Supporting Information

Stereoselective synthesis of bicyclo[3.*n*.1]alkenone frameworks by Lewis acid-catalysis

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1. General Information

All reactions were carried out using anhydrous solvents under argon atmosphere (by using a glove-box or standard Schlenk techniques). 2-(1-Alkynyl)-2-alken-1-ones (**1**) were synthesized according to a literature procedure[1] from the corresponding 2-iodo-2-alken-1-ones[2] and spectral data for the compounds above can be found in the following references: **1a**, **1h**, **1p&1q**,[3] **1b&1g**,[4] **1c&1d**,[5] **1f**,[1] **1r**.[6], **1i&1e**.[7] 4 Å molecular sieves (powdered, 2-3 μm) were flame dried for 20-30 minutes in vacuo prior to use. All other starting materials, catalysts, and solvents were purchased from commercial suppliers and were used as received.

^{1}H NMR and ^{13}C NMR spectra were recorded at room temperature in $CDCl_3$ on a Bruker 400 or 500 MHz spectrometer. Chemical shifts (δ) are reported in ppm with the following abbreviations used for the observed multiplicities: s (singlet), d (doublet), t (triplet), q (quartet), br (broad), m (multiplet, for unresolved signals). ^{1}H NMR chemical shifts were referenced to the residual solvent signal for $CHCl_3$ (7.26 ppm), and ^{13}C NMR chemical shifts were referenced to the solvent signal of $CDCl_3$ (77.16 ppm). Analytical TLC was performed on pre-coated silica gel plates. After elution, the plates were visualized by UV illumination at 254−360 nm and by staining with ethanolic $KMnO_4$. Column chromatography was performed using Davisil 60Å silica gel (35-70 μm). HRMS data were recorded on a micrOTOF instrument using ESI technique. X-ray crystallographic data were collected using a Bruker advance D8 single crystal diffractometer. HPLC samples were analyzed by UV detection (at 210.5 nm) on a Waters 2489 HPLC.

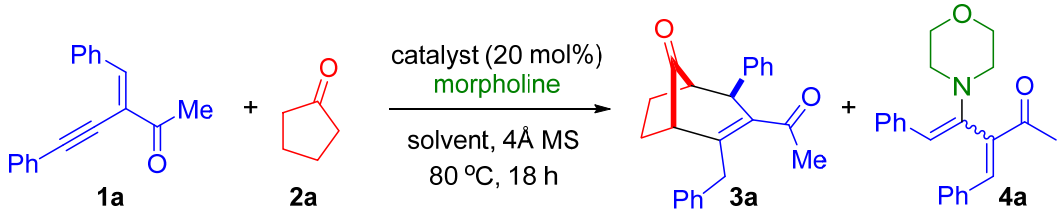
Isomeric ratios of the products were determined by ^{1}H NMR analysis of crude reaction mixtures. Single-crystal X-ray analysis (CCDC 1569101) was used for determination of the relative configuration of compound **3n**. The relative configuration of compounds **3h** and **3q** was determined by 1D-NOE experiments. The enantiomeric excess of compound **3a*** was determined by chiral HPLC using the racemic compound as a reference.

2. Experimental Procedures and Spectral Data

2.1 Screening of Reaction Conditions

To a screw-cap vial equipped with a magnetic stirring bar were added **1a** (0.10 mmol), **2a** (1-2 equiv, see below), morpholine (1-2 equiv, see below), the indicated catalyst, molecular sieves (4 Å) and the indicated solvent under argon (glove-box). The reaction mixture was stirred for 18 hours at 80 ºC and then allowed to cool down to room temperature. The yields were determined by ^{1}H NMR analysis after evaporation of the solvent, using 1,3,5-trimethoxybenzene as an internal standard. The results are summarized in Table S-1.

Table S-1 Screening of reaction conditions



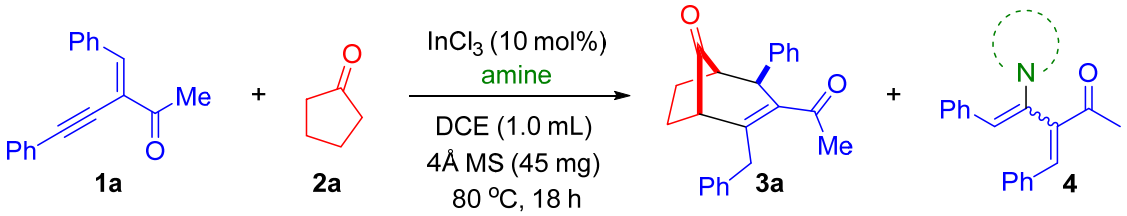
1a **2a** **3a** **4a**

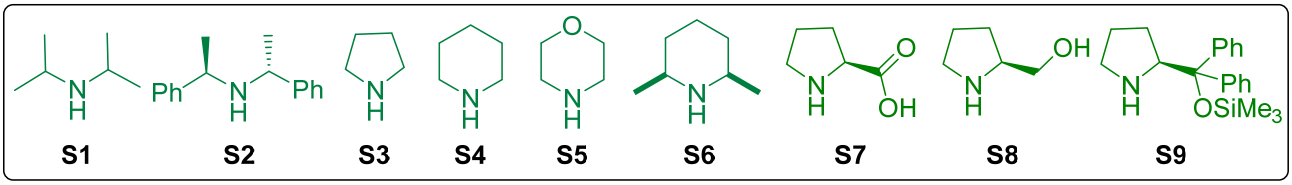
entry	catalyst (20 mol %)	4Å MS (mg)	solvent (1.0 mL)	ratio 1a : 2a : morpholine	yield 3a (%)	yield 4a (%)
1	$InBr_3$	0	DCE (2.0 mL)	1 : 1.5 : 2	61	17
2	$InBr_3$	45	DCE (2.0 mL)	1 : 1.5 : 2	84	2
3	$InBr_3$	45	DCE	1 : 1.5 : 2	89	6
4	$InBr_3$	45	EtOAc	1 : 1.5 : 2	74	4
5	$InBr_3$	45	CH_3CN	1 : 1.5 : 2	79	9
6	$InBr_3$	45	$CDCl_3$	1 : 1.5 : 2	72	1
7	$InBr_3$	45	$PhCH_3$	1 : 1.5 : 2	54	4
8	$InBr_3$	45	DCM	1 : 1.5 : 2	85	2
9	$InBr_3$	45	THF	1 : 1.5 : 2	81	3
10	None	45	DCE	1 : 1.5 : 2	39	16
11	$ScOTf_3$	45	DCE	1 : 1.5 : 2	35	24
12	$ZnOTf_2$	45	DCE	1 : 1.5 : 2	47	7
13	$CuOTf_2$	45	DCE	1 : 1.5 : 2	34	5
14	AgOTf	45	DCE	1 : 1.5 : 2	76	9
15	$InOTf_3$	45	DCE	1 : 1.5 : 2	35	9
16	$In(NTf_2)_3$	45	DCE	1 : 1.5 : 2	54	9
17	$ZnCl_2$	45	DCE	1 : 1.5 : 2	62	6
18	$FeCl_3$	45	DCE	1 : 1.5 : 2	60	2
19	**$InCl_3$**	**45**	**DCE**	**1 : 1.5 : 2**	**91**	**3**
20	$TsOH{\cdot}H_2O$	45	DCE	1 : 1.5 : 2	57	12
21	$InCl_3$ (5 mol%)	45	DCE	1 : 1.5 : 2	74	4
22	**$InCl_3$ (10 mol%)**	**45**	**DCE**	**1 : 1.5 : 2**	**90**	**4**
23	$InCl_3$ (10 mol%)	45	DCE	1 : 1 : 1	46	7
24	$InCl_3$ (10 mol%)	45	DCE	1 : 1.5 : 1	50	6
25	$InCl_3$ (10 mol%)	45	DCE	1 : 2 : 1	42	4
26	$InCl_3$ (10 mol%)	45	DCE	1 : 1.5 : 1.5	76	6
27	$InCl_3$ (10 mol%)	45	DCE	1 : 1 : 2	71	2

2.2 Screening of Amines

To a screw-cap vial equipped with a magnetic stirring bar were added **1a** (0.10 mmol), **2a** (1.5 equiv), amine (0.3-2.0 equiv, see below), $InCl_3$ (10 mol%), molecular sieves (4 Å, 45 mg) and DCE (1.0 mL) under argon (glove-box). The reaction mixture was stirred for 18 hours at 80 ºC and then allowed to cool down to room temperature. The yields were determined by ^1H NMR analysis after evaporation of the solvent, using 1,3,5-trimethoxybenzene as an internal standard. The results are summarized in Table S-2.

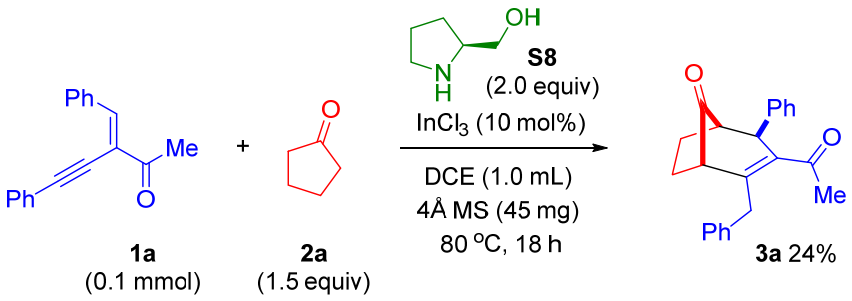
Table S-2 Screening of various amines





entry	amine	amine (X equiv)	yield 3a (%)	yield 4a (%)	SM 1a (%)
1	**S1**	0.3	0	0	95
2	**S1**	2.0	0	0	95
3	**S2**	2.0	0	0	99
4	**S3**	0.3	48	3	0
5	**S3**	1.0	48	2	0
6	**S3**	2.0	69	8	0
7	**S4**	0.3	29	0	32
8	**S4**	1.0	39	3	0
9	**S4**	2.0	57	8	0
10	**S5**	0.3	34	1	21
11	**S5**	1.0	55	7	0
12	**S5**	2.0	90	3	0
13	**S6**	2.0	8	0	70
14	**S7**	0.3	0	0	30
15	**S7**	2.0	4	0	25
16	**S8**	2.0	26	0	0
17	**S9**	0.3	0	0	77
18	**S9**	2.0	13	0	28

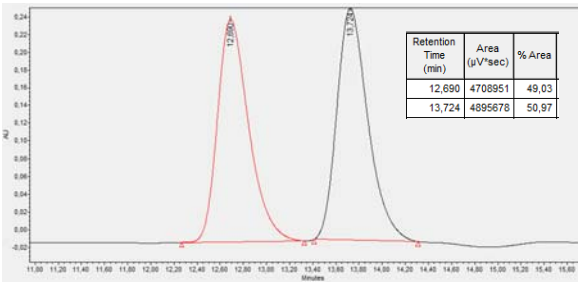
Determination of ee values for reactions carried out with amines S8 and S9



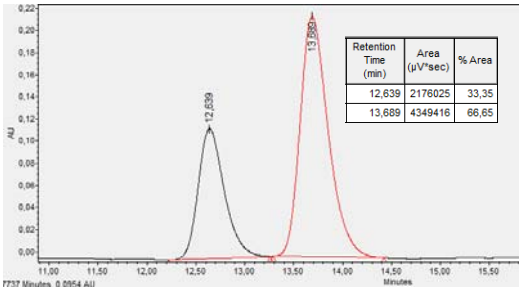
Scheme S-1 Performing the reaction with amine **S8**

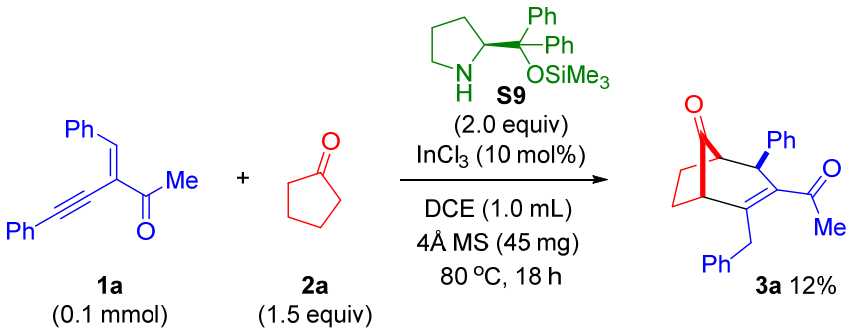
3-Acetyl-2-benzyl-4-phenylbicyclo[3.2.1]oct-2-en-8-one* (3a*): (Amine **S8**, 24% yield, 8.0 mg, colorless solid); HPLC: 33% *ee* (Chiralcel IC, 1.0 mL/min, 10% i-PrOH/hexanes), t_R = 12.64 min (minor), t_R = 13.68 min (major).

(***rac***)-**3a**:



with amine **S8**:

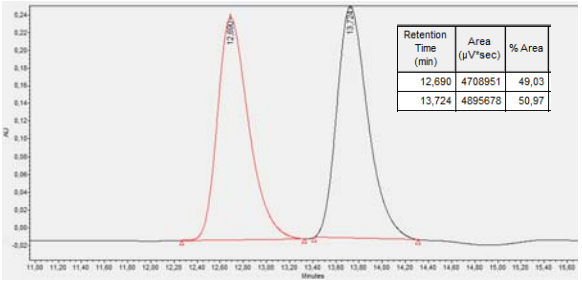




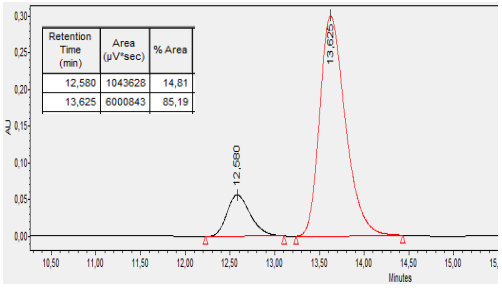
Scheme S-2 Performing the reaction with amine **S9**

3-Acetyl-2-benzyl-4-phenylbicyclo[3.2.1]oct-2-en-8-one* (3a*): (Amine **S9**, 12% yield, 4.0 mg, colorless solid); HPLC: 70% *ee* (Chiralcel IC, 1.0 mL/min, 10% i-PrOH/hexanes), t_R = 12.58 min (minor), t_R = 13.62 min (major).

(***rac***)-**3a**:



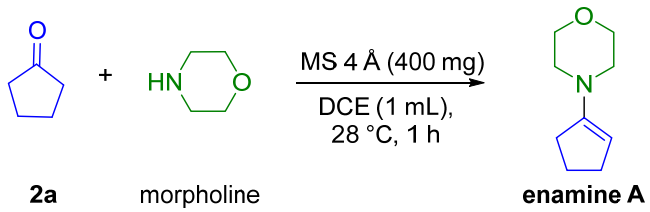
with amine **S9**:



Using a preformed enamine as a starting material

To reduce the requirement of an excess of amine and ketone, a preformed enamine was used as a starting material (in different equivalents) along with **2a** (0-1.0 equiv).

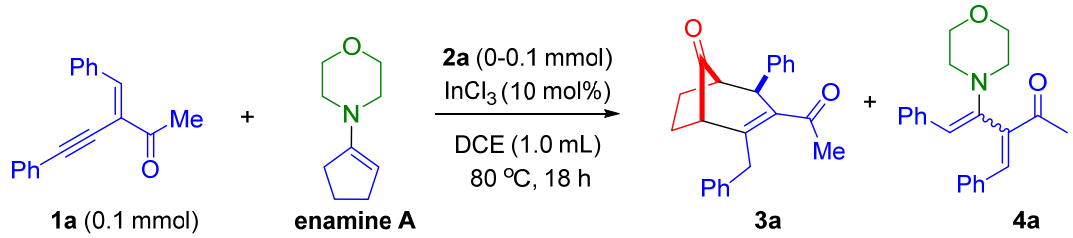
Enamine A: To a screw-cap vial equipped with a magnetic stirring bar were added **2a** (0.10 mmol), morpholine (1.0 equiv), molecular sieves (4 Å, 400 mg) and DCE (1.0 mL) under argon (glove-box). The reaction mixture was stirred for one hour at 28 ºC to obtain **enamine A** in full conversion as judged by ^{1}H NMR. **Enamine A** was used without further purification.



Scheme S-3 Synthesis of **enamine A**

To a screw-cap vial equipped with a magnetic stirring bar were added **1a** (0.10 mmol), **2a** (0-1.0 equiv), $InCl_3$ (10 mol%) and **enamine A** (0.5-1.5 equiv) in DCE (1.0 mL) under argon (glove-box). The reaction mixture was stirred for 18 hours at 80 ºC and then allowed to cool down to room temperature. The yields were determined by ^{1}H NMR analysis after evaporation of the solvent, using 1,3,5-trimethoxybenzene as an internal standard. The outcome of these experiments (Table S-3) indicates that both starting materials, **enamine A** and **2a**, were needed in excess to obtain high yields of product **3**.

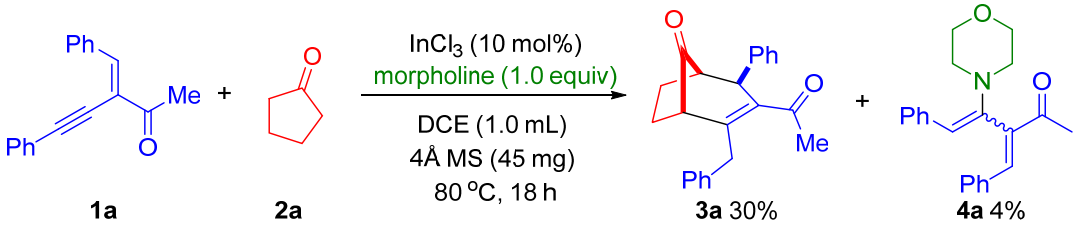
Table S-3 Investigating a preformed enamine as reactant



entry	2a (X equiv)	enamine A (X equiv)	yield 3a (%)	yield 4a (%)	SM 1a (%)
1	--	0.5	21	3	45
2	--	1.0	29	trace	15
3	--	1.5	27	trace	4
4	0.5	0.5	33	trace	55
5	0.5	1.0	59	trace	2
6	1.0	0.5	30	trace	31

Slow addition of amine

To a screw-cap vial equipped with a magnetic stirring bar were added **1a** (0.10 mmol), **2a** (1.5 equiv), $InCl_3$ (10 mol%), molecular sieves (4 Å, 45 mg) and DCE (0.5 mL) under argon (glove-box). Morpholine (1.0 equiv) dissolved in 0.5 mL of DCE was added to the reaction mixture drop-wise over 17 h (0.029 mL/h). The reaction mixture was stirred for one additional hour at 80 ºC, and then allowed to cool down to room temperature. The yield of **3a** (30%) was determined by ^{1}H NMR analysis after evaporation of the solvent, using 1,3,5-trimethoxybenzene as an internal standard.



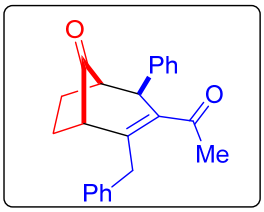
1a **2a** **3a** 30% **4a** 4%

Scheme S-4 Slow addition of morpholine

2.3 General Procedure for the Synthesis of Compounds 3a-3n, 3p-3s.

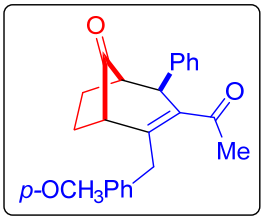
To a microwave vial equipped with a magnetic stirring bar were added 2-(1-alkynyl)-2-alken-1-one **1** (0.30 mmol), ketone **2** (0.45 mmol), morpholine (for **3a-3i**, **3p-3r**) or pyrrolidine (for **3j-3n** and **3s**) (0.60 mmol), anhydrous $InCl_3$ (10 mol %), powdered molecular sieves (4 Å, 135 mg), and 1,2-dichloroethane (3.0 mL) under argon (glove-box). The reaction mixture was stirred for 18 hours at 80 ^oC (unless otherwise stated) and then allowed to cool down to room temperature. After evaporation of the solvent, the crude product was purified by column chromatography (petroleum ether/ethyl acetate) or recrystallized from diethyl ether to obtain analytically pure bicyclic bridged keto compounds **3a-3n**, and **3p-3s**.

3-Acetyl-2-benzyl-4-phenylbicyclo[3.2.1]oct-2-en-8-one (3a)



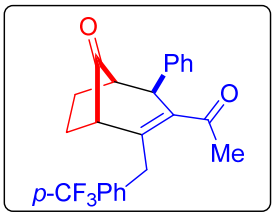
3a: (86% yield, 85.2 mg; (82% yield, 1.085 g for 4.0 mmol scale), colorless solid): **^{1}H NMR** (400 MHz, $CDCl_3$): δ ppm 7.38-7.22 (m, 8H), 7.13-7.10 (m, 2H), 4.36 (bs, 1H), 3.87 (d, J = 14.6 Hz, 1H), 3.45 (dd, J = 14.7, 1.5 Hz, 1H), 2.53-2.51 (m, 1H), 2.37-2.34 (m, 1H), 2.29-2.19 (m, 1H), 2.08-2.01 (m, 4H), 1.96-1.87 (m, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ ppm 213.55, 203.04, 147.27, 139.95, 137.69, 135.57, 129.15, 129.08, 128.99, 127.87, 127.77, 126.96, 60.73, 49.75, 48.11, 39.55, 30.88, 28.08, 25.72; **HRMS** (ESI): *m/z* calcd for $C_{23}H_{22}NaO_2$ $[M+Na]^+$ 353.1512, found 353.1499.

3-Acetyl-2-(4-methoxybenzyl)-4-phenylbicyclo[3.2.1]oct-2-en-8-one (3b)



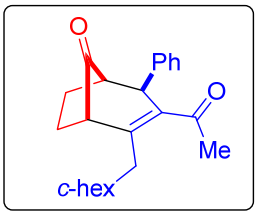
3b: (81% yield, 87.3 mg, colorless solid): **^{1}H NMR** (400 MHz, $CDCl_3$): δ ppm 7.33-7.29 (m, 2H), 7.26-7.22 (m, 3H), 7.12-7.10 (m, 2H), 6.91-6.88 (m, 2H), 4.35 (bs, 1H), 3.82-3.78 (m, 4H), 3.36 (dd, J = 14.5, 1.3 Hz, 1H), 2.52-2.51 (m, 1H), 2.35-2.33 (m, 1H), 2.28-2.20 (m, 1H), 2.08-1.89 (m, 6H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ ppm 213.64, 203.02, 158.60, 147.69, 139.97, 135.18, 130.11, 129.62, 129.02, 127.84, 127.71, 114.38, 60.69, 55.40, 49.74, 47.98, 38.66, 30.83, 28.06, 25.70; **HRMS** (ESI): *m/z* calcd for $C_{24}H_{24}NaO_3$ $[M+Na]^+$ 383.1618, found 383.1630.

