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Graphical Abstract

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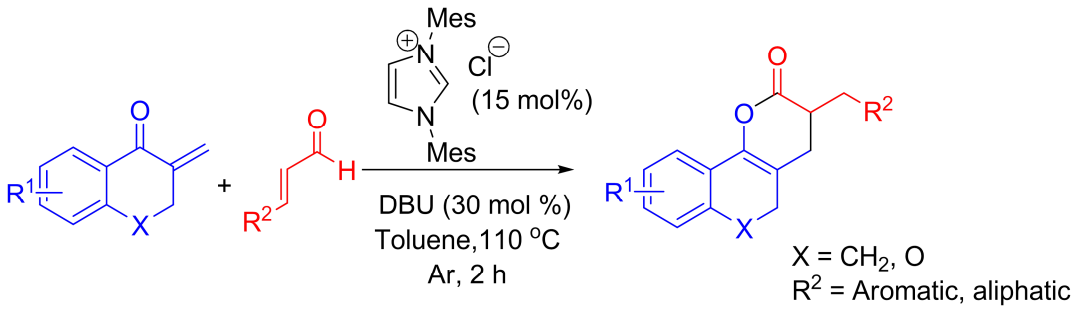

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Expedient Synthesis of Tricyclic Benzopyran-2-ones via N-Heterocyclic Carbene Catalyzed Annulation of Enals to α-Methylene Cycloalkanones[#]

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[#]*This paper is dedicated with best regards to Dr. Stanley Lang in honor of his contributions to Heterocyclic Chemistry and his service to ISHC.*

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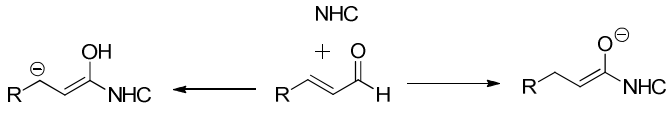
ABSTRACT

Tricyclic benzopyrans are medicinally important biologically active compounds. Synthesis of a series of tricyclic benzopyrans derivatives via N-Heterocyclic carbene (NHC) catalyzed annulation of enals to α-methylidenetetralones/chromanones is described. This reaction afforded the benzopyrans in high yield with aromatic as well as aliphatic enals.

1. Introduction

Ever since the demonstration by Glorius and Bode that N-Heterocyclic Carbenes (NHC) can catalyze the annulation of enals to aldehydes to deliver γ-lactones,[1,2] via the intermediacy of homoenolates, the chemistry of the latter has received extraordinary attention from organic chemists. There have been intense efforts in exploiting homoenolate reactivity in several laboratories including our own.[3] These explorations have succeeded in directing homoenolate reactivity towards a variety of electrophiles leading to the synthesis of a wide range of products.[4] Contemporaneous to the development of homoenolate chemistry, as early as 2004, Bode[5] and Rovis[6] independently observed that NHC can transform α-functionalized aldehydes to ester enolate equivalents that can participate in a variety of interesting reactions. More recently it was reported by Scheidt[7] and others[8] that, under controlled experimental conditions and with the use of appropriate base, homoenolate can endure β-protonation thus transforming it to enol (enolate) (Scheme 1).



Scheme 1. NHC mediated homoenolate and enolate formation

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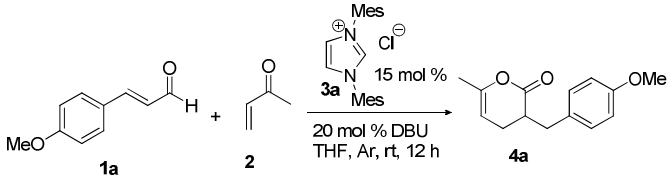
This reactivity has been utilized in the synthesis of dihydropyranones,[8b,9] and dihydropyridones.[10] The observation that in contrast to the well-established synthesis of cyclopentenes by the homoenolate annulation of chalcones, vinyl ketones afforded dihydropyranones (scheme 2) is noteworthy.[9c]



Scheme 2. Homoenolate annulation of vinyl ketones

In this context, it was of interest to explore the possibility of developing a synthesis of benzopyranones, mainly because of the impressive medicinal properties displayed by several natural and synthetic benzopyranones.[11] Some selected benzopyranones endowed with medicinal properties are shown in figure 1.

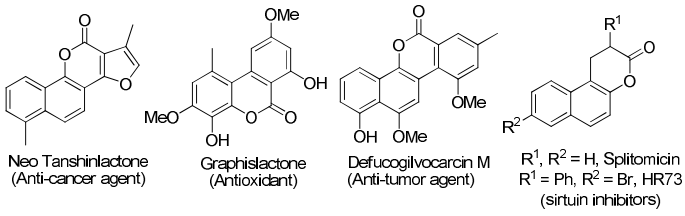
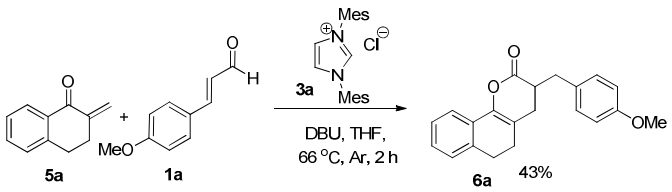


Figure 1. Biologically active tricyclic benzopyranones

2. Results and Discussion

Our studies commenced by refluxing a mixture of 4-methoxycinnamaldehyde and 2-methylene-3,4-dihydronaphthalen-1(2*H*)-one with catalytic amount (15 mol %) of imidazolium salt (IMes·HCl) and DBU (30 mol %) in dry THF under argon atmosphere for about 2 h. Then the reaction mixture was purified by silica gel chromatography (ethyl acetate-hexane (5:95)) to give product as white solid in 43% yield (Scheme 3).



Scheme 3. Synthesis of tricyclic benzopyran-2-one

The structure of the product was established by spectroscopic analysis. The IR spectrum of **6a** showed absorption at 1759 cm^{-1} corresponding to the lactone carbonyl, which was supported by the ^{13}C NMR signal at δ 170.6. Conclusive evidence for the structure of **6a** was obtained from single crystal X-ray analysis of **6b** (Figure 2).[12]

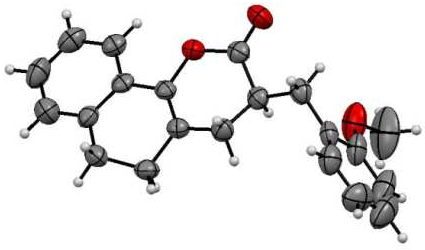
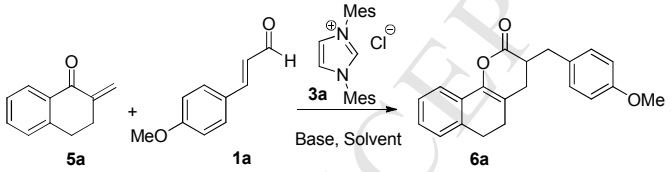


Figure 2. ORTEP of **6b**.

After the catalyst screening,[13] a brief screening of various bases and solvents were undertaken (Table 1). These studies revealed that DBU and toluene under refluxing offered optimum condition for this reaction.

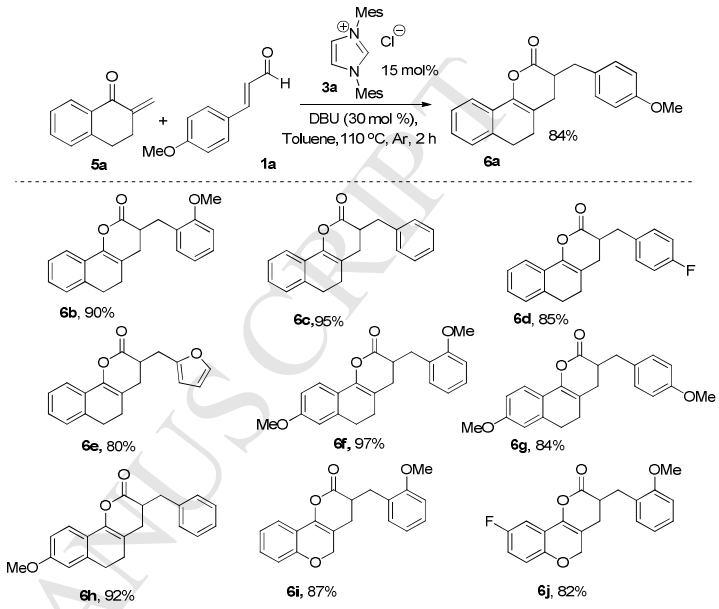
Table 1. Optimization of Reaction



Entry	Base	Solvent	Time (h)	Temperature	Yield[a] (%)
1	DBU	DCM	24	RT	-
2	DBU	THF	24	RT	-
3	DBU	THF	8	66 °C	43
4	DBU	Toluene	24	66 °C	Trace
5	DBU	Toluene	2	110 °C	84[b]
6	DBU	CH_3CN	24	82 °C	38
7	DBU	DMF	24	110 °C	49
8	DMAP	DCM	24	RT	-
9	DMAP	THF	24	66 °C	15
10	DMAP	Toluene	24	RT	-
11	DMAP	Toluene	24	110 °C	22
12	K_2CO_3	THF	24	66 °C	10

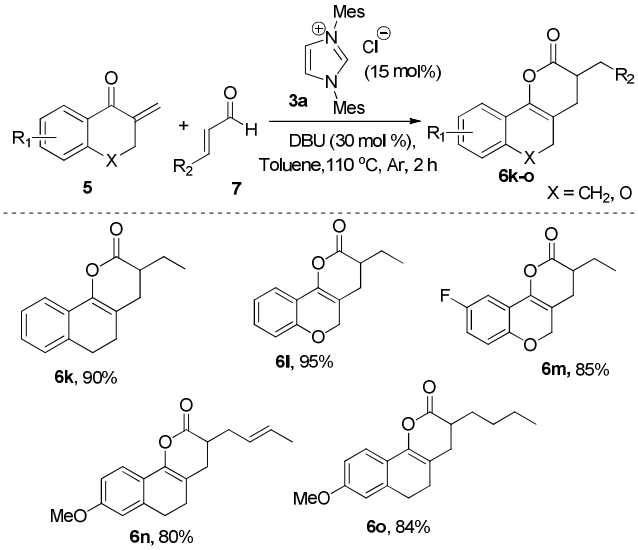
a Overall yield, b Reaction condition: enone **5a** (0.5 mmol), enal **1a** (2.5 mmol), catalyst **3a** (15 mol %), DBU (30 mol %) and toluene 7 mL, refluxed under argon atmosphere for 2 h.

After establishing the most favorable conditions, the generality of the reaction was investigated with various α, β-unsaturated aldehydes and α-methylene tetralones and oxa analogs of the latter. The results are summarized in Scheme 4.



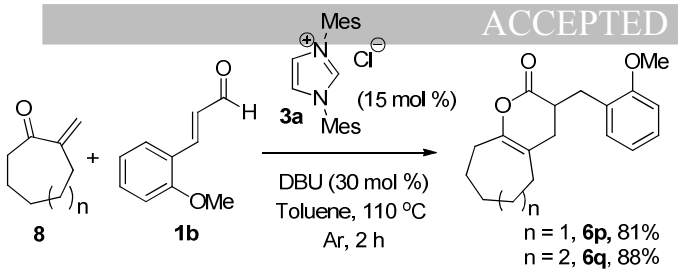
Scheme 4. Scope of the reaction with various aromatic enals

In the view of the interesting results obtained by the reaction of tethered α- methylene ketones with aromatic enals, it was obligatory to extend our studies to aliphatic enals (Scheme 5). Satisfactorily, the reaction of 2-methylene-3,4-dihydronaphthalen-1(2*H*)-one **5a** with crotonaldehyde in presence of IMes.HCl and DBU in an inert atmosphere of argon under reflux condition for 2h, afforded the product **6k** in 90% yield as white solid.



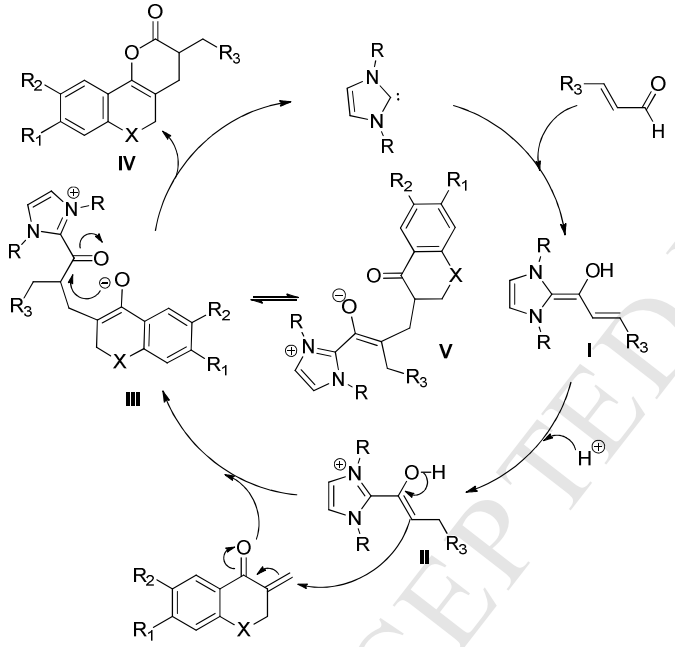
Scheme 5. Scope of the reaction with various aliphatic enals

Encouraged by these results, we extended this strategy to yet another interesting α-methylene cycloalkanones like 2-methylene cycloheptanone and 2-methylene cyclooctanone under similar reaction condition. In these studies also the expected products were obtained in high yields (Scheme 6).



Scheme 6. Extension of the reaction to α-methylene cycloalkanones

A mechanistic rationalization for this unexpected reaction may be postulated as follows (Scheme 7). The homoenolate equivalent **I** formed initially from the enal and NHC undergoes β- protonation to afford the enol **II**. The latter on Michael addition to the exo-methylene cyclanones affords the species **III** which on intramolecular *O*-acylation reaction delivers the product (**IV**). It is noteworthy that isomerization of enolate **III** to a more stable enolate **V** and subsequent intramolecular aldol-type reaction, analogous to the events observed in the case of cyclopentene formation from chalcone, is precluded here since that would involve a four-membered transition state.



Scheme 7. Postulated reaction mechanism

3. Conclusion

In conclusion, we have successfully employed the NHC catalyzed annulation for the synthesis of polycyclic di-hydropyran-2-ones. Parenthetically it may be added that the pyrone motif is present in a number of natural products with important biological activity.

4. Experimental Section

4.1. General Remarks

NMR spectra were recorded at 500 (^{1}H) and 126 (^{13}C) MHz respectively on a Bruker DPX-500 MHz NMR spectrometer. Chemical shifts (d) are reported relative to TMS (^{1}H) and $CDCl_3$ (^{13}C) as the internal standards. Coupling constant (*J*) is reported in Hertz (Hz). Mass spectra were recorded on Thermo Scientific™ Exactive mass Spectrometer for ESI. IR spectra were recorded on a Bruker Alpha-T FT-IR spectrophotometer.

4.2. Preparation of α-methylidene ketones (α-methylidenetetralones)

α-methylidene ketones were prepared according to the known literature procedure.[14] In a 100 mL round bottom flask, added α-tetralone (1.0 mmol) and paraformaldehyde (2.0 mmol) and THF (1.0 mL) into this catalyst-*i*-Pr_2NH:TFA (1.0 mmol), trifluoroacetic acid (0.1 mmol) was added. The reaction mixture was stirred, open to the atmosphere and reflux for 2 h. Reaction mixture was cooled down to room temperature and paraformaldehyde (2.0 mmol) was added again and it was refluxed for 6 h open to the atmosphere. After completion of the reaction, the reaction mixture was cooled down to room temperature, solvent was removed and dissolved in Et_2O and washed with 1N HCl, 1N NaOH, and brine, then dried using Na_2SO_4 and concentrated under vacuum. The crude product was purified by (100-200 mesh) silica-gel column chromatography using 1% EtOAc–Hexane as eluent.

4.3. Synthesis of substituted dihydropyranones

To a solution of 2-methylene-3,4-dihydronaphthalen-1(2H)-one **5a** (79 mg, 0.5 mmol) and 4-methoxy cinnamaldehyde (203 mg, 2.5 mmol) **1a** in toluene (7 mL) was added IMes.HCl (15 mol %) and DBU (30 mol %) in an inert atmosphere of argon under reflux condition for about 2 h. Then the reaction mixture was purified by column chromatography using 100-200 mesh silica using ethyl acetate-hexane (5:95) as eluent to afford the corresponding product **6a** in 84% yield.

*3-(4-Methoxybenzyl)-3,4,5,6-tetrahydro-2H-benzo[h]chromen-2-one (**6a**) :*

Chemical Formula: $C_{21}H_{20}O_3$; Yield:135 mg (84%); mp: 122-124 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.49 (d, *J* = 7.5 Hz, 1H), 7.22 - 7.15 (m, 2H), 7.11 (d, *J* = 8.5 Hz, 3H), 6.83 (d, *J* = 8.5 Hz, 2H), 3.79 (s, 3H), 3.31 (dd, J_1 = 14 Hz, J_2 = 4.5 Hz, 1H), 2.91 – 2.82 (m, 3H), 2.75-2.70 (m,1H), 2.33 (t, *J* = 8.0 Hz, 2H), 2.27 (d, *J* = 8.5 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 170.6, 158.4, 143.7, 135.0, 130.2, 130.1, 128.8, 127.8, 127.3, 126.6, 120.9, 114.0, 110.7, 55.2, 40.8, 35.1, 29.1, 27.5, 26.5. IR (film) ν_{max}: 2955, 2918, 2850, 1759, 1612, 1512, 1247,1129 cm^{-1}. HRMS: m/z (ESI) $(M+H)^+$ calcd. for $C_{21}H_{20}O_3$ is 321.1492; found 321.1499.

