Synthesis

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Supporting Information

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Supporting Information

Synthesis of Benzoazepinone Derivatives via Photoredox Deaminative Radical Cascade Alkylation of 1,7-Dienes- and 1,7-Enynes

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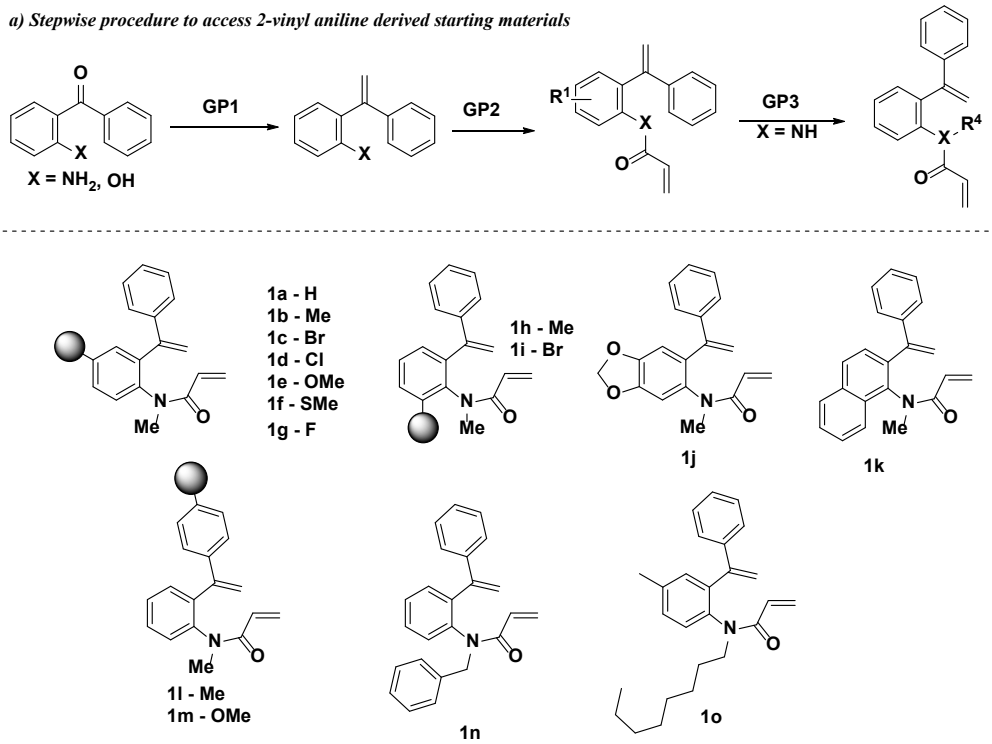
1. General Procedures for the synthesis of starting materials

a) Stepwise procedure to access 2-vinyl aniline derived starting materials



1.1.General Procedure 1 (GP1) - Synthesis of 2-Vinylanilines[1]

To a stirred solution of Ph_3PMeBr (1.5 equiv) in Dry THF (x mL) was added KO*t*Bu (1.5 equiv.) in portions under nitrogen. After the mixture was stirred at room temperature for 0.5 h, a solution of corresponding 2-aminobenzophenone (1 equiv.) in THF (x mL) was added dropwise. The reaction mixture was then stirred at room temperature under nitrogen overnight. The reaction mixture was quenched with water and extracted with EtOAc (50 mL x 2). The combined organic layers were washed with saturated $NaHCO_3$ (50 mL) and brine (50 mL), dried over anhydrous Na_2SO_4, and concentrated on rotary evaporator under vacuum and the residue was purified by column chromatography on silica gel.

1.2.General Procedure 2 (GP2) - Synthesis of *N*-phenylacrylamide[2]

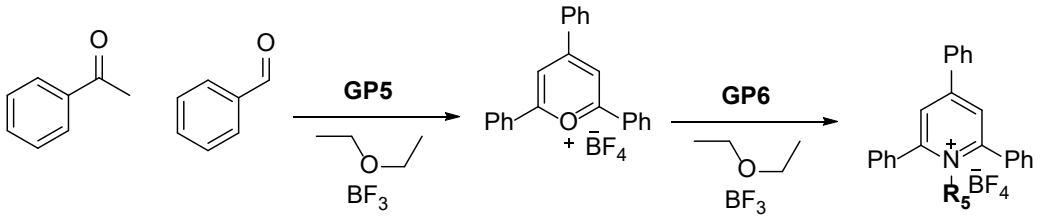
To solution of $P(OMe)_3$ (1.5 equiv.) in dichloromethane (15 mL), cooled with ice bath, was added I_2 (1.5 equiv.). After the solid iodine was completely dissolved, the corresponding acrylic acid (1.5 equiv.) and Et_3N (2.5 equiv.) were added in a sequential order. The solution was stirred for 10 minutes in the cooling bath. Next, vinylaniline was

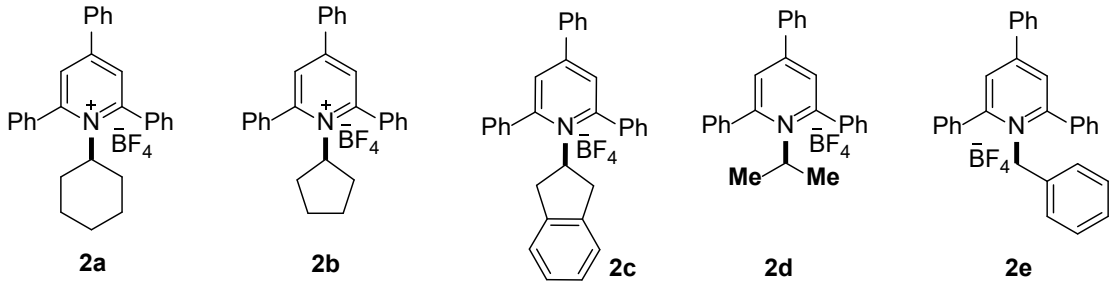
added to the corresponding mixture (1.0 equiv.), which was left to stir for additional 10 minutes. The reaction was warmed up to room temperature and stirred for 3 hours (monitoring by TLC), then the solvent was removed under vacuum and the crude product was treated with saturated aqueous solution of $NaHCO_3$ and extracted with EtOAc (3 x 30 mL). The combined organic layer was sequentially washed with water, 1 $mol \cdot L^{-1}$ HCl, water and brine, dried over anhydrous Na_2SO_4 and then purified by silica column chromatography to afford *N*-phenylacrylamide.

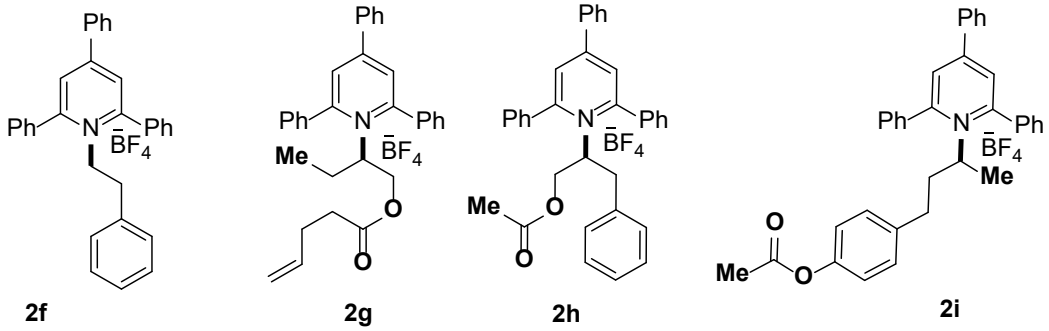
1.3.General Procedure 3 (GP3) - Synthesis of *N*-methyl-*N*-(2-(1-phenylvinyl)phenyl) acrylamide [3]

To a suspension of NaH (2.0 equiv) in THF (5.0 mL) at 0 °C, a solution of *N*-phenylacrylamide (1.0 equiv) in THF (5.0 mL) was added dropwise. The reaction mixture was stirred for 30 min and afterwards iodomethane (3.0 equiv.) was added. The reaction was stirred overnight at room temperature, quenched by water and extracted with EtOAc for (3 x 20 mL). The combined organic layers were washed with brine and dried over anhydrous Na_2SO_4. The solvent was removed under vacuum and the residue was purified by flash column chromatography.

b) Stepwise procedure to access Katritzky derived starting materials







1.4.General Procedure 4 (GP4) - Synthesis of triphenylpyrylium tetrafluoroborate

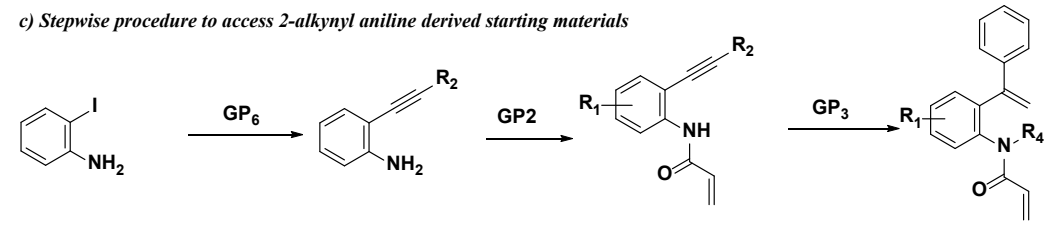
Synthesis of triphenylpyrylium tetrafluoroborate: Benzaldehyde (1 equiv) and acetophenone (2 equiv) were placed in a closed two-necked flask equipped with a magnetic stirrer, then boron trifluoride etherate (2.5 equiv) was added dropwise under argon treatment. The mixture was reacted at 100 ºC for two hours and cooled to ambient temperature. Ether was added to the reaction mixture and the resulting suspension stirred at ambient temperature. The solid was collected by filtration and washed with ether. Recrystallization by acetone and hexane to get pure light yellow solid.

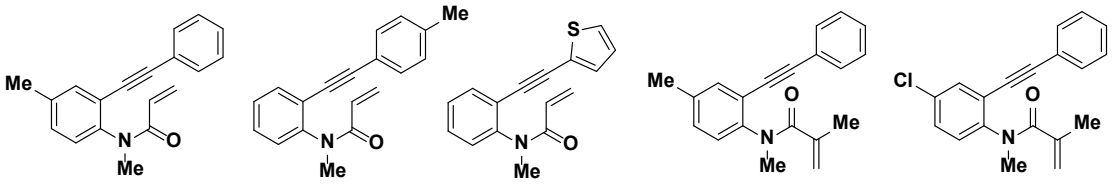
1.5.General Procedure 5 (GP5) - Synthesis of pyridinium salts

A Schlenk tube equipped with a magnetic stirrer bar was charged with triphenylpyrylium tetrafluoroborate (1.0 equiv.) and, if solid, the corresponding primary amine (1.2 equiv.). Ethanol (1.0 M) was added to the reaction vessel and the tube sealed. No precautions to protect the reaction mixture from air and moisture were taken. The reaction mixture was heated to 85-90 °C and after 4 h cooled to ambient temperature. If precipitation occurred

during this step, the solid was collected by filtration and washed with ethanol and diethyl ether. In case no precipitation occurred, diethyl ether was added to the reaction mixture and the resulting suspension stirred at room temperature for at least 1 h to complete the precipitation process. The solid was collected by filtration and washed with diethyl ether. After the operations required the solids were dried under reduced pressure to obtain the analytically pure pyridinium salts.

c) Stepwise procedure to access 2-alkynyl aniline derived starting materials





5a 5b 5c 5d 5e

1.6.General Procedure 6 (GP6) – Synthesis of 2-Alkynyl aniline[4]

To an organic halide (1.0 equiv.) and the respective alkyne (1.5 equiv.) dissolved in triethylamine (30 mL/mmol), was added dichlorobis(triphenylphosphine) palladium (II) (5 mol%) and copper iodide (10 mol%) to the reaction mixture. The mixture was stirred for 4-16 h at room temperature. Upon completion (monitored by TLC), the reaction mixture was diluted with water and the aqueous phase extracted with DCM (3 x 20 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated under reduced pressure. The crude mixture was purified by column chromatography.

1.7. General Procedure 7 (GP7)

To a dried Schlenk tube was treated with 1a (0.20 mmol, 1.0 equiv), 2a-2i (0.1 mmol, 1.1 equiv), photocatalyst (0.00265 mmol, 2,5 mol %). Subsequently, DMA (2.0 mL), 2,6-lutidine (0.12mmol, 1.2 equiv) were added. And then this mixture solution was degassed for 3 times via ‘freeze-pump-thaw’ procedure. After that, this resulting solution was stirred at a distance of ~2 cm under irradiation by 2*3 W blue LEDs at room temperature

for 48 h. The solvent was evaporated, and the crude product was purified by column chromatography using hexane/ethyl acetate as eluent (8:2), affording the desired product.

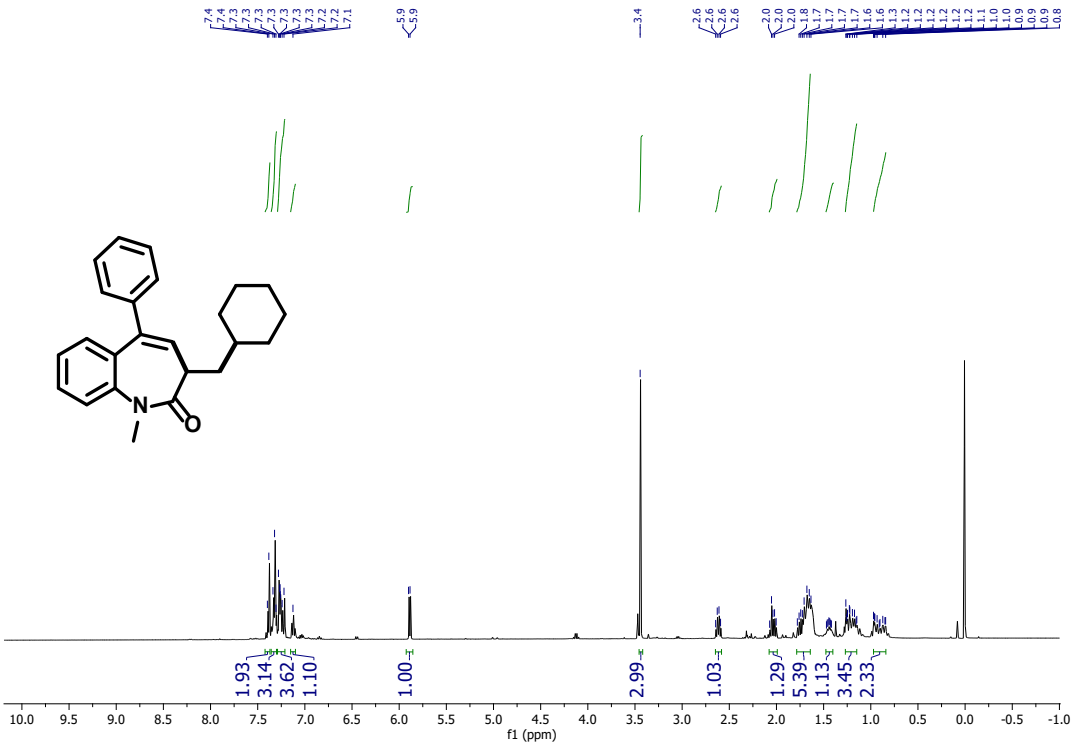
Set-up of the reaction

1.8.General Procedure 8 (GP8)

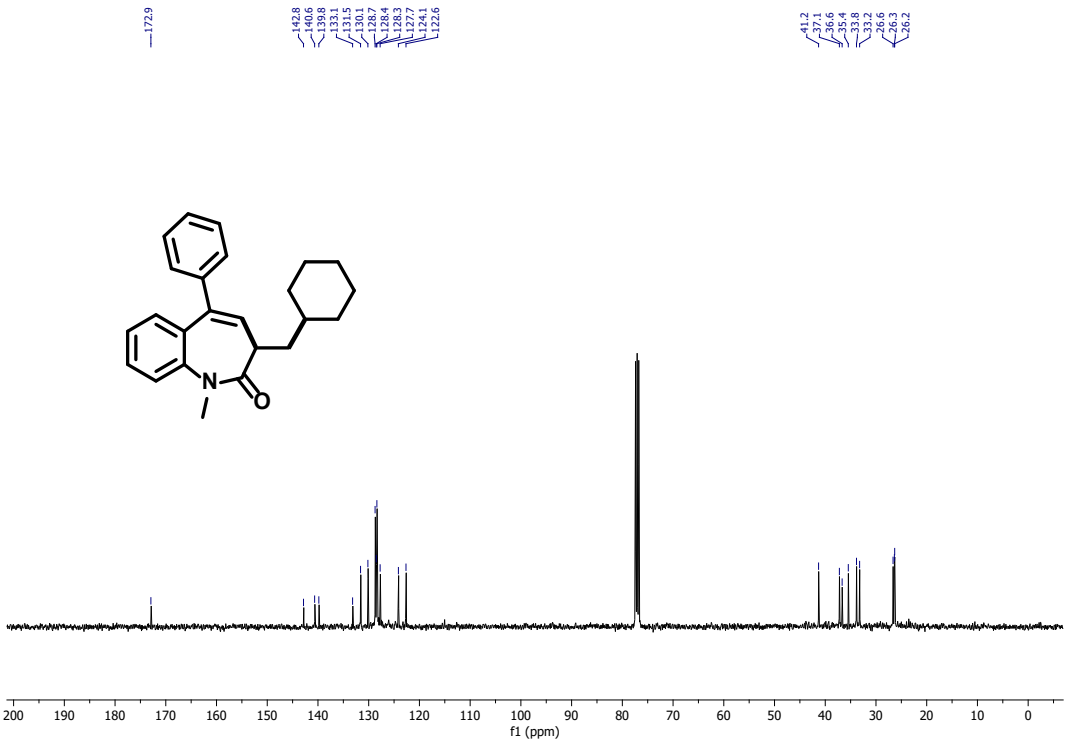
To a dried Schlenk tube was treated with 5a-5e (0.20 mmol, 1.0 equiv), 2a (0.1 mmol, 1.1 equiv), photocatalyst (0.00265 mmol, 2,5 mol %). Subsequently, DMA (2.0 mL), 2,6-lutidine (0.12mmol, 1.2 equiv) were added. And then this mixture solution was degassed for 3 times via ‘freeze-pump-thaw’ procedure. After that, this resulting solution was stirred at a distance of ~2 cm under irradiation by 2*3 W blue LEDs at room temperature for 48 h. The solvent was evaporated, and the crude product was purified by column chromatography using hexane/ethyl acetate as eluent (8:2), affording the desired product.

2. NMR Spectra of photoreactions

3-(cyclohexylmethyl)-1-methyl-5-phenyl-1,3-dihydro-2H-benzo[*b*]azepin-2-one (3a)

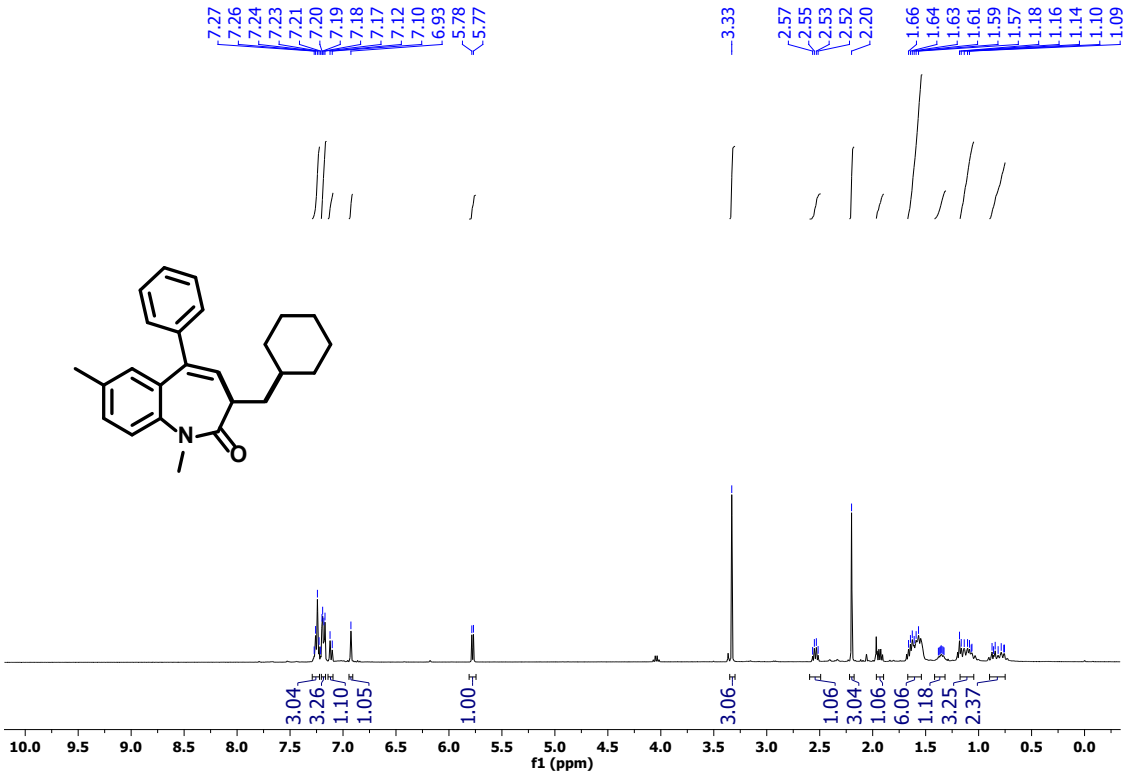


^{1}H NMR(400 MHz, $CDCl_3$) of compound **3a**

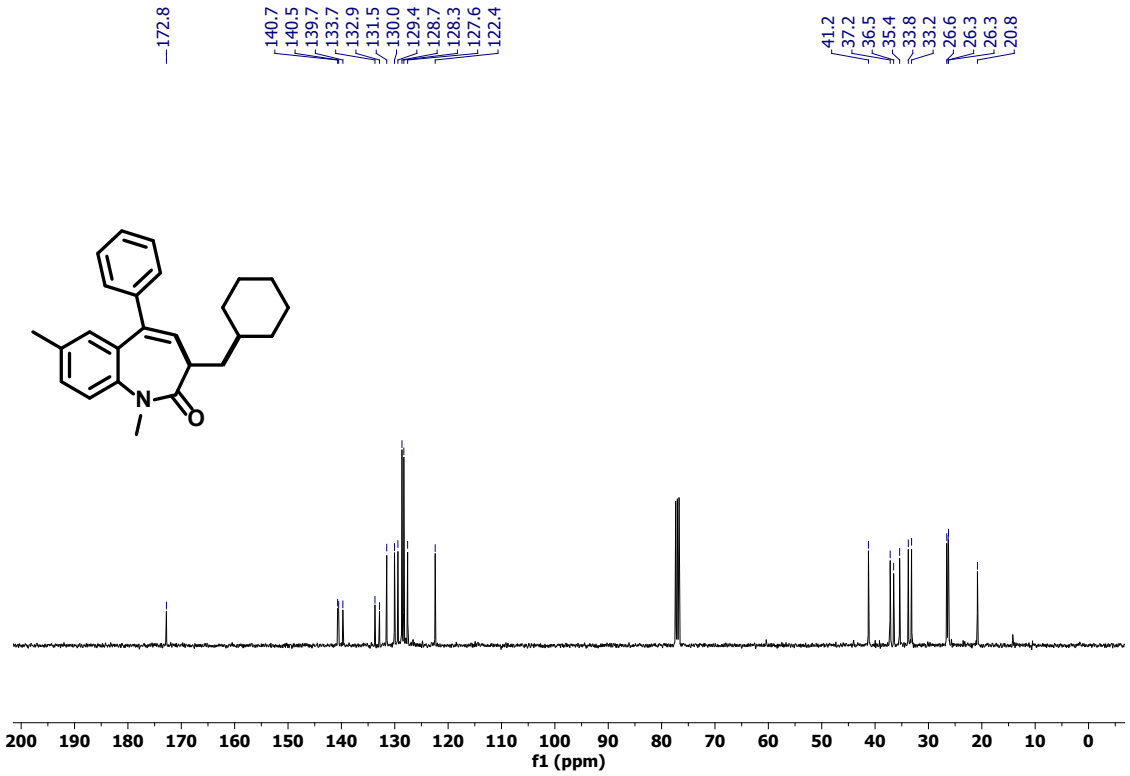


^{13}C NMR(100 MHz, $CDCl_3$) of compound **3a**

3-(cyclohexylmethyl)-1,7-dimethyl-5-phenyl-1,3-dihydro-2H-benzo[b]azepin-2-one (3b)

