Supporting Information

Synthesis of Coumarins *via* Pd-catalyzed Oxidative Cyclocarbonylation of 2-vinylphenols

*Jamie Ferguson, Fanlong Zeng, and Howard Alper**

Centre for Catalysis Research and Innovation, Department of Chemistry, University of Ottawa, 10 Marie Curie, Ottawa, Ontario, Canada, K1N 6N5

E-mail: howard.alper@uottawa.ca

Experimental Section (Supporting Information)

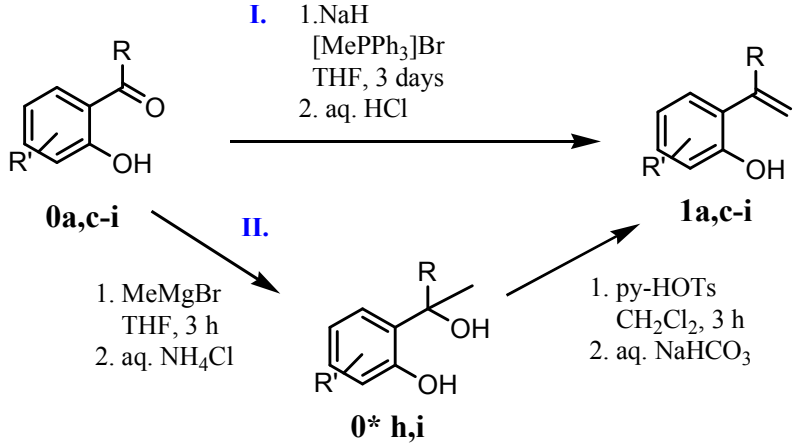
Contents:

I. General Considerations

Unless otherwise noted, all the materials were purchased from commercial suppliers and used as received. Solvents were freshly distilled by standard procedure prior to use. Flash chromatography was performed on silica gel 60Å (Aldrich, 200-425 mesh) with the indicated eluant. All ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra were recorded on a Bruker 400 MHz spectrometer. The NMR chemical shift values refer to $CDCl_3$ (δ (^{1}H), 7.26 ppm; δ (^{13}C), 77.16 ppm). Mass spectra were obtained on a VG7070E mass spectrometer.

II. Procedures for the Preparation of 2-vinylphenols, 1a-i

Compound **1b** was prepared according to a literature method.[1] All other substrates (**1a,c-i**) were prepared from the appropriate 2'-hydroxyacetophenone or 2'-hydroxybenzaldehyde (**0, Scheme 1**), either directly *via* a Wittig reaction (**I**), or in two steps (**II**), *via* Grignard addition, followed by dehydration.



Scheme 1

[1] X. Wang, A. Guram, S. Caille, J. Hu, J. P. Preston, M. Ronk, S. Walker, *Org. Lett.*, 2011, 13, 1881-1883.

Preparation of 1a,c-g (I, Scheme 1). Under a dry N_2 atmosphere in a 2-necked flask, THF was added to sodium hydride (4 equiv. to **1**), and the flask was cooled in an ice bath. Methyltriphenylphosphonium bromide (2 equiv. to **1**) was added slowly (*e.g.* 5 g per 5 min), and the mixture was stirred at 0 °C (1 h). **1** (*ca.* 10 mmol) was then added dropwise at 0 °C. The mixture was allowed to warm to room temperature. After being stirred for 2-3 days, the flask was cooled in an ice bath, and the reaction mixture was quenched by dropwise addition of 1M $HCl_{(aq.)}$, turning its appearance from a single, opaque, bright yellow phase to two transparent, pale or colorless phases. The mixture was transferred to a separatory funnel, and the organic phase was collected and dried with anhydrous $MgSO_4$. The dried solution was filtered through a glass sintered funnel, and solvent was removed under reduced pressure. The residue was separated by flash chromatography with a gradient of hexanes to diethyl ether/hexanes (v/v = 1:9) as the eluant, to yield the olefin product as a yellow or colorless oil after the evaporation of solvent. Whenever the product and the starting compound eluted very closely together, final purification was achieved by distillation under high vacuum. Note that 2-vinylphenol (**1c**) crystallized to a white solid when it was stored in a freezer.

Preparation of 1h and 1i (II, Scheme 1). Under a dry N_2 atmosphere in a 2-necked flask, compound **0h** or **0i** (5 mmol) was dissolved in THF (10 mL). The flask was cooled in an ice bath, and to it was added dropwise a solution of methylmagnesium bromide (3 M in diethyl ether, 4 mL). The solution was warmed to 40 °C and stirred for 3 h, while the reaction was monitored by TLC. The reaction mixture was then cooled in an ice bath and quenched by addition of saturated aqueous NH_4Cl. After transferring the mixture into a separatory funnel, the alcohol product (**0***) was extracted into diethyl ether and washed once with saturated aqueous NaCl. The organic phase was collected and dried with anhydrous $MgSO_4$, then filtered through a

glass sintered funnel, and solvent was removed under reduced pressure. The residue was separated by flash chromatography with a gradient of hexanes to diethyl ether/hexanes (v/v = 1:4). After solvent evaporation, the alcohol product was obtained as a white solid (**0*h**) or as a yellow oil (**0*i**), in quantitative yield.

In a 2-necked flask, the alcohol **0*** (4 mmol) was dissolved in CH_2Cl_2 (12 mL) under N_2 atmosphere, and pyridinium *p*-toluenesulfonate complex (0.8 mmol) was added. The flask was sealed under a bubbler and stirred in an oil bath at 40 °C for 2.5 h. The reaction mixture was washed with saturated aqueous $NaHCO_3$ and transferred into a separatory funnel. The product **1** was extracted with diethyl ether, and washed with saturated aqueous NaCl. The organic phase was collected and dried with anhydrous $MgSO_4$, then filtered through a glass sintered funnel, and solvent was removed under reduced pressure. The residue was separated by flash chromatography with a gradient of hexanes to diethyl ether/hexanes (v/v = 1:19). Products **1h** and **1i** were obtained as yellow oils in 79% and 40% yield, respectively.

