Palladium-catalyzed decarboxylative (4+3) cycloadditions of bicyclobutanes with 2-alkylidenetrimethylene carbonates for the synthesis of 2-oxabicyclo[4.1.1]octanes

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Supporting Information

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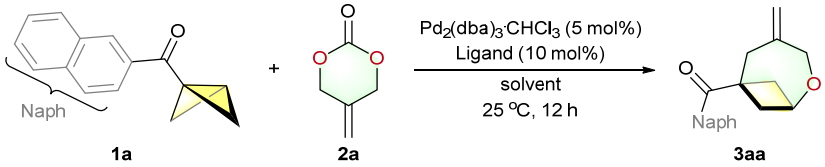
1 General Information

All reactions were performed in flame-dried glassware using conventional Schlenk techniques under a static pressure of nitrogen unless otherwise stated. Liquids and solutions were transferred with syringes. Bicyclo[1.1.0]butanes (BCBs)[1] and 2-alkylidenetrimethylene carbonates (**ADTMCs**)[2] were prepared according to reported procedures. $Pd_2(dba)_3{\cdot}CHCl_3$ (98%, *Energy Chemical* and other commercially available reagents were purchased from *Sigma-Adrich*, *Leyan*, *Energy Chemical* and *Bide* Chemical Company and used as received.) 1,4-dioxane was purchased from *Energy Chemical* (99%, Extra Dry) and used as received. All other solvents (CH_3CN, THF, toluene and 1,2-dichloroethane *etc*.) were dried and purified following standard procedures. Technical grade solvents for extraction or chromatography (Petroleum ether, CH_2Cl_2, and ethyl acetate) were distilled prior to use. Analytical thin layer chromatography (TLC) was performed on silica gel 60 F254 glass plates by *Merck*. Flash column chromatography was performed on silica gel 60 (40–63 μm, 230–400 mesh, ASTM) by *Grace* using the indicated solvents. ^1H, ^{13}C NMR spectra were recorded in $CDCl_3$ on Bruker AV400 or 600 instruments. Chemical shifts are reported in parts per million (ppm) and are referenced to the residual solvent resonance as the internal standard ($CDCl_3$: δ = 7.26 ppm for ^1H NMR and $CDCl_3$: δ = 77.0 ppm for ^{13}C NMR). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplett, q = quartet, m = multiplet), coupling constants (Hz), and integration. The full-scan mass spectra were taken on a hybrid quadrupole-orbitrap mass spectrometer equipped with a heated electrospray ionization source (ThermoFischer Scientific, Bremen, Germany). The configuration was determined by single crystal X-ray diffraction analysis on Bruker D8 Venture dual system with a Cu micro-focus source. Acknowledgement: the ^1H, ^{13}C NMR spectra, single crystal X-ray diffraction and HRMS (ESI) were performed at Analytical Instrumentation Center of Hunan University.

2 Optimization Study

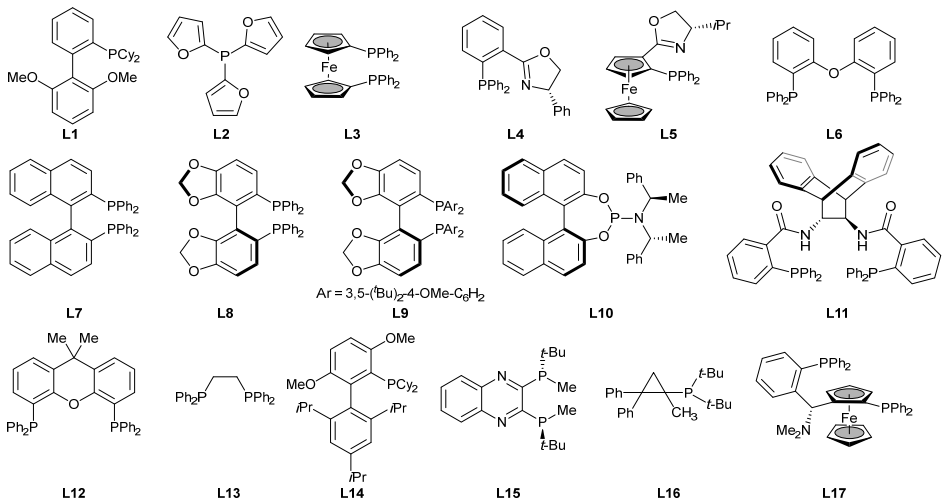
Table S1. Screening of ligand and solvent for the (4+3) cycloaddition of BCB 1a and ADTMC 2a[a]



1a **2a** **3aa**

Entry	Ligand	Solvent	Conversion of **1a** [%][b]	Conversion of **2a** [%][b]	Yield of **3aa** [%][b]
1	**L1**	toluene	36	100	0
2	**L2**	toluene	<5	100	0
3	**L3**	toluene	34	100	0
4	**L4**	toluene	42	100	11
5	**L5**	toluene	58	100	14
6	**L6**	toluene	44	100	0
7	**L7**	toluene	50	100	0
8	**L8**	toluene	10	100	0
9	**L9**	**toluene**	**66**	**100**	**49**
10	**L10**	toluene	8	73	0
11	**L11**	toluene	15	100	0
12	**L12**	toluene	35	100	0
13	**L13**	toluene	32	100	0
14	**L14**	toluene	16	75	0
15	**L15**	toluene	25	100	0
16	**L16**	toluene	24	100	0
17	**L17**	toluene	20	100	0
18	**L9**	PhCl	75	100	40
19	**L9**	CH_2Cl_2	30	100	10
20	**L9**	EtOAc	64	100	53
21	**L9**	CH_3CN	32	97	7
22	**L9**	THF	85	100	71
23	**L9**	**1,4-dioxane**	**>99**	**100**	**96**
24	**L9**	HFIP	38	12	0

[a] Reaction conditions: **1a** (0.10 mmol), **2a** (0.12 mmol), $Pd_2(dba)_3$•$CHCl_3$ (5 mol%) and ligand (10 mol%), solvent (2 mL), 25 °C, under N_2 for 12 h. [b] Determined by ^1H NMR analysis using CH_2Br_2 as the internal reference. HFIP = Hexafluoroisopropanol.

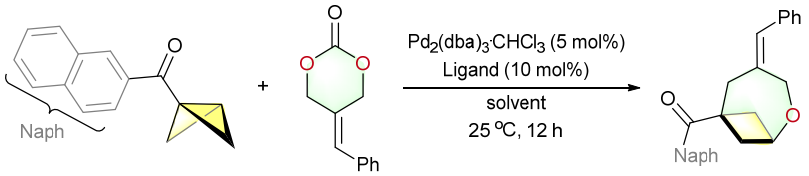


The primary side reaction in the present decarboxylative (4+3) cycloadditions of BCBs is the rapid decomposition of 2-alkylidenetrimethylene carbonates (ADTMCs). Ligands like **L4**, **L7**, **L8**, and **L10** have been identified as effective for the palladium-catalyzed decarboxylative cycloadditions of ADTMCs (ref 29j: *Angew. Chem. Int. Ed.*, **2020**, *59*, 11316; ref 29b*:Org. Lett.*, **2023**, *25*, 5011 in the main text). However, these ligands yielded unsatisfactory results in the current decarboxylative (4+3) cycloadditions of BCBs. These results suggest that the benefits of employing DTBM-Segphos **L9** may stem from the formation of a relatively stable intermediate **int-II**, preventing its rapid decomposition, and promoting subsequent reactions (Scheme 5 in the main text) through steric hindrance or dispersion interactions.

In 2013, the Wanbin Zhang group reported the asymmetric hydrogenation of α-acyloxy-1-arylethanones using Pd and DTBM-Segphos as the catalyst (*Angew. Chem. Int. Ed.* **2013**, *52*, 11632). Unlike SegPHOS **L8**, which did not yield the desired products, the use of DTBM-Segphos **L9** as the ligand resulted in the formation of the desired products with high yield and excellent *ee*. The DFT results demonstrated that an extensive network of C-H … H-C interactions provided by the heavily substituted phenyl rings of DTBM-SegPHOS leads to increased stabilities of all intermediates and transition states in the corresponding catalytic cycles compared with the unsubstituted analogues (K. N. Houk, *et al. Org. Chem. Front.*, **2023**, *10*, 3485; I. D. Gridnev, *et al. iScience* **2020**, *23*, 100960).

Due to the formation of 1,4-O/C dipole species **int-II** in the reaction, a polar solvent may serve as a stabilizing agent for this intermediate. The use of CH_2Cl_2 resulted in a low yield of product **3aa** (Table S1, entry 19), whereas an O-containing polar solvent such as EtOAc, THF and 1,4-dioxane led to a higher yield of **3aa** (Table S1, entries 20, 22-23). Oxygen atoms in the solvent could coordinate with the palladium catalyst to enhance the reaction.

Table S2. Screening of ligand and solvent for the (4+3) cycloaddition of BCB 1a and ADTMC 2b[a]



1a **2b** **3ab**

Entry	Ligand	Solvent	Conversion of **1a** [%][b]	Conversion of **2b** [%][b]	Yield of **3ab** [%][b]
1	**L1**	1,4-dioxane	36	70	12
2	**L2**	1,4-dioxane	15	34	0
3	**L3**	1,4-dioxane	15	44	0
4	**L4**	1,4-dioxane	34	18	4
5	**L5**	1,4-dioxane	51	28	14
6	**L6**	**1,4-dioxane**	**71**	**95**	**19**
7	**L7**	1,4-dioxane	37	84	4
8	**L8**	1,4-dioxane	16	89	<3
9	**L9**	1,4-dioxane	42	100	13
10	**L10**	1,4-dioxane	8	<5	<5
11	**L11**	1,4-dioxane	28	42	0
12	**L12**	1,4-dioxane	20	90	<5
13	**L13**	1,4-dioxane	55	56	9
14	**L14**	1,4-dioxane	19	13	6
15	**L15**	1,4-dioxane	34	53	7
16	**L16**	1,4-dioxane	25	71	4
17	**L17**	1,4-dioxane	36	90	14
18	**L18**	1,4-dioxane	45	86	15

19	**L19**	1,4-dioxane	26	54	0
20	**L20**	1,4-dioxane	25	51	<5
21	**L21**	1,4-dioxane	23	100	0
22	**L22**	1,4-dioxane	17	100	0
23	**L23**	1,4-dioxane	64	97	0
24	**L24**	1,4-dioxane	17	24	2
25	**L25**	1,4-dioxane	60	100	7
26	**L26**	1,4-dioxane	60	91	10
27	**L27**	1,4-dioxane	46	82	8
28	**L6**	THF	47	88	13
29	**L6**	toluene	45	96	10
30	**L6**	CH_2Cl_2	35	93	7
31	**L6**	EtOAc	42	90	9
32	**L6**	CH_3CN	36	64	<5

[a] Reaction conditions: **1a** (0.10 mmol), **2a** (0.12 mmol), $Pd_2(dba)_3$•$CHCl_3$ (5 mol%) and ligand (10 mol%), solvent (2 mL), 25 °C, under N_2 for 12 h. [b] Determined by ^1H NMR analysis using CH_2Br_2 as the internal reference.

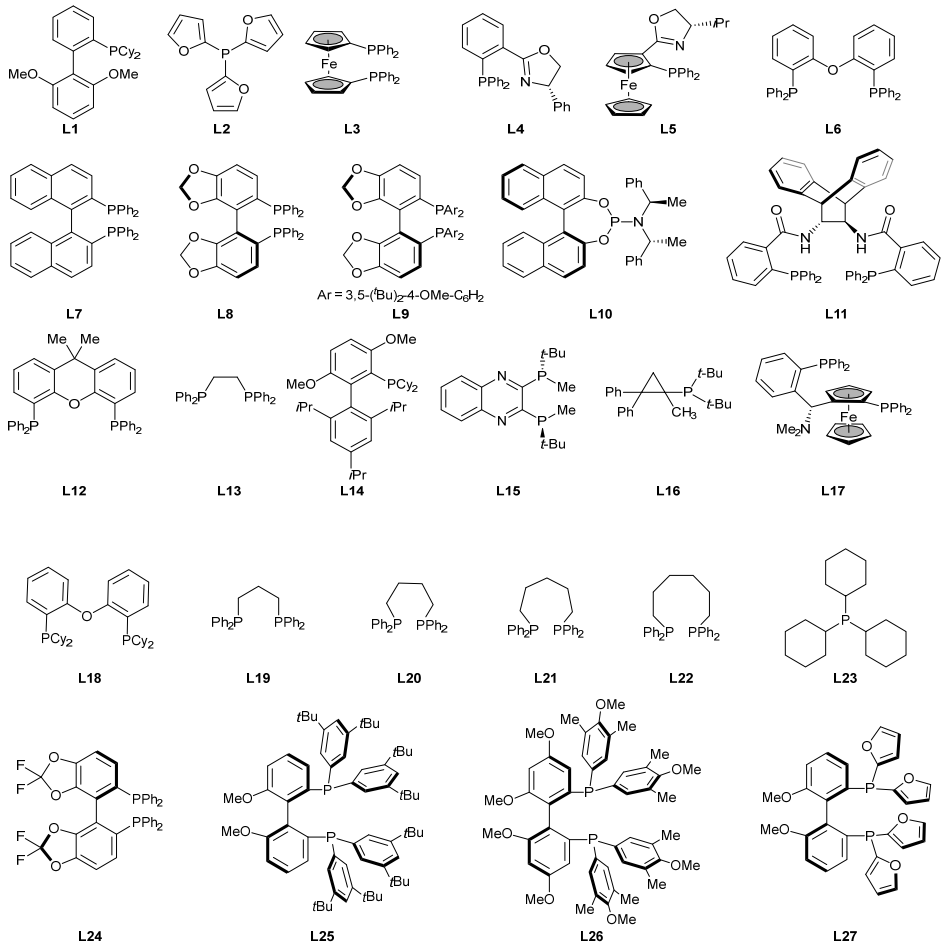
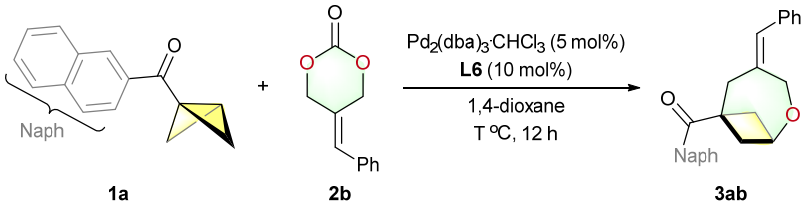


Table S3. Screening of temperature and the stoichiometric amount of 2b for the (4+3) cycloaddition of BCB 1a [a]

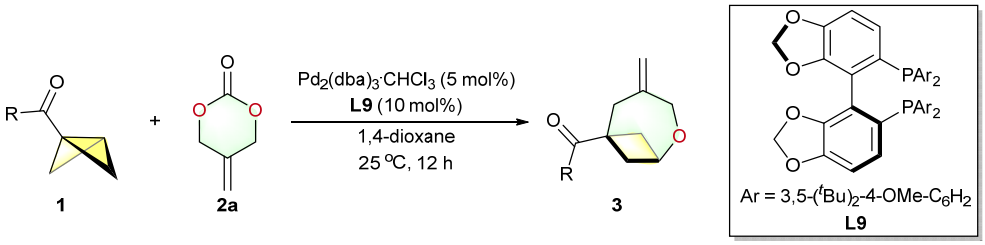


1a **2b** **3ab**

Entry	T (°C)	**1a** (equiv.)	**2b** (equiv.)	Conversion of **1a** [%][b]	Conversion of **2a** [%][b]	Yield of **3ab** [%][b]
1[c]	0	1.0	1.2	53	87	5
2	25	1.0	1.2	71	95	19
3	65	1.0	1.2	76	>99	30
4	85	1.0	1.2	77	97	34
5	100	1.0	1.2	90	97	42
6	**100**	**1.0**	**2.0**	**100**	**99**	**53**
7	100	1.0	3.0	100	98	46

[a] Reaction conditions: **1a** (0.10 mmol, 1.0 equiv.), **2a** (x equiv.), $Pd_2(dba)_3$•$CHCl_3$ (5 mol%) and **L6** (10 mol%), 1,4-dioxane (2 mL), T °C, under N_2 for 12 h. [b] Determined by ^1H NMR analysis using CH_2Br_2 as the internal reference. [c] THF was used.

3 General Procedure for the (4+3) Cycloadditions of BCBs 1 and ADTMC 2a (GP1)

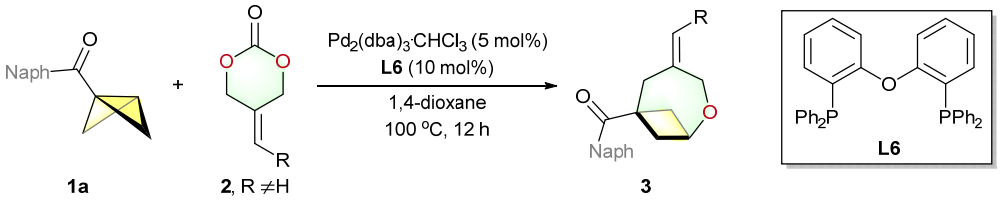


1 **2a** **3**

Under an atmosphere of N_2, to a 25 mL oven-dried Schlenk tube were added BCBs **1** (0.20 mmol, 1.0 equiv), ADTMC **2a** (27.4 mg, 0.24 mmol, 1.2 equiv), $Pd_2(dba)_3{\cdot}CHCl_3$ (10.24 mg, 0.010 mmol, 5 mol%), **L9** (23.6 mg, 0.020 mmol, 10 mol%) and 1,4-dioxane (4.0 mL). Then the resulting mixture was stirred at 25 °C for 12 h. After the solvent was removed under reduced pressure, the residue was directly subjected to a column

chromatography purification using petroleum ether /EtOAc (10:1, v/v) as the eluent, to afford the desired product **3**.

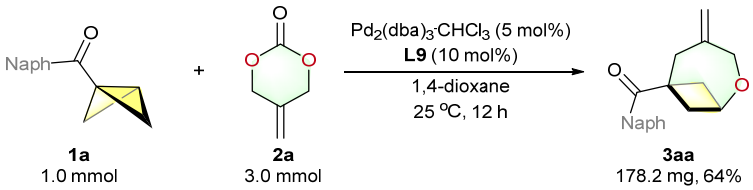
4 General Procedure for the (4+3) Cycloadditions of BCBs and substituted ADTMCs (GP2)



1a **2**, R ≠H **3**

Under an atmosphere of N_2, to a 25 mL oven-dried Schlenk tube were added BCB **1a** (20.83 mg, 0.10 mmol, 1.0 equiv), ADTMC **2** (0.20 mmol, 2.0 equiv), $Pd_2(dba)_3{\cdot}CHCl_3$ (5.12 mg, 0.005 mmol, 5 mol%), **L6** (5.39 mg, 0.010 mmol, 10 mol%) and 1,4-dioxane (2.0 mL). Then the resulting mixture was stirred at 100 °C for 12 h. After the solvent was removed under reduced pressure, the residue was directly subjected to a column chromatography purification using petroleum ether /EtOAc (15:1, v/v) as the eluent, to afford the desired product **3**.

5 Scale-Up Experiment



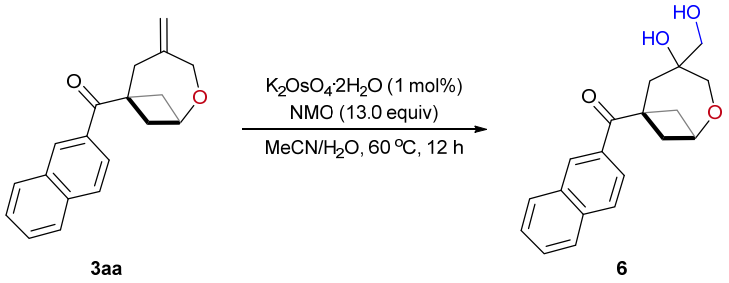
1a
1.0 mmol

2a
3.0 mmol

3aa
178.2 mg, 64%

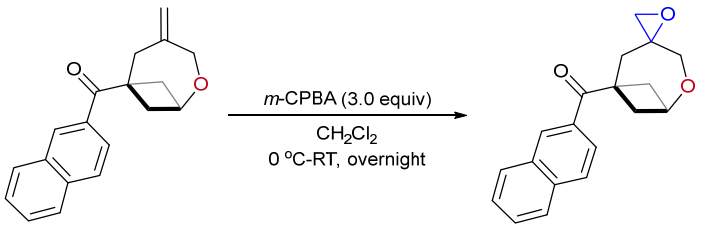
Under an atmosphere of N_2, to a 25 mL oven-dried Schlenk tube were added $Pd_2(dba)_3{\cdot}CHCl_3$ (51.2 mg, 0.05 mmol, 5 mol%) and **L9** (118.0 mg, 0.1 mmol, 10 mol%), followed by 5.0 mL of anhydrous 1,4-dioxane. The solution was stirred at 25 °C for 10 mintus. The **1a** (208.3 mg, 1.0 mmol, 1.0 equiv), **2a** (342.3 mg, 3.0 mmol) and 1,4-dioxane (7.0 mL) were added. Then the resulting mixture was stirred at 25 °C for 12 h. After removal of the solvents under reduced pressure, the crude product was purified by flash chromatography on silica gel (petroleum ether/EtOAc = 10/1) to afford analytically pure product **3aa** as a white solid (178.2 mg, 64% yield).

6 Synthetic Transformations



3aa **6**

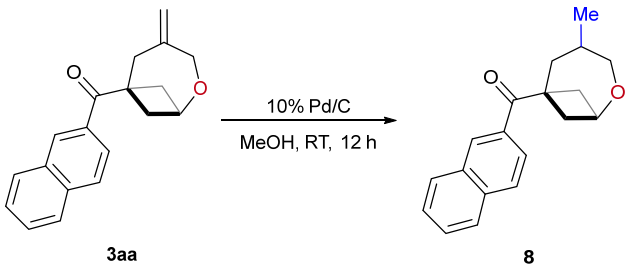
Synthesis of (6): To a solution of **3aa** (0.10 mmol, 27.84 mg, 1.0 equiv) in MeCN (1.6 mL) and H_2O (0.4 mL) was added $K_2OsO_4 \cdot 2H_2O$ (1.0 umol, 0.3 mg, 1 mol%), *N*-methylmorpholine-*N*-oxide (NMO) (1.30 mmol, 152.3 mg, 13.0 equiv). The reaction mixture was stirred at 60 °C for 12 h. After completion (monitored by TLC), the mixture was then quenched with aqueous $Na_2S_2O_3$ and stirred for 30 mins. The biphasic reaction mixture was then extracted with EtOAc and the combined organic layers were washed with brine, dried over Na_2SO_4. The filtrate was evaporated under *vacuo*, and purified by silica gel column chromatography (petroleum ether/EtOAc = 1/1) to afford **6** as a white solid (29.0 mg, 93% yield).



3aa **7**

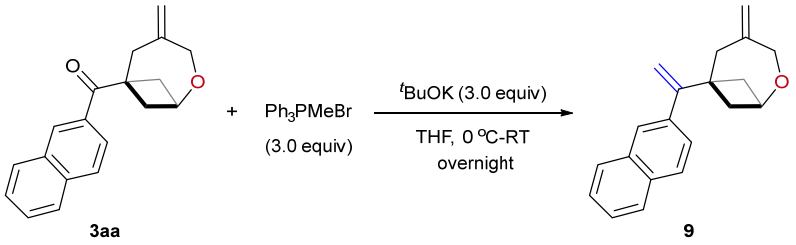
Synthesis of (7): To a 25 mL Schlenk tube equipped with a stir bar was charged with **3aa** (0.10 mmol, 27.8 mg, 1.0 equiv) and dichloromethane (2 mL). The mixture was cooled to 0 °C and then *m*-CPBA (85%) (0.3 mmol, 51.8 mg, 3.0 equiv) was added to the reaction. The mixture was slowly warmed to room temperature and stirred overnight. Then, the mixture was quenched with a saturated aqueous $NaHCO_3$ solution, then diluted with water. The aqueous phase was extracted twice with dichloromethane. The combined organic phases were washed by brine and dried over Na_2SO_4 and concentrated under reduced pressure after filtration. The residue was directly purified

by silica gel column chromatography using (petroleum ether/EtOAc = 3/1) as the eluent to give product **7** as a white solid (18.2 mg, 62% yield).



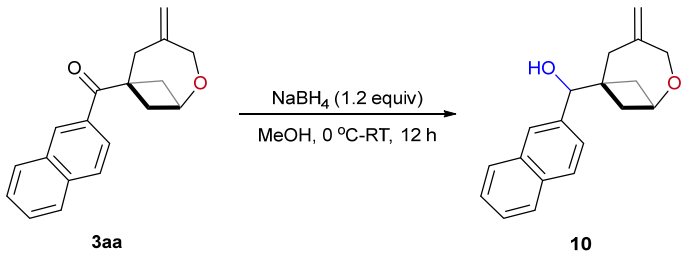
3aa **8**

Synthesis of (8): To a solution of **3aa** (0.15 mmol, 41.8 mg, 1.0 equiv) in MeOH (3.0 mL) was added Pd/C (10 wt%) (4.2 mg). This flask was in a vacuum and back-filled with H_2 (1 atm). After being stirred at room temperature overnight, the reaction solution was filtered, and the filtered-cake was washed with EtOAc (5.0 mL). The filtrate was evaporated under *vacuo*, and purified by silica gel column chromatography (petroleum ether/EtOAc = 20/1) to afford **8** as a yellow oil (32.4 mg, 77% yield).



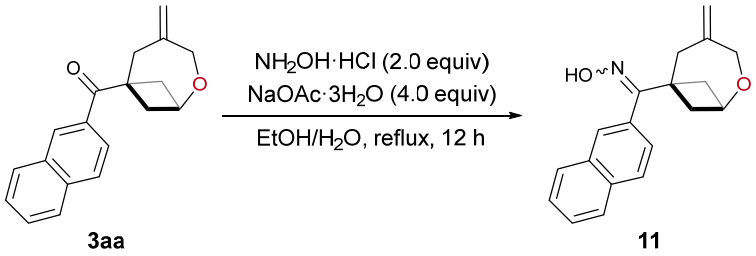
3aa **9**

Synthesis of (9): To a 25 mL Schlenk tube equipped with a stir bar was charged with methyl triphenylphosphonium bromide (0.30 mmol, 107.2 mg, 3.0 equiv) and anhydrous THF (1 mL). The mixture was cooled to 0 °C and then ^{t}BuOK (0.3 mmol, 33.7 mg, 3.0 equiv) was added to the reaction. The resulting yellow suspension was stirred at 0 °C for 45 min, then a solution of **3aa** (0.10 mmol, 27.8 mg, 1.0 equiv) in THF (1 mL) added dropwise. The resulting mixture was warmed gradually to room temperature and stirred until **3aa** disappeared (monitored by TLC). The reaction mixture was quenched with water, extracted with EtOAc, dried over Na_2SO_4, filtered and concentrated in *vacuo*. The residue was purification by flash chromatography on silica gel (petroleum ether/EtOAc = 30/1) to afford analytically pure product **9** as a white solid (26.3 mg, 95% yield).



3aa **10**

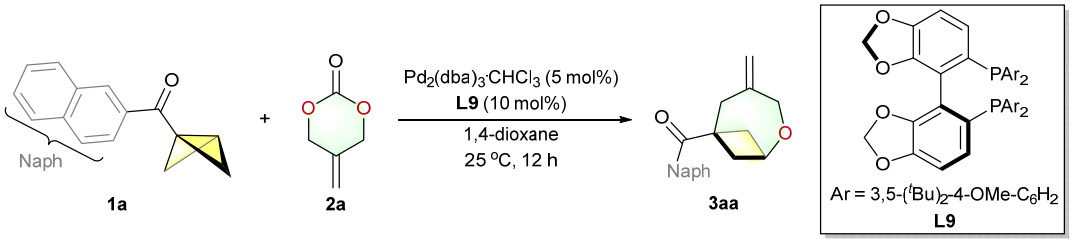
Synthesis of (10): To a solution of **3aa** (0.10 mmol, 27.8 mg, 1.0 equiv) in the MeOH (2.0 mL) was added $NaBH_4$ (4.5 mg, 0.12 mmol, 1.2 equiv) at 0 °C. The mixture was slowly warmed to room temperature and stirred overnight. Then aqueous saturated NH_4Cl solution (5 mL) was added to quench the reaction. The aqueous phase was extracted with EtOAc. The combined organic phases were washed by brine and dried over Na_2SO_4 and concentrated under reduced pressure after filtration. The crude residue was purified by silica gel column chromatography (petroleum ether/EtOAc = 5/1) to afford **10** as a colorless oil (23.9 mg, 85% yield).



3aa **11**

Synthesis of (11): 3aa (0.10 mmol, 27.8 mg, 1.0 equiv) and hydroxylamine hydrochloride (0.20 mmol, 13.9 mg, 2.0 equiv) were dissolved in EtOH (0.5 mL) and H_2O (1 mL). To the mixture was added $NaOAc·3H_2O$ (0.4 mmol, 54.4 mg, 4.0 equiv) and the reaction was heated under reflux for 12 h. After completion of the reaction, the reaction mixture was cooled to room temperature, and water (5 mL) were added. The aqueous layer was extracted three times with EtOAc (3×15 mL). The combined organic phases were washed by brine and dried over Na_2SO_4 and concentrated under reduced pressure after filtration. The product was purified by column chromatography on silica gel (petroleum ether/ EtOAc = 1:1) to afford **11** (the major isomer: 16.2 mg, 55%; the minor isomer: 12.8 mg, 44%) as a white solid.

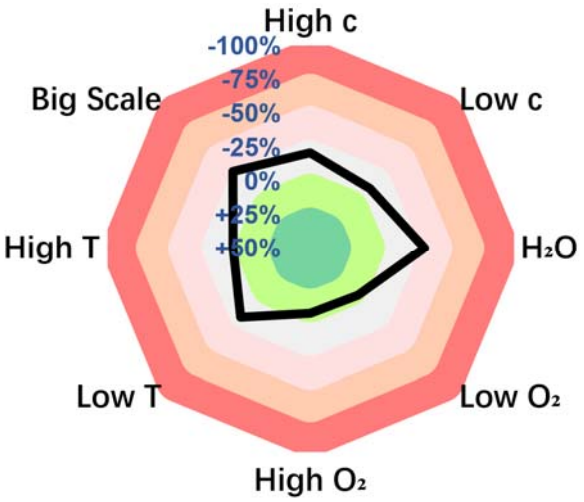
7 Sensitivity Assessment[3]



Standard conditions: Under an atmosphere of N_2, to a 25 mL oven-dried Schlenk tube were added BCB **1a** (0.10 mmol, 20.8 mg, 1.0 equiv), ADTMC **2a** (0.12 mmol, 13.7 mg, 1.2 equiv), $Pd_2(dba)_3{\cdot}CHCl_3$ (5.12 mg, 0.005 mmol, 5 mol%), **L9** (11.8 mg, 0.010 mmol, 10 mol%) and 1,4-dioxane (2.0 mL). Then the resulting mixture was stirred at 25 °C for 12 h. After the solvent was removed under reduced pressure, CH_2Br_2 (0.10 mmol, 17.4 mg) was added as an internal standard, and the yield was determined by ^1H NMR analysis of the crude mixture.

Table S4. Sensitivity assessment

Entry	Description	Deviation from standard condition	Yield	Deviation
1	High *c*	1,4-dioxane (1 mL)	75%	-21%
2	Low *c*	1,4-dioxane (3 mL)	83%	-13%
3	H_2O	+5 μL H_2O	61%	-35%
4	Low O_2	degassed solvent	96%	0%
5	High O_2	+5 mL air	97%	+1%
6	Low *T*	at 15 °C	73%	-23%
7	High *T*	at 40 °C	89%	-7%
8	Big Scale	1.0 mmol scale (10 times of standard scale)	65%	-31%
9	control	-	96%	-

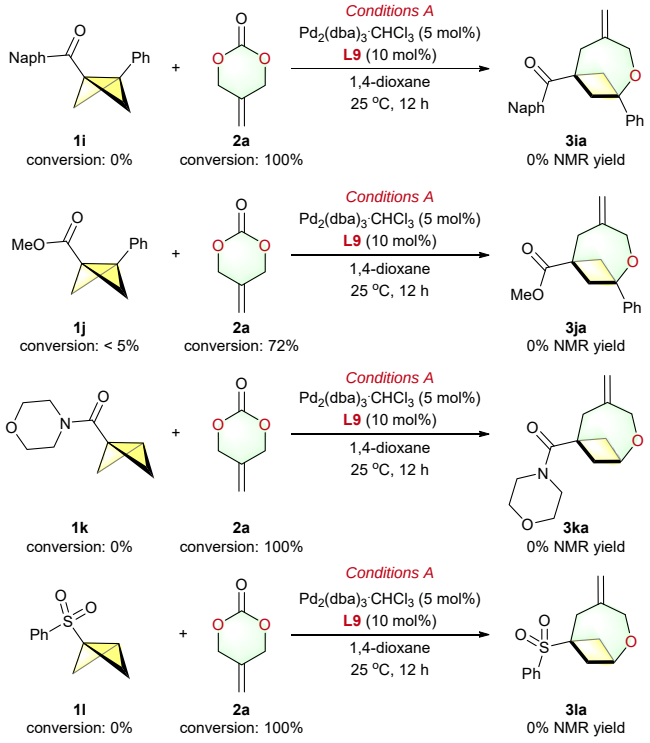


Comment: we conducted condition-based sensitivity screening, revealing that the O_2 level had no significant impact on the reaction. However, this reaction exhibited moderate sensitivity to concentration, moisture, temperature, and scale.

