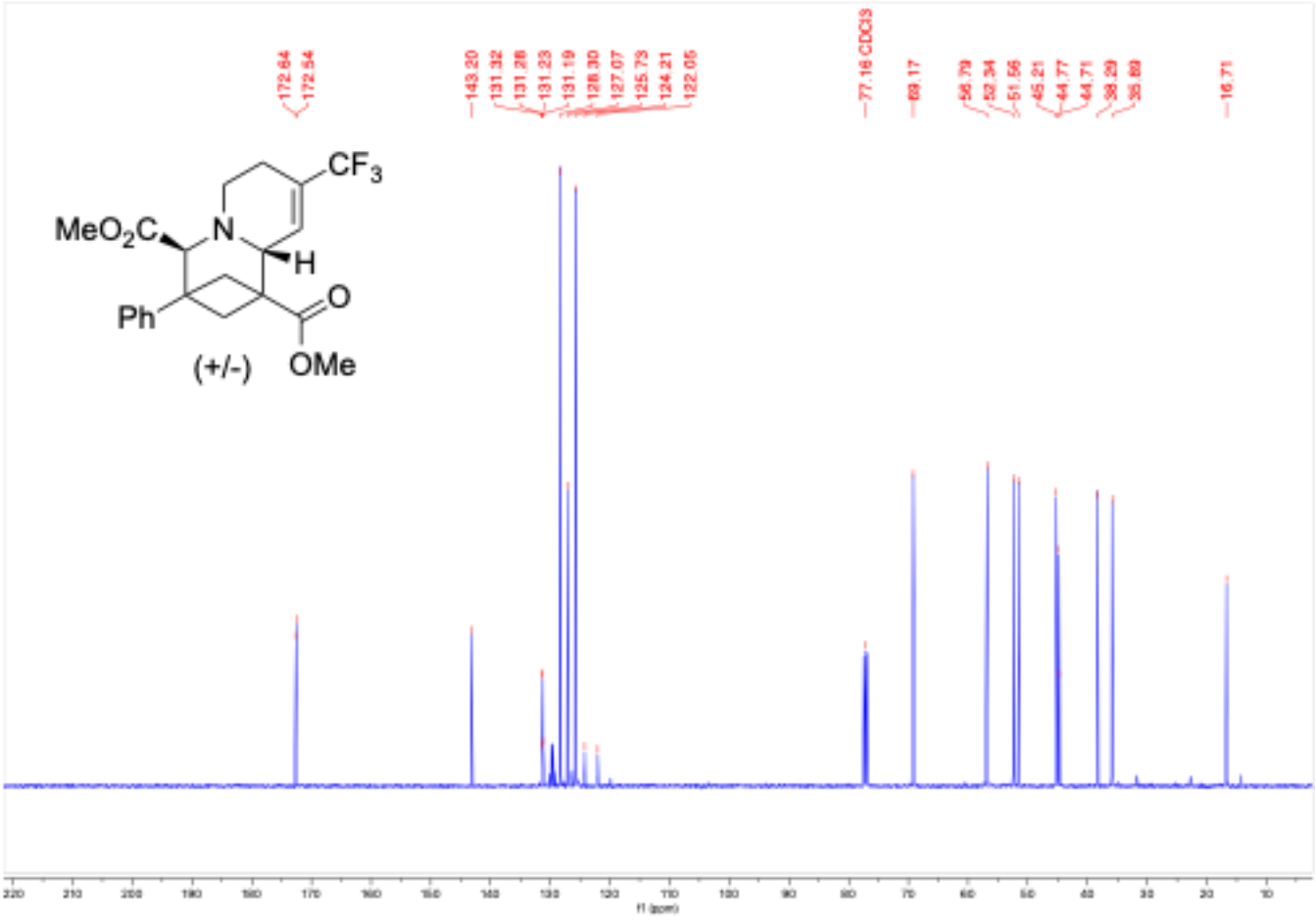
^{1}H NMR (500 MHz, $CDCl_3$, 292 K, ppm): δ 7.31 – 7.23 (m, 2H), 7.23 – 7.18 (m, 1H), 7.08 – 6.97 (m, 2H), 6.31 (s, 1H), 4.45 (s, 1H), 3.71 (m, 4H), 3.26 (s, 3H), 3.17 (dd, J = 8.9, 7.6 Hz, 1H), 3.10 (ddd, J = 14.2, 11.8, 4.0 Hz, 1H), 2.95 (dd, J = 14.4, 5.3 Hz, 1H), 2.45 (m, 3H), 1.99 (dt, J = 17.7, 3.4 Hz, 1H), 1.90 (dd, J = 9.7, 7.7 Hz, 1H).



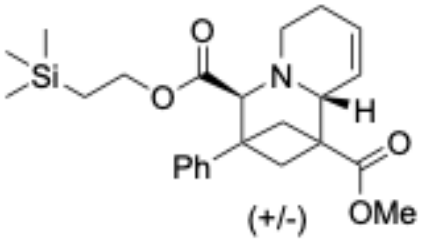
^{19}F NMR (500 MHz, $CDCl_3$, 292 K, ppm): δ 69.84



^{13}C NMR (126 MHz, $CDCl_3$, 292 K, ppm): δ 172.64, 172.54, 143.20, quartet (131.32, 131.28, 131.23, 131.19), 128.30, 127.07, 125.73, 124.21, 122.05, 69.17, 56.79, 52.34, 51.56, 45.21, 44.77, 44.71, 38.29, 35.89, 16.71.



