Supplementary Information (SI) for Reaction Chemistry & Engineering.
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SUPPORTING INFORMATION

Fast and Scalable Continuous Flow Synthesis of Butenolides and Coumarins

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1. GENERAL INFORMATION

Reagents and solvents were bought from Sigma Aldrich, Ambeed and were used as received. The crude products were purified by flash column chromatography on silica gel (60 Å, 220-440 mesh, 35-75 μM). TLC analysis was performed using silica on aluminum foils TLC plates (F254, Sigma Aldrich) with visualization under ultraviolet light (254 nm). Organic solutions were concentrated under reduced pressure on a Büchi rotary evaporator (in vacuo at 40 ºC, ~20 mbar). The crude was analyzed by ^{1}H NMR through the integration of diagnostic signals. ^{1}H (400/500/600 MHz), ^{13}C (100/125/150 MHz) spectra were recorded on ambient temperature using a Bruker-Avance 400/500/600. ^{1}H NMR spectra were reported in parts per million (ppm) downfield relative to $CDCl_3$ (7.26 ppm) and ^{13}C NMR spectra were reported in ppm relative to $CDCl_3$ (77.16 ppm). NMR spectra used the following abbreviations to describe the multiplicity: s (singlet), d (doublet), t (triplet), q (quartet), p (pentet), h (hextet), hept (heptet), m (multiplet), dd (double doublet), td (triple doublet). Coupling constants (J) were reported in hertz (Hz). NMR data were processed using the MestReNova 14 software package. Known products were characterized by comparing to the corresponding ^{1}H NMR and ^{13}C NMR from literature. High-resolution mass spectra (HRMS) were recorded by Q Exactive – Orbitrap Thermo. The names of all products were generated using the PerkinElmer ChemBioDraw Ultra v. 18.0.0 software package.

2. SETUP OF THE REACTION IN FLOW

For the optimization experiments and the evaluation of the scope, an Uniqsis device with a HPFA reactor was used. The active reactor volume was 14 mL, using a coil of PFA (ID: 0.79 mm) (**figure 1.a** and **1.b**). The injection of the crude was performed through a 2.5 mL coil of PFA (ID: 0.79 mm) (**figure 1.c**)

Figure S1.Uniqsis device (a) Picture of full reactor, (b) HPFA Coil reactor (V = 14 mL) and (c) 2.5 mL HPFA coil.

3. REACTION OPTIMIZATION

3.1 Fed-batch synthesis of butenolide

For the development of the transformation, we evaluate the process using the hydroxyketone **1e** as the standard and the corresponding ester **I**. Initially, a solution containing TMD, serving as ketene precursor, and the hydroxyketone, as nucleophile, was introduced into a 2.5 mL looping chamber and subsequently injected into a reactor with a predefined flow rate. The crude product was collected in an Erlenmeyer flask after a specified residence time then the solvent was evaporated. The yield of the product was determined by ^{1}H NMR spectroscopy with 1,3,5-trimethoxybenzene used as the internal standard. The signals used for yield determination included the (CH_2) α O-ester and CH_3 of acetyl group in **3ea** and the conversion CH_2 of aliphatic group in **1e**. The signals are depicted in **figure 2**.

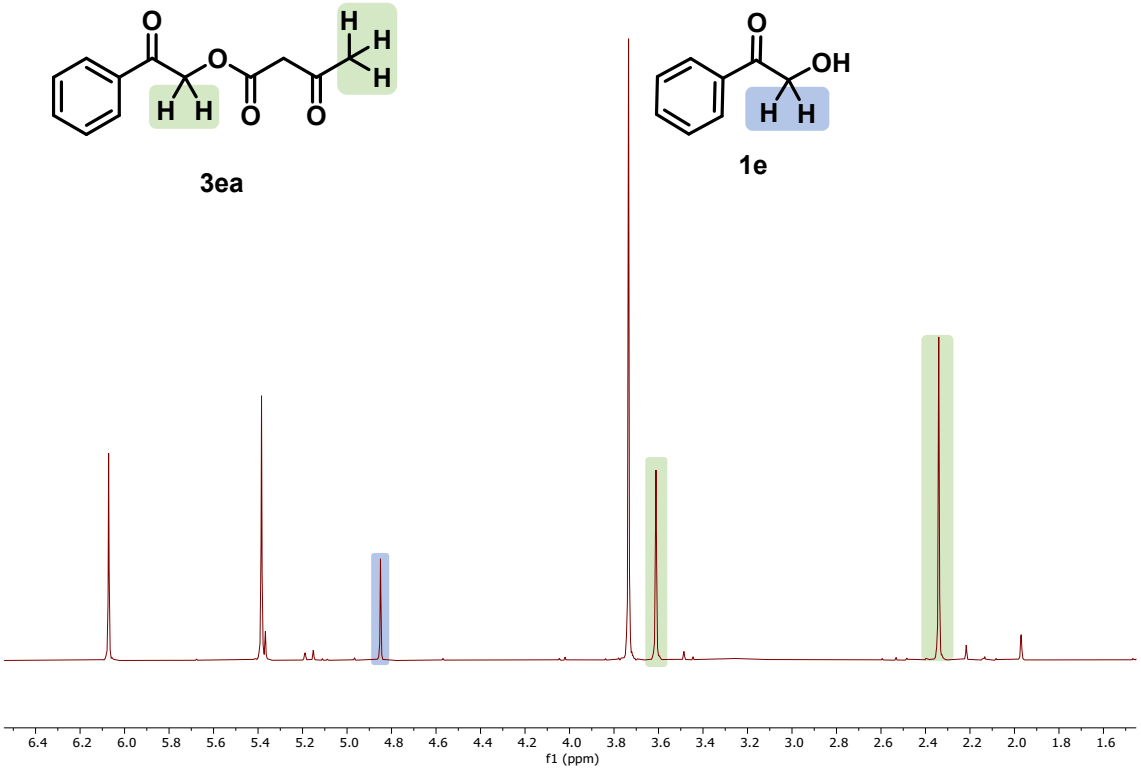
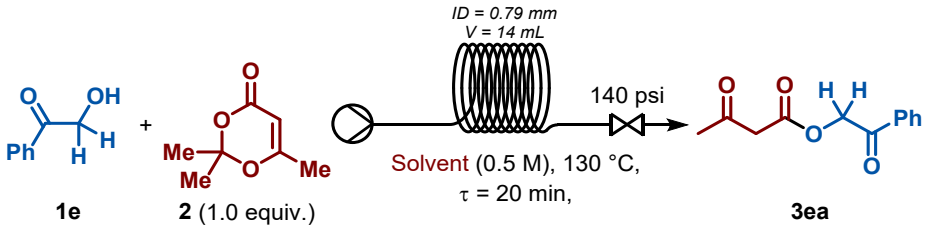


Figure S2. Spectra of crude containing internal standard and the structures of **1e** and **3ea** with groups highlighted.

3.1.1 Solvent screening

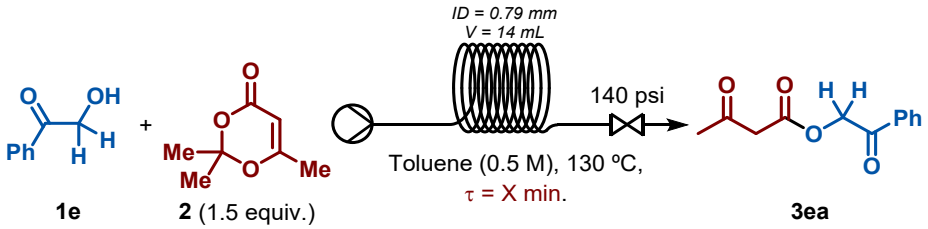


Entry	Solvent	Conversion (%)	Yield (%)[a]
1	EtOAc	70	10
2	THF	58	9
3	Toluene	68	24

[a] Yield and conversion were determined by ^{1}H NMR using 1,3,5-trimethoxybenzene as internal standard.

Initially, we selected solvents based on their non-nucleophilic characteristics, owing to the known high electrophilicity of ketenes. Experiments conducted in polar solvents (Entries 1 and 2) resulted in a lower yield compared to those conducted in a non-polar solvent (3).

3.1.2 Residence time

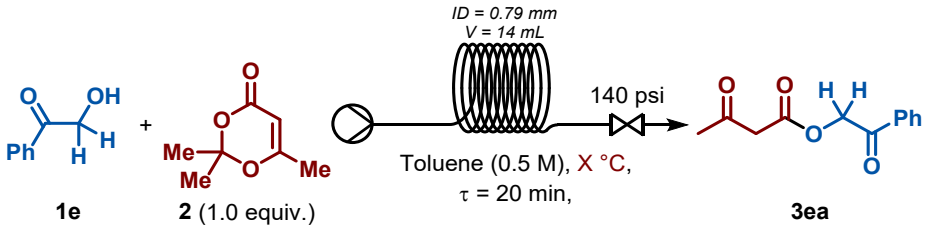


Entry	Residence time (min)	Yield (%)[a]
1	20	24
2	40	27

[a] Yield and conversion were determined by ^{1}H NMR using 1,3,5-trimethoxybenzene as internal standard.

When the reaction was conducted with a residence time of 20 minutes (Entry 1), 24% of product was obtained. In the other hand, with 40 minutes of residence time, no relevant increase was detected (Entry 2).

3.1.3 Temperature screening

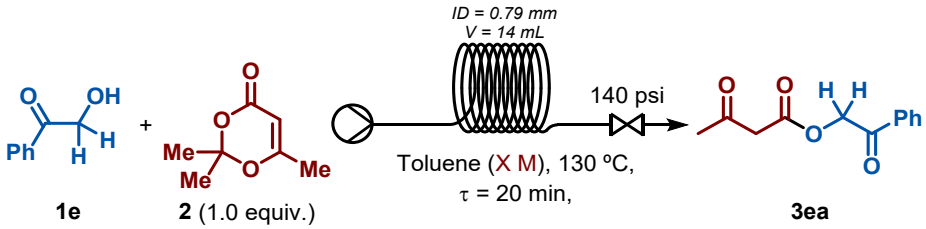


Entry	Temperature (ºC)	Yield (%)[a]
1	110	24
2	130	52
3	150	55

[a] Yield and conversion were determined by ^{1}H NMR using 1,3,5-trimethoxybenzene as internal standard.

According to the most recent publication from our group, the formation of ketenes from TMD occurs only at temperatures exceeding 100°C. Consequently, we initiated our experiments at 110°C (Entry 1). Although the highest yield was achieved at 150°C (Entry 3), the pressure approached the maximum limit of 20 bar for the PFA Coil. Therefore, we opted for 130°C to ensure greater safety while maintaining effective reaction conditions (Entry 2).

3.1.4 Concentration

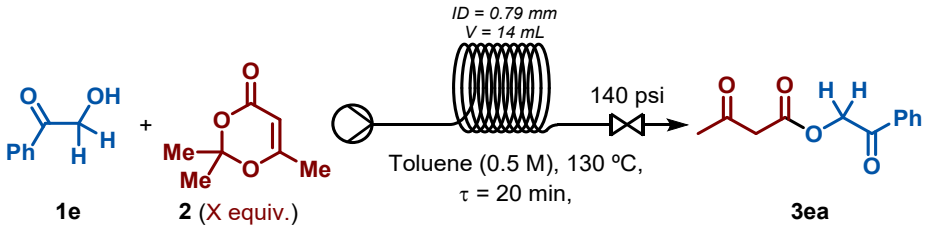


Entry	Concentration (M)	Yield (%)[a]
1	0.5	58
2	0.25	51
3	0.1	52

[a] Yield and conversion were determined by ^{1}H NMR using 1,3,5-trimethoxybenzene as internal standard.

. Under more diluted conditions, the yield decreased significantly (Entries 2 and 3). Conversely, at more concentrated medium, the yield increased (Entry 1). Therefore, a concentration of 0.5 M was determined to be the optimal condition.

3.1.5 Equivalents of ketene precursor



Entry	TMD (equiv.)	Yield (%)[a]
1	1.0	58
2	1.5	81
3	2.0	64

[a] Yield and conversion were determined by ^{1}H NMR using 1,3,5-trimethoxybenzene as internal standard.

As the equivalence of TMD was increased, the stability of the ketene intermediate in the reactor improved. The yield increased when 1.5 equivalents of TMD were used (Entries 1 and 2). Although, 2.0 equivalents decreased the yield (Entry 3).

3.2 One step synthesis of butenolides

For the development of the transformation, we evaluated the process using the hydroxyketone **1a** as standard and the corresponding butenolide **3a**. Initially, a solution containing TMD, serving as the ketene precursor, and the hydroxyketone acting as the nucleophile, was introduced into a 2.5 mL looping chamber and subsequently injected into a reactor with a predefined flow rate. The crude product was collected in an Erlenmeyer flask after the specified residence time, and the solvent was then evaporated. The yield of the product was determined by ^{1}H NMR spectroscopy, with 1,3,5-trimethoxybenzene used as the internal standard. The signals used for yield determination included the CH_3 groups of the acetyl group (O) or $(CH3)_2$ of compound **3a**, and for conversion, the $(CH_3)_2$ group of compound **1a**, as depicted in the structures shown in **Figure 3**.

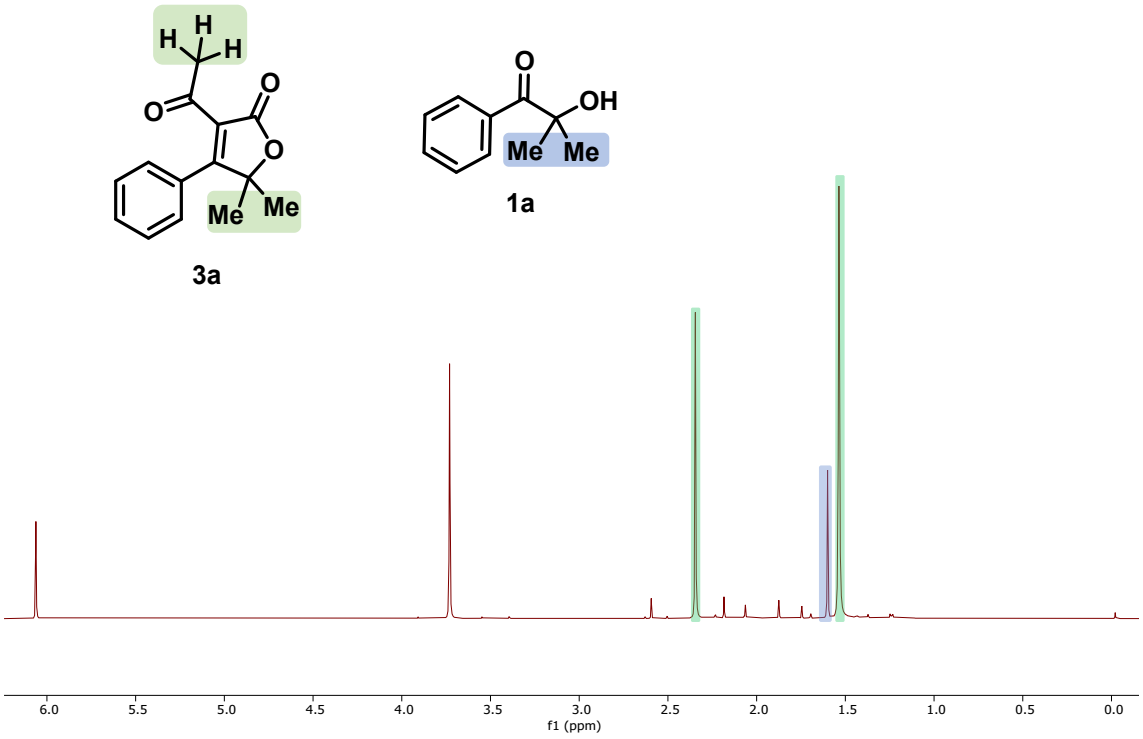
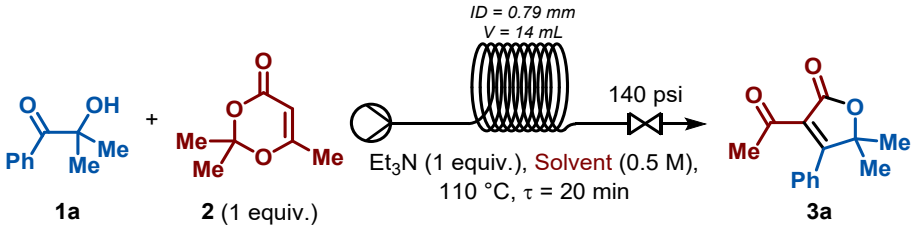


Figure S3. Spectra of crude containing internal standard and the structures of **1a** and **3a** with groups highlighted.

3.2.1 Solvent screening

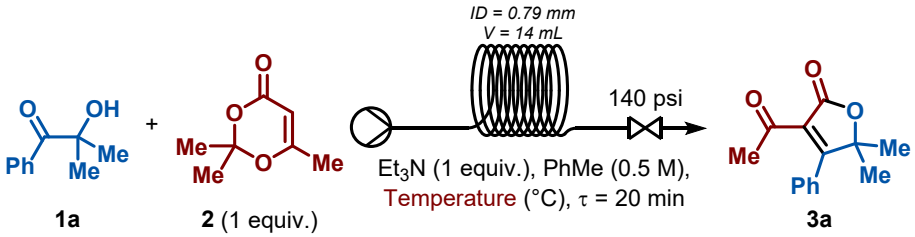


Entry	Solvent	Conversion (%)	Yield (%)[a]
1	EtOAc	90	2
2	THF	96	5
3	Toluene	93	13

[a] Yield and conversion were determined by ^{1}H NMR using 1,3,5-trimethoxybenzene as internal standard.

Initially, we selected solvents based on their non-nucleophilic characteristics, owing to the known high electrophilicity of ketenes. Experiments conducted in polar solvents (Entries **1** and **2**) resulted in a lower yield compared to those conducted in a non-polar solvent (**3**). It is noteworthy that, in all cases, a high conversion of hydroxyketone was consistently observed.

3.2.2 Temperature screening

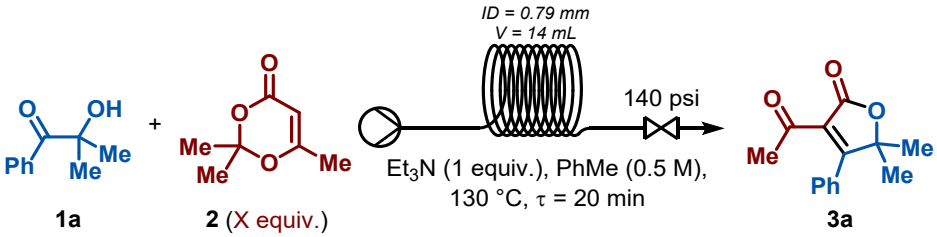


Entry	Temperature (ºC)	Yield (%)[a]
1	110	16
2	130	25
3	150	28

[a] Yield and conversion were determined by ^{1}H NMR using 1,3,5-trimethoxybenzene as internal standard.

According to the most recent publication from our group, the formation of ketenes from TMD occurs only at temperatures exceeding 100°C. Consequently, we initiated our experiments at 110°C (Entry 1). Although the highest yield was achieved at 150°C (Entry 3), the pressure approached the maximum limit of 20 bar for the PFA Coil. Therefore, we opted for 130°C to ensure greater safety while maintaining effective reaction conditions (Entry 2).

3.2.3 Equivalents of ketene precursor

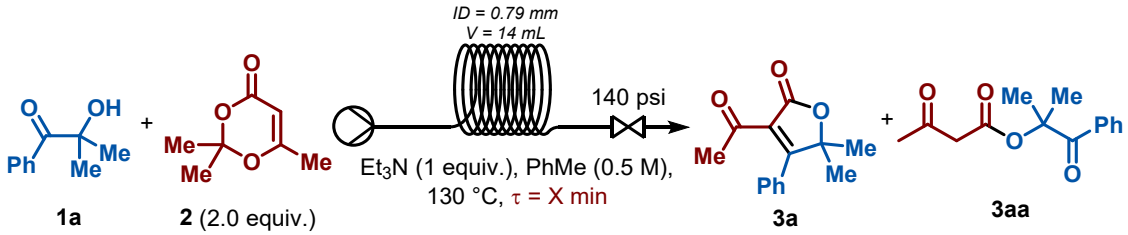


Entry	TMD (equiv.)	Yield (%)[a]
1	1.2	18
2	1.5	33
3	2.0	42
4	2.5	45

[a] Yield and conversion were determined by ^{1}H NMR using 1,3,5-trimethoxybenzene as internal standard.

As the equivalence of TMD was increased, the stability of the ketene intermediate in the reactor improved. The yield increased when 2.0 equivalents of TMD were used (Entries 1, 2 and 3). However, the use of 2.5 equivalents proved unnecessary, as no additional benefit was observed (Entry 4).

3.2.4 Residence time

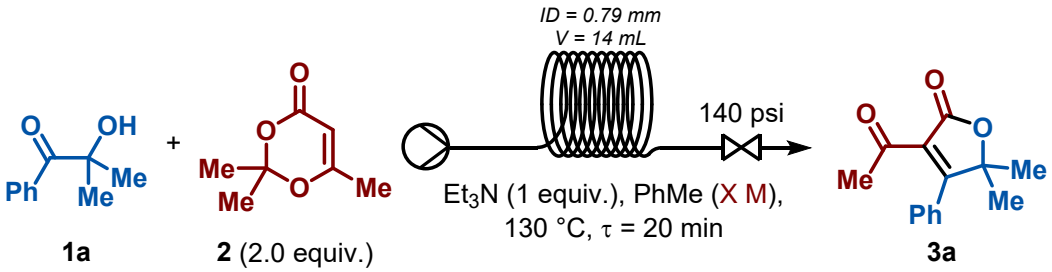


Entry	Residence time (min)	Yield (%)[a]
1	10	--
2	20	42
3	30	--

[a] Yield and conversion were determined by ^{1}H NMR using 1,3,5-trimethoxybenzene as internal standard.

When the reaction was conducted with a residence time of 10 minutes, only the reaction intermediate was observed in the NMR spectra (Entry 1). In contrast, with a residence time of 30 minutes, neither the desired product nor the intermediate was detected in the NMR spectra; instead, only hydroxyketone (HK) was present (entry 2). We hypothesize that, at elevated temperatures, the butenolide may degrade. Consequently, a residence time of 20 minutes was determined to be optimal (Entry 2).

3.2.5 Concentration

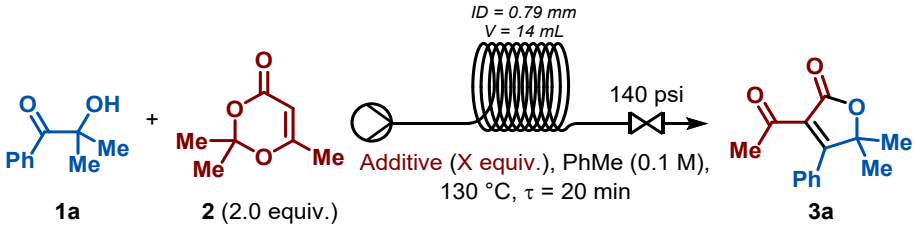


Entry	Concentration (M)	Yield (%)[a]
1	1.0	41
2	0.75	43
3	0.25	50
4	0.1	54

[a] Yield and conversion were determined by ^{1}H NMR using 1,3,5-trimethoxybenzene as internal standard.

In the context of a two-step reaction involving an initial intermolecular step followed by an intramolecular step, it was important to investigate how concentration affects the transformation. Under more concentrated conditions, the yield decreased significantly (Entries 1 and 2). Conversely, at more dilute concentrations, the yield increased (Entries 3 and 4). Therefore, a concentration of 0.1 M was determined to be the optimal condition.

3.2.6 Screening of base

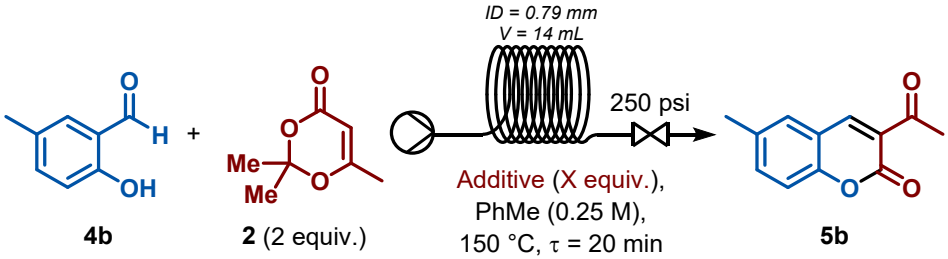


Entry	Additive (X equiv.)	Yield (%)[a]
1	Et_3N (1.5)	63
2	Et_3N (2.0)	76 (**71**)
3	Et_3N (2.5)	71
4	DBU (2.0)	65
5	Imidazole (2.0)	72
6	Tetramethylguanidine (2.0)	46

[a] Yield and conversion were determined by ^1H NMR using 1,3,5-trimethoxybenzene as internal standard.

Initially, we assessed the quantity of base required to maximize the yield of the desired product. Increasing the amount of base to 2.0 equivalents resulted in a significant improvement in yield. However, using 2.5 equivalents caused a decline in yield. After determining the optimal amount, we tested additional bases. Strong bases were found to be more effective when used in larger volumes (Entries 4 and 6). An aromatic base also produced a notable yield, approaching the optimal condition (Entry 5).