3-Acetyl-4-phenyl-2-(4-(trifluoromethyl)benzyl)bicyclo[3.2.1]oct-2-en-8-one (3c)



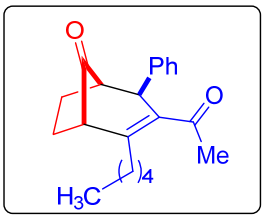
3c: (75% yield, 89.5 mg, colorless solid): **^{1}H NMR** (400 MHz, $CDCl_3$): δ ppm 7.62 (d, J = 8.2 Hz, 2H), 7.47 (d, J = 8.2 Hz, 2H), 7.34-7.23 (m, 3H), 7.10-7.08 (m, 2H), 4.39 (bs, 1H), 4.02 (d, J = 14.4 Hz, 1H), 3.39 (d, J = 14.5 Hz, 1H), 2.46 (d, J = 5.3 Hz, 1H), 2.39-2.37 (m, 1H), 2.33-2.22 (m, 1H), 2.11-1.93 (m, 6H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ ppm 212.83, 202.15, 147.38, 142.07, 139.63, 135.87, 129.49, 129.27 (q, $^2J_{C\text{-}CF_3}$ = 32.2 Hz), 129.15, 127.89, 127.76, 125.87 (q, $^3J_{C\text{-}CF_3}$ = 3.7 Hz), 124.33 (q, $^1J_{C\text{-}F}$ = 272.0 Hz), 60.63, 49.72, 48.24, 39.36, 30.39, 27.99, 25.70; **HRMS** (ESI): *m/z* calcd for $C_{24}H_{21}F_3NaO_2$ $[M+Na]^+$ 421.1386, found 421.1371.

3-Acetyl-2-(cyclohexylmethyl)-4-phenylbicyclo[3.2.1]oct-2-en-8-one (3d)



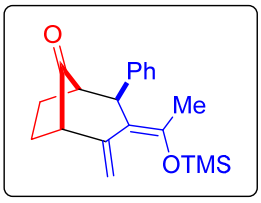
3d: (66% yield, 67.0 mg, colorless solid): **^{1}H NMR** (500 MHz, $CDCl_3$): δ ppm 7.30-7.27 (m, 2H), 7.24-7.20 (m, 1H), 7.08-7.05 (m, 2H), 4.29 (bs, 1H), 2.60 (d, J = 4.8 Hz, 1H), 2.37-2.33 (m, 2H), 2.31-2.23 (m, 1H), 2.15-2.00 (m, 7H), 1.78-1.74 (m, 4H), 1.70-1.61 (m, 2H), 1.33-0.79 (m, 7H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ ppm 214.07, 203.02, 148.77, 140.13, 135.10, 129.00, 127.86, 127.66, 61.07, 50.04, 48.97, 41.57, 37.05, 33.71, 33.42, 30.98, 28.09, 26.54, 26.49, 25.85; **HRMS** (ESI): *m/z* calcd for $C_{23}H_{28}NaO_2$ $[M+Na]^+$ 359.1982, found 359.1984.

3-Acetyl-2-pentyl-4-phenylbicyclo[3.2.1]oct-2-en-8-one (3e)



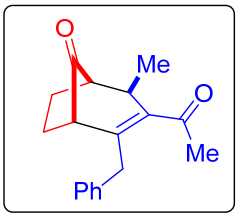
3e: (66% yield, 61.7 mg, colorless solid): **^{1}H NMR** (400 MHz, $CDCl_3$): δ ppm 7.29-7.19 (m, 3H), 7.06-7.04 (m, 2H), 4.31 (bs, 1H), 2.56-2.45 (m, 2H), 2.35-2.24 (m, 2H), 2.16-1.93 (m, 7H), 1.67-1.52 (m, 2H), 1.42-1.33 (m, 4H) 0.94-0.91 (m, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ ppm 213.80, 202.56, 150.99, 140.20, 133.58, 128.96, 127.80, 127.64, 60.59, 49.96, 48.96, 34.65, 32.18, 30.71, 28.35, 28.11, 25.69, 22.60, 14.15; **HRMS** (ESI): *m/z* calcd for $C_{21}H_{26}NaO_2$ $[M+Na]^+$ 333.1825, found 333.1818

(*Z*)-2-Methylene-4-phenyl-3-(1-((trimethylsilyl)oxy)ethylidene)bicyclo[3.2.1]octan-8-one (3f)



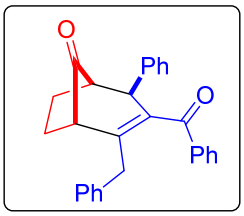
3f: (42% yield, 40.9 mg, colorless solid): **^{1}H NMR** (500 MHz, $CDCl_3$): δ ppm 7.26-7.22 (m, 2H), 7.18-7.15 (m, 3H), 5.35 (d, J = 1.6 Hz, 1H), 5.16 (d, J = 1.6 Hz, 1H), 3.91 (d, J = 3.3 Hz, 1H), 2.80 (d, J = 6.2 Hz, 1H), 2.49-2.48 (m, 1H), 2.15-2.07 (m, 1H), 2.03-1.94 (m, 1H), 1.91-1.82 (m, 5H), 0.23 (s, 9H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ ppm 215.24, 149.74, 146.90, 142.56, 128.45, 127.30, 126.70, 114.37, 113.51, 55.88, 55.32, 51.21, 24.15, 24.00, 20.33, 1.06; **HRMS** (ESI): *m/z* calcd for $C_{20}H_{26}NaO_2Si$ $[M+Na]^+$ 349.1594, found 349.1591.

3-Acetyl-2-benzyl-4-methylbicyclo[3.2.1]oct-2-en-8-one (3g)



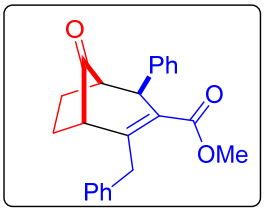
3g: (29% yield, 23.6 mg, colorless solid): **^{1}H NMR** (400 MHz, $CDCl_3$): δ ppm 7.32-7.26 (m, 2H), 7.22-7.17 (m, 3H), 3.51-3.44 (m, 1H), 3.38 (s, 2H), 2.40 (dd, J = 5.3, 1.2 Hz, 1H), 2.30-2.21 (m, 4H), 2.01-1.94 (m, 1H), 1.87-1.72 (m, 2H), 1.66-1.60 (m, 1H), 1.08 (d, J = 7.1 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ ppm 215.40, 205.48, 140.65, 138.89, 137.73, 129.06, 128.78, 126.80, 43.59, 39.37, 30.42, 28.21, 18.44, 16.46; **HRMS** (ESI): *m/z* calcd for $C_{18}H_{20}NaO_2$ $[M+Na]^+$ 291.1356, found 291.1357.

3-Benzoyl-2-benzyl-4-phenylbicyclo[3.2.1]oct-2-en-8-one (3h)



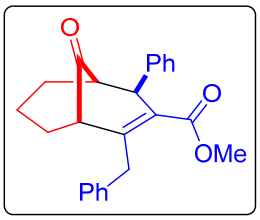
3h: (63% yield, 74.0 mg, colorless solid): **^{1}H NMR** (500 MHz, $CDCl_3$): δ ppm 7.76-7.75 (m, 2H), 7.50-7.47 (m, 1H), 7.38-7.35 (m, 2H), 7.31-7.28 (m, 2H), 7.24-7.19 (m, 5H), 7.15-7.13 (m, 3H), 4.39 (bs, 1H), 3.42 (d, J = 14.8 Hz, 1H), 3.37 (d, J = 14.8 Hz, 1H), 2.62 (d, J = 5.4 Hz, 1H), 2.42 (d, J = 7.5 Hz, 1H), 2.31-2.24 (m, 1H), 2.19-2.13 (m, 1H), 1.98-1.87 (m, 2H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ ppm 214.56, 198.18, 144.62, 139.73, 137.42, 137.21, 134.45, 133.40, 129.26, 129.14, 128.83, 128.71, 128.66, 128.19, 127.49, 126.92, 61.32, 49.31, 47.77, 40.43, 28.61, 26.05; **HRMS** (ESI): *m/z* calcd for $C_{28}H_{24}NaO_2$ $[M+Na]^+$ 415.1669, found 415.1680.

Methyl-2-benzyl-8-oxo-4-phenylbicyclo[3.2.1]oct-2-ene-3-carboxylate (3i)



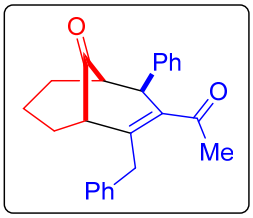
3i: (78% yield, 84.7 mg; colorless solid): **^{1}H NMR** (400 MHz, $CDCl_3$): δ ppm 7.36-7.27 (m, 7H), 7.23-7.20 (m, 1H), 7.10-7.08 (m, 2H), 4.48 (bs, 1H), 4.17 (d, J = 14.1 Hz, 1H), 3.56 (s, 3H), 3.51 (dd, J = 14.1, 1.5 Hz, 1H), 2.54-2.53 (m, 1H), 2.34-2.32 (m, 1H), 2.26-2.15 (m, 2H), 2.08-1.90 (m, 4H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ ppm 213.19, 167.68, 152.58, 140.66, 137.82, 129.22, 128.91, 128.76, 127.53, 127.35, 126.91, 126.50, 59.92, 51.82, 49.57, 48.45, 40.04, 28.04, 25.33; **HRMS** (ESI): *m/z* calcd for $C_{23}H_{22}NaO_3$ $[M+Na]^+$ 369.1461, found 369.1452.

Methyl-2-benzyl-9-oxo-4-phenylbicyclo[3.3.1]non-2-ene-3-carboxylate (3j)



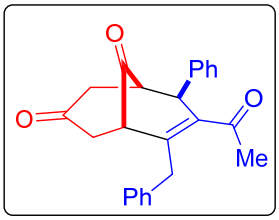
3j: (pyrrolidine was used, 82% yield, 92.1 mg, colorless solid): **^{1}H NMR** (500 MHz, $CDCl_3$): δ ppm 7.34-7.16 (m, 8H), 7.05-7.03 (m, 2H), 4.37 (d, J = 1.1 Hz, 1H), 4.15 (d, J = 14.3 Hz, 1H), 3.56 (s, 3H), 3.31 (dd, J = 14.3, 1.9 Hz, 1H), 2.90 (bs, 1H), 2.55 (bs, 1H), 2.28-2.24 (m, 1H), 2.09-1.82 (m, 4H), 1.62-1.57 (m, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ ppm 213.71, 167.59, 144.44, 142.58, 137.97, 132.22, 129.06, 128.85, 128.76, 127.22, 127.02, 126.78, 54.60, 53.59, 51.67, 50.15, 38.76, 37.14, 32.66, 17.61; **HRMS** (ESI): *m/z* calcd for $C_{24}H_{24}NaO_3$ $[M+Na]^+$ 383.1618, found 383.1621.

3-Acetyl-2-benzyl-4-phenylbicyclo[3.3.1]non-2-en-9-one (3k)



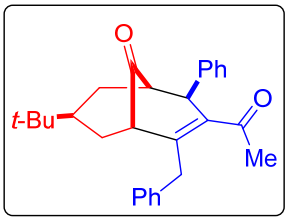
3k: (pyrrolidine was used, 58% yield (33% with morpholine), 59.7 mg, colorless solid): **^{1}H NMR** (500 MHz, $CDCl_3$): δ ppm 7.35-7.19 (m, 8H), 7.07-7.05 (m, 2H), 4.21 (d, J = 1.2 Hz, 1H), 3.75 (d, J = 15.0 Hz, 1H), 3.33 (dd, J = 15.0, 1.8 Hz, 1H), 2.87 (bs, 1H), 2.58 (bs, 1H), 2.27-2.23 (m, 1H), 2.08-1.89 (m, 6H), 1.86-1.78 (m, 1H), 1.61-1.57 (m, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ ppm 204.27, 204.45, 142.12, 141.97, 137.69, 137.56, 129.26, 128.98, 128.91, 127.51, 127.44, 126.94, 55.24, 53.71, 49.66, 38.25, 37.19, 32.55, 31.42, 17.59; **HRMS** (ESI): *m/z* calcd for $C_{24}H_{24}NaO_2$ $[M+Na]^+$ 367.1669, found 367.1683.

7-Acetyl-6-benzyl-8-phenylbicyclo[3.3.1]non-6-ene-3,9-dione (3l)



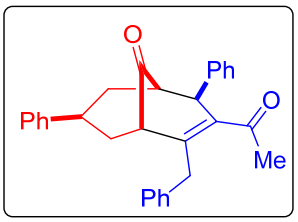
3l: (pyrrolidine was used, reaction time 20 h, 32% yield, 34.9 mg, colorless solid): **^{1}H NMR** (500 MHz, $CDCl_3$): δ ppm 7.35-7.22 (m, 8H), 7.01-6.99 (m, 2H), 4.25 (bs, 1H), 3.92 (d, J = 14.9 Hz, 1H), 3.21 (dd, J = 14.9, 1.7 Hz, 1H), 3.04-2.99 (m, 2H), 2.90-2.79 (m, 4H), 2.10 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ ppm 208.81, 204.06, 202.34, 140.30, 139.74, 137.41, 137.10, 129.40, 129.17, 129.12, 128.12, 127.51, 127.26, 55.91, 52.60, 48.89, 47.04, 45.21; **HRMS** (ESI): *m/z* calcd for $C_{24}H_{22}NaO_3$ $[M+Na]^+$ 381.1461, found 381.1447.

3-Acetyl-2-benzyl-7-(*tert*-butyl)-4-phenylbicyclo[3.3.1]non-2-en-9-one (3m)



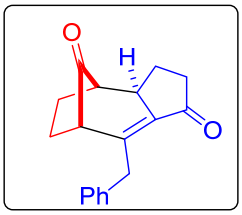
3m: (pyrrolidine was used, 41% yield, 49.0 mg, colorless solid): **^{1}H NMR** (500 MHz, $CDCl_3$): δ ppm 7.34-7.26 (m, 5H), 7.25-7.19 (m, 3H), 7.07-7.05 (m, 2H), 4.18 (bs, 1H), 3.68 (d, J = 14.9 Hz, 1H), 3.41 (d, J = 14.9 Hz, 1H), 2.85-2.82 (m, 1H), 2.59-2.54 (m, 1H), 2.25-2.21 (m, 1H), 1.99 (s, 3H), 1.91-1.88 (m, 1H), 1.74 (dt, J = 13.1, 4.3 Hz, 1H), 1.57 (m, 2H), 0.85 (s, 9H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ ppm 214.92, 204.37, 142.05, 141.81, 137.65, 129.25, 129.03, 128.98, 127.53, 127.44, 126.95, 55.64, 52.98, 49.32, 38.69, 38.45, 38.22, 33.68, 32.0, 31.51, 27.86; **HRMS** (ESI): *m/z* calcd for $C_{28}H_{32}NaO_2$ $[M+Na]^+$ 423.2295, found 423.2297.

3-Acetyl-2-benzyl-4,7-diphenylbicyclo[3.3.1]non-2-en-9-one (3n)



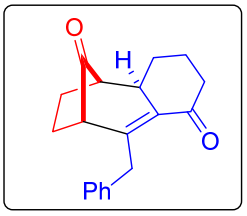
3n: (pyrrolidine was used, 51% yield, 64.0 mg, colorless solid): **^{1}H NMR** (400 MHz, $CDCl_3$): δ ppm 7.36-7.19 (m, 13H), 7.11-7.08 (m, 2H), 4.35 (bs, 1H), 3.77 (d, J = 15.1 Hz, 1H), 3.53-3.42 (m, 2H), 2.94 (bs, 1H), 2.69 (bs, 1H), 2.45-2.39 (m, 1H), 2.19 (ddd, J = 15.3, 4.2, 4.1 Hz, 1H), 2.13-1.98 (m, 5H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ ppm 213.73, 204.56, 142.86, 142.34, 141.79, 137.74, 137.53, 129.35, 129.09, 128.89, 128.79, 127.60, 127.55, 127.22, 127.08, 126.98, 55.49, 53.27, 49.44, 43.85, 39.48, 38.57, 35.42,31.59; **HRMS** (ESI): *m/z* calcd for $C_{30}H_{28}NaO_2$ $[M+Na]^+$ 443.1982, found 443.1974.

8-Benzyl-3,3a,4,5,6,7-hexahydro-4,7-methanoazulene-1,9(2*H*)-dione (3p)



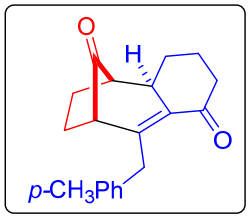
3p: (73% yield, 58.2 mg, colorless solid): **^{1}H NMR** (400 MHz, $CDCl_3$): δ ppm 7.28-7.16 (m, 5H), 4.42 (d, J = 13.5 Hz, 1H), 3.58 (dd, J = 13.6, 1.4 Hz, 1H), 3.49-3.39 (m, 1H), 2.56-2.35 (m, 4H), 2.02-1.78 (m, 6H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ ppm 213.86, 205.21, 152.31, 137.80, 130.55, 129.33, 128.89, 126.90, 51.34, 48.60, 46.96, 40.33, 36.69, 28.63, 23.77, 18.53; **HRMS** (ESI): *m/z* calcd for $C_{18}H_{18}NaO_2$ $[M+Na]^+$ 289.1199, found 289.1196.

9-Benzyl-2,3,4,4a,5,6,7,8-octahydro-1*H*-5,8-methanobenzo[7]annulene-1,10-dione (3q)



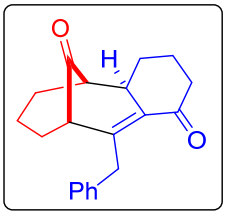
3q: (52% yield, 43.8 mg, colorless solid): **^{1}H NMR** (500 MHz, $CDCl_3$): δ ppm 7.28-7.25 (m, 2H), 7.20-7.18 (m, 3H), 3.94 (d, J = 13.9 Hz, 1H), 3.38 (dd, J = 13.9, 1.2 Hz, 1H), 3.23 (dt, J = 12.2, 3.8 Hz, 1H), 2.62-2.57 (m, 1H), 2.47-2.40 (m, 2H), 2.31-2.29 (m, 1H), 2.18-2.08 (m, 2H), 1.97-1.78 (m, 5H), 1.70-1.65 (m, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ ppm 214.13, 201.87, 150.48, 138.14, 132.24, 129.22, 128.65, 126.62, 51.43, 49.48, 48.56, 43.30, 39.30, 28.85, 28.31, 23.74, 19.29; **HRMS** (ESI): *m/z* calcd for $C_{19}H_{20}NaO_2$ $[M+Na]^+$ 303.1356, found 303.1345.

9-(4-Methylbenzyl)-2,3,4,4a,5,6,7,8-octahydro-1*H*-5,8-methanobenzo[7]annulene-1,10-dione (3r)



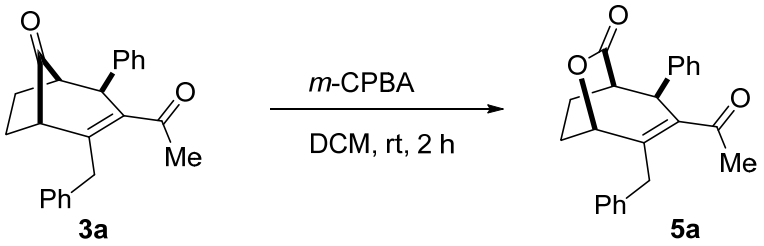
3r: (56% yield, 49.4 mg, colorless solid): **^{1}H NMR** (400 MHz, $CDCl_3$): δ ppm 7.12-7.02 (m, 4H), 3.89 (d, J = 13.9 Hz, 1H), 3.35 (dd, J = 13.9, 1.2 Hz, 1H), 3.26-3.18 (m, 1H), 2.63-2.56 (m, 1H), 2.47-2.37 (m, 2H), 2.32-2.27 (m, 4H), 2.19-2.07 (m, 2H), 1.98-1.77 (m, 5H), 1.71-1.64 (m, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ ppm 214.30, 201.91, 150.86, 136.12, 135.04, 132.02, 129.38, 129.13, 51.48, 49.48, 48.63, 43.34, 38.91, 28.90, 28.37, 23.79, 21.18, 19.32; **HRMS** (ESI): *m/z* calcd for $C_{20}H_{22}NaO_2$ $[M+Na]^+$ 317.1512, found 317.1496.

10-Benzyl-3,4,4a,5,6,7,8,9-octahydro-5,9-methanobenzo[8]annulene-1,11(2*H*)-dione (3s)



3s: (pyrrolidine was used, 71% yield, 63.7 mg, colorless solid): **^{1}H NMR** (500 MHz, $CDCl_3$): δ ppm 7.27-7.24 (m, 2H), 7.20-7.17 (m, 3H), 3.66 (d, J = 14.4 Hz, 1H), 3.45 (d, J = 14.4 Hz, 1H), 2.80-2.77 (m, 2H), 2.58-2.54 (m, 1H), 2.38-2.27 (m, 2H), 2.08-2.02 (m, 1H), 1.99-1.92 (m, 2H), 1.88-1.75 (m, 3H), 1.74-1.62 (m, 3H), 1.56-1.52 (m, 1H), 1.43-1.40 (m, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ ppm 213.91, 205.16, 140.48, 138.33, 138.30, 128.91, 128.72, 126.66, 51.93, 51.80, 51.37, 43.15, 38.65, 36.55, 33.75, 32.84, 24.60, 17.46; **HRMS** (ESI): *m/z* calcd for $C_{20}H_{22}NaO_2$ $[M+Na]^+$ 317.1512, found 317.1511.

2.4 Procedure for the Oxidation of 3a



Compound **5a** was synthesized by an adapted literature procedure.[8] To a screw-cap vial equipped with a magnetic stirring bar was added **3a** (0.30 mmol, 99.0 mg), $NaHCO_3$ (1.8 mmol) in CH_2Cl_2 (3.0 mL). Then 77% *m*-CPBA (0.45 mmol, 110.0 mg) was added. The reaction mixture was stirred at room temperature for 2 hours and then an additional 30 minutes after the addition of Na_2SO_3 (175.0 mg) and H_2O (0.5 mL). The organic layer was separated and dried over anhydrous Na_2SO_4. After evaporation of the solvent, the crude product was purified by column chromatography (petroleum ether/ethyl acetate) to obtain analytically pure compound **5a**.

