

Electronic Supplementary Information (ESI)

Iodocyclization *versus* Diiodination in the Reaction of 3-Alkynyl-4-methoxycoumarins with Iodine: Synthesis of 3-Iodofuro[2,3-*b*]chromones.

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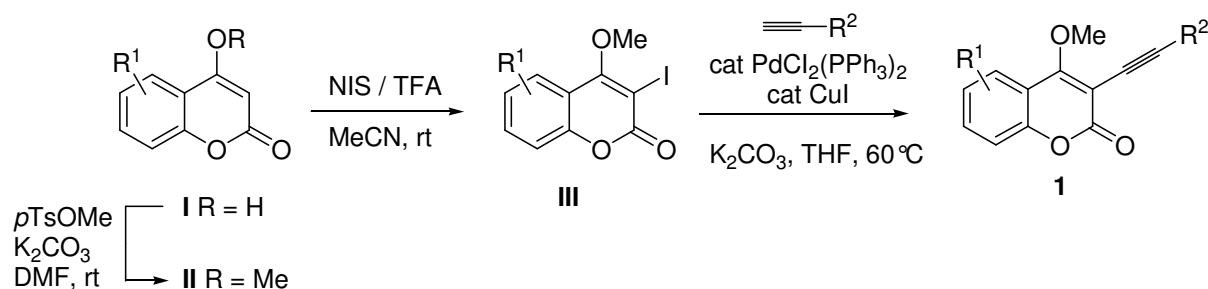
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1. General Remarks.

All reactions were run under open atmosphere using commercial grade solvents except for reactions catalysed by palladium which were carried out under argon atmosphere using dry THF (distilled over Na/Benzophenone). Commercial available reagents were used as purchased. Analytical thin-layer chromatography (TLC) was carried out on Merck silica 60/F-240 aluminium-backed plates. Visualization of the developed chromatogram was done by UV absorbance. Flash chromatography was performed using Merck silica gel 60 (40-63 μm). Melting points are uncorrected. NMR spectra were recorded either on a 300 MHz or 400 MHz spectrometers in the indicated solvent. Chemical shifts (δ) are given from TMS (δ = 0.00) in parts per million (ppm) with the residual signals of deuterated solvent used as standards [CDCl₃: ¹H NMR δ = 7.26 ppm (s); ¹³C NMR δ = 77.0 ppm (t)]. Coupling constants (J) are expressed in hertz (Hz) and spin multiplicities are given as s (singlet), d (doublet), dd (double doublet), t (triplet), m (multiplet) and br (broad). Mass spectra were performed using ESI or FAB ionization mode. Infrared spectra were obtained on FT-IR spectrometer in neat condition or as KBr plates and are reported in wavenumber (cm⁻¹).

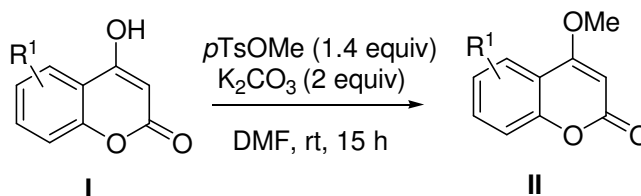
2. Preparation of starting materials 1a-i and 4 (Table 1)

The 3-alkynyl-4-methoxycoumarins (**1**) have been prepared as depicted in the following scheme:



1/ Preparation of 4-methoxycoumarins.

4-Methoxycoumarin and 6-methyl-4-methoxy-2-pyrone are commercially available compounds. 6-Chloro-4-methoxy-, 6-methyl-4-methoxy-, and 4,7-dimethoxycoumarins were prepared as follows:



General procedure: The selected 4-hydroxycoumarin **I** (2.45 mmol) and potassium carbonate (4.9 mmol) were dissolved in dry DMF (13 mL) and the suspension was cooled to 0° C. Methyl paratoluenesulfonate (3.43 mmol) was slowly added and the reaction mixture was allowed to reach room temperature and left to stir overnight. The reaction mixture was then poured into ice-cold water and then extracted twice with dichloromethane. The combined organic layers were washed with saturated aqueous NaCl and water and then dried over MgSO₄ and concentrated *in vacuo*. The residue was purified by flash chromatography to afford the desired 4-methoxycoumarin **II**.

6-Chloro-4-methoxycoumarin: 81% yield, white solid, mp (from AcOEt): 163-164 °C. FTIR (KBr): $\nu_{\text{max}}/\text{cm}^{-1}$ 1708 (C=O). ¹H NMR (300 MHz, CDCl₃): δ . 4.00 (s, 3H), 5.72 (s, 1H), 7.27 (d, *J* = 8.7 Hz, 1H), 7.50 (dd, *J* = 8.7 and 2.5 Hz, 1H), 7.79 (d, *J* = 2.5 Hz, 1H), ¹³C NMR (75 MHz, CDCl₃): δ . 56.7, 90.9, 116.8, 118.3, 122.8, 129.6, 132.5, 151.7, 162.3, 165.4. GC/MS: *m/z* 210.

6-Methyl-4-methoxycoumarin:¹ 83% yield, white solid, mp (from AcOEt): 119-121 °C. FTIR (KBr): $\nu_{\text{max}}/\text{cm}^{-1}$ 1695 (C=O). ¹H NMR (300 MHz, CDCl₃): δ . 2.40 (s, 3H), 3.98 (s, 3H), 5.67 (s, 1H), 7.20 (d, *J* = 8.5 Hz, 1H), 7.35 (dd, *J* = 8.5 and 1.8 Hz, 1H), 7.59 (d, *J* = 1.8 Hz, 1H), ¹³C NMR (75 MHz, CDCl₃): δ . 20.9, 56.4, 90.0, 115.3, 116.5, 122.7, 133.4, 133.5, 151.5, 163.2, 166.5. GC/MS: *m/z* 190.

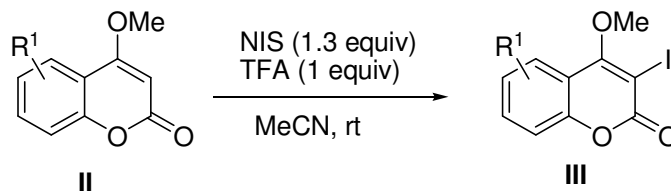
4,7-Dimethoxymethoxycoumarin:² 73% yield, white solid, mp (from AcOEt): 158-160 °C (Lit.² 157-159 °C). FTIR (KBr): $\nu_{\text{max}}/\text{cm}^{-1}$ 1724 (C=O). ¹H NMR (300 MHz, CDCl₃): δ . 3.87 (s, 3H), 3.97 (s, 3H), 5.57 (s, 1H), 6.80 (d, *J* = 2.3 Hz, 1H), 6.84 (dd, *J* = 8.8 and 2.3 Hz), 7.70 (d, *J* = 8.8 Hz, 1H), ¹³C NMR (75 MHz, CDCl₃): δ . 55.8, 56.3, 87.7, 100.5, 108.9, 112.2, 124.14, 155.2, 163.3, 163.5, 166.9. GC/MS: *m/z* 206.

¹ J.I. Okogun, V.U. Enyenihi, D.E.U. Ekong, *Tetrahedron*, 1978, **34**, 1221.

² Büchi, G.; Klaubert, D.; Shank, R.C.; Weinreb, S.M.; Wogan, G.N. *J. Org. Chem.* 1971, **36**, 1147.

2/ Preparation of 3-iodocoumarins.

3-Iodo-4-methoxy-6-methyl-2-pyrone was prepared according to a literature procedure.³ 3-Iodocoumarins were prepared as follows:



A solution of the selected 4-methoxycoumarin (17.25 mmol) **II** and *N*-iodosuccinimide (22.42 mmol) in MeCN (50 mL) was treated with TFA (17.25 mmol) and left to stir in dark at room temperature for the indicated time (TLC) and then concentrated *in vacuo*. The residue was diluted with CH₂Cl₂ and then washed with aqueous Na₂S₂O₃ and 1N NaOH (thrice). The aqueous layer was extracted twice with CH₂Cl₂ and the combined organic layers were dried over MgSO₄ and concentrated *in vacuo* to give the desired iodocoumarins **III**.

3-Iodo-4-methoxycoumarin:⁴ (60 h) 92% yield, yellow solid, mp: 88-89 °C.

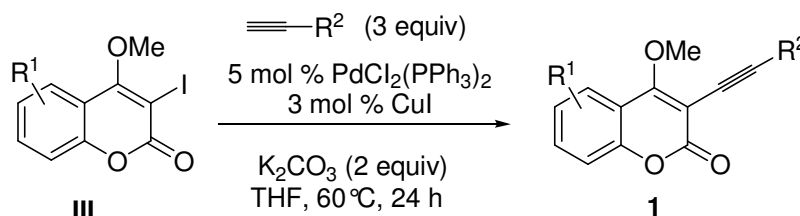
6-Chloro-3-iodo-4-methoxycoumarin: (15 d) 65% yield, yellow solid, mp: 155-157 °C. FTIR (KBr): $\nu_{\max}/\text{cm}^{-1}$ 1713 (C=O). ¹H NMR (300 MHz, CDCl₃): δ . 4.17 (s, 3H), 7.33 (d, J = 8.8 Hz, 1H), 7.55 (dd, J = 8.8 and 2.4 Hz, 1H), 7.72 (d, J = 2.4 Hz, 1H), ¹³C NMR (75 MHz, CDCl₃): δ . 61.8, 75.2, 118.0, 118.4, 122.7, 130.2, 132.9, 151.6, 159.5, 168.9. GC/MS: m/z 336.

3-Iodo-4-methoxy-6-methylcoumarin: (40 h) 89% yield, yellow solid, mp: 124-126 °C. FTIR (KBr): $\nu_{\max}/\text{cm}^{-1}$ 1712 (C=O). ¹H NMR (300 MHz, CDCl₃): δ . 2.41 (s, 3H), 4.09 (s, 3H), 7.20 (d, J = 8.5 Hz, 1H), 7.36 (dd; J = 8.5 and 1.9 Hz, 1H), 7.46 (br. s, 1H) ¹³C NMR (75 MHz, CDCl₃): δ . 21.1, 61.7, 76.7, 116.6, 116.7, 122.8, 134.1, 134.5, 151.6, 160.2, 170.2. GC/MS: m/z 316.

3-Iodo-4,7-dimethoxycoumarin: (5 h) 94% yield, yellow solid, Mp: 128-130 °C. FTIR (KBr): $\nu_{\max}/\text{cm}^{-1}$ 1708 (C=O). ¹H NMR (300 MHz, CDCl₃): δ . 3.87 (s, 3H), 4.09 (s, 3H), 6.81 (d, J = 2.5 Hz, 1H), 6.85 (dd, J = 8.8 and 2.5 Hz, 1H), 7.61 (d, J = 8.8 Hz, 1H), ¹³C NMR (75 Hz, CDCl₃): δ . 56.0, 61.7, 72.5, 100.7, 110.4, 112.9, 124.5, 155.3, 160.5, 163.8, 170.4. GC/MS: m/z 332.

3/ Preparation of the 3-alkynylcoumarins 1.

3-Alkynylcoumarins **1a**, **1c**, **1d**, and **1i**,⁵ as well as 3-alkynyl-2-pyrone **4**⁶ have been previously prepared in our laboratories using the Sonogashira cross-coupling methodology. The following procedure was used to synthesize alkynylcoumarins **1b** and **1e-h**:



³ S. Cerezo, M. Moreno-Mañas, R. Pleixats, *Tetrahedron* 1998, **54**, 7813.

⁴ Fukuyama N., H. Nishino, K. Kurosawa, *Bull. Chem. Soc. Jpn.*, 1987, **60**, 4363.

⁵ G. Raffa, M. Rusch, G. Balme, N. Monteiro, *Org. Lett.*, 2009, **22**, 5254.

⁶ D. Conreux, S. Belot, P. Desbordes, N. Monteiro, G. Balme, *J. Org. Chem.*, 2008, **73**, 8619.

General procedure: In a glass tube fitted with a Teflon screw seal, PdCl₂(PPh₃)₂ (0.166 mmol), CuI (0.1 mmol), K₂CO₃ (6.64 mmol) and the selected terminal alkyne (9.96 mmol) were added to a solution of 3-iodo-4-methoxycoumarin (3.32 mmol) in dry, degassed THF (16 mL). The reactor was flushed with argon and the reaction mixture was left to stir at 60 °C for 24 h and then concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, appropriate mixture of cyclohexane/CH₂Cl₂) and then recrystallized (MeOH) to afford the corresponding 3-alkynyl-4-methoxycoumarin.

