

# Supporting Information

Visible-light-mediated Achmatowicz rearrangement  
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## General:

Furan and 2-methylfuran were freshly distilled for each reaction. Inhibitor-free diethyl ether, anhydrous acetone, and anhydrous DCM were obtained from a JC Meyer Solvent System. 2-methyltetrahydrofuran and *N,N*-dimethylformamide were dried over molecular sieves (4 Å, 0.4 nm, type 514, pearls, Carl Roth). Celite was purchased from Sigma-Aldrich (Celite 535). Unless otherwise noted, all other reagents and solvents were purchased from commercial suppliers and used without further purification. All reactions were carried out under an argon atmosphere. Analytical thin layer chromatography (TLC) was performed on Macherey-Nagel Pre-coated TLC-sheets, ALUGRAM Xtra SIL G/UV<sub>254</sub> sheets and visualized with 254 nm light, 2,5-dinitrophenylhydrazine (DNPH) and/or KMnO<sub>4</sub> staining solutions followed by heating. Purification of the reaction products was carried out by flash chromatography using the Reveleris X2 Flash Chromatography System from GRACE, using a prepacked column with 12 g, 40 μm silica gel at a 30 mL/min elution flow rate. Macherey-Nagel Silica 60 M (0.04-0.063 mm) silica gel was used for dry loading of the crude compounds on the flash chromatography system. <sup>1</sup>H NMR spectra were recorded on a 400 MHz Varian spectrometer and are reported in ppm relative to the residual solvent peaks (CDCl<sub>3</sub> at 7.26 ppm). Peaks are reported as: s = singlet, d = doublet, t = triplet, q = quartet, quint = quintet, m = multiplet or unresolved, bs = broad signal, with coupling constants in Hz. <sup>13</sup>C NMR spectra were recorded with <sup>1</sup>H-decoupling on a 101 MHz Varian spectrometer and are reported in ppm relative to the residual solvent peak (CDCl<sub>3</sub> at 77.16 ppm). High-resolution mass spectral data were obtained using a Waters XEVO G2-XS 4K spectrometer (#186008532) with the XEVO G2-XS QTOF capability kit (#1860083535). Samples were prepared in LC-MS CHROMASOLV water and acetonitrile, and analyzed in the respective mixtures. Fluorescence intensity measurements were taken using a Molecular Devices Spectra Max M5 plate reader system.

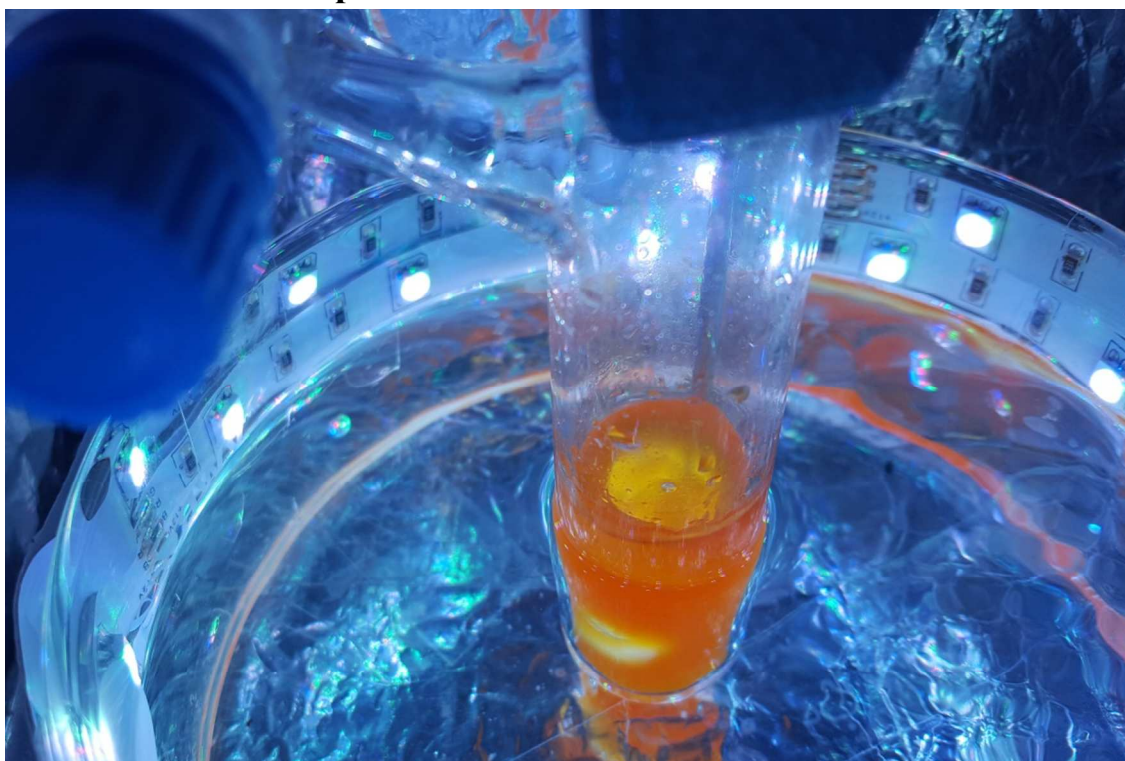
## Hair Bleach Titration

Blond-Booster Ultra Plus from Schwarzkopf was used for the hair bleach reactions. The ingredients listed are potassium persulfate, sodium silicate, sodium persulfate, ammonium persulfate, aqua, silica, disodium EDTA, potassium sulfate, ammonium sulfate, sodium sulfate. The hair bleach was titrated according to the procedure outlined in the FMC Persulfates brochure.<sup>1</sup> To 2-20 mL of persulfate solution (depending on the approximate solution concentration) was added 50 mL of about 1 N H<sub>2</sub>SO<sub>4</sub> solution and 40 mL of 0.5 N ferrous ammonium sulfate solution. With 0.5 N Ce(SO<sub>4</sub>)<sub>2</sub> the solution was titrated to a Ferroin indicator endpoint. This was done for ammonium persulfate and hair bleach. Hair bleach was determined to have 0.59 times the oxidizing power as ammonium persulfate, or a molecular weight of 1.69 times the molecular weight of ammonium persulfate (385.66 g/mol)

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<sup>1</sup>FMC Persulfates-PeroxyChem: [www.peroxychem.com/media/90826/aod\\_brochure\\_persulfate.pdf](http://www.peroxychem.com/media/90826/aod_brochure_persulfate.pdf) (Accessed October 6, 2016)

## Batch Photoreactor Setup



**Figure S1.** Typical photoreactor setup for General Procedure B (see page 9)

A flexible 3 meter, red/green/blue, 16.2 W LED band was wrapped around a 115 mm borosilicate evaporating dish which was placed inside of a cardboard syringe box lined with aluminum foil. White light (illumination of all three LED colors, red/green/blue) was used at full power. The evaporating dish was filled with isopropanol with compressed air flowing over the top. This cooling system maintained a bath temperature between 19-22° C. The Schlenk tube was placed at the center of the reactor and stirred rapidly (1400 rpm).

## Sunlight Photoreactor Setup



**Figure S2.** Typical setup for sunlight reactions.

An old solvent bottle was cut so that the bottom and half of the body remained to form a curved container open on one side as shown above. This bottle was lined with aluminum foil to increase the reflected light. The Schlenk tube was placed at the center of the reactor and stirred rapidly (1400 rpm).

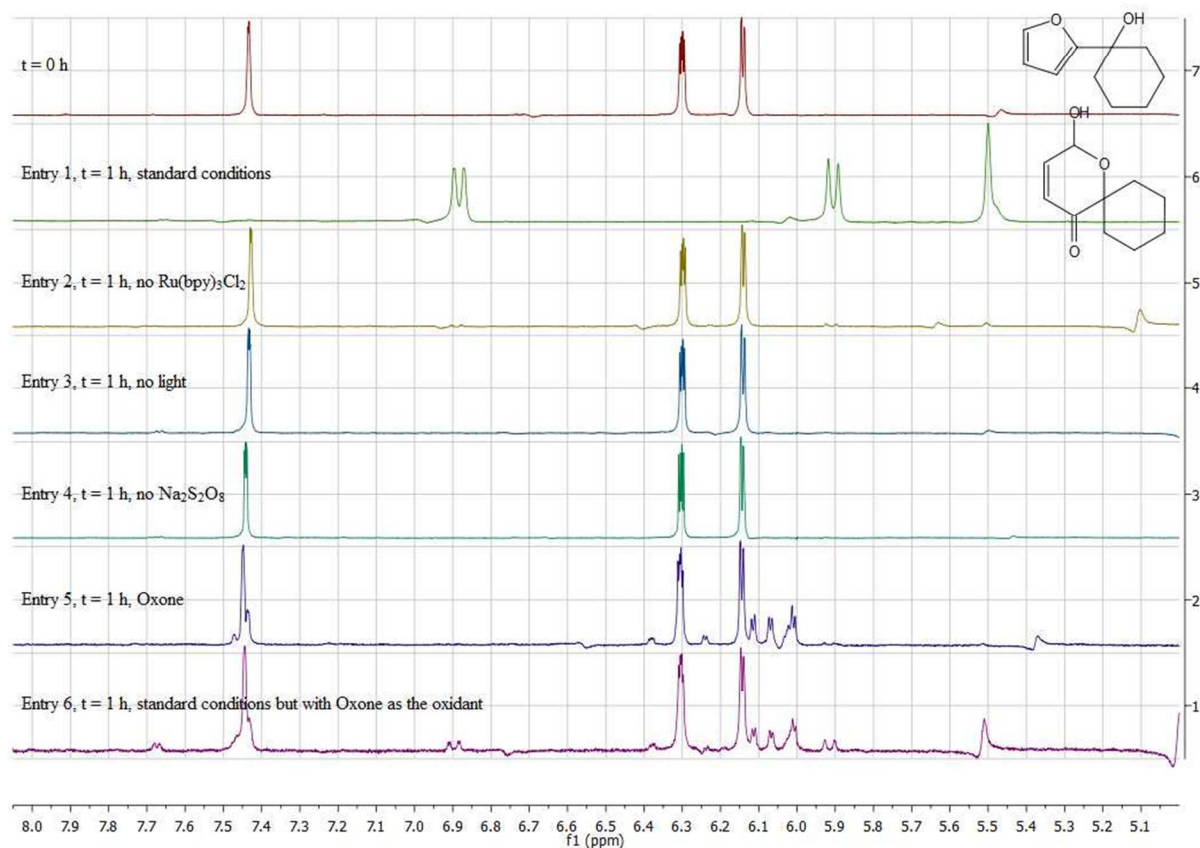
### Control Studies

An oven dried flask was evacuated and filled with argon three times. To this flask was added 10 mL of diethyl ether, followed by furan (0.23 mL, 3.2 mmol, 1.6 equiv). The solution was stirred (600 rpm) and cooled to 0° C, and then *n*-BuLi (1.5 mL, 1.2 equiv, 1.6 M solution in hexanes) was added slowly. The reaction mixture was allowed to stir at 0° C for 1 hour at which point the reaction mixture was cooled to -78° C. Cyclohexanone (0.196 g, 2 mmol) was then added slowly and the reaction mixture was allowed to stir and warm to room temperature over 16 hours. The resulting reaction mixture was quenched under inert atmosphere via slow addition of 5 mL of saturated ammonium chloride solution followed by 5 mL of saturated sodium chloride solution. The aqueous phase was extracted three times with ethyl acetate. The combined organic phase was dried over sodium sulfate and concentrated via rotary evaporator. The resulting crude

**cyclohexyl(furan-2-yl)methanol (1a)** was taken up in ethyl acetate and separated into four equi-volume fractions which were subsequently concentrated via rotary evaporator.

A Schlenk tube was charged with sodium persulfate (0.125 g, 0.525 mmol, 1.05 equiv) and  $\text{Ru}(\text{bpy})_3\text{Cl}_2 \cdot 6 \text{H}_2\text{O}$  (2 mg, 2.6  $\mu\text{mol}$ , 0.5 mol%). To this tube was added water (1 mL), followed by crude **cyclohexyl(furan-2-yl)methanol (1a)** (0.5 mmol) in a 1:1 acetonitrile:DMSO mixture (1 mL). The reaction mixture was kept in the dark while argon was bubbled through it for 15 minutes. Then the reaction mixture was irradiated in the batch photoreactor with rapid stirring (1400 rpm) for 1 hour. 0.1 mL of the crude reaction mixture was diluted with 0.4 mL  $d_6$ -DMSO and analyzed by  $^1\text{H}$  NMR (Figure S3, Entry 1).

The other three fractions were run and analyzed under the same conditions but in the absence of catalyst, light, or oxidant (Figure S3, Entries 2-4 respectively). Two additional fractions prepared by the same procedure were reacted with only Oxone (no light, no photocatalyst, Figure S3, Entry 5) and with Oxone instead of sodium persulfate under standard photoredox conditions (Figure S3, Entry 6).



**Figure S3.** Control Studies: crude  $^1\text{H}$  NMR spectra of 0.1 mL of reaction mixture in 0.4 mL  $d_6$ -DMSO

## Reaction Robustness and Sustainability

The aforementioned procedure in **Control Studies** was used to obtain crude **cyclohexyl(furan-2-yl)methanol (1a)** in four fractions. The following photoreactions were performed using the same general procedure and analysis outlined above, with the following changes:

Entry 1: Instead of white light (red/green/blue), only blue light was used to irradiate the solution.

Entry 2: Instead of white light, the reaction mixture was exposed to direct sunlight (see above for sunlight photoreactor setup).

Entry 3: Seawater obtained from the Adriatic Sea was used instead of deionized water.

Entry 4: Beer (Krombacher Pils) was used instead of deionized water.

Entry 5: Hair bleach (0.203g, 1.05 equiv.) was used instead of sodium persulfate

Entry 6: Hair bleach (0.675g, 3.50 equiv.) was used instead of sodium persulfate

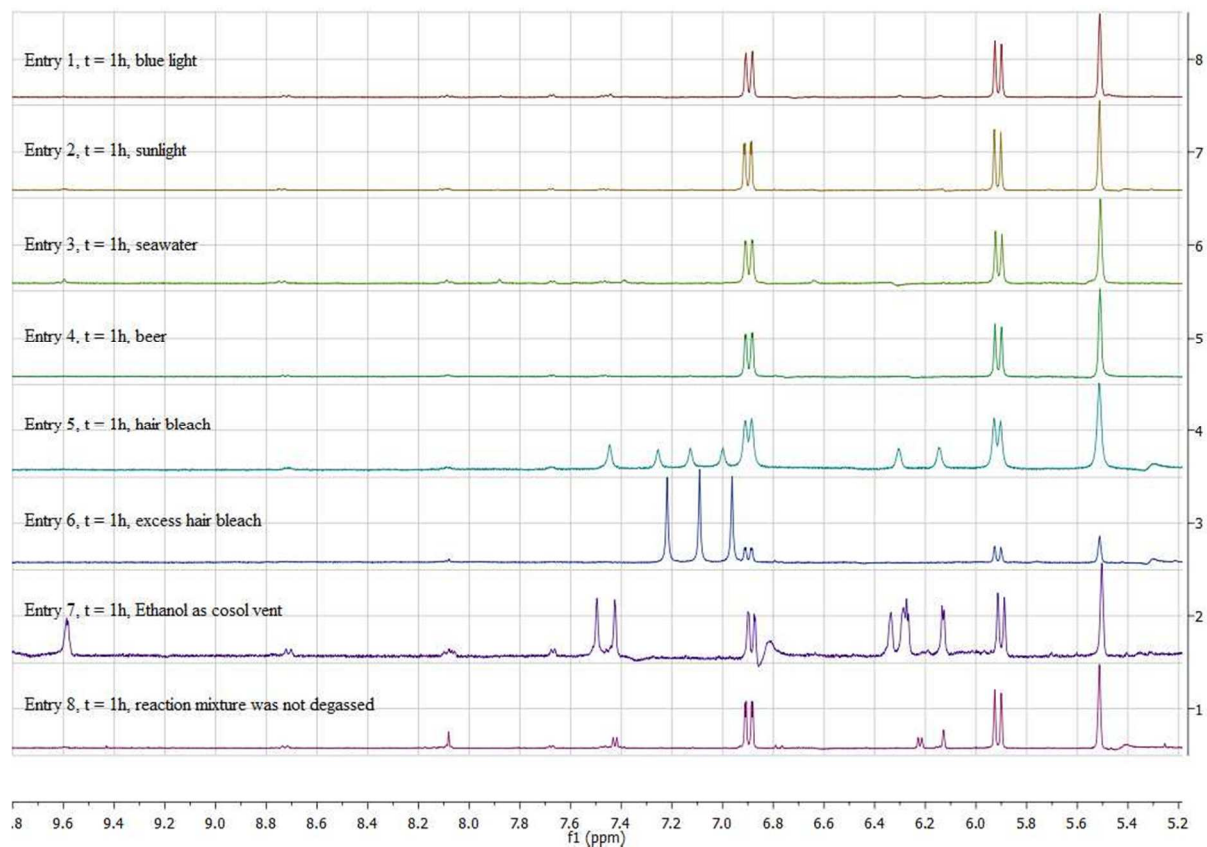
Entry 7: Instead of DMSO and MeCN, 1 mL of EtOH was used. The major side-product was acetaldehyde.  $^1\text{H NMR } \delta$  9.59 (q,  $J = 2.5$  Hz, 1H). The other side-products were unidentified.

Entry 8: The reaction was run using standard conditions, however not degassed. The main side-product was **5-Hydroxy-2(5H)-furanone**.  $^1\text{H NMR } \delta$  7.42 (d,  $J = 5.7$  Hz, 1H), 6.22 (d,  $J = 5.6$  Hz, 1H), 6.13 (s, 1H). After work up and column  $^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )  $\delta$  171.4, 152.0, 125.0, 98.5. Both spectra are in agreement with literature values.<sup>2</sup> The expected co-side-product, cyclohexanone, although not isolated, is also probably present in the crude  $^1\text{H NMR}$  with a characteristic triplet appearing at 2.26 ppm with a  $J = 6.6$  Hz coupling constant.

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<sup>2</sup>Wahlen, J.; Moens, B.; De Vos, D. E.; Alsters, P. L.; Jacobs, P. A., *Adv. Synth. Catal.* **2004**, *346*, 333-338.





**Figure S4.** Robustness and Sustainability Experiments: crude  $^1\text{H}$  NMR spectra of 0.1 mL of reaction mixture in 0.4 mL  $\text{d}_6\text{-DMSO}$

## Stern-Volmer Experiments

Stock solution **1** was prepared by dissolving 14.95 mg of Ru(bpy)<sub>3</sub>Cl<sub>2</sub> 6H<sub>2</sub>O with a 2:1:1 water:DMSO:acetonitrile solvent mixture and diluting to 10 mL (2.0 mM).

Stock solution **2** was prepared by dissolving 0.952 g of sodium persulfate with a 2:1:1 water:DMSO:Acetonitrile solvent mixture and diluting to 10 mL (0.4 M).

Stock solution **3** was prepared using crude **1g** (2 mmol), taken up in acetonitrile and diluted to 5 mL using acetonitrile (0.4 M).

Fluorescence intensities were measured at a fixed wavelength (610 nm) with a fixed excitation (450 nm). All samples contained 0.2 mL of stock solution **1** (0.20 mM Ru(bpy)<sub>3</sub>Cl<sub>2</sub> 6H<sub>2</sub>O), the designated amount of stock solution **2** or **3**, and were diluted to 2 mL with a 2:1:1 water:DMSO:Acetonitrile solvent mixture (sodium persulfate) or acetonitrile (compound **1g**). All concentrations were prepared in triplicate and the reported fluorescence intensities reported as the average of three samples.

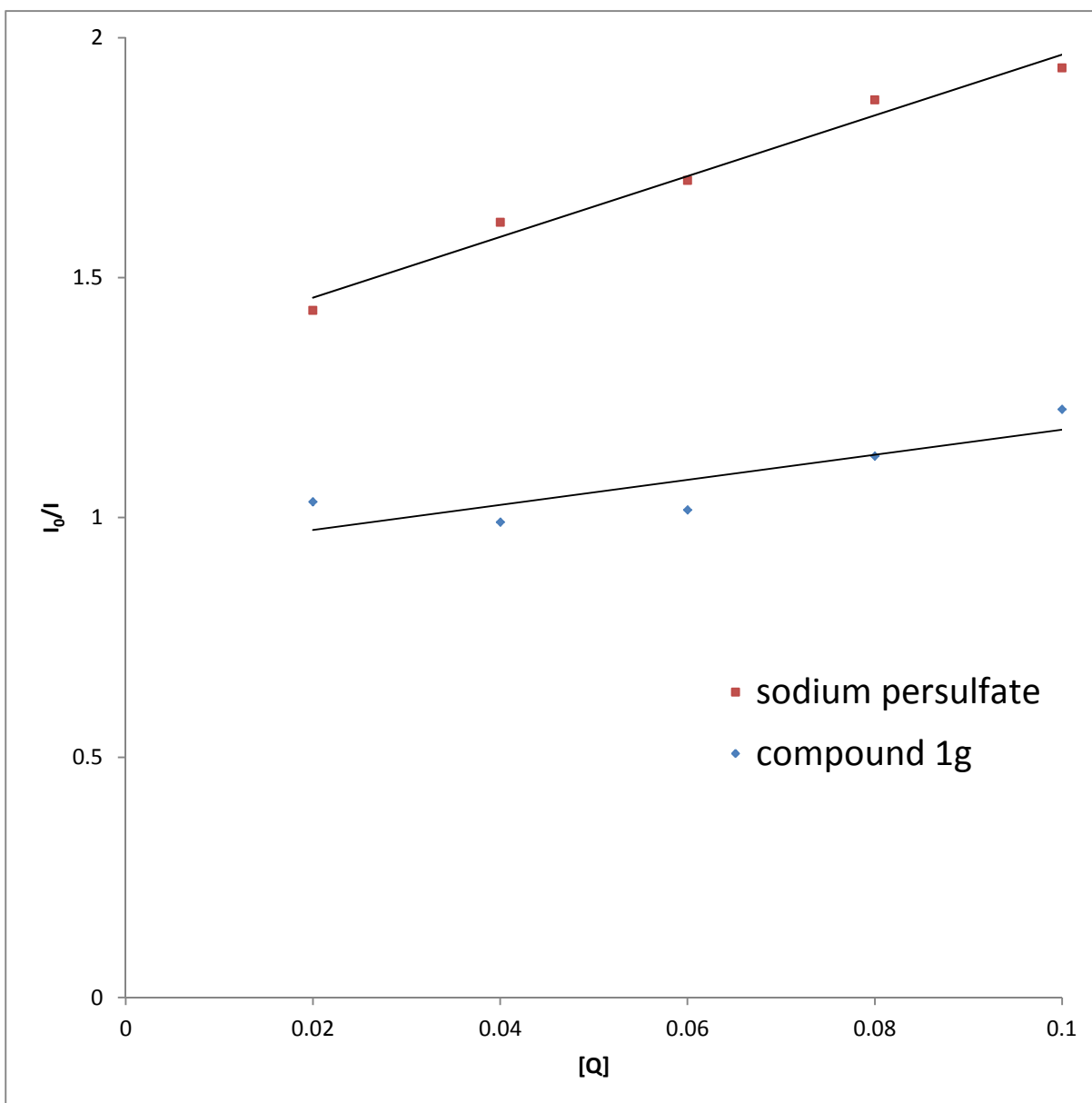
In the absence of quencher, the average fluorescence intensity was 2900.0 in a 2:1:1 water:DMSO:Acetonitrile solvent mixture.

- 1 - 0.05 mL stock solution **2** (0.02 M) - 2025.5
- 2 - 0.10 mL stock solution **2** (0.04 M) - 1795.6
- 3 - 0.15 mL stock solution **2** (0.06 M) - 1703.6
- 4 - 0.20 mL stock solution **2** (0.08 M) - 1550.3
- 5 - 0.25 mL stock solution **2** (0.10 M) - 1497.3

In the absence of quencher, the average fluorescence intensity was 2459.2 in acetonitrile

- 1 - 0.05 mL stock solution **3** (0.02 M) - 2380.0
- 2 - 0.10 mL stock solution **3** (0.04 M) - 2482.5
- 3 - 0.15 mL stock solution **3** (0.06 M) - 2420.5
- 4 - 0.20 mL stock solution **3** (0.08 M) - 2179.3
- 5 - 0.25 mL stock solution **3** (0.10 M) - 2006.7

The quotient of fluorescence intensity ( $I_0$ ) and fluorescence intensity with quencher ( $I$ ) was plotted versus the concentration of the quencher,  $[Q]$  (Figure S5).



**Figure S5.** Stern-Volmer plot for sodium persulfate and compound **1g**.

## Synthesis and Characterization of Products

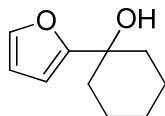
### General Procedure A: the Synthesis of Furfuryl Alcohols

An oven dried flask was evacuated and filled with argon three times. To this flask was added 10 mL of diethyl ether, followed by furan (0.23 mL, 3.2 mmol, 1.6 equiv). The solution was stirred (600 rpm) and cooled to 0° C, and then *n*-BuLi (1.5 mL, 1.2 equiv, 1.6 M solution in hexanes) was added slowly. The reaction mixture was allowed to stir at 0° C for 1 hour at which point the reaction mixture was cooled to -78° C. The corresponding carbonyl compound (2 mmol) was added slowly and the reaction mixture was allowed to stir and warm to room temperature over 16 hours. The resulting reaction mixture was quenched under inert atmosphere via slow addition of 5 mL of saturated ammonium chloride solution followed by 5 mL of saturated sodium chloride solution. The aqueous phase was extracted three times with ethyl acetate. The combined organic phase was dried over sodium sulfate and concentrated via rotary evaporator. The resulting crude product was kept under argon and used without further modification in the subsequent reaction.

### General Procedure B: the Photoredox Achmatowicz Rearrangement

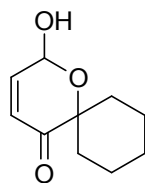
To a Schlenk tube was added with sodium persulfate (0.500 g, 2.1 mmol, 1.05 equiv) and Ru(bpy)<sub>3</sub>Cl<sub>2</sub>•6 H<sub>2</sub>O (2 mg, 2.6 μmol, 0.1 mol%). To this tube was added water (4 mL), followed by the crude furfuryl alcohol substrate (2 mmol) in a 1:1 acetonitrile:DMSO mixture (4 mL). The reaction mixture was kept in the dark while argon was bubbled through it for 15 minutes. Then the reaction mixture was irradiated in the batch photoreactor with rapid stirring (1400 rpm) for 2 hours. The reaction mixture was diluted with 5 mL saturated sodium chloride solution and extracted three times with ethyl acetate. The combined organic phases were dried over sodium sulfate and concentrated via rotary evaporator. The resulting crude product was adsorbed onto silica gel (2 equiv by weight) for loading onto the Reveleris flash chromatography system with the corresponding hexane:ethyl acetate mixture.

### 1-(furan-2-yl)cyclohexanol (1a)



The corresponding compound was prepared following the **general procedure A** by using **furan** and **cyclohexanone**. The reaction was run for 16 h and judged complete by TLC and crude <sup>1</sup>H NMR. The crude product was obtained as a yellowish oil and used in the subsequent reaction without purification. R<sub>f</sub> = 0.21 (Hexane:Ethyl acetate 4:1). <sup>1</sup>H NMR (400 MHz, Chloroform-*d*) δ 7.38 (d, *J* = 1.1 Hz, 1H), 6.35 (dd, *J* = 3.2, 1.8 Hz, 1H), 6.24 (d, *J* = 3.3 Hz, 1H), 2.08 - 1.94 (m, 2H), 1.92 - 1.83 (m, 2H), 1.81 - 1.45 (m, 6H).

## 2-hydroxy-1-oxaspiro[5.5]undec-3-en-5-one (2a)



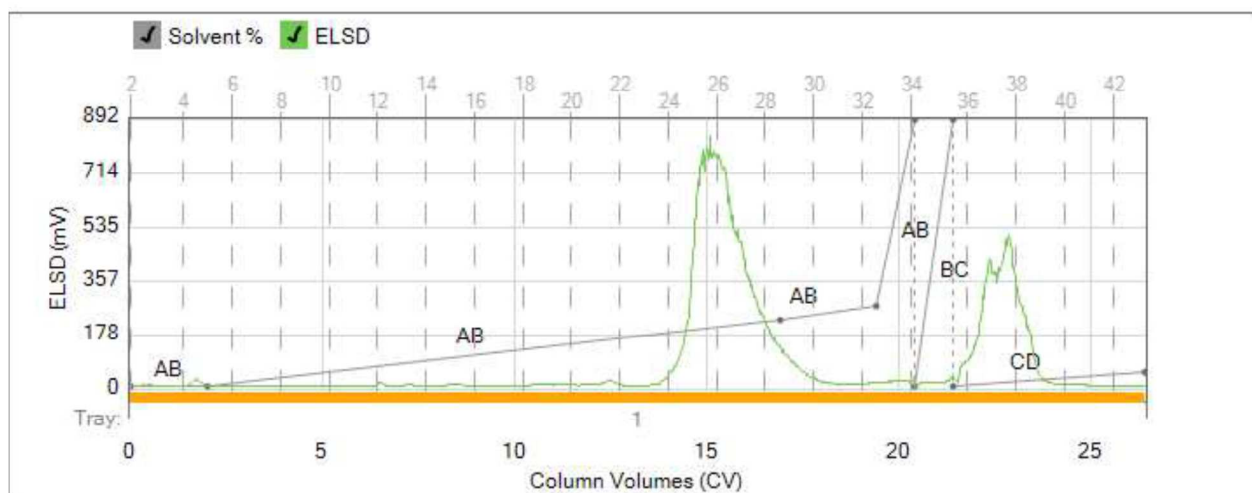
The corresponding compound was prepared following the **general procedure B** by using crude **1-(furan-2-yl)cyclohexanol (1a)**. The reaction was run for 2 h and determined to be complete by TLC and  $^1\text{H}$  NMR. An elution of 0-30% ethyl acetate in hexane over 17.5 CV was used for purification on the flash chromatography system. The product was obtained as a yellowish oil (0.289 g, 79% yield).  $R_f = 0.27$  (Hexane:Ethyl acetate 1:1).  $^1\text{H}$  NMR (400 MHz, Chloroform-*d*)  $\delta$  6.82 (d,  $J = 10.3$  Hz, 1H), 6.00 (d,  $J = 10.3$  Hz, 1H), 5.65 (s, 1H), 4.47 (bs, 1H), 1.90 – 1.46 (m, 9H), 1.14-1.30 (m, 1H).  $^{13}\text{C}$  NMR (101 MHz, Chloroform-*d*)  $\delta$  199.8, 146.1, 126.7, 87.4, 80.6, 33.4, 31.0, 25.1, 21.0, 20.5. HRMS (ESI):  $[\text{M}-\text{OH}]^+$  calcd for  $\text{C}_{10}\text{H}_{13}\text{O}_2^+$  165.0911, found 165.0913.

Column: Reveleris® Silica 12g  
Flow Rate: 30 mL/min  
Equilibration: 0.0 CV  
Run Length: 26.5 CV  
Mode: Flash Dry

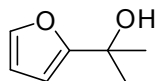
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Solvent C: Acetone  
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UV1 Wavelength: N/A  
UV2 Wavelength: N/A  
UV3 Wavelength: N/A

ELSD Threshold: N/A  
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Per-Vial Volume: 15 mL  
Non-Peak Volume: 15 mL

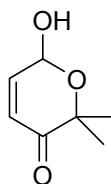


## 2-(furan-2-yl)propan-2-ol (1b)



The corresponding compound was prepared following the **general procedure A** by using **furan** and **acetone**. The reaction was run for 16 h and judged complete by TLC and crude  $^1\text{H}$  NMR. The crude product was obtained as a yellowish oil and used in the subsequent reaction without purification.  $R_f = 0.17$  (Hexane:Ethyl acetate 4:1).  $^1\text{H}$  NMR (400 MHz, Chloroform-*d*)  $\delta$  7.34 (s, 1H), 6.30 (d,  $J = 3.1$  Hz, 1H), 6.18 (d,  $J = 3.1$  Hz, 1H), 1.58 (s, 6H).

### 6-hydroxy-2,2-dimethyl-2H-pyran-3(6H)-one (2b)



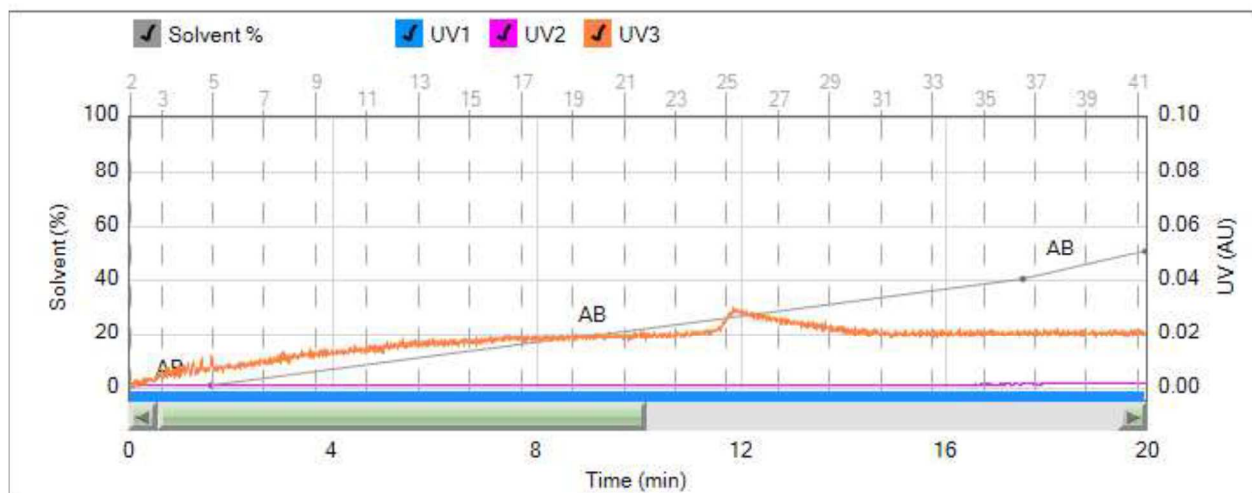
The corresponding compound was prepared following the **general procedure B** by using crude **2-(furan-2-yl)propan-2-ol (1b)**. The reaction was run for 2 h and determined to be complete by TLC and  $^1\text{H}$  NMR. An elution of 0-40% ethyl acetate in hexane over 20 CV was used for purification on the flash chromatography system. The product was obtained as a clear oil (0.182 g, 64% yield).  $R_f = 0.27$  (Hexane:Ethyl acetate 1:1).  $^1\text{H}$  NMR (400 MHz, Chloroform-*d*)  $\delta$  6.82 (d,  $J = 10.3$  Hz, 1H), 5.98 (d,  $J = 10.3$  Hz, 1H), 5.61 (s, 1H), 4.87 (bs, 1H), 1.38 (s, 3H), 1.29 (s, 3H).  $^{13}\text{C}$  NMR (101 MHz, Chloroform-*d*)  $\delta$  199.3, 146.4, 126.4, 87.8, 79.5, 26.5, 23.7. HRMS (ESI):  $[2\text{M}+\text{Na}^+]^+$  calcd for  $\text{C}_{14}\text{H}_{20}\text{NaO}_6^+$  307.1153, found 307.1157.

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Flow Rate: 30 mL/min  
Equilibration: 0.0 min  
Run Length: 39.2 min  
Mode: Flash Dry

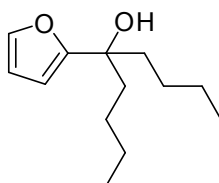
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Solvent B: Ethyl acetate  
Solvent C: Acetone  
Solvent D: i-Propanol  
Slope Detection: Off

UV Threshold: N/A  
UV Sensitivity: High  
UV1 Wavelength: 254 nm  
UV2 Wavelength: 300 nm  
UV3 Wavelength: 345 nm

ELSD Threshold: N/A  
ELSD Sensitivity: High  
Collection: Collect All  
Per-Vial Volume: 15 mL  
Non-Peak Volume: 15 mL



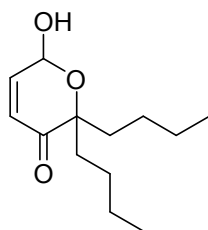
### 5-(furan-2-yl)nonan-5-ol (1c)



The corresponding compound was prepared following the **general procedure A** by using **furan** and **5-nonanone**. The reaction was run for 16 h and was determined to be complete by TLC and crude  $^1\text{H}$  NMR. The crude product was obtained as a yellowish oil and used in the subsequent reaction without purification.  $R_f = 0.40$  (Hexane:Ethyl acetate 4:1).  $^1\text{H}$  NMR (400 MHz,

Chloroform-*d*)  $\delta$  7.33 (dd,  $J = 1.8, 0.8$  Hz, 1H), 6.29 (dd,  $J = 3.2, 1.8$  Hz, 1H), 6.16 (dd,  $J = 3.2, 0.8$  Hz, 1H), 1.86 – 1.70 (m, 4H), 1.33 – 1.08 (m, 8H), 0.86 (t,  $J = 7.1$  Hz, 6H).