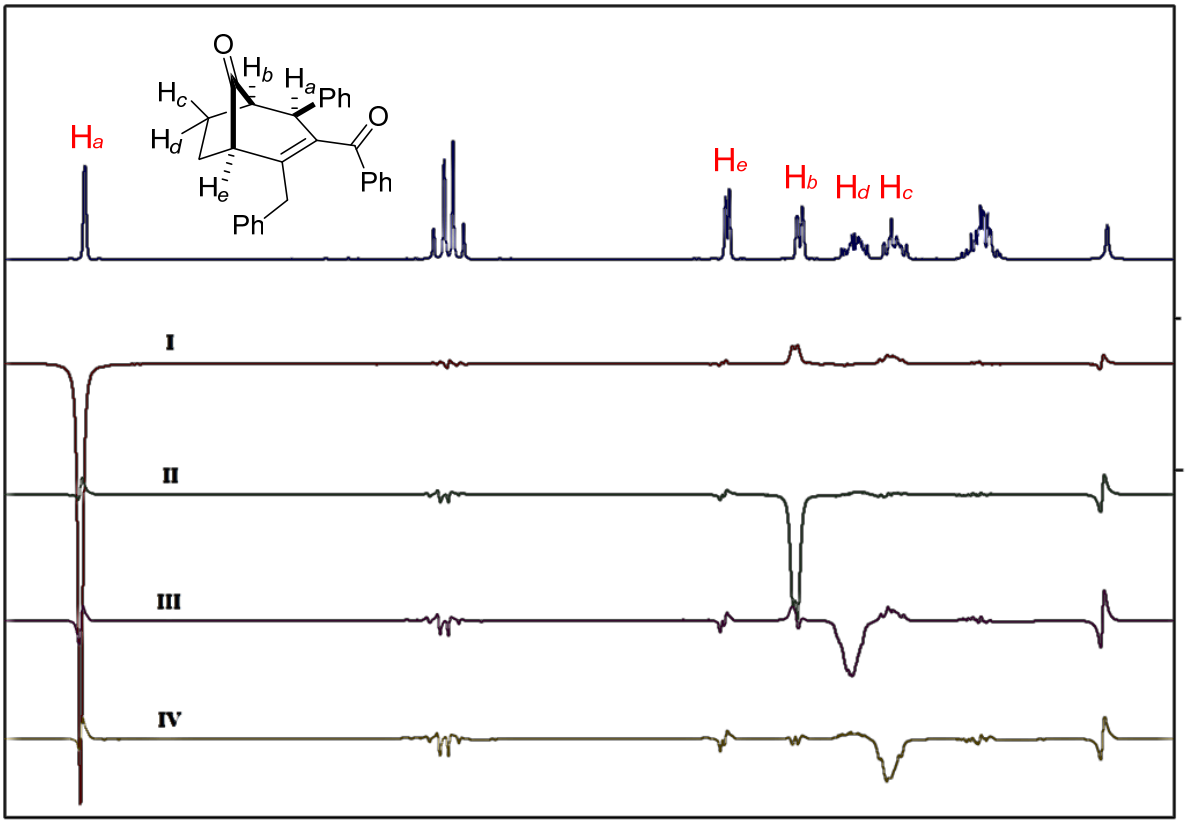
3-Acetyl-4-benzyl-2-phenyl-6-oxabicyclo[3.2.2]non-3-en-7-one (5a)

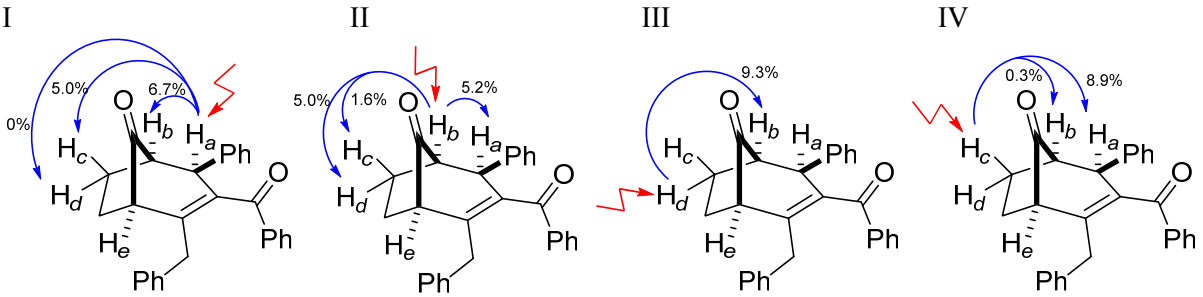
(92% yield, 95.6 mg, colorless solid): **^{1}H NMR** (400 MHz, $CDCl_3$): δ ppm 7.39-7.33 (m, 4H), 7.30-7.26 (m, 4H), 7.23-7.20 (m, 2H), 4.72 (dd, J = 7.8, 2.6 Hz, 1H), 3.97 (d, J = 2.2 Hz, 1H), 3.65 (d, J = 14.9 Hz, 1H), 3.56 (d, J = 14.9 Hz, 1H), 3.20 (dd, J = 4.9, 2.3 Hz, 1H), 2.30-2.20 (m, 1H), 2.00-1.86 (m, 5H), 1.83 (m, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ ppm 205.92, 172.32, 139.42, 138.05, 136.55, 135.76, 129.15, 129.08, 129.06, 128.99, 128.02, 127.30, 78.37, 55.11, 45.17, 41.56, 32.00, 25.68, 23.70; **HRMS** (ESI): *m/z* calcd for $C_{23}H_{22}NaO_3$ $[M+Na]^+$ 369.1461, found 369.1455.

2.5 Differential NOE Spectra of 3h and 3q

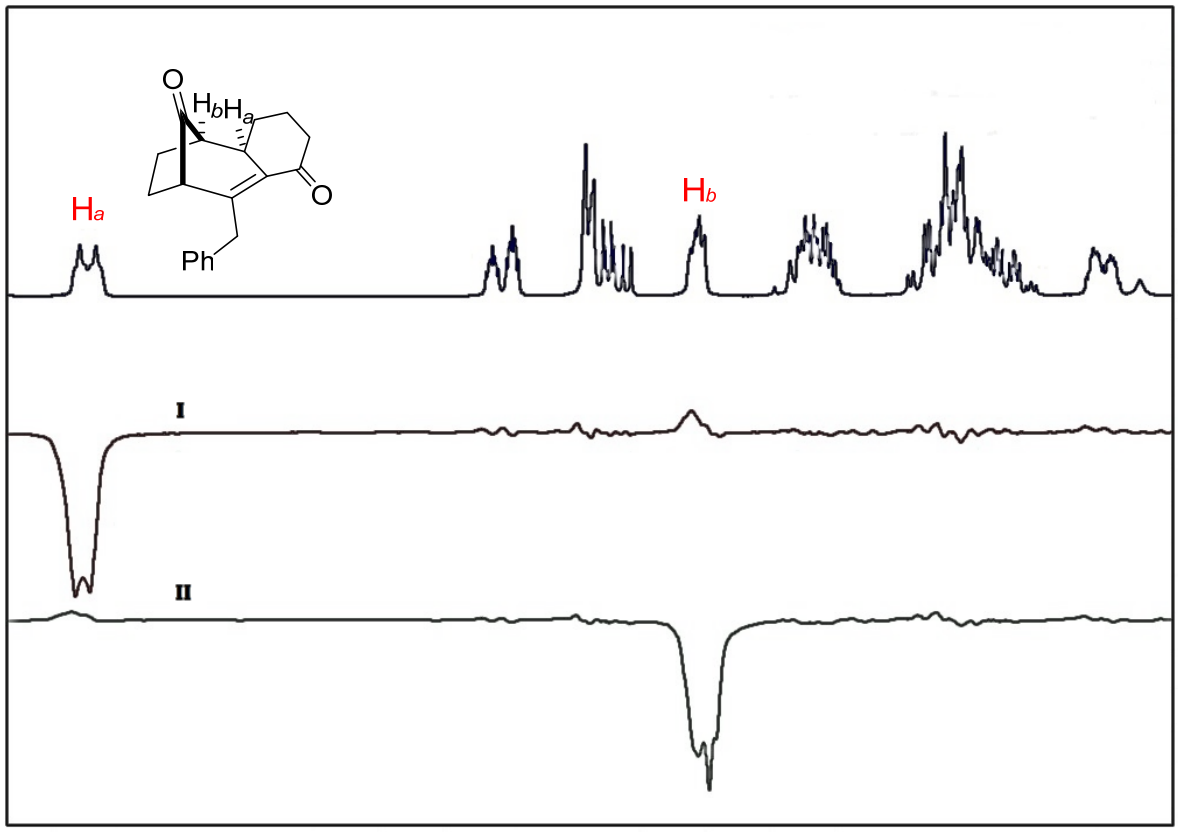
The relative stereochemistry of compounds **3h** and **3q** was established by 1D differential NOE experiments according to the figures and spectra below.

Product **3h**:

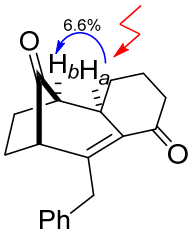




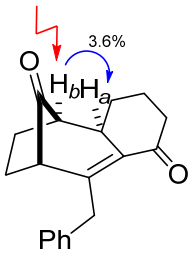
Product **3q**:



I

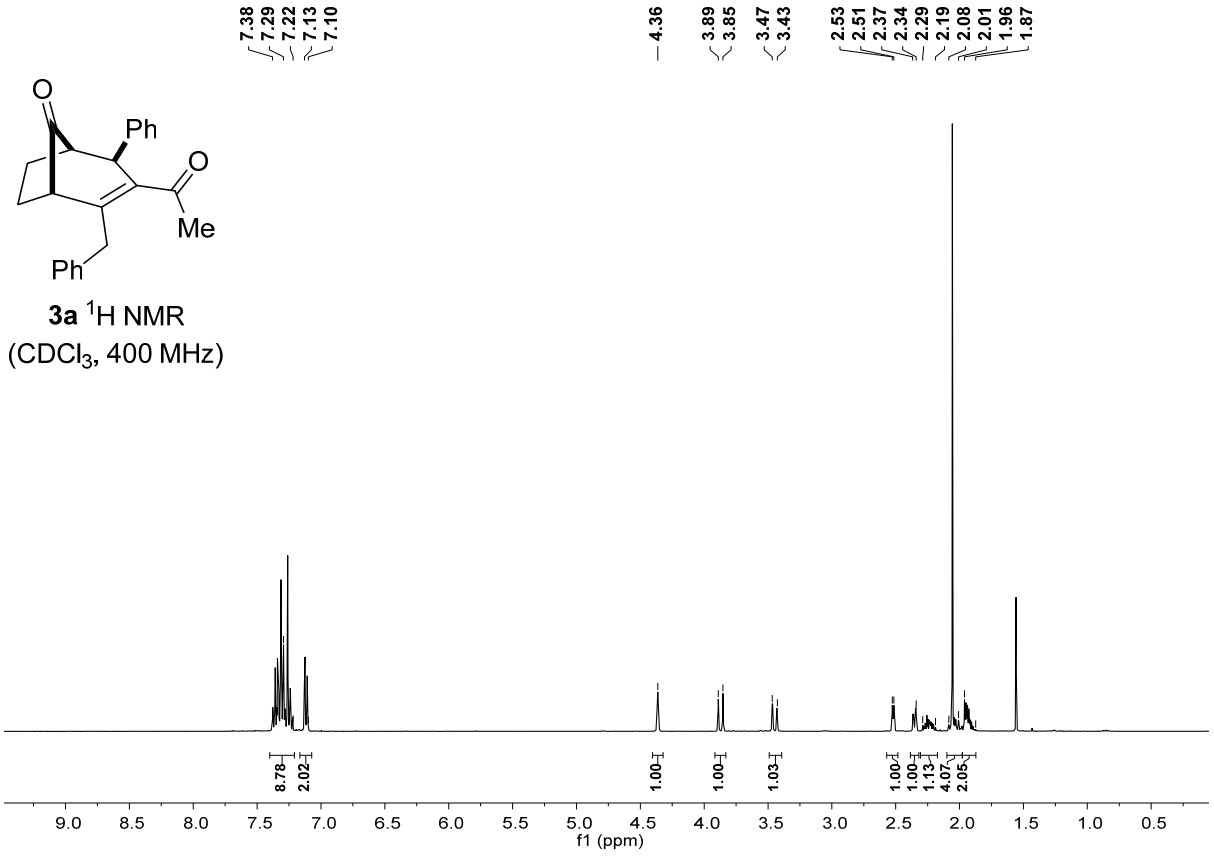


II

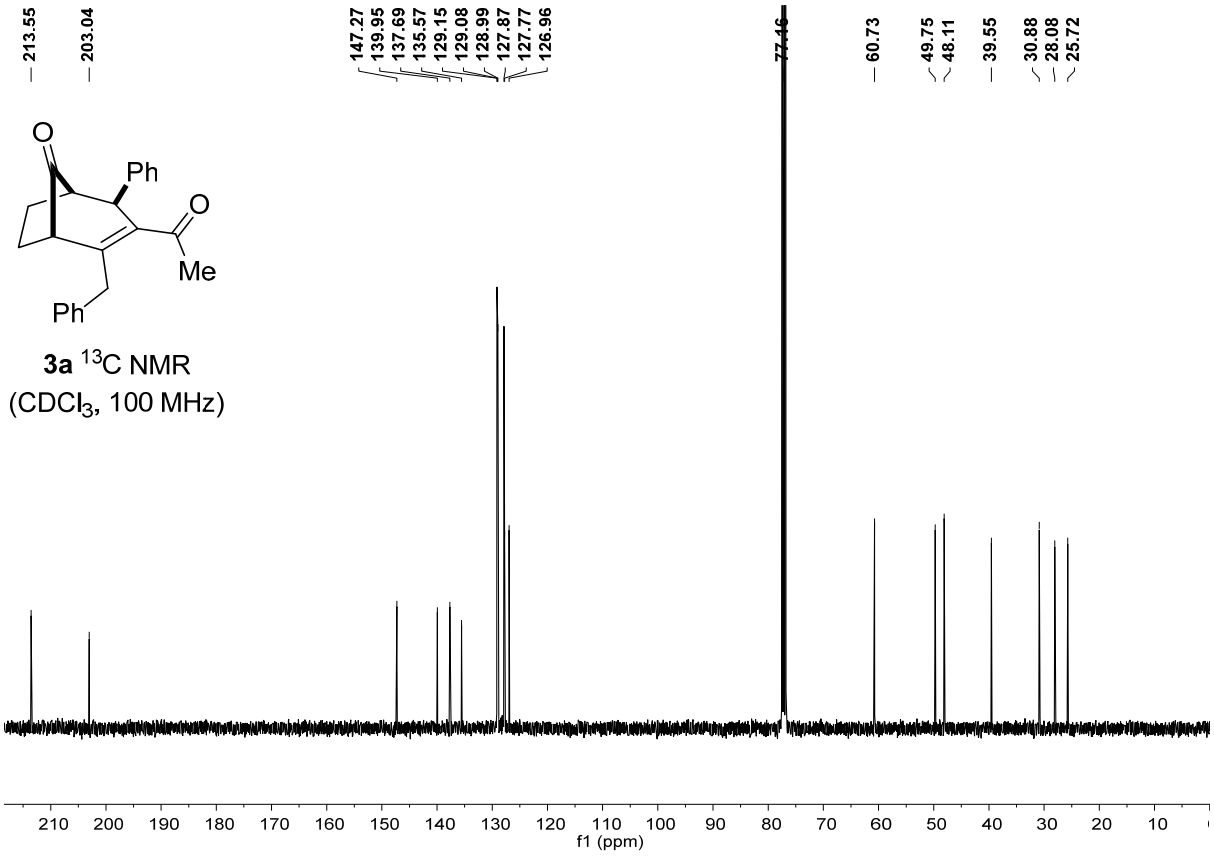


Although the NOE for product **3q** resembles the one for product **3h**, we can not rule out the opposite relative configuration (with respect to H_a and H_b) in **3q** due to signal overlap.

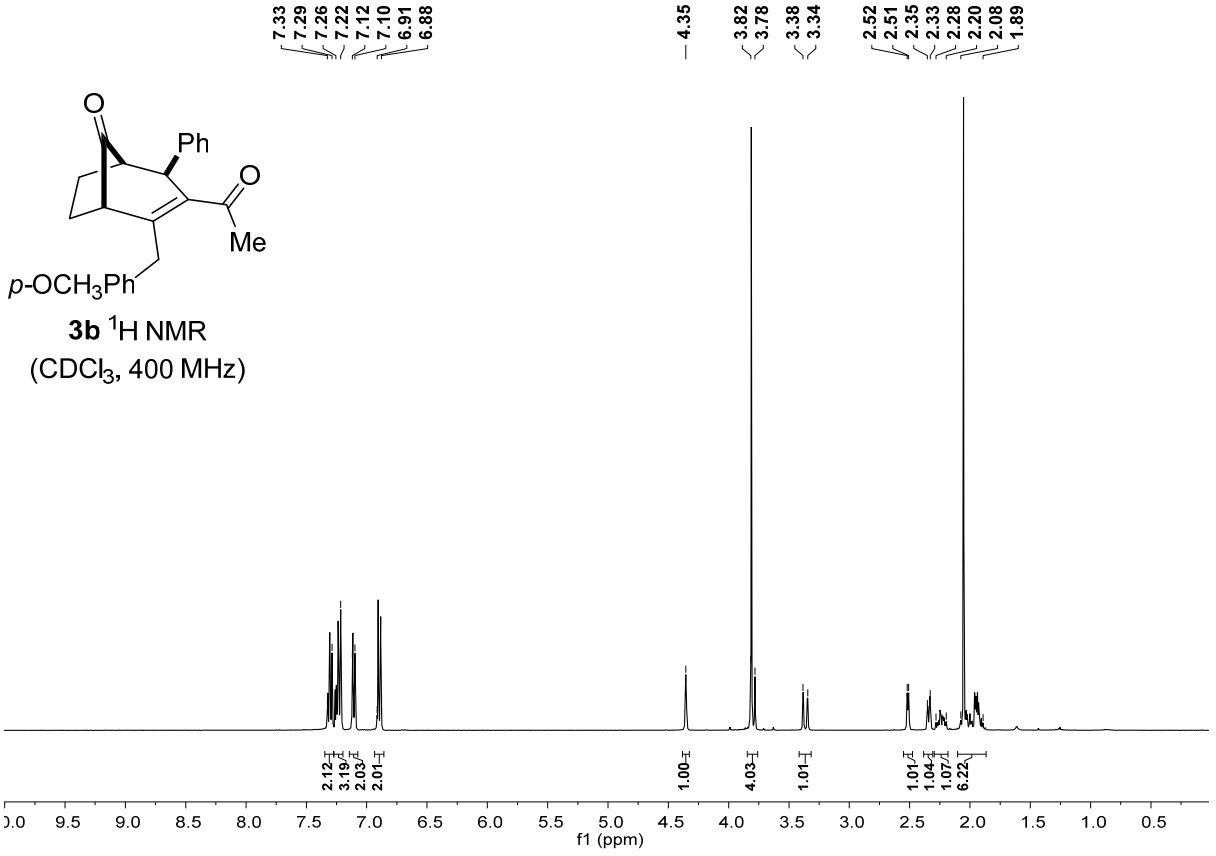
3. ^{1}H and ^{13}C NMR Spectra



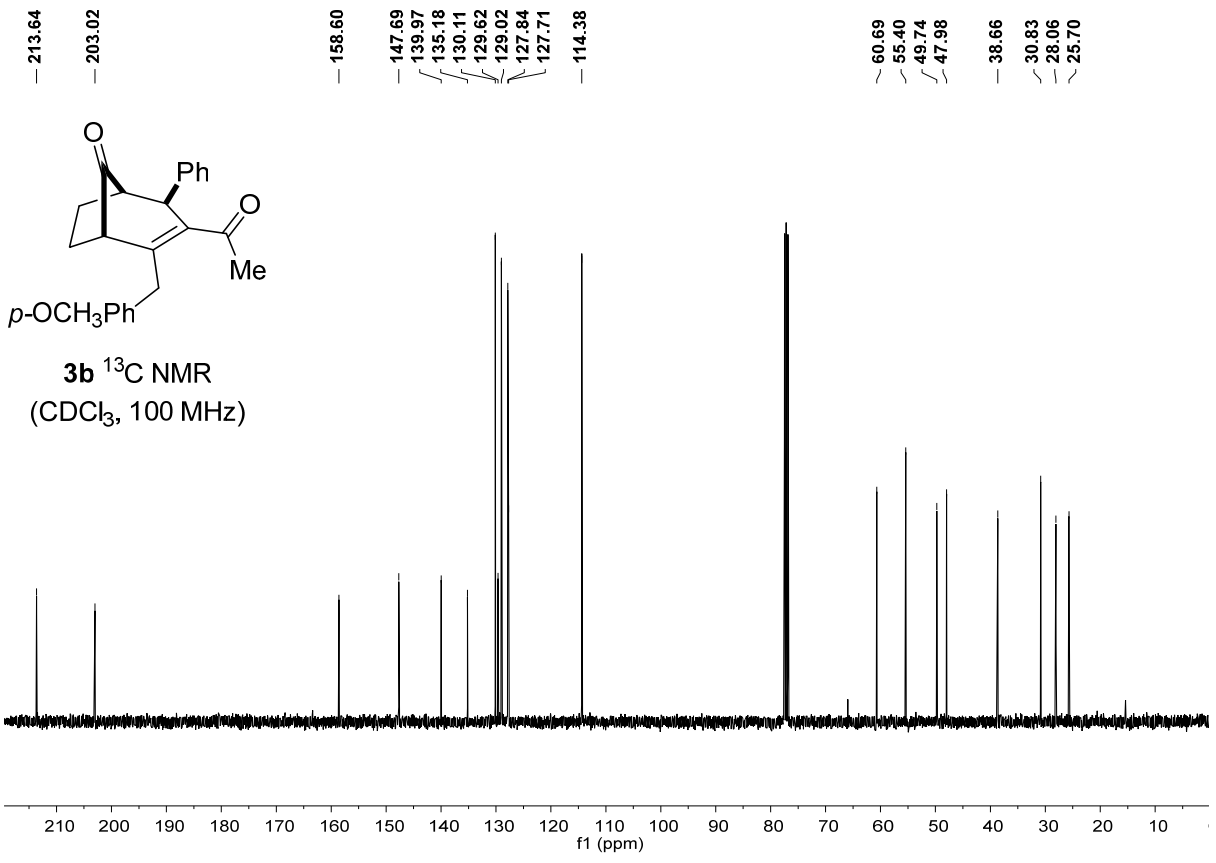
3a ^{1}H NMR
($CDCl_3$, 400 MHz)



