SUPPORTING INFORMATION

Assembly of Multicyclic Isoquinoline Scaffolds from Pyridines: Formal Total Synthesis of Fredericamycin A

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This version of the ESI published 14/07/2021 replaces the previous version published 28/06/2021. All spectra data now included.

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General

All moisture or oxygen-sensitive reactions were carried out under an argon atmosphere in heat-dried flasks. The solvents used were purified by distillation over the drying agents indicated and were transferred under argon: THF (Na), CH_2Cl_2 (CaH_2), acetone ($CaSO_4$). Other solvents were all bought from Sigma-Aldrich as anhydrous reagent. All reactions were monitored by thin-layer chromatography (TLC) on silica gel F_{254} plates using UV light as visualizing agent (if applicable), and a solution of ammonium molybdate tetrahydrate (50 g/L) in EtOH followed by heating as developing agents. The products were purified by flash column chromatography on silica gel (200-300 meshes).

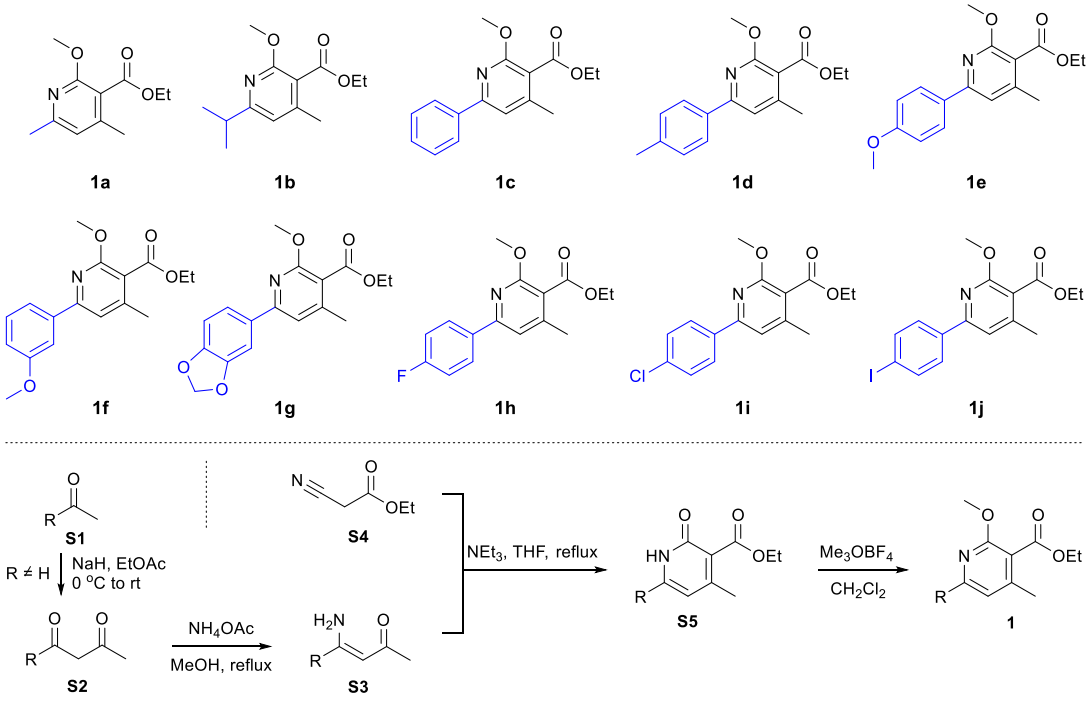
^{1}H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$, acetonitrile-d_3, DMSO-d_6 solution on a Bruker AVIII 400 MHz or AV 500 MHz instrument. Chemical shifts were denoted in ppm (δ), and calibrated by using residual undeuterated solvent ($CDCl_3$ (7.27 ppm), acetonitrile-d_3 (1.94 ppm), DMSO-d_6 (2.50 ppm) or tetramethylsilane (0.00 ppm)) as internal reference for ^{1}H NMR and the deuterated solvent ($CDCl_3$ (77.00 ppm), acetonitrile-d_3 (1.32 ppm), DMSO-d_6 (39.52 ppm) or tetramethylsilane (0.00 ppm)) as internal standard for ^{13}C NMR. The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, br = broad, m = multiplet, dd = double doublet, dt = double triplet, dq = double quartet. High-resolution mass spectral analysis (HRMS) data were measured on a Q-tof mass spectrometer by means of the ESI technique. The IR spectra were recorded on SHIMADZU IRAffinity-1 FTIR spectrometer. The X-ray single-crystal determination was performed on a Bruker APEX II X-ray single crystal diffractometer.

1. Conditions Screening for Isoquinoline Synthesis from Pyridine

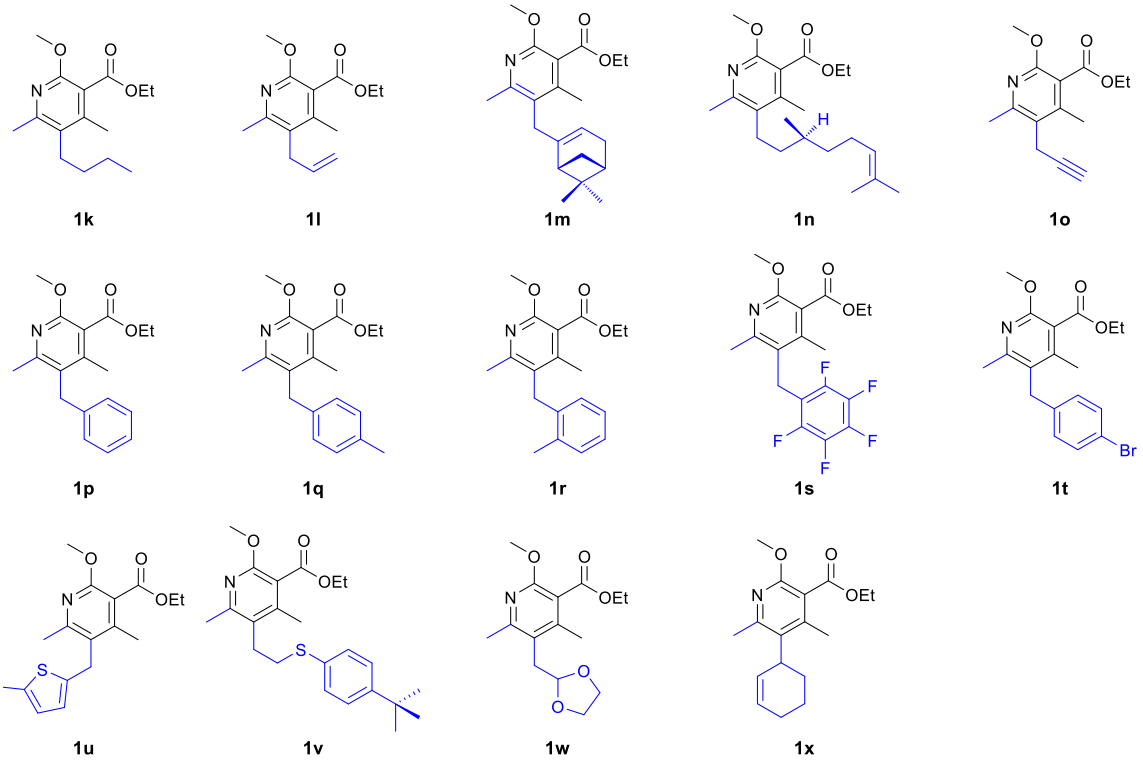
Many attempts have been made to optimize the reaction conditions. Firstly, we have synthesized or bought the substrates needed and tested the Staunton–Weinreb-type annulation conditions with cycloenones bearing different *α*- or *β*-substitutes. Below are the details.

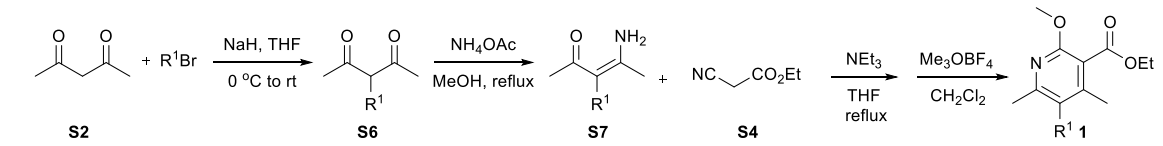
1.1. General Scheme for Preparation of Compound 1

Part 1: **1a**, **1b**, **1c**, **1d**, **1e**, **1f**, **1g**, **1h**, **1i**, **1j**

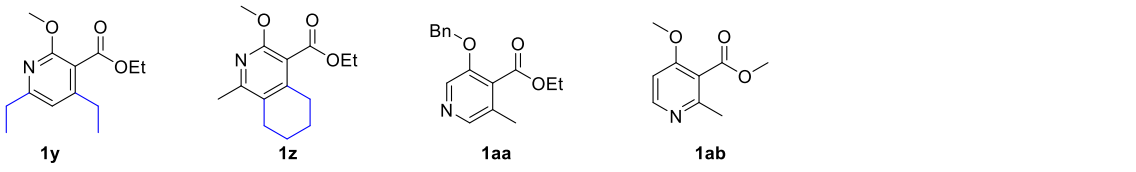


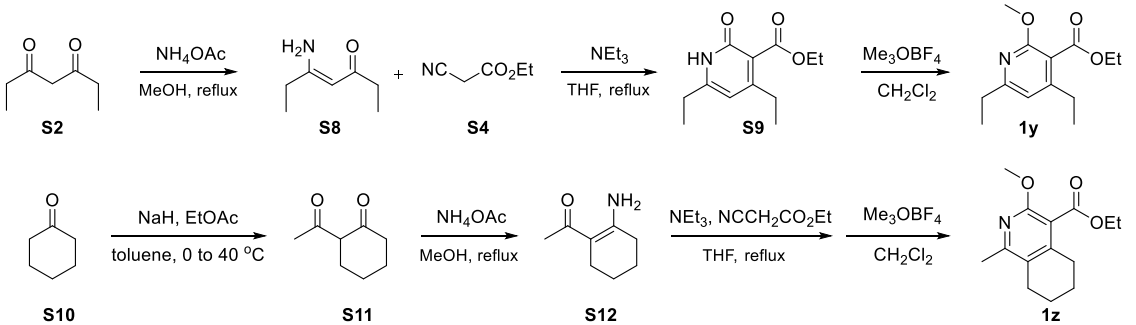
Part 2: **1k**, **1l**, **1m**, **1n**, **1o**, **1p**, **1q**, **1r**, **1s**, **1t**, **1u**, **1v**, **1w**, **1x**

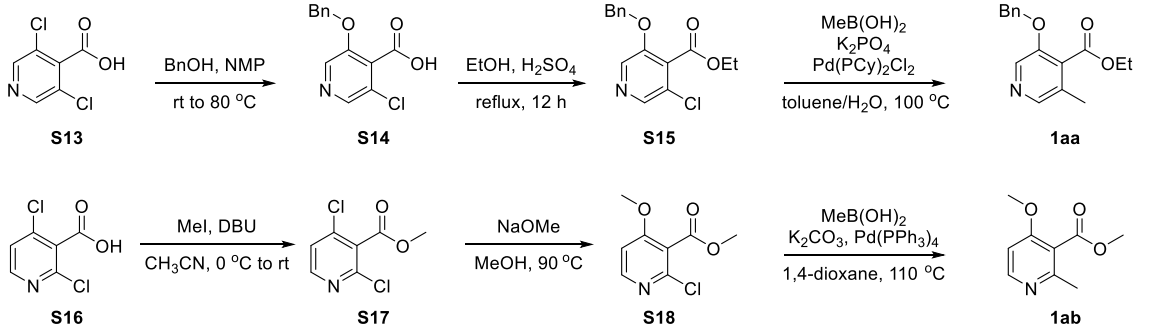




Part 3: **1y**, **1z**, **1aa**, **1ab**

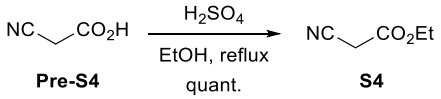






All the substrates pertaining to **1** could be synthesized via schemes demonstrated in part 1 to 3. Particularly, **1a** is commercially available and the details for synthesis of this model substrate in large scale are shown below.

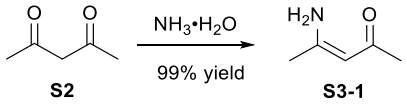
1.1.1. Preparation of Compound S4



To a stirred solution of **Pre-S4** (50.0 g, 590.0 mmol, 1.0 equiv) in EtOH (200 mL) was dropwise added concentrated H_2SO_4 (3.2 mL, 59.0 mmol, 0.1 equiv) at room temperature. The resulting mixture was stirred at reflux overnight. After cooling to room temperature, the mixture was concentrated under reduced pressure. EtOAc (200 mL) and water (200 mL) were added to the residue. The organic phase was separated, and the aqueous layer was extracted with EtOAc (2 × 200 mL). The combined extracts were washed with brine (200 mL), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The crude **S4** (66.7 g, 590.0 mmol, quant.) was obtained as a colorless liquid and pure enough for the next step.

S4: **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 4.27 (q, J = 7.1 Hz, 2H), 3.54 (s, 2H), 1.32 ppm (t, J = 7.1 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 167.6, 113.4, 62.5, 24.4, 13.6 ppm.

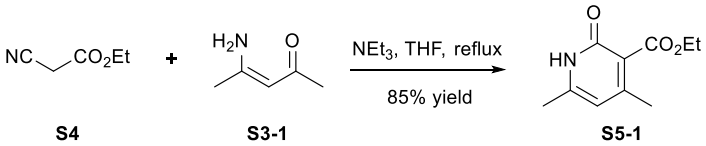
1.1.2. Preparation of Compound S3-1



To suspension of silica gel (50 g) in **S2** (50.0 g, 499.8 mmol, 1.0 equiv) was dropwise added ammonia (28% in water, 40.5 mL, 599.8 mmol, 1.2 equiv) at room temperature. The resulting mixture was stirred for 12 h. CH_2Cl_2 (200 mL) and water (200 mL) were added to the mixture. The organic phase was separated, and the aqueous layer was extracted with CH_2Cl_2 (2 × 200 mL). The combined extracts were washed with brine (200 mL), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel eluting with *n*-hexane/AcOEt (1:1) to afford **S3-1** (49.0 g, 494.8 mmol, 99% yield) as a colorless solid.

S3-1: **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 9.57 (br, 1H), 5.72 (br, 1H), 4.90 (s, 1H), 1.90 (s, 3H), 1.80 ppm (s, 3H).

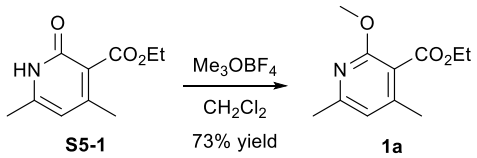
1.1.3. Preparation of Compound S5-1



To a stirred solution of **S4** (50.0 g, 442.3 mmol, 1.0 equiv) and NEt_3 (61.6 mL, 442.3 mmol, 1.0 equiv) in THF (100 mL) was dropwise added **S3-1** (43.8 g, 442.3 mmol, 1.0 equiv) in THF (100 mL). The resulting mixture was brought to reflux and stirred overnight. After cooling to room temperature, additional NEt_3 (61.6 mL, 442.3 mmol, 1.0 equiv) was added and the mixture was brought to reflux and stirred for additional 12 h. After cooling to room temperature, CH_2Cl_2 (400 mL) and water (400 mL) were added. The organic phase was separated, and the aqueous layer was extracted with CH_2Cl_2 (2 × 200 mL). The combined extracts were washed with brine (400 mL), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The pure **S5-1** (73.4 g, 376.0 mmol, 85% yield) was obtained as a white solid by recrystallization from ethanol.

S5-1: **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 13.25 (br, 1H), 5.93 (s, 1H), 4.37 (q, J = 7.0 Hz, 2H), 2.30 (s, 3H), 2.22 (s, 3H), 1.36 ppm (t, J = 7.0 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 166.7, 162.8, 152.2, 146.8, 120.0, 108.9, 61.0, 20.0, 18.9, 14.2 ppm.

1.1.4. Preparation of Compound 1a

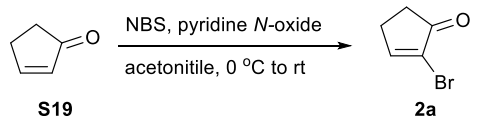


S5-1 1a

To a stirred solution of **S5-1** (50.0 g, 256.3 mmol, 1.0 equiv) in CH_2Cl_2 (200 mL) was added Me_3OBF_4 (41.7 g, 281.9 mmol, 1.1 equiv). The resulting mixture was stirred vigorously for 2 d. A saturated aqueous solution of $NaHCO_3$ (200 mL) was dropwise added to the stirred solution (caution: a lot of gas emerged). After addition of water (200 mL), the organic phase was separated, and the aqueous layer was extracted with CH_2Cl_2 (2 × 200 mL). The combined extracts were washed with brine (400 mL), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel eluting with *n*-hexane/AcOEt (4:1) to afford the pyridine **1a** (39.1 g, 187.1 mmol, 73% yield; 95% yield brsm) as a colorless liquid.

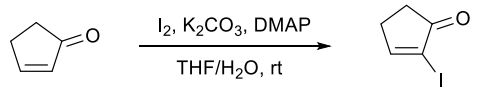
1a: **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 6.48 (s, 1H), 4.29 (q, J = 7.5 Hz, 2H), 3.85 (s, 3H), 2.30 (s, 3H), 2.17 (s, 3H), 1.28 ppm (t, J = 7.5 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 167.0, 160.0, 156.6, 147.1, 117.3, 114.0, 60.8, 53.2, 23.6, 18.6, 13.9 ppm.

1.2. General Scheme for Preparation of Compound 2



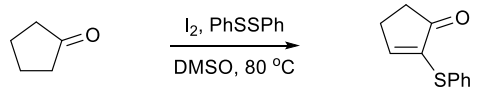
S19 2a

Ohfusa, T. and Nishida, A. *Tetrahedron* **2011**, *67*, 1893–1906.



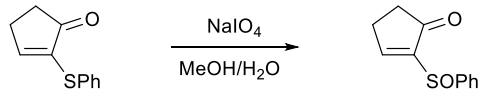
S19 2b

Lin, H.; Xiao, L.-J.; Zhou, M.-J.; Yu, H.-M.; Xie, J.-H. and Zhou, Q.-L. *Org. Lett.* **2006**, *18*, 1434–1437.



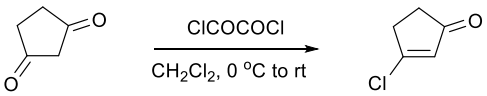
S20 2c

Ge, W.; Zhu, X. and Wei, Y. *Adv. Synth. Catal.* **2013**, *355*, 3014–3021.



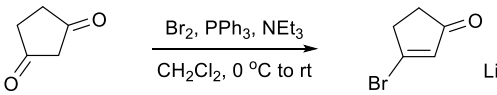
2c 2d

Yechezkel, T.; Ghera, E.; Ostercamp, D. and Hassner, A. *J. Org. Chem.* **1995**, *60*, 5135–5142.



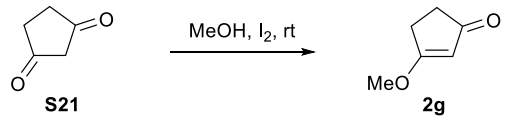
S21 2e

Eckelbarger,J. D.; Wilmot, J. T.; Epperson, M. T.;Thakur, C. S.; Shum, D.; Antczak, C.; Tarassishin, L.; Djaballah, H.; and Gin, D. Y. *Chem. Eur. J.* **2008**, *14*, 4293–4306.

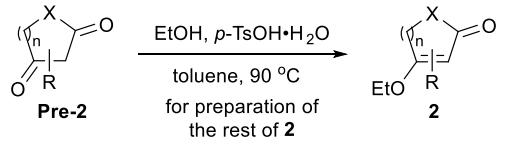


S21 2f

Lin, H.-H.; Chiang, T.-C.; Wu, R.-X.; Chang, Y.-M.; Wang, H.-W.; Liu, S.-T. and Yeh, M.-C. P. *Adv. Synth. Catal.* **2019**, *361*, 1277–1282.



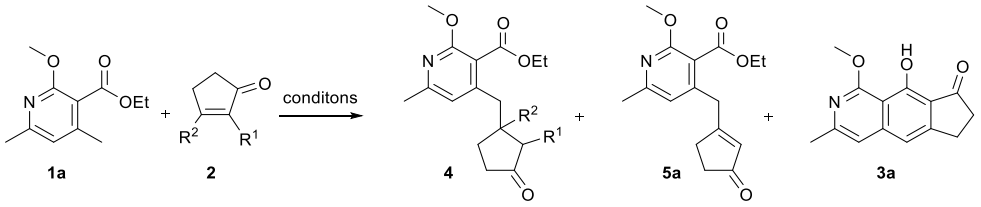
Bhosale, R. S.; Bhosale, S. V.; Bhosale, S. V.; Wang, T. and Zubaidha, P. K. *Tetrahedron Lett.* **2004**, *45*, 7187–7188.



Brenninger, C.; Pöthig, A. and Bach, T. *Angew. Chem. Int. Ed.* **2017**, *56*, 4337–4341.

As we can see from the scheme above, all the substrates pertaining to **2** could be synthesized according to the known literature reported previously.

1.3. Main Scheme for Conditions Screening[a]



Entry	Substrate	Conditions	Result
1	**2a** (R^1 = Br, R^2 = H)	LDA, LDA, THF, –78 °C to rt, THF,	no product
2	**2b** (R^1 = I, R^2 = H)	LDA, THF, –78 °C to rt	no product
3[b]	**2c** (R^1 = SPh, R^2 = H)	LDA, THF, –78 °C to rt	**4a**: 55% yield; **5a**, **3a**: 0%
4[b]	**2d** (R^1 = SOPh, R^2 = H)	LDA, THF, –78 °C to rt	**4b**: 66% yield; **5a**, **3a**: 0%
5	**2e** (R^1 = H, R^2 = Cl)	LDA, CuI, TMSCl, THF, –78 °C to rt	no product
6	**2f** (R^1 = H, R^2 = Br)	LDA, CuI, TMSCl, THF, –78 °C to rt	no product
7[c]	**2g** (R^1 = H, R^2 = OCH_3)	LDA, THF, –78 °C to rt	**4**: 0%; **5a**: 5% yield; **3a**: 10% yield
8[c,d]	**2g** (R^1 = H, R^2 = OCH_3)	LDA, THF, –78 °C	**4**: 0%; **5a**: 25% yield; **3a**: 8% yield

[a]Unless otherwise noted, reactions were conducted as follows: **1a** (0.1 mmol) and LDA (0.1 mmol) reacted in THF at –78 °C for 1 h; **2** (0.1 mmol) was added to the mixture before warming up to rt in 10 min. the reaction was quenched by addition of saturated NH_4Cl after completion monitored by TLC. [b]Compound **4a** or **4b** can't be transformed into **3a** under various conditions. [c]Compound **5a** can't be transformed into **3a** under various conditions. [d]Compound **2** was recovered in 16% yield.

As demonstrated in the scheme, α-substituted enones (entries 1–4) are not suitable substrates for the Staundon–Weinreb-type annulation, as we just got the recovered starting material (entries 1–2) or just the Michael addition by-products **4a/4b** (entries 3–4) without any detection of products **3a**. It should be noted that the by-product **4a/4b** can't be transformed further into the desired product **3a** in the presence of various bases (such as NaH, LiHMDS, LDA, KO*t*Bu, DBU, $NaOCH_3$) and different solvents. On the other hand, for the β-substitution pattern, we found that incorporation of halide (entries 5–6) is not a good choice. When the β-site was replaced by OCH_3 group (entries 7–8), the desired product **3a** could be isolated in 8%–10% yield together with the by-product enone **5a** (5%–25% yield). The by-product **5a** could not be transformed further into the desired product **3a** under various conditions. The low yield of **3a** might be attributed to its relatively unstable characteristic to column chromatography. With this idea in mind, we decided to conduct the methylation of the new formed phenol directly without trying any isolation or purification, which turned out to be correct.

4a (R^1 = SPh, R^2 = H, *dr* > 14:1): yellow oil. $\mathbf{R_f}$ = 0.55 (silica, *n*-hexane/AcOEt = 4/1). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.47 (dd, *J* = 7.5, 2.0 Hz, 2H), 7.33–7.24 (m, 3H), 6.51 (s, 1H), 4.43–4.30 (m, 2H), 3.94 (s, 3H), 3.19–3.11 (m, 1H), 2.75–2.64 (m, 1H), 2.54 (dd, *J* = 13.5, 9.5 Hz, 1H), 2.39 (s, 3H), 2.37–2.31 (m, 1H), 2.31–2.23 (m, 1H), 2.16–2.05 (m, 1H), 2.04–1.96 (m, 1H), 1.60–1.49 (m, 1H), 1.39–1.33 ppm (m, 3H). **^{13}C NMR** (125 MHz,

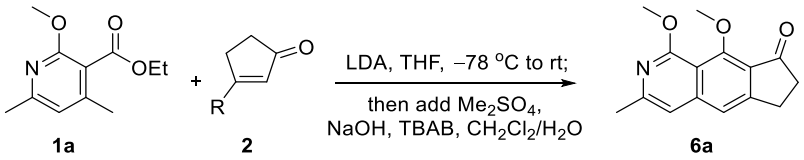
$CDCl_3$): δ = 213.3, 167.2, 160.4, 157.1, 148.1, 133.2, 132.8, 128.9, 127.8, 116.7, 114.7, 61.4, 58.9, 53.6, 43.1, 36.4, 36.2, 26.1, 24.0, 14.1 ppm. **IR**: $\bar{\upsilon}$ = 2980, 1728, 1599, 1456, 1369, 1281, 1096, 737 cm^{-1}. **HRMS** (ESI): *m/z* calcd for $C_{22}H_{26}NO_4S$ $[M + H]^+$: 400.1577; found: 400.1583. The two diastereoisomers can't be separated through column chromatography and the ^1H and ^{13}C NMR spectra only show the major diastereomer.

4b (R^1 = SOPh, R^2 = H, *dr* ~ 2:3): colorless oil. $\mathbf{R_f}$ = 0.6 (silica, *n*-hexane/AcOEt = 2/1). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.56–7.47 (m, 3H), 7.45–7.39 (m, 2H), 6.68 (s, 0.4H), 6.22 (s, 0.6H), 4.44–4.35 (m, 0.85H), 4.35–4.25 (m, 1.15H), 3.94 (s, 1.3H), 3.89 (s, 1.7H), 3.47 (d, *J* = 7.0 Hz, 0.43H), 3.16 (d, *J* = 5.4 Hz, 0.57H), 3.08–2.90 (m, 1.5H), 2.79–2.71 (m, 0.4H), 2.44 (s, 1.3H), 2.43–2.34 (m, 1H), 2.31 (s, 1.7H), 2.29–2.08 (m, 2H), 1.92–1.80 (m, 1H), 1.71–1.62 (m, 0.6H), 1.58–1.44 (m, 0.4H), 1.38–1.29 ppm (m, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 211.7, 209.0, 167.3, 167.0, 160.4, 160.1, 157.4, 157.2, 147.7, 147.4, 141.4, 140.4, 131.3, 131.0, 129.0, 128.9, 124.7, 123.9, 116.6, 116.1, 114.7, 114.4, 74.5, 72.2, 61.6, 61.5, 53.7, 53.6, 39.4, 37.8, 37.7, 36.9, 34.6, 27.4, 26.4, 24.12, 24.08, 14.1 ppm. The ^{13}C NMR signals of two carbons missed. **IR**: $\bar{\upsilon}$ = 3466, 2951, 1728, 1599, 1572, 1369, 1281, 849 cm^{-1}. **HRMS** (ESI): *m/z* calcd for $C_{22}H_{26}NO_5S$ $[M + H]^+$: 416.1526; found: 416.1532. The two diastereoisomers can't be separated through column chromatography.

5a: colorless liquid, $\mathbf{R_f}$ = 0.4 (silica, *n*-hexane/AcOEt = 2/1). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 6.54 (s, 1H), 5.85–5.82 (m, 1H), 4.29 (q, *J* = 7.1 Hz, 2H), 3.92 (s, 3H), 3.67 (s, 2H), 2.51 (dd, *J* = 4.7, 3.1 Hz, 2H), 2.40 (s, 3H), 2.36 (dt, *J* = 4.7, 3.2 Hz, 2H), 1.29 ppm (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 209.0, 178.0, 166.7, 160.6, 157.9, 146.2, 131.2, 116.9, 114.1, 61.3, 53.7, 36.7, 35.3, 31.0, 24.0, 14.0 ppm. **IR**: $\bar{\upsilon}$ = 3489, 2982, 1709, 1456, 1369, 1200, 1096, 866 cm^{-1}. **HRMS** (ESI): *m/z* calcd for $C_{16}H_{20}NO_4$ $[M + H]^+$: 290.1387; found: 290.1392.

3a: off-white solid, mp = 164−166 °C. $\mathbf{R_f}$ = 0.4 (silica, *n*-hexane/AcOEt = 4/1). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 10.68 (br, 1H), 7.01 (s, 1H), 6.90 (s, 1H), 4.16 (s, 3H), 3.18–3.11 (m, 2H), 2.78–2.71 (m, 2H), 2.49 ppm (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 207.0, 161.8, 157.4, 153.8, 152.9, 146.1, 118.4, 113.2, 113.0, 106.4, 54.0, 36.4, 25.3, 24.1 ppm. **IR**: $\bar{\upsilon}$ = 3053, 2986, 2305, 1628, 1422, 1265, 895, 741 cm^{-1}. **HRMS** (ESI): *m/z* calcd for $C_{14}H_{14}NO_3$ $[M + H]^+$: 244.0968; found: 244.0974.

1.4. Further Optimization

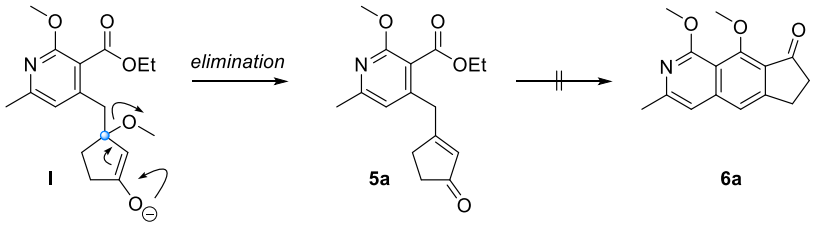


1a **2** **6a**

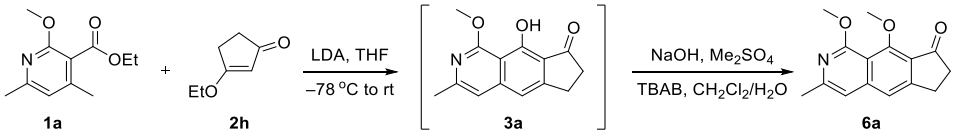
Entry	R	Ratio of 1a and 2	Yield (%)
1	OCH_3	**1a**: 0.10 mmol, **2**: 0.10 mmol	32
2	OCH_3	**1a**: 0.15 mmol, **2**: 0.10 mmol	49
3	OCH_3	**1a**: 0.20 mmol, **2**: 0.10 mmol	65
4^b	OEt	**1a**: 0.20 mmol, **2**: 0.10 mmol	72

Unless otherwise noted, reactions were conducted as follows: **1a** and LDA (the same ratio as for **1a**) reacted in THF (1 mL) at −78 °C for 1 h; **2** (1.0 eq.) was added to the mixture before warming up to rt in 10 min. When the reaction was in completion monitored by TLC, saturated aqueous NH_4Cl was added to the mixture and extraction was conducted by ethyl acetate and the solvent was removed under reduced pressure. The residue was treated with TBAB (0.2 eq.), NaOH (2.0 eq.) in water (1 mL), Me_2SO_4 (4.0 eq.) in CH_2Cl_2 (1 mL) and the complex mixture was vigorously stirred overnight.

As shown in this table, entry 4 indicated that OEt in the β position of enone **2** is a better substitution compared with the corresponding OCH_3 (72% yield *vs* 65% yield). This is possibly because EtOH is a relatively weaker acid compared with CH_3OH (pKa: 15.5 for CH_3OH, 16.0 for EtOH). That is to say, CH_3O^- is a weaker conjugated base and a better leaving group, thus accelerating the undesired pathway from **I** to **5a**. As **5a** can't be transformed further into **6a**, a lower yield was observed in this case.



Further optimization focused on pyridine **1a** and *α,β*-unsaturated cycloenone **2h** as the model substrates. Bases, solvents, substrates ratios and temperature were screened systematically. Details are listed in the table below.



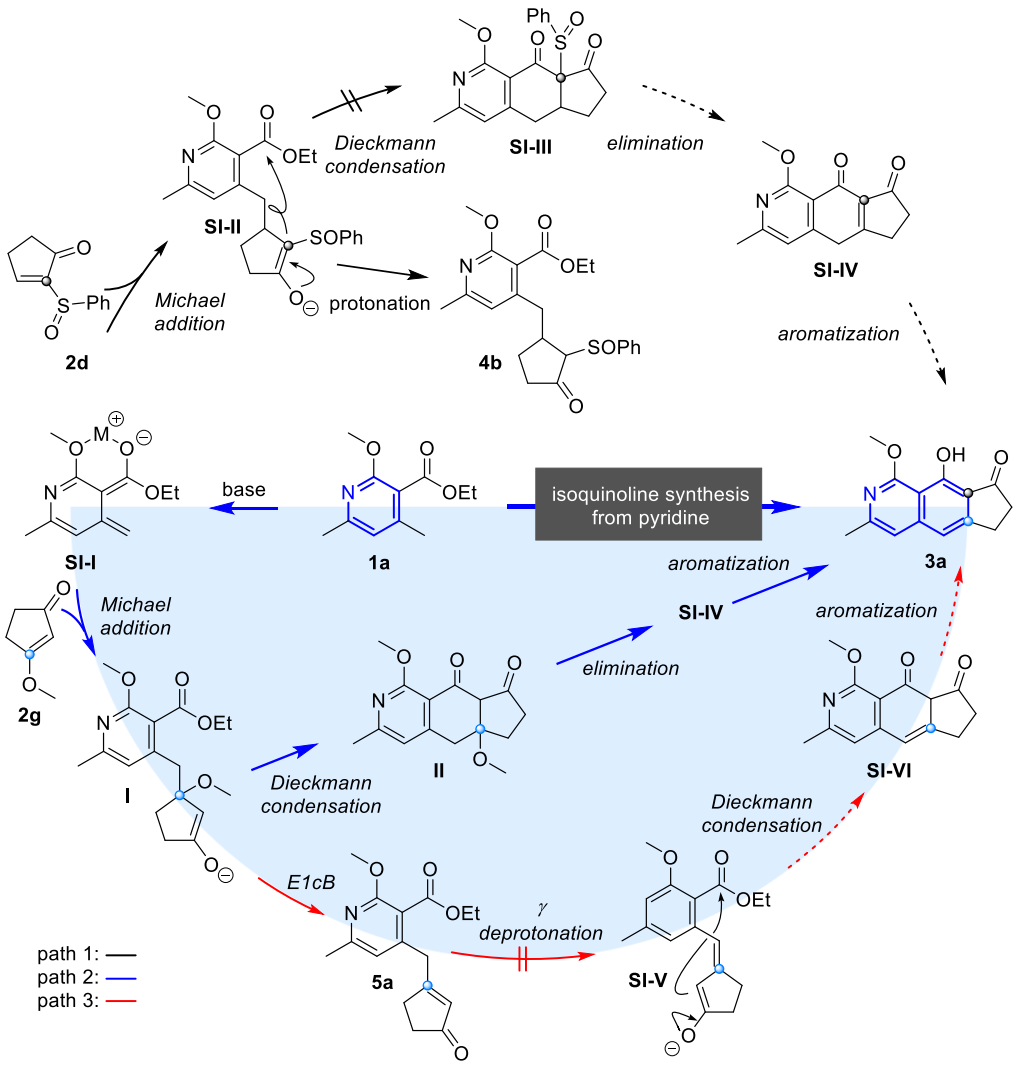
Entry	Variation from standard conditions[a]	Yield (%)[b]
1	none	72
2	no methylation	14
3	OCH_3 instead of OEt in **2h**	65
4[b]	DABCO, DBU, DMAP, LiHMDS and KHMDS instead of LDA	0–42
5	Other solvents in step 1	<41
6	**1a**:**2h** = 1:1	39
7	**1a**:**2h** = 1.5:1	54
8	**1a**:**2h** = 1:1.5	42
9[c]	−78 °C for step 1	23
10	H instead of OCH_3 in **1a**	0

[a]Standard conditions: **1a** (0.2 mmol) and LDA (0.2 mmol) reacted in THF at –78 °C for 1 h; **2h** (0.1 mmol) was added dropwise to the mixture before warming up to rt in 10 min. The reaction was quenched by addition of saturated aqueous solution of NH_4Cl after completion monitored by TLC. After removal of solvents, the crude residue was treated directly with TBAB (0.2 eq.), NaOH (2.0 eq.) in water (1 mL), Me_2SO_4 (4.0 eq.) in CH_2Cl_2 (1 mL) and vigorously stirred overnight. [b]Isolated yield. [c]Recovered starting material **2h**: 16% yield.

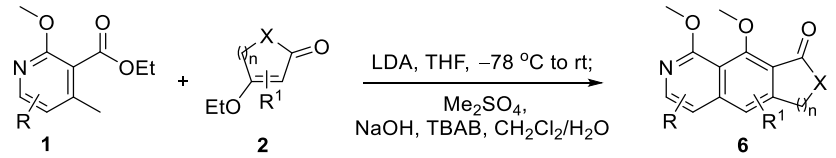
1.5. Tentative Explanation for Reaction Pathways

Generally, we proposed three main synthetic routes (color: path 1 in black, path 2 in blue and path 3 in red) for the construction of isoquinoline **3a** (see the scheme below). Path 1 goes with pyridine **1a** and the α-substituted cycloenone **2d**. Deprotonation of **1a** gives a metal ate complex **SI-I**, in which Michael addition occurs with enone **2d** to deliver intermediate **SI-II**. Subsequent Dieckmann condensation of enolate **SI-II** is followed by thermally promoted sulfoxide elimination of **SI-III**, forming intermediate **SI-IV**. Finally, spontaneous aromatization of **SI-IV** delivers the tricyclic isoquinoline **3a**. On the other hand, if we start the sequence with pyridine **1a** and the β-substituted enone **2g**, the Michael product **I** might be transformed into **5a** via a competitive E1cB. The following γ deprotonation of **5a** and Dieckmann condensation of **SI-V** produced intermediate **SI-VI**. Late-stage aromatization ensured the formation of compound **3a** (path 3). If Dieckmann condensation dominates the following transformation of Michael product **I** over E1cB, the intermediate **II** would be formed. Subsequent β-elimination of **II** and aromatization of **SI-IV** could also yield the isoquinoline **3a** (path 2).

Systematic study demonstrated that the Dieckmann condensation from intermediates **SI-II** to **SI-III** can't go through, excluding the possibility of path 1. The elimination product **5a** couldn't be transformed further into the isoquinoline **3a** under various conditions, which ruled out the reasonability for path 3. Taken together, path 2 might be a possible approach towards the isoquinoline **3a**.



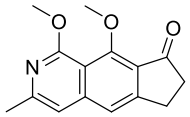
1.6. A General Procedure for Isoquinoline Synthesis



To a stirred solution of **1** (0.2 mmol, 2.0 equiv) in THF (1 mL) was dropwise added freshly prepared LDA (1.0 mol/L, 0.2 mL, 0.2 mmol, 2.0 equiv) at −78 °C. The resulting mixture was stirred at the same temperature for 1 h. After slow addition of **2** (0.1 mmol, 1.0 equiv) in THF solution (0.5 mL) at −78 °C, the mixture was warmed to ambient temperature in 10 min. Saturated aqueous solution of NH_4Cl (2 mL) was added to quench the reaction after completion of the reaction monitored by TLC. Water (2 mL) and EtOAc (2 mL) was added into the mixture. The organic phase was separated, and the aqueous layer was extracted with EtOAc (2 × 2 mL). The combined extracts were washed with brine (4 mL) and concentrated under reduced pressure (note: all substrates including the insoluble should be collected). The residue was directly subjected to the next step without further purification.

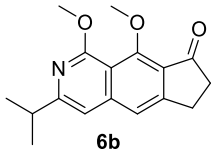
To the residue obtained above was added NaOH (8.0 mg, 0.2 mmol, 2.0 equiv) in water (1 mL), Me_2SO_4 (38 μL, 0.4 mmol, 4.0 equiv), TBAB (6.4 mg, 0.02 mmol, 0.2 equiv), CH_2Cl_2 (1 mL) and the reaction mixture were stirred vigorously. Saturated aqueous solution of NH_4Cl (2 mL) was added to quench the reaction after completion of the reaction monitored by TLC. The organic phase was separated, and the aqueous layer was extracted with CH_2Cl_2 (2 × 2 mL). The combined extracts were washed with brine (4 mL), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel eluting with *n*-hexane/AcOEt (10:1 to 1:2) to afford the isoquinoline **6**.

1.7. Characterization of Isoquinoline Products



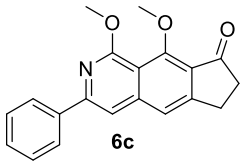
6a

6a: 72% yield, off-white solid, mp 145−146 °C. $\mathbf{R_f}$ = 0.45 (silica, *n*-hexane/AcOEt = 4/1). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.30 (s, 1H), 6.92 (s, 1H), 4.11 (s, 3H), 4.06 (s, 3H), 3.20–3.12 (m, 2H), 2.75–2.68 (m, 2H), 2.49 ppm (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 203.3, 161.8, 158.7, 154.4, 152.1, 145.6, 125.7, 117.8, 112.3, 111.9, 63.0, 53.9, 37.2, 25.1, 24.0 ppm. **IR**: $\bar{\upsilon}$ = 3053, 2305, 1717, 1616, 1421, 1265, 895, 739 cm^{-1}. **HRMS** (ESI): *m/z* calcd for $C_{15}H_{16}NO_3$ $[M + H]^+$: 258.1125; found: 258.1130.



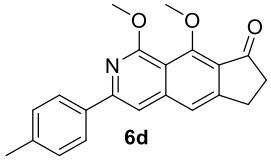
6b

6b: 63% yield, light yellow solid, mp 92−94 °C. $\mathbf{R_f}$ = 0.5 (silica, *n*-hexane/AcOEt = 4/1). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.37 (s, 1H), 6.94 (s, 1H), 4.14 (s, 3H), 4.08 (s, 3H), 3.19 (t, *J* = 6.5 Hz, 2H), 3.06–2.94 (m, 1H), 2.74 (t, *J* = 6.5 Hz, 2H), 1.35 (s, 3H), 1.33 ppm (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 203.4, 161.8, 161.1, 158.6, 154.2, 145.9, 125.7, 118.3, 112.3, 109.5, 63.1, 53.8, 37.3, 35.6, 25.1, 22.0 ppm. **IR**: $\bar{\upsilon}$ = 2964, 2854, 1441, 1377, 1287, 1158, 949, 705 cm^{-1}. **HRMS** (ESI): *m/z* calcd for $C_{17}H_{20}NO_3$ $[M + H]^+$: 286.1438; found: 286.1443.



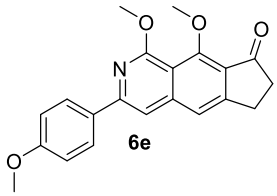
6c

6c: 66% yield, light yellow solid, mp 149−151 °C. $\mathbf{R_f}$ = 0.4 (silica, *n*-hexane/AcOEt = 4/1). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 8.18 (d, *J* = 7.5 Hz, 2H), 7.60 (s, 1H), 7.55–7.47 (m, 3H), 7.43 (t, *J* = 7.2 Hz, 1H), 4.27 (s, 3H), 4.13 (s, 3H), 3.29–3.12 (m, 2H), 2.83–2.66 ppm (m, 2H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 203.2, 162.1, 158.7, 154.7, 150.2, 145.8, 138.4, 129.1, 128.7, 126.8, 126.4, 119.0, 112.9, 109.9, 63.2, 54.1, 37.3, 25.2 ppm. **IR**: $\bar{\upsilon}$ = 3054, 2930, 1442, 1375, 1203, 1156, 955, 744 cm^{-1}. **HRMS** (ESI): *m/z* calcd for $C_{20}H_{18}NO_3$ $[M + H]^+$: 320.1281; found: 320.1286.

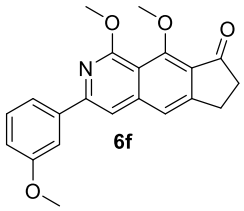


6d

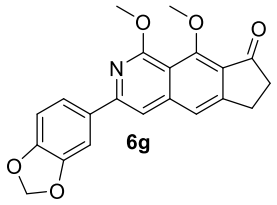
6d: 82% yield, white solid, mp 171−173 °C. $\mathbf{R_f}$ = 0.35 (silica, *n*-hexane/AcOEt = 4/1). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 8.07 (d, *J* = 8.1 Hz, 2H), 7.56 (s, 1H), 7.47 (s, 1H), 7.30 (d, *J* = 8.0 Hz, 2H), 4.26 (s, 3H), 4.12 (s, 3H), 3.25–3.15 (m, 2H), 2.82–2.70 (m, 2H), 2.44 ppm (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 203.2, 162.0, 158.7, 154.6, 150.2, 145.9, 139.2, 135.7, 129.4, 126.7, 126.2, 118.9, 112.8, 109.3, 63.2, 54.0, 37.3, 25.1, 21.3 ppm. **IR**: $\bar{\upsilon}$ = 3423, 2944, 1702, 1606, 1568, 1373, 1112, 738 cm^{-1}. **HRMS** (ESI): *m/z* calcd for $C_{21}H_{20}NO_3$ $[M + H]^+$: 334.1438; found: 334.1443.



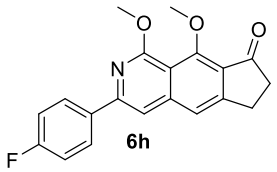
6e: 81% yield, off-white solid, mp 159−161 °C. $\mathbf{R_f}$ = 0.25 (silica, *n*-hexane/AcOEt = 4/1). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 8.13 (d, *J* = 8.7 Hz, 2H), 7.51 (s, 1H), 7.45 (s, 1H), 7.02 (d, *J* = 8.7 Hz, 2H), 4.25 (s, 3H), 4.11 (s, 3H), 3.89 (s, 3H), 3.30–3.15 (m, 2H), 2.80–2.70 ppm (m, 2H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 203.2, 162.0, 160.6, 158.7, 154.6, 150.0, 146.0, 131.1, 128.1, 126.0, 118.7, 114.1, 112.5, 108.6, 63.2, 55.4, 54.0, 37.3, 25.1 ppm. **IR**: $\bar{\upsilon}$ = 3542, 3208, 1480, 1404, 1293, 1028, 802, 730 cm^{-1}. **HRMS** (ESI): *m/z* calcd for $C_{21}H_{20}NO_4$ $[M + H]^+$: 350.1387; found: 350.1392.



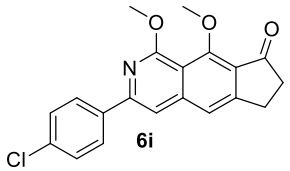
6f: 65% yield, yellow solid, mp 118−121 °C. $\mathbf{R_f}$ = 0.25 (silica, *n*-hexane/AcOEt = 4/1). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.79–7.76 (m, 1H), 7.74 (d, *J* = 7.8 Hz, 1H), 7.60 (s, 1H), 7.50 (s, 1H), 7.42 (t, *J* = 7.9 Hz, 1H), 6.99 (dd, *J* = 8.0, 2.3 Hz, 1H), 4.26 (s, 3H), 4.12 (s, 3H), 3.93 (d, *J* = 4.1 Hz, 3H), 3.28–3.16 (m, 2H), 2.82–2.73 ppm (m, 2H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 203.3, 162.0, 160.0, 158.7, 154.7, 149.9, 145.8, 140.0, 129.7, 126.5, 119.2, 119.0, 114.5, 113.0, 112.6, 110.1, 63.2, 55.4, 54.1, 37.3, 25.2 ppm. **IR**: $\bar{\upsilon}$ = 3463, 2933, 1466, 1421, 1351, 1291, 1098, 794 cm^{-1}. **HRMS** (ESI): *m/z* calcd for $C_{21}H_{20}NO_4$ $[M + H]^+$: 350.1387; found: 350.1392.



6g: 86% yield, light yellow solid, mp 236−239 °C. $\mathbf{R_f}$ = 0.3 (silica, *n*-hexane/AcOEt = 4/1). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.74–7.66 (m, 2H), 7.52 (s, 1H), 7.45 (s, 1H), 6.93 (d, *J* = 8.1 Hz, 1H), 6.02 (s, 2H), 4.24 (s, 3H), 4.11 (s, 3H), 3.26–3.15 (m, 2H), 2.81–2.70 ppm (m, 2H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 203.3, 161.9, 158.7, 154.7, 149.7, 148.5, 148.2, 145.9, 133.0, 126.2, 120.9, 118.8, 112.7, 109.0, 108.4, 107.2, 101.3, 63.2, 54.0, 37.3, 25.2 ppm. **IR**: $\bar{\upsilon}$ = 4199, 3011, 2988, 1510, 1447, 1287, 1183, 807 cm^{-1}. **HRMS** (ESI): *m/z* calcd for $C_{21}H_{18}NO_5$ $[M + H]^+$: 364.1179; found: 364.1184.

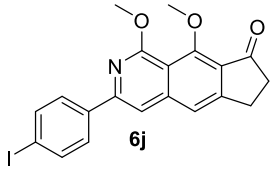


6h: 44% yield, yellow solid, mp 185−187 °C. $\mathbf{R_f}$ = 0.35 (silica, *n*-hexane/AcOEt = 4/1). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 8.19–8.13 (m, 2H), 7.54 (s, 1H), 7.49 (s, 1H), 7.22–7.15 (m, 2H), 4.25 (s, 3H), 4.12 (s, 3H), 3.27–3.19 (m, 2H), 2.82–2.72 ppm (m, 2H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 203.2, 162.6, 162.2, 158.7, 154.8, 149.2, 145.8, 134.6, 128.62, 128.55, 126.4, 118.9, 115.7, 115.5, 112.8, 109.5, 63.2, 54.1, 37.3, 25.2 ppm. **^{19}F NMR** (376 MHz, $CDCl_3$): δ = -112.6 ppm. **IR**: $\bar{\upsilon}$ = 3431, 2923, 1600, 1507, 1352, 1261, 1015, 805 cm^{-1}. **HRMS** (ESI): *m/z* calcd for $C_{20}H_{17}FNO_3$ $[M + H]^+$: 338.1187; found: 338.1193.



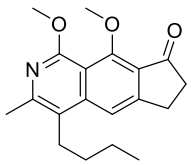
6i

6i: 57% yield, off-white solid, mp 148−150 °C. $\mathbf{R_f}$ = 0.32 (silica, *n*-hexane/AcOEt = 4/1). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 8.10 (d, *J* = 8.5 Hz, 2H), 7.56 (s, 1H), 7.51–7.42 (m, 3H), 4.25 (s, 3H), 4.12 (s, 3H), 3.29–3.15 (m, 2H), 2.82–2.72 ppm (m, 2H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 203.2, 162.2, 158.7, 154.9, 148.9, 145.7, 136.9, 135.1, 128.8, 128.0, 126.6, 119.0 113.0, 109.8, 63.2, 54.1, 37.3, 25.2 ppm. **IR**: $\bar{\upsilon}$ = 2959, 2852, 1695, 1436, 1263, 1012, 810, 703 cm^{-1}. **HRMS** (ESI): *m/z* calcd for $C_{20}H_{17}ClNO_3$ [*M* + H]$^+$: 354.0891; found: 354.0896.



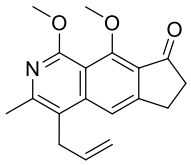
6j

6j: 60% yield, light yellow solid, mp 179−181 °C. $\mathbf{R_f}$ = 0.35 (silica, *n*-hexane/AcOEt = 4/1). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 8.19–8.12 (m, 2H), 7.55 (s, 1H), 7.49 (s, 1H), 7.18 (t, *J* = 8.7 Hz, 2H), 4.26 (s, 3H), 4.14 (s, 3H), 3.26–3.20 (m, 2H), 2.81–2.74 ppm (m, 2H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 203.2, 162.6, 162.2, 158.7, 154.9, 149.2, 145.8, 134.6, 128.62, 128.56, 126.5, 118.9, 115.7, 115.5, 112.9, 109.5, 63.3, 54.1, 37.3, 25.2 ppm. **IR**: $\bar{\upsilon}$ = 3064, 2853, 1695, 1616, 1264, 1112, 821, 738 cm^{-1}. **HRMS** (ESI): *m/z* calcd for $C_{20}H_{17}INO_3$ [*M* + H]$^+$: 446.0248; found: 446.0252.



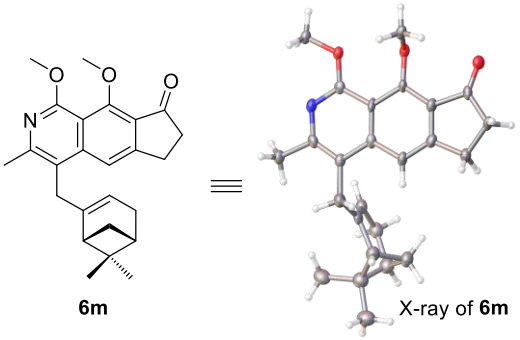
6k

6k: 76% yield, colorless liquid. $\mathbf{R_f}$ = 0.38 (silica, *n*-hexane/AcOEt = 4/1). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.55 (s, 1H), 4.10 (s, 3H), 4.07 (s, 3H), 3.29–3.20 (m, 2H), 2.90–2.83 (m, 2H), 2.79–2.72 (m, 2H), 2.56 (s, 3H), 1.59–1.47 (m, 4H), 1.01 ppm (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 203.4, 159.8, 159.0, 154.1, 149.2, 144.3, 125.0, 121.2, 115.0, 112.5, 63.1, 53.6, 37.4, 31.9, 28.0, 25.5, 23.1, 22.2, 14.0 ppm. **IR**: $\bar{\upsilon}$ = 3342, 2956, 2859, 1731, 1624, 1325, 1182, 738 cm^{-1}. **HRMS** (ESI): *m/z* calcd for $C_{19}H_{24}NO_3$ [*M* + H]$^+$: 314.1751; found: 314.1755.



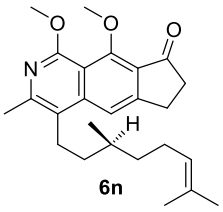
6l

6l: 83% yield, light yellow solid, mp 109−111 °C. $\mathbf{R_f}$ = 0.55 (silica, *n*-hexane/AcOEt = 4/1). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.49 (s, 1H), 6.03–5.93 (m, 1H), 5.04 (dd, *J* = 10.2, 1.4 Hz, 1H), 4.89 (dd, *J* = 17.2, 1.5 Hz, 1H), 4.11 (s, 3H), 4.06 (s, 3H), 3.62 (d, *J* = 5.3 Hz, 2H), 3.20 (t, *J* = 6.5 Hz, 2H), 2.72 (t, *J* = 6.5 Hz, 2H), 2.52 ppm (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 203.3, 160.3, 158.8, 154.2, 150.2, 144.3, 135.1, 125.1, 117.8, 115.6, 115.1, 112.4, 63.0, 53.6, 37.3, 32.1, 25.4, 22.1 ppm. **IR**: $\bar{\upsilon}$ = 3077, 2928, 2858, 1709, 1616, 1386, 1184, 734 cm^{-1}. **HRMS** (ESI): *m/z* calcd for $C_{18}H_{20}NO_3$ [*M* + H]$^+$: 298.1438; found: 298.1443.

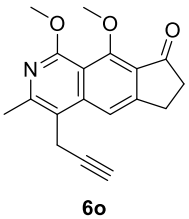


6m: 93% yield, white solid, mp 160−161 °C. $\mathbf{R_f}$ = 0.75 (silica, *n*-hexane/AcOEt = 4/1). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.43 (s, 1H), 4.67 (s, 1H), 4.12 (s, 3H), 4.08 (s, 3H), 3.52, 3.44 (ABq, *J* = 17.5 Hz, 2H), 3.22–3.14 (m, 2H), 2.79–2.70 (m, 2H), 2.50 (s, 3H), 2.43 (dt, *J* = 8.3, 5.6 Hz, 1H), 2.21–2.04 (m, 4H), 1.32 (s, 3H), 1.22 (d, *J* = 8.5 Hz, 1H), 0.91 ppm (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 203.4, 160.2, 158.8, 153.9, 150.4, 145.5, 144.8, 125.0, 118.0, 117.0, 115.7, 112.3, 63.1, 53.7, 46.6, 41.0, 38.2, 37.3, 35.3, 31.7, 31.2, 26.3, 25.4, 22.2, 21.1 ppm. **IR**: $\bar{\upsilon}$ = 3052, 2942, 1722, 1608, 1589, 1264, 1081, 731 cm^{-1}. **HRMS** (ESI): *m/z* calcd for $C_{25}H_{30}NO_3$ [*M* + H]$^+$: 392.2220; found: 392.2225.

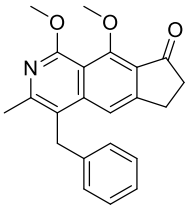
The single crystal of **6m** (CCDC 2061702), which was used for determination of the absolute configuration via X-ray crystallographic analysis, was obtained from a recrystallization from a solution of **6m** in a mixed solvent of petroleum ether and ethyl acetate.



6n: 71% yield, white solid, mp 178−180 °C. $\mathbf{R_f}$ = 0.7 (silica, *n*-hexane/AcOEt = 4/1). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.53 (s, 1H), 5.15 (t, *J* = 7.1 Hz, 1H), 4.10 (s, 3H), 4.07 (s, 3H), 3.24 (t, *J* = 6.5 Hz, 2H), 2.95–2.79 (m, 2H), 2.76 (t, *J* = 6.5 Hz, 2H), 2.55 (s, 3H), 2.15–1.95 (m, 2H), 1.72 (s, 3H), 1.63 (s, 3H), 1.62 (s, 3H), 1.62–1.28 (m, 4H), 1.07 ppm (d, *J* = 6.6 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 203.4, 159.9, 159.0, 154.1, 149.0, 144.2, 131.3, 125.0, 124.7, 121.4, 114.8, 112.5, 63.1, 53.6, 37.3, 36.8, 36.6, 33.1, 25.8, 25.7, 25.6, 25.5, 22.1, 19.6, 17.7 ppm. **IR**: $\bar{\upsilon}$ = 3429, 2925, 1653, 1617, 1140, 795, 603, 551 cm^{-1}. **HRMS** (ESI): *m/z* calcd for $C_{25}H_{34}NO_3$ [*M* + H]$^+$: 396.2533; found: 396.2538.

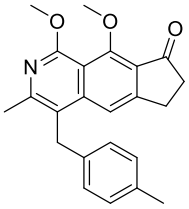


6o: 57% yield, light yellow solid, mp 166−168 °C. $\mathbf{R_f}$ = 0.4 (silica, *n*-hexane/AcOEt = 4/1). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.66 (s, 1H), 4.12 (s, 3H), 4.08 (s, 3H), 3.75 (s, 2H), 3.27 (t, *J* = 6.4 Hz, 2H), 2.76 (t, *J* = 6.4 Hz, 2H), 2.62 (s, 3H), 2.04 ppm (s, 1H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 203.3, 160.8, 159.0, 154.9, 149.9, 143.7, 125.4, 115.7, 114.9, 112.7, 81.5, 69.0, 63.2, 53.9, 37.3, 25.6, 22.4, 18.2 ppm. **IR**: $\bar{\upsilon}$ = 3447, 2962, 1700, 1611, 1257, 1136, 856, 795 cm^{-1}. **HRMS** (ESI): *m/z* calcd for $C_{18}H_{18}NO_3$ [*M* + H]$^+$: 296.1281; found: 296.1286.



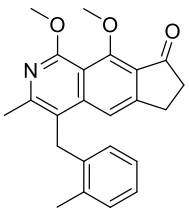
6p

6p: 75% yield, light yellow solid, mp 141−143 °C. $\mathbf{R_f}$ = 0.45 (silica, *n*-hexane/AcOEt = 4/1). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.44 (s, 1H), 7.29–7.22 (m, 2H), 7.21–7.15 (m, 1H), 7.08 (d, *J* = 7.4 Hz, 2H), 4.29 (s, 2H), 4.14 (s, 3H), 4.08 (s, 3H), 3.13–3.07 (m, 2H), 2.74–2.65 (m, 2H), 2.54 ppm (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 203.3, 160.6, 158.9, 154.5, 150.9, 144.8, 139.6, 128.6, 127.8, 126.1, 125.3, 118.5, 115.4, 112.6, 63.1, 53.8, 37.2, 33.8, 25.4, 22.5 ppm. **IR**: $\bar{\upsilon}$ = 2918, 2849, 1693, 1609, 1558, 1261, 1062, 850, 738 cm^{-1}. **HRMS** (ESI): *m/z* calcd for $C_{22}H_{22}NO_3$ $[M + H]^+$: 348.1594; found: 348.1599.



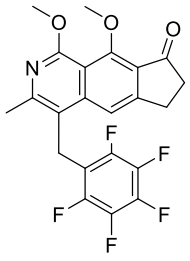
6q

6q: 71% yield, white solid, mp 140−141 °C. $\mathbf{R_f}$ = 0.42 (silica, *n*-hexane/AcOEt = 4/1). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.46 (s, 1H), 7.07 (d, *J* = 7.9 Hz, 2H), 6.98 (d, *J* = 8.0 Hz, 2H), 4.26 (s, 2H), 4.15 (s, 3H), 4.09 (s, 3H), 3.15–3.09 (m, 2H), 2.73–2.66 (m, 2H), 2.56 (s, 3H), 2.30 ppm (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 203.4, 160.5, 158.9, 154.5, 150.8, 144.8, 136.4, 135.6, 129.2, 127.7, 125.2, 118.7, 115.5, 112.5, 63.1, 53.7, 37.2, 33.3, 25.4, 22.5, 20.9 ppm. **IR**: $\bar{\upsilon}$ = 3054, 2925, 2860, 1716, 1616, 1361, 1258, 1115, 737 cm^{-1}. **HRMS** (ESI): *m/z* calcd for $C_{23}H_{24}NO_3$ $[M + H]^+$: 362.1751; found: 362.1756.



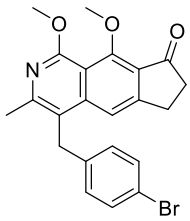
6r

6r: 85% yield, white solid, mp 165−167 °C. $\mathbf{R_f}$ = 0.5 (silica, *n*-hexane/AcOEt = 4/1). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.26 (d, *J* = 7.4 Hz, 2H), 7.12 (t, *J* = 7.2 Hz, 1H), 6.96 (t, *J* = 7.4 Hz, 1H), 6.50 (d, *J* = 7.5 Hz, 1H), 4.17 (s, 3H), 4.15 (s, 2H), 4.12 (s, 3H), 3.10 (t, *J* = 6.5Hz, 2H), 2.70 (t, *J* = 6.5Hz, 2H), 2.54 (s, 3H), 2.48 ppm (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 203.3, 160.6, 158.9, 154.6, 151.1, 144.9, 137.2, 136.1, 129.9, 126.7, 126.2, 126.1, 125.3, 118.1, 115.3, 112.5, 63.1, 53.8, 37.2, 31.2, 25.4, 22.3, 19.8 ppm. **IR**: $\bar{\upsilon}$ = 3052, 2936, 2858, 1699, 1608, 1261, 1064, 956, 733 cm^{-1}. **HRMS** (ESI): *m/z* calcd for $C_{23}H_{24}NO_3$ $[M + H]^+$: 362.1751; found: 362.1756.



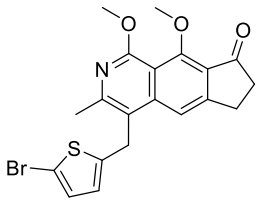
6s

6s: 66% yield, white solid, mp 192−194 °C. $\mathbf{R_f}$ = 0.65 (silica, *n*-hexane/AcOEt = 4/1). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.45 (s, 1H), 4.30 (s, 2H), 4.12 (s, 3H), 4.07 (s, 3H), 3.19 (t, *J* = 7 Hz, 2H), 2.73 (t, *J* = 7 Hz, 2H), 2.62 ppm (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 203.1, 160.7, 159.1, 154.9, 151.2, 146.3 (br), 144.4 (br), 144.0, 140.8 (br), 138.6 (br), 136.6 (br), 125.4, 115.6, 114.2, 113.5 (br), 112.5, 63.2, 53.8, 37.2, 25.5, 22.6, 22.4 ppm.**^{19}F NMR** (376 MHz, $CDCl_3$): δ = -141.83 (dd, *J* = 22.1, 7.5 Hz, 2F), -156.62 (t, *J* = 18.8 Hz, 1F), -162.26 ppm (td, *J* = 21.8, 7.7 Hz, 2F). **IR**: $\bar{\upsilon}$ = 3453, 2954, 1722, 1564, 1489, 1122, 995, 858 cm^{-1}. **HRMS** (ESI): *m/z* calcd for $C_{22}H_{17}F_5NO_3$ [*M* + H]$^+$: 438.1123; found: 438.1128.



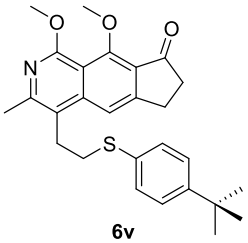
6t

6t: 69% yield, light yellow solid, mp 171−173 °C. $\mathbf{R_f}$ = 0.5 (silica, *n*-hexane/AcOEt = 4/1). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.39–7.33 (m, 3H), 6.95 (d, *J* = 8.3 Hz, 2H), 4.22 (s, 2H), 4.14 (s, 3H), 4.09 (s, 3H), 3.15–3.08 (m, 2H), 2.74–2.67 (m, 2H), 2.52 ppm (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 203.2, 160.6, 158.9, 154.7, 150.9, 144.6, 138.6, 131.6, 129.5, 125.3, 119.8, 117.9, 115.1, 112.5, 63.1, 53.8, 37.2, 33.2, 25.4, 22.5 ppm. **IR**: $\bar{\upsilon}$ = 3054, 1700, 1608, 1486, 1264, 1138, 1010, 736 cm^{-1}. **HRMS** (ESI): *m/z* calcd for $C_{22}H_{21}BrNO_3$ [*M* + H]$^+$: 426.0699; found: 426.0704.



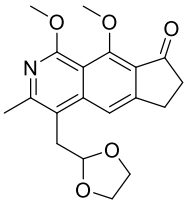
6u

6u: 82% yield, white solid, mp 158−160 °C. $\mathbf{R_f}$ = 0.5 (silica, *n*-hexane/AcOEt = 4/1). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.48 (s, 1H), 6.82 (d, *J* = 3.5 Hz, 1H), 6.44 (d, *J* = 3.5 Hz, 1H), 4.32 (s, 2H), 4.13 (s, 3H), 4.09 (s, 3H), 3.18 (t, *J* = 6.5 Hz, 2H), 2.72 (t, *J* = 6.5 Hz, 2H), 2.58 ppm (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 203.2, 160.8, 159.0, 154.8, 150.7, 144.8, 144.2, 129.6, 125.4, 124.8, 117.8, 114.9, 112.5, 109.5, 63.2, 53.8, 37.2, 29.0, 25.5, 22.3 ppm. **IR**: $\bar{\upsilon}$ = 3054, 2950, 2855, 1732, 1614, 1350, 1006, 704 cm^{-1}. **HRMS** (ESI): *m/z* calcd for $C_{20}H_{19}BrNO_3S$ [*M* + H]$^+$: 432.0264; found: 432.0269.



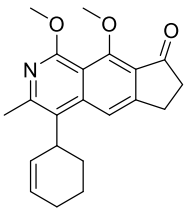
6v

6v: 72% yield, white solid, mp 144−146 °C. $\mathbf{R_f}$ = 0.65 (silica, *n*-hexane/AcOEt = 4/1). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.40 (q, *J* = 8.5 Hz, 4H), 7.33 (s, 1H), 4.09 (s, 3H), 4.06 (s, 3H), 3.20–3.13 (m, 4H), 3.09–3.01 (m, 2H), 2.80–2.70 (m, 2H), 2.49 (s, 3H), 1.34 ppm (s, 9H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 203.2, 160.3, 159.1, 154.5, 150.1, 150.0, 144.0, 132.2, 130.6, 126.1, 125.2, 118.8, 114.4, 112.5, 63.1, 53.7, 37.3, 34.5, 33.8, 31.3, 28.7, 25.5, 22.2 ppm. **IR**: $\bar{\upsilon}$ = 3054, 2986, 2305, 1710, 1612, 1265, 1137, 895 cm^{-1}. **HRMS** (ESI): *m/z* calcd for $C_{27}H_{32}NO_3S$ [*M* + H]$^+$: 450.2097; found: 450.2102.



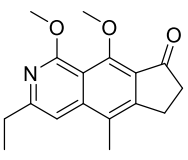
6w

6w: 74% yield, white solid, mp 152−154 °C. $\mathbf{R_f}$ = 0.2 (silica, *n*-hexane/AcOEt = 4/1). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.67 (s, 1H), 5.12 (t, *J* = 4.8 Hz, 1H), 4.11 (s, 3H), 4.06 (s, 3H), 4.03–3.97 (m, 2H), 3.86–3.81 (m, 2H), 3.31 (d, *J* = 4.8 Hz, 2H), 3.27–3.21 (m, 2H), 2.78–2.72 (m, 2H), 2.63 ppm (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 203.4, 160.5, 158.9, 154.2, 151.6, 144.9, 125.2, 115.4, 115.2, 112.4, 104.2, 65.0, 63.1, 53.7, 37.3, 33.0, 25.5, 22.9 ppm. **IR**: $\bar{\upsilon}$ = 2956, 2927, 2305, 1708, 1613, 1264, 1139, 734 cm^{-1}. **HRMS** (ESI): *m/z* calcd for $C_{19}H_{22}NO_5$ [*M* + H]$^+$: 344.1492; found: 344.1497.



6x

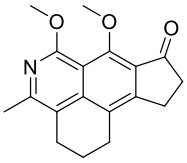
6x: 88% yield, white solid, mp 150−152 °C. $\mathbf{R_f}$ = 0.7 (silica, *n*-hexane/AcOEt = 4/1). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 8.00 (s, 1H), 5.86 (s, 1H), 5.78 (s, 1H), 4.10 (s, 3H), 4.06 (s, 3H), 3.19 (s, 2H), 2.73 (d, *J* = 5.8 Hz, 2H), 2.58 (d, *J* = 15.1 Hz, 3H), 2.24 (s, 2H), 2.09–1.79 ppm (m, 4H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 203.4, 160.0, 158.8, 153.0, 149.6, 144.1, 132.5, 126.5, 124.9, 123.7, 117.0, 113.1, 63.0, 53.6, 38.1, 37.3, 28.4, 25.5, 24.7, 23.4, 23.0 ppm. **IR**: $\bar{\upsilon}$ =2923, 2853, 1709, 1611, 1569, 1363, 958, 735 cm^{-1}. **HRMS** (ESI): *m/z* calcd for $C_{21}H_{24}NO_3$ [*M* + H]$^+$: 338.1751; found: 338.1756.



6y

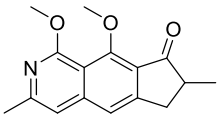
6y: 89% yield, white solid, mp 92−94 °C. $\mathbf{R_f}$ = 0.5 (silica, *n*-hexane/AcOEt = 4/1). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.08 (s, 1H), 4.14 (s, 3H), 4.03 (s, 3H), 3.18–3.06 (m, 2H), 2.82 (q, *J* = 7.5 Hz, 2H), 2.74 (dd, *J* = 7.8, 5.6 Hz, 2H), 2.46 (s, 3H), 1.37 ppm (t, *J* = 7.5 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 204.0, 162.5, 157.3, 156.7,

151.8, 144.3, 125.1, 124.0, 112.1, 107.3, 62.9, 53.9, 37.1, 31.2, 24.6, 13.9, 13.4 ppm. **IR**: $\bar{\upsilon}$ = 3448, 3067, 2126, 1731, 1644, 1381, 1292, 1197, 738 cm^{-1}. **HRMS** (ESI): *m/z* calcd for $C_{17}H_{20}NO_3$ $[M + H]^+$: 286.1438; found: 286.1443.



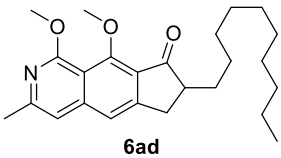
6z

6z: 92% yield, light yellow solid, mp 172−174 °C. $\mathbf{R_f}$ = 0.35 (silica, *n*-hexane/AcOEt = 4/1). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 4.09 (s, 3H), 4.01 (s, 3H), 3.04 (t, *J* = 6.5 Hz, 2H), 2.87–2.81 (m, 4H), 2.72 (t, *J* = 6.5 Hz, 2H), 2.48 (s, 3H), 2.06–1.93 ppm (m, 2H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 204.0, 159.8, 156.2, 150.0, 147.3, 141.1, 126.1, 124.7, 118.0, 112.0, 62.8, 53.5, 37.2, 26.0, 25.8, 24.0, 21.63, 21.57 ppm. **IR**: $\bar{\upsilon}$ = 2985, 2921, 2848, 1722, 1539, 1259, 1026, 740 cm^{-1}. **HRMS** (ESI): *m/z* calcd for $C_{18}H_{20}NO_3$ $[M + H]^+$: 298.1438; found: 298.1443.



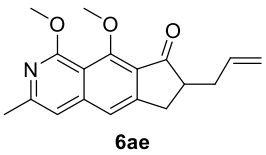
6ac

6ac: 81% yield, white solid, mp 117−119 °C. $\mathbf{R_f}$ = 0.6 (silica, *n*-hexane/AcOEt = 4/1). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.31 (s, 1H), 6.95 (s, 1H), 4.12 (s, 3H), 4.08 (s, 3H), 3.44 (dd, *J* = 18.2, 9.6 Hz, 1H), 2.84–2.69 (m, 2H), 2.51 (s, 3H), 1.33 ppm (d, *J* = 6.9 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 205.6, 161.9, 158.8, 152.6, 152.1, 145.7, 125.0, 117.6, 112.3, 112.0, 63.1, 53.9, 43.0, 34.3, 24.1, 16.4 ppm. **IR**: $\bar{\upsilon}$ = 3055, 2985, 2302, 1558, 1265, 1180, 1120, 737 cm^{-1}. **HRMS** (ESI): *m/z* calcd for $C_{16}H_{18}NO_3$ $[M + H]^+$: 272.1281; found: 272.1286.



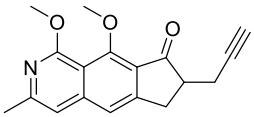
6ad

6ad: 86% yield, colorless liquid. $\mathbf{R_f}$ = 0.8 (silica, *n*-hexane/AcOEt = 4/1). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.31 (s, 1H), 6.95 (s, 1H), 4.12 (s, 3H), 4.08 (s, 3H), 3.36 (dd, *J* = 17.5, 8.5 Hz, 1H), 2.86 (dd, *J* = 17.2, 4.3 Hz, 1H), 2.73–2.66 (m, 1H), 2.51 (s, 3H), 2.02–1.92 (m, 1H), 1.54–1.38 (m, 3H), 1.39–1.19 (m, 14H), 0.88 ppm (t, *J* = 6.9 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 205.4, 161.9, 158.7, 153.0, 152.1, 145.7, 125.6, 117.6, 112.3, 112.0, 63.1, 53.9, 48.3, 32.3, 31.9, 31.7, 29.7, 29.64, 29.61, 29.5, 29.3, 27.3, 24.1, 22.7, 14.1 ppm. **IR**: $\bar{\upsilon}$ = 3396, 2919, 2850, 1695, 1616, 1606, 1262, 796 cm^{-1}. **HRMS** (ESI): *m/z* calcd for $C_{25}H_{36}NO_3$ $[M + H]^+$: 398.2690; found: 398.2695.