4-Methoxy-3-(4-fluorophenyl)ethynylcoumarin (1b): 62% yield, off-white solid, mp: 156-158 °C. FTIR (neat): $\nu_{\max}/\text{cm}^{-1}$ 1719 (C=O). ¹H NMR (300 MHz, CDCl₃): δ . 4.62 (s, 3H), 7.02-7.08 (m, 2H), 7.30-7.33 (m, 2H), 7.50-7.58 (m, 3H), 7.85 (d, $J=8.1$ Hz, 1H); ¹³C NMR (100 MHz, CDCl₃): δ . 60.7, 81.4, 92.3, 97.0, 115.8 (d, $J=21.8$ Hz), 116.5, 116.6, 119.1 (d, $J=3.6$ Hz), 123.7, 124.3, 132.8, 132.2 (d, $J=8.7$ Hz), 151.8, 162.1, 163.1 (d, $J=248.6$ Hz), 166.1. HRMS (EI): M⁺, 294.0697, Calc. for C₁₈H₁₁FO₃: 294.0687.

4-Methoxy-3-(3,4,5-trimethoxyphenyl)ethynylcoumarin (1e): 58% yield, white solid, mp: 165-167 °C. FTIR (neat): $\nu_{\max}/\text{cm}^{-1}$ 1711 (CO). ¹H NMR (300 MHz, CDCl₃): δ . 3.87 (s, 9H), 4.63 (s, 3H), 6.76 (s, 2H), 7.29-7.33 (m, 2H), 7.55, (ddd, $J=8.4, 7.2$ and 1.4 Hz, 1H), 7.85 (dd, $J=8.0$ and 1.4 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃): δ . 56.3, 60.7, 61.0, 80.7, 92.5, 98.3, 108.6, 116.5, 116.6, 117.9, 123.7, 124.3, 132.7, 139.3, 151.8, 153.2, 162.2, 166.0. HRMS (EI): M⁺, 366.1107, Calc. for C₂₁H₁₈O₆: 366.1098.

6-Chloro-4-methoxy-3-phenylethynylcoumarin (1f): 43% yield, white solid, mp: 205-207 °C. FTIR (neat): $\nu_{\max}/\text{cm}^{-1}$ 1715 (CO). ¹H NMR (300 MHz, CDCl₃): δ . 4.64 (s, 3H), 7.24-7.26 (m, 1H), 7.36-7.37 (m, 3H), 7.46-7.54 (m, 3H), 7.82 (d, $J=2.2$ Hz, 1H); ¹³C NMR (100 MHz, CDCl₃): δ . 60.9, 81.3, 93.3, 99.0, 117.8, 118.2, 122.8, 123.3, 128.6, 129.1, 130.0, 131.4, 132.7, 150.2, 161.6, 164.7. HRMS (EI): M⁺, 310.0384, Calc. for C₁₈H₁₁ClO₃: 310.0391.

4-Methoxy-6-methyl-3-phenylethynylcoumarin (1g): 33% yield, white solid, mp: 155-157 °C. FTIR (neat): $\nu_{\max}/\text{cm}^{-1}$ 1708 (CO). ¹H NMR (300 MHz, CDCl₃): δ . 2.41 (s, 3H), 4.63 (s, 3H), 7.20 (s, $J=8.5$ Hz, 1H), 7.34-7.36 (m, 4H), 7.52-7.55 (m, 2H), 7.63 (br. s, 1H); ¹³C NMR (100 MHz, CDCl₃): δ . 21.0, 60.7, 81.9, 92.4, 98.1, 116.2, 116.3, 123.0, 123.3, 128.4, 128.7, 131.3, 133.8, 134.1, 150.0, 162.3, 166.1. HRMS (EI): M⁺, 290.0942, Calc. for C₁₉H₁₄O₃: 290.0937.

4,7-Dimethoxy-3-phenylethynylcoumarin (1h): 41% yield, yellow solid, Mp: 178-179 °C. FTIR (neat): $\nu_{\max}/\text{cm}^{-1}$ 1712 (CO). ¹H NMR (300 MHz, CDCl₃): δ . 3.87 (s, 3H), 4.61 (s, 3H), 6.78 (d, $J=2.2$ Hz, 1H), 6.85 (dd, $J=8.8$ and 2.2 Hz, 1H), 7.33-7.35 (m, 3H), 7.51-7.54 (m, 2H), 7.73 (d, $J=8.8$ Hz, 1H); ¹³C NMR (75 MHz, CDCl₃): δ . 55.9, 60.6, 82.0, 90.0, 97.4, 100.3, 109.8, 112.7, 123.2, 124.9, 128.4, 128.6, 131.2, 153.7, 162.7, 163.6, 166.5. HRMS (EI): M⁺, 306.0879, Calc. for C₁₉H₁₄O₄: 306.0892.

3. Preparation of diiodoalkene 3a (Scheme 2).

A solution of 4-methoxy-3-phenylethynylcoumarin (1a) (0.72 mmol) was treated with iodine (1.44 mmol) in MeCN (4 mL) and left to stir at room temperature for 5 h. The reaction mixture was then diluted with dichloromethane and washed thrice with aqueous Na₂S₂O₃. The aqueous layer was extracted with dichloromethane and the combined organic layers were dried over MgSO₄ and concentrated *in vacuo* at room temperature. The residue was recrystallized (AcOEt) to give 230 mg (60% yield) of the corresponding (*E*)-1,2-diiodoethenylcoumarin 3a as a yellow solid Mp: 108-110 °C (dec.). ¹H NMR (300 MHz, CDCl₃): δ . 4.57 (s, 3H), 7.29-7.44 (m, 7H), 7.56-7.61 (m, 1H), 7.93 (dd, $J=7.9$ and 1.3 Hz, 1H), ¹³C NMR (75 MHz, CDCl₃): δ . 59.8, 89.8, 104.9, 114.7, 115.8, 115.9, 123.4, 123.6, 127.1, 127.7, 128.1, 131.8, 145.4, 151.5, 159.5. HRMS (ESI): MH⁺, 530.8956, Calc. for C₁₈H₁₃I₂O₃: 530.8949.

4. X-Ray crystallographic information of products **2a** and **3a**:

Crystal data for 2a: single crystals were recrystallized from dichloromethane

$C_{17}H_9IO_3$	$F(000) = 752$
$M_r = 388.16$	$D_x = 1.833 \text{ Mg m}^{-3}$
Monoclinic, $P2_1/c$	Mo $K\alpha$ radiation, $\lambda = 0.7107 \text{ \AA}$
Hall symbol: $-P 2ybc$	Cell parameters from 2573 reflections
$a = 12.173 (2) \text{ \AA}$	$\theta = 3.4\text{--}29.5^\circ$
$b = 14.445 (2) \text{ \AA}$	$\mu = 2.28 \text{ mm}^{-1}$
$c = 8.223 (2) \text{ \AA}$	$T = 293 \text{ K}$
$\beta = 103.46 (2)^\circ$	Plate, Colorless
$V = 1406.2 (5) \text{ \AA}^3$	$0.52 \times 0.29 \times 0.08 \text{ mm}$
$Z = 4$	

Crystal data for 3a: single crystals were recrystallized from dichloromethane

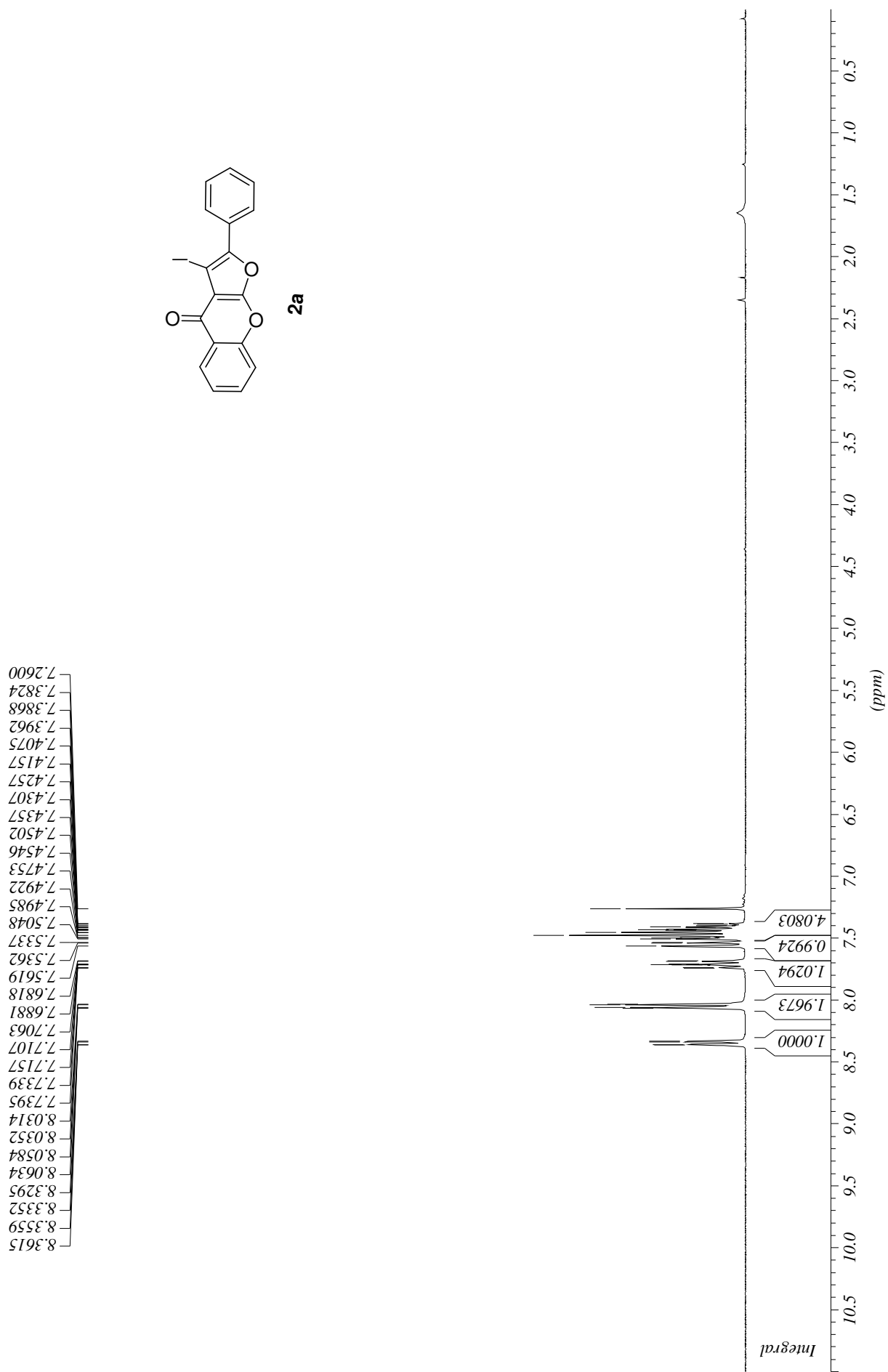
$C_{18}H_{12}I_2O_3$	$F(000) = 2000$
$M_r = 530.08$	$D_x = 1.999 \text{ Mg m}^{-3}$
Monoclinic, $P2_1/c$	Mo $K\alpha$ radiation, $\lambda = 0.7107 \text{ \AA}$
Hall symbol: $-P 2ybc$	Cell parameters from 22776 reflections
$a = 18.6185 (3) \text{ \AA}$	$\theta = 2.9\text{--}29.2^\circ$
$b = 14.0017 (3) \text{ \AA}$	$\mu = 3.58 \text{ mm}^{-1}$
$c = 14.1965 (3) \text{ \AA}$	$T = 293 \text{ K}$
$\beta = 107.820 (2)^\circ$	Plate, Colorless
$V = 3523.34 (13) \text{ \AA}^3$	$0.37 \times 0.20 \times 0.05 \text{ mm}$
$Z = 8$	

