Advanced Synthesis & Catalysis

Supporting Information

Cobalt-Catalyzed Regioselective [4+2] Annulation/Lactonization of Benzamides with 4-Hydroxy-2-Alkynoates under Aerobic Conditions

Nachimuthu Muniraj, Anil Kumar, and Kandikere Ramaiah Prabhu*

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General experimental

All reactions were carried out using distilled solvents. Reactions were monitored by using precoated silica TLC plates. Mass spectra were recorded on EI, and ESI (TOF) modes. NMR spectra were recorded in 400 MHz spectrometers in $CDCl_3$, DMSO-d_6, tetramethylsilane (TMS; δ = 0.00 ppm) served as an internal standard for ^{1}H NMR. The corresponding residual non-deuterated solvent signal ($CDCl_3$; δ = 77.00 ppm and DMSO-d_6; δ = 39.52 ppm) was used as internal standard for ^{13}C NMR. Column chromatography was carried out on silica gel 230-400 mesh or 100-200 mesh (Merck), and thin-layer chromatography was carried out using SILICA GEL GF-254. Chemicals obtained from commercial suppliers were used without further purification.

All benzamide derivatives[1], *N*-(5-methoxyquinolin-8-yl)benzamide[2], 4-hydroxy-2-alkynoate derivatives[3] were prepared according to reported literature procedure.

General experimental procedure:

(a) Experimental procedure for [4+2] annulation/Lactonization of benzamides with 4-hydroxy-2-alkynoates

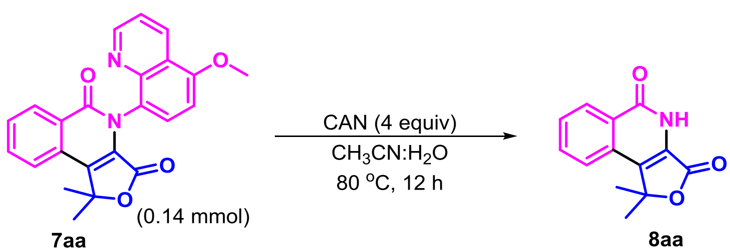
In a 10-mL round-bottom flask, benzamide derivatives **1** (0.2 mmol), 4-hydroxy-2-alkynoates **2** (0.3 mmol), $Co(acac)_2$ (7.7 mg, 15 mol%), NaOPiv. xH_2O (12.4 mg, 50 mol%) in DCE (1.5 mL) were taken and the reaction mixture was refluxed at 80 °C for 12 h in open-air. After completion of the reaction (monitored by TLC), the reaction mixture was concentrated under vacuum. The crude products were purified on a silica gel column using EtOAc/petroleum ether mixture.

(b) Experimental procedure for the scale-up reaction

In a 50-mL round-bottom flask, benzamide derivatives **1a** (496 mg, 2 mmol), 4-hydroxy-2-alkynoates **2a** (468 mg, 3 mmol), $Co(acac)_2$ (77 mg, 15 mol%), NaOPiv. xH_2O (124 mg, 50 mol%) in DCE (15 mL) were taken and the reaction mixture was refluxed at 80 °C for 12 h in oxygen atmosphere. After completion of the reaction (monitored by TLC), the reaction mixture was concentrated under vacuum. The crude products were purified on a silica gel column using EtOAc/petroleum ether mixture.

(c) Experimental procedure for removal of auxiliary directing group

The auxiliary directing group was removed using a slightly modified procedure of previously reported method.[4]

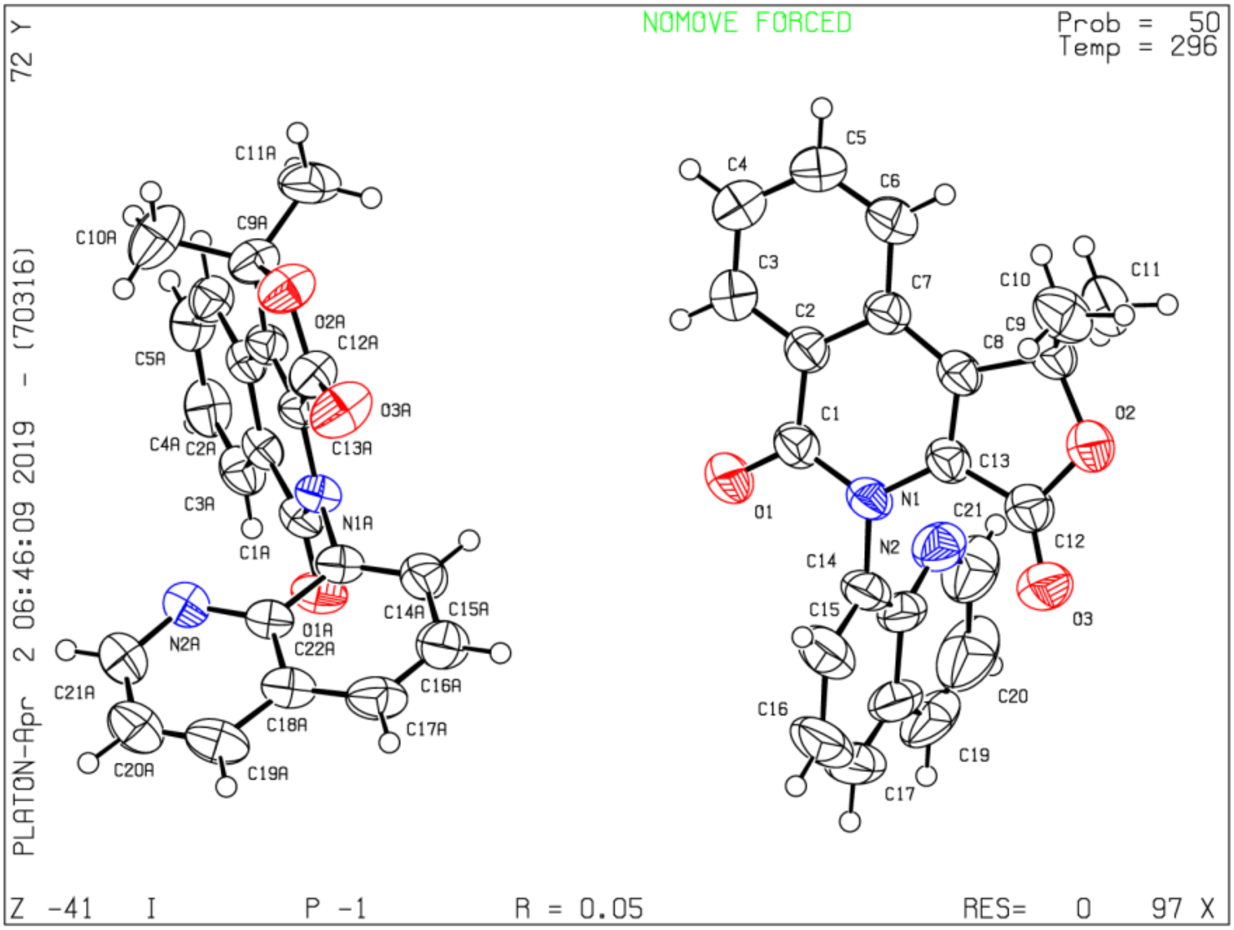


The compound **7aa** (0.14 mmol) was dissolved in a mixture of CH_3CN/H_2O (2.0 mL/0.4 mL) at room temperature. After the addition of CAN (312 mg, 4 equiv), the reaction mixture was stirred at 60 ^{o}C for 12 h. Then the reaction mixture was diluted with water (5 mL), extracted with ethyl acetate, washed with water, saturated aqueous $NaHCO_3$ and brine. The organic layer was dried over anhydrous Na_2SO_4. After removal of the solvent, the residue was purified on a flash column (silica gel) using ethylacetate/petroleum ether mixture to give the deprotected product **8aa** in 51% yield.

Crystal data for compound 3aa (CCDC 1914826)

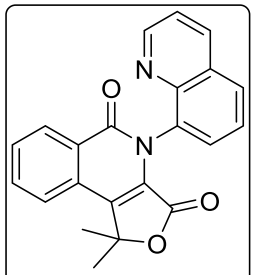
Empirical formula	$C_{22} H_{16} N_2 O_3$
Formula weight	356.37
Temperature	296(2) K
Wavelength	0.71073 Å
Crystal system	Triclinic
Space group	P -1
Unit cell dimensions	a = 10.149(6) Å α = 107.029(7)°. b = 12.088(7) Å β = 97.099(8)°. c = 15.908(9) Å γ = 103.463(8)°.
Volume	1775.7(17) $Å^3$
Z	4
Density (calculated)	1.333 Mg/m^3
Absorption coefficient	0.090 mm^{-1}
F(000)	744
Crystal size	0.082 x 0.070 x 0.067 mm^3
Theta range for data collection	1.368 to 28.357°.
Index ranges	-13<=h<=13, -16<=k<=16, -21<=l<=21
Reflections collected	63914
Independent reflections	8844 [R(int) = 0.0551]
Completeness to theta = 25.242°	100.0 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.7457 and 0.7049
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	8844 / 0 / 491
Goodness-of-fit on F^2	1.010
Final R indices [I>2sigma(I)]	R1 = 0.0508, wR2 = 0.1197
R indices (all data)	R1 = 0.1118, wR2 = 0.1500
Extinction coefficient	n/a
Largest diff. peak and hole	0.233 and -0.277 e.$Å^{-3}$

Crystal structure for compound 3aa (CCDC 1914826)



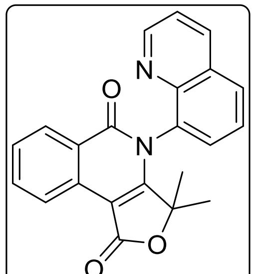
Characterization data for the products

1. **1,1-Dimethyl-4-(quinolin-8-yl)-1,4-dihydrofuro[3,4-c]isoquinoline-3,5-dione (3aa).** Brown solid; Yield – (60 mg, 84%); ***mp***: 239-241 °C; R_f (50% EtOAc/petroleum ether) 0.25; Prepared as shown in general experimental procedure (a). **IR** (Neat, cm^{-1}): 1761, 1672; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 1.88 (s, 3 H) 1.91 (s, 3 H) 7.39 (dd, *J* =8.24, 4.27 Hz, 1 H) 7.66 - 7.75 (m, 3 H) 7.79 - 7.81 (m, 1 H) 7.83 - 7.88 (m, 1 H) 7.98 (d, *J* =8.24 Hz, 1 H) 8.23 (dd, *J* =8.39, 1.37 Hz, 1 H) 8.64 (d, *J* =7.93 Hz, 1 H) 8.75 (dd, *J* =3.97, 1.53 Hz, 1 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 27.0, 82.8, 121.6, 123.7, 126.0, 126.9, 128.9, 129.5, 129.6, 129.8, 130.1, 130.6, 133.2, 133.4, 136.3, 144.6, 150.8, 162.5, 163.2; **HRESI-MS** *(mz)*: Calculated for $C_{22}H_{16}N_2O_3$ $(M + H)^+$: 357.1239, found $(M + H)^+$: 357.1237.



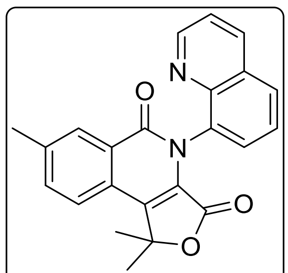
3aa

2. **3,3-Dimethyl-4-(quinolin-8-yl)furo[3,4-c]isoquinoline-1,5(3H,4H)-dione (3aa').** White solid; Yield – (8.5 mg mg, 12%); ***mp***: >250 °C; R_f (50% EtOAc/petroleum ether) 0.4; Prepared as shown in general experimental procedure (a). **IR** (Neat, cm^{-1}): 1751, 1679; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 0.81 (s, 3 H) 1.54 (s, 3 H) 7.47 (dd, *J*= 8.24, 4.27 Hz, 1 H) 7.59 (t, *J*= 7.63 Hz, 1 H) 7.73 (t, *J*= 7.78 Hz, 1 H) 7.80 - 7.86 (m, 2 H) 8.08 (d, *J*= 8.24 Hz, 1 H) 8.27 (d, *J*= 8.24 Hz, 1 H) 8.39 (d, *J*= 7.93 Hz, 1 H) 8.70 (d, *J*= 7.93 Hz, 1 H) 8.84 (d, *J*= 2.75 Hz, 1 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 24.6, 82.6, 100.7, 122.4, 123.3, 124.7, 125.7, 128.1, 128.9, 129.1, 130.8, 131.1, 131.6, 134.0, 136.3, 144.8, 151.7, 162.6, 163.9, 167.6; **HRESI-MS** *(mz)*: Calculated for $C_{22}H_{16}N_2O_3$ $(M + H)^+$: 357.1239, found $(M + H)^+$: 357.1242.



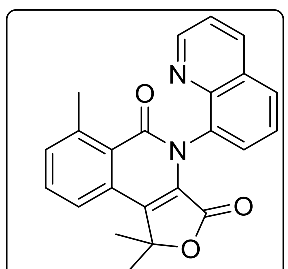
3aa'

3. **1,1,7-trimethyl-4-(quinolin-8-yl)-1,4-dihydrofuro[3,4-c]isoquinoline-3,5-dione (3ba).** Brown solid; Yield – (68 mg, 92%); ***mp***: >250 °C; R_f (50% EtOAc/petroleum ether) 0.25; Prepared as shown in general experimental procedure (a). **IR** (Neat, cm^{-1}): 1759, 1671; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 1.87 (s, 3 H) 1.90 (s, 3 H) 2.57 (s, 3 H) 7.41 (dd, *J*= 8.24, 4.27 Hz, 1 H) 7.63 - 7.71 (m, 3 H) 7.81 (dd, *J*=7.32, 1.22 Hz, 1 H) 7.99 (dd, *J*= 8.24, 1.22 Hz, 1 H) 8.24 (dd, *J*= 8.39, 1.37 Hz, 1 H) 8.46 (s, 1 H) 8.78 (dd, *J*= 4.27, 1.53 Hz, 1 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 21.8, 27.0, 82.7, 121.7, 123.7, 126.0, 126.0, 127.7, 128.8, 129.0, 129.5, 129.6, 130.5, 133.5, 134.5, 135.6, 136.4, 140.6, 144.6, 150.7, 162.5, 163.3; **HRESI-MS** *(mz)*: Calculated for $C_{23}H_{18}N_2O_3$ $(M + H)^+$: 371.1396, found $(M + H)^+$: 371.1396.



3ba

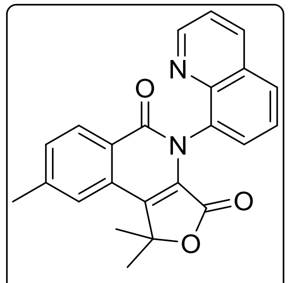
4. **1,1,6-Trimethyl-4-(quinolin-8-yl)-1,4-dihydrofuro[3,4-c]isoquinoline-3,5-dione (3ca).** brown solid; Yield – (68 mg, 92%); ***mp***: 208-210 °C; R_f (50% EtOAc/petroleum ether) 0.3;



3ca

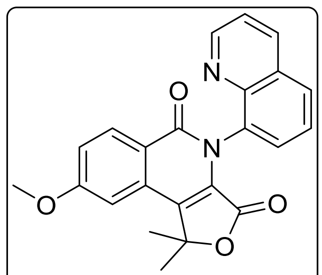
Prepared as shown in general experimental procedure (a). **IR** (Neat, cm^{-1}): 1760, 1673; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 1.87 (s, 3 H) 1.90 (s, 3 H) 2.93 (s, 3 H) 7.40 (dd, *J*= 8.24, 3.97 Hz, 1 H) 7.50 (d, *J*= 7.63 Hz, 1 H) 7.57 (d, *J*= 7.63 Hz, 1 H) 7.70 (t, *J*= 7.78 Hz, 2 H) 7.80 (d, *J*= 6.71 Hz, 1 H) 7.98 (d, *J*=7.93 Hz, 1 H) 8.23 (d, *J*= 8.24 Hz, 1 H) 8.77 (d, *J*= 2.75 Hz, 1 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 24.5, 83.1, 121.7, 122.0, 126.1, 126.8, 127.0, 129.1, 129.4, 129.7, 131.7, 132.4, 133.4, 133.6, 135.1, 136.4, 147.8, 145.0, 150.8, 163.1, 163.4; **HRESI-MS** *(mz)*: Calculated for $C_{23}H_{18}N_2O_3$ $(M + H)^+$: 371.1396, found $(M + H)^+$: 371.1395.

5. **1,1,8-Trimethyl-4-(quinolin-8-yl)-1,4-dihydrofuro[3,4-c]isoquinoline-3,5-dione (3da).** Brown solid; Yield – (65 mg, 88%); ***mp***: >250 °C; R_f (50% EtOAc/petroleum ether) 0.25; Prepared as shown in general experimental procedure (a). **IR** (Neat, cm^{-1}): 1759, 1670; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 1.88 (s, 3 H) 1.92 (s, 3 H) 2.61 (s, 3 H) 7.40 (dd, *J*= 8.24, 4.27 Hz, 1 H) 7.49 (s, 1 H) 7.54 (d, *J*= 8.24 Hz, 1 H) 7.69 (t, *J*= 7.78 Hz, 1 H) 7.80 (dd, *J*= 7.32, 1.22 Hz, 1 H) 7.98 (dd, *J*= 8.24, 1.22 Hz, 1 H) 8.24 (d, *J*= 7.32 Hz, 1 H) 8.53 (d, *J*= 8.24 Hz, 1 H) 8.76 (dd, *J*= 3.97, 1.53 Hz, 1 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 22.2, 27.1, 82.8, 121.7, 123.6, 126.0, 126.6, 126.9, 129.0, 129.5, 129.6, 130.2, 130.6, 131.2, 133.5, 135.1, 136.3, 144.2, 144.7, 150.8, 162.6, 163.3; **HRESI-MS** *(mz)*: Calculated for $C_{23}H_{18}N_2O_3$ $(M + H)^+$: 371.1396, found $(M + H)^+$: 371.1393.



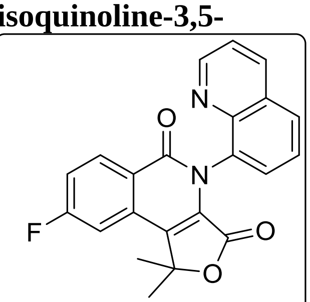
3da

6. **8-Methoxy-1,1-dimethyl-4-(quinolin-8-yl)-1,4-dihydrofuro[3,4-c]isoquinoline-3,5-dione (3ea).** Brown solid; Yield – (65 mg, 84%); ***mp***: >250 °C; R_f (50% EtOAc/petroleum ether) 0.2; Prepared as shown in general experimental procedure (a). **IR** (Neat, cm^{-1}): 1760, 1669; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 1.86 (s, 3 H) 1.89 (s, 3 H) 3.97 (s, 3 H) 7.08 (d, *J* =2.44 Hz, 1 H) 7.25 - 7.28 (m, 1 H) 7.38 (dd, *J*=8.39, 4.12 Hz, 1 H) 7.67 (t, *J* =7.74 Hz, 1 H) 7.78 - 7.80 (m, 1 H) 7.97 (d, *J*= 8.24 Hz, 1 H) 8.22 (dd, *J*= 8.24, 1.53 Hz, 1 H) 8.57 (d, *J*= 8.85 Hz, 1 H) 8.75 (dd, *J*=3.97, 1.53 Hz, 1 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 26.9, 55.8, 82.7, 107.2, 116.7, 121.6, 122.2, 126.0, 127.5, 129.0, 129.4, 129.6, 131.9, 132.8, 133.4, 134.6, 136.3, 144.7, 150.8, 162.3, 163.2, 163.3; **HRESI-MS** *(mz)*: Calculated for $C_{23}H_{18}N_2O_4$ $(M + H)^+$: 387.1345, found $(M + H)^+$: 387.1341.



3ea

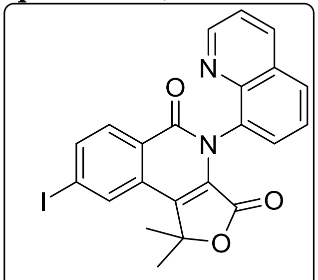
7. **8-Fluoro-1,1-dimethyl-4-(quinolin-8-yl)-1,4-dihydrofuro[3,4-c]isoquinoline-3,5-dione (3fa).** Brown solid; Yield – (67.5 mg, 90%); ***mp***: 219-221 °C; R_f (50% EtOAc/petroleum ether) 0.25; Prepared as shown in general experimental procedure (a). **IR** (Neat, cm^{-1}): 1761, 1674; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 1.86 (s, 3 H) 1.89 (s, 3 H) 7.33 - 7.44 (m, 3 H) 7.68 (t, *J*= 7.40 Hz, 1 H) 7.79 (dd,



3fa

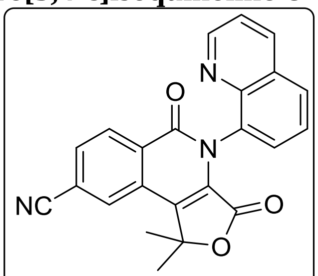
J= 7.33, 1.26 Hz, 1 H) 7.99 (dd, *J*= 8.27, 1.33 Hz, 1 H) 8.23 (dd, *J*= 8.34, 1.64 Hz, 1 H) 8.66 (dd, *J*= 8.91, 5.75 Hz, 1 H) 8.75 (dd, *J*= 4.23, 1.71 Hz, 1 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 26.8, 26.9, 82.7, 109.5 (d, $J_{C\text{-}F}$ = 23.3 Hz), 117.9 (d, $J_{C\text{-}F}$ = 22.5 Hz), 121.8, 125.3 (d, $J_{C\text{-}F}$ = 2.0 Hz), 126.0, 128.2, 129.0, 129.5, 129.6, 132.2 (d, $J_{C\text{-}F}$ = 9.6 Hz), 133.0, 133.9 (d, $J_{C\text{-}F}$ = 9.8 Hz), 134.0 (d, $J_{C\text{-}F}$ = 3.6 Hz), 136.4, 144.5, 150.8, 161.9, 162.8, 165.5 (d, $J_{C\text{-}F}$ = 254.0 Hz); **HRESI-MS** *(mz)*: Calculated for $C_{22}H_{15}FN_2O_3$ $(M + H)^+$: 375.1145, found $(M + H)^+$: 375.1145.

8. **8-Iodo-1,1-dimethyl-4-(quinolin-8-yl)-1,4-dihydrofuro[3,4-c]isoquinoline-3,5-dione (3ga).** Pale Brown solid; Yield – (81 mg, 84%); ***mp***: 250-252 °C; R_f (50% EtOAc/petroleum ether) 0.25; Prepared as shown in general experimental procedure (a). **IR** (Neat, cm^{-1}): 1762, 1673; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 1.87 (s, 3 H) 1.90 (s, 3 H) 7.40 (dd, *J*= 8.21, 4.17 Hz, 1 H) 7.69 (t, *J*= 7.77 Hz, 1 H) 7.79 (dd, *J*= 7.33, 1.26 Hz, 1 H) 7.97 - 8.06 (m, 3 H) 8.23 (dd, *J*= 8.34, 1.52 Hz, 1 H) 8.32 (d, *J*= 8.46 Hz, 1 H) 8.74 (dd, *J*= 4.17, 1.52 Hz, 1 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 27.0, 27.1, 82.7, 101.2, 121.7, 126.0, 128.0, 128.0, 129.0, 129.5, 129.6, 131.6, 132.0, 132.5, 133.0, 133.4, 136.4, 138.7, 144.4, 150.8, 162.3, 162.7; **HRESI-MS** *(mz)*: Calculated for $C_{22}H_{15}IN_2O_3$ $(M + H)^+$: 483.0206, found $(M + H)^+$: 483.0208.



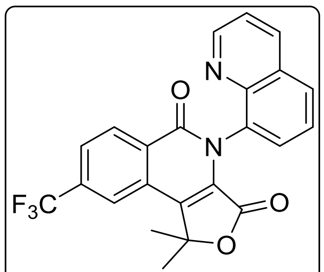
3ga

9. **1,1-Dimethyl-3,5-dioxo-4-(quinolin-8-yl)-1,3,4,5-tetrahydrofuro[3,4-c]isoquinoline-8-carbonitrile (3ha).** White solid; Yield – (60 mg, 79%); ***mp***: 250 °C; R_f (50% EtOAc/petroleum ether) 0.25; Prepared as shown in general experimental procedure (a). **IR** (Neat, cm^{-1}): 2233, 1762, 1674; **^{1}H NMR** (400 MHz, DMSO-d_6): δ 1.84 (s, 6 H) 7.56 (dd, *J*= 8.27, 4.23 Hz, 1 H) 7.74 (t, *J*= 7.83 Hz, 1 H) 7.91 (dd, *J*= 7.33, 1.26 Hz, 1 H) 8.16 (td, *J*=9.03, 1.26 Hz, 2 H) 8.48 - 8.53 (m, 2 H) 8.64 (s, 1 H) 8.75 (dd, *J*= 4.23, 1.58 Hz, 1 H); **^{13}C NMR** (100 MHz, DMSO-d_6): δ 26.1, 26.5, 83.6, 116.7, 118.0, 122.3, 126.3, 127.9, 128.7, 129.3, 129.8, 130.0, 130.1, 130.6, 130.7, 132.8, 133.0, 133.8, 136.8, 144.1, 151.2, 161.1, 162.5; **HRESI-MS** *(mz)*: Calculated for $C_{23}H_{15}N_3O_3$ $(M + H)^+$: 382.1192, found $(M + H)^+$: 382.1195.



3ha

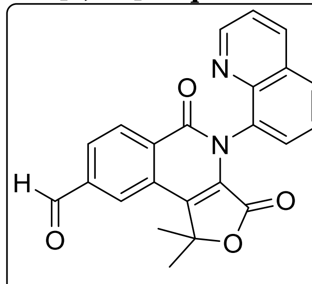
10. **1,1-Dimethyl-4-(quinolin-8-yl)-8-(trifluoromethyl)-1,4-dihydrofuro[3,4-c]isoquinoline-3,5-dione (3ia).** White solid; Yield – (68 mg, 82%); ***mp***: 238-240 °C; R_f (5% EtOAc/DCM) 0.3; Prepared as shown in general experimental procedure (a). **IR** (Neat, cm^{-1}): 1766, 1679; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 1.94 (s, 3 H) 1.95 (s, 3 H) 7.42 (dd, *J*= 8.34, 4.17 Hz, 1 H) 7.70 (t, *J*= 7.77 Hz, 1 H) 7.81 (dd, *J*=7.33, 1.26 Hz, 1 H) 7.93 - 7.95 (m, 2 H) 8.01 (dd, *J*= 8.34, 1.14 Hz, 1 H) 8.24 (dd, *J*= 8.34, 1.52 Hz, 1 H) 8.73 - 8.78 (m, 2 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 27.0,



3ia

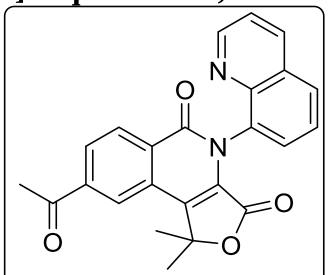
27.1, 82.7, 120.6 (q, $J_{C\text{-}F}$ = 7.5 Hz) 121.8, 123.3 (q, $J_{C\text{-}F}$ = 271.0 Hz), 125.8 (q, $J_{C\text{-}F}$ = 6.2 Hz), 125.9, 128.4, 129.0, 129.4, 129.7, 130.4, 131.2, 131.7, 132.8, 133.9, 135.0 (q, $J_{C\text{-}F}$ = 32.4 Hz), 136.3, 144.4, 150.8, 161.7, 162.6 ; **HRESI-MS** *(mz)*: Calculated for $C_{23}H_{15}F_3N_2O_3$ $(M + H)^+$: 425.1113, found $(M + H)^+$: 425.1112.

11. 1,1-Dimethyl-3,5-dioxo-4-(quinolin-8-yl)-1,3,4,5-tetrahydrofuro[3,4-c]isoquinoline-8-carbaldehyde (3ja). Brown solid; Yield – (58 mg, 75%); ***mp***: >250 °C; R_f (50% EtOAc/petroleum ether) 0.25; Prepared as shown in general experimental procedure (a). **IR** (Neat, cm^{-1}): 1761, 1705, 1671; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 1.96 (s, 3 H) 1.93 (s, 3 H) 7.43 (dd, *J*= 8.27, 4.23 Hz, 1 H) 7.68 (t, *J*= 7.60 Hz, 1 H) 7.80 - 7.82 (m, 1 H) 8.02 (d, *J*= 8.21 Hz, 1 H) 8.16 - 8.26 (m, 3 H) 8.76 - 8.81 (m, 2 H) 10.27 (s, 1 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 27.1, 27.1, 82.9, 121.8, 124.6, 126.0, 128.1, 129.0, 129.5, 129.7, 130.6, 131.8, 132.6, 132.8, 134.6, 136.5, 139.1, 144.3, 150.8, 161.9, 162.7, 191.1; **HRESI-MS** *(mz)*: Calculated for $C_{23}H_{16}N_2O_4$ $(M + H)^+$: 385.1188, found $(M + H)^+$: 385.1186.



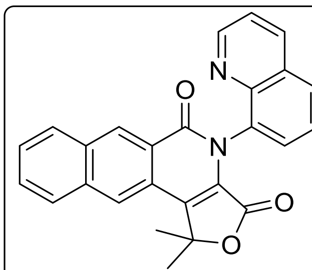
3ja

12. 8-Acetyl-1,1-dimethyl-4-(quinolin-8-yl)-1,4-dihydrofuro[3,4-c]isoquinoline-3,5-dione (3ka). white solid; Yield – (62 mg, 78%); ***mp***: >250 °C; R_f (50% EtOAc/petroleum ether) 0.2; Prepared as shown in general experimental procedure (a). **IR** (Neat, cm^{-1}): 1762, 1673; **^{1}H NMR** (400 MHz, DMSO-d_6): δ 1.86 (s, 6 H) 2.79 (s, 3 H) 7.56 (dd, *J*= 8.21, 4.17 Hz, 1 H) 7.75 (t, *J*= 7.83 Hz, 1 H) 7.91 (d, *J*= 7.20 Hz, 1 H) 8.15 (d, *J*= 8.08 Hz, 1 H) 8.28 - 8.30 (m, 2 H) 8.48 – 8.53 (m, 1 H) 8.75 (d, *J*= 2.91 Hz, 1 H); **^{13}C NMR** (100 MHz, DMSO-d_6): δ 26.5, 26.9, 27.6, 83.3, 122.3, 124.1, 126.4, 127.3, 128.7, 129.1, 129.7, 129.9, 130.2, 130.4, 130.8, 133.2, 134.8, 136.9, 140.9, 144.2, 151.2, 161.5, 162.7, 198.4 ; **HRESI-MS** *(mz)*: Calculated for $C_{24}H_{18}N_2O_4$ $(M + H)^+$: 399.1345, found $(M + H)^+$: 399.1346.



3ka

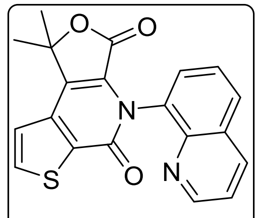
13. 1,1-Dimethyl-4-(quinolin-8-yl)-1,4-dihydrobenzo[g]furo[3,4-c]isoquinoline-3,5-dione (3la). Pale Brown solid; Yield – (75 mg, 92%); ***mp***: >250 °C; R_f (50% EtOAc/petroleum ether) 0.3; Prepared as shown in general experimental procedure (a). **IR** (Neat, cm^{-1}): 1757, 1672; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 1.98 (s, 3 H) 2.01 (s, 3 H) 7.41 (dd, *J*= 8.21, 4.17 Hz, 1 H) 7.65 - 7.74 (m, 3 H) 7.85 (d, *J*= 7.20 Hz, 1 H) 8.00 (d, *J*= 8.21 Hz, 1 H) 8.08 (d, *J*= 8.34 Hz, 1 H) 8.14 (d, *J*= 8.08 Hz, 1 H) 8.17 (s, 1 H) 8.25 (d, *J*= 7.96 Hz, 1 H) 8.76 (d, *J*= 4.04 Hz, 1 H) 9.22 (s, 1 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 27.1, 82.8, 121.6, 123.4, 125.7, 126.0,



3la

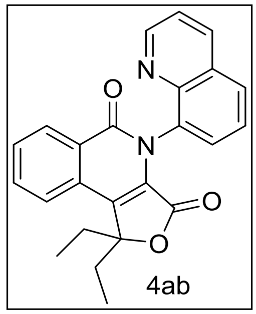
126.5, 127.8, 128.2, 129.0, 129.2, 129.4, 129.8, 129.8, 132.3, 133.0, 133.5, 135.0, 135.8, 136.4, 144.8, 150.7, 163.1, 163.5; **HRESI-MS** *(mz)*: Calculated for $C_{26}H_{18}N_2O_3$ (M + H)$^+$: 407.1396, found (M + H)$^+$: 407.1396.

14. 1,1-Dimethyl-4-(quinolin-8-yl)-1,4-dihydrofuro[3,4-b]thieno[3,2-d]pyridine-3,5-dione (3ma). Brown solid; Yield – (65 mg, 90%); ***mp***: >250 °C; R_f (50% EtOAc/petroleum ether) 0.2; Prepared as shown in general experimental procedure (a). **IR** (Neat, cm^{-1}): 1761, 1663; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 1.81 (s, 3 H) 1.85 (s, 3 H) 7.39 - 7.42 (m, 2 H) 7.69 (t, *J*=7.77 Hz, 1 H) 7.82 (dd, *J*=7.33, 1.26 Hz, 1 H) 7.95 - 8.01 (m, 2 H) 8.23 (dd, *J*=8.34, 1.52 Hz, 1 H) 8.77 (dd, *J*=4.17, 1.64 Hz, 1 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 26.9, 82.1, 121.7, 121.9, 125.9, 127.9, 129.0, 129.6, 129.7, 132.7, 134.2, 135.9, 136.3, 136.6, 137.2, 144.6, 150.9, 158.6, 163.0; **HRESI-MS** *(mz)*: Calculated for $C_{20}H_{14}N_2O_3S$ (M + H)$^+$: 363.0803, found (M + H)$^+$: 363.0804.



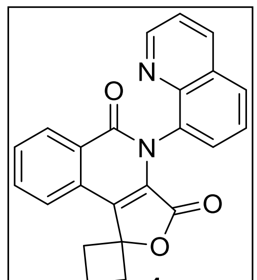
3ma

15. 1,1-Diethyl-4-(quinolin-8-yl)-1,4-dihydrofuro[3,4-c]isoquinoline-3,5-dione (4ab). Pale Brown solid; Yield – (62 mg, 81%); ***mp***: 178-181 °C; R_f (50% EtOAc/petroleum ether) 0.25; Prepared as shown in general experimental procedure (a). **IR** (Neat, cm^{-1}): 1757, 1674; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 0.78 (t, *J*= 7.32 Hz, 3 H) 0.89 (t, *J*= 7.17 Hz, 3 H) 2.16 - 2.36 (m, 4 H) 7.37 (dd, *J*= 8.24, 3.97 Hz, 1 H) 7.68 - 7.73 (m, 3 H) 7.81 - 7.87 (m, 2 H) 7.97 (d, *J*= 8.24 Hz, 1 H) 8.21 (d, *J*= 8.24 Hz, 1 H) 8.63 - 8.67(m, 2 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 7.4, 7.6, 31.1, 31.4, 88.5, 121.6, 123.2, 125.9, 128.6, 128.9, 129.1, 129.3, 129.5, 129.8, 130.4, 130.6, 131.0, 133.3, 133.4, 136.1, 144.5, 150.5, 162.6, 164.0 ; **HRESI-MS** *(mz)*: Calculated for $C_{24}H_{20}N_2O_3$ (M + H)$^+$: 385.1552, found (M + H)$^+$: 385.1554.



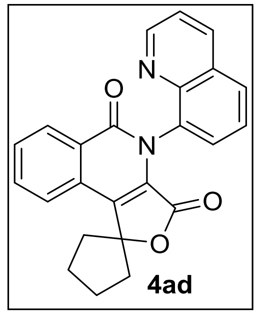
4ab

16. 4'-(Quinolin-8-yl)-3'H-spiro[cyclobutane-1,1'-furo[3,4-c]isoquinoline]-3',5'(4'H)-dione (4ac). Pale yellow solid; Yield – (69 mg, 94%); ***mp***: 220-222 °C; R_f (50% EtOAc/petroleum ether) 0.25; Prepared as shown in general experimental procedure (a). **IR** (Neat, cm^{-1}): 1763, 1671; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 2.23 - 2.33 (m, 1 H) 2.42 - 2.54 (m, 1 H) 2.79 (qd, *J*= 9.26, 4.27 Hz, 2 H) 3.04 - 3.17 (m, 2 H) 7.40 (dd, *J*= 8.24, 4.27 Hz, 1 H) 7.66 - 7.70 (m, 1 H) 7.73 - 7.77 (m, 2 H) 7.91 (t, *J*= 7.32 Hz, 1 H) 7.97 – 8.03 (m, 2 H) 8.22 - 8.24 (m, 1 H) 8.65 (d, *J*= 7.93 Hz, 1 H) 8.77 (dd, *J*= 3.97, 1.22 Hz, 1 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 13.8, 32.8, 32.9, 85.8, 121.6, 123.0, 126.0, 126.8, 128.8, 129.0, 129.5, 129.6, 129.8, 130.6, 130.7, 131.6, 133.3, 133.4, 136.3, 144.6, 150.8, 162.4, 163.0; **HRESI-MS** *(mz)*: Calculated for $C_{23}H_{16}N_2O_3$ (M + H)$^+$: 369.1239, found (M + H)$^+$: 369.1241.

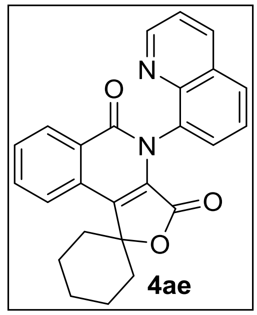


4ac

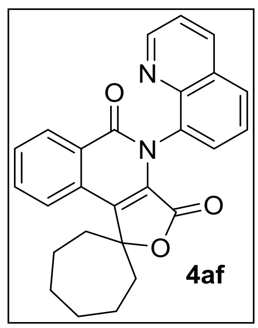
17. 4'-(Quinolin-8-yl)-3'H-spiro[cyclopentane-1,1'-furo[3,4-c]isoquinoline]-3',5'(4'H)-dione (4ad). Pale Brown solid; Yield – (68 mg, 89%); ***mp***: 241-243 °C; R_f (50% EtOAc/petroleum ether) 0.25; Prepared as shown in general experimental procedure (a). **IR** (Neat, cm^{-1}): 1764, 1674; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 2.03 - 2.17 (m, 6 H) 2.45 - 2.55 (m, 2 H) 7.39 (dd, *J*= 8.24, 3.97 Hz, 1 H) 7.63 - 7.72 (m, 3 H) 7.77 - 7.84 (m, 2 H) 7.96 – 7.98 (m, 1 H) 8.22 (dd, *J*= 8.55, 1.53 Hz, 1 H) 8.64 (d, *J*= 7.93 Hz, 1 H) 8.76 (dd, *J*= 4.27, 1.53 Hz, 1 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 25.3, 25.4, 38.4, 38.5, 92.8, 121.6, 123.3, 125.9, 127.2, 128.8, 129.0, 129.5, 129.5, 129.7, 130.3, 130.6, 132.0, 133.1, 133.4, 136.3, 144.6, 150.8, 162.5, 163.2; **HRESI-MS** *(mz)*: Calculated for $C_{24}H_{18}N_2O_3$ $(M + H)^+$: 383.1396, found $(M + H)^+$: 383.1394.



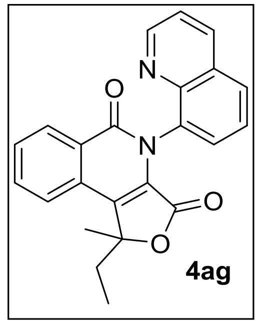
18. 4'-(quinolin-8-yl)-3'H-spiro[cyclohexane-1,1'-furo[3,4-c]isoquinoline]-3',5'(4'H)-dione (4ae). White solid; Yield – (66 mg, 83%); ***mp***: >250 °C; R_f (50% EtOAc/petroleum ether) 0.25; Prepared as shown in general experimental procedure (a). **IR** (Neat, cm^{-1}): 1760, 1672; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 1.41 - 1.48 (m, 1 H) 1.84 - 2.04 (m, 7 H) 2.29 - 2.37 (m, 2 H) 7.39 (dd, *J*= 8.24, 4.27 Hz, 1 H) 7.66 - 7.72 (m, 2 H) 7.77 - 7.79 (m, 1 H) 7.82 - 7.87 (m, 2 H) 7.98 (d, *J*= 7.93 Hz, 1 H) 8.22 (dd, *J*= 8.39, 1.37 Hz, 1 H) 8.64 (d, *J*= 7.93 Hz, 1 H) 8.75 (dd, *J*= 3.97, 1.53 Hz, 1 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 22.2, 24.7, 84.5, 121.6, 123.8, 125.9, 127.1, 128.9, 129.0, 129.4, 129.5, 129.6, 130.4, 130.6, 133.0, 133.5, 135.1, 136.2, 144.7, 150.7, 162.5, 163.3; **HRESI-MS** *(mz)*: Calculated for $C_{25}H_{20}N_2O_3$ $(M + H)^+$: 397.1552, found $(M + H)^+$: 397.1555.



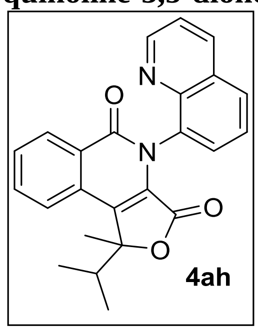
19. 4'-(Quinolin-8-yl)-3'H-spiro[cycloheptane-1,1'-furo[3,4-c]isoquinoline]-3',5'(4'H)-dione (4af). Pale Brown solid; Yield – (66 mg, 80%); ***mp***: 244-246 °C; R_f (50% EtOAc/petroleum ether) 0.25; Prepared as shown in general experimental procedure (a). **IR** (Neat, cm^{-1}): 1759, 1671; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 1.69 - 1.88 (m, 6 H) 2.00 - 2.13 (m, 4 H) 2.40 - 2.47 (m, 2 H) 7.38 (dd, *J*= 8.39, 4.12 Hz, 1 H) 7.65 - 7.72 (m, 2 H) 7.77 - 7.86 (m, 3 H) 7.97 (d, *J*= 8.24 Hz, 1 H) 8.22 (d, *J*= 8.24 Hz, 1 H) 8.63 (d, *J*= 7.93 Hz, 1 H) 8.75 (d, *J*= 3.66 Hz, 1 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 22.8, 22.8, 27.4, 27.4, 39.3, 87.5, 121.6, 123.9, 125.9, 126.1, 129.0, 129.4, 129.5, 130.2, 130.6, 133.0, 133.5, 136.3, 136.8, 144.7, 150.7, 162.4, 163.5; **HRESI-MS** *(mz)*: Calculated for $C_{26}H_{22}N_2O_3$ $(M + H)^+$: 411.1709, found $(M + H)^+$: 411.1712.