*3-(2-Methoxybenzyl)-3,4,5,6-tetrahydro-2H-benzo[h]chromen-2-one (**6b**):*

Chemical Formula: $C_{21}H_{20}O_3$; Yield:144 mg (90%); mp: 104-106 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.50 (d, *J* = 7.5 Hz, 1H), 7.23 – 7.10 (m, 5H), 6.90 (t, *J* = 7.5 Hz, 1H), 6.86 (d, *J* = 8.0 Hz, 1H), 3.81 (s, 3H), 3.43 (dd, J_1 = 13.5 Hz, J_2 = 4.5 Hz, 1H), 3.10 – 3.04 (m, 1H), 2.83 (t, *J* = 8.5 Hz, 2H), 2.75 – 2.71 (m, 1H), 2.31 (t, *J* = 8.0 Hz, 2H), 2.27 – 2.20 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 171.3, 157.7, 143.5, 131.2, 128.1, 127.7, 127.3, 126.7, 126.6, 120.8, 120.5, 111.2, 110.3, 55.2, 38.8, 31.2, 29.3, 27.5, 26.5. IR (film) ν_{max}: 2933, 2887, 2834, 1759, 1587, 1493, 1243, 1132 cm^{-1}. HRMS: m/z (ESI) $(M+H)^+$ calcd. for $C_{21}H_{20}O_3$ is 321.1492; found 321.1497.

*3-Benzyl-3,4,5,6-tetrahydro-2H-benzo[h]chromen-2-one(**6c**):*

Chemical Formula: $C_{20}H_{18}O_2$; Yield:139 mg (95%); mp: 110-112 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.40 (d, *J* = 7.5 Hz, 1H), 7.21 - 7.18 (m, 2H), 7.15 - 7.05 (m, 5H), 7.00 (d, *J* = 7.0 Hz, 1H), 3.30 (dd, J_1 = 14.0 Hz, J_2 = 4.5 Hz, 1H), 2.87 - 2.79 (m, 1H), 2.73 (t, *J* = 8.0 Hz, 2H), 2.69 – 2.64 (m, 1H), 2.22 (t, *J* = 8.0 Hz, 2H), 2.18 – 2.16 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 170.4, 143.7, 138.3, 135.0, 129.1, 128.8, 128.6, 127.8, 127.3, 126.7,

126.6, 120.9, 110.7, 40.6, 36.0, 29.6, 27.5, 26.5. IR (film) ν_{max}: 3028, 2926, 2855, 1777, 1682, 1454, 1225, 1158 cm^{-1}. HRMS: m/z (ESI) $(M+H)^+$ calcd. for $C_{20}H_{18}O_2$ is 291.1385; found 291.1391.

*3-(4-Fluorobenzyl)-3,4,5,6-tetrahydro-2H-benzo[h]chromen-2-one (**6d**):*

Chemical Formula: $C_{20}H_{17}FO_2$; Yield:131 mg (85%); mp: 142-144 ^oC; ^1H NMR (500 MHz, $CDCl_3$) δ: 7.47 (d, *J* = 7.5 Hz, 1H), 7.21 – 7.15 (m, 4H), 7.09 (d, *J* = 7.5Hz, 1H), 6.98 (t, *J* = 8.5 Hz, 2H), 3.32 (dd, J_1 = 14.0 Hz, J_2 = 4.5 Hz, 1H), 2.91 – 2.87 (m, 1H), 2.83 (t, *J* = 8.0 Hz, 2H), 2.79 – 2.74 (m, 1H), 2.32 (t, *J* = 8.0 Hz, 2H), 2.29 – 2.24 (m, 2H). ^{13}C NMR (126 MHz, CDCl3) δ: 170.1, 162.7, 160.8, 143.8, 134.9, 133.9, 130.6, 130.5, 128.7, 127.9, 127.3, 126.6, 120.9, 115.6, 115.4, 110.5, 40.6, 35.2, 29.2, 27.5, 26.5. IR (film) ν_{max}: 2955, 2918, 2851, 1730, 1681, 1510, 1223, 1158 cm^{-1}. HRMS: m/z (ESI) $(M+H)^+$ calcd. for $C_{20}H_{17}FO_2$ is 309.1290; found 309.1291.

*3-(Furan-2-ylmethyl)-3,4,5,6-tetrahydro-2H-benzo[h]chromen-2-one (**6e**):*

Chemical Formula: $C_{18}H_{16}O_3$; Yield: 112 mg (80%), Viscous liquid; ^1H NMR (500 MHz, $CDCl_3$) δ: 7.47 (d, *J* = 7.5 Hz, 1H), 7.31 (d, *J* = 7.0 Hz, 1H), 7.20 – 7.14 (m, 2H), 7.09 (d, *J* = 7.5 Hz, 1H), 6.28 (s, 1H), 6.11 (d, *J* = 2.0 Hz, 1H), 3.33 (dd, J_1 = 15.0 Hz, J_2 = 4.5 Hz, 1H), 3.04 – 2.96 (m, 1H), 2.91 – 2.81 (m, 3H), 2.36 – 2.32 (m, 4H). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 169.9, 152.2, 143.7, 141.6, 135.0, 128.7, 127.8, 127.3, 126.6, 120.8, 110.9, 110.4, 107.3, 38.5, 29.6, 28.5, 27.5, 26.5. IR (film) ν_{max}: 2956, 2918, 2851, 1732, 1681, 1600, 1435, 1224, 1156 cm^{-1}. HRMS: m/z (ESI) $(M+H)^+$ calcd. for $C_{18}H_{16}O_3$ is 281.1177; found 281.1183.

*8-Methoxy-3-(2-methoxybenzyl)-3,4,5,6-tetrahydro-2H-benzo[h]chromen-2-one (**6f**):*

Chemical Formula: $C_{22}H_{22}O_4$; Yield:170 mg (97%); mp: 109-111 ^oC; ^1H NMR (500 MHz, $CDCl_3$) δ: 7.41 (d, *J* = 8.5 Hz, 1H), 7.22 – 7.19 (m, 1H), 7.12 (dd, J_1 = 7.5 Hz, J_2 = 1.5 Hz, 1H), 6.89 - 6.83 (m, 2H), 6.70 (dd, J_1 = 8.5 Hz, J_2 =2.5 Hz, 1H), 6.65 (d, *J* = 2.5 Hz, 1H), 3.81 (s, 3H), 3.79 (s, 3H), 3.42 (dd, J_1 = 13.5 Hz, J_2 = 4.5 Hz, 1H), 3.07- 3.01 (m, 1H), 2.79 (t, *J* = 8.0 Hz, 2H), 2.73 – 2.68 (m, 1H), 2.28 (t, *J* = 8.0 Hz, 2H), 2.25 – 2.16 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ: 171.1, 159.3, 157.6, 143.5, 137.0, 131.2, 128.0, 126.7, 122.1, 122.0, 120.5, 113.9, 110.8, 110.3, 108.1, 55.1, 38.9, 31.2, 29.3, 28.0, 26.5. IR (film) ν_{max}: 2937, 2838, 1703, 1776, 1672, 1598, 1494, 1244, 1159 cm^{-1}. HRMS: m/z (ESI) $(M+H)^+$ calcd. for $C_{22}H_{22}O_4$ is 351.1596; found 351.1598.

*8-Methoxy-3-(4-methoxybenzyl)-3,4,5,6-tetrahydro-2H-benzo[h]chromen-2-one (**6g**)*

Chemical Formula: $C_{22}H_{22}O_4$; Yield:147 mg (84%); mp: 105-107 ^oC; ^1H NMR (500 MHz, $CDCl_3$) δ: 7.40 (d, *J* = 8.5 Hz, 1H), 7.11 – 7.09 (m, 2H), 6.83 – 6.82 (m, 2H), 6.71 (dd, J_1 = 8.5 Hz, J_2 = 2.5 Hz, 1H), 6.66 (d, *J* = 2.5 Hz, 1H), 3.79 (s, 3H), 3.78 (s, 3H), 3.29 (dd, , J_1 = 14.0 Hz, J_2 = 5.0 Hz, 1H), 2.90 – 2.83 (m, 1H), 2.79 (t, *J* = 8.0 Hz, 2H), 2.73 – 2.68 (m, 1H), 2.31 - 2.28 (m, 2H), 2.23 (d, *J* = 9.0 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 170.8, 159.3, 158.4, 143.5, 136.9, 130.2, 130.1, 122.1, 121.8, 114.4, 114.0, 113.9, 110.8, 107.9, 55.2, 55.1, 40.9, 35.1, 28.9, 27.9, 26.5. IR (film) ν_{max}: 2922, 2839, 1774, 1731, 1672, 1598, 1494, 1244, 1159 cm^{-1}. HRMS: m/z (ESI) $(M+H)^+$ calcd. for $C_{22}H_{22}O_4$ is 351.1596; found 351.1599.

*3-Benzyl-8-methoxy-3,4,5,6-tetrahydro-2H-benzo[h]chromen-2-one (**6h**)*

Chemical Formula: $C_{21}H_{20}O_3$; Yield:147 mg (92%); mp: 113-115 ^oC; ^1H NMR (500 MHz, $CDCl_3$) δ: 7.40 (d, *J* = 8.5 Hz, 1H), 7.29 (t, *J* = 7.0 Hz, 2H), 7.24 – 7.12 (m, 3H), 6.70 (dd, J_1 = 8.5 Hz, J_2 = 2.6 Hz, 1H), 6.65 (d, *J* = 2.5 Hz, 1H), 3.78 (s, 3H), 3.38 (dd, J_1 = 13.8 Hz, J_2 = 4.5 Hz, 1H), 2.96 – 2.87 (m, 1H), 2.84 – 2.71 (m, 3H), 2.30 – 2.21 (m, 4H). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 170.7, 159.4, 143.6, 138.4, 137.0, 129.1, 128.6, 126.7, 122.2, 121.8, 114.0, 110.8, 107.9, 55.1, 40.7, 36.0, 29.0, 27.9, 26.5. IR (film) ν_{max}: 3028, 2927, 2843, 1777, 1731, 1673, 1596, 1495, 1247, 1158 cm^{-1}. HRMS: m/z (ESI) $(M+H)^+$ calcd. for $C_{21}H_{20}O_3$ is 321.1490; found 321.1494.

*3-(2-Methoxybenzyl)-3,4-dihydropyrano[3,2-c]chromen-2(5H)-one (**6i**):*

Chemical Formula: $C_{20}H_{18}O_4$; Yield:140 mg (87%); mp: 132-134 ^oC; ^1H NMR (500 MHz, $CDCl_3$) δ: 7.83 (d, *J* = 7.5 Hz, 1H), 7.43 (t, *J* = 8.0 Hz, 1H), 7.20 - 7.14 (m, 2H), 6.97 (t, *J* = 7.5 Hz, 1H), 6.92 (d, *J* = 8.5 Hz, 1H), 6.87 (t, *J* = 7.5 Hz, 1H), 6.80 (d, *J* = 8.0 Hz, 1H), 4.56 (d, *J* = 11.5 Hz, 1H), 4.32 (d, *J* = 11.5 Hz, 1H), 3.78 (s, 3H), 3.70 – 3.62 (m, 1H), 2.77 – 2.72 (m, 1H), 2.68 – 2.55 (m, 2H), 2.43 – 2.39 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ: 160.3, 156.3, 135.1, 127.0, 126.7, 125.6, 120.7, 119.7, 116.8, 109.3, 69.0, 59.9, 54.1, 44.8, 34.1, 31.7. IR (film) ν_{max}: 3068, 2928, 2838, 1737, 1684, 1604, 1493, 1242, 1179 cm^{-1}. HRMS: m/z (ESI) $(M+H)^+$ calcd. for $C_{20}H_{18}O_4$ is 323.1283; found 323.1286.

*9-Fluoro-3-(2-methoxybenzyl)-3,4-dihydropyrano[3,2-c]chromen-2(5H)-one (**6j**):*

Chemical Formula: $C_{20}H_{17}FO_4$; Yield:140 mg (82%); mp: 164-166 ^oC; ^1H NMR (500 MHz, $CDCl_3$) δ: 7.21 (t, *J* = 7.5 Hz, 1H), 7.11 (d, *J* = 7.5 Hz, 1H), 7.07 (dd, J_1 = 8.5 Hz, J_2 = 2.5 Hz, 1H), 6.88 (t, *J* = 7.5 Hz, 1H), 6.85 – 6.79 (m, 2H), 6.71- 6.68 (m, 1H), 4.73 (s, 2H), 3.83 (s, 3H), 3.42 (dd, J_1 = 13.5 Hz, J_2 = 4.5 Hz, 1H), 3.14 – 3.07 (m, 1H), 2.76 – 2.71 (m, 1H), 2.18 – 2.08 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 169.1, 158.5, 157.6, 156.6, 149.8, 140.2, 131.1, 128.3, 126.0, 120.6, 118.3, 116.5, 116.4, 116.0, 115.8, 110.3, 108.2, 108.0, 105.5, 67.6, 55.2, 38.5, 31.2, 25.5. IR (film) ν_{max}: 2956, 2920, 2851, 1770, 1743, 1650, 1439, 1245, 1179cm^{-1}. HRMS: m/z (ESI) $(M+H)^+$ calcd. For $C_{20}H_{17}FO_4$ is 341.1189; found 341.1190.

*3-Ethyl-3,4,5,6-tetrahydro-2H-benzo[h]chromen-2-one (**6k**):*

Chemical Formula: $C_{15}H_{16}O_2$; Yield:103 mg (90%); mp: 75-77 ^oC; ^1H NMR (500 MHz, $CDCl_3$) δ: 7.48 (d, *J* = 7.0 Hz, 1H), 7.25 - 7.15 (m, 2H), 7.12 - 7.06 (m, 1H), 2.87 (t, *J* = 8.0 Hz, 2H), 2.63 – 2.57 (m, 1H), 2.48 (dd, J_1 = 17.0 Hz, J_2 = 7.0 Hz, 1H), 2.40 – 2.32 (m, 3H), 2.02 – 1.94 (m, 1H), 1.66 – 1.54 (m, 1H), 1.05 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ: 170.8, 143.5, 134.9, 128.9, 127.7, 127.3, 126.6, 120.9, 110.7, 40.3, 29.8, 27.6, 26.7, 23.3, 11.4. IR (film) ν_{max}: 2961, 2925, 2857, 1731, 1682, 1600, 1455, 1223, 1157 cm^{-1}. HRMS: m/z (ESI) $(M+H)^+$ calcd. for $C_{15}H_{16}O_2$ is 229.1228; found 229.1230.

*3-Ethyl-3,4-dihydropyrano[3,2-c]chromen-2(5H)-one (**6l**):*

Chemical Formula: $C_{14}H_{14}O_3$; Yield:109 mg (95%); mp: 205-207 ^oC; ^1H NMR (500 MHz, $CDCl_3$ δ: 7.34 (d, *J* = 7.5 Hz, 1H), 7.14 (t, *J* = 7.5 Hz, 1H), 6.91 (t, *J* = 7.5 Hz, 1H), 6.78 (d, *J* = 8.0 Hz, 1H), 4.88 - 4.82 (m, 2H), 2.67 – 2.62 (m, 1H), 2.40 – 2.35 (m, 1H), 2.24 – 2.19 (m, 1H), 2.04 – 1.95 (m, 1H), 1.66 – 1.59 (m, 1H), 1.04 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ:

169.7, 154.0, 140.7, 129.9, 121.3, 121.1, 117.1, 115.6, 103.9, 67.5, 40.1, 25.9, 23.4, 11.3. IR (film) ν_{max}: 2966, 2932, 2877, 1787, 1697, 1579, 1478, 1296, 1185 cm^{-1}. HRMS: m/z (ESI) $(M+H)^+$ calcd. for $C_{14}H_{14}O_3$ is 231.1021; found 231.1025.

*3-Ethyl-9-fluoro-3,4-dihydropyrano[3,2-c]chromen-2(5H)-one (**6m**):*

Chemical Formula: $C_{14}H_{13}FO_3$; Yield:106 mg (85%); mp: 116-118 ^oC; ^1H NMR (500 MHz, $CDCl_3$) δ: 7.07 (dd, J_1 = 8.5 Hz, J_2 = 2.7 Hz, 1H), 6.84 (td, J_1 = 8.5 Hz, J_2 = 2.7 Hz, 1H), 6.73 (dd, J_1 = 8.8 Hz, J_2 = 4.4 Hz, 1H), 4.88 – 4.76 (m, 2H), 2.66 (dq, J_1 = 13.7 Hz, J_2 = 6.9 Hz, 1H), 2.41 (dd, J_1 = 17.2 Hz, J_2 = 7.2 Hz, 1H), 2.25 (dd, J_1 = 17.2 Hz, J_2 = 10.5 Hz, 1H), 2.07 – 1.93 (m, 1H), 1.69 – 1.59 (m, 1H), 1.05 (t, J = 7.5 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 169.2, 158.5, 156.9, 149.8, 140.2, 118.2, 116.6, 116.5, 116.1, 115.9, 108.2, 108.0, 105.3, 67.6, 40.1, 26.0, 23.4, 11.3. IR (film) ν_{max}: 2966, 2931, 2879, 1788, 1622, 1581, 1486, 1274, 1184 cm^{-1}. HRMS: m/z (ESI) $(M+H)^+$ calcd. for $C_{14}H_{13}FO_3$ is 249.1629; found 249.1631.