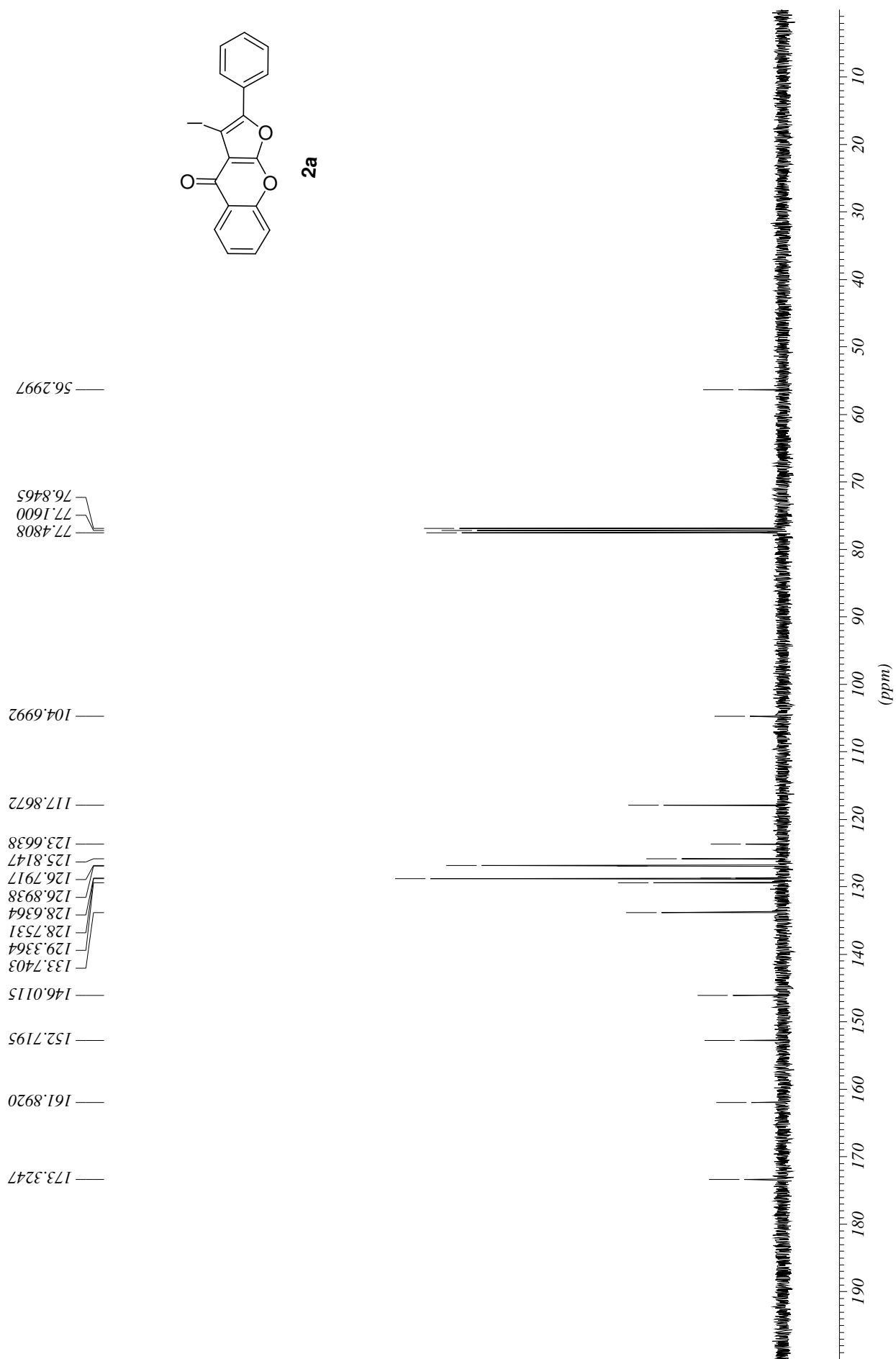
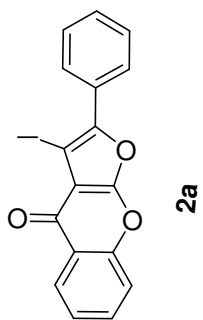
For more details please see the CIF files attached with supporting information. The crystal data of the products have been deposited at Cambridge Crystallographic Data Center, UK, and the reference numbers are CCDC 798397 for structure **2a** and CCDC 798398 for structure **3a**.

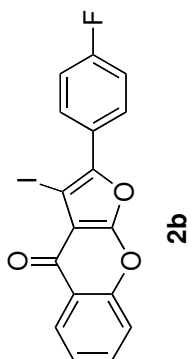
5. ^1H and ^{13}C NMR spectra for compounds **2a-j**, and **5**

All spectra were recorded in CDCl_3 .