20. 1-Ethyl-1-methyl-4-(quinolin-8-yl)-1,4-dihydrofuro[3,4-c]isoquinoline-3,5-dione (4ag)-Diastereomer-I: White solid; Yield – (38 mg, 51%); ***mp***: 203-205 °C; R_f (50% EtOAc/petroleum ether) 0.25; Prepared as shown in general experimental procedure (a). **IR** (Neat, cm^{-1}): 1760, 1672; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 0.91 (t, *J*= 7.32 Hz, 3 H) 1.86 (s, 3 H) 2.27 (qq, *J*= 14.61, 7.36 Hz, 2 H) 7.37 (dd, *J*= 8.24, 4.27 Hz, 1 H) 7.68 - 7.73 (m, 3 H) 7.82 - 7.86 (m, 2 H) 7.97 (d, *J*= 7.93 Hz, 1 H) 8.21 (d, *J*= 7.63 Hz, 1 H) 8.63 - 8.67 (m, 2 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 7.7, 25.8, 32.3, 85.4, 121.6, 123.5, 125.9, 128.2, 128.8, 128.9, 129.3, 129.5, 129.7, 130.3, 130.6, 133.1, 133.2, 133.4, 136.2, 144.6, 150.6, 162.7, 163.7; **HRESI-MS** *(mz)*: Calculated for $C_{23}H_{18}N_2O_3$ $(M + H)^+$: 371.1396, found $(M + H)^+$: 371.1396. **Diastereomer-II:** Brown solid; Yield – (30 mg, 40%); ***mp***: 166-168 °C; R_f (50% EtOAc/petroleum ether) 0.2; Prepared as shown in general experimental procedure (a). **IR** (Neat, cm^{-1}): 1760, 1672; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 0.82 (t, *J*= 7.32 Hz, 3 H) 1.89 (s, 3 H) 2.16 - 2.24 (m, 1 H) 2.27 - 2.36 (m, 1 H) 7.40 (dd, *J*= 8.24, 4.27 Hz, 1 H) 7.67 - 7.74 (m, 3 H) 7.79 - 7.86 (m, 2 H) 7.98 (d, *J*= 7.93 Hz, 1 H) 8.22 - 8.24 (m, 1 H) 8.64 (d, *J*= 7.63 Hz, 1 H) 8.76 (d, *J*= 2.75 Hz, 1 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 7.9, 25.8, 32.1, 85.5, 121.7, 123.5, 126.0, 127.6, 128.7, 129.0, 129.5, 129.5, 129.9, 130.2, 130.6, 133.3, 133.6, 136.4, 144.6, 150.8, 162.6, 163.5; **HRESI-MS** *(mz)*: Calculated for $C_{23}H_{18}N_2O_3$ $(M + H)^+$: 371.1396, found $(M + H)^+$: 371.1399.

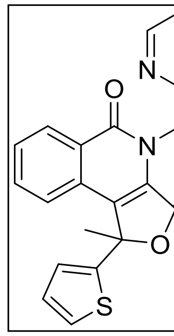


21. 1-Isopropyl-1-methyl-4-(quinolin-8-yl)-1,4-dihydrofuro[3,4-c]isoquinoline-3,5-dione (4ah)-Diastereomer-I: White solid; Yield – (47 mg, 61%); ***mp***: 202-204 °C; R_f (50% EtOAc/petroleum ether) 0.25; Prepared as shown in general experimental procedure (a). **IR** (Neat, cm^{-1}): 1759, 1673; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 0.87 (d, *J*= 6.71 Hz, 3 H) 1.26 (d, *J*=6.71 Hz, 3 H) 1.86 (s, 3 H) 2.54 (dt, *J*= 13.66, 6.75 Hz, 1 H) 7.36 (dd, *J*= 8.39, 4.12 Hz, 1 H) 7.68 - 7.76 (m, 3 H) 7.82 (d, *J*=7.32 Hz, 1 H) 7.87 (d, *J*=7.02 Hz, 1 H) 7.97 (d, *J*= 8.24 Hz, 1 H) 8.20 (d, *J*= 8.24 Hz, 1 H) 8.63 - 8.35 (m, 2 H); **^{13}C NMR** (100 MHz): δ 16.8, 17.1, 23.9, 35.8, 87.2, 121.6, 123.7, 125.9, 127.7, 128.8, 128.9, 129.2, 129.5, 129.7, 130.2, 130.6, 133.2, 133.3, 134.4, 136.1, 144.5, 150.5, 162.7, 164.1; **HRESI-MS** *(mz)*: Calculated for $C_{24}H_{20}N_2O_3$ $(M + H)^+$: 385.1552, found $(M + H)^+$: 385.1553. **Diastereomer-II:** Pale brown solid; Yield – (20 mg, 26%); ***mp***: 178-180 °C; R_f (50% EtOAc/petroleum ether) 0.2; Prepared as shown in general experimental procedure (a). **IR** (Neat, cm^{-1}): 1760, 1673; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 0.73 (d, *J*= 6.71 Hz, 3 H) 1.27 (d, *J*= 7.02 Hz, 3 H) 1.90 (s, 3 H) 2.48 - 2.59 (m, 1 H) 7.40 (dd, *J*= 8.24, 4.27 Hz, 1 H) 7.67 - 7.85 (m, 5 H) 7.98 (d, *J*= 7.93 Hz, 1 H) 8.23 (d, *J*= 8.54 Hz, 1 H) 8.64 (d, *J*= 7.93 Hz, 1 H) 8.76 (d, *J*= 3.97 Hz, 1 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 16.8, 17.0, 24.1, 35.5, 87.2, 121.7, 123.7, 126.0, 127.0, 128.7, 129.0, 129.5, 129.6, 129.9,



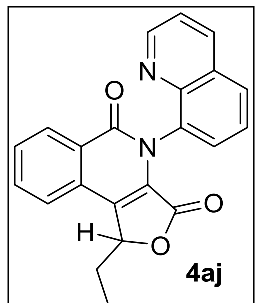
130.2, 130.6, 133.2, 134.8, 136.4, 144.6, 150.8, 162.5, 163.8; **HRESI-MS** *(mz)*: Calculated for $C_{24}H_{20}N_2O_3$ (M + H)$^+$: 385.1552, found (M + H)$^+$: 385.1553.

22. 1-Methyl-4-(quinolin-8-yl)-1-(thiophen-2-yl)-1,4-dihydrofuro[3,4-c]isoquinoline-3,5-dione (4ai)-diastereomer-I: Pale yellow solid; Yield – (40 mg, 47%); ***mp***: 200-202 °C; R_f (50% EtOAc/petroleum ether) 0.25; Prepared as shown in general experimental procedure (a). **IR** (Neat, cm^{-1}): 1766, 1675; ^{1}**H NMR** (400 MHz, $CDCl_3$): δ 2.33 (s, 3 H) 7.02 (s, 1 H) 7.39 (d, *J*= 4.27 Hz, 2 H) 7.45 (d, *J*= 7.02 Hz, 1 H) 7.67 - 7.73 (m, 3 H) 7.91 (d, *J*= 7.02 Hz, 1 H) 7.99 (d, *J*= 7.93 Hz, 1 H) 8.22 (d, *J*= 8.24 Hz, 1 H) 8.62 (d, *J*= 7.02 Hz, 1 H) 8.77 (s, 1 H); ^{13}**C NMR** (100 MHz, $CDCl_3$): δ 26.3, 81.6, 121.7, 124.3, 125.9, 127.2, 127.5, 127.5, 128.0, 128.9, 129.0, 129.4, 129.6, 129.8, 130.1, 130.3, 133.0, 133.2, 133.2, 136.3, 142.7, 144.8, 150.8, 162.7, 162.9; **HRESI-MS** *(mz)*: Calculated for $C_{25}H_{16}N_2O_3S$ (M + H)$^+$: 425.0960, found (M + H)$^+$: 425.0959. **Diastereomer-II:** Brown solid; Yield – (32 mg, 38%); ***mp***: 176-178 °C; R_f (50% EtOAc/petroleum ether) 0.2; Prepared as shown in general experimental procedure (a). **IR** (Neat, cm^{-1}): 1766, 1675; ^{1}**H NMR** (400 MHz, $CDCl_3$): δ 2.35 (s, 3 H) 6.99 - 7.01 (m, 1 H) 7.16 (d, *J*= 2.75 Hz, 1 H) 7.37 (d, *J*= 4.58 Hz, 1 H) 7.41 - 7.45 (m, 2 H) 7.66 - 7.73 (m, 3 H) 7.87 (d, *J*= 7.02 Hz, 1 H) 8.01 (d, *J*= 7.93 Hz, 1 H) 8.26 (d, *J*= 8.24 Hz, 1 H) 8.63 (d, *J*= 7.02 Hz, 1 H) 8.81 (d, *J*= 2.75 Hz, 1 H); ^{13}**C NMR** (100 MHz, $CDCl_3$): δ 26.7, 81.8, 121.7, 124.5, 126.1, 127.1, 127.2, 127.5, 127.6, 128.0, 128.9, 129.1, 129.6, 129.7, 129.9, 130.2, 130.3, 133.1, 133.5, 136.5, 142.7, 144.5, 150.8, 162.7; **HRESI-MS** *(mz)*: Calculated for $C_{25}H_{16}N_2O_3S$ (M + H)$^+$: 425.0960, found (M + H)$^+$: 425.0956.



4ai

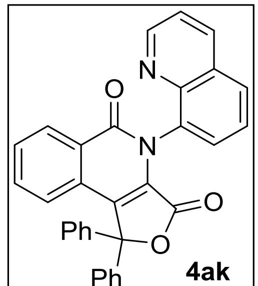
23. 1-Ethyl-4-(quinolin-8-yl)-1,4-dihydrofuro[3,4-c]isoquinoline-3,5-dione (4aj)-Diastereomer-I: White solid; Yield – (15 mg, 21%); ***mp***: >250 °C; R_f (50% EtOAc/petroleum ether) 0.3; Prepared as shown in general experimental procedure (a). **IR** (Neat, cm^{-1}): 1762, 1672; ^{1}**H NMR** (400 MHz, $CDCl_3$): δ 1.07 (t, *J*= 7.32 Hz, 3 H) 1.99 - 2.10 (m, 1 H) 2.40 – 2.50 (m, 1 H) 5.60 (dd, *J*= 6.71, 3.05 Hz, 1 H) 7.39 (dd, *J*= 8.39, 4.12 Hz, 1 H) 7.68 - 7.75 (m, 3 H) 7.81 - 7.86 (m, 2 H) 7.97 – 7.99 (m, 1 H) 8.23 (dd, *J*= 8.24, 1.53 Hz, 1 H) 8.62 (d, *J*= 7.93 Hz, 1 H) 8.72 (dd, *J*= 4.12, 1.68 Hz, 1 H); ^{13}**C NMR** (100 MHz, $CDCl_3$): δ 8.3, 27.4, 78.8, 121.7, 123.2, 126.0, 128.1, 128.6, 129.0, 129.4, 129.5, 130.1, 130.4, 130.5, 130.6, 133.2, 133.3, 136.2, 144.6, 150.7, 162.6, 164.3; **HRESI-MS** *(mz)*: Calculated for $C_{22}H_{16}N_2O_3$ (M + H)$^+$: 357.1239, found (M + H)$^+$: 357.1237. **Diastereomer-II:** Brown solid; Yield – (35 mg, 49%); ***mp***: 247-249 °C; R_f (50% EtOAc/petroleum ether) 0.25; Prepared as shown in general experimental procedure (a). **IR** (Neat, cm^{-1}): 1760, 1672; ^{1}**H NMR** (100 MHz, $CDCl_3$): δ 1.02 (t, *J*= 7.32 Hz, 3 H) 1.90 – 2.01 (m, 1 H) 2.44 (ddd, *J*=14.65, 7.32, 3.05 Hz, 1 H) 5.60 (dd, *J*= 7.17, 2.90 Hz, 1 H) 7.39 (dd, *J*= 8.24, 4.27 Hz, 1 H) 7.67 - 7.74 (m, 3 H) 7.80 - 7.85 (m, 2 H) 7.98 - 8.00 (m, 1 H) 8.23 (dd, *J*= 8.24, 1.22 Hz, 1 H) 8.61 (d, *J*= 7.93 Hz, 1 H) 8.76



4aj

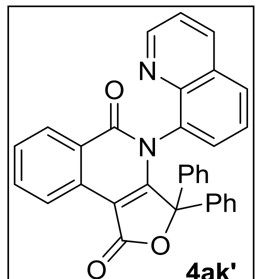
(dd, *J*= 4.12, 1.37 Hz, 1 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 8.6, 27.4, 79.0, 121.7, 123.4, 126.0, 127.7, 128.4, 129.0, 129.6, 129.7, 130.2, 130.4, 130.6, 133.2, 133.4, 136.5, 144.6, 150.9, 162.6, 164.2 ; **HRESI-MS** *(mz)*: Calculated for $C_{22}H_{16}N_2O_3$ $(M + H)^+$: 357.1239, found $(M + H)^+$: 357.1241.

24. 1,1-Diphenyl-4-(quinolin-8-yl)-1,4-dihydrofuro[3,4-c]isoquinoline-3,5-dione (4ak): Brown solid; Yield – (34 mg, 35%); ***mp***: >250 °C; R_f (50% EtOAc/petroleum ether) 0.3; Prepared as shown in general experimental procedure (a). **IR** (Neat, cm^{-1}): 1767, 1674; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.39 - 7.51 (m, 12 H) 7.58 - 7.65 (m, 2 H) 7.73 (t, *J*= 7.78 Hz, 1 H) 7.90 - 7.92 (m, 1 H) 8.00 (d, *J*= 8.24 Hz, 1 H) 8.26 (d, *J*= 7.93 Hz, 1 H) 8.59 (dd, *J*= 6.71, 2.75 Hz, 1 H) 8.79 (d, *J*= 2.75 Hz, 1 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 89.8, 121.7, 125.5, 126.0, 128.5, 128.5, 128.7, 129.0, 129.0, 129.1, 129.5, 129.8, 130.1, 132.9, 132.9, 133.1, 136.4, 138.1, 138.7, 144.5, 150.7, 162.7, 163.6; **HRESI-MS** *(mz)*: Calculated for $C_{32}H_{20}N_2O_3$ $(M + H)^+$: 481.1552, found $(M + H)^+$: 481.1550.



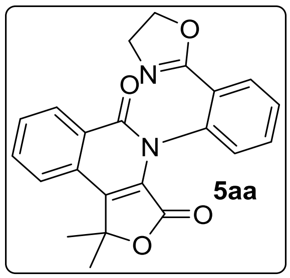
4ak

25. 3,3-Diphenyl-4-(quinolin-8-yl)furo[3,4-c]isoquinoline-1,5(3H,4H)-dione (4ak'): White solid; Yield – (55 mg, 57%); ***mp***: >250 °C; R_f (50% EtOAc/petroleum ether) 0.35; Prepared as shown in general experimental procedure (a). **IR** (Neat, cm^{-1}): 1755, 1683; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 6.49 - 6.52 (m, 4 H) 6.64 (td, *J*= 5.49, 3.05 Hz, 1 H) 7.14 (dd, *J*= 8.24, 4.27 Hz, 1 H) 7.30 (t, *J*= 7.78 Hz, 1 H) 7.36 - 7.46 (m, 6 H) 7.65 (t, *J*= 7.63 Hz, 1 H) 7.77 (d, *J*= 8.24 Hz, 1 H) 7.89 – 8.02 (m, 2 H) 8.30 (d, *J*= 3.05 Hz, 1 H) 8.43 (d, *J*= 7.93 Hz, 1 H) 8.81 (d, *J*= 8.24 Hz, 1 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 89.5, 102.5, 121.4, 123.7, 125.2, 125.2, 126.7, 127.7, 128.2, 128.4, 128.4, 128.6, 129.1, 129.2, 129.7, 130.2, 130.4, 131.2, 133.4, 133.6, 134.1, 135.2, 137.9, 144.3, 150.8, 160.4, 164.1, 168.0; **HRESI-MS** *(mz)*: Calculated for $C_{32}H_{20}N_2O_3$ $(M + H)^+$: 481.1552, found $(M + H)^+$: 481.1555.



4ak'

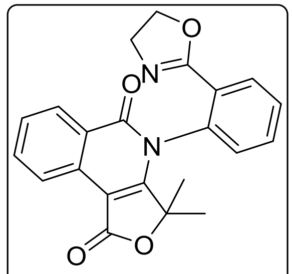
26. 4-(2-(4,5-Dihydrooxazol-2-yl)phenyl)-1,1-dimethyl-1,4-dihydrofuro[3,4-c]isoquinoline-3,5-dione (5aa): White solid; Yield – (25 mg, 33%); ***mp***: 153-155 °C; R_f (50% EtOAc/petroleum ether) 0.25; Prepared as shown in general experimental procedure (a). **IR** (Neat, cm^{-1}): 1760, 1672, 1638; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 1.84 (s, 3 H) 1.89 (s, 3 H) 3.71 (t, *J*= 9.46 Hz, 2 H) 4.11 (t, *J*= 9.46 Hz, 2 H) 7.38 (d, *J*= 7.93 Hz, 1 H) 7.57 (t, *J*= 7.48 Hz, 1 H) 7.63 (t, *J*= 7.02 Hz, 1 H) 7.69 - 7.72 (m, 2 H) 7.83 - 7.86 (m, 1 H) 8.12 (d, *J*= 7.32 Hz, 1 H) 8.60 (d, *J*= 7.93 Hz, 1 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 26.7. 27.3. 55.4. 66.5. 82.8. 123.6, 125.9, 126.7, 128.8, 129.3, 129.6, 129.9, 130.0, 130.4,



5aa

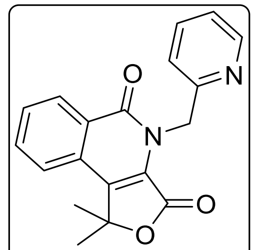
130.7, 131.7, 133.1, 135.0, 135.1, 161.5, 162.7, 163.5; **HRESI-MS** *(mz)*: Calculated for $C_{22}H_{18}N_2O_4$ $(M + H)^+$: 375.1345, found $(M + H)^+$: 375.1343.

27. 4-(2-(4,5-Dihydrooxazol-2-yl)phenyl)-3,3-dimethylfuro[3,4-c]isoquinoline 1,5(3H,4H)-dionee (5aa'): Brown solid; Yield – (38 mg, 51%); ***mp***: 219-221 °C; R_f (50% EtOAc/petroleum ether) 0.4; Prepared as shown in general experimental procedure (a). **IR** (Neat, cm^{-1}): 1751, 1678, 1634; ^{1}**H NMR** (400 MHz, $CDCl_3$): δ 1.20 (s, 3 H) 1.49 (s, 3 H) 3.76 (t, *J*= 9.16 Hz, 2 H) 4.13 (t, *J*= 9.00 Hz, 2 H) 7.40 (d, *J*= 7.93 Hz, 1 H) 7.57 (t, *J*= 7.48 Hz, 1 H) 7.63 - 7.69 (m, 2 H) 7.82 (t, *J*= 7.63 Hz, 1 H) 8.20 (d, *J*= 6.71 Hz, 1 H) 8.36 (d, *J*= 7.93 Hz, 1 H) 8.65 (d, *J*= 7.93 Hz, 1 H); ^{13}**C NMR** (100 MHz, $CDCl_3$): δ 24.5, 26.7, 55.3, 67.1, 82.6, 100.8, 123.2, 124.8, 127.4, 127.9, 128.7, 130.5, 131.2, 131.4, 131.5, 131.7, 133.9, 135.0, 161.1, 162.0, 164.2, 167.7; **HRESI-MS** *(mz)*: Calculated for $C_{22}H_{18}N_2O_4$ $(M + H)^+$: 375.1345, found $(M + H)^+$: 375.1341.



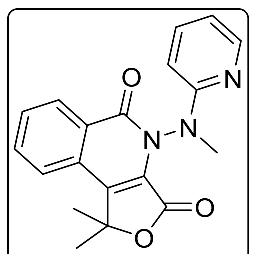
5aa'

28. 1,1-Dimethyl-4-(pyridin-2-ylmethyl)-1,4-dihydrofuro[3,4-c]isoquinoline-3,5-dione (5ba): White solid; Yield – (36 mg, 56%); ***mp***: 187-189 °C; R_f (50% EtOAc/petroleum ether) 0.4; Prepared as shown in general experimental procedure (a). **IR** (Neat, cm^{-1}): 1754, 1666; ^{1}**H NMR** (400 MHz, $CDCl_3$): δ 1.87 (s, 6 H) 5.93 (s, 2 H) 5.93 (s, 2 H) 7.09 - 7.13 (m, 1 H) 7.27 - 7.28 (m, 1 H) 7.61 (t, *J*= 7.17 Hz, 1 H) 7.67 - 7.72 (m, 2 H) 7.80 - 7.84 (m, 1 H) 8.45 (br. s., 1 H) 8.60 (d, *J*= 7.93 Hz, 1 H); ^{13}**C NMR** (100 MHz, $CDCl_3$): δ 27.0, 46.4, 83.0, 121.5, 122.1, 123.6, 125.7, 128.4, 129.5, 129.8, 130.4, 133.1, 135.9, 136.4, 149.4, 156.1, 162.3, 164.3; **HRESI-MS** *(mz)*: Calculated for $C_{19}H_{16}N_2O_3$ $(M + H)^+$: 321.1239, found $(M + H)^+$: 321.1241.



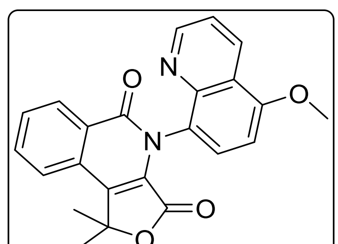
5ba

29. 3,3-Dimethyl-4-(methyl(pyridin-2-yl)amino)furo[3,4-c]isoquinoline-1,5(3H,4H)-dione (5ca): White solid; Yield – (25 mg, 37%); ***mp***: 178-180 °C; R_f (50% EtOAc/petroleum ether) 0.4; Prepared as shown in general experimental procedure (a). **IR** (Neat, cm^{-1}): 1761, 1680, 1595; ^{1}**H NMR** (400 MHz, $CDCl_3$): δ 1.87 (s, 1 H) 1.88 (s, 1 H) 3.59 (s, 3 H) 6.51 (d, *J*= 8.59 Hz, 1 H) 6.69 - 6.72 (m, 1 H) 7.48 - 7.52 (m, 1 H) 7.70 - 7.74 (m, 2 H) 7.84 - 7.88 (m, 1 H) 8.11 (d, *J*= 4.80 Hz, 1 H) 8.61 (dd, *J*= 7.96, 0.63 Hz, 1 H); ^{13}**C NMR** (100 MHz, $CDCl_3$): δ 26.9, 27.1, 82.7, 105.8, 115.0, 123.9, 126.4, 129.5, 129.6, 129.9, 130.6, 135.5, 136.9, 137.8, 148.0, 157.4, 161.1, 161.8; **HRESI-MS** *(mz)*: Calculated for $C_{19}H_{17}N_3O_3$ $(M + H)^+$: 336.1348, found $(M + H)^+$: 336.1348.



5ca

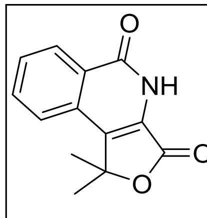
30. 4-(5-Methoxyquinolin-8-yl)-3,3-dimethylfuro[3,4-c]isoquinoline-1,5(3H,4H)-dione (7aa): White solid; Yield – (69 mg, 89%); ***mp***: >250 °C; R_f (50% EtOAc/petroleum ether) 0.25; Prepared as shown in



7aa

general experimental procedure (a). **IR** (Neat, cm^{-1}): 1760, 1671; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 1.92 (s, 3 H) 1.89 (s, 3 H) 4.08 (s, 3 H) 6.98 (d, *J*= 8.34 Hz, 1 H) 7.38 (dd, *J*= 8.40, 4.23 Hz, 1 H) 7.68 – 7.74 (m, 3 H) 7.83 - 7.87 (m, 1 H) 8.61 - 8.65 (m, 2 H) 8.74 (dd, *J*= 4.11, 1.45 Hz, 1 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 27.1, 55.9, 82.7, 103.5, 120.7, 121.4, 123.6, 125.7, 128.9, 129.4, 129.7, 130.1, 130.6, 131.3, 133.1, 135.1, 145.1, 150.9, 155.9, 162.8, 163.3; **HRESI-MS** *(mz)*: Calculated for $C_{23}H_{18}N_2O_4$ $(M + H)^+$: 387.1345, found $(M + H)^+$: 387.1346.

31. **1,1-Dimethyl-1,4-dihydrofuro[3,4-c]isoquinoline-3,5-dione (8aa):** White solid; Yield – (16.5 mg, 51%); ***mp***: 210-212 °C; R_f (50% EtOAc/petroleum ether) 0.6; Prepared as shown in experimental procedure (c). **IR** (Neat, cm^{-1}): 3236, 1765, 1670; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 1.85 (s, 6 H) 7.65 (d, *J*= 8.24 Hz, 1 H) 7.70 - 7.74 (m, 1 H) 7.82 - 7.86 (m, 1 H) 8.63 - 8.65 (m, 1 H) 9.95 (br. s., 1 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 26.8, 85.4, 123.7, 124.8, 128.9, 129.9, 130.2, 130.4, 133.6, 135.0, 162.5, 164.4; **HRESI-MS** *(mz)*: Calculated for $C_{13}H_{11}NO_3$ $(M + H)^+$: 230.0817, found $(M + H)^+$: 230.0814.



8aa

References

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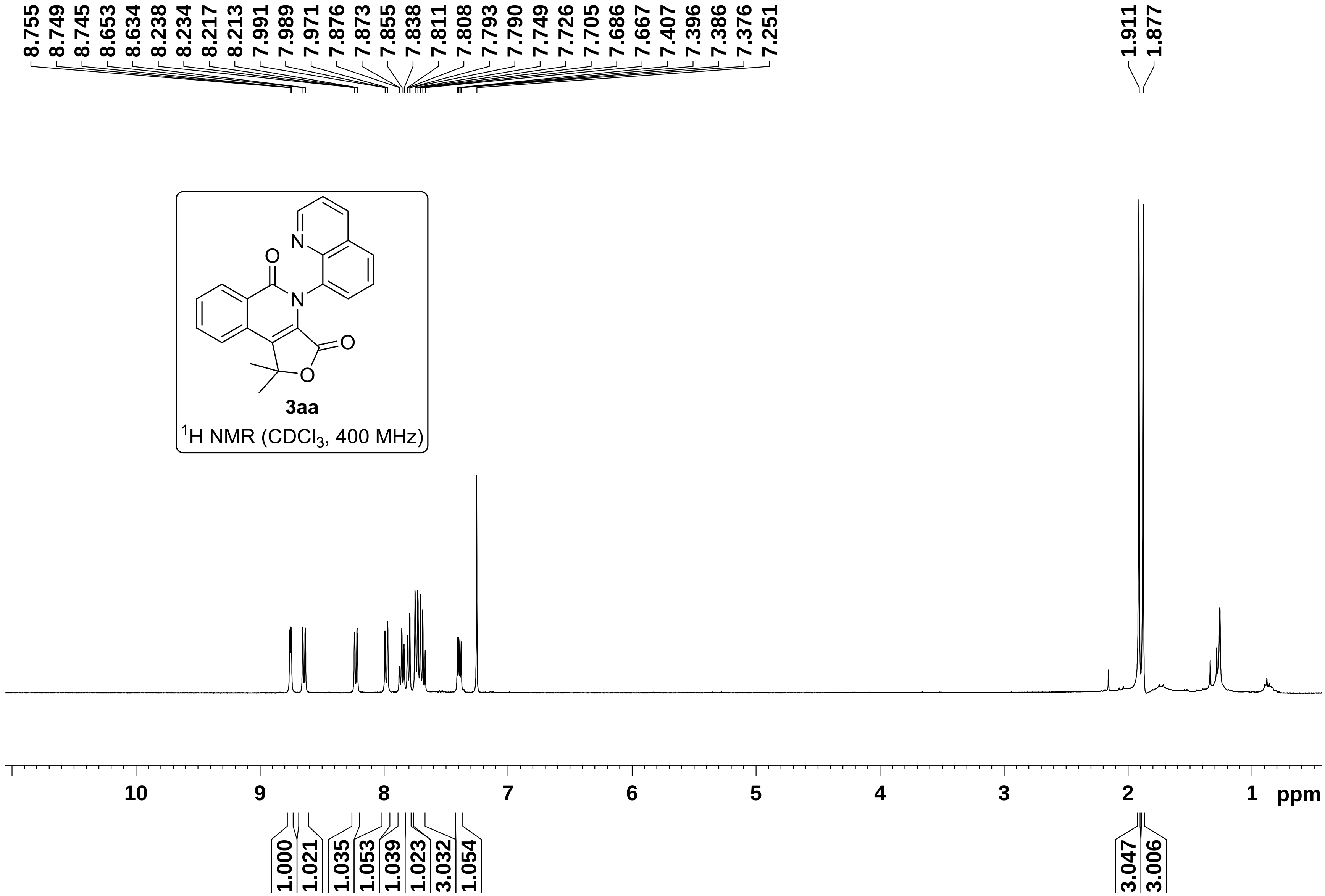
3. a) G. Liao, H. Song, X.-S. Yin, B.-F. Shi, *Chem. Commun.* **2017**, *53*, 7824; b) Y. Xu, B. Li, X. Zhang, X. Fan, *Adv. Synth. Catal.* **2018**, *360*, 2613.
4. X. Wu, K. Yang, Y. Zhao, H. Sun, G. Li, H. Ge, *Nat. Commun*. **2015**, *6*, 6462.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1.911 1.877
O
N
N
O
O
3aa
^{1}H NMR ($CDCl_3$, 400 MHz)
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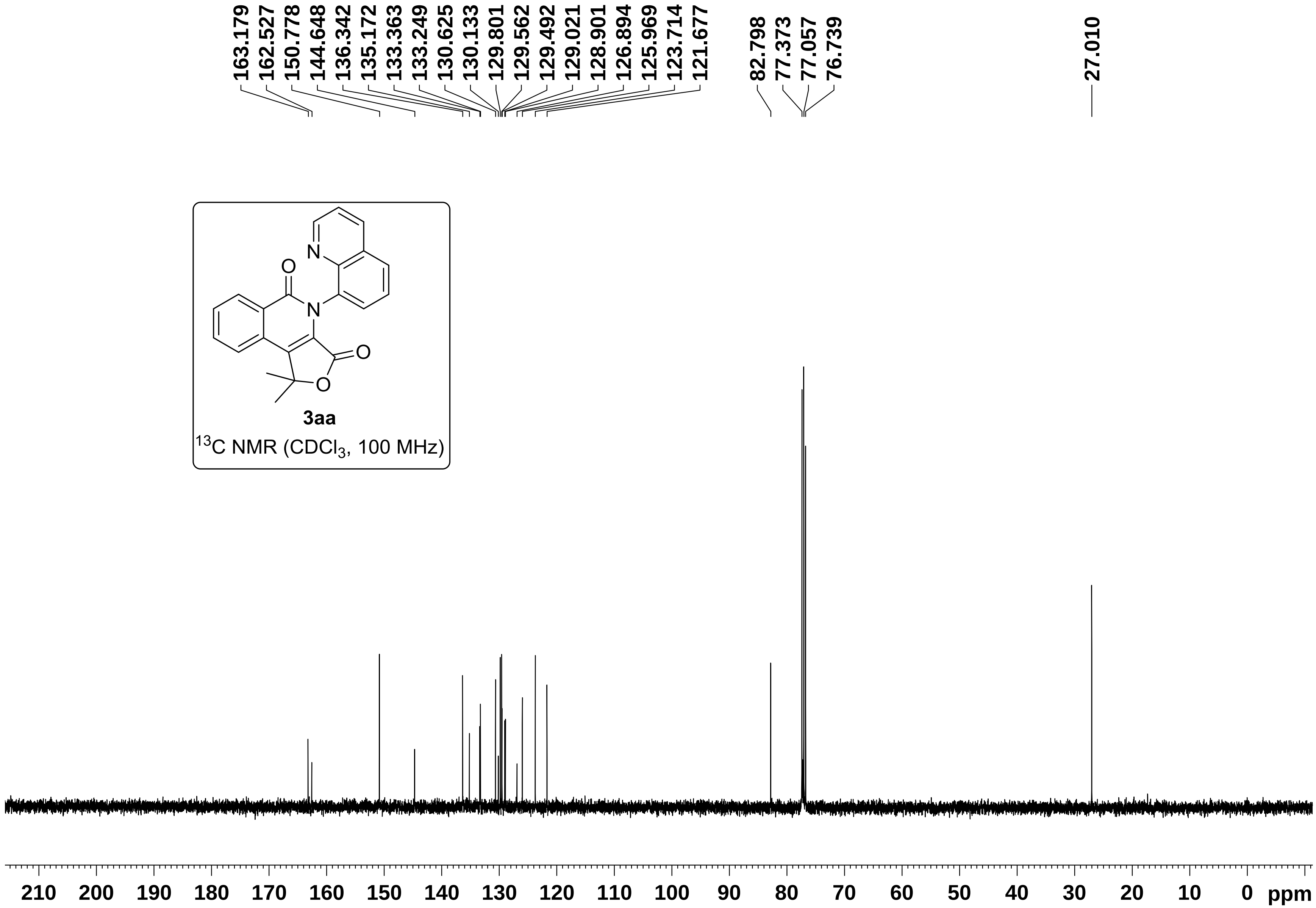
3.047 3.006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128.901
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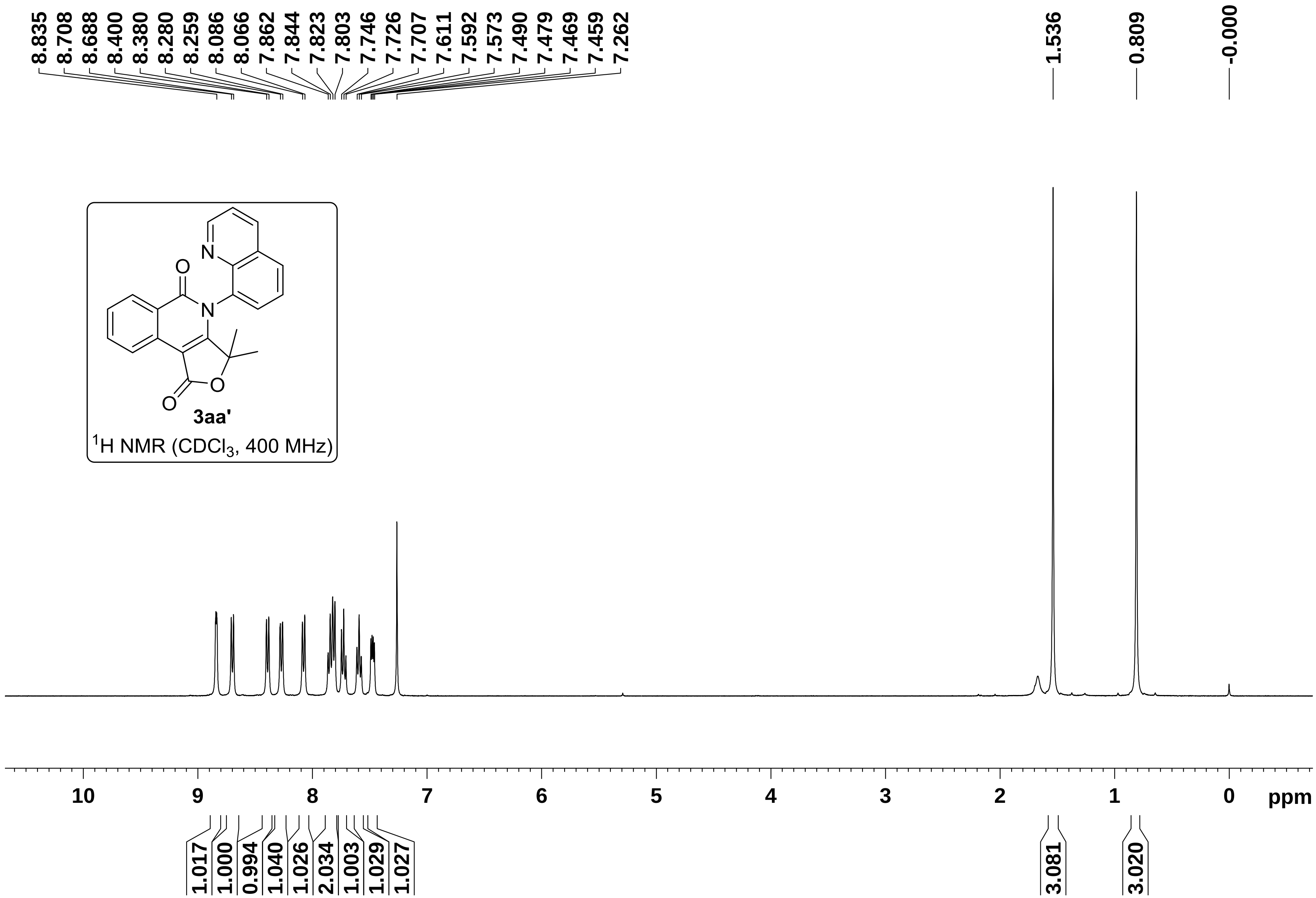
125.969
123.714
121.677
82.798
77.373
77.057
76.739
27.010
N
O
N
O
O
3aa
^{13}C NMR ($CDCl_3$, 100 MHz)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm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7.803
7.746
7.726
7.707
7.611
7.592
7.573
7.490
7.479
7.469
7.459
7.262
1.536
0.809
-0.000
N
O
N
O
O
3aa'
^{1}H NMR (CDCl$_3$, 400 MHz)
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9
8
7
6
5
4
3
2
1
0
ppm
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2.034
1.003
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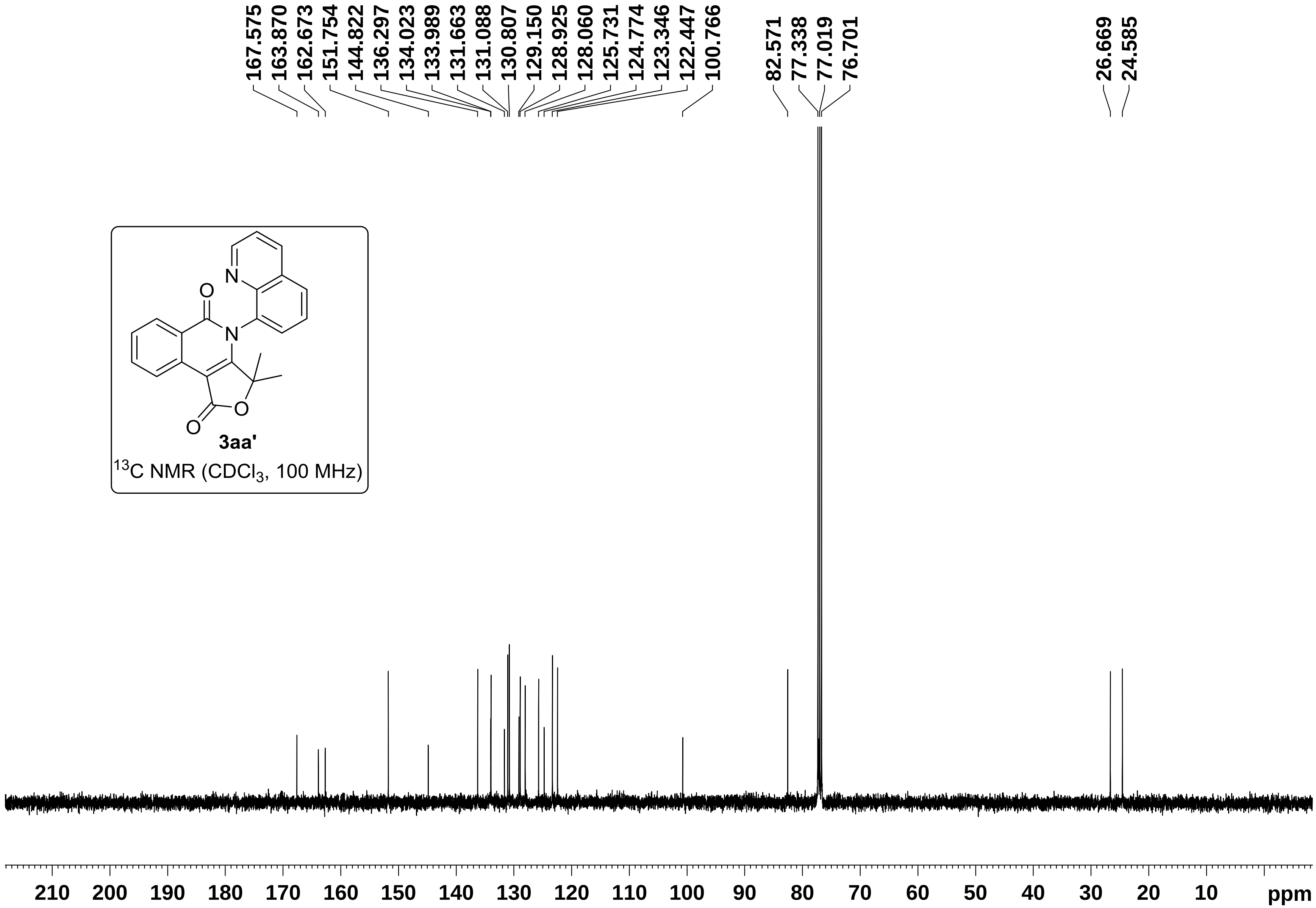
3.020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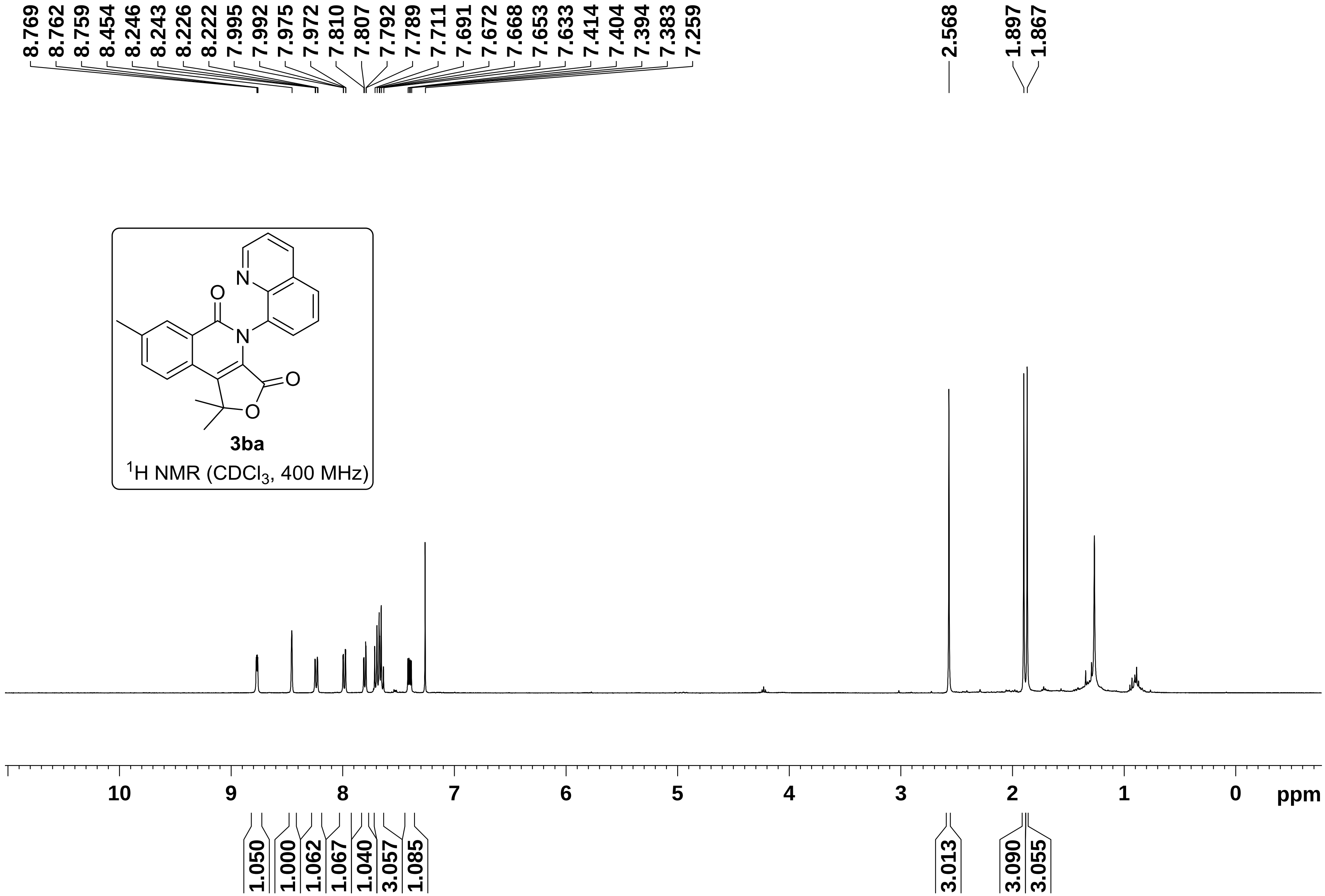
123.346
122.447
100.766
82.571
77.338
77.019
76.701
26.669
24.585
N
O
N
O
O
O
3aa'
^{13}C NMR ($CDCl_3$, 100 MHz)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm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8.222
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7.789
7.711
7.691
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7.668
7.653
7.633
7.414
7.404
7.394
7.383
7.259
2.568
1.897
1.867
N
O
N
O
O
3ba
1H NMR (CDCl3, 400 MHz)
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9
8
7
6
5
4
3
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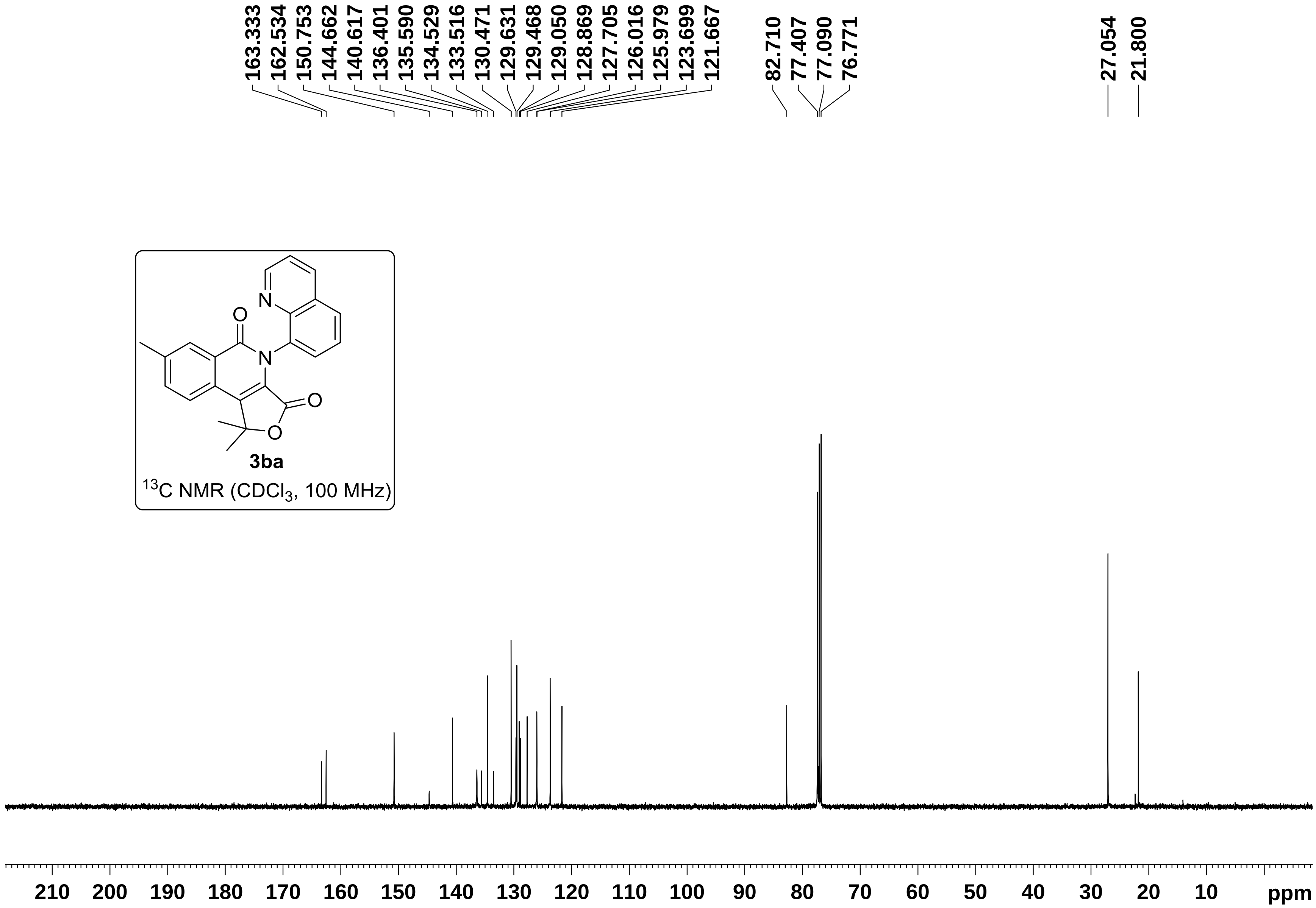
3.055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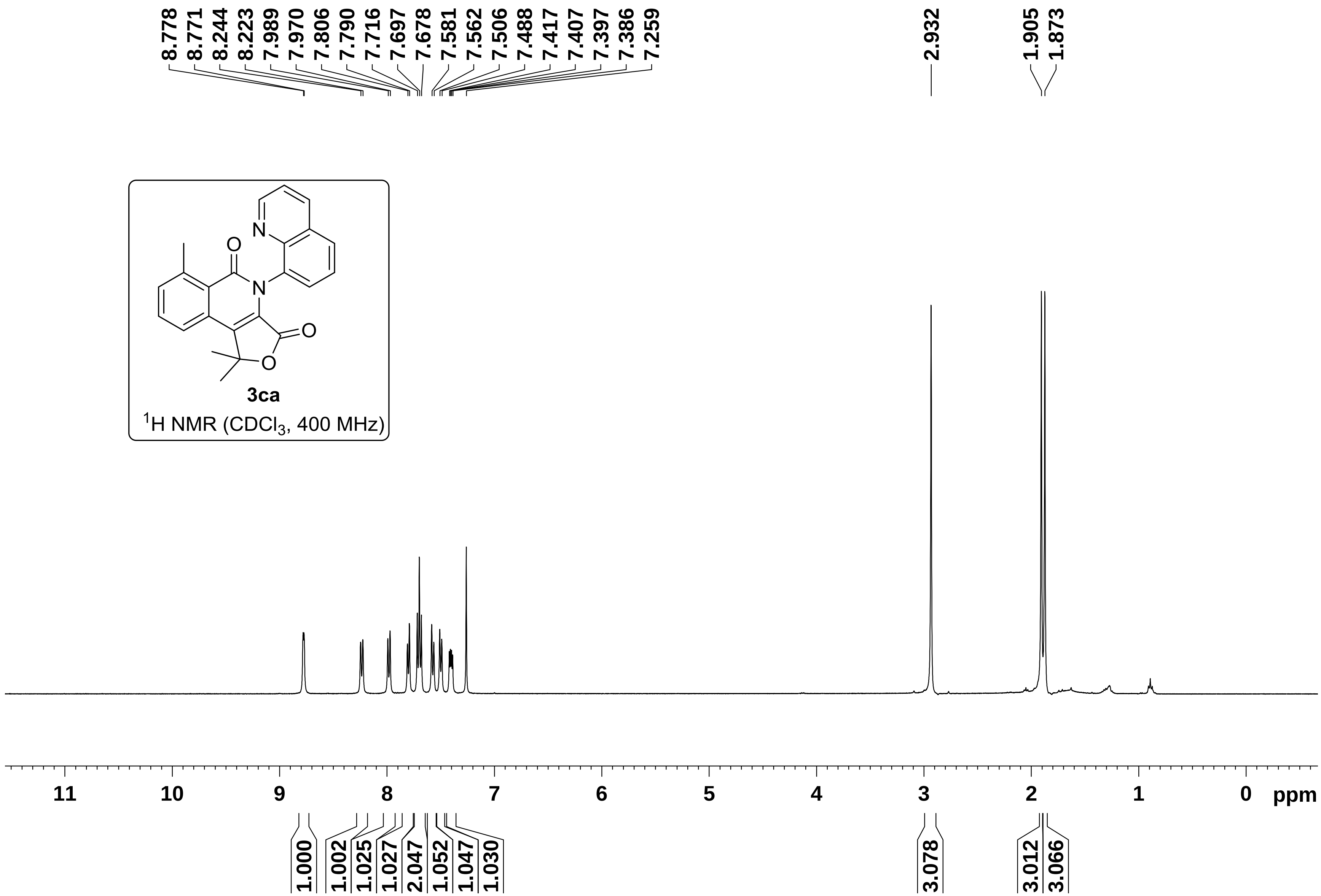
128.869
127.705
126.016
125.979
123.699
121.667
82.710
77.407
77.090
76.771
27.054
21.800
N
O
N
O
O
3ba
^{13}C NMR ($CDCl_3$, 100 MHz)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm



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7.562
7.506
7.488
7.417
7.407
7.397
7.386
7.259
2.932
1.905
1.873
3ca
^{1}H NMR ($CDCl_3$, 400 MHz)
11 10 9 8 7 6 5 4 3 2 1 0 ppm
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1.047
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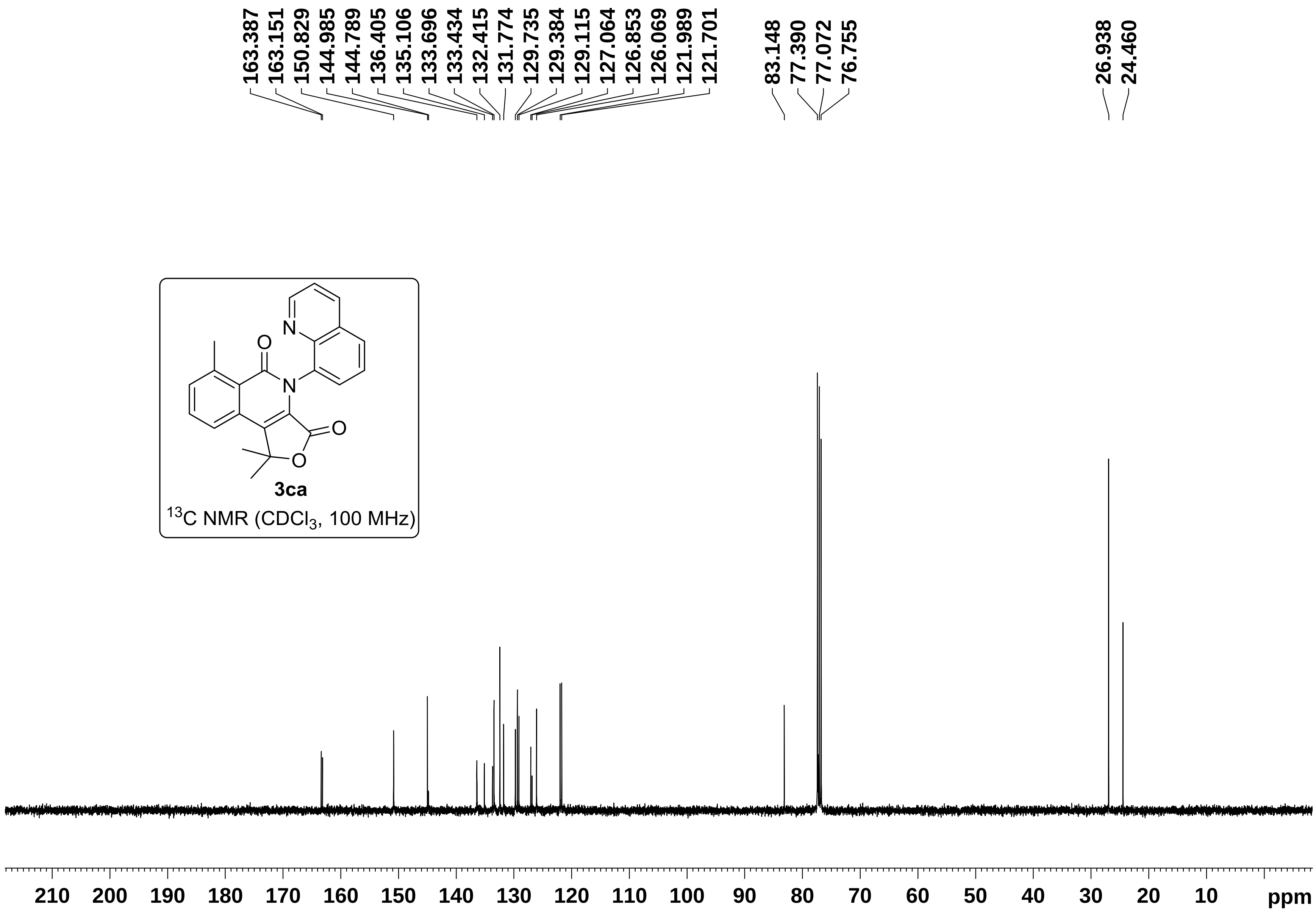
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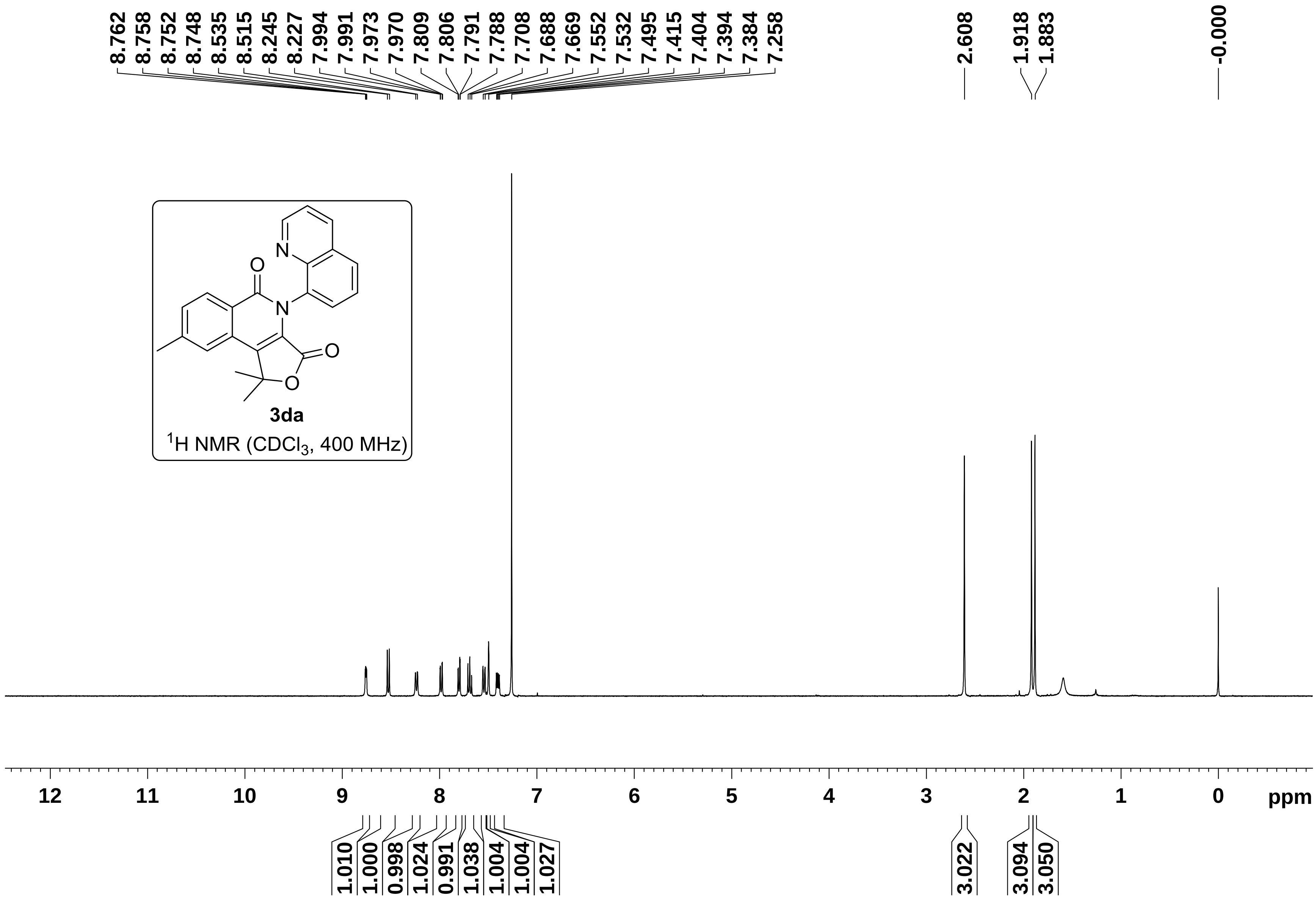
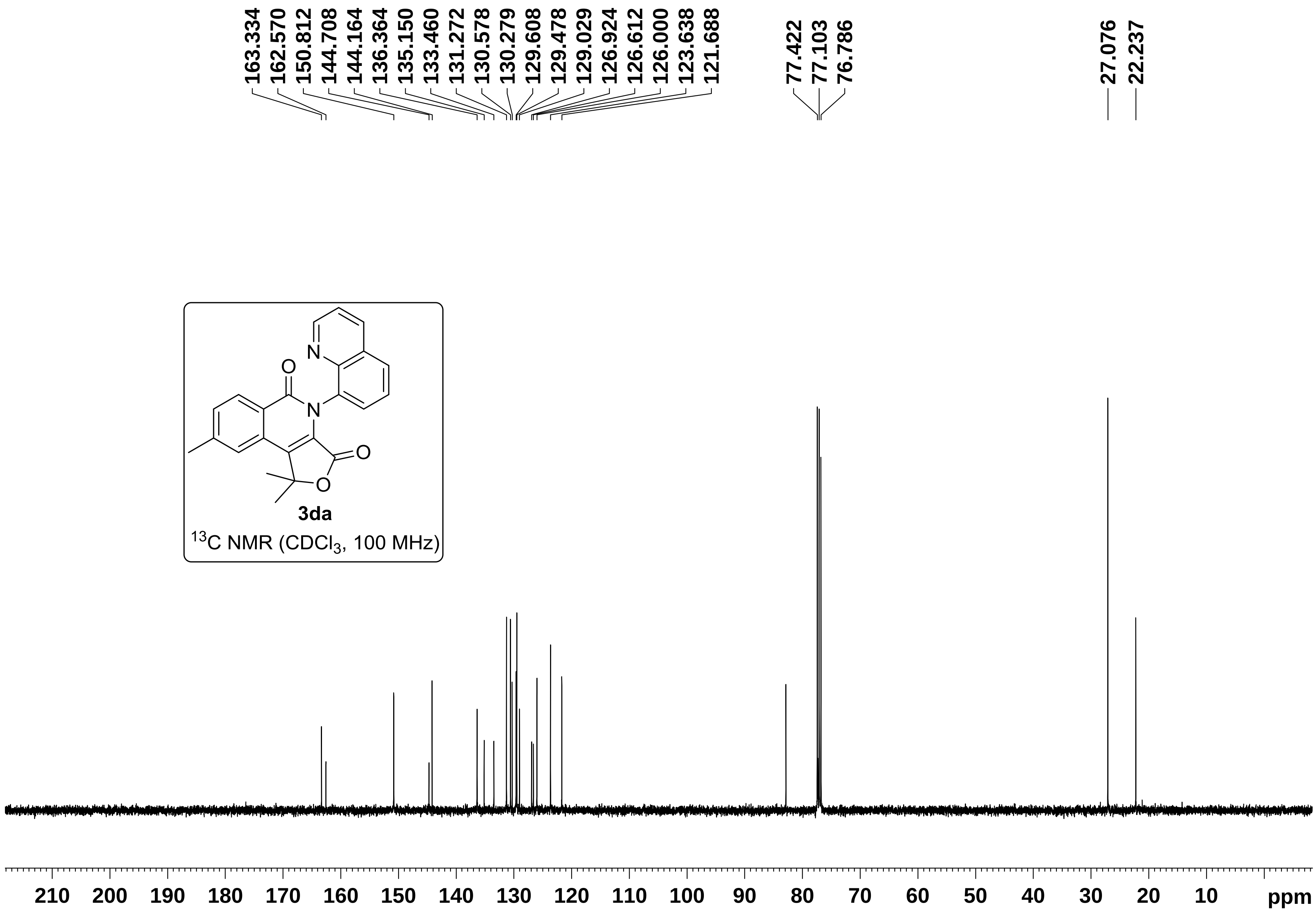
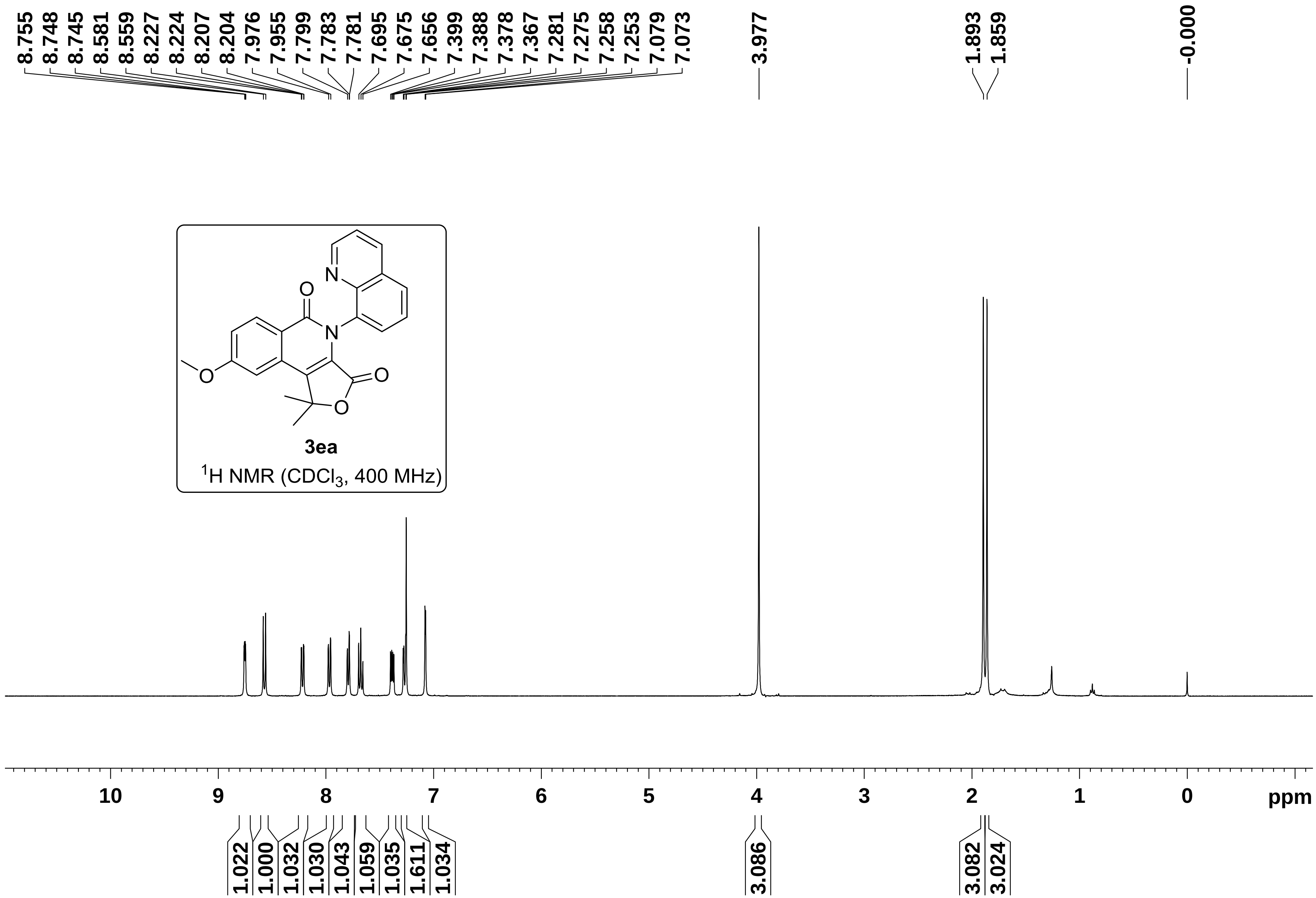
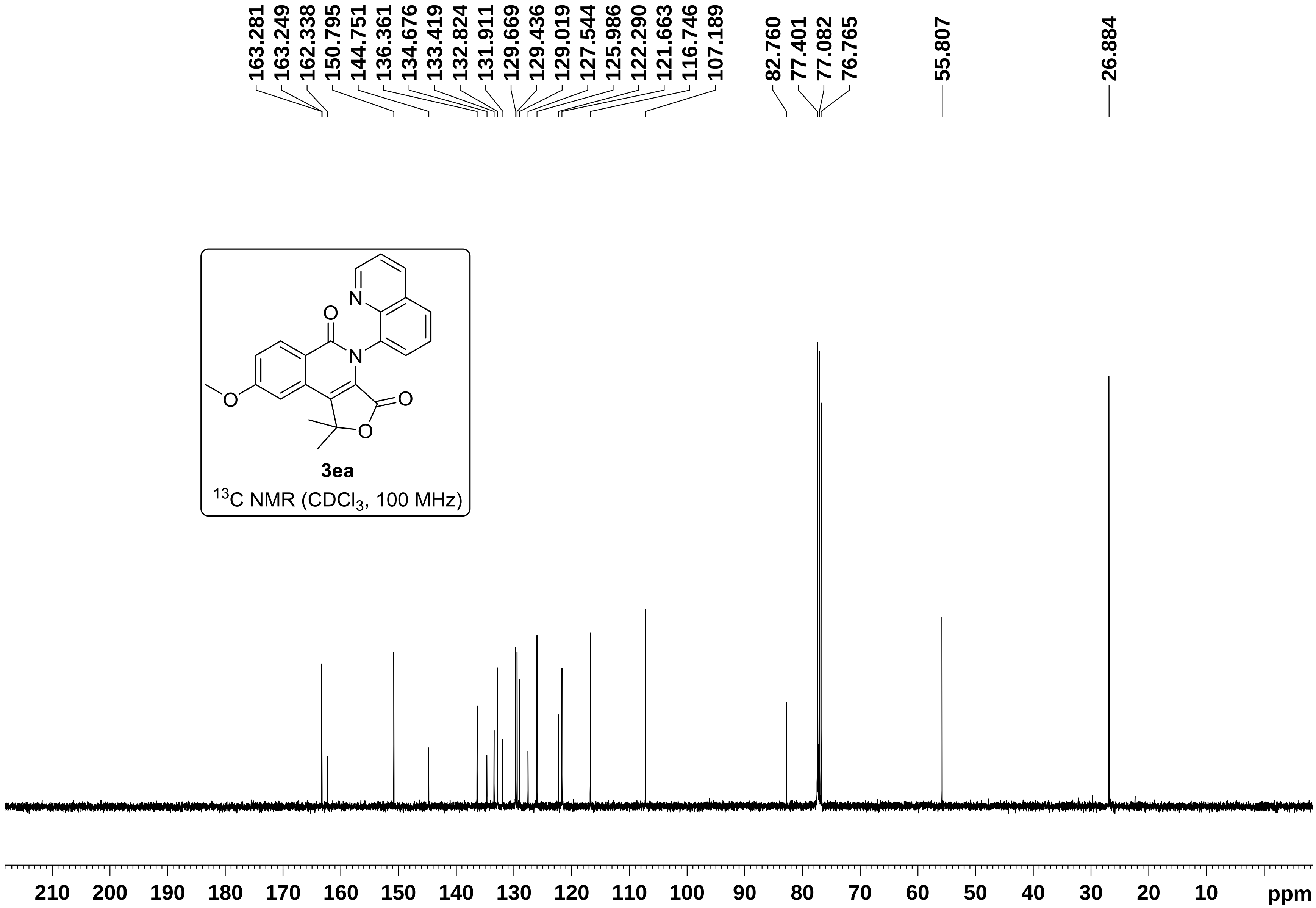
129.384
129.115
127.064
126.853
126.069
121.989
121.701
83.148
77.390
77.072
76.755
26.938
24.460
3ca
^{13}C NMR ($CDCl_3$, 100 MHz)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


8.762
8.758
8.752
8.748
8.535
8.515
8.245
8.227
7.994
7.991
7.973
7.970
7.809
7.806
7.791
7.788
7.708
7.688
7.669
7.552
7.532
7.495
7.415
7.404
7.394
7.384
7.258
2.608
1.918
1.883
-0.000
O
N
N
O
O
3da
^{1}H NMR ($CDCl_3$, 400 MHz)
12
11
10
9
8
7
6
5
4
3
2
1
0
ppm
1.010
1.000
0.998
1.024
0.991
1.038
1.004
1.004
1.027
3.022
3.094
3.050


163.334
162.570
150.812
144.708
144.164
136.364
135.150
133.460
131.272
130.578
130.279
129.608
129.478
129.029
126.924
126.612
126.000
123.638
121.688
77.422
77.103
76.786
27.076
22.237
N
O
N
O
O
3da
^{13}C NMR (CDCl$_3$, 100 MHz)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

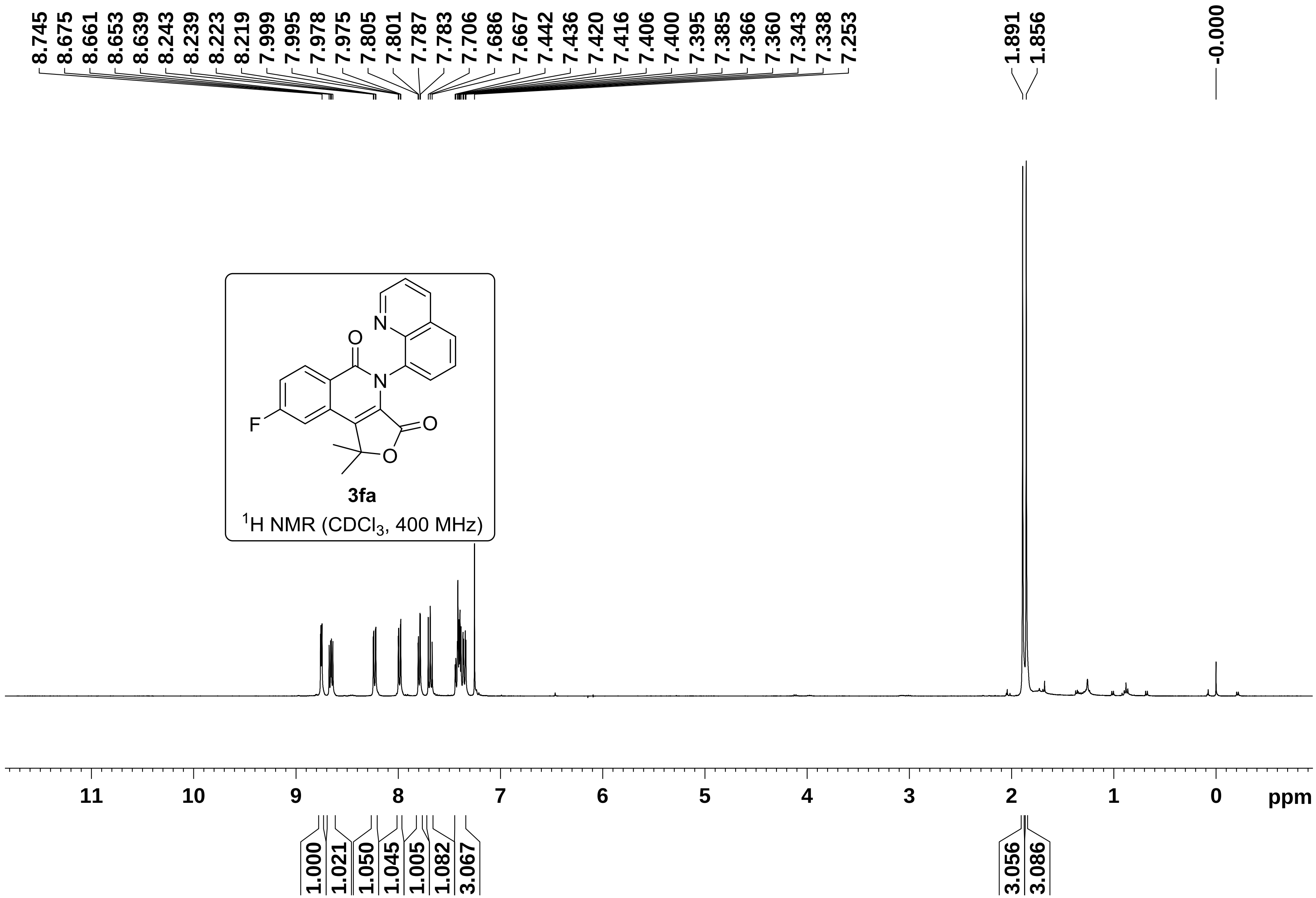


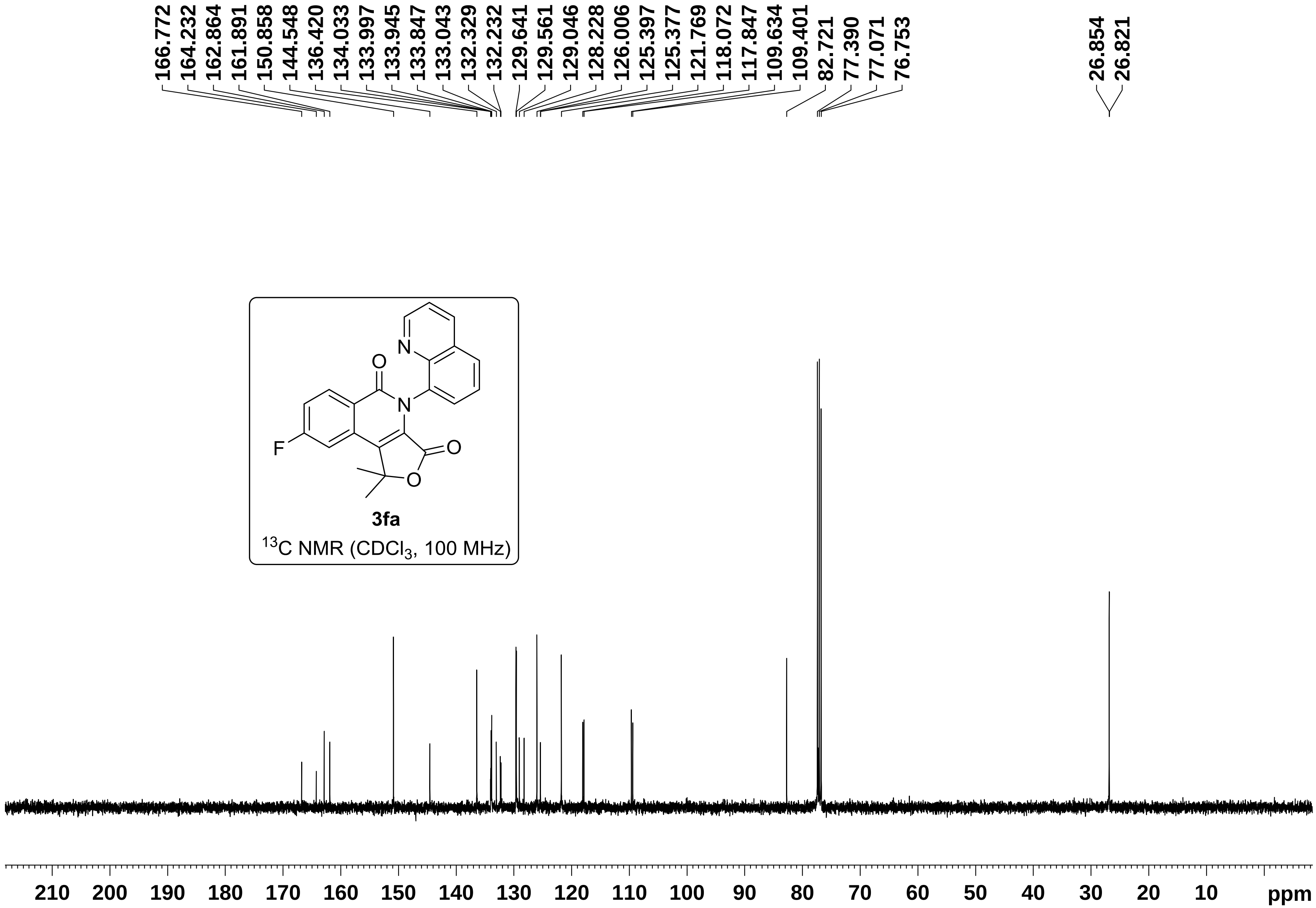
8.755
8.748
8.745
8.581
8.559
8.227
8.224
8.207
8.204
7.976
7.955
7.799
7.783
7.781
7.695
7.675
7.656
7.399
7.388
7.378
7.367
7.281
7.275
7.258
7.253
7.079
7.073
3.977
1.893
1.859
-0.000
N
O
N
O
O
O
3ea
1H NMR (CDCl3, 400 MHz)
10
9
8
7
6
5
4
3
2
1
0
ppm
1.022
1.000
1.032
1.030
1.043
1.059
1.035
1.611
1.034
3.086
3.082
3.024



3ea

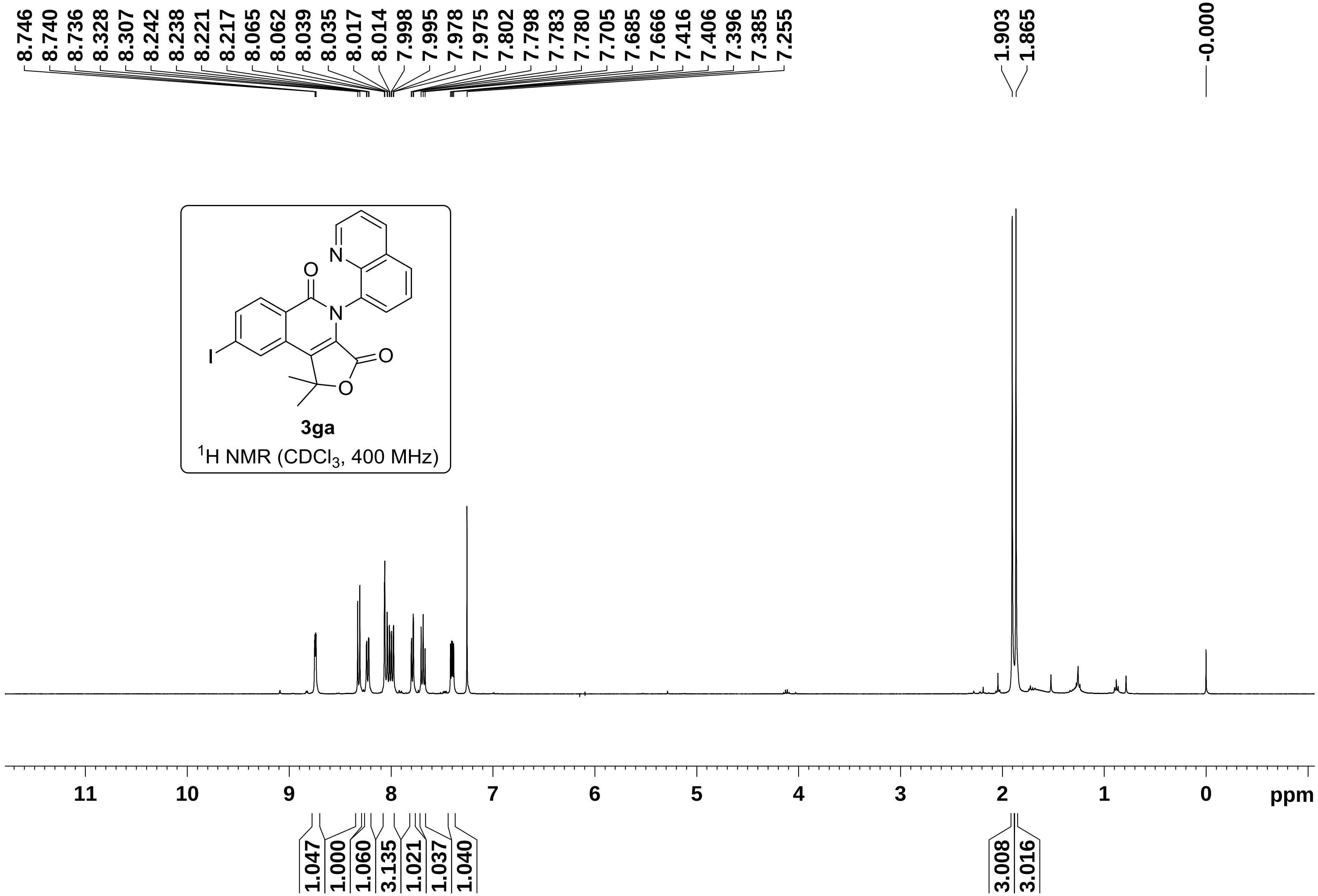
^{13}C NMR ($CDCl_3$, 100 MHz)

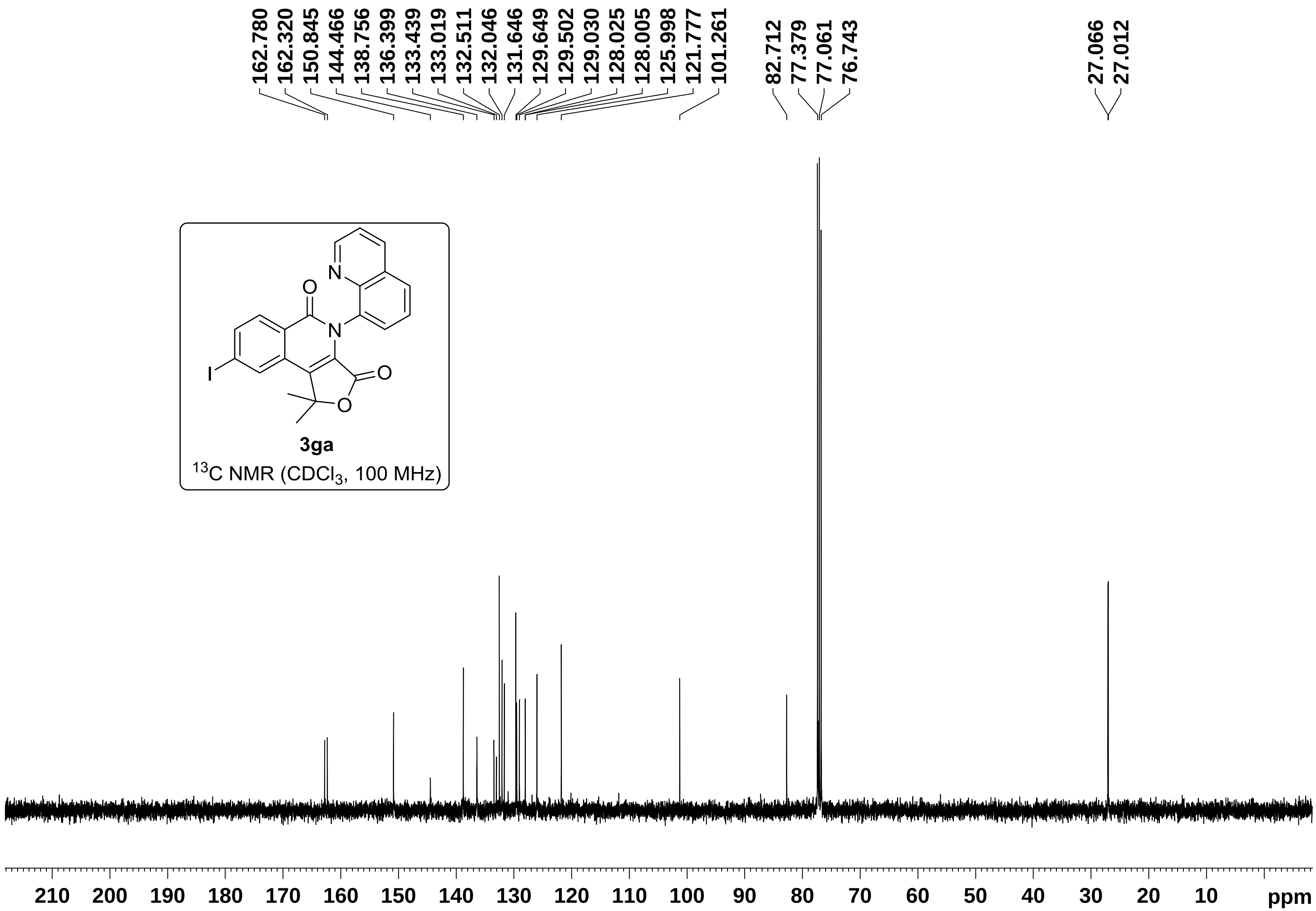

8.745
8.675
8.661
8.653
8.639
8.243
8.239
8.223
8.219
7.999
7.995
7.978
7.975
7.805
7.801
7.787
7.783
7.706
7.686
7.667
7.442
7.436
7.420
7.416
7.406
7.400
7.395
7.385
7.366
7.360
7.343
7.338
7.253
1.891
1.856
-0.000
3fa
1H NMR (CDCl3, 400 MHz)
11
10
9
8
7
6
5
4
3
2
1
0
ppm
1.000
1.021
1.050
1.045
1.005
1.082
3.067
3.056
3.086