*3-(But-2-enyl)-8-methoxy-3,4,5,6-tetrahydro-2H-benzo[h]chromen-2-one (**6n**):*

Chemical Formula: $C_{18}H_{20}O_3$; Yield:115 mg (81%); mp: 95-97 ^oC; ^1H NMR (500 MHz, $CDCl_3$) δ: 7.40 (d, J = 8.5 Hz, 1H), 6.70 (dd, J_1 = 8.5 Hz, J_2 = 2.5 Hz, 1H), 6.67 (s, 1H), 5.56 - 5.49 (m, 1H), 5.46 – 5.39 (m, 1H), 3.79 (s, 3H), 2.82 (t, J = 8.0 Hz, 2H), 2.73 – 2.63 (m, 1H), 2.60 - 2.55 (m, 1H), 2.40 – 2.30 (m, 5H), 1.68 (dd, J_1 = 6.2 Hz, J_2 = 1.0 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 170.7, 159.3, 143.4, 136.9, 128.5, 127.1, 122.1, 121.9, 113.9, 110.8, 108.1, 55.1, 39.0, 33.2, 28.0, 26.5, 18.0. IR (film) ν_{max}: 2918, 2851, 1775, 1674, 1597, 1495, 1250,1160 cm^{-1}. HRMS: m/z (ESI) $(M+H)^+$ calcd. for $C_{18}H_{20}O_3$ is 285.1490; found 285.1494.

*3-Butyl-8-methoxy-3,4,5,6-tetrahydro-2H-benzo[h]chromen-2-one (**6o**):*

Chemical Formula: $C_{18}H_{22}O_3$; Yield:120.3 mg (77%); mp: 128-130 ^oC; ^1H NMR (500 MHz, $CDCl_3$) δ: 7.40 (d, J = 8.5 Hz, 1H), 6.71 (dd, J_1 = 8.5 Hz, J_2 = 2.5 Hz, 1H), 6.68 (d, J = 2.0 Hz, 1H), 3.80 (s, 3H), 2.83 (t, J = 8.0 Hz, 2H), 2.68 – 2.61 (m, 1H), 2.45 – 2.44 (m, 1H), 2.39 -2.35 (m, 2H), 2.32 – 2.27 (m, 1H), 1.99 – 1.92 (m, 1H), 1.56 - 1.49 (m, 1H), 1.45 – 1.33 (m, 4H), 0.93 (t, J = 7.0 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 171.2, 159.3, 143.4, 136.9, 122.1, 121.9, 113.9, 110.8, 107.9, 55.2, 39.0, 30.1, 29.9, 29.1, 28.0, 26.6, 22.6, 14.0; IR (film) ν_{max}: 2955, 2926, 2857, 1778, 1675, 1598, 1495, 1251, 1160 cm^{-1}. HRMS: m/z (ESI) $(M+H)^+$ calcd. for $C_{18}H_{22}O_3$ is 287.1647; found 287.1643.

*3-(2-Methoxybenzyl)-3,4,6,7,8,9-hexahydrocyclohepta[b]pyran-2(5H)-one (**6p**):*

Chemical Formula: $C_{18}H_{22}O_3$; Yield:116 mg (81%), Viscous liquid; ^1H NMR (500 MHz, $CDCl_3$) δ: 7.20 (t, J = 8.0 Hz, 1H), 7.09 (d, J = 7.5 Hz, 1H), 6.89 - 6.83 (m, 2H), 3.81 (s, 3H), 3.35 (dd, J_1 = 13.5 Hz, J_2 = 5.0 Hz, 1H), 2.87 - 2.80 (m, 1H), 2.68 – 2.60 (m, 1H), 2.33 (t, J = 5.5 Hz, 2H), 2.13 - 1.98 (m, 4H), 1.73 – 1.53 (m, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 171.6, 157.6, 149.6, 131.1, 127.9, 127.0, 120.4, 113.5, 110.2, 55.1, 38.4, 31.7, 31.6, 31.5, 30.8, 30.5, 26.5, 25.1. IR (film) ν_{max}: 2928, 2855, 1774, 1703, 1601, 1494 cm^{-1}. HRMS: m/z (ESI) $(M+H)^+$ calcd. for $C_{18}H_{22}O_3$ is 287.1647; found 287.1650.

*3-(2-Methoxybenzyl)-3,4,5,6,7,8,9,10-octahydro-2H-cycloocta[b]pyran-2-one (**6q**):*

Chemical Formula: $C_{19}H_{24}O_3$; Yield:132 mg (88%), Viscous liquid; ^1H NMR (500 MHz, $CDCl_3$) δ: 7.18 (t, J = 8.0 Hz, 1H), 7.09 (d, J = 7.0 Hz, 1H), 6.87 – 6.81 (m, 2H), 3.81 (s, 3H), 3.37 (dd, J_1 = 13.5 Hz, J_2 = 5.0 Hz, 1H), 2.92 – 2.84 (m, 1H), 2.65 – 2.6 (m, 1H), 2.15-2.03 (dd, J_1 = 11.0 Hz, J_2 = 5.1 Hz, 2H), 2.15 – 2.02 (m, 3H), 1.97 (m, 1H), 1.65 – 1.67 (m, 2H), 1.58 – 1.48 (m, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 171.7, 157.6, 147.3, 131.0, 127.9, 127.0, 120.5, 110.9, 110.3, 55.1, 38.7, 31.1, 30.0, 29.2, 28.9, 28.7, 28.5, 26.5, 26.2. IR (film) ν_{max}: 2925,2855, 1698 (broad), 1602, 1464 cm^{-1}. HRMS: m/z (ESI) $(M+H)^+$ calcd. for $C_{19}H_{24}O_3$ is 301.1803 found 301.1806.

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Expedient Synthesis of Tricyclic Benzopyran-2-ones via N-Heterocyclic Carbene Catalyzed Annulation of Enals to α-Methylene Cycloalkanones

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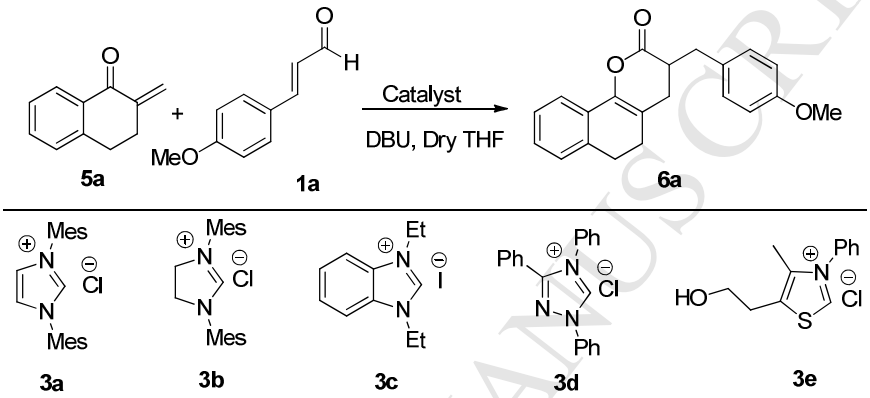
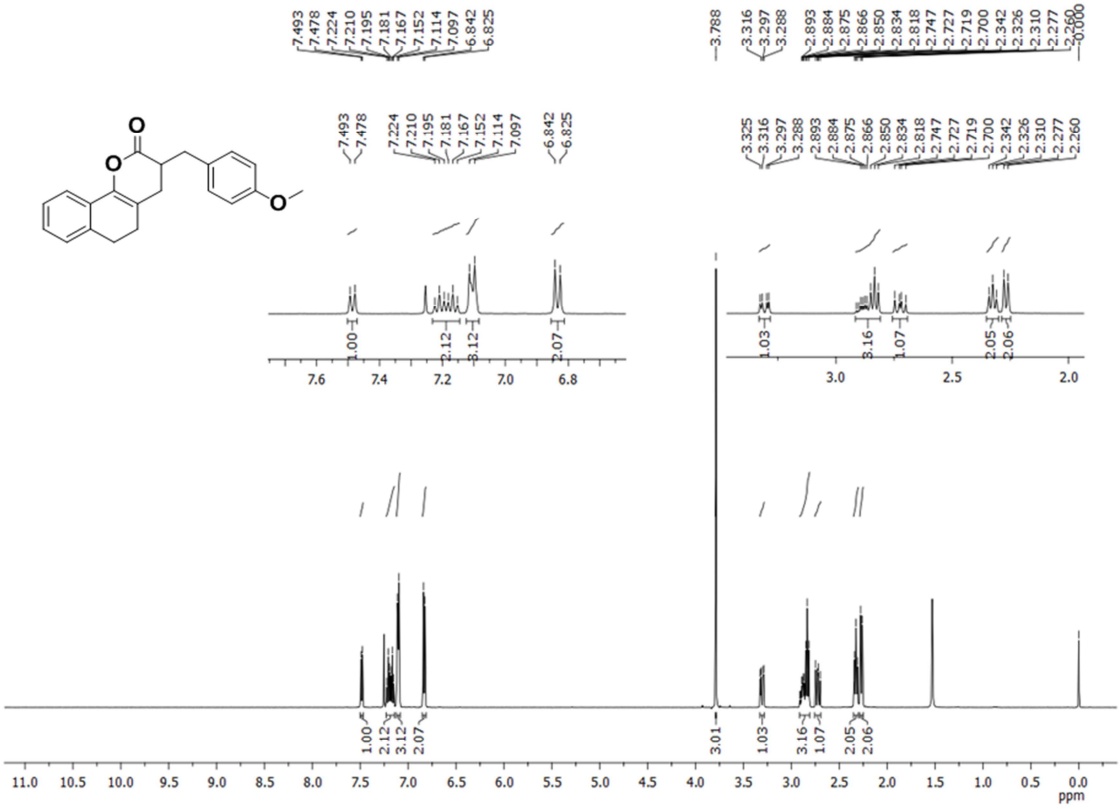
Optimization Reactions



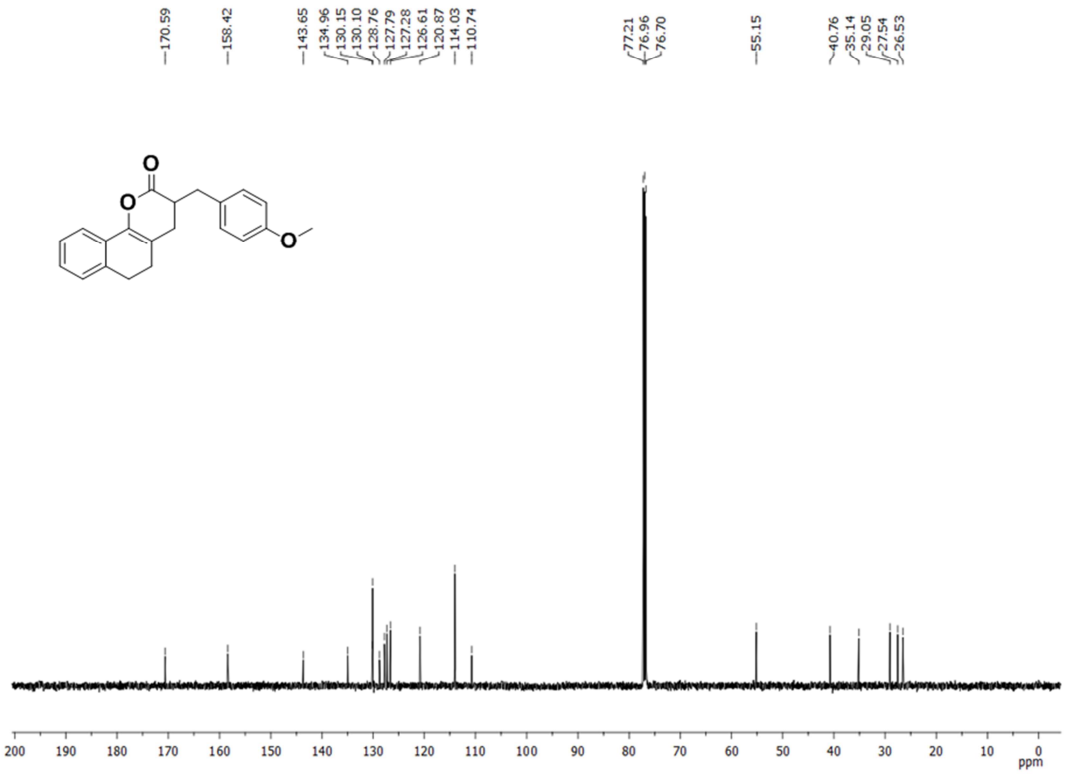
Entry	Catalyst	Condition	Time (h)	Yield[a] (%)
1	**3a**	DBU, DCM, rt	24	-
2	**3a**	DBU, THF, rt	24	-
3	**3a**	DBU, THF, 66 ^{O}C	8	43
4	**3b**	DBU, THF, 66 ^{O}C	24	Trace
5	**3c**	DBU, THF, 66 ^{O}C	24	-
6	**3d**	DBU, THF, 66 ^{O}C	24	-
7	**3e**	DBU, THF, 66 ^{O}C	24	-
8	**3a**	DBU, Toluene, 66 ^{O}C	24	Trace
9	**3a**	DBU, Toluene, 110 ^{O}C	2	84
10	**3a**	DBU, CH_3CN, 82 ^{O}C	24	38
11	**3a**	DBU, DMF, 110 ^{O}C	24	49
12	**3a**	DMAP, DCM, rt	24	-
13	**3a**	DMAP, DCM, 66 ^{O}C	24	15
14	**3a**	DMAP, Toluene, rt	24	-
15	**3a**	DMAP, Toluene, 110 ^{O}C	24	22
16	**3a**	K_2CO_3, THF, 66 ^{O}C	24	10

[a]Isolated yield

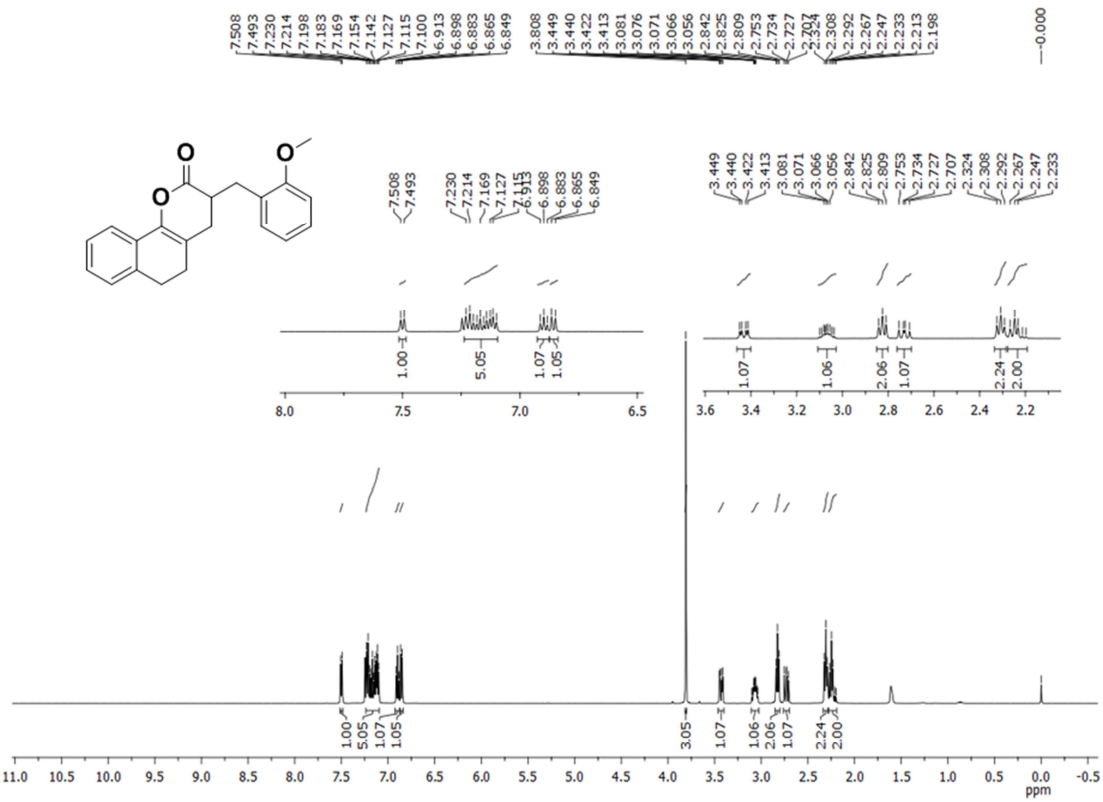
^{1}H NMR (500 MHz, $CDCl_3$) of Compound 6a



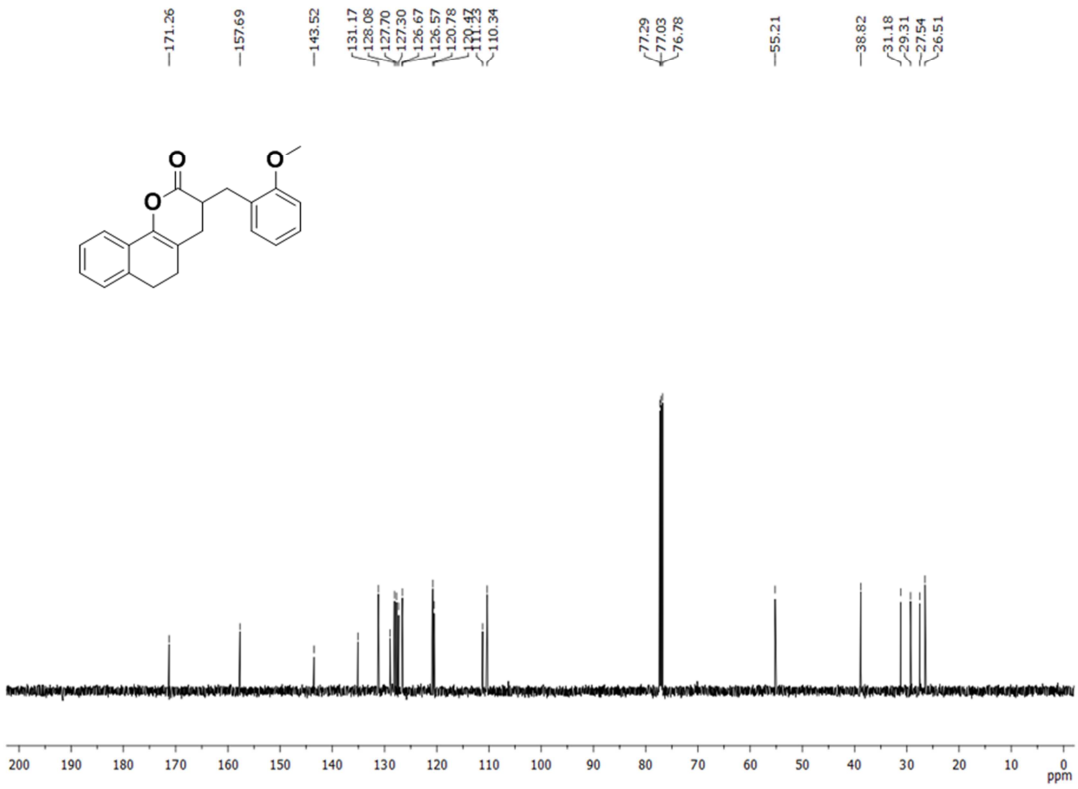
^{13}C NMR (126 MHz, $CDCl_3$) of Compound 6a