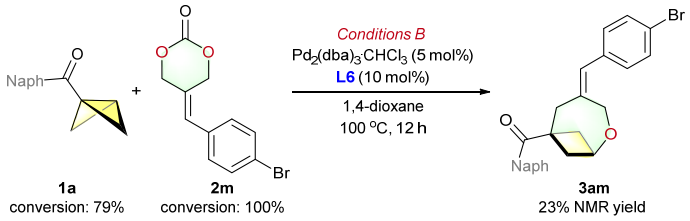
8 Unsuccessful Substrates

The following Scheme S1 and Scheme S2 list the BCB and ADTMC substrates that were unsuccessfully tested. The reactions were carried out according to General Procedure and were analyzed by crude ^{1}H NMR with CH_2Br_2 as an internal standard.

Scheme S1. Unsuccessful BCB substrates

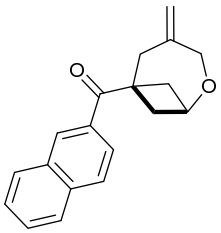


Scheme S2. Unsuccessful ADTMC substrates



1a conversion: 79% **2m** conversion: 100% **3am** 23% NMR yield

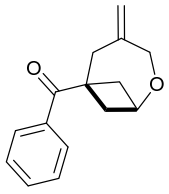
9 Characterization Data of the Products



3aa
$C_{19}H_{18}O_2$
M = 278.35 g/mol

(4-Methylene-2-oxabicyclo[4.1.1]octan-6-yl)(naphthalen-2-yl)methanone (**3aa**): Prepared from bicyclo[1.1.0]butan-1-yl(naphthalen-2-yl)methanone (**1a**, 41.7 mg, 0.20 mmol) and 5-methylene-1,3-dioxan-2-one (**2a**, 27.4 mg, 0.24 mmol) according to the **GP1** at 25 °C for 12 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (10/1) afforded **3aa** as a white solid (51.8 mg, 93% yield).

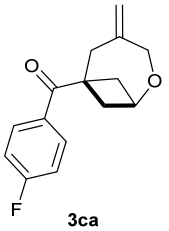
3aa: $\mathbf{R_f}$ = 0.30 (petroleum ether/EtOAc = 10/1). **^{1}H NMR** (600 MHz, $CDCl_3$): δ 8.31 (s, 1H), 7.95 (d, *J* = 7.8 Hz, 1H), 7.90-7.88 (m, 3H), 7.62 (t, *J* = 7.2 Hz, 1H), 7.56 (t, *J* = 7.2 Hz, 1H), 5.33 (s, 1H), 5.14 (s, 1H), 4.48 (t, *J* = 6.0 Hz, 1H), 4.41 (s, 2H), 2.87-2.84 (m, 4H), 2.64 (d, *J* = 11.4 Hz, 2H) ppm. **^{13}C NMR** (150 MHz, $CDCl_3$): δ 203.6, 144.3, 135.4, 132.4, 131.2, 130.6, 129.6, 128.6, 128.5, 127.7, 126.8, 124.6, 119.6, 72.6, 68.7, 50.9, 43.6, 37.1 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{19}H_{19}O_2$: 279.1380; found: 279.1272.



3ba
$C_{15}H_{16}O_2$
M = 228.29 g/mol

(4-Methylene-2-oxabicyclo[4.1.1]octan-6-yl)(phenyl)methanone (**3ba**): Prepared from bicyclo[1.1.0]butan-1-yl(phenyl)methanone (**1b**, 31.6 mg, 0.20 mmol) and 5-methylene-1,3-dioxan-2-one (**2a**, 27.4 mg, 0.24 mmol) according to the **GP1** at 25 °C for 12 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (15/1) afforded **3ba** as a yellow oil (34.2 mg, 75% yield).

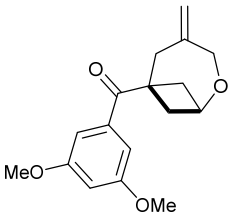
3ba: $\mathbf{R_f}$ = 0.35 (petroleum ether/EtOAc = 15/1). **^{1}H NMR** (600 MHz, $CDCl_3$): δ 7.82 (d, *J* = 7.8 Hz, 2H), 7.55 (t, *J* = 7.2 Hz, 1H), 7.46 (t, *J* = 7.8 Hz, 2H), 5.29 (s, 1H), 5.10 (s, 1H), 4.44 (t, *J* = 6.6 Hz, 1H), 4.37 (s, 2H), 2.79-2.76 (m, 4H), 2.56 (d, *J* = 14.4 Hz, 2H) ppm. **^{13}C NMR** (150 MHz, $CDCl_3$): δ 203.5, 144.3, 134.0, 132.9, 128.9, 128.6, 119.5, 72.5, 68.7, 50.8, 43.4, 36.9 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{15}H_{17}O_2$: 229.1223; found: 229.1220.



3ca
$C_{15}H_{15}FO_2$
M = 246.28 g/mol

(4-Fluorophenyl)(4-methylene-2-oxabicyclo[4.1.1]octan-6-yl)methanone (**3ca**): Prepared from bicyclo[1.1.0]butan-1-yl(4-fluorophenyl)methanone (**1c**, 26.4 mg, 0.15 mmol) and 5-methylene-1,3-dioxan-2-one (**2a**, 20.5 mg, 0.18 mmol) according to the **GP1** at 25 °C for 12 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (10/1) afforded **3ca** as a white solid (16.0 mg, 43% yield).

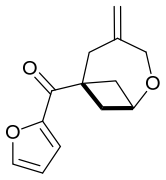
3ca: $\mathbf{R_f}$ = 0.30 (petroleum ether/EtOAc = 15/1). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.85 (dd, *J* = 8.4, 5.6 Hz, 2H), 7.15 (t, *J* = 8.4 Hz, 2H), 5.30 (s, 1H), 5.11 (s, 1H), 4.43 (t, *J* = 6.4 Hz, 1H), 4.36 (s, 2H), 2.79-2.74 (m, 4H), 2.57-2.52 (m, 2H) ppm. **^{13}C NMR** (150 MHz, $CDCl_3$): δ 201.9, 165.5 (d, *J* = 253.7 Hz), 144.1, 131.6 (d, *J* = 9.2 Hz), 130.3 (d, *J* = 3.0 Hz), 119.7, 115.8 (d, *J* = 21.8 Hz), 72.4, 68.6, 50.6, 43.4, 36.9 ppm. ^{19}F NMR (376 MHz, $CDCl_3$) δ -104.92 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{15}H_{16}FO_2$: 247.1129; found: 247.1139.



3da
$C_{17}H_{20}O_4$
M = 288.34 g/mol

(3,5-Dimethoxyphenyl)(4-methylene-2-oxabicyclo[4.1.1]octan-6-yl)methanone (**3da**): Prepared from bicyclo[1.1.0]butan-1-yl(3,5-dimethoxyphenyl)methanone (**1d**, 43.7 mg, 0.20 mmol) and 5-methylene-1,3-dioxan-2-one (**2a**, 27.4 mg, 0.24 mmol) according to the **GP1** at 25 °C for 12 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (10/1) afforded **3da** as a white solid (42.9 mg, 74% yield).

3da: $\mathbf{R_f}$ = 0.3 (petroleum ether/EtOAc = 10/1). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 6.95 (s, 2H), 6.64 (s, 1H), 5.29 (s, 1H), 5.11 (s, 1H), 4.42 (t, *J* = 6.0 Hz, 1H), 4.35 (s, 2H), 3.83 (s, 6H), 2.79-2.73 (m, 4H), 2.56-2.51 (m, 2H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ 203.2, 160.7, 144.3, 135.7, 119.5, 106.7, 105.1, 72.4, 68.6, 55.5, 50.8, 43.5, 37.0 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{17}H_{21}O_4$: 289.1434; found: 289.1427.

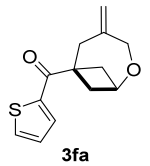


3ea
$C_{13}H_{14}O_3$
M = 218.25 g/mol

Furan-2-yl(4-methylene-2-oxabicyclo[4.1.1]octan-6-yl)methanone (**3ea**): Prepared from bicyclo[1.1.0]butan-1-yl(furan-2-yl)methanone (**1e**, 29.6 mg, 0.20 mmol) and 5-methylene-1,3-dioxan-2-one (**2a**, 27.4 mg, 0.24 mmol) according to the **GP1** at 25 °C for 12 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (10/1) afforded **3ea** as a white solid (26.1 mg, 60% yield).

3ea: $\mathbf{R_f}$ = 0.3 (petroleum ether/EtOAc = 15/1). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.59 (s, 1H), 7.14 (d, *J* = 3.2 Hz, 1H), 6.55-6.54 (m, 1H), 5.28 (s, 1H), 5.09 (s, 1H), 4.43 (t, *J* =

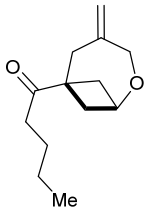
6.4 Hz, 1H), 4.35 (s, 2H), 2.74 (s, 2H), 2.71-2.65 (m, 2H), 2.52-2.47 (m, 2H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ 192.5, 150.8, 146.1, 144.3, 119.5, 118.1, 112.1, 72.4, 68.6, 49.8, 42.5, 35.7 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{13}H_{15}O_3$: 219.1016; found: 219.1028.



3fa
$C_{13}H_{14}O_2S$
M = 234.31 g/mol

(4-Methylene-2-oxabicyclo[4.1.1]octan-6-yl)(thiophen-2-yl)methanone (**3fa**): Prepared from bicyclo[1.1.0]butan-1-yl(thiophen-2-yl)methanone (**1f**, 24.6 mg, 0.15 mmol) and 5-methylene-1,3-dioxan-2-one (**2a**, 20.5 mg, 0.18 mmol) according to the **GP1** at 25 °C for 12 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (10/1) afforded **3fa** as a white solid (26.3 mg, 75% yield).

3fa: $\mathbf{R_f}$ = 0.30 (petroleum ether/EtOAc = 15/1). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.64 (d, *J* = 4.4 Hz, 2H), 7.56 (d, *J* = 3.6 Hz, 2H), 7.13 (t, *J* = 4.4 Hz, 2H), 5.29 (s, 1H), 5.11 (s, 1H), 4.43 (t, *J* = 6.4 Hz, 1H), 4.35 (s, 2H), 2.79 (s, 2H), 2.78-2.72 (m, 2H), 2.56-2.55 (m, 1H), 2.53-2.51 (m, 1H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ 196.8, 144.2, 140.8, 133.4, 132.2, 128.1, 119.6, 72.2, 68.6, 50.7, 43.7, 36.6 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{13}H_{15}O_2S$: 236.0866; found: 236.0873.

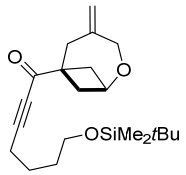


3ga
$C_{13}H_{20}O_2$
M = 208.30 g/mol

1-(4-Methylene-2-oxabicyclo[4.1.1]octan-6-yl)pentan-1-one (**3ga**): Prepared from bicyclo[1.1.0]butan-1-yl(naphthalen-2-yl)methanone (**1g**, 27.6 mg, 0.20 mmol) and 5-methylene-1,3-dioxan-2-one (**2a**, 27.4 mg, 0.24 mmol) according to the **GP1** at 100 °C

for 12 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (15/1) afforded **3ga** as a yellow oil (18.7 mg, 42% yield).

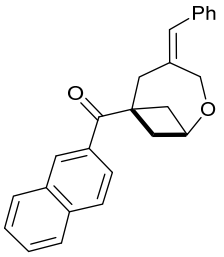
3ga: $\mathbf{R_f}$ = 0.35 (petroleum ether/EtOAc = 15/1). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 5.24 (s, 1H), 5.07 (s, 1H), 4.37 (t, *J* = 5.6 Hz, 1H), 4.28 (s, 2H), 2.56 (s, 2H), 2.53-2.48 (m, 2H), 2.42 (t, *J* = 7.2 Hz, 2H), 2.26-2.22 (s, 2H), 1.62-1.52 (m, 2H), 1.38-1.26 (m, 2H), 0.92 (t, *J* = 7.2 Hz, 3H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ 213.1, 144.2, 119.4, 71.6, 68.4, 53.4, 51.2, 41.4, 36.1, 34.6, 25.8, 22.4, 13.9 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{13}H_{21}O_2$: 210.1614; found: 210.1608.



3ha
$C_{21}H_{34}O_3Si$
M = 362.59 g/mol

7-((*tert*-Butyldimethylsilyl)oxy)-1-(4-methylene-2-oxabicyclo[4.1.1]octan-6-yl)hept-2-yn-1-one (**3ha**): Prepared from 1-(bicyclo[1.1.0]butan-1-yl)-8-((*tert*-butyldimethylsilyl)oxy)oct-3-yn-1-one (**1h**, 61.3 mg, 0.20 mmol) and 5-methylene-1,3-dioxan-2-one (**2a**, 27.4 mg, 0.24 mmol) according to the **GP1** at 100 °C for 12 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (10/1) afforded **3ha** as a yellow oil (47.4 mg, 63% yield).

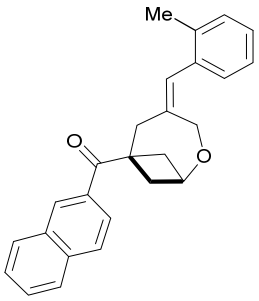
3ha: $\mathbf{R_f}$ = 0.30 (petroleum ether/EtOAc = 20/1). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 5.23 (s, 1H), 5.09 (s, 1H), 4.41 (t, *J* = 6.0 Hz, 1H), 4.27 (s, 2H), 3.64 (t, *J* = 5.2 Hz, 2H), 2.68 (s, 2H), 2.66-2.62 (m, 2H), 2.45 (t, *J* = 5.6 Hz, 2H), 2.26-2.22 (m, 2H), 1.72-1.62 (m, 4H), 0.89 (s, 9H), 0.05 (s, 6H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ 190.6, 144.0, 119.5, 97.1, 78.3, 71.8, 68.4, 67.0, 62.3, 51.5, 40.5, 34.9, 31.8, 25.9, 24.4, 18.9, 18.3, -5.4 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{21}H_{35}O_3Si$: 363.2350; found: 363.2344.



3ab
$C_{25}H_{22}O_2$
M = 354.45 g/mol

(4-((*Z*)-benzylidene)-2-oxabicyclo[4.1.1]octan-6-yl)(naphthalen-2-yl)methanone ((*Z*)-**3ab**): Prepared from bicyclo[1.1.0]butan-1-yl(naphthalen-2-yl)methanone (**1a**, 20.8 mg, 0.10 mmol) and 5-benzylidene-1,3-dioxan-2-one (**2b**, 38.0 mg, 0.20 mmol) according to the **GP2** at 100 °C for 12 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (15/1) afforded **3ab** as a white solid (16.3 mg, 46% yield).

(*Z*)-**3ab**: $\mathbf{R_f}$ = 0.35 (petroleum ether/EtOAc = 15/1). (*Z*)-**3ab: ^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.33 (s, 1H), 7.95-7.87 (m, 4H), 7.61 (t, *J* = 7.2 Hz, 1H), 7.55 (t, *J* = 7.6 Hz, 1H), 7.47 (d, *J* = 7.6 Hz, 2H), 7.41 (t, *J* = 7.2 Hz, 2H), 7.31 (t, *J* = 7.6 Hz, 1H), 6.69 (s, 1H), 4.57 (t, *J* = 6.4 Hz, 1H), 4.52 (s, 2H), 2.92 (s, 2H), 2.91-2.86 (m, 2H), 2.81-2.77 (m, 2H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ 203.6, 137.2, 136.5, 135.4, 133.4, 132.5, 131.2, 130.6, 129.6, 129.0, 128.6, 128.5, 128.4, 127.7, 127.4, 126.8, 124.7, 73.2, 62.7, 51.7, 45.6, 37.4 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{25}H_{23}O_2$: 355.1693; found: 355.1688.

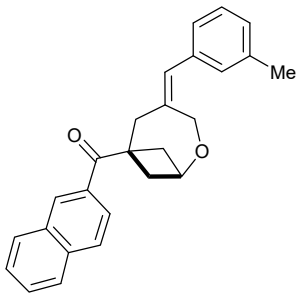


3ac
$C_{26}H_{24}O_2$
M = 368.48 g/mol

(4-((*Z*)-2-Methylbenzylidene)-2-oxabicyclo[4.1.1]octan-6-yl)(naphthalen-2-yl)methanone ((*Z*)-**3ac**): Prepared from bicyclo[1.1.0]butan-1-yl(naphthalen-2-yl)methanone (**1a**, 20.8 mg, 0.10 mmol) and 5-(2-methylbenzylidene)-1,3-dioxan-2-one (**2c**, 40.9 mg, 0.20 mmol)

according to the **GP2** at 100 °C for 12 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (20/1) afforded **3ac** as a white solid (23.6 mg, 64% yield).

(*Z*)-**3ac**: $\mathbf{R_f}$ = 0.30 (petroleum ether/EtOAc = 20/1). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.34 (s, 1H), 7.95-7.87 (m, 4H), 7.62-7.55 (m, 3H), 7.26-7.20 (m, 3H), 6.67 (s, 1H), 4.55 (t, *J* = 6.0 Hz, 1H), 4.44 (s, 2H), 2.97 (s, 2H), 2.92-2.88 (m, 2H), 2.78 (d, *J* = 11.6 Hz, 2H), 2.28 (s, 3H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ 203.6, 136.9, 136.3, 135.6, 135.4, 132.6, 132.4, 131.3, 130.6, 129.83, 129.77, 129.6, 128.54, 128.46, 127.7, 127.6, 126.8, 125.8, 124.7, 73.0, 62.8, 51.6, 45.5, 37.3, 20.0 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{26}H_{25}O_2$: 369.1849; found: 369.1843.

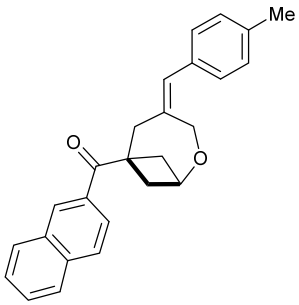


3ad
$C_{26}H_{24}O_2$
M = 368.48 g/mol

(4-((*Z*)-3-methylbenzylidene)-2-oxabicyclo[4.1.1]octan-6-yl)(naphthalen-2-yl)methanone ((*Z*)-**3ad**): Prepared from bicyclo[1.1.0]butan-1-yl(naphthalen-2-yl)methanone (**1a**, 20.8 mg, 0.10 mmol) and 5-(3-methylbenzylidene)-1,3-dioxan-2-one (**2d**, 40.9 mg, 0.20 mmol) according to the **GP2** at 100 °C for 12 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (15/1) afforded **3ad** as a white solid (16.3 mg, 44% yield).

(*Z*)-**3ad**: $\mathbf{R_f}$ = 0.35 (petroleum ether/EtOAc = 15/1). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.33 (s, 1H), 7.95-7.87 (m, 4H), 7.60 (t, *J* = 7.2 Hz, 1H), 7.54 (t, *J* = 7.6 Hz, 1H), 7.30-7.25 (m, 3H), 7.14-7.12 (m, 1H), 6.65 (s, 1H), 4.56 (t, *J* = 6.4 Hz, 1H), 4.52 (s, 2H), 2.91 (s, 2H), 2.89-2.86 (m, 2H), 2.79-2.76 (m, 2H), 2.40 (s, 3H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ 203.6, 138.0, 137.0, 136.5, 135.4, 133.5, 132.5, 131.3, 130.6, 129.64,

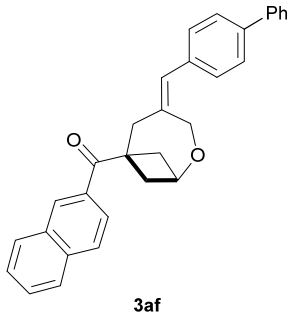
129.59, 128.6, 128.5, 128.3, 128.1, 127.7, 126.8, 126.1, 124.7, 73.2, 62.8, 51.7, 45.7, 37.4, 21.5 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{26}H_{25}O_2$: 369.1849; found: 369.1841.



3ae
$C_{26}H_{24}O_2$
M = 368.48 g/mol

((1s,6r)-4-((*Z*)-4-methylbenzylidene)-2-oxabicyclo[4.1.1]octan-6-yl)(naphthalen-2-yl)methanone ((*Z*)-**3ae**): Prepared from bicyclo[1.1.0]butan-1-yl(naphthalen-2-yl)methanone (**1a**, 20.8 mg, 0.10 mmol) and 5-(4-methylbenzylidene)-1,3-dioxan-2-one (**2e**, 40.9 mg, 0.20 mmol) according to the **GP2** at 100 °C for 12 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (15/1) afforded **3ae** as a white solid (15.2 mg, 41% yield).

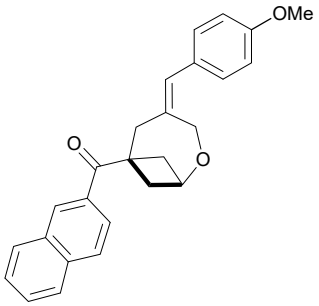
(*Z*)-**3ae**: $\mathbf{R_f}$ = 0.30 (petroleum ether/EtOAc = 15/1). **^{1}H NMR** (600 MHz, $CDCl_3$): δ 8.33 (s, 1H), 7.95-7.87 (m, 4H), 7.61 (t, *J* = 7.2 Hz, 1H), 7.55 (t, *J* = 7.8 Hz, 1H), 7.37 (d, *J* = 7.8 Hz, 2H), 7.22 (d, *J* = 7.8 Hz, 2H), 6.66 (s, 1H), 4.57 (t, *J* = 6.0 Hz, 1H), 4.52 (s, 2H), 2.91 (s, 2H), 2.89-2.87 (m, 2H), 2.80-2.76 (m, 2H), 2.39 (s, 3H) ppm. **^{13}C NMR** (150 MHz, $CDCl_3$): δ 203.7, 137.2, 136.4, 135.4, 133.6, 133.3, 132.4, 131.2, 130.6, 129.6, 129.1, 128.9, 128.6, 128.5, 127.7, 126.8, 124.7, 73.2, 62.8, 51.7, 45.6, 37.4, 21.2 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{26}H_{25}O_2$: 369.1849; found: 369.1840.



3af
$C_{31}H_{26}O_2$
M = 430.55 g/mol

(*Z*)-4-([1,1'-Biphenyl]-4-ylmethylene)-2-oxabicyclo[4.1.1]octan-6-yl)(naphthalen-2-yl) methanone ((*Z*)-**3af**): Prepared from bicyclo[1.1.0]butan-1-yl(naphthalen-2-yl)methanone (**1a**, 20.8 mg, 0.10 mmol) and 5-([1,1'-biphenyl]-4-ylmethylene)-1,3-dioxan-2-one (**2f**, 53.3 mg, 0.20 mmol) according to the **GP2** at 100 °C for 12 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (15/1) afforded **3af** as a white solid (22.1 mg, 51% yield).

(*Z*)-**3af**: $\mathbf{R_f}$ = 0.30 (petroleum ether/EtOAc = 15/1). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.34 (s, 1H), 7.96-7.87 (m, 4H), 7.65-7.62 (m, 5H), 7.59-7.54 (m, 3H), 7.46 (t, *J* = 7.2 Hz, 2H), 7.36 (t, *J* = 7.2 Hz, 1H), 6.72 (s, 1H), 4.60-4.57 (m, 3H), 2.94 (s, 2H), 2.90-2.89 (m, 2H), 2.80 (d, *J* = 11.6 Hz, 2H) ppm.**^{13}C NMR** (100 MHz, $CDCl_3$): δ 203.6, 140.7, 140.2, 137.4, 135.5, 135.4, 133.0, 132.4, 131.2, 130.6, 129.6, 129.5, 128.8, 128.6, 128.5, 127.7, 127.4, 127.1, 127.0, 126.8, 124.7, 73.3, 62.8, 51.7, 45.7, 37.4 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{31}H_{27}O_2$: 431.2006; found: 431.1998.

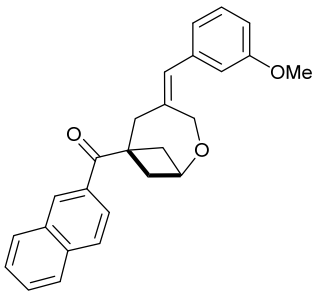


3ag
$C_{26}H_{24}O_3$
M = 384.48 g/mol

(4-((*Z*)-4-Methoxybenzylidene)-2-oxabicyclo[4.1.1]octan-6-yl)(naphthalen-2-yl)methanone ((*Z*)-**3ag**): Prepared from bicyclo[1.1.0]butan-1-yl(naphthalen-2-yl)methanone (**1a**, 20.8 mg,

0.10 mmol) and 5-(4-methoxybenzylidene)-1,3-dioxan-2-one (**2g**, 44.0 mg, 0.20 mmol) according to the **GP2** at 100 °C for 12 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (15/1) afforded **3ag** as a yellow solid (17.8 mg, 46% yield).

(*Z*)-**3ag**: $\mathbf{R_f}$ = 0.25 (petroleum ether/EtOAc = 15/1). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.32 (s, 1H), 7.95-7.87 (m, 4H), 7.60 (t, *J* = 7.2 Hz, 1H), 7.54 (t, *J* = 7.2 Hz, 1H), 7.41 (d, *J* = 7.6 Hz, 2H), 6.94 (d, *J* = 7.6 Hz, 2H), 6.63 (s, 1H), 4.56 (t, *J* = 6.4 Hz, 1H), 4.52 (s, 2H), 3.84 (s, 3H), 2.90 (s, 2H), 2.87-2.85 (m, 2H), 2.78 (d, *J* = 11.2 Hz, 2H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ 203.7, 159.0, 135.8, 135.4, 132.9, 132.5, 131.3, 130.6, 130.3, 129.7, 129.1, 128.5, 128.4, 127.7, 126.8, 124.7, 113.8, 73.2, 62.8, 55.3, 51.8, 45.6, 37.4 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{26}H_{25}O_3$: 385.1798; found: 385.1792.

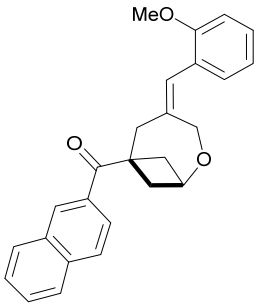


3ah
$C_{26}H_{24}O_3$
M = 384.48 g/mol

(4-((*Z*)-3-Methoxybenzylidene)-2-oxabicyclo[4.1.1]octan-6-yl)(naphthalen-2-yl)methanone ((*Z*)-**3ah**): Prepared from bicyclo[1.1.0]butan-1-yl(naphthalen-2-yl)methanone (**1a**, 20.8 mg, 0.10 mmol) and 5-(3-methoxybenzylidene)-1,3-dioxan-2-one (**2h**, 44.0 mg, 0.20 mmol) according to the **GP2** at 100 °C for 12 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (15/1) afforded **3ah** as a white solid (16.7 mg, 43% yield).

(*Z*)-**3ah**: $\mathbf{R_f}$ = 0.35 (petroleum ether/EtOAc = 15/1). **^{1}H NMR** (600 MHz, $CDCl_3$): δ 8.33 (s, 1H), 7.95-7.88 (m, 4H), 7.61 (t, *J* = 7.2 Hz, 1H), 7.55 (t, *J* = 7.8 Hz, 1H), 7.33 (t, *J* = 7.8 Hz, 1H), 7.09 (d, *J* = 7.2 Hz, 1H), 7.01 (s, 1H), 6.88 (d, *J* = 8.4 Hz, 1H), 6.67 (s, 1H), 4.57 (t, *J* = 6.0 Hz, 1H), 4.53 (s, 2H), 3.85 (s, 3H), 2.92 (s, 2H), 2.89-2.87 (m, 2H),

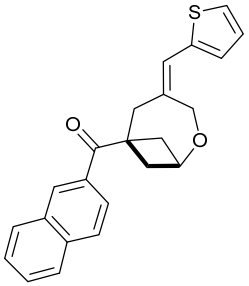
2.79-2.77 (m, 2H) ppm. **^{13}C NMR** (150 MHz, $CDCl_3$): δ 203.7, 159.5, 137.8, 137.5, 135.4, 133.3, 132.4, 131.2, 130.6, 129.6, 129.4, 128.6, 128.5, 127.7, 126.8, 124.7, 121.5, 114.3, 113.0, 73.2, 62.7, 55.2, 51.6, 45.6, 37.4 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{26}H_{25}O_3$: 385.1798; found: 385.1788.



3ai
$C_{26}H_{24}O_3$
M = 384.48 g/mol

(4-((*Z*)-2-Methoxybenzylidene)-2-oxabicyclo[4.1.1]octan-6-yl)(naphthalen-2-yl)methanone ((*Z*)-**3ai**): Prepared from bicyclo[1.1.0]butan-1-yl(naphthalen-2-yl)methanone (**1a**, 20.8 mg, 0.10 mmol) and 5-(2-methoxybenzylidene)-1,3-dioxan-2-one (**2i**, 44.0 mg, 0.20 mmol) according to the **GP2** at 100 °C for 12 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (15/1) afforded **3ai** as a white solid (26.7 mg, 69% yield).

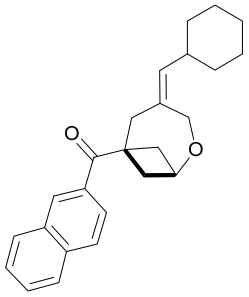
(*Z*)-**3ai**: $\mathbf{R_f}$ = 0.30 (petroleum ether/EtOAc = 15/1). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.32 (s, 1H), 7.94-7.86 (m, 4H), 7.67 (d, *J* = 7.2 Hz, 1H), 7.60 (t, *J* = 7.2 Hz, 1H), 7.54 (t, *J* = 7.6 Hz, 1H), 7.32 (t, *J* = 8.0 Hz, 1H), 7.04 (t, *J* = 7.2 Hz, 1H), 6.90 (d, *J* = 8.4 Hz, 1H), 6.79 (s, 1H), 4.56 (t, *J* = 4.8 Hz, 1H), 4.51 (s, 2H), 3.82 (s, 3H), 2.97 (s, 2H), 2.90-2.85 (m, 2H), 2.80-2.76 (m, 2H) ppm.**^{13}C NMR** (100 MHz, $CDCl_3$): δ 203.7, 157.1, 136.6, 135.3, 132.4, 131.2, 130.9, 130.6, 129.6, 129.4, 129.0, 128.5, 128.4, 127.7, 126.7, 125.3, 124.7, 120.5, 110.2, 73.2, 63.1, 55.3, 51.7, 45.7, 37.4 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{26}H_{25}O_3$: 385.1798; found: 385.1793.



3aj
$C_{23}H_{20}O_2S$
M = 360.47g/mol

Naphthalen-2-yl((*Z*)-4-(thiophen-2-ylmethylene)-2-oxabicyclo[4.1.1]octan-6-yl)methanone ((*Z*)-**3aj**): Prepared from bicyclo[1.1.0]butan-1-yl(naphthalen-2-yl)methanone (**1a**, 20.8 mg, 0.10 mmol) and 5-(thiophen-2-ylmethylene)-1,3-dioxan-2-one (**2j**, 39.2 mg, 0.20 mmol) according to the **GP2** at 100 °C for 12 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (15/1) afforded **3aj** as a white solid (12.5 mg, 35% yield).

(*Z*)-**3aj**: $\mathbf{R_f}$ = 0.35 (petroleum ether/EtOAc = 15/1). **^{1}H NMR** (600 MHz, $CDCl_3$): δ 8.32 (s, 1H), 7.95 (d, *J* = 7.8 Hz, 1H), 7.92-7.88 (m, 3H), 7.62 (t, *J* = 4.8 Hz, 1H), 7.56 (t, *J* = 7.2 Hz, 1H), 7.34 (d, *J* = 4.8 Hz, 1H), 7.22-7.21 (m, 1H), 7.07 (t, *J* = 3.0 Hz, 1H), 6.68 (s, 1H), 4.71 (s, 2H), 4.55 (t, *J* = 6.0 Hz, 1H), 2.91 (s, 2H), 2.89-2.85 (m, 2H), 2.76-2.73 (m, 2H) ppm.**^{13}C NMR** (150 MHz, $CDCl_3$): δ 203.6, 138.6, 136.7, 135.4, 132.4, 131.2, 130.6, 129.6, 128.6, 128.5, 128.1, 127.7, 127.3, 126.8, 126.0, 125.5, 124.6, 73.2, 62.8, 51.6, 45.8, 37.3 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{23}H_{21}O_2S$: 361.1257; found: 361.1249.