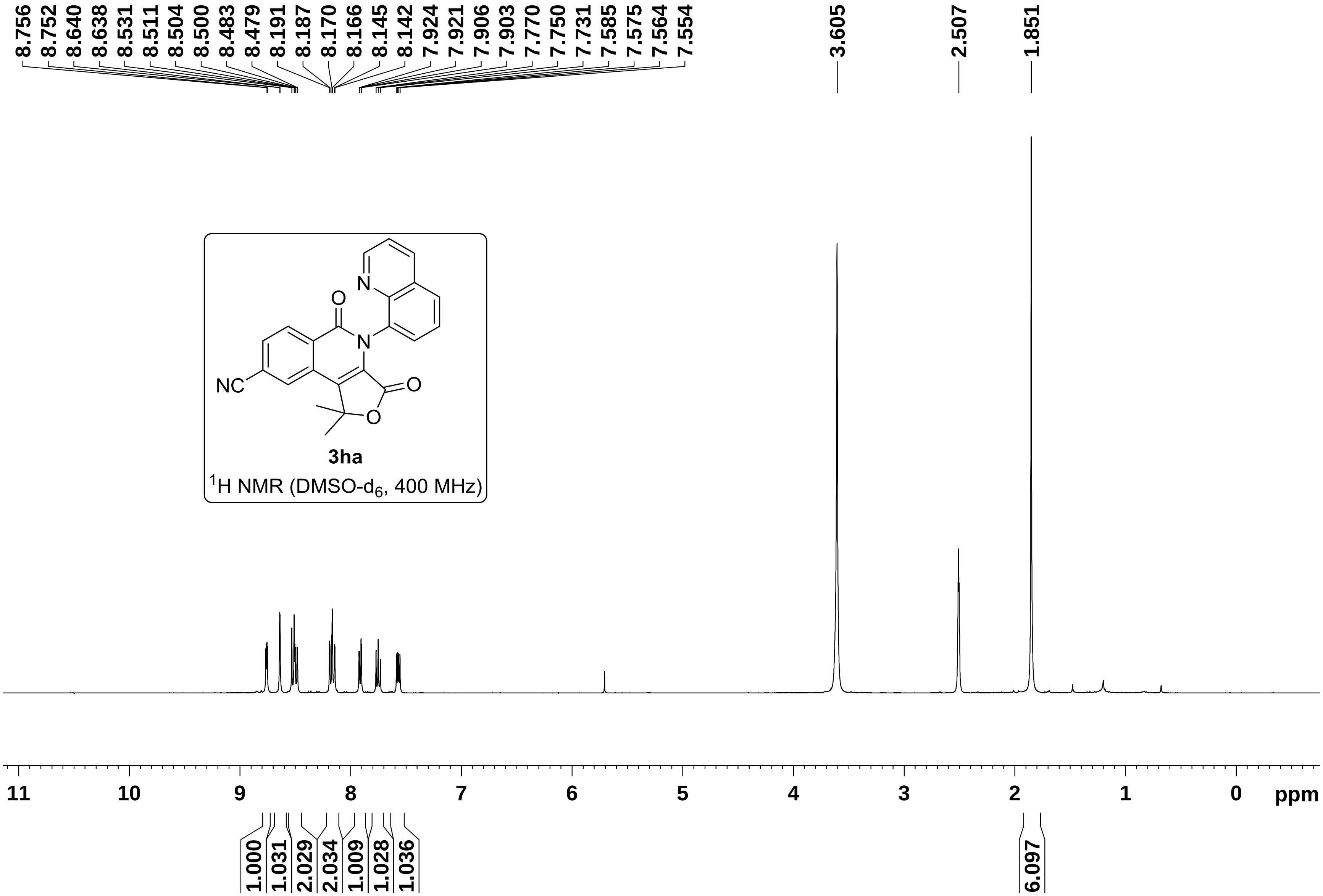


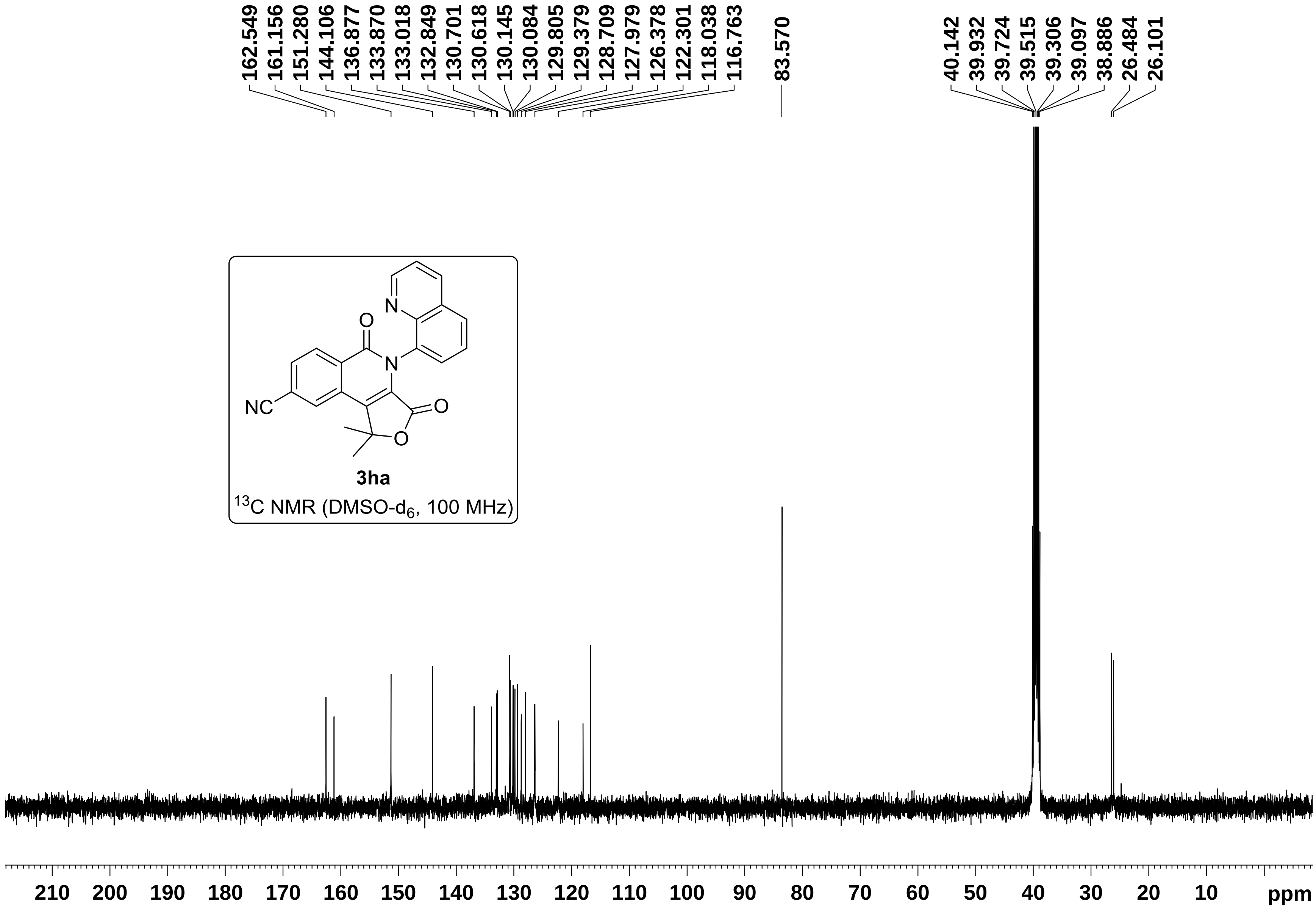
3fa

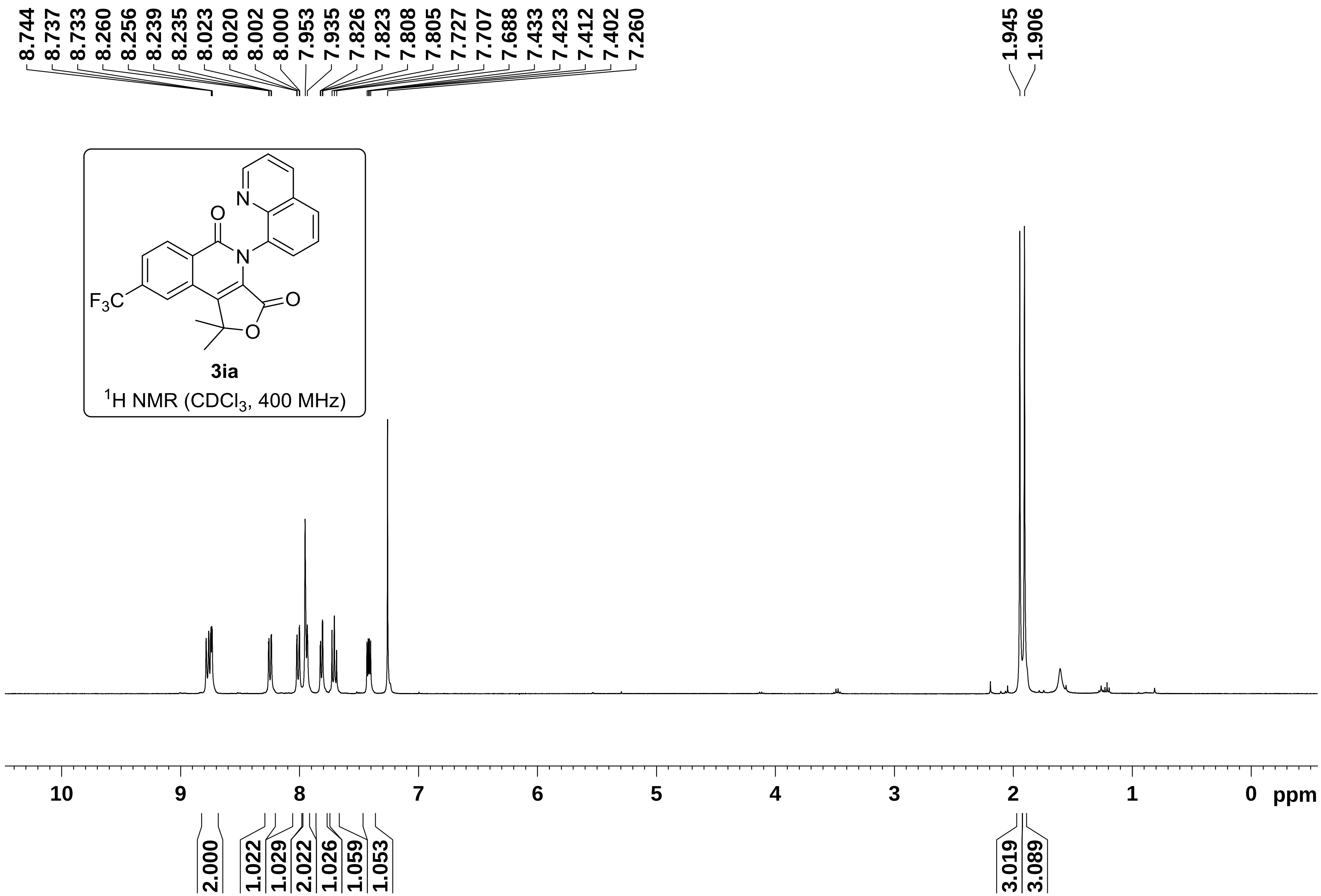
^{13}C NMR ($CDCl_3$, 100 MHz)

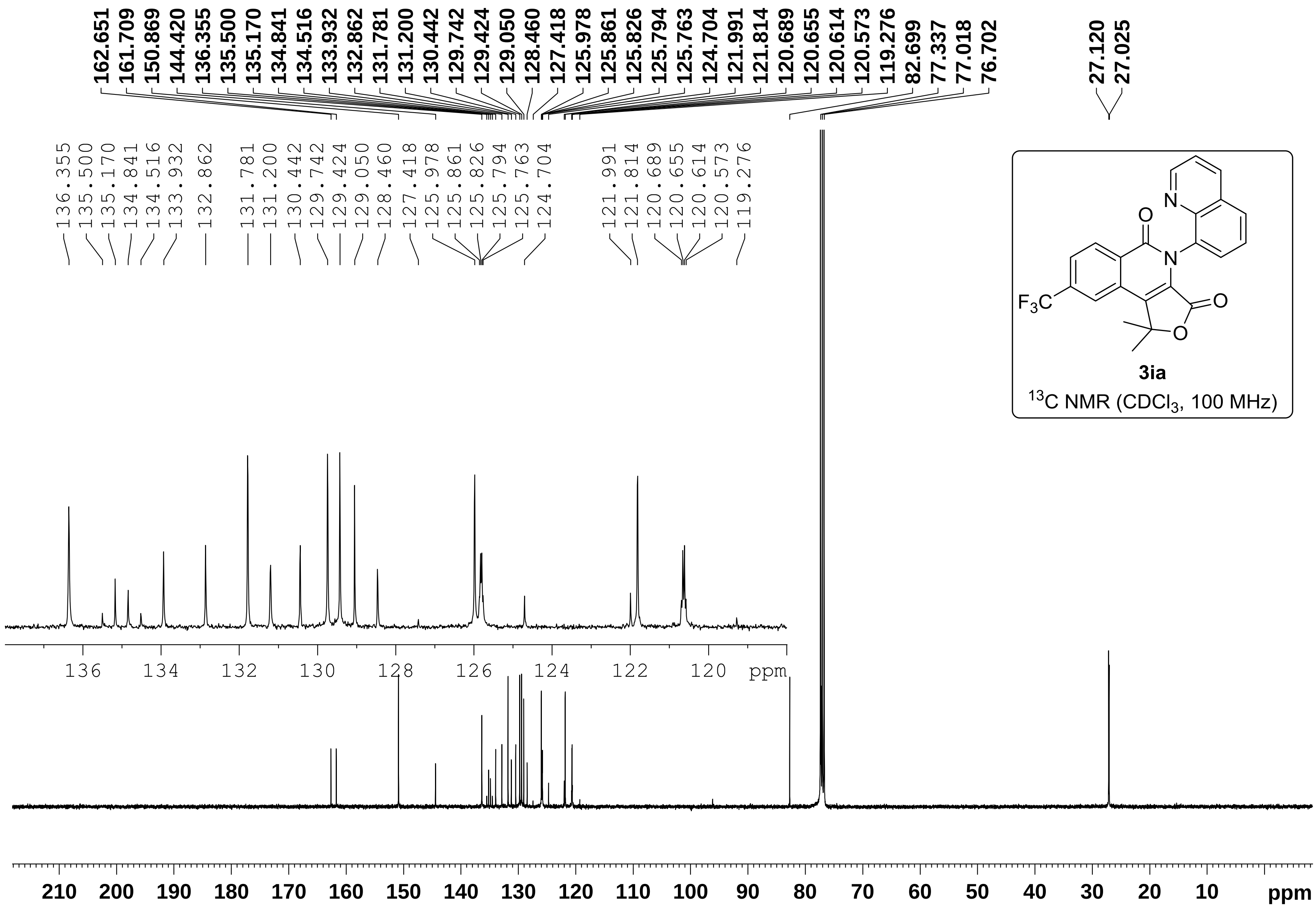

8.746 8.740 8.736 8.328 8.307 8.242 8.238 8.221 8.217 8.065 8.062 8.039 8.035 8.017 8.014 7.998 7.995 7.978 7.975 7.802 7.798 7.783 7.780 7.705 7.685 7.666 7.416 7.406 7.396 7.385 7.255
1.903 1.865
-0.000
N
O
N
O
I
O
3ga
1H NMR (CDCl3, 400 MHz)
11 10 9 8 7 6 5 4 3 2 1 0 ppm
1.047 1.000 1.060 3.135 1.021 1.037 1.040
3.008 3.016

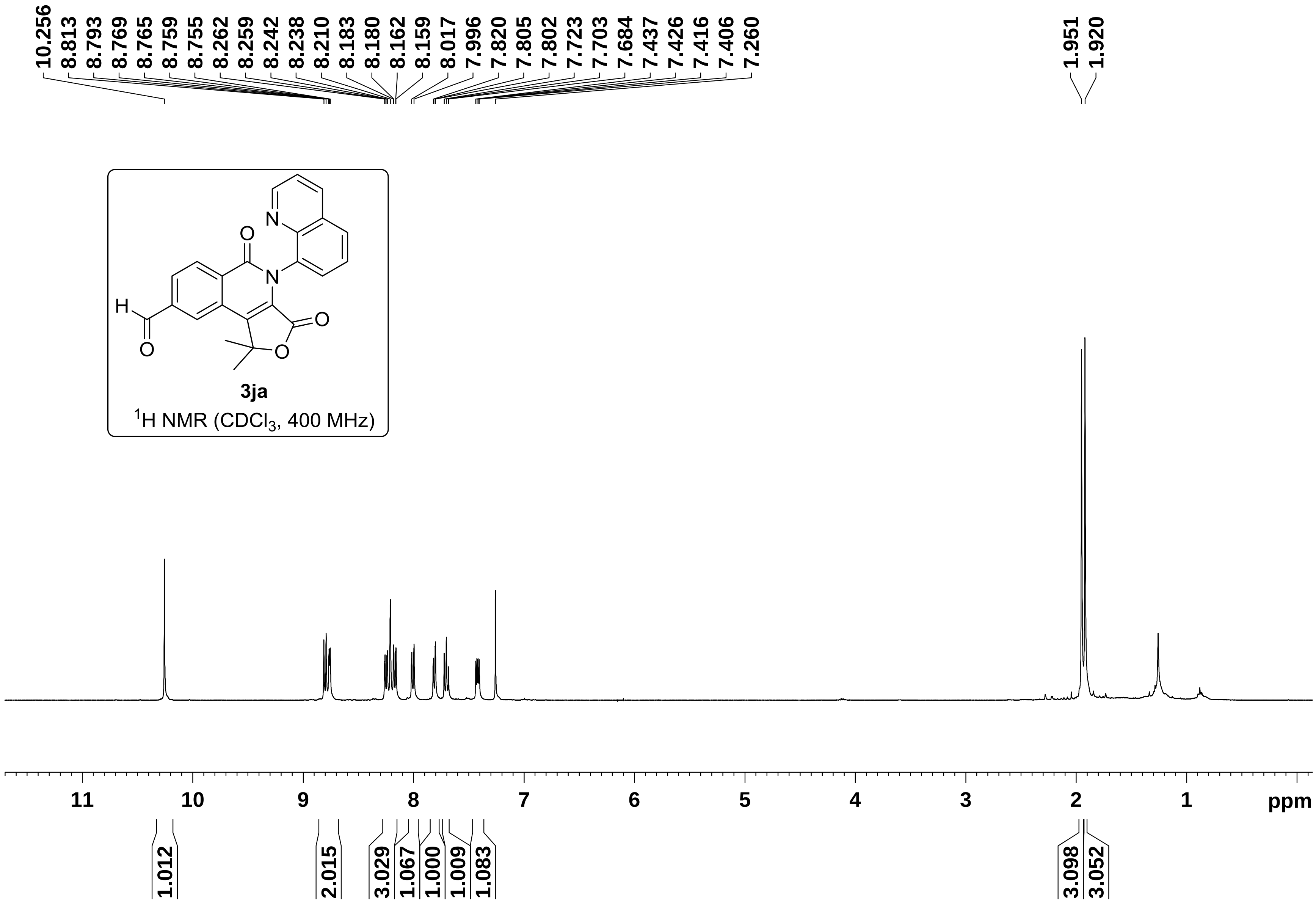

162.780
162.320
150.845
144.466
138.756
136.399
133.439
133.019
132.511
132.046
131.646
129.649
129.502
129.030
128.025
128.005
125.998
121.777
101.261
82.712
77.379
77.061
76.743
27.066
27.012
3ga
^{13}C NMR ($CDCl_3$, 100 MHz)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

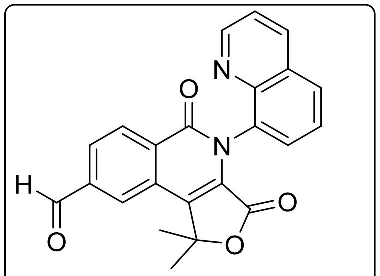

8.756
8.752
8.640
8.638
8.531
8.511
8.504
8.500
8.483
8.479
8.191
8.187
8.170
8.166
8.145
8.142
7.924
7.921
7.906
7.903
7.770
7.750
7.731
7.585
7.575
7.564
7.554
3.605
2.507
1.851
NC
O
N
N
O
O
3ha
1H NMR (DMSO-d6, 400 MHz)
11
10
9
8
7
6
5
4
3
2
1
0
ppm
1.000
1.031
2.029
2.034
1.009
1.028
1.036
6.097


162.549
161.156
151.280
144.106
136.877
133.870
133.018
132.849
130.701
130.618
130.145
130.084
129.805
129.379
128.709
127.979
126.378
122.301
118.038
116.763
83.570
40.142
39.932
39.724
39.515
39.306
39.097
38.886
26.484
26.101
N
O
N
NC
O
O
3ha
^{13}C NMR (DMSO-d$_6$, 100 MHz)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


8.744
8.737
8.733
8.260
8.256
8.239
8.235
8.023
8.020
8.002
8.000
7.953
7.935
7.826
7.823
7.808
7.805
7.727
7.707
7.688
7.433
7.423
7.412
7.402
7.260
1.945
1.906
N
O
N
F3C
O
O
3ia
1H NMR (CDCl3, 400 MHz)
10
9
8
7
6
5
4
3
2
1
0
ppm
2.000
1.022
1.029
2.022
1.026
1.059
1.053
3.019
3.089

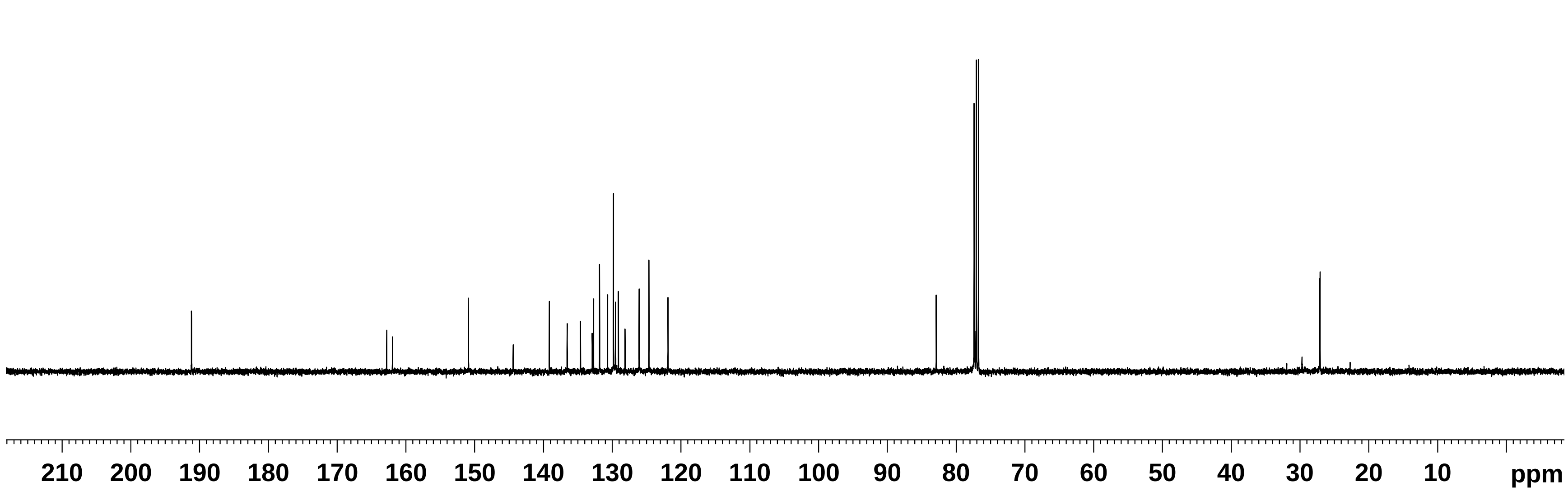

162.651
161.709
150.869
144.420
136.355
135.500
135.170
134.841
134.516
133.932
132.862
131.781
131.200
130.442
129.742
129.424
129.050
128.460
127.418
125.978
125.861
125.826
125.794
125.763
124.704
121.991
121.814
120.689
120.655
120.614
120.573
119.276
82.699
77.337
77.018
76.702
27.120
27.025
3ia
^{13}C NMR ($CDCl_3$, 100 MHz)
136 134 132 130 128 126 124 122 120 ppm
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

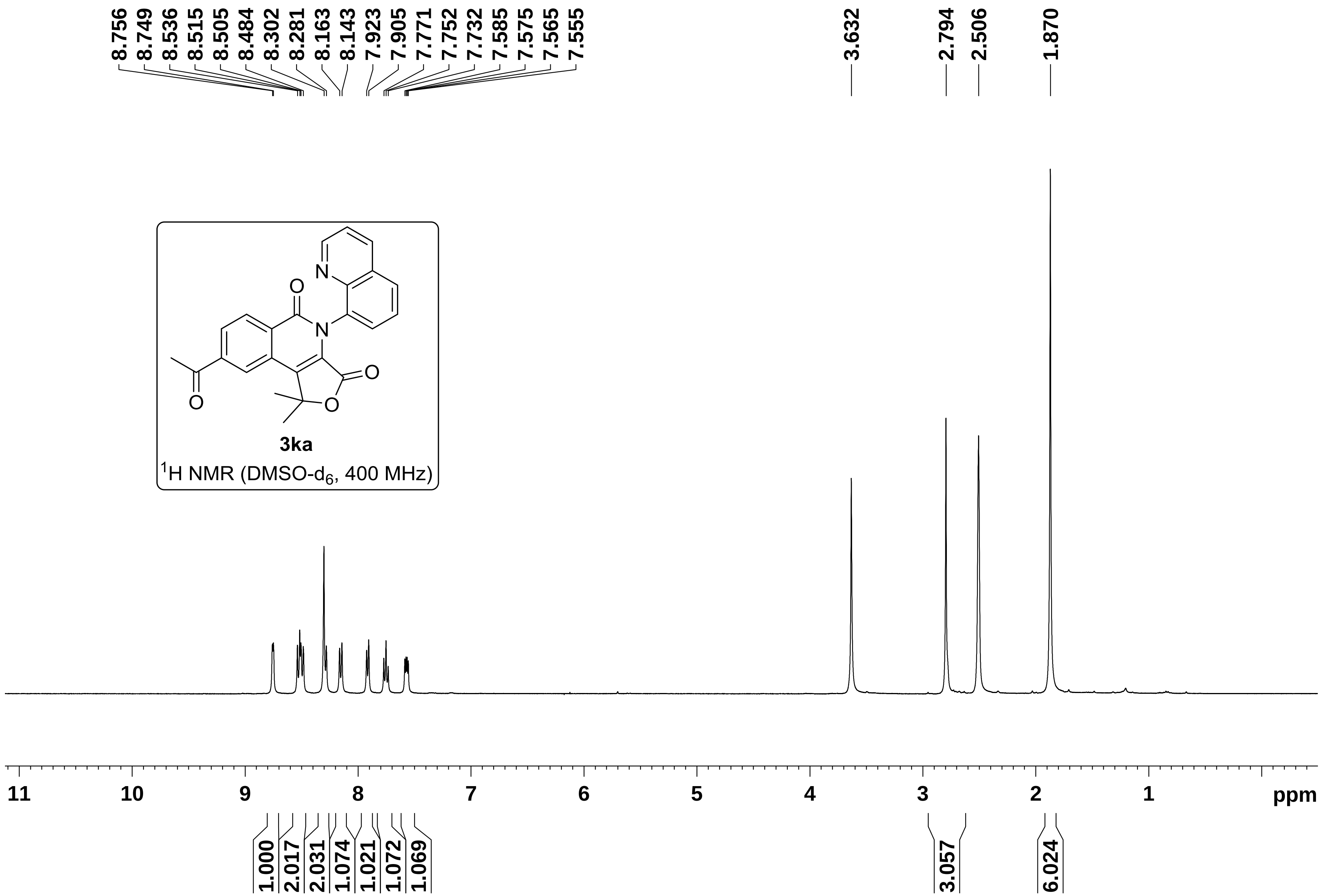

10.256
8.813
8.793
8.769
8.765
8.759
8.755
8.262
8.259
8.242
8.238
8.210
8.183
8.180
8.162
8.159
8.017
7.996
7.820
7.805
7.802
7.723
7.703
7.684
7.437
7.426
7.416
7.406
7.260
1.951
1.920
3ja
^{1}H NMR ($CDCl_3$, 400 MHz)
11
10
9
8
7
6
5
4
3
2
1
ppm
1.012
2.015
3.029
1.067
1.000
1.009
1.083
3.098
3.052

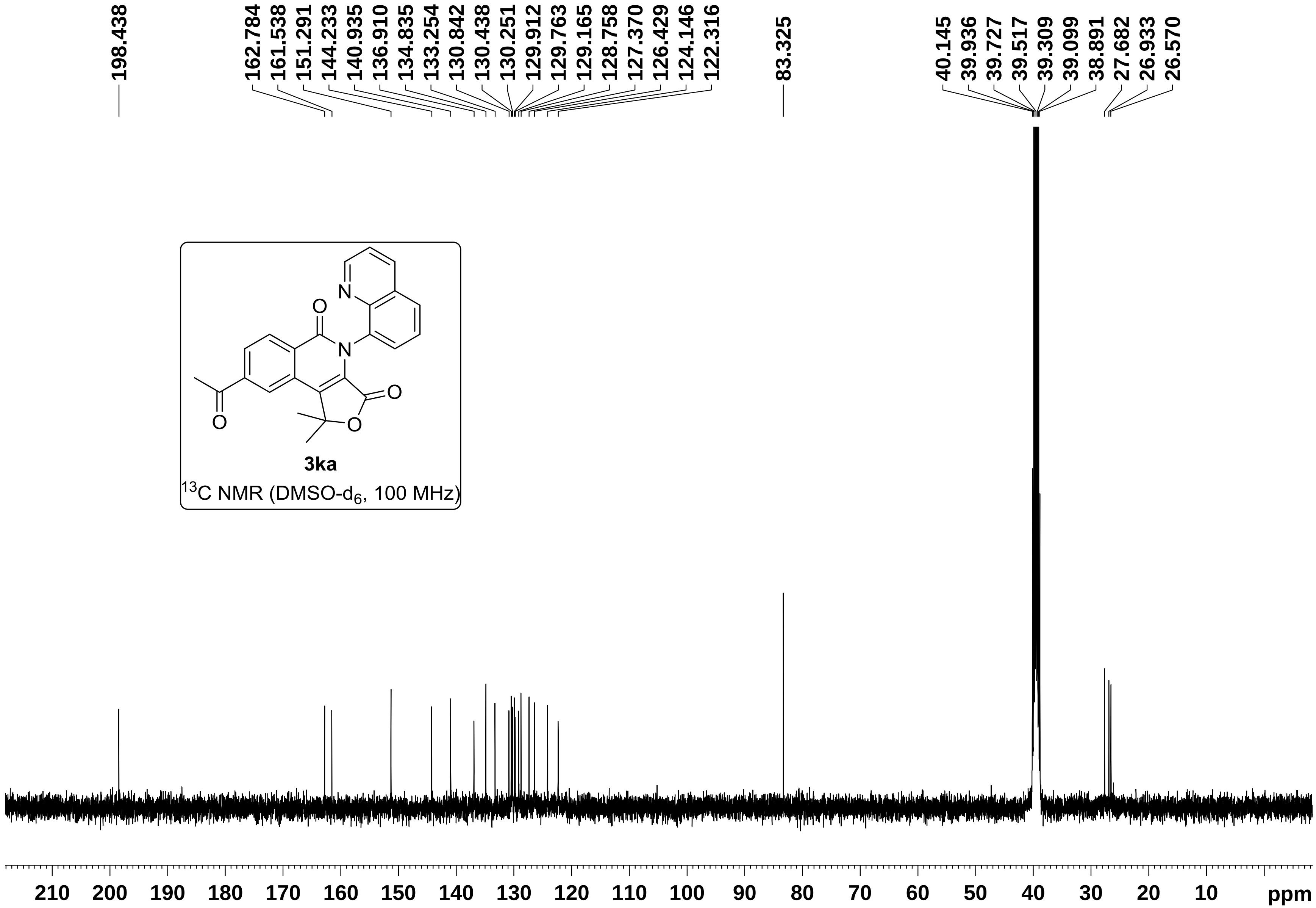


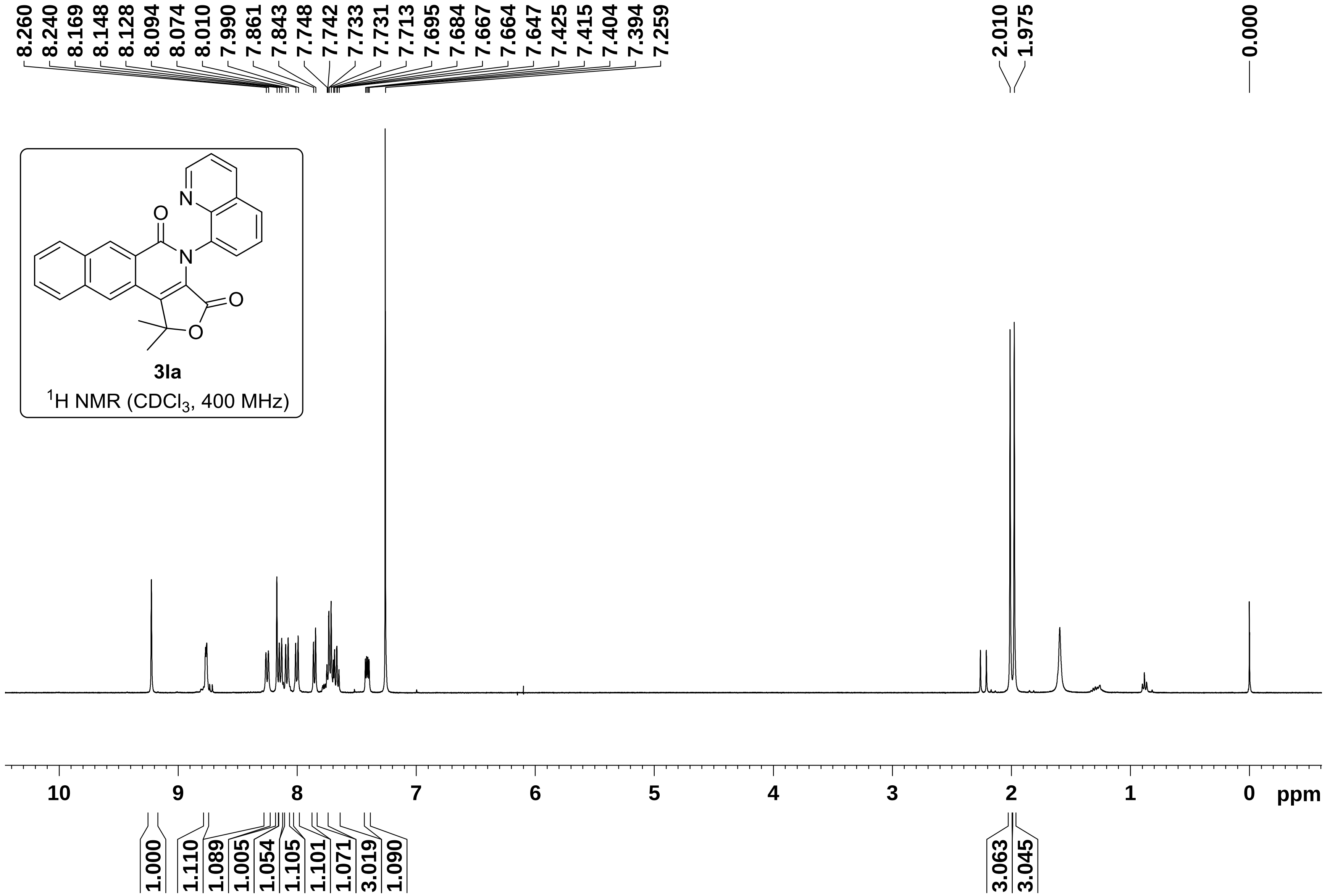
3ja

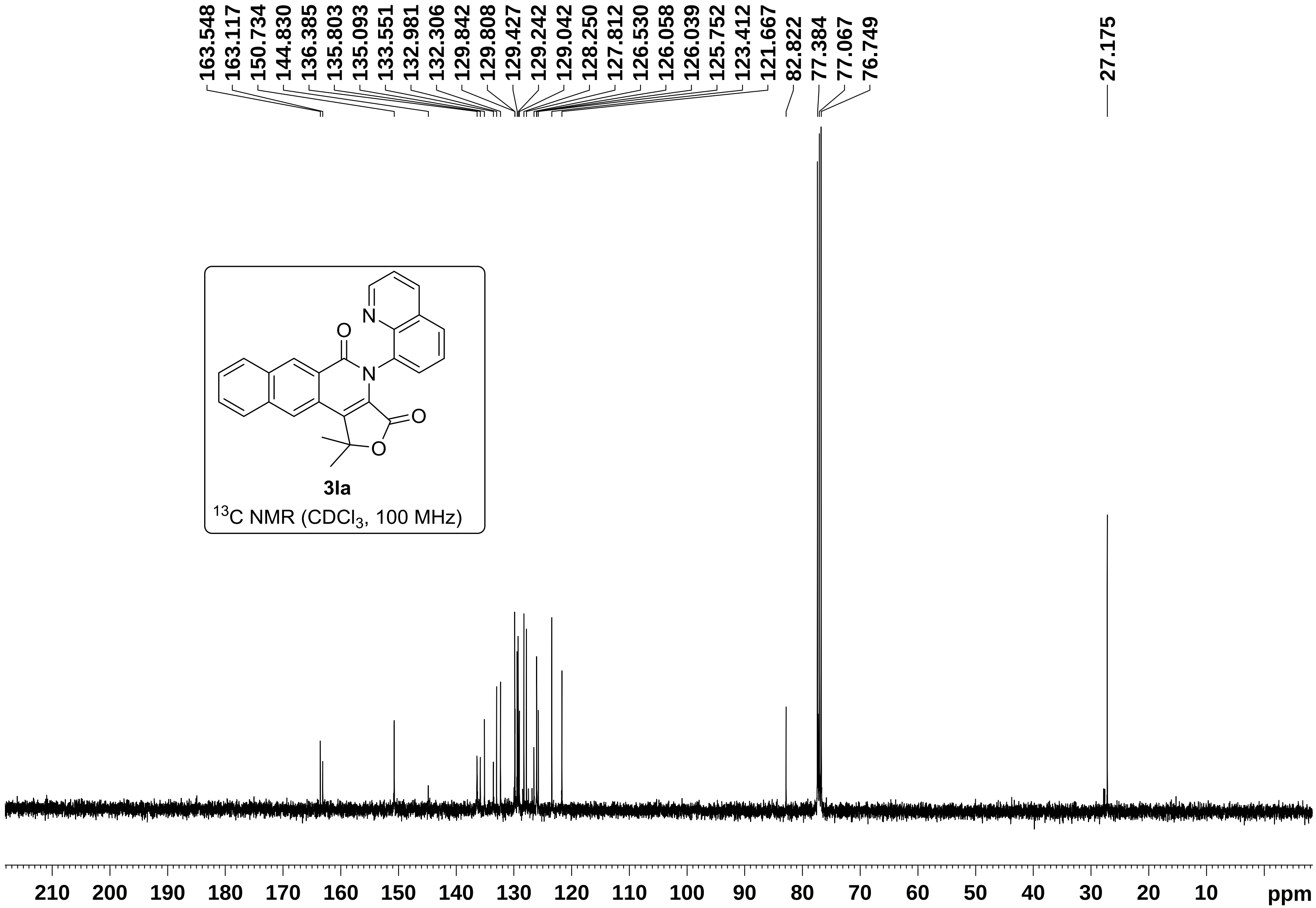
^{13}C NMR ($CDCl_3$, 100 MHz)