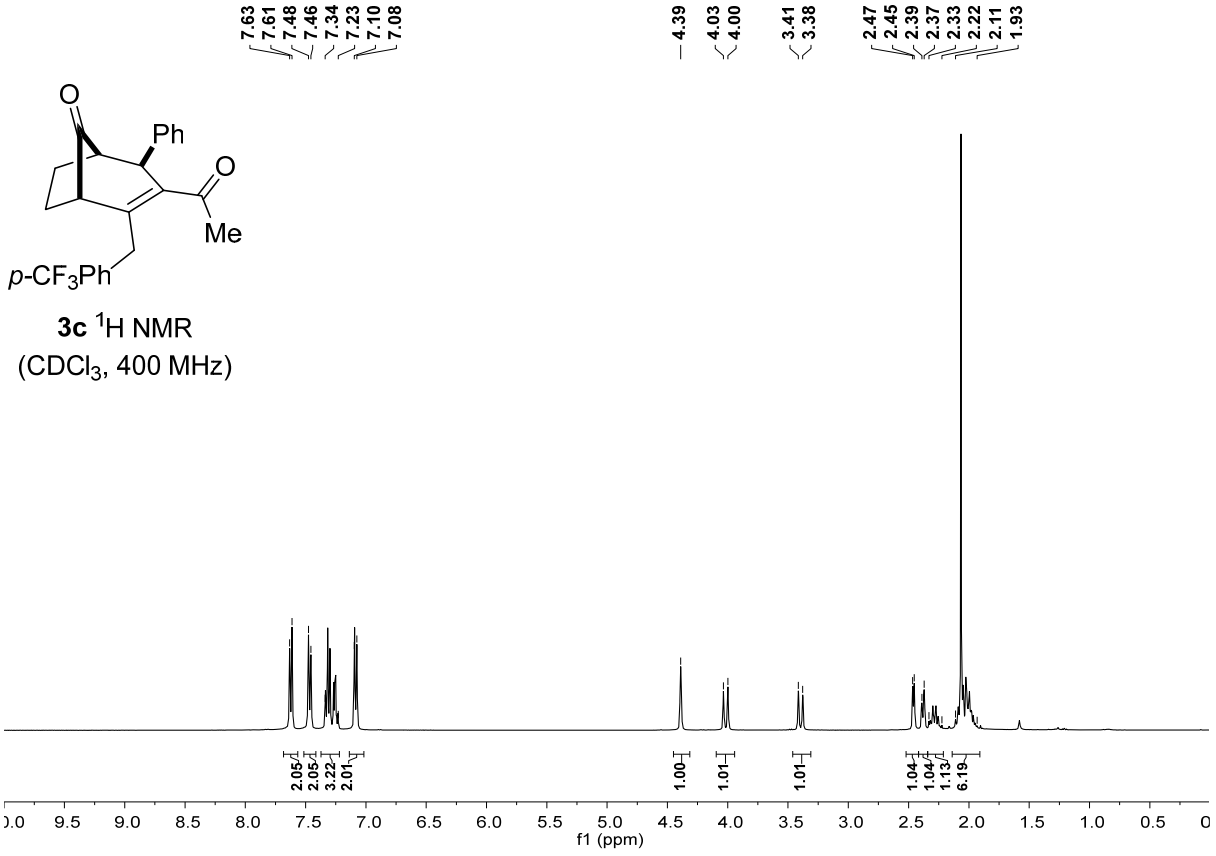
3a ^{13}C NMR
($CDCl_3$, 100 MHz)



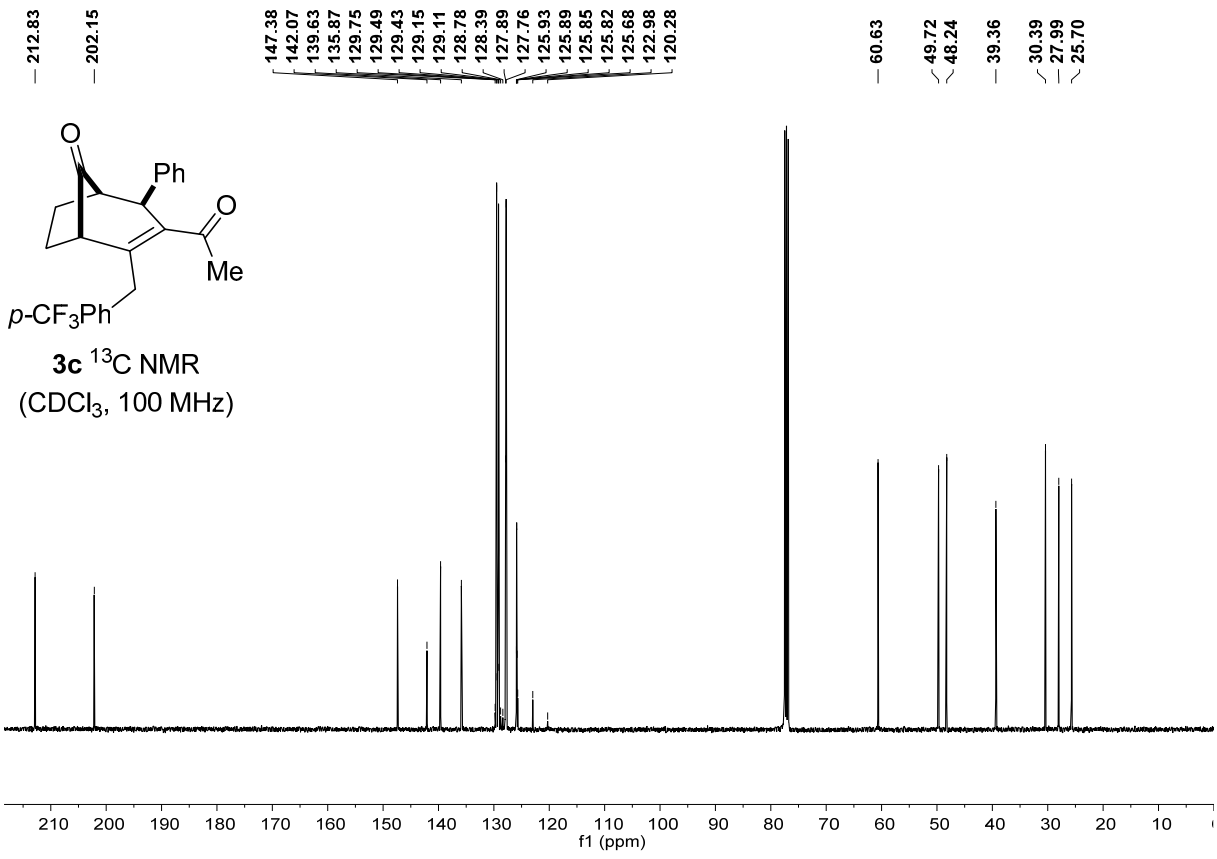
3b ^{1}H NMR
($CDCl_3$, 400 MHz)



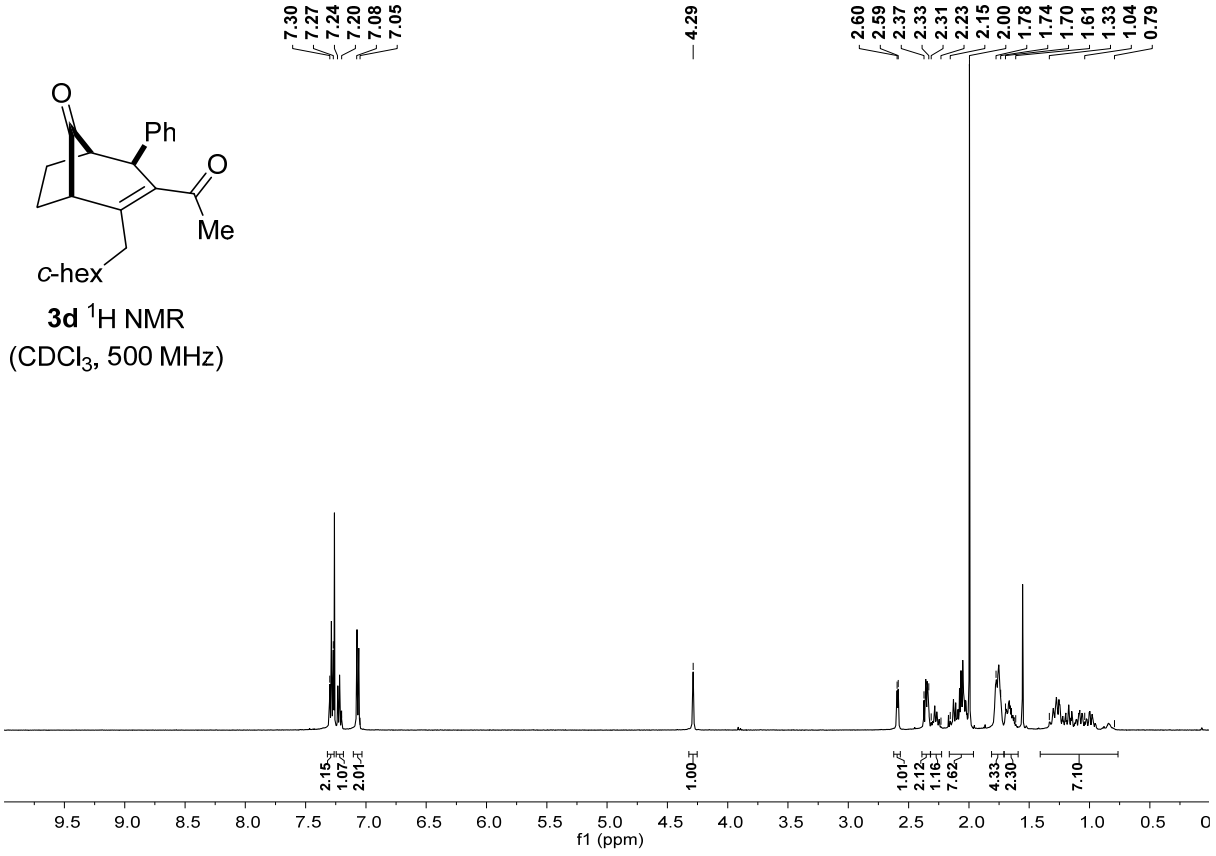
3b ^{13}C NMR
($CDCl_3$, 100 MHz)



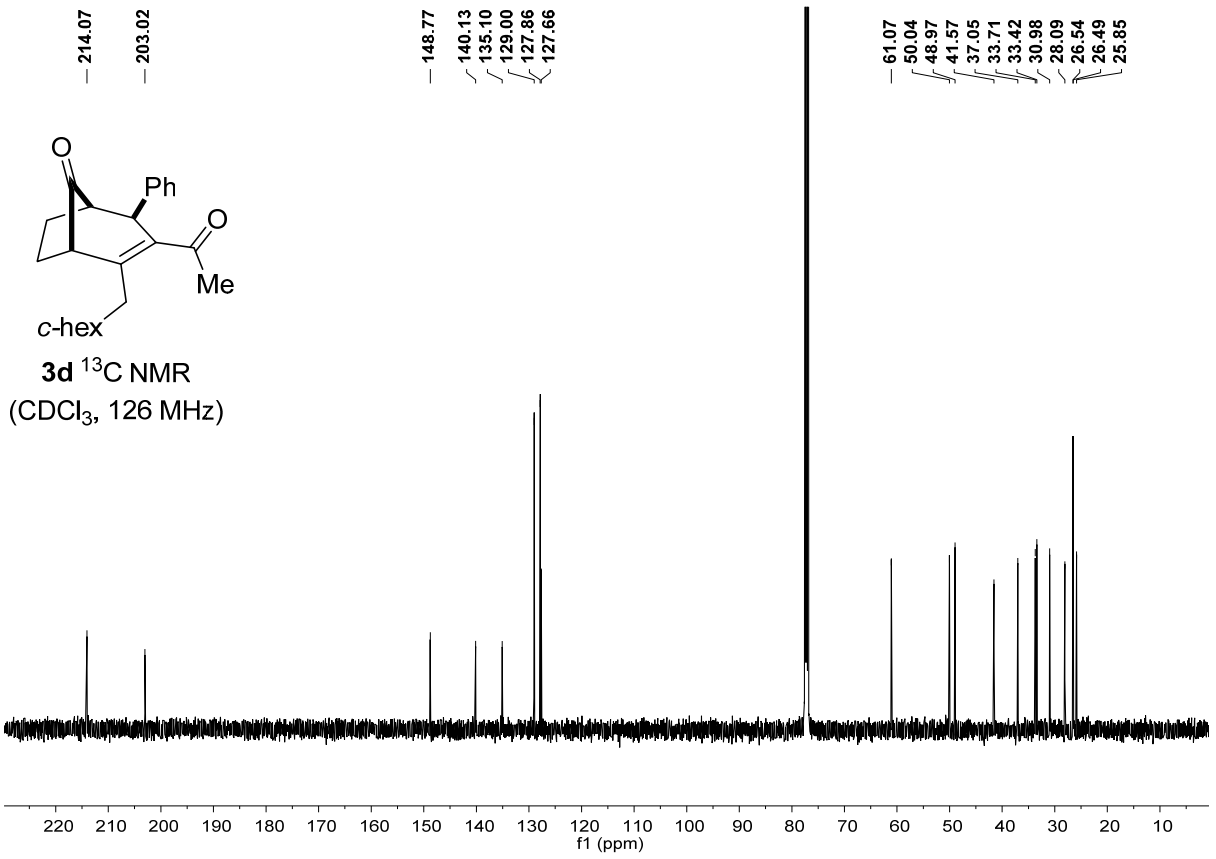
3c ^{1}H NMR
($CDCl_3$, 400 MHz)



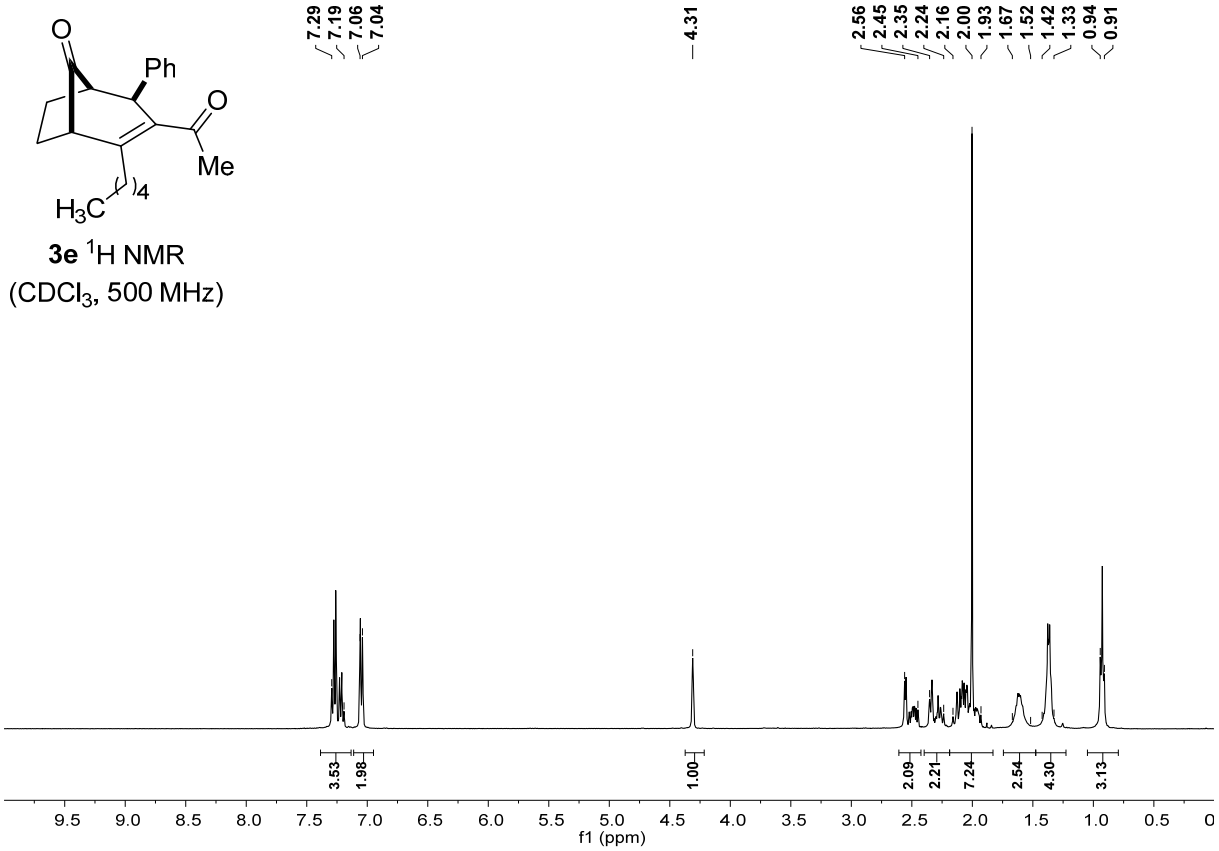
3c ^{13}C NMR
($CDCl_3$, 100 MHz)



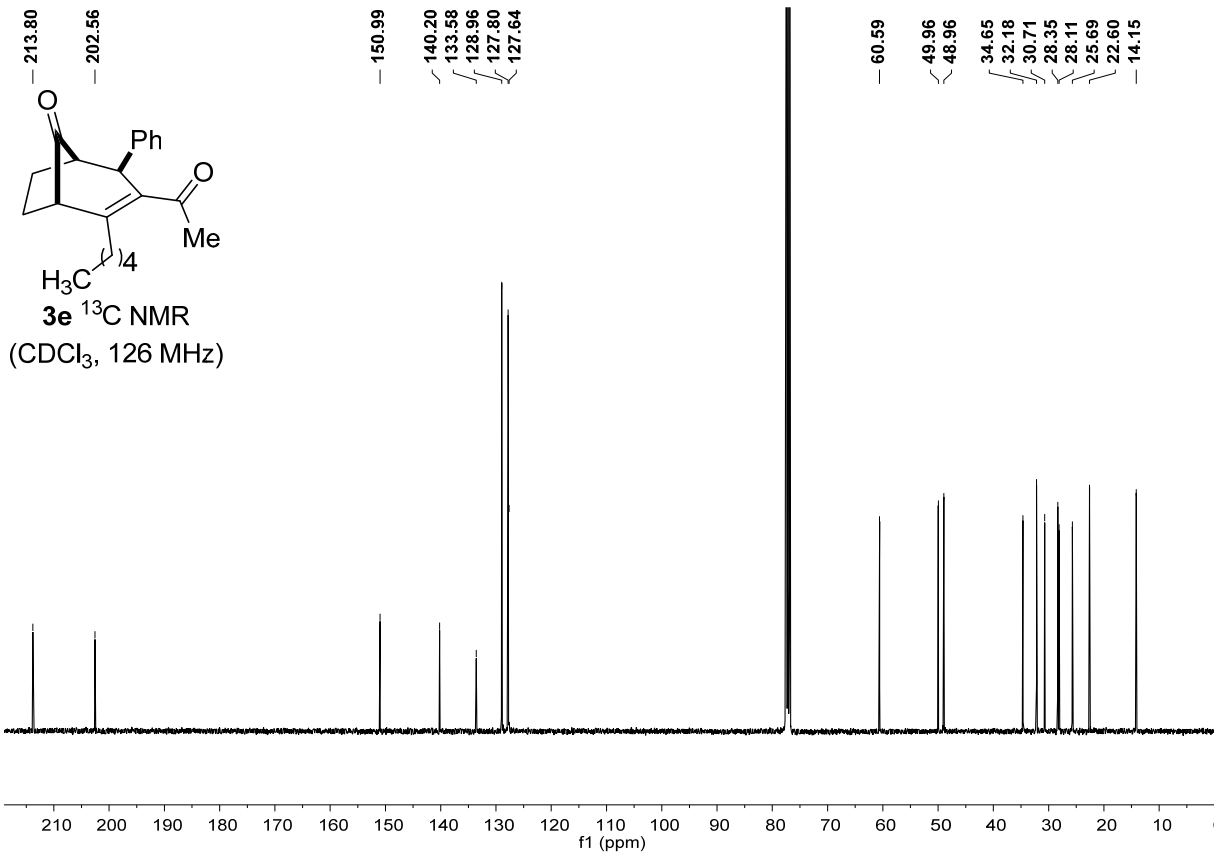
3d ^{1}H NMR
($CDCl_3$, 500 MHz)



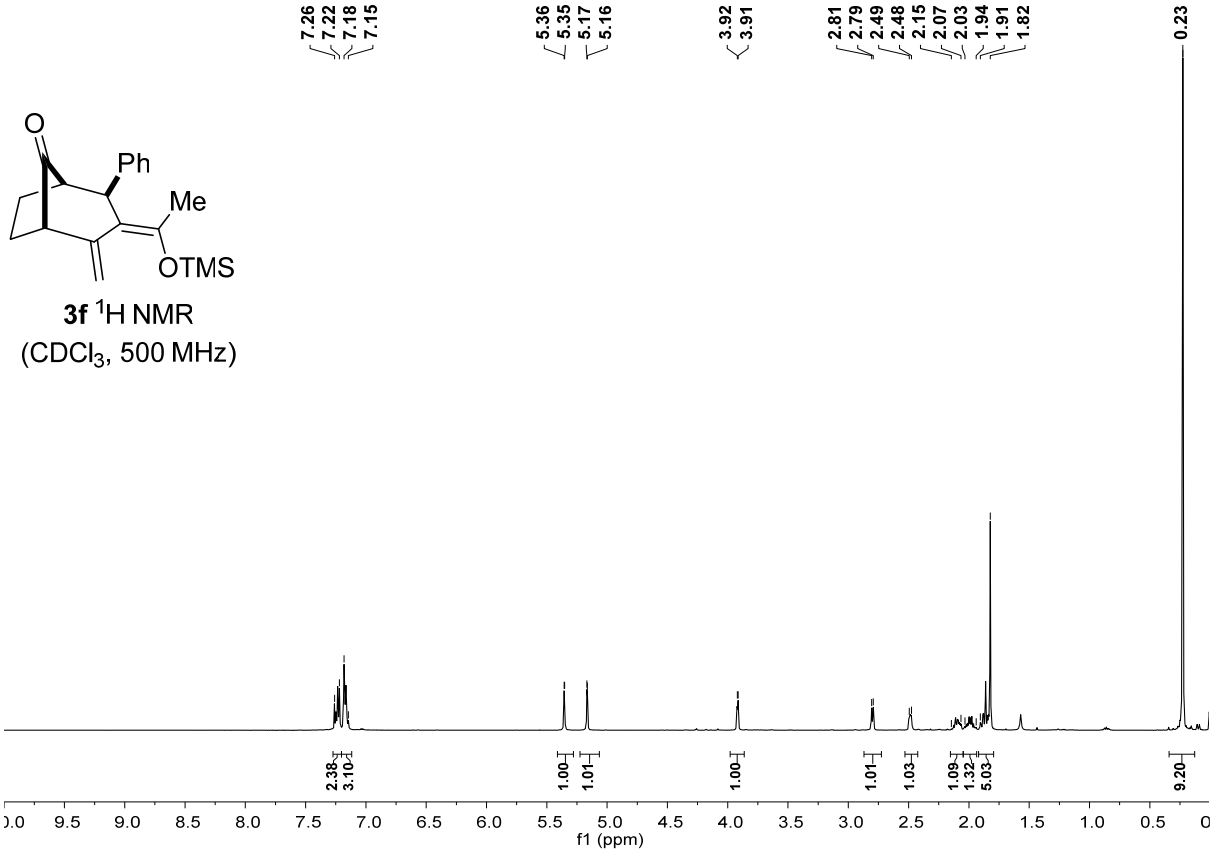
3d ^{13}C NMR
($CDCl_3$, 126 MHz)