1-Methyl 4-(2-(trimethylsilyl)ethyl) 3-phenyl-3,4,7,9a-tetrahydro-2*H*-1,3-methanoquinolizine-1,4(6*H*)-dicarboxylate (4q)

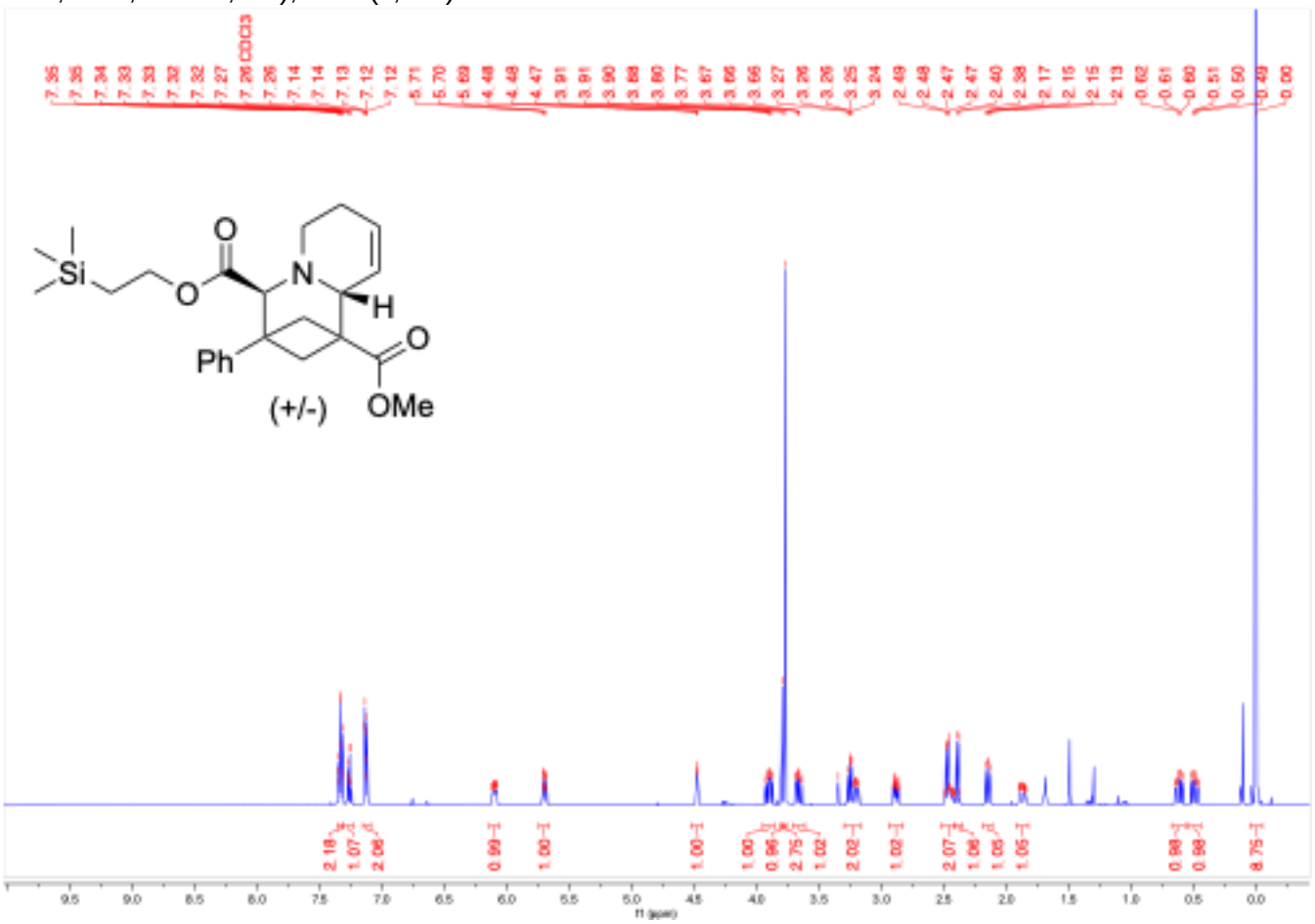


To a 4 mL vial was added the pyridinium salt **2q** (1.25 equiv., 119.4 mg, 0.38 mmol)**,** K_3PO_4, (2.5 equiv., 159.2 mg, 0.75 mmol) and a stir bar. Acetonitrile (0.6 mL) was added, and the mixture stirred for 5 minutes at room temperature. Then, bicyclobutane **1a** (1 equiv, 75.7 g, 0.30 mmol) was weighed into a 1 mL vial. Using acetonitrile (0.6 mL), **1a** was quantitatively transferred to the reaction vial. The mixture was stirred for 24 hours at room temperature. Then, an equal volume of methanol (1.2 mL) and additional