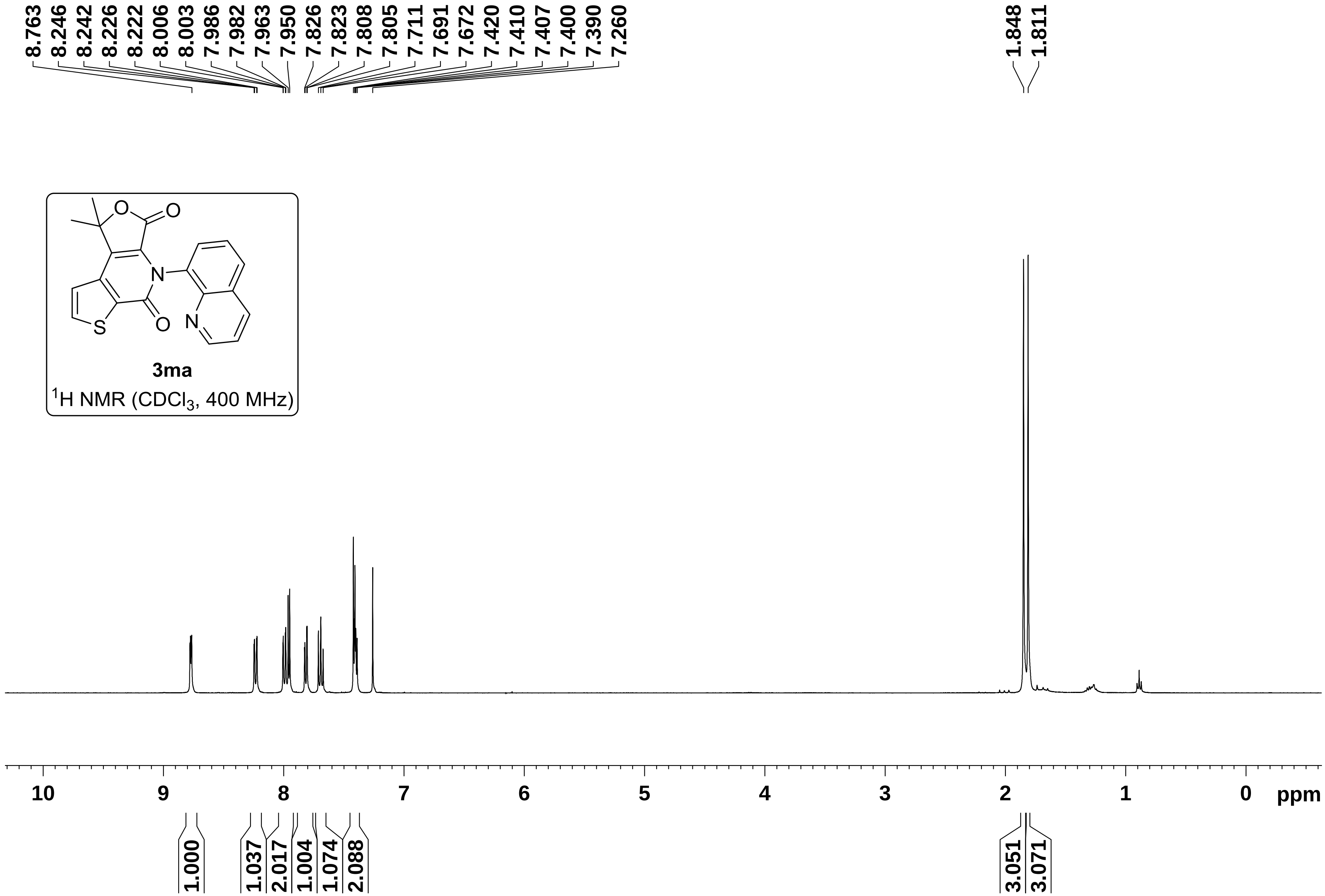


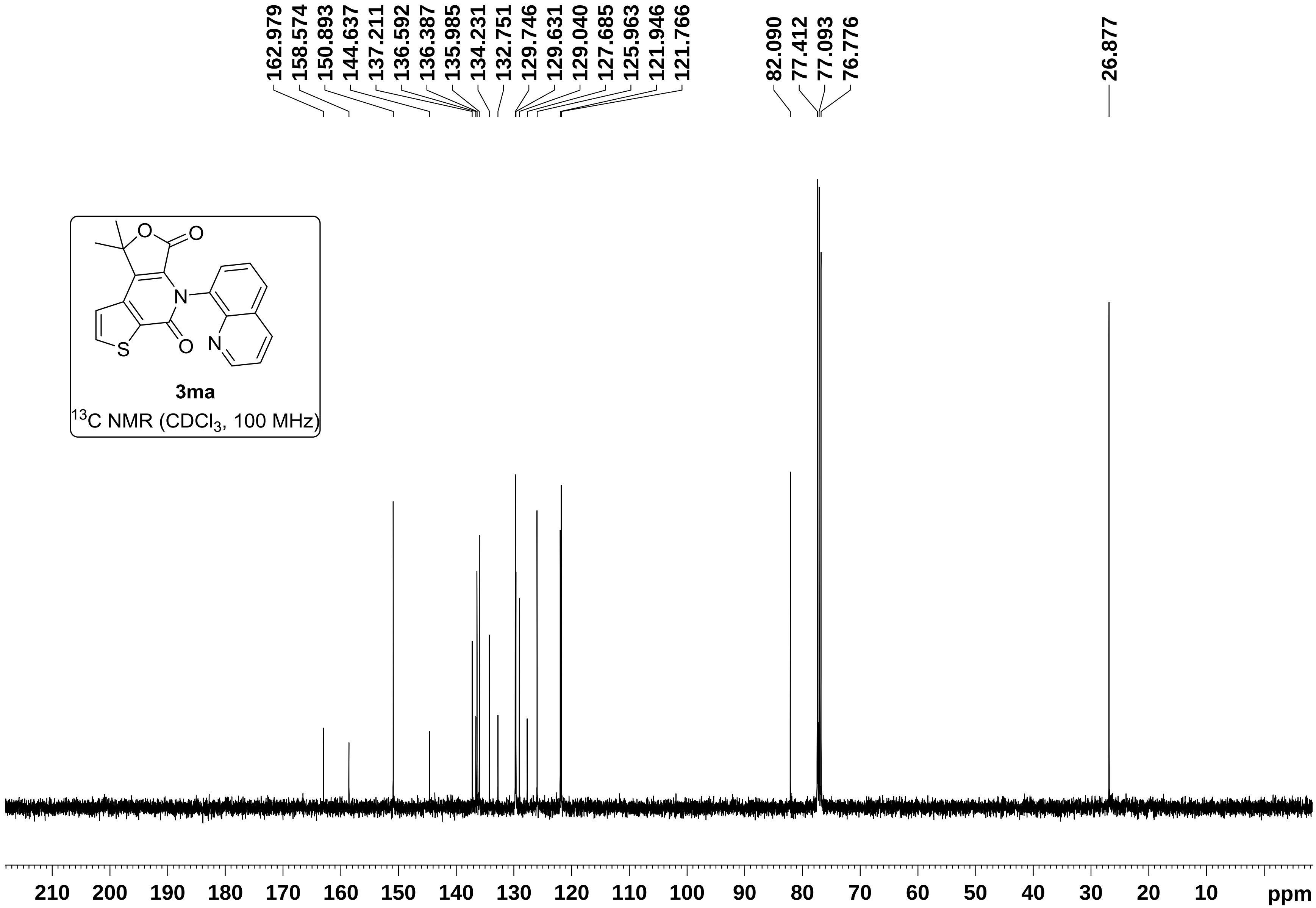

8.756
8.749
8.536
8.515
8.505
8.484
8.302
8.281
8.163
8.143
7.923
7.905
7.771
7.752
7.732
7.585
7.575
7.565
7.555
3.632
2.794
2.506
1.870
N
O
N
O
O
O
3ka
¹H NMR (DMSO-d6, 400 MHz)
11
10
9
8
7
6
5
4
3
2
1
ppm
1.000
2.017
2.031
1.074
1.021
1.072
1.069
3.057
6.024


198.438
162.784
161.538
151.291
144.233
140.935
136.910
134.835
133.254
130.842
130.438
130.251
129.912
129.763
129.165
128.758
127.370
126.429
124.146
122.316
83.325
40.145
39.936
39.727
39.517
39.309
39.099
38.891
27.682
26.933
26.570
N
O
O
O
O
O
3ka
13C NMR (DMSO-d6, 100 MHz)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


8.260 8.240 8.169 8.148 8.128 8.094 8.074 8.010 7.990 7.861 7.843 7.748 7.742 7.733 7.731 7.713 7.695 7.684 7.667 7.664 7.647 7.425 7.415 7.404 7.394 7.259
2.010 1.975
0.000
3la
1H NMR (CDCl3, 400 MHz)
10 9 8 7 6 5 4 3 2 1 0 ppm
1.000 1.110 1.089 1.005 1.054 1.105 1.101 1.071 3.019 1.090
3.063 3.045

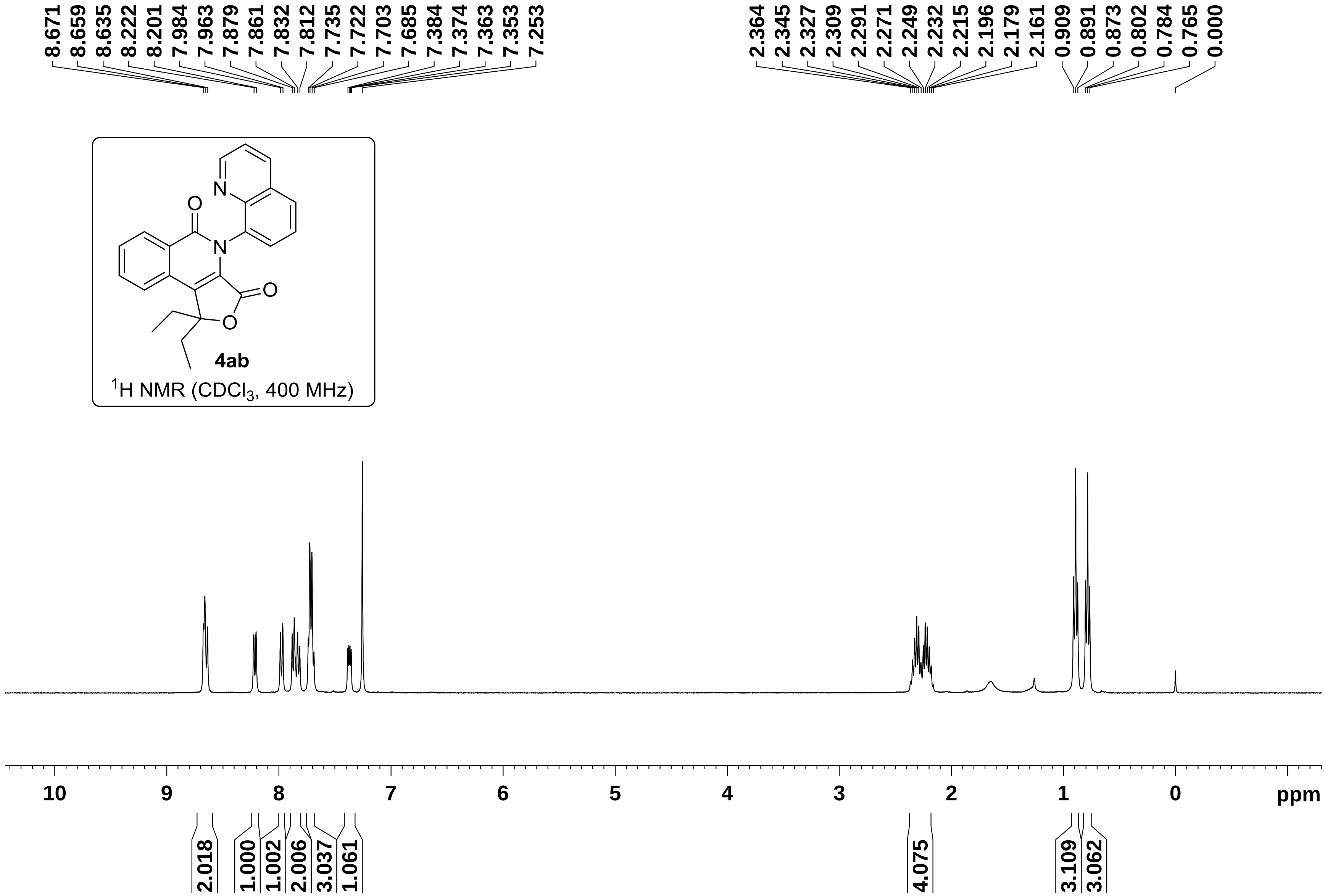

163.548
163.117
150.734
144.830
136.385
135.803
135.093
133.551
132.981
132.306
129.842
129.808
129.427
129.242
129.042
128.250
127.812
126.530
126.058
126.039
125.752
123.412
121.667
82.822
77.384
77.067
76.749
27.175
N
O
N
O
O
3la
^{13}C NMR (CDCl$_3$, 100 MHz)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

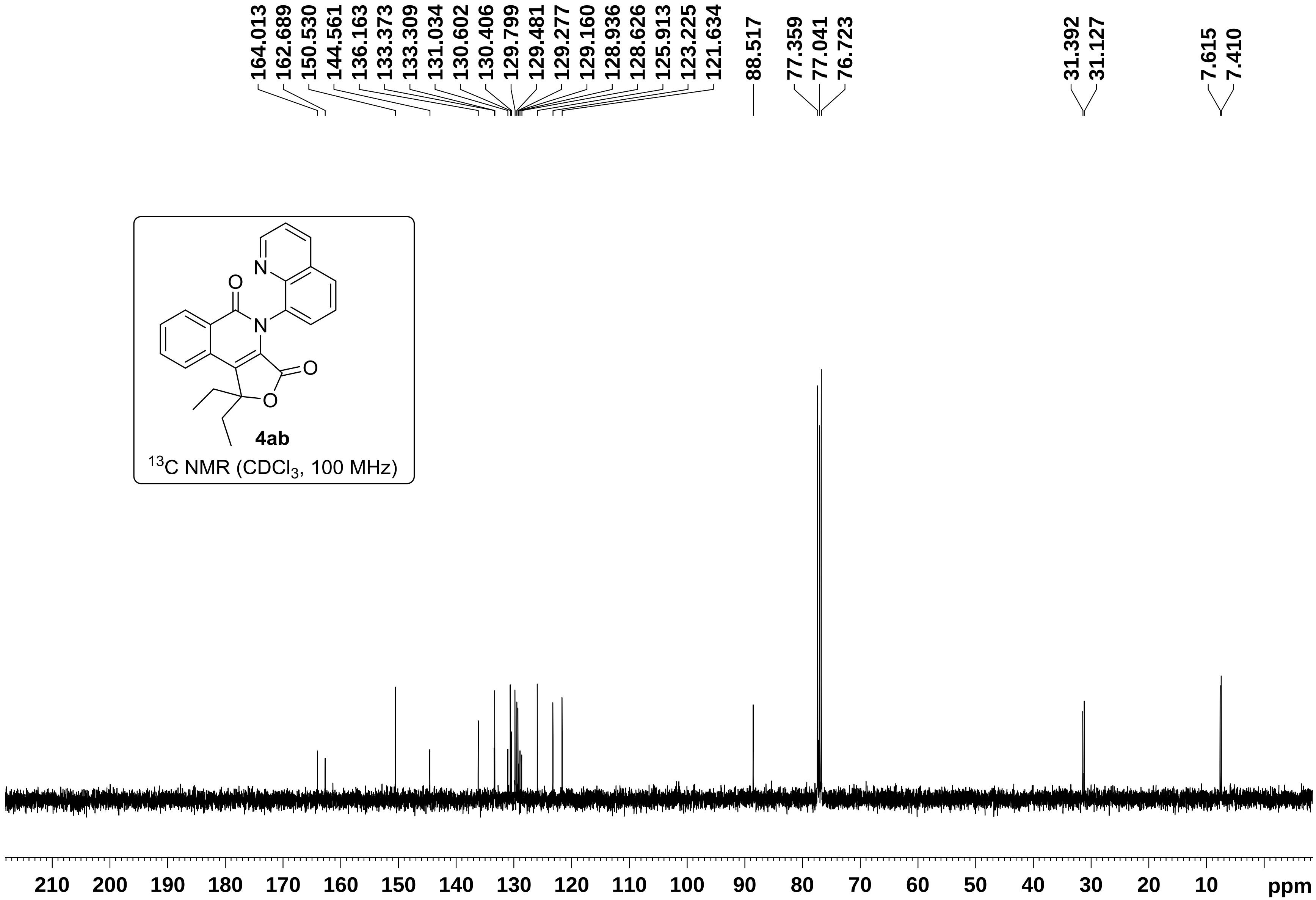

8.763
8.246
8.242
8.226
8.222
8.006
8.003
7.986
7.982
7.963
7.950
7.826
7.823
7.808
7.805
7.711
7.691
7.672
7.420
7.410
7.407
7.400
7.390
7.260
1.848
1.811
3ma
1H NMR (CDCl3, 400 MHz)
10
9
8
7
6
5
4
3
2
1
0
ppm
1.000
1.037
2.017
1.004
1.074
2.088
3.051
3.071



3ma

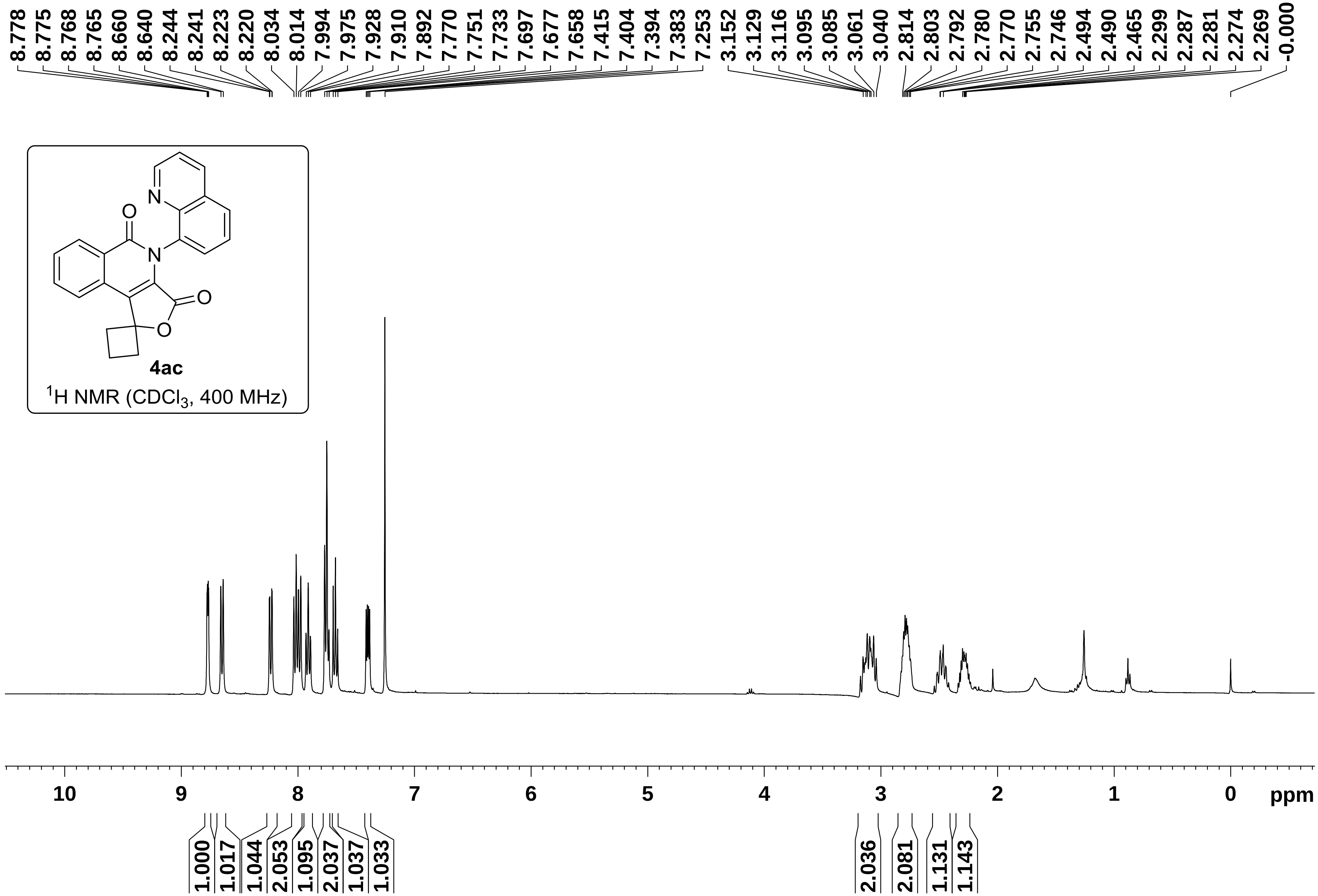
^{13}C NMR ($CDCl_3$, 100 MHz)


8.671
8.659
8.635
8.222
8.201
7.984
7.963
7.879
7.861
7.832
7.812
7.735
7.722
7.703
7.685
7.384
7.374
7.363
7.353
7.253
2.364
2.345
2.327
2.309
2.291
2.271
2.249
2.232
2.215
2.196
2.179
2.161
0.909
0.891
0.873
0.802
0.784
0.765
0.000
O
N
N
O
O
4ab
^{1}H NMR (CDCl$_3$, 400 MHz)
10
9
8
7
6
5
4
3
2
1
0
ppm
2.018
1.000
1.002
2.006
3.037
1.061
4.075
3.109
3.062



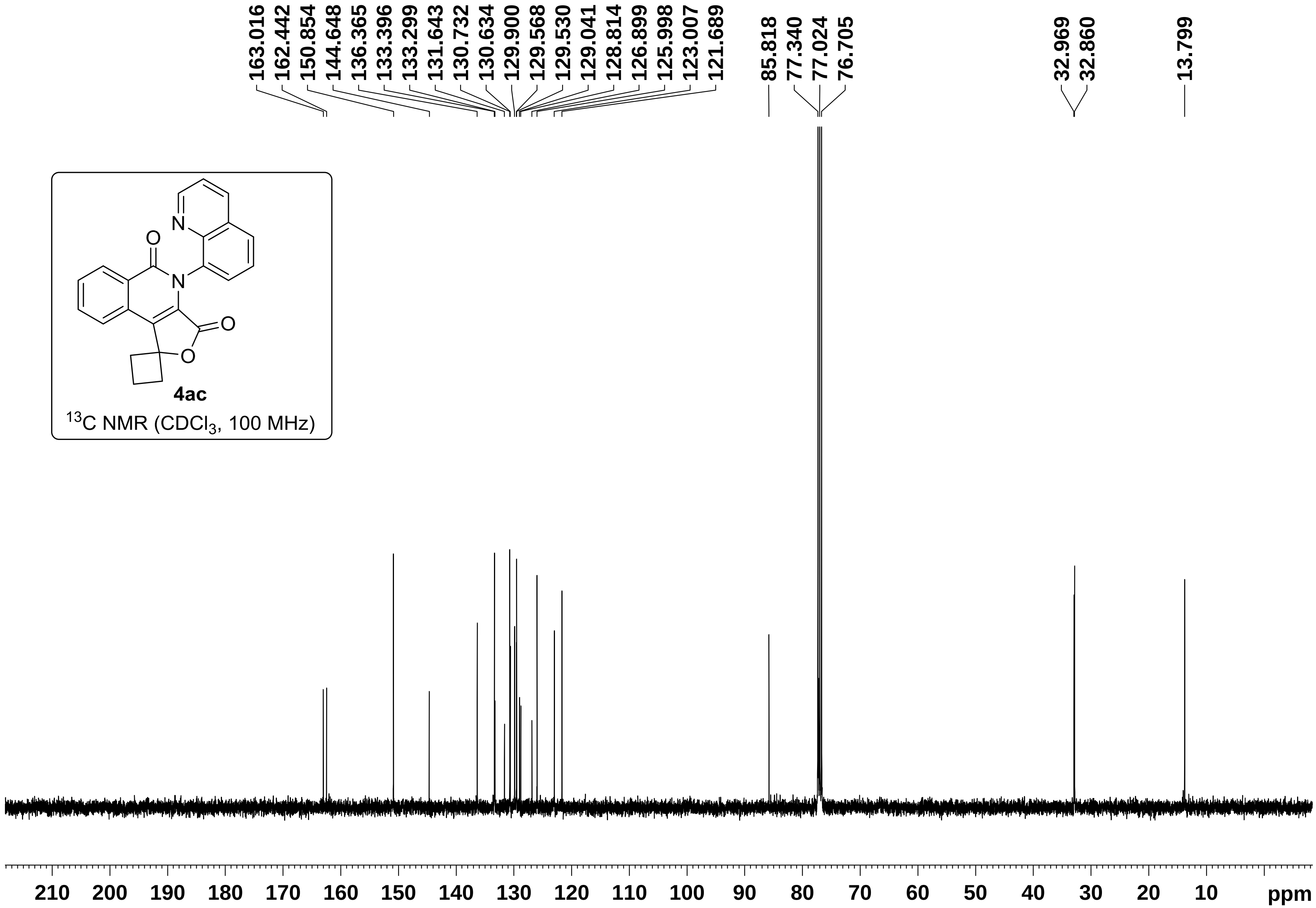
4ab

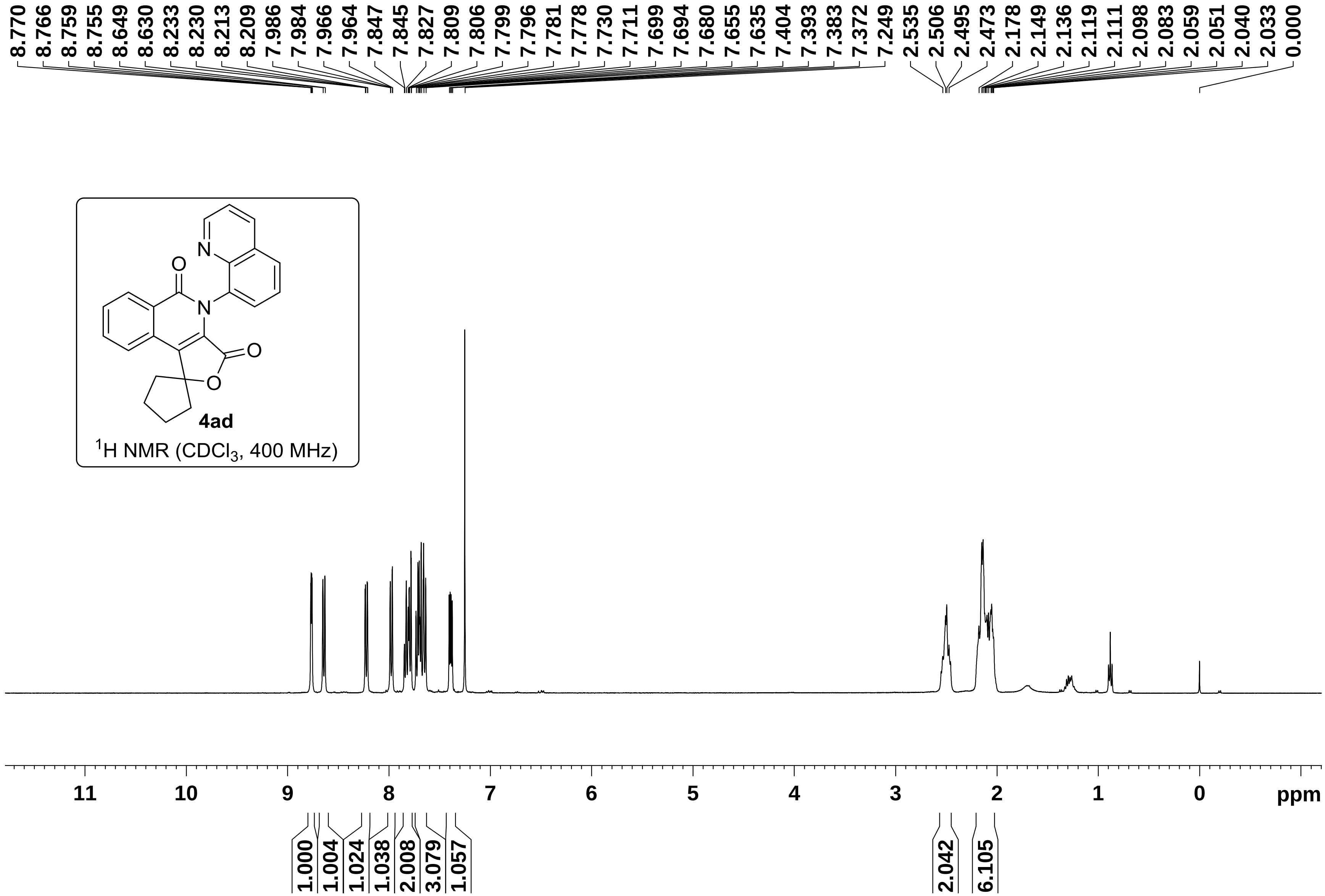
^{13}C NMR (CDCl$_3$, 100 MHz)

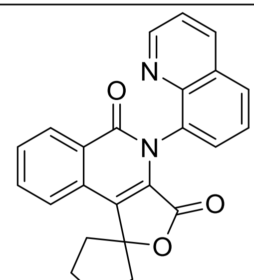


4ac

^{1}H NMR ($CDCl_3$, 400 MHz)

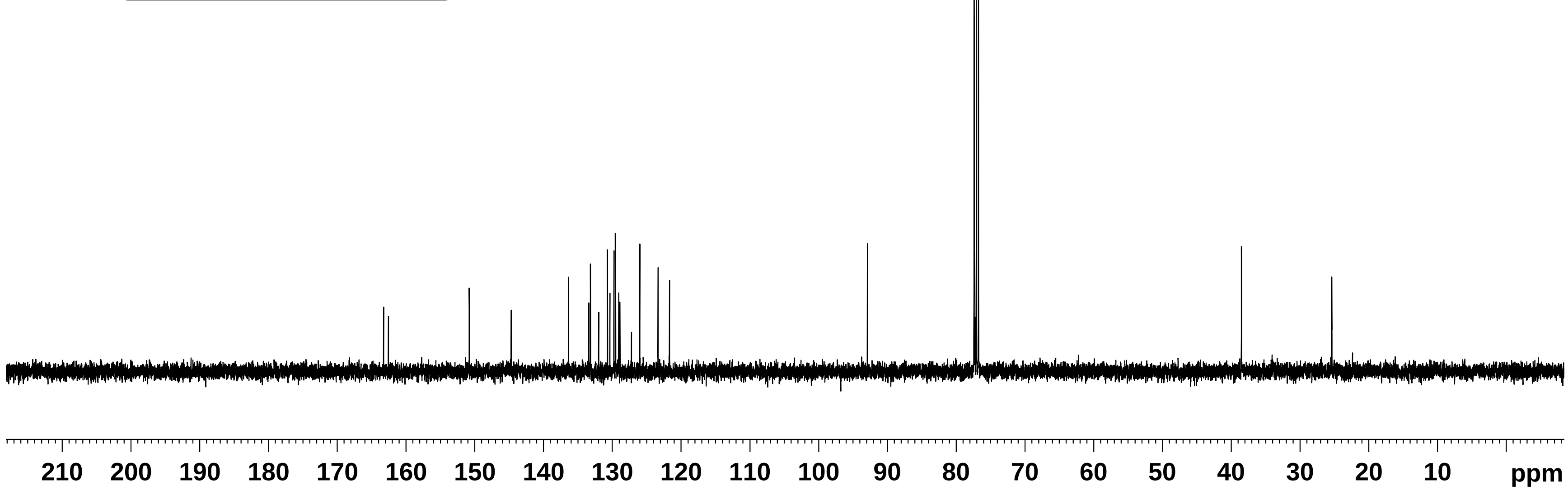

163.016
162.442
150.854
144.648
136.365
133.396
133.299
131.643
130.732
130.634
129.900
129.568
129.530
129.041
128.814
126.899
125.998
123.007
121.689
85.818
77.340
77.024
76.705
32.969
32.860
13.799
N
O
N
O
O
4ac
13C NMR (CDCl3, 100 MHz)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

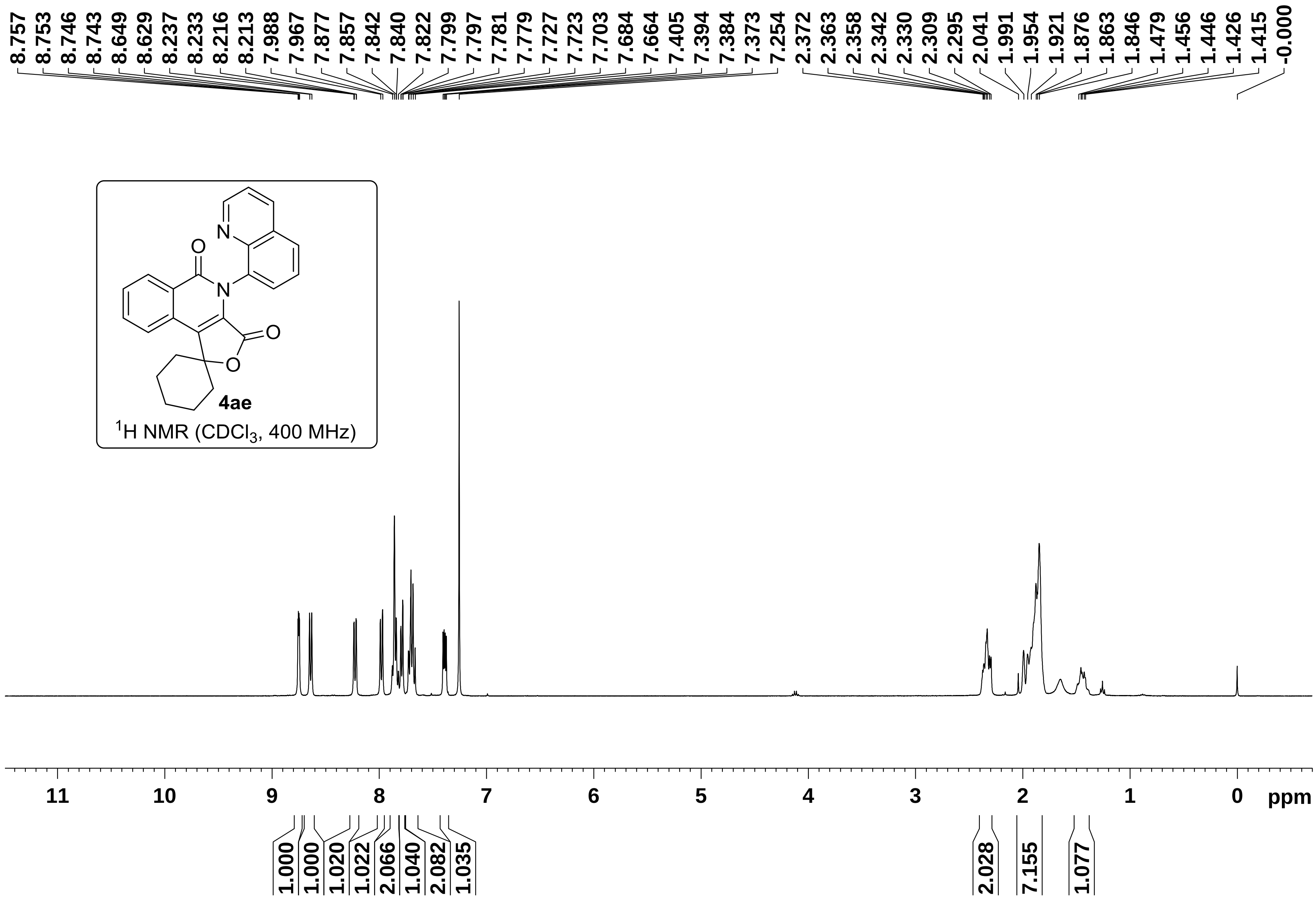

8.770
8.766
8.759
8.755
8.649
8.630
8.233
8.230
8.213
8.209
7.986
7.984
7.966
7.964
7.847
7.845
7.827
7.809
7.806
7.799
7.796
7.781
7.778
7.730
7.711
7.699
7.694
7.680
7.655
7.635
7.404
7.393
7.383
7.372
7.249
2.535
2.506
2.495
2.473
2.178
2.149
2.136
2.119
2.111
2.098
2.083
2.059
2.051
2.040
2.033
0.000
N
O
N
O
O
4ad
1H NMR (CDCl3, 400 MHz)
11
10
9
8
7
6
5
4
3
2
1
0
ppm
1.000
1.004
1.024
1.038
2.008
3.079
1.057
2.042
6.105

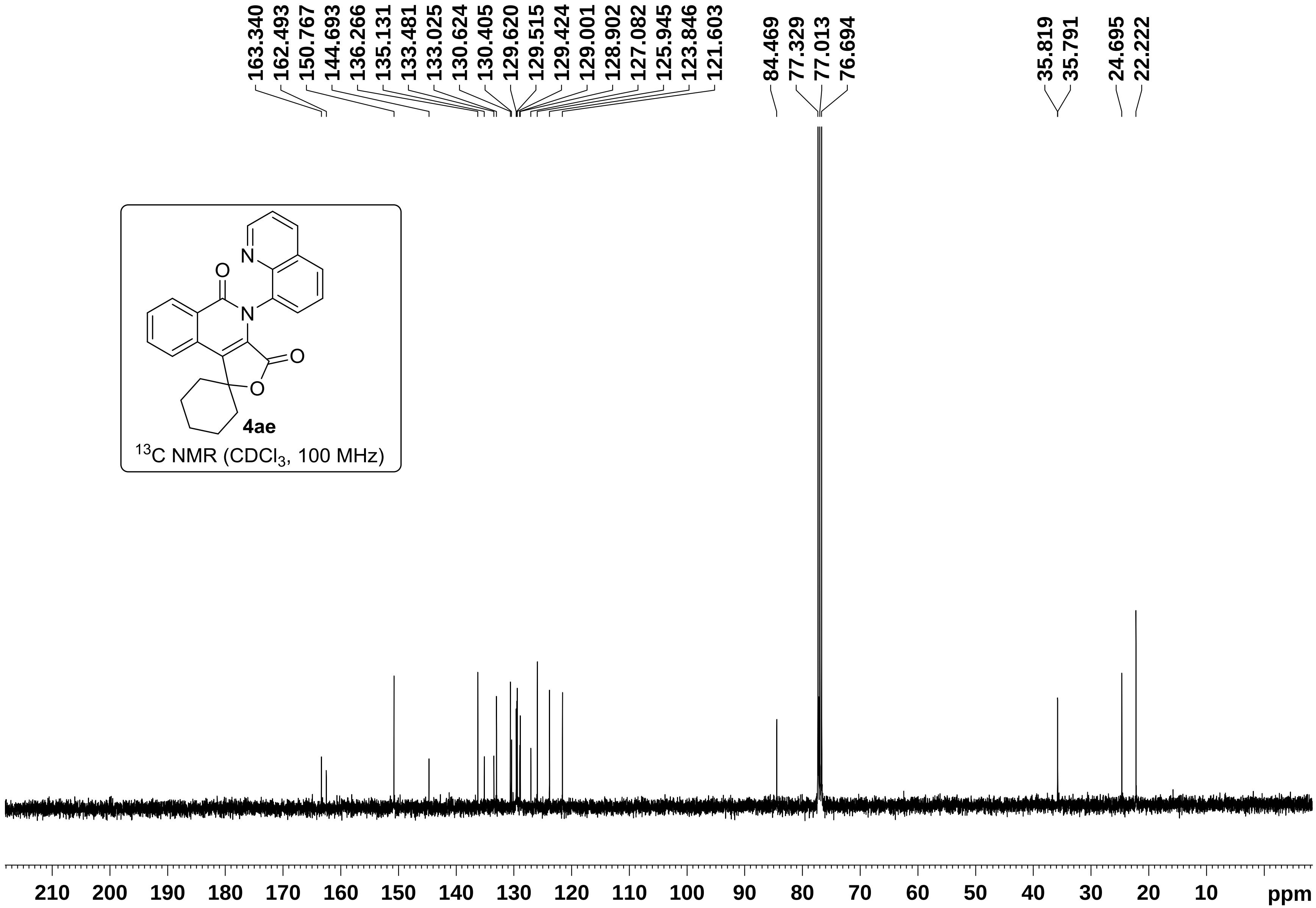


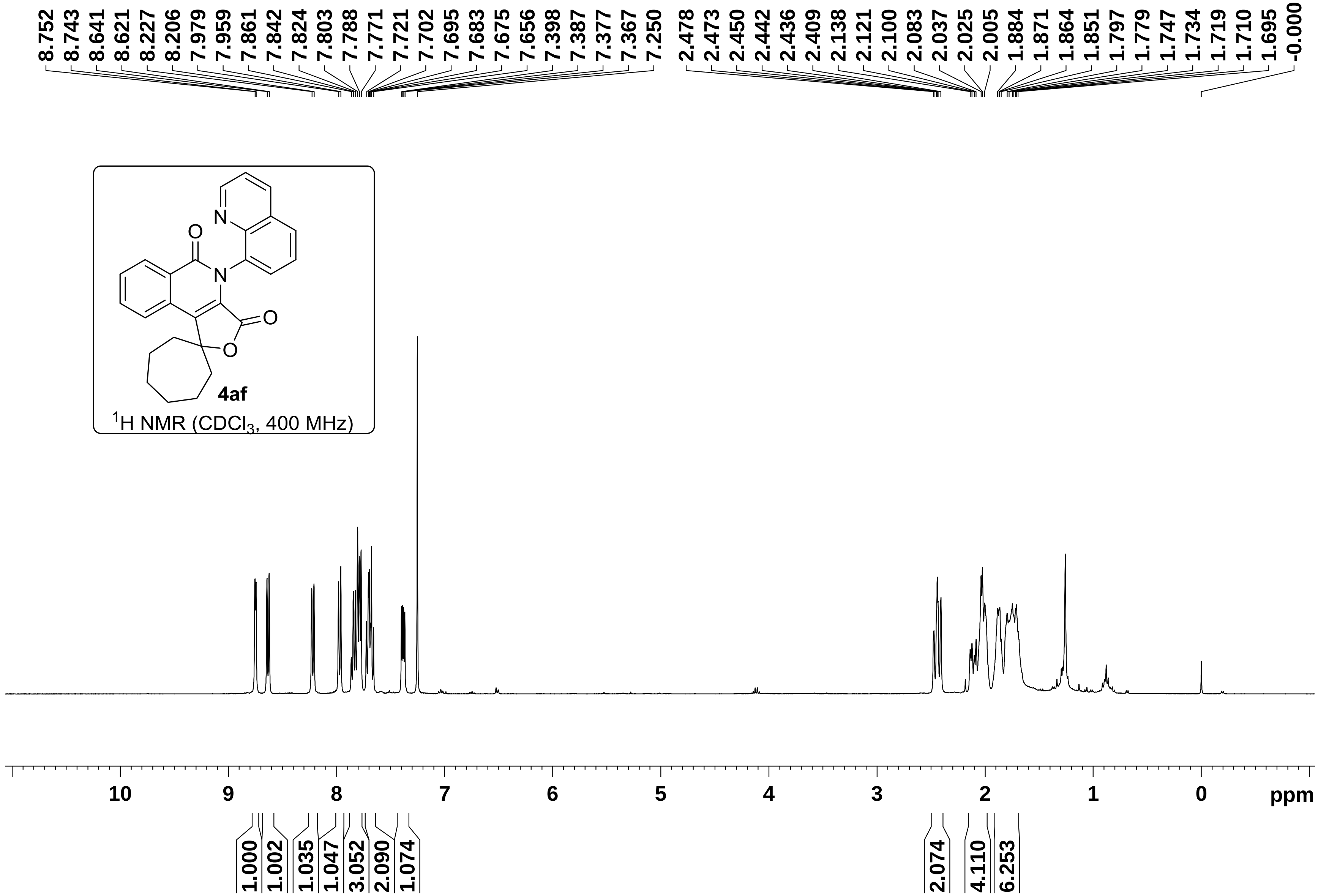
4ad

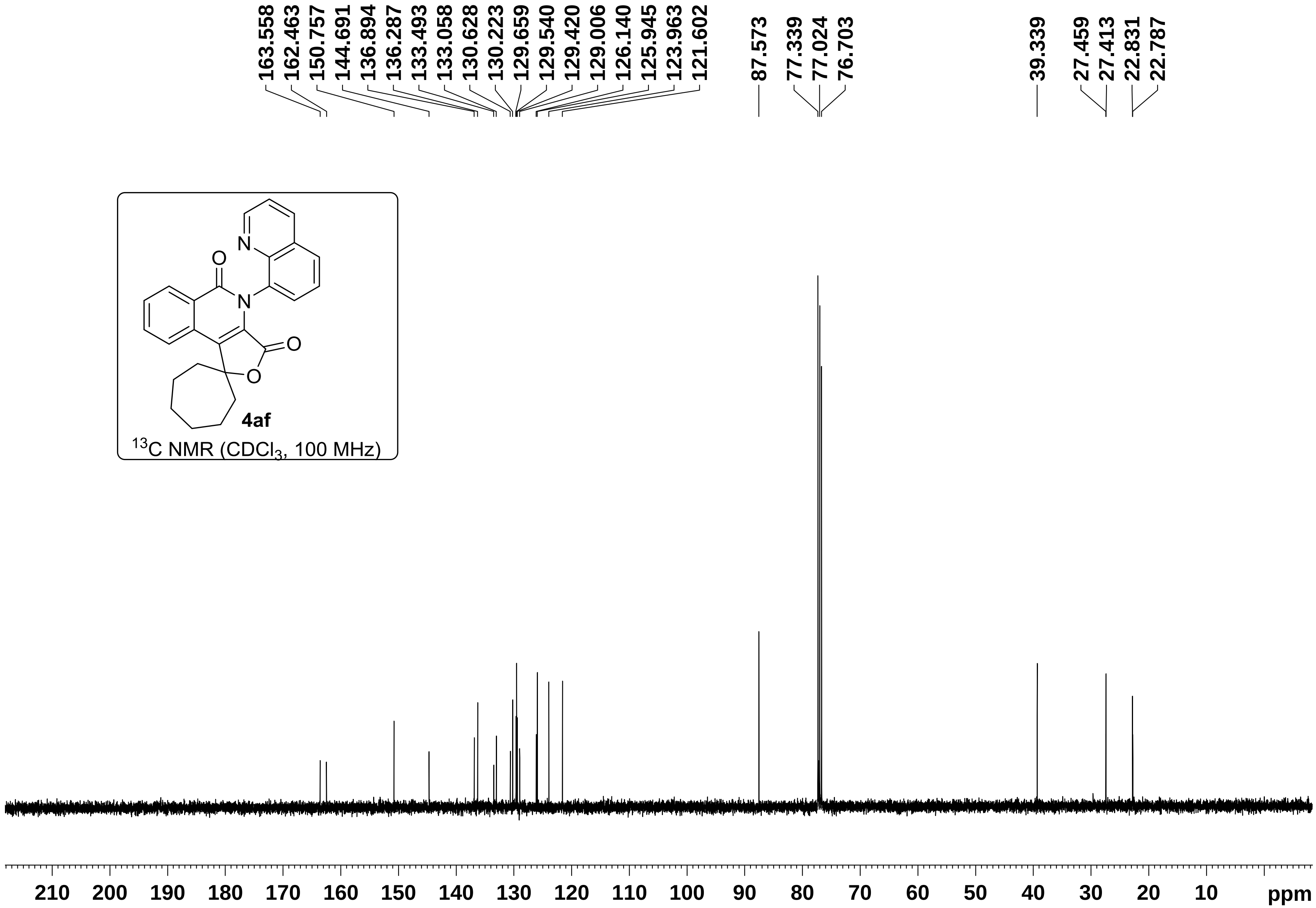
^{13}C NMR (CDCl$_3$, 100 MHz)