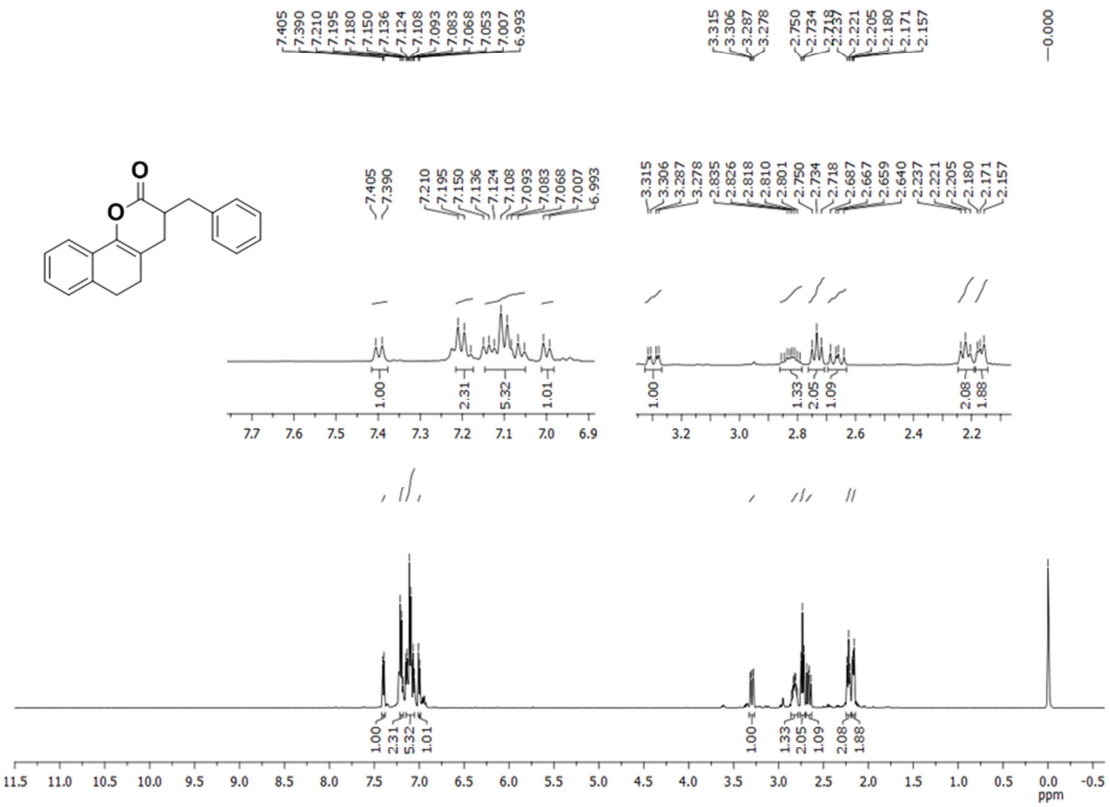
^{1}H NMR (500 MHz, $CDCl_3$) of Compound 6b



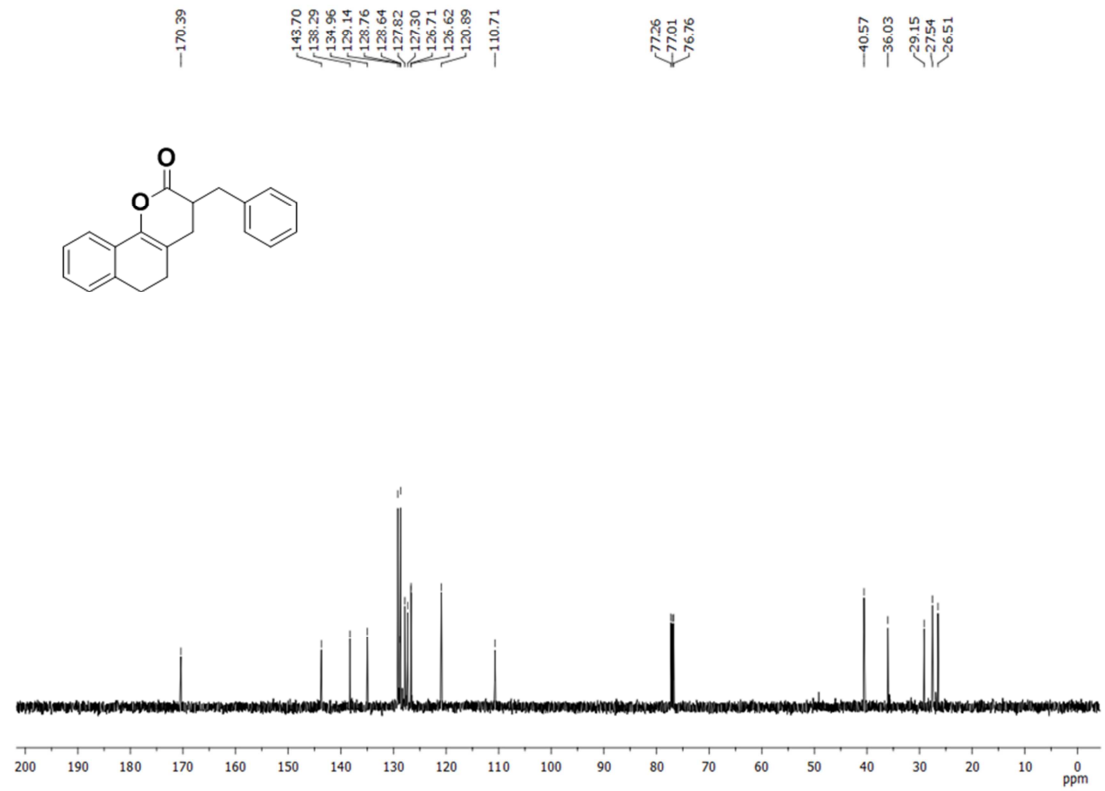
^{13}C NMR (126 MHz, $CDCl_3$) of Compound 6b



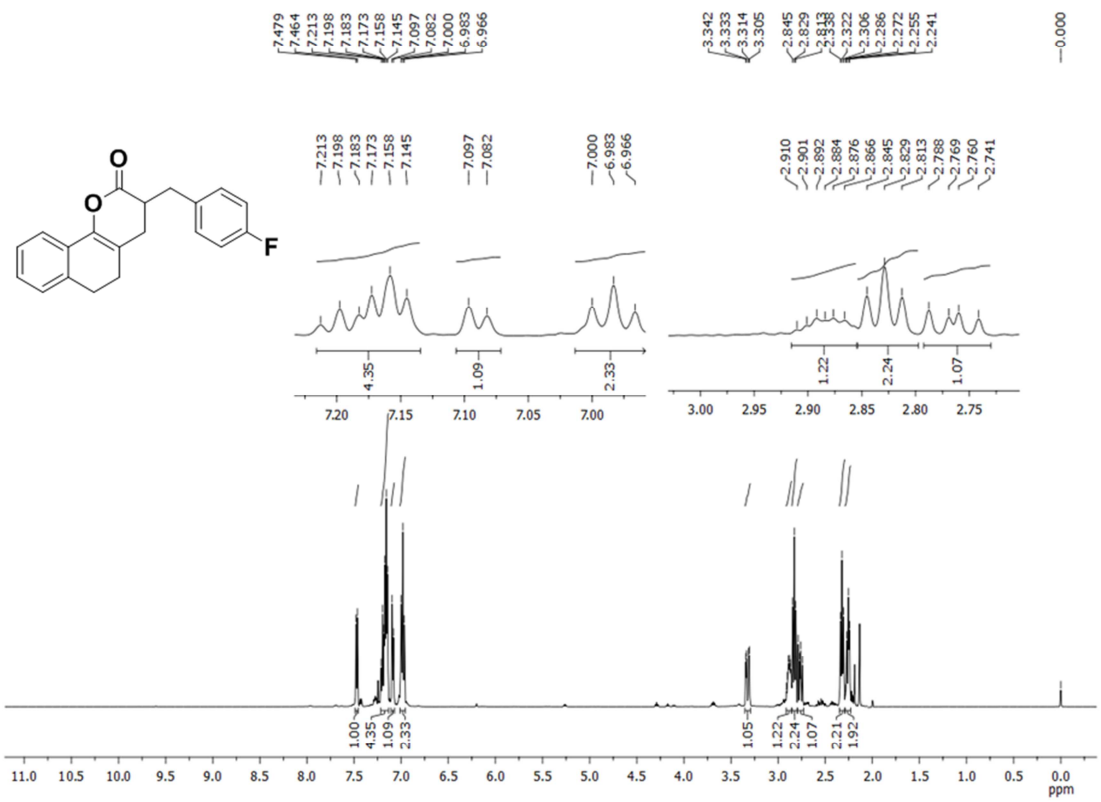
^{1}H NMR (500 MHz, $CDCl_3$) of Compound 6c



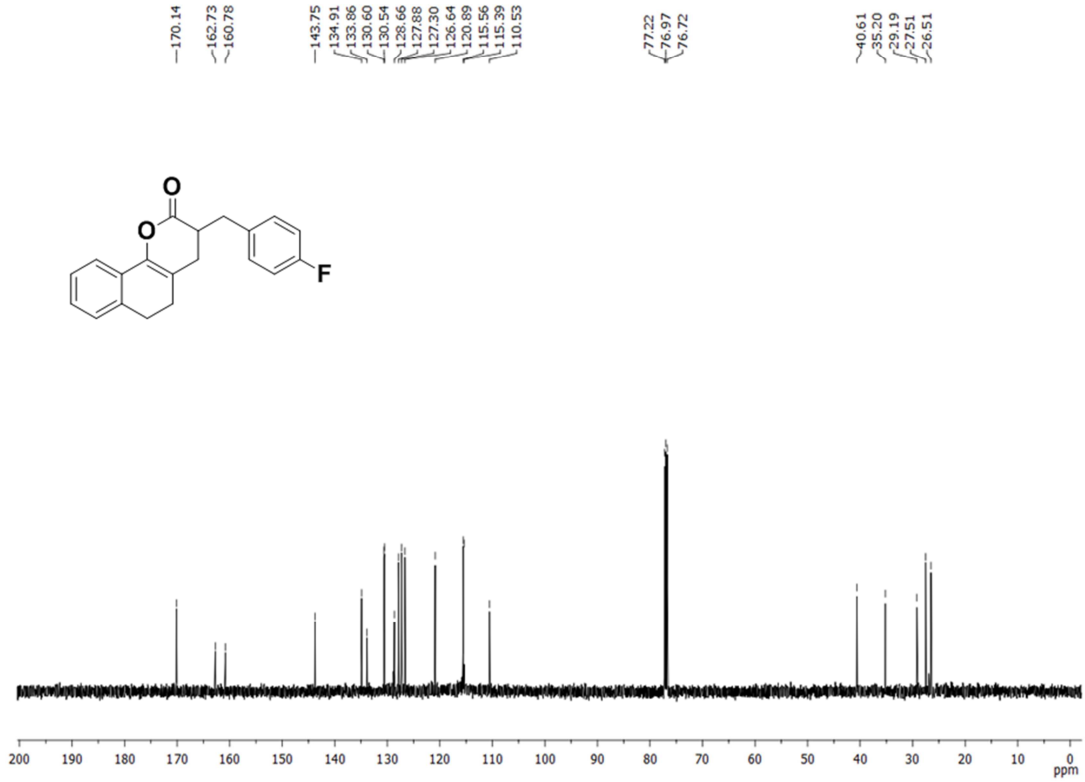
^{13}C NMR (126 MHz, $CDCl_3$) of Compound 6c



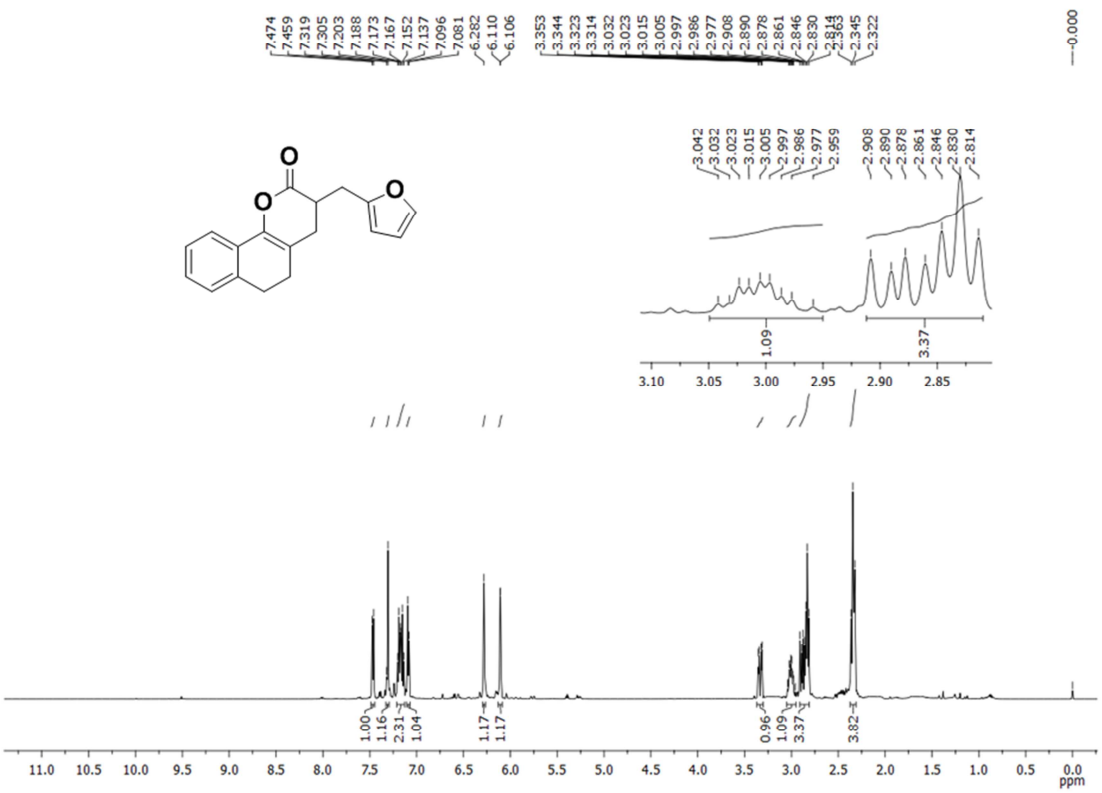
^{1}H NMR (500 MHz, $CDCl_3$) of Compound 6d



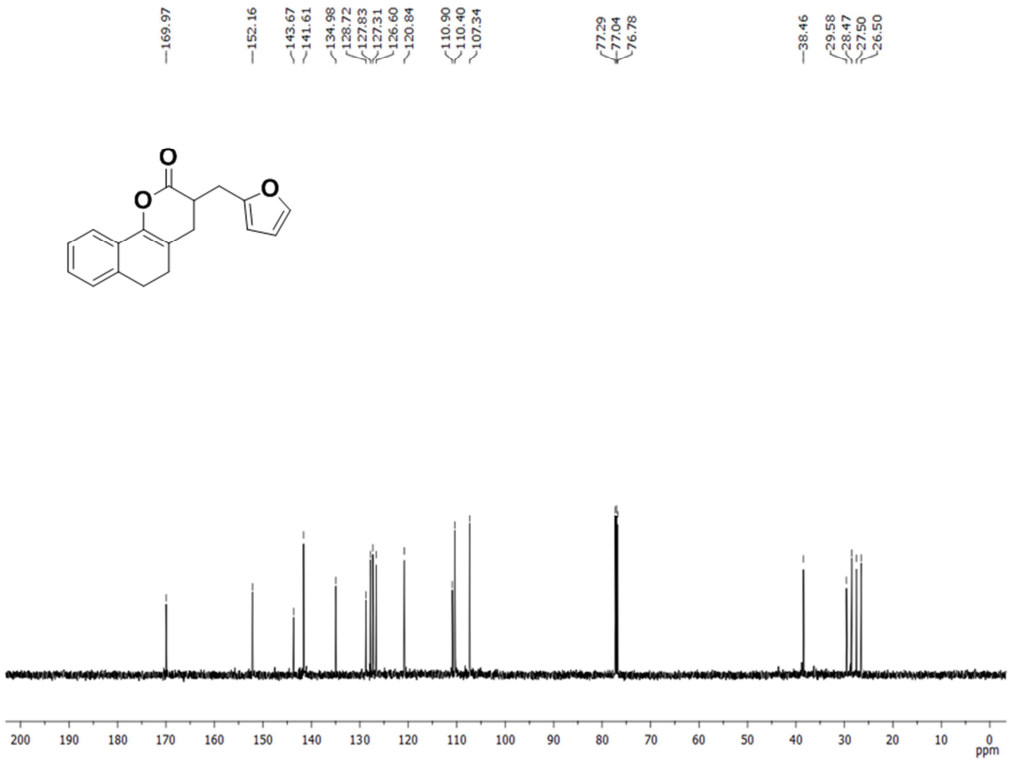
^{13}C NMR (126 MHz, $CDCl_3$) of Compound 6d