4. BASE SCREENING FOR COUMARINS



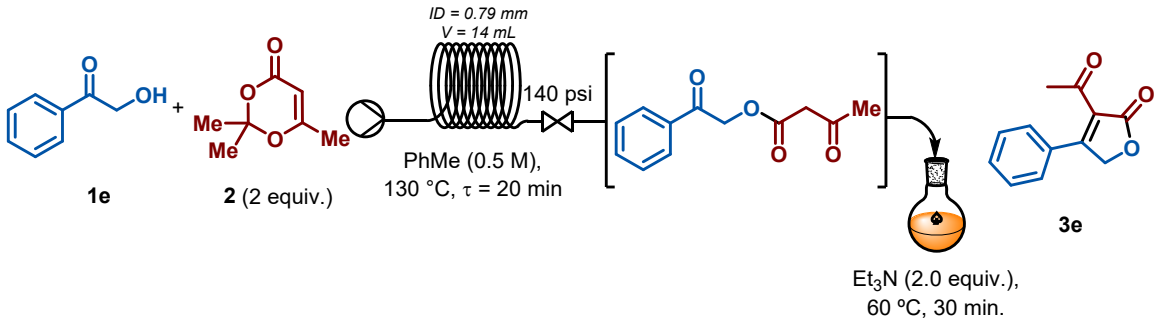
Entry	Additive (X equiv.)	Yield (%)[a]
1	Et_3N (1.1)	50
2	Et_3N (2.0)	50
3	Et_3N (5.0)	45
4	DBU (1.1)	19
5	Imidazole (1.1)	44

[a] Yield and conversion were determined by ^1H NMR using mesitylene as internal standard.

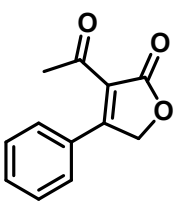
Since we previously conducted a screening for a similar transformation, optimizing the synthesis of coumarins was straightforward. As described earlier, we assessed the quantity of additive required, selecting those additives that had previously demonstrated significant results. In this instance, bases used in larger volumes were found to decrease the yield (Entry 4). In contrast, the aromatic base did not exhibit a significant decrease in yield, consistent with earlier observations for butenolides (Entry 5).

5 SYNTHETIC PROCEDURES

5.1 General procedure A: Fed-batch synthesis of butenolides



In a solution of toluene [0.1M] were added the respective HK **1e** (81.7 mg, 1.0 equiv., 0.6 mmol); TMD **2** (126 µL, 1.5 equiv., 0.9 mmol). The mixture was pumped through a coil of HPFA (ID: 0.79 mm; V = 2.5 mL) with a rate of 0.700 mL/min into a HPFA reactor (ID: 0.79; 14.0 mL) at 130 ºC and back-pressure regulator of 140 psi. The resulting mixture was collected (≈ 7 min) in a round-bottom flask containing Et_3N (175 µL, 2.0 equiv., 1.2 mmol) and heated to 60 ºC for 30 minutes. When the crude reach to room temperature, was diluted in 10 mL of AcOEt and washed with HCl (1M) (1x10 mL). The resulting organic layer was dried with Na_2SO_4, filtered and concentrated under reduced pressure. The crude was purified with column chromatography.

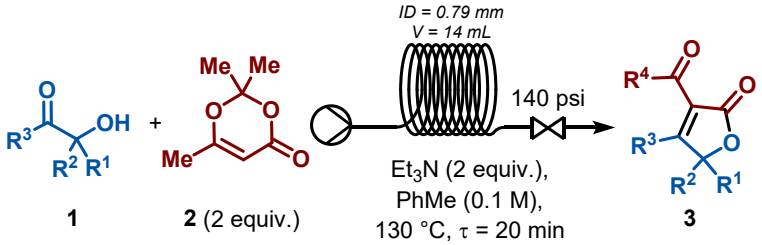


3-acetyl-4-phenylfuran-2(5*H*)-one (**3e**)[1]**:** Compound **3e** was prepared according to the general procedure A using 2-hydroxy-1-phenylethan-1-one (35.4 mg, 1.0 equiv., 0.26 mmol) as substrate. Product was not allowed to separate from starting material and yield was determined by ^{1}H NMR using 1,3,5-trimethoxybenzene as internal standard (Yield: 30%).

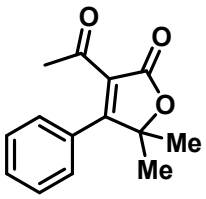
^{1}H NMR (500 MHz, $CDCl_3$): 7.56-7.51 (m, 3H); 7.49-7.45 (m, 2H); 5.15 (s, 2H); 2.57 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): 196.2. 171.0, 165.0, 132.3, 129.6, 129.2, 128.3, 126.1, 70.9, 30.8.

5.2 General procedure B: One step synthesis of the butenolides



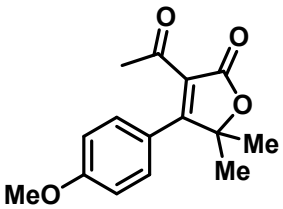
In a solution of toluene [0.1M] were added the respective HK (**1**) (1.0 equiv.); TMD (**2**) (2.0 equiv.) and Et_3N (2.0 equiv.). The mixture was pumped through a coil of HPFA (ID: 0.79 mm; V = 2.5 mL) with a rate of 0.700 mL/min into a HPFA reactor (ID: 0.79; 14.0 mL) at 130 ºC and back-pressure regulator of 140 psi. The resulting mixture obtained was diluted in 10 mL of AcOEt and washed with HCl (1M) (1x10 mL). The resulting organic layer was dried with Na_2SO_4, filtered and concentrated under reduced pressure. The crude was purified with column chromatography.



3-acetyl-5,5-dimethyl-4-phenylfuran-2(5H)-one (**3a**)[2]: Compound **3a** was prepared according to the general procedure B using 2-hydroxy-2-methyl-1-phenylpropan-1-one (90.9 mg; 1.0 equiv.; 0.51 mmol) as substrate and looping of 5.0 mL The compound was purified with column chromatography (SiO_2; Hex:AcOEt 9:1; rf = 0.26; Vanillin as orange spot) to afford an light yellow oil (82 mg, 0.356 mmol, 71%).

^{1}H NMR (600 MHz, $CDCl_3$): 7.48-7.46 (m, 3H), 7.24-7.22 (m, 2H), 2.38 (s, 3H); 1.56 (s, 6H).

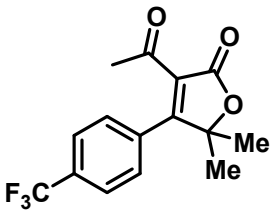
^{13}C NMR (150 MHz, $CDCl_3$): 194.4; 176.0; 168.5; 168.4; 130.9; 129.9; 128.8; 126.8; 86.3; 30.5; 24.8.



3-acetyl-4-(4-methoxyphenyl)-5,5-dimethylfuran-2(5H)-one (**3b**)[3]: Compound **3b** was prepared according to the general procedure B using 2-hydroxy-1-(4-methoxyxphenyl)-2-methylpropan-1-one) (50.5 mg; 1.0 equiv.; 0.26 mmol) as substrate. The compound was purified with column chromatography (SiO_2; Hex:AcOEt 9:1; rf = 0.26; Vanillin as orange spot) to afford a yellow oil (32.9 mg, 0.126 mmol, 51%).

^{1}H NMR (500 MHz, $CDCl_3$): 7.24 (dt, J = 2.1 Hz, J = 8.8 Hz, 2H); 6.97 (dt, J = 2.1 Hz and J = 8.8 Hz, 2H); 3.86 (s, 3H); 2.41 (s, 3H);1.57 (s, 6H).

^{13}C NMR (125 MHz, $CDCl_3$): 195.3; 175.5; 168.8; 161.3; 129.2; 125.8; 122.7; 114.4; 86.4; 55.5; 30.6; 25.3.

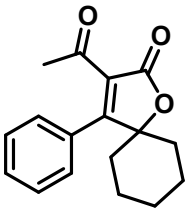


3-acetyl-5,5-dimethyl-4-(4-(trifluoromethyl) phenyl) furan-2(5*H*)-one (**3c**): Compound **3c** was prepared according to the general procedure B using 2-hydroxy-2-methyl-1-(4-(trifluoromethyl)phenyl)propan-1-one (25 mg; 1.0 equiv.; 0.108 mmol) as substrate and looping of 1.0 mL The compound was purified with column chromatography (SiO_2; Hex:AcOEt 9:1; rf = 0.26; $KMnO_4$) to afford an light yellow oil (29.2 mg; 0.0979 mmol, 91%).

^{1}H NMR (500 MHz, $CDCl_3$): 7.73 (d, J = 8.2 Hz, 2H); 7.33 (d, J = 8.2 Hz, 2H), 2.48 (s, 3H), 1.55 (s, 6H).

^{13}C NMR (125 MHz, $CDCl_3$):193.9, 175.3, 168.3, 134.8, 132.2 (q, J = 33.1 Hz), 127.4, 126.9, 125.8 (q, J = 3.8 Hz), 124.8, 122.7, 86.3, 30.4, 24.7.

^{19}F NMR (500 MHz, $CDCl_3$): - 62.9.

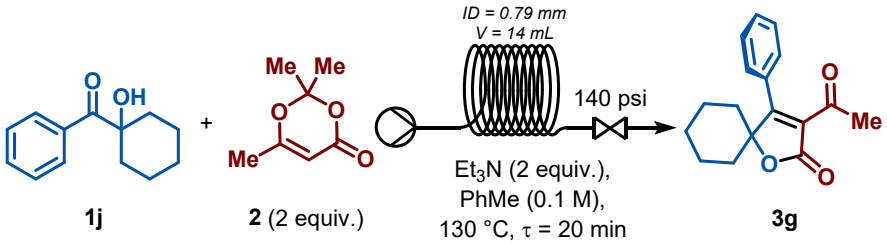


3-acetyl-4-phenyl-1-oxaspiro [4.5] dec-3-en-2-one (**3g**): Compound **3g** was prepared according to the general procedure B using 1-(hydroxy cyclohexyl) (phenyl)methanone (53.1 mg; 1.0 equiv.; 0.26 mmol) as substrate. The compound was purified with column chromatography (SiO_2; Hex: Acetone 9:1; rf = 0.28; Vanillin, orange spot) to afford a white solid (40.5 mg, 0.15 mmol, 60%).

^{1}H NMR (500 MHz, $CDCl_3$): 7.45-7.44 (m, 3H); 7.16-7.14 (m, 2H); 2.35 (s, 3H), 1.78-1.69 (m, 10H).

^{13}C NMR (125 MHz, $CDCl_3$):194.4, 176.9, 168.9, 131.4, 129.6, 128.7, 126.8, 88.1, 33.1, 30.6, 24.3, 21.8.

5.3 General procedure C: Gram scale synthesis



In a volumetric flask (50 mL) were added 1-(hydroxy cyclohexyl) (phenyl)methanone (1.746g; 1.0 equiv.; 10 mmol); TMD (2.80 mL; 2.0 equiv.; 20 mmol) and Et_3N (2.9 mL; 2.0 equiv.; 20 mmol) and filled with toluene. The mixture was pumped into a reactor HPFA (ID: 0.79 mm; 14 mL) with a flow of 0.700 mL/min at 130 ºC and 140 as back pressure regulator. The mixture obtained was

washed with HCl (1M) (1x 20 mL). The residual organic layer was dried with Na_2SO_4, filtered and concentrated under reduced pressure. The crude was purified by recrystallization (Hexane, 25 mL) and slow addition of $CHCl_3$ until residual solid was completely soluble to afford a white needled solid (1.25g, 46%).

5.2.1 Crystallography data

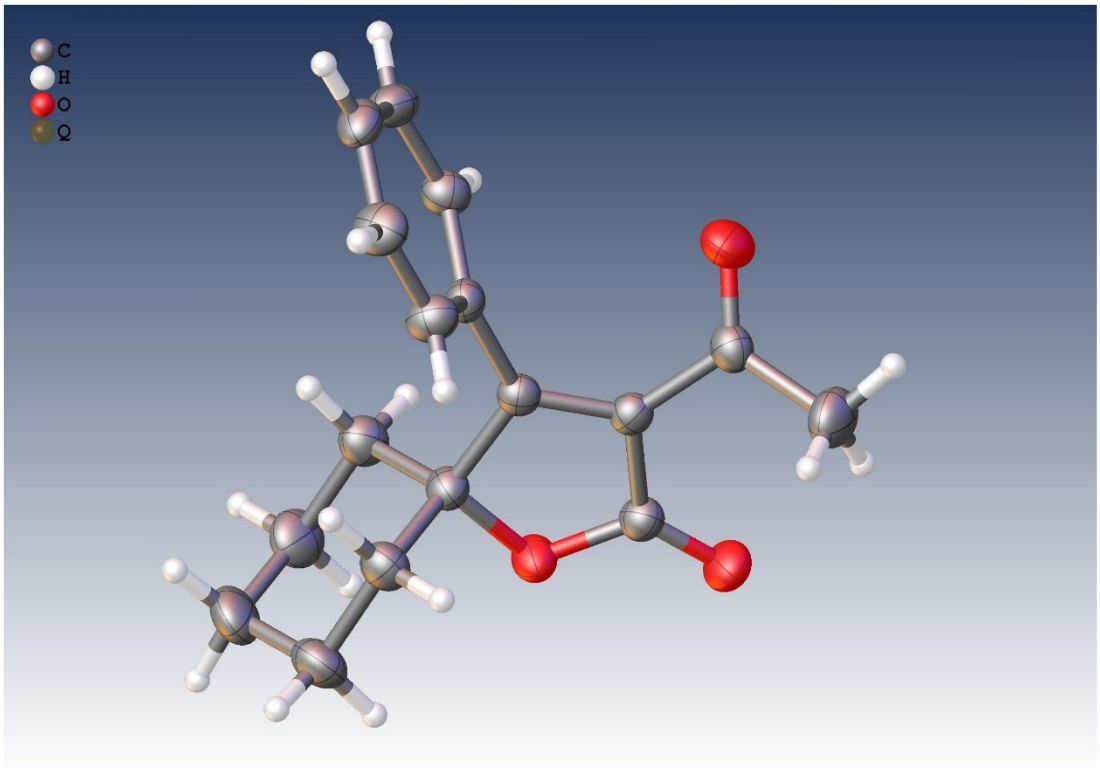


Table S1. Crystal data and structure refinement for (**3g**).

Identification code	**3g**
Formula	$C_{17}H_{18}O_3$
$D_{calc.}$/ g cm^{-3}	1.283
□/mm^{-1}	0.701
Formula Weight	270.31
Colour	None None None
Shape	?
Size/mm^3	0.28×0.04×0.03
T/K	210(2)
Crystal System	monoclinic
Space Group	$P2_1/c$
a/Å	10.3477(2)
b/Å	15.8799(2)

c/Å	8.92800(10)
□/°	90
□/°	107.442(2)
□/°	90
V/Å^3	1399.60(4)
Z	4
Z'	1
Wavelength/Å	1.54184
Radiation type	CuK□
□$_{min}$/°	4.479
□$_{max}$/°	79.606
Measured Refl.	15929
Independent Refl.	3039
Reflections with I > 2(I)	2688
R_{int}	0.0331
Parameters	182
Restraints	0
Largest Peak	0.218
Deepest Hole	-0.192
GooF	1.082
wR_2 (all data)	0.0979
wR_2	0.0944
R_1 (all data)	0.0430
R_1	0.0380

Table S2. Fractional Atomic Coordinates (×10^4) and Equivalent Isotropic Displacement Parameters (Å^2×10^3) for **Amostra_304**. U_{eq} is defined as 1/3 of the trace of the orthogonalised U_{ij}.

Atom	x	y	z	U_{eq}
O3	5399.7(8)	4522.8(5)	7643.1(9)	35.9(2)
O2	3448.7(8)	4130.3(6)	5898.2(10)	40.8(2)
O1	5838.4(10)	3159.4(6)	3244.1(10)	47.9(2)
C4	6885.9(11)	3857.3(6)	6515.1(12)	26.4(2)
C3	5621.0(10)	3705.9(7)	5607.4(12)	27.4(2)
C12	8175.1(10)	3579.6(7)	6282.2(12)	27.1(2)

Atom	x	y	z	U_{eq}
C2	5199.1(11)	3163.9(7)	4176.4(12)	31.3(2)
C6	4672.1(11)	4116.7(7)	6333.4(12)	30.8(2)
C13	8733.7(12)	4038.0(7)	5296.6(13)	33.1(2)
C5	6844.3(10)	4374.6(7)	7922.5(12)	29.0(2)
C17	8851.6(12)	2872.7(8)	7055.8(14)	35.6(3)
C14	9958.1(13)	3794.7(8)	5108.0(14)	37.5(3)
C16	10071.3(12)	2630.8(8)	6836.1(15)	40.4(3)
C7	7548.5(13)	5224.4(7)	8008.8(14)	36.5(3)
C15	10629.4(11)	3093.1(8)	5878.7(14)	37.9(3)
C11	7370.7(13)	3894.4(8)	9471.8(13)	36.7(3)
C10	7243.2(15)	4421.1(9)	10853.9(14)	46.4(3)
C8	7432.0(15)	5743.8(9)	9405.6(16)	47.1(3)
C9	7960.5(16)	5259.1(10)	10941.8(16)	51.9(4)
C1	4012.7(14)	2598.4(9)	4013.8(18)	49.8(3)

Table S3. Anisotropic Displacement Parameters ($\times 10^4$) **Amostra_304**. The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2} \times U_{11} + \ldots + 2hka^* \times b^* \times U_{12}]$

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
O3	27.0(4)	46.4(5)	34.1(4)	-9.1(3)	9.0(3)	3.6(3)
O2	25.3(4)	55.0(5)	41.3(5)	-3.7(4)	8.7(3)	3.1(4)
O1	49.9(5)	60.6(6)	37.2(5)	-13.1(4)	18.9(4)	-8.5(4)
C4	28.1(5)	25.1(5)	26.1(5)	2.1(4)	8.5(4)	0.8(4)
C3	26.3(5)	28.1(5)	27.6(5)	2.1(4)	8.1(4)	0.5(4)
C12	24.6(5)	28.7(5)	26.8(5)	-4.0(4)	6.1(4)	-1.3(4)
C2	29.7(5)	32.3(5)	29.0(5)	-0.6(4)	4.4(4)	2.0(4)
C6	27.6(5)	34.7(6)	29.8(5)	1.6(4)	8.3(4)	1.7(4)
C13	37.0(6)	31.1(5)	32.9(5)	-0.3(4)	12.9(5)	0.4(4)
C5	25.3(5)	32.8(5)	28.6(5)	-2.3(4)	7.7(4)	2.2(4)
C17	33.8(6)	35.9(6)	38.7(6)	5.5(5)	13.4(5)	4.5(5)
C14	37.6(6)	40.2(6)	39.9(6)	-5.1(5)	19.7(5)	-6.9(5)
C16	34.3(6)	42.6(7)	43.8(6)	3.6(5)	11.1(5)	12.0(5)
C7	40.7(6)	31.9(6)	37.3(6)	-2.6(5)	12.3(5)	-2.4(5)
C15	25.7(5)	47.1(7)	41.3(6)	-10.7(5)	10.9(5)	0.3(5)
C11	39.9(6)	38.9(6)	30.3(5)	1.3(4)	9.1(5)	0.6(5)

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
C10	52.4(8)	59.0(8)	27.9(6)	-2.0(5)	12.4(5)	1.5(6)
C8	53.7(8)	38.6(7)	49.6(7)	-15.6(6)	16.8(6)	-6.2(6)
C9	51.5(8)	63.9(9)	37.6(7)	-20.4(6)	9.1(6)	-5.4(7)
C1	43.5(7)	48.5(8)	56.8(8)	-16.7(6)	14.2(6)	-14.0(6)

Table S4. Bond Lengths in Å for **Amostra_304**.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
O3	C6	1.3499(14)	C2	C1	1.4926(17)
O3	C5	1.4589(13)	C13	C14	1.3823(16)
O2	C6	1.2079(14)	C5	C7	1.5246(16)
O1	C2	1.2085(14)	C5	C11	1.5296(15)
C4	C3	1.3386(15)	C17	C16	1.3883(16)
C4	C12	1.4778(14)	C14	C15	1.3823(18)
C4	C5	1.5127(14)	C16	C15	1.3780(18)
C3	C6	1.4803(15)	C7	C8	1.5298(17)
C3	C2	1.4931(15)	C11	C10	1.5288(17)
C12	C17	1.3918(16)	C10	C9	1.514(2)
C12	C13	1.3940(15)	C8	C9	1.524(2)

Table S5. Bond Angles in ° for **Amostra_304**.

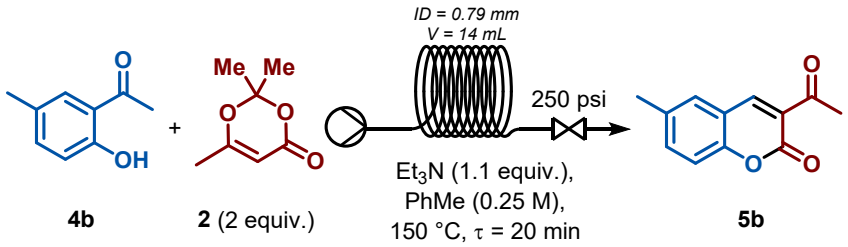
Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
C6	O3	C5	110.36(8)	O2	C6	C3	129.48(10)
C3	C4	C12	128.42(9)	O3	C6	C3	108.59(9)
C3	C4	C5	109.53(9)	C14	C13	C12	119.97(11)
C12	C4	C5	122.05(9)	O3	C5	C4	103.20(8)
C4	C3	C6	108.20(9)	O3	C5	C7	108.40(9)
C4	C3	C2	127.12(10)	C4	C5	C7	112.98(9)
C6	C3	C2	124.51(9)	O3	C5	C11	107.69(9)
C17	C12	C13	119.50(10)	C4	C5	C11	112.92(9)
C17	C12	C4	120.79(9)	C7	C5	C11	111.12(9)
C13	C12	C4	119.71(10)	C16	C17	C12	119.76(11)
O1	C2	C1	122.24(11)	C13	C14	C15	120.45(11)
O1	C2	C3	120.85(10)	C15	C16	C17	120.53(11)
C1	C2	C3	116.81(10)	C5	C7	C8	111.42(10)
O2	C6	O3	121.92(10)	C16	C15	C14	119.79(11)

Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
C10	C11	C5	111.33(10)	C9	C8	C7	111.51(11)
C9	C10	C11	111.29(11)	C10	C9	C8	111.04(11)

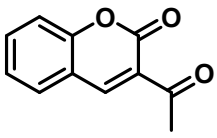
Table S6. Hydrogen Fractional Atomic Coordinates ($\times 10^4$) and Equivalent Isotropic Displacement Parameters ($Å^2 \times 10^3$) for **Amostra_304**. U_{eq} is defined as 1/3 of the trace of the orthogonalised U_{ij}.

Atom	x	y	z	U_{eq}
H13	8277.92	4512.34	4760.45	40
H17	8484.01	2560.23	7724.58	43
H14	10336.89	4108.48	4451.11	45
H16	10520.07	2147.75	7344.42	48
H7A	7139.96	5537.15	7035.37	44
H7B	8507.17	5134.41	8106.23	44
H15	11463.76	2931.84	5750.2	45
H11A	6854.84	3371.34	9410.36	44
H11B	8323.16	3745.09	9644.33	44
H10A	6283.05	4519.07	10738.15	56
H10B	7634.66	4109.99	11833.26	56
H8A	7949.85	6266.47	9472.25	56
H8B	6481.2	5894.48	9241.88	56
H9A	8935.73	5163.15	11166.78	62
H9B	7819.84	5594.48	11801.18	62
H1A	3818.51	2290.09	3033.29	75
H1B	3229.99	2933.22	4018.69	75
H1C	4218.67	2204.35	4883.67	75

5.3 General procedure C: Synthesis of coumarins



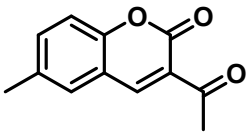
To a volumetric flask (2 mL) were added the desired salicylaldehyde (1.0 equiv., 0.5 mmol), TMD (142 µL, 2.0 equiv., 1.0 mmol) and Et_3N (80 µL, 1.1 equiv., 0.55 mmol) and filled with AcOEt. The mixture was loaded into a HPFA coil (ID: 0.79 mm, 1 mL) and pumped to a reactor of HPFA (V = 18.0 mL) with a flow of 0.900 mL/min at 150 ºC and back pressure regulator of 250 psi. The crude obtained was purified through column chromatography (dry load).



3-acetyl-2H-chromen-2-one (**5a**)[4]**:** Compound **5a** was prepared according to general procedure C using 2-hydroxybenzaldehyde (61.1 mg, 1.0 equiv., 0.5 mmol) as substrate. The compound was purified through column chromatography (SiO_2, Hex:AcOEt) to afford a white solid (46.6 mg, 0.2475 mmol, 99%), m.p. 120-122 ºC.

^{1}H NMR (500 MHz, $CDCl_3$): 8.52 (s, 1H), 7.71-7.61 (m, 2H), 7.42-7.30 (m, 2H), 2.74 (s, 3H).

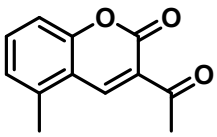
^{13}C NMR (125 MHz, $CDCl_3$): 195.5; 159.3; 155.4; 147.5; 134.4; 130.3; 125.0; 124.5; 118.3; 116.7; 30.6



3-acetyl-6-methyl-2*H*-chromen-2-one (**5b**)[5]**:** Compound **5b** was prepared according to general procedure C using 2-hydroxy-5-methylbenzaldehyde (68.1 mg, 1.0 equiv., 0.5 mmol) as substrate. The compound was purified through column chromatography (SiO_2, Hex:AcOEt) to afford a white solid (48.5 mg, 0.24 mmol, 96%), m.p. 127-129 ºC.

^{1}H NMR (400 MHz, $CDCl_3$): 8.39 (s, 1H); 7.42-7.33 (m, 2H), 7.23-7.17 (m, 1H), 2.65 (s, 3H), 2.36 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): 195.7; 159.5; 153.5; 147.5; 135.6; 134.8; 129.8; 124.4; 118.0; 116.4; 30.6; 20.7.

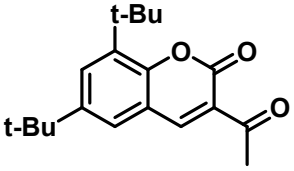


3-acetil-5-methyl-2*H*-chromen-2-one (**5c**)[6]**:** Compound **5c** was prepared according to general procedure C using 2-hydroxy-6-methylbenzaldehyde (68 mg, 1.0 equiv., 0.5 mmol)

as substrate. The compound was purified through column chromatography (SiO_2, Hex:AcOEt 9:1, rf = 0.3, UV = 254 nm) to afford a white solid (28 mg, 0.138 mmol, 55%), m.p. 119-121 ºC.

^{1}H NMR (400 MHz, $CDCl_3$): 8.47 (s, 1H), 7.48 (t, J = 7.8 Hz, 2H); 7.22 (t, J = 7.8 Hz, 1H), 2.72 (s, 3H), 2.47 (s, 3H).

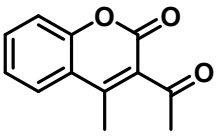
^{13}C NMR (100 MHz, $CDCl_3$): 195.8; 159.5; 153.8; 148.0; 135.8; 128.0; 126.4; 124.7; 124.3; 118.1; 30.7; 15.5.



3-acetyl-6,8-di-*tert*- butyl-2*H*-chromen-2-one (**5d**)[7]**:** Compound **5d** was prepared according to general procedure C using 3,5-di-*tert*-butyl-2-hydroxybenzaldehyde (117.2 mg, 1.0 equiv., 0.5 mmol) as substrate. The compound was purified through column chromatography (SiO_2, Hex:AcOEt) to afford a white solid (67.5 mg, 0.225 mmol, 90%), m.p. 150-153 ºC.

^{1}H NMR (500 MHz, $CDCl_3$): 8.50 (s, 1H), 7.69 (d, J = 2.1 Hz, 1H), 7.45 (d, J = 2.1 Hz, 1H), 2.72 (s, 3H), 1.52 (s, 9H), 1.35 (s, 9H).

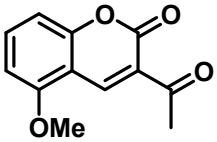
^{13}C NMR (125 MHz, $CDCl_3$): 195.7; 159.2; 152.3; 148.9; 147.4; 137.4; 129.9; 124.7; 123.2; 118.3; 35.2; 34.7; 30.6; 29.8.



3-acetyl-4-methyl-2*H*-chromen-2-one (**5e**)[8]**:** Compound **5e** was prepared according to general procedure C using 2-hydroxybenzaldehyde (61 mg, 1.0 equiv., 0.5 mmol) as substrate. The compound was purified through column chromatography (SiO_2, Hex:AcOEt) to afford a white solid (25 mg, 0.125 mmol, 50%), m.p. 97-98 ºC.

^{1}H NMR (400 MHz, $CDCl_3$): 7.68-7.59 (m, 1H), 7.56-7.46 (m, 1H), 7.32-7.21 (m, 2H), 2.52 (s, 3H), 2.39 (s, 3H).

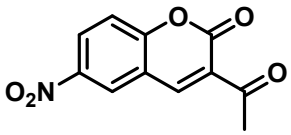
^{13}C NMR (100 MHz, $CDCl_3$): 200.7; 158.8; 152.9; 150.4; 132.8; 127.4; 125.7 124.7; 119.7; 117.1; 31.2; 15.5.



3-acetyl-5-methoxy-2*H*-chromen-2-one (**5f**)[9]**:** Compound **5f** was prepared according to general procedure C using 2-hydroxy-6-methoxybenzaldehyde (76.1 mg, 1.0 equiv., 0.5 mmol) as substrate. The compound was purified through column chromatography (SiO_2, Hex:AcOEt) to afford a white solid (28 mg, 0.13 mmol, 51%), m.p. 150-152 ºC.

^{1}H NMR (500 MHz, $CDCl_3$): 8.90 (s, 1H), 7.55 (t, J = 8.4 Hz, 1H), 6.93 (d, J = 8.4 Hz, 1H), 6.73 (d, J = 8.3 Hz,1H), 3.96 (s, 3H), 2.71 (s, 3H).

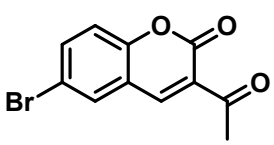
^{13}C NMR (125 MHz, $CDCl_3$): 195.5; 159.4; 158.1; 156.3; 143.2; 135.4; 122.3; 109.5; 108.7; 105.4; 30.6.



3-acetyl-6-nitro-2*H*-chromen-2-one (**5g**)[7]**:** Compound **5g** was prepared according to general procedure C using 2-hydroxy-5-nitrobenzaldehyde (83.6 mg, 1.0 equiv., 0.5 mmol) as substrate. The compound was purified through column chromatography (SiO_2, Hex:AcOEt) to afford a white solid (19 mg, 0.055 mmol, 31%), m.p. 194-196 ºC.

^{1}H NMR (400 MHz, $CDCl_3$): 8.66-8.42 (m, 3H), 7.52 (d, J = 9.2 Hz, 1H), 2.74 (s, 3H).

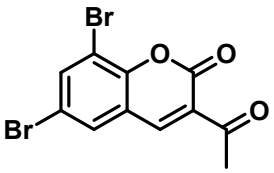
13C NMR (100 MHz, $CDCl_3$): 194.3; 158.4; 157.6; 145.9; 144.4; 128.6; 126.4; 125.8; 118.2; 30.5.



3-acetyl-6-bromo-2*H*-chromen-2-one (**5h**)[5]**:** Compound **5h** was prepared according to general procedure C using 5-bromo-2-hydroxybenzaldehyde (101 mg, 1.0 equiv., 0.5 mmol) as substrate. The compound was purified through column chromatography (SiO_2, Hex:AcOEt) to afford a light-yellow solid (56.5 mg, 0.21 mmol, 85%), m.p. 218-220 ºC.

^{1}H NMR (500 MHz, DMSO-d6): 8.60 (s, 1H), 8.21 (d, J = 2.5 Hz, 1H), 7.89 (dd, J = 8.8 Hz, 2.5 Hz, 1H), 7.44 (d, J = 8.8 Hz, 1H), 2.58 (s, 3H).

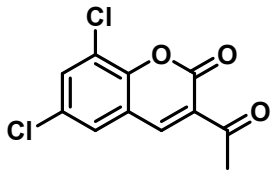
^{13}C NMR (126 MHz, DMSO-d6): 194.9, 158.0, 153.6, 145.6, 136.6, 132.5, 125.4, 120.0, 118.4, 116.3, 30.0.



3-acetyl-6,8-dibromo-2*H*-chromen-2-one (**5i**)[10]**:** Compound **5i** was prepared according to general procedure C using 3,5-dibromo-2-hydroxybenzaldehyde (140 mg, 1.0 equiv., 0.5 mmol) as substrate. The compound was purified through column chromatography (SiO_2, Hex:AcOEt) to afford a light-yellow solid (27 mg, 0.0775 mmol, 31%), m.p. 220-222 ºC.

^{1}H NMR (600 MHz, $CDCl_3$): 8.35 (s, 1H), 7.98 (d, J = 2.2 Hz, 1H), 7.73 (d, J = 2.2 Hz, 1H), 2.72 (s, 3H).

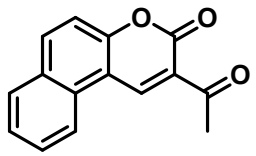
^{13}C NMR (150 MHz, $CDCl_3$): 195.2; 158.5; 149.8; 146.0; 134.8; 131.1; 128.0; 126.9; 123.2; 121.0; 31.2.



3-acetyl-6,8-dichloro-2*H*-chromen-2-one (**5j**)[11]**:** Compound **5j** was prepared according to general procedure C using 3,5-dichloro-2-hydroxybenzaldehyde (95.5 mg, 1.0 equiv., 0.5 mmol) as substrate. The compound was purified through column chromatography (SiO_2, Hex:AcOEt) to afford a light-yellow solid (18 mg, 0.07 mmol, 28%), m.p. 174-177 ºC.

^{1}H NMR (400 MHz, $CDCl_3$): 8.38 (s, 1H), 7.69 (d, J = 2.4 Hz, 1H), 7.54 (d, J = 2.4 Hz, 1H), 2.73 (s, 3H).

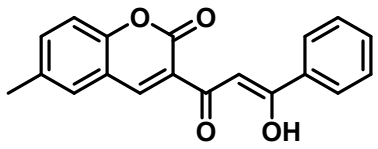
^{13}C NMR (100 MHz, $CDCl_3$): 194.6; 157.5; 149.5; 145.7; 134.0; 130.1; 127.6; 126.1; 122.8; 120.0; 30.5.



2-acetyl-3*H*- benzo[*f*]chromen-3-one (**5k**)[7]**:** Compound **5k** was prepared according to general procedure C using 2-hydroxy-1-naphthaldehyde (86 mg, 1.0 equiv., 0.5 mmol) as substrate. The compound was purified through column chromatography (SiO_2, Hex:AcOEt) to afford a white solid (57.8 mg, 0.2425 mmol, 97%), m.p. 191-194 ºC.

^{1}H NMR (400 MHz, $CDCl_3$): 9.32 (s, 1H), 8.37 (d, J = 8.4 Hz, 1H), 8.10 (d, J = 9.0 Hz, 1H), 7.93 (d, J = 8.1 Hz, 1H), 7.75 (ddd, J = 8.4, 7.0, 1.3 Hz, 1H), 7.62 (ddd, J = 8.1, 7.0, 1.0 Hz), 7.48 (d, J = 9.0 Hz, 1H), 2.79 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): 195.6; 159.5; 143.3; 136.3; 129.9; 129.3; 129.2; 126.7; 122.5; 121.7; 116.6; 112.8; 30.7.

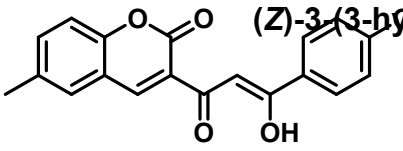


(*Z*)-3-(3-hydroxy-3-phenylacryloyl)-6-methyl-2*H*-chromen-2-one (**5l**): Compound **5l** was prepared according to general procedure C using 2-hydroxy-5-methylbenzaldehyde (68.1 mg, 1.0 equiv., 0.5 mmol) as substrate. The compound was purified through column chromatography (SiO_2, Hex:AcOEt) to afford a yellow solid (78 mg, 0.2475 mmol, 99%), m.p. 180-182 ºC.

^{1}H NMR (500 MHz, $CDCl_3$): 16.64 (s, 1H), 8.69 (s, 1H), 8.06 (d, J = 8.3 Hz, 2H), 7.79 (d, J = 8.3 Hz, 1H), 7.62-7.54 (m, 1H), 7.53-7.43 (m, 4H), 7.32-7.27 (m, 1H), 2.44 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): 190.3; 175.1; 158.5; 152.8; 145.7; 135.9; 135.3; 134.8; 133.0; 129.3; 128.7; 127.9; 120.9; 118.4; 116.4; 97.9; 20.8.

HRMS (ES) calc. for $[M+H]^+$ $C_{19}H_{15}O_4$: 307.0970, found: 307.0974.

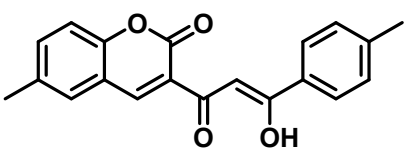


(*Z*)-3-(3-hydroxy-3-(4-methoxyphenyl) acryloyl)-6-methyl-2*H*-chromen-2-one (**5m**)**:** Compound **5m** was prepared according to the general procedure C using 2-hydroxy-5-methylbenzaldehyde (68.1 mg, 1.0 equiv., 0.5 mmol) as substrate. The compound was purified through column chromatography (SiO_2, Hex: AcOEt, 4:1) to afford a yellow solid (81.6 mg, 0.2425 mmol, 97%), m.p. 165-169 ºC.

^{1}H NMR (500 MHz, $CDCl_3$): 8.68 (s, 1H), 8.06 (d, *J* = 8.9 Hz, 2H), 7.75 (s, 1H), 7.45 (d, *J* = 6.8 Hz, 2H), 7.29 (*s*, 1H), 6.99 (d, *J* = 8.9 Hz, 2H), 3.90 (s, 3H), 2.44 (s, 3H).

13C NMR (126 MHz, CDCl3): 190.3, 173.4, 163.9, 158.7, 152.8, 145.3, 135.2, 134.9, 132.0, 130.3, 129.3, 128.8, 121.1, 116.5, 114.2, 97.6, 55.7, 20.9.

HRMS (ES) calc. for $[M+H]^+$ $C_{20}H_{17}O_5$: 337.1076, found: 337.1076.

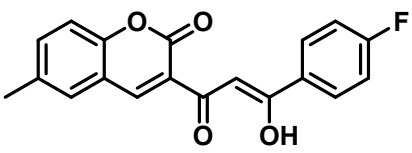


(*Z*)-3-(3-hydroxy-3-(p-tolyl)acryloyl)-6-methyl-2H-chromen-2-one (**5n**): Compound **5n** was prepared according to the general procedure C using 2-hydroxy-5-methylbenzaldehyde (68.1 mg, 1.0 equiv., 0.5 mmol) as substrate. The compound was purified through column chromatography (SiO_2, Hex: AcOEt, 4:1) to afford a pale-yellow solid (73.7 mg, 0.23 mg, 92%), m.p. 179-184 ºC.

^{1}H NMR (500 MHz, $CDCl_3$): 8.68 (s, 1H), 7.96 (d, J = 8.2 Hz, 2H), 7.77 (s, 1H), 7.49 – 7.39 (m, 2H), 7.32 – 7.26 (m, 3H), 2.44 (s, 6H).

^{13}C NMR (126 MHz, $CDCl_3$): 190.6, 174.6, 158.7, 152.9, 145.6, 144.1, 135.3, 134.9, 133.4, 129.6, 129.4, 128.1, 121.2, 118.6, 116.5, 97.8, 21.9, 20.9.

HRMS (ES) calc. for $[M+H]^+$ $C_{20}H_{17}O_4$: 321.1127, found: 321.1127.



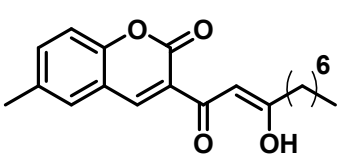
(*Z*)-3-(3-(4-fluorophenyl)-3-hydroxyacryloyl)-6-methyl-2*H*-chromen-2- one (**5o**)**:** Compound **5o** was prepared according to the general procedure C using 2-hydroxy-5-methylbenzaldehyde (68.1 mg, 1.0 equiv., 0.5 mmol) as substrate. The compound was purified through column chromatography (SiO_2, Hex: AcOEt, 4:1) to afford a pale-yellow solid (66.9 mg, 0.205 mmol, 82%), m.p. 195-199 ºC.

^{1}H NMR (500 MHz, CDCl3): 8.72 (s, 1H), 8.11 (dd, J = 8.9, 5.4 Hz, 2H), 7.79 (s, 1H), 7.51 – 7.46 (m, 2H), 7.33 (s, 1H), 7.20 (t, J = 8.6 Hz, 2H), 2.47 (s, 3H).

^{13}C NMR (126 MHz, CDCl3) δ 189.5 (s), 174.6 (s), 165.9 (d, J = 254.8 Hz), 158.6 (s), 152.9 (s), 145.8 (s), 135.5 (s), 135.0 (s), 132.4 (d, J = 3.0 Hz), 130.6 (d, J = 9.3 Hz), 129.4 (s), 120.8 (s), 118.5 (s), 116.5 (s), 116.0 (d, J = 21.9 Hz), 97.7 (s), 20.9 (s).

^{19}F NMR (471 MHz, $CDCl_3$): -105.32.

HRMS (ES) calc. for $[M+H]^+$ $C_{19}H_{14}O_4F$: 325.0876, found: 325.0870.



(*Z*)-3-(3-hydroxydec-2-enoyl)-6-methyl-2*H*-chromen-2-one (**5p**): Compound 5p was prepared according to the general procedure C using 2-hydroxy-5-methylbenzaldehyde (68.1 mg, 1.0 equiv., 0.5 mmol) as substrate. The compound was purified through column chromatography (SiO_2, Hex: AcOEt, 4:1) to afford a white solid (60.9 mg, 0.1850 mmol, 74%), m.p. 94-96 ºC.

^{1}H NMR (400 MHz, $CDCl_3$): 8.60 (s, 1H), 7.46 – 7.40 (m, 2H), 7.27 (s, 1H), 7.02 (s, 1H), 2.50 (t, 2H), 2.43 (s, 3H), 1.39 – 1.23 (m, 10H), 0.88 (t, *J* = 6.9 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): 211.1, 192.2, 163.4, 145.5, 135.2, 132.9, 129.3, 124.5, 116.5, 109.3, 101.2, 60.1, 40.9, 31.8, 29.4, 29.2, 25.6, 22.8, 20.9, 14.2.

HRMS (ES) calc. for $[M+H]^+$ $C_{20}H_{25}O_4$: 329.1753, found: 329.1756.

6.PROPOSAL MECHANISMS

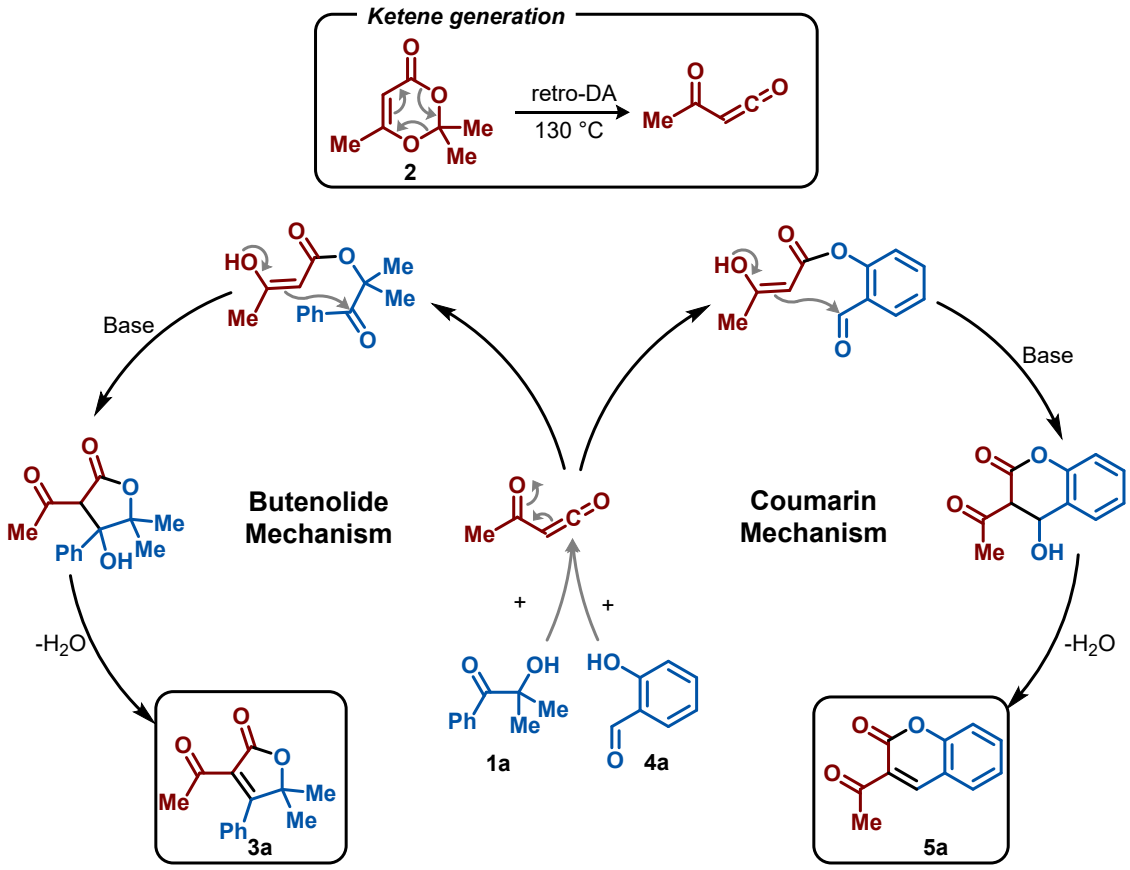


Figure S4: Proposal mechanism for synthesis of butenolide and coumarin.

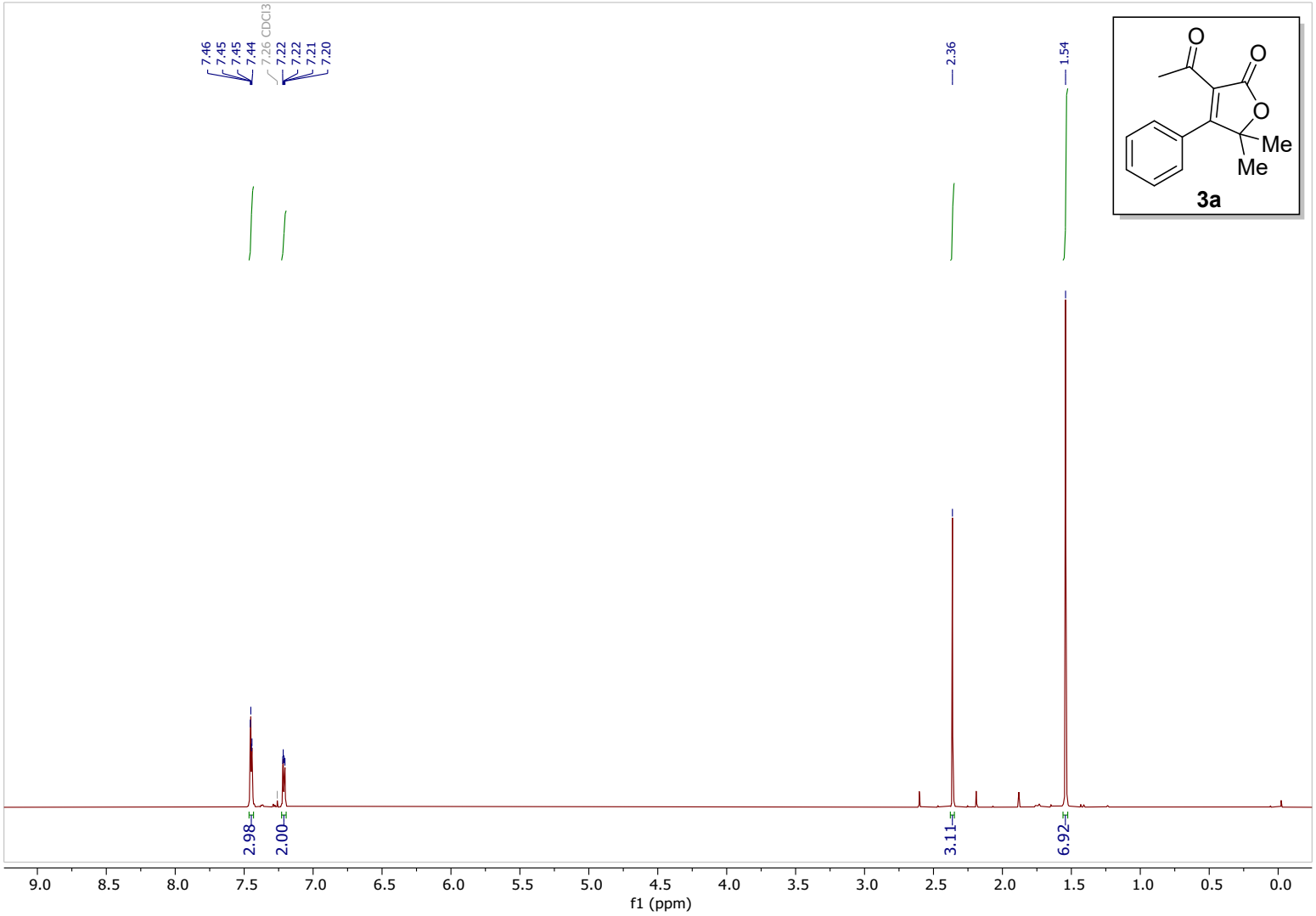
7. REFERENCES

1 B. J. Huffman, S. Chen, J. L. Schwarz, R. E. Plata, E. N. Chin, L. L. Lairson, K. N. Houk and R. A. Shenvi, *Nat. Chem.*, 2020, **12**, 310–317.
2 United States, US20110065962A1, 2011.
3 Q. Zhang, Y. Li, B. Zhao, L. Xu, H. Ma and M. Wang, *Molecules*, 2022, **27**, 6541.
4 S. Gond, A. Kumar Singh, P. Yadav, P. Kumar, S. Srikrishna and V. P. Singh, *Journal of Photochemistry and Photobiology A: Chemistry*, 2024, **454**, 115744.
5 L. Chen, Q. Lv, J. Cai, J. Liang, Z. Liang, J. Lin, Y. Xiao, R. Chen, Z. Zhang, Y. Hong and H. Ji, *Front. Pharmacol.*, 2023, **14**, DOI:10.3389/fphar.2023.1141121.
6 P. Kisanga, X. Fei and J. Verkade, *Synthetic Communications*, 2002, **32**, 1135–1144.
7 K. D. Dhawale, A. P. Ingale, M. S. Pansare, S. S. Gaikwad, N. M. Thorat and L. R. Patil, *Polycyclic Aromatic Compounds*, 2023, **43**, 3588–3600.
8 V. N. Toan and N. D. Thanh, *Med Chem Res*, 2021, **30**, 1868–1885.
9 B.-F. Ruan, H.-J. Cheng, J. Ren, H.-L. Li, L.-L. Guo, X.-X. Zhang and C. Liao, *European Journal of Medicinal Chemistry*, 2015, **103**, 185–190.
10 S. Rahimi, M. Ghandi, M. Fallahnezhad and A. Abbasi, *Mol Divers*, 2024, **28**, 133–142.
11 A. Varluvothu, K. Vaarla, K. Vermeire and P. Leelavathi, *Journal of Heterocyclic Chemistry*, 2022, **59**, 1604–1615.

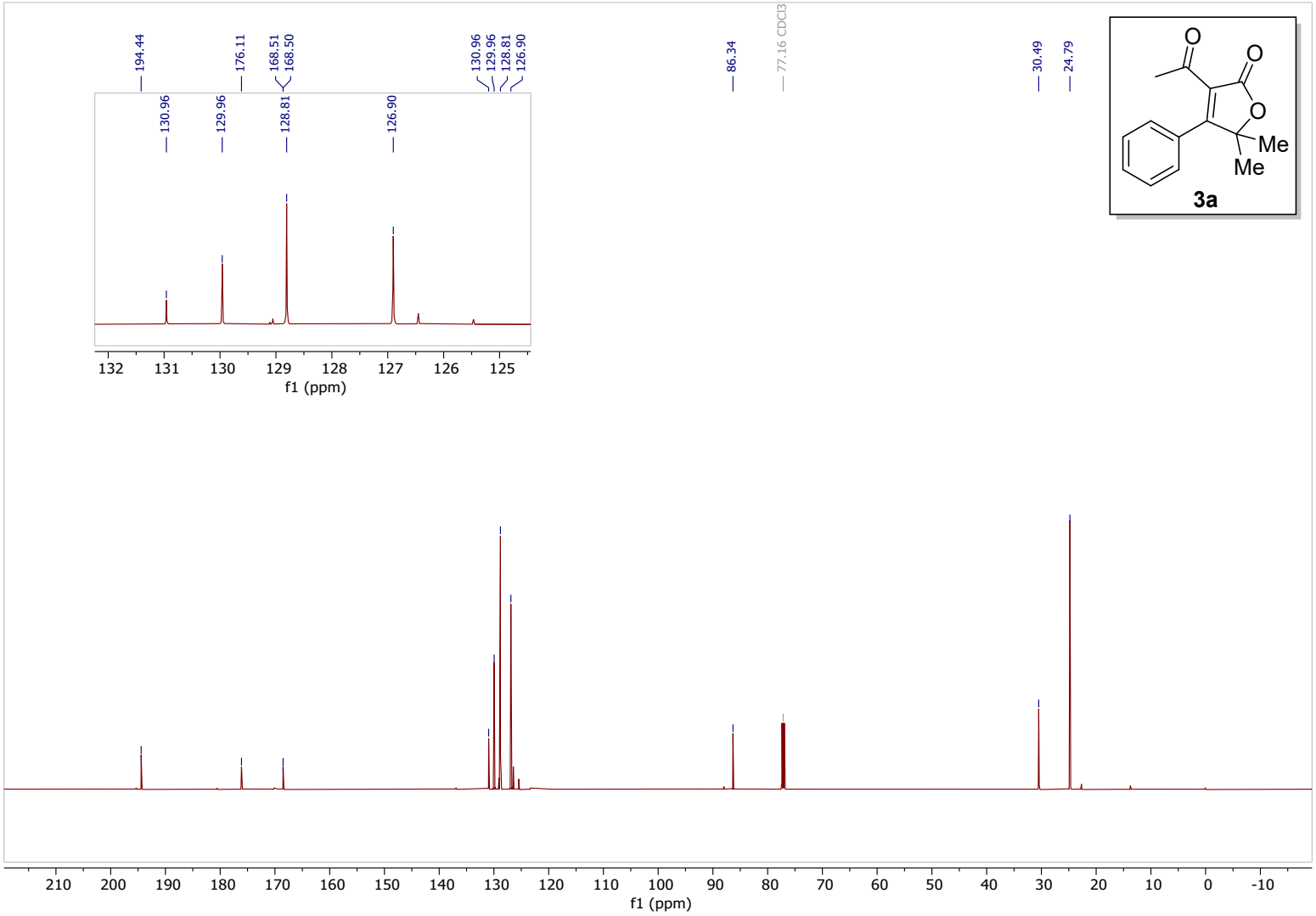
7. NMR DATA

7.1 NMR of butenolides

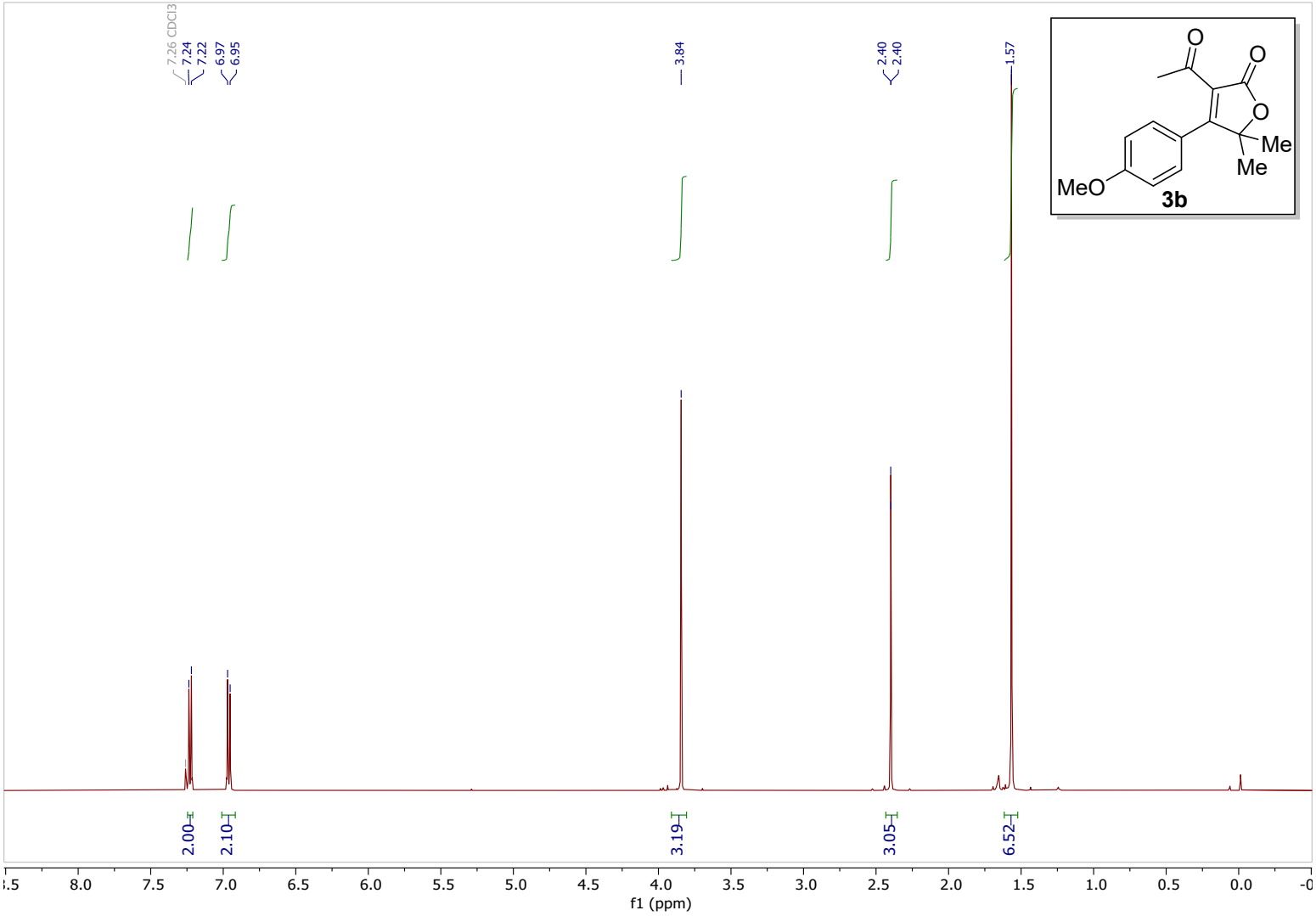
^{1}H NMR (600 MHz, $CDCl_3$) – **3a**



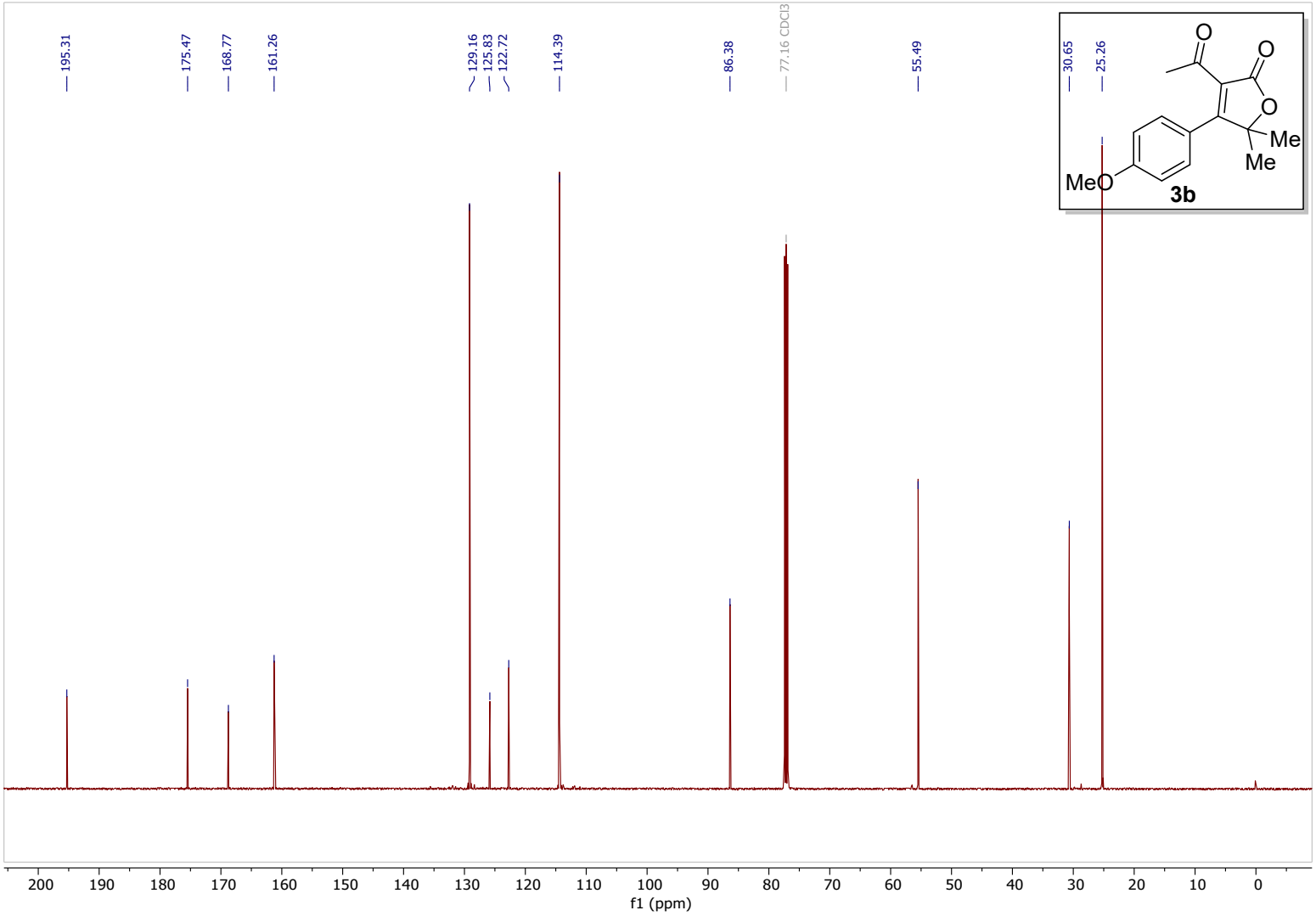
^{13}C NMR (125 MHz, $CDCl_3$) – **3a**



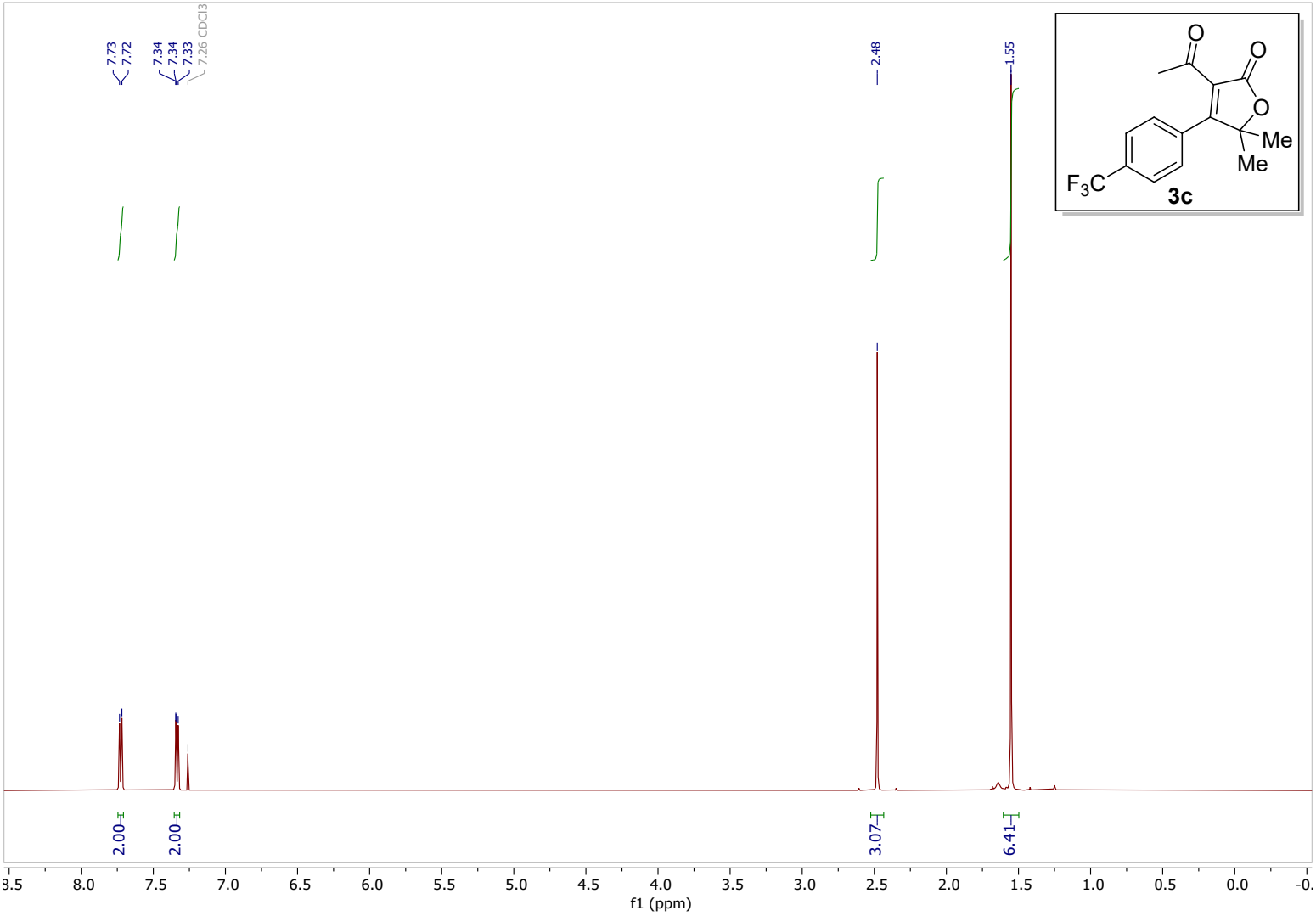
^{1}H NMR (500 MHz, $CDCl_3$) – **3b**



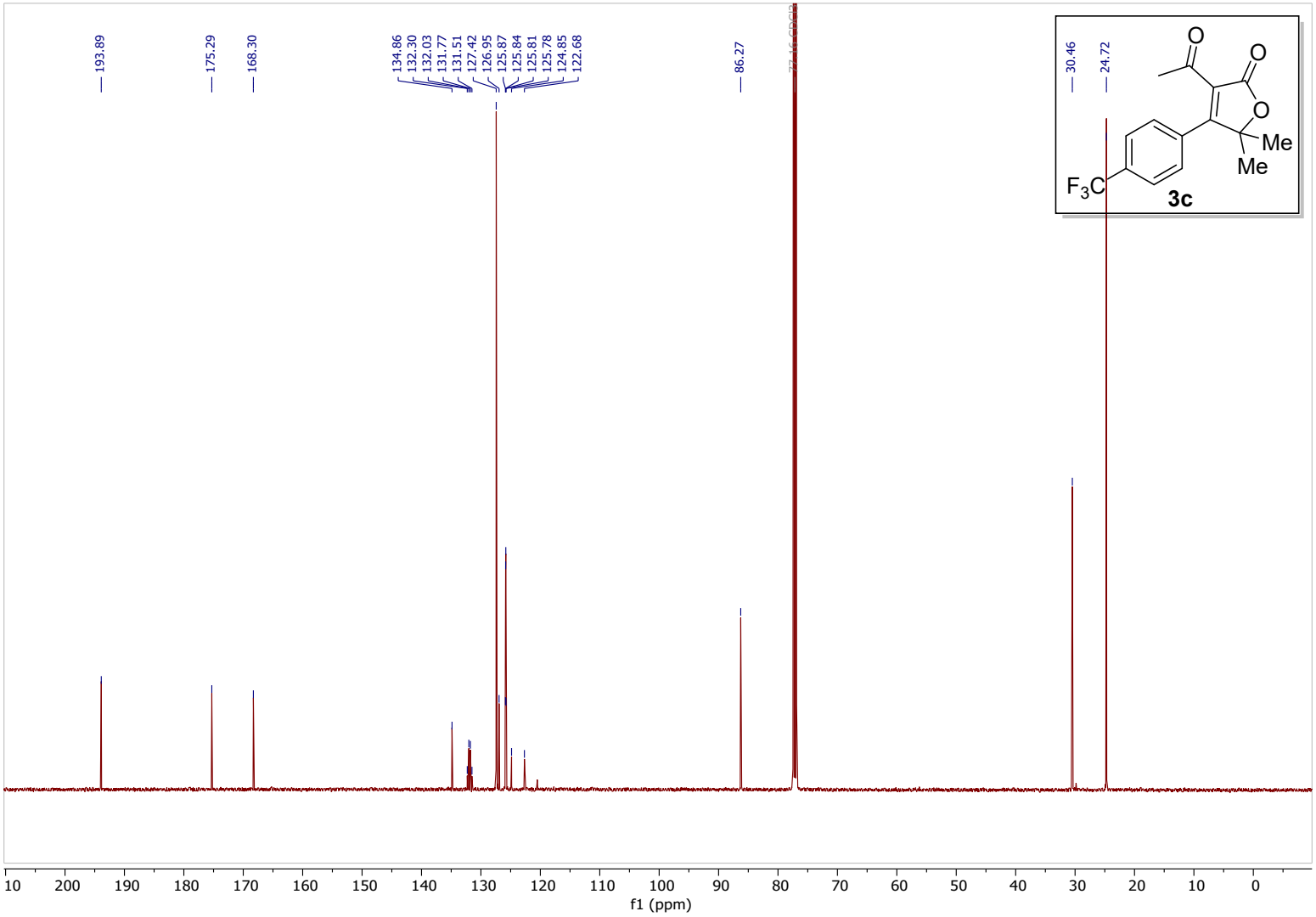
^{13}C NMR (125 MHz, $CDCl_3$) – **3b**



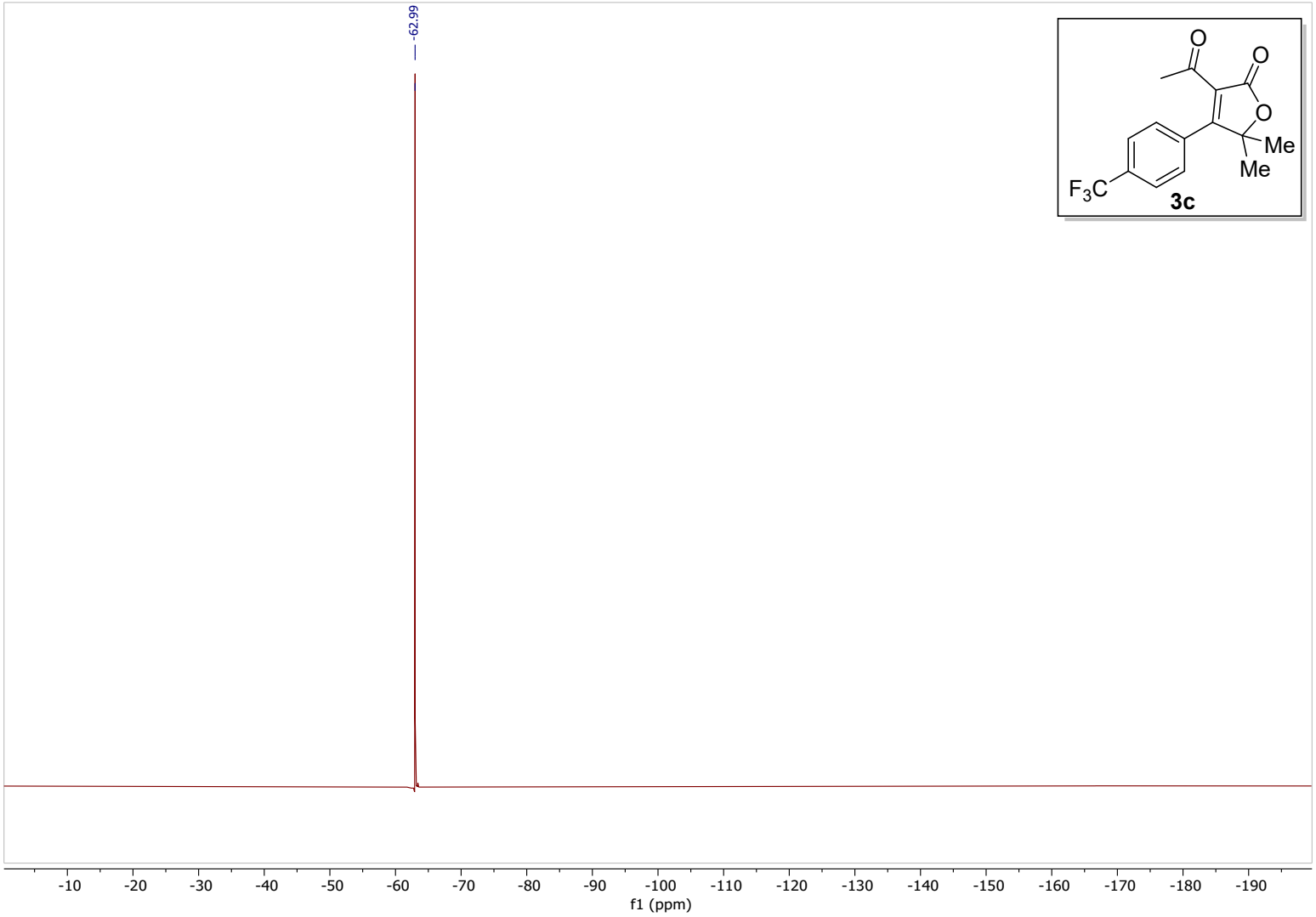
^{1}H NMR (125 MHz, $CDCl_3$) – **3c**