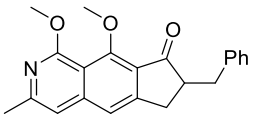
6ae

6ae: 84% yield, off-white solid, mp 76−78 °C. $\mathbf{R_f}$ = 0.7 (silica, *n*-hexane/AcOEt = 4/1). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.31 (s, 1H), 6.95 (s, 1H), 5.82 (ddt, *J* = 17.0, 10.1, 6.9 Hz, 1H), 5.18–5.00 (m, 2H), 4.12 (s, 3H), 4.08 (s, 3H), 3.33 (dd, *J* = 17.3, 8.6 Hz, 1H), 2.97–2.87 (m, 1H), 2.86–2.78 (m, 1H), 2.77–2.68 (m, 1H), 2.51 (s, 3H), 2.35–2.24 ppm (m, 1H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 204.4, 161.9, 158.8, 152.4, 152.2, 145.8, 135.4, 125.4, 117.7, 117.0, 112.3, 112.0, 63.1, 53.9, 47.4, 35.8, 31.4, 24.1 ppm. **IR**: $\bar{\upsilon}$ = 3053, 2917, 1693, 1614, 1350, 1265, 1115, 738 cm^{-1}. **HRMS** (ESI): *m/z* calcd for $C_{18}H_{20}NO_3$ $[M + H]^+$: 298.1438; found: 298.1443.



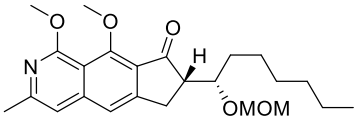
6af

6af: 86% yield, light yellow solid, mp 102−104 °C. $\mathbf{R_f}$ = 0.5 (silica, *n*-hexane/AcOEt = 4/1). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.32 (s, 1H), 6.95 (s, 1H), 4.12 (s, 3H), 4.08 (s, 3H), 3.44 (ddd, *J* = 17.3, 8.7, 0.7 Hz, 1H), 3.13 (ddd, *J* = 17.3, 5.5, 1.1 Hz, 1H), 2.94–2.86 (m, 1H), 2.82–2.73 (m, 1H), 2.62–2.54 (m, 1H), 2.50 (s, 3H), 1.91 ppm (t, *J* = 2.6 Hz, 1H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 202.6, 161.9, 159.0, 152.5, 152.4, 145.8, 125.0, 117.6, 112.3, 112.0, 81.2, 69.7, 63.2, 53.9, 46.5, 31.3, 24.1, 20.2 ppm. **IR**: $\bar{\upsilon}$ = 3304, 3054, 2986, 1709, 1617, 1564, 1350, 1265, 738 cm^{-1}. **HRMS** (ESI): *m/z* calcd for $C_{18}H_{18}NO_3$ $[M + H]^+$: 296.1281; found: 296.1286.



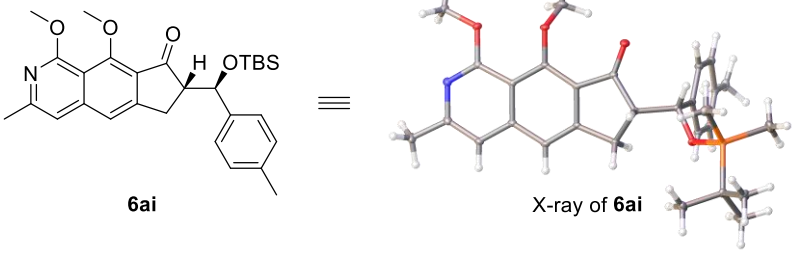
6ag

6ag: 78% yield, yellow solid, mp 98−99 °C. $\mathbf{R_f}$ = 0.65 (silica, *n*-hexane/AcOEt = 4/1). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.35–7.18 (m, 6H), 6.93 (s, 1H), 4.13 (s, 3H), 4.11 (s, 3H), 3.41 (dd, *J* = 14.0, 4.0 Hz, 1H), 3.22 (dd, *J* = 17.1, 8.5 Hz, 1H), 3.10–3.01 (m, 1H), 2.91 (dd, *J* = 17.1, 4.8 Hz, 1H), 2.74 (dd, *J* = 13.8, 10.2 Hz, 1H), 2.50 ppm (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 204.0, 161.9, 158.9, 152.6, 152.3, 145.7, 139.5, 129.0, 128.5, 126.3, 125.3, 117.6, 112.3, 112.0, 63.2, 54.0, 49.8, 37.2, 31.5, 24.1 ppm. **IR**: $\bar{\upsilon}$ = 3054, 2986, 2927, 2305, 1709, 1615, 1262, 744 cm^{-1}. **HRMS** (ESI): *m/z* calcd for $C_{22}H_{22}NO_3$ $[M + H]^+$: 348.1594; found: 348.1599.



6ah

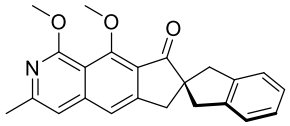
6ah: 86% yield, light yellow liquid. $\mathbf{R_f}$ = 0.6 (silica, *n*-hexane/AcOEt = 4/1). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.34 (s, 1H), 6.95 (s, 1H), 4.71, 4.73 (ABq, *J* = 7.0 Hz, 2H), 4.12 (s, 3H), 4.10 (t, *J* = 3.5 Hz, 1H), 4.07 (s, 3H), 3.36 (s, 3H), 3.31–3.20 (m, 3H), 2.51 (s, 3H), 1.51–1.39 (m, 2H), 1.36–1.15 (m, 8H), 0.83 ppm (t, *J* = 6.9 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 202.9, 161.9, 158.7, 153.6, 152.3, 145.7, 126.2, 117.6, 112.3, 112.0, 96.2, 79.1, 63.1, 55.7, 53.9, 51.4, 31.7, 30.7, 29.2, 27.8, 26.1, 24.1, 22.5, 14.0 ppm. **IR**: $\bar{\upsilon}$ = 2958, 2926, 1705, 1616, 1348, 1265, 1116, 738 cm^{-1}. **HRMS** (ESI): *m/z* calcd for $C_{24}H_{34}NO_5$ $[M + H]^+$: 416.2431; found: 416.2436.



6ai ≡ X-ray of **6ai**

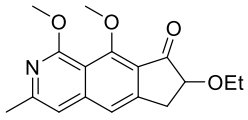
6ai: 61% yield, colorless solid, mp 123−125 °C. $\mathbf{R_f}$ = 0.75 (silica, *n*-hexane/AcOEt = 4/1). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.19 (d, *J* = 8.0 Hz, 2H), 7.14 (s, 1H), 6.95 (d, *J* = 7.9 Hz, 2H), 6.84 (s, 1H), 5.47 (d, *J* = 4.4 Hz, 1H), 4.09 (s, 3H), 4.07 (s, 3H), 3.28–3.22 (m, 1H), 3.21–3.07 (m, 2H), 2.46 (s, 3H), 2.19 (s, 3H), 0.91 (s, 9H), 0.11 (s, 3H), -0.02 ppm (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 202.5, 161.8, 158.6, 153.6, 152.0, 145.5, 137.9, 136.6, 128.4, 126.5, 126.2, 117.4, 112.2, 111.7, 74.2, 63.0, 56.6, 53.9, 27.0, 25.6, 24.0, 21.0, 18.2, -4.8, -5.1 ppm. **IR**: $\bar{\upsilon}$ = 3054, 2928, 2305, 1617, 1421, 1264, 895, 740 cm^{-1}. **HRMS** (ESI): *m/z* calcd for $C_{29}H_{38}NO_4Si$ $[M + H]^+$: 492.2565; found: 492.2570.

The single crystal of **6ai** (CCDC 2061701), which was used for determination of the relative configuration via X-ray crystallographic analysis, was obtained from a recrystallization from a solution of **6ai** in a mixed solvent of petroleum ether and ethyl acetate.



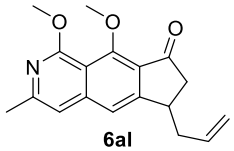
6aj

6aj: 52% yield, white solid, mp 151−154 °C. $\mathbf{R_f}$ = 0.7 (silica, *n*-hexane/AcOEt = 4/1). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.30 (s, 1H), 7.25–7.18 (m, 4H), 6.96 (s, 1H), 4.14 (s, 3H), 4.13 (s, 3H), 3.53 (d, *J* = 15.5 Hz, 2H), 3.22 (s, 2H), 2.86 (d, *J* = 15.5 Hz, 2H), 2.52 ppm (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 205.1, 161.9, 159.2, 152.4, 151.5, 145.8, 141.4, 126.8, 124.9, 124.5, 117.8, 112.4, 112.2, 63.2, 58.5, 54.0, 44.7, 42.8, 24.1 ppm. **IR**: $\bar{\upsilon}$ = 3054, 2986, 2301, 1710, 1615, 1351, 1264, 734 cm^{-1}. **HRMS** (ESI): *m/z* calcd for $C_{23}H_{22}NO_3$ [*M* + H]$^+$: 360.1594; found: 360.1599.



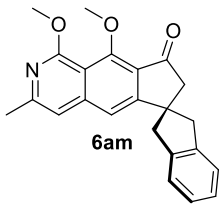
6ak

6ak: 61% yield, white solid, mp 119−122 °C. $\mathbf{R_f}$ = 0.45 (silica, *n*-hexane/AcOEt = 4/1). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.56 (s, 1H), 7.01 (s, 1H), 5.08 (dd, *J* = 6.8, 3.4 Hz, 1H), 4.12 (s, 3H), 4.08 (s, 3H), 3.71 (qd, *J* = 7.0, 3.5 Hz, 2H), 3.03 (dd, *J* = 18.2, 7.0 Hz, 1H), 2.73 (dd, *J* = 18.2, 3.5 Hz, 1H), 2.51 (s, 3H), 1.31 ppm (t, *J* = 7.0 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 199.4, 161.8, 158.4, 152.9, 152.5, 145.8, 124.9, 118.2, 112.9, 112.8, 74.4, 65.2, 63.2, 54.0, 45.3, 24.0, 15.4 ppm. **IR**: $\bar{\upsilon}$ = 3054, 2940, 2306, 1713, 1616, 1564, 1350, 1264, 1113, 740 cm^{-1}. **HRMS** (ESI): *m/z* calcd for $C_{17}H_{20}NO_4$ [*M* + H]$^+$: 302.1387; found: 302.1392.



6al

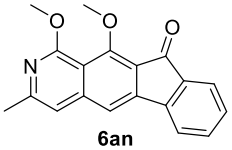
6al: 64% yield, white solid, mp 124−126 °C. $\mathbf{R_f}$ = 0.55 (silica, *n*-hexane/AcOEt = 4/1). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.39 (s, 1H), 6.98 (s, 1H), 5.77 (ddt, *J* = 17.1, 10.2, 6.9 Hz, 1H), 5.12 (dd, *J* = 20.8, 5.3 Hz, 2H), 4.12 (s, 3H), 4.08 (s, 3H), 3.50 (tt, *J* = 8.3, 4.2 Hz, 1H), 2.86 (dd, *J* = 18.8, 8.3 Hz, 1H), 2.75–2.64 (m, 1H), 2.51 (s, 3H), 2.48 (dd, *J* = 18.8, 4.1 Hz, 1H), 2.42–2.33 ppm (m, 1H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 202.3, 161.9, 158.5, 157.4, 152.2, 145.6, 135.1, 125.6, 117.7, 117.0, 112.5, 112.1, 63.1, 54.0, 43.5, 40.2, 36.7, 24.1 ppm. **IR**: $\bar{\upsilon}$ = 3054, 2985, 2306, 1709, 1615, 1350, 1264, 1115, 740 cm^{-1}. **HRMS** (ESI): *m/z* calcd for $C_{18}H_{20}NO_3$ [*M* + H]$^+$: 298.1438; found: 298.1443.



6am

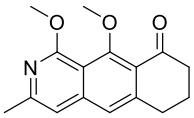
6am: 65% yield, light yellow solid, mp 155−157 °C. $\mathbf{R_f}$ = 0.7 (silica, *n*-hexane/AcOEt = 4/1). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.27–7.25 (m, 4H), 7.23 (s, 1H), 6.88 (s, 1H), 4.13 (s, 3H), 4.11 (s, 3H), 3.45, 3.23 (ABq, *J* = 15.5 Hz, 4H), 2.86 (s, 2H), 2.48 ppm (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 201.6, 161.8, 161.2, 158.3, 152.3, 145.9, 141.8, 127.0, 125.0, 124.5, 114.8, 112.7, 112.2, 63.2, 54.0, 53.7, 49.1, 48.5, 24.0 ppm. **IR**: $\bar{\upsilon}$ = 3054, 2936, 2305,

1717, 1615, 1580, 1351, 1116, 728 cm^{-1}. **HRMS** (ESI): *m/z* calcd for $C_{23}H_{22}NO_3$ $[M + H]^+$: 360.1594; found: 360.1599.



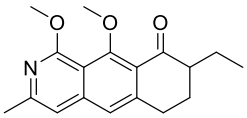
6an

6an: 89% yield, yellow solid, mp 130−132 °C. $\mathbf{R_f}$ = 0.7 (silica, *n*-hexane/AcOEt = 4/1). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.73 (d, *J* = 7.0 Hz, 1H), 7.67 (d, *J* = 7.5 Hz, 1H), 7.54 (t, *J* = 7.5 Hz, 1H), 7.41 (s, 1H), 7.38 (t, *J* = 7.5 Hz, 1H), 6.97 (s, 1H), 4.17 (s, 3H), 4.12 (s, 3H), 2.51 ppm (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 189.8, 162.0, 159.4, 153.7, 146.4, 143.9, 142.6, 136.7, 134.2, 129.9, 124.0, 121.6, 120.9, 113.9, 112.9, 63.1, 54.0, 24.0 ppm. The ^{13}C NMR signal of one carbon missed. **IR**: $\bar{\upsilon}$ = 3054, 2927, 1706, 1568, 1458, 1352, 1264, 1108, 746 cm^{-1}. **HRMS** (ESI): *m/z* calcd for $C_{19}H_{16}NO_3$ $[M + H]^+$: 306.1125; found: 306.1130. Note: 3 days were needed for the methylation of the in-situ formed phenol derivative as the reaction rate is relatively low. Meanwhile, addition of additional reagents including NaOH, TBAB, Me_2SO_4 was needed to secure the accomplishment of this transformation.



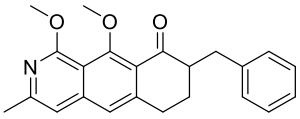
6ao

6ao: 59% yield, light yellow solid, mp 112−114 °C. $\mathbf{R_f}$ = 0.45 (silica, *n*-hexane/AcOEt = 4/1). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.18 (s, 1H), 6.88 (s, 1H), 4.11 (s, 3H), 3.96 (s, 3H), 2.99 (t, *J* = 5.5 Hz, 2H), 2.68 (t, *J* = 6.5 Hz, 2H), 2.49 (s, 3H), 2.11–2.04 ppm (m, 2H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 196.6, 161.0, 152.0, 145.7, 143.5, 124.0, 120.13, 120.13, 112.3, 111.9, 63.2, 53.9, 41.0, 31.1, 24.0, 22.5 ppm. **IR**: $\bar{\upsilon}$ = 3055, 2948, 1681, 1615, 1546, 1457, 1349, 1008, 734 cm^{-1}. **HRMS** (ESI): *m/z* calcd for $C_{16}H_{18}NO_3$ $[M + H]^+$: 272.1281; found: 272.1286.



6ap

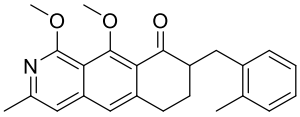
6ap: 54% yield, white solid, mp 94−96 °C. $\mathbf{R_f}$ = 0.8 (silica, *n*-hexane/AcOEt = 4/1). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.17 (s, 1H), 6.90 (s, 1H), 4.12 (s, 3H), 3.97 (s, 3H), 3.12–2.94 (m, 2H), 2.50 (s, 3H), 2.49–2.42 (m, 1H), 2.26–2.17 (m, 1H), 2.01–1.89 (m, 1H), 1.88–1.77 (m, 1H), 1.64–1.51 (m, 1H), 1.00 ppm (t, *J* = 7.5 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 199.7, 160.9, 160.4, 151.7, 145.4, 143.3, 124.7, 120.0, 112.2, 111.9, 63.5, 53.9, 50.8, 29.3, 27.4, 24.0, 23.7, 11.5 ppm. **IR**: $\bar{\upsilon}$ = 3054, 2929, 1727, 1681, 1615, 1548, 1456, 1350, 1263, 734 cm^{-1}. **HRMS** (ESI): *m/z* calcd for $C_{18}H_{22}NO_3$ $[M + H]^+$: 300.1594; found: 300.1599.



6aq

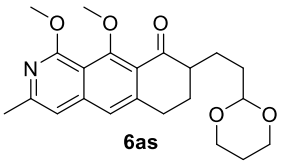
6aq: 71% yield, light yellow solid, mp 98−100 °C. $\mathbf{R_f}$ = 0.7 (silica, *n*-hexane/AcOEt = 4/1). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.33–7.28 (m, 2H), 7.26–7.20 (m, 3H), 7.16 (s, 1H), 6.89 (s, 1H), 4.14 (s, 3H), 4.00 (s, 3H), 3.47 (dd, *J* = 13.8, 4.1 Hz, 1H), 3.03 (dt, *J* = 16.4, 4.3 Hz, 1H), 2.98–2.88 (m, 1H), 2.84–2.76 (m, 1H), 2.67 (dd, *J* = 13.7, 9.9 Hz, 1H), 2.50 (s, 3H), 2.10–2.03 (m, 1H), 1.81–1.71 ppm (m, 1H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 198.4, 161.0, 160.8, 152.0, 145.3, 143.4, 140.0, 129.2, 128.4, 126.1, 124.3, 120.1, 112.3, 111.9, 63.5, 53.9, 51.2, 36.6, 29.6, 27.2,

24.0 ppm. **IR**: $\bar{\upsilon}$ = 3053, 2985, 2304, 1614, 1421, 1350, 1265, 739 cm^{-1}. **HRMS** (ESI): *m/z* calcd for $C_{23}H_{24}NO_3$ [*M* + H]$^+$: 362.1751; found: 362.1756.



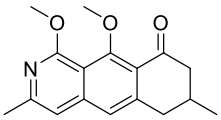
6ar

6ar: 68% yield, light yellow solid, mp 103−105 °C. $\mathbf{R_f}$ = 0.8 (silica, *n*-hexane/AcOEt = 4/1). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.20–7.13 (m, 5H), 6.90 (s, 1H), 4.14 (s, 3H), 4.02 (s, 3H), 3.57 (dd, *J* = 14.0, 3.7 Hz, 1H), 3.04 (dt, *J* = 16.6, 4.3 Hz, 1H), 2.98–2.87 (m, 1H), 2.81–2.72 (m, 1H), 2.59 (dd, *J* = 14.0, 10.5 Hz, 1H), 2.51 (s, 3H), 2.37 (s, 3H), 2.12–2.03 (m, 1H), 1.87–1.73 ppm (m, 1H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 198.5, 161.0, 160.8, 151.9, 145.3, 143.4, 138.2, 136.5, 130.4, 130.0, 126.3, 125.8, 124.4, 120.2, 112.2, 111.9, 63.5, 53.9, 49.9, 33.8, 29.7, 27.4, 24.0, 19.5 ppm. **IR**: $\bar{\upsilon}$ = 3054, 2950, 2305, 1681, 1615, 1350, 1264, 1116, 738 cm^{-1}. **HRMS** (ESI): *m/z* calcd for $C_{24}H_{26}NO_3$ [*M* + H]$^+$: 376.1907; found: 376.1912.



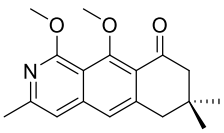
6as

6as: 53% yield, white solid, mp 100−102 °C. $\mathbf{R_f}$ = 0.3 (silica, *n*-hexane/AcOEt = 4/1). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.16 (s, 1H), 6.89 (s, 1H), 4.57 (t, *J* = 5.1 Hz, 1H), 4.12 (s, 3H), 4.12–4.05 (m, 2H), 3.96 (s, 3H), 3.76 (tdd, *J* = 12.1, 5.3, 2.5 Hz, 2H), 3.13–2.92 (m, 2H), 2.58–2.51 (m, 1H), 2.49 (s, 3H), 2.26–2.19 (m, 1H), 2.14–1.99 (m, 2H), 1.87–1.77 (m, 1H), 1.76–1.66 (m, 2H), 1.61–1.54 (m, 1H), 1.33 ppm (d, *J* = 13.5 Hz, 1H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 199.2, 160.9, 160.5, 151.7, 145.3, 143.3, 124.5, 120.0, 112.2, 111.9, 102.4, 66.9, 63.5, 53.9, 49.1, 32.6, 29.4, 27.9, 25.8, 25.0, 24.0 ppm. **IR**: $\bar{\upsilon}$ = 3054, 2305, 1615, 1421, 1350, 1264, 1144, 895, 730 cm^{-1}. **HRMS** (ESI): *m/z* calcd for $C_{22}H_{28}NO_5$ [*M* + H]$^+$: 386.1962; found: 386.1967.



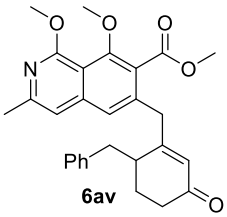
6at

6at: 52% yield, white solid, mp 109−111 °C. $\mathbf{R_f}$ = 0.5 (silica, *n*-hexane/AcOEt = 4/1). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.18 (s, 1H), 6.89 (s, 1H), 4.12 (s, 3H), 3.96 (s, 3H), 3.04 (d, *J* = 15.4 Hz, 1H), 2.83–2.65 (m, 2H), 2.50 (s, 3H), 2.41–2.23 (m, 2H), 1.13 ppm (d, *J* = 6.2 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 196.7, 161.1, 161.0, 152.1, 145.0, 143.6, 123.4, 120.4, 112.3, 111.9, 63.1, 53.9, 49.2, 39.3, 29.6, 24.0, 21.2 ppm. **IR**: $\bar{\upsilon}$ = 3054, 2929, 2306, 1681, 1546, 1375, 1264, 1116, 739 cm^{-1}. **HRMS** (ESI): *m/z* calcd for $C_{17}H_{20}NO_3$ [*M* + H]$^+$: 286.1438; found: 286.1443.



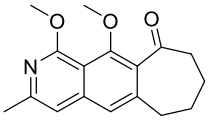
6au

6au: 95% yield, white solid, mp 131−133 °C. $\mathbf{R_f}$ = 0.7 (silica, *n*-hexane/AcOEt = 4/1). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.16 (s, 1H), 6.88 (s, 1H), 4.11 (s, 3H), 3.95 (s, 3H), 2.88 (s, 2H), 2.52 (s, 2H), 2.49 (s, 3H), 1.06 ppm (s, 6H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 196.5, 161.1, 161.0, 152.1, 144.2, 143.7, 122.8, 121.0, 112.3, 111.8, 63.0, 54.6, 53.9, 44.8, 32.7, 28.1, 24.0 ppm. **IR**: $\bar{\upsilon}$ = 3054, 2957, 2306, 1686, 1614, 1539, 1344, 731 cm^{-1}. **HRMS** (ESI): *m/z* calcd for $C_{18}H_{22}NO_3$ [*M* + H]$^+$: 300.1594; found:300.1599.



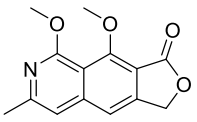
6av

6av: 50% yield, colorless liquid. $\mathbf{R_f}$ = 0.45 (silica, *n*-hexane/AcOEt = 4/1). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.30–7.25 (m, 2H), 7.22–7.18 (m, 1H), 7.17–7.14 (m, 2H), 6.55 (s, 1H), 5.82 (s, 1H), 3.95 (s, 3H), 3.84 (s, 3H), 3.48 (s, 2H), 3.36–3.29 (m, 1H), 2.53–2.45 (m, 2H), 2.43 (s, 3H), 2.26–2.13 (m, 2H), 1.96–1.88 (m, 1H), 1.64–1.53 ppm (m, 1H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 200.4, 167.3, 161.2, 160.7, 158.0, 146.6, 139.8, 129.2, 128.3, 127.2, 126.1, 117.1, 114.0, 53.9, 52.3, 47.6, 40.8, 35.2, 28.6, 26.9, 24.1 ppm. **IR**: $\bar{\upsilon}$ = 3055, 2951, 1728, 1668, 1598, 1456, 1207, 1097, 736 cm^{-1}. **HRMS** (ESI): *m/z* calcd for $C_{28}H_{30}NO_5$ $[M + H]^+$: 460.2118; found:460.2123.



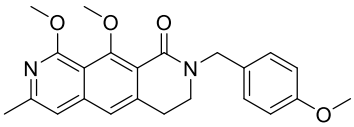
6aw

6aw: 45% yield, white solid, mp 87−89 °C. $\mathbf{R_f}$ = 0.75 (silica, *n*-hexane/AcOEt = 4/1). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.14 (s, 1H), 6.95 (s, 1H), 4.13 (s, 3H), 3.92 (s, 3H), 2.84 (t, *J* = 6.1 Hz, 2H), 2.73–2.63 (m, 2H), 2.51 (s, 3H), 1.90–1.77 ppm (m, 4H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 207.2, 159.7, 154.0, 150.3, 142.5, 140.4, 133.6, 120.9, 112.4, 111.2, 64.9, 53.8, 42.9, 33.1, 26.5, 23.8, 23.7 ppm. **IR**: $\bar{\upsilon}$ = 3054, 2942, 1694, 1621, 1556, 1456, 1348, 1265, 735 cm^{-1}. **HRMS** (ESI): *m/z* calcd for $C_{17}H_{20}NO_3$ $[M + H]^+$: 286.1438; found: 286.1443.



6ax

6ax: 61% yield, white solid, mp 159−162 °C. $\mathbf{R_f}$ = 0.2 (silica, *n*-hexane/AcOEt = 4/1). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.32 (s, 1H), 7.01 (s, 1H), 5.32 (s, 2H), 4.18 (s, 3H), 4.14 (s, 3H), 2.53 ppm (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 168.0, 161.3, 160.4, 152.9, 146.4, 145.4, 113.9, 113.6, 112.8, 112.5, 68.2, 63.8, 54.1, 24.0 ppm. **IR**: $\bar{\upsilon}$ = 3054, 2986, 2305, 1763, 1630, 1353, 1264, 745 cm^{-1}. **HRMS** (ESI): *m/z* calcd for $C_{14}H_{14}NO_4$ $[M + H]^+$: 260.0917; found: 260.0922.

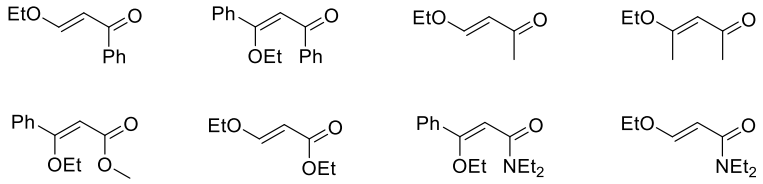


6ay

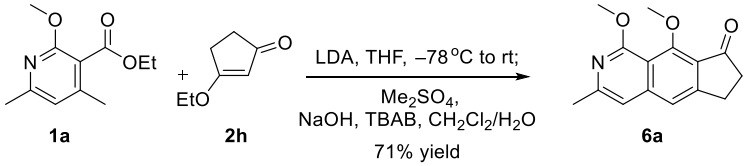
6ay: 70% yield, colorless solid, 119−121 °C. $\mathbf{R_f}$ = 0.15 (silica, *n*-hexane/AcOEt = 4/1). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.28 (d, *J* = 8.6 Hz, 2H), 7.10 (s, 1H), 6.89 (s, 1H), 6.86 (d, *J* = 8.6 Hz, 2H), 4.77 (s, 2H), 4.13 (s, 3H), 4.08 (s, 3H), 3.80 (s, 3H), 3.40 (t, *J* = 6.0 Hz, 2H), 2.92 (t, *J* = 6.0 Hz, 2H), 2.50 ppm (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 162.5, 160.6, 160.3, 159.0, 151.3, 142.8, 141.4, 129.8, 129.4, 120.5, 118.8, 114.0, 112.8, 112.0, 63.7, 55.2, 53.8, 49.5, 44.7, 30.3, 23.9 ppm. **IR**: $\bar{\upsilon}$ = 3053, 2929, 1730, 1647, 1512, 1348, 1265, 739 cm^{-1}. **HRMS** (ESI): *m/z* calcd for $C_{23}H_{25}N_2O_4$ $[M + H]^+$: 393.1809; found: 393.1814.

Note: Preliminary experiments showcased that acyclic vinylogous systems do not deliver any positive result in this annulation under the optimized conditions. No reaction, decomposition of the starting material or complex mixture

always occurred when the linear *β*-ethoxy *α*,*β*-unsaturated carbonyl compounds were exposed to the alkaline conditions. Below are the failed substrates.



2. Preparation of Compound 6a

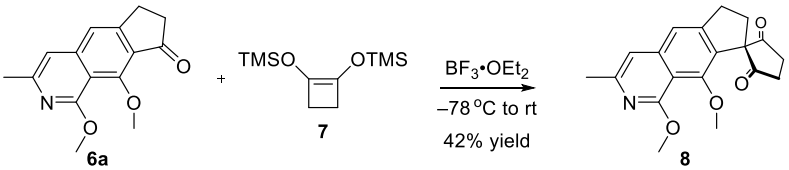


To a stirred solution of **1a** (8.33 g, 39.84 mmol, 2.0 equiv) in THF (150 mL) was dropwise added freshly prepared LDA (1.0 mol/L, 39.84 mL, 39.84 mmol, 2.0 equiv) at –78 °C. The resulting mixture was stirred at the same temperature for 1 h. After slow addition of **2h** (2.51 g, 19.92 mmol, 1.0 equiv) in THF solution (50 mL) at –78 °C, the mixture was warmed to ambient temperature in 10 min. Saturated aqueous NH_4Cl (20 mL) was added to quench the reaction after completion of the reaction monitored by TLC. Water (200 mL) and EtOAc (200 mL) was added into the mixture. The organic phase was separated, and the aqueous layer was extracted with EtOAc (2 × 100 mL). The combined extractswere washed with brine (200 mL) and concentrated under reduced pressure. (note: all substrates including the insoluble should be collected) The residue was directly subjected to the next step without further purification.

To the residue obtained above was added NaOH (1.59 g, 39.84 mmol, 2.0 equiv) in water (20 mL), Me_2SO_4 (4.73 mL, 49.80 mmol, 2.5 equiv), TBAB (0.64 g, 1.99 mmol, 0.1 equiv) and CH_2Cl_2 (20 mL) and the reaction mixture were stirred vigorously. Saturated aqueous NH_4Cl (10 mL) was added to quench the reaction after completion of the reaction monitored by TLC. The organic phase was separated, and the aqueous layer was extracted with CH_2Cl_2 (2 × 50 mL). The combined extracts were washed with brine (50 mL), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel eluting with *n*-hexane/AcOEt (4:1) to afford the isoquinoline **6a** (3.64 g, 14.14 mmol, 71% yield, mp 145−146 °C) as a white solid.

6a: 72% yield, off-white solid, mp 145−146 °C. $\mathbf{R_f}$ = 0.45 (silica, *n*-hexane/AcOEt = 4/1). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.30 (s, 1H), 6.92 (s, 1H), 4.11 (s, 3H), 4.06 (s, 3H), 3.20–3.12 (m, 2H), 2.75–2.68 (m, 2H), 2.49 ppm (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 203.3, 161.8, 158.7, 154.4, 152.1, 145.6, 125.7, 117.8, 112.3, 111.9, 63.0, 53.9, 37.2, 25.1, 24.0 ppm. **IR**: $\bar{\upsilon}$ = 3053, 2305, 1717, 1616, 1421, 1265, 895, 739 cm^{-1}. **HRMS** (ESI): *m/z* calcd for $C_{15}H_{16}NO_3$ $[M + H]^+$: 258.1125; found: 258.1130.

3. Preparation of Compound 8

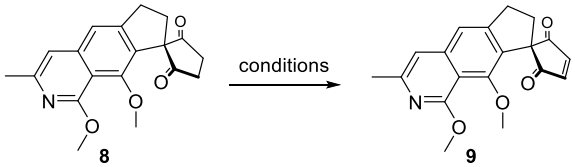


To a stirred solution of **6a** (3.00 g, 11.67 mmol, 1.0 equiv) in CH_2Cl_2 (25 mL) was added freshly distilled BF_3 Ɛt_2O (2.16 mL, 17.50 mmol, 1.5 equiv) at –78 °C. 5 min later, compound **7** (6.00 mL, 23.34 mmol, 2.0 equiv) was added to the reaction mixture and the resulting mixture was stirred at the same temperature for 1 h. The mixture was warmed to ambient temperature in 10 min and stirred overnight. A saturated aqueous solution of $NaHCO_3$ (20 mL) was added to quench the reaction. The organic phase was separated, and the aqueous layer was extracted with CH_2Cl_2 (2 × 25 mL). The combined extracts were washed with brine (50 mL), dried over anhydrous

Na_2SO_4, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel eluting with *n*-hexane/AcOEt (4:1) to afford the diketone **8** (1.59 g, 4.90 mmol, 42% yield, mp 121−122 °C) as a yellow solid.

8: $\mathbf{R_f}$ = 0.5 (silica, *n*-hexane/AcOEt = 2/1). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.25 (s, 1H), 6.94 (s, 1H), 4.09 (s, 3H), 3.72 (s, 3H), 3.27 (t, *J* = 7.4 Hz, 2H), 3.19–3.05 (m, 2H), 2.96–2.82 (m, 2H), 2.47 (s, 3H), 2.37 ppm (t, *J* = 7.4 Hz, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 215.3, 158.6, 151.6, 149.1, 149.0, 143.2, 134.5, 117.3, 112.9, 110.6, 65.3, 62.3, 53.6, 36.2, 35.9, 32.2, 23.6 ppm. **IR**: $\bar{\upsilon}$ = 3454, 2945, 1720, 1628, 1570, 1342, 1182, 1095 cm^{-1}. **HRMS** (ESI): *m/z* calcd for $C_{19}H_{20}NO_4$ $[M + H]^+$: 326.1387; found: 326.1392.

4. Preparation of Compound 9



Entry	Conditions	Result
1	DDQ (1. 2 eq.), *p*-TsOH (0.25 eq.), toluene, reflux	mixture (no main point)
2	DDQ (1. 2 eq.), *p*-TsOH (0.25 eq.), toluene, 80 ℃, 24 h	47% yield (64% yield brsm)
3	DDQ (2. 2 eq.), *p*-TsOH (0.50 eq.), toluene, 90 ℃, 5 h	62% yield
4	$CuBr_2$ (2.2 eq.), CH_3OH, 50 °C	rsm
5	$CuBr_2$ (2.2 eq.), CH_3OH, reflux	trace

As we can see from this table, DDQ could oxidize **8** in the presence of *p*-TsOH to deliver tetracyclic enone **9** in an acceptable yield of 62%. Temperature and the equivalent of acid should be carefully balanced. Meanwhile, $CuBr_2$ is not a good oxidant. It should be noted that for this reaction, a scale of 100 mg is good and it's not suitable for large scale synthesis as the product might not be stable enough in the acidic conditions. However, we could conduct more than 10 parallel reactions at the same time to get enough material for further transformations. A general procedure for entry 3 is as follows:

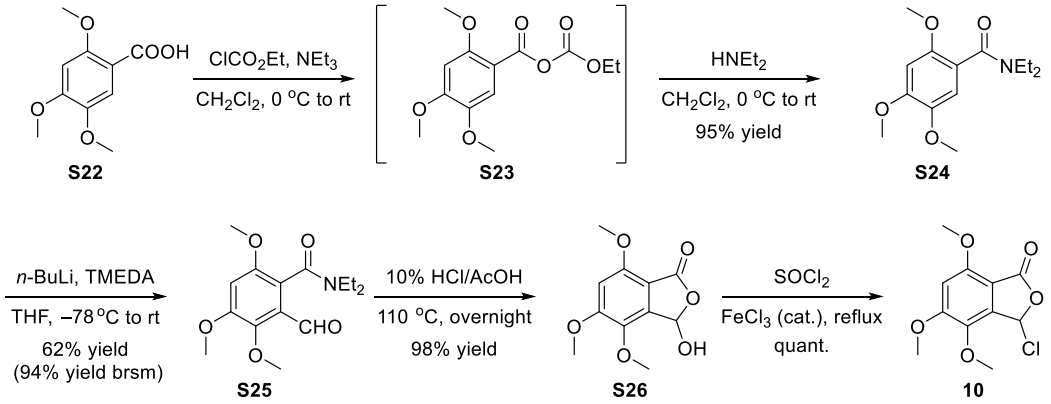
To a stirred solution of **8** (100 mg, 0.308 mmol, 1.0 equiv) in toluene (3 mL) was sequentially added DDQ (167.8 mg, 0.739 mmol, 2.4 equiv) and *p*-TsOH (29.3 mg, 0.154 mmol, 0.5 equiv). The resulting mixture was stirred at 90 °C for 5 h. After cooled to rt, saturated aq. $NaHCO_3$ (2 mL) was added to the mixture. The organic phase was separated, and the aqueous layer was extracted with EtOAc (3 × 2 mL). The combined extracts were washed with brine (5 mL), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel eluting with *n*-hexane/AcOEt (4:1) to afford the diketone **9** (61.7 mg, 0.191 mmol, 62% yield, mp 104−106 °C) as a light yellow solid.

9: $\mathbf{R_f}$ = 0.45 (silica, *n*-hexane/AcOEt = 4/1). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.42 (s, 2H), 7.29 (s, 1H), 6.96 (s, 1H), 4.07 (s, 3H), 3.60 (s, 3H), 3.31 (t, *J* = 7.2 Hz, 2H), 2.48 (s, 3H), 2.38 ppm (t, *J* = 7.5 Hz, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 205.3, 158.8, 152.6, 149.5, 149.2, 148.4, 143.3, 131.8, 117.3, 112.9, 110.9, 62.8, 60.6, 53.6, 34.3, 32.0, 23.7 ppm. **IR**: $\bar{\upsilon}$ = 3053, 2985, 1707, 1421, 1346, 1285, 1103, 736 cm^{-1}. **HRMS** (ESI): *m/z* calcd for $C_{19}H_{18}NO_4$ $[M + H]^+$: 324.1230; found: 324.1236.

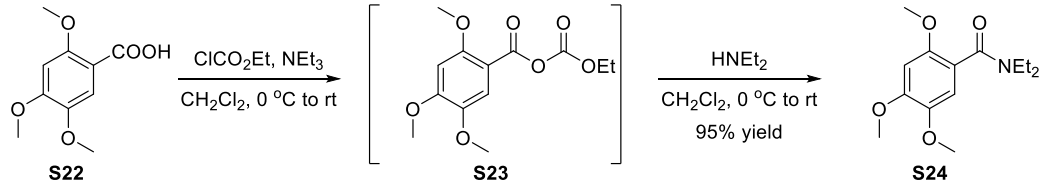
5. Main Scheme for Preparation of Compound 10

For the synthesis of **10**, we selected the commercially available benzoic acid **S22** as the starting material. Following the known procedure (Evans, J. C.; Klix, R. C. and Bach, R. D. *J. Org. Chem.* **1988**, *53*, 5519–5527), we can obtain phthalidyl chloride **10** in 4 known steps.

Outline for the synthesis of **10** is as follows:



5.1. Preparation of Compound S24

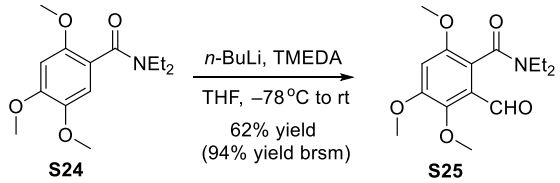


To a stirred solution of **S22** (10.0 g, 47.2 mmol, 1.0 equiv) in CH_2Cl_2 (50 mL) was added NEt_3 (19.7 mL, 141.6 mmol, 3.0 equiv). The resulting mixture was cooled to 0 °C and $ClCO_2Et$ (6.74 mL, 70.8 mmol, 1.5 equiv) was added dropwise to the mixture. After 0.5 h, $HNEt_2$ (14.6 mL, 141.6 mmol, 3.0 equiv) was added dropwise to the mixture at 0 °C and the reaction mixture was warmed to room temperature and stirred for 2 h. H_2O (50 mL) was added to the mixture. The organic phase was separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 20 mL). The combined extracts were washed with brine (50 mL), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel eluting with *n*-hexane/AcOEt (1:1) to afford the amide **S24** (12.0 g, 44.8 mmol, 95% yield) as a light yellow liquid.

S22: **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.60 (s, 1H), 6.56 (s, 1H), 4.06 (s, 3H), 3.96 (s, 3H), 3.88 ppm (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 165.5, 154.6, 153.8, 144.3, 114.7, 109.1, 96.5, 57.5, 56.5, 56.4 ppm.

S24: $\mathbf{R_f}$ = 0.4 (silica, *n*-hexane/AcOEt = 1/1). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 6.52 (s, 1H), 6.32 (s, 1H), 3.65 (s, 3H), 3.59 (d, 3H), 3.55 (s, 3H), 3.30 (br, 2H), 2.95 (q, J = 7.1 Hz, 2H), 0.99 (t, J = 7.1 Hz, 3H), 0.81ppm (t, J = 7.1 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 167.8, 149.5, 149.0, 142.5, 117.4, 110.7, 97.0, 55.83, 55.77, 55.4, 42.2, 38.2, 13.4, 12.2 ppm.

5.2. Preparation of Compound S25

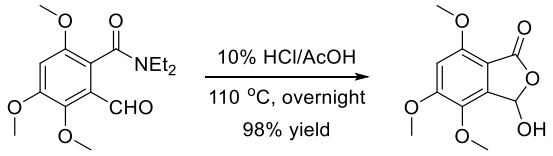


To a stirred solution of **S24** (11.0 g, 41.2 mmol, 1.0 equiv) in THF (50 mL) was added TMEDA (7.4 mL, 49.4 mmol, 1.2 equiv). The resulting mixture was cooled to −78 °C and *n*-BuLi (2.0 M in cyclohexane, 61.8 mL, 123.6 mmol, 3.0 equiv) was added dropwise to the mixture. After 0.5 h, dry DMF (15.9 mL, 206.0 mmol, 5.0 equiv) was added dropwise at the same temperature and the reaction mixture was warmed to room temperature after 30 min and stirred overnight. A saturated aqueous solution of NH_4Cl (50 mL) was added carefully to the mixture. AcOEt (50 mL) was added to the mixture and the organic phase was separated, and the aqueous layer was extracted with AcOEt (3 × 50 mL). The combined extracts were washed with brine (100 mL), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel

eluting with *n*-hexane/AcOEt (1:2) to afford the aldehyde **S25** (7.5 g, 25.5 mmol, 62% yield, 94% yield based on the recovered starting material) as a light yellow liquid.

S25: $\mathbf{R_f}$ = 0.2 (silica, *n*-hexane/AcOEt = 1/1). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 10.34 (s, 1H), 6.74 (s, 1H), 3.92 (s, 3H), 3.89 (s, 3H), 3.80 (s, 3H), 3.70 (dt, *J* = 17.2, 7.1 Hz, 1H), 3.44 (dq, *J* = 14.1, 7.1 Hz, 1H), 3.05 (q, *J* = 7.2 Hz, 2H), 1.28 (t, *J* = 7.1 Hz, 3H), 0.97 ppm (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 189.6, 166.4, 153.6, 152.0, 146.4, 126.9, 118.0, 102.7, 62.4, 56.4, 56.2, 42.5, 38.5, 13.3, 12.1 ppm.

5.3. Preparation of Compound S26



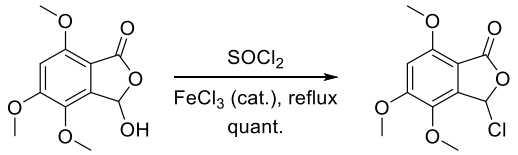
S25 **S26**

S25 (7.0 g, 23.7 mmol) was dissolved in 10% HCl (10 mL)/AcOH (10 mL) and the mixture was brought to 110 °C. After vigorously stirred overnight, the resulting mixture was cooled to room temperature and the solvents were concentrated under reduced pressure. A saturated aqueous solution of $NaHCO_3$ (50 mL) and AcOEt (50 mL) were added to the residue. The organic phase was separated, and the aqueous layer was extracted with AcOEt (3 × 50 mL). The combined extracts were washed with brine (100 mL), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel eluting with *n*-hexane/AcOEt (1:2) to afford the hemiacetal **S26** (5.6 g, 23.2 mmol, 98% yield) as an off-white solid.

Caution: The hemiacetal is not easy to dissolve in most of solvents. For large scale, filtration is advised.

S26: $\mathbf{R_f}$ = 0.75 (silica, AcOEt). **^{1}H NMR** (500 MHz, DMSO-d_6): δ = 7.90 (br, 1H), 6.78 (s, 1H), 6.52 (s, 1H), 3.94 (s, 3H), 3.90 (s, 3H), 3.76 ppm (s, 3H). **^{13}C NMR** (125 MHz, DMSO-d_6): δ = 165.6, 158.9, 154.7, 140.4, 137.2, 105.1, 99.0, 94.8, 60.6, 56.7, 56.3 ppm.

5.4. Preparation of Compound 10



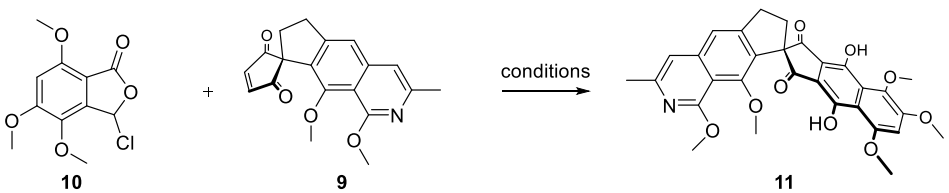
S26 **10**

To a stirred solution of hemiacetal **S26** (5.0 g, 20.8 mmol) in $SOCl_2$ (5 mL) was added $FeCl_3$ (16.9 mg, 0.104 mmol, 0.005 equiv). The mixture was brought to reflux (86 °C) and stirred for 2 h. After cooling to room temperature, the solvents were concentrated under reduced pressure. The residue was dissolved in CH_2Cl_2 and filtrated to deliver phthalidyl chloride **10** (5.4 g, 20.8 mmol, quant., mp 245−246 °C) as an off-white solid.

Caution: phthalidyl chloride **10** is easy to hydrolyze in DMSO-d_6 possibly because of the presence of H_2O.

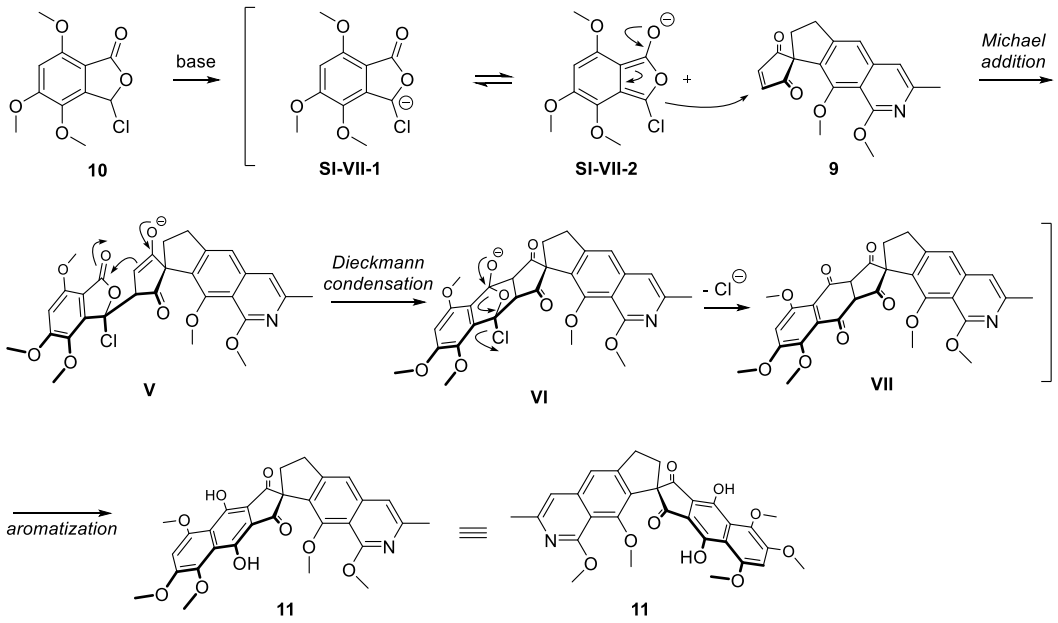
10: $\mathbf{R_f}$ = 0.5 (silica, *n*-hexane/AcOEt = 1/1). **^{1}H NMR** (500 MHz, CD_3CN): δ = 7.13 (s, 1H), 6.76 (s, 1H), 3.99 (s, 3H), 3.97 (s, 3H), 3.86 ppm (s, 3H). **^{13}C NMR** (125 MHz, CD_3CN): δ = 165.3, 161.2, 156.8, 141.6, 137.6, 103.2, 100.5, 84.5, 61.4, 57.7, 57.4 ppm. **IR**: $\bar{\nu}$ = 3460, 3055, 1784, 1512, 1364, 1265, 989, 739 cm^{-1}. **HRMS** (ESI): *m/z* calcd for $C_{11}H_{12}ClO_5$ $[M + H]^+$: 259.0368; found: 259.0373.

6. Conditions Screening for Hauser–Kraus-Type Annulation and Preparation of Kita Intermediate 12



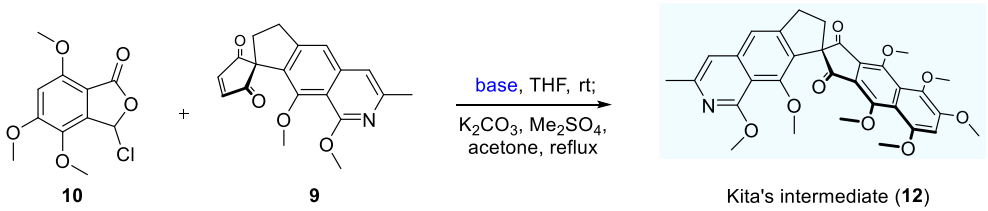
10 **9** **11**

With phthalidyl chloride **10** and diketone **9** in hand, as shown in the scheme above, we hope to obtain the Hauser-Kraus annulation product **11** following the designed reaction pathway. Mechanistically, after benzylic deprotonation of the phthalidyl chloride **10**, the resonance structures **VIII-1** and **VIII-2** were formed. Intermolecular Michael addition of **VIII** and **9** was followed by successive transformations involving Dieckmann condensation of enolate **V**, extrusion of chloride anion from the diketone **VI** and last aromatization of the advanced intermediate **VII** to afford the hexacyclic diphenol **11** with the full skeleton embedded in fredericamycin A.



6.1. Screening of Bases

As the Hauser-Kraus-type annulation product is not that stable, dimethylation was conducted *in-situ* to deliver Kita's intermediate **12** directly. As shown in the table below, we have screened a series of bases. Among them, most bases didn't give the desired products. LiO^{t}Bu gave the desired product in 51% yield for 2 steps.

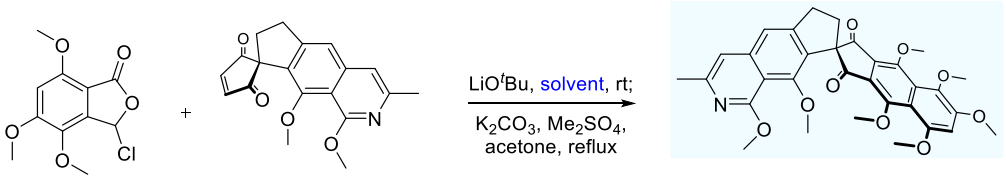


Entry	Base	Result
1	K_2CO_3	no reaction
2	K_3PO_4	no reaction
3	KOAc	no reaction
4	KO^{t}Bu	no product
5	KOH	no product
6	NaO^{t}Bu	no product
7	NaOEt	no reaction
8	$NaOCH_3$	no product
9	NaOAc	no reaction
10	LiO^{t}Bu	51% yield
11	Li_2CO_3	no reaction
12	LiOH $\cdot H_2O$	no product
13	$LiOCH_3$	no product
14	DBU	no product

15	DABCO	no reaction
16	Cs_2CO_3	no product
17	CsOAc	no reaction
18	DIPEA	no reaction
19	NEt_3	no reaction
20	DMAP	no reaction
21	KHMDS	trace
22	LiHMDS	32% yield

6.2. Screening of Solvents

As shown in the table below, a series of solvents have been tested. Among them, most solvents didn't give the desired products. THF is the only solvent that gave the desired product.

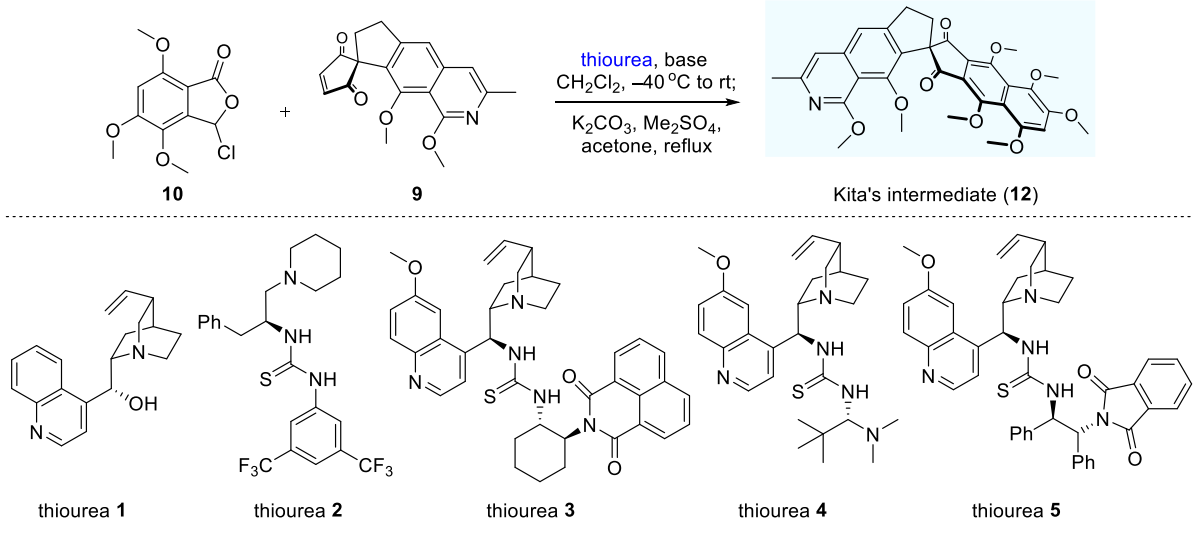


10 **9** Kita's intermediate (**12**)

Entry	Solvent	Result
1	THF	51% yield
2	CH_2Cl_2	no reaction
3	toluene	no product
4	DMF	no product
5	DMSO	no product
6	1,4-dioxane	no reaction
7	acetonitrile	no product
8	DCE	no reaction
9	Et_2O	no product

6.3. Screening of Thiourea Catalysts

As shown in the table below, a series of combination of thiourea catalysts and bases have been examined with the hope of achieving the asymmetric version of this transformation. In most cases, no good ee has been yielded, indicating that thiourea catalysts are not good choices for this transformation.

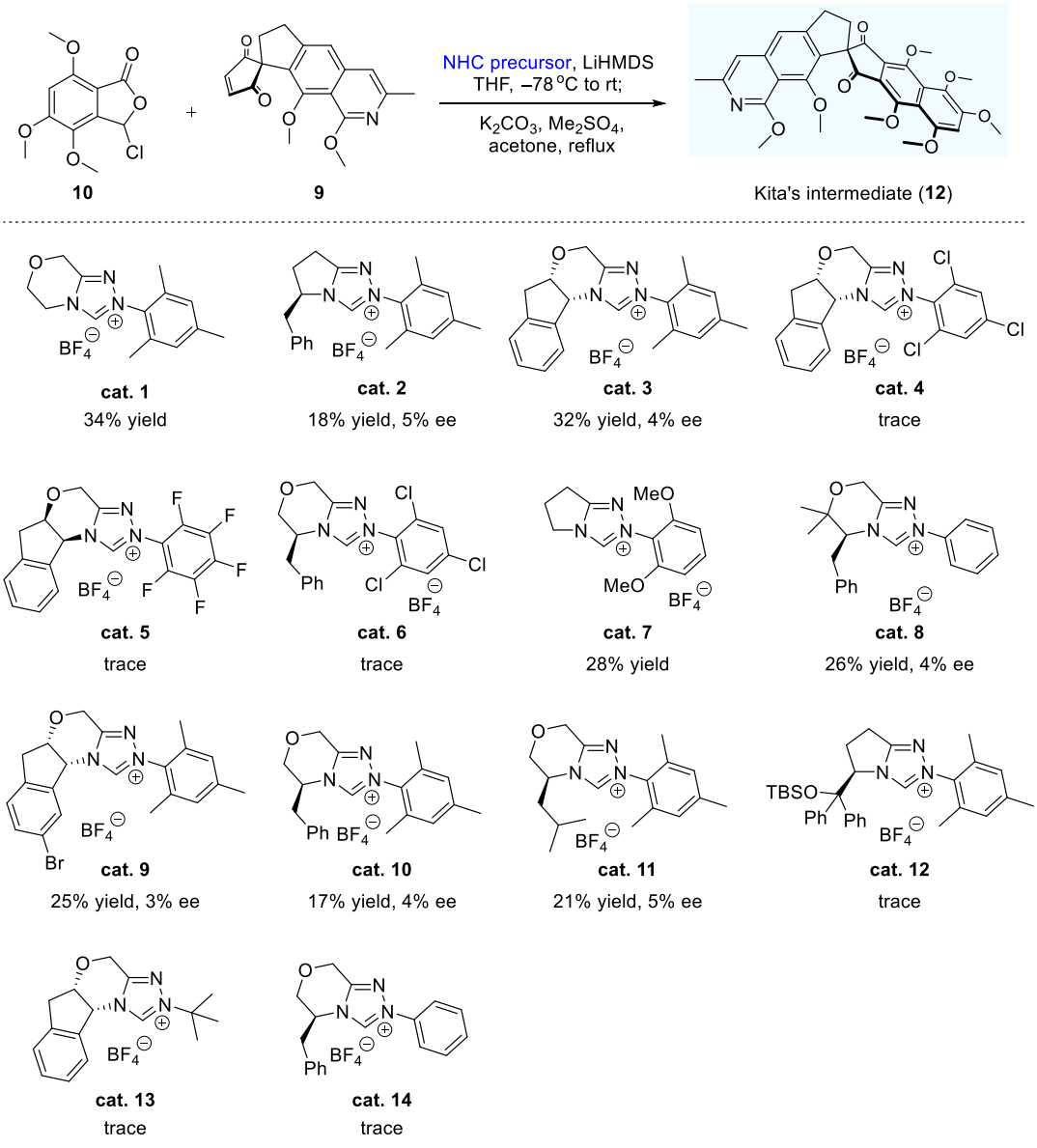


10 **9** Kita's intermediate (**12**)

thiourea **1** thiourea **2** thiourea **3** thiourea **4** thiourea **5**

Entry	Conditions	Result
1	LiHMDS (in THF), thiourea **1**	39% yield, 6% ee
2	LiHMDS (in THF), thiourea **2**	trace
3	LiHMDS (in THF), thiourea **3**	31% yield, 4% ee
4	LiHMDS (in THF), thiourea **4**	trace
5	KHMDS (in toluene), thiourea **1**	no reaction
6	KHMDS (in toluene), thiourea **2**	no reaction
7	KHMDS (in toluene), thiourea **3**	no reaction
8	KHMDS (in toluene), thiourea **4**	no reaction
9	KHMDS (in toluene), thiourea **5**	no reaction
10	LiO^{t}Bu, thiourea **2**	trace
11	LiO^{t}Bu, thiourea **3**	trace
12	LiO^{t}Bu, thiourea **4**	trace

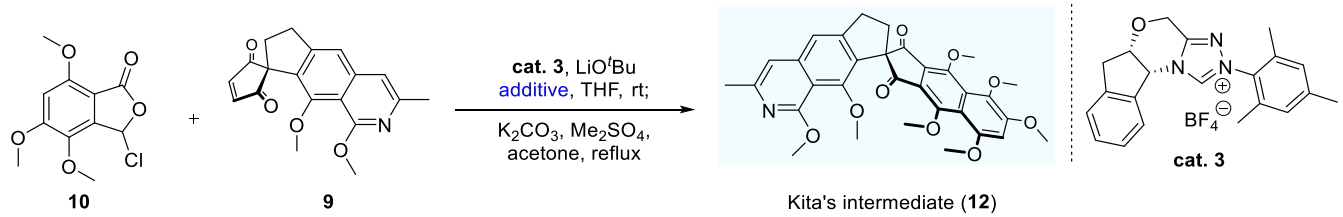
6.4. Screening of NHC Precursors



As shown in the scheme above, LiHMDS was chosen as the base for this reaction. Most of the NHC precursors tested are not good. Low yield and nearly no ee value showcased that NHC can't involve in this transformation to induce the newly formed chiral center.

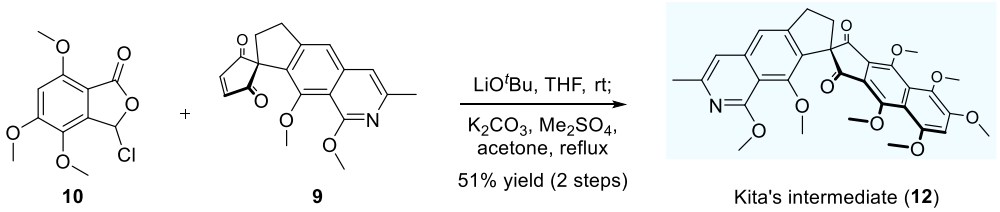
6.5. Screening of Salts

We wanted to improve the ee value by introduction of additives. As shown in the table below, In the presence of NaI, Kita's intermediate could be obtained in 31% yield but only with 5% ee. Other additives such as $AgPF_6$, $AgNO_3$, Ag_2CO_3 and $AgClO_4$ didn't even give the annulation product.



Entry	Base	Result
1	NaI	31% yield, 5% ee
2	$AgPF_6$	no product
3	$AgNO_3$	trace
4	Ag_2CO_3	no product
5	$AgClO_4$	no product

6.6. Preparation of Kita's Intermediate 12



To a stirred solution of phthalidyl chloride **10** (95.7 mg, 0.371 mmol, 1.2 equiv), diketone **9** (100.0 mg, 0.309 mmol, 1.0 equiv) in THF (10 mL) was added LiO^{t}Bu (34.6 mg, 0.433 mmol, 1.4 equiv) and stirred overnight at room temperature. Saturated aqueous solution of NH_4Cl (10 mL) and AcOEt (20 mL) were added to the mixture after completion of the reaction monitored by TLC. The organic phase was separated, and the aqueous layer was extracted with AcOEt (2 × 10 mL). The combined extracts were washed with brine (20 mL), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was directly exposed to the next reaction without further purification.

To the residue mentioned above in acetone (5 mL) was added K_2CO_3 (127.9 mg, 0.927 mmol, 3.0 equiv) and Me_2SO_4 (0.15 mL, 1.545 mmol, 5.0 equiv). The resulting mixture was brought to reflux and stirred overnight. After cooling to room temperature, a saturated aqueous solution of NH_4Cl (10 mL) and AcOEt (10 mL) were added to the mixture. The organic phase was separated, and the aqueous layer was extracted with AcOEt (2 × 10 mL). The combined extracts were washed with brine (20 mL), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel eluting with *n*-hexane/AcOEt (2:1) to afford Kita's intermediate **12** (90.3 mg, 0.158 mmol, 51% yield, mp 99−100 °C) as a light yellow solid.

12: $\mathbf{R_f}$ = 0.4 (silica, *n*-hexane/AcOEt = 1/1). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.32 (s, 1H), 6.96 (s, 1H), 6.93 (s, 1H), 4.07 (s, 6H), 4.06 (s, 3H), 4.05 (s, 3H), 4.00 (s, 3H), 3.91 (s, 3H), 3.49 (s, 3H), 3.44–3.36 (m, 2H), 2.55 (t, J = 7.3 Hz, 2H), 2.47 ppm (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 200.5, 199.3, 159.0, 156.9, 153.9, 153.6, 152.4, 150.9, 150.0, 148.7, 143.2, 139.3, 134.5, 131.1, 127.7, 124.5, 121.2, 117.2, 113.0, 111.1, 99.8, 66.2, 63.3, 63.1, 62.5, 62.3, 57.4, 56.6, 53.4, 36.2, 32.4, 23.7 ppm. **IR**: $\bar{\upsilon}$ = 3053, 2928, 2304, 1732, 1265, 1045, 894, 737 cm^{-1}. **HRMS** (ESI): *m/z* calcd for $C_{32}H_{32}NO_9$ $[M + H]^+$: 574.2072; found: 574.2077.

6.7. Comparison of NMR Spectral Data of Kita's Intermediate 12

Yasuyuki Kita reported his intermediate **12** in 2001 (Kita, Y., Higuchi, K., Yoshida, Y., Iio, K., Kitagaki, S., Ueda, K., Akai, S. and Fujioka, H. *J. Am. Chem. Soc.* **2001**, *123*, 3214−3222) and its absolute configuration was determined by CD analysis.

^{1}H and ^{13}C NMR spectral data of our synthetic Kita's intermediate **12** are in good accord with those from Kita's lab. Below is the comparison of ^{1}H and ^{13}C NMR spectral data from these two labs.

Comparison of ^{13}H NMR Spectral Data of Kita's Intermediate

Kita's lab ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) [a]	Our lab **^{1}H NMR** (400 MHz, $CDCl_3$) **δ (ppm)**	**$\Delta\delta$ (ppm)**
7.24 (s, 1H)	7.32 (s, 1H),	–0.08
6.87 (s, 1H)	6.96 (s, 1H)	–0.09
6.84 (s, 1H)	6.93 (s, 1H)	–0.09
3.99 (s, 6H)	4.07 (s, 6H)	–0.08
3.99 (s, 3H)	4.06 (s, 3H)	–0.07
3.96 (s, 3H)	4.05 (s, 3H)	–0.09
3.92 (s, 3H)	4.00 (s, 3H)	–0.08
3.82 (s, 3H)	3.91 (s, 3H)	–0.09
3.41 (s, 3H)	3.49 (s, 3H)	–0.08
3.33 (t, *J* = 7.5 Hz, 2H)	3.44–3.36 (m, 2H)	–0.07
2.47 (t, *J* = 7.5 Hz, 2H)	2.55 (t, *J* = 7.3 Hz, 2H)	–0.08
2.38 (s, 3H)	2.47 ppm (s, 3H)	–0.09

[a] For the reference, see: Kita, Y., Higuchi, K., Yoshida, Y., Iio, K., Kitagaki, S., Ueda, K., Akai, S. and Fujioka, H., *J. Am. Chem. Soc.* **2001**, *123*, 3214-3222.

Comparison of ^{13}C NMR Spectral Data of Kita's Intermediate

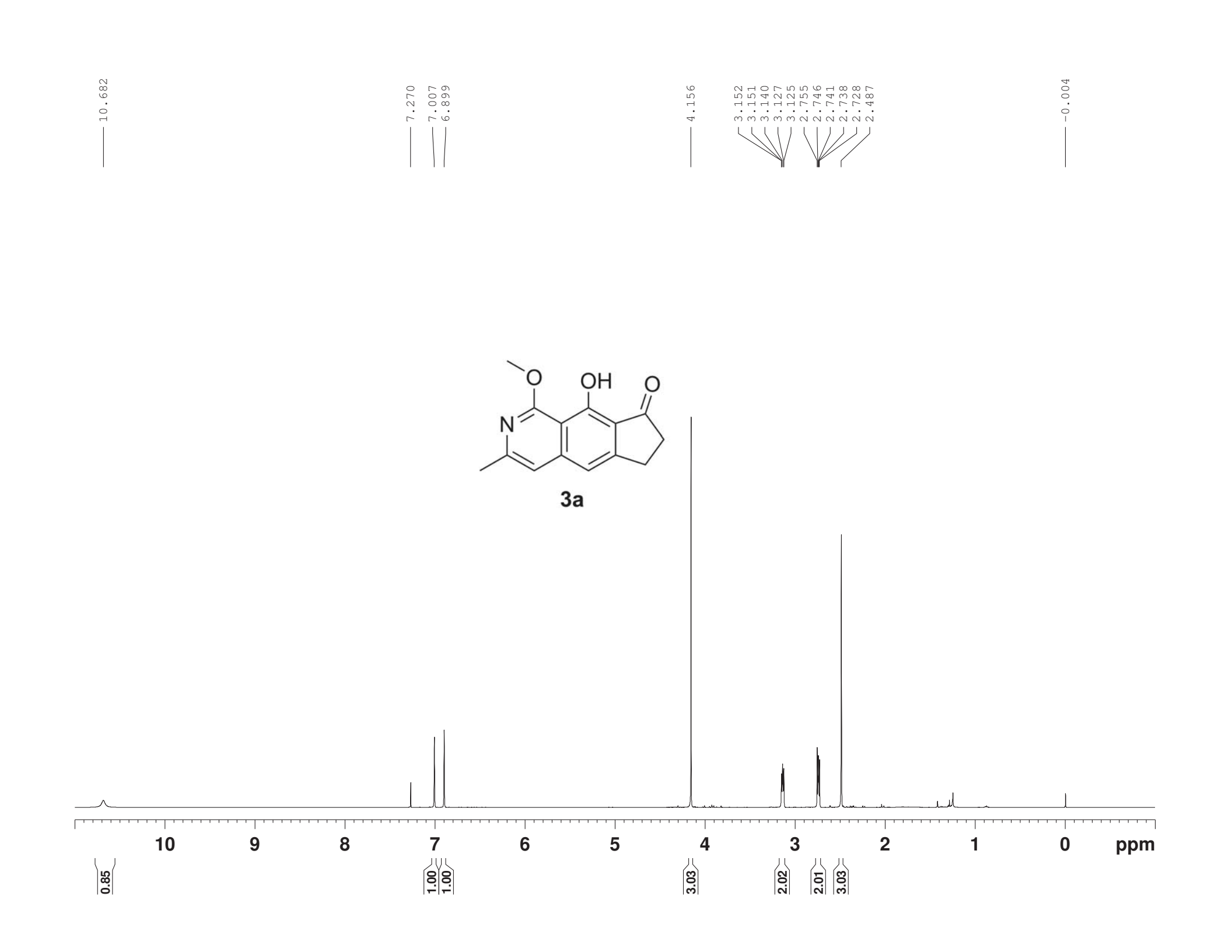
Kita's lab ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) [a]	Our lab **^{13}C NMR** (100 MHz, $CDCl_3$) **δ (ppm)**	**$\Delta\delta$ (ppm)**
200.4	200.5	–0.1
199.2	199.3	–0.1
158.9	159.0	–0.1
156.8	156.9	–0.1
153.9	153.9	0.0
153.6	153.6	0.0
152.4	152.4	0.0
150.8	150.9	–0.1
150.0	150.0	0.0
148.6	148.7	–0.1
143.2	143.2	0.0

139.2	139.3	–0.1
134.5	134.5	0.0
131.0	131.1	–0.1
127.6	127.7	–0.1
124.4	124.5	–0.1
121.1	121.2	–0.1
117.1	117.2	–0.1
112.9	113.0	–0.1
111.1	111.1	0.0
99.7	99.8	–0.1
66.2	66.2	0.0
63.2	63.3	–0.1
63.0	63.1	–0.1
62.5	62.5	0.0
62.2	62.3	–0.1
57.3	57.4	–0.1
56.5	56.6	–0.1
53.4	53.4	0.0
36.2	36.2	0.0
32.3	32.4	–0.1
23.7	23.7	0.0

[a] For the reference, see: Kita, Y., Higuchi, K., Yoshida, Y., Iio, K., Kitagaki, S., Ueda, K., Akai, S. and Fujioka, H., *J. Am. Chem. Soc.* **2001**, *123*, 3214-3222.