### 2,2-dibutyl-6-hydroxy-2H-pyran-3(6H)-one (2c)



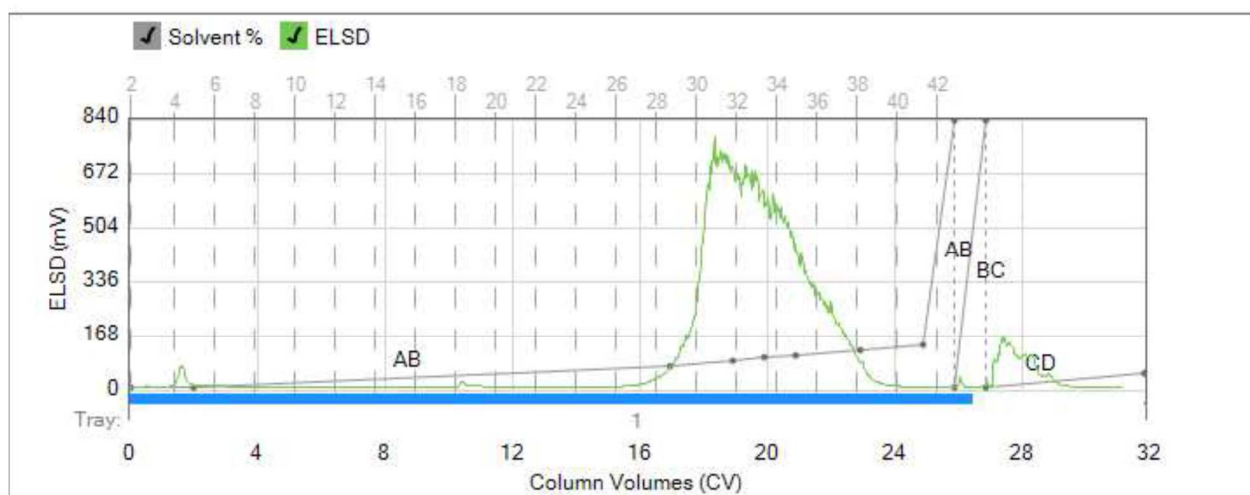
The corresponding compound was prepared following the **general procedure B** by using crude **5-(furan-2-yl)nonan-5-ol (1c)**. The reaction was run for 2 h and determined to be complete by TLC and  $^1\text{H}$  NMR. An elution of 0-16% ethyl acetate in hexane over 23 CV was used for purification on the flash chromatography system. The product was obtained as a yellowish oil (0.401 g, 89% yield).  $R_f = 0.18$  (Hexane:Ethyl acetate 4:1).  $^1\text{H}$  NMR (400 MHz, Chloroform-*d*)  $\delta$  6.84 (d,  $J = 10.3$  Hz, 1H), 6.06 (d,  $J = 10.3$  Hz, 1H), 5.71 (s, 1H), 2.99 (d,  $J = 6.5$  Hz, 1H), 1.93 - 1.54 (m, 5H), 1.44-1.18 (m, 8H), 0.88 (t,  $J = 6.9$  Hz, 6H).  $^{13}\text{C}$  NMR (101 MHz, Chloroform-*d*)  $\delta$  199.2, 145.4, 127.5, 87.9, 84.8, 37.3, 35.3, 25.7, 25.6, 23.2, 14.14, 14.11. HRMS (ESI):  $[\text{M-OH}]^+$  calcd for  $\text{C}_{13}\text{H}_{21}\text{O}_2^+$  209.1537, found 209.1534.

Column: Reveleris® Silica 12g  
Flow Rate: 30 mL/min  
Equilibration: 0.0 CV  
Run Length: 32.0 CV  
Mode: Flash Dry

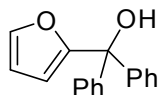
Solvent A: Hexane  
Solvent B: Ethyl acetate  
Solvent C: Acetone  
Solvent D: i-Propanol  
Slope Detection: Off

UV Threshold: N/A  
UV Sensitivity: Low  
UV1 Wavelength: N/A  
UV2 Wavelength: N/A  
UV3 Wavelength: N/A

ELSD Threshold: N/A  
ELSD Sensitivity: Low  
Collection: Collect None  
Per-Vial Volume: 15 mL  
Non-Peak Volume: 15 mL

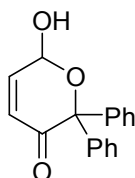


### furan-2-ylidiphenylmethanol (1d)



The corresponding compound was prepared following the **general procedure A** by using **furan** and **benzophenone** (added as a solution in diethyl ether). The reaction was run for 16 h and judged complete by TLC and crude  $^1\text{H}$  NMR. The crude product was obtained as a white solid and used in the subsequent reaction without purification.  $R_f = 0.33$  (Hexane:Ethyl acetate 4:1).  $^1\text{H}$  NMR (400 MHz, Chloroform-*d*)  $\delta$  7.45 (dd,  $J = 1.8, 0.9$  Hz, 1H), 7.35 – 7.28 (m, 10H), 6.33 (dd,  $J = 3.3, 1.8$  Hz, 1H), 5.92 (dd,  $J = 3.3, 0.8$  Hz, 1H), 3.06 (bs, 1H).

### 6-hydroxy-2,2-diphenyl-2H-pyran-3(6H)-one (2d)



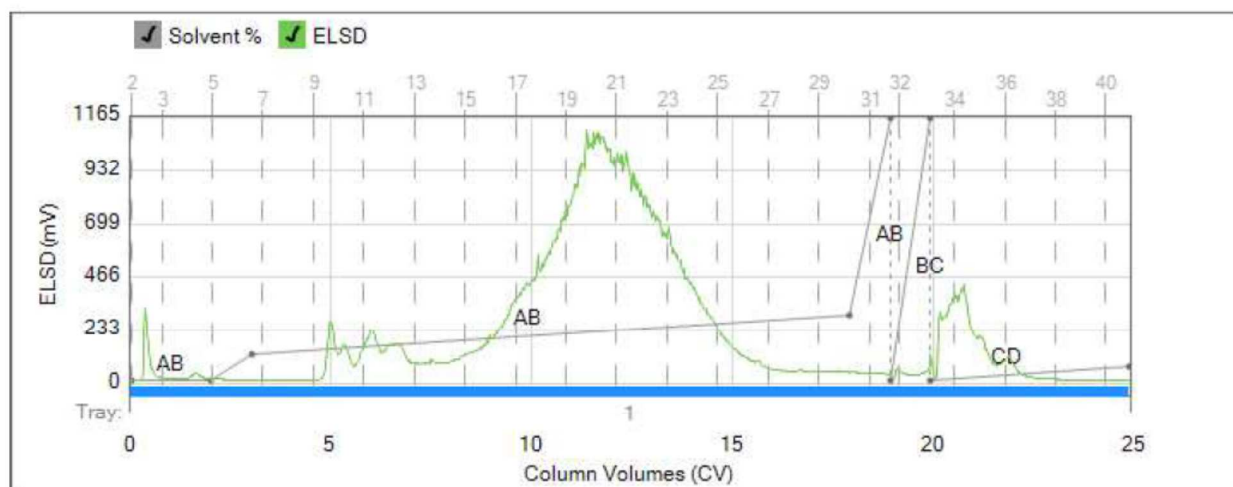
The corresponding compound was prepared following the **general procedure B** by using crude **furan-2-ylidiphenylmethanol (1d)**. The reaction was run for 2 h and determined to be complete by TLC and  $^1\text{H}$  NMR. An elution of 0-20% ethyl acetate in hexane over 15 CV was used for purification on the flash chromatography system. The product was obtained as a sticky yellow solid (0.401 g, 76% yield).  $R_f = 0.41$  (Hexane:Ethyl acetate 1:1).  $^1\text{H}$  NMR (400 MHz, Chloroform-*d*)  $\delta$  7.35 – 7.15 (m, 10H), 6.82 (d,  $J = 10.2$  Hz, 1H), 6.23 (d,  $J = 10.3$  Hz, 1H), 5.42 (bs, 1H).  $^{13}\text{C}$  NMR (101 MHz, Chloroform-*d*)  $\delta$  194.4, 147.4, 141.4, 137.6, 129.2, 128.8, 128.7, 128.0, 127.9, 127.7, 127.6, 89.0, 87.1. HRMS (ESI):  $[\text{M-OH}]^+$  calcd for  $\text{C}_{17}\text{H}_{13}\text{O}_2^+$  249.0911, found 249.0909.

Column: Reveleris® Silica 12g  
Flow Rate: 30 mL/min  
Equilibration: 0.0 CV  
Run Length: 25.0 CV  
Mode: Flash Dry

Solvent A: Hexane  
Solvent B: Ethyl acetate  
Solvent C: Acetone  
Solvent D: i-Propanol  
Slope Detection: Off

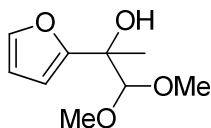
UV Threshold: N/A  
UV Sensitivity: High  
UV1 Wavelength: N/A  
UV2 Wavelength: N/A  
UV3 Wavelength: N/A

ELSD Threshold: N/A  
ELSD Sensitivity: Low  
Collection: Collect All  
Per-Vial Volume: 15 mL  
Non-Peak Volume: 15 mL



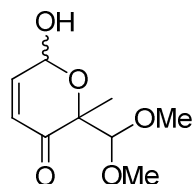


### 2-(furan-2-yl)-1,1-dimethoxypropan-2-ol (**1e**)



The corresponding compound was prepared following the **general procedure A** by using **furan** and **methylglyoxal 1,1-dimethyl acetal**. The reaction was run for 16 h and judged complete by TLC and crude  $^1\text{H}$  NMR. The crude product was obtained as a yellowish oil and used in the subsequent reaction without purification.  $R_f = 0.11$  (Hexane:Ethyl acetate 4:1).  $^1\text{H}$  NMR (400 MHz, Chloroform-*d*)  $\delta$  7.41 (dd,  $J = 1.8, 0.8$  Hz, 1H), 6.37 (dd,  $J = 3.3, 1.8$  Hz, 1H), 6.34 (dd,  $J = 3.3, 0.9$  Hz, 1H), 4.45 (s, 1H), 3.52 (s, 3H), 3.43 (s, 3H), 2.75 (bs, 1H), 1.56 (s, 3H).

### 2-(dimethoxymethyl)-6-hydroxy-2-methyl-2H-pyran-3(6H)-one (**2e**)



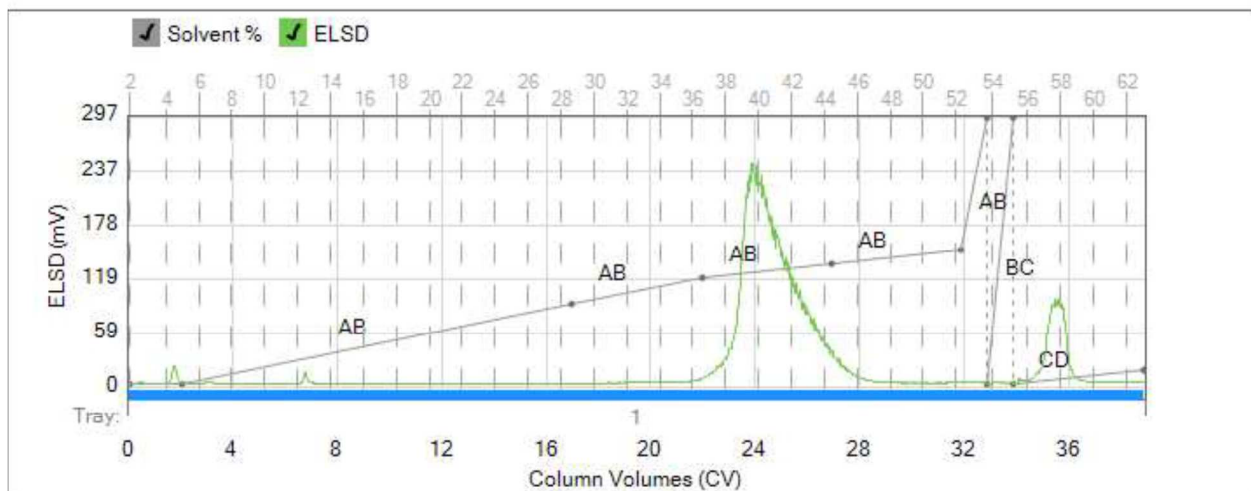
The corresponding compound was prepared following the **general procedure B** by using crude **2-(furan-2-yl)-1,1-dimethoxypropan-2-ol (1e)**. The reaction was run for 2 h and determined to be complete by TLC and  $^1\text{H}$  NMR. An elution of 0-50% ethyl acetate in hexane over 30 CV was used for purification on the flash chromatography system. The product was obtained as a mixture of diastereomers as a yellowish oil (0.183 g, 45% yield).  $R_f = 0.38$  (Hexane:Ethyl acetate 1:1).  $^1\text{H}$  NMR (400 MHz, Chloroform-*d*) Major isomer:  $\delta$  6.84 (dd,  $J = 10.3, 2.1$  Hz, 1H), 6.02 (dd,  $J = 10.4, 1.2$  Hz, 1H), 5.90 (m, 1H), 4.84 (bs, 1H), 4.36 (s, 1H), 3.49 (s, 3H), 3.33 (s, 3H), 1.40 (s, 3H). Minor isomer:  $\delta$  6.84 (dd,  $J = 10.4, 2.1$  Hz, 1H), 6.02 (dd,  $J = 10.4, 1.4$  Hz, 1H), 5.42 (m, 1H), 4.94 (bs, 1H), 4.31 (s, 1H), 3.52 (s, 3H), 3.40 (s, 3H), 1.32 (s, 3H).  $^{13}\text{C}$  NMR (101 MHz, Chloroform-*d*) Major isomer:  $\delta$  196.0, 146.5, 125.9, 106.8, 86.9, 83.4, 58.2, 57.8, 21.3. Minor isomer:  $\delta$  196.8, 146.8, 126.8, 108.6, 88.3, 83.3, 58.0, 57.5, 22.6. HRMS (ESI):  $[\text{M}+\text{Na}^+]^+$  calcd for  $\text{C}_9\text{H}_{14}\text{O}_5^+$  225.0734, found 225.0730.

Column: Reveleris® Silica 12g  
 Flow Rate: 30 mL/min  
 Equilibration: 0.0 CV  
 Run Length: 39.0 CV  
 Mode: Flash Dry

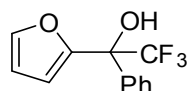
Solvent A: Hexane  
 Solvent B: Ethyl acetate  
 Solvent C: Acetone  
 Solvent D: i-Propanol  
 Slope Detection: Off

UV Threshold: N/A  
 UV Sensitivity: High  
 UV1 Wavelength: N/A  
 UV2 Wavelength: N/A  
 UV3 Wavelength: N/A

ELSD Threshold: N/A  
 ELSD Sensitivity: Low  
 Collection: Collect All  
 Per-Vial Volume: 15 mL  
 Non-Peak Volume: 15 mL

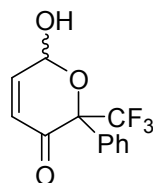


### 2,2,2-trifluoro-1-(furan-2-yl)-1-phenylethanol (**1f**)



The corresponding compound was prepared following the **general procedure A** by using **furan** and **2,2,2-trifluoroacetophenone**. The reaction was run for 16 h and judged complete by TLC and crude  $^1\text{H}$  NMR. The crude product was obtained as a yellowish oil and used in the subsequent reaction without purification.  $R_f = 0.26$  (Hexane:Ethyl acetate 4:1).  $^1\text{H}$  NMR (400 MHz, Chloroform-*d*)  $\delta$  7.61 – 7.33 (m, 6H), 6.50 (s, 1H), 6.42 (s, 1H).  $^{19}\text{F}$  NMR (376 MHz, Chloroform-*d*)  $\delta$  -77.06.

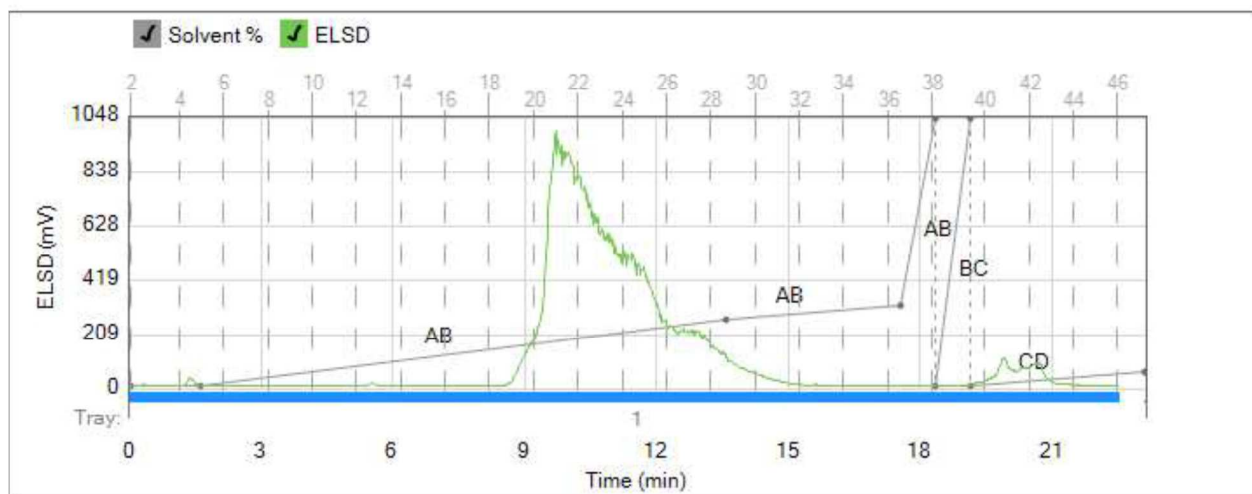
### 6-hydroxy-2-phenyl-2-(trifluoromethyl)-2H-pyran-3(6H)-one (**2f**)



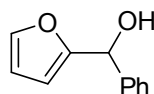
The corresponding compound was prepared following the **general procedure B** by using crude **2,2,2-trifluoro-1-(furan-2-yl)-1-phenylethanol (1f)**. The reaction was run for 6 h and determined to be complete by TLC and  $^1\text{H}$  NMR. An elution of 0-30% ethyl acetate in hexane over 16 CV was used for purification on the flash chromatography system. The product was obtained as a yellow solid comprised of a mixture of diastereomers (0.461 g, 89% yield).  $R_f = 0.46$  (Hexane:Ethyl acetate 1:1). mp = 91-93 °C;  $^1\text{H}$  NMR (400 MHz, Chloroform-*d*)  $\delta$  7.58 – 7.34 (m, 5H), 6.85 (d,  $J = 10.4$  Hz, 1H), 6.27 (d,  $J = 10.5$  Hz, 1H), 5.62 (s, 1H), 4.21 (bs, 1H). Minor isomer:  $\delta$  7.70 (d,  $J = 6.6$  Hz, 1H), 7.58 – 7.34 (m, 4H), 6.93 (d,  $J = 10.7$  Hz, 1H), 6.27 (d,

$J = 10.5$  Hz, 1H), 5.96 (s, 1H), 3.60 (bs, 1H).  $^{19}\text{F}$  NMR (376 MHz, Chloroform- $d$ )  $\delta$  -75.30, -76.12. HRMS (ESI):  $[\text{M-OH}]^+$  calcd for  $\text{C}_{12}\text{H}_8\text{F}_3\text{O}_2^+$  241.0471, found 241.0463.

Column: <none>	Solvent A: Hexane	UV Threshold: N/A	ELSD Threshold: N/A
Flow Rate: 30 mL/min	Solvent B: Ethyl acetate	UV Sensitivity: High	ELSD Sensitivity: Low
Equilibration: 0.0 min	Solvent C: Acetone	UV1 Wavelength: N/A	Collection: Collect All
Run Length: 23.2 min	Solvent D: i-Propanol	UV2 Wavelength: N/A	Per-Vial Volume: 15 mL
Mode: Flash Dry	Slope Detection: Off	UV3 Wavelength: N/A	Non-Peak Volume: 15 mL

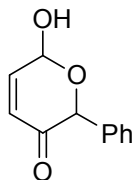


### furan-2-yl(phenyl)methanol (**1g**)



The corresponding compound was prepared following the **general procedure A** by using **furan** and **benzaldehyde**. The reaction was run for 16 h and judged complete by TLC and crude  $^1\text{H}$  NMR. The crude product was obtained as a yellowish oil and used in the subsequent reaction without purification.  $R_f = 0.22$  (Hexane:Ethyl acetate 4:1).  $^1\text{H}$  NMR (400 MHz, Chloroform- $d$ )  $\delta$  7.47 – 7.29 (m, 6H), 6.32 (dd,  $J = 3.2, 1.8$  Hz, 1H), 6.12 (dt,  $J = 3.3, 0.8$  Hz, 1H), 5.84 (d,  $J = 3.3$  Hz, 1H) 2.40 (d,  $J = 3.9$  Hz, 1H).

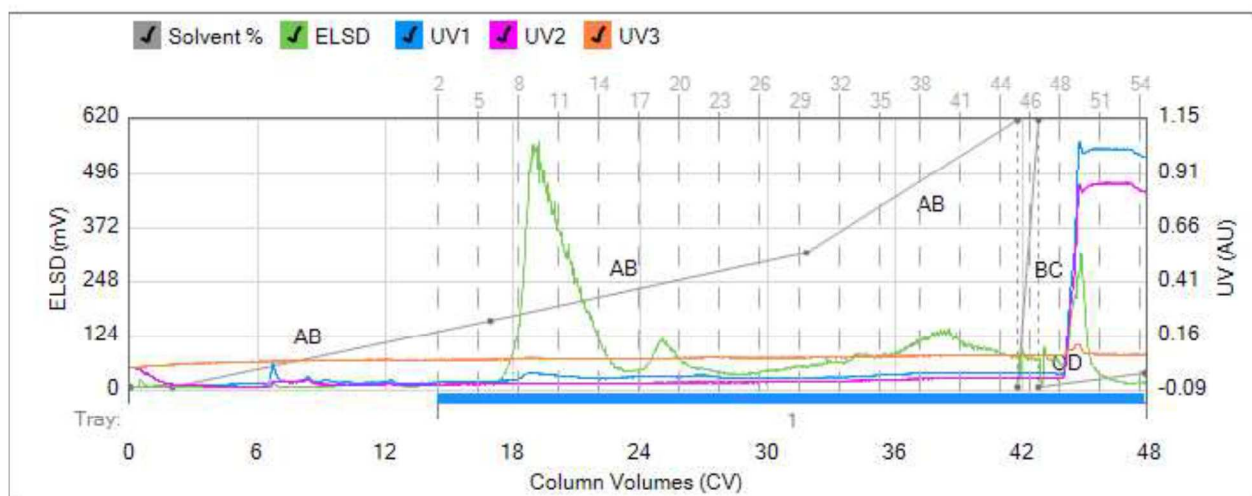
### 6-hydroxy-2-phenyl-2H-pyran-3(6H)-one (**2g**)



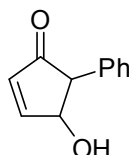
The corresponding compound was prepared following the **general procedure B** by using crude **furan-2-yl(phenyl)methanol (1g)**. The reaction was run for 2 h and determined to be complete by TLC and  $^1\text{H}$  NMR. An elution of 0-50% ethyl acetate in hexane over 30 CV was used for purification on the flash chromatography system. The product was obtained as a yellowish oil which darkened upon storage (0.181 g, 48% yield).  $R_f = 0.28$  (Hexane:Ethyl acetate

1:1).  $^1\text{H}$  NMR (400 MHz, Chloroform-*d*) Major isomer:  $\delta$  7.33 (m, 5H), 6.88 (m, 1H), 6.16 (m, 1H), 5.65 – 5.51 (m, 2H), 4.45 (bs, 1H). Minor isomer:  $\delta$  7.33 (m, 5H), 6.88 (m, 1H), 6.16 (m, 1H), 5.65 – 5.51 (m, 1H), 4.99 (s, 1H), 4.76 (bs, 1H).  $^{13}\text{C}$  NMR (101 MHz, Chloroform-*d*) Major isomer:  $\delta$  195.1, 145.5, 135.3, 128.7, 128.5, 128.0, 127.5, 87.8, 76.9. Minor isomer:  $\delta$  194.7, 149.0, 135.4, 129.1, 128.7, 128.5, 128.0, 91.4, 81.1. HRMS (ESI):  $[\text{M-OH}]^+$  calcd for  $\text{C}_{11}\text{H}_9\text{O}_2^+$  173.0598, found 173.0592.

Column: Revelenis® Silica 12g	Solvent A: Hexane	UV Threshold: N/A	ELSD Threshold: N/A
Flow Rate: 30 mL/min	Solvent B: Ethyl acetate	UV Sensitivity: High	ELSD Sensitivity: Low
Equilibration: 0.0 CV	Solvent C: Acetone	UV1 Wavelength: 254 nm	Collection: Collect All
Run Length: 48.0 CV	Solvent D: i-Propanol	UV2 Wavelength: 300 nm	Per-Vial Volume: 15 mL
Mode: Flash Dry	Slope Detection: Off	UV3 Wavelength: 345 nm	Non-Peak Volume: 15 mL

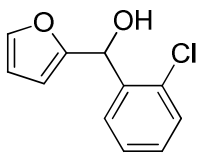


#### 4-hydroxy-5-phenylcyclopent-2-enone<sup>3</sup>

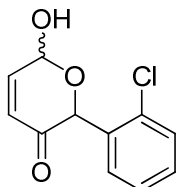


**4-hydroxy-5-phenylcyclopent-2-enone** was isolated as the major side-product for the conversion of **furan-2-yl(phenyl)methanol (1c)** to **6-hydroxy-2-phenyl-2H-pyran-3(6H)-one (2c)**.  $^1\text{H}$  NMR (400 MHz, Chloroform-*d*)  $\delta$  7.61 (dd,  $J = 5.8, 2.2$  Hz, 1H), 7.41 – 7.27 (m, 4H), 7.18 – 7.08 (m, 2H), 6.33 (d,  $J = 5.7$  Hz, 1H), 4.98 (s, 1H), 3.44 (d,  $J = 2.9$  Hz, 1H), 2.47 – 2.29 (m, 1H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  205.4, 161.7, 136.9, 134.7, 129.1, 128.5, 127.6, 79.2, 62.3. LRMS (ESI):  $[\text{M-OH}]^+$  calcd for  $\text{C}_{11}\text{H}_9\text{O}^+$  157.1, found 157.0.  $[\text{M+H}]^+$  calcd for  $\text{C}_{11}\text{H}_{11}\text{O}_2^+$  175.1, found 175.0.  $[\text{M+NH}_4]^+$  calcd for  $\text{C}_{11}\text{H}_{14}\text{NO}_2^+$  192.1, found 192.0.  $[\text{M+Na}]^+$  calcd for  $\text{C}_{11}\text{H}_{10}\text{NaO}_2^+$  197.1, found 197.0.

<sup>3</sup> Kalaitzakis, D.; Triantafyllakis, M.; Alexopoulou, I.; Sofiadis, M.; Vassilikogiannakis, G. *Angew. Chem. Int. Ed.* 2014, 53, 13201-13205.

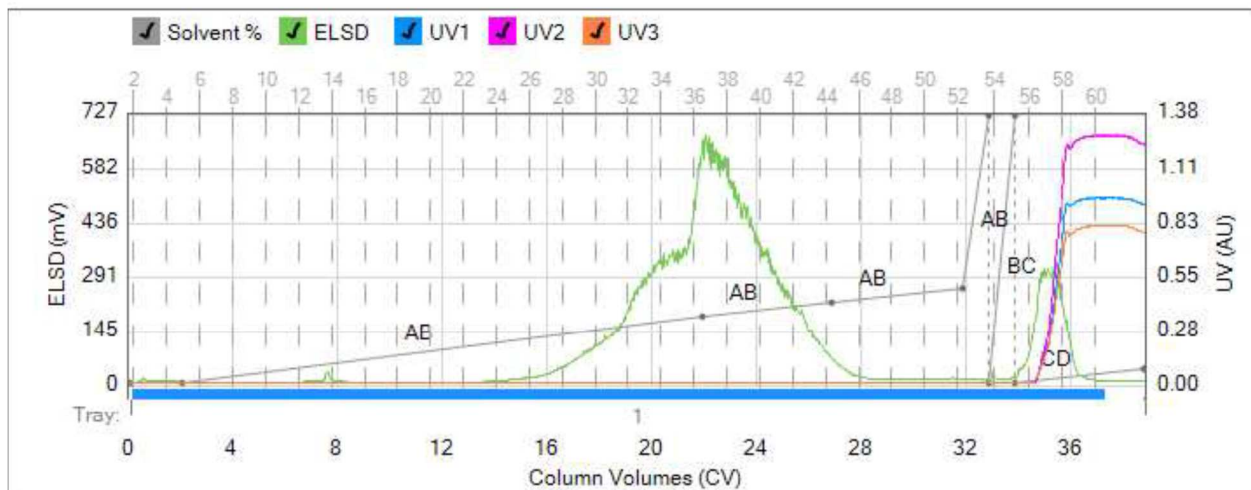
**(2-chlorophenyl)(furan-2-yl)methanol (1h)**

The corresponding compound was prepared following the **general procedure A** by using **furan** and **2-chlorobenzaldehyde**. **2-chlorobenzaldehyde** was purified by extracting once with saturated sodium bicarbonate and then drying over sodium sulfate. The reaction was run for 16 h and judged complete by TLC and crude  $^1\text{H}$  NMR. The crude product was obtained as a yellowish oil and used in the subsequent reaction without purification.  $R_f = 0.31$  (Hexane:Ethyl acetate 4:1).  $^1\text{H}$  NMR (400 MHz, Chloroform-*d*)  $\delta$  7.68 (dd,  $J = 7.6, 1.7$  Hz, 1H), 7.40 (m, 1H), 7.32-7.37 (m, 2H), 7.28 (dd,  $J = 7.7, 1.8$  Hz, 1H), 6.32 (dd,  $J = 3.3, 1.8$  Hz, 1H), 6.23 (s, 1H), 6.08 (d,  $J = 3.3$  Hz, 1H).

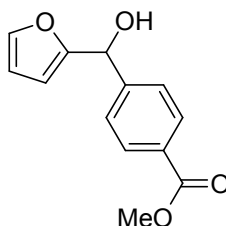
**2-(2-chlorophenyl)-6-hydroxy-2H-pyran-3(6H)-one (2h)**

The corresponding compound was prepared following the **general procedure B** by using crude **(2-chlorophenyl)(furan-2-yl)methanol (1h)**. The reaction was run for 2 h and determined to be complete by TLC and  $^1\text{H}$  NMR. An elution of 0-35% ethyl acetate in hexane over 30 CV was used for purification on the flash chromatography system. The product was obtained as a mixture of diastereomers as a yellowish oil (0.380 g, 85% yield).  $R_f = 0.28$  (Hexane:Ethyl acetate 1:1).  $^1\text{H}$  NMR (400 MHz, Chloroform-*d*) Major isomer:  $\delta$  7.36 – 7.32 (m, 1H), 7.31 – 7.27 (m, 1H), 7.25 – 7.17 (m, 2H), 6.87 (dd,  $J = 10.3, 3.6$  Hz, 1H), 6.15 (d,  $J = 10.3$  Hz, 1H), 5.95 (s, 1H), 5.66 (d,  $J = 3.5$  Hz, 1H), 3.48 (bs, 1H). Minor isomer:  $\delta$  7.37 – 7.32 (m, 1H), 7.30 – 7.27 (m, 1H), 7.25 – 7.18 (m, 2H), 6.92 – 6.89 (m, 1H), 6.20 (dd,  $J = 10.3, 1.6$  Hz, 1H), 5.74 (s, 1H), 5.46 (d,  $J = 1.2$  Hz, 1H), 3.75 (bs, 1H).  $^{13}\text{C}$  NMR (101 MHz, Chloroform-*d*) Major isomer:  $\delta$  193.8, 144.2, 134.5, 133.8, 130.1, 129.94, 129.86, 127.8, 127.1, 88.4, 74.3. Minor isomer:  $\delta$  193.2, 148.3, 134.1, 133.5, 130.1, 129.7, 129.4, 127.2, 92.1, 78.4. HRMS (ESI):  $[\text{M-OH}]^+$  calcd for  $\text{C}_{11}\text{H}_8\text{ClO}_2^+$  207.0208, found 207.0218.

Column: Reveleris® Silica 12g	Solvent A: Hexane	UV Threshold: N/A	ELSD Threshold: N/A
Flow Rate: 30 mL/min	Solvent B: Ethyl acetate	UV Sensitivity: High	ELSD Sensitivity: Low
Equilibration: 0.0 CV	Solvent C: Acetone	UV1 Wavelength: 254 nm	Collection: Collect None
Run Length: 39.0 CV	Solvent D: i-Propanol	UV2 Wavelength: 260 nm	Per-Vial Volume: 15 mL
Mode: Flash Dry	Slope Detection: Off	UV3 Wavelength: 300 nm	Non-Peak Volume: 15 mL

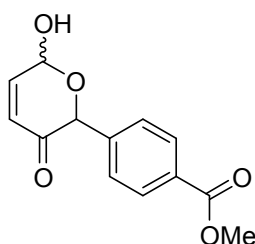


### methyl 4-(furan-2-yl(hydroxy)methyl)benzoate (**1i**)



The corresponding compound was prepared following a modified procedure reported by Ng et al.<sup>4</sup> To a solution of **furan** (0.436 g, 6.40 mmol, 3.2 equiv) in MeTHF (5 mL) at  $-20^{\circ}\text{C}$  was added *n*-BuLi (3.0 mL, 4.80 mmol, 1.6 M solution in hexanes). The reaction was allowed to stir at this temperature for 1 h. Then it was added to a slurry of copper(I) cyanide (0.215 g, 2.4 mmol, 1.2 equiv) in MeTHF (5 mL) at  $-20^{\circ}\text{C}$ . The reaction mixture quickly became clear after addition and was immediately cooled to  $-78^{\circ}\text{C}$ . Then a solution of **methyl 4-formylbenzoate** (0.328 g, 2.0 mmol) in MeTHF (2 mL) was added and left to stir and warm to room temperature over 16 h. The next day the reaction mixture was poured into a mixture of saturated ammonium chloride (20 mL) and water (20 mL). The aqueous layer quickly turned a deep blue. The extra water was to help dissolve and break up the copper solids that remained. The solution was extracted 3 times with ethyl acetate. The combined organic phase was dried over sodium sulfate and concentrated via rotary evaporator. The product **1i** was obtained as a yellow oil and was used in the subsequent step without further purification.  $R_f = 0.10$  (Hexane:Ethyl acetate 4:1).  $^1\text{H NMR}$  (400 MHz, Chloroform-*d*)  $\delta$  8.05 (d,  $J = 8.1$  Hz, 2H), 7.52 (d,  $J = 8.1$  Hz, 2H), 7.40 (s, 1H), 6.32 (s, 1H), 6.12 (d,  $J = 3.1$  Hz, 1H), 5.90 (s, 1H), 3.92 (s, 3H).

<sup>4</sup>Ng, J. S.; Behling, J. R.; Campbell, A. L.; Nguyen, D.; Lipshutz, B. *Tetrahedron Lett.* **1988**, *29*, 3045-3048.