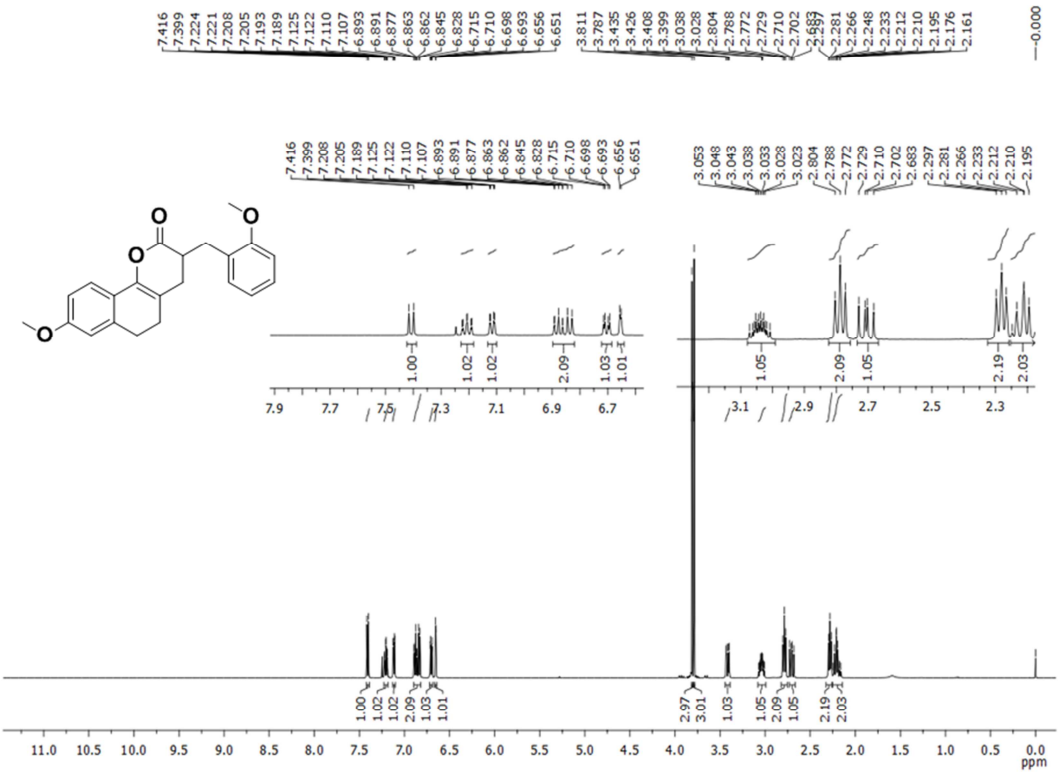
^{1}H NMR (500 MHz, $CDCl_3$) of Compound 6e



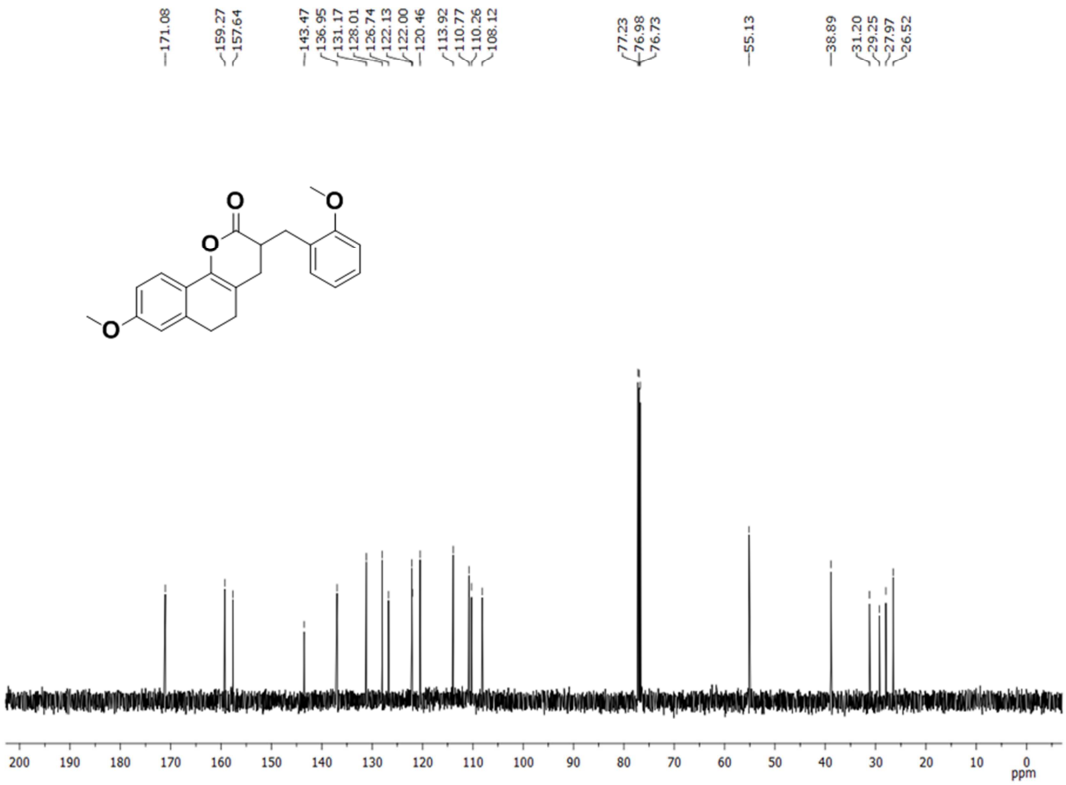
^{13}C NMR (126 MHz, $CDCl_3$) of Compound 6e



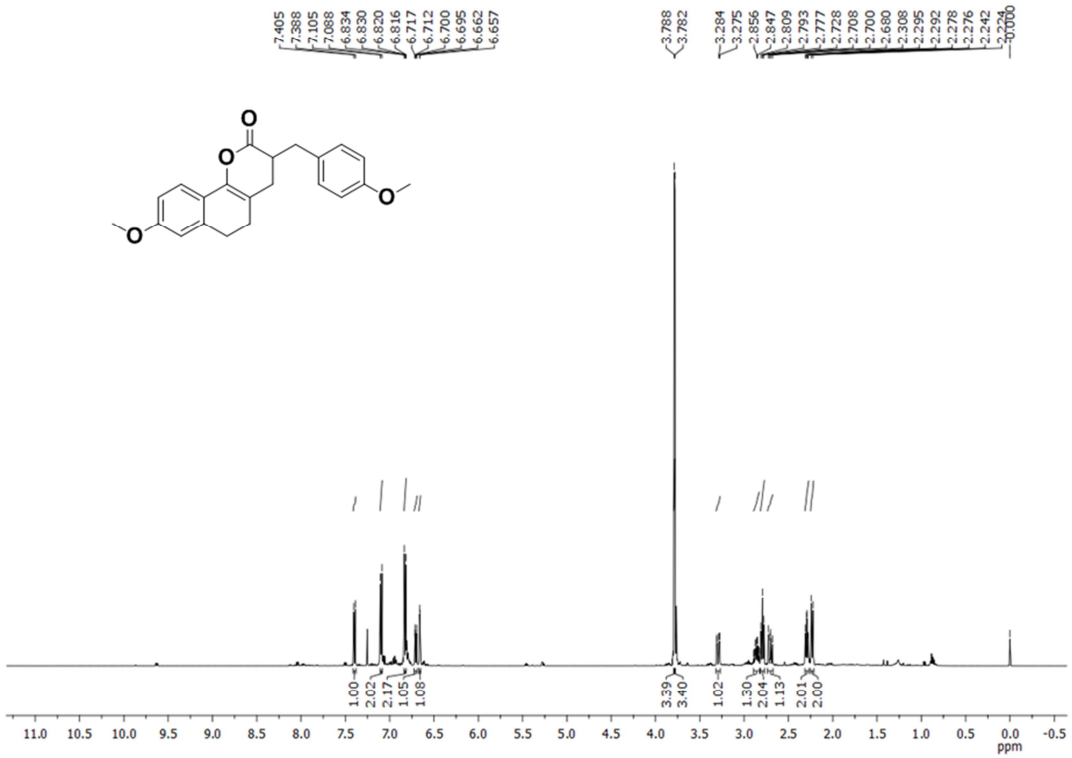
^{1}H NMR (500 MHz, $CDCl_3$) of Compound 6f



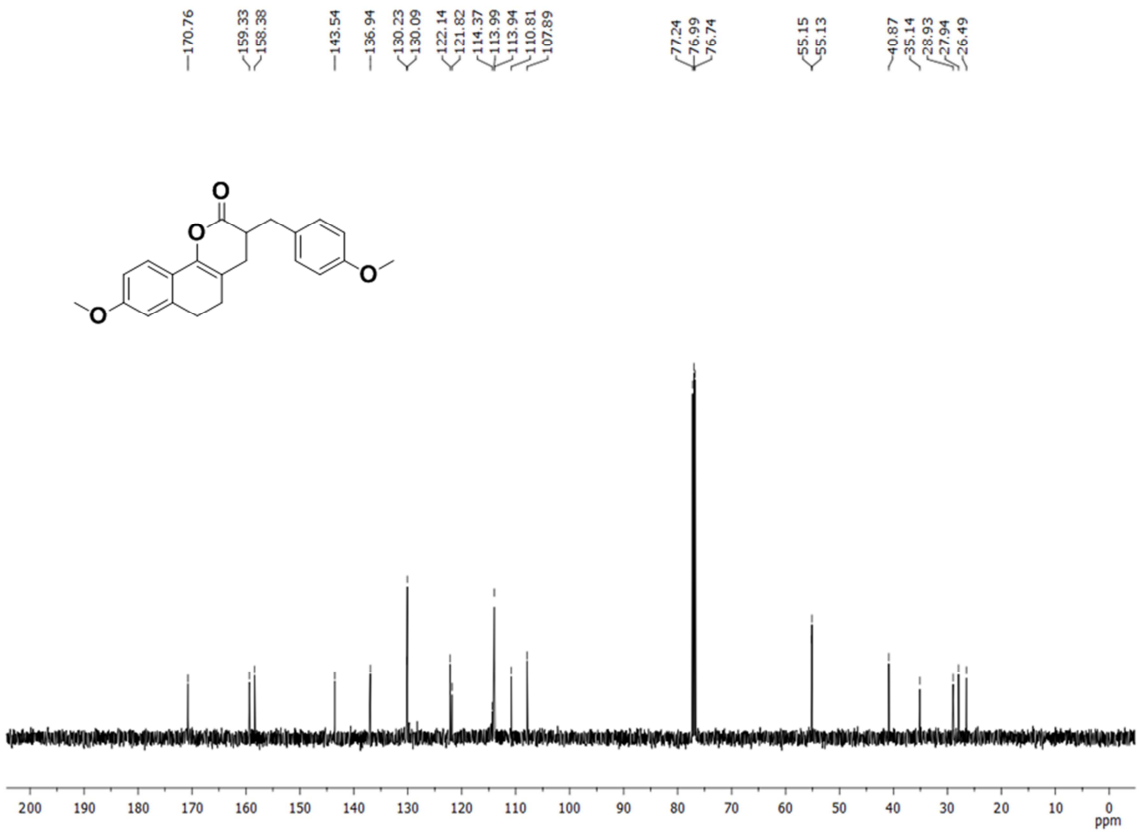
^{13}C NMR (126 MHz, $CDCl_3$) of Compound 6f



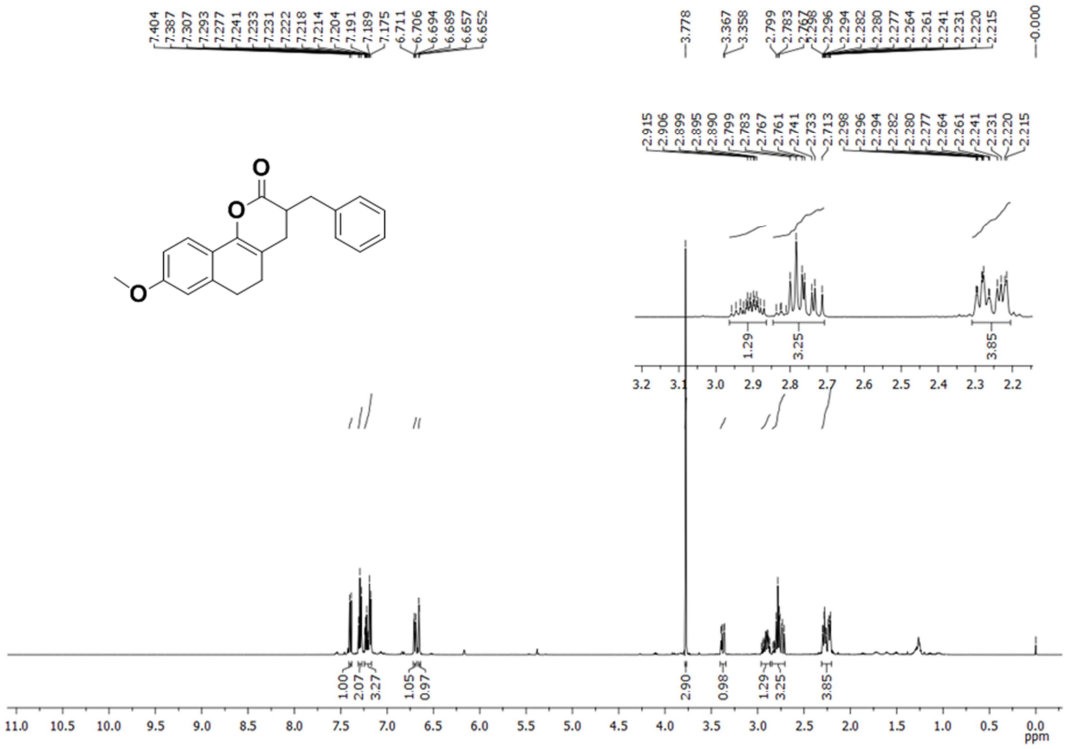
^{1}H NMR (500 MHz, $CDCl_3$) of Compound 6g



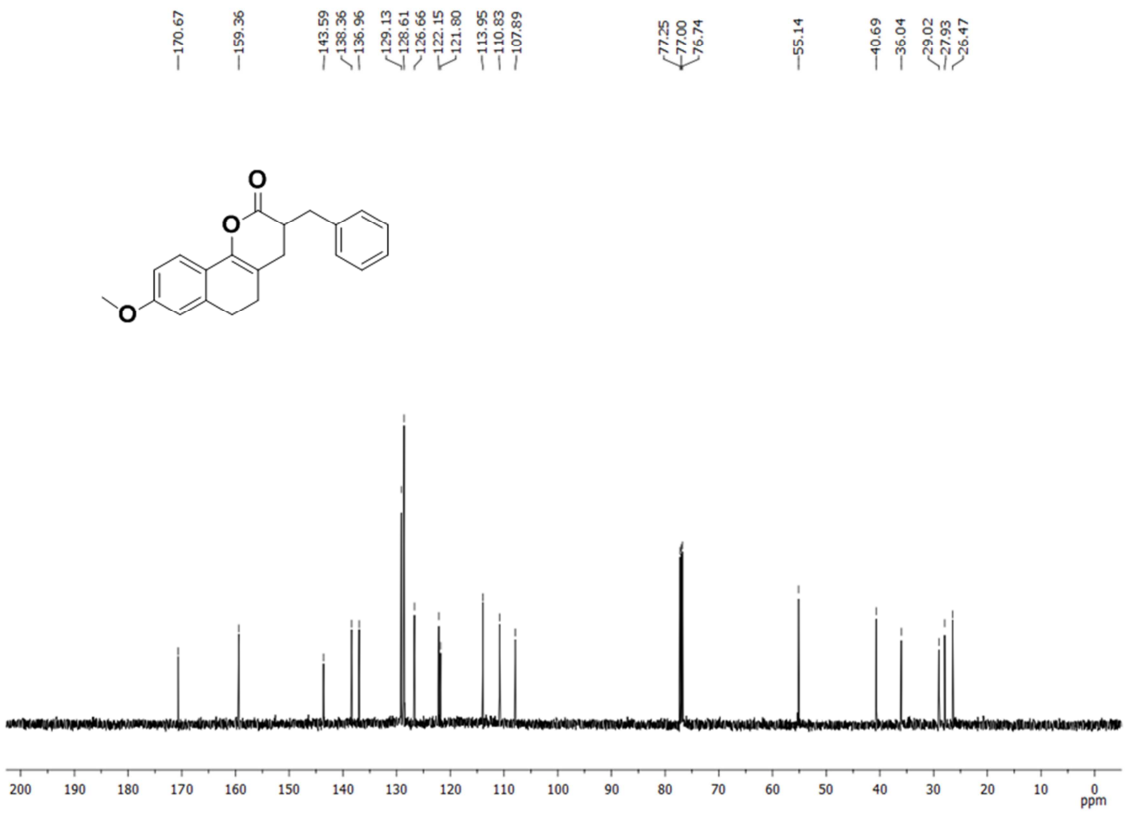
^{13}C NMR (126 MHz, $CDCl_3$) of Compound 6g