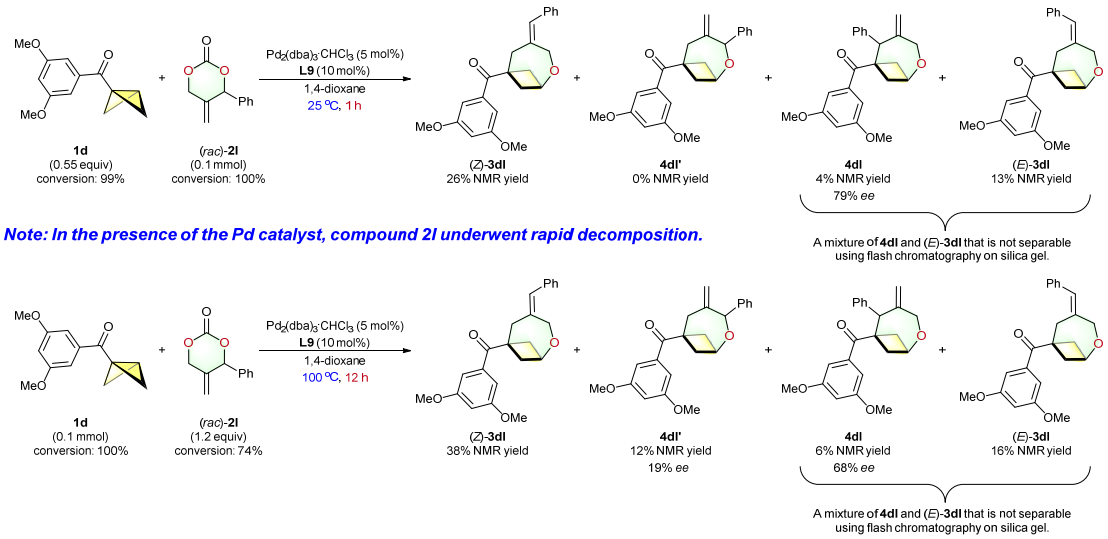


3ak
$C_{25}H_{28}O_2$
M = 360.50 g/mol

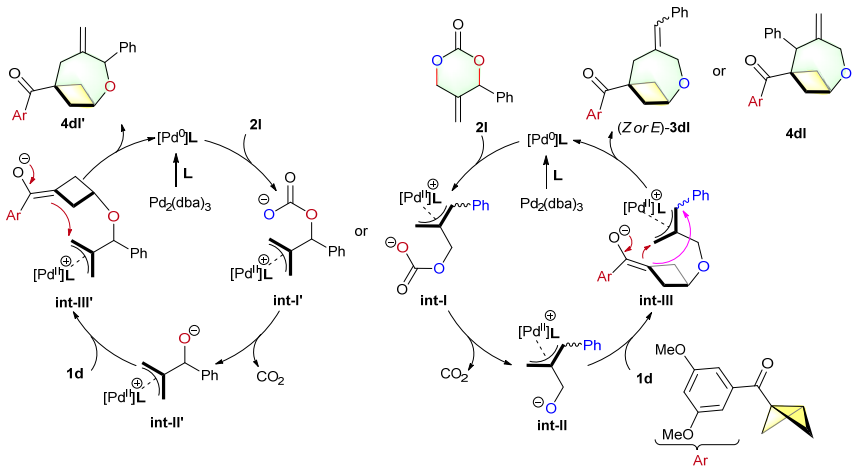
((*Z*)-4-(Cyclohexylmethylene)-2-oxabicyclo[4.1.1]octan-6-yl)(naphthalen-2-yl)methanone ((*Z*)-**3ak**): Prepared from bicyclo[1.1.0]butan-1-yl(naphthalen-2-yl)methanone (**1a**, 20.8 mg,

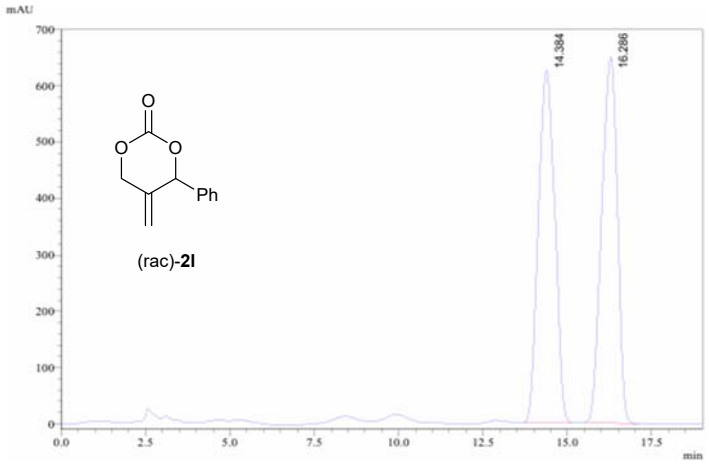
0.10 mmol) and 5-(cyclohexylmethylene)-1,3-dioxan-2-one (**2k**, 39.3 mg, 0.20 mmol) according to the **GP2** at 100 °C for 12 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (20/1) afforded **3ak** as a colorless oil (15.3 mg, 42% yield).

(*Z*)-**3ak**: $\mathbf{R_f}$ = 0.35 (petroleum ether/EtOAc = 20/1). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.29 (s, 1H), 7.94-7.86 (m, 4H), 7.62-7.54 (m, 2H), 5.38 (d, *J* = 9.2 Hz, 1H), 4.45-4.43 (m, 3H), 2.81-2.77 (m, 2H), 2.72 (s, 2H), 2.67-2.62 (m, 2H), 2.54-2.46 (m, 1H), 1.76-1.67 (m, 4H), 1.40-1.31 (m, 2H), 1.25-1.12 (m, 4H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ 203.9, 140.6, 135.3, 132.40, 132.36, 131.4, 130.6, 129.6, 128.5, 128.4, 127.7, 126.7, 124.7, 72.7, 61.9, 51.4, 45.5, 37.1, 36.8, 33.7, 25.9, 25.8 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{25}H_{29}O_2$: 361.2162; found: 361.2157.



Scheme 3. Proposed mechanism for the reaction involving **1d** and **2l**.



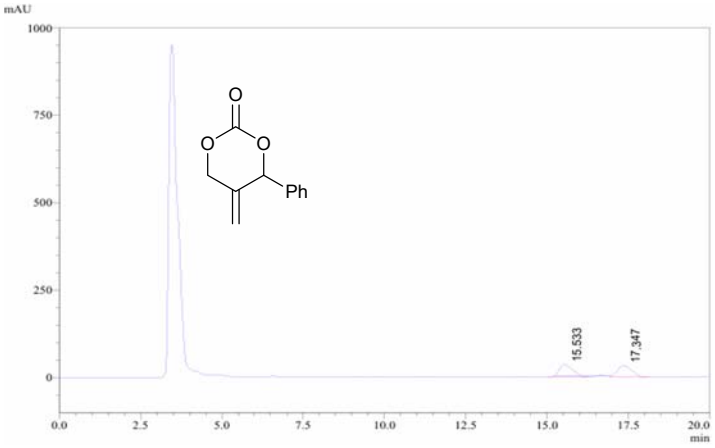


(rac)-**2l**

Detector A Channel 2 220nm

Peak#	Ret. Time [min]	Peak Start [min]	Height [mAU]	Area [mAU*min]	Area%
1	14.384	13.708	625062	21247750	50.188
2	16.286	15.492	649358	21088443	49.812
Total			1274420	42336193	100.000

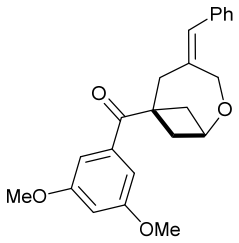
The unreacted ADTMC 2l was obtained with an enantiomeric excess of 1%



Detector A Channel 2 220nm

Peak#	Ret. Time [min]	Peak Start [min]	Height [mAU]	Area [mAU*min]	Area%
1	15.533	15.042	35696	1023688	50.572
2	17.347	16.917	32857	1000530	49.428
Total			68553	2024218	100.000

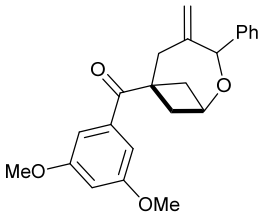
HPLC analysis (Chiralpak AD-H, ^{i}PrOH/hexane = 10/90, 1.0 mL/min, 220 nm; tr (major) = 15.53 min, tr (minor) = 17.35 min) gave the isomeric composition of the unreacted ADTMC **2l**: 1% *ee*.



(*Z*)-**3dl**
$C_{23}H_{24}O_4$
M = 364.44 g/mol

(4-((*Z*)-benzylidene)-2-oxabicyclo[4.1.1]octan-6-yl)(3,5-dimethoxyphenyl)methanone ((*Z*)-**3dl**): Prepared from bicyclo[1.1.0]butan-1-yl(3,5-dimethoxyphenyl)methanone (**1d**, 21.8 mg, 0.10 mmol) and 5-methylene-4-phenyl-1,3-dioxan-2-one (**2l**, 22.8 mg, 0.12 mmol) according to the **GP1** at 100 °C for 12 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (15/1) afforded (*Z*)-**3dl** as a white solid (9.2 mg, 25% yield).

(*Z*)-**3dl**: $\mathbf{R_f}$ = 0.20 (petroleum ether/EtOAc = 15/1). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.44-7.37 (m, 4H), 7.31-7.28 (m, 1H), 6.97 (s, 2H), 6.66 (s, 1H), 6.64 (s, 1H), 4.52 (t, *J* = 6.8 Hz, 1H), 4.47 (s, 2H), 3.82 (s, 6H), 2.84 (s, 2H), 2.82-2.78 (m, 2H), 2.70-2.66 (m, 2H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ 203.3, 160.8, 137.1, 136.5, 135.8, 133.4, 129.0, 128.4, 127.3, 106.8, 105.0, 73.1, 62.7, 55.5, 51.6, 45.5, 37.3 ppm. **HRMS** (ESI) *m/z*: $[M+Na]^+$ calcd. for $C_{23}H_{24}O_4Na$: 387.1567; found: 387.1560.



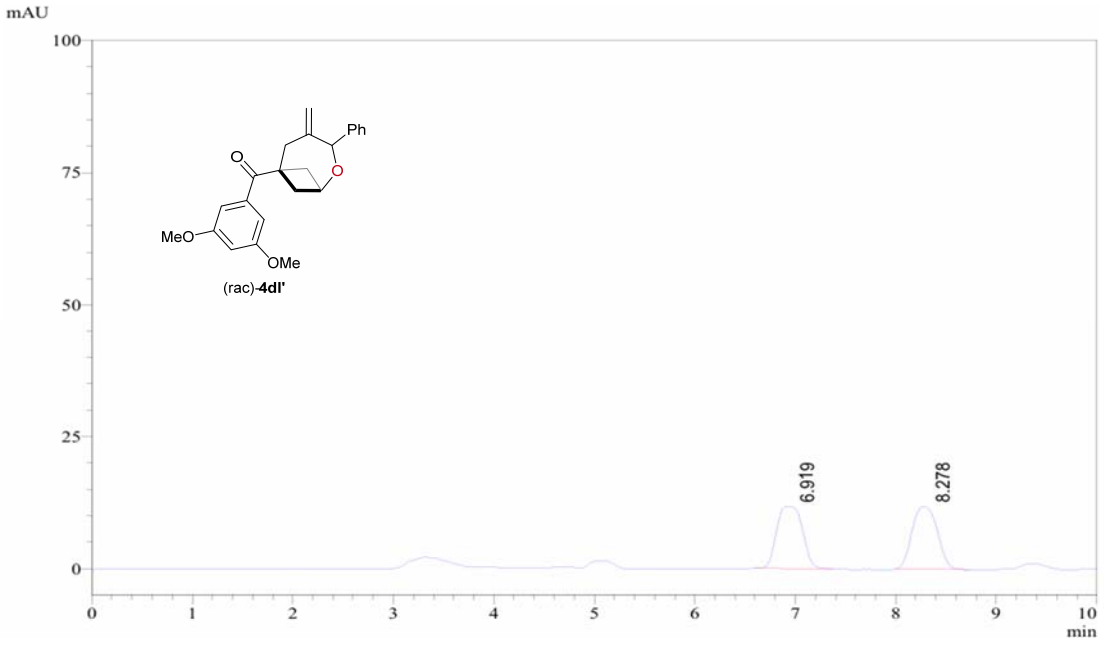
4dl'
$C_{23}H_{24}O_4$
M = 364.44 g/mol

(3,5-dimethoxyphenyl)(4-methylene-3-phenyl-2-oxabicyclo[4.1.1]octan-6-yl)methanone (**4dl'**): Prepared from bicyclo[1.1.0]butan-1-yl(3,5-dimethoxyphenyl)methanone (**1d**, 21.8 mg, 0.10 mmol) and 5-methylene-4-phenyl-1,3-dioxan-2-one (**2l**, 22.8 mg, 0.12 mmol) according to the **GP1** at 100 °C for 12 h. Purification by flash chromatography on silica

gel using petroleum ether/EtOAc (20/1) afforded **4dl'** as a white solid (3.1 mg, 9% yield, 19% *ee*).

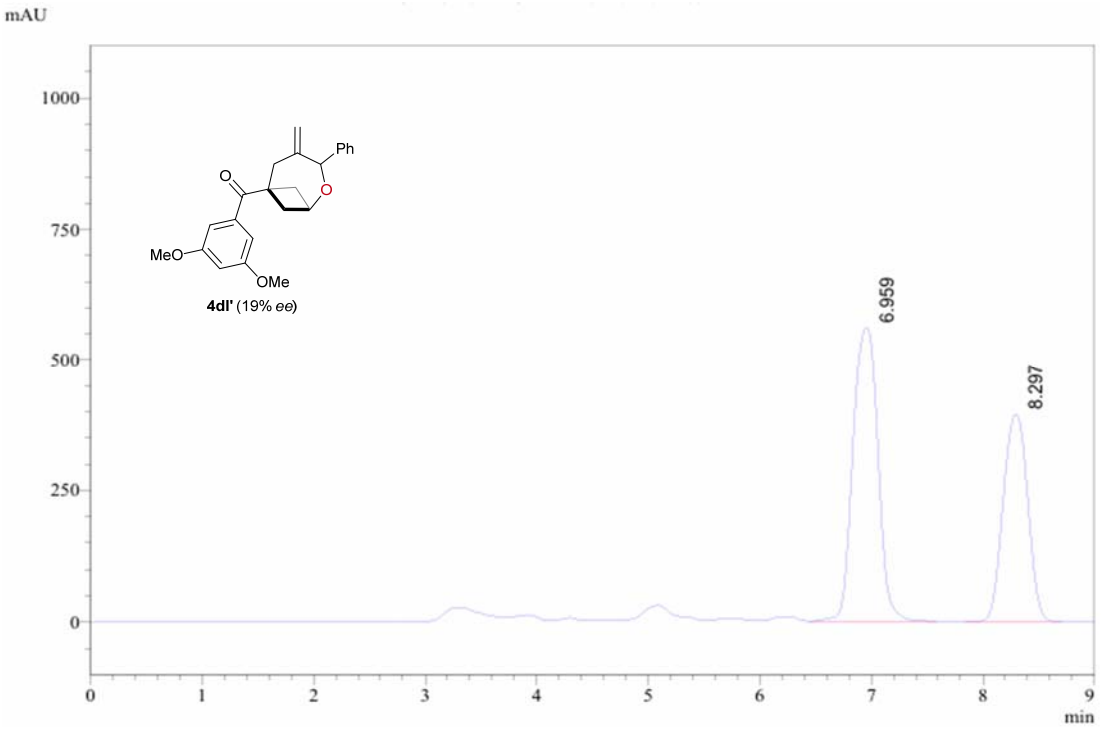
4dl': $\mathbf{R_f}$ = 0.25 (petroleum ether/EtOAc = 20/1). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.43 (d, *J* = 6.8 Hz, 2H), 7.37 (t, *J* = 6.8 Hz, 2H), 7.30 (d, *J* = 6.8 Hz, 1H), 6.97 (s, 2H), 6.64 (s, 1H), 5.53 (s, 1H), 5.15 (s, 1H), 4.73 (s, 1H), 4.62 (t, *J* = 5.2 Hz, 1H), 3.82 (s, 6H), 2.96-2.86 (m, 3H), 2.80-2.75 (m, 1H), 2.73-2.68 (m, 1H), 2.53-2.49 (m, 1H) ppm. **^{13}C NMR** (150 MHz, $CDCl_3$): δ 203.1, 160.8, 147.7, 140.5, 135.8, 128.1, 127.4, 127.1, 120.7, 106.7, 105.2, 77.7, 72.6, 55.5, 50.9, 44.7, 39.5, 35.2 ppm. **HRMS** (ESI) *m/z*: $[M+Na]^+$ calcd. for $C_{23}H_{24}O_4Na$: 387.1567; found: 387.1559.

HPLC analysis of **4dl'** (Chiralpak AD-H, ^{i}PrOH/hexane = 10/90, 1.0 mL/min, 254 nm; tr (major) = 6.96 min, tr (minor) = 8.30 min) gave the isomeric composition of the product: 19% *ee*.



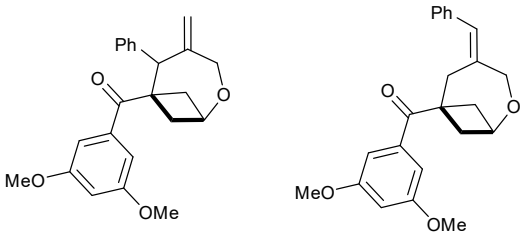
Detector A Channel 1 254nm

Peak#	Ret. Time [min]	Peak Start [min]	Height [mAU]	Area [mAU*min]	Area%
1	6.919	6.592	11714	207631	50.218
2	8.278	8.000	11820	205826	49.782
Total			23534	413457	100.000



Detector A Channel 1 254nm

Peak#	Ret. Time [min]	Peak Start [min]	Height [mAU]	Area [mAU*min]	Area%
1	6.957	6.500	123607	1930165	59.514
2	8.296	7.942	86493	1313029	40.486
Total			210100	3243194	100.000



4dl
$C_{23}H_{24}O_4$
M = 364.44 g/mol

(*E*)-**3dl**
$C_{23}H_{24}O_4$
M = 364.44 g/mol

A mixture of **4dl** and (*E*)-**3dl** that is not separable using flash chromatography on silica gel.

(3,5-dimethoxyphenyl)(4-methylene-5-phenyl-2-oxabicyclo[4.1.1]octan-6-yl)methanone (**4dl**) and **(4-((*E*)-benzylidene)-2-oxabicyclo[4.1.1]octan-6-yl)(3,5-dimethoxyphenyl)methanone** ((*E*)-**3dl**): Prepared from bicyclo[1.1.0]butan-1-yl(3,5-dimethoxyphenyl)methanone (**1d**, 21.8 mg, 0.10 mmol) and 5-methylene-4-phenyl-1,3-dioxan-2-one (**2l**, 22.8 mg, 0.12 mmol) according to the **GP1** at 100 °C for 12 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (20/1) afforded a mixture of **4dl** and (*E*)-**3dl** as a

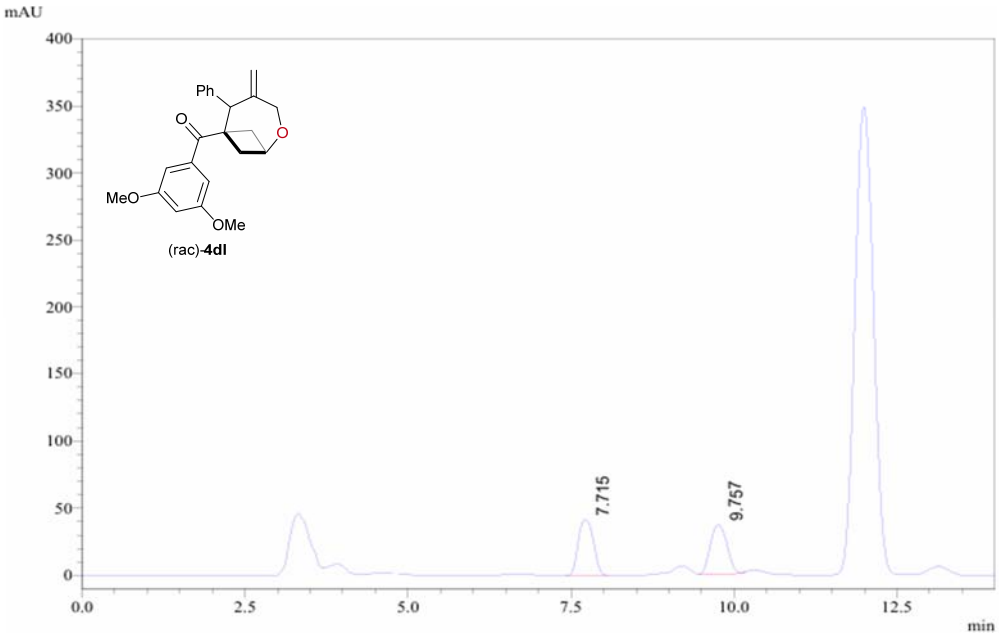
colorless oil that is not separable using flash chromatography on silica gel (8.2 mg, 23% combined isolated yield).

4dl: R_f = 0.20 (petroleum ether/EtOAc = 20/1). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.29-7.26 (m, 2H), 7.22-7.18 (m, 2H), 6.94-6.92 (m, 1H), 6.62 (s, 2H), 6.54 (s, 1H), 5.42 (s, 1H), 4.89 (s, 1H), 4.52 (s, 2H), 4.46 (t, *J* = 5.2 Hz, 1H), 4.29 (s, 1H), 3.74 (s, 6H), 3.24-3.19 (m, 1H), 2.92-2.87 (m, 1H), 2.84-2.79 (m, 1H), 2.37-2.31 (m, 1H) ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{23}H_{25}O_4$: 365.1747; found: 365.1739.

(*E*)-3dl: R_f = 0.20 (petroleum ether/EtOAc = 20/1). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.29-7.26 (m, 2H), 7.22-7.18 (m, 2H), 7.15-7.13 (m, 1H), 6.89 (s, 1H), 6.81 (s, 2H), 6.56 (s, 1H), 4.52 (s, 2H), 4.46 (t, *J* = 5.2 Hz, 1H), 3.65 (s, 6H), 2.98 (s, 2H), 2.76-2.72 (m, 2H), 2.56-2.52 (m, 2H) ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{23}H_{25}O_4$: 365.1747; found: 365.1736.

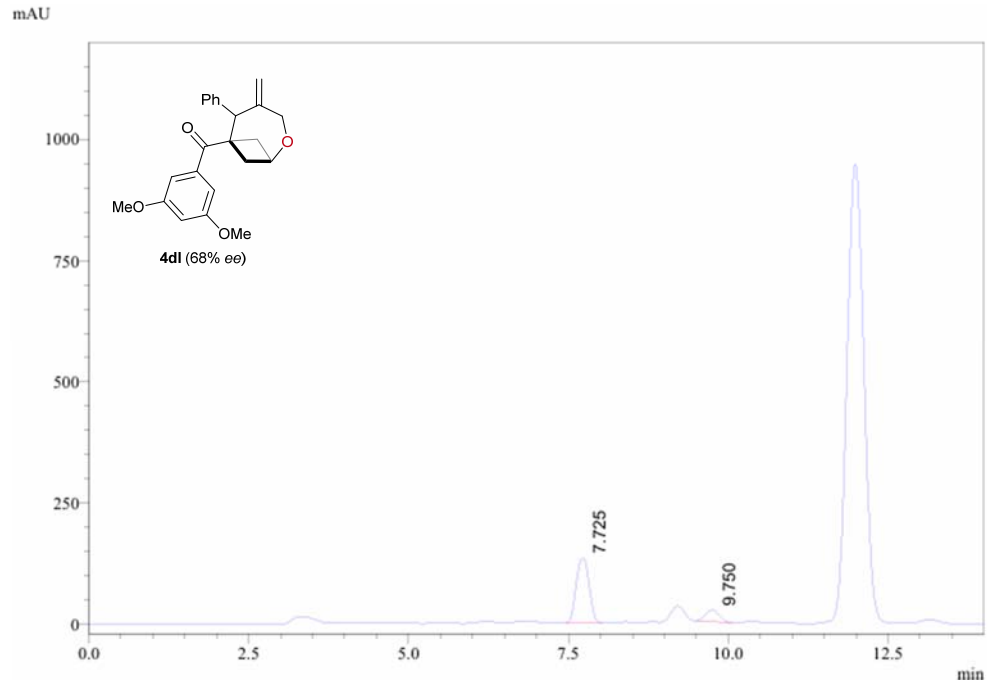
^{13}C NMR (150 MHz, $CDCl_3$): δ 203.3 (for **(*E*)-3dl**), 203.1 (for **4dl**), 160.6 (for **(*E*)-3dl**), 160.4 (for **4dl**), 147.9, 139.6, 137.8, 136.9, 136.5, 135.7, 133.8, 128.7, 128.5, 128.3, 128.2, 127.1, 126.7, 121.4, 106.5, 106.1, 105.5, 104.3, 72.7, 72.3, 70.7, 70.5, 68.5, 55.5, 55.4, 55.2, 51.1, 40.4, 37.1, 36.8 ppm.

HPLC analysis of **4dl** (Chiralpak AD-H, ^{i}PrOH/hexane = 10/90, 1.0 mL/min, 254 nm; tr (major) = 7.73 min, tr (minor) = 9.75 min) gave the isomeric composition of the product: 68% *ee*.



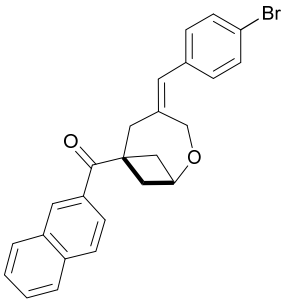
Detector A Channel 2 220nm

Peak#	Ret. Time [min]	Peak Start [min]	Height [mAU]	Area [mAU*min]	Area%
1	7.715	7.417	41258	668142	50.296
2	9.757	9.458	36709	660269	49.704
Total			77967	1328412	100.000



Detector A Channel 1 254nm

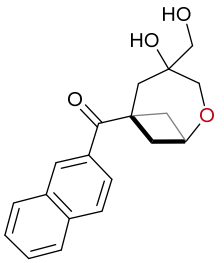
Peak#	Ret. Time [min]	Peak Start [min]	Height [mAU]	Area [mAU*min]	Area%
1	7.725	7.450	134421	1881283	83.934
2	9.750	9.500	23130	360092	16.066
Total			157551	2241375	100.000



3am
$C_{25}H_{21}BrO_2$
M = 433.35 g/mol

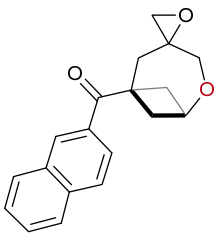
(4-((*Z*)-4-bromobenzylidene)-2-oxabicyclo[4.1.1]octan-6-yl)(naphthalen-2-yl)methanone ((*Z*)-**3am**): Prepared from bicyclo[1.1.0]butan-1-yl(naphthalen-2-yl)methanone (**1a**, 20.8 mg, 0.10 mmol) and 5-(4-bromobenzylidene)-1,3-dioxan-2-one (**2m**, 53.8 mg, 0.20 mmol) according to the **GP2** at 100 °C for 12 h. Purification by flash chromatography on silica gel using petroleum ether/EtOAc (20/1) afforded **3am** as a white solid (9.2 mg, 21% yield).

(*Z*)-**3am**: $\mathbf{R_f}$ = 0.30 (petroleum ether/EtOAc = 20/1). **^{1}H NMR** (600 MHz, $CDCl_3$): δ 8.32 (s, 1H), 7.95 (d, *J* = 8.4 Hz, 1H), 7.91 (s, 2H), 7.89 (d, *J* = 7.8 Hz, 1H), 7.62 (t, *J* = 7.2 Hz, 1H), 7.56 (t, *J* = 7.8 Hz, 1H), 7.53 (d, *J* = 8.4 Hz, 2H), 7.34 (d, *J* = 8.4 Hz, 2H), 6.61 (s, 1H), 4.57 (t, *J* = 6.0 Hz, 1H), 4.48 (s, 2H), 2.91-2.89 (m, 4H), 2.76 (d, *J* = 11.4 Hz, 2H) ppm.**^{13}C NMR** (150 MHz, $CDCl_3$): δ 203.5, 138.1, 135.4, 135.3, 132.4, 132.2, 131.5, 131.1, 130.64, 130.61, 129.6, 128.6, 128.5, 127.8, 126.8, 124.6, 121.4, 73.3, 62.6, 51.6, 45.5, 37.3 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{25}H_{22}BrO_2$: 433.0803; found: 4333.0792.



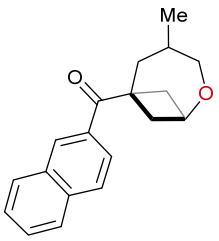
6
$C_{19}H_{20}O_4$
M = 312.37 g/mol

(4-Hydroxy-4-(hydroxymethyl)-2-oxabicyclo[4.1.1]octan-6-yl)(naphthalen-2-yl) methanone (**6**): $\mathbf{R_f}$ = 0.20 (petroleum ether/EtOAc = 1/2). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.41 (s, 1H), 7.95 (t, *J* = 7.2 Hz, 2H), 7.87 (t, *J* = 8.4 Hz, 2H), 7.60 (t, *J* = 7.2 Hz, 1H), 7.54 (t, *J* = 8.0 Hz, 1H), 4.55 (t, *J* = 5.6 Hz, 1H), 4.16 (d, *J* = 13.6 Hz, 1H), 4.03 (d, *J* = 13.6 Hz, 1H), 3.51 (d, *J* = 11.2 Hz, 1H), 3.41 (d, *J* = 11.2 Hz, 1H), 3.23-3.16 (m, 2H), 2.80 (dd, *J* = 14.0 Hz, 6.0 Hz, 1H), 2.69 (dd, *J* = 12.4 Hz, 5.6 Hz, 1H), 2.59 (dd, *J* = 13.6 Hz, 7.6 Hz, 1H), 2.39 (d, *J* = 14.4 Hz, 2H), 1.75 (d, *J* = 14.8 Hz, 1H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ 203.0, 135.4, 132.4, 130.9, 130.8, 129.7, 128.6, 128.5, 127.7, 126.7, 124.7, 76.2, 73.0, 67.7, 67.4, 53.2, 41.8, 40.6, 32.3 ppm. **HRMS** (ESI) *m/z*: $[M+Na]^+$ calcd. for $C_{19}H_{21}O_4Na$: 335.1254; found: 335.1251.



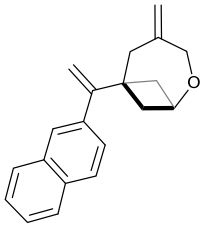
7
$C_{19}H_{18}O_3$
M = 294.35 g/mol

Naphthalen-2-yl(5-oxaspiro[bicyclo[4.1.1]octane-3,2'-oxiran]-1-yl)methanone (**7**): $\mathbf{R_f}$ = 0.20 (petroleum ether/EtOAc = 3/1). **^{1}H NMR** (600 MHz, $CDCl_3$): δ 8.36 (s, 1H), 7.96 (d, *J* = 7.8 Hz, 1H), 7.92-7.86 (m, 3H), 7.61 (t, *J* = 7.2 Hz, 1H), 7.56 (t, *J* = 7.2 Hz, 1H), 4.56 (t, *J* = 6.6 Hz, 1H), 4.31 (d, *J* = 13.2 Hz, 1H), 3.72 (d, *J* = 13.2 Hz, 1H), 3.03-2.95 (m, 2H), 2.91 (dd, *J* = 12.6 Hz, 6.0 Hz, 1H), 2.83 (d, *J* = 4.2 Hz, 1H), 2.78 (d, *J* = 4.2 Hz, 1H), 2.64 (dd, *J* = 13.8 Hz, 7.2 Hz, 1H), 2.44 (d, *J* = 14.4 Hz, 1H), 2.14 (d, *J* = 14.4 Hz, 1H) ppm. **^{13}C NMR** (150 MHz, $CDCl_3$): δ 202.8, 135.3, 132.3, 130.9, 130.7, 129.7, 128.6, 128.5, 127.7, 126.8, 124.6, 72.3, 69.1, 57.8, 52.0, 51.9, 42.4, 39.4, 34.6 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{19}H_{19}O_3$: 295.1329; found: 295.1327.



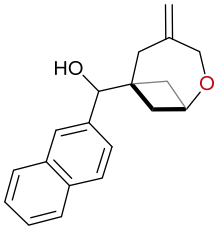
8
$C_{19}H_{20}O_2$
M = 280.37 g/mol

(4-Methyl-2-oxabicyclo[4.1.1]octan-6-yl)(naphthalen-2-yl)methanone (**8**): $\mathbf{R_f}$ = 0.30 (petroleum ether/EtOAc = 20/1). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.32 (s, 1H), 7.96-7.85 (m, 4H), 7.61-7.53 (m, 2H), 4.44 (t, *J* = 5.6 Hz, 1H), 3.90-3.79 (m, 2H), 2.85-2.80 (m, 1H), 2.76-2.72 (m, 1H), 2.63-2.53 (m, 3H), 2.25-2.20 (m, 1H), 1.57 (t, *J* = 12.4 Hz, 1H), 0.95 (d, *J* = 6.4 Hz, 3H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ 203.9, 135.3, 132.4, 131.5, 130.4, 129.5, 128.4, 128.3, 127.7, 126.7, 124.7, 72.3, 70.6, 53.0, 42.5, 40.0, 33.8, 33.6, 18.2 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{19}H_{21}O_2$: 281.1536; found: 281.1535.



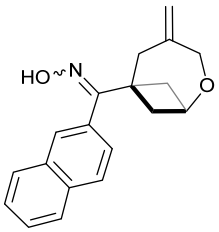
9
$C_{20}H_{20}O$
M = 276.38 g/mol

(4-Methylene-6-(1-(naphthalen-2-yl)vinyl)-2-oxabicyclo[4.1.1]octane (**9**): $\mathbf{R_f}$ = 0.30 (petroleum ether/EtOAc = 30/1). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.82-7.76 (m, 3H), 7.70 (s, 1H), 7.49-7.42 (m, 3H), 5.34 (s, 1H), 5.16 (s, 1H), 5.11 (s, 1H), 4.97 (s, 1H), 4.44 (t, *J* = 6.4 Hz, 1H), 4.30 (s, 2H), 2.62-2.57 (m, 4H), 2.52 (d, *J* = 11.6 Hz, 2H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ 156.3, 145.6, 137.8, 133.2, 132.5, 128.1, 127.6, 127.5, 126.1, 125.84, 125.79, 125.5, 118.3, 111.9, 71.8, 68.7, 46.9, 45.9, 38.4 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{20}H_{21}O$: 277.1587; found: 277.1584.



10
$C_{19}H_{20}O_2$
M = 280.37 g/mol

(4-Methylene-2-oxabicyclo[4.1.1]octan-6-yl)(naphthalen-2-yl)methanol (**10**): **R_f** = 0.25 (petroleum ether/EtOAc = 5/1). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.83-7.78 (m, 3H), 7.72 (s, 1H), 7.50-7.45 (m, 2H), 7.39 (d, *J* = 8.4 Hz, 1H), 5.06 (s, 1H), 4.90 (s, 1H), 4.68 (s, 1H), 4.40 (t, *J* = 6.4 Hz, 1H), 4.12 (s, 2H), 2.55-2.48 (m, 2H), 2.29 (d, *J* = 14.0 Hz, 2H), 2.15-2.06 (m, 2H), 2.01-1.96 (m, 1H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ 145.3, 138.9, 133.0, 132.9, 127.9, 127.8, 127.6, 126.2, 125.9, 125.4, 124.6, 118.2, 79.6, 71.9, 68.4, 45.1, 40.9, 34.0, 33.6 ppm. **HRMS** (ESI) *m/z*: $[M+Na]^+$ calcd. for $C_{19}H_{20}O_2Na$: 303.1356; found: 303.1357.