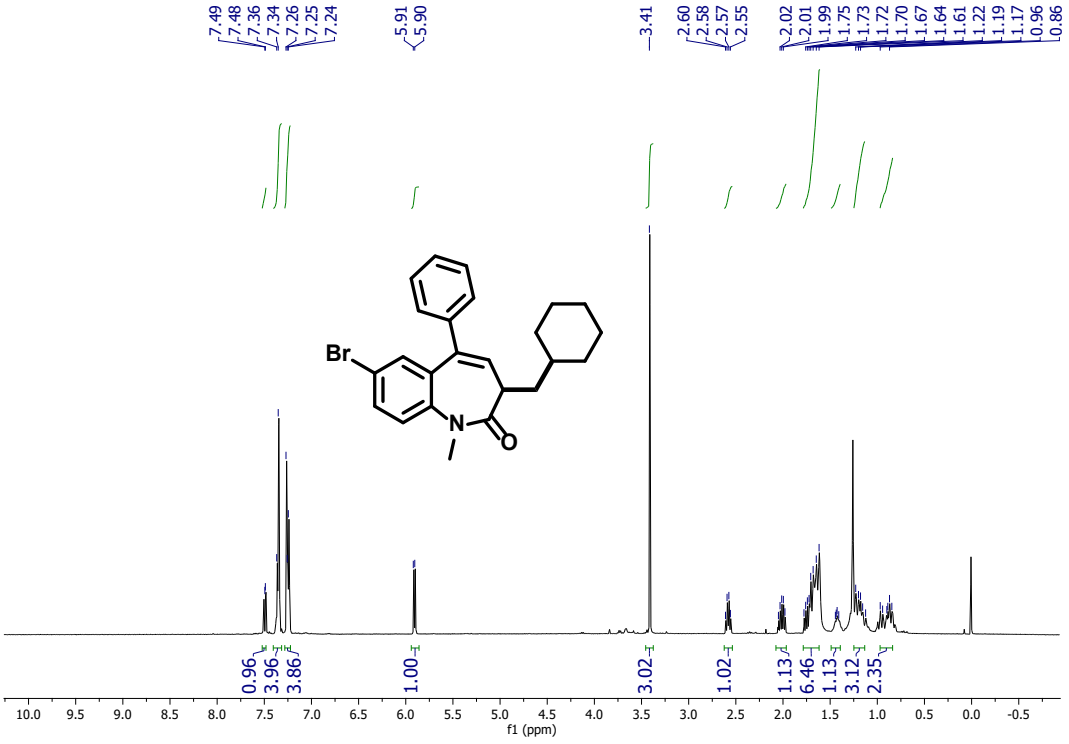


^{1}H NMR(400 MHz, $CDCl_3$) of compound **3b**

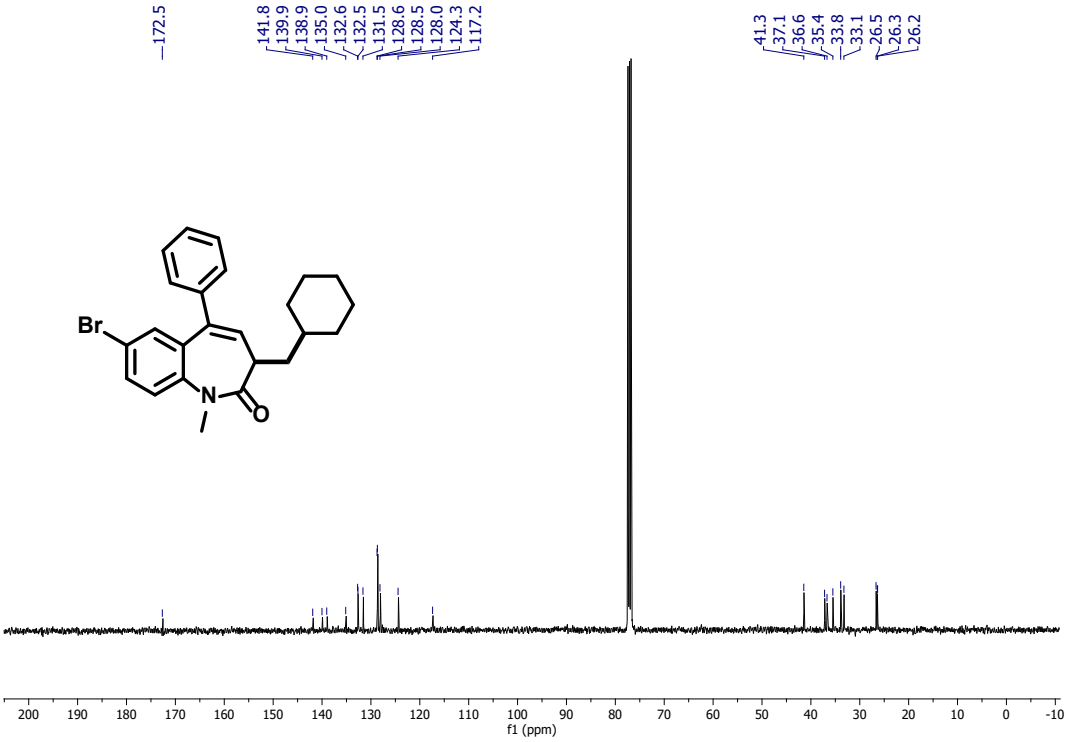


^{13}C NMR(100 MHz, $CDCl_3$) of compound **3b**

7-bromo-3-(cyclohexylmethyl)-1-methyl-5-phenyl-1,3-dihydro-2H-benzo[b]azepin-2-one (3c)

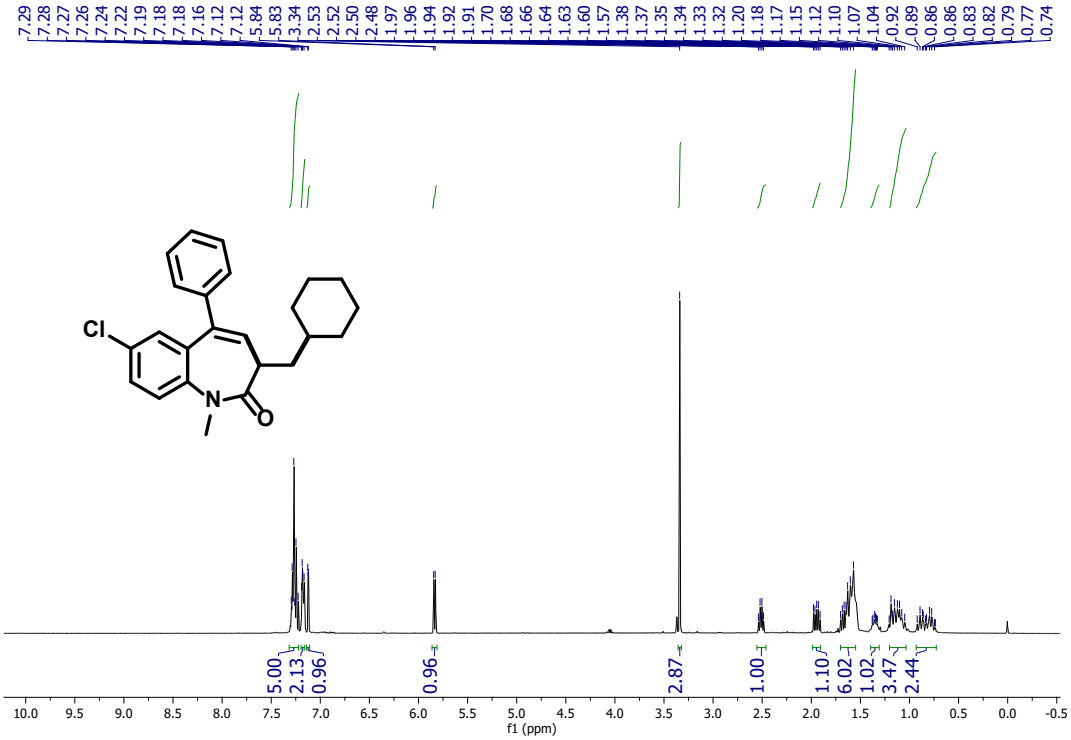


^{1}H NMR(400 MHz, $CDCl_3$) of compound **3c**

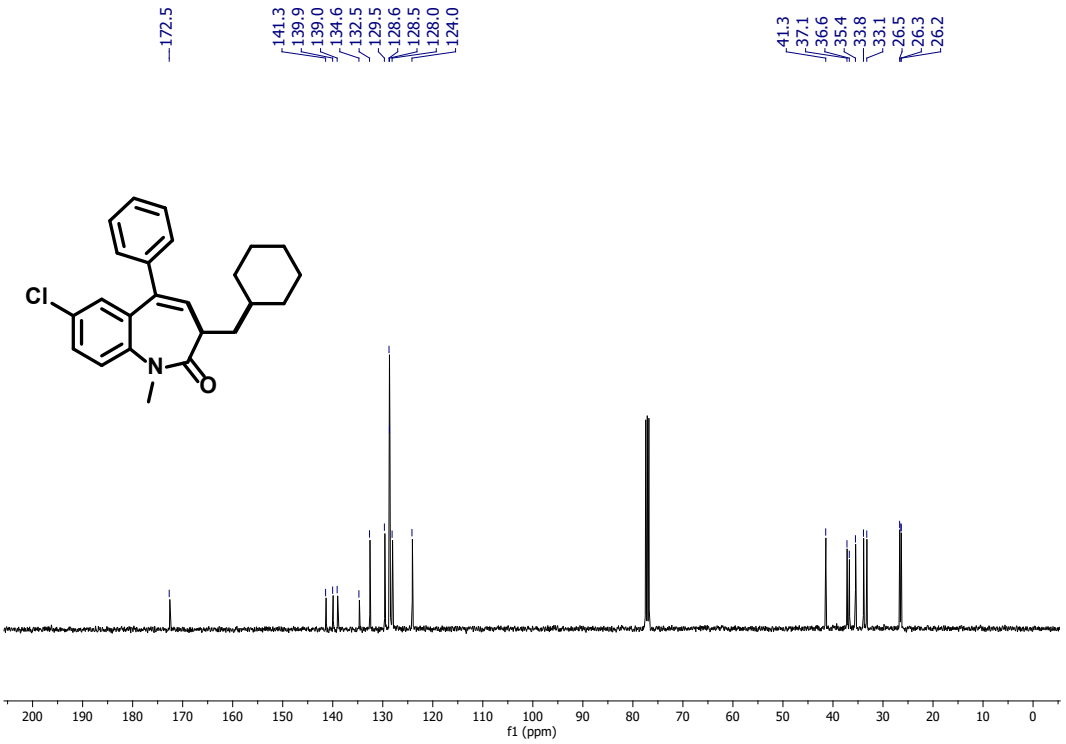


^{13}C NMR(100 MHz, $CDCl_3$) of compound **3c**

7-chloro-3-(cyclohexylmethyl)-1-methyl-5-phenyl-1,3-dihydro-2H-benzo[*b*]azepin-2-one (3d)

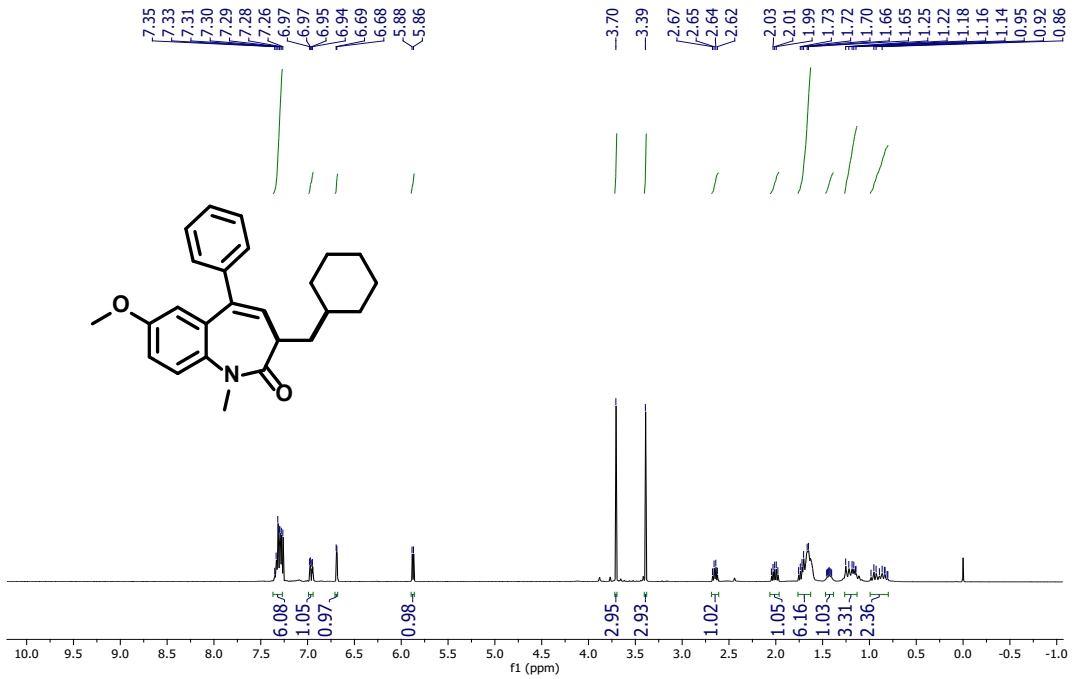


^{1}H NMR(400 MHz, $CDCl_3$) of compound **3d**

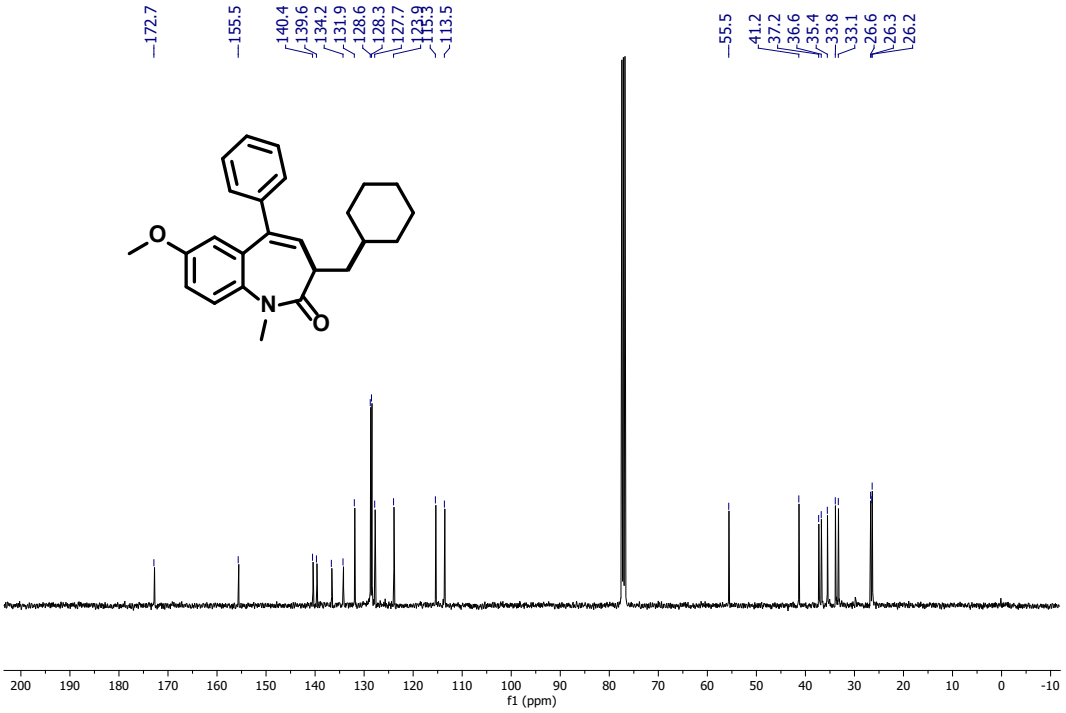


^{13}C NMR(100 MHz, $CDCl_3$) of compound **3d**

3-(cyclohexylmethyl)-7-methoxy-1-methyl-5-phenyl-1,3-dihydro-2H-benzo[b]azepin-2-one (3e)

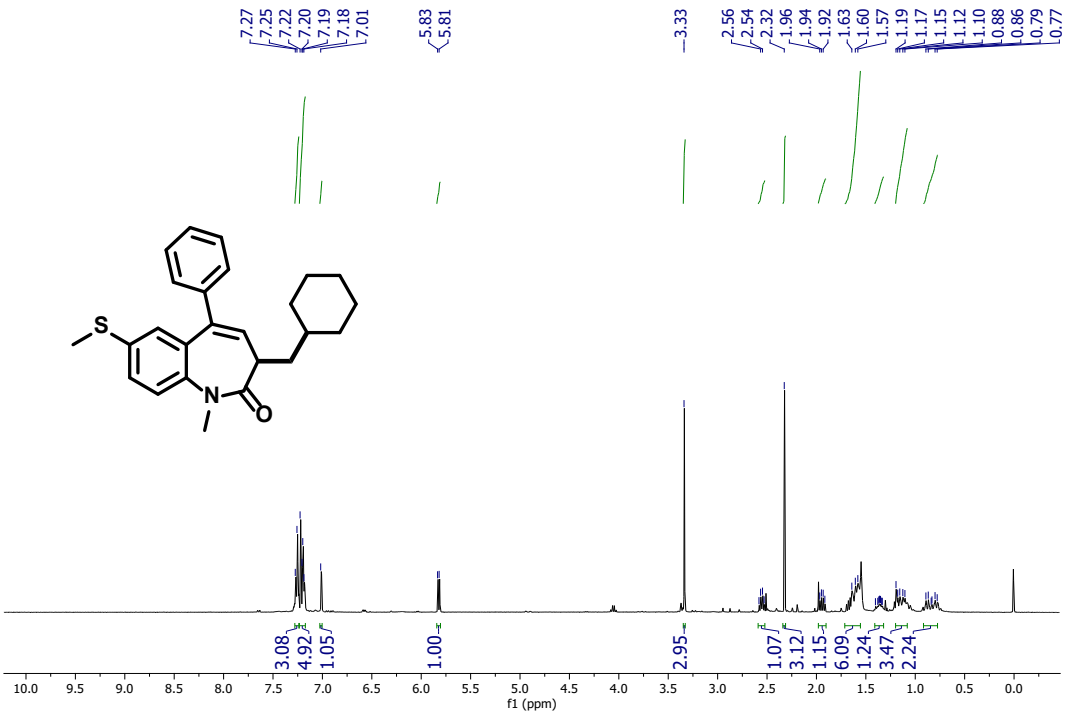


^{1}H NMR(400 MHz, $CDCl_3$) of compound **3e**

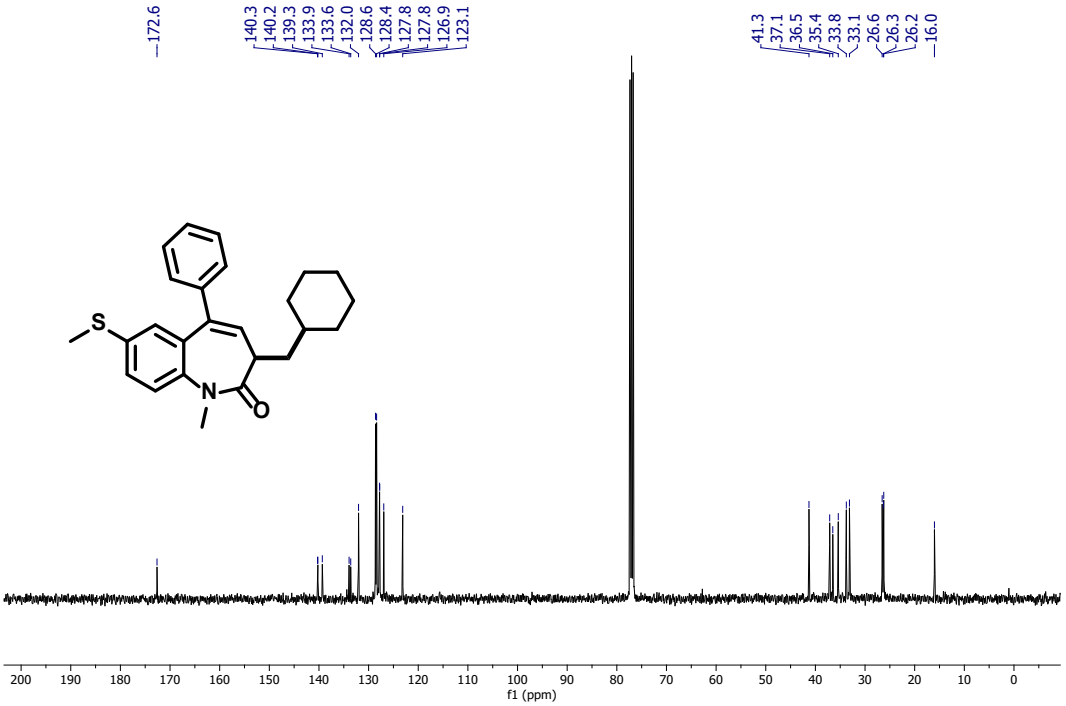


^{13}C NMR(100 MHz, $CDCl_3$) of compound **3e**

3-(cyclohexylmethyl)-1-methyl-7-(methylthio)-5-phenyl-1,3-dihydro-2H-benzo[b]azepin-2-one (3f)