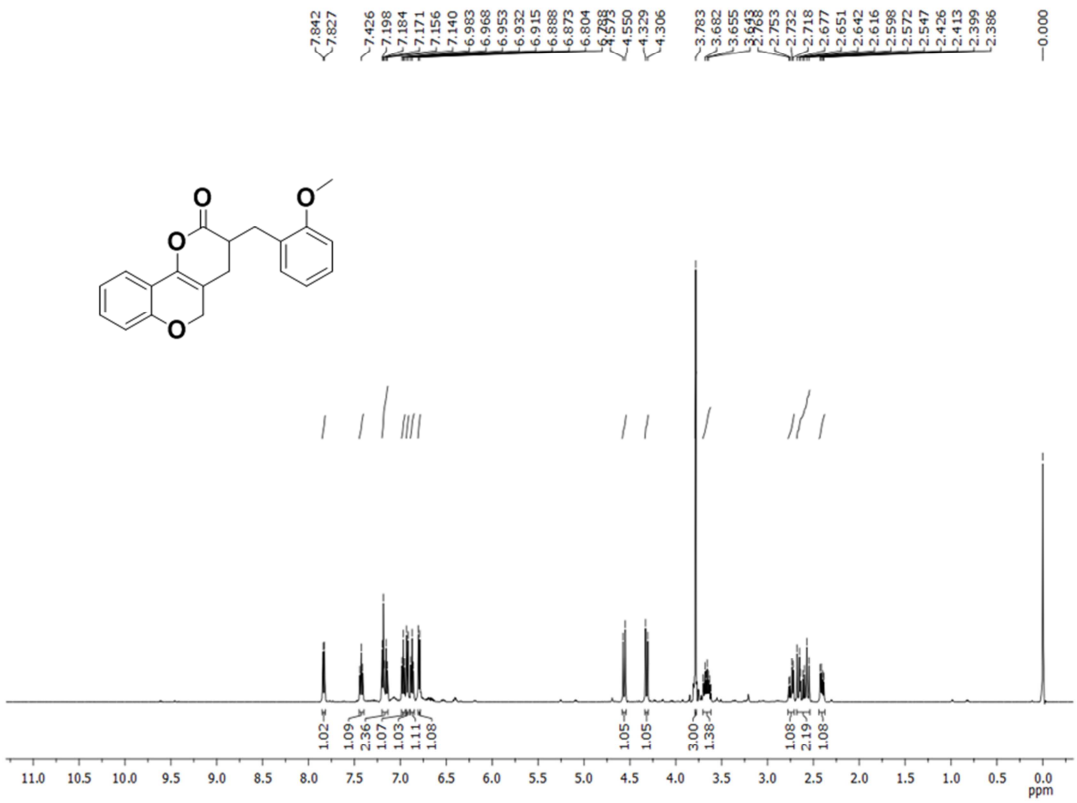
^{1}H NMR (500 MHz, $CDCl_3$) of Compound 6h



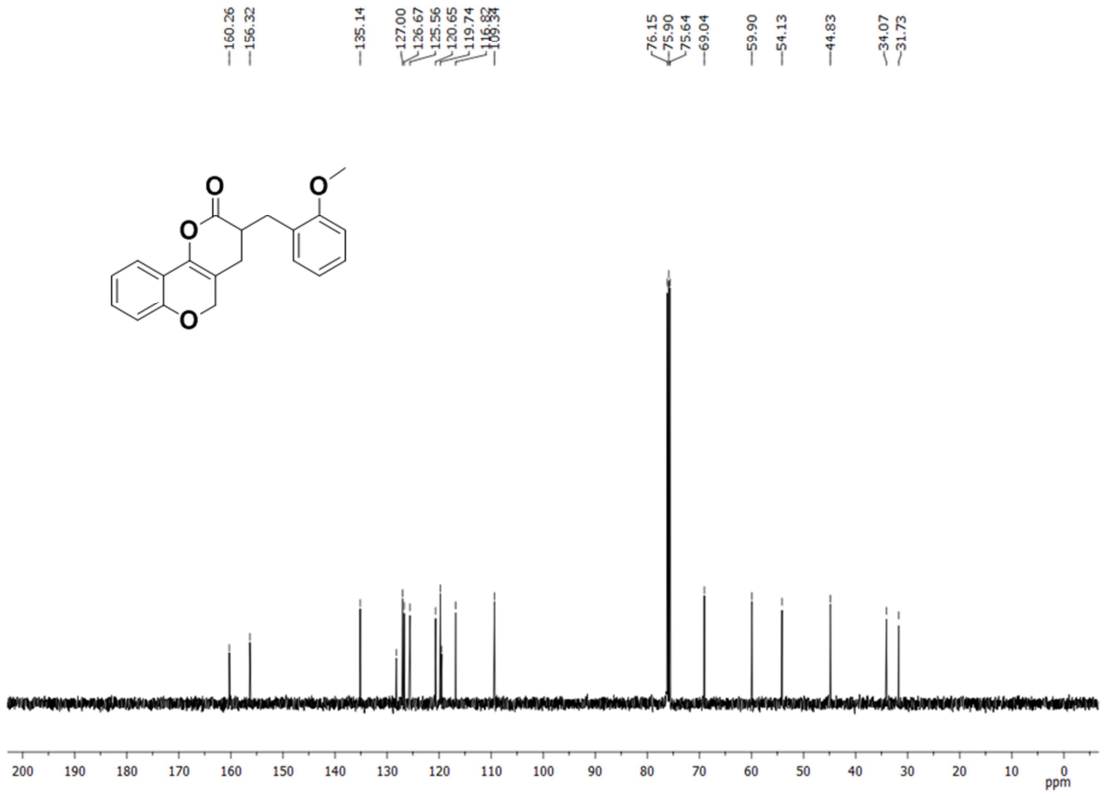
^{13}C NMR (126 MHz, $CDCl_3$) of Compound 6h



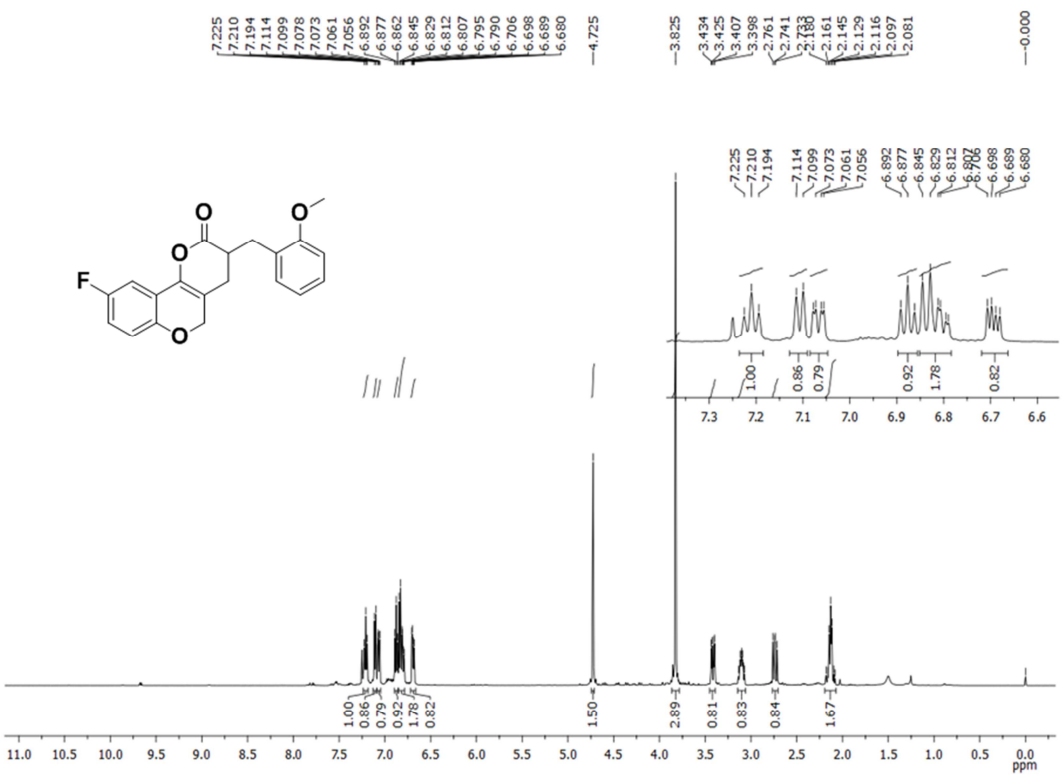
^{1}H NMR (500 MHz, $CDCl_3$) of Compound 6i



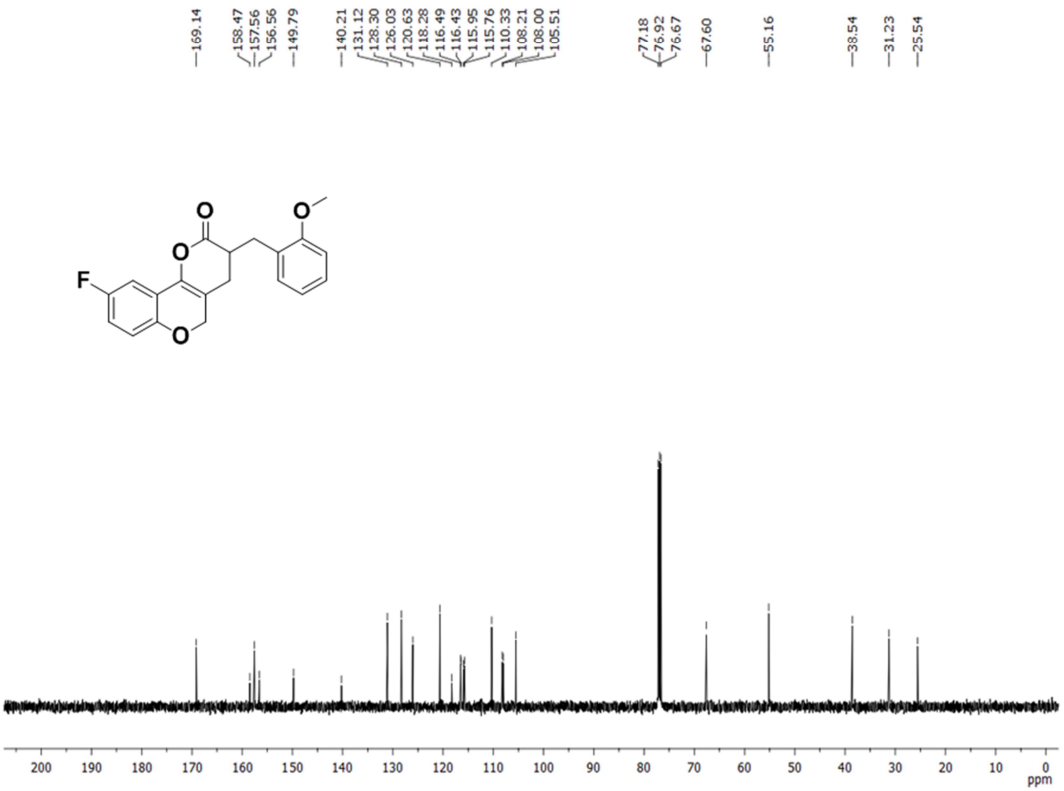
^{13}C NMR (126 MHz, $CDCl_3$) of Compound 6i



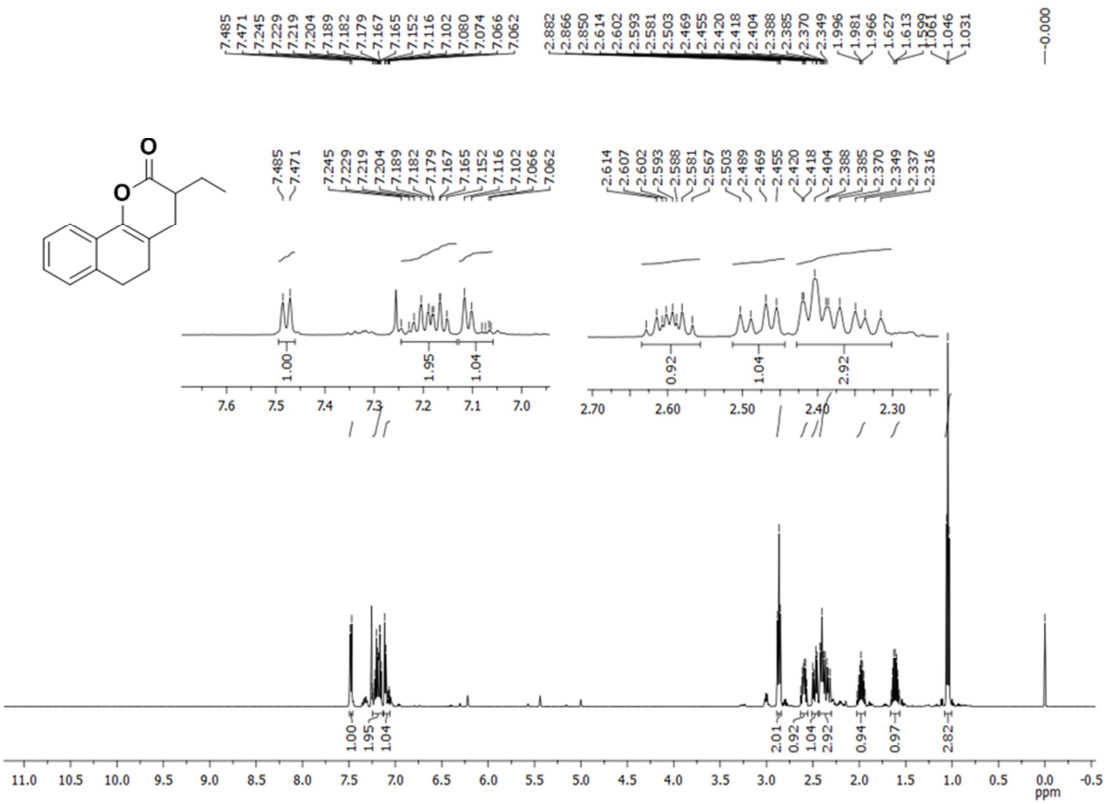
^{1}H NMR (500 MHz, $CDCl_3$) of Compound 6j



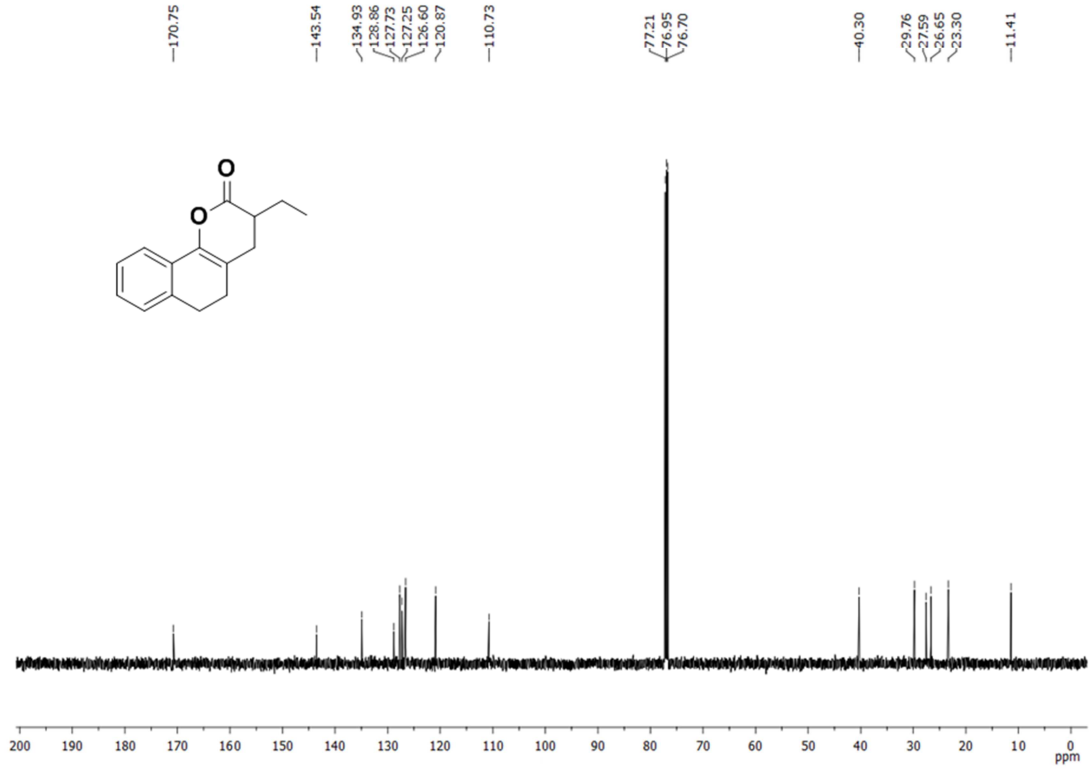
^{13}C NMR (126 MHz, $CDCl_3$) of Compound 6j