11
$C_{19}H_{19}NO_2$
M = 293.37 g/mol

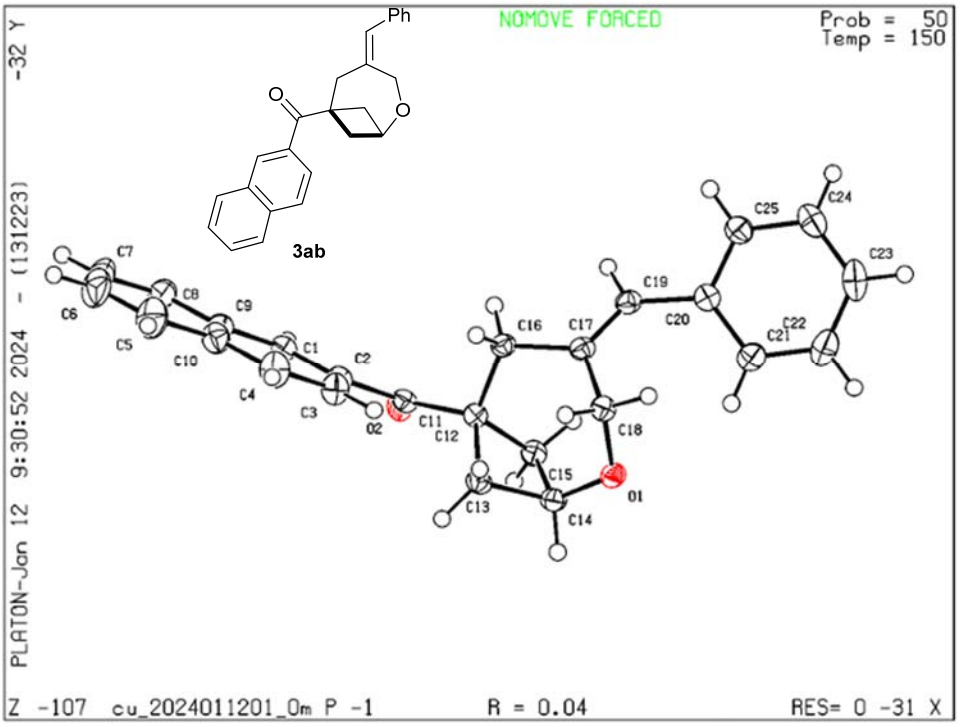
(4-Methylene-2-oxabicyclo[4.1.1]octan-6-yl)(naphthalen-2-yl)methanone oxime (**11**)**: The major isomer: R_f** = 0.30 (petroleum ether/EtOAc = 5/1). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.86-7.80 (m, 4H), 7.52-7.46 (m, 3H), 5.29 (s, 1H), 5.18 (s, 1H), 4.37-4.34 (m, 3H), 3.08 (s, 2H), 2.67-2.62 (m, 2H), 2.45-2.40 (m, 2H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ 164.2, 144.9, 133.3, 132.9, 132.3, 128.4, 128.1, 127.7, 126.6, 126.43, 126.36, 124.3, 119.1, 73.5, 68.7, 44.4, 42.2, 38.8 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{19}H_{20}NO_2$: 294.1489; found: 294.1483.

The minor isomer: R_f = 0.25 (petroleum ether/EtOAc = 5/1). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.19 (broad s, 1H), 7.91-7.86 (m, 3H), 7.71 (s, 1H), 7.55-7.50 (m, 2H), 7.34

(d, *J* = 8.4 Hz, 1H), 5.14 (s, 1H), 4.94 (s, 1H), 4.43 (t, *J* = 6.4 Hz, 1H), 4.22 (s, 2H), 2.80-2.75 (m, 2H), 2.56 (s, 2H), 2.36-2.33 (m, 2H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ 163.4, 144.5, 133.1, 132.9, 129.9, 128.3, 128.0, 127.8, 126.70, 126.6, 126.4, 125.4, 119.2, 72.2, 68.5, 45.3, 44.2, 36.2 ppm. **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{19}H_{20}NO_2$: 294.1489; found: 294.1481.

10 Crystal Structure of 3ab

Note: The thermal ellipsoids are 50% probability level. The crystals are grown by slow solvent (CH_2Cl_2/*n*-Hexane/Et_2O) evaporation at room temperature. CCDC number of **3ab** is 2352144.



Datablock: cu_2024011201_0m

Bond precision: C-C = 0.0018 A Wavelength=1.54178

Cell: a=6.0617(2) b=11.9065(3) c=14.3836(4)
alpha=113.136(1) beta=99.600(1) gamma=90.492(1)
Temperature: 150 K

	Calculated	Reported
Volume	938.11(5)	938.11(5)
Space group	P -1	P -1
Hall group	-P 1	-P 1
Moiety formula	C25 H22 O2	C25 H22 O2
Sum formula	C25 H22 O2	C25 H22 O2
Mr	354.43	354.42
Dx,g cm-3	1.255	1.255
Z	2	2
Mu (mm-1)	0.612	0.612
F000	376.0	376.0
F000'	377.06	
h,k,lmax	7,14,17	7,14,17
Nref	3444	3424
Tmin,Tmax	0.852,0.975	0.818,0.975
Tmin'	0.811	

Correction method= # Reported T Limits: Tmin=0.818 Tmax=0.975
AbsCorr = MULTI-SCAN

Data completeness= 0.994 Theta(max)= 68.263

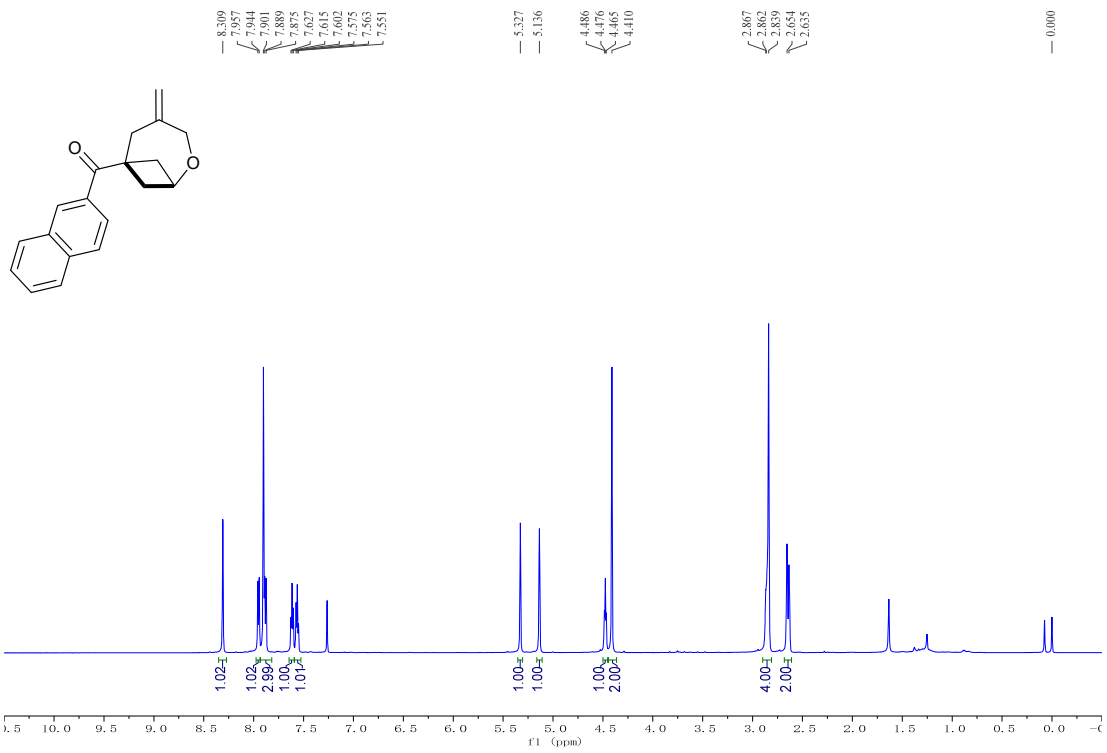
R(reflections)= 0.0355(3062) wR2(reflections)= 0.0958(3424)

S = 1.074 Npar= 245

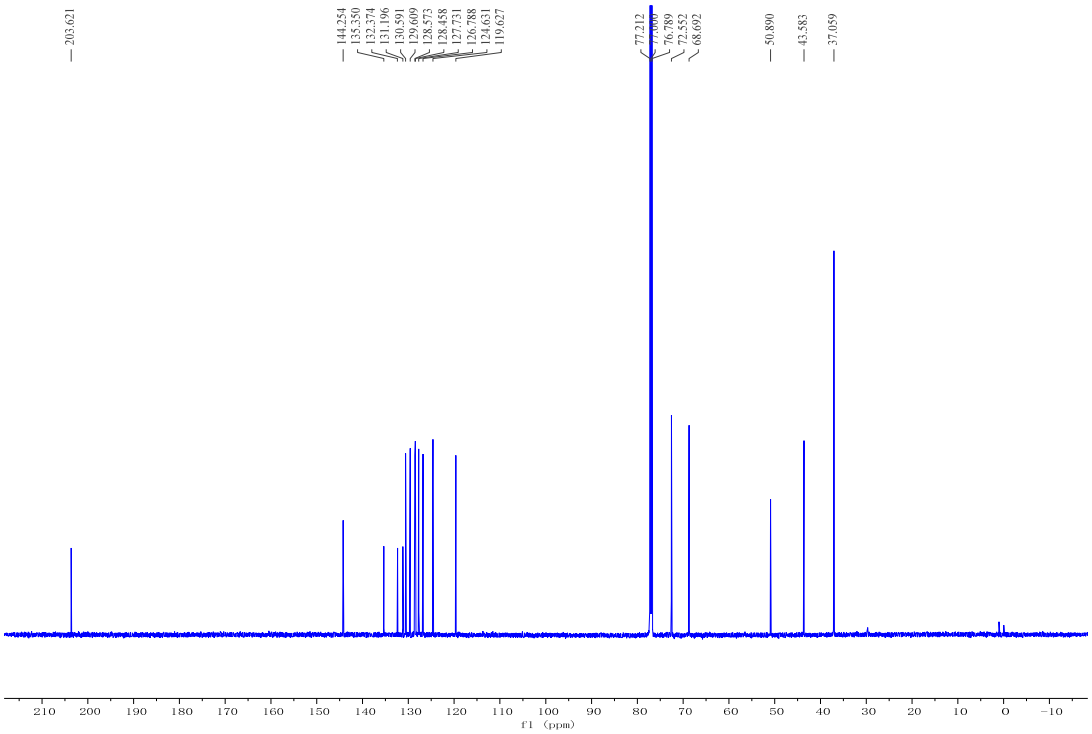
11 NMR Spectra

^{1}H and ^{13}C NMR Spectra for Compound 3aa:

^{1}H NMR (600 MHz, $CDCl_3$)

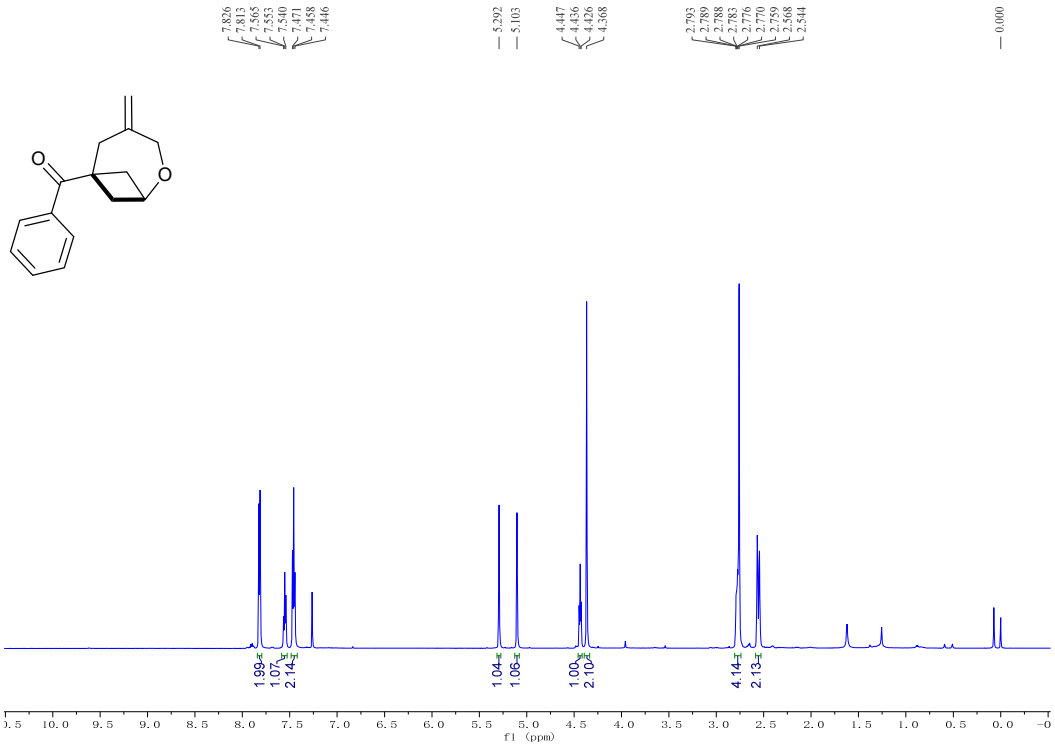


^{13}C NMR (150 MHz, $CDCl_3$)

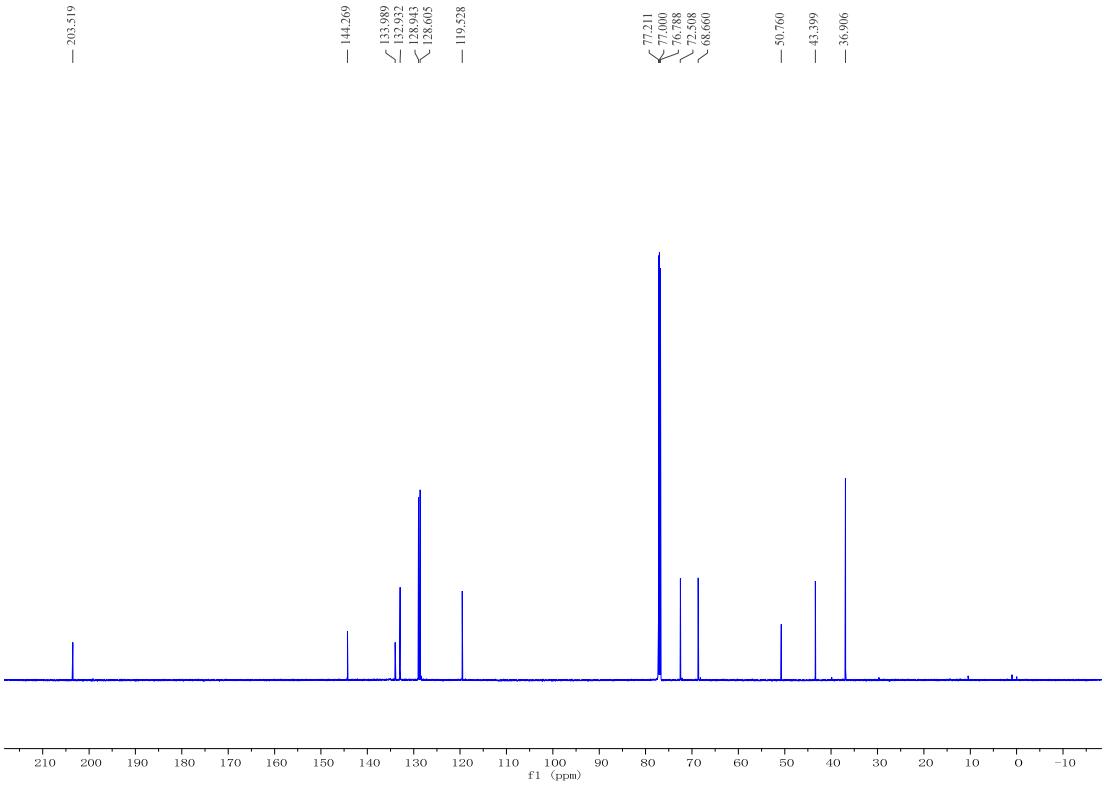


^{1}H and ^{13}C NMR Spectra for Compound **3ba**:

^{1}H NMR (600 MHz, $CDCl_3$)

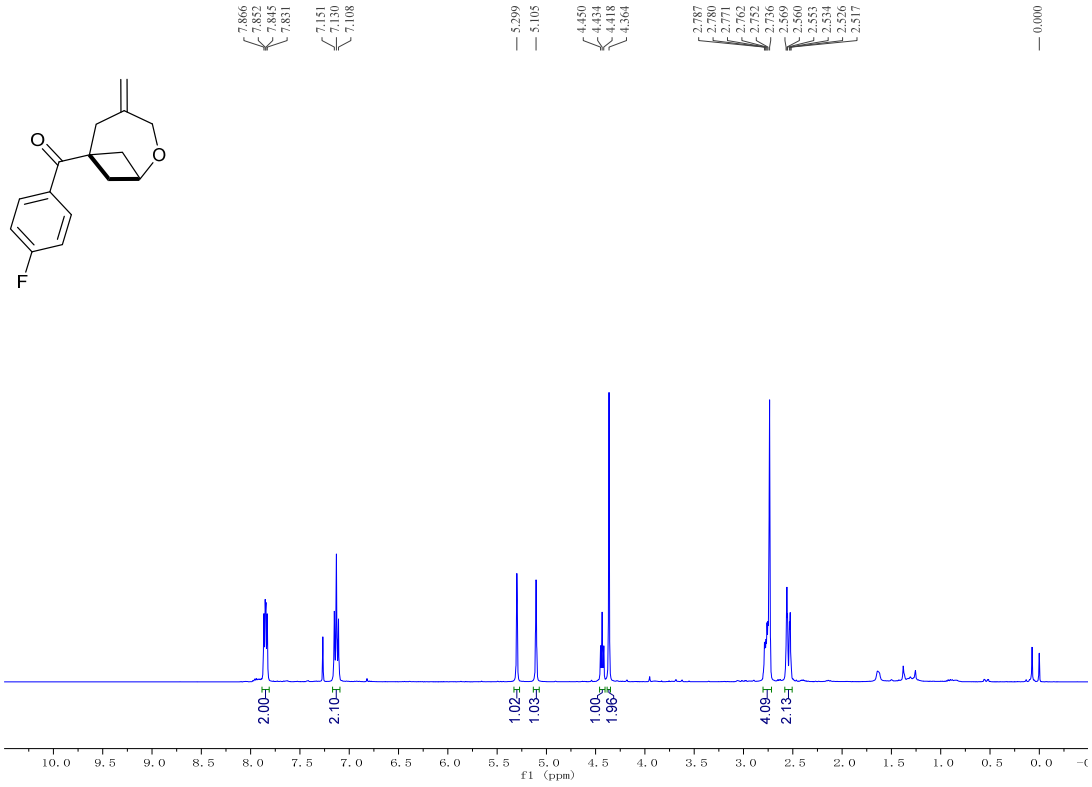


^{13}C NMR (150 MHz, $CDCl_3$)

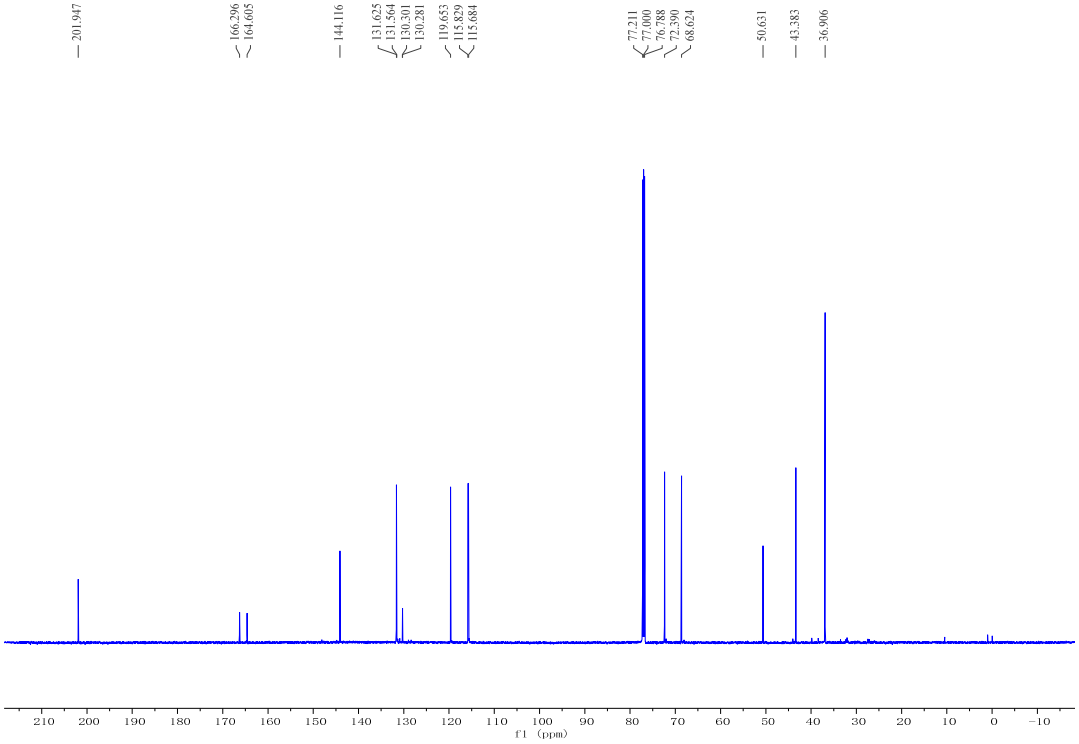


^{1}H ,^{13}C NMR and ^{19}F NMR Spectra for Compound 3ca:

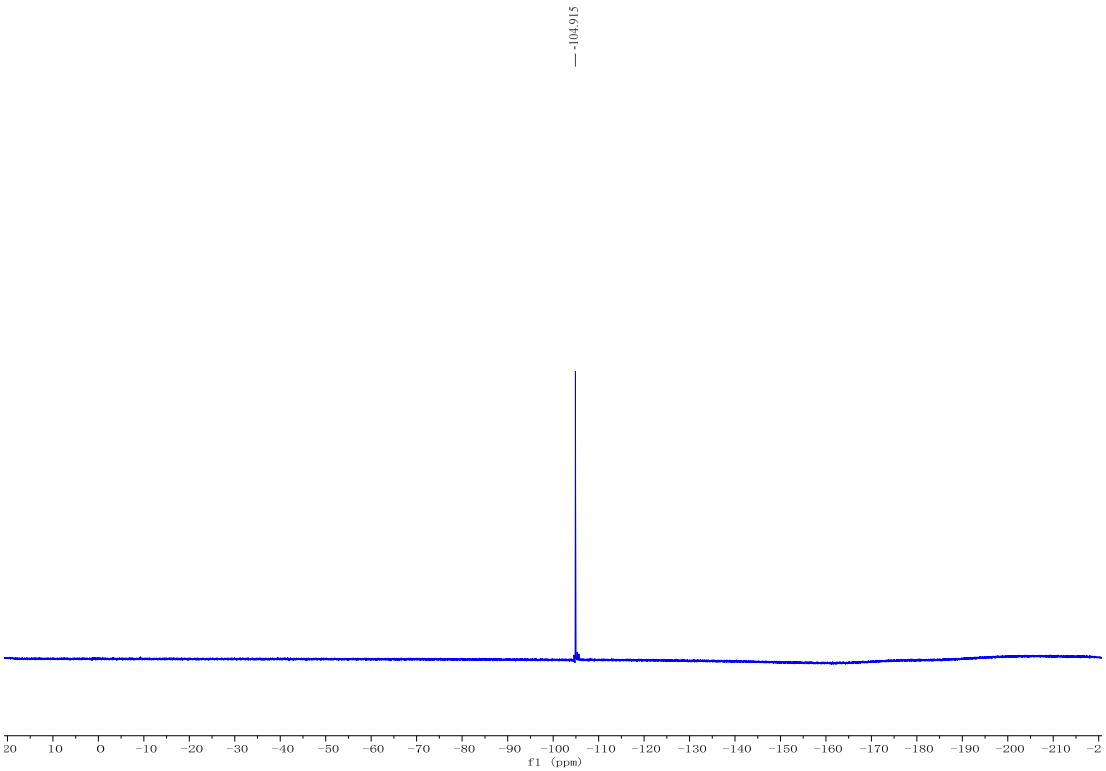
^{1}H NMR (400 MHz, $CDCl_3$)



^{13}C NMR (150 MHz, $CDCl_3$)

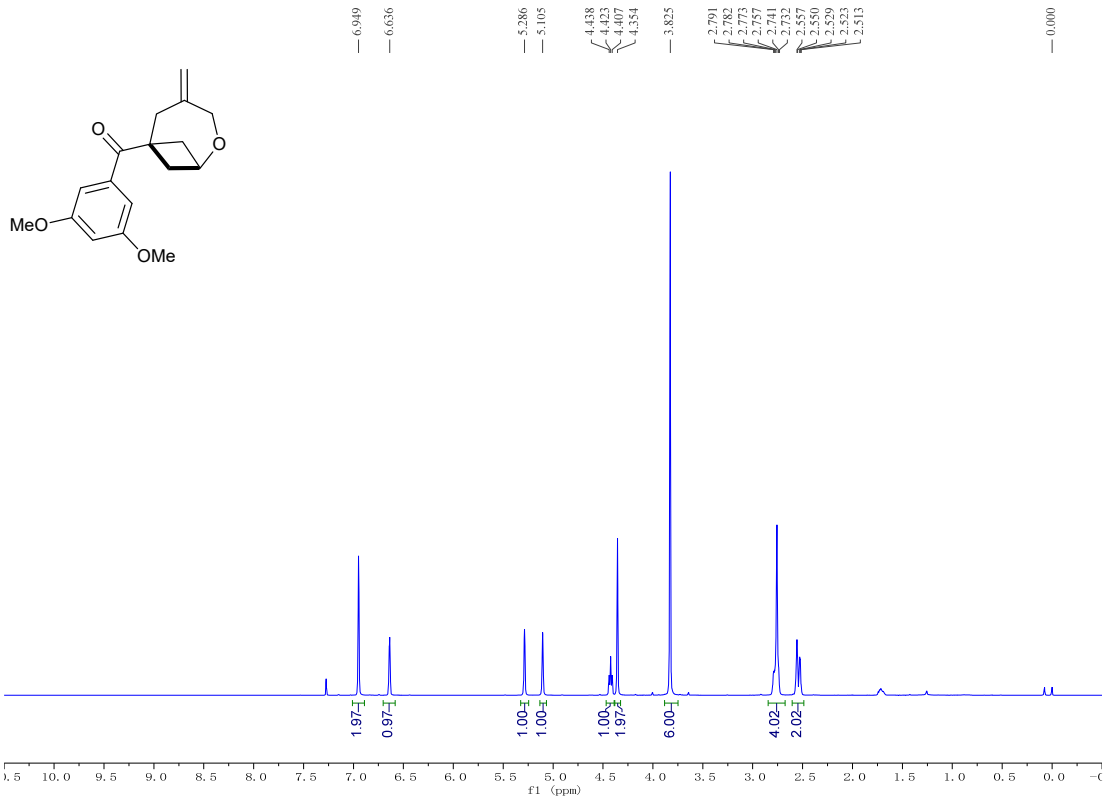


^{19}F NMR (376 MHz, $CDCl_3$)

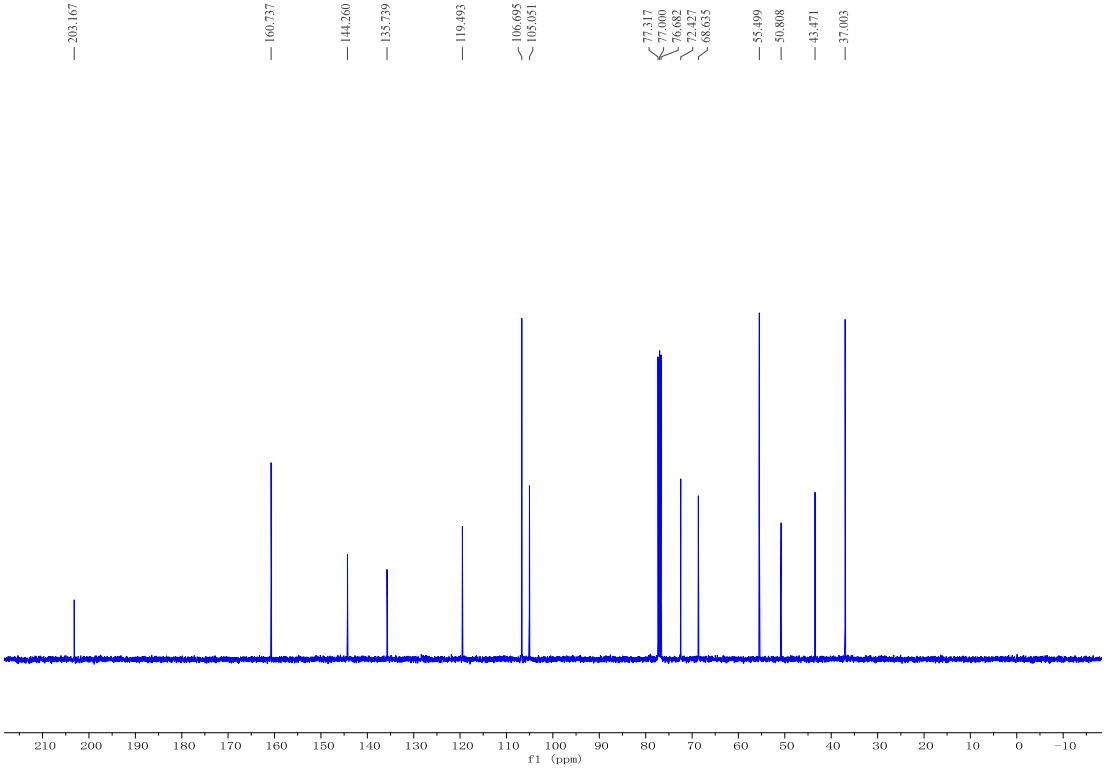


^{1}H and ^{13}C NMR Spectra for Compound 3da:

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

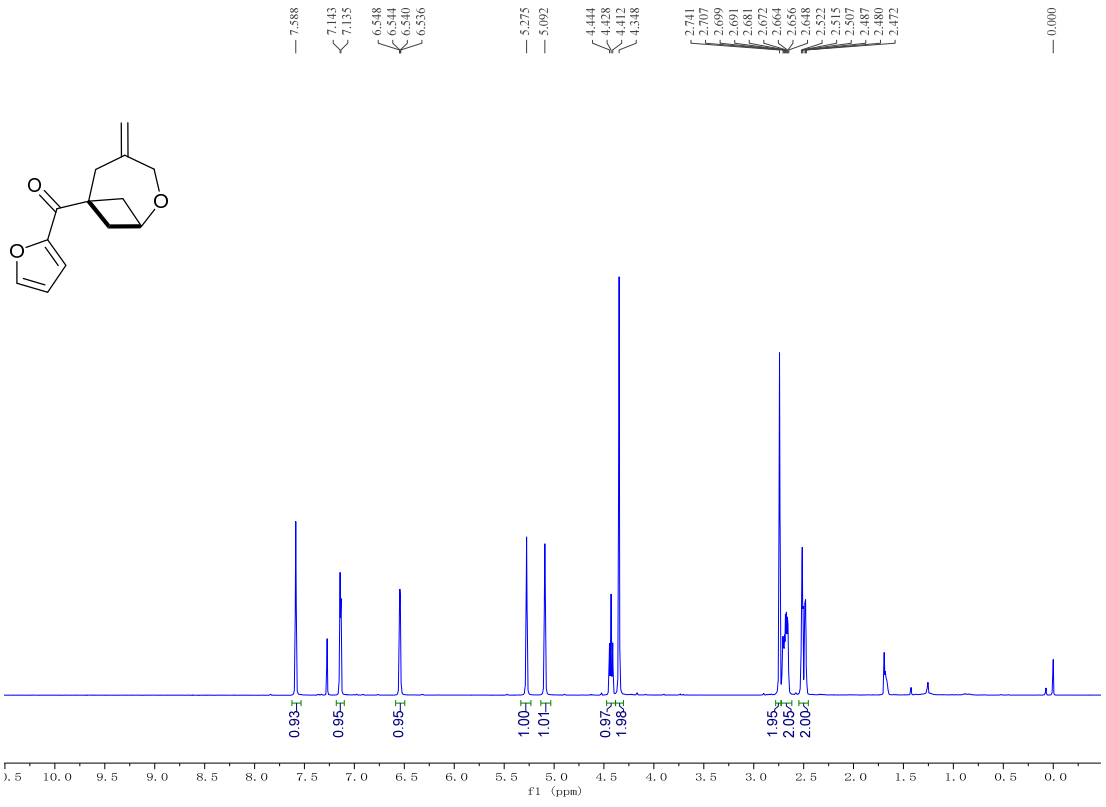


^{13}C NMR (100 MHz, $CDCl_3$)