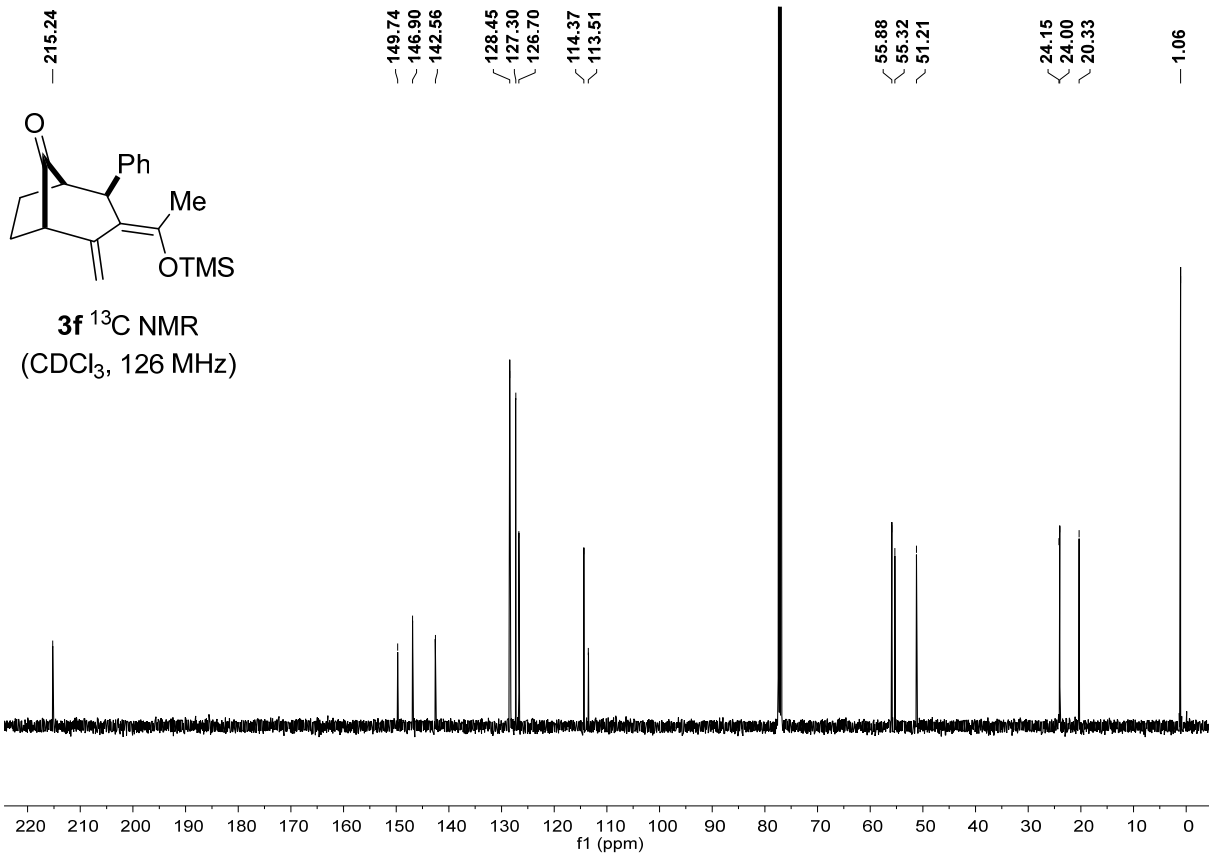
3e ^{1}H NMR
($CDCl_3$, 500 MHz)



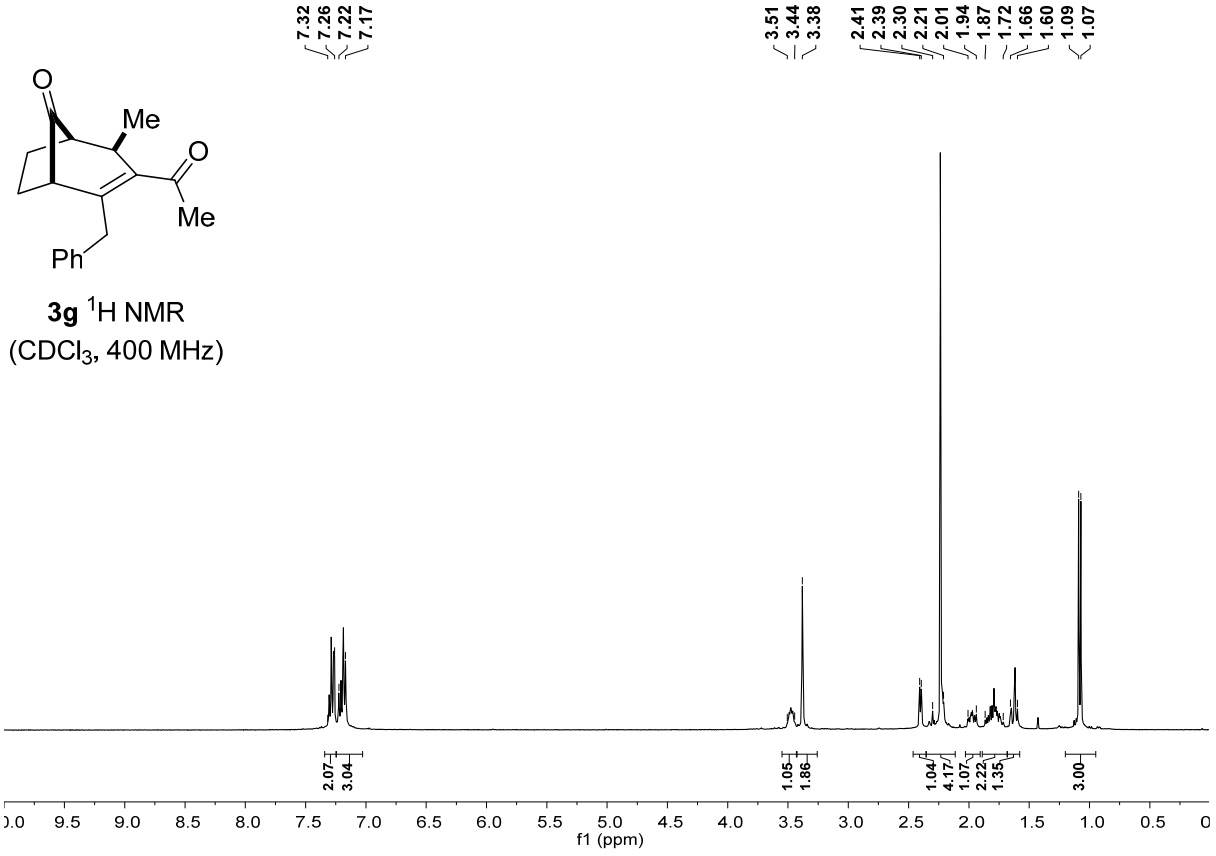
3e ^{13}C NMR
($CDCl_3$, 126 MHz)



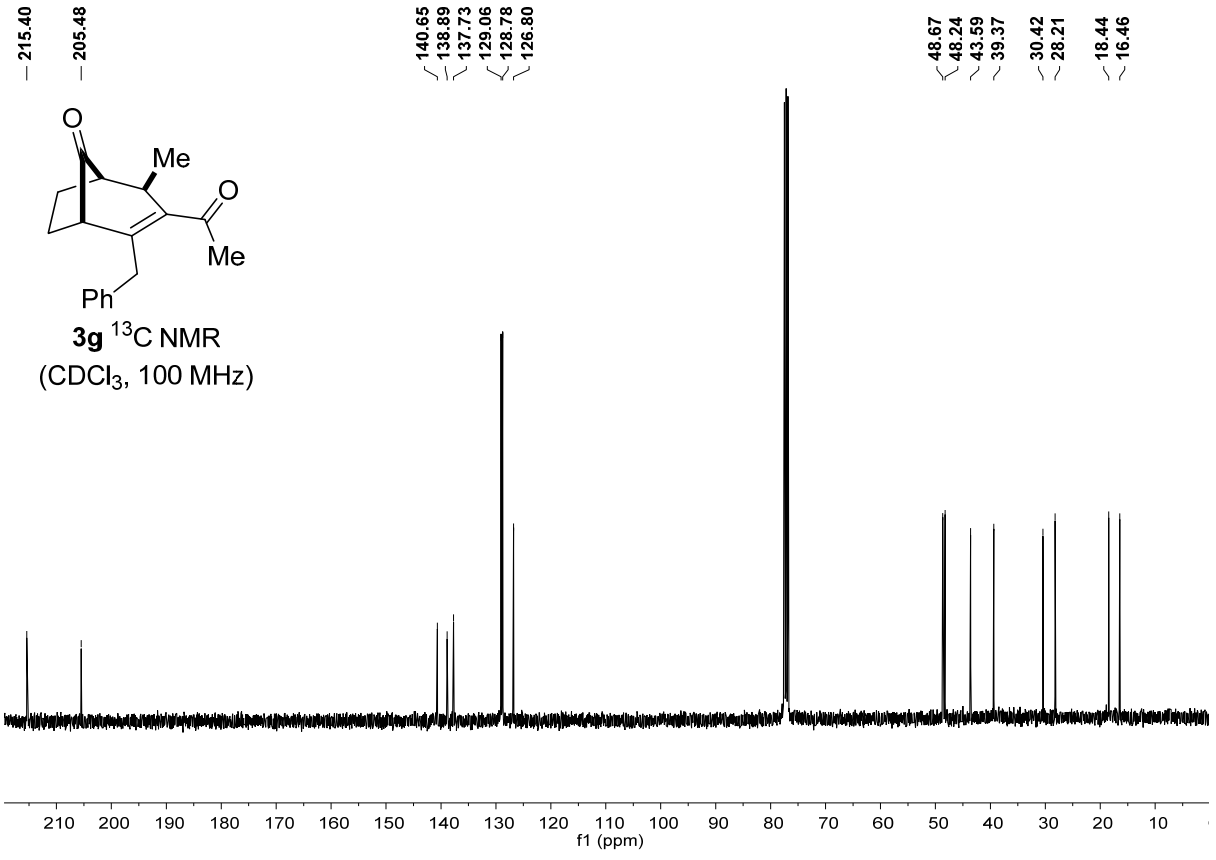
3f ^{1}H NMR
($CDCl_3$, 500 MHz)



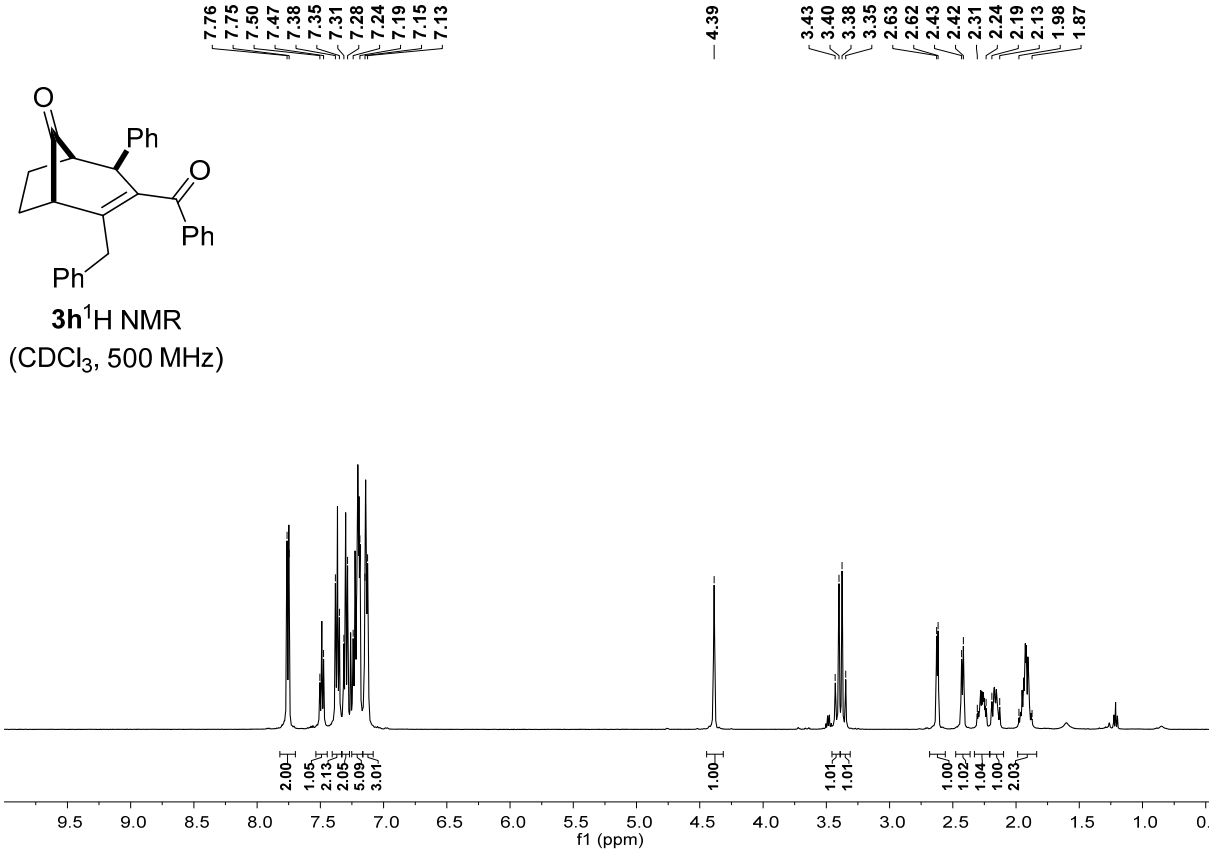
3f ^{13}C NMR
($CDCl_3$, 126 MHz)



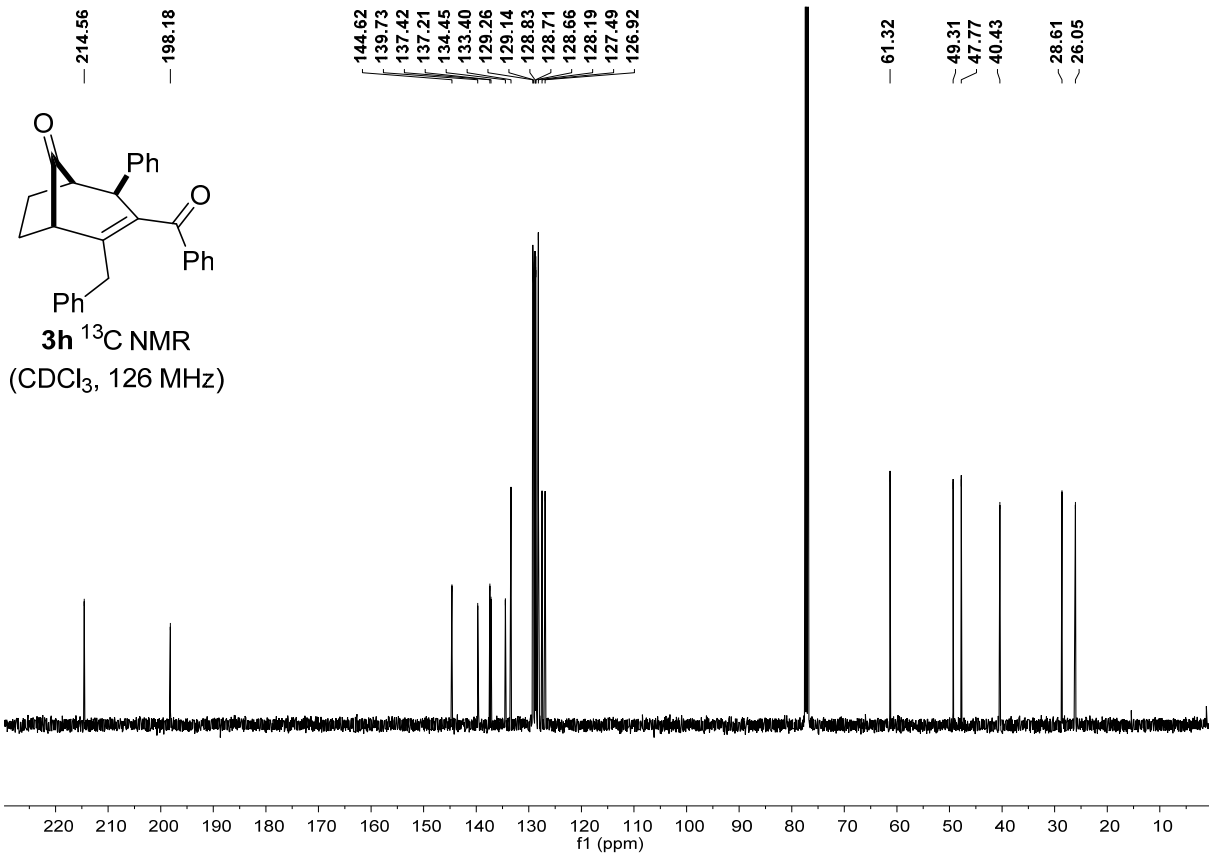
3g ^{1}H NMR
($CDCl_3$, 400 MHz)



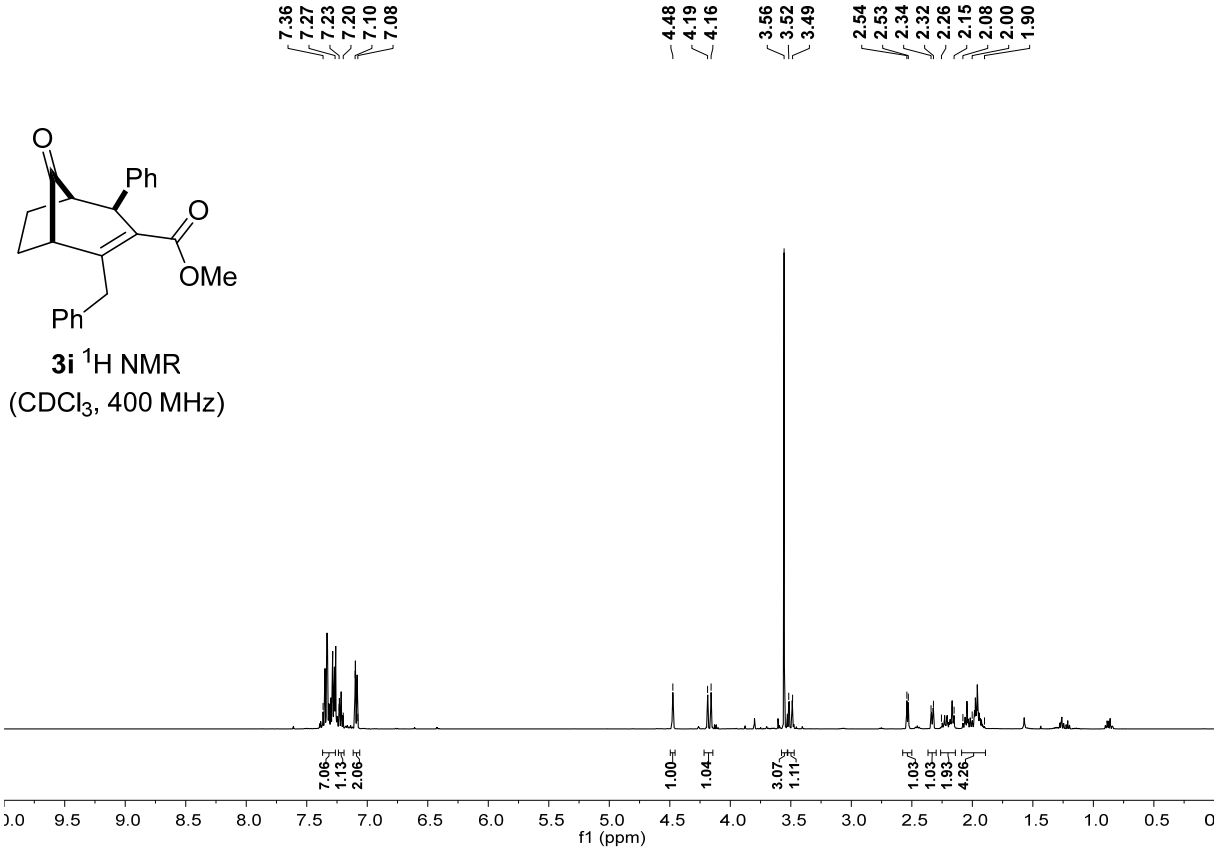
3g ^{13}C NMR
($CDCl_3$, 100 MHz)



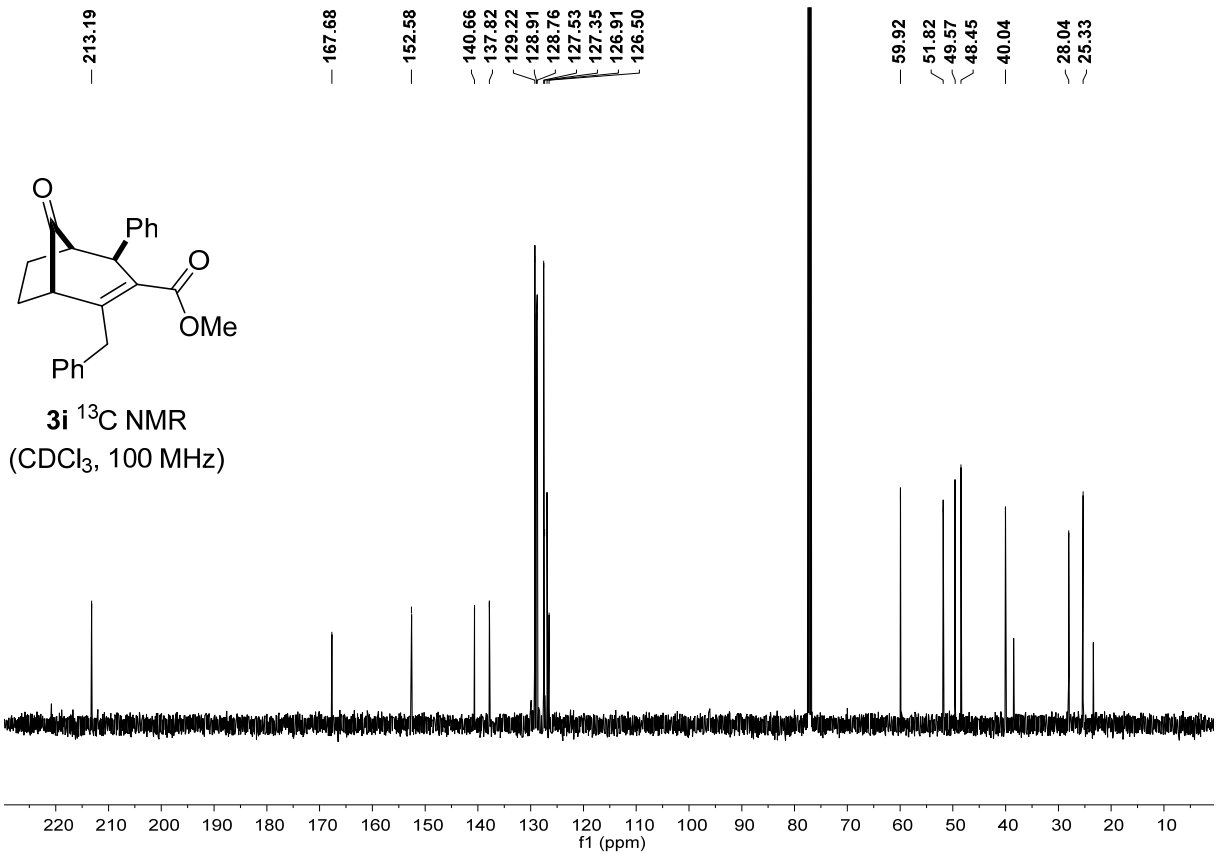
3h ^{1}H NMR
($CDCl_3$, 500 MHz)