**methyl 4-(6-hydroxy-3-oxo-3,6-dihydro-2H-pyran-2-yl)benzoate (2i)**


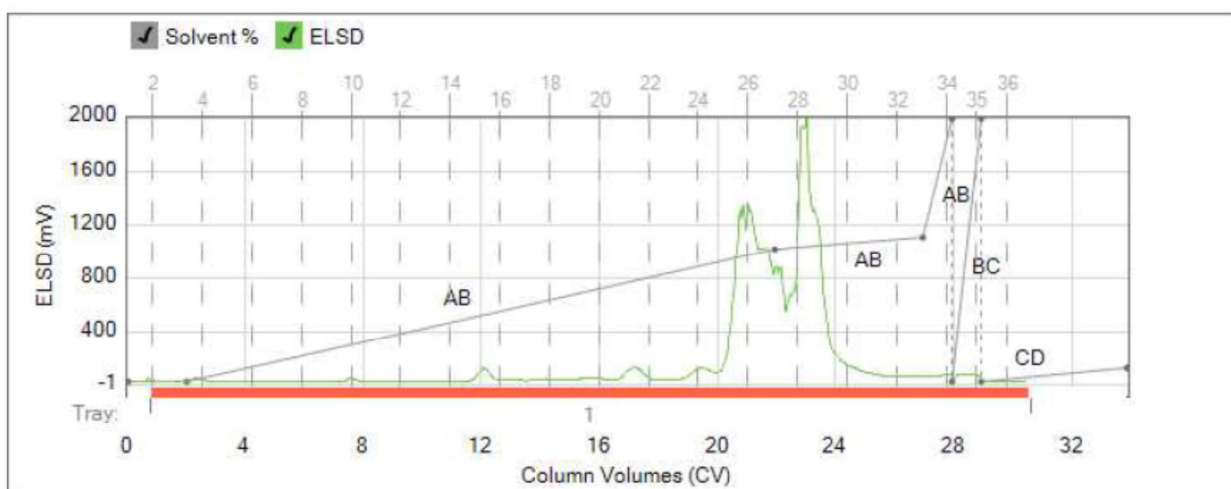
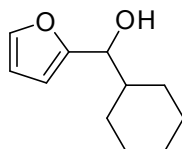
The corresponding compound was prepared following the **general procedure B** by using crude **methyl 4-(furan-2-yl(hydroxy)methyl)benzoate (1i)**. The reaction was run for 2 h and determined to be complete by TLC and  $^1\text{H}$  NMR. An elution of 0-55% ethyl acetate in hexane over 25 CV was used for purification on the flash chromatography system. The product was obtained as a mixture of diastereomers as a white solid (0.313 g, 63% yield).  $R_f = 0.15$  (Hexane:Ethyl acetate 1:1). mp = 135-136.  $^1\text{H}$  NMR (400 MHz, Chloroform-*d*) Major isomer:  $\delta$  8.05 (d,  $J = 8.1$  Hz, 3H), 7.44 (d,  $J = 8.5$  Hz, 2H), 7.02 (dd,  $J = 10.3, 3.3$  Hz, 1H), 6.23 (d,  $J = 10.3$  Hz, 1H), 5.82 (d,  $J = 2.8$  Hz, 1H), 5.67 (s, 1H), 3.92 (s, 3H). Minor isomer:  $\delta$  8.05 (d,  $J = 8.1$  Hz, 2H), 7.47 (d,  $J = 8.8$  Hz, 2H), 7.06 (d,  $J = 10.4$  Hz, 1H), 6.29 (d,  $J = 10.7$  Hz, 1H), 5.87 (bs, 1H), 5.18 (s, 1H).  $^{13}\text{C}$  NMR (101 MHz, Chloroform-*d*)  $\delta$  193.6, 193.2, 167.0, 148.3, 144.7, 140.20, 140.15, 130.3, 129.74, 129.72, 129.4, 127.92, 127.85, 127.7, 110.2, 91.7, 88.3, 80.5, 76.3, 52.38, 52.37. HRMS (ESI):  $[\text{M-OH}]^+$  calcd for  $\text{C}_{13}\text{H}_{11}\text{O}_4^+$  231.0652, found 231.0662.

Column: Generic Silica 12g  
Flow Rate: 28 mL/min  
Equilibration: 0.0 CV  
Run Length: 34.0 CV  
Mode: Flash Dry

Solvent A: Hexane  
Solvent B: Ethyl acetate  
Solvent C: Acetone  
Solvent D: i-Propanol  
Slope Detection: Off

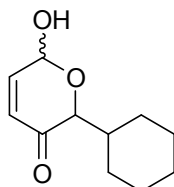
UV Threshold: N/A  
UV Sensitivity: High  
UV1 Wavelength: N/A  
UV2 Wavelength: N/A  
UV3 Wavelength: N/A

ELSD Threshold: N/A  
ELSD Sensitivity: Low  
Collection: Collect All  
Per-Vial Volume: 15 mL  
Non-Peak Volume: 15 mL


**cyclohexyl(furan-2-yl)methanol (1j)**


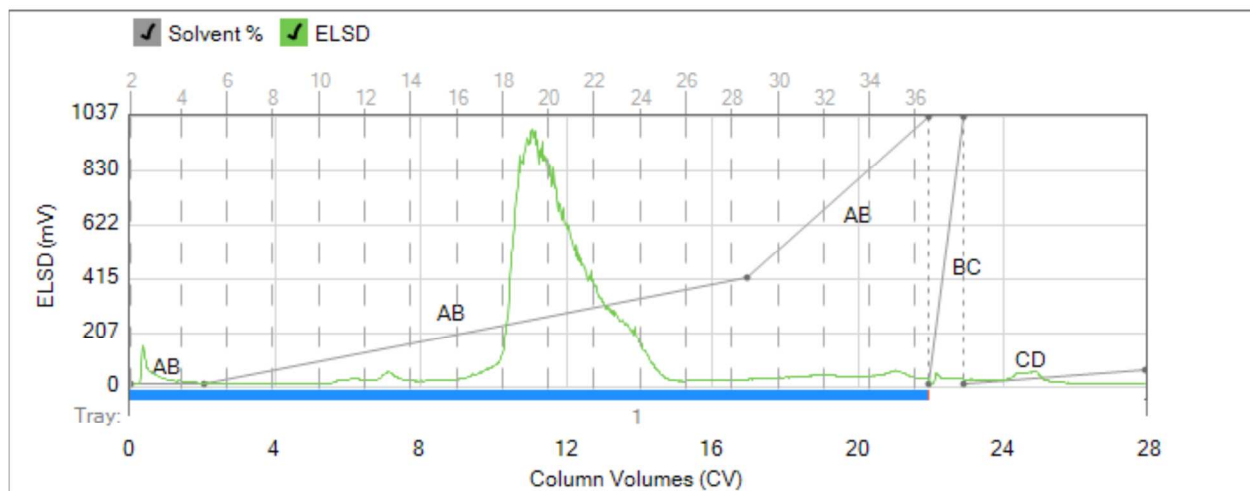
The corresponding compound was prepared following the **general procedure A** by using **furan** and **cyclohexylcarbaldehyde**. The reaction was run for 16 h and judged complete by TLC and crude  $^1\text{H}$  NMR. The crude product was obtained as a yellowish oil and used in the subsequent reaction without purification.  $R_f = 0.26$  (Hexane:Ethyl acetate 4:1).  $^1\text{H}$  NMR (400 MHz, Chloroform- $d$ )  $\delta$  7.38 (dd,  $J = 1.8, 0.8$  Hz, 1H), 6.33 (dd,  $J = 3.2, 1.8$  Hz, 1H), 6.22 (d,  $J = 3.2$  Hz, 1H), 4.38 (d,  $J = 7.5$  Hz, 1H), 2.13 – 0.83 (m, 11H).

### 2-cyclohexyl-6-hydroxy-2H-pyran-3(6H)-one (2j)

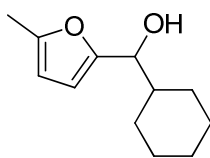


The corresponding compound was prepared following the **general procedure B** by using crude **cyclohexyl(furan-2-yl)methanol (1j)**. The reaction was run for 2 h and complete by TLC and  $^1\text{H}$  NMR. An elution of 0-40% ethyl acetate in hexane over 15 CV was used for purification on the flash chromatography system. The product was obtained as a mixture of diastereomers as a clear, colorless oil (0.335 g, 86% yield).  $R_f = 0.39$  (Hexane:Ethyl acetate 3:4)  $^1\text{H}$  NMR (400 MHz, Chloroform- $d$ ) Major isomer:  $\delta$  6.89 (dd,  $J = 10.3, 3.4$  Hz, 1H), 6.09 (s, 1H), 5.66 (d,  $J = 3.4$  Hz, 1H), 4.38 (d,  $J = 3.1$  Hz, 1H), 2.94 (bs, 1H), 2.11 (m, 1H), 1.84 – 1.54 (m, 4H), 1.50 – 1.03 (m, 6H). Minor isomer:  $\delta$  6.92 (dd,  $J = 8.9, 1.4$  Hz, 1H), 6.14 (dd,  $J = 10.2, 1.6$  Hz, 1H), 5.62 (d,  $J = 1.9$  Hz, 1H), 3.88 (dd,  $J = 3.5, 1.4$  Hz, 0H), 3.18 (bs, 1H), 2.11 (m, 1H), 1.84 – 1.54 (m, 6H), 1.50 – 1.03 (m, 8H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{cdCl}_3$ )  $\delta$  196.6, 196.2, 147.9, 144.3, 129.7, 128.4, 91.3, 87.8, 83.2, 78.6, 38.8, 38.6, 29.6, 29.5, 26.8, 26.7, 26.6, 26.6, 26.3, 26.3, 26.3. HRMS (ESI):  $[\text{M-OH}]^+$  calcd for  $\text{C}_{11}\text{H}_{15}\text{O}_2^+$  179.1067, found 179.1063.

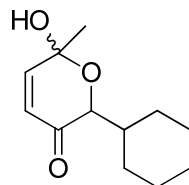
Column: Revelens® Silica 12g	Solvent A: Hexane	UV Threshold: N/A	ELSD Threshold: N/A
Flow Rate: 30 mL/min	Solvent B: Ethyl acetate	UV Sensitivity: Low	ELSD Sensitivity: Low
Equilibration: 0.0 CV	Solvent C: Acetone	UV1 Wavelength: N/A	Collection: Collect None
Run Length: 28.0 CV	Solvent D: i-Propanol	UV2 Wavelength: N/A	Per-Vial Volume: 15 mL
Mode: Flash Dry	Slope Detection: Off	UV3 Wavelength: N/A	Non-Peak Volume: 15 mL





**cyclohexyl(5-methylfuran-2-yl)methanol (1k)**

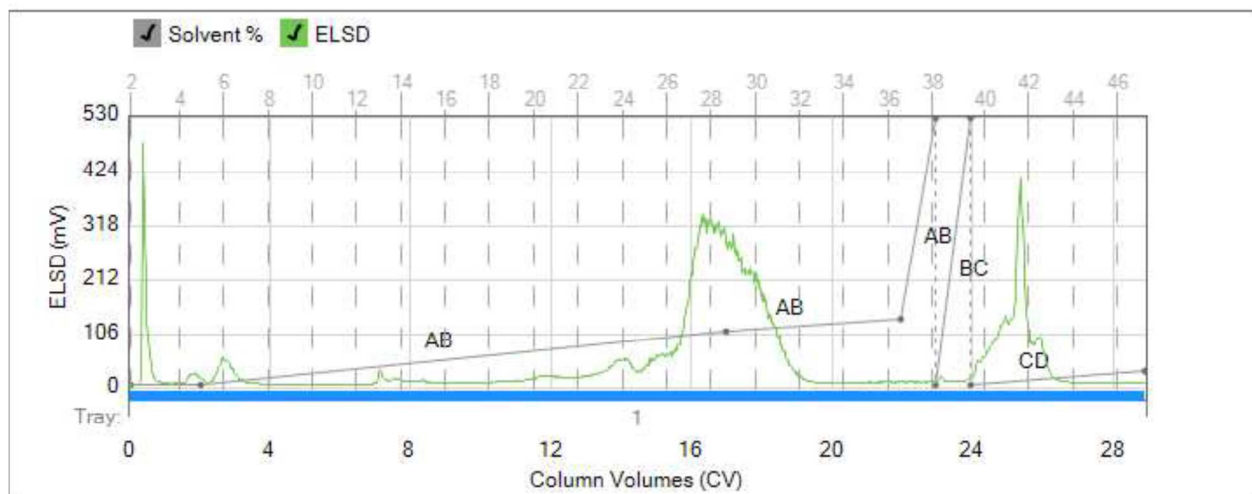
The corresponding compound was prepared following a modified **general procedure A** by using **2-methylfuran** and **cyclohexylcarbaldehyde**. The 2-methylfuran and *n*-BuLi were stirred for 5 hours at 0° C, rather than 1 hour. After the addition of **cyclohexylcarbaldehyde**, the reaction was run for 16 h and judged complete by TLC and crude <sup>1</sup>H NMR. The crude product was obtained as a clear oil and used in the subsequent reaction without purification.  $R_f = 0.28$  (Hexane:Ethyl acetate 4:1). <sup>1</sup>H NMR (400 MHz, Chloroform-*d*)  $\delta$  6.08 (d,  $J = 3.0$  Hz, 1H), 5.93 – 5.85 (m, 1H), 4.29 (d,  $J = 7.7$  Hz, 1H), 2.28 (s, 3H), 1.83 – 1.72 (m, 2H), 1.70 - 1.59 (m, 2H), 1.53 – 0.97 (m, 6H).

**2-cyclohexyl-6-hydroxy-6-methyl-2H-pyran-3(6H)-one (2k)**

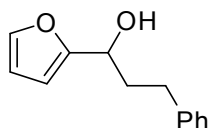
The corresponding compound was prepared following the **general procedure B** by using crude **cyclohexyl(5-methylfuran-2-yl)methanol (1k)**. The reaction was run for 2 h and complete by TLC and <sup>1</sup>H NMR. An elution of 0-25% ethyl acetate in hexane over 20 CV was used for purification on the flash chromatography system. The product was obtained as a mixture of diastereomers as a white solid (0.242 g, 58% yield).  $R_f = 0.46$  (Hexane:Ethyl acetate 1:1). mp = 126-128° C; Compound **2g** could be analyzed by <sup>1</sup>H NMR in Chloroform-*d* immediately after dissolution, however it quickly became a mixture of compounds and was therefore characterized

as such (see page 50). HRMS (ESI):  $[M-OH]^+$  calcd for  $C_{12}H_{17}O_2^+$  193.1224, found 193.1221.

Column: Reveleris® Silica 12g	Solvent A: Hexane	UV Threshold: N/A	ELSD Threshold: N/A
Flow Rate: 30 mL/min	Solvent B: Ethyl acetate	UV Sensitivity: High	ELSD Sensitivity: Low
Equilibration: 0.0 CV	Solvent C: Acetone	UV1 Wavelength: N/A	Collection: Collect All
Run Length: 29.0 CV	Solvent D: i-Propanol	UV2 Wavelength: N/A	Per-Vial Volume: 15 mL
Mode: Flash Dry	Slope Detection: Off	UV3 Wavelength: N/A	Non-Peak Volume: 15 mL

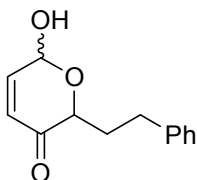


### 1-(furan-2-yl)-3-phenylpropan-1-ol (11)



The corresponding compound was prepared following the **general procedure A** by using **furan** and **hydrocinnamaldehyde**. The reaction was run for 16 h and judged complete by TLC and crude  $^1H$  NMR. The crude product was obtained as a yellowish oil and used in the subsequent reaction without purification.  $R_f = 0.22$  (Hexane:Ethyl acetate 4:1).  $^1H$  NMR (400 MHz, Chloroform- $d$ )  $\delta$  7.37 (d,  $J = 1.8$  Hz, 1H), 7.30 – 7.25 (m, 2H), 7.19 (d,  $J = 7.6$  Hz, 3H), 6.35 – 6.29 (m, 1H), 6.23 (d,  $J = 3.3$  Hz, 1H), 4.67 (t,  $J = 6.8$  Hz, 1H), 2.82 – 2.62 (m, 2H), 2.23 – 2.10 (m, 2H).

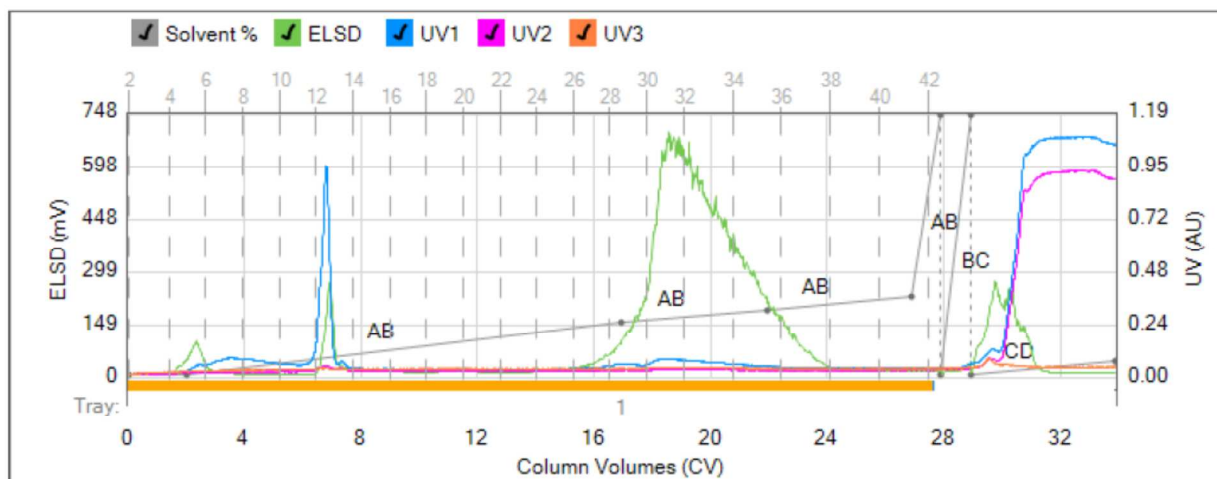
### 6-hydroxy-2-phenethyl-2H-pyran-3(6H)-one (21)



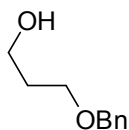
The corresponding compound was prepared following the **general procedure B** by using crude **1-(furan-2-yl)-3-phenylpropan-1-ol (11)**. The reaction was run for 2 h and determined to be complete by TLC and  $^1H$  NMR. An elution of 0-30% ethyl acetate in hexane over 25 CV was used for purification on the flash chromatography system. The product was obtained as a mixture of diastereomers as a yellowish oil (0.307 g, 71% yield).  $R_f = 0.27$  (Hexane:Ethyl acetate 1:1).

$^1\text{H}$  NMR (400 MHz, Chloroform-*d*) Major isomer:  $\delta$  7.27 – 7.06 (m, 5H), 6.84 (d,  $J$  = 10.5 Hz, 1H), 6.03 (d,  $J$  = 10.3 Hz, 1H), 5.61 (s, 1H), 4.48 (d,  $J$  = 8.3 Hz, 1H), 2.95 (bs, 1H), 2.60 - 2.80 (m, 2H), 2.27 – 2.14 (m, 1H), 2.00 – 1.89 (m, 1H). Minor isomer:  $\delta$  7.27 – 7.06 (m, 5H), 6.86 (d,  $J$  = 10.6 Hz, 1H), 6.08 (d,  $J$  = 10.7 Hz, 1H), 5.58 (s, 1H), 3.97 (d,  $J$  = 8.8 Hz, 1H), 3.24 (bs, 1H), 2.60 – 2.80 (m, 2H), 2.27 – 2.14 (m, 1H), 2.08 – 1.99 (m, 1H).  $^{13}\text{C}$  NMR (101 MHz, Chloroform-*d*) Major isomer:  $\delta$  196.5, 144.3, 141.5, 128.7, 128.55, 126.16, 87.9, 73.3, 31.5, 31.1. Minor isomer:  $\delta$  196.1, 147.7, 141.3, 129.0, 128.8, 128.58, 126.19, 91.1, 77.9, 32.3, 31.2. HRMS (ESI):  $[\text{M}-\text{OH}]^+$  calcd for  $\text{C}_{13}\text{H}_{13}\text{O}_2^+$  201.0911, found 201.0908.

Column: Reveleris® Silica 12g	Solvent A: Hexane	UV Threshold: N/A	ELSD Threshold: N/A
Flow Rate: 30 mL/min	Solvent B: Ethyl acetate	UV Sensitivity: High	ELSD Sensitivity: Low
Equilibration: 0.0 CV	Solvent C: Acetone	UV1 Wavelength: 254 nm	Collection: Collect None
Run Length: 34.0 CV	Solvent D: i-Propanol	UV2 Wavelength: 300 nm	Per-Vial Volume: 20 mL
Mode: Flash Dry	Slope Detection: Off	UV3 Wavelength: 345 nm	Non-Peak Volume: 20 mL



### 3-(benzyloxy)propan-1-ol

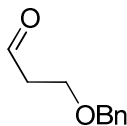


**3-(benzyloxy)propan-1-ol** was prepared using a modified procedure reported by Fonvielle et al.<sup>5</sup> To a slurry of sodium hydride (3.40 g, 85 mmol, 1 equiv) in DMF (100 mL) at 0° C was added slowly, a solution of propane-1,3-diol (25.9 g, 340 mmol, 4 equiv) in DMF (25 mL). The reaction mixture was allowed to stir for 1 h at which point the effervescence had nearly stopped. Then benzyl bromide (10.1 mL, 85 mmol, 1 equiv) was added and the reaction mixture was allowed to stir and warm over 16 h. Then reaction mixture was diluted with 100 mL water, extracted 5 times with diethyl ether, dried with sodium sulfate and concentrated via rotary evaporator. The resulting viscous liquid was directly injected into flash chromatography system and purified using an elution of 0-40% over 20 CV. The product was obtained as a clear colorless liquid (8.99

<sup>5</sup>Fonvielle, M.; Coinçon, M.; Daher, R.; Desbenoit, N.; Kosieradzka, K.; Barilone, N.; Gicquel, B.; Sygusch, J.; Jackson, M.; Therisod, M. *Chem. Eur. J.* **2008**, *14*, 8521-8529.

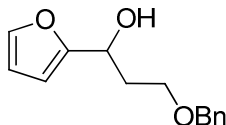
g, 64% yield).  $R_f = 0.16$  (Hexane:Ethyl acetate 3:2).  $^1\text{H NMR}$  (400 MHz, Chloroform-*d*)  $\delta$  7.42 – 7.20 (m, 5H), 4.53 (s, 2H), 3.79 (t,  $J = 5.6$  Hz, 2H), 3.67 (t,  $J = 5.8$  Hz, 2H), 2.16 (bs, 1H), 1.87 (quint,  $J = 5.7$  Hz, 2H).  $^{13}\text{C NMR}$  (101 MHz, Chloroform-*d*)  $\delta$  138.2, 128.6, 127.9, 127.8, 73.4, 69.6, 62.1, 32.2.

### 3-(benzyloxy)propanal



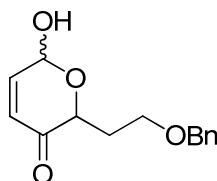
To a slurry of PCC (7.78 g, 36.1 mmol, 1.5 equiv) and celite (7.8 g) in  $\text{CH}_2\text{Cl}_2$  (75 mL) was added drop-wise a solution of **3-(benzyloxy)propan-1-ol** (4.0 g, 24.06 mmol) in  $\text{CH}_2\text{Cl}_2$  (25 mL). The reaction mixture was allowed to stir at room temperature for 16 h at which point, the black solid was filtered over a bed of celite and washed with  $\text{CH}_2\text{Cl}_2$ . The solution was concentrated into a brown liquid which was directly injected into the chromatography system and purified using an elution of 0-16% over 20 CV. The product was obtained as a clear colorless liquid (1.86 g, 47% yield).  $R_f = 0.18$  (Hexane:Ethyl acetate 5:1).  $^1\text{H NMR}$  (400 MHz, Chloroform-*d*)  $\delta$  9.80 (t,  $J = 1.8$  Hz, 1H), 7.39 – 7.23 (m, 6H), 4.54 (s, 2H), 3.82 (t,  $J = 6.1$  Hz, 2H), 2.70 (td,  $J = 6.1, 1.8$  Hz, 2H).  $^{13}\text{C NMR}$  (101 MHz, Chloroform-*d*)  $\delta$  201.3, 138.0, 128.6, 127.93, 127.85, 73.4, 64.0, 44.0.

### 3-(benzyloxy)-1-(furan-2-yl)propan-1-ol (1m)



The corresponding compound was prepared following the **general procedure A** by using **furan** and **3-(benzyloxy)propanal**. The reaction was run for 16 h and judged complete by TLC and crude  $^1\text{H NMR}$ . The crude product was obtained as an orangish oil and used in the subsequent reaction without purification.  $R_f = 0.13$  (Hexane:Ethyl acetate 4:1).  $^1\text{H NMR}$  (400 MHz, Chloroform-*d*)  $\delta$  7.40 – 7.27 (m, 7H), 6.32 (dd,  $J = 3.1, 1.8$  Hz, 1H), 6.24 (d,  $J = 3.2$  Hz, 1H), 4.95 (dd,  $J = 6.9, 5.2$  Hz, 1H), 4.53 (s, 2H), 3.75 – 3.60 (m, 2H), 3.11 (bs, 1H), 2.16 (m, 2H).

### 2-(2-(benzyloxy)ethyl)-6-hydroxy-2H-pyran-3(6H)-one (2m)



The corresponding compound was prepared following the **general procedure B** by using crude **3-(benzyloxy)-1-(furan-2-yl)propan-1-ol (1m)**. The reaction was run for 2 h and

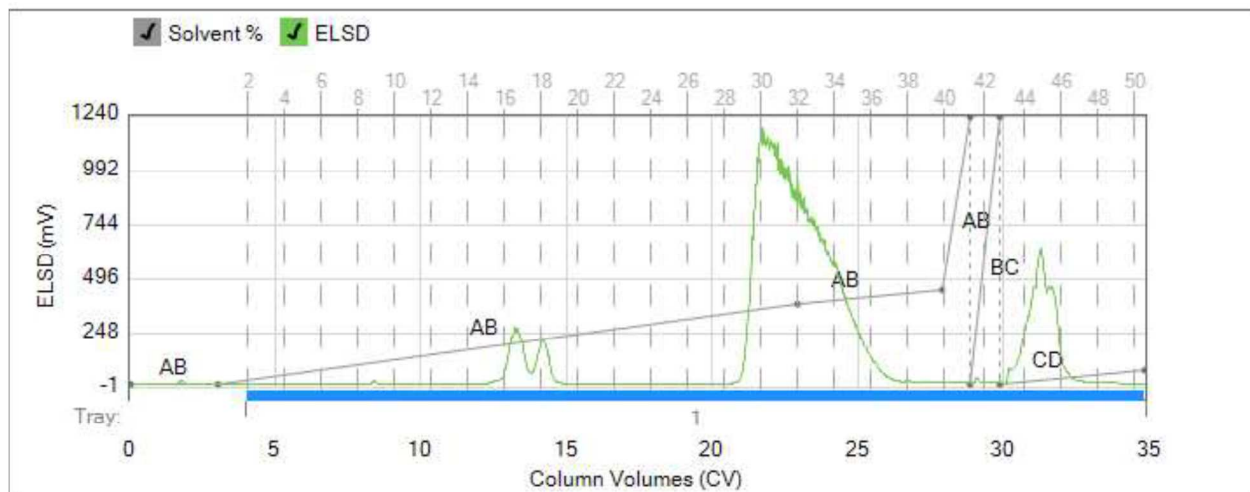
determined to be complete by TLC and  $^1\text{H}$  NMR. An elution of 0-35% ethyl acetate in hexane over 25 CV was used for purification on the flash chromatography system. The product was obtained as a mixture of diastereomers as a clear colorless oil (0.355 g, 72% yield).  $R_f = 0.22$  (Hexane:Ethyl acetate 1:1).  $^1\text{H}$  NMR (400 MHz, Chloroform-*d*) Major isomer:  $\delta$  7.37 – 7.27 (m, 5H), 6.82 (dd,  $J = 10.3, 3.5$  Hz, 1H), 6.07 (d,  $J = 10.3$  Hz, 1H), 5.52 (d,  $J = 3.5$  Hz, 1H), 4.73 (dd,  $J = 8.2, 4.0$  Hz, 1H), 4.56 – 4.44 (m, 2H), 3.90 (bs, 1H), 3.71 – 3.58 (m, 2H), 2.39 – 2.26 (m, 1H), 2.05 – 1.79 (m, 1H). Minor isomer:  $\delta$  7.37 – 7.27 (m, 5H), 6.87 – 6.84 (m, 1H), 6.10 (dd,  $J = 10.3, 1.5$  Hz, 1H), 5.54 – 5.49 (m, 1H), 4.56 – 4.44 (m, 2H), 4.25 (dd,  $J = 8.7, 3.9$  Hz, 1H), 3.71 – 3.58 (m, 2H), 2.39 – 2.26 (m, 1H), 2.05 – 1.79 (m, 1H).  $^{13}\text{C}$  NMR (101 MHz, Chloroform-*d*) Major isomer:  $\delta$  196.6, 144.5, 138.24, 128.5, 127.91, 127.78, 127.5, 87.6, 72.7, 71.1, 65.8, 29.7. Minor isomer:  $\delta$  196.3, 148.1, 138.21, 128.6, 128.5, 127.92, 127.80, 90.8, 75.8, 72.9, 65.8, 30.8. HRMS (ESI):  $[\text{M}+\text{Na}^+]^+$  calcd for  $\text{C}_{14}\text{H}_{16}\text{NaO}_4^+$  271.0941, found 271.0945.

Column: Reveleris® Silica 12g  
Flow Rate: 30 mL/min  
Equilibration: 3.3 CV  
Run Length: 35.0 CV  
Mode: Flash Dry

Solvent A: Hexane  
Solvent B: Ethyl acetate  
Solvent C: Acetone  
Solvent D: i-Propanol  
Slope Detection: Off

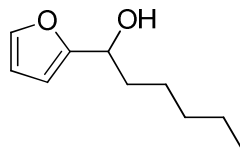
UV Threshold: N/A  
UV Sensitivity: High  
UV1 Wavelength: N/A  
UV2 Wavelength: N/A  
UV3 Wavelength: N/A

ELSD Threshold: N/A  
ELSD Sensitivity: Low  
Collection: Collect All  
Per-Vial Volume: 15 mL  
Non-Peak Volume: 15 mL



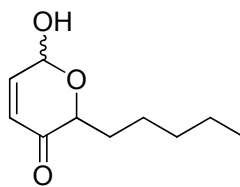
## Formal synthesis of ( $\pm$ )-Monanchorin: Synthesis of *tert*-butyl (5-oxo-6-pentyl-5,6-dihydro-2*H*-pyran-2-yl) carbonate

### 1-(furan-2-yl)hexan-1-ol (**1n**)



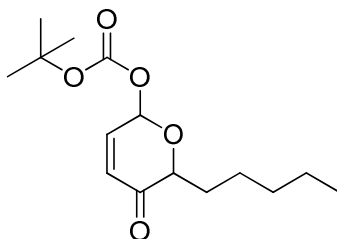
The corresponding compound was prepared following the **general procedure A** by using **furan** and **hexanal**. The reaction was run for 16 h and judged complete by TLC and crude  $^1\text{H}$  NMR. The crude product was obtained as a yellowish oil and used in the subsequent reaction without purification.  $R_f = 0.22$  (Hexane:Ethyl acetate 4:1).  $^1\text{H}$  NMR (400 MHz, Chloroform-*d*)  $\delta$  7.40 (d,  $J = 1.8$  Hz, 1H), 6.35 (dd,  $J = 3.2, 1.9$  Hz, 1H), 6.25 (d,  $J = 3.2$  Hz, 1H), 4.70 (t,  $J = 6.8$  Hz, 1H), 1.92 – 1.82 (m, 2H), 1.59 (bs, 1H), 1.52 – 1.41 (m, 1H), 1.39 – 1.31 (m, 5H), 0.95 – 0.87 (m, 3H).

### 6-hydroxy-2-pentyl-2*H*-pyran-3(6*H*)-one (**2n**)



The corresponding compound was prepared following the **general procedure B** by using crude **1-(furan-2-yl)hexan-1-ol (1n)**. The reaction was run for 3 h and determined to be complete by TLC and  $^1\text{H}$  NMR. The product was obtained as a mixture of diastereomers as a yellowish oil.  $R_f = 0.38$  (Hexane:Ethyl acetate 1:1).  $^1\text{H}$  NMR (400 MHz, Chloroform-*d*) Major isomer:  $\delta$  6.92 (dd,  $J = 10.2, 3.4$  Hz, 1H), 6.13 (d,  $J = 10.2$  Hz, 1H), 5.68 (s, 1H), 4.58 (dd,  $J = 8.1, 3.8$  Hz, 1H) signals below 2 ppm were indecipherable from minor isomer. Minor isomer:  $\delta$  6.95 (dd,  $J = 10.4, 1.7$  Hz, 1H), 6.17 (dd,  $J = 10.3, 1.6$  Hz, 1H), 5.68 (s, 1H), 4.10 (ddd,  $J = 8.3, 4.0, 1.2$  Hz, 1H), signals below 2 ppm were indecipherable from major isomer.

### *tert*-butyl (5-oxo-6-pentyl-5,6-dihydro-2*H*-pyran-2-yl) carbonate (**4n**)

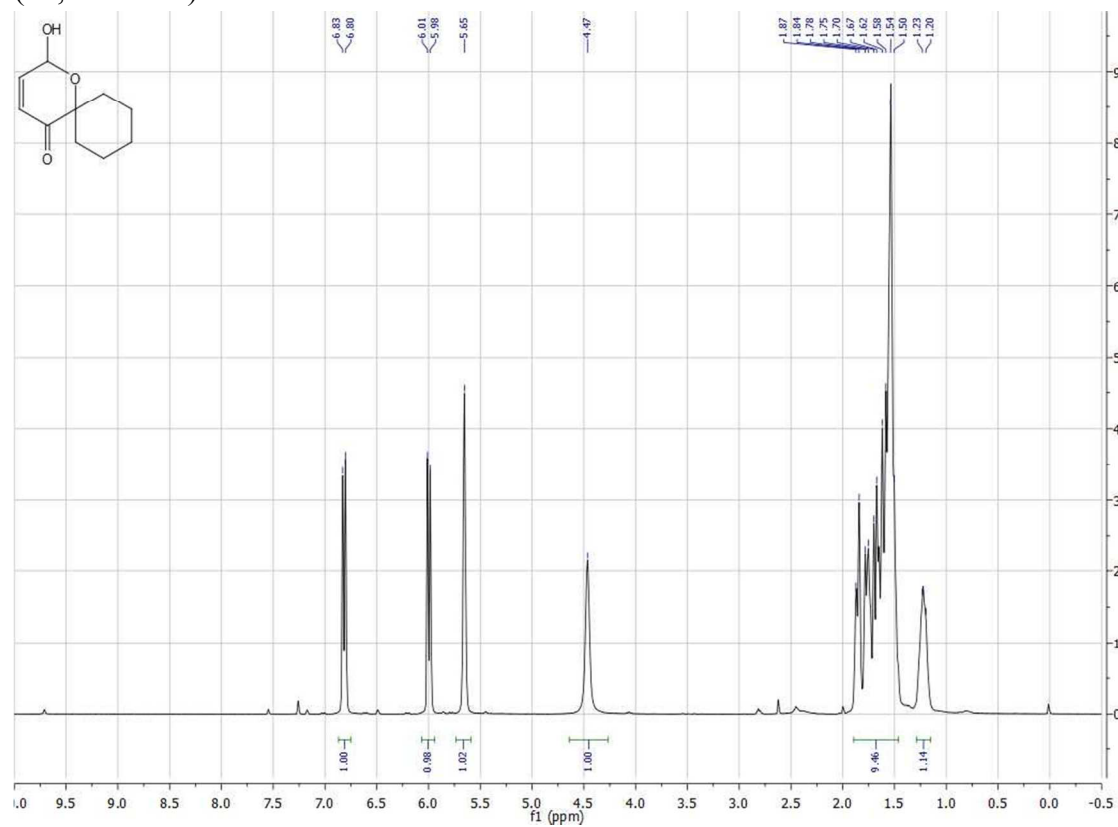


To a stirred solution of crude **6-hydroxy-2-pentyl-2*H*-pyran-3(6*H*)-one (2n)** (2 mmol) in 6 mL of anhydrous DCM was added at  $0^\circ\text{C}$  di-*tert*-butyl dicarbonate (0.655 g, 3.0 mmol, 1.5 equiv.), triethylamine (0.304 g, 3.0 mmol, 1.5 equiv.) and *N,N*-dimethylpyridin-4-amine (0.012 g, 0.05 equiv.) in 2 mL of anhydrous DCM. The reaction was allowed to stir and warm to room

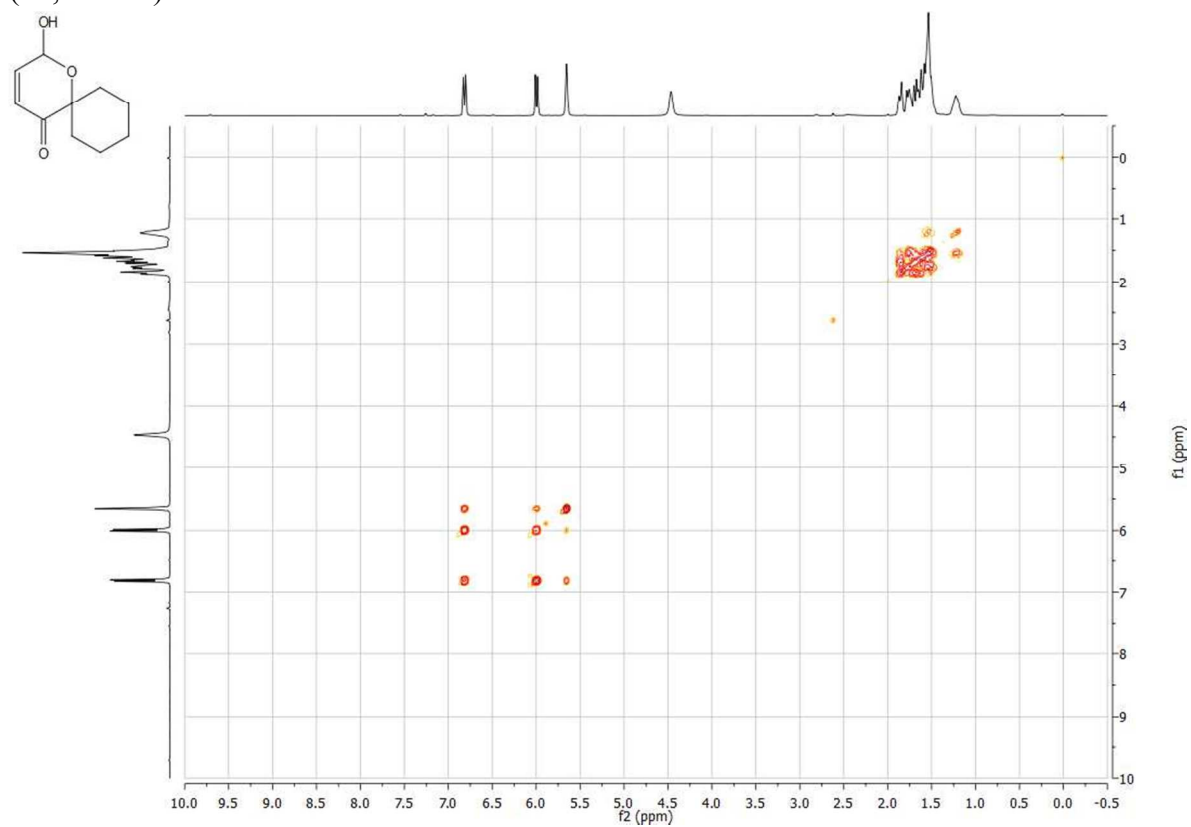
temperature over 16 hours. An aliquot was worked up and determined to be complete by TLC and  $^1\text{H}$  NMR. The reaction mixture was quenched with 10 mL of aqueous saturated ammonium chloride and extracted three times with DCM. The combined organic phases were dried over sodium sulfate and concentrated via rotary evaporator. The crude brownish oil was purified on the flash chromatography system using 0-5% ethyl acetate in hexanes over 25 CV. The diastereomers were poorly separable under these conditions and the product was characterized as a mixture of diastereomers (~2.3:1) as a yellowish oil (0.333 g, 59% yield).  $R_f = 0.49$  (Hexane:Ethyl acetate 9:1).  $^1\text{H}$  NMR (400 MHz, Chloroform-*d*) Major isomer:  $\delta$  6.86 (dd,  $J = 10.2, 3.7$  Hz, 1H), 6.34 (d,  $J = 3.7$  Hz, 1H), 6.19 (d,  $J = 10.2$  Hz, 1H), 4.51 (dd,  $J = 7.8, 3.8$  Hz, 1H), 1.94 (m, 1H), 1.72 (m, 1H), 1.52 (s, 9H), 1.44 – 1.38 (m, 2H), 1.33 – 1.25 (m, 4H), 0.87 (t,  $J = 6.7$  Hz, 3H). Minor isomer:  $\delta$  6.83 (dd,  $J = 10.4, 3.1$  Hz, 1H), 6.36 (d,  $J = 3.0$  Hz, 1H), 6.19 (d,  $J = 10.4$  Hz, 1H), 4.20 (dd,  $J = 10.2, 4.3$  Hz, 1H), 1.88 (m, 1H), 1.76 (m, 1H) 1.52 (s, 9H), 1.44 – 1.38 (m, 2H), 1.33 – 1.25 (m, 4H), 0.87 (t,  $J = 6.7$  Hz, 3H).  $^{13}\text{C}$  NMR (101 MHz, Chloroform-*d*) Major isomer:  $\delta$  196.1, 152.1, 141.9, 128.3, 89.5, 83.59, 79.9, 33.6, 31.49, 27.8, 25.2, 22.6, 14.13. Minor isomer:  $\delta$  195.7, 152.0, 140.9, 129.0, 89.4, 83.62, 75.8, 31.53, 29.5, 27.8, 24.4, 22.6, 14.10. LRMS (ESI):  $[\text{M}+\text{Na}^+]^+$  calcd for  $\text{C}_{15}\text{H}_{24}\text{NaO}_5^+$  307.2, found 307.2.