III. Optimized Procedures for the Pd-Catalyzed Synthesis of Coumarins from 2-vinylphenols

Optimized procedure using 1,4-benzoquinone as oxidant. A mixture of $Pd(OAc)_2$, (0.1 mmol), dppb (0.1 mmol), 1,4-benzoquinone (1.5 mmol), **1** (1 mmol), and CH_3CN (5 mL) were sequentially added to a 45 mL glass-lined autoclave. After sealing, the autoclave was purged three times with CO and pressurized with 100 psi of CO, and then stirred and heated at 110 °C for 20 h.

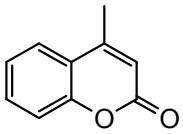
The autoclave was removed from the oil bath and cooled to room temperature prior to the release of excess carbon monoxide. Solvent was removed under reduced pressure, and the

residue was purified by flash chromatography with a gradient of hexanes to ethyl acetate / diethyl ether / hexanes (1:1:8 v/v/v) as the eluant, to afford the products **2a-i** as white solids.

Optimized procedure using air as oxidant. A mixture of $Pd(OAc)_2$, (0.1 mmol), 1,10-phenanthroline (0.1 mmol), **1** (1 mmol), and CH_3CN (5 mL) were added sequentially to a 150 mL heavy glass autoclave. After sealing, the autoclave was pressurized sequentially with 20 psi of air and 20 psi of CO, and then stirred and heated at 110 °C for 20 h.

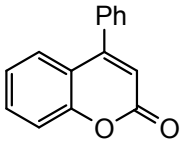
The autoclave was removed from the oil bath and cooled to room temperature prior to the release of gas pressure. Solvent was removed under reduced pressure, and the residue was purified by flash chromatography with a gradient of hexanes to ethyl acetate / hexanes (1:4 v/v) as the eluant, to afford the products **2a, 2c, 2d, 2g,** and **2h** as orange or white solids.

IV. NMR Spectroscopic and High-Resolution Mass Spectrometry Data for Coumarin Products, 2a-i



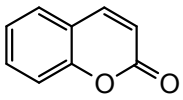
4-Methyl-2H-chromen-2-one (2a)

^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.56 (m, 1 H), 7.48 (m, 1 H), 7.33-7.22 (m, 2 H), 6.24 (s, 1 H), 2.40 (m, 3 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 160.7, 153.4, 152.3, 131.7, 124.5, 124.1, 119.8, 116.9, 115.0, 18.6; HRMS (EI) *m/z* calcd for $C_{10}H_8O_2$ (M^+) 160.0524, found 160.0521.



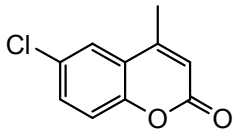
4-Phenyl-2H-chromen-2-one (2b)

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.55-7.20 (m, 8 H), 7.14 (m, 1 H), 6.28 (m, 1 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 160.6, 155.6, 154.1, 135.1, 131.9, 129.6, 128.8, 128.3, 126.9, 124.1, 118.9, 117.2, 115.1; HRMS (EI) *m/z* calcd for $C_{15}H_{10}O_2$ (M^+) 222.0681, found 222.0681.



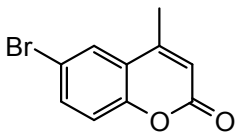
2H-Chromen-2-one (2c)

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.65 (d, *J*=9.46 Hz, 1 H), 7.45 (m, 2 H), 7.23 (m, 2 H), 6.36 (d, *J*=9.50 Hz, 1 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 160.7, 154.0, 143.4, 131.8, 127.8, 124.4, 118.8, 116.9, 116.7; HRMS (EI) *m/z* calcd for $C_9H_6O_2$ (M^+) 146.0368, found 146.0365.



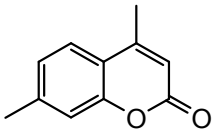
6-Chloro-4-methyl-2H-chromen-2-one (2d)

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.50 (d, *J*=2.45 Hz, 1 H), 7.41 (dd, *J*=8.82, 2.45 Hz, 1 H), 7.21 (m, 1 H), 6.26 (m, 1 H), 2.36 (d, *J*=1.32 Hz, 3 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 160.0, 151.9, 151.2, 131.6, 129.6, 124.2, 121.1, 118.5, 116.1, 18.6; HRMS (EI) *m/z* calcd for $C_{10}H_7O_2Cl$ (M^+) 194.0135, found 194.0135.



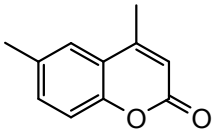
6-Bromo-4-methyl-2H-chromen-2-one (2e)

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.73 (m, 1 H), 7.63 (m, 1 H), 7.24 (d, *J*=8.00 Hz, 1 H), 6.34 (m, 1 H), 2.44 (d, *J*=1.32 Hz, 3 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 160.0, 152.4, 151.2, 134.5, 127.2, 121.6, 118.8, 117.0, 116.1, 18.6; HRMS (EI) *m/z* calcd for $C_{10}H_7O_2Br$ (M^+) 237.9629, found 237.9635.



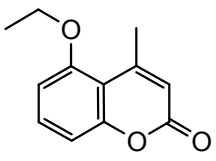
4,7-Dimethyl-2H-chromen-2-one (2f)

^{1}H NMR (400 MHz, CDCl3) δ ppm 7.35 (d, *J*=8.00 Hz, 1 H), 6.98 (m, 2 H), 6.08 (m, 1 H), 2.30 (m, 6 H); ^{13}C NMR (101 MHz, CDCl3) δ ppm 160.8, 153.2, 152.3, 142.7, 125.1, 124.1, 117.3, 116.8, 113.6, 21.3, 18.3; HRMS (EI) *m/z* calcd for $C_{11}H_{10}O_2$ (M^+) 174.0681, found 174.0691.



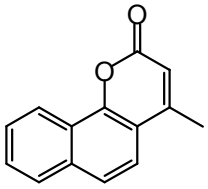
4,6-Dimethyl-2H-chromen-2-one (2g)

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.32 (m, 2 H), 7.19 (d, *J*=8.43 Hz, 1 H), 6.24 (m, 1 H), 2.41 (m, 6 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 160.9, 152.3, 151.5, 133.7, 132.6, 124.3, 119.5, 116.6, 114.9, 20.9, 18.6; HRMS (EI) *m/z* calcd for $C_{11}H_{10}O_2$ (M^+) 174.0681, found 174.0699.