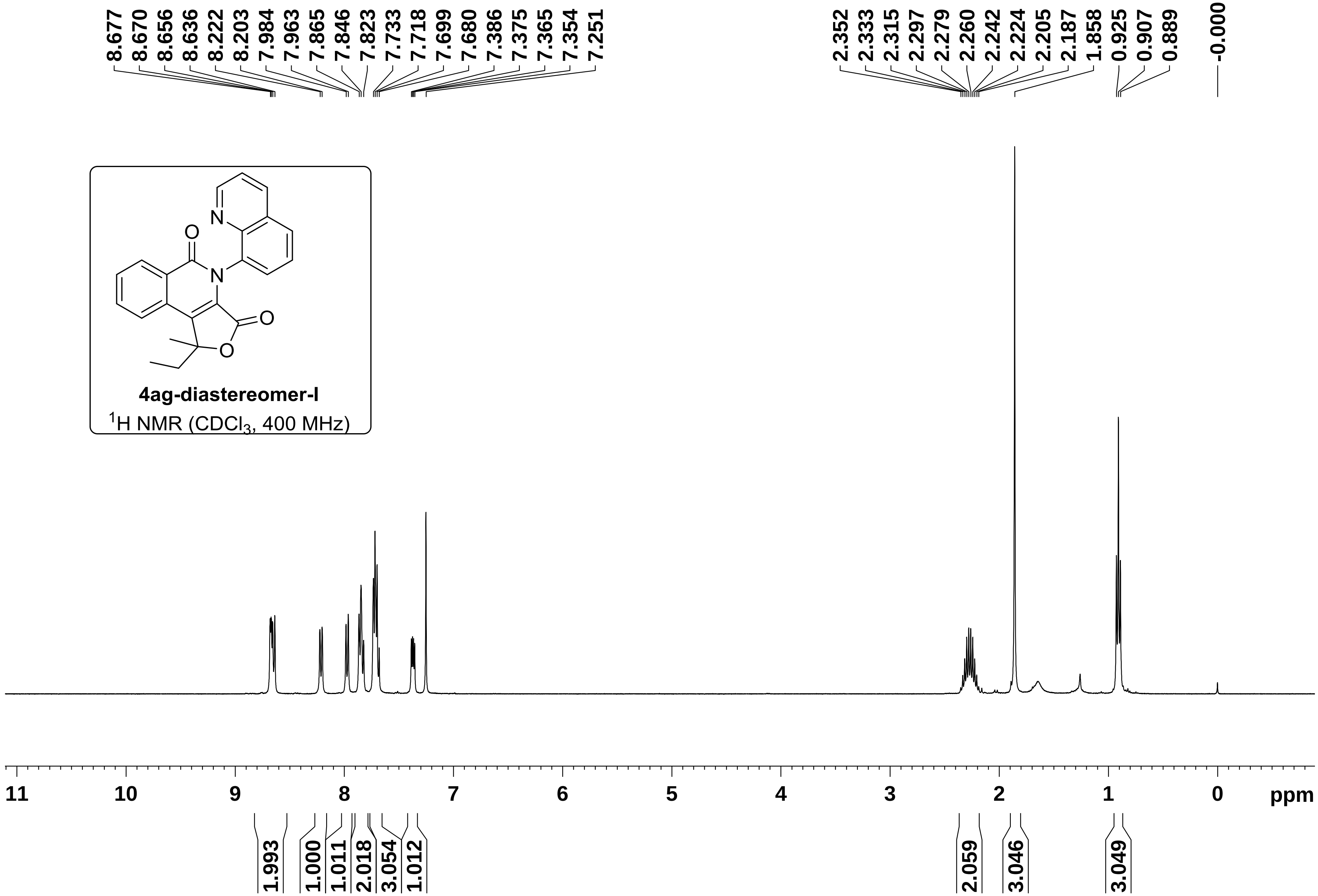



8.757
8.753
8.746
8.743
8.649
8.629
8.237
8.233
8.216
8.213
7.988
7.967
7.877
7.857
7.842
7.840
7.822
7.799
7.797
7.781
7.779
7.727
7.723
7.703
7.684
7.664
7.405
7.394
7.384
7.373
7.254
2.372
2.363
2.358
2.342
2.330
2.309
2.295
2.041
1.991
1.954
1.921
1.876
1.863
1.846
1.479
1.456
1.446
1.426
1.415
-0.000
O
N
N
O
O
4ae
1H NMR (CDCl3, 400 MHz)
11
10
9
8
7
6
5
4
3
2
1
0
ppm
1.000
1.000
1.020
1.022
2.066
1.040
2.082
1.035
2.028
7.155
1.077

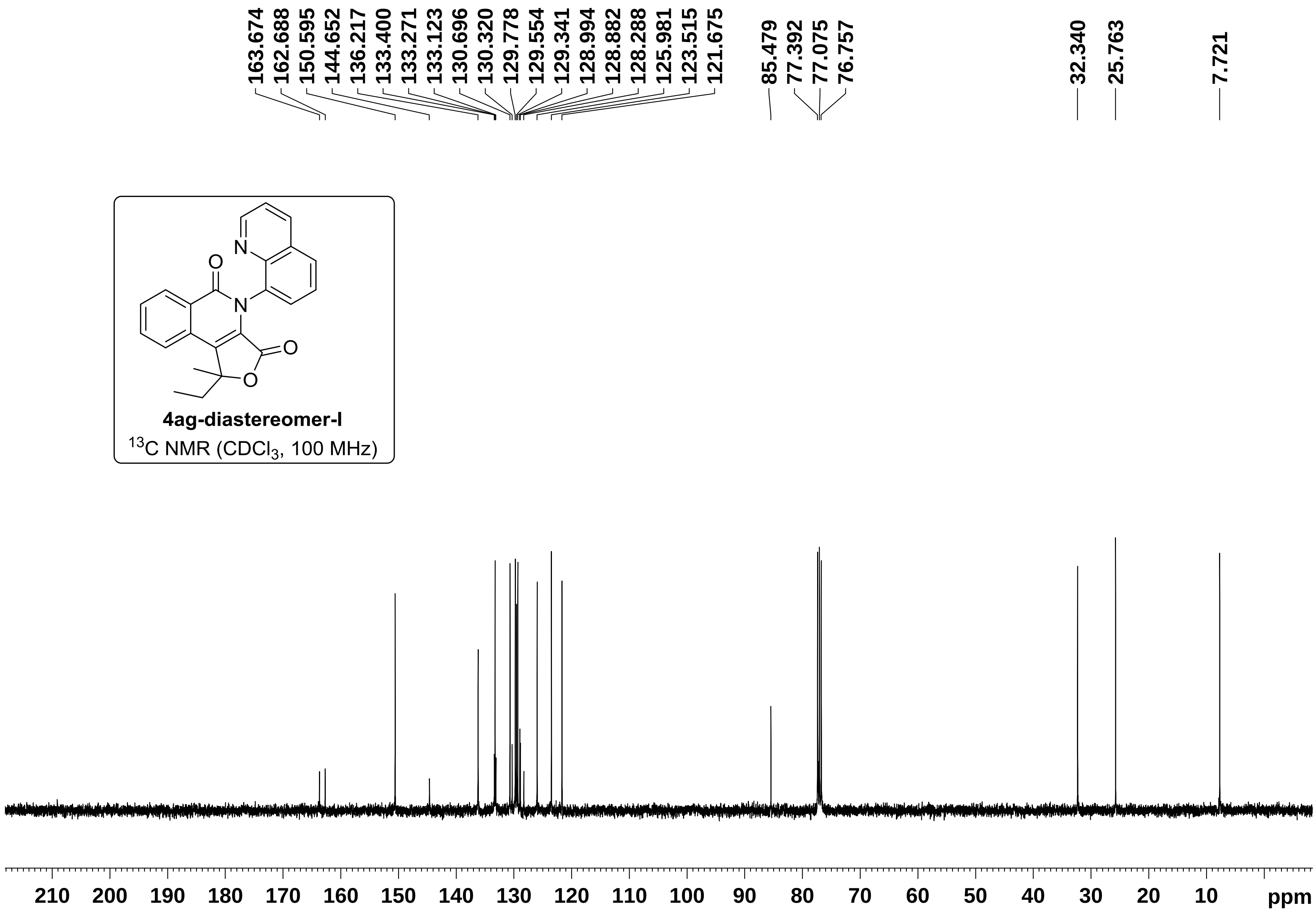

163.340
162.493
150.767
144.693
136.266
135.131
133.481
133.025
130.624
130.405
129.620
129.515
129.424
129.001
128.902
127.082
125.945
123.846
121.603
84.469
77.329
77.013
76.694
35.819
35.791
24.695
22.222
N
O
N
O
O
4ae
13C NMR (CDCl3, 100 MHz)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

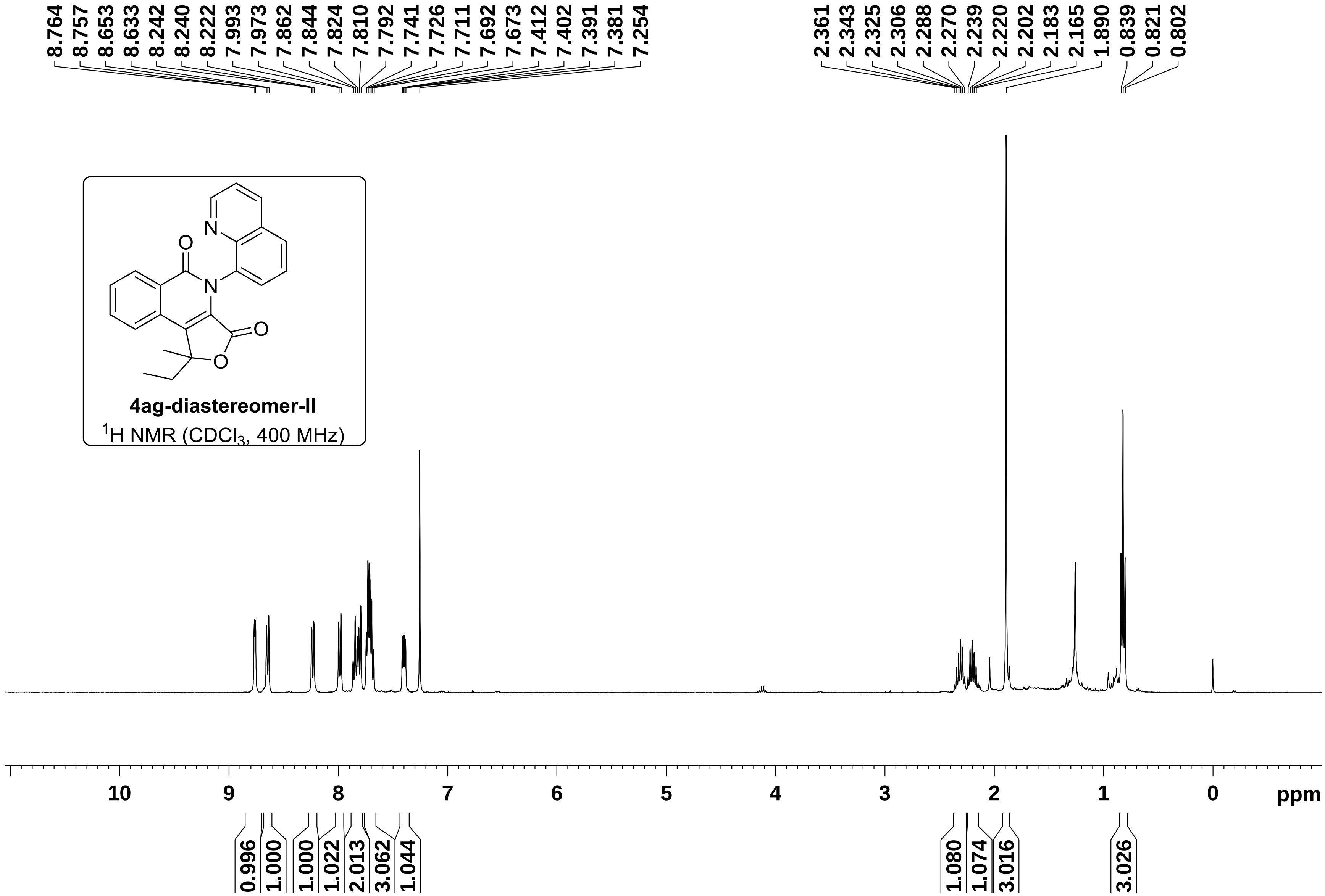

8.752
8.743
8.641
8.621
8.227
8.206
7.979
7.959
7.861
7.842
7.824
7.803
7.788
7.771
7.721
7.702
7.695
7.683
7.675
7.656
7.398
7.387
7.377
7.367
7.250
2.478
2.473
2.450
2.442
2.436
2.409
2.138
2.121
2.100
2.083
2.037
2.025
2.005
1.884
1.871
1.864
1.851
1.797
1.779
1.747
1.734
1.719
1.710
1.695
-0.000
N
O
N
O
O
4af
1H NMR (CDCl3, 400 MHz)
10
9
8
7
6
5
4
3
2
1
0
ppm
1.000
1.002
1.035
1.047
3.052
2.090
1.074
2.074
4.110
6.253


163.558
162.463
150.757
144.691
136.894
136.287
133.493
133.058
130.628
130.223
129.659
129.540
129.420
129.006
126.140
125.945
123.963
121.602
87.573
77.339
77.024
76.703
39.339
27.459
27.413
22.831
22.787
4af
13C NMR (CDCl3, 100 MHz)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

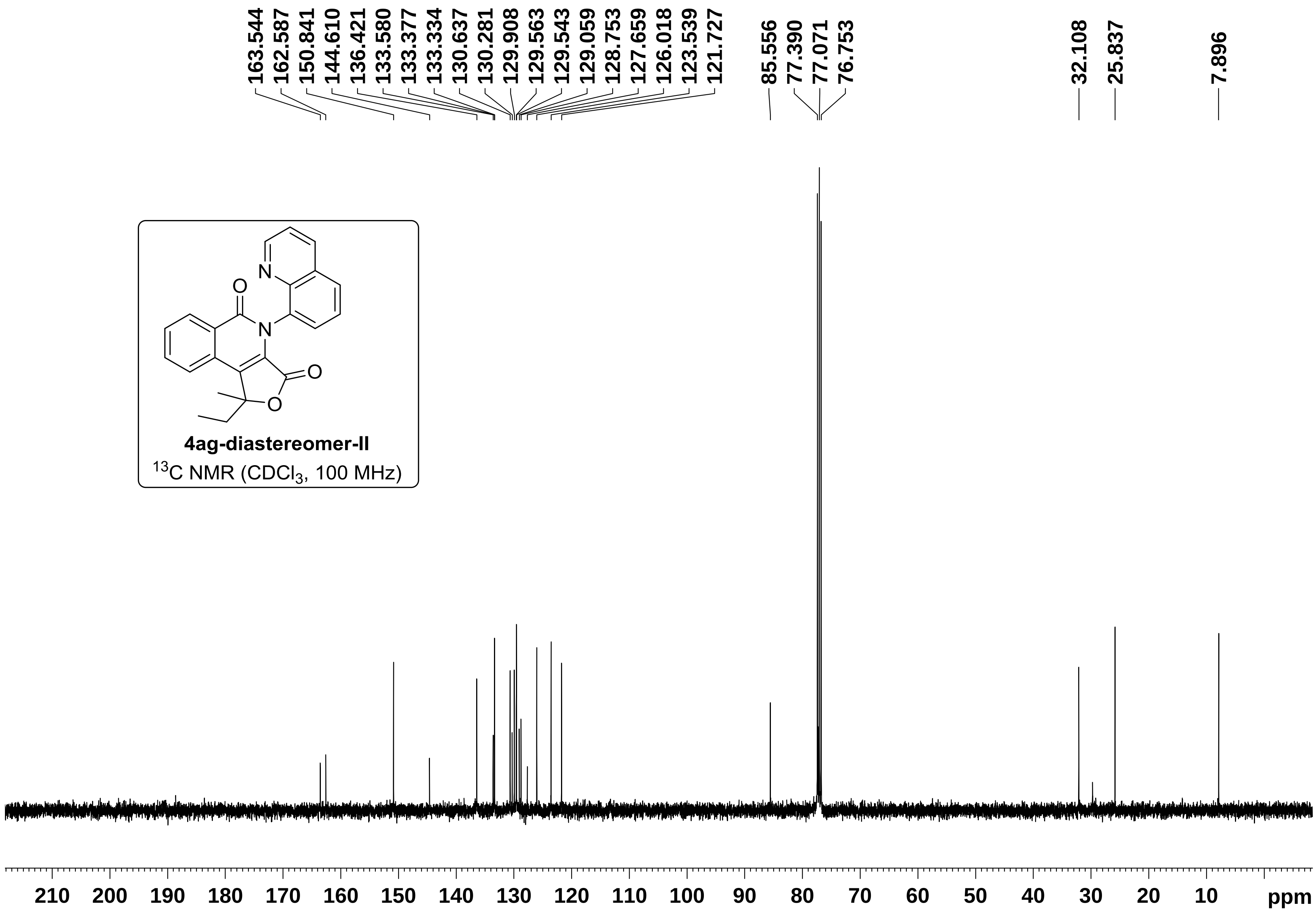

8.677
8.670
8.656
8.636
8.222
8.203
7.984
7.963
7.865
7.846
7.823
7.733
7.718
7.699
7.680
7.386
7.375
7.365
7.354
7.251
2.352
2.333
2.315
2.297
2.279
2.260
2.242
2.224
2.205
2.187
1.858
0.925
0.907
0.889
-0.000
O
N
N
O
O
4ag-diastereomer-I
1H NMR (CDCl3, 400 MHz)
11
10
9
8
7
6
5
4
3
2
1
0
ppm
1.993
1.000
1.011
2.018
3.054
1.012
2.059
3.046
3.049

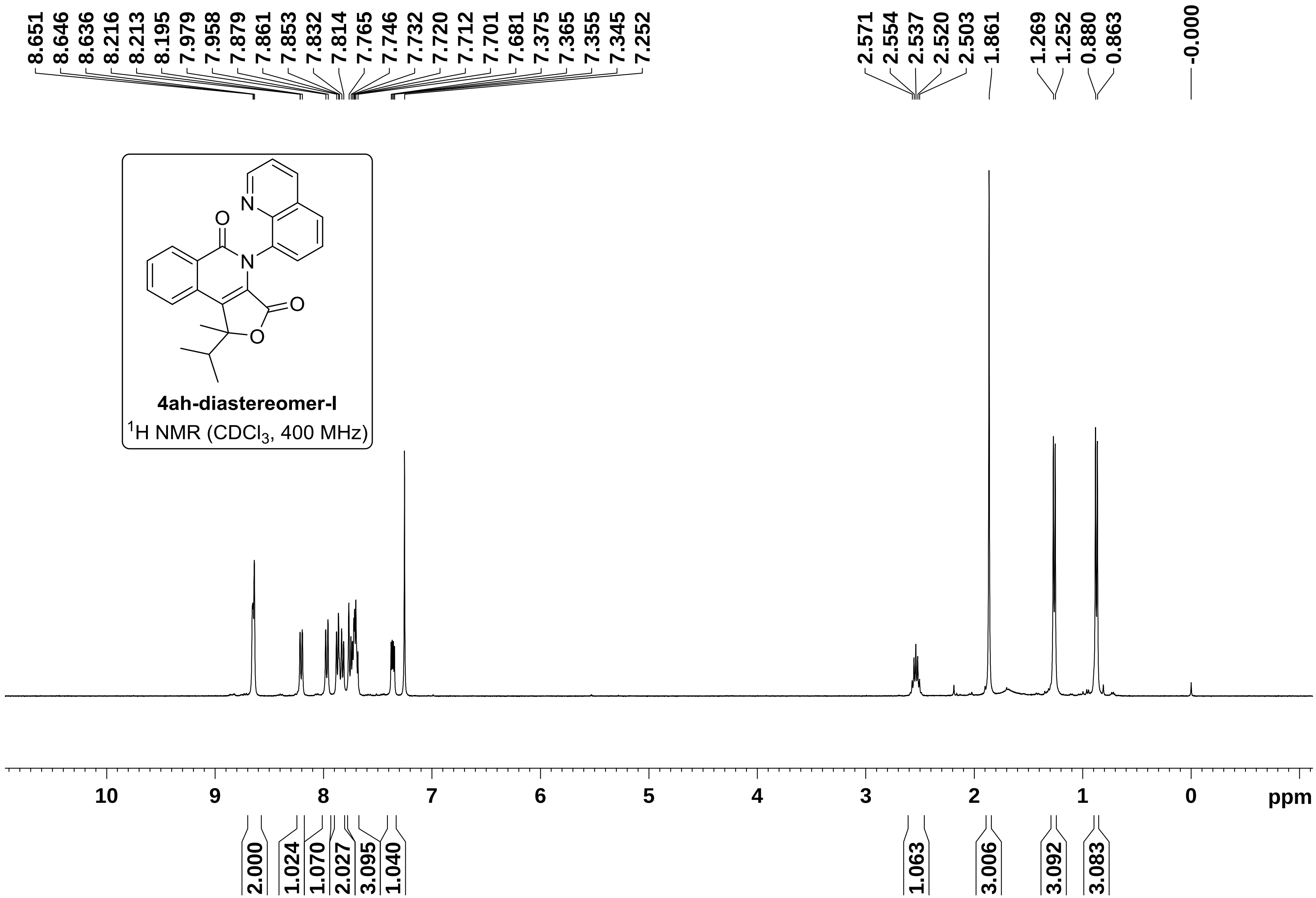
Muniraj, Anil, Prabhu/Organic chemistry/IISc

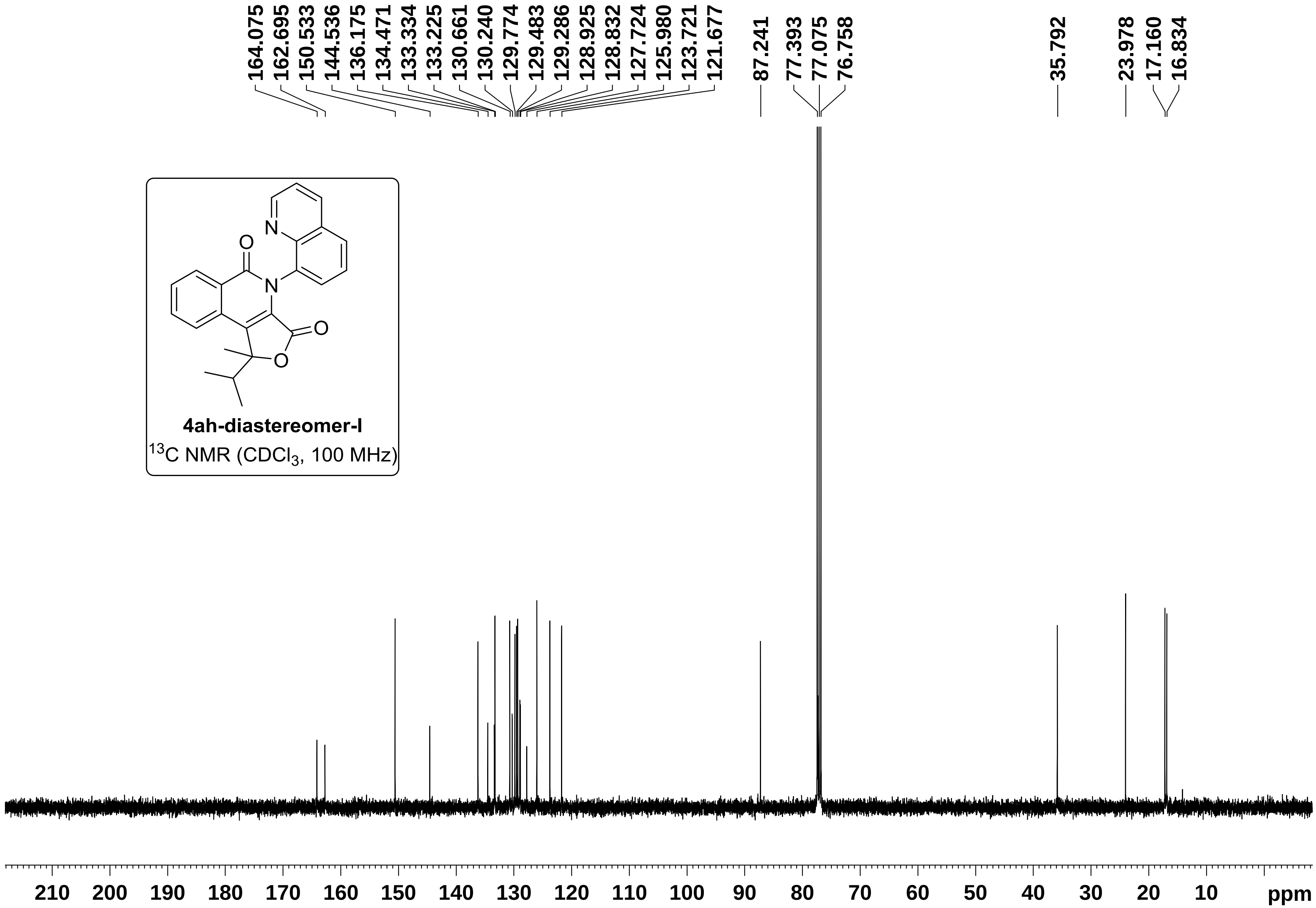



8.764
8.757
8.653
8.633
8.242
8.240
8.222
7.993
7.973
7.862
7.844
7.824
7.810
7.792
7.741
7.726
7.711
7.692
7.673
7.412
7.402
7.391
7.381
7.254
2.361
2.343
2.325
2.306
2.288
2.270
2.239
2.220
2.202
2.183
2.165
1.890
0.839
0.821
0.802
O
N
N
O
O
4ag-diastereomer-II
1H NMR (CDCl3, 400 MHz)
10
9
8
7
6
5
4
3
2
1
0
ppm
0.996
1.000
1.000
1.022
2.013
3.062
1.044
1.080
1.074
3.016
3.026

Muniraj, Anil, Prabhu/Organic chemistry/IISc

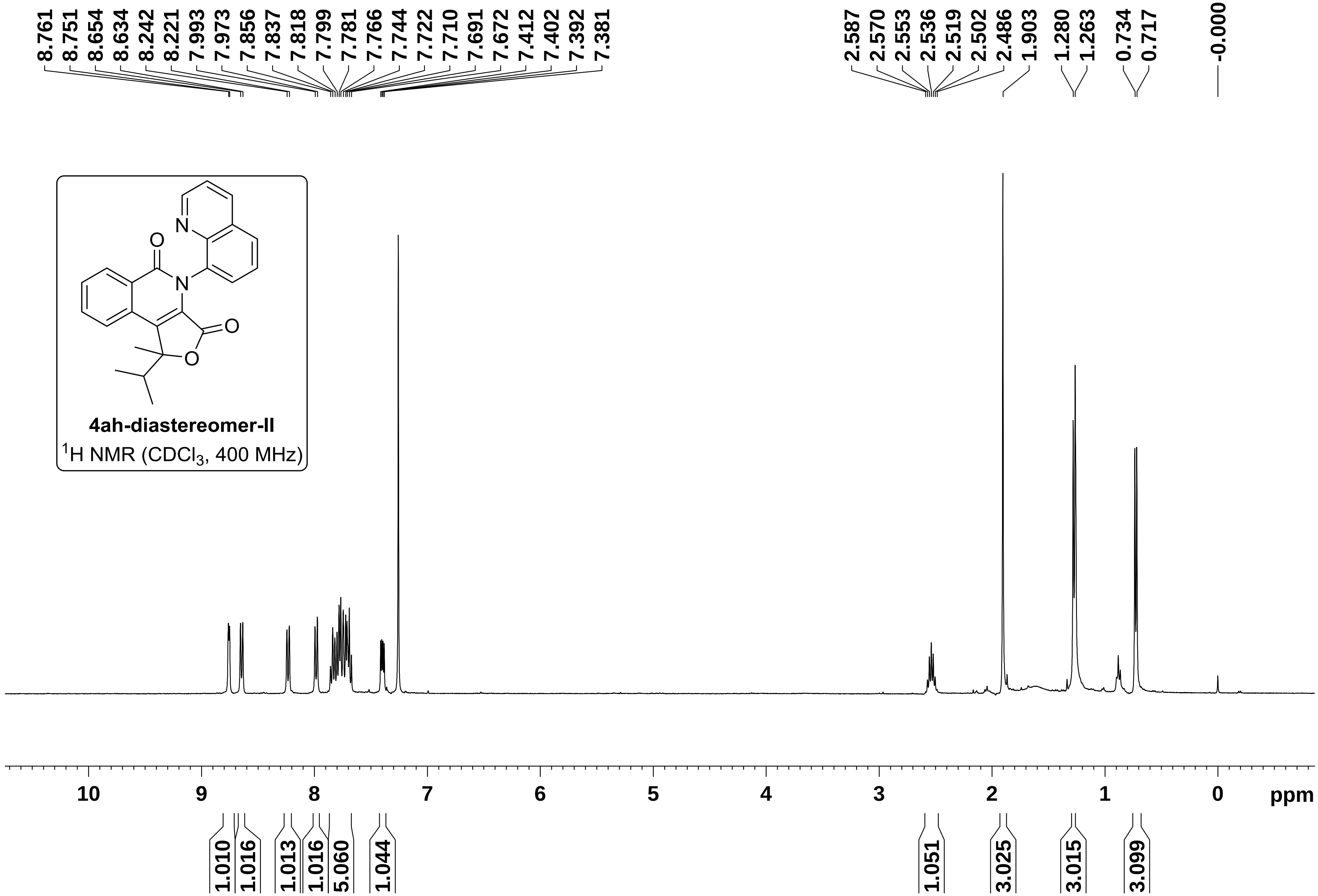


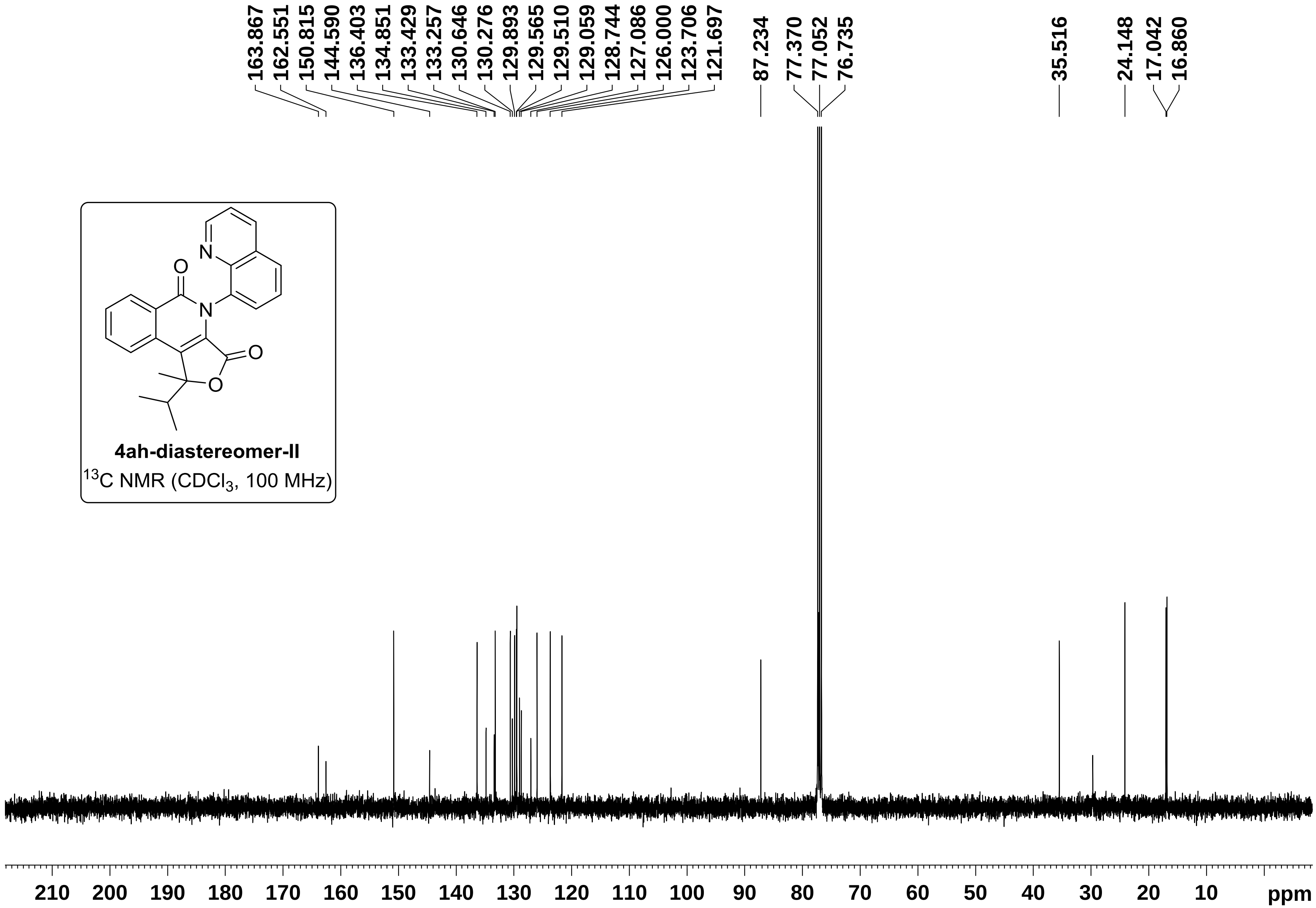

8.651
8.646
8.636
8.216
8.213
8.195
7.979
7.958
7.879
7.861
7.853
7.832
7.814
7.765
7.746
7.732
7.720
7.712
7.701
7.681
7.375
7.365
7.355
7.345
7.252
2.571
2.554
2.537
2.520
2.503
1.861
1.269
1.252
0.880
0.863
-0.000
O
N
N
O
O
4ah-diastereomer-I
1H NMR (CDCl3, 400 MHz)
10
9
8
7
6
5
4
3
2
1
0
ppm
2.000
1.024
1.070
2.027
3.095
1.040
1.063
3.006
3.092
3.083



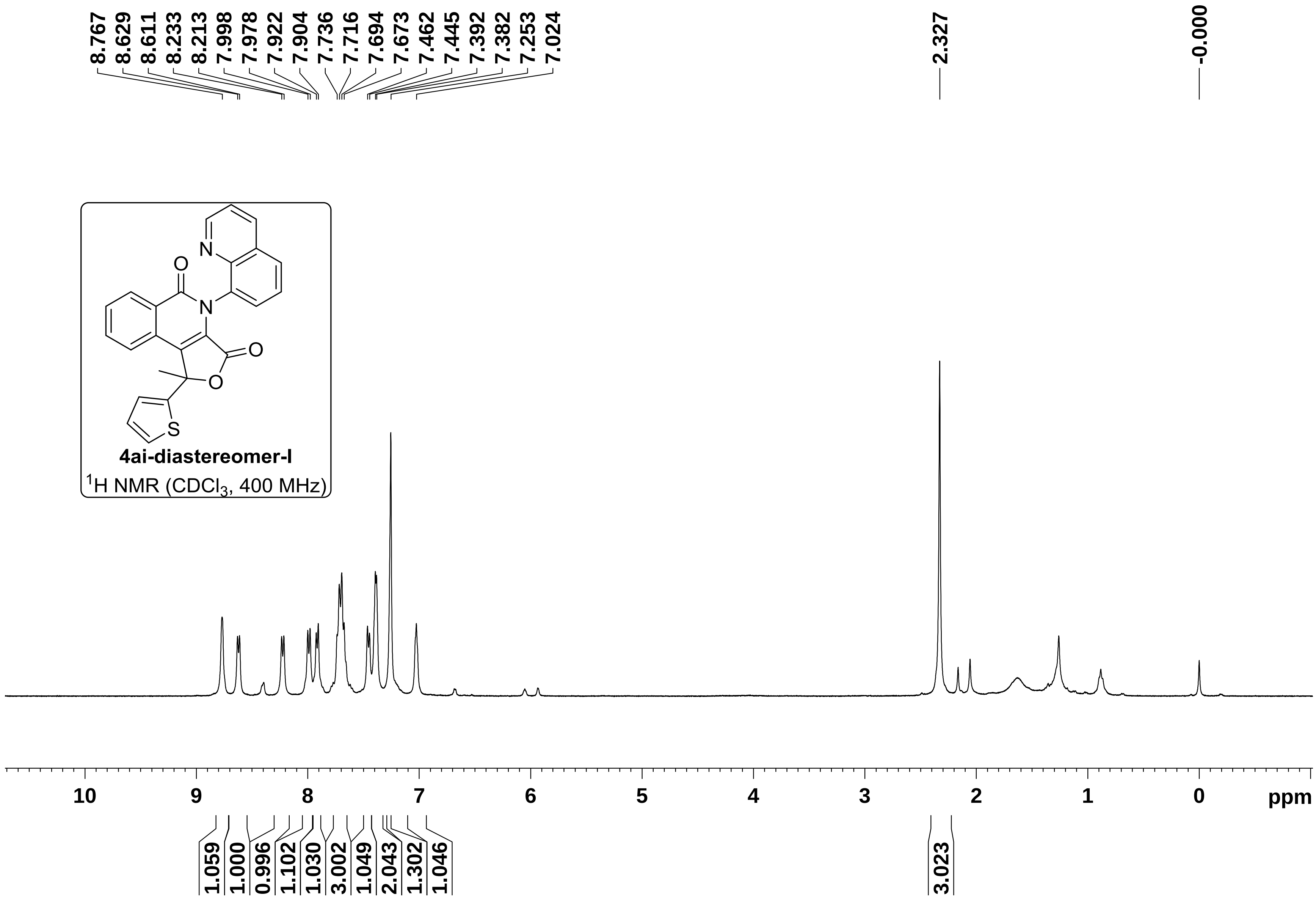
4ah-diastereomer-I

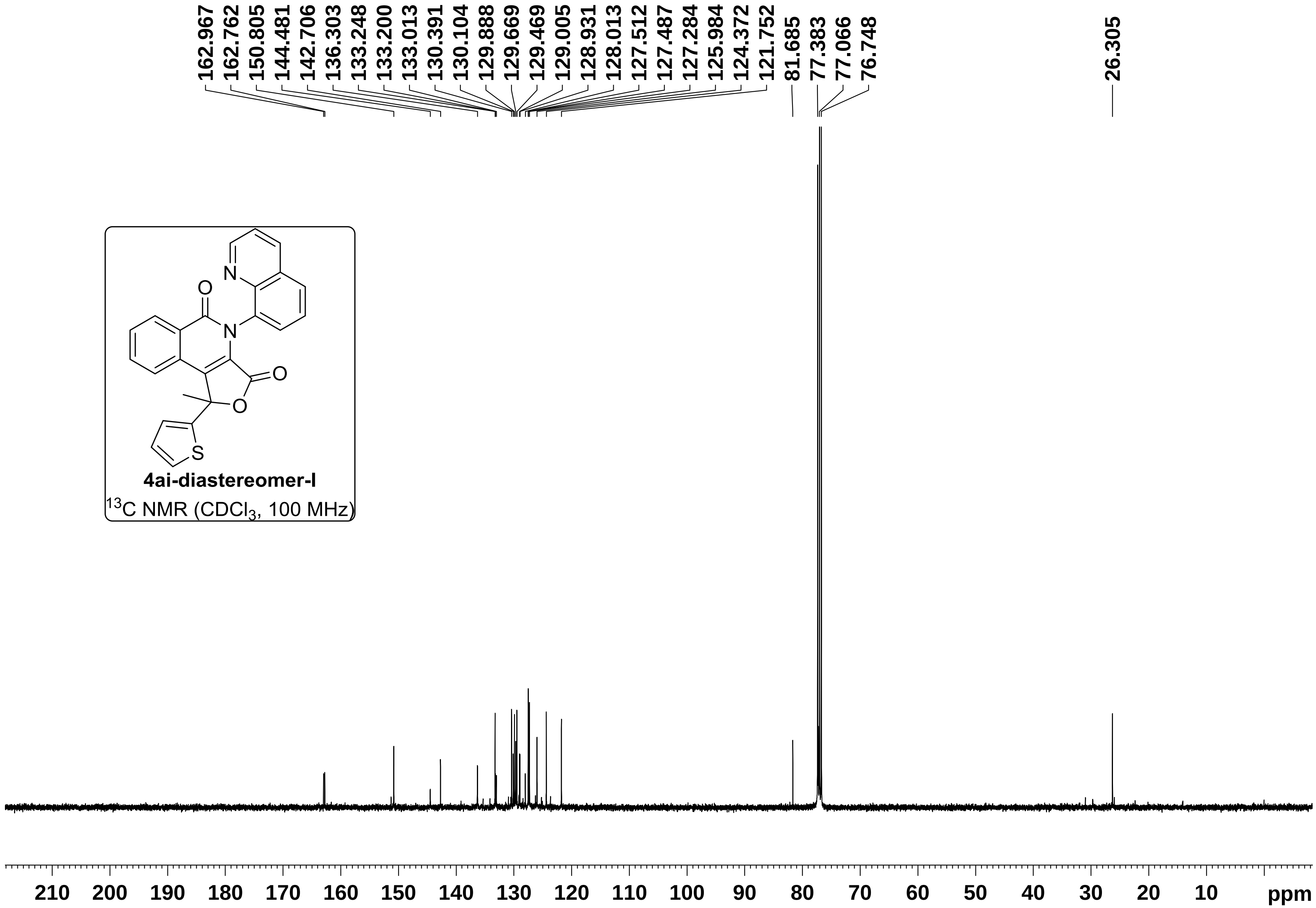
^{13}C NMR ($CDCl_3$, 100 MHz)


8.761
8.751
8.654
8.634
8.242
8.221
7.993
7.973
7.856
7.837
7.818
7.799
7.781
7.766
7.744
7.722
7.710
7.691
7.672
7.412
7.402
7.392
7.381
2.587
2.570
2.553
2.536
2.519
2.502
2.486
1.903
1.280
1.263
0.734
0.717
-0.000
N
O
N
O
O
4ah-diastereomer-II
^{1}H NMR ($CDCl_3$, 400 MHz)
10
9
8
7
6
5
4
3
2
1
0
ppm
1.010
1.016
1.013
1.016
5.060
1.044
1.051
3.025
3.015
3.099


163.867
162.551
150.815
144.590
136.403
134.851
133.429
133.257
130.646
130.276
129.893
129.565
129.510
129.059
128.744
127.086
126.000
123.706
121.697
87.234
77.370
77.052
76.735
35.516
24.148
17.042
16.860
O
N
N
O
O
4ah-diastereomer-II
13C NMR (CDCl3, 100 MHz)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