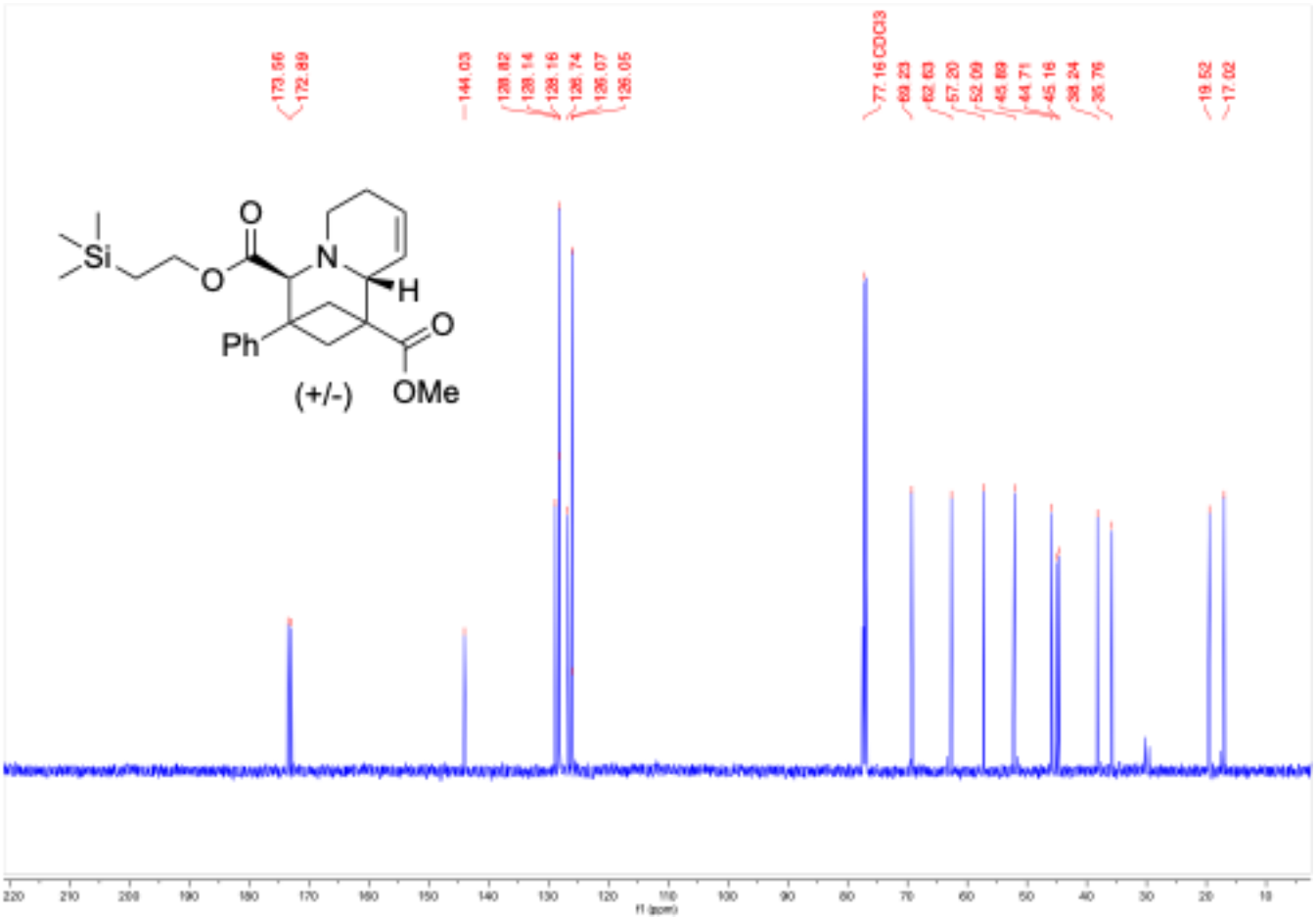
K_3PO_4 (1.0 equiv, 63.7 mg, 0.30 mmol) were added to the reaction mixture, which was stirred at rt for 24 hours. Then, the solvent was evaporated *in vacuo* and the residue was redissolved in methanol (3 mL), filtered quantitatively though a 0.45 µm syringe filter and the solution was cooled down to 0°C. Then $NaBH_3CN$ (47.1 mg, 2.5 equiv., 0.75 mmol) and acetic acid (17.2 µL, 1 equiv., 0.30 mmol) was added to the reaction vial and it was allowed to warm to room temperature and left to stir overnight. The reaction mixture was quenched with $NaHCO_3$ (5 mL) and then extracted DCM (3 x 5 mL). The organic layers were combined then dried with Mg_2SO_4. The solution was filtered, and the solvent was evaporated to give the crude product. The product was purified further by column chromatography (Biotage® Sfär 5g Column, 0-100% EtOAc/hexanes, eluted at 25% EtOAc) to obtain a white solid (14.0 mg, 11% Yield over three steps).

HRMS(ESI): calc'd for [$C_{24}H_{33}NO_4Si + H^+$], 428.22517; found: 428.22500.

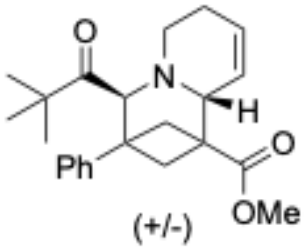
^{1}H NMR (500 MHz, $CDCl_3$, 292 K, ppm): δ 7.36 – 7.32 (m, 2H), 7.31 – 7.23 (m, 1H), 7.16 – 7.09 (m, 2H), 6.14 – 6.07 (m, 1H), 5.70 (ddt, J = 10.3, 2.8, 1.4 Hz, 1H), 4.53 – 4.44 (m, 1H), 3.90 (ddd, J = 11.8, 10.8, 5.7 Hz, 1H), 3.80 (s, 1H), 3.77 (s, 3H), 3.66 (ddd, J = 12.0, 10.8, 5.3 Hz, 1H), 3.30 – 3.17 (m, 2H), 2.89 (ddt, J = 14.1, 5.4, 1.2 Hz, 1H), 2.52 – 2.41 (m, 2H), 2.39 (d, J = 8.8 Hz, 1H), 2.15 (dd, J = 9.4, 7.5 Hz, 1H), 1.87 (ddt, J = 17.3, 4.2, 1.3 Hz, 1H), 0.62 (ddd, J = 13.7, 12.0, 5.7 Hz, 1H), 0.49 (ddd, J = 13.7, 11.8, 5.3 Hz, 1H), 0.00 (s, 9H).



^{13}C NMR (126 MHz, $CDCl_3$, 292 K, ppm): δ 173.56, 172.89, 144.03, 128.82, 128.16, 128.14, 126.74, 126.07, 126.05, 69.23, 62.63, 57.20, 52.09, 45.89, 45.16, 44.71, 38.24, 35.76, 19.52, 17.02.



Methyl 3-phenyl-4-pivaloyl-3,4,7,9a-tetrahydro-2*H*-1,3-methanoquinolizine-1(6*H*)-carboxylate (4ab)