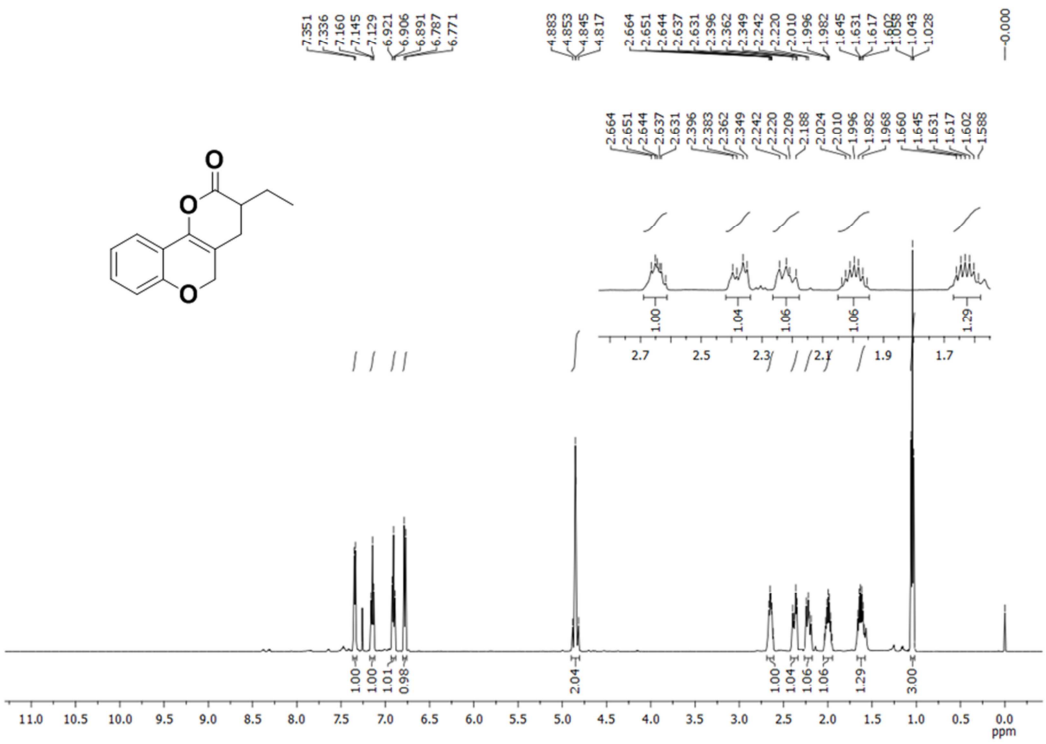
^{1}H NMR (500 MHz, $CDCl_3$) of Compound 6k



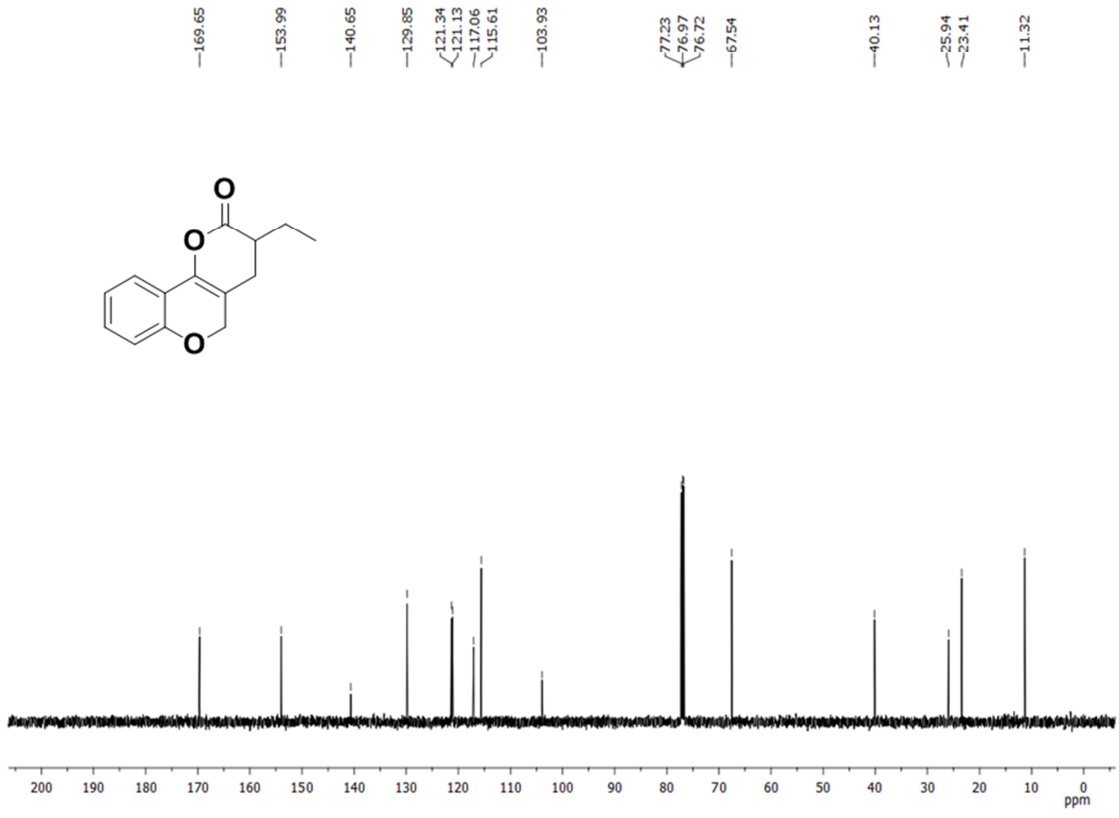
^{13}C NMR (126 MHz, $CDCl_3$) of Compound 6k



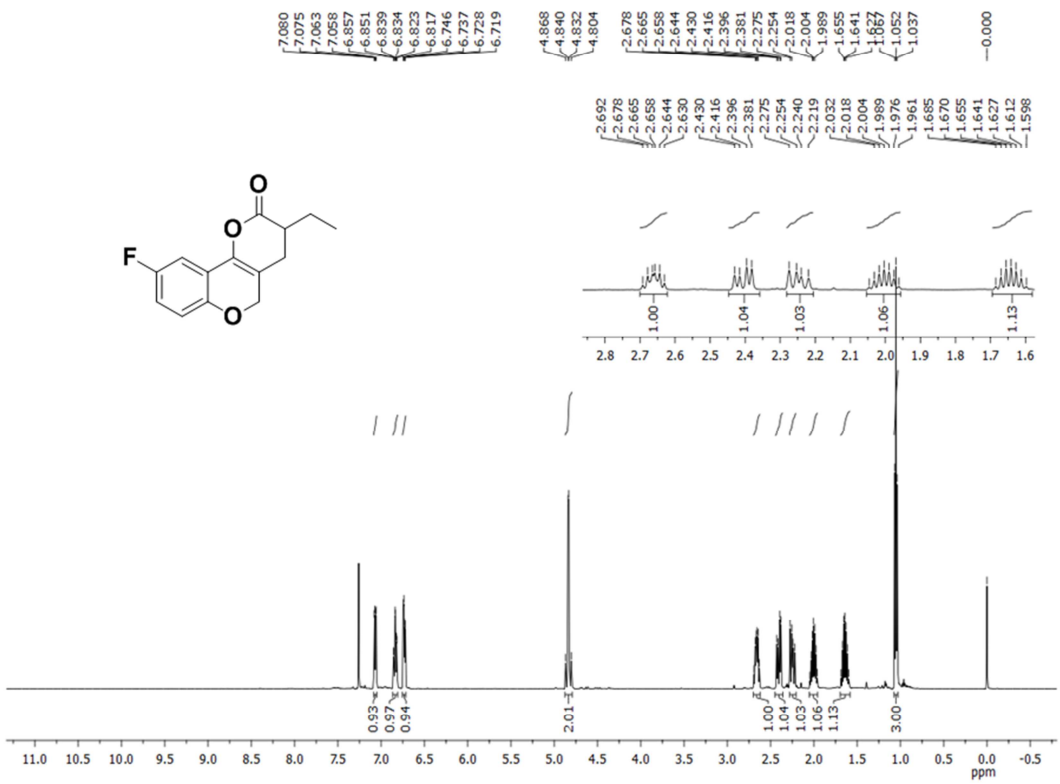
^{1}H NMR (500 MHz, $CDCl_3$) of Compound 6l



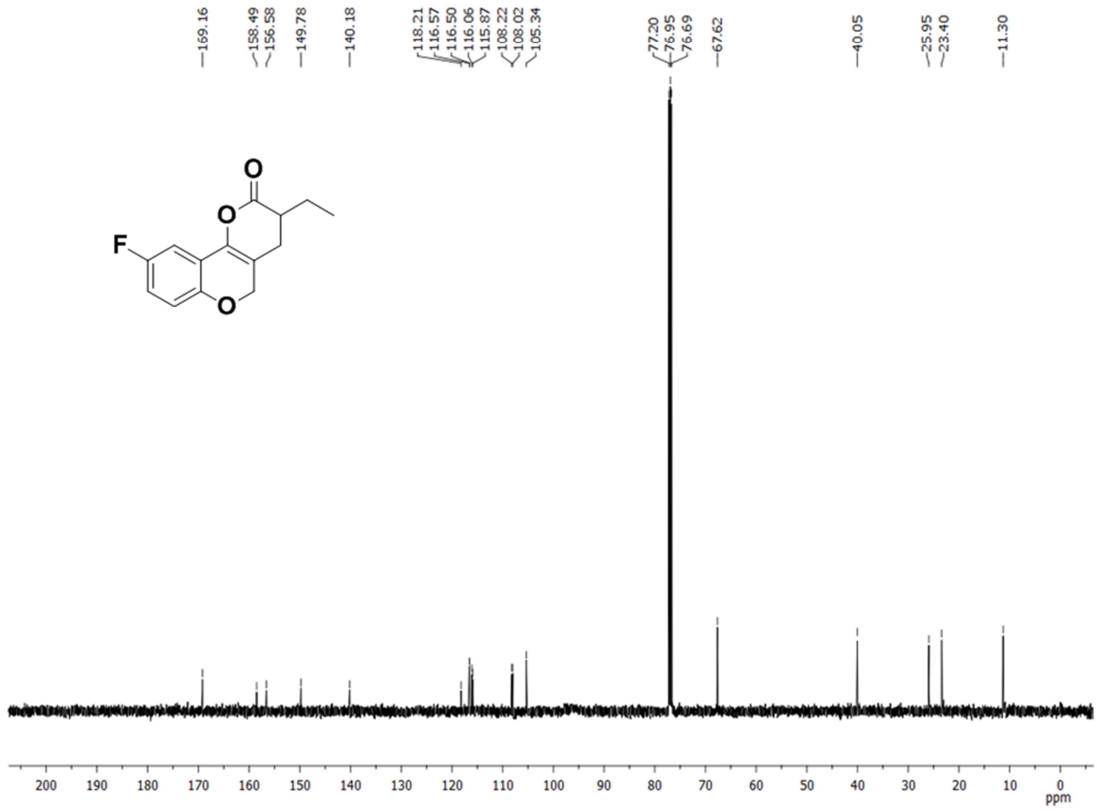
^{13}C NMR (126 MHz, $CDCl_3$) of Compound 6l



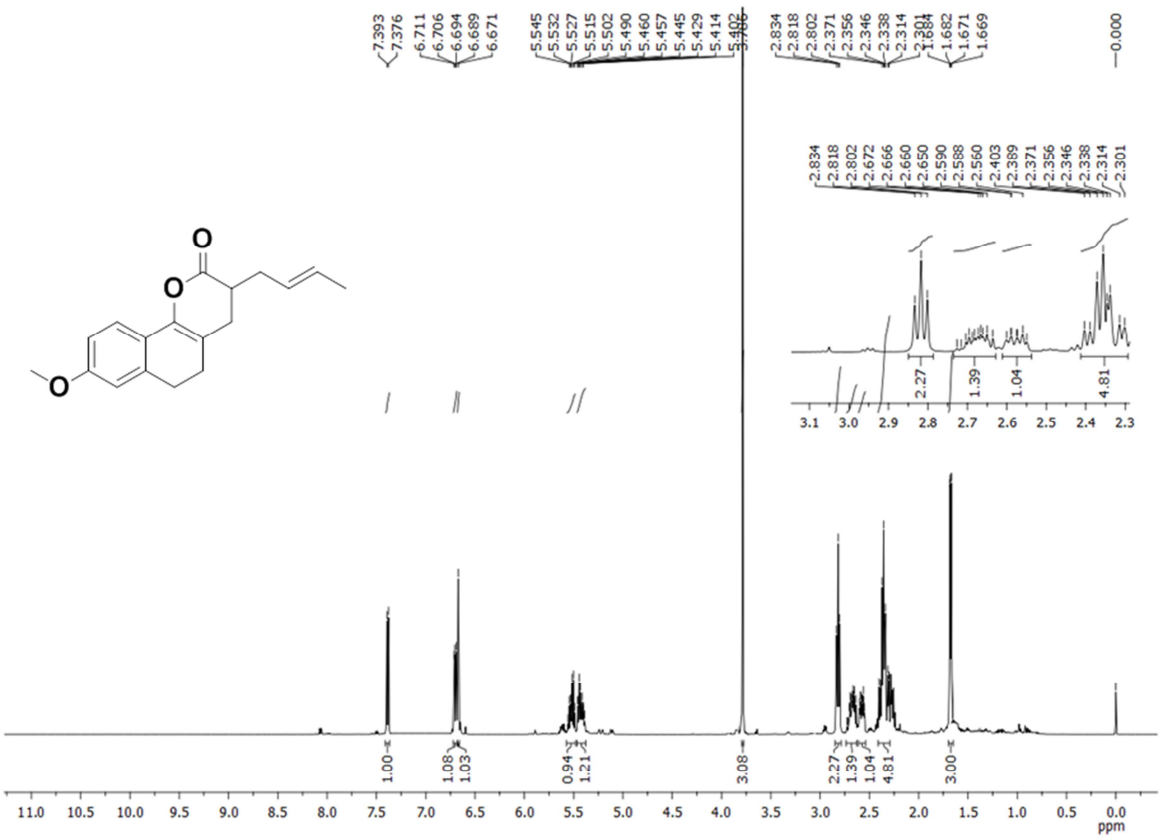
^{1}H NMR (500 MHz, $CDCl_3$) of Compound 6m



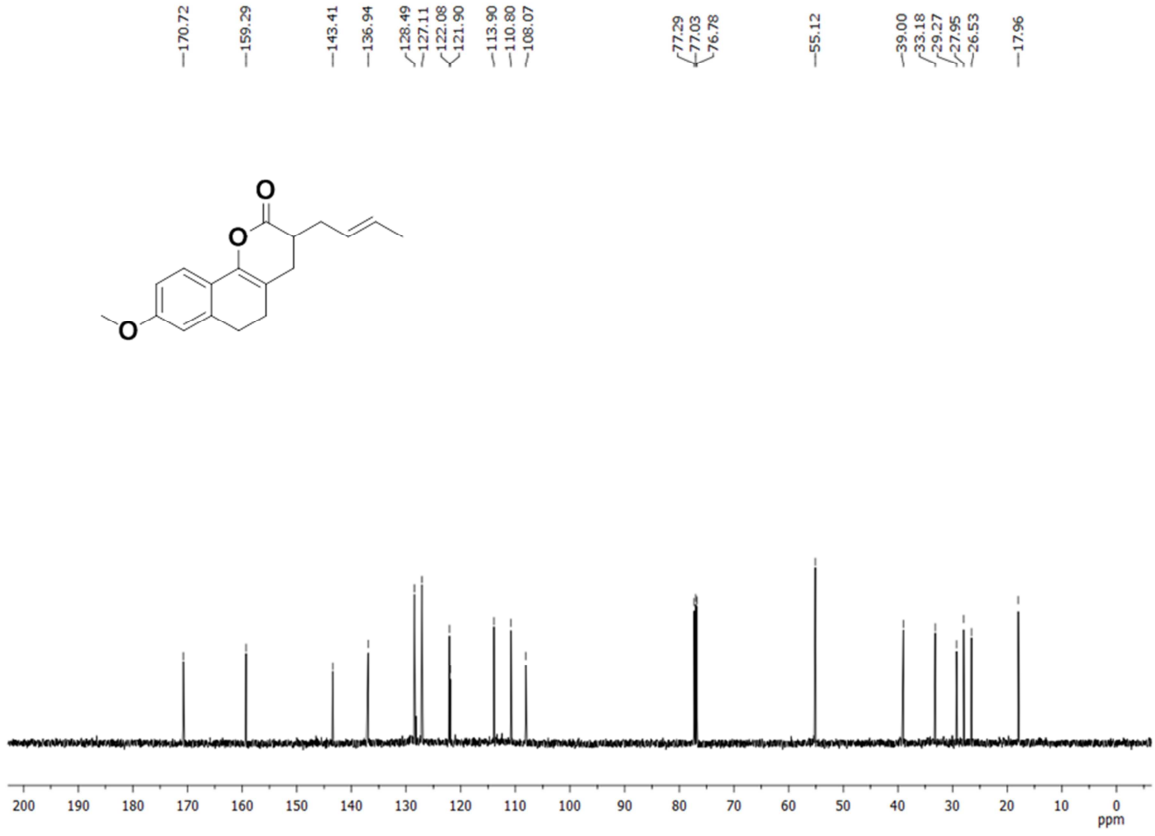
^{13}C NMR (126 MHz, $CDCl_3$) of Compound 6m