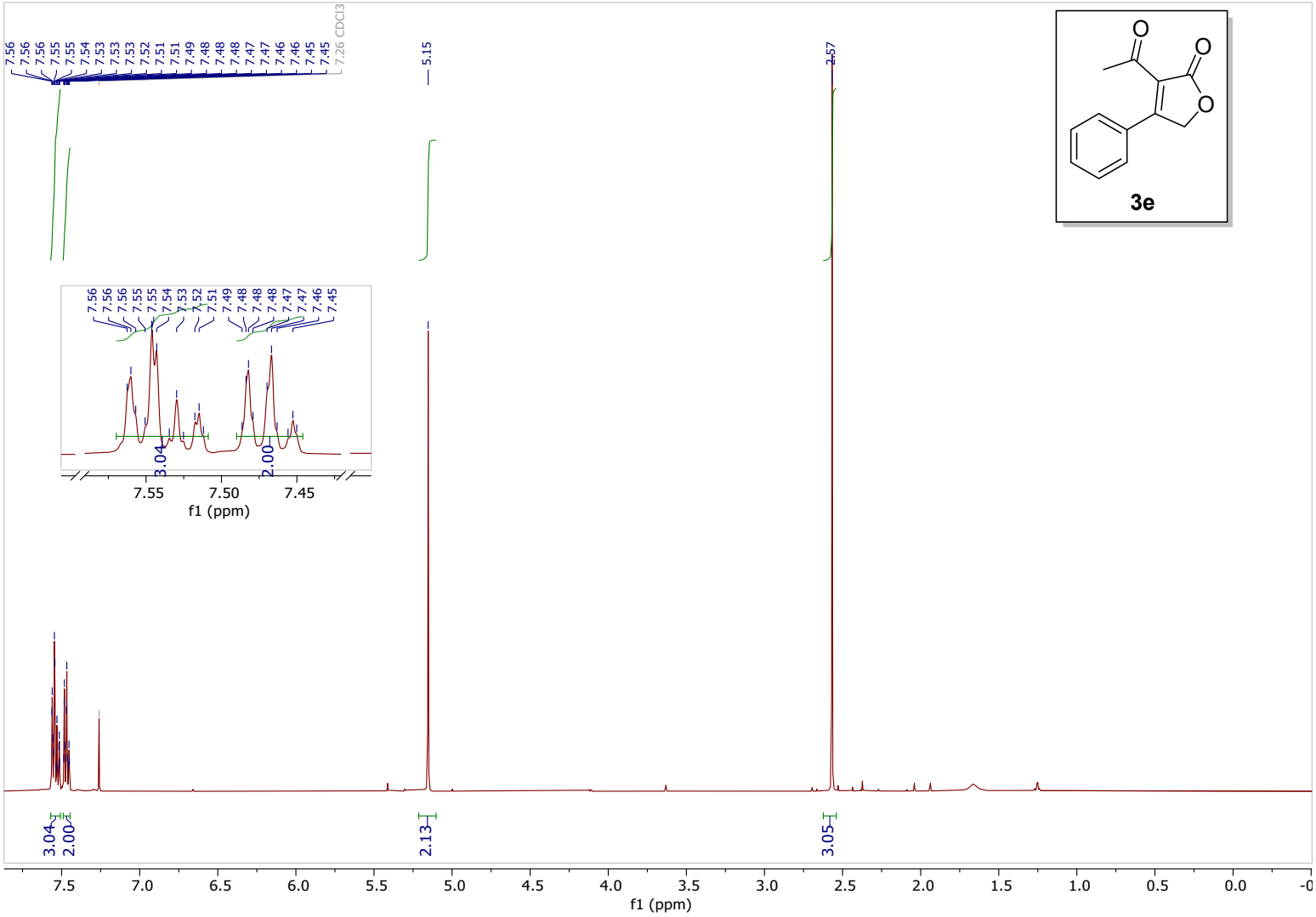
^{13}C NMR (125 MHz, $CDCl_3$) – **3c**



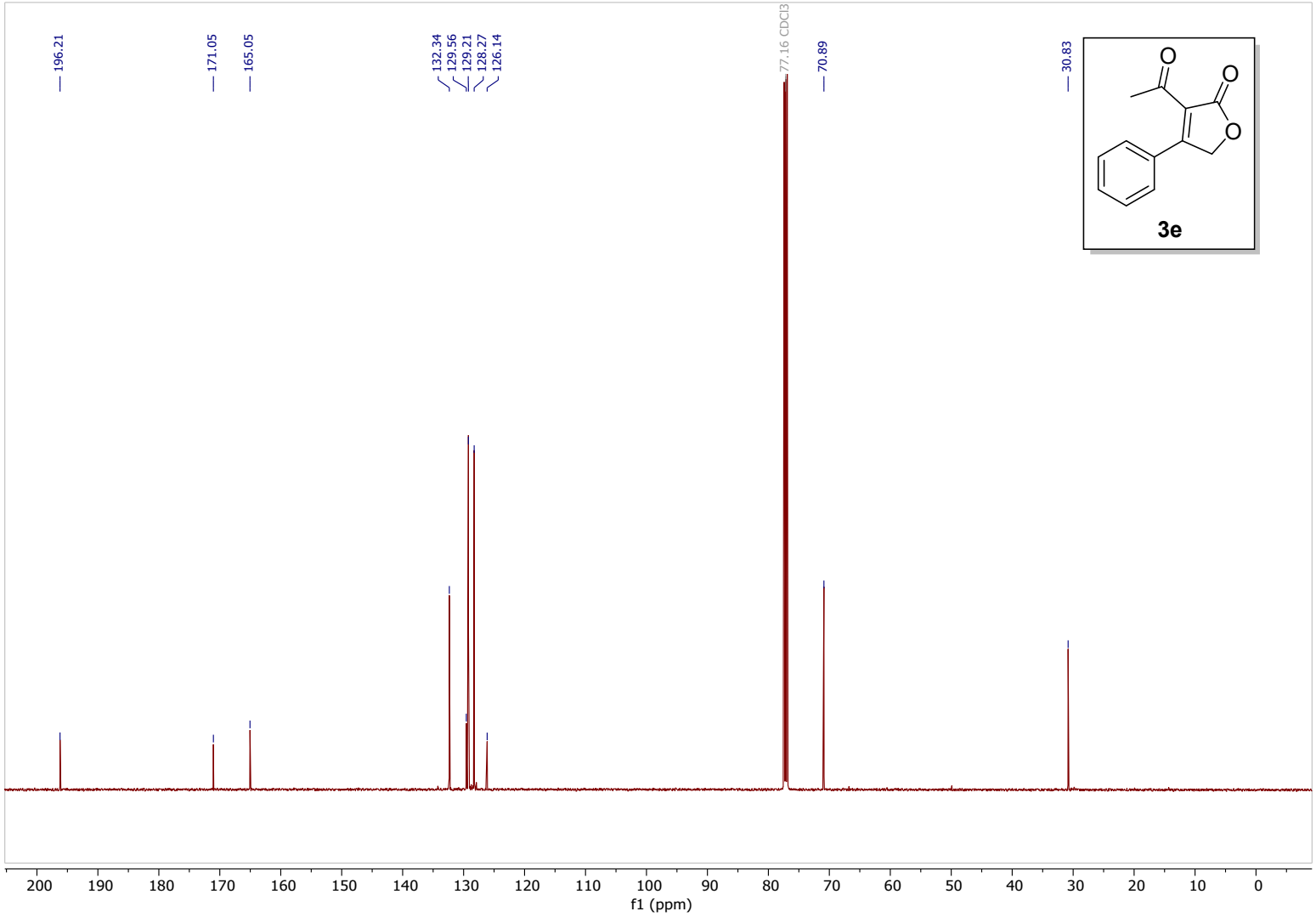
19F NMR (500 MHz, $CDCl_3$): **3c**



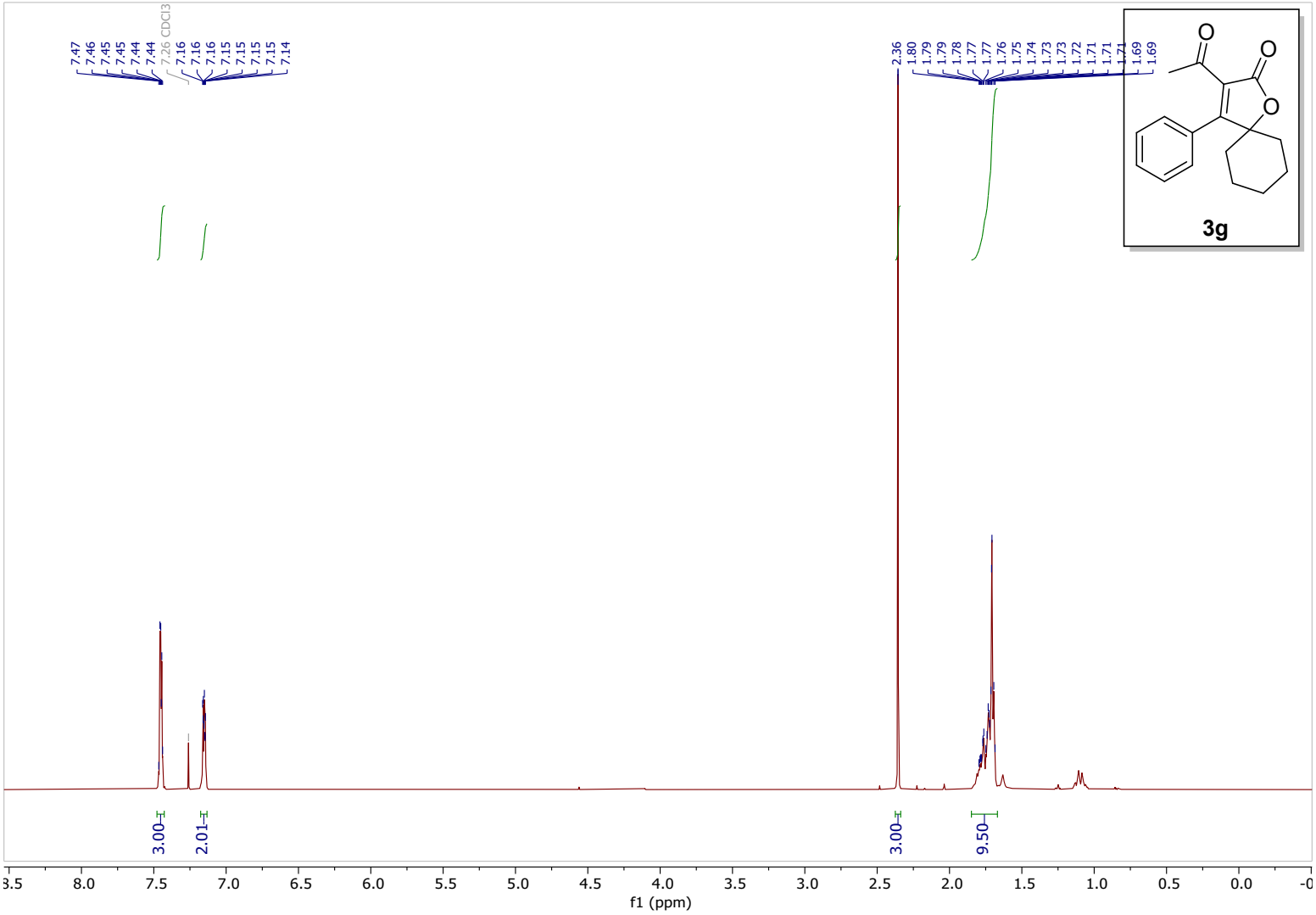
^{1}H NMR (500 MHz, $CDCl_3$) – **3e**



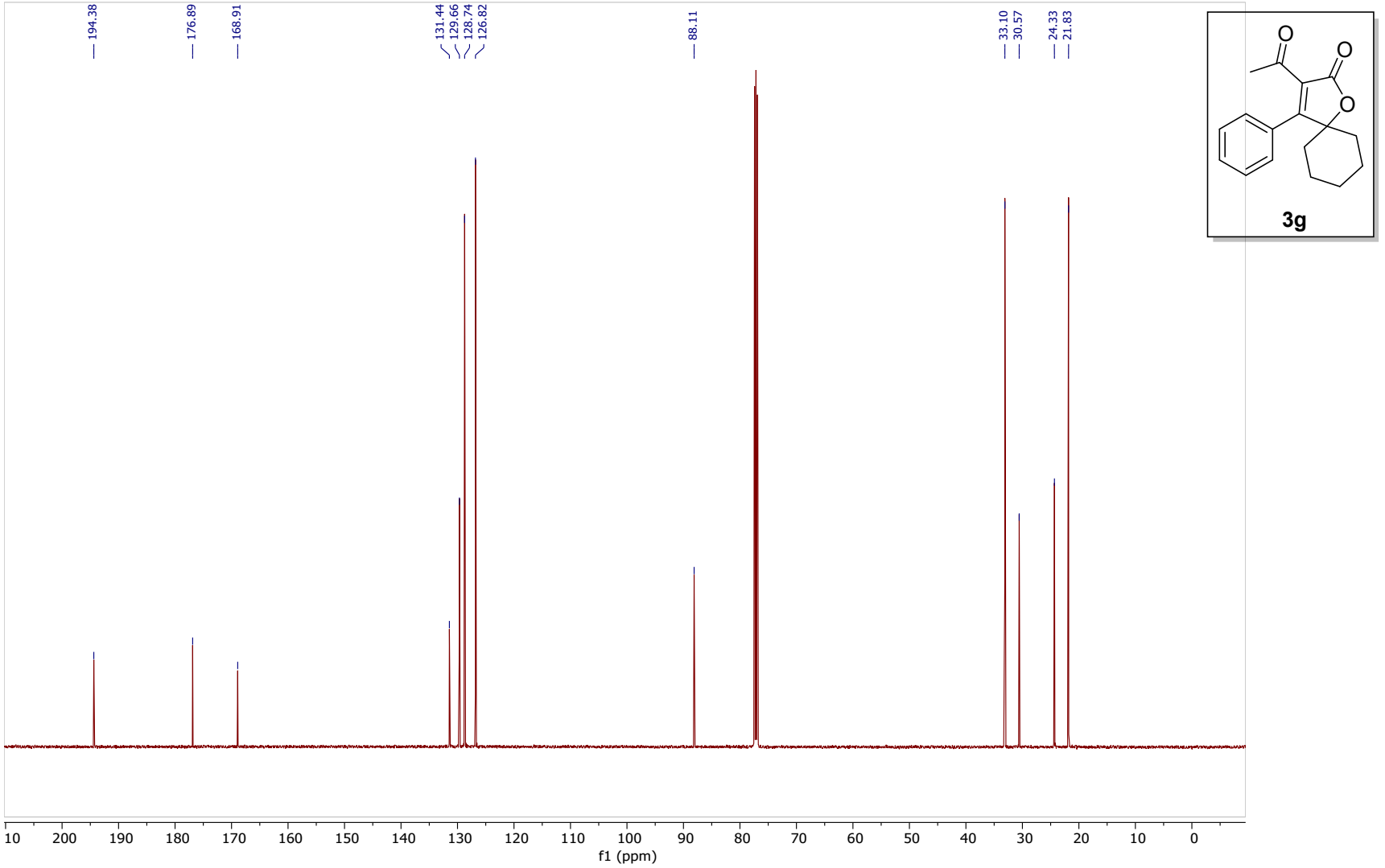
^{13}C NMR (125 MHz, $CDCl_3$) – **3e**



^{1}H NMR (500 MHz, $CDCl_3$) – **3g**

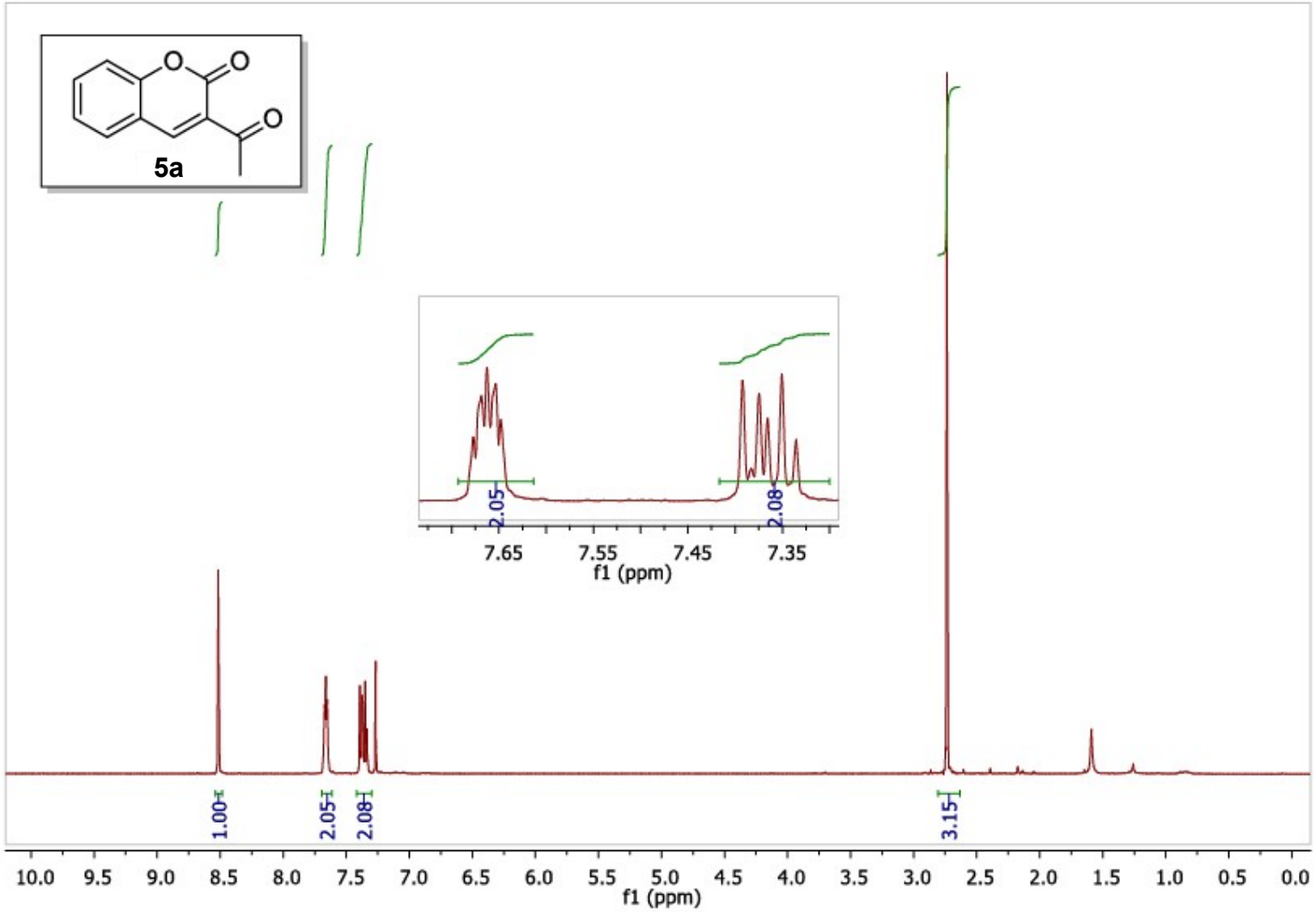


^{13}C NMR (125 MHz, $CDCl_3$) – **3g**

