**Supporting Information**

# Continuous-Flow Approach for the Multi-Gram Scale Synthesis of C2-Alkyl- or β-Amino Functionalized 1,3-Dicarbonyl Derivatives and Ondansetron Drug Using 1,3-Dicarbonyls

Nirmala Mohanta, Krishna Nair, Dasharath Vishambar Sutar, Boopathy Gnanaprakasam*

Department of Chemistry,
Indian Institute of Science Education and Research,
Dr. Homi Bhabha Road, Pashan, Pune - 411008, India.
*Email- gnanaprakasam@iiserpune.ac.in

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## 1. General information and data collection:

Commercially available reagents and solvents were used for the starting material without further purification. All the alcohols and 1,3-dione were purchased from Sigma-Aldrich, while Amberlyst®-15 from SD Fine-Chem. Visualization was accomplished with UV light and/or PMA stain followed by heating. Column chromatographic separations performed over 100-200 Silica-gel. The flow chemistry experiments were carried on Vapourtec R-series with glass column (Omntifit, 6.6 x 150 mm) for heterogeneous system, while homogeneous reactions were performed in SS coiled tubular reactor. 1H and 13C NMR spectra were recorded on 400 and 100 MHz respectively, using a Bruker 400 MHz and JEOL 400 MHz spectrometers. Abbreviations used in the NMR follow-up experiments: b, broad; s, singlet; d, doublet; t, triplet; q, quartet; p, pentet; m, multiplet. High-resolution mass spectra were obtained with Waters-synapt G2 using electrospray ionization (ESI). Fourier-transform infrared (FT-IR) spectra were obtained with a Bruker Alpha-II Fourier transform infrared spectrometer.

## 2. EXPERIMENTAL SECTION:

**A) General procedure for the formation of C-C bond by using Amberlyst®-15 under batch reaction:** The 1,3-dione (0.5 mmol), Amberlyst®-15 (2:1 Amberlyst®-15:1,3-dione**,** w/w ratio) and secondary alcohol (0.6 mmol) were charged to a 20 mL glass tube followed by 3 mL of acetonitrile. The tube was sealed using a crimper and the reaction mixture was stirred at 100 °C for 12 hrs. After cooling to room temperature, the reaction mixture solution was decanted to a round bottom flask. The Amberlyst®-15 was washed 5 times with DCM and added to the same round bottom flask. The organic layer was concentrated under reduced pressure and the residue was subjected to column chromatography purification (EtOAc : n-hexane = 20:80) afforded desired C-C bond formation

product as a pure compound **3a**. Similar reaction protocol was followed for the synthesis of other C2- substituted 1,3-dicarbonyl derivatives **3** by taking 1,3-dione (0.5 mmol) and Amberlyst®-15.

**B) General procedure for the formation of C-C bond by using Amberlyst®-15 under continuous-flow:** 0.1 M solution of the 1,3-dione (1 mmol in 10 mL ACN ) in a 30 mL vial and 0.12 M of alcohol (1.2mmol in 10 mL ACN ) was taken in another 30 mL vial and flown through the packed bed reactor (Omnifit®, 6.6 mm i.d. × 150.0 mm length) loaded with Amberlyst®-15 up to 5 cm (1.0 g, void volume = 1.56 mL swollen up to 6 cm after passing solvent) of bed heated at 100 $^{o}$C temperature and 3.5 bar pressure. The organic layer was concentrated under reduced pressure and the residue was subjected to column chromatography (EtOAc: n-hexane = 25:75) purification afforded corresponding C-C bond formation product **3**.

**C) General procedure for Mannich reaction under continuous-flow:** 0.1 M solution of 1,3-cyclodiketone was made with ACN in a vial. 1 mmol the aldehyde and 1 mmol of piperidine were dissolved in another vial with 10 mL of ACN. Then, both reagent solutions was flown through the 5 mL SS coil in room temperature at 3.3 bar pressure. The organic layer was concentrated under reduced pressure followed by column chromatography (Methanol: DCM = 10:90 or EtOAc : n-hexane = 20:80) purification afforded corresponding β-amino-C2 substituted 1,3-dicarbonyl derivatives compounds **4**.

**D) Study of life time of catalyst and gram scale synthesis:** The multi-gram of 2-benzhydryl-3-hydroxycyclohex-2-en-1-one (**3a**) was prepared by using general procedure A. 0.1 M solution of 1,3-cyclohexadione (3.360g in 300 mL ACN) and 0.12 M of diphenylmethanol (6.624 g in 300 mL ACN) was prepared and flown continuously (without washing the catalyst) through packed bed reactor (Omnifit®, 6.6 mm i.d. × 150.0 mm length) loaded with amberlyst®-15 up to 5 cm (1 g, swollen up to 7 cm after passing solvent) heated at 100 °C temperature with 3.5 bar pressure.

Evaporation of the solvent and column purification afforded 6.027 g (67%) of compound **3a** as a white powder.

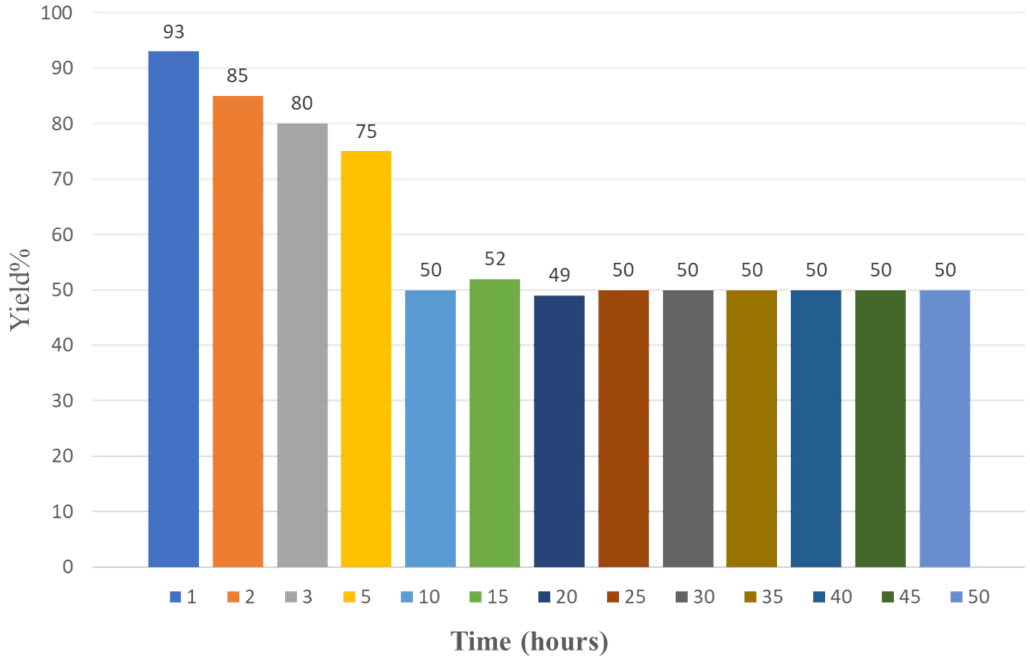



**Figure S1':** Gram scale synthesis of **3a** without recycling of catalyst

**E) The large scales synthesis of Mannich reaction product**:

0.1 M solution of cyclohexane-1,3-dione (10 mmol) was made with 100 mL of ACN in a vial. 10 mmol the formaldehyde and 10 mmol of piperidine were dissolved in another vial with 100 mL of ACN. Then, both reagent solutions were flown 0.15 mL/min each through the 5 mL SS coil in room temperature at 3.3 bar pressure. The organic layer was concentrated under reduced pressure followed by column chromatography (methanol : DCM = 10:90 or EtOAc: n-hexane = 20:80 ) purification afforded 2-(piperidin-1-ylmethyl)cyclohexane-1,3-dione **4a** (1.00, 83%) .

**F) General procedure for Ondansetron:**

**i) Synthesis of 9-methyl-1,2,3,9-tetrahydro-4H-carbazol-4-one (5) in continuous-flow:**

0.1 M of 1,3-cyclohexadione (280 mg in 25 mL of water) and 0.12 M of phenylhydrazine (366 mg in 25 ml of ethanol) was taken in 30 mL of vial separately. The solutions 1,3-cyclohexadione and phenylhydrazine were flown to the 10 mL of tubular SS coil reactor heated at 100 oC and subsequently the reaction mixture was passed continuously to packed bed reactor (Omnifit®, 6.6 mm i.d. × 150.0 mm length) loaded with amberlyst®-15 up to 7 cm of bed heated at 110 $^{o}$C temperature with 3.5 bar pressure. After completion of the reaction, the ethanol was evaporated under high vaccum. 490 mg (75%) of 9-methyl-1,2,3,9-tetrahydro-4H-carbazol-4-one was afforded as yellowish solid compound by recrystallization process.

**ii) Synthesis of Ondansetron 7:** 0.5 mmol of 9-methyl-1,2,3,9-tetrahydro-4H-carbazol-4-one was taken in a 20 ml resealable vial charged with paraformaldehyde (1.5 mmol), N, N-dimethylamine hydrochloride (1,5 mmol) and amberlyst®-15 (200 mg) in 5 mL of toluene. The reaction mixture was heated at 120 $^{o}$C for 24 hrs. After complete consumption of 9-methyl-1,2,3,9-tetrahydro-4H-carbazol-4-one (monitor by TLC), 2-methylimidazole was added to the same reaction mixture and heated at 120 $^{o}$C for 24 hrs. After cooling the reaction mixture to room temperature, the toluene was evaporated under high vacuum. The reaction mass was washed by water and 255 mg of ondansetron **7** was afforded as white solid compound.

**3. Procedure for the recyclability of catalyst**

0.1 M solution of 1,3-cyclohexadione (3.360 g in 300 mL ethanol) and 0.12 M of diphenylmethanol (6.624g in 300 mL) was prepared and flown continuous (without washing the catalyst) through packed bed reactor (Omnifit®, 6.6 mm i.d. × 150.0 mm length) loaded with Amberlyst®-15 up to 5 cm (1 g, swollen up to 7 cm after passing solvent) heated at 100 $^{o}$C temperature at 3.5 bar pressure

upto 10 hours. Depletion of rate of product formation was observed. Thus, 50 mL solution of 0.1 M of HCl in MeOH was passed through the Amberlyst®-15 packed bed at flow rate 0.25 mL/min to regain the catalytic activity of catalyst. Then, Amberlyst®-15 was washed by pure methanol untill the pH of the solution is nearly 7. The Amberlyst®-15 was heated in the reactor bed at 110 °C for 1.5 hour to dried the catalyst. Similarly, the catalyst were washed periodically with 0.1 M of HCl in MeOH and pure MeOH and reactivated after each 5 hours. The resulted conversion of starting material was shown below.

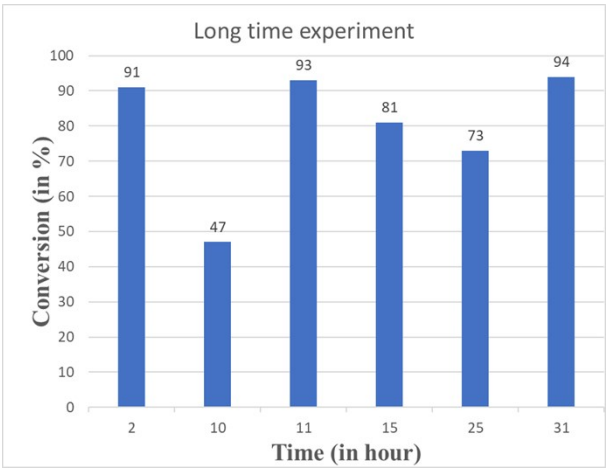
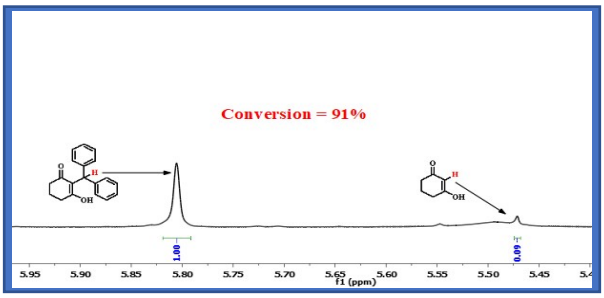
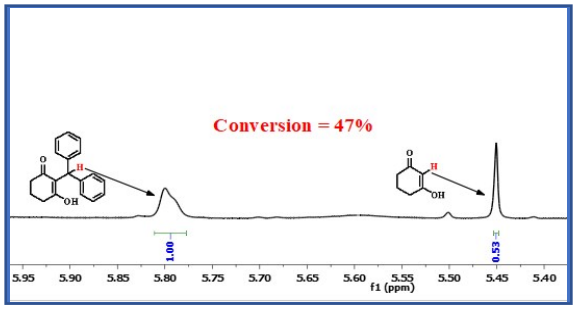



**Figure S1:** Recyclability of catalyst




**A)**

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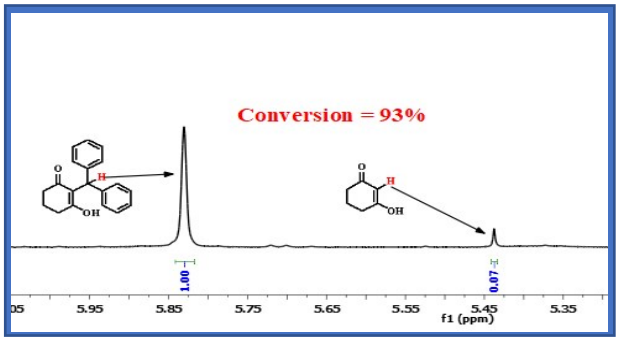
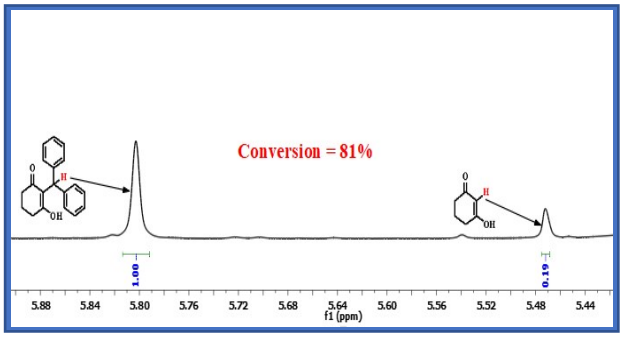
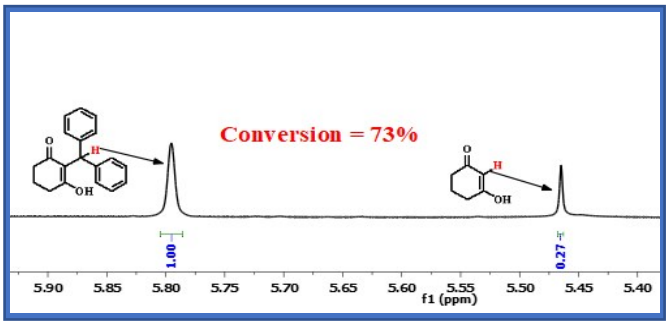
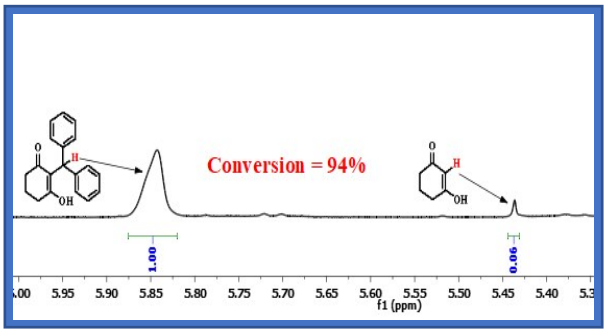



**C)**

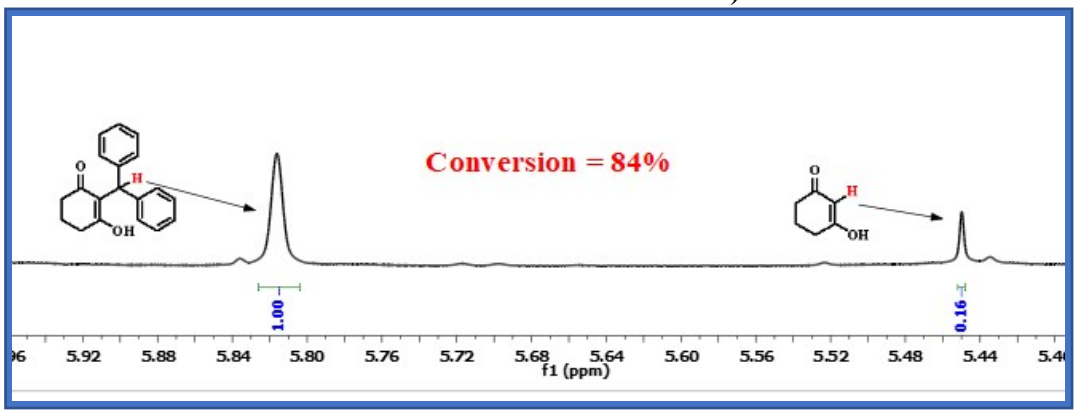
**D)**



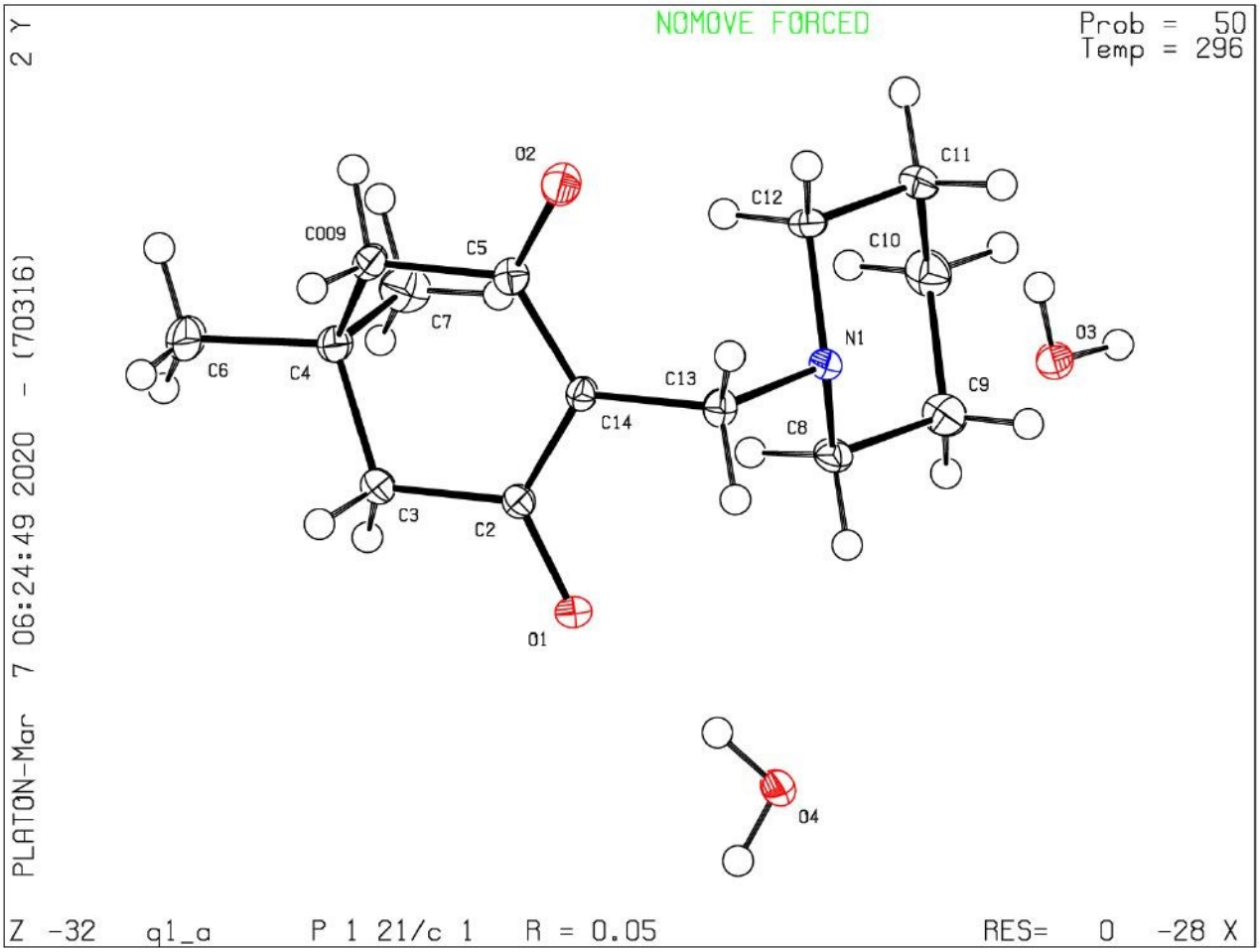

**E)**

**F)**




**G)**

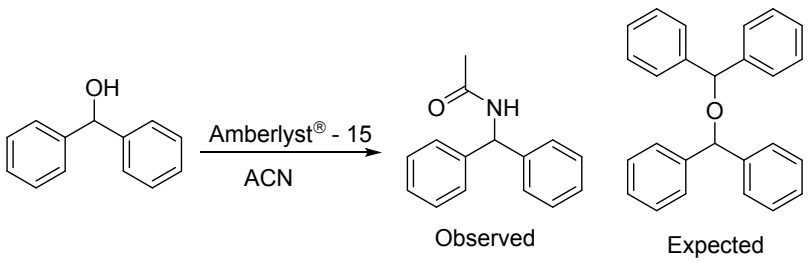
**Figure S2:** $^{1}$H-NMR monitoring reaction mixture over long run experiments: A) After 2 h; B) After 10 h; C) After 11 h; D) 15 hour before washing of amberlyst®-15; E) 24 h before washing of Amberlyst®-15; F) 31 h after washing of amberlyst®-15; G) 36 h after washing of Amberlyst®-15.



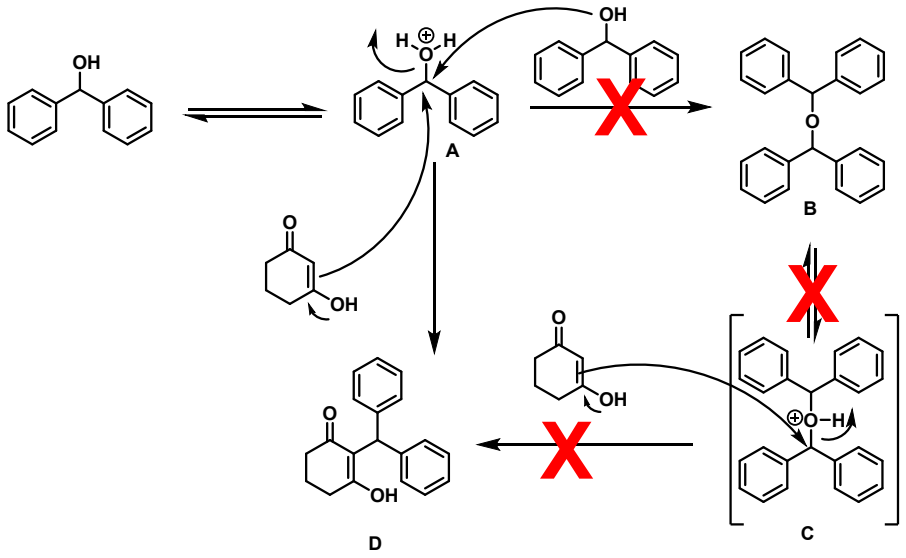

Crystal structure of compound **4c**

**4. Mechanism for C2- substituted alkylation of 1,3-dicarbonyl compound**

**A) Experiment for the synthesis of intermediate B**



1 mmol of diphenyl methanol was taken in a reaction vial followed by 4 mL of ACN and heated at 100 °C for 12 hours. To confirm the formation of intermediate the reaction was monitor by TLC. But the expected intermediate B was not observed.




**Scheme S1: Mechanism of C-C bond formation**

**5. Analytical data for the product:**

2-Benzhydryl-3-hydroxycyclohex-2-en-1-one **(3a)**: Synthesized by following the experimental procedure B by using 1,3-cyclohexadione (0.1 M solution in 10 mL ACN) and diphenyl methanol (0.12M solution in 10 mL ACN) afforded 96% (267.4 mg) as a white solid powder. mp 144-146 °C. $^{1}$H NMR (400 MHz, CDCl3) δ 7.35-7.31 (m, 4H), 7,27-7.24 (m, 3H), 7.18-7.16 (m, 3H), 5.94 (s, 1H) 5.87 (s, 1H), 2.48(t, $J$ = 6.4 Hz, 2H), 2.43 (t, $J$ = 6.4 Hz, 2H), 2.03 (m, 2H) ppm.$^{13}$C{$^{1}$H} NMR (100 MHz, CDCl3) δ 197.5, 172.4, 141.7, 129.2, 128.8, 127.2 118.6, 44.5, 36.8, 29.6 ppm. FTIR: 3030, 2925, 1700, 1576, 1372, 1272, 1190, 1083, 700 cm$^{-1}$. HRMS (ESI-TOF) m/z calculated for $C_{19}H_{18}O_2$ $(M+H)^+$: 279.1385, found: 279.1385.

3-Hydroxy-2-(phenyl(o-tolyl)methyl)cyclohex-2-en-1-one **(3b)**: Synthesized by following the experimental procedure B by using 1,3-cyclohexadione (0.1 M solution in 10 mL ACN) and 2-

methylbenzhydrol (0.12 M solution in 10 mL ACN) afforded 72% (209.6 mg) as a white solid powder. mp 151-152 $^{o}$C. $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.35-7.28 (m, 3H), 7.24-7.18 (m, 2H), 7.16-7.12 (m, 3H), 6.92 (d, *J* = 7.6 Hz, 1H), 6.02 (s, 1H), 5.88 (s, 1H), 2.48 (t, *J* = 6.4 Hz, 2H), 2.43 (t, *J* = 6.4 Hz, 2H), 2.25 (s, 1H), 2.04-1.97 (m, 2H) ppm. $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$) δ 197.4, 172.7, 141.4, 140.3, 138.0, 131.5, 129.3, 128.8, 127.5, 127.4, 127.3, 126.8, 117.1, 42.5, 36.9, 29.7, 20.8, 19.8 ppm. FTIR: 3020, 2920, 2584, 2367, 1731, 1565, 1363, 1191, 737 cm$^{-1}$. HRMS (ESI-TOF) m/z calculated for $C_{20}H_{20}O_2$ $(M+H)^+$: 293.1541, found: 293.1548.

2-(Bis(4-methoxyphenyl)methyl)-3-hydroxycyclohex-2-en-1-one **(3c):** Synthesized by following the experimental procedure B by using 1,3-cyclohexadione (0.1 M solution in 10 mL ACN) and 4,4'-Dimethoxybenzhydrol (0.12 M solution in 10 mL ACN) afforded 90% (350.2 mg) as a white solid powder. mp 177-178 $^{o}$C. $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.09-7.09 (m, 4H), 6.87-6.84 (m, 4H), 6.04 (s, 1H), 5.72 (s, 1H), 3.79 (s, 6H), 2.47 (t, *J* = 6.4 Hz, 2H), 2.42 (t, *J* = 6.4 Hz, 2H), 1.99 (p, *J* = 6.4 Hz, 2H) ppm.$^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$) δ 197.6, 172.3, 158.7, 133.8, 129.8, 118.7, 114.6, 55.4, 42.9, 29.7, 20.8 ppm. FTIR: 2950, 2844, 1712, 1590, 1567, 1454, 1374, 1243, 1169, 935, 826 cm$^{-1}$. HRMS (ESI-TOF) m/z calculated for $C_{21}H_{22}O_2$ $(M+H)^+$: 339.1596, found: 339.1606.

2-(Bis(4-fluorophenyl)methyl)-3-hydroxycyclohex-2-en-1-one **(3d)**: Synthesized by following the experimental procedure B by using 1,3-cyclohexadione (0.1 M solution in 10 mL ACN) and 4,4'-Difluorobenzhydrol (0.12 M solution in 10 mL ACN) afforded 78% (244.5 mg) as a white solid powder. mp 169-170 $^{o}$C. $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.14-7.11 (m, 4H), 7.04-6.97 (m, 4H), 6.01 (s, 1H), 5.78 (s, 1H), 2.49 (t, *J* = 6.4 Hz, 2H), 2.42 (t, *J* = 6.4 Hz, 2H), 2.00 (p, *J* = 6.4 Hz, 2H) ppm.$^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$) δ 197.6, 172.4, 161.8 (d, *J* = 244.69 Hz) 137.1 (d, *J* = 3.21 Hz) 130.1 (d, *J* = 7.88 Hz), 118.3, 43.1, 36.9, 29.8, 20.7 ppm. FTIR: 2922, 2864, 1730, 1572, 1486,

1372, 1256, 1095, 1017, 818 $cm^{-1}$. HRMS (ESI-TOF) m/z calculated for $C_{19}H_{16}F_2O_2$, $(M+H)^+$: 315.1197; found: 315.1204.

2-((4-Chlorophenyl)(phenyl)methyl)-3-hydroxycyclohex-2-en-1-one **(3e):** Synthesized by following the experimental procedure B by using 1,3-cyclohexadione (0.1 M solution in 10 mL ACN) and 4-chlorobenzhydrol (0.12 M solution in 10 mL ACN) afforded 82% (256.2 mg) as a white solid powder. mp 119-121 $^oC$. $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.33-7.24 (m, 7H), 7.19-7.11 (m, 7H), 6.28 (s, 1H),6.18 (d, $J$ = 7.6 Hz, 1H), 5.80 (s, 1H), 2.45 (t, $J$ = 6Hz, 2H), 2.40 (t, $J$ = 6Hz, 2H), 2.00-1.96 (m, 2H) ppm.$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 197.6, 172.6, 169.4, 141.9,140.2, 130.3,129.3, 129.1, 129.0, 128.9, 128.8, 128.7, 128.0,127.6, 127.3, 118.3, 56.7, 36.8, 29.8, 24.0, 20.7 ppm. FTIR: 2945.26, 2854.76, 1719.52, 1539.98, 1485.80, 1130.66, 1031.34, 788.44, 610.97 $cm^{-1}$. HRMS (ESI-TOF) m/z calculated for $C_{19}H_{17}ClO_2$ $(M+H)^+$: 313.0991, found: 313.0995.

2-Benzhydryl-3-hydroxy-5,5-dimethylcyclohex-2-en-1-one **(3f)**[1]: Synthesized by following the experimental procedure B using 5,5-dimethylcyclohexa-1,3-dione (0.1 M solution in 10 mL ACN) and diphenyl methanol (0.12 M solution in 10 mL ACN) afforded 85% (261.4 mg) as a white solid powder. mp 142-143 $^oC$. $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.34-7.31 (m, 4H), 7.27-7.25 (m, 2H), 7.18-7.16 (m, 4H), 5.85 (s, 1H), 2.35 (s, 2H), 2.30 (s, 2H), 1.09 (s, 6H) ppm. $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 197.4, 170.5, 141.7, 129.7, 129.2, 128.8, 127.2, 117.4, 53.2, 50.6, 44.5, 43.3, 32.0, 20.5 ppm. FTIR: 2922, 2864, 1730, 1572, 1486, 1372, 1256, 1095, 1017, 818 $cm^{-1}$. HRMS (ESI-TOF) m/z calculated for $C_{21}H_{22}O_2$ $(M+H)^+$: 307.1698, found: 307.1700.