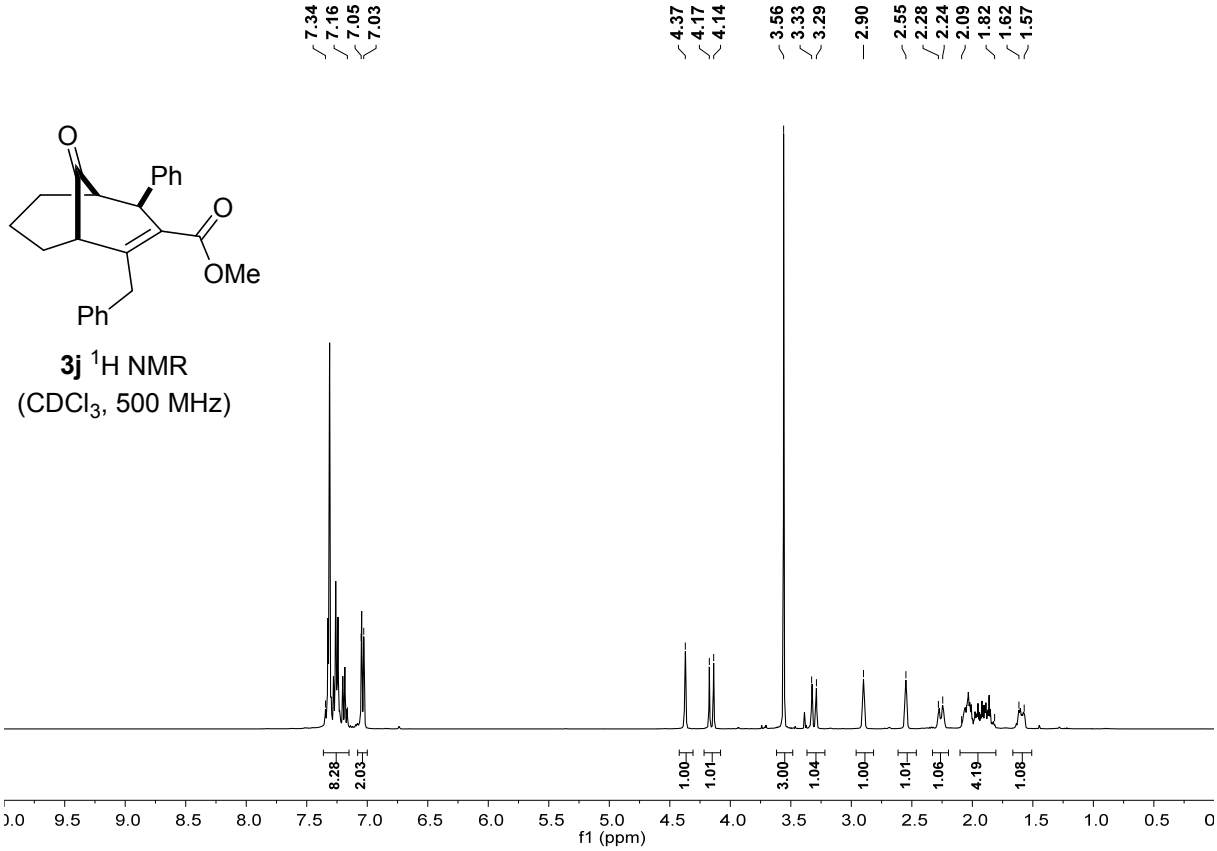
3h ^{13}C NMR
($CDCl_3$, 126 MHz)

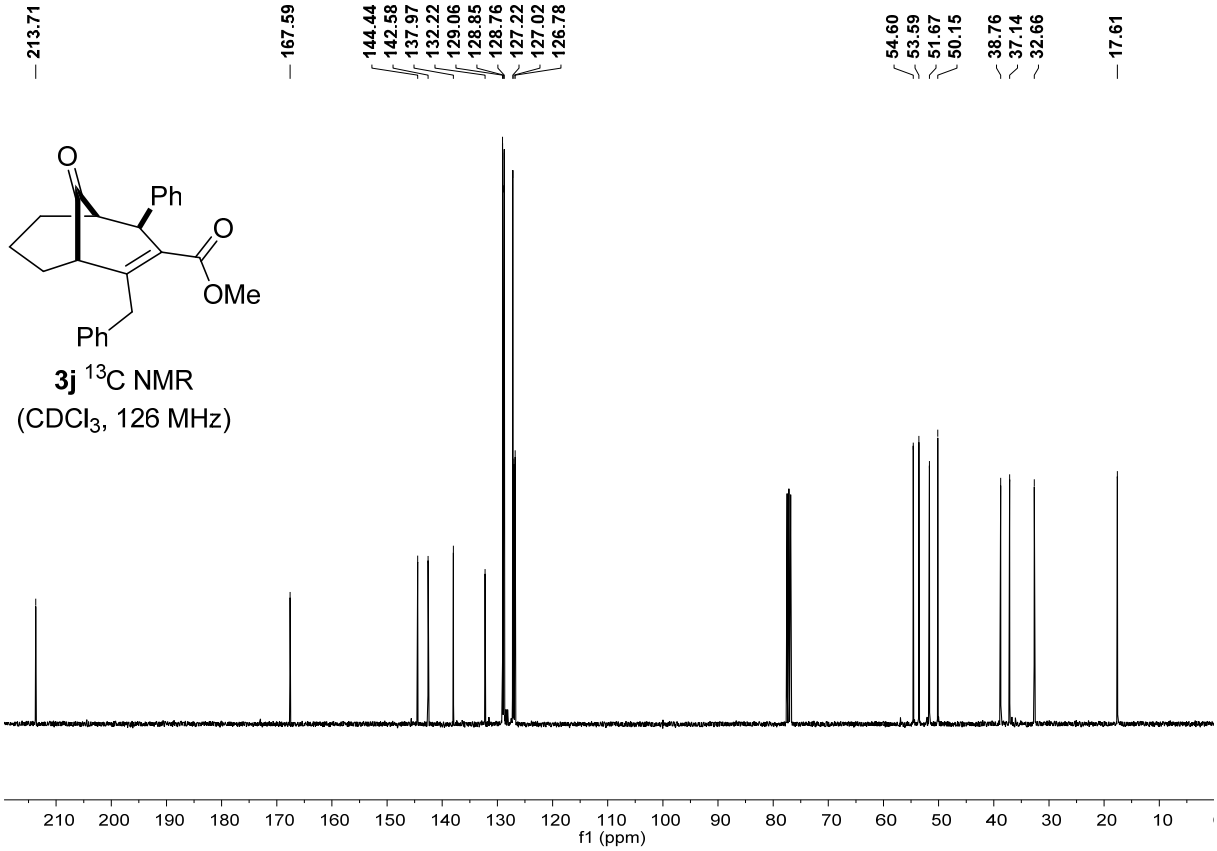


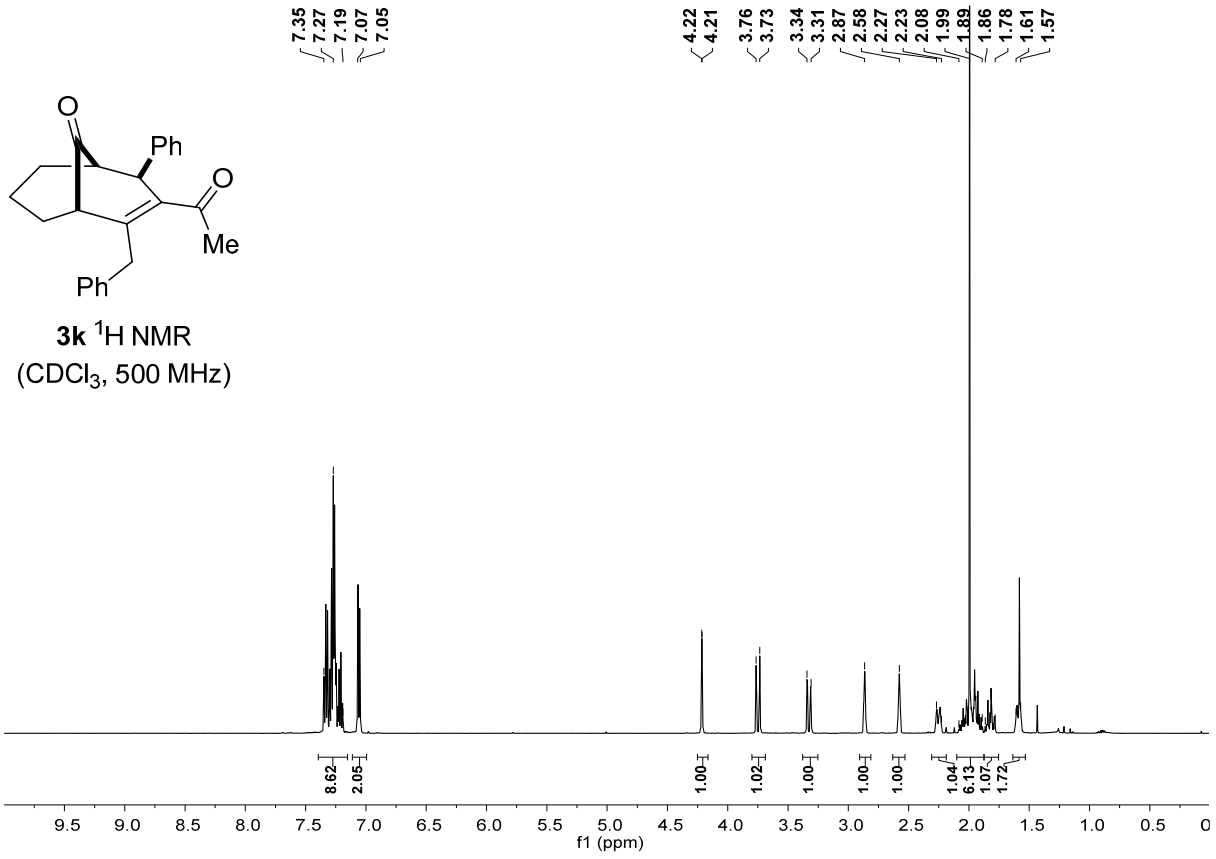
3i ^{1}H NMR
($CDCl_3$, 400 MHz)



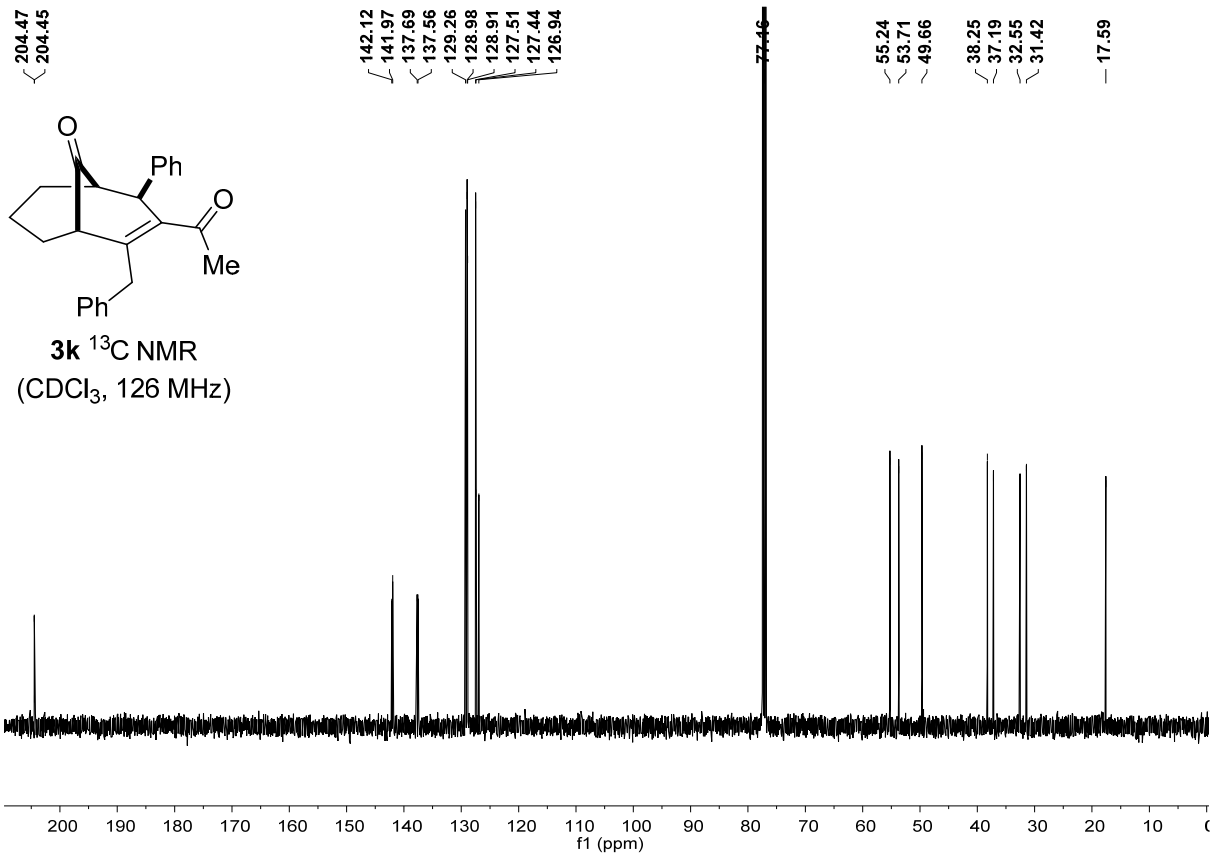
3i ^{13}C NMR
($CDCl_3$, 100 MHz)


7.34
7.16
7.05
7.03
4.37
4.17
4.14
3.56
3.33
3.29
2.90
2.55
2.28
2.24
2.09
1.82
1.62
1.57
O
Ph
O
OMe
Ph
3j 1H NMR
(CDCl3, 500 MHz)
8.28
2.03
1.00
1.01
3.00
1.04
1.00
1.01
1.06
4.19
1.08
f1 (ppm)

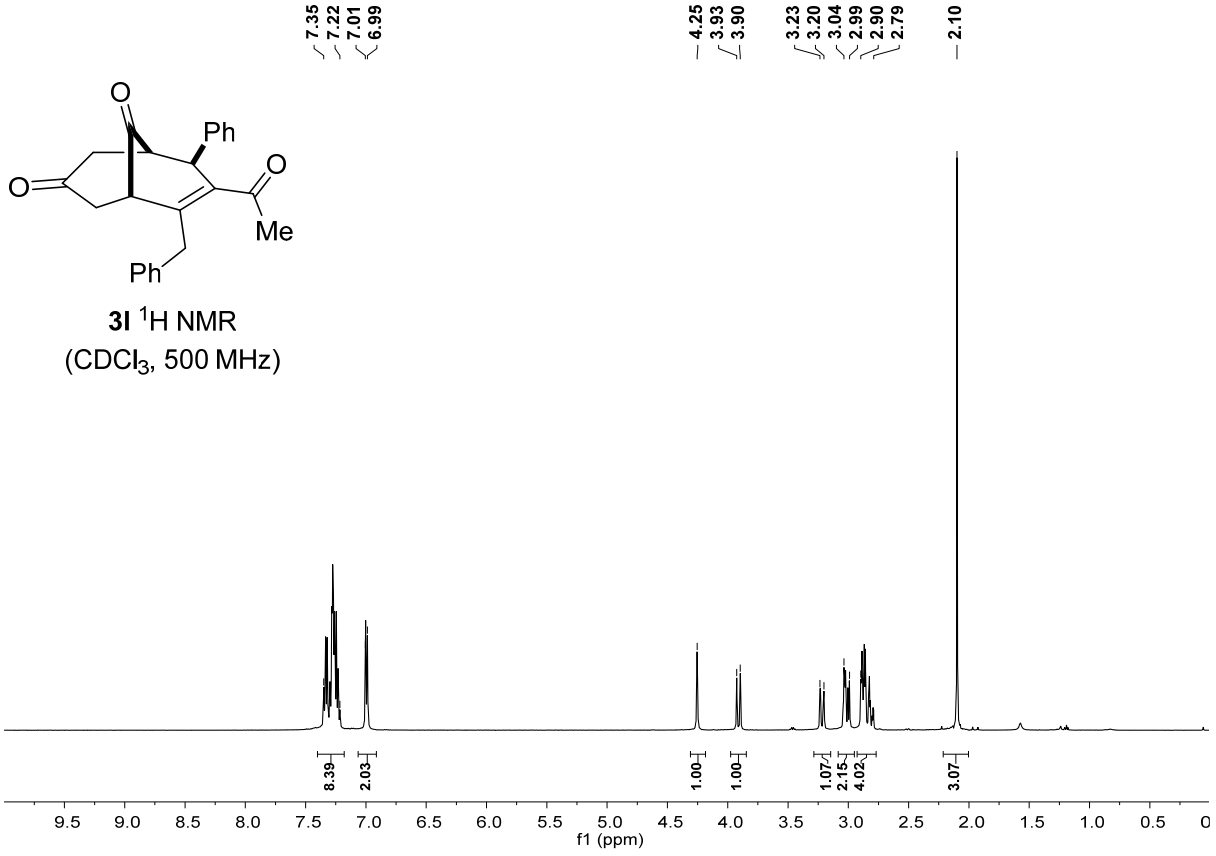

213.71
167.59
144.44
142.58
137.97
132.22
129.06
128.85
128.76
127.22
127.02
126.78
54.60
53.59
51.67
50.15
38.76
37.14
32.66
17.61
O
Ph
O
OMe
Ph
3j 13C NMR
(CDCl3, 126 MHz)
f1 (ppm)



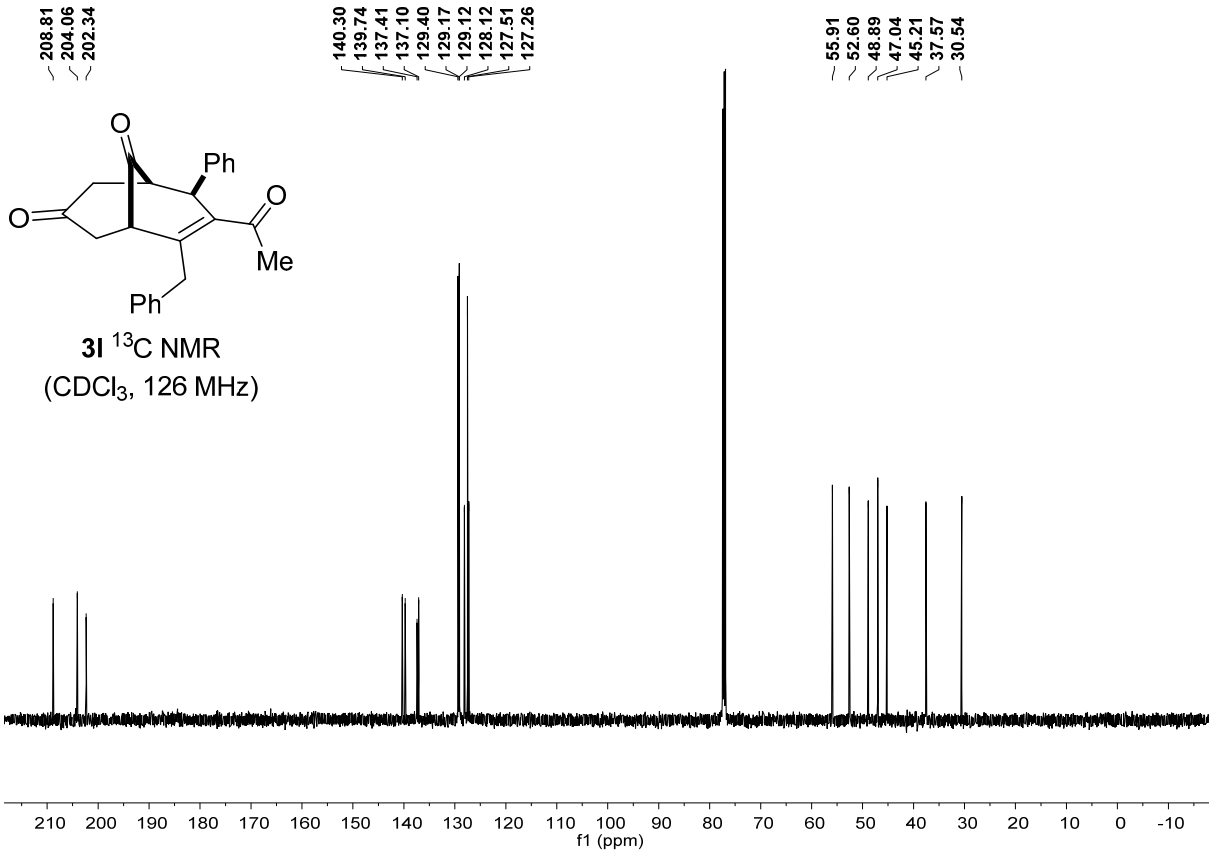
3k ^{1}H NMR
($CDCl_3$, 500 MHz)



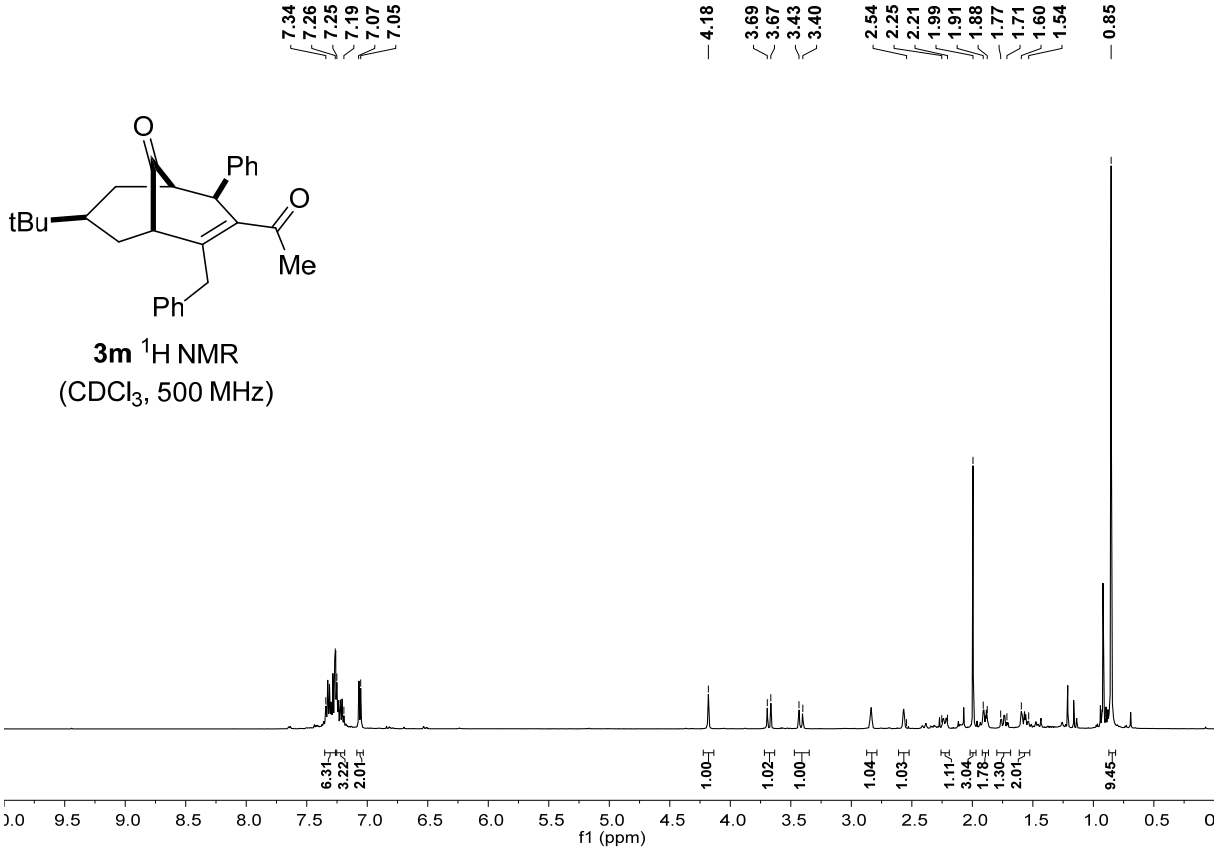
3k ^{13}C NMR
($CDCl_3$, 126 MHz)