7. Copies of NMR Spectra

See the next page.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2.738
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N
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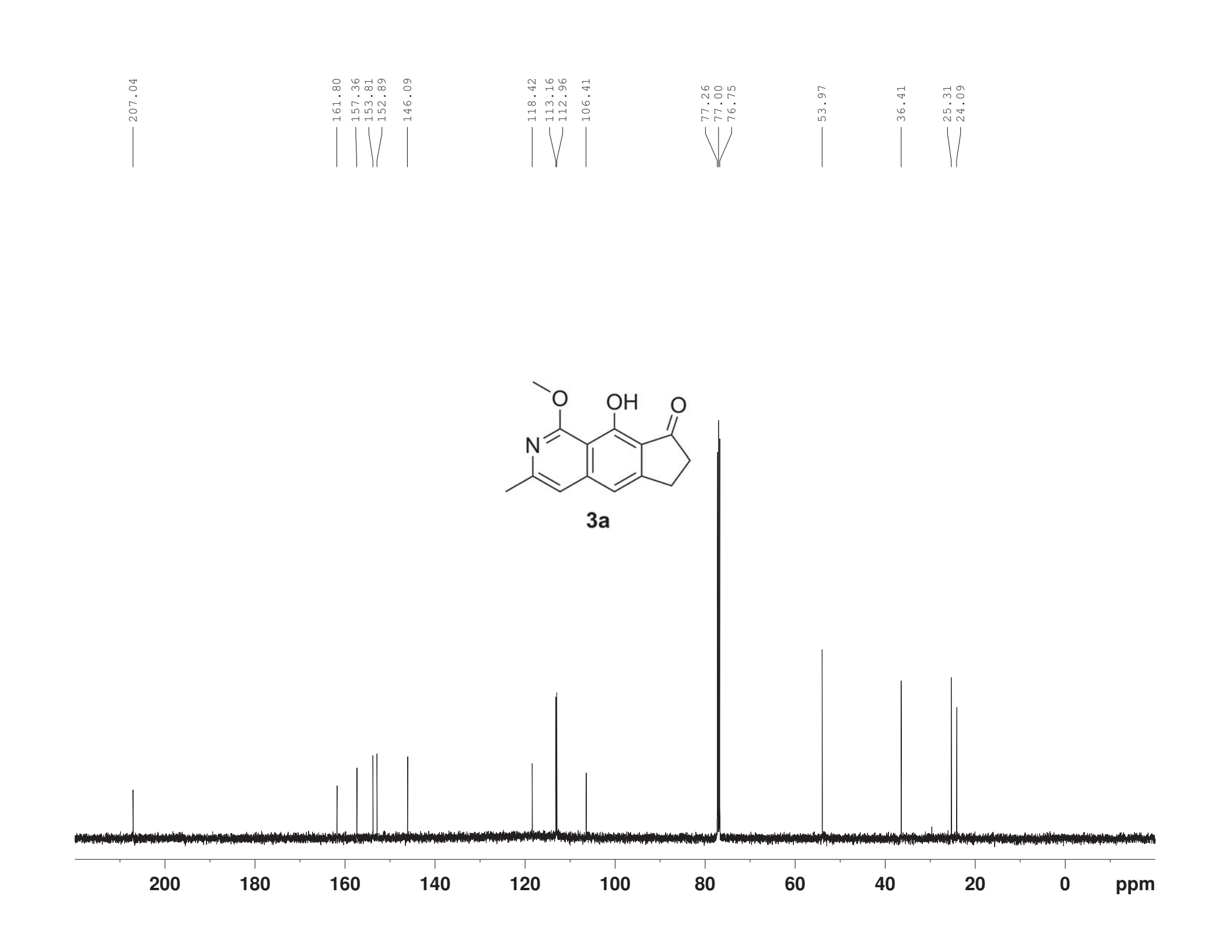
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36.41
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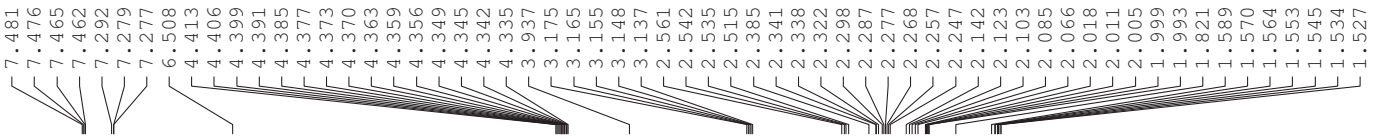
ppm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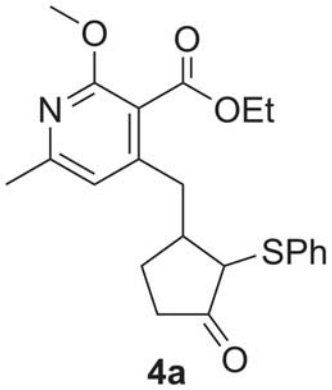
1.527


O
O
N
OEt
SPh
O

4a

10
9
8
7
6
5
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2
1
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ppm
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3.21
0.03
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2.98
0.14
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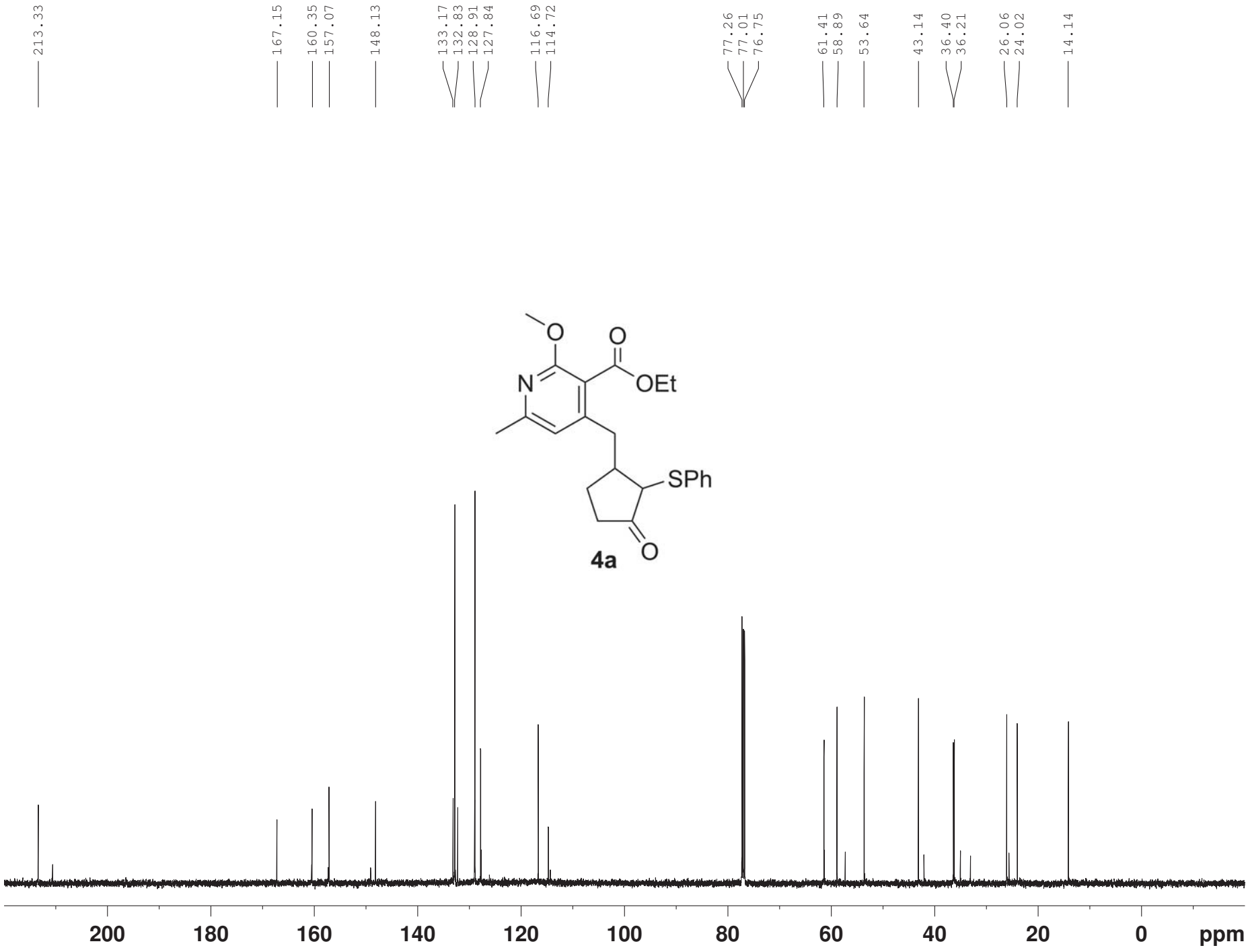
0.98
2.84
1.90
1.05
0.83
0.79
3.07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128.91
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116.69
114.72
77.26
77.01
76.75
61.41
58.89
53.64
43.14
36.40
36.21
26.06
24.02
14.14
O
O
N
OEt
SPh
O
4a
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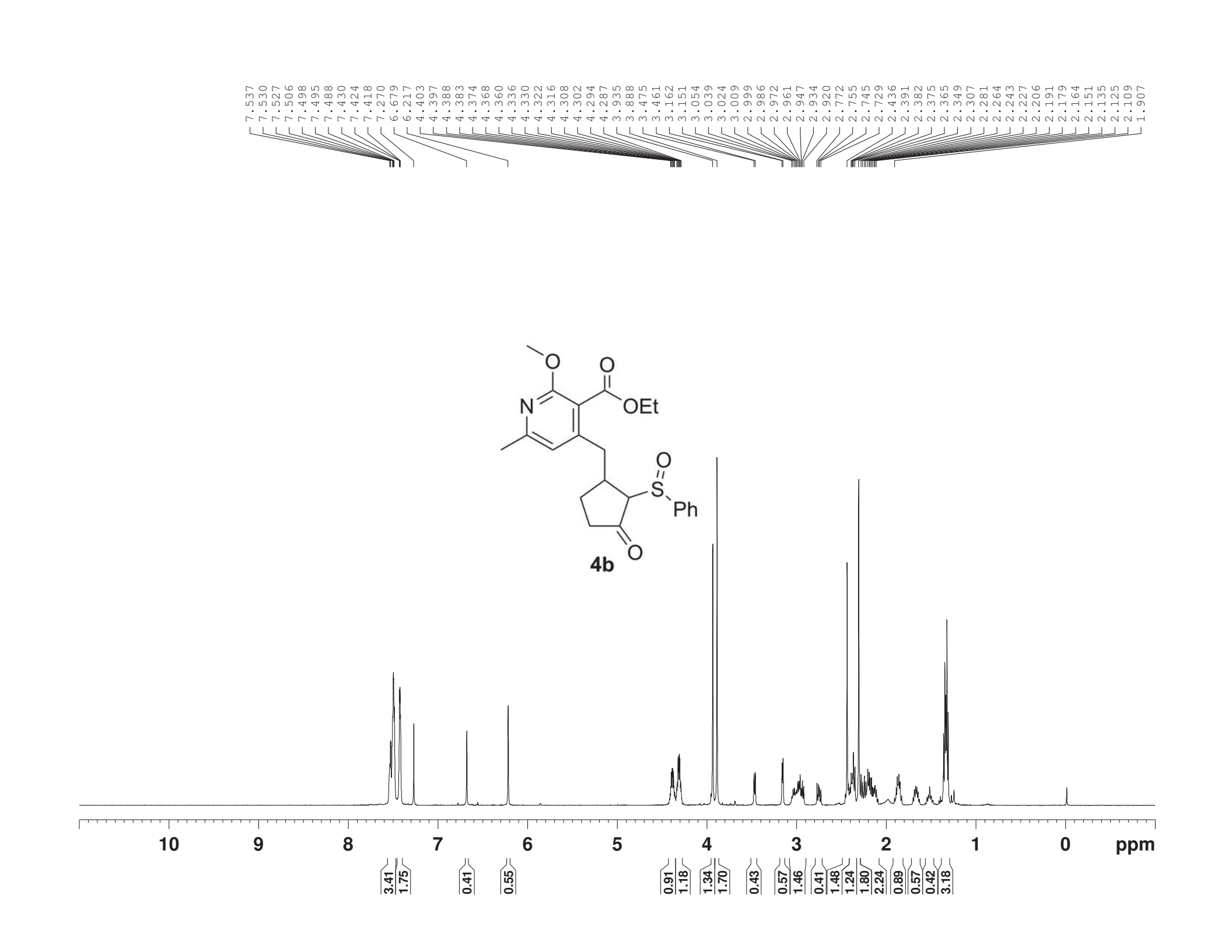
0
ppm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7.527
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7.430
7.424
7.418
7.270
6.679
6.217
4.403
4.397
4.388
4.383
4.374
4.368
4.360
4.336
4.330
4.322
4.316
4.308
4.302
4.294
4.287
3.935
3.888
3.475
3.461
3.162
3.151
3.054
3.039
3.024
3.009
2.999
2.986
2.972
2.961
2.947
2.934
2.920
2.772
2.755
2.745
2.729
2.436
2.391
2.382
2.375
2.365
2.349
2.307
2.281
2.264
2.243
2.227
2.206
2.191
2.179
2.164
2.151
2.135
2.125
2.109
1.907
O
O
N
OEt
O
S
Ph
O
4b
10
9
8
7
6
5
4
3
2
1
0
ppm
3.41
1.75
0.41
0.55
0.91
1.18
1.34
1.70
0.43
0.57
1.46
0.41
1.48
1.24
1.80
2.24
0.89
0.57
0.42
3.18

211.67
209.02

167.30
167.05
160.40
160.13
157.42
157.15
147.70
147.45
141.39
140.36
131.31
131.03
129.03
128.93
124.71
123.87
116.62
116.09
114.74
114.41

77.26
77.00
76.75
74.51
72.24
61.62
61.47
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27.42
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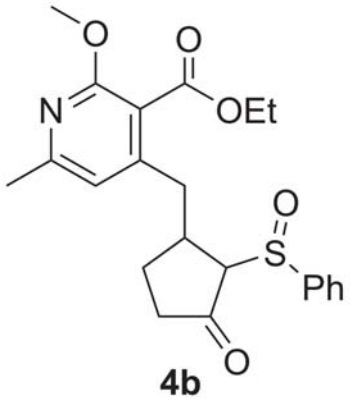
24.12
24.08
14.12



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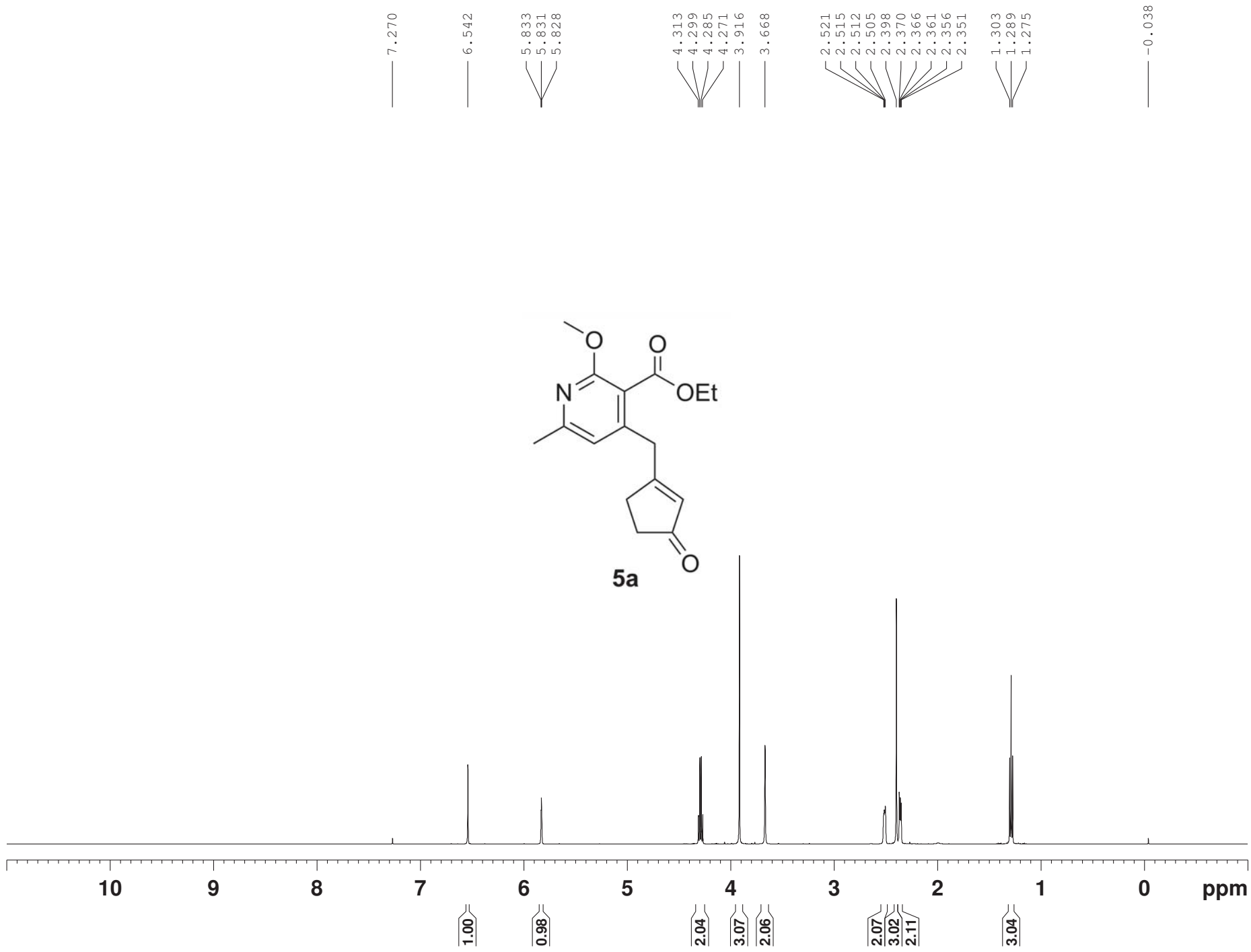
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5.828
4.313
4.299
4.285
4.271
3.916
3.668
2.521
2.515
2.512
2.505
2.398
2.370
2.366
2.361
2.356
2.351
1.303
1.289
1.275
-0.038
O
O
N
OEt
O
5a
10
9
8
7
6
5
4
3
2
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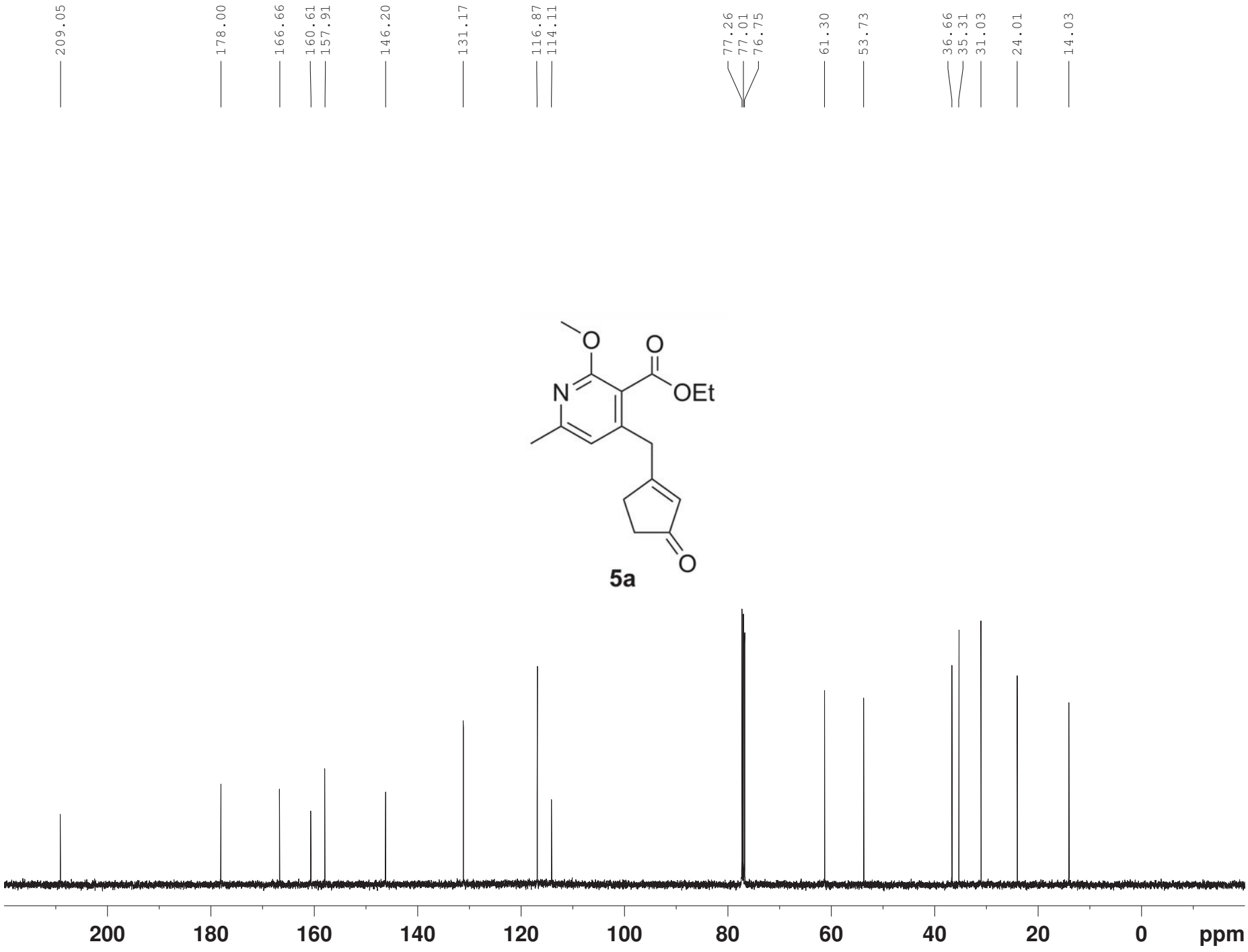
0
ppm
1.00
0.98
2.04
3.07
2.06
2.07
3.02
2.11
3.04


209.05
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160.61
157.91
146.20
131.17
116.87
114.11
77.26
77.01
76.75
61.30
53.73
36.66
35.31
31.03
24.01
14.03
O
O
N
OEt
O
5a
200
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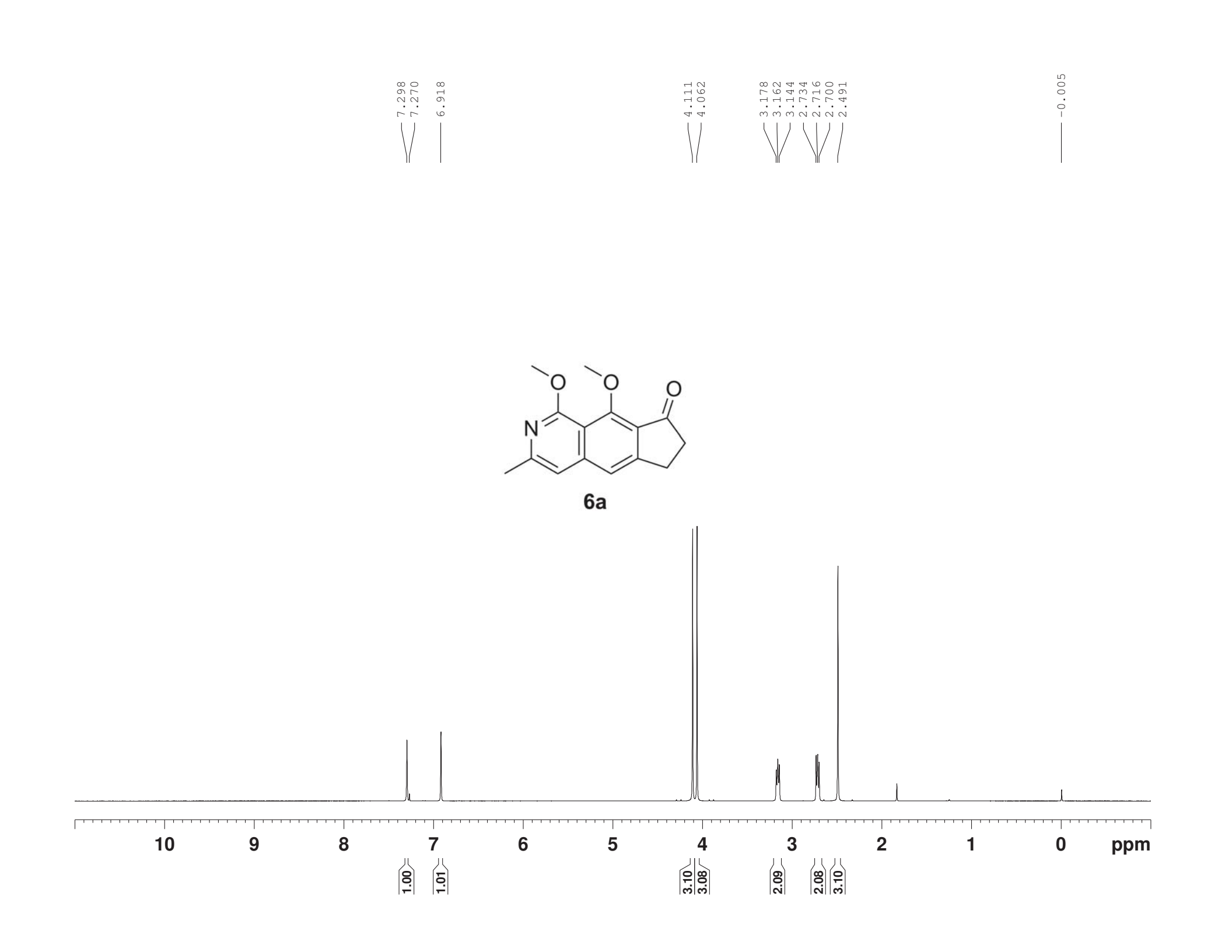
160
140
120
100
80
60
40
20
0
ppm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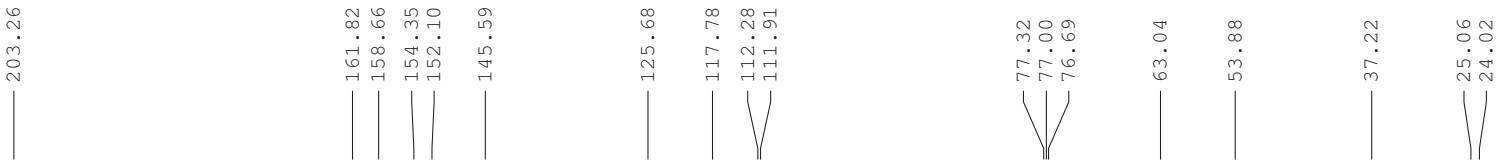
7.270
6.918
4.111
4.062
3.178
3.162
3.144
2.734
2.716
2.700
2.491
-0.005
O
O
O
N
6a
10
9
8
7
6
5
4
3
2
1
0
ppm
1.00
1.01
3.10
3.08
2.09
2.08
3.10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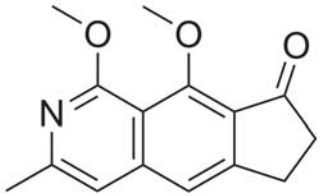
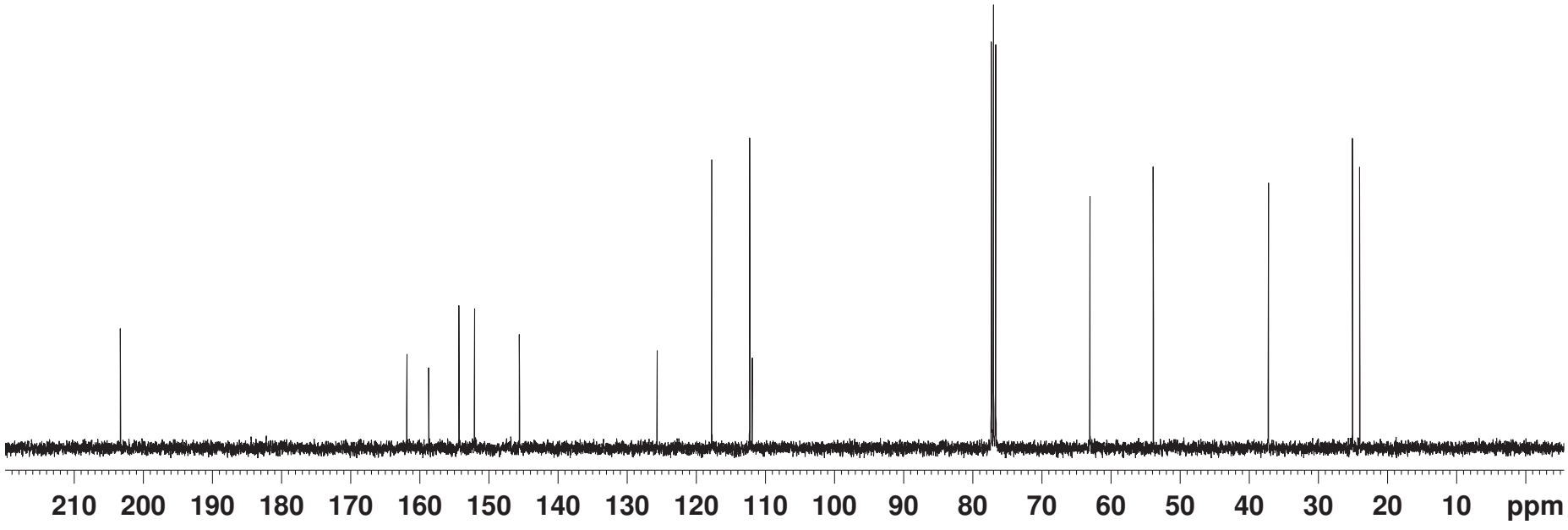
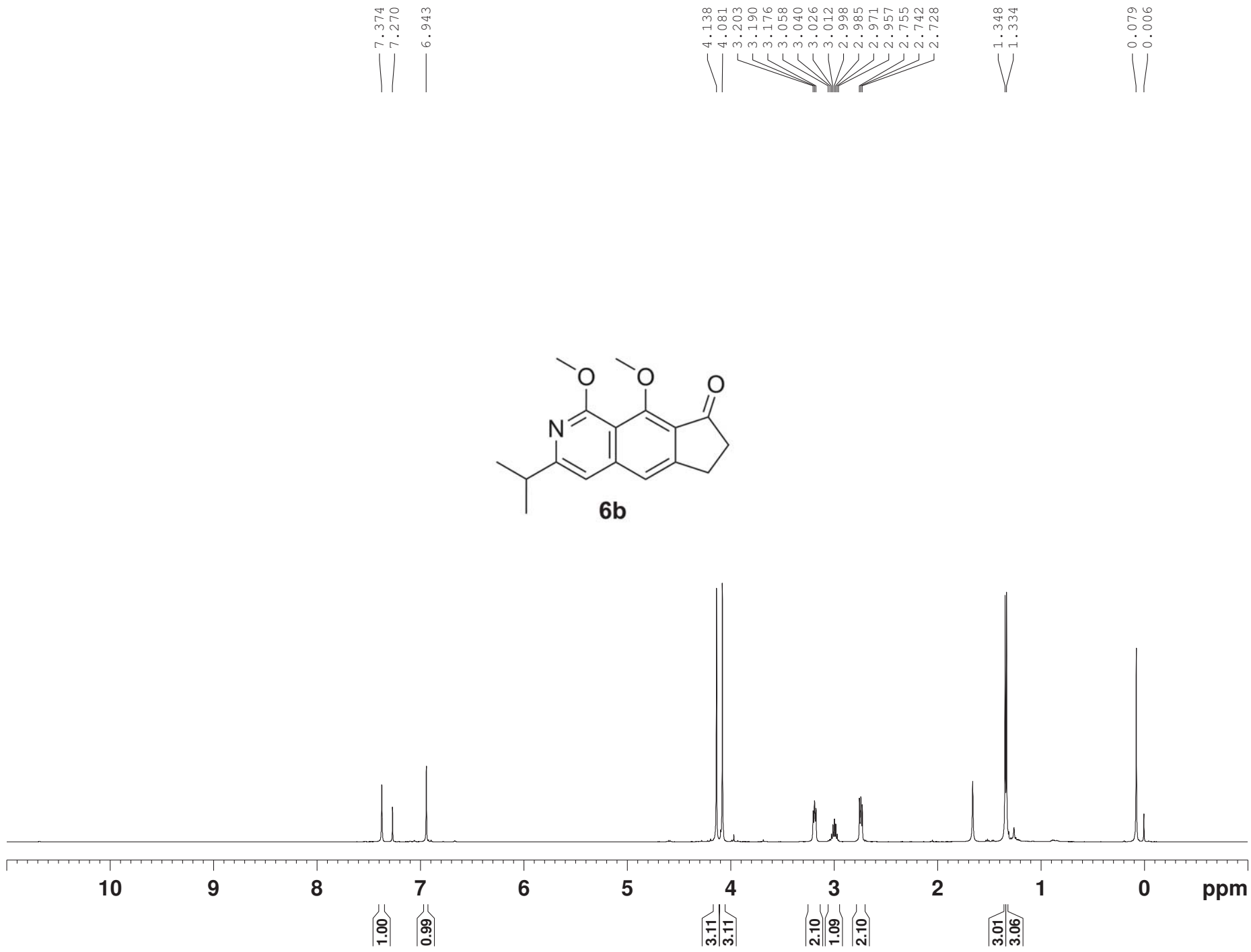
158.66
154.35
152.10
145.59
125.68
117.78
112.28
111.91
77.32
77.00
76.69
63.04
53.88
37.22
25.06
24.02


O
O
O
N

6a


210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm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7.270
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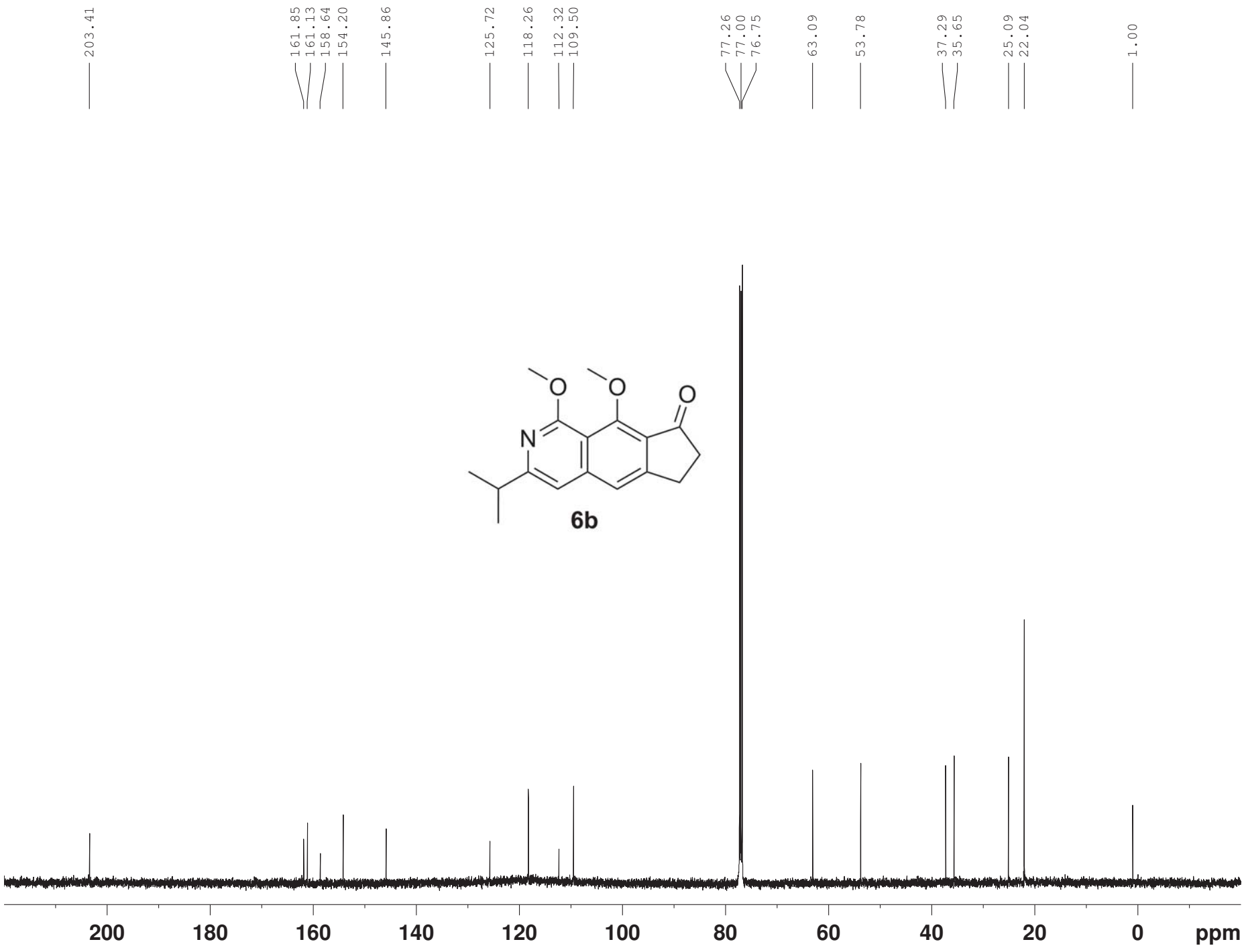
3.203
3.190
3.176
3.058
3.040
3.026
3.012
2.998
2.985
2.971
2.957
2.755
2.742
2.728
1.348
1.334
0.079
0.006
O
O
O
N
6b
10
9
8
7
6
5
4
3
2
1
0
ppm
1.00
0.99
3.11
3.11
2.10
1.09
2.10
3.01
3.06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125.72
118.26
112.32
109.50
77.26
77.00
76.75
63.09
53.78
37.29
35.65
25.09
22.04
1.00
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O
O
N
6b
200
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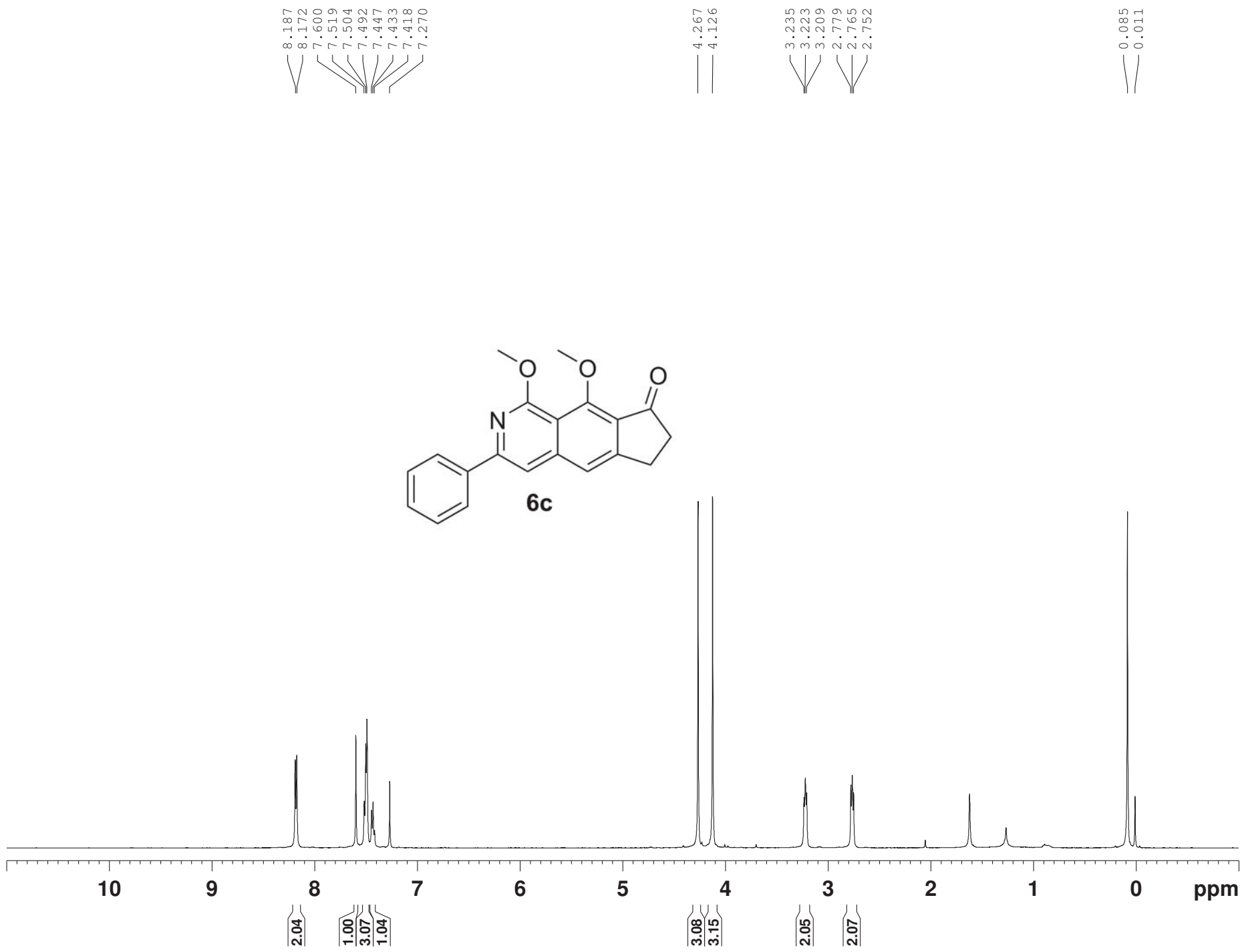
160
140
120
100
80
60
40
20
0
ppm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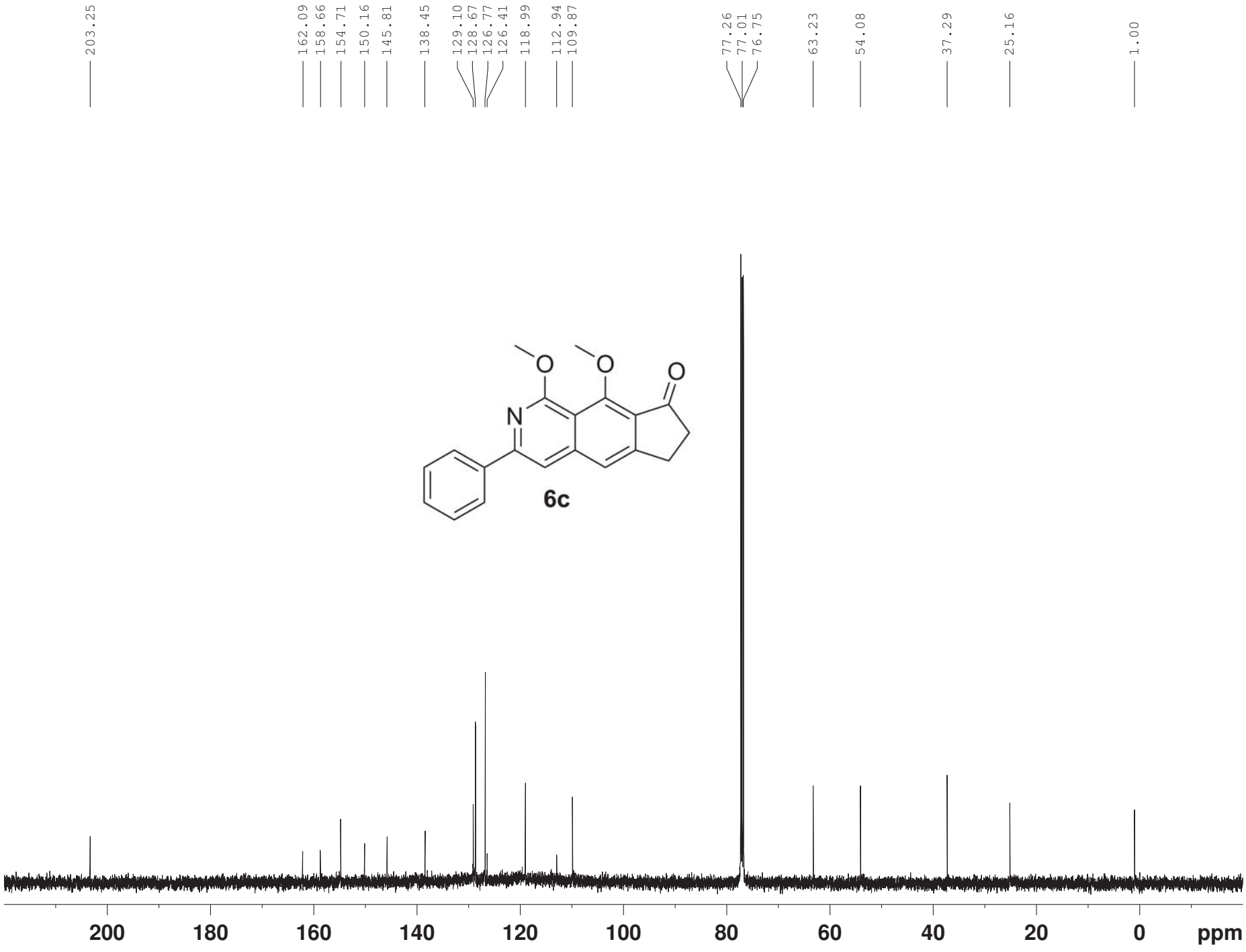
7.504
7.492
7.447
7.433
7.418
7.270
4.267
4.126
3.235
3.223
3.209
2.779
2.765
2.752
0.085
0.011
O
O
O
N
6c
10
9
8
7
6
5
4
3
2
1
0
ppm
2.04
1.00
3.07
1.04
3.08
3.15
2.05
2.07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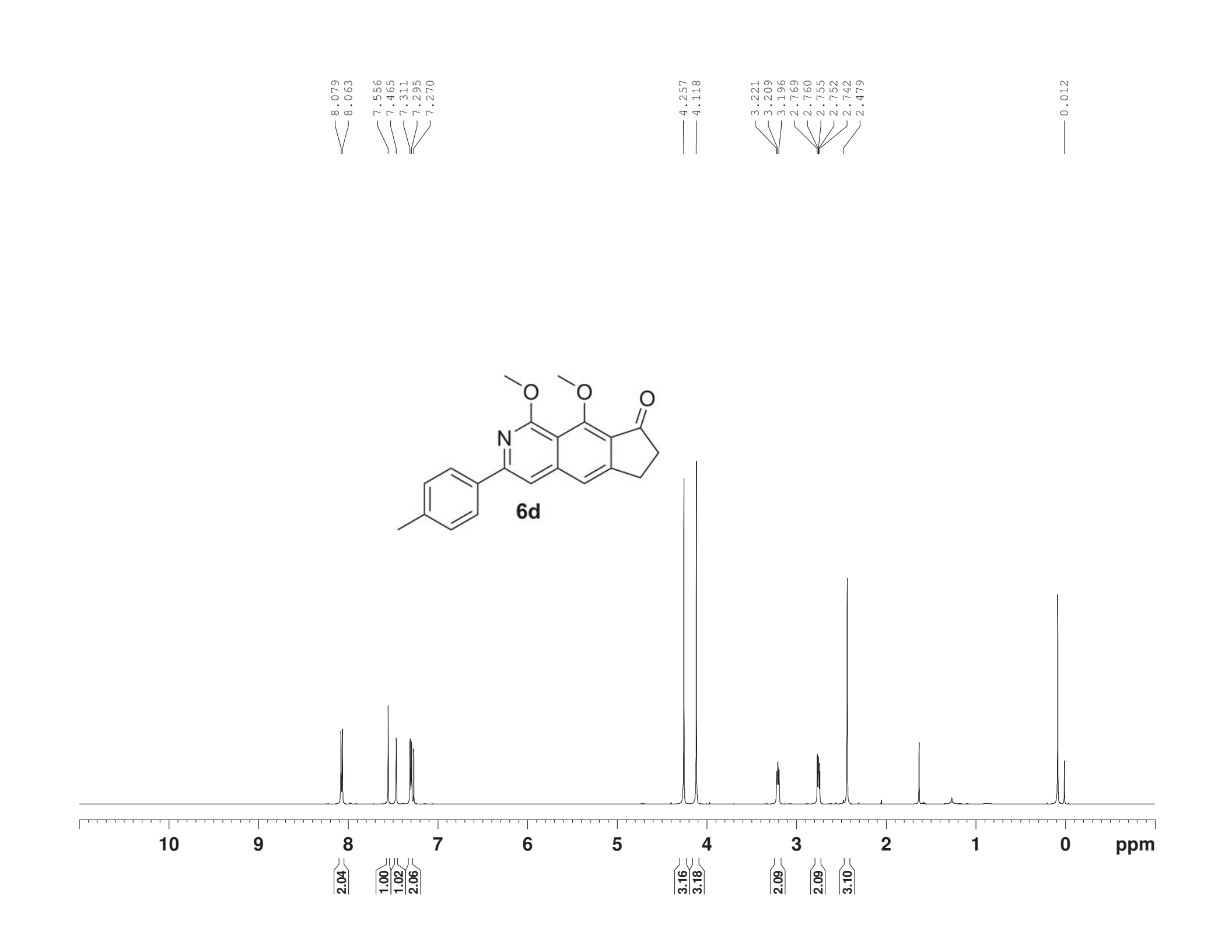
150.16
145.81
138.45
129.10
128.67
126.77
126.41
118.99
112.94
109.87
77.26
77.01
76.75
63.23
54.08
37.29
25.16
1.00
O
O
O
N
6c
200
180
160
140
120
100
80
60
40
20
0
ppm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7.465
7.311
7.295
7.270
4.257
4.118
3.221
3.209
3.196
2.769
2.760
2.755
2.752
2.742
2.479
0.012
O
O
O
N
6d
10
9
8
7
6
5
4
3
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ppm
2.04
1.00
1.02
2.06
3.16
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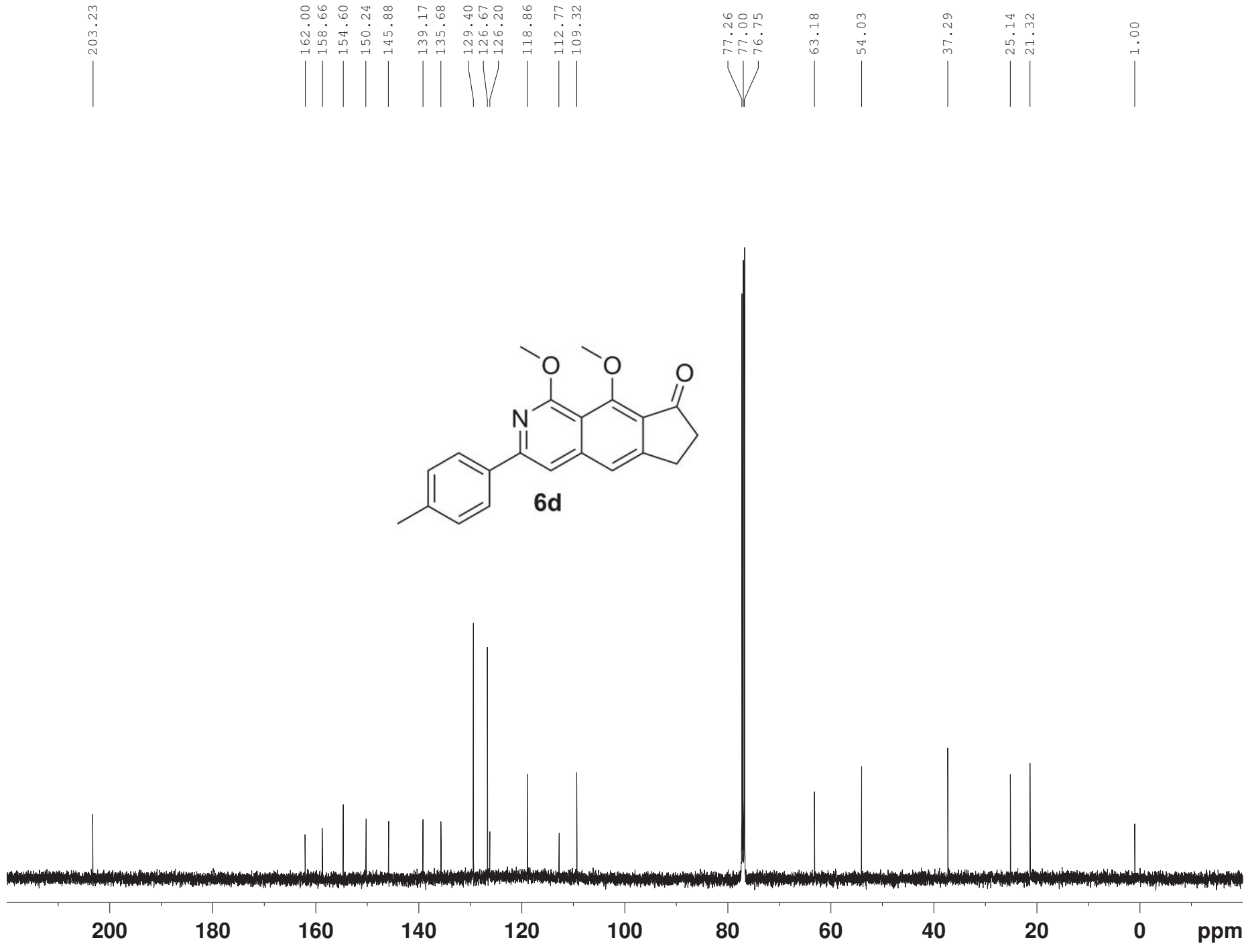
2.09
2.09
3.10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139.17
135.68
129.40
126.67
126.20
118.86
112.77
109.32
77.26
77.00
76.75
63.18
54.03
37.29
25.14
21.32
1.00
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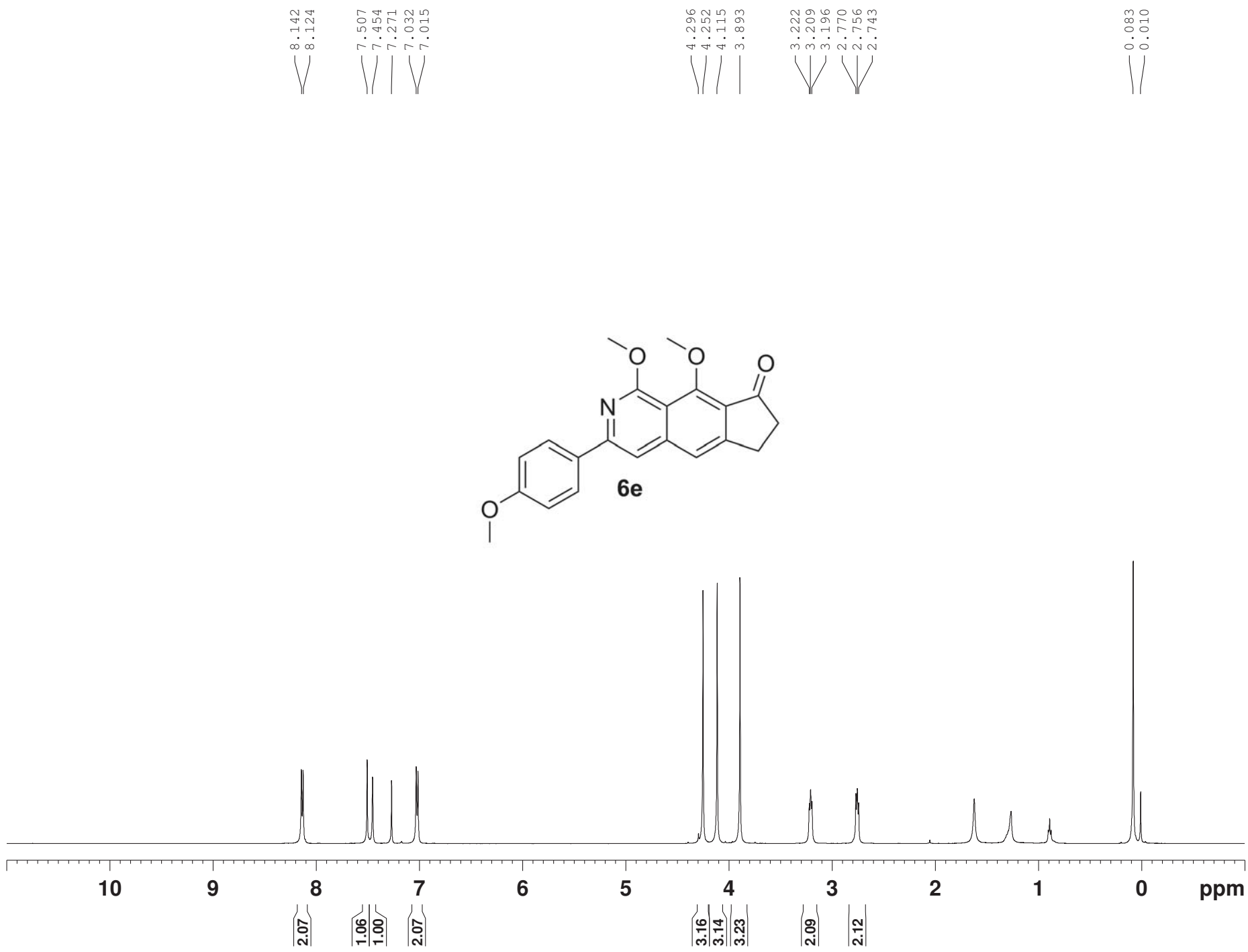
O
O
N
6d
200
180
160
140
120
100
80
60
40
20
0
ppm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4.115
3.893
3.222
3.209
3.196
2.770
2.756
2.743
0.083
0.010
O
O
O
N
O
6e
10
9
8
7
6
5
4
3
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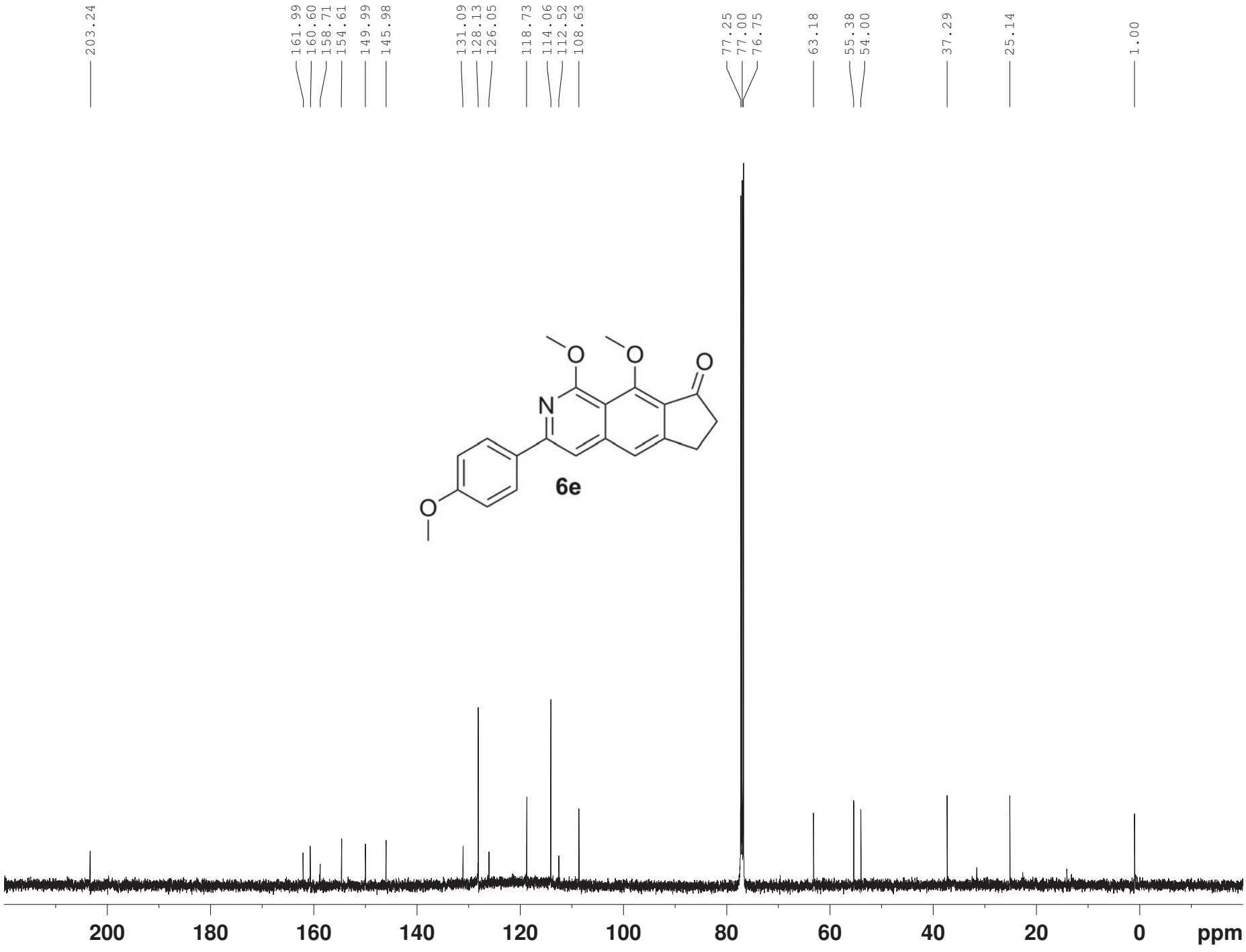
ppm
2.07
1.06
1.00
2.07
3.16
3.14
3.23
2.09
2.12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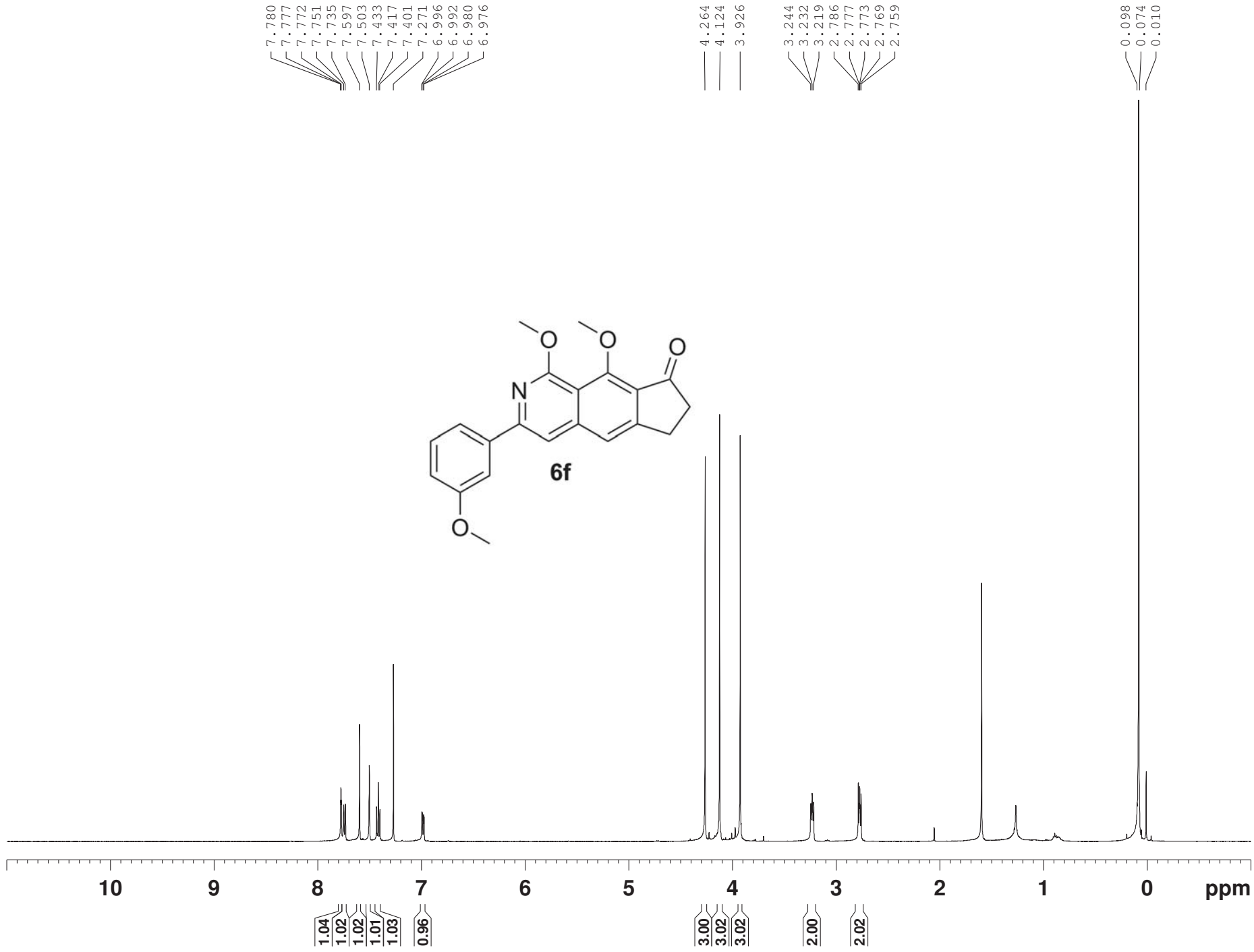
149.99
145.98
131.09
128.13
126.05
118.73
114.06
112.52
108.63
77.25
77.00
76.75
63.18
55.38
54.00
37.29
25.14
1.00
O
O
O
N
O
6e
200
180
160
140
120
100
80
60
40
20
0
ppm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7.433
7.417
7.401
7.271
6.996
6.992
6.980
6.976
4.264
4.124
3.926
3.244
3.232
3.219
2.786
2.777
2.773
2.769
2.759
0.098
0.074
0.010
O
O
O
N
O
6f
10
9
8
7
6
5
4
3
2
1
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ppm
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1.02
1.02
1.01
1.03
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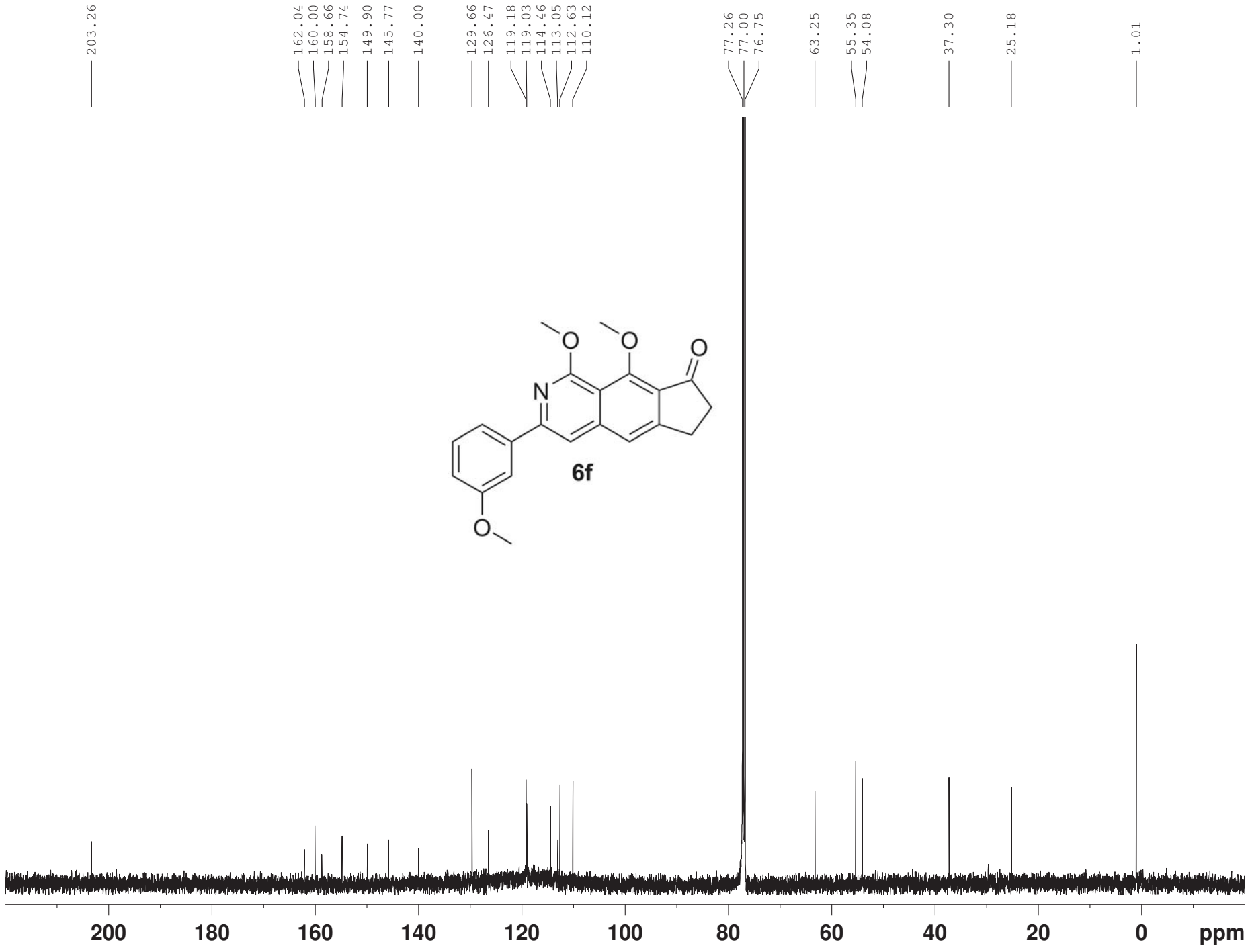
3.02
2.00
2.02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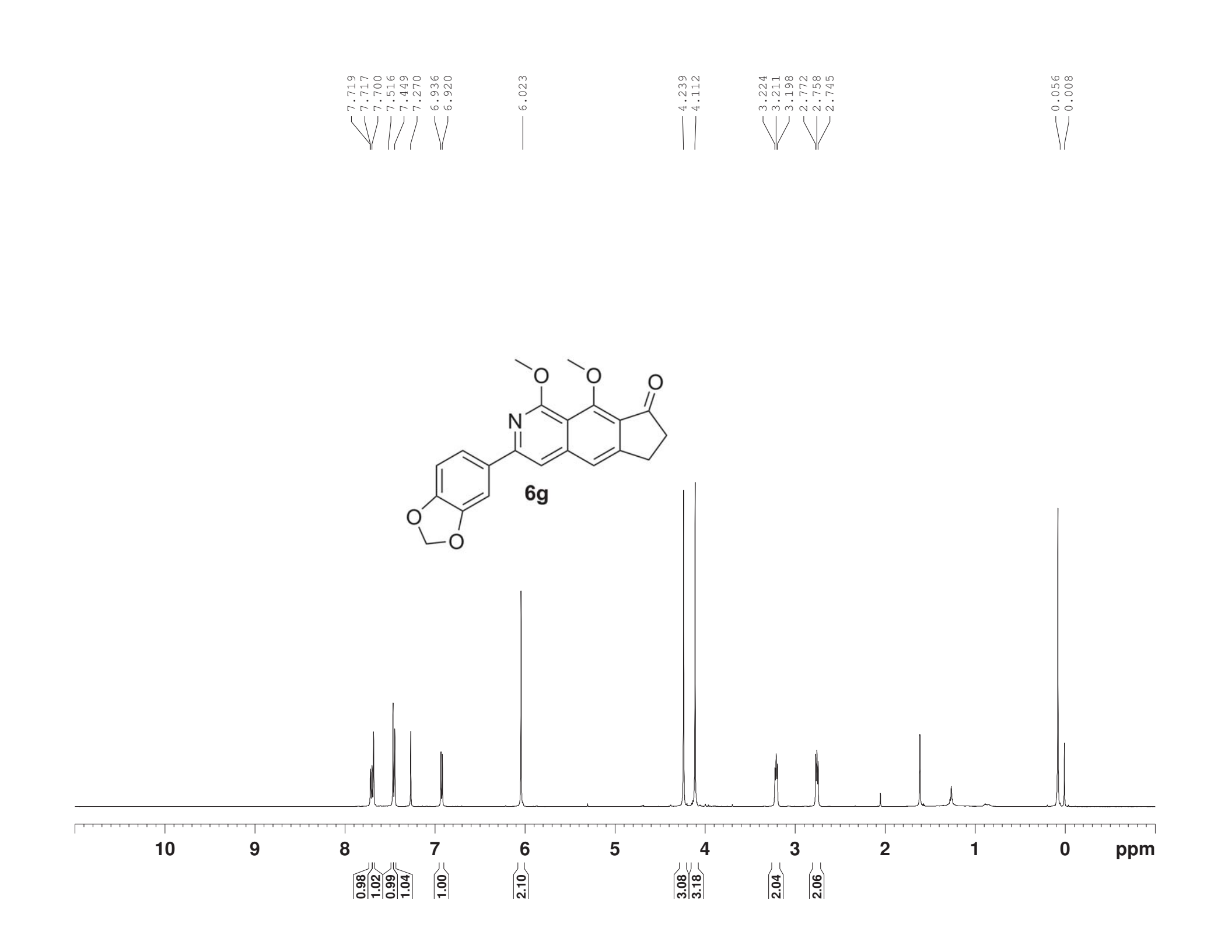
140.00
129.66
126.47
119.18
119.03
114.46
113.05
112.63
110.12
77.26
77.00
76.75
63.25
55.35
54.08
37.30
25.18
1.01
O
O
O
N
O
6f
200
180
160
140
120
100
80
60
40
20
0
ppm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3.211
3.198
2.772
2.758
2.745
0.056
0.008
O
O
O
N
O
O
6g
10
9
8
7
6
5
4
3
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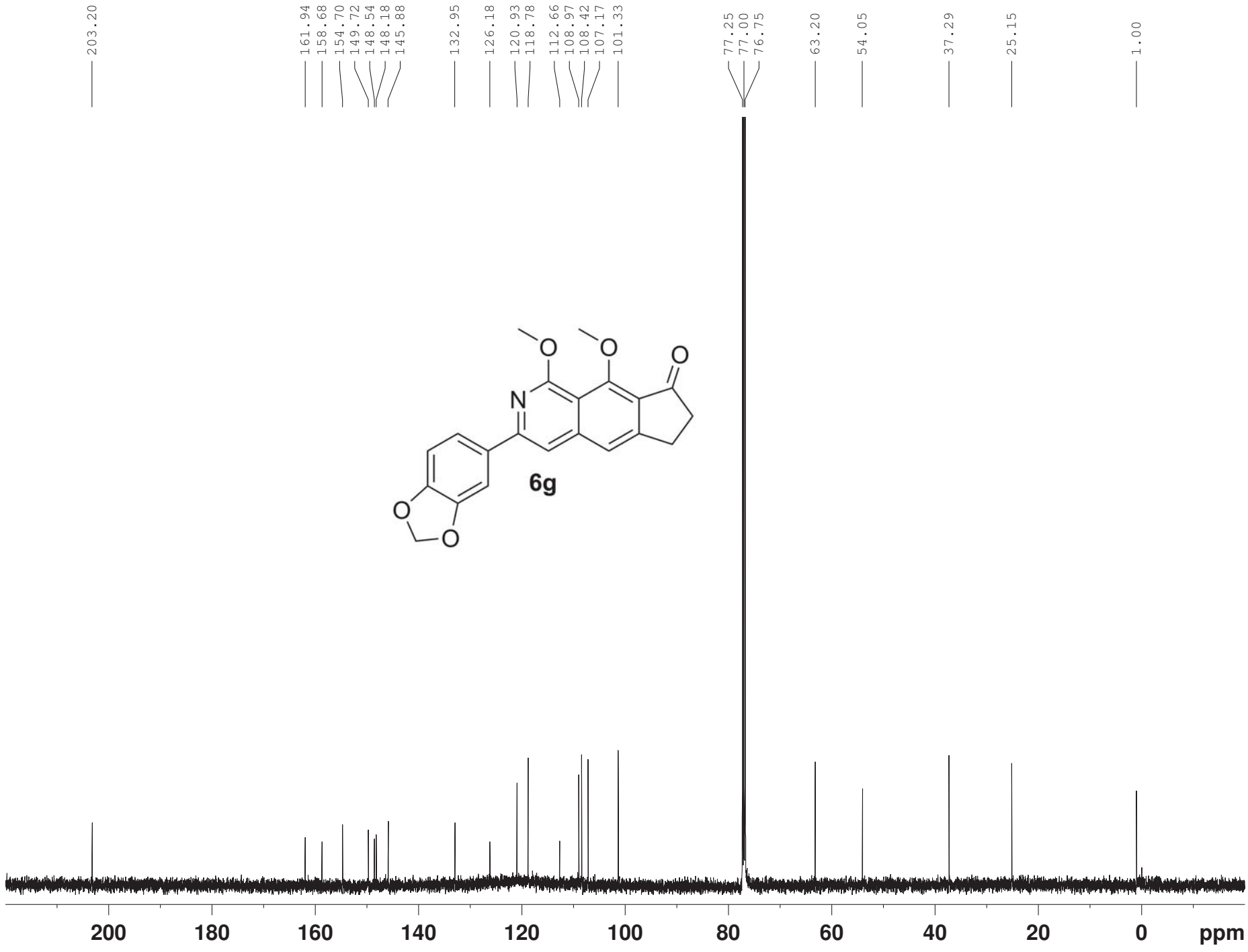
1.00
2.10
3.08
3.18
2.04
2.06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112.66
108.97
108.42
107.17
101.33
77.25
77.00
76.75
63.20
54.05
37.29
25.15
1.00
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O
O
N
O
O
6g
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120
100
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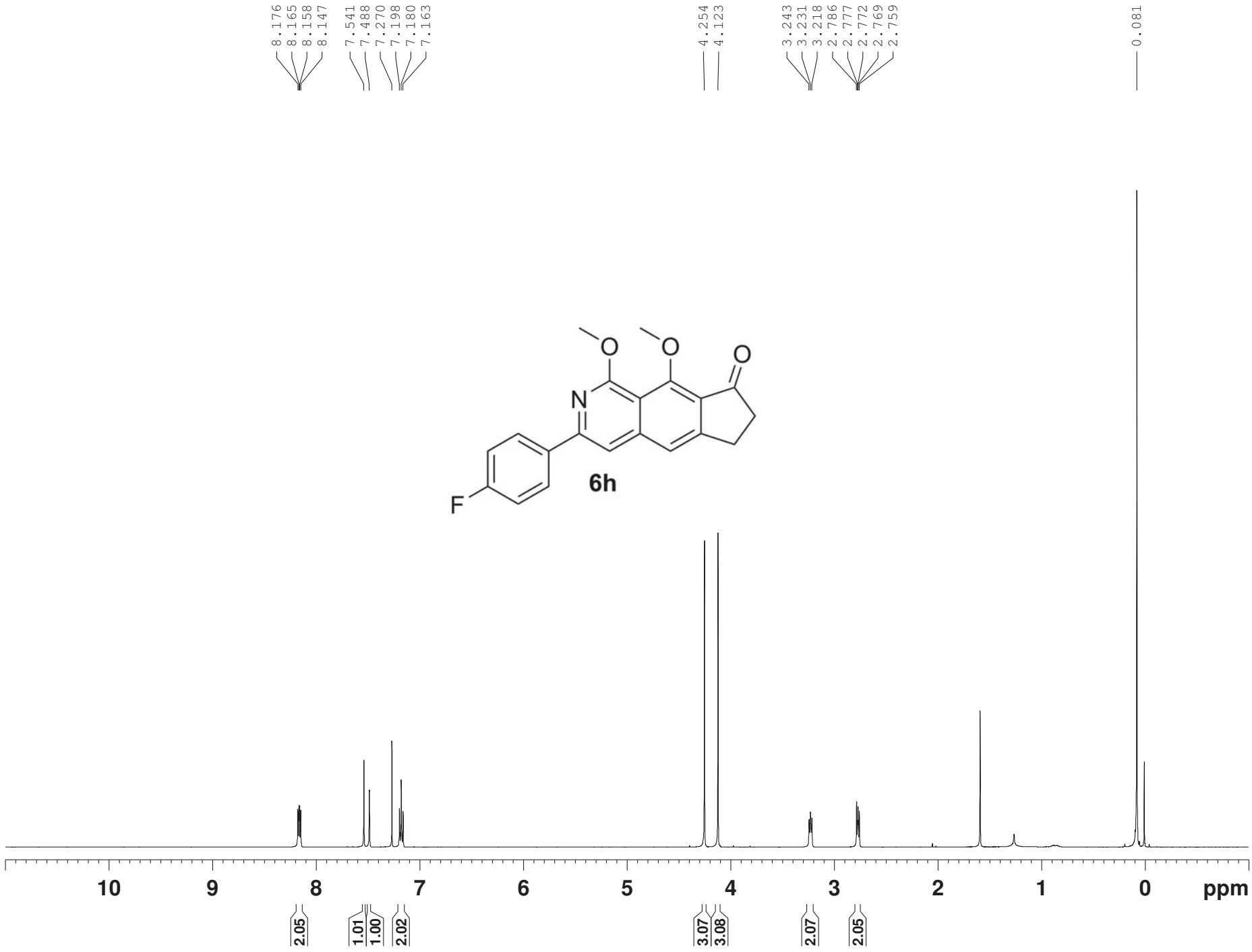
40
20
0
ppm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7.270
7.198
7.180
7.163
4.254
4.123
3.243
3.231
3.218
2.786
2.777
2.772
2.769
2.759
0.081
O
O
O
N
F
6h
10
9
8
7
6
5
4
3
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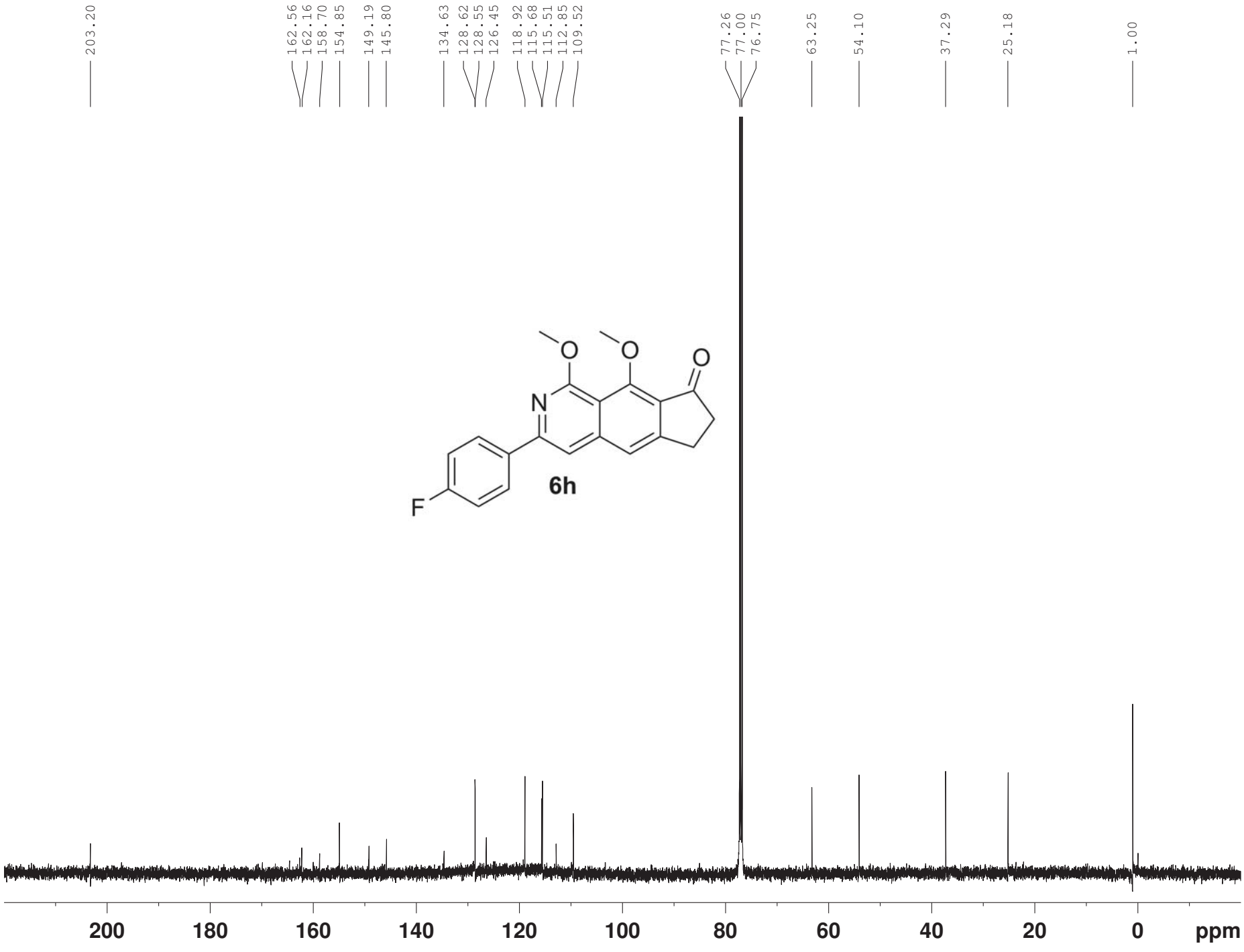
1
0
ppm
2.05
1.01
1.00
2.02
3.07
3.08
2.07
2.05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128.55
126.45
118.92
115.68
115.51
112.85
109.52
77.26
77.00
76.75
63.25
54.10
37.29
25.18
1.00
O
O
O
N
F
6h
200
180
160
140
120
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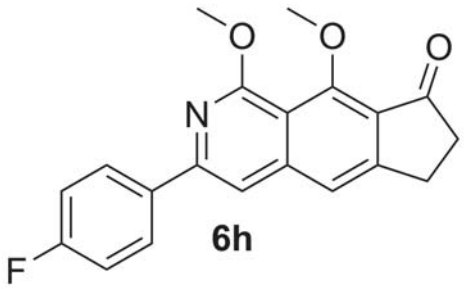
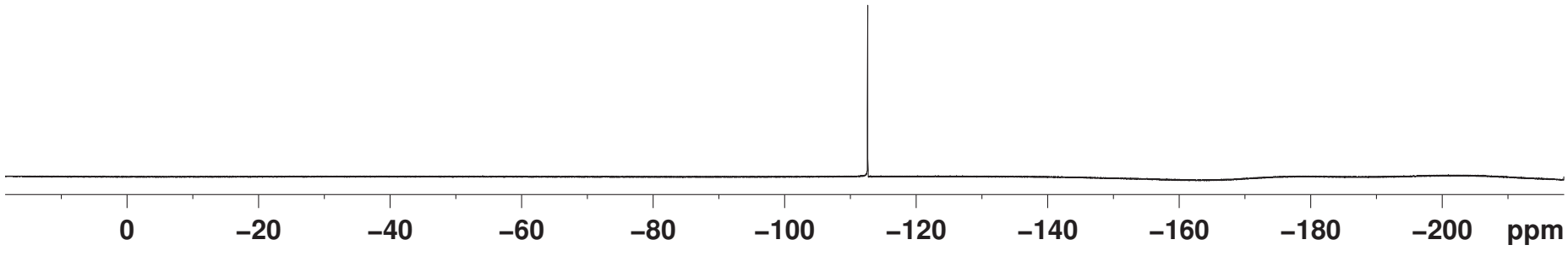
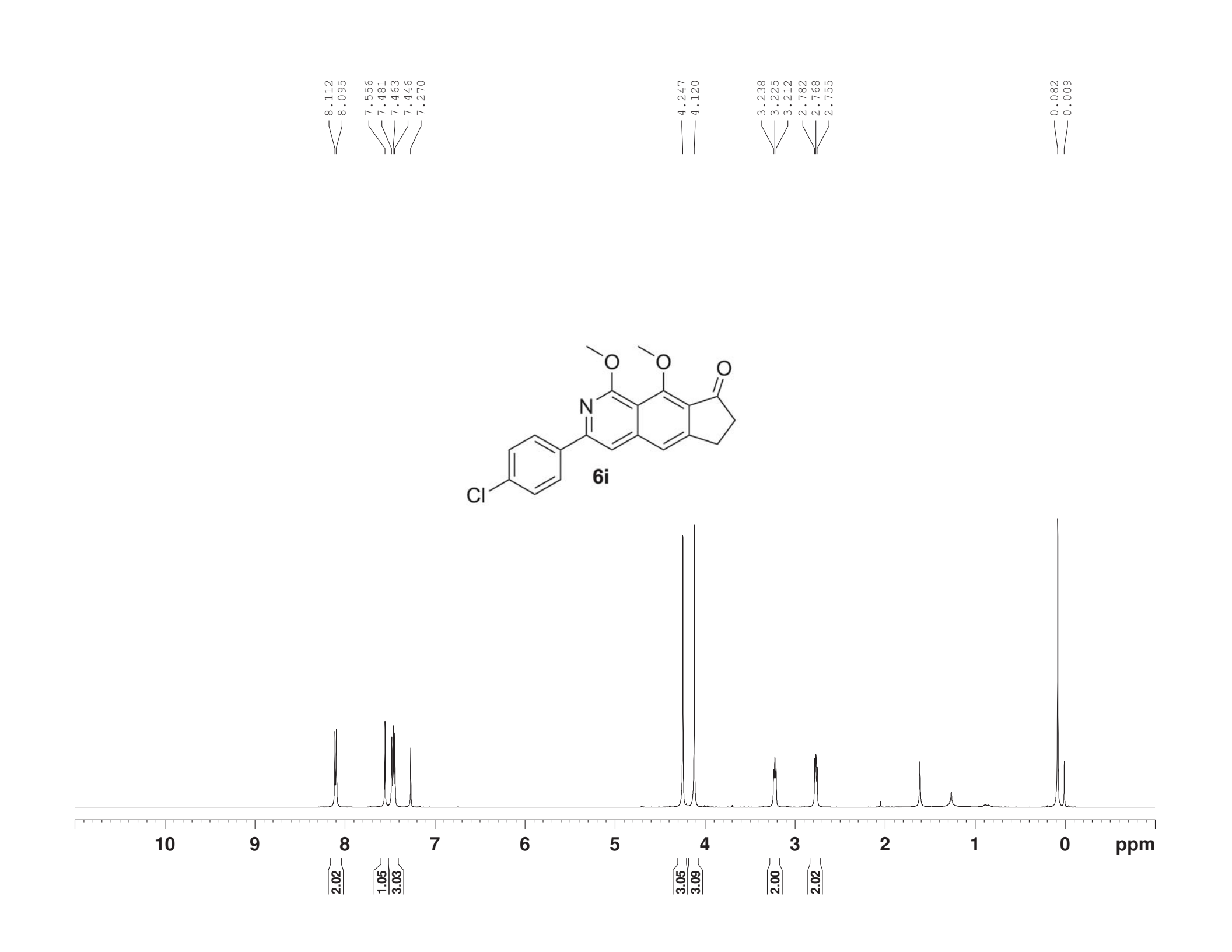
80
60
40
20
0
ppm

-112.64



6h

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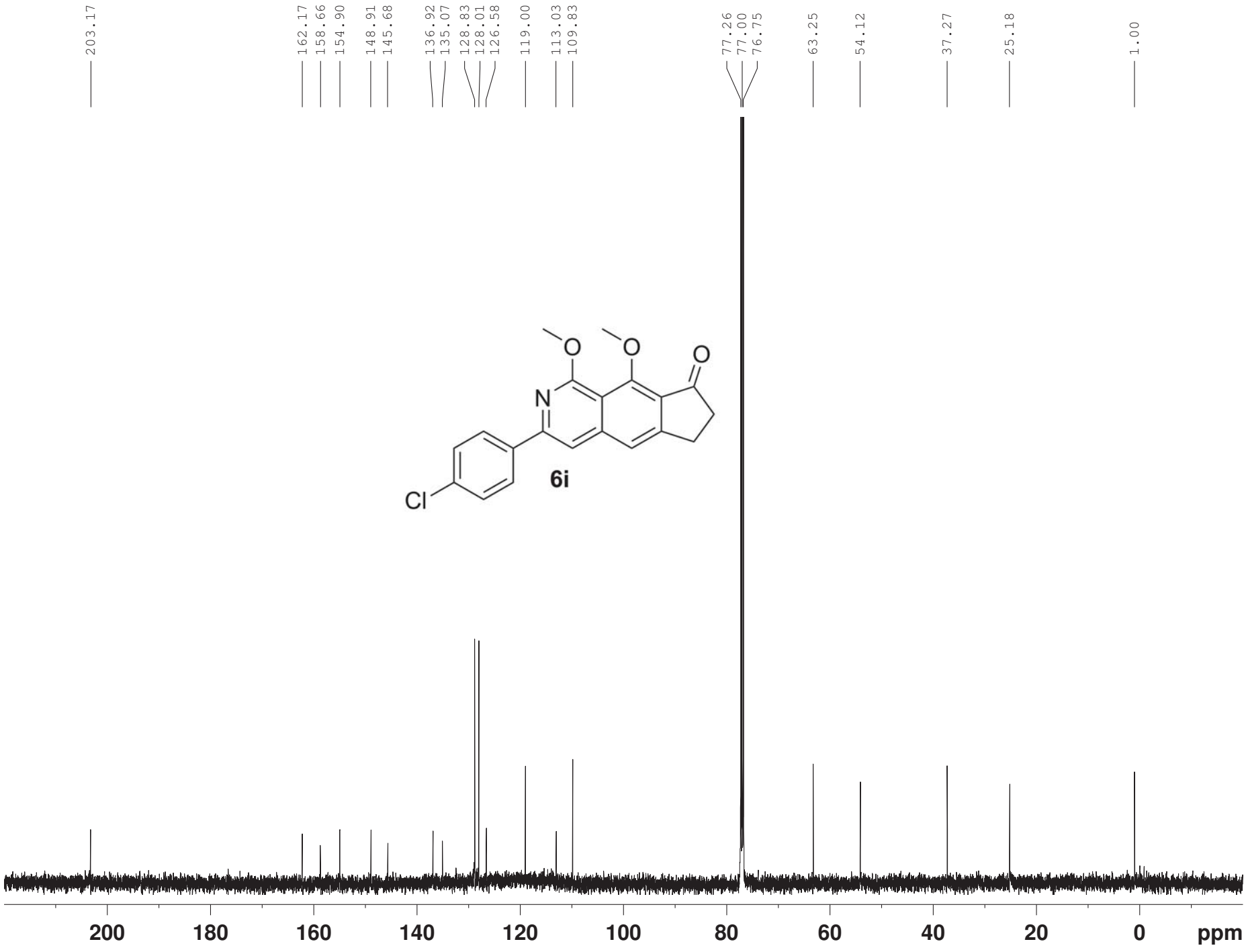
2.768
2.755
0.082
0.009
O
O
O
N
Cl
6i
10
9
8
7
6
5
4
3
2
1
0
ppm
2.02
1.05
3.03
3.05
3.09
2.00
2.02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109.83
77.26
77.00
76.75
63.25
54.12
37.27
25.18
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Cl
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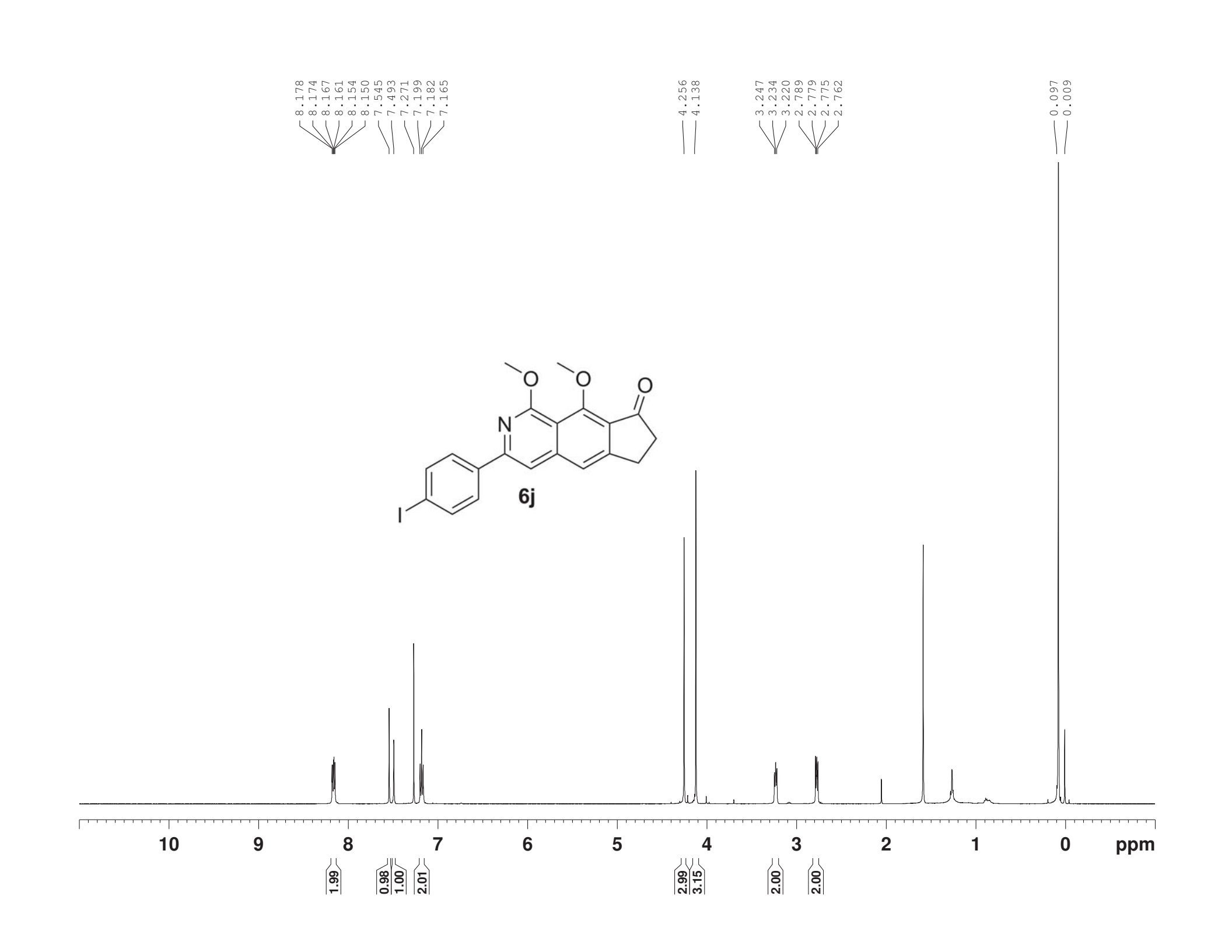
40
20
0
ppm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7.165
4.256
4.138
3.247
3.234
3.220
2.789
2.779
2.775
2.762
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0.009
O
O
O
N
I
6j
10
9
8
7
6
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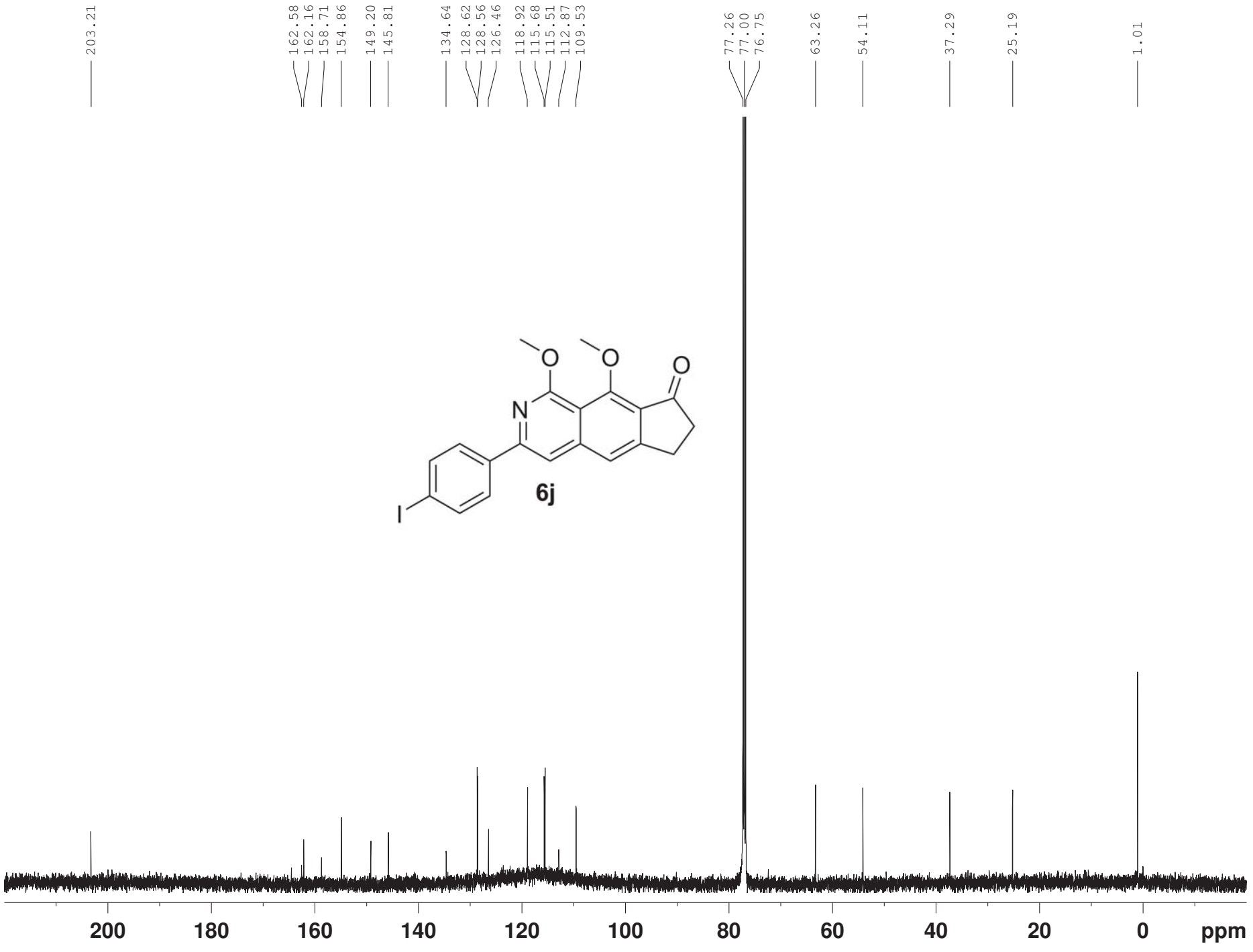
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115.51
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109.53
77.26
77.00
76.75
63.26
54.11
37.29
25.19
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O
N
I
6j
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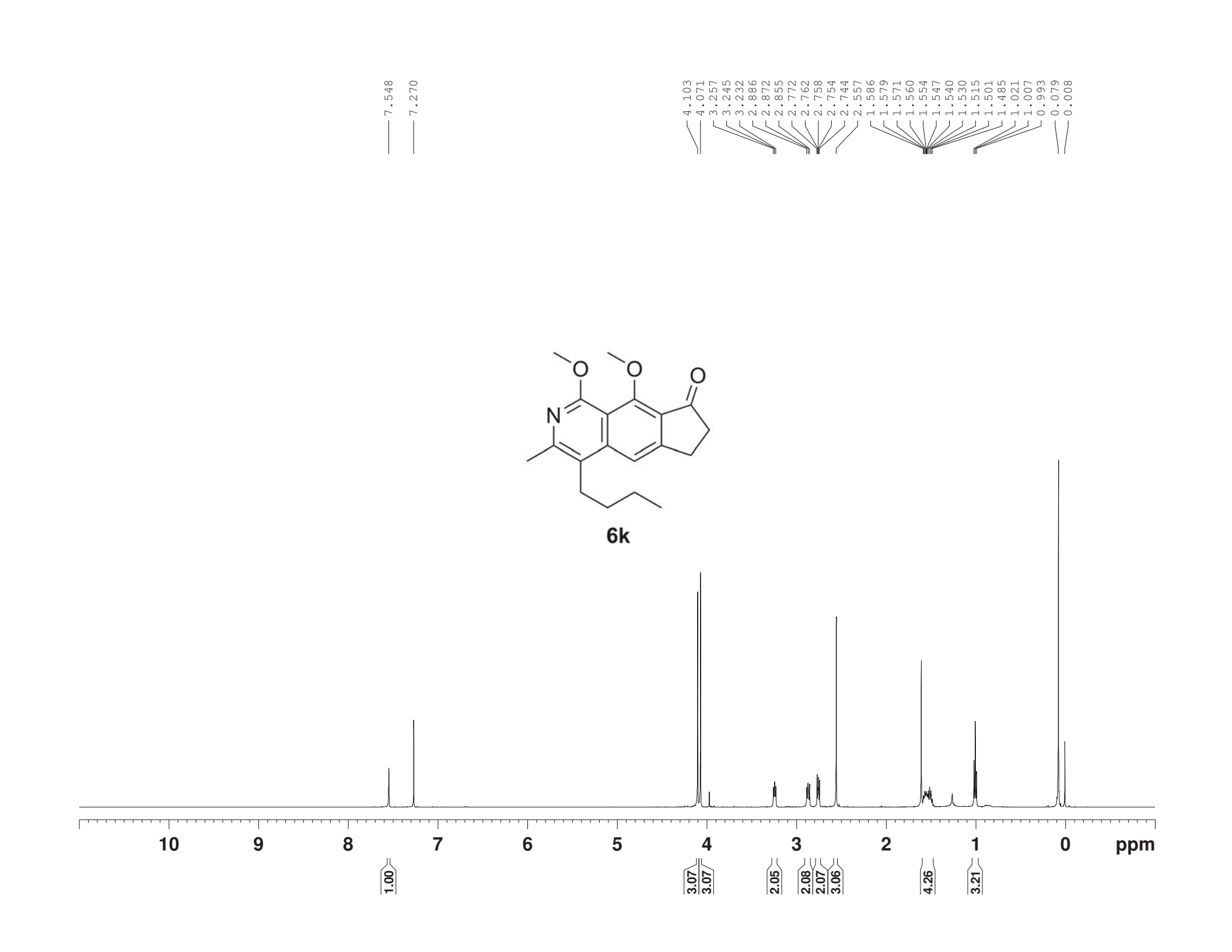
ppm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3.245
3.232
2.886
2.872
2.855
2.772
2.762
2.758
2.754
2.744
2.557
1.586
1.579
1.571
1.560
1.554
1.547
1.540
1.530
1.515
1.501
1.485
1.021
1.007
0.993
0.079
0.008
O
O
O
N
6k
10
9
8
7
6
5
4
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ppm
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2.08
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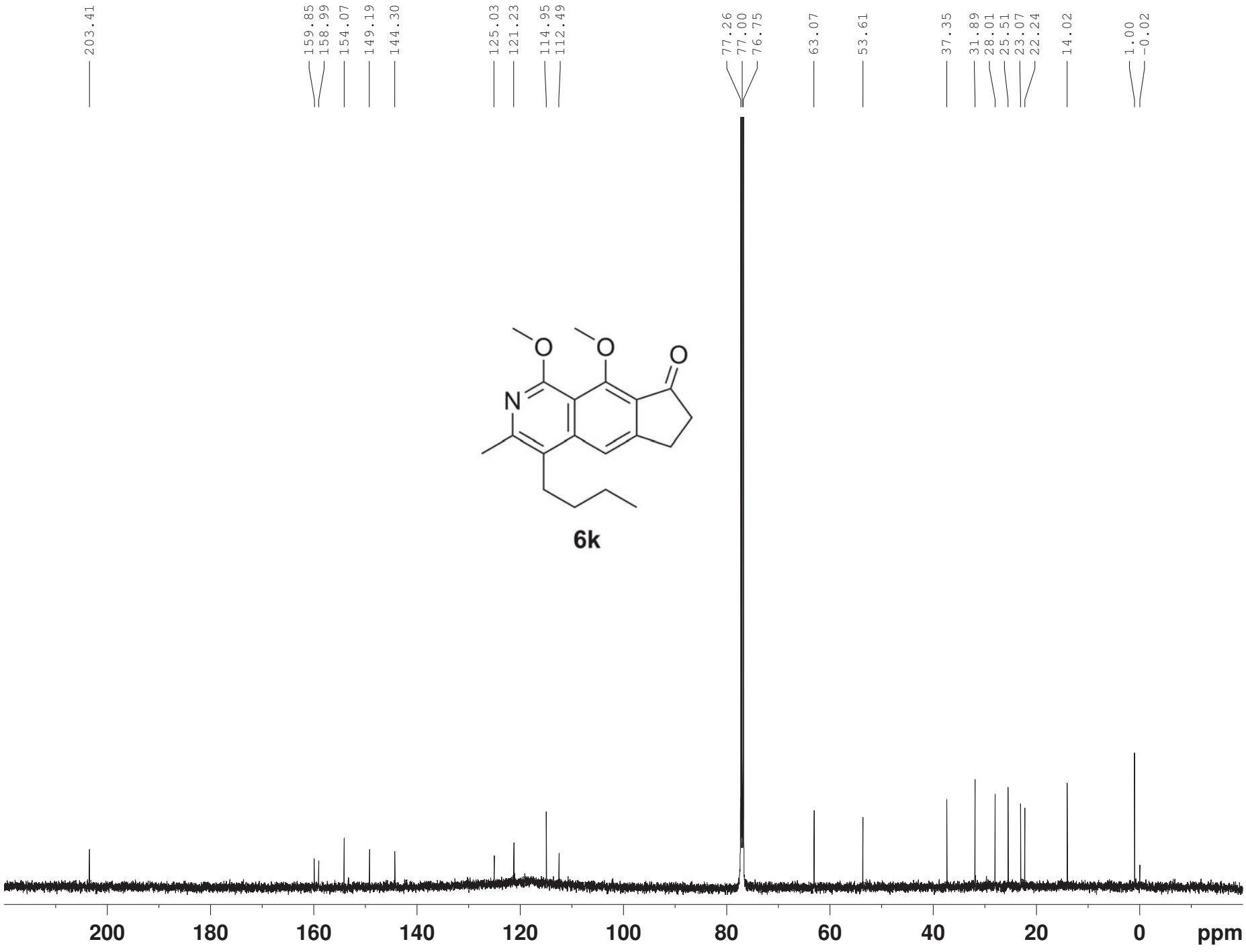
3.21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77.26
77.00
76.75
63.07
53.61
37.35
31.89
28.01
25.51
23.07
22.24
14.02
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O
O
N
6k
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120
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0
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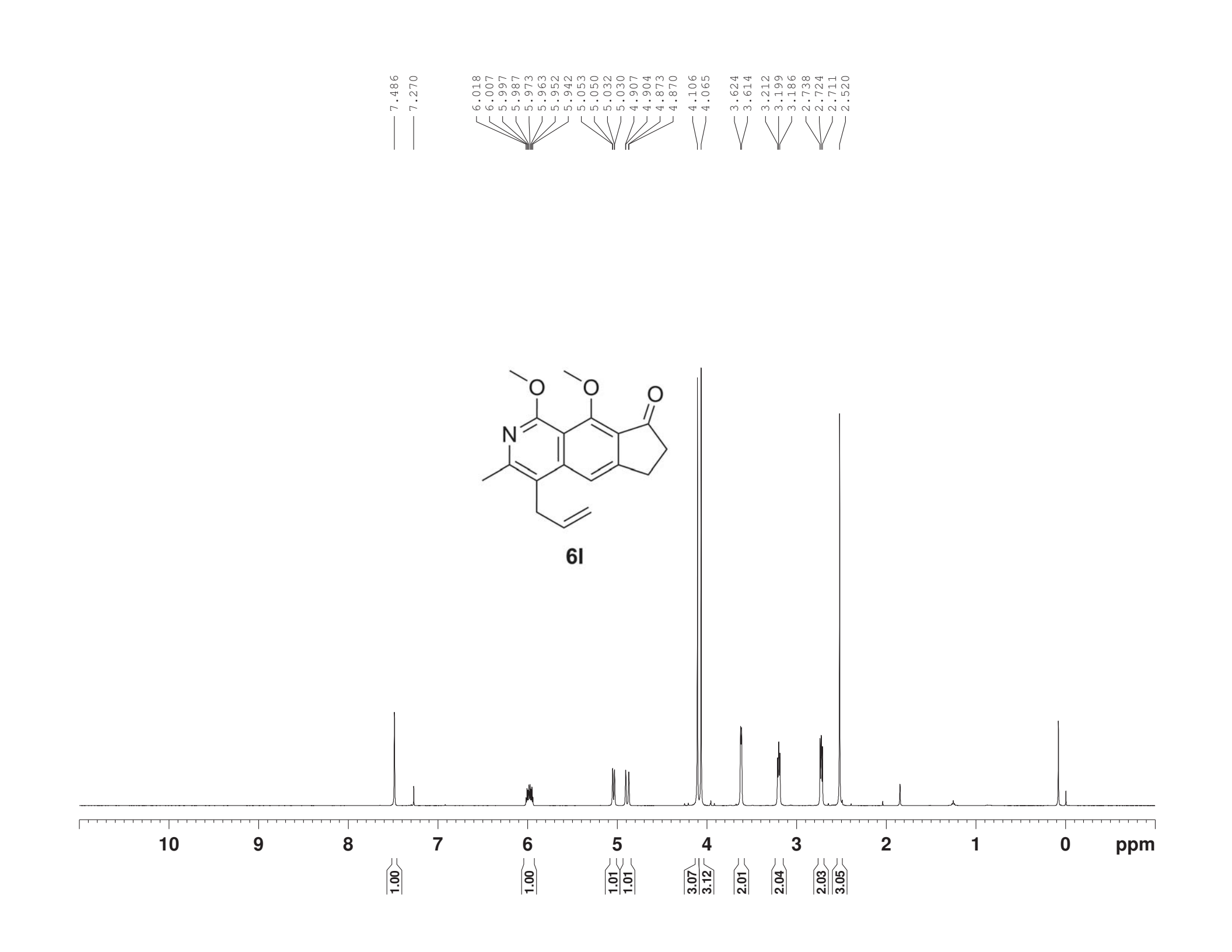
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5.942
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5.050
5.032
5.030
4.907
4.904
4.873
4.870
4.106
4.065
3.624
3.614
3.212
3.199
3.186
2.738
2.724
2.711
2.520
O
O
O
N
6l
10
9
8
7
6
5
4
3
2
1
0
ppm
1.00
1.00
1.01
1.01
3.07
3.12
2.01
2.04
2.03
3.05

203.30
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158.85
154.25
150.18
144.34
135.14
125.08
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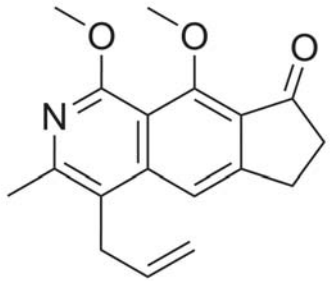

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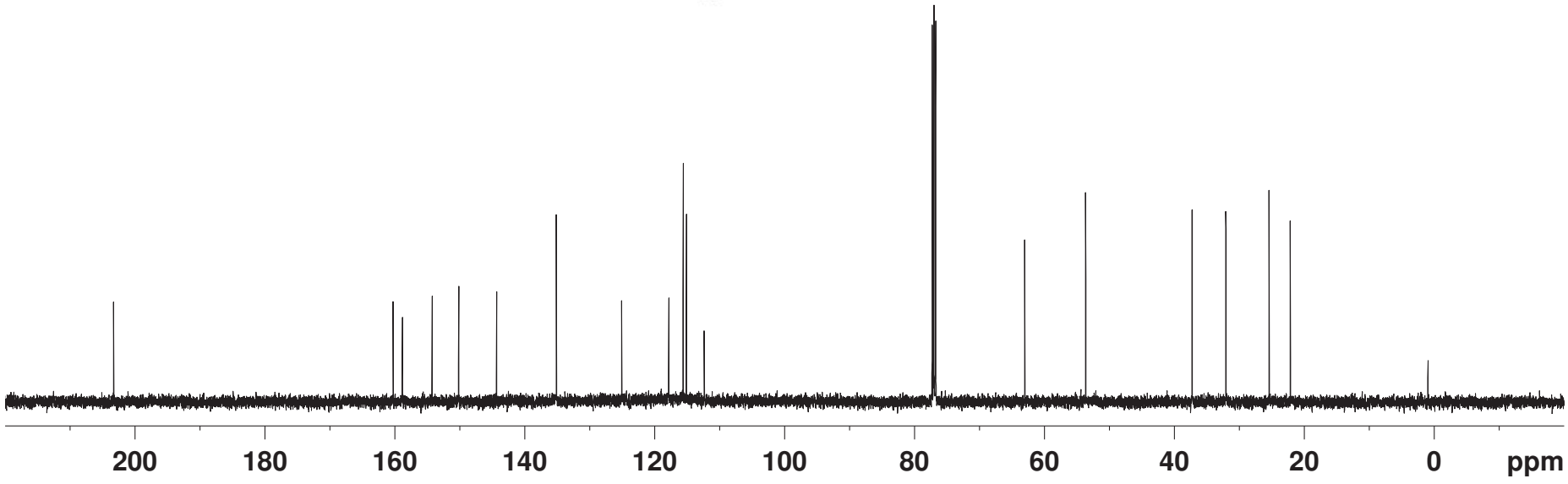

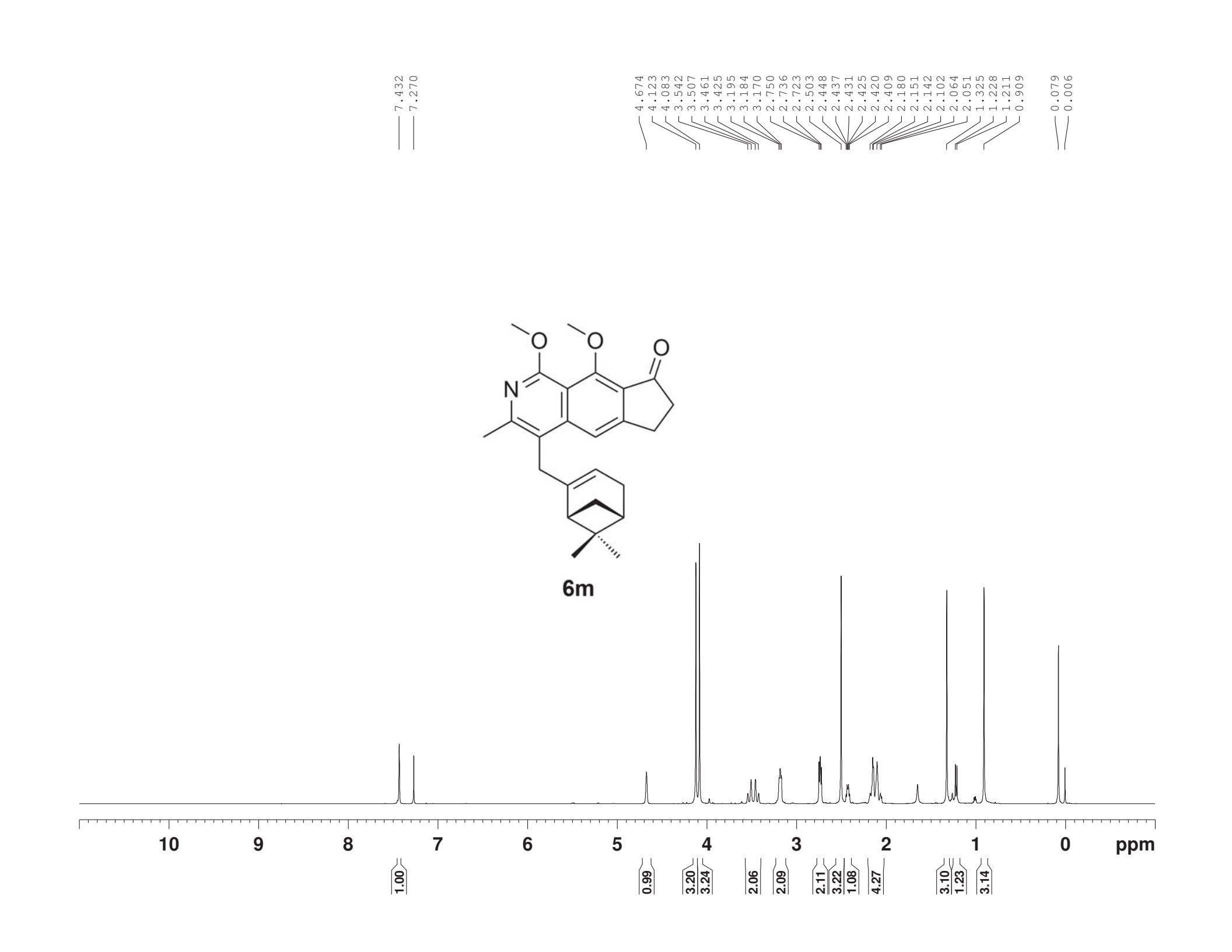
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3.461
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3.195
3.184
3.170
2.750
2.736
2.723
2.503
2.448
2.437
2.431
2.425
2.420
2.409
2.180
2.151
2.142
2.102
2.064
2.051
1.325
1.228
1.211
0.909
0.079
0.006
O
O
O
N
6m
10
9
8
7
6
5
4
3
2
1
0
ppm
1.00
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3.24
2.06
2.09
2.11
3.22
1.08
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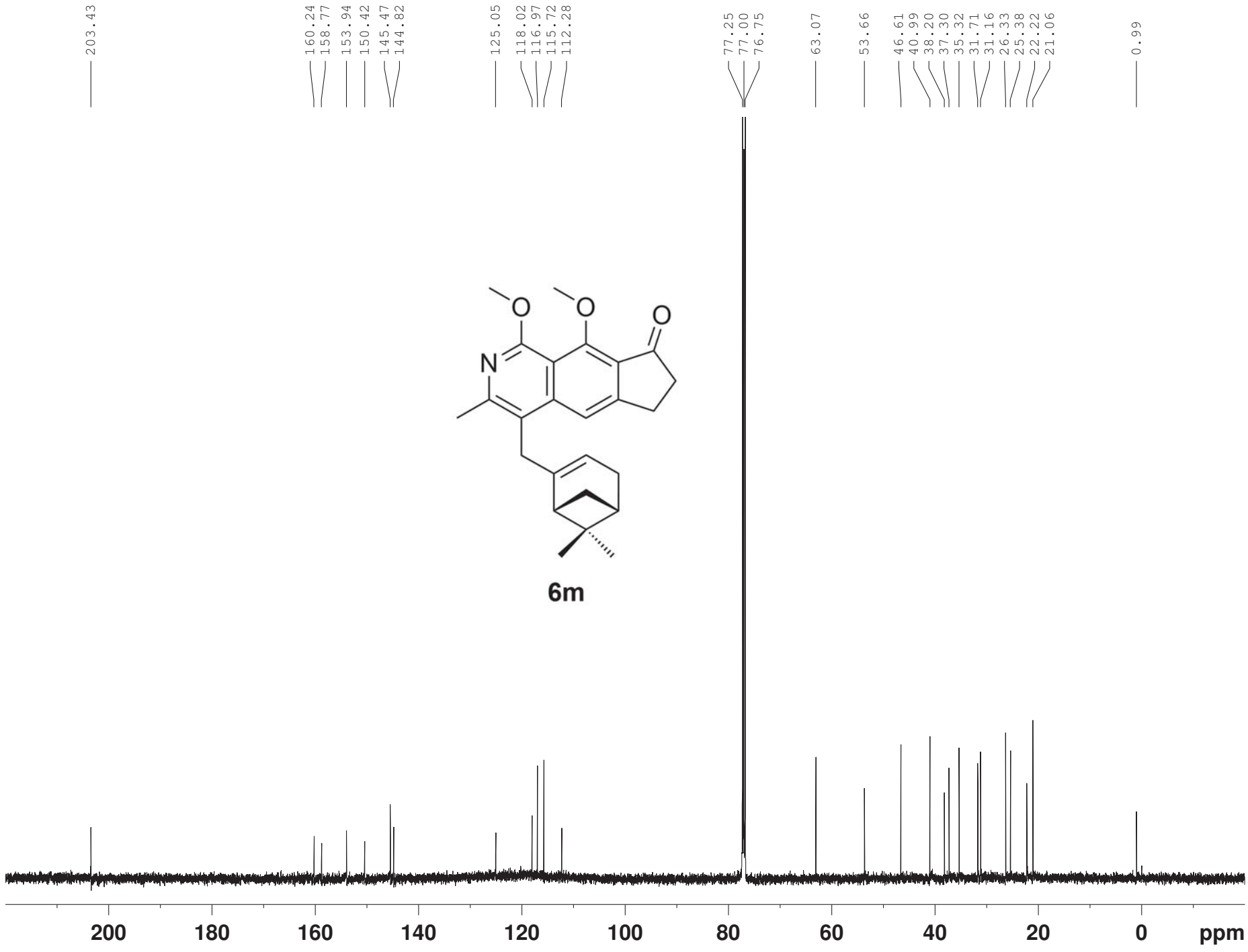
3.10
1.23
3.14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144.82
125.05
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115.72
112.28
77.25
77.00
76.75
63.07
53.66
46.61
40.99
38.20
37.30
35.32
31.71
31.16
26.33
25.38
22.22
21.06
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O
O
N
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120
100
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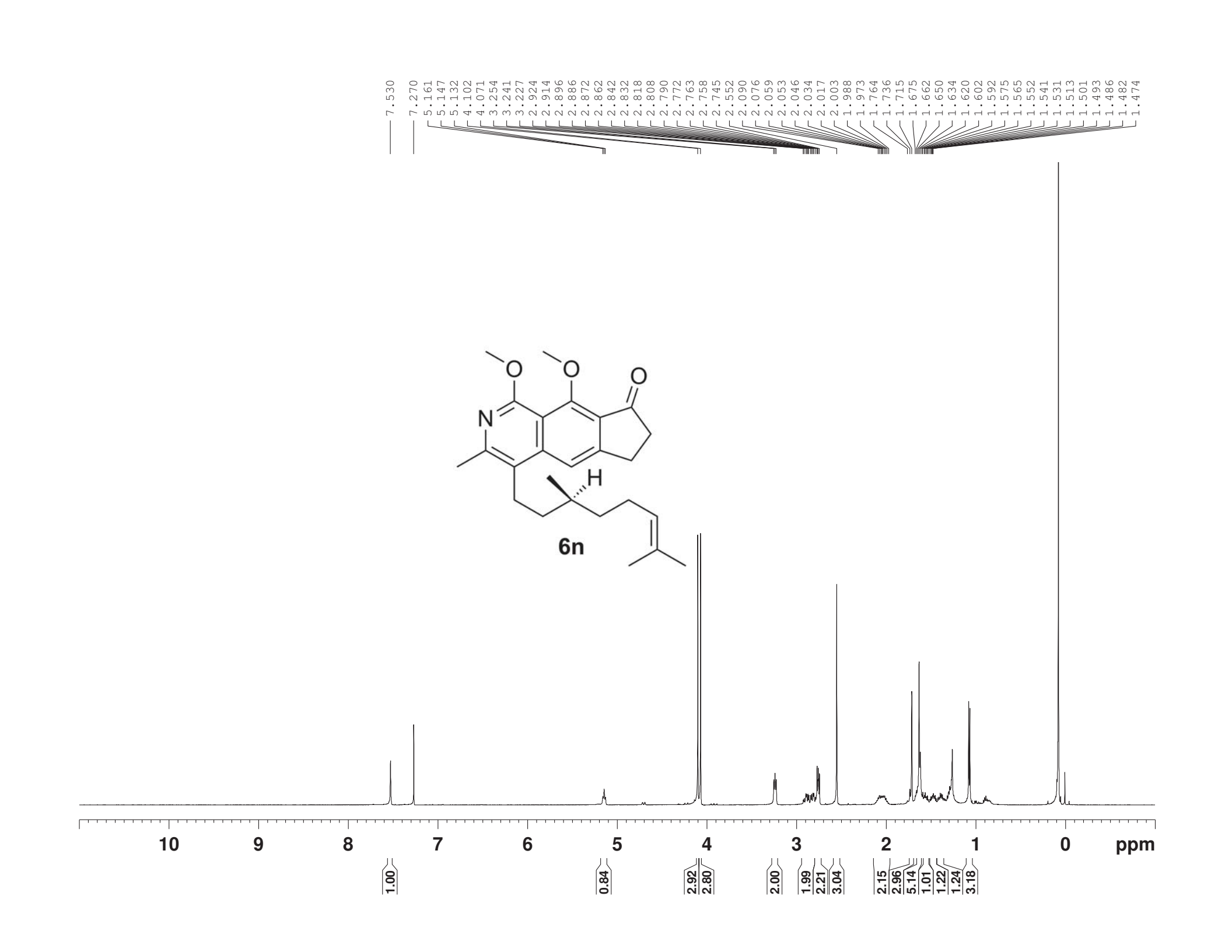
60
40
20
0
ppm

6m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2.886
2.872
2.862
2.842
2.832
2.818
2.808
2.790
2.772
2.763
2.758
2.745
2.552
2.090
2.076
2.059
2.053
2.046
2.034
2.017
2.003
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1.973
1.764
1.736
1.715
1.675
1.662
1.650
1.634
1.620
1.602
1.592
1.575
1.565
1.552
1.541
1.531
1.513
1.501
1.493
1.486
1.482
1.474
O
O
O
N
H
6n
10
9
8
7
6
5
4
3
2
1
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ppm
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1.22
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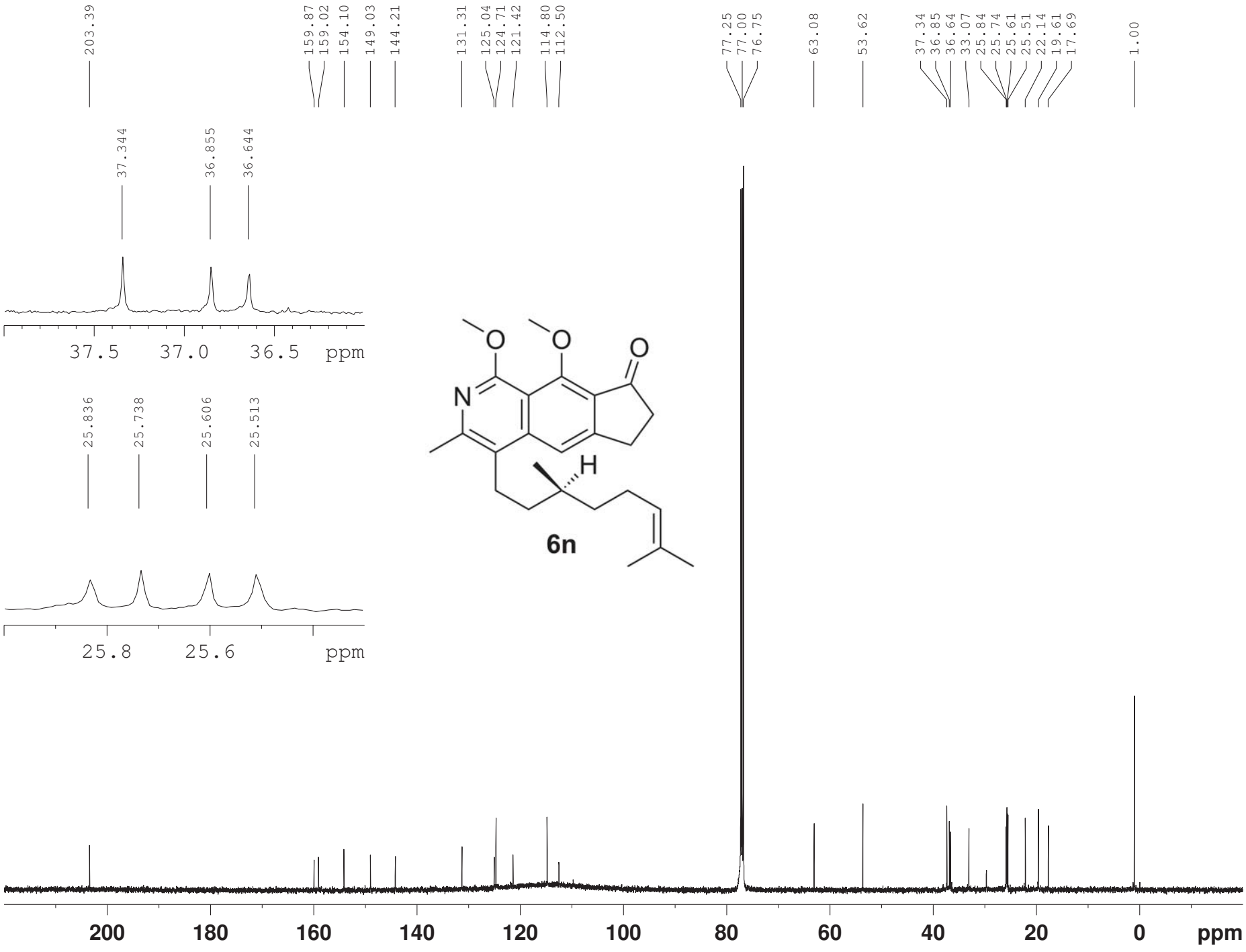
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77.00
76.75
63.08
53.62
37.34
36.85
36.64
33.07
25.84
25.74
25.61
25.51
22.14
19.61
17.69
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36.855
36.644
37.5
37.0
36.5
ppm
25.836
25.738
25.606
25.513
25.8
25.6
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O
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H
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120
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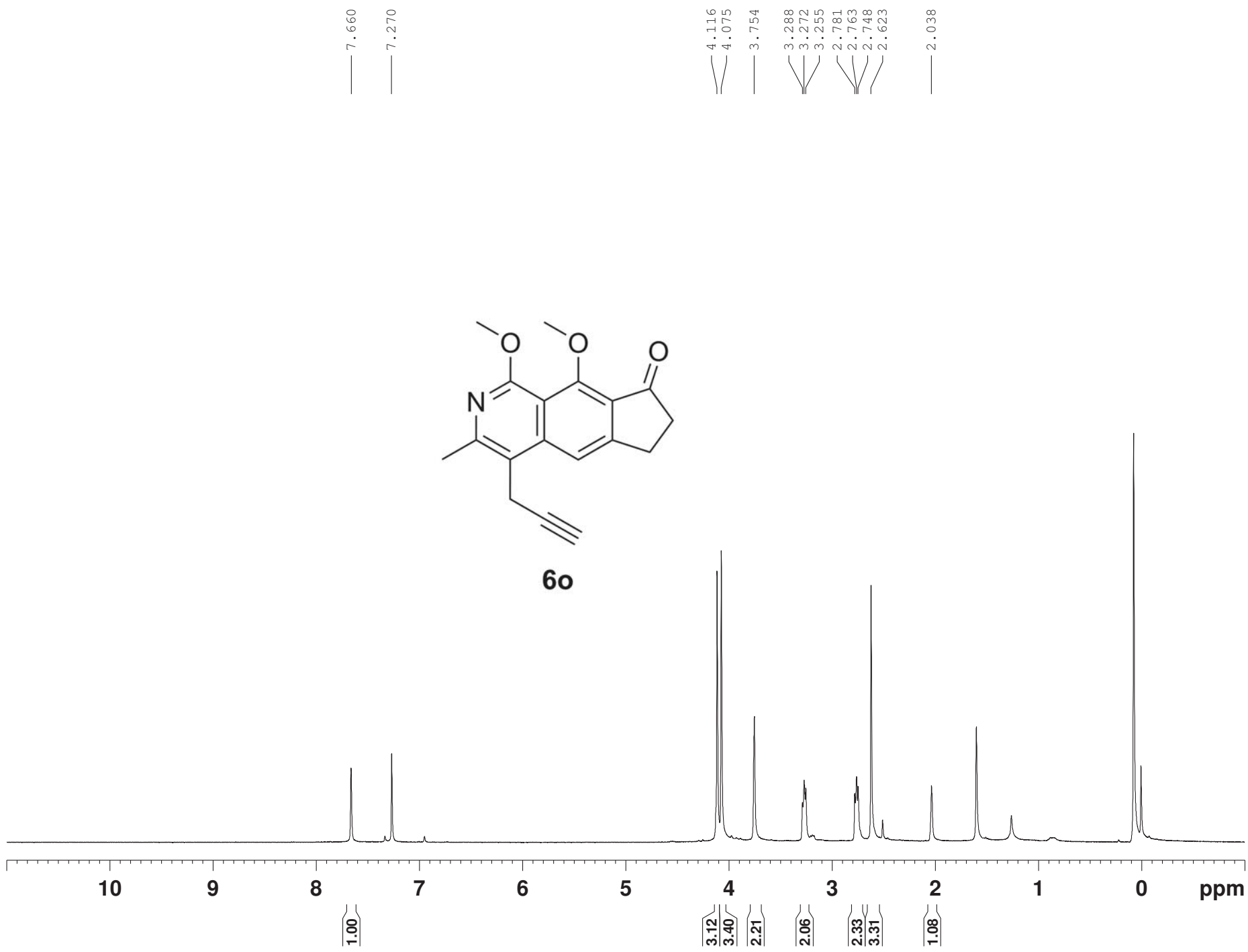
60
40
20
0
ppm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3.255
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2.763
2.748
2.623
2.038
O
O
O
N
6o
10
9
8
7
6
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ppm
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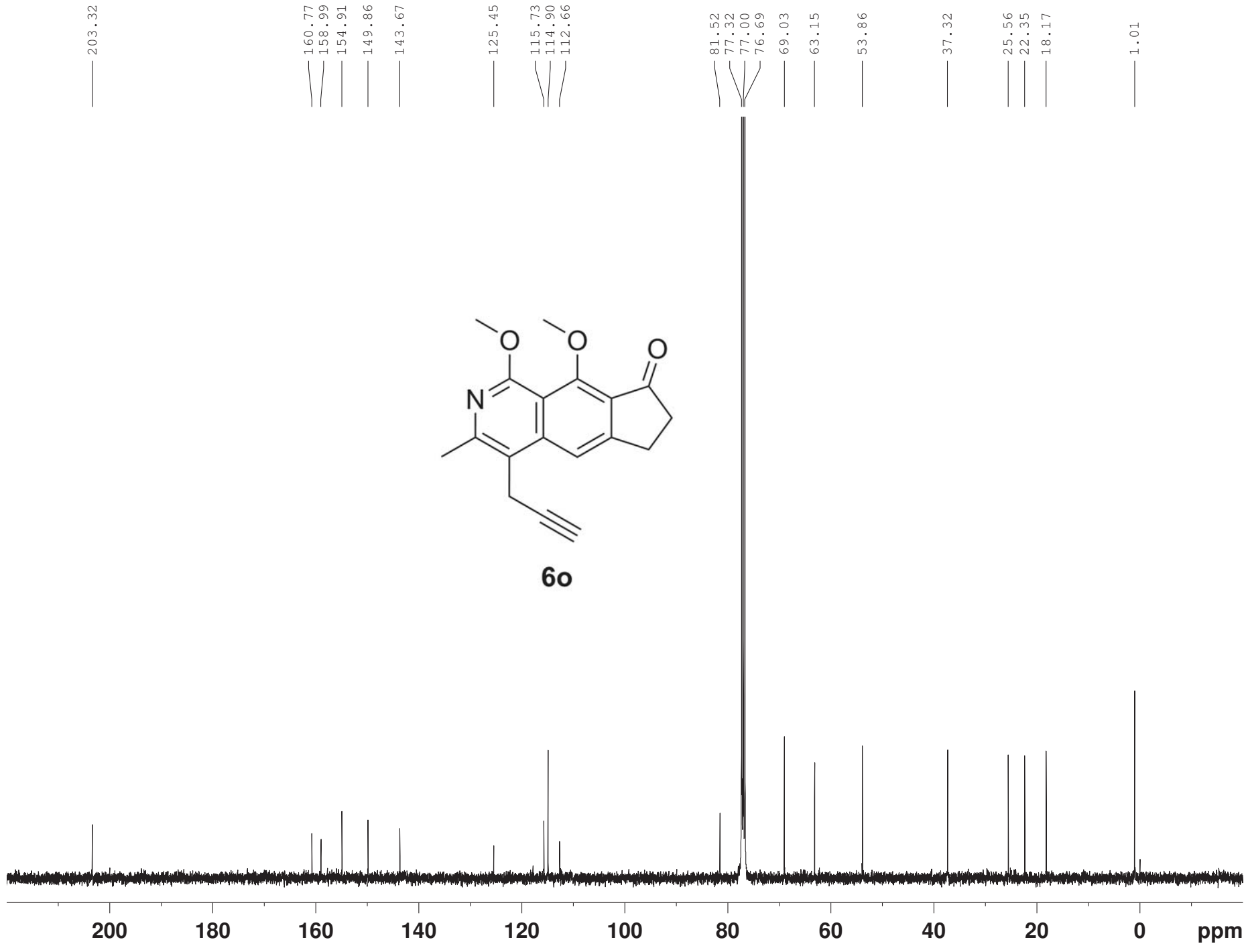
2.21
2.06
2.33
3.31
1.08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81.52
77.32
77.00
76.69
69.03
63.15
53.86
37.32
25.56
22.35
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O
O
N
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100
80
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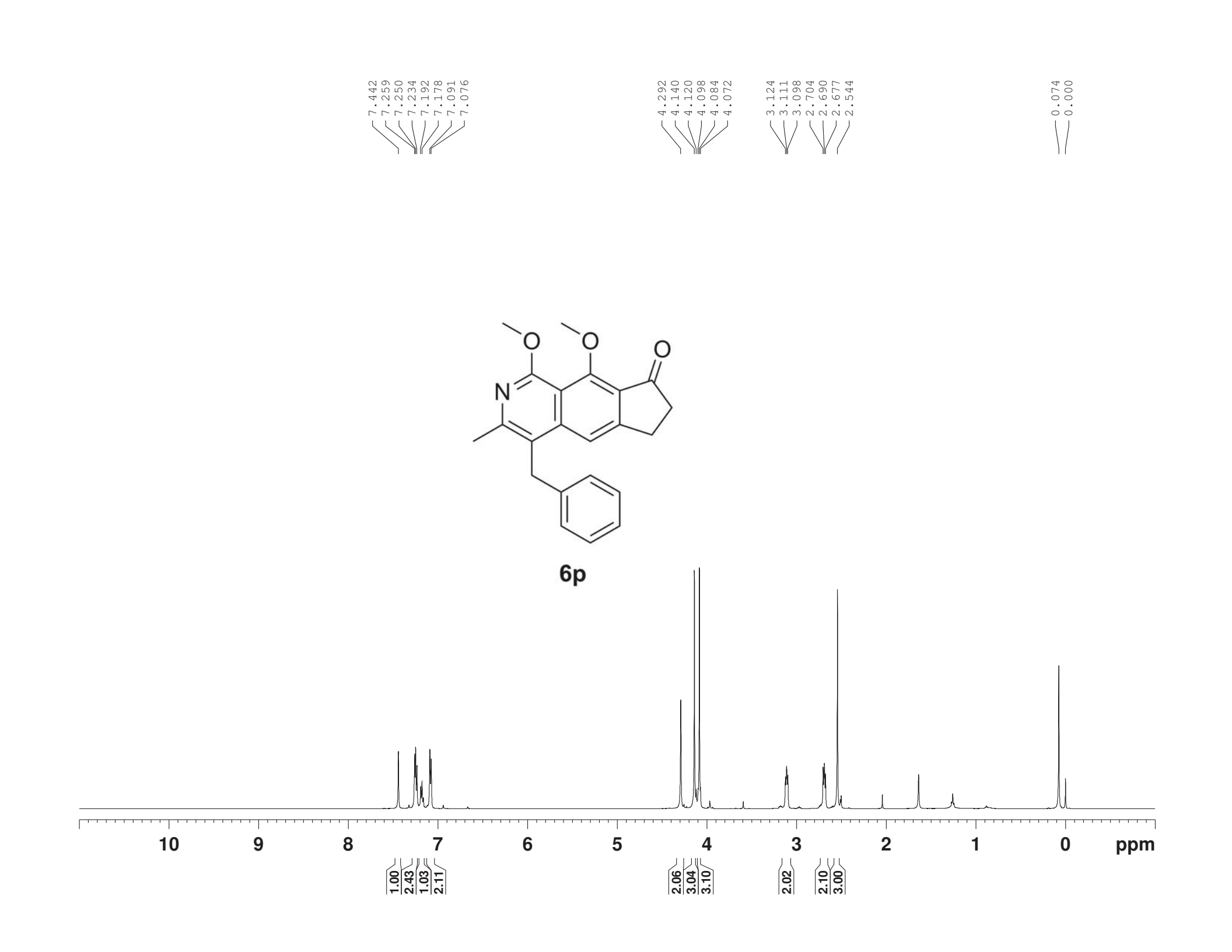
20
0
ppm

6o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4.120
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4.084
4.072
3.124
3.111
3.098
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2.690
2.677
2.544
0.074
0.000
O
O
O
N
6p
10
9
8
7
6
5
4
3
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3.04
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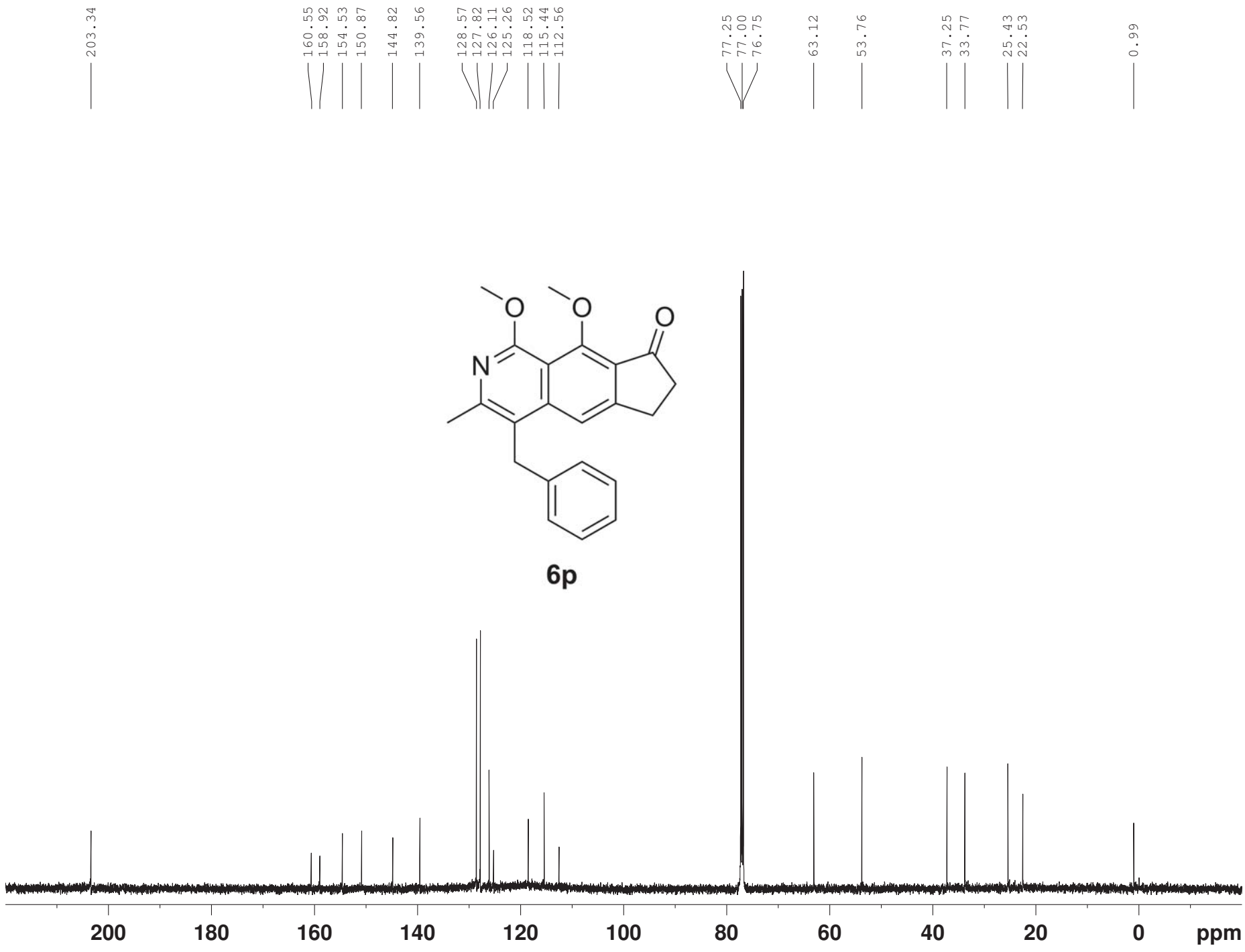
2.10
3.00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125.26
118.52
115.44
112.56
77.25
77.00
76.75
63.12
53.76
37.25
33.77
25.43
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O
O
N
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120
100
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60
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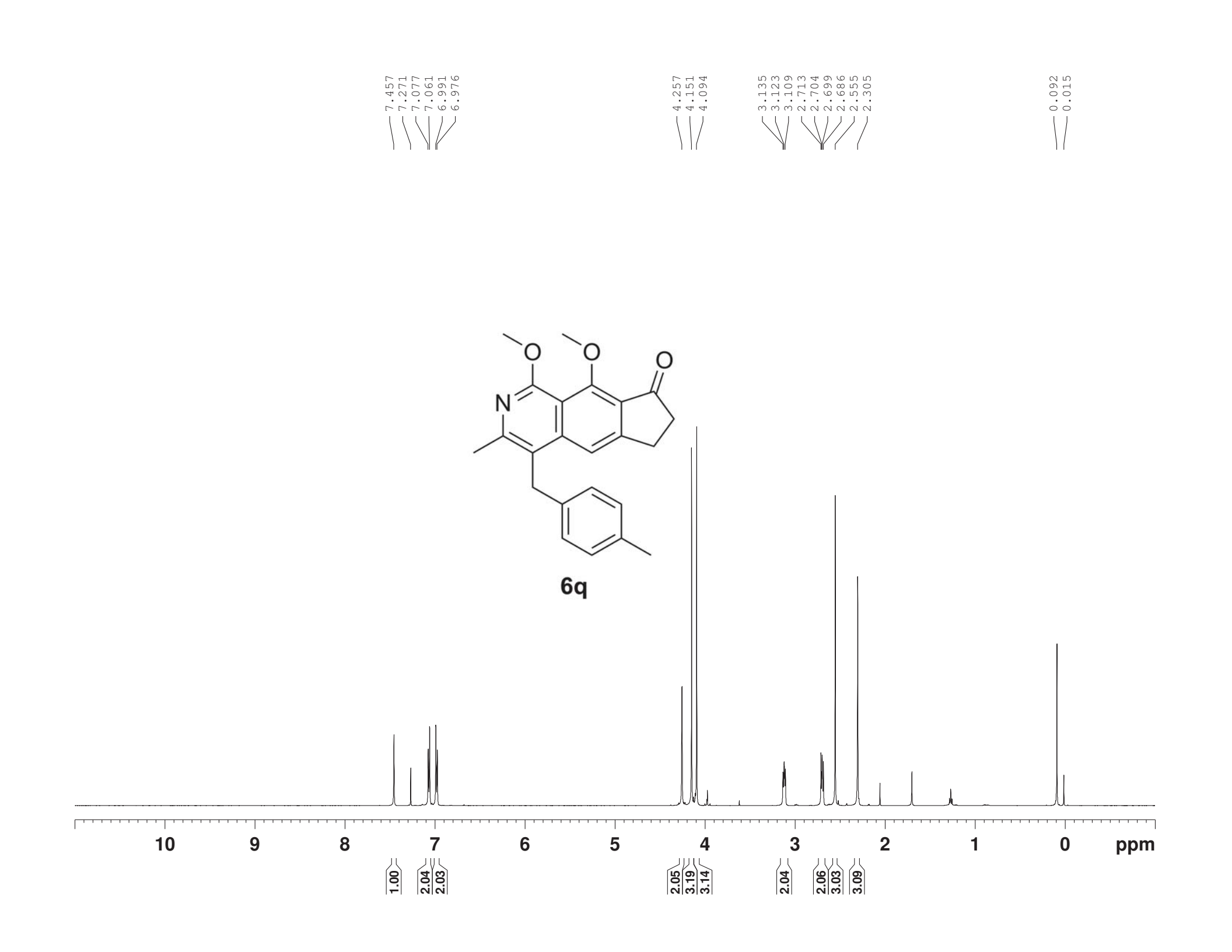
20
0
ppm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3.109
2.713
2.704
2.699
2.686
2.555
2.305
0.092
0.015
O
O
O
N
6q
10
9
8
7
6
5
4
3
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2.04
2.03
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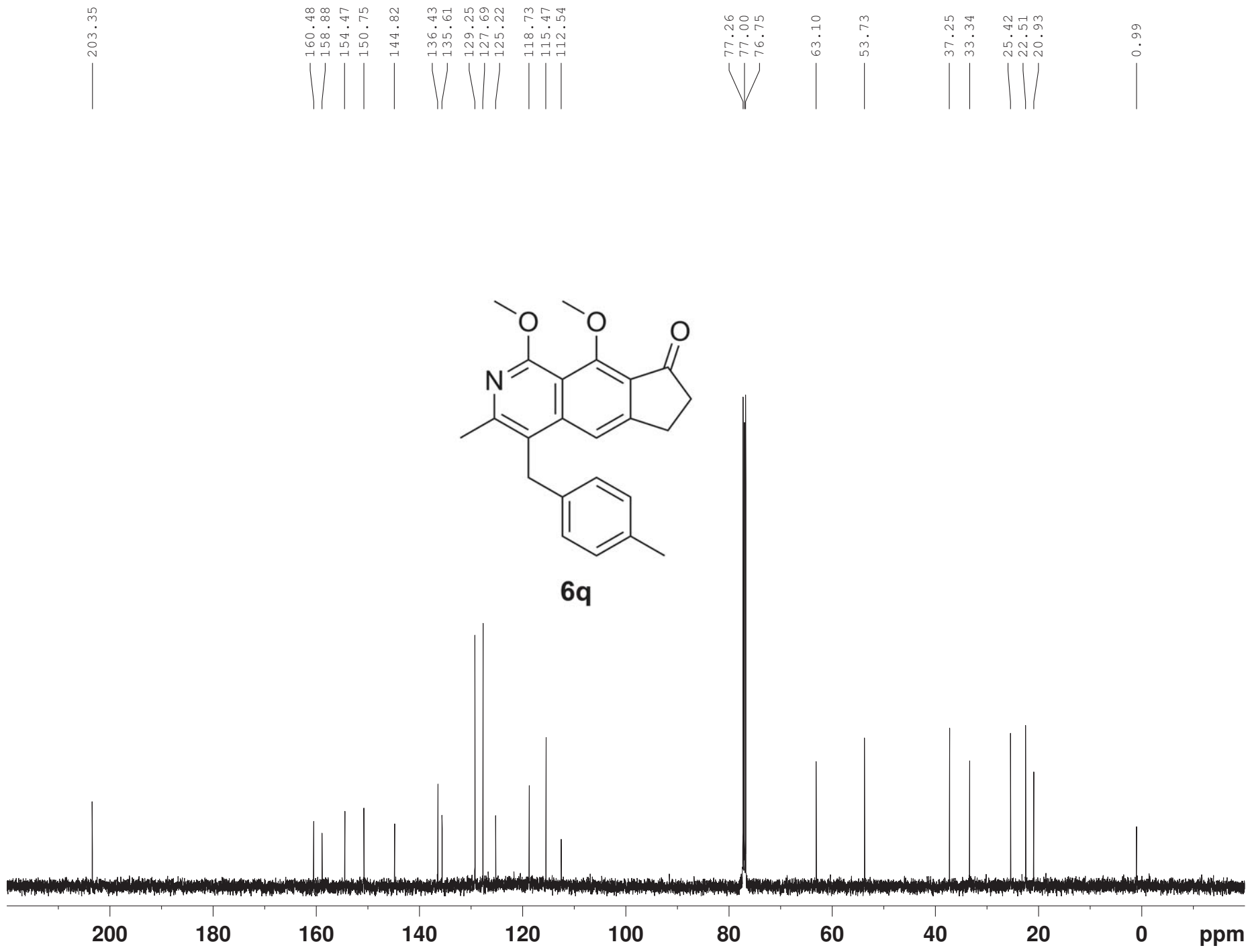
3.09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77.26
77.00
76.75
63.10
53.73
37.25
33.34
25.42
22.51
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O
O
N
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120
100
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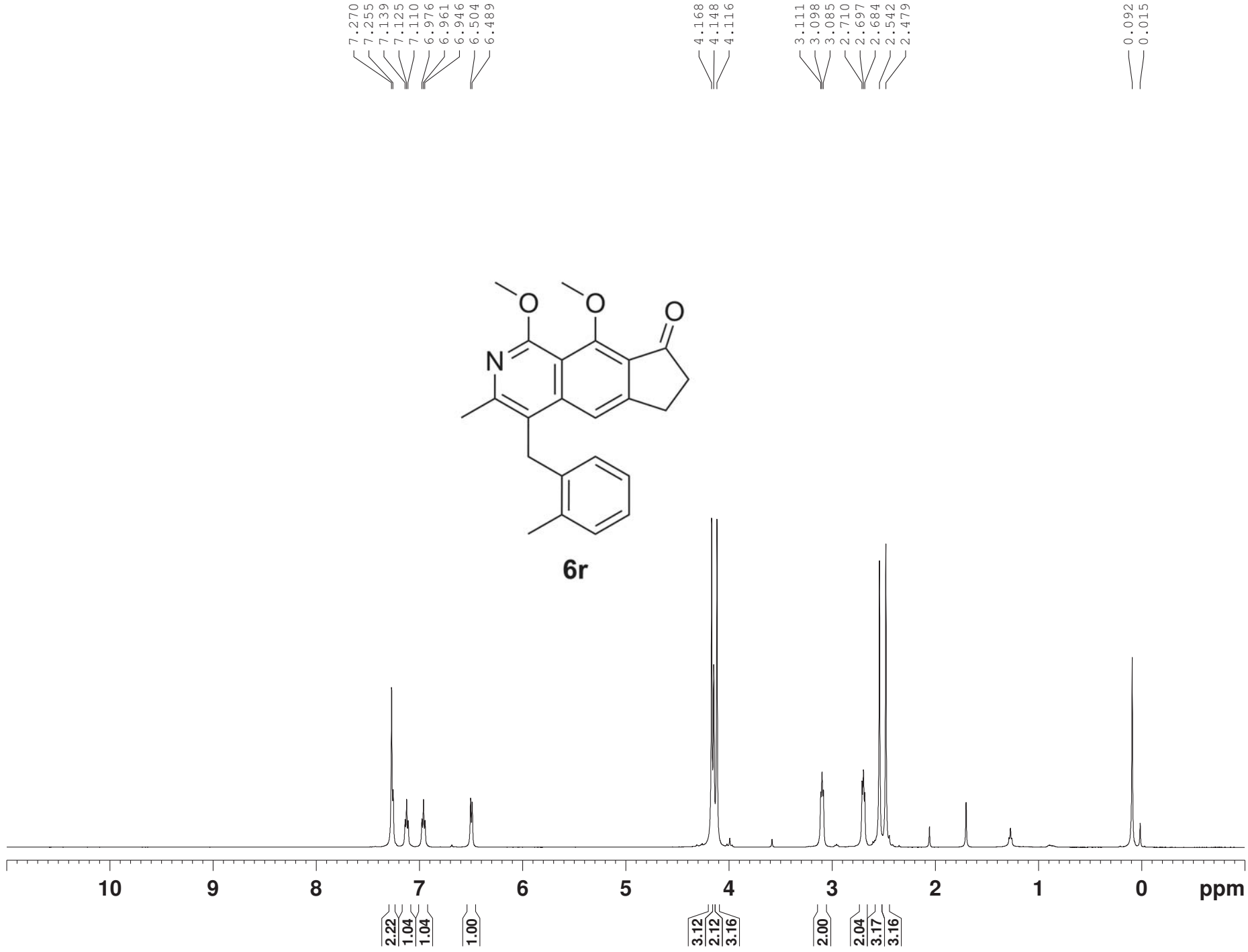
60
40
20
0
ppm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4.116
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3.098
3.085
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2.479
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O
O
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6r
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8
7
6
5
4
3
2
1
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1.04
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3.16
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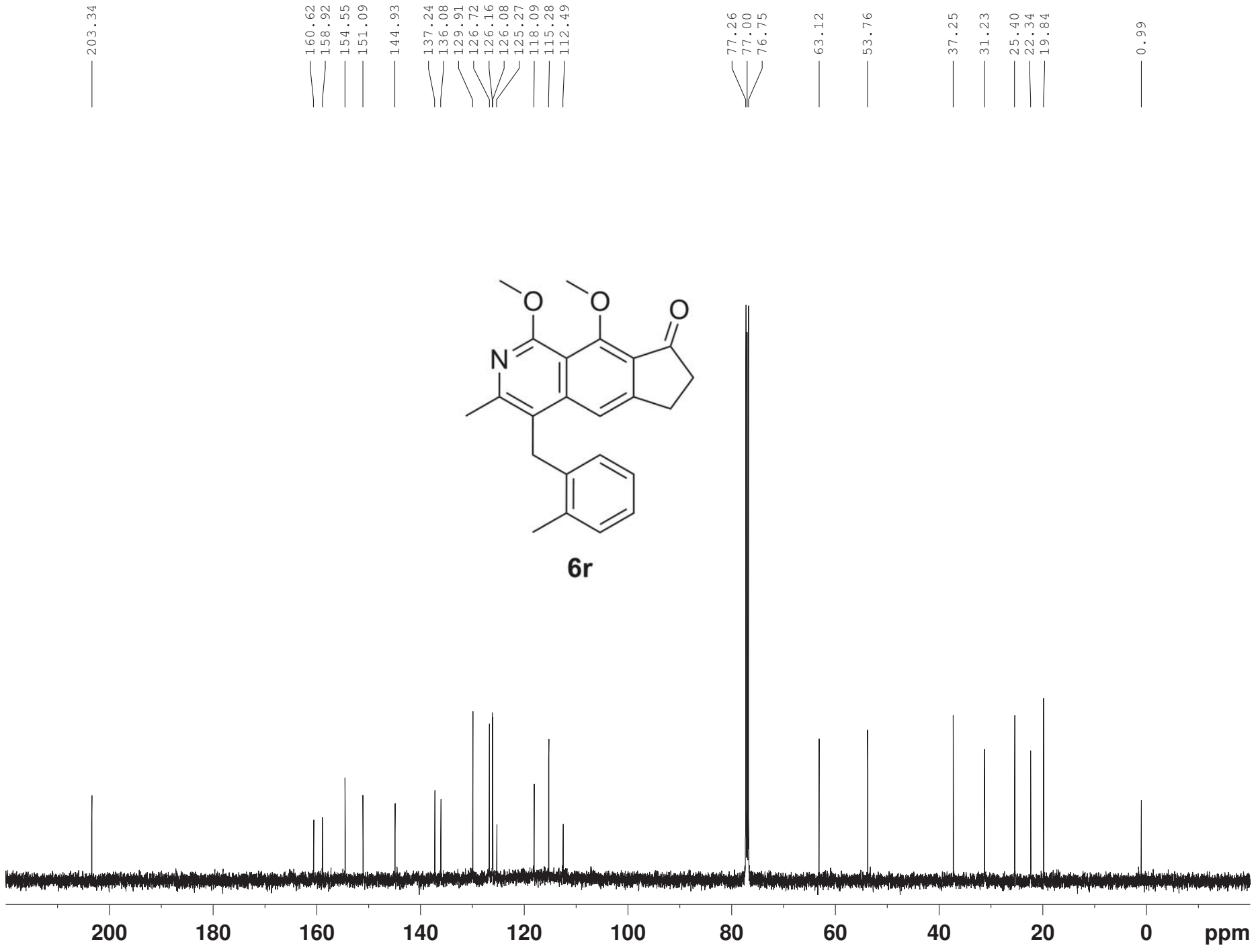
3.16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126.72
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126.08
125.27
118.09
115.28
112.49
77.26
77.00
76.75
63.12
53.76
37.25
31.23
25.40
22.34
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O
O
N
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120
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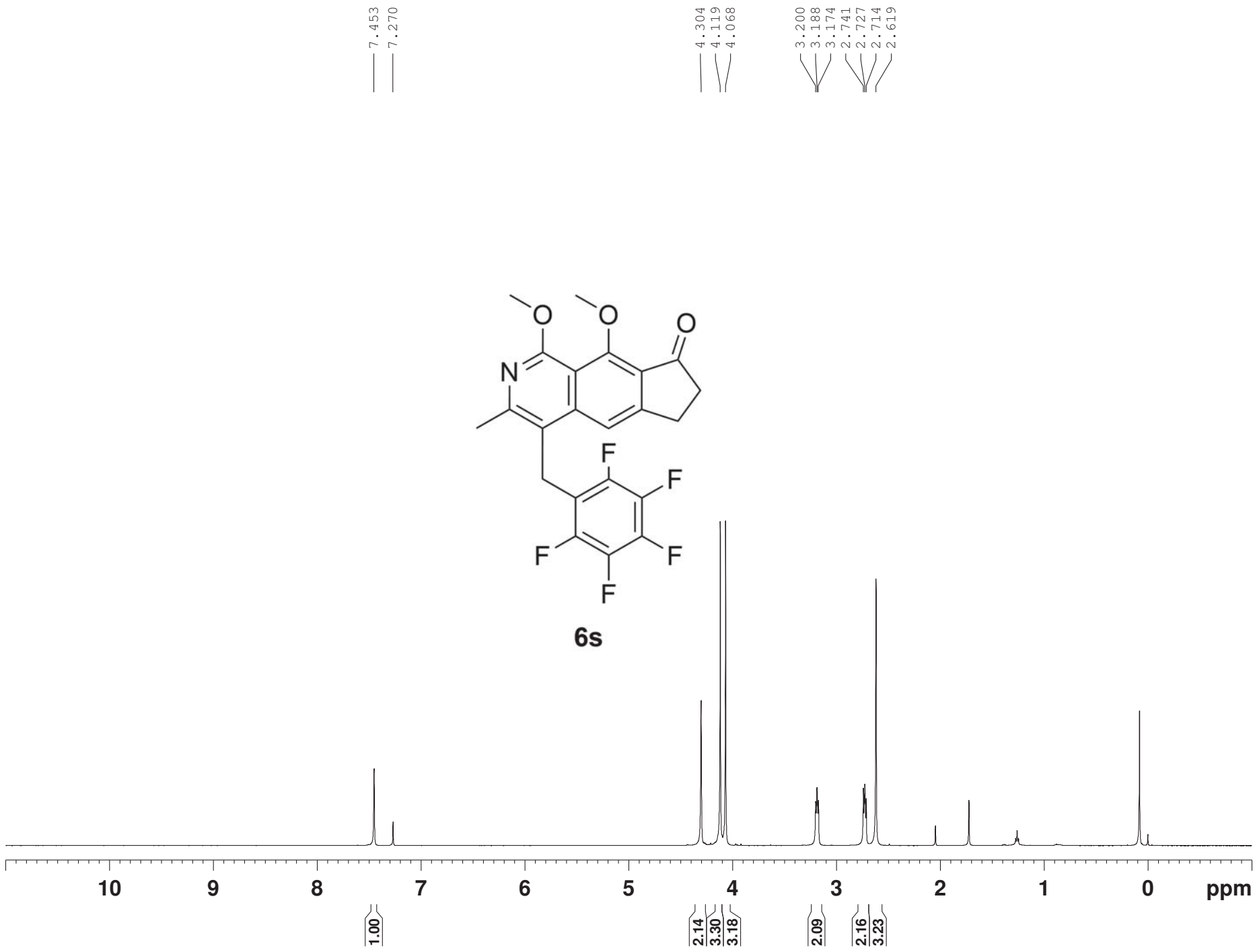
40
20
0
ppm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2.727
2.714
2.619
O
O
O
N
F
F
F
F
F
6s
10
9
8
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6
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2
1
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3.30
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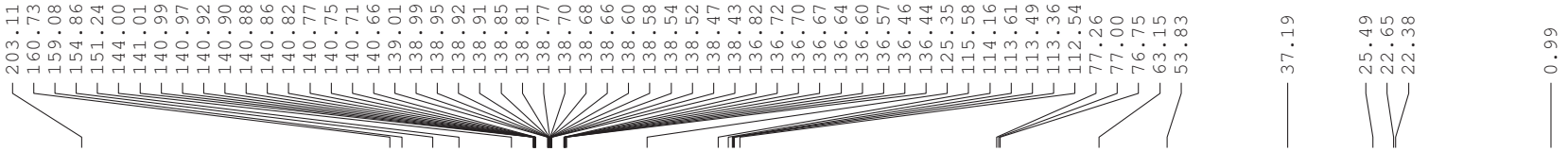
2.09
2.16
3.23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140.82
140.77
140.75
140.71
140.66
139.01
138.99
138.95
138.92
138.91
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138.81
138.77
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138.68
138.66
138.60
138.58
138.54
138.52
138.47
138.43
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136.70
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136.60
136.57
136.46
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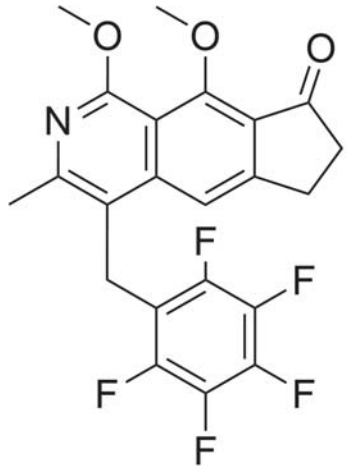
O
O
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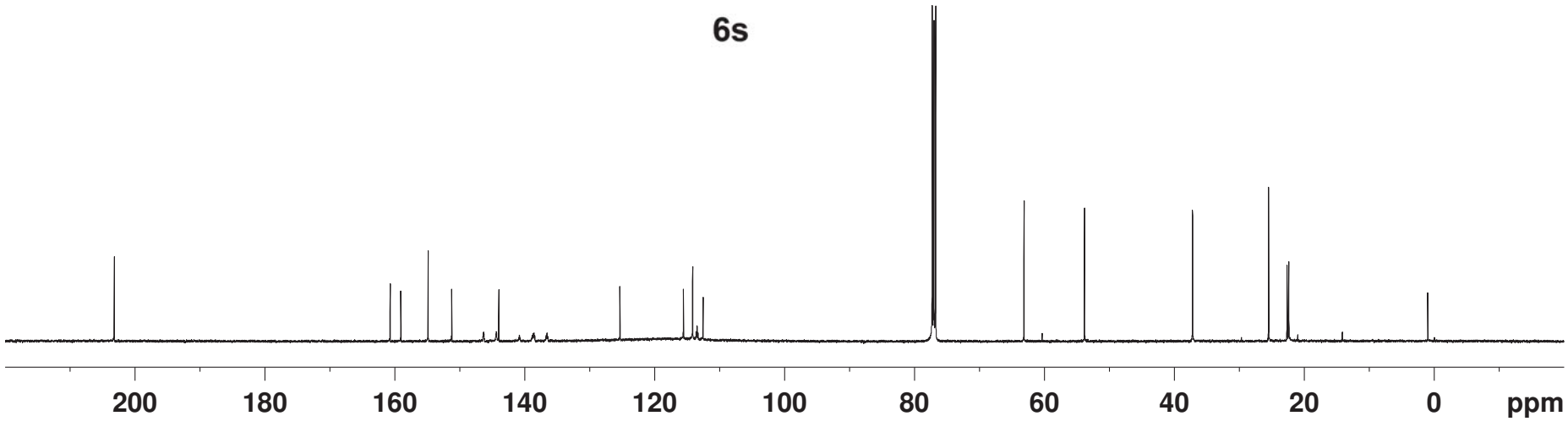
N
F
F
F
F
F

6s


200
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140
120
100
80
60
40
20
0
ppm

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-141.85
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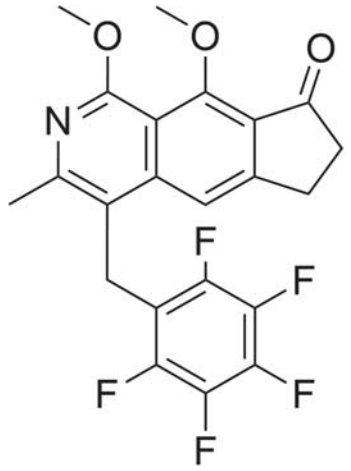
-162.31
-162.33



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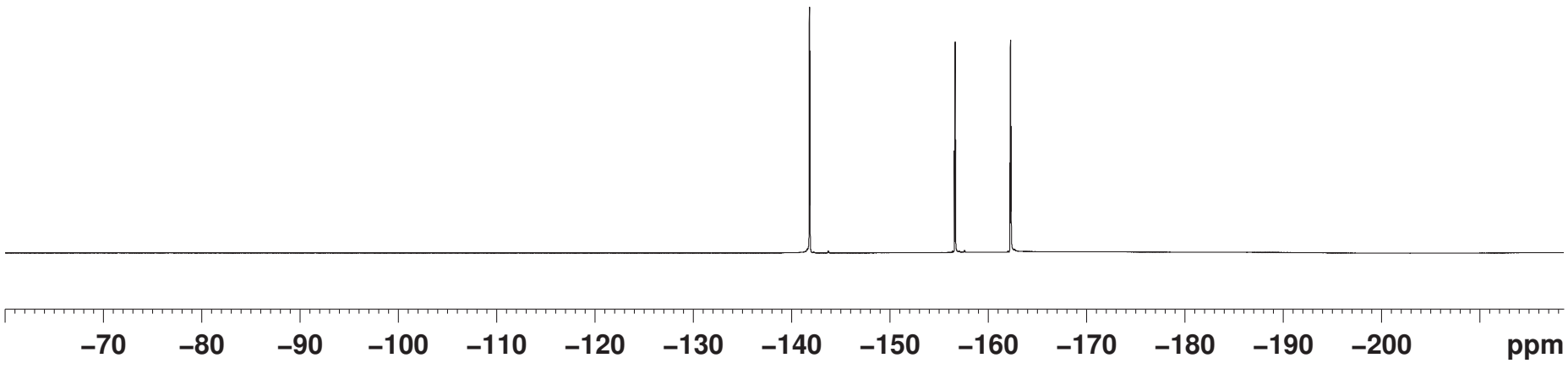

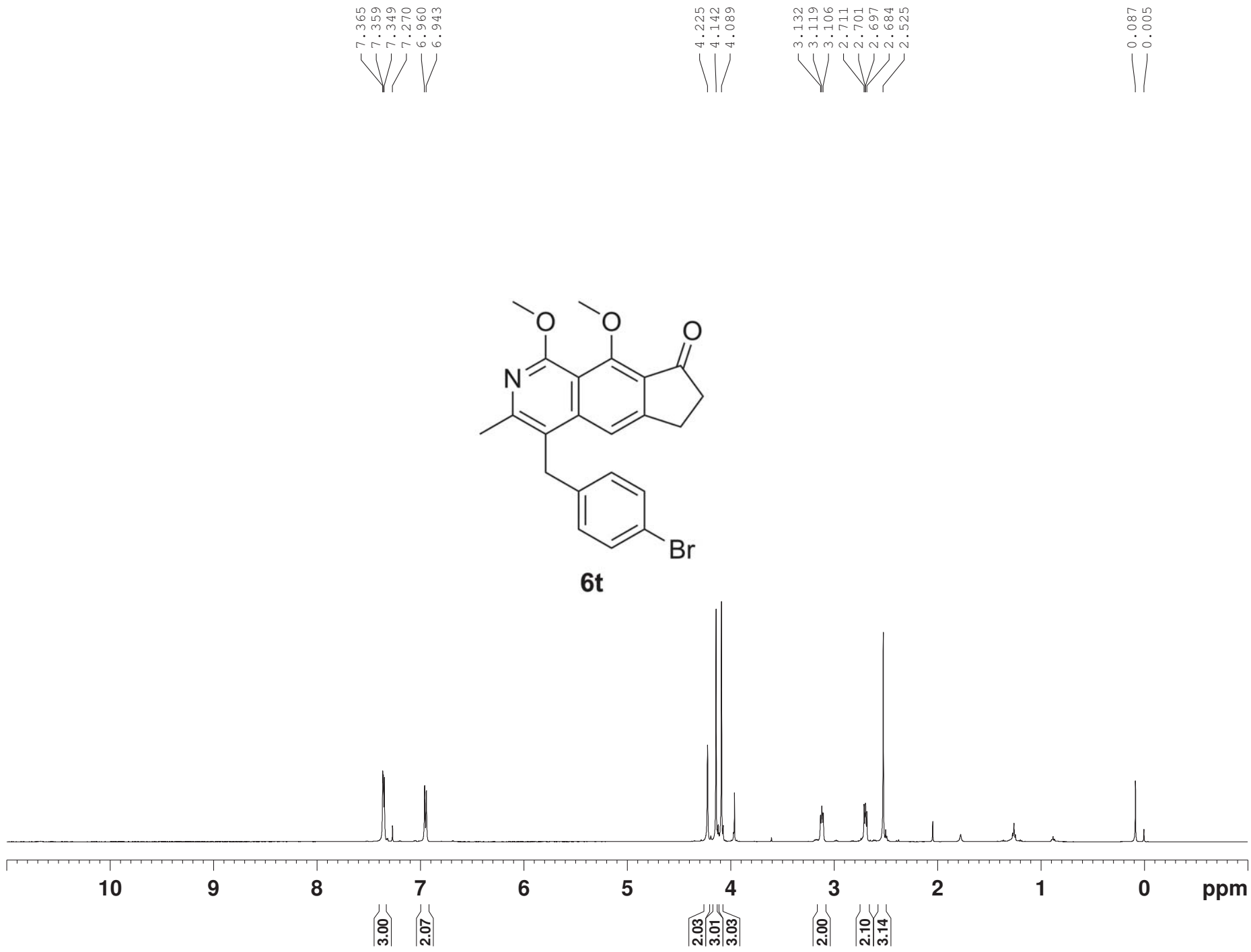
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2.711
2.701
2.697
2.684
2.525
0.087
0.005
O
O
O
N
Br
6t
10
9
8
7
6
5
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1
0
ppm
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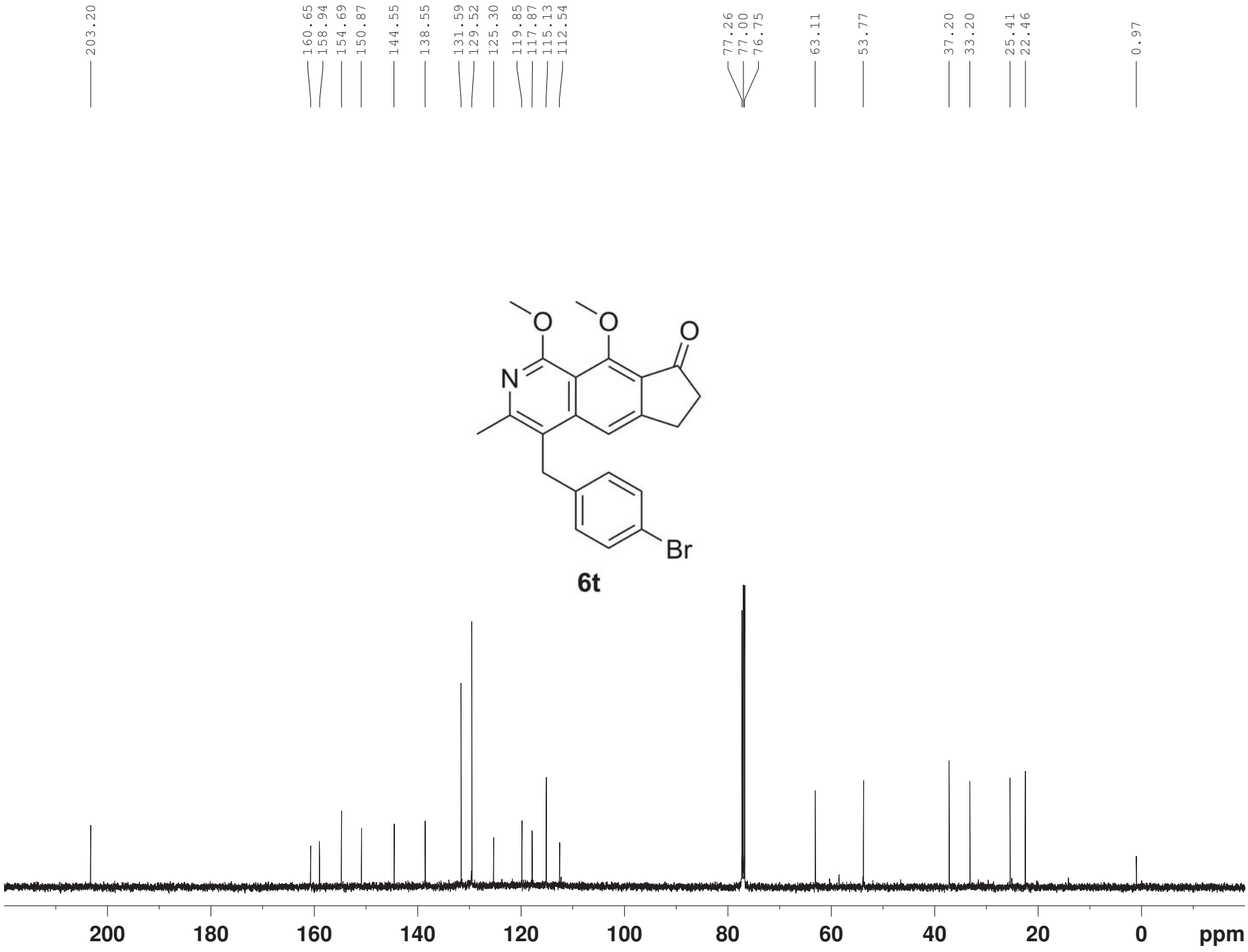
3.01
3.03
2.00
2.10
3.14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125.30
119.85
117.87
115.13
112.54
77.26
77.00
76.75
63.11
53.77
37.20
33.20
25.41
22.46
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O
O
N
Br
6t
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120
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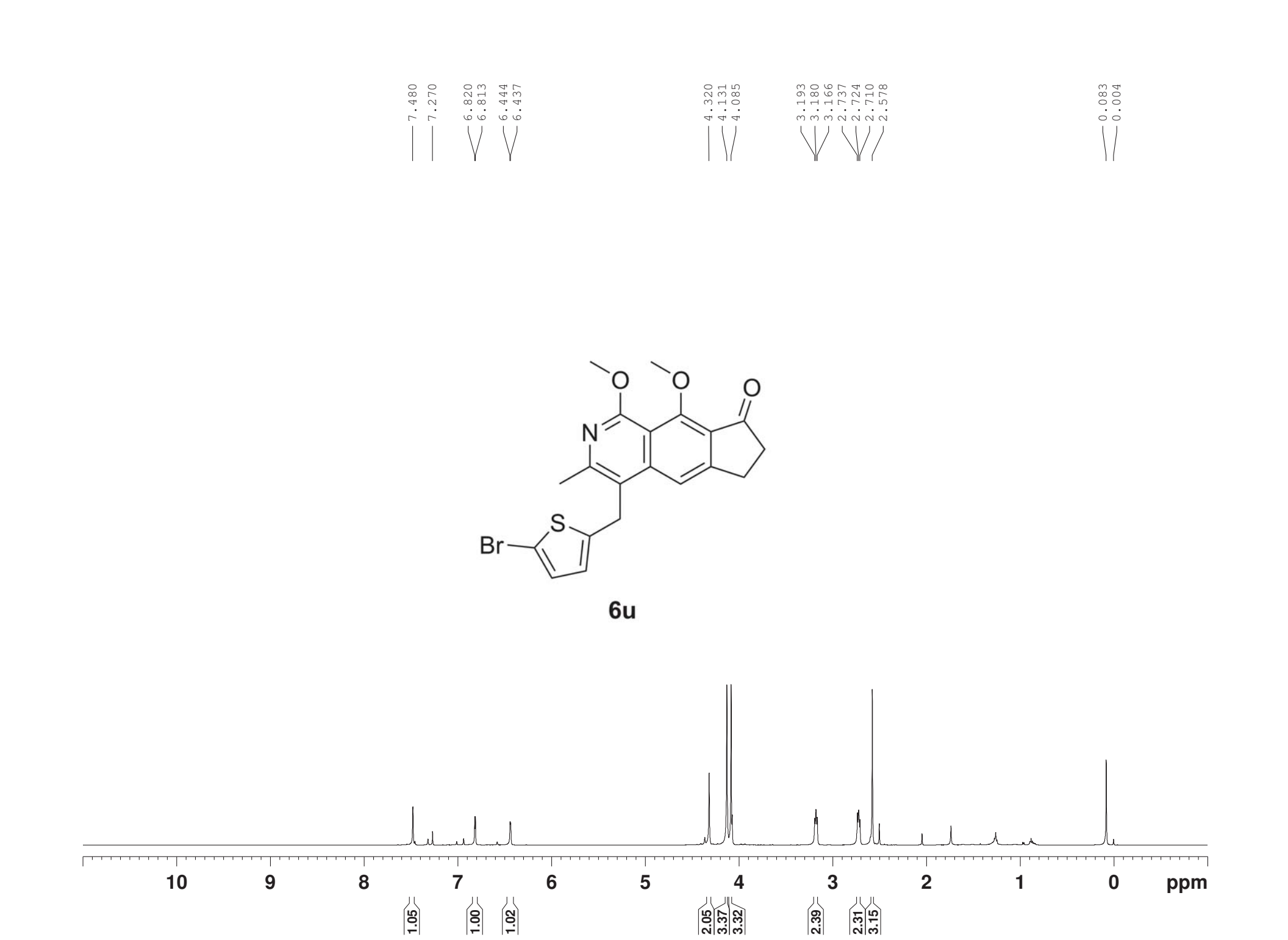
60
40
20
0
ppm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3.180
3.166
2.737
2.724
2.710
2.578
0.083
0.004
O
O
O
N
S
Br
10
9
8
7
6
5
4
3
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1.00
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3.32
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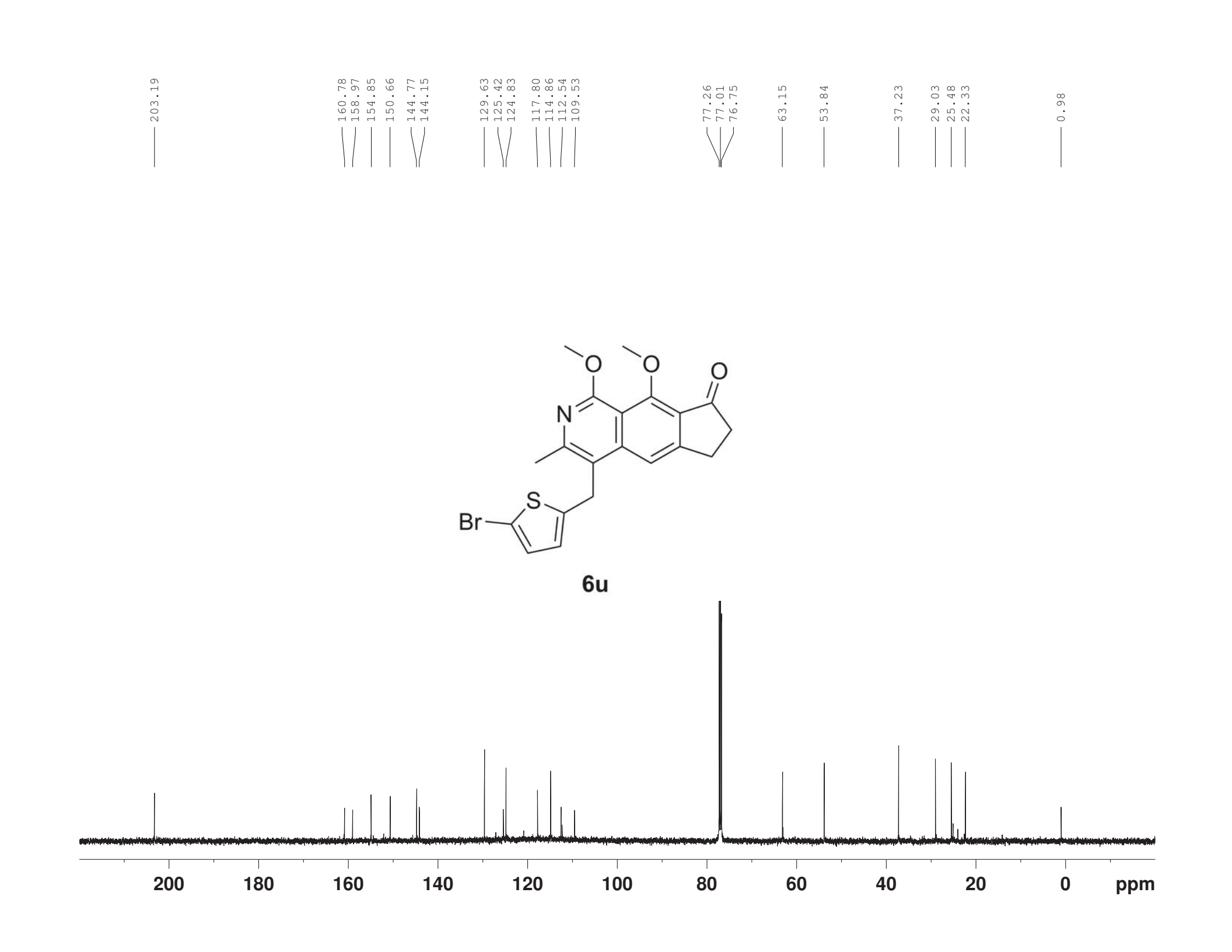
2.31
3.15

6u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117.80
114.86
112.54
109.53
77.26
77.01
76.75
63.15
53.84
37.23
29.03
25.48
22.33
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O
O
N
S
Br
6u
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120
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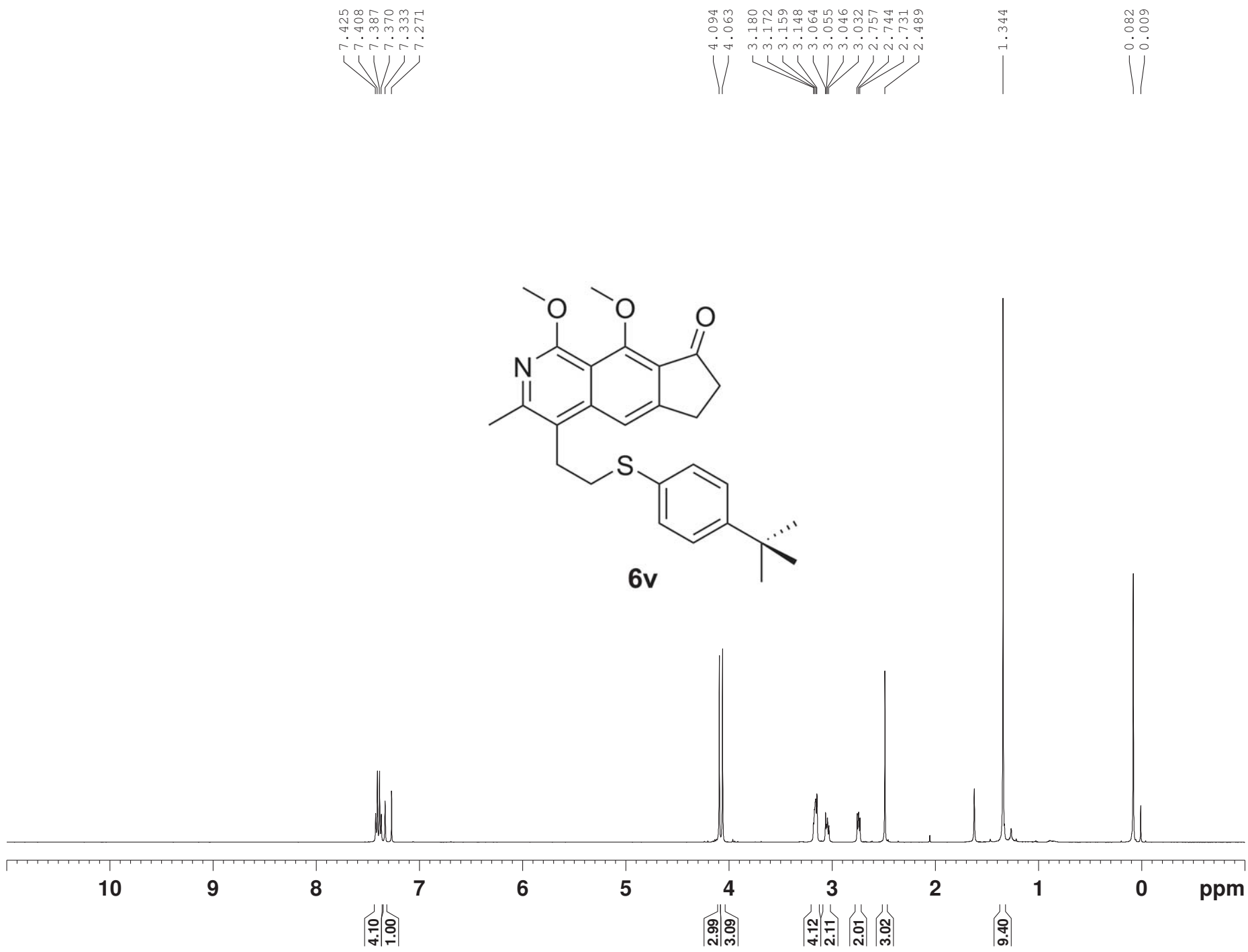
ppm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3.148
3.064
3.055
3.046
3.032
2.757
2.744
2.731
2.489
1.344
0.082
0.009
O
O
O
N
S
6v
10
9
8
7
6
5
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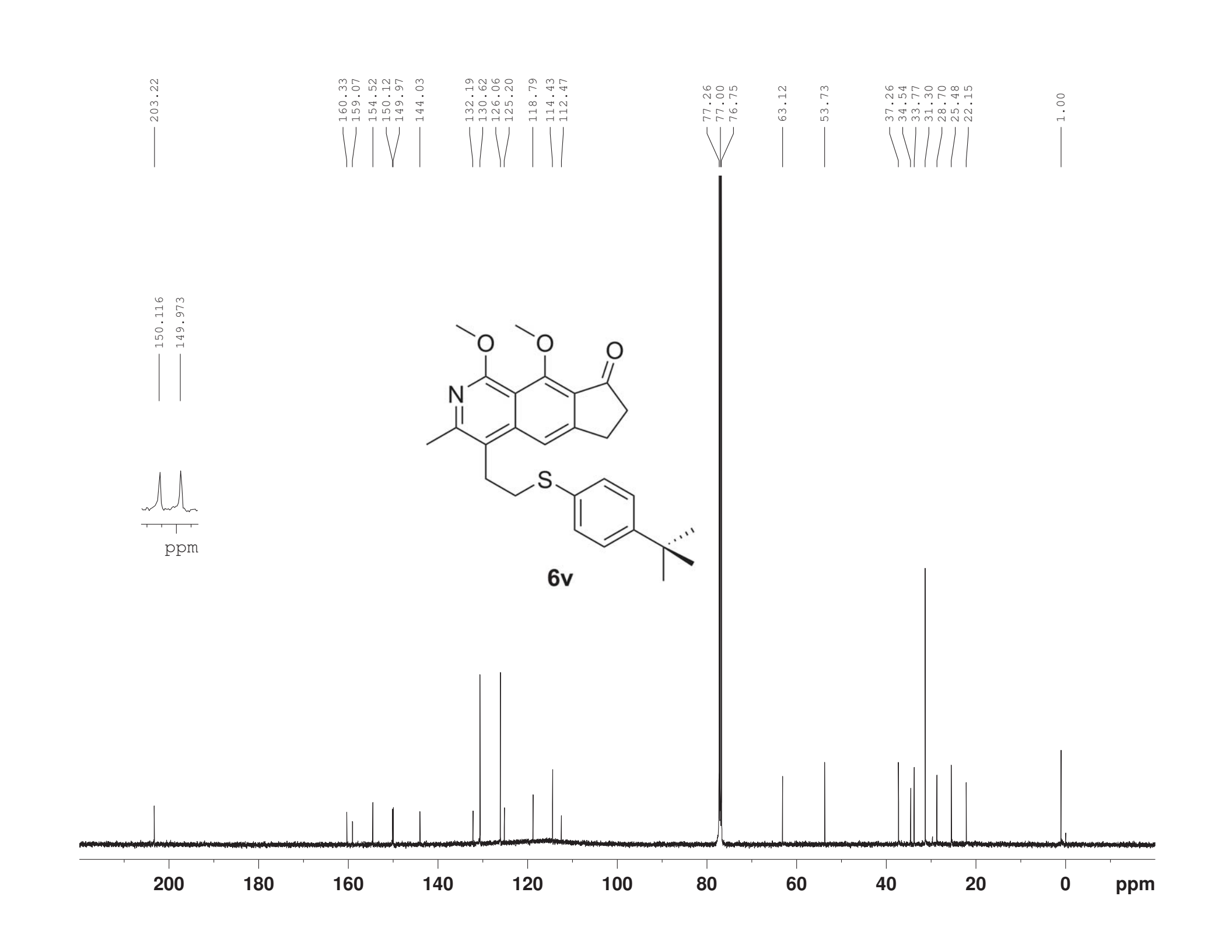
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154.52
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149.97
144.03
132.19
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126.06
125.20
118.79
114.43
112.47
77.26
77.00
76.75
63.12
53.73
37.26
34.54
33.77
31.30
28.70
25.48
22.15
1.00
150.116
149.973
ppm
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S
6v
200
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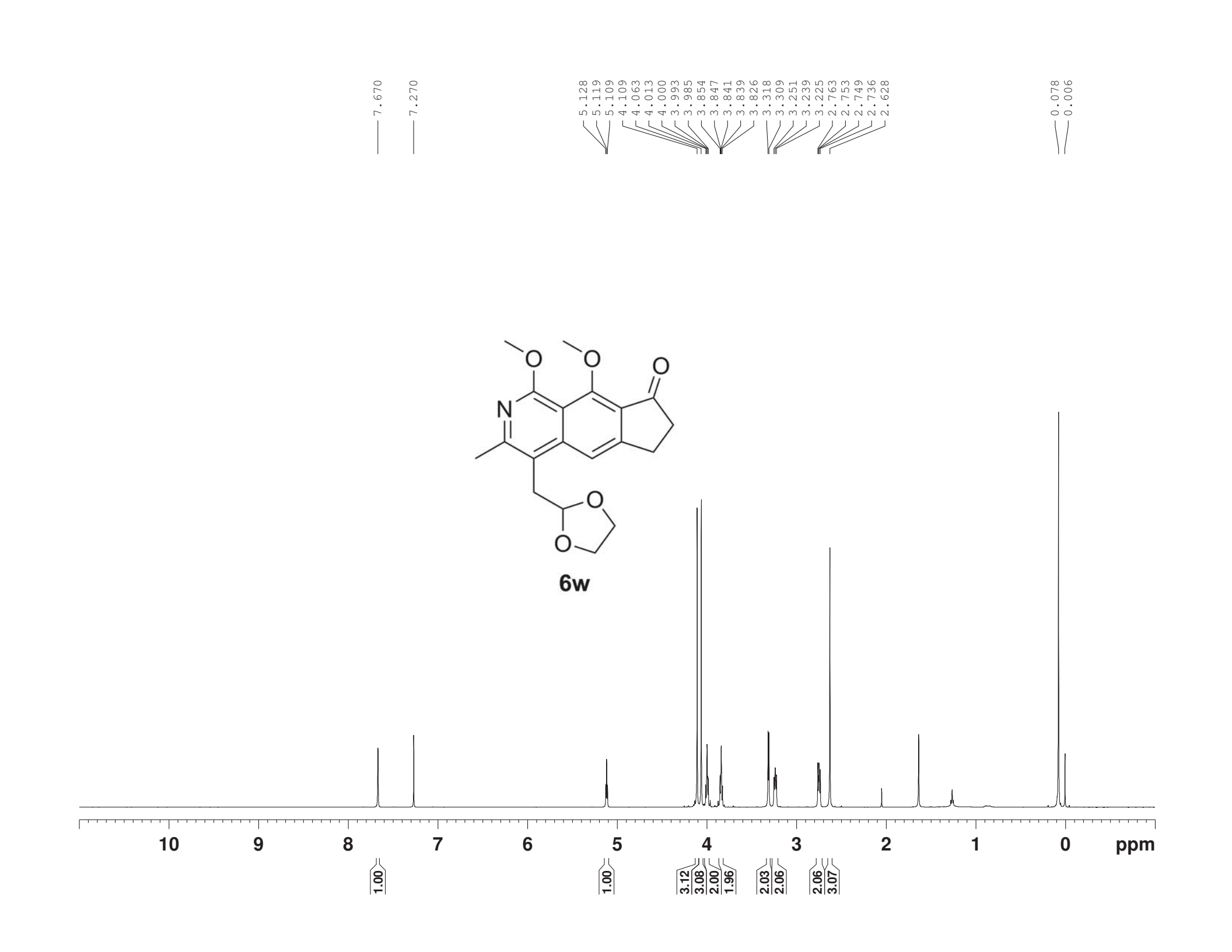
120
100
80
60
40
20
0
ppm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5.119
5.109
4.109
4.063
4.013
4.000
3.993
3.985
3.854
3.847
3.841
3.839
3.826
3.318
3.309
3.251
3.239
3.225
2.763
2.753
2.749
2.736
2.628
0.078
0.006
O
O
O
N
O
O
6w
10
9
8
7
6
5
4
3
2
1
0
ppm
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1.00
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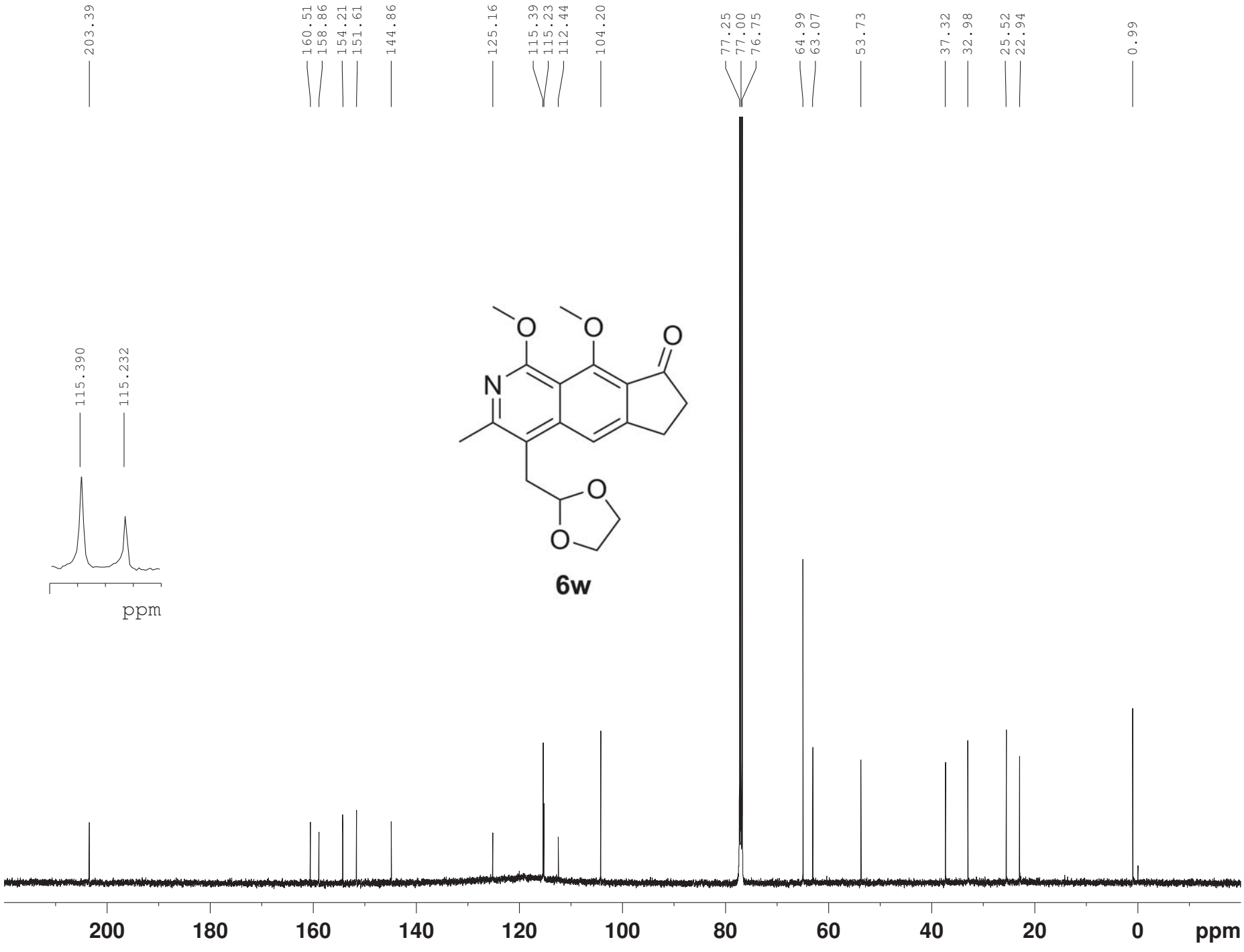
2.00
1.96
2.03
2.06
2.06
3.07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125.16
115.39
115.23
112.44
104.20
77.25
77.00
76.75
64.99
63.07
53.73
37.32
32.98
25.52
22.94
0.99
115.390
115.232
ppm
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O
N
O
O
6w
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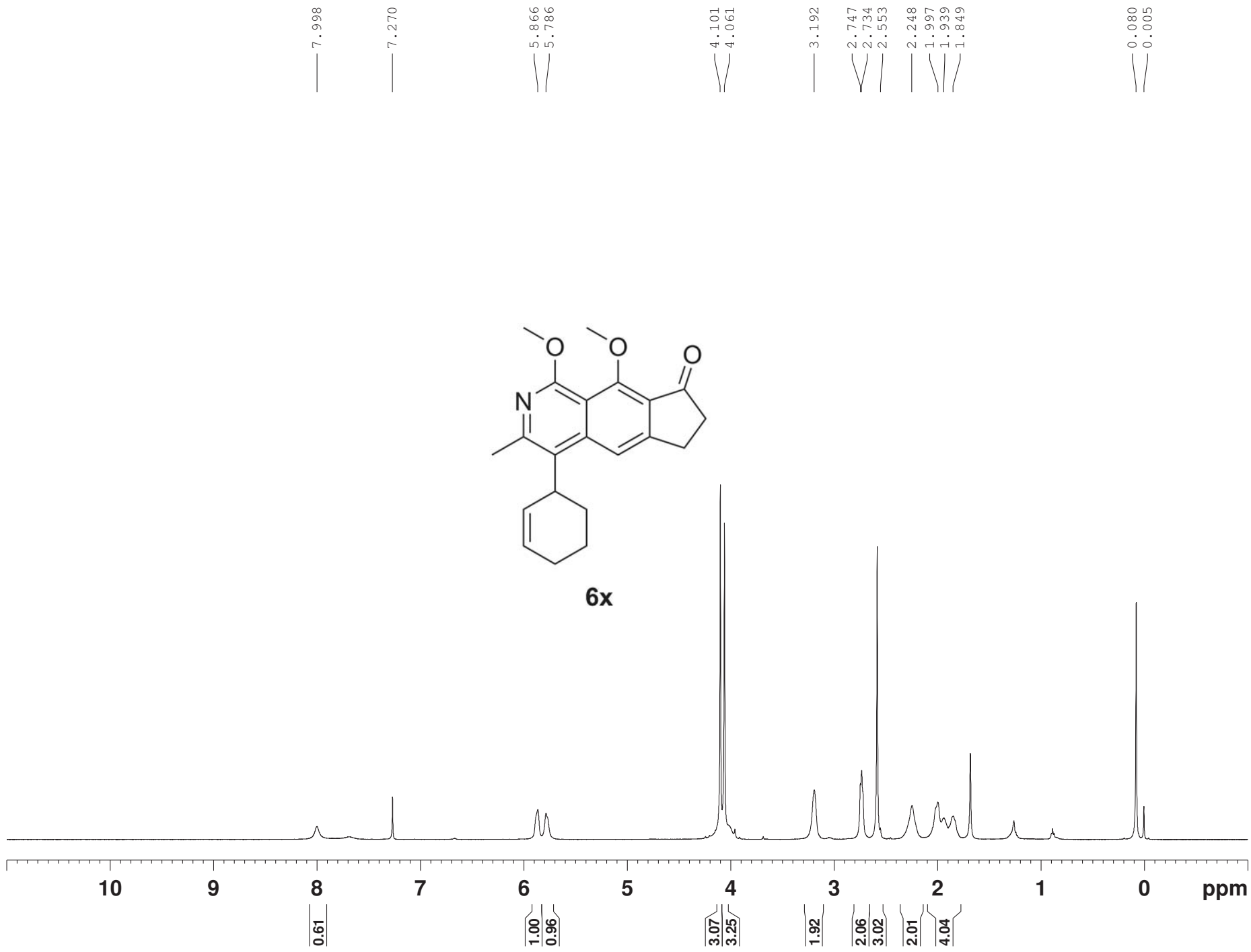
140
120
100
80
60
40
20
0
ppm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5.786
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4.061
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2.747
2.734
2.553
2.248
1.997
1.939
1.849
0.080
0.005
O
O
O
N
6x
10
9
8
7
6
5
4
3
2
1
0
ppm
0.61
1.00
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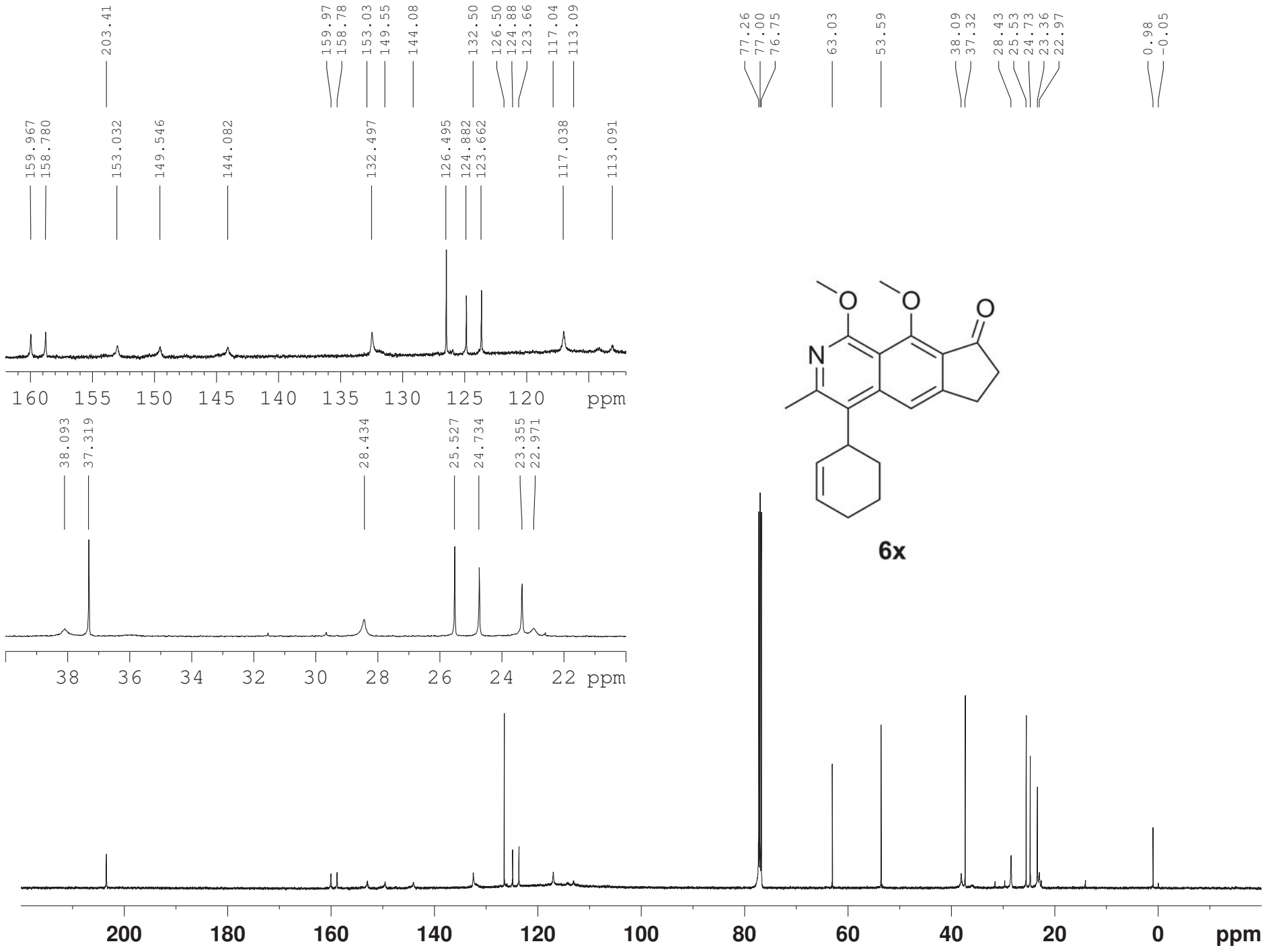
3.25
1.92
2.06
3.02
2.01
4.04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144.08
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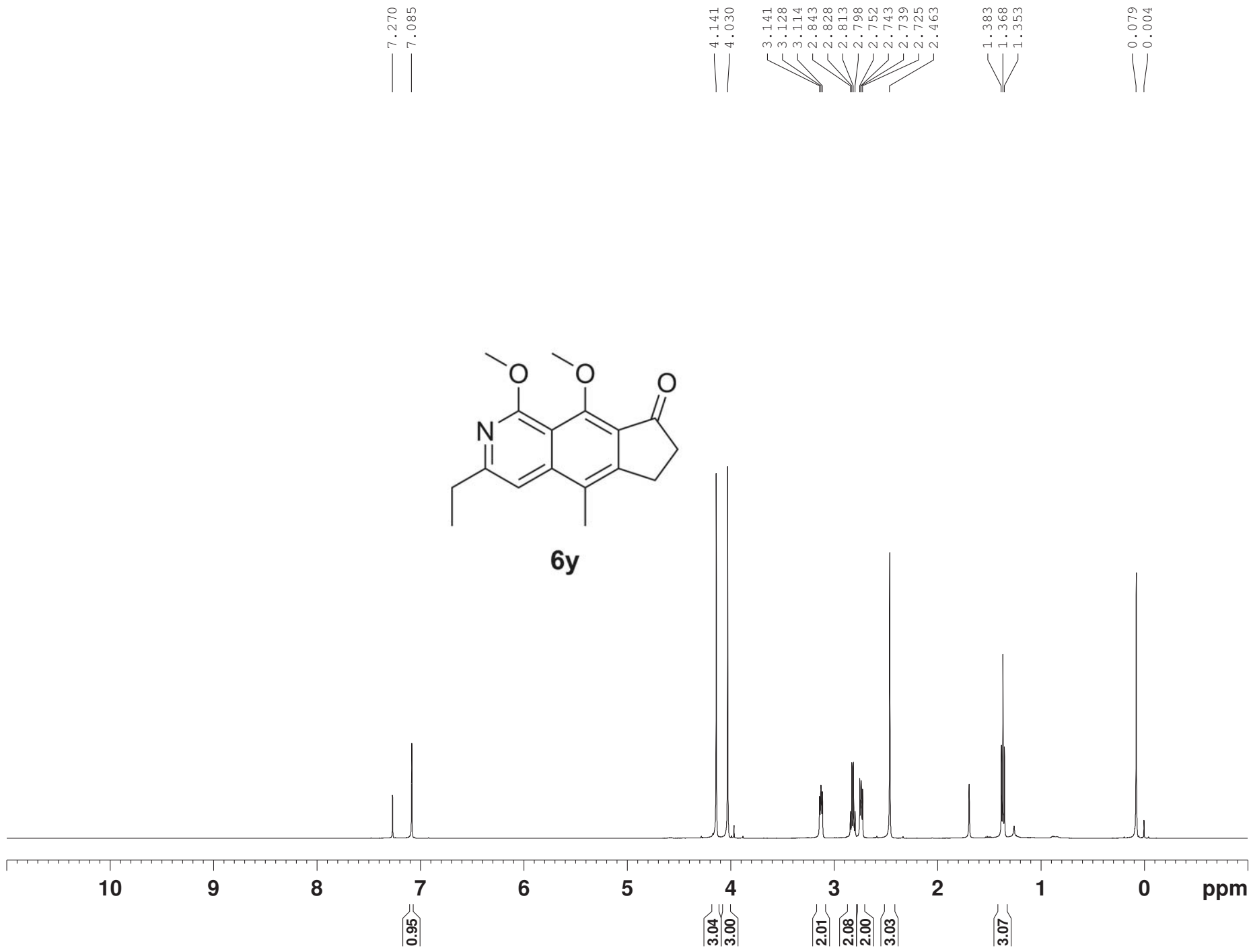
126.50
124.88
123.66
117.04
113.09
77.26
77.00
76.75
63.03
53.59
38.09
37.32
28.43
25.53
24.73
23.36
22.97
0.98
-0.05
159.967
158.780
153.032
149.546
144.082
132.497
126.495
124.882
123.662
117.038
113.091
160 155 150 145 140 135 130 125 120 ppm
38.093
37.319
28.434
25.527
24.734
23.355
22.971
38 36 34 32 30 28 26 24 22 ppm
O
O
O
N
6x
200 180 160 140 120 100 80 60 40 20 0 ppm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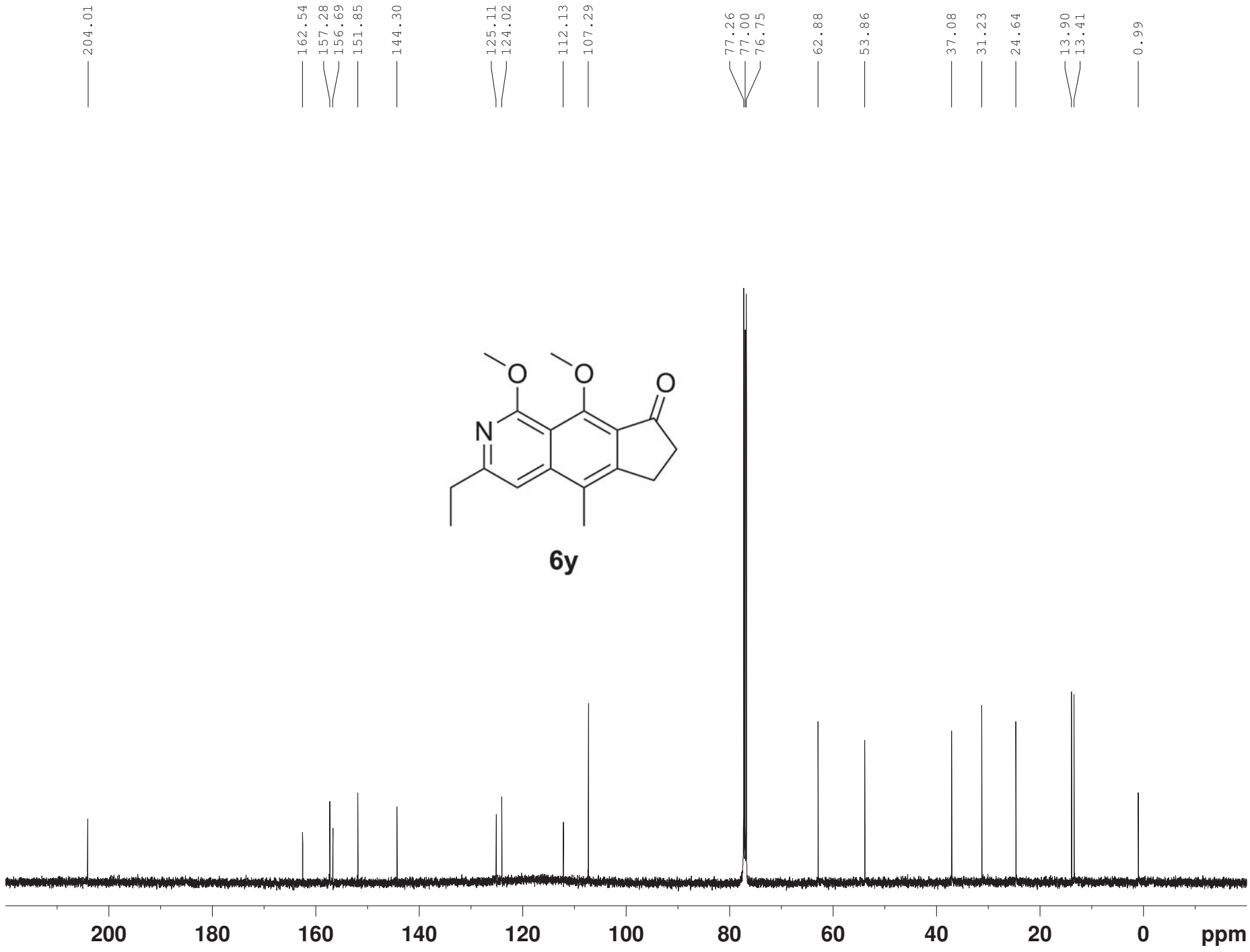
4.141
4.030
3.141
3.128
3.114
2.843
2.828
2.813
2.798
2.752
2.743
2.739
2.725
2.463
1.383
1.368
1.353
0.079
0.004
O
O
O
N
6y
10
9
8
7
6
5
4
3
2
1
0
ppm
0.95
3.04
3.00
2.01
2.08
2.00
3.03
3.07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144.30
125.11
124.02
112.13
107.29
77.26
77.00
76.75
62.88
53.86
37.08
31.23
24.64
13.90
13.41
0.99
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O
O
N
6y
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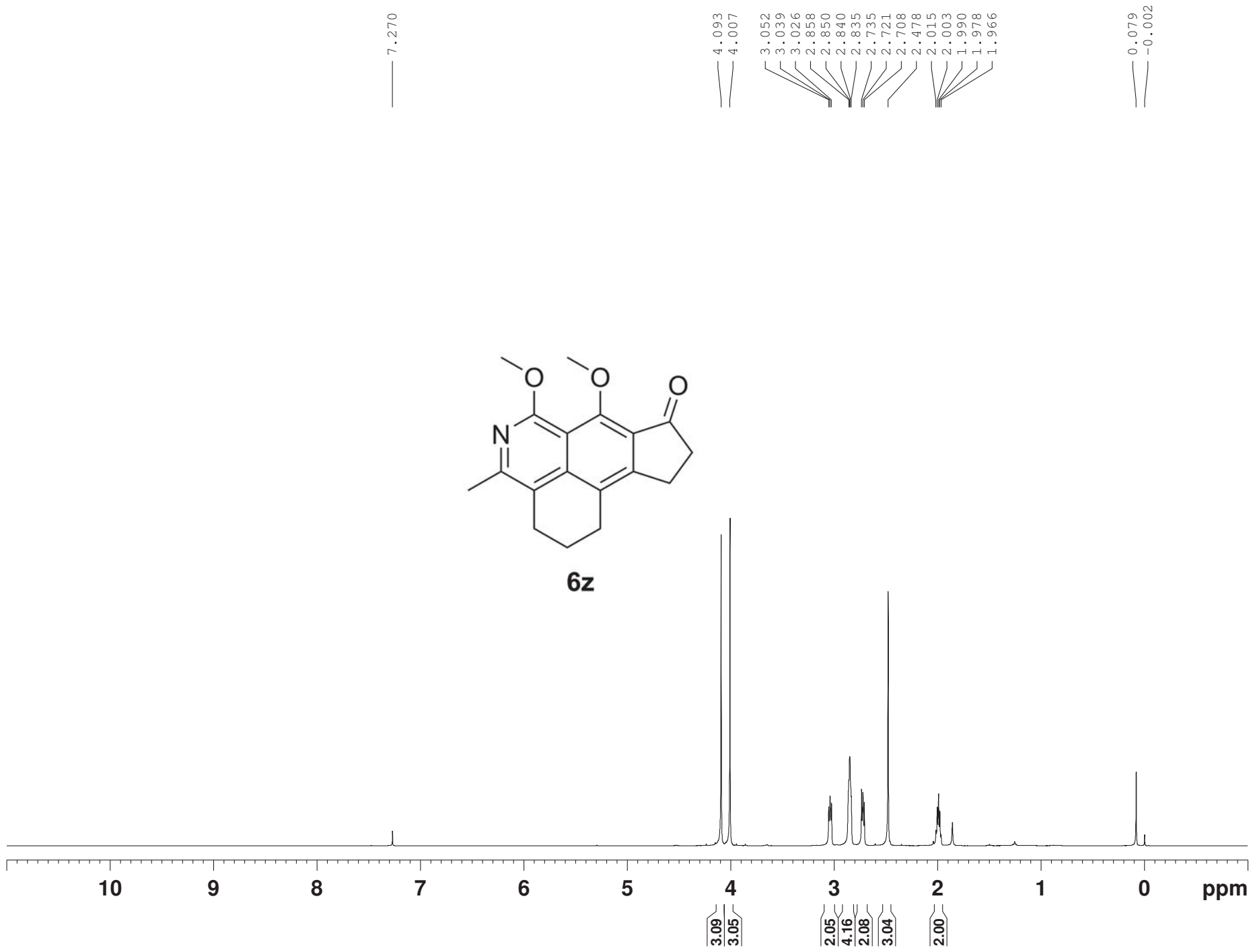
160
140
120
100
80
60
40
20
0
ppm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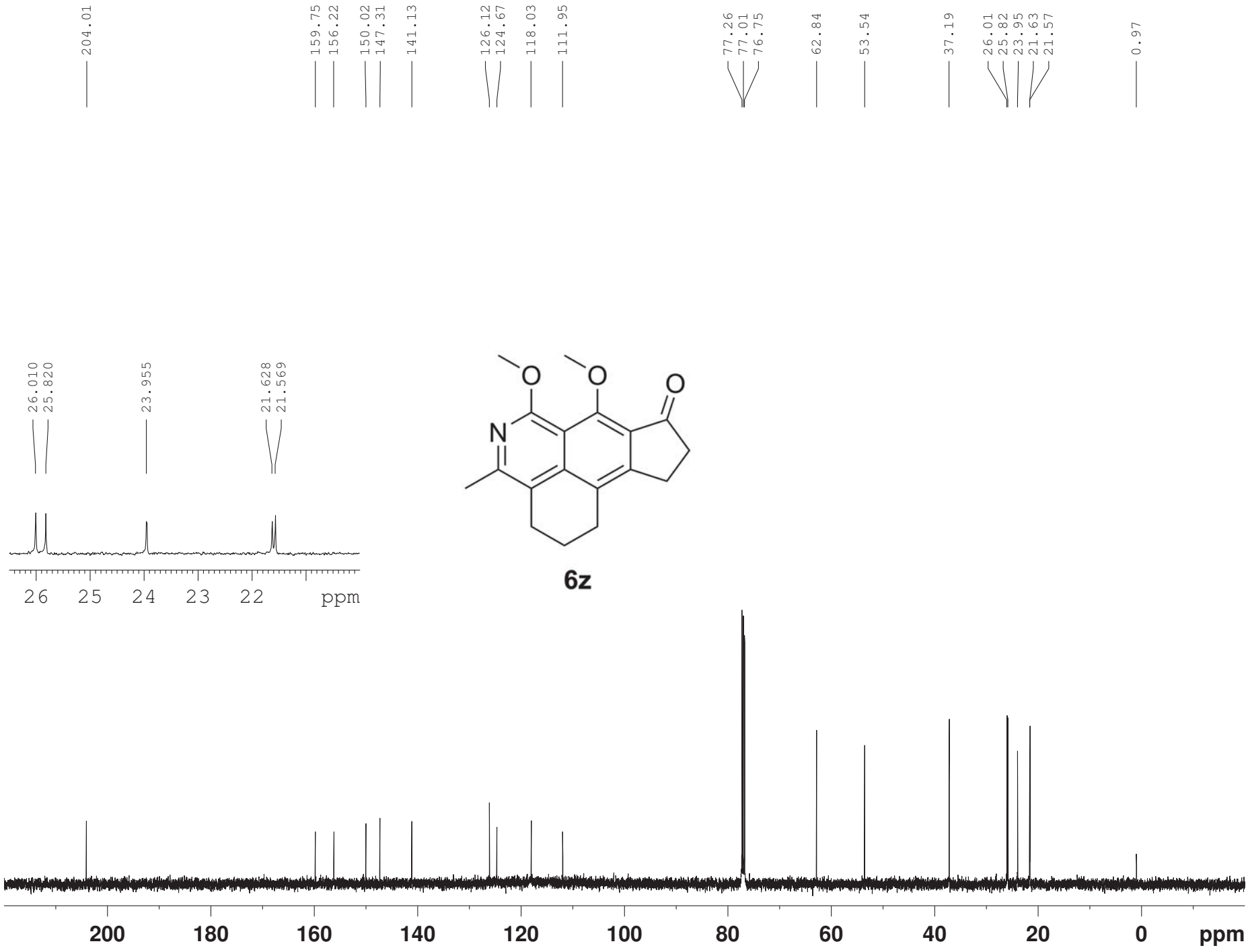
3.039
3.026
2.858
2.850
2.840
2.835
2.735
2.721
2.708
2.478
2.015
2.003
1.990
1.978
1.966
0.079
-0.002
O
O
O
N
6z
10
9
8
7
6
5
4
3
2
1
0
ppm
3.09
3.05
2.05
4.16
2.08
3.04
2.00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126.12
124.67
118.03
111.95
77.26
77.01
76.75
62.84
53.54
37.19
26.01
25.82
23.95
21.63
21.57
0.97
26.010
25.820
23.955
21.628
21.569
26
25
24
23
22
ppm
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O
O
N
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200
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120
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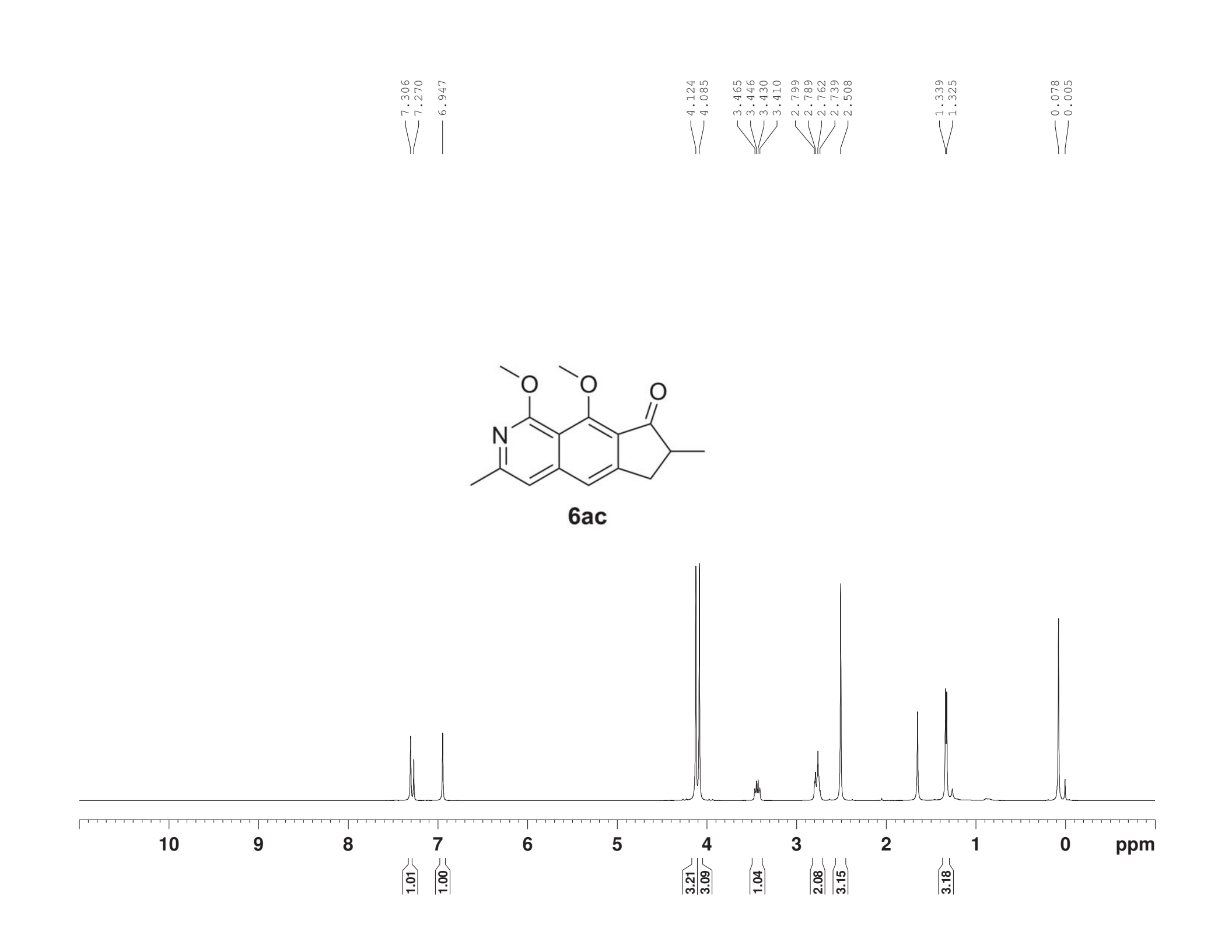
80
60
40
20
0
ppm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4.085
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3.446
3.430
3.410
2.799
2.789
2.762
2.739
2.508
1.339
1.325
0.078
0.005
O
O
O
N
6ac
10
9
8
7
6
5
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ppm
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1.00
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3.09
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2.08
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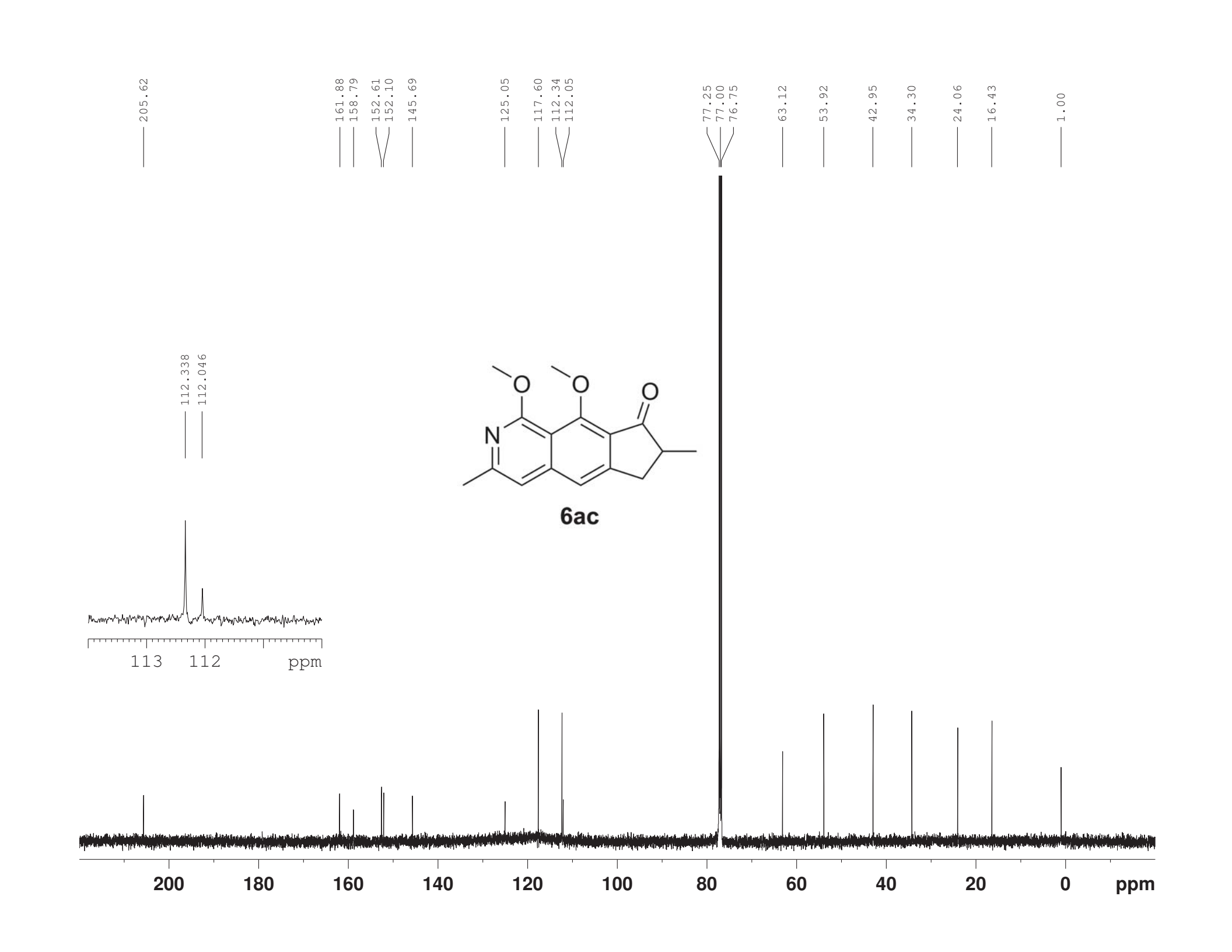
3.18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117.60
112.34
112.05
77.25
77.00
76.75
63.12
53.92
42.95
34.30
24.06
16.43
1.00
112.338
112.046
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112
ppm
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140
120
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80
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40
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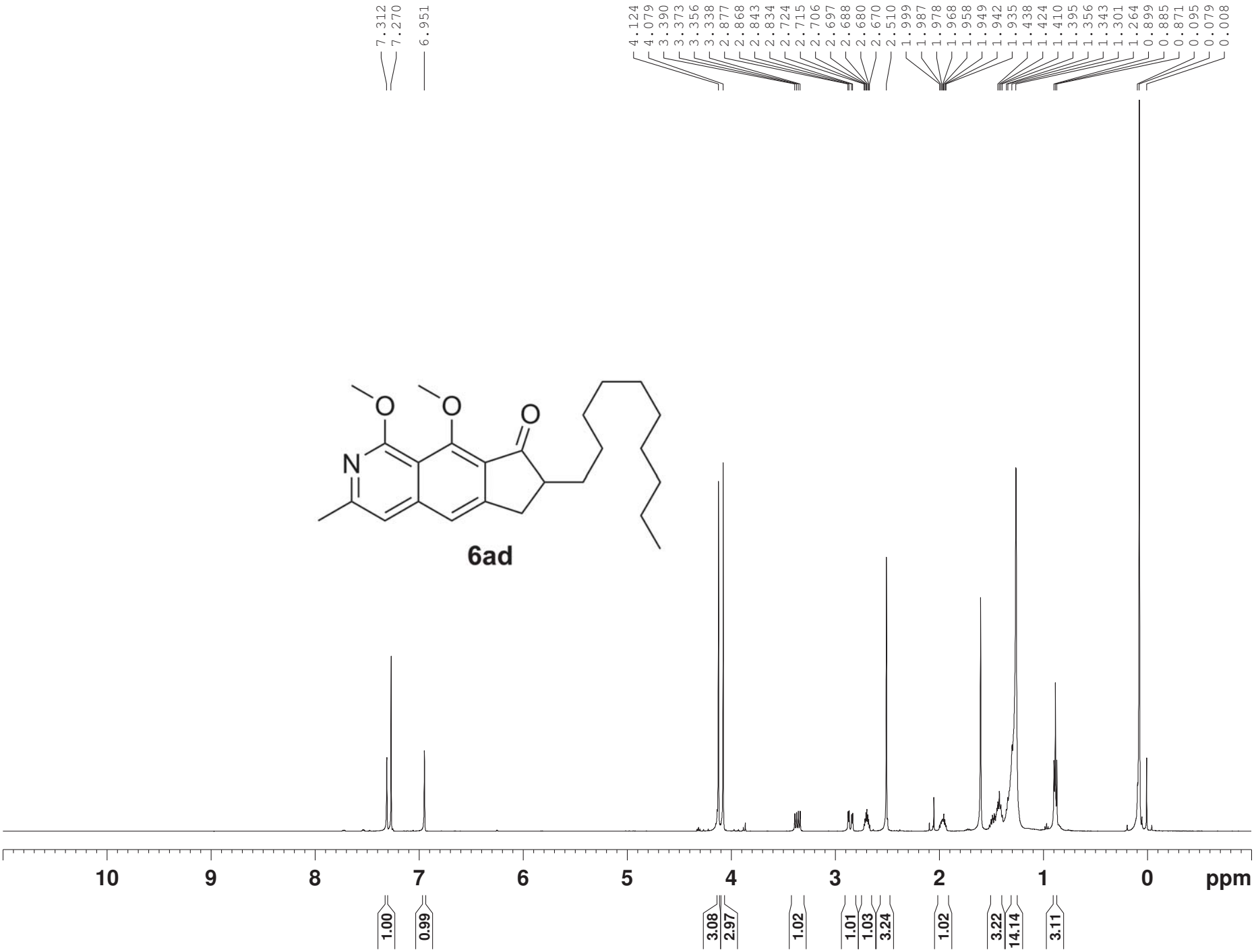
0
ppm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2.724
2.715
2.706
2.697
2.688
2.680
2.670
2.510
1.999
1.987
1.978
1.968
1.958
1.949
1.942
1.935
1.438
1.424
1.410
1.395
1.356
1.343
1.301
1.264
0.899
0.885
0.871
0.095
0.079
0.008
O
O
O
N
6ad
10
9
8
7
6
5
4
3
2
1
0
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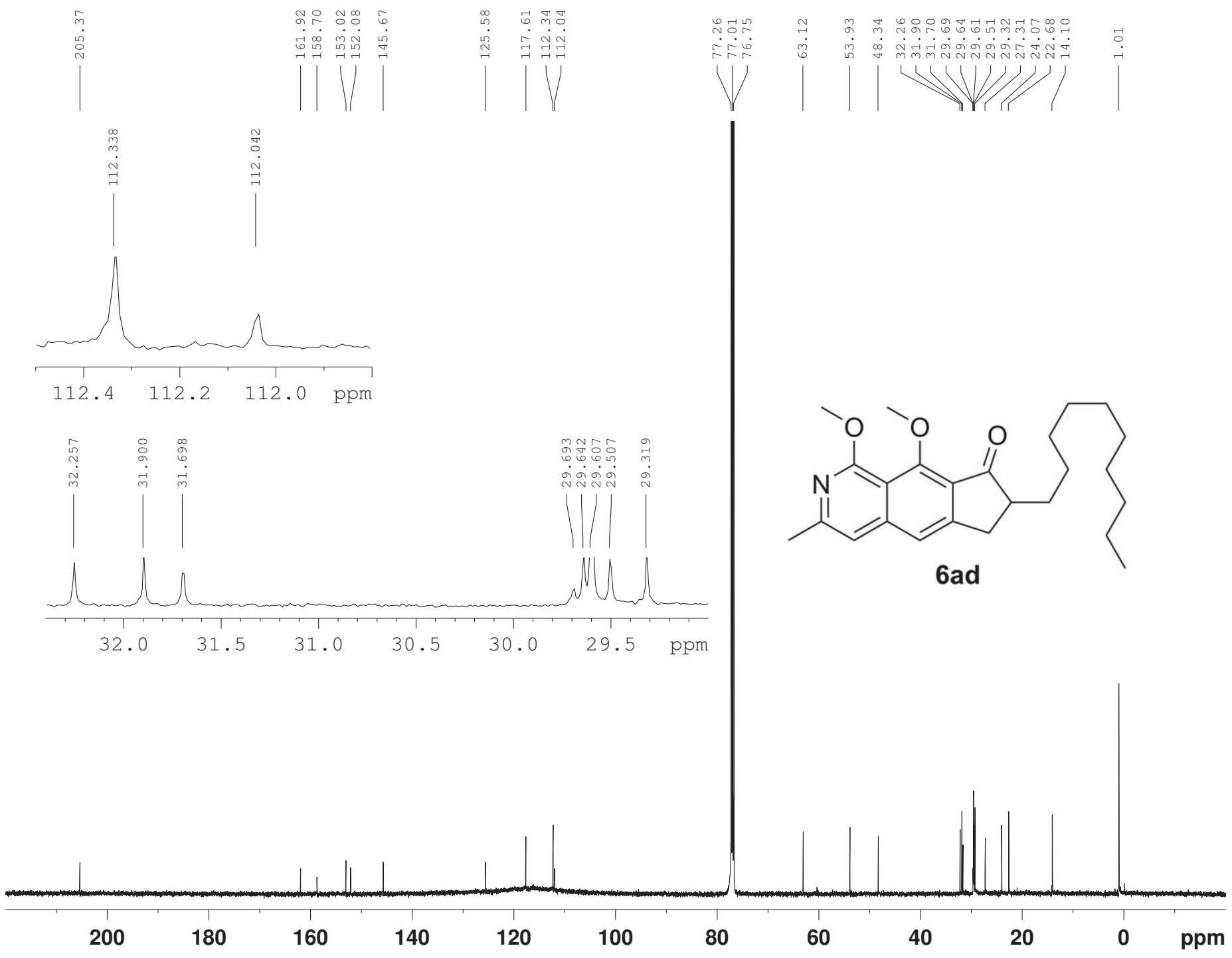
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27.31
24.07
22.68
14.10
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112.2
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29.507
29.319
32.0
31.5
31.0
30.5
30.0
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120
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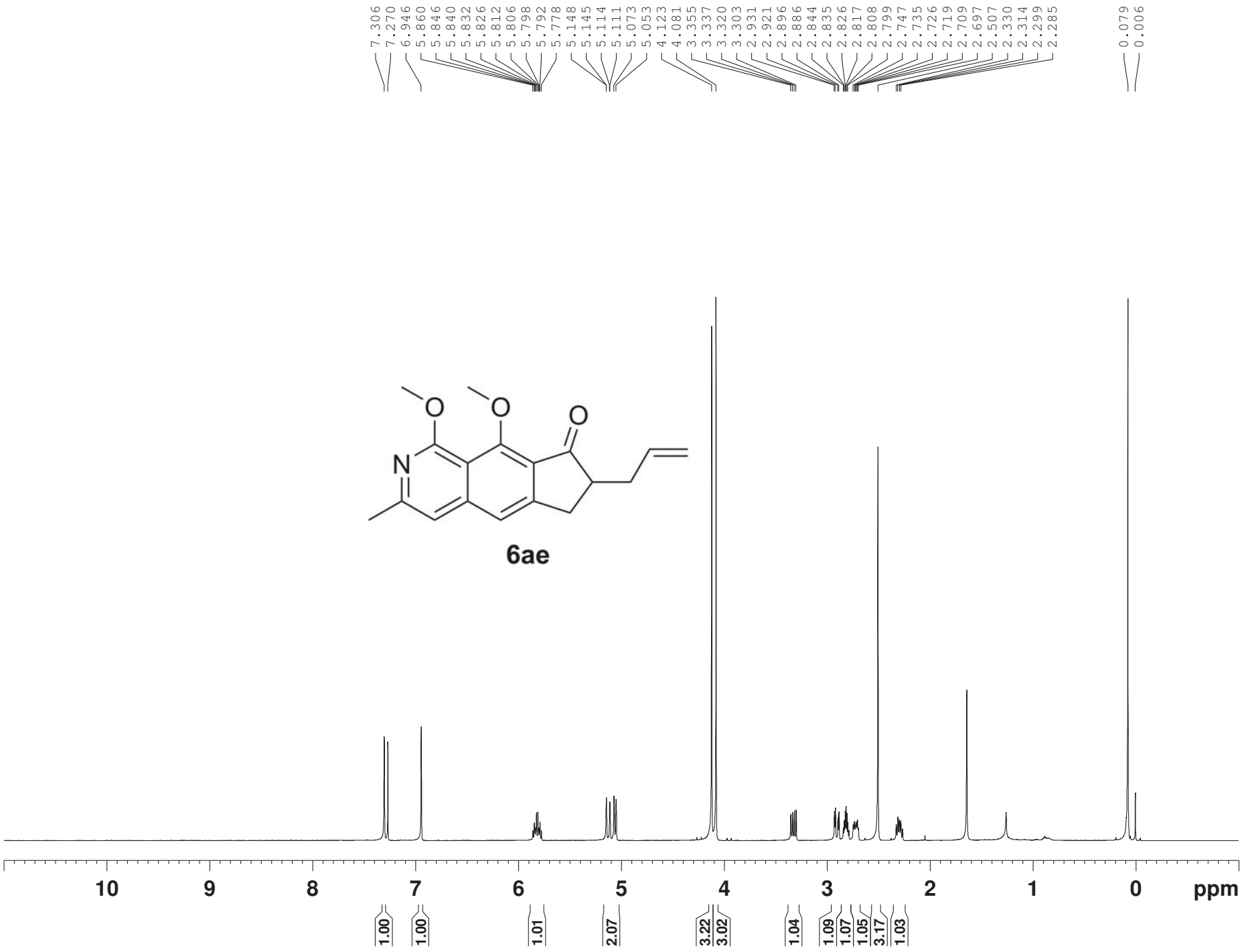
0
ppm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5.778
5.148
5.145
5.114
5.111
5.073
5.053
4.123
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3.303
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2.747
2.735
2.726
2.719
2.709
2.697
2.507
2.330
2.314
2.299
2.285
0.079
0.006
O
O
O
N
6ae
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9
8
7
6
5
4
3
2
1
0
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3.02
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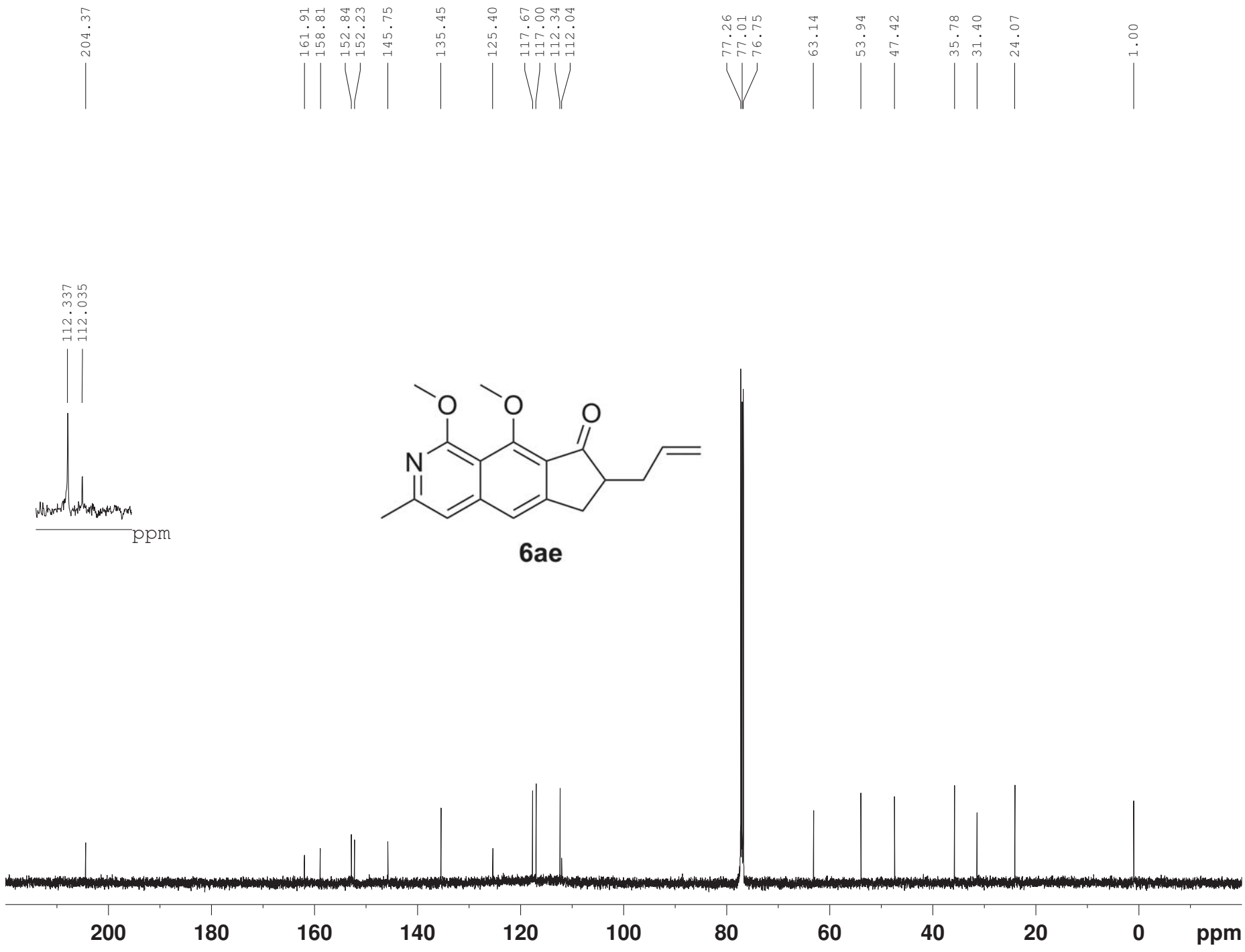
1.09
1.07
1.05
3.17
1.03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125.40
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117.00
112.34
112.04
77.26
77.01
76.75
63.14
53.94
47.42
35.78
31.40
24.07
1.00
112.337
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ppm
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O
O
N
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120
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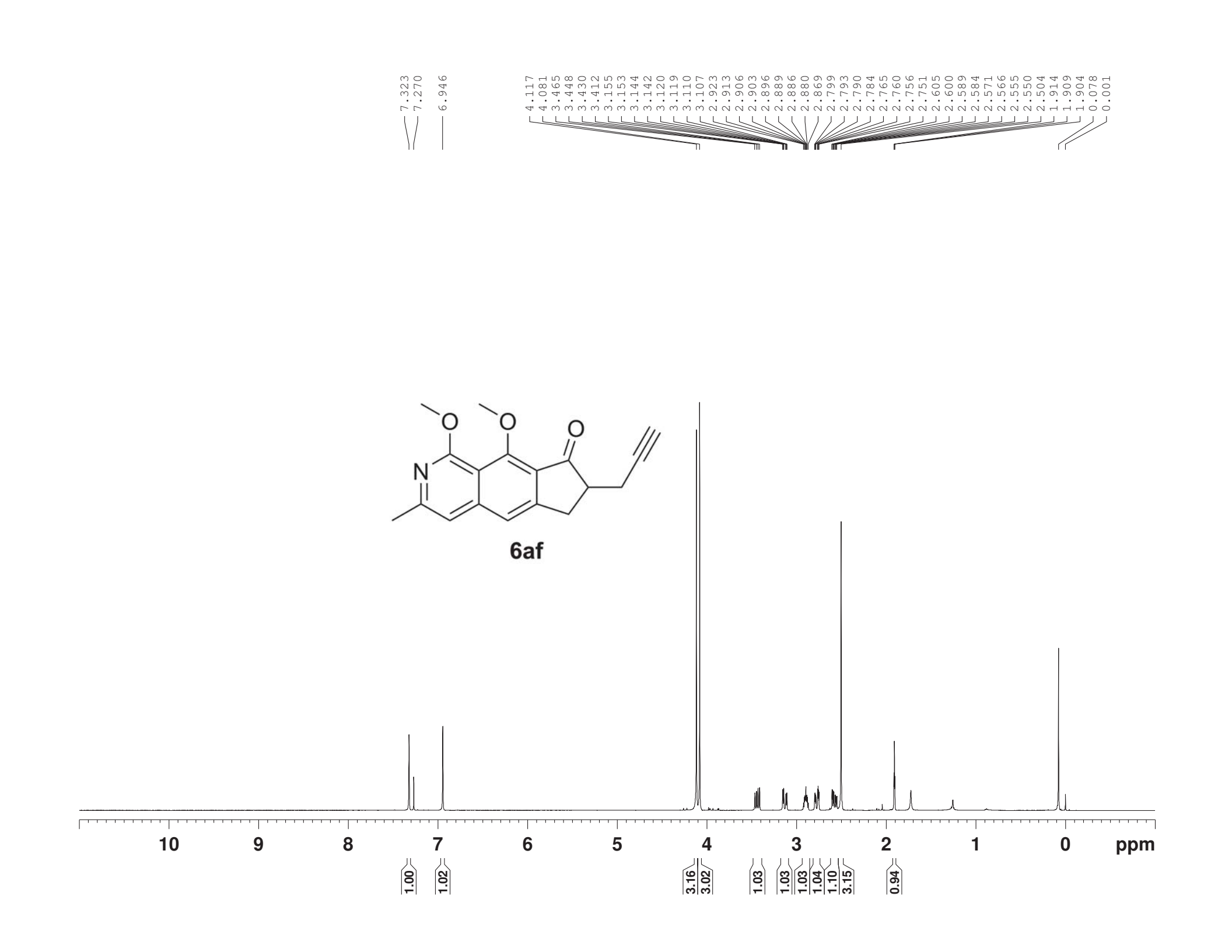
20
0
ppm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3.430
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3.155
3.153
3.144
3.142
3.120
3.119
3.110
3.107
2.923
2.913
2.906
2.903
2.896
2.889
2.886
2.880
2.869
2.799
2.793
2.790
2.784
2.765
2.760
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2.589
2.584
2.571
2.566
2.555
2.550
2.504
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1.909
1.904
0.078
0.001
O
O
O
N
6af
10
9
8
7
6
5
4
3
2
1
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1.03
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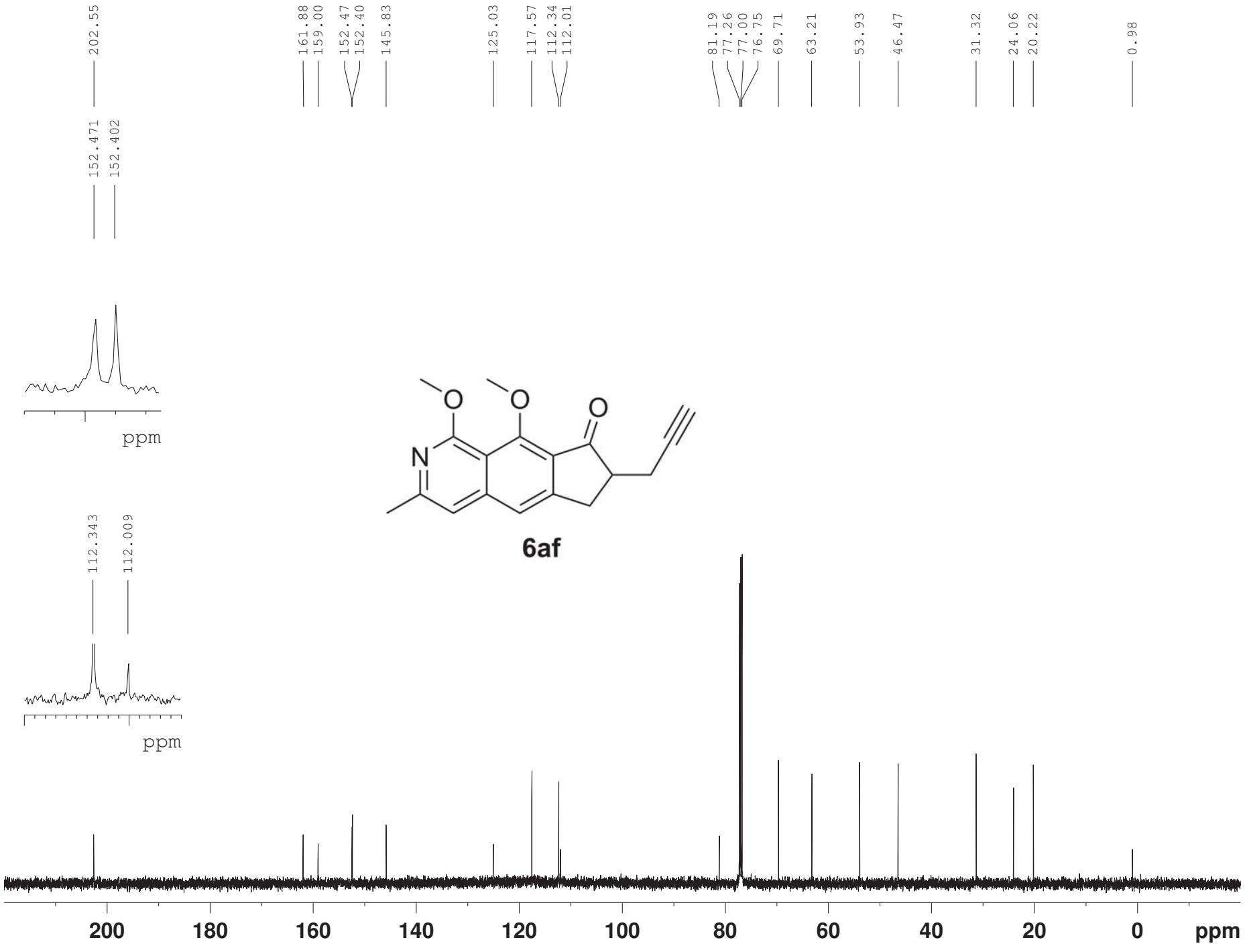
0.94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112.01
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77.00
76.75
69.71
63.21
53.93
46.47
31.32
24.06
20.22
0.98
152.471
152.402
ppm
112.343
112.009
ppm
O
O
O
N
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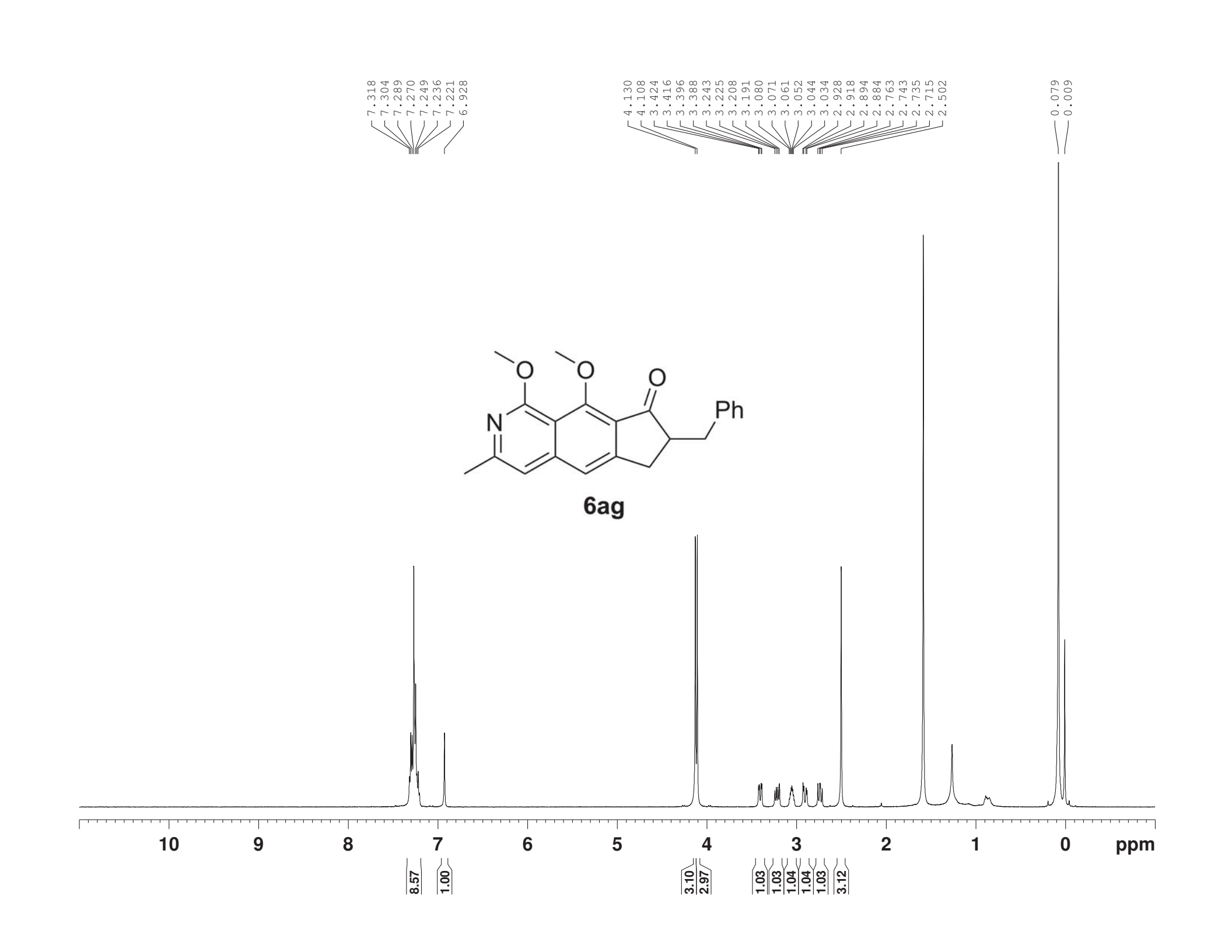
200
180
160
140
120
100
80
60
40
20
0
ppm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4.108
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3.396
3.388
3.243
3.225
3.208
3.191
3.080
3.071
3.061
3.052
3.044
3.034
2.928
2.918
2.894
2.884
2.763
2.743
2.735
2.715
2.502
0.079
0.009
O
O
O
N
Ph
6ag
10
9
8
7
6
5
4
3
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1.03
1.04
1.04
1.03
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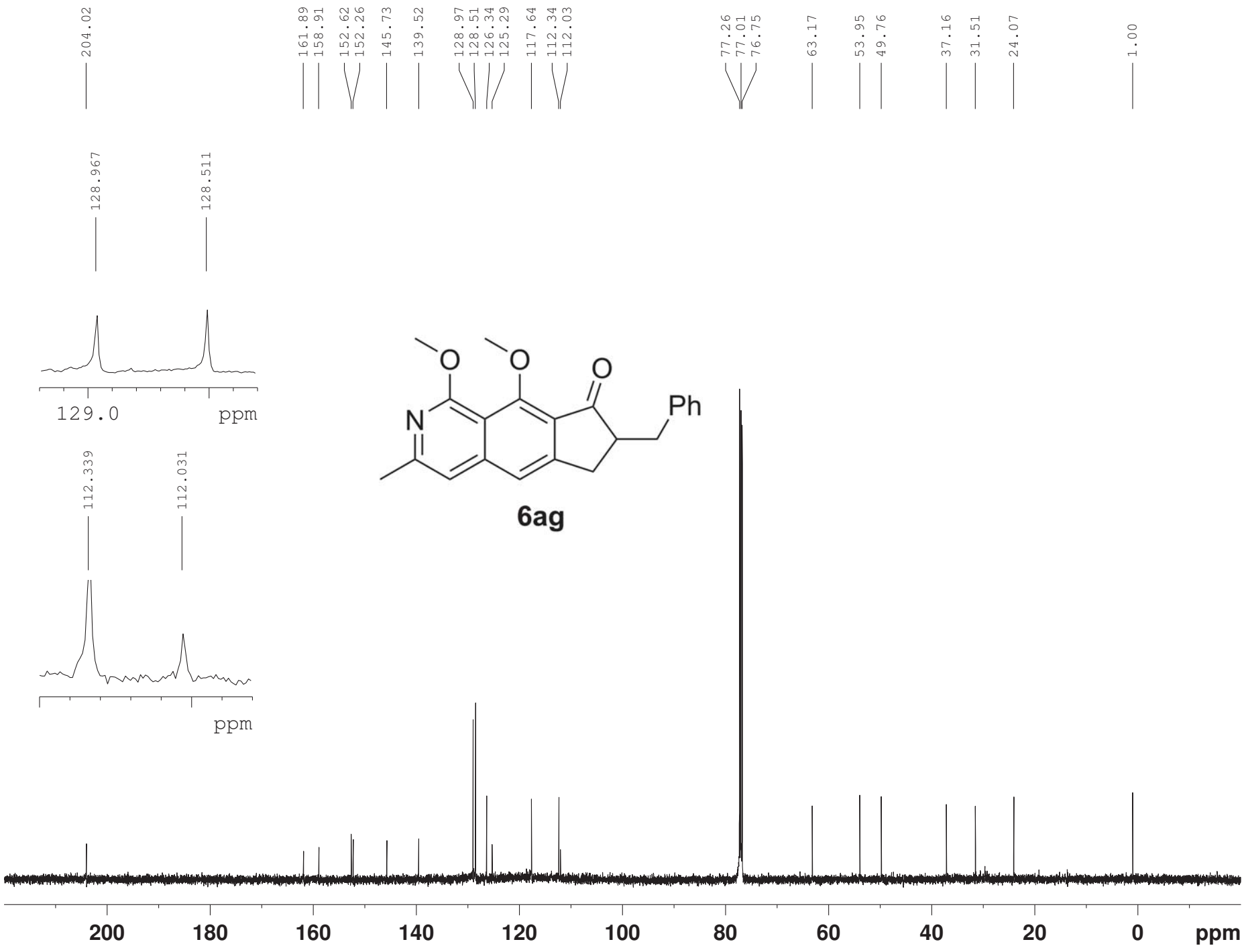
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77.26
77.01
76.75
63.17
53.95
49.76
37.16
31.51
24.07
1.00
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128.511
129.0
ppm
112.339
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O
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Ph
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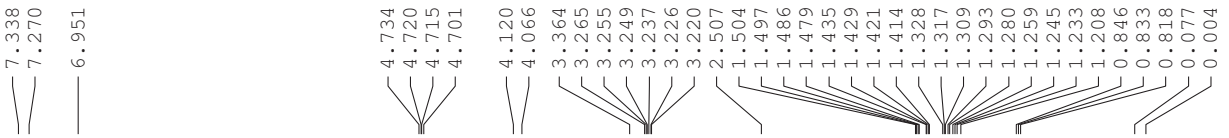
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3.255
3.249
3.237
3.226
3.220
2.507
1.504
1.497
1.486
1.479
1.435
1.429
1.421
1.414
1.328
1.317
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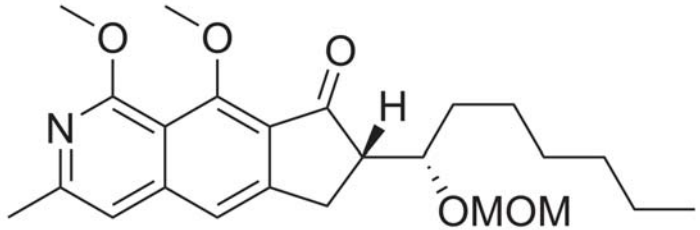
0.004


O
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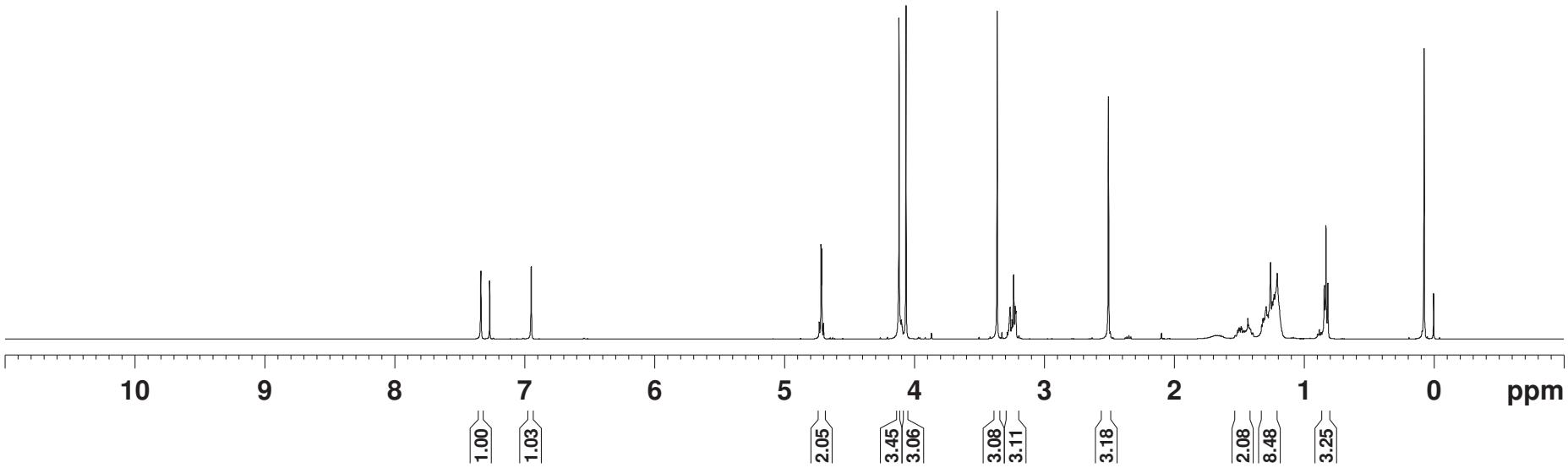
N
OMOM

6ah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3.06
3.08
3.11
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2.08
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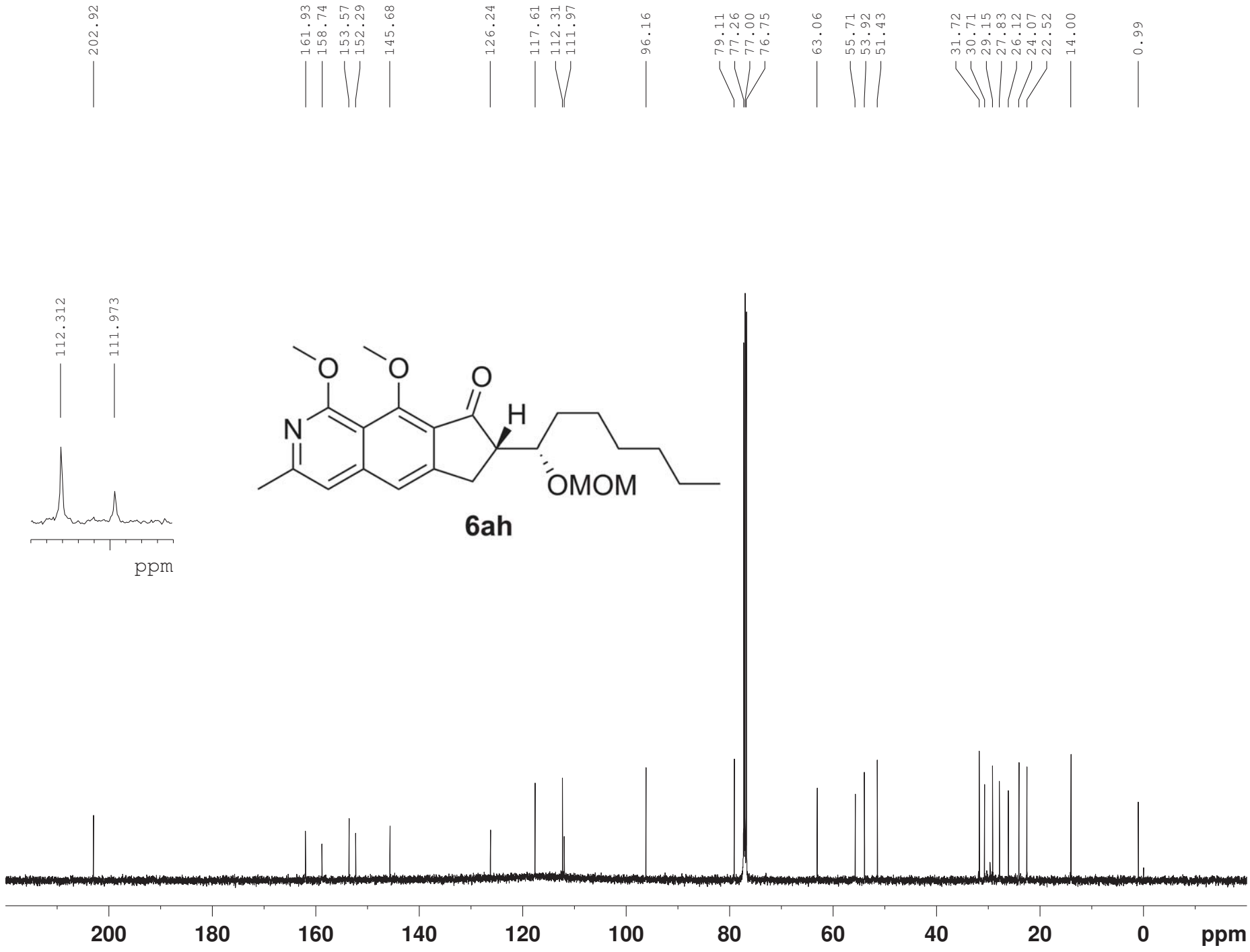
3.25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79.11
77.26
77.00
76.75
63.06
55.71
53.92
51.43
31.72
30.71
29.15
27.83
26.12
24.07
22.52
14.00
0.99
112.312
111.973
ppm
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O
O
N
H
OMOM
6ah
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120
100
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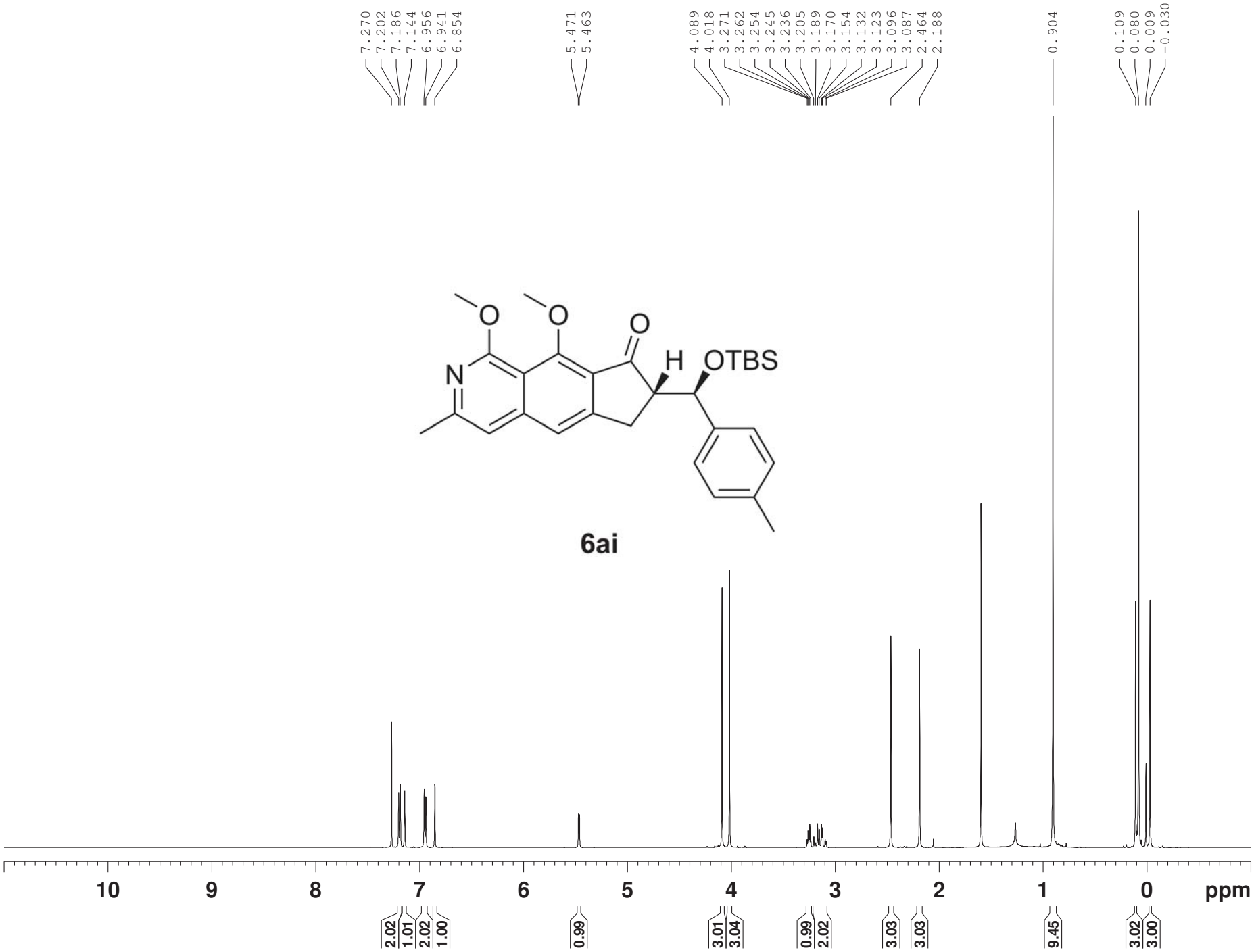
60
40
20
0
ppm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4.018
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3.262
3.254
3.245
3.236
3.205
3.189
3.170
3.154
3.132
3.123
3.096
3.087
2.464
2.188
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0.109
0.080
0.009
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O
O
O
N
H
OTBS
6ai
10
9
8
7
6
5
4
3
2
1
0
ppm
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2.02
1.00
0.99
3.01
3.04
0.99
2.02
3.03
3.03
9.45
3.02
3.00

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158.57
153.55
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77.26
77.01
76.75
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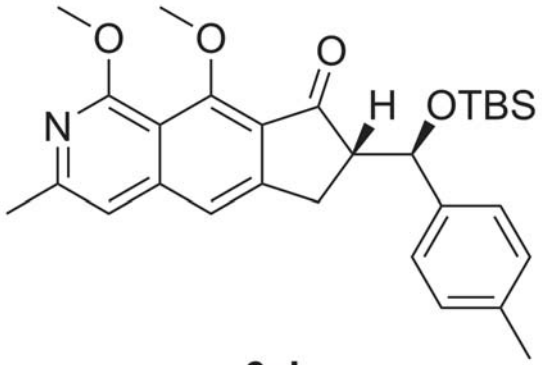

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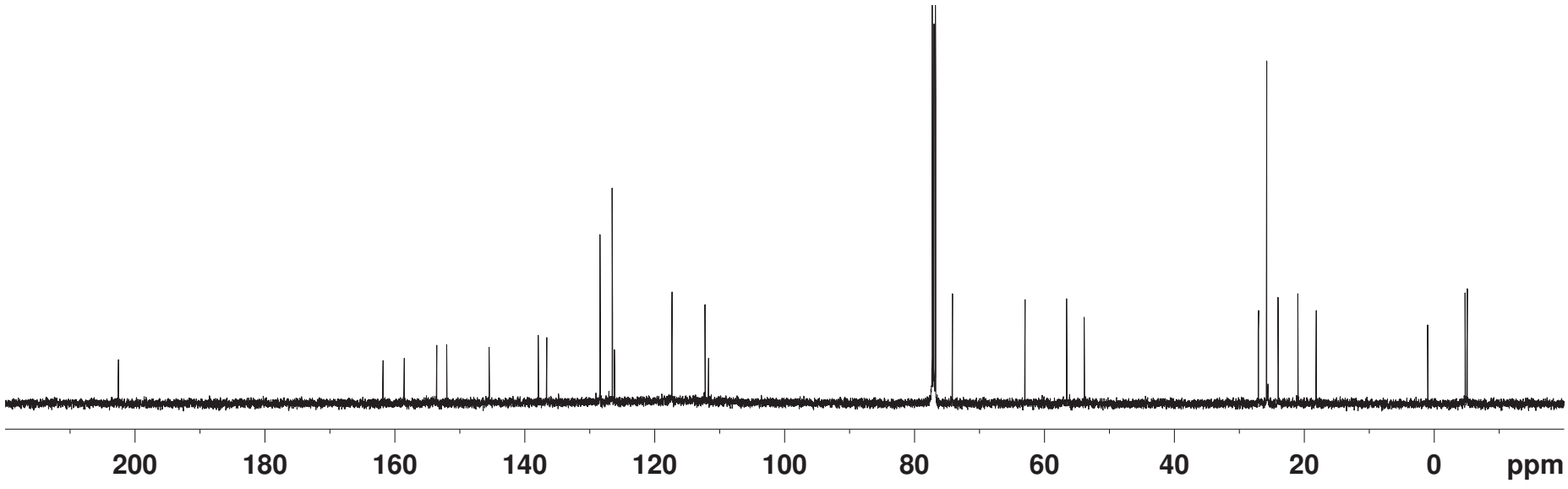

