Supporting information

Synthesis of novel fluorescent 12a-aryl substituted indoxylisoquinolines via aryne-induced domino process

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General information

The aryne precursors were purchased from Sigma-Aldrich and TCI and were used without additional purification. ^{1}H NMR and ^{13}C NMR were recorded on a Bruker AMX-400 (400 MHz for ^{1}H and 100.6 MHz for ^{13}C) and a JEOL JNM ECA (600 MHz and 150.9 MHz, respectively). Proton chemical shifts are reported relative to the residual solvent peak ($CDCl_3$ at δ 7.26 ppm). Carbon chemical shifts are reported relative to $CDCl_3$ at δ 77.2 ppm. Mass spectra were recorded using LCMS-8040 Shimadzu (Japan), ESI. IR spectra were recorded on FT spectrometer Infralum FT-801. For the elemental analyses, a Carlo Erba 1106 was used. Melting points were measured on SMP 10 in open capillaries. TLC on Sorbfil plates was used for the monitoring of reactions. Kieselgel from Macherey-Nagel GmbH&Co (0.04–0.06 mm/230–400 mesh), 60 Å, was used for column chromatography. All solvents were dried according to standard procedures. The absorbance spectra were recorded with a Varian Cary 100 Bio UV-visible Spectrophotometer. Fluorescence excitation and emission spectra were recorded with a Varian Cary Eclipse fluorescence spectrophotometer.

Optimization studies

Table 1. Optimization study

Entry	Aryne	Conditions[a]	Reaction time	Product	Yield, %
1	6a	CsF, MeCN, 20°C	3 days	7a	90
2	6a	CsF, THF, 20°C	1 month	7a	55
3	6a	CsF, MeCN, 50°C	1 day	7a	84
4	6a	TBAT, MeCN, 20°C	2 days	7a	84[b]
5	6a	CsF, THF, 125°C, MW	1,5 h	7a	73
6	6a	CsF, THF, 135°C, MW	1 h	7a	56
7	6a	CsF, MeCN, 150°C, MW	30 min	7a	45
8	6a	TBAT, MeCN, 125°C, MW	40 min	7a	44
9	6a	10 eq.TBAF , THF, 125°C, MW	45 min	Not formed	-
10	6f	CsF, MeCN, 20°C	3 days	7f	85
11	6f	CsF, THF, 125°C, MW	1 h	7f	67
12	6g	CsF, MeCN, 20°C	3 days	7g	87
13	6g	CsF, MeCN, 150°C, MW	45 min	7g	45
14	6h	CsF, MeCN, 20°C	2 days	7h	45
15	6h	CsF, THF MeCN, 125°C, MW	50 min	7h	67

[a] The reaction condition: unless other specified, 3 eq. of fluoride source and 5 mL of solvent were used. [b]The isolated yield after second chromatographic purification.

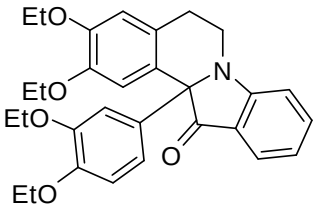
As it could be seen from the table 1 the better yields were achieved with CsF in acetonitrile both at room temperature and at mild heat to 50°C. The use of TBAT (tetrabutylammonium difluorotriphenylsilicate) is also enhancing the reaction time, but in some cases the additional purification of the product is required due to incomplete washout from the catalyst. It was established that the better solvent for reactions conducted at room temperature or slight heat is acetonitrile, while for microwave assisted reactions the use of THF is preferably. The increase of temperature results in reduction of reaction time (entry 3, 5-8), but however decrease the yield and provoke by-products formation which complicate the isolation of product, especially in case of substituted arynes. The use of microwave irradiation obviously reduces the reaction time, but

the yields of desired products were dramatically decreased (entry 6-8, 13), except aryne **6h** (compare entry 14 and 15). The model experiments with THF as a solvent showed that the reaction readily starts only at temperatures above solvent boiling point that can be achieved in microwave reactor. To our surprise the desired indoloisoquinoline **7a** did not form when 10eq TBAF (tetrabutylammonium fluoride) in THF at 125°C (MW) was used; the only isolated product was aromatized isoquinoline (not presented in table).

Based on obtained results the further study of scope and limitation of this reaction was conducted with the use of acetonitrile as a solvent and cesium fluoride as catalyst.

General procedure for the synthesis of indolo[2,1-*a*]isoquinolinones (7a-h, 8a,b).

To a suspension of CsF (3 eq.) in 5-7 mL of dry acetonitrile, the aryloxy substituted isoquinoline **1** or **2** (1 eq.) was added, and after the dissolution of starting material the corresponding (trimethylsilyl)aryltrifluoromethanesulfonate (1.2 eq.) was added into the flask. The mixture was stirred at room temperature for 3 days with TLC monitoring. Upon completion, the solvent was removed under reduced pressure, 5 mL of $CHCl_3$ was added, the white precipitate of CsOTf was filtrated and washed 2 times with $CHCl_3$, the filtrate was evaporated, and the resulting crude oil was then purified by column chromatography (glass column, H=180 mm, d=20 mm, mobile phase: gradient EtOAc-hexane) to give the corresponding indolo[2,1-*a*]isoquinolinones (**7a-h**,**8a,b**) with good yields.



12a-(3,4-Diethoxyphenyl)-2,3-diethoxy-5,12a-dihydroindolo[2,1-*a*]isoquinolin-12(6*H*)-one (7a)

Yellow powder or yellow oil. Yield 90% (105 mg); MP 132-133°C; R_f 0.8 (EtOAc-Hexane, 1:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.59 (d, *J*=8.1 Hz, 1H, 11-H), 7.46 - 7.39 (m, 1H, 9-H), 7.29 (s, 1H, 1-H), 6.90 (d, *J*=8.7 Hz, 1H, 8-H), 6.74 (t, *J*=7.5 Hz, 1H, 1-H), 6.68 (d, *J*=8.1 Hz, 1H, 3'-H), 6.57-6.53 (m, 2H, 2'-H, 6'-H), 6.52 (s, 1H, 4-H), 4.06 - 3.92 (m, 6H, OCH_2CH_3), 3.85 (q, *J*=7.1 Hz, 2H, OCH_2CH_3), 3.74 (ddd, *J*=13.7, 5.6, 3.1 Hz, 1H, 6-CH_2), 3.45 -3.29 (m, 1H, 6-CH_2), 2.92 - 2.73 (m, 1H, 5-CH_2), 2.55 (ddd, 1H, *J*=16.0, 3.6, 3.4 Hz, 5-CH_2), 1.40 - 1.29 (m, 9H, OCH_2CH_3), 1.26 (t, *J*=7.2 Hz, 3H, OCH_2CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 201.1, 160.8, 148.8, 148.7, 148.2, 147.1, 137.2, 134.1, 127.4, 125.9, 125.1, 121.7, 121.3, 118.7, 114.4, 113.3 (2C), 110.0, 74.4, 64.9, 64.7 (2C), 64.6, 39.4, 29.8, 26.4, 14.9 (2C), 14.8, 14.7; ESI MS [M+H] 488; [Found: C, 73.84; H, 6.72; N, 2.91. $C_{30}H_{33}NO_5$ requires C, 73.90; H, 6.82; N, 2.87 %]; IR (KBr) 3392, 2978, 2928, 1699, 1610, 1509, 1477, 1256, 1041, 756 cm^{-1}.

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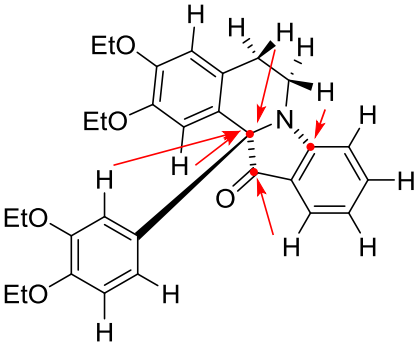

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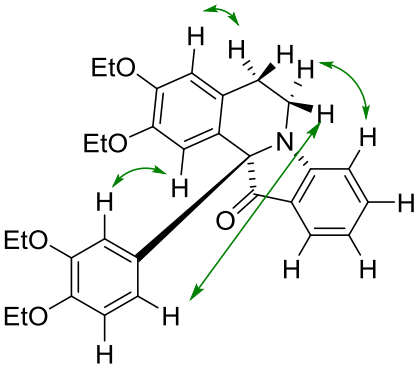

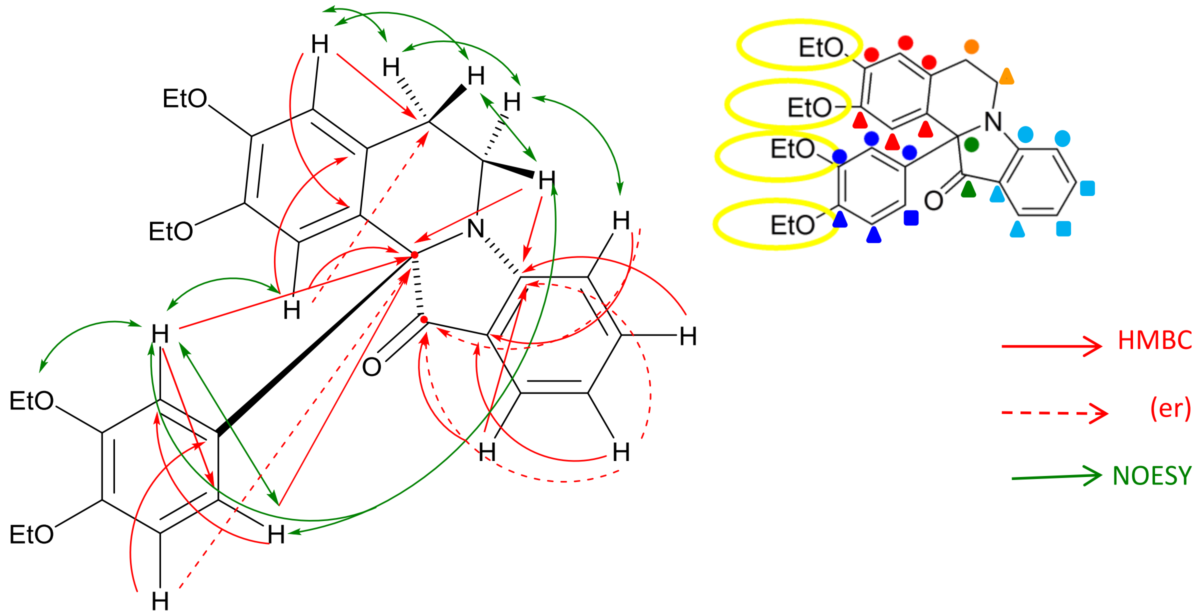
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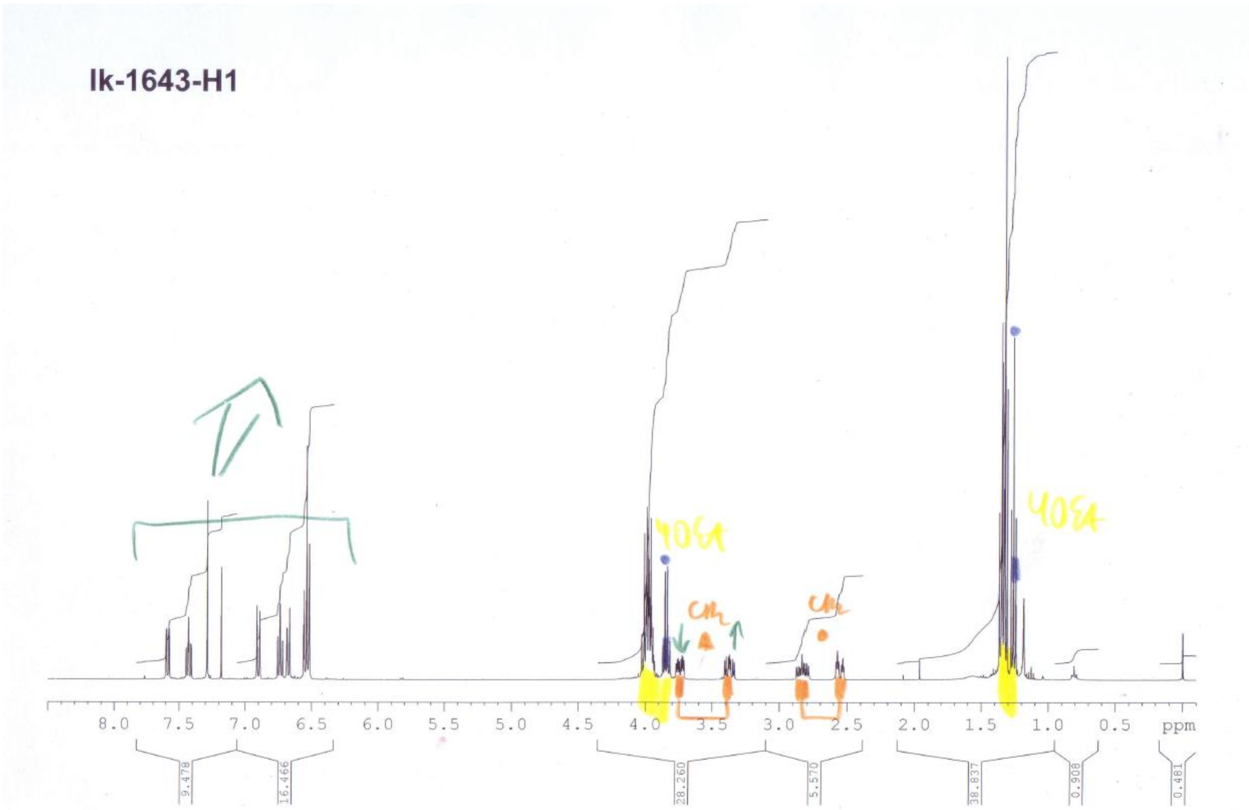
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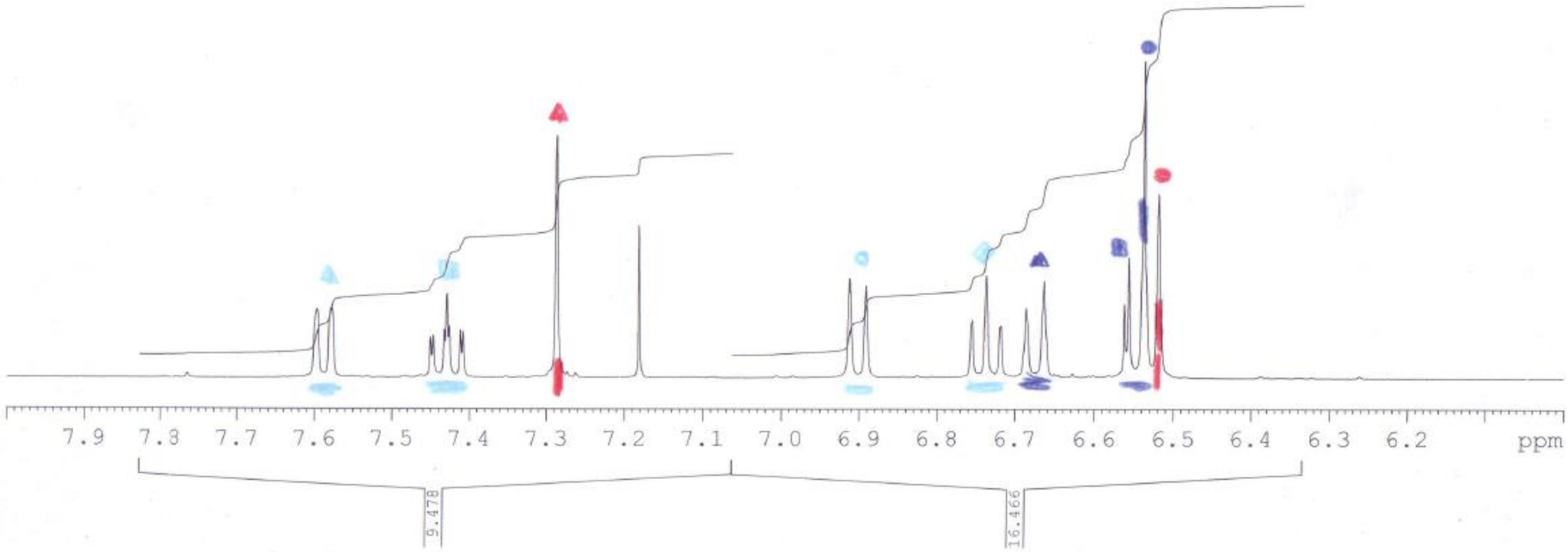
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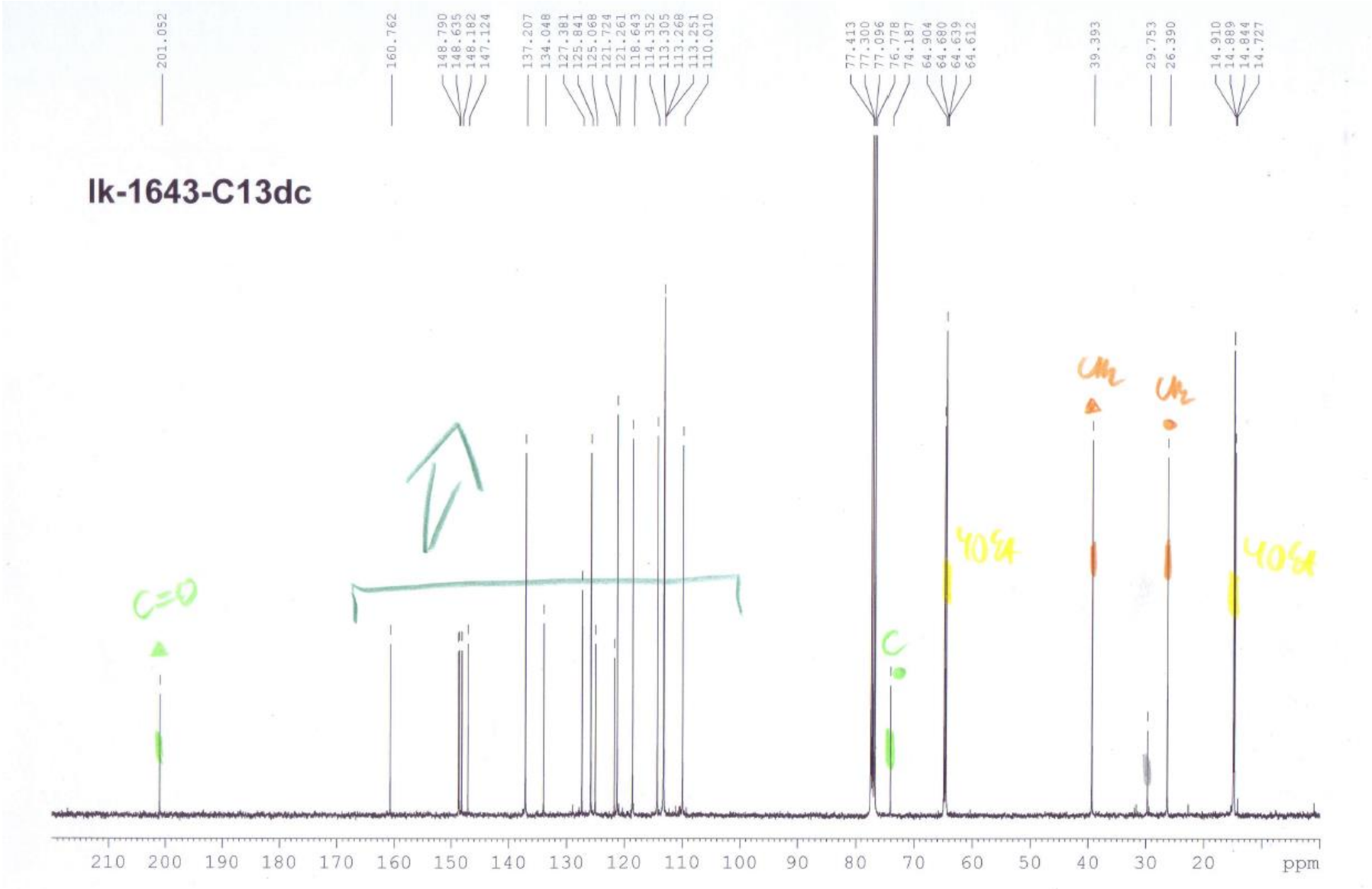
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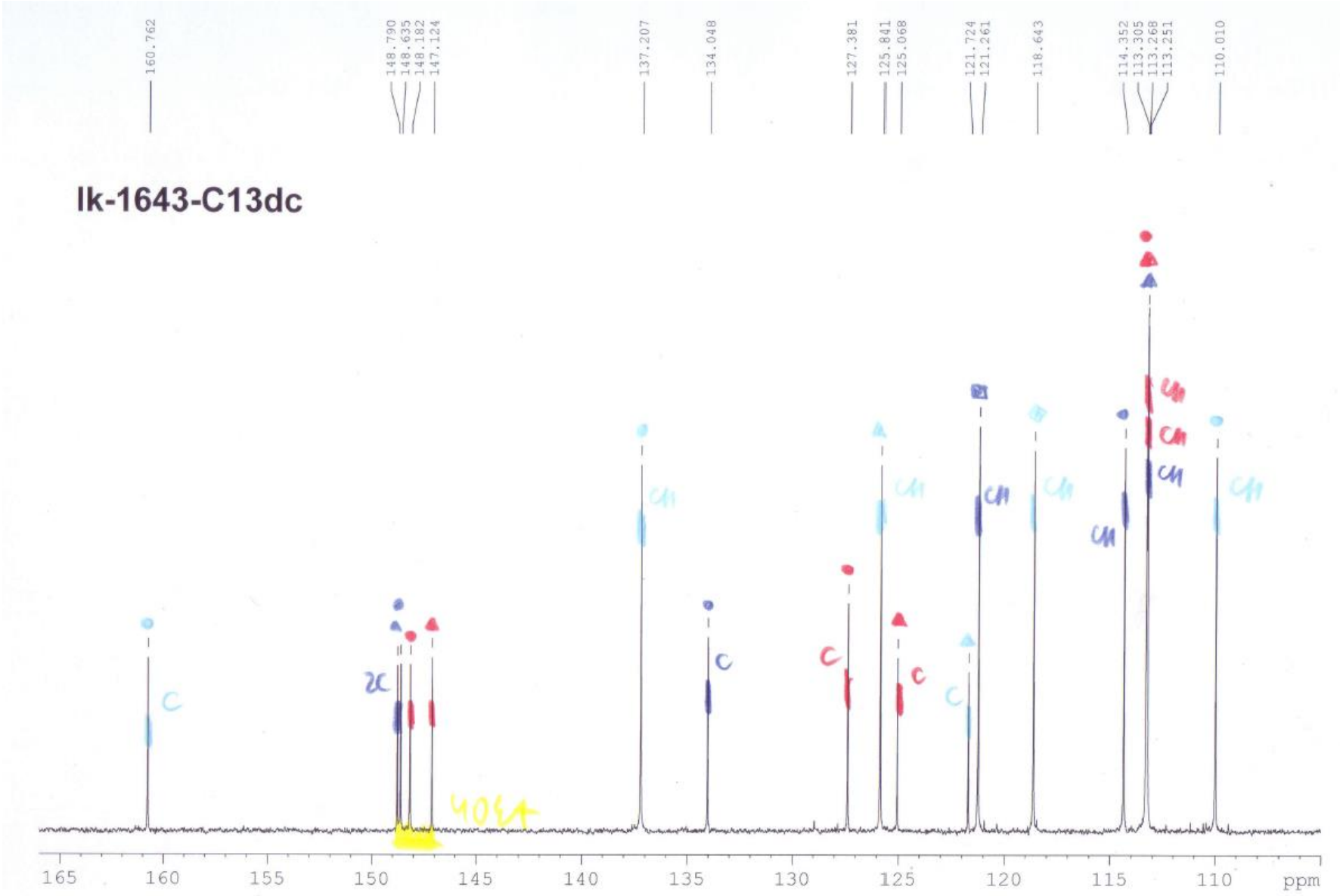
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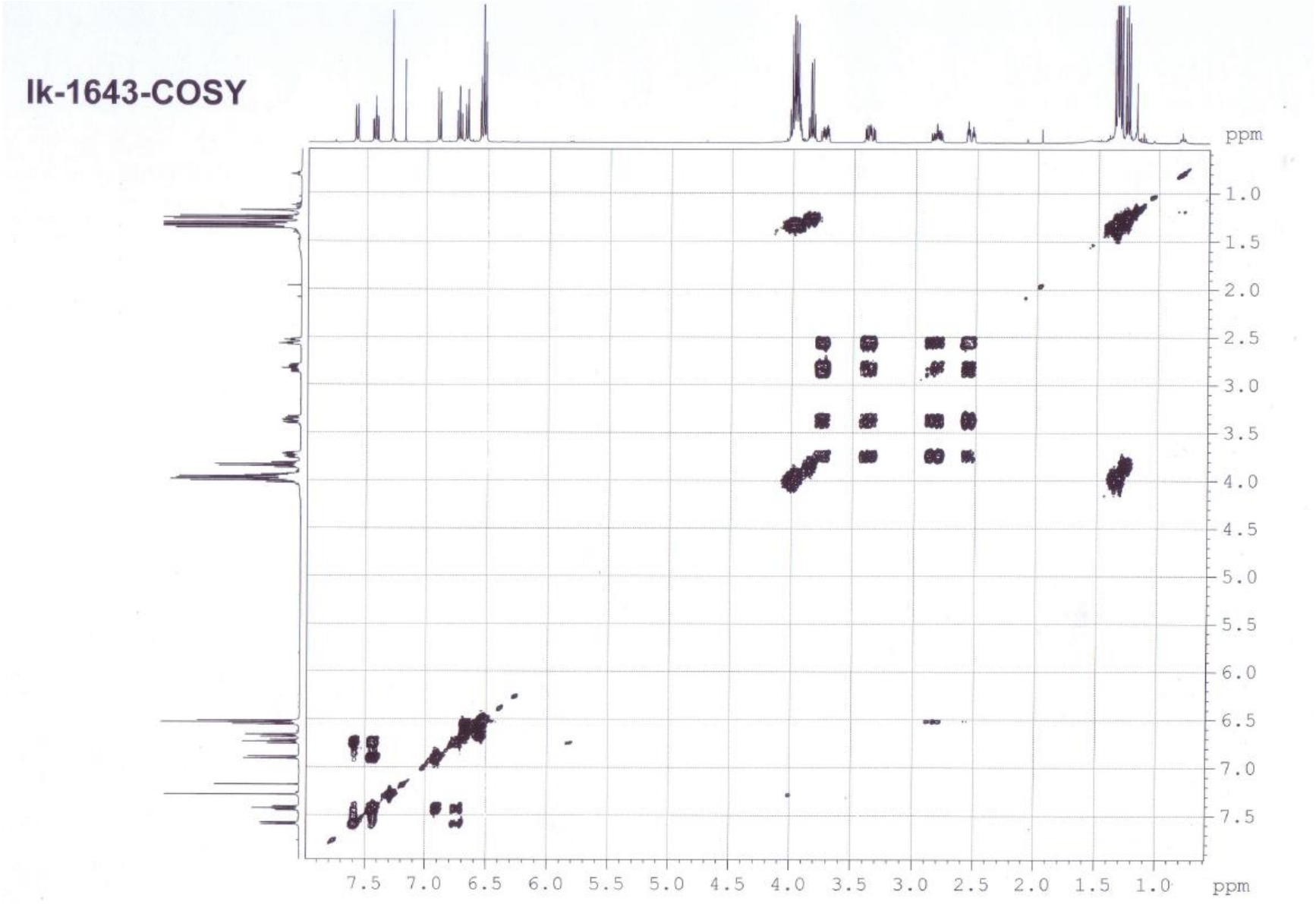
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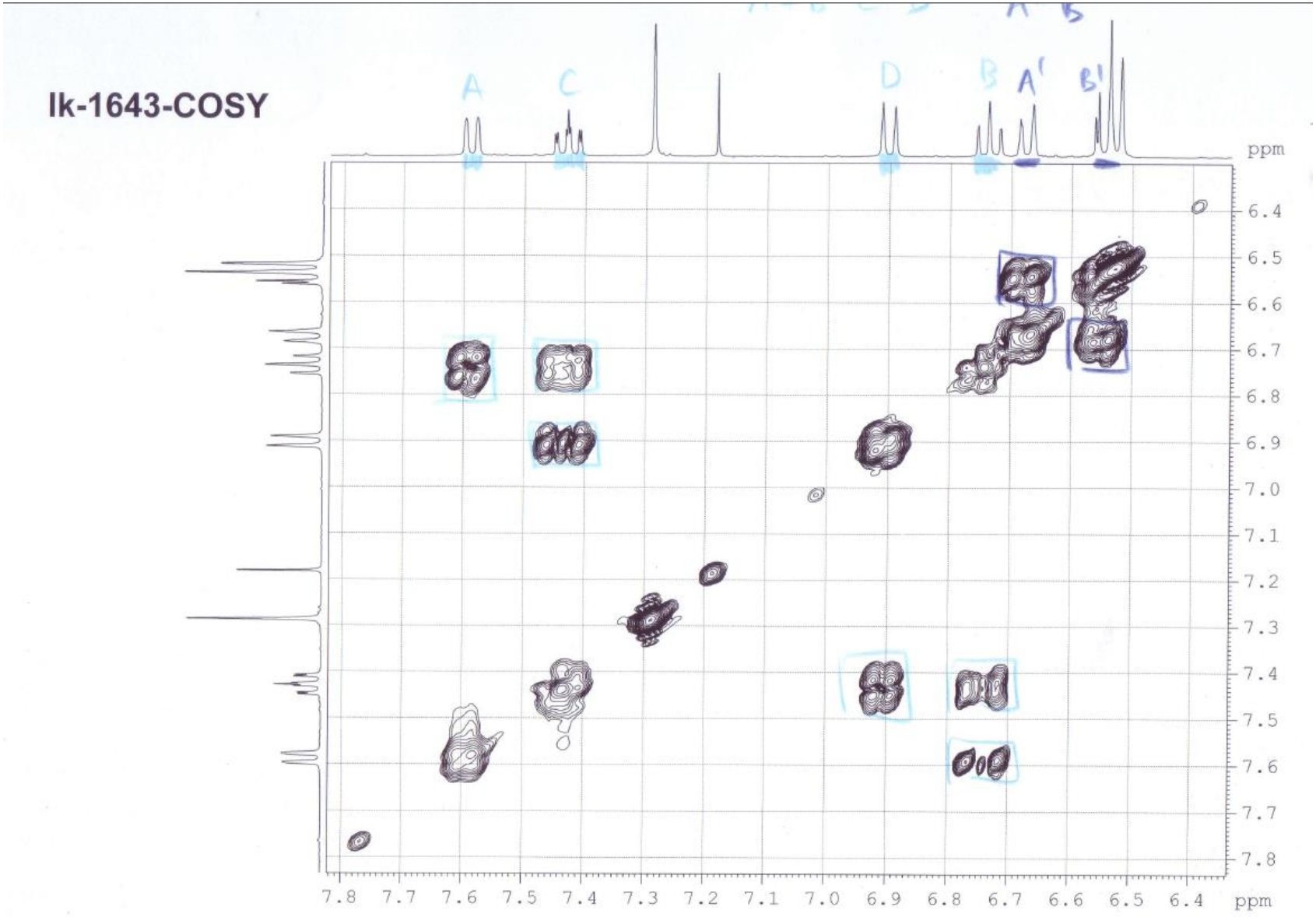
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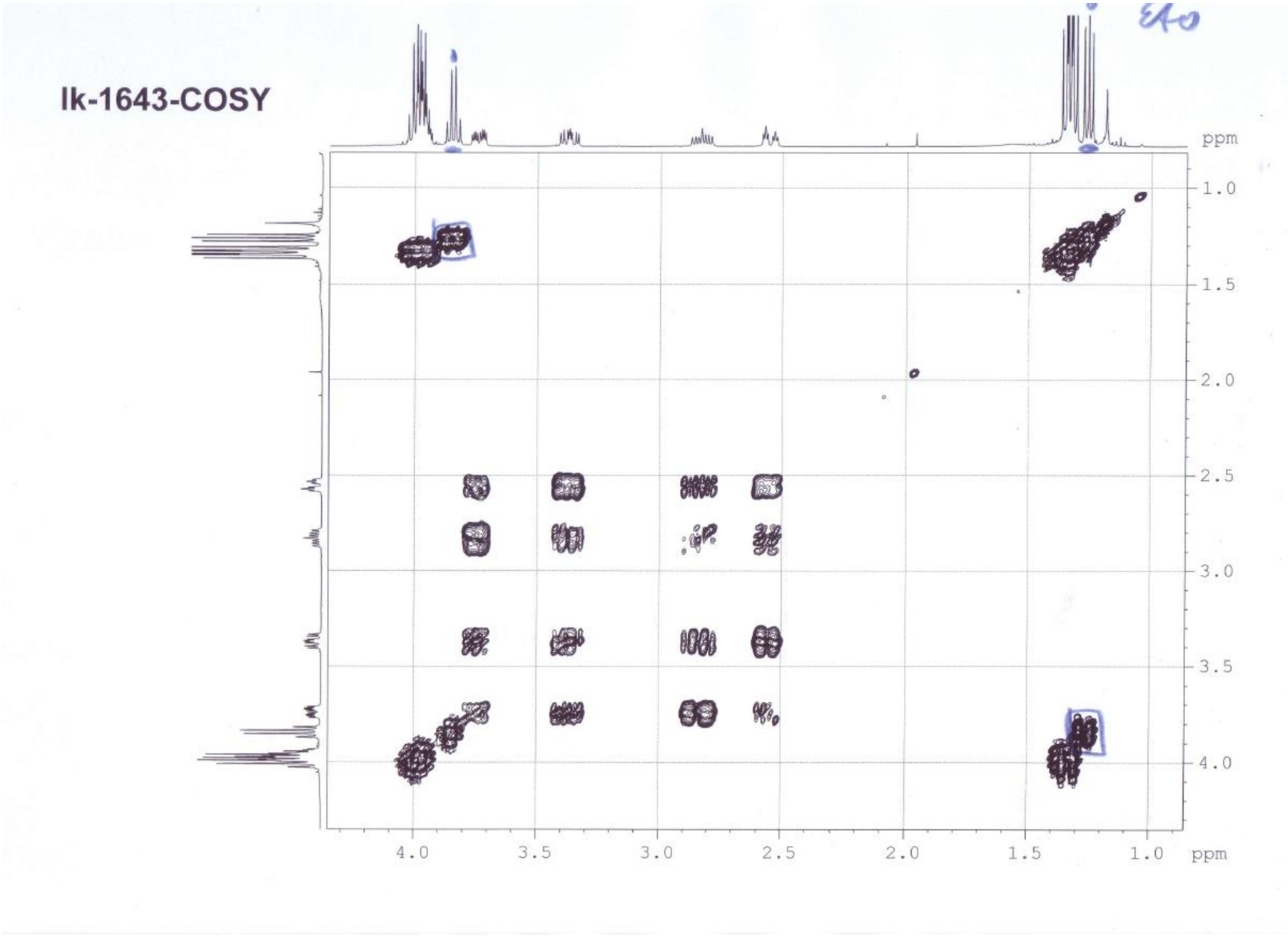
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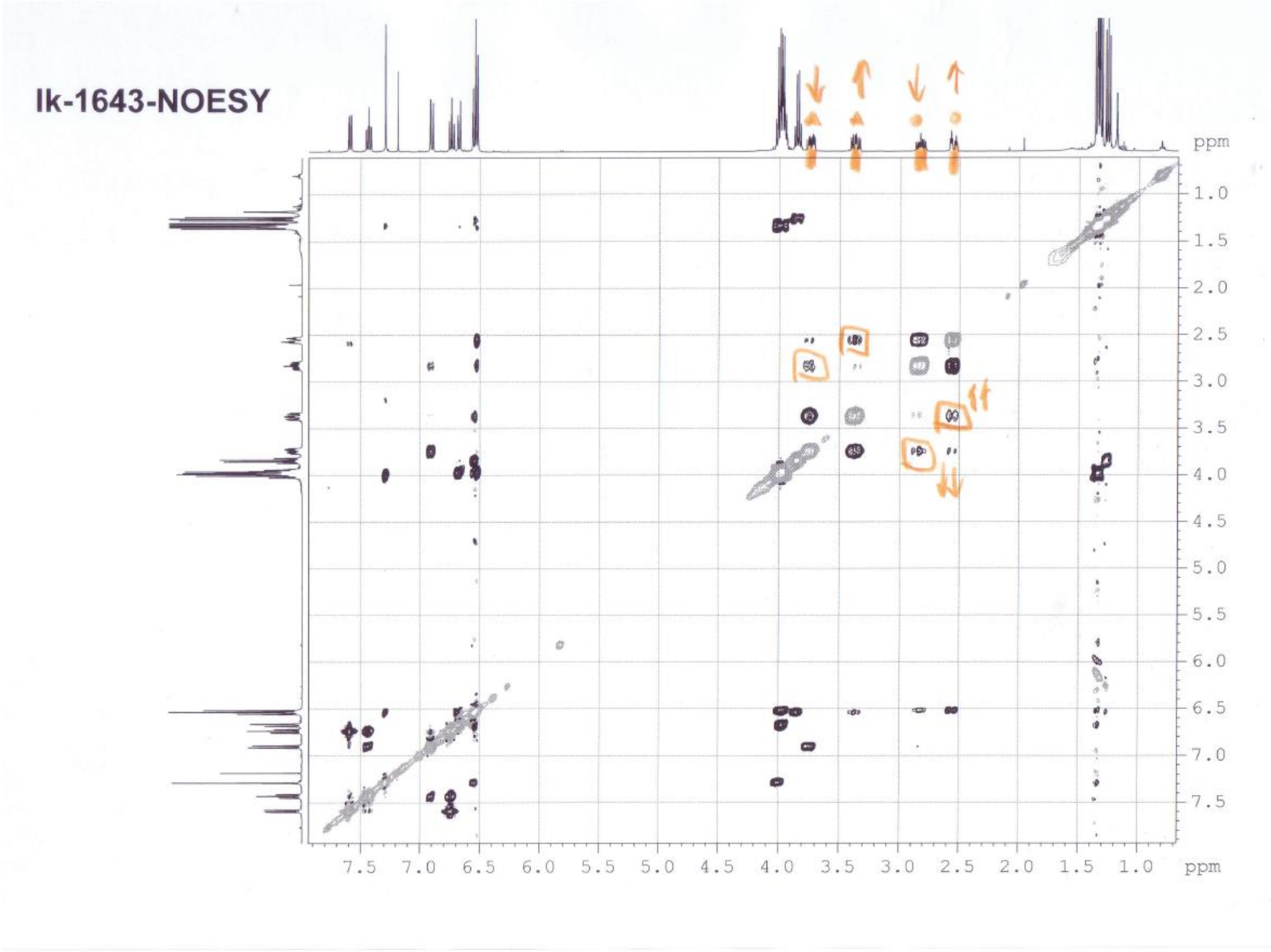
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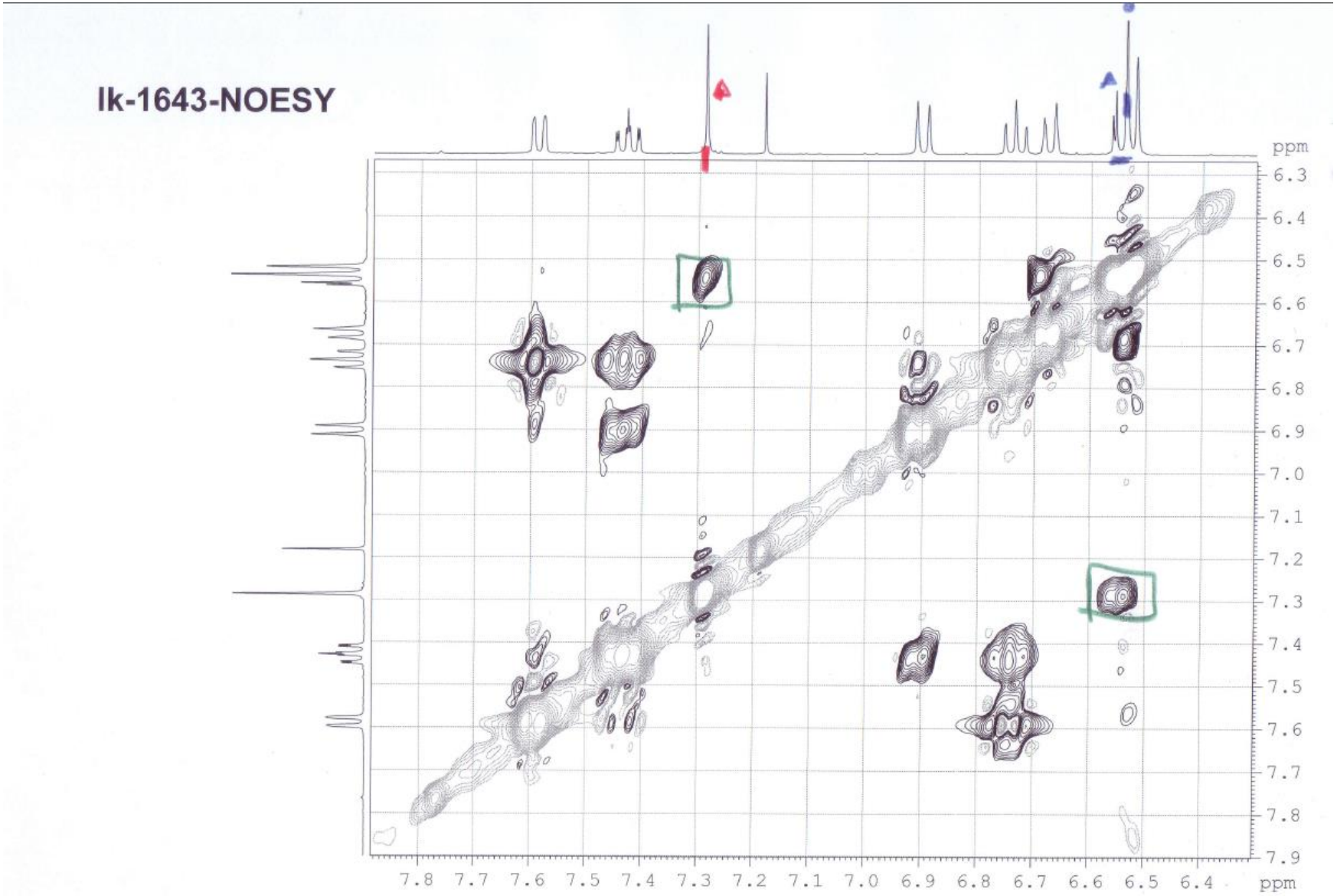
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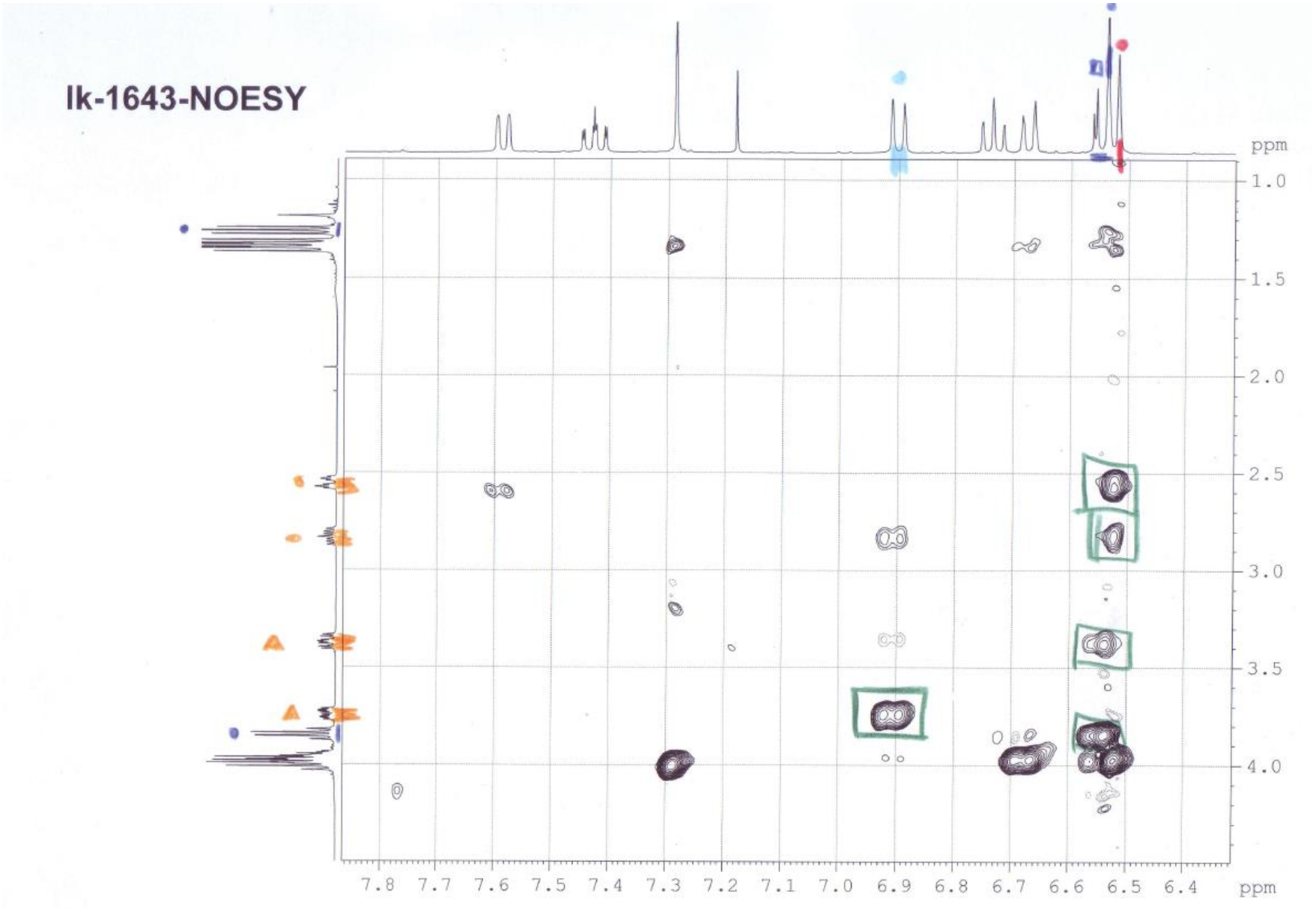
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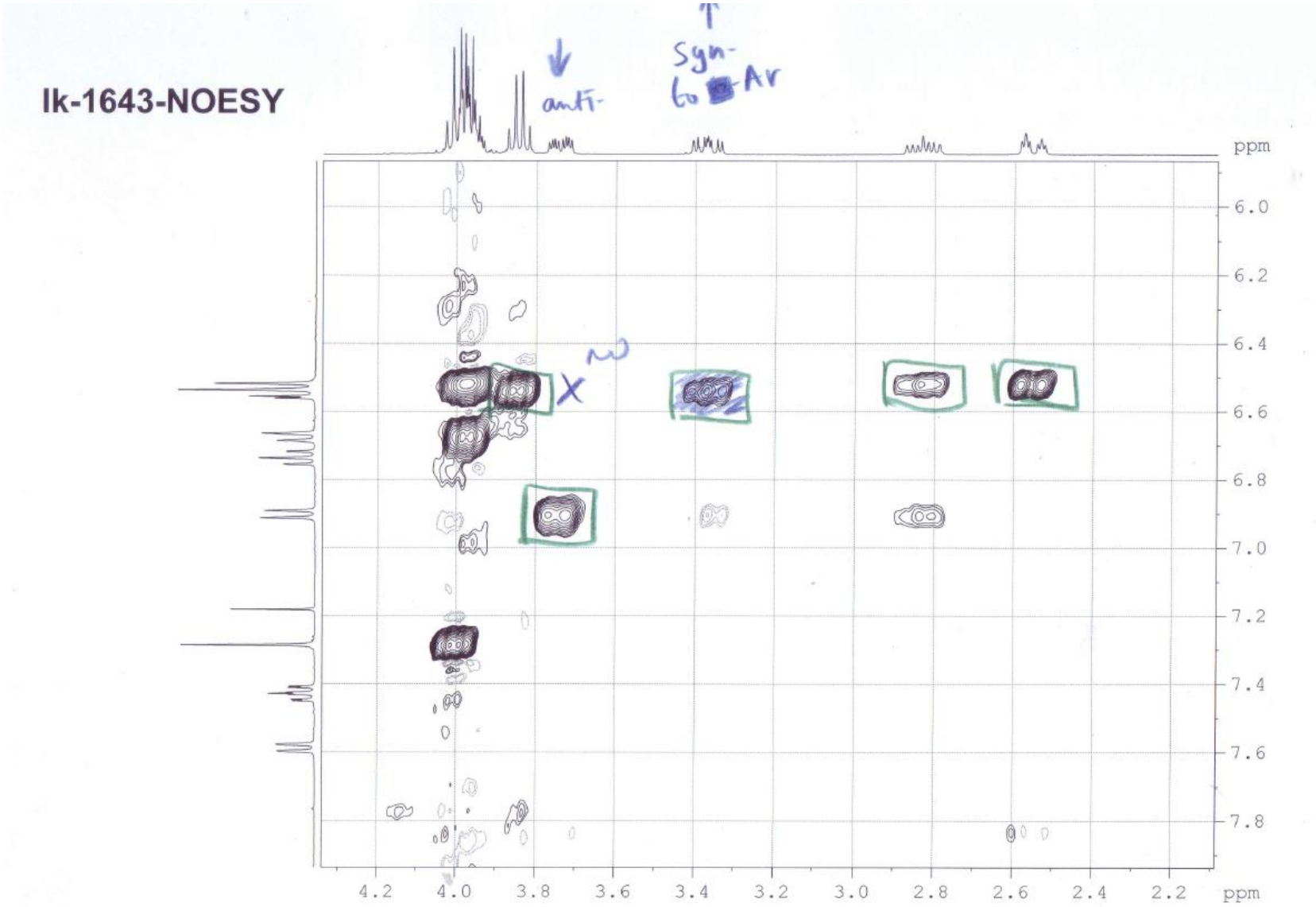
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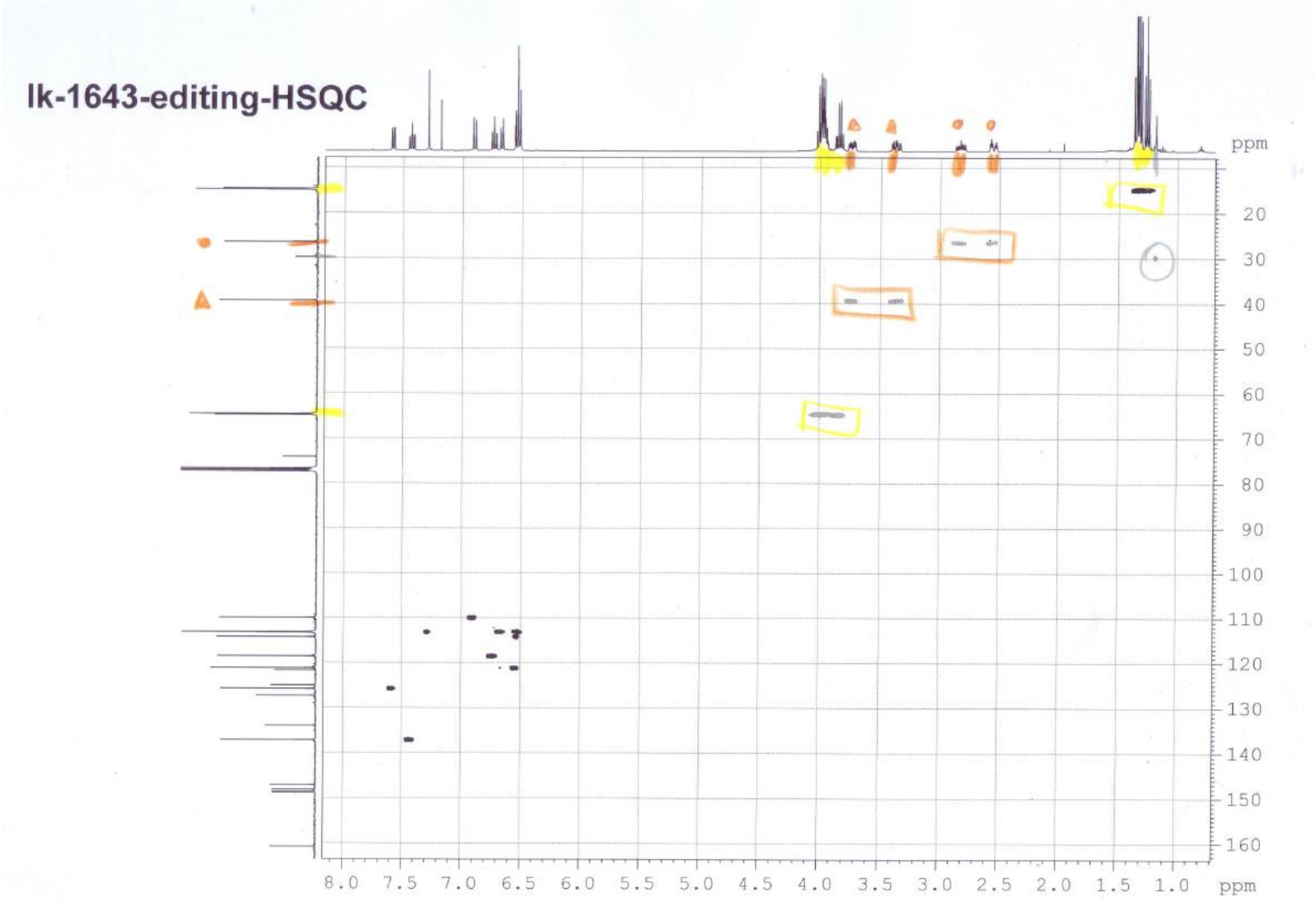
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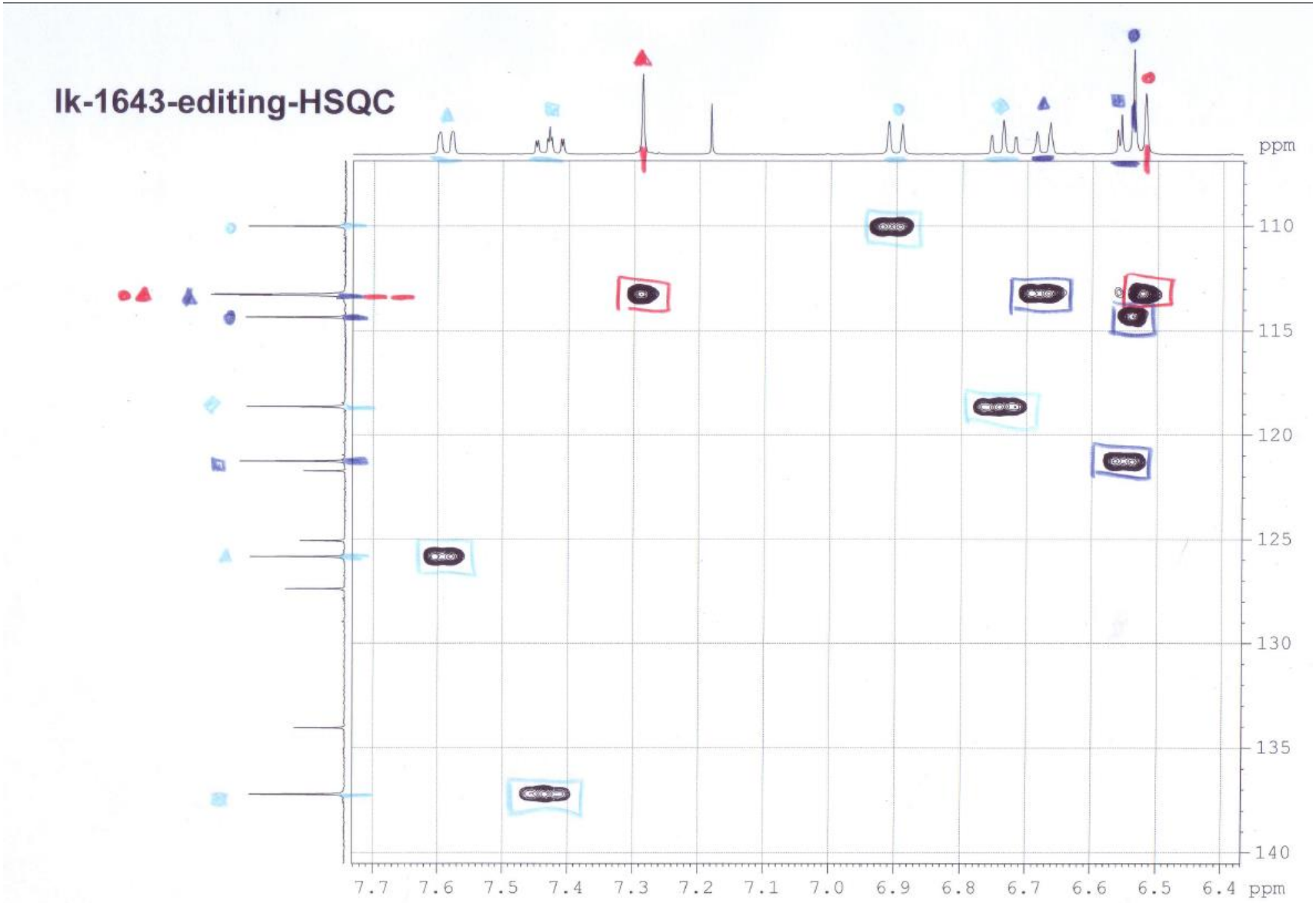
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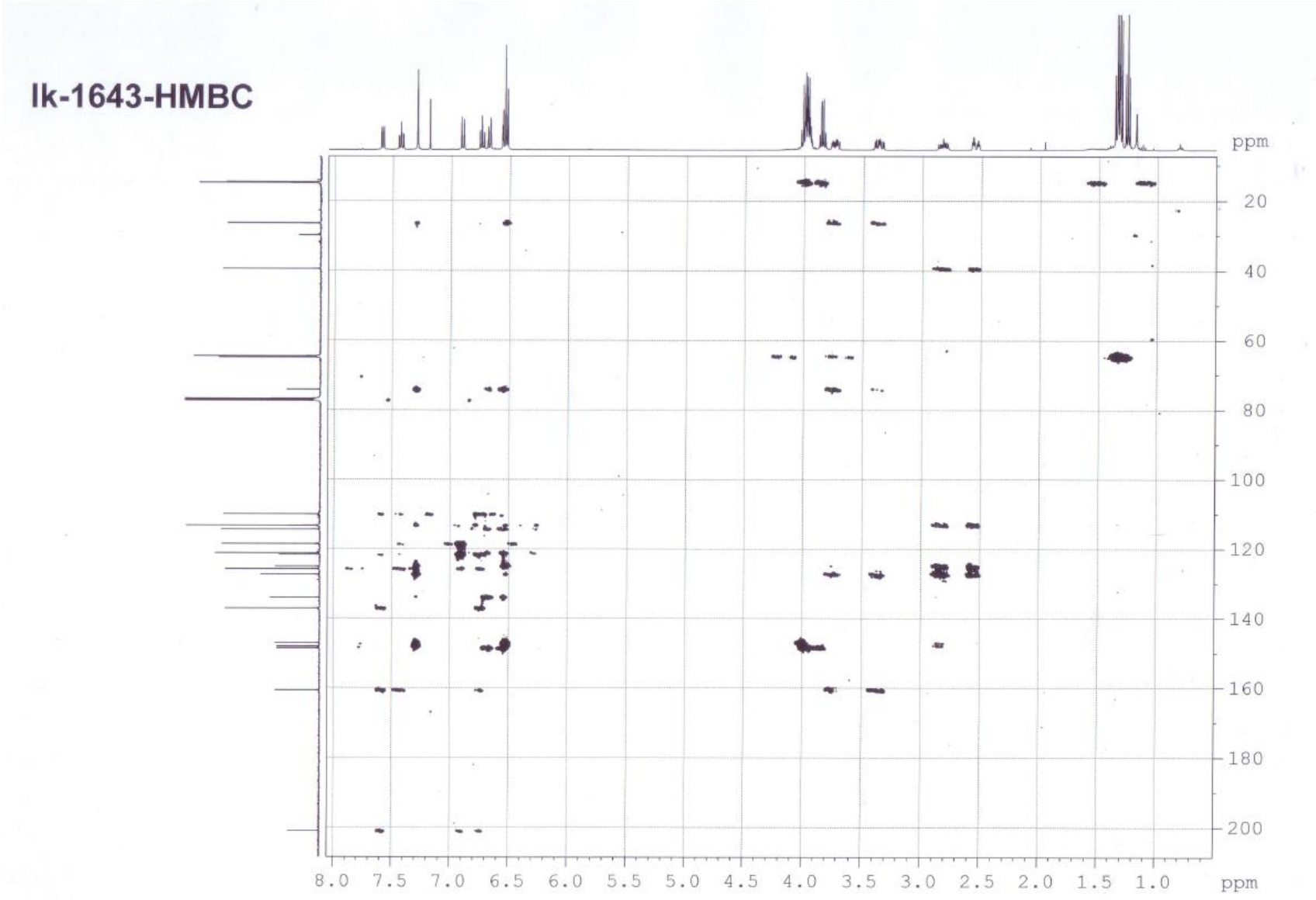
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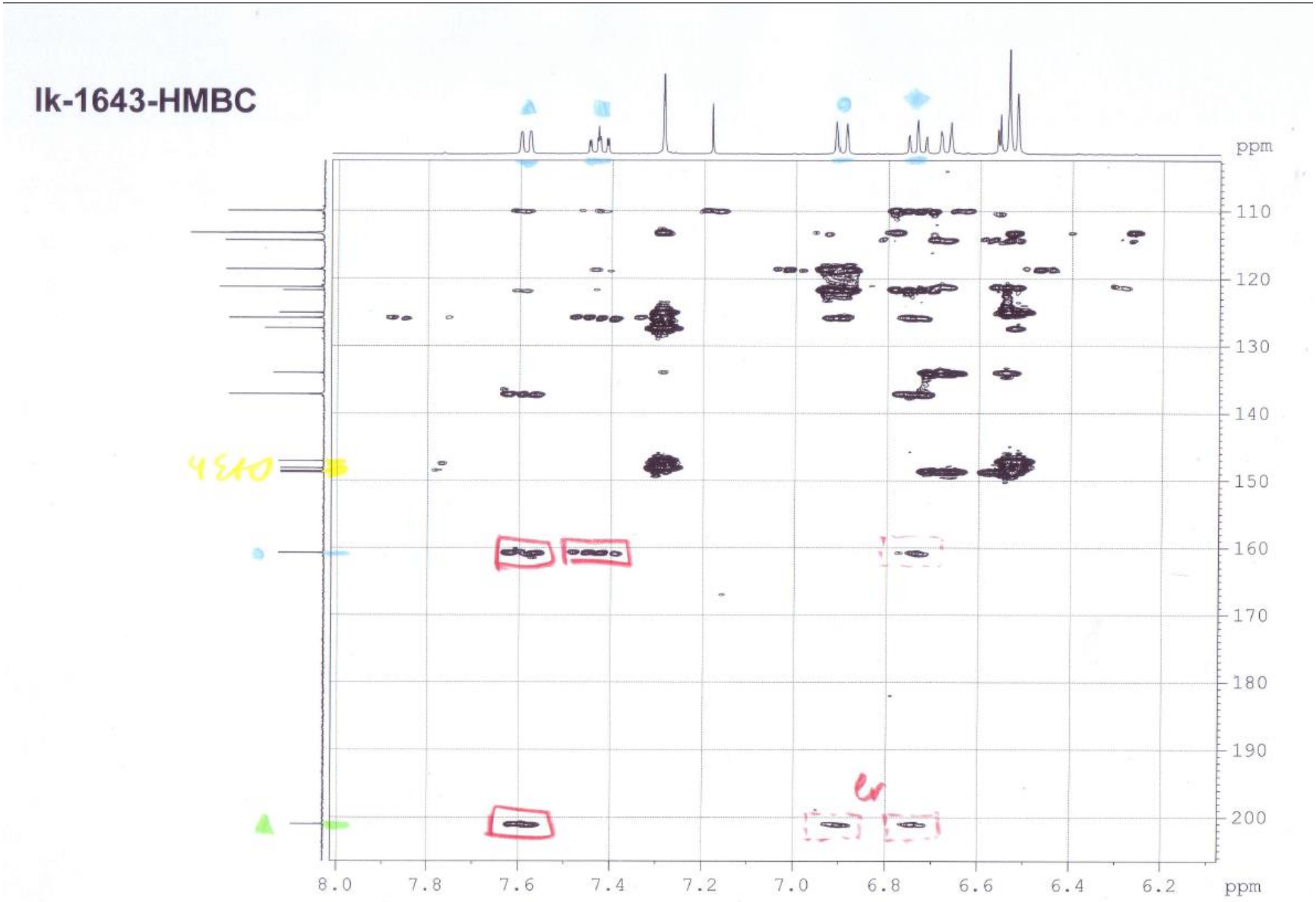
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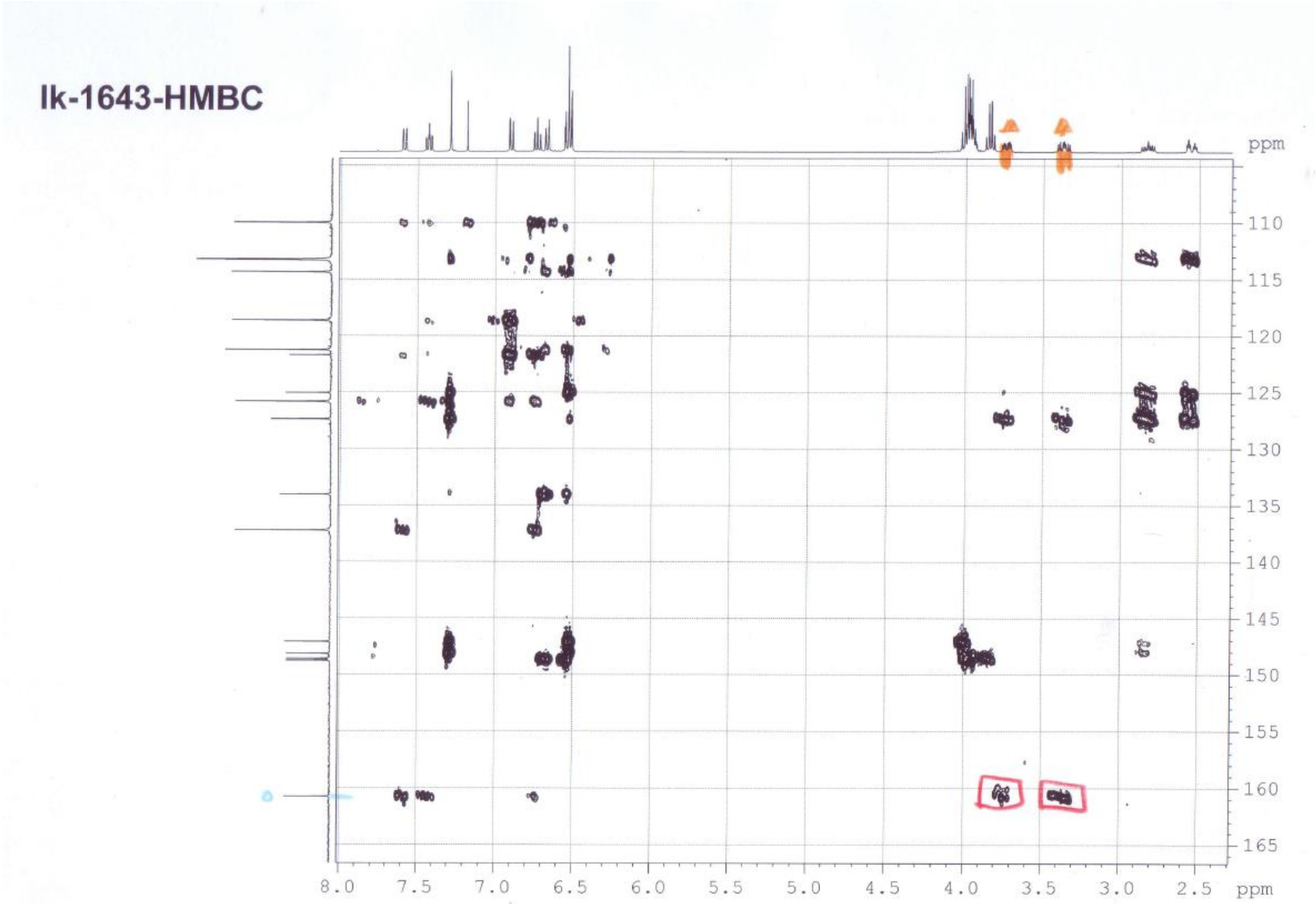
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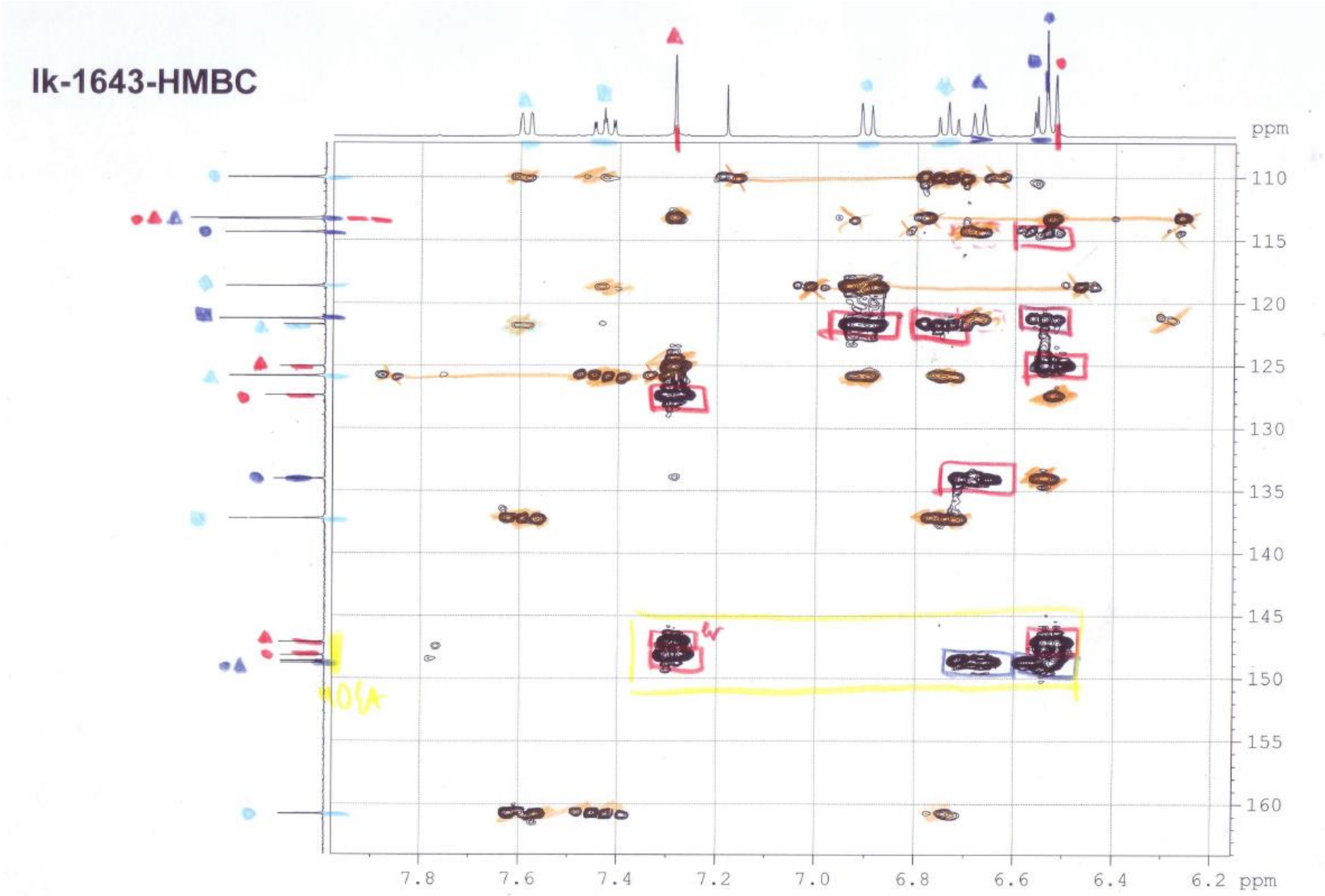
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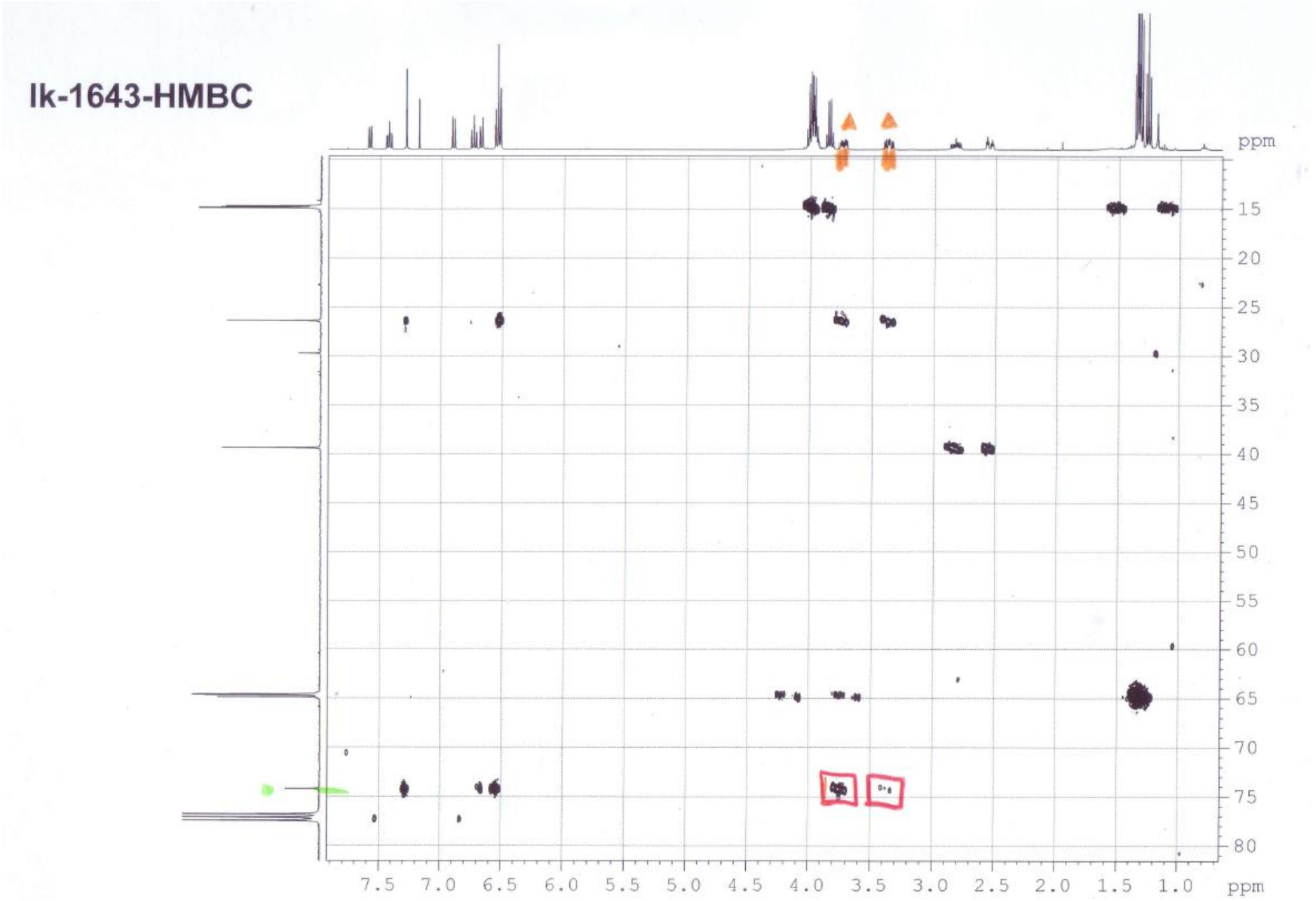
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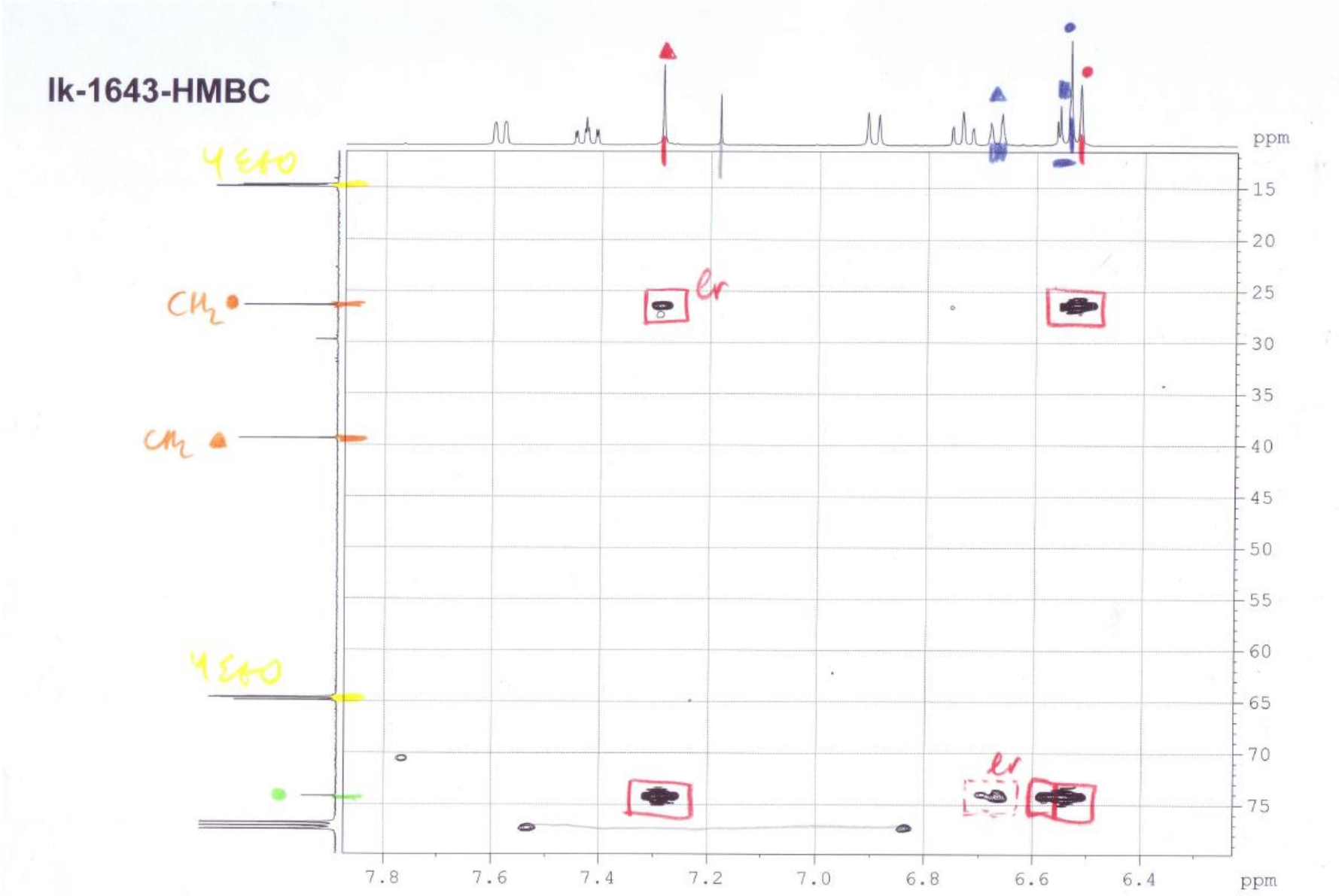
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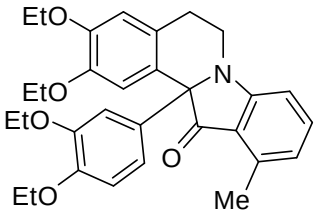
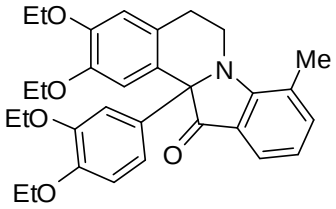


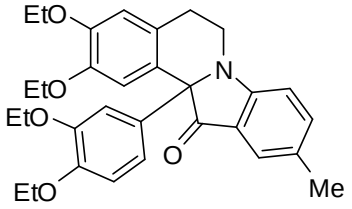
12a-(3,4-Diethoxyphenyl)-2,3-diethoxy-11-methyl-5,12a-dihydroindolo[2,1-*a*]isoquinolin-12(6*H*)-one (7bA)

Yellow powder. Yield 37% (44 mg). Total yield of two isomers is 70%; MP 59-61^{o}C; R_f 0.51 (EtOAc-Hexane, 1:5);^{1}H NMR (400 MHz, $CDCl_3$) □:7.41 (s, 1H, Ar), 7.35 (t, *J*=7.8 Hz, 1H, Ar), 6.78 (dd, *J*=12.1, 8.4 Hz, 2H, Ar), 6.69 - 6.64 (m, 2H, Ar), 6.61 (s, 1H, s), 6.56 (d, *J*=7.5 Hz, 1H, Ar), 4.15 - 4.01 (m, 6H, $OC\underline{H}_2CH_3$), 3.94 (q, *J*=6.9 Hz, 2H, $OC\underline{H}_2CH_3$), 3.80 (ddd, *J*=13.4, 5.6, 3.4 Hz, 1H, 6-H), 3.52 - 3.39 (m, 1H, 6-H), 2.92 (ddd, *J*=16.2, 10.5, 5.6 Hz, 1H, 5-H), 2.66 - 2.59 (m, 1H, 5-H), 2.58 (s, 3H, Me), 1.48 - 1.39 (m, 9H, $OCH_2C\underline{H}_3$), 1.36 (t, *J*=7.2 Hz, 3H, $OCH_2C\underline{H}_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 201.3, 161.3, 148.7, 148.6, 148.1, 147.0, 141.2, 136.4, 134.4, 127.5, 125.6, 121.2, 120.2, 119.7, 114.4, 113.4, 113.3 (2C), 107.2, 73.8, 64.9, 64.7, 64.6 (2C); ESI MS [M+H] 502; [Found: C, 74.18; H, 6.92; N, 2.86. $C_{31}H_{35}NO_5$ requires C, 74.23; H, 7.03; N, 2.79 %]; IR (KBr) 2977, 2926, 2878, 1691, 1599, 1511, 1319, 1256, 1041, 780 cm^{-1}.



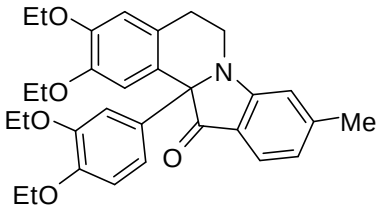
12a-(3,4-Diethoxyphenyl)-2,3-diethoxy-8-methyl-5,12a-dihydroindolo[2,1-*a*]isoquinolin-12(6*H*)-one (7bB)

Yellow oil. Yield 33% (40 mg). Total yield of two isomers is 70%; R_f 0.43 (EtOAc-Hexane, 1:5); ^{1}H NMR (400 MHz, $CDCl_3$) δ:7.55 (d, *J*=7.5 Hz, 1H, Ar), 7.35 (s, 1H, Ar), 7.27 (s, 1H, Ar, overlapped with $CDCl_3$ peak), 6.81 - 6.73 (m, 2H, Ar), 6.66 - 6.57 (m, 3H, Ar), 4.23 (ddd, *J*=13.7, 5.0, 2.5 Hz, 1H, 6-H), 4.14 - 4.00 (m, 6H, $OC\underline{H}_2CH_3$), 3.93 (q, *J*=6.4 Hz, 2H, $OC\underline{H}_2CH_3$), 3.58 - 3.42 (m, 1H, 6-H), 2.84 (ddd, *J*=16.0, 11.4, 5.0 Hz, 1H, 5-H), 2.69 - 2.59 (m, 1H, 5-H), 2.55 (s, 3H, Me), 1.48 - 1.38 (m, 9H, $OCH_2C\underline{H}_3$), 1.35 (t, *J*=6.9 Hz, 3H, $OCH_2C\underline{H}_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 201.6, 159.2, 148.9, 148.6, 148.1, 147.1, 140.1, 134.3, 127.9, 125.1, 123.7, 123.1, 121.9, 121.7, 119.3, 114.8, 113.8, 113.2, 113.1, 75.1, 65.0, 64.7, 64.6, 41.3, 20.7, 15.0, 14.9 (2C), 14.8; ESI MS [M+H] 502; [Found: C, 74.16; H, 6.98; N, 2.83. $C_{31}H_{35}NO_5$ requires C, 74.23; H, 7.03; N, 2.79 %]; IR (KBr) 2977, 2927, 1696, 1621, 1510, 1254, 1042, 756 cm^{-1}.



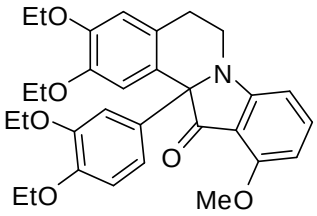
12a-(3,4-Diethoxyphenyl)-2,3-diethoxy-10-methyl-5,12a-dihydroindolo[2,1-*a*]isoquinolin-12(6*H*)-one (7cA)

Yellow oil. Major isomer. Total yield of two isomers is 75% (81 mg); R_f 0.7 (EtOAc-Hexane, 1:1);^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.46 (s, 1H, 11-H), 7.35 (s, 1H, 1-H),7.33 (d, *J*=8.4 Hz, 1H, 8-H), 6.91 (d, *J*=8.4 Hz, 1H, 9-H), 6.73 (dd, *J*=8.3, 2.4 Hz, 1H, 5'-H), 6.61 -6.55 (m, 3H, 2'-H, 6'-H, 4-H), 4.10-3.98 (m, 6H, $OC\underline{H}_2CH_3$), 3.94- 3.86 (m, 2H, $OC\underline{H}_2CH_3$), 3.83 - 3.76 (m, 1H, 6-H),3.45 - 3.33 (m, 1H, 6-H), 2.96- 2.82 (m, 1H, 5-H), 2.65-2.55 (m, 1H, 5-H), 2.28 (s, 3H, Me), 1.45 - 1.36 (m, 9H, $OCH_2C\underline{H}_3$), 1.33 (t, *J*=6.9 Hz, 3H, $OCH_2C\underline{H}_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 201.3, 159.3, 148.6, 148.5, 148.0, 147.0, 138.6, 134.3, 128.3, 127.3, 126.3, 124.9, 122.0, 121.4, 114.2, 113.2, 113.0, 110.2 (2C), 74.6, 64.8, 64.6, 64.5 (2C), 39.5, 26.2, 20.6, 14.9, 14.9, 14.8, 14.7; ESI MS [M+H] 502; IR (KBr) 3436, 2977, 2928, 1695, 1615, 1511, 1254, 1140, 1042, 758 cm^{-1}.



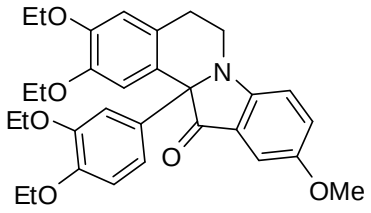
12a-(3,4-Diethoxyphenyl)-2,3-diethoxy-9-methyl-5,12a-dihydroindolo[2,1-*a*]isoquinolin-12(6*H*)-one (7cB)

Yellow oil. Minor isomer. Total yield of two isomers is 75% (81 mg); R_f 0.6 (EtOAc-Hexane, 1:1); ^{1}H NMR (600 MHz, $CDCl_3$) δ:7.55 (d, *J*=7.7 Hz, 1H, 11-H), 7.31 (s, 1H, 1-H), 6.77 (s, 1H, 8-H), 6.73 (dd, *J*=8.3, 2.4 Hz, 1H, 5'-H), 6.64 (d, *J*=7.7 Hz, 1H, 10-H), 6.61 - 6.55 (m, 3H, 2'-H, 6'-H, 4-H), 4.10 - 3.98 (m, 6H, $OC\underline{H}_2CH_3$), 3.94 - 3.86 (m, 2H, $OC\underline{H}_2CH_3$), 3.83 -3.76 (m, 1H, 6-H), 3.45-3.33 (m, 1H, 6-H), 2.96 -2.82 (m, 1H, 5-H), 2.65 - 2.55 (m, 1H, 5-H), 2.39 (s, 3H, Me), 1.45 -1.36 (m, 9H, $OCH_2C\underline{H}_3$), 1.33 (t, *J*=6.9 Hz, 3H, $OCH_2C\underline{H}_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 200.5, 161.2, 148.9, 148.6, 148.5, 148.0, 147.0, 138.6, 134.2, 127.3, 125.6, 125.2, 121.2, 120.5, 119.5, 114.1, 113.1 (2C), 110.2, 74.4, 64.8, 64.6 (2C), 64.5, 39.3, 26.4, 22.8, 14.9, 14.9, 14.8, 14.7; ESI MS [M+H] 502; IR (KBr) 2978, 2928, 2880, 1696, 1621, 1511, 1254, 1140, 1041,756 cm^{-1}.



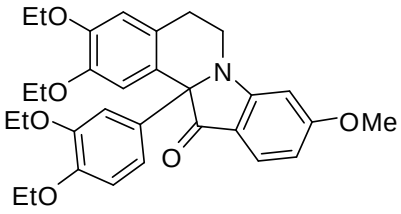
12a-(3,4-Diethoxyphenyl)-2,3-diethoxy-11-methoxy-5,12a-dihydroindolo[2,1-*a*]isoquinolin-12(6*H*)-one(7dA)

Yellow powder.Yield 67% (80 mg); MP 138-140^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.42 (s, 1H, H-1), 7.40 (d, *J*=8.1 Hz, 1H, H-9), 6.72 (d, *J*=8.7 Hz, 1H, 5'-H), 6.66 -6.61 (m, 2H, 2'-H, 6'-H), 6.58 (s,1H, H-4), 6.51 (d, *J*=8.1 Hz, 1H, H-8), 6.19 (d, *J*=8.1 Hz, 1H, H-10), 4.14 - 3.99 (m, 6H, $OC\underline{H}_2CH_3$), 3.92 (dd, *J*=6.8, 3.7 Hz, 2H, $OC\underline{H}_2CH_3$), 3.88 (s, 3H,OMe), 3.76 (ddd, *J*=13.4, 5.6, 3.4 Hz, 2H,6-CH_2), 3.46 -3.35 (m, 1H,6-CH_2), 2.90 (ddd, *J*=15.7, 10.4, 5.6 Hz, 1H,5-CH_2), 2.59 (ddd, *J*=15.7, 3.7, 3.6 Hz, 1H, 5-CH_2), 1.45 - 1.36 (m, 9H, $OCH_2C\underline{H}_3$), 1.33 (t, *J*=6.9 Hz, 3H, $OCH_2C\underline{H}_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 198.2, 162.1, 159.8, 148.7, 148.5, 148.0, 147.2, 138.7, 134.4, 127.2, 125.7, 121.3, 114.5, 113.3 (2C), 113.1, 110.3, 102.1, 99.8, 74.0, 64.9, 64.7, 64.6 (2C), 55.7, 39.6, 26.6, 14.9, 14.9, 14.8, 14.7; ESI MS [M+H] 518; [Found: C, 71.85; H, 6.77; N, 2.75;. $C_{31}H_{35}NO_6$ requires C, 71.93; H, 6.82; N, 2.71%]; IR (KBr) 2977, 2925, 2886, 1694, 1603, 1511, 1493, 1253, 1040, 783 cm^{-1}.



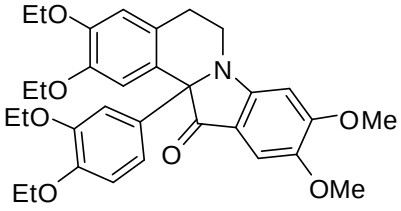
12a-(3,4-Diethoxyphenyl)-2,3-diethoxy-9-methoxy-5,12a-dihydroindolo[2,1-*a*]isoquinolin-12(6*H*)-one (7eA)

Yellow oil. Yield 42% (53mg). Total yield of two isomers 80%; R_f 0.8 (EtOAc: Hexane, 1:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.33 (s, 1H, Ar), 7.21 (dd, *J*=9.0, 2.8 Hz, 1H, Ar), 7.14 (d, *J*=2.5 Hz, 1H, Ar), 6.98 (d, *J*=8.7 Hz, 1H, Ar), 6.76 (d, *J*=8.1 Hz, 1H, Ar), 6.65 - 6.56 (m, 3H, Ar), 4.12 -4.02 (m, 6H, $OC\underline{H}_2CH_3$), 3.98 - 3.89 (m, 2H, $OC\underline{H}_2CH_3$), 3.84-3.80 (m, 1H, 6-CH_2), 3.77 (s, 3H, OMe), 3.47 - 3.29 (m, 1H, 6-CH_2), 2.88 (*J*=16.2, 11.2, 5.6 Hz, 1H, 5-CH_2), 2.67 - 2.56 (m, 1H, 5-CH_2), 1.47 -1.38 (m, 9H,$OCH_2C\underline{H}_3$), 1.35 (t, *J*=7.2 Hz, 3H, $OCH_2C\underline{H}_3$). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 201.2, 156.7, 153.4, 148.7, 148.6, 148.1, 147.1, 134.4, 127.8, 127.3, 124.9, 122.1, 121.4, 114.5, 113.6, 113.2, 113.1, 111.7, 105.9, 75.1, 64.9, 64.7 (2C), 64.6, 55.9, 39.7, 26.2, 15.0, 14.9(2C), 14.7; ESI MS [M+H] 518; [Found: C, 71.89; H, 6.78; N, 2.77;. $C_{31}H_{35}NO_6$ requires C, 71.93; H, 6.82; N, 2.71%]; IR (KBr) 2977, 2930, 1688, 1608, 1510, 1476, 1253, 1229, 1041, 822, 754 cm^{-1}.



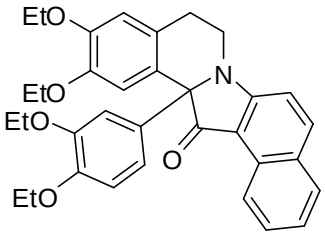
12a-(3,4-Diethoxyphenyl)-2,3-diethoxy-10-methoxy-5,12a-dihydroindolo[2,1-*a*]isoquinolin-12(6*H*)-one(7eB)

Yellow oil. Yield 38% (49 mg).Total yield of two isomers 80%; R_f 0.9 (EtOAc: Hexane, 1:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.59 (d, *J*=8.2 Hz, 1H, Ar), 7.41 (s, 1H, Ar), 6.76 (d, *J*=8.7 Hz, 1H, Ar), 6.66 - 6.59 (m, 3H, Ar), 6.41 (dd, *J*=8.7, 1.9 Hz, 1H, Ar), 6.36 (d, *J*=1.9 Hz, 1H, Ar), 4.14 - 4.04 (m, 6H, $OC\underline{H}_2CH_3$), 3.93 (q, *J*=7.3 Hz, 2H, $OC\underline{H}_2CH_3$), 3.89 (s, 3H,OMe), 3.83 - 3.72 (m, 1H, 6-CH_2), 3.55 - 3.40 (m, 1H, 6-CH_2), 2.94 (ddd, *J*=15.9, 10.3, 5.6 Hz, 1H, 5-CH_2), 2.64 (ddd, *J*=15.7, 4.0, 3.9 Hz, 1H, 5-CH_2), 1.48 - 1.38 (m, 9H, $OCH_2C\underline{H}_3$), 1.35 (t, *J*=6.8 Hz, 3H, $OCH_2C\underline{H}_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 198.7, 168.0, 162.8, 148.7, 148.6, 148.1, 147.1, 134.3, 127.4, 127.2, 125.7, 121.2, 115.1, 114.2, 113.3, 113.2, 113.1, 107.8, 93.0, 74.5, 64.9, 64.7 (3C), 55.7, 39.5, 26.6, 15.0 (2C), 14.9, 14.8; ESI MS [M+H] 518; [Found: C, 71.85; H, 6.74; N, 2.78; $C_{31}H_{35}NO_6$ requires C, 71.93; H, 6.82; N, 2.71%]; IR (KBr) 2977, 2932, 1692, 1493, 1254, 1224, 1039, 754 cm^{-1}.



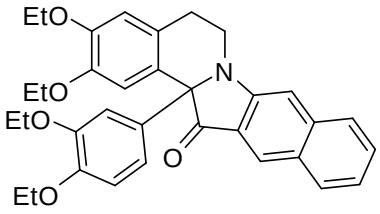
12a-(3,4-Diethoxyphenyl)-2,3-diethoxy-9,10-dimethoxy-5,12a-dihydroindolo[2,1-*a*] isoquinolin-12(6*H*)-one (7f)

Yellow powder. Yield 85% (111 mg); MP 173-175^{o}C; ^{1}H NMR (600 MHz, $CDCl_3$) δ:7.36 (s, 1H, 11-H), 7.09 (s, 1H, 8-H), 6.74 (d, *J*=8.2 Hz, 1H, 3'-H), 6.62 -6.56 (m, 3H, 2'-H, 4-H, 6'-H), 6.43 (s, 1H, 1-H), 4.09 - 4.00 (m, 6H, $OC\underline{H}_2CH_3$), 3.97 (s, 3H, OMe), 3.94 -3.88 (m, 2H, $OC\underline{H}_2CH_3$), 3.82 (s, 3H,OMe), 3.77 (ddd, *J*=13.6, 5.5, 3.1 Hz, 1H, 6-CH_2), 3.48 -3.36 (m, 1H, 6-CH_2), 2.88 (ddd, *J*=15.9, 10.8, 5.5 Hz, 1H, 5-CH_2), 2.62 (dt, *J*=15.1, 3.4 Hz, 1H, 5-CH_2), 1.44- 1.35 (m, 9H, $OCH_2C\underline{H}_3$), 1.33 (t, *J*=7.2 Hz, 3H, $OCH_2C\underline{H}_3$); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 199.1, 158.6, 158.4, 148.7, 148.6, 147.9, 147.1, 144.1, 134.5, 126.9, 125.6, 121.3, 114.2, 113.2, 113.1, 112.9, 105.5, 92.6, 74.5, 64.8, 64.7, 64.6, 64.5 (2C), 56.4, 56.3, 39.8, 26.6, 14.9 (2C), 14.8, 14.7; ESI MS [M+H] 548; [Found: C, 70.09; H, 6.73; N, 2.62. $C_{32}H_{37}NO_7$ requires C, 70.18; H, 6.81; N, 2.56%]; IR (KBr) 3448, 2977, 2897, 1677, 1617, 1510, 1240, 1040, 767 cm^{-1}.



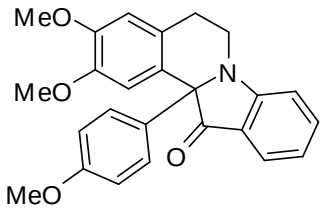
13b-(3,4-Diethoxyphenyl)-11,12-diethoxy-9,13b-dihydrobenzo[4,5]indolo[2,1-*a*]isoquinolin-14(8*H*)-one (7gA)

Orange oil. Yield 87% (112 mg). R_f 0.7; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 8.82 (d, *J*=8.3 Hz, 1H, Ar), 7.95 (d, *J*=8.9 Hz, 1H, Ar), 7.71 (d, *J*=8.3 Hz, 1H, Ar), 7.56 (t, *J*=7.6 Hz, 1H, Ar), 7.51 (s, 1H, Ar), 7.31 (t, *J*=7.6 Hz, 1H, Ar), 7.21 (d, *J*=8.9 Hz, 1H, Ar), 6.75 (d, *J*=8.3 Hz, 1H, Ar), 6.68 - 6.63 (m, 2H, Ar), 6.59 (s, 1H, Ar), 4.14 - 4.07 (m, 2H, $OC\underline{H}_2CH_3$), 4.07 - 4.01 (m, 4H, $CH_3C\underline{H}_2$), 4.01 -3.95 (m, 1H, 6-H), 3.94 - 3.85 (m, 2H, $OC\underline{H}_2CH_3$), 3.57- 3.48 (m, 1 H, 6-H), 2.90 (ddd, *J*=15.8, 10.8, 5.5 Hz, 1H, 5-H), 2.72 (dt, *J*=15.8, 3.4 Hz, 1H, 5-H), 1.44 - 1.37 (m, 9H, $OCH_2C\underline{H}_3$), 1.32 (t, *J*=6.9 Hz, 3H, $OCH_2C\underline{H}_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 205.5, 162.9, 148.9, 148.7, 148.1, 147.4, 139.2, 134.1, 131.3, 129.9, 128.5, 127.9, 126.8, 125.8, 123.9, 123.0, 121.3, 114.4, 113.4, 113.2 (2C), 111.3, 95.8, 74.5, 65.0; 64.7 (2C), 39.7, 29.8, 27.8, 15.0, 14.9 (2C), 14.8; ESI MS [M+H] 538; [Found: C, 75.89; H, 6.48; N, 2.64. $C_{34}H_{35}NO_5$ requires C, 75.95; H, 6.56; N, 2.61%]; IR (KBr) 2978, 2928, 1675, 1624, 1593, 1511, 1475, 1256, 1141, 1041, 816, 761 cm^{-1}.



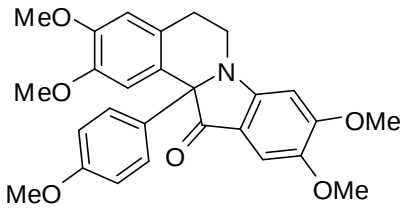
14a-(3,4-Diethoxyphenyl)-2,3-diethoxy-5,14a-dihydrobenzo [5,6]indolo[2,1-*a*]isoquinolin-14(6*H*)-one (7h)

Orange powder. Yield 67% (89 mg); MP 69-71°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.25 (s, 1H, Ar), 7.79 (d, *J*=8.1 Hz, 1H, Ar), 7.68 (d, *J*=8.7 Hz, 1H, Ar), 7.46 (t, *J*=7.5 Hz, 1H, Ar), 7.37 (s,1H, 1-H), 7.22 (t, *J*=7.5 Hz, 1H, Ar), 7.15 (s, 1H, 8-H), 6.75 (d, *J*=8.2 Hz, 1H, 5'-H), 6.71 - 6.66 (m, 2H, 2'-H, 6'-H), 6.61 (s, 1H, 4-H), 4.14 -4.00 (m, 6H,$OC\underline{H}_2CH_3$), 3.93 (m, 3H, 6-CH_2, $OC\underline{H}_2CH_3$), 3.59 - 3.41 (m, 1H, 6-CH_2), 3.06 (ddd, *J*=16.0, 10.7, 5.6 Hz, 1H, 5-CH_2), 2.64 (ddd, *J*=15.7, 3.7, 3.6 Hz, 1H, 5-CH_2), 1.43 (t, *J*=6.9 Hz, 9H,$OCH_2C\underline{H}_3$) ,1.35 (t, *J*=6.9 Hz, 3H, $OCH_2C\underline{H}_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 201.7, 154.3, 148.8, 148.7, 148.3, 147.0, 139.7, 134.1, 130.8, 129.4, 127.9, 127.2, 126.5, 124.8, 123.9, 123.1, 121.4, 114.2, 113.5, 113.3, 113.2, 103.4, 95.1, 74.4, 64.8, 64.7, 64.6, 64.6, 39.4, 25.5, 14.9, 14.9, 14.8, 14.7; ESI MS [M+H] 538; [Found: C, 75.87; H, 6.49; N, 2.65;. $C_{34}H_{35}NO_5$ requires C, 75.95; H, 6.56; N, 2.61%]; IR (KBr) 3745, 3600, 3495, 2976, 2927, 1712, 1628, 1508, 1255, 1042, 749 cm^{-1}.



2,3-Dimethoxy-12a-(4-methoxyphenyl)-5,12a-dihydroindolo[2,1-*a*]isoquinolin-12(6*H*)-one (8a)

Yellow powder. Yield 73% (90 mg); MP 79-81°C; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.69 (d, *J*=7.8 Hz, 1H, Ar), 7.53 (t, *J*=7.8 Hz, 1H, Ar), 7.35 (s, 1H, Ar), 7.03 (d, *J*=9.1 Hz, 2H, Ar), 7.00 (d, *J*=8.3 Hz, 1H, Ar), 6.86 - 6.83 (m, 1H, Ar), 6.81 (d, *J*=8.7 Hz, 2H, Ar), 6.61 (s, 1H, Ar), 3.87 (s, 3H, OMe), 3.86 (s, 3H, OMe), 3.84 (dd, *J*=6.0, 3.1 Hz, 1H, 6-CH_2), 3.78 (s, 3H, OMe), 3.44 (ddd, *J*=13.7, 11.0, 4.5 Hz, 1H, 6-CH_2), 2.95 (ddd, *J*=16.1, 10.7, 5.8 Hz, 1H, 5-CH_2), 2.67 (ddd, *J*=16.0, 3.4, 3.3 Hz, 1H, 5-CH_2); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 201.3, 160.8, 159.4, 148.6, 147.6, 137.3, 133.7, 129.5 (2C), 127.4, 125.9, 125.1, 118.8, 113.9 (2C), 111.4, 111.3, 110.0, 95.8, 74.0, 56.2, 56.0, 55.4, 39.3, 26.5; ESI MS [M+H] 402; [Found: C, 74.75; H, 5.69; N, 3.54; $C_{25}H_{23}NO_4$ requires C, 74.79; H, 5.77; N, 3.49%]; IR (KBr) 3457, 2929, 1692, 1610, 1512, 1481, 1255, 1028, 756.

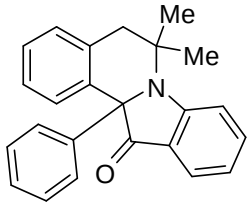


2,3,9,10-Tetramethoxy-12a-(4-methoxyphenyl)-5,12a-dihydroindolo[2,1-*a*]isoquinolin-12(6*H*)-one (8b)

Yellow powder. Yield 77% (110 mg); MP 220-222°C; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.35 (s, 1H, 11-H), 7.10 (s, 1H, 8-H), 6.99 (d, *J*=9.1 Hz, 2H, 2'-H, 6'-H), 6.79 (d, *J*=8.3 Hz, 2H, 3'-H, 5'-H), 6.58 (s, 1H, 4-H), 6.43 (s, 1H, 1-H), 3.97 (s, 3H, OMe), 3.84 (s, 3H, OMe), 3.83 (s, 3H, OMe), 3.82 (s, 3H, OMe), 3.79 - 3.77 (m, 1 H, 6-CH_2), 3.76 (s, 3H, OMe), 3.47 - 3.39 (m, 1H, 6-CH_2), 2.91 (ddd, *J*=15.9, 10.9, 5.4 Hz, 1H, 5-CH_2), 2.68-2.62 (m, 1 H, 5-CH_2); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 199.2, 159.3, 158.8, 158.4, 148.4, 147.6, 144.2, 134.0, 129.5 (2), 127.0, 125.7, 113.9 (2C), 113.1, 111.4, 111.1, 105.6, 92.5, 74.3, 56.4, 56.3, 56.2, 55.9, 55.4, 39.8, 26.7 [Found: C, 70.23; H, 5.94; N, 3.07; $C_{27}H_{27}NO_6$ requires C, 70.27; H, 5.90; N, 3.03%]; ESI MS [M+H] 462; IR (KBr) 2935, 1673, 1618, 1494, 1441, 1255, 1240, 1030, 766 cm^{-1}.

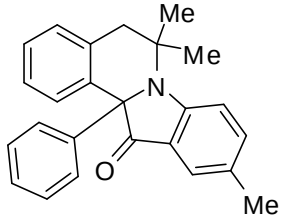
General procedure for the synthesis of indolo[2,1-*a*]isoquinolinones (9a-d, 10a,b, 11a,b).

To a suspension of CsF (3 eq.) in 3 mL of dry acetonitrile, the corresponding 1-benzyloxy-6,6-dimethyl-dihydroisoquinoline (1 eq.) was added, and after the dissolution of starting material the corresponding (trimethylsilyl)aryltrifluoromethanesulfonate (1.2 eq.) was added into the flask. The mixture was stirred at room temperature for 1-3 days with TLC monitoring. The resulting indoloisoquinolines were precipitated from the reaction mixture. The precipitate was filtered and washed with cold water (3×3 mL), then with 3 mL of hexane, and dried. In case of **11a**,**b** the filtrate was evaporated, and purified by column chromatography (glass column, H=100 mm, d=15 mm, mobile phase: EtOAc-hexane, 1:75 to 1:15).



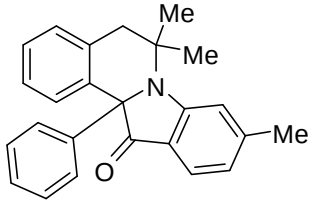
6,6-Dimethyl-12a-phenyl-5,12a-dihydroindolo[2,1-*a*]isoquinolin-12(6*H*)-one (9a)

Yellow powder. Yield 93% (120 mg); MP 233-235°C; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 8.05 (d, *J*=7.6 Hz, 1H, Ar), 7.62 (d, *J*=7.6 Hz, 1H, Ar), 7.48 (t, *J*=7.9 Hz, 1H, Ar), 7.37 (t, *J*=7.6 Hz, 1H, Ar), 7.31 (t, *J*=7.6 Hz,1H, Ar), 7.23 - 7.11 (m, 7H, Ar), 6.75 (t, *J*=7.6 Hz, 1H, Ar), 2.74 (d, *J*=14.4 Hz, 1H, CH_2), 2.46 (d, *J*=14.4 Hz, 1H, CH_2), 1.79 (s, 3H, Me), 1.16 (s, 3H, Me); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 198.2, 159.4, 139.9, 136.9, 136.6, 134.6, 128.8, 128.6 (2C), 127.9, 127.6, 126.5, 126.2, 126.1 (2C), 125.2, 120.4, 117.6, 112.5, 75.1, 56.3, 45.1, 28.8, 23.9; ESI MS [M+H] 340; [Found: C, 84.87; H, 6.21; N, 4.16; $C_{24}H_{21}NO$ requires C, 84.92; H, 6.24; N, 4.13%]; IR (KBr) 3065, 3046, 2987, 1694, 1614, 1476, 1321, 1163, 972, 749 cm^{-1}.



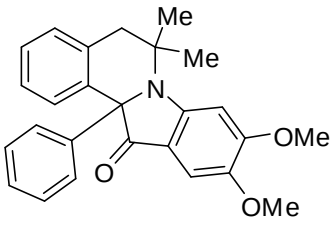
6,6,9-Trimethyl-12a-phenyl-5,12a-dihydroindolo[2,1-*a*]isoquinolin-12(6*H*)-one (9bA)

Yellow powder. Major isomer. Total yield of two isomers is 91% (122 mg); MP 206-207°C; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 8.07 (d, *J*=8.3 Hz, 1H, Ar), 7.51 (d, *J*=8.3 Hz, 1H, Ar), 7.36 (t, *J*=7.6 Hz, 1H, Ar), 7.30 (t, *J*=6.9 Hz, 1H, Ar), 7.21 - 7.13 (m, 6H, Ar), 6.96 (s, 1H, Ar), 6.59 (d, *J*=7.6 Hz, 1H, Ar), 2.73 (d, *J*=14.4 Hz, 1H, CH_2), 2.45 (d, *J*=14.4 Hz, 1H, CH_2), 2.41 (s, 3H, Me), 1.79 (s, 3H, Me), 1.16 (s, 3H, Me); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 197.5, 159.9, 148.4, 140.1, 136.6, 134.8, 128.7, 128.5 (2C), 127.9, 127.5, 126.5, 126.1 (2C), 125.9, 125.3, 119.4, 118.3, 112.6, 75.4, 56.3, 45.1, 28.9, 23.9, 23.1; ESI MS [M+H] 354; [Found: C, 84.87; H, 6.48; N, 3.88; $C_{25}H_{23}NO$ requires C, 84.95; H, 6.56; N, 3.96%]; IR (KBr) 3061, 2972, 2932, 2859, 1689, 1624, 1491, 1338, 1284, 1167, 1058, 816, 752 cm^{-1}.



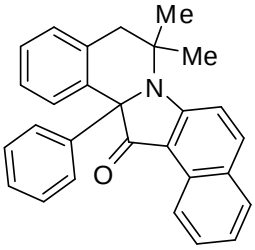
6,6,10-Trimethyl-12a-phenyl-5,12a-dihydroindolo[2,1-*a*]isoquinolin-12(6*H*)-one (9bB)

Yellow powder. Minor isomer. Total yield of two isomers is 91% (122 mg); MP 209-210°C; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 8.04 (d, *J*=7.8 Hz, 1H, Ar), 7.41 (s, 1H, Ar), 7.35 (t, *J*=7.6 Hz, 1H, Ar), 7.33 - 7.27 (m, 2H, Ar), 7.22 - 7.13 (m, 6H, Ar), 7.09 (d, *J*=8.7 Hz, 1H, Ar), 2.73 (d, *J*=14.4 Hz, 1H, CH_2), 2.44 (d, *J*=14.4 Hz, 1H, CH_2), 2.26 (s, 3H, Me), 1.77 (s, 3H, Me), 1.13 (s, 3H, Me); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 198.3, 157.9, 140.2, 138.4, 136.7, 134.7, 128.8, 128.5 (2C), 127.9, 127.5, 127.0, 126.5, 126.1 (2C), 125.5, 125.3, 120.5, 112.5, 75.4, 56.2, 45.0, 29.0, 23.9, 20.3; ESI MS [M+H] 354; [Found: C, 84.89; H, 6.47; N, 3.91; $C_{25}H_{23}NO$ requires C, 84.95; H, 6.56; N, 3.96%]; IR (KBr) 3061, 2972, 2932, 2859, 1689, 1624, 1491, 1338, 1284, 1167, 1058, 816, 752 cm^{-1}.



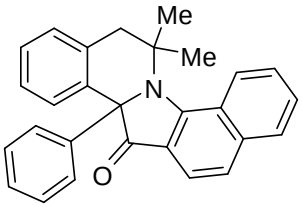
9,10-Dimethoxy-6,6-dimethyl-12a-phenyl-5,12a-dihydroindolo [2,1-*a*]isoquinolin-12(6*H*)-one (9c)

Yellow powder. Yield 94 % (145 mg); MP 295-296 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 8.12 (d, *J*=7.4 Hz, 1H, Ar), 7.38 (t, *J*=7.6 Hz, 1H, Ar), 7.32 (t, *J*=7.0 Hz, 1H, Ar), 7.24 - 7.11 (m, 6H, Ar), 7.06 (s, 1H, Ar), 6.63 (s, 1H, Ar), 4.02 (s, 3H, OMe), 3.83 (s, 3H, OMe), 2.77 (d, *J*=14.0 Hz, 1H, CH_2), 2.46 (d, *J*=14.0 Hz, 1H, CH_2), 1.80 (s, 3H, Me), 1.17 (s, 3H, Me); ^{13}C NMR (MHz, $CDCl_3$) δ: 196.1, 158.0, 157.1, 143.4, 140.4, 136.5, 134.8, 128.6, 128.5 (2C), 127.8, 127.4, 126.5, 126.0 (2C), 125.4, 111.7, 105.7, 95.0 (2C), 75.6, 56.3, 56.2, 45.0, 29.4, 24.2; ESI MS [M+H] 400; [Found: C, 78.15; H, 6.27; N, 3.55; $C_{26}H_{25}NO_3$ requires C, 78.17; H, 6.31; N, 3.51%]; IR (KBr) 2999, 2969, 2932, 2830, 1661, 1619, 1487, 1323, 1248, 1015, 746 cm^{-1}.



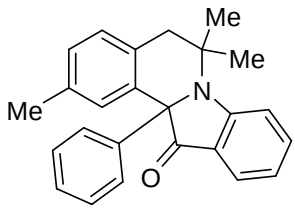
8,8-Dimethyl-13b-phenyl-9,13b-dihydrobenzo[4,5]indolo[2,1-*a*]isoquinolin-14(8*H*)-one (9dA)

Yellow powder. Yield 64% (95 mg). Total yield of two isomers is 72%; MP 292-293°C; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 8.84 (d, *J*=8.3 Hz, 1H, Ar), 8.22 (d, *J*=7.6 Hz, 1H, Ar), 7.91 (d, *J*=8.9 Hz, 1H, Ar), 7.69 (d, *J*=7.6 Hz, 1H, Ar), 7.53 (t, *J*=7.9 Hz, 1H, Ar), 7.45 (d, *J*=9.6 Hz, 1H, Ar), 7.39 (t, *J*=7.6 Hz, 1H, Ar), 7.32 (t, *J*=7.6 Hz, 1H, Ar), 7.29 (t, *J*=7.6 Hz, 1H, Ar), 7.22 - 7.14 (m, 6H, Ar), 2.81 (d, *J*=14.4 Hz, 1H, CH_2), 2.48 (d, *J*=14.4 Hz, 1H, CH_2), 1.86 (s, 3H, Me), 1.23 (s, 3H, Me); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 197.1, 162.3, 139.6, 138.5, 136.5, 134.5, 131.6, 129.9, 128.7, 128.6 (2C), 128.3, 127.9, 127.6, 127.2, 126.7, 126.0 (2C), 125.7, 123.8, 122.9, 114.2, 110.5, 57.0, 45.3, 29.4, 25.3; ESI MS [M+H] 390; [Found: C, 86.29; H, 5.87; N, 3.68; $C_{28}H_{23}NO$ requires C, 86.34; H, 5.95; N, 3.60%]; IR (KBr) 3067, 2978, 2934, 1656, 1622, 1589, 1522, 1465, 1445, 1358, 1166, 758 cm^{-1}.



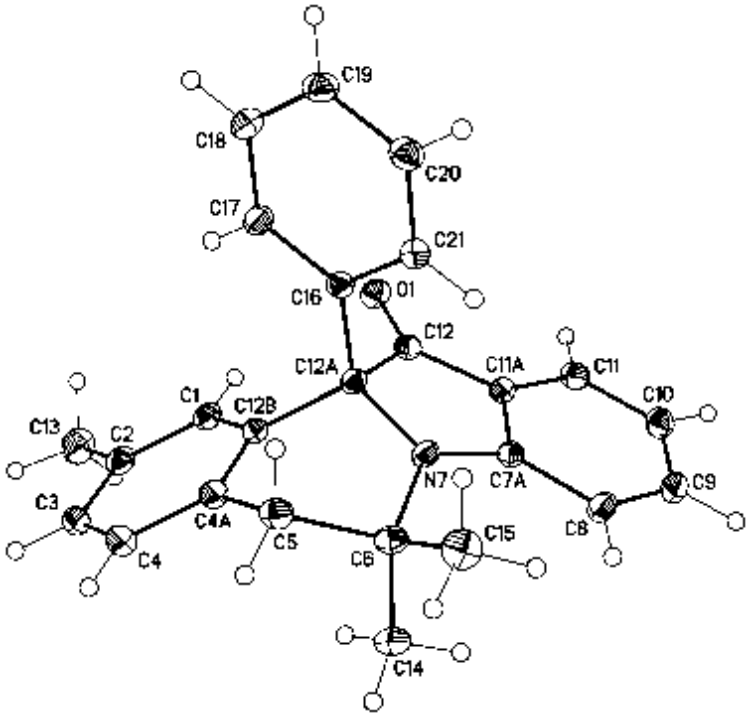
6,6-Dimethyl-14a-phenyl-5,14a-dihydrobenzo[6,7]indolo[2,1-*a*]isoquinolin-14(6*H*)-one (9dB)

Yellow oil. Yield 8% (12 mg). Total yield of two isomers is 72%; MP 167-168°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.71 (d, *J*=8.7 Hz, 1H, Ar), 7.94 (d, *J*=6.8 Hz, 1H, Ar), 7.74 (d, *J*=7.5 Hz, 1H, Ar), 7.57 (d, *J*=8.7 Hz, 1H, Ar), 7.51 (t, *J*=7.2 Hz, 1H, Ar), 7.44 (t, *J*=7.2 Hz, 1H, Ar), 7.32 (t, *J*=7.5 Hz, 1H, Ar), 7.27 (t, *J*=6.8 Hz, 1H, Ar), 7.20 - 7.04 (m, 7H, Ar), 2.86 (d, *J*=14.9 Hz, 1H, CH_2), 2.61 (d, *J*=14.9 Hz, 1H, CH_2), 2.02 (s, 3H, Me), 1.31 (s, 3H, Me); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 197.2, 161.0, 140.9, 139.3, 136.6, 134.6, 129.9, 129.1, 128.8, 128.7 (2C), 128.5, 128.2, 127.7, 126.8, 126.4, 126.1 (2C), 124.7, 122.5, 121.3, 120.8, 117.2, 57.7, 48.0, 32.2, 27.4. IR (KBr) 2924, 2853, 1685, 1599, 1456, 1387, 749 cm^{-1}.



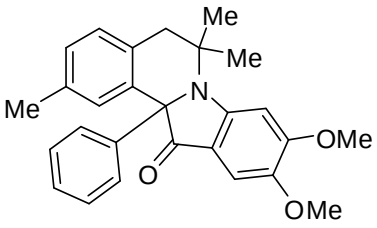
2,6,6-Trimethyl-12a-phenyl-5,12a-dihydroindolo[2,1-*a*]isoquinolin-12(6*H*)-one (10a)

Yellow powder. Yield 69% (75 mg). MP 201-205^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.88 (s, 1H, 1-H), 7.63 (d, *J*=7.5 Hz, 1H, Ar), 7.47 (t, *J*=7.2 Hz, 1H, Ar), 7.23 - 7.14 (m, 6H, Ar), 7.10 (q, *J*=7.7 Hz, 2H, Ar), 6.75 (t, *J*=7.2 Hz, 1H, Ar), 2.70 (d, *J*=14.3 Hz, 1H, CH_2), 2.47 - 2.35 (m, 4H, Me, CH_2), 1.77 (s, 3H, Me), 1.16 (s, 3H, Me); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 198.3, 159.4, 140.0, 136.9, 136.2, 134.3, 133.5, 128.7, 128.6 (2C), 128.4, 127.5, 126.2, 126.1 (2C), 125.9, 120.3, 117.5, 112.5, 75.2, 56.3, 44.7, 28.8, 23.8, 21.6; ESI MS [M+H] 354; [Found: C, 84.81; H, 6.48; N, 4.02;. $C_{25}H_{23}NO$ requires C, 84.95; H, 6.56; N, 3.96%]; IR (KBr) 3437, 2976, 2924, 2854, 1688, 1612, 1483, 1321, 1163, 748 cm^{-1}.



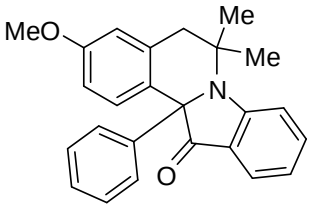
The structure of the product **10a** was unambiguously established by X-ray diffraction study. The central tetrahydropyridine ring in **10a** adopts a distorted *boat* conformation with deviations of the C5 and C12a atoms by 0.6246(16) and 0.4709(15) Å, respectively, from the mean plane of the other ring atoms. The dihydroindole fragment is almost planar (r.m.s. deviation is 0.036 Å), and forms the dihedral angle of 47.17(2)° to the terminal C1/C2/C3/C4/C4a/C12b benzene plane. The N7 nitrogen atom has a slightly pyramidalized configuration (the sum of bond angles is 356.9(3)°).Compound 1is chiral and has an asymmetric center at the C12a atom. The geometry of this quaternary carbon atom is sterically strained. So, the C12-C12a (1.5558(15) Å) and C12a-C16 (1.5430(14) Å) bonds are significantly elongated in compared to the typical value for C_{sp^2}-C_{sp^3} bond of 1.50 Å, and the C12-C12a-N7 (103.27(8)°), C12-C12a-C12b (114.13(9)°) and C12-C12a-C16 (105.49(8)°) bond angles substantially differ from the ideal tetrahedral one of 109.5°.The crystal of **10a** is racemate.

X-ray structure determination. The yellow prismatic crystal of **10a** ($C_{25}H_{23}NO$, M= 353.44) is monoclinic, space group $P2_1/n$, at T= 120 K: a= 10.6168(8) Å, b= 13.0290(10) Å, c= 13.6786(10) Å, β = 91.367(1)°, V= 1891.6(2) Å^3, Z= 4, d_{calc} = 1.241 g/cm^3, $F(000)$ = 752, μ = 0.075 mm^{-1}. 23457 total reflections (5514 unique reflections, R_{int} = 0.052) were measured on a three-circle Bruker APEX-II CCD diffractometer (λ(MoK$_\alpha$)-radiation, graphite monochromator,φ and ω scan mode, $2\theta_{max}$ = 60°). The structure was determined by direct methods and refined by full-matrix least squares technique on F^2 with anisotropic displacement parameters fornon-hydrogen atoms. The hydrogen atoms were placed in calculated positions and refined within riding model with fixed isotropic displacement parameters [U_{iso}(H) = 1.5U_{eq}(C) for the methyl groups and 1.2U_{eq}(C) for the other groups]. The final divergence factors were R_1 = 0.0454 for 4334 independent reflections with $I > 2\sigma(I)$ and wR_2 = 0.1257 for all independent reflections, S = 1.073. All calculations were carried out using the SHELXTL program.
Crystallographic data for **10a** have been deposited with the Cambridge Crystallographic Data Center, CCDC 1043893. Copies of this information may be obtained free of charge from the Director, CCDC, 12 Union Road, CambridgeCB2 1EZ, UK (fax: +44 1223 336033; e-mail: deposit@ccdc.cam.ac.uk or www.ccdc.cam.ac.uk).



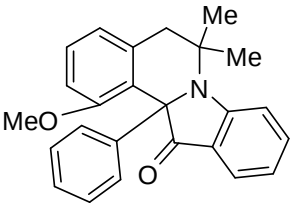
9,10-Dimethoxy-2,6,6-trimethyl-12a-phenyl-5,12a-dihydro-indolo[2,1-*a*]isoquinolin-12(6*H*)-one (10b)

Yellow powder. Yield 87% (129 mg); MP 222-224°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.93 (s, 1H, Ar), 7.24 - 7.05 (m, 8H, Ar), 6.62 (s, 1H, Ar), 4.02 (s, 3H, OMe), 3.83 (s, 3H, OMe), 2.72 (d, *J*=14.3 Hz, 1H, CH_2), 2.45 - 2.36 (m, 4H, Me, CH_2), 1.78 (s, 3H, Me), 1.16 (s, 3H, Me); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 196.2, 168.0, 158.1, 157.3, 143.4, 140.4, 136.3, 134.6, 133.4, 128.5 (2C), 128.4, 127.4, 126.1 (2C), 126.0 (2C), 111.7, 105.7, 94.9, 75.7, 56.3, 56.2, 44.7, 29.4, 24.2, 21.6; ESI MS [M+H] 414; [Found: C, 78.31; H, 6.48; N, 3.43; $C_{27}H_{27}NO_3$ requires C, 78.42; H, 6.58; N, 3.39%]; IR (KBr) 3448, 2971, 1661, 1620, 1491, 1256, 1235, 1015, 733 cm^{-1}.



3-Methoxy-6,6-dimethyl-12a-phenyl-5,12a-dihydroindolo[2,1-*a*]isoquinolin-12(6*H*)-one (11a)

Yellow powder. Yield 57% (105 mg); MP 203-204°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.97 (d, *J*=8.7 Hz, 1H, Ar), 7.62 (d, *J*=8.1 Hz, 1H, Ar), 7.51 - 7.43 (m, 1H, Ar), 7.22 -7.13 (m, 6H, Ar), 6.87 (dd, *J*=8.7, 2.5 Hz, 1H, Ar),6.79 - 6.71 (m, 2H, Ar), 3.82 (s, 3H, OMe), 2.73 (d, *J*=14.3 Hz, 1H, CH_2), 2.40 (d, *J*=14.3 Hz, 1H, CH_2), 1.77 (s, 3H, Me), 1.17 (s, 3H, Me). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 198.5, 159.4, 159.3, 140.2, 138.1, 136.9, 128.6 (3C), 127.5, 126.7, 126.4, 126.2, 126.1, 120.4, 117.5, 115.3, 112.6, 110.6, 74.8, 56.2, 55.4, 45.2, 28.9, 23.9; ESI MS [M+H] 370; [Found: C, 81.17; H, 6.21; N, 3.83; $C_{25}H_{23}NO_2$ requires C, 81.27; H, 6.27; N, 3.79%]; IR (KBr) 2975, 2834, 1701, 1612, 1475, 1347, 1321, 1264, 1166, 1059, 750 cm^{-1}.



1-Methoxy-6,6-dimethyl-12a-phenyl-5,12a-dihydroindolo[2,1-*a*]isoquinolin-12(6*H*)-one (11b)

Yellow powder. Yield 21% (38mg); MP 163-165°C; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.64 (d, *J*=7.6 Hz, 1H, Ar), 7.41 (t, *J*=7.2 Hz, 1H, Ar), 7.27 - 7.24 (m, 1H, Ar), 7.22 - 7.16 (m, 3H, Ar), 7.09 (t, *J*=7.6 Hz, 3H, Ar), 6.87 (d, *J*=8.3 Hz, 1H, Ar), 6.78 (d, *J*=6.9 Hz, 1H, Ar), 6.73 (t, *J*=7.2 Hz, 1H, Ar), 3.78 (s, 3H, OMe), 2.73 (d, *J*=14.4 Hz, 1H, CH_2), 2.34 (d, *J*=14.4 Hz, 1H, CH_2), 1.70 (s, 3H, Me), 1.12 (s, 3H, Me); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 198.6, 159.7, 159.3, 141.2, 138.1, 136.5,134.7, 130.8 (2C), 128.5 (2C), 127.1, 126.8, 126.4, 126.1, 120.3, 117.8, 113.6, 111.0, 74.7, 56.4, 55.8, 45.7, 28.6, 24.5; ESI MS [M+H] 370; [Found: C, 81.23; H, 6.18; N, 3.81; $C_{25}H_{23}NO_2$ requires C, 81.27; H, 6.27; N, 3.79%]; IR (KBr) 2975, 1702, 1612, 1475, 1320, 1263, 1166, 1059, 750 cm^{-1}.

Table S1. Spectral properties of indolo[2,1-*a*]isoquinolinones in different solvents

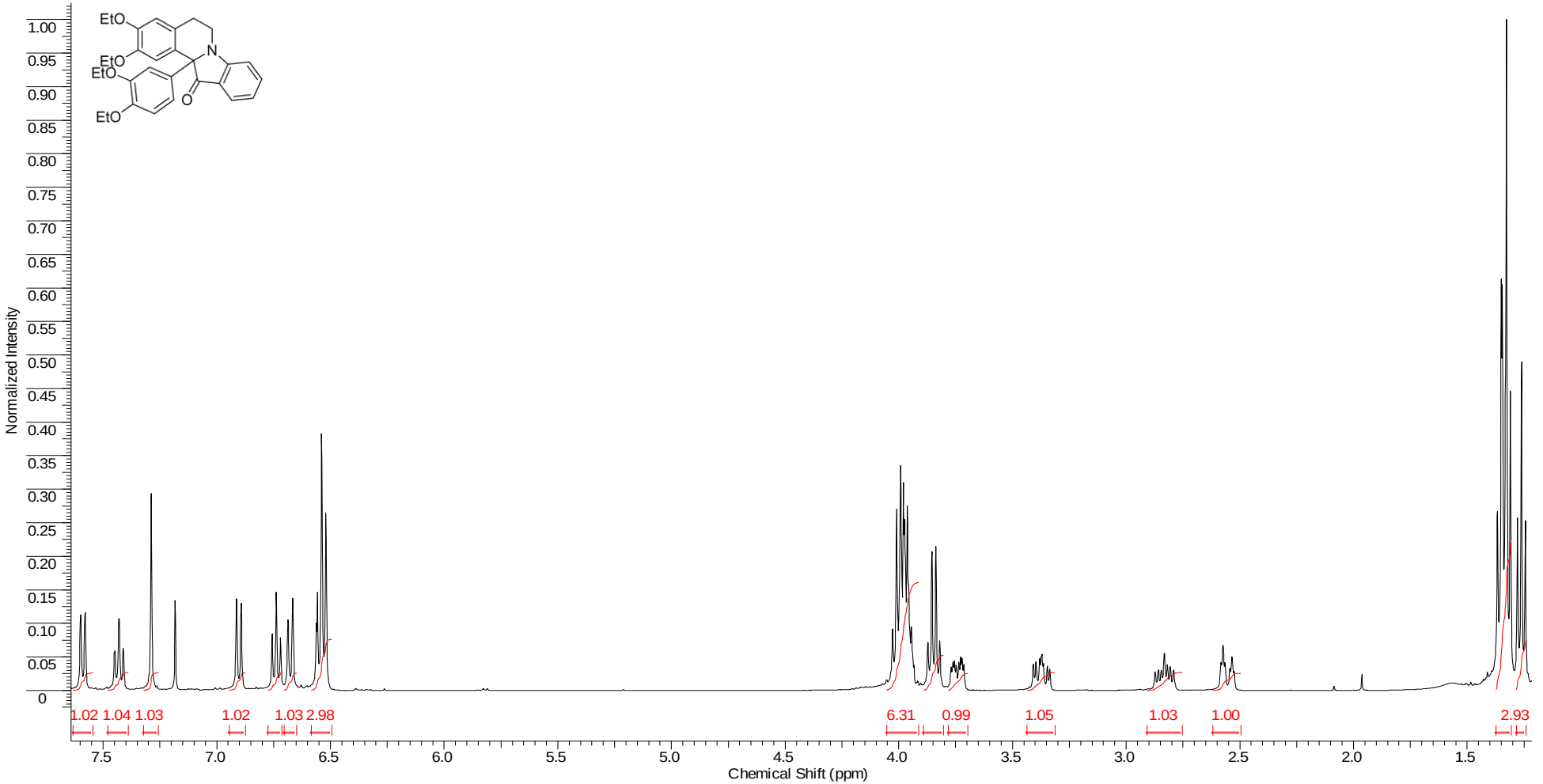
Solvent		**7a**	**7 dA**	**7f**	**7h**	**8a**	**8b**	**9a**	**9c**	**9dA**	**10a**	**10b**	**11a**
EtOH	Abs	404 (4400)[a]	395 (3600)	405 (6900)	468 (1600)	405 (4200)	405 (6500)	419 (3900)	417 (5600)	425 (4300)	419 (4500)	417 (5800)	419 (3600)
	Em	502	488	501	613	502	501	488	494	472	486	492	491
Toluene	Abs	397 (4500)	385 (3900)	396 (7100)	461 (2000)	397 (4400)	396 (6700)	407 (4100)	409 (5600)	423 (4600)	408 (4000)	409 (5000)	407 (3800)
	Em	461	463	475	553	463	474	450	465	463	451	465	451
DMSO	Abs	402 (4300)	392 (3900)	401 (6300)	468 (1800)	402 (4300)	401 (6500)	416 (4200)	415 (5600)	424 (4600)	417 (4100)	415 (4900)	415 (3800)
	Em	479	471	481	585	478	482	465	475	468	466	477	466
MeCN	Abs	399 (4200)	389 (3600)	398 (6300)	463 (1700)	399 (3900)	397 (5500)	414 (4100)	413 (5500)	423 (4400)	413 (3800)	413 (4800)	413 (3600)
	Em	474	466	479	581	478	481	465	476	467	464	477	465

[a] peak maximum in nm (extinction coefficient in $(mol\ cm)^{-1}$)

Table S2. Absorption and emission maxima of **7a** in various solvents

Solvent	Max abs	Max em
Et_2O	395[a] (6100)[b]	459
Toluene	397 (4500)	461
EtOH	404 (4400)	502
Dioxane	397 (4400)	471
DCM	401 (5200)	475
THF	397 (4700)	463
MeCN	399 (4200)	474
DMSO	402 (4300)	479
DMF	400 (4200)	476
EtOAc	397 (4200)	465

[a] peak maximum in nm; [b] extinction coefficient in $(mol\ cm)^{-1}$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EtO
EtO
EtO
N
O
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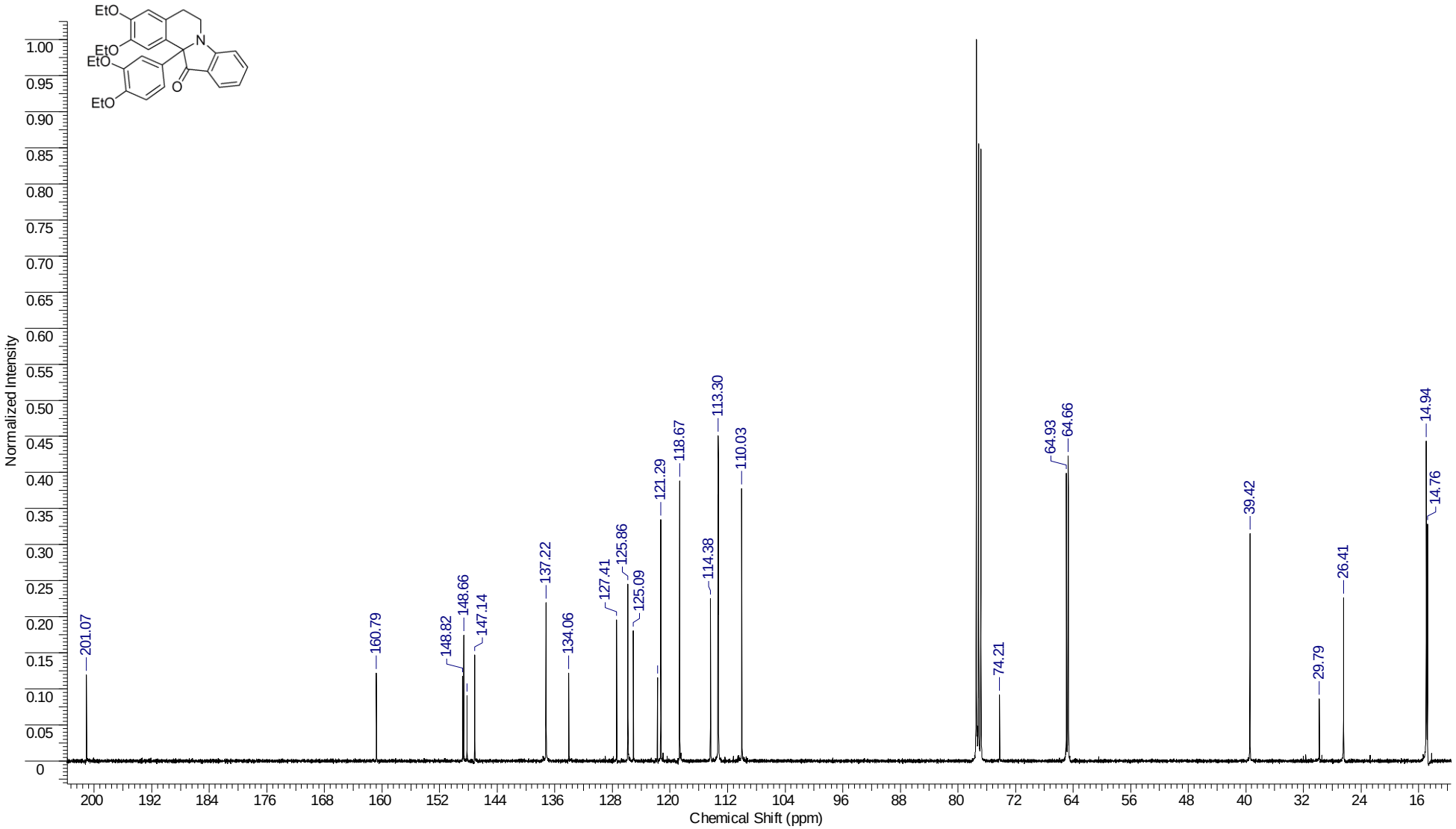
0.85
0.80
0.75
0.70
0.65
0.60
0.55
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
1.02 1.04 1.03 1.02 1.03 2.98 6.31 0.99 1.05 1.03 1.00 2.93
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5
Chemical Shift (ppm)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EtO
EtO
EtO
N
O
Normalized Intensity
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0.70
0.65
0.60
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0.50
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0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
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147.14
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134.06
127.41
125.86
125.09
121.29
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114.38
113.30
110.03
74.21
64.93
64.66
39.42
29.79
26.41
14.94
14.76
200
192
184
176
168
160
152
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32
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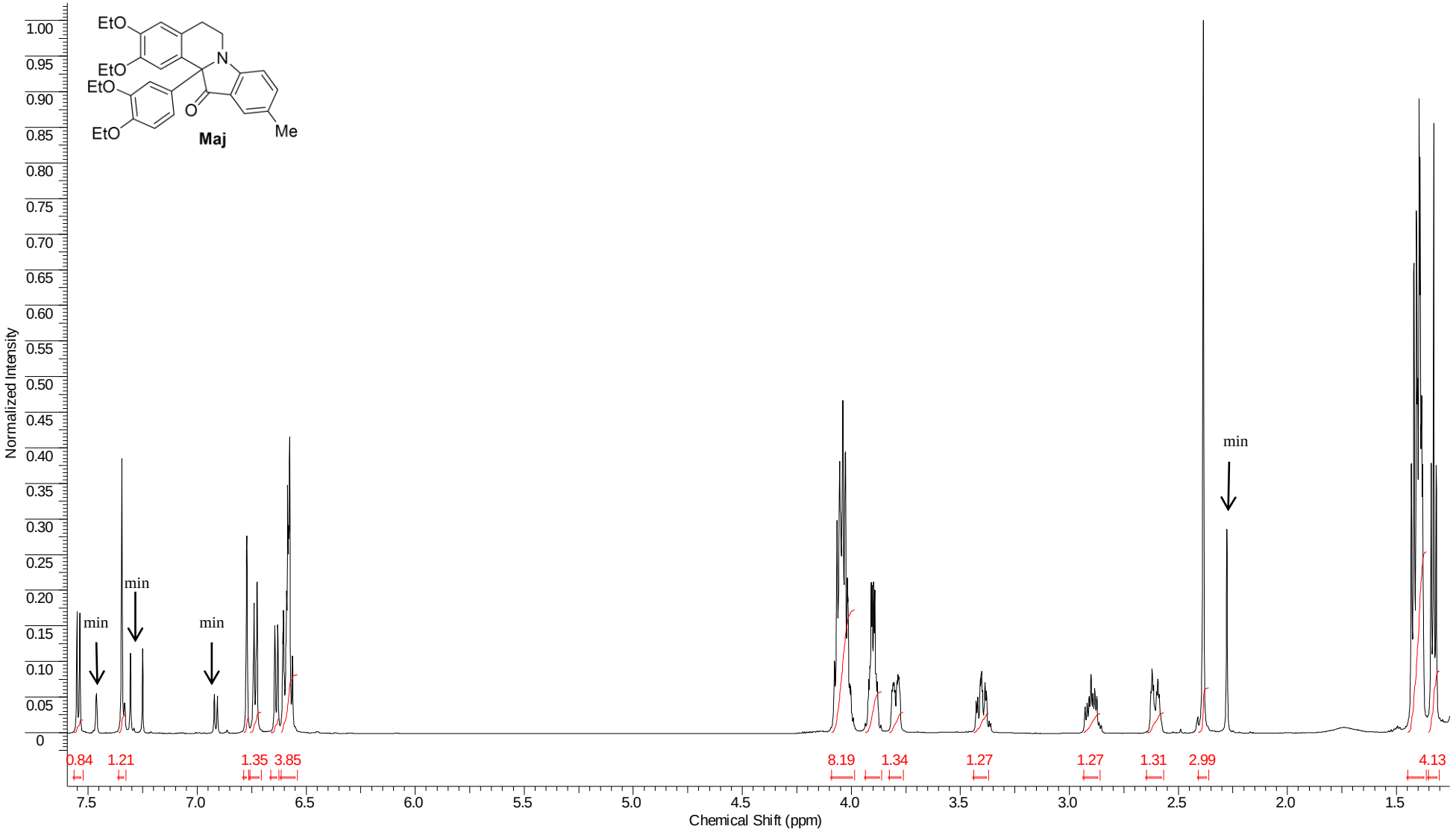
Chemical Shift (ppm)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EtO
EtO
EtO
N
O
Me
Maj
Normalized Intensity
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0.60
0.55
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0.30
0.25
0.20
0.15
0.10
0.05
0
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min
min
min
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1.21
1.35
3.85
8.19
1.34
1.27
1.27
1.31
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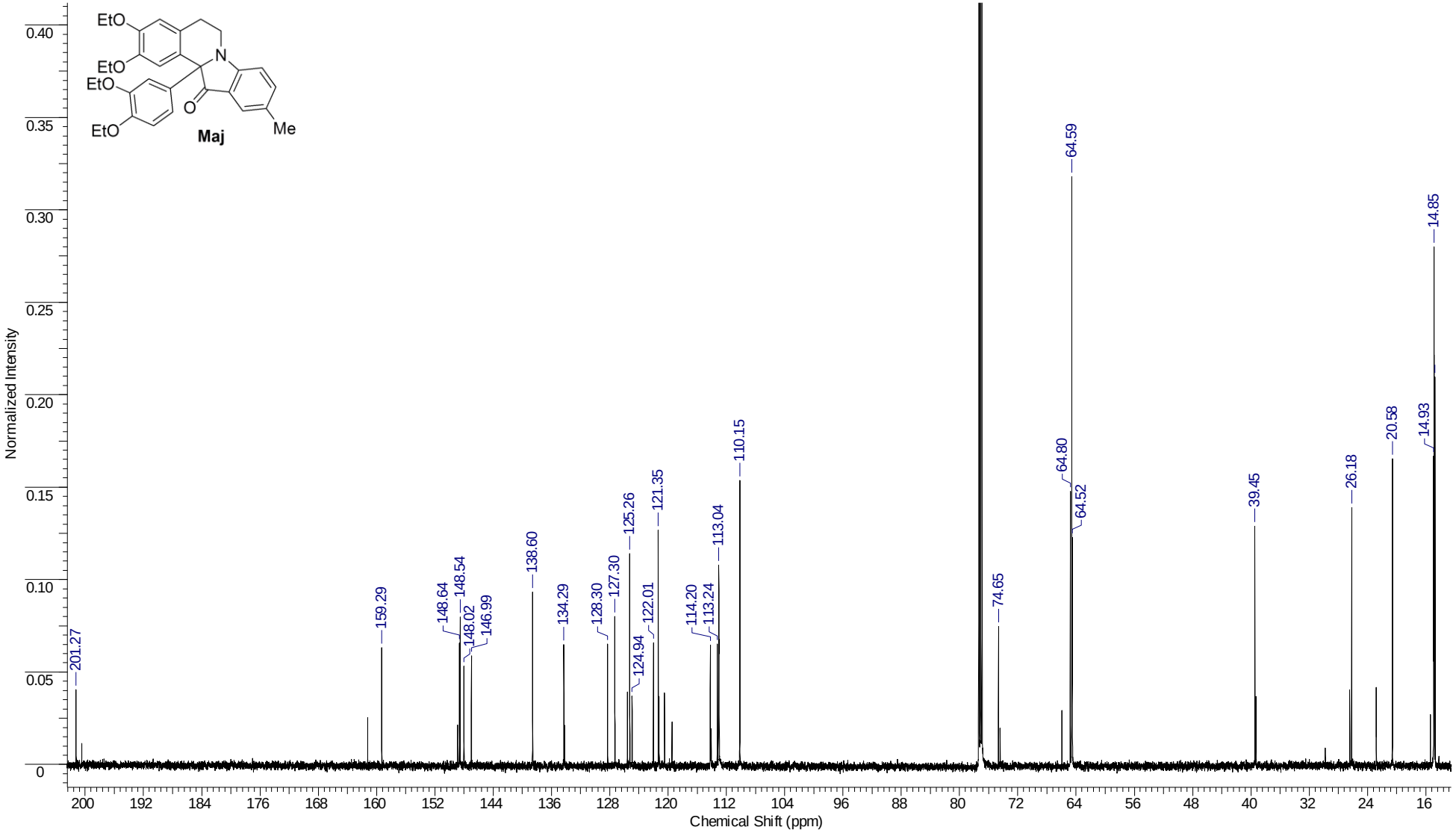
Chemical Shift (ppm)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EtO
EtO
EtO
N
O
Me
Maj
Normalized Intensity
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0.15
0.10
0.05
0
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146.99
138.60
134.29
128.30
127.30
125.26
124.94
122.01
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114.20
113.24
113.04
110.15
74.65
64.80
64.59
64.52
39.45
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14.93
14.85
200
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176
168
160
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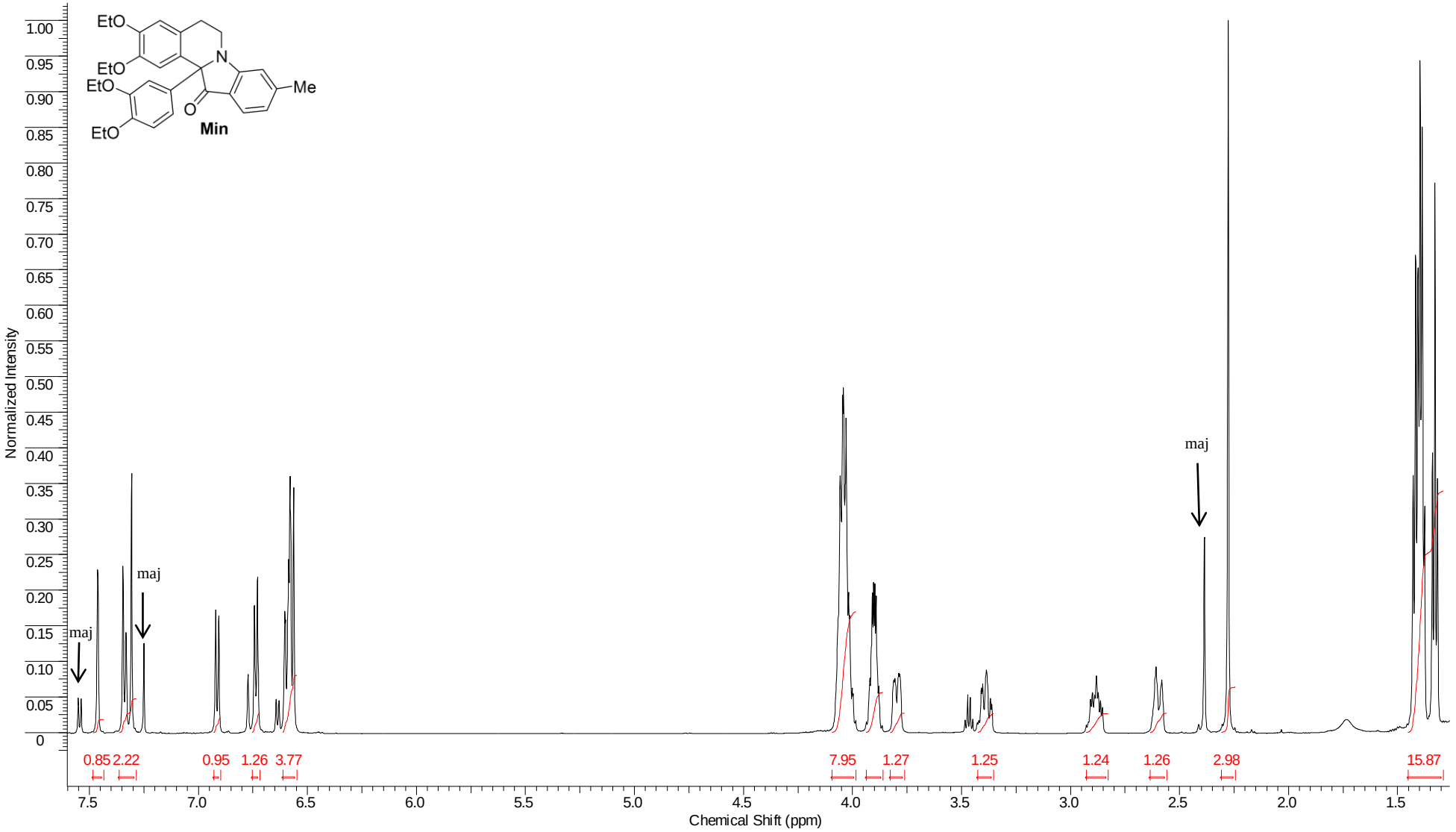
Chemical Shift (ppm)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EtO
N
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Me
Min
Normalized Intensity
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maj
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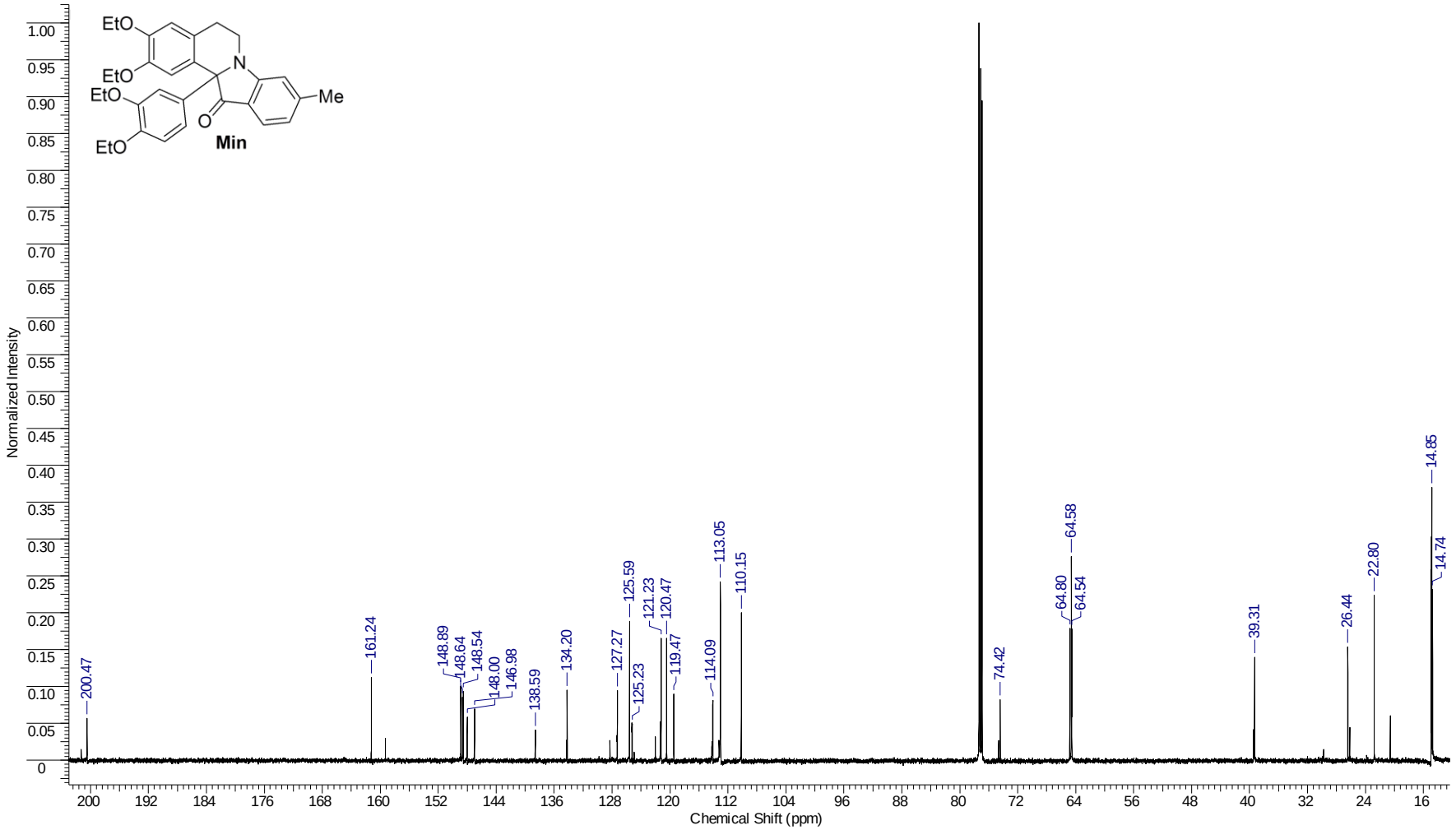
Chemical Shift (ppm)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EtO
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O
Me
Min
Normalized Intensity
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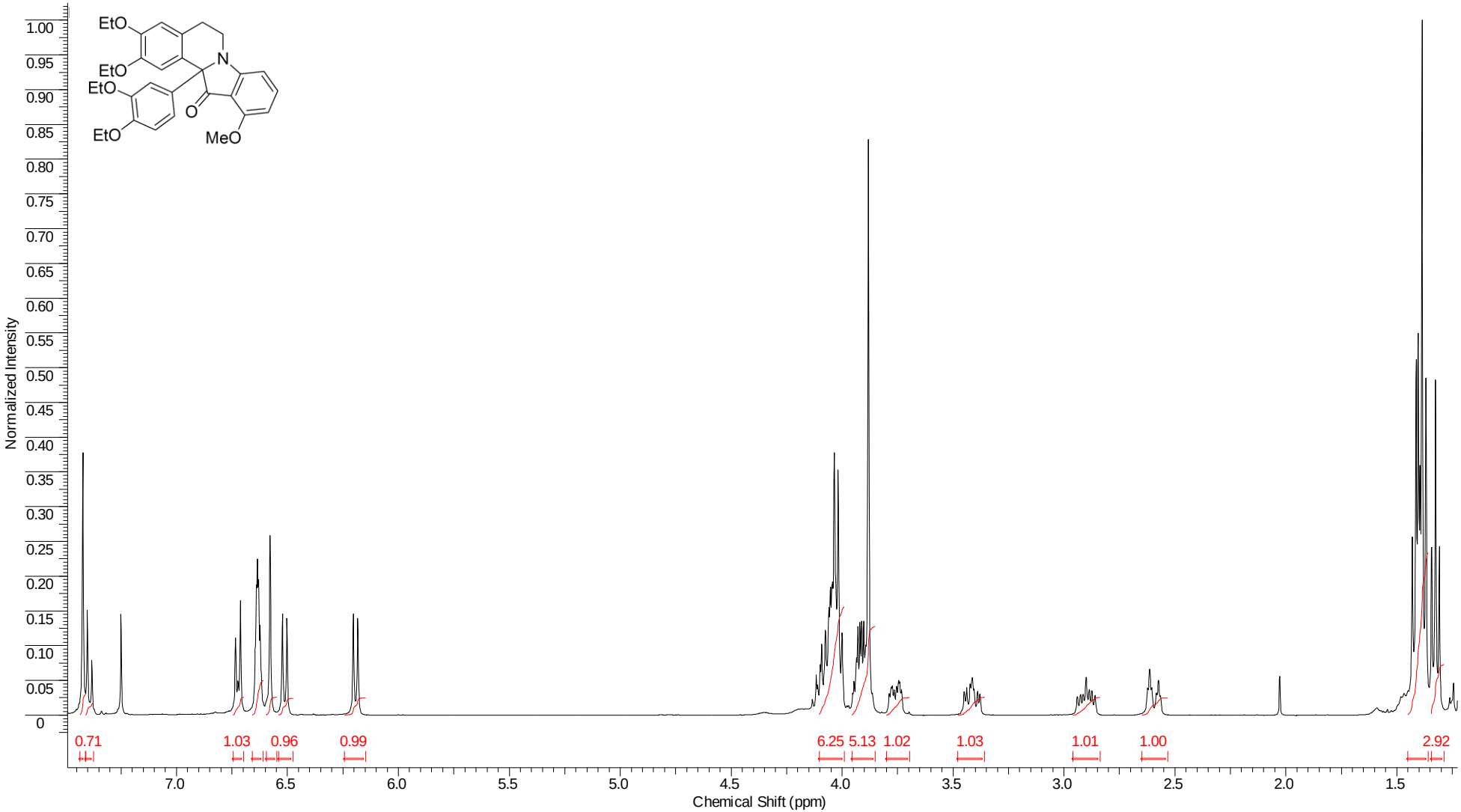
14.74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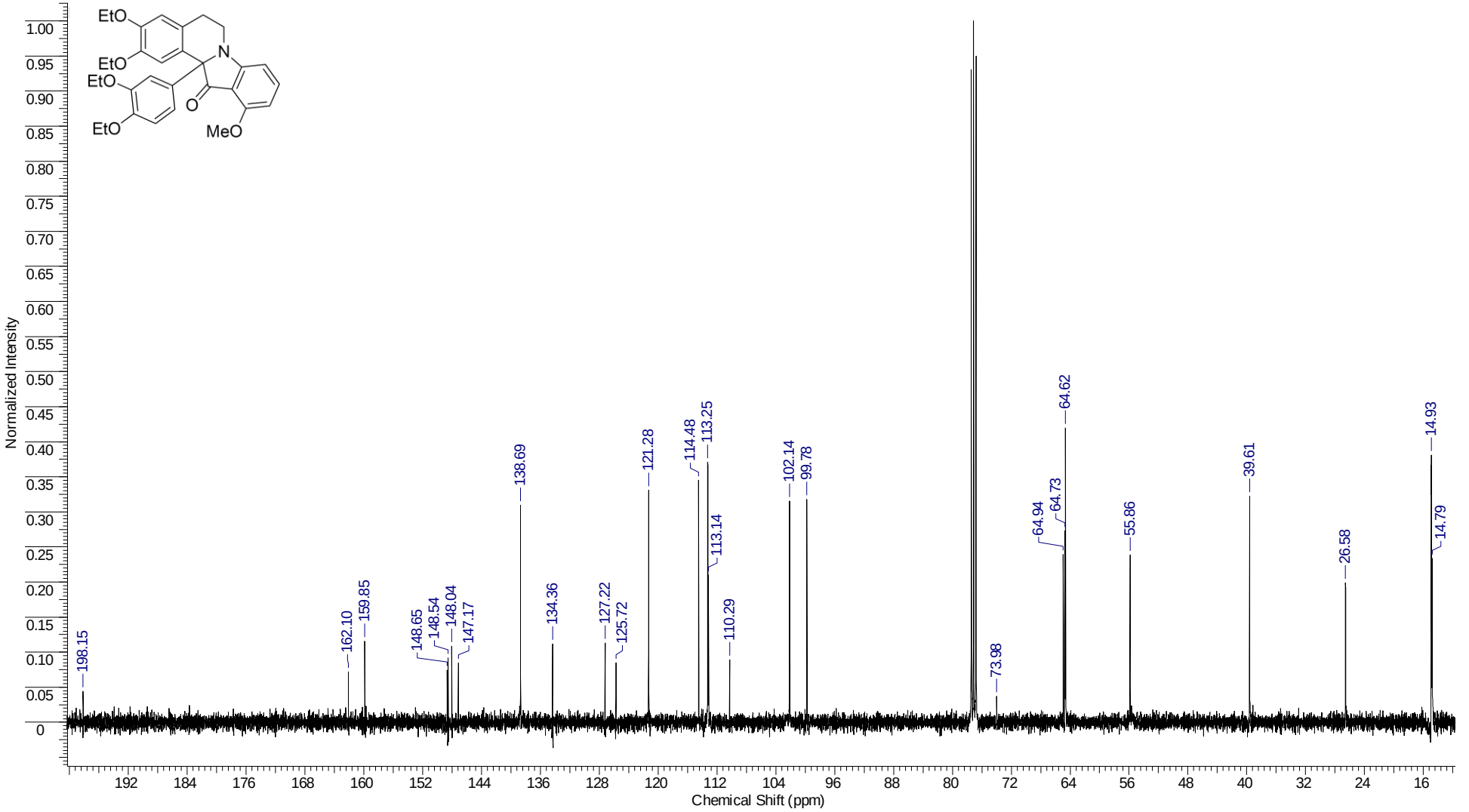
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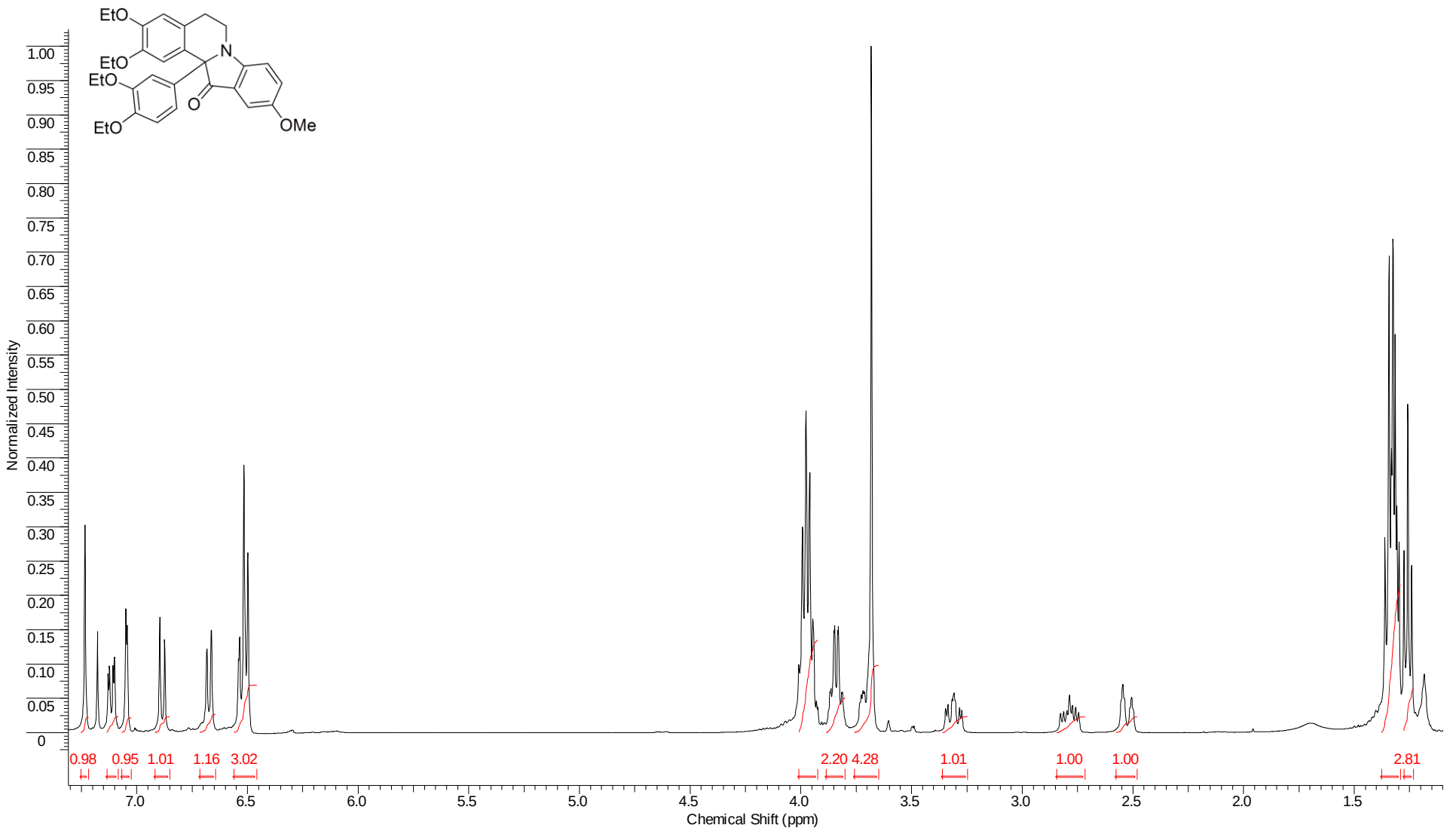
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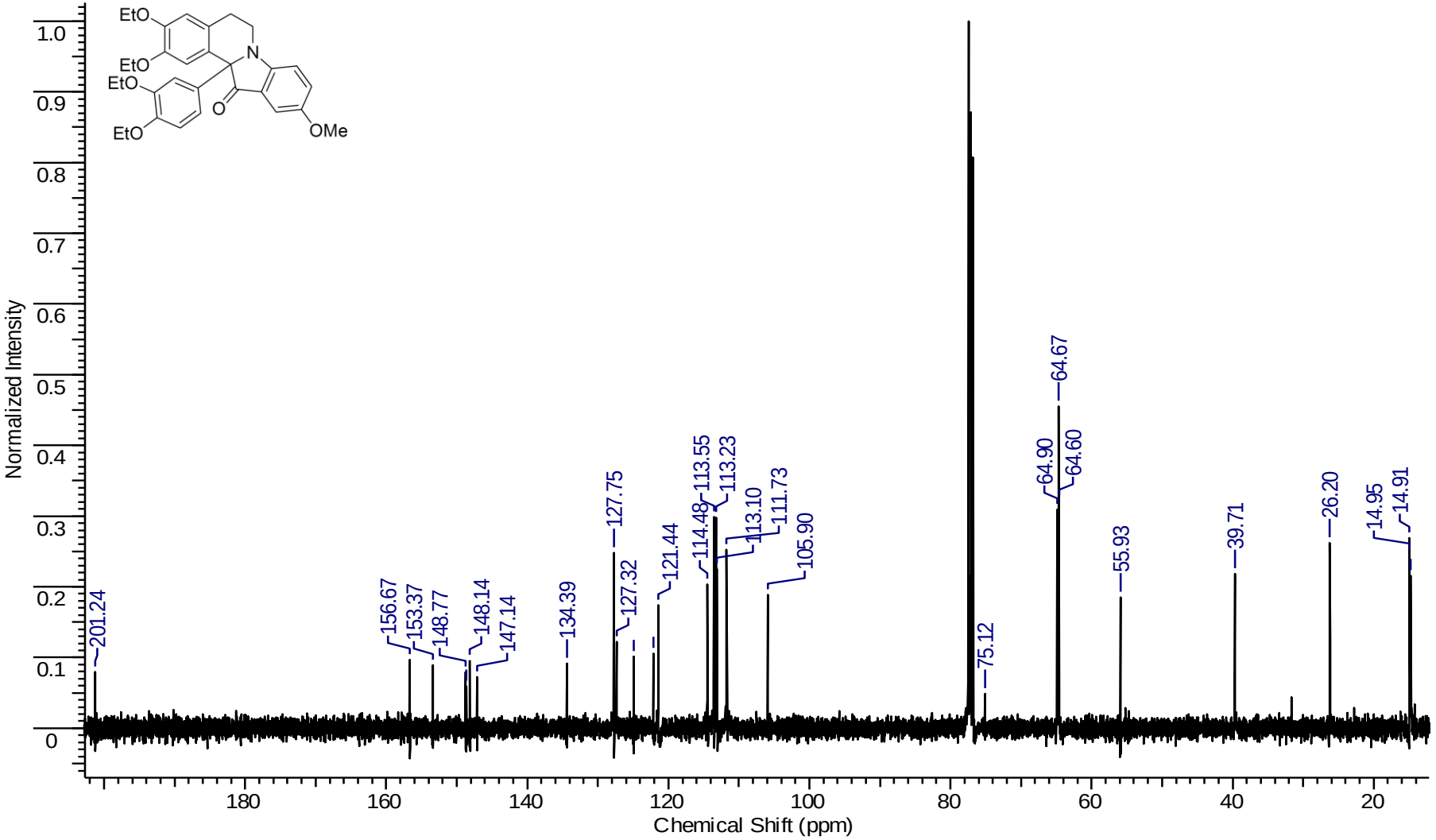
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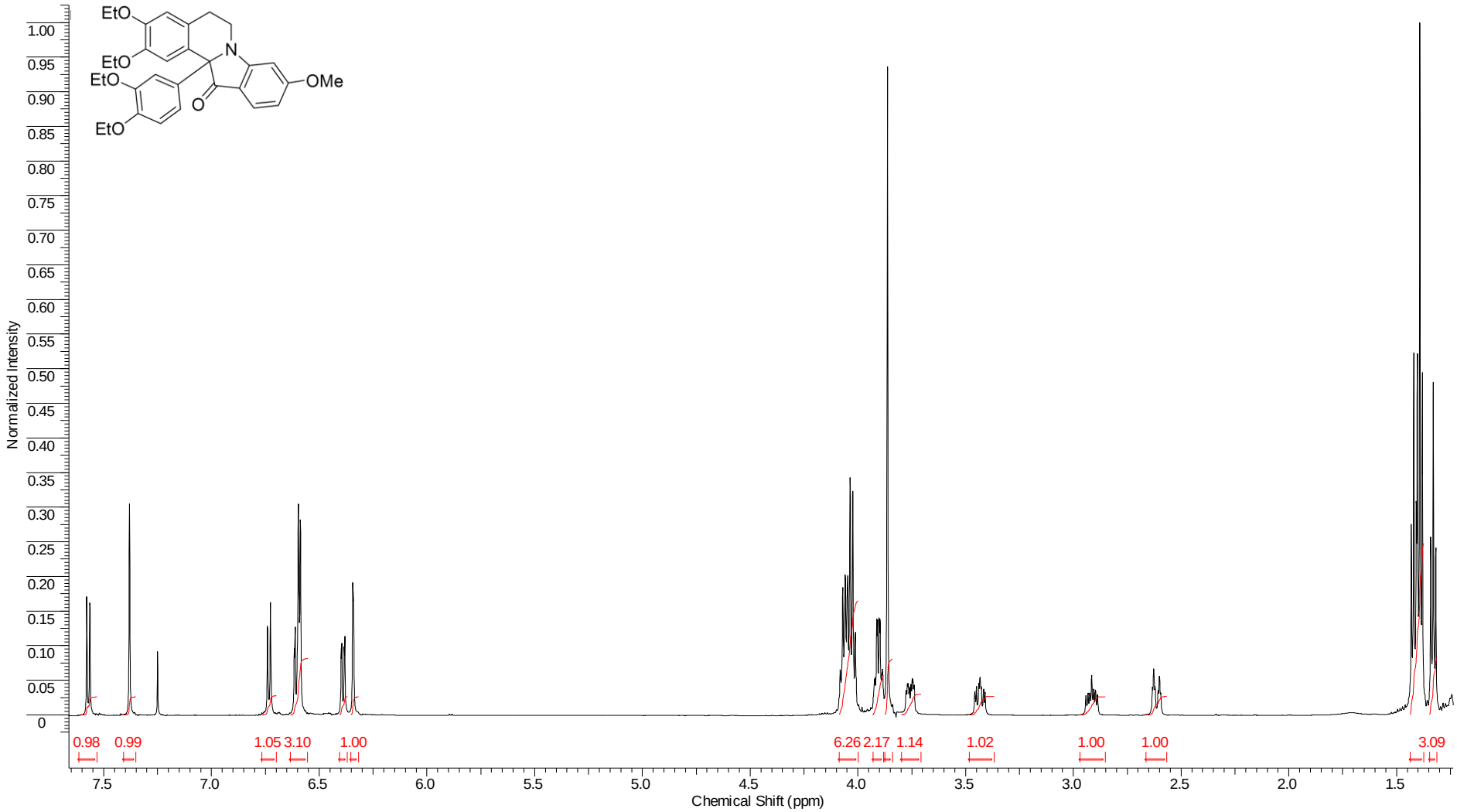
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0.15
0.10
0.05
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0.99
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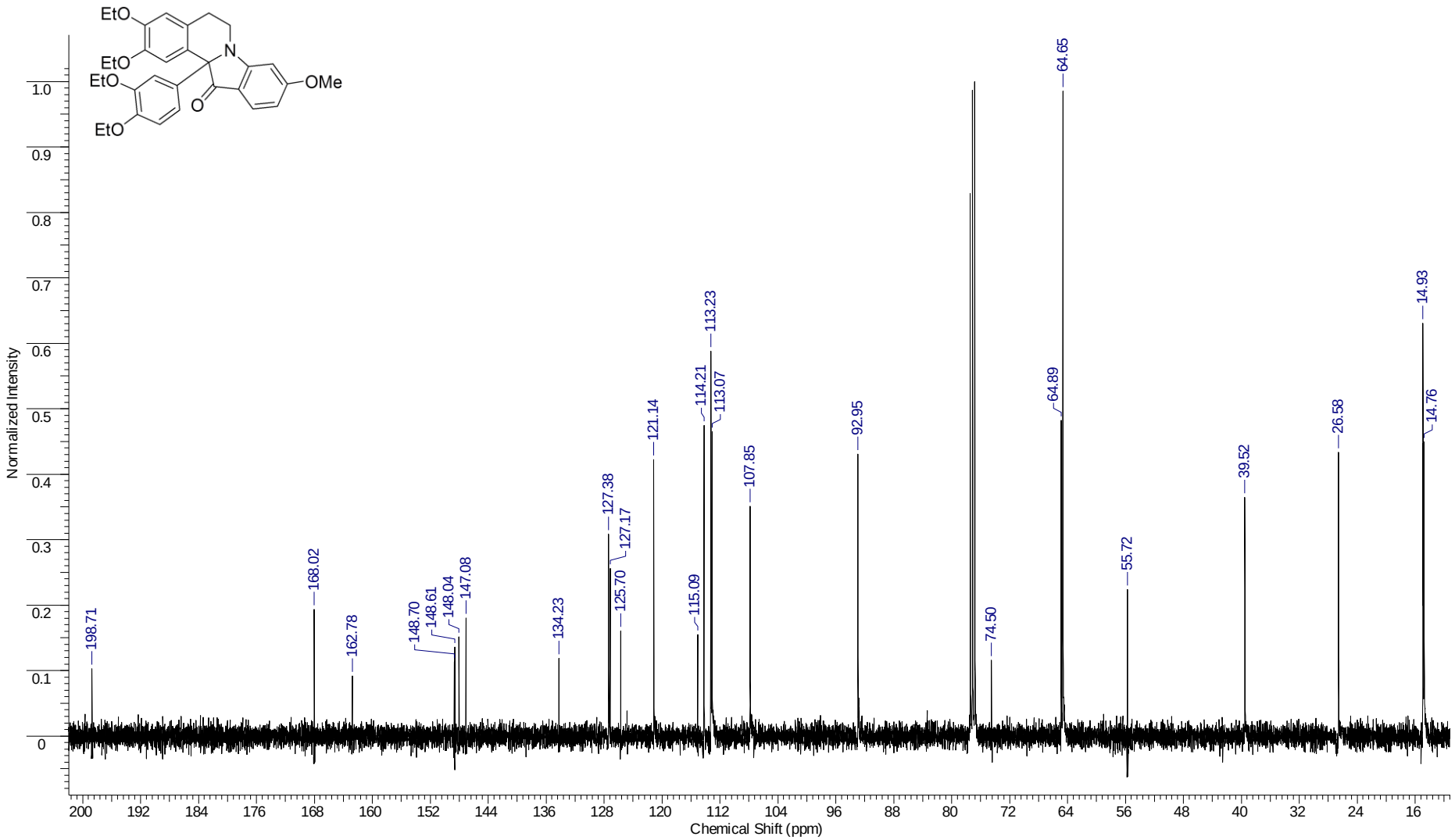
Chemical Shift (ppm)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EtO
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O
OMe
Normalized Intensity
Chemical Shift (ppm)
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125.70
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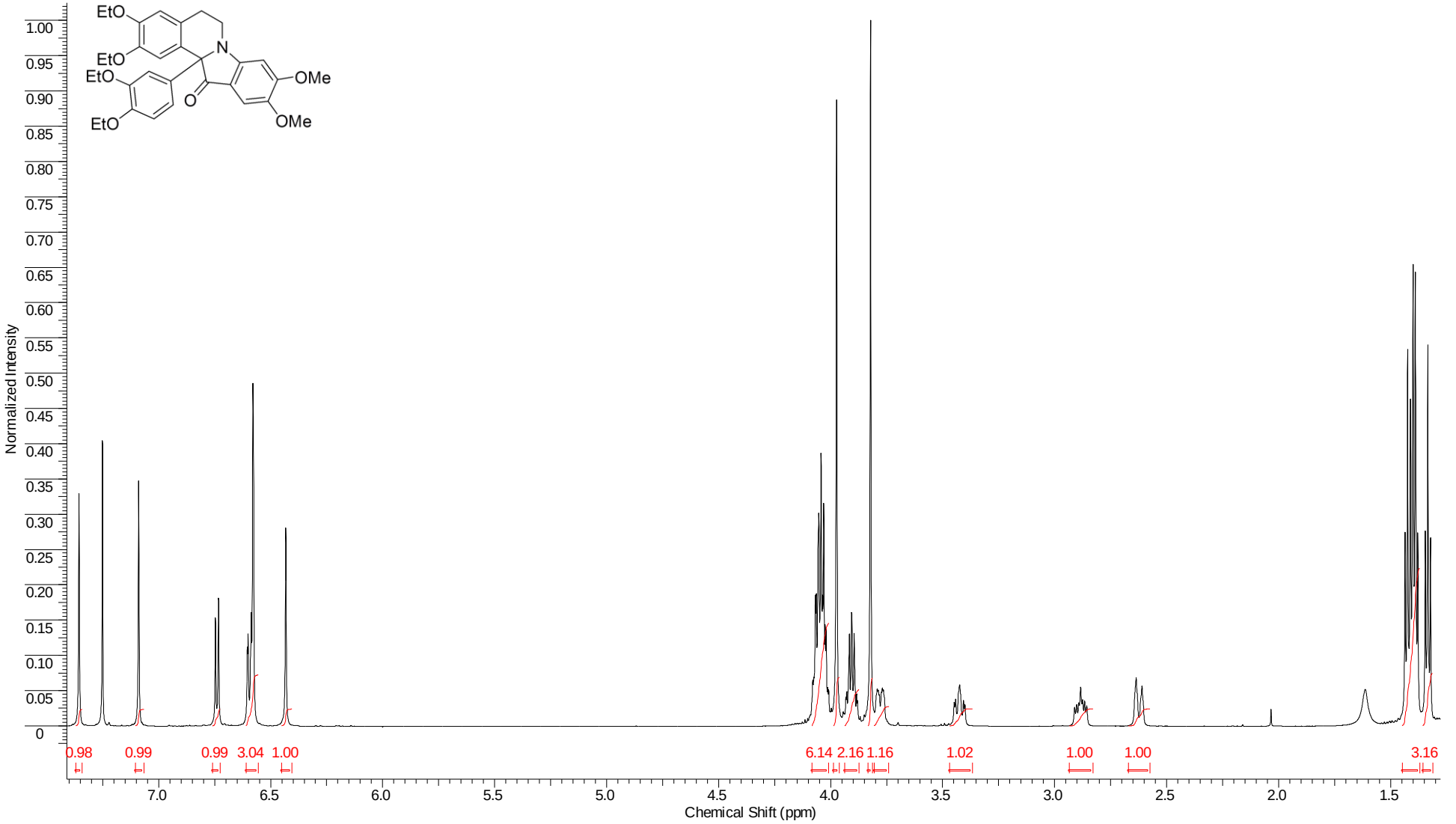
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EtO
EtO
EtO
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O
OMe
OMe
Normalized Intensity
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0.75
0.70
0.65
0.60
0.55
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
0.98
0.99
0.99
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1.02
1.00
1.00
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2.5
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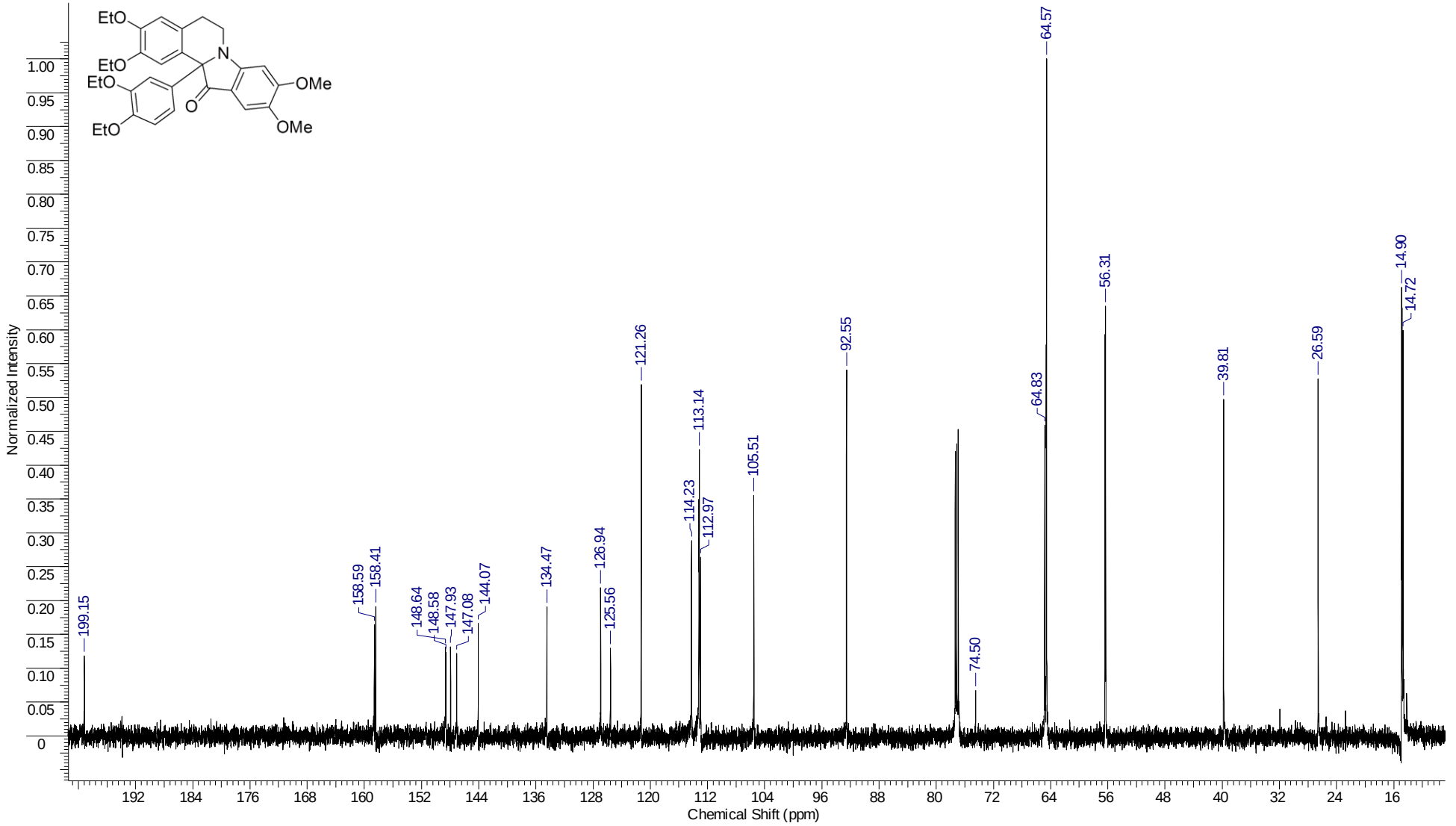
1.5
Chemical Shift (ppm)


EtO
EtO
EtO
EtO
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OMe
OMe
Normalized Intensity
1.00
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0.90
0.85
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0.75
0.70
0.65
0.60
0.55
0.50
0.45
0.40
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0.30
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72
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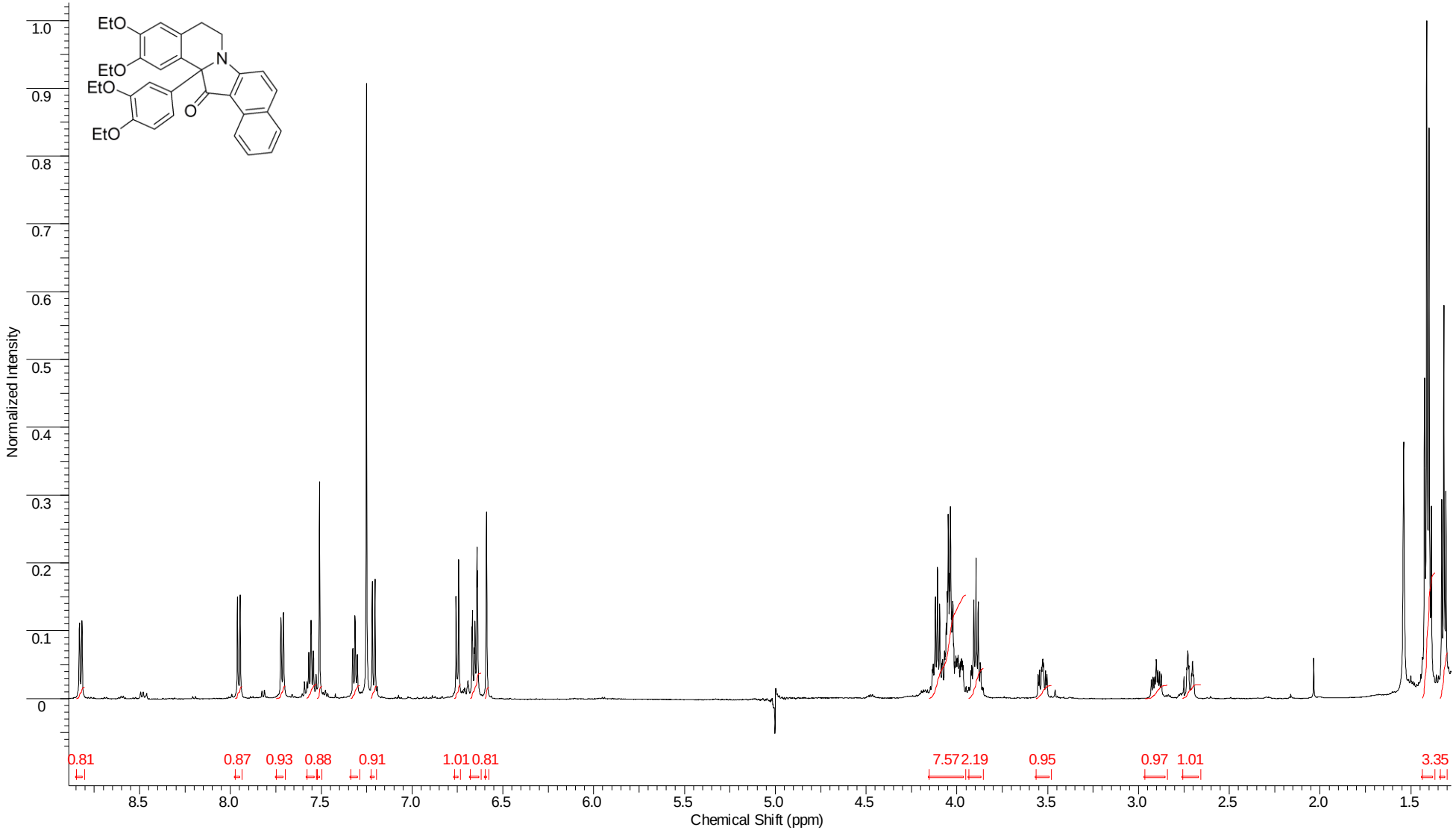
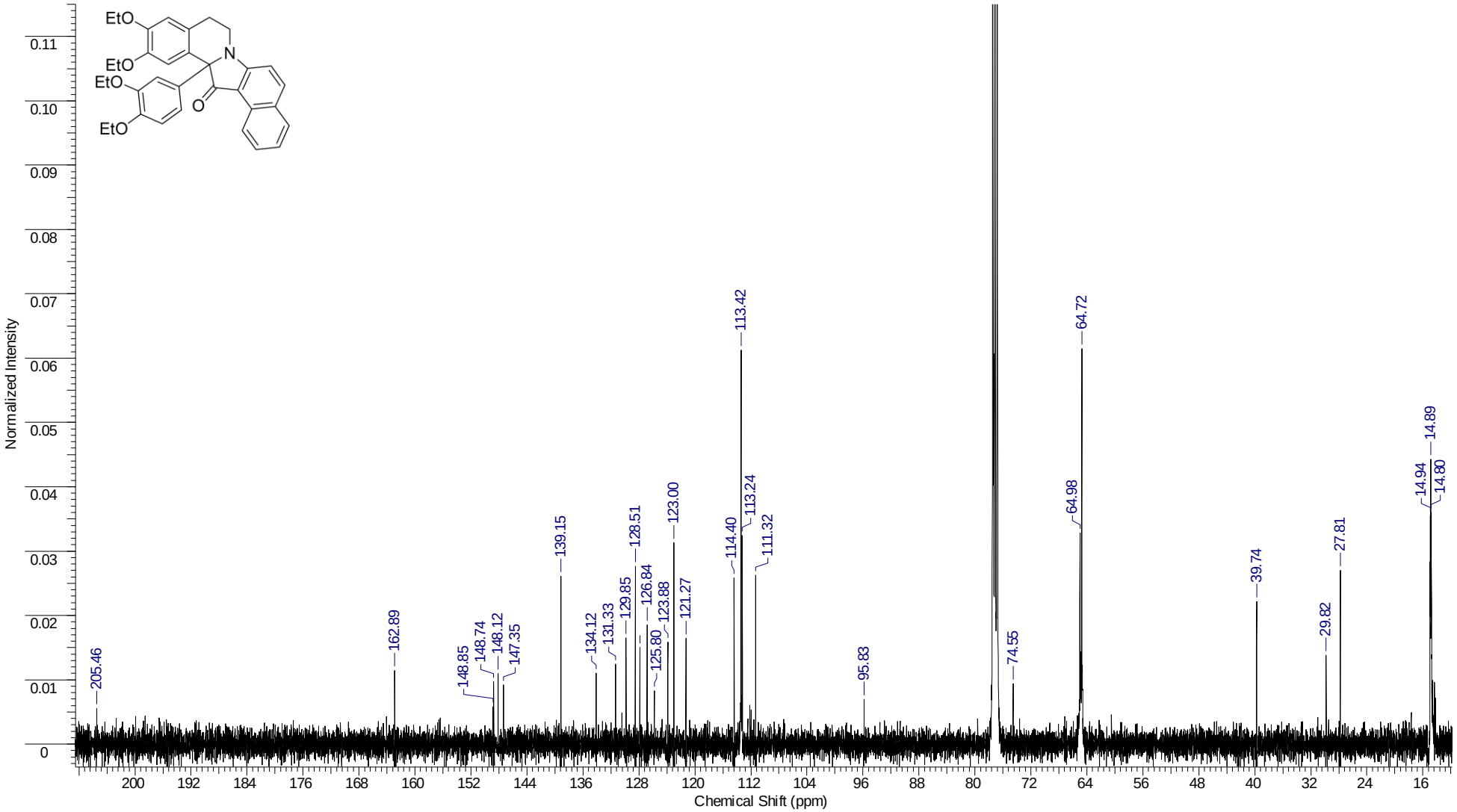
48
40
32
24
16
Chemical Shift (ppm)


EtO
EtO
EtO
EtO
N
O
Normalized Intensity
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
0.81
0.87
0.93
0.88
0.91
1.01
0.81
7.57
2.19
0.95
0.97
1.01
3.35
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
Chemical Shift (ppm)


EtO
EtO
EtO
EtO
N
O
Normalized Intensity
0.11
0.10
0.09
0.08
0.07
0.06
0.05
0.04
0.03
0.02
0.01
0
205.46
162.89
148.85
148.74
148.12
147.35
139.15
134.12
131.33
129.85
128.51
126.84
125.80
123.88
123.00
121.27
114.40
113.42
113.24
111.32
95.83
74.55
64.98
64.72
39.74
29.82
27.81
14.94
14.89
14.80
200
192
184
176
168
160
152
144
136
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112
104
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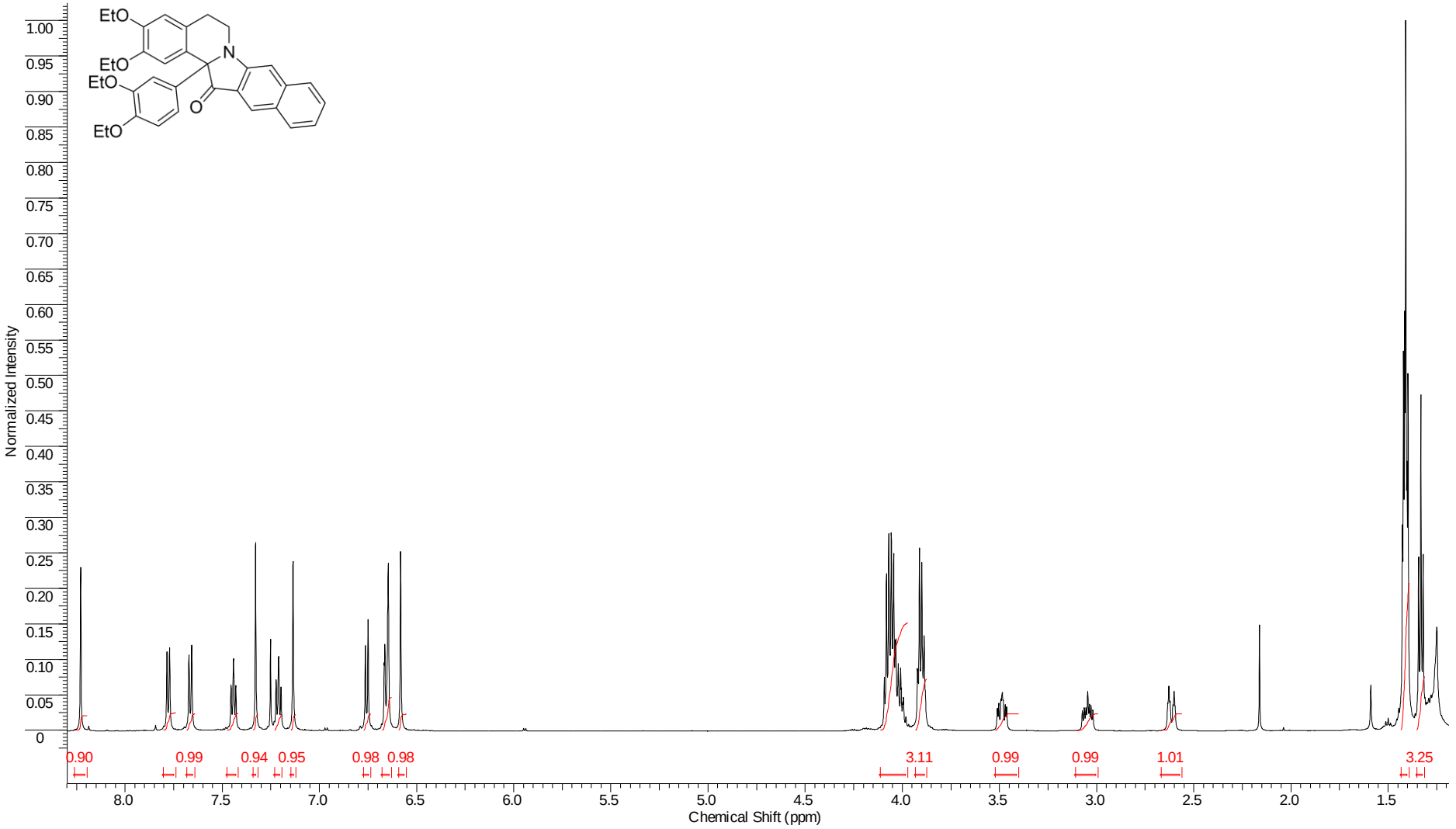
88
80
72
64
56
48
40
32
24
16
Chemical Shift (ppm)


EtO
EtO
EtO
EtO
N
O
Normalized Intensity
1.00
0.95
0.90
0.85
0.80
0.75
0.70
0.65
0.60
0.55
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
0.90
0.99
0.94
0.95
0.98
0.98
3.11
0.99
0.99
1.01
3.25
8.0
7.5
7.0
6.5
6.0
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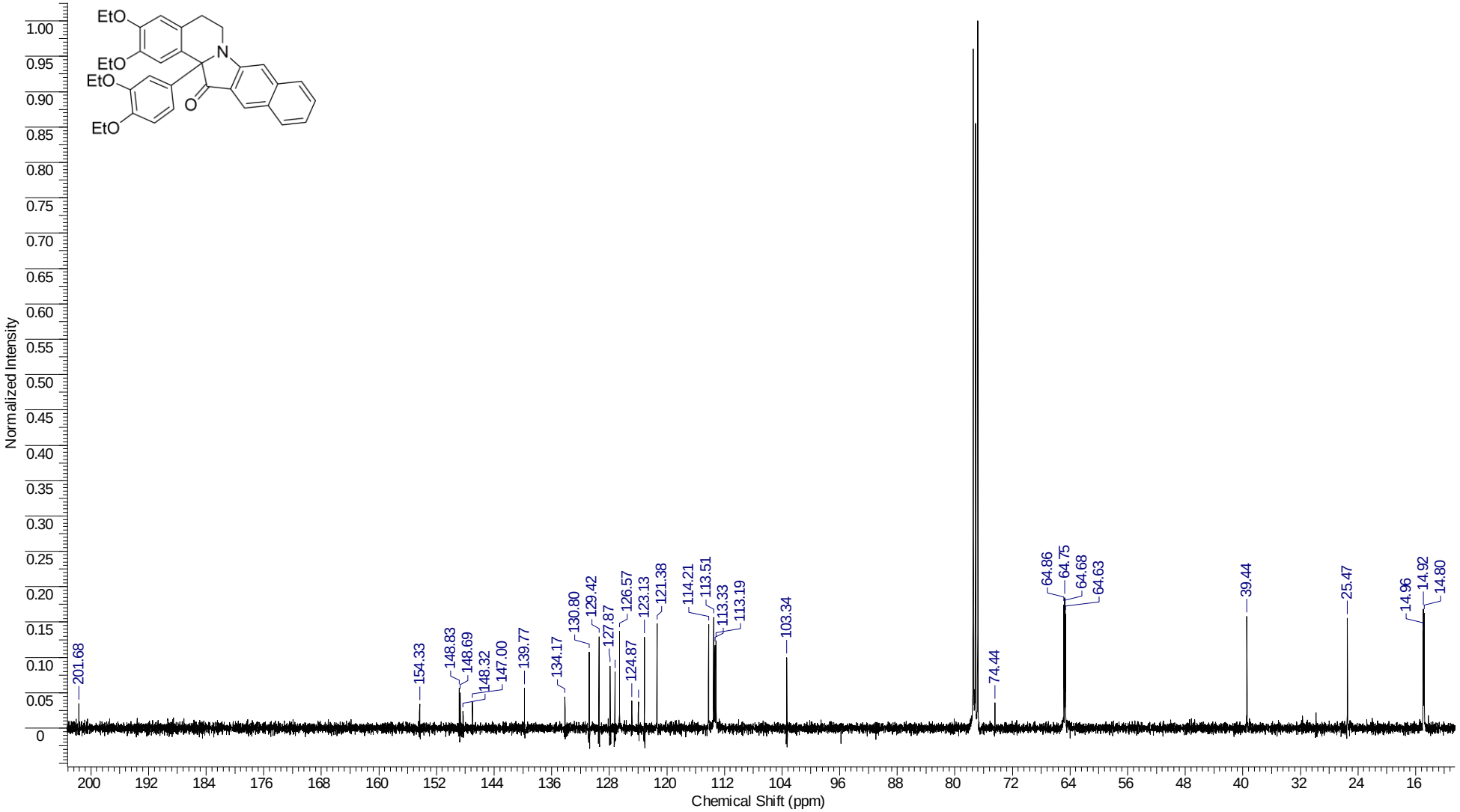
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
Chemical Shift (ppm)


EtO
EtO
EtO
EtO
N
O
Normalized Intensity
1.00
0.95
0.90
0.85
0.80
0.75
0.70
0.65
0.60
0.55
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
201.68
154.33
148.83
148.69
148.32
147.00
139.77
134.17
130.80
129.42
127.87
126.57
124.87
123.13
121.38
114.21
113.51
113.33
113.19
103.34
74.44
64.86
64.75
64.68
64.63
39.44
25.47
14.96
14.92
14.80
200
192
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176
168
160
152
144
136
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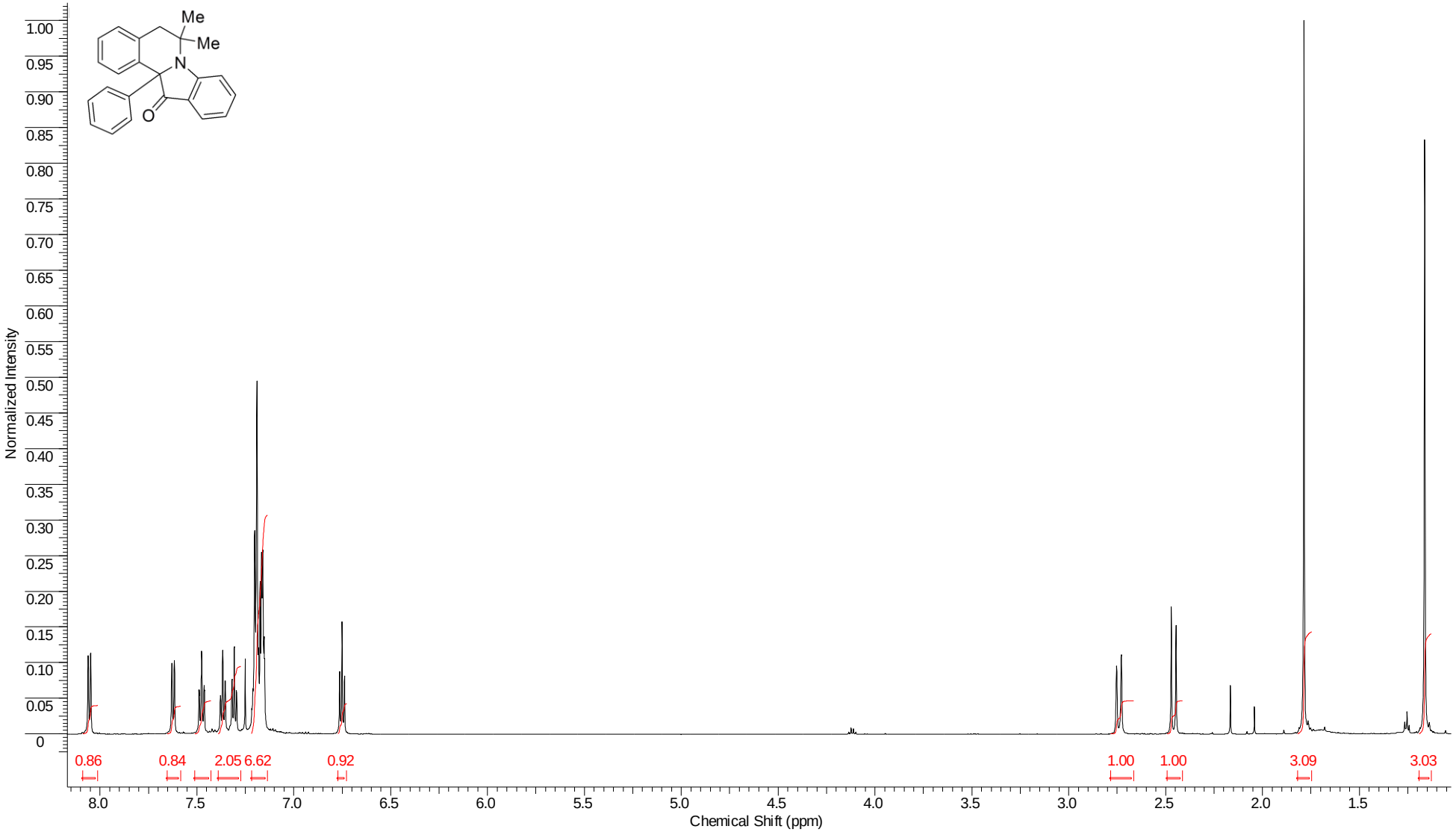
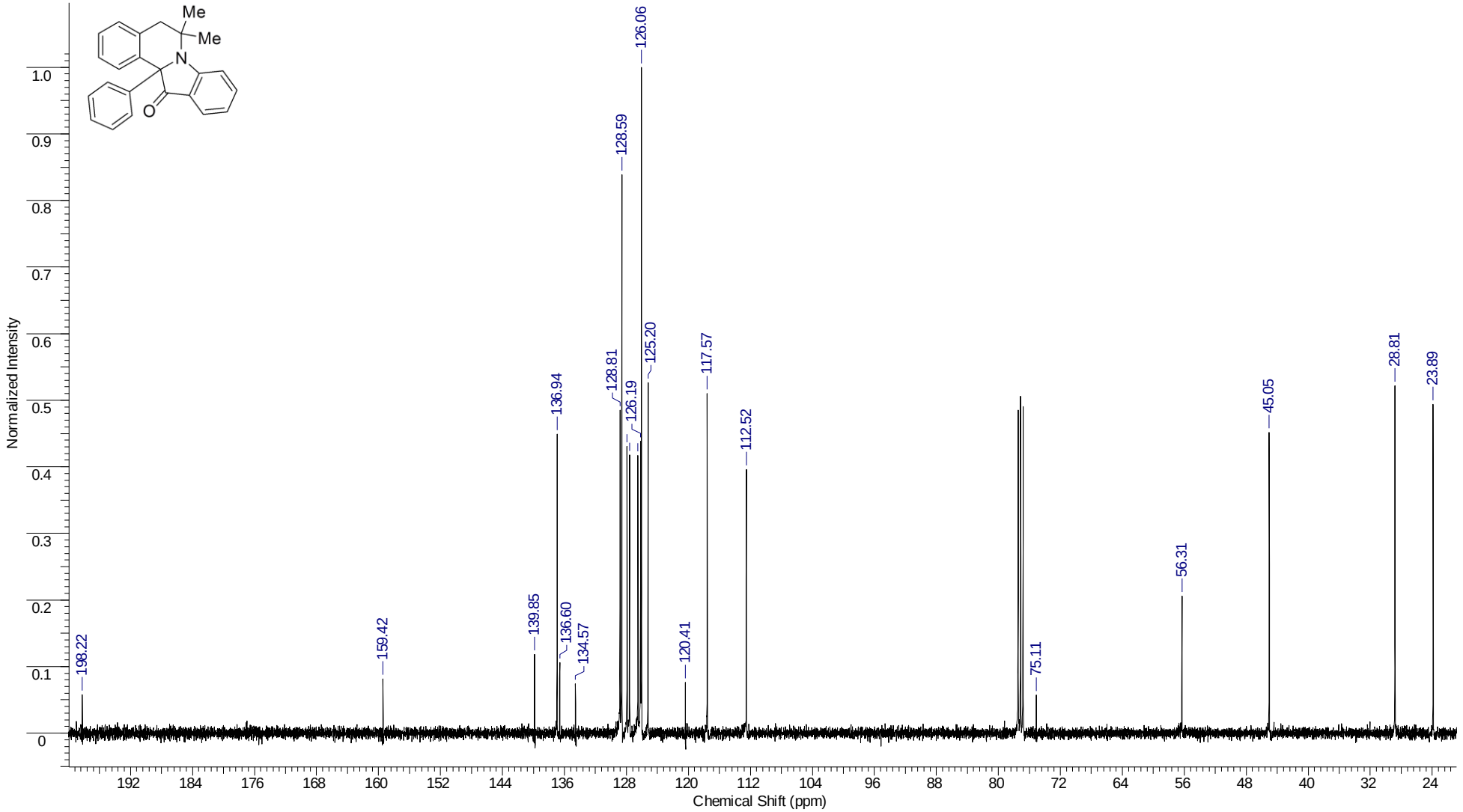
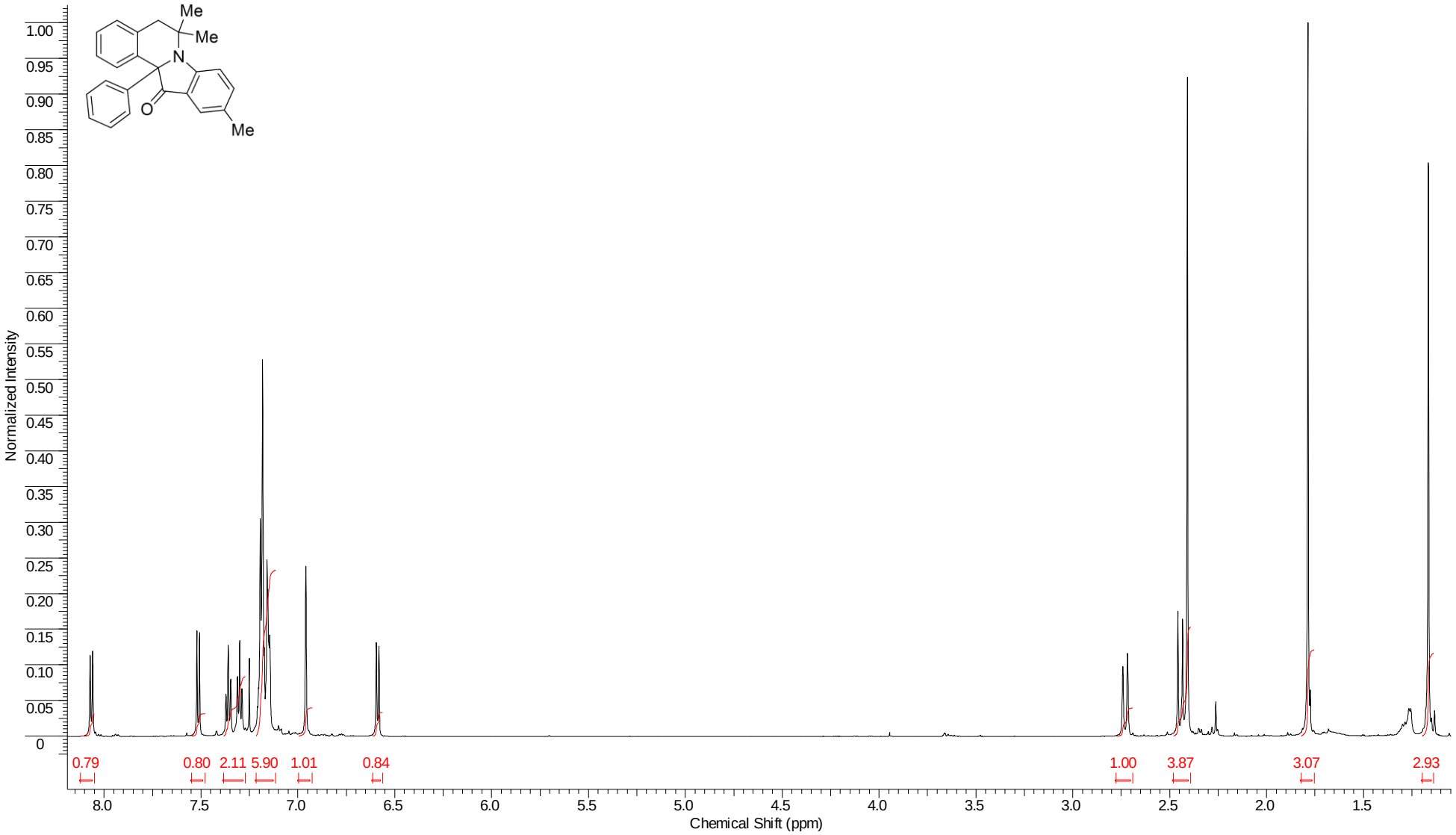
120
112
104
96
88
80
72
64
56
48
40
32
24
16
Chemical Shift (ppm)


Me
Me
N
O
Normalized Intensity
1.00
0.95
0.90
0.85
0.80
0.75
0.70
0.65
0.60
0.55
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
0.86
0.84
2.05
6.62
0.92
1.00
1.00
3.09
3.03
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
Chemical Shift (ppm)


Me
Me
N
O
Normalized Intensity
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
198.22
159.42
139.85
136.94
136.60
134.57
128.81
128.59
126.19
126.06
125.20
120.41
117.57
112.52
75.11
56.31
45.05
28.81
23.89
192
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
Chemical Shift (ppm)


Me
Me
N
O
Me
Normalized Intensity
1.00
0.95
0.90
0.85
0.80
0.75
0.70
0.65
0.60
0.55
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
0.79
0.80
2.11
5.90
1.01
0.84
1.00
3.87
3.07
2.93
8.0
7.5
7.0
6.5
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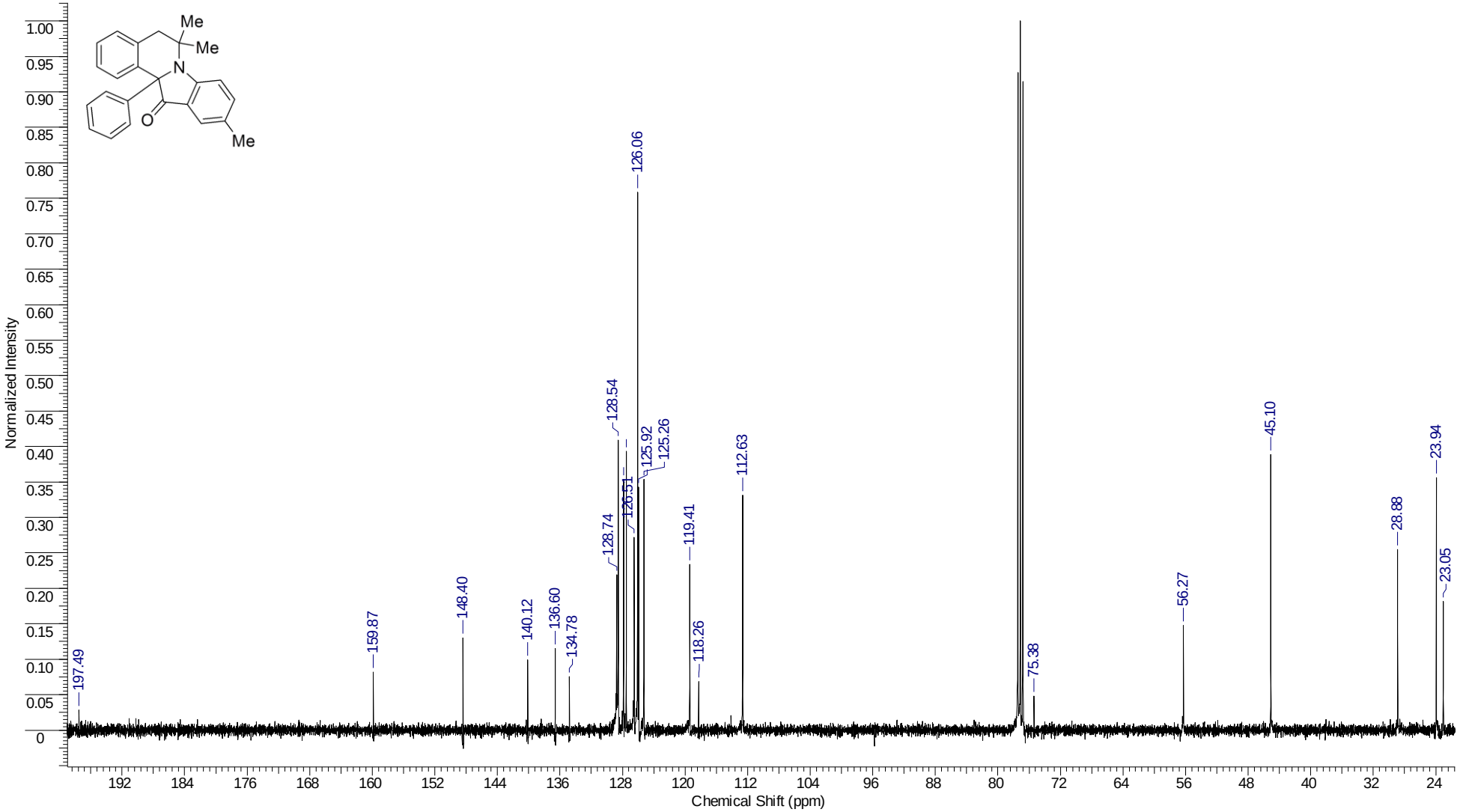
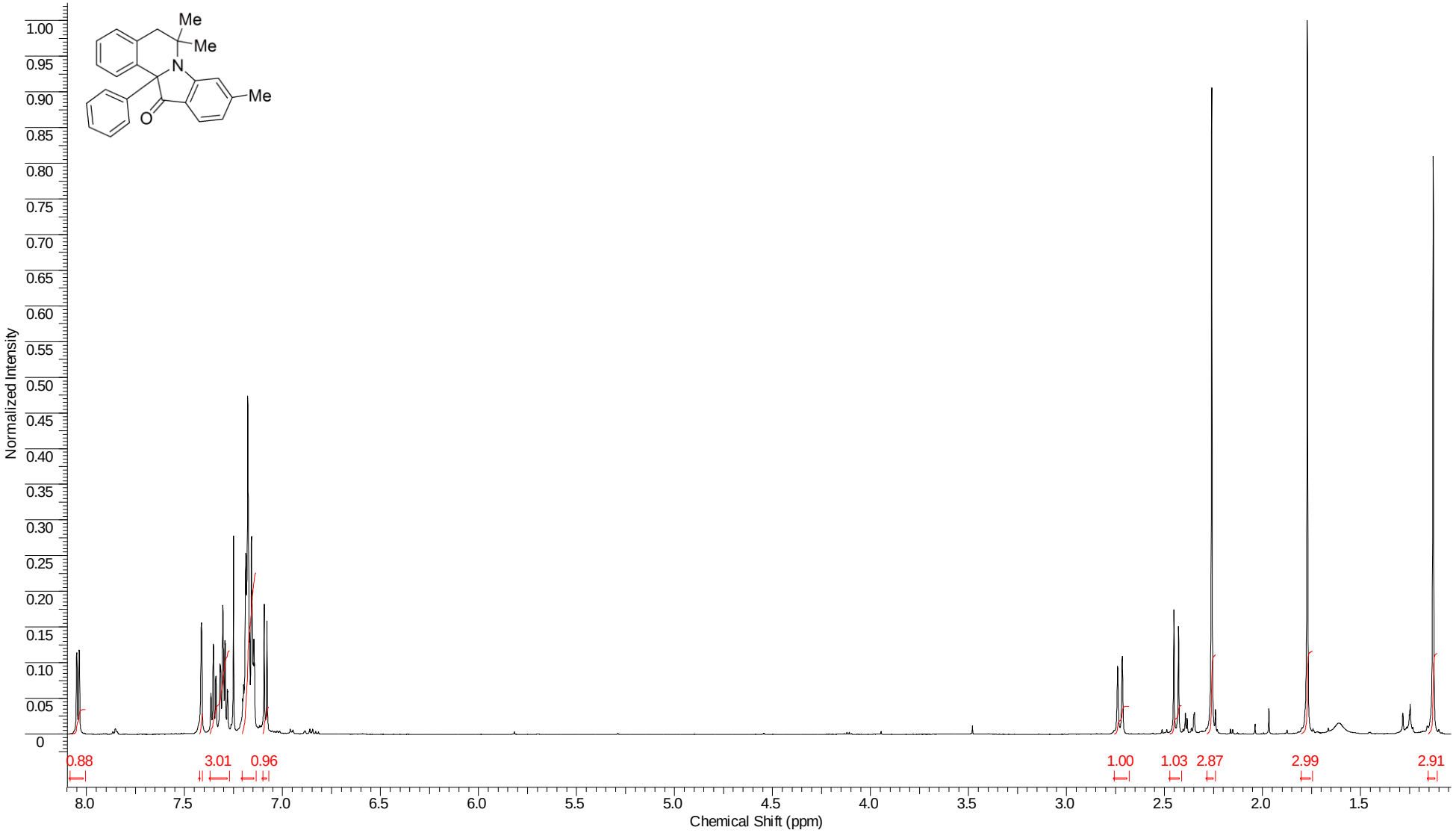
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
Chemical Shift (ppm)


Me
Me
N
O
Me
Normalized Intensity
1.00
0.95
0.90
0.85
0.80
0.75
0.70
0.65
0.60
0.55
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
197.49
159.87
148.40
140.12
136.60
134.78
128.74
128.54
126.51
126.06
125.92
125.26
119.41
118.26
112.63
75.38
56.27
45.10
28.88
23.94
23.05
192
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
Chemical Shift (ppm)


Me
Me
N
Me
O
Normalized Intensity
1.00
0.95
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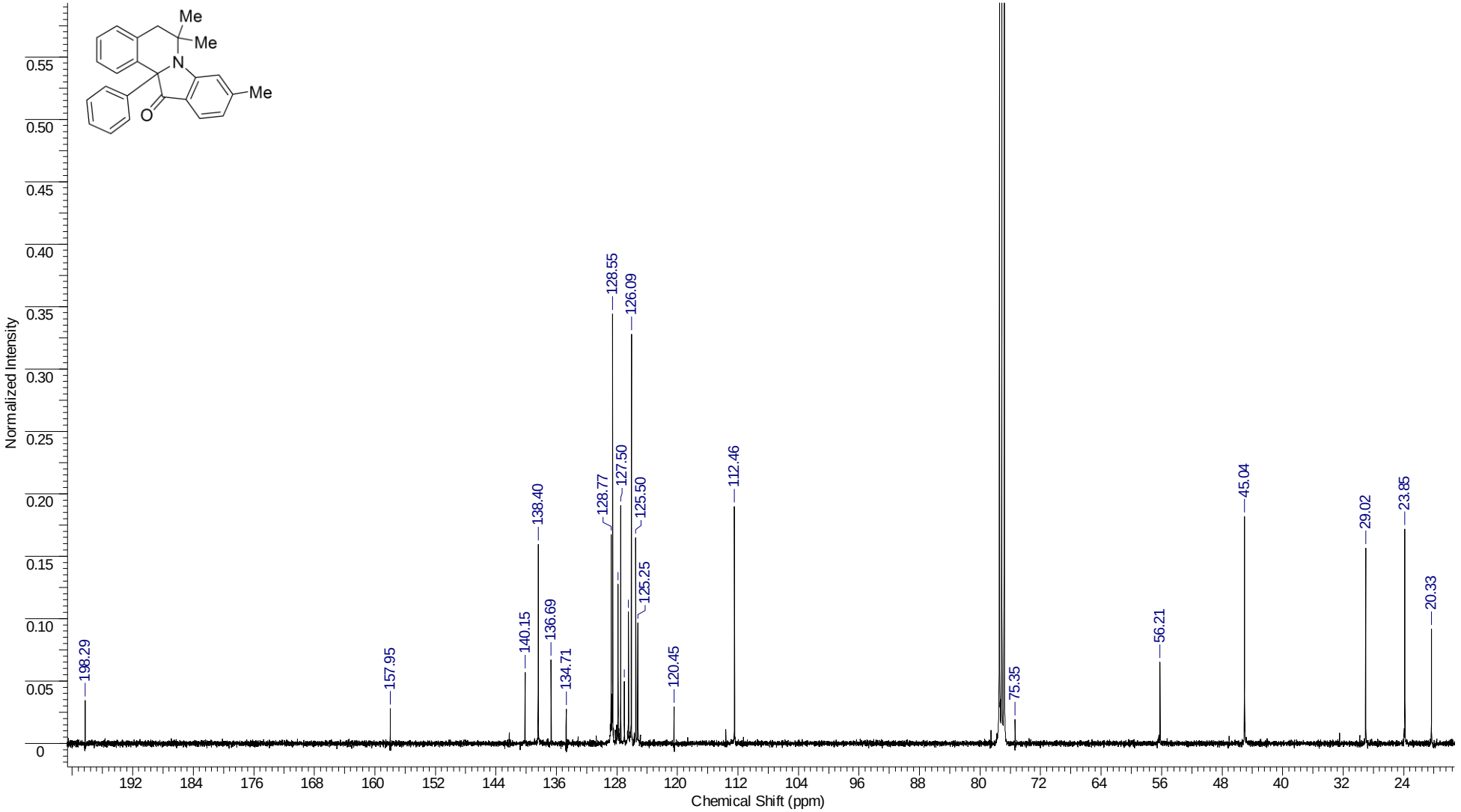
0.85
0.80
0.75
0.70
0.65
0.60
0.55
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
0.88
3.01
0.96
1.00
1.03
2.87
2.99
2.91
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
Chemical Shift (ppm)


Me
Me
N
Me
O
Normalized Intensity
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0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
198.29
157.95
140.15
138.40
136.69
134.71
128.77
128.55
127.50
126.09
125.50
125.25
120.45
112.46
75.35
56.21
45.04
29.02
23.85
20.33
192
184
176
168
160
152
144
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128
120
112
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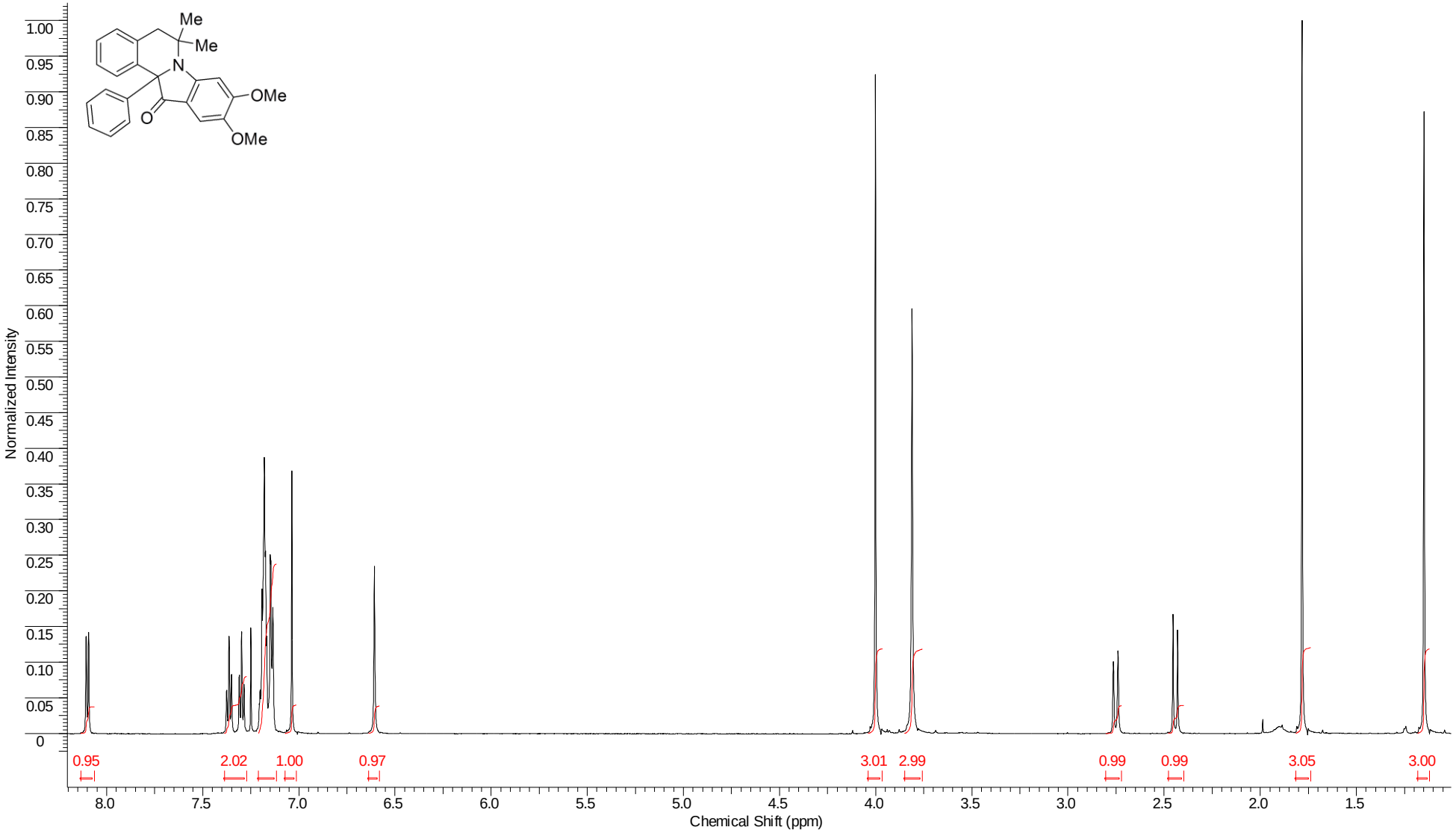
96
88
80
72
64
56
48
40
32
24
Chemical Shift (ppm)


Me
Me
N
O
OMe
OMe
Normalized Intensity
1.00
0.95
0.90
0.85
0.80
0.75
0.70
0.65
0.60
0.55
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
0.95
2.02
1.00
0.97
3.01
2.99
0.99
0.99
3.05
3.00
8.0
7.5
7.0
6.5
6.0
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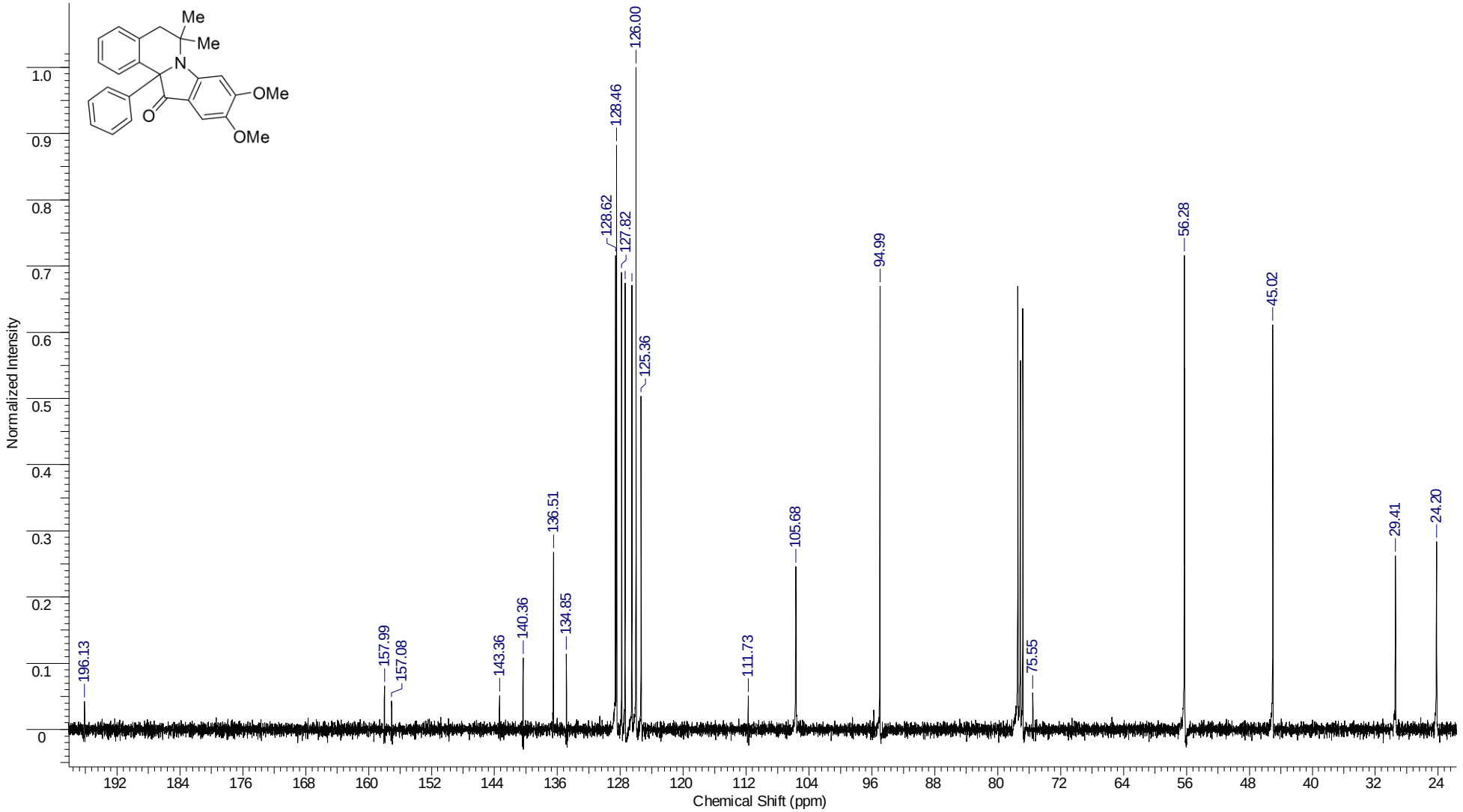
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
Chemical Shift (ppm)


Me
Me
N
O
OMe
OMe
Normalized Intensity
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0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
196.13
157.99
157.08
143.36
140.36
136.51
134.85
128.62
128.46
127.82
126.00
125.36
111.73
105.68
94.99
75.55
56.28
45.02
29.41
24.20
192
184
176
168
160
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144
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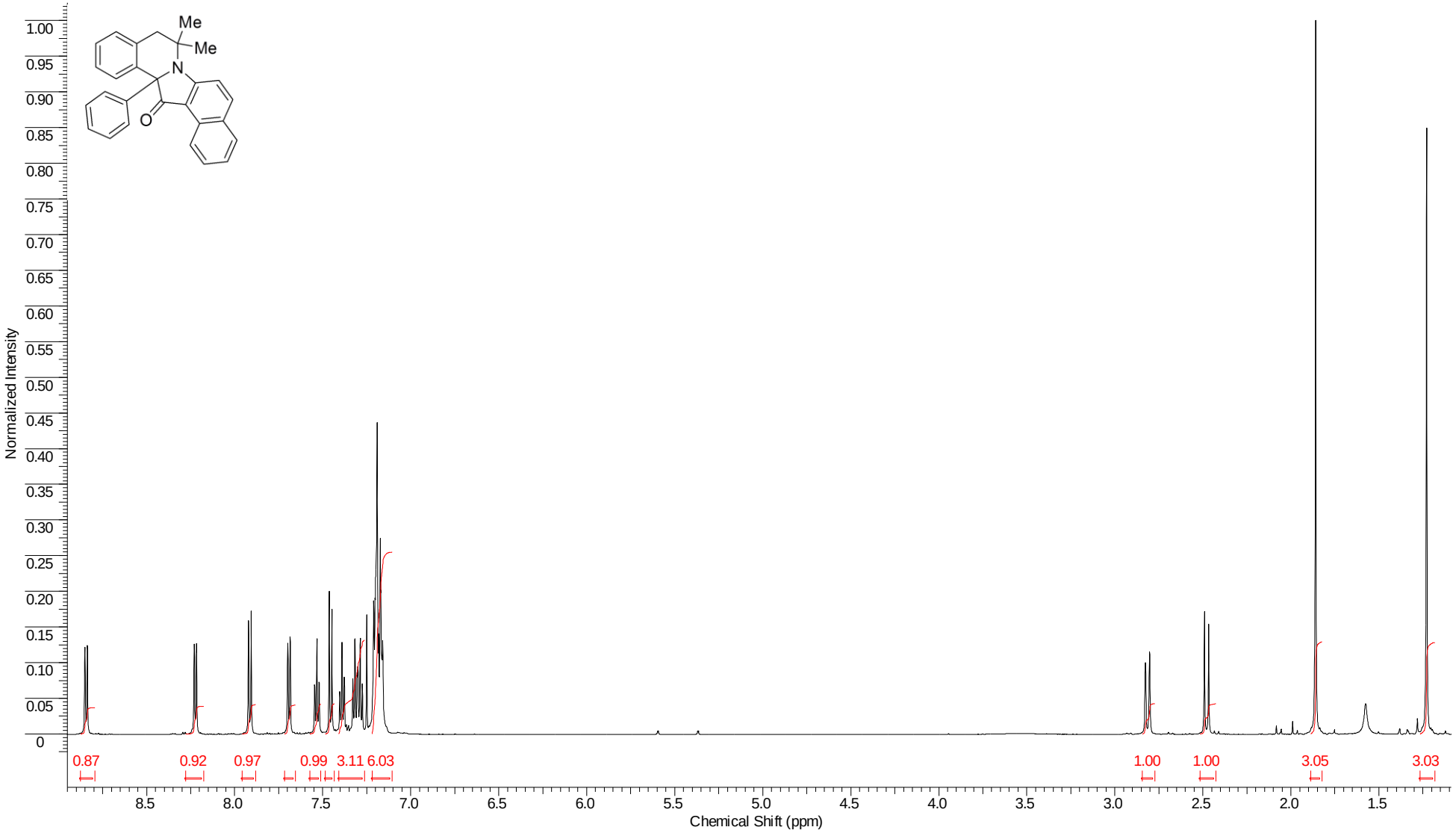
128
120
112
104
96
88
80
72
64
56
48
40
32
24
Chemical Shift (ppm)


Me
Me
N
O
Normalized Intensity
1.00
0.95
0.90
0.85
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0.75
0.70
0.65
0.60
0.55
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
0.87
0.92
0.97
0.99
3.11
6.03
1.00
1.00
3.05
3.03
8.5
8.0
7.5
7.0
6.5
6.0
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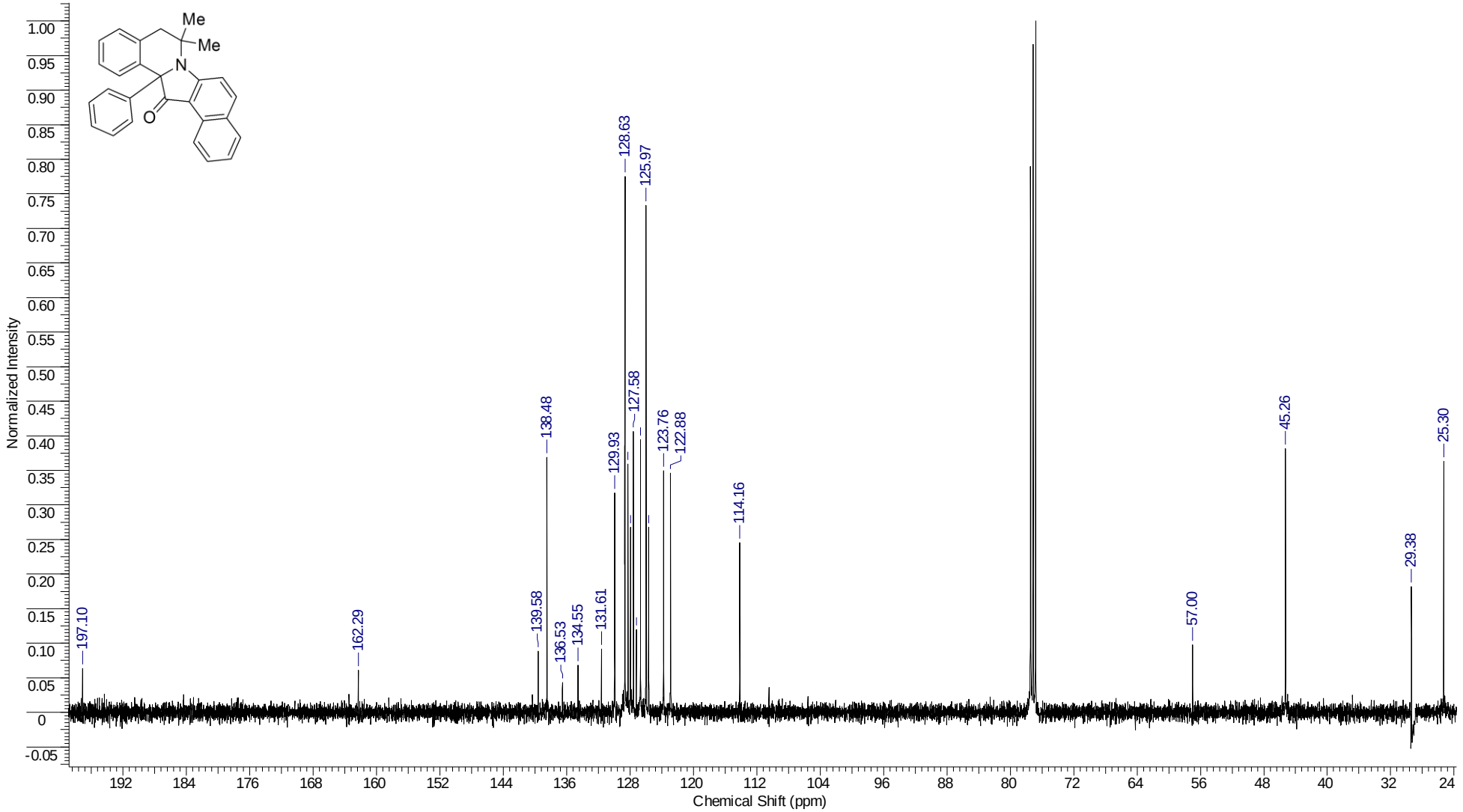
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
Chemical Shift (ppm)


Me
Me
N
O
Normalized Intensity
1.00
0.95
0.90
0.85
0.80
0.75
0.70
0.65
0.60
0.55
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
-0.05
197.10
162.29
139.58
138.48
136.53
134.55
131.61
129.93
128.63
127.58
125.97
123.76
122.88
114.16
57.00
45.26
29.38
25.30
192
184
176
168
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152
144
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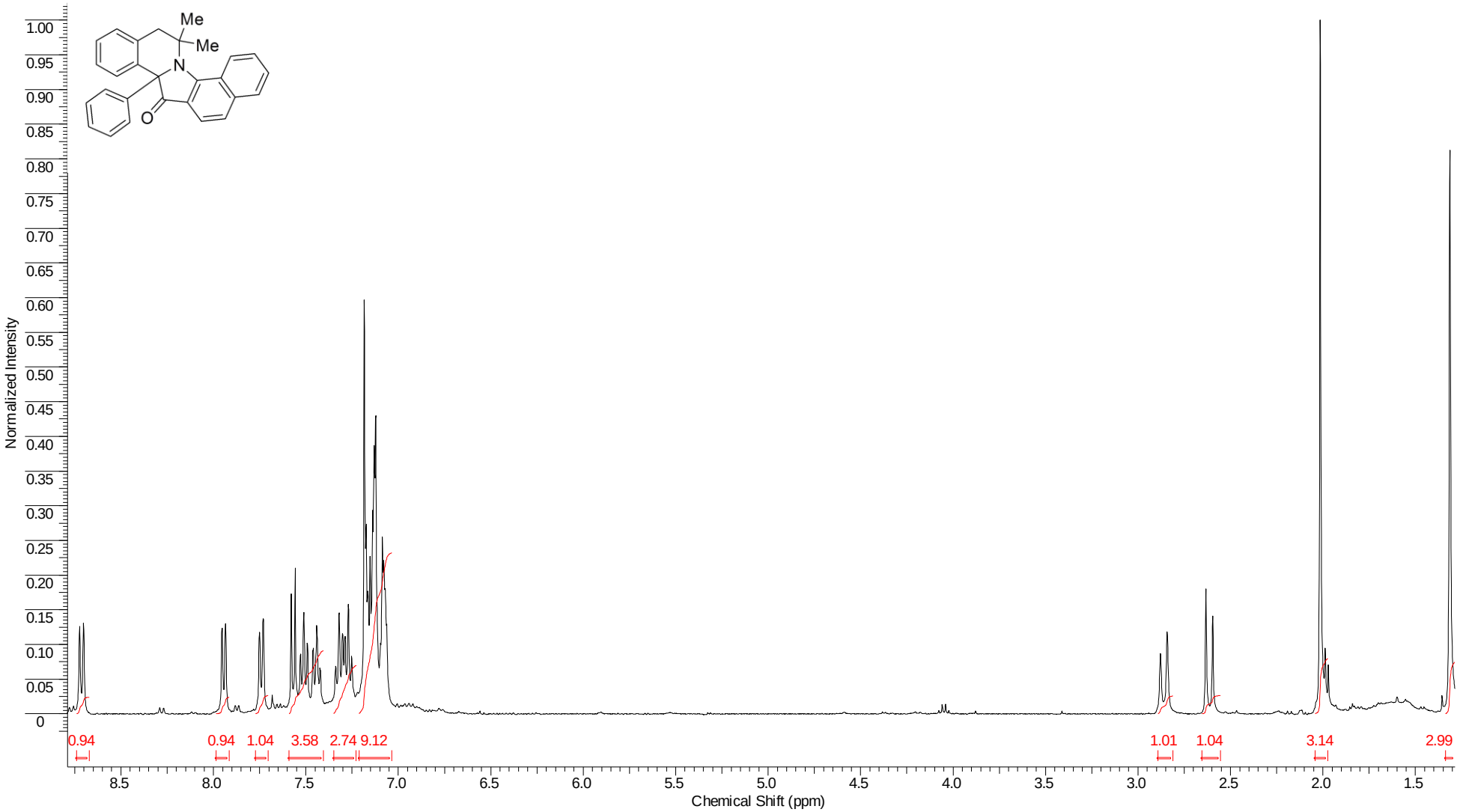
128
120
112
104
96
88
80
72
64
56
48
40
32
24
Chemical Shift (ppm)


Me
Me
N
O
Normalized Intensity
1.00
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0.90
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0.75
0.70
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0.60
0.55
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
0.94
0.94
1.04
3.58
2.74
9.12
1.01
1.04
3.14
2.99
8.5
8.0
7.5
7.0
6.5
6.0
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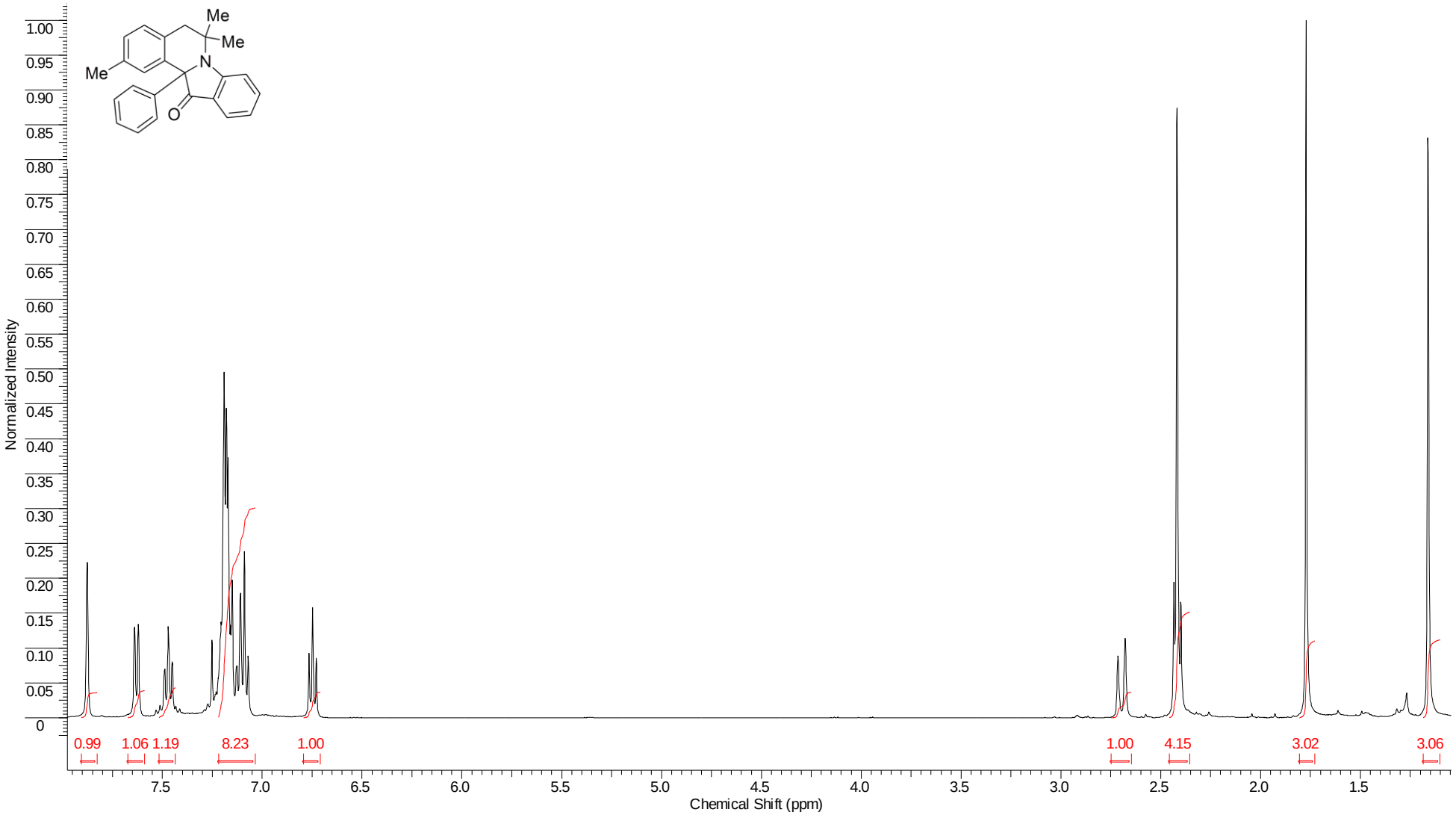
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
Chemical Shift (ppm)


Me
Me
Me
N
O
Normalized Intensity
1.00
0.95
0.90
0.85
0.80
0.75
0.70
0.65
0.60
0.55
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
0.99
1.06
1.19
8.23
1.00
1.00
4.15
3.02
3.06
7.5
7.0
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6.0
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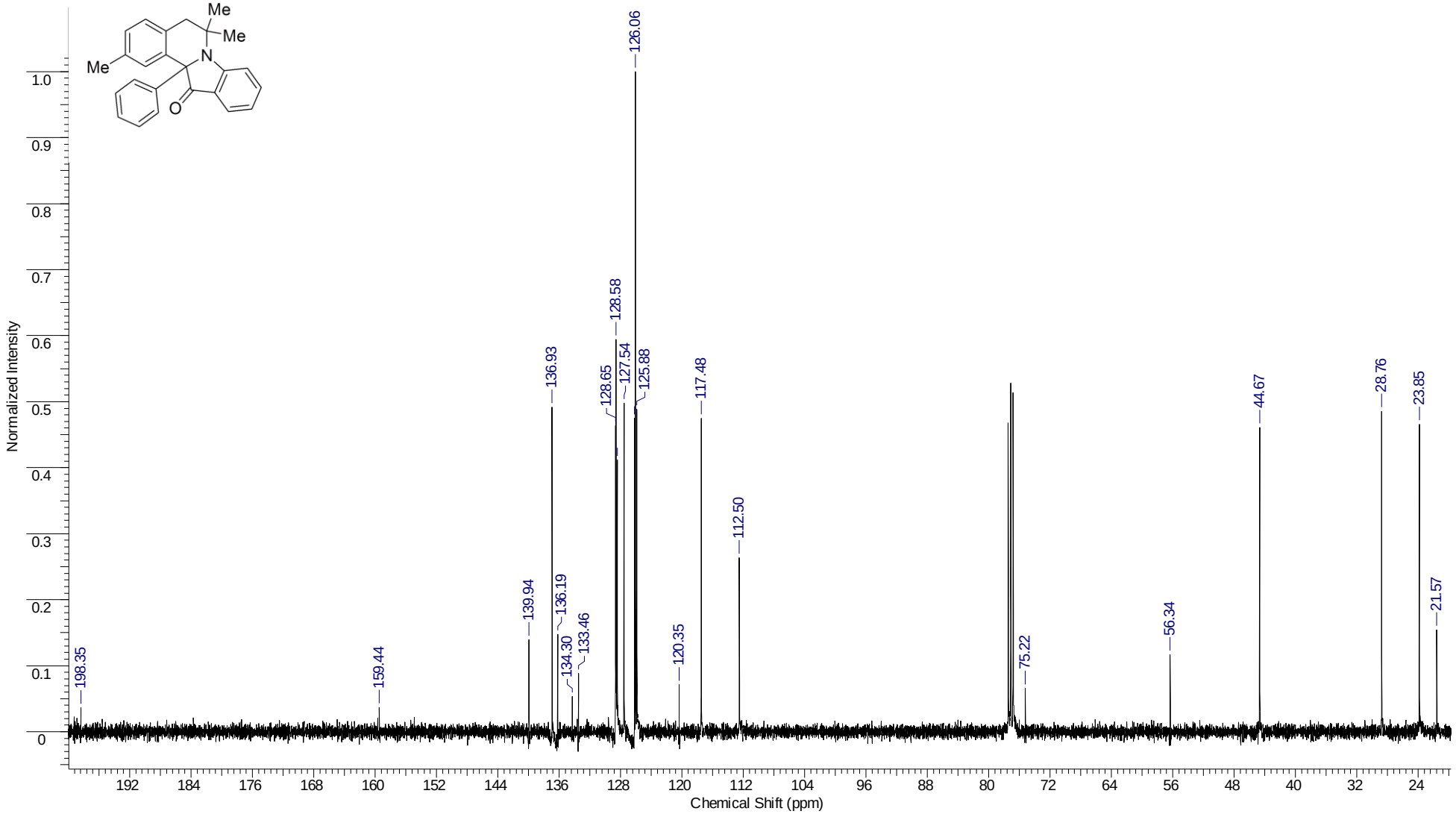
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
Chemical Shift (ppm)


Me
Me
Me
N
O
Normalized Intensity
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
198.35
159.44
139.94
136.93
136.19
134.30
133.46
128.65
128.58
127.54
126.06
125.88
120.35
117.48
112.50
75.22
56.34
44.67
28.76
23.85
21.57
192
184
176
168
160
152
144
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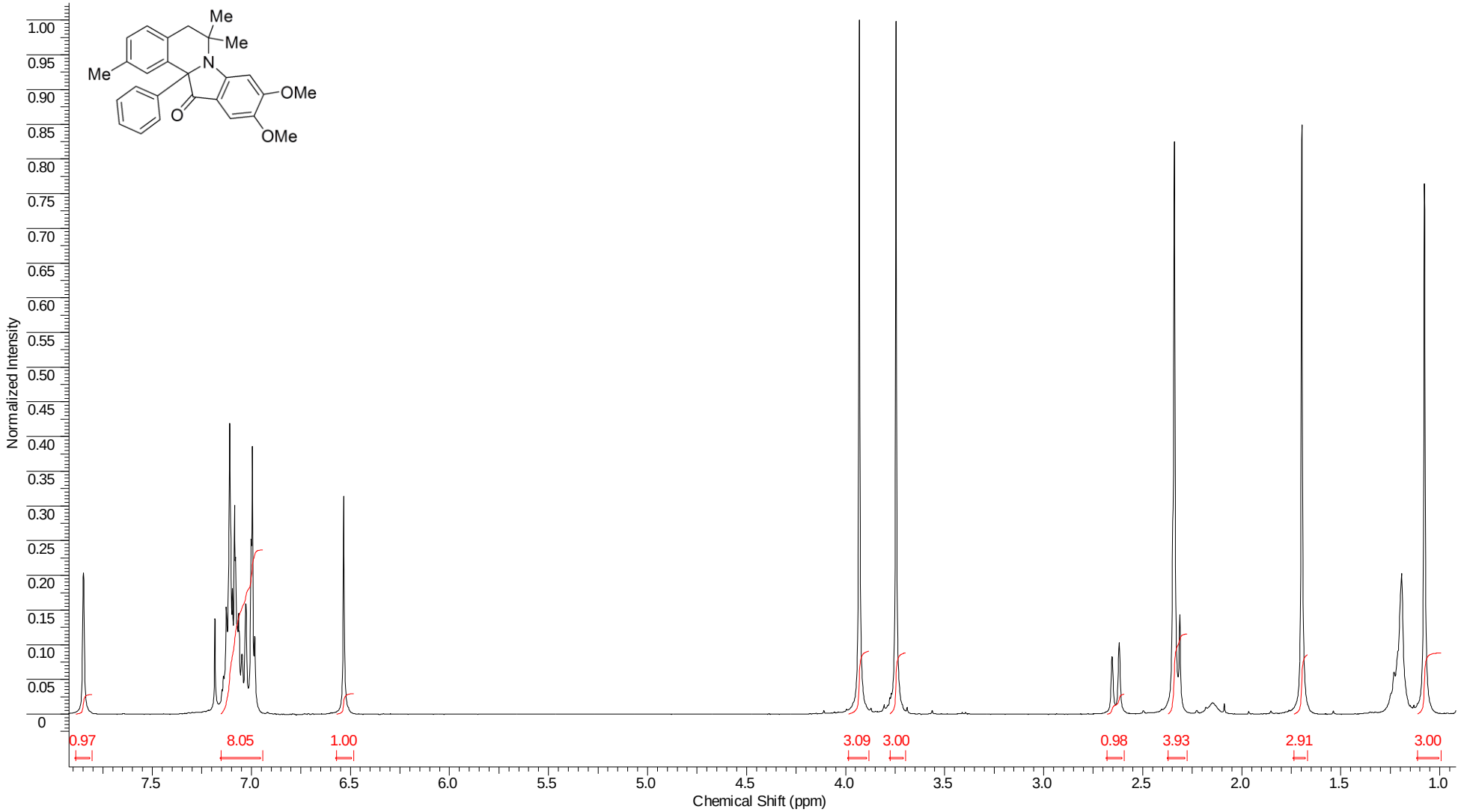
128
120
112
104
96
88
80
72
64
56
48
40
32
24
Chemical Shift (ppm)


Me
Me
Me
N
OMe
O
OMe
Normalized Intensity
1.00
0.95
0.90
0.85
0.80
0.75
0.70
0.65
0.60
0.55
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
0.97
8.05
1.00
3.09
3.00
0.98
3.93
2.91
3.00
7.5
7.0
6.5
6.0
5.5
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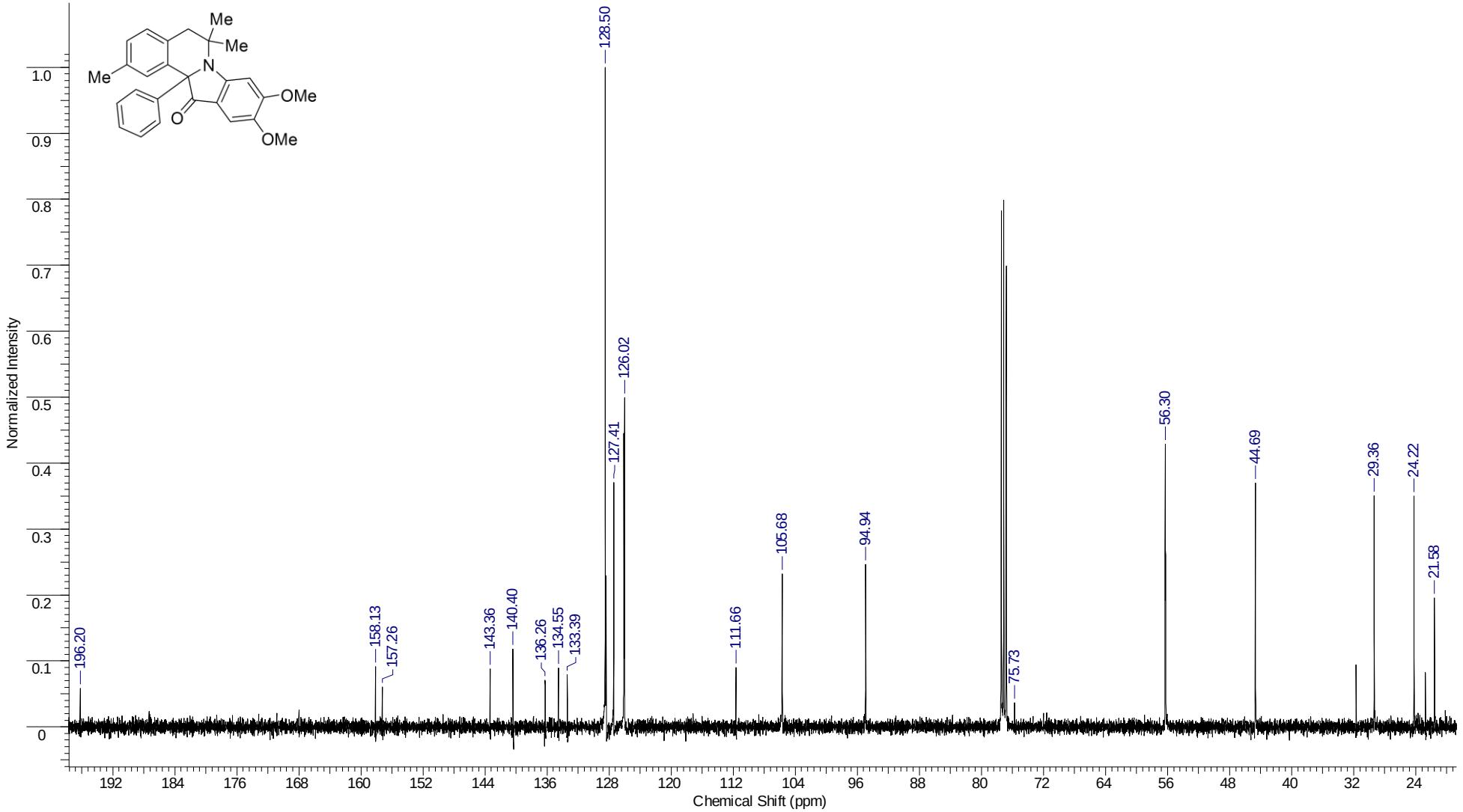
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
Chemical Shift (ppm)


Me
Me
Me
N
OMe
O
OMe
Normalized Intensity
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
196.20
158.13
157.26
143.36
140.40
136.26
134.55
133.39
128.50
127.41
126.02
111.66
105.68
94.94
75.73
56.30
44.69
29.36
24.22
21.58
192
184
176
168
160
152
144
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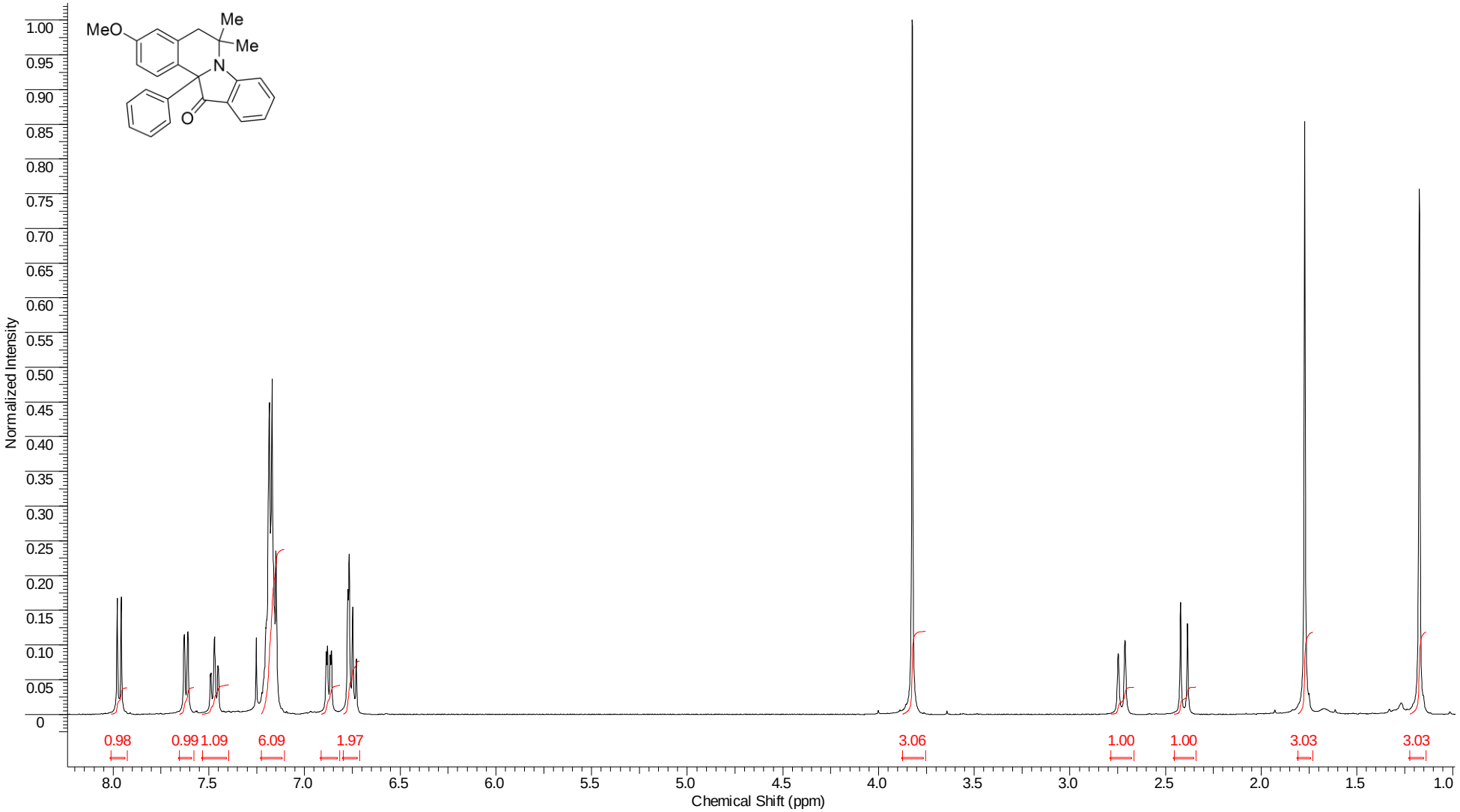
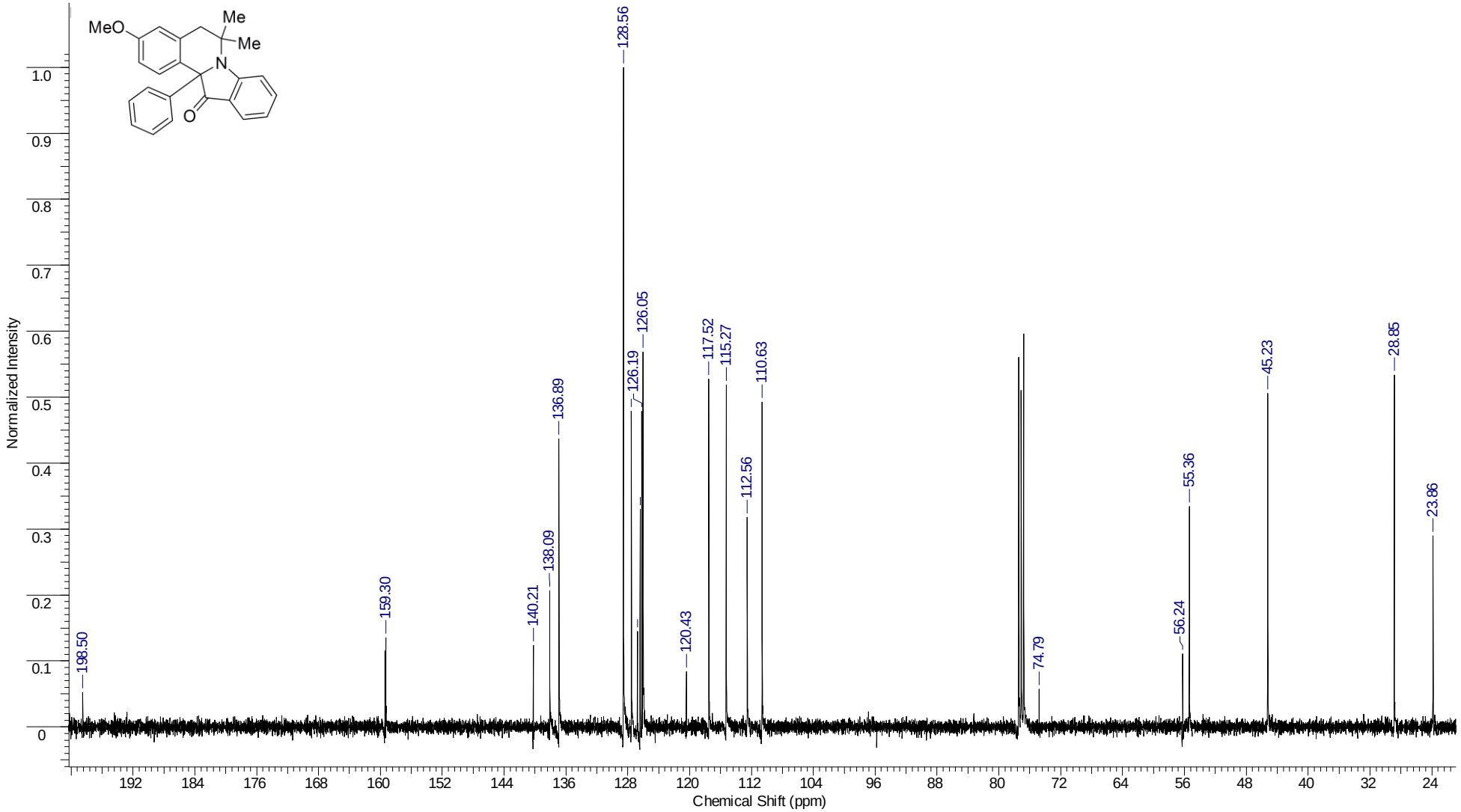
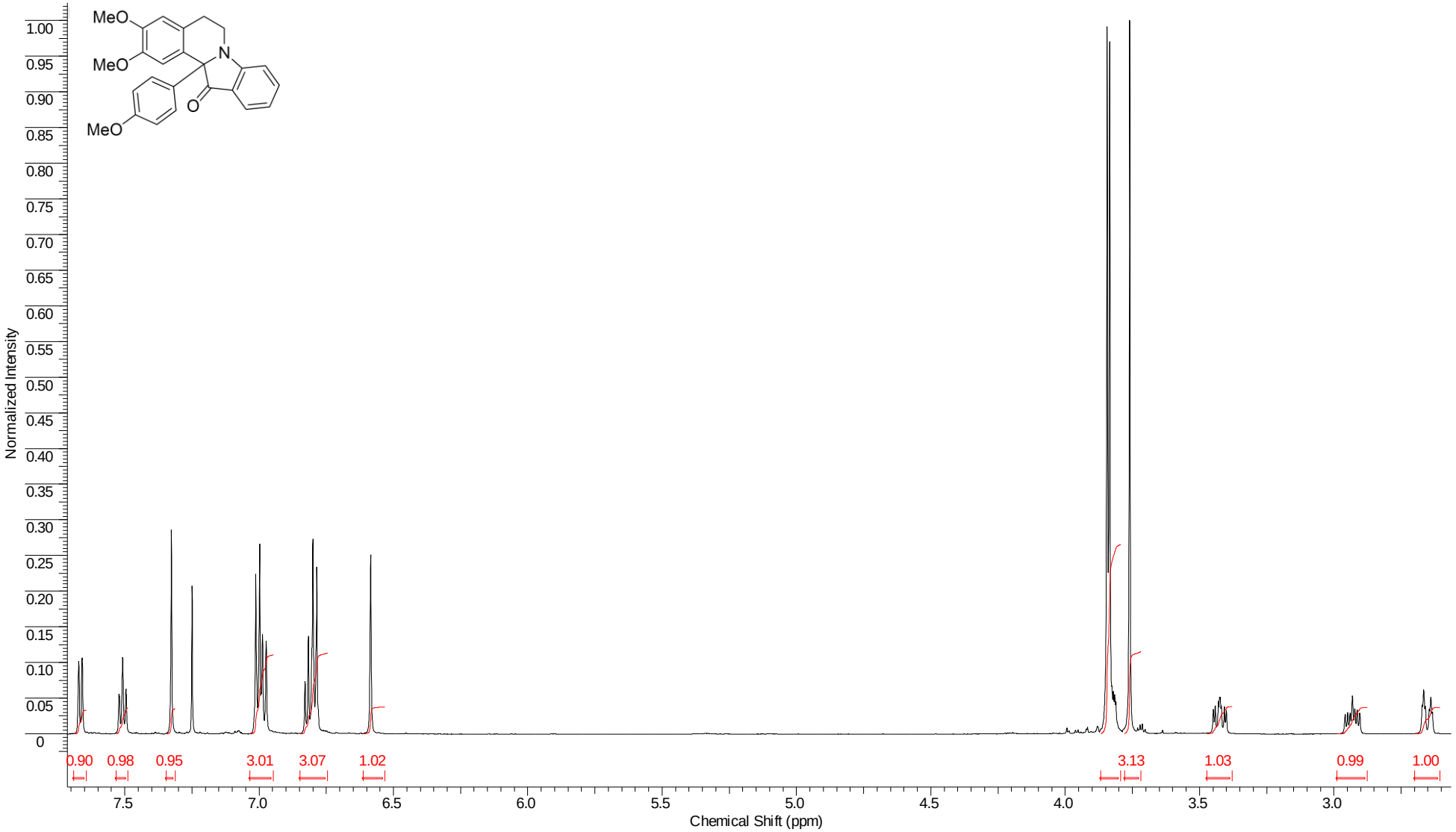
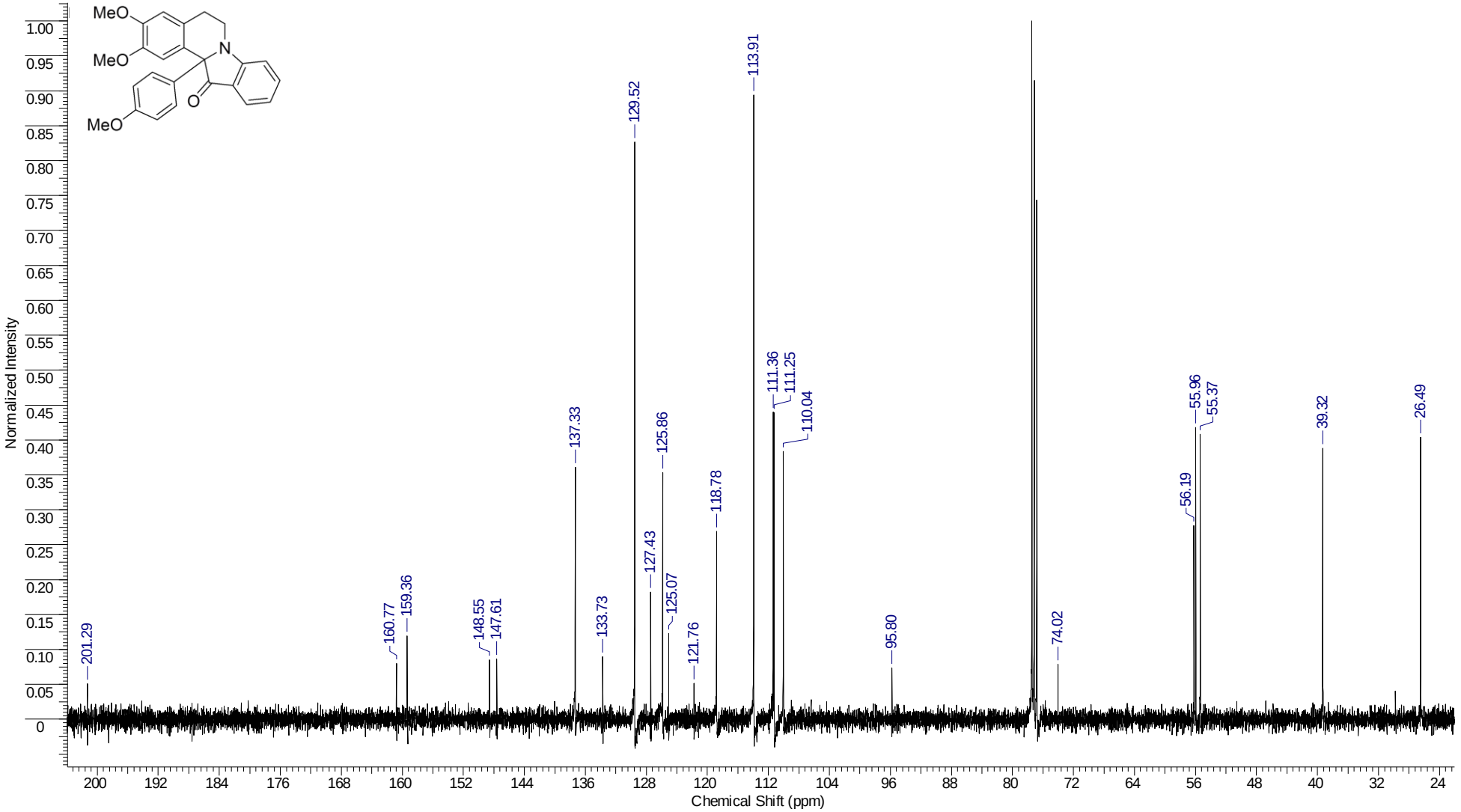
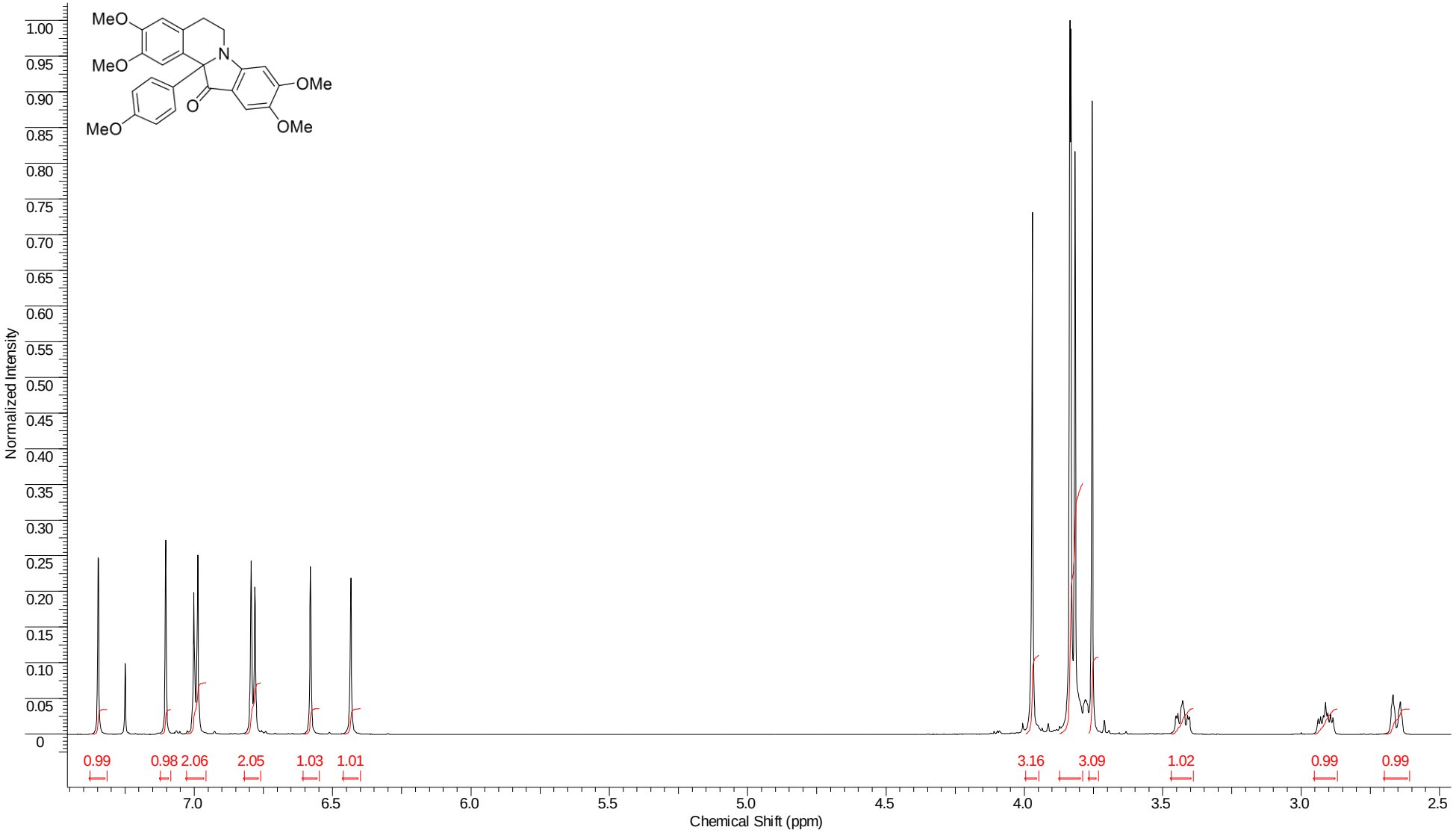
128
120
112
104
96
88
80
72
64
56
48
40
32
24
Chemical Shift (ppm)

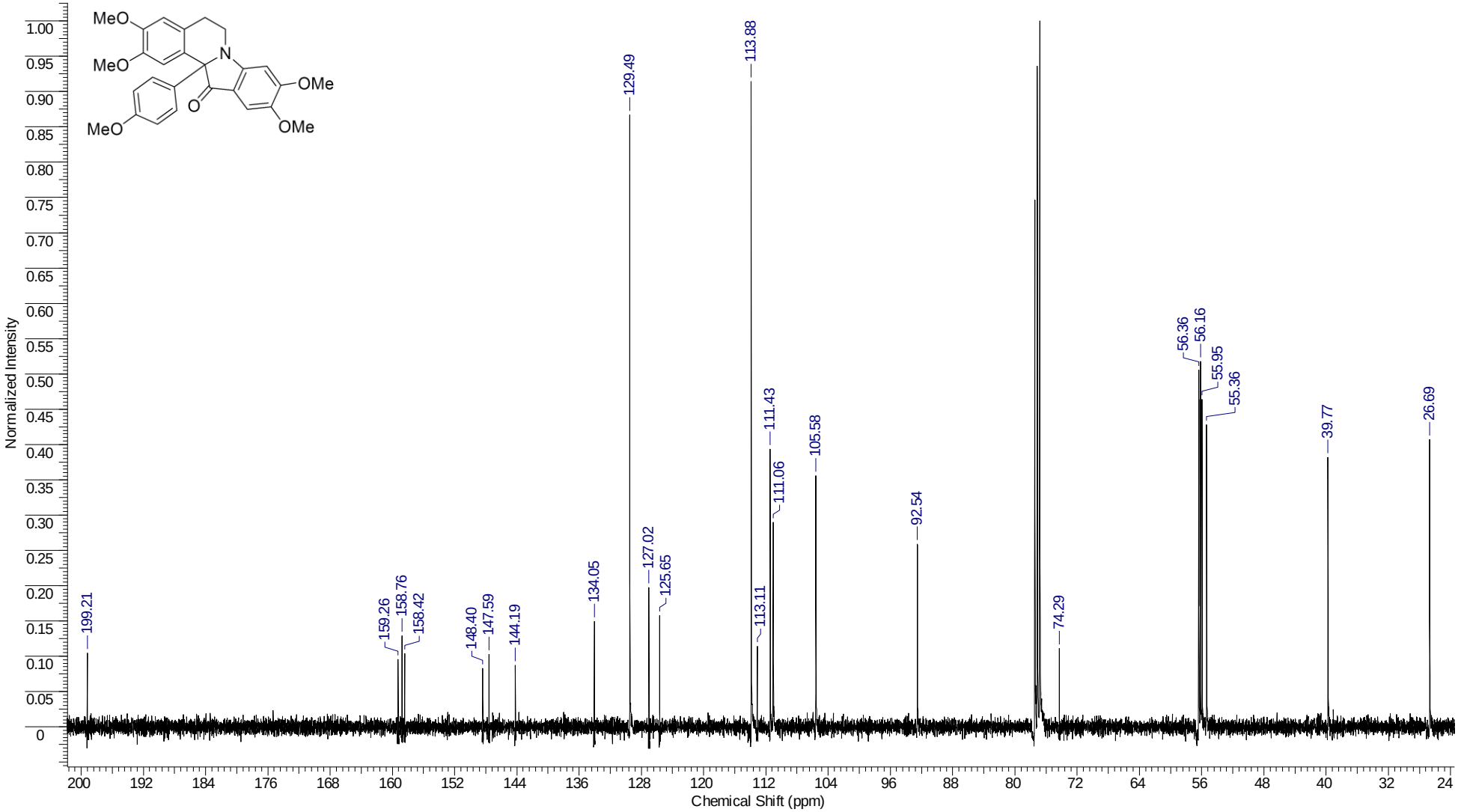

MeO
Me
Me
N
O
Normalized Intensity
1.00
0.95
0.90
0.85
0.80
0.75
0.70
0.65
0.60
0.55
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
0.98
0.99
1.09
6.09
1.97
3.06
1.00
1.00
3.03
3.03
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
Chemical Shift (ppm)


MeO
Me
Me
N
O
198.50
159.30
140.21
138.09
136.89
128.56
126.19
126.05
120.43
117.52
115.27
112.56
110.63
74.79
56.24
55.36
45.23
28.85
23.86
Normalized Intensity
Chemical Shift (ppm)


MeO
MeO
MeO
N
O
Normalized Intensity
1.00
0.95
0.90
0.85
0.80
0.75
0.70
0.65
0.60
0.55
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
0.90
0.98
0.95
3.01
3.07
1.02
3.13
1.03
0.99
1.00
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
Chemical Shift (ppm)


MeO
MeO
MeO
N
O
Normalized Intensity
1.00
0.95
0.90
0.85
0.80
0.75
0.70
0.65
0.60
0.55
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
201.29
160.77
159.36
148.55
147.61
137.33
133.73
129.52
127.43
125.86
125.07
121.76
118.78
113.91
111.36
111.25
110.04
95.80
74.02
56.19
55.96
55.37
39.32
26.49
200
192
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
Chemical Shift (ppm)


MeO
MeO
MeO
OMe
OMe
O
N
Normalized Intensity
1.00
0.95
0.90
0.85
0.80
0.75
0.70
0.65
0.60
0.55
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
0.99
0.98
2.06
2.05
1.03
1.01
3.16
3.09
1.02
0.99
0.99
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
Chemical Shift (ppm)


MeO
MeO
MeO
OMe
OMe
O
N
Normalized Intensity
Chemical Shift (ppm)
199.21
159.26
158.76
158.42
148.40
147.59
144.19
134.05
129.49
127.02
125.65
113.88
113.11
111.43
111.06
105.58
92.54
74.29
56.36
56.16
55.95
55.36
39.77
26.69