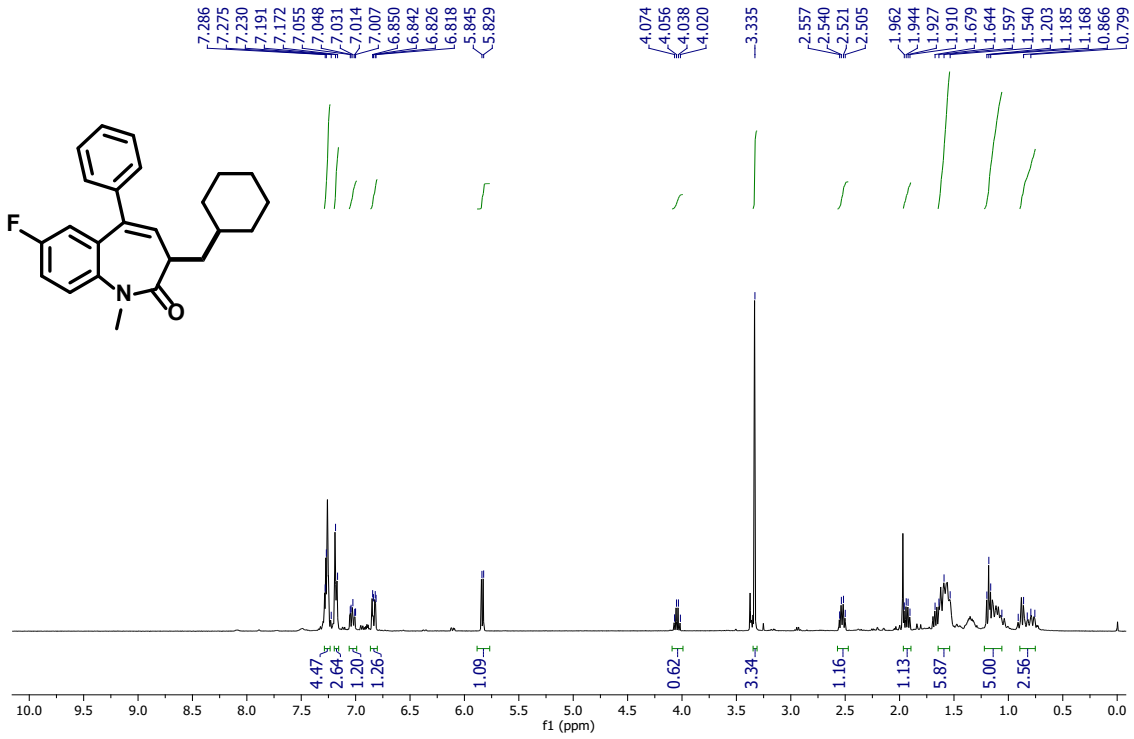


^{1}H NMR(400 MHz, $CDCl_3$) of compound **3f**

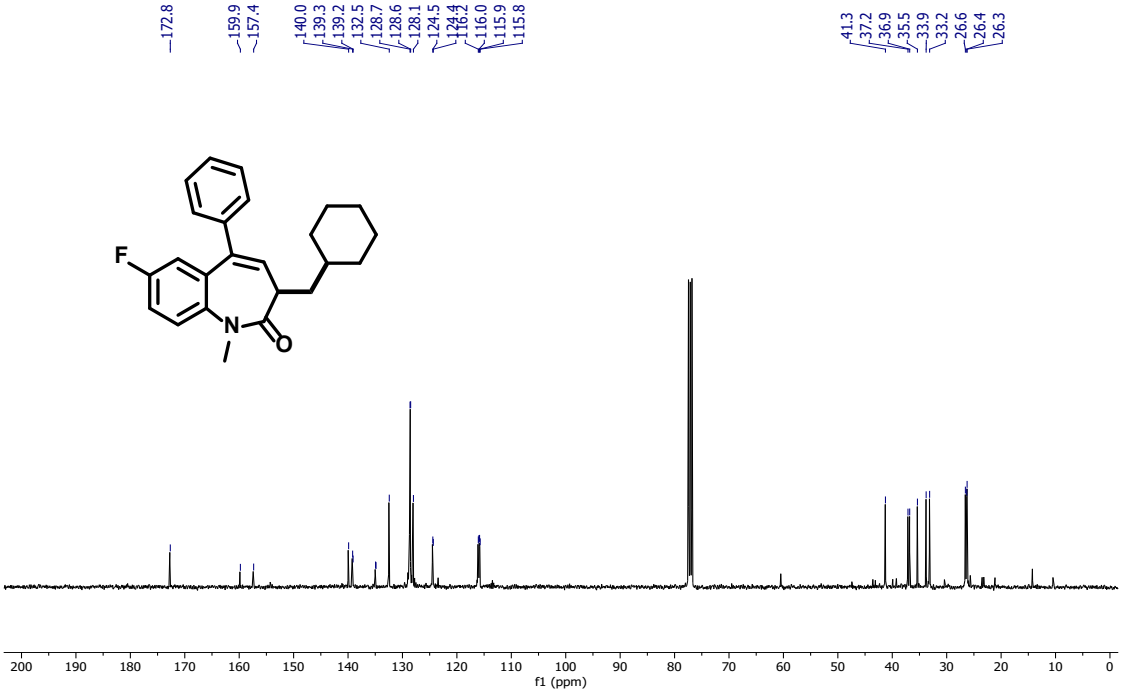


^{13}C NMR(100 MHz, $CDCl_3$) of compound **3f**

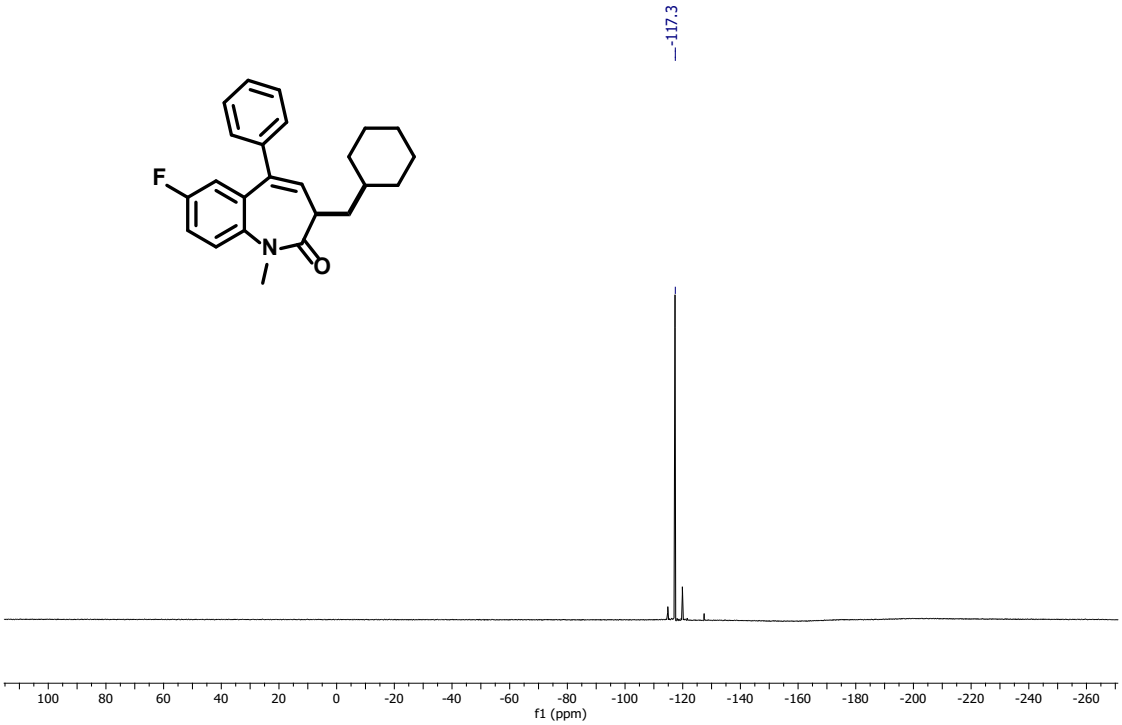
3-(cyclohexylmethyl)-7-fluoro-1-methyl-5-phenyl-1,3-dihydro-2H-benzo[b]azepin-2-one (3g)



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

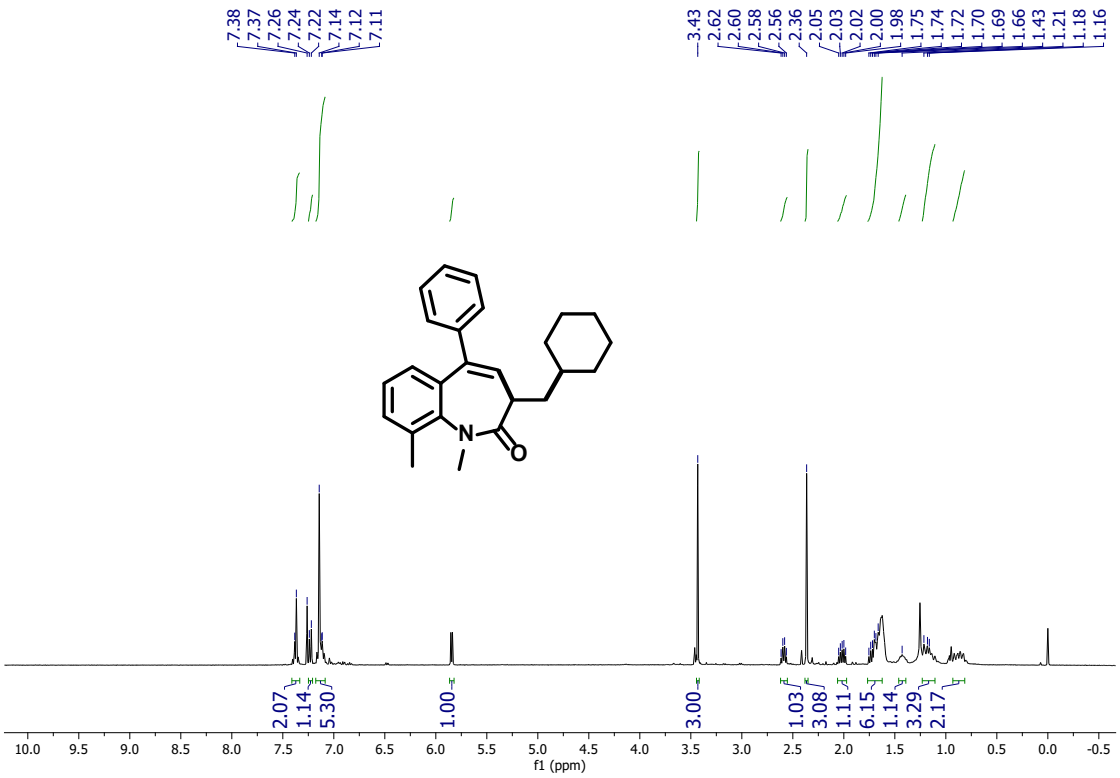


^{13}C NMR(100 MHz, $CDCl_3$) of compound **3g**

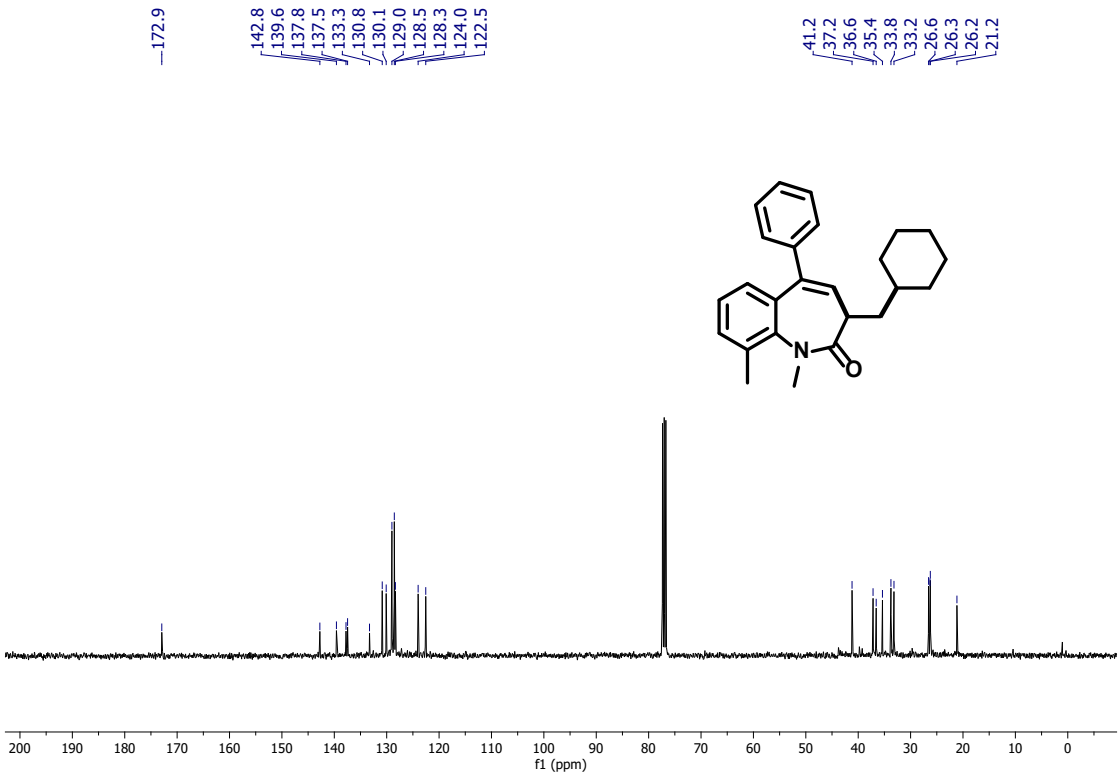


^{19}F NMR NMR (377 MHz, $CDCl_3$) of compound **3g**

<u>3-(cyclohexylmethyl)-1,9-dimethyl-5-phenyl-1,3-dihydro-2H-benzo[b]azepin-2-one (3h)</u>

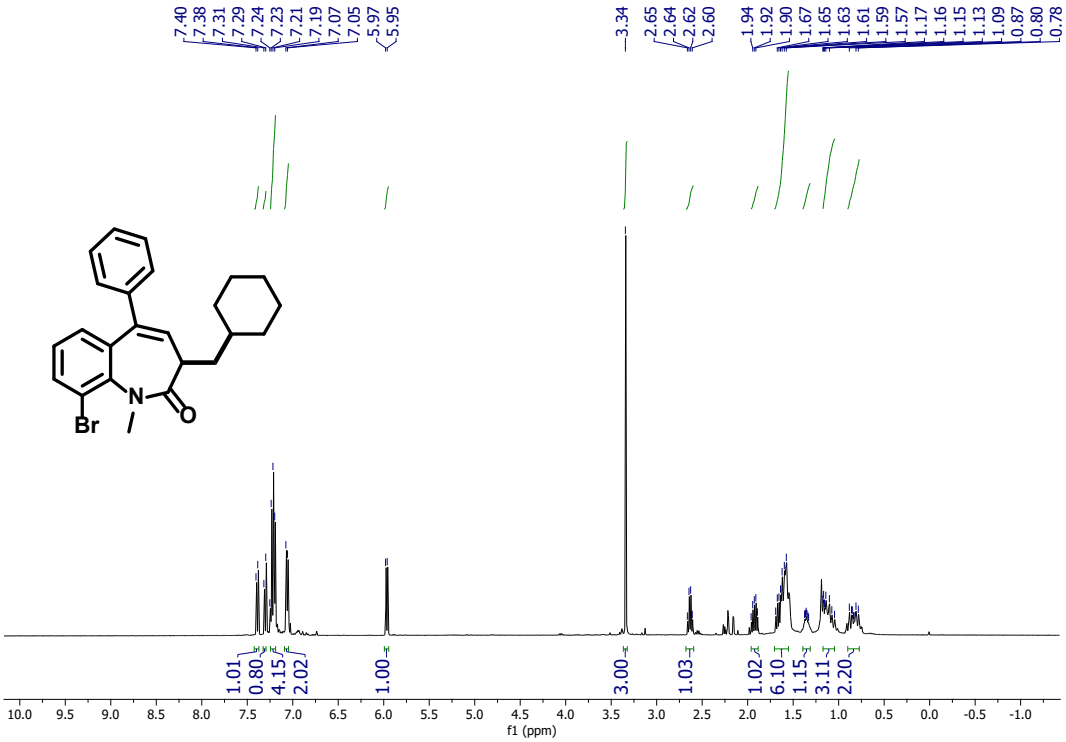


^{1}H NMR(400 MHz, $CDCl_3$) of compound **3h**

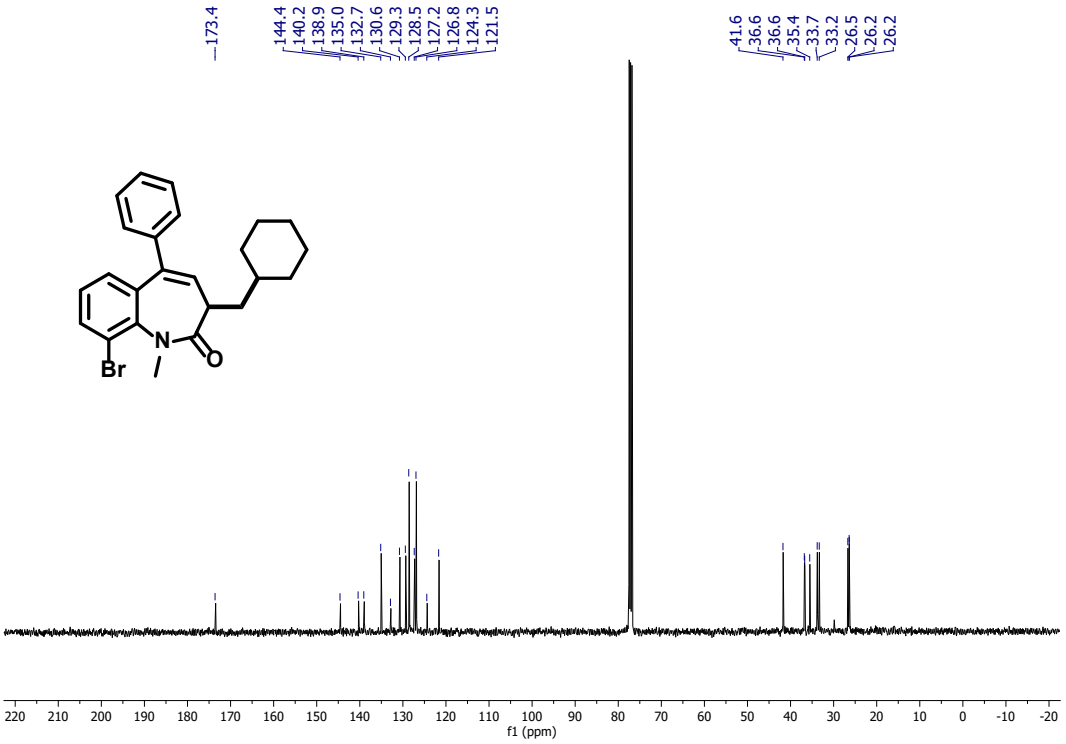


^{13}C NMR(100 MHz, $CDCl_3$) of compound **3h**

9-bromo-3-(cyclohexylmethyl)-1-methyl-5-phenyl-1,3-dihydro-2H-benzo[b]azepin-2-one (3i)