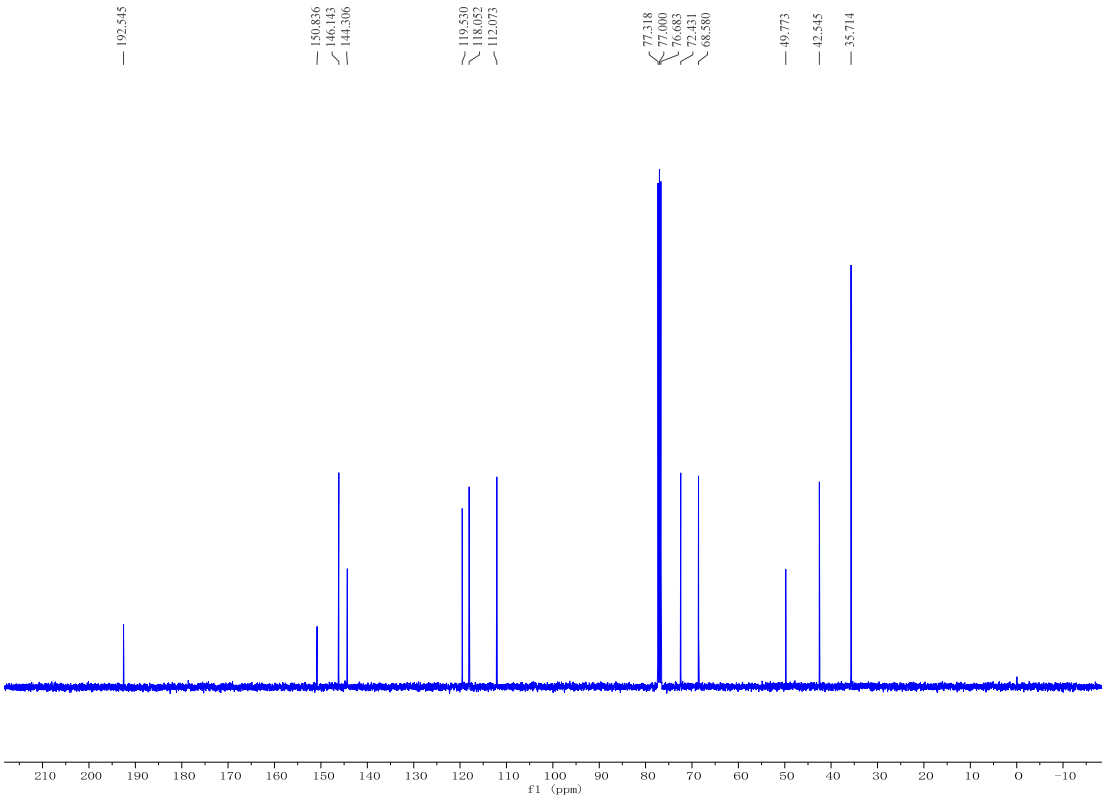


^{1}H and ^{13}C NMR Spectra for Compound 3ea:

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

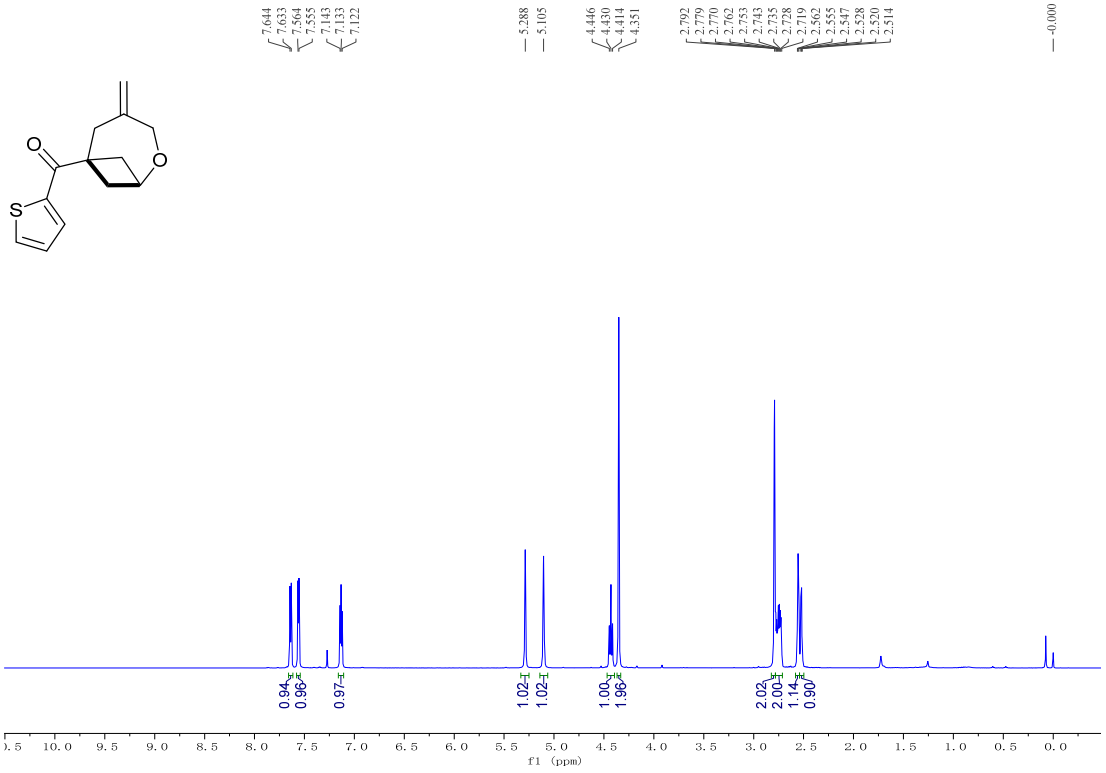


^{13}C NMR (100 MHz, $CDCl_3$)

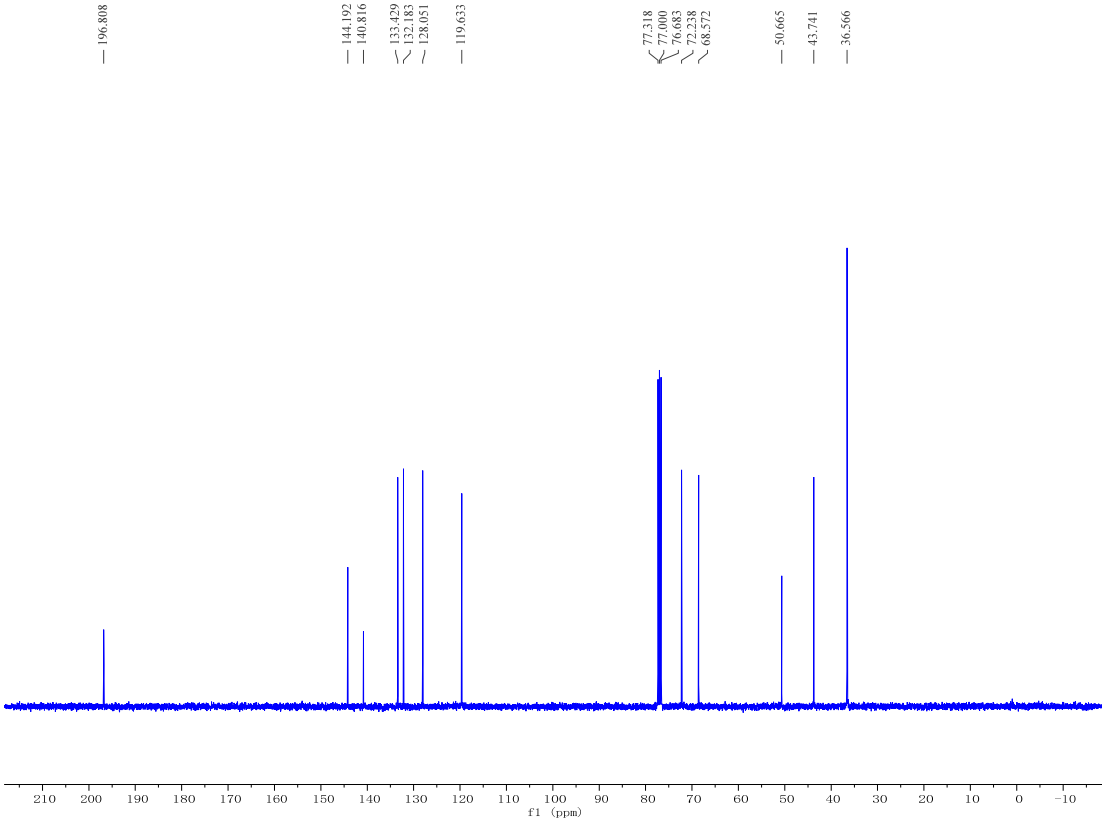


^{1}H and ^{13}C NMR Spectra for Compound 3fa:

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

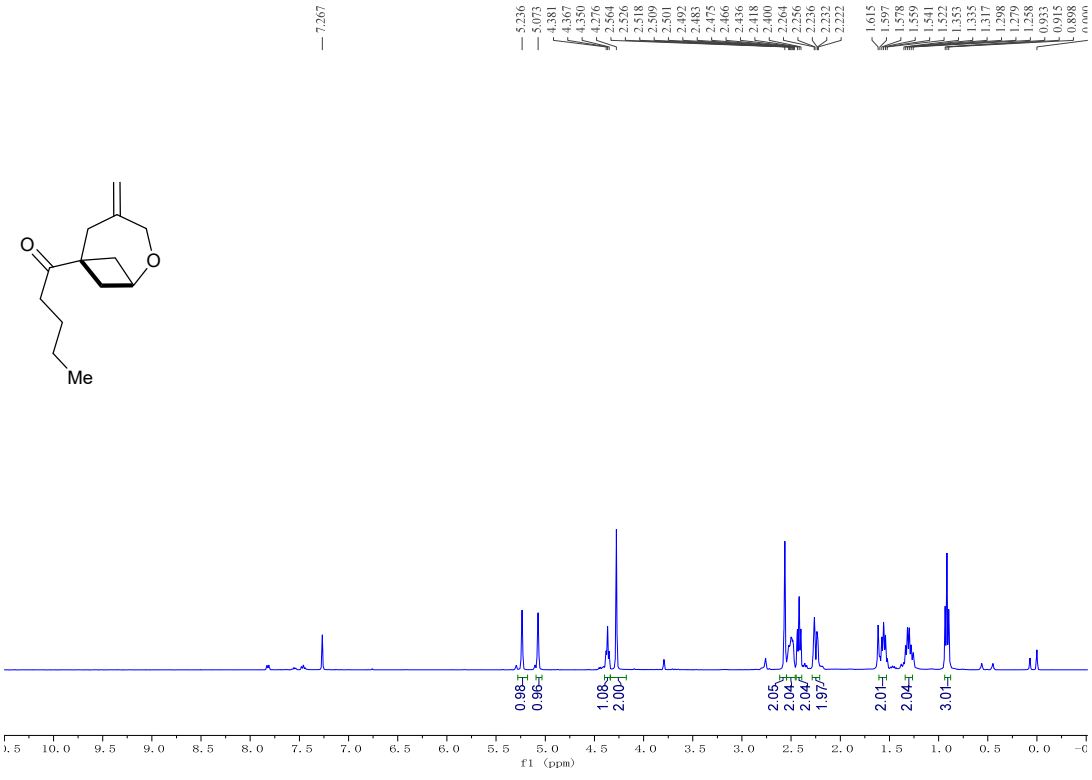


^{13}C NMR (100 MHz, $CDCl_3$)

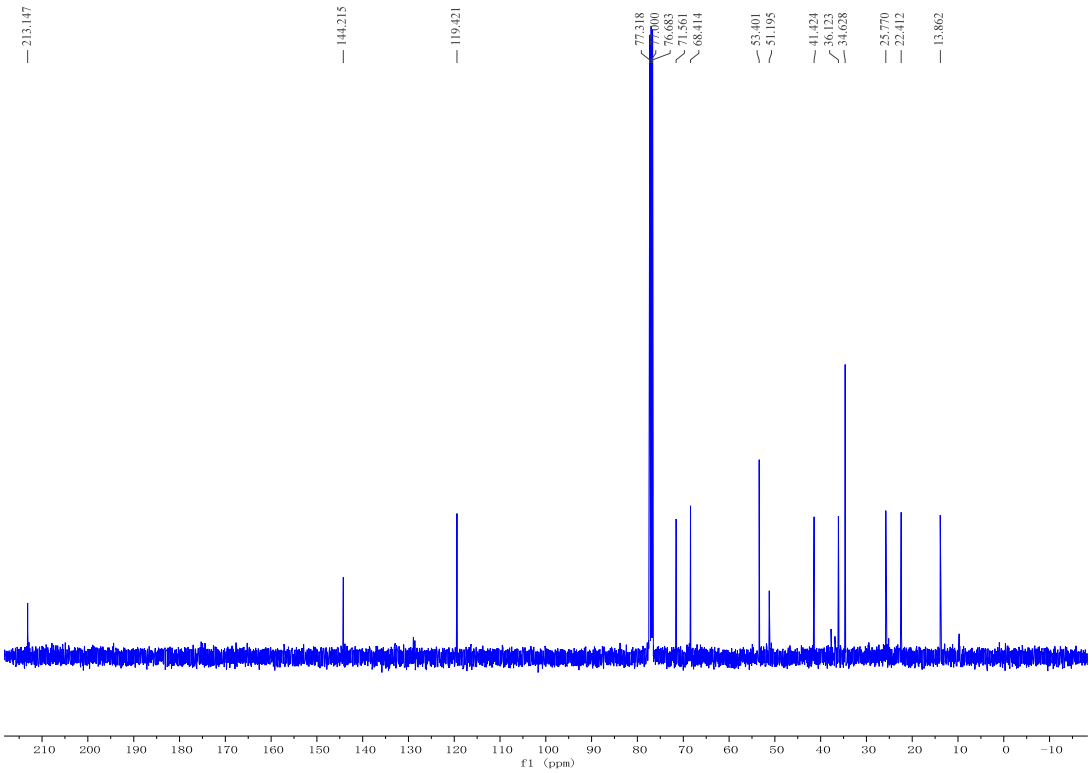


^{1}H and ^{13}C NMR Spectra for Compound 3ga:

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

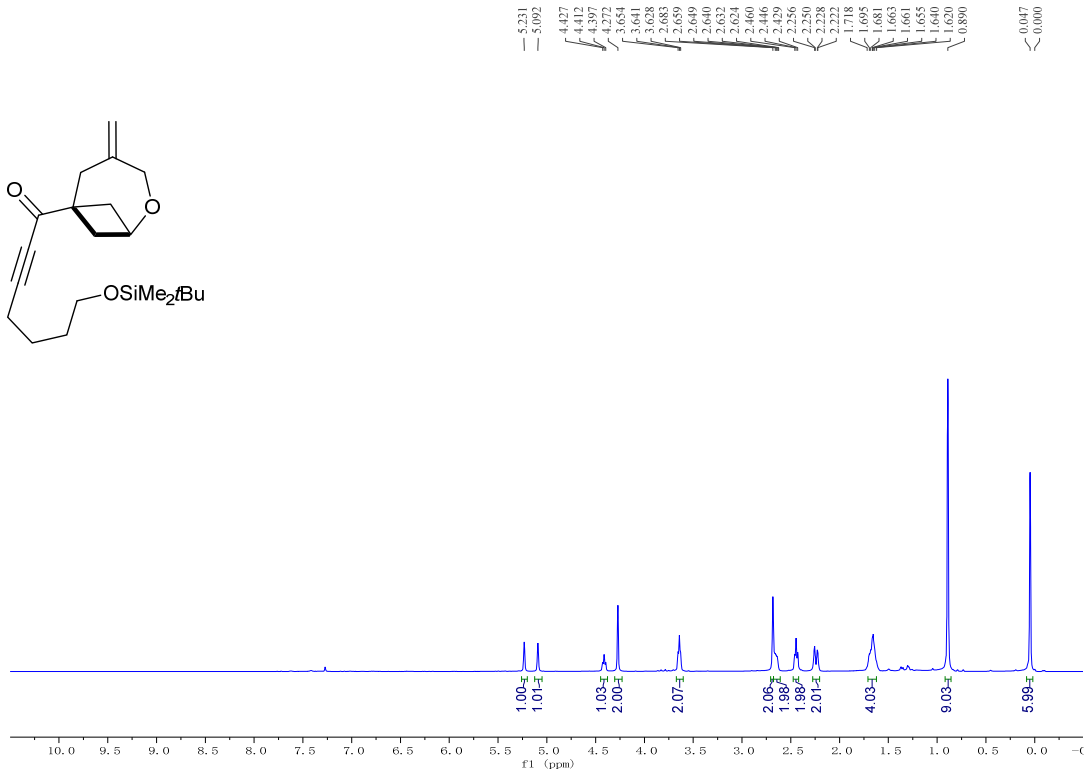


^{13}C NMR (100 MHz, $CDCl_3$)

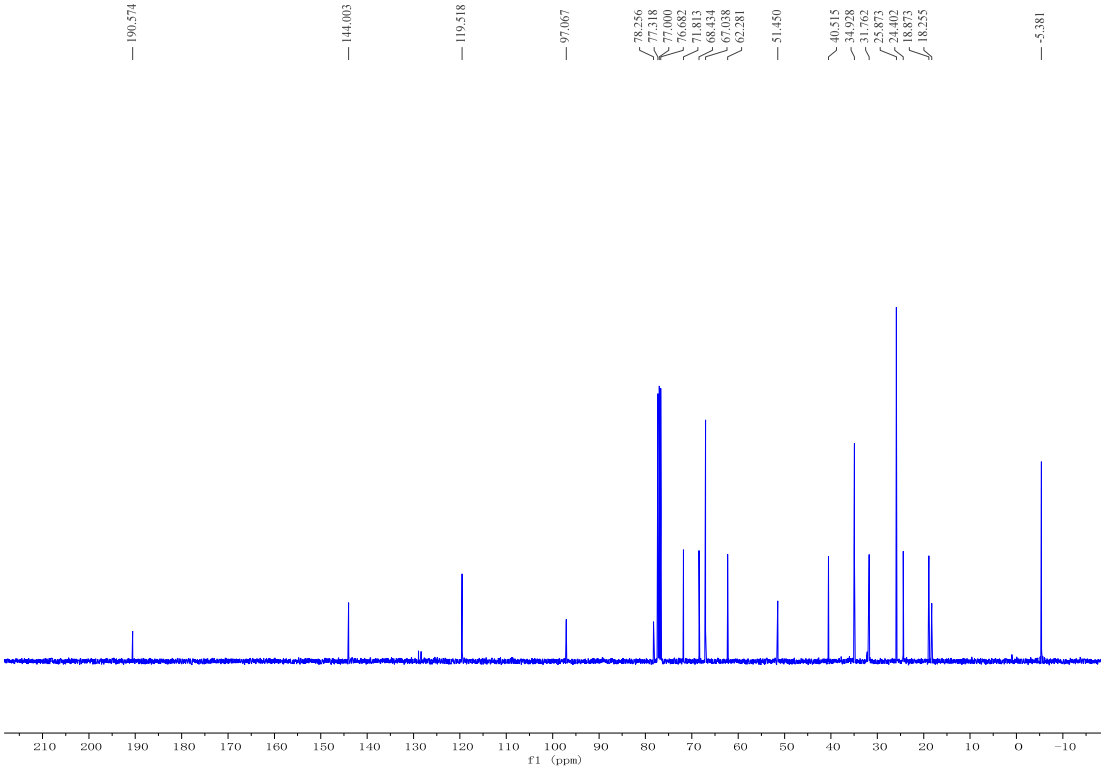


^{1}H and ^{13}C NMR Spectra for Compound 3ha:

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

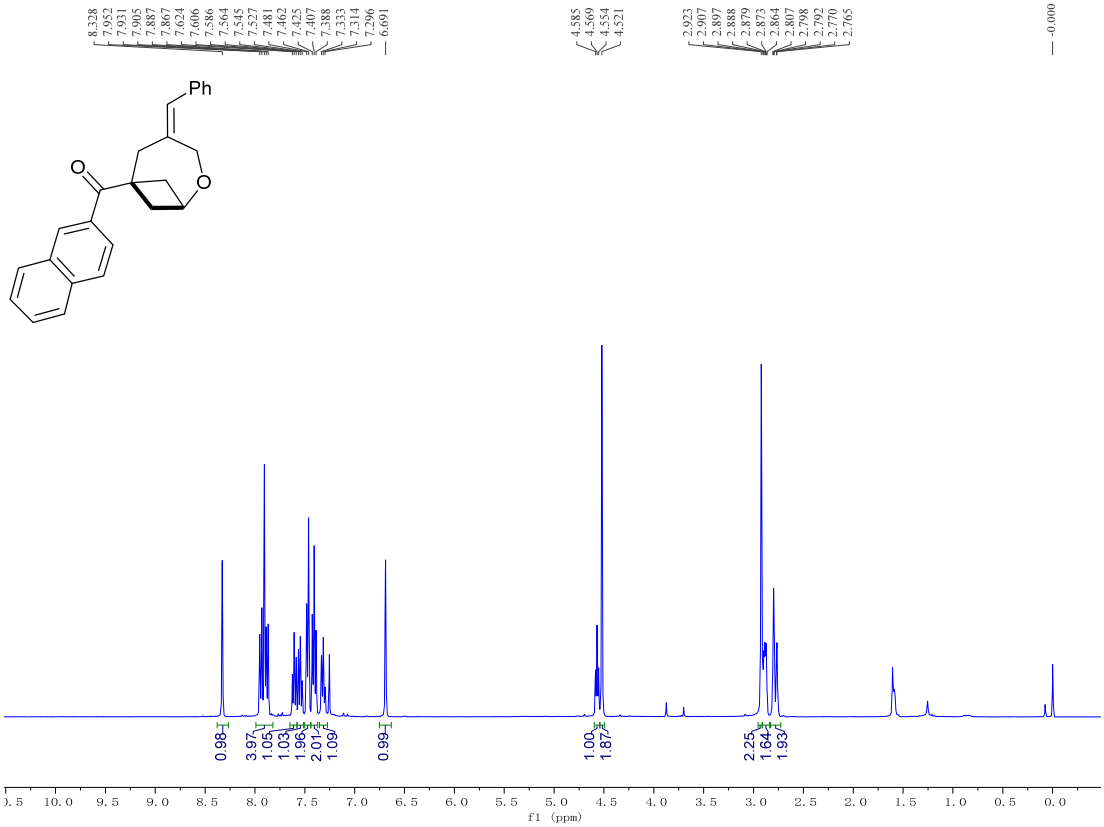


^{13}C NMR (100 MHz, $CDCl_3$)

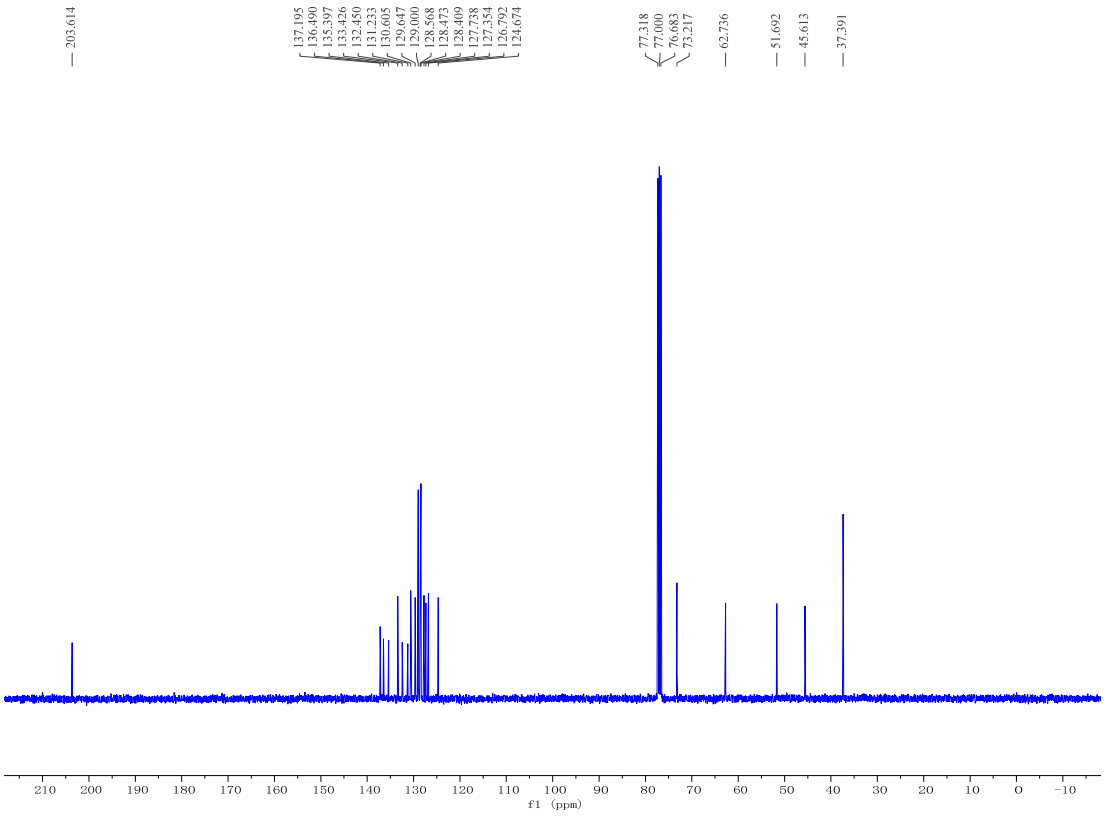


^{1}H and ^{13}C NMR Spectra for Compound 3ab

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

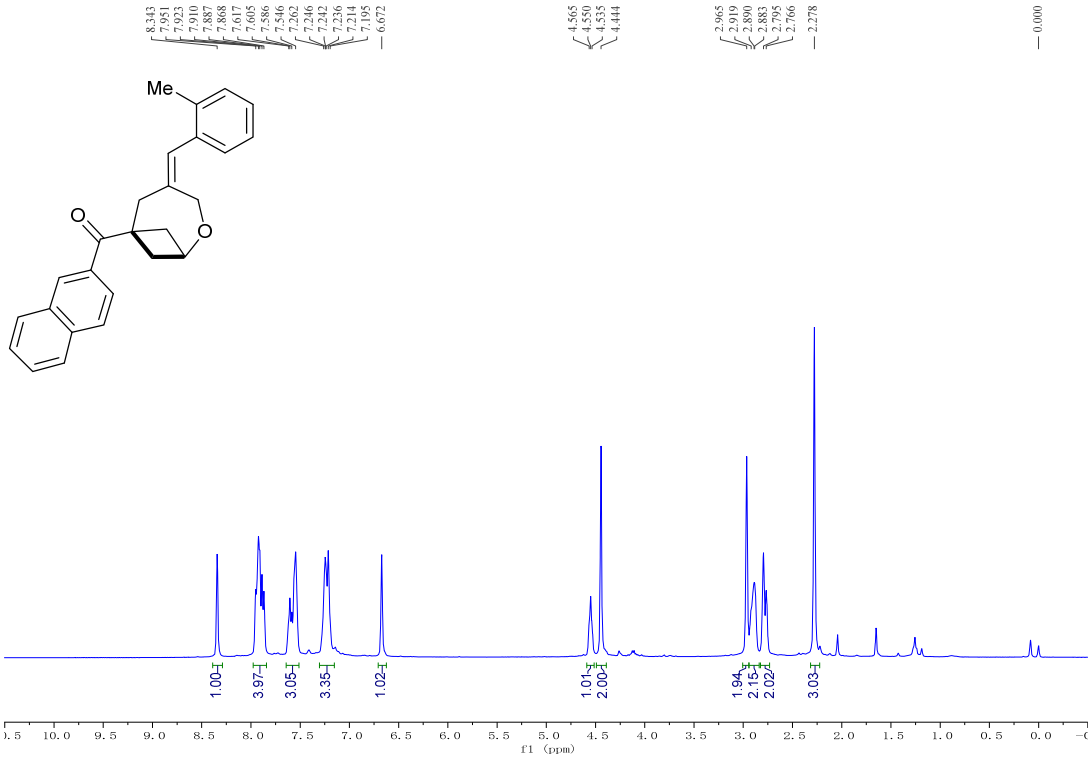


^{13}C NMR (100 MHz, $CDCl_3$)

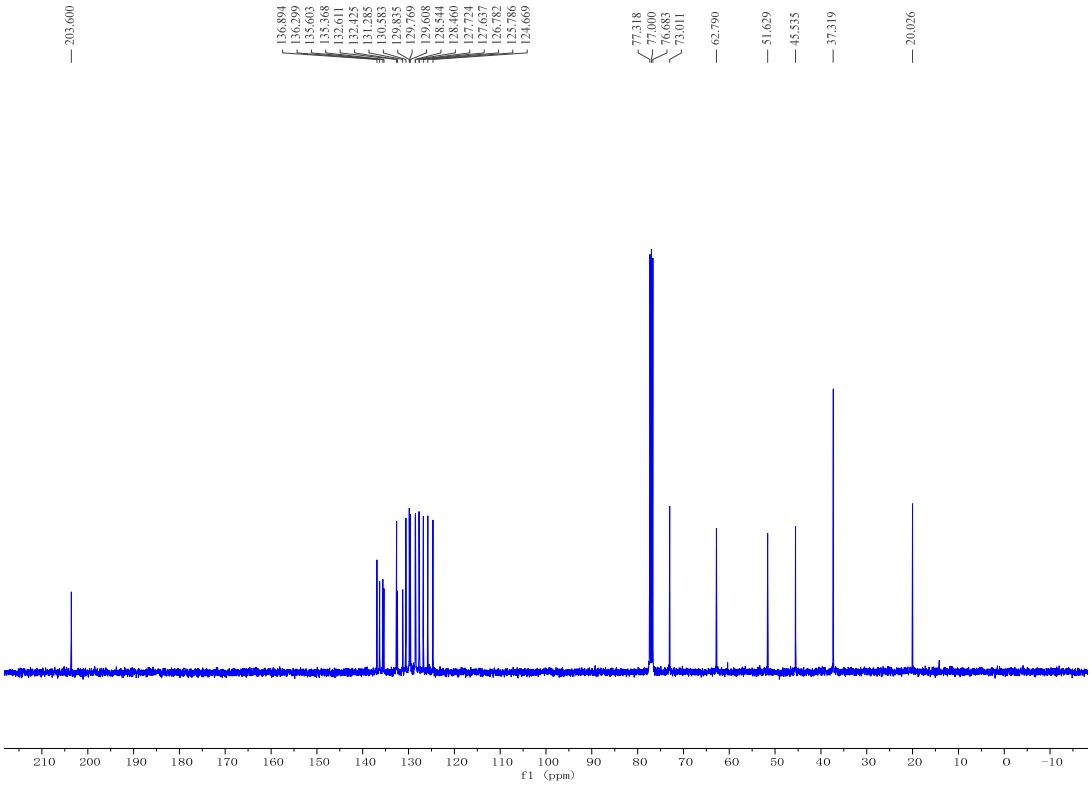


^{1}H and ^{13}C NMR Spectra for Compound 3ac:

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

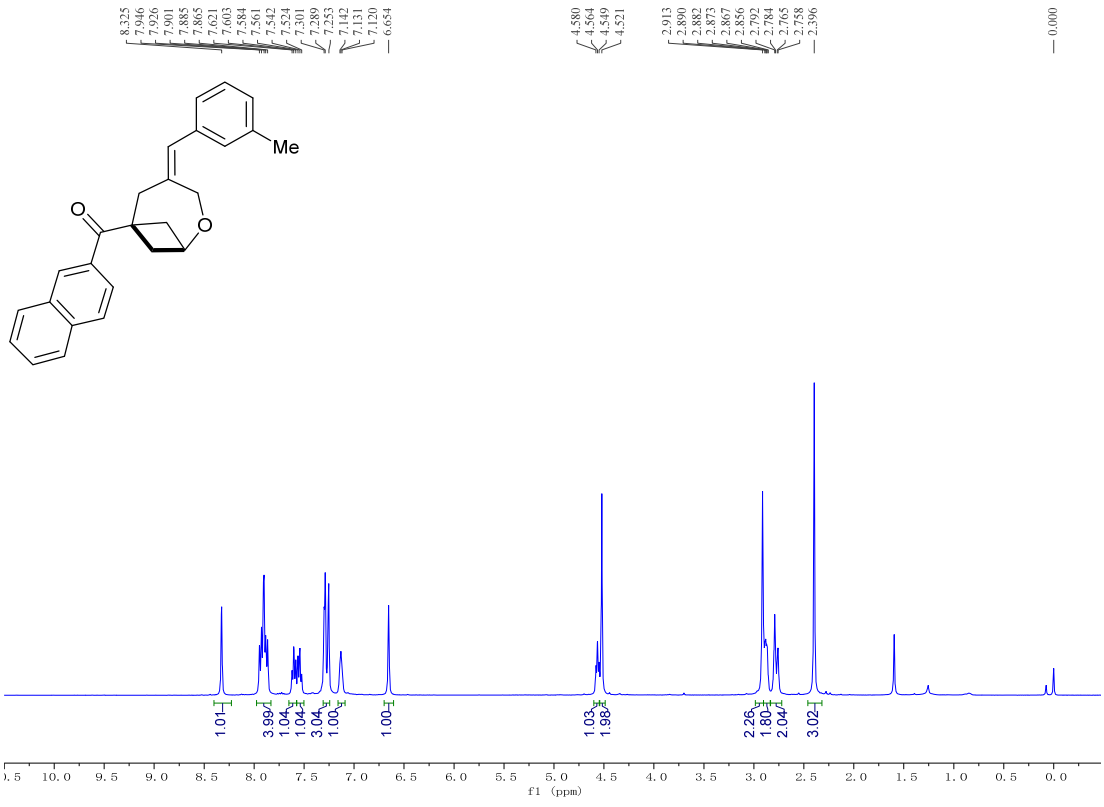


^{13}C NMR (100 MHz, $CDCl_3$)