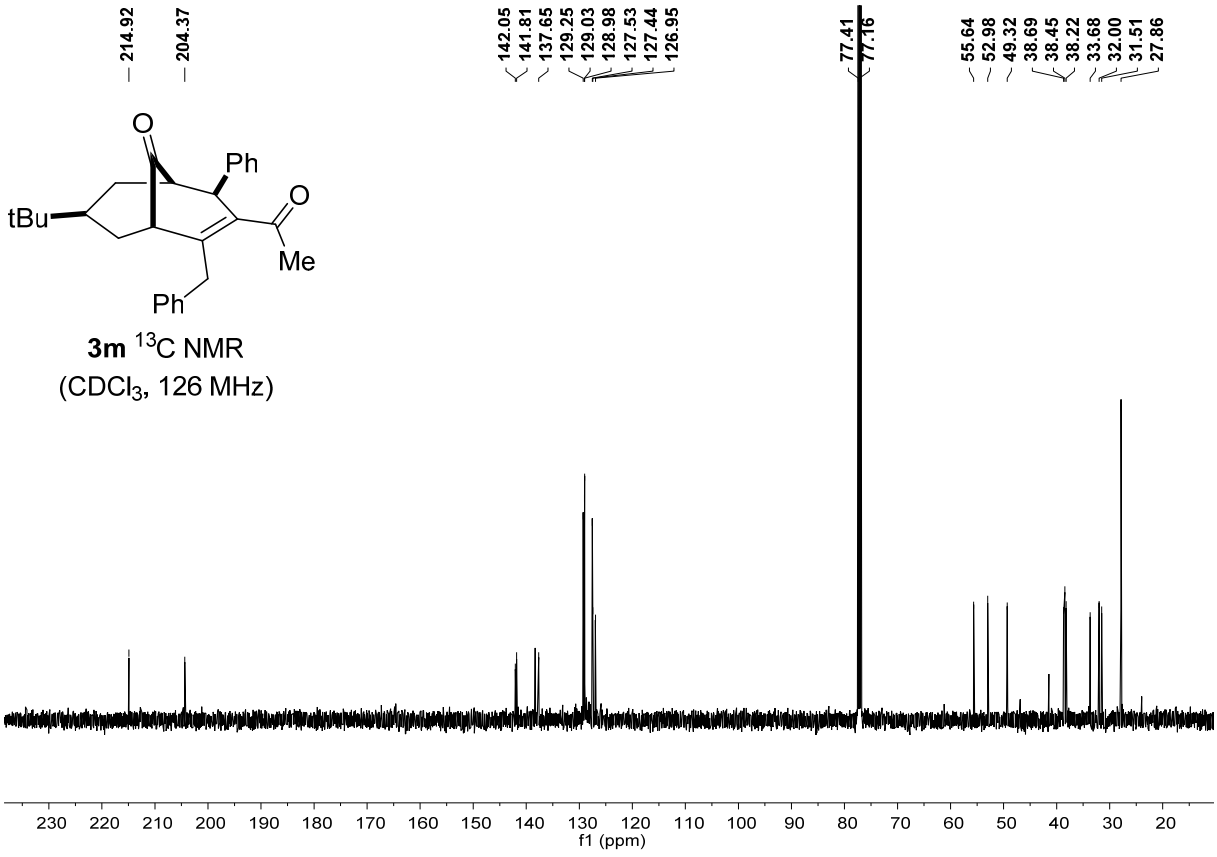
3l ^{1}H NMR
($CDCl_3$, 500 MHz)



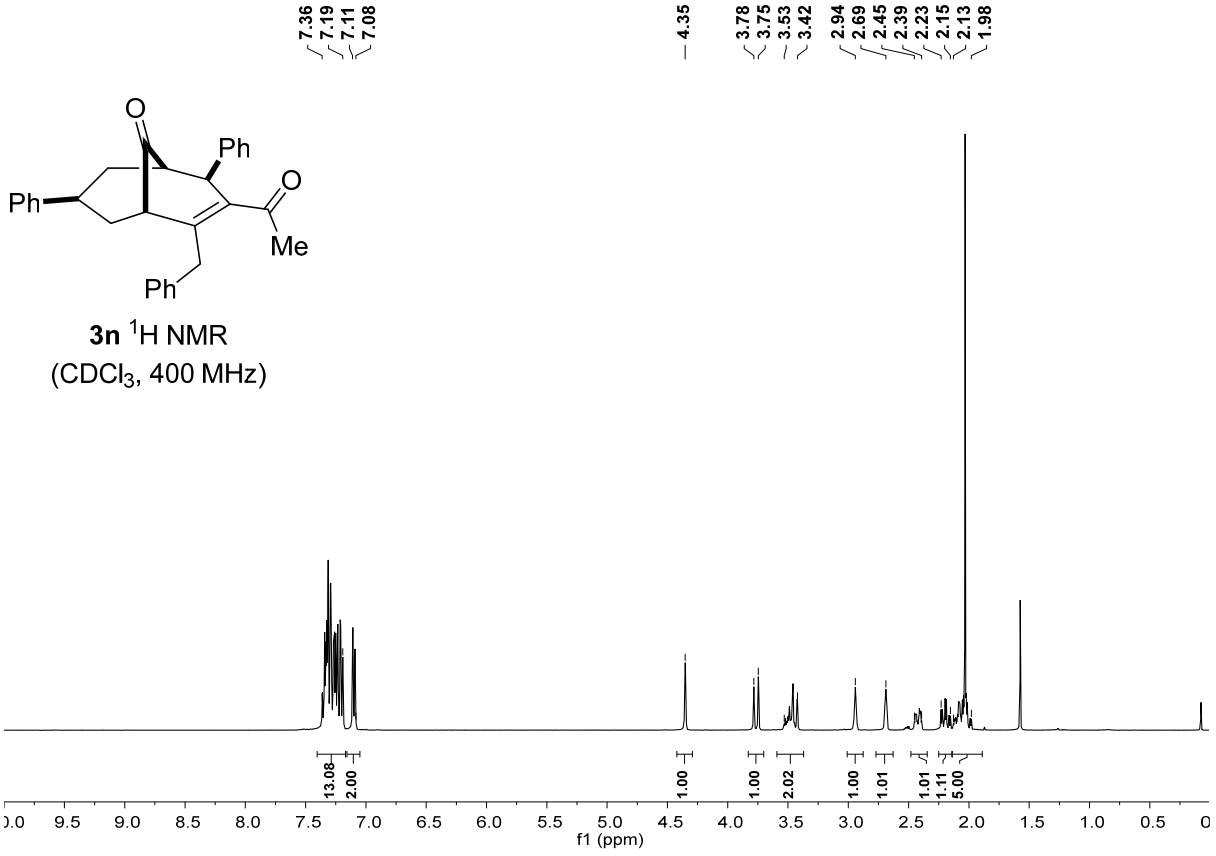
3l ^{13}C NMR
($CDCl_3$, 126 MHz)



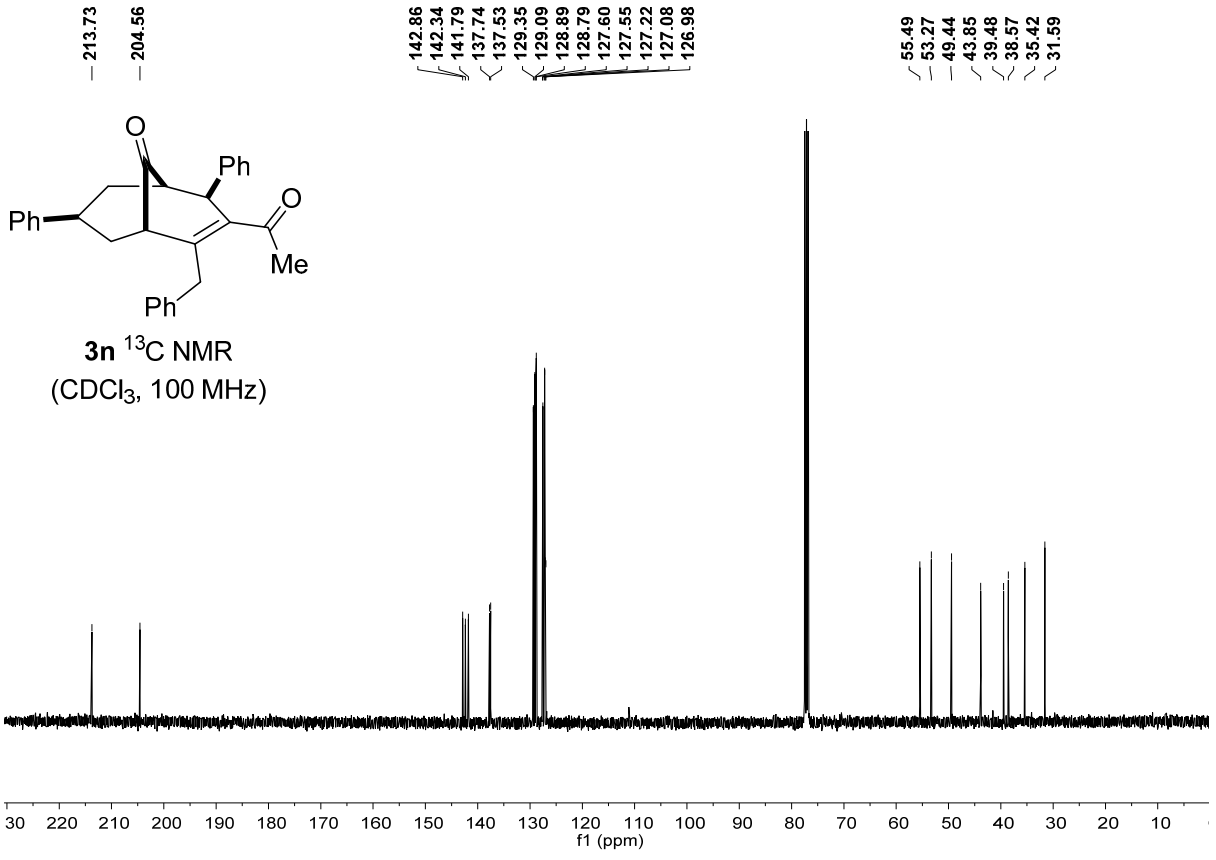
3m ^{1}H NMR
($CDCl_3$, 500 MHz)



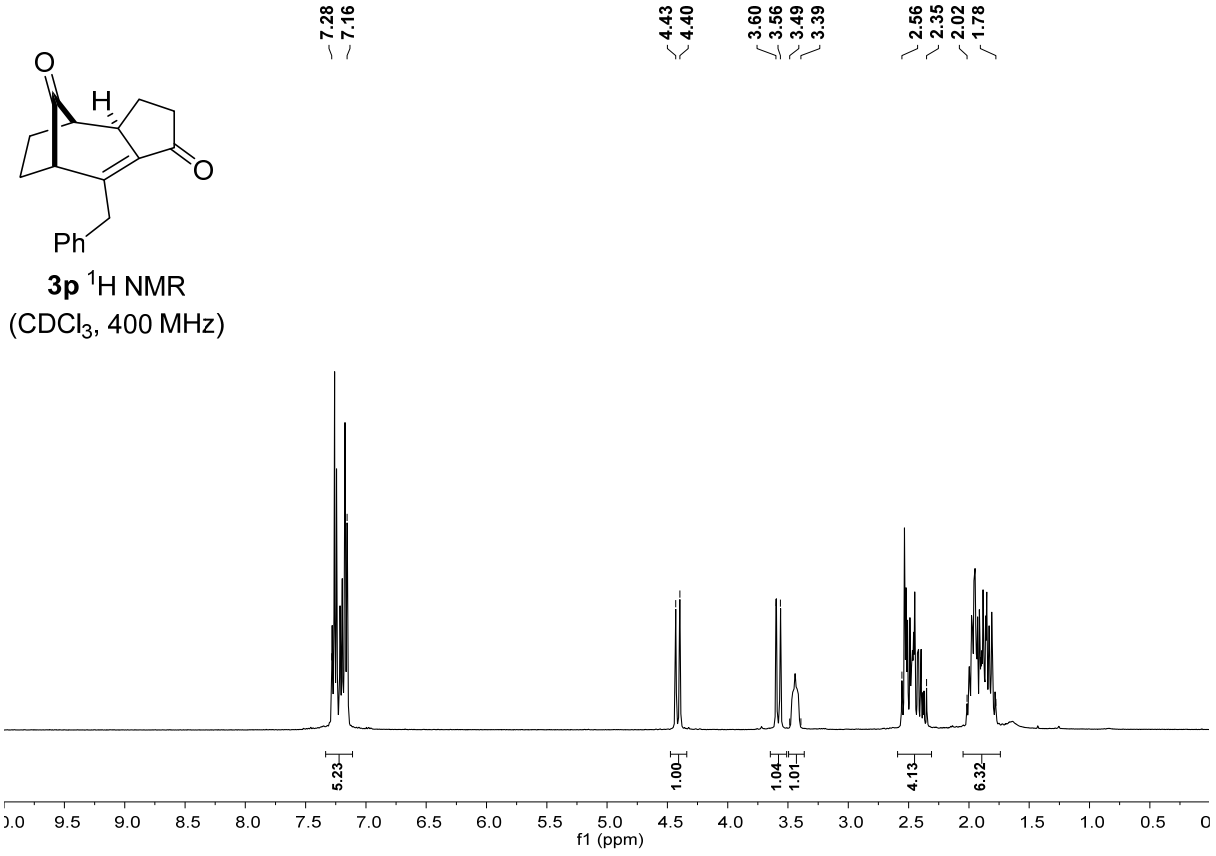
3m ^{13}C NMR
($CDCl_3$, 126 MHz)



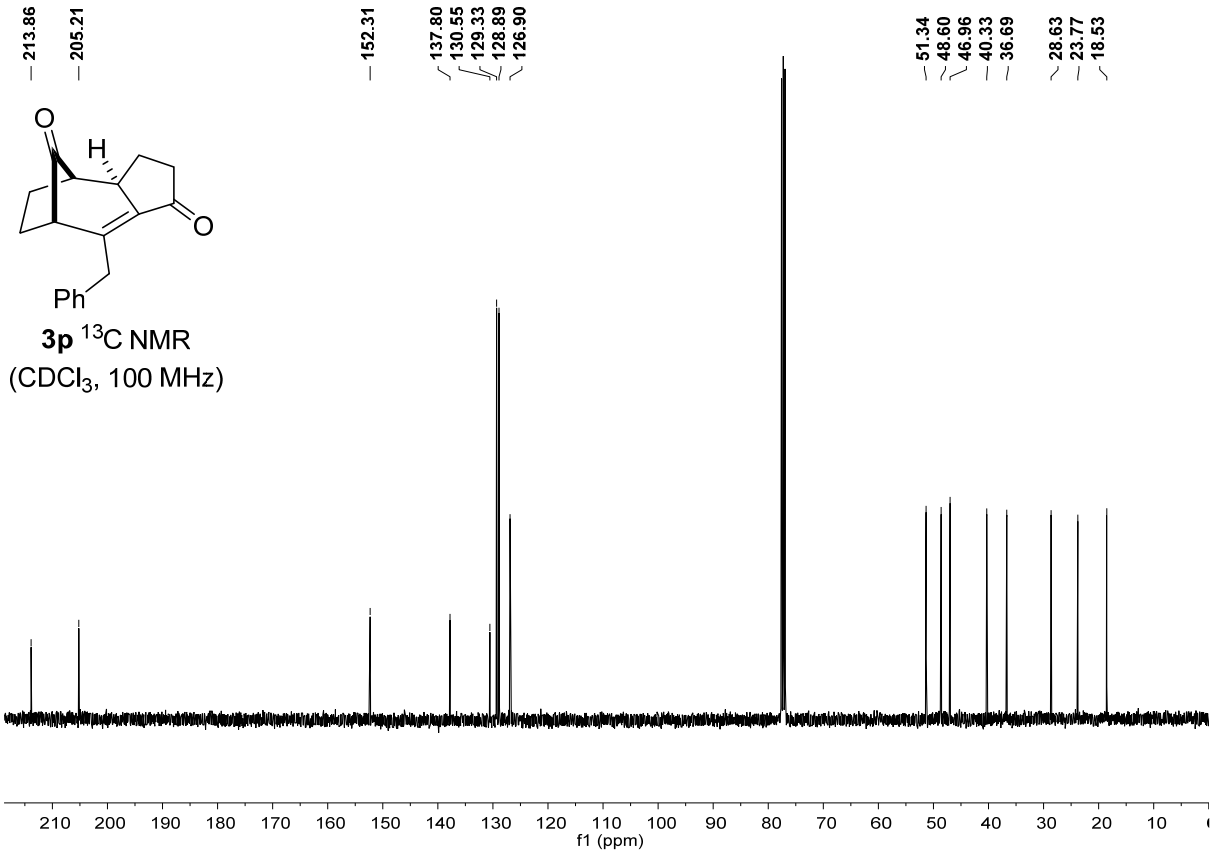
3n ^{1}H NMR
($CDCl_3$, 400 MHz)



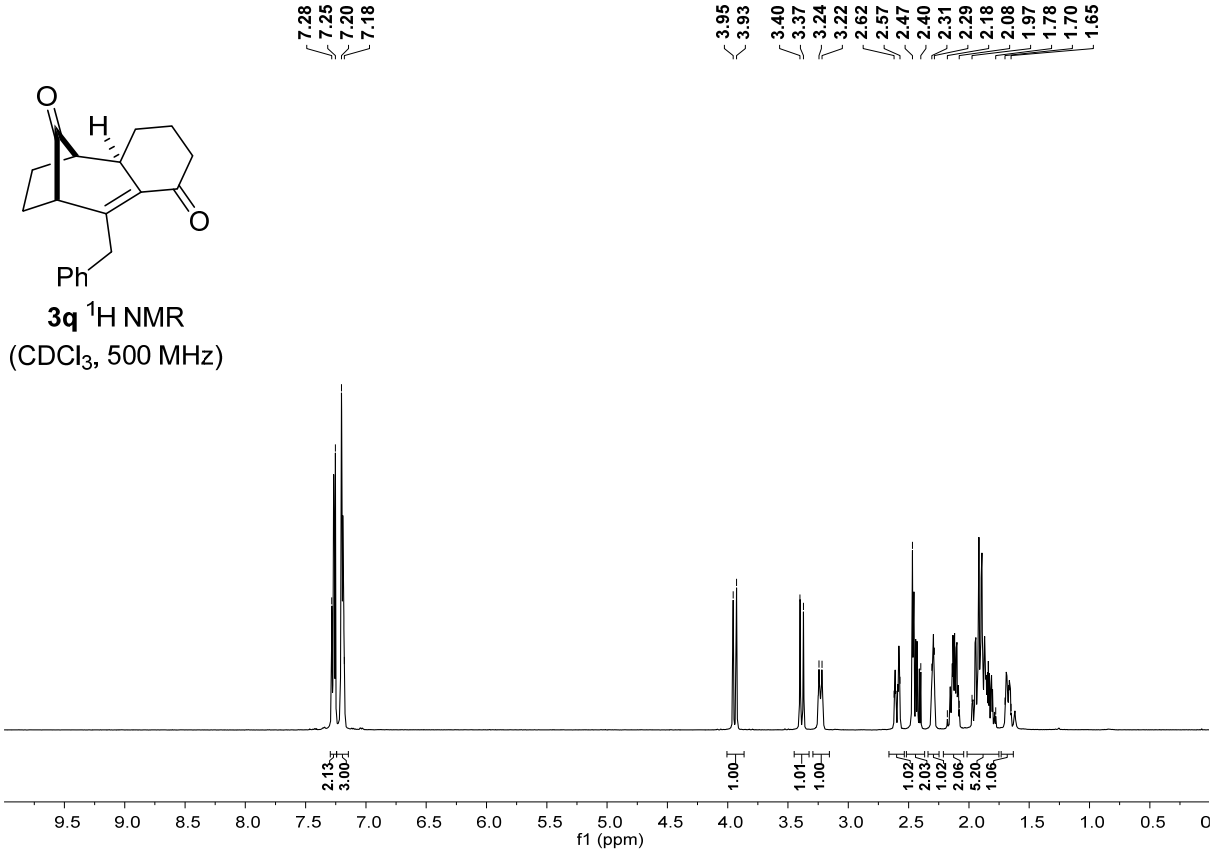
3n ^{13}C NMR
($CDCl_3$, 100 MHz)