5-Ethoxy-4-methyl-2H-chromen-2-one (2h)

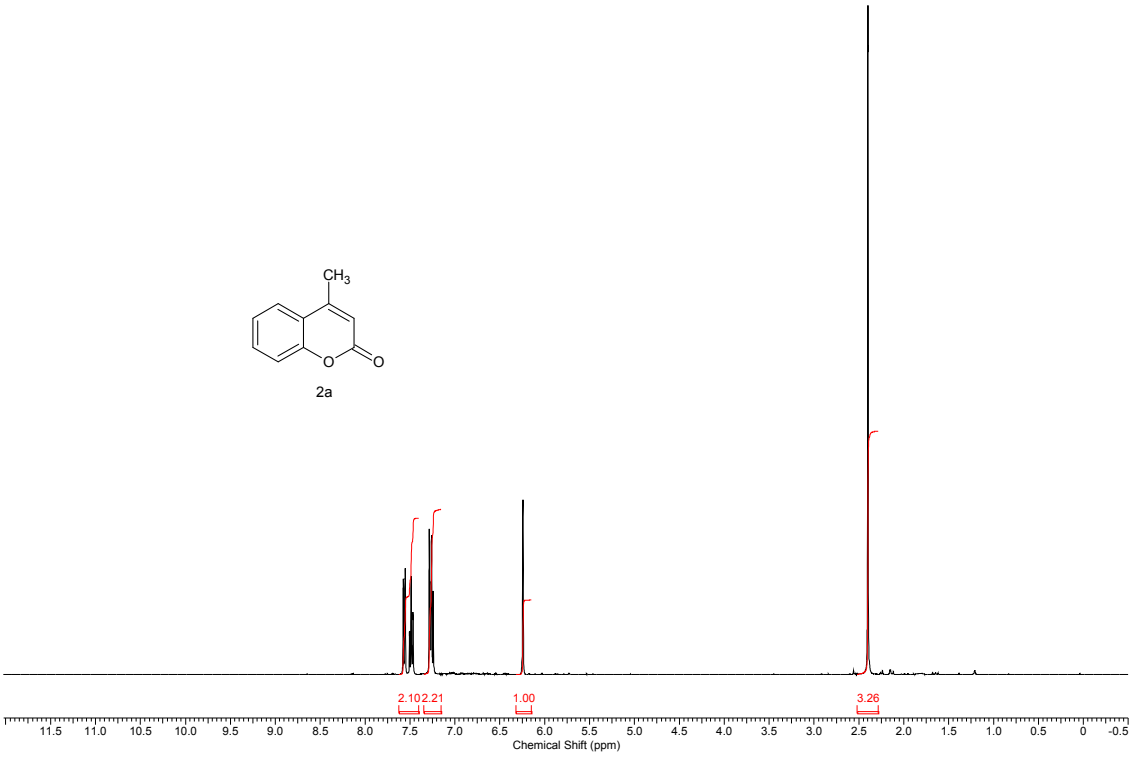
^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.37 (t, *J*=8.00 Hz, 1 H), 6.90 (m, 1 H), 6.68 (m, 1 H), 6.08 (m, 1 H), 4.10 (q, *J*=6.96 Hz, 2 H), 2.59 (d, *J*=4.00 Hz, 3 H), 1.48 (t, *J*=6.96 Hz, 3 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 160.7, 157.4, 155.2, 154.3, 131.7, 114.3, 110.4, 109.6, 106.6, 64.6, 24.6, 14.6; HRMS (EI) *m/z* calcd for $C_{12}H_{12}O_3$ (M^+) 204.0786, found 204.0790.