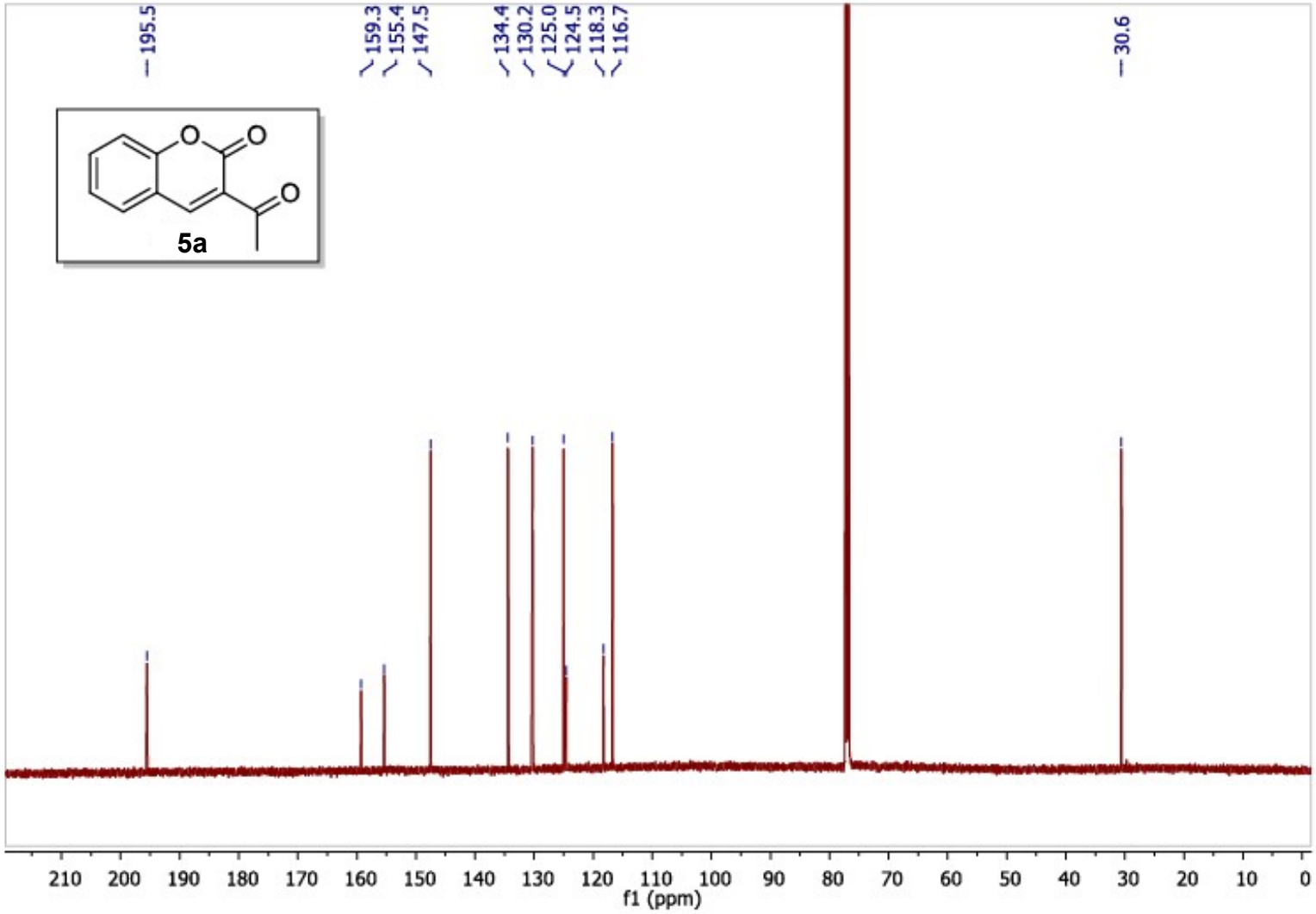


7.2 NMR of coumarins

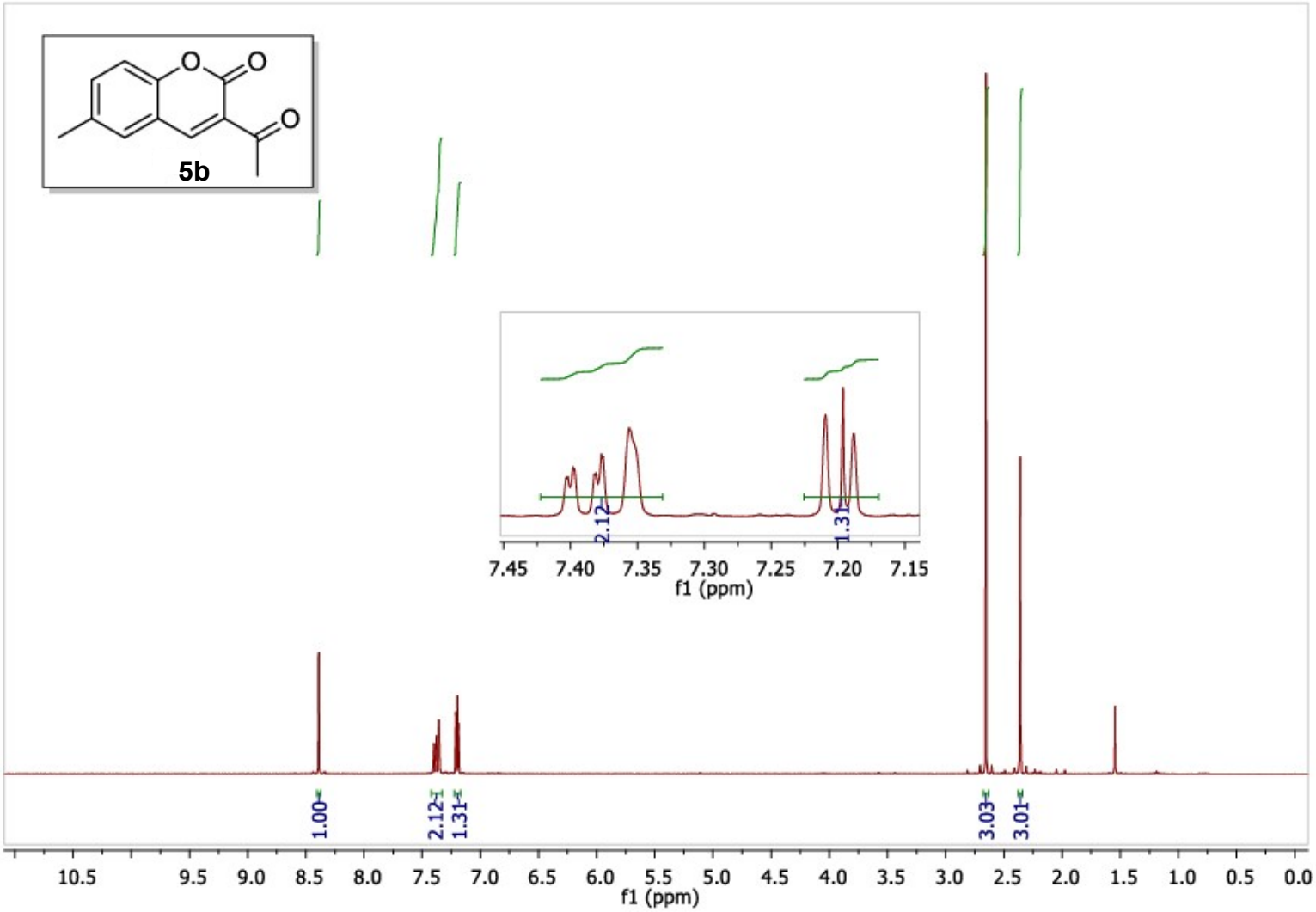
^{1}H NMR (500 MHz, $CDCl_3$) – **5a**



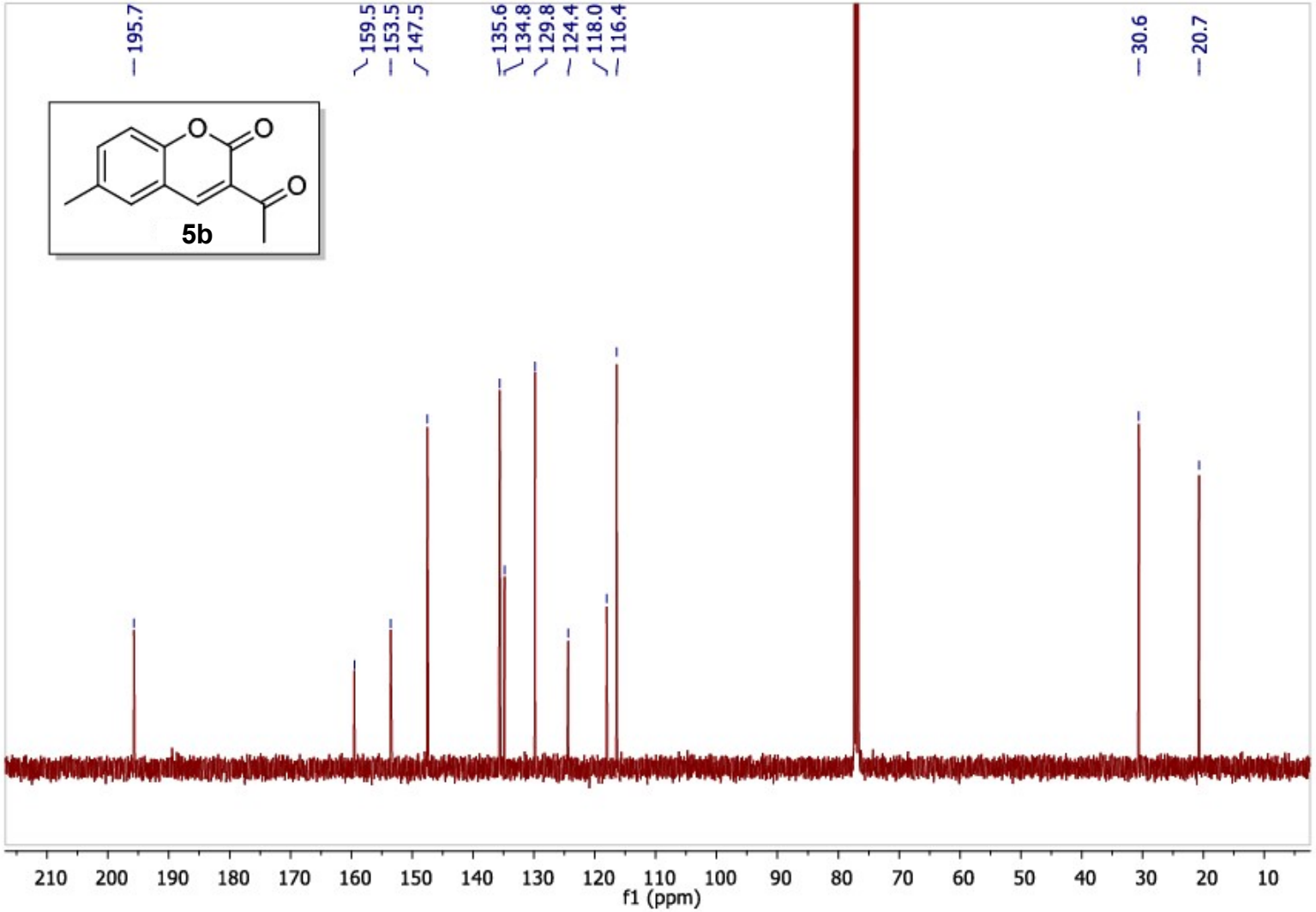
^{13}C NMR (125 MHz, $CDCl_3$) – **5a**



^{1}H NMR (400 MHz, $CDCl_3$) – **5b**



^{13}C NMR (100 MHz, $CDCl_3$) – **5b**



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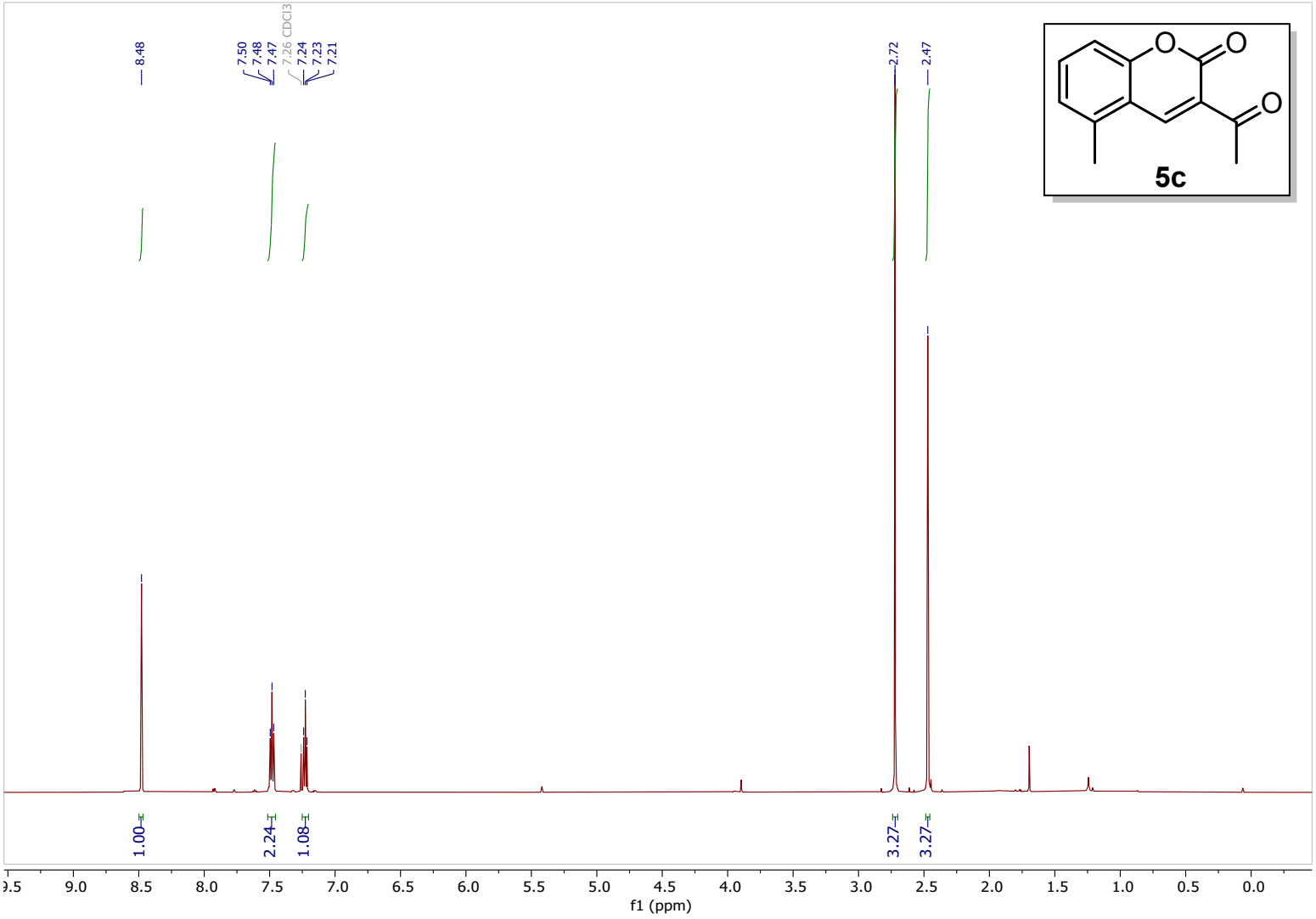
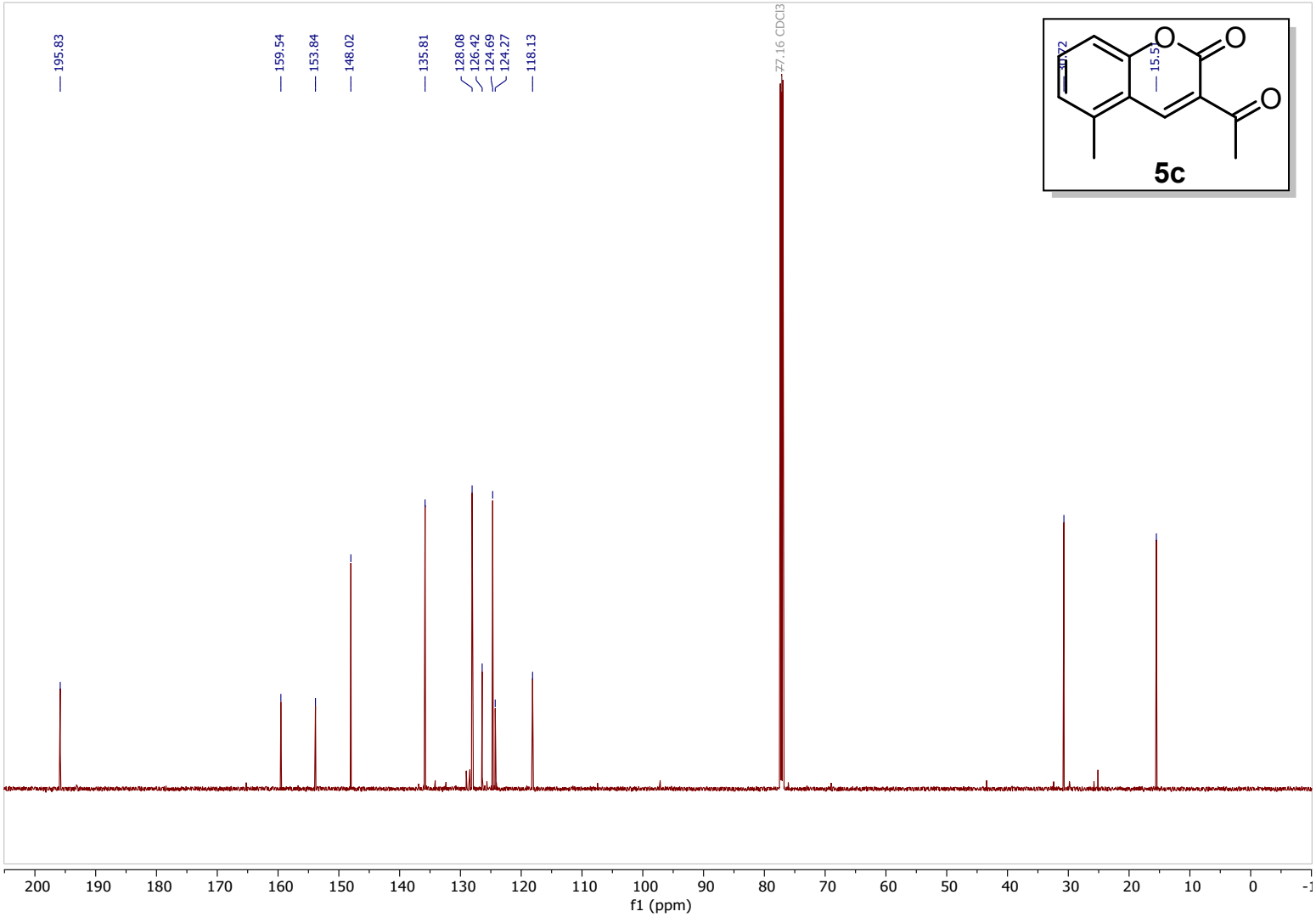
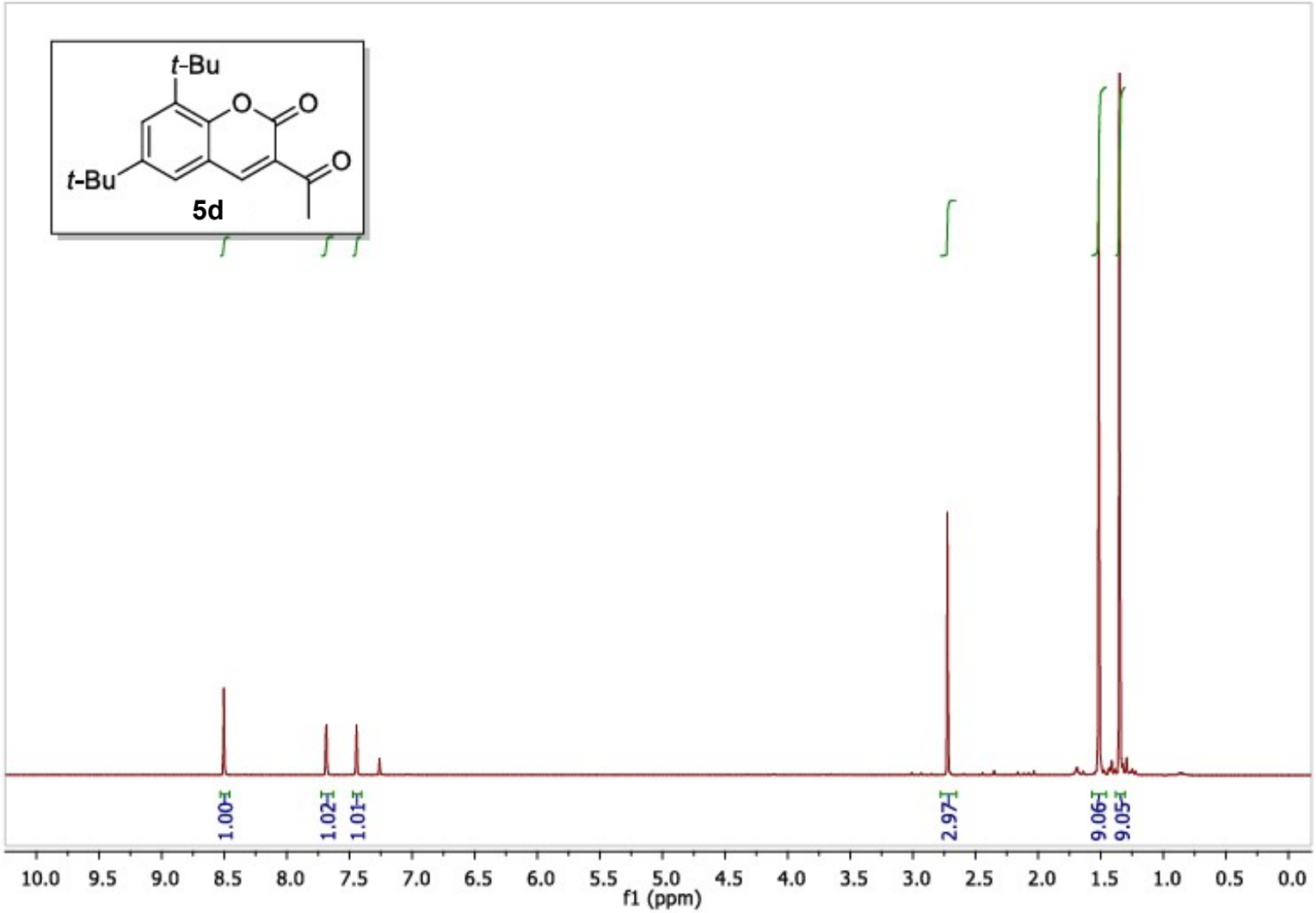


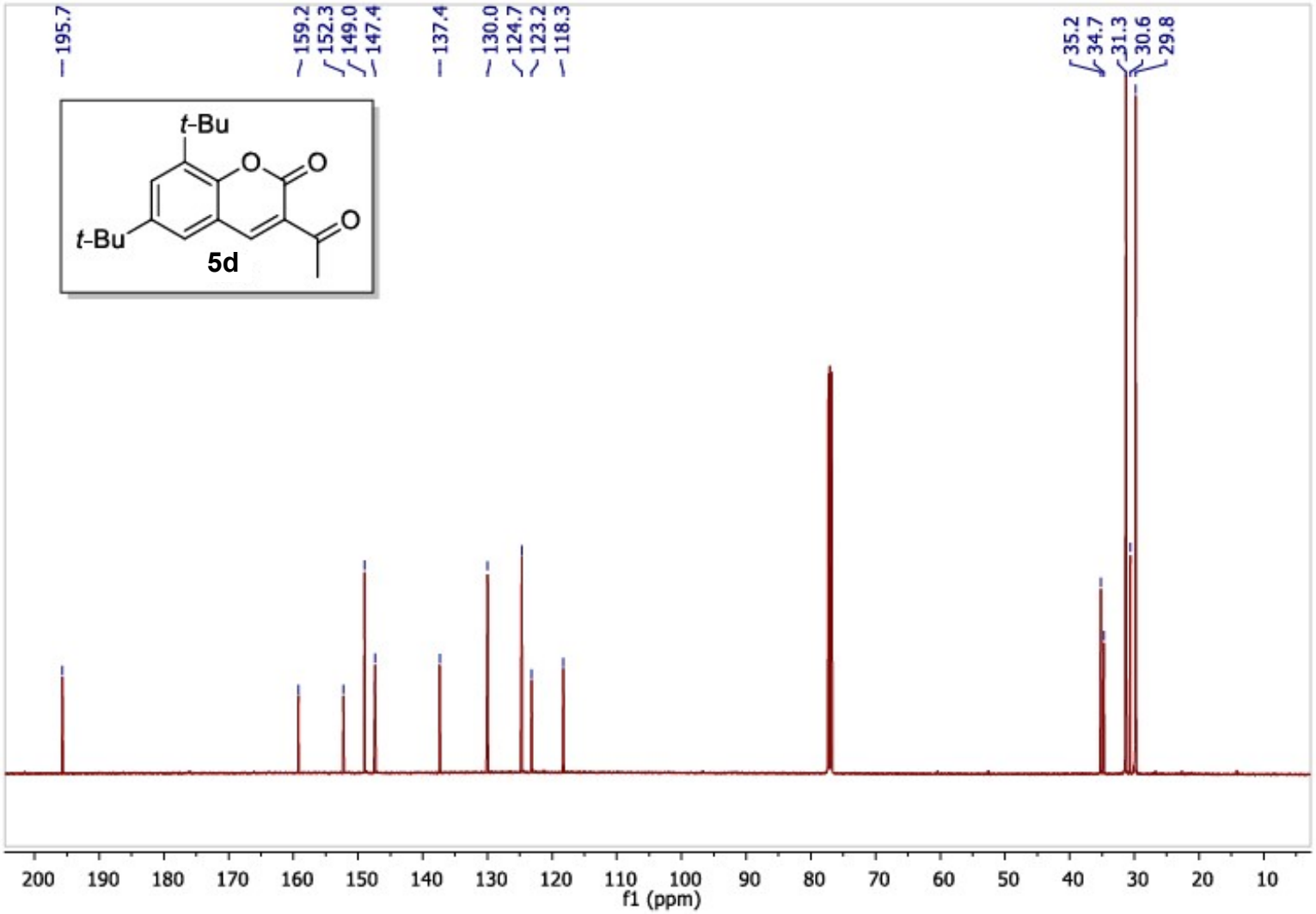
^{13}C NMR (400 MHz, $CDCl_3$) – **5c**



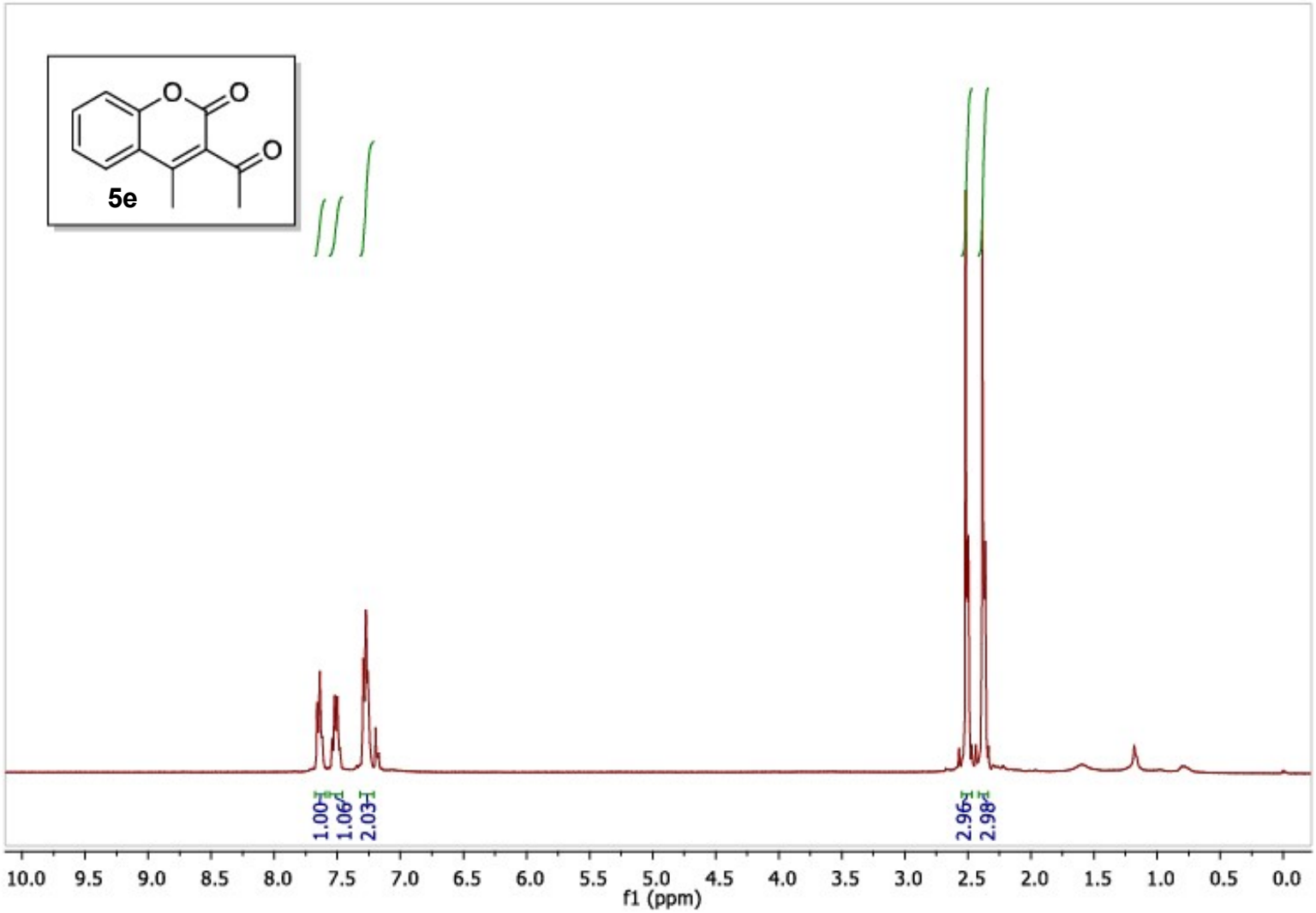
^{1}H NMR (500 MHz, $CDCl_3$) – **5d**



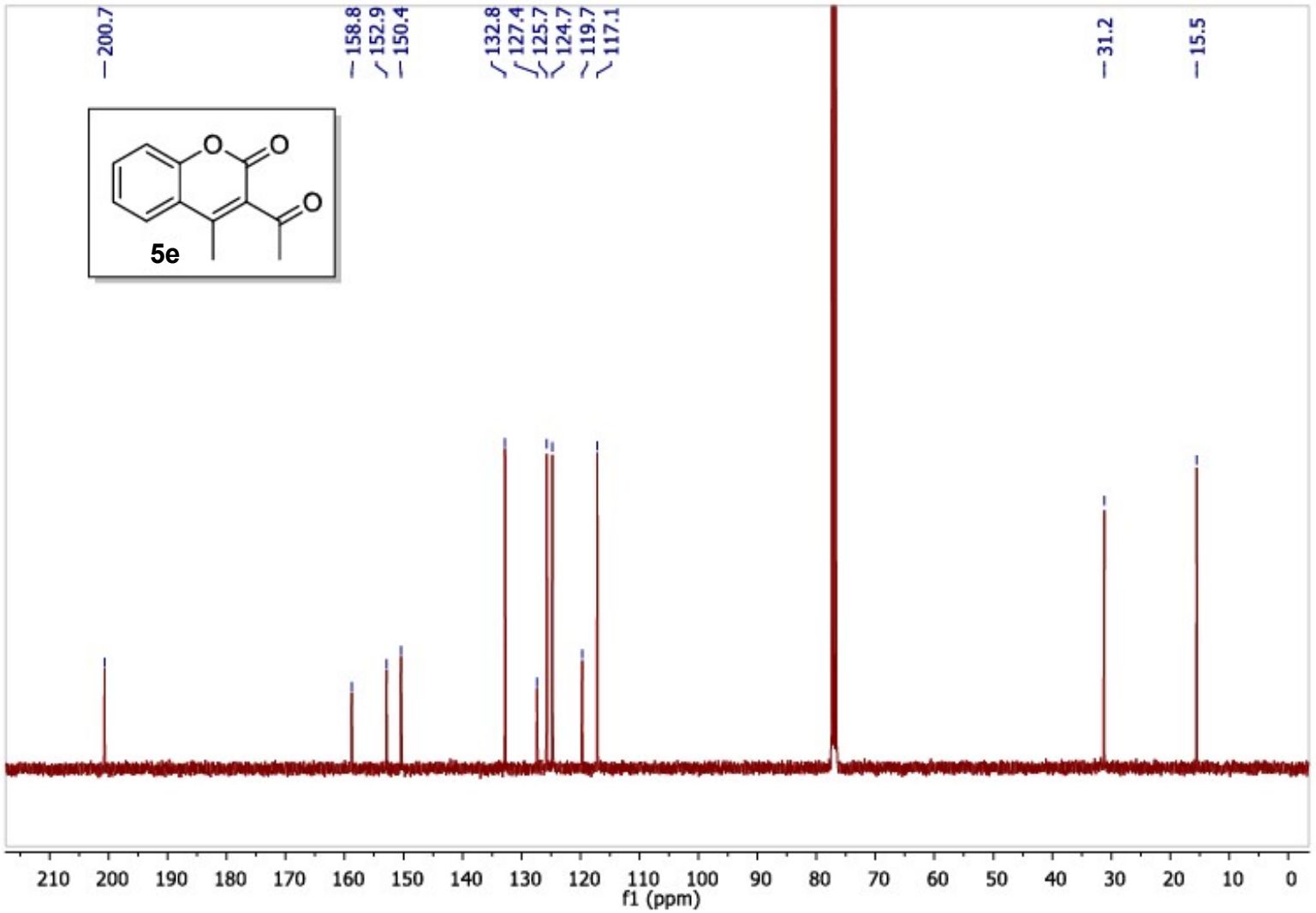
^{13}C NMR (125 MHz, $CDCl_3$) – **5d**



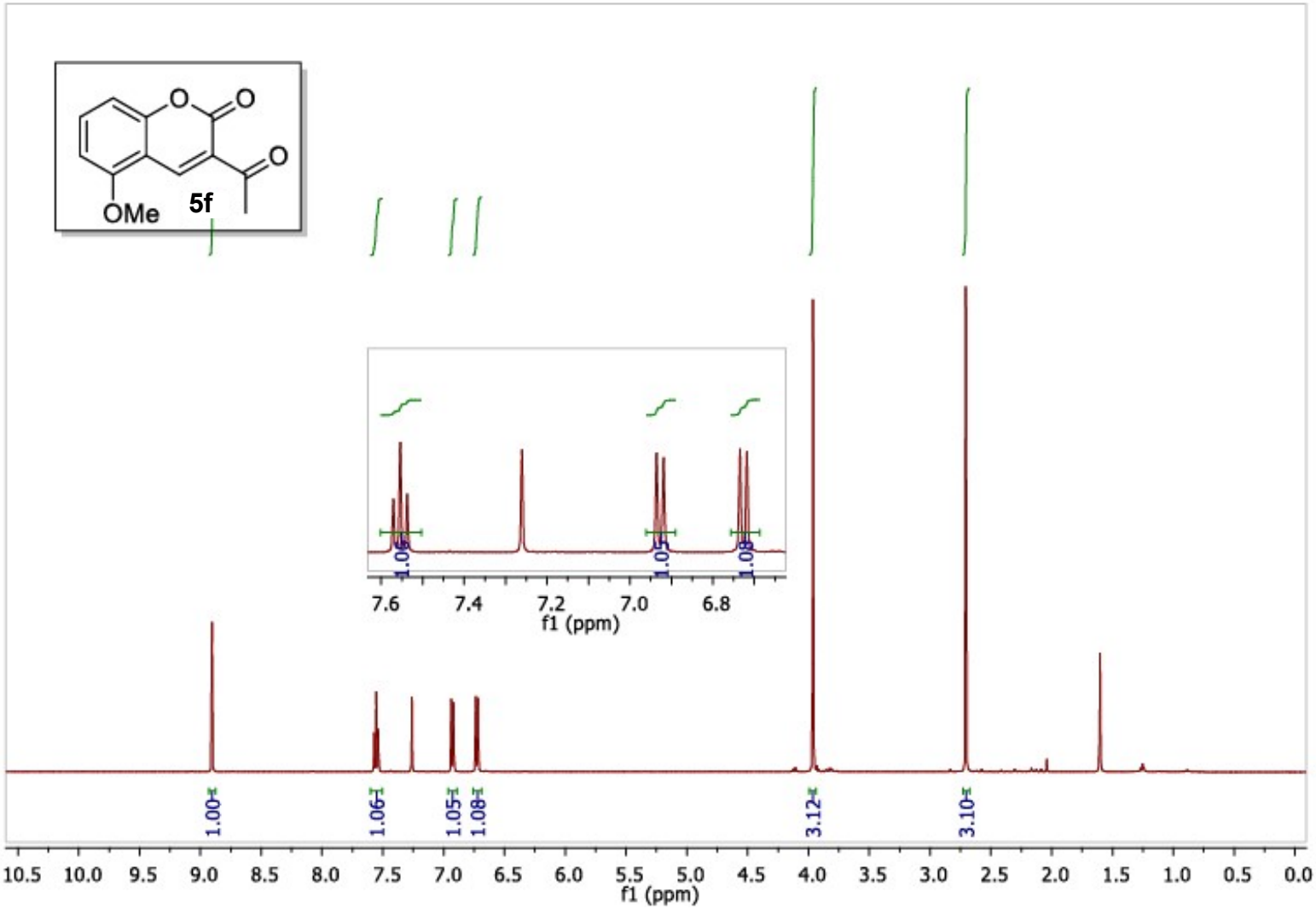
^{1}H NMR (400 MHz, $CDCl_3$) – **5e**



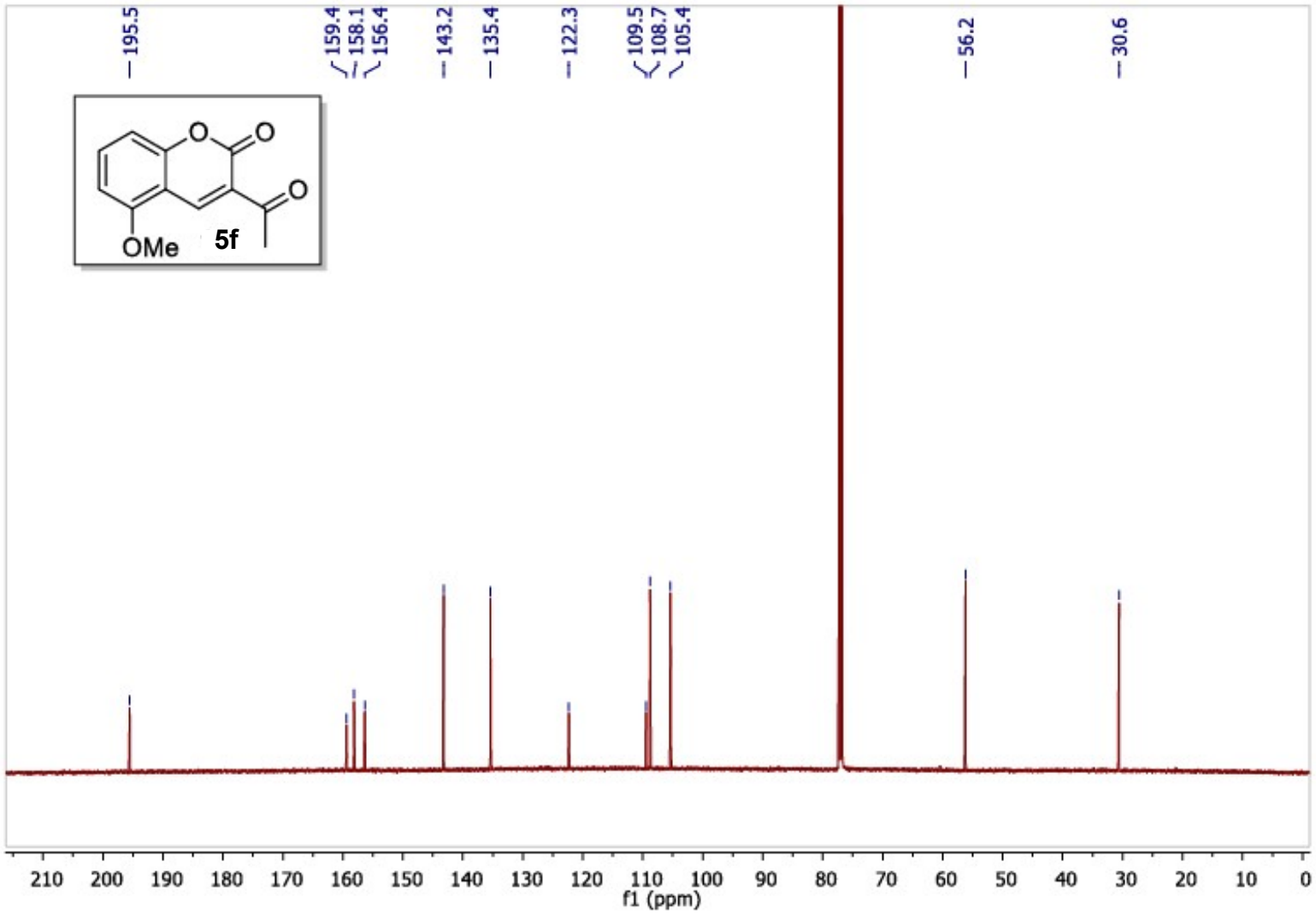
^{13}C NMR (100 MHz, $CDCl_3$) – **5e**



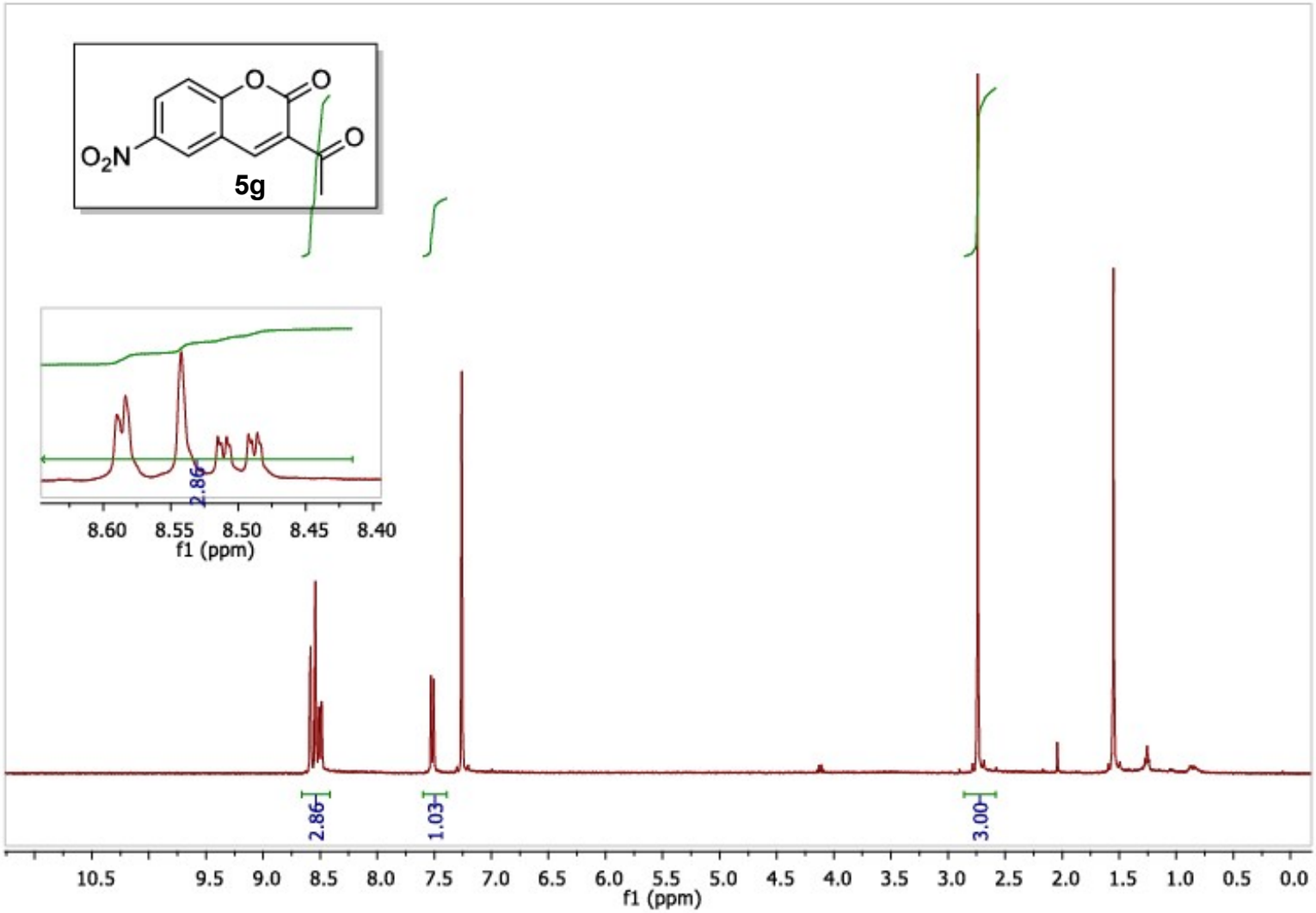
^{1}H NMR (500 MHz, $CDCl_3$) – **5f**



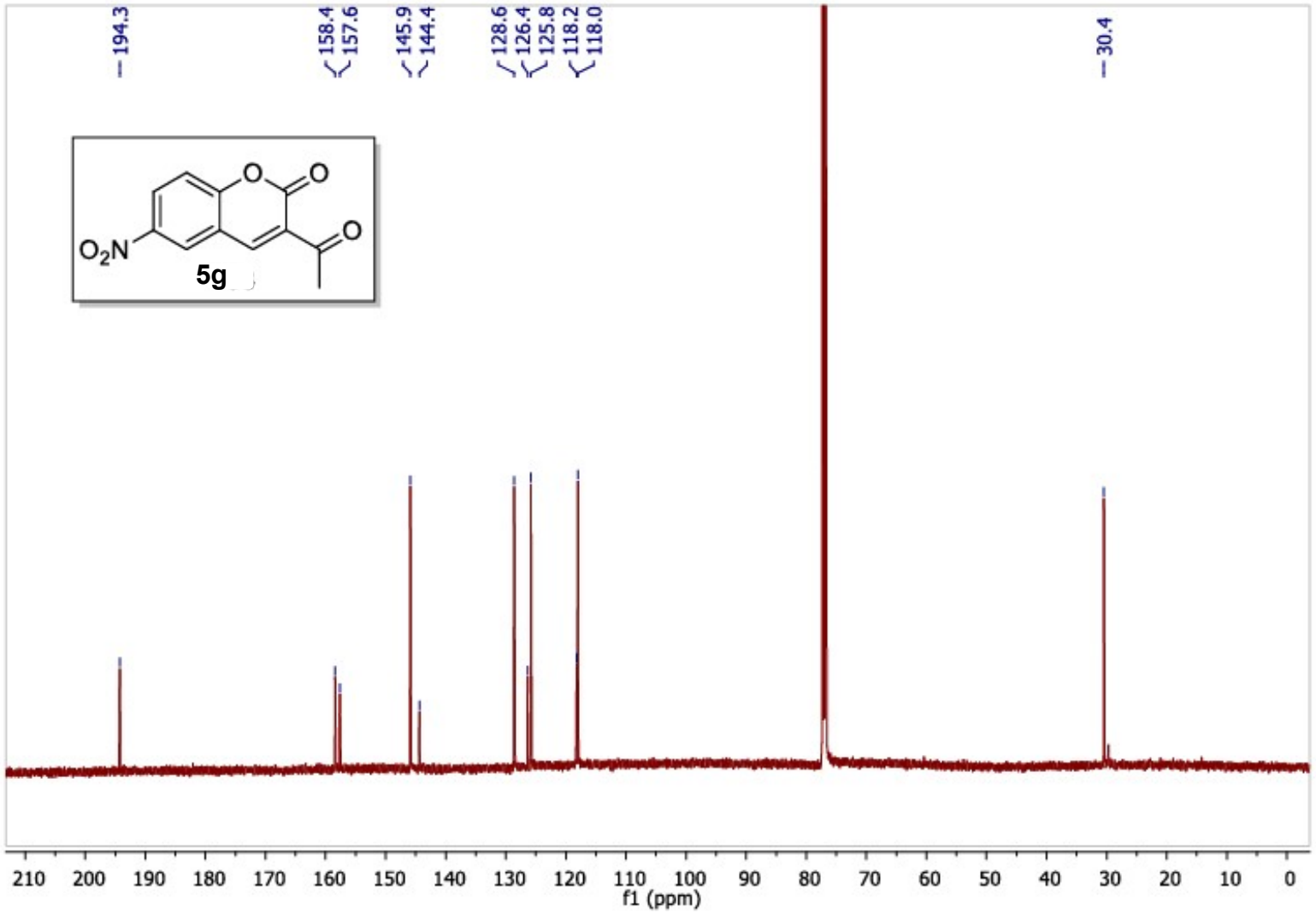
^{13}C NMR (125 MHz, $CDCl_3$) – **5f**



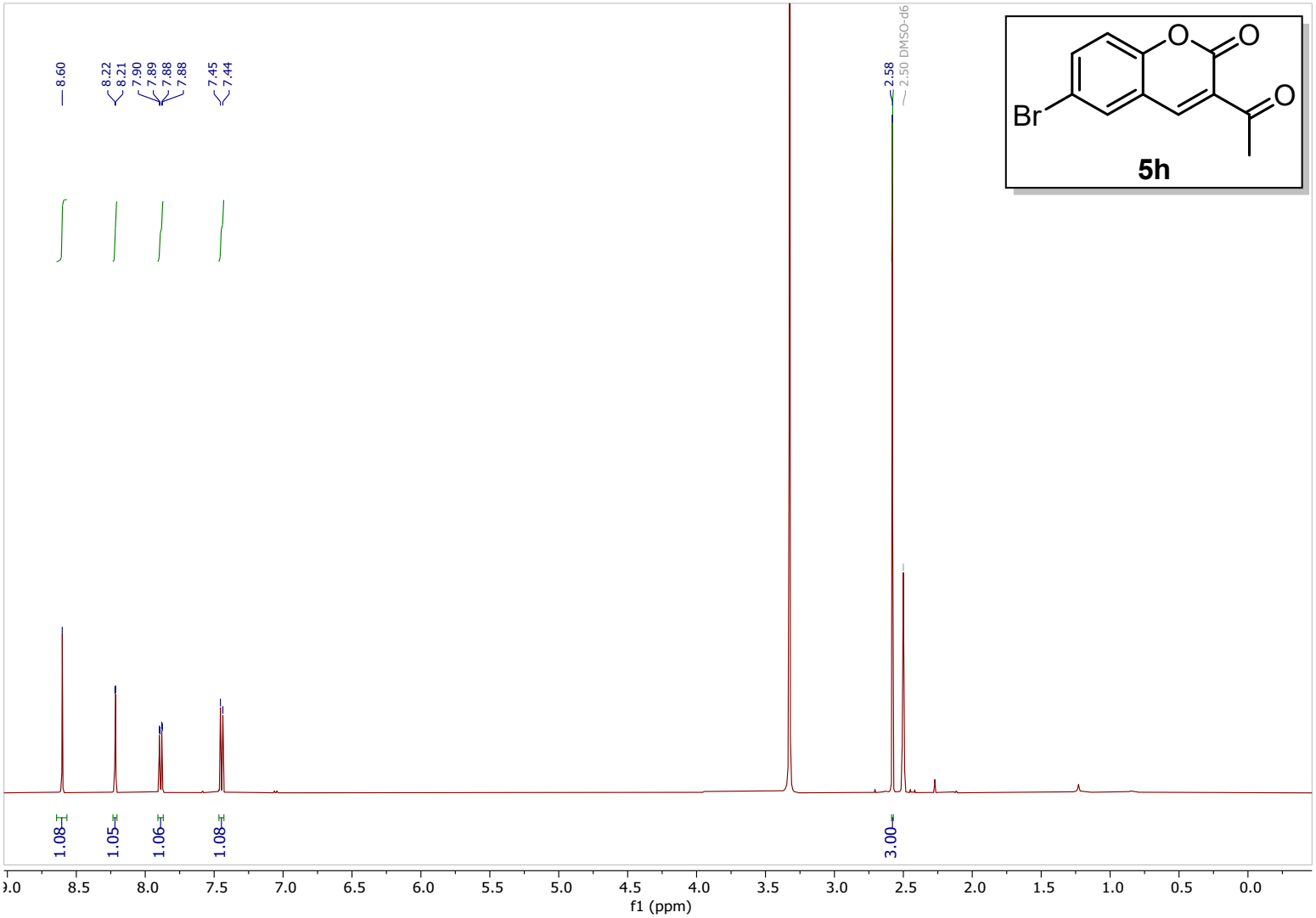
^{1}H NMR (400 MHz, $CDCl_3$) – **5g**



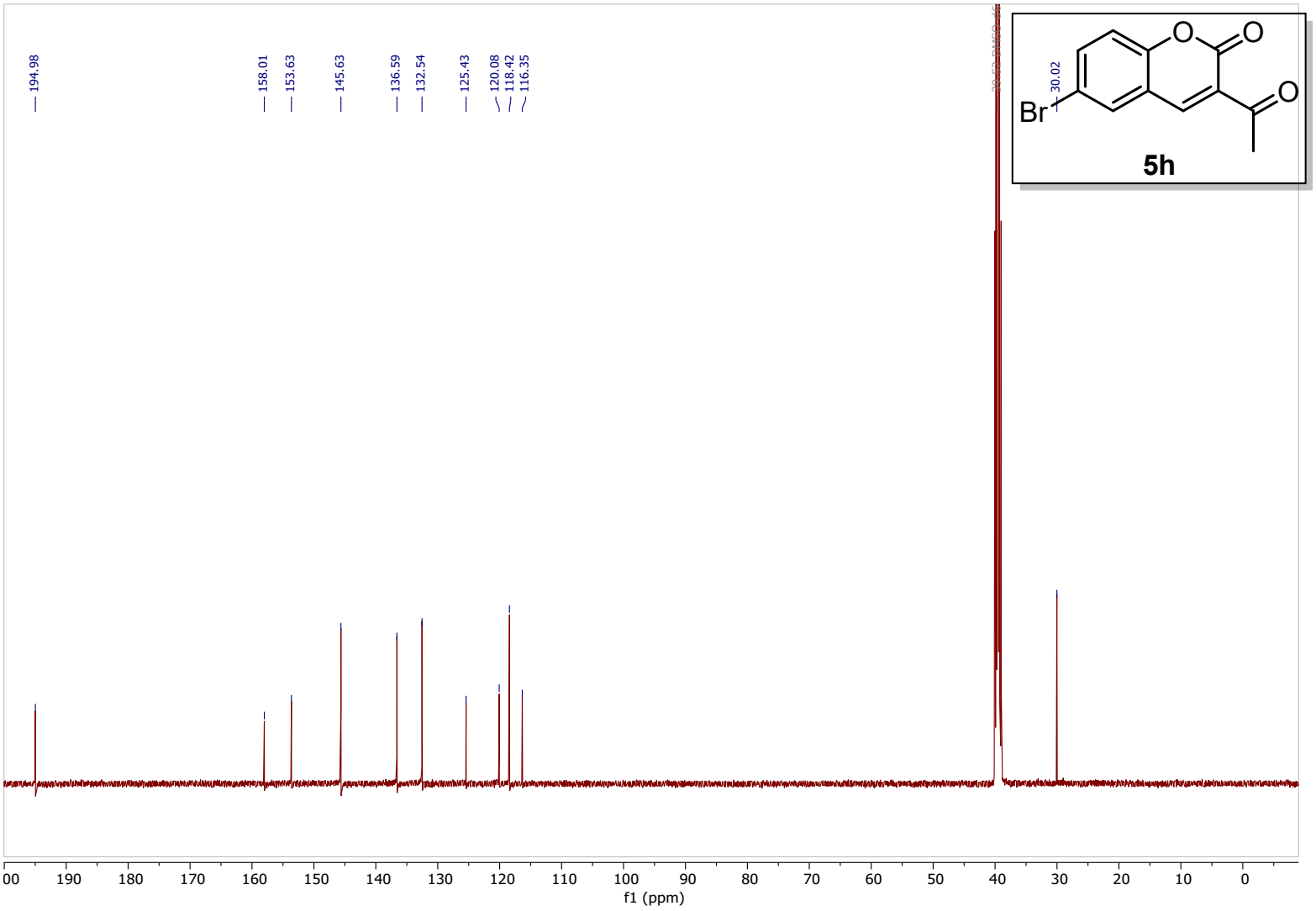
^{13}C NMR (100 MHz, $CDCl_3$) – **5g**



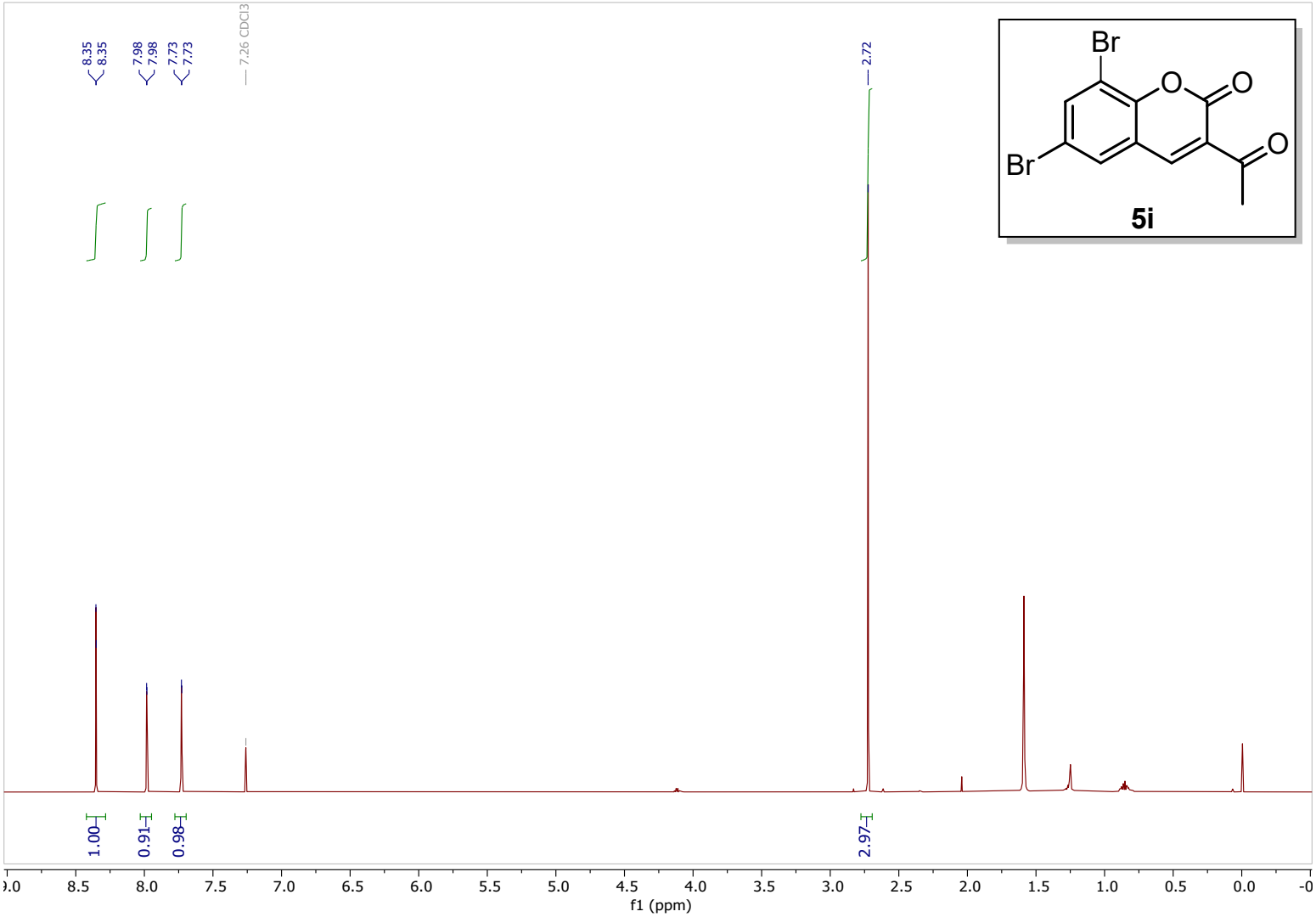
^{1}H NMR (500 MHz, DMSO-*d*6) – **5h**



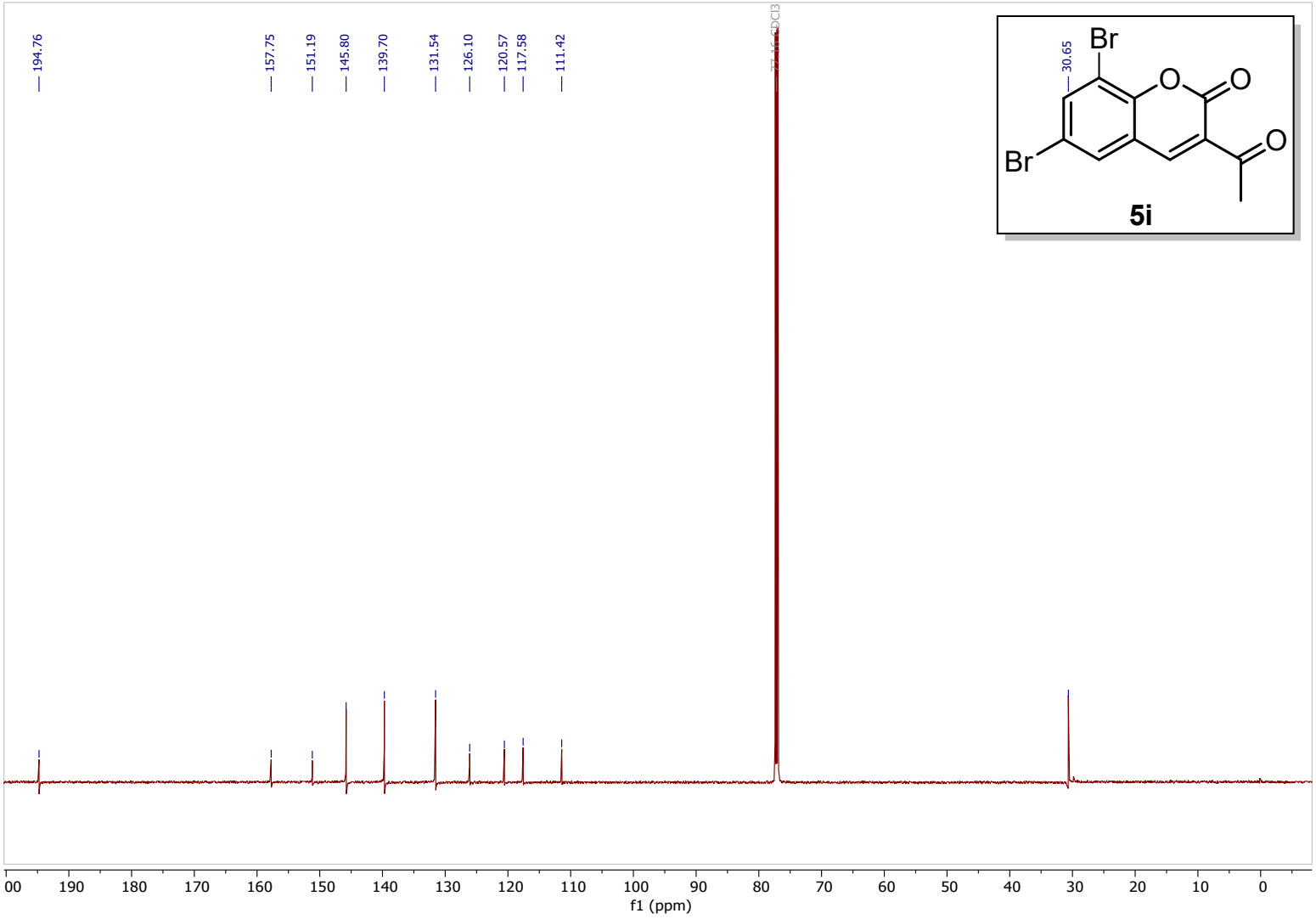
^{13}C NMR (125 MHz, DMSO-*d*6) – **5h**



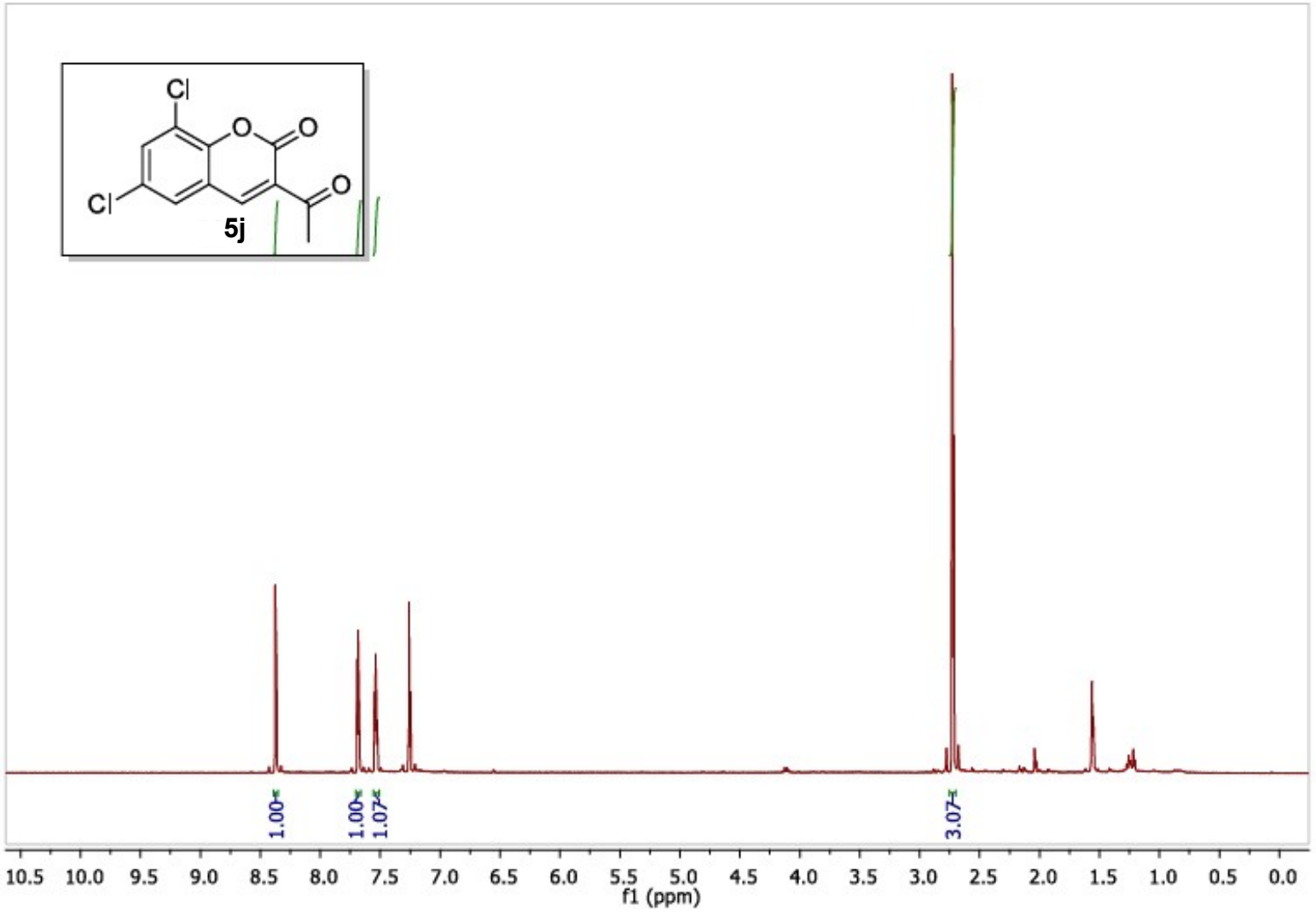
^{1}H NMR (600 MHz, $CDCl_3$) – **5i**



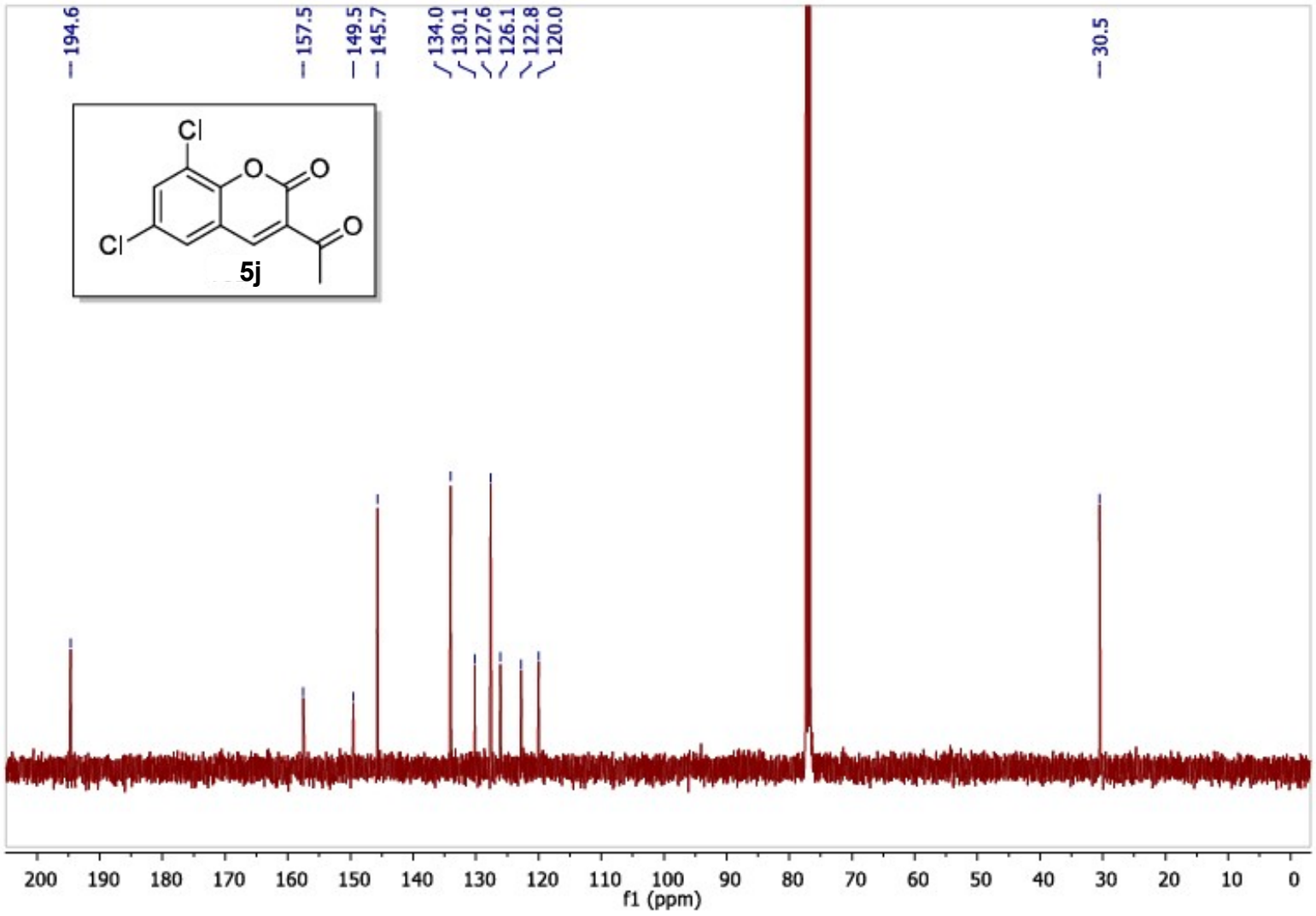
^{13}C NMR (150 MHz, $CDCl_3$) – **5i**



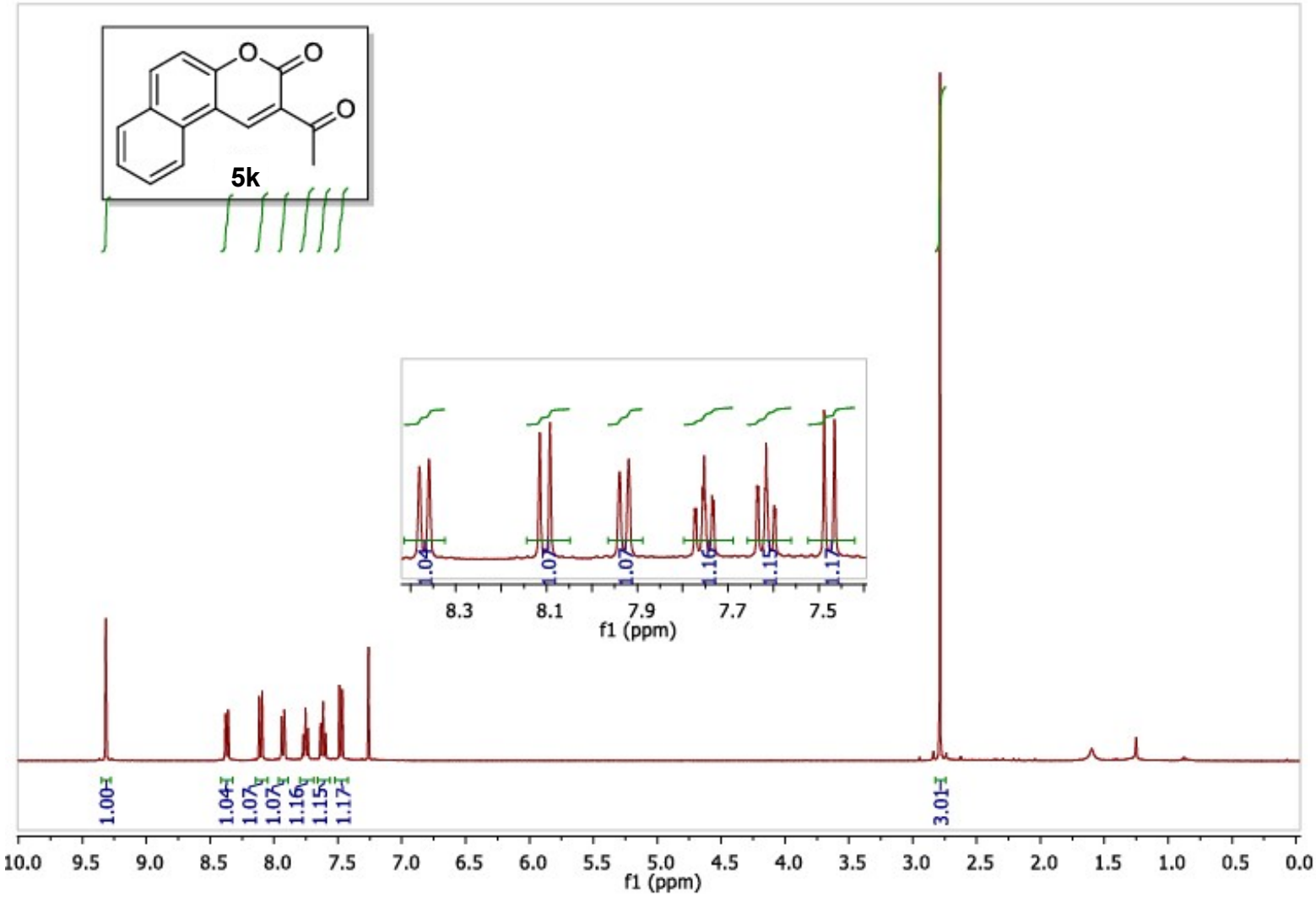
^{1}H NMR (400 MHz, $CDCl_3$) – **5j**



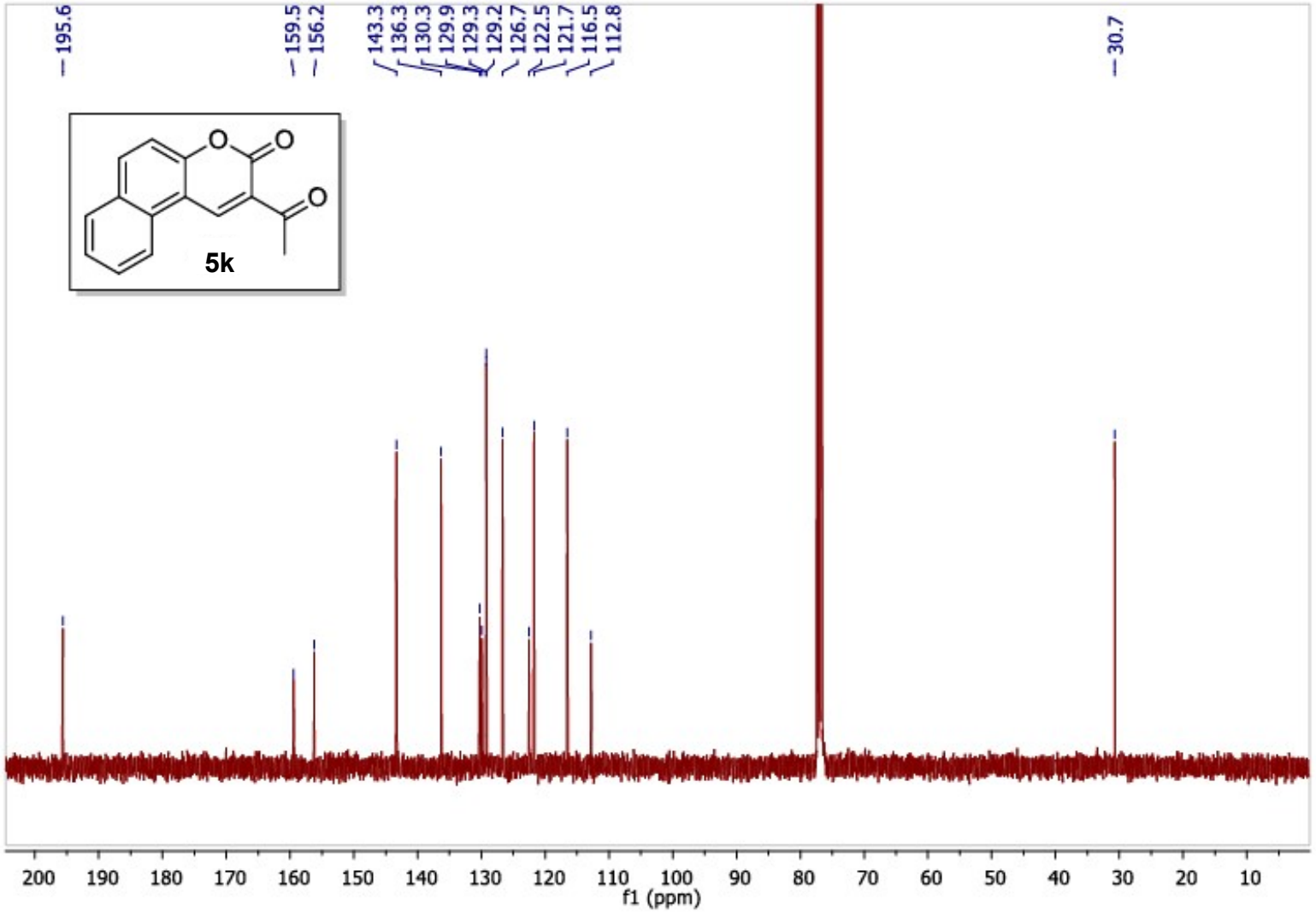
^{1}H NMR (400 MHz, $CDCl_3$) – **5j**



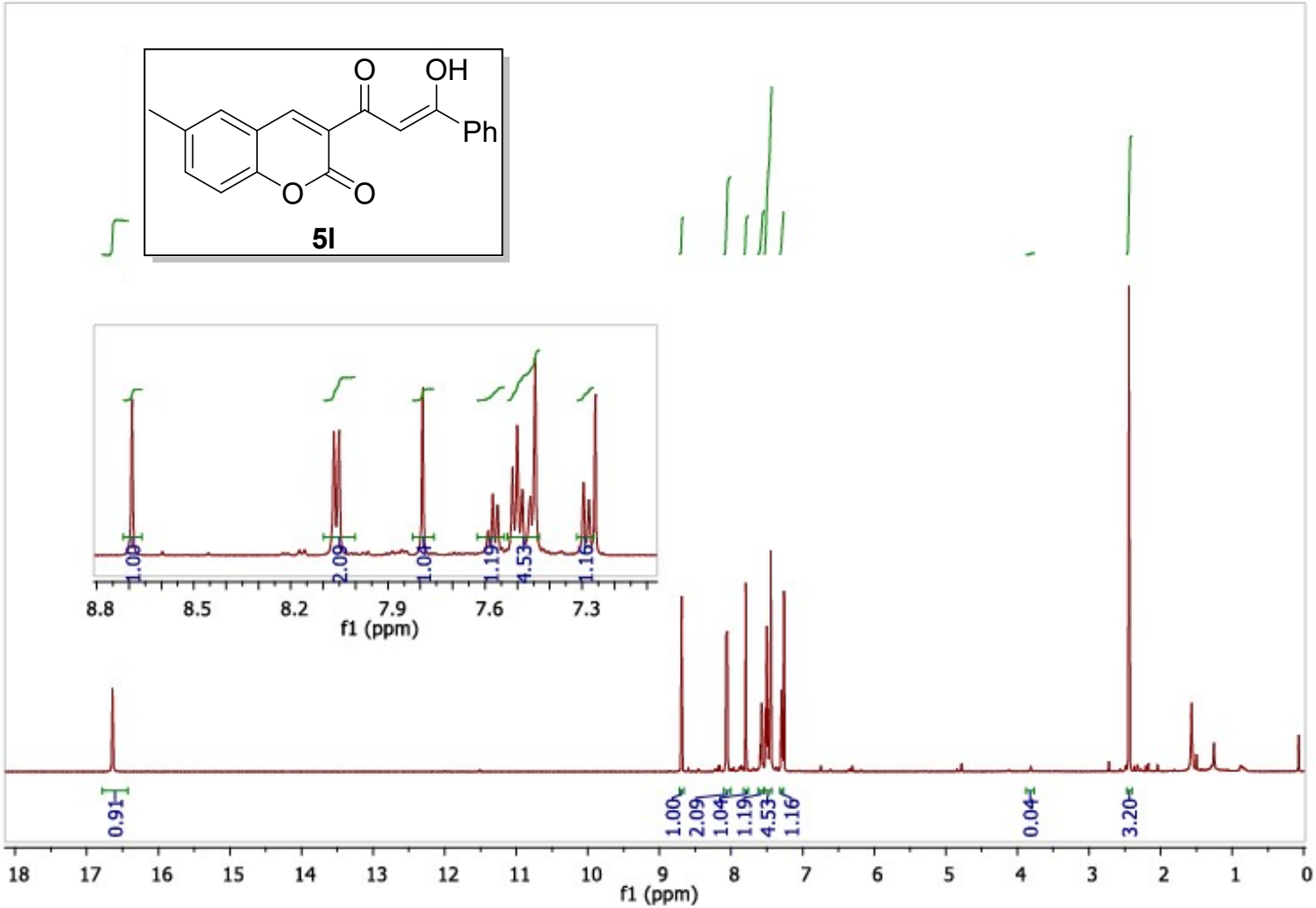
^{1}H NMR (400 MHz, $CDCl_3$) – **5k**



^{13}C NMR (100 MHz, $CDCl_3$) – **5k**



^{1}H NMR (500 MHz, $CDCl_3$) – **5l**



^{13}C NMR (125 MHz, $CDCl_3$) – **5l**