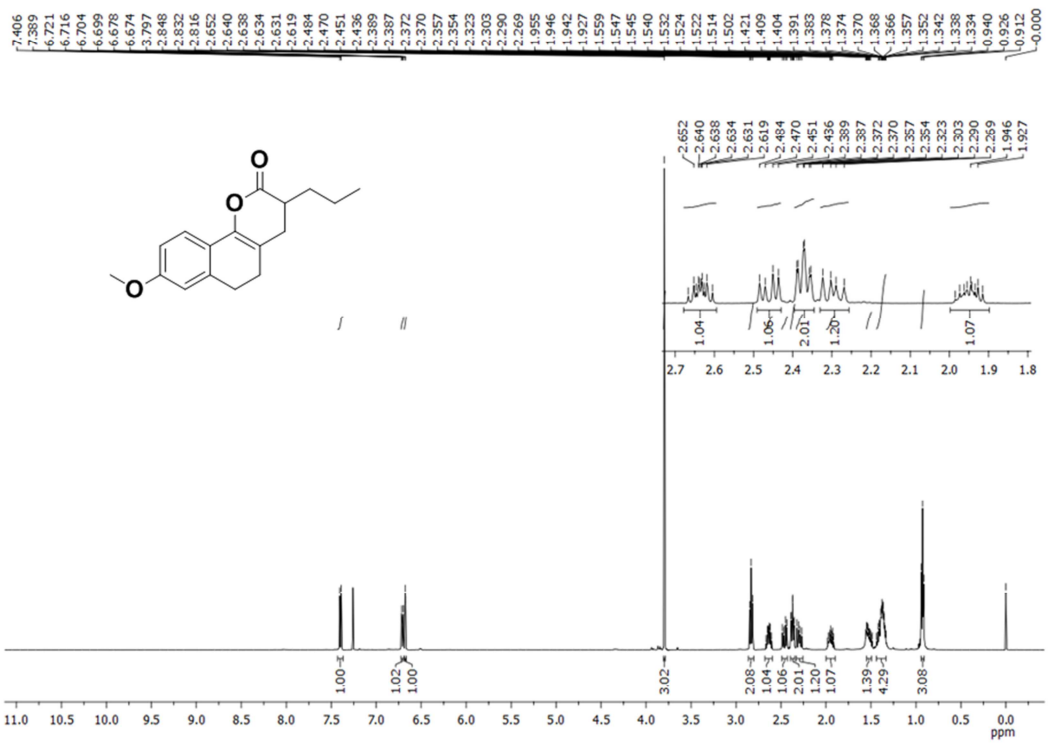
^{1}H NMR (500 MHz, $CDCl_3$) of Compound 6n



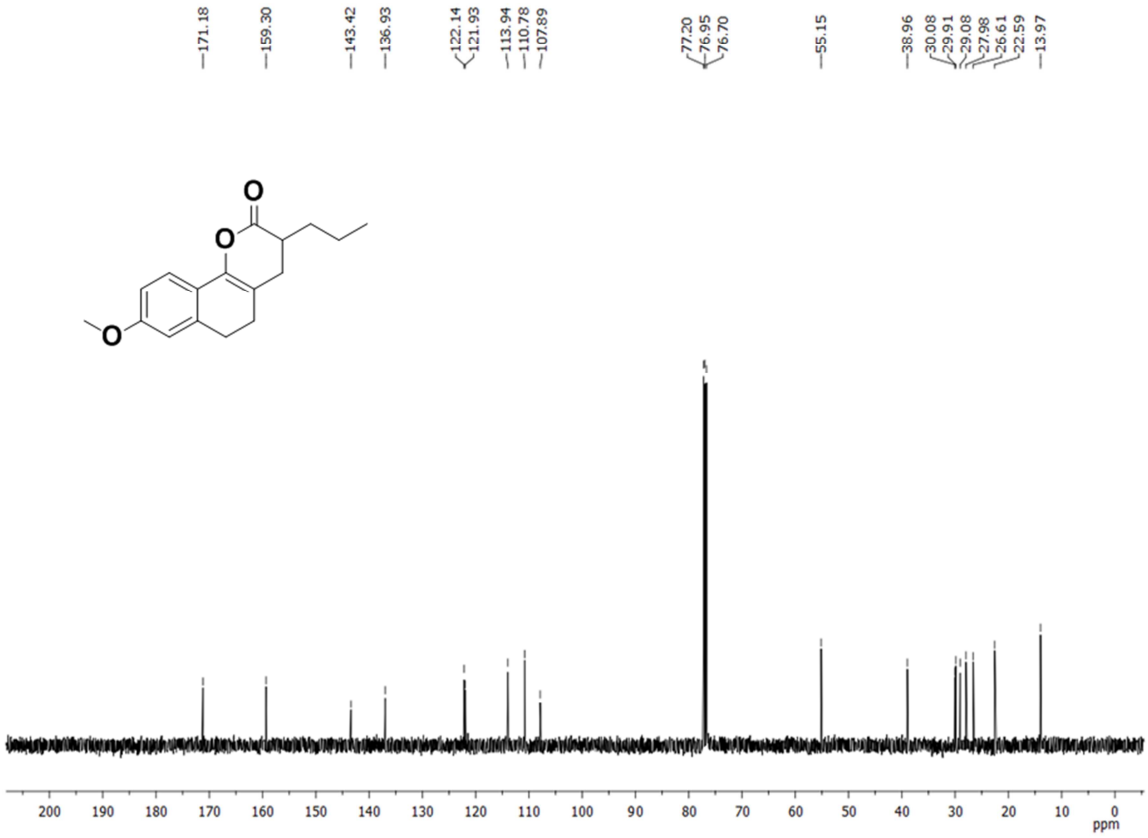
^{13}C NMR (126 MHz, $CDCl_3$) of Compound 6n



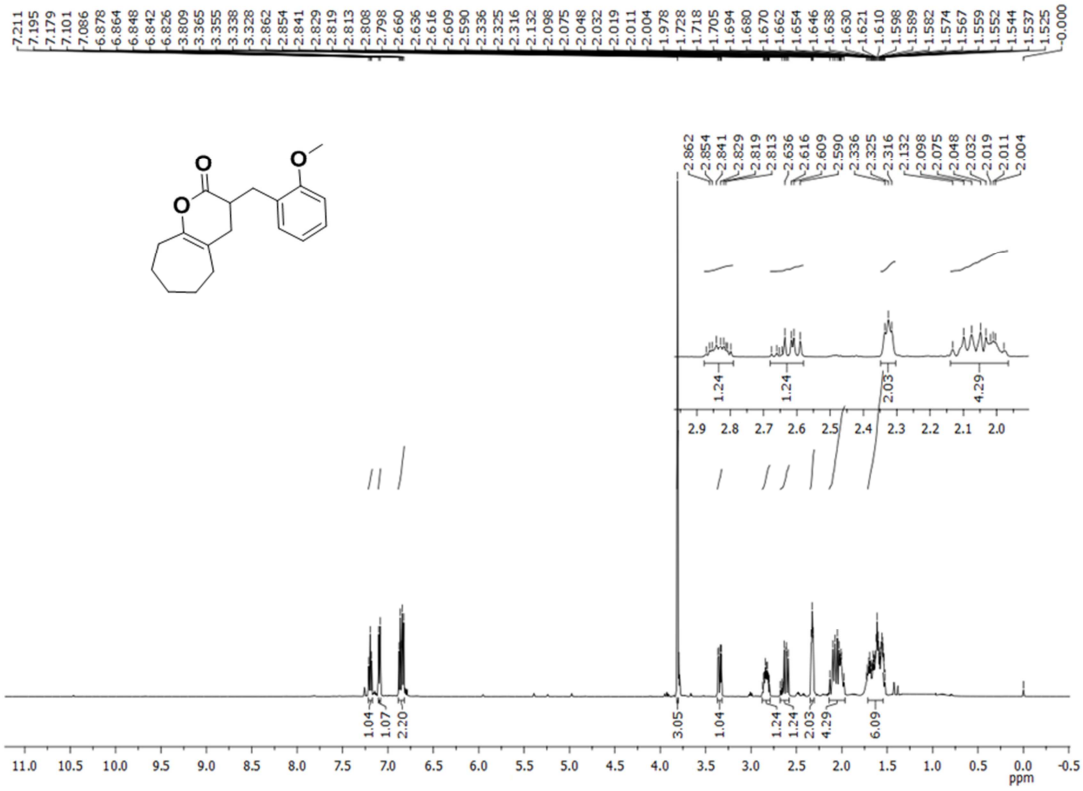
^{1}H NMR (500 MHz, $CDCl_3$) of Compound 6o



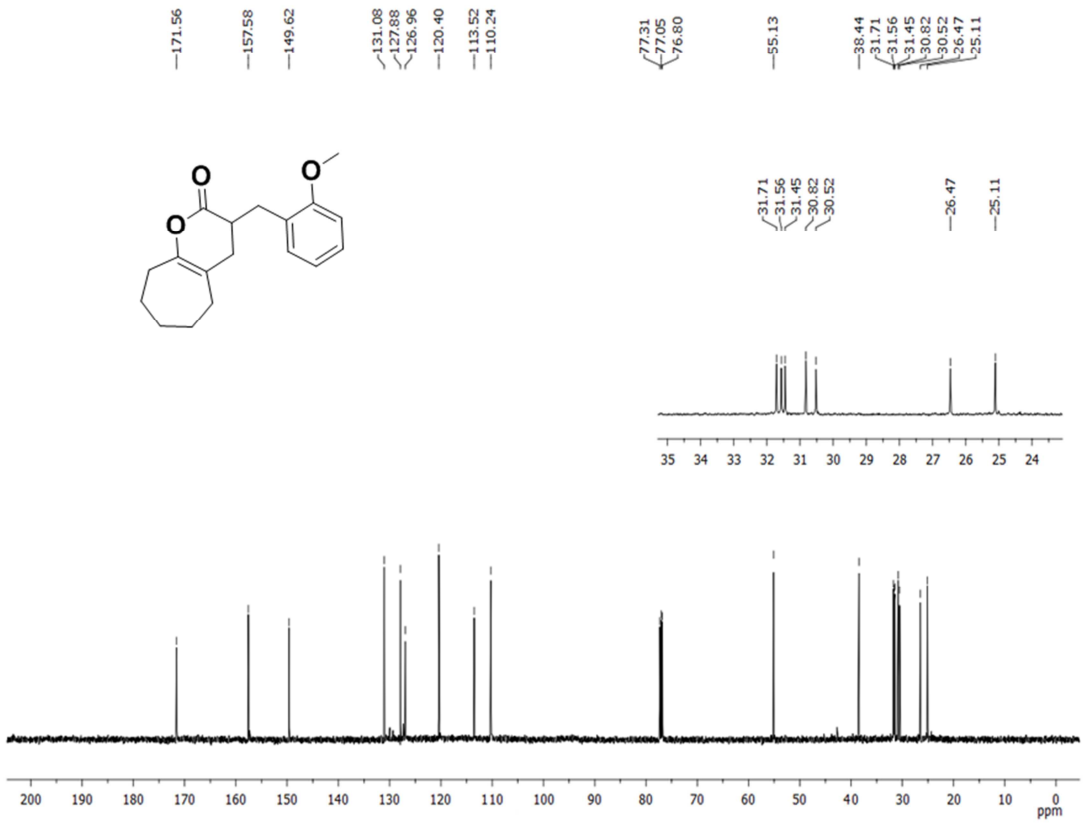
^{13}C NMR (126 MHz, $CDCl_3$) of Compound 6o



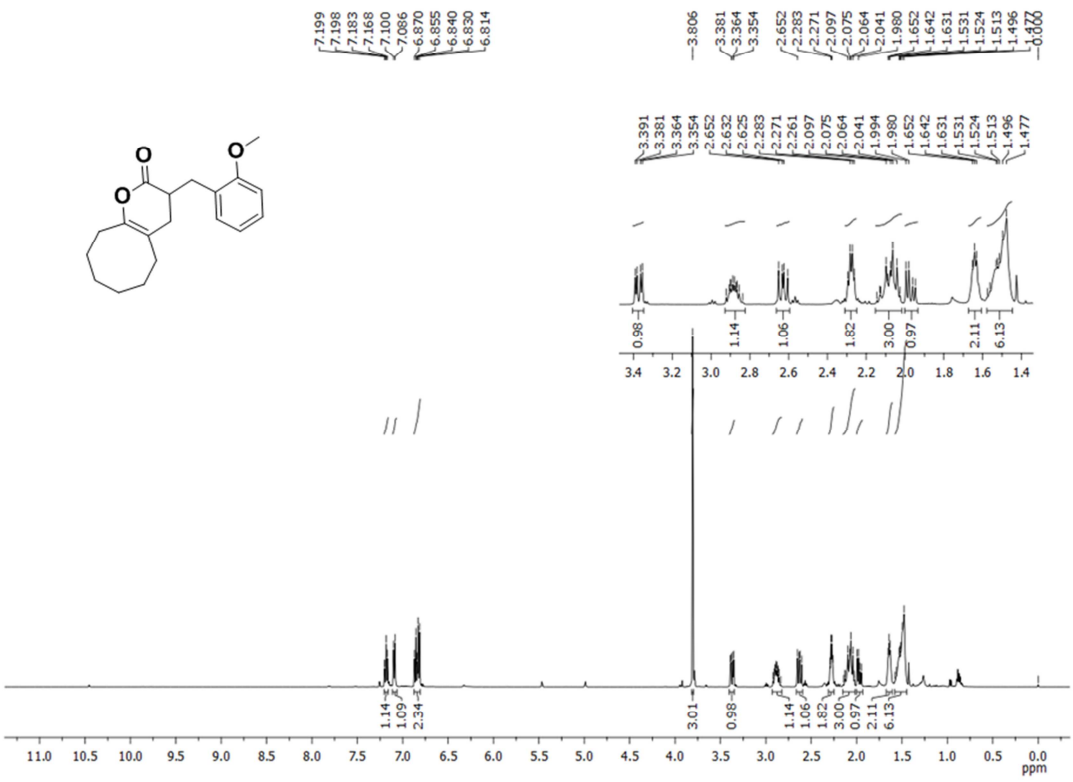
^{1}H NMR (500 MHz, $CDCl_3$) of Compound 6p



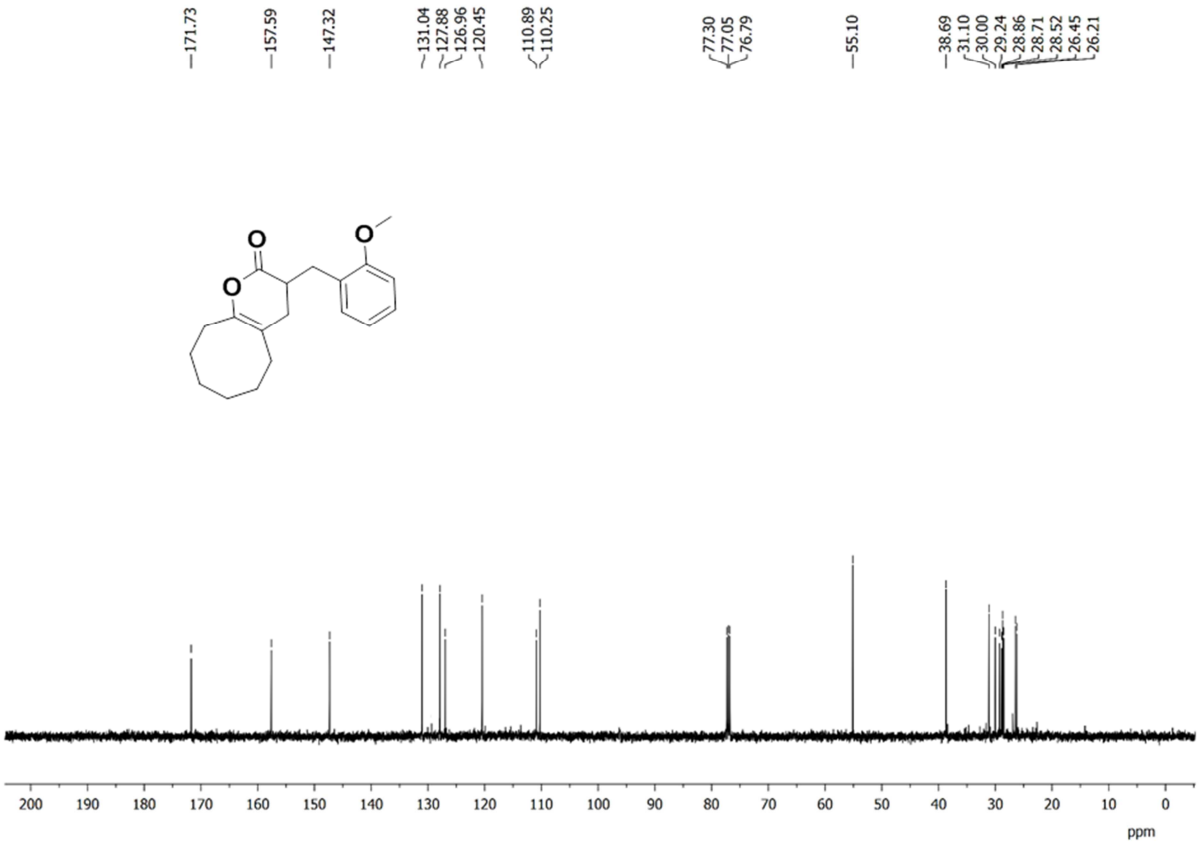
^{13}C NMR (126 MHz, $CDCl_3$) of Compound 6p

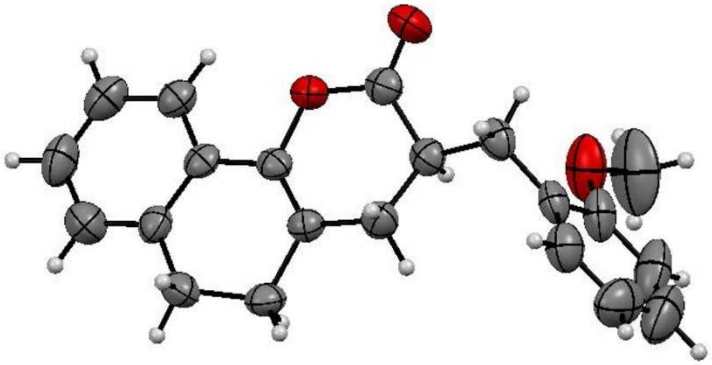


^{1}H NMR (500 MHz, $CDCl_3$) of Compound 6q



^{13}C NMR (126 MHz, $CDCl_3$) of Compound 6q





ORTEP of 6b, CCDC number: 1054134