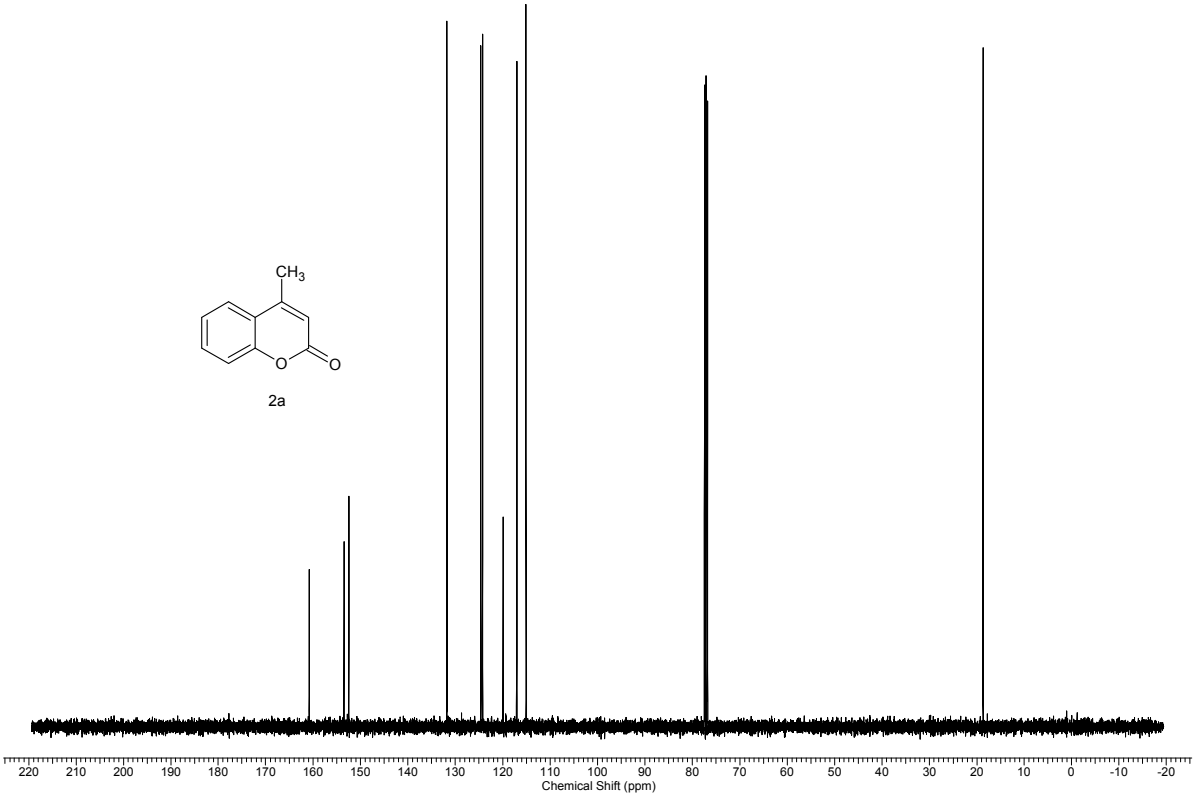


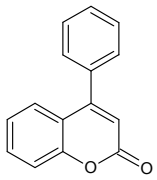
4-Methyl-2H-benzo[h]chromen-2-one (2i)

^{1}H NMR (400 MHz, $CDCl_3$) *δ* ppm 8.59 (m, 1 H), 7.89 (s, 1 H), 7.75-7.60 (m, 4 H), 6.40 (m, 1 H), 2.55 (d, *J* = 1.22 Hz, 3 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 160.9, 153.4, 150.7, 134.8, 128.6, 127.6, 127.2, 124.2, 123.2, 122.7, 120.3, 115.2, 114.4, 19.3; HRMS (EI) *m/z* calcd for $C_{14}H_{10}O_2$ (M^+) 210.0681, found 210.0699.

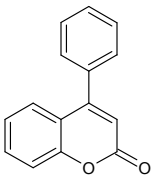
V. ^{1}H and ^{13}C NMR spectra for Coumarins 2a-i