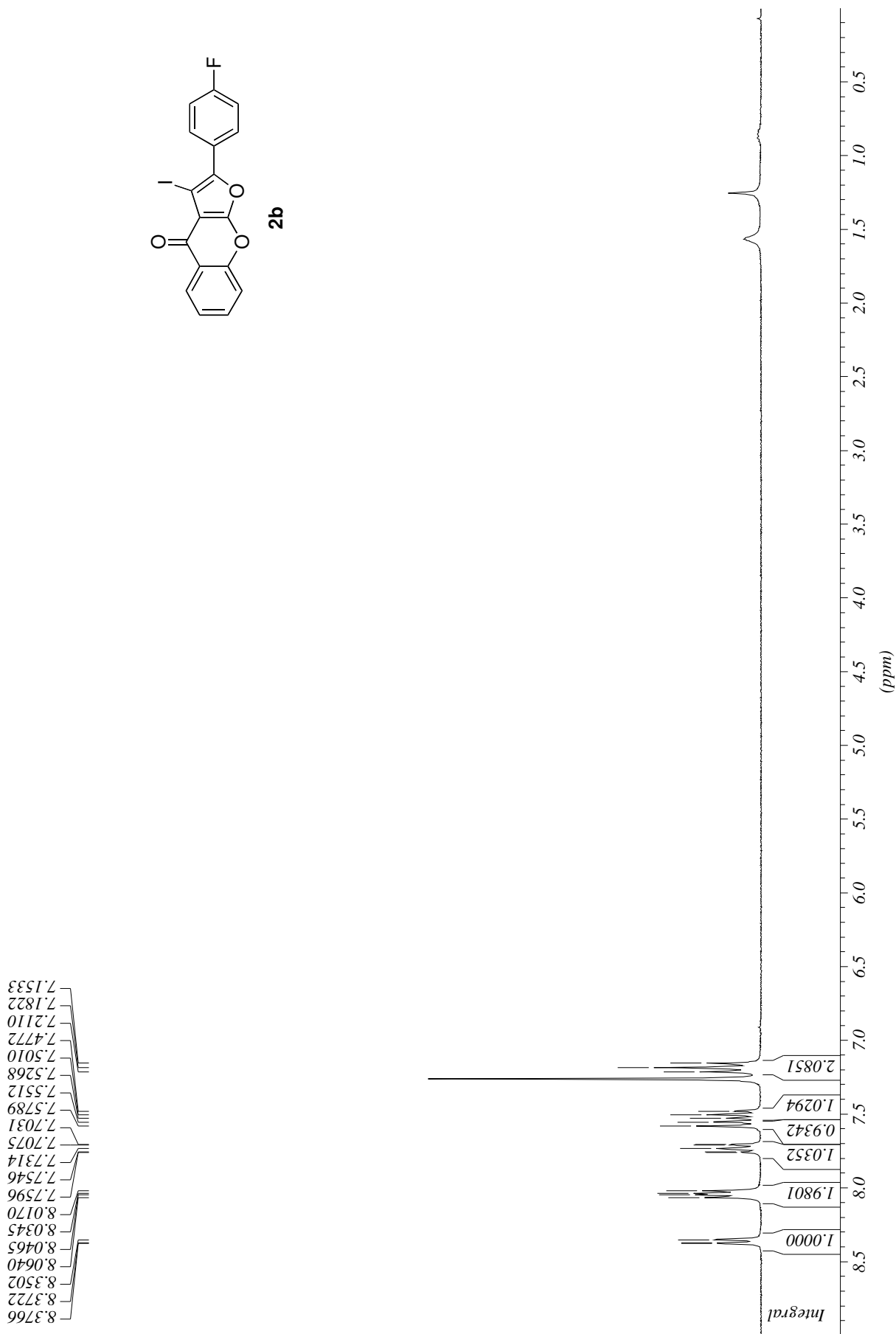
S6

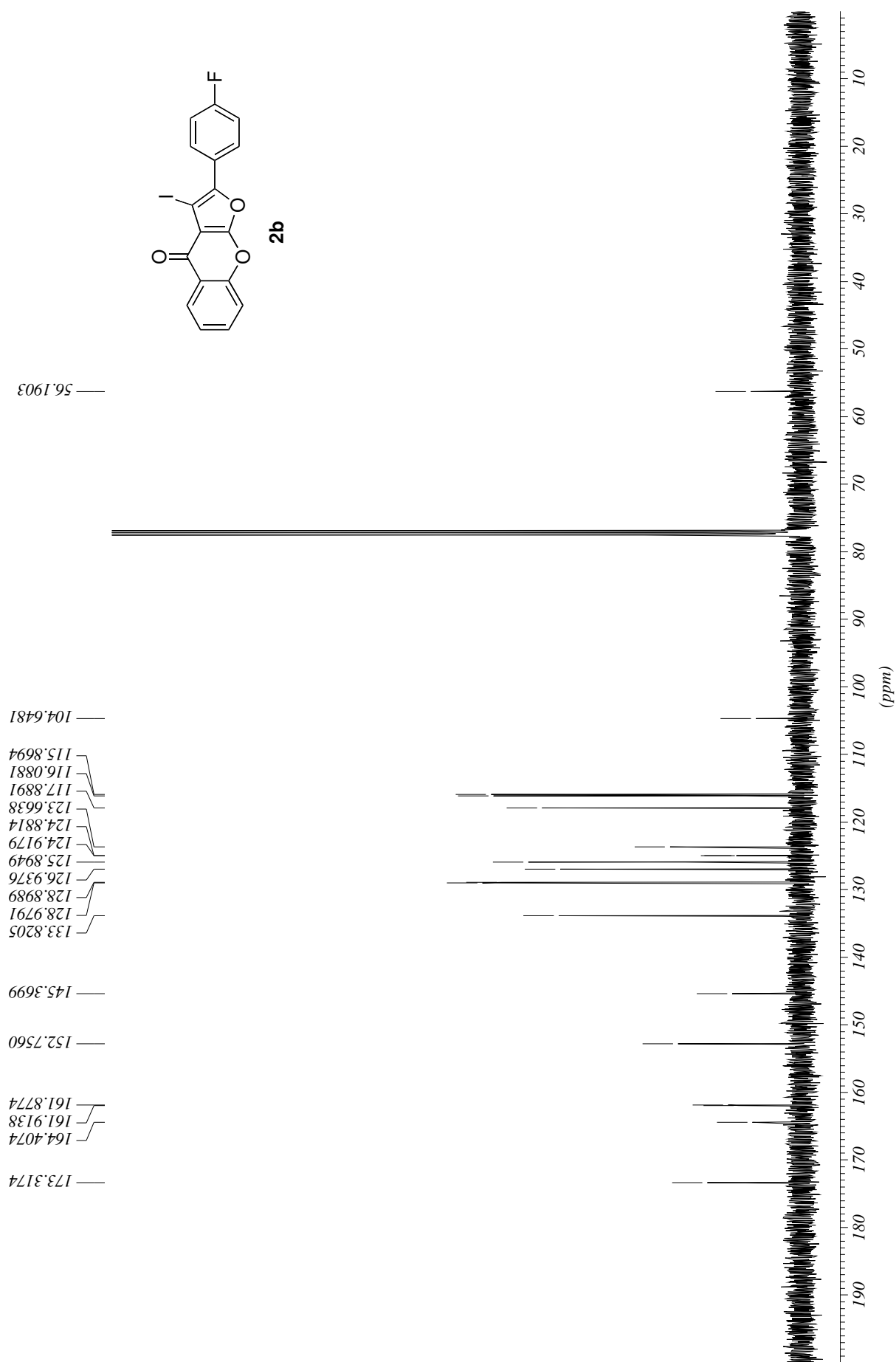




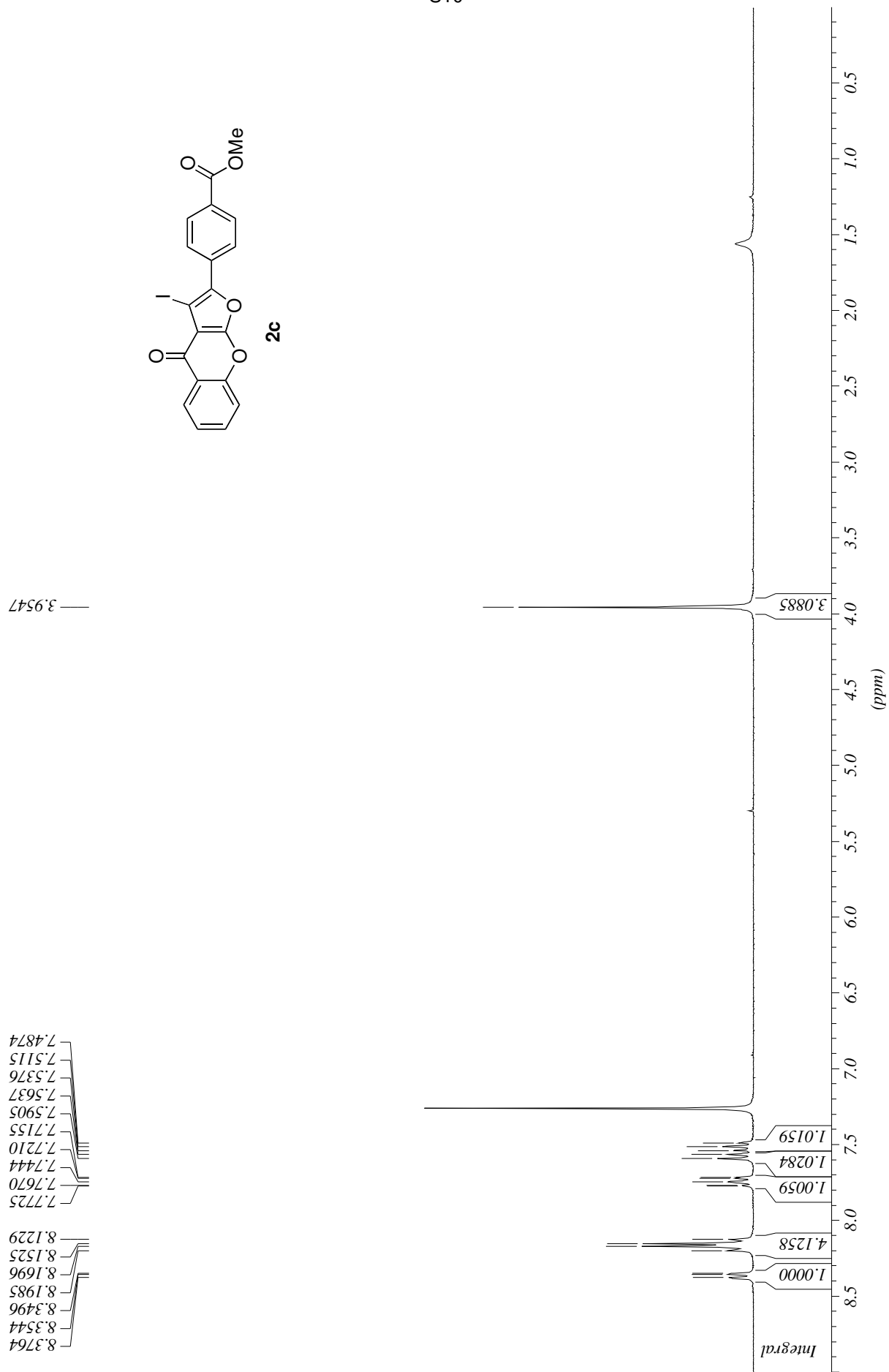
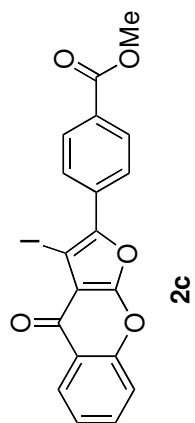