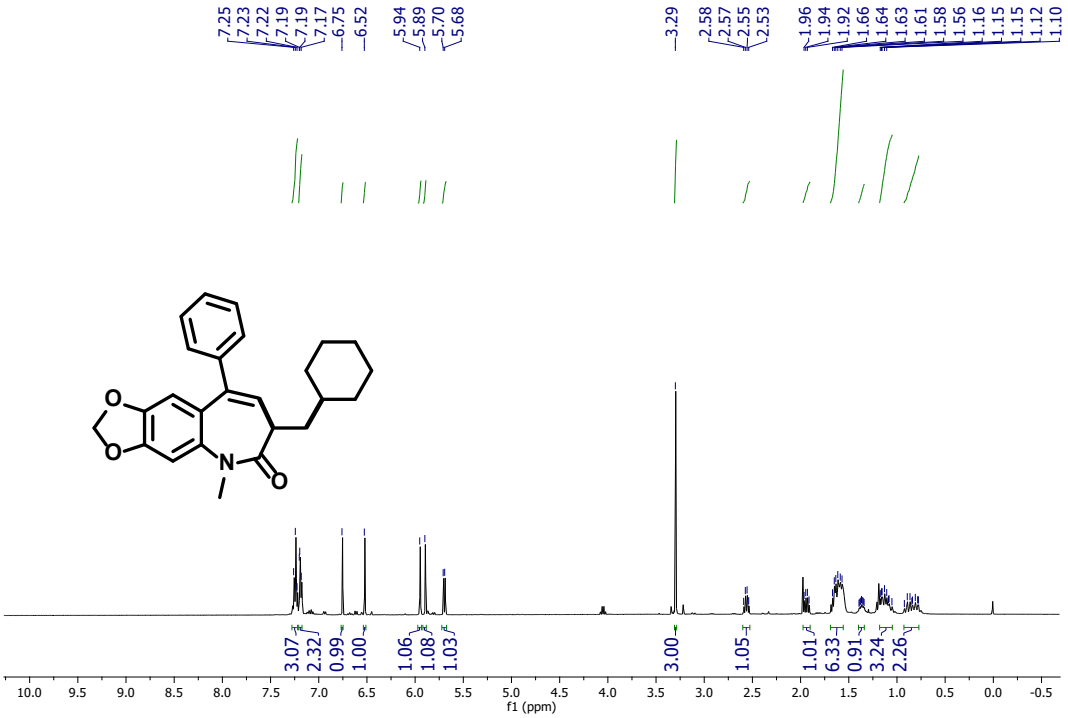


^{1}H NMR(400 MHz, $CDCl_3$) of compound **3i**

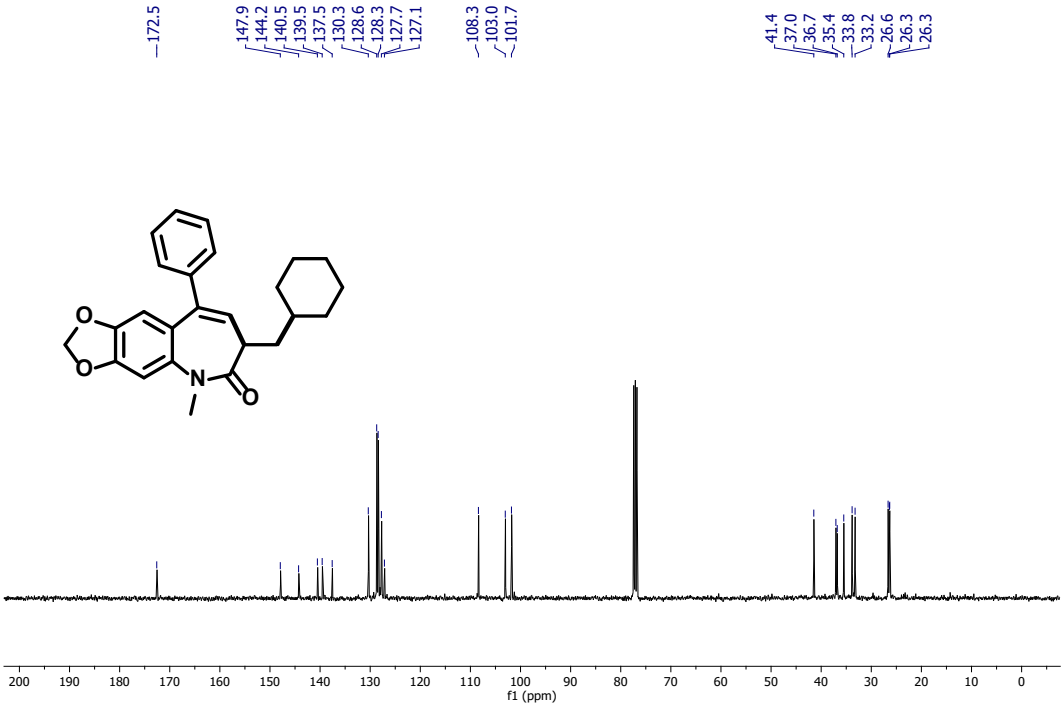


^{13}C NMR(100 MHz, $CDCl_3$) of compound **3i**

7-(cyclohexylmethyl)-5-methyl-9-phenyl-5,7-dihydro-6H-[1,3]dioxolo[4',5':4,5]benzo[1,2-b]azepin-6-one (3j)

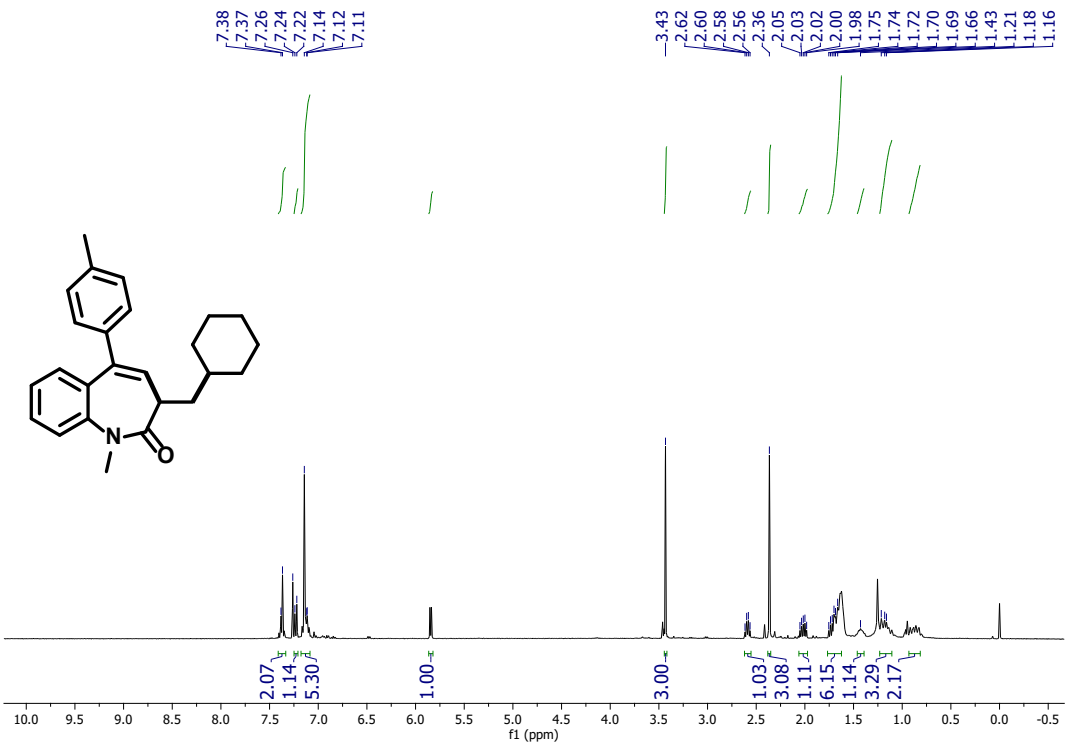


^{1}H NMR(400 MHz, $CDCl_3$) of compound **3j**

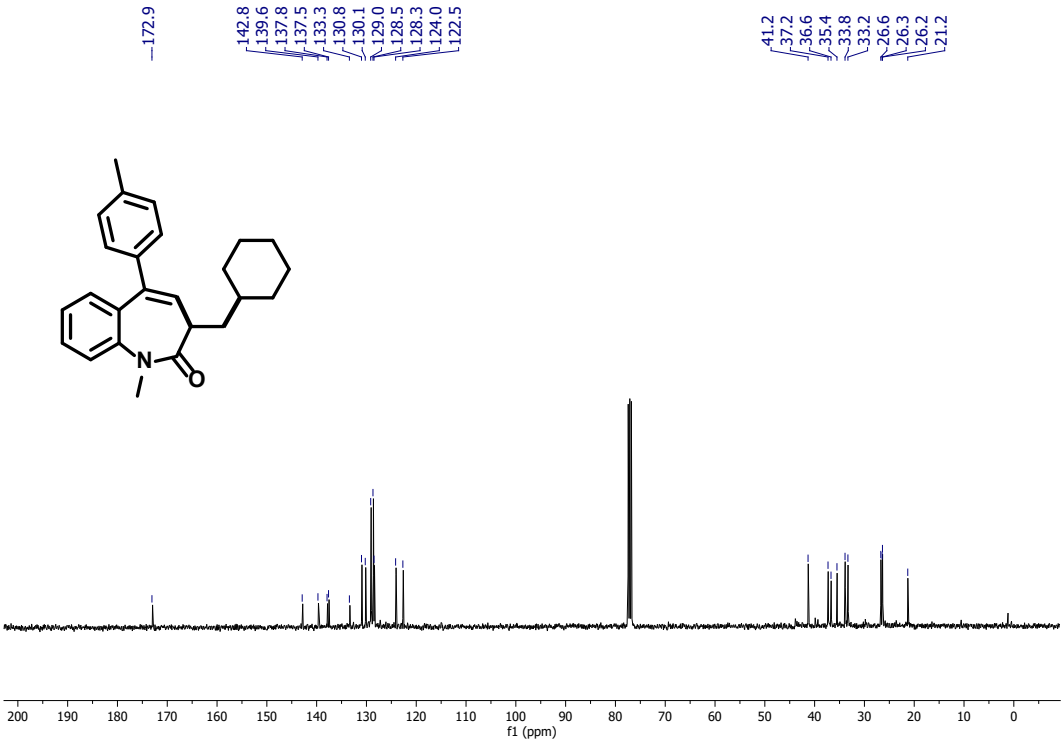


^{13}C NMR(100 MHz, $CDCl_3$) of compound **3j**

3-(cyclohexylmethyl)-1-methyl-5-(p-tolyl)-1,3-dihydro-2H-benzo[b]azepin-2-one (3k)

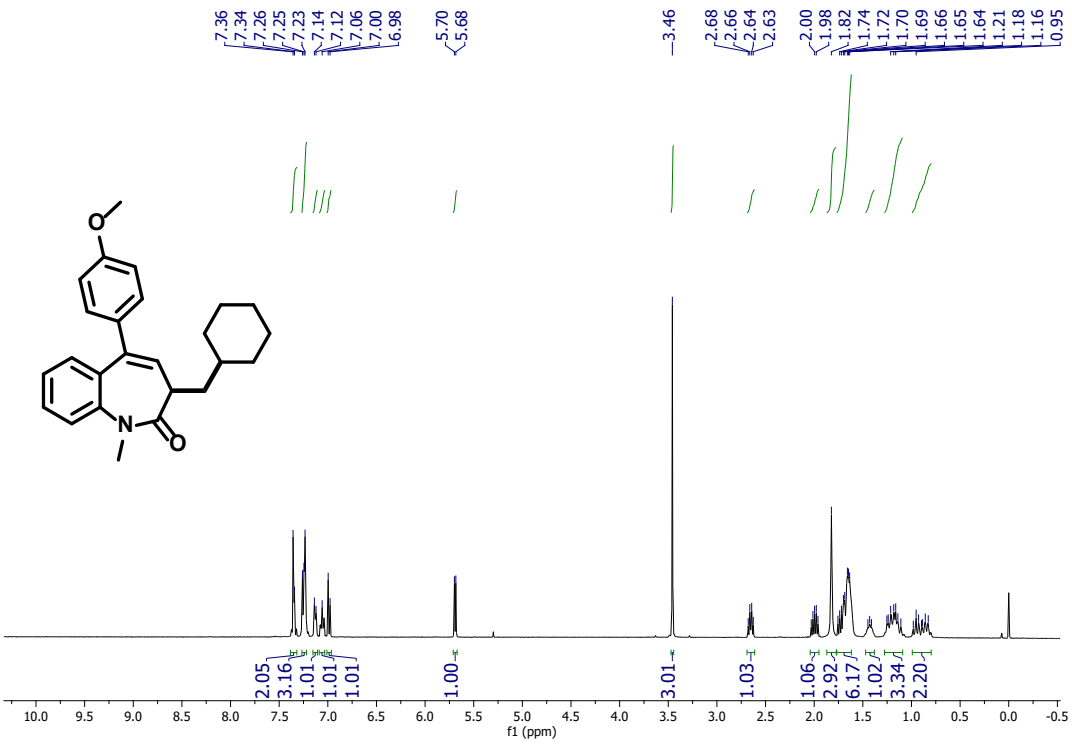


^{1}H NMR(400 MHz, $CDCl_3$) of compound **3k**

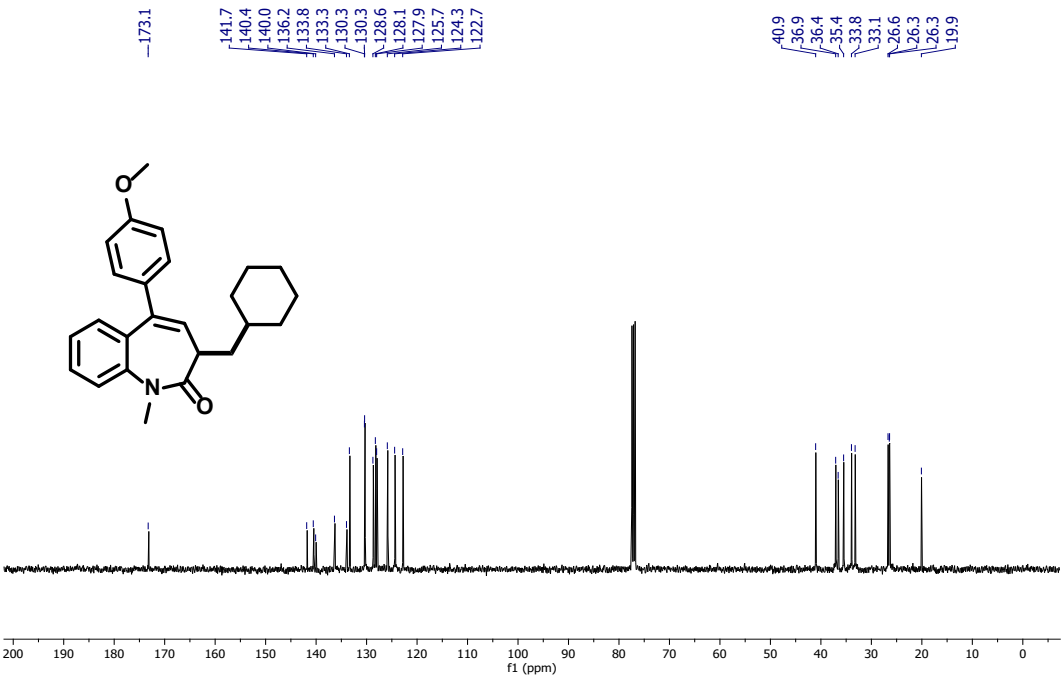


^{13}C NMR(100 MHz, $CDCl_3$) of compound **3k**

3-(cyclohexylmethyl)-5-(4-methoxyphenyl)-1-methyl-1,3-dihydro-2H-benzo[b]azepin-2-one (3l)

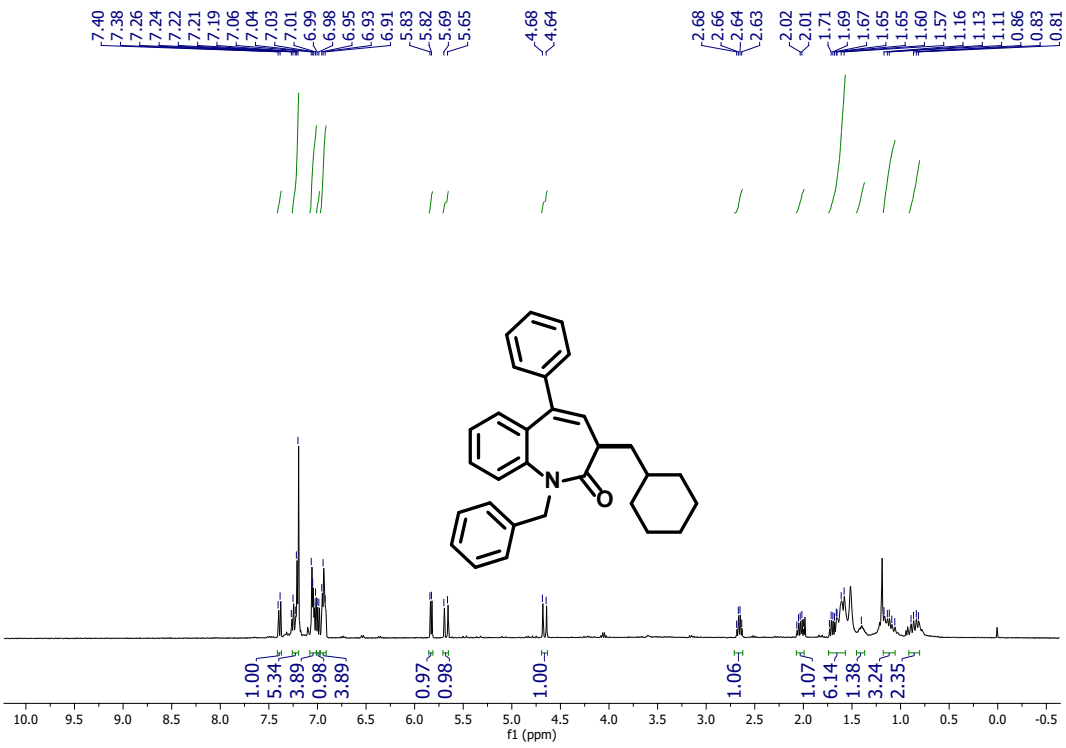


^{1}H NMR(400 MHz, $CDCl_3$) of compound **3l**

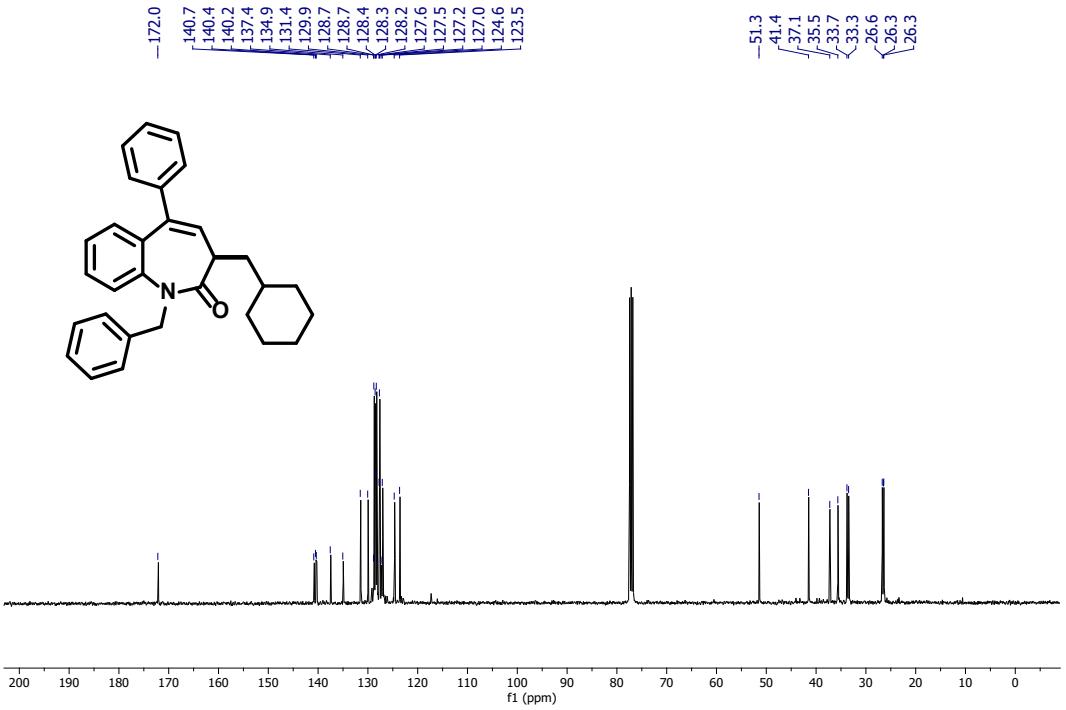


^{13}C NMR(100 MHz, $CDCl_3$) of compound **3l**

1-benzyl-3-(cyclohexylmethyl)-5-phenyl-1,3-dihydro-2H-benzo[b]azepin-2-one (3m)