2-(Bis(4-fluorophenyl)methyl)-3-hydroxy-5,5-dimethylcyclohex-2-en-1-one **(3g):** Synthesized by following the experimental procedure B using 5,5-dimethylcyclohexa-1,3dione (0.1 M solution in 10 mL ACN) 4,4'-Difluorobenzhydrol (0.12 M solution in 10 mL ACN) afforded 94% (320.3 mg) as a

white solid powder. mp 228-230 $^{o}$C. $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.30-7.34 (m, 1H), 7.14 – 7.11 (m, 4H), 7.02-6.94 (m, 3H), 5.76 (s, 1H), 2.36 (s, 2H), 2.29 (s, 2H), 1.08 (s, 6H) ppm. $^{13}$C{$^{1}$H} NMR (100 MHz, DMSO-$d_6$ + $CDCl_3$) δ 196.8, 177.1, 157.9, (d, $J$ = 246 Hz), 139.0, 129.8 (d, $J$ =7.54 Hz), 116.4, 113.8 (d, $J$ =7.54 Hz), 50.4, 43.4, 42.5, 31.4, 27.8 ppm. FTIR**:** 2945, 1715, 1590, 1375, 1256, 1153, 1021, 736 cm$^{-1}$. HRMS (ESI-TOF) m/z calculated for $C_{21}H_{20}F_2O_2$ $(M+H)^+$: 343.1510, found: 343.1519.

2-(Bis(4-methoxyphenyl)methyl)-3-hydroxy-5,5-dimethylcyclohex-2-en-1-one **(3h):** Synthesized by following the experimental procedure B using 5,5-dimethylcyclohexa-1,3dione (0.1 M solution in 10 mL ACN) and 4,4'-Dimethoxybenzhydrol (0.12 M solution in 10 mL ACN) afforded 97% (356 mg) as a white solid powder. mp 194-195 $^{o}$C. $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.08-7.06 (m, 4H), 6.88-6.84 (m, 4H), 5.99 (s, 1H), 5.70 (s, 1H), 3.79 (s, 6H), 2.34 (s, 2H), 2.29 (s, 2H), 1.08 (s, 6H) ppm. $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$) δ 197.3, 170.3, 158.7, 133.7, 129.8, 117.7, 114.6, 55.4, 56.6, 43.6, 42.9, 31.9, 28.4 ppm. FTIR: 2944, 1720, 1582, 1507, 1371, 1310, 1245, 1172, 1028, 827 cm-$^{1}$. HRMS (ESI-TOF) m/z calculated for $C_{23}H_{26}O_4$ $(M+H)^+$: 367.1907, found: 367.1909.

3-Hydroxy-5,5-dimethyl-2-(phenyl(otolyl)methyl)cyclohex-2-en-1-one **(3i):** Synthesized by following the experimental procedure B using 5,5-dimethylcyclohexa-1,3dione (0.1M solution in 10 mL ACN) and 2-methylbenzhydrol (0.12M solution in 10 mL ACN) afforded 71% (227 mg) as a white solid powder. mp 155-156 $^{o}$C. $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.34-7.31 (m, 2H), 7.27-7.18 (m, 3H), 7.15-7.12 (m, 3H), 6.93 (d, $J$ = 7.2 Hz, 1H), 6.05 (s, 1H), 5.86 (s, 1H), 2.35 (s, 2H), 2.30 (s, 2H), 1.09 (d, $J$ = 4.4 Hz, 6H) ppm. $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$) δ 197.1, 170.8, 141.6, 140.2, 137.9, 131.4, 129.3, 128.8, 127.5, 127.4,127.2, 126.8, 116.1, 50.6, 43.3, 42.5, 31.8, 28.6, 28.5, 19.7 ppm. FTIR (neat): 3268.29, 3050.31, 2933.95, 1594, 1370, 1278, 1089, 835, 700 cm$^{-1}$. HRMS (ESI-TOF) m/z calculated for $C_{22}H_{24}O_2$ $(M+H)^+$: 321.1855, found: 321.1860.

2-Benzhydryl-3-hydroxy-5-methylcyclohex-2-en-1-one **(3j):** Synthesized by following the experimental procedure B using 5-methylcyclohexa-1,3-dione (0.1M solution in 10 mL ACN) diphenyl methanol (0.12M solution in 10 mL ACN) afforded 82% (240.7 mg) as a white solid powder. mp 142-143 $^{o}$C. $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.32-7.27 (m, 6H), 7.09 -7.06 (m, 4H), 6.00 (s, 1H), 5.74 (s, 1H), 2.53-2.44 (m, 2H), 2.30-2.25 (m, 2H), 2.13-2.07, (m, 1H), 1.07 (d, *J* = 6, 3H) ppm. $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$) δ 197.4, 171.7, 139.1, 133.1, 130.1, 129.3, 129.2, 128.9, 117.6, 44.9, 43.4, 37.9 ppm. FTIR: 3041, 2942, 1545, 1378, 1152, 1078, 892, 710 cm$^{-1}$. HRMS (ESI-TOF) m/z calculated for $C_{20}H_{20}O_2$ $(M+H)^+$: 293.1542, found: 293.1548

2-(Bis(4-fluorophenyl)methyl)-3-hydroxy-5-methylcyclohex-2-en-1-one **(3k):** Synthesized by following the experimental procedure B using 5-methylcyclohexa-1,3-dione (0.1M solution in 10 mL ACN) and 4,4'-difluorobenzhydrol (0.12M solution in 10 mL ACN) afforded 95% (310.9 mg) as a white solid powder. mp 209-210 $^{o}$C. $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.14-7.09 (m, 4H), 7.04 - 6.99 (m, 4H), 5.77 (s, 1H), 5.78 (s, 1H), 2.55-2.45 (m, 2H), 2.30-2.26 (m, 2H), 2.15-2.08, (m, 1H), 1.08 (d, *J* = 6, 3H) ppm. $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$) δ 197.4, 171.6, 162.0 (d, *J* = 244 Hz), 137.1, 130.3 (d, *J* = 3.89), 130.2 (d, *J* = 3.94), 118.0, 116.2 (d, *J* = 10.24 Hz), 116.0 (d, *J* = 10.35 Hz), 45.0, 43.1, 37.7, 29.9, 28.2, 21.0 ppm. FTIR: 2921, 2857, 2362, 1723, 1504, 1375, 1227, 1156, 1015, 753 cm$^{-1}$. HRMS (ESI-TOF) m/z calculated for $C_{11}H_{18}F_2O_2$ $(M+H)^+$: 329.1353, found: 329.1358.

2-(Bis(4-methoxyphenyl)methyl)-3-hydroxy-5-methylcyclohex-2-en-1-one **(3l):** was synthesized by following the experimental procedure B using 5-methylcyclohexa-1,3-dione (0.1M solution in 10 mL ACN) and 4,4'-dimethoxybenzhydrol (0.12M solution in 10 mL ACN) afforded 98% (344.8 mg) as a white solid powder. mp 127-129 $^{o}$C. $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.07 (t, *J* = 8.4, 4H), 6.85 (d, *J* = 8.4 Hz, 4H), 6.06 (s, 1H), 5.70 (s, 1H), 3.78 (d, *J* = 1.2 Hz, 6H), 2.53-2.40 (m, 2H), 2.26 – 2.24 (m, 2H ), 2.13-2.04 (m, 1H), 1.07 (d, *J* = 6, 3H) ppm. $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$) δ

197.6, 171.6, 158.7, 158.7, 133.8, 133.7, 129.8, 129.8, 118.3, 114.7, 129.8, 118.3, 114.6, 114.5, 55.4, 45.1, 43.0, 32.7, 28.2, 21.0 ppm. FTIR: 3403, 2923, 2857, 1731, 1606, 1510, 1457, 1375, 1247, 1178, 1031, 833, 638 $cm^{-1}$. HRMS (ESI-TOF) m/z calculated for $C_{22}H_{24}O_4$ $(M+H)^+$: 353.1753, found: 353.1754.

3-Hydroxy-5-methyl-2-(phenyl(o-tolyl)methyl)cyclohex-2-en-1-one **(3m):** Synthesized by following the experimental procedure B using 5-methylcyclohexa-1,3-dione (0.1M solution in 10 mL ACN) and 2-methylbenzhydrol (0.12M solution in 10 mL ACN) afforded 52% (160.2 mg) as a white solid powder. mp 240-242 $^oC$. $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.34-7.30 (m, 2H), 7.27-7.25 (m, 1H), 7.23-7.18 (m, 2H), 7.16-7.11 (m, 3H), 6.94-6.89 (m, 1H), 6.08 (s, 1H), 5.86 ( d, *J* = 8.8 Hz, 1H), 2.54 – 2.40 (m, 2H ), 2.30-2.24 (m, 5H), 2,15-2.06 (m, 1H), 1.08 (d, *J* = 5.6, 3H) ppm. $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, selected signal for one of the diastereoisomer) δ 197.3, 172.1, 131.5, 129.3, 128.8, 127.5, 127.4, 126.8, 116.7, 45.1, 42.6, 37.8, 28.4, 21.0, 19.8 ppm. FTIR: 2925, 2637, 2600, 1580, 1508, 1376, 1247, 1174, 1029, 829 $cm^{-1}$. HRMS (ESI-TOF) m/z calculated for $C_{21}H_{22}O_2$ $(M+H)^+$: 307.1698, found: 307.1702.

2-Benzhydryl-3-hydroxycyclopent-2-en-1-one **(3n):** Synthesized by following the experimental procedure B using 1,3-cyclopentadione (0.1M solution in 10 mL ACN) and diphenyl methanol (0.12M solution in 10 mL ACN) afforded 52% (137.8 mg) as a white solid powder. mp 178-180 $^oC$. $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.35-7.31 (m, 4H), 7.28-7.24 (m, 2H), 7.16-7.13 (m, 4H), 5.27 (s, 1H), 2.51 (s, 4H) ppm. $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 141.0, 129.1, 128.8, 127.3, 119.6, 50.0, 31.0, 29.9 ppm. FTIR (neat): 2948, 2854, 1772, 1542, 1371, 1256, 1205, 733 $cm^{-1}$. HRMS (ESI-TOF) m/z calculated for $C_{18}H_{16}O_2$ $(M+H)^+$: 265.1229, found: 265.1233.

3-Hydroxy-2-(phenyl(o-tolyl)methyl)cyclopent-2-en-1-one **(3o):** was synthesized by following the experimental procedure B using 1,3-cyclopentadione (0.1M solution in 10 mL ACN) and 2-methylbenzhydrol (0.12M solution in 10 mL ACN) afforded 27% (76.5 mg) as a white solid powder. mp 191-193 $^{o}$C. $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.35-7.32 (m, 2H), 7.29-7.27 (m, 1H), 7.23-7.19 (m, 2H), 7.18-7.12 (m, 3H), 6.92-6.90 (d, *J* = 8, 1H), 5.95 (s, 1H), 5.37 (s, 1H), 2.58 (s, 1H), 2.48 (s, 1H), 2.24 (s, 3H) ppm. $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$) δ 140.7, 139.2, 137.4, 131.5, 129.3, 128.7, 127.5, 127.4, 126.6, 118.6, 42.2, 29.9, 19.9 ppm. FTIR: 2918, 2854, 1732, 1562, 1373, 1271, 1206, 1057, 733 cm$^{-1}$. HRMS (ESI-TOF) m/z calculated for $C_{19}H_{18}O_2$ $(M+H)^+$: 279.1385, found: 279.1386.

2-(Bis(4-methoxyphenyl)methyl)-3-hydroxycyclopent-2-en-1-one **(3p):** Synthesized by following the experimental procedure B using 1,3-cyclopentadione (0.1M solution in 10 mL ACN) and 4,4'-dimethoxybenzhydrol (0.12M solution in 10 mL ACN) afforded 79% (255.8 mg) as a white solid powder. mp 207-208 $^{o}$C. $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.06 (d, *J* = 8.4 Hz, 4H), 6.85 (d, *J* = 8.4, 4H), 5.17 (s, 1H), 3.78 (s, 6H) 2.49 (s, 4H) ppm. $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$) δ 158.5, 133.6, 129.8, 120.1, 114.2, 55.4, 43.3, 30.2 ppm. FTIR: 3258, 3050, 2921, 2855, 1688, 1647, 1593, 1448, 1285, 1195, 1085, 751, 698 cm$^{-1}$. HRMS (ESI-TOF) m/z calculated for $C_{20}H_{20}O_4$ $(M+H)^+$: 325.1440, found: 325.1445.

2-(Bis(4-fluorophenyl)methyl)-3-hydroxycyclopent-2-en-1-one **(3q):** Synthesized by following the experimental procedure B using 1,3-cyclopentadione (0.1M solution in 10 mL ACN) and 4,4'-Difluorobenzhydrol (0.12M solution in 10 mL ACN) afforded 65% (195.6 mg) as a white solid powder. mp 234-235 $^{o}$C. $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.13-7.11 (m, 4H), 7.09-7.00 (m, 4H), 5.23 (s, 1H), 2.54 (s, 4H) ppm. $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$) 162.0 (d, *J* = 8.34 Hz), 159.6, 138.1, 132.3, 130.5 (d, *J* = 7.83Hz), 124.0, 123.6, 116.3 (d, *J* = 20.27 Hz ) 114.8 ( d, *J* = 20. 99 Hz),

107.5 ppm. FTIR : 2923, 2842, 1574, 1508, 1377, 1248, 823, 734 $cm^{-1}$ . HRMS (ESI-TOF) m/z calculated for $C1_8H_{14}O_2F_2(M+H)^+$: 301.1040 found: 301.1042.

3-Benzhydryl-4-hydroxy-2H-chromen-2-one **(3r)**[19]**:** Synthesized by following the experimental procedure B using 4-hydroxy-2H-chromen-2-one (0.1M solution in 9:1 mL of ACN:THF) and diphenyl methanol (0.12M solution in 10 mL ACN) afforded 57% (187.3 mg) as a white solid powder. mp 179-180 $^oC$. $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.70 (d, *J* = 8 Hz, 1H), 7.51 (t, *J* = 8.4 Hz, 1H), 7.38-7.34 (m, 4H) 7.32-7.29 (m, 3H), 7.26-7.21 (m, 5H), 5.96 (s, 1H) ppm. $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 163.4, 160.8, 152.9, 140.1, 132.3, 129.6, 128.9, 128.0, 124.0, 123.3, 116.6, 109.9, 47.5 ppm. FTIR (neat): 3252, 3067, 2923, 1611, 1556, 1503, 1385, 1224, 1104, 831, 752 $cm^{-1}$. HRMS (ESI-TOF) m/z calculated for $C_{22}H_{16}O_3$ $(M+H)^+$: 329.1177, found: 329.1183.

3-(Bis(4-methoxyphenyl)methyl)-4-hydroxy-2H-chromen-2-one **(3s)**[2]**:** Synthesized by following the experimental procedure B using 4-hydroxy-2H-chromen-2-one (0.1M solution in 9:1 mL of ACN:THF) and 4,4'-dimethoxybenzhydrol (0.12M solution in 10 mL ACN) afforded 79% (306.7 mg) as a white solid powder. mp 146-148 $^oC$. $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.75 (dd, J = 8 Hz, J = 1.2 Hz, 1H ); 7.57-7.53 ( m, 1H), 7.34 (d, *J* = 8.4 Hz, 1H), 7.30-7.28 ( m, 1H), 7.21 (d, *J* =8.8 Hz, 4H), 6.93 (d, *J* = 8.8 Hz, 4H), 6.44 (s, 1H), 5.86 (s, 1H), 3.83 (s, 6H) ppm. $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) 163.3, 160.7, 159.8, 132.1, 129.9, 124.00, 123.2, 116.6, 116.5, 114.9, 108.2, 55.4, 46.0 ppm. FTIR: 3097, 2930, 2844, 1693.10, 1614, 1505, 11246, 1177, 1034, 901, 737 $cm^{-1}$. HRMS (ESI-TOF) m/z calculated for $C_{24}H_{20}O_5$ $(M+H)^+$: 389.1389, found: 389.1391.

3-(Bis(4-fluorophenyl)methyl)-4-hydroxy-2H-chromen-2-one **(3t)**[2]**:** Synthesized by following the experimental procedure B using 4-hydroxy-2H-chromen-2-one (0.1M solution in 9:1 mL of ACN:THF) and 4,4'-difluorobenzhydrol (0.12M solution in 10 mL ACN) afforded 81% (295.2 mg)

as a white solid powder . mp 199-200 $^{o}$C. $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 8 Hz, 1H); 7.56 (t, *J* = 8.4 Hz, 1H), 7.34-7.28 (m, 2H), 7.24-7.22 ( m, 4H), 7.08 (t, *J* =8.8 Hz, 4H), 6.14 (s, 1H), 5.92 (s, 1H) ppm. $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$) δ 163.6, 163.2, 161.9 (d, *J* = 243 Hz), 152.9, 135.6 (d, *J* = 3.25), 130.5 (d, *J* = 8.02 Hz), 116.7 (d, *J* = 21.37), 116.7, 115.9, 107.6, 46.0 ppm. FTIR: 3282, 2920, 1598, 1375, 1285, 1228, 1094, 829, 750 cm$^{-1}$. HRMS (ESI) m/z calculated for $C_{22}H_{16}O_3F_2$ $(M+H)^+$ : 365.0989, found: 365.0990.

2-Benzhydryl-1,3-diphenylpropane-1,3-dione **(3u)**[2,3]**:** Synthesized by following the experimental procedure B using 1,3-cyclopentadione (0.1M solution in 10 mL ACN) diphenyl methanol (0.12M solution in 10 mL ACN) afforded 76% (296.3 mg) as a white solid powder. mp 200-201 $^{o}$C. $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.84-7.81 (m, 3H); 7.49-7.45 ( m, 2H), 7.35-7.31 (m, 5H), 7.29-7.27 ( m, 1H), 7.24-7.22 (m, 4H), 7.16-7.12 ( m, 3H), 7.07-7.03 ( m, 2H), 6.34 (d, *J* = 11.6 Hz, 1H), 5.34 (d, *J* = 11.6 Hz, 1H) ppm. $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$) 194.2,141.8, 137.1, 133.3, 128.8, 128.8, 128.7, 128.4, 127.7, 127.6, 126.8, 62.5, 57.2, 52.6 ppm. FTIR: 2920, 2857, 1732, 1570, 1376, 1224, 943 cm$^{-1}$. HRMS (ESI-TOF) m/z calculated for $C_{28}H_{22}O_2$ $(M+H)^+$: 413.1517; found: 413.1522.

2-(Bis(4-fluorophenyl)methyl)-1,3-diphenylpropane-1,3-dione **(3u')**[3]: Synthesized by following the experimental procedure B using 1,3-diphenylpropane-1,3-dione (0.1M solution in 10 mL ACN) and 4,4'-difluorobenzhydrol (0.12M solution in 10 mL ACN) afforded 92% (391.4 mg) as a white solid powder. mp 216-217 $^{o}$C. $^{1}$H NMR (400 MHz, $CDCl_3$+ $CCl_4$) δ 7.84-7.81 (m, 4H); 7.48 (tt, *J* = 8.5 Hz, *J* = 12 Hz, 2H), 7.37-7.33 (m, 4H), 7.16-7.13 (m, 4H), 6.86-6.81 ( m, 4H), 6.12 (d, *J* = 11.6 Hz, 1H), 5.28 (d, *J* = 11.6 Hz, 1H) ppm. $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$) 193.4, 161.8 (d, *J* = 244.97 Hz), 137.6 (d, *J* = 3.18 Hz), 137.1, 133.5, 129.9 (d, *J* = 7.85 Hz), 128.9 (d, *J* = 3.08 Hz), 115.7 (d, *J* = 21.2), 63.6, 50.6 ppm. FTIR: 2918, 1687, 1594, 1504, 1254, 972, 824, 753 cm$^{-1}$. HRMS (ESI-TOF) m/z calculated for $C_{28}H_{20}O_2F_2$ $(M+H)^+$: 427.1510; found: 427.1517.

2-Benzhydryl-1,3-bis(4-methoxyphenyl)propane-1,3-dione **(3v)**[4]**:** Synthesized by following the experimental procedure B using 1,3-bis(4-methoxyphenyl)propane-1,3-dione (0.1M solution in 10 mL ACN) and diphenyl methanol (0.12M solution in 10 mL ACN) afforded 84% (378.8 mg) as a white solid powder. mp 161-163 $^{o}$C. $^{1}$H NMR (400 MHz, MeOH-$d_4$) δ 7.35-7.29 (m, 2H), 7.25-7.22 (m, 4H), 7.16-7.12 (m, 2H), 7.07-7.03 (m, 2H), 6.82-6.79 (m, 4H), 6.26 (d, *J* = 8 Hz, 1H), 6.19 (d, *J* = 11.6 Hz, 1H), 3.81(s, 6H) ppm. $^{13}$C{$^{1}$H} NMR (100 MHz, MeOH-$d_4$) δ 192.7, 163.7, 142.2, 141.6, 131.2, 128.8, 128.6, 128,4, 127.6, 126.6, 113.8, 57.2, 55.5, 52.4 ppm. FTIR: 3043, 2923, 2853, 1667, 1595, 1510, 1262, 1025, 839, 700 cm$^{-1}$. HRMS (ESI-TOF) m/z calculated for $C_{30}H_{26}O_4$ $(M+H)^+$: 451.1909, found: 451.1908.

3-Hydroxy-2-(piperidin-1-ylmethyl)cyclohex-2-en-1-one **(4a):** Synthesized by following the experimental procedure C using 1,3-cyclohexadione (0.1M solution in 10 mL ACN), formaldehyde and piperidine (1 mmol of each in 10 ml ACN ) afforded 85% (177.8 mg) as a yellowish semi-solid . $^{1}$H NMR (400 MHz, $CDCl_3$) δ 3.90 (s, 2H), 3.35 (d, *J* = 13.2 Hz, 2H), 2.55 (t, *J* = 12 Hz, 2H), 2.32, (t, *J* = 6.4 Hz), 1.95-1.87 (m, 6H), 1.71-1.67 (m, 2H) ppm. $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$) δ 193.4, 101.3, 55.0, 52.3, 35.5, 32.5, 29.8, 24.1, 22.8, 21.7 ppm. FTIR: 2937, 1615, 1494, 1037, 729 cm$^{-1}$. HRMS (ESI-TOF) m/z calculated for $C_{12}H_{19}NO_2$ $(M+H)^+$: 210.1494, found: 210.1496.

3-Hydroxy-5-methyl-2-(piperidin-1-ylmethyl)cyclohex-2-en-1-one **(4b):** Synthesized by following the experimental procedure C using 5-methylcyclohexa-1,3-dione (0.1M solution in 10 mL ACN), formaldehyde and piperidine ( 1 mmol of each in 10 ml ACN ) afforded 75% (167.1 mg) as a white solid powder. mp 144-146 $^{o}$C. $^{1}$H NMR (400 MHz, $CDCl_3$) δ 3.88 (s, 2H), 3.34 (d, *J* = 11 Hz, 2H), 2.54 (t, *J* = 11.6 Hz, 2H), 2.36-2.32 (m, 2H), 2.08-2.00 (m, 2H), 1.89-1.70 (m, 6H), 1.40 (m, 1H), 1.01 (d, *J* = 6.4 Hz, 3 Hz) ppm. $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$) δ 193.0, 100.9, 54.8, 52.3, 43.9,

29.8, 29.0, 24.0, 22.8, 21.5 ppm. FTIR: 2957, 2881, 1754, 1654, 1423, 1242, 1059, 757 $cm^{-1}$. HRMS (ESI-TOF) m/z calculated for $C_{13}H_{21}NO_2$ $(M+H)^+$: 224.1650, found: 224.1655.

3-Hydroxy-5,5-dimethyl-2-(piperidin-1-ylmethyl)cyclohex-2-en-1-one **(4c):** Synthesized by following the experimental procedure C using 5,5-dimethylcyclohexa-1,3dione (0.1M solution in 10 mL ACN), formaldehyde and piperidine (1 mmol of each in 10 ml ACN ) afforded 67% (158.8 mg) as a white solid powder. mp 152-154 $^oC$. $^1H$ NMR (400 MHz, $CDCl_3$) δ 3.88 (s, 2H), 3.32 (m, 2H), 2.54 (t; $J$ = 10 Hz, 2H), 2.19 (bs, 4H), 1.74 (m, 5H), 1.40 (s, 1H), 1.03 (s, 6H) ppm. $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 192.1, 100.0, 54.8, 52.3, 49.2, 46.1, 32.1, 29.8, 28.9, 24.0, 22.8 ppm. FTIR: 2937, 1582, 1496, 1420, 1135, 1079, 923 $cm^{-1}$. HRMS (ESI-TOF) m/z calculated for $C_{19}H_{23}NO_2$ $(M+H)^+$: 238.1807, found: 238.1808.

3-Hydroxy-2-(piperidin-1-ylmethyl)cyclopent-2-en-1-one **(4d):** Synthesized by following the experimental procedure C using 1,3-cyclopentadione (0.1M solution in 10 mL ACN), formaldehyde and piperidine (1 mmol of each in 10 ml ACN ) afforded 82% (195.8 mg) as a white solid powder. mp 212-213 $^oC$. $^1H$ NMR (400 MHz, $CDCl_3$) δ 3.58 (s, 2H), 2.70 (s, 2H), 2.25 (m, 4H), 1.86 (s, 5H), 1.39 (s, 1H) ppm. $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 203.0, 102.6, 53.9,50.9, 44.6, 32.8, 29.7, 23.2, 22.2 ppm. FTIR: 2922, 2816, 2342, 1721, 1618, 1423, 1222, 1054, 751$cm^{-1}$. HRMS (ESI-TOF) m/z calculated for $C_{16}H_{25}NO_3$ $(M+H)^+$: 272.1260, found: 272.1266.

3-Hydroxy-2-(phenyl(piperidin-1-yl)methyl)cyclopent-2-en-1-one **(4e):** Synthesized by following the experimental procedure C using 1,3-cyclopentadione (0.1M solution in 10 mL ACN), benzaldehyde and piperidine ( 1 mmol of each in 10 ml ACN ) afforded 78% (271.1 mg) as a white solid powder. mp 260-261 $^oC$. $^1H$ NMR (400 MHz, $CDCl_3$) δ 12.35 (bs, 1H), 7.28-7.26 (m, 1H), 7.24-7.23 (m, 2H), 7.19-7.14 (m, 1H), 7.11-7.09 (m, 2H), 5.47 (s, 1H), 2.66-2.55 (m, 4H), 2.49-2.34

(m, 5H), 2.07-2.00 (m, 4H) ppm. $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 192.0, 190.9, 137.8, 128.2, 126.5, 125.9, 116.4, 33.5, 32.9, 20.1 ppm. FTIR: 2936, 1731, 1591, 1373, 1159, 854, 734 $cm^{-1}$. HRMS (ESI-TOF) m/z calculated for $C_{16}H_{25}NO_3$ $(M+H)^+$: 272.1260, found: 272.1266.

4-Hydroxy-3-(piperidin-1-ylmethyl)-2H-chromen-2-one **(4f):** Synthesized by following the experimental procedure C using 4-hydroxy-2H-chromen-2-one (0.1M solution in 9:1 mL of ACN:THF), benzaldehyde and piperidine ( 1 mmol of each in 10 ml ACN )afforded 72% (267.4 mg) as a white solid powder . mp 180-181 $^{o}C$. $^{1}H$ NMR (400 MHz, $CDCl_3$) δ 7.88-7.86 (m, 1H), 7.39-7.34 (m, 1H), 7.21-7.06 (m, 2H), 4.16 (s, 2H), 3.59 (d, *J* = 12.4 Hz, 2H), 2.81 (m, 2H), 1.94-1.85 (m, 6H) ppm. $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 179.8, 176.3, 167.4, 166.0, 154.2, 154.9, 132.1, 131.4, 125.3, 124.4, 123.2, 123.2, 121.4, 120.00, 116.6, 116.5, 88.0, 86.5, 55.3, 52.8, 23.5, 22.5, 22.0, 20.1 ppm. FTIR: 2940, 2863, 2576, 1650, 1601, 1527, 1420, 1272, 1217, 1045, 920, 752, 684 $cm^{-1}$. HRMS (ESI-TOF) m/z calculated for $C_{16}H_{17}NO_3$ $(M+H)^+$: 260.1286, found: 260.1297.

4-Hydroxy-3-(phenyl(piperidin-1-yl)methyl)-2H-chromen-2-one **(4g)**[5]**:** synthesized by following the experimental procedure C using 4-hydroxy-2H-chromen-2-one (0.1M solution in 9:1 mL of ACN:THF), benzaldehyde and piperidine ( 1 mmol of each in 10 ml ACN ) afforded 79% (264.4 mg) as a white solid powder. mp 153-154 $^{o}C$. $^{1}H$ NMR (400 MHz, $CDCl_3$) δ 8.01-7.98 (m, 1H), 7.62-7.52 (m, 2H), 7.47-7.43 (m, 1H), 7.35-7.30 (m, 3H), 7.24-7.21 (m, 2H), 5.13 (s, 1H), 3.83 (d, *J* = 12.4 Hz), 2.99 (d, *J* = 12.4 , 1H), 2.75 (t, *J* = 12 Hz, 1H), 2.34-2.31 (m, 2H), 1.93-167 (m, 6H) ppm. $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 174.0, 164.4, 154.2, 136.2, 131.5, 129.4, 129.3, 124.3, 123.1, 121.0, 116.7, 95.0, 71.6, 54.0, 51.8, 24.4, 22.6 ppm. FTIR: 3049, 2949, 2877, 2373, 1714, 1580, 1373, 1256, 1151, 1021, 735 $cm^{-1}$. HRMS (ESI-TOF) m/z calculated for $C_{21}H_{21}NO_3$ $(M+H)^+$: 336.1600, found: 336.1608.

3-(Piperidin-1-ylmethyl)-1H-indole **(4h)**[6]**:** Synthesized by following the experimental procedure C using indole (0.1M solution in 10 mL ACN), formaldehyde and piperidine ( 1 mmol of each in 10 ml ACN ) heated at 80°C afforded 32% (69.4 mg) as a oil liquid. $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.70-7.68 (m, 1H), 7.45-7.43 (m, 1H), 7.22-7.20 (m, 1H), 7.18-7.13 (m, 2H), 4.81 (s, 1H), 2.53-2.50 (m, 4H), 1.62-1.55 (m, 3H), 1.43-1.26 (m, 3H) ppm. $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$) δ 137.4, 128.9, 121.7, 119.5, 119.3, 110.9, 110.3, 68.7, 54.4, 53.9, 51.9, 26.0, 26.0, 24.4, 24.0 ppm. FTIR: 3342, 2932, 1579, 1467.37, 1201.92, 1059, 757.02 cm$^{-1}$. HRMS (ESI-TOF) m/z calculated for $C_{14}H_{18}N_2$ $(M+H)^+$: 215.1548, found: 215.1552.

