

Synthesis of alpha-pyrones and chromen-2-ones by transition-metal catalyzed annulations of sulfoxonium and iodonium ylides with *cis*-stilbene acids

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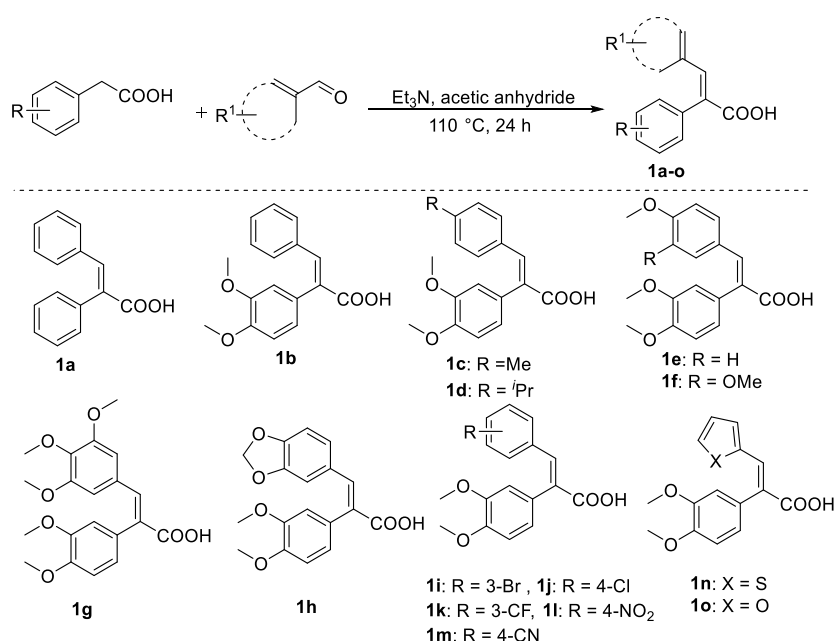
1. General Information

All the chemicals, starting materials, reagents and solvents were procured from commercial sources and were used without further purification. Thin layer chromatography was performed on MERCK precoated silica gel 60F-254 (0.5 mm) aluminum plates and visualized under UV light at 254 nm. Column chromatography was performed using silica gel #60-120 and #100-200 mesh. The ^1H NMR spectra were recorded on NMR Bruker instrument operated at 500 MHz. Chemical shifts are reported in ppm with the solvent resonance as the internal standard (CDCl_3 : δ 7.25 ppm). ^{13}C NMR spectra were recorded on NMR Bruker instrument operated at 125 MHz with complete proton decoupling. Chemical shifts are reported in ppm with the solvent resonance as the internal standard (CDCl_3 : δ 77.16 ppm). The following abbreviations were used for ^1H NMR spectra to indicate the signal multiplicity: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), dd (doublet of doublet) and dt (doublet of triplet). HRMS was measured in ESI-MS mass spectrophotometer.

2. Preparation of starting precursor

2.1. General procedure for synthesis of 1a-o

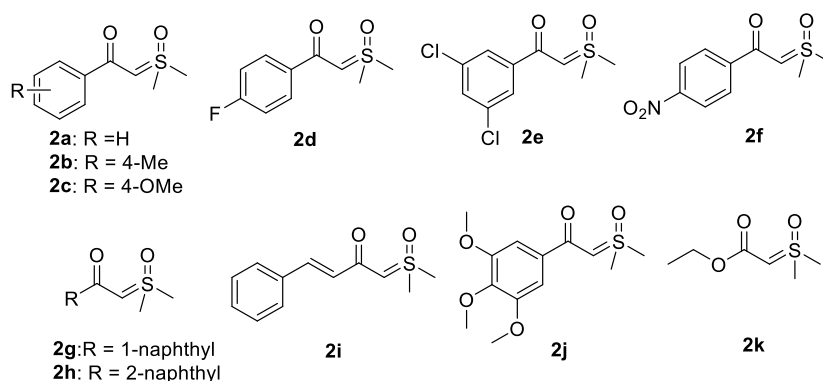
The *cis*-stilbene acids were synthesized using the previous literature report.¹



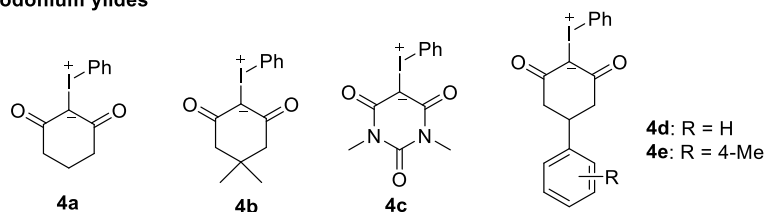
2.2. General procedure for the synthesis of ylides 2a-k and 4a-e

The sulfoxonium ylides were prepared using reported literature procedure. Similarly, the hypervalent iodonium ylides were prepared using reported method.²

Sulfoxonium ylides

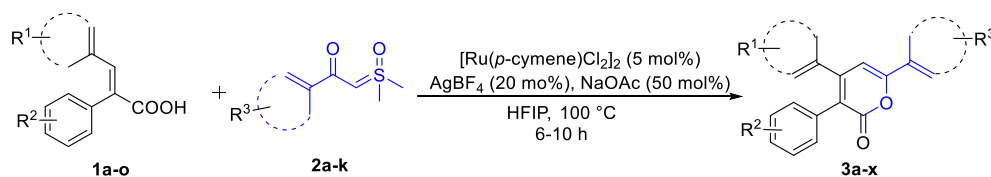


Iodonium ylides



3. General procedure for synthesis of α -pyrones and chromene-2-ones

3.1. General procedure for synthesis of **3**

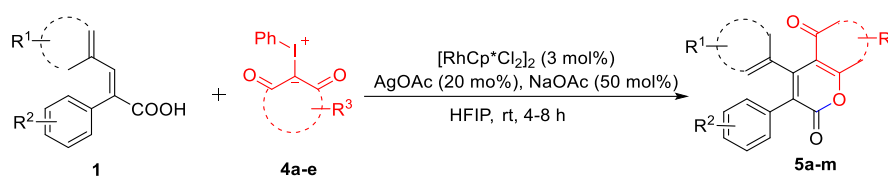


An oven dried pressure reaction tube with a magnetic stir bar was charged with substituted *cis*-stilbene analogues **1a-o** (1.0 equiv.), substituted sulfoxonium ylide **2a-k** (1.2 equiv.), [Ru(*p*-cymene)Cl₂]₂ (5 mol%), AgBF₄ (20 mol%), NaOAc (50 mol%) in 1 mL of HFIP. The reaction mixture was then heated at 100 °C for 6-10 h until the reaction was complete as indicated by TLC. Upon completion of reaction, the solvent was evaporated under reduced pressure and the crude product was directly purified by a silica gel column chromatography using ethyl acetate/hexane (20-40%) as the eluent to afford the corresponding products **3a-x**. All the synthesized compounds were thoroughly characterized by IR, ¹H and ¹³C NMR and HRMS (ESI).

Table S1. Additional condition variation for optimization of synthesis of α -pyrones

Entry	Deviation from standard condition	Yield (%)
1.	Catalyst [Ru(<i>p</i> -cymene)Cl ₂] ₂ (2.5 mol%)	46
2	Base NaOAc (25 mol%)	50
	NaOAc (1 equiv.)	78
3	Additive AgBF ₄ (10 mol%)	65
	AgBF ₄ (30 mol%)	78

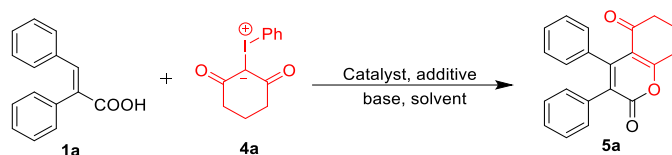
3.2. General procedure for synthesis of compound 5



An oven dried reaction tube with a magnetic stir bar was charged with substituted *cis*-stilbene analogues **1** (1.0 equiv.), substituted hypervalent iodonium ylides **4a-e** (1.2 equiv.), [RhCp*Cl₂]₂ (3 mol%), AgOAc (20 mol%) and NaOAc (50 mol%) in 1 mL of HFIP. The reaction mixture was then stirred at room temperature until the reaction is complete as indicated by TLC. Upon completion of reaction, the solvent was evaporated under reduced pressure and the crude product was directly purified by column chromatography (silica gel) by using ethyl acetate/ hexane (20-30%) as the eluent to afford the corresponding products **5a-m**. All the synthesized compounds were thoroughly characterized by IR, ¹H and ¹³C NMR and HRMS (ESI).

4. Optimization of Rh(III)-catalyzed C-H activation with iodonium ylide

Table S2. Optimization of Rh(III)-catalyzed carbene insertion through iodonium ylide^a

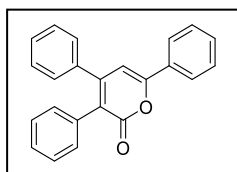


Entry	Catalyst	Additive	Base	Solvent	Temp. (°C)	Yield (%) ^d
1	[Ru(<i>p</i> -cymene)Cl ₂] ₂	AgBF ₄	NaOAc	HFIP	80	10
2	[Ru(<i>p</i> -cymene)Cl ₂] ₂	AgBF ₄	NaOAc	TFE	120	10
3	[Ru(<i>p</i> -cymene)Cl ₂] ₂	AgBF ₄	Cs ₂ CO ₃	HFIP	80	NR
4	[Ru(<i>p</i> -cymene)Cl ₂] ₂	AgBF ₄	NaOAc	HFIP	100	NR
5	[Ru(<i>p</i> -cymene)Cl ₂] ₂	AgBF ₄	Zn(OAc) ₂	HFIP	100	NR
6	[Ru(<i>p</i> -cymene)Cl ₂] ₂	AgBF ₄	Zn(OAc) ₂ + NaOAc	HFIP	100	NR
7	[Ru(<i>p</i> -cymene)Cl ₂] ₂	AgBF ₄	Zn(OAc) ₂ + NaOAc	HFIP+H ₂ O	100	NR
8	[Ru(<i>p</i> -cymene)Cl ₂] ₂	AgBF ₄	NaOAc	HFIP	100	NR
9	[Ru(<i>p</i> -cymene)Cl ₂] ₂	AgOAc	NaOAc	HFIP	80	20
10	[Ru(<i>p</i> -cymene)Cl ₂] ₂	AgOAc	NaOAc	DCE	80	10
11	[Ru(<i>p</i> -cymene)Cl ₂] ₂	AgOAc	NaOAc	DCE	120	10
12	[Ru(<i>p</i> -cymene)Cl ₂] ₂	AgOAc	NaOAc	ACN	120	NR
13	[Ru(<i>p</i> -cymene)Cl ₂] ₂	AgOAc	NaOAc	THF	80	NR
14	[Ru(<i>p</i> -cymene)Cl ₂] ₂	AgOAc	NaOAc	DCM	80	10
15	[Ru(<i>p</i> -cymene)Cl ₂] ₂	AgOAc	NaOAc	CHCl ₃	60	10
16	[Ru(<i>p</i> -cymene)Cl ₂] ₂	AgOAc	NaOAc	DMF	100	NR
17	[Ru(<i>p</i> -cymene)Cl ₂] ₂	AgOAc	NaOAc	Dioxane	100	NR
18	[Ru(<i>p</i> -cymene)Cl ₂] ₂	AgOAc	NaOAc	MeOH	80	NR
19	[Ru(<i>p</i> -cymene)Cl ₂] ₂	AgOAc	NaOAc	TFE	120	NR
20	[Ru(<i>p</i> -cymene)Cl ₂] ₂	AgOAc	Mn(OAc) ₃	HFIP	80	NR
21	[Ru(<i>p</i> -cymene)Cl ₂] ₂	AgOAc	Mn(OAc) ₃ + NaOAc	HFIP	80	NR
22	[Ru(<i>p</i> -cymene)Cl ₂] ₂	AgOAc	CsOAc	HFIP	80	NR
23	[Rh(Cp*Cl ₂) ₂]	-	NaOAc	HFIP	80	75
24	[Rh(Cp*Cl ₂) ₂]	-	NaOAc	HFIP	25	72 ^c
25	[Rh(Cp*Cl ₂) ₂]	AgOAc	NaOAc	HFIP	25	83 ^b
26	[Rh(Cp*Cl₂)₂]	AgOAc	NaOAc	HFIP	25	85
27	[Rh(Cp*Cl ₂) ₂]	AgOAc	NaOAc	DCE	25	30
28	[Rh(Cp*Cl ₂) ₂]	AgOAc	NaOAc	TFE	25	50

^aReaction conditions: **1a** (0.31mmol), **4a** (0.37 mmol), [Ru(*p*-cymene)Cl₂]₂ (5 mol%), additive (20 mol%), base (50 mol%), solvent (1 mL), 12 h in pressure tube. ^bCatalyst (3 mol%), ^ctime = 4 h. ^dIsolated yield, NR = No Reaction.

5. Characterization data

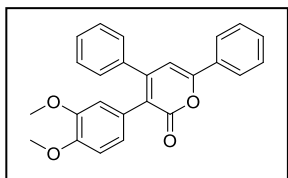
3,5,6-Triphenyl-2H-pyran-2-one (3a): 80% yield (81.0 mg), yellow solid, mp: 175-178 °C, FT-



IR (cm⁻¹): 2977, 1704, 1694, 1598, 1575; ¹H NMR (500 MHz, CDCl₃): δ 7.91 (dd, *J* = 6.6, 3.0 Hz, 2H), 7.48 (dd, *J* = 5.0, 2.0 Hz, 3H), 7.27 (d, *J* = 6.6 Hz, 4H), 7.23 (s, 2H), 7.21–7.19 (m, 2H), 7.18–7.15 (m, 2H), 6.85 (s, 1H) ppm; ¹³C NMR (125 MHz, CDCl₃): δ 162.7, 158.3, 152.7, 137.8,

133.8, 131.4, 130.9, 130.7, 128.9, 128.7, 128.7, 128.4, 128.0, 127.7, 125.6, 123.2, 105.0 ppm; HRMS (ESI-QTOF): m/z $[M+H]^+$ calcd. for $C_{23}H_{17}O_2$ 325.1223 found 325.1223.

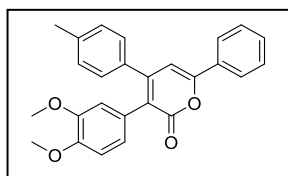
6-(3,4-Dimethoxyphenyl)-3,5-diphenyl-2H-pyran-2-one (3b): 85% yield (80.4 mg), yellow



solid, mp: 134-137 °C, FT-IR (cm)⁻¹: 3005, 2849, 1715, 1624, 1541; ¹H NMR (500 MHz, CDCl₃): δ 7.92–7.89 (m, 2H), 7.47 (dd, J = 5.1, 2.0 Hz, 3H), 7.28 (dd, J = 5.0, 1.8 Hz, 3H), 7.22–7.16 (m, 2H), 6.88 (dd, J = 8.3, 2.0 Hz, 1H), 6.83 (s, 1H), 6.76 (d, J = 8.3 Hz, 1H), 6.63

(d, J = 2.0 Hz, 1H), 3.85 (s, 3H), 3.61 (s, 3H) ppm; ¹³C NMR (125 MHz, CDCl₃): δ 162.8, 157.9, 152.3, 148.5, 148.2, 138.2, 131.4, 130.7, 129.0, 128.6, 128.6, 128.5, 126.0, 125.5, 123.7, 122.8, 114.3, 110.7, 105.0, 55.8, 55.7 ppm; HRMS (ESI-QTOF): m/z $[M+H]^+$ calcd. for $C_{25}H_{21}O_4$ 385.1434 found 385.1468.

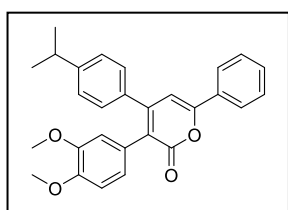
6-(3,4-Dimethoxyphenyl)-3-phenyl-5-(p-tolyl)-2H-pyran-2-one (3c): 79% yield (73.8 mg),



yellow solid, mp: 145-148 °C, FT-IR (cm)⁻¹: 2972, 1714, 1625, 1540, 1509; ¹H NMR (500 MHz, CDCl₃): δ 7.90 (d, J = 6.0 Hz, 2H), 7.47 (d, J = 5.2 Hz, 3H), 7.08 (s, 4H), 6.88 (d, J = 7.8 Hz, 1H), 6.83 (s, 1H), 6.78 (d, J = 8.3 Hz, 1H), 6.64 (s, 1H), 3.86 (s, 3H), 3.62 (s, 3H),

2.32 (s, 3H) ppm; ¹³C NMR (125 MHz, CDCl₃): δ 162.9, 157.8, 152.3, 148.5, 148.2, 138.7, 135.2, 131.5, 130.6, 129.1, 129.0, 128.9, 128.8, 128.5, 126.3, 125.5, 123.7, 122.5, 114.3, 110.7, 105.1, 55.8, 55.7, 21.2 ppm; HRMS (ESI-QTOF): m/z $[M+H]^+$ calcd. for $C_{26}H_{23}O_4$ 399.1591 found 399.1593.

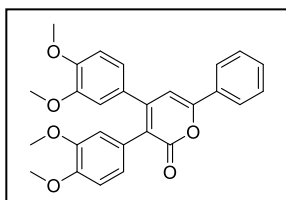
6-(3,4-Dimethoxyphenyl)-5-(4-isopropylphenyl)-3-phenyl-2H-pyran-2-one (3d): 75% yield



(68.6 mg), yellow solid, mp: 157-159 °C, FT-IR (cm)⁻¹: 2955, 1701, 1625, 1535, 1514; ¹H NMR (500 MHz, CDCl₃): δ 7.90 (dd, J = 6.8, 2.9 Hz, 2H), 7.47 (dd, J = 5.2, 2.1 Hz, 3H), 7.15-7.11 (m, 4H), 6.98-6.96 (m, 1H), 6.84 (s, 1H), 6.80 (d, J = 8.3 Hz, 1H), 6.56 (d, J = 2.1

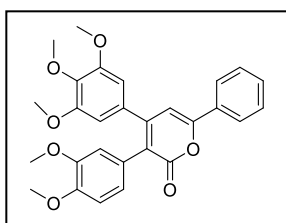
Hz, 1H), 3.86 (s, 3H), 3.55 (s, 3H), 2.91–2.86 (m, 1H), 1.22 (d, J = 6.9 Hz, 6H) ppm; ¹³C NMR (125 MHz, CDCl₃): δ 162.9, 157.8, 152.2, 149.7, 148.5, 148.2, 135.6, 131.5, 130.6, 128.9, 128.6, 126.5, 126.2, 125.5, 123.8, 122.4, 114.4, 110.7, 105.2, 55.8, 55.6, 33.9, 23.8 ppm; HRMS (ESI-QTOF): m/z $[M+H]^+$ calcd. for $C_{28}H_{27}O_4$ 427.1904 found 427.1914.

5,6-Bis(3,4-dimethoxyphenyl)-3-phenyl-2H-pyran-2-one (3f): 72% yield (65.0 mg), yellow



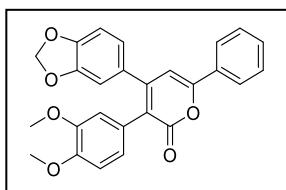
solid, mp: 150-153 °C, FT-IR (cm)⁻¹: 2978, 1718, 1649, 1580, 1541; ¹H NMR (500 MHz, CDCl₃): δ 7.91 (dd, *J* = 6.7, 2.9 Hz, 2H), 7.48 (dd, *J* = 5.3, 2.0 Hz, 3H), 6.90 (dd, *J* = 8.3, 2.1 Hz, 1H), 6.86 (s, 1H), 6.83 – 6.80 (m, 2H), 6.78 (d, *J* = 8.3 Hz, 1H), 6.75 (d, *J* = 1.9 Hz, 1H), 6.60 (d, *J* = 2.0 Hz, 1H), 3.88 (s, 3H), 3.86 (s, 3H), 3.69 (s, 3H), 3.58 (s, 3H) ppm; ¹³C NMR (125 MHz, CDCl₃): δ 163.0, 157.9, 151.9, 149.5, 148.6, 148.5, 131.5, 130.7, 130.2, 129.0, 126.7, 125.6, 123.6, 122.1, 121.5, 114.1, 112.3, 110.9, 110.8, 104.9, 55.9, 55.9, 55.8, 55.8 ppm; HRMS (ESI-QTOF): *m/z* [M+H]⁺ calcd. for C₂₇H₂₅O₆ 445.1646 found 445.1618.

6-(3,4-Dimethoxyphenyl)-3-phenyl-5-(3,4,5-trimethoxyphenyl)-2H-pyran-2-one (3g): 73%



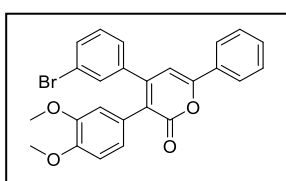
yield (65.4 mg), yellow solid, mp: 152-155 °C, FT-IR (cm)⁻¹: 3009, 2833, 1703, 1627, 1585; ¹H NMR (500 MHz, CDCl₃): δ 7.91 (dd, *J* = 6.6, 3.0 Hz, 2H), 7.49 (dd, *J* = 5.2, 2.0 Hz, 3H), 6.85 (d, *J* = 4.0 Hz, 2H), 6.80 (d, *J* = 8.3 Hz, 1H), 6.72 (d, *J* = 2.0 Hz, 1H), 6.41 (s, 2H), 3.86 (s, 3H), 3.84 (s, 3H), 3.68 (s, 3H), 3.66 (s, 6H) ppm; ¹³C NMR (125 MHz, CDCl₃): δ 162.8, 158.1, 153.1, 152.0, 148.7, 148.6, 133.1, 131.4, 130.8, 129.0, 127.8, 126.5, 125.6, 123.5, 114.0, 110.9, 108.2, 106.3, 104.6, 61.0, 56.2, 55.9, 55.9 ppm; HRMS (ESI-QTOF): *m/z* [M+H]⁺ calcd. for C₂₈H₂₇O₇ 475.1751 found 475.1757.

5-(Benzo[d][1,3]dioxol-5-yl)-6-(3,4-dimethoxyphenyl)-3-phenyl-2H-pyran-2-one (3h): 78%



yield (71.2 mg), yellow solid, mp: 153-156 °C, FT-IR (cm)⁻¹: 2970, 1707, 1620, 1600, 1537; ¹H NMR (500 MHz, CDCl₃): δ 7.95–7.86 (m, 2H), 7.52–7.45 (m, 2H), 6.92 (dd, *J* = 8.2, 2.1 Hz, 1H), 6.89–6.80 (m, 3H), 6.78 – 6.68 (m, 3H), 6.61 (d, *J* = 2.1 Hz, 1H), 5.93 (s, 2H), 3.89 (s, 3H), 3.61 (s, 3H) ppm; ¹³C NMR (125 MHz, CDCl₃): δ 162.0, 155.0, 153.3, 151.3, 149.0, 148.7, 148.6, 138.8, 136.9, 132.5, 126.2, 125.8, 124.6, 124.3, 123.5, 113.9, 110.9, 107.2, 106.2, 100.0, 61.0, 56.2, 55.9, 55.9 ppm; HRMS (ESI-QTOF): *m/z* [M+H]⁺ calcd. for C₂₆H₂₁O₆ 429.1333 found 429.1328.

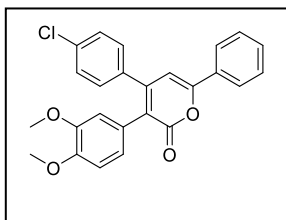
5-(3-Bromophenyl)-6-(3,4-dimethoxyphenyl)-3-phenyl-2H-pyran-2-one (3i): 82% yield (73.2



mg), yellow solid, mp: 186-188, FT-IR (cm)⁻¹: 2997, 2837, 1711, 1627, 1531; ¹H NMR (500 MHz, CDCl₃): δ 7.92–7.89 (m, 2H), 7.50–7.47 (m, 3H), 7.43 (d, *J* = 8.9 Hz, 2H), 7.11 (t, *J* = 7.8 Hz, 1H), 7.04

(d, $J = 7.7$ Hz, 1H), 6.81 (dd, $J = 8.2, 2.0$ Hz, 1H), 6.77 (d, $J = 8.5$ Hz, 2H), 6.68 (d, $J = 2.0$ Hz, 1H), 3.86 (s, 3H), 3.68 (s, 3H) ppm; ^{13}C NMR (125 MHz, CDCl_3): δ 162.5, 158.3, 150.6, 148.8, 148.4, 140.2, 131.6, 131.2, 131.2, 130.9, 130.0, 129.0, 127.4, 125.6, 125.5, 123.8, 123.3, 122.5, 114.1, 110.8, 104.4, 55.8, 55.8 ppm; HRMS (ESI-QTOF): m/z $[\text{M}+\text{H}]^+$ calcd. for $\text{C}_{25}\text{H}_{19}\text{BrO}_4\text{S}$ 463.0539 found 463.0546.

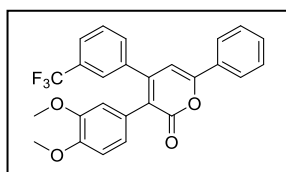
5-(4-Chlorophenyl)-6-(3,4-dimethoxyphenyl)-3-phenyl-2H-pyran-2-one (**3j**): 84% yield (77.2



mg), yellow solid, mp: 130-132 °C, FT-IR (cm^{-1}): 2937, 2836, 1703, 1623, 1586; ^1H NMR (500 MHz, CDCl_3): δ 7.92–7.88 (m, 2H), 7.48 (d, $J = 4.3$ Hz, 3H), 7.27 (d, $J = 2.0$ Hz, 1H), 7.26 (d, $J = 2.0$ Hz, 1H), 7.16–7.10 (m, 2H), 6.81 (dd, $J = 8.3, 1.9$ Hz, 1H), 6.79–6.75 (m, 2H), 6.66 (d, $J = 2.0$ Hz, 1H), 3.86 (s, 3H), 3.67 (s, 3H) ppm; ^{13}C NMR

(125 MHz, CDCl_3): δ 162.6, 158.3, 150.9, 148.7, 148.4, 136.5, 134.8, 131.2, 130.8, 130.0, 129.0, 128.8, 125.7, 125.6, 123.7, 123.0, 114.1, 110.8, 104.5, 55.8, 55.7 ppm; HRMS (ESI-QTOF): m/z $[\text{M}+\text{H}]^+$ calcd. for $\text{C}_{25}\text{H}_{20}\text{ClO}_4$ 419.1045 found 419.1046.

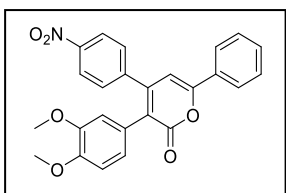
6-(3,4-Dimethoxyphenyl)-3-phenyl-5-(3-(trifluoromethyl)phenyl)-2H-pyran-2-one (**3k**): 81%



yield (76.9 mg), yellow solid, mp: 142-144 °C, FT-IR (cm^{-1}): 2997, 2936, 1714, 1647, 1587; ^1H NMR (500 MHz, CDCl_3): δ 7.90 (dd, $J = 6.6, 3.0$ Hz, 2H), 7.56 (d, $J = 8.0$ Hz, 2H), 7.49 (q, $J = 3.9, 3.3$ Hz, 3H), 7.33 (d, $J = 8.0$ Hz, 2H), 6.83–6.73 (m, 3H), 6.66–6.62 (m, 1H),

3.85 (s, 3H), 3.63 (s, 3H) ppm; ^{13}C NMR (125 MHz, CDCl_3): δ 162.4, 158.5, 150.6, 148.9, 148.4, 141.9, 131.1, 131.0, 129.8 (q, $J = 282$) 129.0, 125.5 (q, $J = 3.76$), 125.4 (q, $J = 3.73$ Hz), 125.3, 124.8, 123.8, 123.5, 114.1, 110.8, 104.3, 55.8, 55.7 ppm; ^{19}F NMR (470 MHz, CDCl_3): δ -60.7 ppm, HRMS (ESI-QTOF): m/z $[\text{M}+\text{H}]^+$ calcd. for $\text{C}_{26}\text{H}_{20}\text{F}_3\text{O}_4$ 453.1308 found 453.1356.

6-(3,4-Dimethoxyphenyl)-5-(4-nitrophenyl)-3-phenyl-2H-pyran-2-one (**3l**): 78% yield (73.0

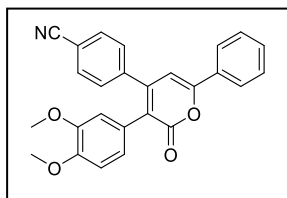


mg), yellow solid, mp: 166-169 °C, FT-IR (cm^{-1}): 3005, 2968, 1715, 1627, 1544; ^1H NMR (500 MHz, CDCl_3): δ 8.15 (d, $J = 8.7$ Hz, 2H), 7.90 (dt, $J = 5.4, 1.7$ Hz, 2H), 7.52–7.48 (m, 3H), 7.41–7.37 (m, 2H), 6.78 (s, 1H), 6.74–6.67 (m, 3H), 3.85 (s, 3H), 3.70 (s, 3H) ppm; ^{13}C

NMR (125 MHz, CDCl_3): δ 162.2, 158.8, 149.8, 149.1, 148.6, 147.5, 144.8, 131.1, 131.0,

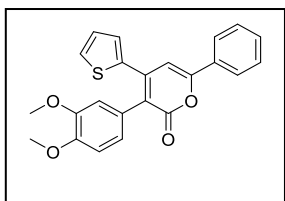
129.7, 129.1, 125.6, 125.1, 123.8, 123.7, 113.9, 110.9, 103.8, 55.8, 55.8 ppm; HRMS (ESI-QTOF): m/z $[M+H]^+$ calcd. for $C_{25}H_{20}NO_6$ 430.1285 found 430.1286.

4-(6-(3,4-Dimethoxyphenyl)-2-oxo-3-phenyl-2H-pyran-5-yl)benzonitrile (**3m**): 80% yield



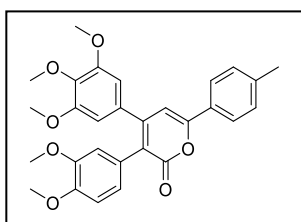
(74.1 mg), yellow solid, mp: 148-150 °C, FT-IR (cm)⁻¹: 2937, 2227, 1714, 1626, 1581; ¹H NMR (500 MHz, CDCl₃): δ 7.89 (dd, J = 6.8, 3.0 Hz, 2H), 7.58 (d, J = 7.9 Hz, 2H), 7.50–7.47 (m, 4H), 7.32 (d, J = 8.0 Hz, 2H), 6.76 (s, 1H), 6.73–6.71 (m, 1H), 6.69 (s, 1H), 3.85 (s, 3H), 3.68 (s, 3H) ppm; ¹³C NMR (125 MHz, CDCl₃): δ 157.5, 154.0, 145.3, 144.3, 143.8, 138.1, 127.5, 126.3, 126.3, 124.6, 124.3, 120.8, 120.4, 119.1, 118.9, 113.4, 109.2, 107.7, 106.1, 99.1, 51.1 ppm; HRMS (ESI-QTOF): m/z $[M+H]^+$ calcd. for $C_{26}H_{20}NO_4$ 410.1387 found 410.1393.

6-(3,4-Dimethoxyphenyl)-3-phenyl-5-(thiophen-2-yl)-2H-pyran-2-one (**3n**): 70% yield (65.8



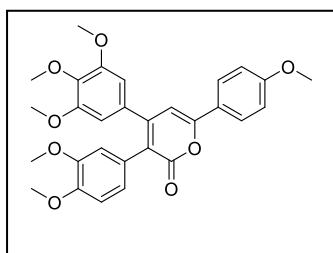
mg), yellow solid, mp: 180-183 °C, FT-IR (cm)⁻¹: 3079, 2964, 1689, 1578, 1540; ¹H NMR (500 MHz, CDCl₃): δ 7.93–7.90 (m, 2H), 7.49 (dd, J = 5.2, 2.0 Hz, 3H), 7.37 (dd, J = 5.1, 1.2 Hz, 1H), 7.15 (dd, J = 3.7, 1.2 Hz, 1H), 7.03 (d, J = 1.1 Hz, 1H), 6.98–6.96 (m, 1H), 6.95–6.90 (m, 2H), 6.80 (d, J = 1.8 Hz, 1H), 3.93 (s, 3H), 3.80 (s, 3H) ppm; ¹³C NMR (125 MHz, CDCl₃): δ 163.0, 157.9, 149.4, 149.4, 144.5, 139.0, 131.5, 130.8, 130.2, 130.1, 129.0, 127.2, 126.5, 125.6, 123.2, 121.1, 113.5, 111.6, 102.9, 55.9, 55.9 ppm; HRMS (ESI-QTOF): m/z $[M+H]^+$ calcd. for $C_{23}H_{19}O_4S$ 391.0999 found 391.1028.

6-(3,4-Dimethoxyphenyl)-3-(*p*-tolyl)-5-(3,4,5-trimethoxyphenyl)-2H-pyran-2-one (**3p**): 78%



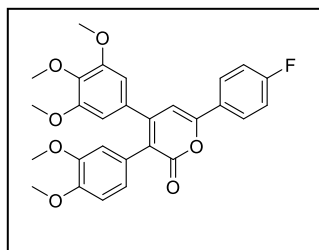
yield (71.2 mg), yellow solid, mp: 174-176 °C, FT-IR (cm)⁻¹: 2941, 2841, 1703, 1622, 1581; ¹H NMR (500 MHz, CDCl₃): δ 7.81 (d, J = 8.3 Hz, 2H), 7.31–7.28 (m, 2H), 6.85 (dd, J = 8.3, 2.0 Hz, 1H), 6.81–6.77 (m, 2H), 6.71 (d, J = 2.0 Hz, 1H), 6.41 (s, 2H), 3.86 (s, 3H), 3.84 (s, 3H), 3.68 (s, 3H), 3.66 (s, 6H), 2.43 (s, 3H) ppm; ¹³C NMR (125 MHz, CDCl₃): δ 162.9, 158.3, 153.1, 152.2, 148.6, 148.5, 141.3, 138.4, 133.2, 129.7, 128.6, 126.6, 125.5, 123.5, 122.1, 114.0, 110.9, 106.2, 104.0, 61.0, 56.2, 55.9, 55.8, 21.5 ppm; HRMS (ESI-QTOF): m/z $[M+H]^+$ calcd. for $C_{29}H_{29}O_7$ 489.1909 found 489.1948.

6-(3,4-Dimethoxyphenyl)-3-(4-methoxyphenyl)-5-(3,4,5-trimethoxyphenyl)-2H-pyran-2-one



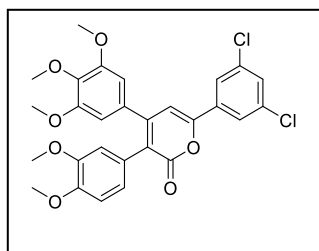
(**3q**): 76% yield (71.6 mg), yellow solid, mp: 161-163 °C, FT-IR (cm)⁻¹: 2933, 2896, 1708, 1620, 1604; ¹H NMR (500 MHz, CDCl₃): δ 7.88–7.84 (m, 2H), 6.99 (d, *J* = 8.9 Hz, 2H), 6.85 (dd, *J* = 8.3, 2.0 Hz, 1H), 6.81–6.77 (m, 1H), 6.74 (s, 1H), 6.70 (d, *J* = 2.0 Hz, 1H), 6.41 (s, 2H), 3.88 (s, 3H), 3.85 (s, 3H), 3.83 (s, 3H), 3.68 (s, 3H), 3.66 (s, 6H) ppm; ¹³C NMR (125 MHz, CDCl₃): δ 162.9, 161.8, 158.3, 153.1, 152.4, 148.6, 148.5, 138.4, 133.3, 127.3, 126.7, 123.9, 123.5, 121.3, 114.4, 114.1, 114.1, 110.9, 106.3, 103.2, 61.0, 56.2, 55.9, 55.8, 55.5 ppm; HRMS (ESI-QTOF): *m/z* [M+H]⁺ calcd. for C₂₉H₂₉O₈ 505.1857 found 505.1860.

6-(3,4-Dimethoxyphenyl)-3-(4-fluorophenyl)-5-(3,4,5-trimethoxyphenyl)-2H-pyran-2-one



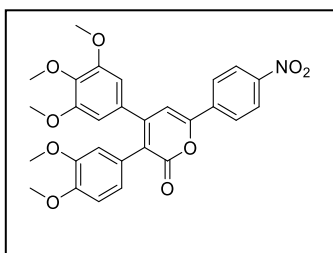
(**3r**): 79% yield (72.7 mg), yellow solid, mp: 160-163 °C, FT-IR (cm)⁻¹: 2971, 1710, 1625, 1582, 1523; ¹H NMR (500 MHz, CDCl₃): δ 7.93–7.88 (m, 2H), 7.18 (t, *J* = 8.6 Hz, 2H), 6.85 (dd, *J* = 8.2, 2.0 Hz, 1H), 6.81–6.77 (m, 2H), 6.71 (d, *J* = 2.0 Hz, 1H), 6.40 (s, 2H), 3.86 (s, 3H), 3.84 (s, 3H), 3.68 (s, 3H), 3.66 (s, 6H) ppm; ¹³C NMR (125 MHz, CDCl₃): δ 164.2 (d, *J* = 252.2 Hz), 163.2, 162.6, 157.1, 153.1, 152.1, 148.7, 148.6, 138.5, 133.0, 127.7 (d, *J* = 8.6 Hz), 126.3, 123.5, 122.4, 116.2 (d, *J* = 21.8 Hz), 114.0, 110.9, 106.2, 104.4, 61.0, 56.2, 55.9, 55.9 ppm; ¹⁹F NMR (470 MHz, CDCl₃): δ -106.1 ppm; HRMS (ESI-QTOF): *m/z* [M+H]⁺ calcd. for C₂₈H₂₆FO₇ 493.1657 found 493.1655.

3-(3,5-Dichlorophenyl)-6-(3,4-dimethoxyphenyl)-5-(3,4,5-trimethoxyphenyl)-2H-pyran-2-one



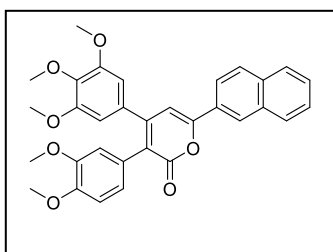
(**3s**): 82% yield (89.6 mg), yellow solid, mp: 141-143 °C, FT-IR (cm)⁻¹: 2938, 1713, 1630, 1588, 1563; ¹H NMR (500 MHz, CDCl₃): δ 7.78 (d, *J* = 1.8 Hz, 2H), 7.45 (t, *J* = 1.8 Hz, 1H), 6.86 (dd, *J* = 8.3, 2.0 Hz, 1H), 6.83 (s, 1H), 6.80 (d, *J* = 8.3 Hz, 1H), 6.70 (d, *J* = 2.0 Hz, 1H), 6.39 (s, 2H), 3.86 (s, 3H), 3.84 (s, 3H), 3.68 (s, 3H), 3.67 (s, 6H) ppm; ¹³C NMR (125 MHz, CDCl₃): δ 162.0, 154.8, 153.2, 151.5, 148.9, 148.6, 138.7, 135.9, 134.1, 132.6, 130.4, 125.9, 124.0, 123.8, 123.5, 113.8, 110.9, 106.2, 106.0, 61.0, 56.2, 55.9, 55.9 ppm; HRMS (ESI-QTOF): *m/z* [M+H]⁺ calcd. for C₂₈H₂₅Cl₂O₇ 543.0972 found 543.0966.

6-(3,4-Dimethoxyphenyl)-3-(4-nitrophenyl)-5-(3,4,5-trimethoxyphenyl)-2H-pyran-2-one (3t):



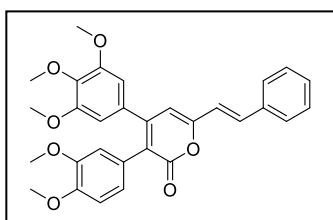
83% yield (86.8 mg), yellow solid, mp: 133-137 °C, FT-IR (cm)⁻¹: 2939, 1716, 1583, 1517, 1416; ¹H NMR (500 MHz, CDCl₃): δ 8.34 (d, *J* = 9.0 Hz, 2H), 8.10–8.05 (m, 2H), 6.99 (s, 1H), 6.88 (dd, *J* = 8.3, 2.0 Hz, 1H), 6.81 (d, *J* = 8.3 Hz, 1H), 6.72 (d, *J* = 2.0 Hz, 1H), 6.41 (s, 2H), 3.87 (s, 3H), 3.85 (s, 3H), 3.68 (s, 3H), 3.67 (s, 6H) ppm; ¹³C NMR (125 MHz, CDCl₃): δ 162.9, 158.0, 152.1, 149.6, 148.5, 147.5, 147.1, 131.5, 130.7, 130.0, 128.9, 128.8, 128.0, 127.8, 125.6, 124.7, 121.5, 112.3, 111.2, 110.9, 108.3, 104.8, 101.0, 55.9, 55.7, 55.3 ppm; HRMS (ESI-QTOF): *m/z* [M+H]⁺ calcd. for C₂₈H₂₆NO₉ 520.1602 found 520.1597.

6-(3,4-Dimethoxyphenyl)-3-(naphthalen-2-yl)-5-(3,4,5-trimethoxyphenyl)-2H-pyran-2-one (3v):



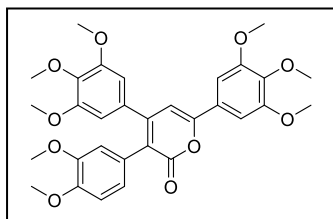
85% yield (89.8 mg), yellow solid, mp: 166-168 °C, FT-IR (cm)⁻¹: 2969, 1711, 1622, 1582, 1530; ¹H NMR (500 MHz, CDCl₃): δ 8.52 (t, *J* = 1.1 Hz, 1H), 8.00–7.92 (m, 1H), 7.93–7.85 (m, 3H), 7.61–7.54 (m, 2H), 6.98 (s, 1H), 6.89 (dd, *J* = 8.3, 2.0 Hz, 1H), 6.81 (d, *J* = 8.3 Hz, 1H), 6.74 (d, *J* = 2.0 Hz, 1H), 6.45 (s, 2H), 3.87 (s, 3H), 3.85 (s, 3H), 3.69 (s, 3H), 3.68 (s, 6H) ppm; ¹³C NMR (125 MHz, CDCl₃): δ 162.8, 158.0, 153.2, 152.1, 148.7, 148.6, 138.5, 134.3, 133.2, 133.2, 129.0, 128.8, 128.4, 127.8, 127.7, 127.0, 126.5, 126.1, 123.6, 122.0, 114.1, 111.0, 106.3, 105.0, 61.0, 56.2, 55.9, 55.9 ppm; HRMS (ESI-QTOF): *m/z* [M+H]⁺ calcd. for C₃₂H₂₉O₇ 525.1908 found 525.1899.

E-6-(3,4-Dimethoxyphenyl)-3-styryl-5-(3,4,5-trimethoxyphenyl)-2H-pyran-2-one (3w):



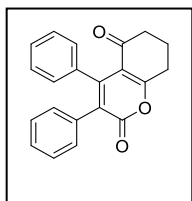
80% yield (80.6 mg), yellow solid, mp: 144-146 °C, FT-IR (cm)⁻¹: 2942, 2841, 1709, 1622, 1582; ¹H NMR (500 MHz, CDCl₃): δ 7.55 (d, *J* = 7.6 Hz, 2H), 7.40 (t, *J* = 7.5 Hz, 3H), 7.36 (d, *J* = 7.1 Hz, 1H), 6.89–6.77 (m, 3H), 6.75–6.67 (m, 2H), 6.38 (s, 2H), 3.86 (s, 3H), 3.83 (s, 3H), 3.68 (s, 3H), 3.65 (s, 6H) ppm; ¹³C NMR (125 MHz, CDCl₃): δ 162.6, 156.8, 153.1, 151.9, 148.7, 135.5, 135.1, 132.8, 129.4, 129.0, 127.4, 126.6, 123.5, 122.7, 118.7, 114.0, 110.9, 108.5, 106.2, 61.0, 56.1, 55.9, 55.9 ppm; HRMS (ESI-QTOF): *m/z* [M+H]⁺ calcd. for C₃₀H₂₉O₇ 501.1908 found 501.1909.

6-(3,4-Dimethoxyphenyl)-3,5-bis(3,4,5-trimethoxyphenyl)-2H-pyran-2-one (**3x**): 70% yield



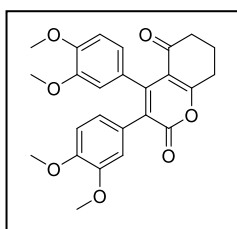
(79.6 mg), yellow solid, mp: 150-153 °C, FT-IR (cm)⁻¹: 2814, 2156, 1718, 1678, 1589; ¹H NMR (500 MHz, CDCl₃): δ 7.10 (s, 2H), 6.85 (dd, *J* = 8.2, 1.9 Hz, 1H), 6.80 (d, *J* = 8.3 Hz, 1H), 6.75 (s, 1H), 6.71 (d, *J* = 1.9 Hz, 1H), 6.41 (s, 2H), 3.95 (s, 6H), 3.92 (s, 3H), 3.86 (s, 3H), 3.84 (s, 3H), 3.68 (s, 3H), 3.67 (s, 6H) ppm; ¹³C NMR (125 MHz, CDCl₃): δ 162.8, 157.9, 153.6, 153.2, 152.2, 148.7, 148.5, 140.6, 138.5, 133.2, 126.8, 126.4, 123.5, 122.2, 114.0, 110.9, 106.2, 104.4, 103.1, 61.0, 61.0, 56.5, 56.2, 55.9, 55.8 ppm; HRMS (ESI-QTOF): *m/z* [M+H]⁺ calcd. for C₃₁H₃₃O₁₀ 565.2068 found 565.2068.

3,4-Diphenyl-7,8-dihydro-2H-chromene-2,5(6H)-dione (**5a**): 85% yield (83.9 mg), yellow



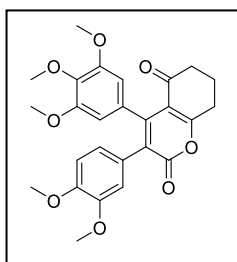
solid, mp: 171-173 °C, FT-IR (cm)⁻¹: 3062, 2906, 1731, 1676, 1594; ¹H NMR (500 MHz, CDCl₃): δ 7.18–7.13 (m, 6H), 7.00–6.97 (m, 2H), 6.91–6.88 (m, 2H), 3.00 (t, *J* = 6.4 Hz, 2H), 2.54–2.50 (m, 2H), 2.18 (dq, *J* = 7.8, 6.4 Hz, 2H) ppm; ¹³C NMR (125 MHz, CDCl₃): δ 193.3, 173.0, 160.4, 152.1, 136.3, 132.8, 130.4, 127.8, 127.7, 127.6, 127.5, 127.4, 126.1, 115.0, 38.5, 29.1, 19.8 ppm; HRMS (ESI-QTOF): *m/z* [M+H]⁺ calcd. for C₂₁H₁₇O₃ 317.1172 found 317.1170.

3,4-Bis(3,4-dimethoxyphenyl)-7,8-dihydro-2H-chromene-2,5(6H)-dione (**5b**): 71% yield (62.9



mg), yellow solid, mp: 175-178 °C, FT-IR (cm)⁻¹: 3011, 1730, 1689, 1517, 1511; ¹H NMR (500 MHz, CDCl₃): δ 6.71 (d, *J* = 8.3 Hz, 2H), 6.66 (dd, *J* = 8.3, 2.0 Hz, 1H), 6.50 (dd, *J* = 8.2, 2.0 Hz, 1H), 6.45 (d, *J* = 2.0 Hz, 1H), 6.39 (d, *J* = 2.0 Hz, 1H), 3.83 (s, 3H), 3.82 (s, 3H), 3.62 (s, 3H), 3.61 (s, 3H), 2.98 (t, *J* = 6.3 Hz, 2H), 2.54 (t, *J* = 6.7 Hz, 2H), 2.18 (p, *J* = 6.4 Hz, 2H) ppm; ¹³C NMR (125 MHz, CDCl₃): δ 193.4, 172.6, 160.6, 151.3, 148.5, 148.4, 148.3, 148.2, 128.8, 125.6, 125.4, 123.2, 120.8, 115.2, 113.8, 112.0, 110.5, 110.2, 55.8, 55.7, 55.7, 38.6, 29.1, 19.9 ppm; HRMS (ESI-QTOF): *m/z* [M+H]⁺ calcd. for C₂₅H₂₅O₇ 437.1595 found 437.1583.

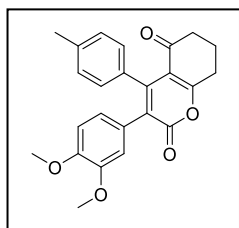
3-(3,4-Dimethoxyphenyl)-4-(3,4,5-trimethoxyphenyl)-7,8-dihydro-2H-chromene-2,5(6H)-



dione (5c): 70% yield (65.8mg), yellow solid, mp: 176-179 °C, FT-IR (cm)⁻¹: 3090, 1738, 1699, 1654, 1513; ¹H NMR (500 MHz, CDCl₃): δ 6.72 (d, *J* = 8.3 Hz, 1H), 6.68 (dd, *J* = 8.3, 2.0 Hz, 1H), 6.46 (d, *J* = 2.0 Hz, 1H), 6.13 (s, 2H), 3.81 (d, *J* = 2.7 Hz, 6H), 3.62 (d, *J* = 3.7 Hz, 9H), 2.99 (t, *J* = 6.3 Hz, 2H), 2.55 (t, *J* = 6.7 Hz, 2H), 2.19 (p, *J* = 6.5 Hz, 2H)

ppm; ¹³C NMR (125 MHz, CDCl₃): δ 193.1, 172.7, 160.4, 152.7, 151.2, 148.5, 148.2, 137.6, 131.7, 125.6, 125.3, 123.1, 114.9, 113.6, 110.5, 106.1, 61.0, 56.1, 55.8, 55.7, 38.5, 29.1, 19.9 ppm; HRMS (ESI-QTOF): *m/z* [M+H]⁺ calcd. for C₂₆H₂₇O₈ 467.1700 found 467.1690.

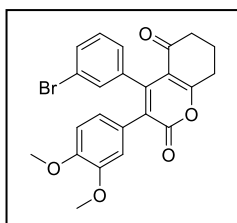
3-(3,4-Dimethoxyphenyl)-4-(p-tolyl)-7,8-dihydro-1H-isochromene-1,5(6H)-dione (5d): 79%



yield (72.3 mg), yellow solid, mp: 179-181 °C, FT-IR (cm)⁻¹: 3014, 2899, 1727, 1627, 1596; ¹H NMR (500 MHz, CDCl₃): δ 6.99 (d, *J* = 7.7 Hz, 2H), 6.79 (d, *J* = 7.7 Hz, 2H), 6.73 (d, *J* = 1.9 Hz, 2H), 6.35 (s, 1H), 3.82 (s, 3H), 3.56 (s, 3H), 2.98 (t, *J* = 6.3 Hz, 2H), 2.51 (t, *J* = 6.6 Hz, 2H), 2.28 (s, 3H), 2.17 (p, *J* = 6.4 Hz, 2H) ppm; ¹³C NMR (125 MHz, CDCl₃): δ

193.5, 172.6, 160.6, 151.8, 148.2, 147.9, 137.2, 133.6, 128.3, 127.8, 125.5, 125.1, 123.4, 115.2, 113.9, 110.4, 55.7, 55.6, 38.5, 29.1, 21.3, 19.9 ppm; HRMS (ESI-QTOF): *m/z* [M+H]⁺ calcd. for C₂₄H₂₃O₅ 391.1540 found 391.1575.

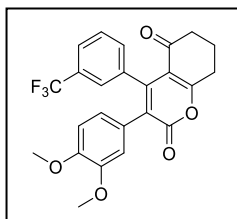
4-(3-Bromophenyl)-3-(3,4-dimethoxyphenyl)-7,8-dihydro-2H-chromene-2,5(6H)-dione (5e):



81% yield (71.1 mg), yellow solid, mp: 138-141 °C, FT-IR (cm)⁻¹: 2954, 2833, 1729, 1681, 1592; ¹H NMR (500 MHz, CDCl₃): δ 7.32 (ddd, *J* = 8.0, 2.0, 1.0 Hz, 1H), 7.13 (t, *J* = 1.8 Hz, 1H), 7.05 (t, *J* = 7.9 Hz, 1H), 6.82 (ddd, *J* = 7.7, 1.6, 1.0 Hz, 1H), 6.73 (d, *J* = 8.3 Hz, 1H), 6.68 (dd, *J* = 8.3, 2.0 Hz, 1H), 6.39 (d, *J* = 2.0 Hz, 1H), 3.82 (s, 3H), 3.64 (s, 3H),

2.99 (t, *J* = 6.3 Hz, 2H), 2.52 (t, *J* = 6.6 Hz, 2H), 2.18 (p, *J* = 6.5 Hz, 2H) ppm; ¹³C NMR (125 MHz, CDCl₃): δ 193.2, 173.0, 160.3, 149.9, 148.5, 148.1, 138.7, 130.8, 130.5, 129.2, 126.4, 126.1, 124.5, 123.3, 121.5, 114.6, 113.7, 110.5, 55.8, 55.7, 38.4, 29.1, 19.8 ppm; HRMS (ESI-QTOF): *m/z* [M+H]⁺ calcd. for C₂₃H₂₀BrO₅ 455.0489 found 455.0444.

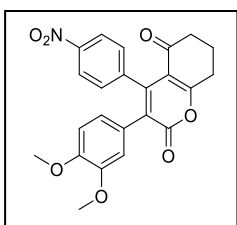
3-(3,4-Dimethoxyphenyl)-4-(3-(trifluoromethyl)phenyl)-7,8-dihydro-2H-chromene-2,5(6H)-



dione (**5f**): 84% yield (74.1 mg), yellow solid, mp: 185-188 °C, FT-IR (cm)⁻¹: 2956, 1725, 1680, 1601, 1539; ¹H NMR (500 MHz, CDCl₃): δ 7.49–7.43 (m, 2H), 7.10–7.03 (m, 2H), 6.70 (d, *J* = 8.3 Hz, 1H), 6.64 (dd, *J* = 8.3, 2.0 Hz, 1H), 6.36 (d, *J* = 2.0 Hz, 1H), 3.81 (s, 3H), 3.58 (s, 3H), 3.00 (t, *J* = 6.3 Hz, 2H), 2.52 (dd, *J* = 7.4, 6.0 Hz, 2H), 2.28–2.09 (m, 2H)

ppm; ¹³C NMR (125 MHz, CDCl₃): δ 193.3, 173.2, 160.2, 149.8, 148.7, 148.2, 140.5, 129.7, 129.4 (q, *J* = 280 Hz), 128.3, 126.1, 125.0, 124.5 (q, *J* = 3.8 Hz), 124.2, 123.4, 114.6, 113.7, 110.5, 55.7, 55.7, 38.3, 29.1, 19.8 ppm; ¹⁹F NMR (470 MHz, CDCl₃): δ -62.6 ppm; HRMS (ESI-QTOF): *m/z* [M+H]⁺ calcd. for C₂₄H₂₀F₃O₅ 445.1257 found 445.1274.

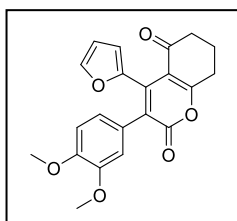
3-(3,4-Dimethoxyphenyl)-4-(4-nitrophenyl)-7,8-dihydro-2H-chromene-2,5(6H)-dione



(**5g**): 80% yield (71.6 mg), yellow solid, mp: 220-222 °C, FT-IR (cm)⁻¹: 2960, 2837, 1722, 1679, 1534; ¹H NMR (500 MHz, CDCl₃): δ 8.07 (d, *J* = 8.7 Hz, 2H), 7.11 (d, *J* = 8.7 Hz, 2H), 6.66 (d, *J* = 8.4 Hz, 1H), 6.55 (dd, *J* = 8.3, 2.0 Hz, 1H), 6.45 (d, *J* = 2.1 Hz, 1H), 3.80 (s, 3H), 3.65 (s, 3H), 3.01 (t, *J* = 6.3 Hz, 2H), 2.52 (dd, *J* = 7.4, 5.9 Hz, 2H), 2.20 (p, *J* = 6.4

Hz, 2H) ppm; ¹³C NMR (125 MHz, CDCl₃): δ 193.3, 173.6, 159.9, 149.1, 148.9, 148.3, 146.8, 143.8, 128.9, 126.3, 124.0, 123.3, 122.9, 114.3, 113.4, 110.6, 55.8, 55.7, 38.2, 29.1, 19.8 ppm; HRMS (ESI-QTOF): *m/z* [M+H]⁺ calcd. for C₂₃H₂₀NO₇ 422.1234 found 422.1247.

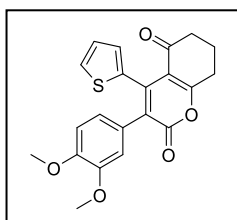
3-(3,4-Dimethoxyphenyl)-4-(furan-2-yl)-7,8-dihydro-2H-chromene-2,5(6H)-dione (**5h**): 68%



yield (63.5 mg), yellow solid, mp: 133-135 °C, FT-IR (cm)⁻¹: 2814, 1713, 1698, 1609, 1562; ¹H NMR (500 MHz, CDCl₃): δ 7.44 (d, *J* = 1.8 Hz, 1H), 6.83 (d, *J* = 8.3 Hz, 1H), 6.78 (dd, *J* = 8.2, 2.0 Hz, 1H), 6.56 (d, *J* = 2.0 Hz, 1H), 6.28 (dd, *J* = 3.4, 1.8 Hz, 1H), 5.82 (d, *J* = 3.4 Hz, 1H), 3.87 (s, 3H), 3.84 (s, 3H), 2.95 (t, *J* = 6.3 Hz, 2H), 2.58 (t, *J* = 6.7 Hz, 2H), 2.19

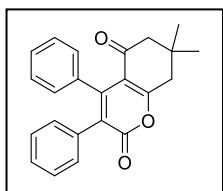
(p, *J* = 6.4 Hz, 2H) ppm; ¹³C NMR (125 MHz, CDCl₃): δ 192.8, 172.4, 148.5, 147.5, 142.7, 125.3, 122.5, 112.9, 111.7, 111.4, 110.8, 55.8, 38.0, 28.9, 19.9 ppm; HRMS (ESI-QTOF): *m/z* [M+H]⁺ calcd. for C₂₁H₁₉O₆ 367.1176 found 367.1190.

3-(3,4-Dimethoxyphenyl)-4-(thiophen-2-yl)-7,8-dihydro-2H-chromene-2,5(6H)-dione (5i):



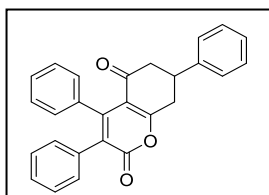
65% yield (59.9 mg), yellow solid, mp: 160-163 °C, FT-IR (cm)⁻¹: 2888, 2150, 1717, 1673, 1599; ¹H NMR (500 MHz, CDCl₃): δ 7.41–7.35 (m, 1H), 7.14 (dd, *J* = 3.5, 1.2 Hz, 1H), 7.11 (dd, *J* = 8.5, 2.0 Hz, 1H), 7.07 (dd, *J* = 5.2, 3.5 Hz, 1H), 6.93 (d, *J* = 2.1 Hz, 1H), 6.81 (d, *J* = 8.4 Hz, 1H), 3.88 (s, 3H), 3.67 (s, 3H), 2.98 (t, *J* = 6.3 Hz, 2H), 2.57–2.48 (m, 2H), 2.22 (p, *J* = 6.2 Hz, 2H) ppm; ¹³C NMR (125 MHz, CDCl₃): δ 193.7, 165.6, 150.5, 149.1, 148.6, 132.8, 128.4, 127.1, 126.4, 122.4, 121.6, 119.2, 111.1, 111.0, 109.5, 109.5, 55.9, 55.5, 38.6, 23.7, 22.4 ppm; HRMS (ESI-QTOF): *m/z* [M+H]⁺ calcd. for C₂₁H₁₉O₅S 383.0948 found 383.1000.

7,7-Dimethyl-3,4-diphenyl-7,8-dihydro-2H-chromene-2,5(6H)-dione (5j): 77% yield (82.7



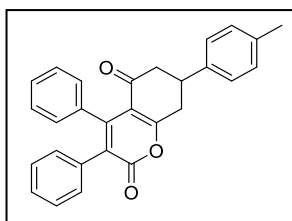
mg), yellow solid, mp: 189-191 °C, FT-IR (cm)⁻¹: 2961, 1787, 1696, 1608; ¹H NMR (500 MHz, CDCl₃): δ 7.19–7.12 (m, 6H), 7.03–6.96 (m, 2H), 6.90–6.86 (m, 2H), 2.86 (s, 2H), 2.40 (s, 2H), 1.19 (s, 6H) ppm; ¹³C NMR (125 MHz, CDCl₃): δ 193.4, 171.6, 160.7, 151.8, 136.1, 132.8, 130.4, 127.9, 127.7, 127.6, 127.6, 127.5, 127.4, 125.8, 114.1, 52.6, 42.7, 32.0, 28.3 ppm; HRMS (ESI-QTOF): *m/z* [M+H]⁺ calcd. for C₂₃H₂₁O₃ 345.1485 found 345.1481.

3,4,7-Triphenyl-7,8-dihydro-2H-chromene-2,5(6H)-dione (5l): 82% yield (100.4 mg), yellow



solid, mp: 160-162 °C, FT-IR (cm)⁻¹: 3023, 1735, 1685, 1672, 1611; ¹H NMR (500 MHz, CDCl₃): δ 7.40 (dd, *J* = 8.2, 6.9 Hz, 2H), 7.36–7.28 (m, 1H), 7.31–7.26 (m, 2H), 7.21–7.13 (m, 6H), 7.04–6.97 (m, 2H), 6.92 (s, 2H), 3.57 (p, *J* = 8.4 Hz, 1H), 3.24–3.19 (m, 2H), 2.78 (d, *J* = 8.6 Hz, 2H) ppm; ¹³C NMR (125 MHz, CDCl₃): δ 192.5, 172.1, 160.4, 151.9, 141.2, 136.1, 132.7, 130.4, 129.1, 127.9, 127.8, 127.7, 127.6, 127.6, 127.5, 126.6, 126.2, 114.7, 45.5, 37.9, 36.5 ppm; HRMS (ESI-QTOF): *m/z* [M+H]⁺ calcd. for C₂₇H₂₁O₃ 393.1485 found 393.1498

3,4-Diphenyl-7-(p-tolyl)-7,8-dihydro-2H-chromene-2,5(6H)-dione (5m): 81% yield (102.7

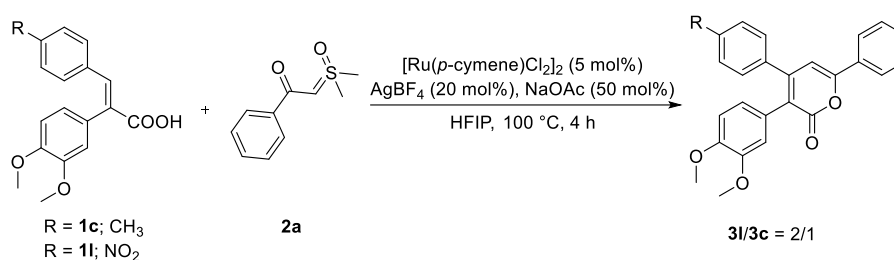


mg), yellow solid, mp: 166-168 °C, FT-IR (cm)⁻¹: 3022, 1718, 1699, 1534, 1511; ¹H NMR (500 MHz, CDCl₃): δ 7.22–7.12 (m, 10H), 7.00 (dd, *J* = 6.9, 2.6 Hz, 2H), 6.92 (s, 2H), 3.53 (p, *J* = 8.5 Hz, 1H), 3.20 (d, *J* = 9.3 Hz, 2H), 2.75 (d, *J* = 8.5 Hz, 2H), 2.36 (s, 3H) ppm; ¹³C NMR (125 MHz, CDCl₃): δ 192.6, 172.2, 160.4, 151.9, 138.2, 137.3,

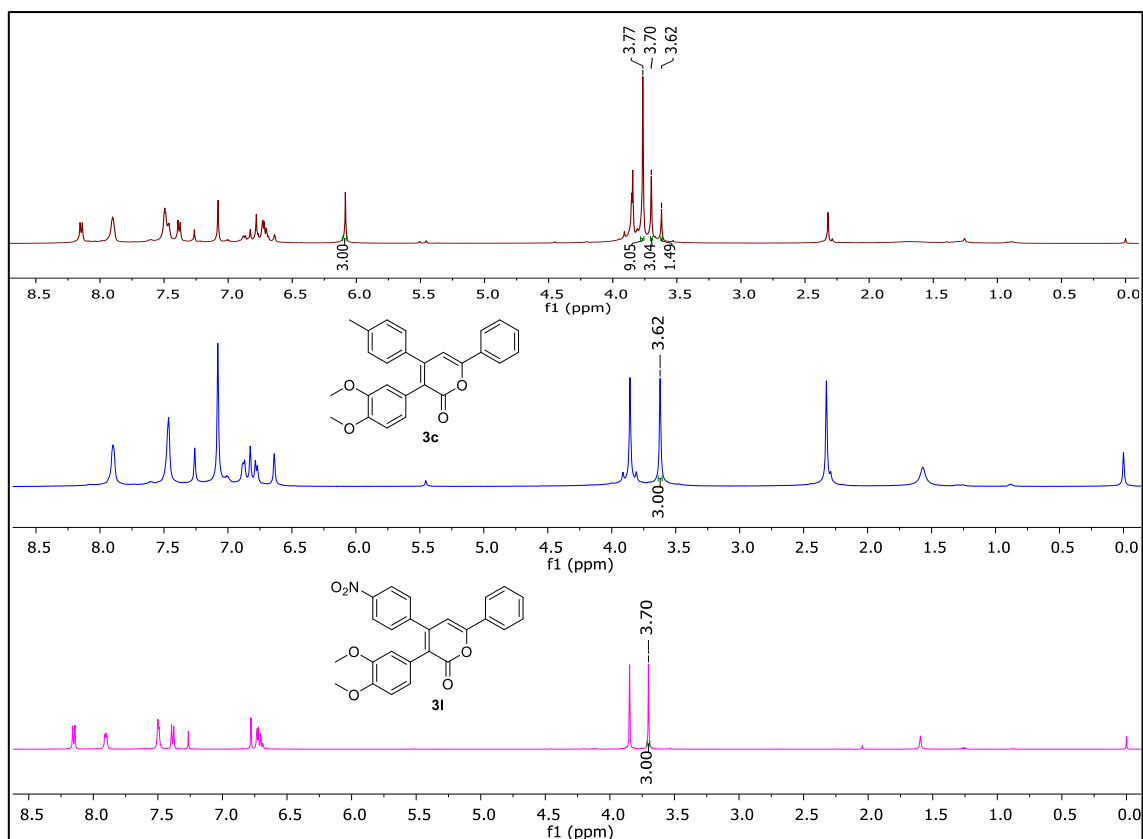
136.1, 132.7, 130.4, 129.7, 127.9, 127.7, 127.7, 127.6, 127.5, 126.4, 126.2, 114.7, 45.6, 37.5, 36.7, 21.1 ppm; HRMS (ESI-QTOF): m/z . $[M+H]^+$ calcd. For $C_{28}H_{23}O_3$ 407.1642 found 407.1645.

6. Mechanistic studies for ruthenium-catalyzed α -pyrone synthesis

6.1. Competitive reaction between *cis*-stilbene acids

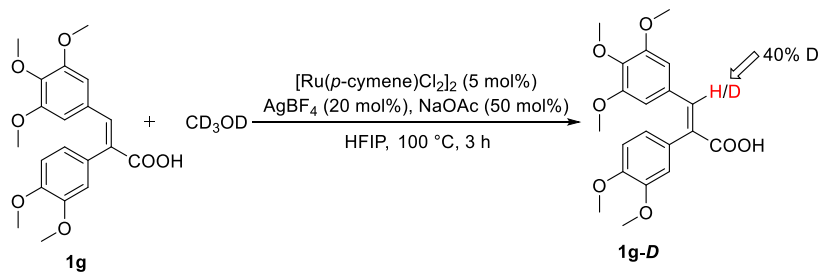


A pressure tube with a magnetic stir bar was charged with **1c** (1.0 equiv.), **1I** (1.0 equiv.), **2a** (1.2 equiv.), $[Ru(p\text{-cymene})Cl_2]_2$ (5.0 mol%), $AgBF_4$ (20 mol%), NaOAc (50 mol%) and HFIP (1 mL). The resulting mixture was stirred at 100 °C for 4 h. After 4 h, trimethoxy benzene (1.0 equiv.) was added to the reaction mixture as the standard. Thereafter, the reaction solvent was evaporated under reduced pressure and the crude product containing mixture of the product **3** and **3I** was directly submitted for 1H NMR analysis. The 1H NMR analysis demonstrated that the compounds **3I/3c** have been formed with the ratio of 2/1. It indicated that, the reaction rate of the electron deficient substrate is twice than the reaction rate of electron rich substrate.

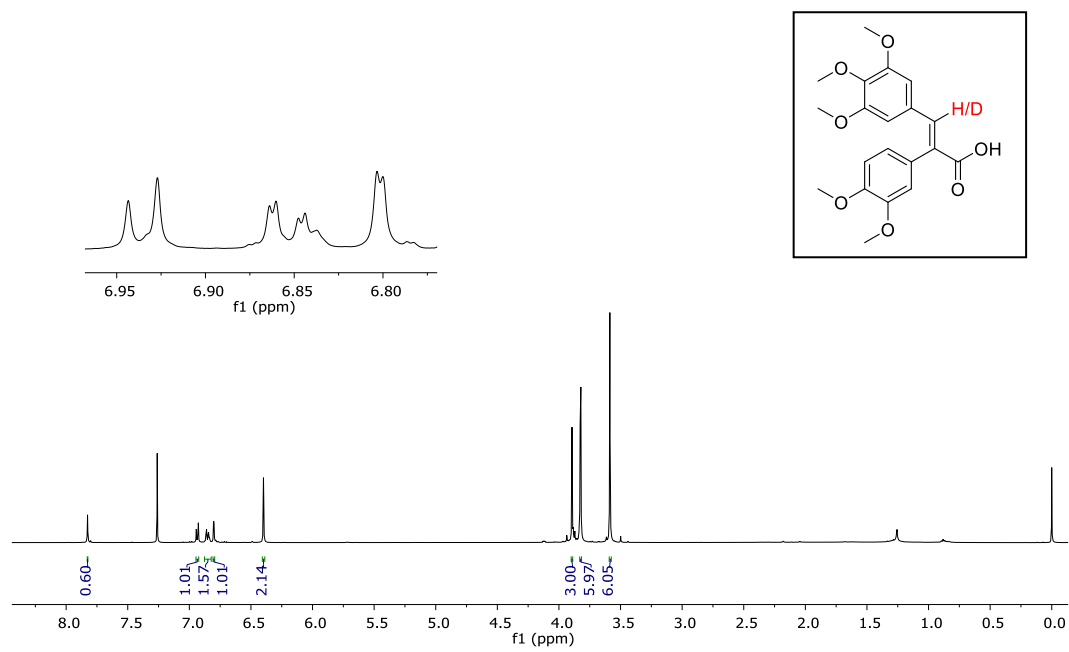


^1H NMR overlay of competitive reaction, ^1H NMR of **3c** and **3l** (CDCl_3 , 500 MHz)

6.2. H/D Exchange Experiment



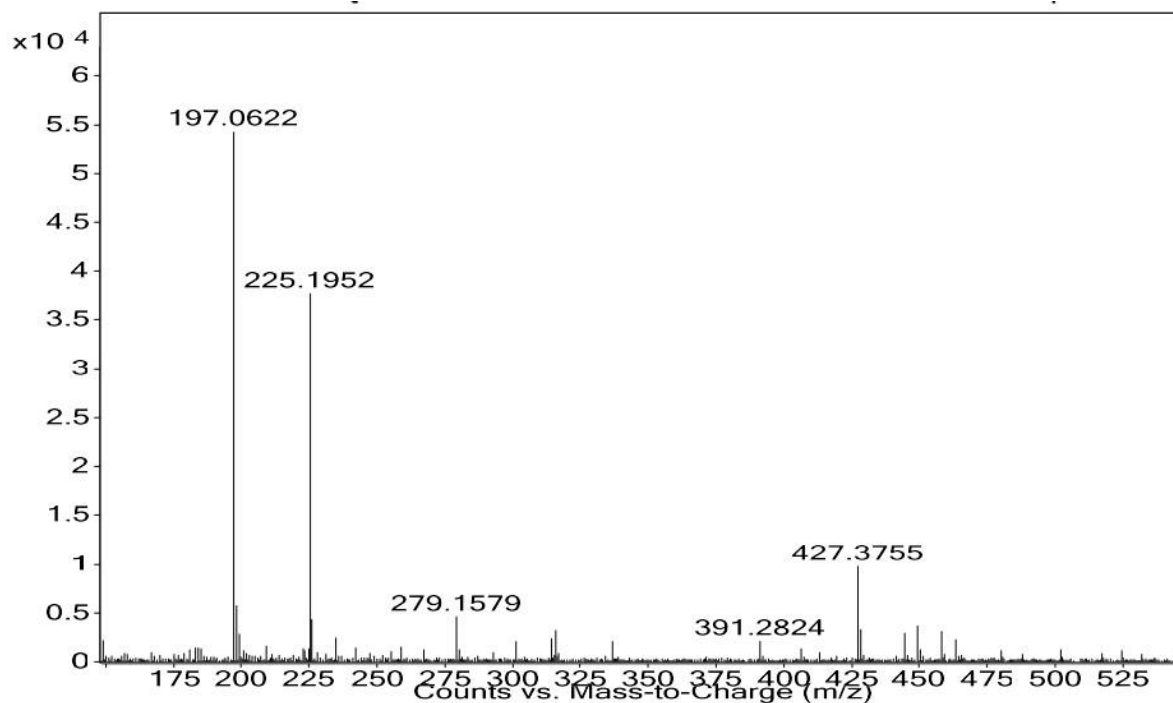
A pressure tube was charged with *cis*-stilbene acid (**1g**, 1 equiv.), $[\text{Ru}(p\text{-cymene})\text{Cl}_2]_2$ (5 mol%), AgBF_4 (20 mol%), NaOAc (50 mol%), CD_3OD (10 equiv.), and HFIP (1 mL). The reaction mixture was stirred at $100\text{ }^\circ\text{C}$ for 3 h. The solvent was removed under reduced pressure and the residue was purified by silica gel chromatography using EA/hexane (40:60) to afford the deuterated compound, which was characterized by ^1H NMR spectroscopy. ^1H NMR analysis of **1g** revealed 40% deuteration at the olefinic-position of *cis*-stilbene acid.



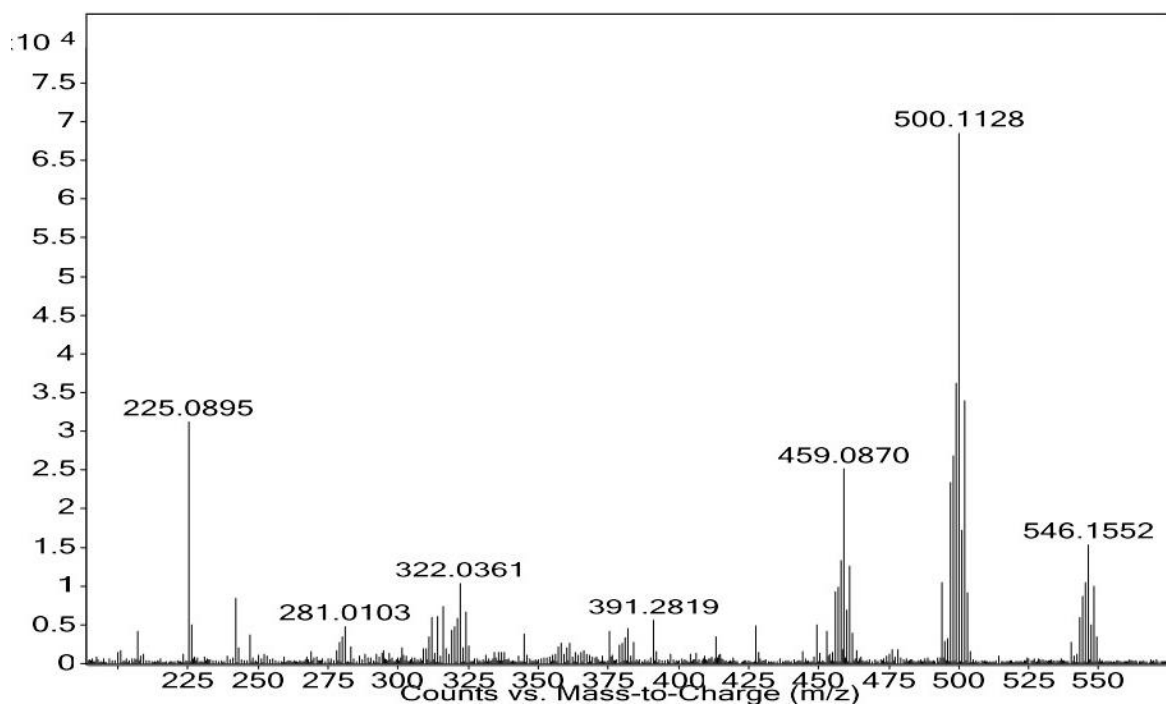
¹H NMR of **1g-Din** in CDCl₃ (500MHz)

7. Mass studies

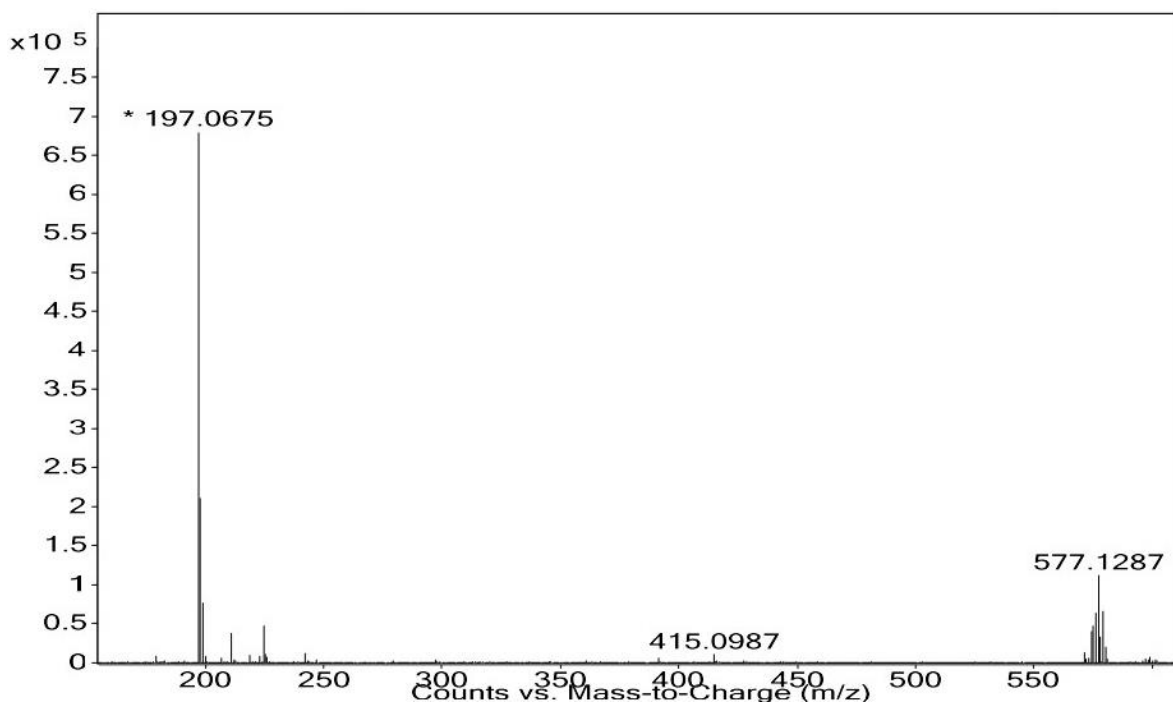
To identify the intermediate species involved the reaction was run under standard conditions. The reaction mixture was then analysed at specific time intervals.



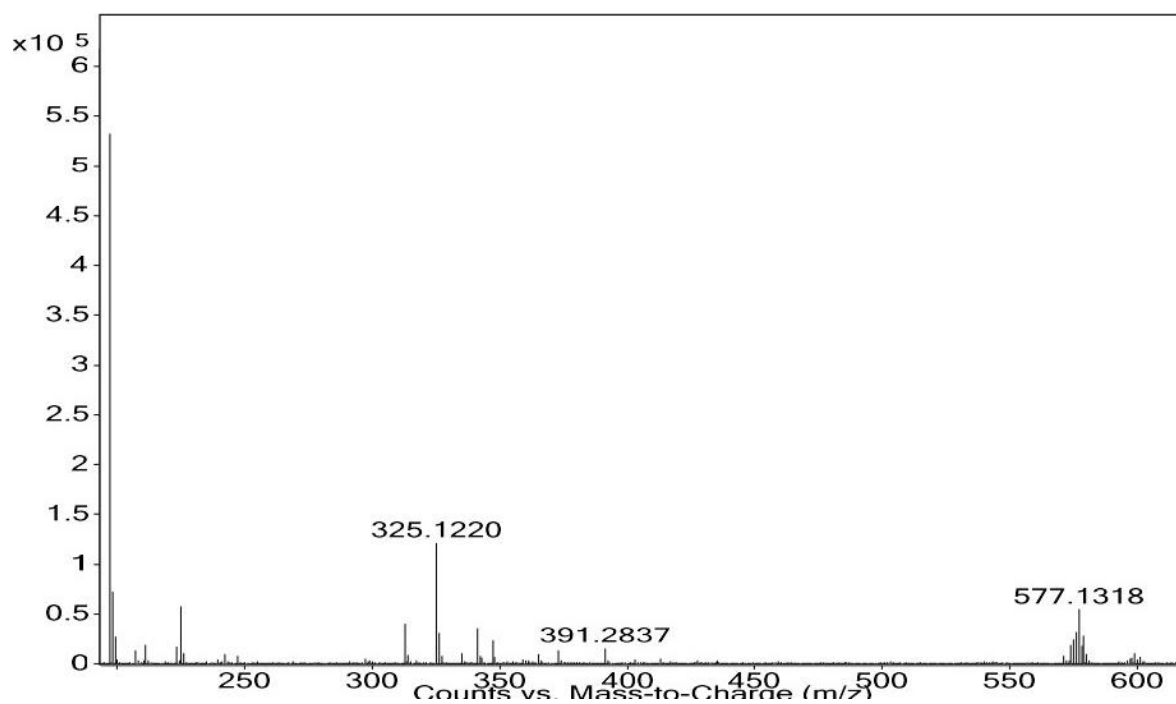
ESI-MS data of reaction mixture at 0 min.



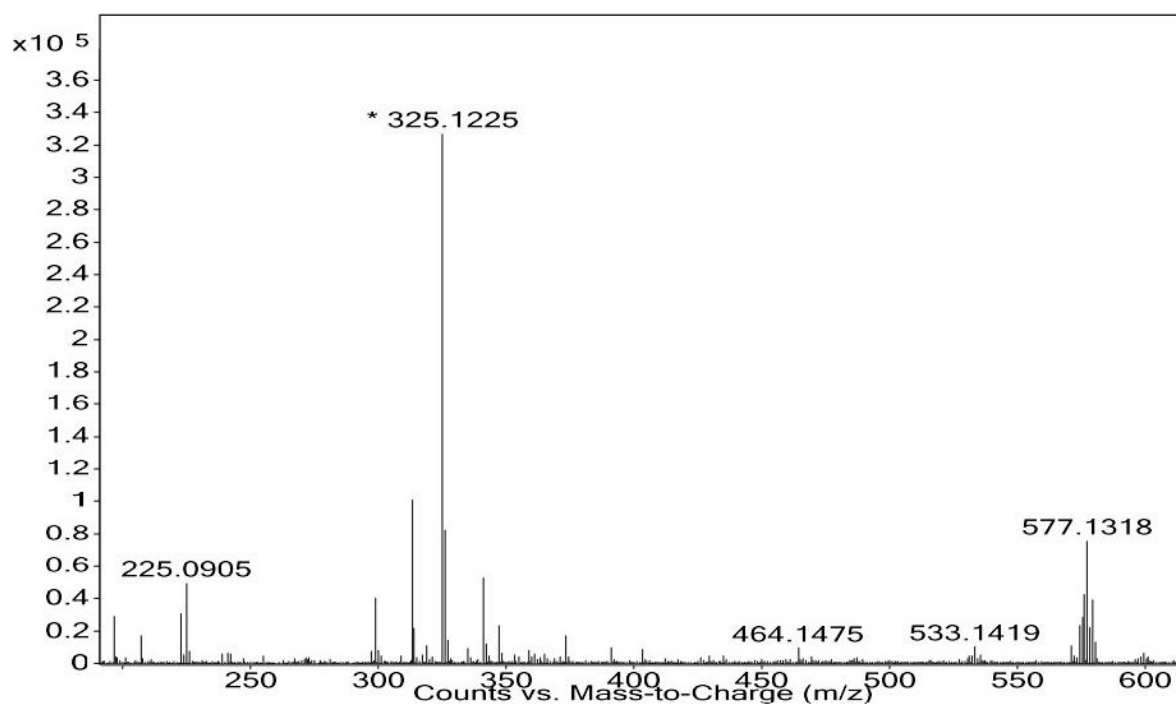
ESI-MS data of reaction mixture after 2 min.



ESI-MS data of reaction mixture after 5 min.



ESI-MS data of reaction mixture after 30 min.



ESI-MS data of reaction mixture after 6 h.

8. Gram-Scale Preparation and Transformations

8.1. Gram-Scale Synthesis of **3i**

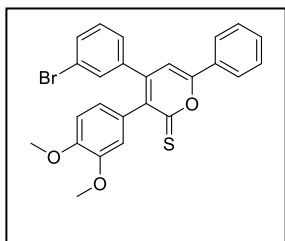
To demonstrate the scalability of the reaction, a gram-scale synthesis was performed using **1i** (1.0 g, 1.0 equiv.) and **2a** (1.2 equiv.) under the optimized conditions, as discussed in

the general procedure. The reaction proceeded efficiently to give the desired product **3i** (1.04 g) in 80% yield.

8.2. Synthesis of thione (**6**)

The synthetic transformation of the keto-group in the pyrone to thio-ketone was demonstrated by using **3i** (50 mg, 1.0 equiv.), Lawesson's reagent (2.0 equiv.) was refluxed in toluene for 12 h. After completion the solvent was evaporated under reduced pressure and extracted using ethyl acetate and water. The organic layer was then concentrated, dried over Na₂SO₄ and subjected to column chromatography using ethyl acetate/ hexane (30:70) to obtain **6**.

4-(3-Bromophenyl)-3-(3,4-dimethoxyphenyl)-6-phenyl-2H-pyran-2-thione (**6**): 75% yield



(54.4mg), yellow solid, mp: 190-193 °C, FT-IR (cm)⁻¹: 2900, 2356, 1716, 1689, 1012; ¹H NMR (500 MHz, CDCl₃): δ 7.99–7.95 (m, 2H), 7.52 (d, *J* = 6.6 Hz, 3H), 7.42–7.36 (m, 2H), 7.08 (t, *J* = 8.2 Hz, 1H), 7.03–6.96 (m, 2H), 6.81–6.72 (m, 3H), 6.70 (d, *J* = 1.9 Hz, 1H), 3.86 (s, 3H), 3.72 (s, 3H) ppm; ¹³C NMR (125 MHz, CDCl₃): δ 197.1, 163.7, 148.7, 148.6, 146.1, 139.9, 137.1, 131.7, 131.6, 131.1, 130.5, 129.8, 129.2, 128.6, 127.1, 125.9, 123.5, 122.4, 114.2, 110.8, 107.9, 55.9, 55.8 ppm; HRMS (ESI-QTOF): *m/z* [M+H]⁺ calcd. for C₂₅H₂₀NO₅S 479.0311 found 479.0269.

8.3. Gram-Scale Synthesis of **5a**

To demonstrate the scalability employing the hypervalent iodonium ylide, a gram-scale synthesis was performed using **1a** (1.0 g, 1.0 equiv.) and **4a** (1.2 equiv.) under the optimized conditions, as discussed in the general procedure. The reaction proceeded efficiently to give the desired product **5a** (1.11 g) in 79% yield.

9. Application

9.1. Photophysical study

The excitation and emission experiments were performed in a 3.0 mL quartz cuvette on Agilent Cary Eclipse fluorescence spectrophotometer (Singapore) at 20 °C. The excitation and emission slit widths were 10 nm each, while the scanning speed was 600 nm per minute with 10 millisecond integration time. The resulting data were plotted as fluorescence intensity versus wavelength plots. The fluorescence emission spectrum of compounds at 5 μM was recorded in

water. The excitation wavelength for compounds **3a**, **3c**, **3i**, **3l** and **3k** ranged from 344-390 nm whereas for compounds **5d**, **5e**, **5f** and **5g** ranged from 276-284. The emission spectrum was recorded between 290–600 nm for chromone-2-one series and 400-700nm for α -pyrone series. All compounds were dissolved in DMSO to make the stock solution and then diluted in an aqueous medium for working solutions.

9.2. Molecular docking

The docking for the tubulin-binding potential was performed using the tubulin protein obtained from protein data bank (PDB ID: 4O2B). The receptor model was prepared using the protein preparation tool (Schrödinger 2017-1). The missing side chains and loops were added with removal of water molecules with a distance of more than 5 Å away from the active pocket. The receptor grid was generated with 20 Å distance equally in each direction X, Y and Z. The Ligprep model of Schrödinger suite was used to sketch the ligands (**3a-x**, **5a-m**) along with different conformer generation. The ligands were docked using GLIDE-XP 7.4 (Extra Precision) mode. The docking score obtained along with the co-crystal (colchicine-known tubulin inhibitor) is tabulated below (Table S3).

Table S3. Docking scores of the synthesized analogues along with colchicine

α -pyrone series				Isochromene-one series	
Entry	Docking score	Entry	Docking score	Entry	Docking score
3a	-5.713	3n	-7.333	5a	-5.251
3b	-6.570	3p	-4.852	5b	-4.422
3c	-6.513	3q	-4.876	5c	-6.767
3d	-5.388	3r	-6.942	5d	-6.182
3f	-4.825	3s	-5.319	5e	-5.833
3g	-4.639	3t	-4.955	5f	-7.304
3h	-6.599	3v	-6.819	5g	-6.771
3i	-6.628	3w	-5.660	5h	-7.588
3j	-6.620	3x	-5.896	5i	-6.037
3k	-6.601			5j	-4.768
3l	-6.546			5l	-5.591
3m	-6.540			5m	-4.865
Colchicine	-6.395				

9.3. MTT Assay

MTT assay is a colorimetric assay based on the conversion of MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide) into insoluble formazan by succinate

dehydrogenase enzyme (mitochondrial enzyme). The viability of cells is indicated by the ability of the live cells to reduce MTT level. The assay initiates with the seeding of cells in 96-well plates (density = 1000- 4000 cell/well) in 100 μ L of medium and grown for 24 h. The media was replaced with fresh media and cells were treated with 20 μ M concentration of compounds and standard for 48 h period. After 48 h of incubation media removal was followed by the addition of 100 μ L of MTT solution in media (0.5 mg/mL) and incubated for 4 h at 37 $^{\circ}$ C. The whole media was removed and 100 μ L of DMSO was added to dissolve formazan crystal and kept for 20 min at 37 $^{\circ}$ C. The amount of formazan was determined utilizing spectrophotometric microtiter plate reader at 570 nm wavelength.

Table S4. Percentage inhibition on cancer cell lines (HCT-116 and A549) at 20 μ M after 48 h

Compound	Cell lines		Compound	Cell lines	
	HCT-116	A549		HCT-116	A549
3a	30.99	29.01	3s	73.15	70.17
3b	45.31	35.88	3t	22.10	20.14
3c	41.56	39.76	3v	71.74	55.95
3d	30.18	12.90	3w	86.33	77.00
3f	55.09	45.54	3x	89.36	82.94
3g	70.89	61.11	5a	26.11	30.92
3h	79.09	30.15	5b	45.16	49.76
3i	56.76	50.72	5c	60.41	61.23
3j	68.45	52.34	5d	30.56	41.15
3k	75.34	69.10	5e	66.42	63.17
3l	46.94	33.18	5f	77.80	71.45
3m	30.90	21.38	5g	56.38	45.67
3n	71.77	66.63	5h	73.15	65.15
3p	56.09	47.19	5i	46.77	68.66
3q	81.18	77.16	5j	36.73	52.14
3r	30.21	11.18	5l	49.49	69.58
Colchicine	85.22	90.10	5m	59.56	71.77

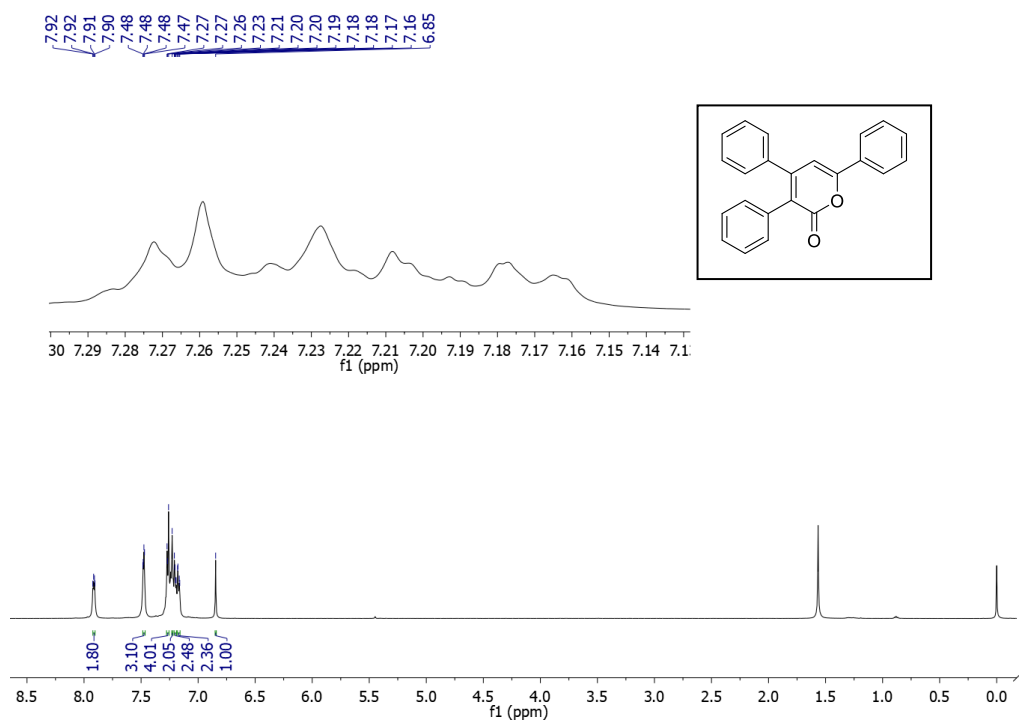
*HCT-116: human colon cancer cell line, A549: human lung cancer cell

10. References

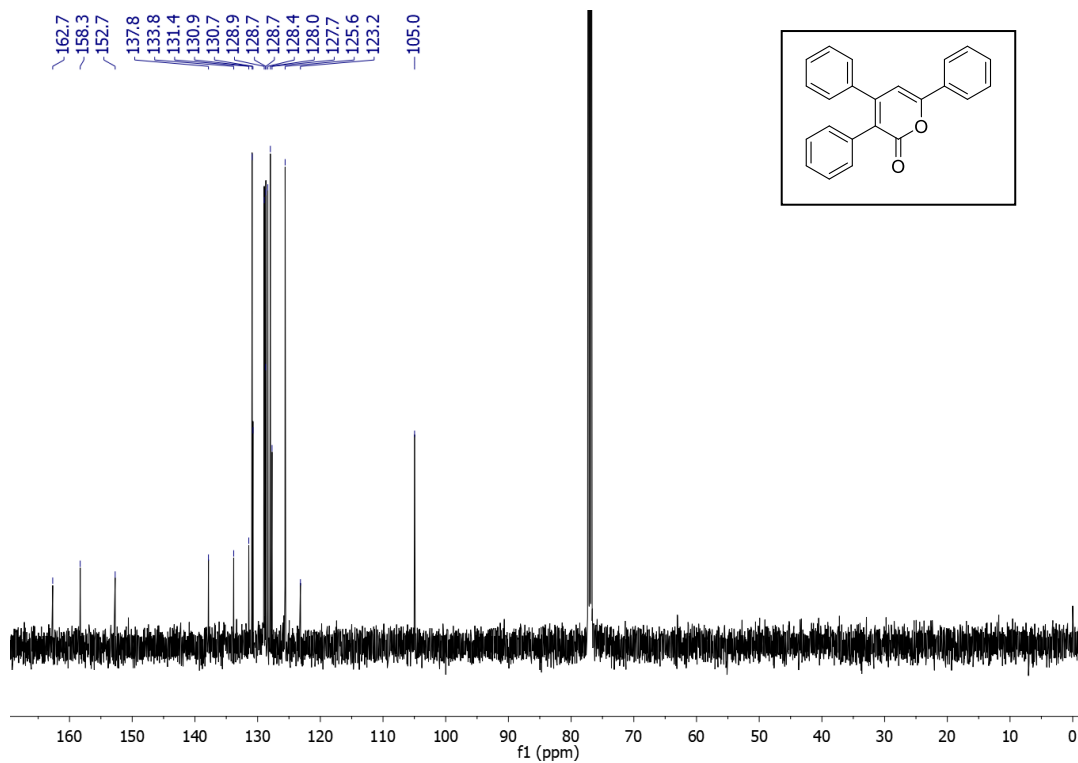
1. C. Jadala, M. Sathish, T. S. Reddy, V. G. Reddy, R. Tokala, S. K. Bhargava, N. Shankaraiah, N. Nagesh, A. Kamal, Synthesis and in vitro cytotoxicity evaluation of β -carboline-combretastatin carboxamides as apoptosis inducing agents: DNA intercalation and topoisomerase-II inhibition, *Bioorg. Med. Chem.* **2019**, 27, 3285-3298.
2. S. Kumar, S. Nunewar, and V. Kanchupalli, Rh(III)-Catalyzed Cross-Coupling/Annulation of Two Carbene Precursors: Construction of Dihydrobenzo[c]chromen-6-one Scaffolds and Application in the Total Synthesis of Cannabinol. *Asian. J. Org. Chem.* 2022, 11, e202100689. doi: [10.1002/ajoc.202100689](https://doi.org/10.1002/ajoc.202100689).

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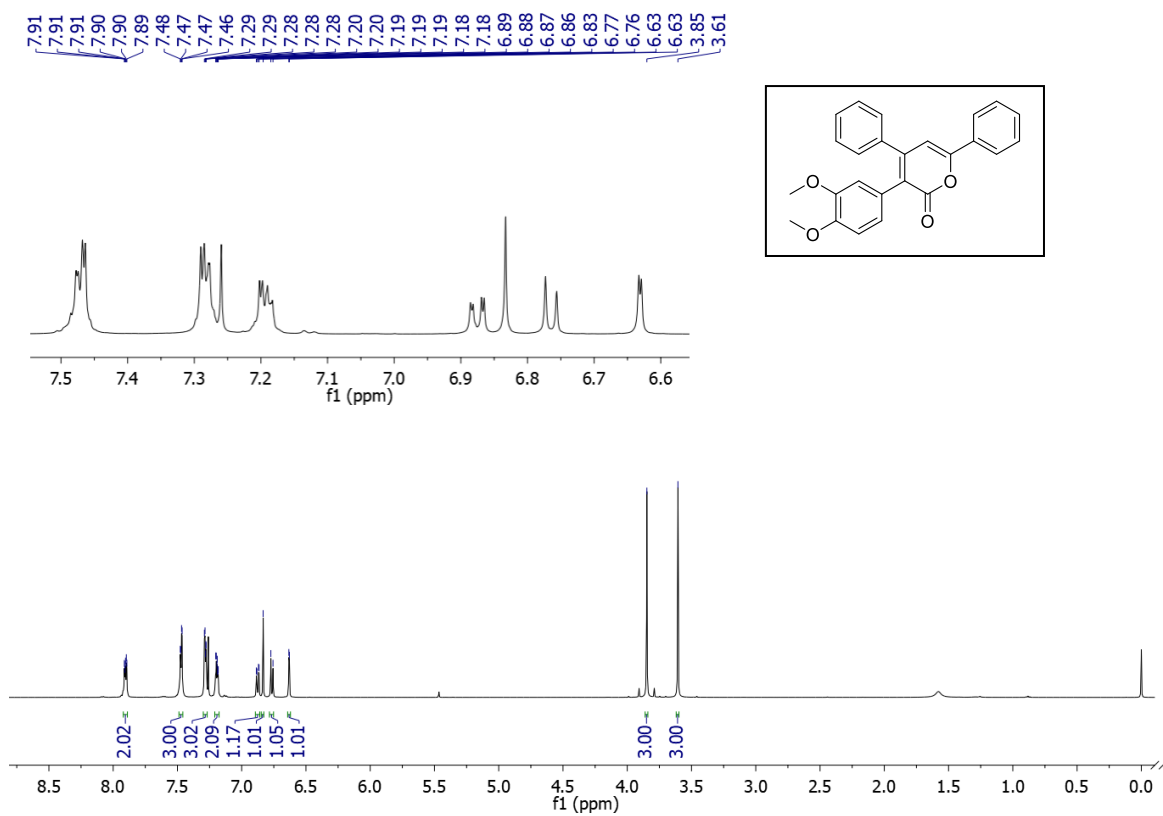
11. Spectral Data



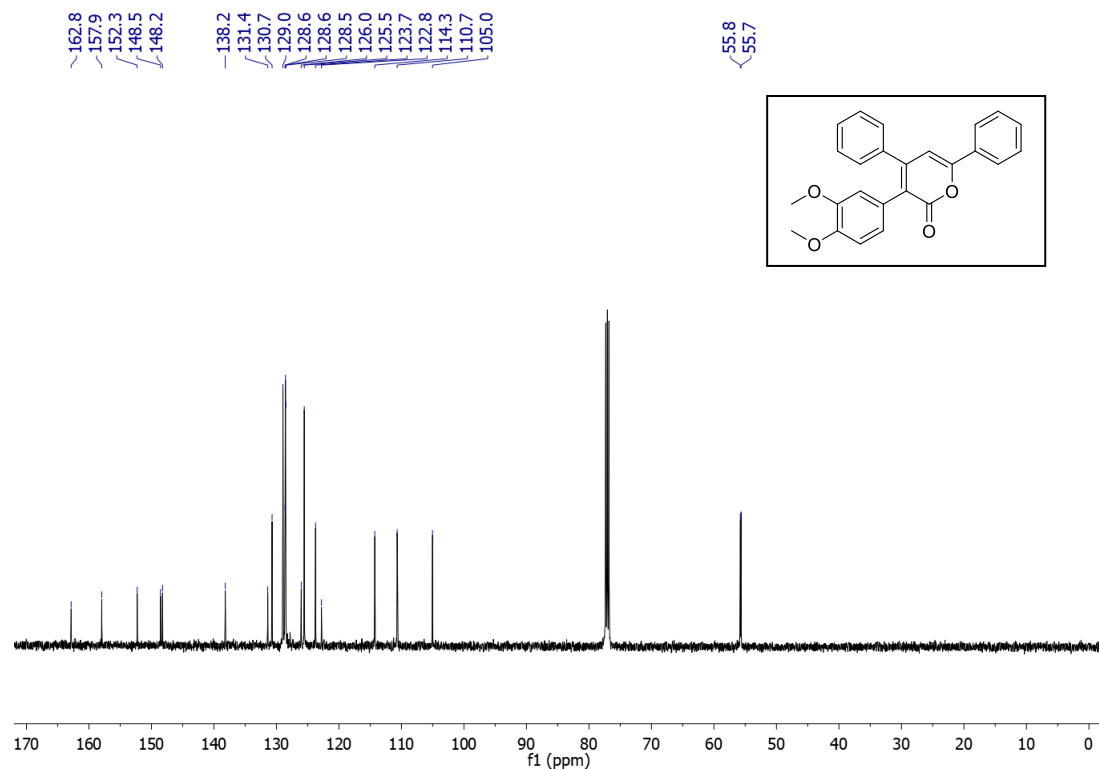
¹H NMR (500 MHz, CDCl₃) of compound **3a³**



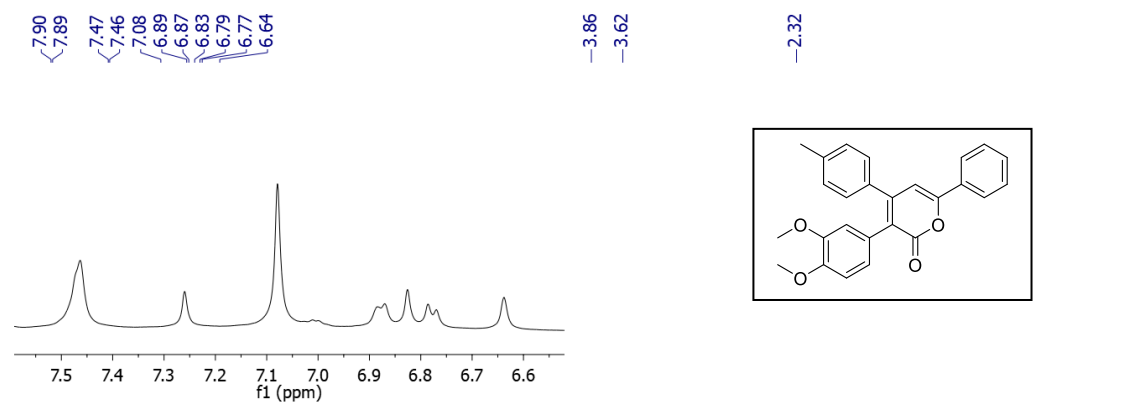
¹³C NMR (125 MHz, CDCl₃) of compound **3a³**



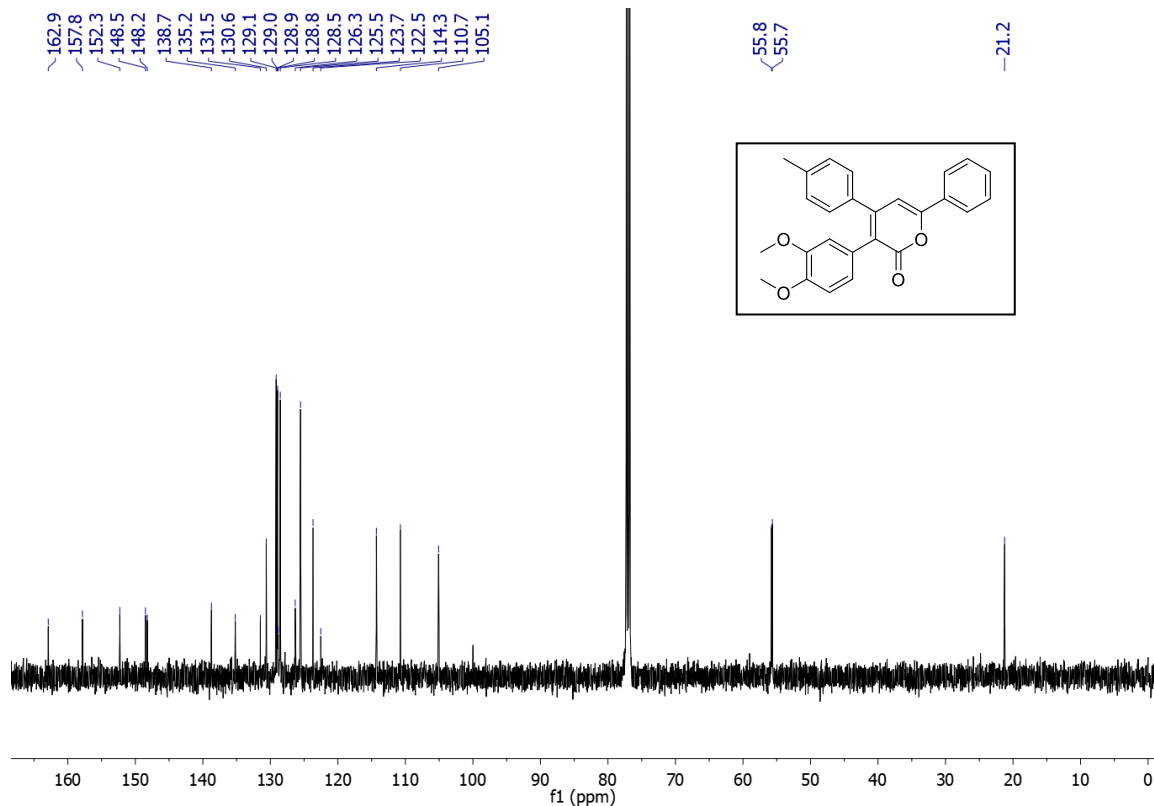
¹H NMR (500 MHz, CDCl₃) of compound **3b**



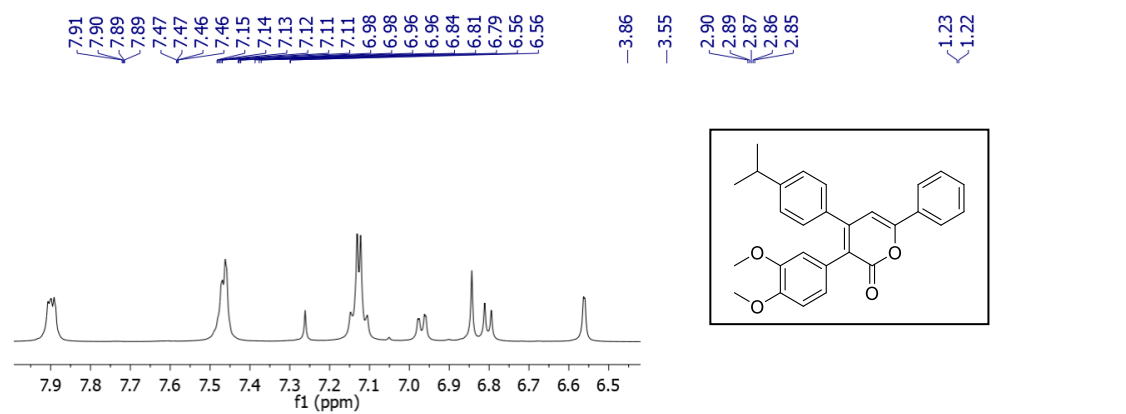
¹³C NMR (125 MHz, CDCl₃) of compound **3b**



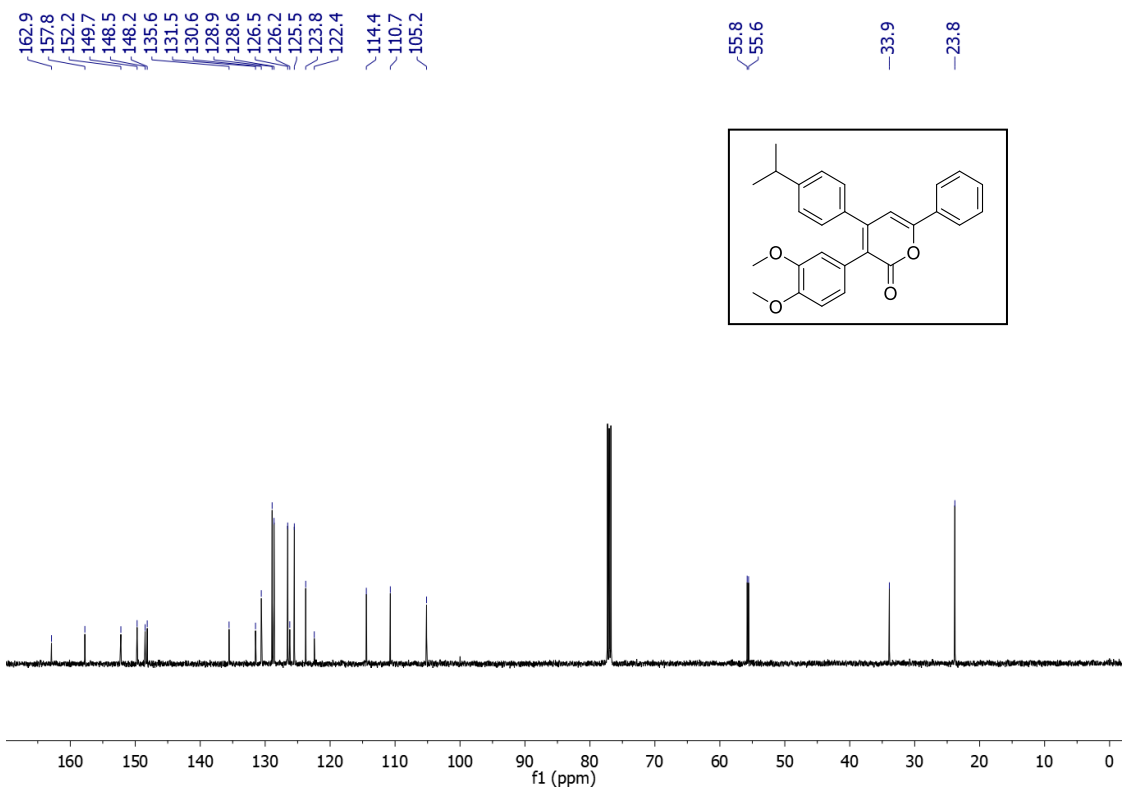
¹H NMR (500 MHz, CDCl₃) of compound **3c**



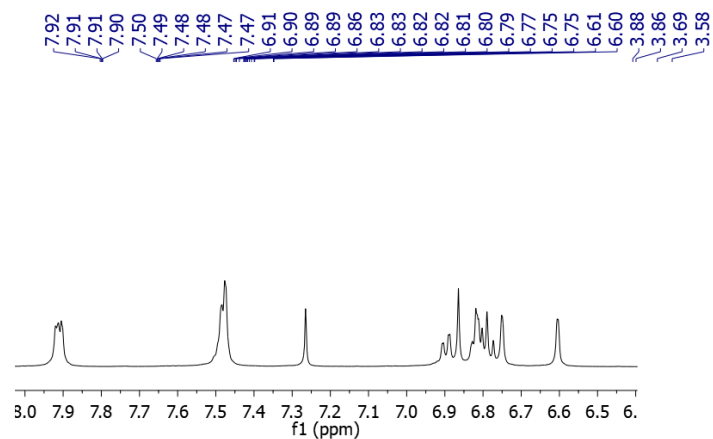
¹³C NMR (125 MHz, CDCl₃) of compound **3c**



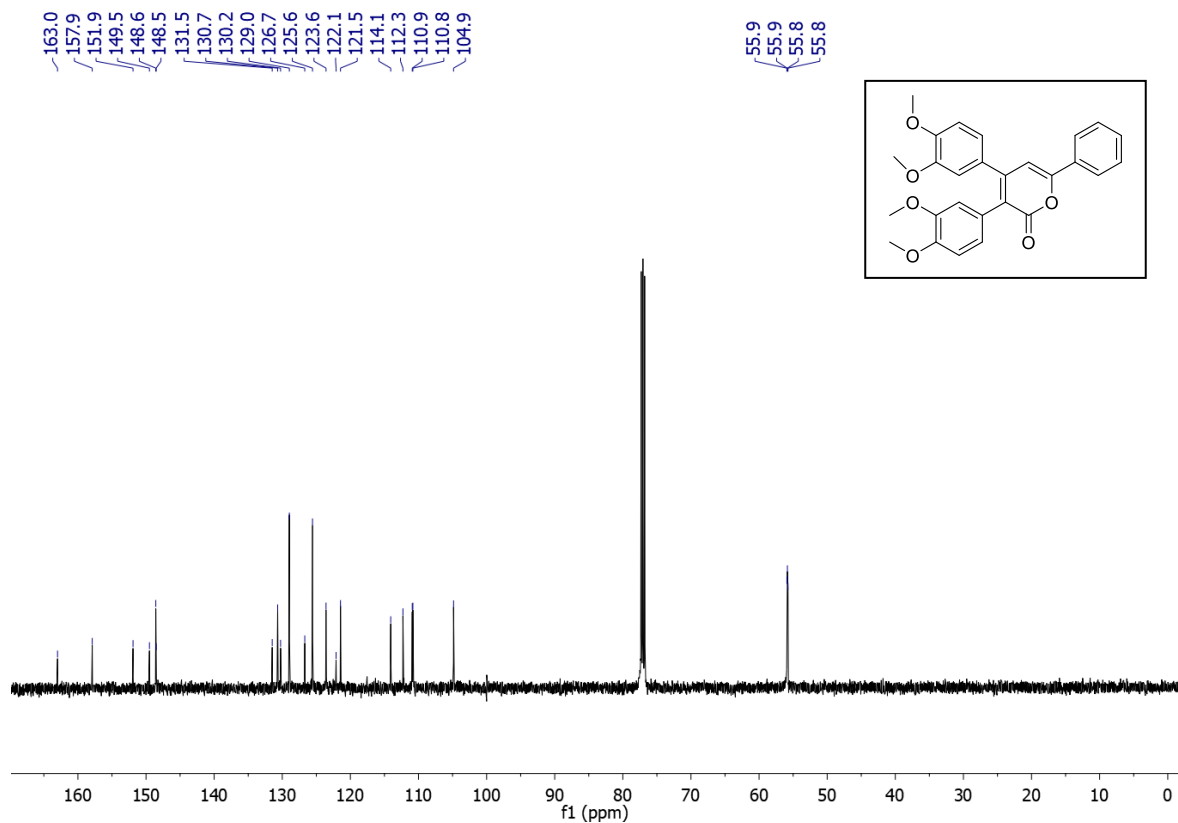
¹H NMR (500 MHz, CDCl₃) of compound **3d**



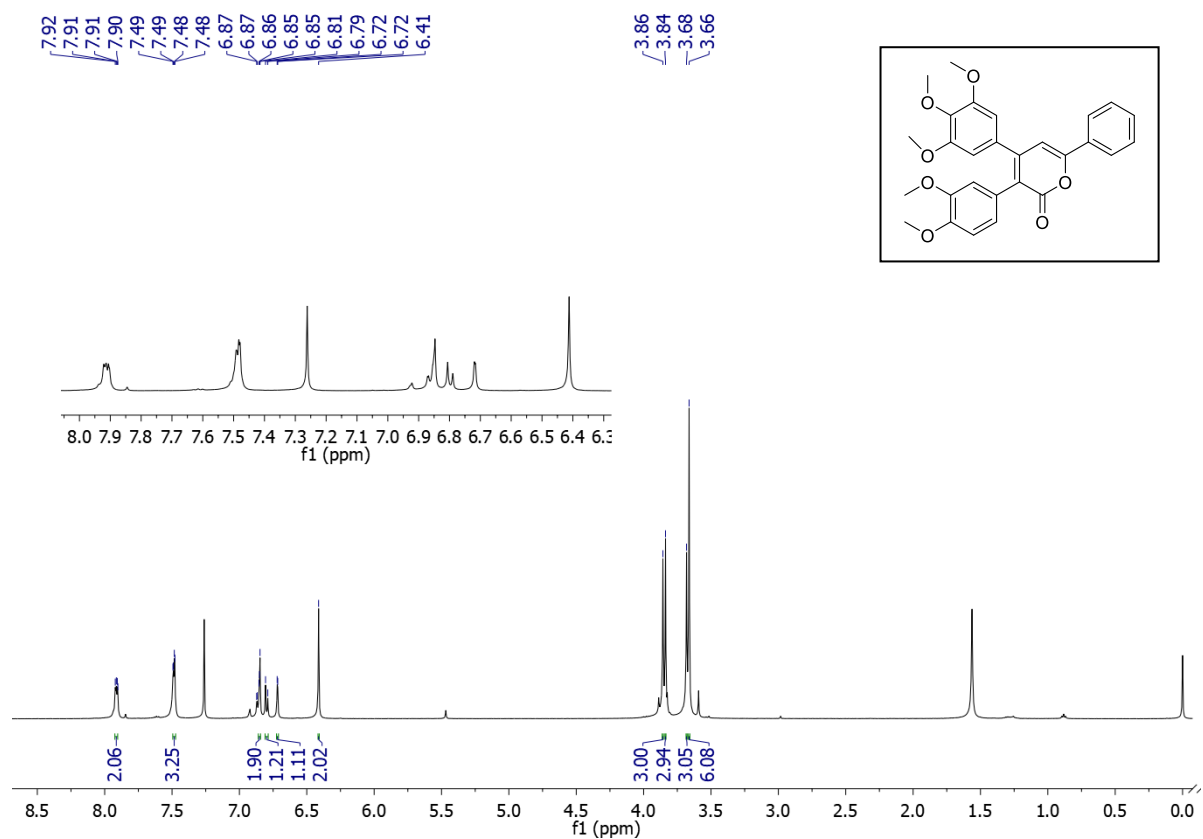
¹³C NMR (125 MHz, CDCl₃) of compound **3d**



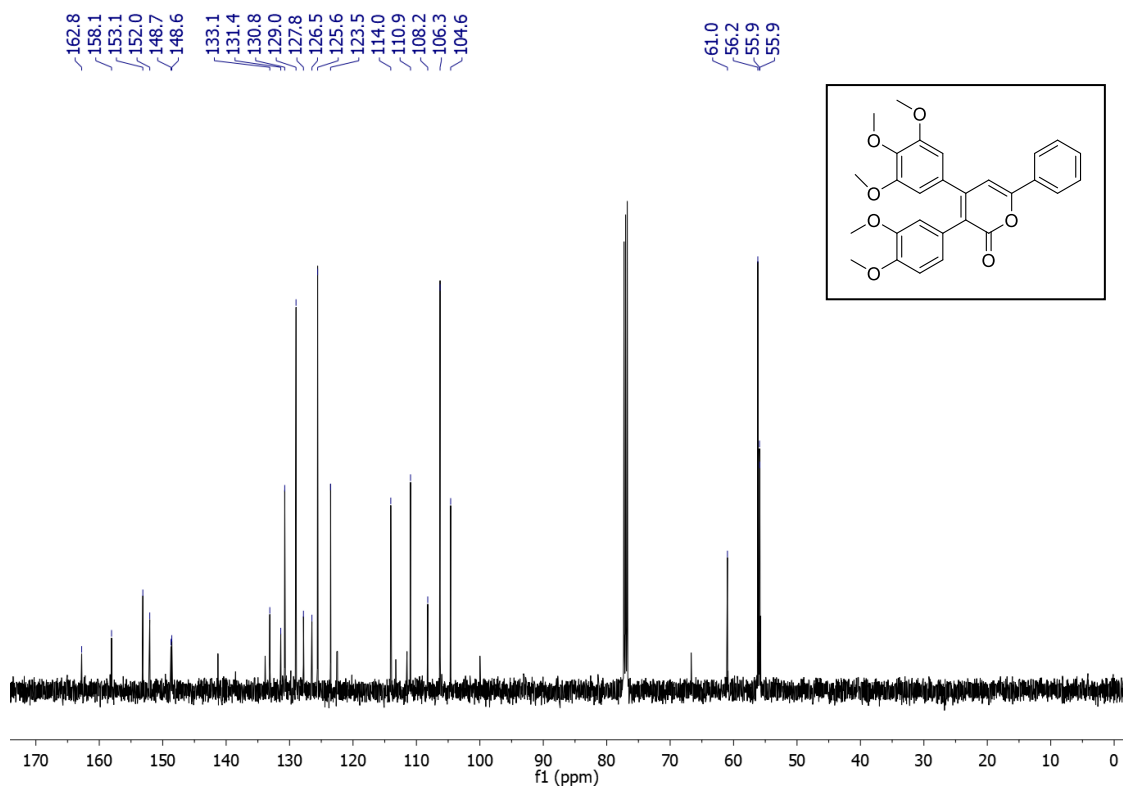
¹H NMR (500 MHz, CDCl₃) of compound **3f**



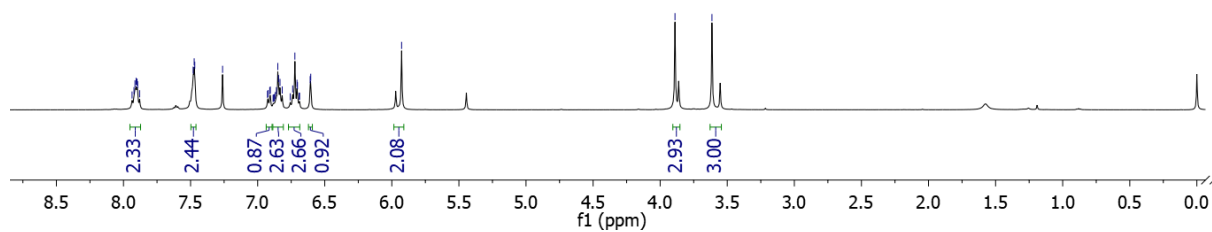
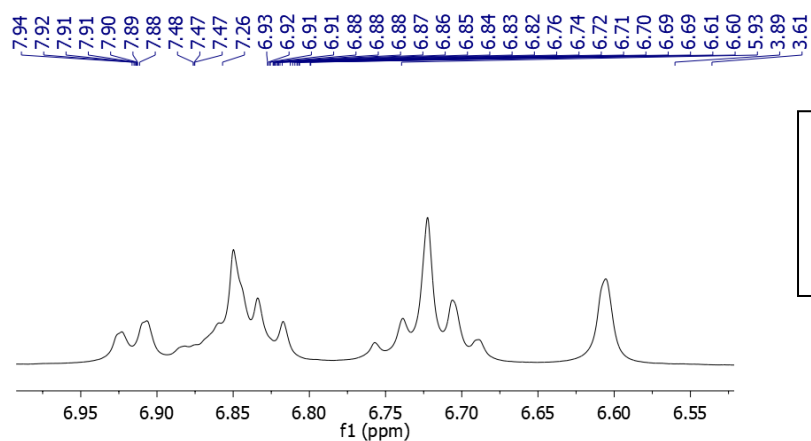
¹³C NMR (125 MHz, CDCl₃) of compound **3f**



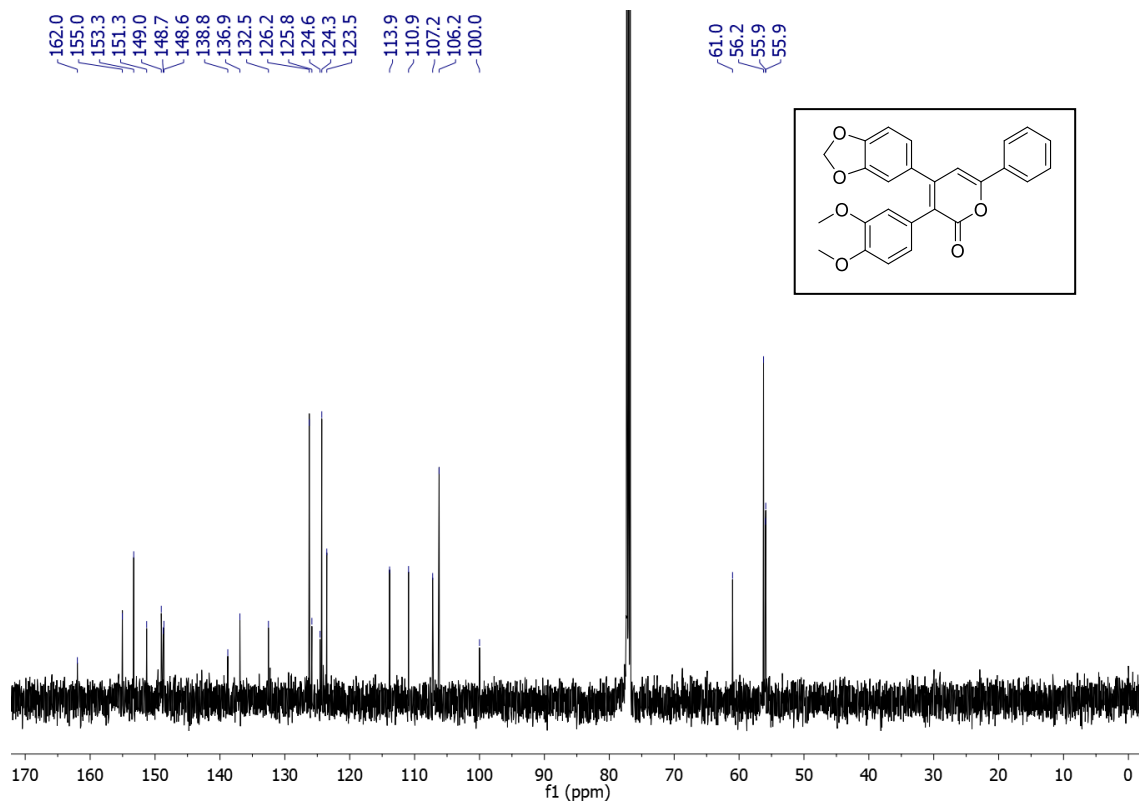
¹H NMR (500 MHz, CDCl₃) of compound **3g**



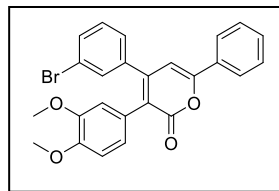
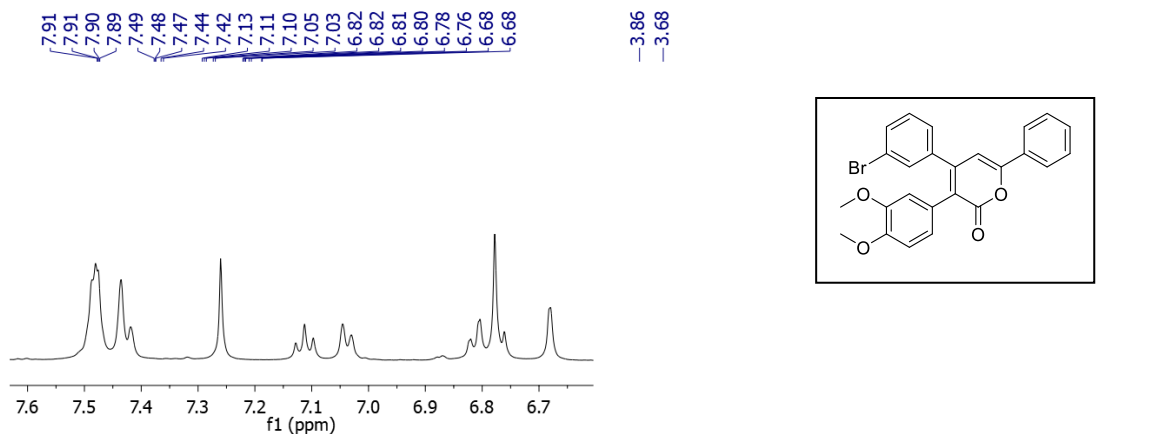
¹³C NMR (125 MHz, CDCl₃) of compound **3g**



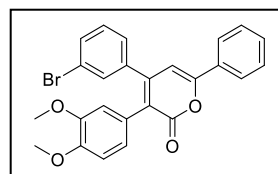
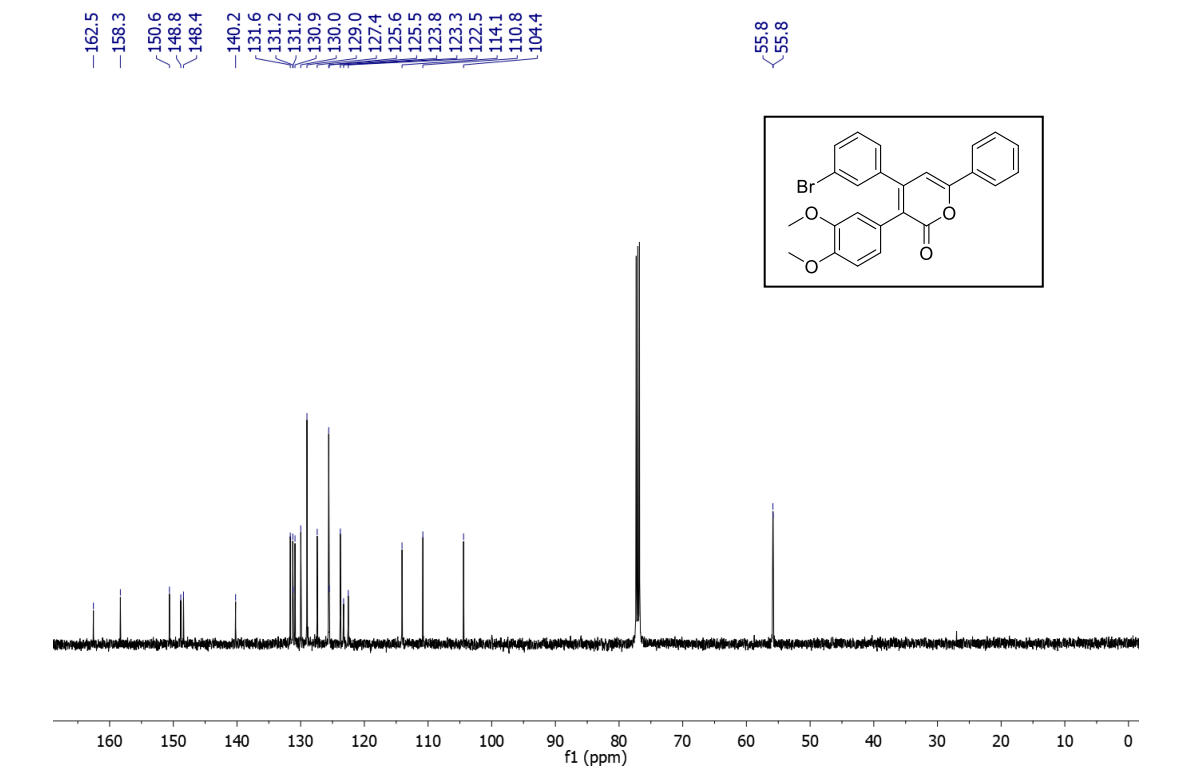
¹H NMR (500 MHz, CDCl₃) of compound **3h**



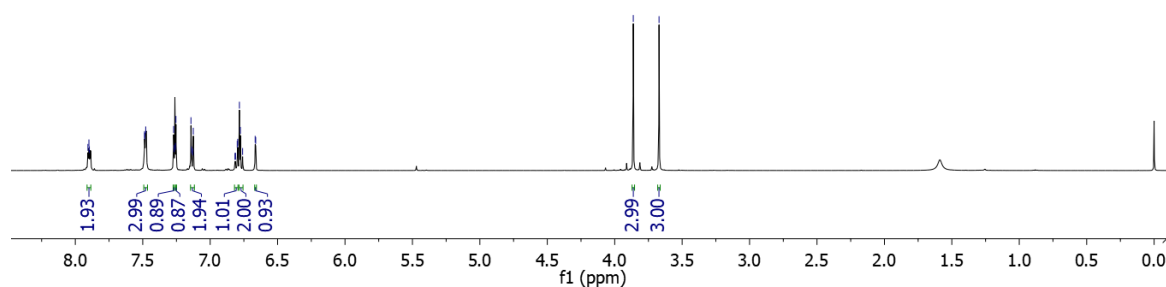
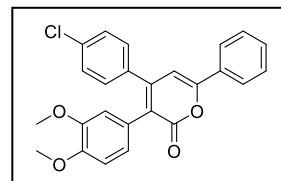
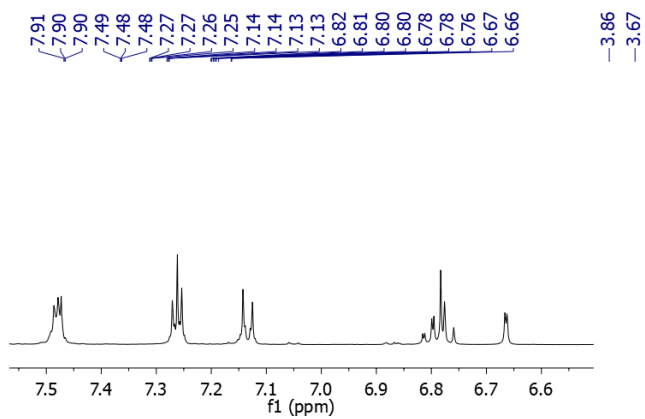
¹³C NMR (125 MHz, CDCl₃) of compound **3h**



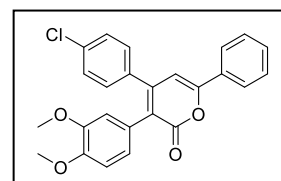
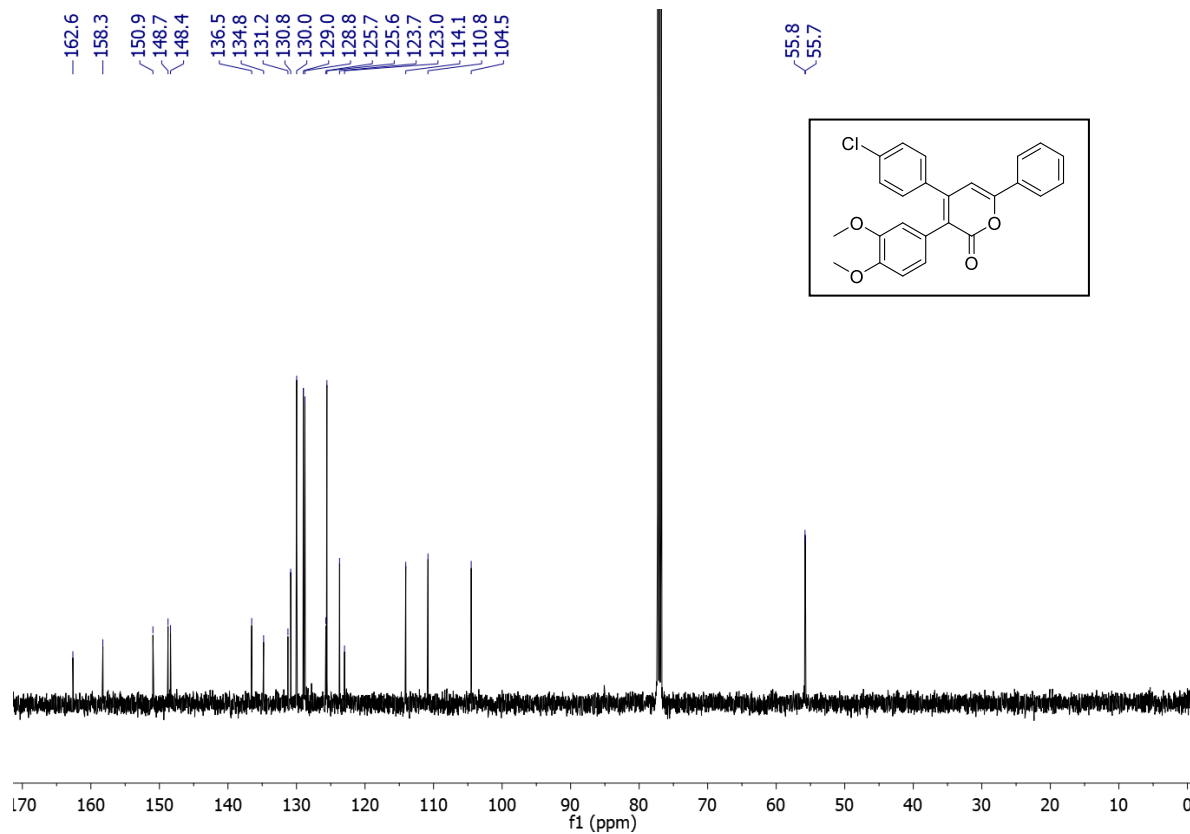
¹H NMR (500 MHz, CDCl₃) of compound **3i**



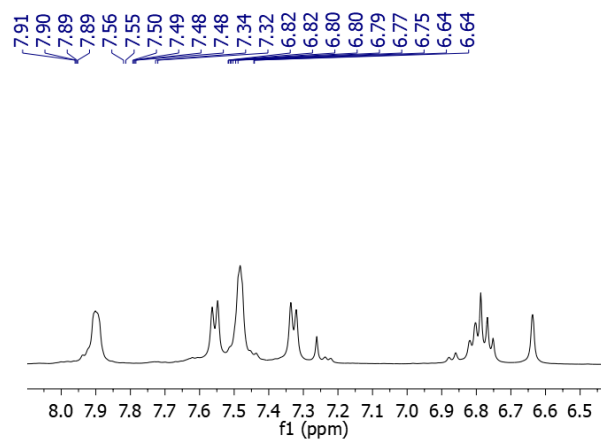
¹³C NMR (125 MHz, CDCl₃) of compound **3i**



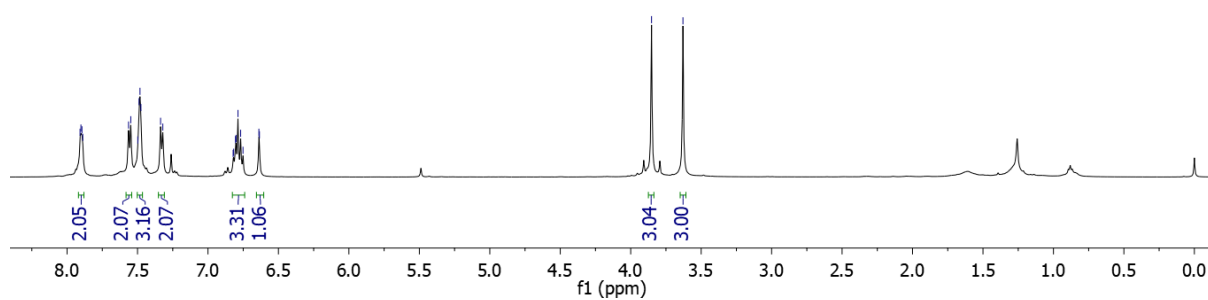
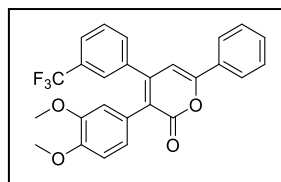
^1H NMR (500 MHz, CDCl_3) of compound **3j**



^{13}C NMR (125 MHz, CDCl_3) of compound **3j**



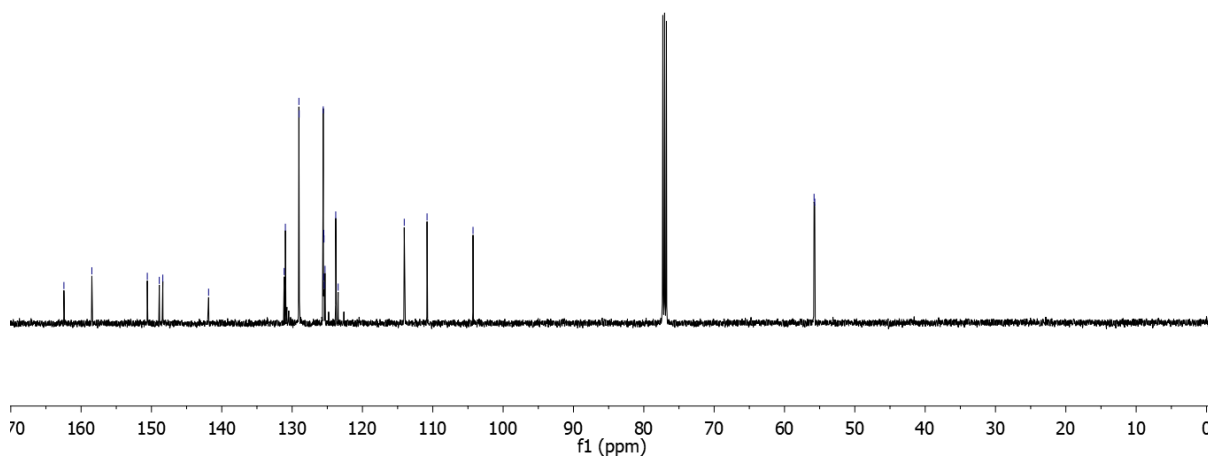
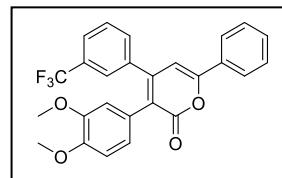
3.85
3.63



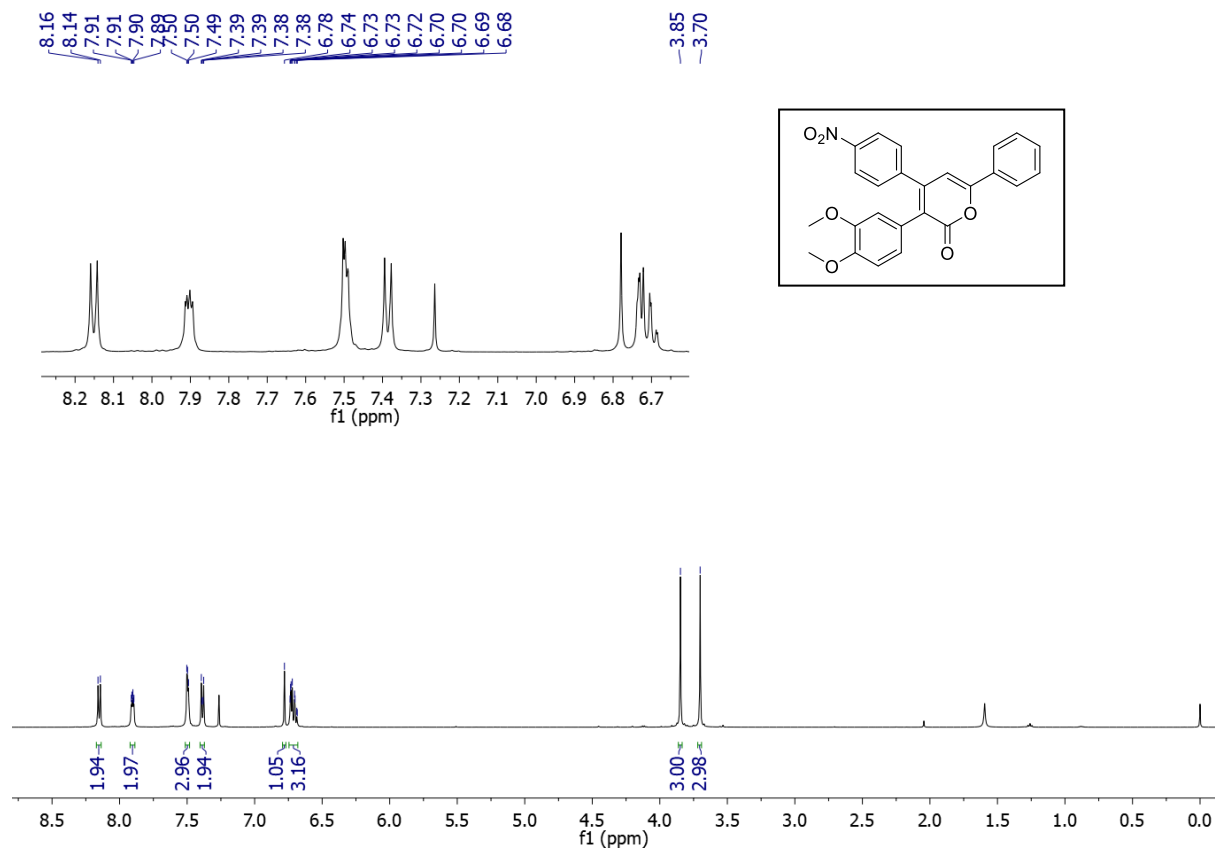
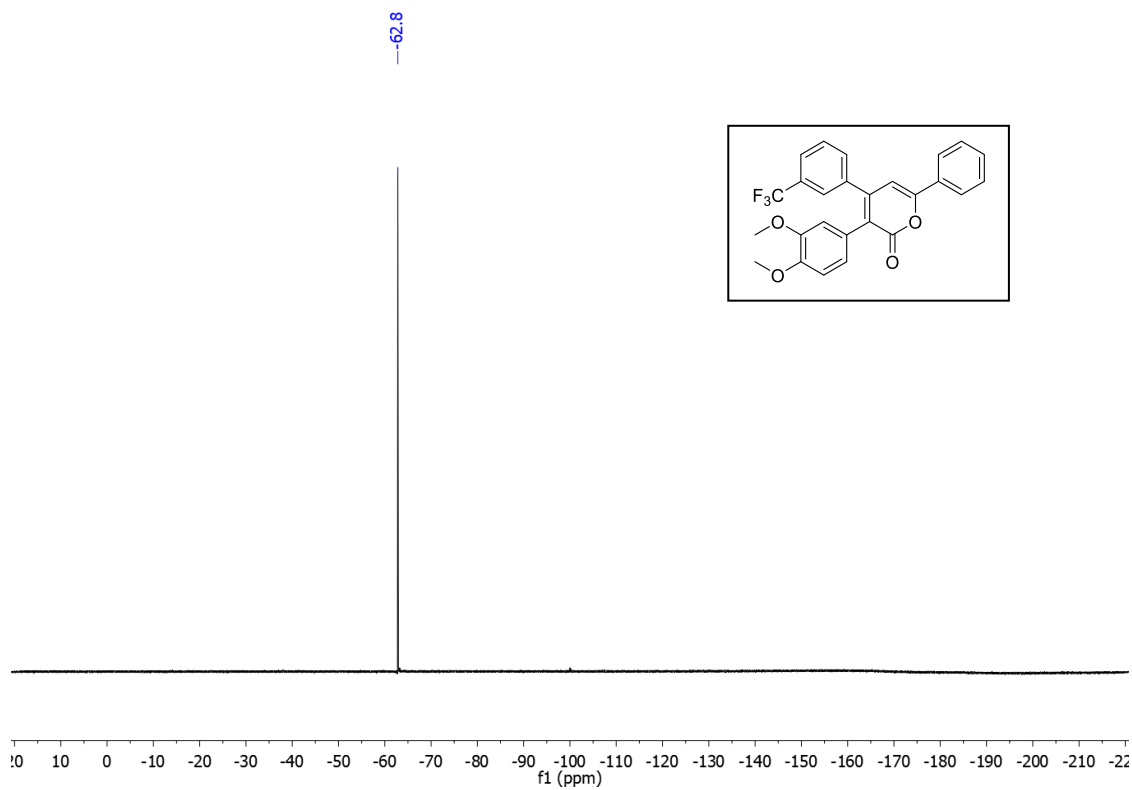
¹H NMR (500 MHz, CDCl₃) of compound **3k**

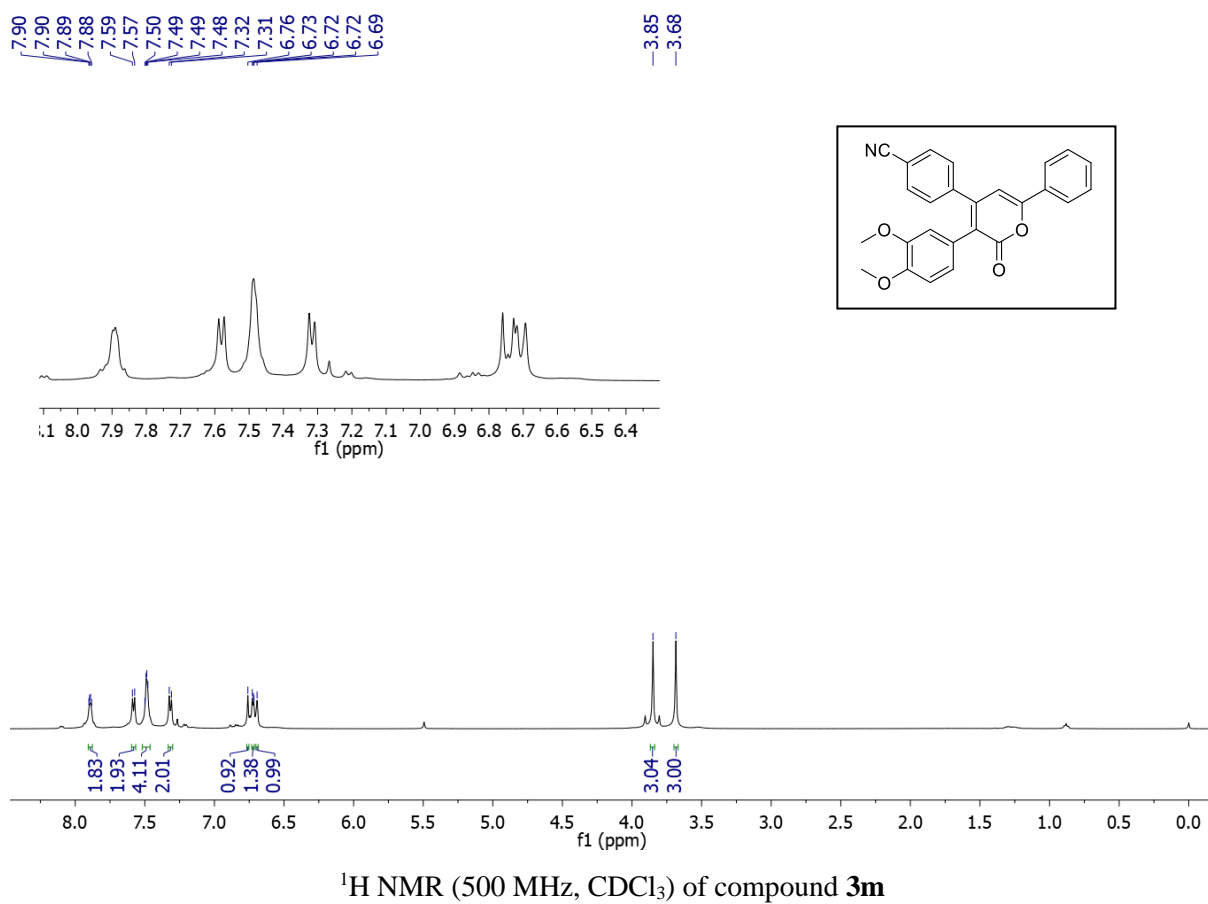
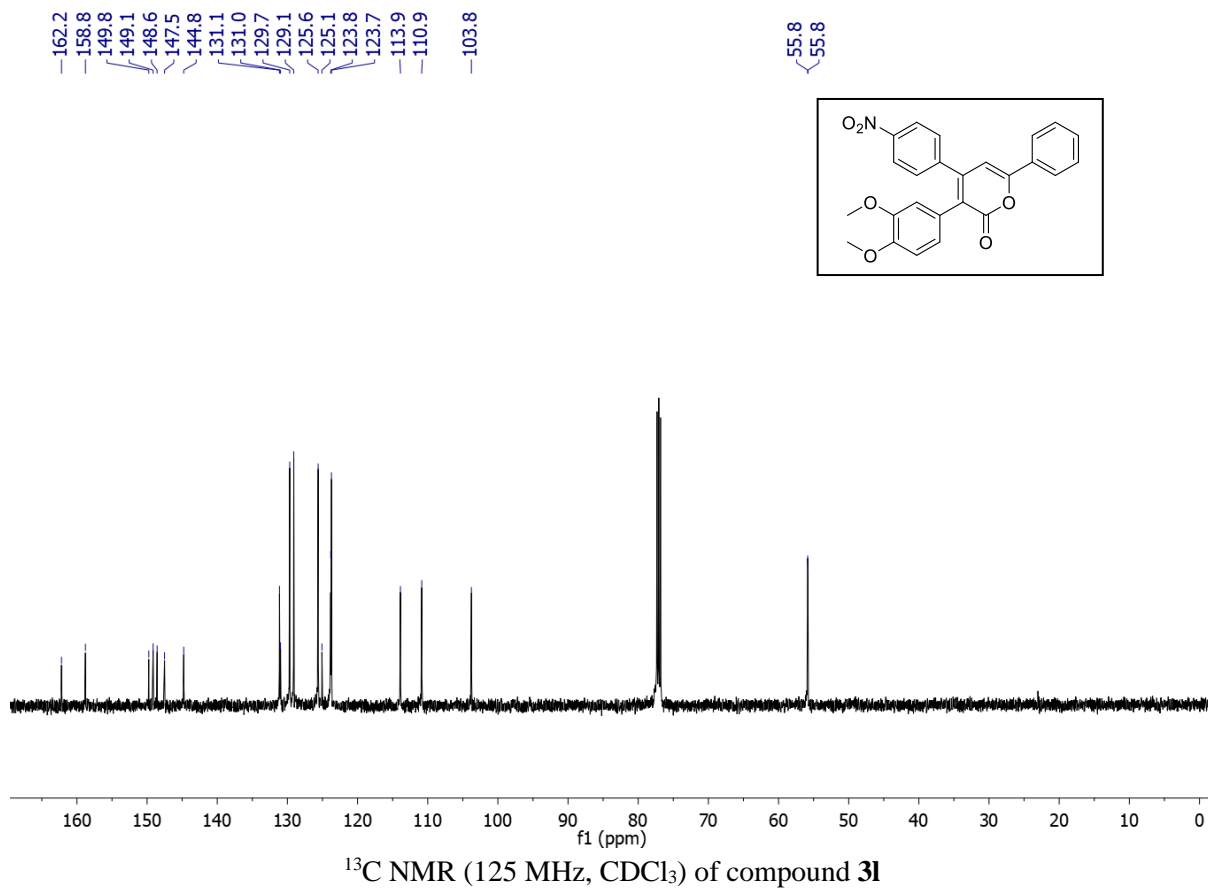
162.4
158.5
150.6
148.9
148.4
141.9
131.1
131.0
129.0
129.0
125.6
125.5
125.5
125.5
125.4
125.3
123.8
123.5
114.1
110.8
104.3

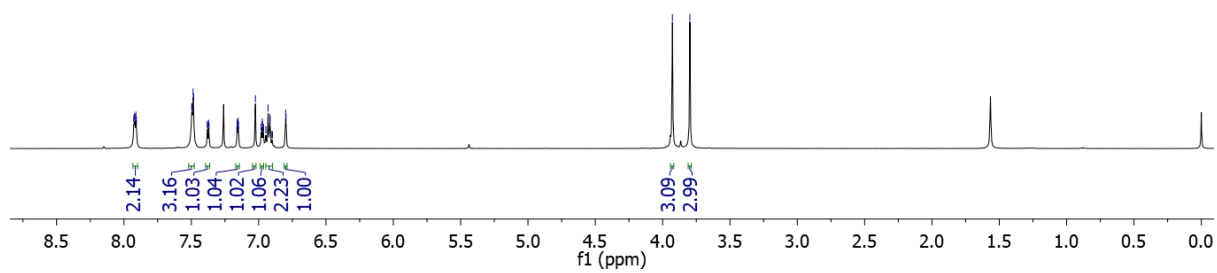
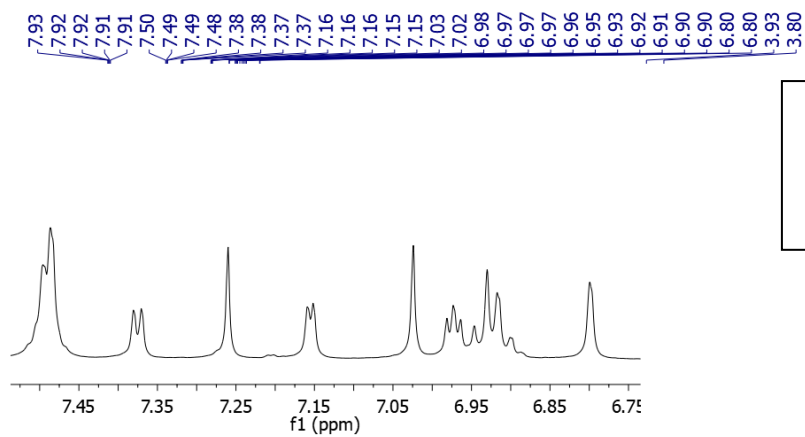
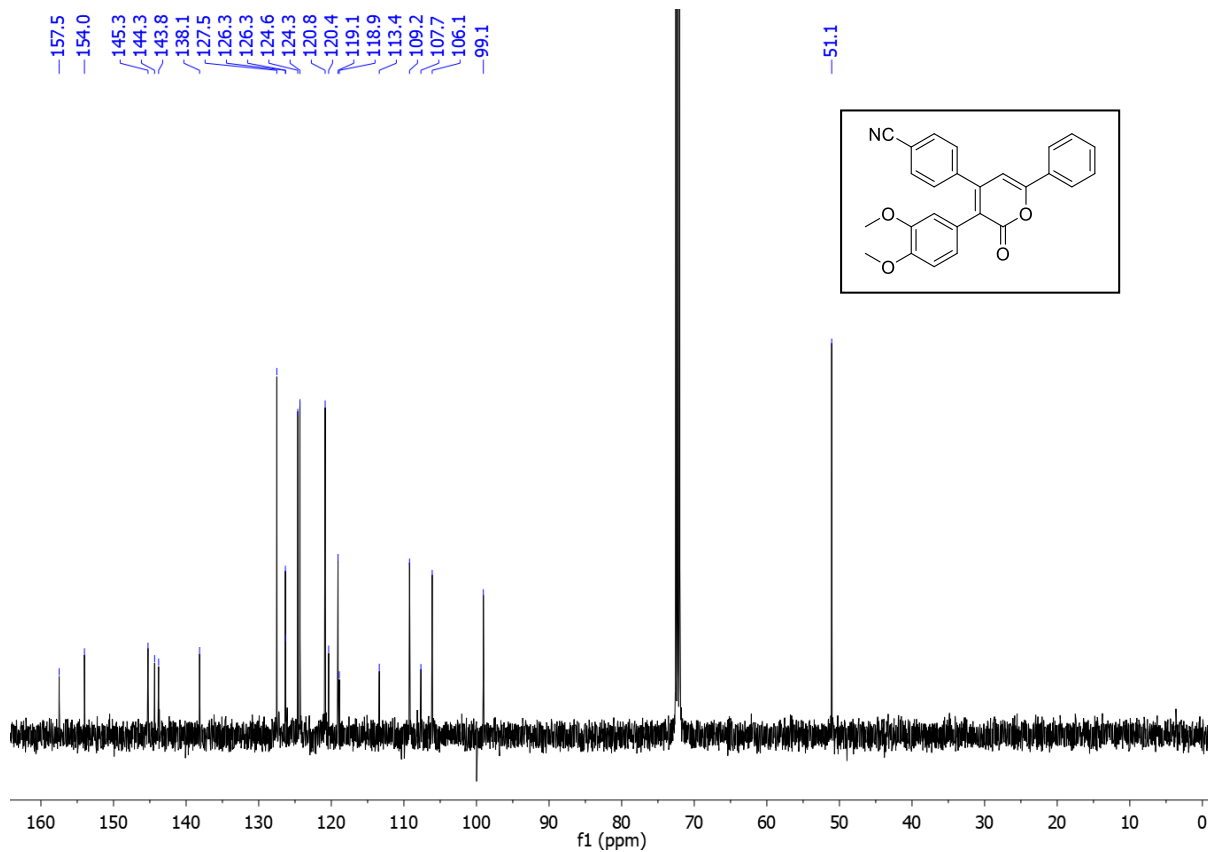
55.8
55.7

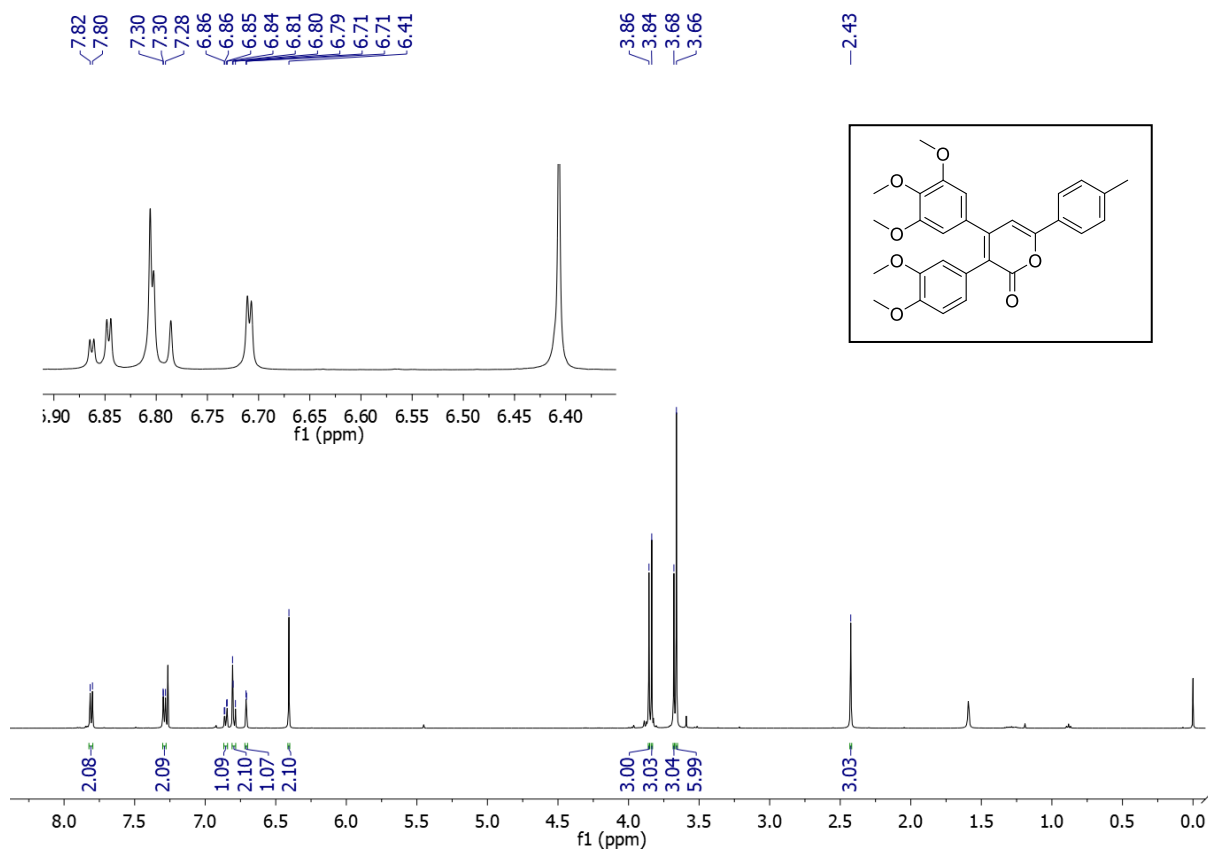
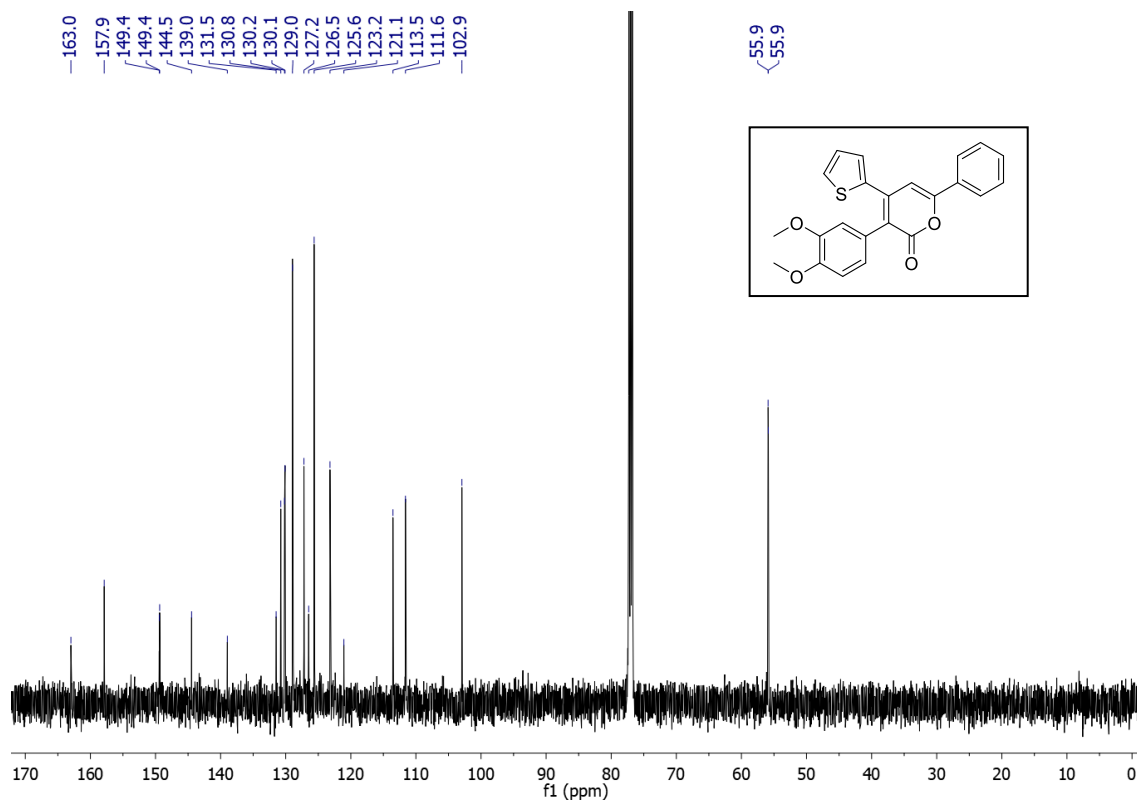


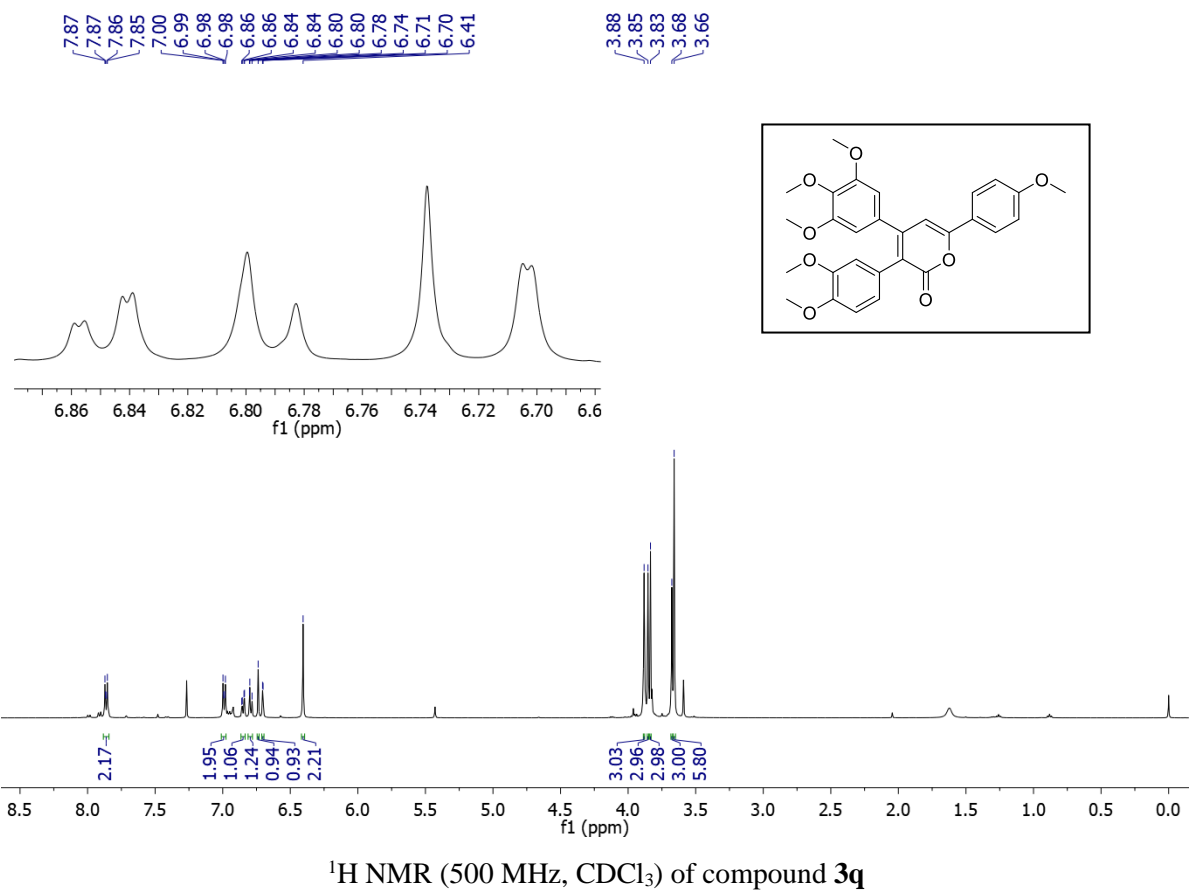
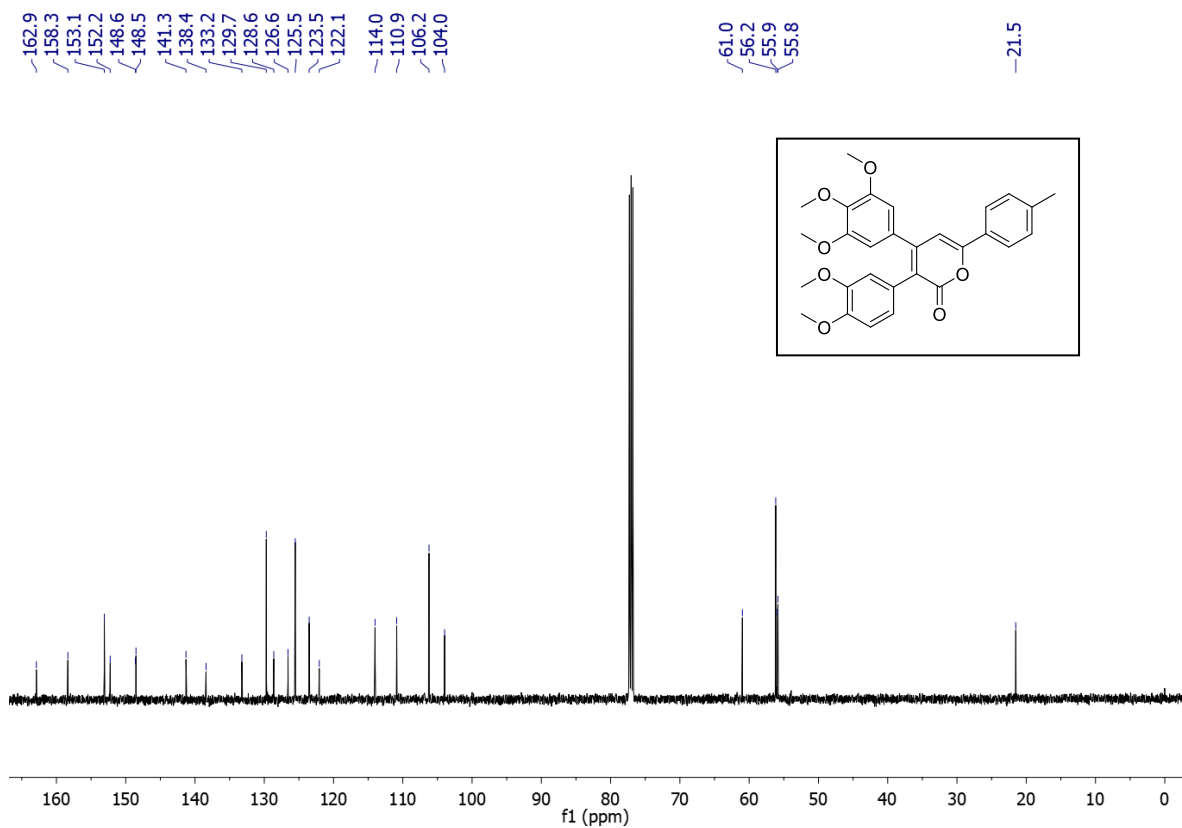
¹³C NMR (125 MHz, CDCl₃) of compound **3k**

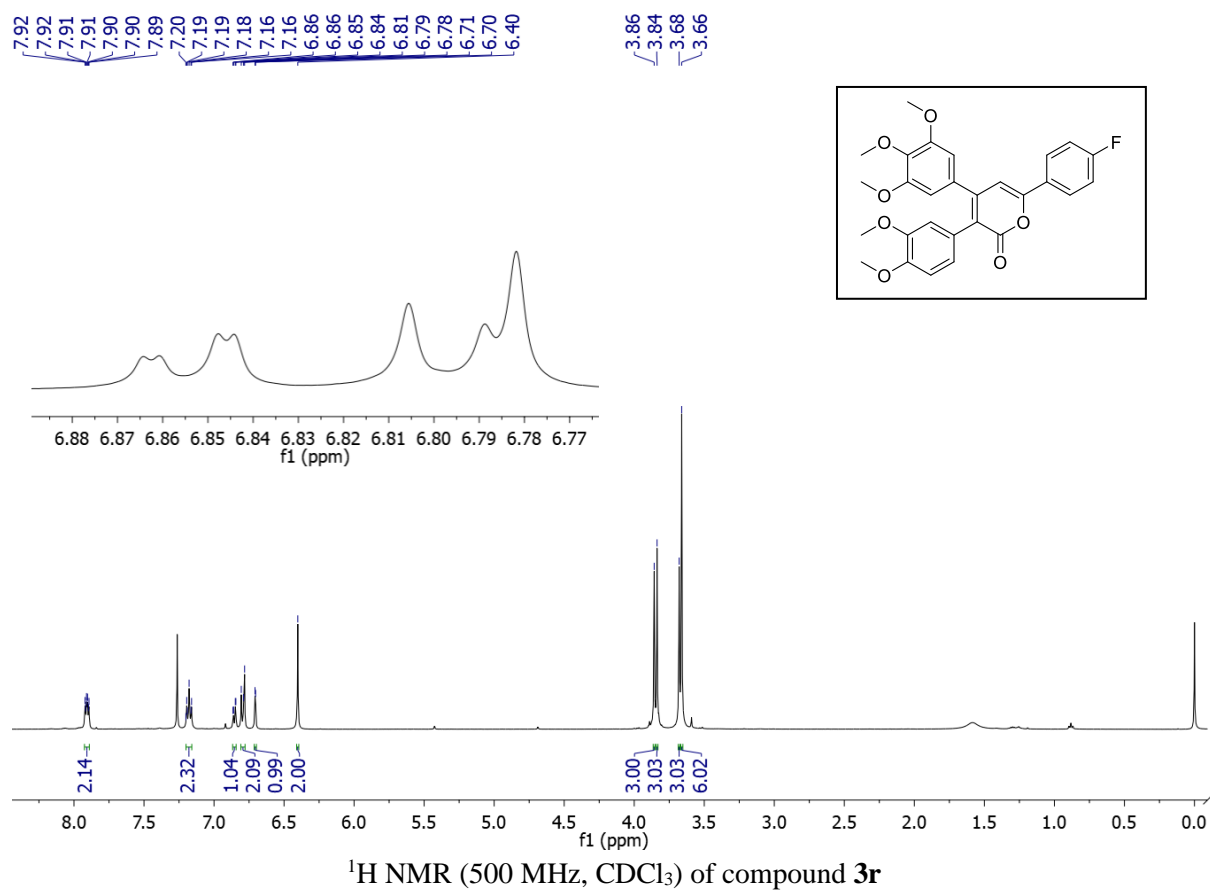
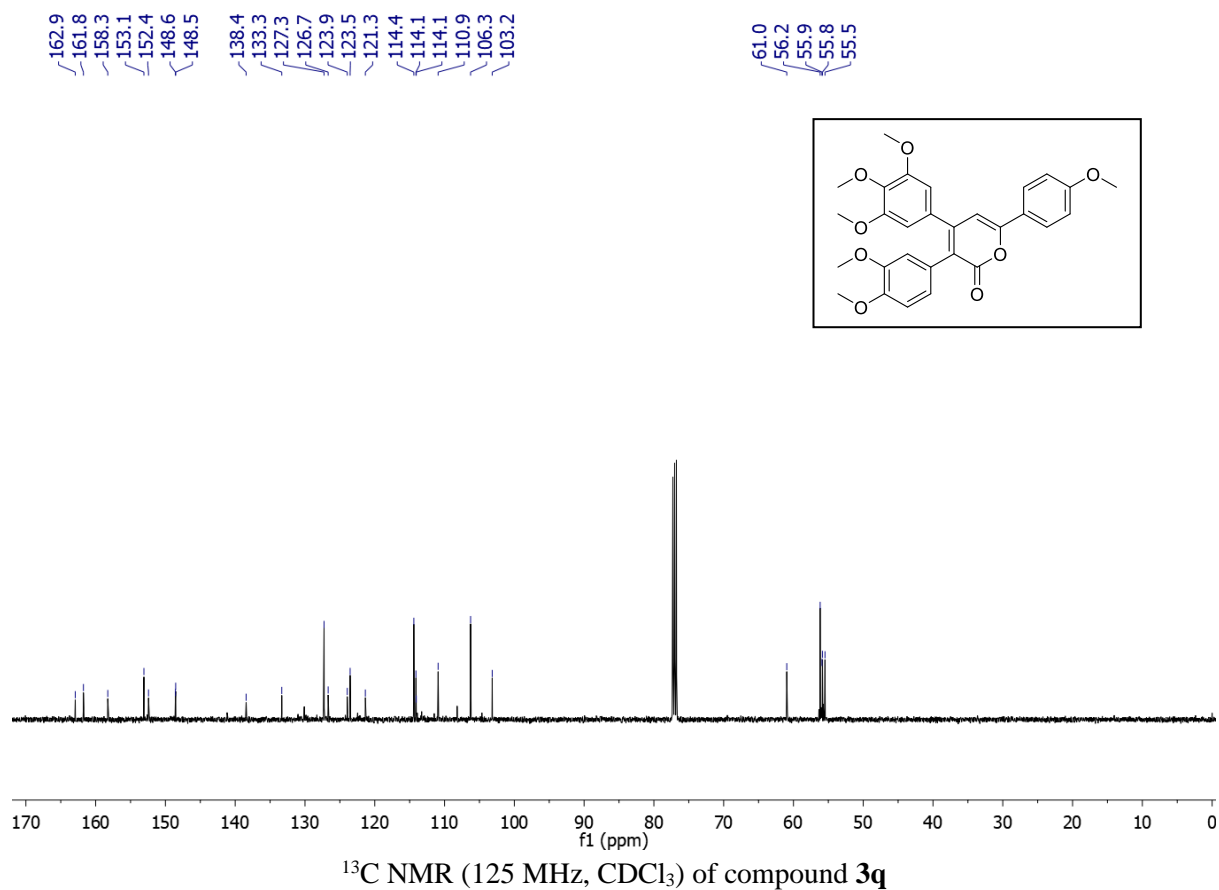






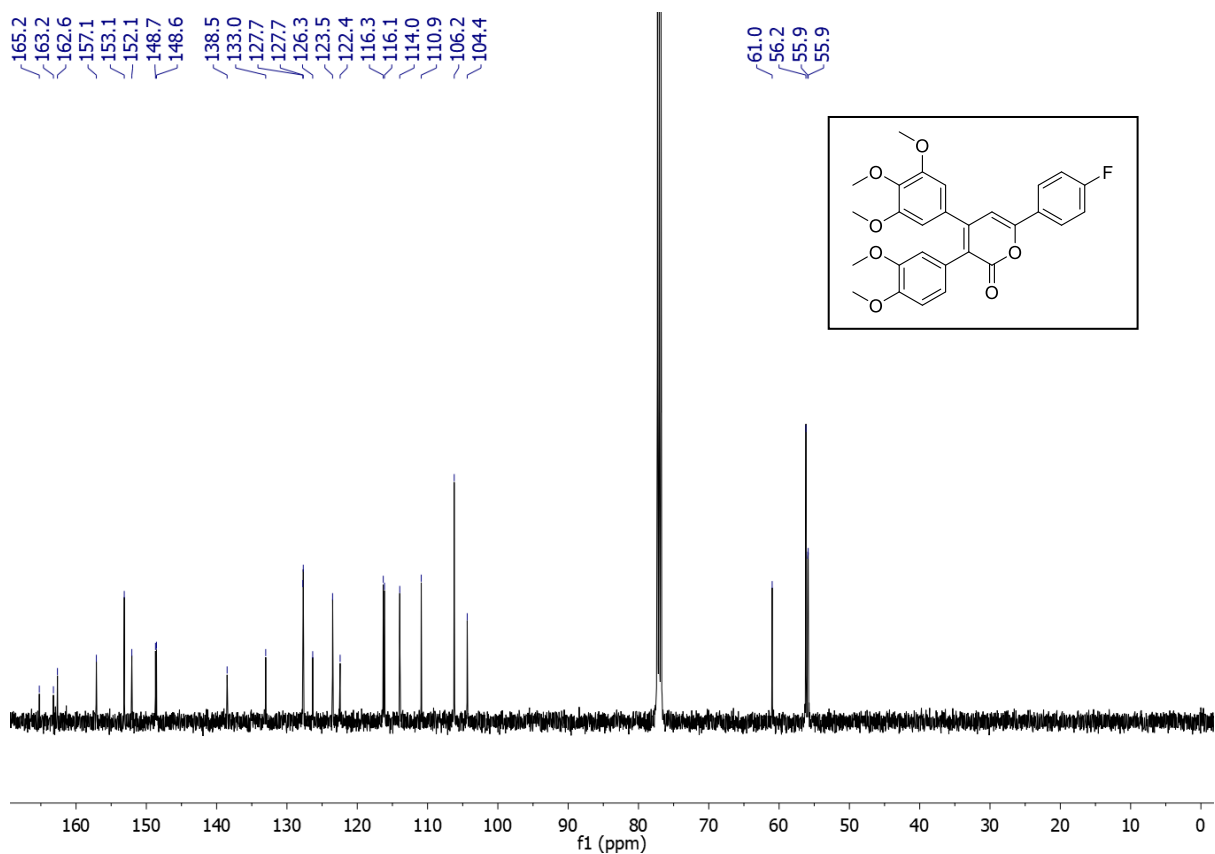
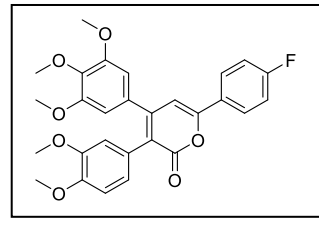






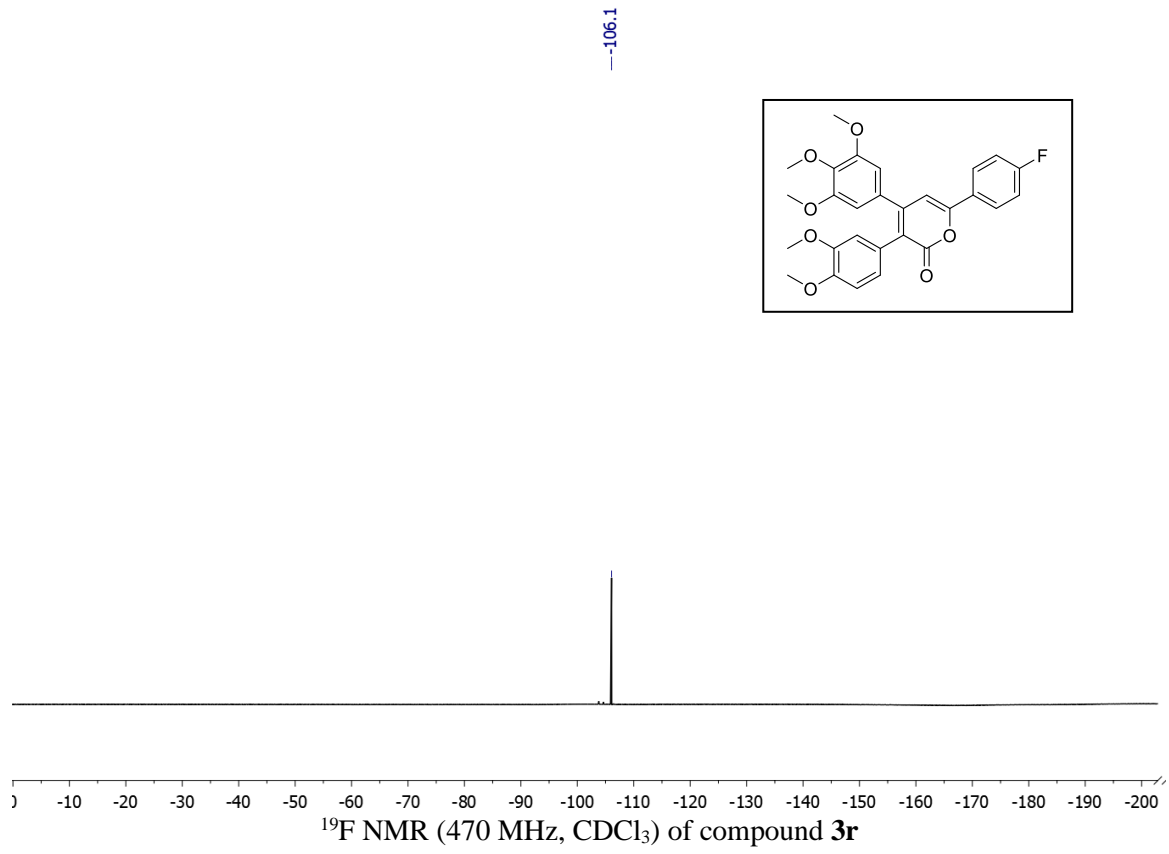
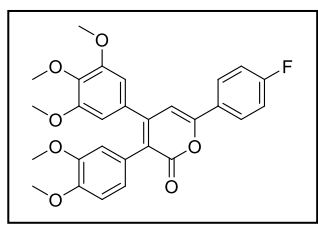
165.2
163.2
162.6
157.1
153.1
152.1
148.7
148.6
138.5
133.0
127.7
127.7
126.3
123.5
122.4
116.3
116.1
114.0
110.9
106.2
104.4

61.0
56.2
55.9
55.9

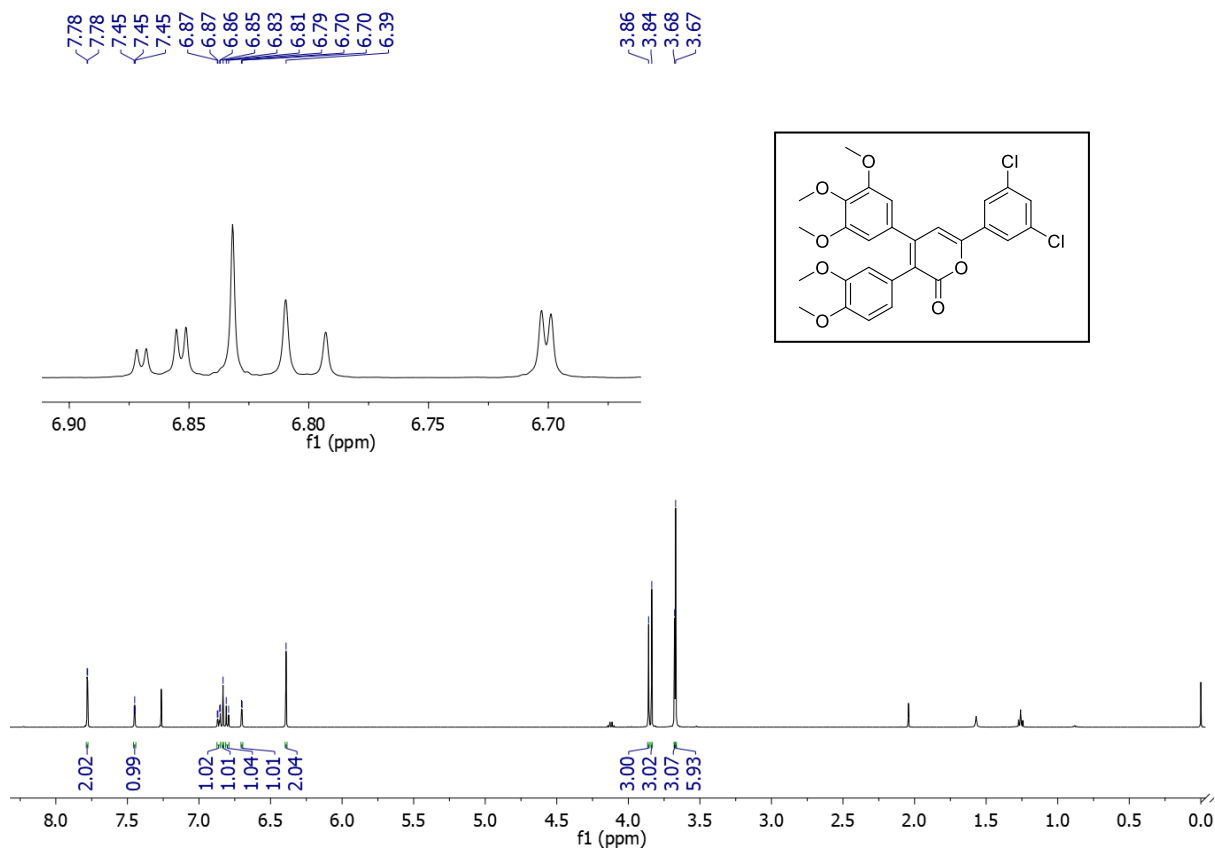


^{13}C NMR (125 MHz, CDCl_3) of compound **3r**

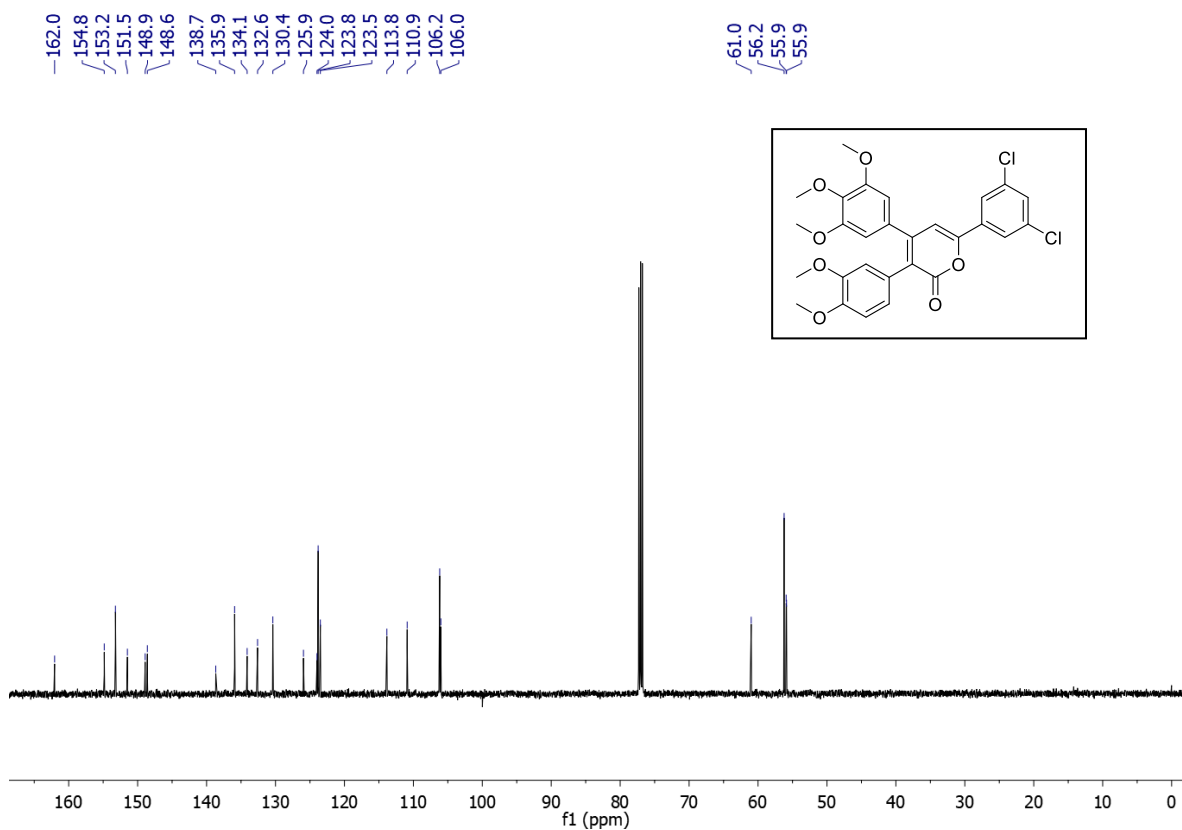
-106.1



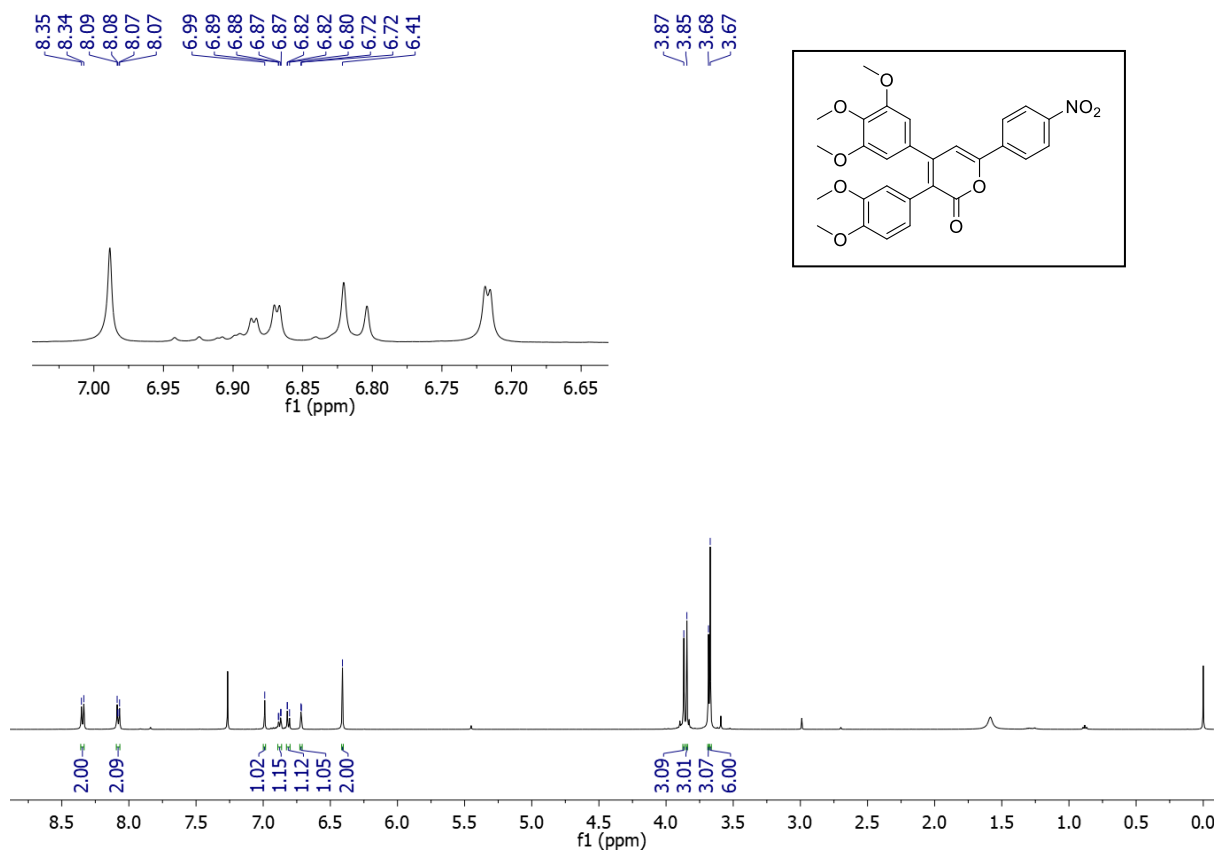
^{19}F NMR (470 MHz, CDCl_3) of compound **3r**



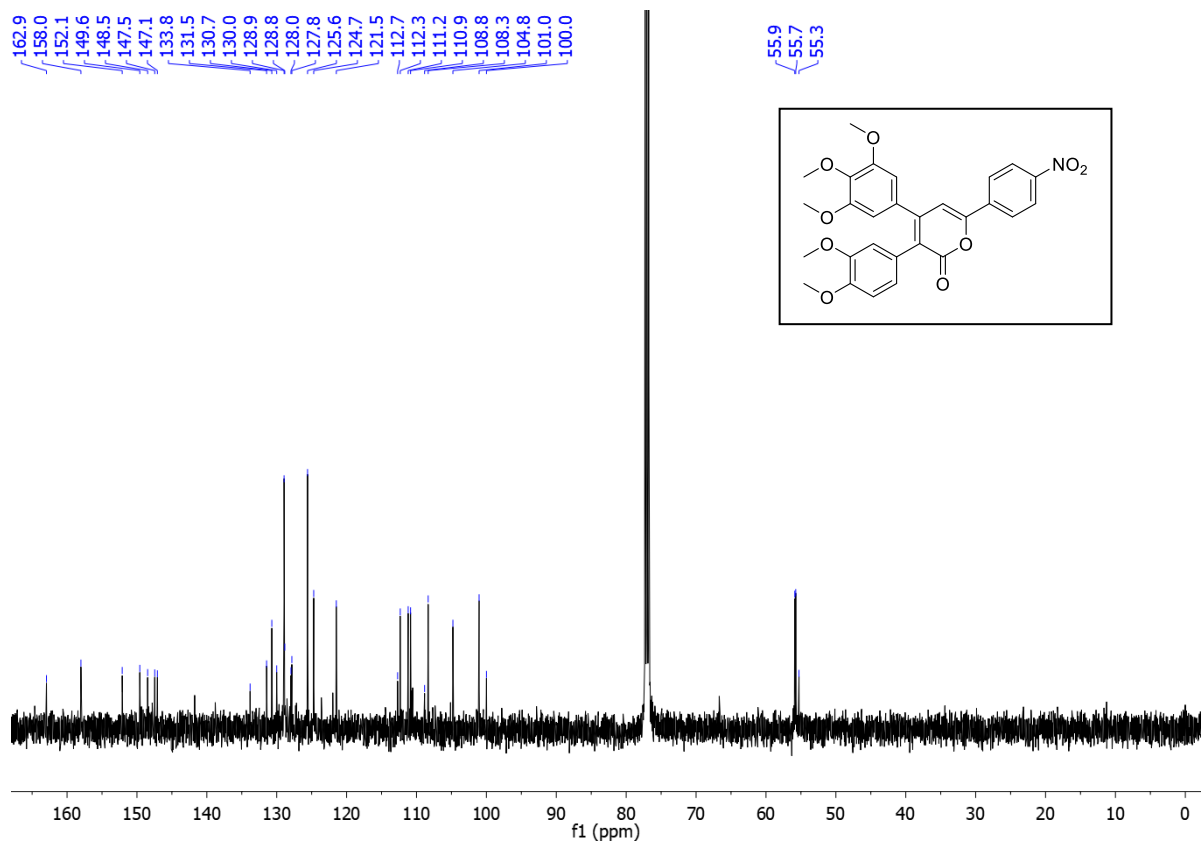
¹H NMR (500 MHz, CDCl₃) of compound **3s**



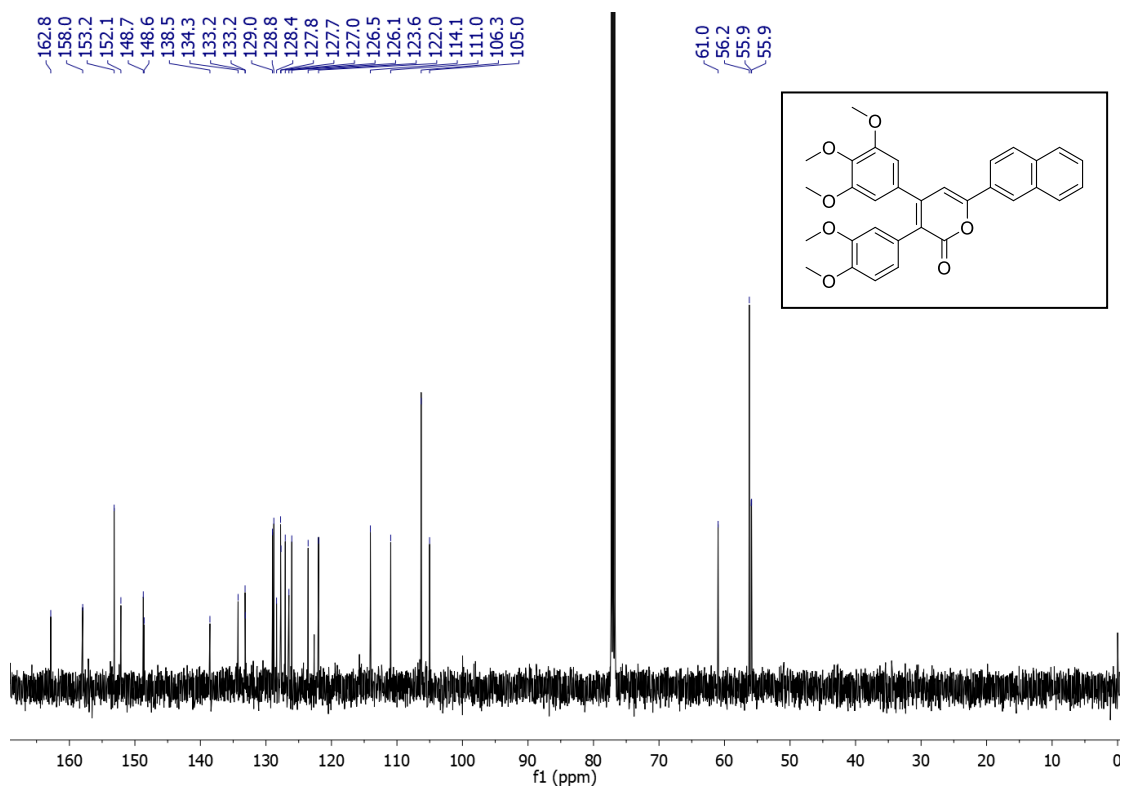
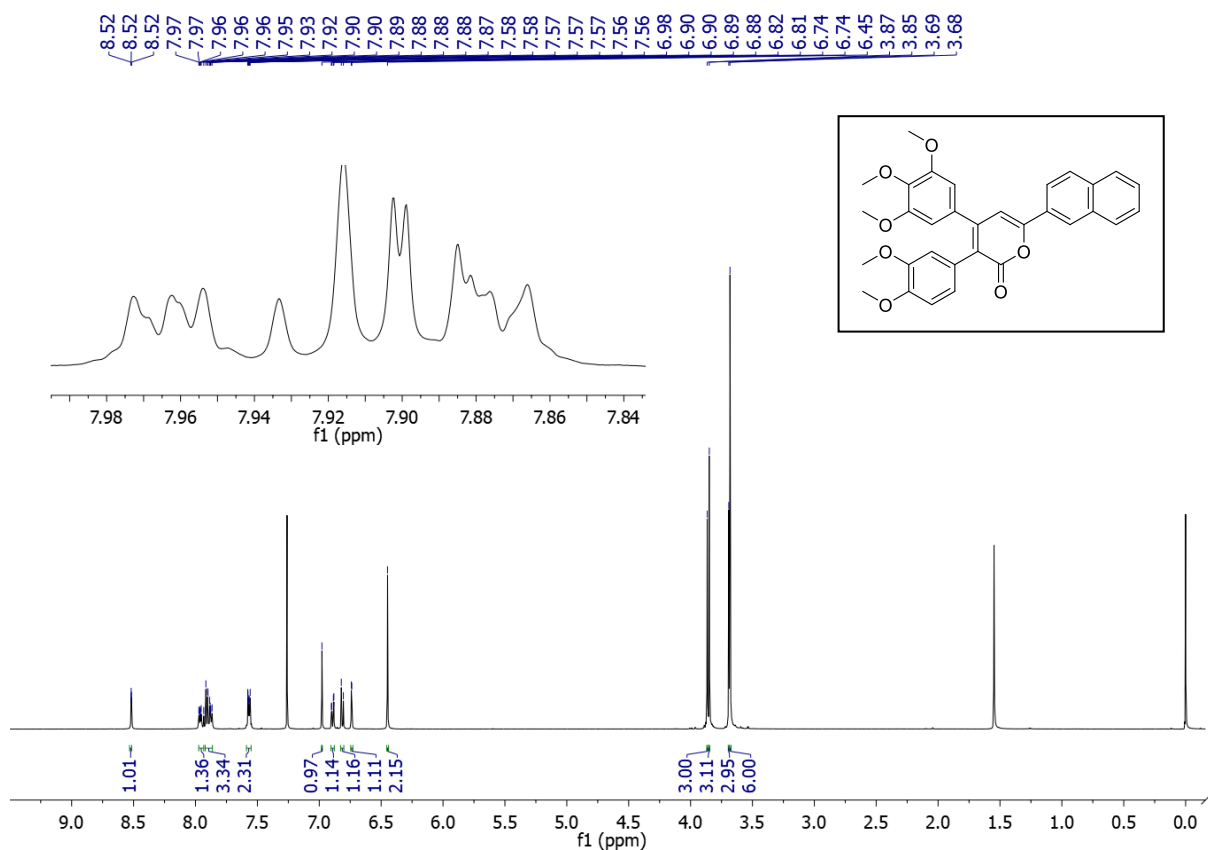
¹³C NMR (125 MHz, CDCl₃) of compound **3s**

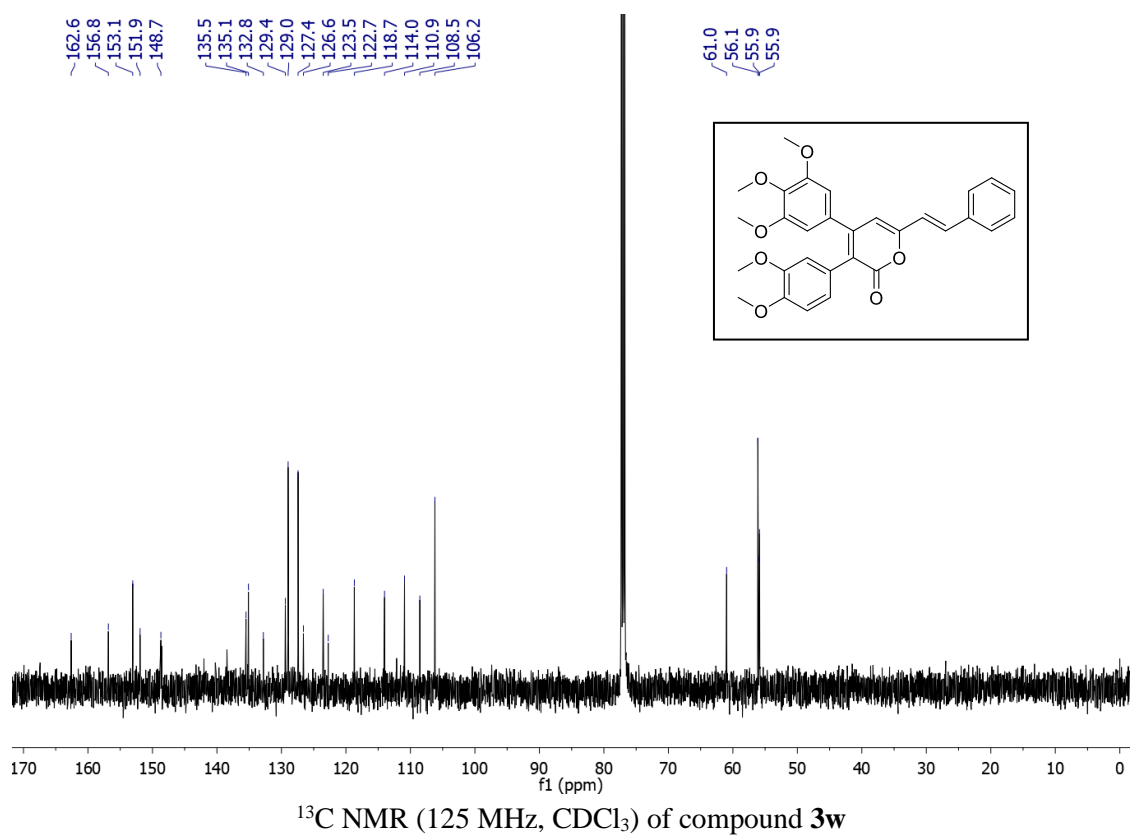
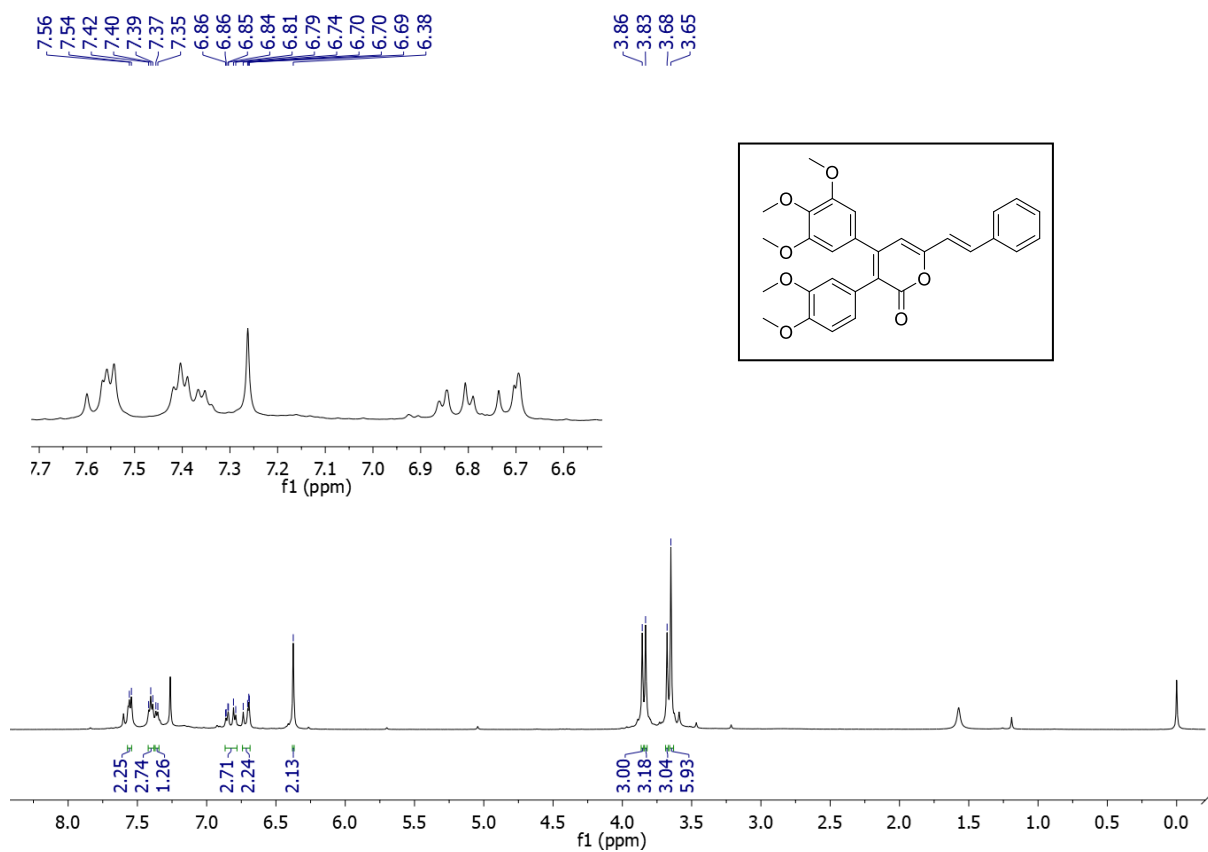


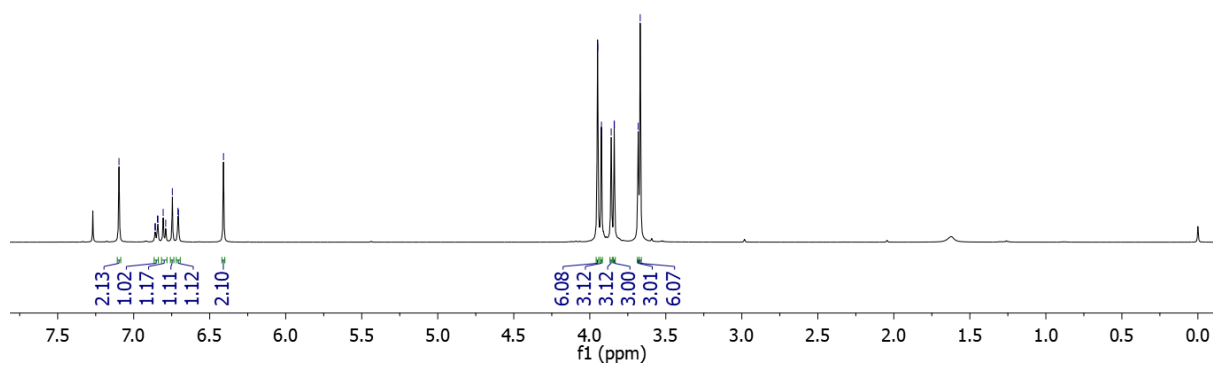
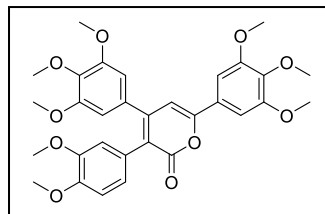
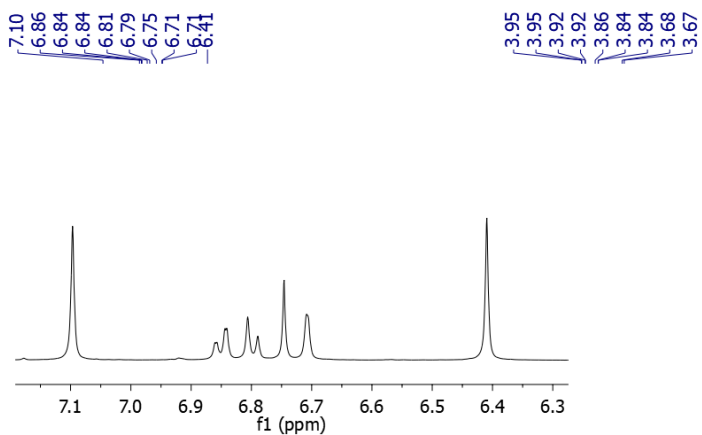
¹H NMR (500 MHz, CDCl₃) of compound **3t**



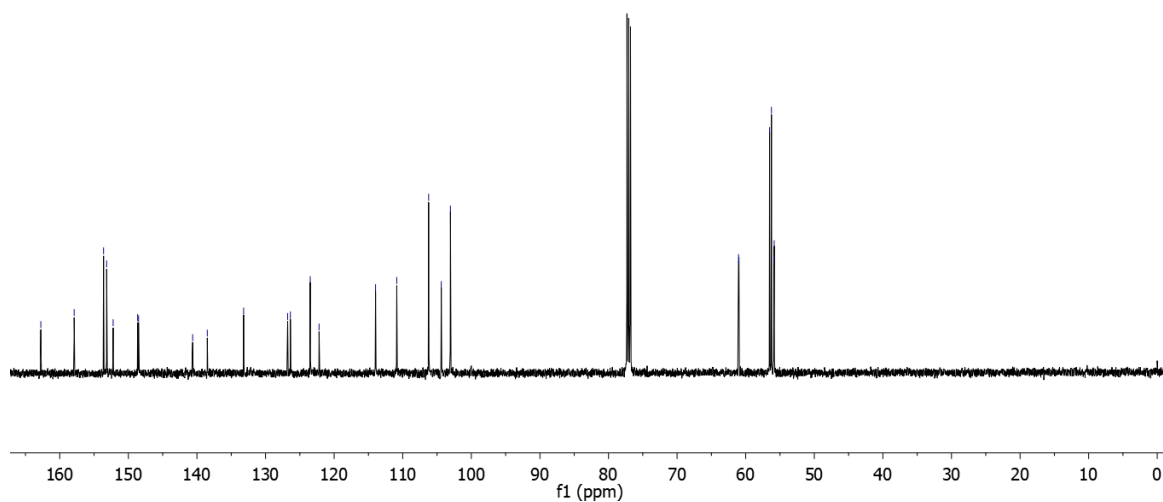
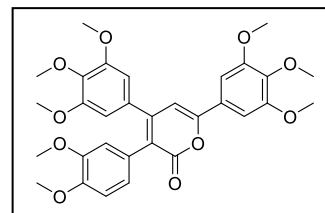
¹³C NMR (125 MHz, CDCl₃) of compound **3t**



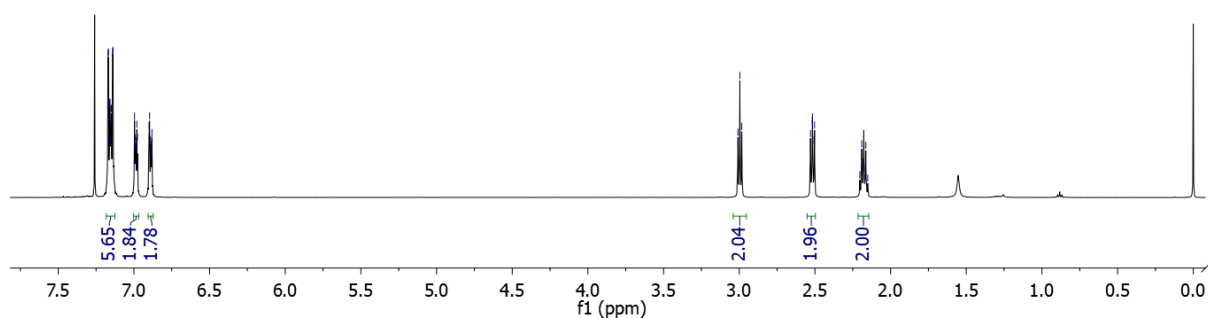
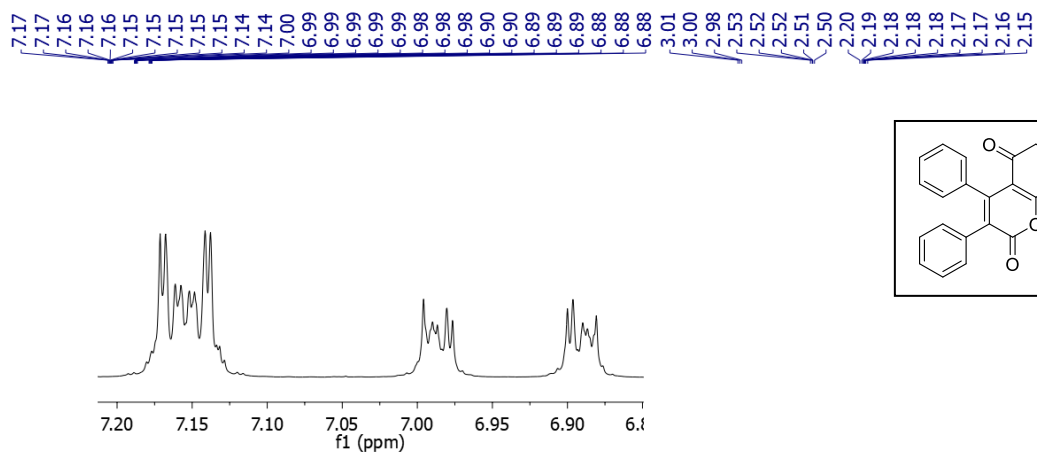




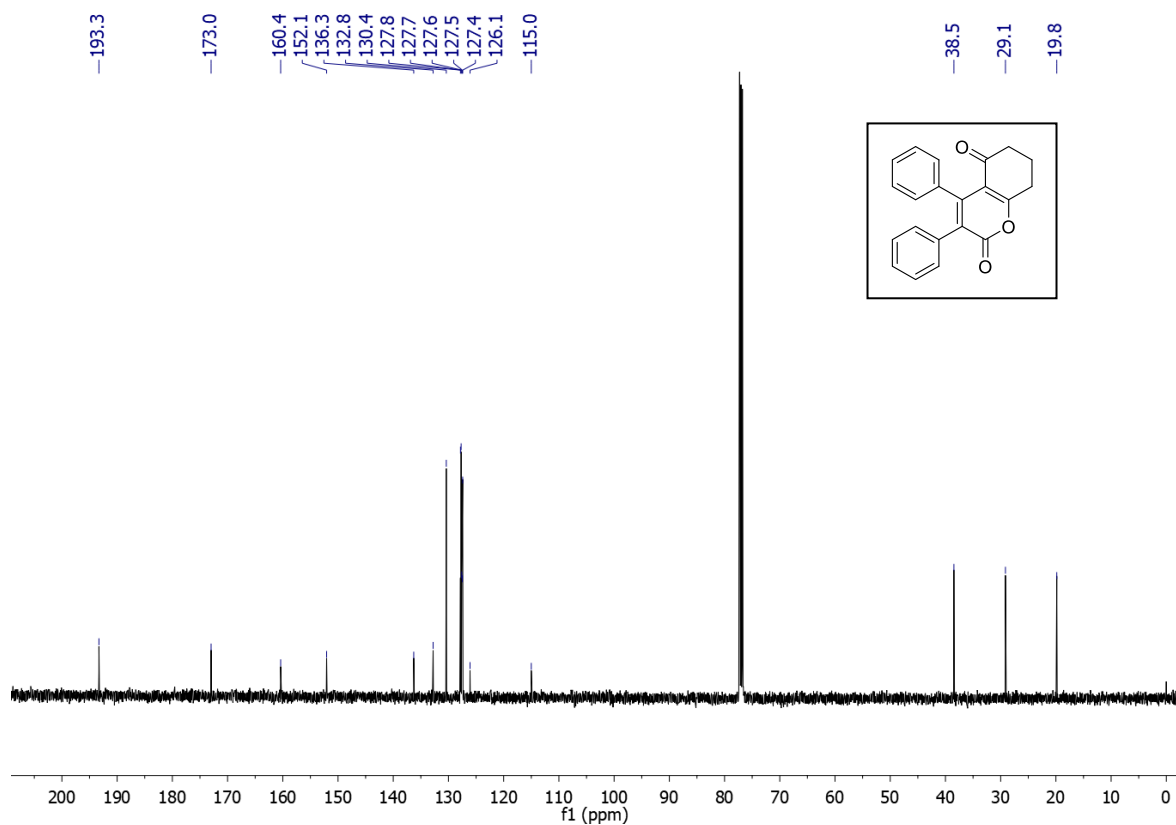
^1H NMR (500 MHz, CDCl_3) of compound **3x**



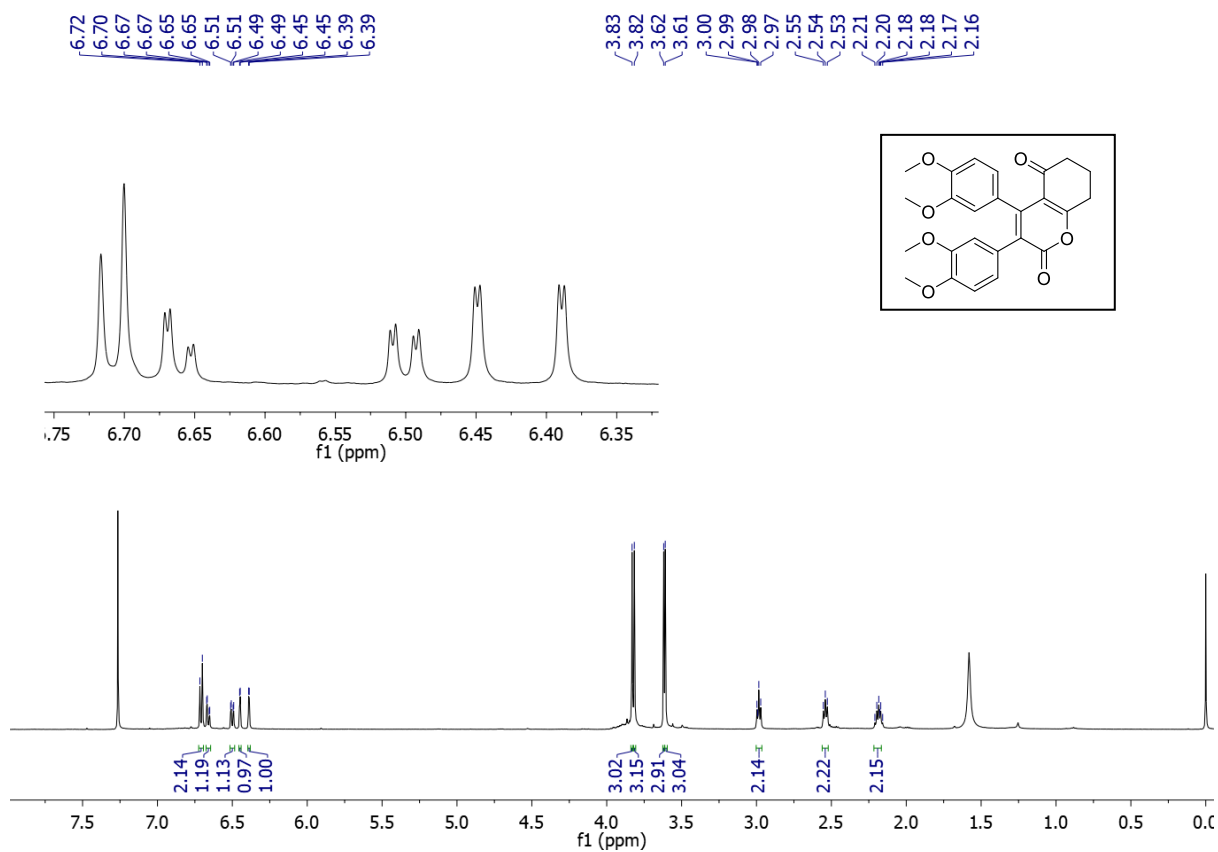
^{13}C NMR (125 MHz, CDCl_3) of compound **3x**



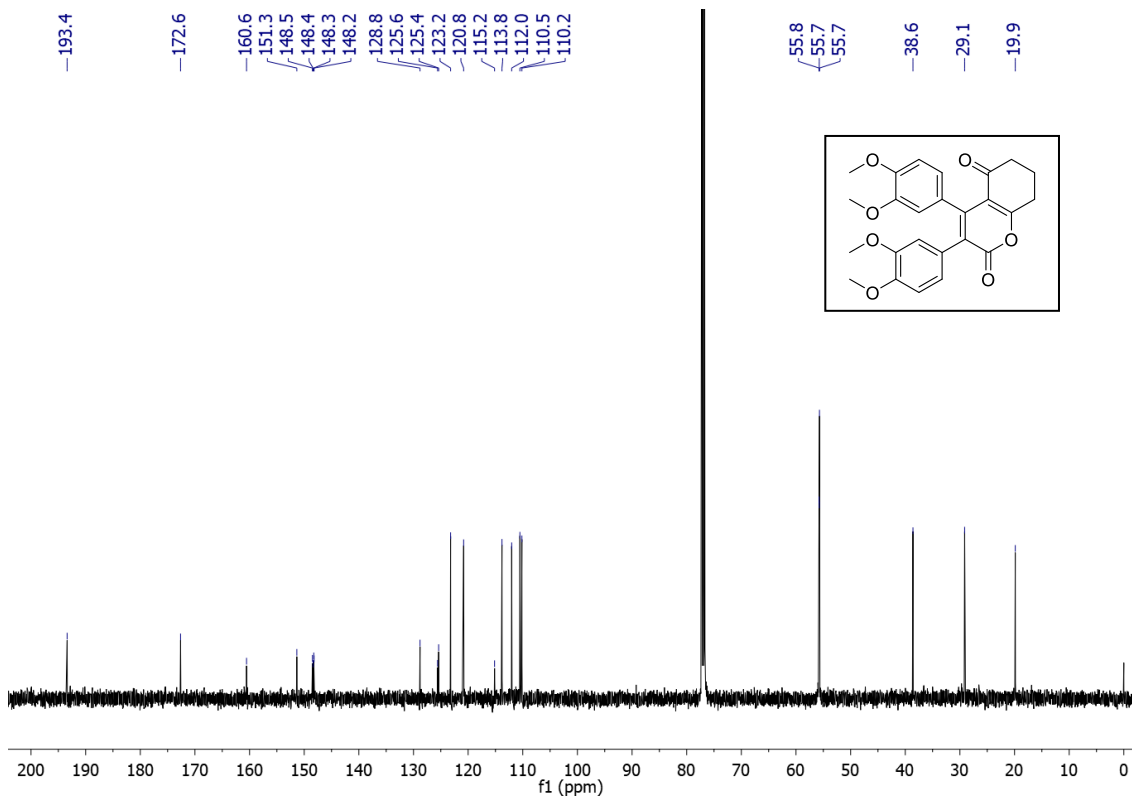
¹H NMR (500 MHz, CDCl₃) of compound **5a**



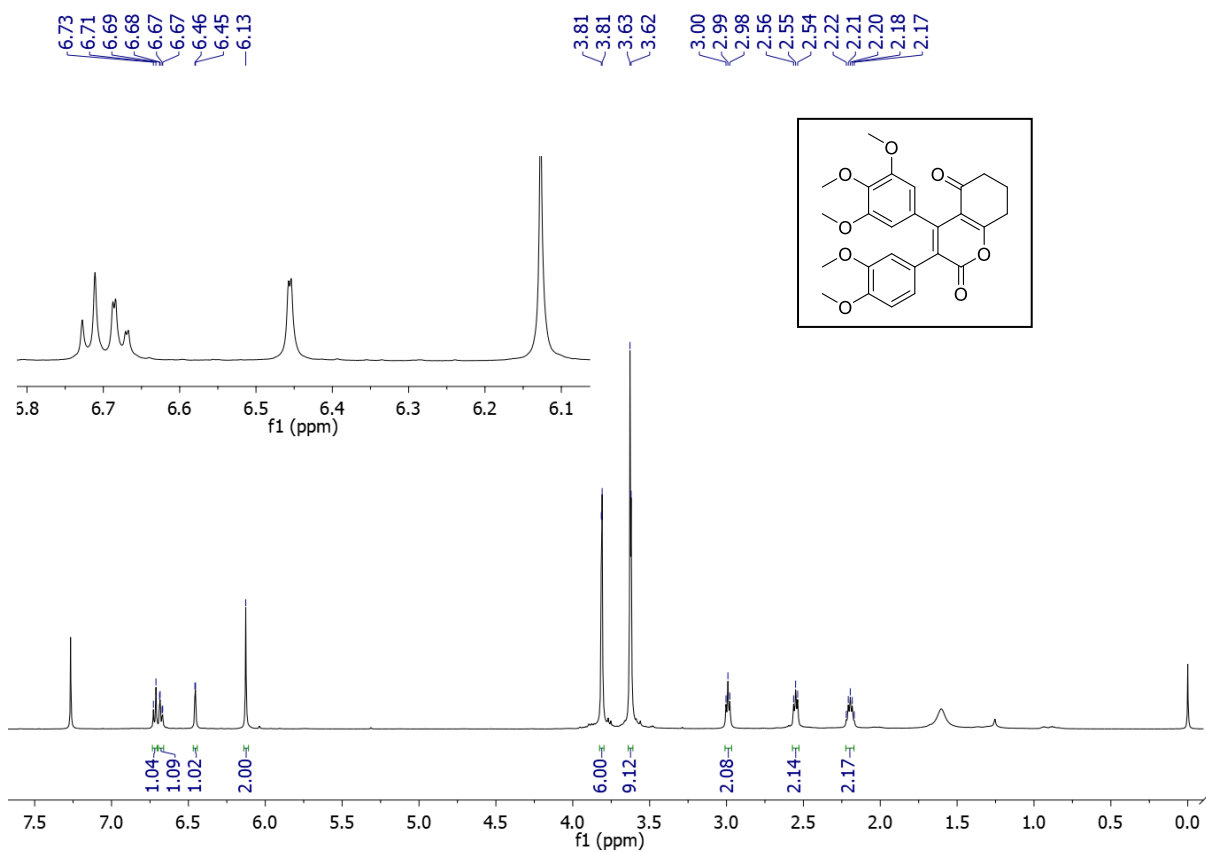
¹³C NMR (125 MHz, CDCl₃) of compound **5a**



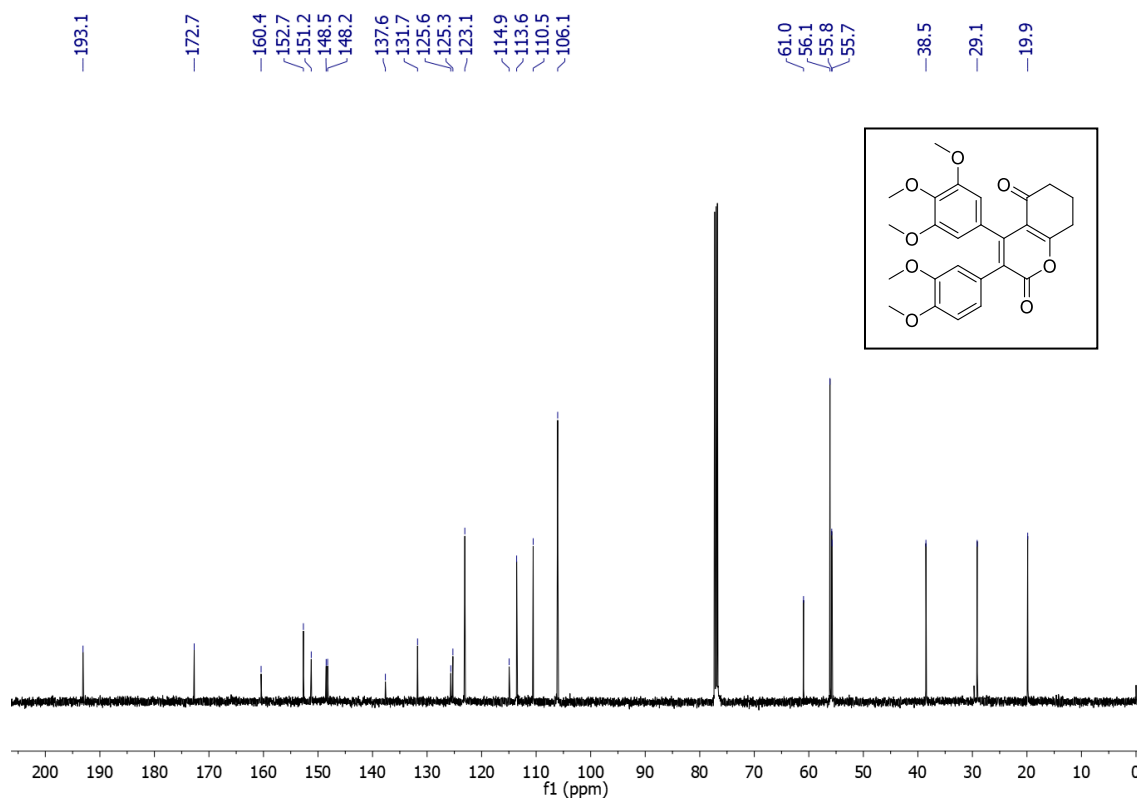
¹H NMR (500 MHz, CDCl₃) of compound **5b**



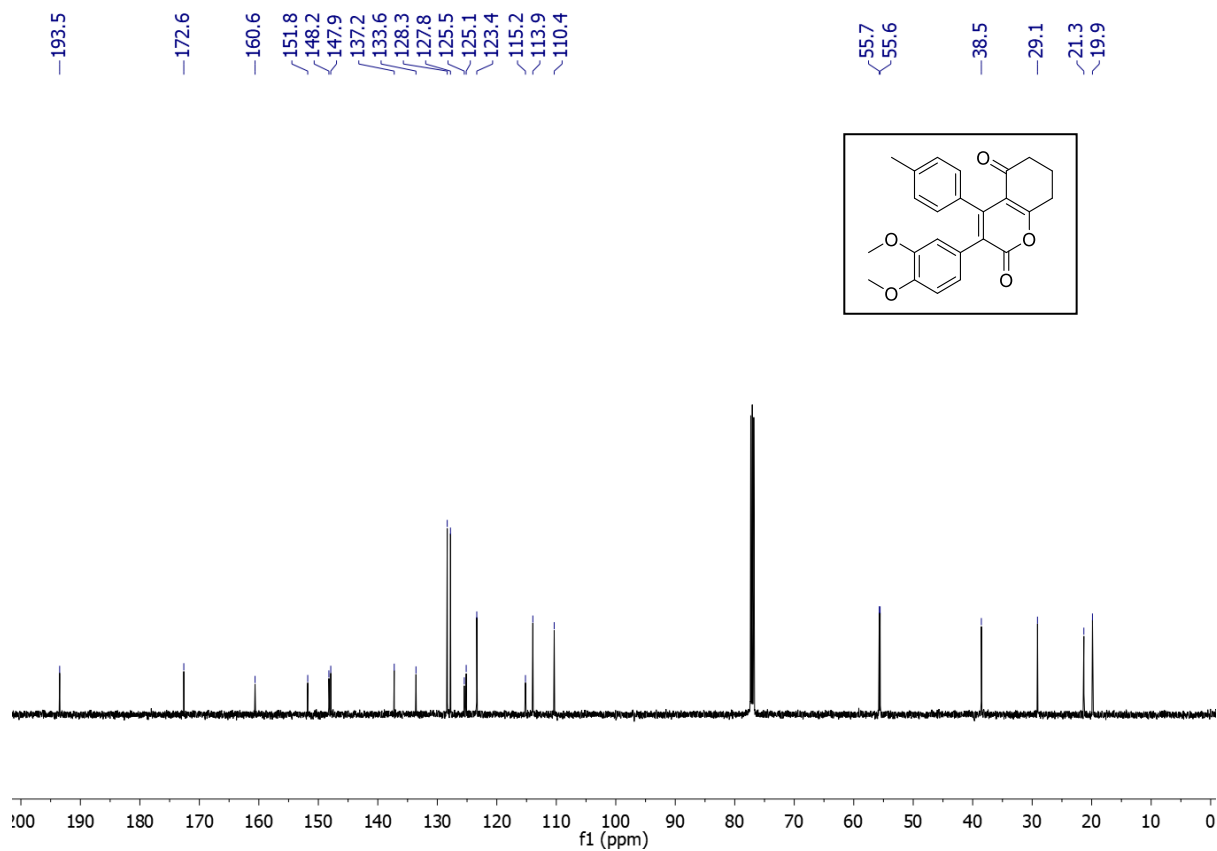
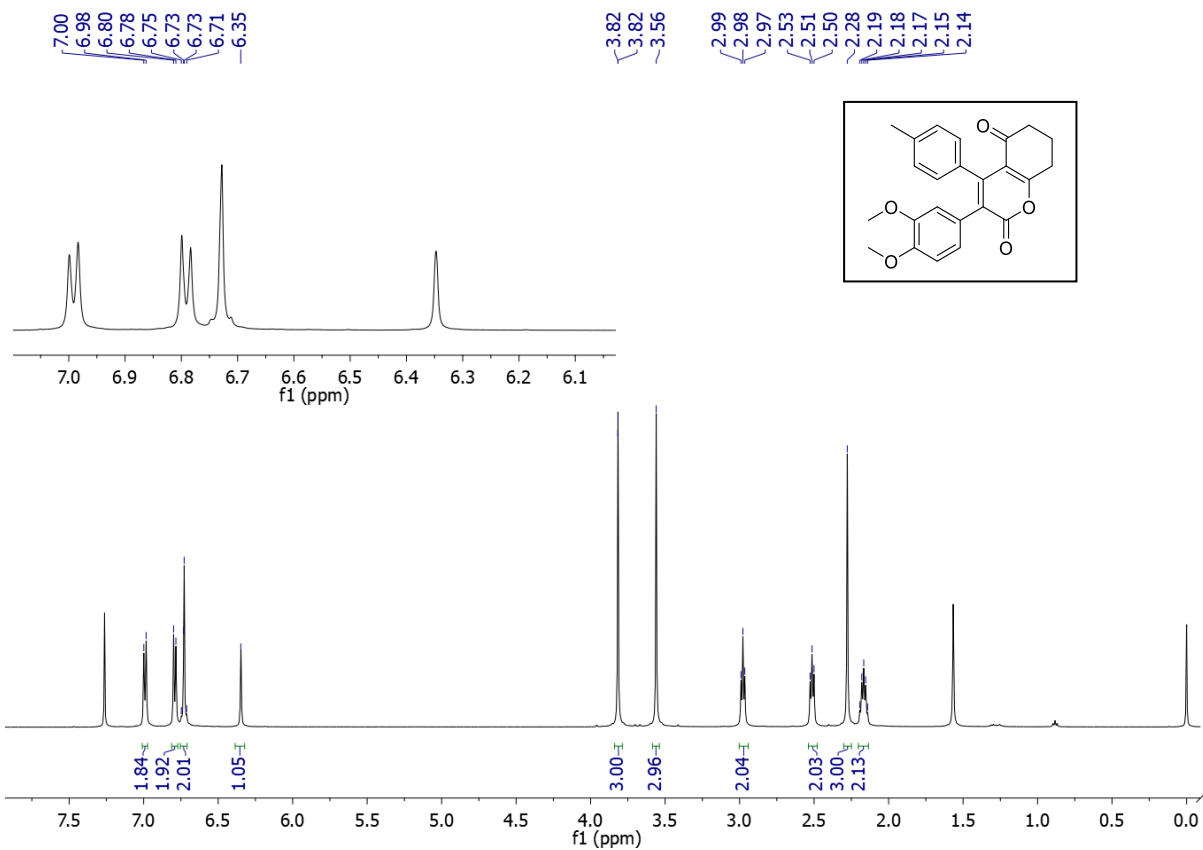
¹³C NMR (125 MHz, CDCl₃) of compound **5b**

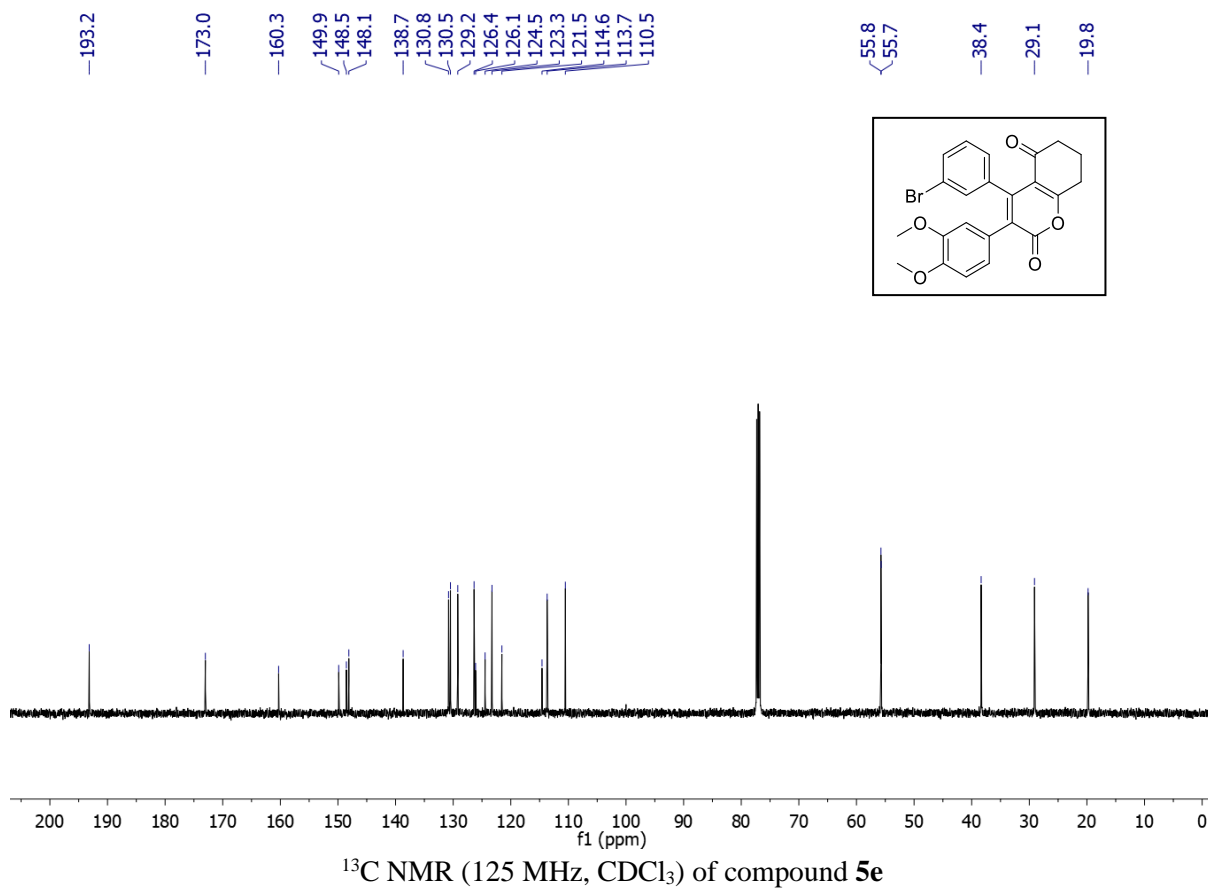
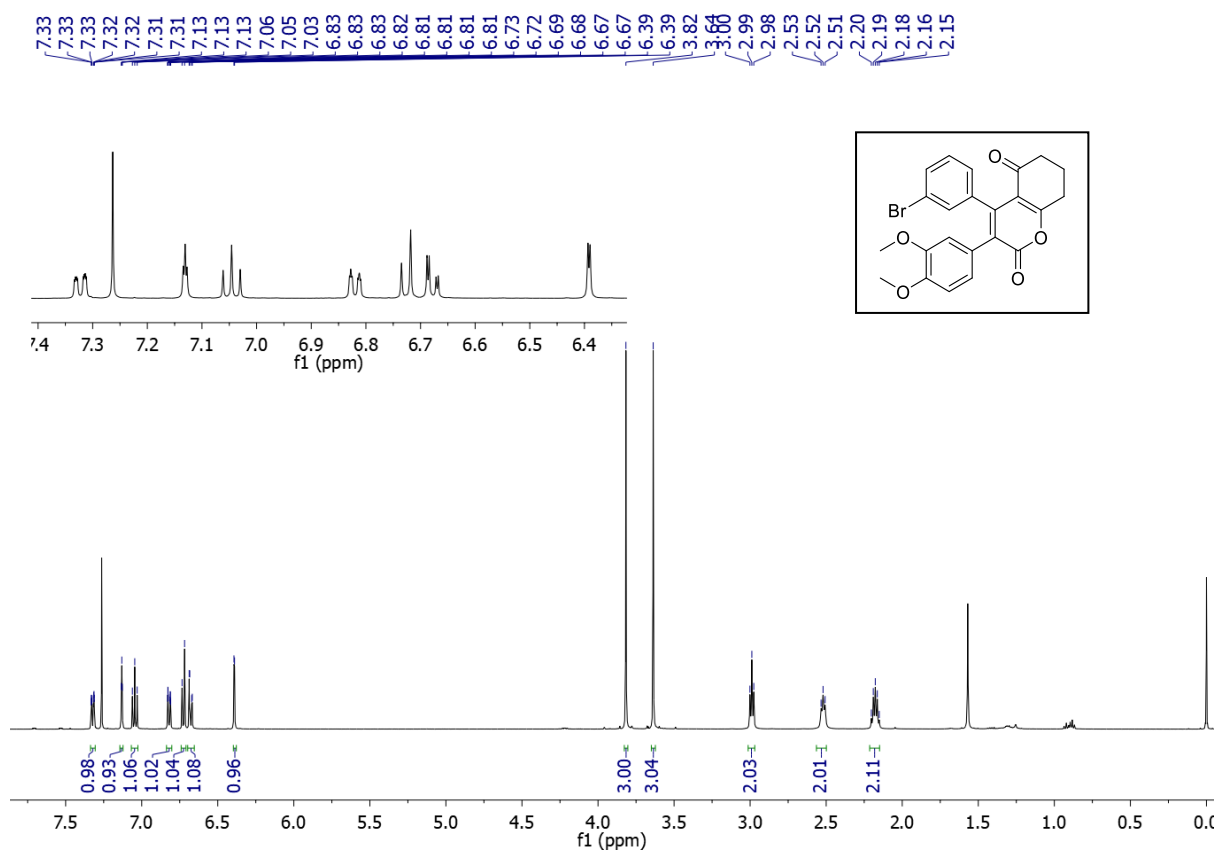


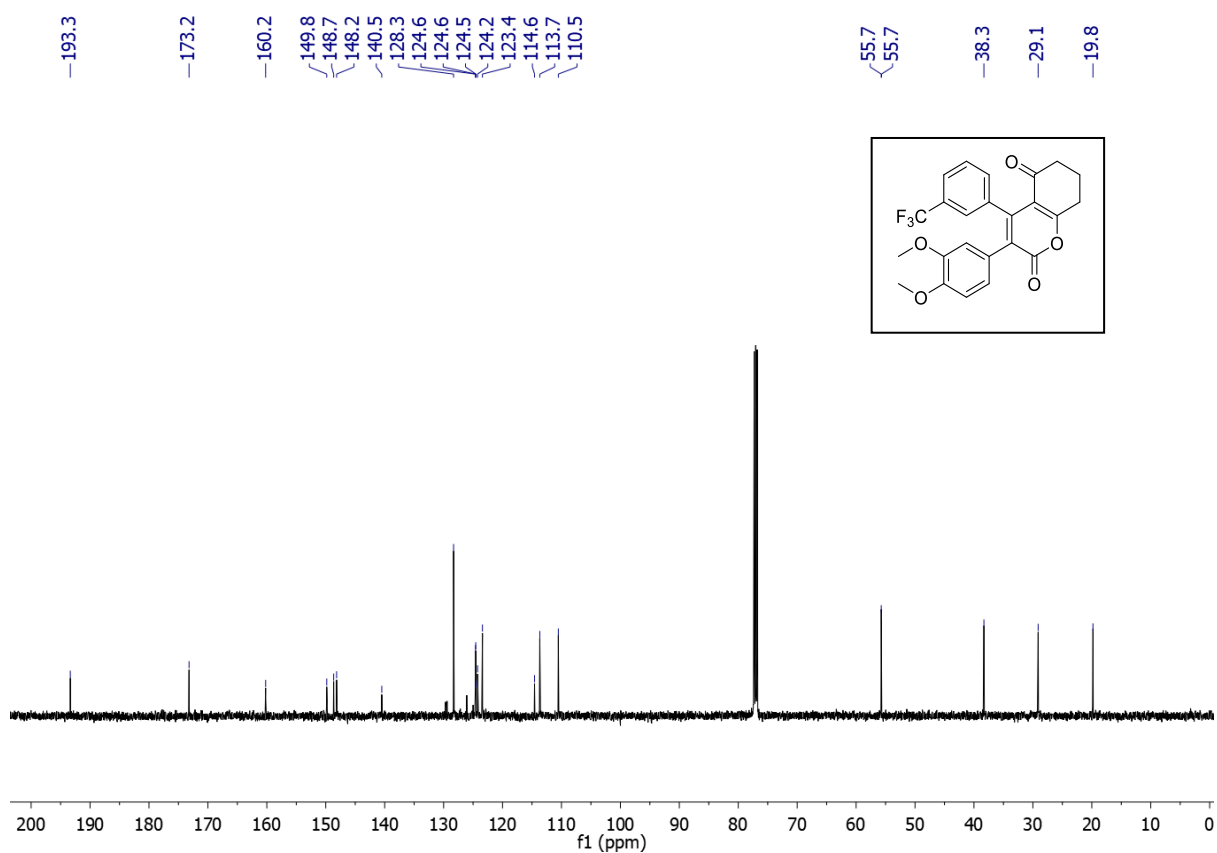
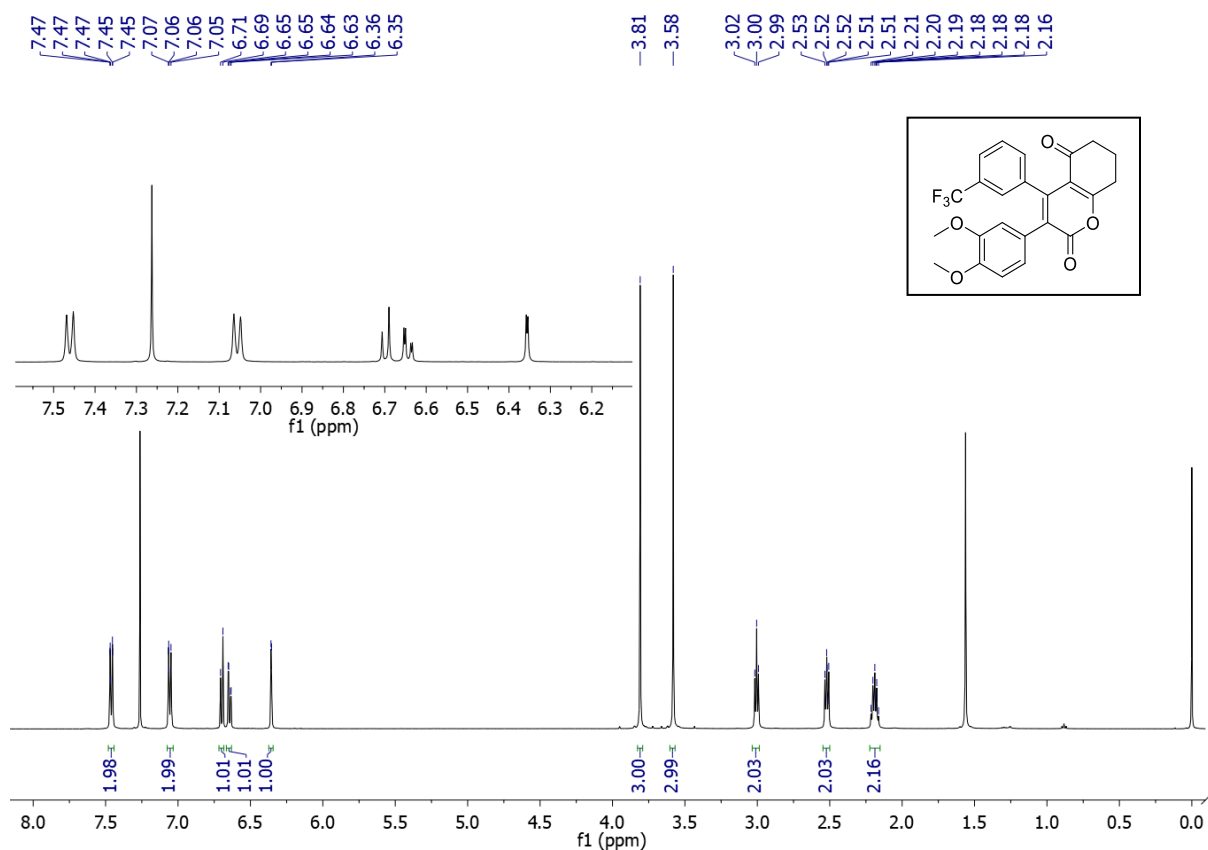
¹H NMR (500 MHz, CDCl₃) of compound **5c**

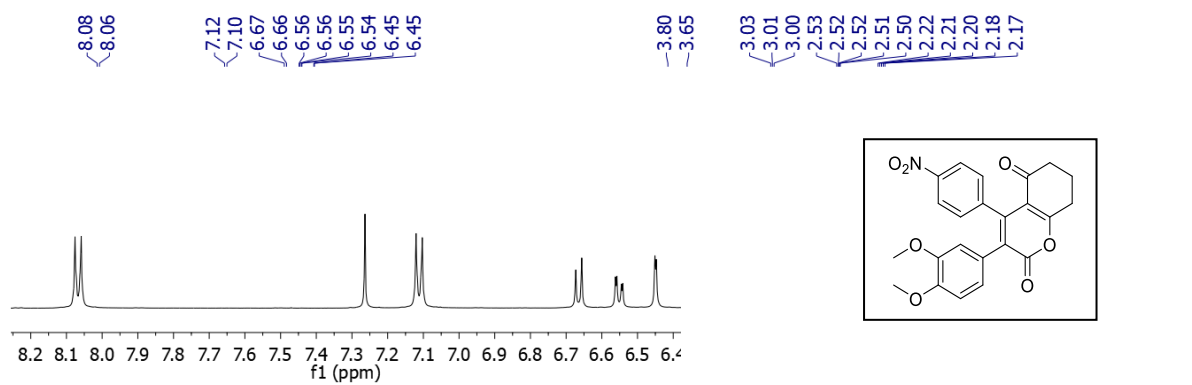
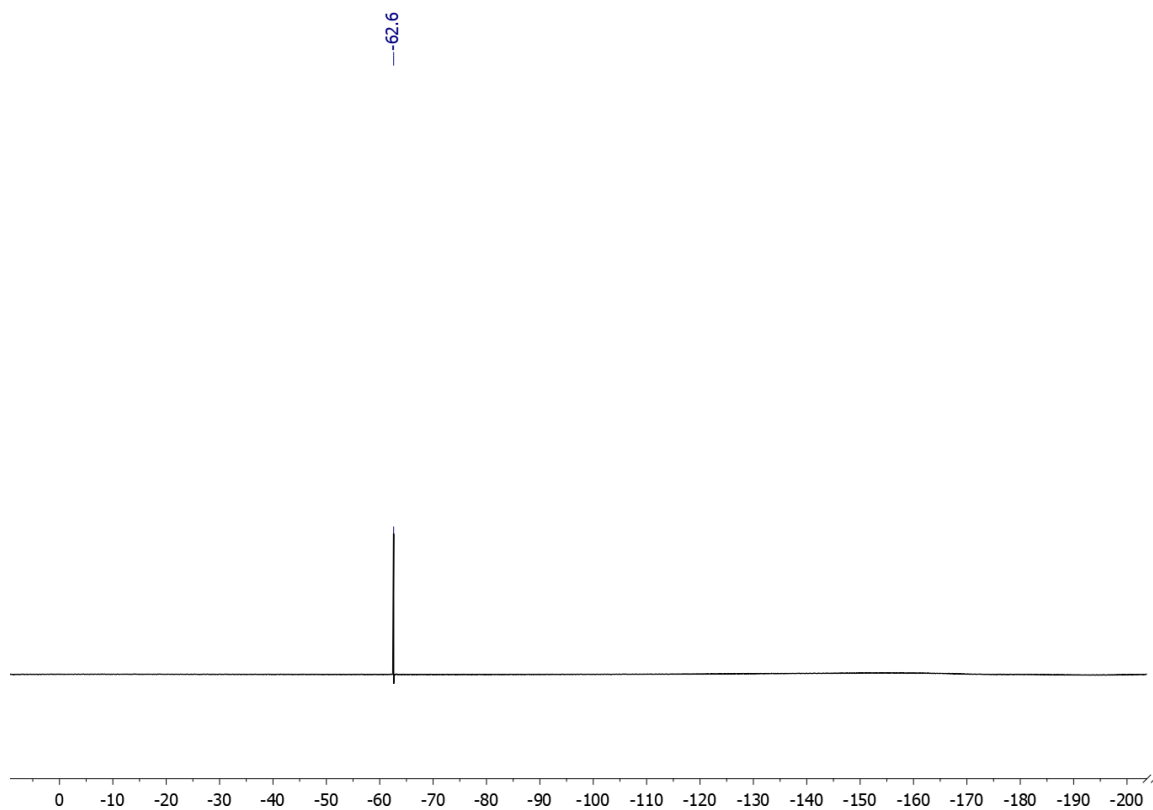


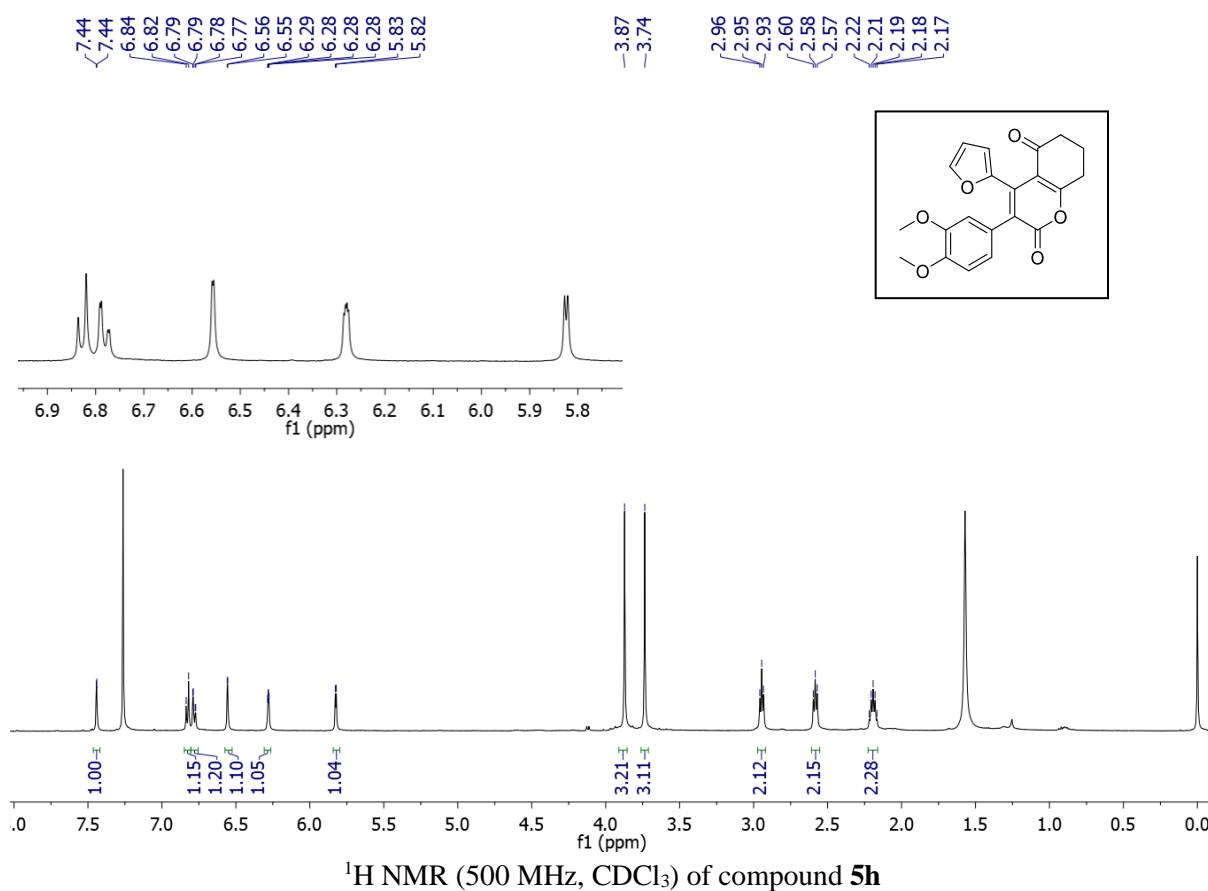
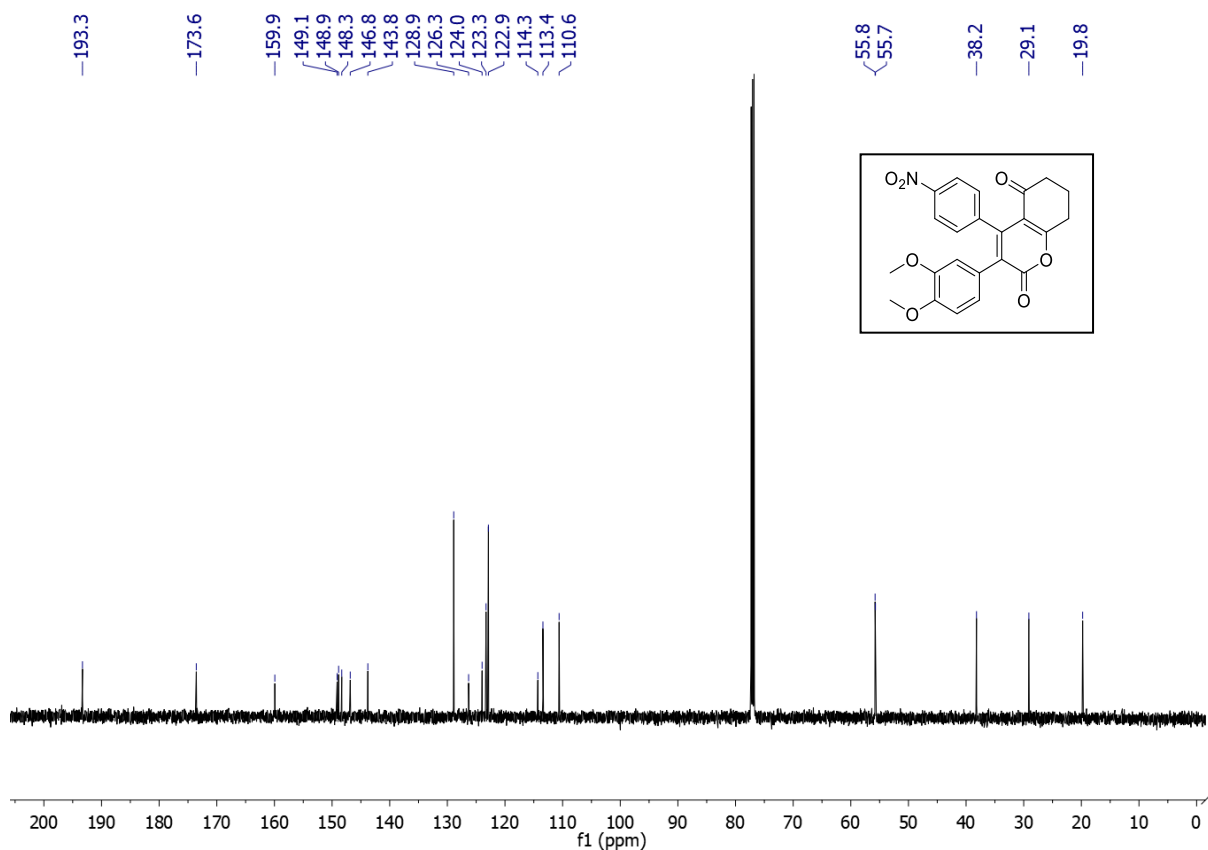
¹³C NMR (125 MHz, CDCl₃) of compound **5c**

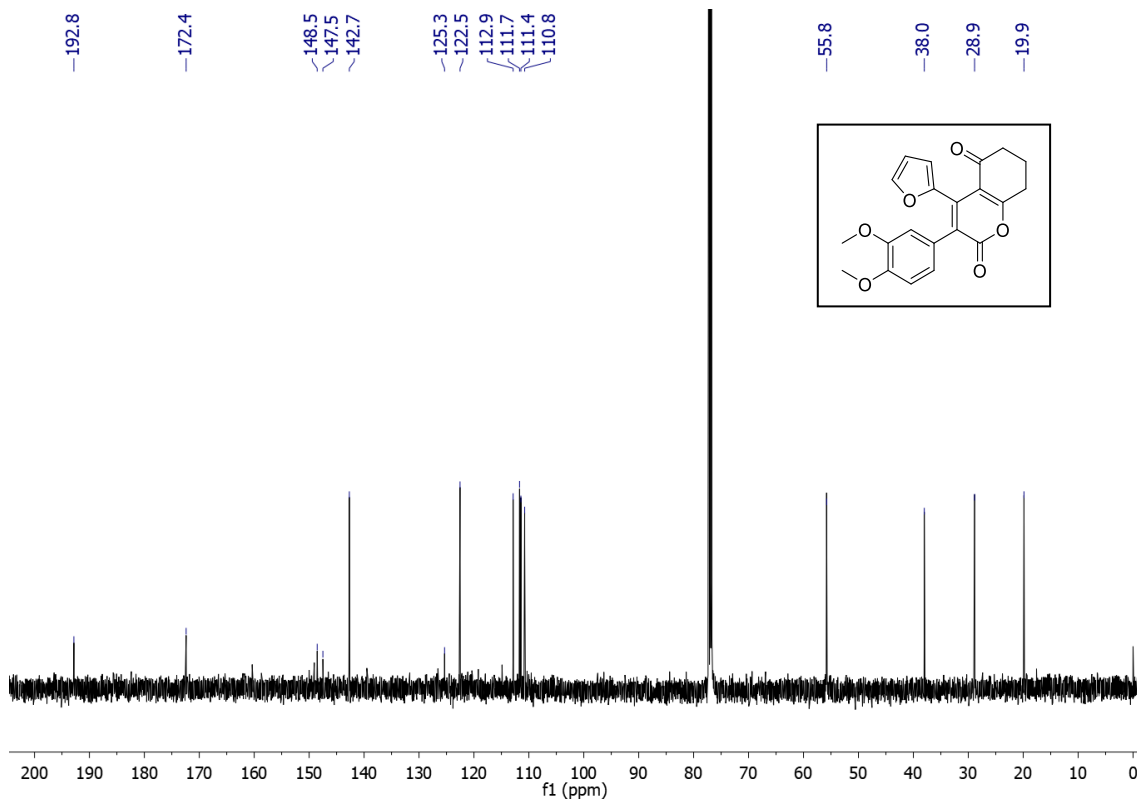




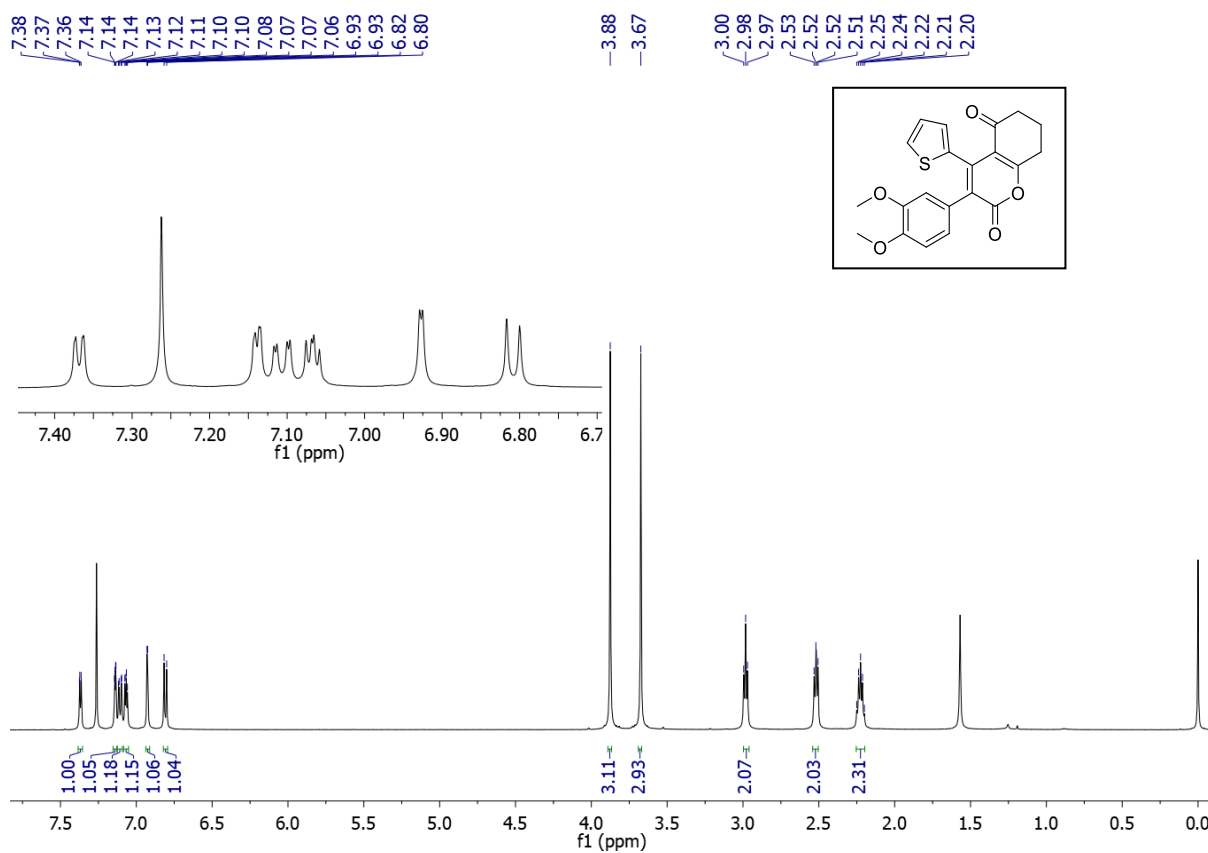








^{13}C NMR (125 MHz, CDCl_3) of compound **5h**



^1H NMR (500 MHz, CDCl_3) of compound **5i**