# NMR Spectra

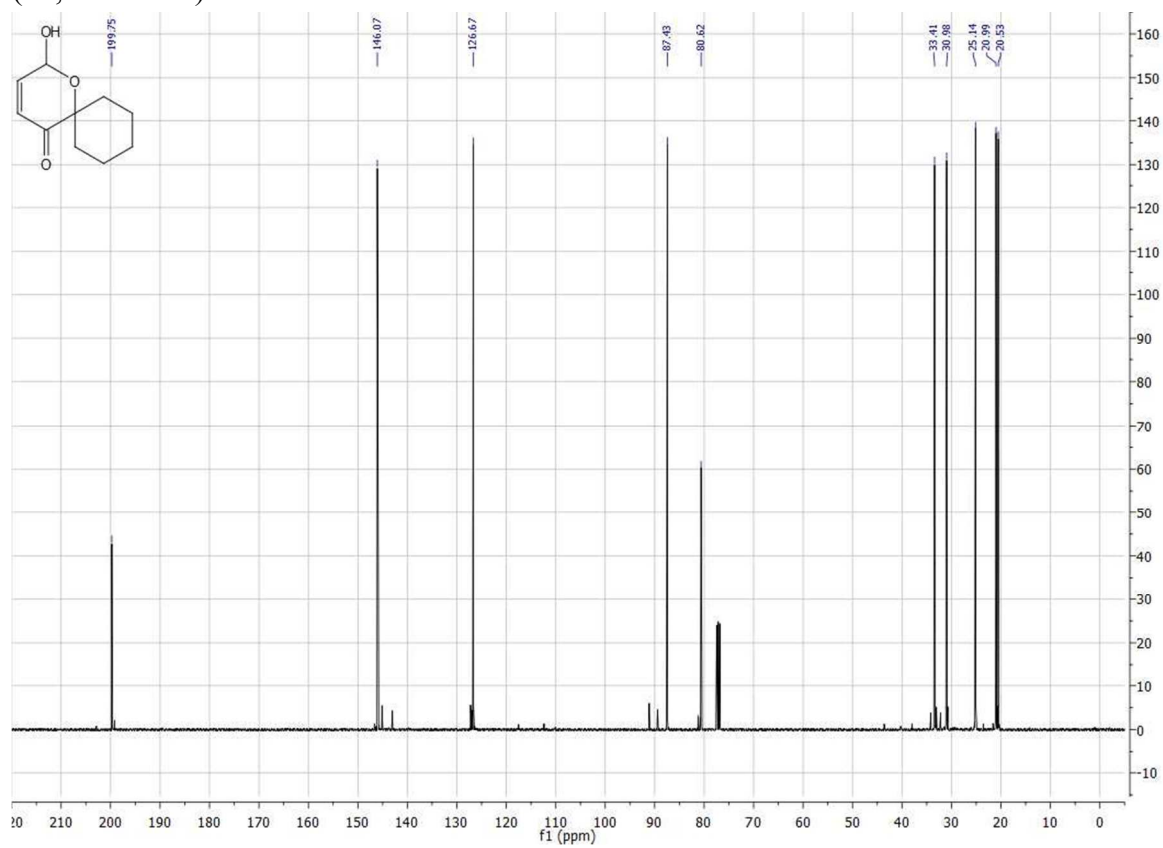
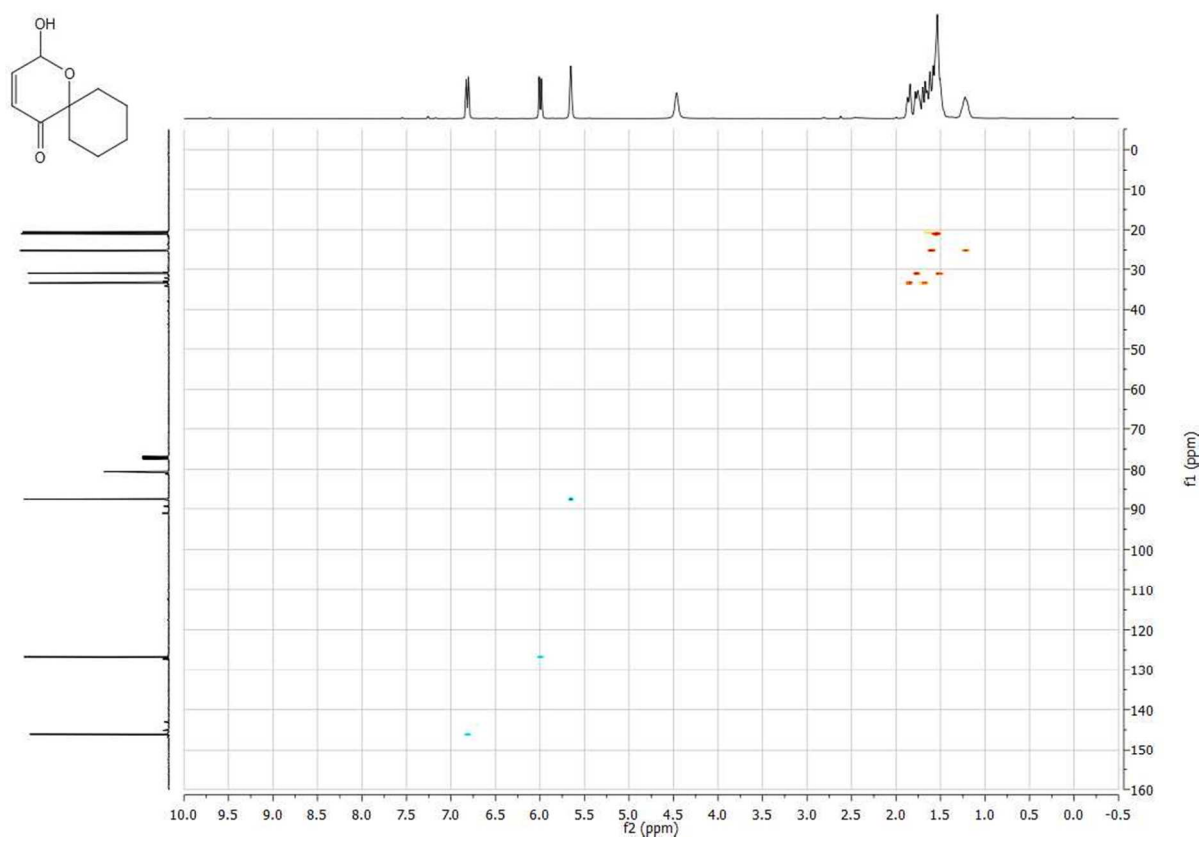
(2a,  $^1\text{H}$  NMR)

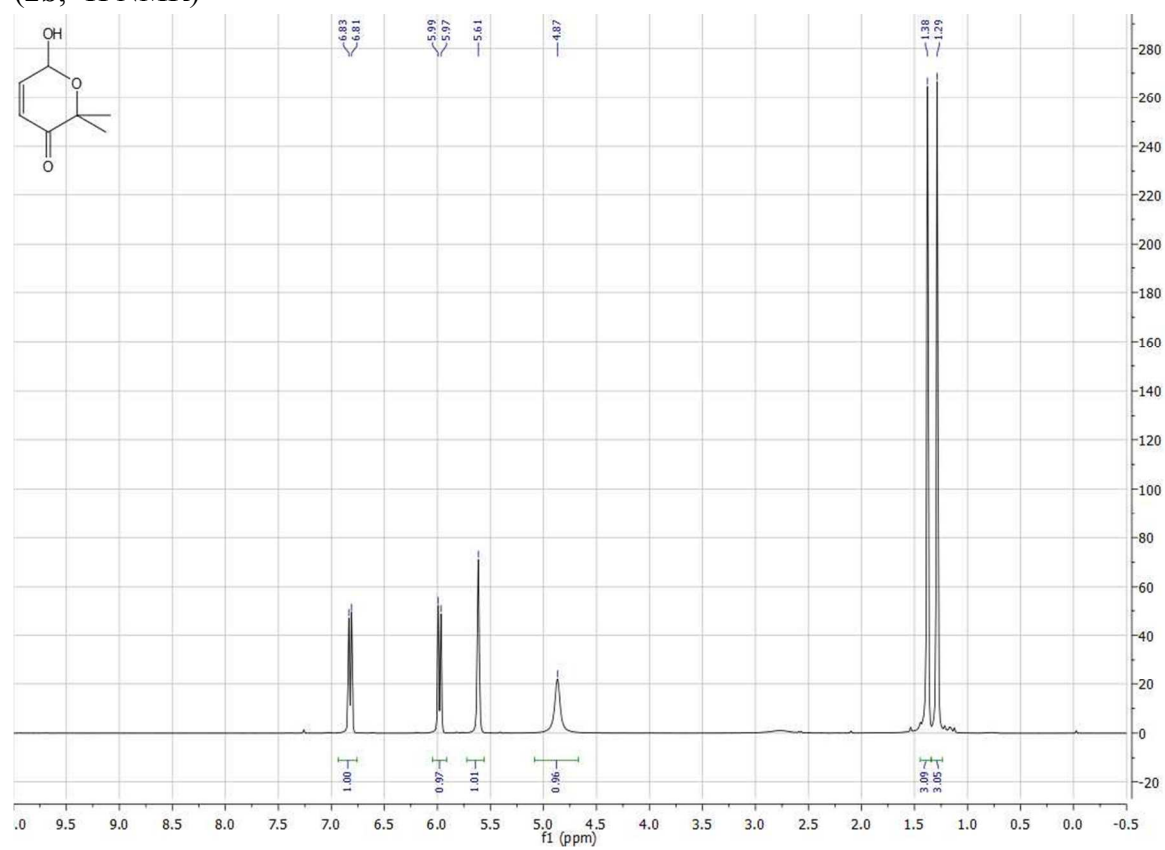
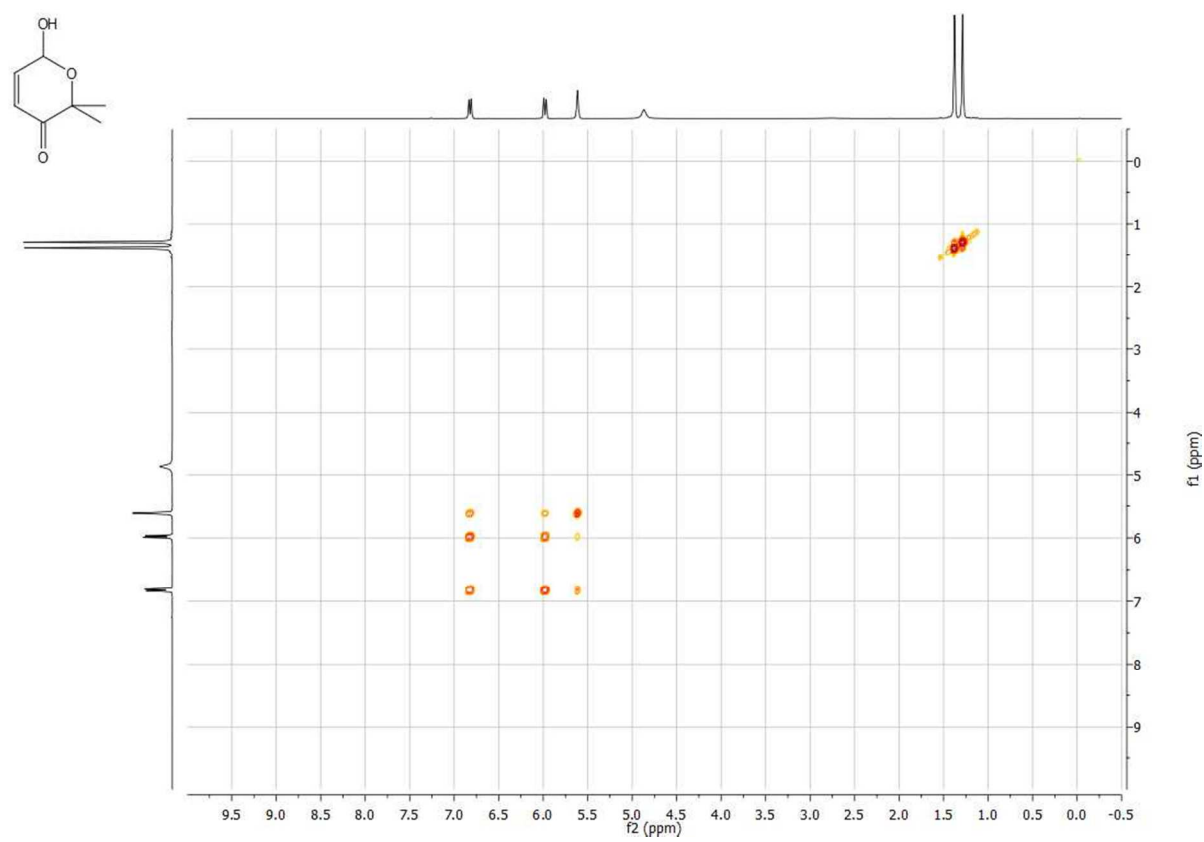


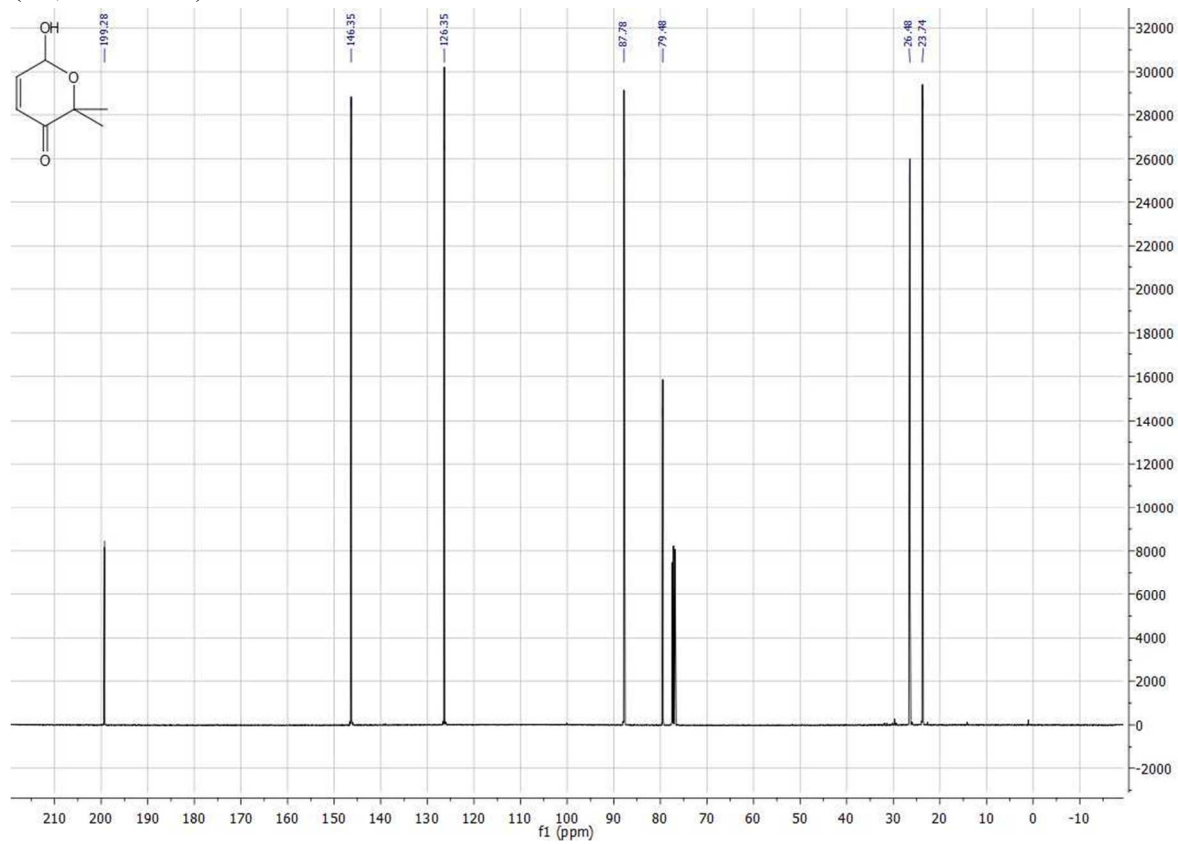
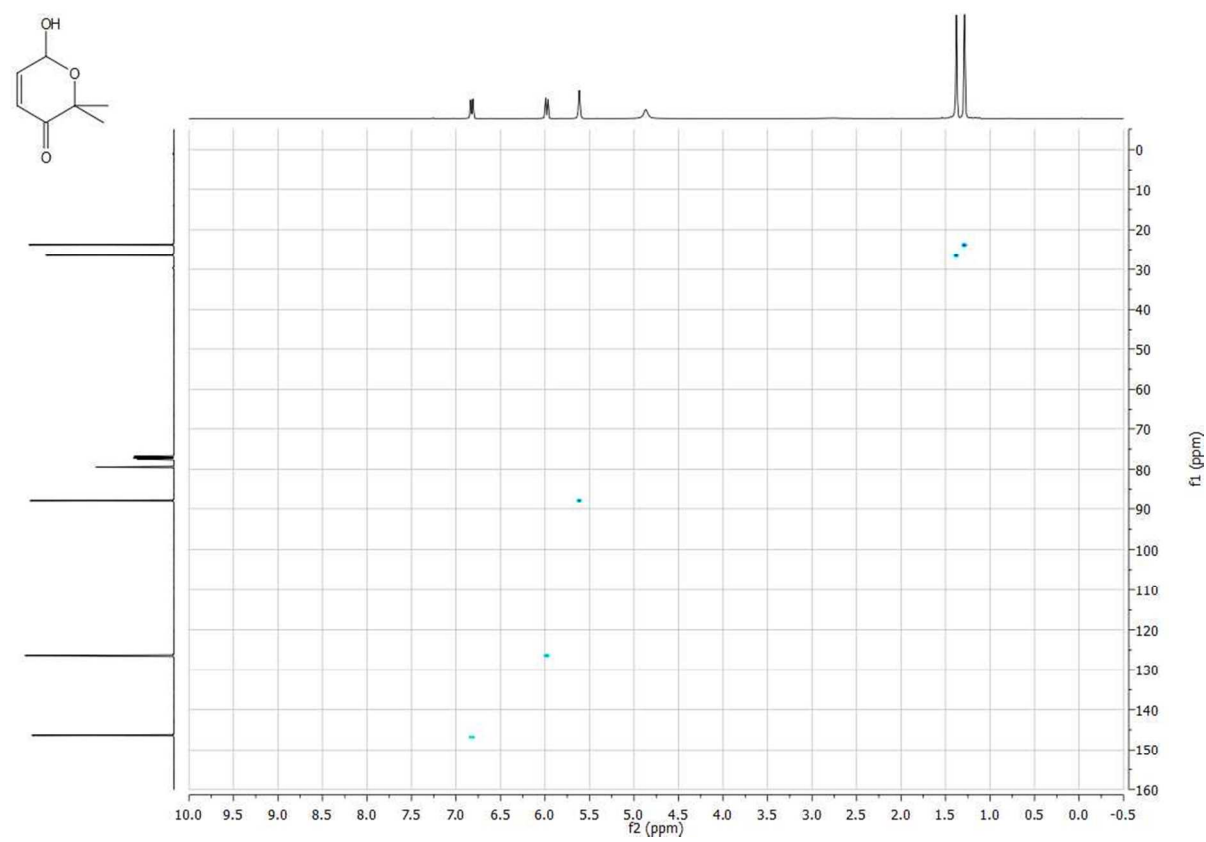
(2a, COSY)

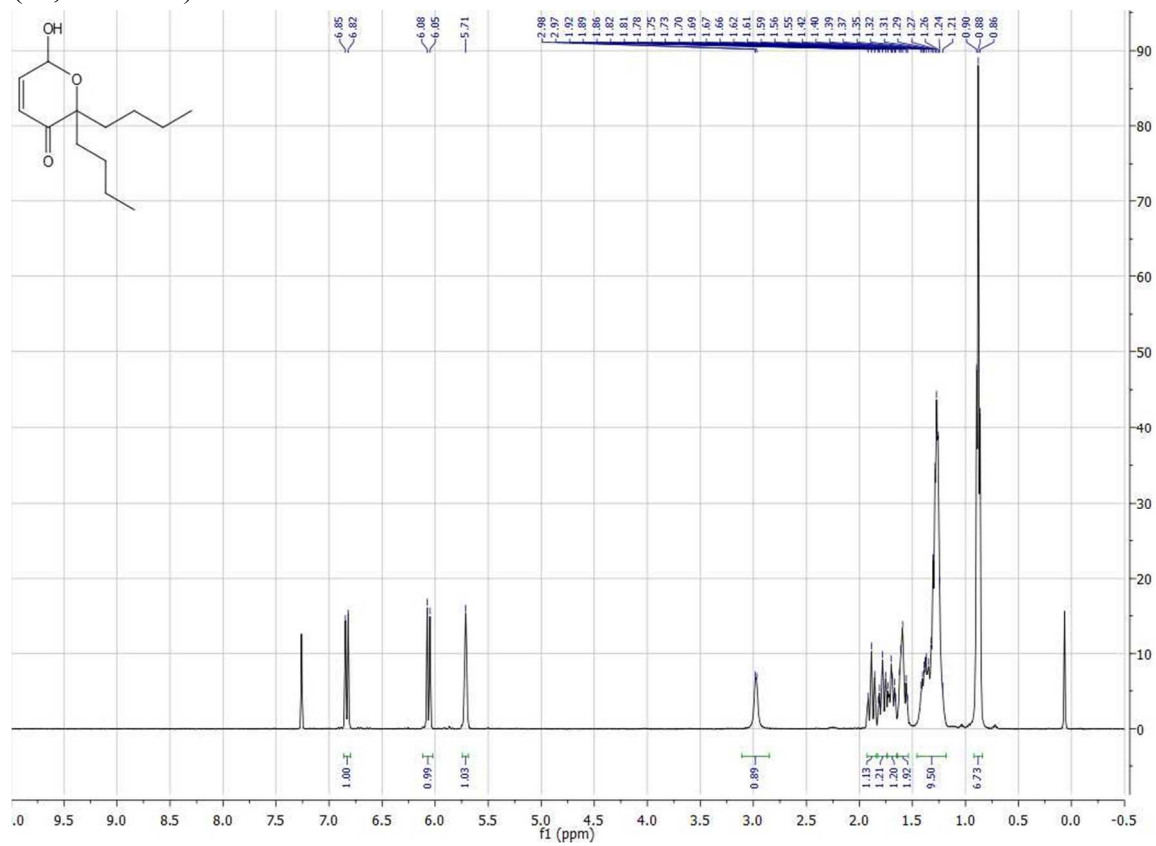
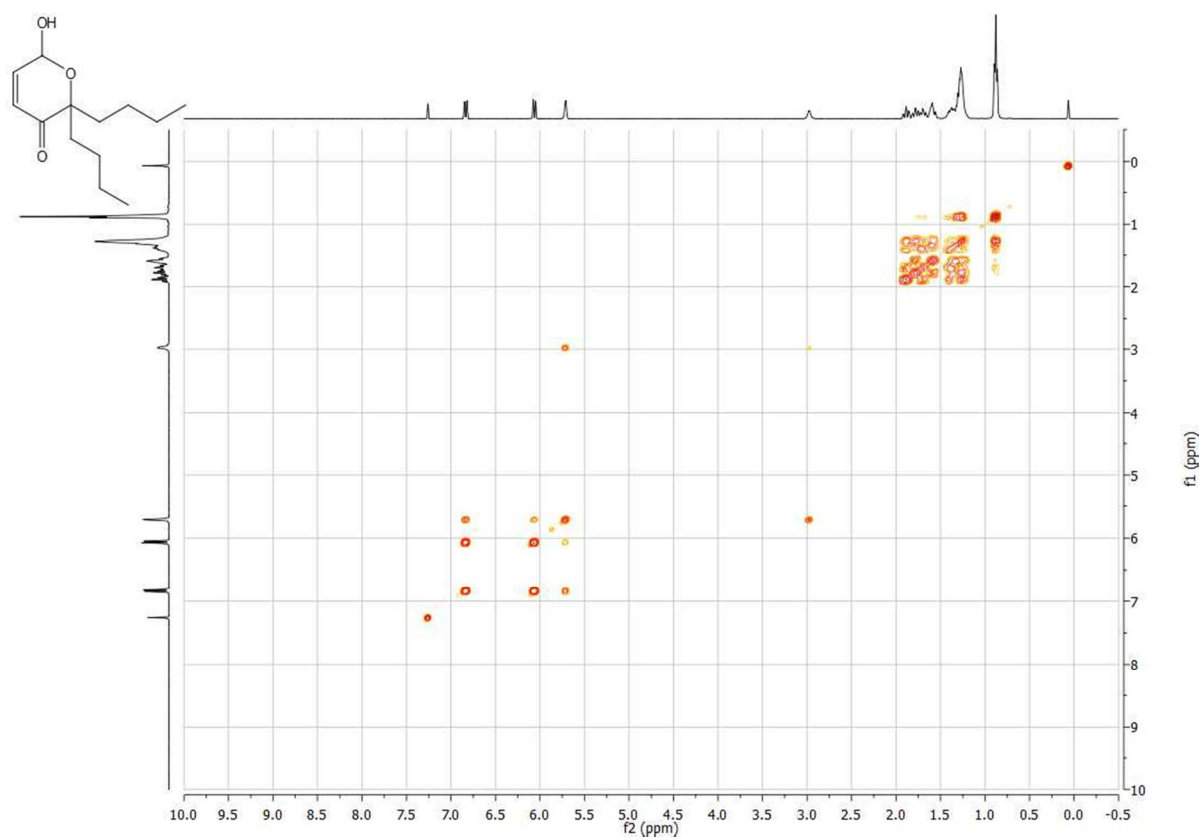


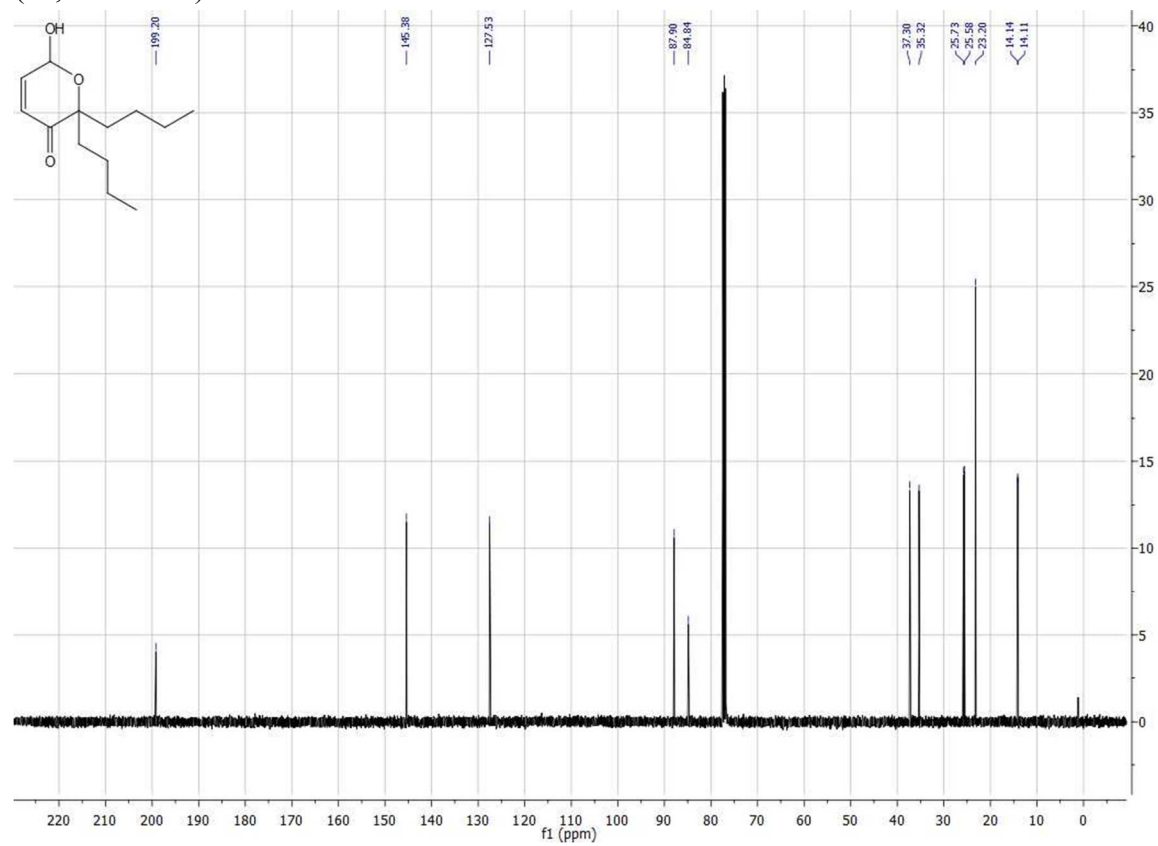
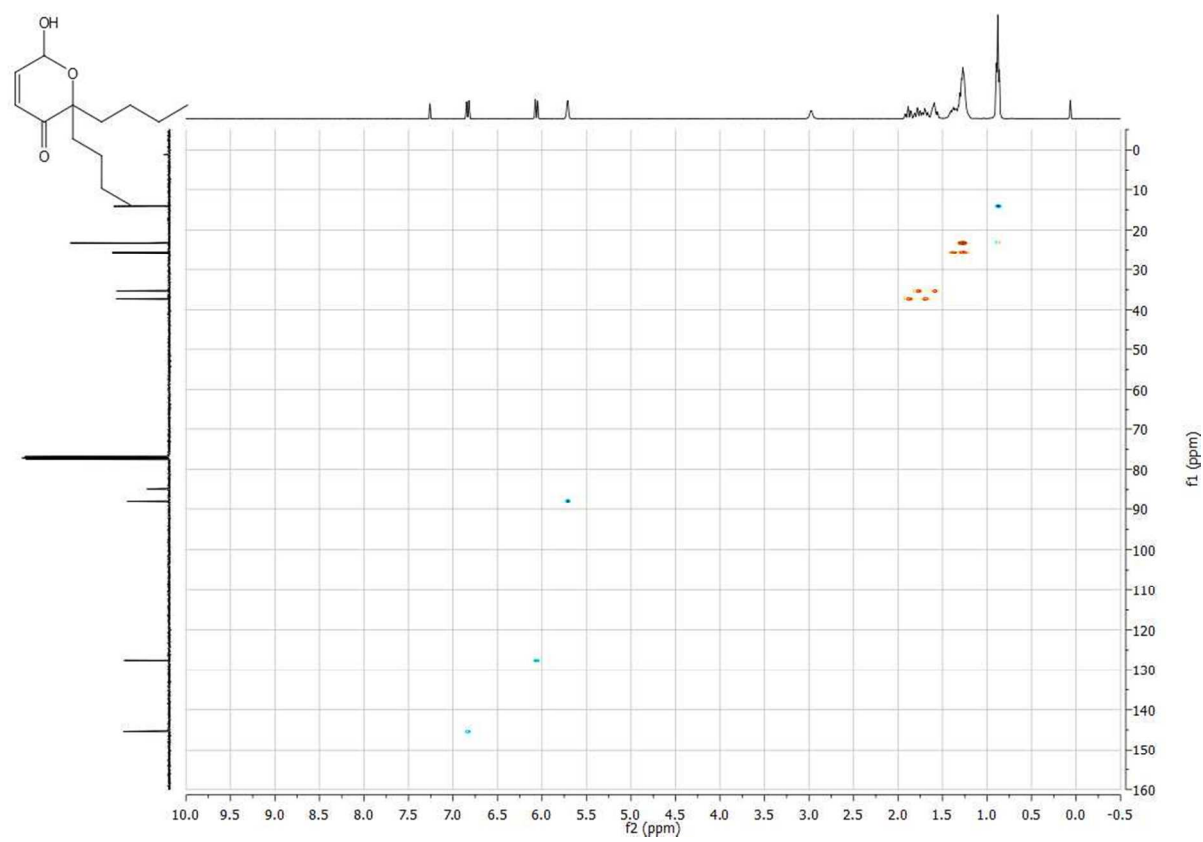