9-Methyl-1,2,3,9-tetrahydro-4H-carbazol-4-one **(5)**[7] was synthesized by following the experimental procedure F(i). mp 193-194 °C. $^{1}$H NMR (400 MHz, $CDCl_3$) δ 8.27-8.24 (m, 1H), 7.30-7.27 (m, 3H), 3.72 (s, 3H), 2.95 (t, *J* = 6 Hz, 2H), 2.58 (t, *J* = 6 Hz, 2H), 2.30-2.23 (m, 2H) ppm. $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$) δ 193.9, 152.0, 137.5, 124.8, 123.9, 123.1, 122.7, 121.8, 112.8, 109.2, 38.0, 30.0, 23.4, 22.3 ppm. HRMS (ESI-TOF) m/z calculated for $C_{13}H_{13}NO$ $(M+H)^+$: 200.1075, found: 200.1078.

9-Methyl-3-methylene-1,2,3,9-tetrahydro-4H-carbazol-4-one **(6)** was synthesized by following the experimental procedure F(ii). mp 118-119 °C. $^{1}$H NMR (400 MHz, $CDCl_3$) δ 8.34-8.31(m, 1H), 7.31-7.30 (m, 3H ), 6.15-6.14 (m, 1H), 5.39-5.38 (m, 1H), 3.71 (s, 3H), 3.05-3.04 (m, 2H), 2.99-2.98 (m, 2H) ppm. $^{13}$C{1H} NMR (100 MHz, CDCl3) δ 183.4, 151.8, 143.7, 125.3, 123.4, 122.9, 122.1, 119.0, 109.4, 31.1, 30.0, 22.7 ppm. HRMS (ESI-TOF) m/z calculated for $C_{14}H_{13}NO$ (M+H)+: 212.1075, found: 212.1079.

9-Methyl-3-((2-methyl-1H-imidazol-1-yl)methyl)-1,2,3,9-tetrahydro-4H-carbazol-4-one **(7)** was synthesized by following the experimental procedure F(ii). mp 221-222 °C. $^{1}$H NMR (400 MHz,

$CDCl_3$) δ 8.26-8.24(m, 1H), 7.32-7.29 (m, 3H ), 6.93 (d, *J* = 1.2 Hz, 1H), 6.89 (d, *J* = 1.6 Hz, 1H) 4.67 (dd, *J* = 14.8 Hz, *J* = 4 Hz, 1H) 4.08 (dd, *J* = 14.8 Hz, *J* = 2.2 Hz, 1H), 3.70 (s, 3H), 2.99-2.97 (m, 1H), 2.92-2.82 (m, 2H), 2.43 (s, 3H), 2.22-2.17 (m, 1H) 1.95-1.85 (m, 1H) ppm. $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 191.7, 151.4, 145.1, 137.8, 127.5, 124.8, 123.6, 123.1, 121.7, 119.9, 112.4, 109.5, 47.4, 45.8, 30.0, 26.7, 21.6, 13.4 ppm. HRMS (ESI-TOF) m/z calculated for $C_{18}H_{19}N_3O$ $(M+H)^+$: 294.1606, found: 294.1608.