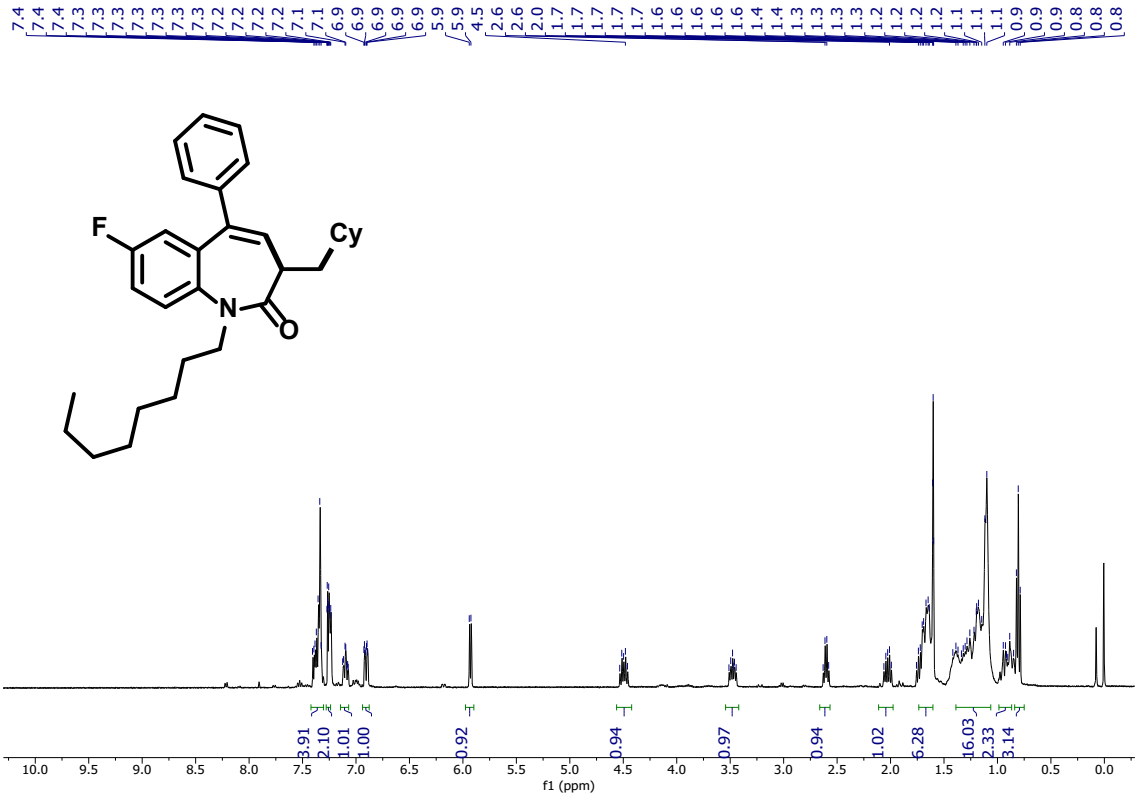


^{1}H NMR(400 MHz, $CDCl_3$) of compound **3m**

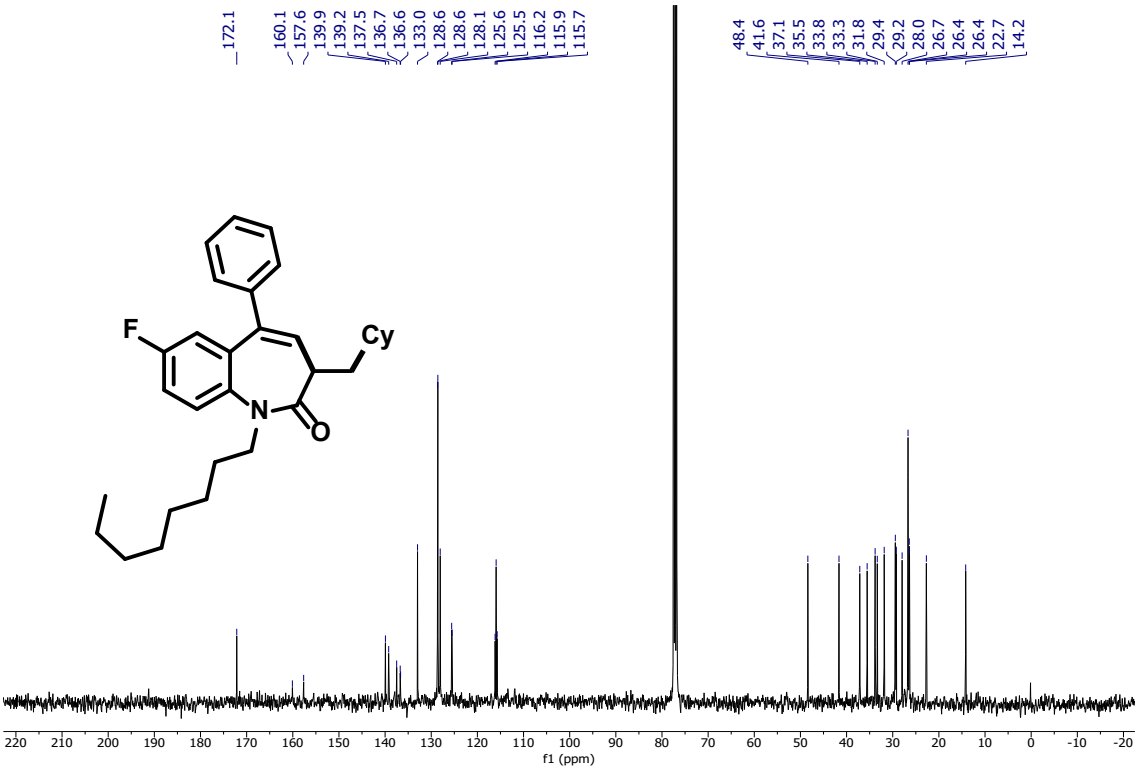


^{13}C NMR(100 MHz, $CDCl_3$) of compound **3m**

3-(cyclohexylmethyl)-7-fluoro-1-octyl-5-phenyl-1,3-dihydro-2H-benzo[b]azepin-2-one (3n)

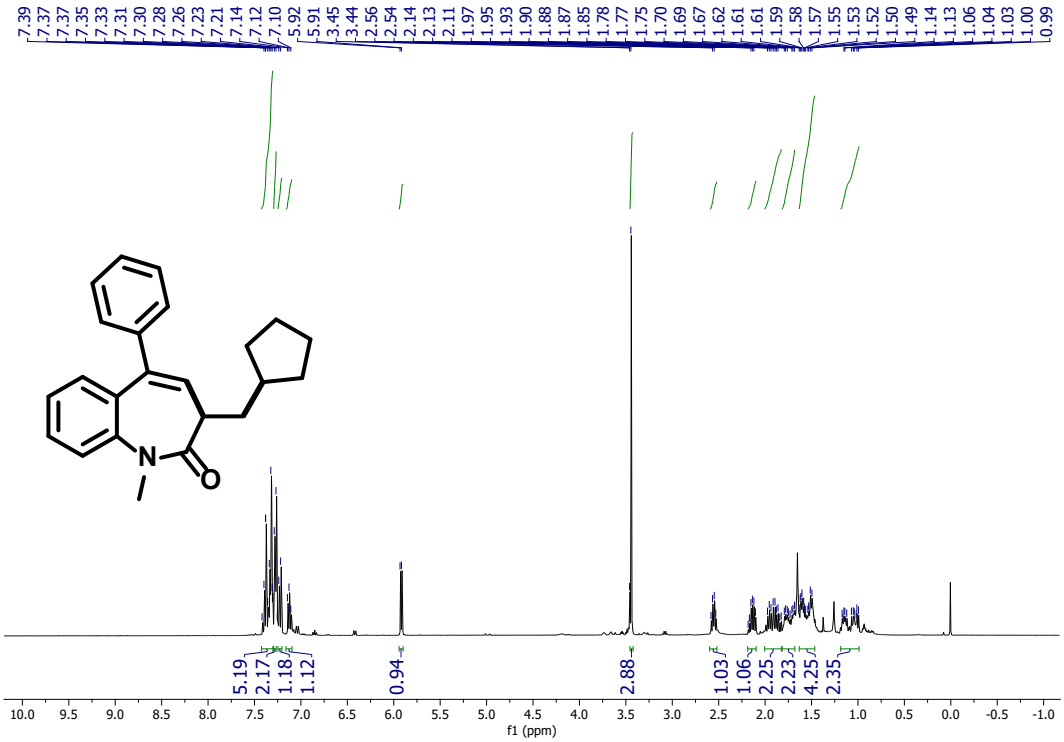


^{1}H NMR(400 MHz, $CDCl_3$) of compound **3n**

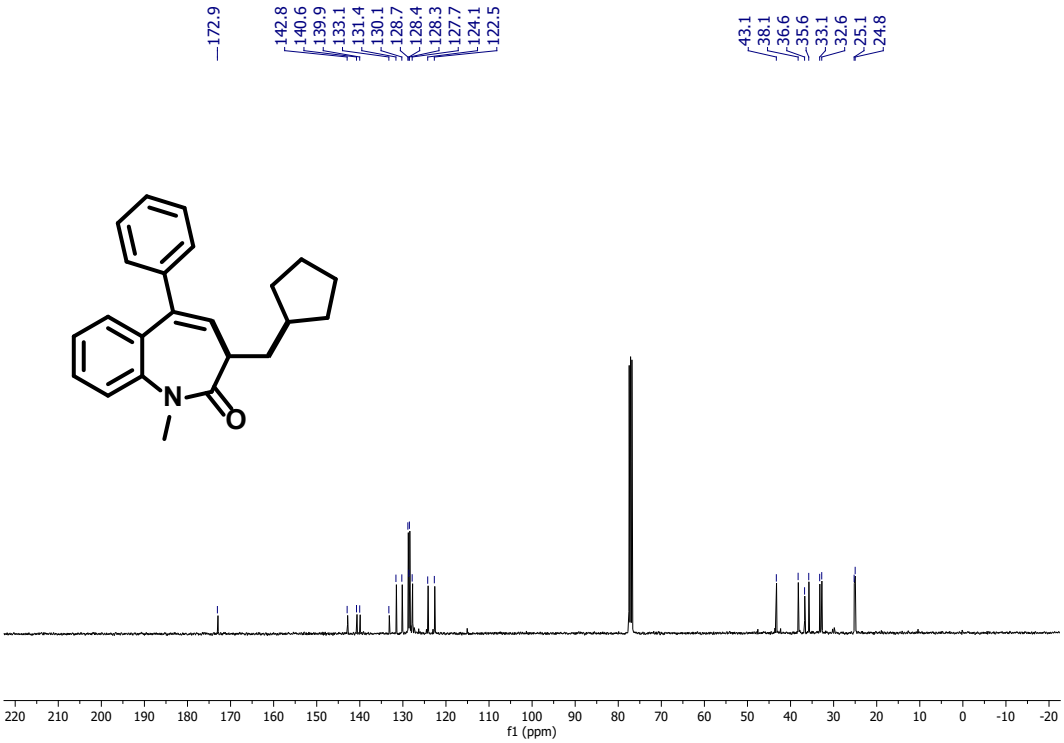


^{13}C NMR(100 MHz, $CDCl_3$) of compound **3n**

3-(cyclopentylmethyl)-1-methyl-5-phenyl-1,3-dihydro-2H-benzo[b]azepin-2-one (3o)

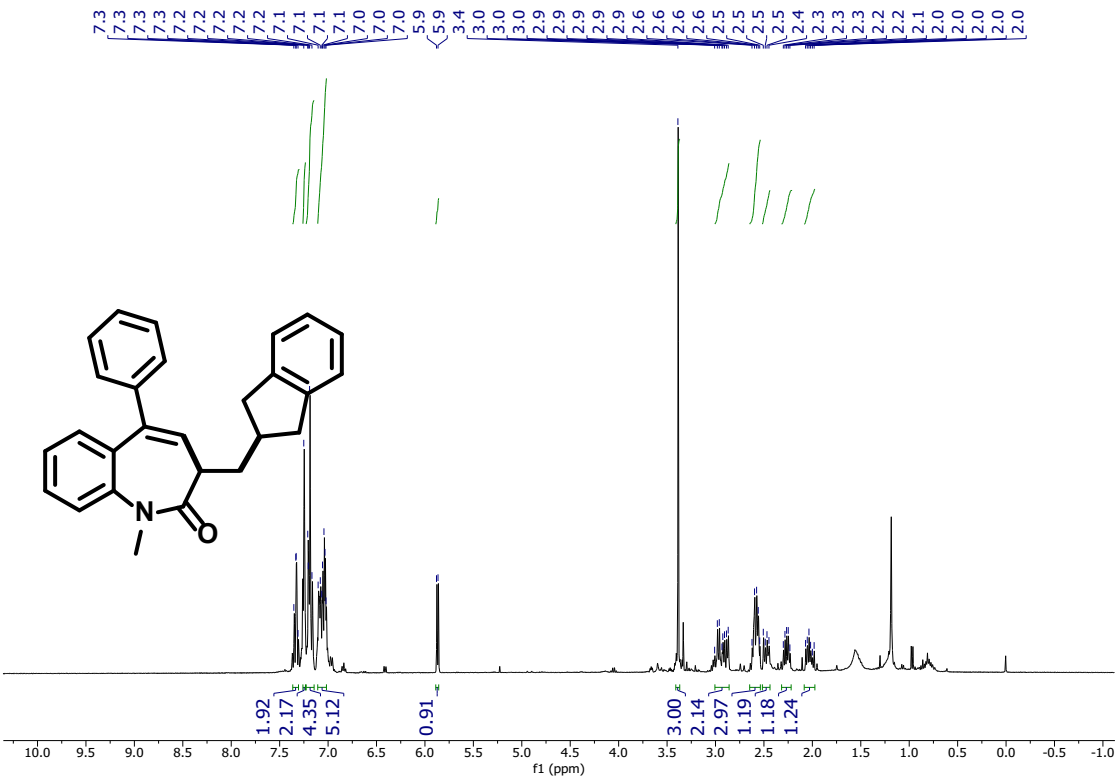


^{1}H NMR(400 MHz, $CDCl_3$) of compound **3o**

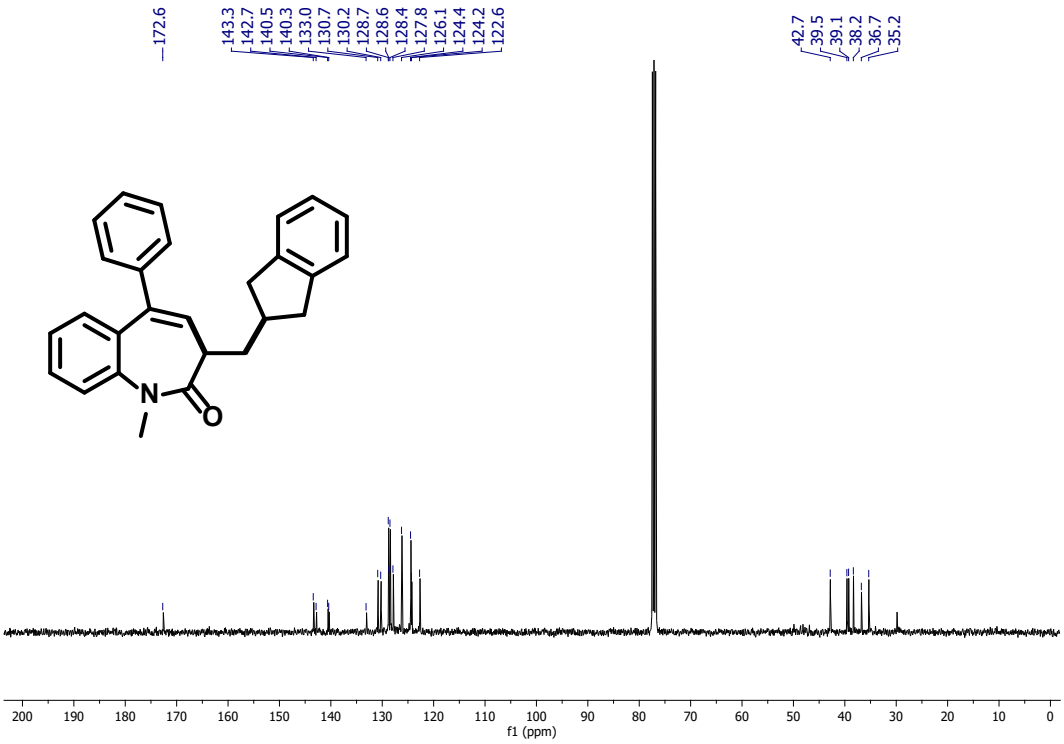


^{13}C NMR(100 MHz, $CDCl_3$) of compound **3o**

3-((2,3-dihydro-1H-inden-2-yl)methyl)-1-methyl-5-phenyl-1,3-dihydro-2H-benzo[b]azepin-2-one (3p)

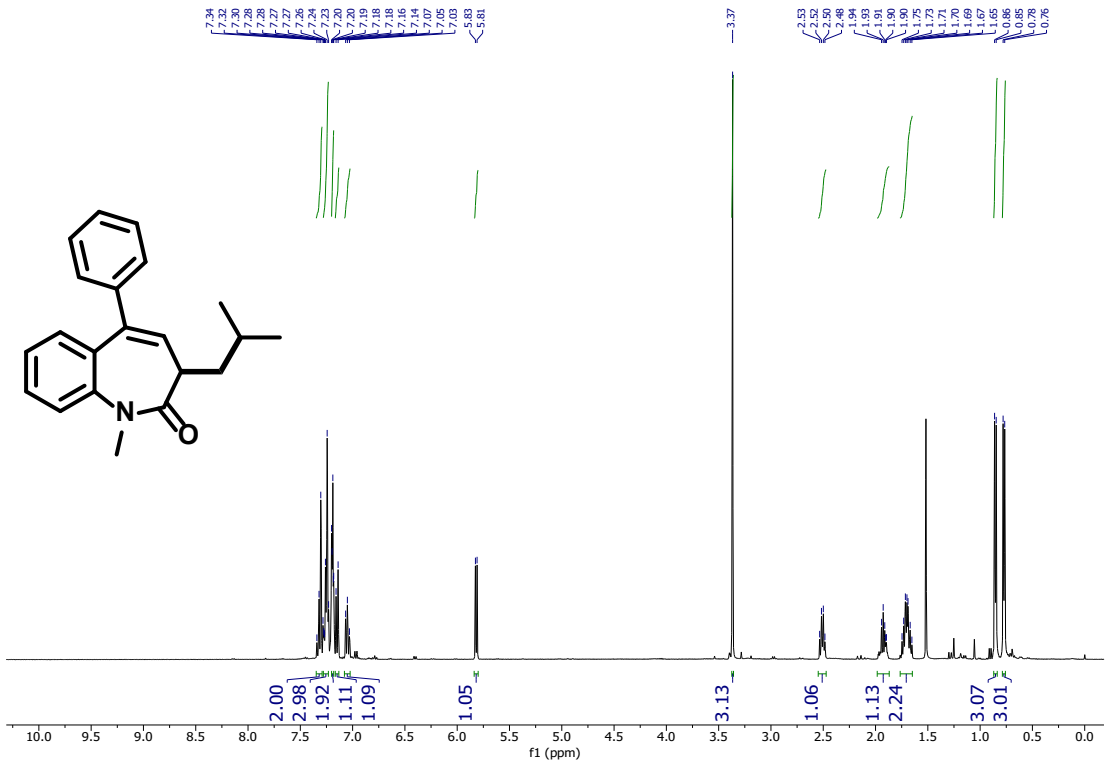


^{1}H NMR(400 MHz, $CDCl_3$) of compound **3p**

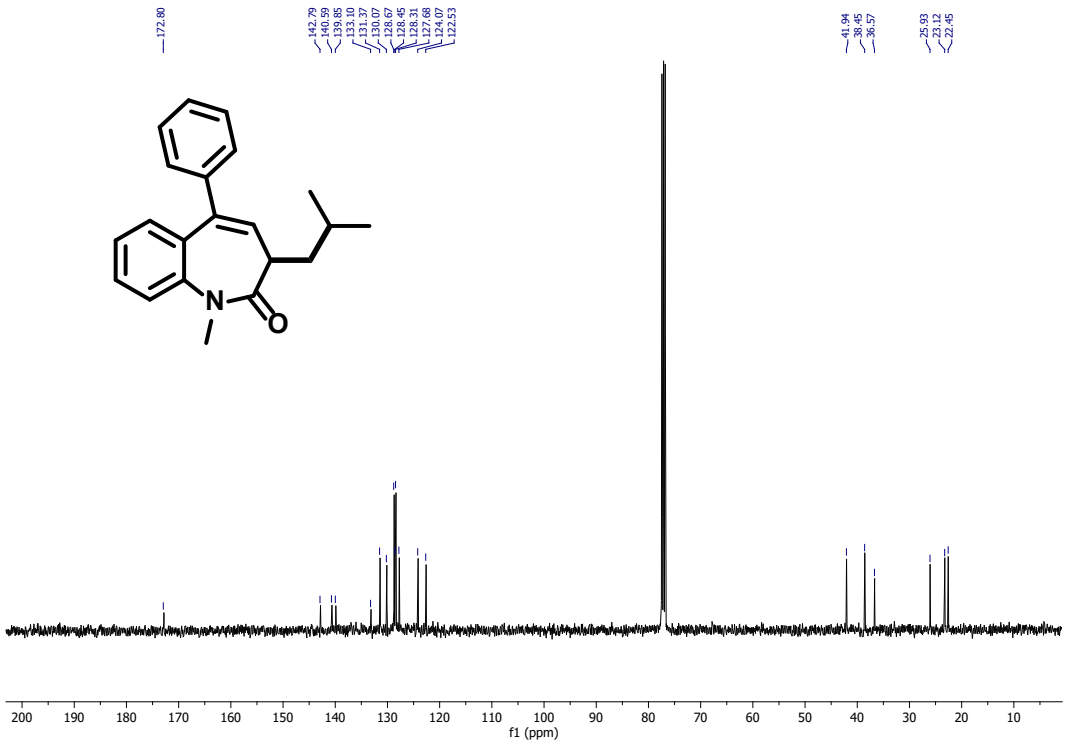


^{13}C NMR(100 MHz, $CDCl_3$) of compound **3p**

3-isobutyl-1-methyl-5-phenyl-1,3-dihydro-2H-benzo[b]azepin-2-one (3q)

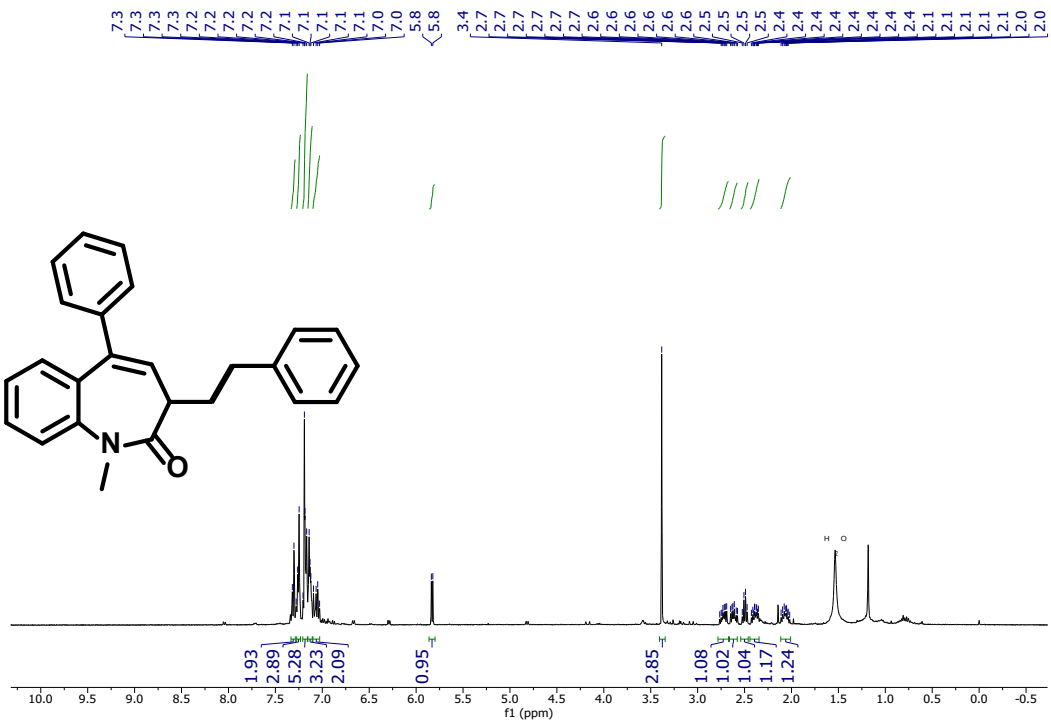


^{1}H NMR(400 MHz, $CDCl_3$) of compound **3q**

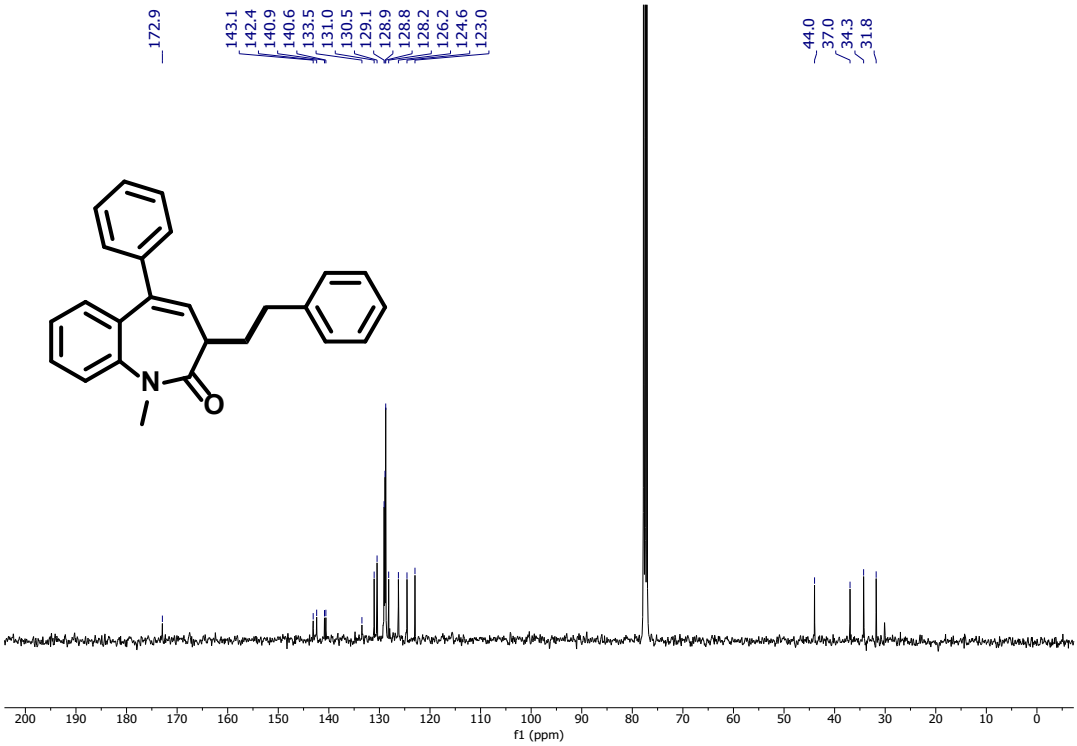


^{13}C NMR(100 MHz, $CDCl_3$) of compound **3q**

1-methyl-3-phenethyl-5-phenyl-1,3-dihydro-2H-benzo[b]azepin-2-one (3r)