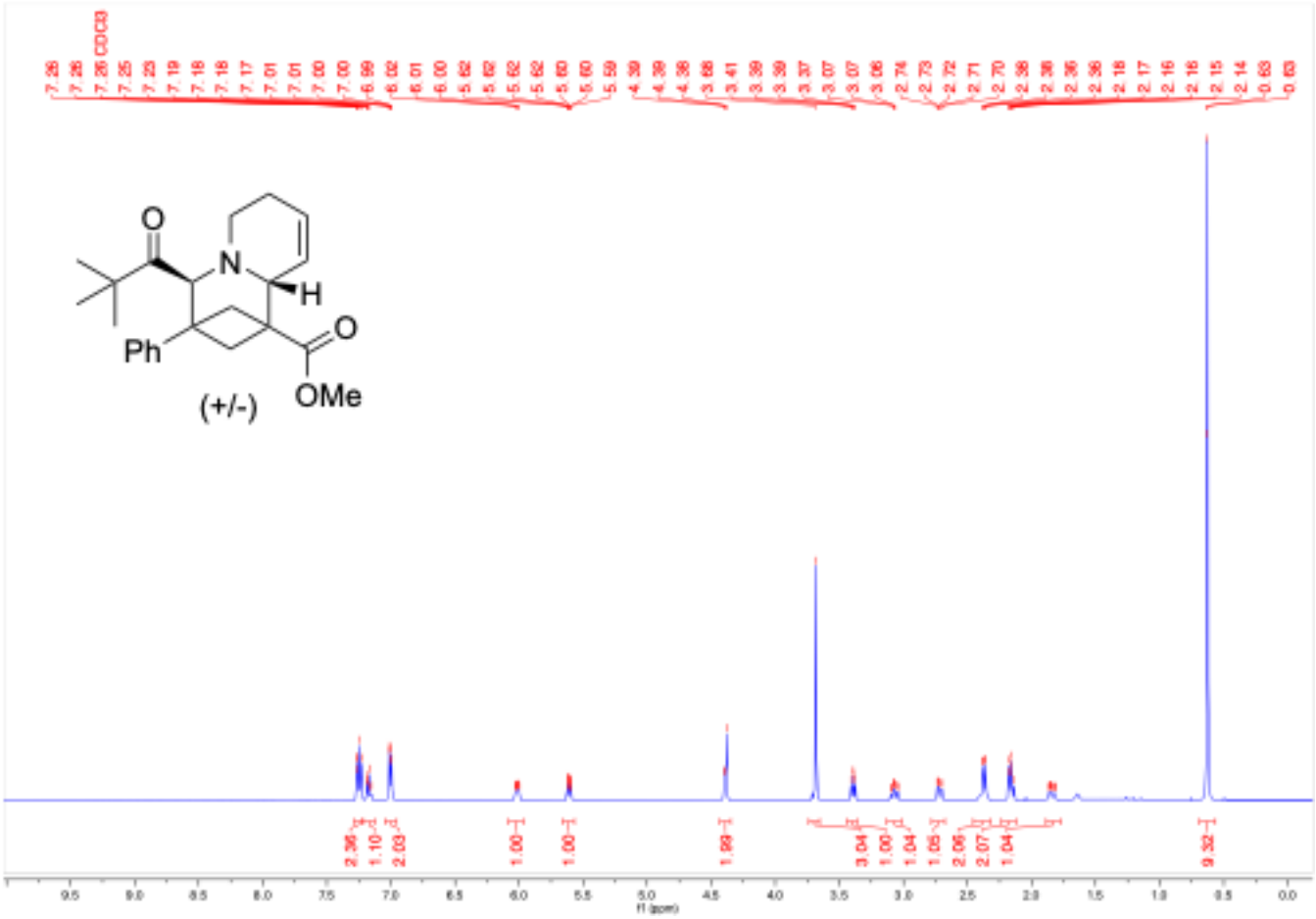


To a 4 mL vial was added the pyridinium salt **2ab** (1.25 equiv., 96.8 mg, 0.38 mmol), $NaPF_6$ (1.3 equiv., 65.5 mg, 0.39 mmol), and a stir bar. Acetonitrile (0.6 mL) was added, and the solution was stirred for 2 hours at room temperature. K_3PO_4, (2.5 equiv., 159.2 mg, 0.75 mmol) was added to the vial and the mixture stirred for 5 minutes at room temperature. Then, bicyclobutane **1a** (1 equiv., 75.7 g, 0.30 mmol) was weighed into a 1 mL vial. Using acetonitrile (0.6 mL), **1a** was quantitatively transferred to the reaction vial. The mixture was stirred for 24 hours at room temperature. Then, an equal volume of methanol (1.2 mL) and additional K_3PO_4 (1.0 equiv, 63.7 mg, 0.30 mmol) were added to the reaction mixture, which was stirred at rt for 24 hours. Then, the solvent was evaporated *in vacuo* and the residue was redissolved in methanol (3 mL), filtered quantitatively though a 0.45 µm syringe filter and the solution was cooled

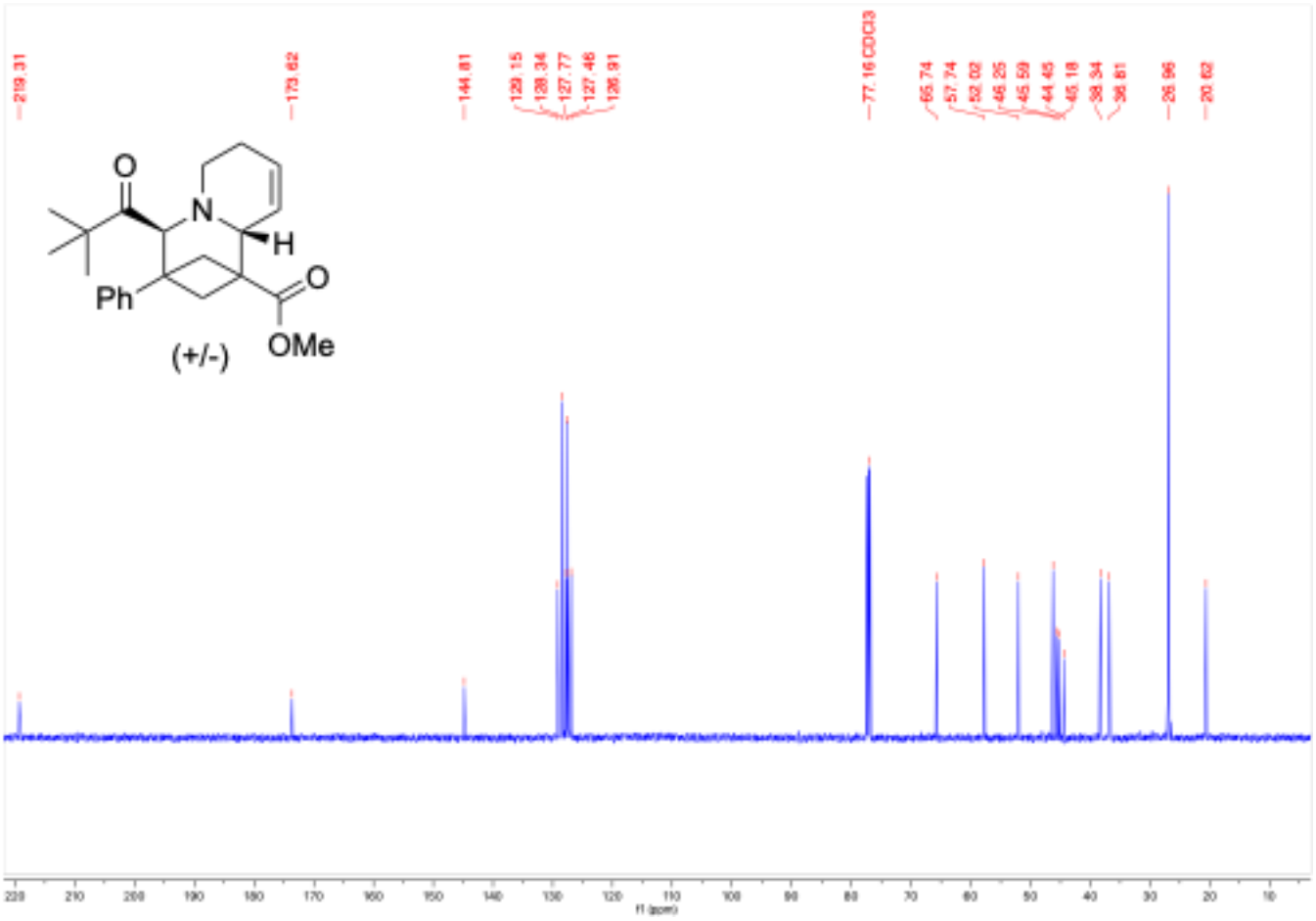
down to 0°C. Then $NaBH_3CN$ (47.1 mg, 2.5 equiv., 0.75 mmol) and acetic acid (17.2 µL, 1 equiv., 0.30 mmol) was added to the reaction vial and it was allowed to warm to room temperature and left to stir overnight. The reaction mixture was quenched with $NaHCO_3$ (5 mL) and then extracted DCM (3 x 5 mL). The organic layers were combined then dried with Mg_2SO_4. The solution was filtered, and the solvent was evaporated to give the crude product. The product was purified further by column chromatography (Biotage® Sfär 5g Column, 0-100% EtOAc/hexanes, eluted at 25% EtOAc) to obtain a white solid (25.0 mg, 23% Yield (20% of the major diastereomer and 3% of the minor diastereomer isolated separately) over three steps).

HRMS(ESI): calc'd for [$C_{23}H_{29}NO_3$ + H^+], 368.22202; found: 368.22250.

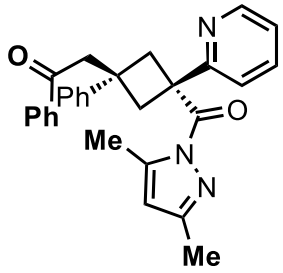
^{1}H NMR (500 MHz, $CDCl_3$, 292 K, ppm): δ 7.29 – 7.22 (m, 2H), 7.22 – 7.12 (m, 1H), 7.05 – 6.95 (m, 2H), 6.08 – 5.96 (m, 1H), 5.61 (ddt, J = 10.4, 2.9, 1.4 Hz, 1H), 4.39 (m, 2H), 3.68 (s, 3H), 3.44 – 3.36 (m, 1H), 3.07 (ddd, J = 13.9, 11.9, 4.0 Hz, 1H), 2.78 – 2.68 (m, 1H), 2.46 – 2.32 (m, 2H), 2.23 – 2.12 (m, 2H), 1.89 – 1.77 (m, 1H), 0.63 (s, 9H).



^{13}C NMR (126 MHz, $CDCl_3$, 292 K, ppm): δ 219.31, 173.62, 144.81, 129.15, 128.34, 127.77, 127.46, 126.91, 65.74, 57.74, 52.02, 46.25, 45.59, 45.18, 44.45, 38.34, 36.81, 26.96, 20.62.



(3-benzoyl-3-phenyl-1-(pyridin-2-yl)cyclobutyl)(3,5-dimethyl-1H-pyrazol-1-yl)methanone (4m)