## 6. Copies of NMR spectra

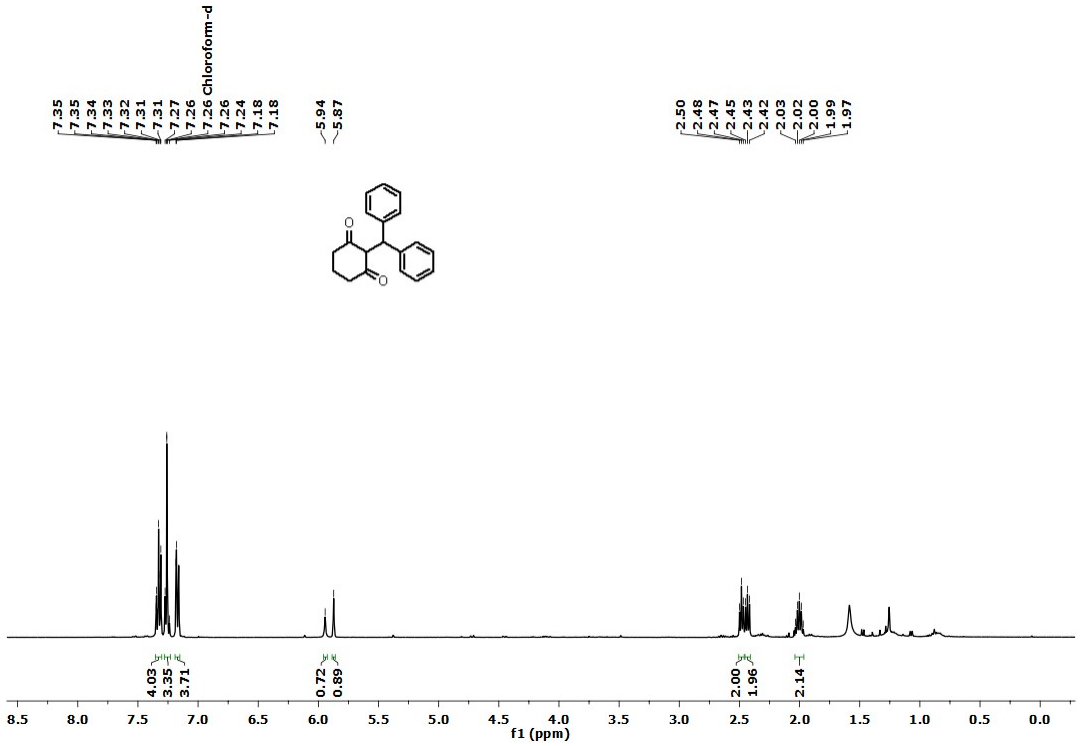



**Figure S3:** $^{1}$H NMR of Compound **3a**

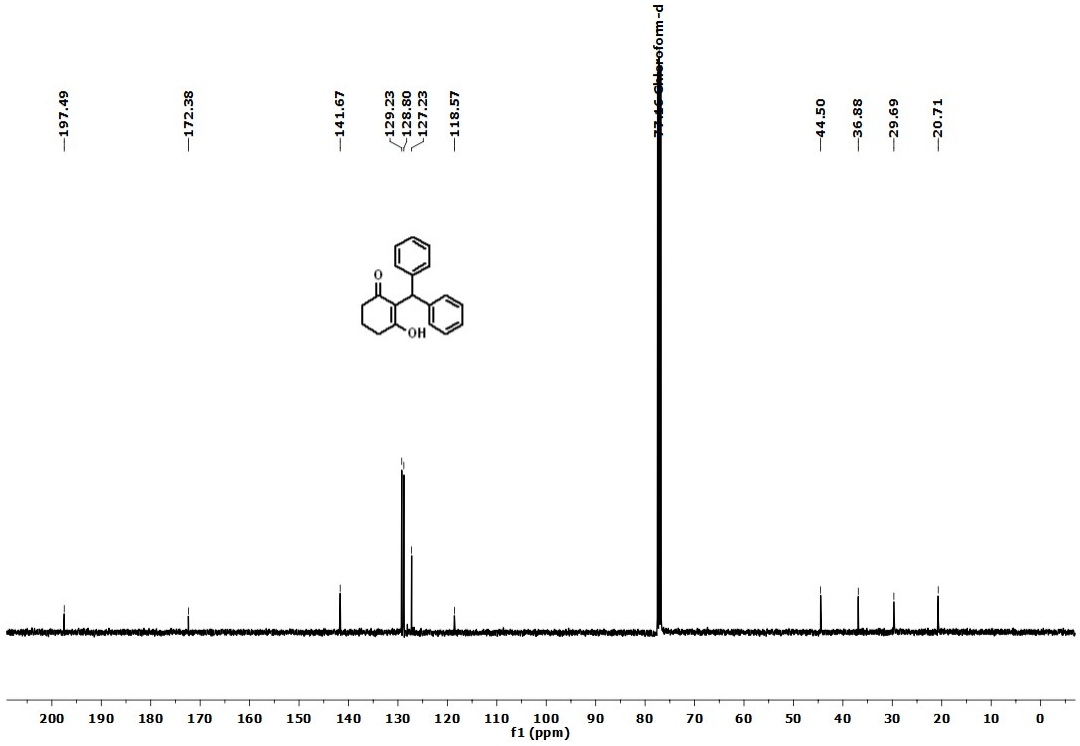



**Figure S4:** $^{13}$C NMR of Compound **3a**

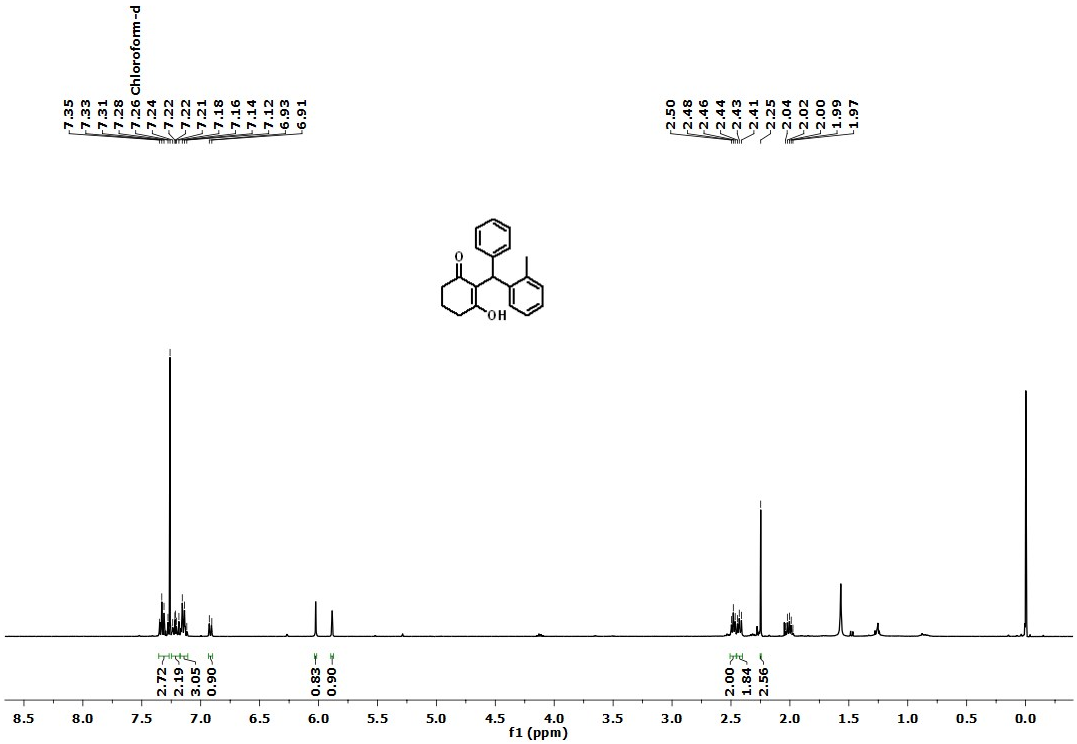



**Figure S5:** $^{1}$H NMR of Compound **3b**

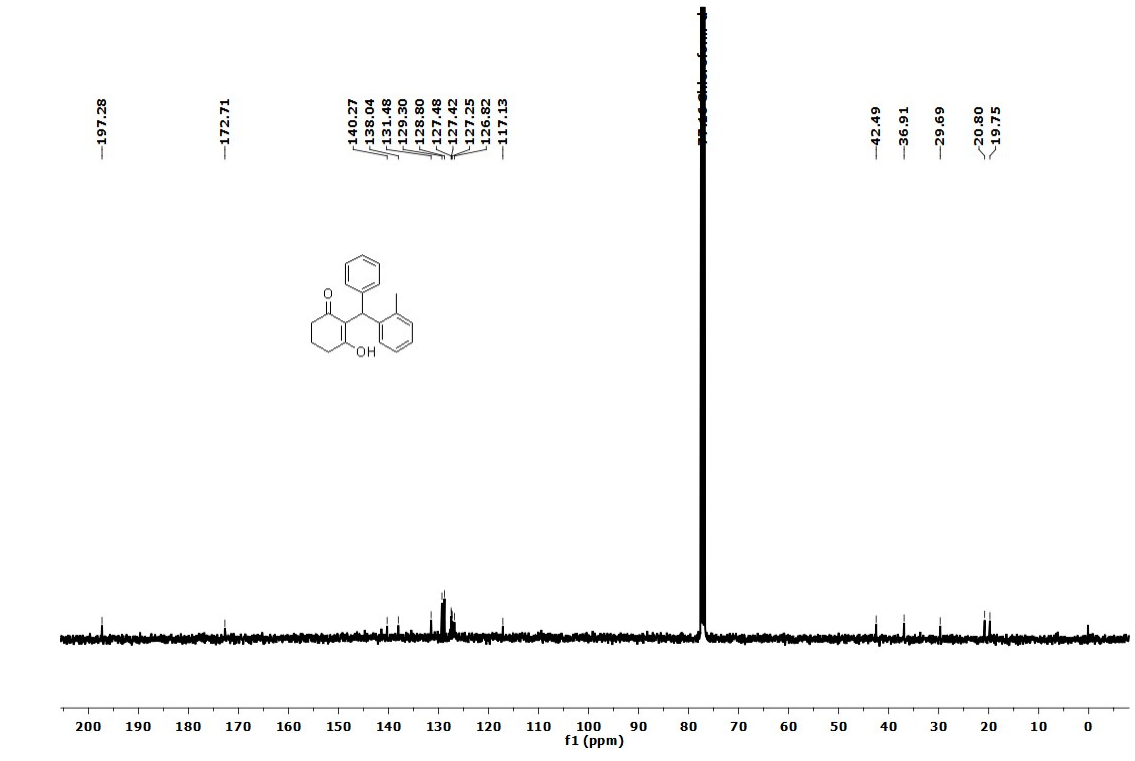



**Figure S6:** $^{13}$C NMR of Compound **3b**

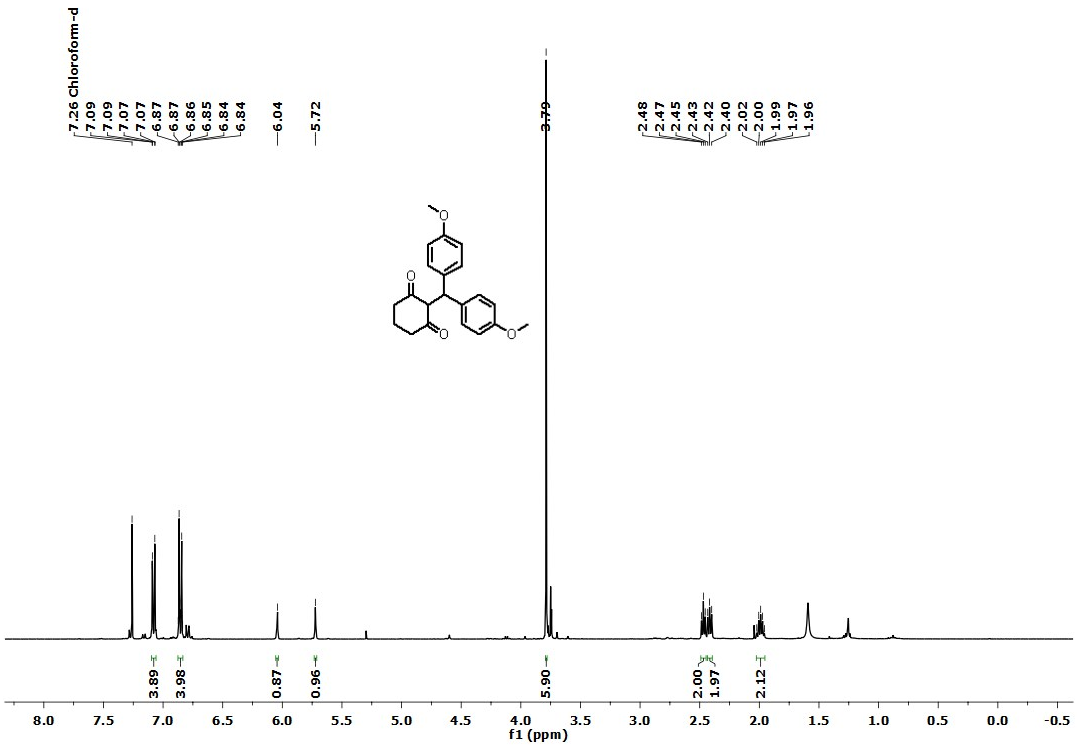



**Figure S7:** $^{1}$H NMR of Compound **3c**

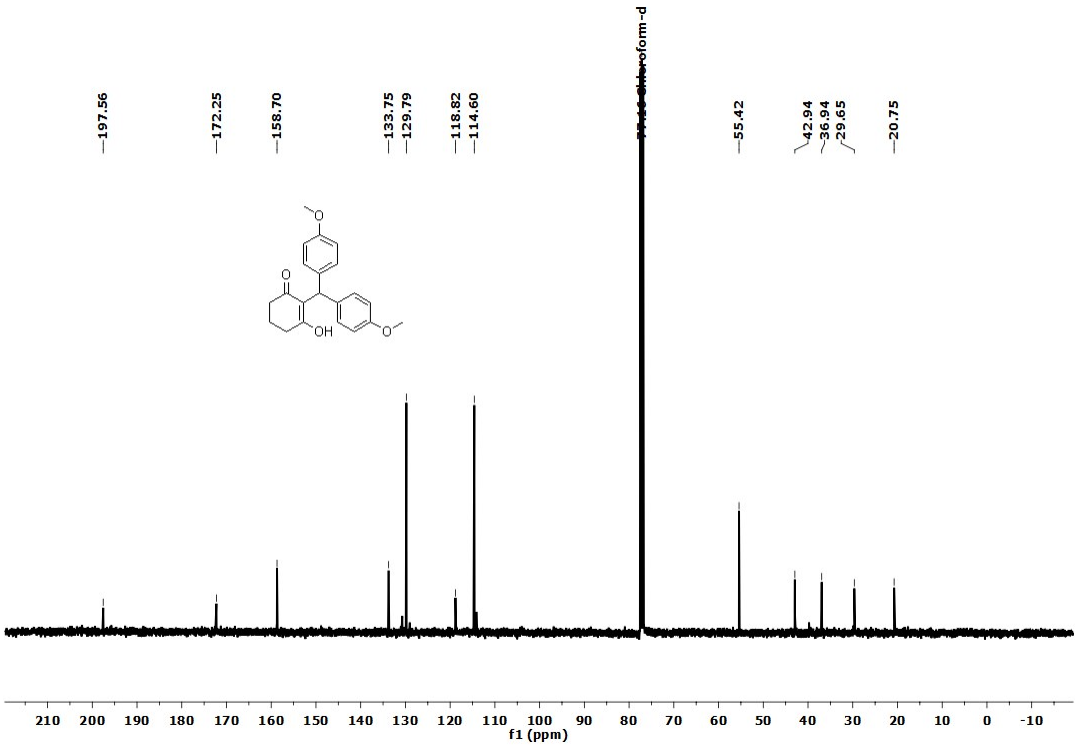



**Figure S8:** $^{13}$C NMR of Compound **3c**

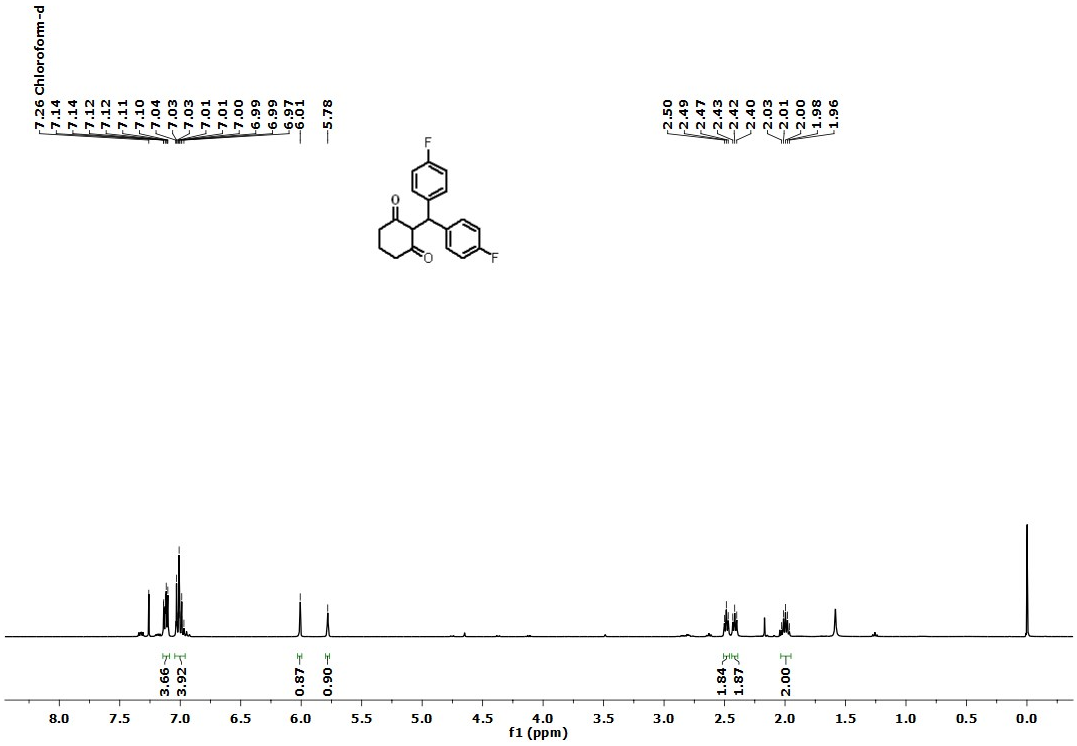



**Figure S9:**[1] H NMR of Compound **3d**

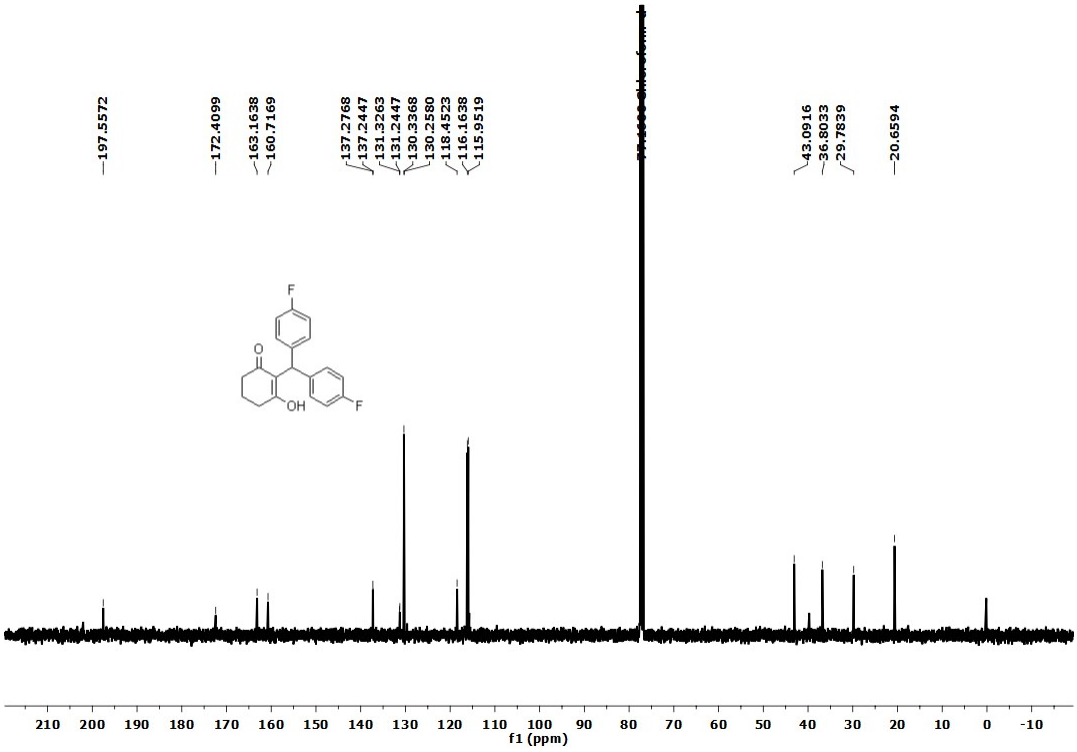



**Figure S10:** [13]C NMR of Compound **3d**

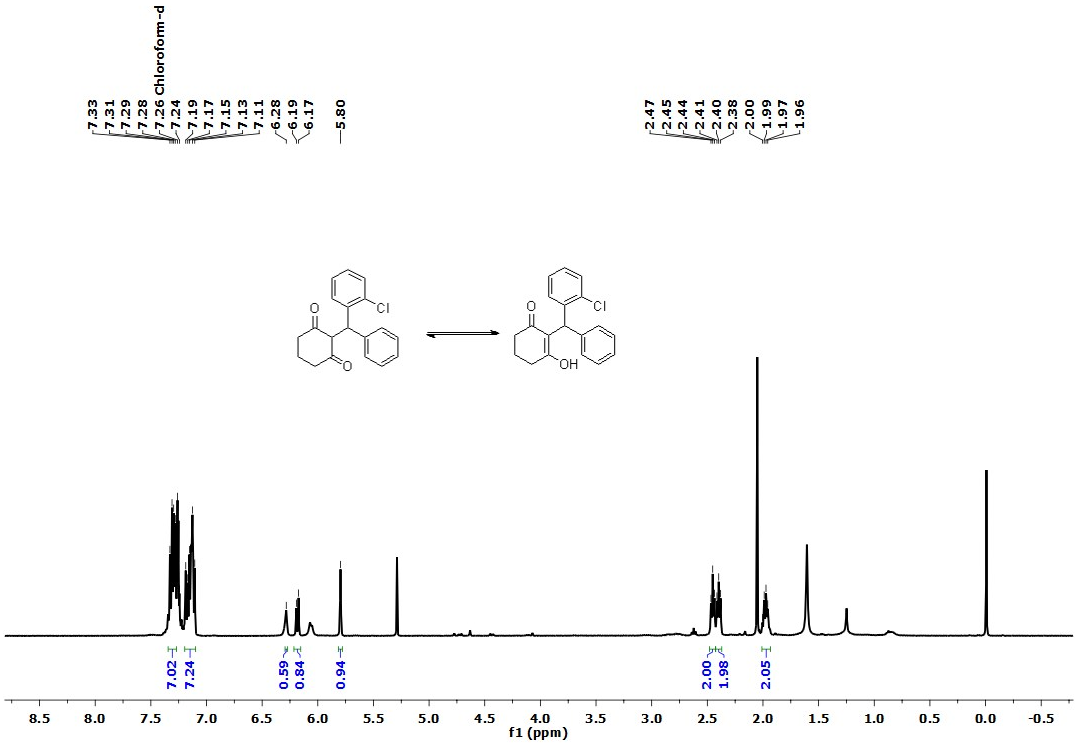



**Figure S11:**[1] H NMR of Compound **3e**

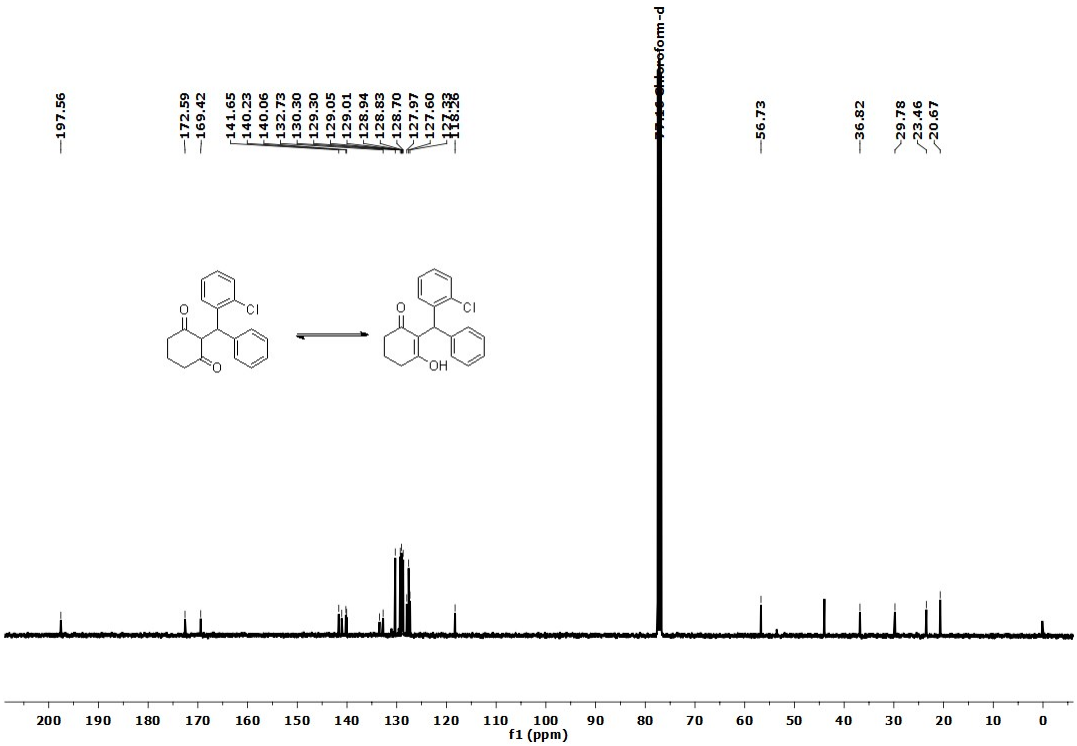



**Figure S12:** [13]C NMR of Compound **3e**

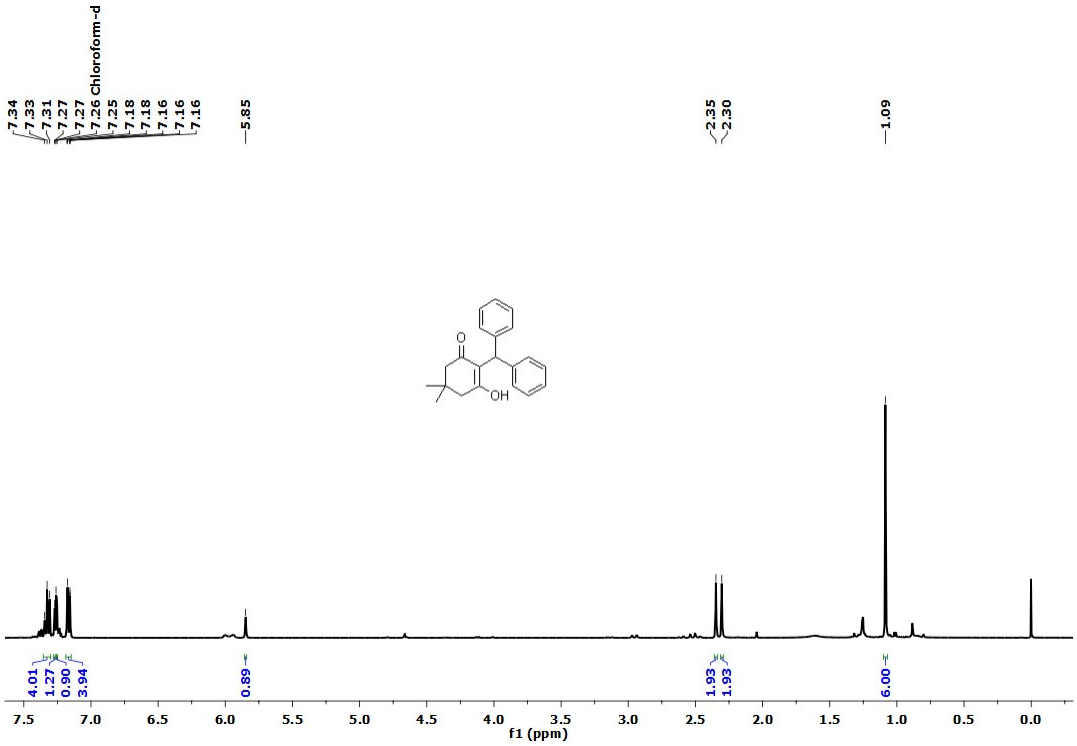



**Figure S13:** $^{1}$H NMR of Compound **3f**

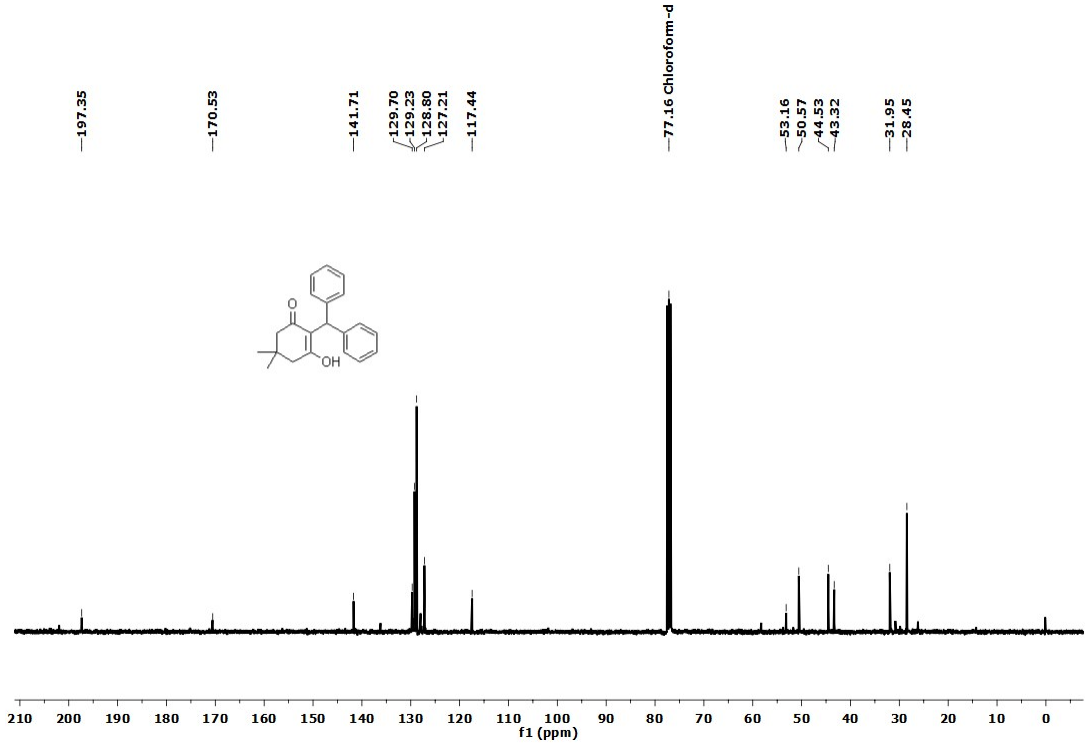



**Figure S14:** $^{13}$C NMR of Compound **3f**

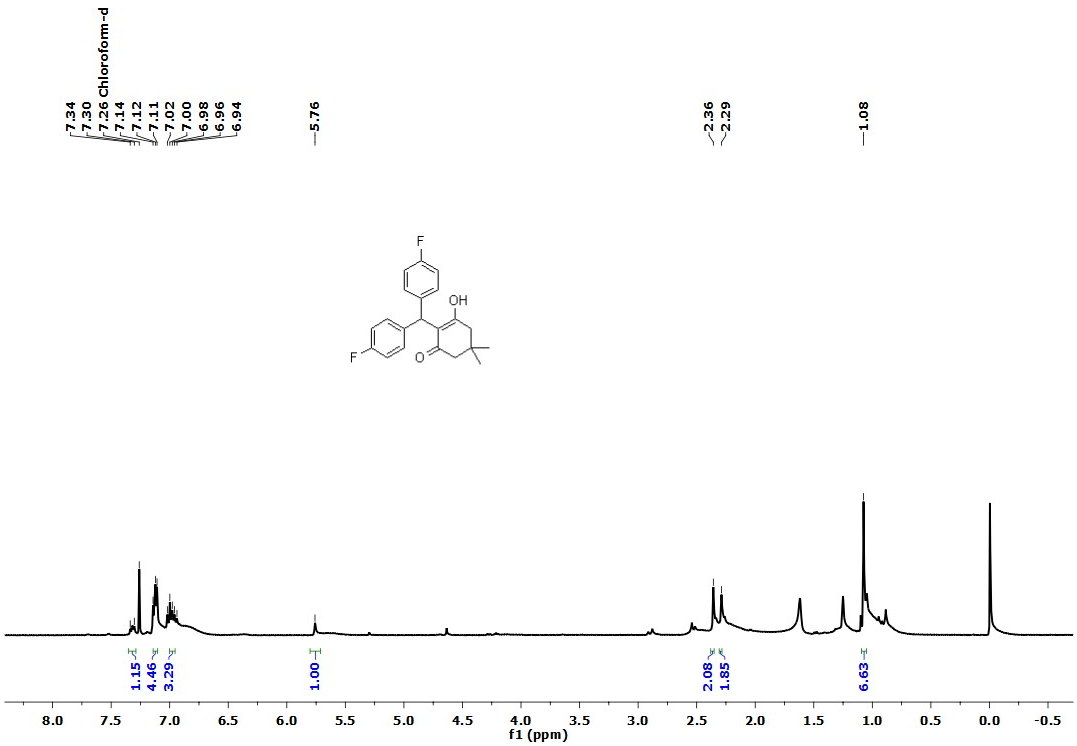



**Figure S15:**[1]H NMR of Compound **3g**

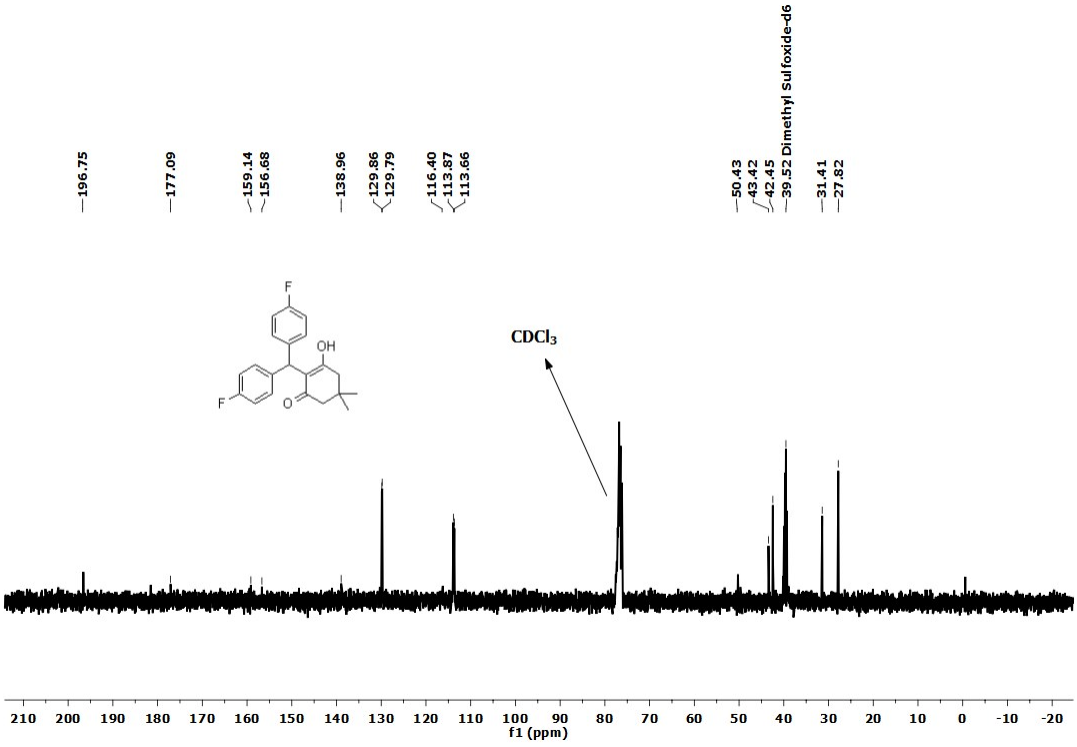



**Figure S16:**[13]C NMR of Compound **3g**

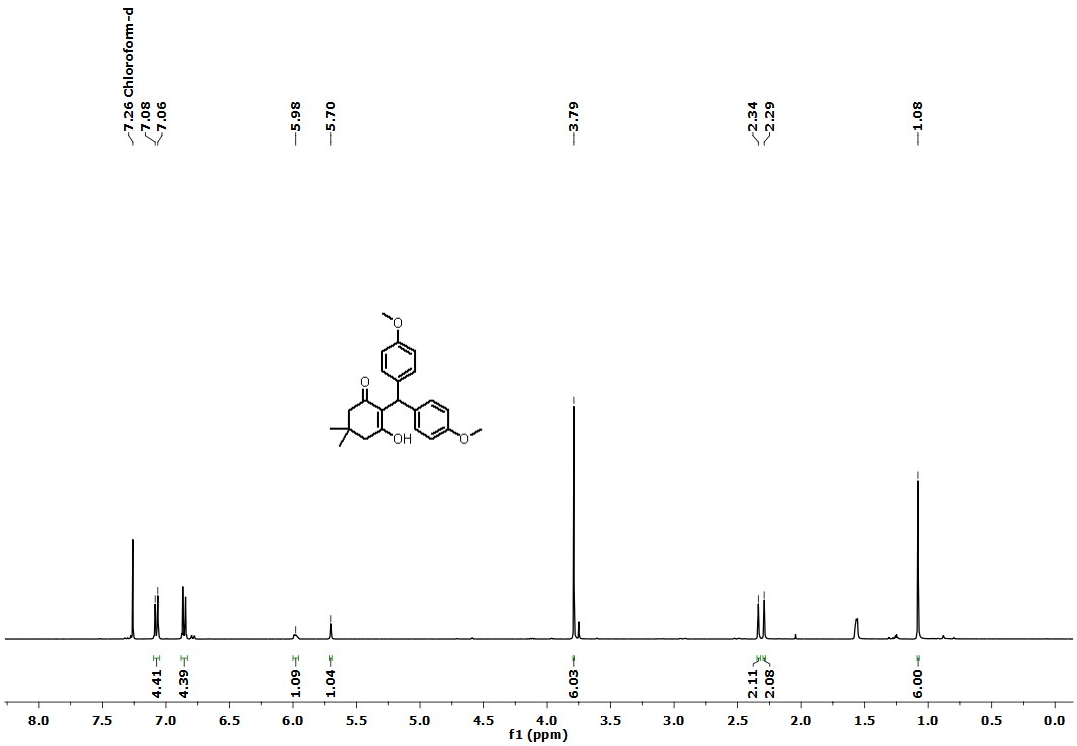