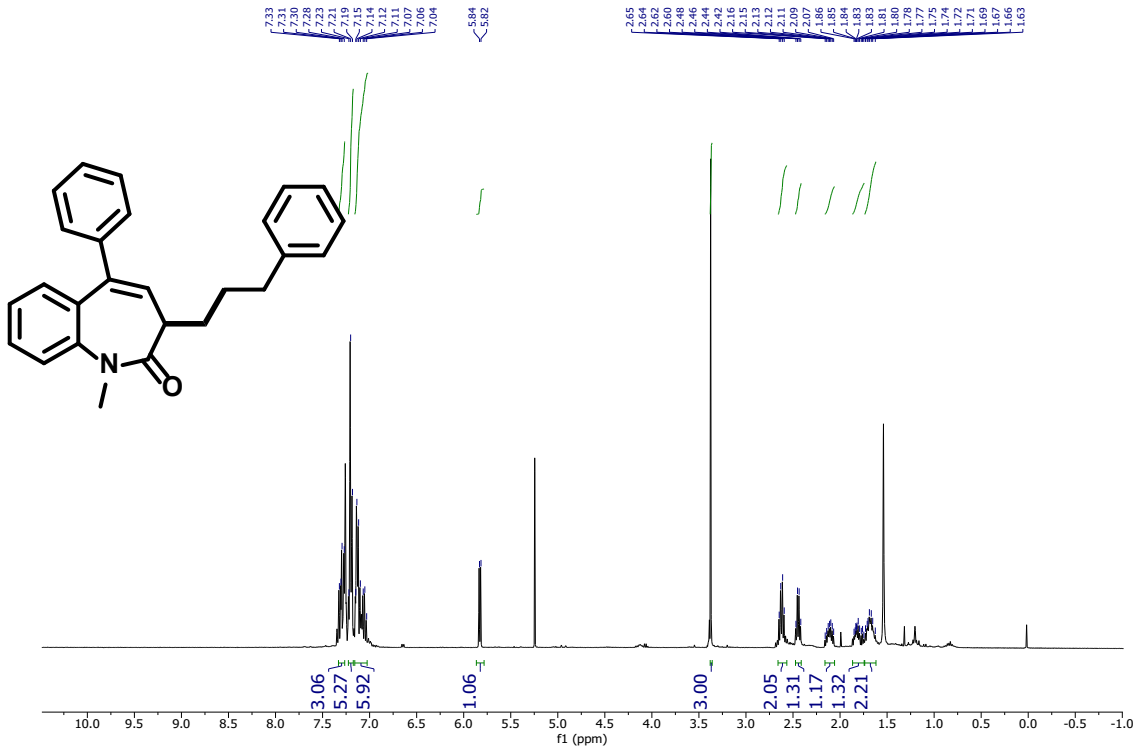


^{1}H NMR(400 MHz, $CDCl_3$) of compound **3r**

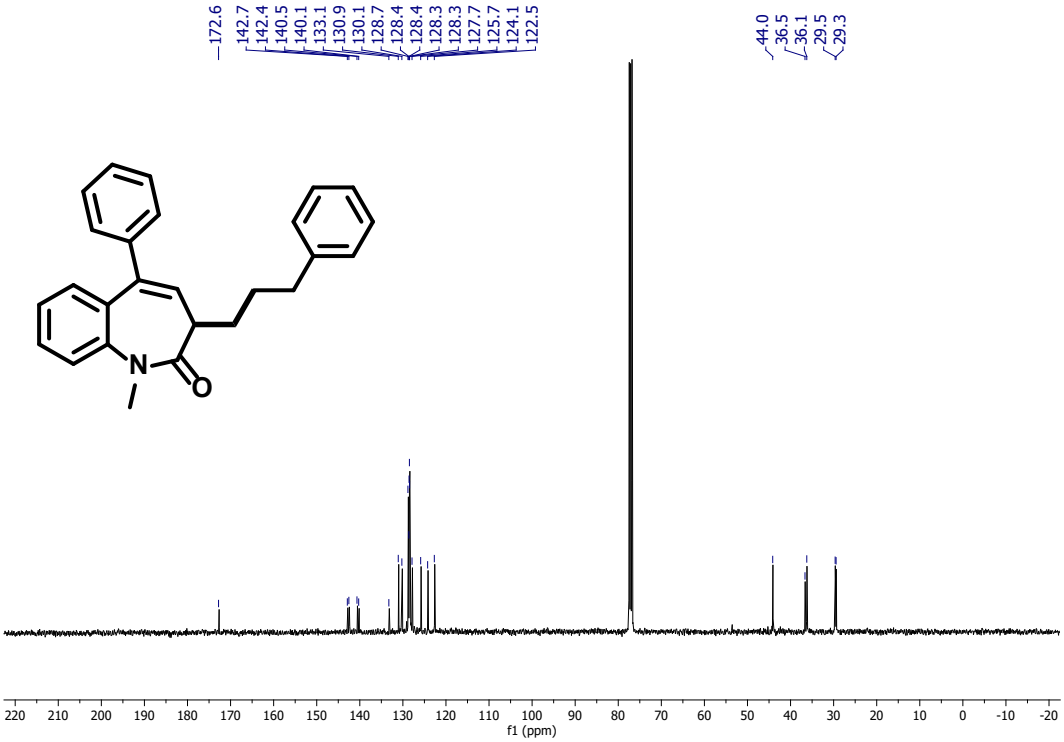


^{13}C NMR(100 MHz, $CDCl_3$) of compound **3r**

1-methyl-5-phenyl-3-(3-phenylpropyl)-1,3-dihydro-2H-benzo[b]azepin-2-one (3s)

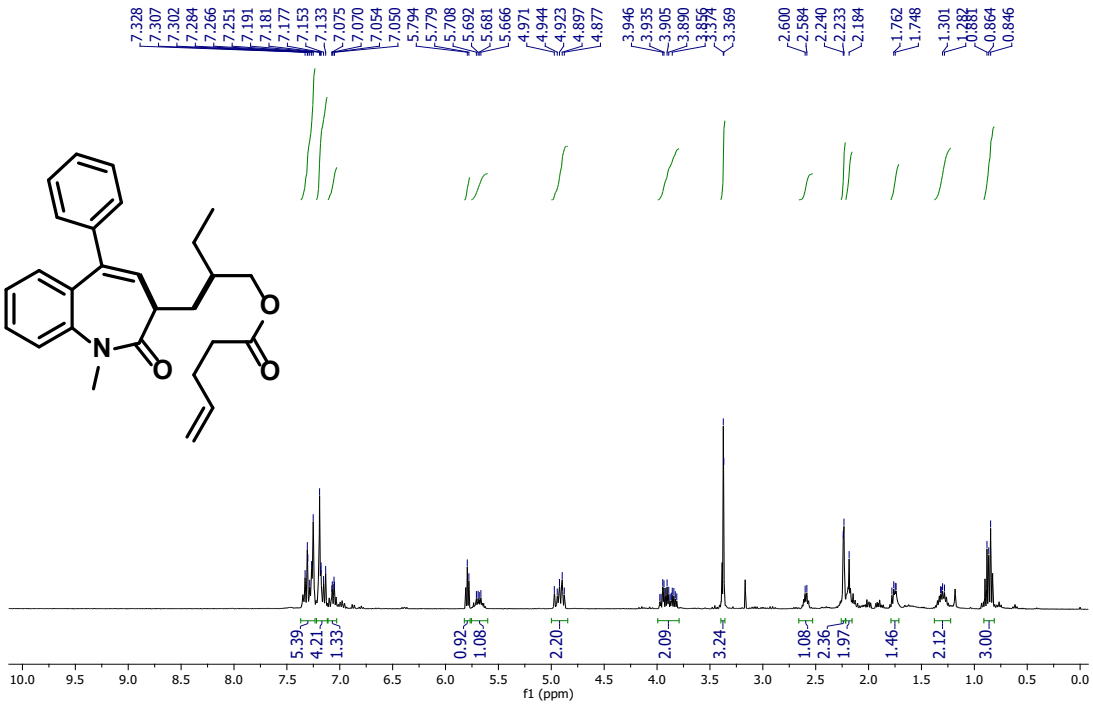


^{1}H NMR(400 MHz, $CDCl_3$) of compound **3s**

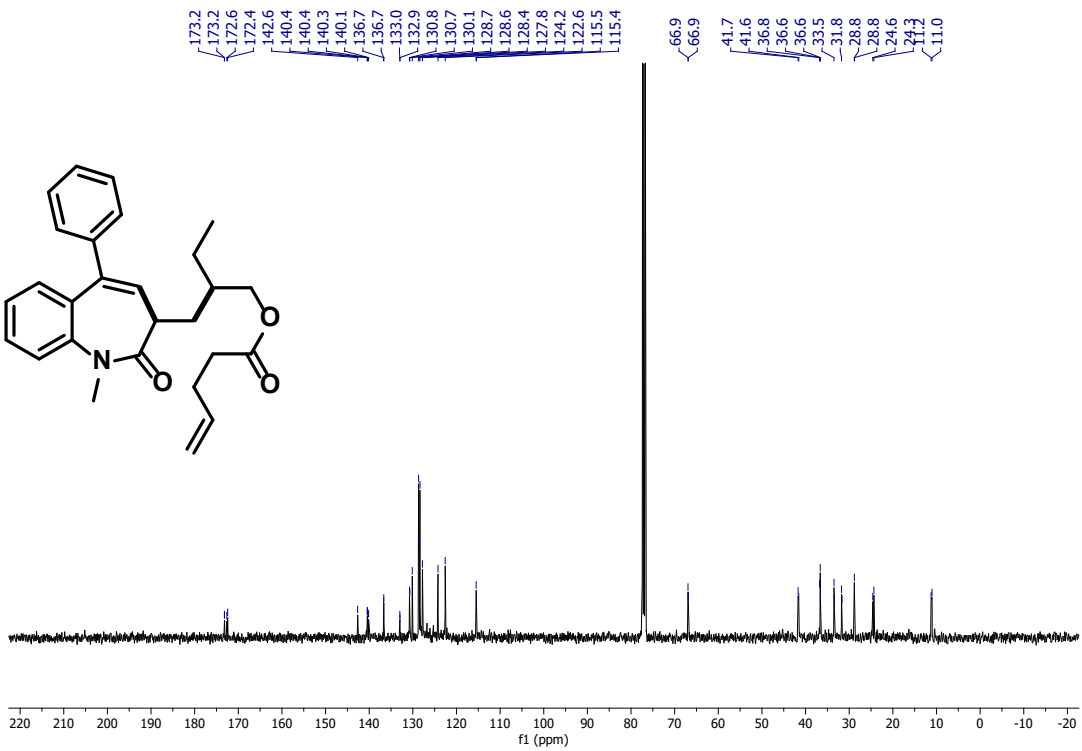


^{13}C NMR(100 MHz, $CDCl_3$) of compound **3s**

2-(((R)-1-methyl-2-oxo-5-phenyl-2,3-dihydro-1H-benzo[b]azepin-3-yl)methyl)butyl pent-4-enoate (3t)

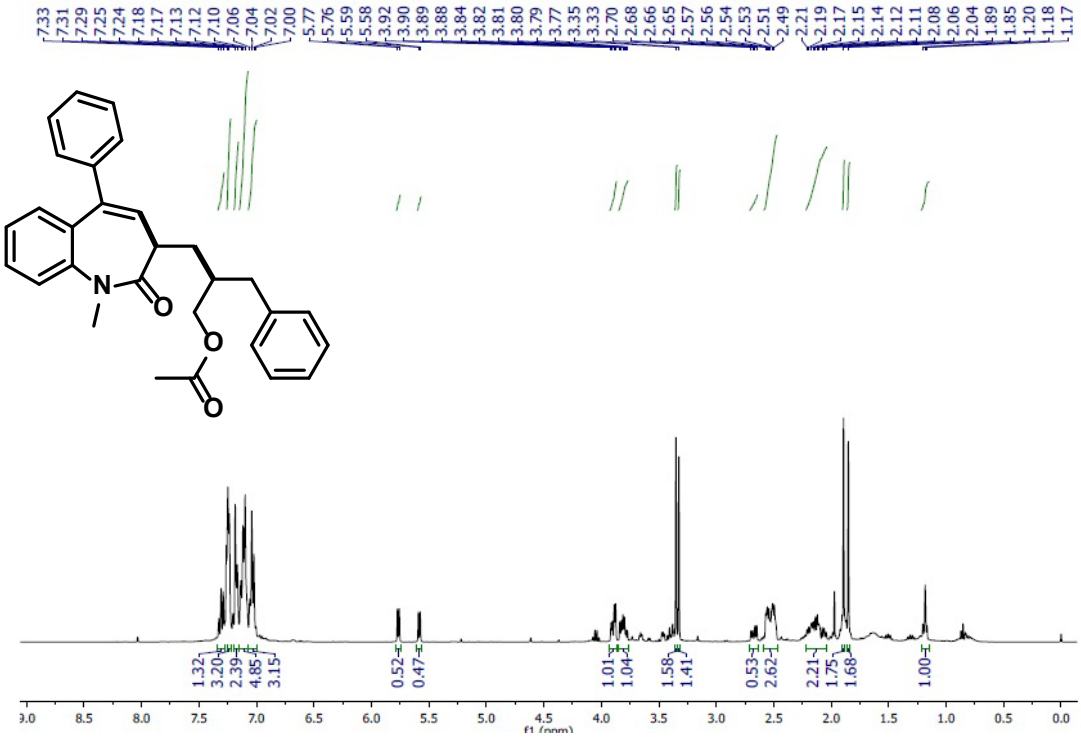


^{1}H NMR(400 MHz, $CDCl_3$) of compound **3t**

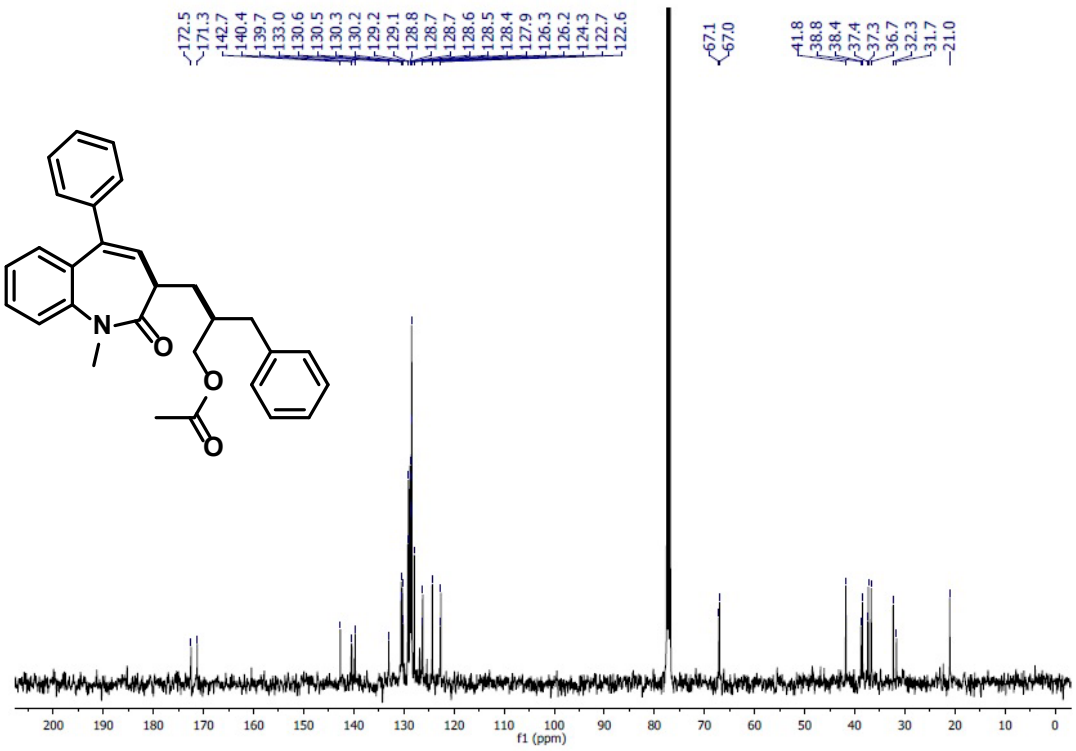


^{13}C NMR(100 MHz, $CDCl_3$) of compound **3t**

2-benzyl-3-(1-methyl-2-oxo-5-phenyl-2,3-dihydro-1H-benzo[b]azepin-3-yl)propyl acetate (3u)

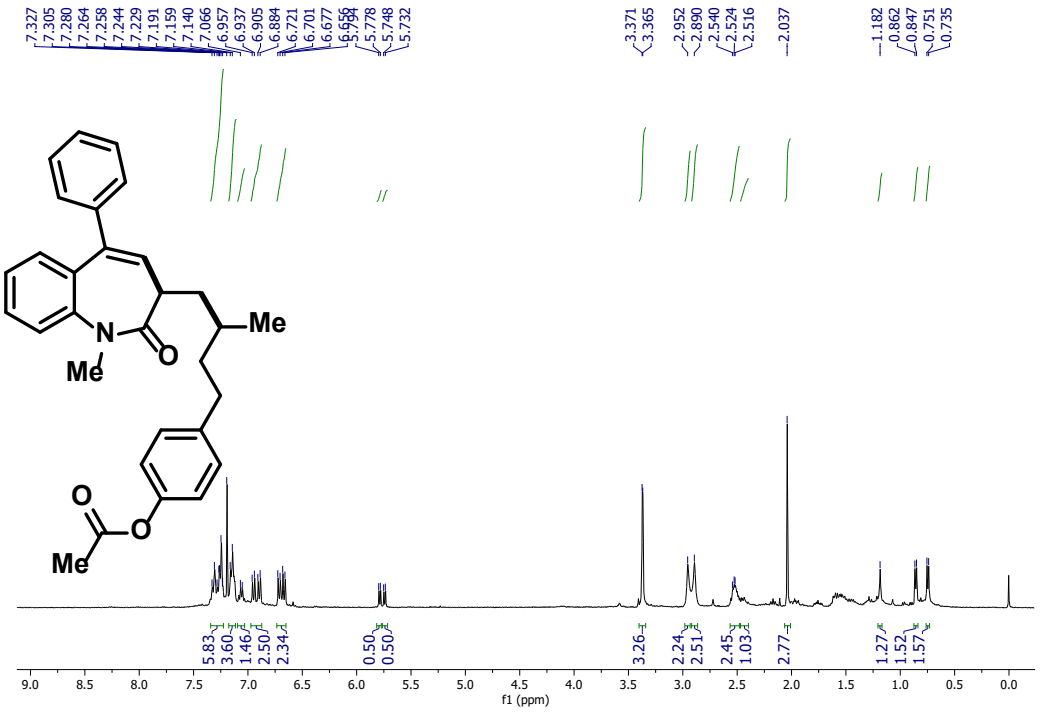


^{1}H NMR(400 MHz, $CDCl_3$) of compound **3u**

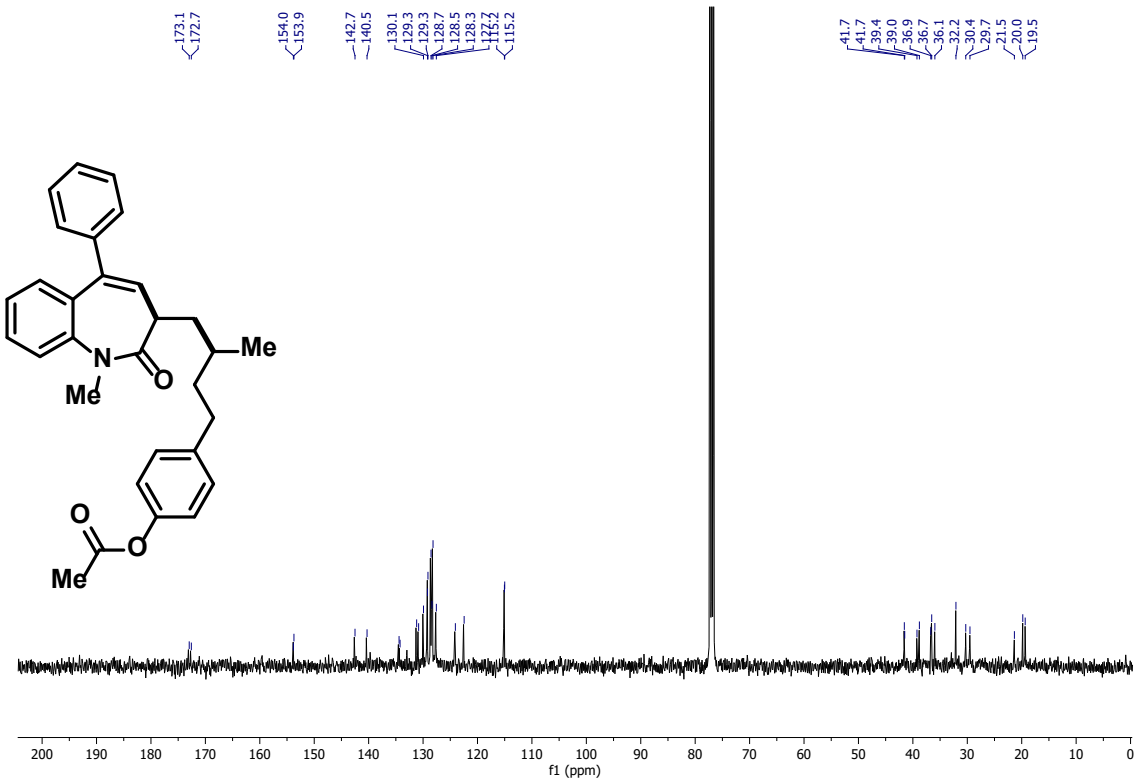


^{13}C NMR(100 MHz, $CDCl_3$) of compound **3u**

4-(3-methyl-4-(1-methyl-2-oxo-5-phenyl-2,3-dihydro-1H-benzo[b]azepin-3-yl)butyl) phenyl acetate (3v)