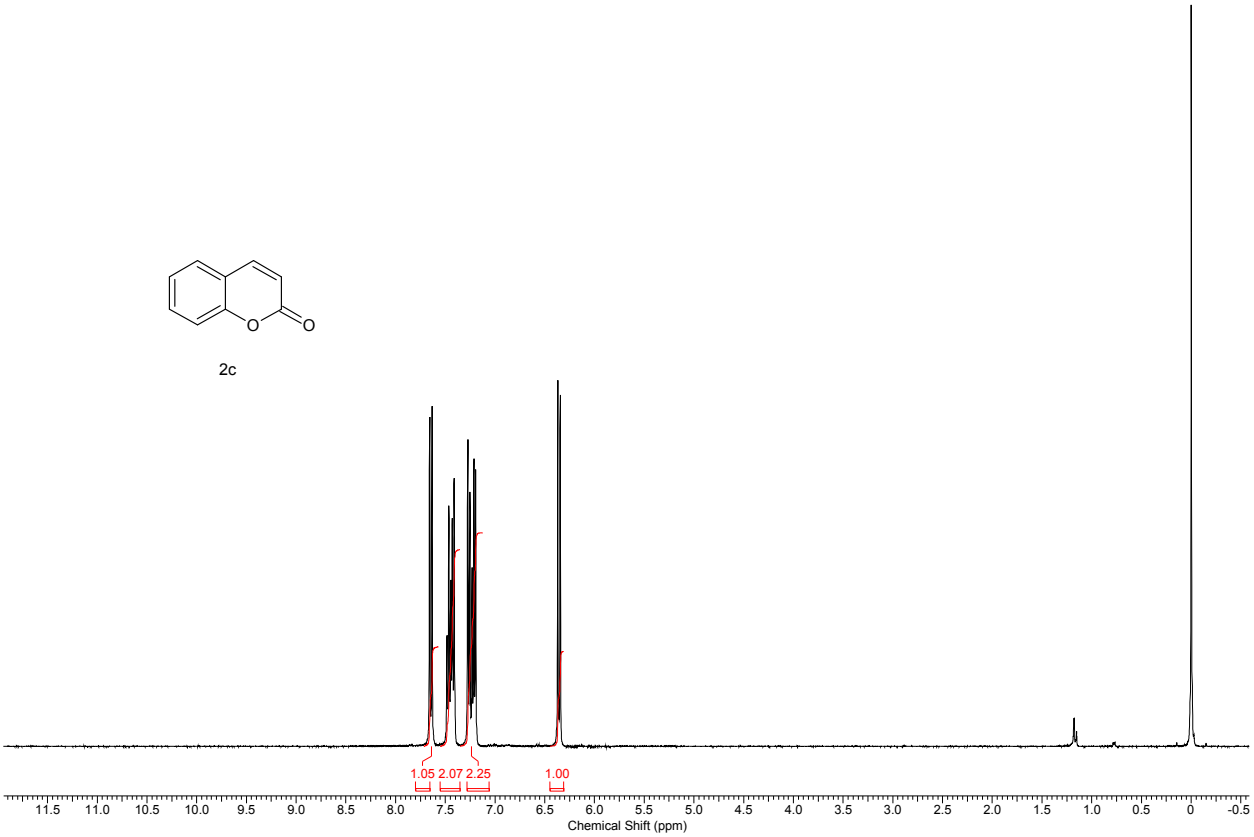




2b



2b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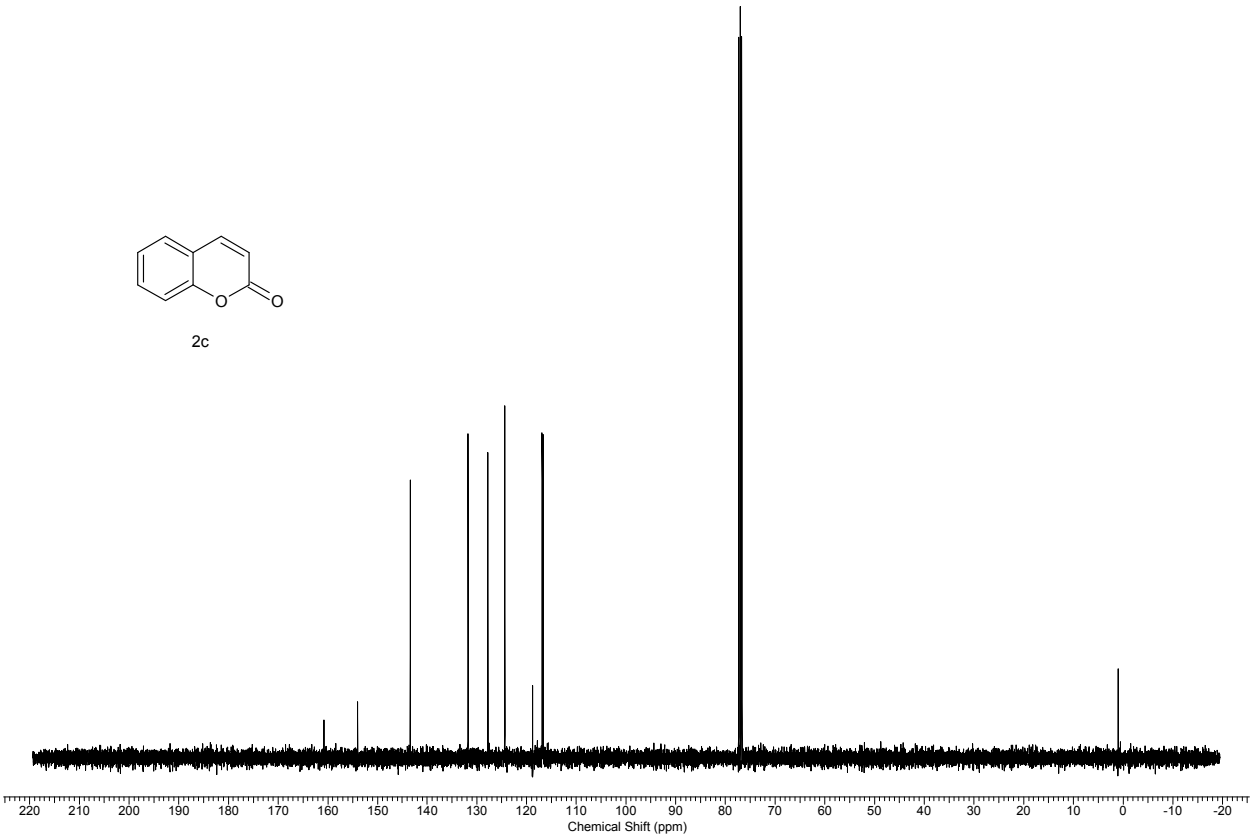
2.25
1.00
Chemical Shift (ppm)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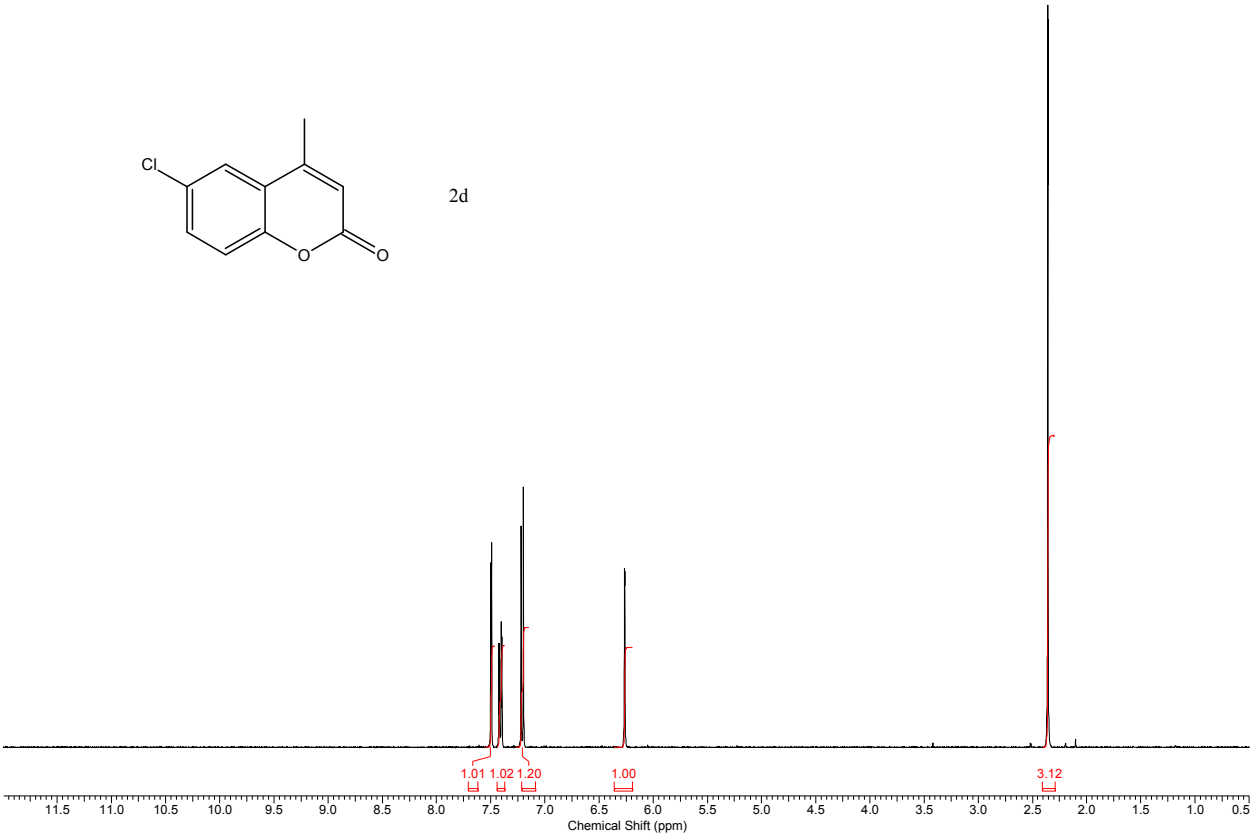