2b

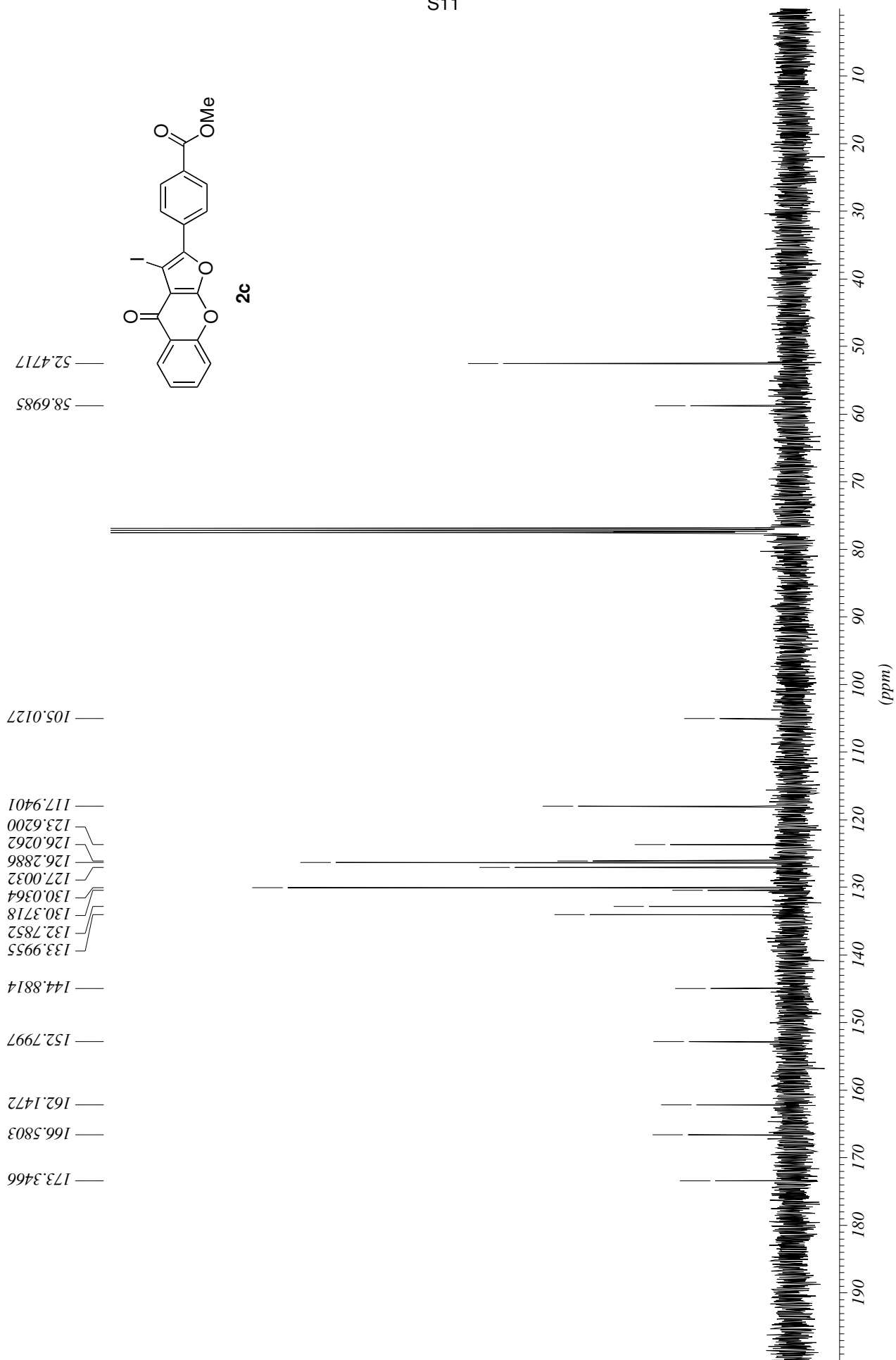




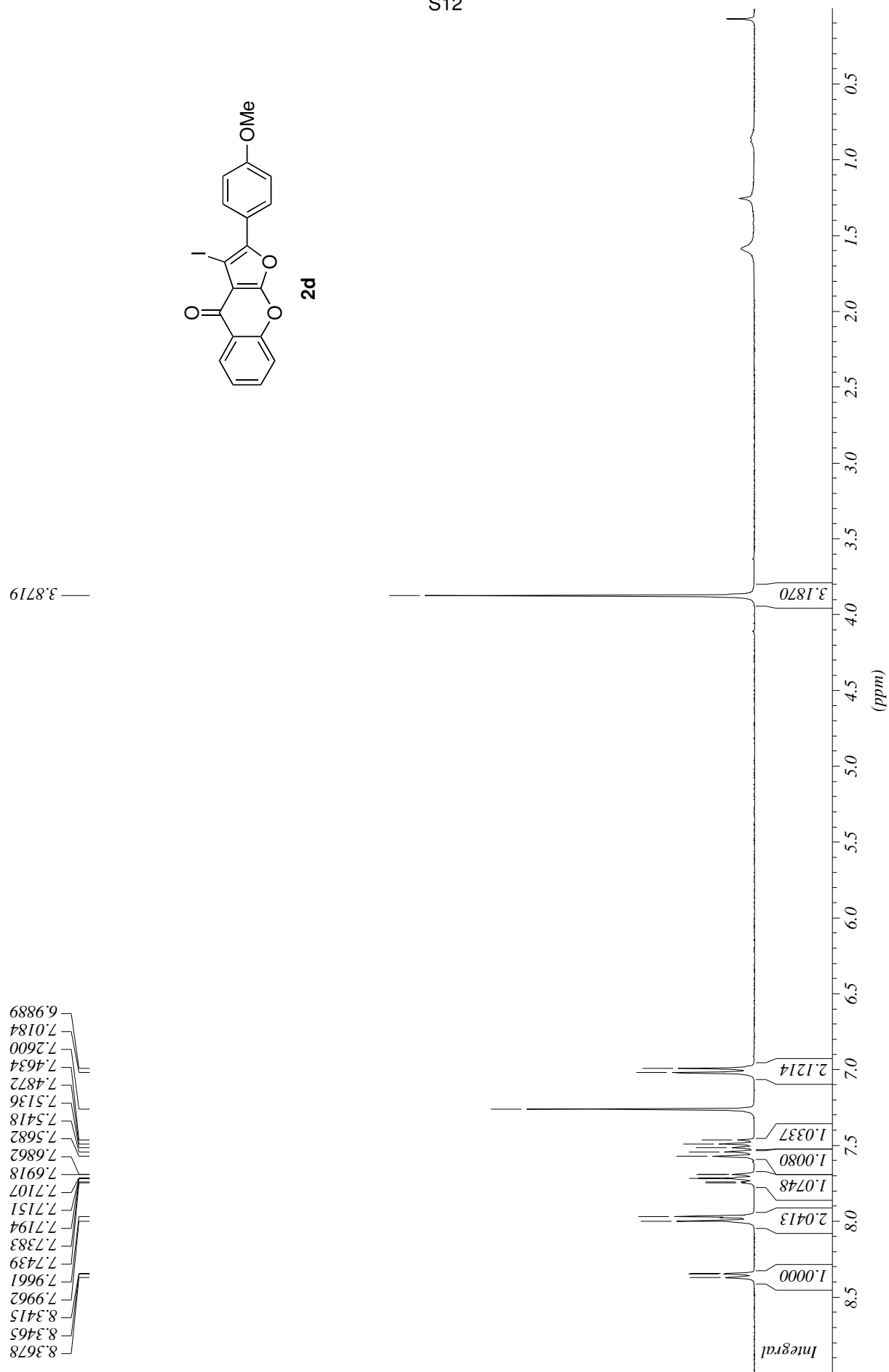
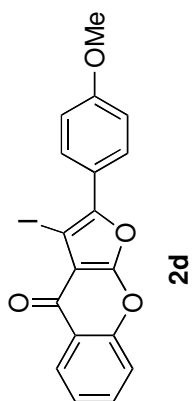
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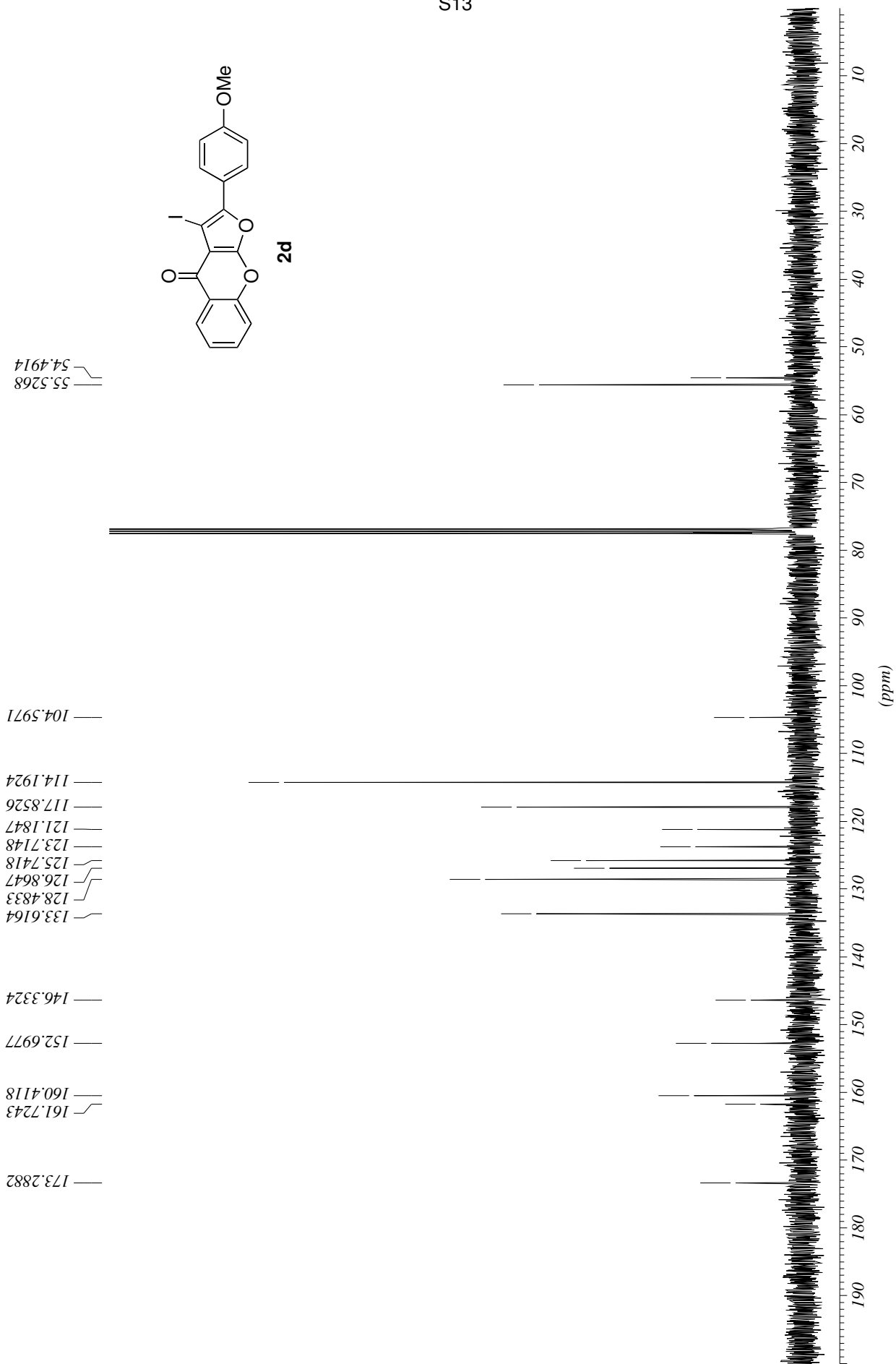
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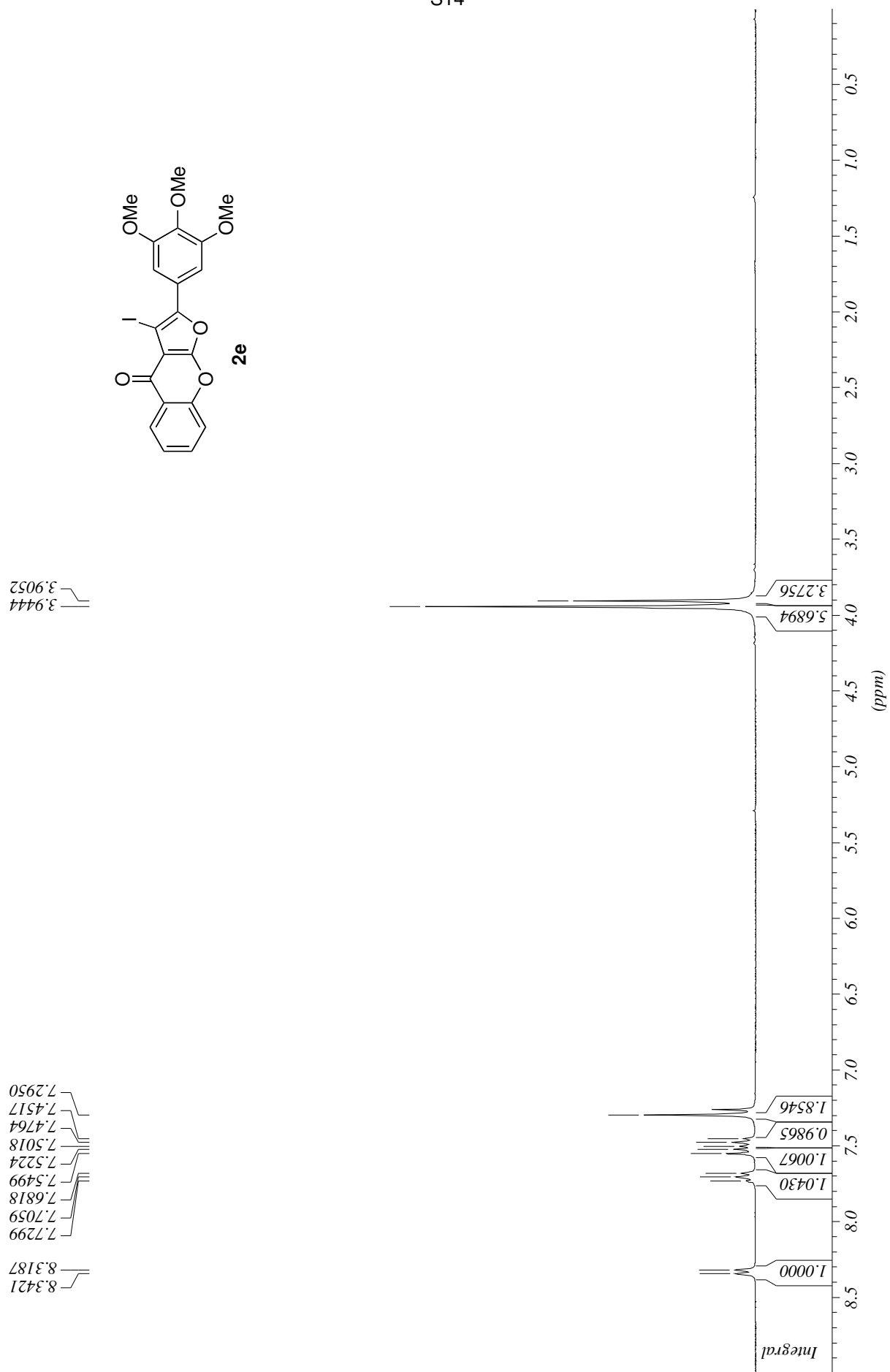
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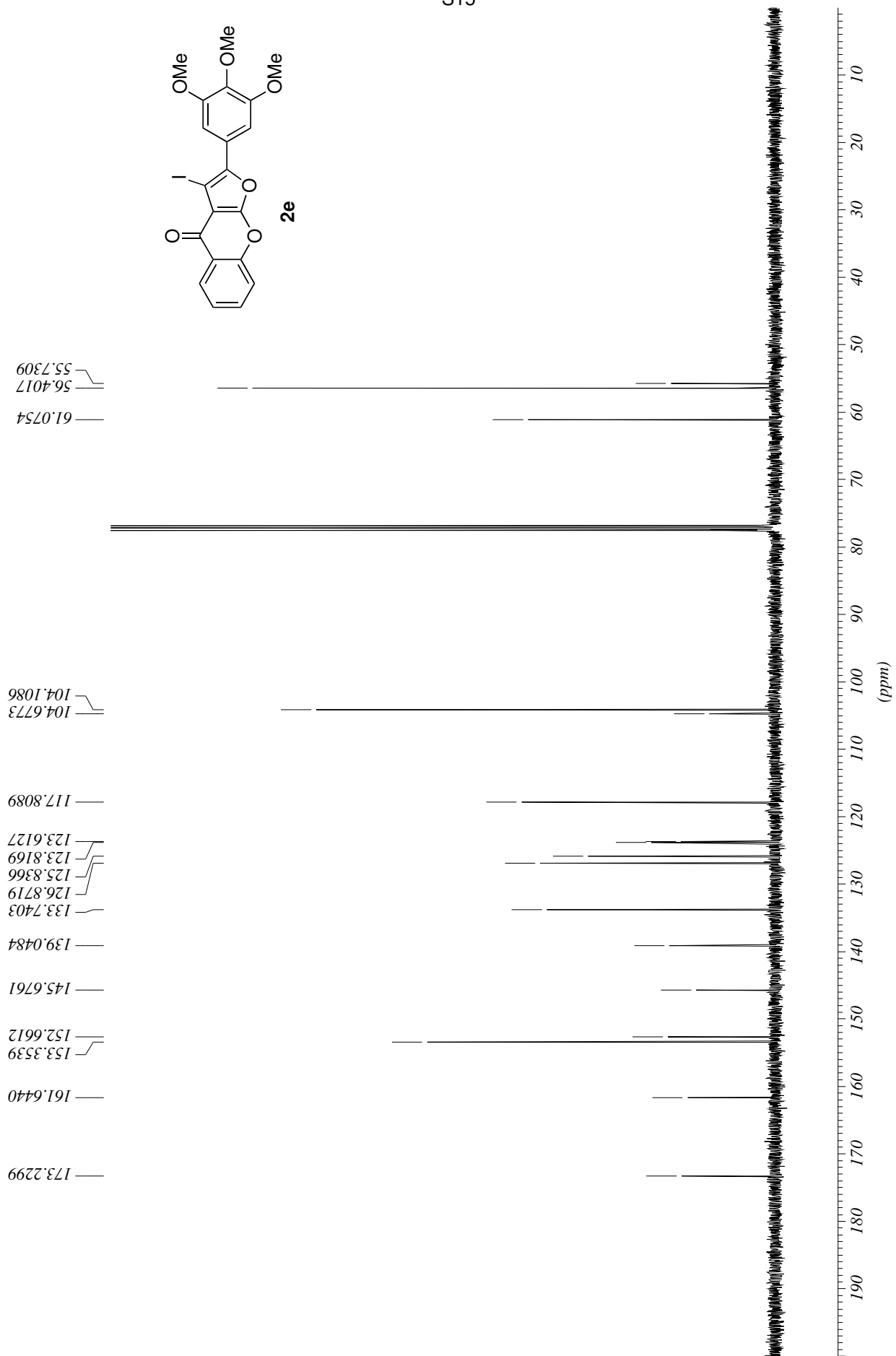
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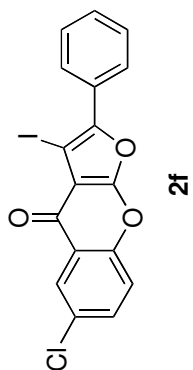
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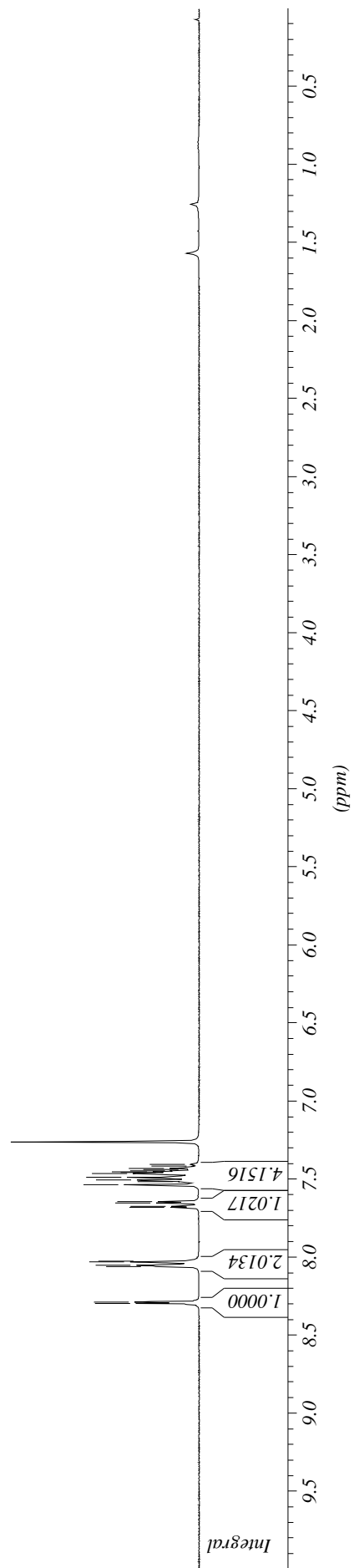
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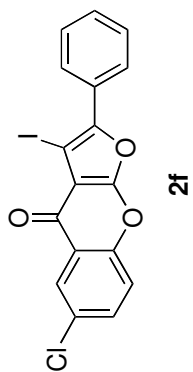
S16