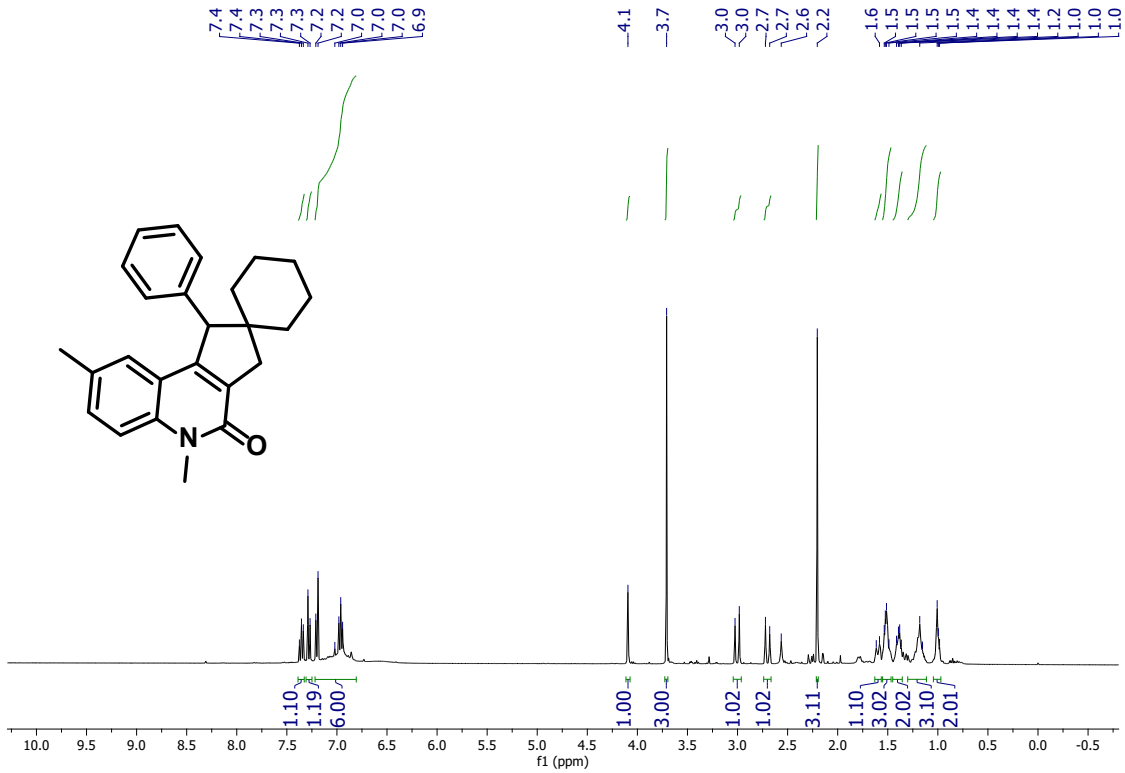


^{1}H NMR(400 MHz, $CDCl_3$) of compound **3v**

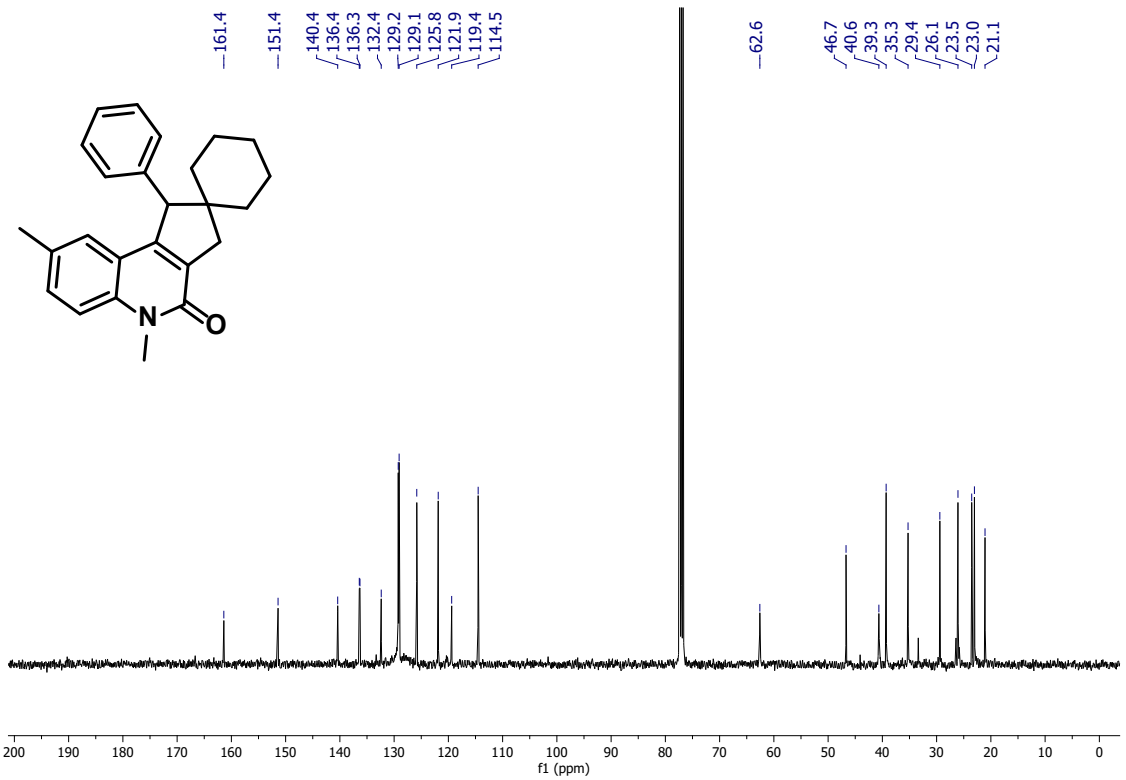


^{13}C NMR(100 MHz, $CDCl_3$) of compound **3v**

5',8'-dimethyl-1'-phenyl-3',5'-dihydrospiro[cyclohexane-1,2'-cyclopenta[c]quinolin]-4'(1'H)-one (6a)

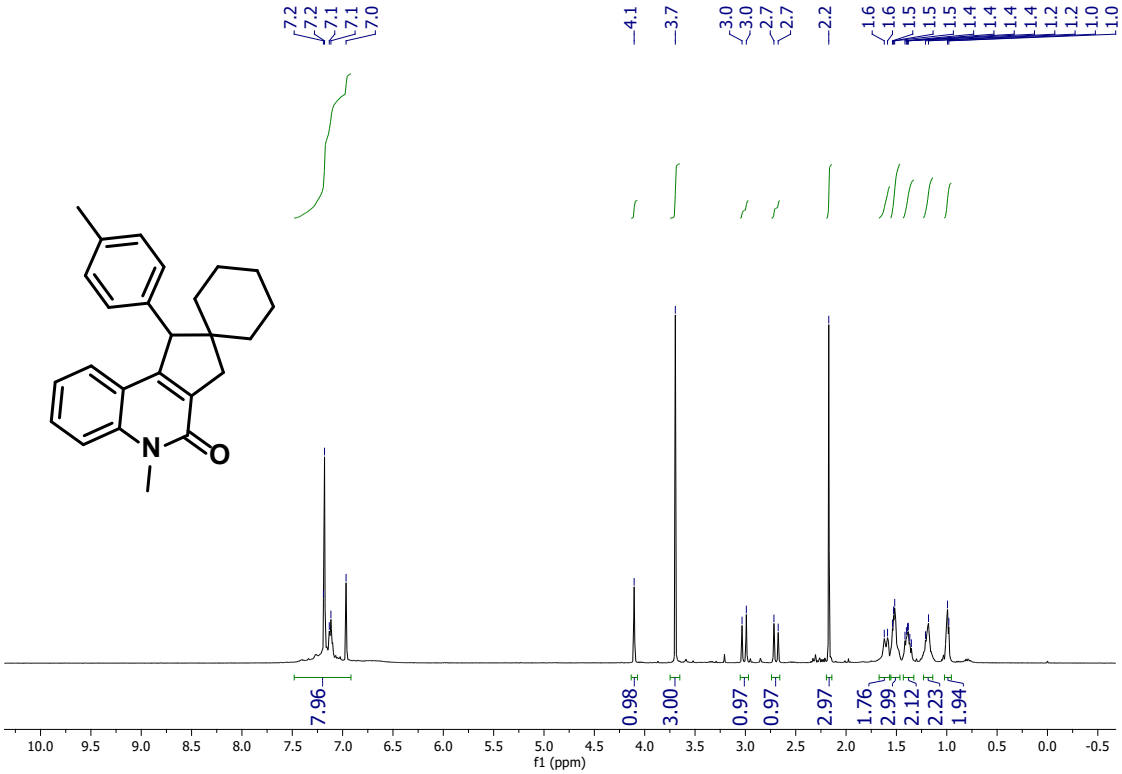


^{1}H NMR(400 MHz, $CDCl_3$) of compound **6**[a]

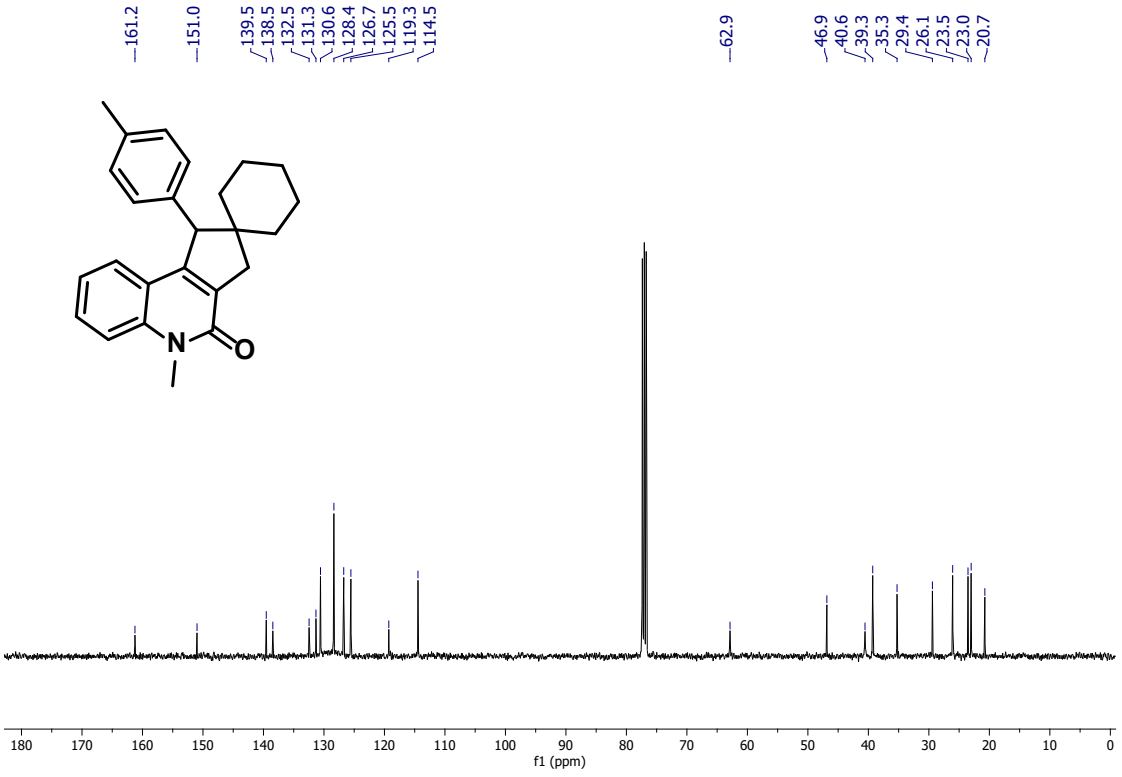


^{13}C NMR(100 MHz, $CDCl_3$) of compound **6a**

5'-methyl-1'-(p-tolyl)-3',5'-dihydrospiro[cyclohexane-1,2'-cyclopenta[c]quinolin]-4'(1'H)-one (6b)

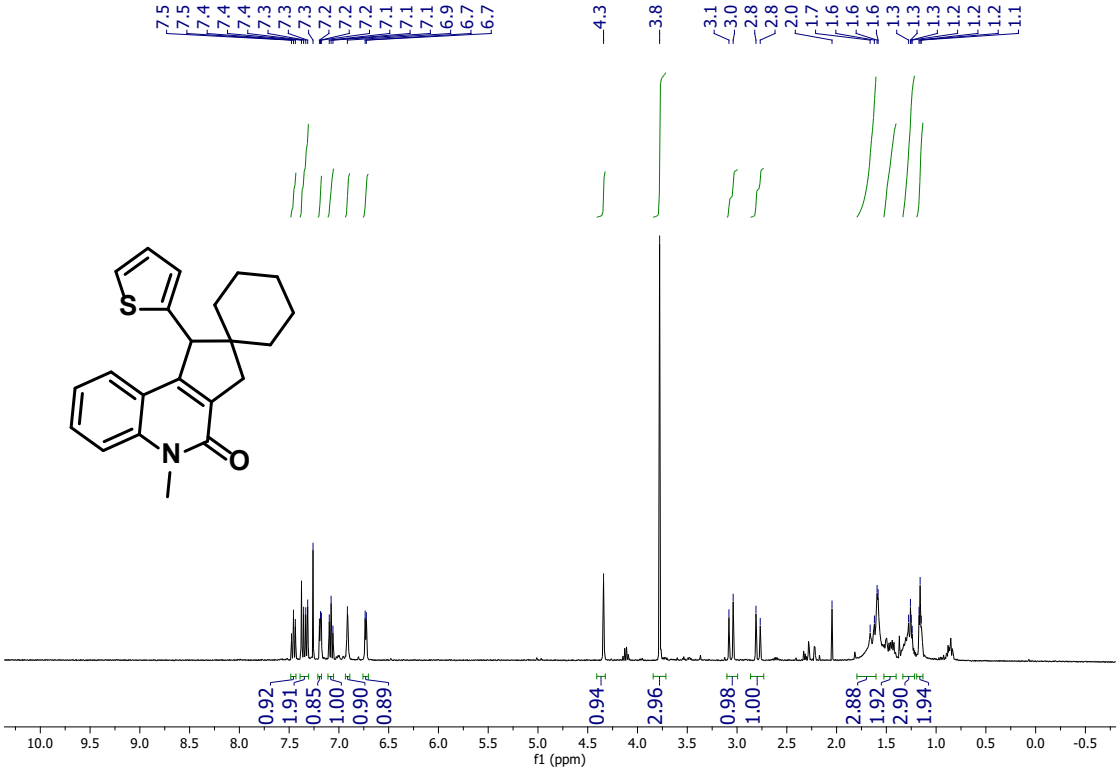


^{1}H NMR(400 MHz, $CDCl_3$) of compound **6b**

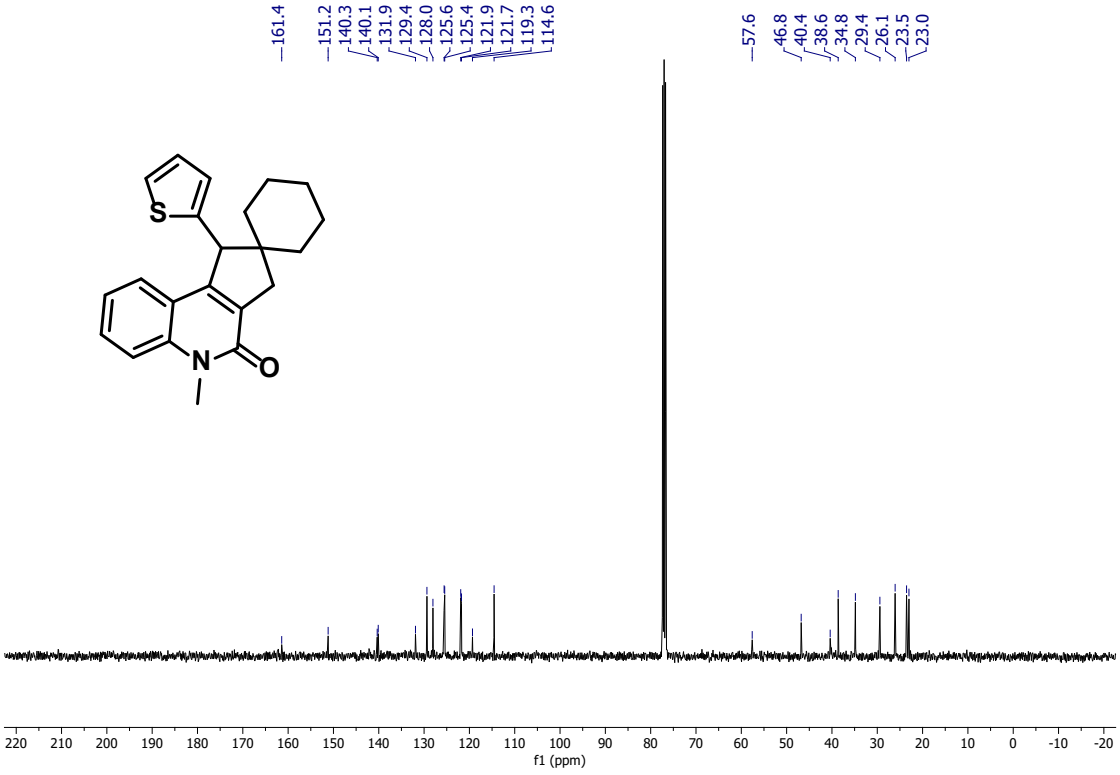


^{13}C NMR(100 MHz, $CDCl_3$) of compound **6b**

5'-methyl-1'-(thiophen-2-yl)-3',5'-dihydrospiro[cyclohexane-1,2'-cyclopenta[c]quinolin]-4'(1'H)-one (6c)