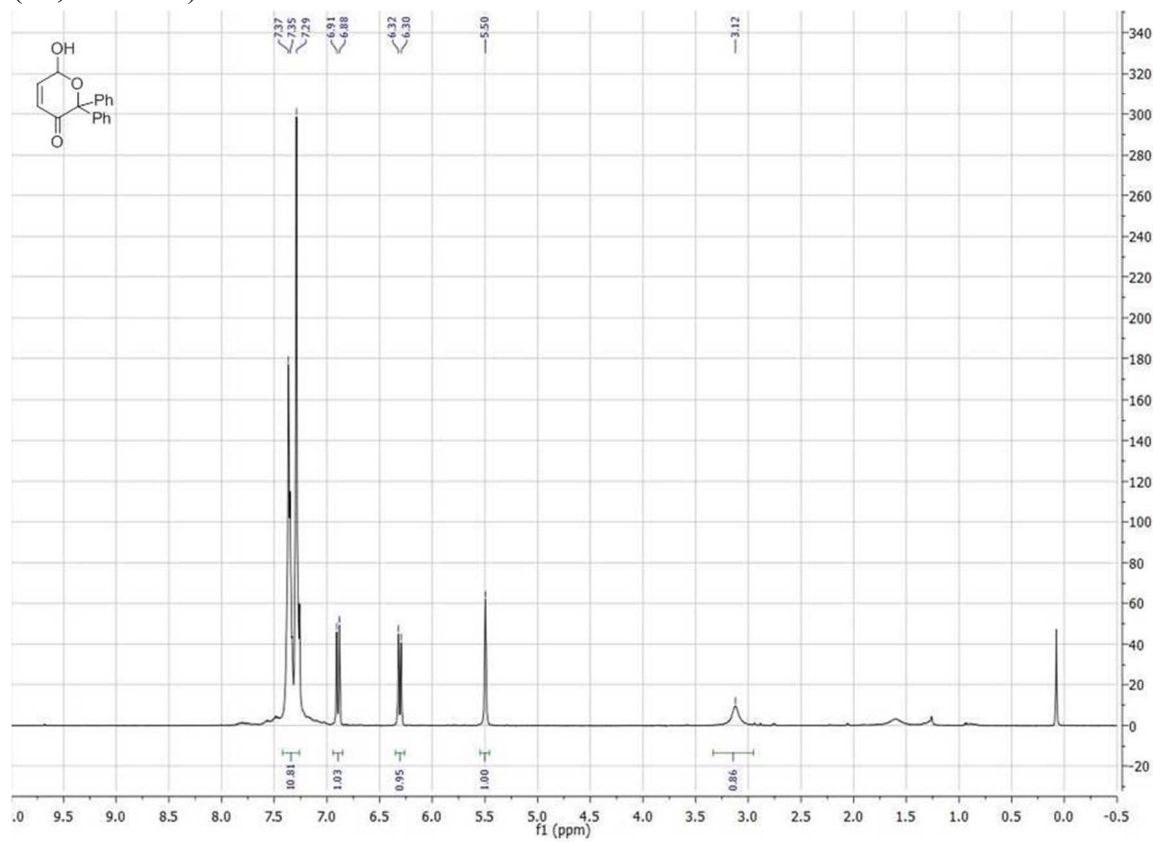
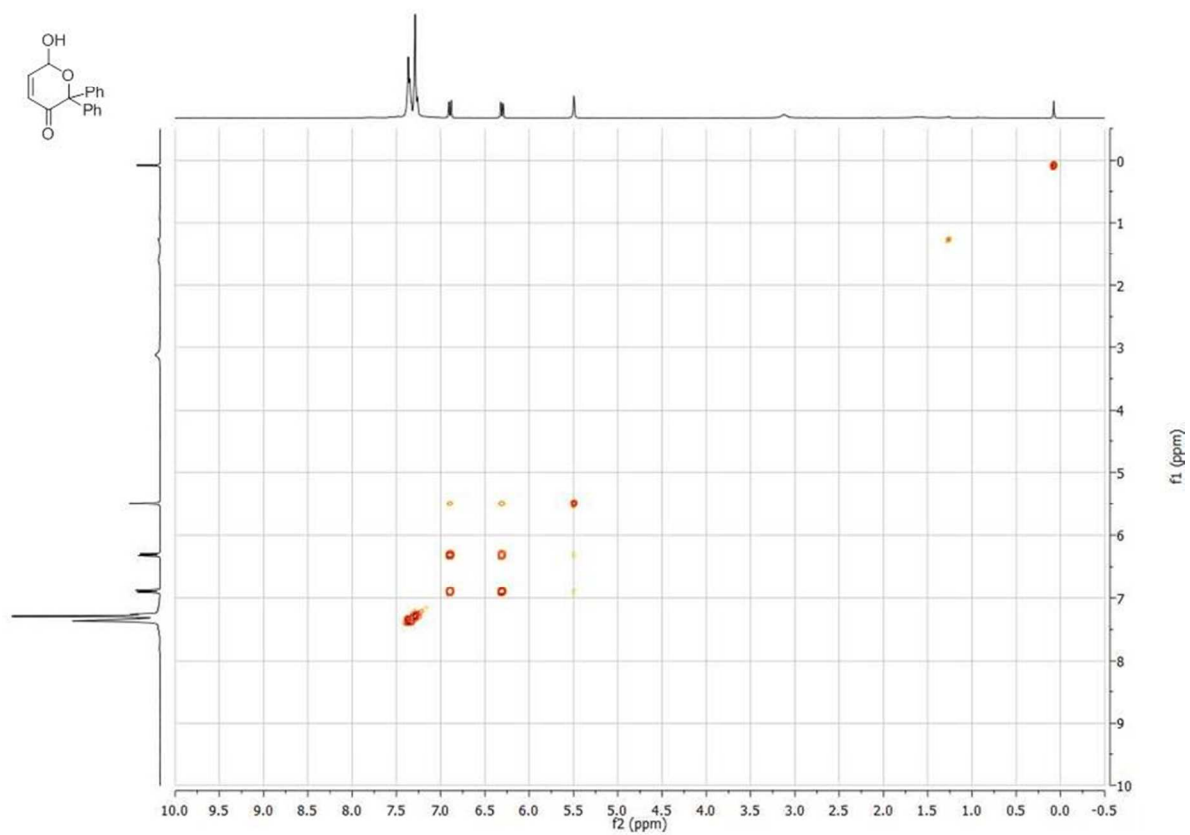
**(2a,  $^{13}\text{C}$  NMR)****(2a, HSQC)**

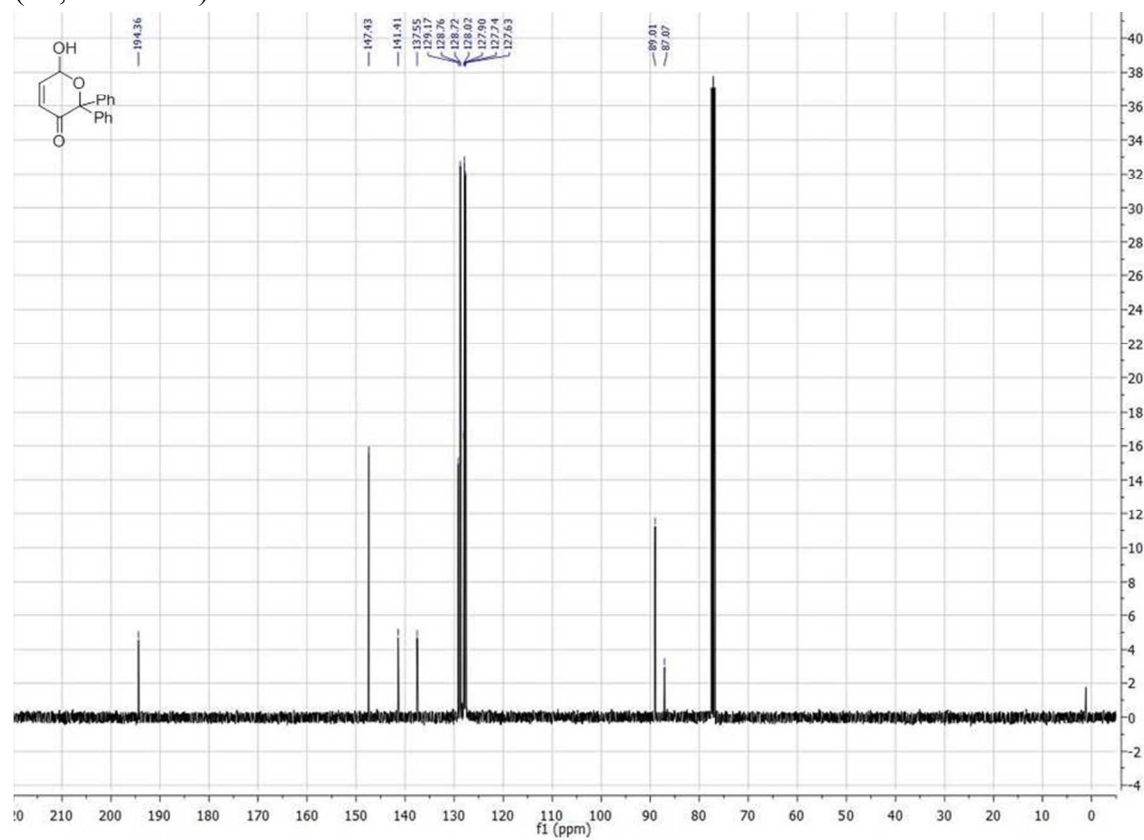
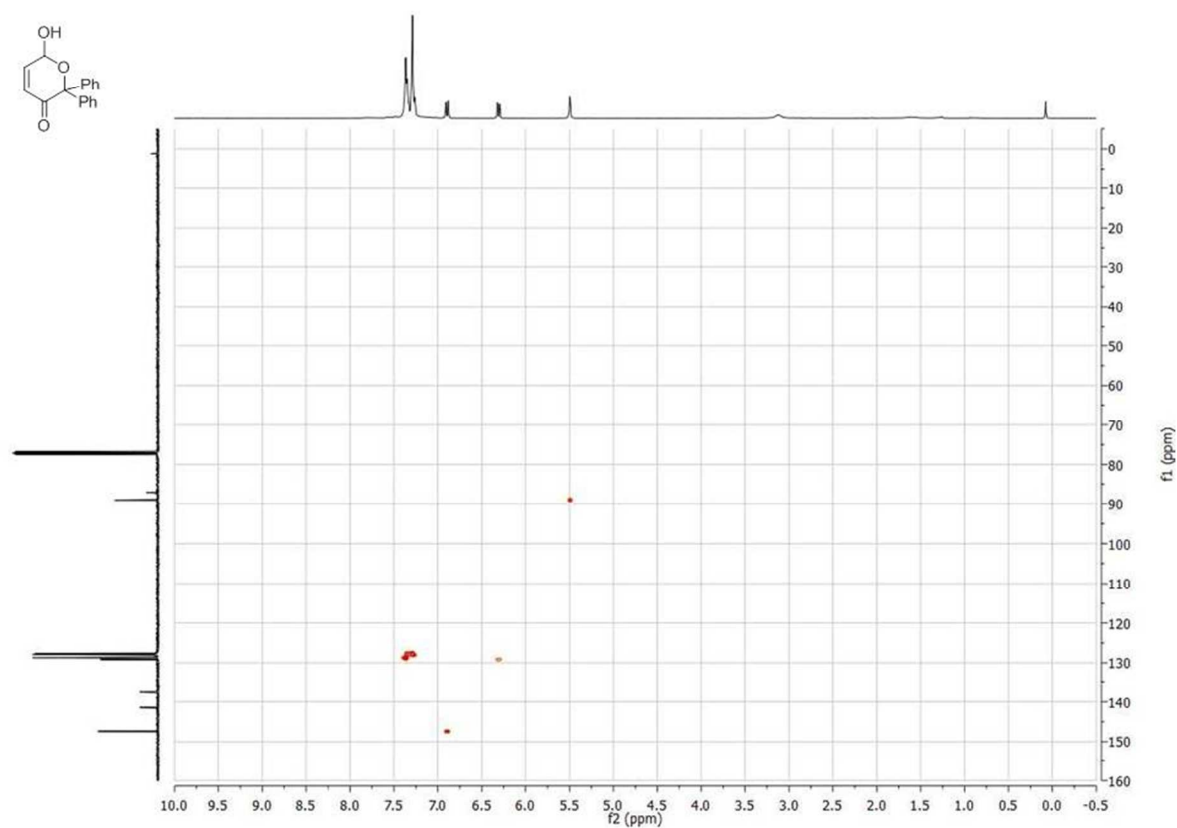
**(2b,  $^1\text{H}$  NMR)****(2b, COSY)**

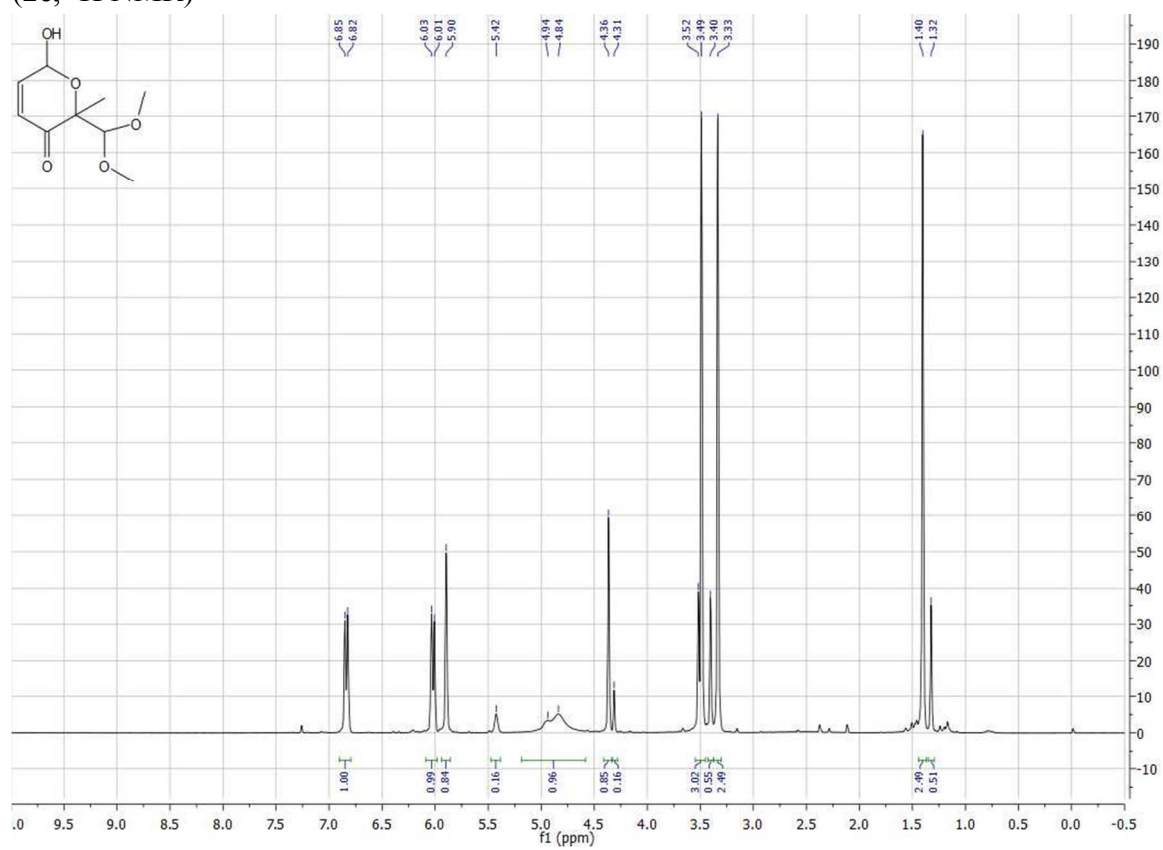
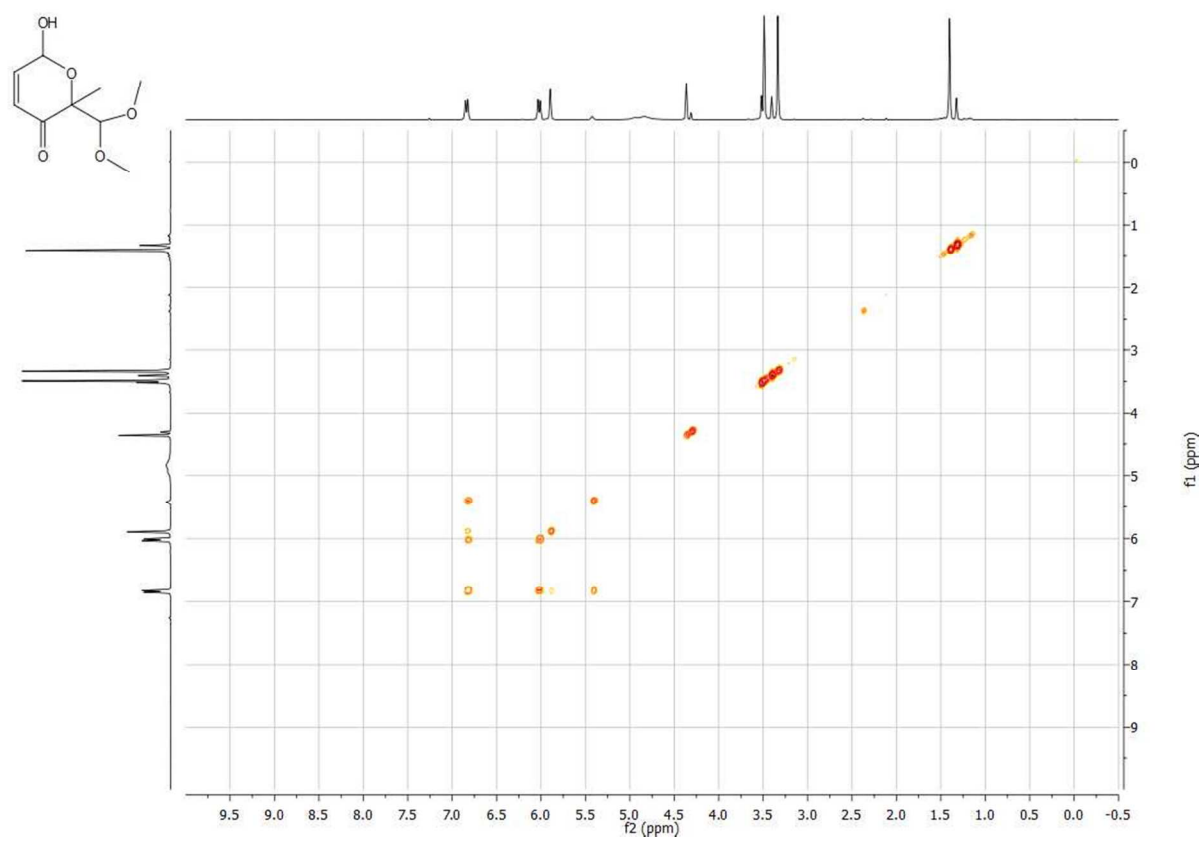
**(2b,  $^{13}\text{C}$  NMR)****(2b, HSQC)**

**(2c,  $^1\text{H}$  NMR)****(2c, COSY)**

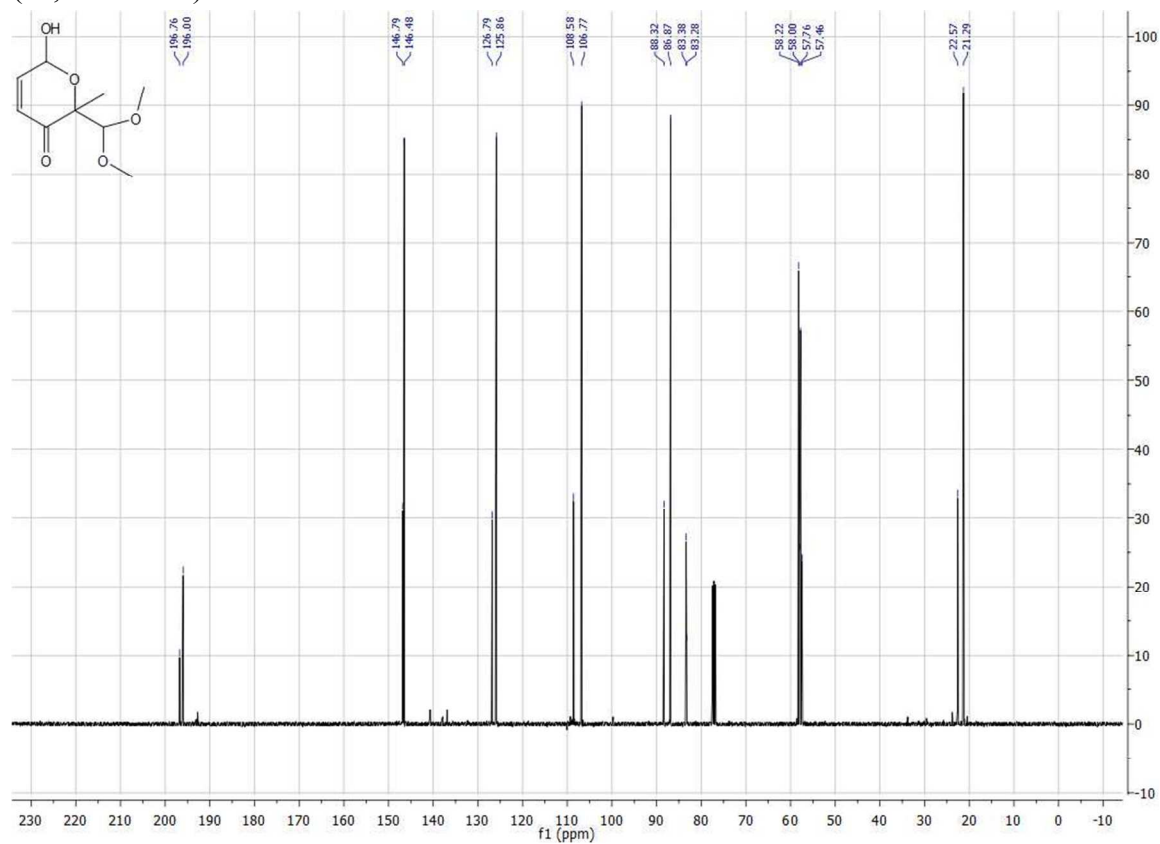
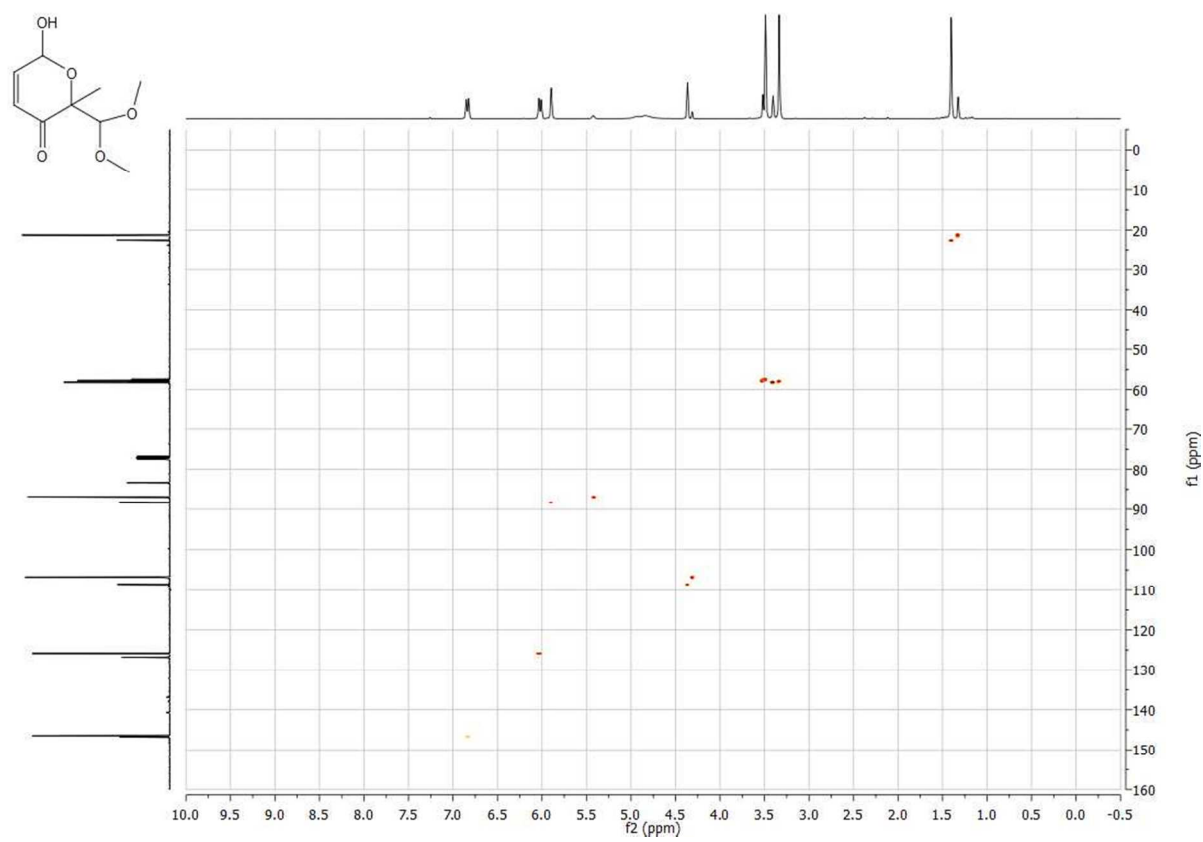
**(2c,  $^{13}\text{C}$  NMR)****(2c, HSQC)**

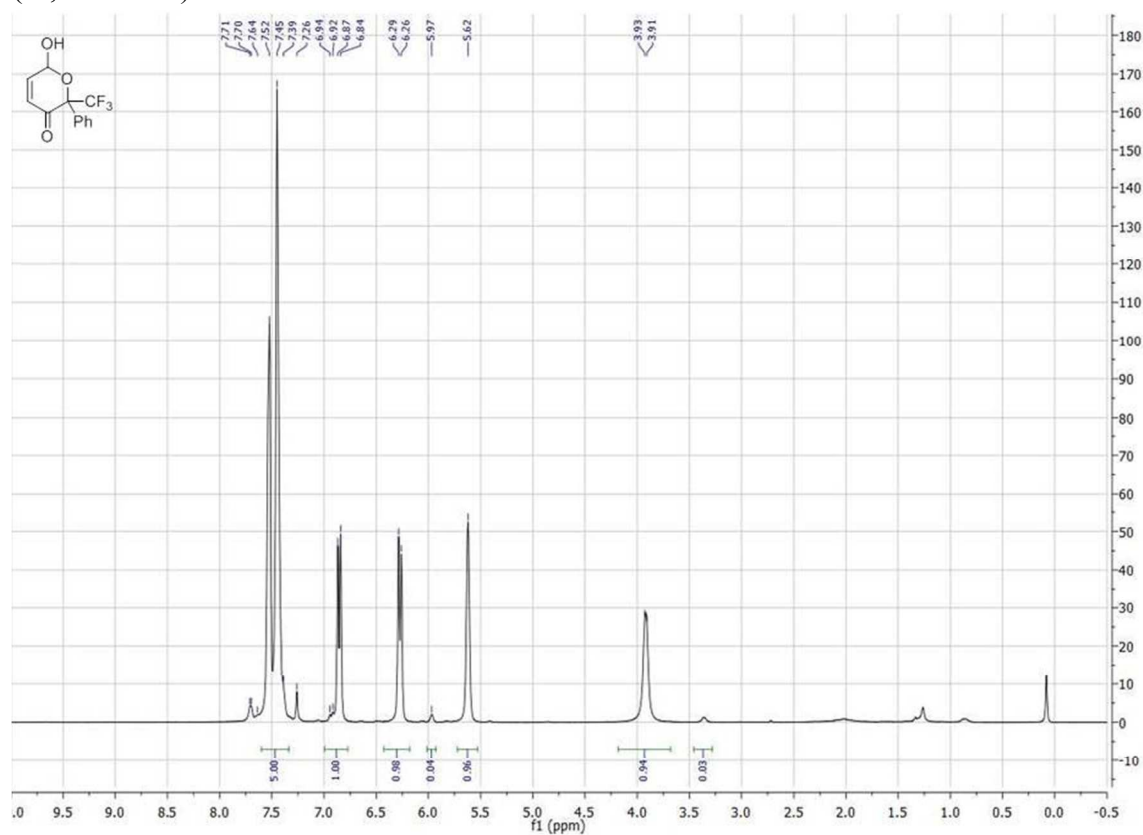
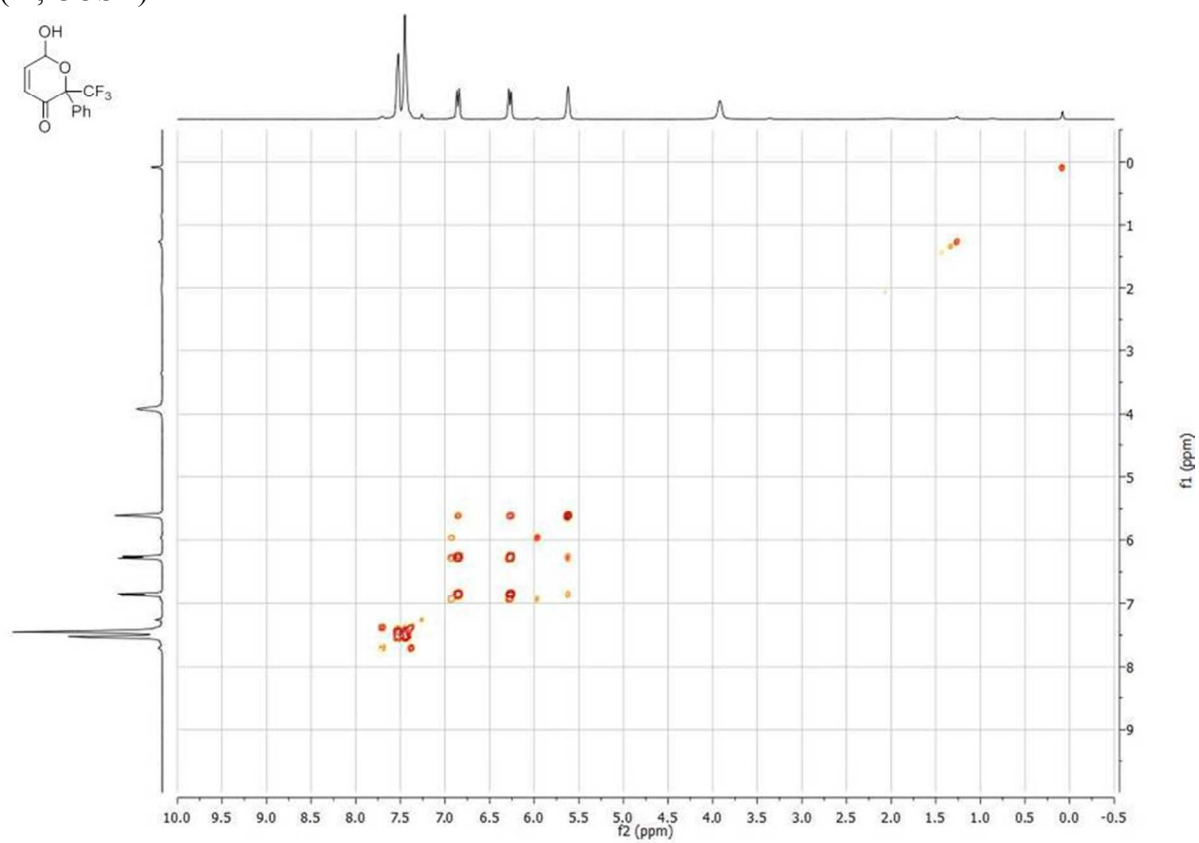
**(2d,  $^1\text{H}$  NMR)****(2d, COSY)**

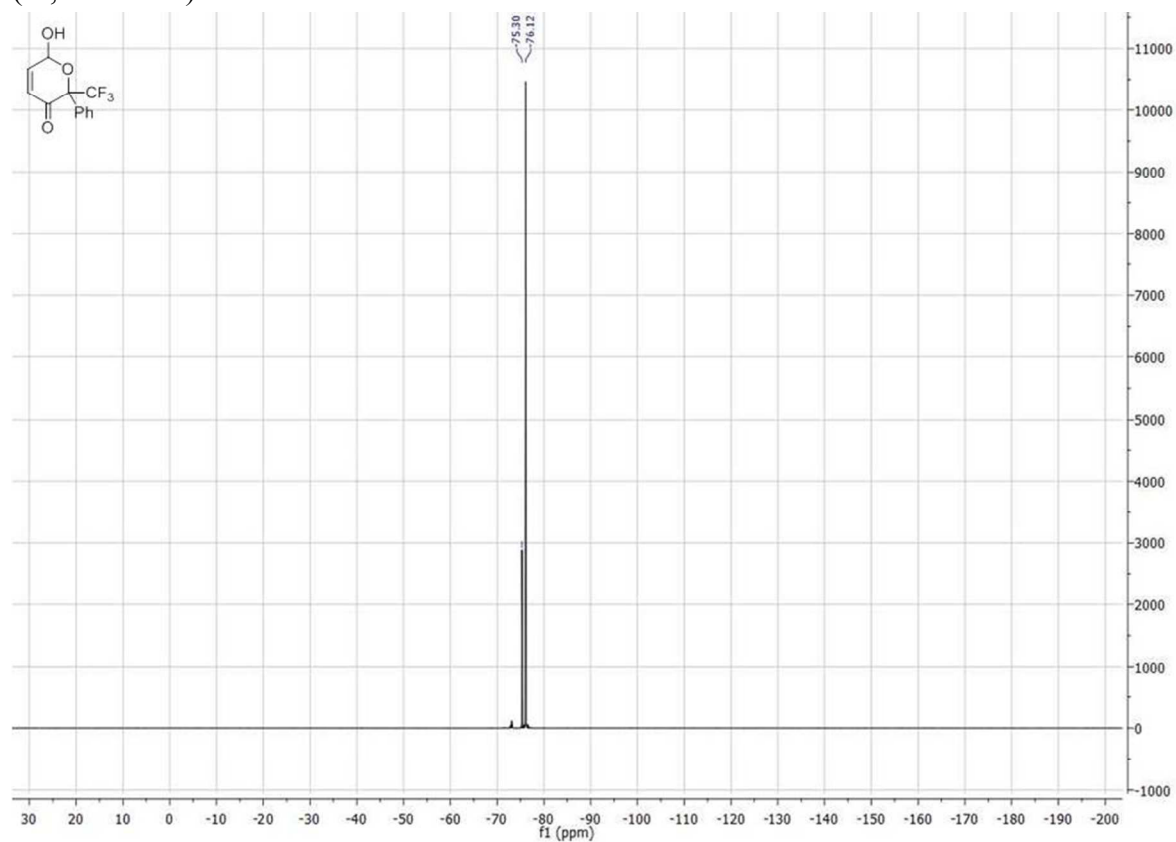
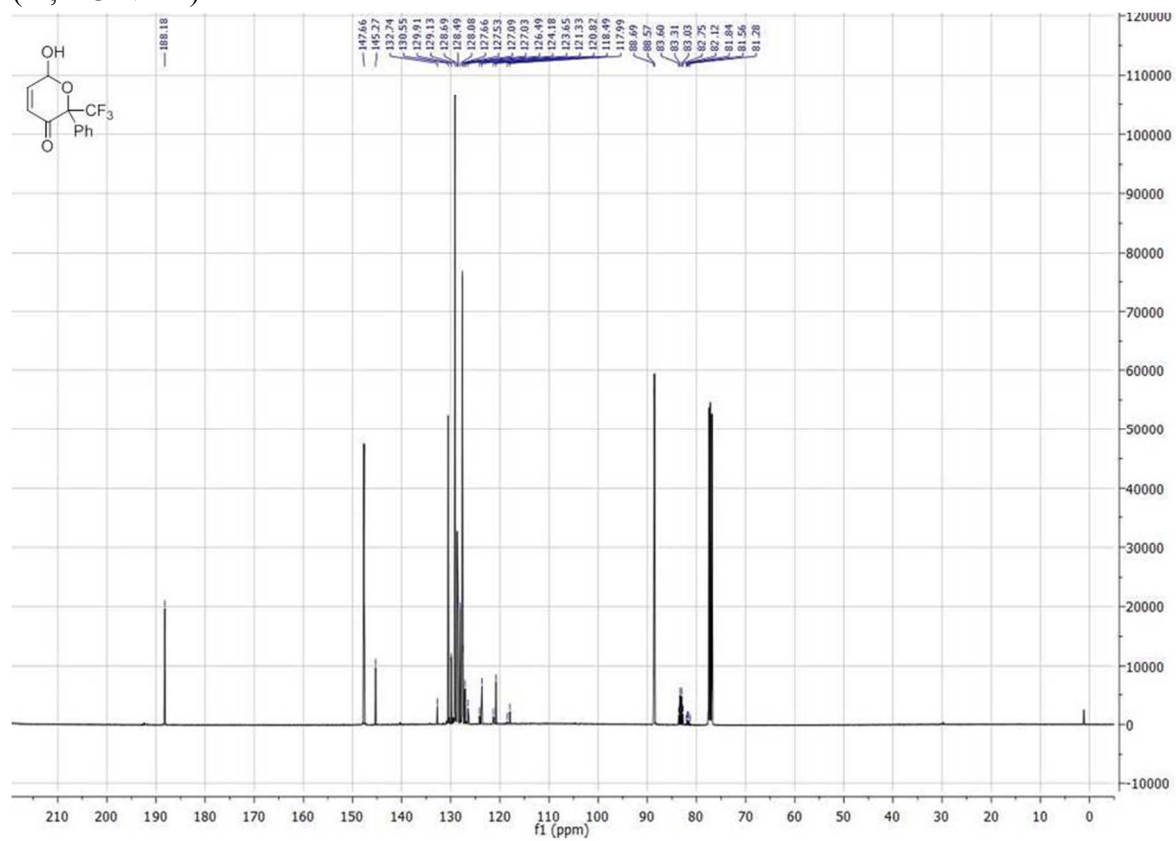
**(2d,  $^{13}\text{C}$  NMR)****(2d, HSQC)**