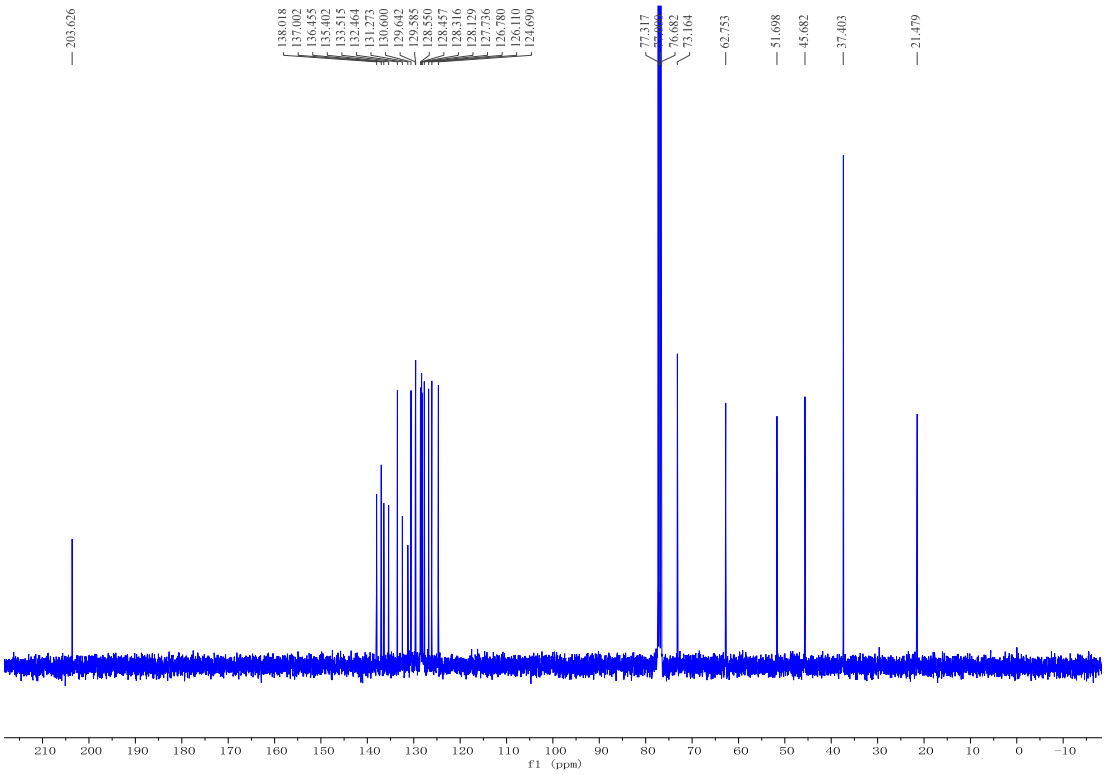


^{1}H and ^{13}C NMR Spectra for Compound 3ad:

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

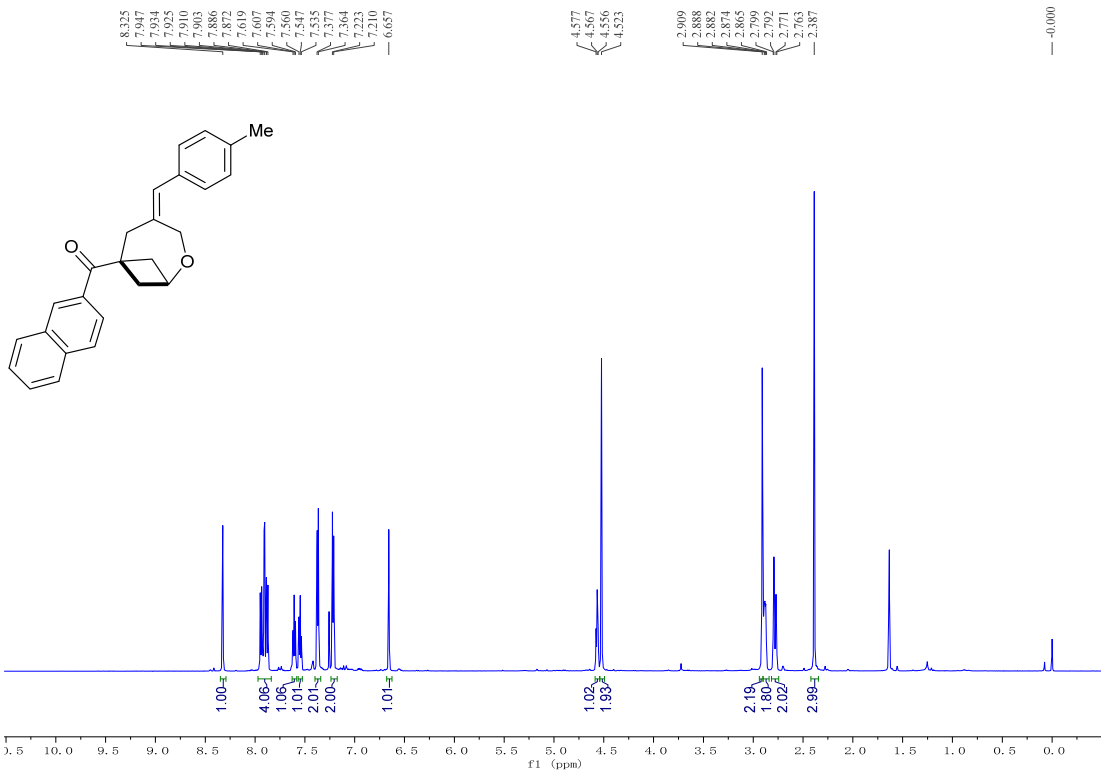


^{13}C NMR (100 MHz, $CDCl_3$)

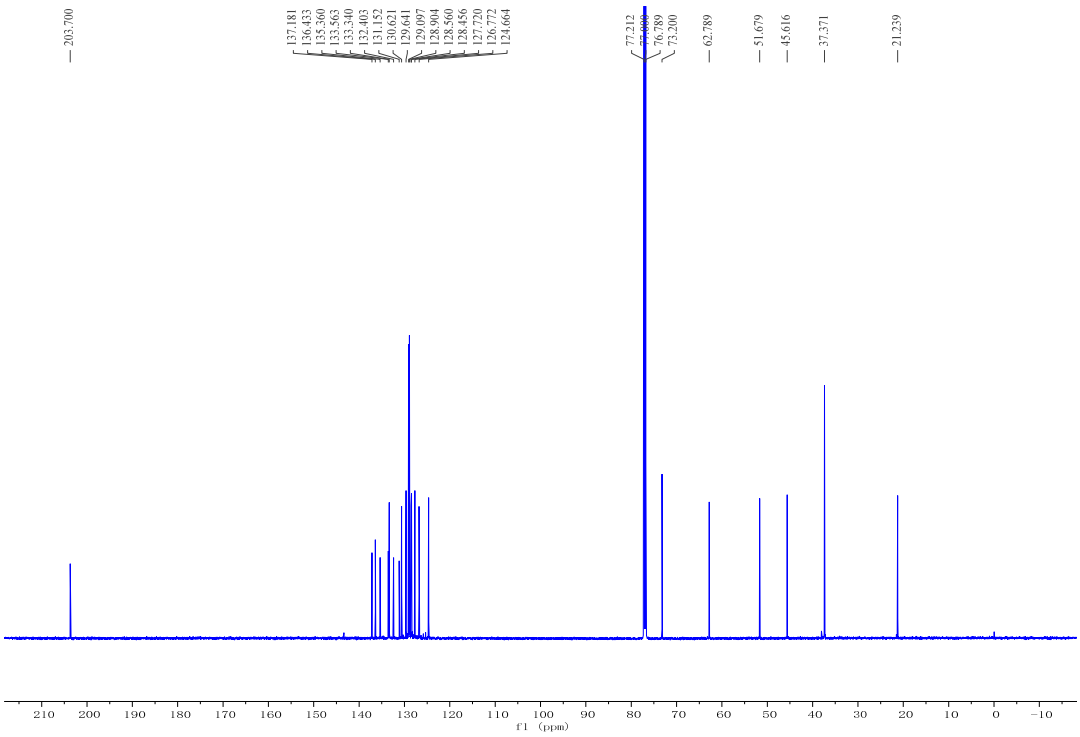


^{1}H and ^{13}C NMR Spectra for Compound 3ae

^{1}H NMR (600 MHz, $CDCl_3$)

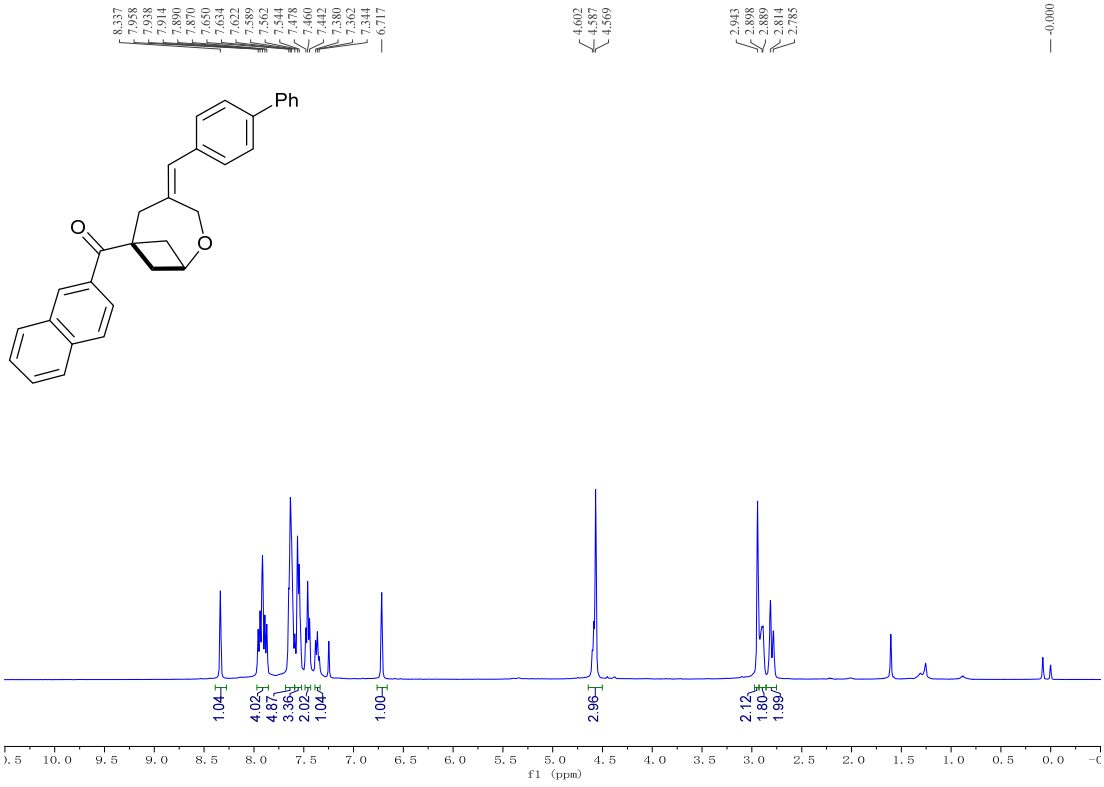


^{13}C NMR (150 MHz, $CDCl_3$)

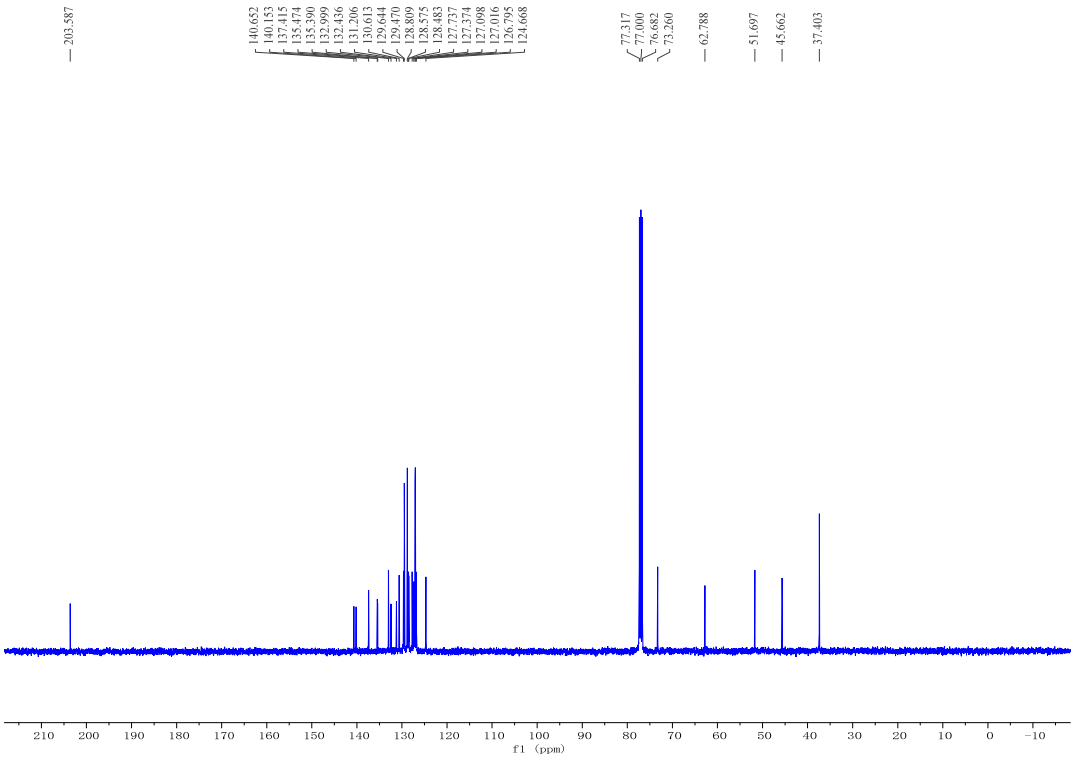


^{1}H and ^{13}C NMR Spectra for Compound 3af:

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

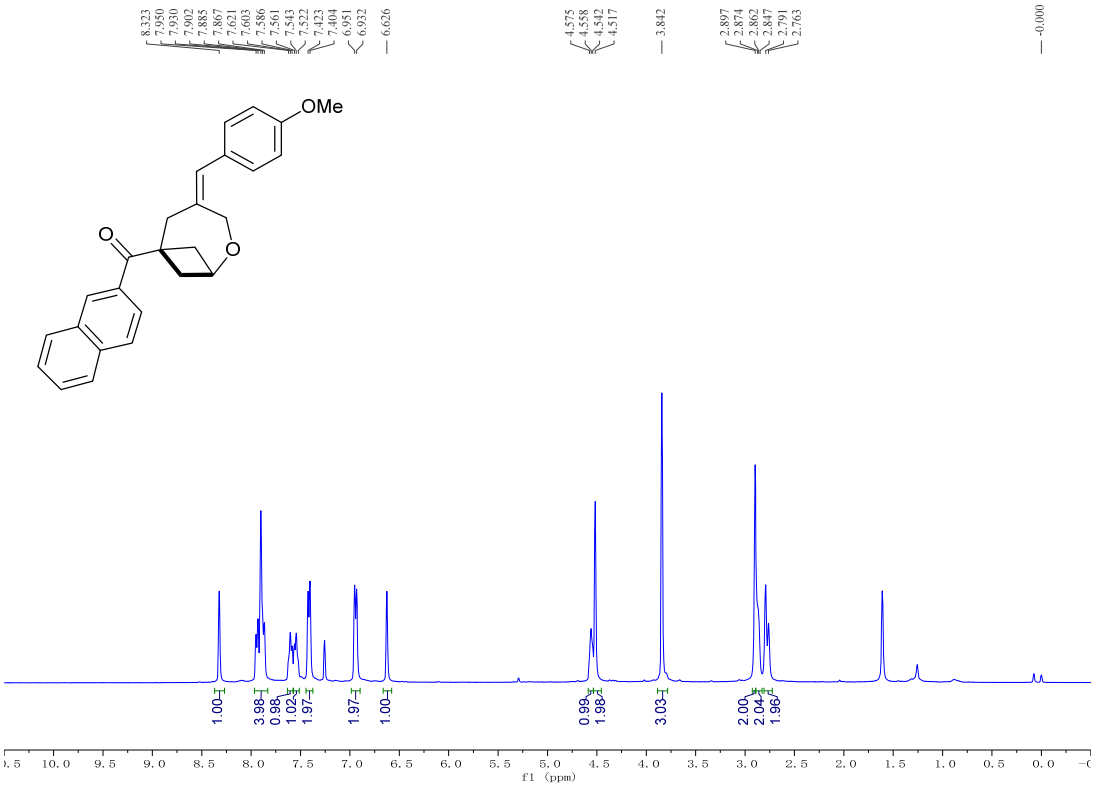


^{13}C NMR (100 MHz, $CDCl_3$)

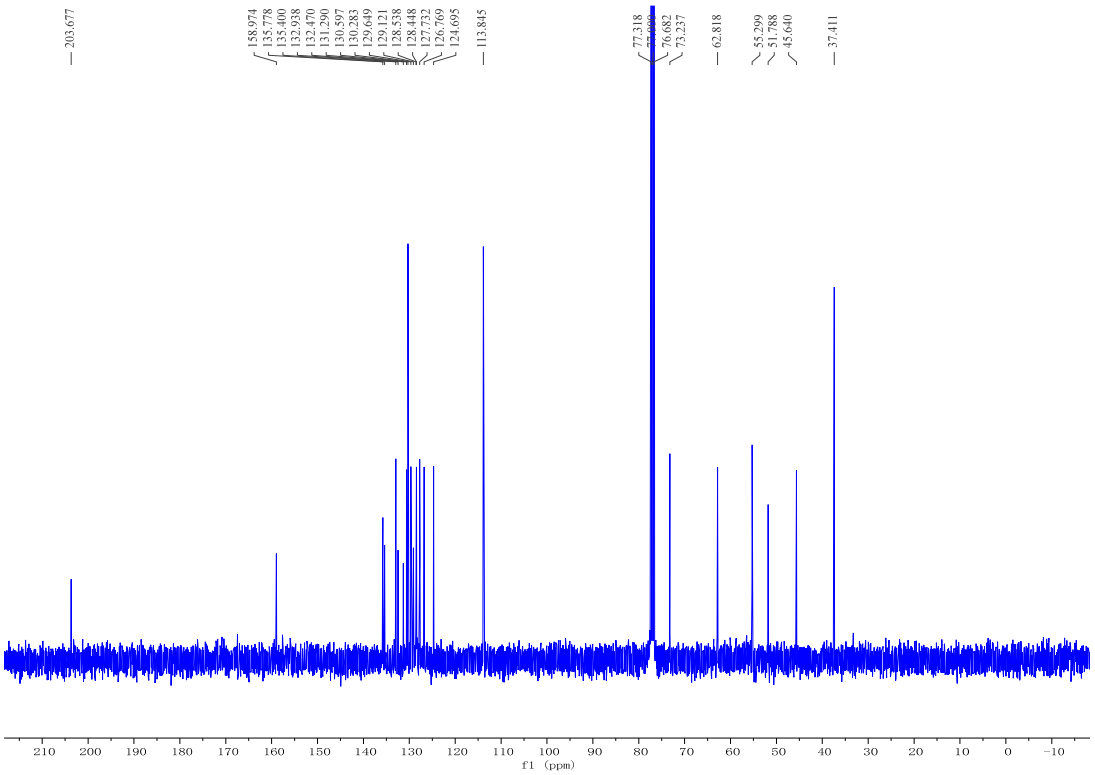


^{1}H and ^{13}C NMR Spectra for Compound 3ag:

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

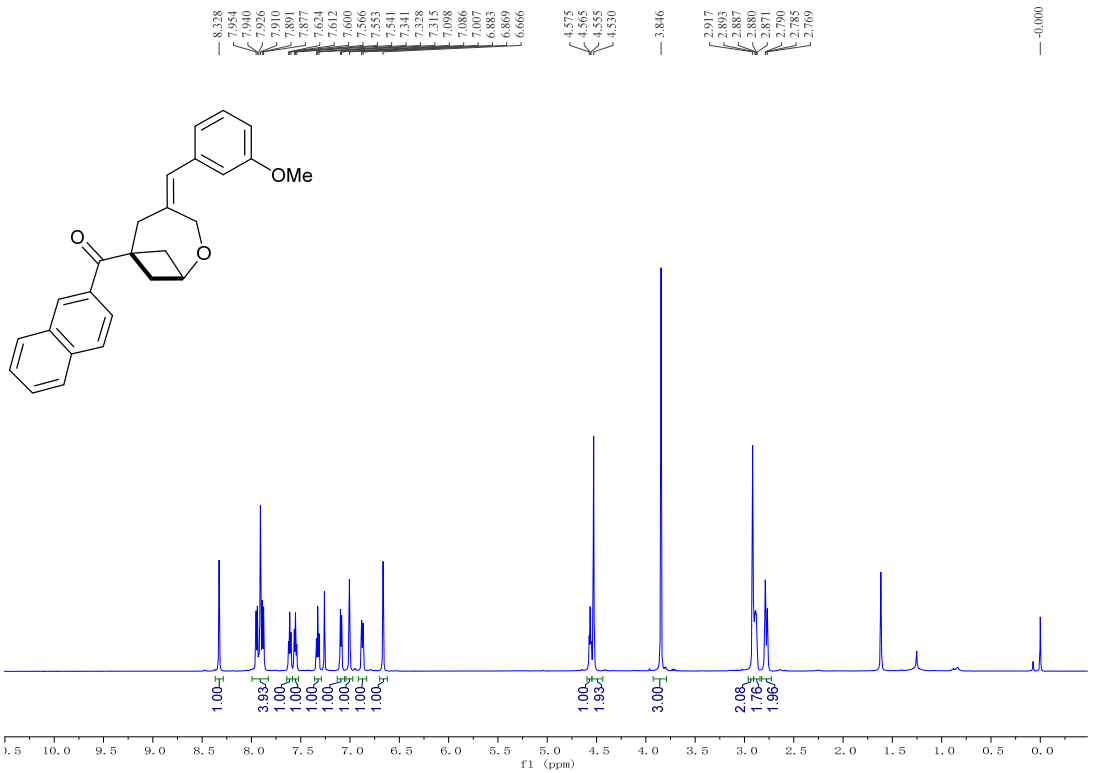


^{13}C NMR (100 MHz, $CDCl_3$)

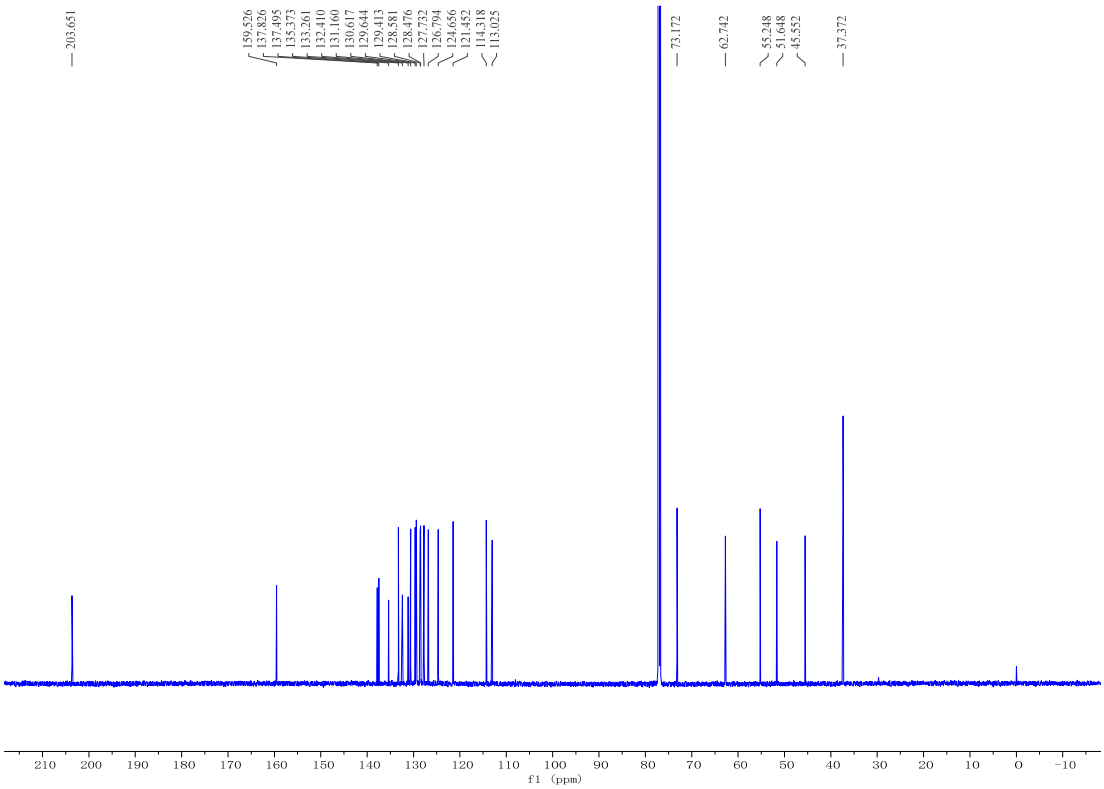


^{1}H and ^{13}C NMR Spectra for Compound 3ah:

^{1}H NMR (600 MHz, $CDCl_3$)

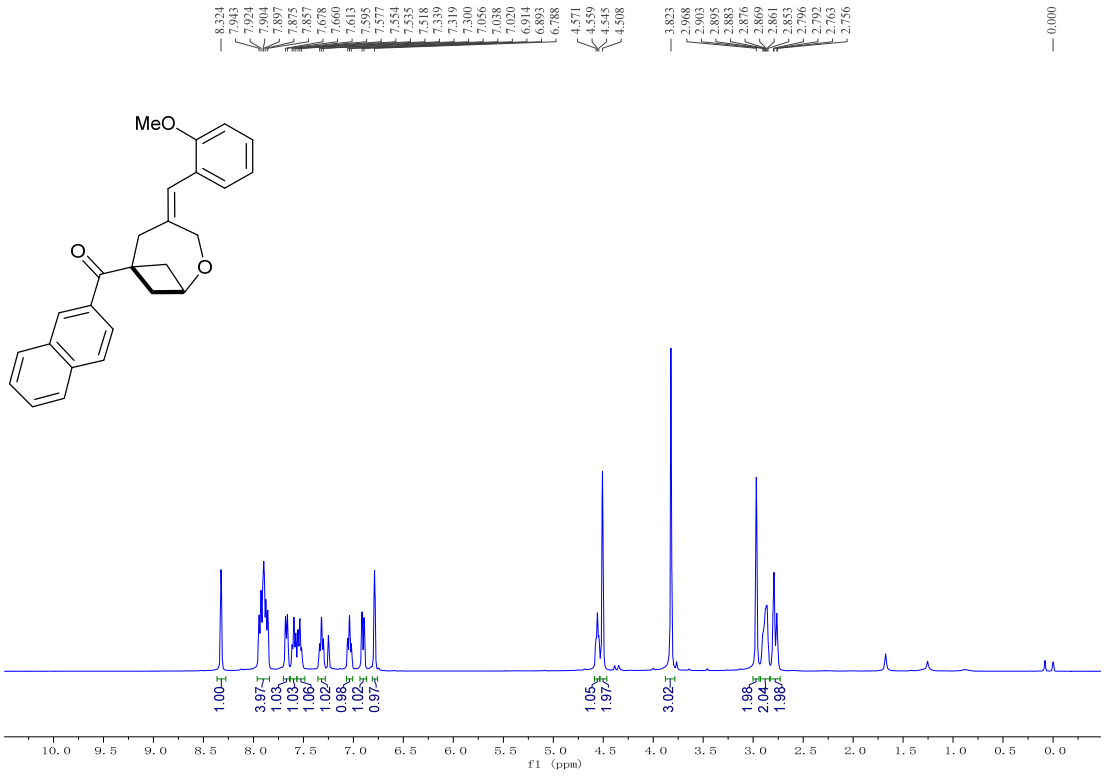


^{13}C NMR (150 MHz, $CDCl_3$)

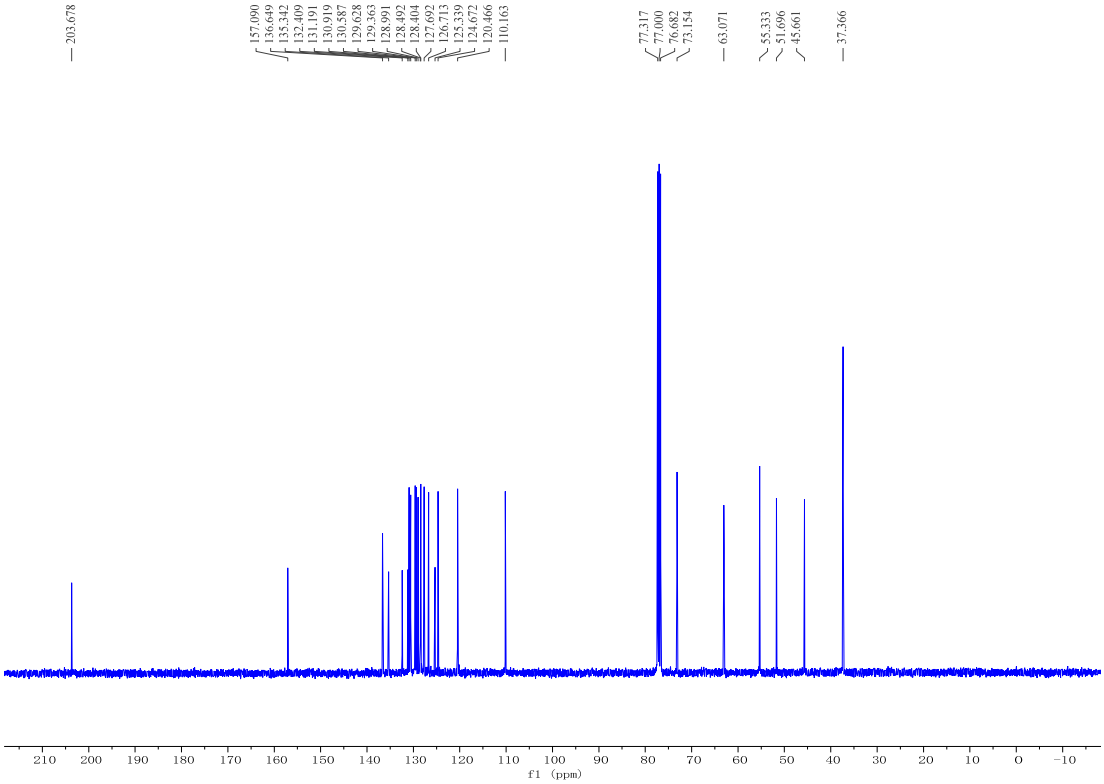


^{1}H and ^{13}C NMR Spectra for Compound 3ai:

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

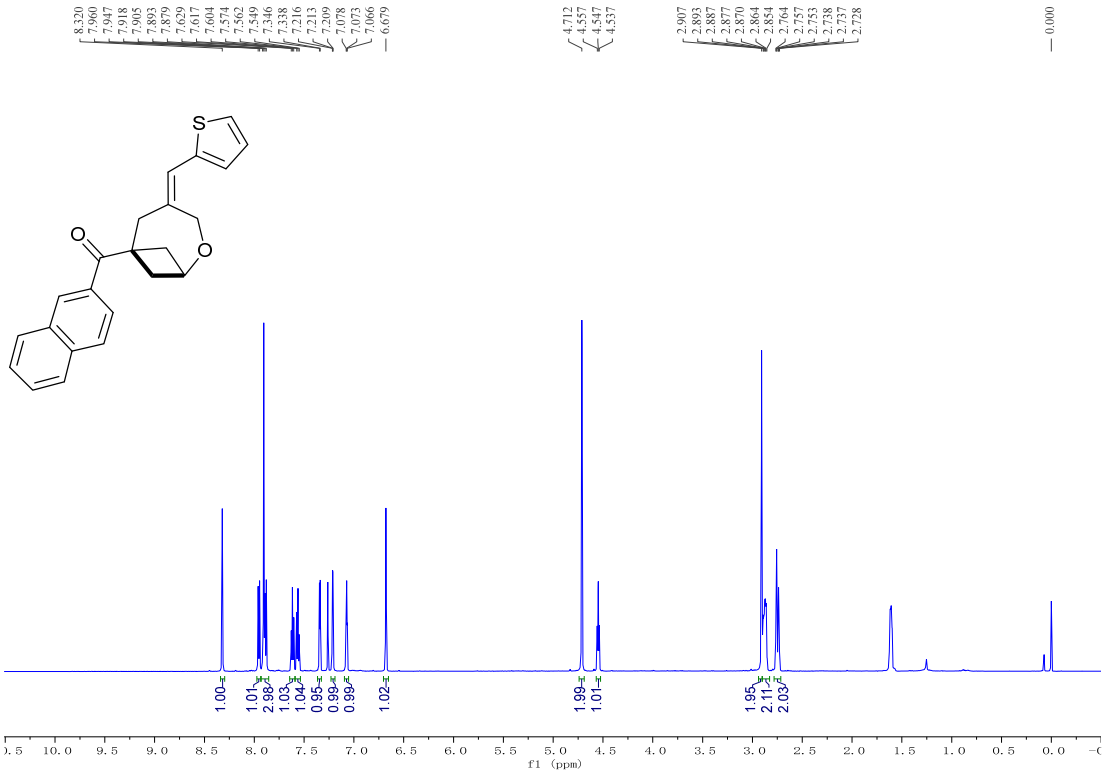


^{13}C NMR (100 MHz, $CDCl_3$)