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S17



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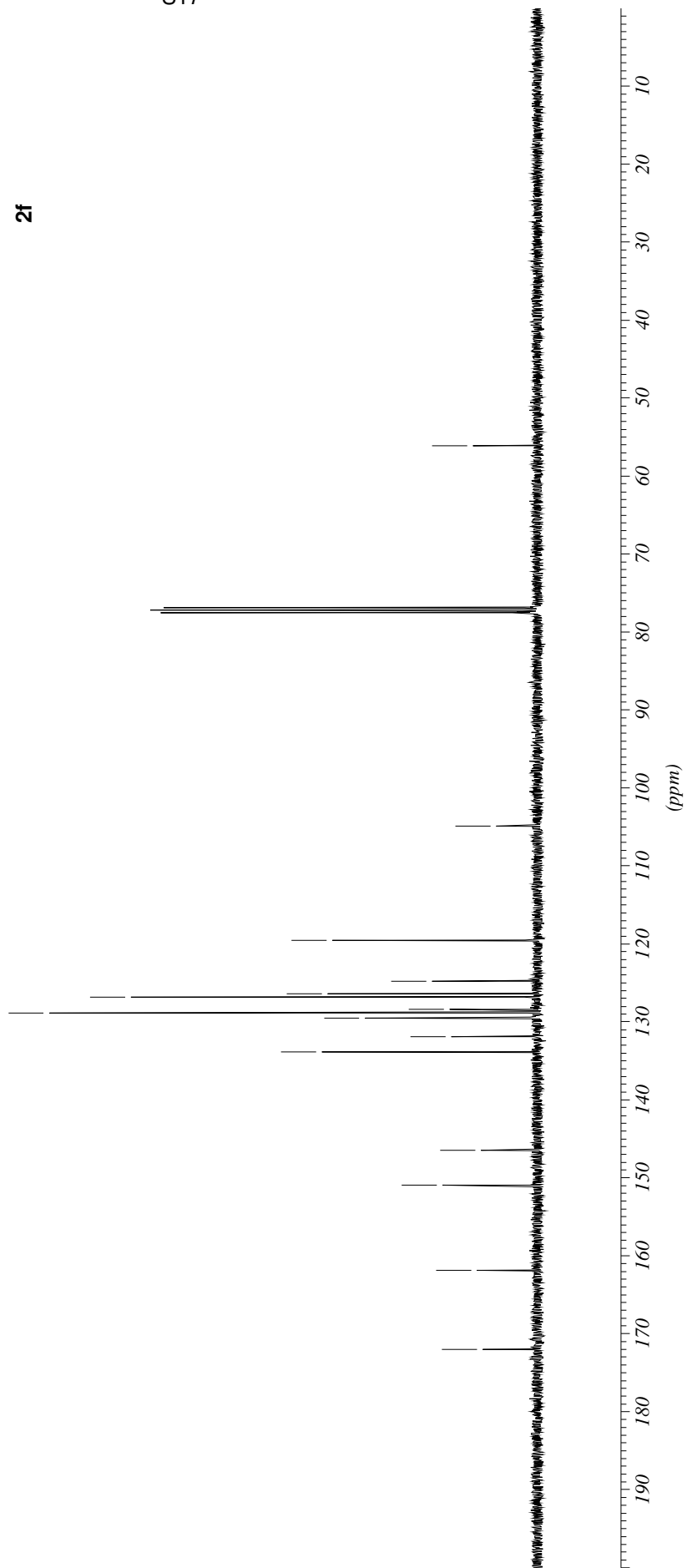
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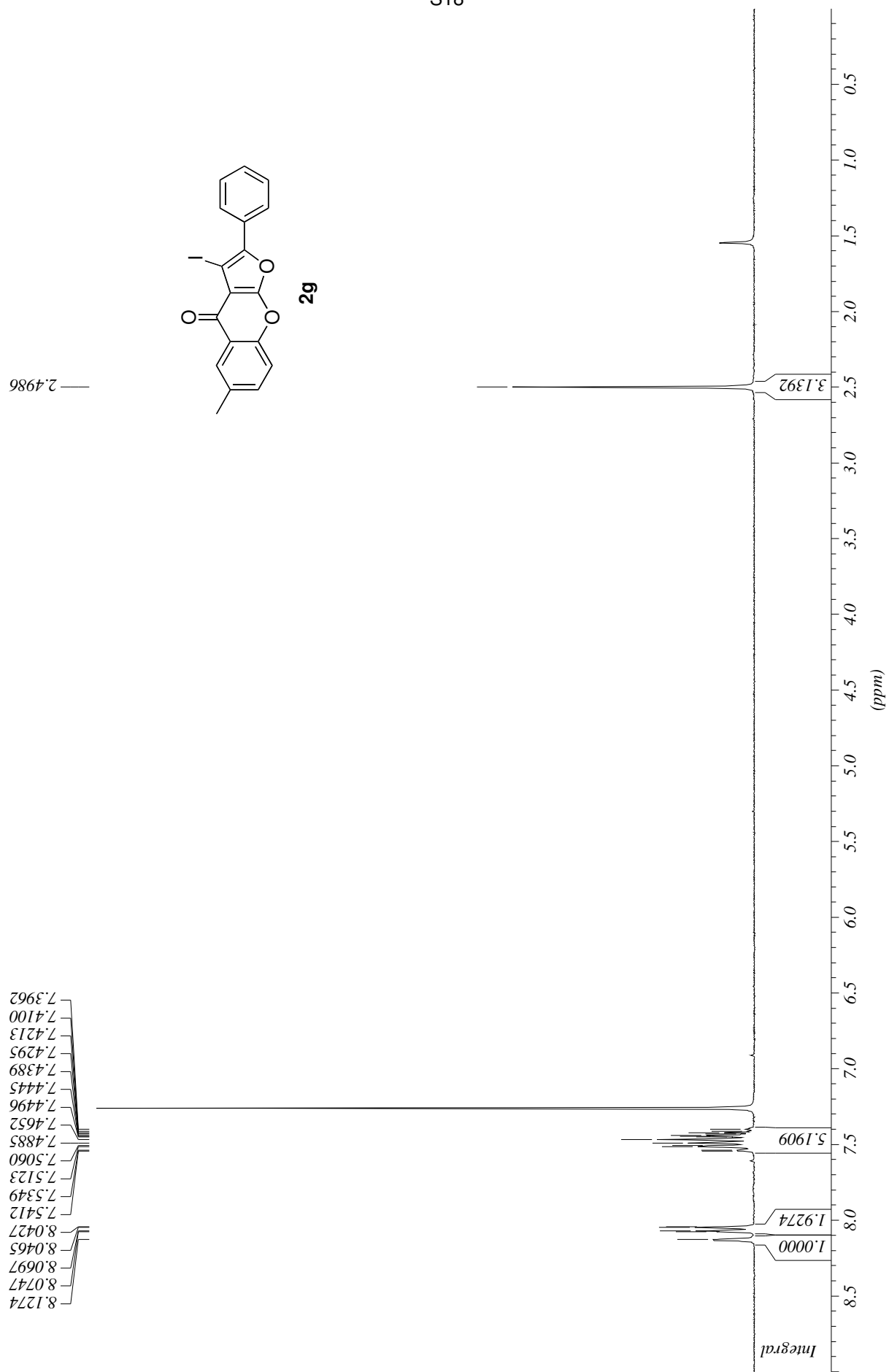
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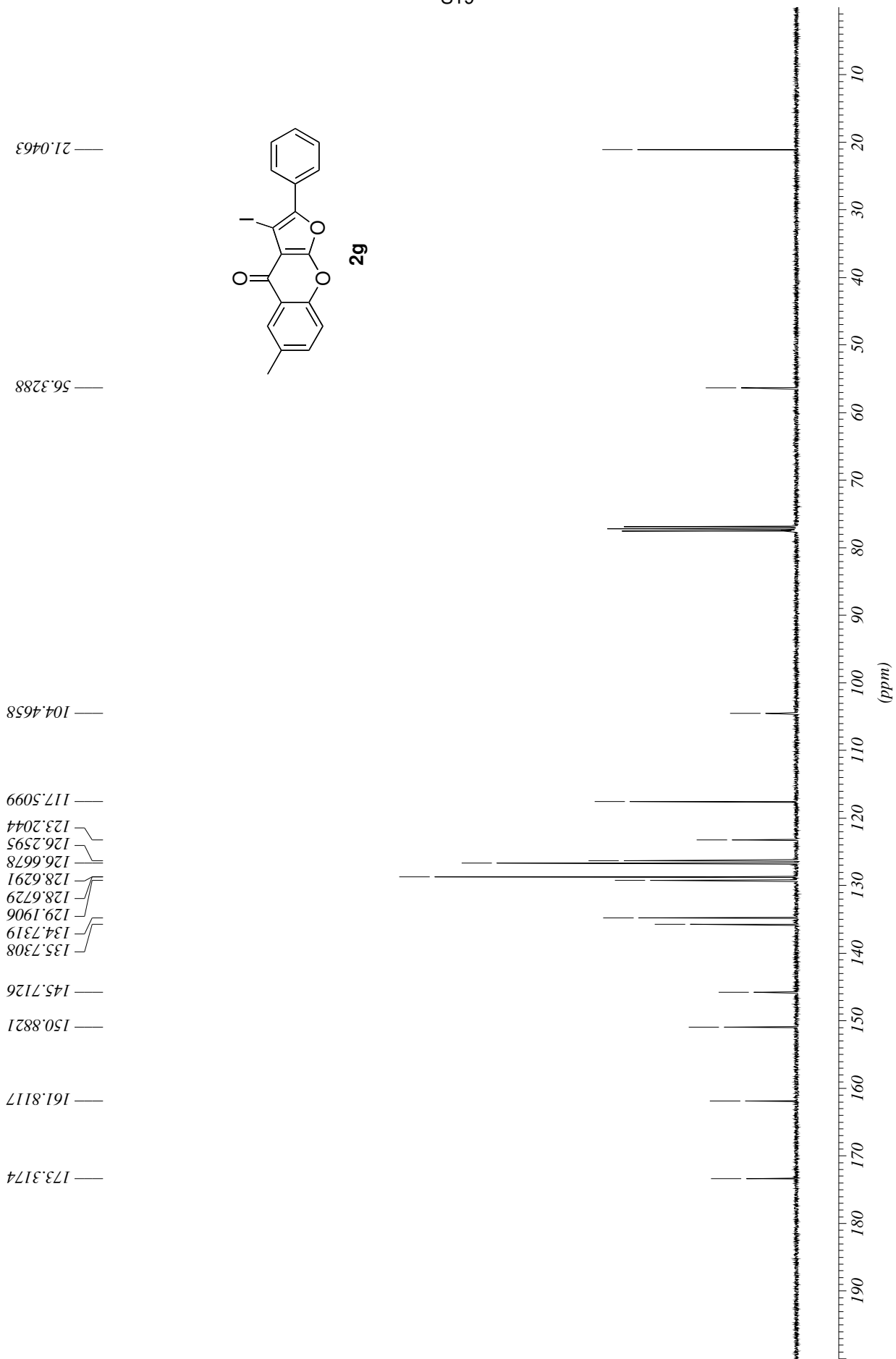