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2d
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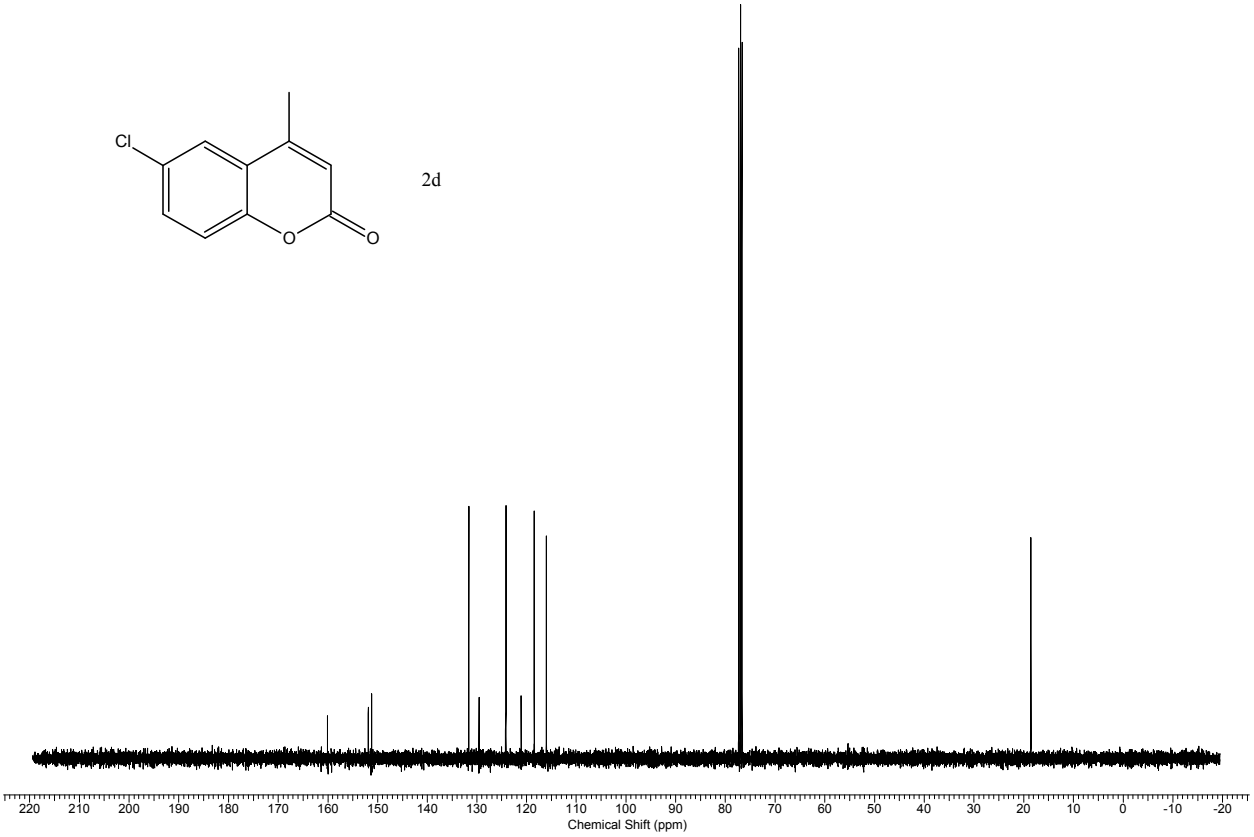
1.02
1.20
1.00
3.12
Chemical Shift (ppm)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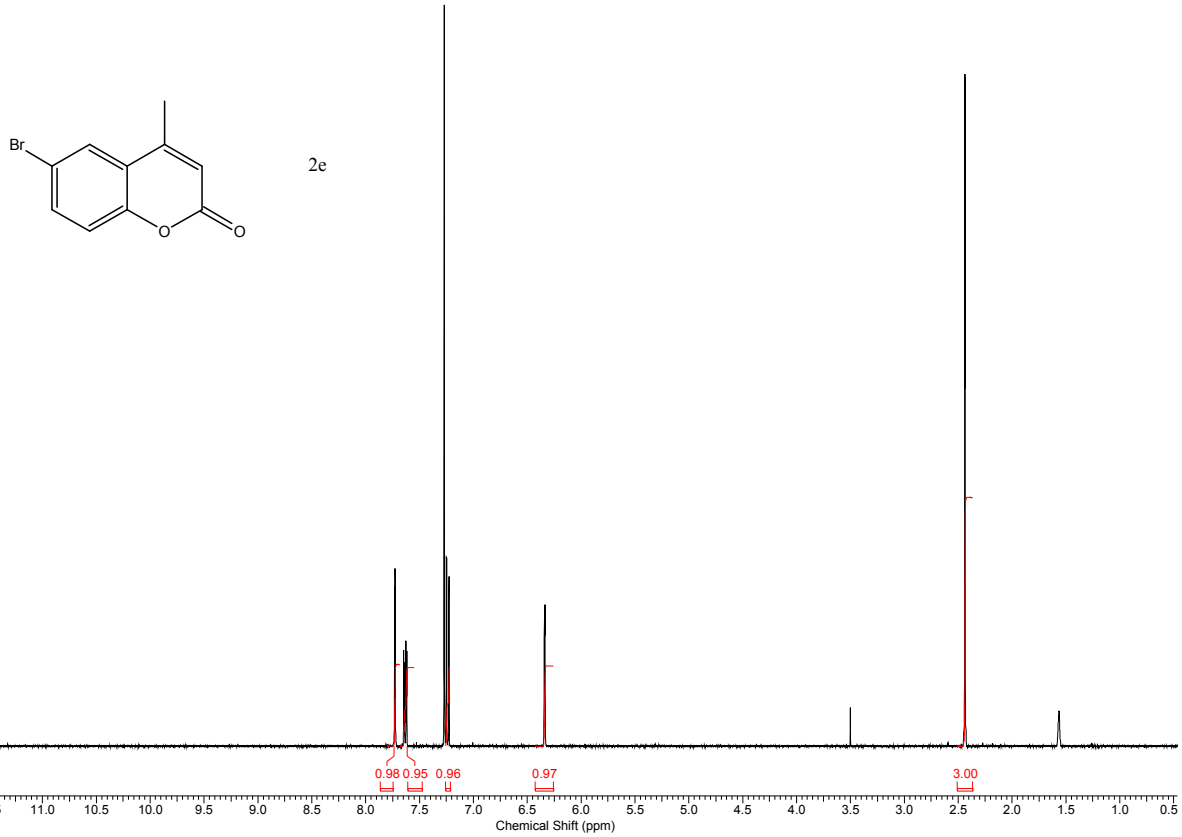
O
O
2d
Chemical Shift (ppm)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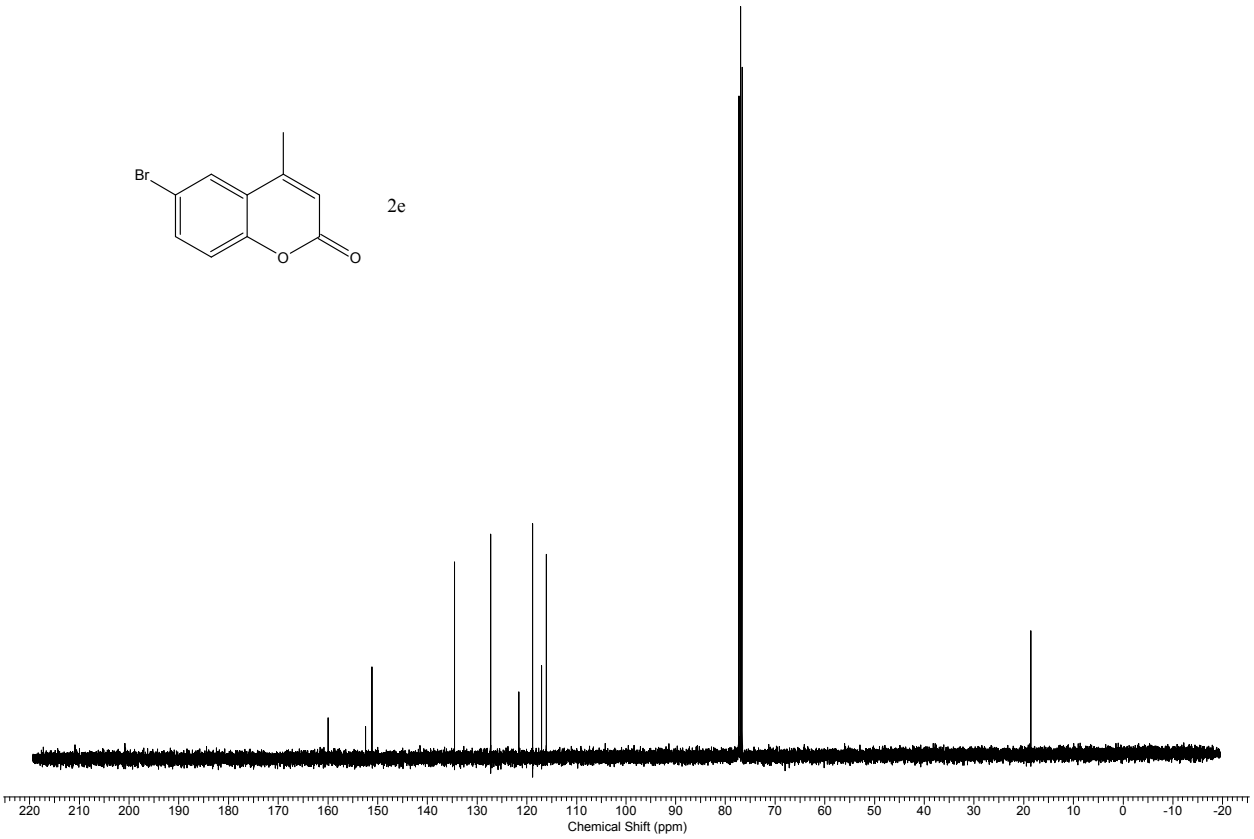
0.96
0.97
3.00
Chemical Shift (ppm)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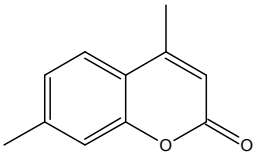
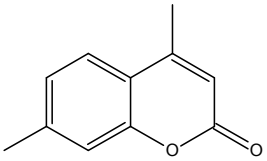
O
O
2e
Chemical Shift (ppm)