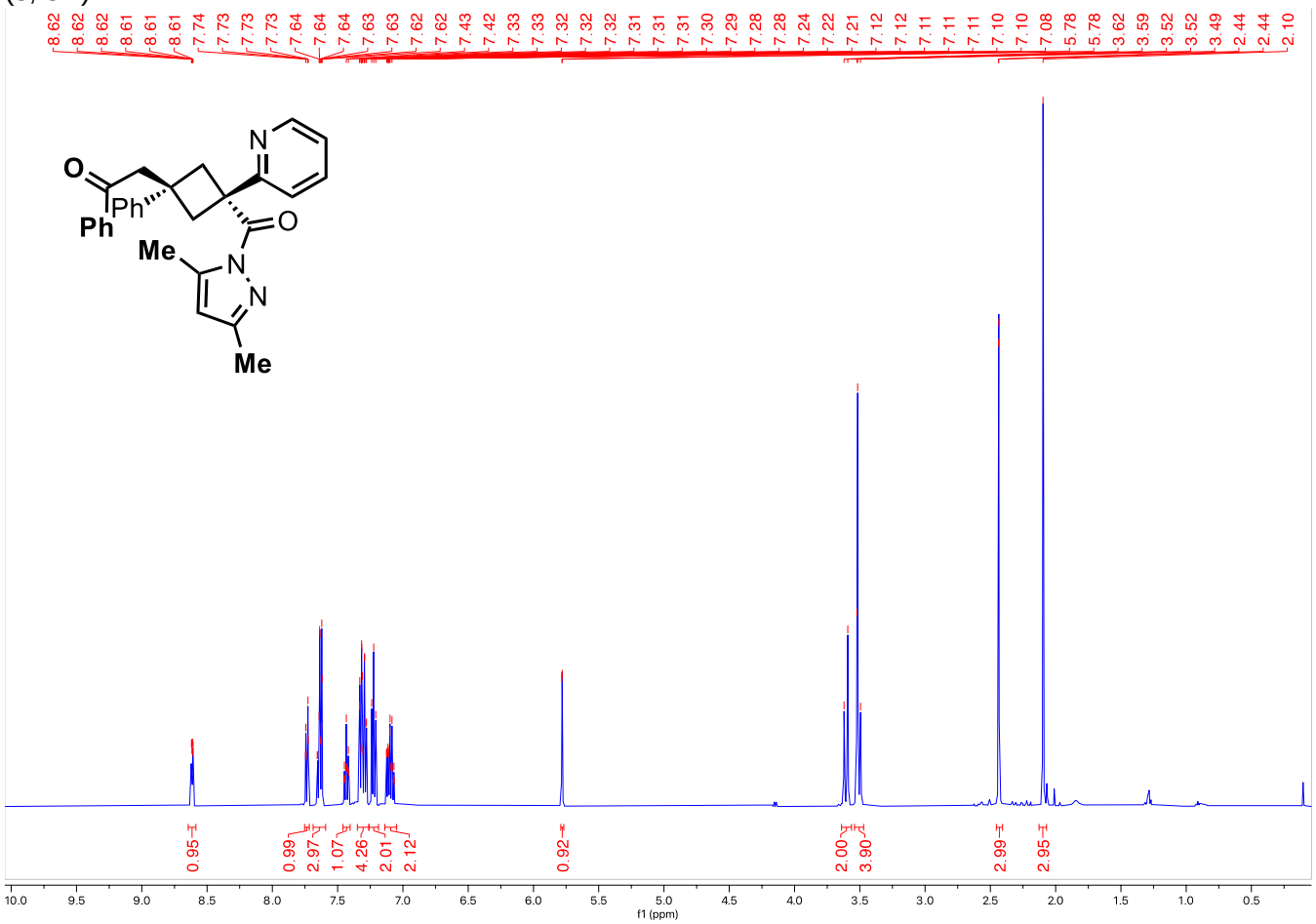


3-Azabicyclo[2.1.1]heptane **3m** (89.8 mg, 0.2 mmol) was added to a 27 mL test tube, which was sealed with a rubber septum and flushed with N_2 for 15 minutes. Then, anhydrous acetonitrile (8 mL, 0.025M) was added to the test tube, which was then shaken until all of the starting material was dissolved. The solution was irradiated with blue light (470 nm) with fan cooling. The distance between the sample and the lamp was 1 cm, and the power output of the Lumidox lamp was 1 W. The test tube was shaken periodically after every hour. After 6 hours, the solvent was evaporated to give the crude product. The product was purified by column chromatography (Biotage® Sfär 5g Column, 0-100% EtOAc/hexanes, eluted at 53% EtOAc) to obtain an orange oil (**41.8 mg, 47% Yield**).

HRMS(ESI): calc'd for [$C_{29}H_{27}N_3O_2$ + H^+], 450.21761; found: 450.21738.

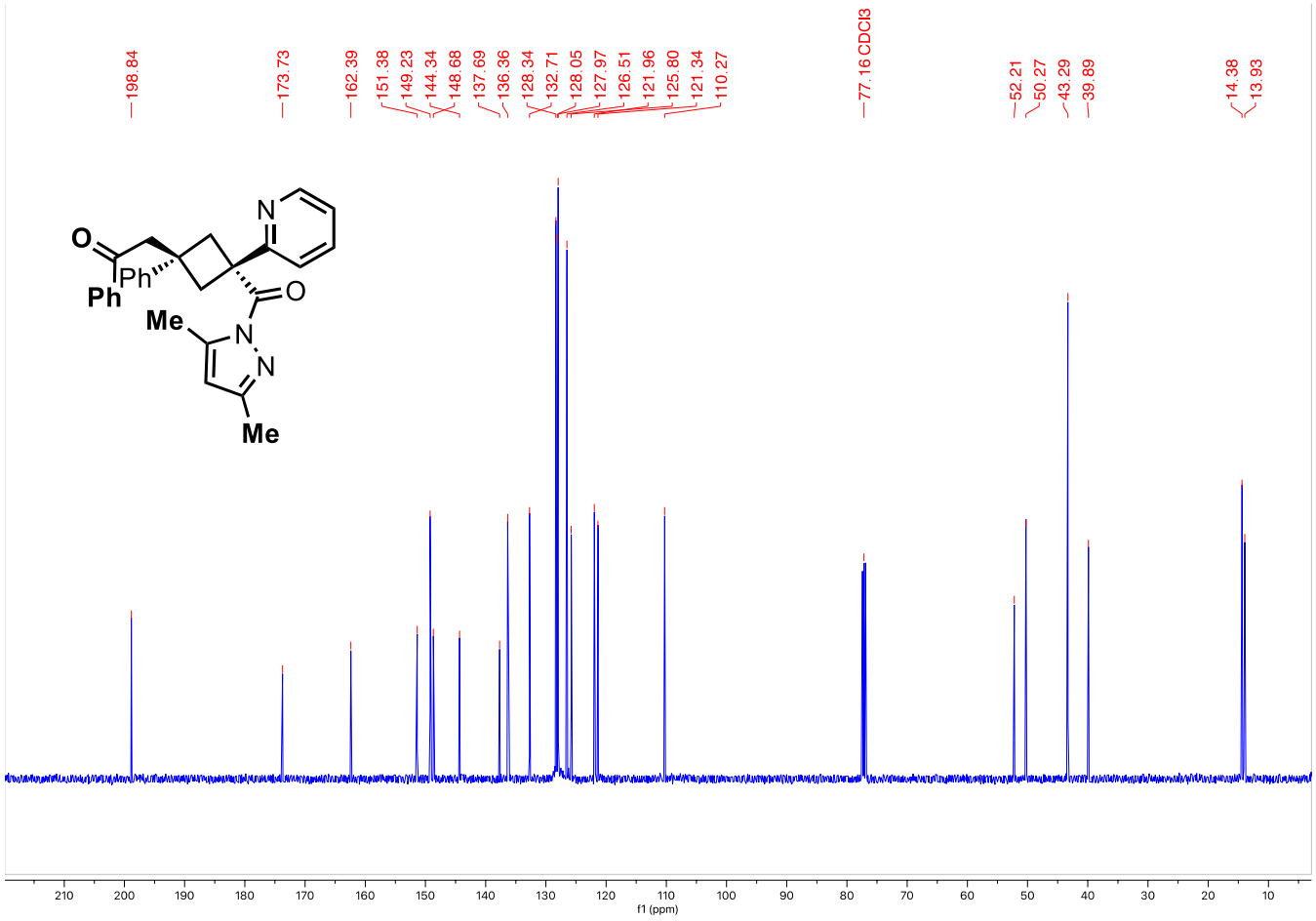
^{1}H NMR (500 MHz, $CDCl_3$, 292 K, ppm): δ 8.64 – 8.59 (m, 1H), 7.74 (dt, J = 8.1, 1.0 Hz, 1H), 7.69 – 7.59 (m, 3H), 7.46 – 7.40 (m, 1H), 7.35 – 7.26 (m, 4H), 7.22 (t, J = 7.7 Hz, 2H), 7.14 – 7.05 (m, 2H), 5.78 (d, J = 1.3 Hz, 1H), 3.61 (d, J = 14.0 Hz, 2H), 3.54 – 3.47 (m, 4H), 2.44 (d, J = 1.1 Hz, 3H), 2.10