**Figure S17:** $^{1}$H NMR of Compound **3h**

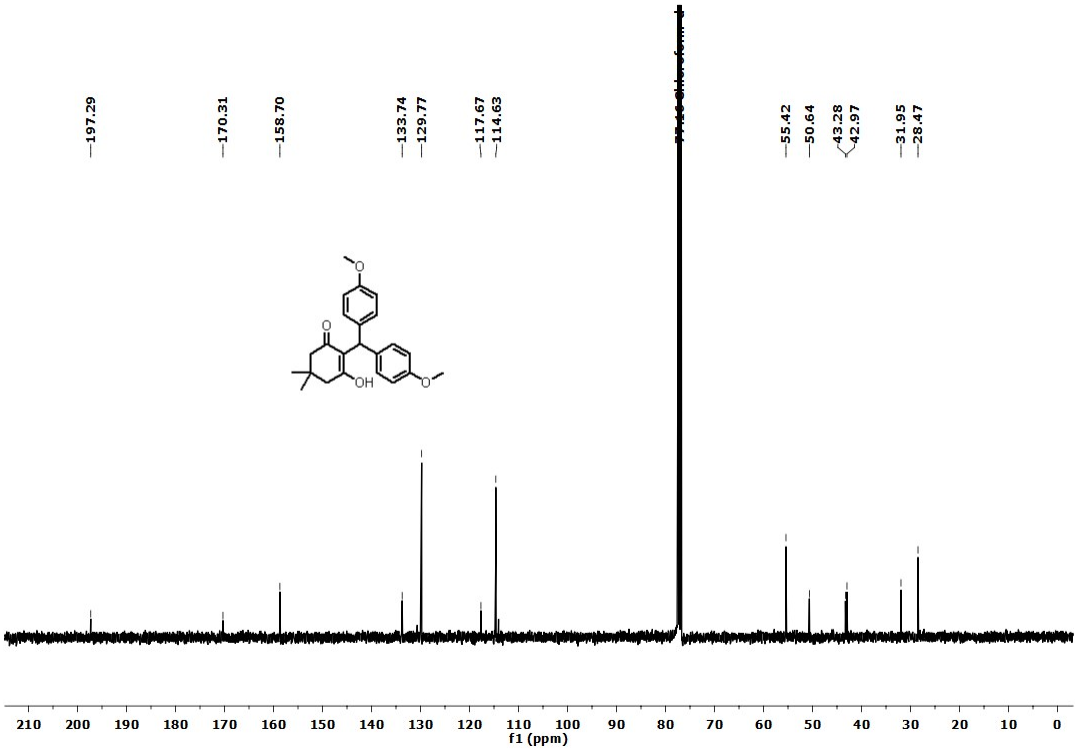



**Figure S18:** $^{13}$C NMR of Compound **3h**

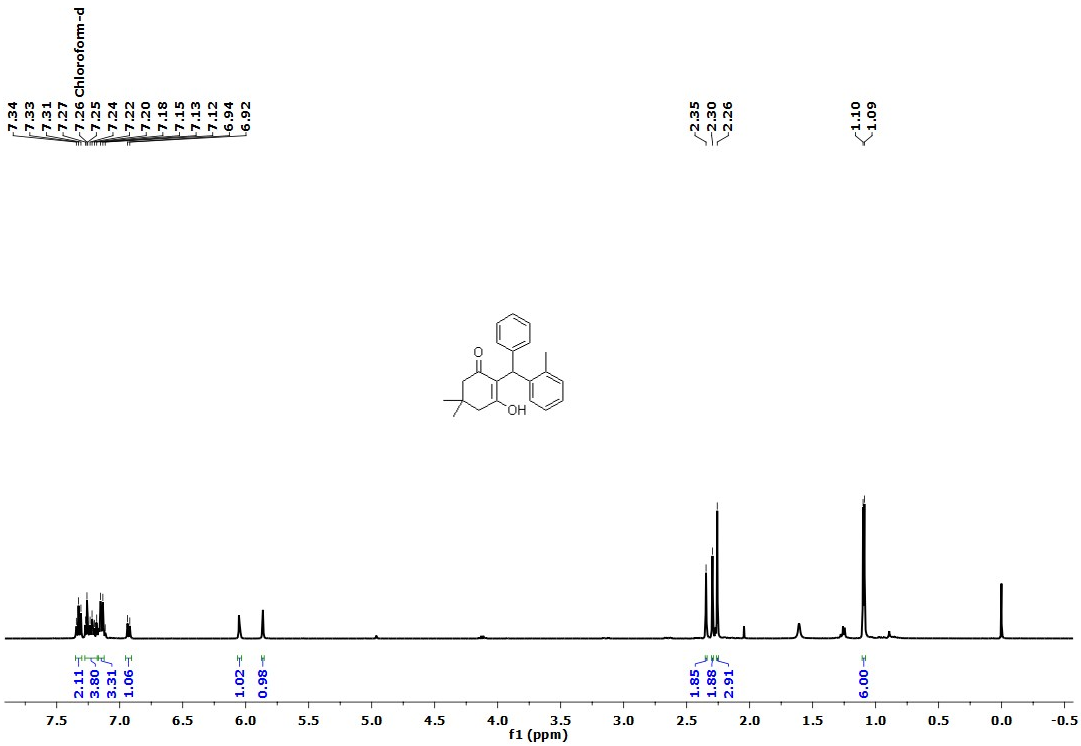



**Figure S19:** $^{1}$H NMR of Compound **3i**

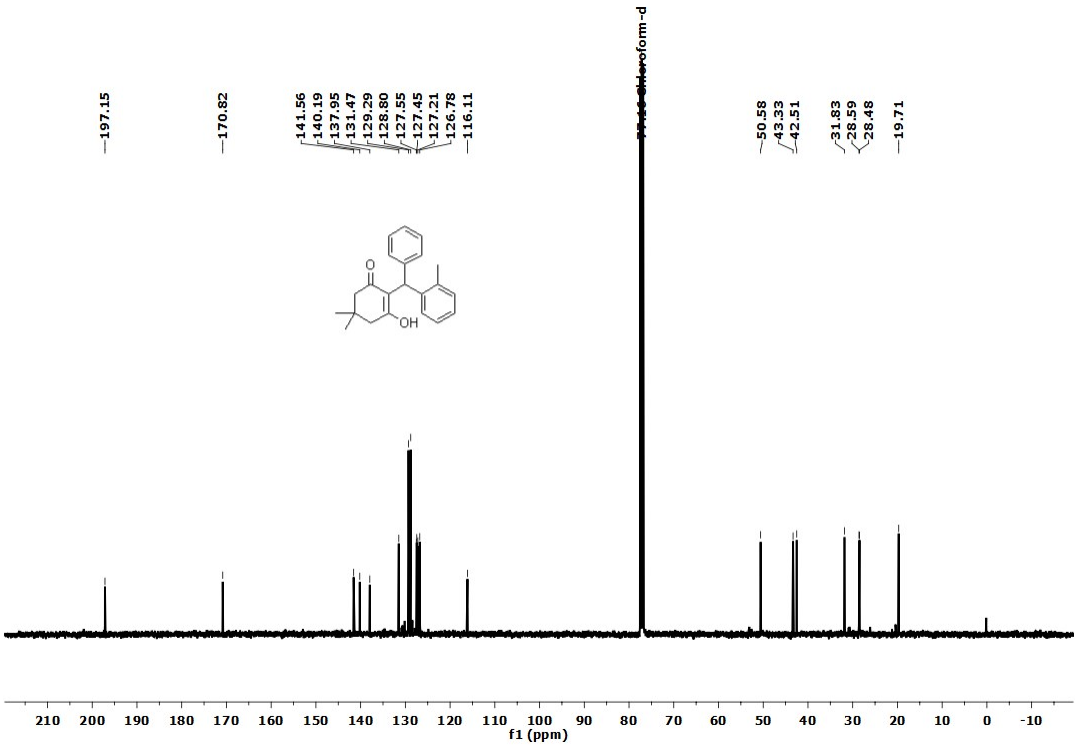



**Figure S20:** $^{13}$C NMR of Compound **3i**

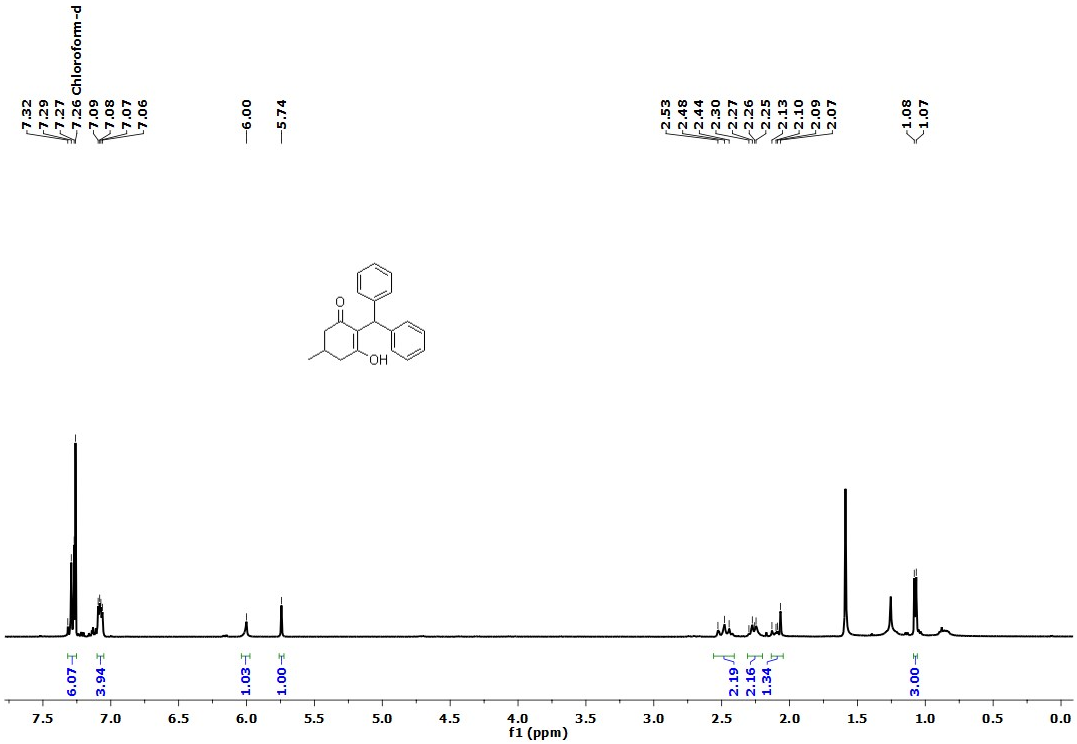



**Figure S21:** $^{1}$H NMR of Compound **3j**

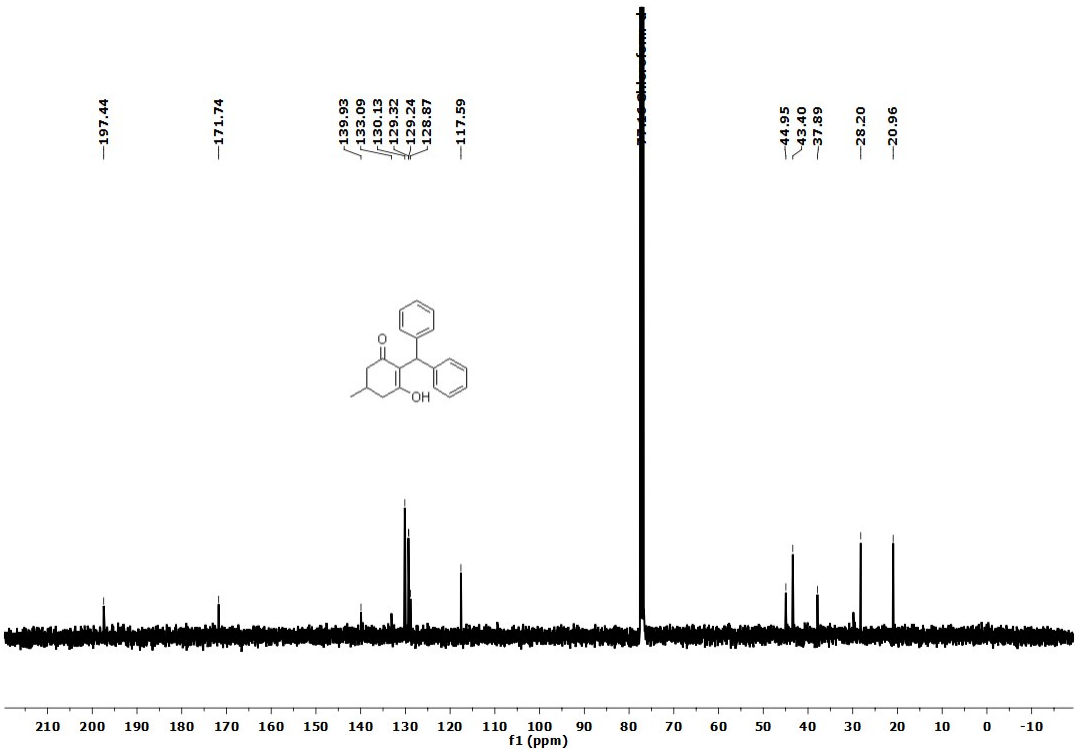



**Figure S22:**$^{13}$C NMR of Compound **3j**

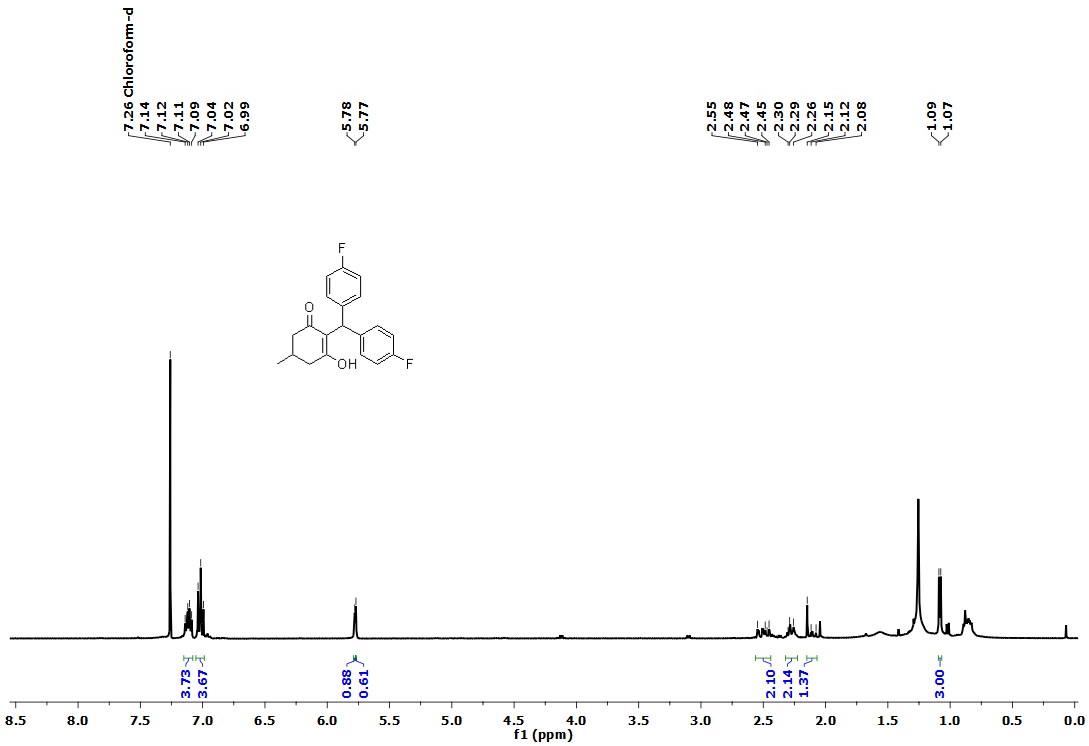



**Figure S23:**[1]H NMR of Compound **3k**

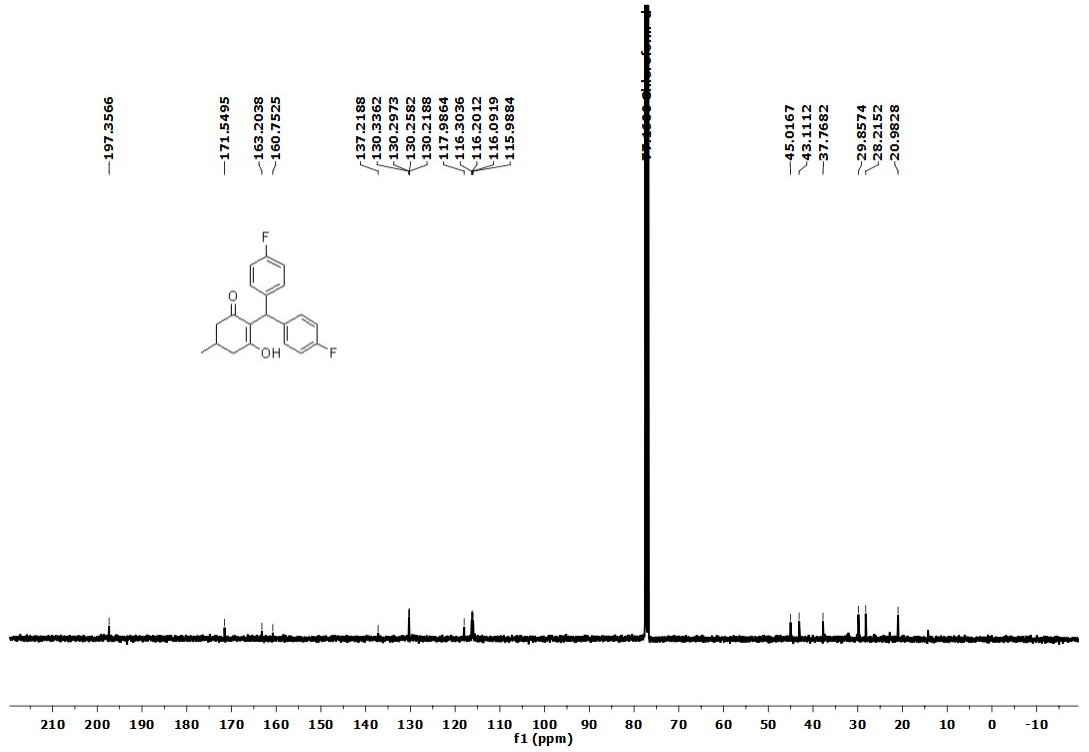



**Figure S24:** [13]C NMR of Compound **3k**

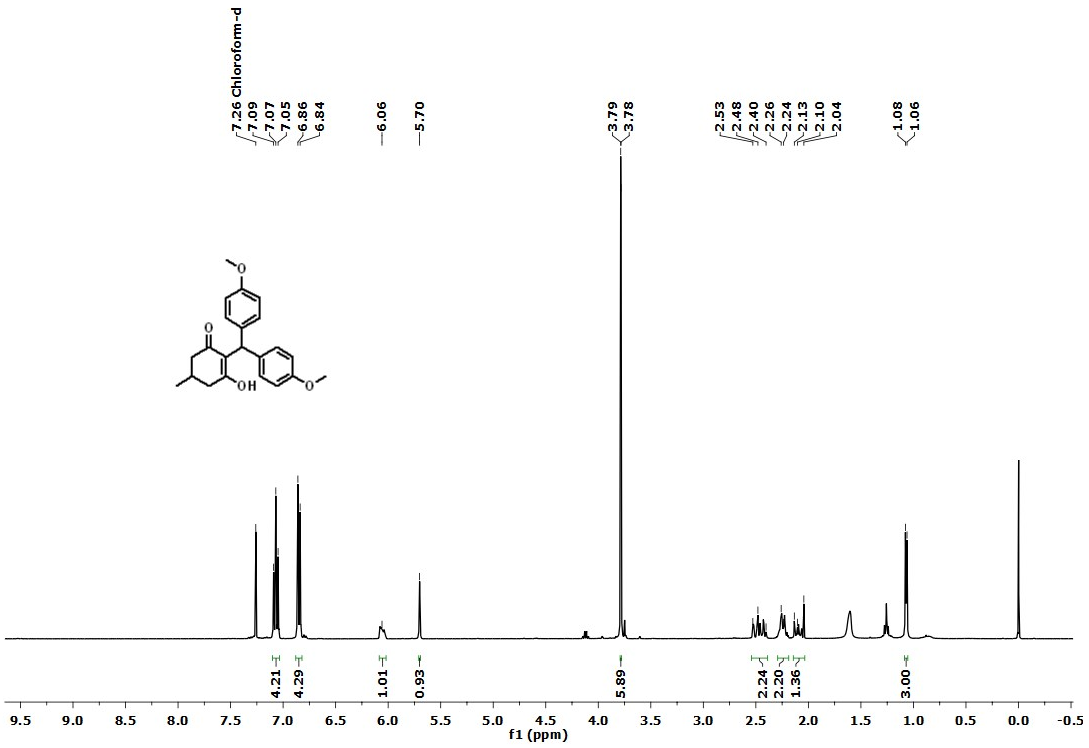



**Figure S25:** $^{1}$H NMR of Compound **3l**

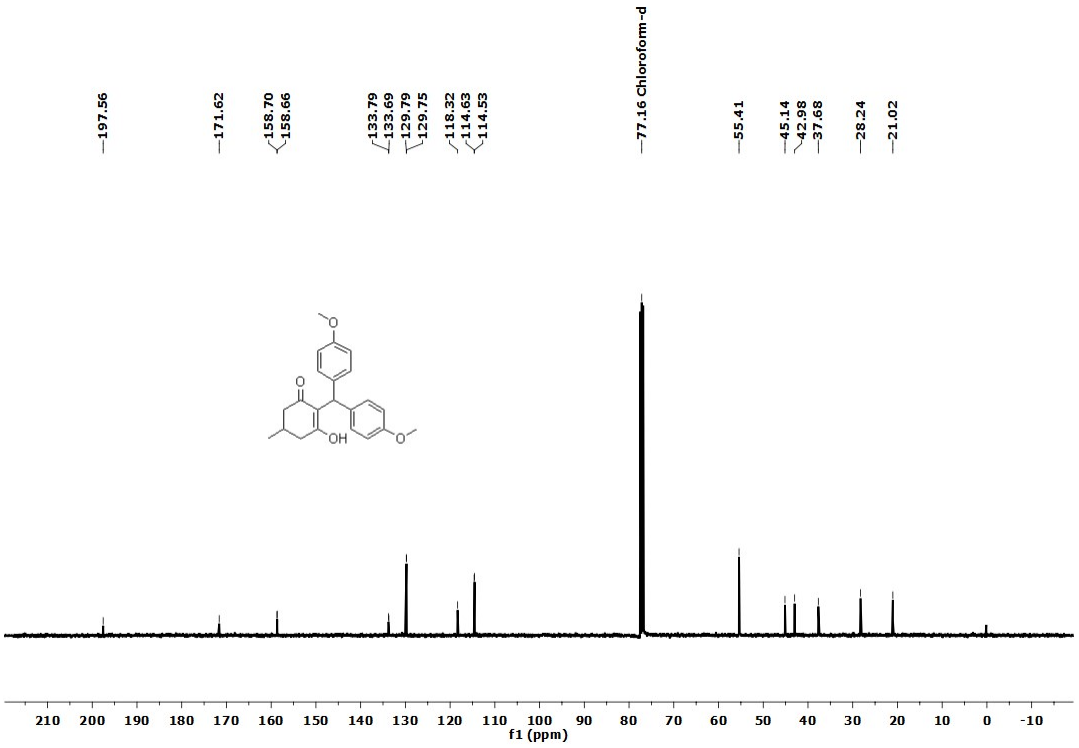



**Figure S26:** $^{13}$C NMR of Compound **3l**

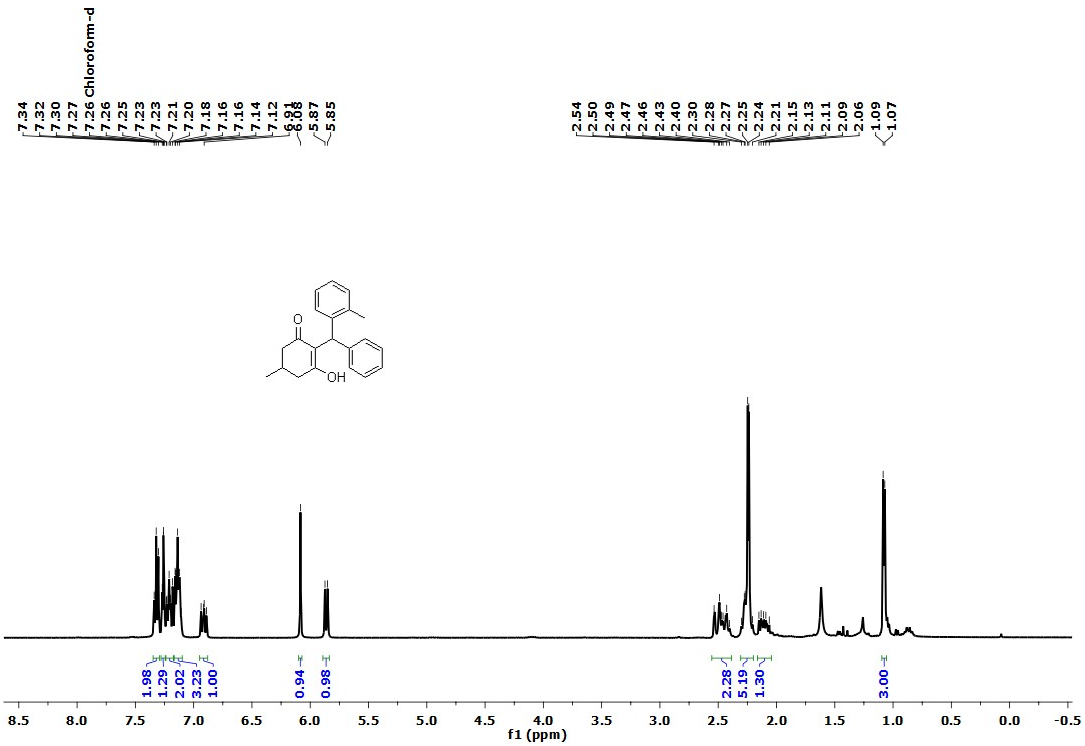



**Figure S27:** $^{1}$H NMR of Compound **3m**

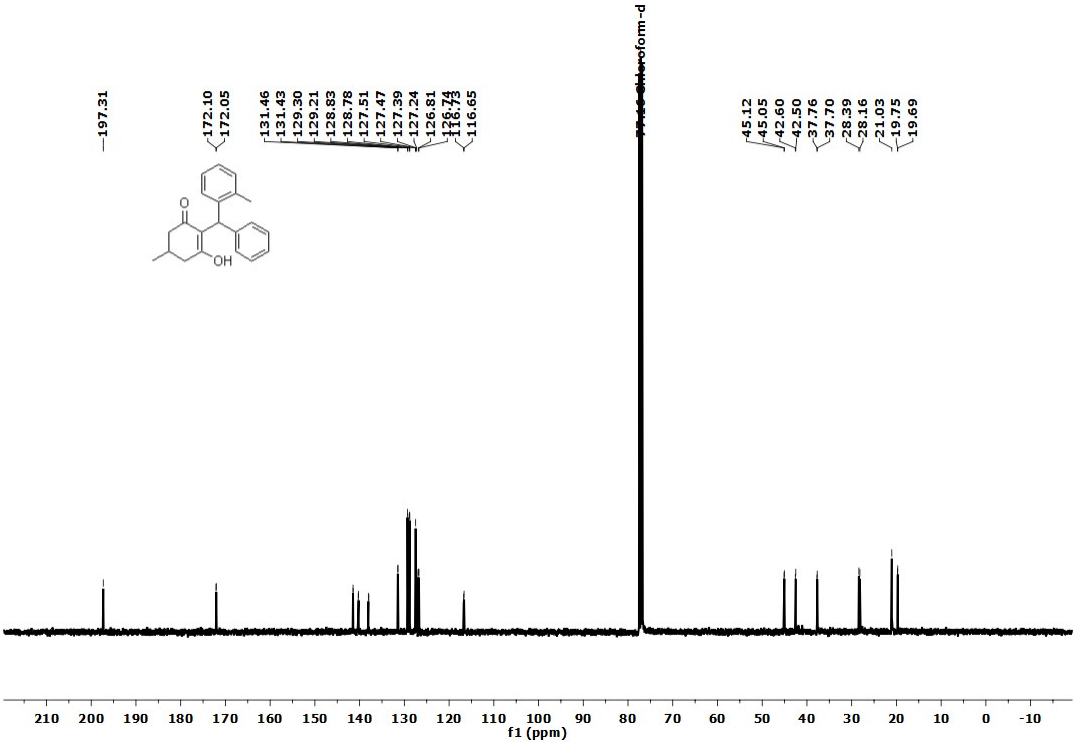



**Figure S28:** $^{13}$C NMR of Compound **3m**

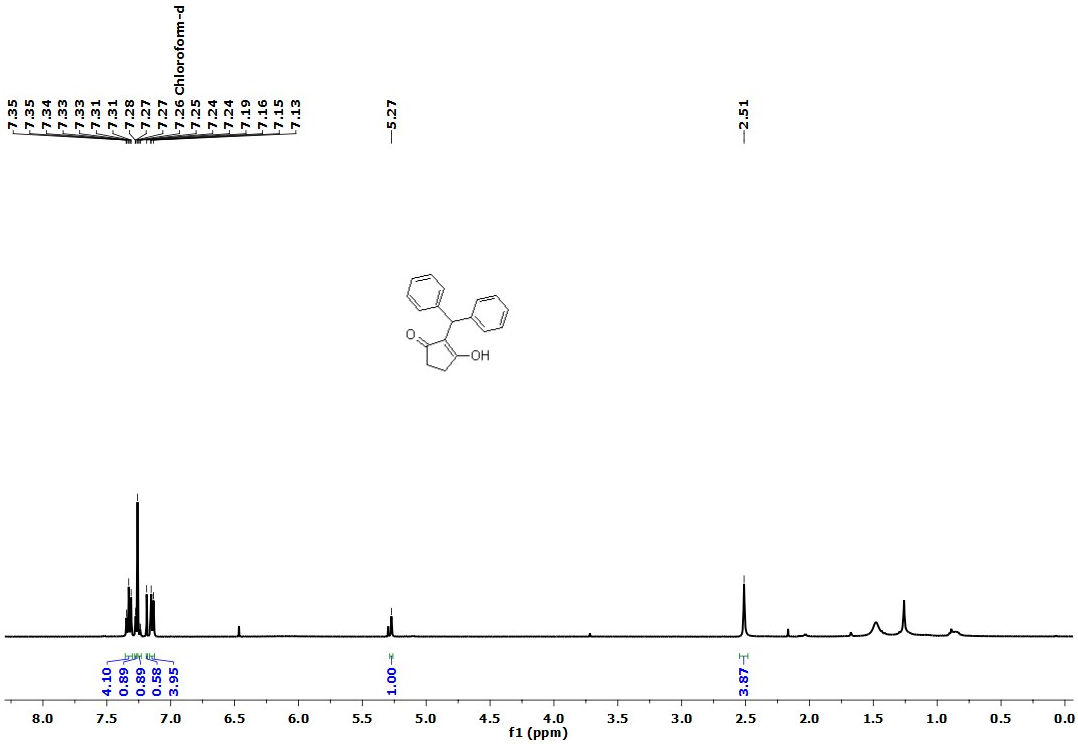



**Figure S29:** $^{1}$H NMR of Compound **3n**

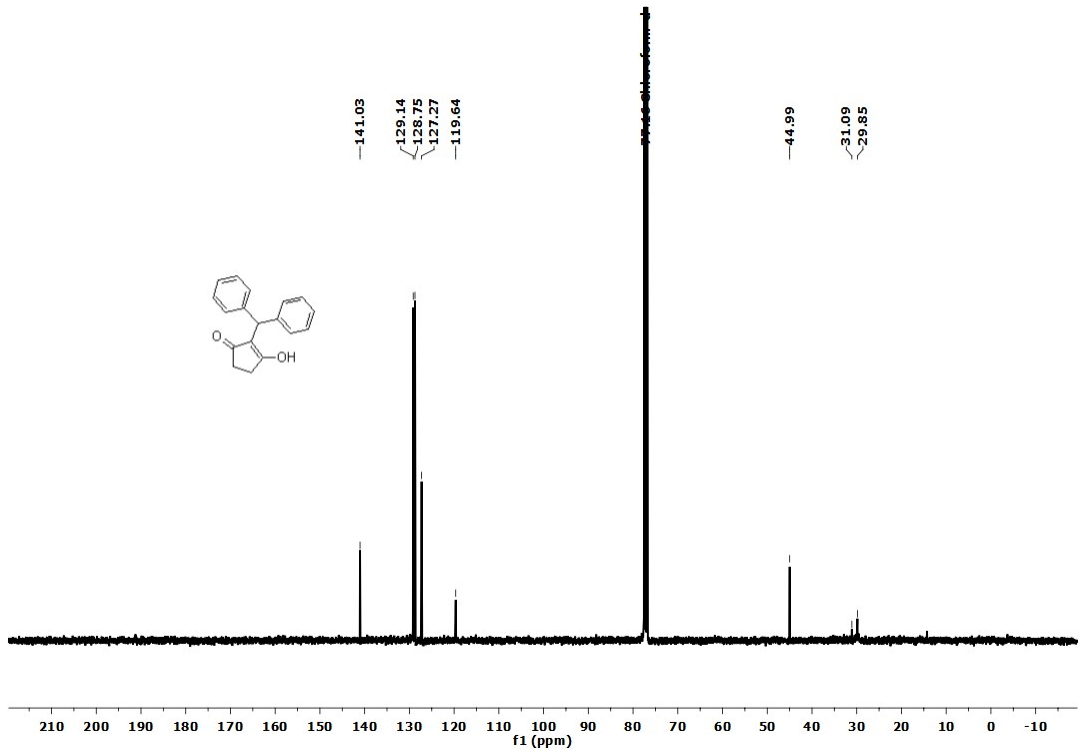



**Figure S30:** $^{13}$C NMR of Compound **3n**

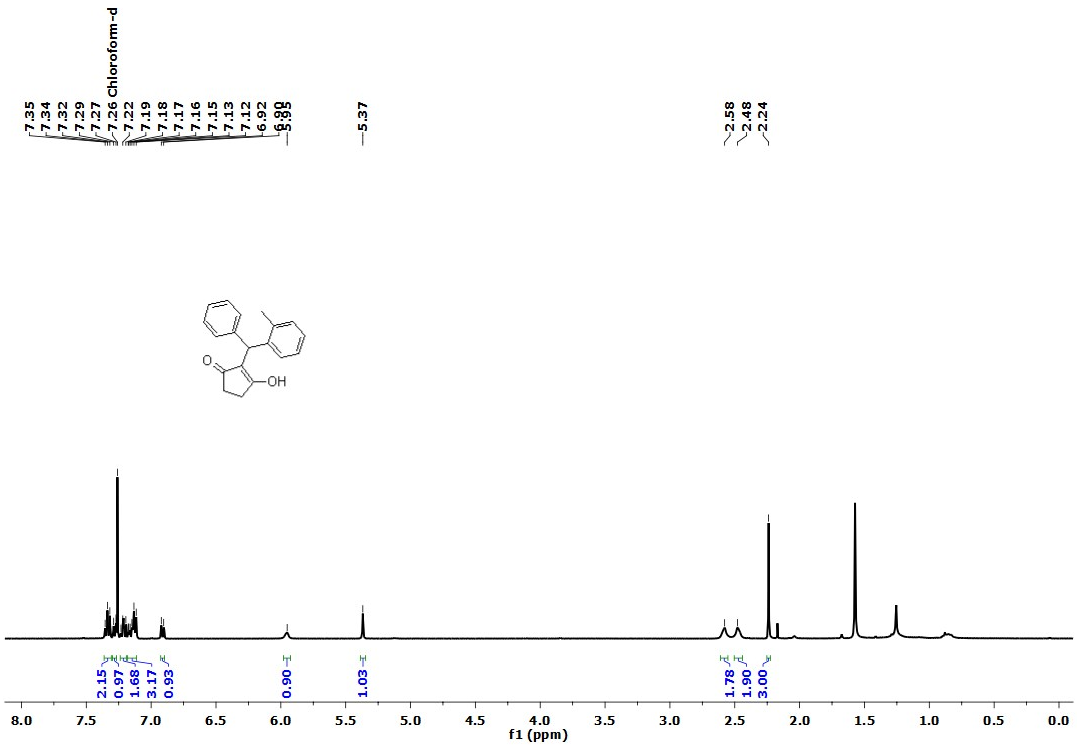