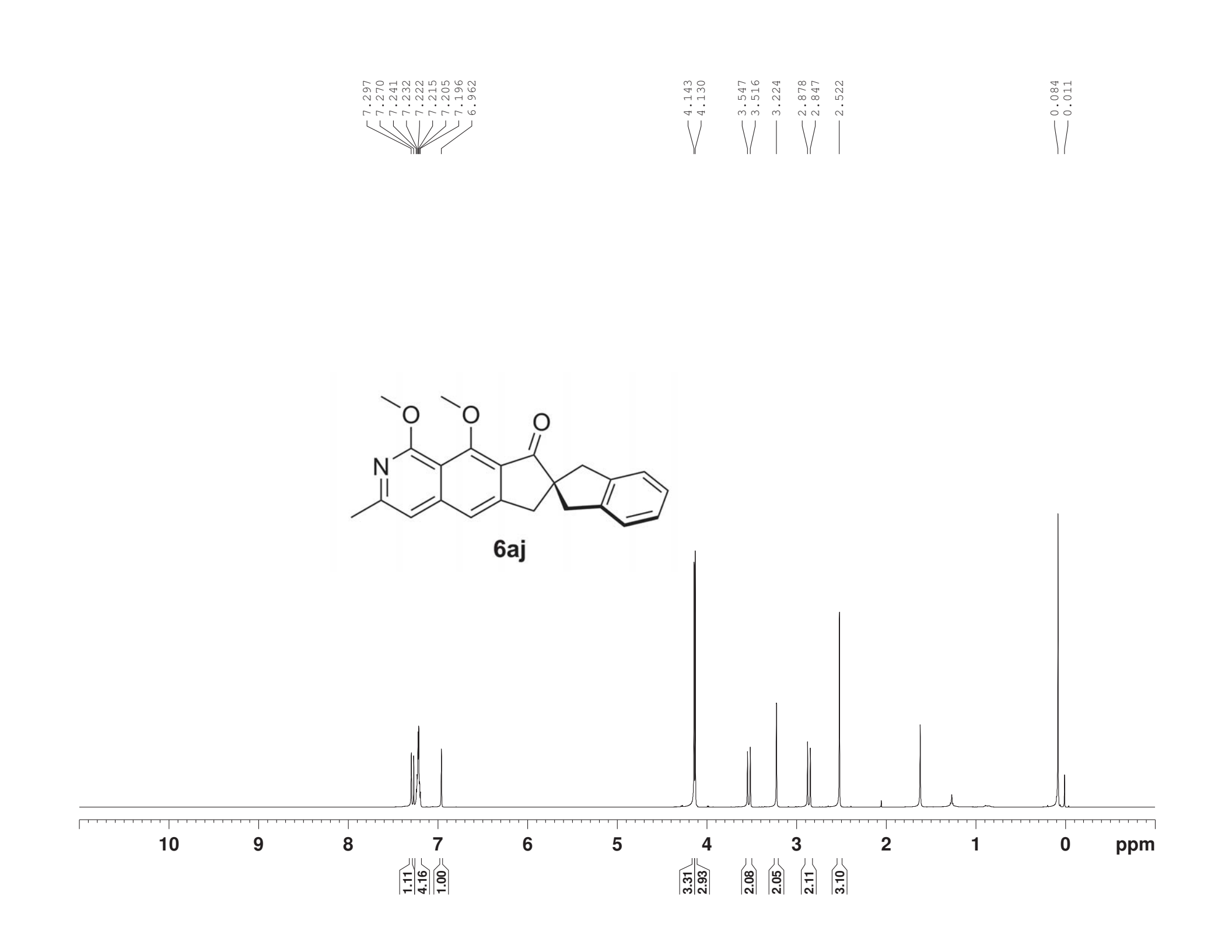
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7.241
7.232
7.222
7.215
7.205
7.196
6.962
4.143
4.130
3.547
3.516
3.224
2.878
2.847
2.522
0.084
0.011
O
O
O
N
6aj
10
9
8
7
6
5
4
3
2
1
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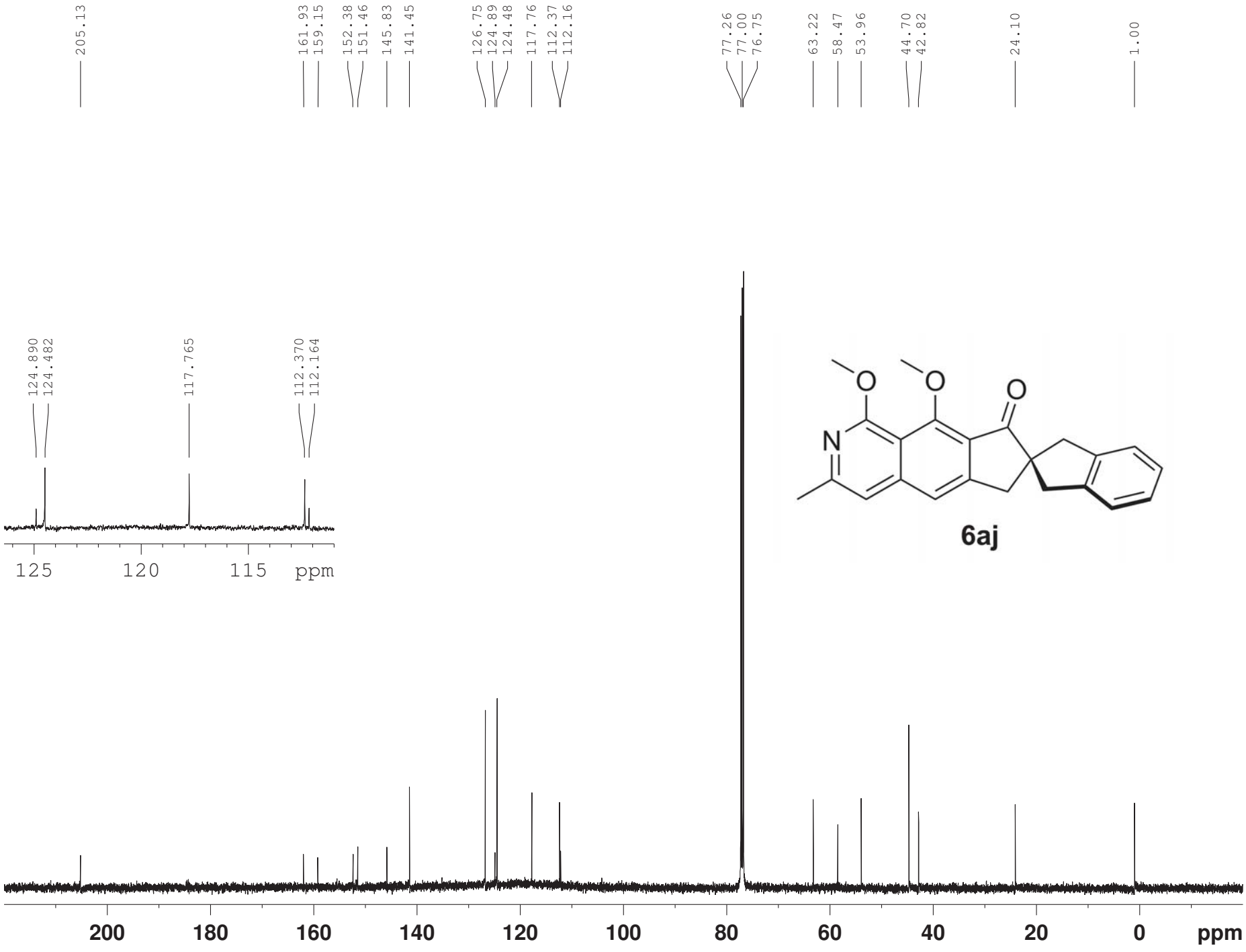
ppm
1.11
4.16
1.00
3.31
2.93
2.08
2.05
2.11
3.10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145.83
141.45
126.75
124.89
124.48
117.76
112.37
112.16
77.26
77.00
76.75
63.22
58.47
53.96
44.70
42.82
24.10
1.00
124.890
124.482
117.765
112.370
112.164
125
120
115
ppm
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O
O
N
6aj
200
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120
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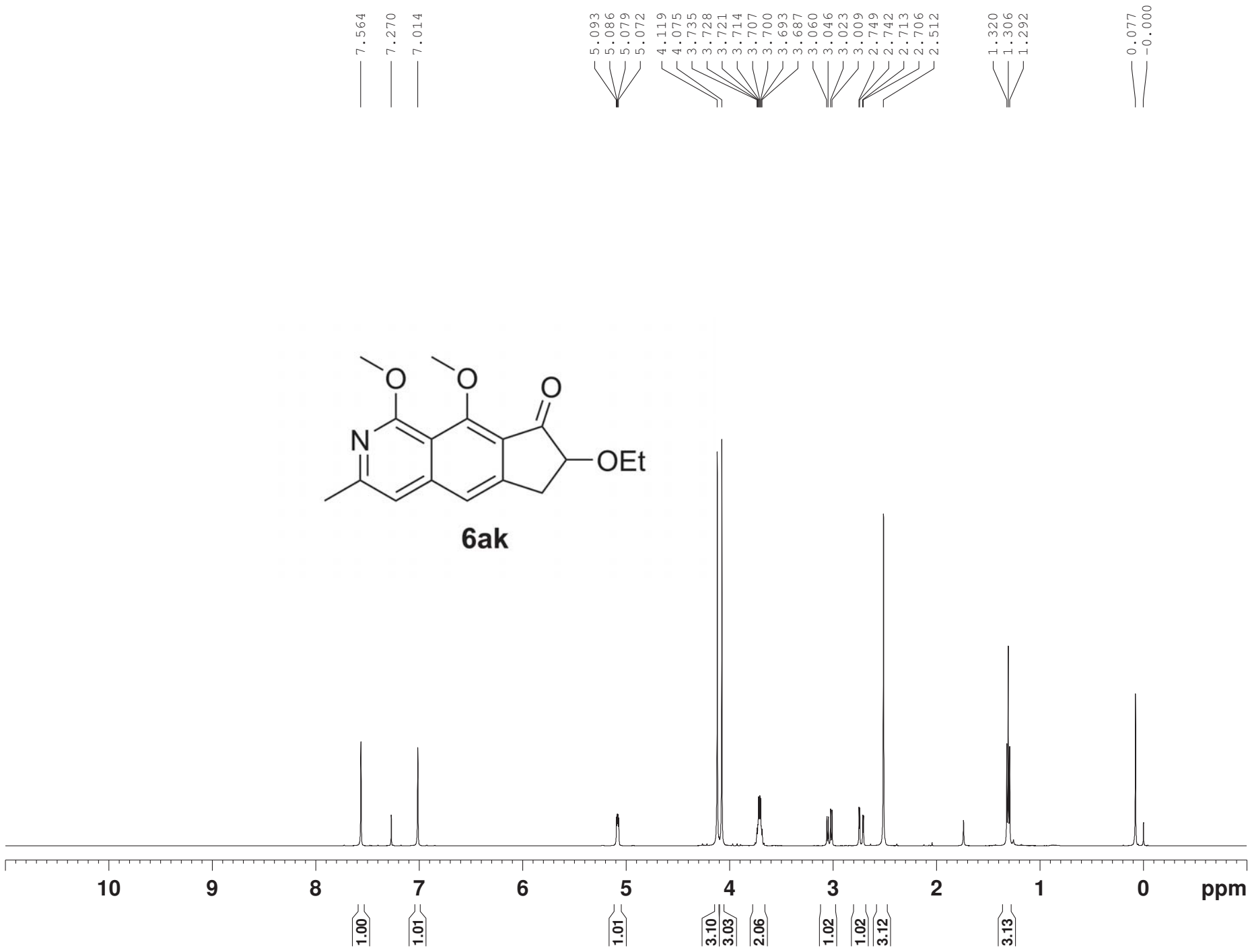
80
60
40
20
0
ppm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5.072
4.119
4.075
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3.728
3.721
3.714
3.707
3.700
3.693
3.687
3.060
3.046
3.023
3.009
2.749
2.742
2.713
2.706
2.512
1.320
1.306
1.292
0.077
-0.000
O
O
O
N
OEt
6ak
10
9
8
7
6
5
4
3
2
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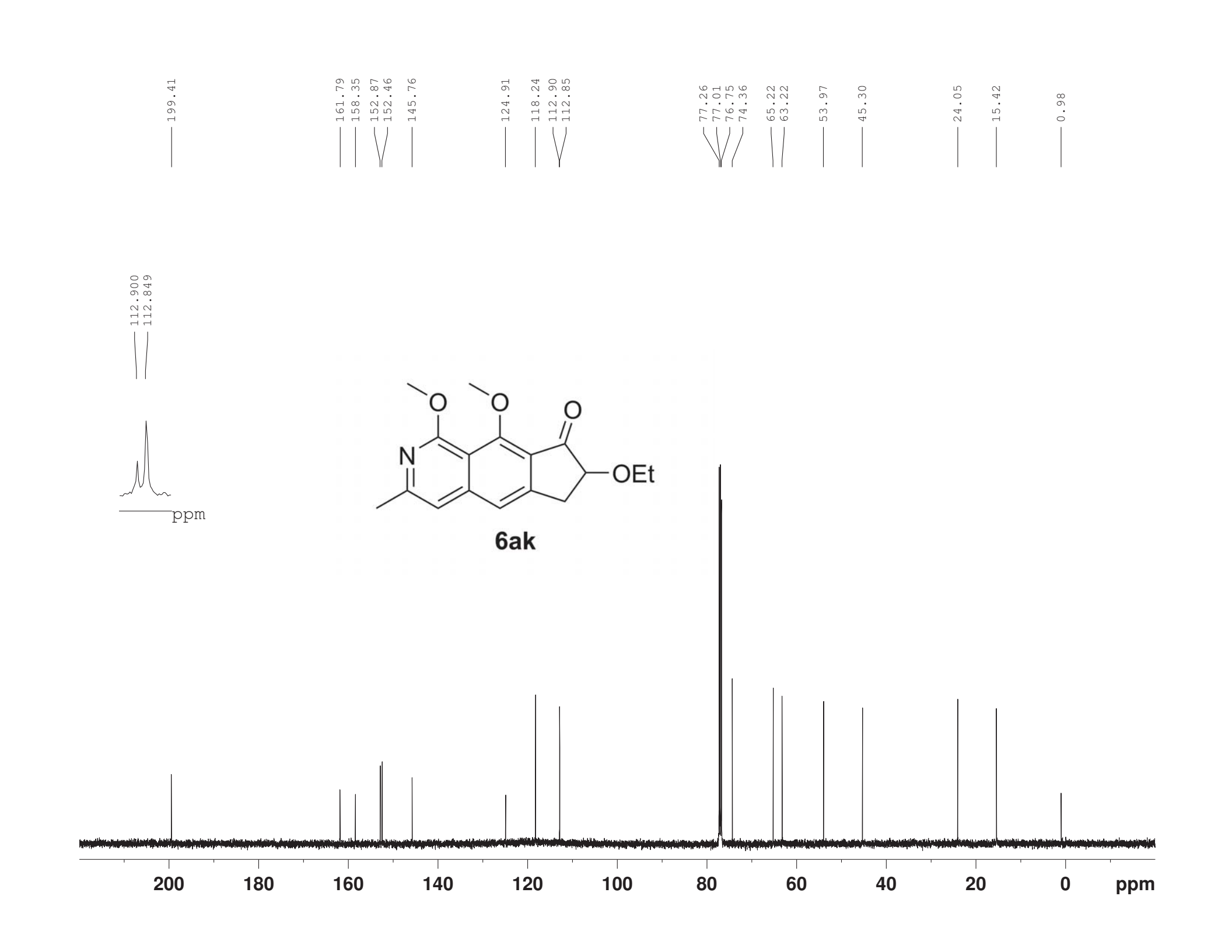
1.01
1.01
3.10
3.03
2.06
1.02
1.02
3.12
3.13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112.85
77.26
77.01
76.75
74.36
65.22
63.22
53.97
45.30
24.05
15.42
0.98
112.900
112.849
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O
N
OEt
6ak
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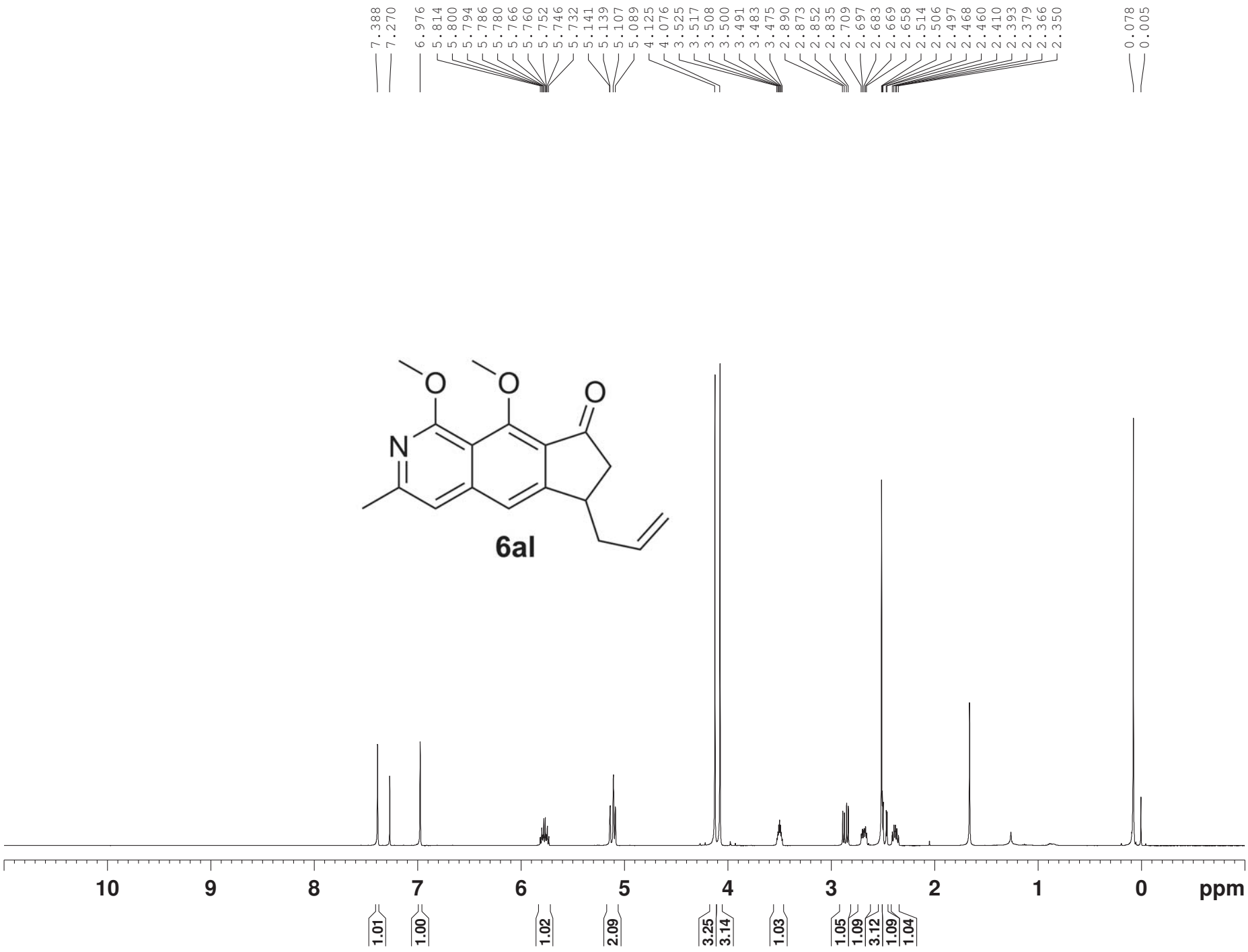
120
100
80
60
40
20
0
ppm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5.786
5.780
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5.760
5.752
5.746
5.732
5.141
5.139
5.107
5.089
4.125
4.076
3.525
3.517
3.508
3.500
3.491
3.483
3.475
2.890
2.873
2.852
2.835
2.709
2.697
2.683
2.669
2.658
2.514
2.506
2.497
2.468
2.460
2.410
2.393
2.379
2.366
2.350
0.078
0.005
O
O
O
N
6al
10
9
8
7
6
5
4
3
2
1
0
ppm
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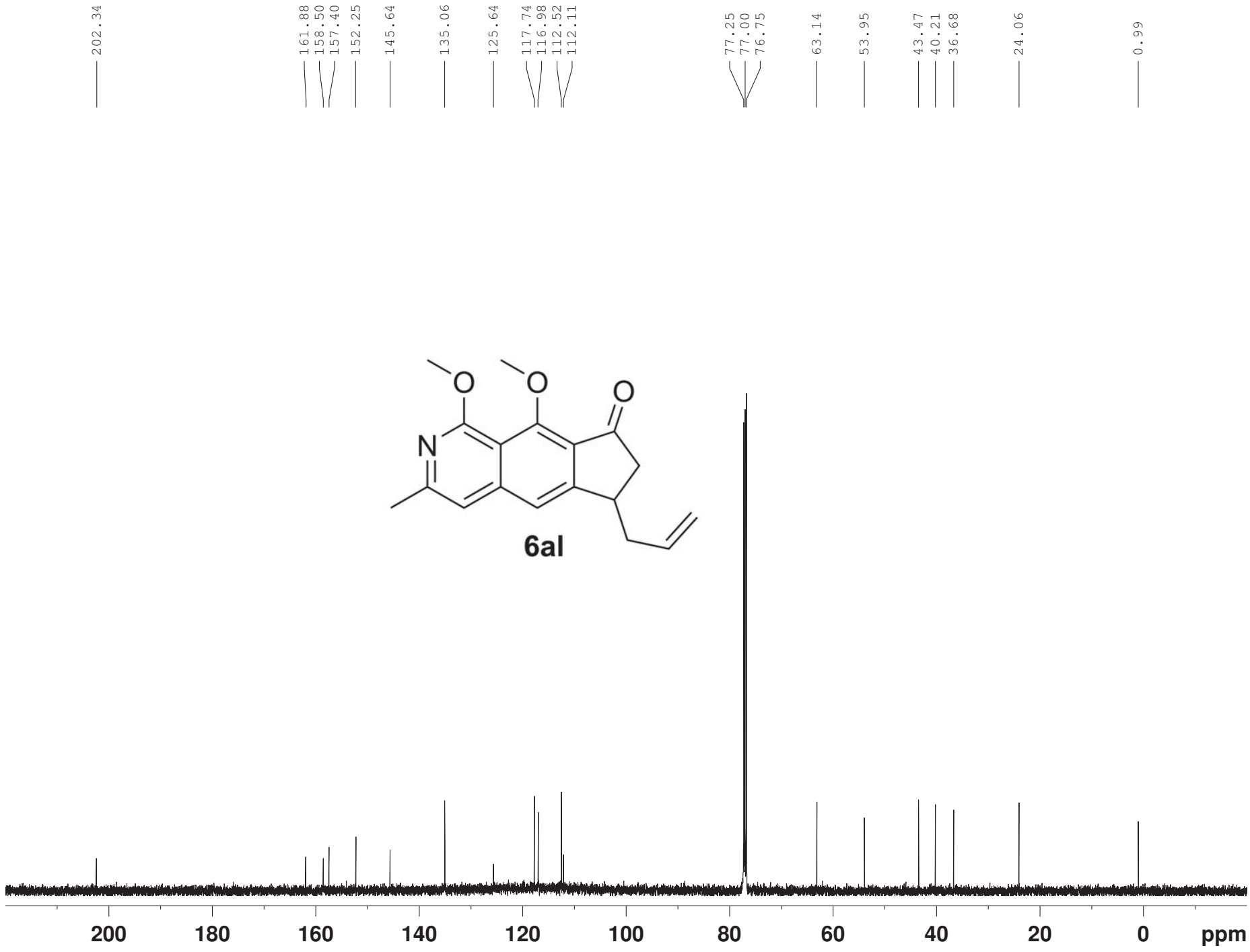
1.00
1.02
2.09
3.25
3.14
1.03
1.05
1.09
3.12
1.09
1.04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145.64
135.06
125.64
117.74
116.98
112.52
112.11
77.25
77.00
76.75
63.14
53.95
43.47
40.21
36.68
24.06
0.99
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O
O
N
6al
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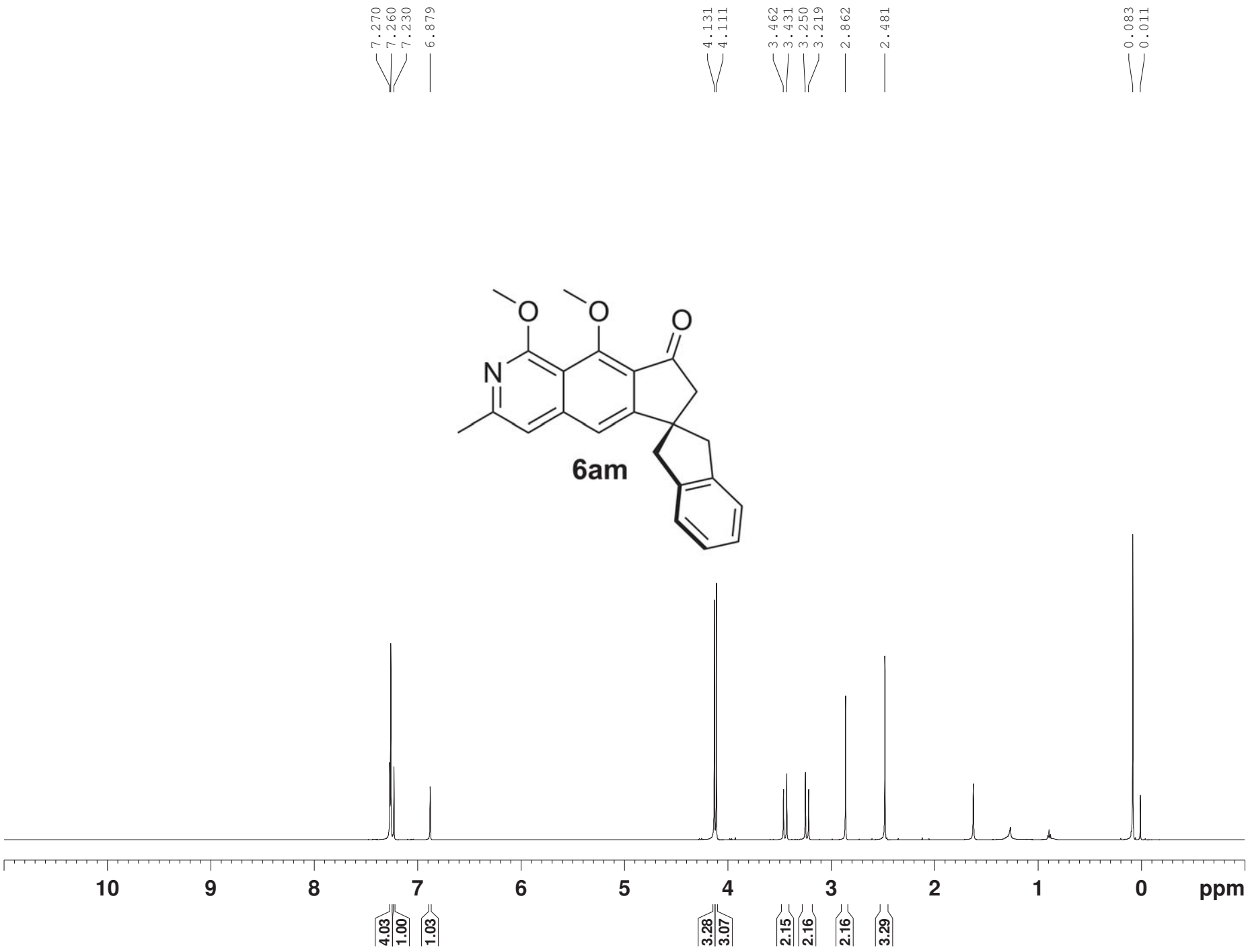
160
140
120
100
80
60
40
20
0
ppm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4.111
3.462
3.431
3.250
3.219
2.862
2.481
0.083
0.011
O
O
O
N
6am
10
9
8
7
6
5
4
3
2
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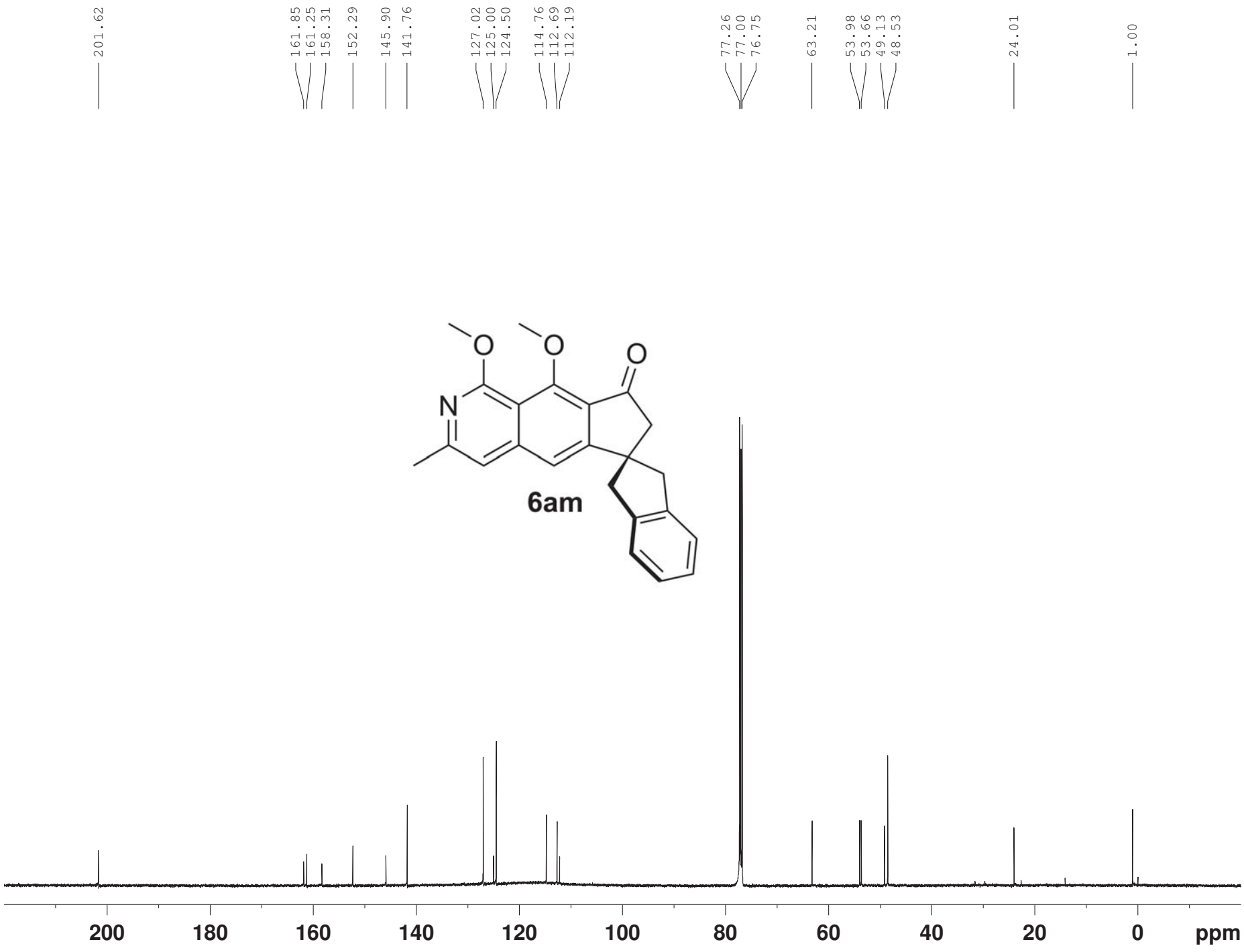
ppm
4.03
1.00
1.03
3.28
3.07
2.15
2.16
2.16
3.29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161.25
158.31
152.29
145.90
141.76
127.02
125.00
124.50
114.76
112.69
112.19
77.26
77.00
76.75
63.21
53.98
53.66
49.13
48.53
24.01
1.00
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O
O
N
6am
200
180
160
140
120
100
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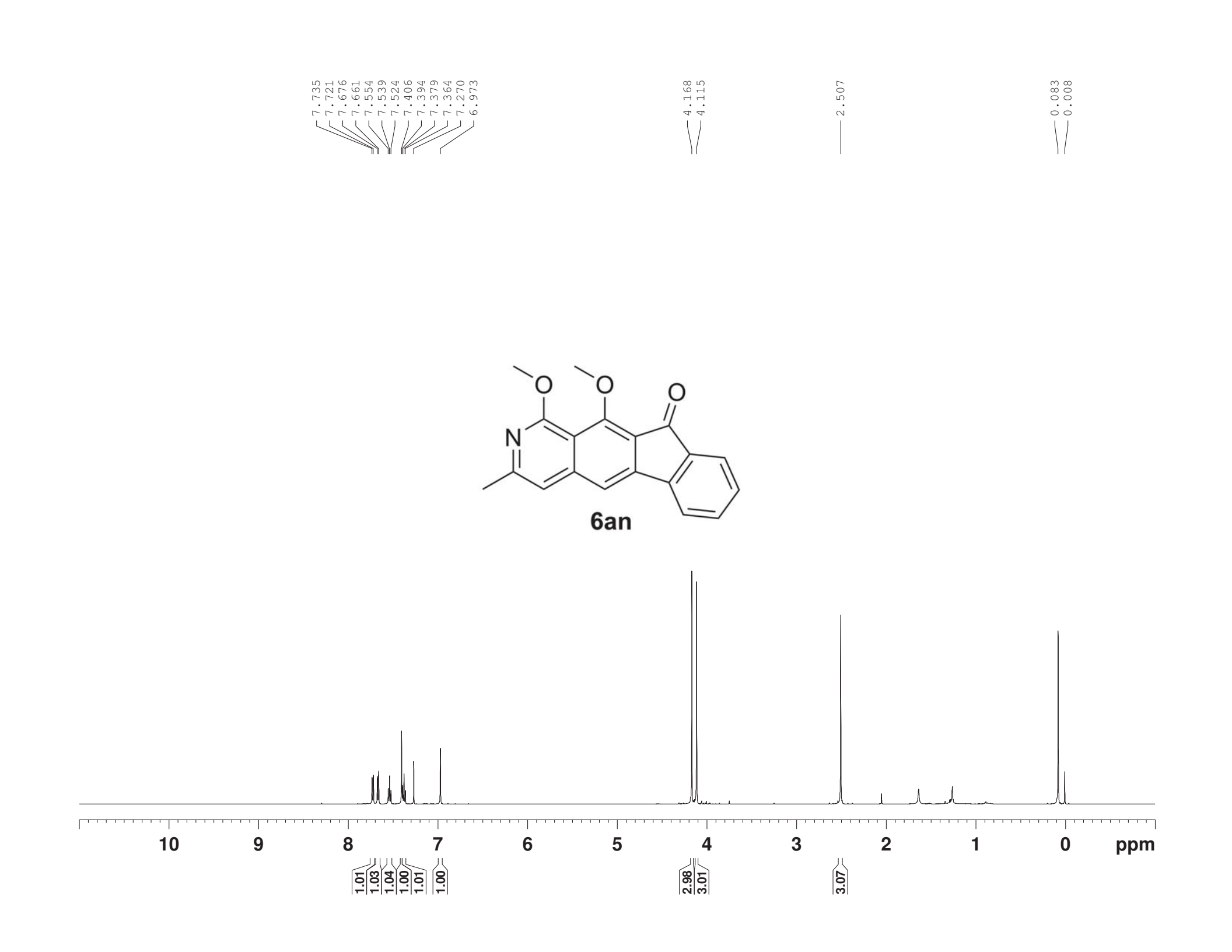
60
40
20
0
ppm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7.539
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7.406
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7.379
7.364
7.270
6.973
4.168
4.115
2.507
0.083
0.008
O
O
O
N
6an
10
9
8
7
6
5
4
3
2
1
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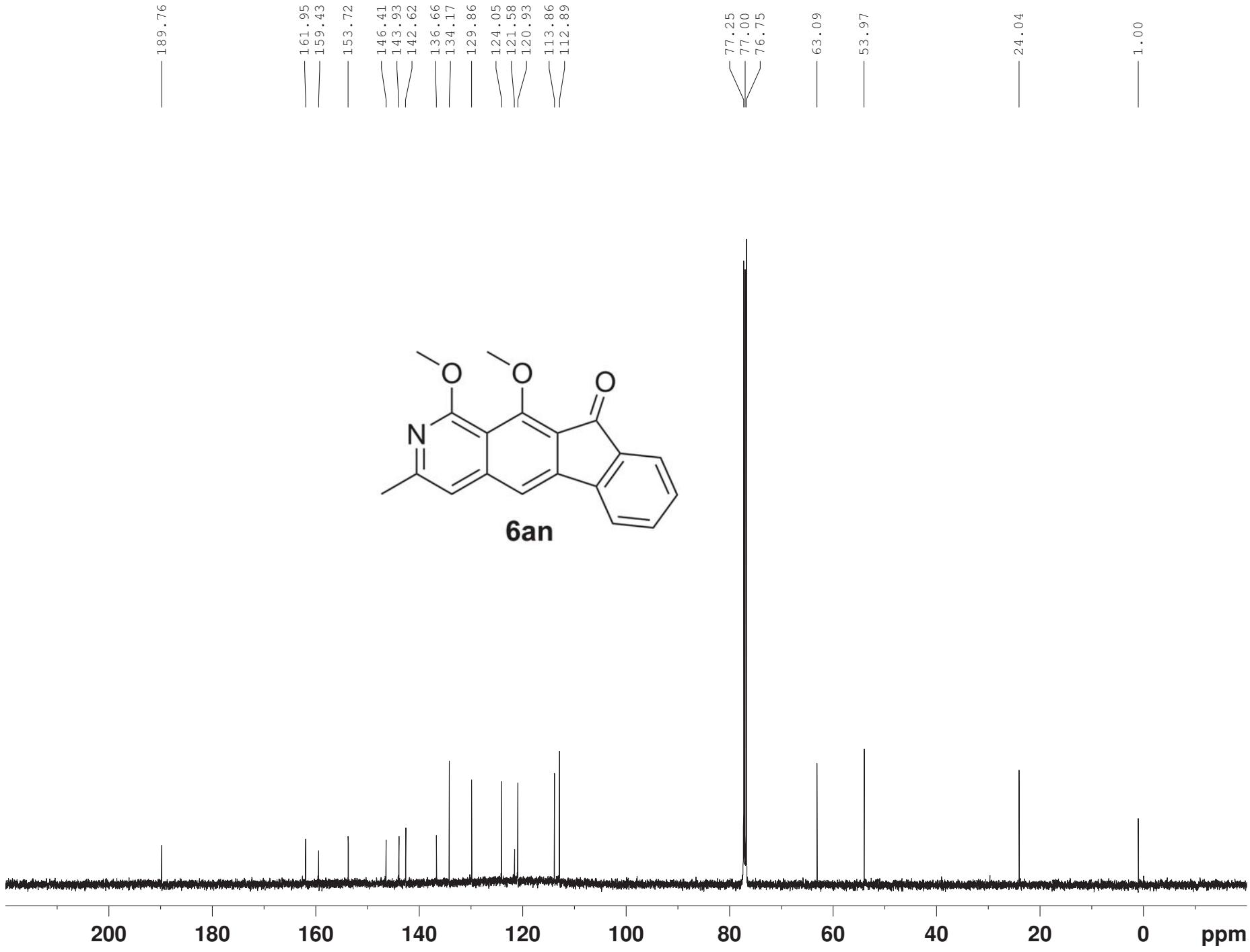
ppm
1.01
1.03
1.04
1.00
1.01
1.00
2.98
3.01
3.07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136.66
134.17
129.86
124.05
121.58
120.93
113.86
112.89
77.25
77.00
76.75
63.09
53.97
24.04
1.00
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O
O
N
6an
200
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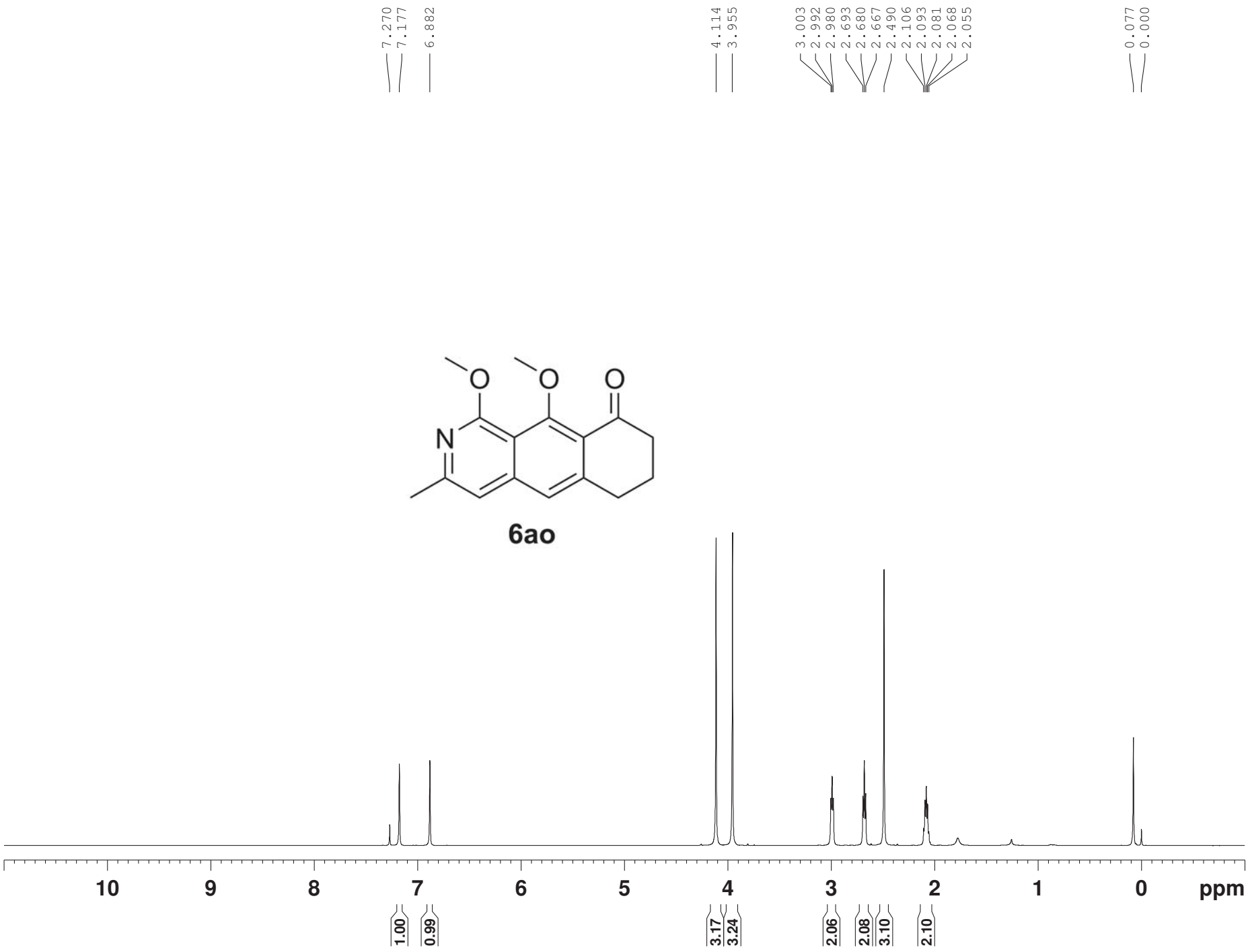
160
140
120
100
80
60
40
20
0
ppm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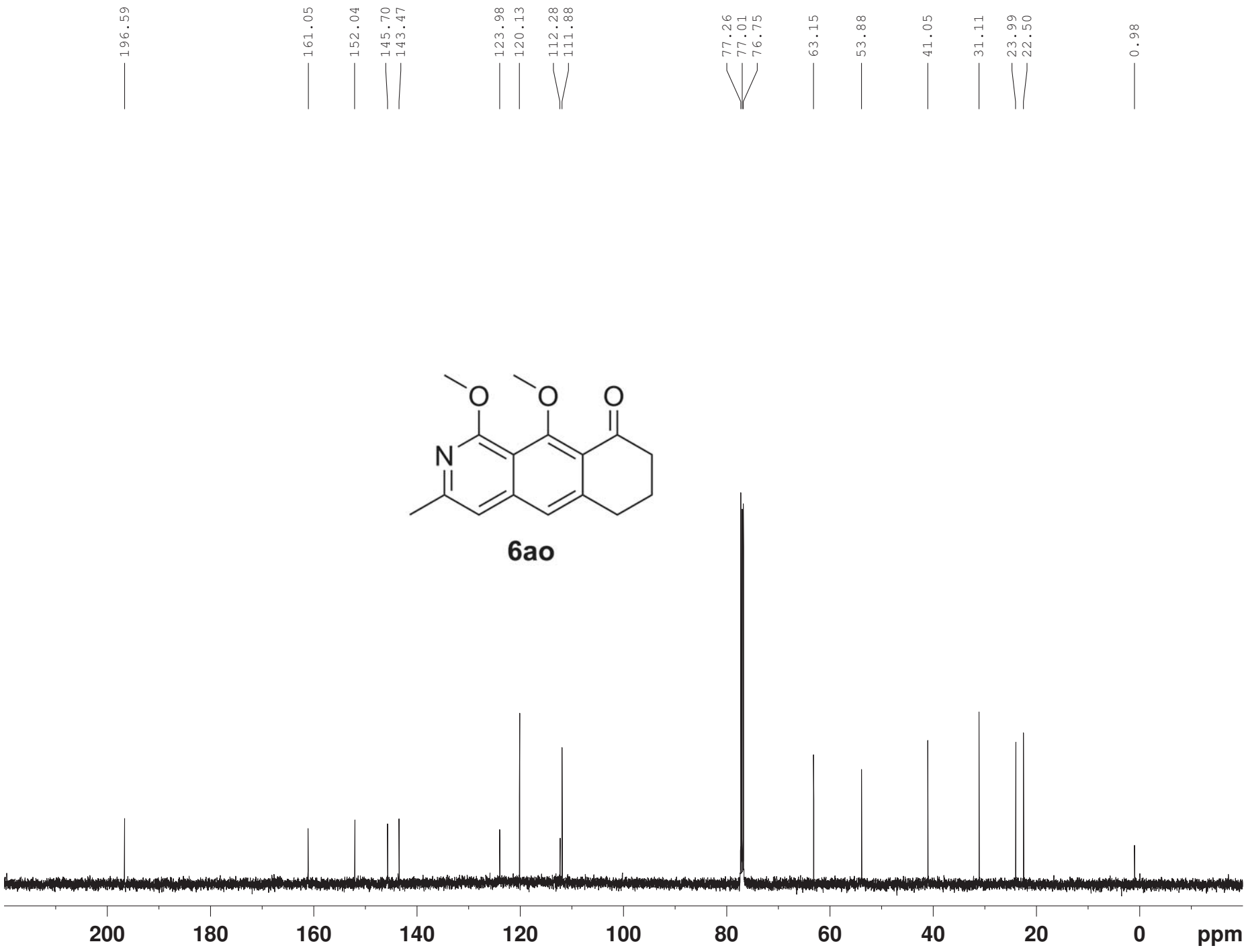
2.980
2.693
2.680
2.667
2.490
2.106
2.093
2.081
2.068
2.055
0.077
0.000
O
O
O
N
6ao
10
9
8
7
6
5
4
3
2
1
0
ppm
1.00
0.99
3.17
3.24
2.06
2.08
3.10
2.10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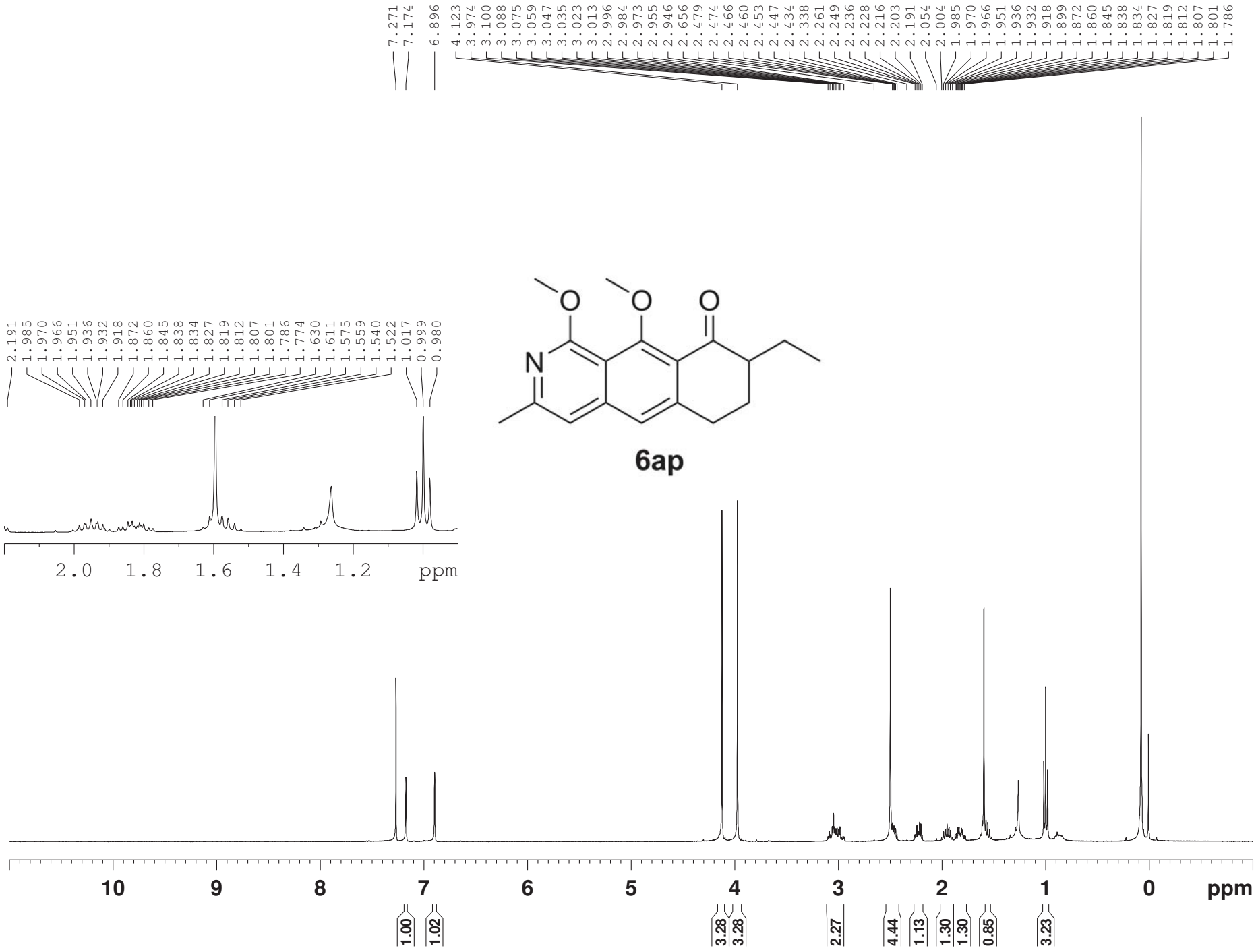
123.98
120.13
112.28
111.88
77.26
77.01
76.75
63.15
53.88
41.05
31.11
23.99
22.50
0.98
O
O
O
N
6ao
200
180
160
140
120
100
80
60
40
20
0
ppm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3.023
3.013
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2.984
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2.955
2.946
2.656
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2.434
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2.261
2.249
2.236
2.228
2.216
2.203
2.191
2.054
2.004
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1.936
1.932
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1.838
1.834
1.827
1.819
1.812
1.807
1.801
1.786
2.191
1.985
1.970
1.966
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1.936
1.932
1.918
1.872
1.860
1.845
1.838
1.834
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1.807
1.801
1.786
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1.611
1.575
1.559
1.540
1.522
1.017
0.999
0.980
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O
O
N
6ap
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1.8
1.6
1.4
1.2
ppm
10
9
8
7
6
5
4
3
2
1
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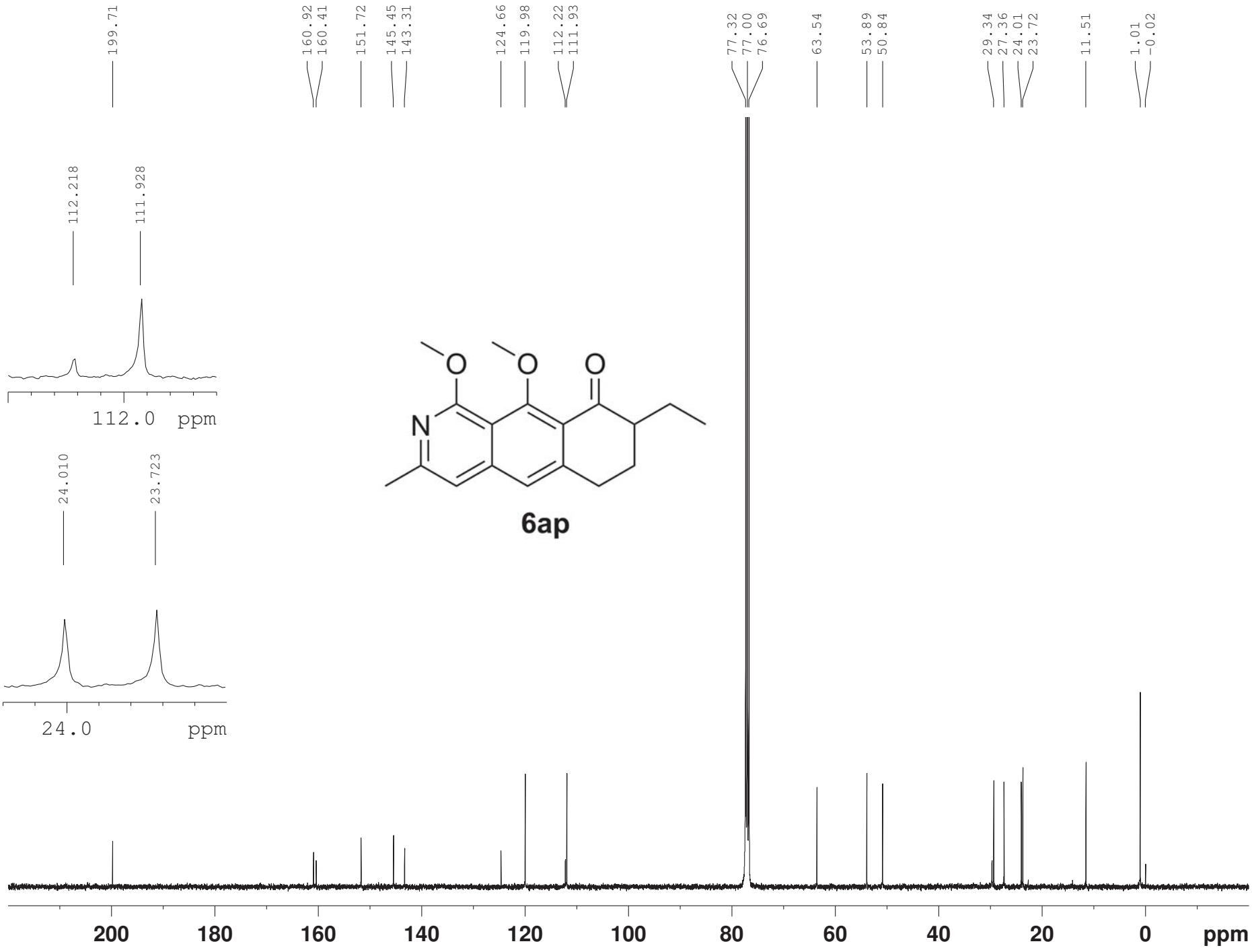
3.23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143.31
124.66
119.98
112.22
111.93
77.32
77.00
76.69
63.54
53.89
50.84
29.34
27.36
24.01
23.72
11.51
1.01
-0.02
112.218
111.928
112.0 ppm
24.010
23.723
24.0 ppm
O
O
O
N
6ap
200
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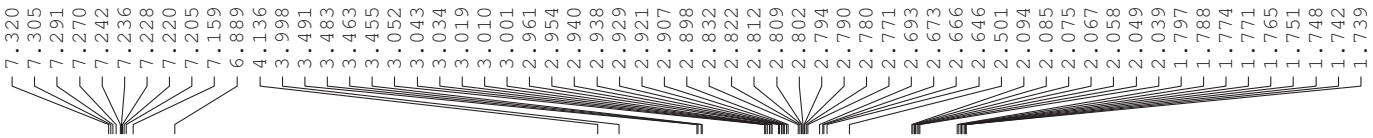
140
120
100
80
60
40
20
0
ppm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6.889
4.136
3.998
3.491
3.483
3.463
3.455
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3.043
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3.019
3.010
3.001
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2.940
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2.929
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2.802
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2.780
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2.085
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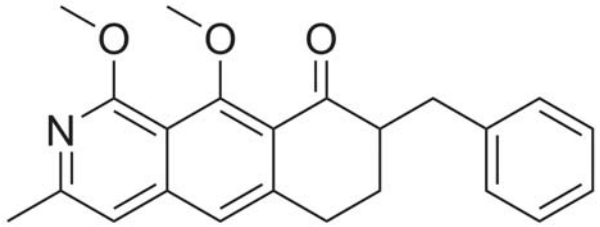
1.739


O
O
O
N

6aq

10
9
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4
3
2
1
0
ppm
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1.00
3.22
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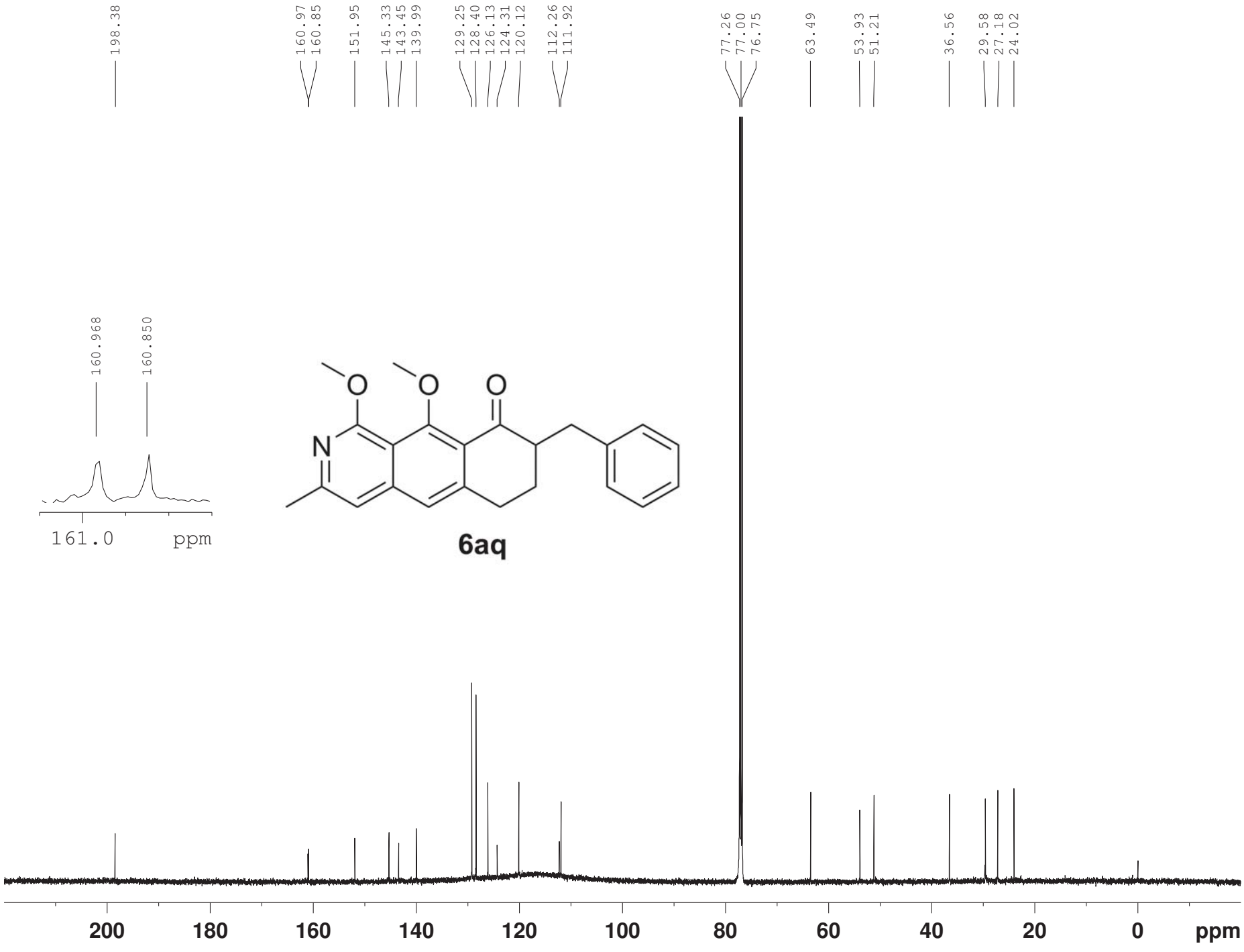
1.09
1.12
1.10
1.08
3.14
1.12
1.19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111.92
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77.00
76.75
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24.02
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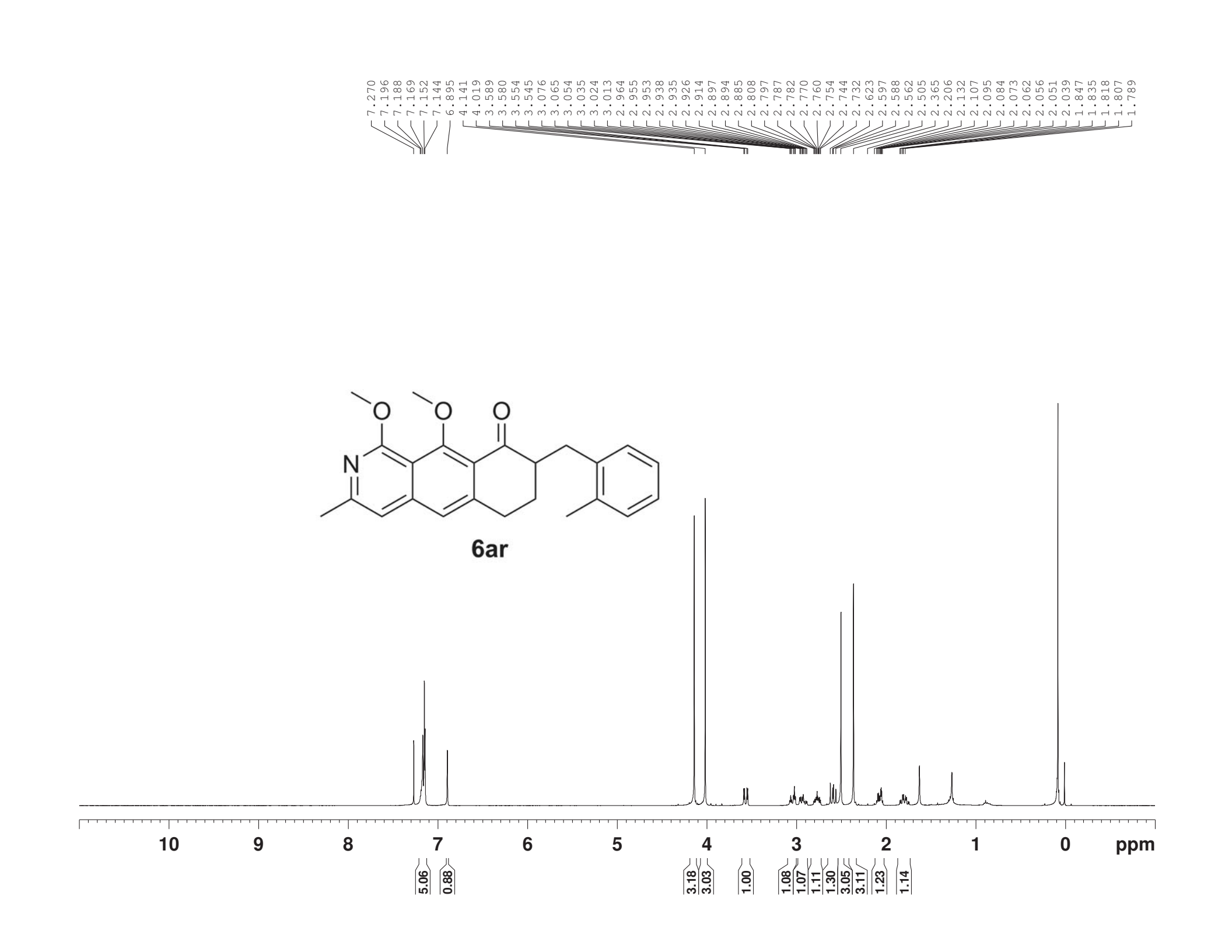
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3.076
3.065
3.054
3.035
3.024
3.013
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2.955
2.953
2.938
2.935
2.926
2.914
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2.894
2.885
2.808
2.797
2.787
2.782
2.770
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2.754
2.744
2.732
2.623
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2.588
2.562
2.505
2.365
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2.132
2.107
2.095
2.084
2.073
2.062
2.056
2.051
2.039
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1.818
1.807
1.789
O
O
O
N
6ar
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9
8
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6
5
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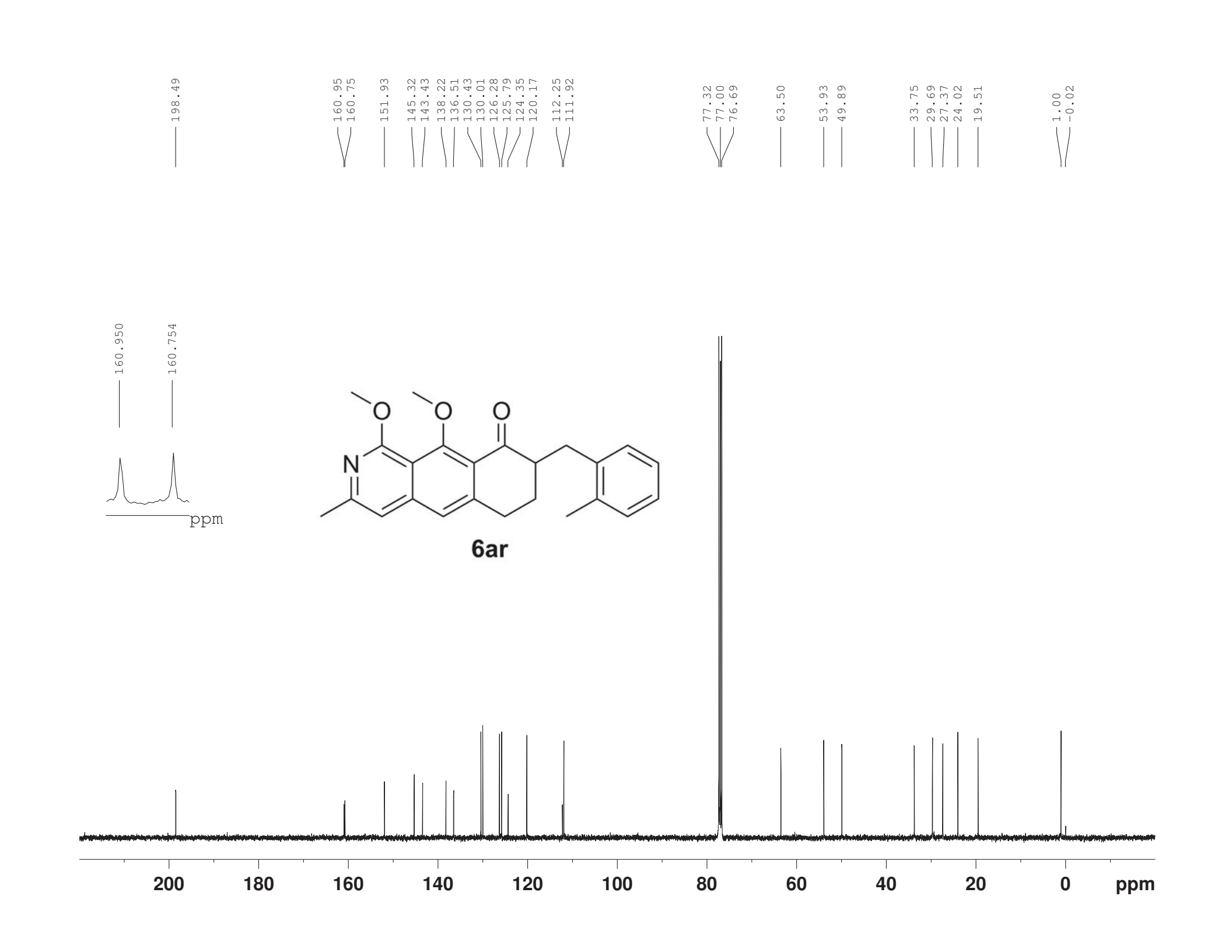
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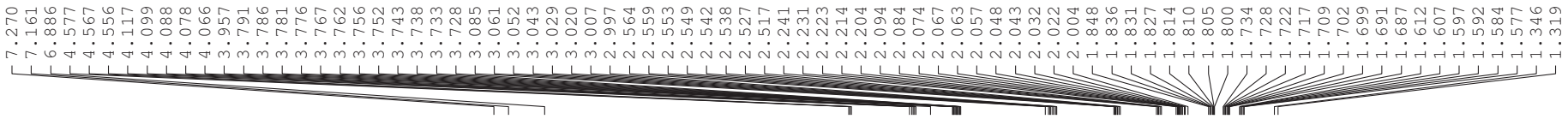
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4.066
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3.786
3.781
3.776
3.767
3.762
3.756
3.752
3.743
3.738
3.733
3.728
3.085
3.061
3.052
3.043
3.029
3.020
3.007
2.997
2.564
2.559
2.553
2.549
2.542
2.538
2.527
2.517
2.241
2.231
2.223
2.214
2.204
2.094
2.084
2.074
2.067
2.063
2.057
2.048
2.043
2.032
2.022
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1.722
1.717
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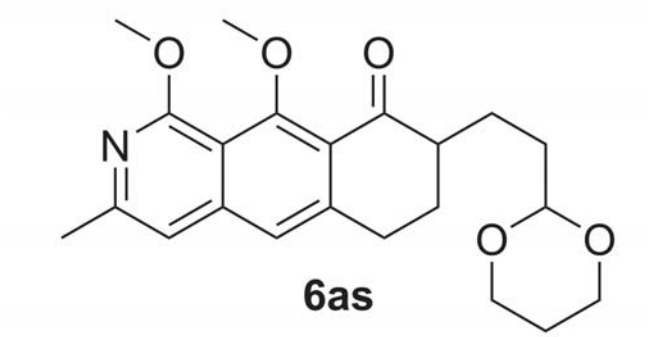
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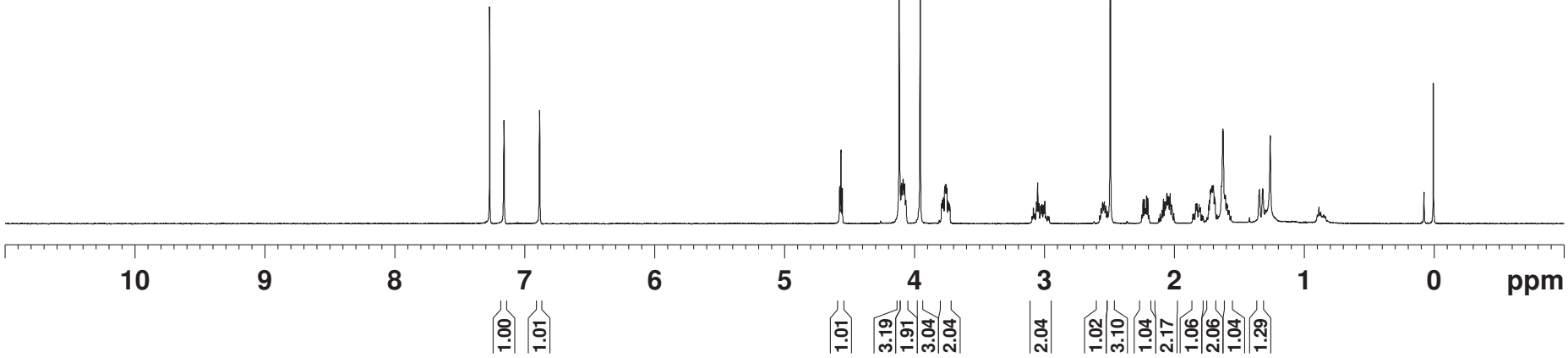
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1.01
3.19
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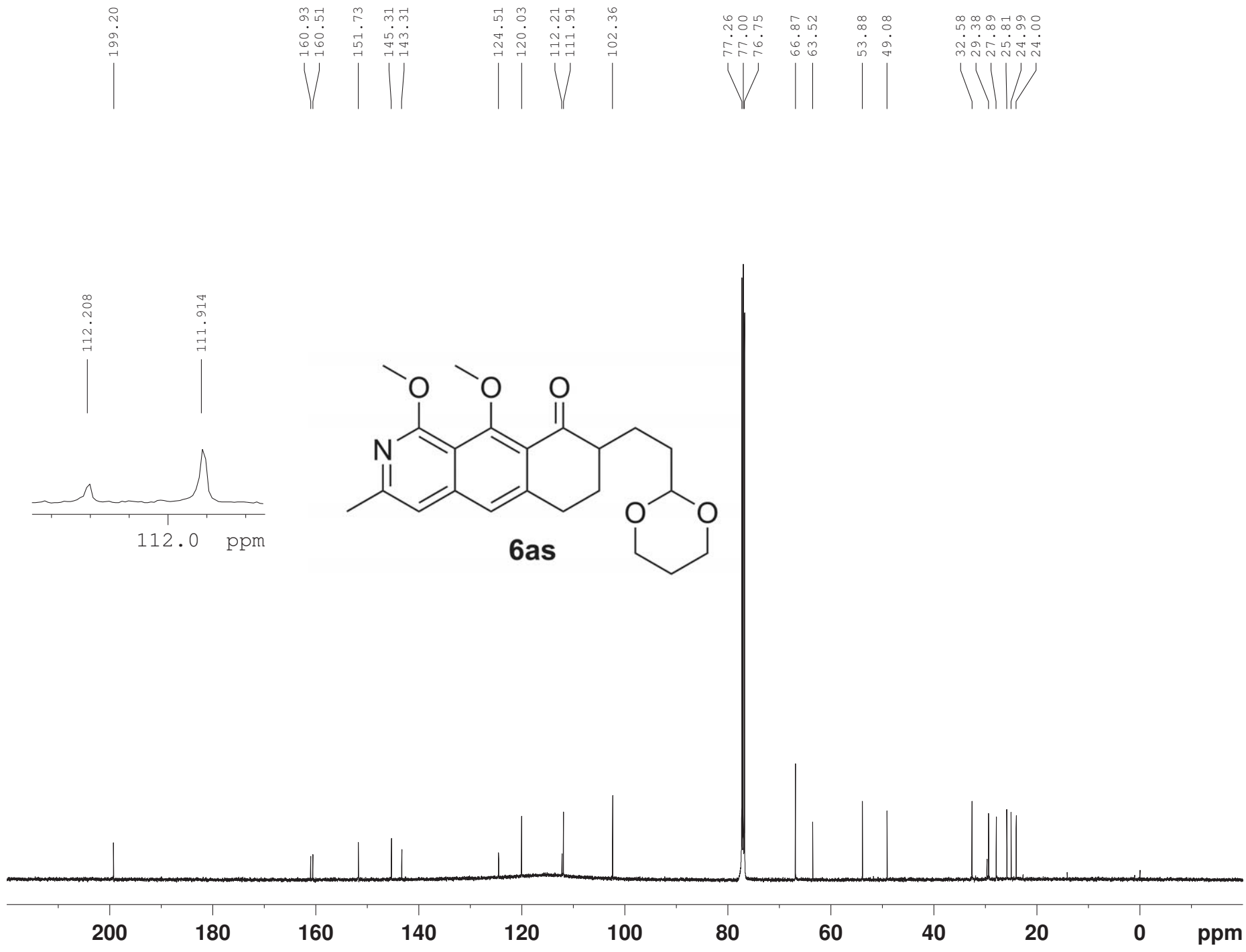
2.04
1.02
3.10
1.04
2.17
1.06
2.06
1.04
1.29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77.26
77.00
76.75
66.87
63.52
53.88
49.08
32.58
29.38
27.89
25.81
24.99
24.00
112.208
111.914
112.0 ppm
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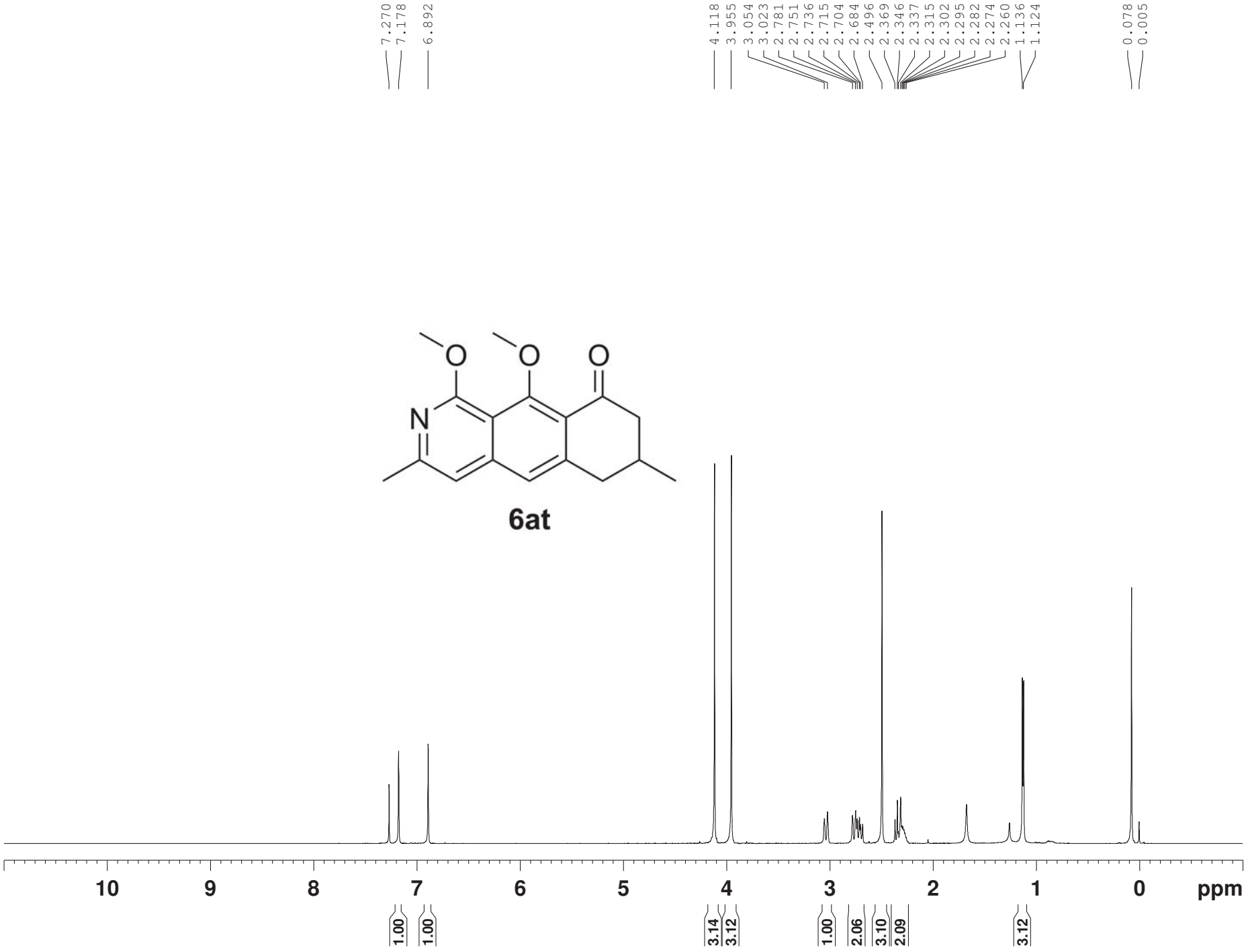
20
0
ppm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2.715
2.704
2.684
2.496
2.369
2.346
2.337
2.315
2.302
2.295
2.282
2.274
2.260
1.136
1.124
0.078
0.005
O
O
O
N
6at
10
9
8
7
6
5
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ppm
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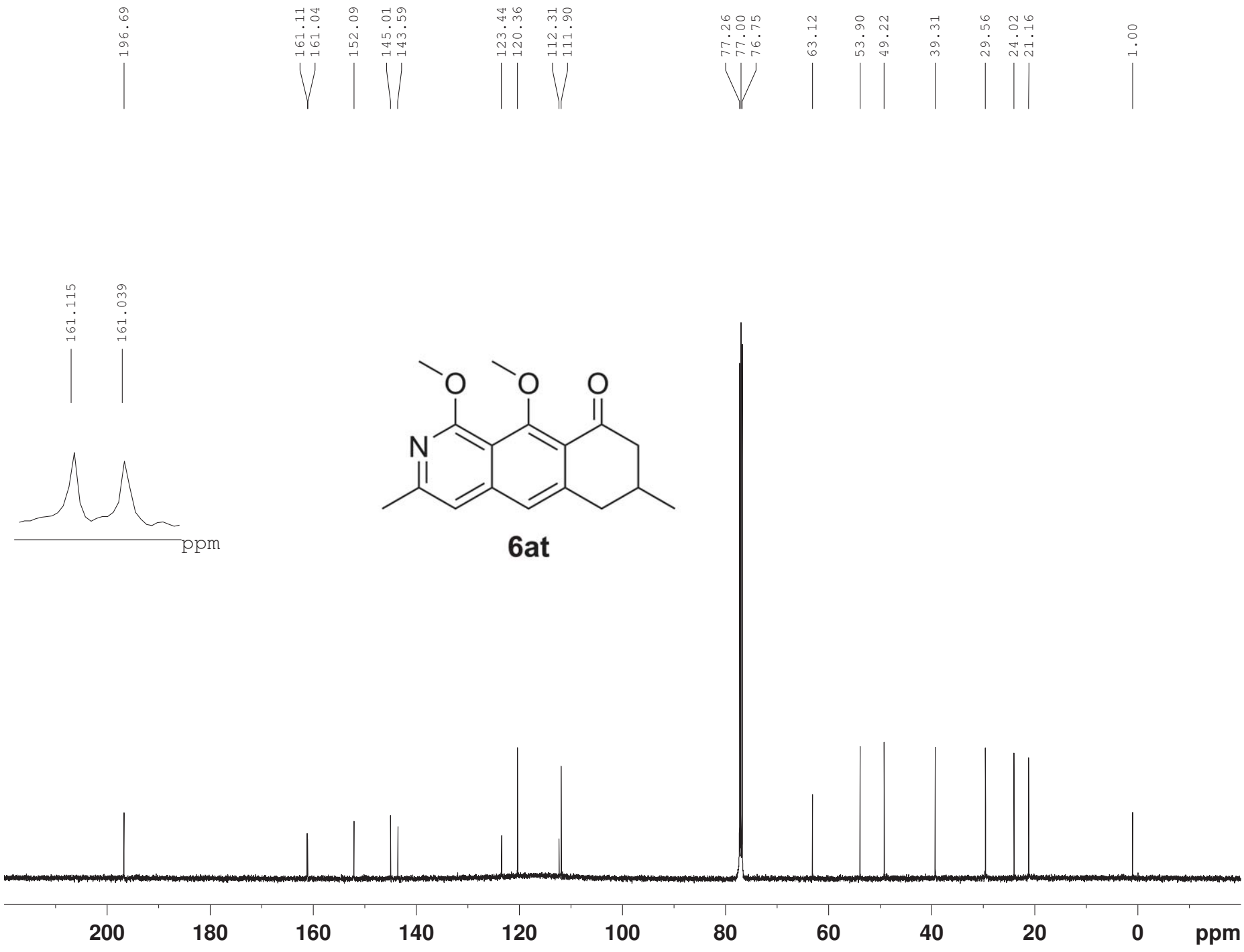
2.09
3.12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120.36
112.31
111.90
77.26
77.00
76.75
63.12
53.90
49.22
39.31
29.56
24.02
21.16
1.00
161.115
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120
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20
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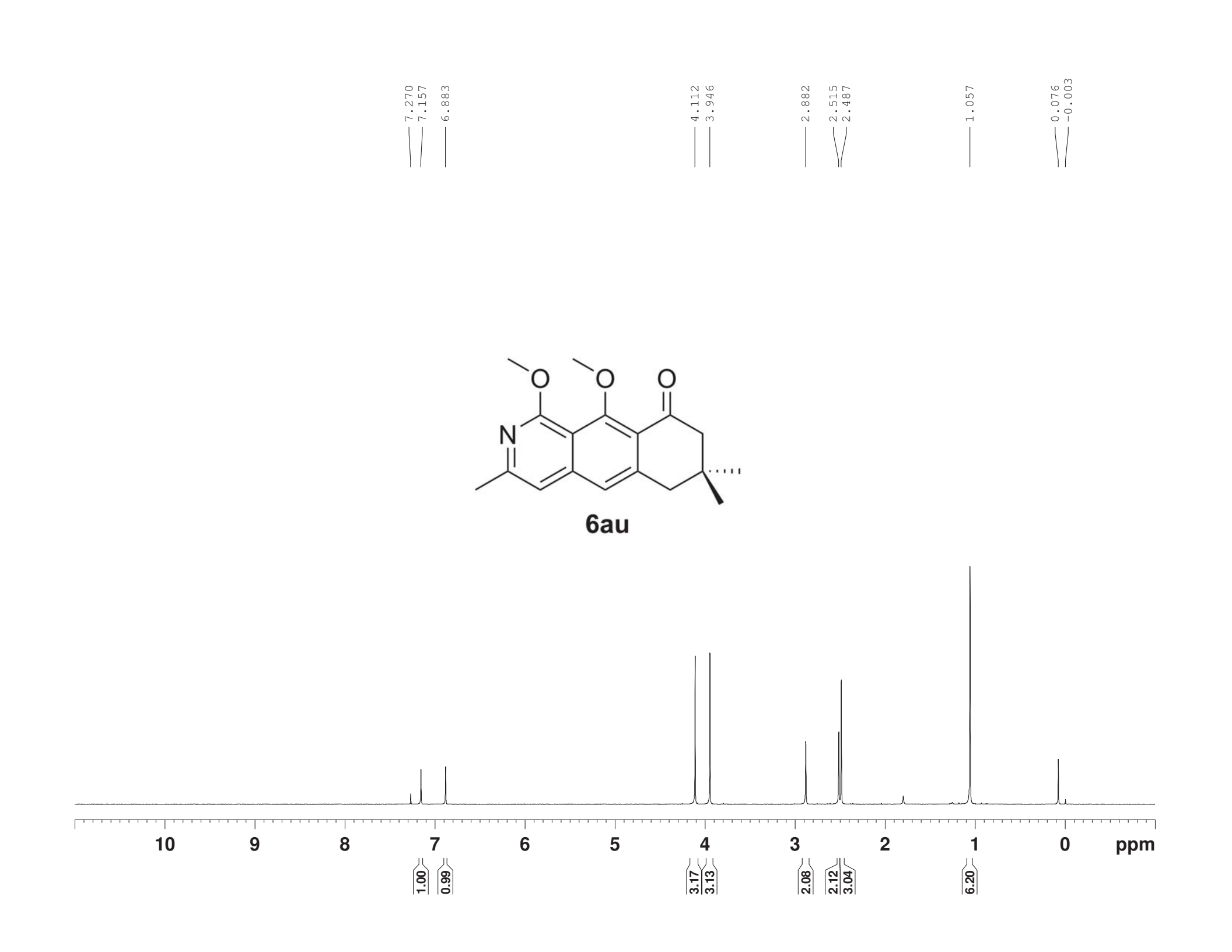
ppm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0.076
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O
O
N
6au
10
9
8
7
6
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3.13
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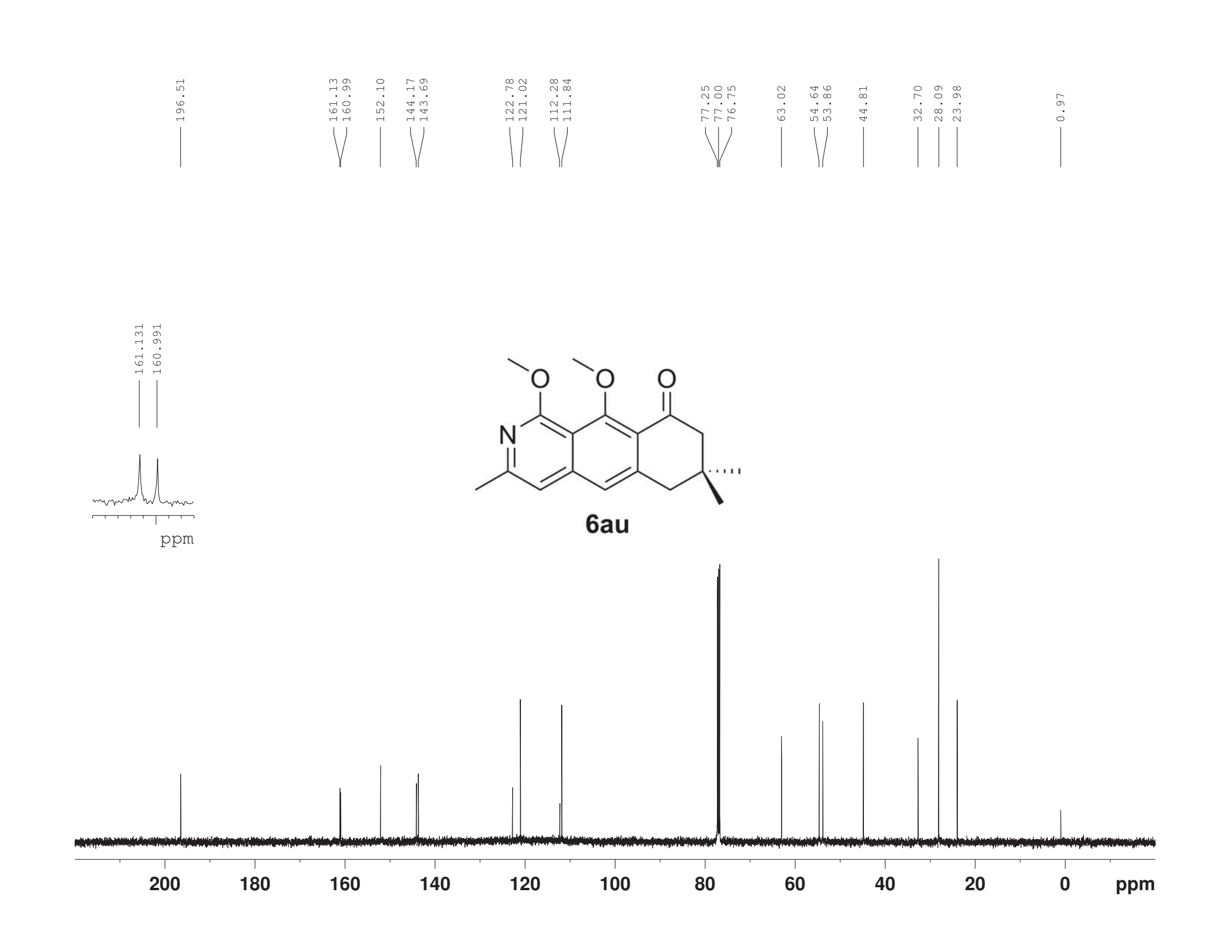
2.12
3.04
6.20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121.02
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77.00
76.75
63.02
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53.86
44.81
32.70
28.09
23.98
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120
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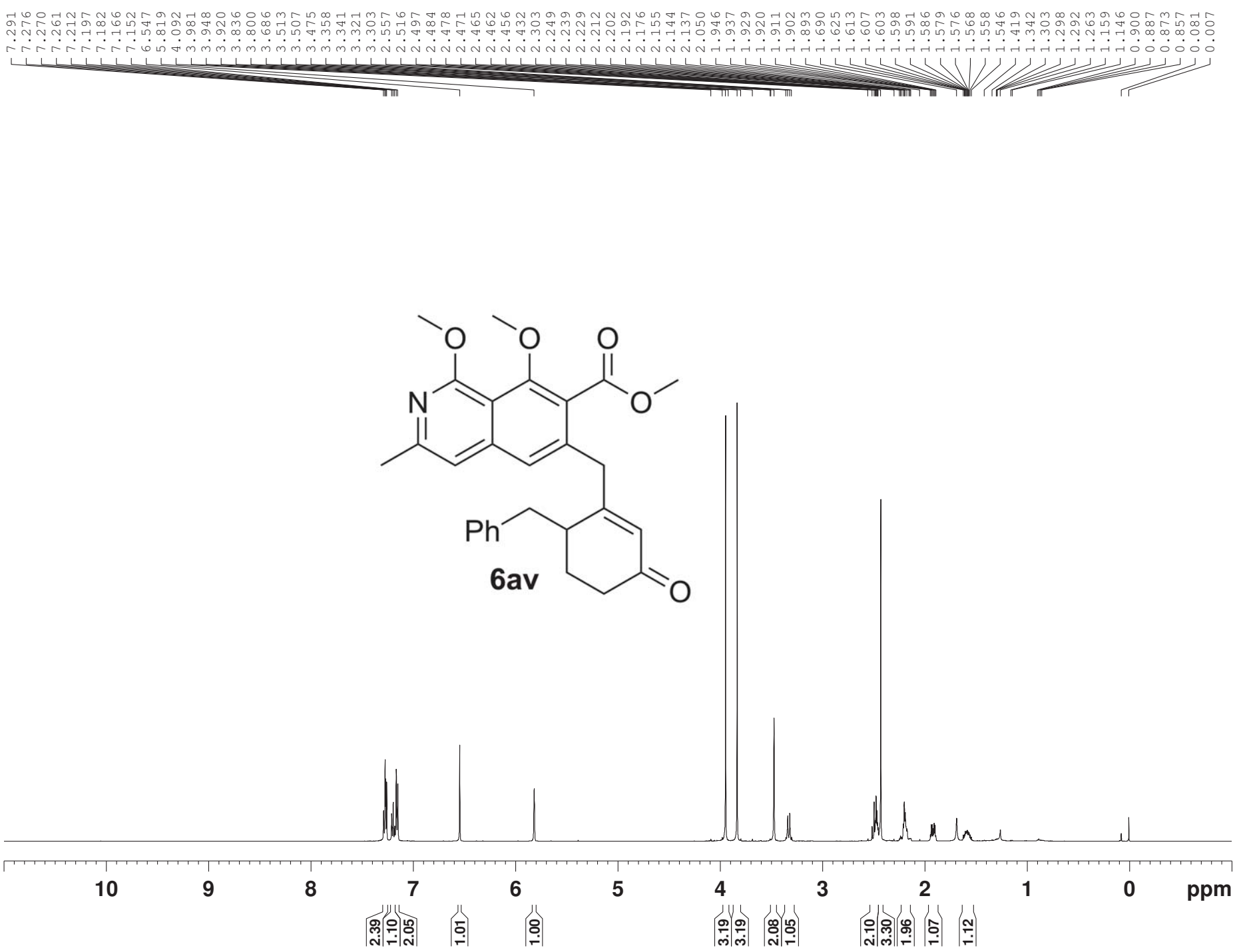
ppm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7.166
7.152
6.547
5.819
4.092
3.981
3.948
3.920
3.836
3.800
3.686
3.513
3.507
3.475
3.358
3.341
3.321
3.303
2.557
2.516
2.497
2.484
2.478
2.471
2.465
2.462
2.456
2.432
2.303
2.249
2.239
2.229
2.212
2.202
2.192
2.176
2.155
2.144
2.137
2.050
1.946
1.937
1.929
1.920
1.911
1.902
1.893
1.690
1.625
1.613
1.607
1.603
1.598
1.591
1.586
1.579
1.576
1.568
1.558
1.546
1.419
1.342
1.303
1.298
1.292
1.263
1.159
1.146
0.900
0.887
0.873
0.857
0.081
0.007
O
O
O
N
O
Ph
O
6av
10
9
8
7
6
5
4
3
2
1
0
ppm
2.39
1.10
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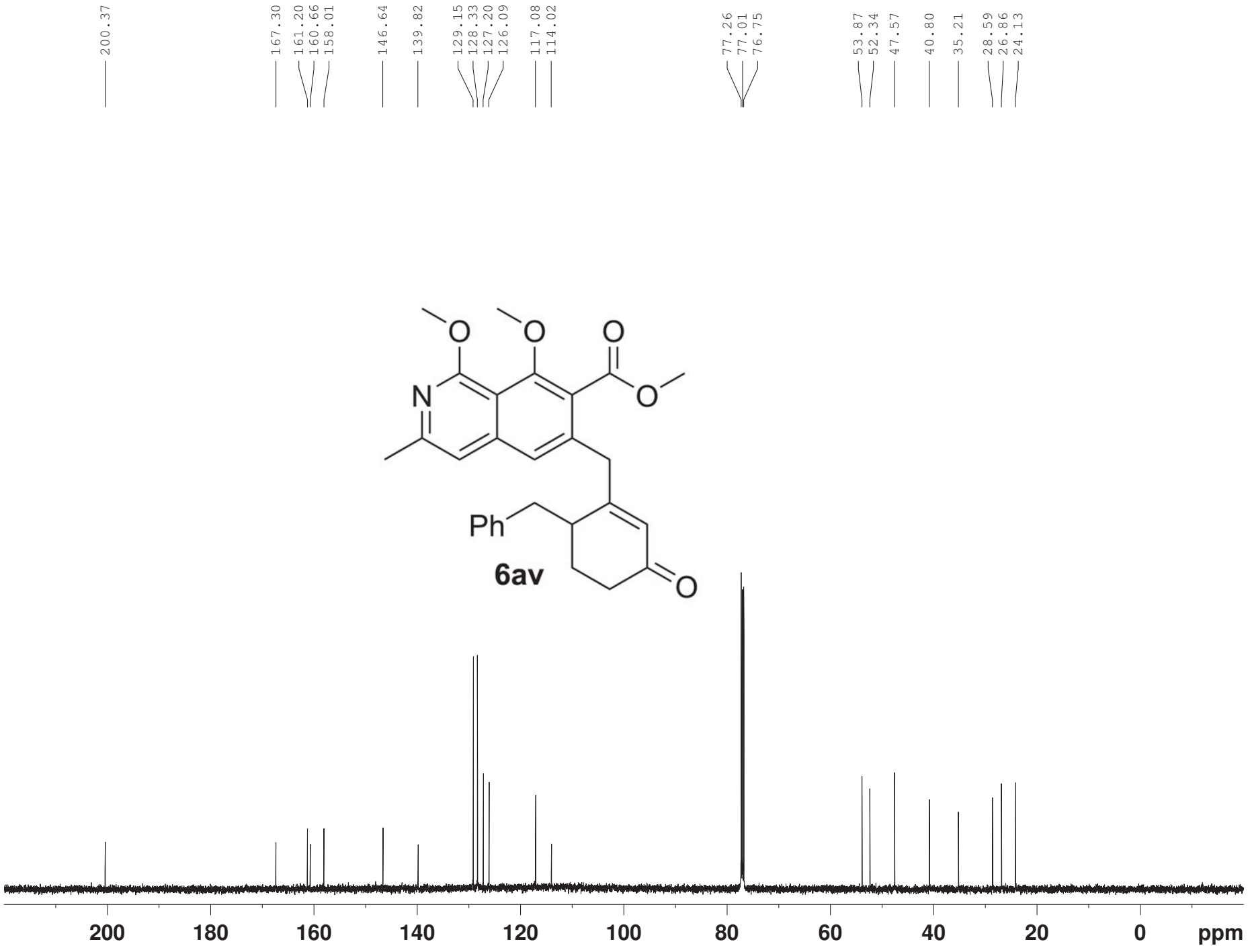
1.01
1.00
3.19
3.19
2.08
1.05
2.10
3.30
1.96
1.07
1.12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139.82
129.15
128.33
127.20
126.09
117.08
114.02
77.26
77.01
76.75
53.87
52.34
47.57
40.80
35.21
28.59
26.86
24.13
O
O
O
N
O
Ph
O
6av
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120
100
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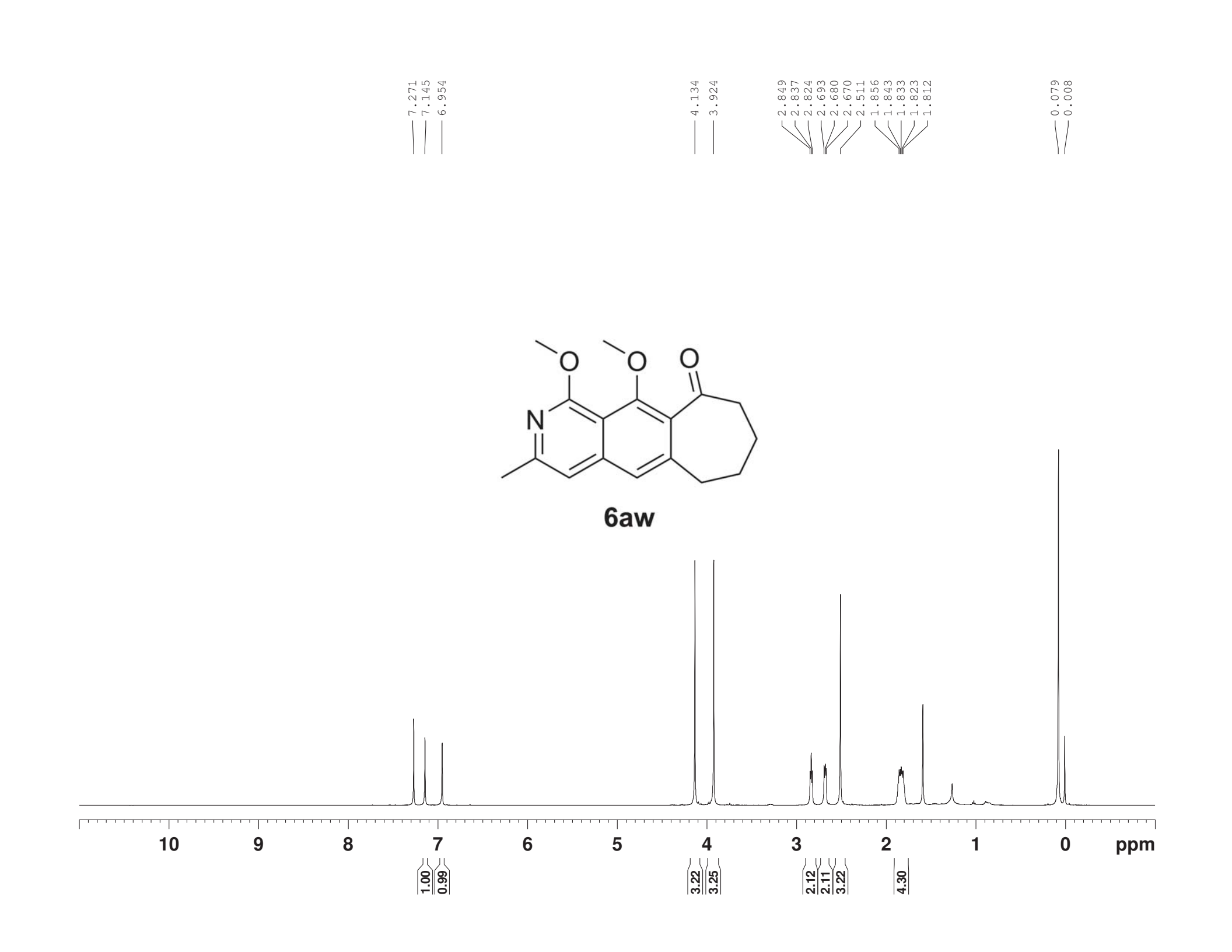
60
40
20
0
ppm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2.837
2.824
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2.680
2.670
2.511
1.856
1.843
1.833
1.823
1.812
0.079
0.008
O
O
O
N
6aw
10
9
8
7
6
5
4
3
2
1
0
ppm
1.00
0.99
3.22
3.25
2.12
2.11
3.22
4.30