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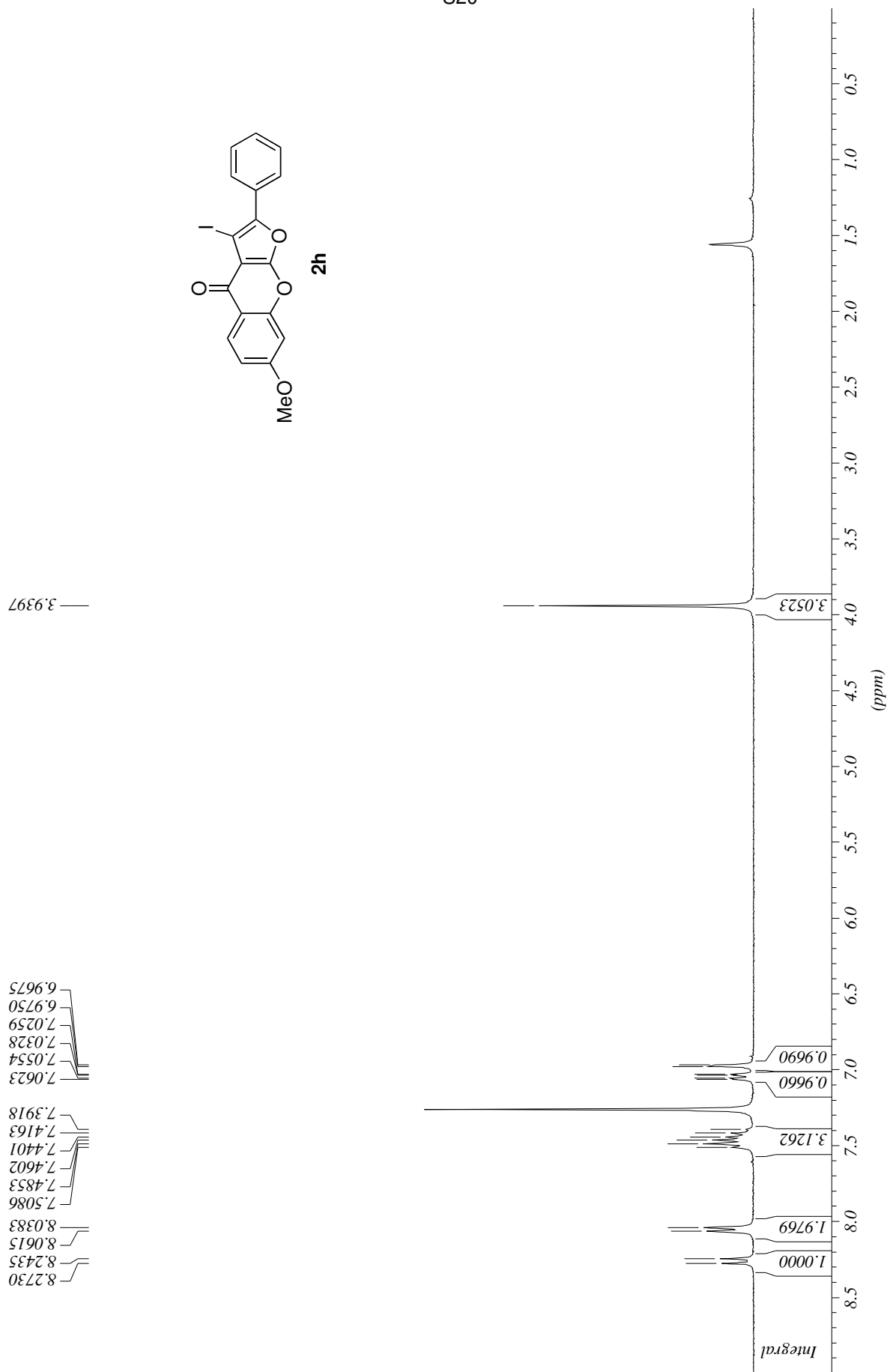
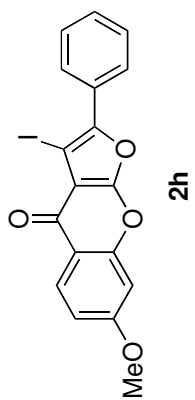
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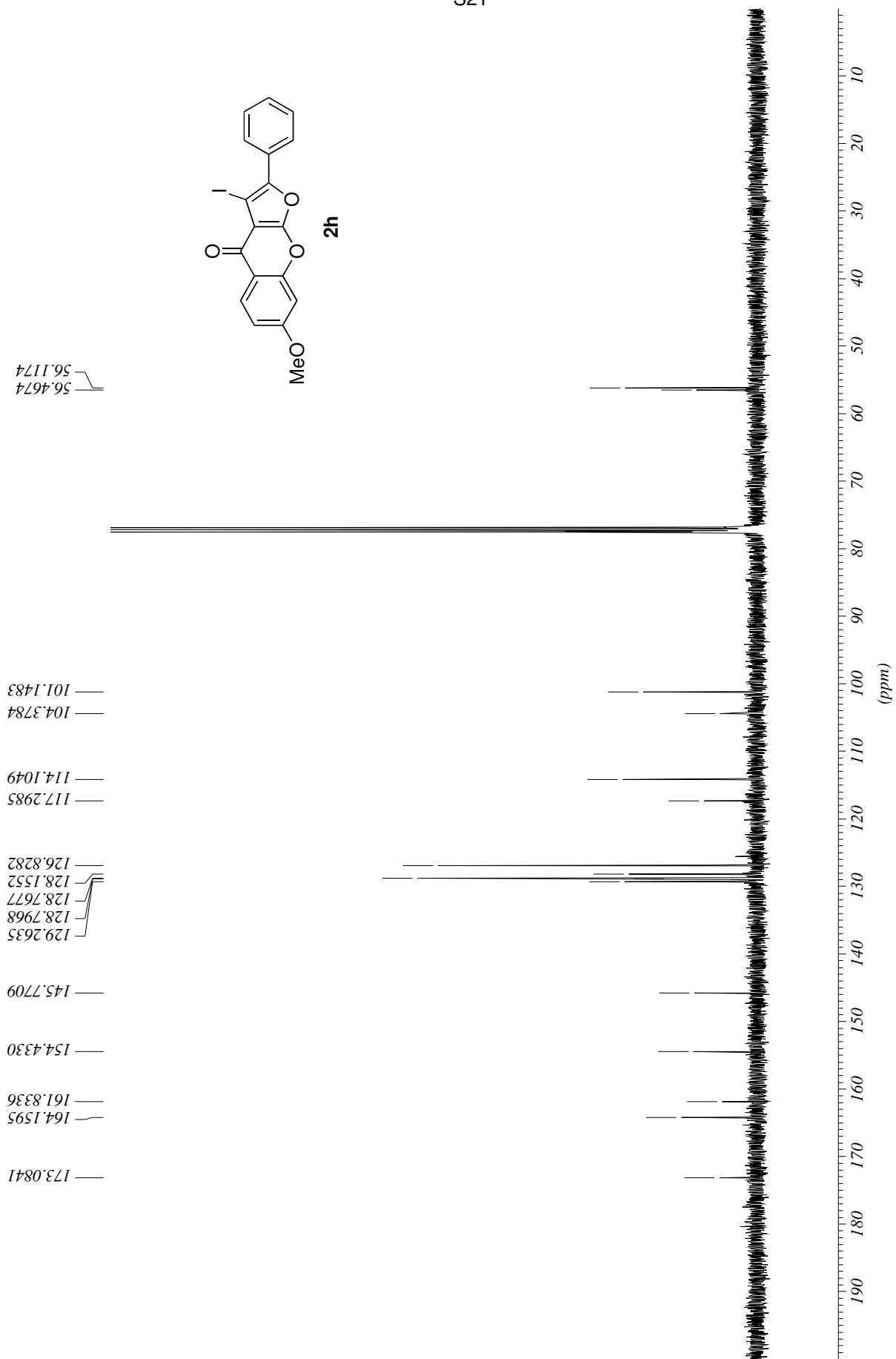
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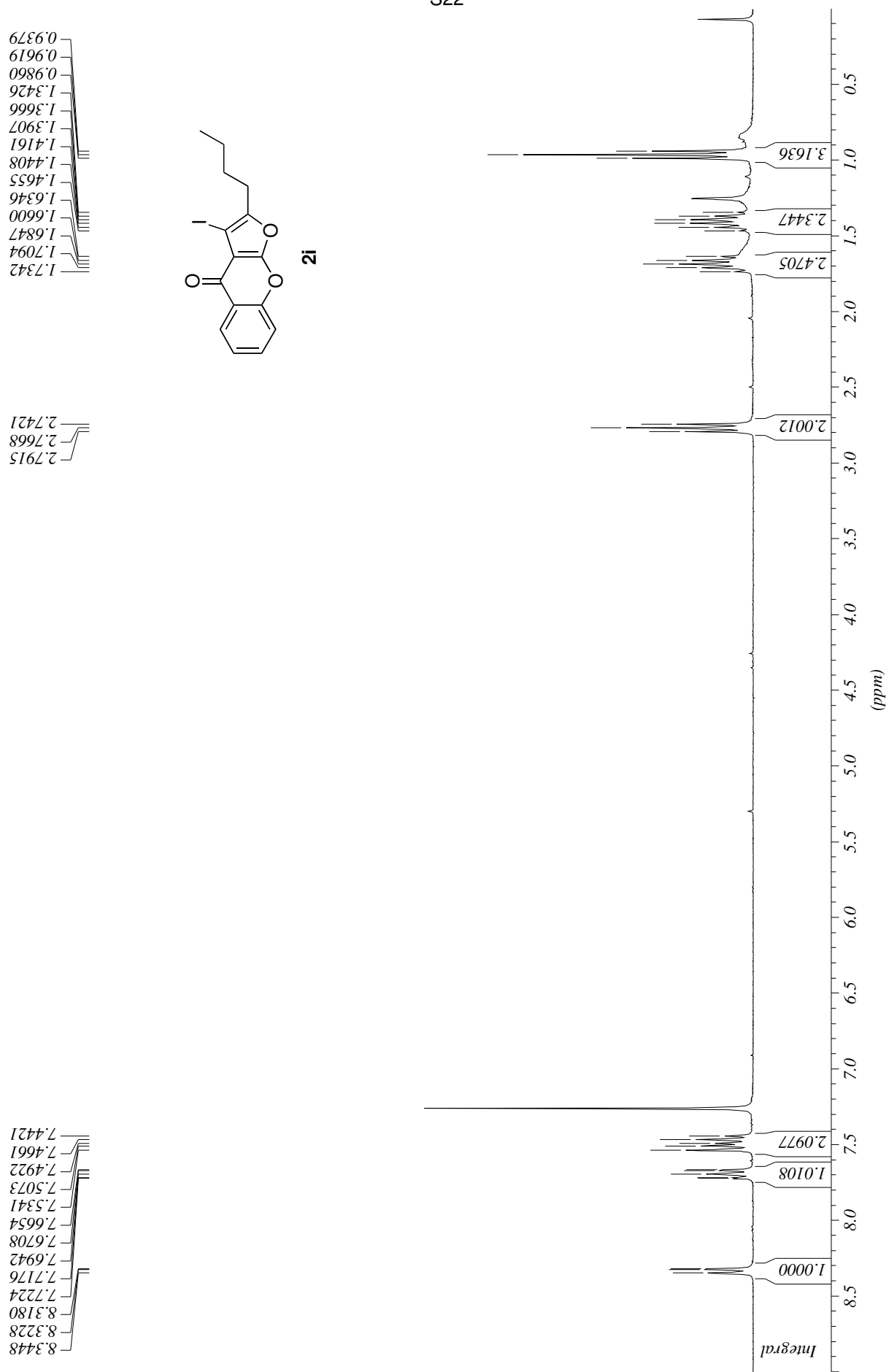
S20