**Figure S31:** $^{1}$H NMR of Compound **3o**

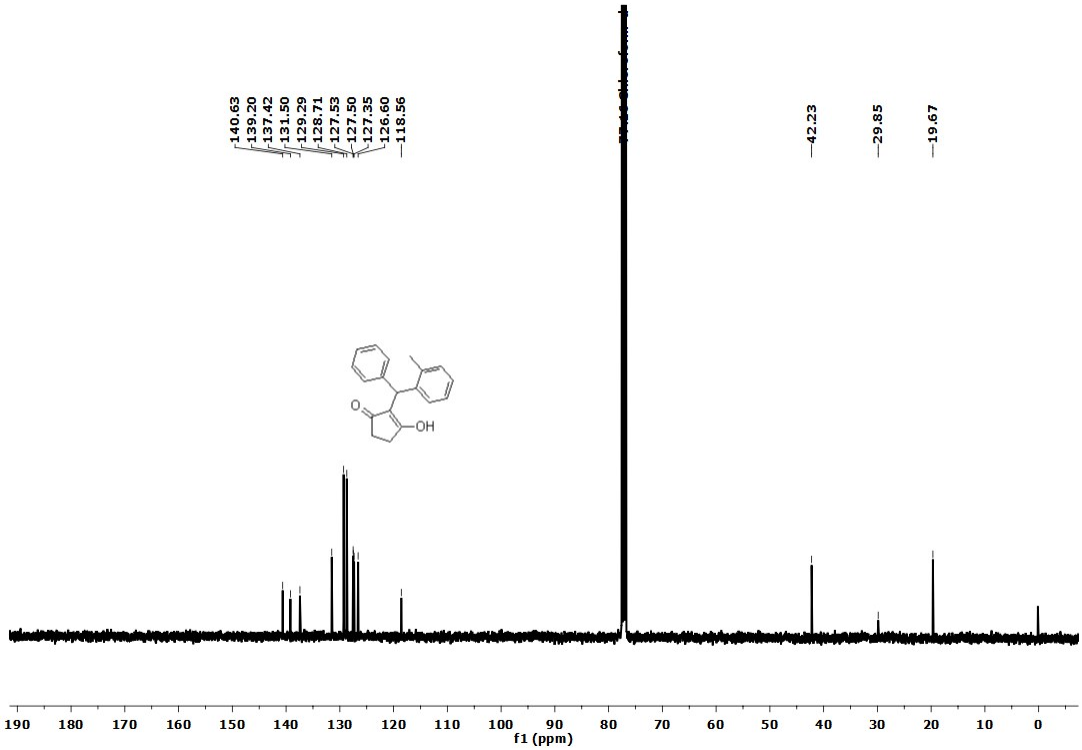



**Figure S32:** $^{13}$C NMR of Compound **3o**

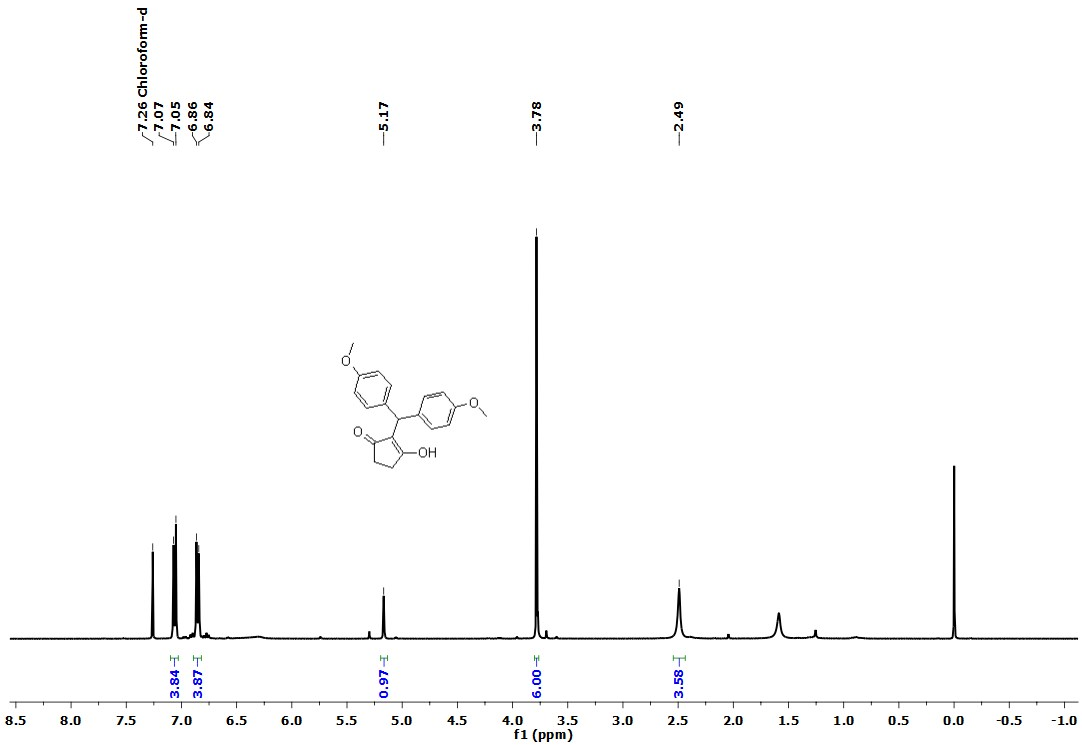



**Figure S33:** $^{1}$H NMR of Compound **3p**

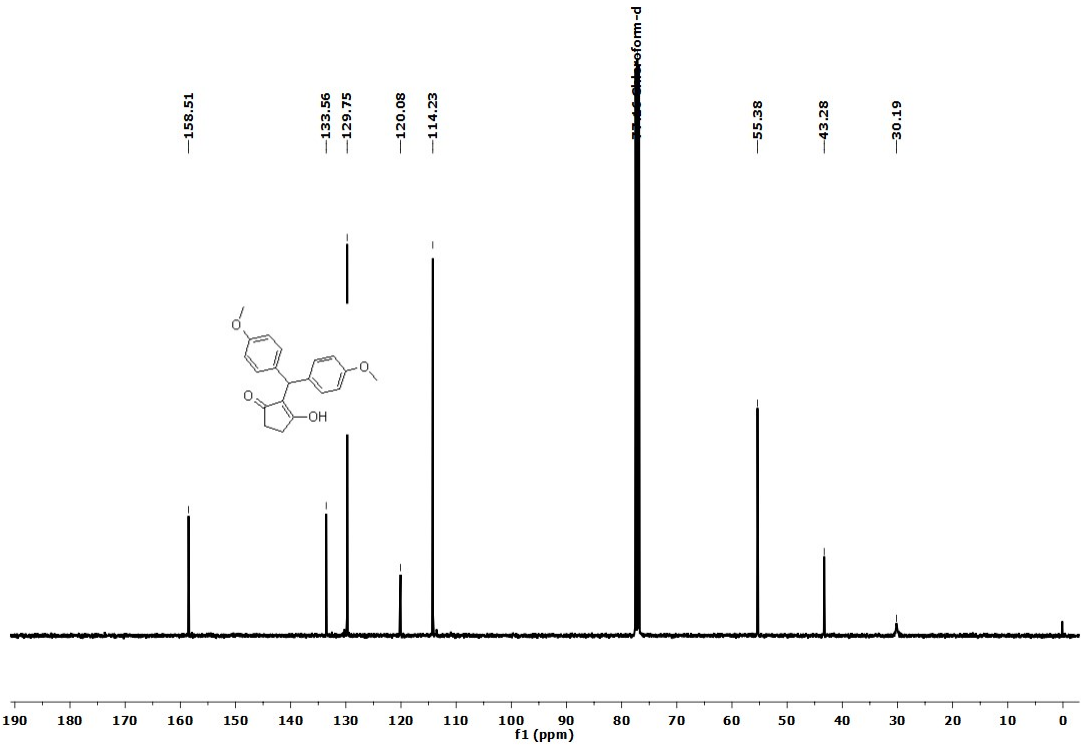



**Figure S34:**$^{13}$C NMR of Compound **3p**

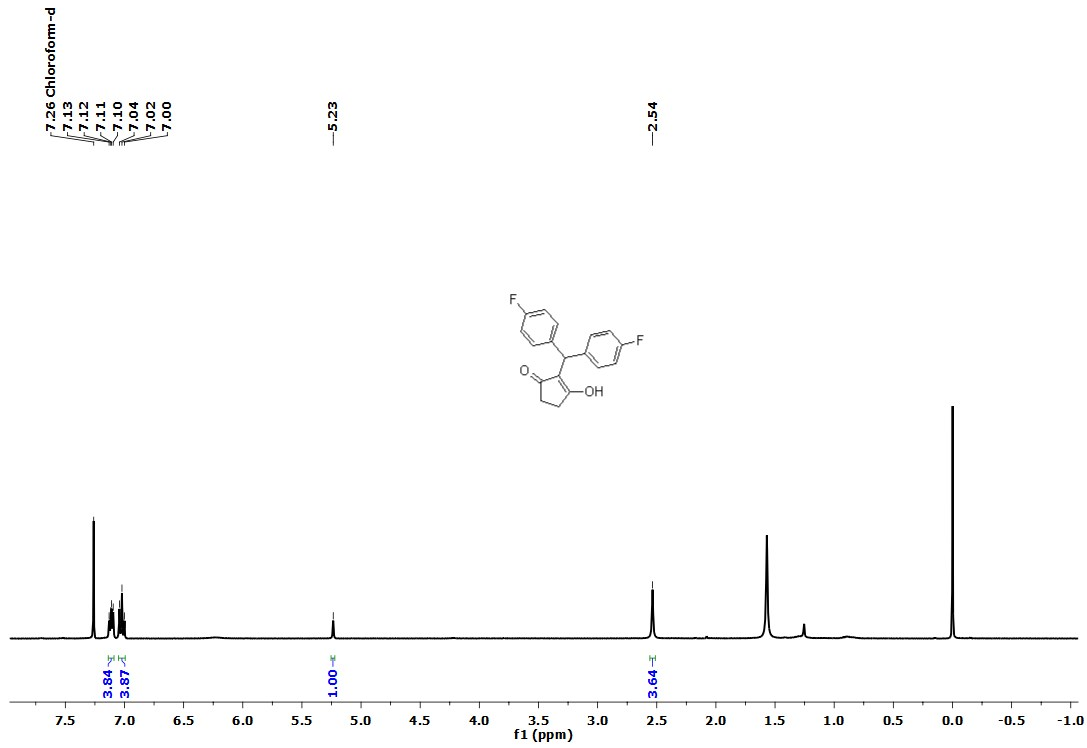



**Figure S35:** $^{1}$H NMR of Compound **3q**

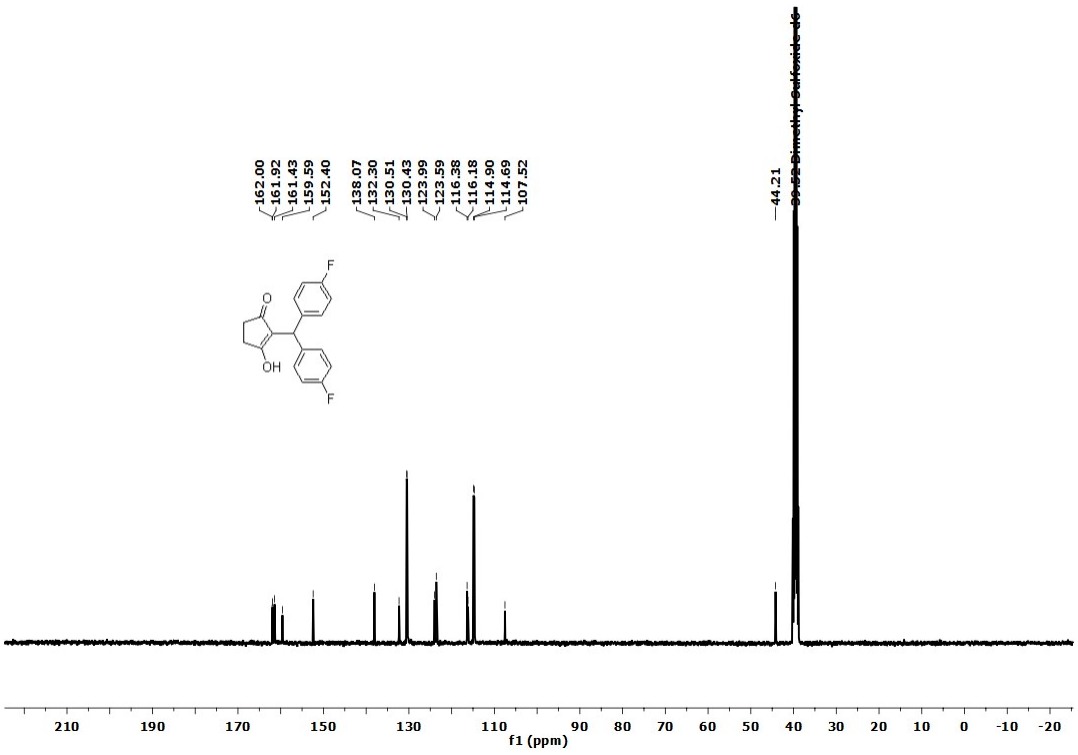



**Figure S36:**$^{13}$C NMR of Compound **3q**

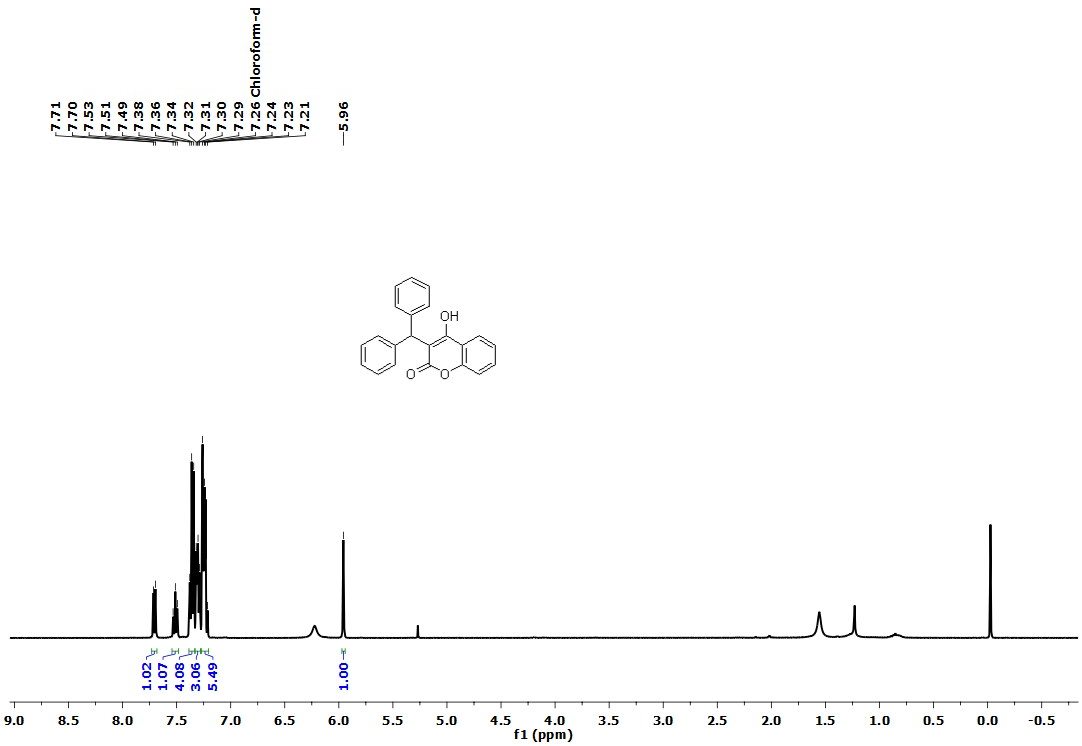



**Figure S37:** $^{1}$H NMR of Compound **3r**

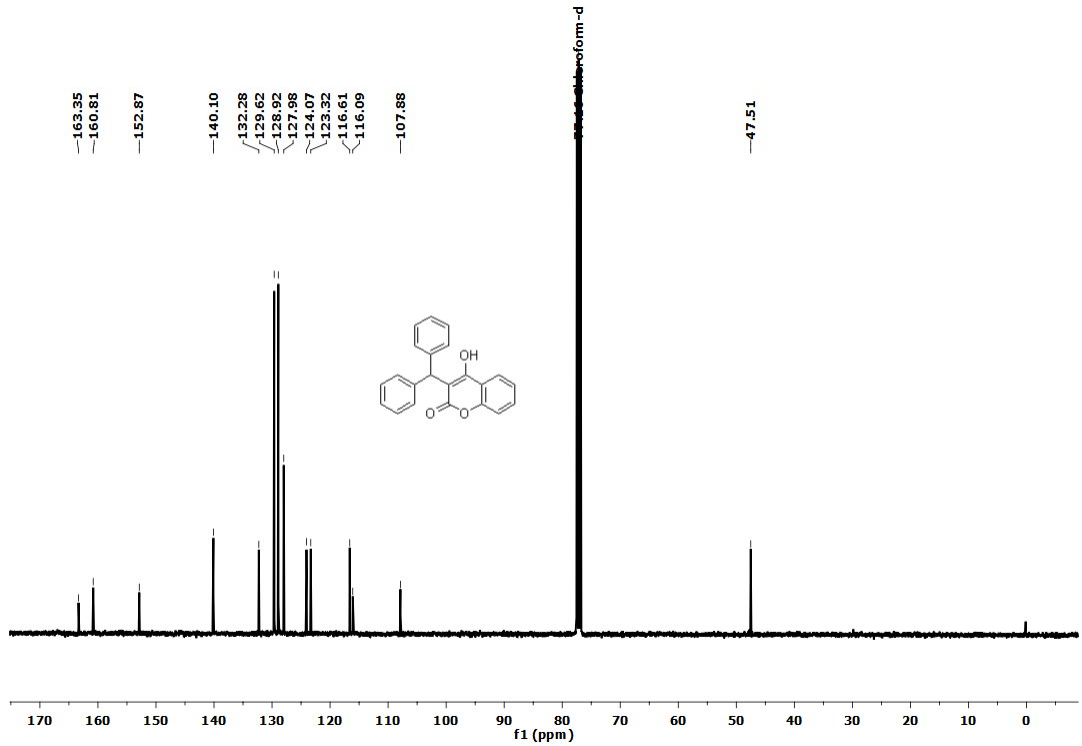



**Figure S38:** $^{13}$C NMR of Compound **3r**

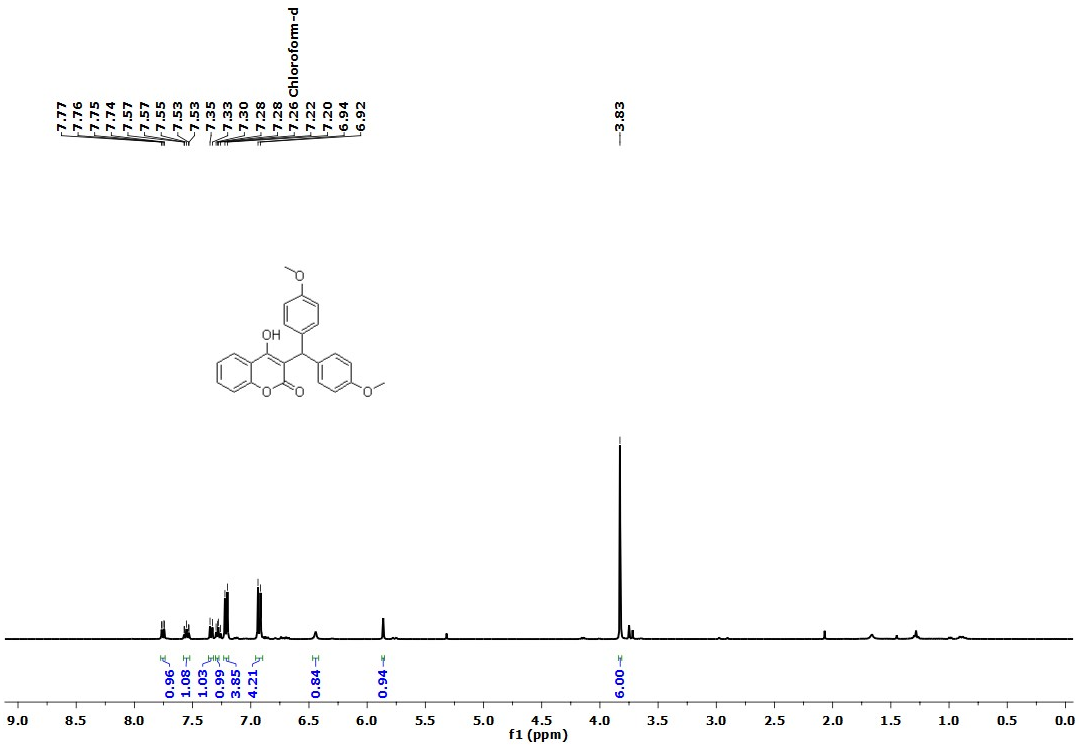



**Figure S39:** $^{1}$H NMR of Compound **3s**

**Figure S40:** $^{13}$C NMR of Compound **3s**

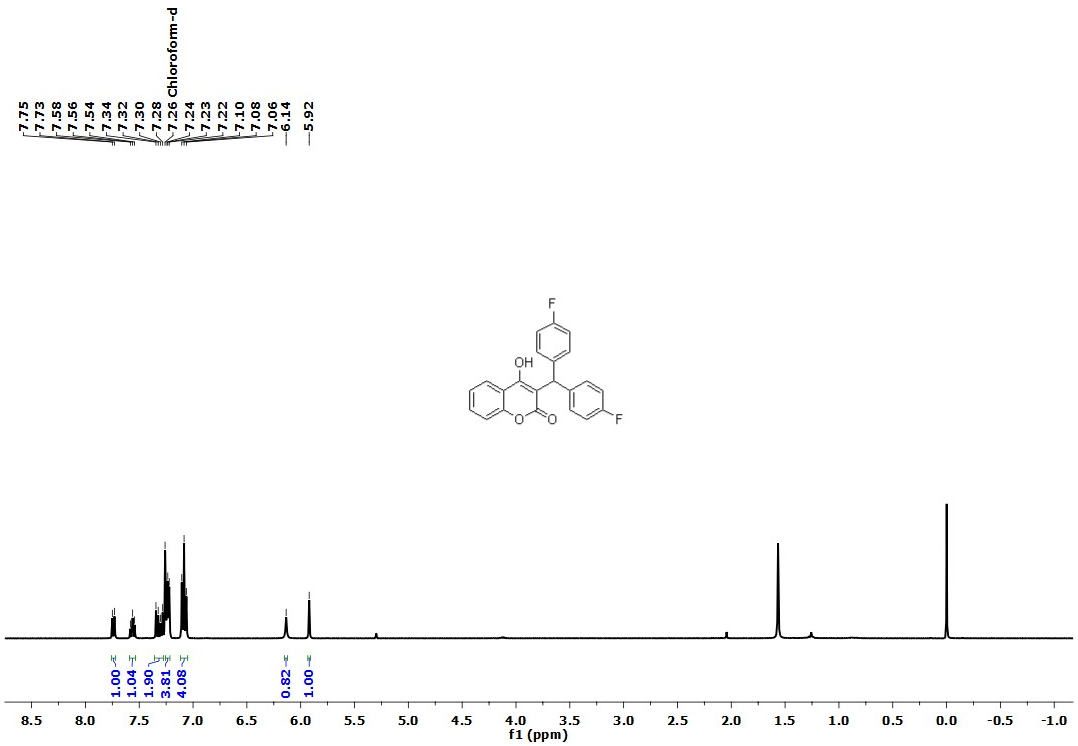



**Figure S41:** $^{1}$H NMR of Compound **3t**

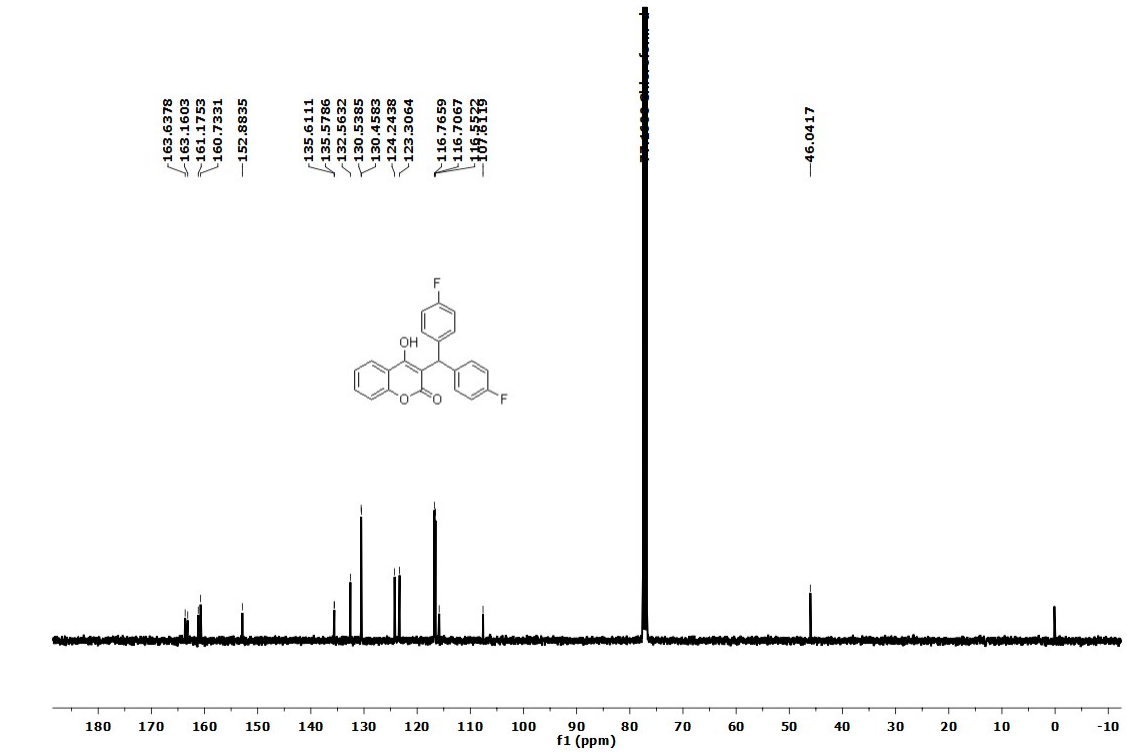



**Figure S42:** $^{13}$C NMR of Compound **3t**

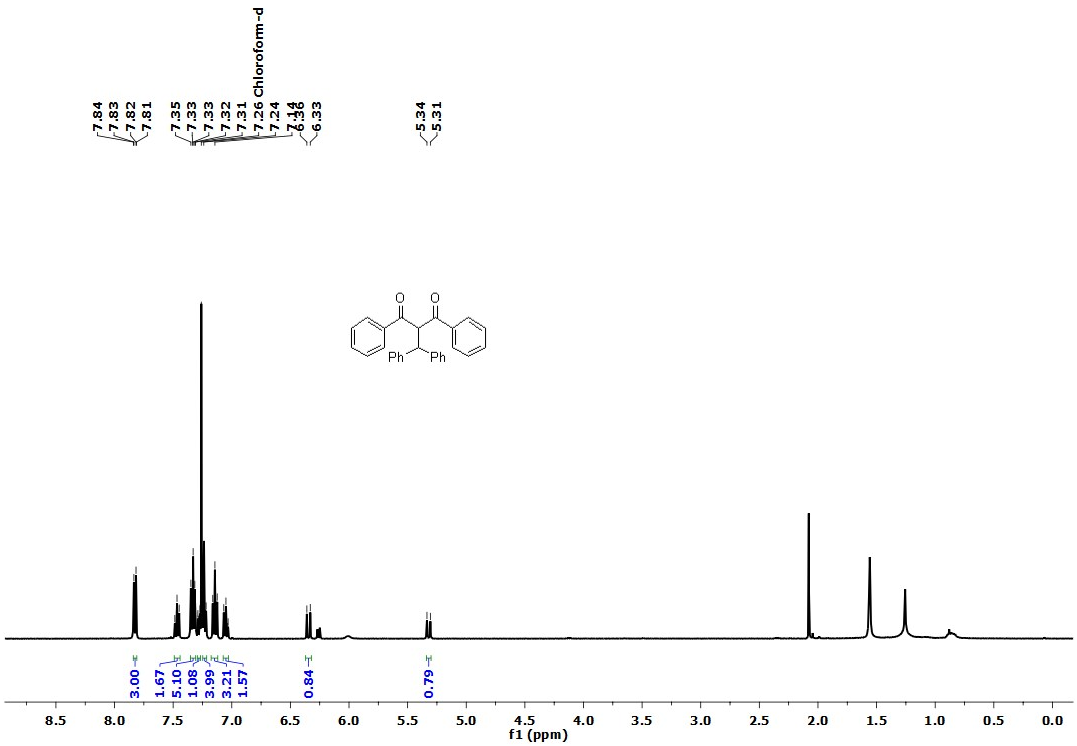



**Figure S43:**[1]H NMR of Compound **3u**

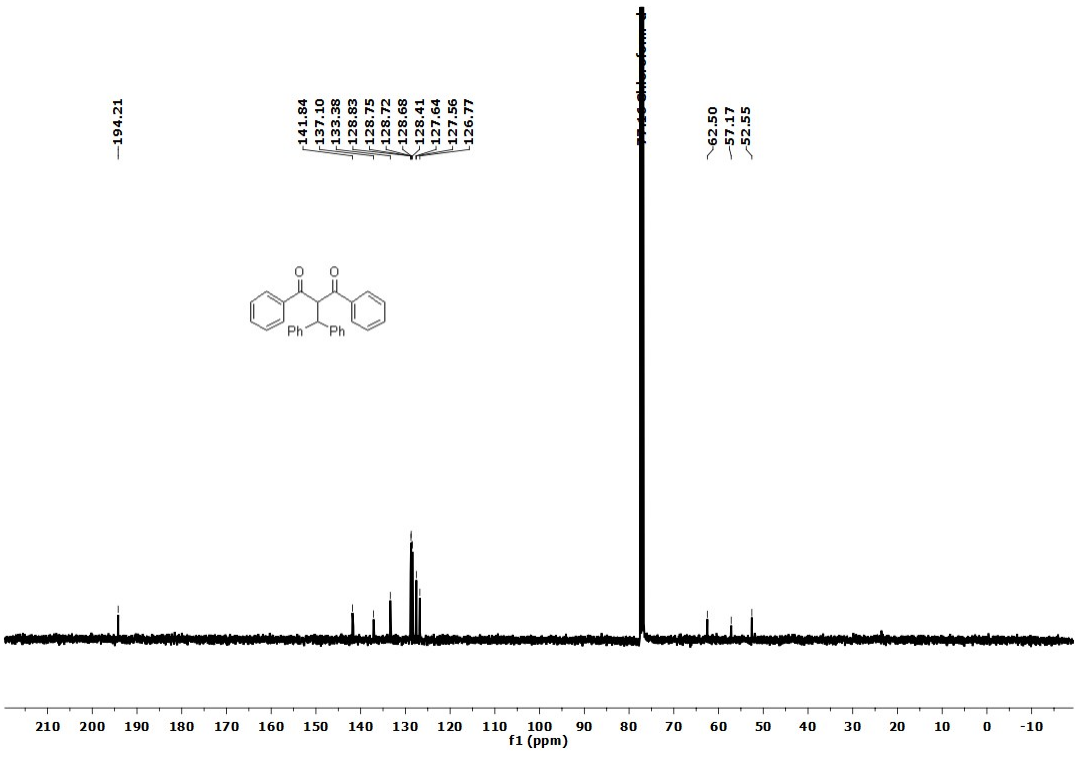



**Figure S44:** [13]C NMR of Compound **3u**

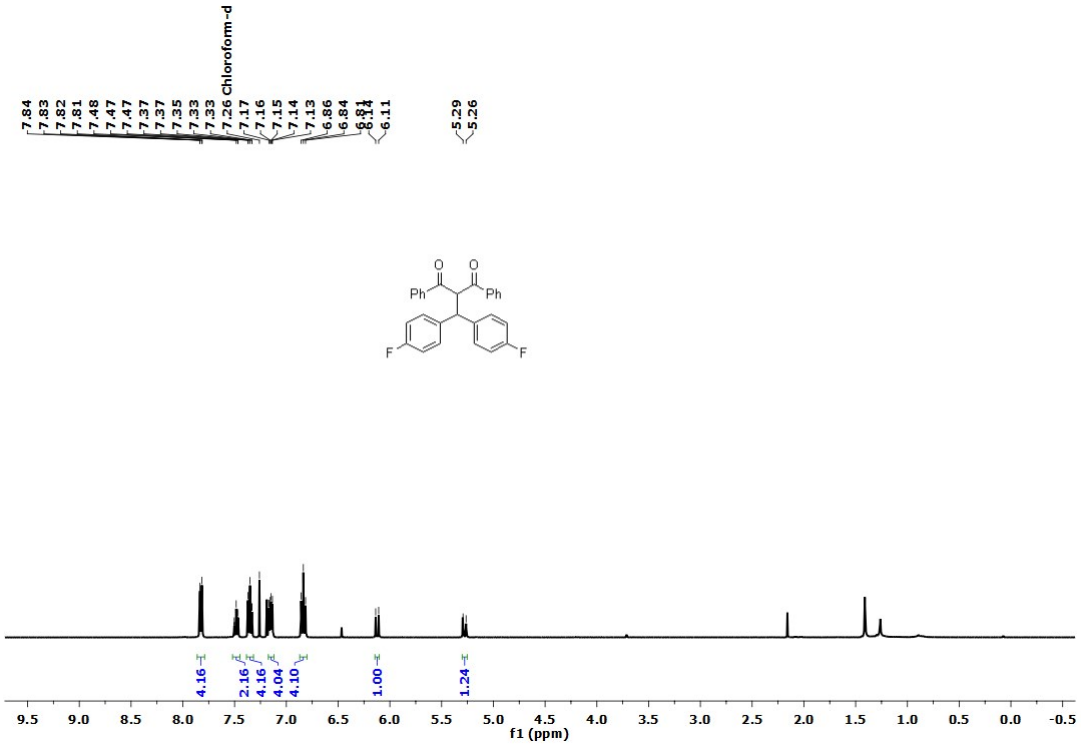