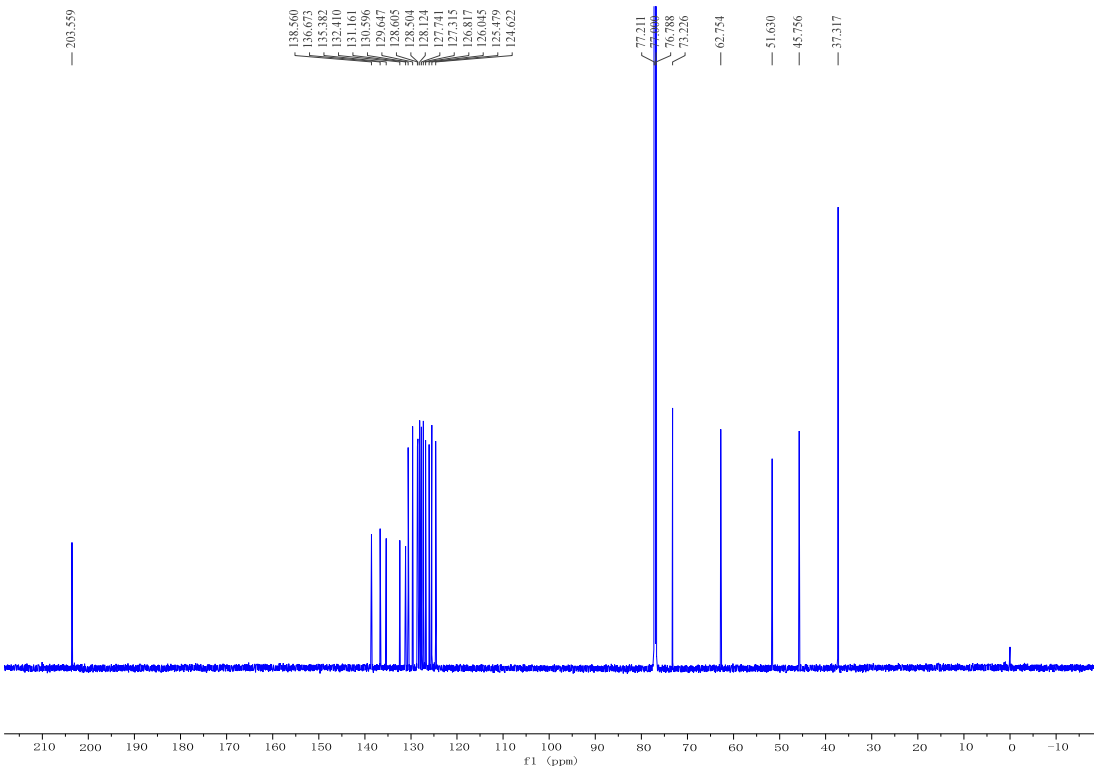


^{1}H and ^{13}C NMR Spectra for Compound 3aj:

^{1}H NMR (600 MHz, $CDCl_3$)

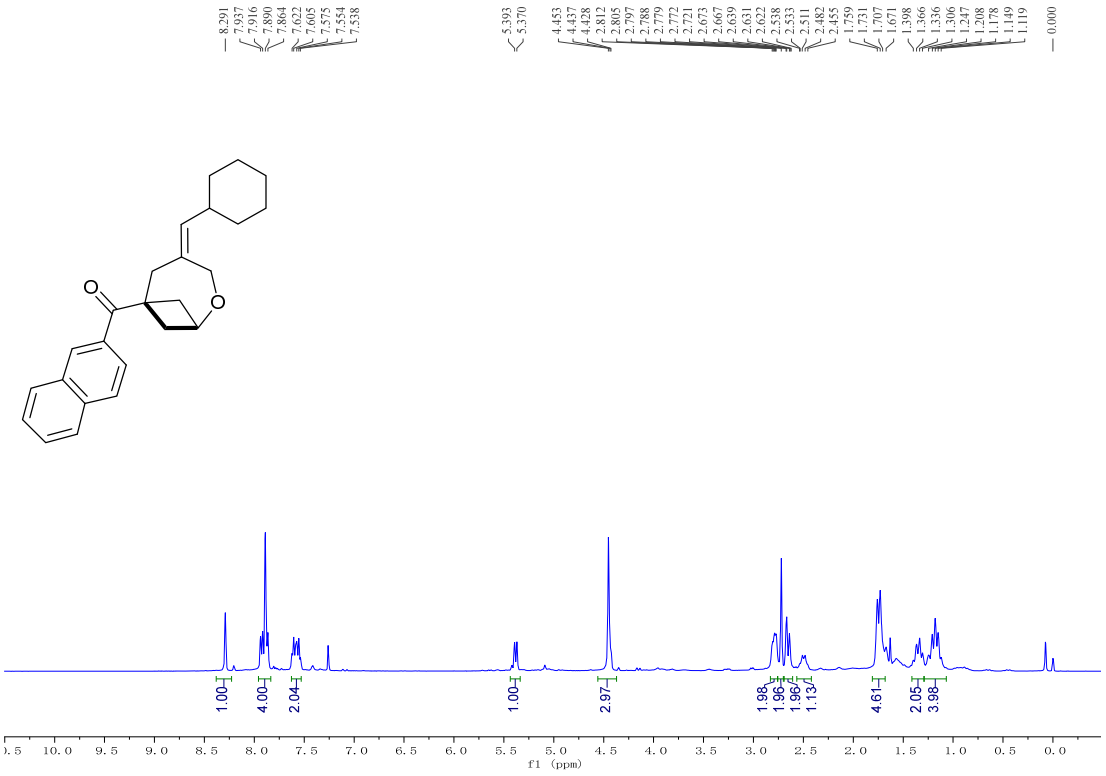


^{13}C NMR (150 MHz, $CDCl_3$)

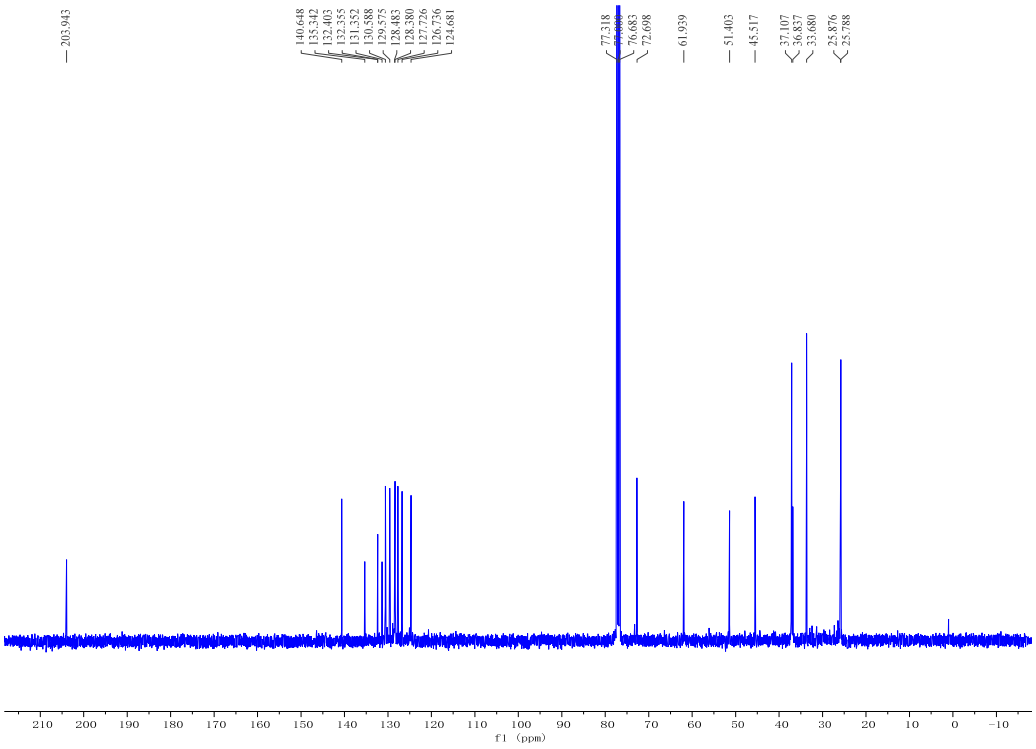


^{1}H and ^{13}C NMR Spectra for Compound 3ak:

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

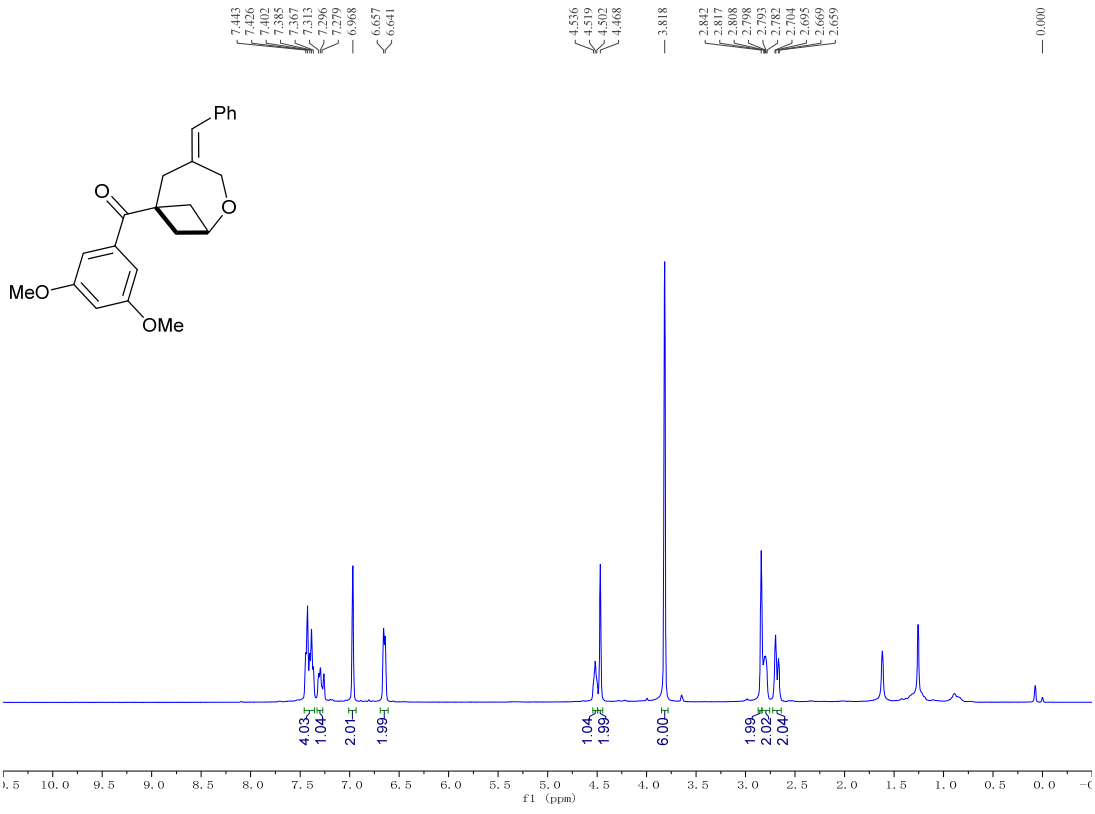


^{13}C NMR (100 MHz, $CDCl_3$)

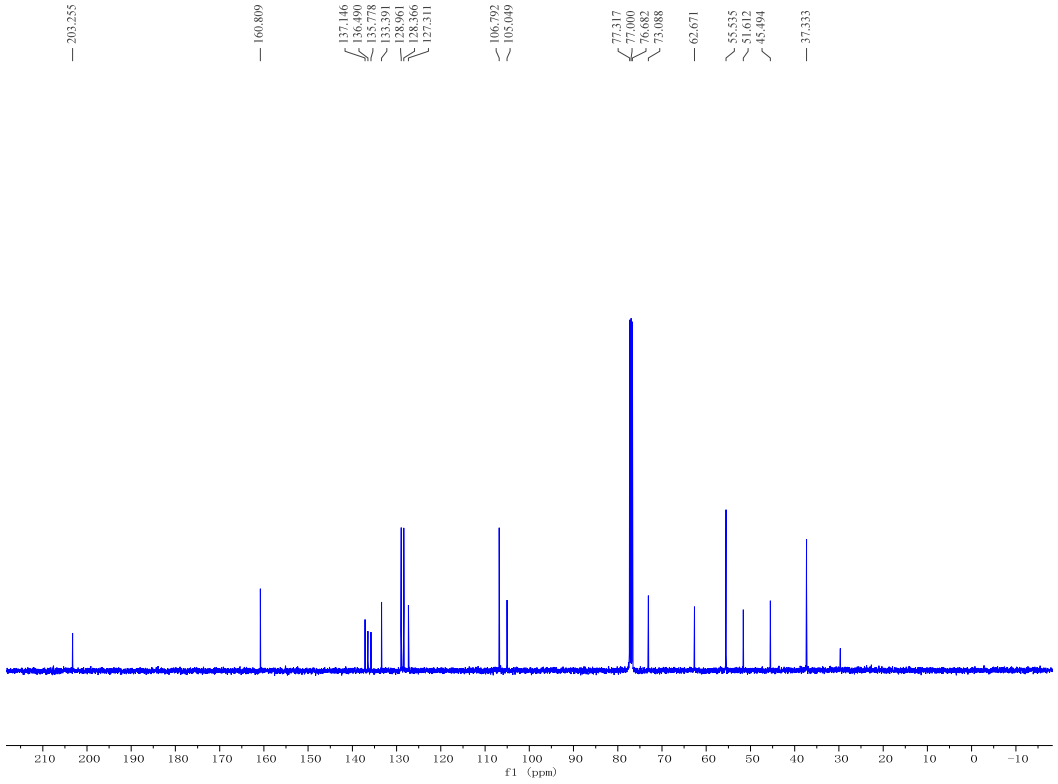


^{1}H and ^{13}C NMR Spectra for Compound (*Z*)-3dl:

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

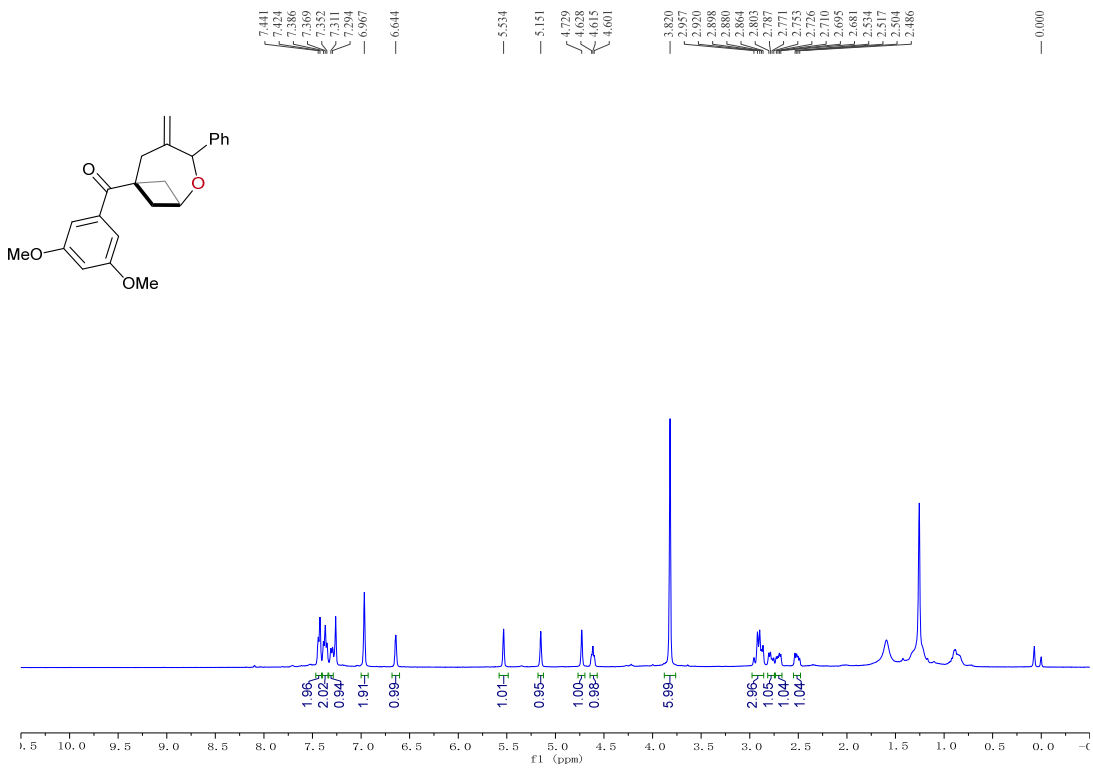


^{13}C NMR (100 MHz, $CDCl_3$)

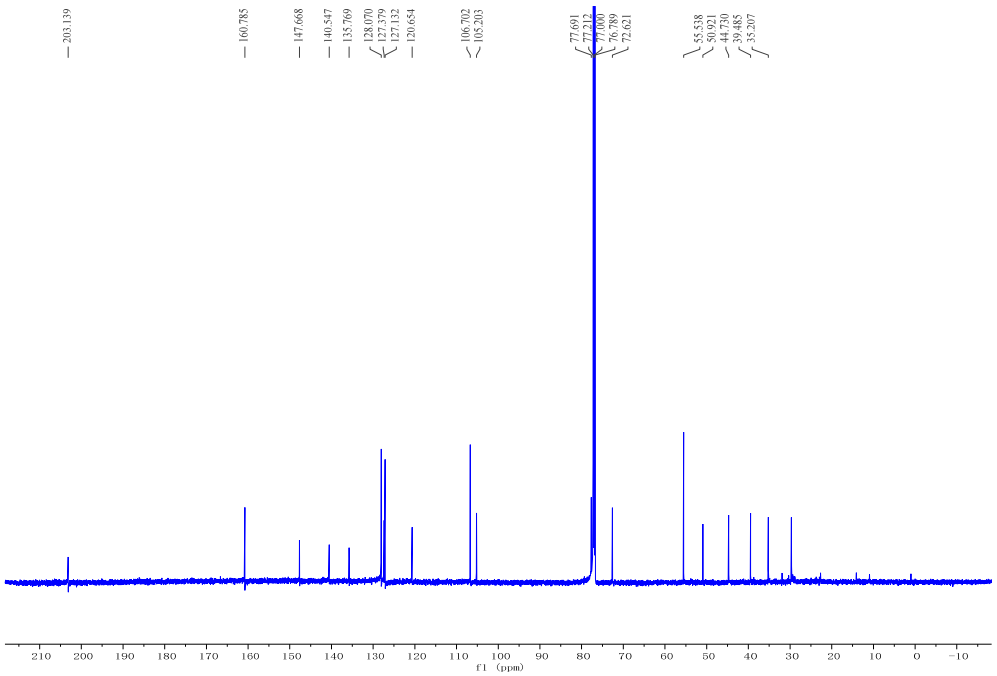


^{1}H and ^{13}C NMR Spectra for Compound 4dl':

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

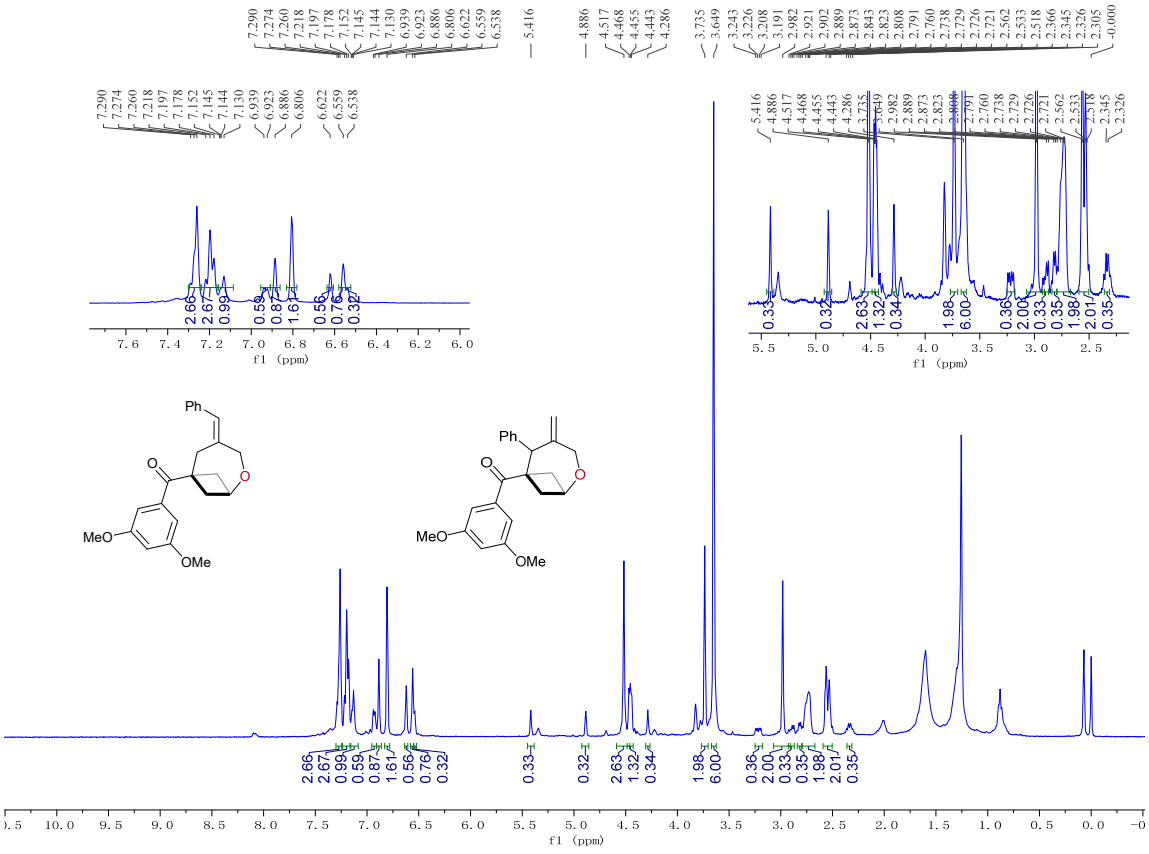


^{13}C NMR (150 MHz, $CDCl_3$)

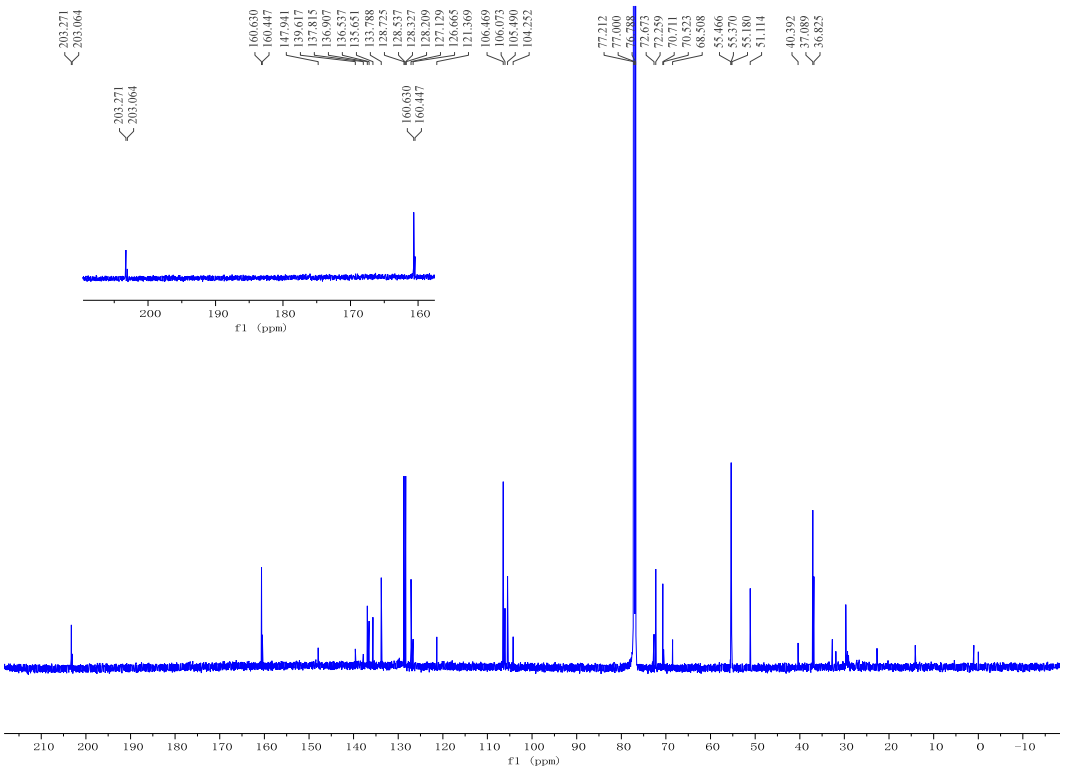


^{1}H and ^{13}C NMR Spectra for Compound (*E*)-3dl and 4dl:

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

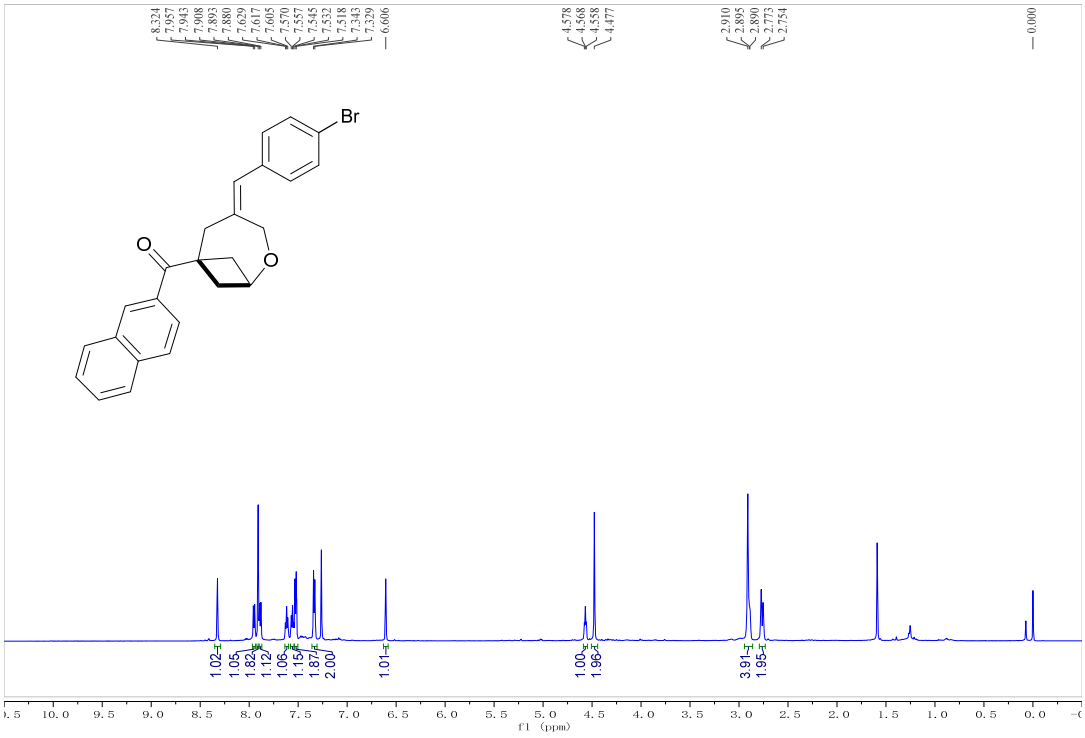


^{3}C NMR (150 MHz, $CDCl_3$)

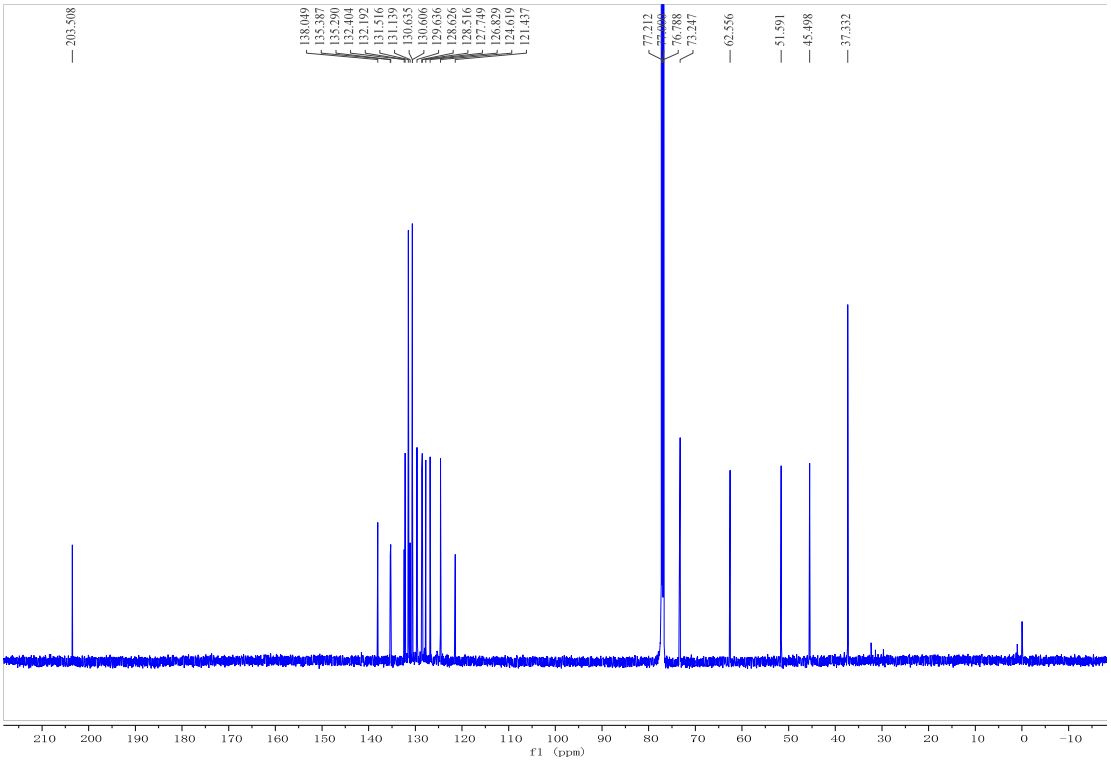


^{1}H and ^{13}C NMR Spectra for Compound 3am:

^{1}H NMR (600 MHz, $CDCl_3$)

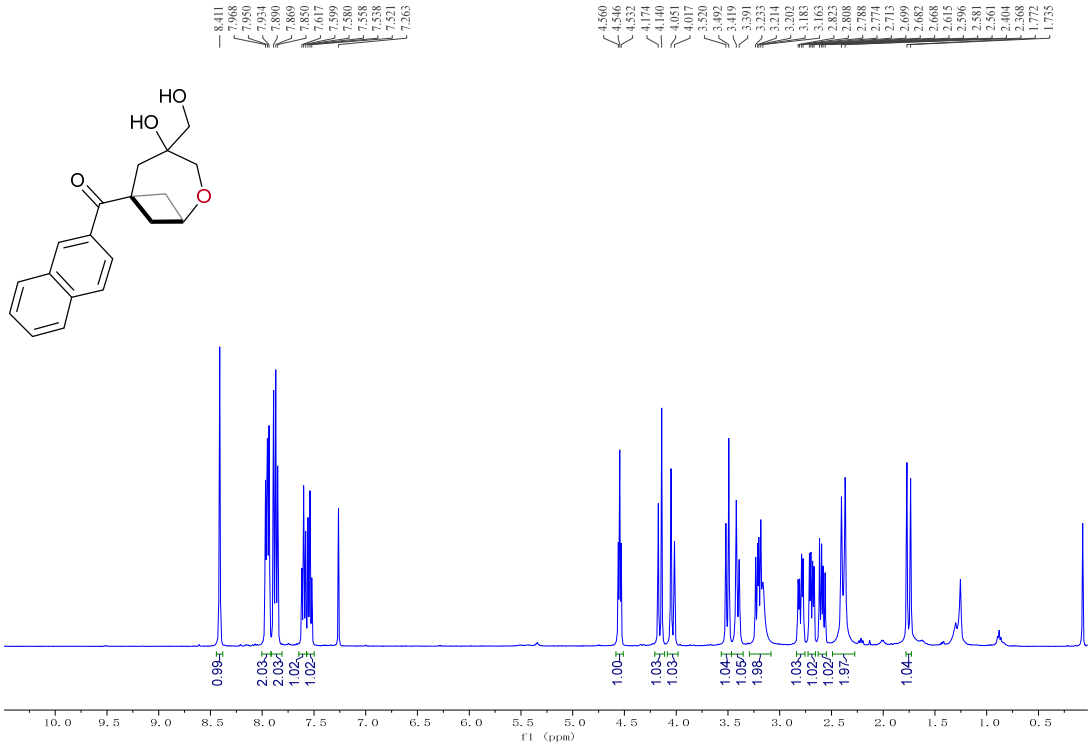


^{13}C NMR (150 MHz, $CDCl_3$)