O
O

2f

1.02
2.19
1.00
6.56
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
Chemical Shift (ppm)


O
O

2f

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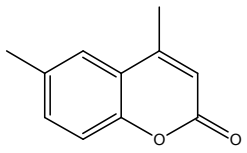
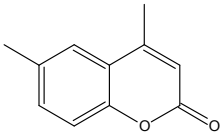


2g



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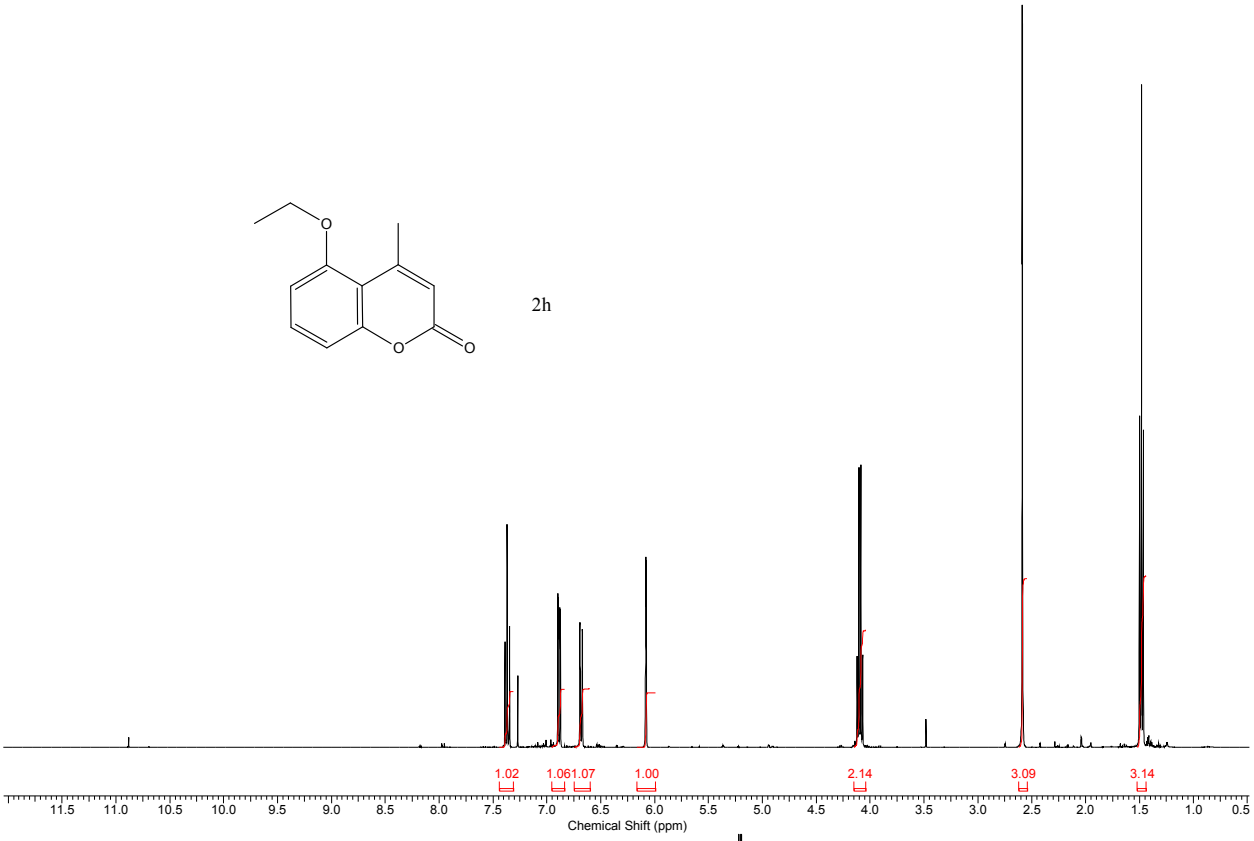
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1.07
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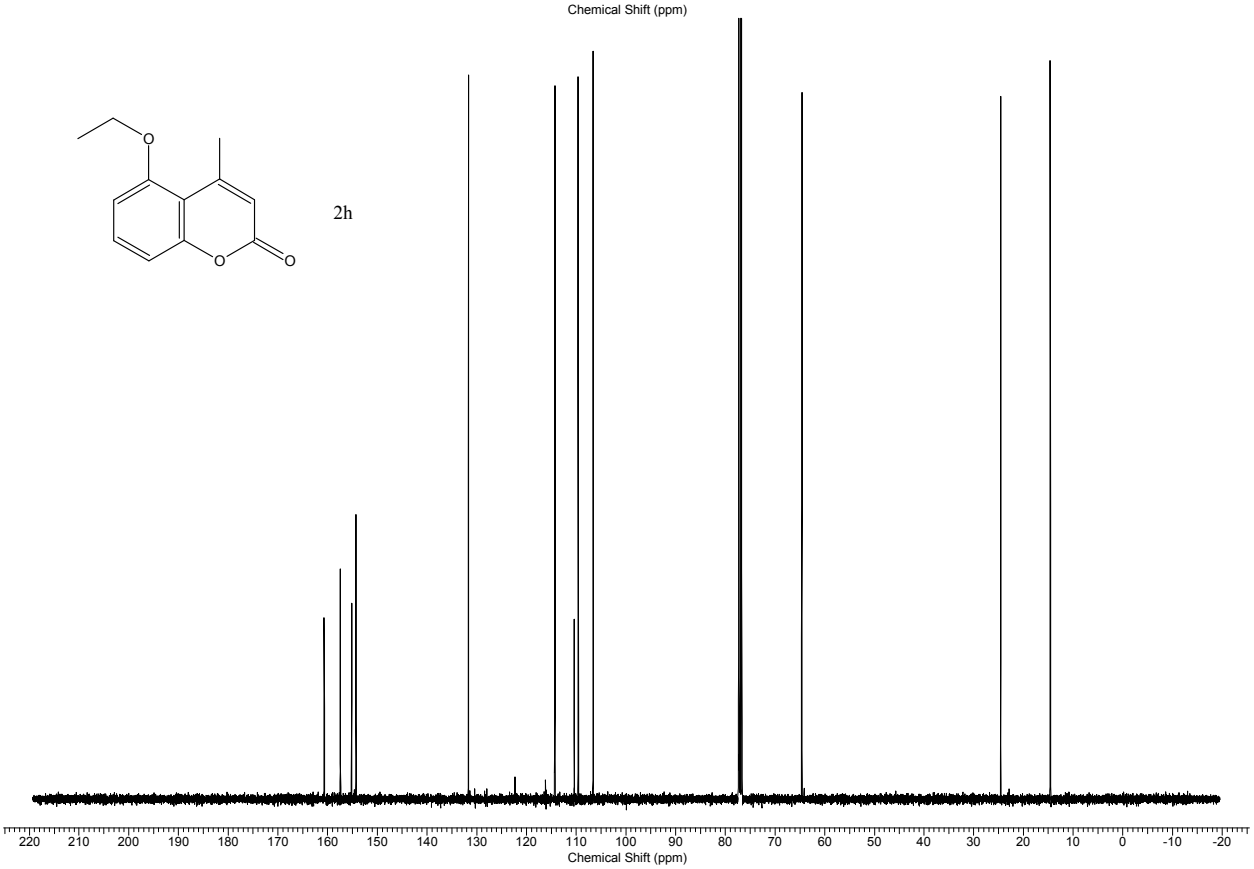
3.14
Chemical Shift (ppm)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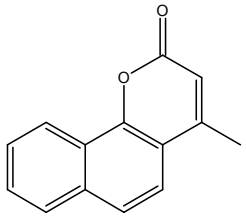
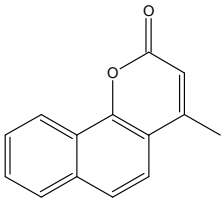
Chemical Shift (ppm)



2i



2i