(s, 3H).



^{13}C NMR (126 MHz, $CDCl_3$, 292 K, ppm): δ 198.84, 173.73, 162.39, 151.38, 149.23, 148.68, 144.34, 137.69, 136.36, 132.71, 128.34, 128.05, 127.97, 126.51, 125.80, 121.96, 121.34, 110.27, 52.21, 50.27,

43.29, 39.89, 14.38, 13.93.



X: X-Ray Crystallography

A suitable crystal of each sample (**3c** and **4b**) was selected for analysis and mounted in a polyimide loop. Measurements on **3c** were made at Vanderbilt University on a Rigaku Oxford Diffraction Supernova Eos CCD with filtered Cu-Kα radiation at a temperature of 100 K. This dataset was collected by Prof. Nathan Schley.

Measurements on **4b** were made at the University of British Columbia on a Bruker Apex DUO CCD with filtered Cu-Kα radiation at a temperature of 100 K. This dataset was collected by Dr. Brian Patrick.

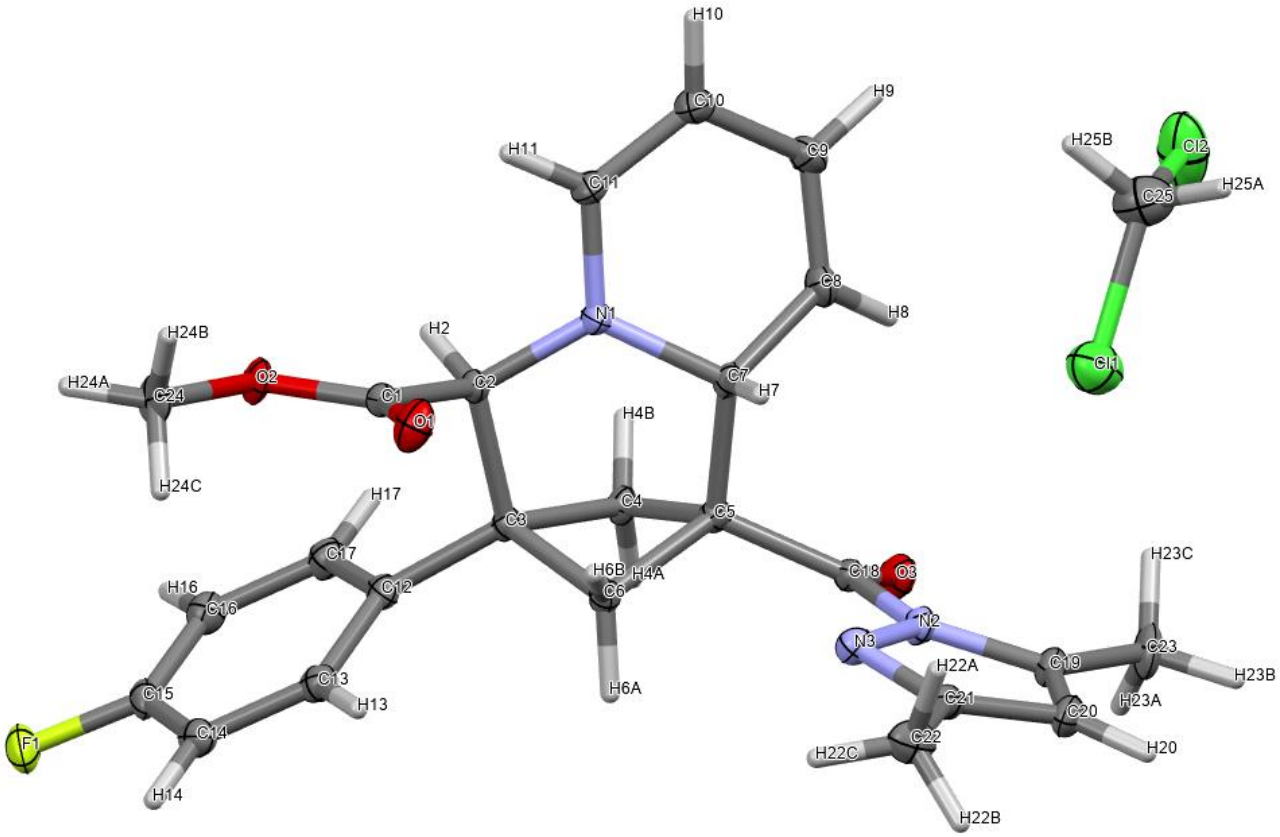
Using Olex2, the structures were solved with the ShelXT structure solution program using Direct Methods and refined with the ShelXL refinement package using Least Squares minimization. Solutions of both structures were carried out by Prof. Nathan Schley.

The structure of **3c** was refined as a racemic twin. Twinning was identified using the TWINROTMAT tool in Platon which was resolved by generating and refining against a detwinned HKLF5 reflection file.

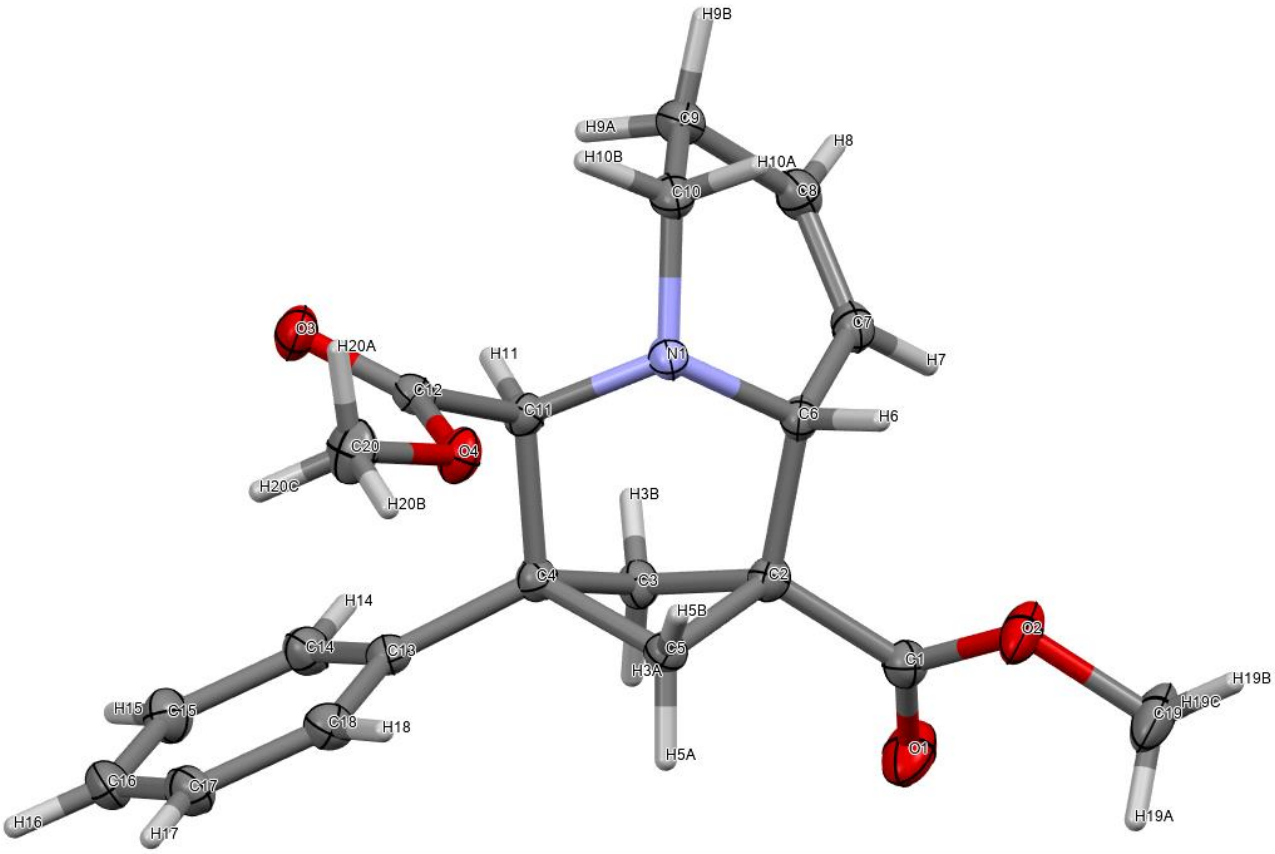
The structure of **4b** was refined without additional restraints.

CIFs of **3c** and **4b** are available from the Cambridge Crystallographic Data Centre (CCDC) with deposition numbers CCDC 2374388-2374389.

Solid state molecular structure of 3c, crystallized as a dichloromethane solvate:



Solid state molecular structure of 4b:



XI: References

1. Liang, Y.; Paulus, F.; Daniliuc, C. G.; Glorius, F. *Angew. Chem. Int. Ed.*, **2023**, *62*, e202305043.
2. Ren, H.; Li, T.; Xing, J.; Li, Z.; Zhang, Y.; Yu, X.; Zheng, J. *Org. Lett.*, **2024**, *26,* 1745-1750.
3. G. P. Kondratenko, N. I. Geonya, L. A. Perel'man, L. M. Litvinenko. *Khimiko-Farmatsevticheskii Zhurnal*. **1979**, *10*, 68-71.
4. W. P. Walter. PhD Dissertation, *Brigham Young University*, Provo, UT, **1970**. 323.
5. J. Brioche, C. Meyer, J. Cossy. *Org. Lett.* **2015**, *17*, 2800–2803.
6. O. Tsuge, S. Kanemasa, S. Takenaka. *Bull. Chem. Soc. Jpn* **1986**, *59*, 3631–3635.
7. S. Bonte, I. O. Ghinea, R. Dinica, I. Baussanne, M. Demeunynck. *Molecules/Molecules online/Molecules annual* **2016**, *21*, 332–332.
8. Y. F. Zhang, W. D. Duan, J. Chen, Y. Hu. *J. Org. Chem.* **2019**, *84*, 4467–4472.
9. O. Tsuge; S. Kanemasa; S. Takenaka. *Bull. Chem. Soc. Jpn* **1985**, 58, 3137–3157.
10. J. B. Xia, Y. Su, N. X. Guo. *Synthesis* **2023**, *55*, 2159–2165.
11. P. N. Praveen Rao, M. Amini, H. Li, E. E. Knaus. *J. Med. Chem*. **2003**, *46*, 4872–4882.
12. S. Malik, K. Pandey, K. C. Gupta, B. Raj. *J. Chem. Eng. Data* **1983**, *28*, 430–431.
13. G. P. Kondratenko, N. I. Geonya, L. A. Perel'man, L. M. Litvinenko*. Khimiko-Farmatsevticheskii Zhurnal* **1976**. *10*, 68-71.
14. K. Senga, K. Shimizu, S. Nishigaki. A New Synthesis of 6-Hydroxypteridine Derivatives. *Heterocycles* **1977**, *6*, 1907–1907.
15. R. K. Bansal, G. Bhagchandani. *Ind. J. Chem.* **1980**, 19B, 801-802.
16. P. Desmazeau, G. Doerflinger, Y. Ribeill, E. Bacque, J. Barriere, G. Dutruc-rosset, G. Puchault. *WO9943699*, **1999**.
17. T. N. Maksimova, V. B. Mochalin, B. V. Unkovskii. *Russ. J. Gen. Chem.* **1975**, *5*, 64–67.