**Figure S45:** $^{1}$H NMR of Compound **3u'**

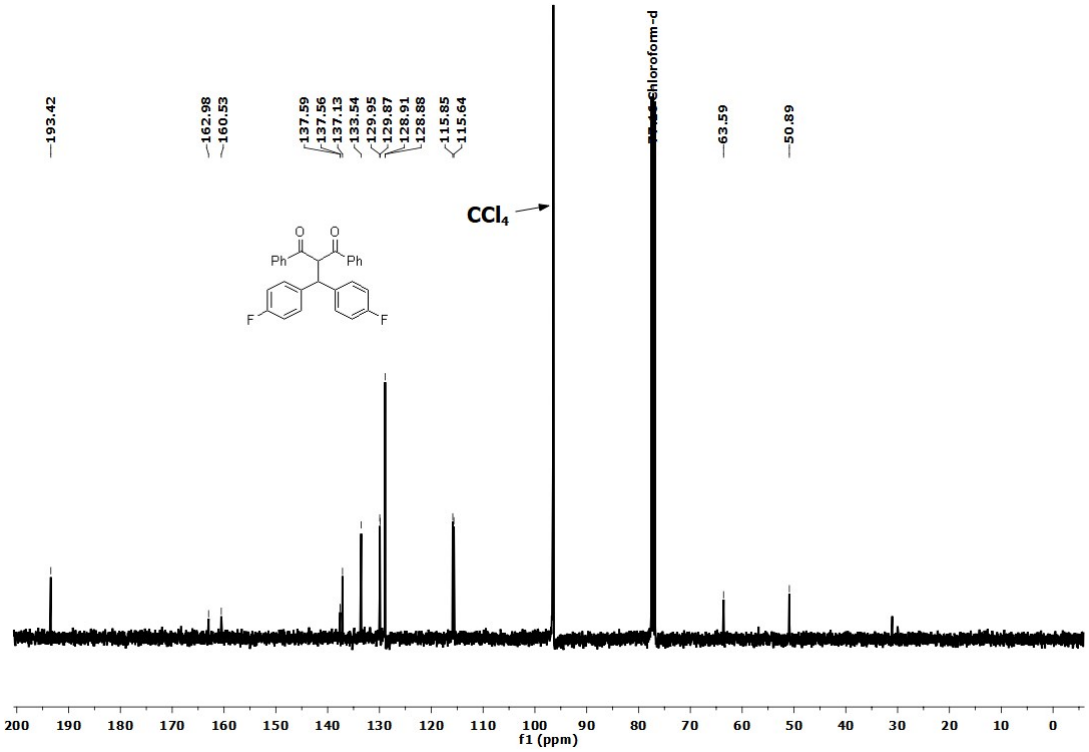



**Figure S46:** $^{13}$C NMR of Compound **3u'**

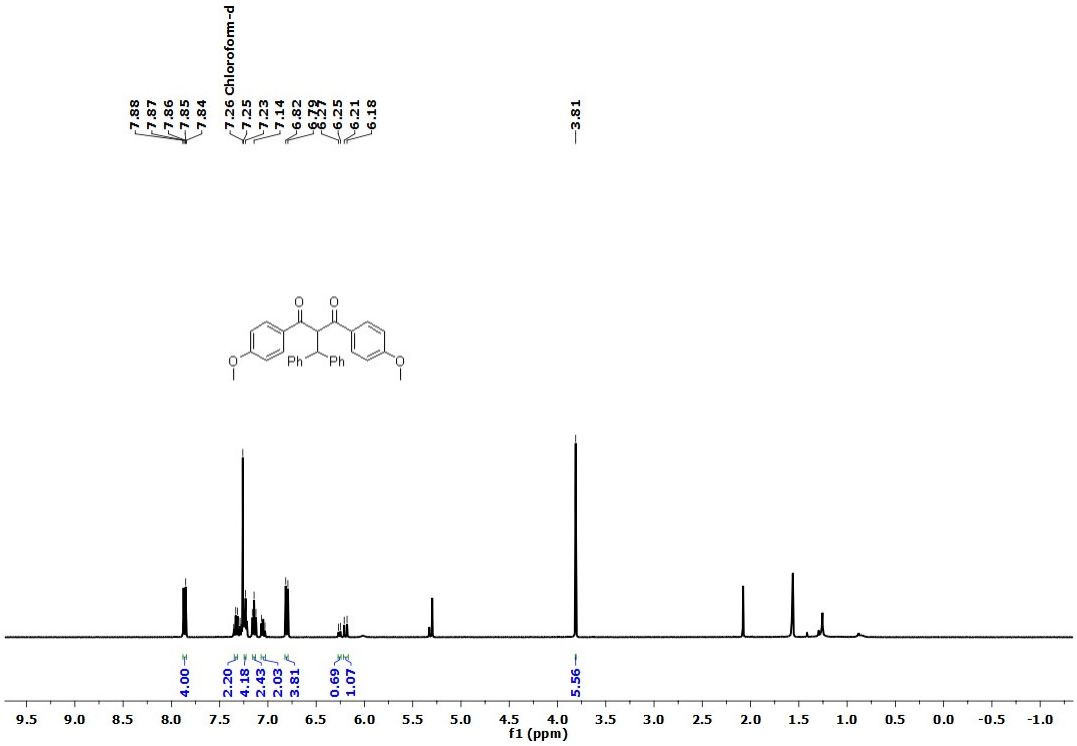



**Figure S47:** $^{1}$H NMR of Compound **3v**

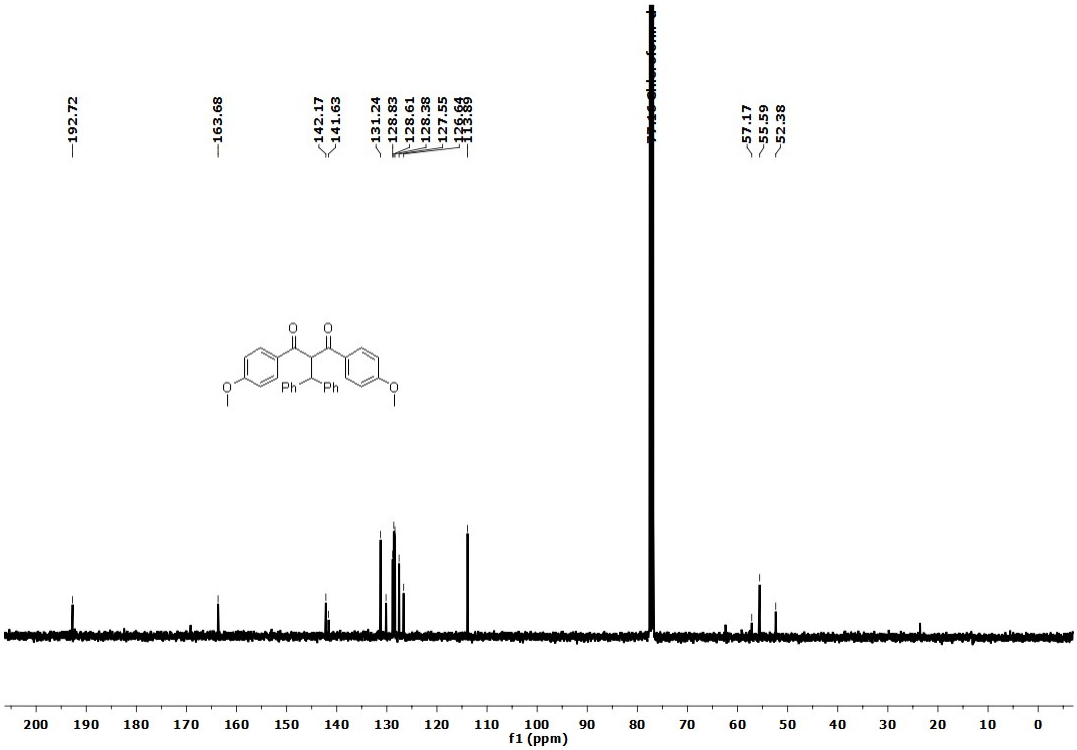



**Figure S48:** $^{13}$C NMR of Compound **3v**

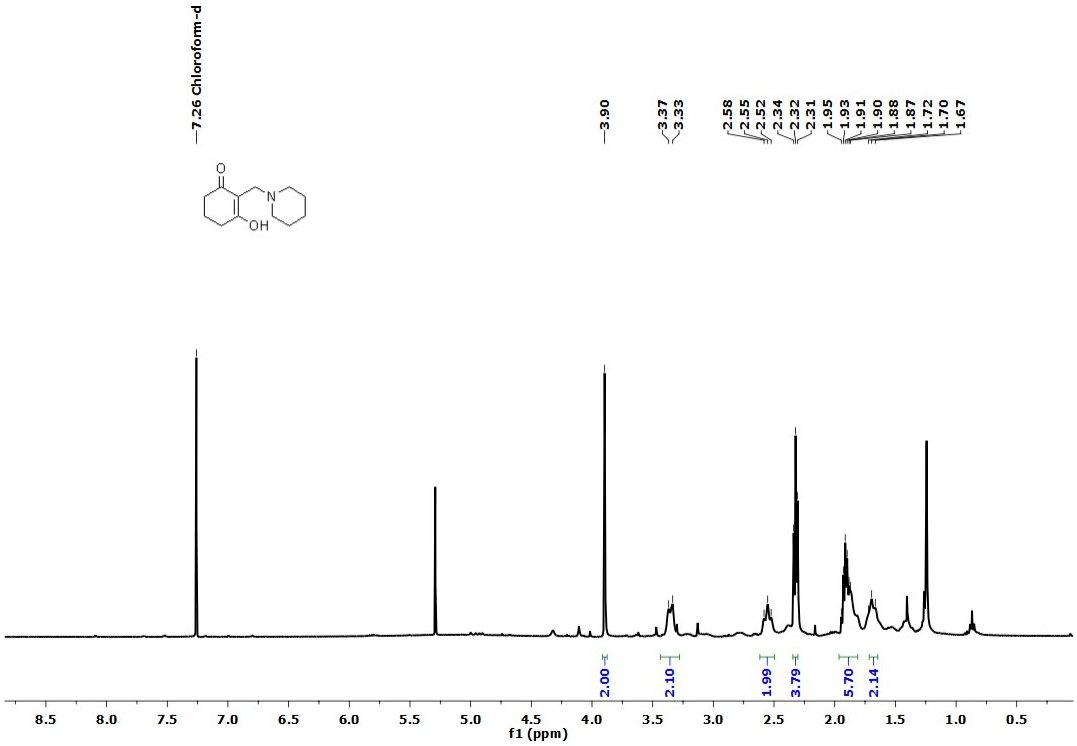



**Figure S49:** $^{1}$H NMR of Compound **4a**

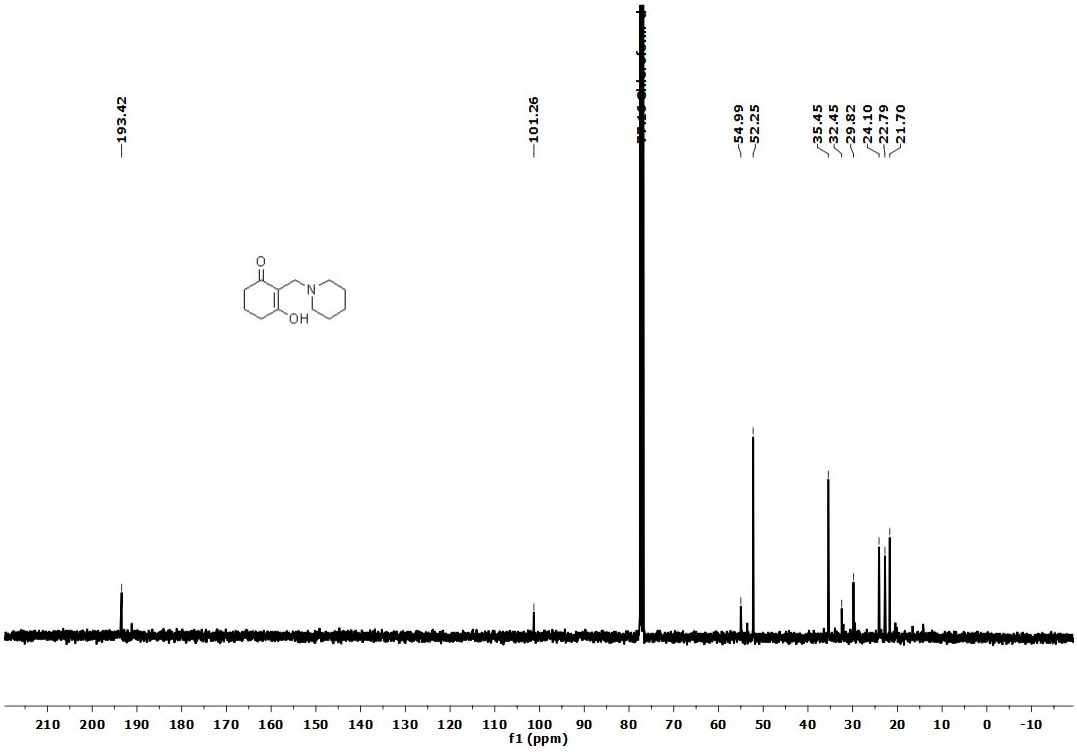



**Figure S50:** $^{13}$C NMR of Compound **4a**

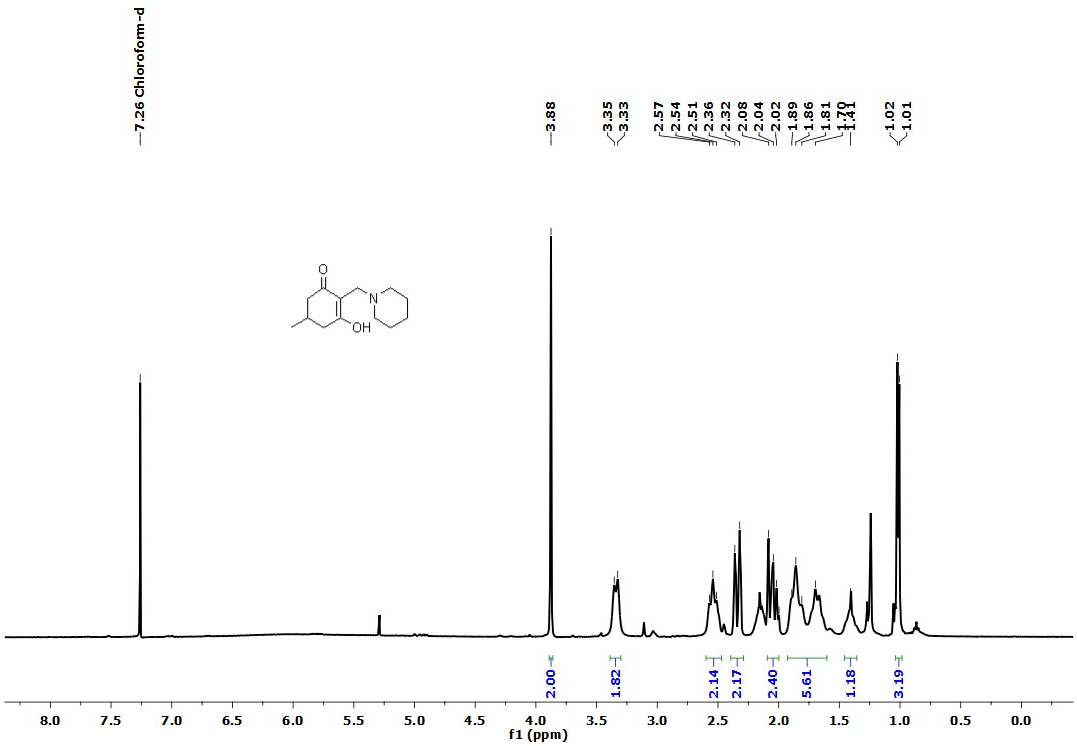



**Figure S51:** $^{1}$H NMR of Compound **4b**

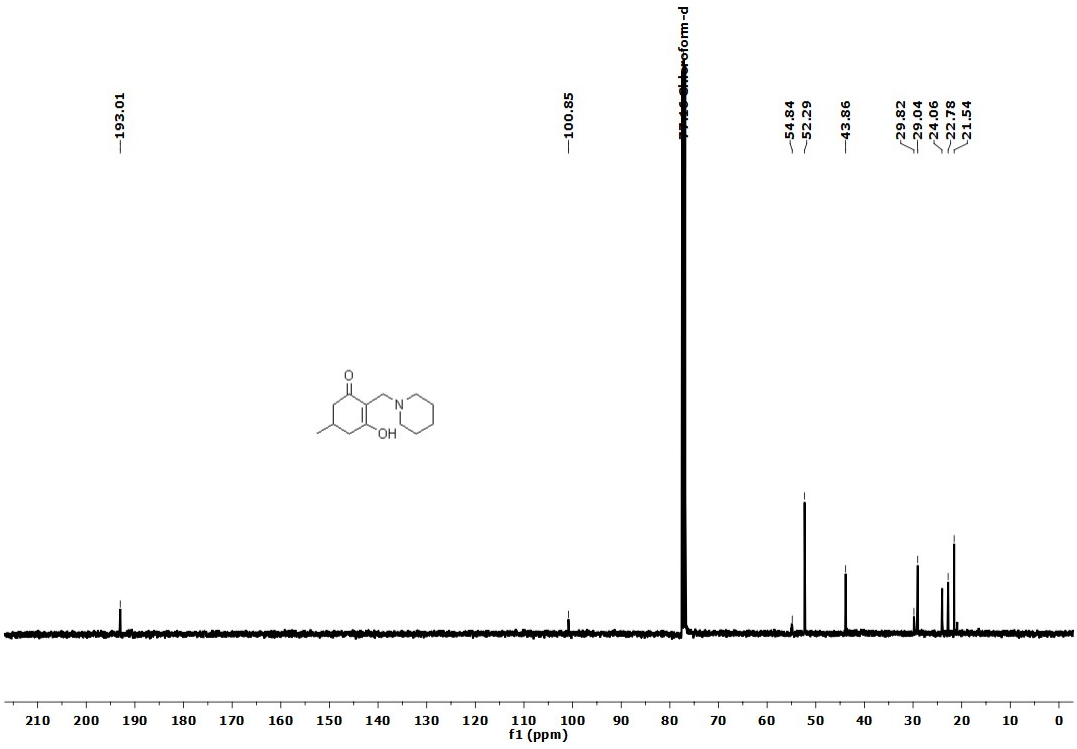



**Figure S52:** $^{13}$C NMR of Compound **4b**

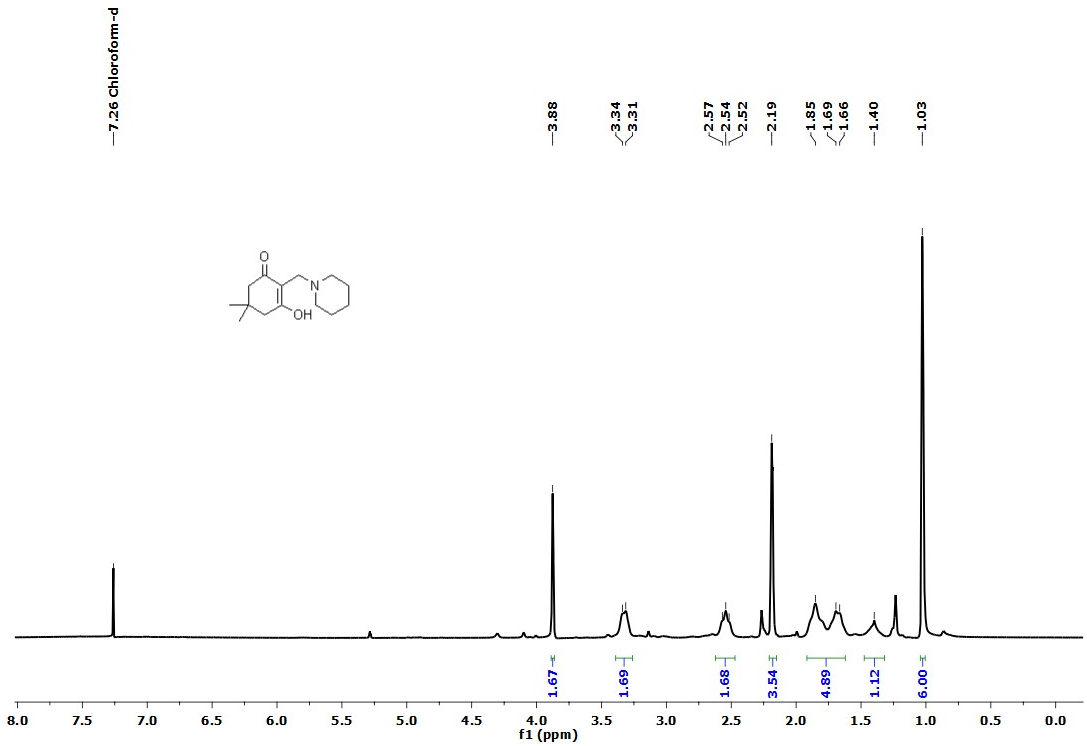



**Figure S53:** $^{1}$H NMR of Compound **4c**

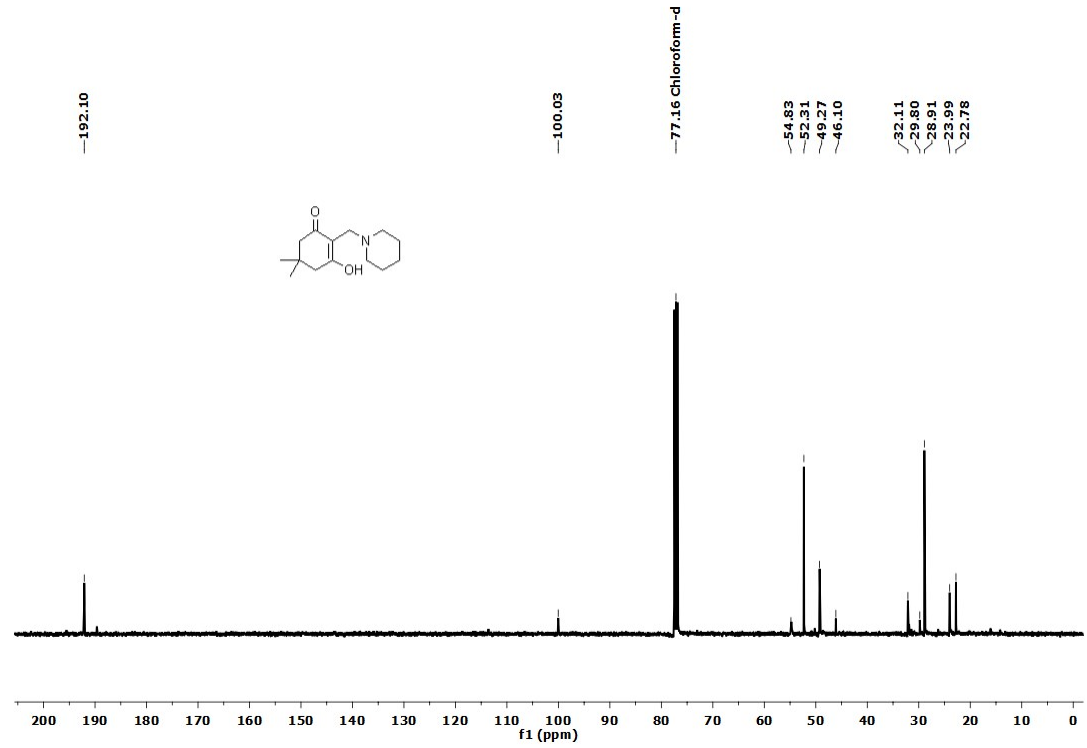



**Figure S54:** $^{13}$C NMR of Compound **4c**

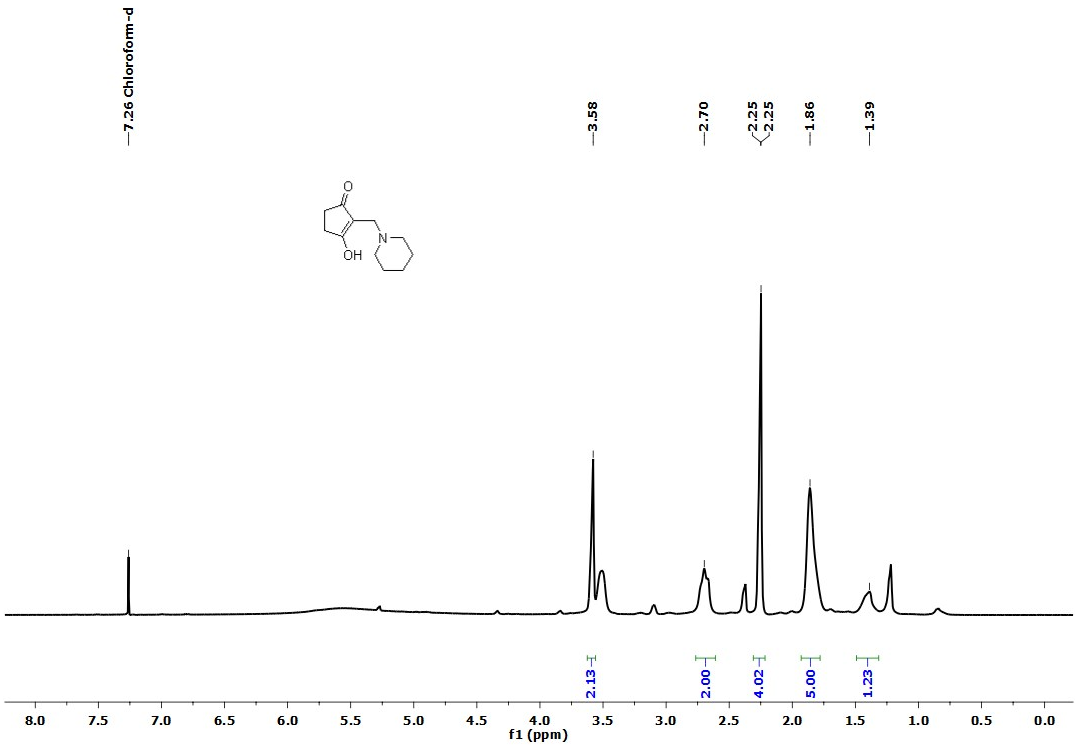



**Figure S55:** $^{1}$H NMR of Compound **4d**

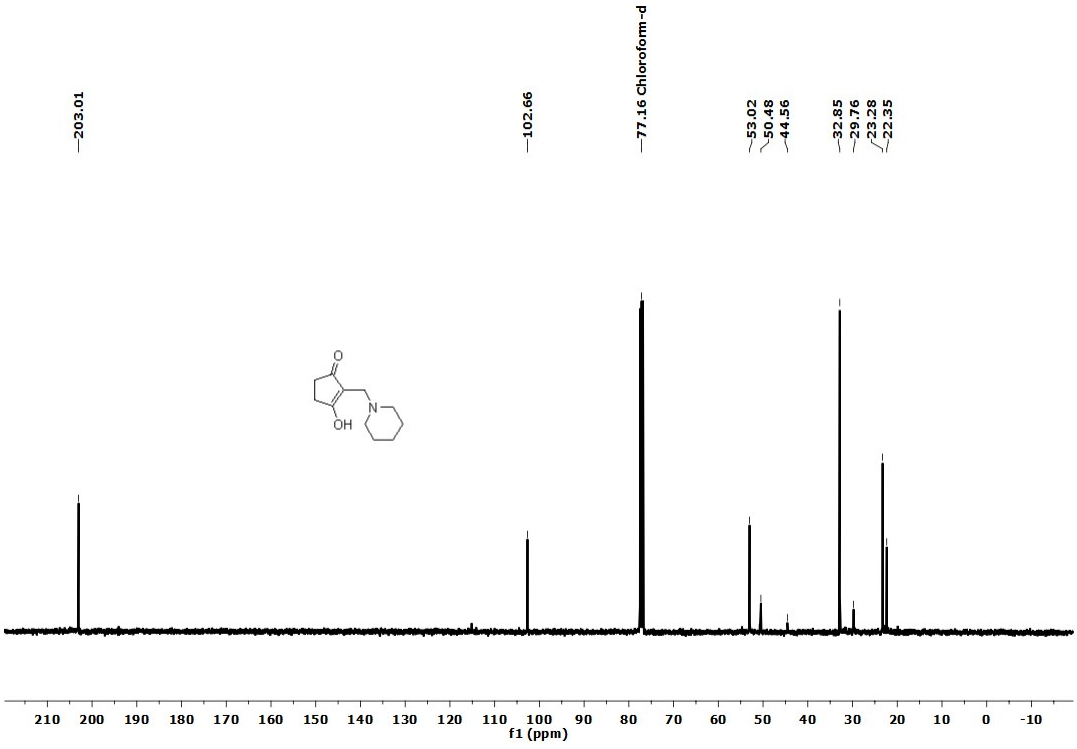



**Figure S56:** $^{13}$C NMR of Compound **4d**

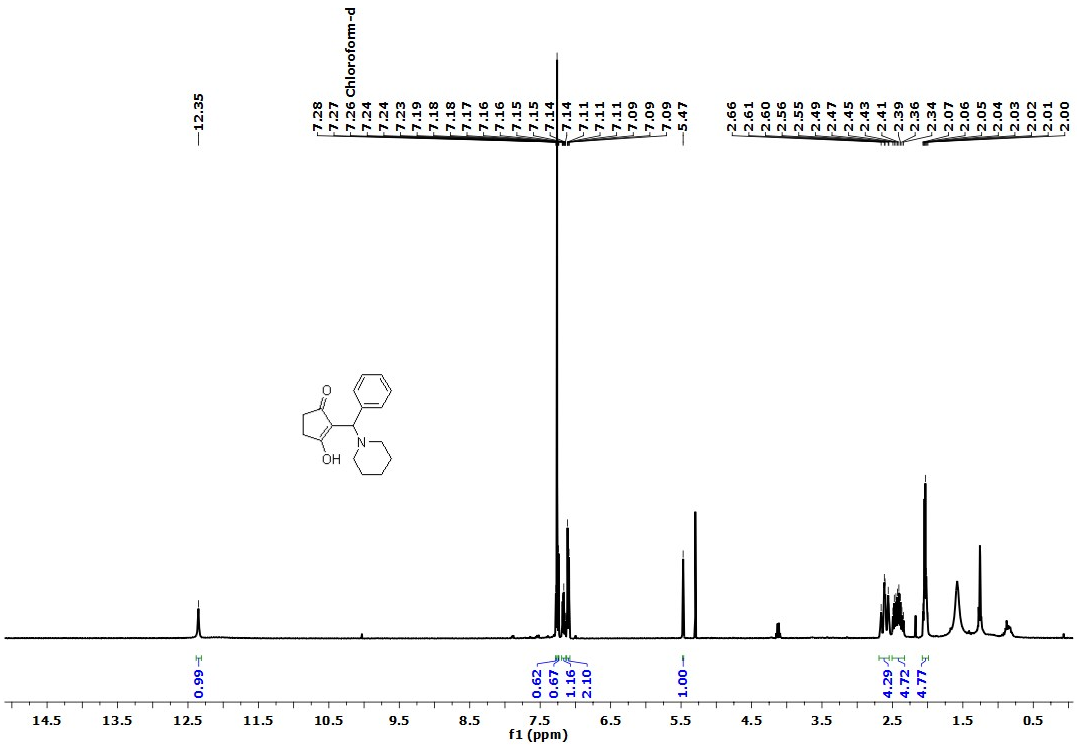



**Figure S57:** $^{1}$H NMR of Compound **4e**

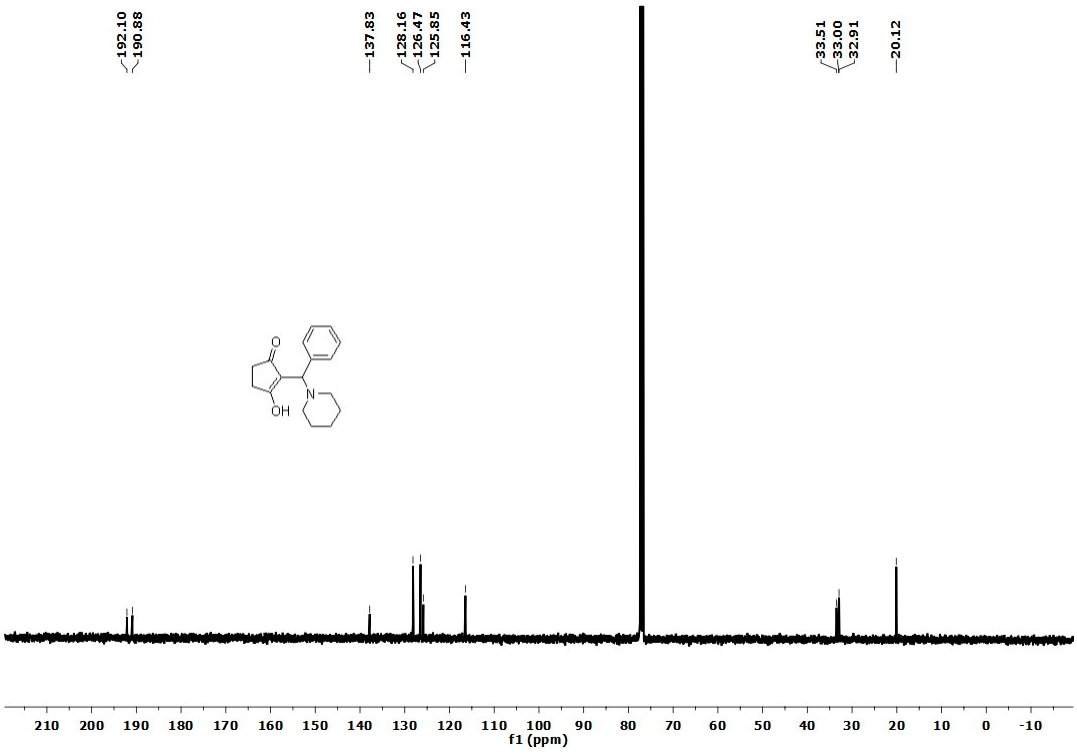



**Figure S58:** $^{13}$C NMR of Compound **4e**

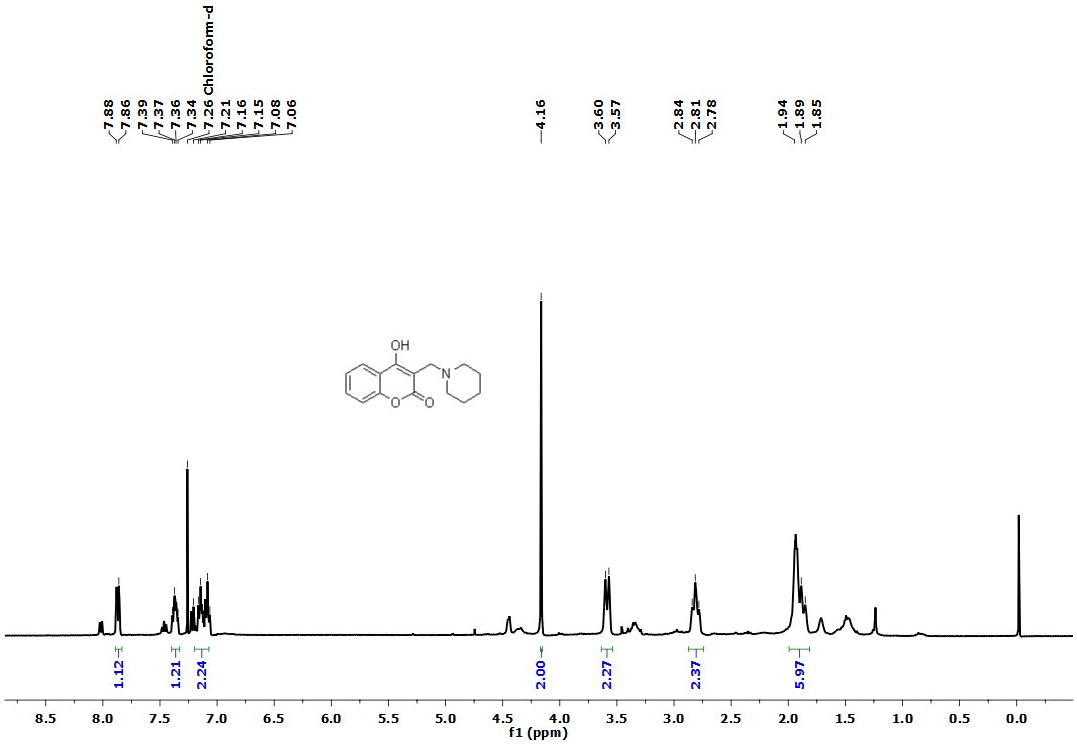



**Figure S59:** $^{1}$H NMR of Compound **4f**

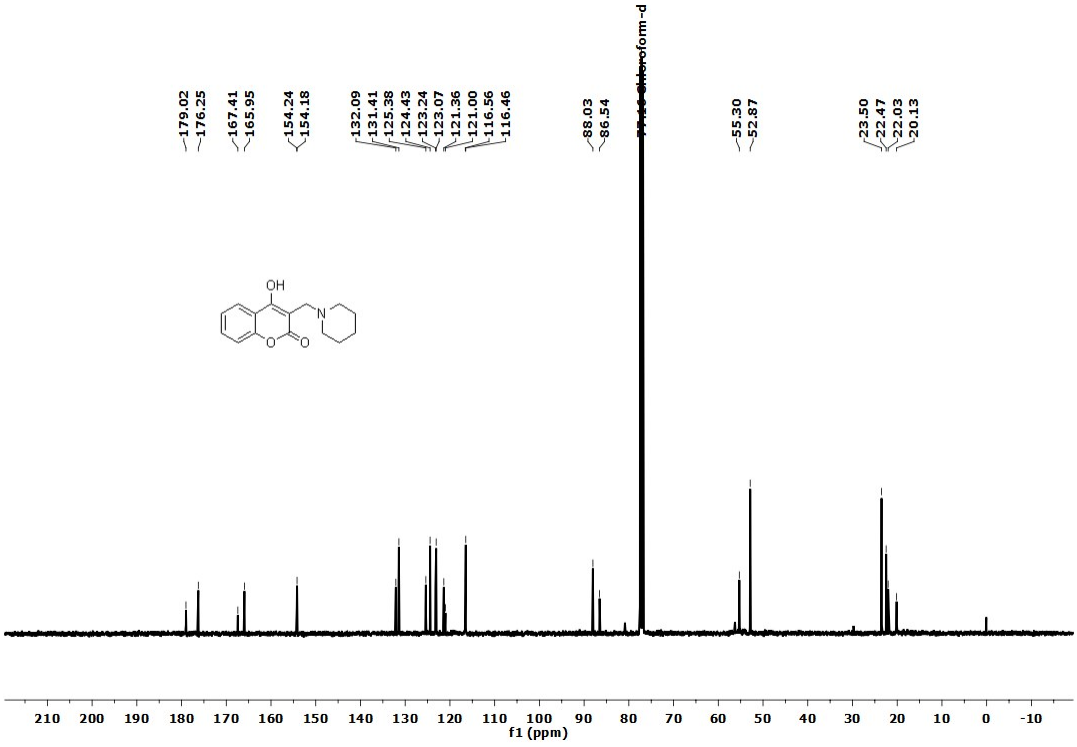



**Figure S60:** $^{13}$C NMR of Compound **4f**

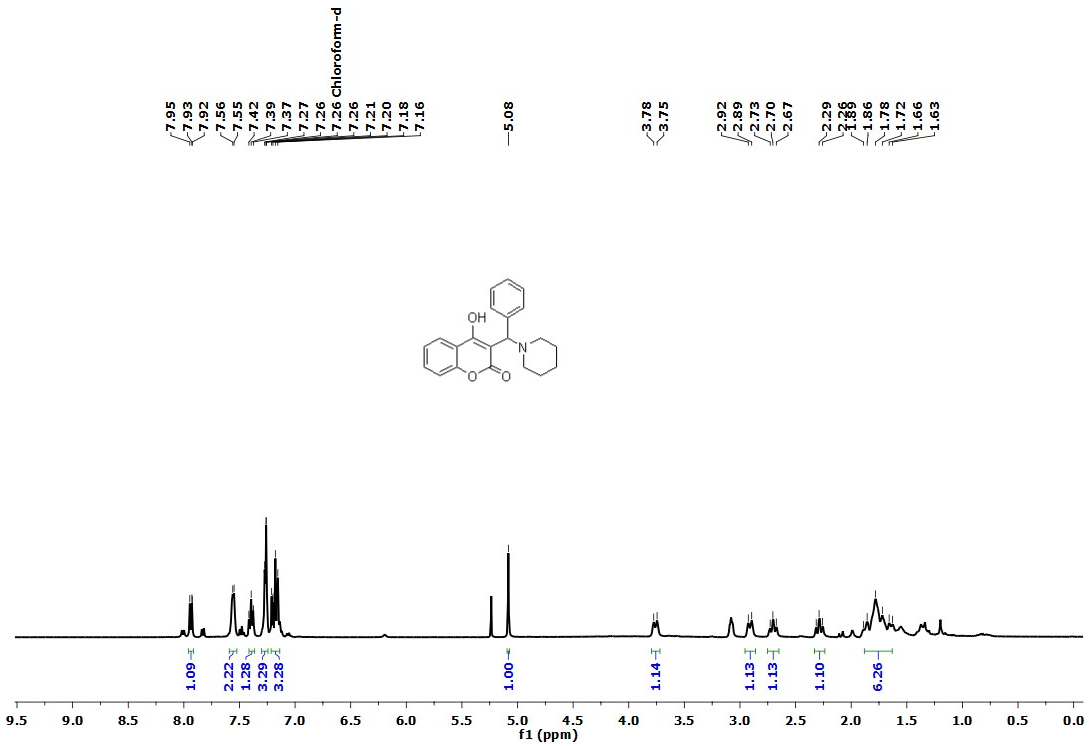



**Figure S61:** $^{1}$H NMR of Compound **4g**

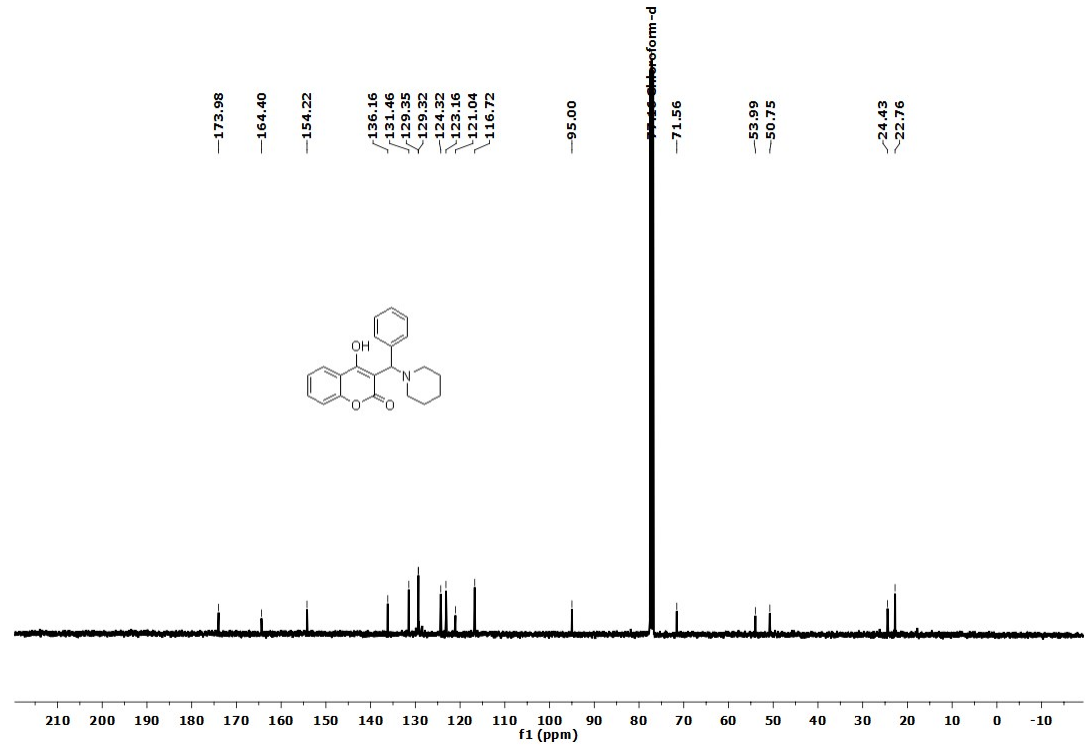



**Figure S62:** $^{13}$C NMR of Compound **4g**

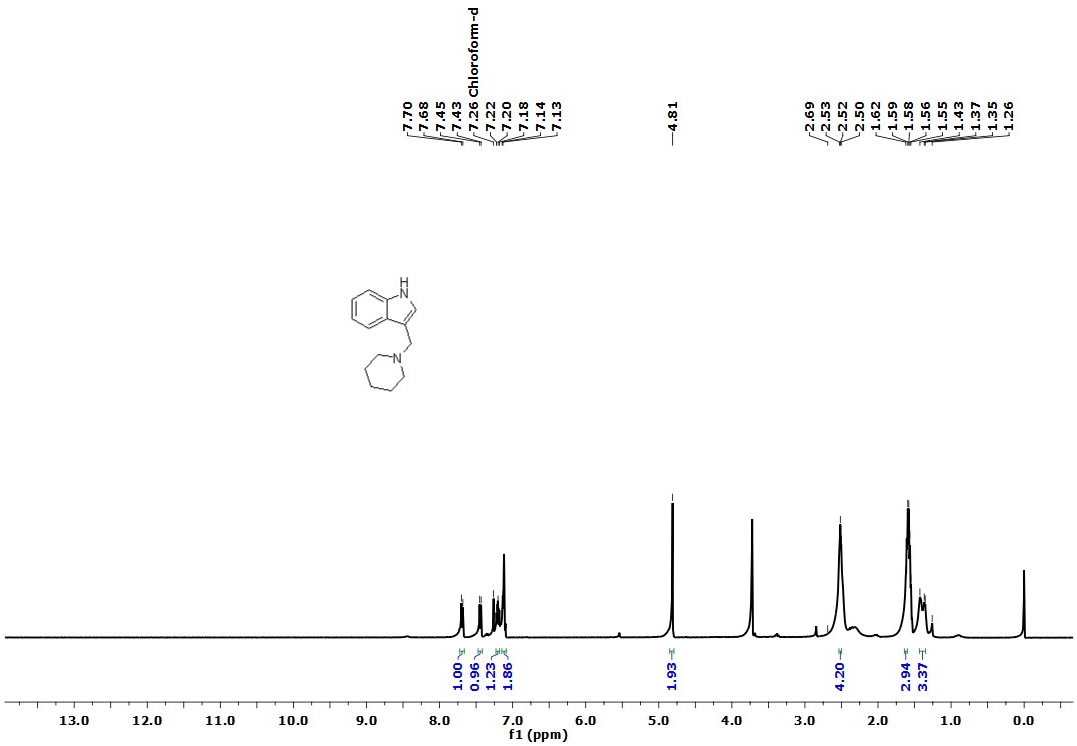



**Figure S63:** $^{1}$H NMR of Compound **4h**

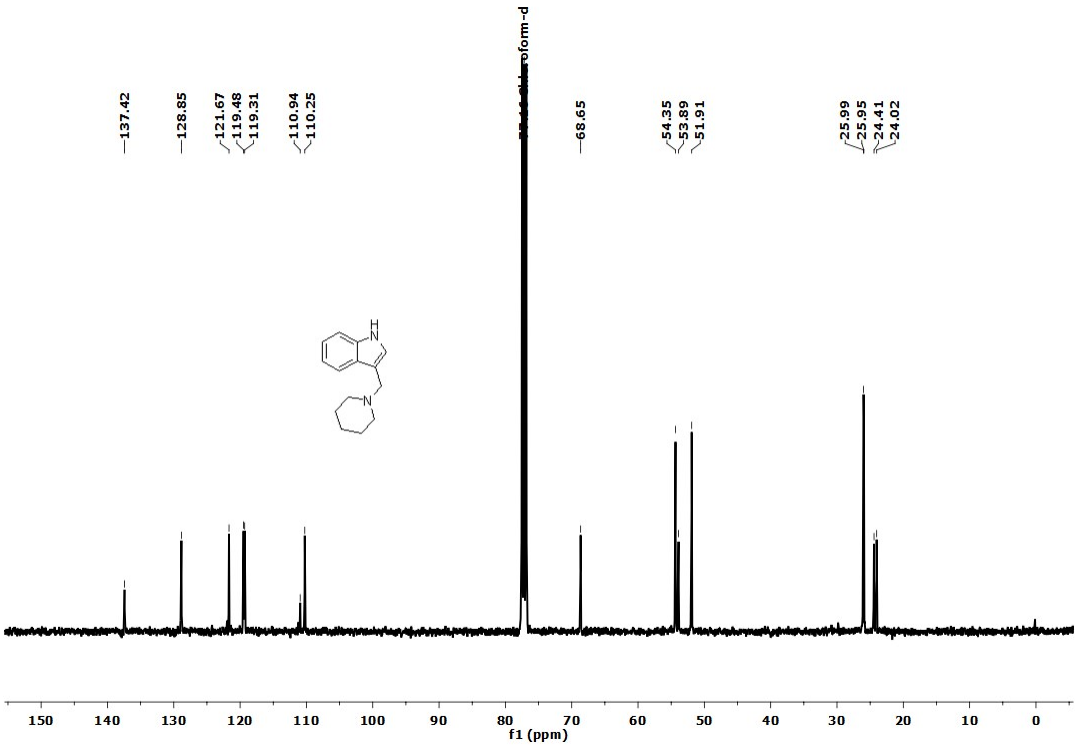



**Figure S64:**$^{13}$C NMR of Compound **4h**

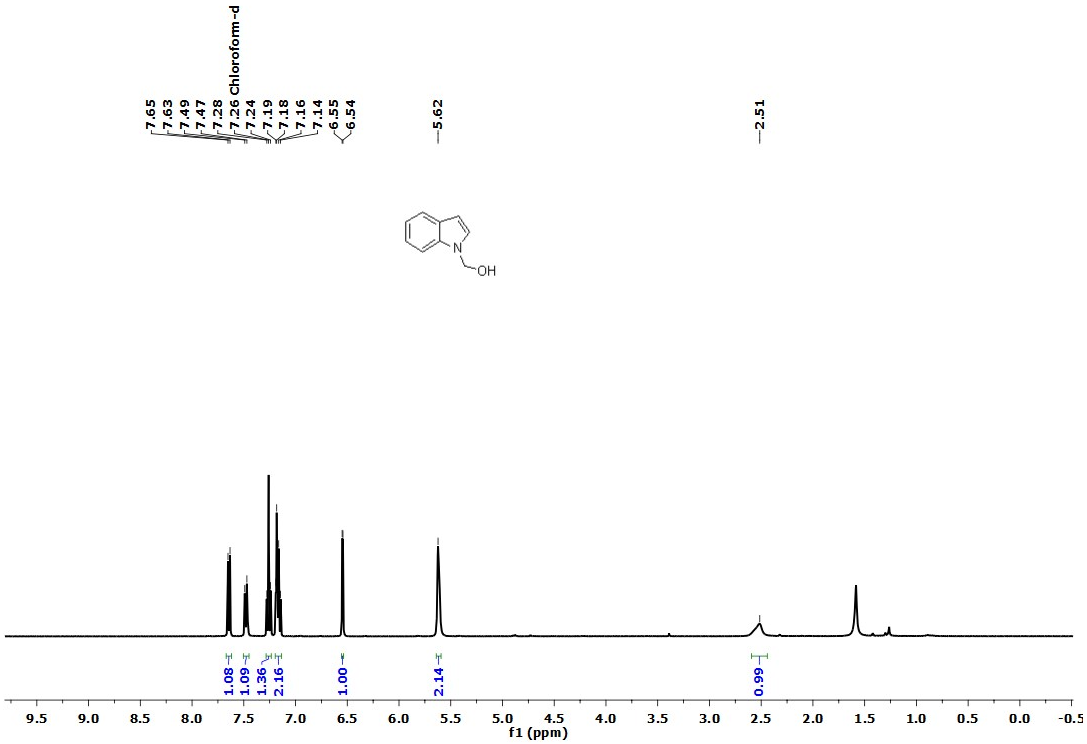



**Figure S65:** $^{1}$H NMR of Compound **4i**

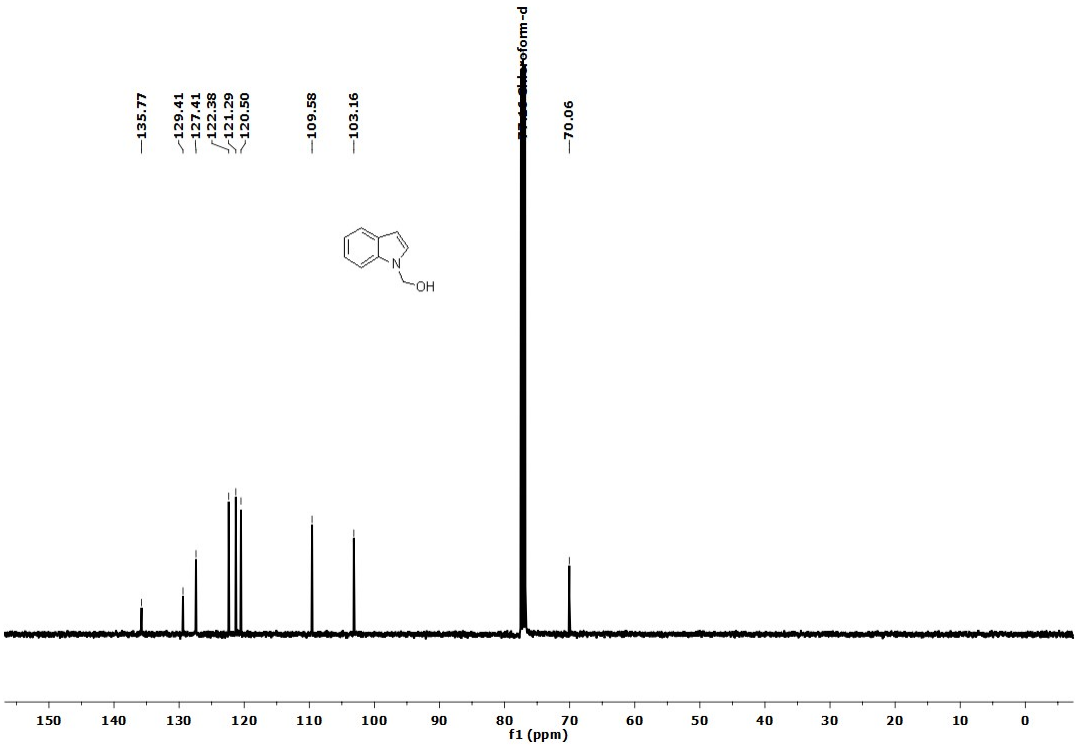



**Figure S66:** $^{13}$C NMR of Compound **(1H-indol-1-yl)methanol**

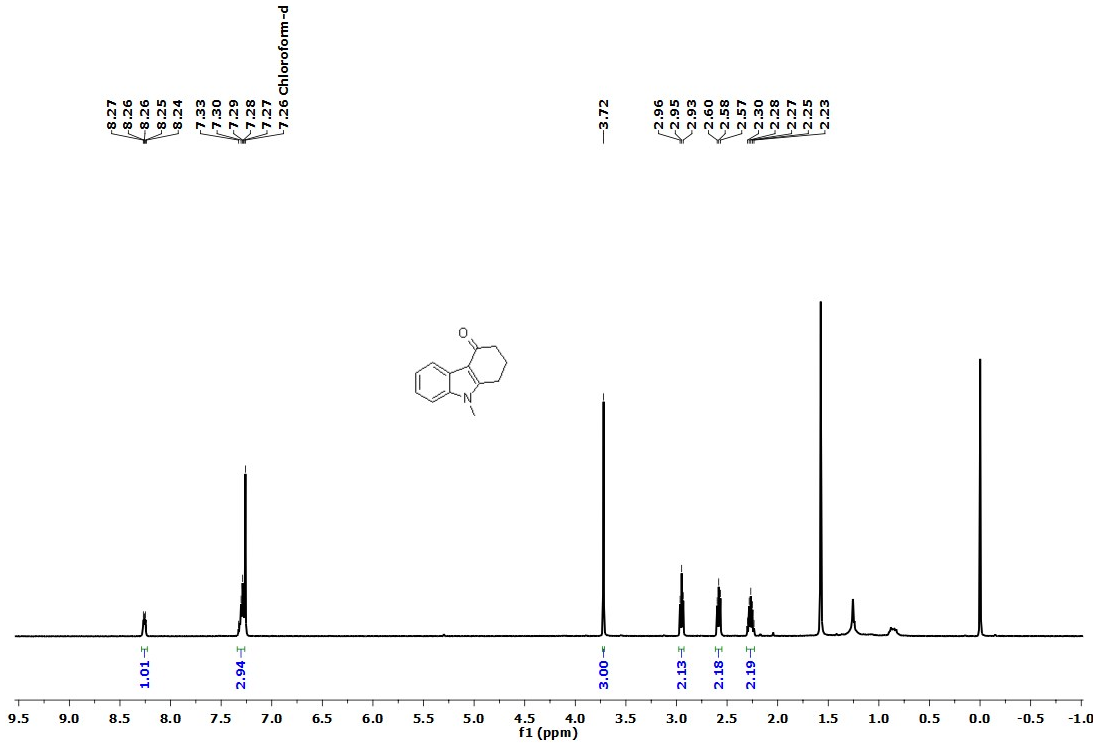



**Figure S67:** $^{1}$H NMR of Compound **5**

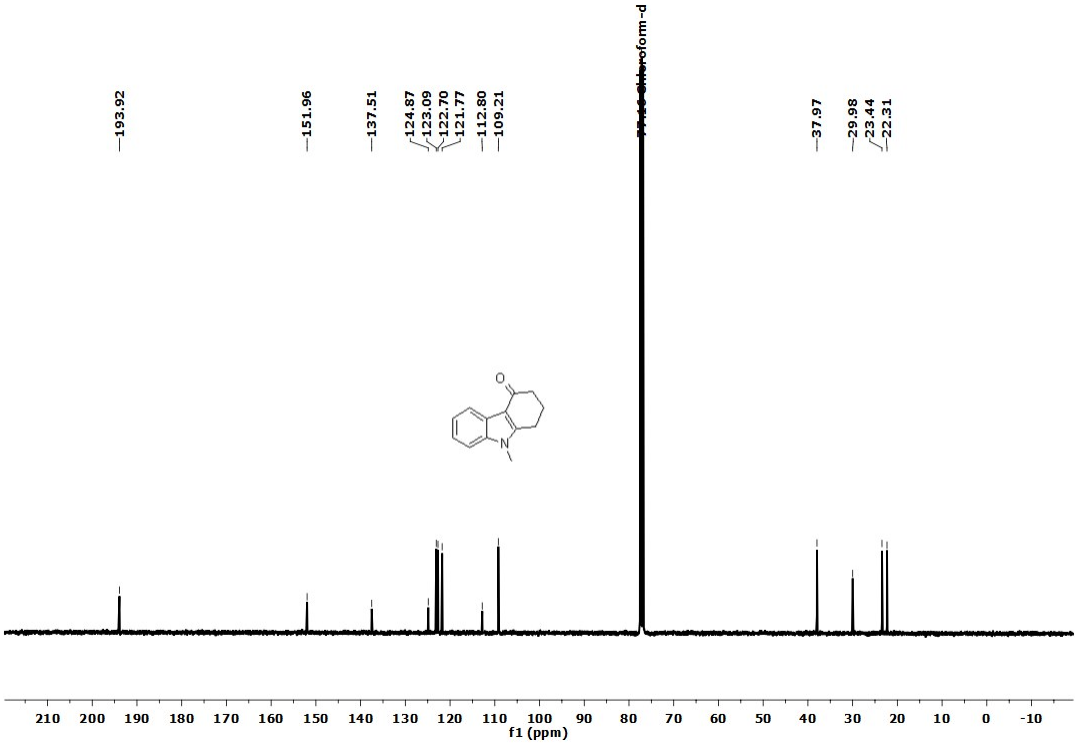



**Figure S68:** $^{13}$C NMR of Compound **5**

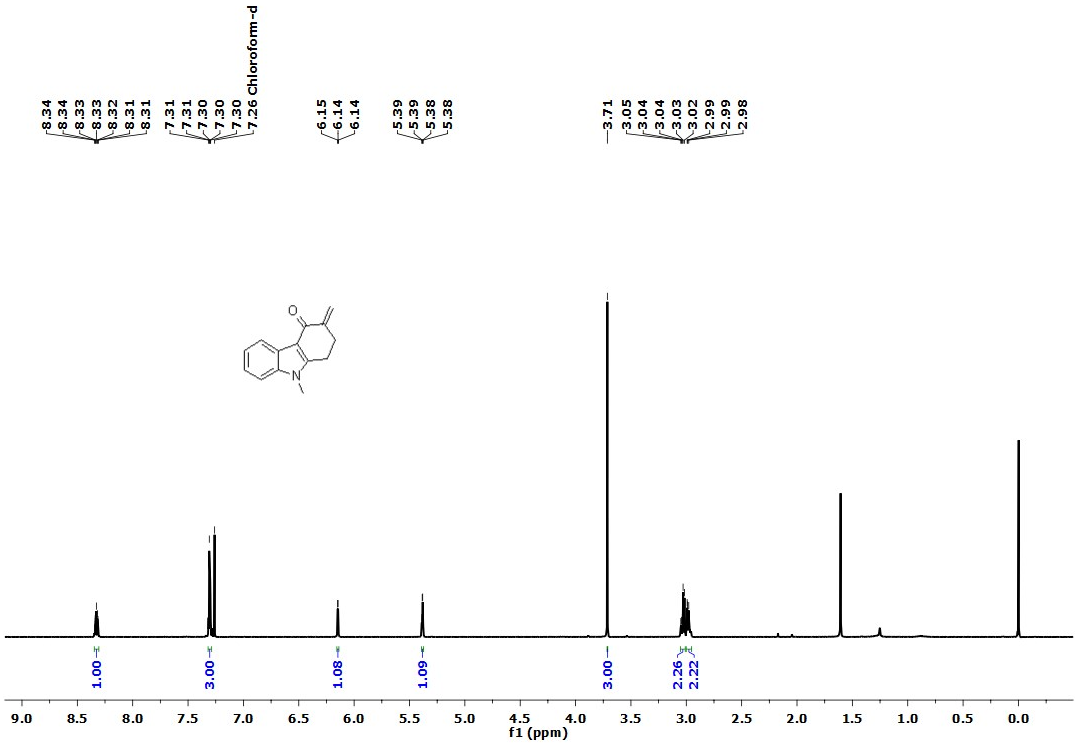



**Figure S69:** $^{1}$H NMR of Compound **6**

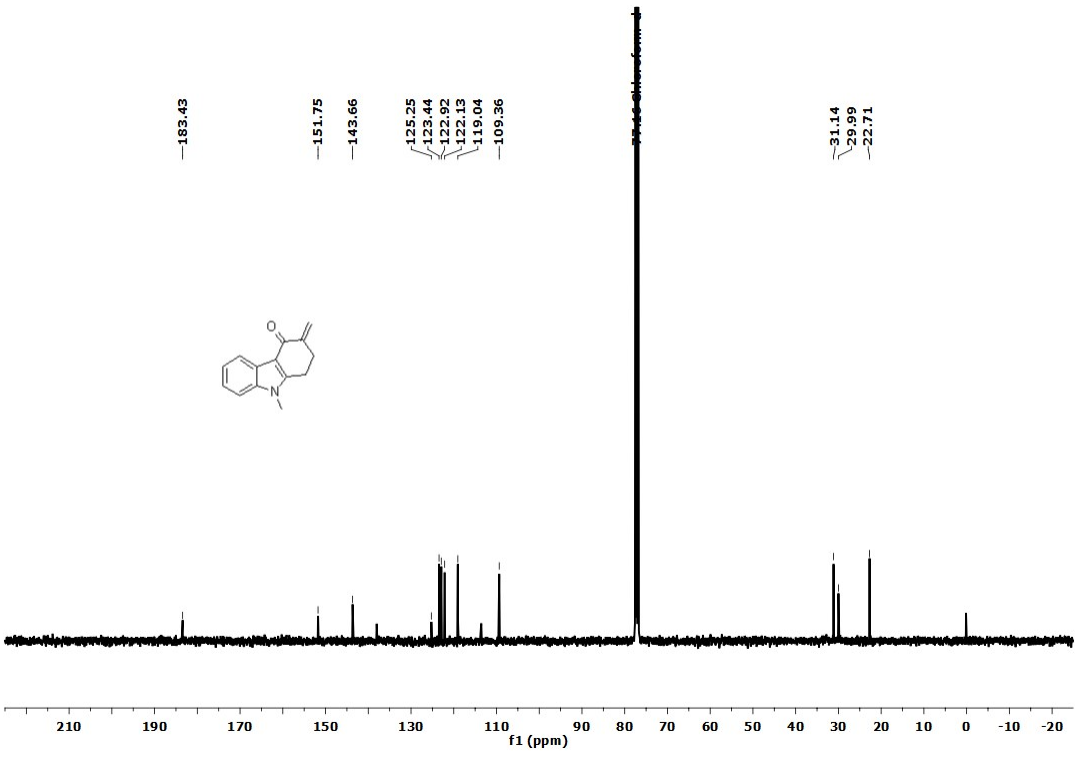



**Figure S70:** $^{13}$C NMR of Compound **6**

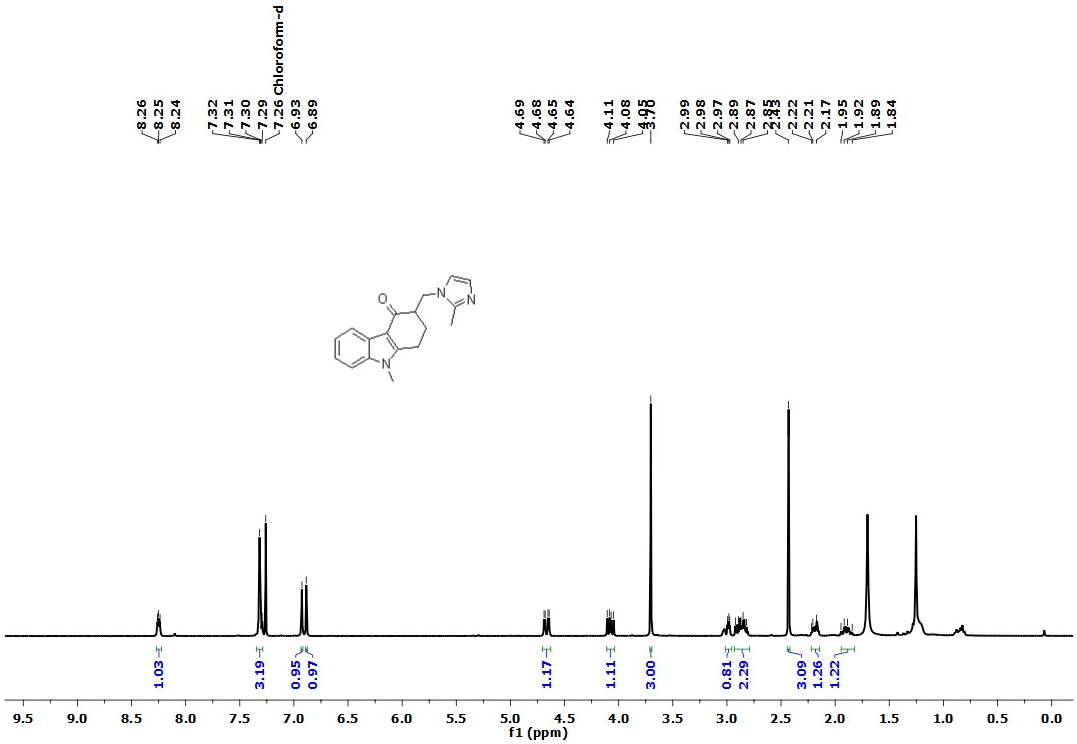



**Figure S69:** $^{1}$H NMR of Compound **7**

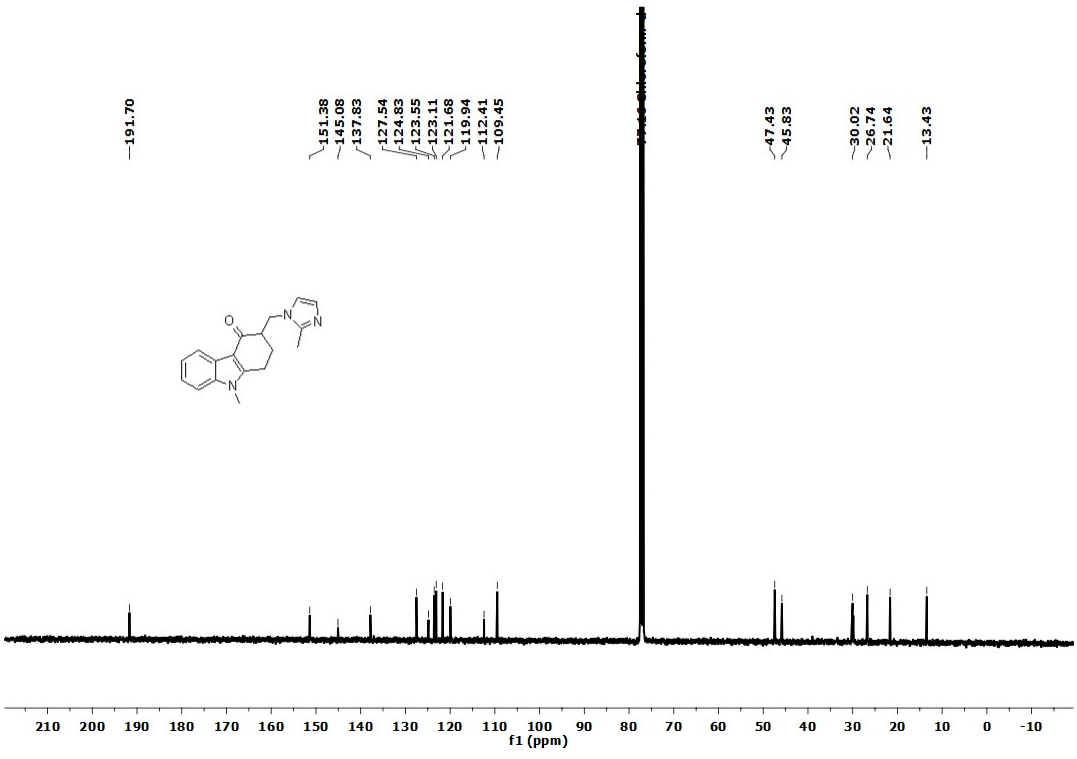



**Figure S70:** $^{13}$C NMR of Compound **7**

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