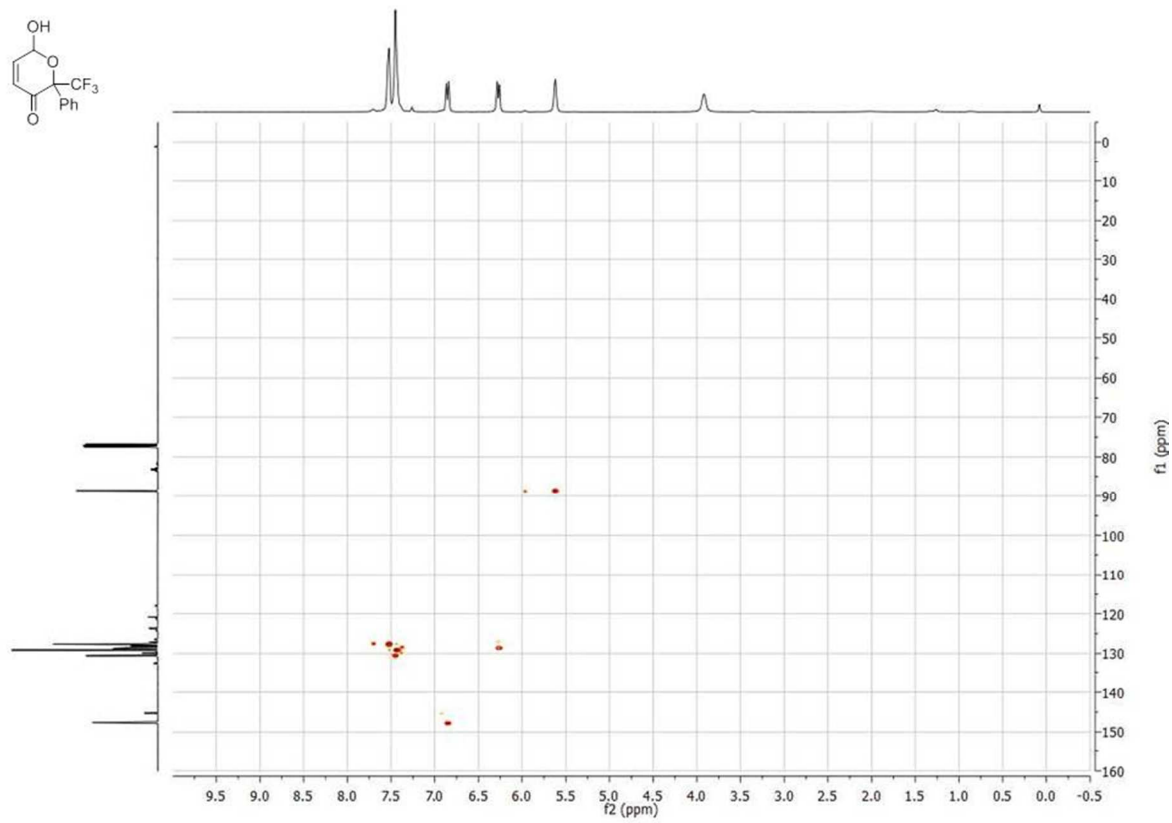
**(2e,  $^1\text{H}$  NMR)****(2e, COSY)**

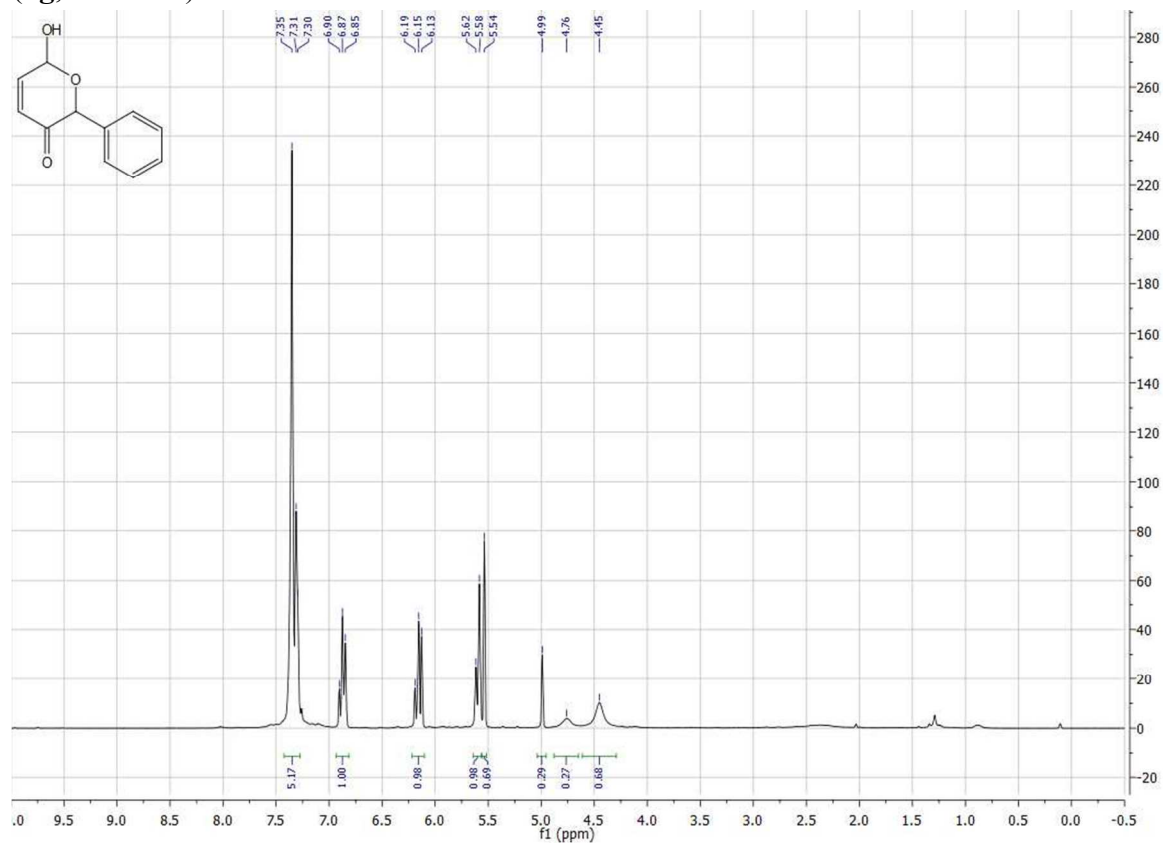
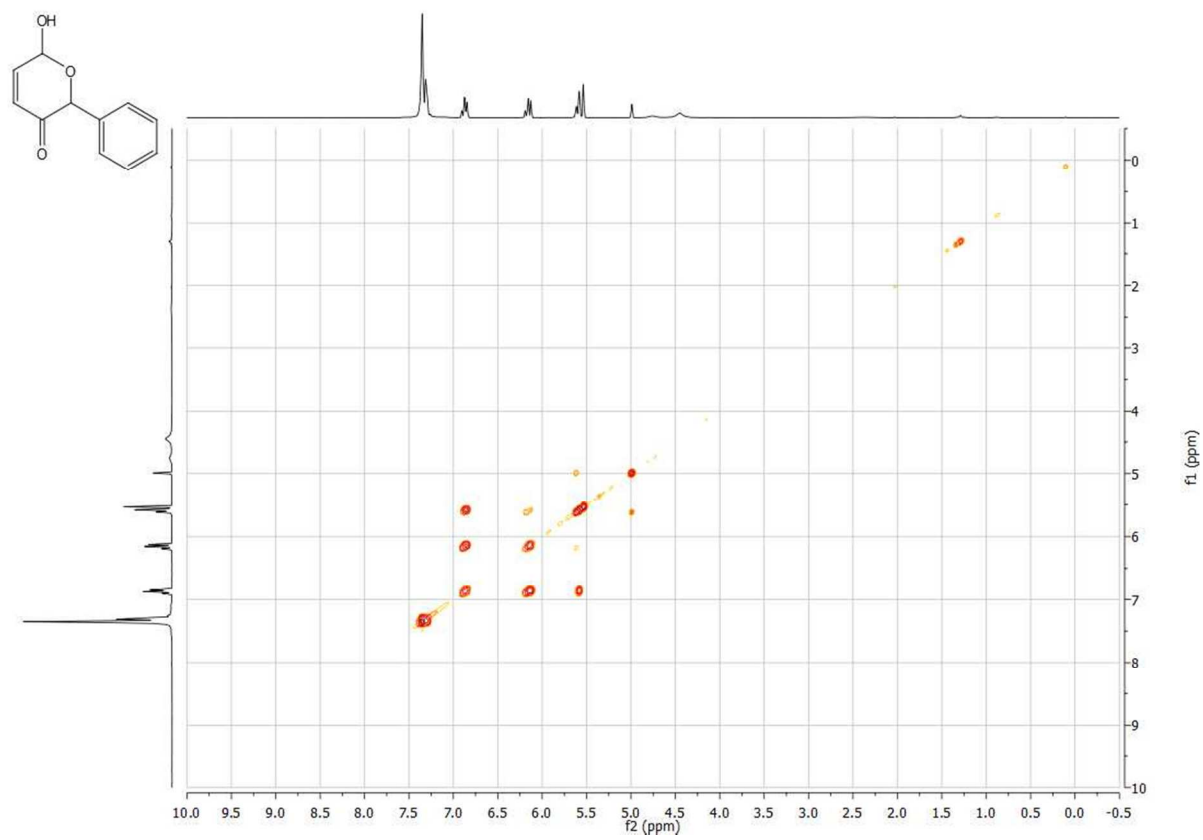


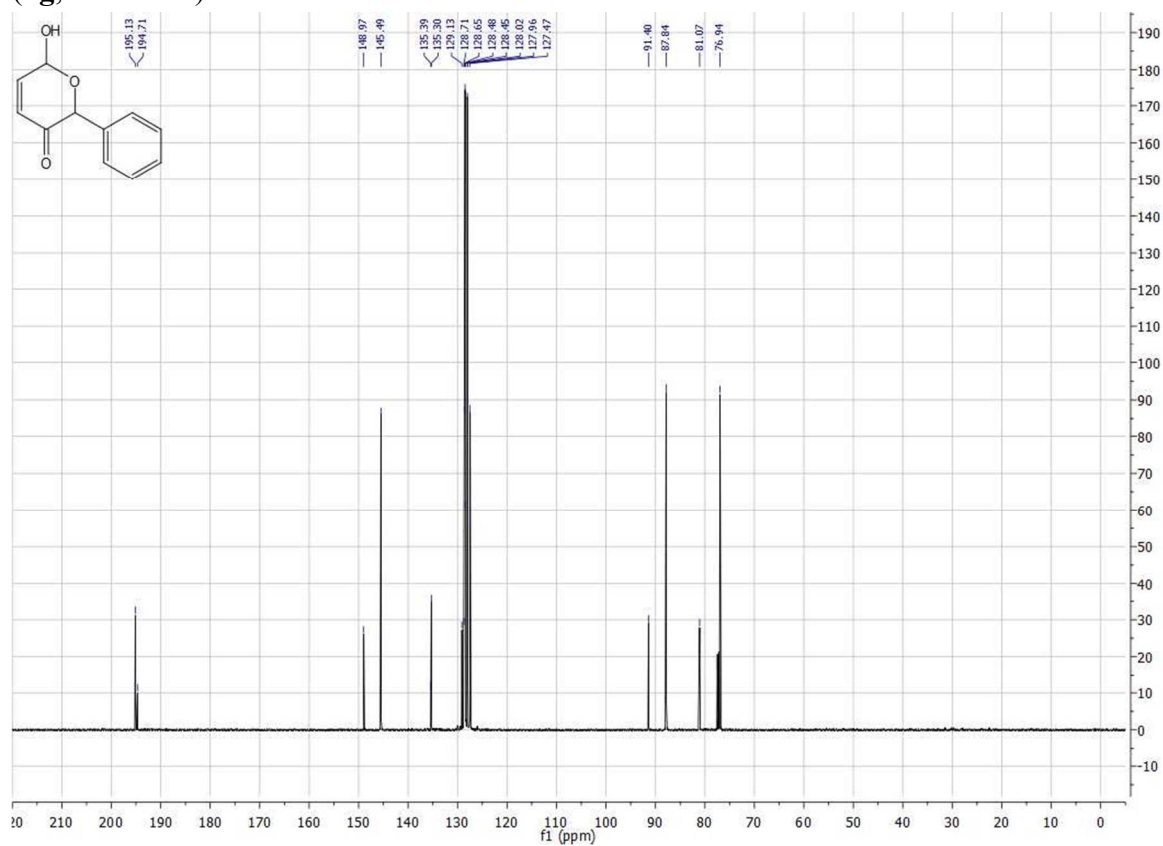
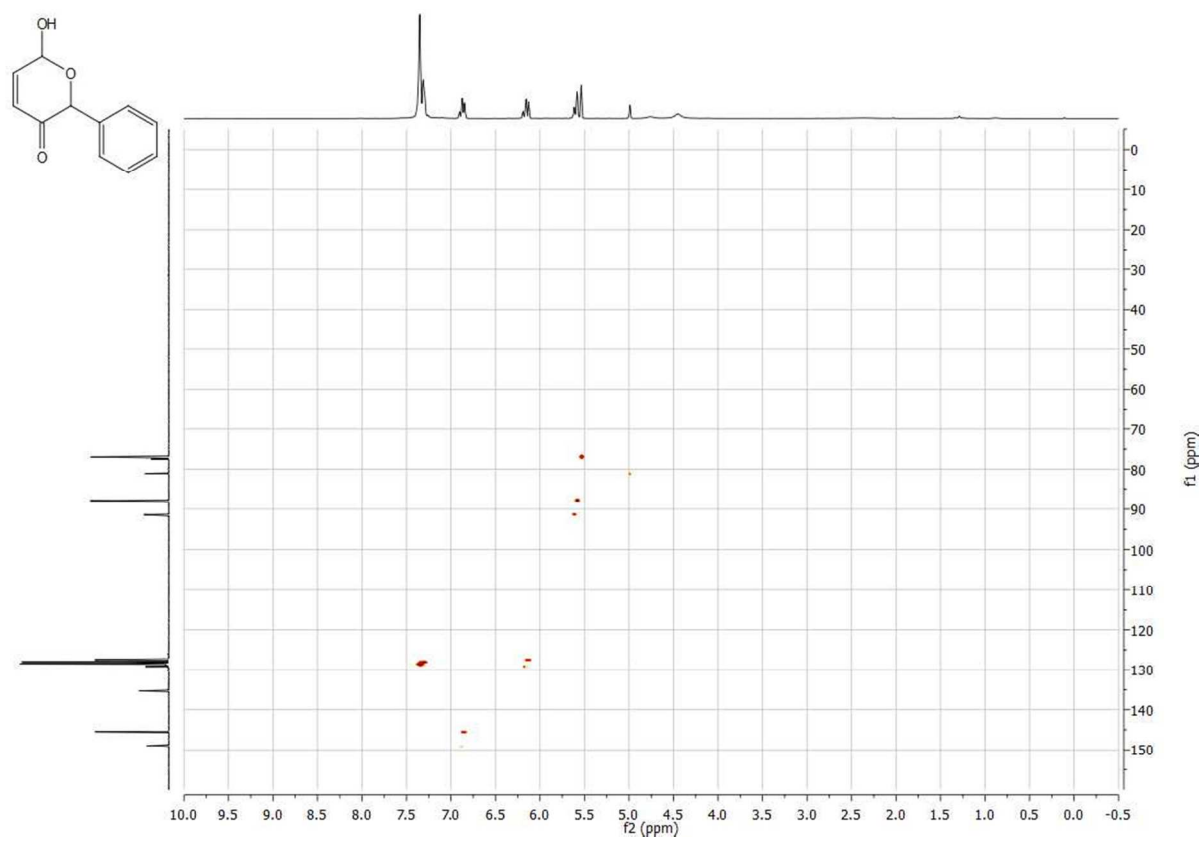
**(2e,  $^{13}\text{C}$  NMR)****(2e, HSQC)**

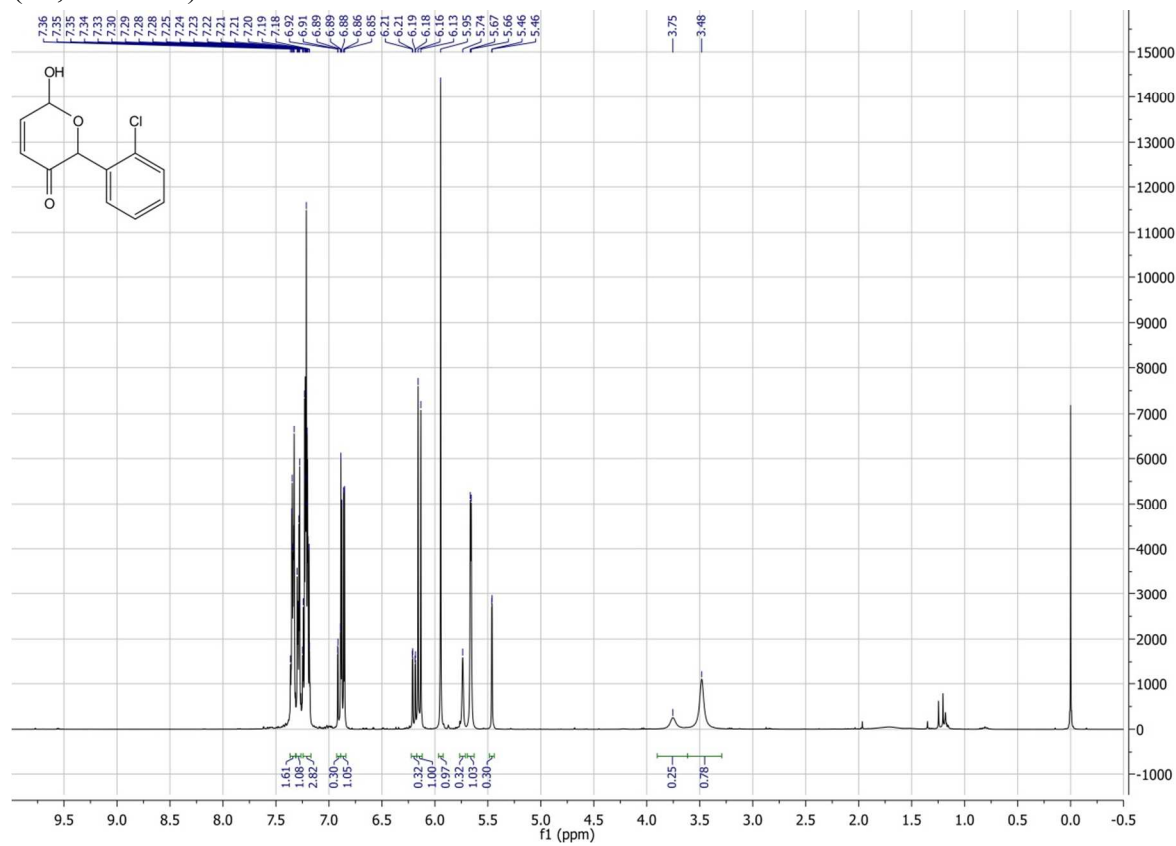
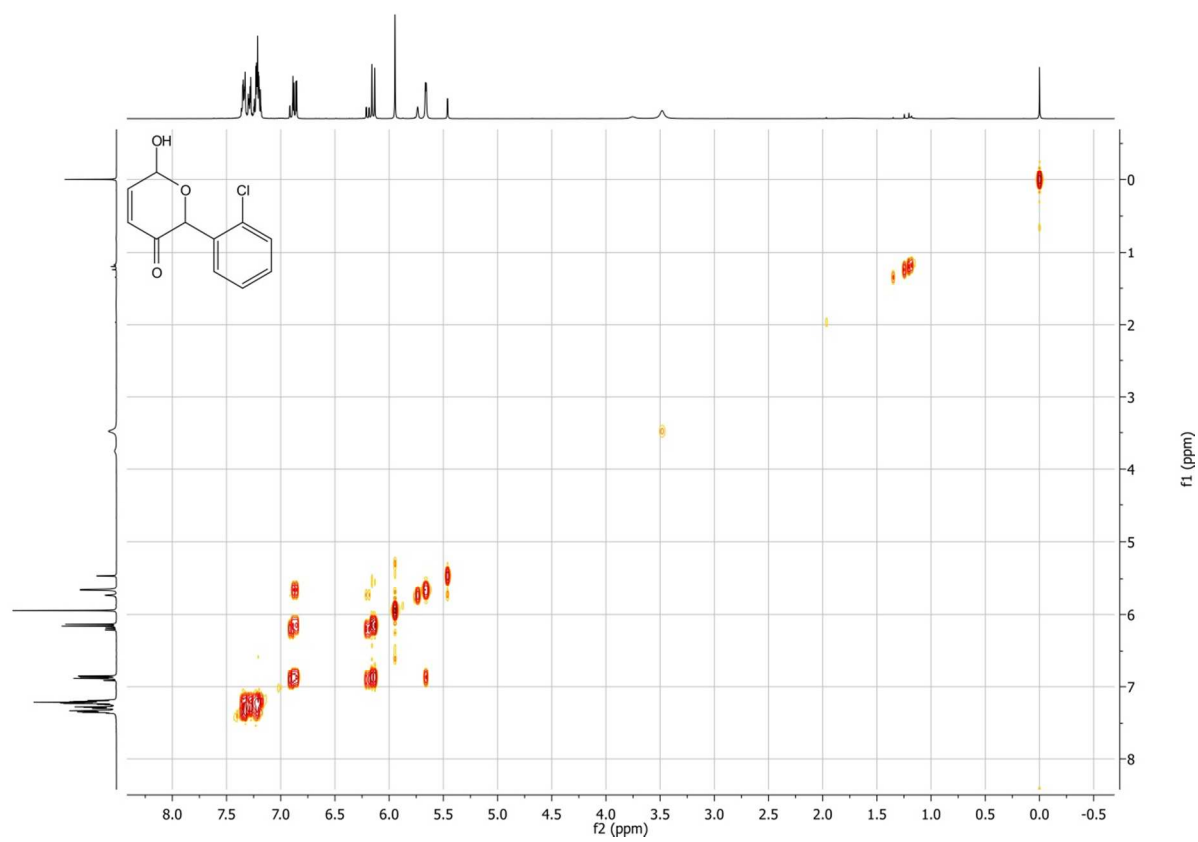
**(2f, <sup>1</sup>H NMR)****(2f, COSY)**

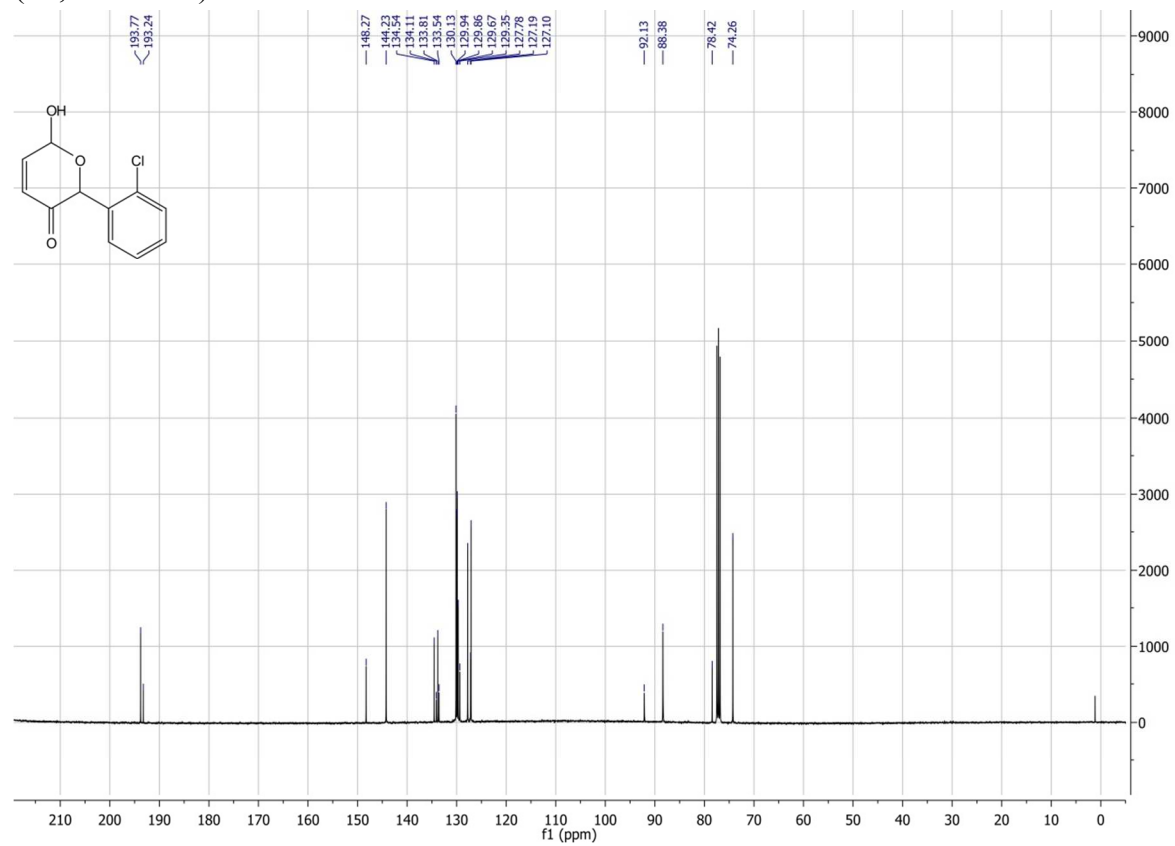
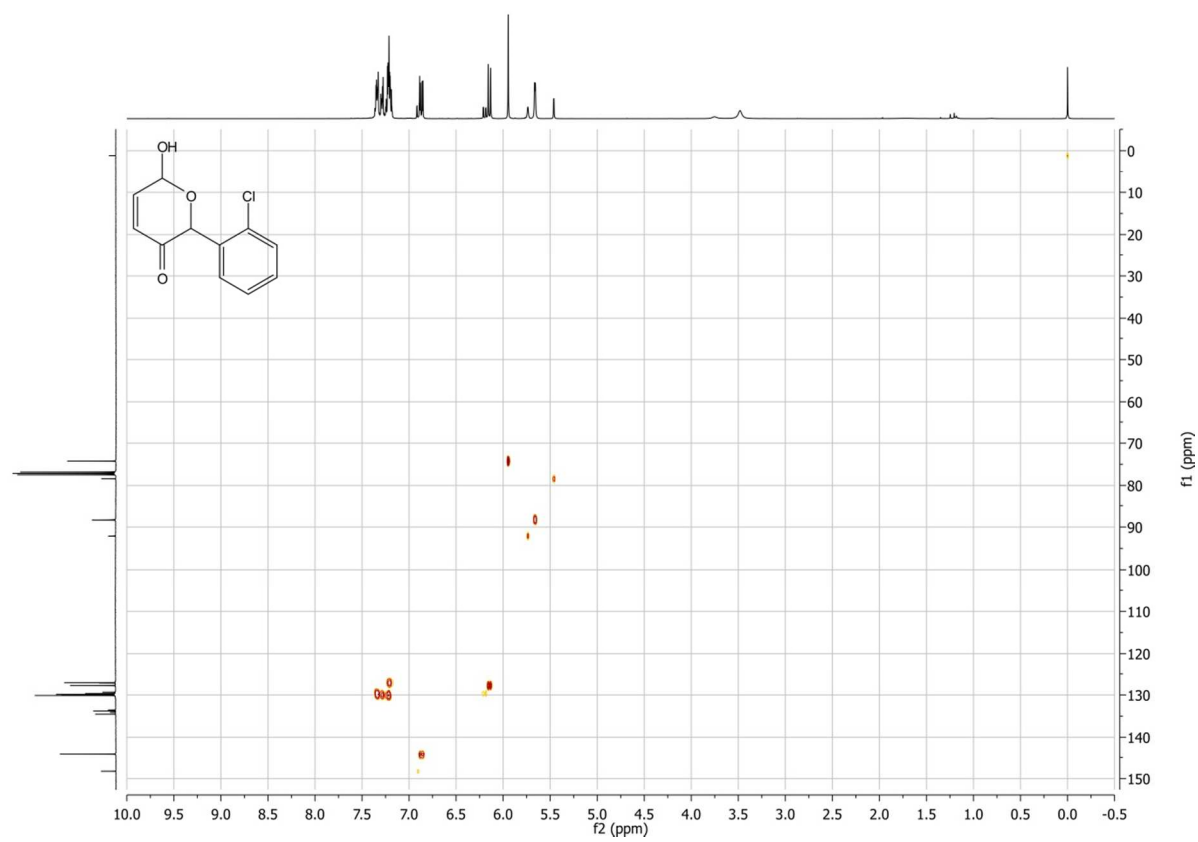
**(2f, <sup>19</sup>F NMR)****(2f, <sup>13</sup>C NMR)**

**(2f, HSQC)**

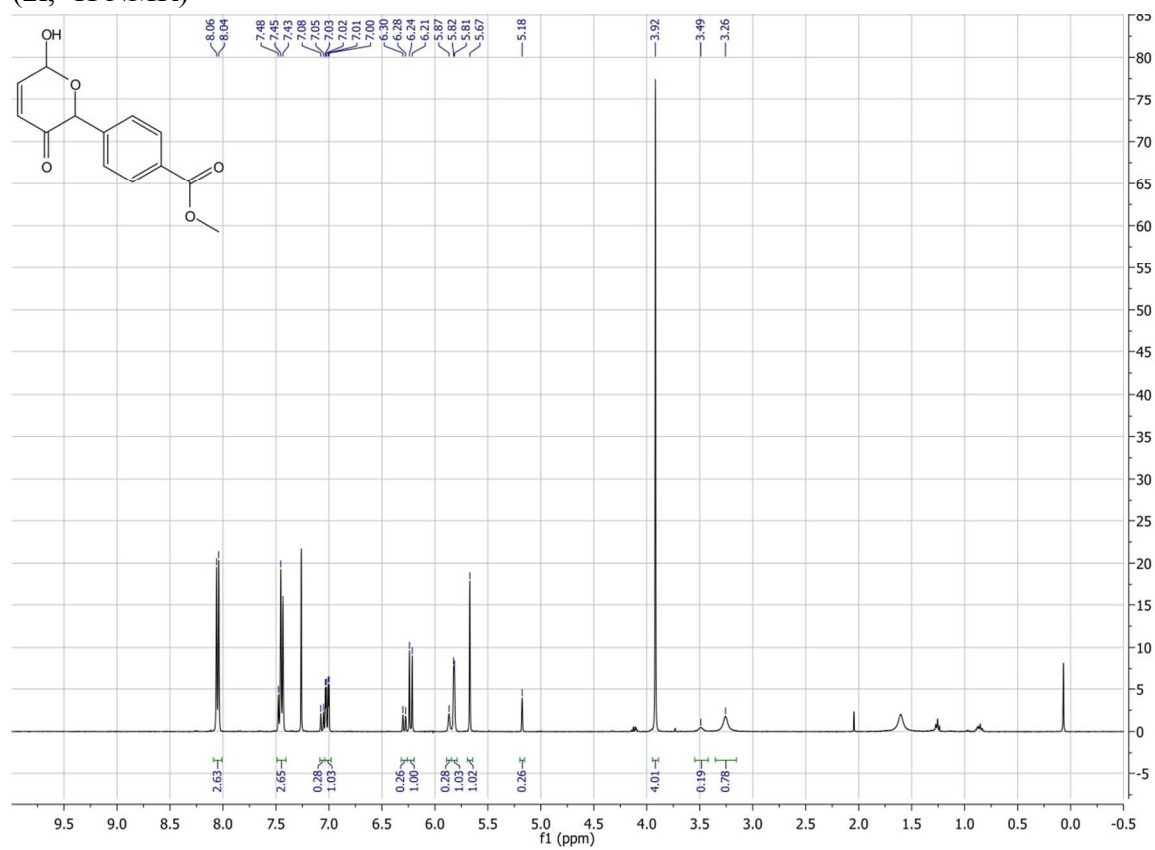
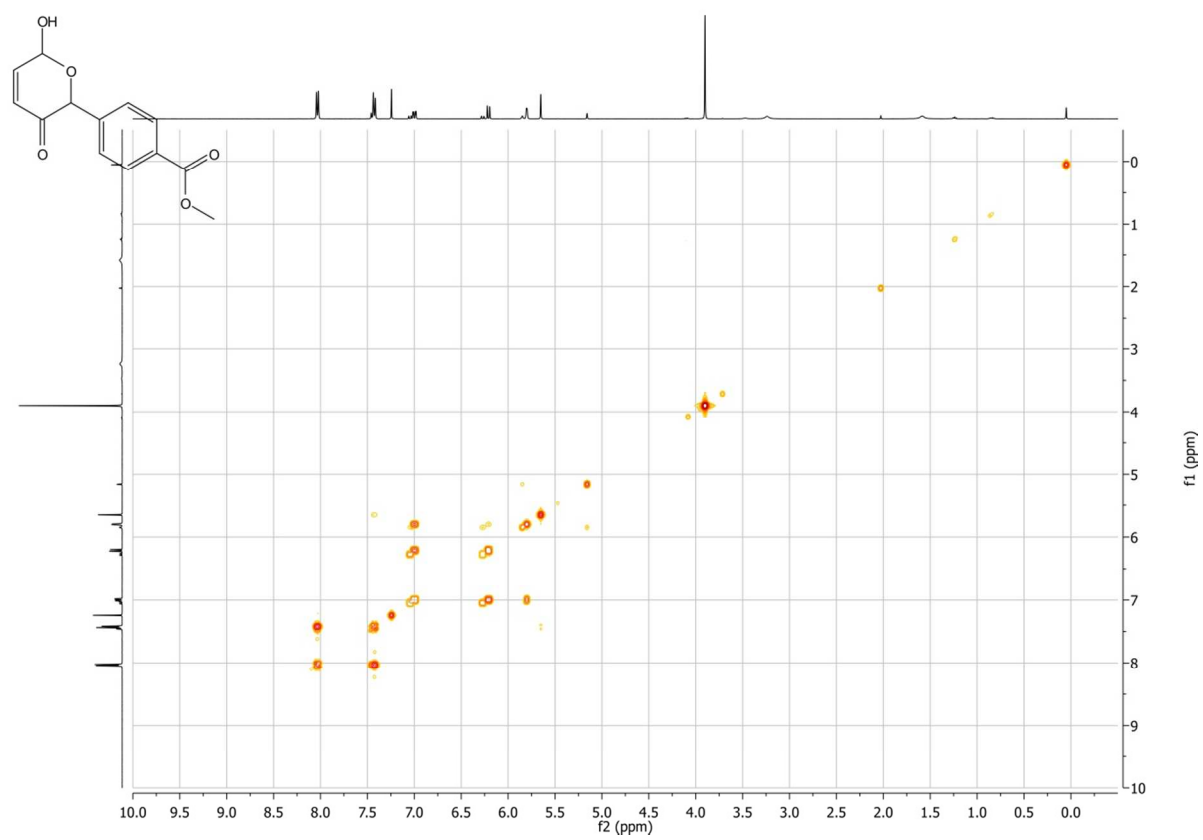
**(2g,  $^1\text{H}$  NMR)****(2g, COSY)**