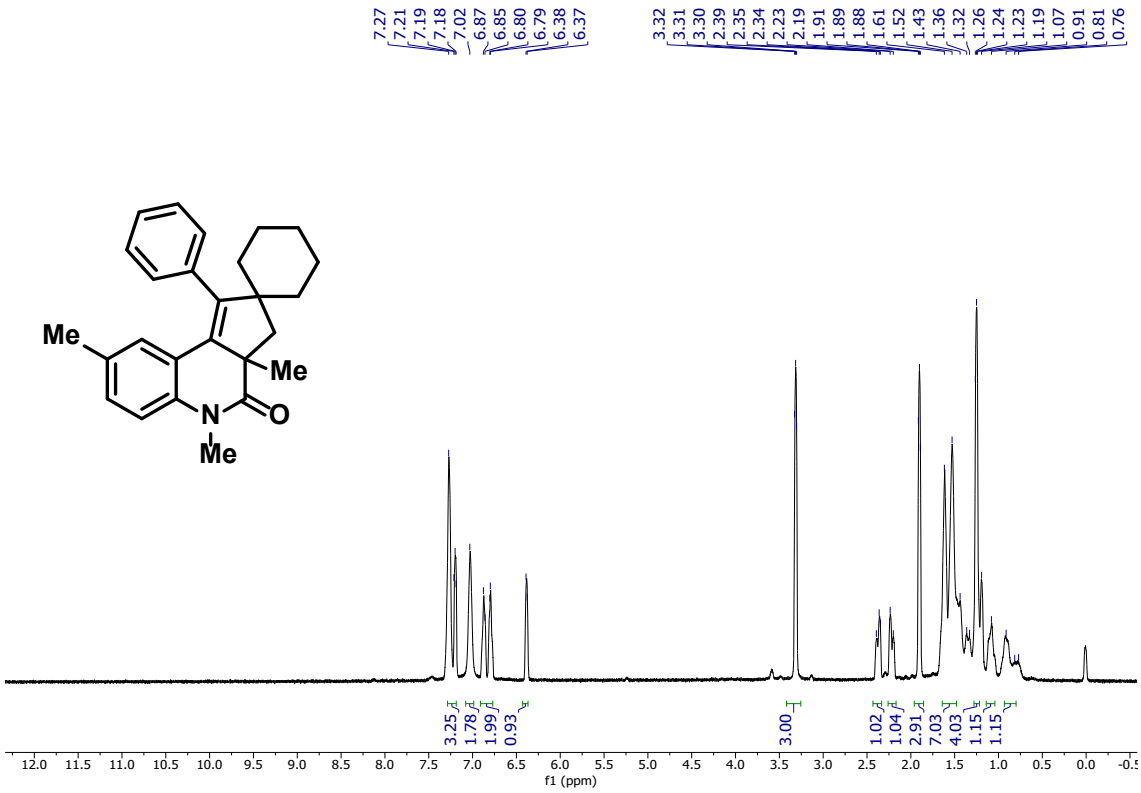


^{1}H NMR(400 MHz, $CDCl_3$) of compound **6c**

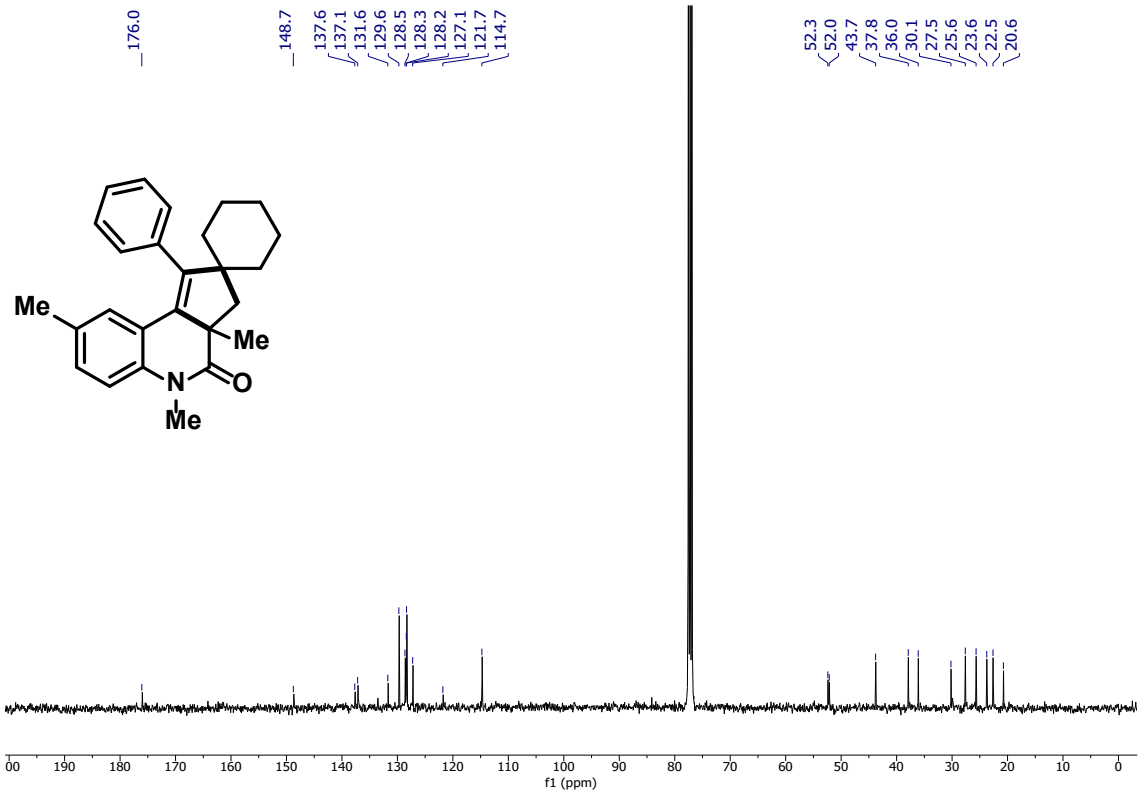


^{13}C NMR(100 MHz, $CDCl_3$) of compound **6c**

3a',5',8'-trimethyl-1'-phenyl-3',3a'-dihydrospiro[cyclohexane-1,2'-cyclopenta[c]quinolin]-4'(5'H)-one (6d)

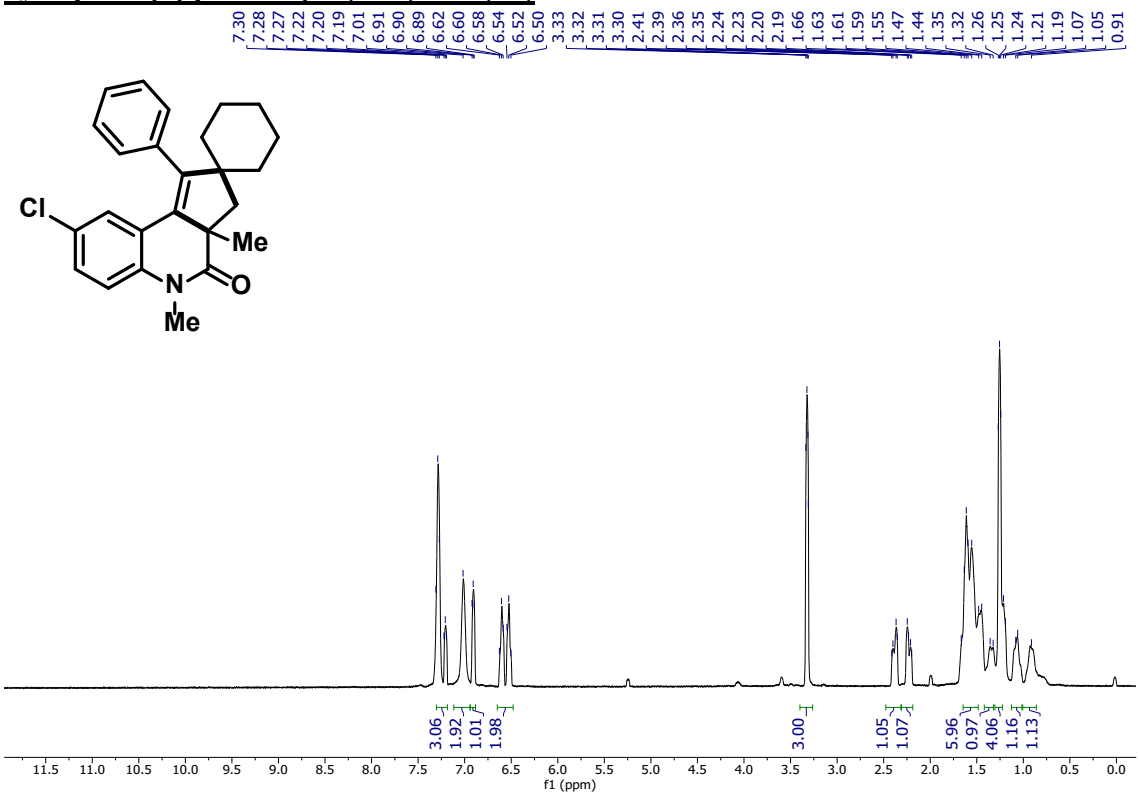


^{1}H NMR(400 MHz, $CDCl_3$) of compound **6d**

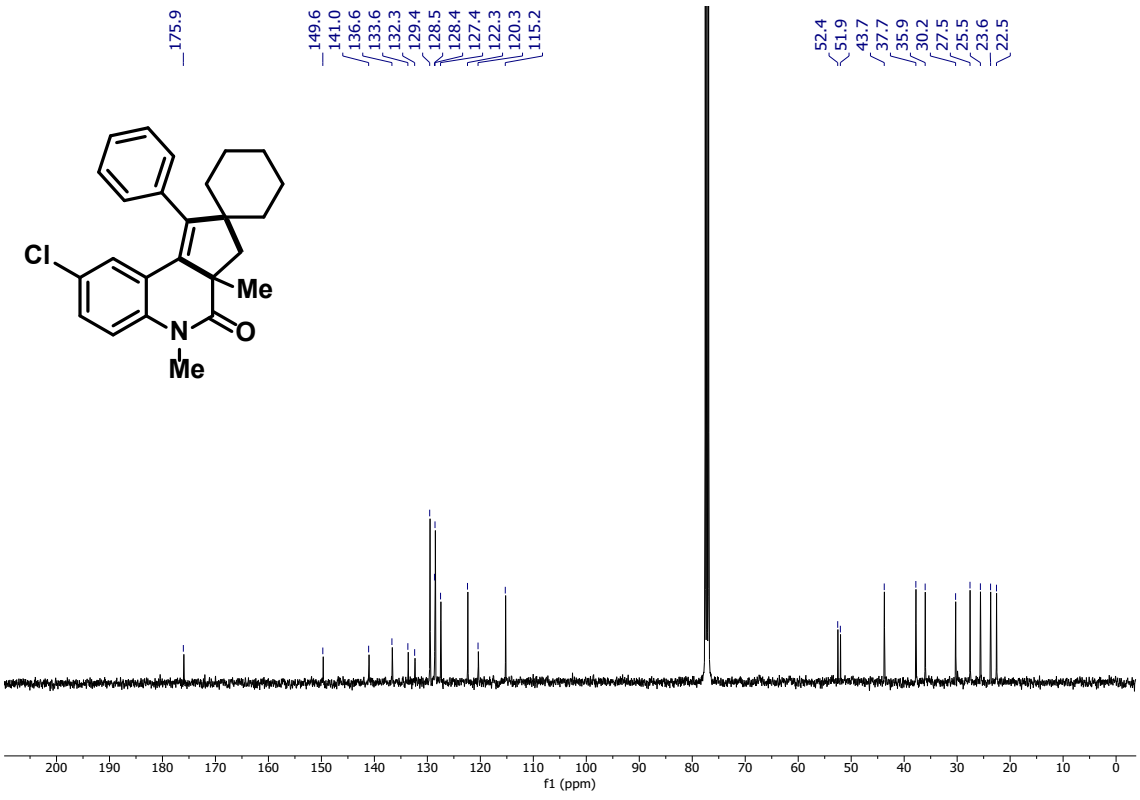


^{13}C NMR(100 MHz, $CDCl_3$) of compound **6d**

8'-chloro-3a',5'-dimethyl-1'-phenyl-3',3a'-dihydrospiro[cyclohexane-1,2'-cyclopenta[c]quinolin]-4'(5'H)-one (6e)

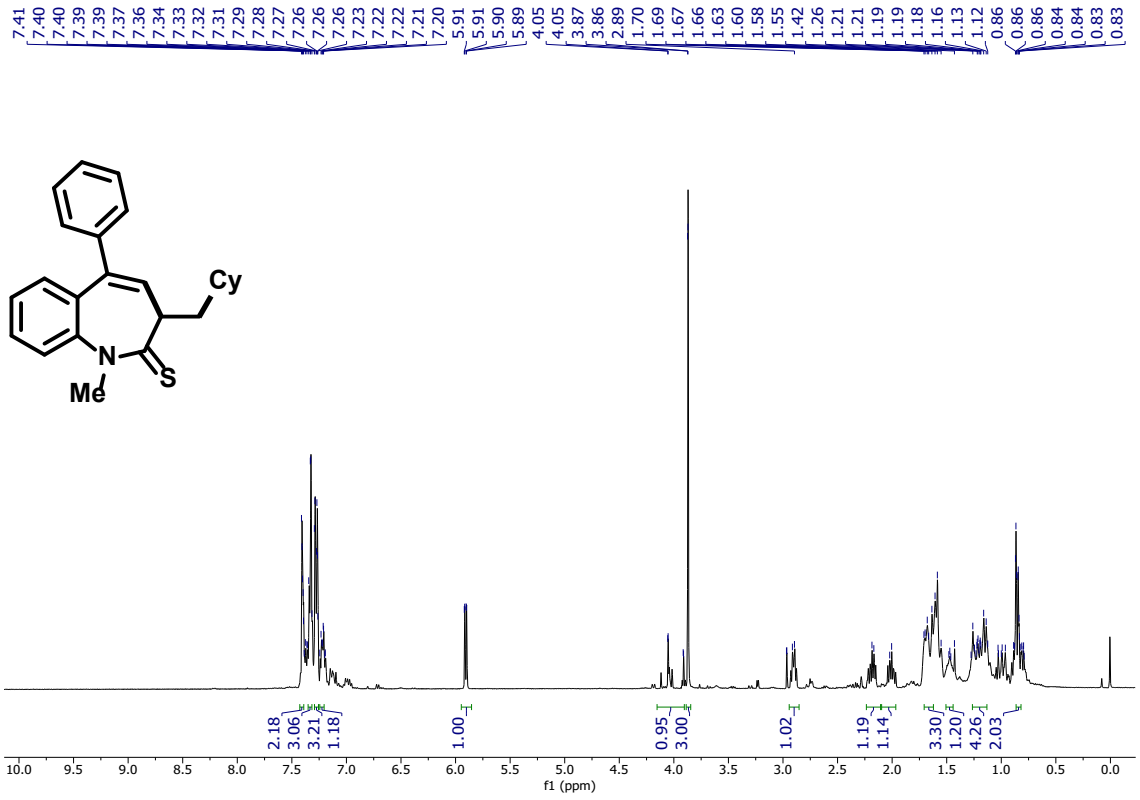


^{1}H NMR(400 MHz, $CDCl_3$) of compound **6e**

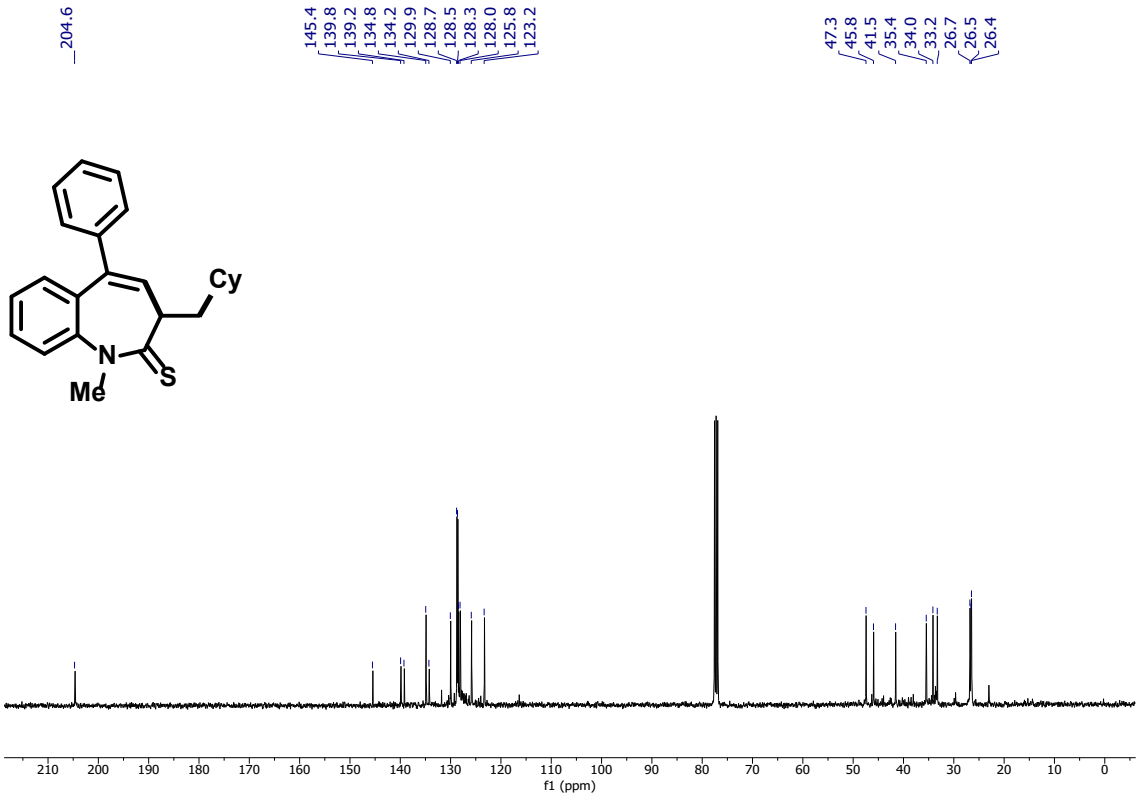


^{13}C NMR(100 MHz, $CDCl_3$) of compound **6e**

3-(cyclohexylmethyl)-1-methyl-5-phenyl-1,3-dihydro-2H-benzo[b]azepine-2-thione (7)

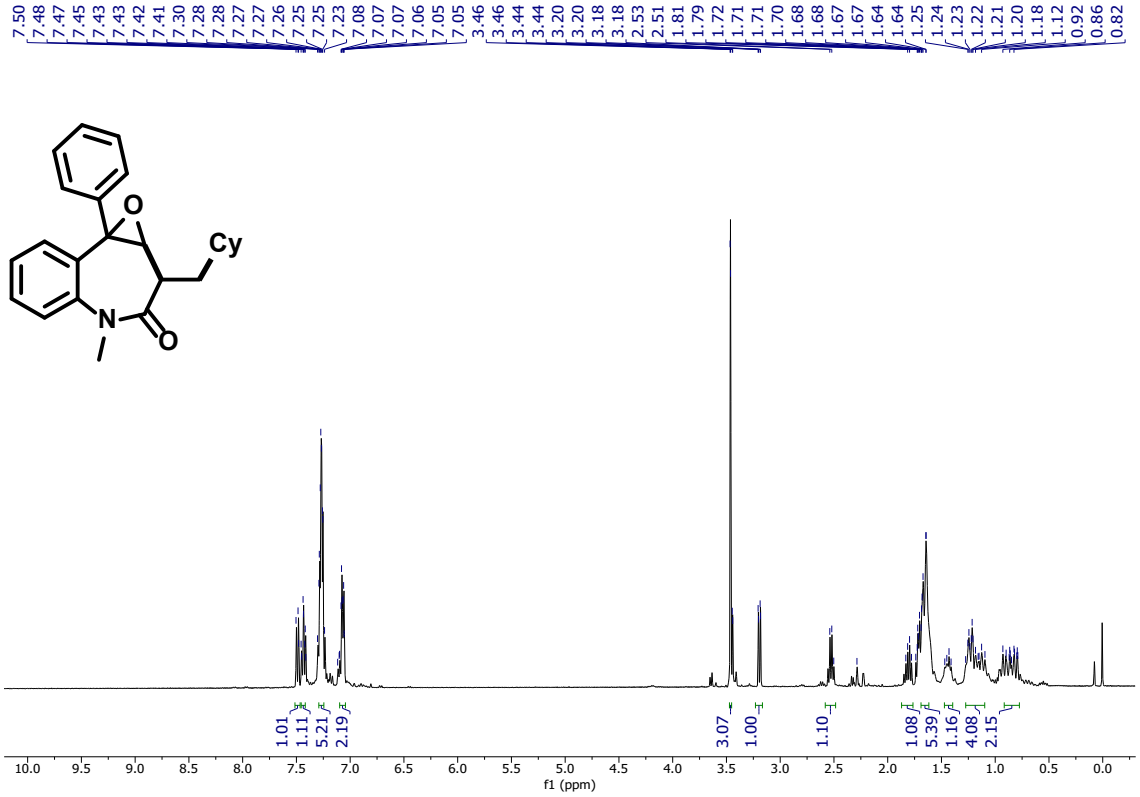


^{1}H NMR(400 MHz, $CDCl_3$) of compound **7**

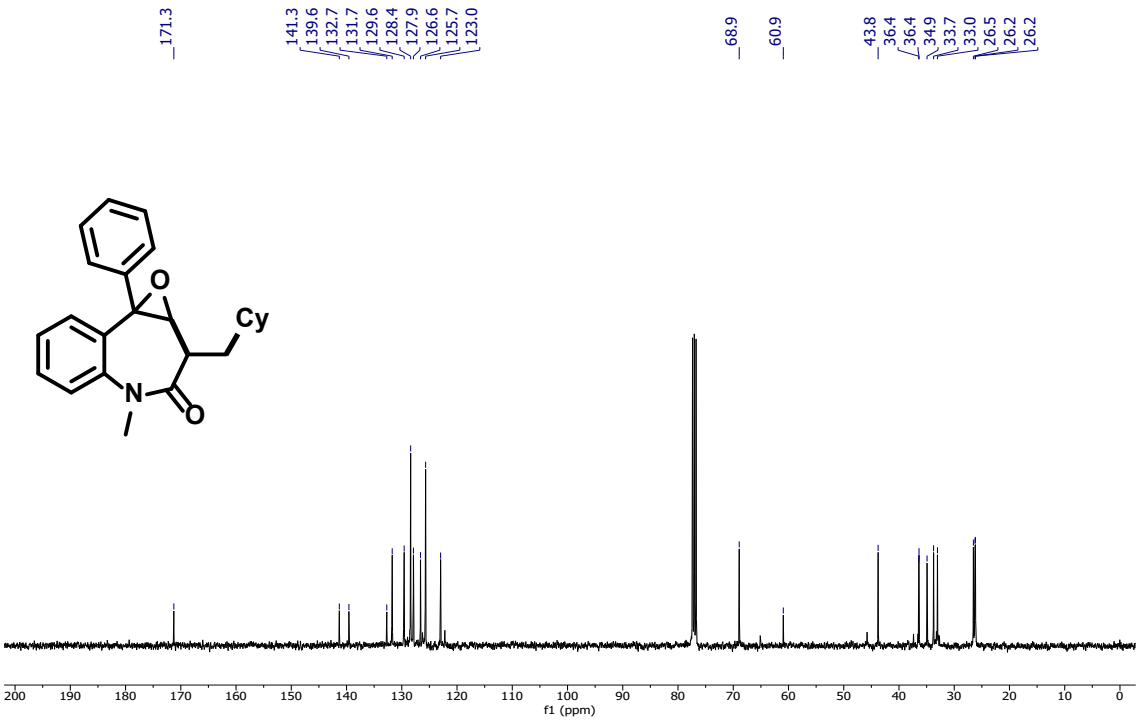


^{13}C NMR(100 MHz, $CDCl_3$) of compound **7**

(cyclohexylmethyl)-4-methyl-8b-phenyl-1a,2,4,8b-tetrahydro-3H-benzo[b]oxireno[2,3-d]azepin-3-one [2,3-d]azepin-3-one (8)



^{1}H NMR(400 MHz, $CDCl_3$) of compound **8**



^{13}C NMR(100 MHz, $CDCl_3$) of compound **8**

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[2] Luo, Q.-L.; Lv, L.; Li, Y.; Tan, J.-P.; Nan, W.; Hui. Q. *Eur. J. Org Chem.* **2011**, *34*, 6916-6922.

[3] Yu, L.-Z.; Xu, Q.; Tang, X.-Y.; Shi, M. ACS Catal. 2016, 6, 526–531. (d) Koester, D. C.; Werz, D. B. *Beilstein J. Org. Chem.* **2012**, *8*, 675–682.

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