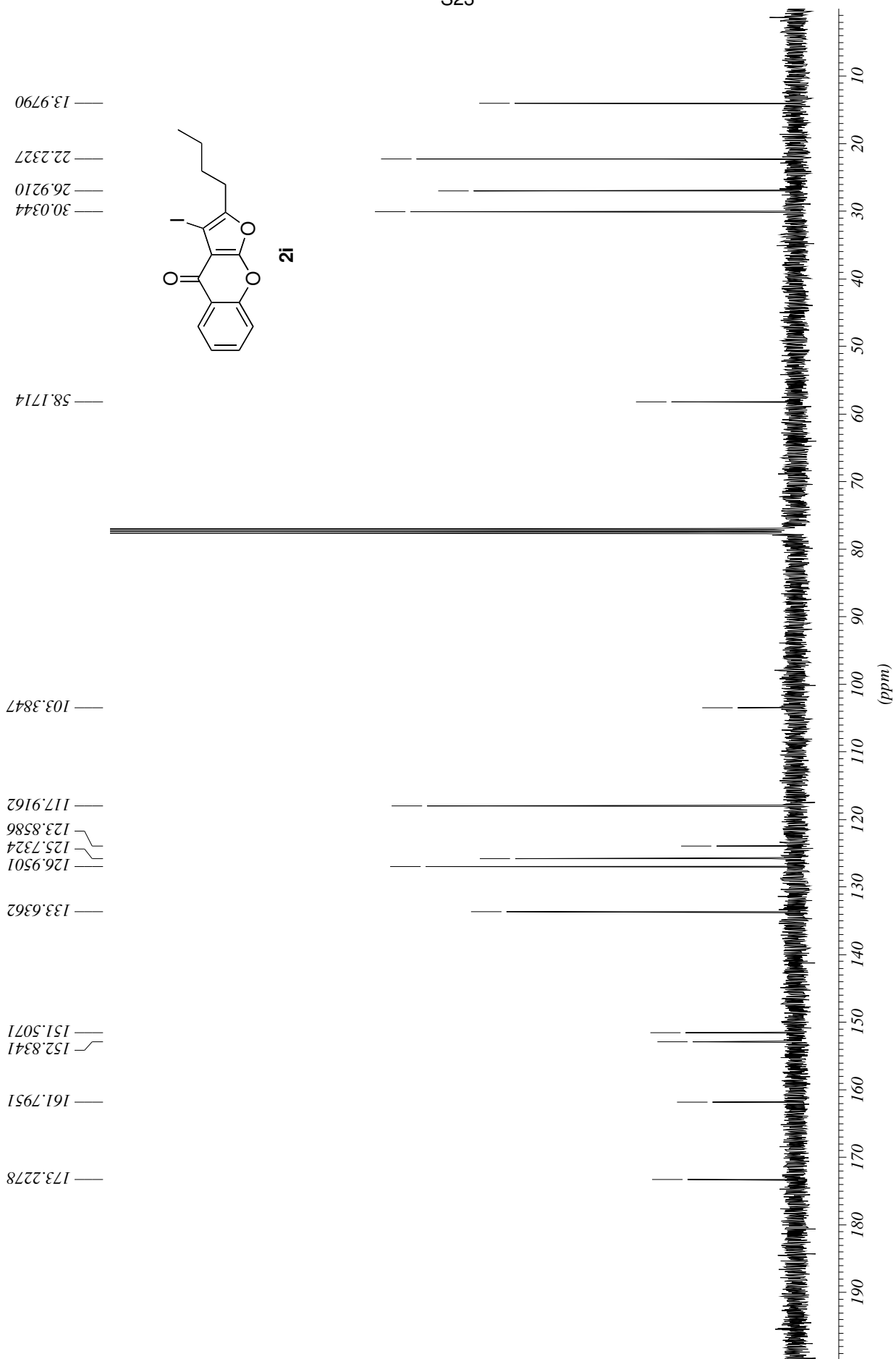
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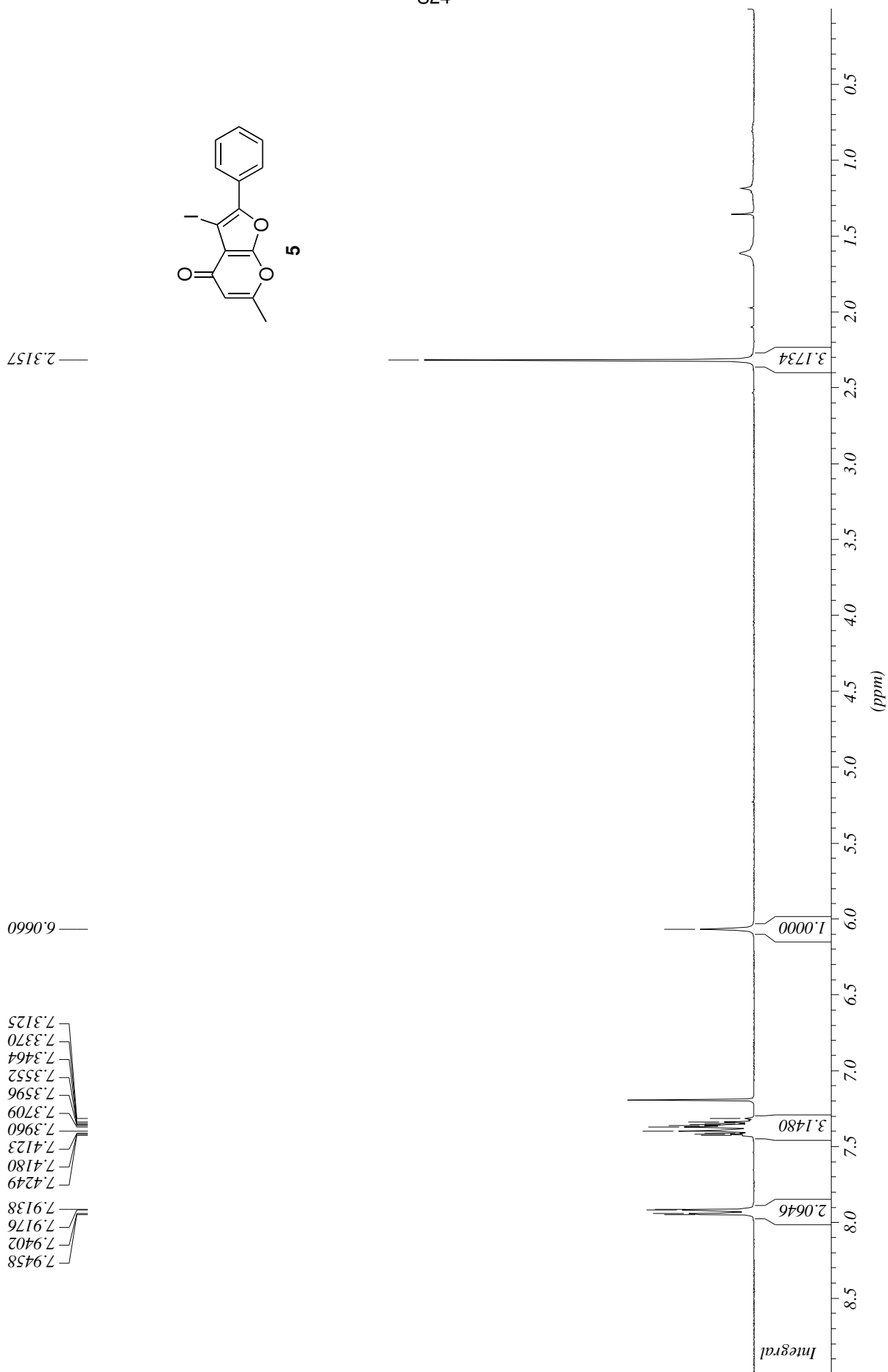
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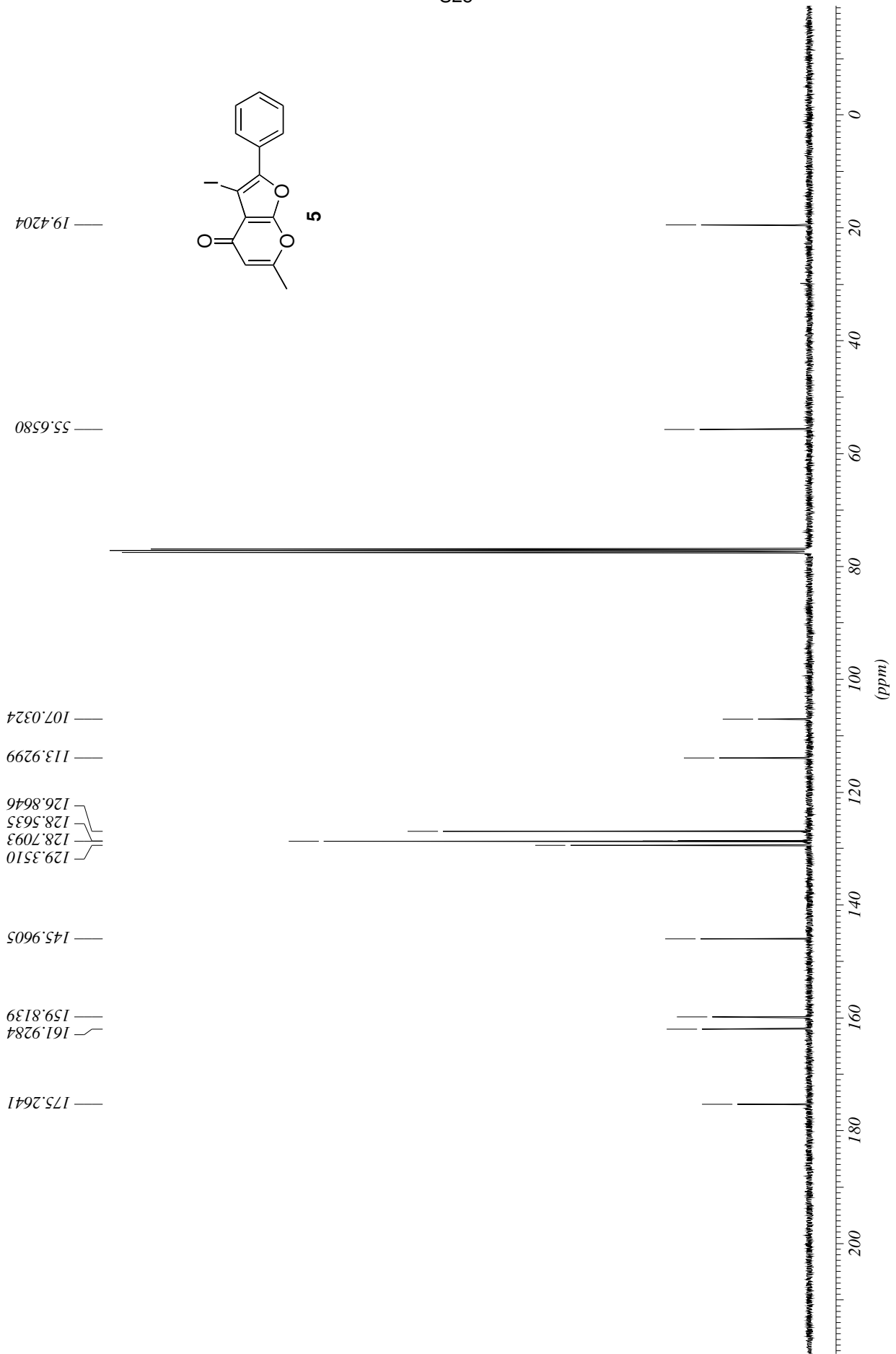
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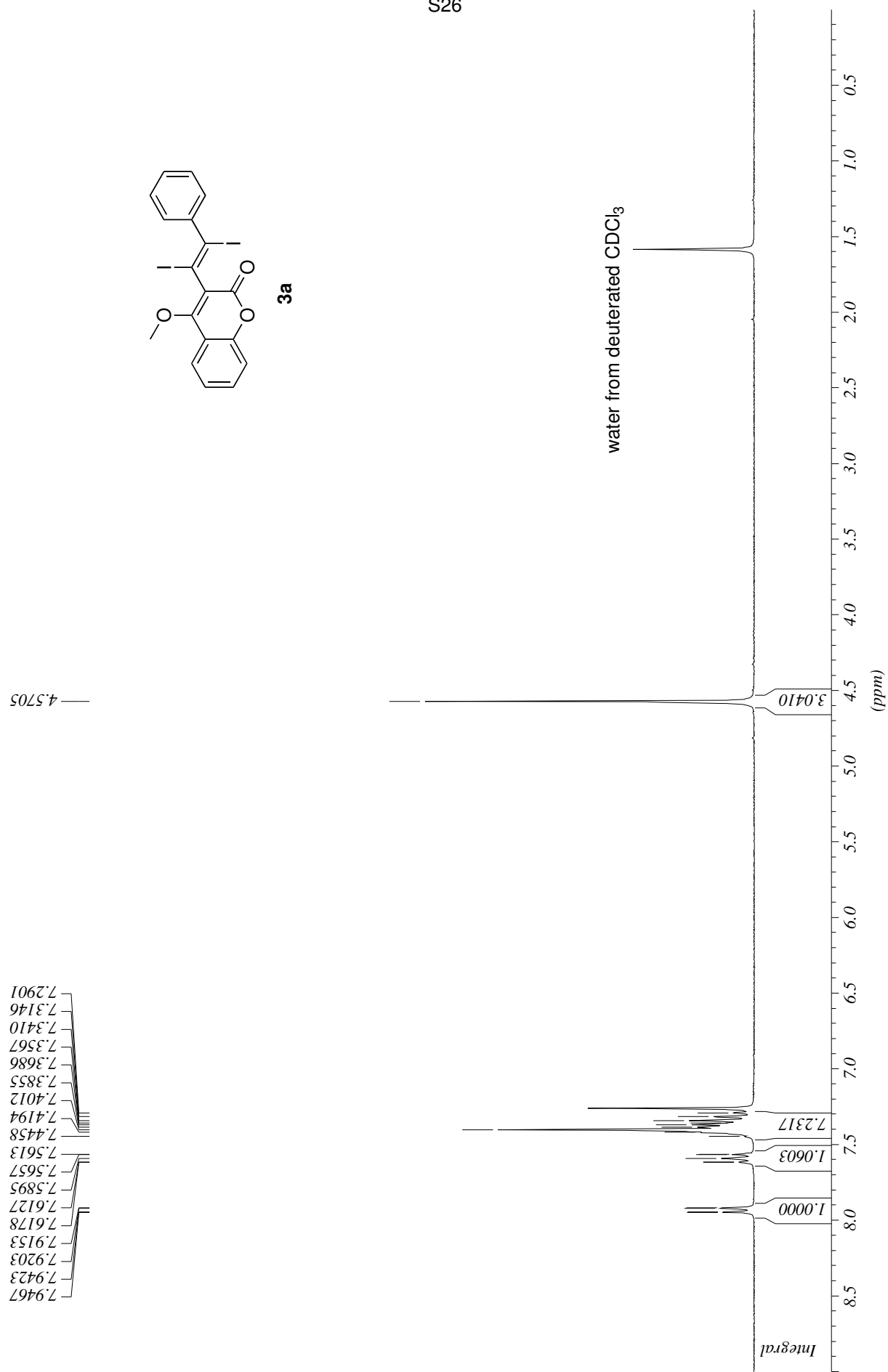
S24



S25



S26



S27