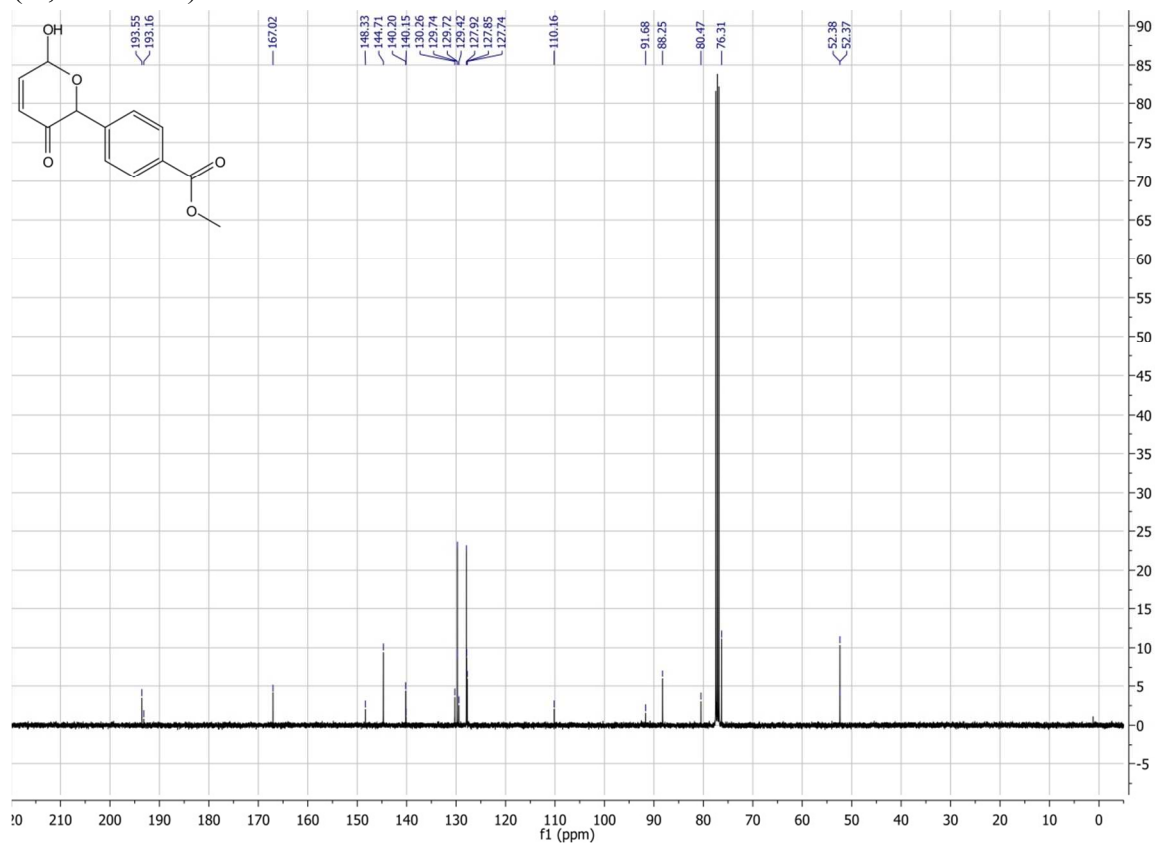
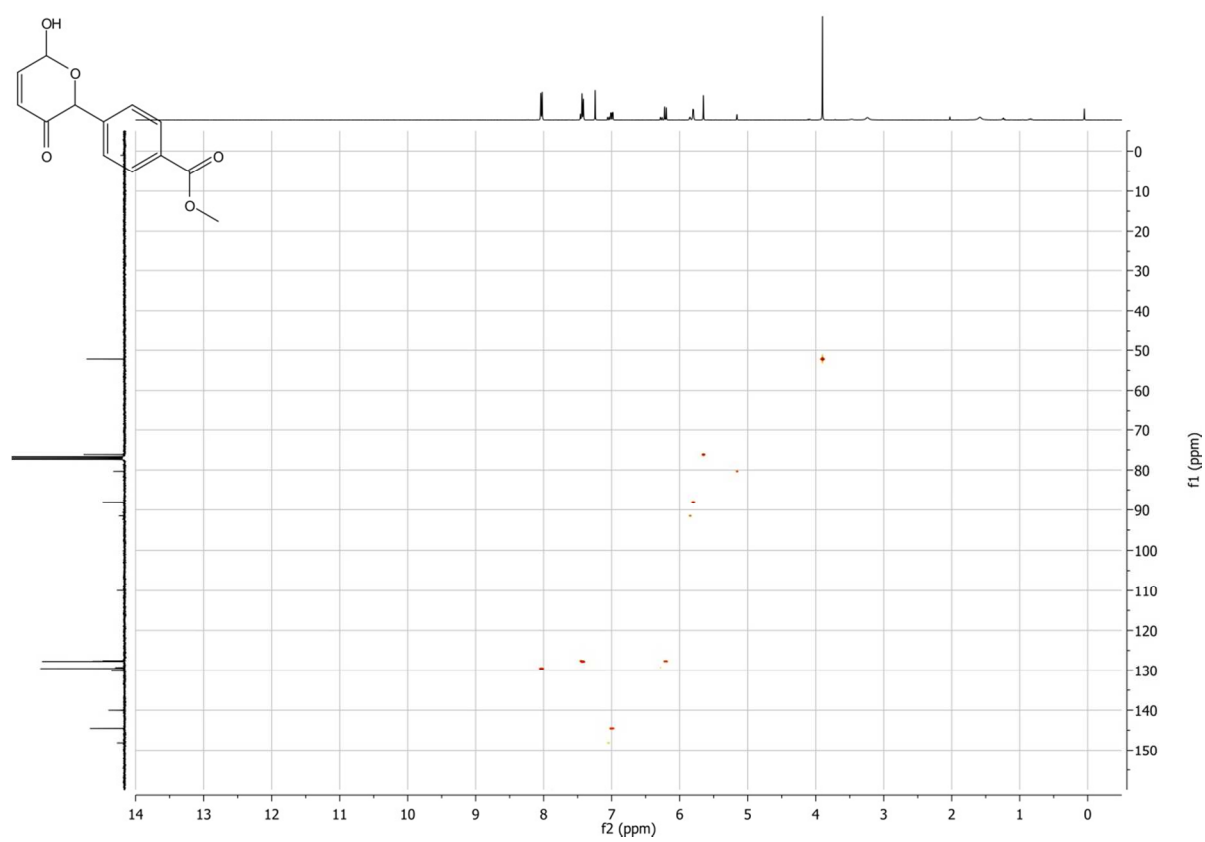
**(2g,  $^{13}\text{C}$  NMR)****(2g, HSQC)**

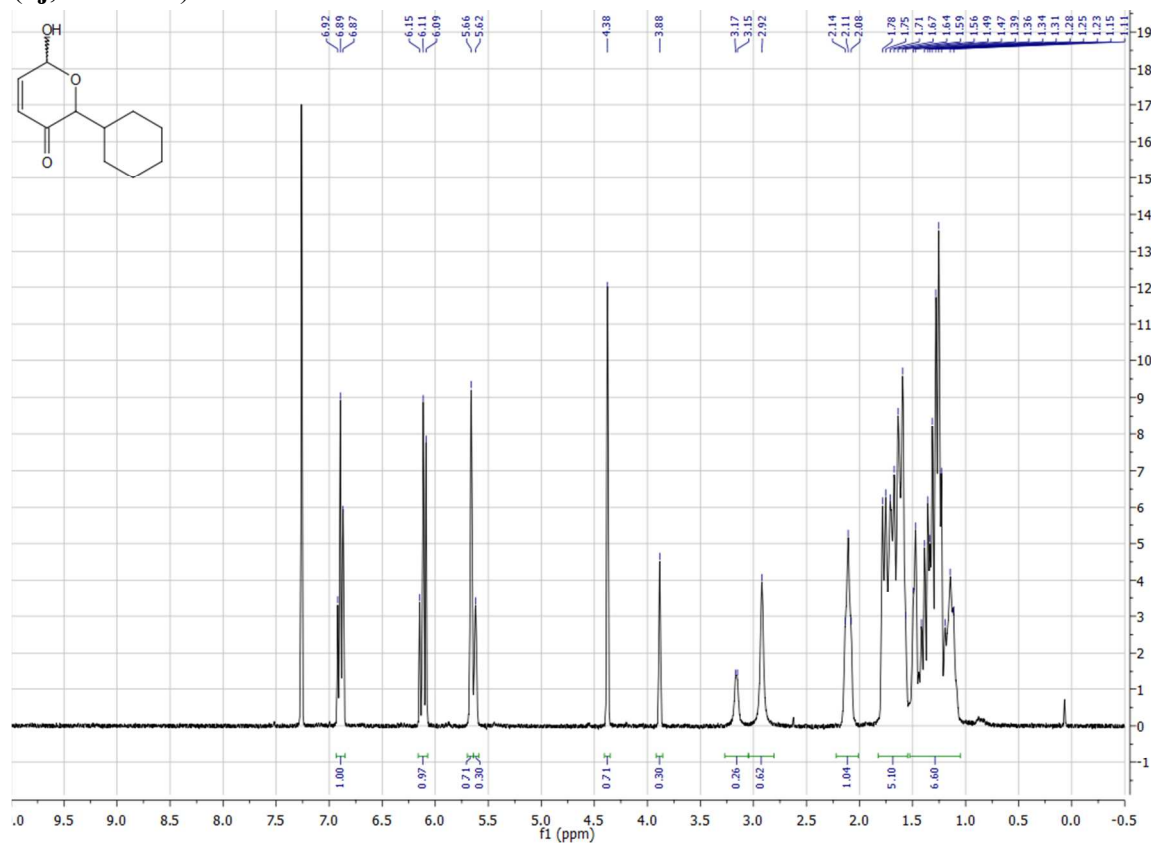
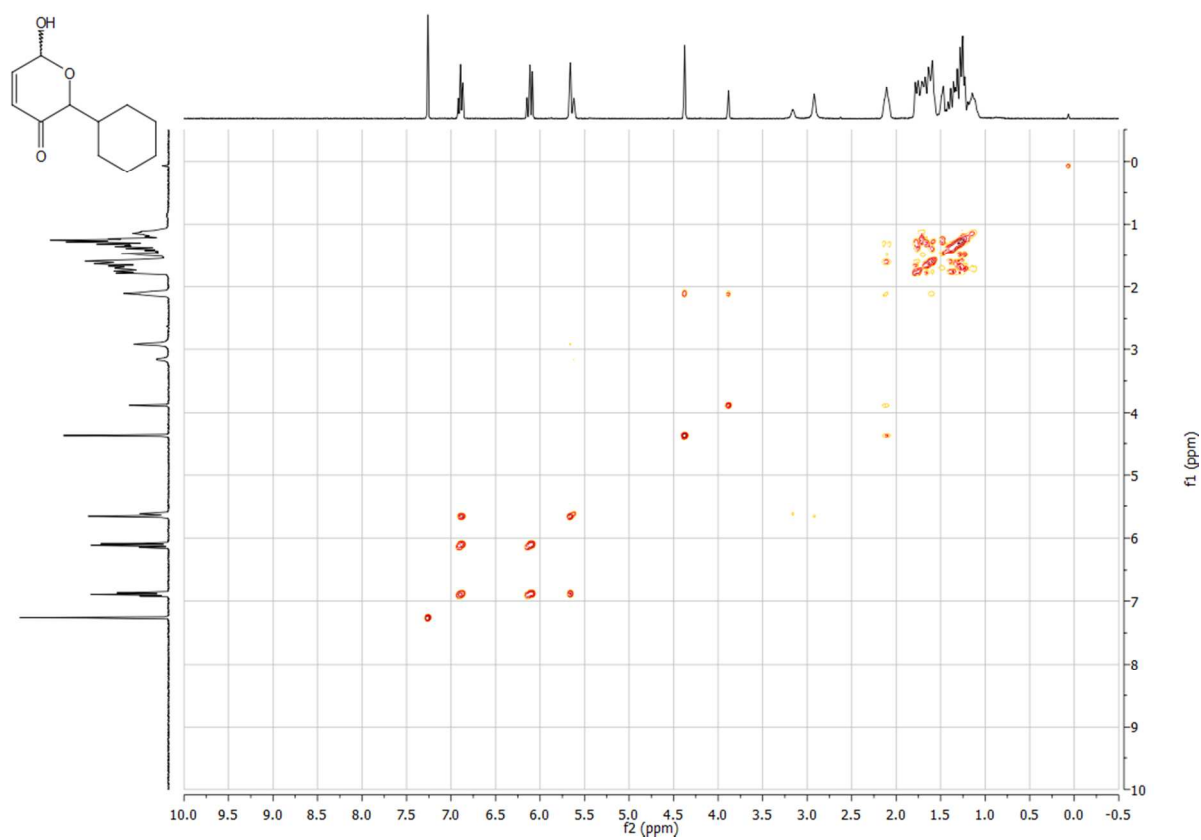
**(2h,  $^1\text{H NMR}$ )****(2h, COSY)**

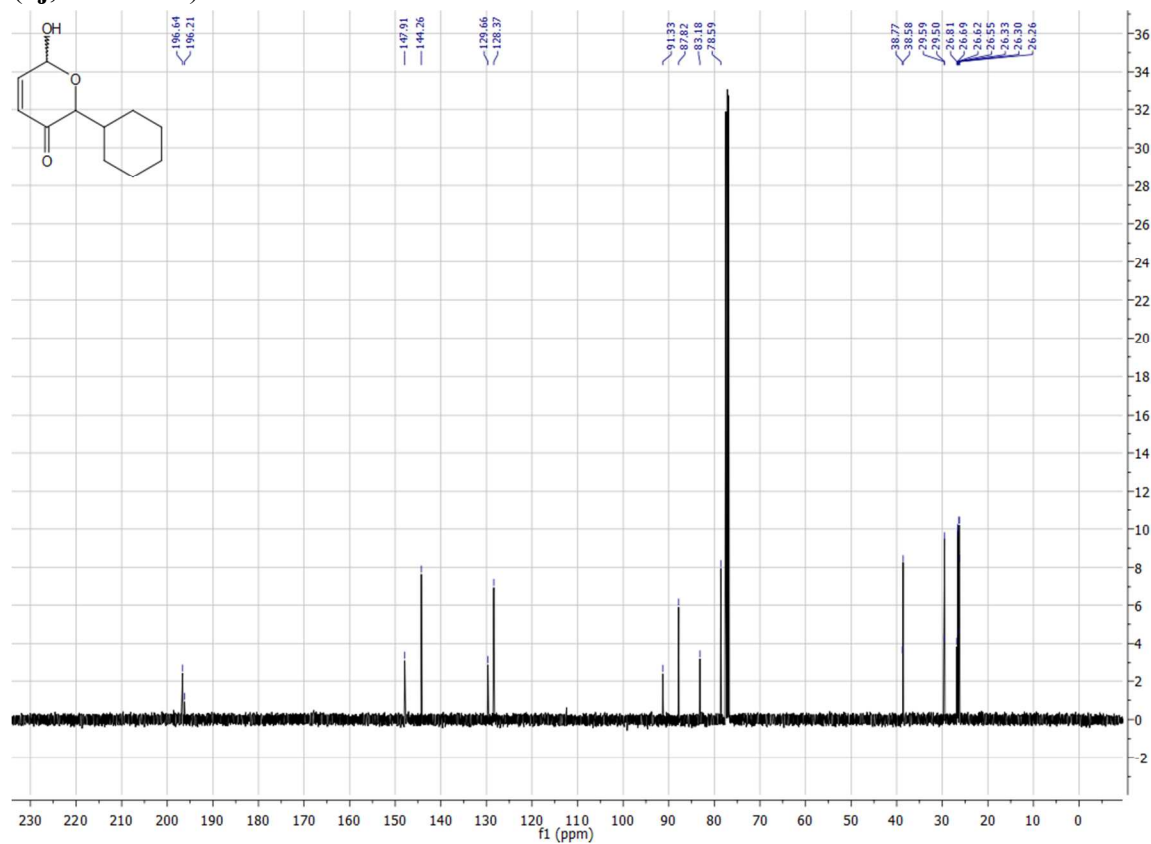
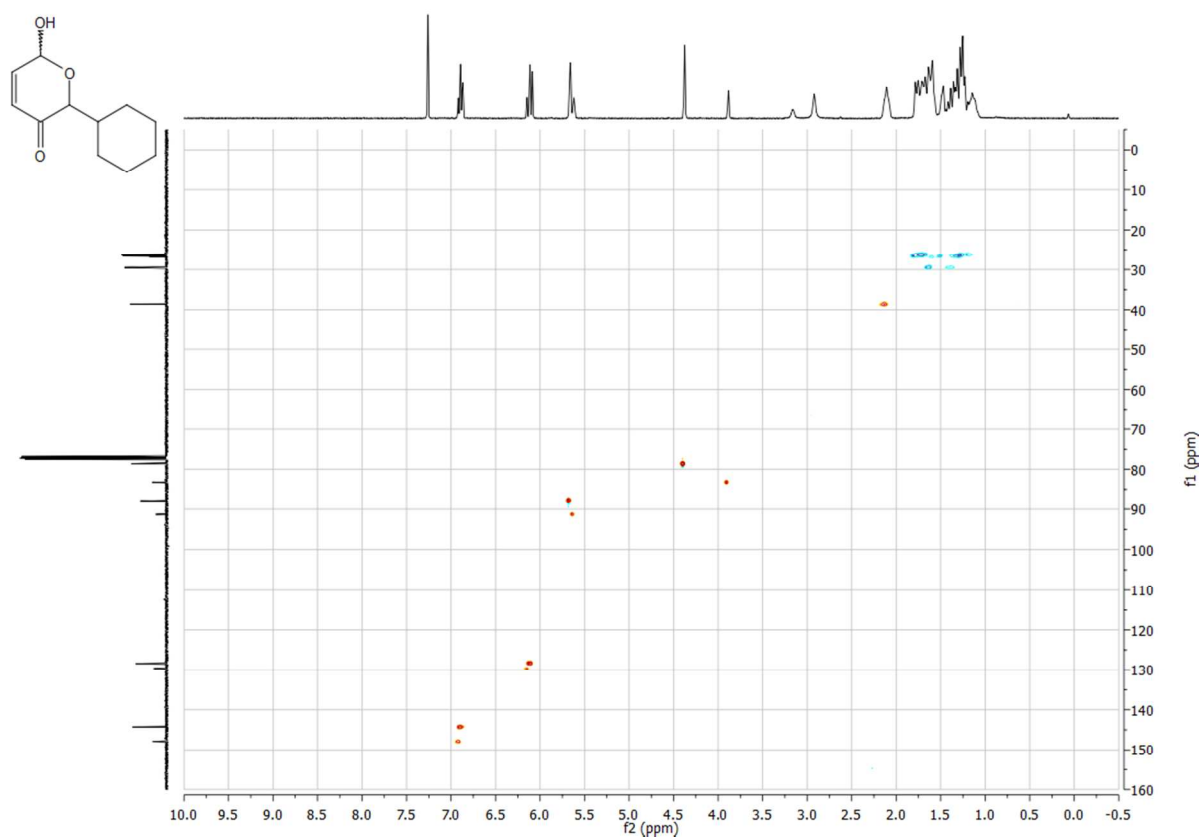
**(2h,  $^{13}\text{C}$  NMR)****(2h, HSQC)**



**(2i,  $^1\text{H}$  NMR)****(2i, COSY)**

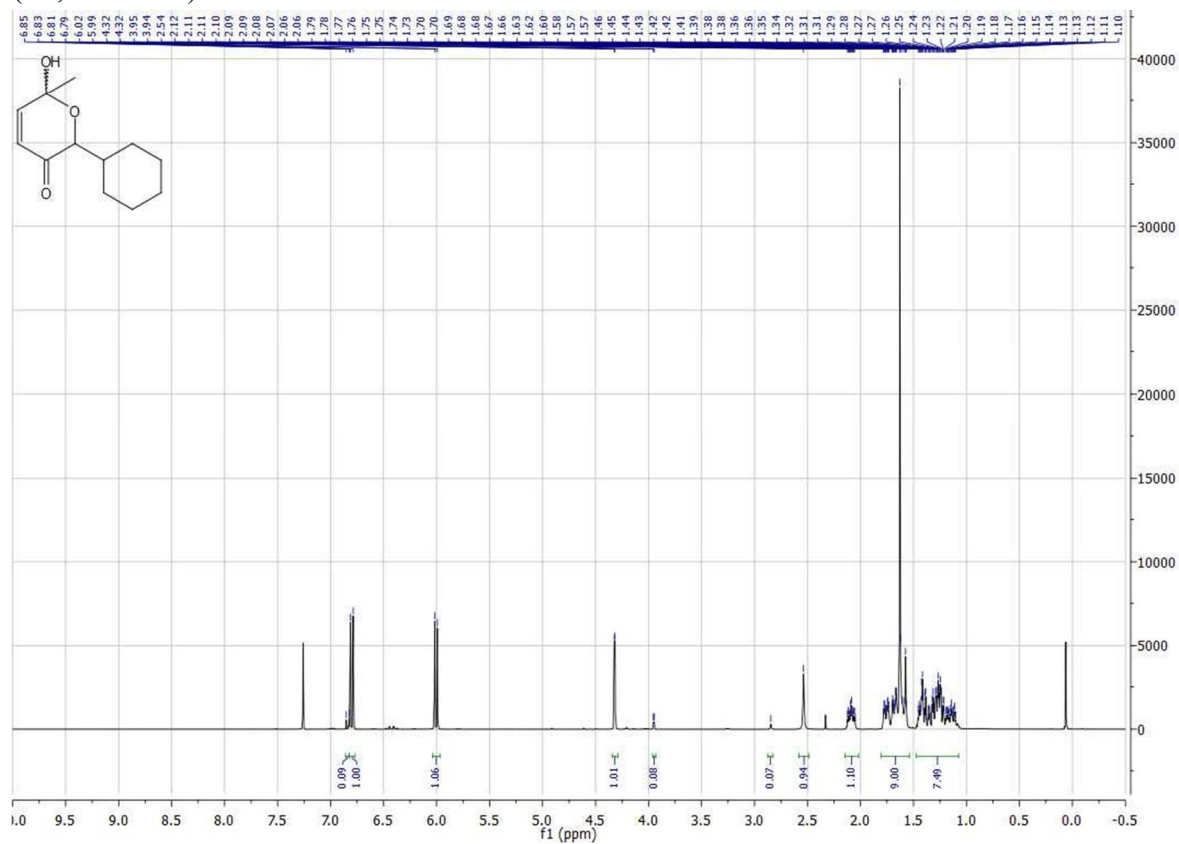
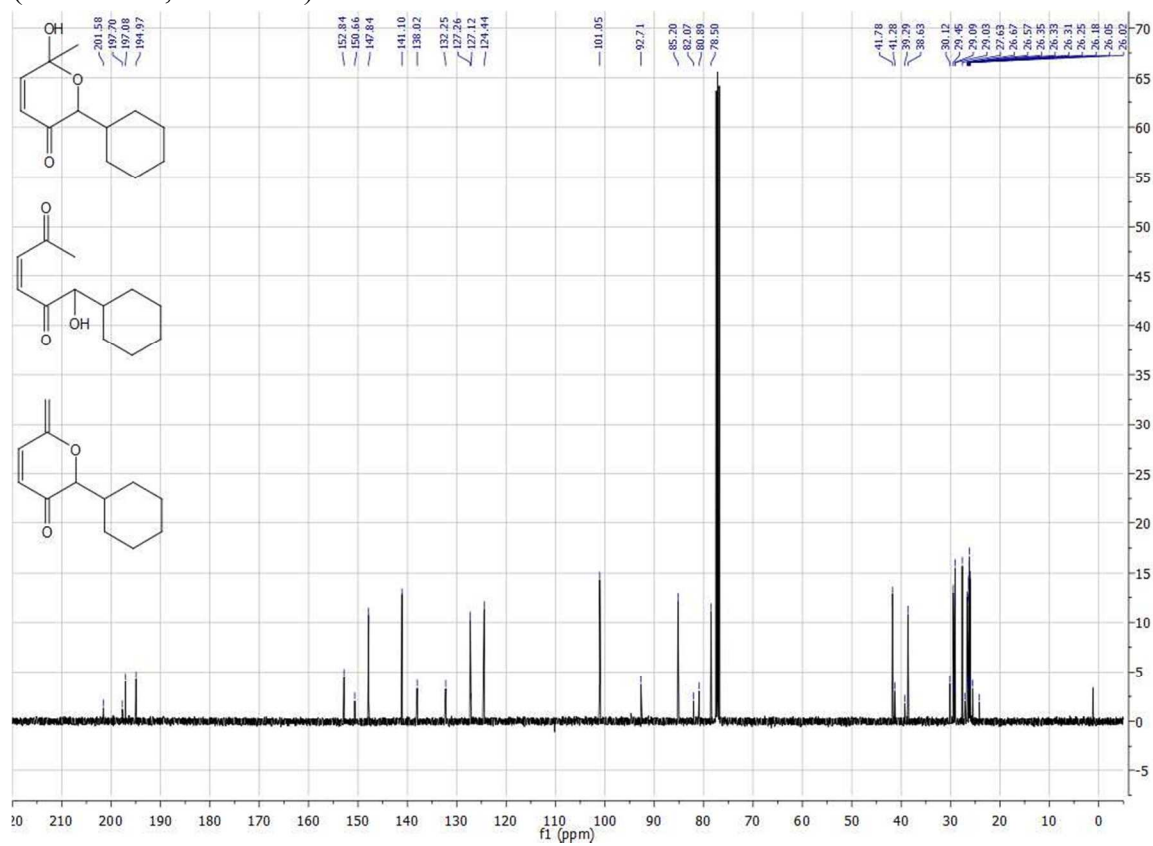
**(2i, <sup>13</sup>C NMR)****(2i, HSQC)**

**(2j,  $^1\text{H}$  NMR)****(2j, COSY)**

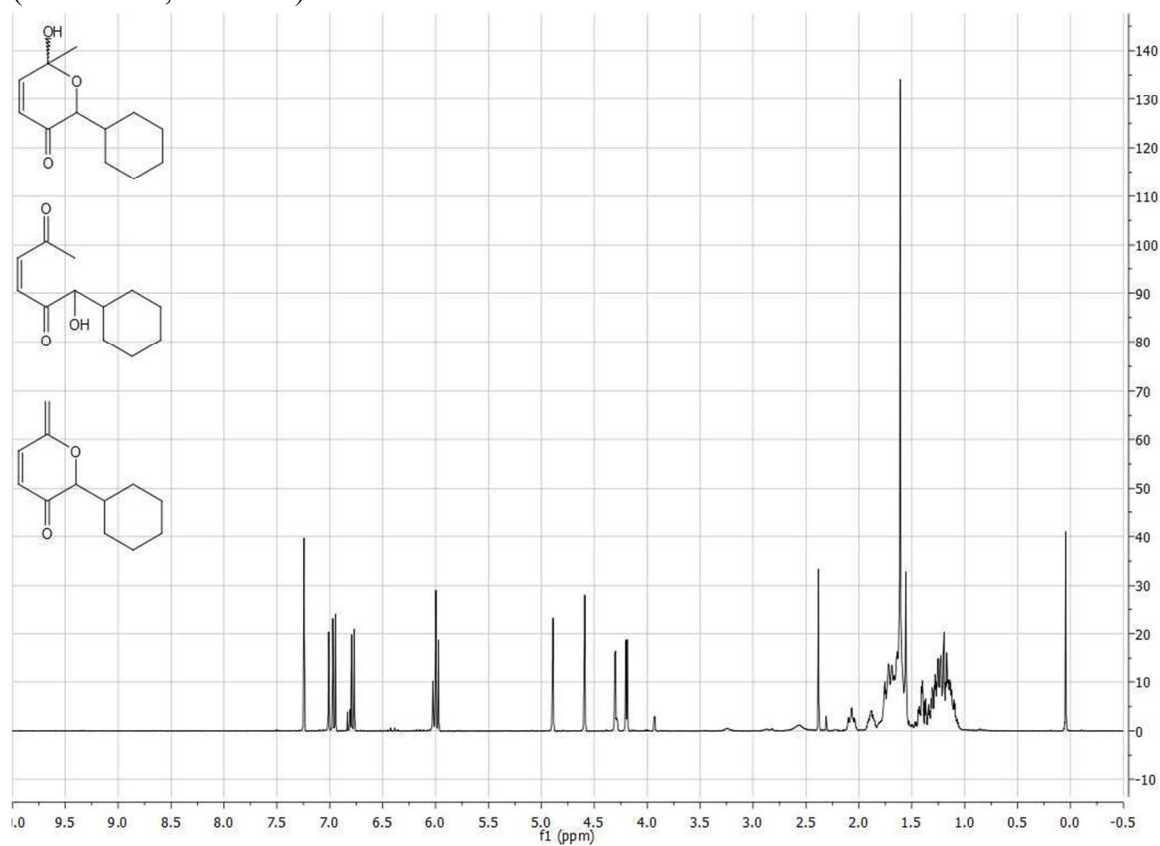
**(2j,  $^{13}\text{C}$  NMR)****(2j, HSQC)**

### NMR Analysis of compound **2k**

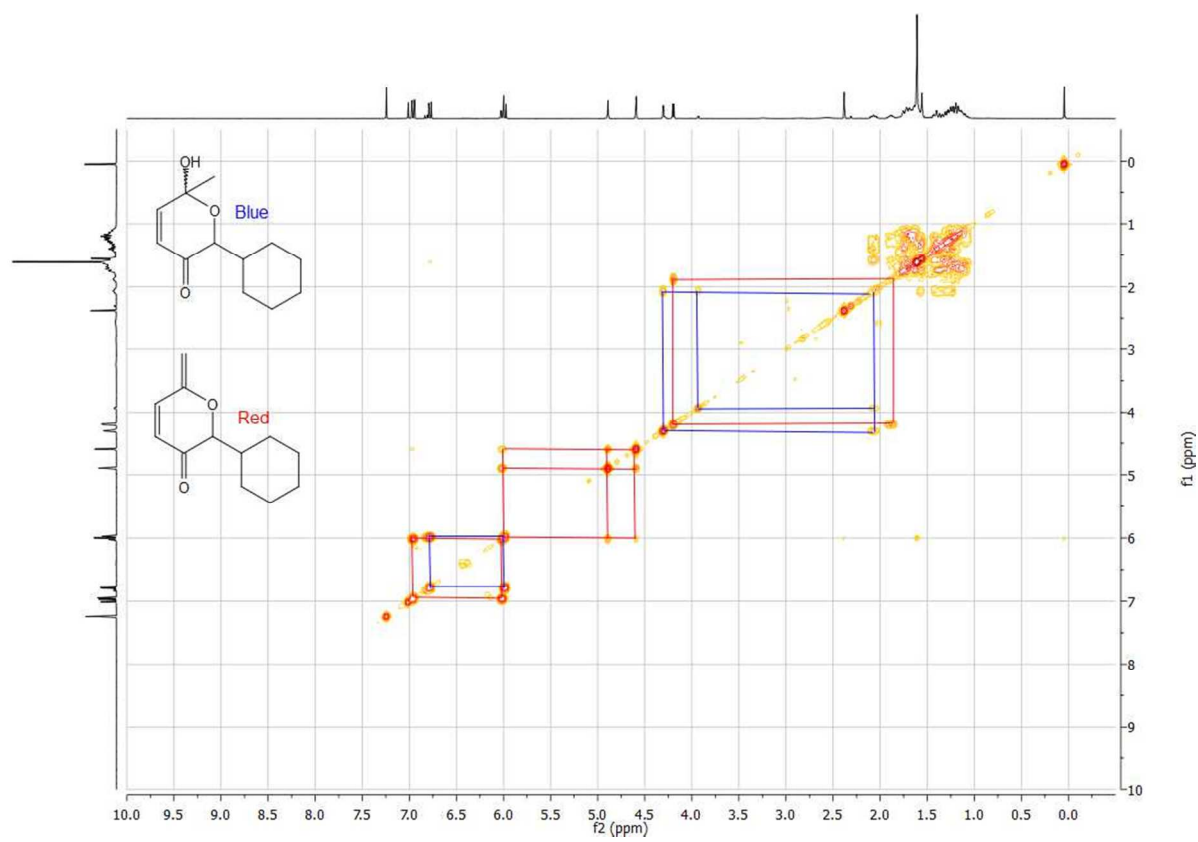
While compound **2k** was isolated as a white solid, analysis by NMR spectroscopy was complicated by conversion to other species in solution. Dissolution, followed by an immediate  $^1\text{H}$  NMR measurement shows compound **2k** as the primary component with the minor diastereomer comprising roughly 8% of the mixture (Page 51, Top). After a longer  $^{13}\text{C}$  NMR measurement a mixture of compounds is already observed (Page 51, Bottom). Acquiring another  $^1\text{H}$  NMR spectrum showed that now a mixture of compounds was present (Page 52, Top). Characteristic gem-alkenyl peaks helped us identify one component as **2k** after the loss of water (shown below in **red**).  $^{13}\text{C}$  NMR and HSQC helped us identify the other major component as the keto-form of compound **2k** (shown below in **orange**). The composition of the sample was observed over the course of eleven days. The ratio between the major and minor diastereomer of **2k** and the **dehydrated** compound remains relatively constant over the course of 11 days, where as the signals from of the **ring-open ketone** increase in intensity (Page 53, Bottom).