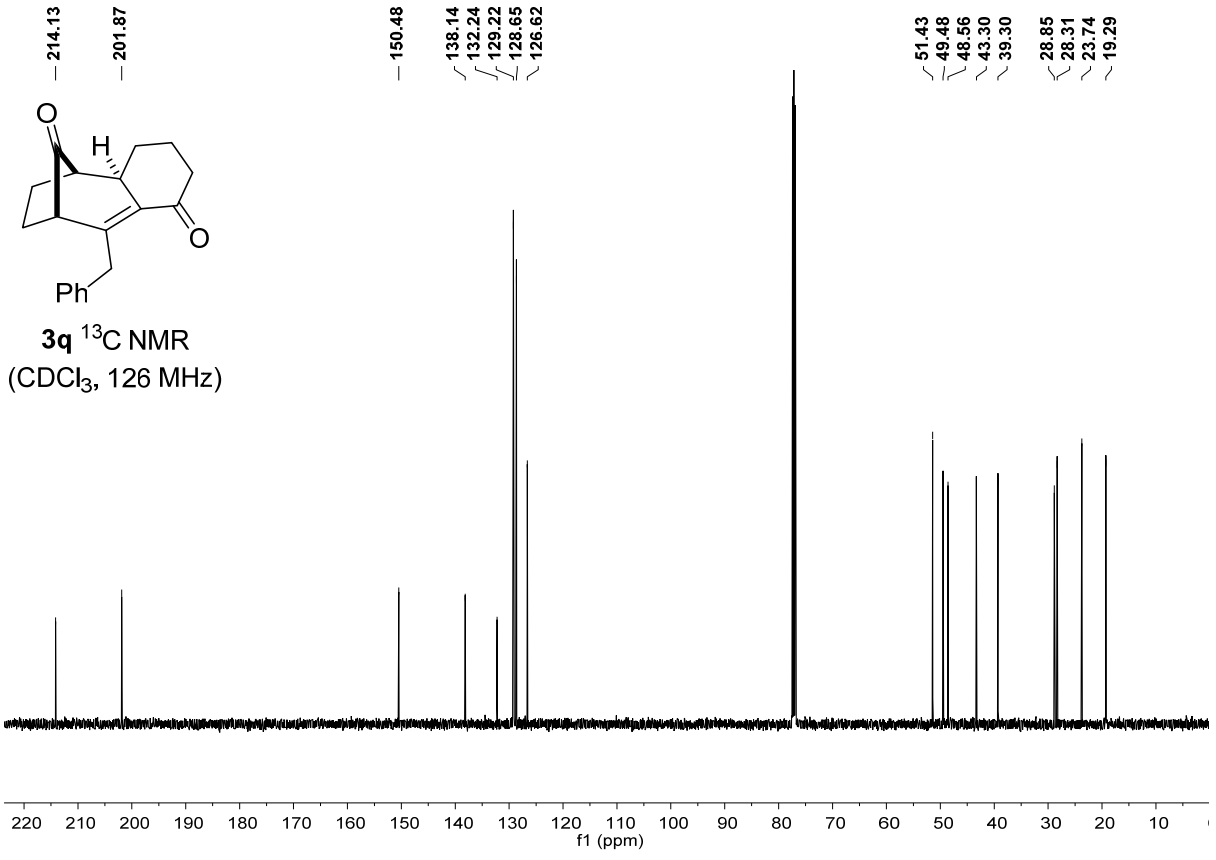
3p ^{1}H NMR
($CDCl_3$, 400 MHz)



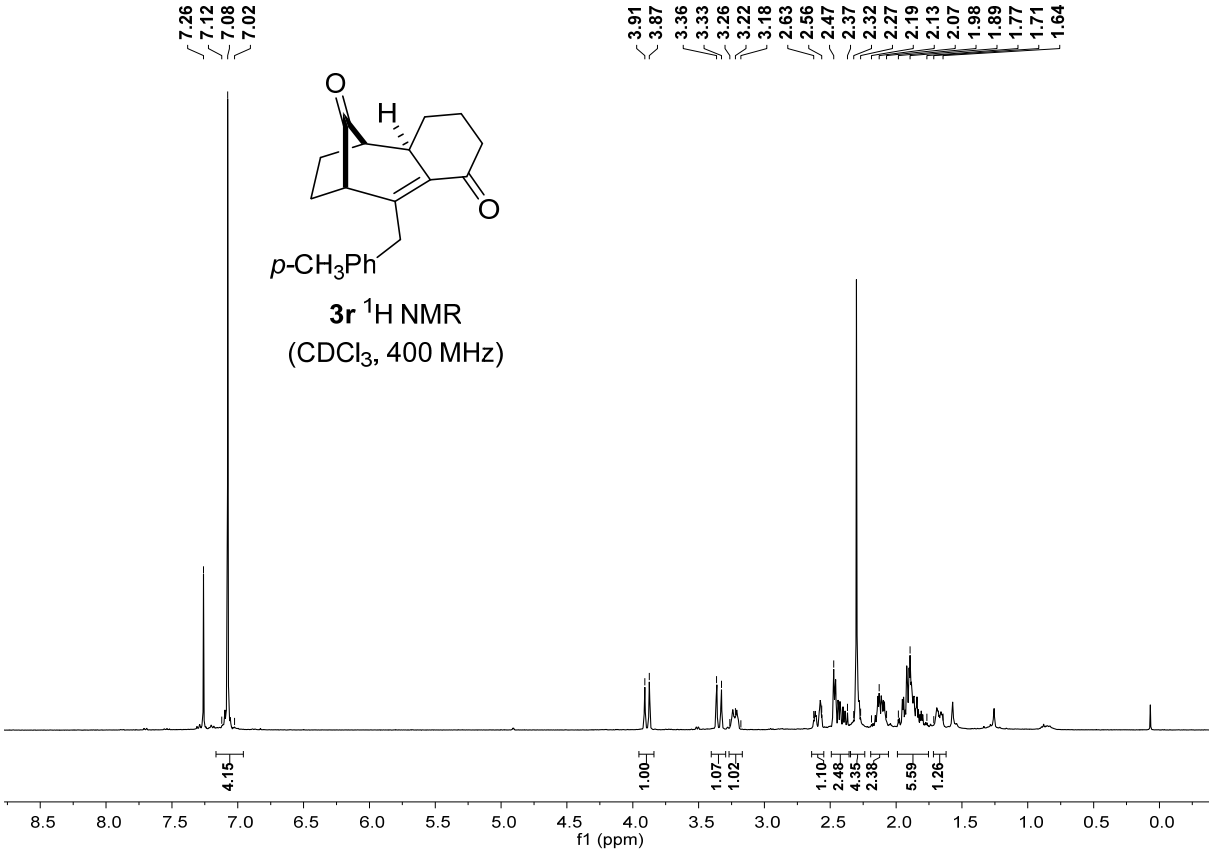
3p ^{13}C NMR
($CDCl_3$, 100 MHz)

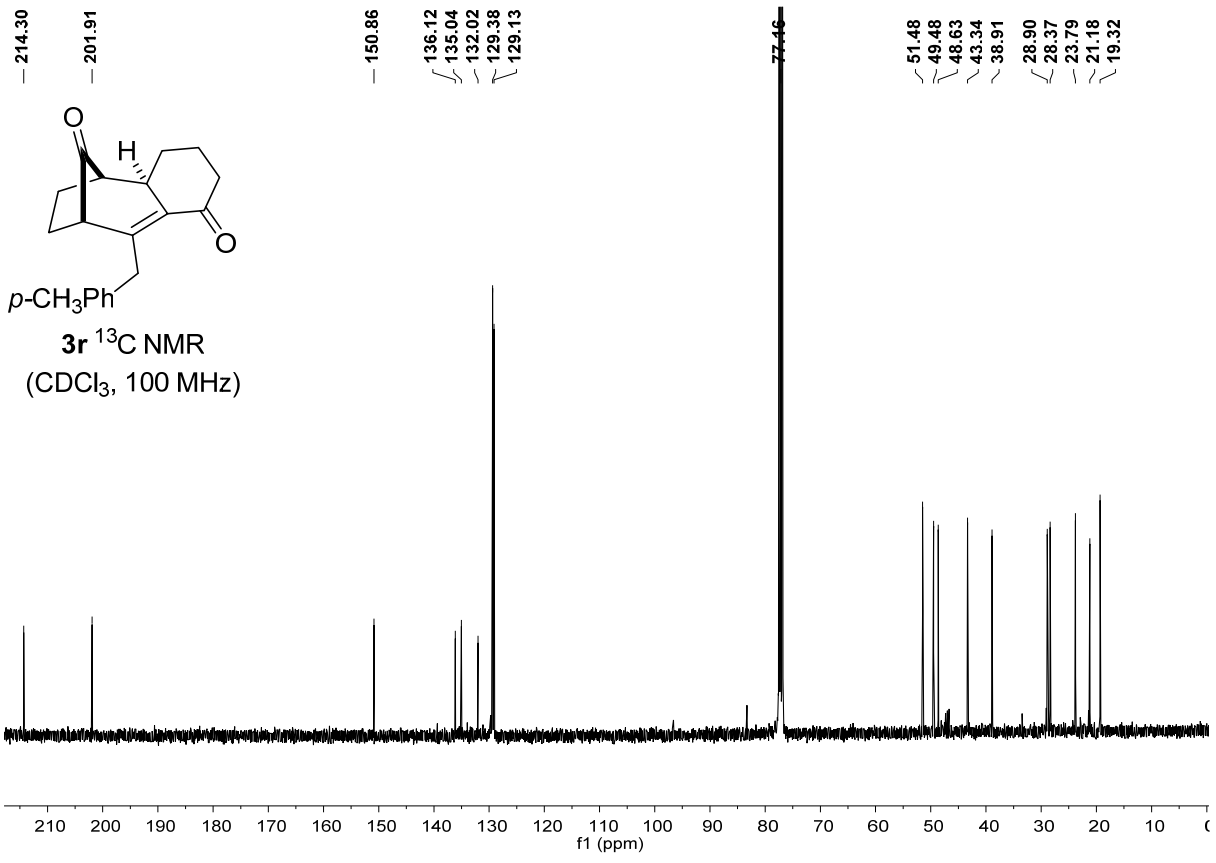


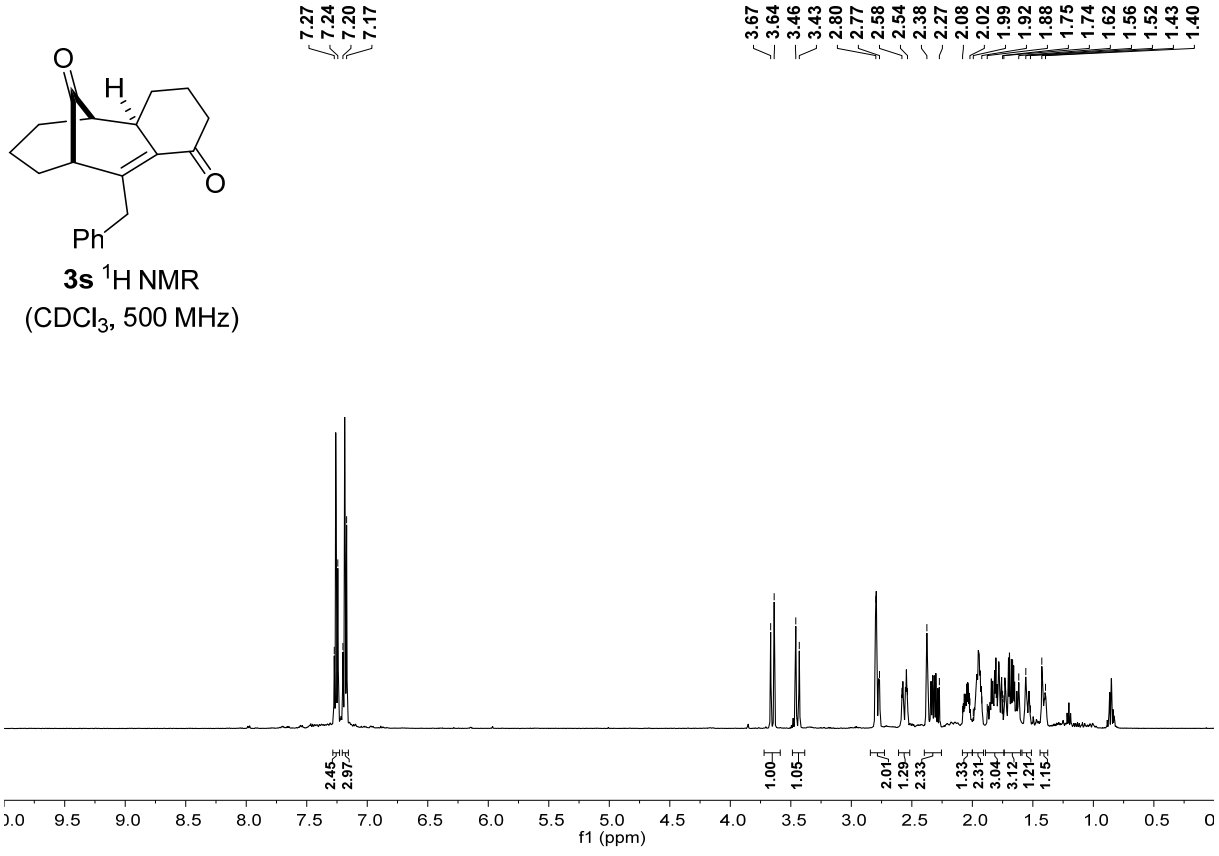
3q ^{1}H NMR
($CDCl_3$, 500 MHz)



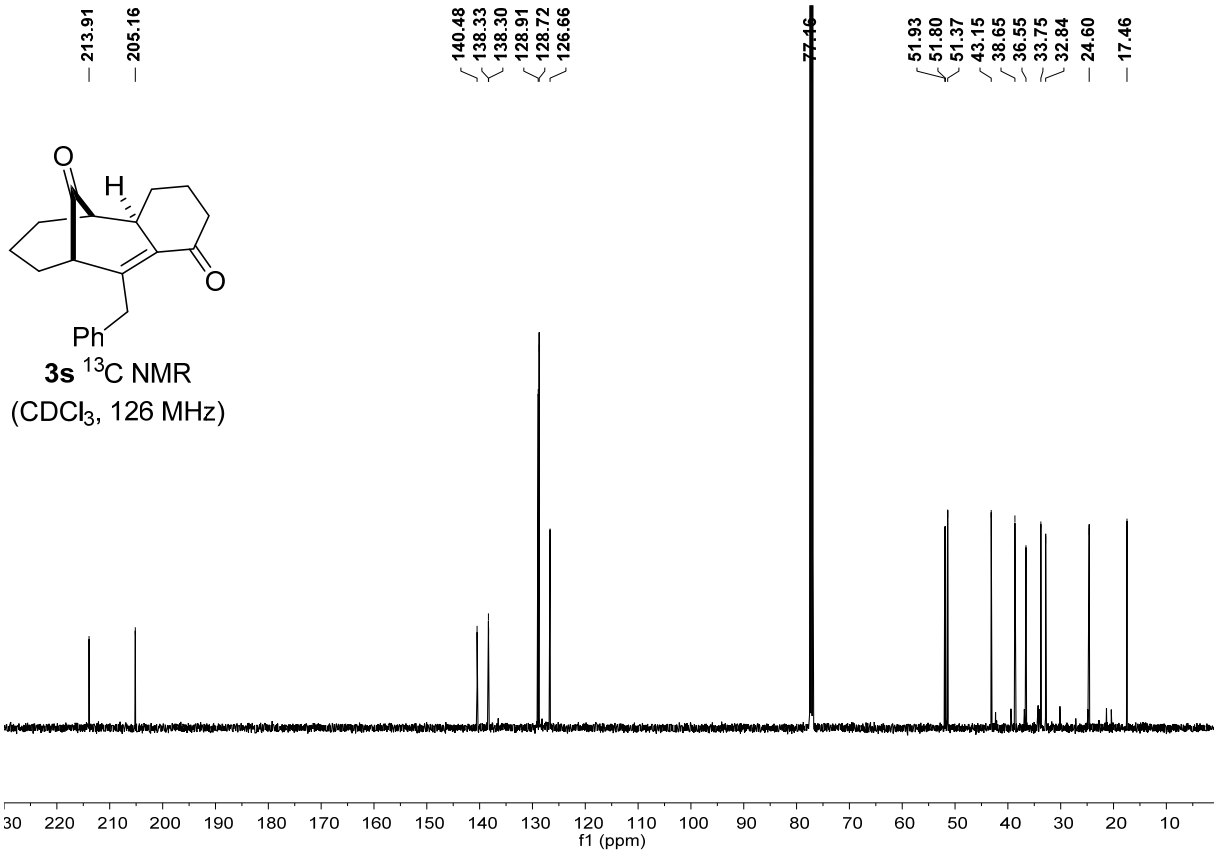
3q ^{13}C NMR
($CDCl_3$, 126 MHz)


7.26
7.12
7.08
7.02
3.91
3.87
3.36
3.33
3.26
3.22
3.18
2.63
2.56
2.47
2.37
2.32
2.27
2.19
2.13
2.07
1.98
1.89
1.77
1.71
1.64
O
H
O
p-CH3Ph
3r 1H NMR
(CDCl3, 400 MHz)
4.15
1.00
1.07
1.02
1.10
2.48
4.35
2.38
5.59
1.26
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

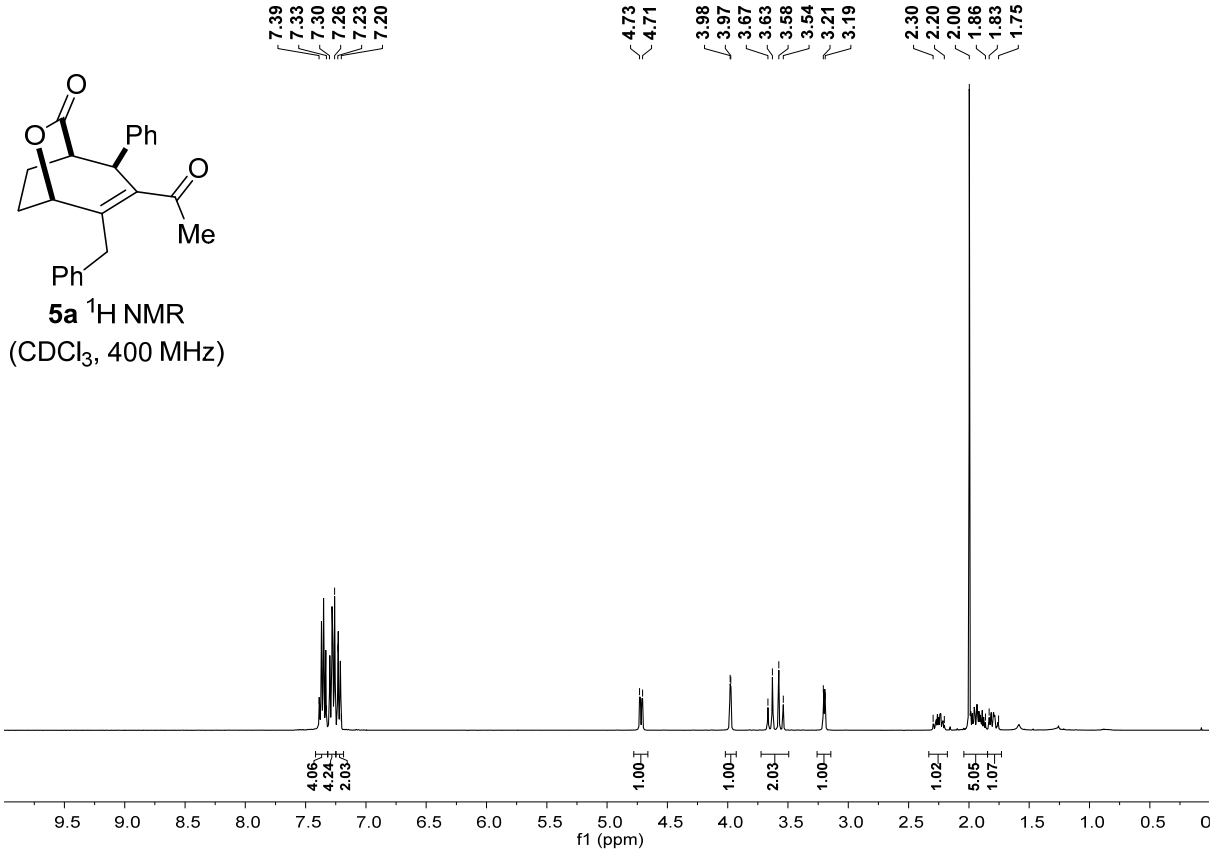

214.30
201.91
150.86
136.12
135.04
132.02
129.38
129.13
77.46
51.48
49.48
48.63
43.34
38.91
28.90
28.37
23.79
21.18
19.32
O
H
O
p-CH3Ph
3r 13C NMR
(CDCl3, 100 MHz)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)



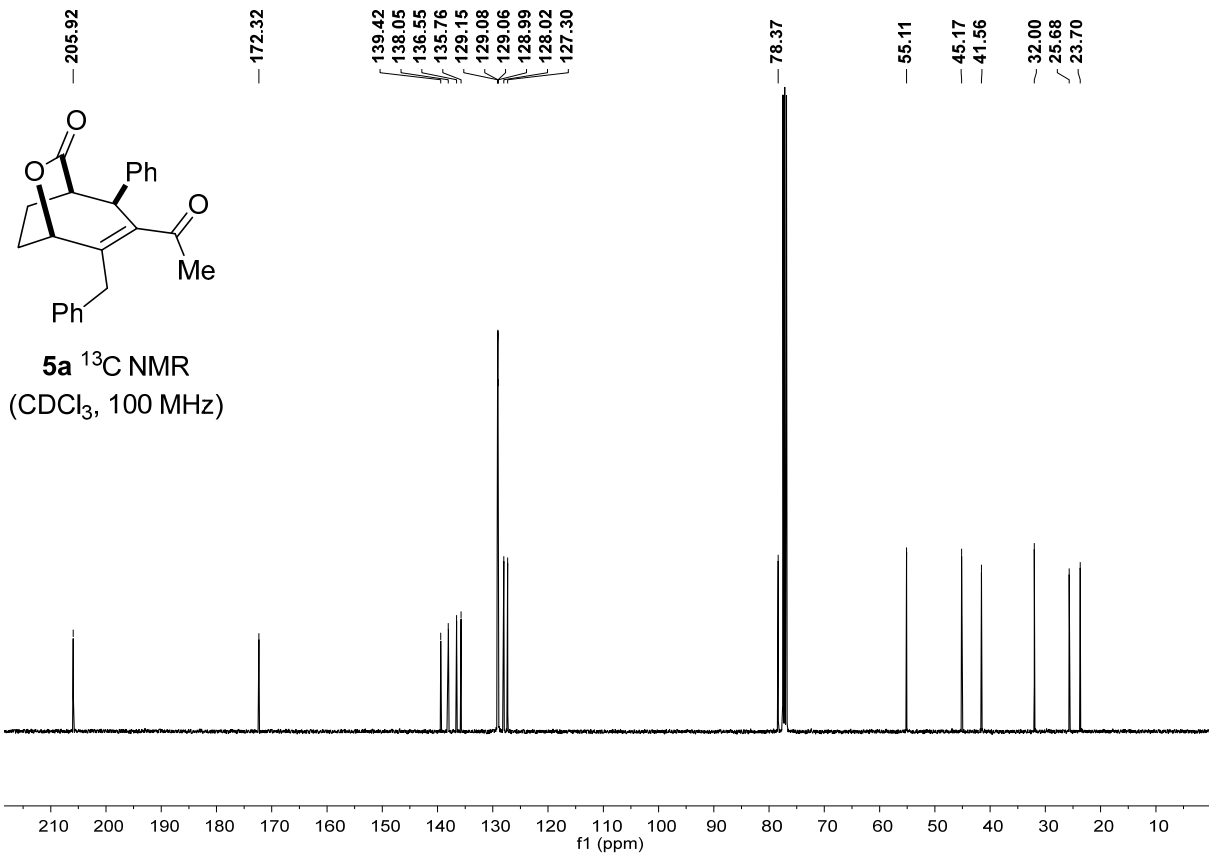
3s ^{1}H NMR
($CDCl_3$, 500 MHz)



3s ^{13}C NMR
($CDCl_3$, 126 MHz)



5a ^{1}H NMR
($CDCl_3$, 400 MHz)



5a ^{13}C NMR
($CDCl_3$, 100 MHz)

4. References

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4. S. R. Pathipati, A. van der Werf, L. Eriksson and N. Selander, *Angew. Chem. Int. Ed.*, 2016, **55**, 11863.
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