207.23
159.69
153.98
150.34
142.50
140.44
133.57
120.86
112.41
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77.01
76.75
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53.75
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33.10
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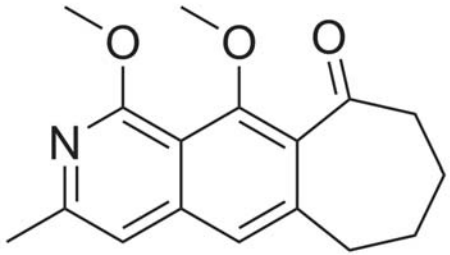

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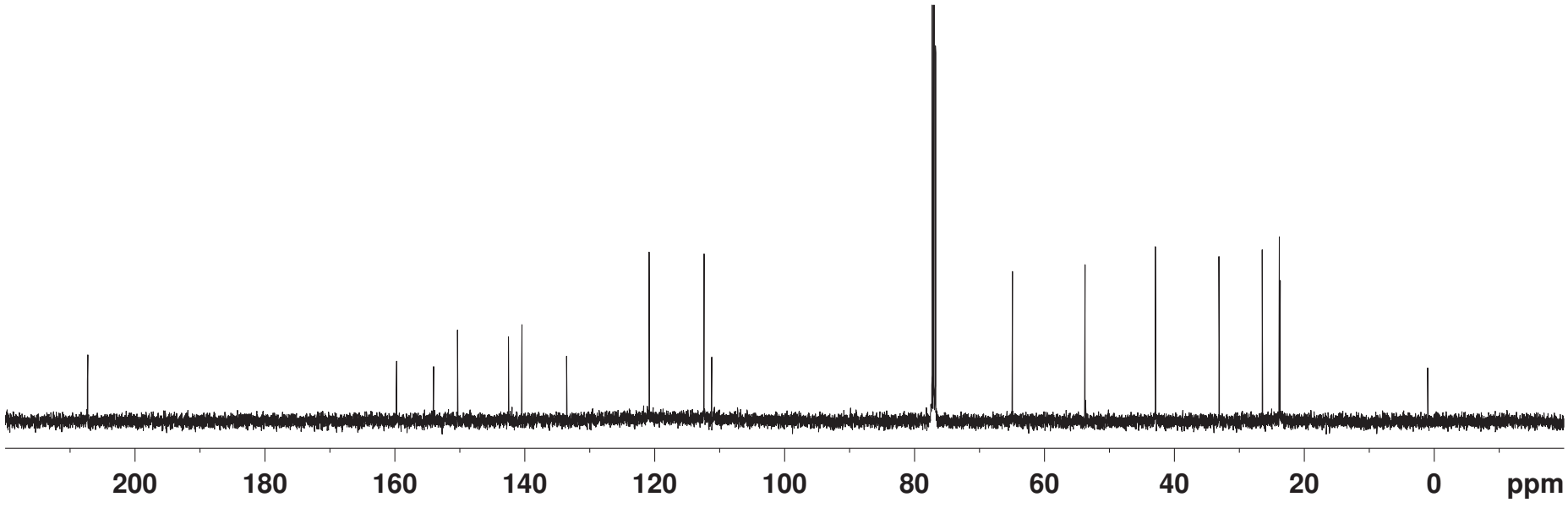

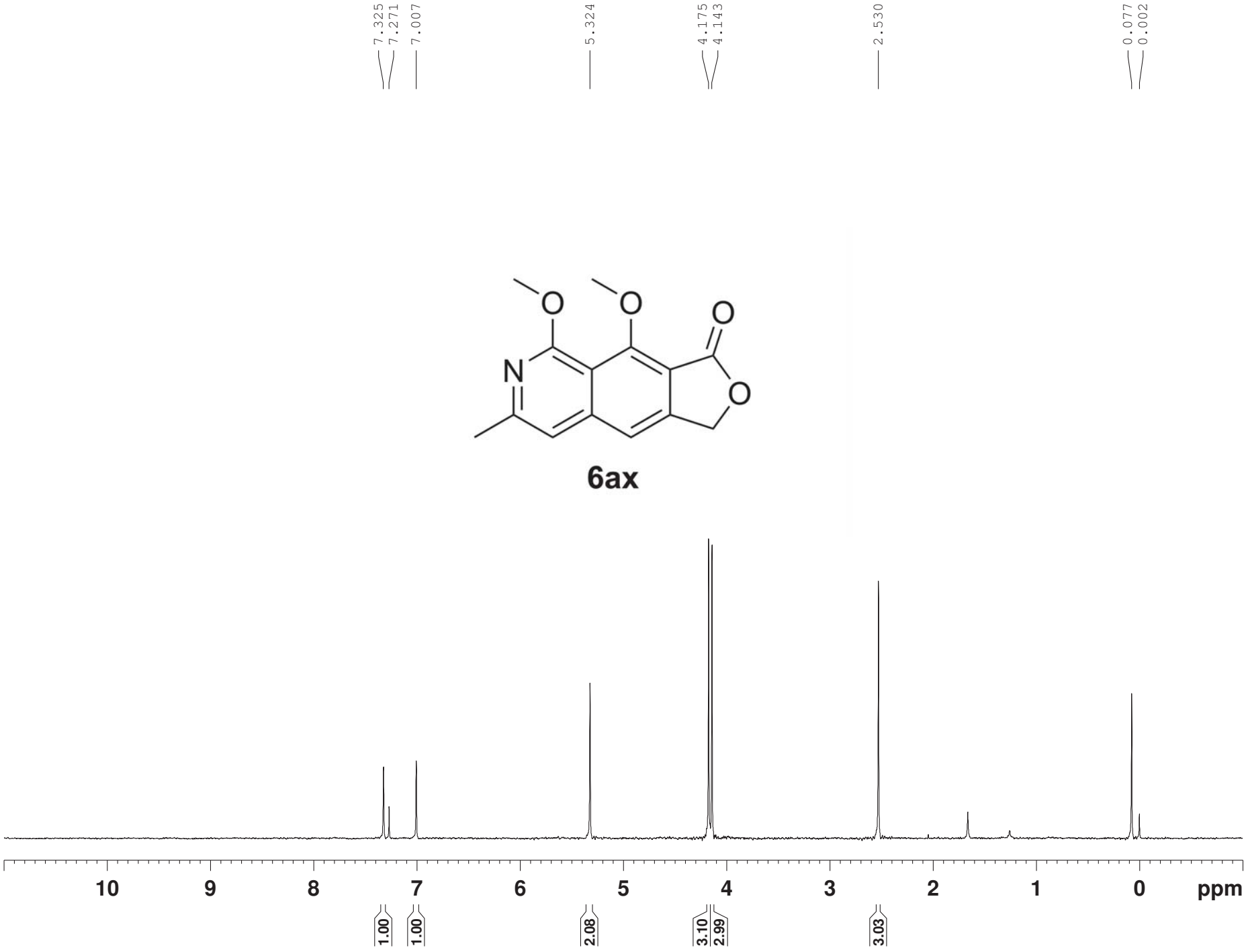
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0.002
O
O
O
N
O
6ax
10
9
8
7
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5
4
3
2
1
0
ppm
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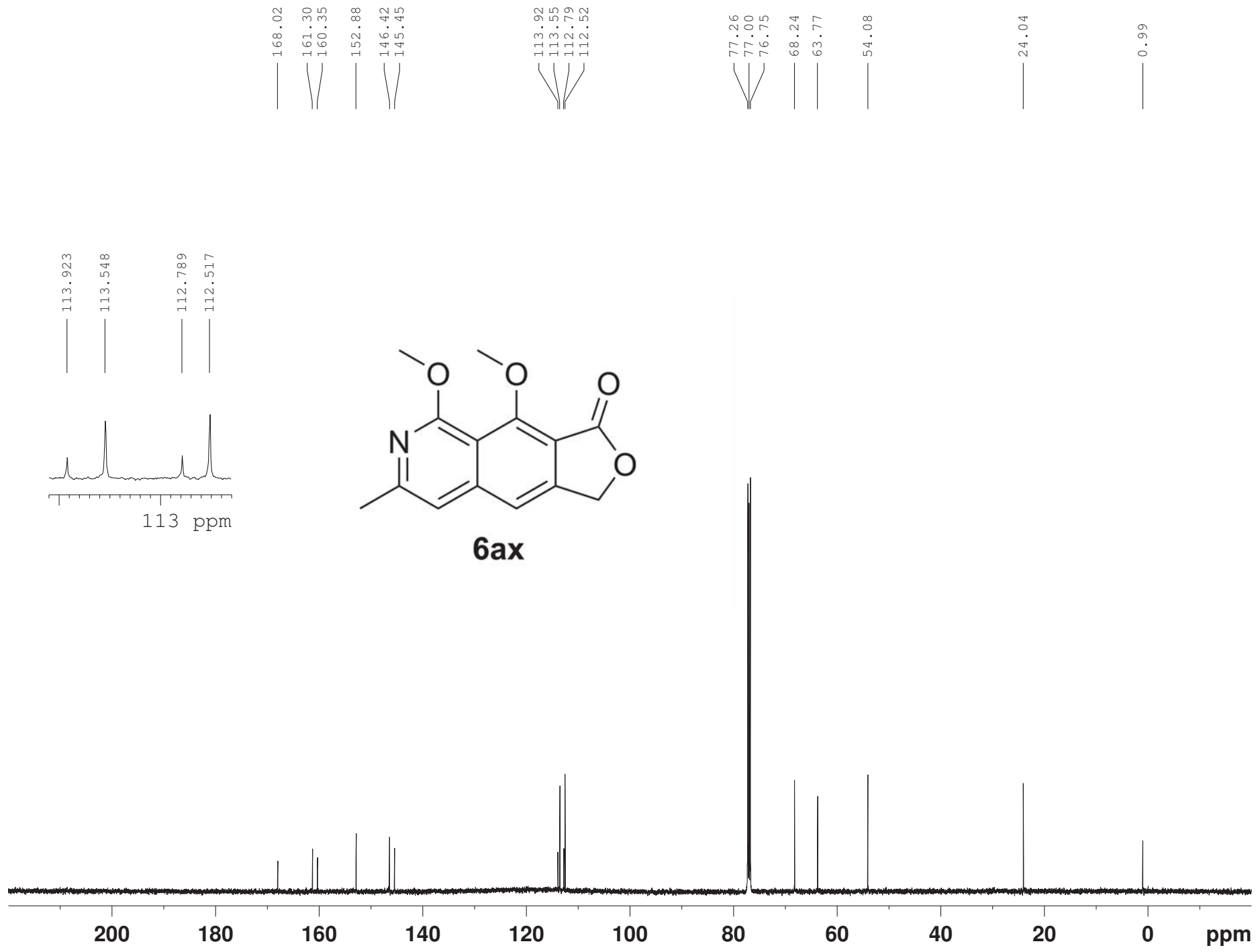
1.00
2.08
3.10
2.99
3.03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113.92
113.55
112.79
112.52
77.26
77.00
76.75
68.24
63.77
54.08
24.04
0.99
113.923
113.548
112.789
112.517
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O
N
O
6ax
200
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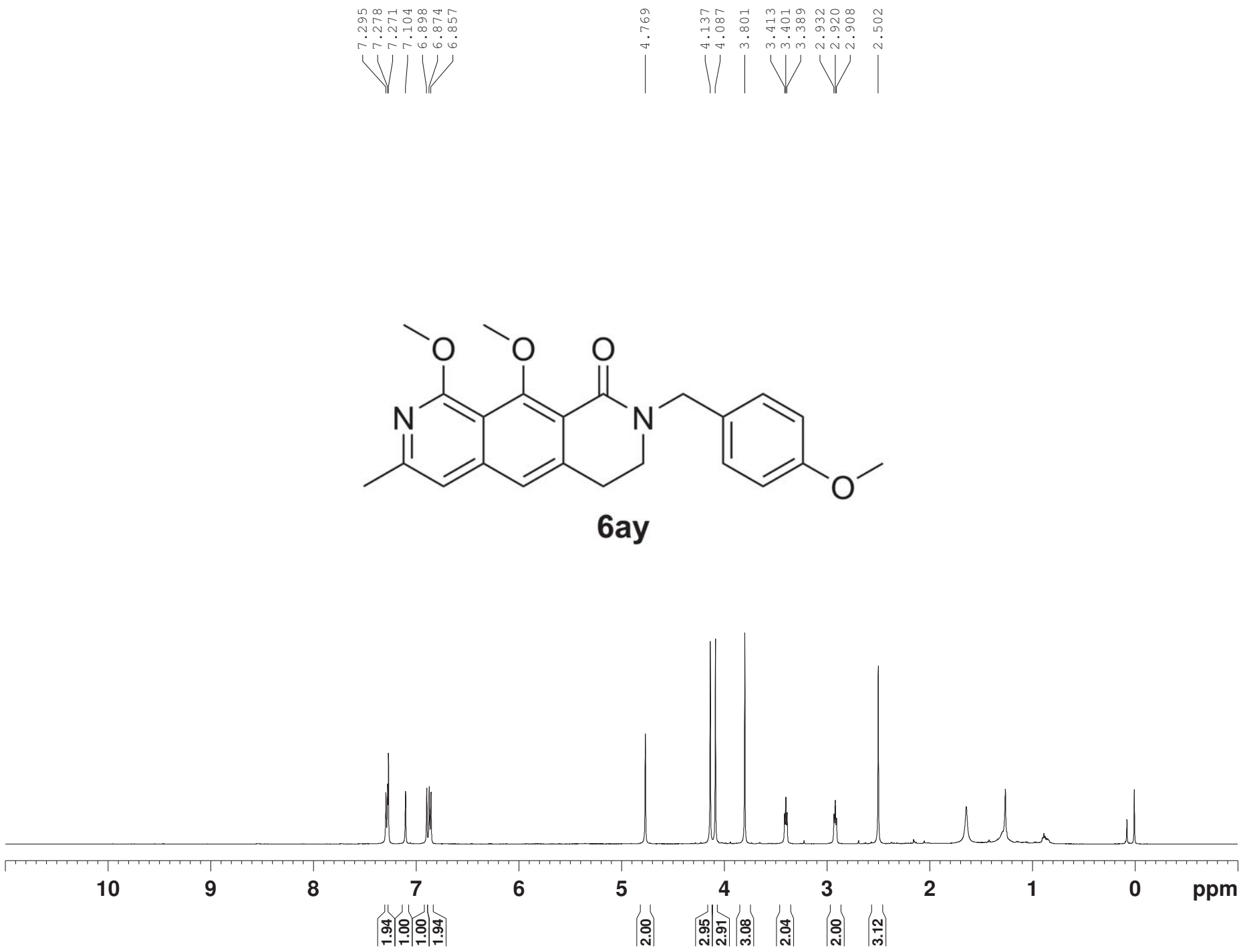
160
140
120
100
80
60
40
20
0
ppm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4.087
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3.401
3.389
2.932
2.920
2.908
2.502
O
O
O
N
N
O
6ay
10
9
8
7
6
5
4
3
2
1
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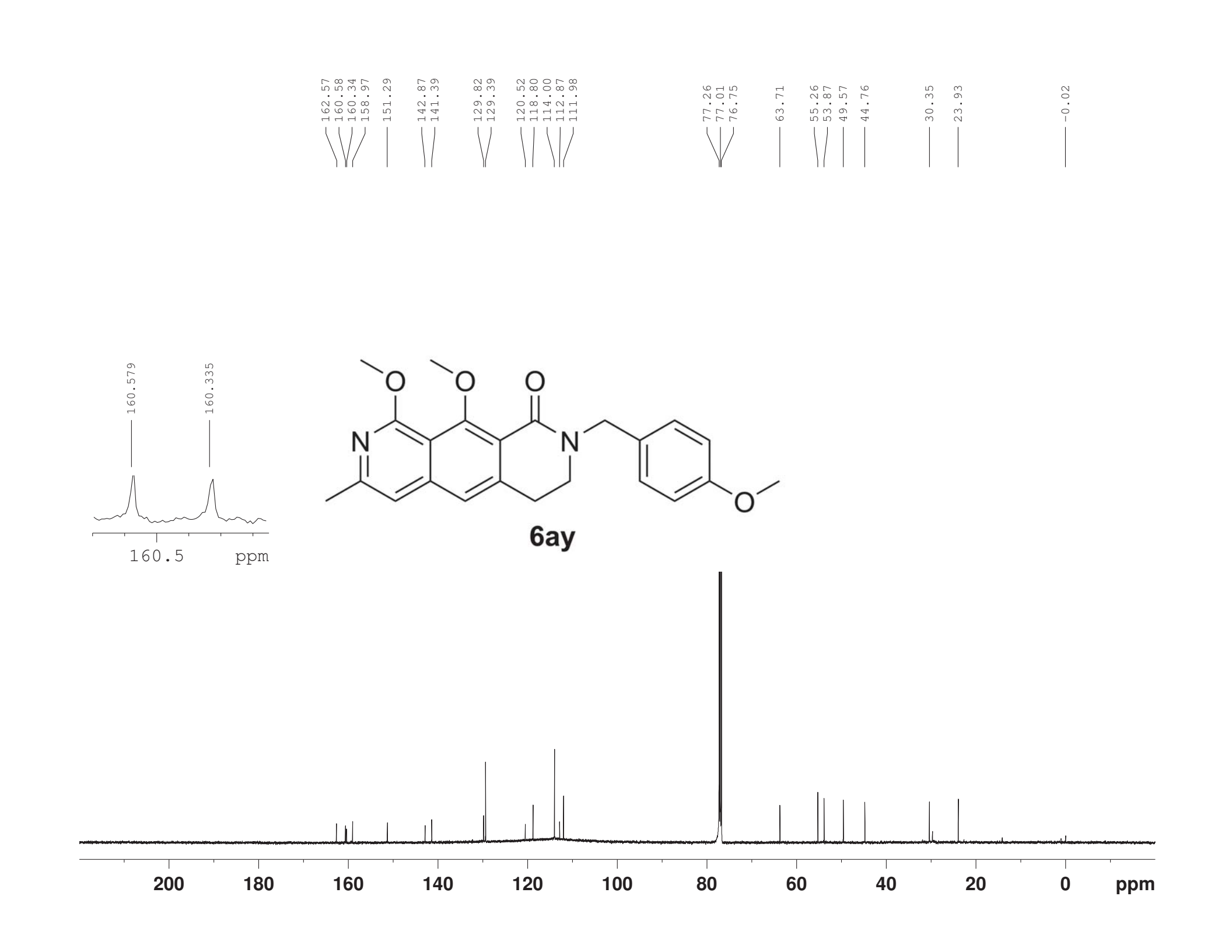
3.12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129.82
129.39
120.52
118.80
114.00
112.87
111.98
77.26
77.01
76.75
63.71
55.26
53.87
49.57
44.76
30.35
23.93
-0.02
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160.335
160.5
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N
N
O
6ay
200
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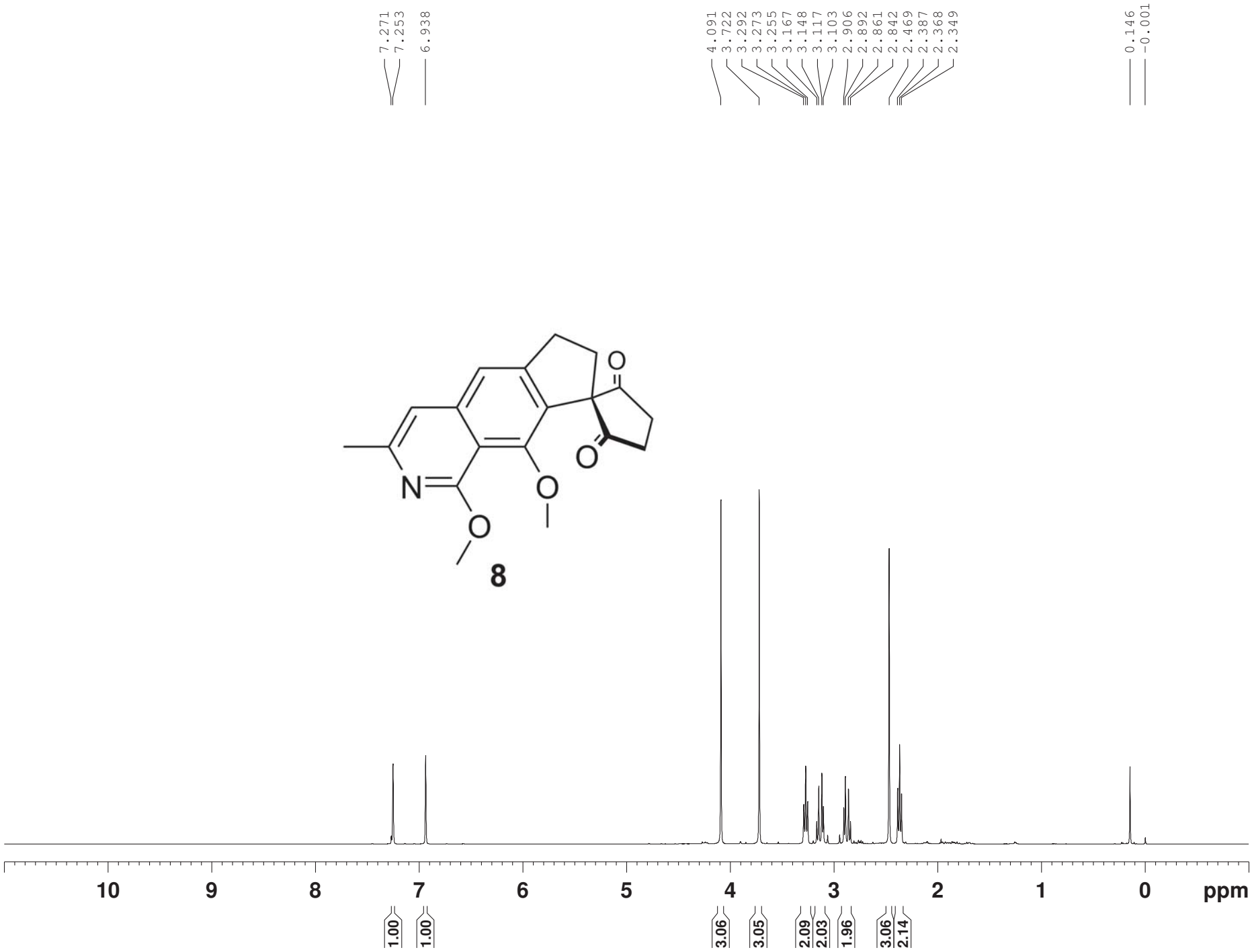
160
140
120
100
80
60
40
20
0
ppm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3.722
3.292
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3.148
3.117
3.103
2.906
2.892
2.861
2.842
2.469
2.387
2.368
2.349
0.146
-0.001
O
O
N
O
O
8
10
9
8
7
6
5
4
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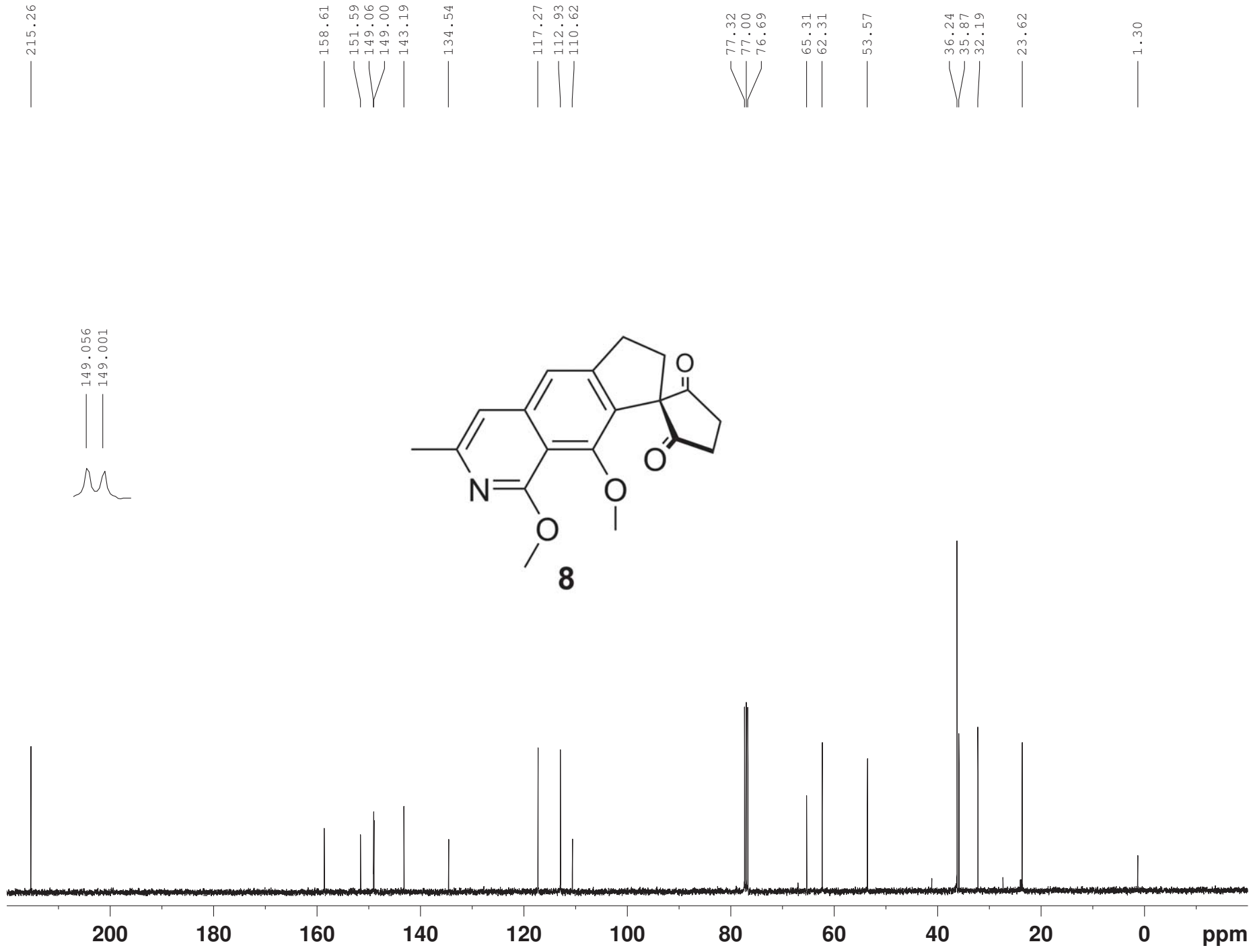
ppm
1.00
1.00
3.06
3.05
2.09
2.03
1.96
3.06
2.14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143.19
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117.27
112.93
110.62
77.32
77.00
76.69
65.31
62.31
53.57
36.24
35.87
32.19
23.62
1.30
149.056
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N
O
O
8
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140
120
100
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60
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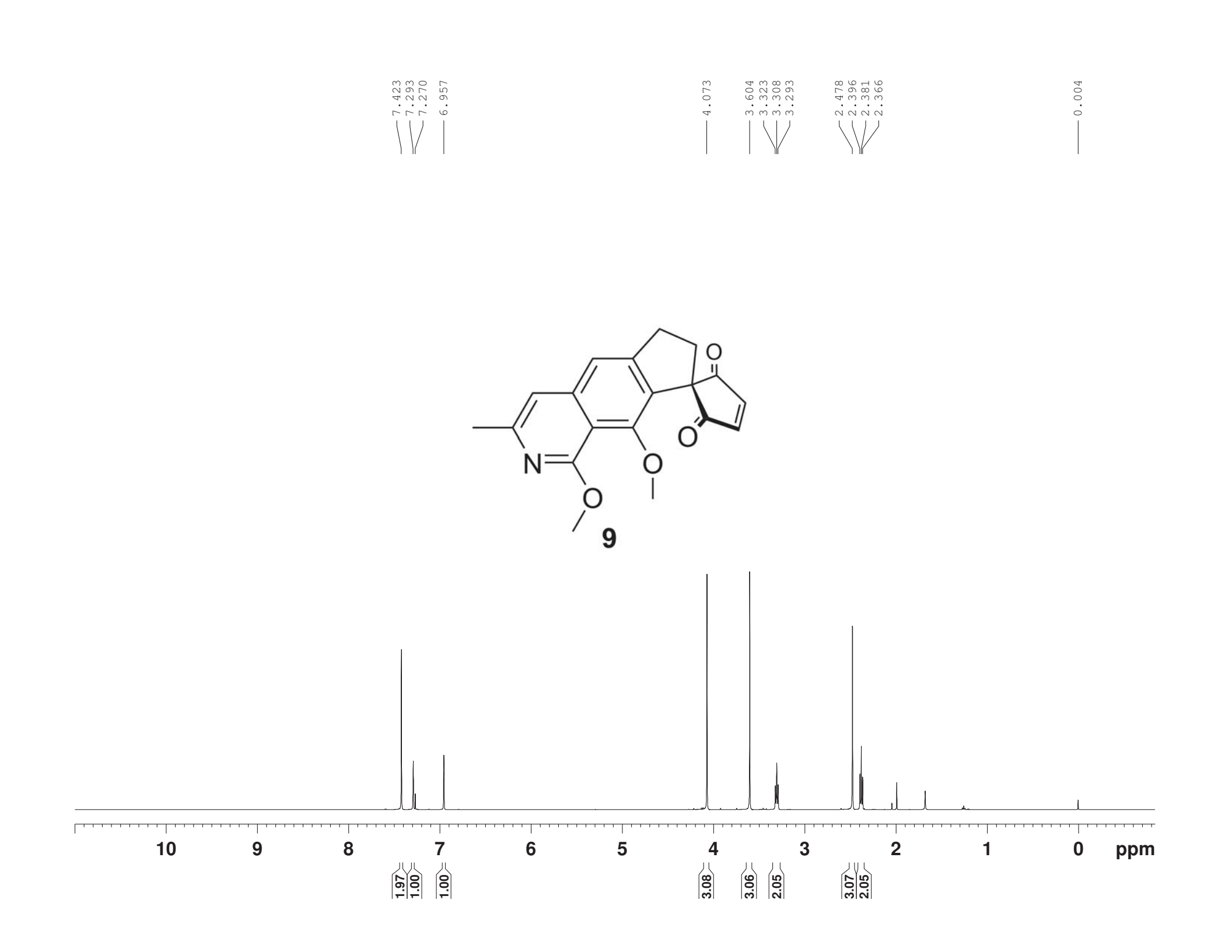
20
0
ppm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2.396
2.381
2.366
0.004
O
O
N
O
O
9
10
9
8
7
6
5
4
3
2
1
0
ppm
1.97
1.00
1.00
3.08
3.06
2.05
3.07
2.05

205.32
158.78
152.58
149.49
149.15
148.39
143.31
131.76
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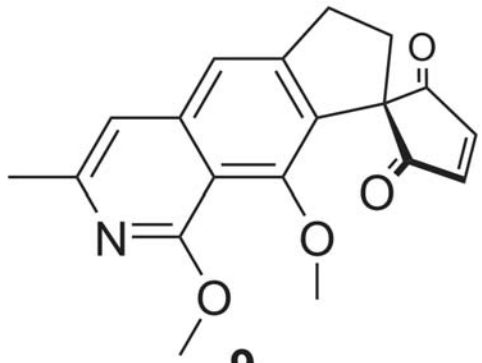
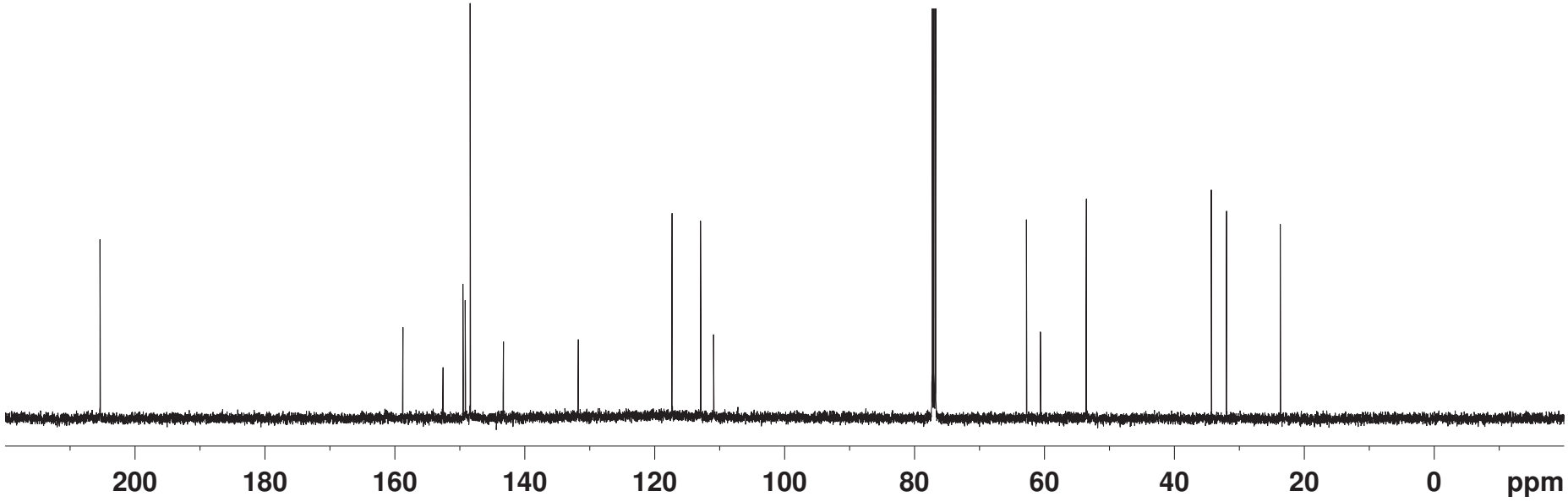
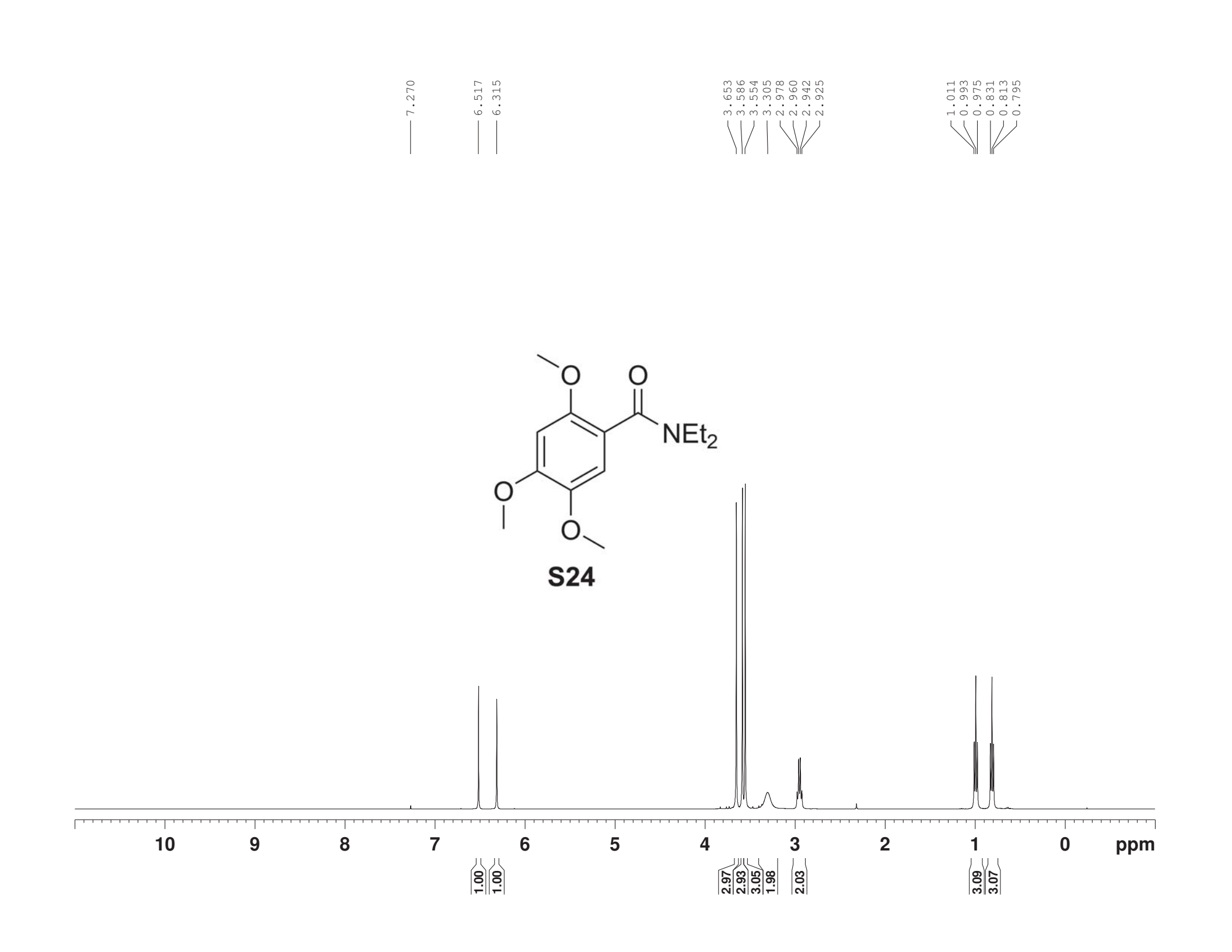
23.69



9

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3.554
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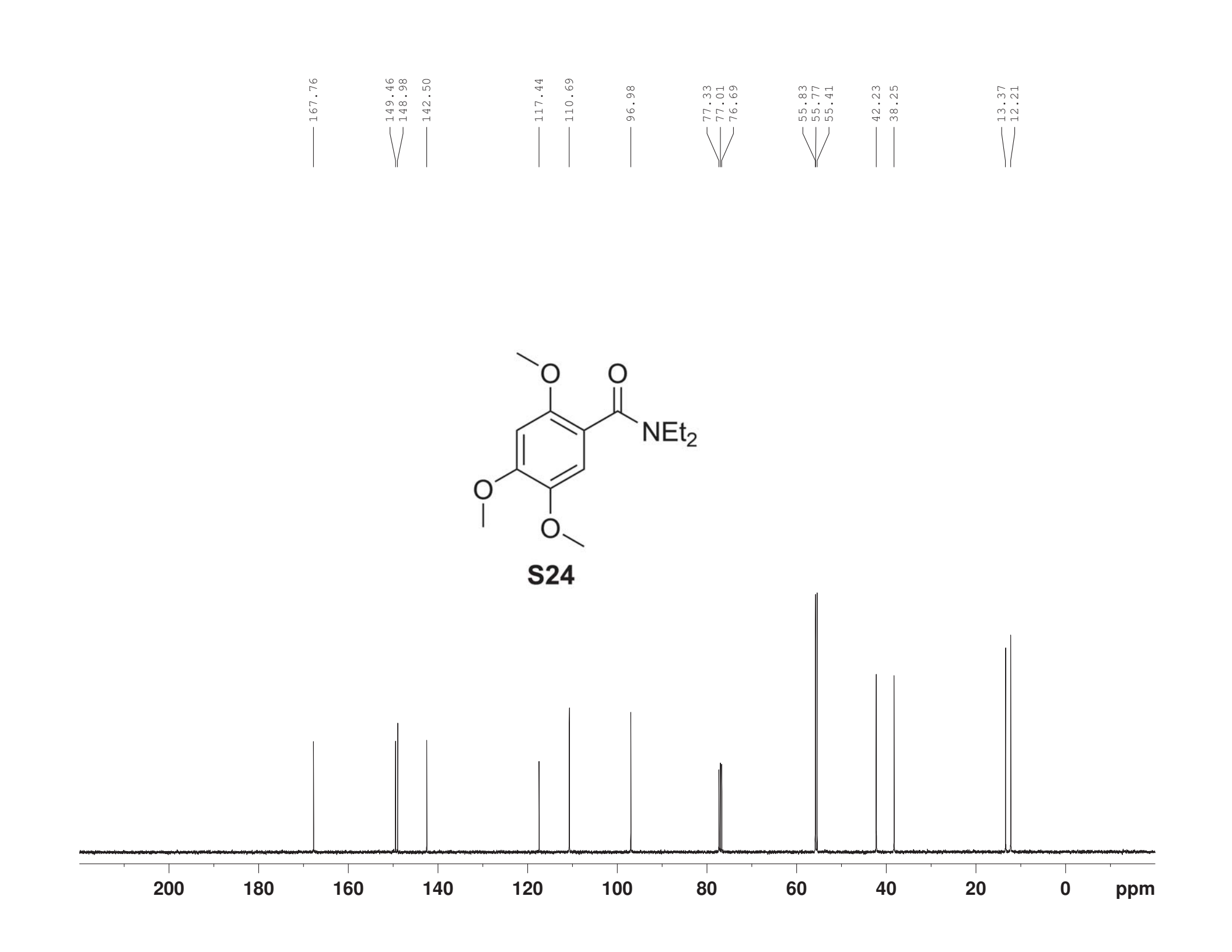
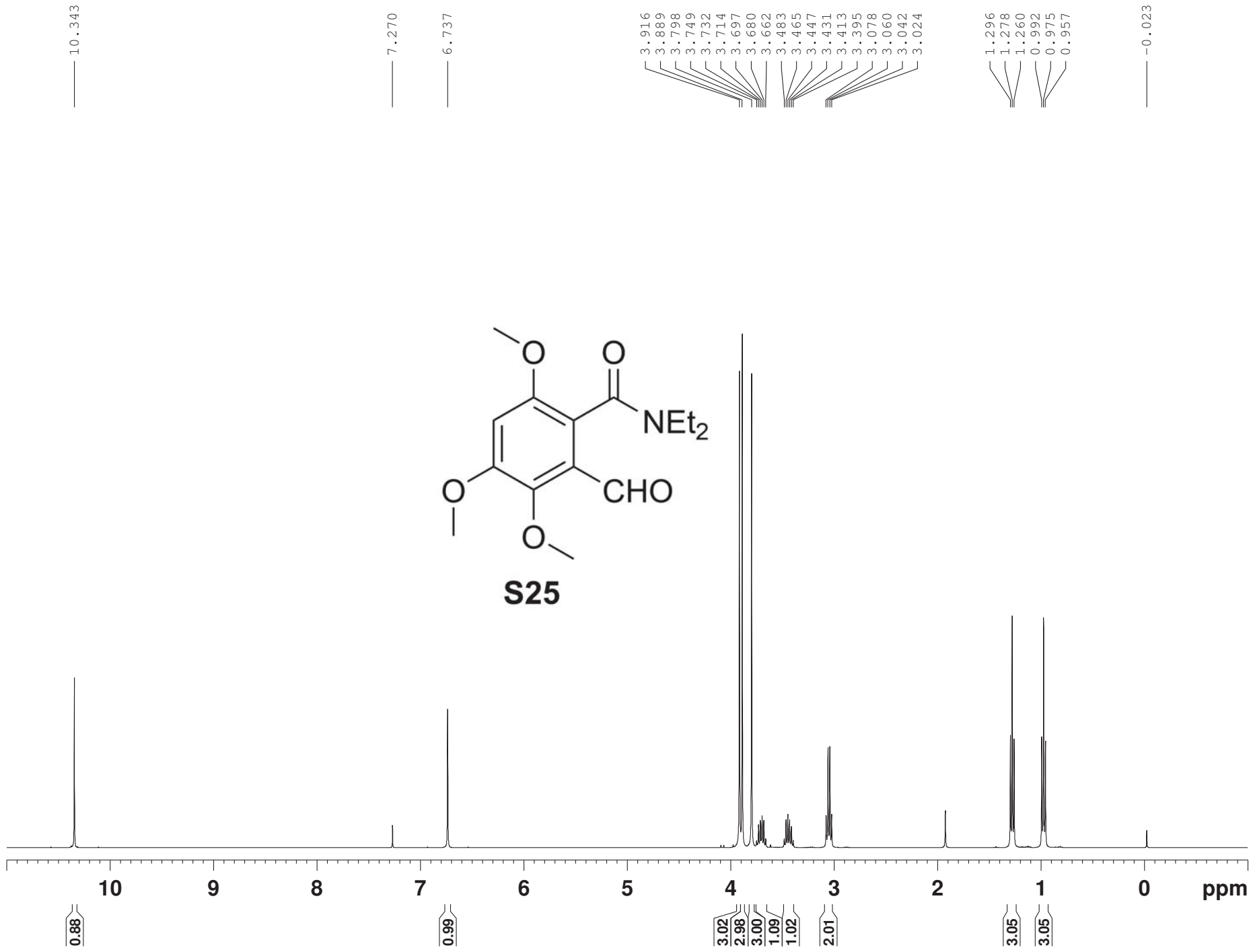
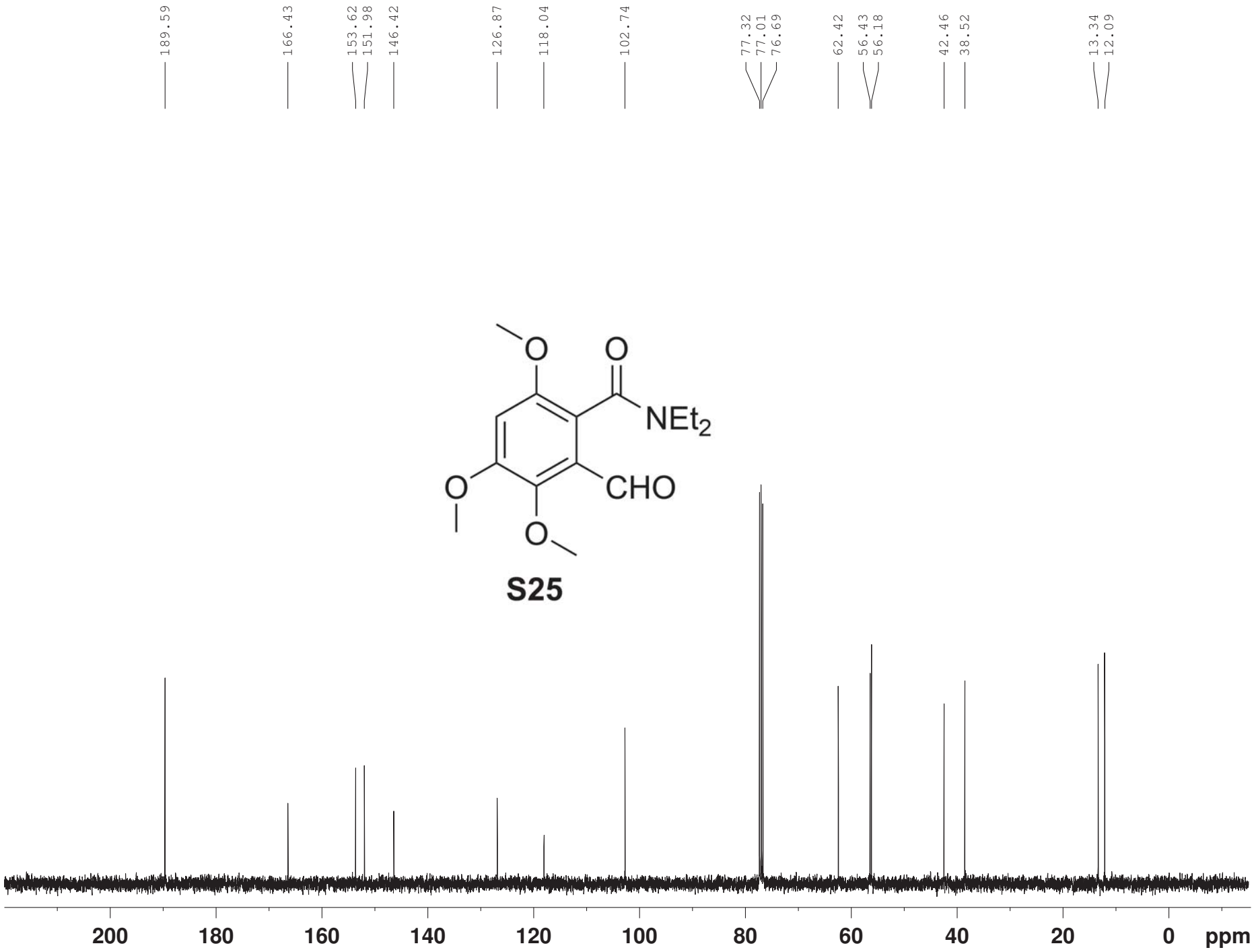
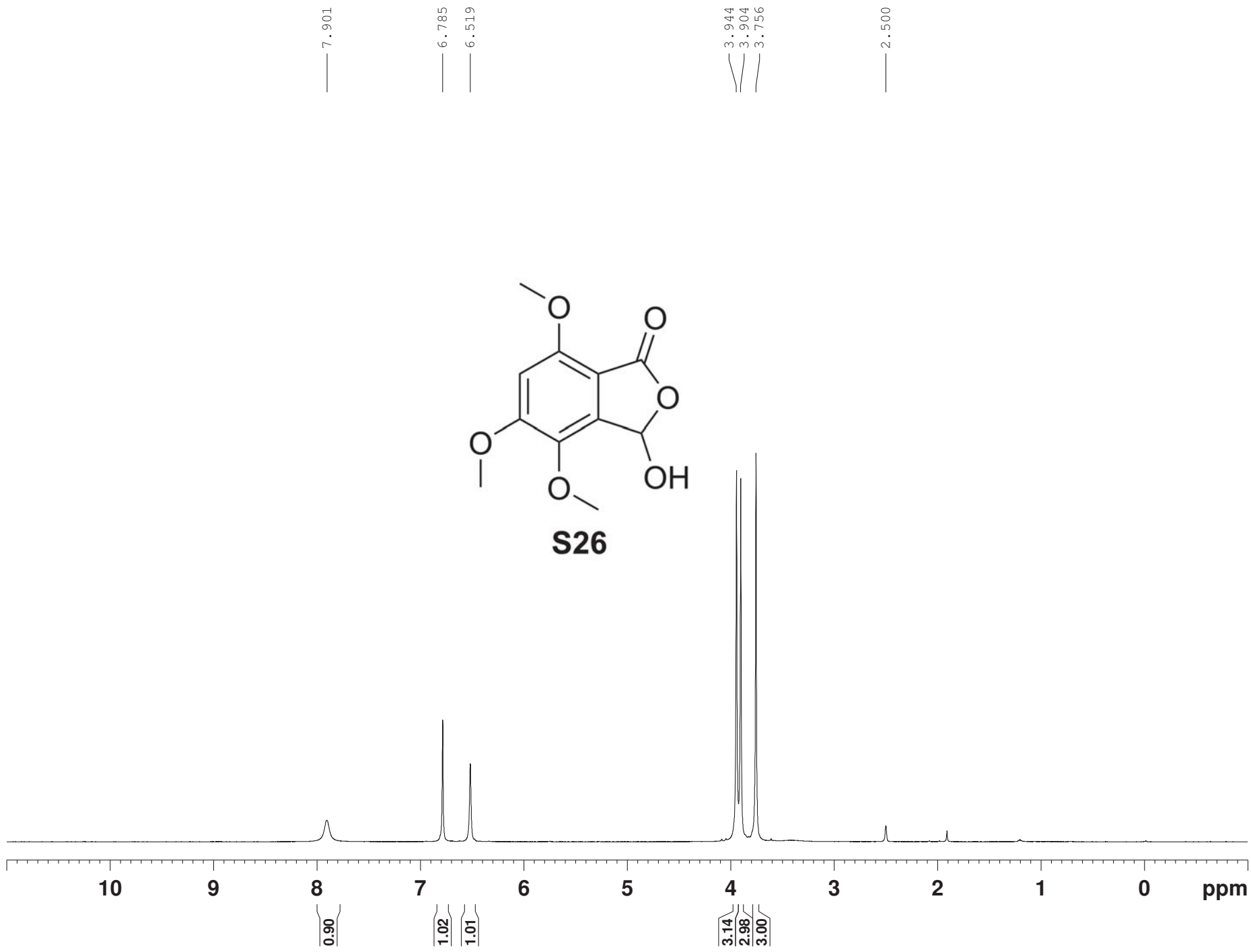
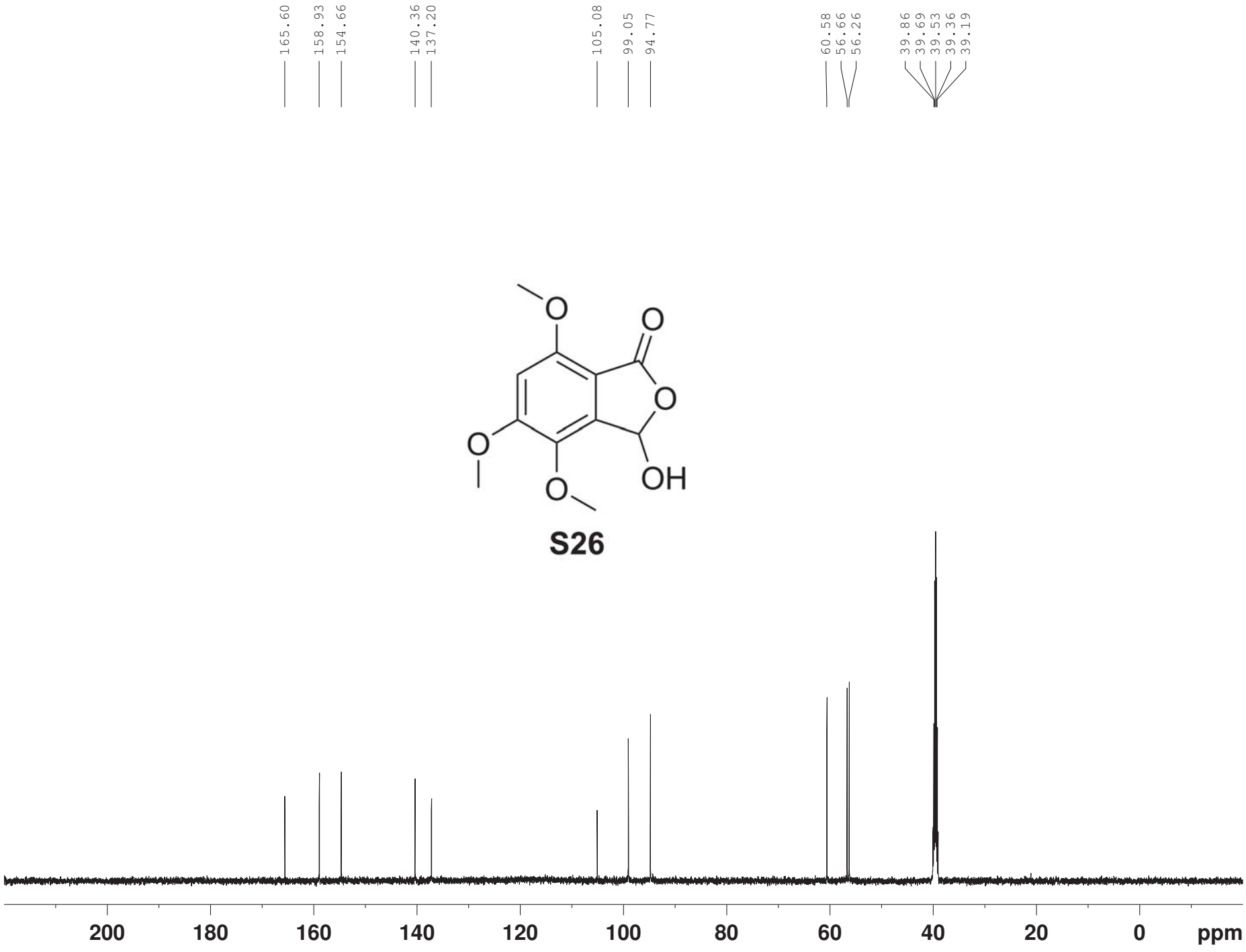
2.960
2.942
2.925
1.011
0.993
0.975
0.831
0.813
0.795
O
O
NEt2
O
O
S24
10
9
8
7
6
5
4
3
2
1
0
ppm
1.00
1.00
2.97
2.93
3.05
1.98
2.03
3.09
3.07


167.76
149.46
148.98
142.50
117.44
110.69
96.98
77.33
77.01
76.69
55.83
55.77
55.41
42.23
38.25
13.37
12.21
O
O
NEt2
O
O
S24
200
180
160
140
120
100
80
60
40
20
0
ppm

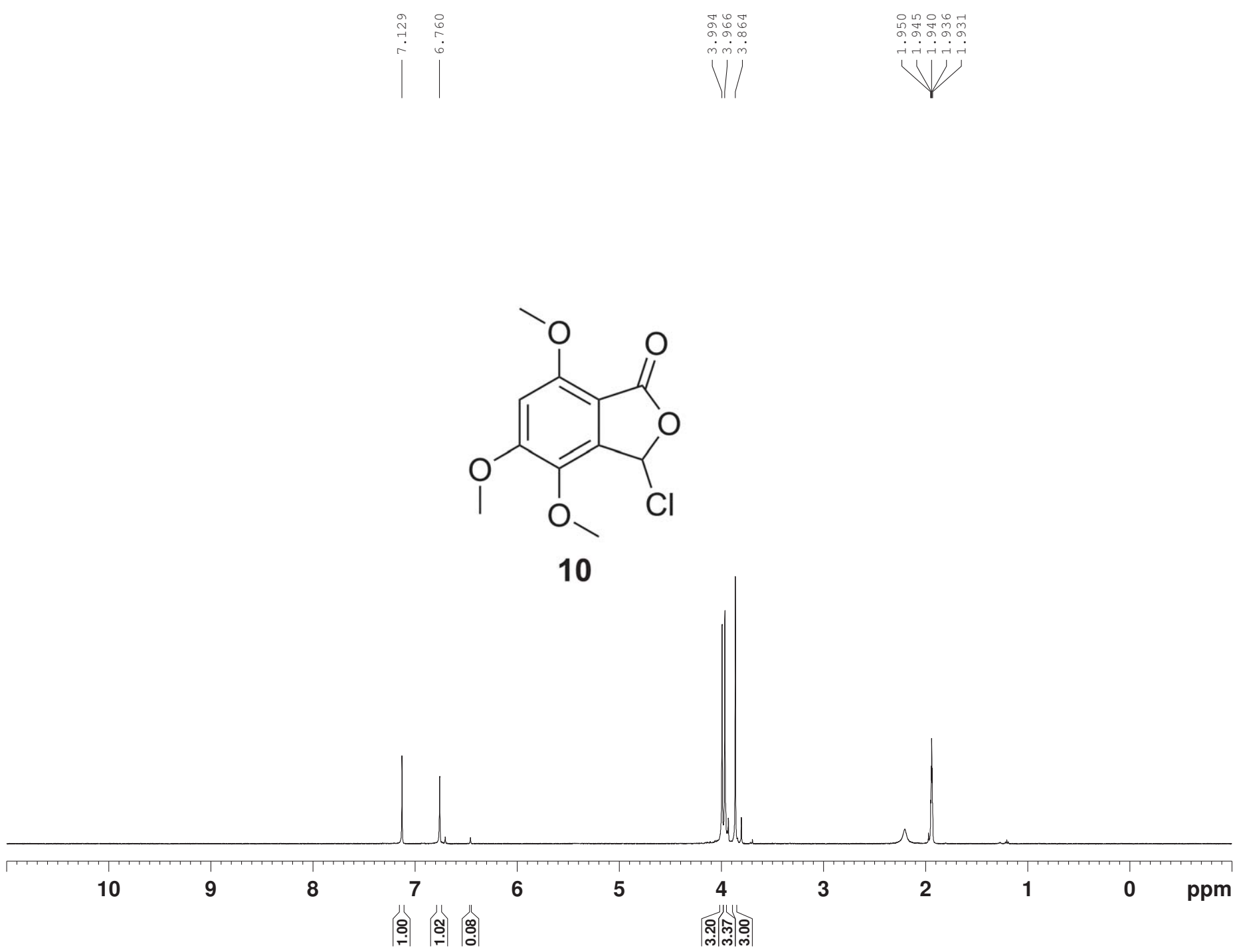

10.343
7.270
6.737
3.916
3.889
3.798
3.749
3.732
3.714
3.697
3.680
3.662
3.483
3.465
3.447
3.431
3.413
3.395
3.078
3.060
3.042
3.024
1.296
1.278
1.260
0.992
0.975
0.957
-0.023
O
O
NEt2
O
CHO
O
S25
10
9
8
7
6
5
4
3
2
1
0
ppm
0.88
0.99
3.02
2.98
3.00
1.09
1.02
2.01
3.05
3.05

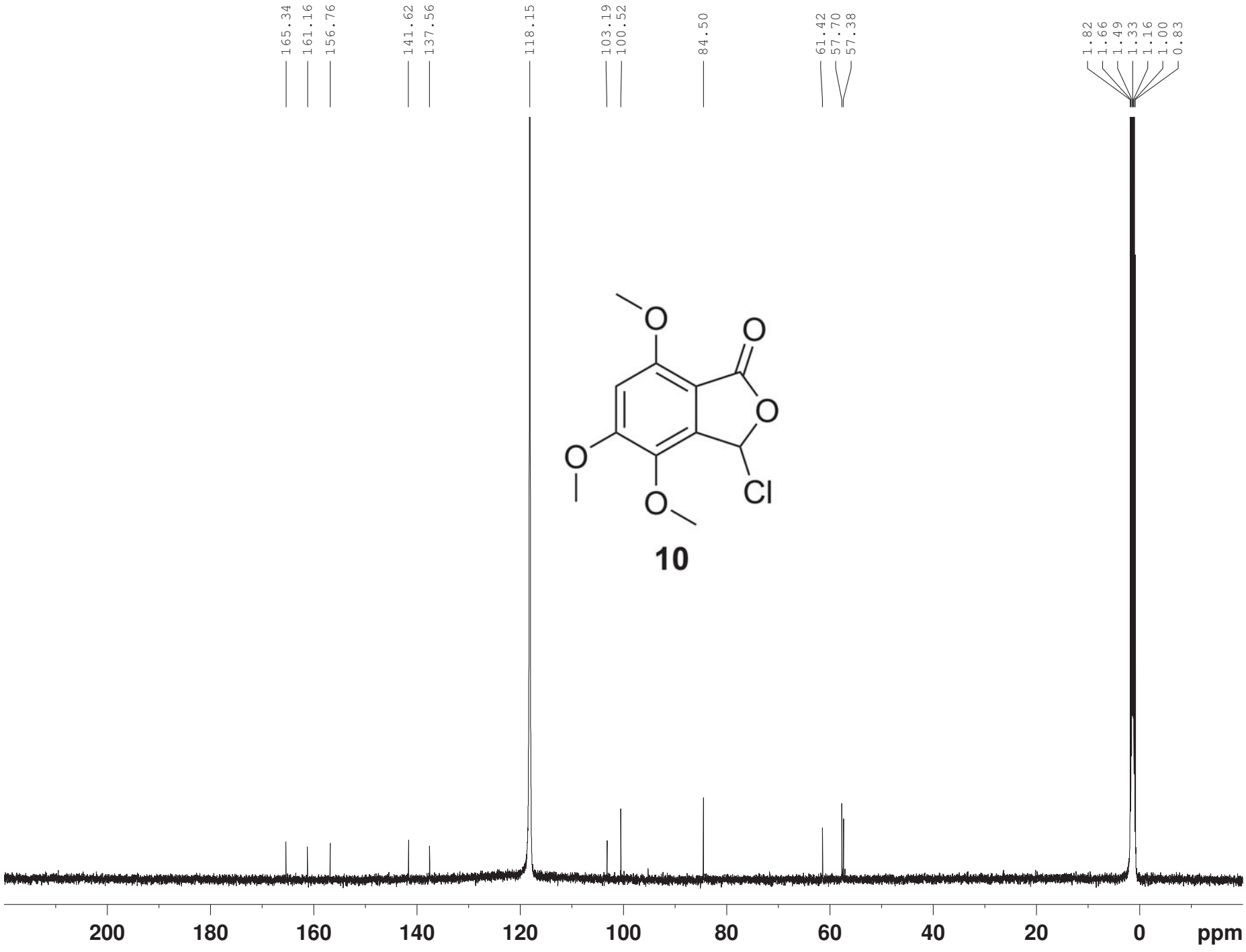

189.59
166.43
153.62
151.98
146.42
126.87
118.04
102.74
77.32
77.01
76.69
62.42
56.43
56.18
42.46
38.52
13.34
12.09
O
O
NEt2
CHO
O
O
S25
200
180
160
140
120
100
80
60
40
20
0
ppm


7.901
6.785
6.519
3.944
3.904
3.756
2.500
O
O
O
O
O
OH
S26
10
9
8
7
6
5
4
3
2
1
0
ppm
0.90
1.02
1.01
3.14
2.98
3.00

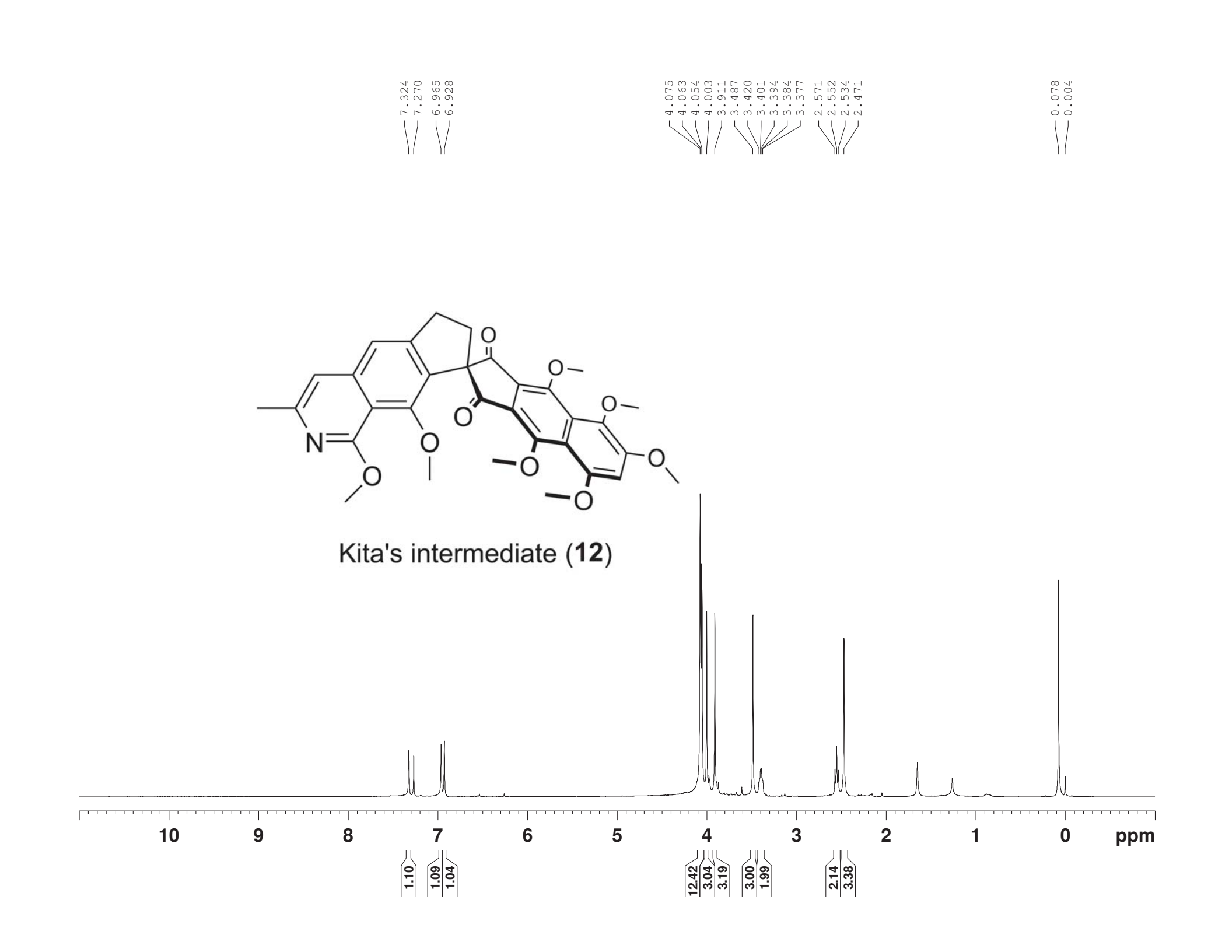

165.60
158.93
154.66
140.36
137.20
105.08
99.05
94.77
60.58
56.66
56.26
39.86
39.69
39.53
39.36
39.19
O
O
O
O
O
OH
200
180
160
140
120
100
80
60
40
20
0
ppm

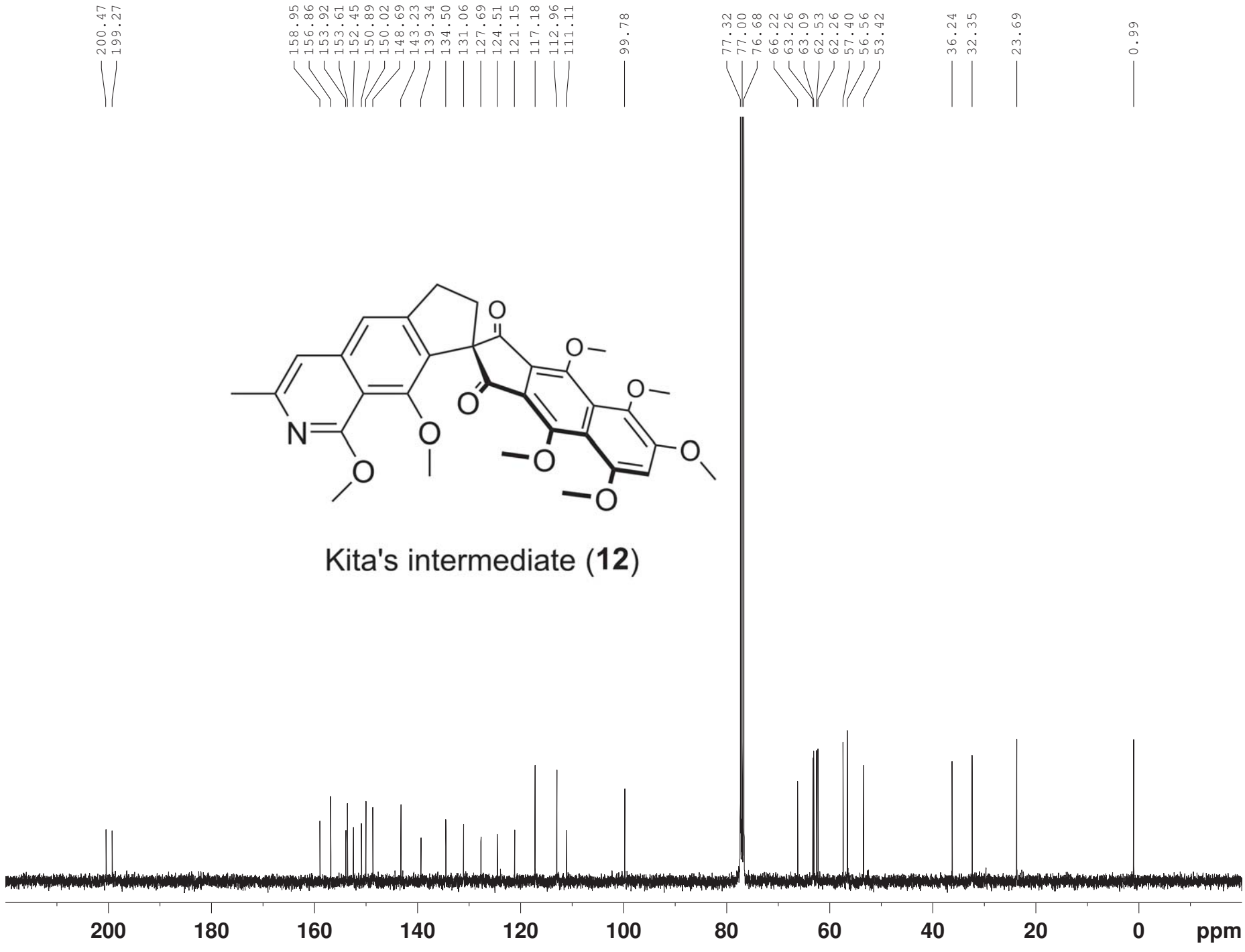
S26


7.129
6.760
3.994
3.966
3.864
1.950
1.945
1.940
1.936
1.931
O
O
O
O
O
Cl
10
10
9
8
7
6
5
4
3
2
1
0
ppm
1.00
1.02
0.08
3.20
3.37
3.00


165.34
161.16
156.76
141.62
137.56
118.15
103.19
100.52
84.50
61.42
57.70
57.38
1.82
1.66
1.49
1.33
1.16
1.00
0.83
O
O
O
O
O
Cl
200
180
160
140
120
100
80
60
40
20
0
ppm

10


7.324
7.270
6.965
6.928
4.075
4.063
4.054
4.003
3.911
3.487
3.420
3.401
3.394
3.384
3.377
2.571
2.552
2.534
2.471
0.078
0.004
Kita's intermediate (12)
10
9
8
7
6
5
4
3
2
1
0
ppm
1.10
1.09
1.04
12.42
3.04
3.19
3.00
1.99
2.14
3.38


200.47
199.27
158.95
156.86
153.92
153.61
152.45
150.89
150.02
148.69
143.23
139.34
134.50
131.06
127.69
124.51
121.15
117.18
112.96
111.11
99.78
77.32
77.00
76.68
66.22
63.26
63.09
62.53
62.26
57.40
56.56
53.42
36.24
32.35
23.69
0.99
Kita's intermediate (12)
200
180
160
140
120
100
80
60
40
20
0
ppm