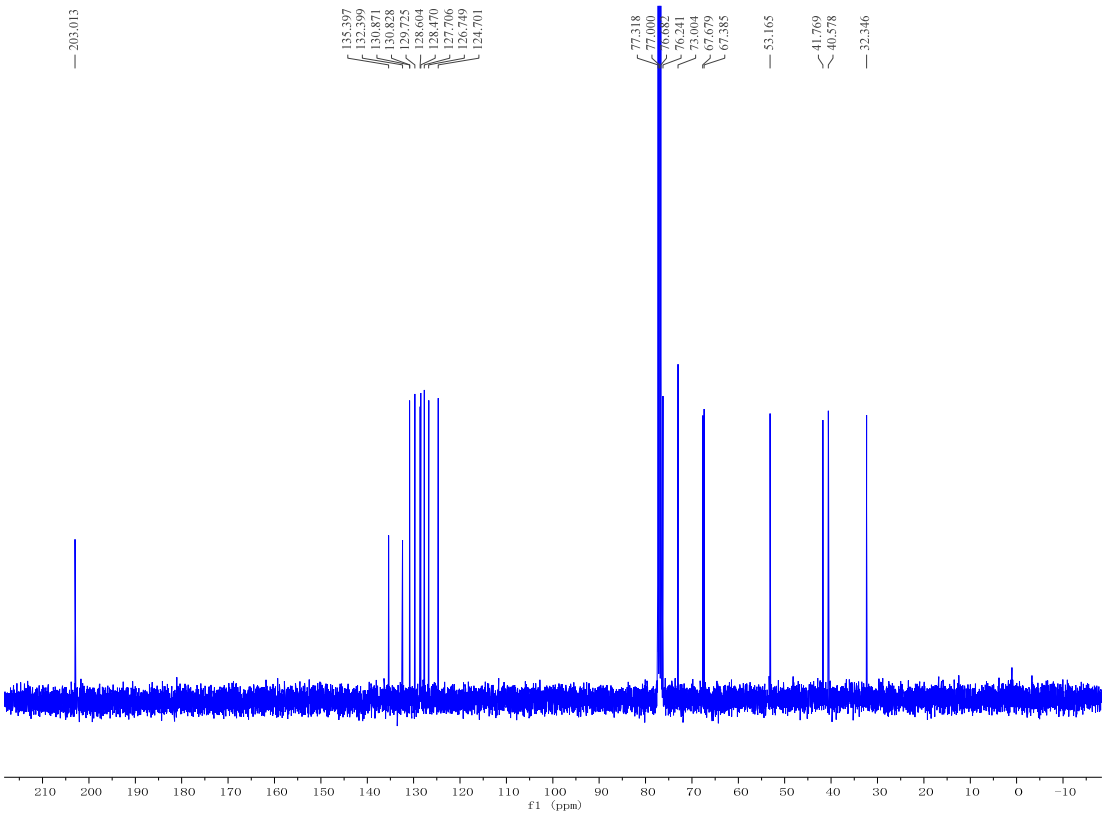


^{1}H and ^{13}C NMR Spectra for Compound 6

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

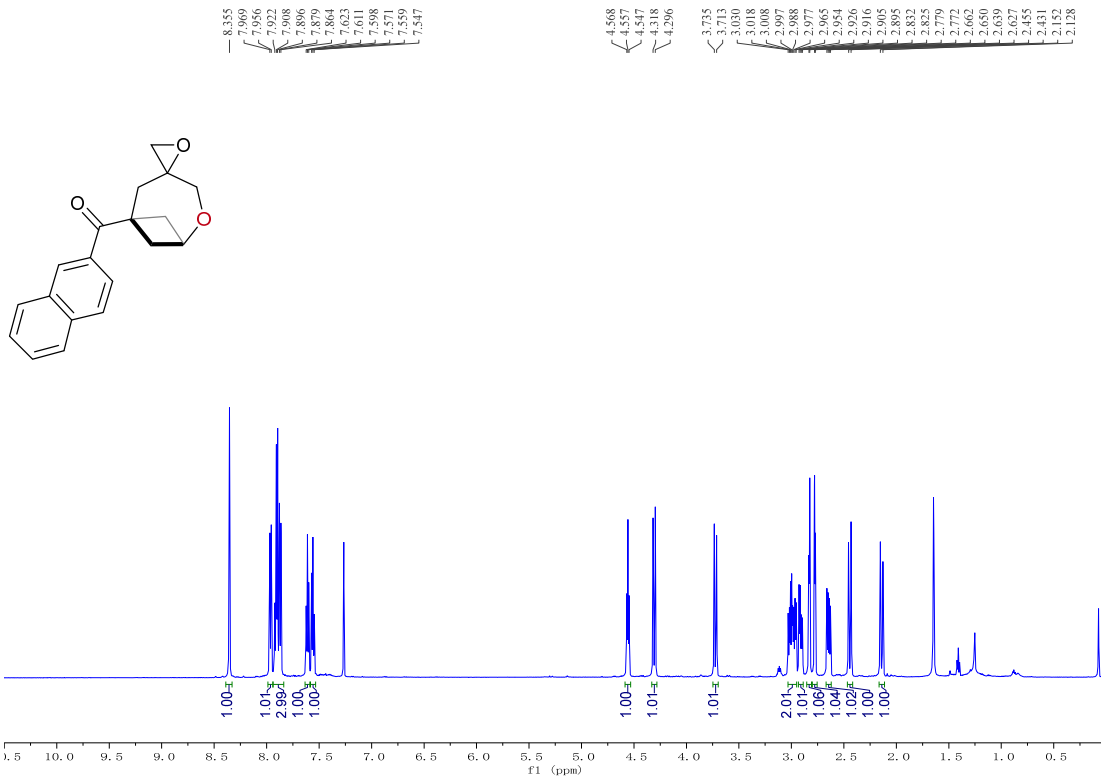


^{13}C NMR (100 MHz, $CDCl_3$)

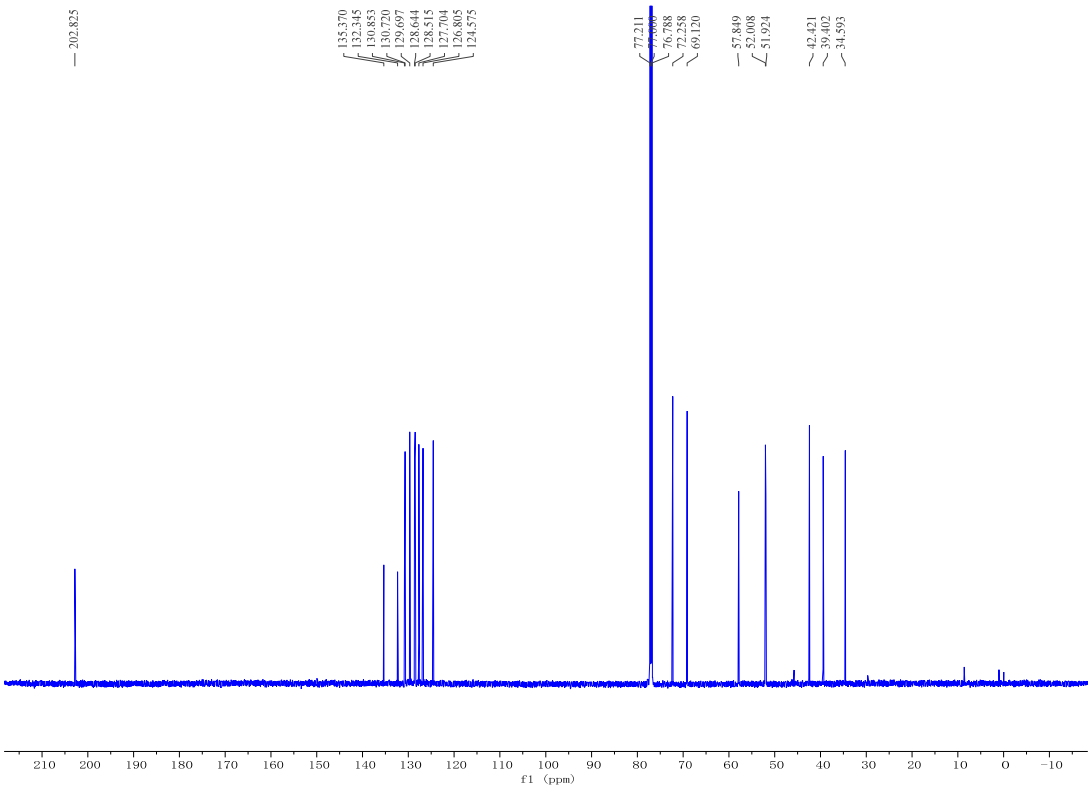


^{1}H and ^{13}C NMR Spectra for Compound 7

^{1}H NMR (600 MHz, $CDCl_3$)

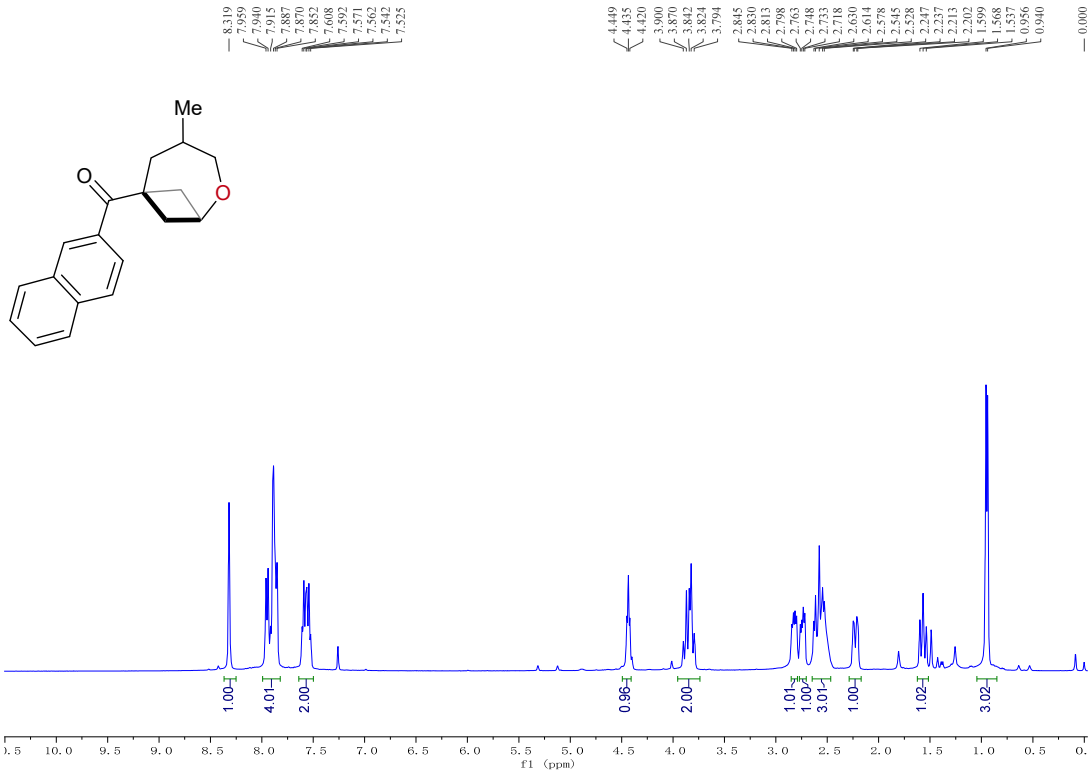


^{13}C NMR (100 MHz, $CDCl_3$)

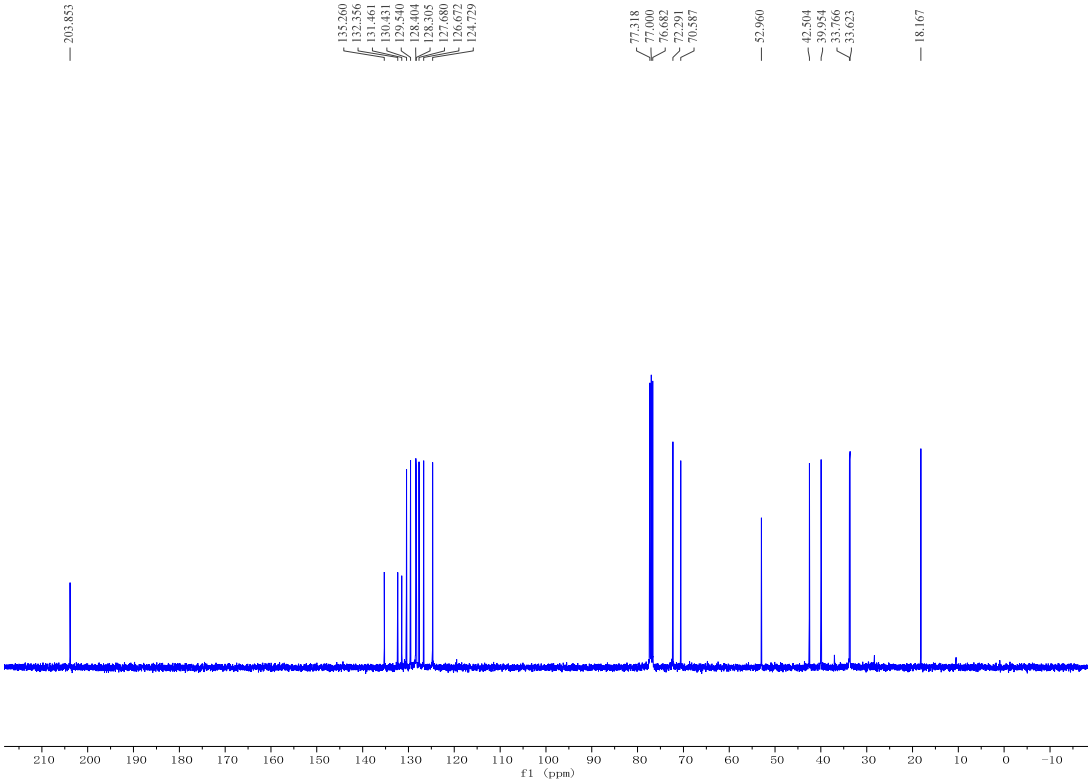


^{1}H and ^{13}C NMR Spectra for Compound 8

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

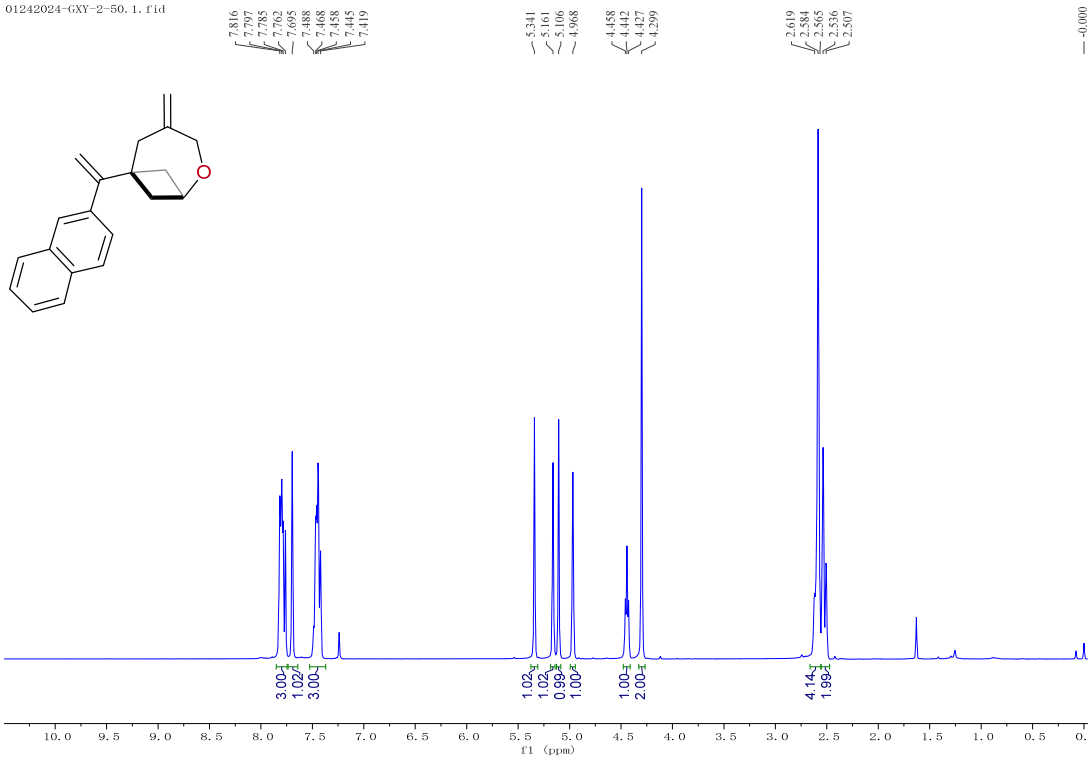


^{13}C NMR (100 MHz, $CDCl_3$)

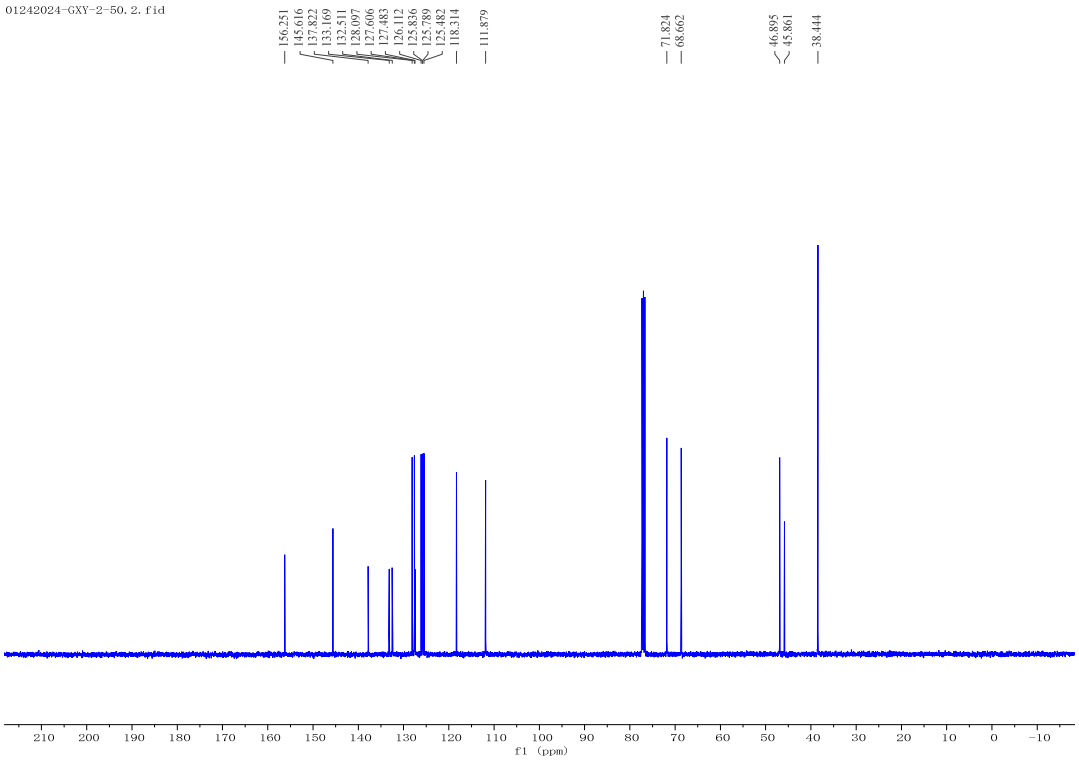


^{1}H and ^{13}C NMR Spectra for Compound 9

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

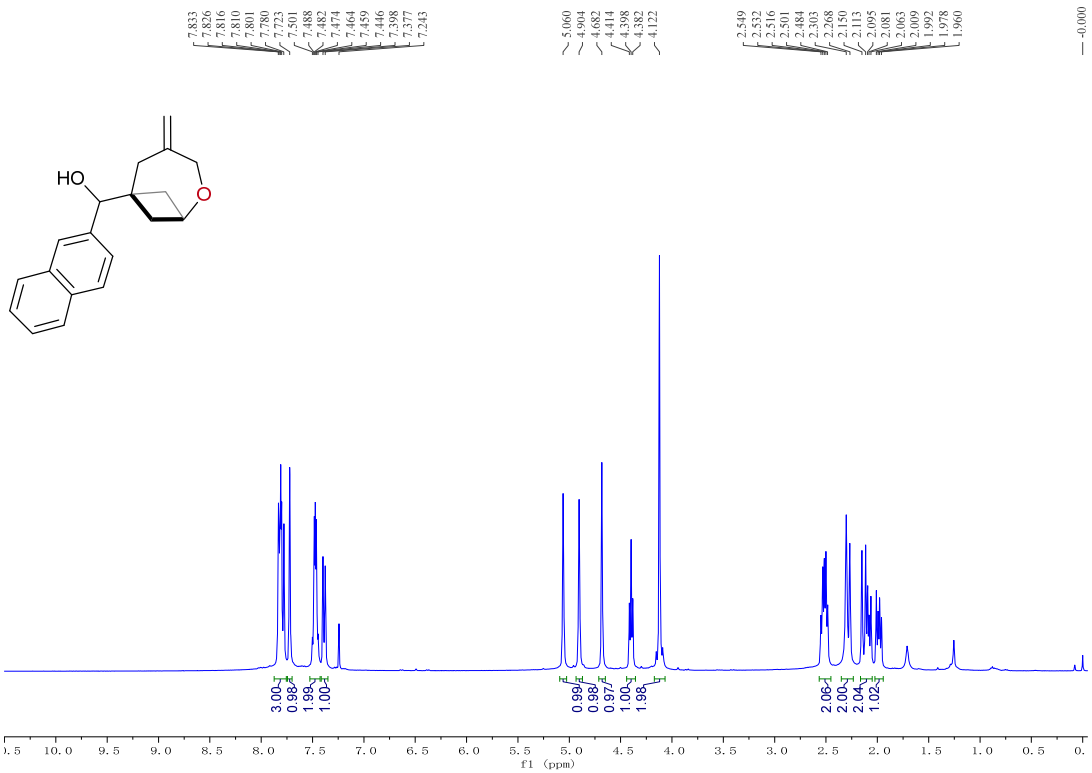


^{13}C NMR (100 MHz, $CDCl_3$)

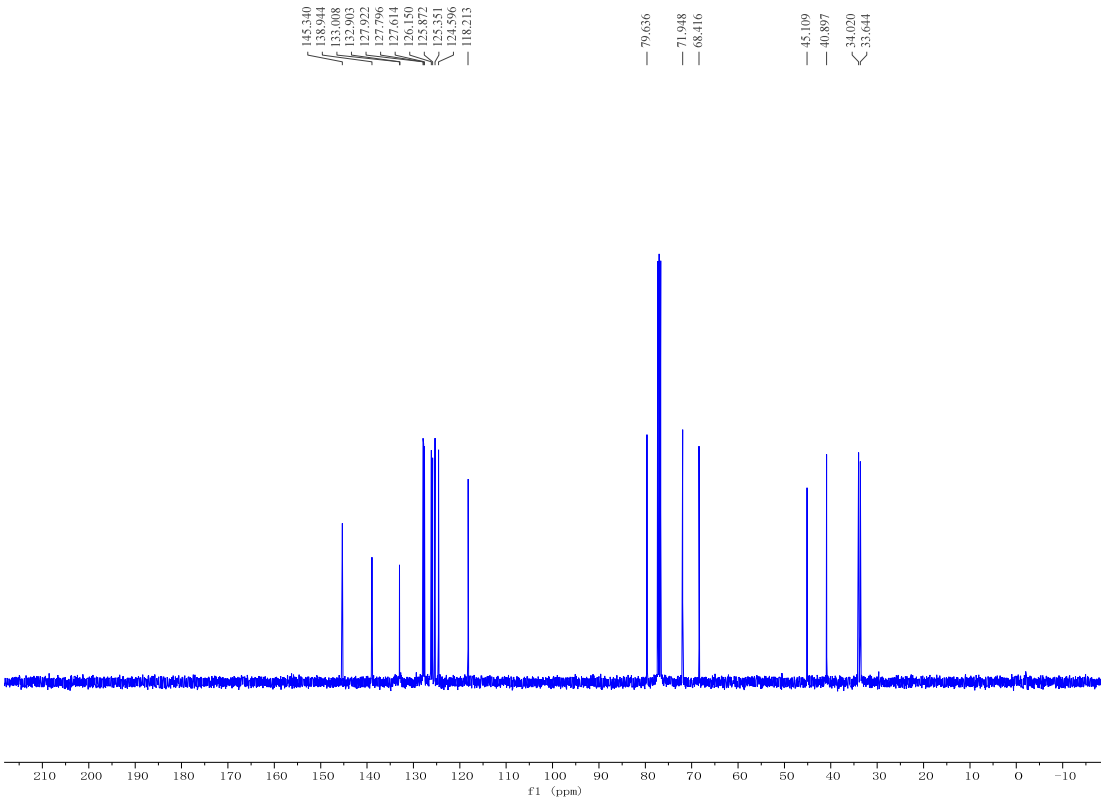


^{1}H and ^{13}C NMR Spectra for Compound 10

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

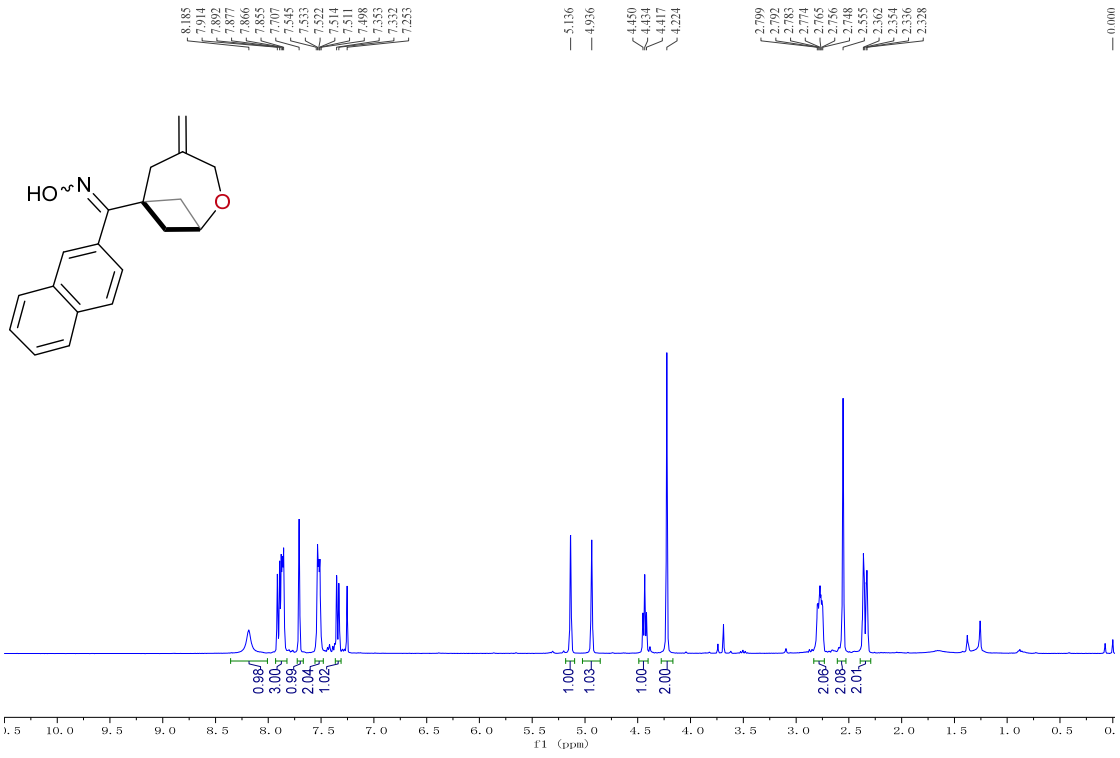


^{13}C NMR (100 MHz, $CDCl_3$)

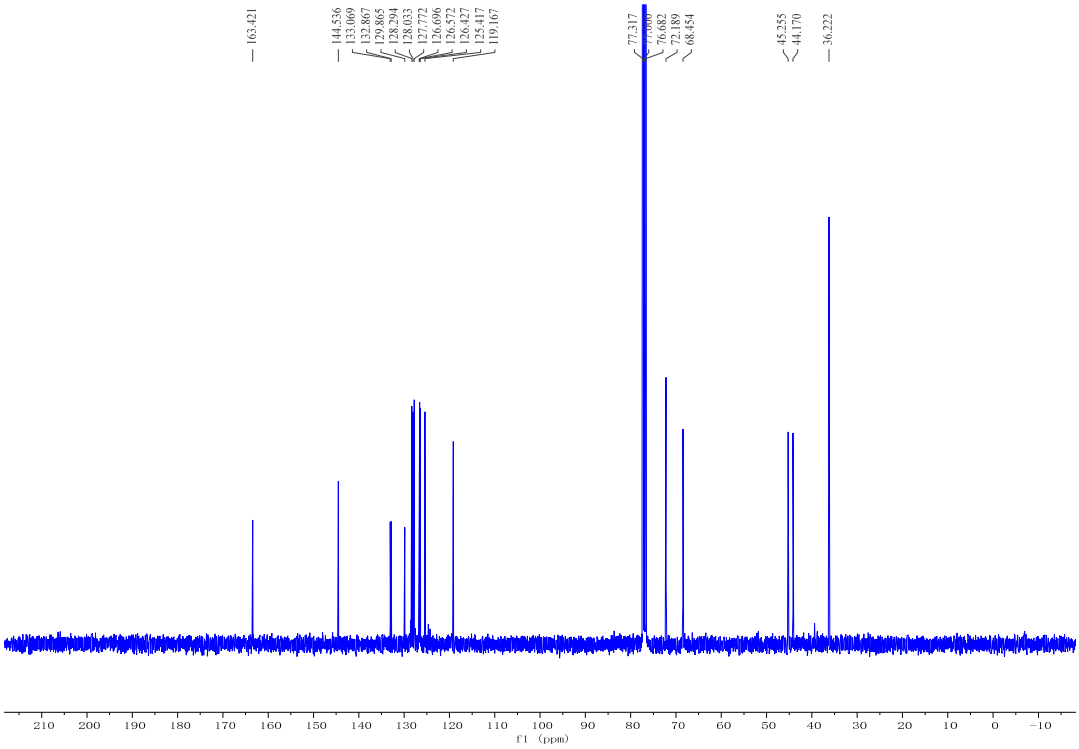


^{1}H and ^{13}C NMR Spectra for Compound 11

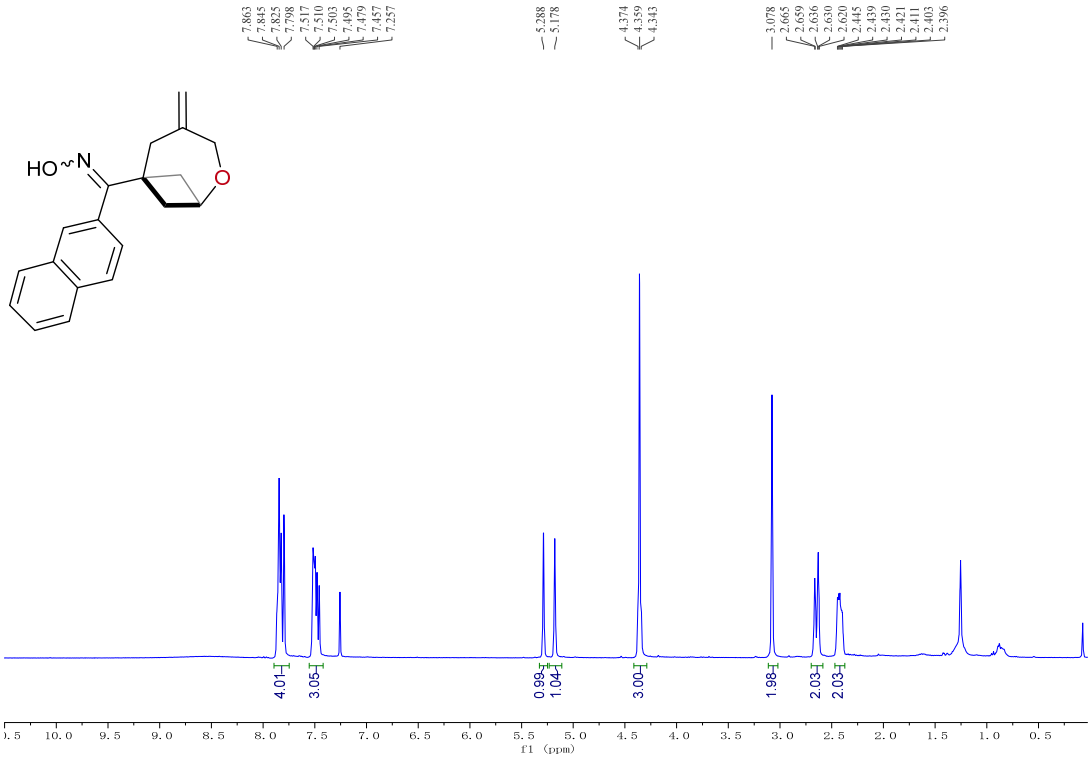
^{1}H NMR (400 MHz, $CDCl_3$) for the major isomer



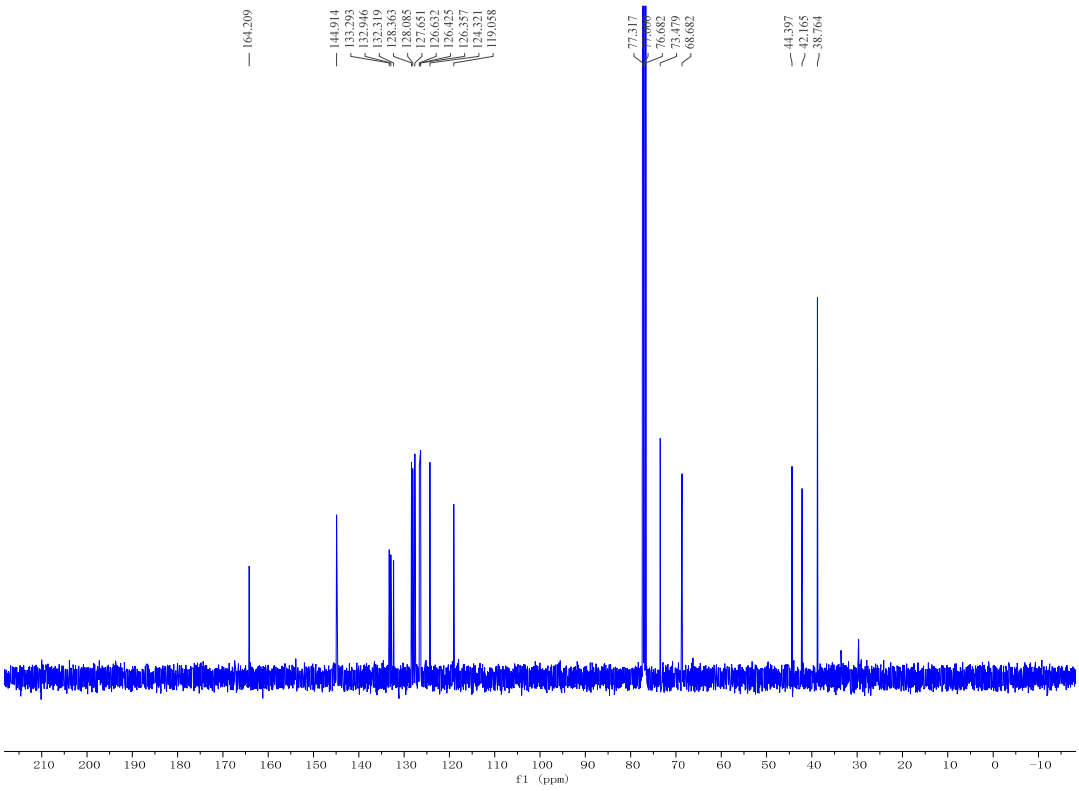
^{13}C NMR (100 MHz, $CDCl_3$) for the major isomer



^{1}H NMR (400 MHz, $CDCl_3$) for the minor isomer



^{13}C NMR (100 MHz, $CDCl_3$) for the minor isomer



12 References

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