**(2k,  $^1\text{H}$  NMR)****(2k mixture,  $^{13}\text{C}$  NMR)**

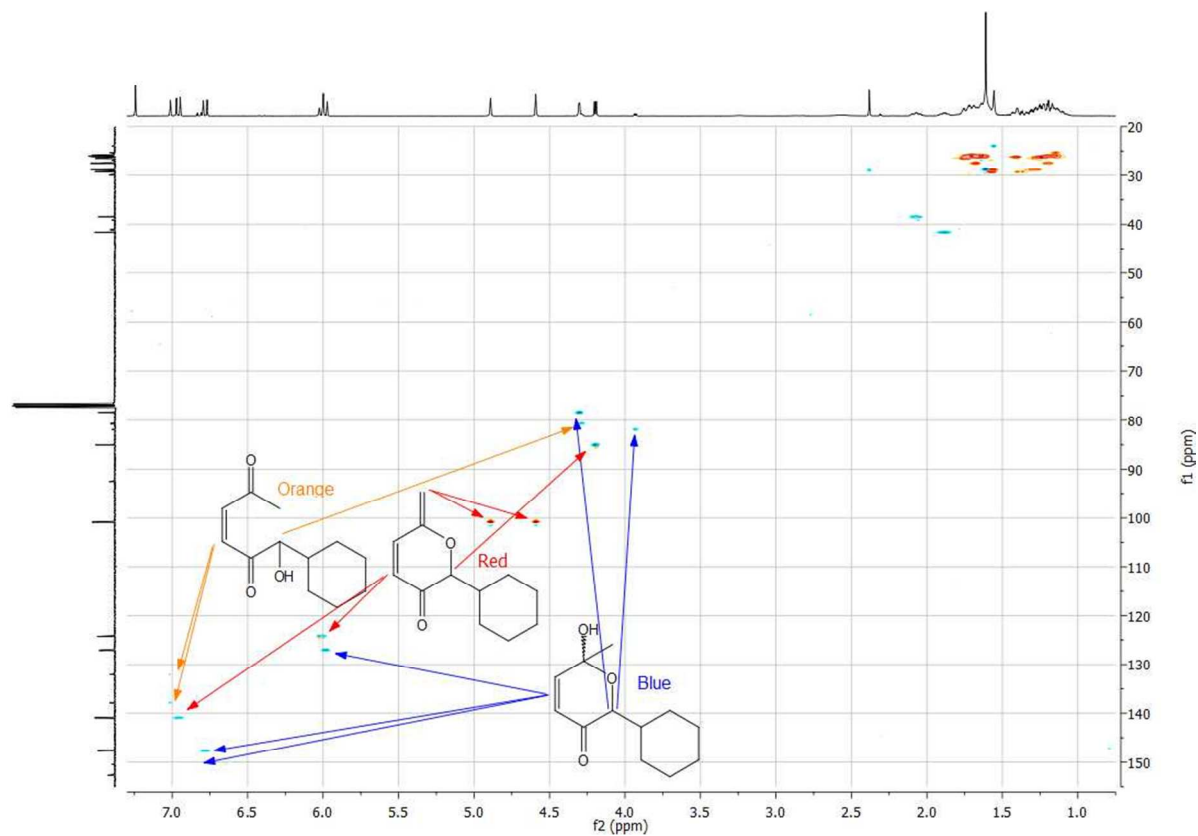
(2k mixture,  $^1\text{H}$  NMR)



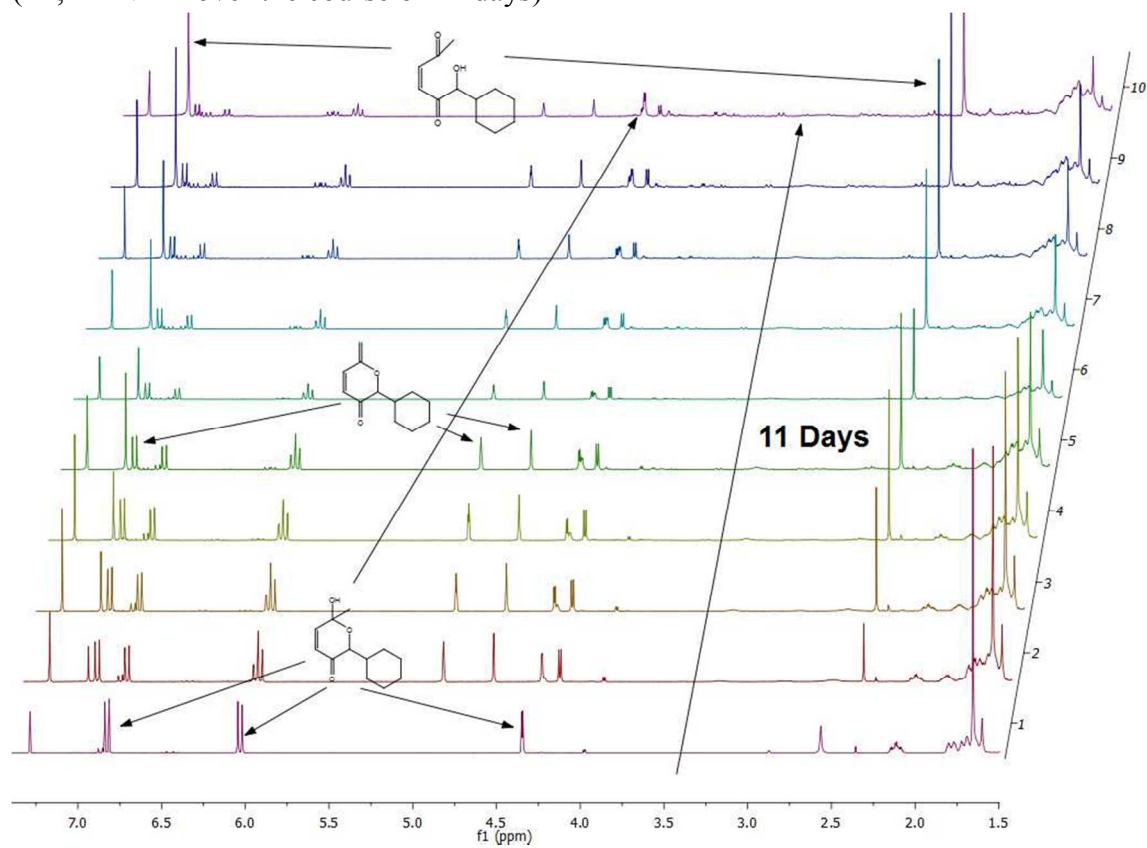
(2k mixture, COSY)



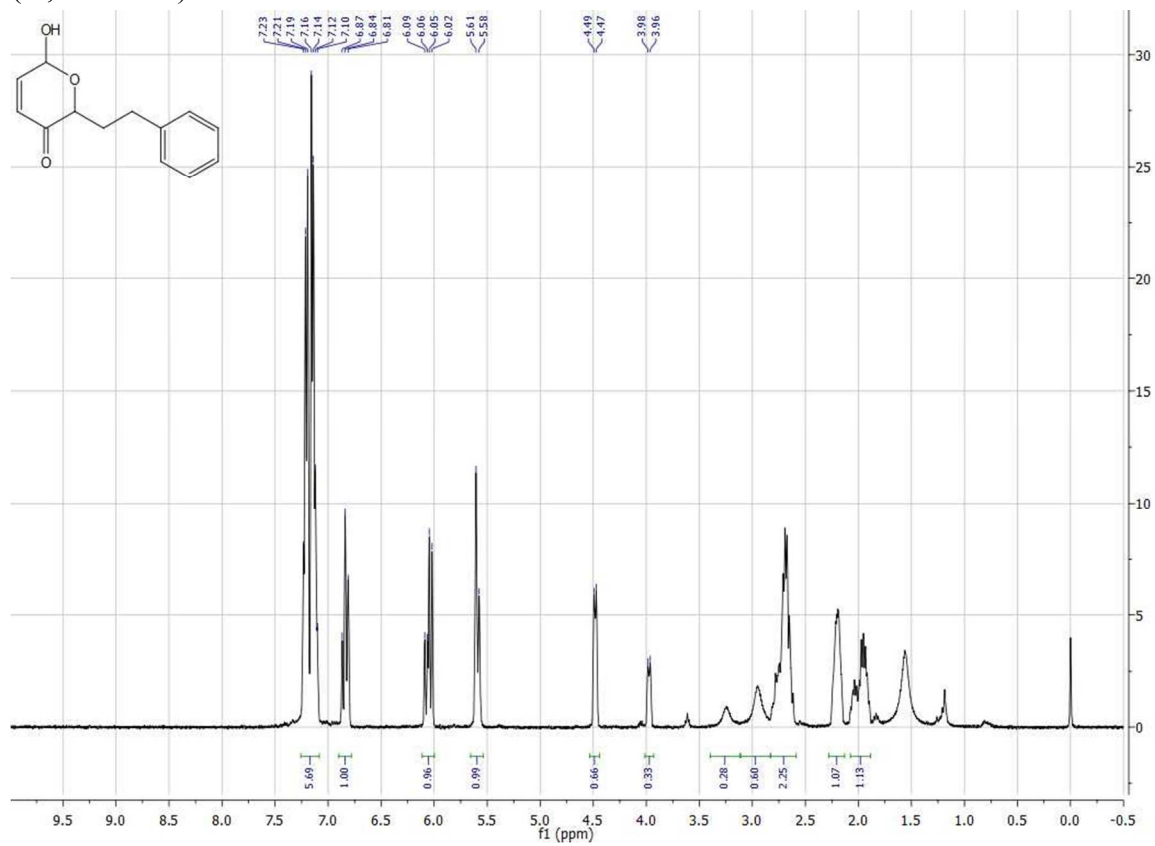
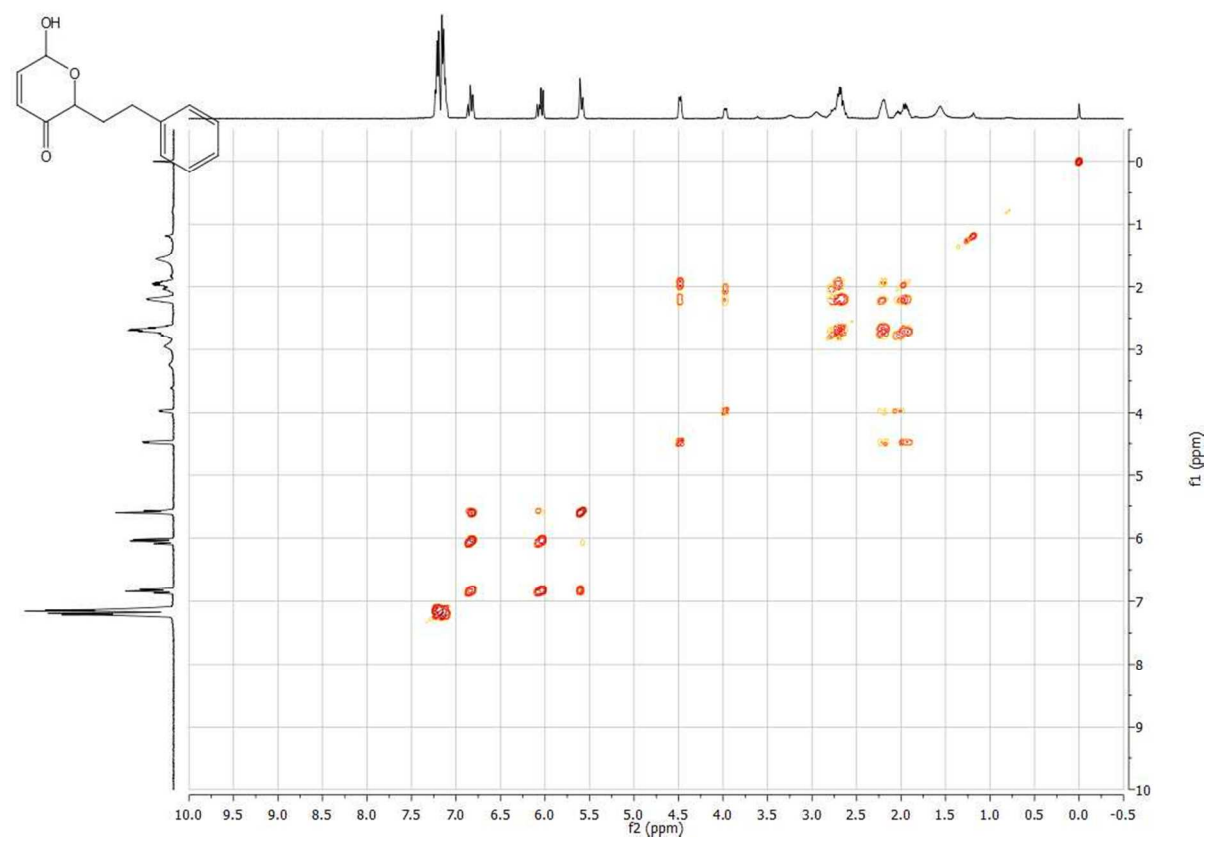
(2k mixture, HSQC)

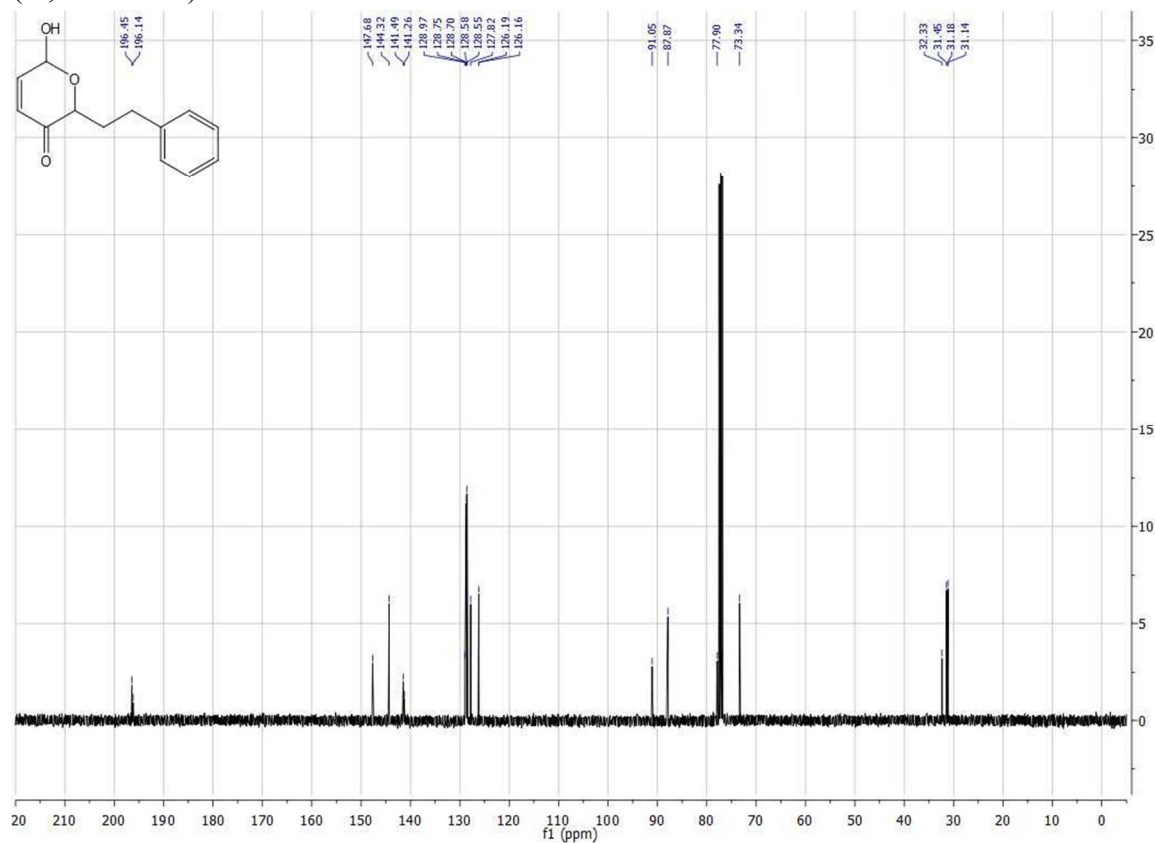
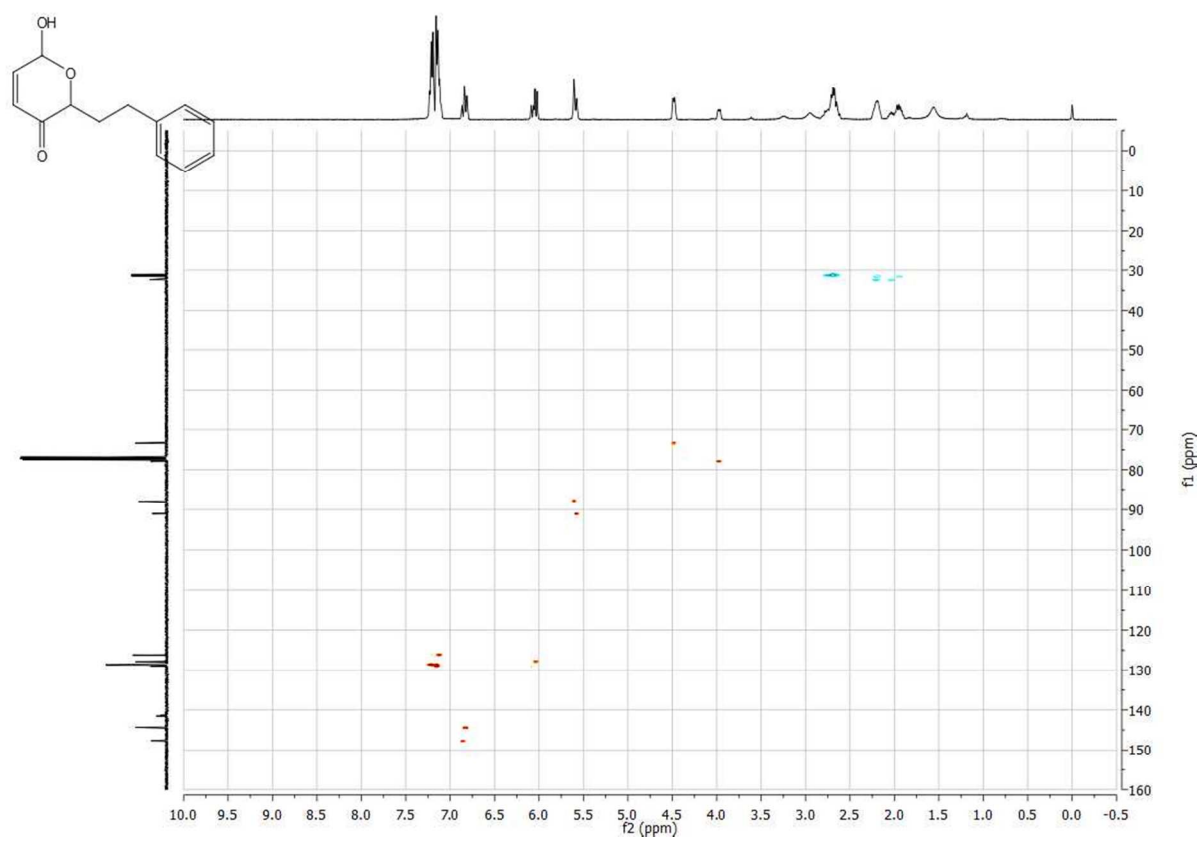


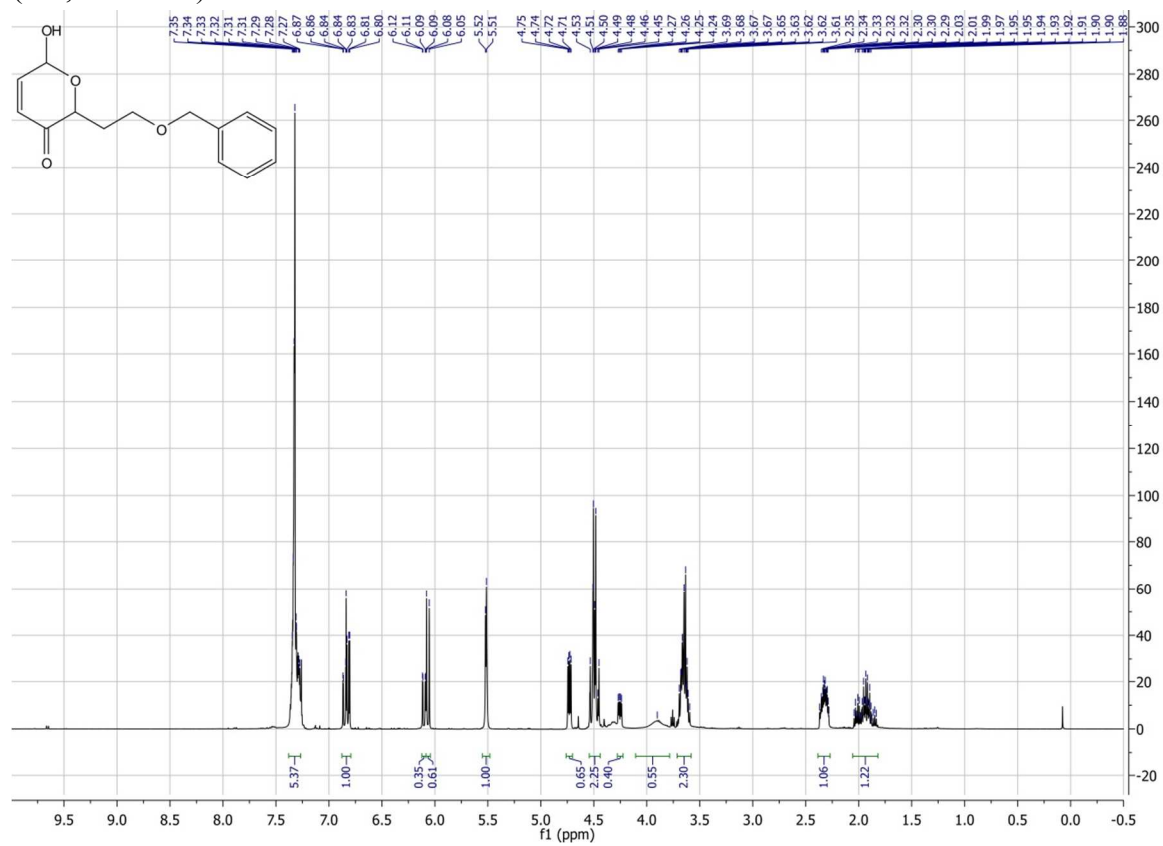
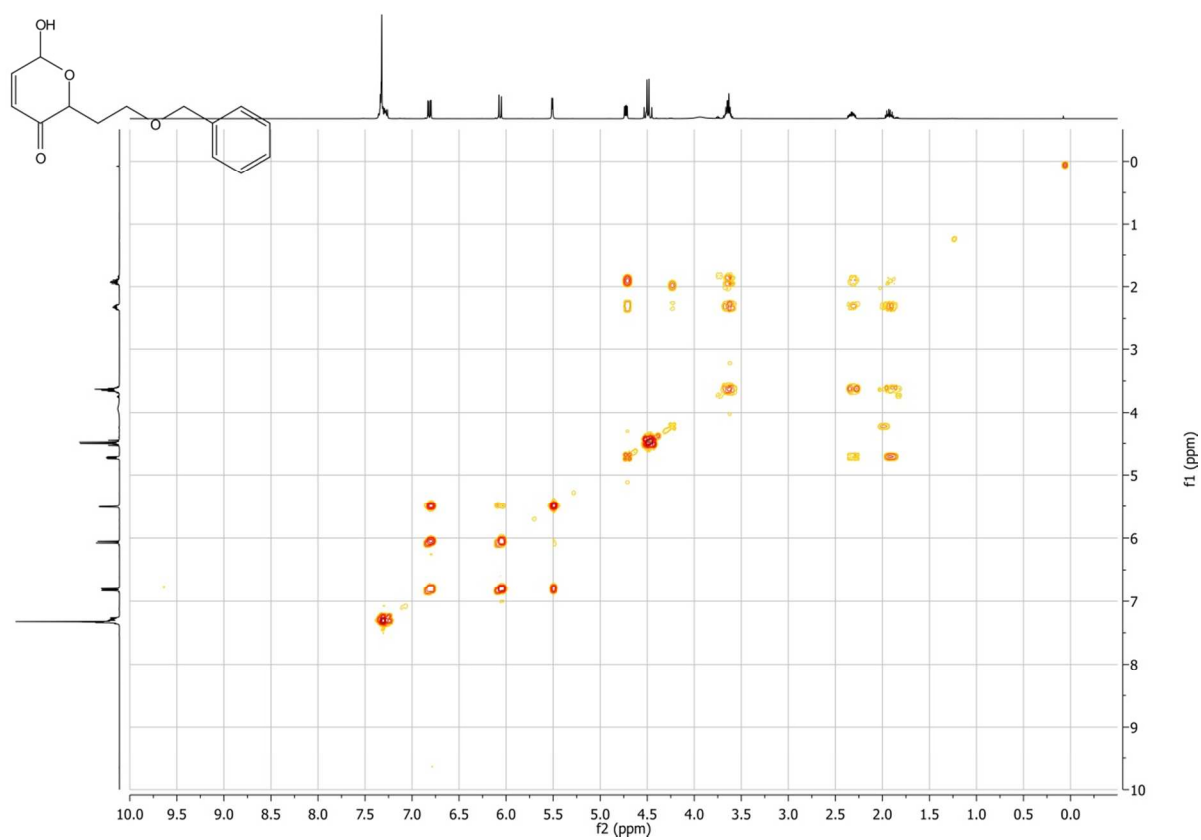
(2k,  $^1\text{H}$  NMR over the course of 11 days)

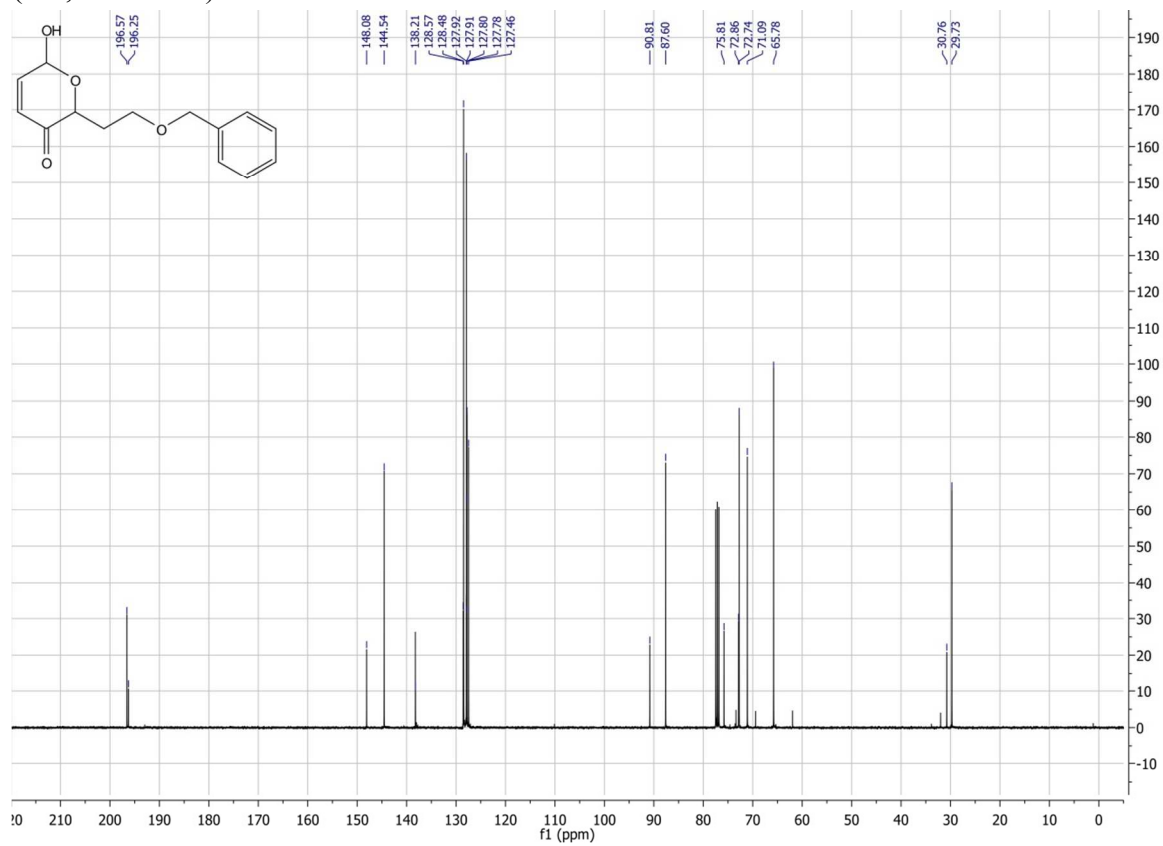
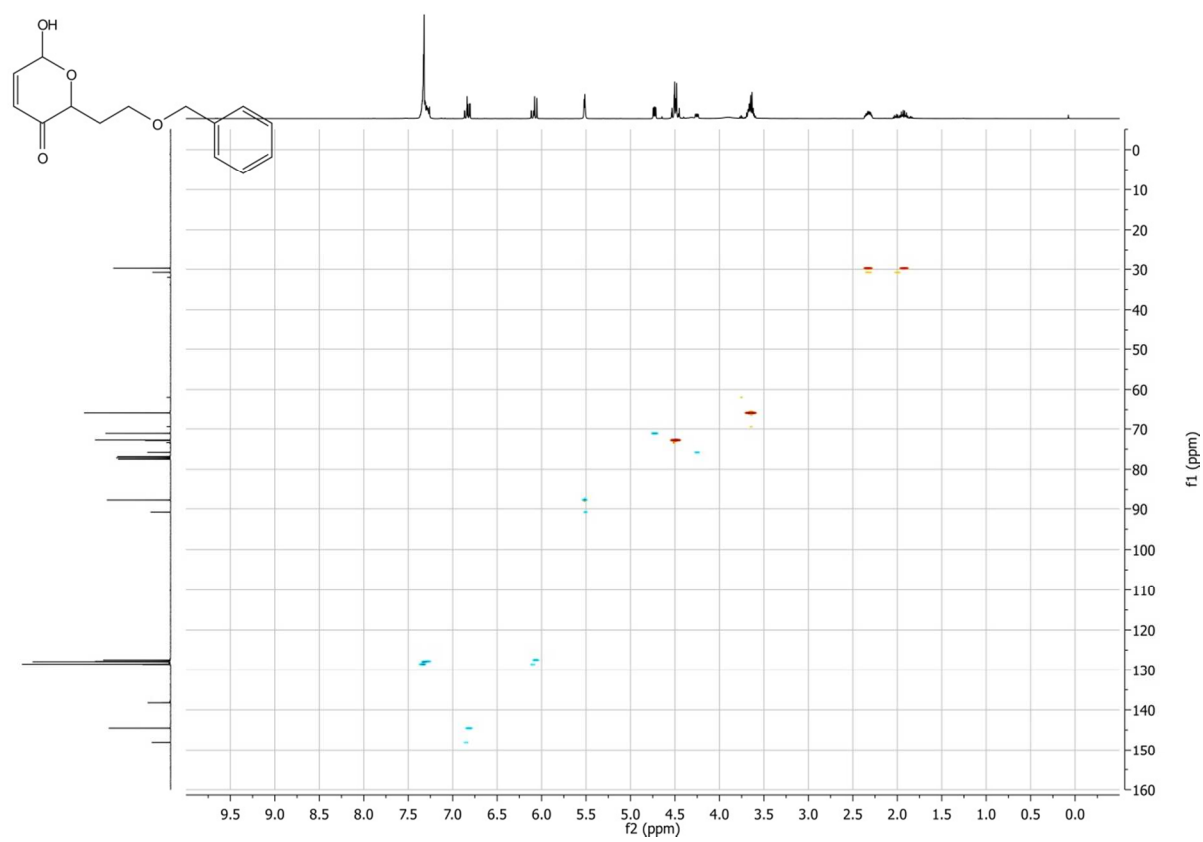


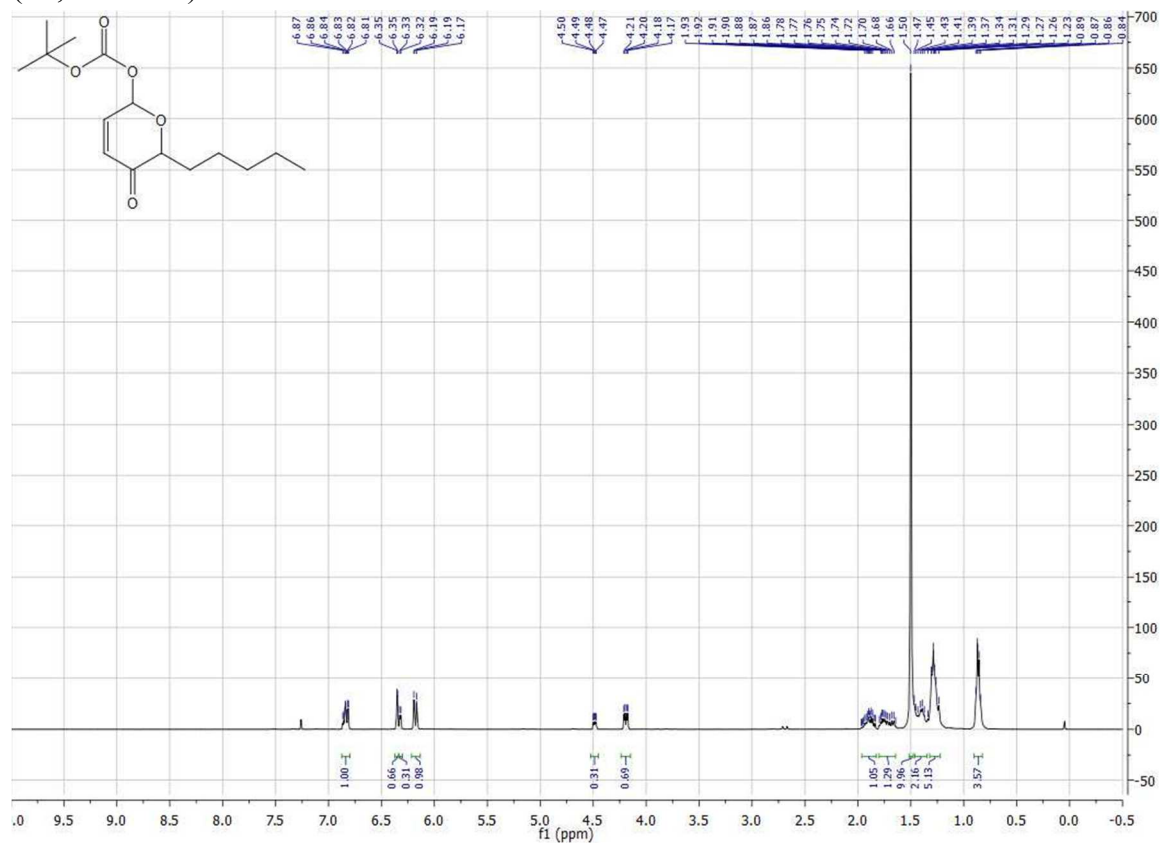
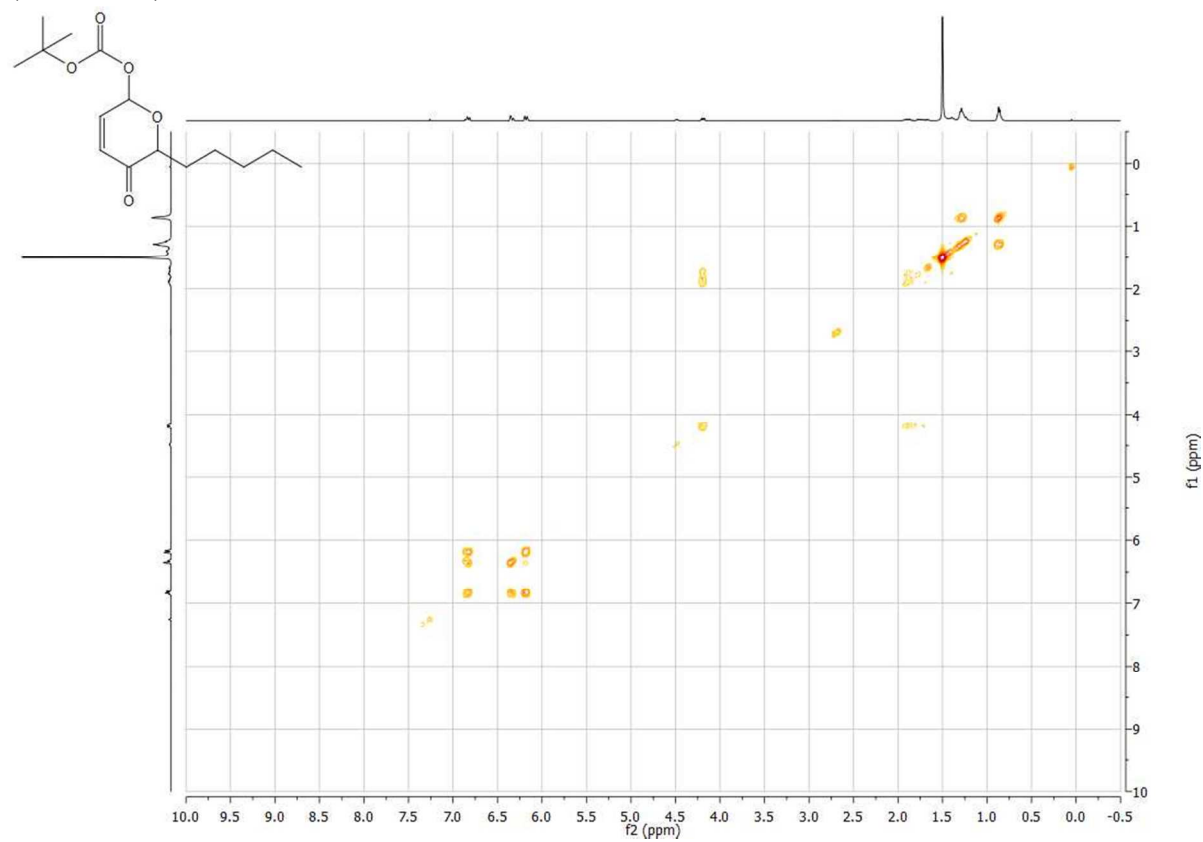


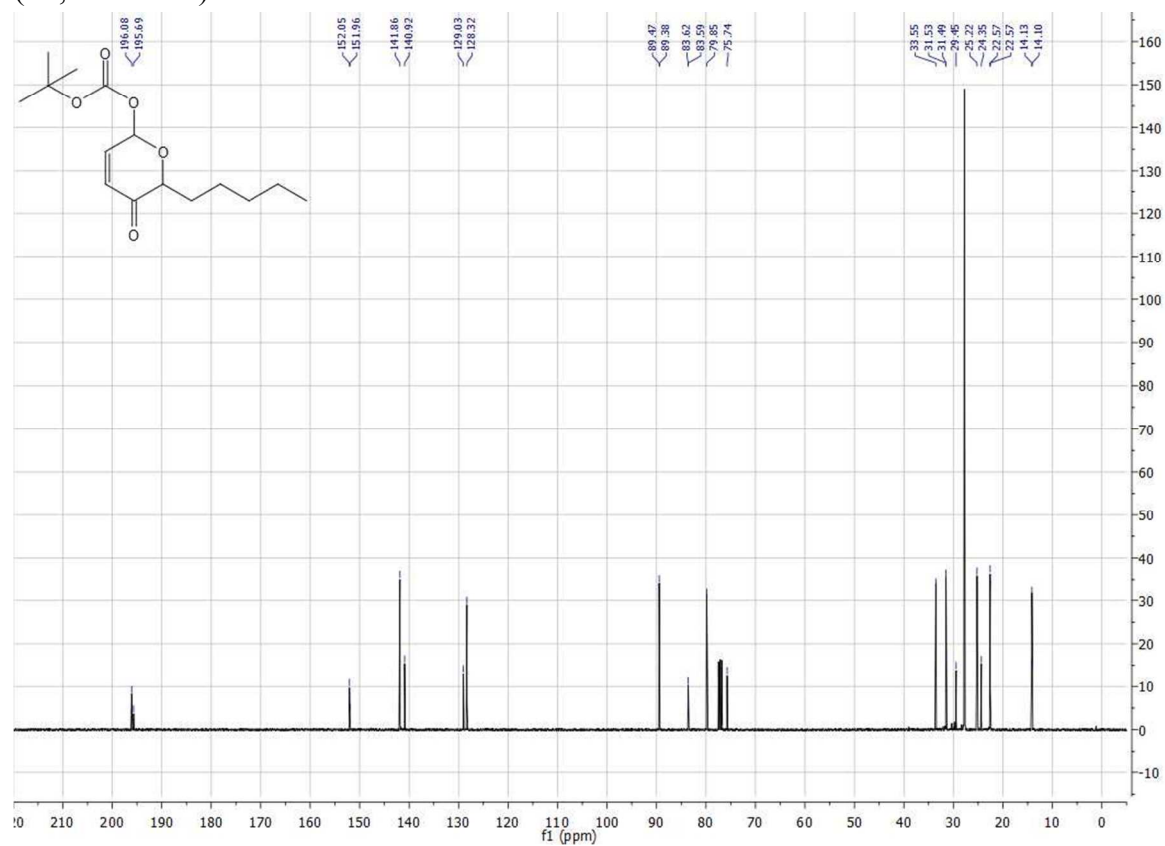
**(21,  $^1\text{H}$  NMR)****(21, COSY)**

**(21,  $^{13}\text{C}$  NMR)****(21, HSQC)**

**(2m,  $^1\text{H}$  NMR)****(2m, COSY)**

**(2m,  $^{13}\text{C}$  NMR)****(2m, HSQC)**

**(4n,  $^1\text{H}$  NMR)****(4n, COSY)**

**(4n,  $^{13}\text{C}$  NMR)****(4n, HSQC)**