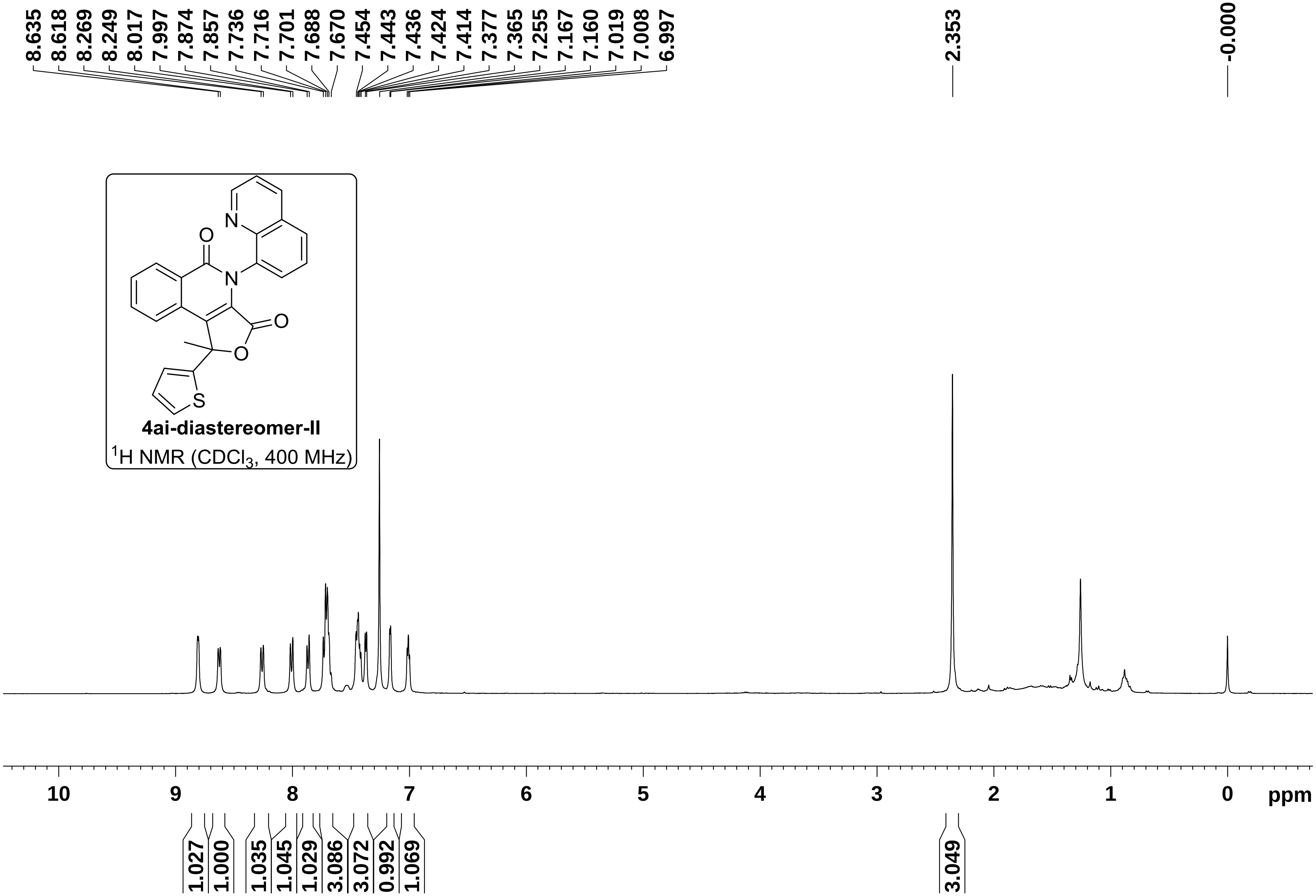
Muniraj, Anil, Prabhu/Organic chemistry/IISc

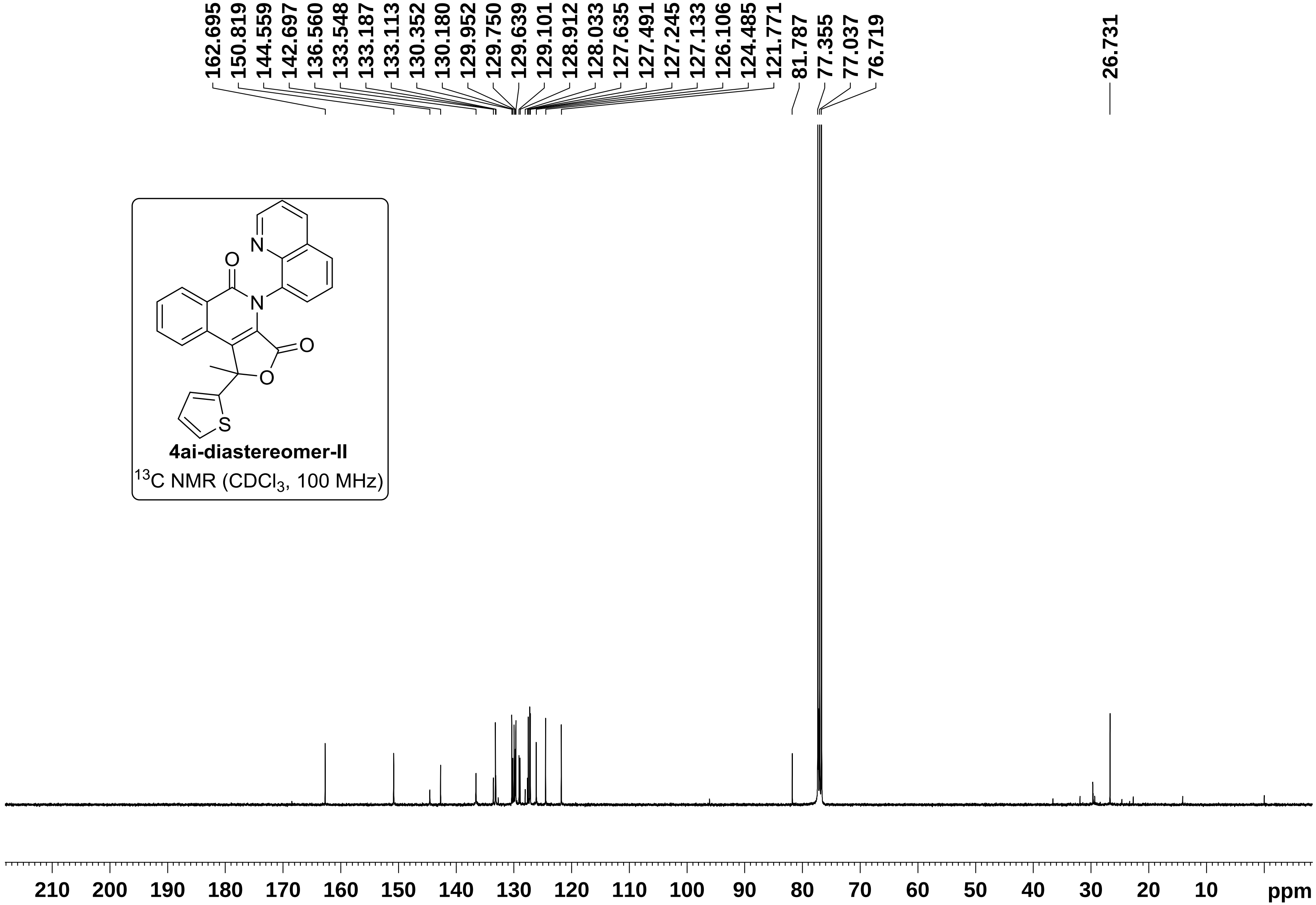


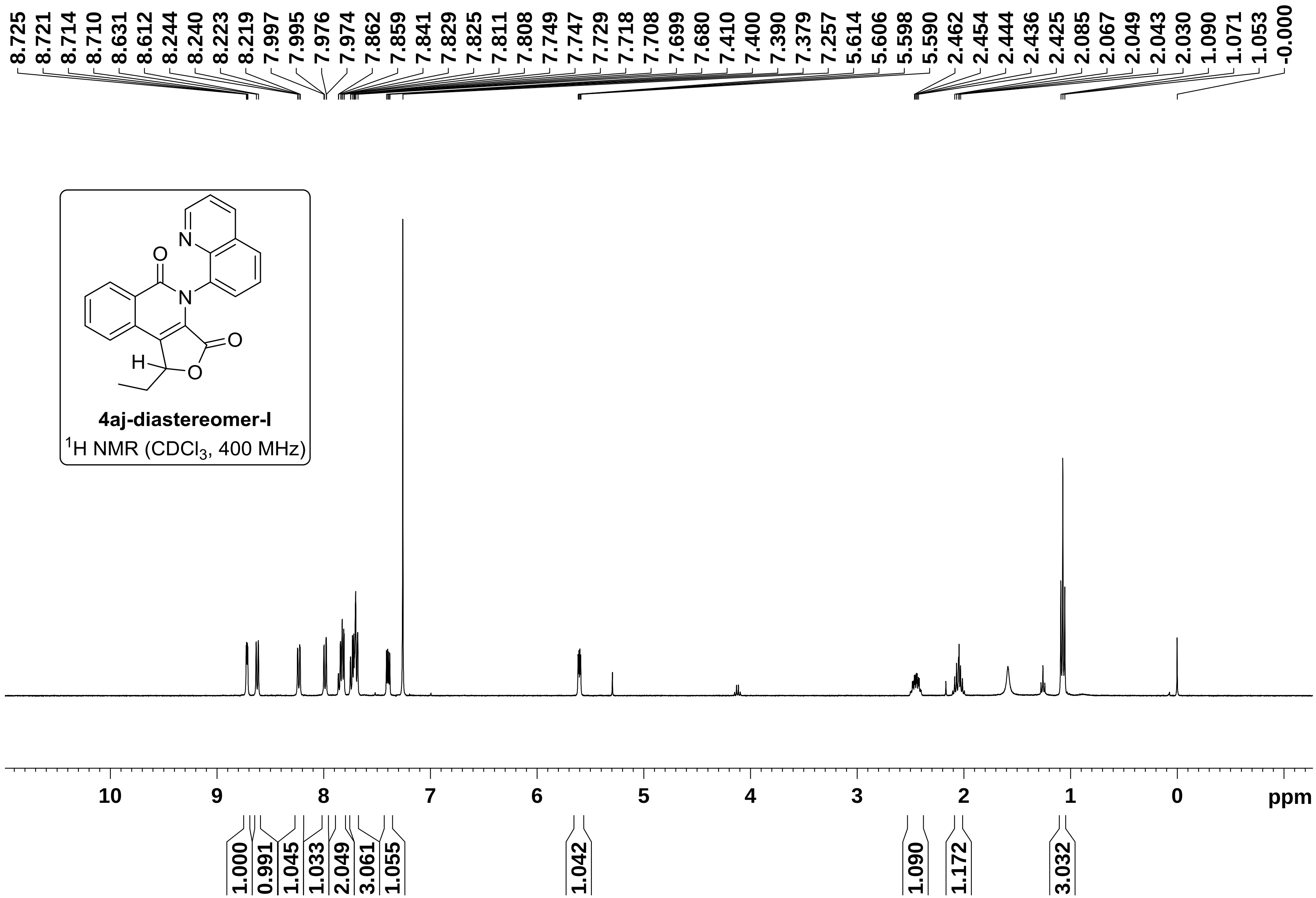


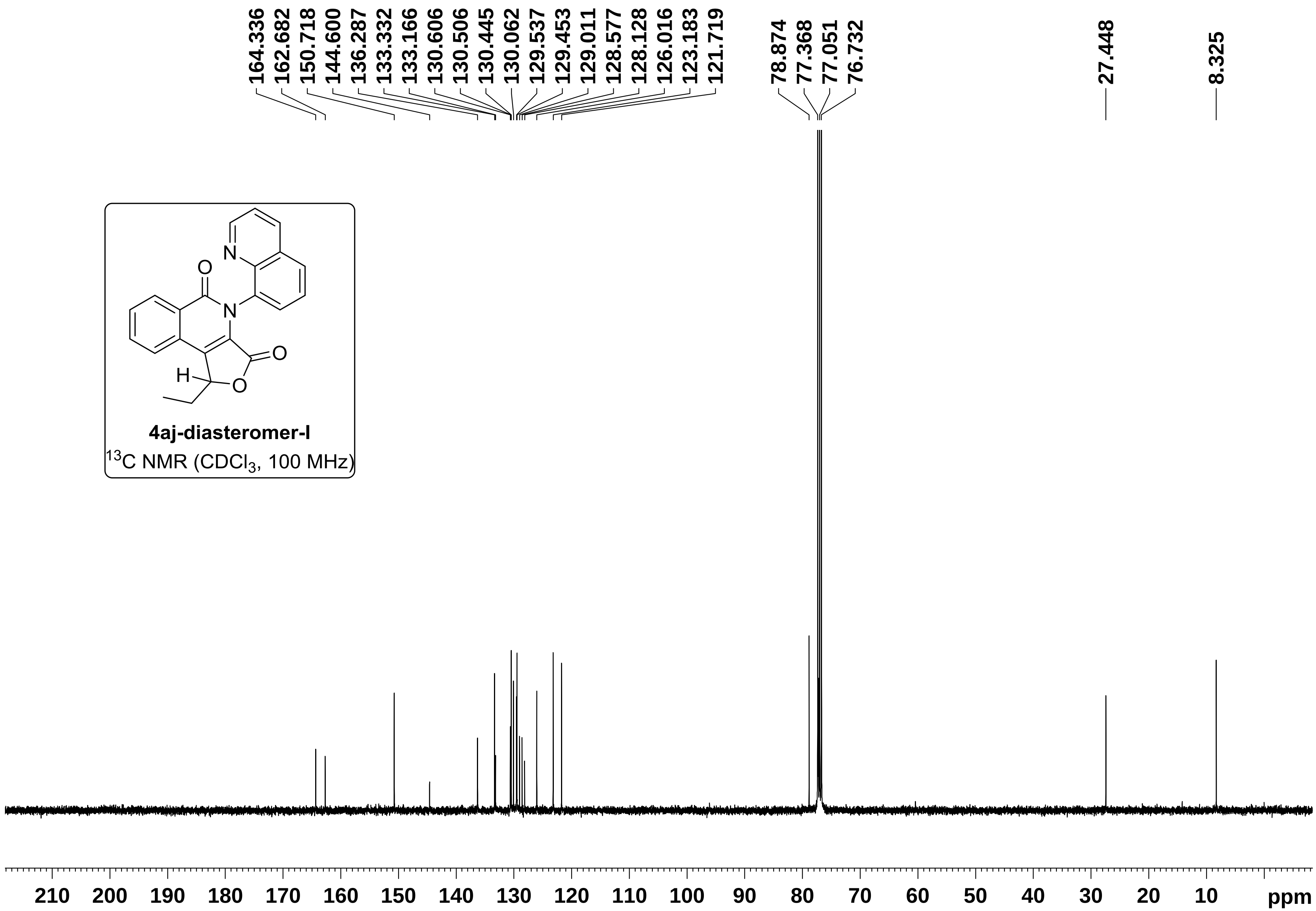
4ai-diastereomer-I

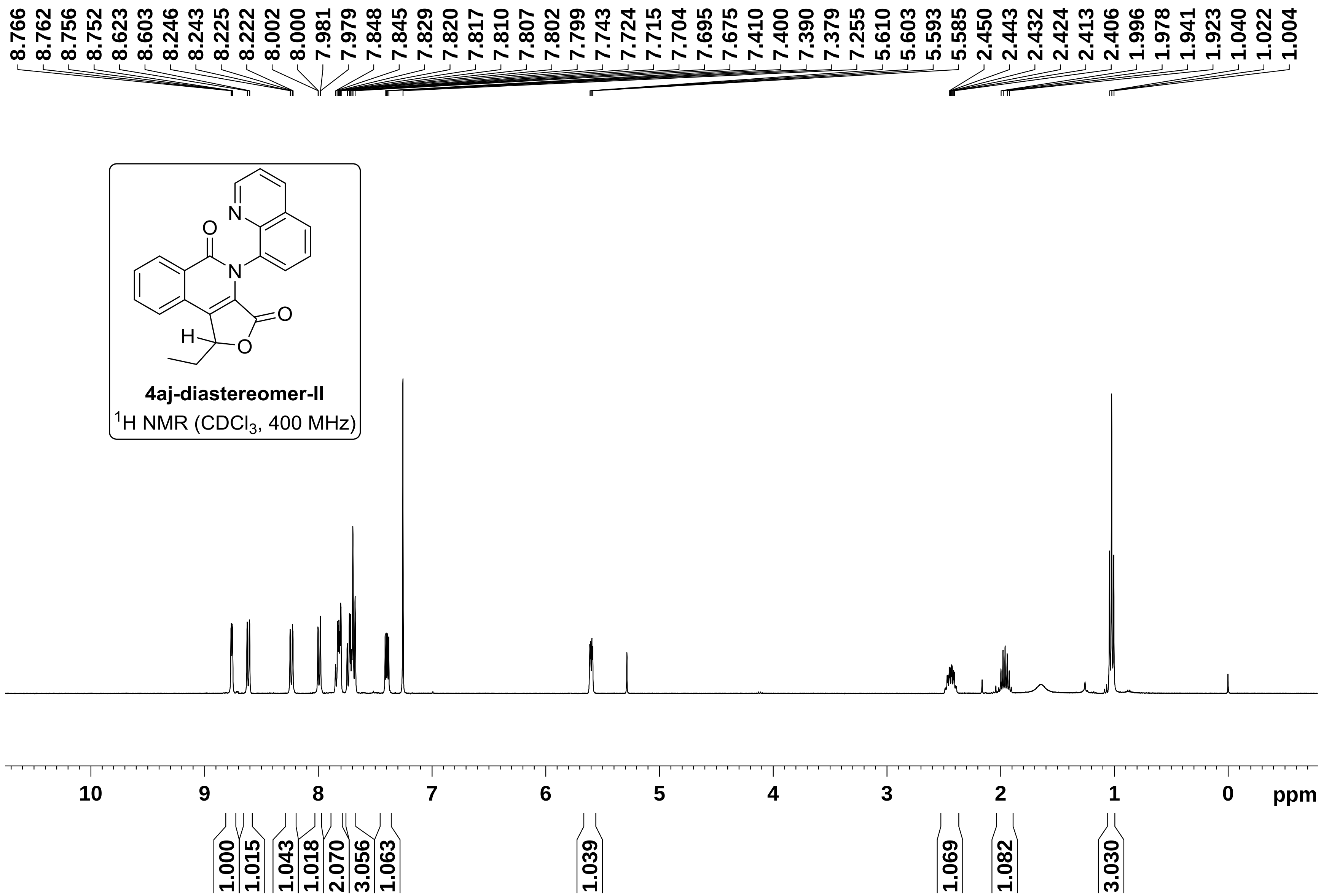
^{13}C NMR ($CDCl_3$, 100 MHz)

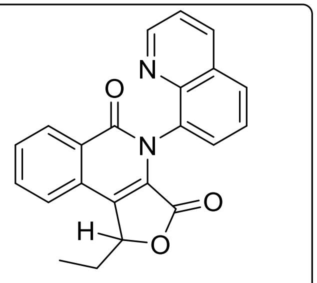

8.635
8.618
8.269
8.249
8.017
7.997
7.874
7.857
7.736
7.716
7.701
7.688
7.670
7.454
7.443
7.436
7.424
7.414
7.377
7.365
7.255
7.167
7.160
7.019
7.008
6.997
2.353
-0.000
N
O
N
O
O
S
4ai-diastereomer-II
1H NMR (CDCl3, 400 MHz)
10
9
8
7
6
5
4
3
2
1
0
ppm
1.027
1.000
1.035
1.045
1.029
3.086
3.072
0.992
1.069
3.049


162.695
150.819
144.559
142.697
136.560
133.548
133.187
133.113
130.352
130.180
129.952
129.750
129.639
129.101
128.912
128.033
127.635
127.491
127.245
127.133
126.106
124.485
121.771
81.787
77.355
77.037
76.719
26.731
O
N
N
O
O
S
4ai-diastereomer-II
13C NMR (CDCl3, 100 MHz)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


8.725 8.721 8.714 8.710 8.631 8.612 8.244 8.240 8.223 8.219 7.997 7.995 7.976 7.974 7.862 7.859 7.841 7.829 7.825 7.811 7.808 7.749 7.747 7.729 7.718 7.708 7.699 7.680 7.410 7.400 7.390 7.379 7.257 5.614 5.606 5.598 5.590 2.462 2.454 2.444 2.436 2.425 2.085 2.067 2.049 2.043 2.030 1.090 1.071 1.053 -0.000
N
O
N
O
H
O
4aj-diastereomer-I
^{1}H NMR ($CDCl_3$, 400 MHz)
10
9
8
7
6
5
4
3
2
1
0
ppm
1.000
0.991
1.045
1.033
2.049
3.061
1.055
1.042
1.090
1.172
3.032

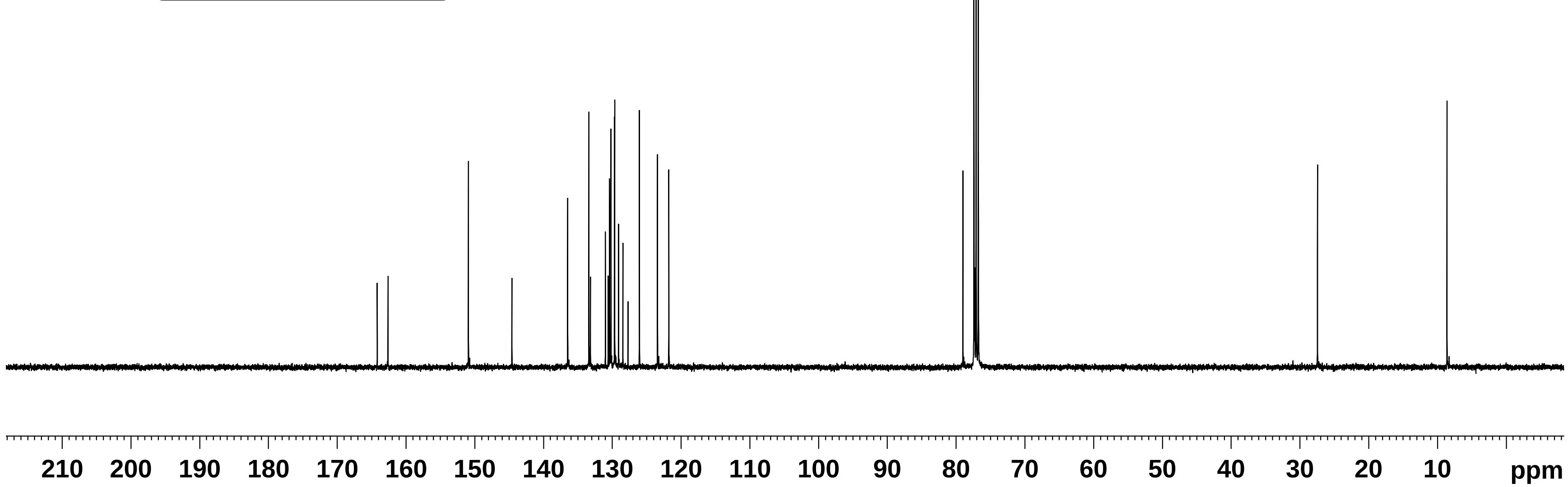

164.336
162.682
150.718
144.600
136.287
133.332
133.166
130.606
130.506
130.445
130.062
129.537
129.453
129.011
128.577
128.128
126.016
123.183
121.719
78.874
77.368
77.051
76.732
27.448
8.325
N
O
N
O
H
O
4aj-diasteromer-I
13C NMR (CDCl3, 100 MHz)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

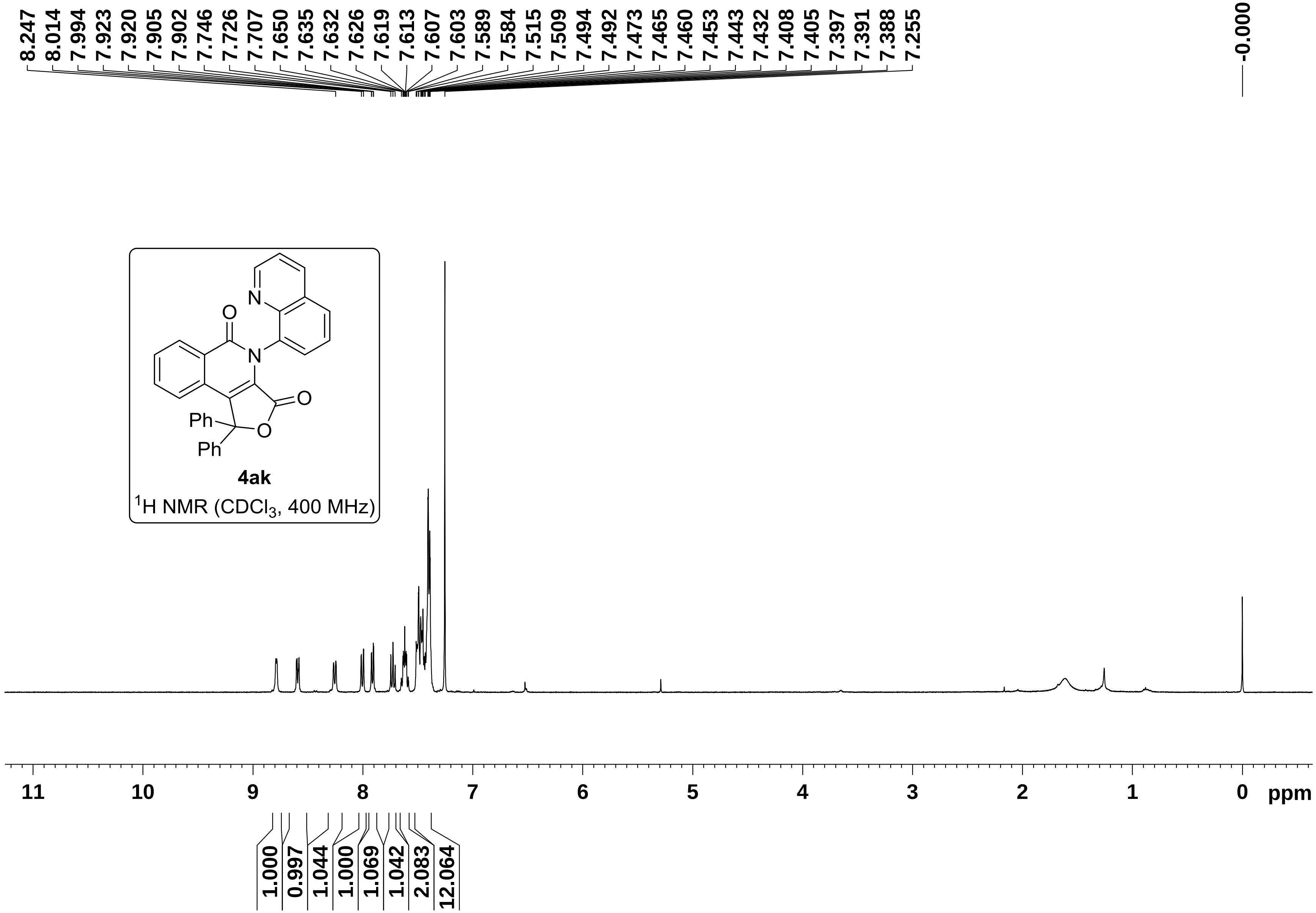

8.766
8.762
8.756
8.752
8.623
8.603
8.246
8.243
8.225
8.222
8.002
8.000
7.981
7.979
7.848
7.845
7.829
7.820
7.817
7.810
7.807
7.802
7.799
7.743
7.724
7.715
7.704
7.695
7.675
7.410
7.400
7.390
7.379
7.255
5.610
5.603
5.593
5.585
2.450
2.443
2.432
2.424
2.413
2.406
1.996
1.978
1.941
1.923
1.040
1.022
1.004
4aj-diastereomer-II
^{1}H NMR ($CDCl_3$, 400 MHz)
10
9
8
7
6
5
4
3
2
1
0
ppm
1.000
1.015
1.043
1.018
2.070
3.056
1.063
1.039
1.069
1.082
3.030

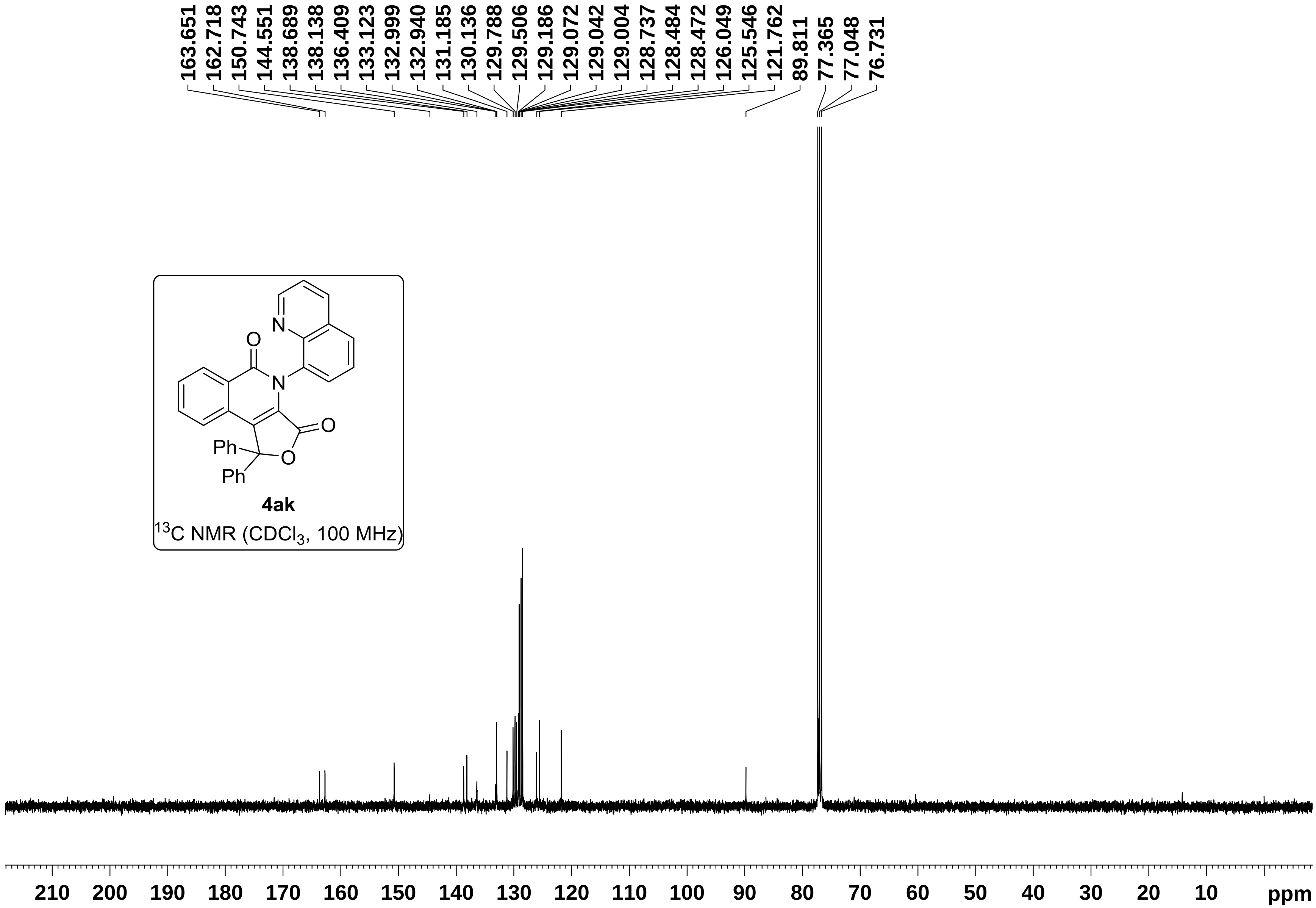


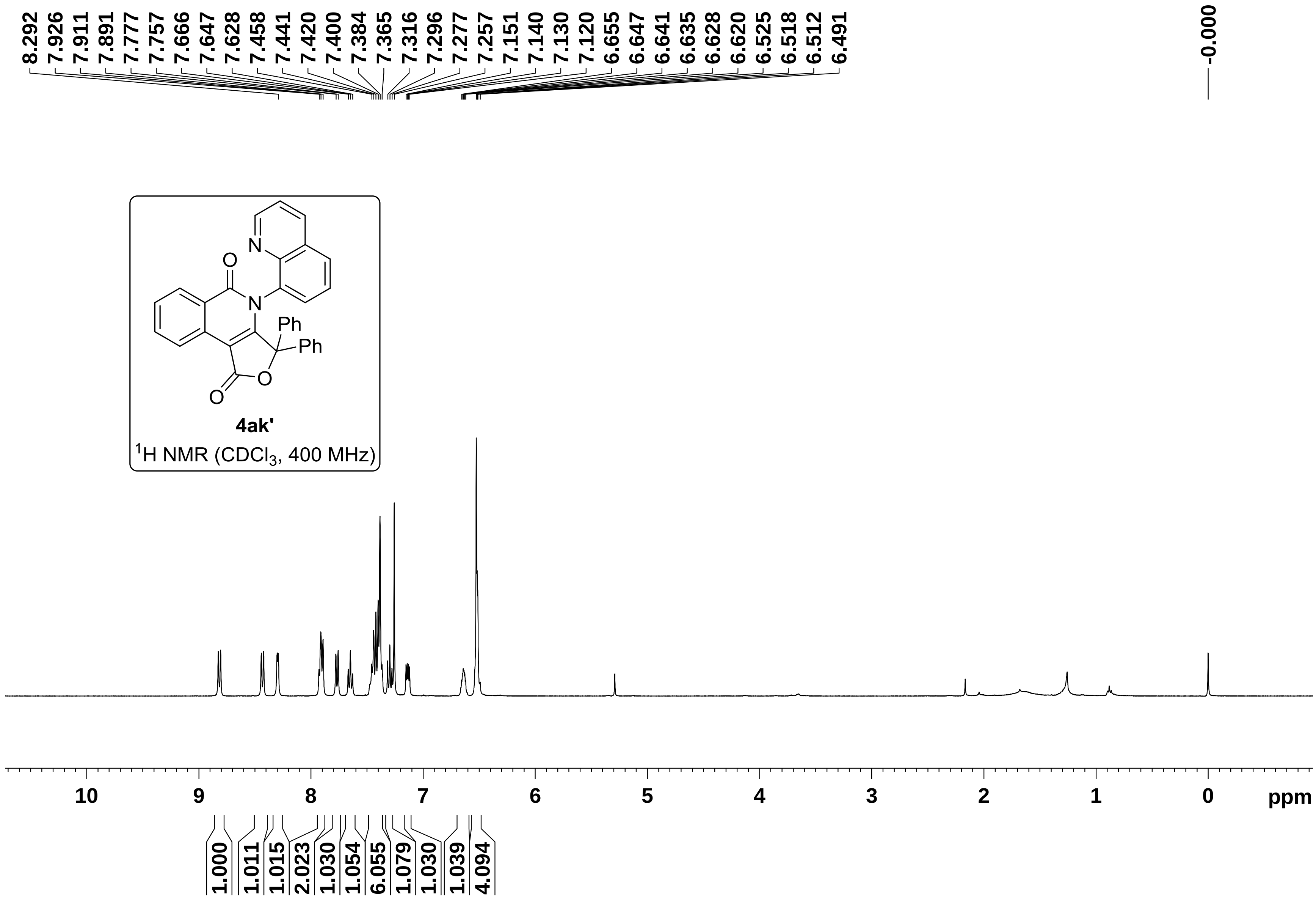
4aj-diasteromer-II

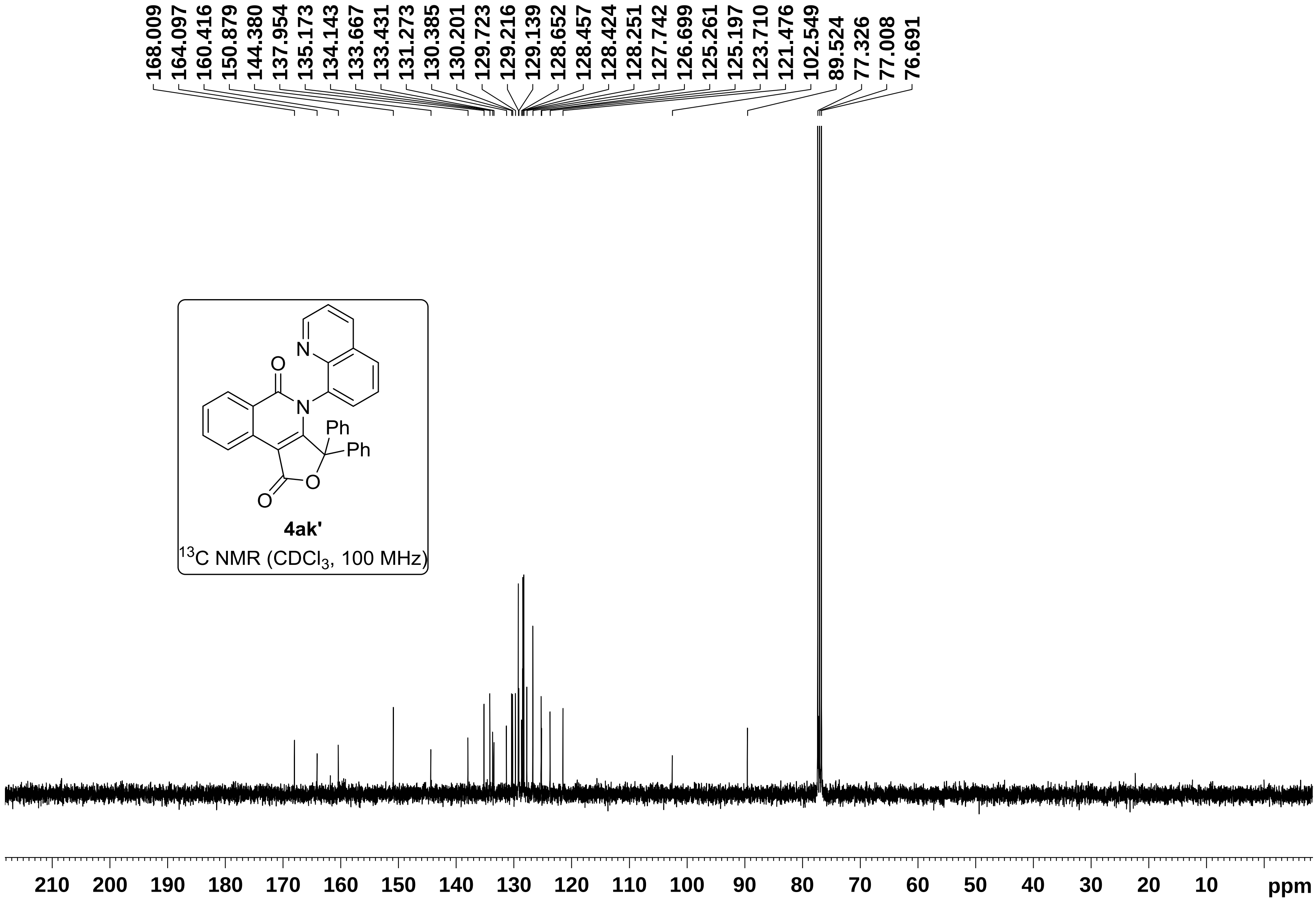
^{13}C NMR ($CDCl_3$, 100 MHz)

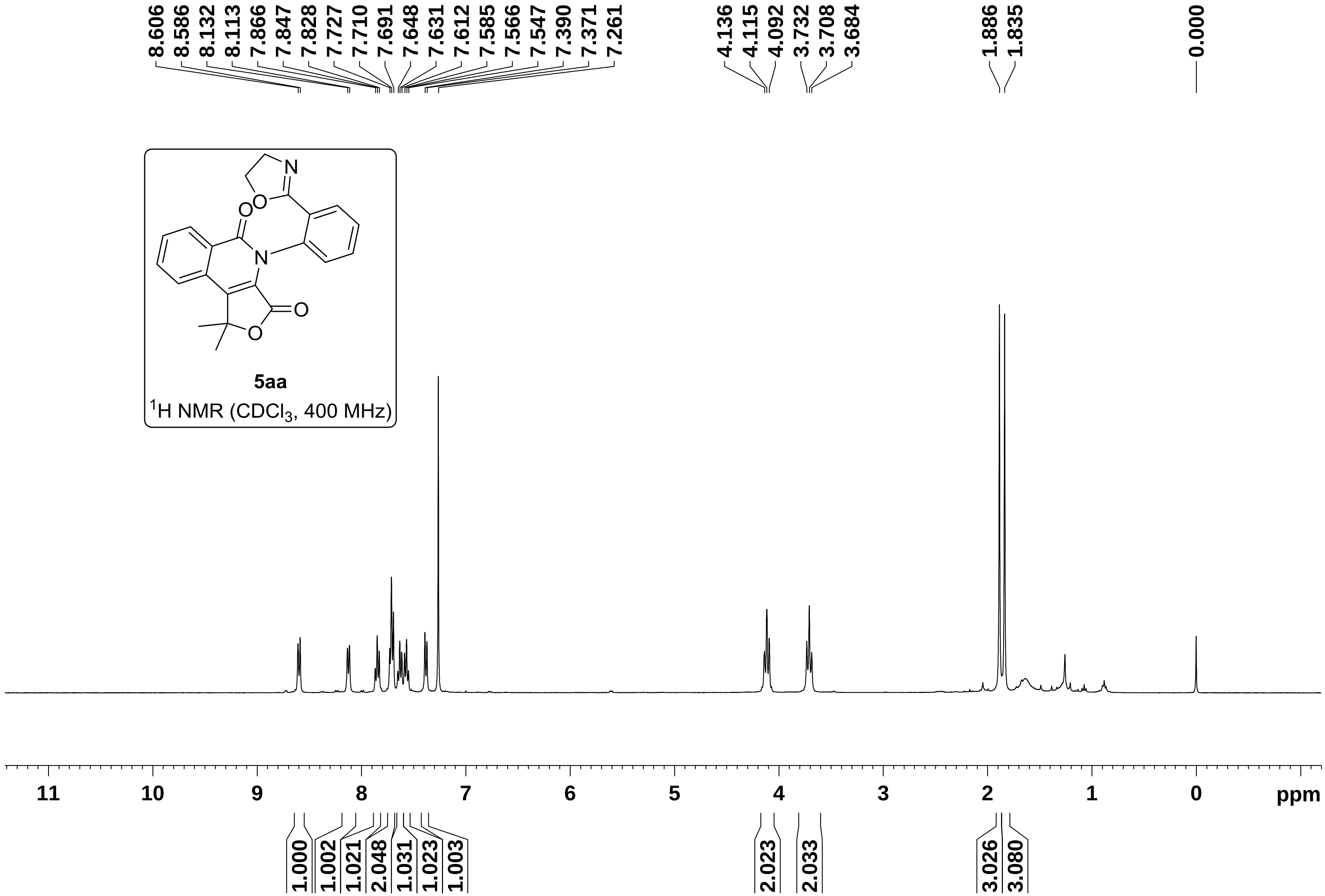


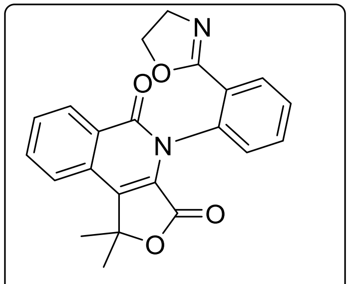

8.247
8.014
7.994
7.923
7.920
7.905
7.902
7.746
7.726
7.707
7.650
7.635
7.632
7.626
7.619
7.613
7.607
7.603
7.589
7.584
7.515
7.509
7.494
7.492
7.473
7.465
7.460
7.453
7.443
7.432
7.408
7.405
7.397
7.391
7.388
7.255
-0.000
N
O
N
O
Ph
O
Ph
4ak
1H NMR (CDCl3, 400 MHz)
11
10
9
8
7
6
5
4
3
2
1
0
ppm
1.000
0.997
1.044
1.000
1.069
1.042
2.083
12.064


163.651
162.718
150.743
144.551
138.689
138.138
136.409
133.123
132.999
132.940
131.185
130.136
129.788
129.506
129.186
129.072
129.042
129.004
128.737
128.484
128.472
126.049
125.546
121.762
89.811
77.365
77.048
76.731
N
O
N
O
Ph
O
Ph
4ak
^{13}C NMR ($CDCl_3$, 100 MHz)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

