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Revisited synthesis of fused diazepines from 3-(3-aryl-3-oxopropenyl)chromen-4-ones and binucleophilic amino enones in a three-step domino process

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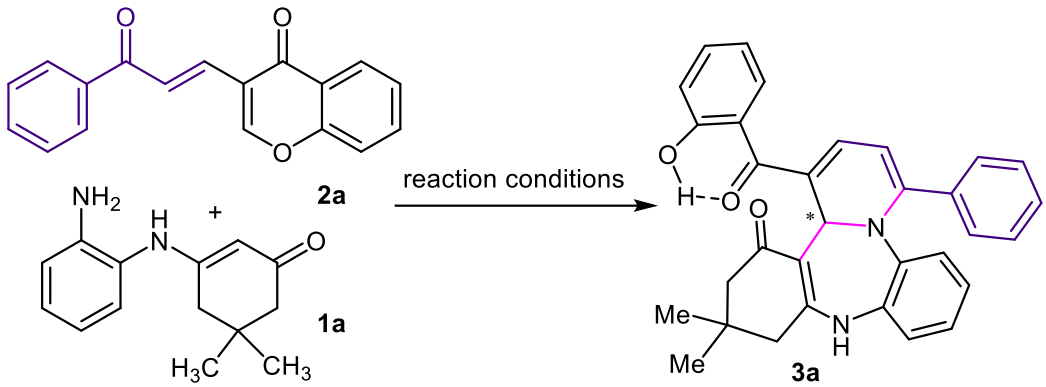
Experimental

The 3-[(2-aminoaryl)amino]-5,5-dimethylcyclohex-2-en-1-ones and 3-(3-aryl-3-oxopropenyl)chromen-4-ones were prepared according to the reported procedure. All other chemicals and solvents were purchased from Merck or Aldrich and were used without further purification. Elemental analyses for C, H, and N were performed using a Heraeus CHN–O–Rapid analyzer. Mass spectra were recorded on a FINNIGAN-MATT 8430 mass spectrometer operating at an ionization potential of 70 eV. ^{1}H NMR (300 MHz), and ^{13}C NMR (75 MHz) spectra were obtained using Bruker DRX-300 AVANCE and Bruker DRX-400 AVANCE spectrometers. IR spectra were recorded as KBr pellets on a NICOLET FT-IR 100 spectrometer; absorbencies are reported in cm^{-1}.

General procedure for preparation of compounds 3 (example for 3a)

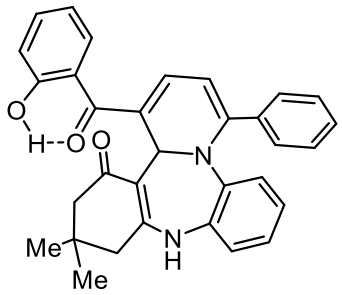
A mixture of dimedone (1.0 mmol) and *o*-phenylenediamine (1.0 mmol) was magnetically stirred in toluene (1.0 mL) at reflux (80 °C) for 3 h, and the resulted binucleophilic amino enone **1a** was added *in situ* to a solution of 3-vinylchromone **2a** (0.85 mmol) in CH_2Cl_2 (1.0 mL), and this was magnetically stirred under reflux for 12 h (monitoring by TLC). Compound **3a** was obtained as a red solid after purification by column chromatography (silica gel, *n*-hexane–EtOAc, 10:1).

Table S1 Different conditions for the synthesis of **3a**



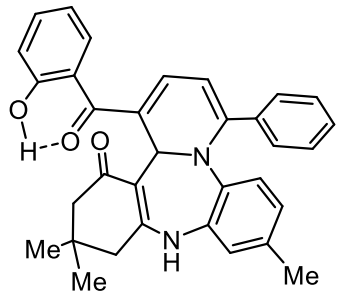
Entry	Solvent for **1a**	Solvent	*T*/°C	*t*/h	Yield of **3a**/(%)
1	toluene	EtOH	76	12	53
2	toluene	DMF	80	12	20
3	toluene	MeCN	80	12	10
4	**toluene**	**CH_2Cl_2**	**80**	**12**	**73**
5	toluene	THF	60	12	0
6	toluene	toluene	100	12	30
7	Solvent free	CH_2Cl_2	40	12	10
8	Solvent free	EtOH	78	12	40
9	EtOH	EtOH	78	12	55
10	EtOH	CH_2Cl_2	78	12	60

1-(2-Hydroxybenzoyl)-12,12-dimethyl-4-phenyl-11,12,13,14b-tetrahydrodibenzo[*b*,*f*]pyrido[1,2-*d*][1,4]diazepin-14(10*H*)-one (3a).



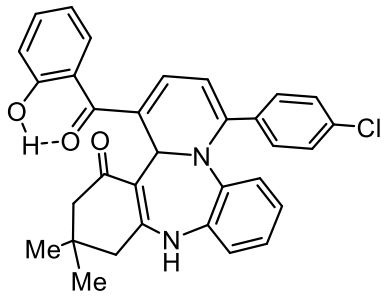
Red powder, mp = 257-259 °C, 0.356 g, yield: 73%. IR (KBr) (ν_{max}, cm^{-1}): 3296 (OH), 3211 (NH), 1608 and 1526 (C=O), 1497 and 1479 (Ar). Anal. Calcd. for $C_{32}H_{28}N_2O_3$ (488.21): C, 78.67; H, 5.78; N, 5.73%. Found: C, 78.64; H, 5.74; N, 5.69%. MS (EI, 70 eV): *m/z* (%) = 488 (74), 470 (24), 367 (100), 282 (13), 220 (87), 116 (37), 76 (26). ^{1}H NMR (300.13 MHz, DMSO): δ_H 1.03 (3H, s, CH_3), 1.05 (3H, s, CH_3), 2.02 (1H, d, $^2J_{HH}$ = 16.4 Hz, CH_2), 2.23 (1H, d, $^2J_{HH}$ = 16.3 Hz, CH_2), 2.57 (1H, d, $^2J_{HH}$ = 16.3 Hz, CH_2), 2.69 (1H, d, $^2J_{HH}$ = 16.2 Hz, CH_2), 5.53 (1H, dd, $^3J_{HH}$ = 6.6 Hz, $^4J_{HH}$ = 1.9 Hz, CH^2), 5.78 (1H, s, CH^{14b}), 6.51 (1H, d, $^3J_{HH}$ = 8.0 Hz, CH^9), 6.66 (1H, d, $^3J_{HH}$ = 6.1 Hz, CH^3), 6.66 (1H, d, $^3J_{HH}$ = 8.0 Hz, CH of Ar), 6.88 (1H, d, $^3J_{HH}$ = 8.0 Hz, CH^8), 6.92 (1H, t, $^3J_{HH}$ = 7.5 Hz, CH^7), 7.04 (1H, t, $^3J_{HH}$ = 7.7 Hz, CH of Ar), 7.14-7.23 (5H, m, 5 CH of Ar), 7.30 (1H, d, $^3J_{HH}$ = 7.9 Hz, CH^6), 7.34 (1H, t, $^3J_{HH}$ = 7.8 Hz, CH of Ar), 7.55 (1H, d, $^3J_{HH}$ = 7.7 Hz, CH of Ar), 9.55 (1H, s, NH), 10.00 (1H, s, OH). ^{13}C NMR (75.00 MHz, DMSO): δ_C 31.45 (CH_3), 31.45 (CH_3), 35.76 (C^{12}), 44.56 (CH_2), 50.76 (CH_2), 56.90 (CH^{14b}), 102.60 (C^{14a}), 112.69 (CH^3), 116.47 (CH of Ar), 118.59 (CH of Ar), 120.30 (CH^6), 122.23 (CH^9), 125.52 (CH^7), 125.81 (C_{ipso}-C=O), 125.95 (CH_{para} of Ph), 127.56 (2 CH_{ortho} of Ph), 128.37 (2 CH_{meta} of Ph), 128.73 (CH^8), 128.75 (CH of Ar), 130.05 (CH of Ar), 130.16 (C_{ipso} of Ph), 131.48 (CH^2), 136.51 (C^{9a}), 136.82 (C^{5a}), 138.54 (C^1), 147.28 (C^{10a}), 155.39 (C^4), 159.09 (C-OH), 193.88 (C=O), 194.07 (C=O).

1-(2-Hydroxybenzoyl)-8,12,12-trimethyl-4-phenyl-11,12,13,14*b*-tetrahydrodibenzo[*b*,*f*]pyrido[1,2-*d*][1,4]diazepin-14(10*H*)-one (3b).



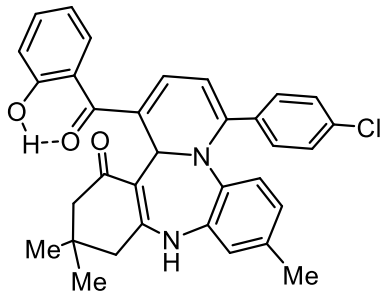
Red powder, mp = 273-275 °C, 0.342 g, yield: 68%. IR (KBr) (ν_{max}, cm^{-1}): 3475 (OH), 3414 (NH), 1616 and 1527 (C=O), 1506 and 1479 (Ar). Anal. Calcd. for $C_{33}H_{30}N_2O_3$ (502.61): C, 78.86; H, 6.02; N, 5.57%. Found: C, 78.82; H, 5.96; N, 5.52%. MS (EI, 70 eV): *m/z* (%) = 503 (56), 484 (84), 465 (51), 399 (27), 381 (100), 331 (29), 209 (22), 121 (36), 77 (29). ^{1}H NMR (300.13 MHz, DMSO): δ_H 0.99 (3H, s, CH_3), 1.02 (3H, s, CH_3), 1.95 (3H, s, CH_3), 2.00 (1H, d, $^2J_{HH}$ = 16.5 Hz, CH_2), 2.16 (1H, d, $^2J_{HH}$ = 16.4 Hz, CH_2), 2.53 (1H, d, $^2J_{HH}$ = 15.2 Hz, CH_2), 2.67 (1H, d, $^2J_{HH}$ = 15.3 Hz, CH_2), 5.49 (1H, dd, $^3J_{HH}$ = 6.5 Hz, $^4J_{HH}$ = 1.8 Hz, CH^2), 5.77 (1H, s, CH^{14b}), 6.33 (1H, s, CH^9), 6.65 (1H, d, $^3J_{HH}$ = 6.3 Hz, CH^3), 6.84 (1H, d, $^3J_{HH}$ = 7.5 Hz, CH of Ar), 6.90 (1H, d, $^3J_{HH}$ = 8.5 Hz, CH^6), 6.90 (1H, t, $^3J_{HH}$ = 7.7 Hz, CH of Ar), 7.09-7.19 (5H, m, 5 CH of Ar), 7.19 (1H, d, $^3J_{HH}$ = 8.3 Hz, CH^7), 7.32 (1H, t, $^3J_{HH}$ = 7.7 Hz, CH of Ar), 7.59 (1H, d, $^3J_{HH}$ = 7.3 Hz, CH of Ar), 9.55 (1H, s, NH), 10.07 (1H, s, OH). ^{13}C NMR (75.00 MHz, DMSO): δ_C 19.86 (CH_3), 27.01 (CH_3), 27.91 (CH_3), 31.46 (C^{12}), 44.63 (CH_2), 50.76 (CH_2), 56.95 (CH^{14b}), 102.53 (C^{14a}), 112.12 (CH^3), 116.51 (CH of Ar), 118.57 (CH of Ar), 120.22 (C_{ipso}-C=O), 122.21 (CH^6), 125.63 (CH^9), 125.57 (CH^7), 126.21 (C_{ipso}-Me), 126.77 (CH_{para} of Ph), 127.55 (2 CH_{ortho} of Ph), 128.40 (2 CH_{meta} of Ph), 128.95 (CH of Ar), 130.09 (CH of Ar), 131.30 (CH^2), 134.60 (C_{ipso} of Ph), 136.19 (C^{9a}), 136.91 (C^{5a}), 138.30 (C^1), 147.31 (C^{10a}), 155.35 (C^4), 159.17 (C-OH), 193.71 (C=O), 194.07 (C=O).

4-(4-Chlorophenyl)-1-(2-hydroxybenzoyl)-12,12-dimethyl-11,12,13,14b-tetrahydrodibenzo[*b*,*f*]pyrido[1,2-*d*][1,4]diazepin-14(10*H*)-one (3c).



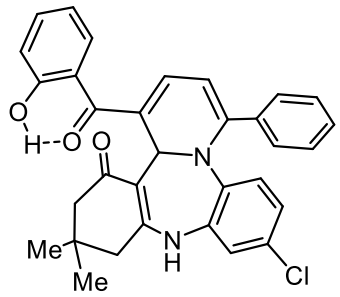
Red powder, mp = 261-263 °C, 0.349 g, yield: 67%. IR (KBr) (ν_{max}, cm^{-1}): 3401 (OH), 3296 (NH), 1615 and 1595 (C=O), 1498 and 1480 (Ar). Anal. Calcd. for $C_{32}H_{27}ClN_2O_3$ (523.03): C, 73.49; H, 5.20; N, 5.36%. Found: C, 73.45; H, 4.16; N, 5.31%. MS (EI, 70 eV): *m/z* (%) = 523 (60), 504 (100), 486 (48), 419 (43), 401 (55), 228 (28), 171 (43), 121 (38), 65 (33). ^{1}H NMR (300.13 MHz, DMSO): δ_H 0.99 (3H, s, CH_3), 1.02 (3H, s, CH_3), 2.00 (1H, d, $^2J_{HH}$ = 16.2 Hz, CH_2), 2.22 (1H, d, $^2J_{HH}$ = 16.3 Hz, CH_2), 2.54 (1H, d, $^2J_{HH}$ = 16.0 Hz, CH_2), 2.68 (1H, d, $^2J_{HH}$ = 16.2 Hz, CH_2), 5.54 (1H, d, $^3J_{HH}$ = 6.2 Hz, CH^2), 5.76 (1H, s, CH^{14b}), 6.50 (1H, d, $^3J_{HH}$ = 7.9 Hz, CH^9), 6.64 (1H, d, $^3J_{HH}$ = 6.2 Hz, CH^3), 6.66 (1H, d, $^3J_{HH}$ = 8.0 Hz, CH of Ar), 6.87 (1H, d, $^3J_{HH}$ = 8.0 Hz, CH^8), 6.88 (1H, t, $^3J_{HH}$ = 8.0 Hz, CH^7), 7.04 (1H, t, $^3J_{HH}$ = 7.7 Hz, CH of Ar), 7.13 (2H, d, $^3J_{HH}$ = 8.3 Hz, 2 CH of Ar), 7.29 (2H, d, $^3J_{HH}$ = 8.6 Hz, 2 CH of Ar), 7.31 (1H, d, $^3J_{HH}$ = 8.3 Hz, CH^6), 7.32 (1H, td, $^3J_{HH}$ = 7.6 Hz, $^4J_{HH}$ = 1.8 Hz, CH of Ar), 7.55 (1H, dd, $^3J_{HH}$ = 7.6 Hz, $^3J_{HH}$ = 1.8 Hz, CH of Ar), 9.57 (1H, s, NH), 10.01 (1H, s, OH). ^{13}C NMR (75.00 MHz, DMSO): δ_C 27.17 (CH_3), 27.73 (CH_3), 31.50 (C^{12}), 44.55 (CH_2), 50.73 (CH_2), 56.92 (CH^{14b}), 102.99 (C^{14a}), 112.74 (CH^3), 116.49 (CH of Ar), 118.69 (CH of Ar), 120.39 (CH^6), 121.95 (C_{ipso}-C=O), 122.85 (CH^9), 125.50 (CH^7), 126.25 (2 CH of Ar), 128.54 (2 CH of Ar), 129.27 (CH^8), 128.85 (CH of Ar), 130.15 (CH of Ar), 131.53 (C_{ipso} of Ph), 133.30 (CH^2), 135.41 (C^{9a}), 136.54 (C^{5a}), 138.52 (C^1), 145.76 (C^{10a}), 155.40 (C^4), 159.07 (C-OH), 193.89 (C=O), 194.17 (C=O).

4-(4-Chlorophenyl)-1-(2-hydroxybenzoyl)-8,12,12-trimethyl-11,12,13,14b-tetrahydrodibenzo[*b*,*f*]pyrido[1,2-*d*][1,4]diazepin-14(10*H*)-one (3d).



Red powder, mp = 273-275 °C, 0.327 g, yield: 61%. IR (KBr) (ν_{max}, cm^{-1}): 3292 (OH), 3213 (NH), 1615 and 1594 (C=O), 1507 and 1478 (Ar). Anal. Calcd. for $C_{33}H_{29}ClN_2O_3$ (536.19): C, 73.80; H, 5.44; N, 5.22%. Found: C, 73.76; H, 5.41; N, 5.18%. MS (EI, 70 eV): *m/z* (%) = 536 (69), 520 (100), 500 (31), 433 (31), 415 (75), 365 (30), 242 (21), 121 (30), 65 (9). ^{1}H NMR (300.13 MHz, DMSO): δ_H 0.99 (3H, s, CH_3), 1.02 (3H, s, CH_3), 2.02 (1H, d, $^2J_{HH}$ = 16.0 Hz, CH_2), 2.20 (1H, d, $^2J_{HH}$ = 15.9 Hz, CH_2), 2.55 (1H, d, $^2J_{HH}$ = 16.2 Hz, CH_2), 2.66 (1H, d, $^2J_{HH}$ = 16.1 Hz, CH_2), 5.52 (1H, d, $^3J_{HH}$ = 6.2 Hz, CH^2), 5.74 (1H, s, CH^{14b}), 6.34 (1H, d, $^4J_{HH}$ = 1.8 Hz, CH^9), 6.62 (1H, d, $^3J_{HH}$ = 6.2 Hz, CH^3), 6.87 (1H, dd, $^3J_{HH}$ = 8.2 Hz, CH of Ar), 6.90 (1H, d, $^3J_{HH}$ = 8.9 Hz, CH^6), 7.12 (1H, t, $^3J_{HH}$ = 8.0 Hz, CH of Ar), 7.14 (2H, d, $^3J_{HH}$ = 8.4 Hz, 2 CH of Ar), 7.19 (1H, d, $^3J_{HH}$ = 8.3 Hz, CH^7), 7.29 (2H, d, $^3J_{HH}$ = 8.6 Hz, 2 CH of Ar), 7.31 (1H, t, $^3J_{HH}$ = 8.1 Hz, CH of Ar), 7.55 (1H, dd, $^3J_{HH}$ = 7.5 Hz, $^3J_{HH}$ = 1.8 Hz, CH of Ar), 9.55 (1H, s, NH), 10.03 (1H, s, OH). ^{13}C NMR (75.00 MHz, DMSO): δ_C 19.88 (CH_3), 27.10 (CH_3), 27.82 (CH_3), 31.48 (C^{12}), 44.61 (CH_2), 50.73 (CH_2), 56.96 (CH^{14b}), 102.93 (C^{14a}), 112.16 (CH^3), 116.50 (CH of Ar), 118.72 (CH of Ar), 120.28 (CH^6), 122.82 (C_{ipso}-C=O), 125.54 (CH^9), 126.66 (CH^7), 126.83 (C_{ipso}-CH_3), 128.53 (2 CH of Ar), 129.21 (2 CH of Ar), 130.11 (CH of Ar), 131.41 (CH of Ar), 131.53 (C_{ipso} of Ph), 133.28 (CH^2), 134.19 (C_{ipso}-CH_3), 135.48 (C^{9a}), 136.16 (C^{5a}), 136.63 (C^1), 145.75 (C^{10a}), 155.35 (C^4), 159.06 (C-OH), 193.68 (C=O), 194.14 (C=O).

8-Chloro-1-(2-hydroxybenzoyl)-12,12-dimethyl-4-phenyl-11,12,13,14b-tetrahydrodibenzo[*b*,*f*]pyrido[1,2-*d*][1,4]diazepin-14(10*H*)-one (3e).



Red powder, mp = 281-283 °C, 0.317 g, yield: 57%. IR (KBr) (ν_{max}, cm^{-1}): 3547 (OH), 3411 (NH), 1615 and 1578 (C=O), 1494 and 1449 (Ar). Anal. Calcd. for $C_{32}H_{27}ClN_2O_3$ (523.03): C, 73.49; H, 5.20; N, 5.36%. Found: C, 73.45; H, 5.17; N, 5.31%. MS (EI, 70 eV): *m/z* (%) = 523 (55), 504 (99), 485 (57), 443 (29), 420 (28), 401 (100), 229 (62), 207 (38), 121 (48), 77 (40). ^{1}H NMR (300.13 MHz, DMSO): δ_H 1.01 (3H, s, CH_3), 1.03 (3H, s, CH_3), 1.89 (1H, d, $^2J_{HH}$ = 14.6 Hz, CH_2), 2.07 (1H, d, $^2J_{HH}$ = 14.0 Hz, CH_2), 2.17 (1H, d, $^2J_{HH}$ = 13.2 Hz, CH_2), 2.32 (1H, d, $^2J_{HH}$ = 13.0 Hz, CH_2), 5.65 (1H, d, $^3J_{HH}$ = 6.3 Hz, CH^2), 5.99 (1H, s, CH^{14b}), 6.52 (1H, d, $^4J_{HH}$ = 1.6 Hz, CH^9), 6.82 (1H, d, $^3J_{HH}$ = 6.2 Hz, CH^3), 7.02 (1H, d, $^3J_{HH}$ = 7.9 Hz, CH of Ar), 6.89 (1H, t, $^3J_{HH}$ = 7.8 Hz, CH of Ar), 7.13 (1H, d, $^3J_{HH}$ = 6.5 Hz, CH^7), 7.15-7.26 (5H, m, 5 CH of Ph), 7.44 (1H, t, $^3J_{HH}$ = 8.1 Hz, CH of Ar), 7.54 (1H, d, $^3J_{HH}$ = 8.0 Hz, CH of Ar), 7.70 (1H, d, $^3J_{HH}$ = 6.5 Hz, CH^6), 8.58 (1H, s, NH), 10.41 (1H, s, OH). ^{13}C NMR (75.00 MHz, DMSO): δ_C 29.36 (CH_3), 29.75 (CH_3), 31.68 (C^{12}), 46.08 (CH_2), 51.08 (CH_2), 56.93 (CH^{14b}), 104.20 (C^{14a}), 114.26 (CH^3), 116.87 (CH of Ar), 117.75 (CH of Ar), 119.45 (CH^9), 121.97 (CH^7), 124.03 (C_{ipso}-Cl), 125.24 (C_{ipso}-C=O), 126.28 (CH^6), 127.33 (CH_{para} of Ph), 127.75 (2 CH_{ortho} of Ph), 128.31 (CH of Ar), 128.66 (2 CH_{meta} of Ph), 129.35 (C_{ipso} of Ph), 130.92 (CH of Ar), 133.07 (CH^2), 135.89 (C^{9a}), 136.68 (C^{5a}), 137.51 (C^1), 148.16 (C^{10a}), 156.99 (C^4), 159.16 (C-OH), 195.28 (C=O), 1967.19 (C=O).

Crystal data for **3e** $C_{32}H_{26}ClN_2O_3$ (CCDC 2216002): M_W = 575.55, monoclinic, P 1 21/c 1, a = 23.001(5) Å, b = 13.972(3) Å, c = 16.662(3) Å, α = 90.0, β = 96.17(3), γ = 90.0, V = 5323.6(19) Å^3, Z = 4, Dc = 1.304 mg/m^3, F (000) = 2188, crystal dimension 0.2 × 0.15 × 0.1 mm, radiation, Mo Kα (λ = 0.71073 Å), $0.890 \leq 2\theta \leq 26.665$, intensity data were collected at 290 K with a Bruker APEX

area-detector diffractometer, and employing $\omega/2\theta$ scanning technique, in the range of -28 ≤ h ≤ 28, -17 ≤ k ≤ 17, -20 ≤ l ≤ 20; the structure was solved by a direct method, all non-hydrogen atoms were positioned and anisotropic thermal parameters refined from 10247 observed reflections with R (into) = 0.0887 by a full-matrix least-squares technique converged to R1 = 0.0714, and wR2 = 0.1511 [I>2sigma(I)].

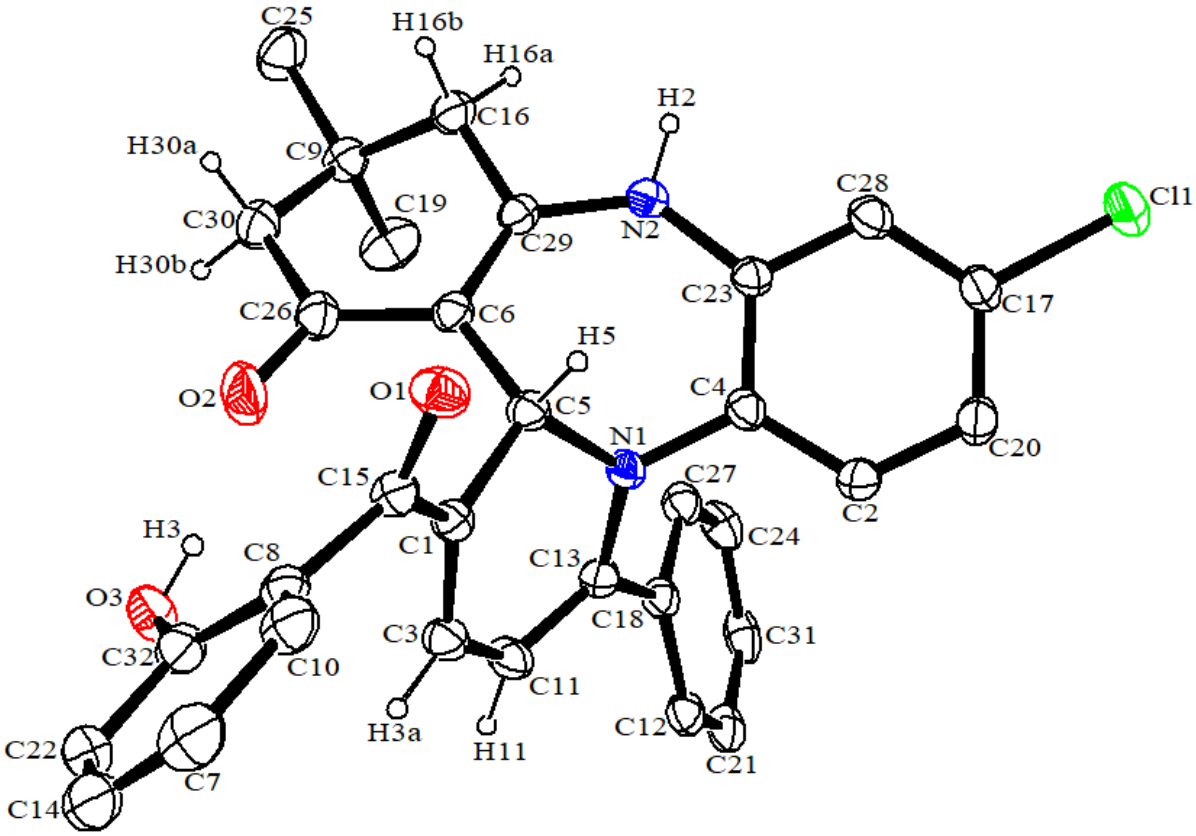
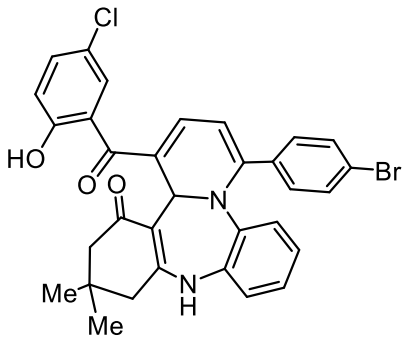
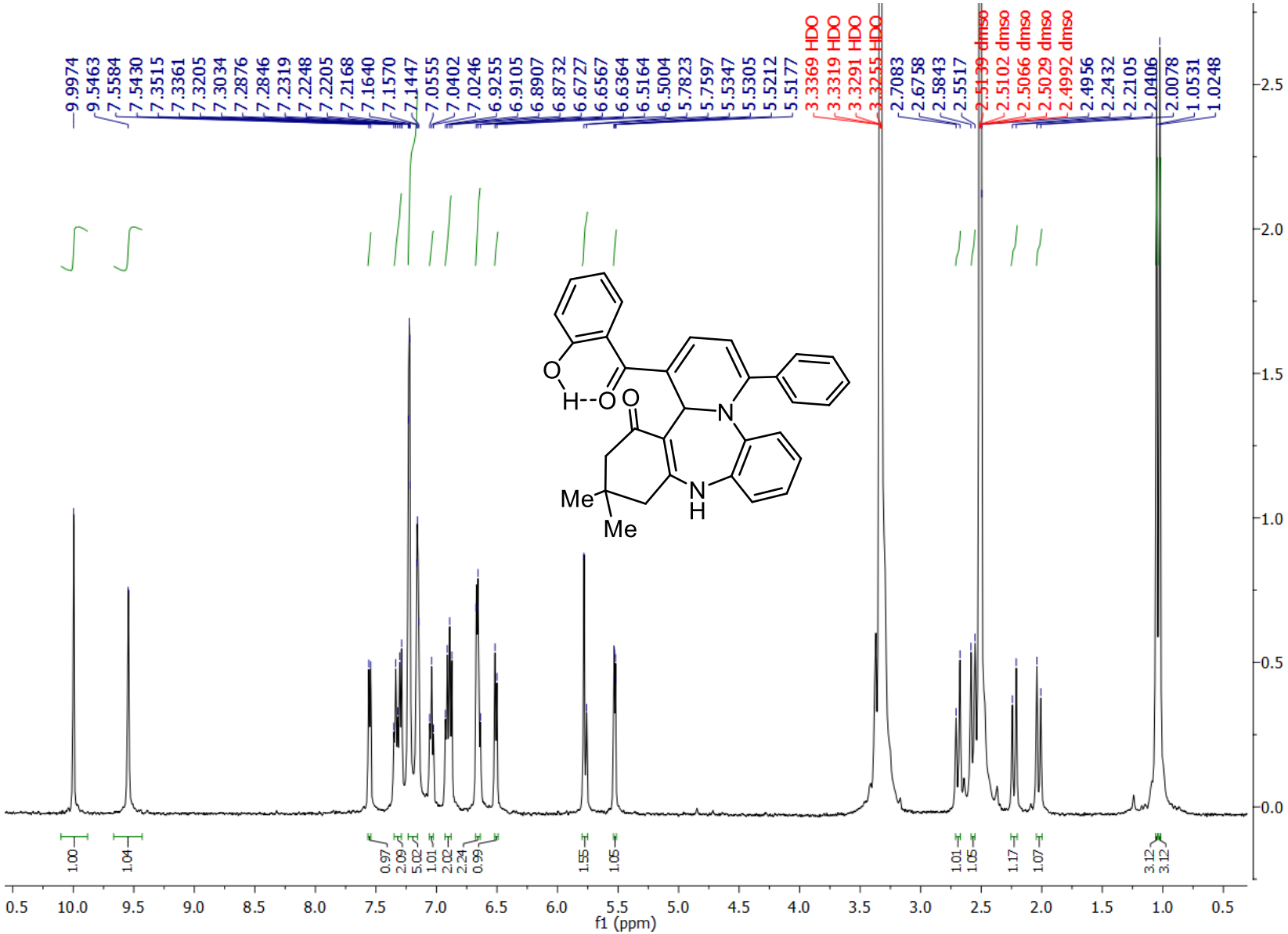


Figure S1 ORTEP diagram of compound **3e**

4-(4-Bromophenyl)-1-(5-chloro-2-hydroxybenzoyl)-12,12-dimethyl-11,12,13,14b-tetrahydrodibenzo[*b*,*f*]pyrido[1,2-*d*][1,4]diazepin-14(10*H*)-one (3f).



Red powder, mp = 291-293 °C, 0.317 g, yield: 59%. IR (KBr) (ν_{max}, cm^{-1}): 3472 (OH), 3414 (NH), 1615 and 1561 (C=O), 1493 and 1463 (Ar). Anal. Calcd. for $C_{32}H_{26}BrClN_2O_3$ (601.93): C, 63.85; H, 4.35; N, 4.65%. Found: C, 63.81; H, 4.32; N, 4.61%. MS (EI, 70 eV): *m/z* (%) = 601 (25), 584 (100), 566 (53), 499 (31), 445 (78), 418 (25), 277 (75), 183 (41), 155 (36), 132 (25). ^{1}H NMR (300.13 MHz, DMSO): δ_H 0.88 (3H, s, CH_3), 1.02 (3H, s, CH_3), 1.76 (1H, d, $^2J_{HH}$ = 17.0 Hz, CH_2), 1.88 (1H, d, $^2J_{HH}$ = 17.0 Hz, CH_2), 2.10 (1H, d, $^2J_{HH}$ = 15.9 Hz, CH_2), 2.27 (1H, d, $^2J_{HH}$ = 15.9 Hz, CH_2), 5.63 (1H, d, $^3J_{HH}$ = 6.5 Hz, CH^2), 5.97 (1H, s, CH^{14b}), 6.51 (1H, d, $^3J_{HH}$ = 7.1 Hz, CH^9), 6.65 (1H, t, $^3J_{HH}$ = 7.4 Hz, CH^8), 6.85 (1H, d, $^3J_{HH}$ = 7.6 Hz, CH of Ar), 6.91 (1H, t, $^3J_{HH}$ = 7.9 Hz, CH^7), 6.99 (2H, d, $^3J_{HH}$ = 8.1 Hz, 2 CH of Ar), 7.15 (1H, d, $^3J_{HH}$ = 6.4 Hz, CH^3), 7.29 (2H, d, $^3J_{HH}$ = 8.5 Hz, 2 CH of Ar), 7.36 (1H, d, $^3J_{HH}$ = 8.8 Hz, $^4J_{HH}$ = 2.6 Hz, CH of Ar), 7.48 (1H, d, $^3J_{HH}$ = 7.7 Hz, CH^6), 7.53 (1H, d, $^4J_{HH}$ = 2.6 Hz, CH of Ar), 8.92 (1H, s, NH), 10.41 (1H, s, OH). ^{13}C NMR (75.00 MHz, DMSO): δ_C 25.87 (CH_3), 29.71 (CH_3), 31.59 (C^{12}), 46.08 (CH_2), 50.81 (CH_2), 57.21 (CH^{14b}), 103.86 (C^{14a}), 113.70 (CH^3), 119.35 (CH of Ar), 120.39 (CH^6), 121.07 (CH^9), 123.46 (C_{ipso}-Br), 124.46 (C_{ipso}-Cl), 126.09 (C_{ipso}-C=O), 126.75 (CH^8), 128.51 (CH of Ar), 128.68 (CH^7), 129.29 (2 CH of Ar), 131.79 (2 CH of Ar), 132.11 (CH of Ar), 132.39 (CH^2), 135.14 (C_{ipso} of Ar), 136.30 (C^{9a}), 137.83 (C^{5a}), 138.52 (C^1), 148.19 (C^{10a}), 154.59 (C^4), 160.41 (C-OH), 194.84 (C=O), 195.45 (C=O).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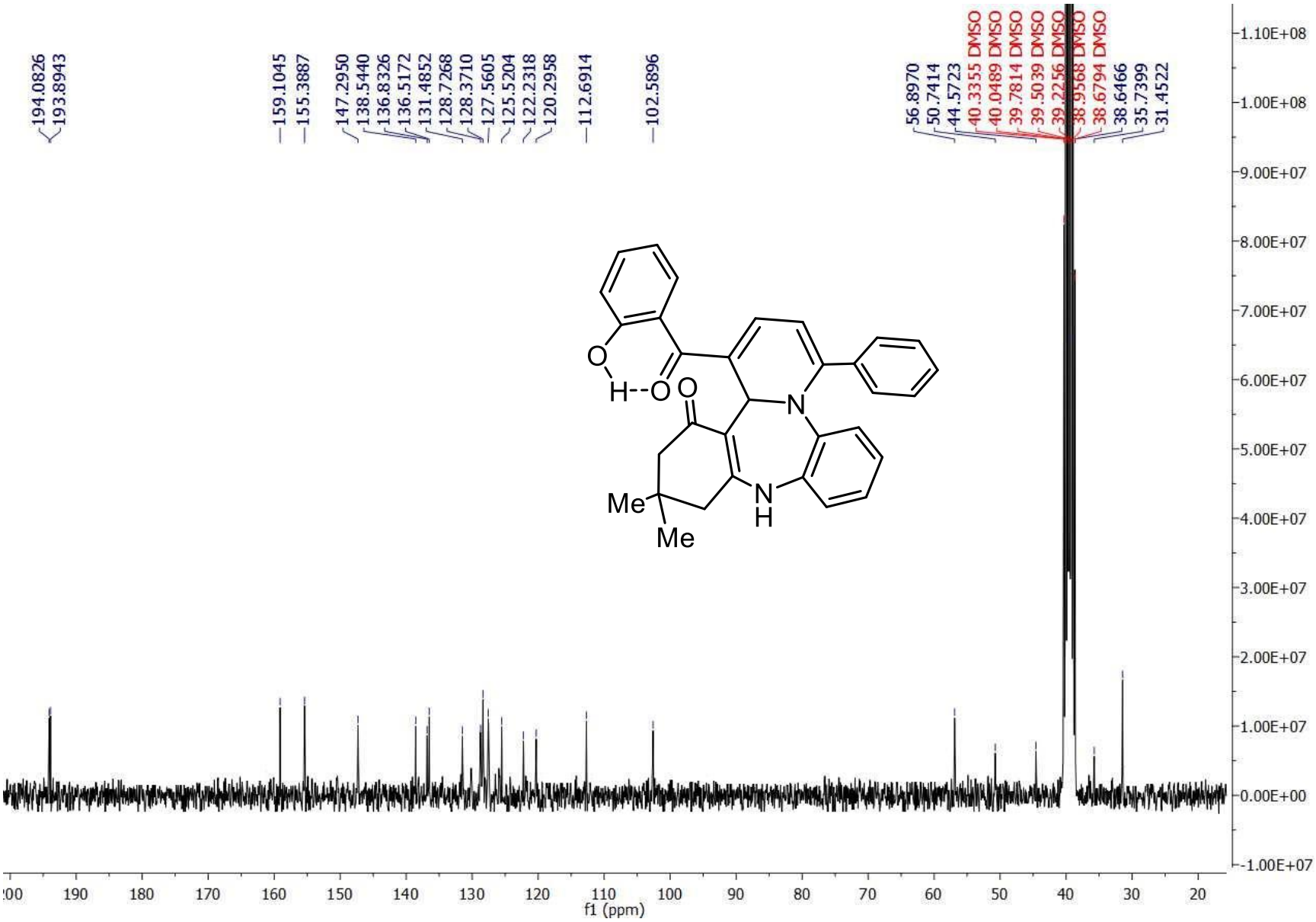
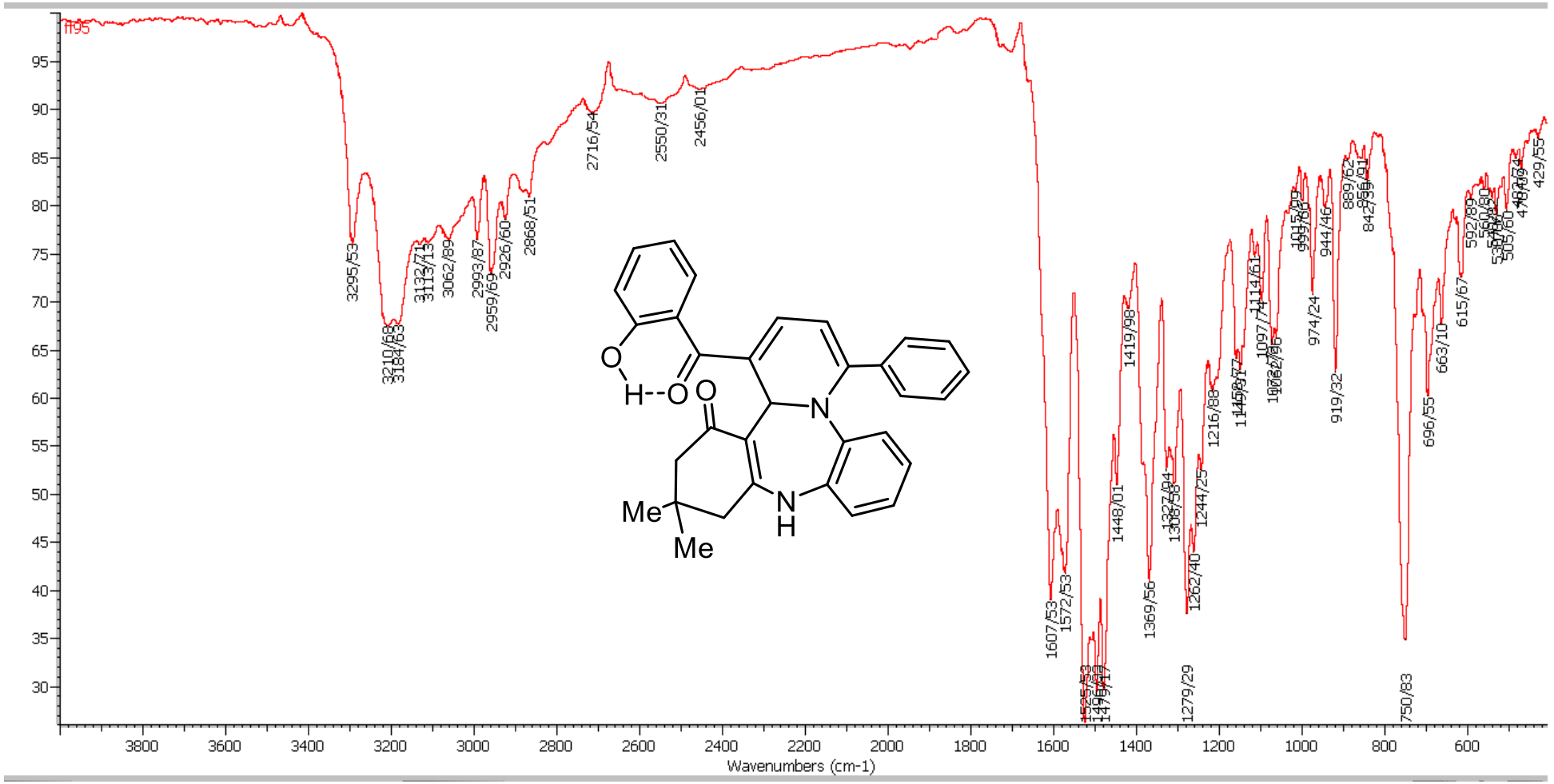
9.5463
7.5584
7.5430
7.3515
7.3361
7.3205
7.3034
7.2876
7.2846
7.2319
7.2248
7.2205
7.2168
7.1640
7.1570
7.1447
7.0555
7.0402
7.0246
6.9255
6.9105
6.8907
6.8732
6.6727
6.6567
6.6364
6.5164
6.5004
5.7823
5.7597
5.5347
5.5305
5.5212
5.5177
3.3369 HDO
3.3319 HDO
3.3291 HDO
3.3255 HDO
2.7083
2.6758
2.5843
2.5517
2.5139 dmso
2.5102 dmso
2.5066 dmso
2.5029 dmso
2.4992 dmso
2.4956
2.2432
2.2105
2.0406
2.0078
1.0531
1.0248
O
H--O
O
N
N
H
Me
Me
1.00
1.04
0.97
2.09
5.02
1.01
2.02
2.24
0.99
1.55
1.05
1.01
1.05
1.17
1.07
3.12
3.12
f1 (ppm)

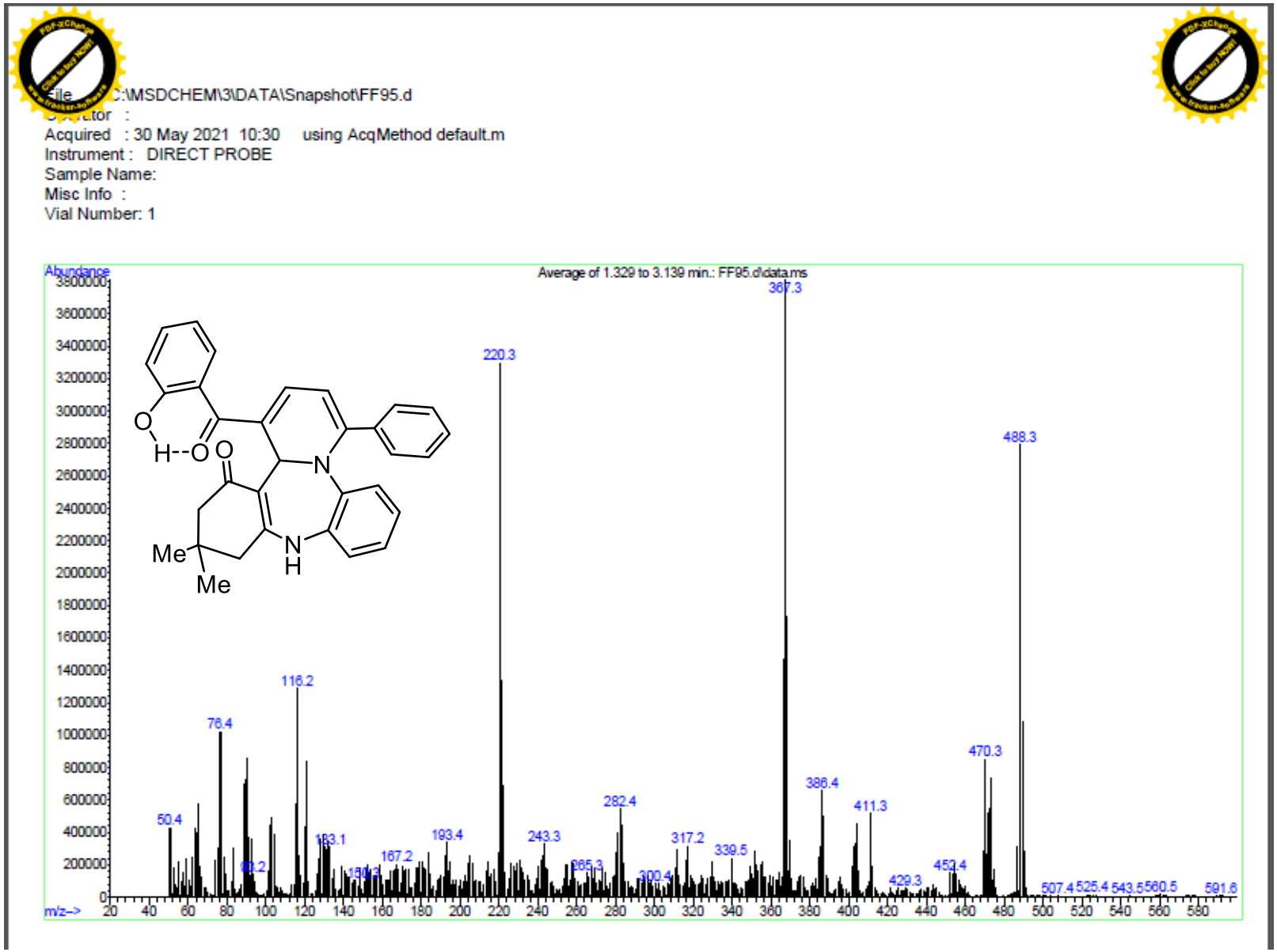
^{1}H NMR of **3a**


194.0826
193.8943
159.1045
155.3887
147.2950
138.5440
136.8326
136.5172
131.4852
128.7268
128.3710
127.5605
125.5204
122.2318
120.2958
112.6914
102.5896
56.8970
50.7414
44.5723
40.3355 DMSO
40.0489 DMSO
39.7814 DMSO
39.5039 DMSO
39.2256 DMSO
38.9568 DMSO
38.6794 DMSO
38.6466
35.7399
31.4522
O
H--O
O
N
N
H
Me
Me
1.10E+08
1.00E+08
9.00E+07
8.00E+07
7.00E+07
6.00E+07
5.00E+07
4.00E+07
3.00E+07
2.00E+07
1.00E+07
0.00E+00
-1.00E+07
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
f1 (ppm)

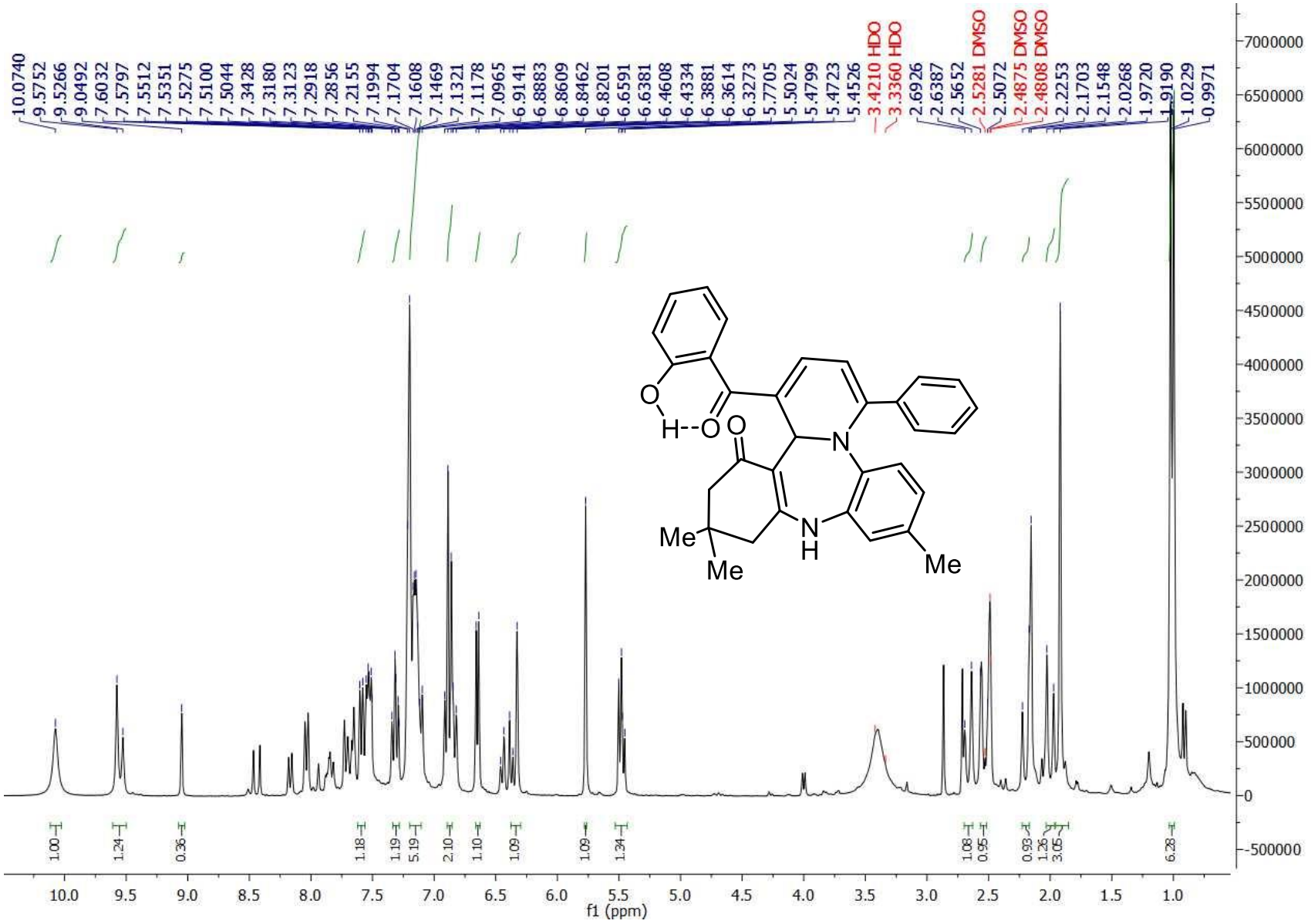
^{13}C NMR of **3a**



IR of **3a**



MS of compound **3a**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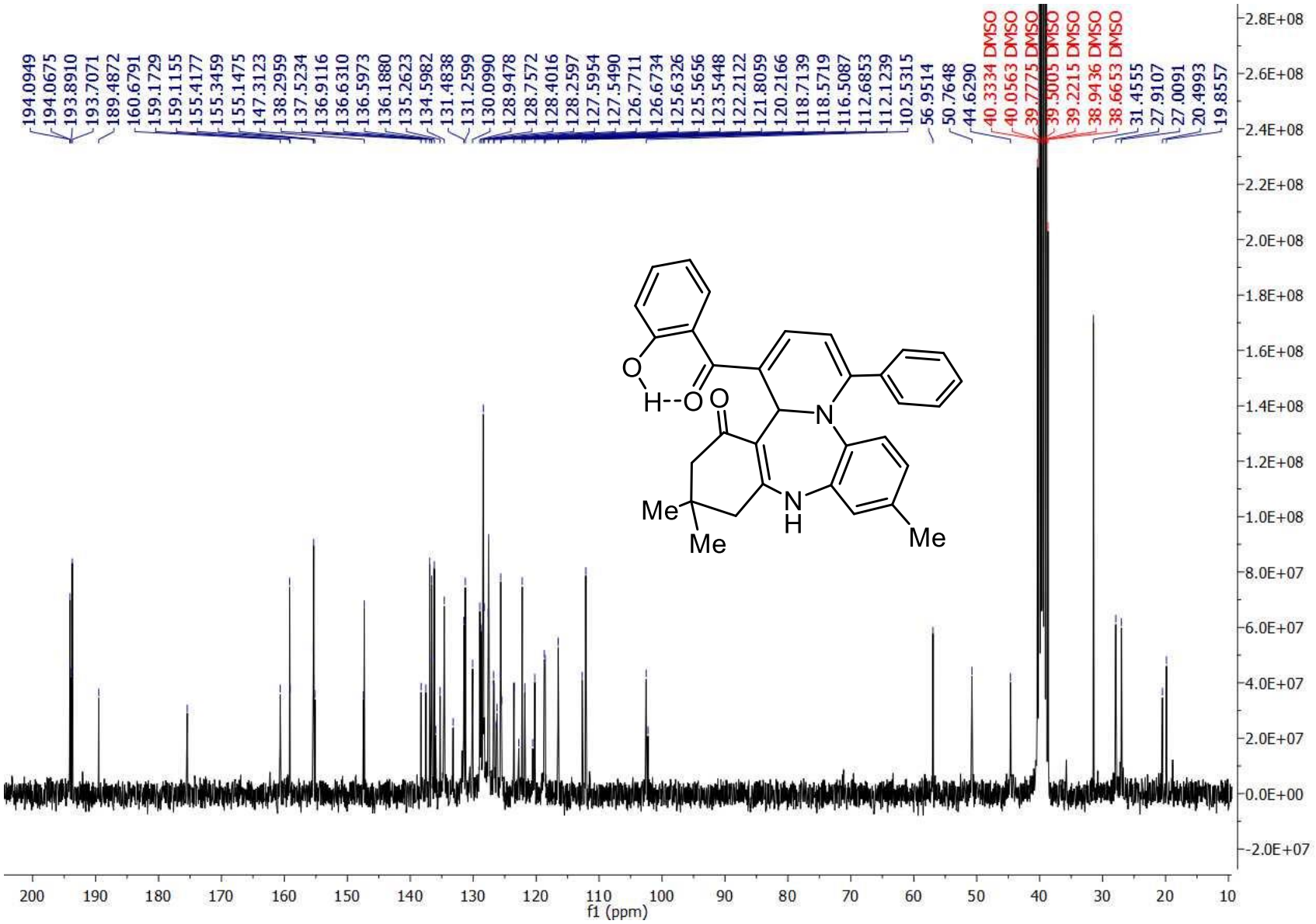
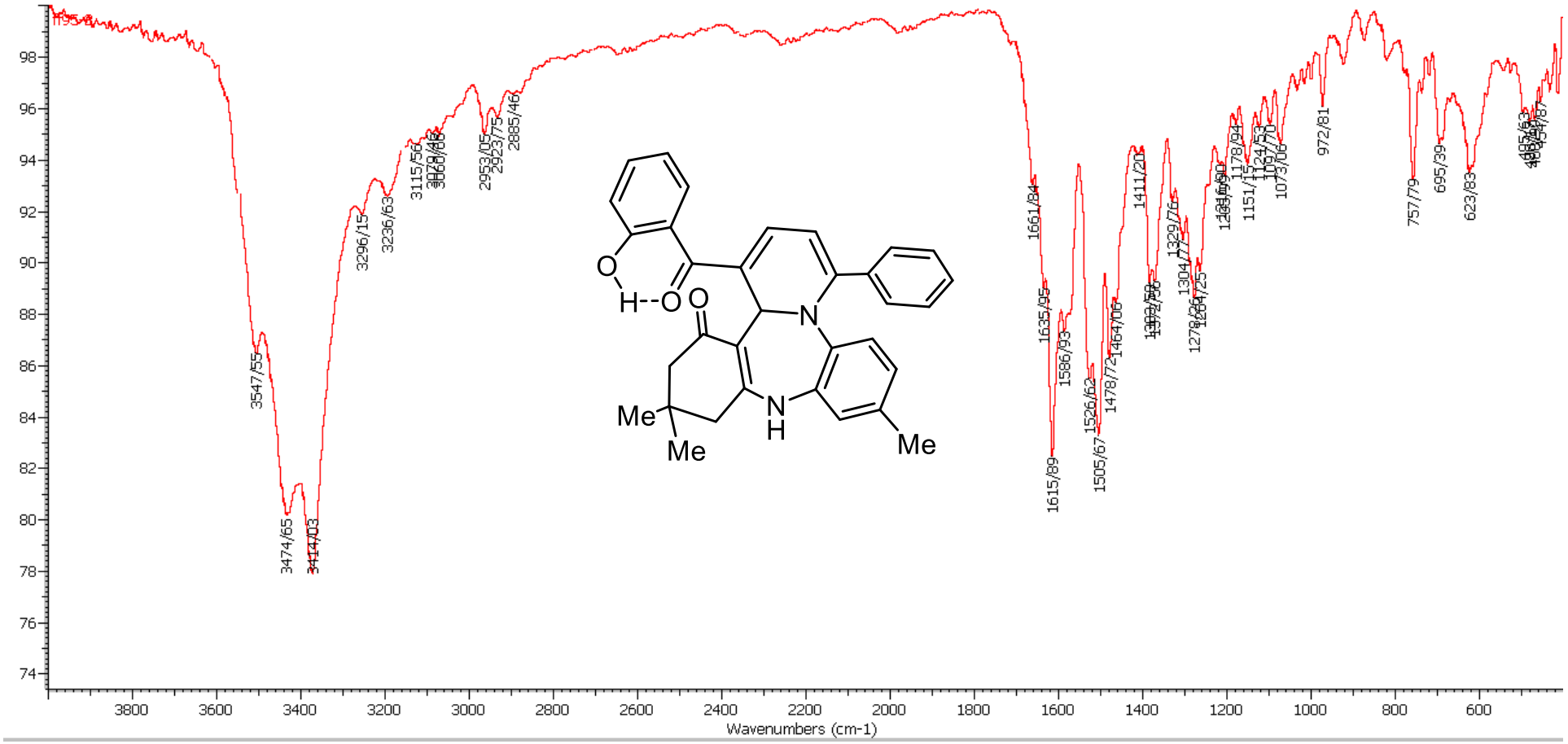
9.5752
9.5266
9.0492
7.6032
7.5797
7.5512
7.5351
7.5275
7.5100
7.5044
7.3428
7.3180
7.3123
7.2918
7.2856
7.2155
7.1994
7.1704
7.1608
7.1469
7.1321
7.1178
7.0965
6.9141
6.8883
6.8609
6.8462
6.8201
6.6591
6.6381
6.4608
6.4334
6.3881
6.3614
6.3273
5.7705
5.5024
5.4799
5.4723
5.4526
3.4210 HDO
3.3360 HDO
2.6926
2.6387
2.5652
2.5281 DMSO
2.5072
2.4875 DMSO
2.4808 DMSO
2.2253
2.1703
2.1548
2.0268
1.9720
1.9190
1.0229
0.9971
O
H
O
O
N
N
H
Me
Me
Me
1.00
1.24
0.36
1.18
1.19
5.19
2.10
1.10
1.09
1.09
1.34
1.08
0.95
0.93
1.26
3.05
6.28
f1 (ppm)

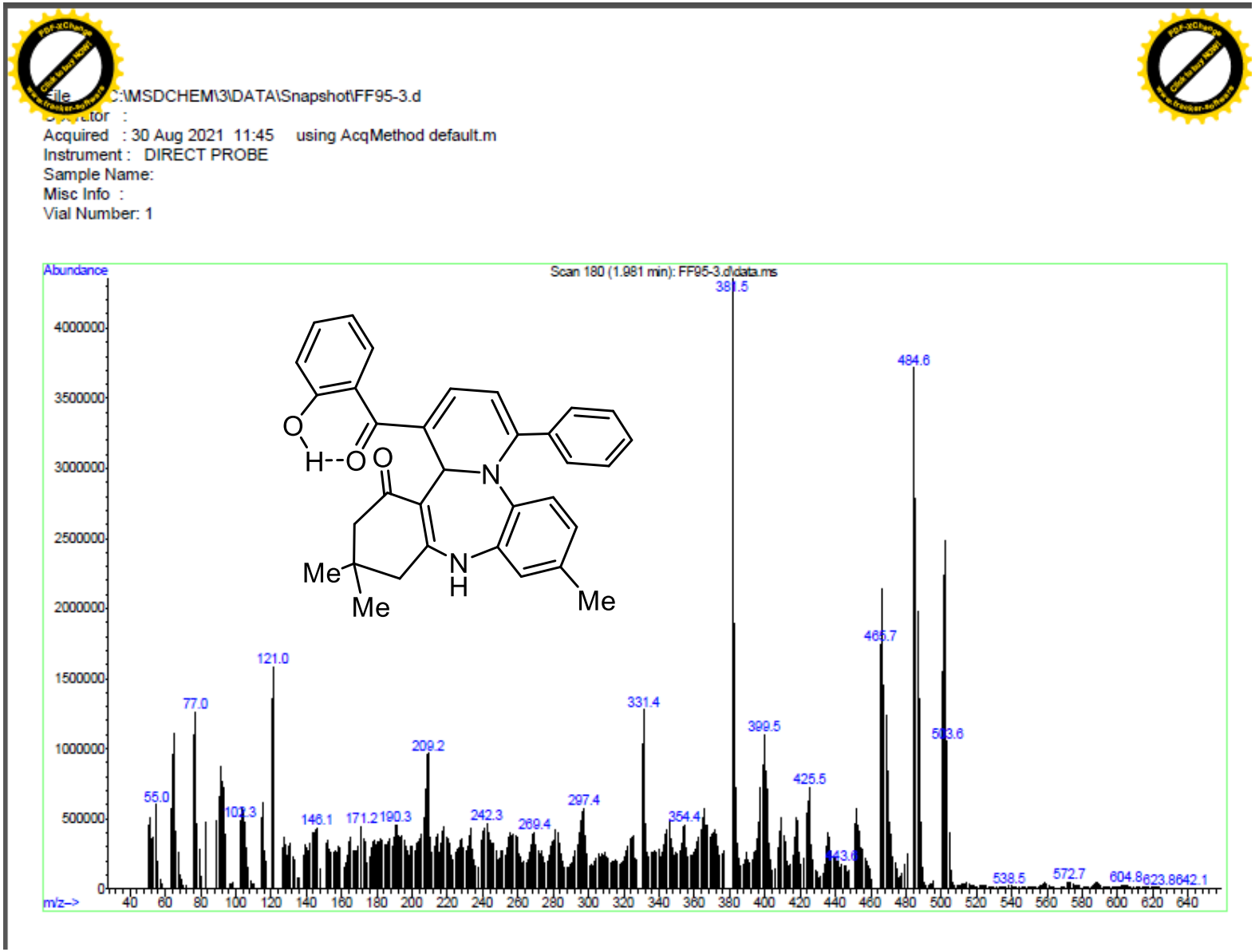
^{1}H NMR of **3b**


194.0949
194.0675
193.8910
193.7071
189.4872
160.6791
159.1729
159.1155
155.4177
155.3459
155.1475
147.3123
138.2959
137.5234
136.9116
136.6310
136.5973
136.1880
135.2623
134.5982
131.4838
131.2599
130.0990
128.9478
128.7572
128.4016
128.2597
127.5954
127.5490
126.7711
126.6734
125.6326
125.5656
123.5448
122.2122
121.8059
120.2166
118.7139
118.5719
116.5087
112.6853
112.1239
102.5315
56.9514
50.7648
44.6290
40.3334 DMSO
40.0563 DMSO
39.7775 DMSO
39.5005 DMSO
39.2215 DMSO
38.9436 DMSO
38.6653 DMSO
31.4555
27.9107
27.0091
20.4993
19.8557
O
H--O
O
N
N
H
Me
Me
Me
2.8E+08
2.6E+08
2.4E+08
2.2E+08
2.0E+08
1.8E+08
1.6E+08
1.4E+08
1.2E+08
1.0E+08
8.0E+07
6.0E+07
4.0E+07
2.0E+07
0.0E+00
-2.0E+07
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

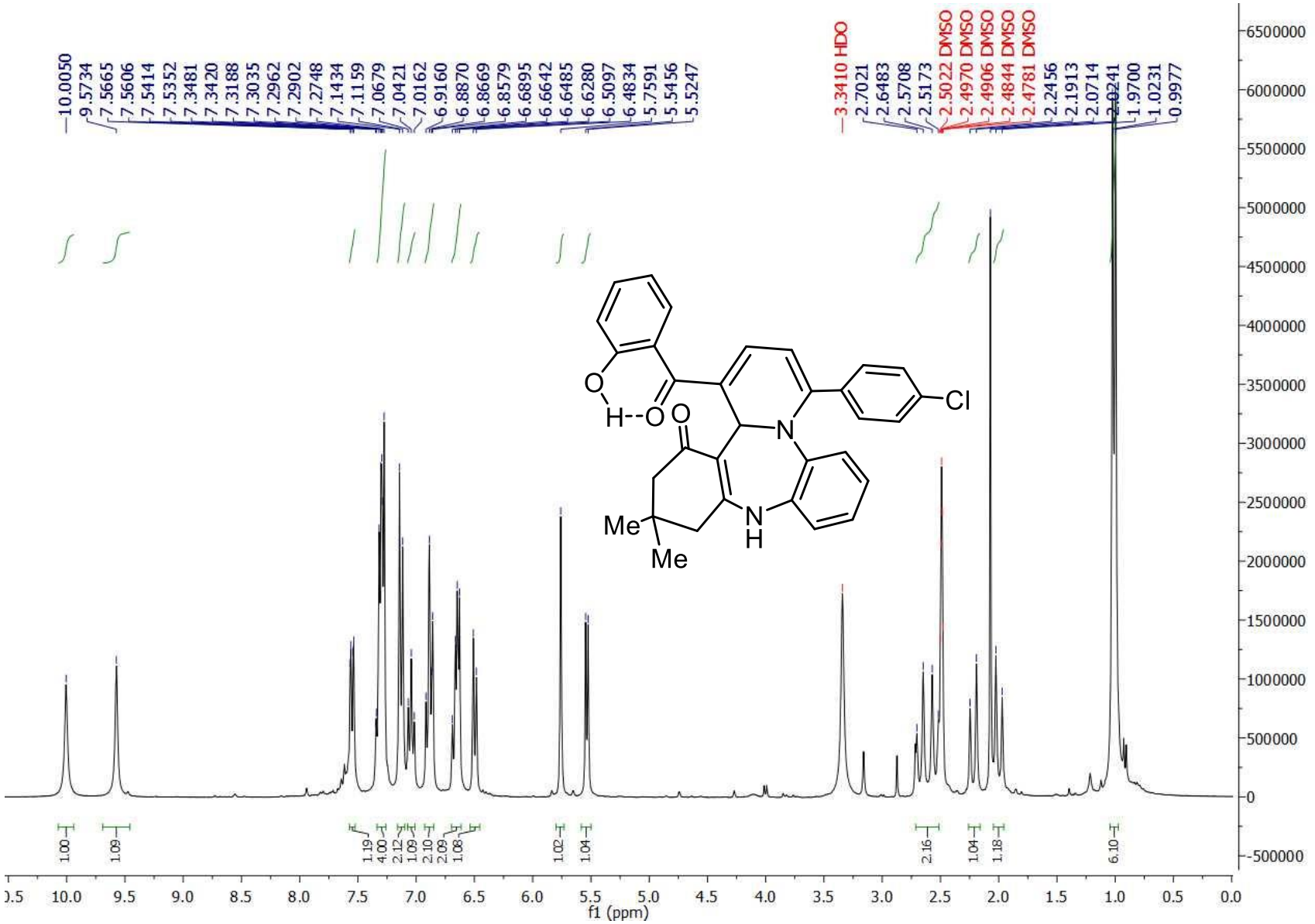
^{13}C NMR of **3b**


Wavenumbers (cm-1)
3547/55
3474/65
3414/03
3296/15
3236/63
3115/56
2953/05
2923/75
2885/46
1661/84
1635/95
1615/89
1586/93
1526/62
1505/67
1478/72
1464/06
1411/20
1329/76
1304/72
1178/94
1151/12
1124/53
1073/06
972/81
757/79
695/39
623/83
O
H--O
O
N
N
H
Me
Me
Me

IR of **3b**



MS of compound **3b**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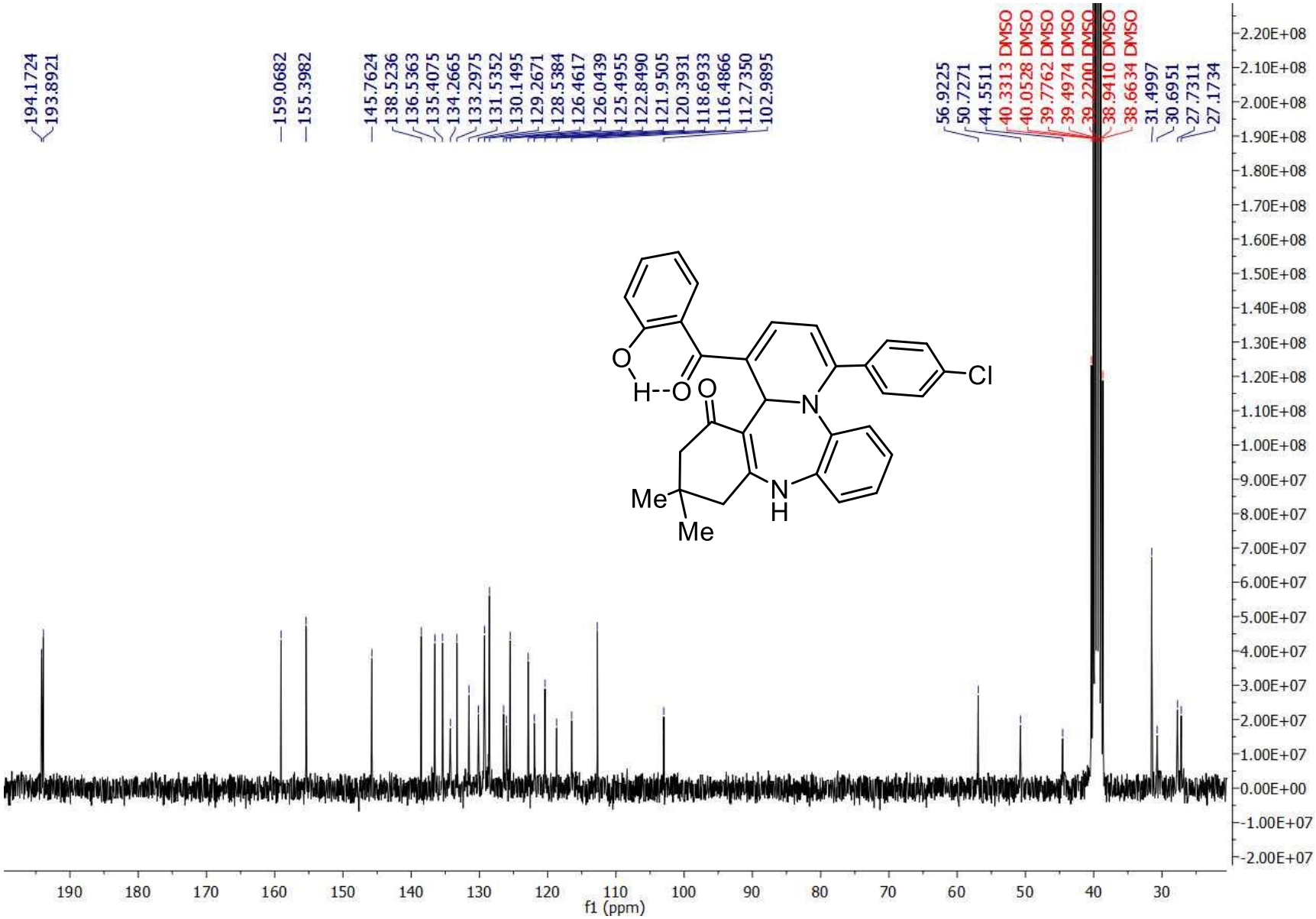
7.5665
7.5606
7.5414
7.5352
7.3481
7.3420
7.3188
7.3035
7.2962
7.2902
7.2748
7.1434
7.1159
7.0679
7.0421
7.0162
6.9160
6.8870
6.8669
6.8579
6.6895
6.6642
6.6485
6.6280
6.5097
6.4834
5.7591
5.5456
5.5247
3.3410 HDO
2.7021
2.6483
2.5708
2.5173
2.5022 DMSO
2.4970 DMSO
2.4906 DMSO
2.4844 DMSO
2.4781 DMSO
2.2456
2.1913
2.0714
2.0241
1.9700
1.0231
0.9977
O
H--O
O
N
Cl
N
H
Me
Me
1.00
1.09
1.19
4.00
2.12
1.09
2.10
2.09
1.08
1.02
1.04
2.16
1.04
1.18
6.10
f1 (ppm)

^{1}H NMR of **3c**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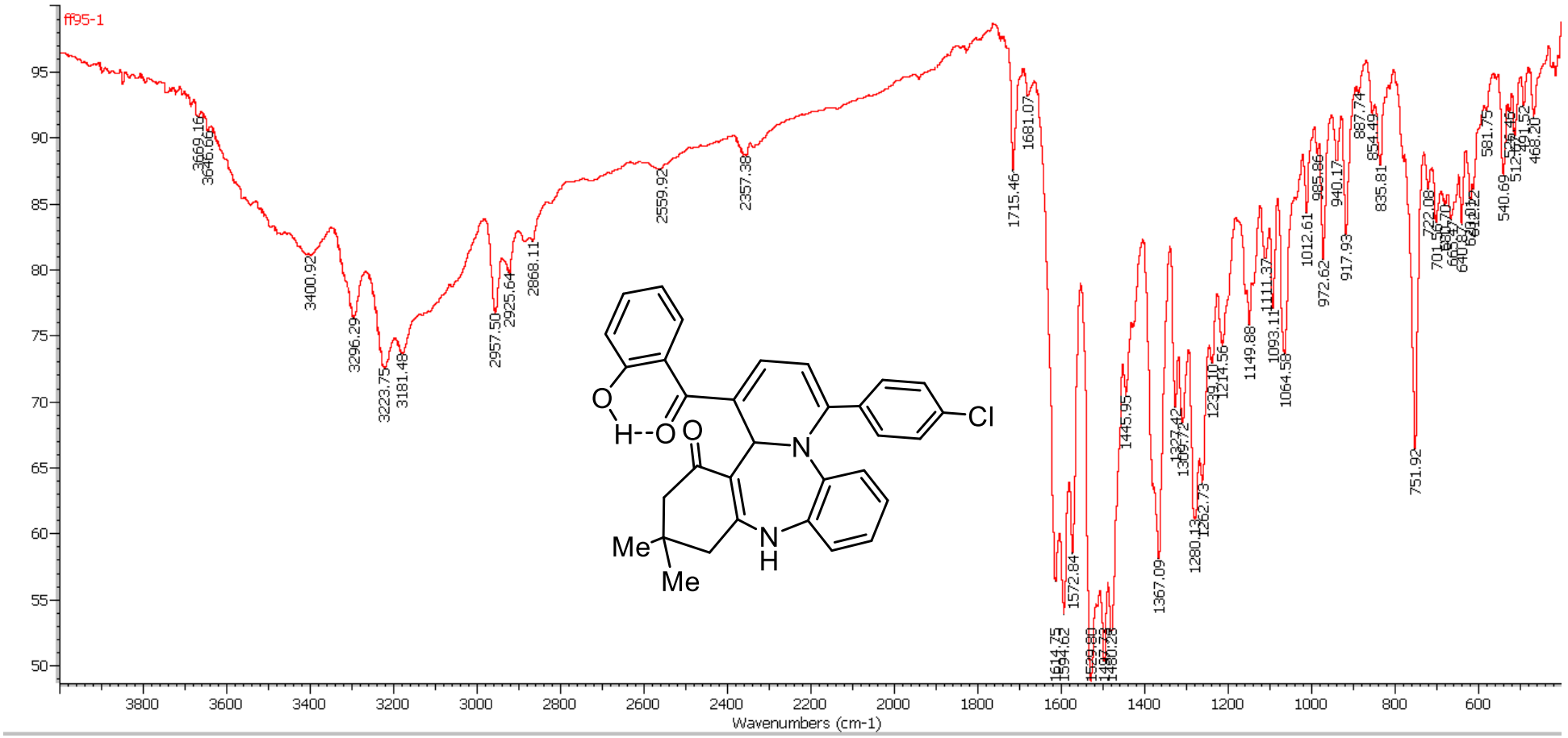
193.8921
159.0682
155.3982
145.7624
138.5236
136.5363
135.4075
134.2665
133.2975
131.5352
130.1495
129.2671
128.5384
126.4617
126.0439
125.4955
122.8490
121.9505
120.3931
118.6933
116.4866
112.7350
102.9895
56.9225
50.7271
44.5511
40.3313 DMSO
40.0528 DMSO
39.7762 DMSO
39.4974 DMSO
39.2200 DMSO
38.9410 DMSO
38.6634 DMSO
31.4997
30.6951
27.7311
27.1734
O
H--O
O
N
Cl
N
H
Me
Me
f1 (ppm)

^{13}C NMR of **3c**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Wavenumbers (cm-1)
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3646.66
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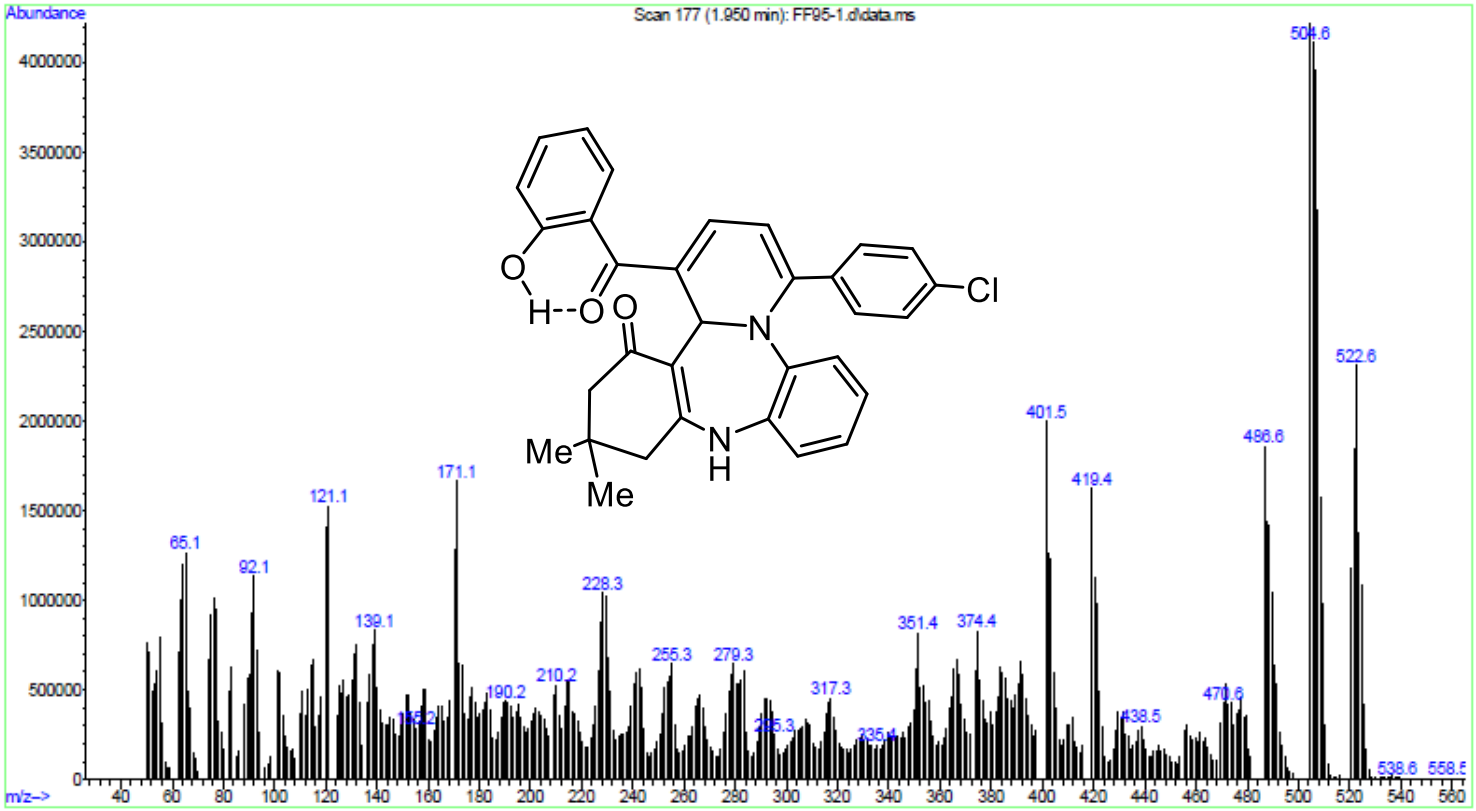
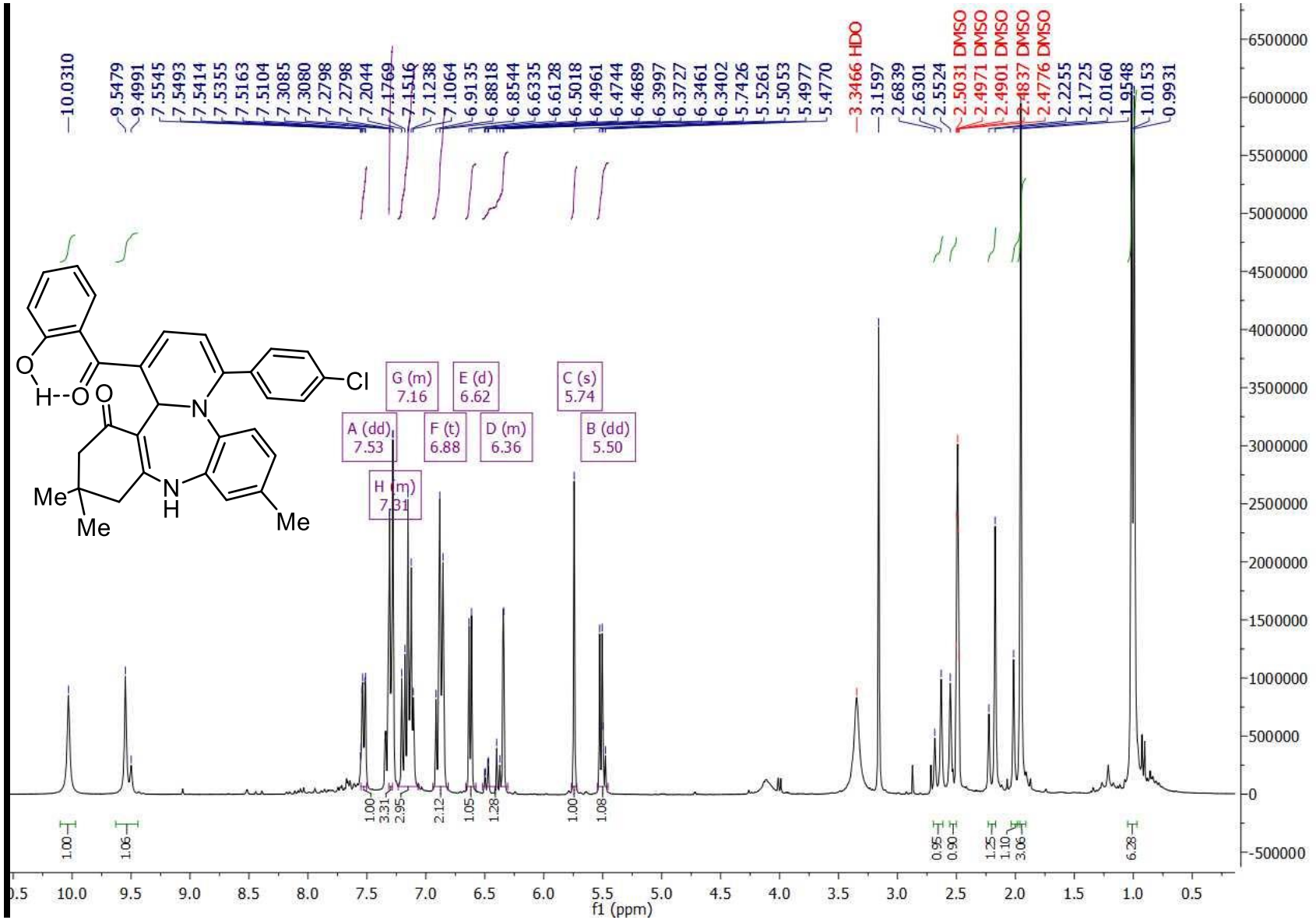
3296.29
3223.75
3181.48
2957.50
2925.64
2868.11
2559.92
2357.38
1715.46
1681.07
1614.75
1594.62
1572.84
1445.95
1367.09
1327.42
1280.13
1262.73
1214.56
1149.88
1111.37
1093.11
1064.58
1012.61
985.86
972.62
940.17
917.93
887.74
854.49
835.81
751.92
722.08
701.70
640.87
581.75
540.69
526.46
512.91
468.20
O
H--O
O
N
N
H
Me
Me
Cl

IR of **3c**

File C:\MSDCHEM\3\DATA\Snapshot\FF95-1.d
Operator :
Acquired : 30 Aug 2021 11:12 using AcqMethod default.m
Instrument : DIRECT PROBE
Sample Name:
Misc Info :
Vial Number: 1



MS of compound **3c**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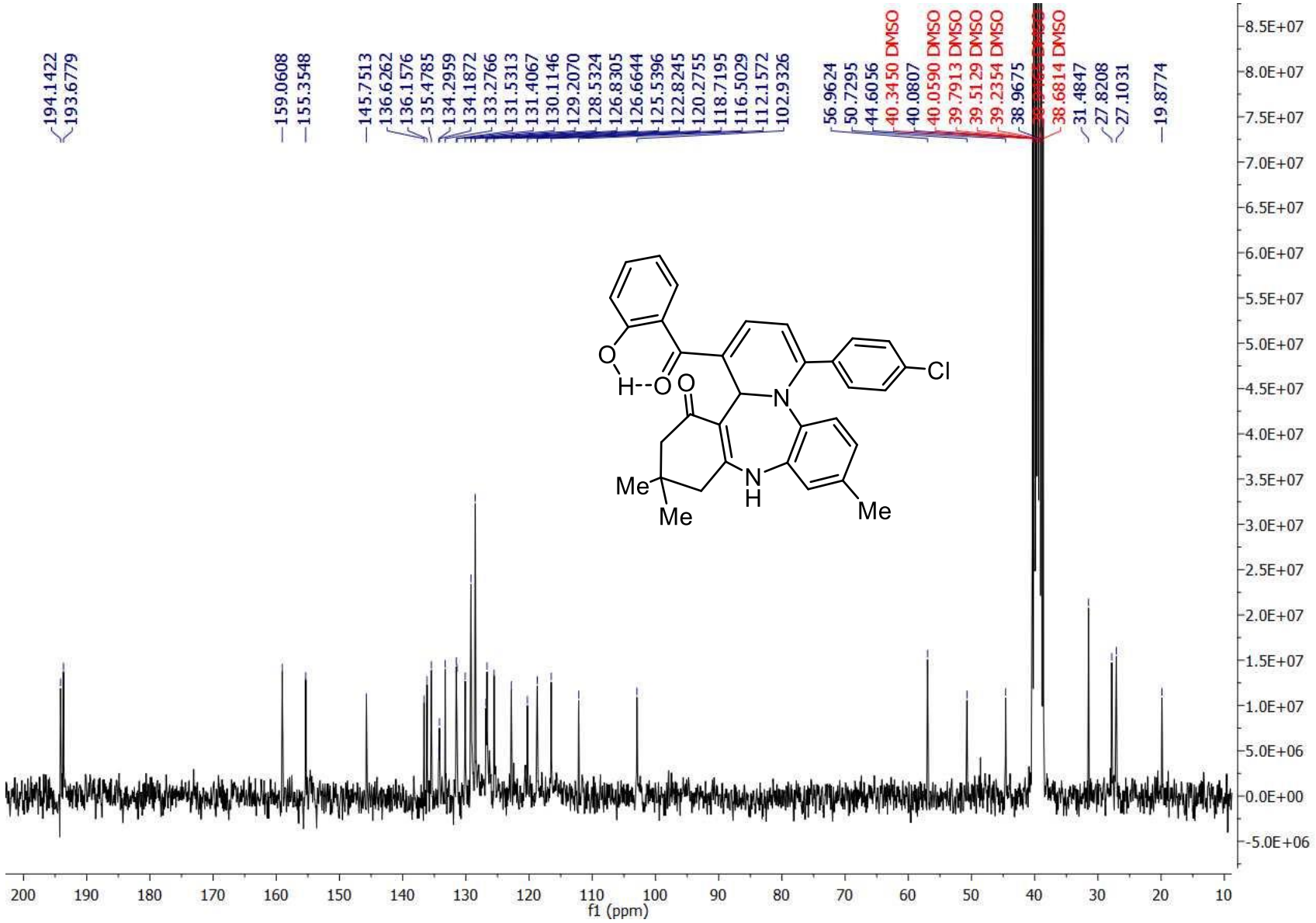
9.4991
7.5545
7.5493
7.5414
7.5355
7.5163
7.5104
7.3085
7.3080
7.2798
7.2798
7.2044
7.1769
7.1516
7.1238
7.1064
6.9135
6.8818
6.8544
6.6335
6.6128
6.5018
6.4961
6.4744
6.4689
6.3997
6.3727
6.3461
6.3402
5.7426
5.5261
5.5053
5.4977
5.4770
3.3466 HDO
3.1597
2.6839
2.6301
2.5524
2.5031 DMSO
2.4971 DMSO
2.4901 DMSO
2.4837 DMSO
2.4776 DMSO
2.2255
2.1725
2.0160
1.9548
1.0153
0.9931
G (m) 7.16
E (d) 6.62
C (s) 5.74
A (dd) 7.53
F (t) 6.88
D (m) 6.36
B (dd) 5.50
H (m) 7.31
Cl
O
H--O
O
N
N
H
Me
Me
Me
1.00
1.06
1.00
3.31
2.95
2.12
1.05
1.28
1.00
1.08
0.95
0.90
1.25
1.10
3.06
6.28
f1 (ppm)

^{1}H NMR of **3d**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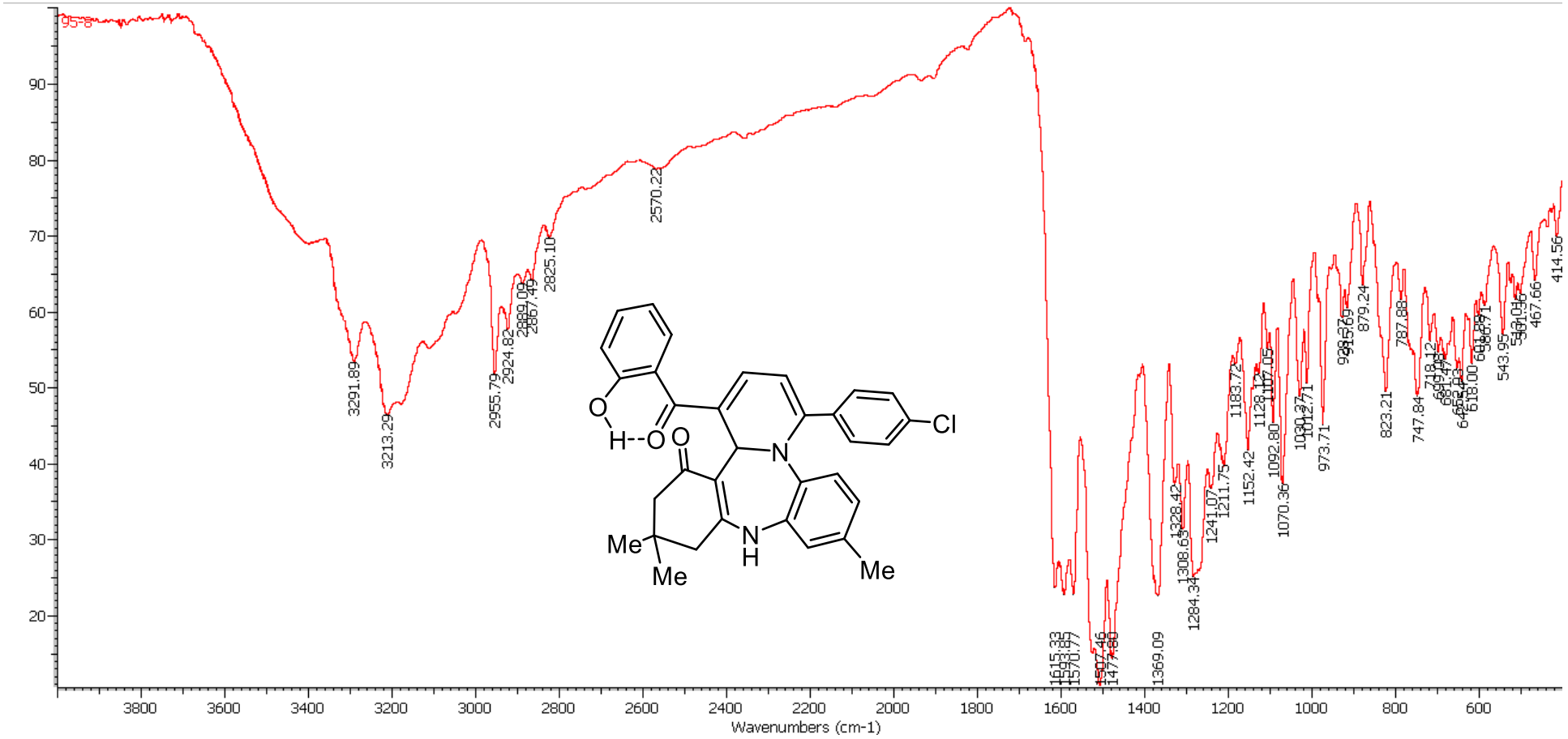
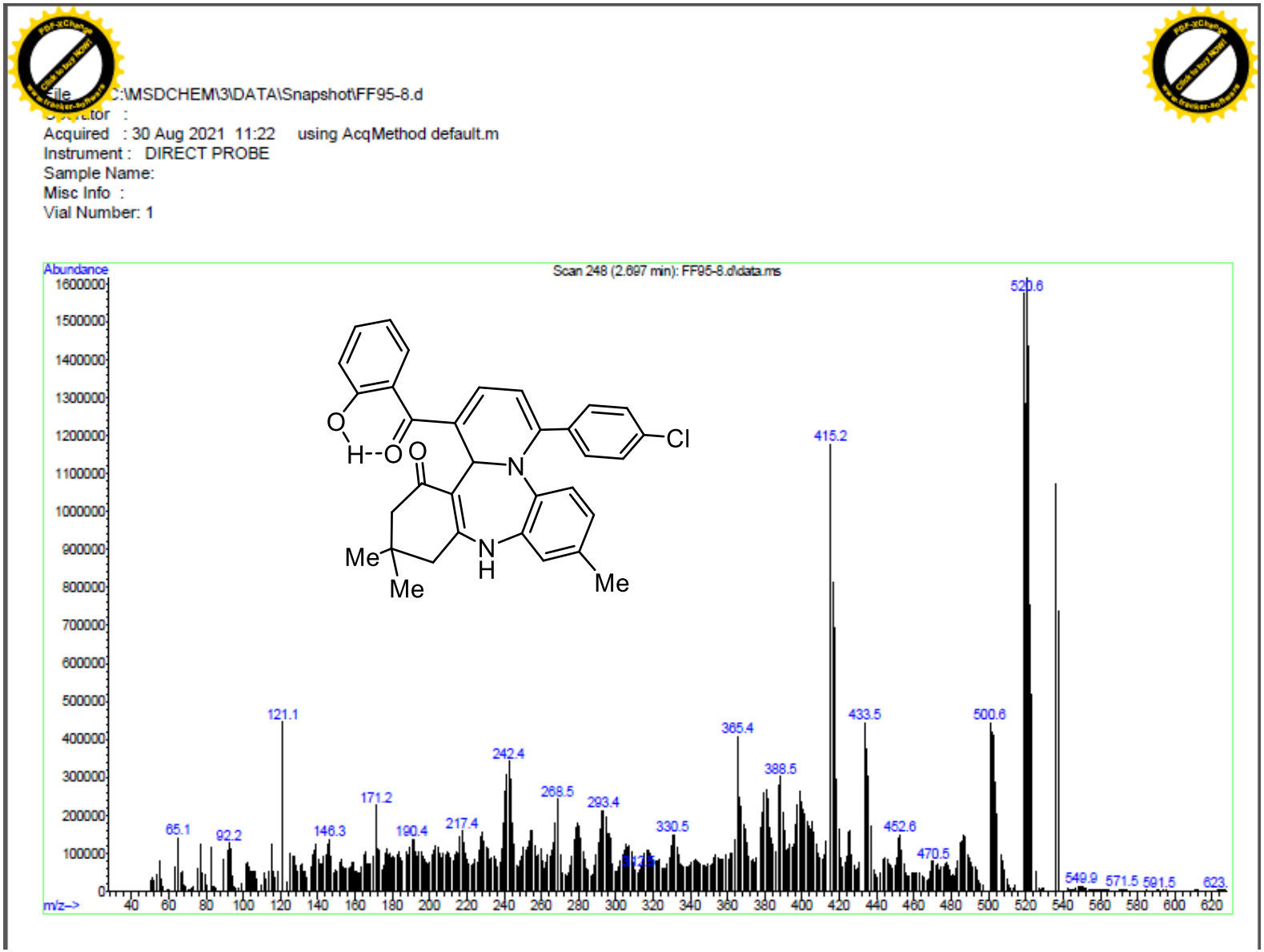
159.0608
155.3548
145.7513
136.6262
136.1576
135.4785
134.2959
134.1872
133.2766
131.5313
131.4067
130.1146
129.2070
128.5324
126.8305
126.6644
125.5396
122.8245
120.2755
118.7195
116.5029
112.1572
102.9326
56.9624
50.7295
44.6056
40.3450 DMSO
40.0807
40.0590 DMSO
39.7913 DMSO
39.5129 DMSO
39.2354 DMSO
38.9675
38.6814 DMSO
31.4847
27.8208
27.1031
19.8774
O
H--O
O
N
Cl
N
H
Me
Me
Me
8.5E+07
8.0E+07
7.5E+07
7.0E+07
6.5E+07
6.0E+07
5.5E+07
5.0E+07
4.5E+07
4.0E+07
3.5E+07
3.0E+07
2.5E+07
2.0E+07
1.5E+07
1.0E+07
5.0E+06
0.0E+00
-5.0E+06
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

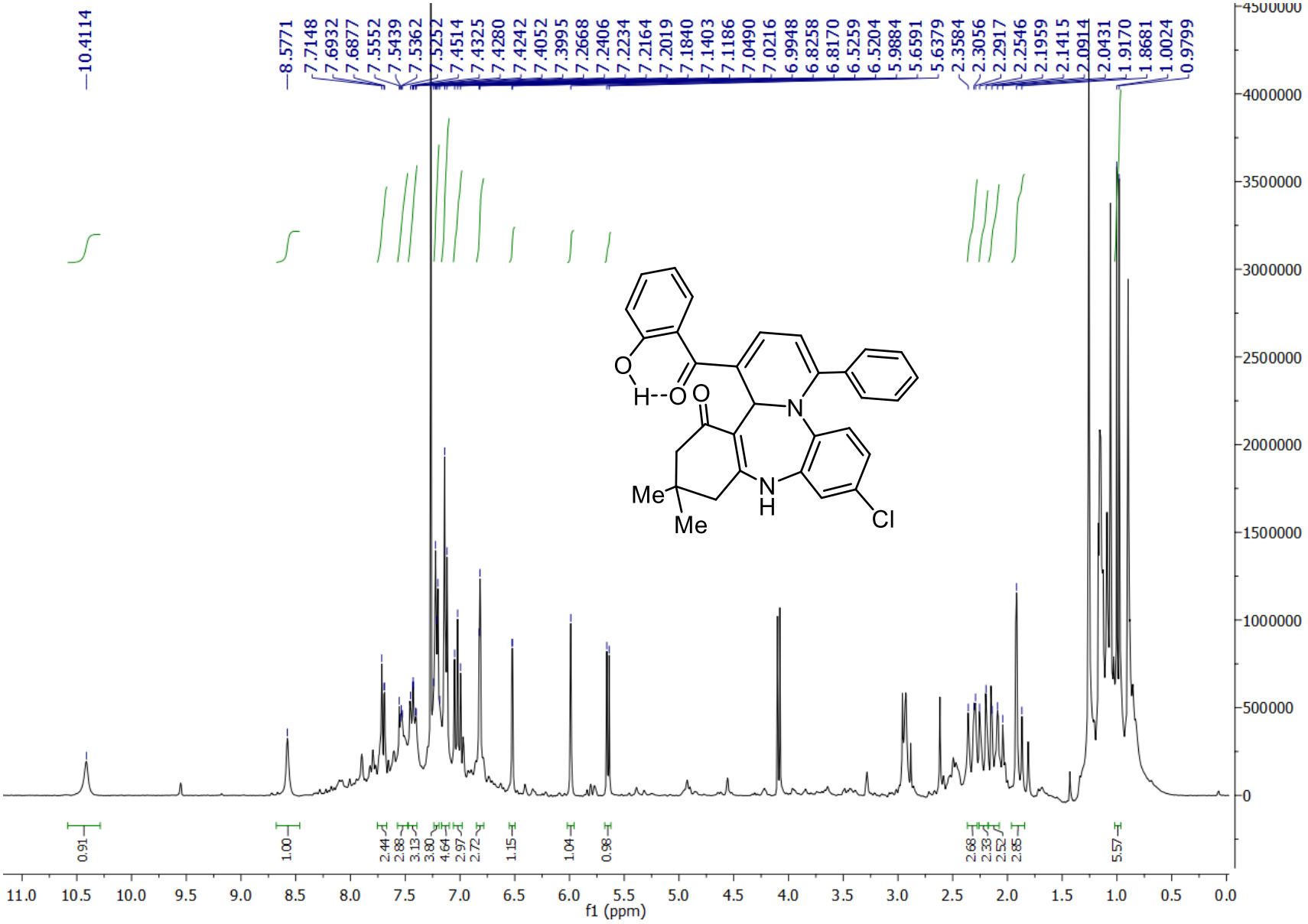
^{13}C NMR of **3d**


95-8
Wavenumbers (cm-1)
3291.89
3213.29
2955.79
2924.82
2889.08
2867.49
2825.10
2570.22
1615.33
1597.46
1577.97
1369.09
1328.42
1308.63
1284.34
1241.07
1211.75
1183.72
1152.42
1128.12
1092.80
1070.36
1030.37
973.71
879.24
823.21
787.88
747.84
543.95
467.66
414.56
O
H--O
O
N
N
H
Me
Me
Me
Cl

IR of **3d**



Mass of compound **3d**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7.7148
7.6932
7.6877
7.5552
7.5439
7.5362
7.5252
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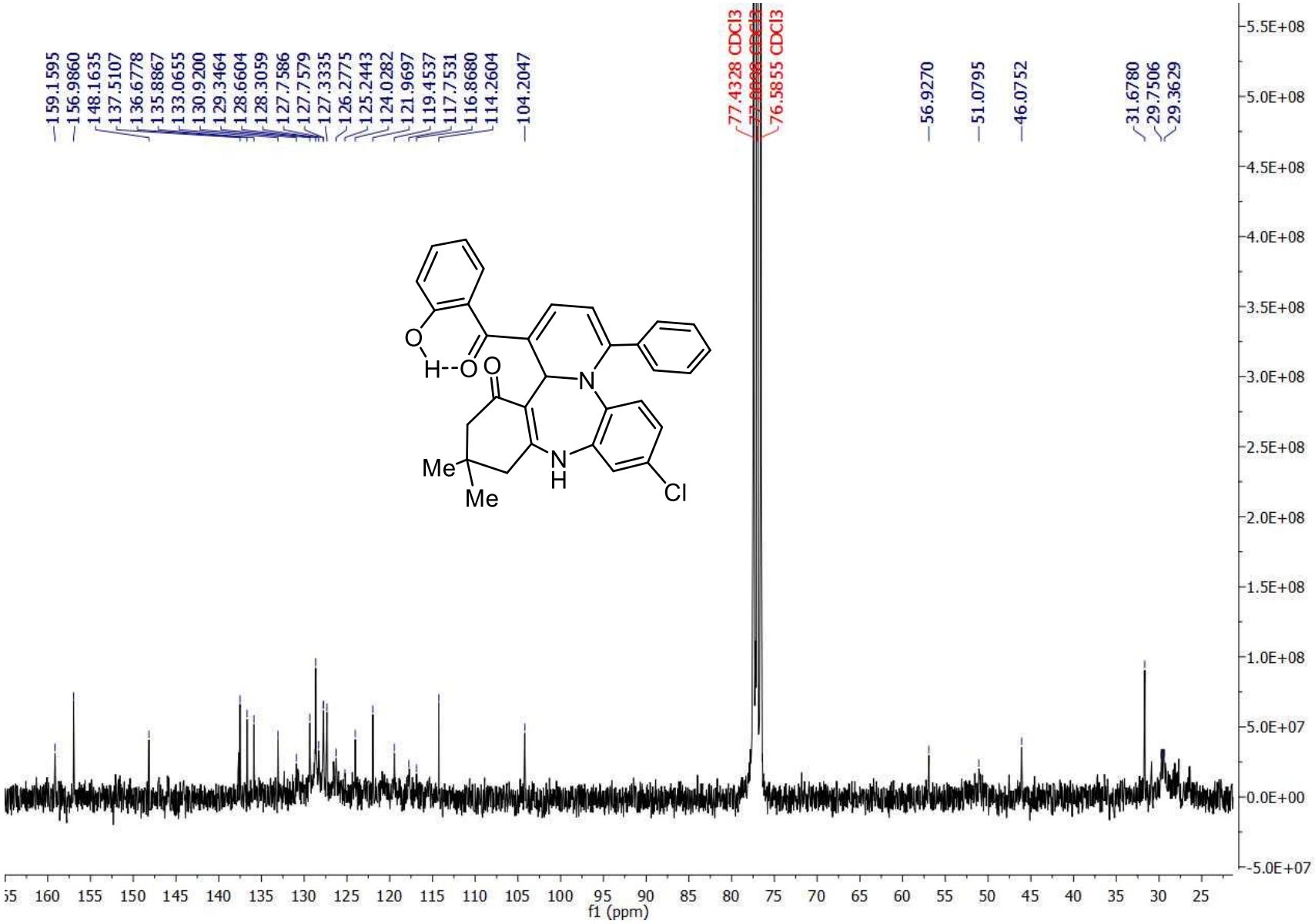
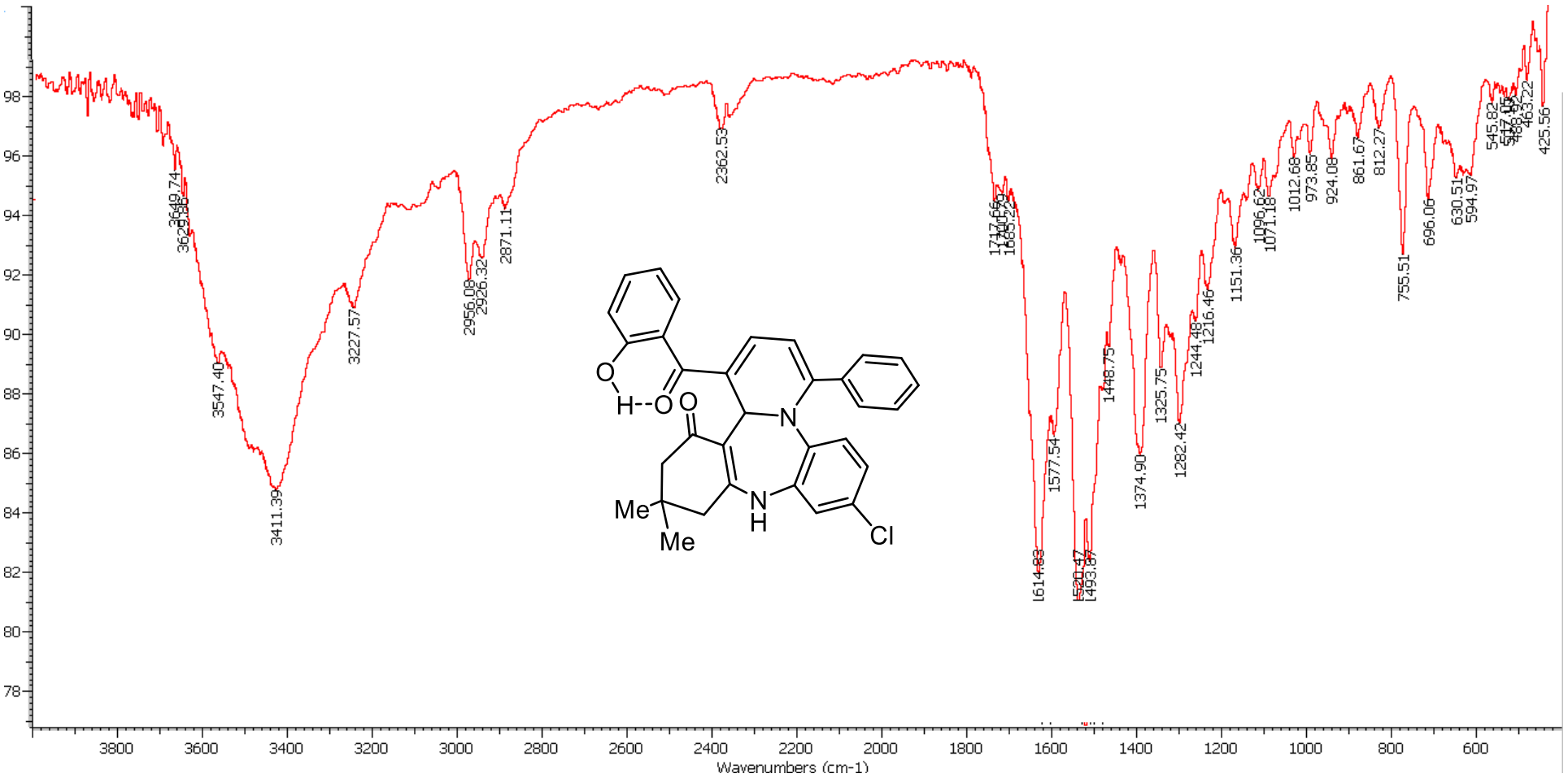
7.4325
7.4280
7.4242
7.4052
7.3995
7.2668
7.2406
7.2234
7.2164
7.2019
7.1840
7.1403
7.1186
7.0490
7.0216
6.9948
6.8258
6.8170
6.5259
6.5204
5.9884
5.6591
5.6379
2.3584
2.3056
2.2917
2.2546
2.1959
2.1415
2.0914
2.0431
1.9170
1.8681
1.0024
0.9799
O
H--O
O
N
N
H
Me
Me
Cl
0.91
1.00
2.44
2.88
3.13
3.80
4.64
2.97
2.72
1.15
1.04
0.98
2.68
2.33
2.52
2.85
5.57
f1 (ppm)

^{1}H NMR of **3e**

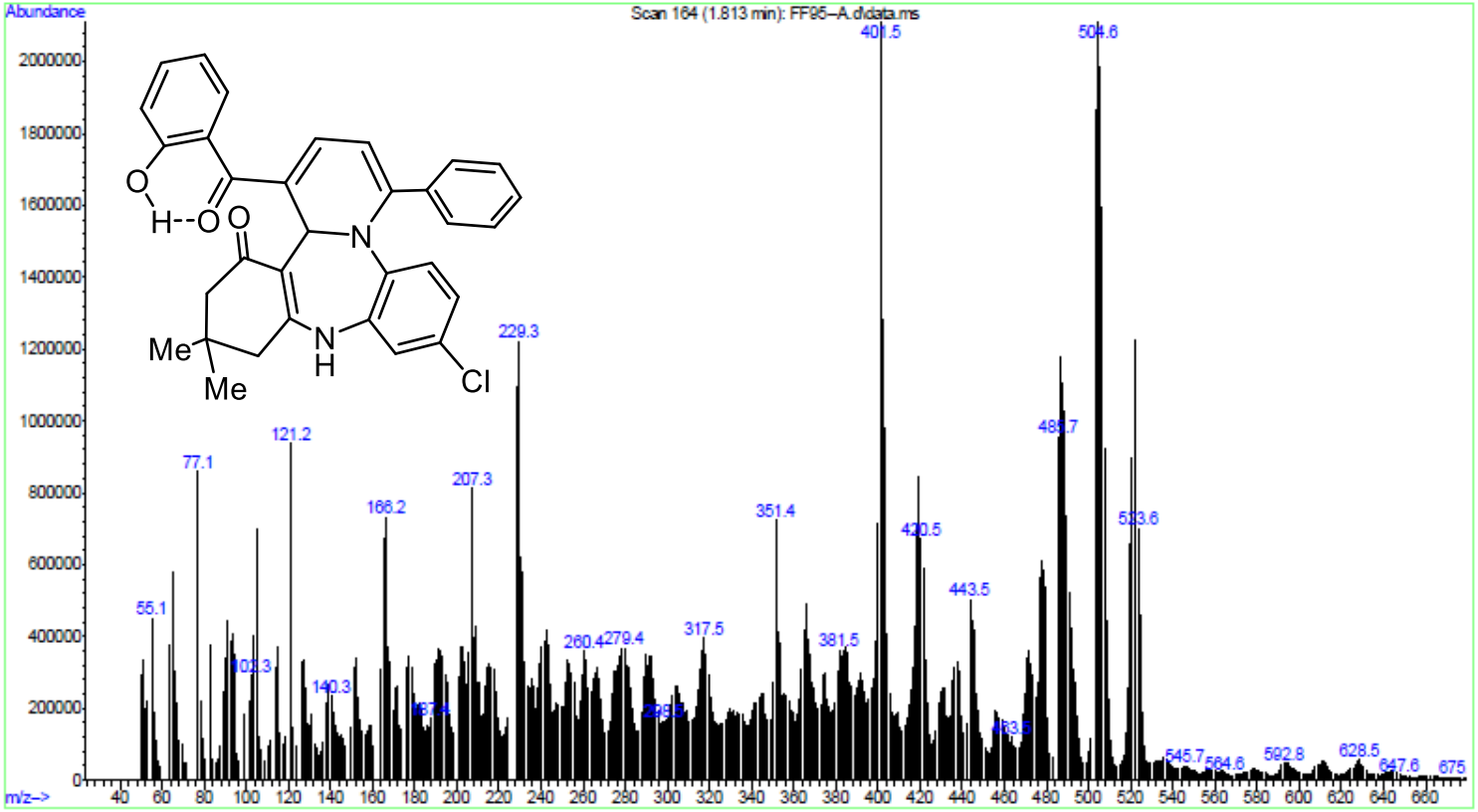

159.1595
156.9860
148.1635
137.5107
136.6778
135.8867
133.0655
130.9200
129.3464
128.6604
128.3059
127.7586
127.7579
127.3335
126.2775
125.2443
124.0282
121.9697
119.4537
117.7531
116.8680
114.2604
104.2047
77.4328 CDCl3
76.5855 CDCl3
56.9270
51.0795
46.0752
31.6780
29.7506
29.3629
O
H--O
O
N
N
H
Me
Me
Cl
5.5E+08
5.0E+08
4.5E+08
4.0E+08
3.5E+08
3.0E+08
2.5E+08
2.0E+08
1.5E+08
1.0E+08
5.0E+07
0.0E+00
-5.0E+07
160 155 150 145 140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25
f1 (ppm)

^{13}C NMR of **3e**

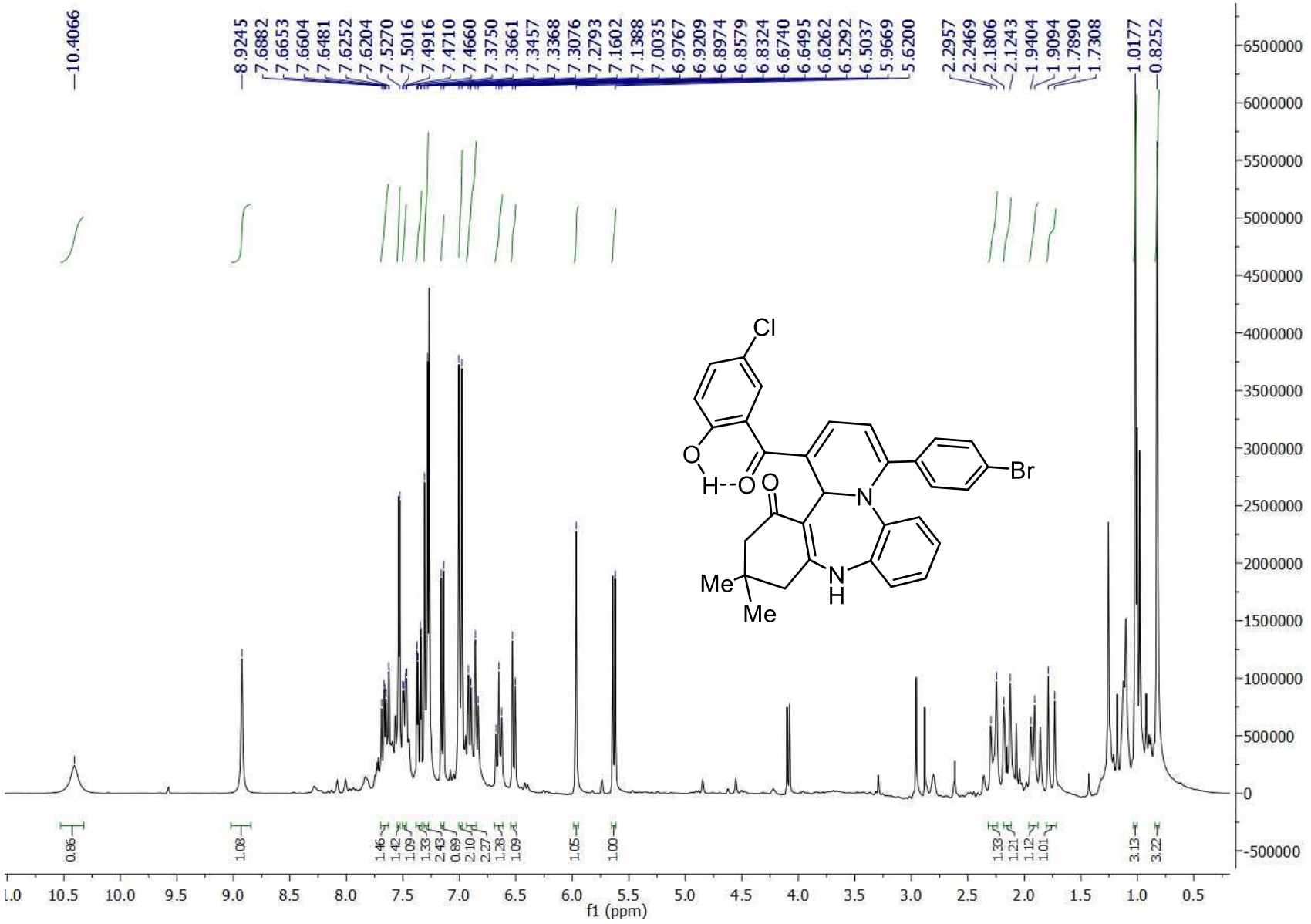

3649.74
3547.40
3411.39
3227.57
2956.09
2926.32
2871.11
2362.53
1717.66
1685.22
1614.83
1577.54
1520.47
1493.87
1448.75
1374.90
1325.75
1282.42
1244.48
1216.46
1151.36
1096.62
1071.18
1012.68
973.85
924.08
861.67
812.27
755.51
696.06
630.51
594.97
545.82
463.22
425.56
O
H--O
O
N
N
H
Me
Me
Cl
Wavenumbers (cm-1)

IR of **3e**

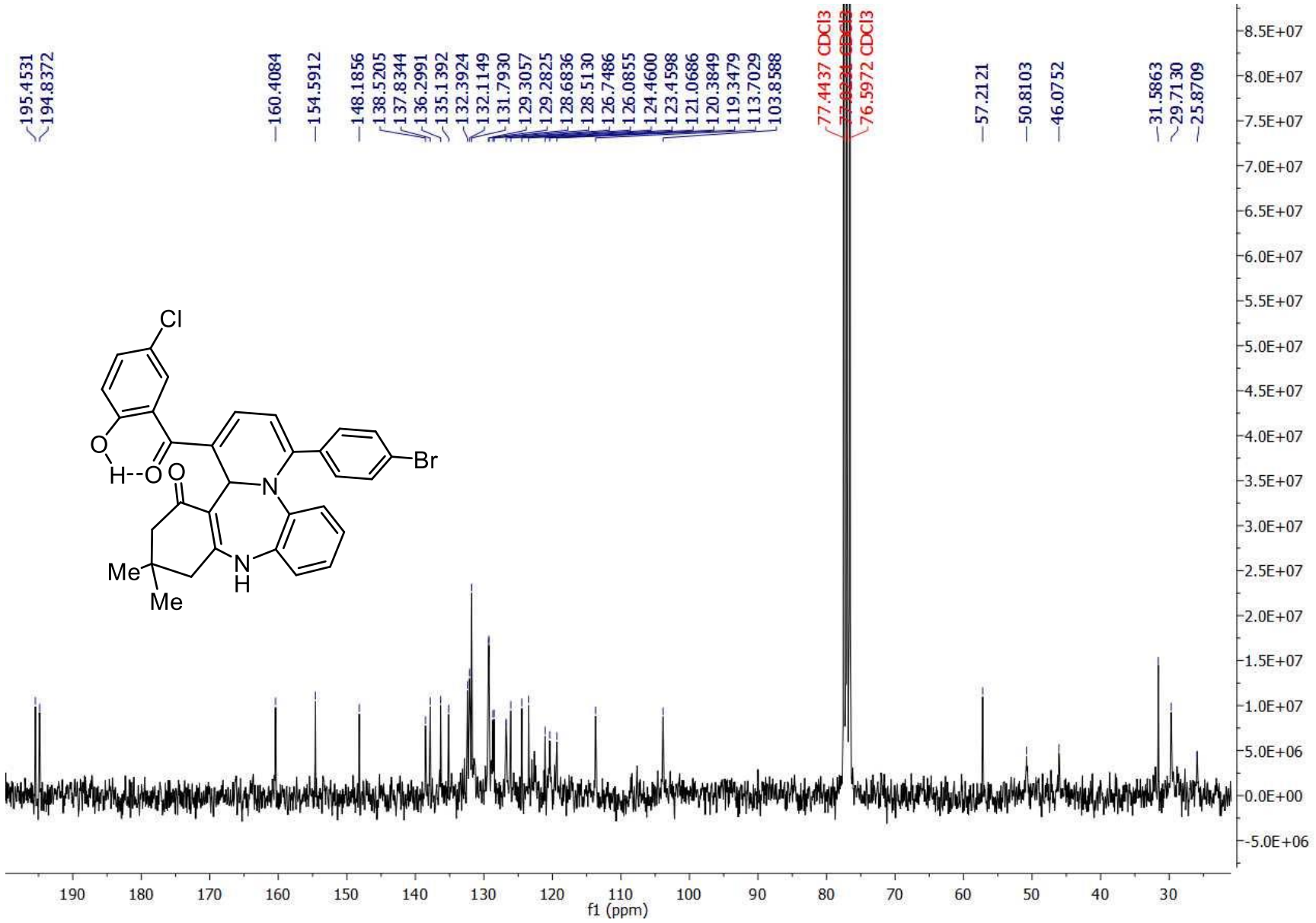
File C:\MSDCHEM\3\DATA\Snapshot\FF95--A.d
Acquired : 30 Aug 2021 12:07 using AcqMethod default.m
Instrument : DIRECT PROBE
Sample Name:
Misc Info :
Vial Number: 1



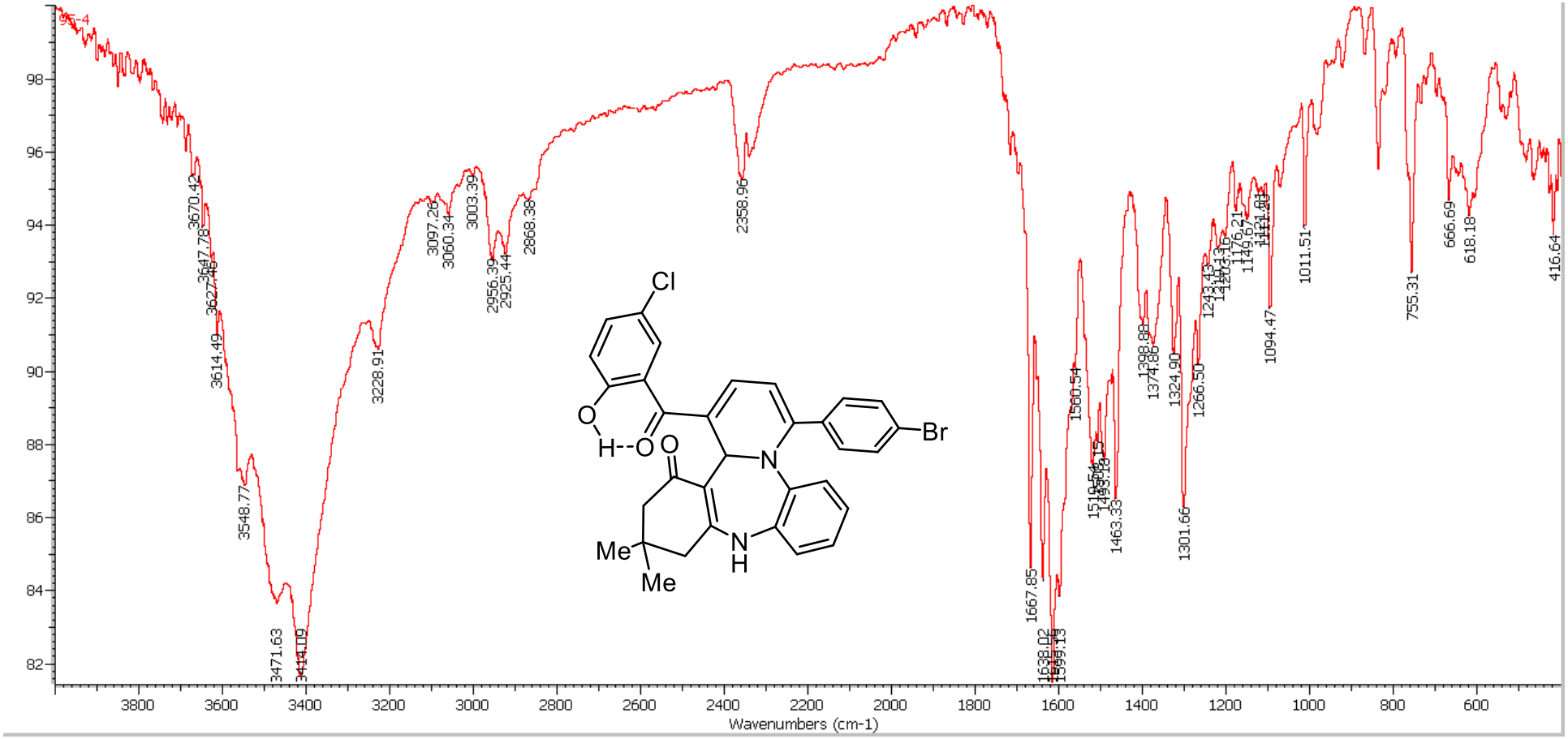
Mass of compound **3e**


10.4066
8.9245
7.6882
7.6653
7.6604
7.6481
7.6252
7.6204
7.5270
7.5016
7.4916
7.4710
7.4660
7.3750
7.3661
7.3457
7.3368
7.3076
7.2793
7.1602
7.1388
7.0035
6.9767
6.9209
6.8974
6.8579
6.8324
6.6740
6.6495
6.6262
6.5292
6.5037
5.9669
5.6200
2.2957
2.2469
2.1806
2.1243
1.9404
1.9094
1.7890
1.7308
1.0177
0.8252
Cl
O
H--O
O
Br
N
N
H
Me
Me
0.86
1.08
1.46
1.42
1.09
1.33
2.43
0.89
2.10
2.27
1.28
1.09
1.05
1.00
1.33
1.21
1.12
1.01
3.13
3.22
f1 (ppm)

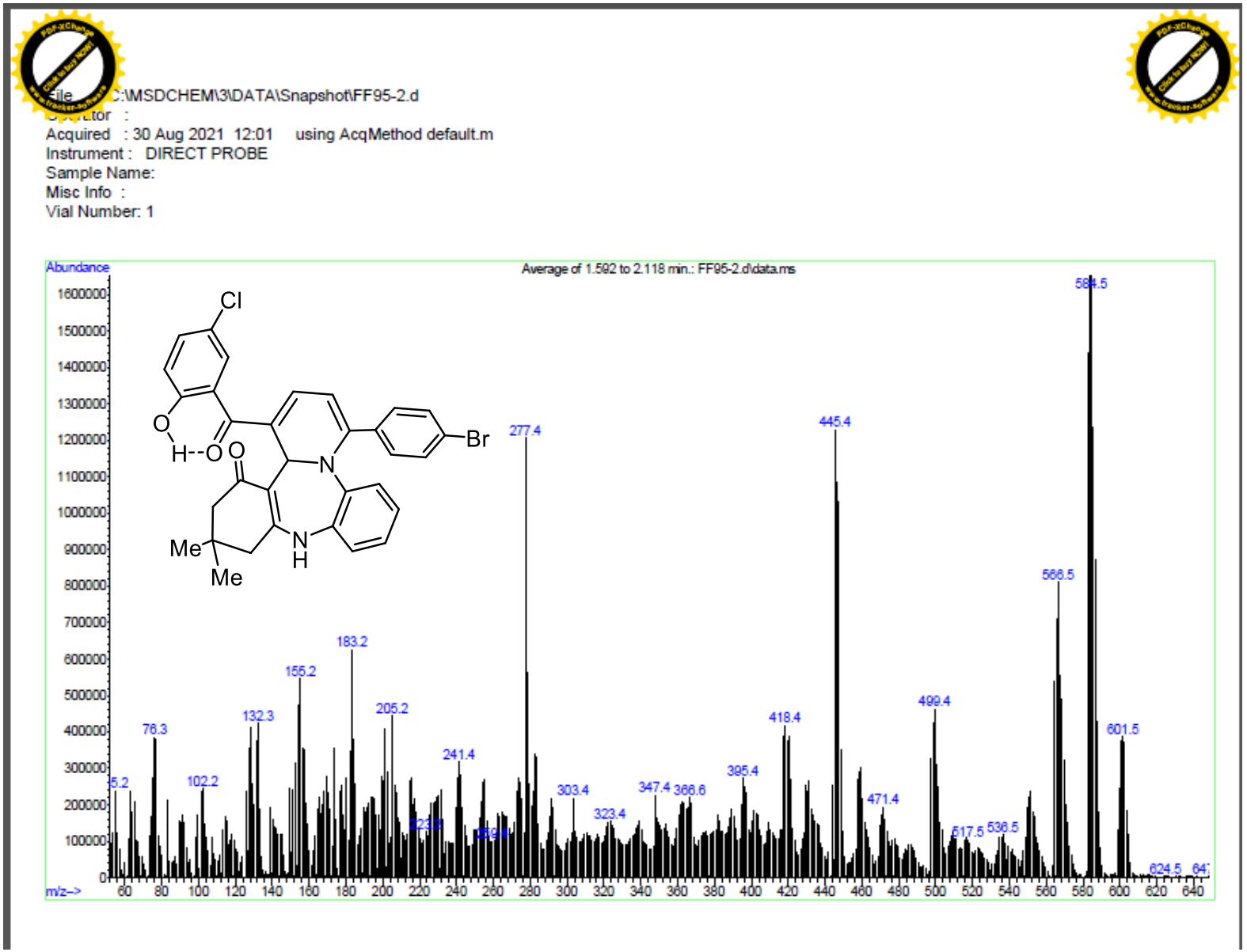
^{1}H NMR of **3f**


195.4531
194.8372
160.4084
154.5912
148.1856
138.5205
137.8344
136.2991
135.1392
132.3924
132.1149
131.7930
129.3057
129.2825
128.6836
128.5130
126.7486
126.0855
124.4600
123.4598
121.0686
120.3849
119.3479
113.7029
103.8588
77.4437 CDCl3
76.5972 CDCl3
57.2121
50.8103
46.0752
31.5863
29.7130
25.8709
Cl
O
H--O
O
N
Br
Me
Me
N
H
8.5E+07
8.0E+07
7.5E+07
7.0E+07
6.5E+07
6.0E+07
5.5E+07
5.0E+07
4.5E+07
4.0E+07
3.5E+07
3.0E+07
2.5E+07
2.0E+07
1.5E+07
1.0E+07
5.0E+06
0.0E+00
-5.0E+06
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
f1 (ppm)

^{13}C NMR of **3f**


Cl
O
H--O
O
N
Br
Me
Me
N
H
3670.42
3614.49
3548.77
3471.63
3414.09
3228.91
3097.26
3060.34
3003.39
2956.39
2925.44
2868.38
2358.96
1667.85
1560.54
1463.33
1398.88
1374.88
1324.90
1301.66
1266.50
1243.43
1094.47
1011.51
755.31
666.69
618.18
416.64
Wavenumbers (cm-1)

IR of **3f**



MS of compound **3f**