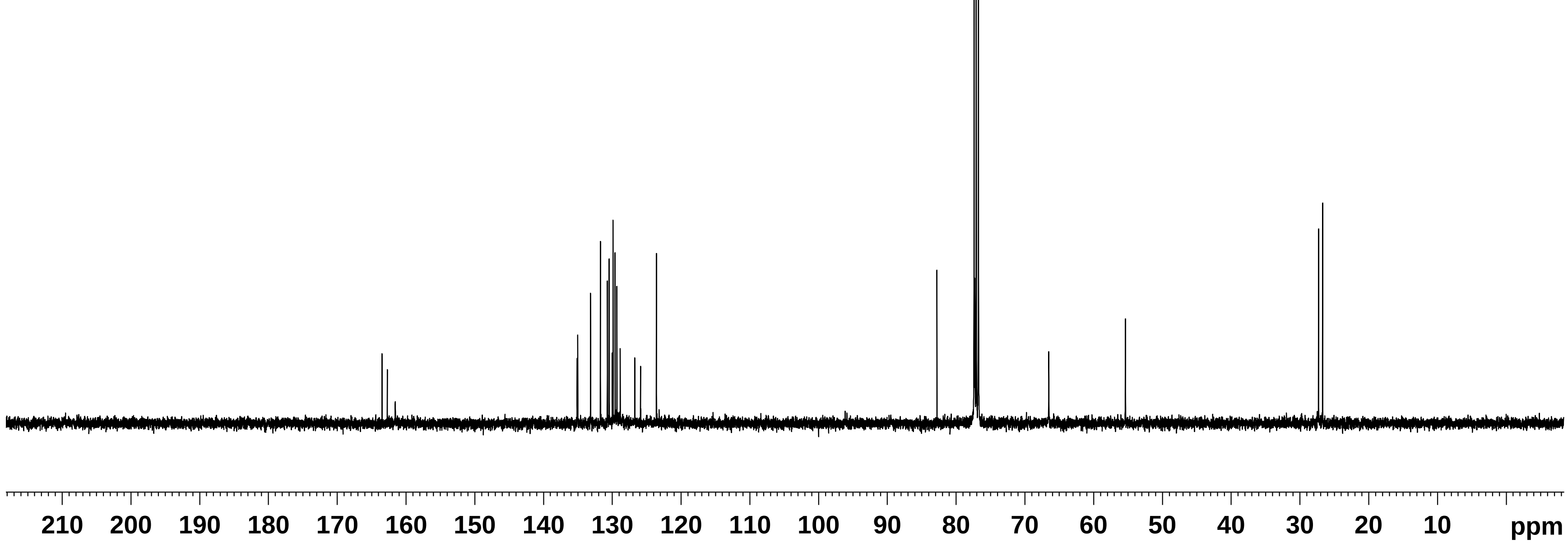

8.292
7.926
7.911
7.891
7.777
7.757
7.666
7.647
7.628
7.458
7.441
7.420
7.400
7.384
7.365
7.316
7.296
7.277
7.257
7.151
7.140
7.130
7.120
6.655
6.647
6.641
6.635
6.628
6.620
6.525
6.518
6.512
6.491
-0.000
N
O
N
Ph
Ph
O
O
4ak'
1H NMR (CDCl3, 400 MHz)
10
9
8
7
6
5
4
3
2
1
0
ppm
1.000
1.011
1.015
2.023
1.030
1.054
6.055
1.079
1.030
1.039
4.094


168.009
164.097
160.416
150.879
144.380
137.954
135.173
134.143
133.667
133.431
131.273
130.385
130.201
129.723
129.216
129.139
128.652
128.457
128.424
128.251
127.742
126.699
125.261
125.197
123.710
121.476
102.549
89.524
77.326
77.008
76.691
O
N
N
Ph
Ph
O
O
4ak'
13C NMR (CDCl3, 100 MHz)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

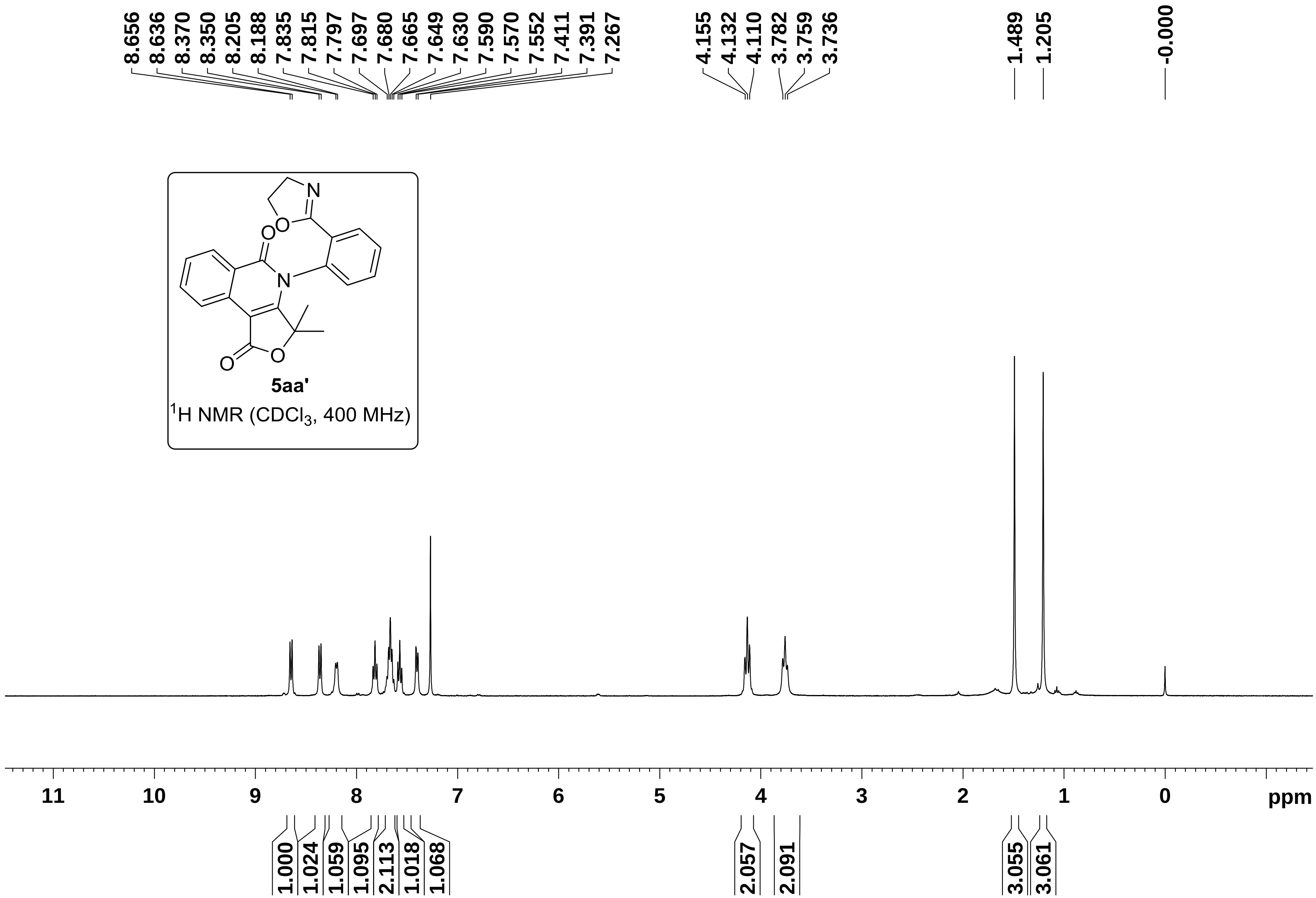

8.606
8.586
8.132
8.113
7.866
7.847
7.828
7.727
7.710
7.691
7.648
7.631
7.612
7.585
7.566
7.547
7.390
7.371
7.261
4.136
4.115
4.092
3.732
3.708
3.684
1.886
1.835
0.000
N
O
O
N
O
O
5aa
1H NMR (CDCl3, 400 MHz)
11
10
9
8
7
6
5
4
3
2
1
0
ppm
1.000
1.002
1.021
2.048
1.031
1.023
1.003
2.023
2.033
3.026
3.080



5aa
^{13}C NMR (CDCl$_3$, 100 MHz)

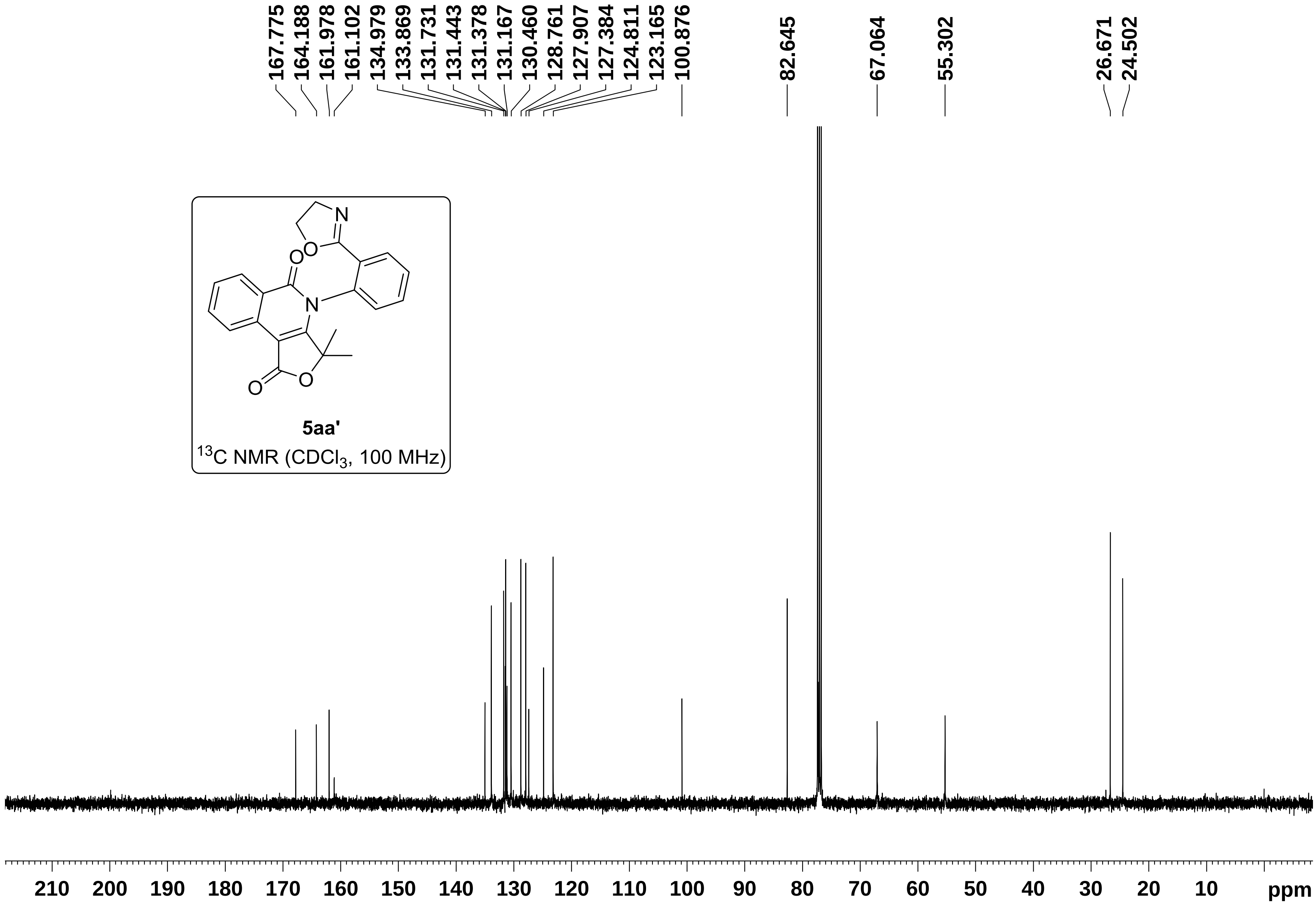


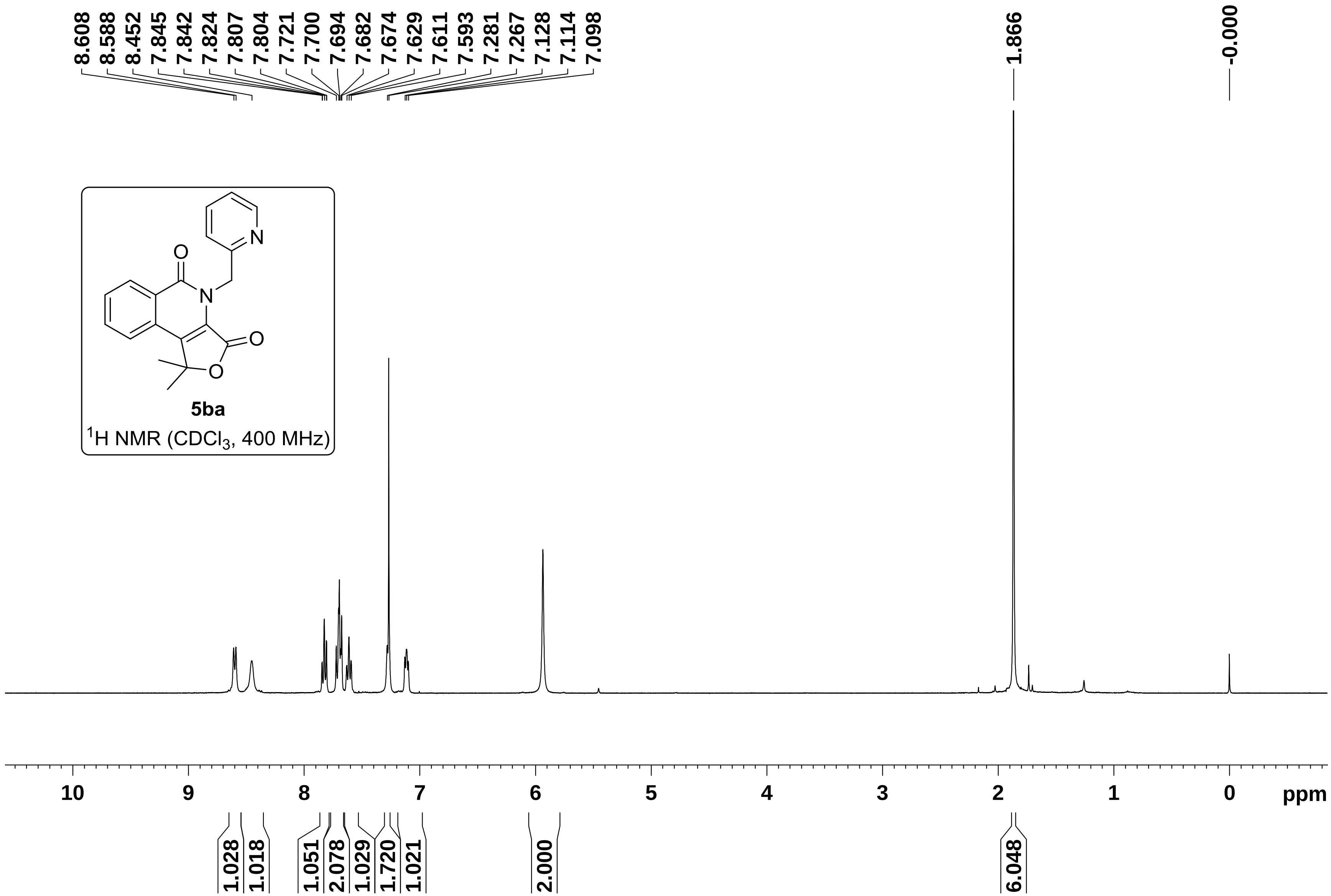
163.472
162.704
161.551
135.096
135.010
133.155
131.710
130.706
130.451
129.989
129.884
129.585
129.320
128.846
126.712
125.870
123.571
82.774
77.372
77.057
76.738
66.511
55.368
27.280
26.692
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

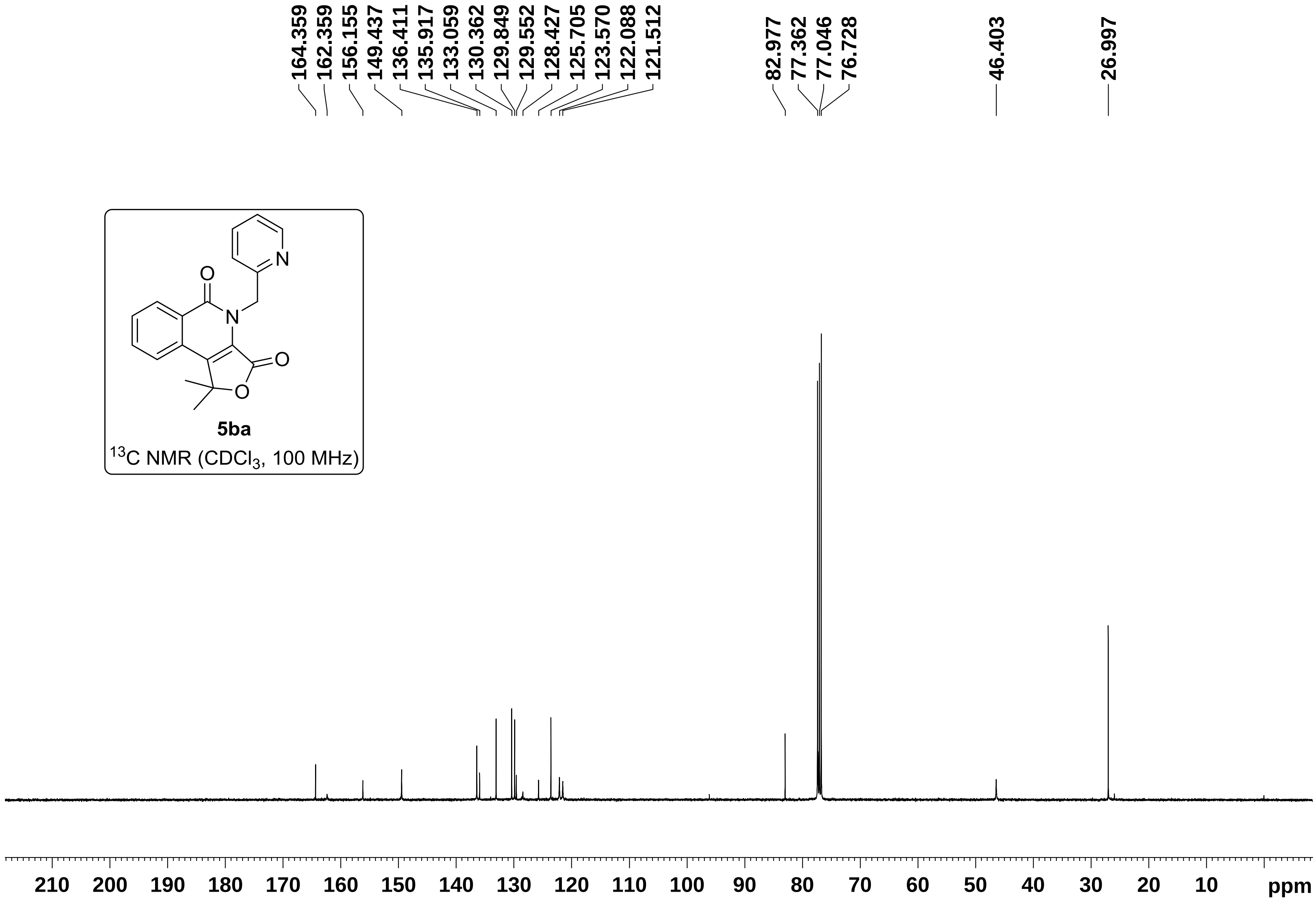


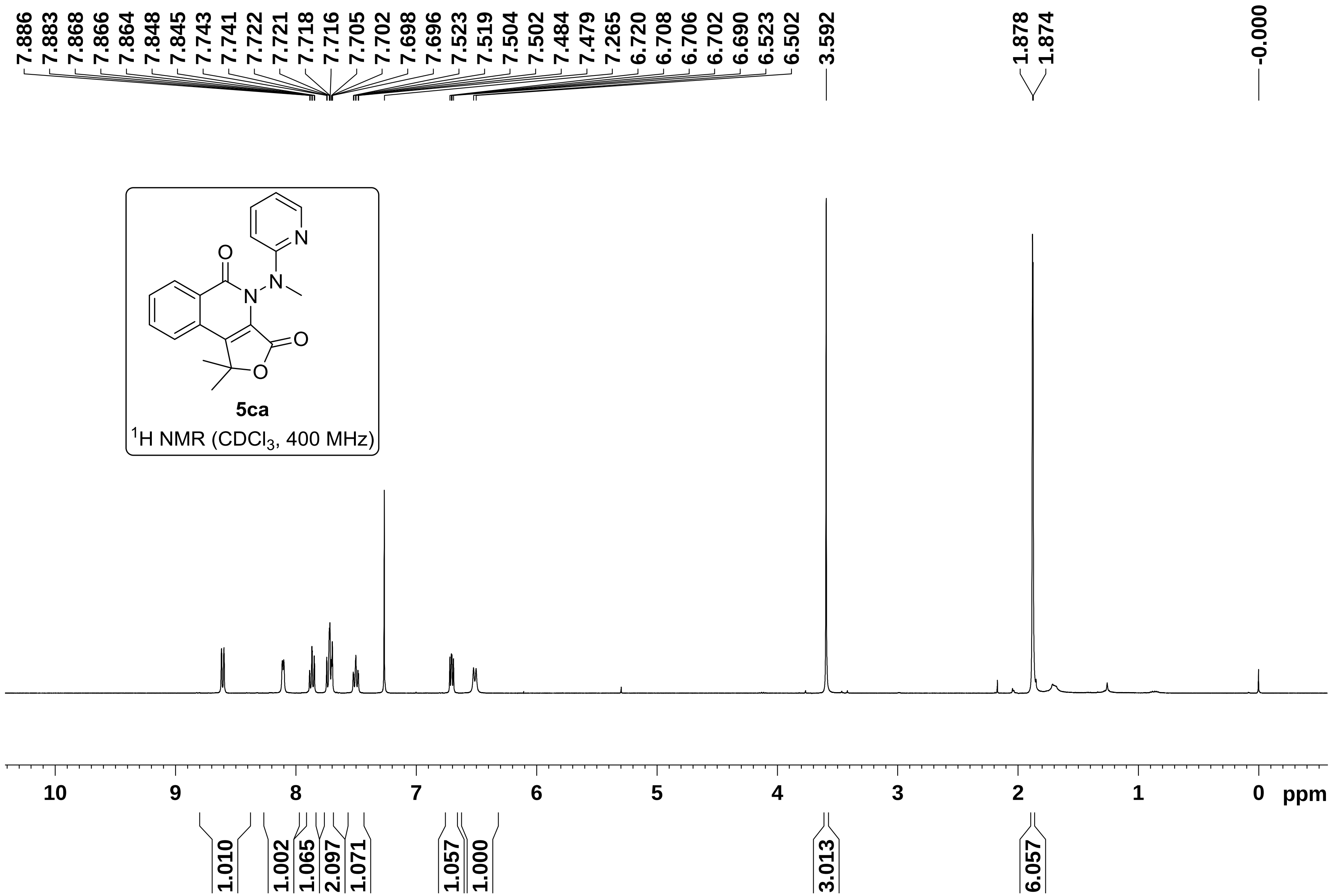
5aa'

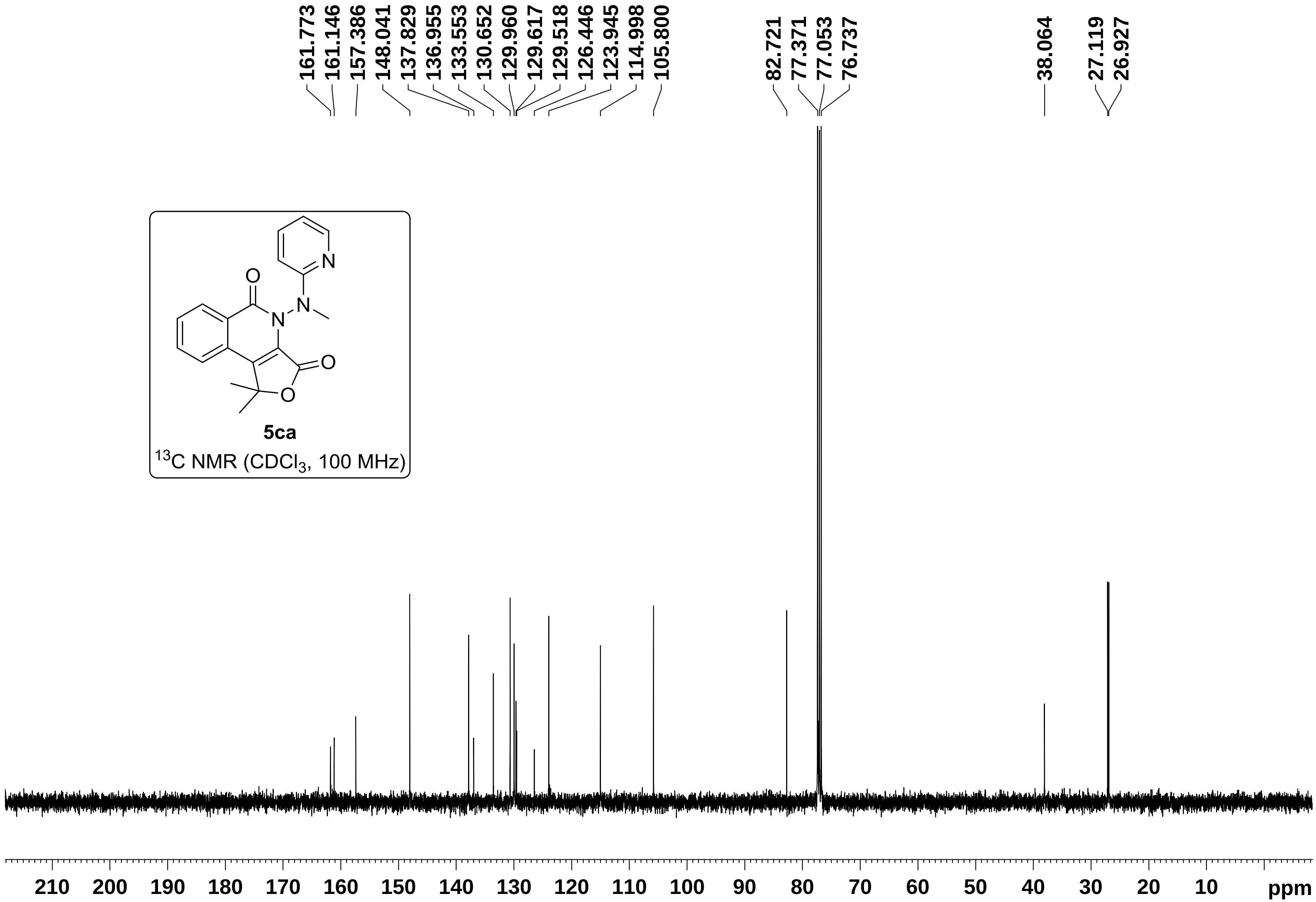
^{1}H NMR ($CDCl_3$, 400 MHz)


167.775
164.188
161.978
161.102
134.979
133.869
131.731
131.443
131.378
131.167
130.460
128.761
127.907
127.384
124.811
123.165
100.876
82.645
67.064
55.302
26.671
24.502
5aa'
^{13}C NMR ($CDCl_3$, 100 MHz)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


8.608
8.588
8.452
7.845
7.842
7.824
7.807
7.804
7.721
7.700
7.694
7.682
7.674
7.629
7.611
7.593
7.281
7.267
7.128
7.114
7.098
1.866
-0.000
O
N
N
O
O
5ba
1H NMR (CDCl3, 400 MHz)
10
9
8
7
6
5
4
3
2
1
0
ppm
1.028
1.018
1.051
2.078
1.029
1.720
1.021
2.000
6.048

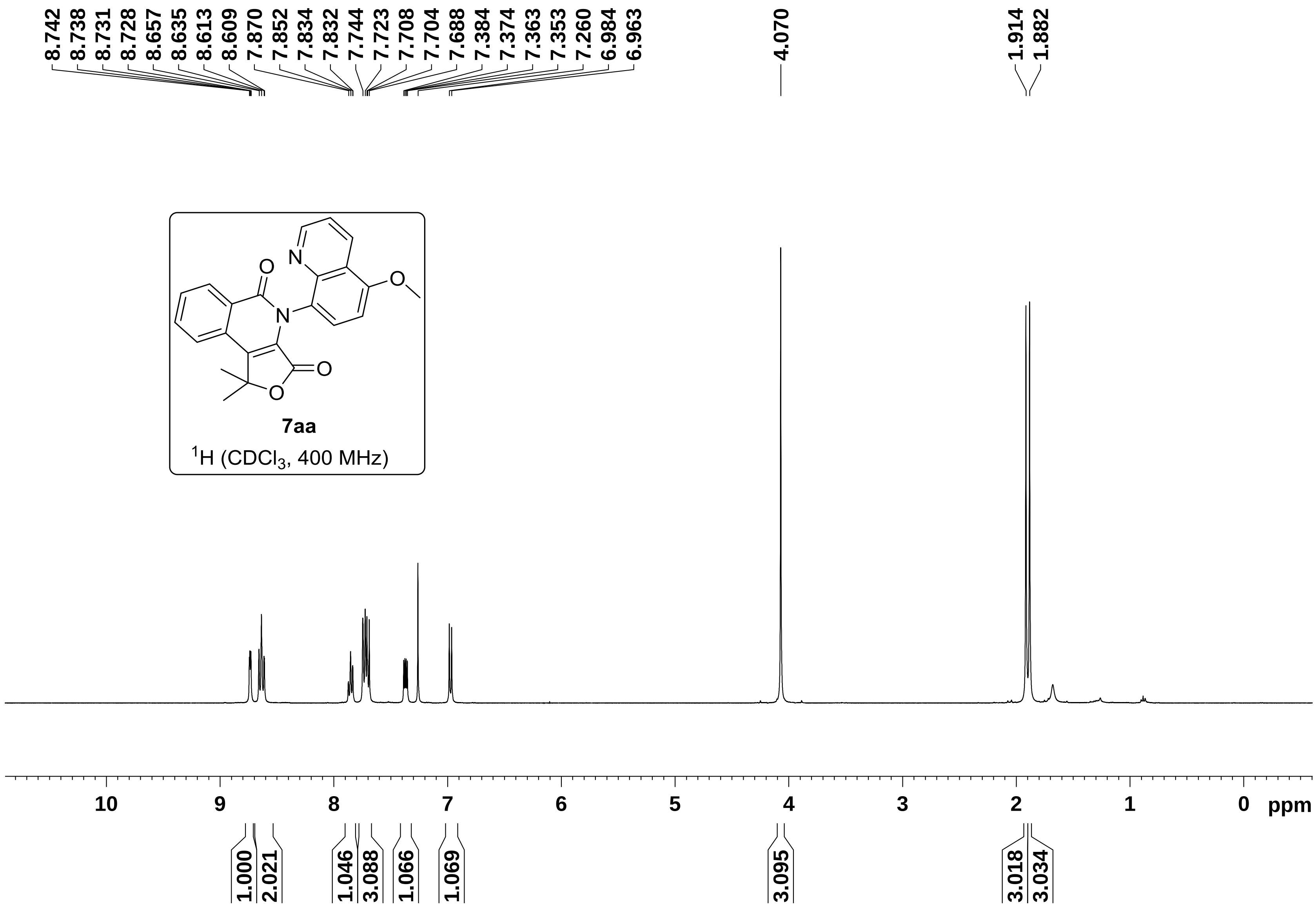

164.359
162.359
156.155
149.437
136.411
135.917
133.059
130.362
129.849
129.552
128.427
125.705
123.570
122.088
121.512
82.977
77.362
77.046
76.728
46.403
26.997
5ba
^{13}C NMR ($CDCl_3$, 100 MHz)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

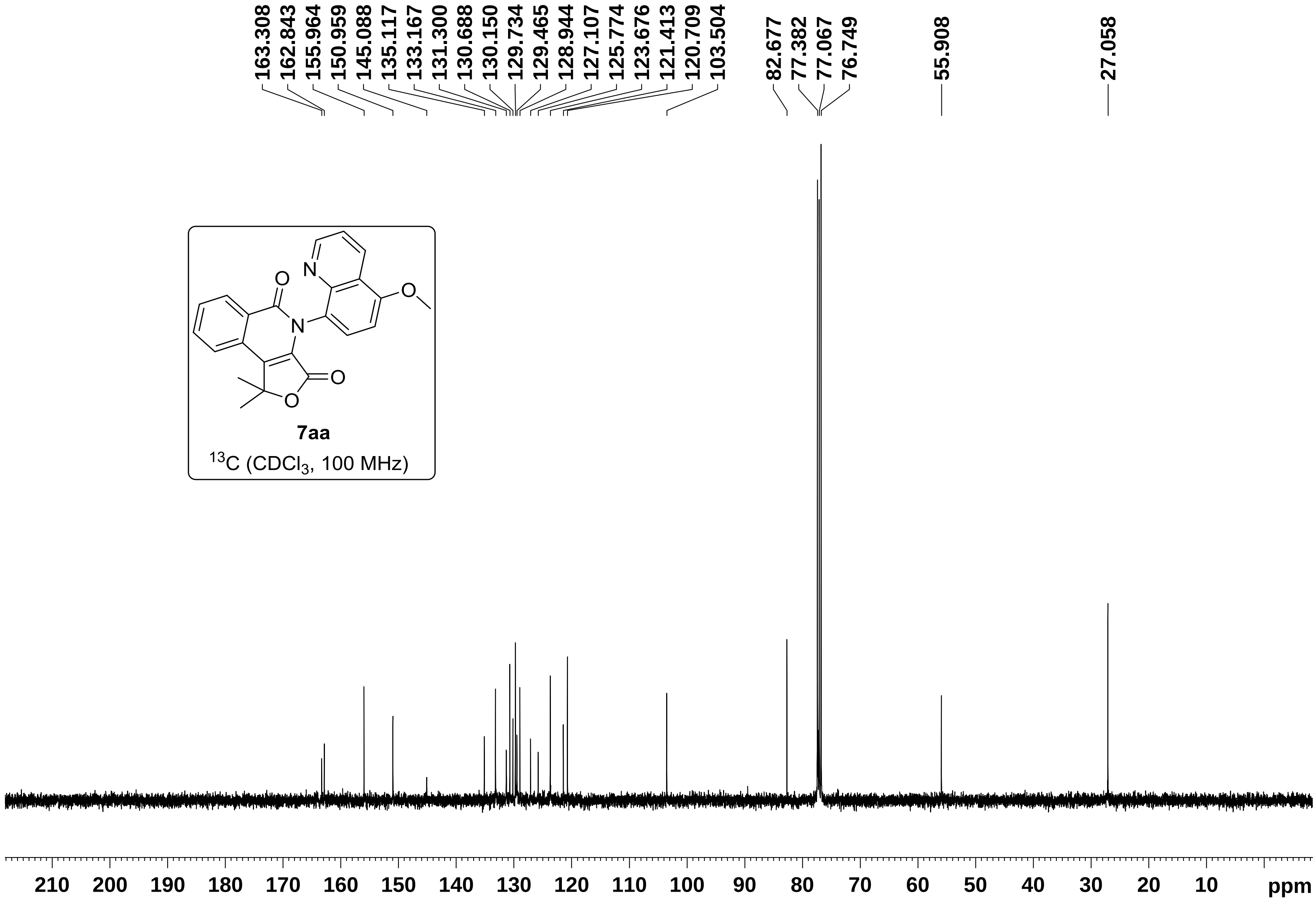

7.886
7.883
7.868
7.866
7.864
7.848
7.845
7.743
7.741
7.722
7.721
7.718
7.716
7.705
7.702
7.698
7.696
7.523
7.519
7.504
7.502
7.484
7.479
7.265
6.720
6.708
6.706
6.702
6.690
6.523
6.502
3.592
1.878
1.874
-0.000
O
N
N
N
O
O
5ca
^{1}H NMR ($CDCl_3$, 400 MHz)
10
9
8
7
6
5
4
3
2
1
0
ppm
1.010
1.002
1.065
2.097
1.071
1.057
1.000
3.013
6.057

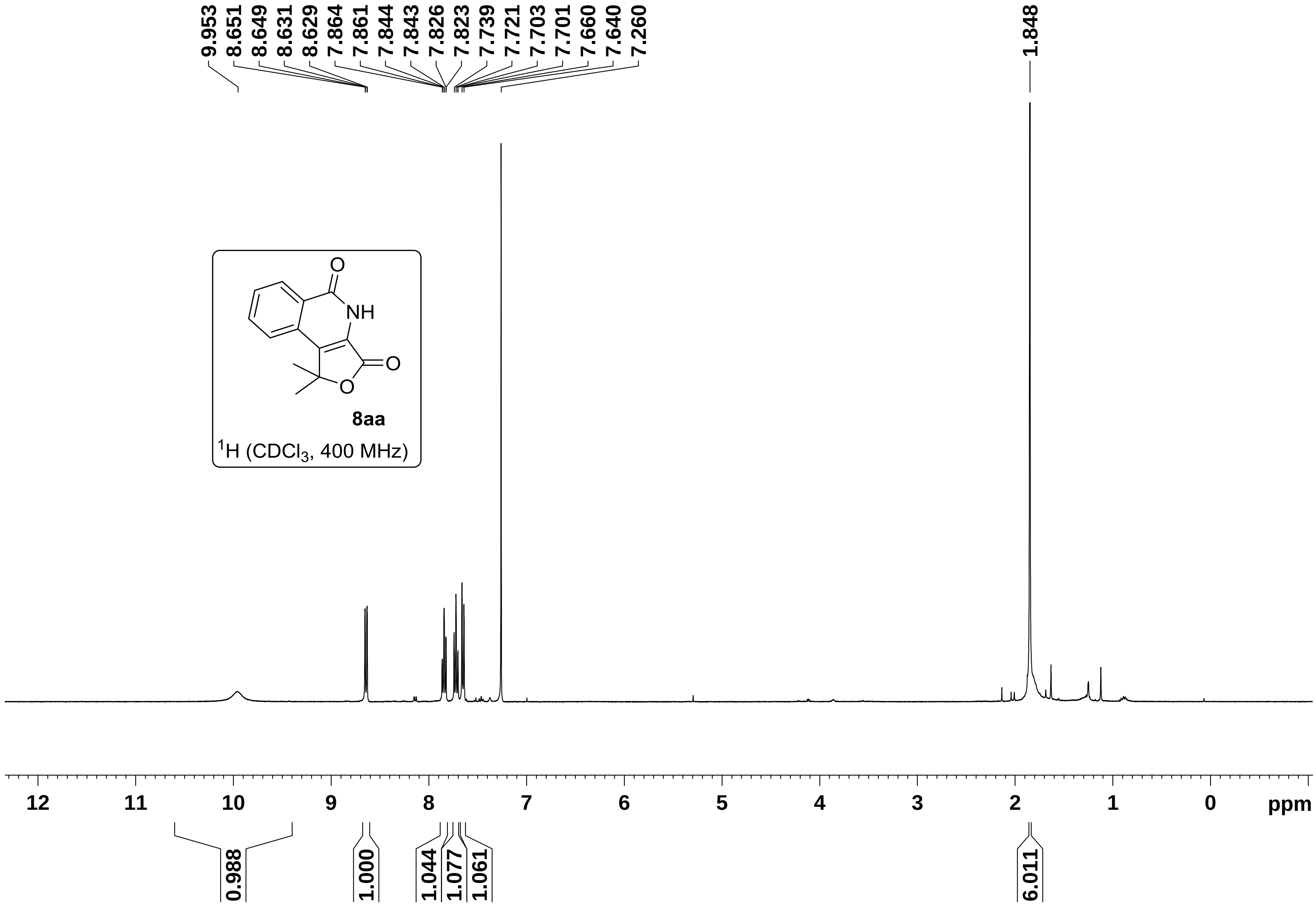


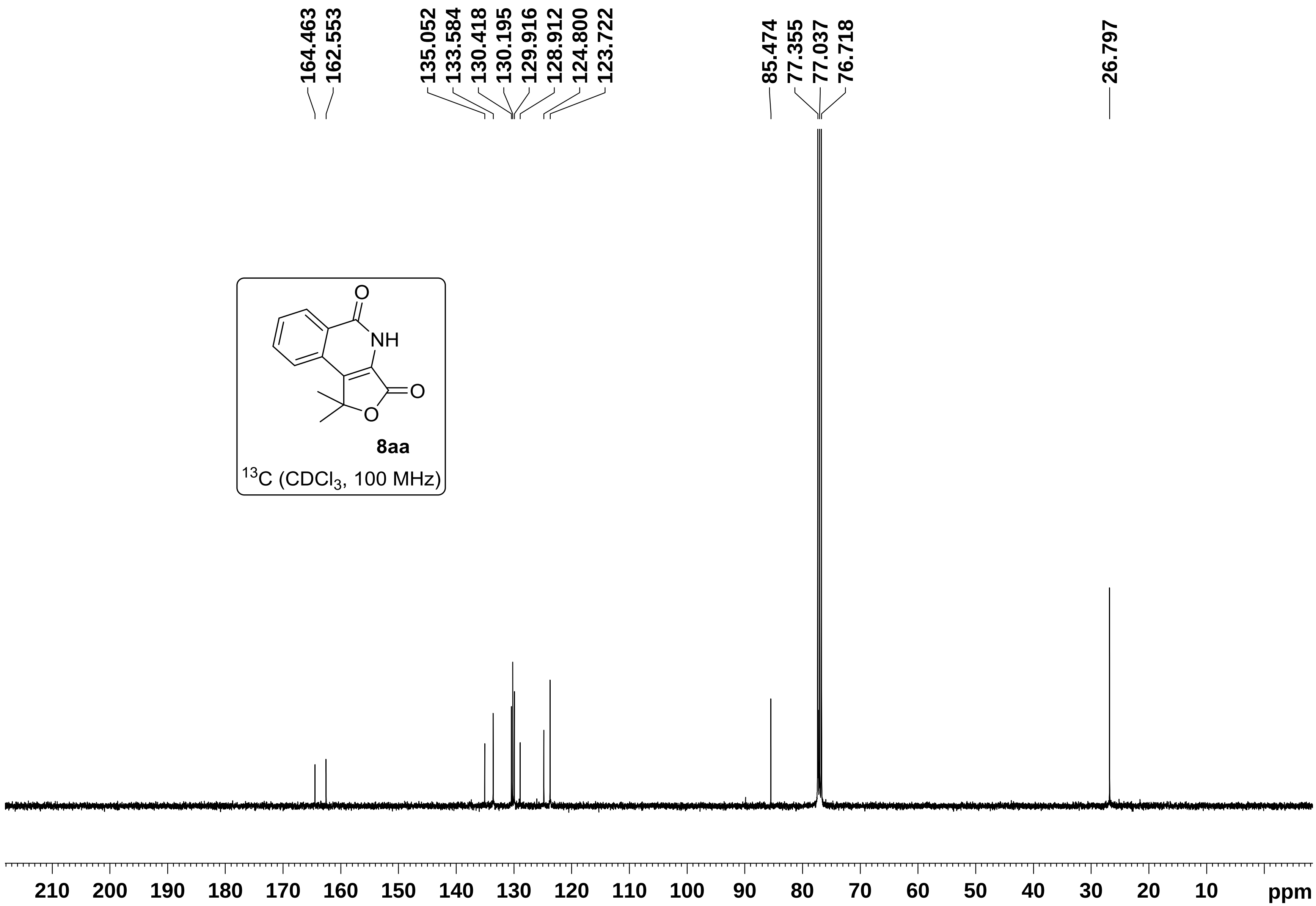
5ca

^{13}C NMR (CDCl$_3$, 100 MHz)


8.742
8.738
8.731
8.728
8.657
8.635
8.613
8.609
7.870
7.852
7.834
7.832
7.744
7.723
7.708
7.704
7.688
7.384
7.374
7.363
7.353
7.260
6.984
6.963
4.070
1.914
1.882
7aa
^{1}H (CDCl$_3$, 400 MHz)
10
9
8
7
6
5
4
3
2
1
0
ppm
1.000
2.021
1.046
3.088
1.066
1.069
3.095
3.018
3.034


163.308
162.843
155.964
150.959
145.088
135.117
133.167
131.300
130.688
130.150
129.734
129.465
128.944
127.107
125.774
123.676
121.413
120.709
103.504
82.677
77.382
77.067
76.749
55.908
27.058
N
O
N
O
O
O
7aa
13C (CDCl3, 100 MHz)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


9.953
8.651
8.649
8.631
8.629
7.864
7.861
7.844
7.843
7.826
7.823
7.739
7.721
7.703
7.701
7.660
7.640
7.260
1.848
O
NH
O
O
8aa
^{1}H (CDCl$_3$, 400 MHz)
12
11
10
9
8
7
6
5
4
3
2
1
0
ppm
0.988
1.000
1.044
1.077
1.061
6.011


164.463
162.553
135.052
133.584
130.418
130.195
129.916
128.912
124.800
123.722
85.474
77.355
77.037
76.718
26.797
O
NH
O
O
8aa
13C (CDCl3, 100 MHz)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm