Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

From α-Keto Acids to Nitrile Oxides Enabled by Copper Nitrate: A Facile Access to Fused Isoxazolines

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Supporting Information

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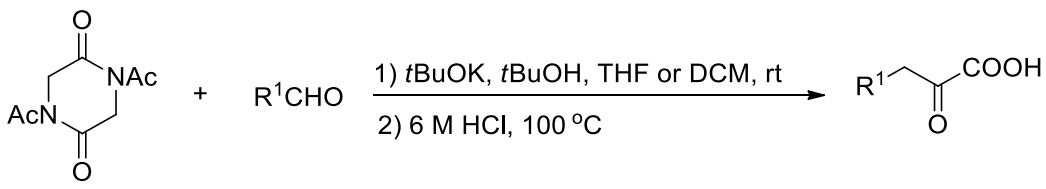
1. General Information

All reagents were obtained from commercial sources without further purification, and commercially available solvents were purified before use. All new compounds were fully characterized. All melting points were taken on a SGWX-4A Digital Melting Point Apparatus without correction. Infrared spectra were obtained using an AVATAR 370 FT-IR spectrometer. ^{1}H and ^{13}C spectra were recorded with a Bruker AV-500 spectrometer operating at 500 MHz and 125 MHz, respectively, with chemical shift values being reported in ppm relative to chloroform (δ = 7.26 ppm), dimethyl sulfoxide (δ = 2.50 ppm), acetone (δ = 2.05 ppm) or TMS (δ = 0.00 ppm) for ^{1}H NMR; chloroform (δ = 77.16 ppm), acetone (δ = 206.68, 29.92 ppm) or dimethyl sulfoxide (δ = 39.52 ppm) for ^{13}C NMR; Mass spectra (MS) and high resolution mass spectra (HRMS) were recorded with an Agilent 5975N or Thermo Fisher Scientific LTQ FTICR-MS using an Electron impact (EI) or Electrospray ionization (ESI) techniques. The crystal structure was recorded on SMART APEXII X-ray diffraction spectrometer. Silica gel plate GF254 was used for thin layer chromatography (TLC) and silica gel 300-400 mesh was used for flash column chromatography. Yields refer to chromatographically and spectroscopically pure compounds, unless otherwise indicated. α-Keto acids including 2-oxobutanoic acid (**1a**), 4-methyl-2-oxopentanoic acid (**1e**), 2-oxo-4-phenylbutanoic acid (**1i**), 2-oxo-3-phenylpropanoic acid (**1m**) were purchased commercially. Ethyl 2-oxo-4-phenylbutanoate **5** is also commercially available. α-Keto acids including 2-oxohexanoic acid (**1b**), 2-oxononanoic acid (**1c**), 5-methyl-2-oxohexanoic acid (**1d**), 3-cyclopentyl-2-oxopropanoic acid (**1f**), 3-cyclohexyl-2-oxopropanoic acid (**1g**), 4,4-dimethyl-2-oxopentanoic acid (**1h**), 2-oxo-3-(*p*-tolyl)propanoic acid (**1n**) and 3-(4-bromophenyl)-2-oxopropanoic acid (**1o**) were prepared from 1,4-diacetylpiperazine-2,5-dione and aldehyde following literature procedure.[1] 2-Oxo-5-phenylpentanoic acid (**1j**), 4-(4-chlorophenyl)-2-oxobutanoic acid (**1k**) and 5-(benzyloxy)-2-oxopentanoic acid (**1l**) were prepared by addition of appropriate Grignard reagents to *tert*-butyl 2-(methoxy(methyl)amino)-2-oxoacetate followed by hydrolysis with trifluoroacetic acid.[2,3]

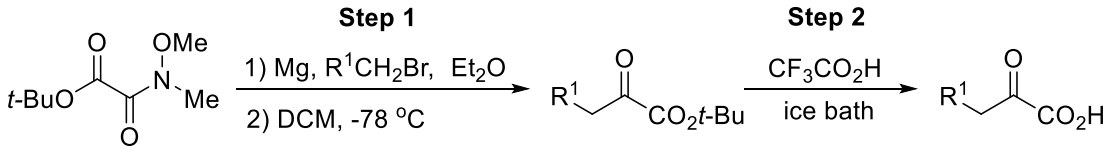
2. Synthesis and Characterization of α-Keto Acids

General Procedure A[1]



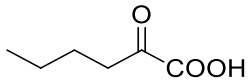
1,4-Diacetyl-piperazine-2,5-dione (5 mmol) was dissolved in dry THF (or DCM) (5 mL) under N_2 atmosphere. aldehyde (5 mmol) were added to this solution. potassium *tert*-butoxide (5 mmol) in a *tert*-butanol (5-10 mL) was added dropwise to this solution over 15 min at room temperature. The reaction mixture was stirred for 3 h, then a saturated aqueous solution of NH_4Cl (10 mL) was added to quench the reaction. The aqueous layer was extracted with DCM (3×10 mL) and the combined organic extracts were washed with water and brine (10 mL), dried over anhydrous Na_2SO_4, filtered and dried in vacuum. The residue was recrystallized from hot DCM/ Hexane to solid. The solid (1.0 mmol) was dissolved in 6 M aqueous HCl (5 mL) and heated to 100 ºC for 8 h. The reaction was then cooled to room temperature and extracted with ethyl acetate (3×5 mL). The combined organic phase was washed with water and brine (5 mL). The organic phase was dried over anhydrous sodium sulfate, and concentrated in vacuo. The residue was recrystallized from hot Hexane or purified by flash column chromatography on silica gel to α-keto acids.

General Procedure B[2,3]

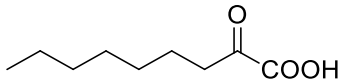


Step 1: A 3-neck round-bottomed flask affixed with a reflux condenser and constant pressure separation funnel was charged with magnesium turnings (14 mmol, 1.4 equiv). The apparatus was flame-dried under high vacuum. Upon cooling to room temperature, the apparatus was placed under an atmosphere of nitrogen, a piece of iodine and diethyl ether (5 mL) was added. A solution of the alkyl bromide (14 mmol, 1.4 equiv) in diethyl ether (15 mL) was added 1/5 from the constant pressure separation funnel. The solution was heated to reflux until the yellow color of iodine had faded out. Following addition, a solution of the alkyl bromide (14 mmol, 1.4 equiv) in diethyl ether (15 mL) was added dropwise from the constant pressure separation funnel over 30 min. The reaction was allowed to age for 1 h at 40 ºC following addition. A flame-dried round-bottomed flask with a low temperature thermometer was charged with *tert*-butyl 2-(methoxy-(methyl)amino)-2-oxoacetate (10 mmol, 1.0 equiv) in methylene chloride (20 mL) under a nitrogen atmosphere. The solution was cooled to -78 ºC. The previously prepared Grignard solution (~0.7 M, 1.4 equiv) was added dropwise to the reaction over 30 min. Following addition, the reaction was allowed to stir for 3 h at -78 ºC. The reaction was quenched with sat. aq. NH_4Cl (30 mL) and allowed to warm to room temperature.[2]

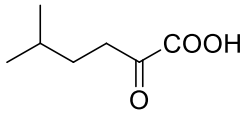
Step 2: The α-keto ester (2 mmol) was added to CF_3CO_2H (5 mL) and stirred in an ice bath. After approximately 3 h, TLC monitoring showed the reaction to be complete and the CF_3CO_2H was removed under reduced pressure. The residue was recrystallized from hot ethyl acetate/hexane or purified by flash column chromatography on silica gel to a-keto acids.[3]



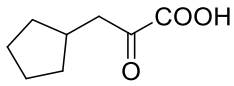
2-Oxohexanoic acid (1b):[4] This compound was prepared according to the General Procedure A using butyraldehyde as the aldehyde and purified by column chromatography (SiO_2, *n*-hexane/ethyl acetate = 5:1) to afford **1b** in 53% yield as brown liquid. IR (KBr, cm^{-1}): 3502, 2930, 2863, 2548, 2370, 1732, 1460, 1390, 1049; ^1H NMR (500 MHz, $CDCl_3$): δ 8.06 (s, br, 1H), 2.94 (t, J = 7.4 Hz, 2H), 1.68-1.62 (m, 2H), 1.41-1.34 (m, 2H), 0.93 (t, J = 7.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 195.95, 159.61, 37.02, 25.11, 22.06, 13.69; MS (ESI): *m/z* 129.1 $[M-H]^+$.



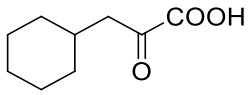
2-Oxononanoic acid (1c):[5] The title compound was prepared according to the General Procedure A using heptanal as the aldehyde and purified by column chromatography (SiO_2, *n*-hexane/ethyl acetate = 5:1) to afford **1c** in 51% yield as brown flake solid. IR (KBr, cm^{-1}): 3515, 2965, 2922, 2876, 1717, 1460, 1265, 1074; M.p.33-35 ^oC; ^1H NMR (500 MHz, $CDCl_3$): δ 8.20 (s, br, 1H), 2.94 (t, J = 7.3 Hz, 2H), 1.69-1.63 (m, 2H), 1.34-1.22 (m, 8H), 0.89-0.87 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 196.20, 159.50, 37.36, 31.70, 29.03, 29.01, 23.24, 22.70, 14.18; MS (ESI): *m/z* 171.2 $[M-H]^+$.



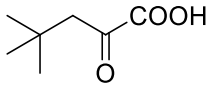
5-Methyl-2-oxohexanoic acid (1d):[6] The title compound was prepared according to the General Procedure A using 3-methylbutanal as the aldehyde and purified by column chromatography (SiO_2, *n*-hexane/ethyl acetate = 5:1) to afford **1d** in 56% yield as brown liquid. IR (KBr, cm^{-1}): 2957, 2872, 1723, 1469, 1386, 1368, 1321, 1211, 1170, 1132, 1064, 1023, 764, 666; ^1H NMR (500 MHz, $CDCl_3$): δ 7.92 (s, br, 1H), 2.94 (t, J = 7.6 Hz, 2H), 1.65-1.53 (m, 3H), 0.92 (d, J = 6.4 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 195.97, 160.41, 35.68, 31.75, 27.55, 22.19; MS (ESI): *m/z* 143.1 $[M-H]^+$.



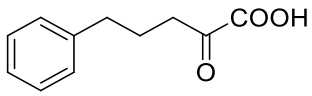
3-Cyclopentyl-2-oxopropanoic acid (1f):[7] The title compound was prepared according to the General Procedure A using cyclopentanecarbaldehyde as the aldehyde and purified by column chromatography (SiO_2, *n*-hexane/ethyl acetate = 5:1) to afford **1f** in 77% yield as brown liquid. IR (KBr, cm^{-1}): 3407, 2955, 2878, 2420, 2345, 1732, 1389, 1360, 1211, 1048; ^1H NMR (500 MHz, $CDCl_3$): δ 8.37 (s, br, 1H), 2.96 (d, J = 7.1 Hz, 2H), 2.35-2.26 (m, 1H), 1.91-1.84 (m, 2H), 1.69-1.55 (m, 4H), 1.19-1.12 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 195.55, 160.47, 43.59, 34.95, 32.42, 24.85; MS (ESI): *m/z* 155.1 $[M-H]^+$.



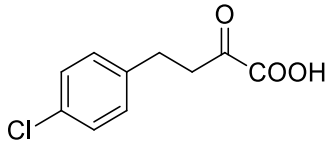
3-Cyclohexyl-2-oxopropanoic acid (1g):[1] The title compound was prepared according to the General Procedure A using cyclohexanecarbaldehyde as the aldehyde and purified by recrystallized from hot hexane to afford **1g** in 91% yield as brown flake solid. IR (KBr, cm^{-1}): 3509, 2924, 2851, 2793, 1733, 1449, 1337, 1280, 1205, 1047; M.p. 36-38 °C; ^1H NMR (500 MHz, $CDCl_3$): δ 9.24 (s, br, 1H), 2.80 (d, J = 6.8 Hz, 2H), 1.94-1.87 (m, 1H), 1.70-1.63 (m, 5H), 1.31-1.24 (m, 2H), 1.18-1.11 (m, 1H), 1.03-0.96 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 195.63, 160.30, 44.76, 33.83, 33.15, 26.10, 26.04; MS (ESI): *m/z* 169.1 $[M-H]^+$.



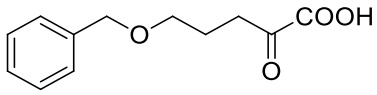
4,4-Dimethyl-2-oxopentanoic acid (1h):[1] The title compound was prepared according to the General Procedure A using pivalaldehyde as the aldehyde and purified by recrystallized from hot hexane to afford **1h** in 40% yield as brown flake solid. IR (KBr, cm^{-1}): 2970, 1727, 1473, 1368, 1307, 1191, 1083; M.p. 44-46 °C; ^1H NMR (500 MHz, $CDCl_3$): δ 7.14 (s, br, 1H), 2.85 (s, 2H), 1.05 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 196.00, 160.28, 48.48, 31.97, 29.59; MS (ESI): *m/z* 143.1 $[M-H]^+$.



2-Oxo-5-phenylpentanoic acid (1j):[8] The title compound was prepared according to the General Procedure B using (3-bromopropyl)benzene as the bromide and purified by recrystallized from hot ethyl acetate/hexane to afford **1j** in 50% yield as white solid. IR (KBr, cm^{-1}): 3538, 3503, 3045, 2938, 2893, 1734, 1694, 1392, 1303, 1084, 752, 701; M.p. 65-67 °C; ^1H NMR (500 MHz, $CDCl_3$): δ 7.58 (s, br, 1H), 7.33-7.30 (m, 2H), 7.25-7.19 (m, 3H), 2.99 (t, J = 7.2 Hz, 2H), 2.70 (t, J = 7.5 Hz, 2H), 2.07-2.01 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 195.79, 159.69, 140.91, 128.68, 128.60, 126.38, 36.88, 34.91, 24.75; MS (ESI): *m/z* 191.1 $[M-H]^+$.

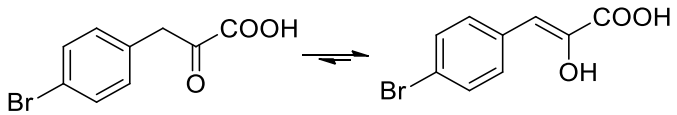


4-(4-Chlorophenyl)-2-oxobutanoic acid (1k):[9] The title compound was prepared according to the General Procedure B using 1-(2-bromoethyl)-4-chlorobenzene as the bromide and purified by column chromatography (SiO_2, *n*-hexane/ethyl acetate = 5:1) to afford **1k** in 52% yield as light-yellow solid. IR (KBr, cm^{-1}): 3458, 3120, 1722, 1493, 1340, 1268, 1083, 1014, 820; M.p. 26-28 °C; ^1H NMR (500 MHz, $CDCl_3$): δ 7.27 (d, J = 8.0 Hz, 2H), 7.14 (d, J = 8.0 Hz, 2H), 3.28 (t, J = 7.5 Hz, 2H), 2.97 (t, J = 7.5 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 194.60, 159.25, 137.95, 132.41, 129.71, 128.78, 38.86, 28.31; MS (ESI): *m/z* 211.0 $[M-H]^+$.

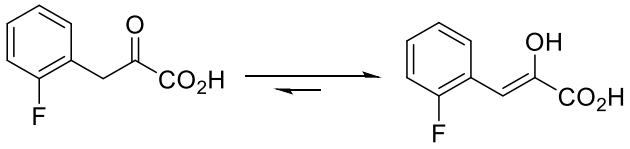


5-(Benzyloxy)-2-oxopentanoic acid (1l): The title compound was prepared according to the General Procedure B using 3-(benzyloxy)propyl bromide as the bromide and purified by column chromatography (SiO_2, *n*-hexane/ethyl acetate = 5:1) to afford **1l** in 57% yield as light yellow liquid. IR (KBr, cm^{-1}): 3453, 2942, 2868, 2371, 1732, 1450, 1361, 1206, 1098, 743, 699; ^1H NMR (500 MHz, $CDCl_3$): δ 7.38-7.35 (m, 2H), 7.33-7.28 (m, 3H), 4.46 (s, 2H), 3.54 (t, J = 5.7 Hz, 2H), 3.02 (t, J = 6.8 Hz, 2H), 2.10-2.05 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 195.68, 160.11, 137.68, 128.43, 127.84, 127.80, 72.93, 68.77, 34.70, 24.79; MS (ESI): *m/z* 221.1 $[M-H]^+$; HRMS (DART) *m/z* calcd for $C_{12}H_{13}O_4$ $[M-H]^+$ 221.0819, found 221.0815.

2-Oxo-3-(p-tolyl)propanoic acid (1n):[10] The title compound was prepared according to the General Procedure A using 4-methylbenzaldehyde as the aldehyde and purified by recrystallized from hot ethyl acetate/hexane to afford **1n** in 39% yield as white dendrites. IR (KBr, cm^{-1}): 3470, 3098, 2971, 2871, 1669, 1449, 1236, 868; M.p. 177-178 °C; ^1H NMR (500 MHz, d_6-DMSO): δ 13.12 (s, 1H), 9.11 (s, 1H), 7.64 (d, J = 8.2 Hz, 2H), 7.16 (d, J = 8.1 Hz, 2H), 6.37 (s, 1H), 2.29 (s, 3H); ^{13}C NMR (125 MHz, d_6-DMSO): δ 166.45, 141.17, 136.61, 132.16, 129.26, 128.96, 109.74, 20.93; MS (ESI): *m/z* 177.1 $[M-H]^+$.



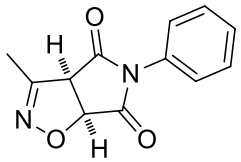
3-(4-Bromophenyl)-2-oxopropanoic acid (1o):[11] The title compound was prepared according to the General Procedure A using 4-bromobenzaldehyde as the aldehyde and purified by recrystallized from hot ethyl acetate/hexane to afford **1o** in 41% yield as white dendrites. IR (KBr, cm^{-1}): 3583, 3479, 2907, 2828, 1691, 1576, 1486, 1220, 872, 818; M.p. 187-189 °C; ^1H NMR (500 MHz, d_6-DMSO): δ 13.30 (s, 1H), 9.50 (s, 1H), 7.71 (d, J = 8.6 Hz, 2H), 7.53 (d, J = 8.6 Hz, 2H), 6.37 (s, 1H); ^{13}C NMR (125 MHz, d_6-DMSO): δ 166.56, 143.08, 134.74, 131.71, 131.58, 120.47, 108.67; MS (ESI): *m/z* 242.9 $[M-H]^+$.



3-(2-Fluorophenyl)-2-oxopropanoic acid (1p):[12] The title compound was prepared according to the General Procedure A using 2-fluorobenzaldehyde as the aldehyde and purified by recrystallized from hot ethyl acetate/hexane to afford **1p** in 46% yield as white solide. M.p. 124-126 °C; ^1H NMR (500 MHz, d_6-DMSO): δ 13.33 (s, 1H), 9.64 (s, 1H), 8.23 (td, J = 8.0, 2.0 Hz, 1H), 7.32-7.24 (m, 1H), 7.23-7.16 (m, 2H), 6.53 (s, 1H); ^{19}F NMR (470 MHz, d_6-DMSO)**:** δ -117.90; ^{13}C NMR (125 MHz,

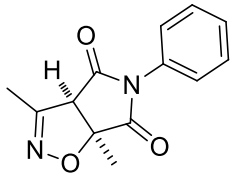
d_6-DMSO): δ 165.92, 159.09 (d, $^1J_{C\text{-}F}$ = 246.3 Hz), 143.48, 130.22 (d, $^4J_{C\text{-}F}$ = 2.5 Hz), 128.89 (d, $^3J_{C\text{-}F}$ = 8.9 Hz), 124.43 (d, $^2J_{C\text{-}F}$ = 16.3 Hz), 122.61 (d, $^3J_{C\text{-}F}$ = 11.3 Hz), 115.00 (d, $^2J_{C\text{-}F}$ = 21.3 Hz), 99.37 (d, $^3J_{C\text{-}F}$ = 7.5 Hz).

3. Synthesis and Characterization of Products



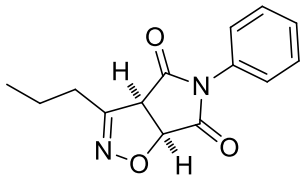
3-Methyl-5-phenyl-3a*H*-pyrrolo[3,4-*d*]isoxazole-4,6(5*H*,6a*H*)-dione (3a):[13] To a 15 mL oven-dried test tube containing $Cu(NO_3)_2{\cdot}3H_2O$ (145.0 mg, 0.6 mmol), 1-phenyl-1*H*-pyrrole-2,5-dione **2a** (103.9 mg, 0.6 mmol) and 2-oxobutanoic acid **1a** (30.6 mg, 0.3 mmol), was added 1.5 mL dioxane and purged with nitrogen. The mixture was stirred at 75 °C for 8 h as monitored by TLC. Upon completion, the reaction mixture was cooled down to room temperature, and purified by flash column chromatography on silica gel (eluted with petroleum ether/ethyl acetate = 2:1) to afford **3a** (50.4 mg, 74%) as a pale-yellow solid. M.p. 181-183 °C; IR (KBr, cm^{-1}): 3066, 2960, 1720, 1495, 1386, 1288, 1197, 870, 742; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.50-7.47 (m, 2H), 7.44-7.41 (m, 1H), 7.28-7.26 (m, 2H), 5.46 (d, J = 9.6 Hz, 1H), 4.40 (d, J = 9.5 Hz, 1H), 2.20 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 171.51, 170.07, 151.53, 130.90, 129.48, 129.35, 126.24, 78.98, 58.05, 11.98; MS (EI) m/z (%): m/z 230 (20) $[M]^+$, 119 (100), 91 (20).

Gram scale preparation of 3a: To a 50 mL flask were added $Cu(NO_3)_2{\cdot}3H_2O$ (4.830 g, 20 mmol), 1-phenyl-1*H*-pyrrole-2,5-dione **2a** (3.463 g, 20 mmol), 2-oxobutanoic acid **1a** (1.121 g, 11 mmol) and 15 mL dioxane. After purged with nitrogen, the mixture was stirred at 75 °C for 9 h as monitored by TLC. Upon completion, the reaction mixture was cooled down to room temperature, and purified by flash column chromatography on silica gel (eluted with petroleum ether/ethyl acetate = 2:1) to afford **3a** (1.66 g, 66%) as a pale-yellow solid.

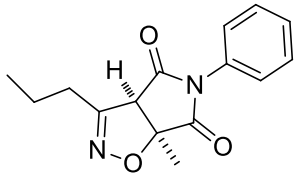


3,6a-Dimethyl-5-phenyl-3a*H*-pyrrolo[3,4-*d*]isoxazole-4,6(5*H*,6a*H*)-dione (3b):[14] Following the same procedure used for **3a** with $Cu(NO_3)_2{\cdot}3H_2O$ (145.0 mg, 0.6 mmol), 3-methyl-1-phenyl-1*H*-pyrrole-2,5-dione **2a'** (112.2 mg, 0.6 mmol) and 2-oxobutanoic acid **1a** (32.5 mg, 0.3 mmol) in dioxane (1.5 mL) for 8 h. The reaction mixture was purified by column chromatography on silica gel (eluted with petroleum ether/ethyl acetate = 2:1) to afford **3b** (41.4 mg, 56%) as a white solid. M.p. 179-181 °C; IR (KBr, cm^{-1}): 3063, 2962, 1716, 1506, 1381,1131, 867, 743, 688; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.51-7.48 (m, 2H), 7.44-7.41 (m, 1H), 7.31-7.29 (m, 2H), 4.01 (d, J

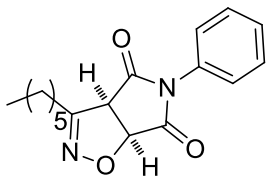
= 0.6 Hz, 1H), 2.19 (d, J = 0.7 Hz, 3H), 1.79 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 173.53, 169.71, 151.59, 131.07, 129.44, 129.28, 126.26, 86.37, 62.52, 19.13, 12.39; MS (ESI): *m/z* 245.1 $[M+H]^+$.



5-Phenyl-3-propyl-3a*H*-pyrrolo[3,4-*d*]isoxazole-4,6(5*H*,6a*H*)-dione (3c):[13]
Following the same procedure used for **3aa** with $Cu(NO_3)_2{\cdot}3H_2O$ (145.0 mg, 0.6 mmol), 1-phenyl-1*H*-pyrrole-2,5-dione **2a** (103.9 mg, 0.6 mmol) and 2-oxohexanoic acid **1b** (39.9 mg, 0.3 mmol) in dioxane (1.5 mL) for 8 h. The reaction mixture was purified by column chromatography on silica gel (eluted with petroleum ether/ethyl acetate = 4:1) to afford **3c** (48.2 mg, 61%) as a white solid. M.p. 134-136 ^{o}C; IR (KBr, cm^{-1}): 3066, 2964, 2877, 1720, 1501, 1385, 1191, 872, 742; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.50-7.47 (m, 2H), 7.44-7.41 (m, 1H), 7.28-7.26 (m, 2H), 5.45 (d, J = 9.6 Hz, 1H), 4.43 (d, J = 9.6 Hz, 1H), 2.62-2.56 (m, 1H), 2.50-2.44 (m, 1H), 1.84-1.77 (m, 1H), 1.73-1.64 (m, 1H), 1.01 (t, J = 7.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 171.66, 170.18, 154.82, 130.93, 129.45, 129.31, 126.24, 78.78, 57.05, 28.38, 19.34, 13.81; MS (ESI): *m/z* 259.1 $[M+H]^+$.

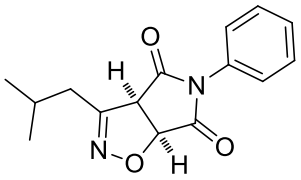


6a-Methyl-5-phenyl-3-propyl-3a*H*-pyrrolo[3,4-*d*]isoxazole-4,6(5*H*,6a*H*)-dione (3d): Following the same procedure used for **3a** with $Cu(NO_3)_2{\cdot}3H_2O$ (145.0 mg, 0.6 mmol), 3-methyl-1-phenyl-1*H*-pyrrole-2,5-dione **2a'** (112.3 mg, 0.6 mmol) and 2-oxohexanoic acid **1b** (39.9 mg, 0.3 mmol) in dioxane (1.5 mL) for 8 h. The reaction mixture was purified by column chromatography on silica gel (eluted with petroleum ether/ethyl acetate = 4:1) to afford **3d** (35.1 mg, 42%) as a white solid. M.p. 137-139 ^{o}C; IR (KBr, cm^{-1}): 2965, 1727, 1501, 1386, 1242, 1140, 751; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.50-7.47 (m, 2H), 7.43-7.41 (m, 1H), 7.30-7.28 (m, 2H), 4.03 (s, 1H), 2.60-2.53 (m, 1H), 2.49-2.43 (m, 1H), 1.84-1.65 (m, 5H), 1.00 (t, J = 7.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 173.56, 169.76, 154.87, 131.05, 129.36, 129.18, 126.20, 86.08, 61.47, 28.65, 19.27, 19.07, 13.76; MS (ESI): *m/z* 273.1 $[M+H]^+$; HRMS (DART) *m/z* calcd for $C_{15}H_{17}O_3N_2$ $[M+H]^+$ 273.1234, found 273.1234.

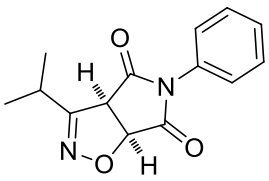


3-Hexyl-5-phenyl-3a*H*-pyrrolo[3,4-*d*]isoxazole-4,6(5*H*,6a*H*)-dione (3e): Following

the same procedure used for **3a** with $Cu(NO_3)_2 \cdot 3H_2O$ (145.0 mg, 0.6 mmol), 1-phenyl-1*H*-pyrrole-2,5-dione **2a** (103.9 mg, 0.6 mmol) and 2-oxononanoic acid **1c** (51.6 mg, 0.3 mmol) in dioxane (1.5 mL) for 8 h. The reaction mixture was purified by column chromatography on silica gel (eluted with petroleum ether/ethyl acetate = 5:1) to afford **3e** (62.7 mg, 70%) as a white solid. M.p. 88-90 °C; IR (KBr, cm^{-1}): 3066, 2928, 2860, 1721, 1498, 1387, 1190, 870, 739; ^1H NMR (500 MHz, $CDCl_3$): δ 7.52-7.49 (m, 2H), 7.47-7.44 (m, 1H), 7.31-7.28 (m, 2H), 5.48 (d, J = 9.6 Hz, 1H), 4.47 (d, J = 9.5 Hz, 1H), 2.68-2.61 (m, 1H), 2.53-2.46 (m, 1H), 1.83-1.63 (m, 2H), 1.43-1.31 (m, 6H), 0.91 (t, J = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 171.64, 170.19, 155.02, 130.94, 129.48, 129.34, 126.25, 78.78, 57.05, 31.46, 28.93, 26.49, 25.85, 22.60, 14.14; MS (ESI): *m/z* 301.1 $[M+H]^+$; HRMS (DART) *m/z* calcd for $C_{17}H_{21}O_3N_2$ $[M+H]^+$ 301.1547, found 301.1551.

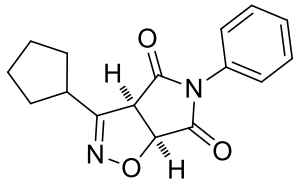


3-Isobutyl-5-phenyl-3aH-pyrrolo[3,4-*d*]isoxazole-4,6(5*H*,6a*H*)-dione (3f):[15]
Following the same procedure used for **3aa** with $Cu(NO_3)_2 \cdot 3H_2O$ (145.0 mg, 0.6 mmol), 1-phenyl-1*H*-pyrrole-2,5-dione **2a** (103.9 mg, 0.6 mmol) and 5-methyl-2-oxohexanoic acid **1d** (44.5 mg, 0.3 mmol) in dioxane (1.5 mL) for 8 h. The reaction mixture was purified by column chromatography on silica gel (eluted with petroleum ether/ethyl acetate = 2:1) to afford **3f** (59.3 mg, 71%) as a white solid. M.p. 145-147 °C; IR (KBr, cm^{-1}): 3068, 2962, 2870, 1720, 1499, 1462, 1388，1190, 830, 745; ^1H NMR (500 MHz, $CDCl_3$): δ 7.50-7.41 (m, 3H), 7.27-7.25 (m, 2H), 5.45 (d, J = 9.5 Hz, 1H), 4.42 (d, J = 9.6 Hz, 1H), 2.44 (d, J = 7.2 Hz, 2H), 2.18-2.13 (m, 1H), 1.05 (d, J = 6.6 Hz, 3H), 0.96 (d, J = 6.6 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 171.54, 170.04, 154.06, 130.81, 129.38, 129.23, 126.11, 78.57, 57.07, 34.95, 25.79, 22.89, 21.96; MS (ESI): *m/z* 273.1 $[M+H]^+$.

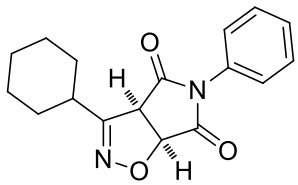


3-Isopropyl-5-phenyl-3a*H*-pyrrolo[3,4-*d*]isoxazole-4,6(5*H*,6a*H*)-dione (3g):[15]
Following the same procedure used for **3a** with $Cu(NO_3)_2 \cdot 3H_2O$ (145.0 mg, 0.6 mmol), 1-phenyl-1*H*-pyrrole-2,5-dione **2a** (103.9 mg, 0.6 mmol) and 4-methyl-2-oxopentanoic acid **1e** (39.5 mg, 0.3 mmol) in dioxane (1.5 mL) for 8 h. The reaction mixture was purified by column chromatography on silica gel (eluted with petroleum ether/ethyl acetate = 2:1) to afford **3g** (40.5 mg, 52%) as a white solid. M.p. 115-117 °C; IR (KBr, cm^{-1}): 3064, 2972, 1721, 1500, 1388, 1191, 870; ^1H NMR (500 MHz, $CDCl_3$): δ 7.50-7.47 (m, 2H), 7.44-7.41 (m, 1H), 7.29-7.27 (m, 2H), 5.47 (d, J = 9.6 Hz, 1H), 4.53 (d, J = 9.7 Hz, 1H), 2.94-2.85 (m, 1H), 1.33 (d, J = 6.8 Hz, 3H), 1.32 (d, J = 6.8 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 171.57, 170.21, 159.18, 130.85,

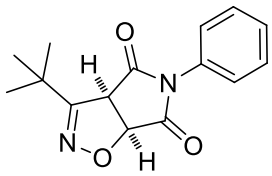
129.35, 129.20, 126.13, 79.01, 55.96, 27.30, 20.40, 19.12; MS (ESI): *m/z* 259.1 $[M+H]^+$.



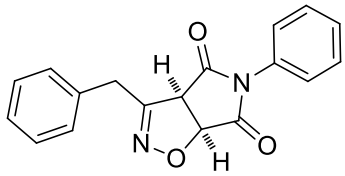
3-Cyclopentyl-5-phenyl-3a*H*-pyrrolo[3,4-*d*]isoxazole-4,6(5*H*,6a*H*)-dione (3h): Following the same procedure used for **3a** with $Cu(NO_3)_2{\cdot}3H_2O$ (145.0 mg, 0.6 mmol), 1-phenyl-1*H*-pyrrole-2,5-dione **2a** (103.9 mg, 0.6 mmol) and **1f** (48.5 mg, 0.3 mmol) in dioxane (1.5 mL) for 8 h. The reaction mixture was purified by column chromatography on silica gel (eluted with petroleum ether/ethyl acetate = 2:1) to afford **3h** (37.7 mg, 44%) as a white solid. M.p. 166-168 °C; IR (KBr, cm^{-1}):2969, 1721, 1502, 1384, 1190; ^1H NMR (500 MHz, $CDCl_3$): δ 7.53-7.49 (m, 2H), 7.47-7.44 (m, 1H), 7.32-7.29 (m, 2H), 5.49 (d, J = 9.6 Hz, 1H), 4.50 (dd, J = 9.6, 0.85 Hz, 1H), 3.02-2.96 (m, 1H), 2.22-2.16 (m, 1H), 2.04-1.90 (m, 2H), 1.84-1.78 (m, 2H), 1.71-1.63 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 171.71, 170.29, 157.88, 130.99, 129.48, 129.32, 126.26, 79.04, 57.22, 37.71, 31.42, 29.62, 25.26, 25.11; MS (ESI): *m/z* 285.1 $[M+H]^+$; HRMS (DART) *m/z* calcd for $C_{16}H_{17}O_3N_2$ $[M+H]^+$ 285.1234, found 285.1233.



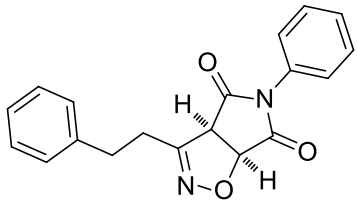
3-Cyclohexyl-5-phenyl-3a*H*-pyrrolo[3,4-*d*]isoxazole-4,6(5*H*,6a*H*)-dione (3i):[13] Following the same procedure used for **3aa** with $Cu(NO_3)_2{\cdot}3H_2O$ (145.0 mg, 0.6 mmol), 1-phenyl-1*H*-pyrrole-2,5-dione **2a** (103.9 mg, 0.6 mmol), and 3-cyclohexyl-2-oxopropanoic acid **1g** (51.0 mg, 0.3 mmol) in dioxane (1.5 mL) for 8 h. The reaction mixture was purified by column chromatography on silica gel (eluted with petroleum ether/ethyl acetate = 2:1) to afford **3i** (48.5 mg, 54%) as a white solid. M.p. 178-180 °C; IR (KBr, cm^{-1}): 3063, 2932, 2857, 1721, 1500, 1388, 1188, 869; ^1H NMR (500 MHz, $CDCl_3$): δ 7.50-7.47 (m, 2H), 7.44-7.41 (m, 1H), 7.29-7.27 (m, 2H) 5.44 (d, J = 9.6 Hz, 1H), 4.52 (d, J = 9.6 Hz, 1H), 2.61-2.56 (m, 1H), 2.12-2.10 (m, 1H), 2.00-1.97 (m, 1H), 1.83-1.81 (m, 2H), 1.72-1.70 (m, 1H), 1.64-1.57 (m, 1H), 1.42-1.24 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 171.68, 170.39, 158.46, 130.98, 129.47, 129.31, 126.24, 78.81, 56.00, 36.38, 30.86, 29.51, 26.00, 25.89, 25.59; MS (ESI): *m/z* 299.1 $[M+H]^+$.



3-(*tert*-Butyl)-5-phenyl-3a*H*-pyrrolo[3,4-*d*]isoxazole-4,6(5*H*,6a*H*)-dione (3j):
Following the same procedure used for **3a** with $Cu(NO_3)_2 \cdot 3H_2O$ (145.0 mg, 0.6 mmol), 1-phenyl-1*H*-pyrrole-2,5-dione **2a** (103.9 mg, 0.6 mmol) and 4,4-dimethyl-2-oxopentanoic acid **1h** (43.2 mg, 0.3 mmol) in dioxane (1.5 mL) for 8 h. The reaction mixture was purified by column chromatography on silica gel (eluted with petroleum ether/ethyl acetate = 5:1) to afford **3j** (38.2 mg, 47%) as a white solid. M.p. 154-156 °C; IR (KBr, cm^{-1}): 3064, 2968, 1722, 1497, 1386, 1197, 883; ^1H NMR (500 MHz, $CDCl_3$): δ 7.53-7.49 (m, 2H), 7.47-7.43 (m, 1H), 7.29-7.27 (m, 2H) 5.52 (d, J = 9.6 Hz, 1H), 4.60 (d, J = 9.6 Hz, 1H), 1.39 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 171.63, 170.87, 161.59, 131.06, 129.53, 129.36, 126.28, 80.05, 55.94, 34.25, 28.72; MS (ESI): *m/z* 273.1 $[M+H]^+$; HRMS (DART) *m/z* calcd for $C_{15}H_{17}O_3N_2$ $[M+H]^+$ 273.1234, found 273.1235.

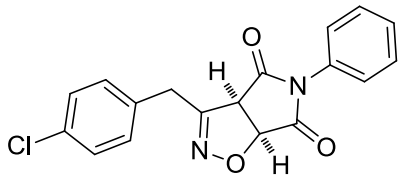


3-Benzyl-5-phenyl-3a*H*-pyrrolo[3,4-*d*]isoxazole-4,6(5*H*,6a*H*)-dione (3k):[13]
Following the same procedure used for **3a** with $Cu(NO_3)_2 \cdot 3H_2O$ (145.0 mg, 0.6 mmol), 1-phenyl-1*H*-pyrrole-2,5-dione **2a** (103.9 mg, 0.6 mmol) and 2-oxo-4-phenylbutanoic acid **1i** (53.4 mg, 0.3 mmol) in dioxane (1.5 mL) for 8 h. The reaction mixture was purified by column chromatography on silica gel (eluted with petroleum ether/ethyl acetate = 3:1) to afford **3k** (72.8 mg, 68%) as a white solid. M.p. 176-178 °C; IR (KBr, cm^{-1}): 1713, 1495, 1385, 1187, 868; ^1H NMR (500 MHz, $CDCl_3$): δ 7.49-7.46 (m, 2H), 7.44-7.36 (m, 5H), 7.32-7.30 (m, 1H), 7.24-7.22 (m, 2H), 5.38 (d, J = 9.7 Hz, 1H), 4.29 (d, J = 9.6 Hz, 1H), 4.04 (d, J = 14.7 Hz, 1H), 3.74 (d, J = 14.7 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 171.28, 169.94, 153.89, 133.86, 130.77, 129.45, 129.35, 129.24, 129.10, 127.65, 126.09, 79.06, 55.64, 32.28; MS (ESI): *m/z* 307.1 $[M+H]^+$.

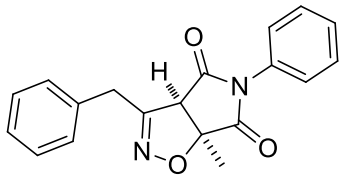


3-Phenethyl-5-phenyl-3a*H*-pyrrolo[3,4-*d*]isoxazole-4,6(5*H*,6a*H*)-dione (3l):[13]
Following the same procedure used for **3a** with $Cu(NO_3)_2 \cdot 3H_2O$ (145.0 mg, 0.6 mmol), 1-phenyl-1*H*-pyrrole-2,5-dione **2a** (103.9 mg, 0.6 mmol) and 2-oxo-5-phenylpentanoic acid **1j** (57.6 mg, 0.3 mmol) in dioxane (1.5 mL) for 8 h. The reaction mixture was purified by column chromatography on silica gel (eluted with petroleum ether/ethyl acetate = 2:1) to afford **3l** (59.3 mg, 62%) as a white solid. M.p. 165-167 °C; IR (KBr, cm^{-1}): 2954, 1715, 1499, 1381, 1184, 877; ^1H NMR (500 MHz, d_6-DMSO): δ 7.53-7.44 (m, 3H), 7.32-7.20 (m, 7H), 5.54 (d, J = 9.4 Hz, 1H), 4.77 (d, J = 9.5 Hz, 1H), 3.02-2.90 (m, 2H), 2.83-2.73 (m, 2H); ^{13}C NMR (125 MHz, d_6-DMSO): δ 172.69, 171.02, 154.74, 140.52, 131.57, 129.00, 128.76, 128.39, 128.25,

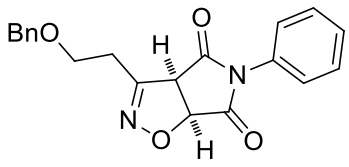
126.86, 126.15, 79.39, 57.55, 30.91, 27.68; MS (ESI): *m/z* 321.1 $[M+H]^+$.



3-(4-Chlorobenzyl)-5-phenyl-3a*H*-pyrrolo[3,4-*d*]isoxazole-4,6(5*H*,6a*H*)-dione (3m): Following the same procedure used for **3a** with $Cu(NO_3)_2 \cdot 3H_2O$ (145.0 mg, 0.6 mmol), 1-phenyl-1*H*-pyrrole-2,5-dione **2a** (103.9 mg, 0.6 mmol) and 4-(4-chlorophenyl)-2-oxobutanoic acid **1k** (63.6 mg, 0.3 mmol) in dioxane (1.5 mL) for 8 h. The reaction mixture was purified by column chromatography on silica gel (eluted with petroleum ether/ethyl acetate = 3:1) to afford **3m** (81.9 mg, 80%) as a white solid. M.p. 155-157 ºC; IR (KBr, cm^{-1}): 2981, 1721, 1498, 1380, 1189, 889; ^1H NMR (500 MHz, $CDCl_3$): δ 7.50-7.47 (m, 2H), 7.45-7.42 (m, 1H), 7.36-7.32 (m, 4H), 7.23-7.21 (m, 2H), 5.42 (d, J = 9.6 Hz, 1H), 4.29 (d, J = 9.7 Hz, 1H), 4.00 (d, J = 14.9 Hz, 1H), 3.71 (d, J = 14.9 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 171.25, 169.99, 153.61, 133.88, 132.41, 130.97, 130.82, 129.52, 129.44, 129.40, 126.17, 79.24, 55.69, 31.84; MS (ESI): *m/z* 341.1 $[M+H]^+$; HRMS (DART) *m/z* calcd for $C_{18}H_{14}O_3N_2Cl$ $[M+H]^+$ 341.0687, found 341.0691.

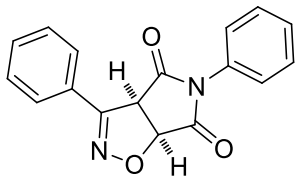


3-Benzyl-6a-methyl-5-phenyl-3a*H*-pyrrolo[3,4-*d*]isoxazole-4,6(5*H*,6a*H*)-dione (3n): Following the same procedure used for **3aa** with $Cu(NO_3)_2 \cdot 3H_2O$ (145.0 mg, 0.6 mmol), 3-methyl-1-phenyl-1*H*-pyrrole-2,5-dione **2a'** (112.2 mg, 0.6 mmol) and 2-oxo-4-phenylbutanoic acid **1i** (53.4 mg, 0.3 mmol) in dioxane (1.5 mL) for 8 h. The reaction mixture was purified by column chromatography on silica gel (eluted with petroleum ether/ethyl acetate = 5:1) to afford **3n** (45.5 mg, 47%) as a white solid. M.p.172-174 ºC; IR (KBr, cm^{-1}): 3060, 2926, 2861, 1728, 1492, 1385, 1240, 1131; ^1H NMR (500 MHz, $CDCl_3$): δ 7.50-7.47 (m, 2H), 7.44-7.38 (m, 5H), 7.34-7.30 (m, 1H), 7.28-7.26 (m, 2H), 4.01 (d, J = 14.8 Hz, 1H), 3.90 (s, 1H), 3.72 (d, J = 14.9 Hz, 1H), 1.69 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 173.43, 169.70, 154.20, 134.31, 131.06, 129.44, 129.42, 129.27, 129.23, 127.70, 126.21, 86.68, 60.08, 32.76, 18.99; MS (ESI): *m/z* 321.1 $[M+H]^+$; HRMS (DART) *m/z* calcd for $C_{19}H_{17}O_3N_2$ $[M+H]^+$ 321.1234, found 321.1232.

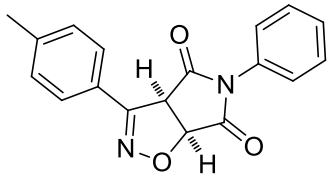


3-(2-(Benzyloxy)ethyl)-5-phenyl-3a*H*-pyrrolo[3,4-*d*]isoxazole-4,6(5*H*,6a*H*)-dione (3o): Following the same procedure used for **3a** with $Cu(NO_3)_2 \cdot 3H_2O$ (145.0 mg, 0.6

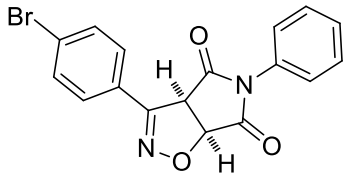
mmol), 1-phenyl-1*H*-pyrrole-2,5-dione **2a** (103.9 mg, 0.6 mmol) and 5-(benzyloxy)-2-oxopentanoic acid **1l** (68.5 mg, 0.3 mmol), in dioxane (1.5 mL) for 8 h. The reaction mixture was purified by column chromatography on silica gel (eluted with petroleum ether/ethyl acetate = 2:1) to afford **3o** (37.7 mg, 35%) as a white solid. M.p. 92-94 °C; IR (KBr, cm^{-1}): 1720, 1502, 1381, 1190, 870; ^1H NMR (500 MHz, $CDCl_3$): δ 7.51-7.47 (m, 2H), 7.46-7.43 (m, 1H), 7.39-7.32 (m, 5H), 7.29-7.27 (m, 2H), 5.45 (d, J = 9.6 Hz, 1H), 4.58 (s, 2H), 4.53 (d, J = 9.6 Hz, 1H), 3.93-3.89 (m, 1H), 3.86-3.82 (m, 1H), 3.00-2.95 (m, 1H), 2.86-2.81 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 171.51, 170.21, 153.28, 137.90, 130.93, 129.44, 129.29, 128.62, 127.98, 127.89, 126.25, 78.96, 73.02, 66.38, 57.23, 26.82; MS (ESI): *m/z* 351.1 $[M+H]^+$; HRMS (DART) *m/z* calcd for $C_{20}H_{19}O_4N_2$ $[M+H]^+$ 351.1339, found 351.1338.



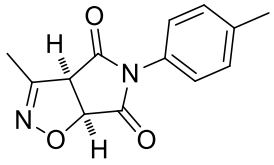
3,5-Diphenyl-3a*H*-pyrrolo[3,4-*d*]isoxazole-4,6(5*H*,6a*H*)-dione (3p):[13] Following the same procedure used for **3a** with $Cu(NO_3)_2{\cdot}3H_2O$ (145.0 mg, 0.6 mmol), 1-phenyl-1*H*-pyrrole-2,5-dione **2a** (103.9 mg, 0.6 mmol) and 2-oxo-3-phenyl-propanoic acid **1m** (49.2 mg, 0.3 mmol), KI (49.8 mg, 0.3 mmol), in dioxane (1.5 mL) for 8 h. The reaction mixture was purified by column chromatography on silica gel (eluted with petroleum ether/ethyl acetate = 2:1) to afford **3p** (42.0 mg, 48%) as a pale-yellow solid. M.p. 171-173 °C; IR (KBr, cm^{-1}): 3064, 1723, 1498, 1387, 1311, 1198, 897; ^1H NMR (500 MHz, $CDCl_3$): δ 8.04-8.02 (m, 2H), 7.47-7.39 (m, 6H), 7.27 (d, J = 8.4 Hz, 2H), 5.66 (d, J = 9.7 Hz, 1H), 4.97 (d, J = 9.7 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.98, 169.95, 152.93, 131.38, 130.96, 129.43, 129.35, 129.00, 128.22, 126.84, 126.28, 80.54, 55.04; MS (ESI): *m/z* 293.1 $[M+H]^+$.



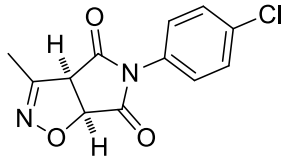
5-Phenyl-3-(*p*-tolyl)-3a*H*-pyrrolo[3,4-*d*]isoxazole-4,6(5*H*,6a*H*)-dione (3q):[16]
Following the same procedure used for **3a** with $Cu(NO_3)_2{\cdot}3H_2O$ (145.0 mg, 0.6 mmol), 1-phenyl-1*H*-pyrrole-2,5-dione **2a** (103.9 mg, 0.6 mmol), 2-oxo-3-(p-tolyl)-propanoic acid **1n** (55.0 mg, 0.3 mmol) and KI (49.8 mg, 0.3 mmol) in dioxane (1.5 mL) for 8 h. The reaction mixture was purified by column chromatography on silica gel (eluted with petroleum ether/ethyl acetate = 3:1) to afford **3q** (34.1 mg, 36%) as a pale-yellow solid. M.p. 170-172 °C; IR (KBr, cm^{-1}): 3051, 2964, 1724, 1498, 1385, 1192, 891; ^1HNMR (500 MHz, $CDCl_3$): δ 7.94 (d, J = 8.3 Hz, 2H), 7.50-7.46 (m, 2H), 7.45-7.41 (m, 1H), 7.31-7.28 (m, 4H), 5.68 (d, J = 9.7 Hz, 1H), 4.98 (d, J = 9.8 Hz, 1H), 2.42 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 171.07, 170.01, 152.86, 141.92, 130.99, 129.72, 129.42, 129.33, 128.18, 126.29, 123.99, 80.37, 55.15, 21.68; MS (ESI): *m/z* 307.1 $[M+H]^+$.



3-(4-Bromophenyl)-5-phenyl-3a*H*-pyrrolo[3,4-*d*]isoxazole-4,6(5*H*,6a*H*)-dione (3r):[17] Following the same procedure used for **3a** with $Cu(NO_3)_2{\cdot}3H_2O$ (145.0 mg, 0.6 mmol), 1-phenyl-1*H*-pyrrole-2,5-dione **2a** (103.9 mg, 0.6 mmol), 3-(4-bromophenyl)-2-oxopropanoic acid **1o** (73.5 mg, 0.3 mmol) and KI (49.8 mg, 0.3 mmol) in dioxane (1.5 mL) for 8 h. The reaction mixture was purified by column chromatography on silica gel (eluted with petroleum ether/ethyl acetate = 2:1) to afford **3r** (51.3 mg, 46%) as a white solid. M.p. 194-196 °C; IR (KBr, cm^{-1}): 3062, 2961, 1722, 1493, 1389, 1190, 890, 832; ^1H NMR (500 MHz, $CDCl_3$): δ 7.94 (d, J = 8.6 Hz, 2H), 7.62 (d, J = 8.6 Hz, 2H), 7.51-7.43 (m, 3H), 7.30-7.28 (m, 2H), 5.71 (d, J = 9.8 Hz, 1H), 4.96 (d, J = 9.8 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.57, 169.71, 152.06, 132.18, 130.71, 129.50, 129.35, 129.32, 126.10, 125.94, 125.66, 80.58, 54.72; MS (ESI): *m/z* 370.9 $[M+H]^+$.

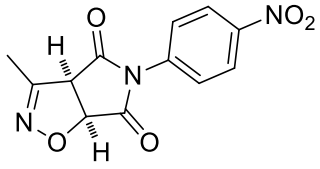


3-Methyl-5-(*p*-tolyl)-3a*H*-pyrrolo[3,4-*d*]isoxazole-4,6(5*H*,6a*H*)-dione (3ab): Following the same procedure used for **3a** with $Cu(NO_3)_2{\cdot}3H_2O$ (145.0 mg, 0.6 mmol), 1-(*p*-tolyl)-1*H*-pyrrole-2,5-dione **2b** (112.3 mg, 0.6 mmol) and 2-oxobutanoic acid **1a** (30.6 mg, 0.3 mmol) in dioxane (1.5 mL) for 8 h. The reaction mixture was purified by column chromatography on silica gel (eluted with petroleum ether/ethyl acetate = 2:1) to afford **3ab** (55.8 mg, 74%) as a white solid. M.p. 174-176 °C; IR (KBr, cm^{-1}): 2965, 1772, 1515, 1388, 1195; ^1H NMR (500 MHz, $CDCl_3$): δ 7.29 (d, J = 8.2 Hz, 2H), 7.15 (d, J = 8.3 Hz, 2H), 5.46 (d, J = 9.5 Hz, 1H), 4.39 (d, J = 9.5 Hz, 1H), 2.39 (s, 3H), 2.21 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 171.7, 170.2, 151.6, 139.6, 130.1, 128.2, 126.0, 79.0, 58.0, 21.4, 11.98; MS (ESI): *m/z* 245.0 $[M+H]^+$; HRMS (DART) *m/z* calcd for $C_{13}H_{13}O_3N_2$ $[M+H]^+$ 245.0921, found 245.0921.

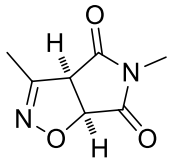


5-(4-Chlorophenyl)-3-methyl-3a*H*-pyrrolo[3,4-*d*]isoxazole-4,6(5*H*,6a*H*)-dione (3ac): Following the same procedure used for **3a** with $Cu(NO_3)_2{\cdot}3H_2O$ (145.0 mg, 0.6 mmol), 1-(4-chlorophenyl)-1*H*-pyrrole-2,5-dione **2c** (124.6 mg, 0.6 mmol) and 2-oxobutanoic acid **1a** (30.6 mg, 0.3 mmol) in dioxane (1.5 mL) for 8 h. The reaction mixture was purified by column chromatography on silica gel (eluted with petroleum ether/ethyl acetate = 2:1) to afford **3ac** (53.0 mg, 65%) as a white solid. M.p. 177-179 °C; IR (KBr, cm^{-1}): 2965, 1720, 1551, 1388, 1195, 837, 771; ^1H NMR (500 MHz,

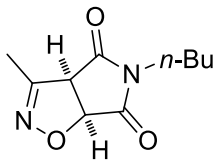
$CDCl_3$): δ 7.47 (d, J = 8.8 Hz, 2H), 7.26 (d, J = 8.8 Hz, 2H), 5.47 (d, J = 9.6 Hz, 1H), 4.41 (dd, J = 9.6, 0.9 Hz, 1H), 2.21 (d, J = 0.8 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 171.18, 169.77, 151.39, 135.27, 129.71, 129.32, 127.45, 78.90, 58.04, 12.00; MS (ESI): *m/z* 265.1 $[M+H]^+$; HRMS (DART) *m/z* calcd for $C_{12}H_{10}O_3N_2Cl$ $[M+H]^+$ 265.0374, found 265.0374.



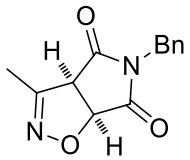
3-Methyl-5-(4-nitrophenyl)-3a*H*-pyrrolo[3,4-*d*]isoxazole-4,6(5*H*,6a*H*)-dione (3ad): Following the same procedure used for **3a** with $Cu(NO_3)_2{\cdot}3H_2O$ (145.0 mg, 0.6 mmol), 1-(4-nitrophenyl)-1*H*-pyrrole-2,5-dione **2d** (130.9 mg, 0.6 mmol) and 2-oxobutanoic acid **1a** (30.6 mg, 0.3 mmol) in dioxane (1.5 mL) for 8 h. The reaction mixture was purified by column chromatography on silica gel (eluted with petroleum ether/ethyl acetate = 2:1) to afford **3ad** (53.6 mg, 65%) as a pale-yellow solid. M.p. 187-189 °C; IR (KBr, cm^{-1}): 2987, 1727, 1525, 1348, 1181, 842; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.36 (d, J = 9.1 Hz, 2H), 7.60 (d, J = 9.1 Hz, 2H), 5.51 (d, J = 9.6 Hz, 1H), 4.47 (dd, J = 9.7, 0.85 Hz, 1H), 2.23 (d, J = 0.8 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.67, 169.27, 151.19, 147.56, 136.32, 126.86, 124.73, 78.87, 58.11, 12.00; MS (EI): *m/z* (%) 275 (60) $[M]^+$, 164 (100), 134 (50); HRMS (DART) *m/z* calcd for $C_{12}H_{10}O_5N_3$ $[M+H]^+$ 276.0615, found 276.0615.



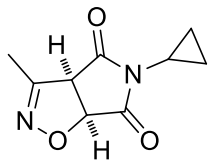
3,5-Dimethyl-3a*H*-pyrrolo[3,4-*d*]isoxazole-4,6(5*H*,6a*H*)-dione (3ae): Following the same procedure used for **3a** with $Cu(NO_3)_2{\cdot}3H_2O$ (145.0 mg, 0.6 mmol), 1-methyl-1*H*-pyrrole-2,5-dione **2e** (66.7 mg, 0.6 mmol) and 2-oxobutanoic acid **1a** (30.6 mg, 0.3 mmol) in dioxane (1.5 mL) for 8 h. The reaction mixture was purified by column chromatography on silica gel (eluted with petroleum ether/ethyl acetate = 2:1) to afford **3ae** (34.3 mg, 68%) as a white solid. M.p. 128-130 °C; IR (KBr, cm^{-1}): 2998, 2967, 1709, 1439, 1387, 1289, 1139, 982, 851; ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.32 (d, J = 9.4 Hz, 1H), 4.25 (d, J = 9.4 Hz, 1H), 3.02 (s, 3H), 2.15 (d, J = 0.95 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 172.57, 171.09, 151.38, 79.01, 58.10, 25.54, 11.92; MS (EI): *m/z* (%) 168 (98) $[M]^+$, 82 (100); HRMS (EI) *m/z* calcd for $C_7H_8N_2O_3$ $[M]^+$ 168.0535, found 168.0536.



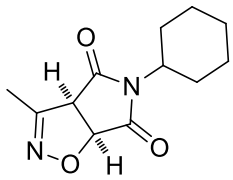
5-Butyl-3-methyl-3a*H*-pyrrolo[3,4-*d*]isoxazole-4,6(5*H*,6a*H*)-dione (3af):
Following the same procedure used for **3a** with $Cu(NO_3)_2 \cdot 3H_2O$ (145.0 mg, 0.6 mmol), 1-butyl-1*H*-pyrrole-2,5-dione **2f** (93.5 mg, 0.6 mmol) and 2-oxobutanoic acid **1a** (29.0 mg, 0.3 mmol) in dioxane (1.5 mL) for 8 h. The reaction mixture was purified by column chromatography on silica gel (eluted with petroleum ether/ethyl acetate = 2:1) to afford **3af** (42.4 mg, 72%) as a colorless liquid. IR (KBr, cm^{-1}): 2965, 1711, 1551, 1363; ^1H NMR (500 MHz, $CDCl_3$): δ 5.30 (d, J = 9.4 Hz, 1H), 4.22 (dd, J = 9.4, 0.85 Hz, 1H), 3.56-3.47 (m, 2H), 2.14 (d, J = 1.0 Hz, 3H), 1.56-1.50 (m, 2H), 1.31-1.24 (m, 2H), 0.91 (t, J = 7.3, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 172.57, 171.15, 151.50, 78.94, 57.99, 39.39, 29.57, 20.00, 13.63, 11.88; MS (ESI): *m/z* 211.1 $[M+H]^+$; HRMS (DART) *m/z* calcd for $C_{10}H_{15}O_3N_2$ $[M+H]^+$ 211.1077, found 211.1077.



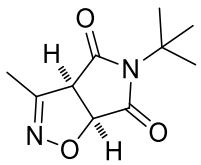
5-Benzyl-3-methyl-3a*H*-pyrrolo[3,4-*d*]isoxazole-4,6(5*H*,6a*H*)-dione (3ag):
Following the same procedure used for **3a** with $Cu(NO_3)_2 \cdot 3H_2O$ (145.0 mg, 0.6 mmol), 1-benzyl-1*H*-pyrrole-2,5-dione **2g** (112.3 mg, 0.6 mmol) and 2-oxobutanoic acid **1a** (33.5 mg, 0.3 mmol) in dioxane (1.5 mL) for 8 h. The reaction mixture was purified by column chromatography on silica gel (eluted with petroleum ether/ethyl acetate = 2:1) to afford **3ag** (51.4 mg, 64%) as a white solid. M.p. 136-138 ºC; IR (KBr, cm^{-1}): 2965, 1713, 1491, 1437, 1395, 1348, 1175, 888, 750, 701; ^1H NMR (500 MHz, $CDCl_3$): δ 7.34-7.28 (m, 5H), 5.28 (d, J = 9.4 Hz, 1H), 4.65 (s, 2H), 4.22 (dd, J = 9.2, 0.5 Hz, 1H), 2.12 (d, J = 0.65 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 172.20, 170.78, 151.39, 134.76, 128.97, 128.49, 128.48, 79.01, 58.07, 43.14, 11.86; MS (ESI): *m/z* 245.1 $[M+H]^+$; HRMS (DART) *m/z* calcd for $C_{13}H_{13}O_3N_2$ $[M+H]^+$ 245.0921, found 245.0921.



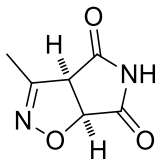
5-Cyclopropyl-3-methyl-3aH-pyrrolo[3,4-*d*]isoxazole-4,6(5*H*,6a*H*)-dione (3ah):
Following the same procedure used for **3a** with $Cu(NO_3)_2 \cdot 3H_2O$ (145.0 mg, 0.6 mmol), 1-cyclopropyl-1*H*-pyrrole-2,5-dione **2h** (82.3 mg, 0.6 mmol) and 2-oxobutanoic acid **1a** (34.0 mg, 0.3 mmol) in dioxane (1.5 mL) for 8 h. The reaction mixture was purified by column chromatography on silica gel (eluted with petroleum ether/ethyl acetate = 2:1) to afford **3ah** (28.2 mg, 44%) as a white solid. M.p. 112-114 ºC; IR (KBr, cm^{-1}): 2967, 1712, 1550, 1450, 1215, 852; ^1H NMR (500 MHz, $CDCl_3$): δ 5.23 (d, J = 9.5 Hz, 1H), 4.17 (d, J = 9.5 Hz, 1H), 2.66-2.61 (m, 1H), 2.14 (d, J = 0.7 Hz, 3H), 1.00-0.96 (m, 3H), 0.92-0.87 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 172.86, 171.44, 151.49, 78.55, 57.63, 22.94, 11.90, 4.98, 4.91; MS (ESI): *m/z* 195.1 $[M+H]^+$; HRMS (DART) *m/z* calcd for $C_9H_{11}O_3N_2$ $[M+H]^+$ 195.0764, found 195.0765.



5-Cyclohexyl-3-methyl-3a*H*-pyrrolo[3,4-*d*]isoxazole-4,6(5*H*,6a*H*)-dione (3ai): Following the same procedure used for **3a** with $Cu(NO_3)_2 \cdot 3H_2O$ (145.0 mg, 0.6 mmol), 1-cyclohexyl-1*H*-pyrrole-2,5-dione **2i** (107.5 mg, 0.6 mmol), 2-oxobutanoic acid **1a** (32.5 mg, 0.3 mmol), in dioxane (1.5 mL) for 8 h. The reaction mixture was purified by column chromatography on silica gel (eluted with petroleum ether/ethyl acetate = 2:1) to afford **3ai** (49.8 mg, 66%) as a white solid. M.p. 145-147 ºC; IR (KBr, cm^{-1}): 2931, 2855, 1706, 1388, 1196, 856; ^1H NMR (500 MHz, $CDCl_3$): δ 5.24 (d, J = 9.45 Hz, 1H), 4.16 (dd, J = 9.4, 0.86 Hz, 1H), 3.97-3.92 (m, 1H), 2.14 (d, J = 0.8 Hz, 3H), 2.11-2.03 (m, 2H), 1.84-1.82 (m, 2H), 1.67-1.65 (m, 1H), 1.58-1.56 (m, 3H), 1.35-1.16 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 172.66 , 171.17, 151.64, 78.63, 57.70, 52.70, 28.77, 28.68, 25.80, 25.78, 24.96, 11.87; MS (ESI): *m/z* 237.1 $[M+H]^+$; HRMS (DART) *m/z* calcd for $C_{12}H_{17}O_3N_2$ $[M+H]^+$ 237.1234 found 237.1234.

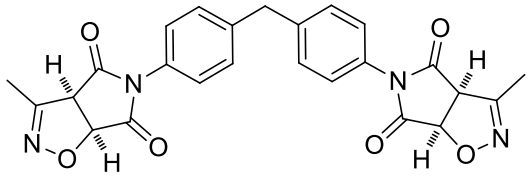


5-(*tert*-Butyl)-3-methyl-3a*H*-pyrrolo[3,4-*d*]isoxazole-4,6(5*H*,6a*H*)-dione (3aj): Following the same procedure used for **3a** with $Cu(NO_3)_2 \cdot 3H_2O$ (145.0 mg, 0.6 mmol), 1-(*tert*-butyl)-1*H*-pyrrole-2,5-dione **2j** (91.9 mg, 0.6 mmol) and 2-oxo-butanoic acid **1a** (38.0 mg, 0.4 mmol) in dioxane (1.5 mL) for 8 h. The reaction mixture was purified by column chromatography on silica gel (eluted with petroleum ether/ethyl acetate = 2:1) to afford **3aj** (40.6 mg, 52%) as a white solid. M.p. 103-105 ºC; IR (KBr, cm^{-1}): 2984, 1709, 1341, 1166, 849; ^1H NMR (500 MHz, $CDCl_3$): δ 5.14 (d, J = 9.55 Hz, 1H), 4.06 (dd, J = 9.7, 1.1 Hz, 1H), 2.13 (d, J = 0.9 Hz, 3H), 1.57 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 173.77, 172.02, 151.94, 78.66, 59.79, 57.81, 28.22, 11.93; MS (ESI): *m/z* 211.0 $[M+H]^+$; HRMS (DART) *m/z* calcd for $C_{10}H_{15}O_3N_2$ $[M+H]^+$ 211.1077, found 211.1078.

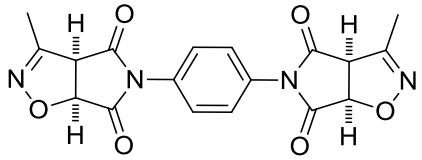


3-Methyl-3a*H*-pyrrolo[3,4-*d*]isoxazole-4,6(5*H*,6a*H*)-dione (3ak): Following the same procedure used for **3a** with $Cu(NO_3)_2 \cdot 3H_2O$ (145.0 mg, 0.6 mmol), 1*H*-pyrrole-2,5-dione **2k** (58.2 mg, 0.6 mmol) and 2-oxobutanoic acid **1a** (32.5 mg, 0.3 mmol) in dioxane (1.5 mL) for 8 h. The reaction mixture was purified by column chromatography on silica gel (eluted with petroleum ether/ethyl acetate = 2:1) to afford **3ak** (27.9 mg, 57%) as a white solid. M.p.172-174 ºC; IR (KBr, cm^{-1}): 3267,

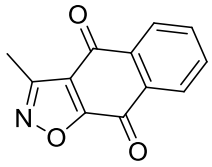
2987, 2732, 1720, 1551, 1344, 1187, 860, 753; ^{1}H NMR (500 MHz, d_6-Acetone): δ 10.54 (s, 1H), 5.38 (d, J = 9.3 Hz, 1H), 4.53 (d, J = 9.3 Hz, 1H), 2.09 (s, 3H); ^{13}C NMR (125 MHz, d_6-Acetone): δ 173.75, 172.23, 151.72, 80.58, 59.25, 10.59; MS (ESI): *m/z* 155.0 $[M+H]^+$; HRMS (DART) *m/z* calcd for $C_6H_7O_3N_2$ $[M+H]^+$ 155.0451, found 155.0451.



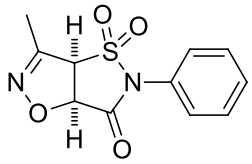
5,5'-(Methylenebis(4,1-phenylene))bis(3-methyl-3a*H*-pyrrolo[3,4-*d*]isoxazole-4,6(5*H*,6a*H*)-dione) (3al): Following the same procedure used for **3a** with $Cu(NO_3)_2{\cdot}3H_2O$ (289.8 mg, 1.2 mmol), 1,1'-(methylenebis(4,1-phenylene))bis(1*H*-pyrrole-2,5-dione) **2l** (107.5 mg, 0.3 mmol) and 2-oxobutanoic acid **1a** (102.0 mg, 1.0 mmol) in dioxane (3.0 mL) for 10 h. The reaction mixture was purified by column chromatography on silica gel (eluted with petroleum ether/ethyl acetate = 1:1) to afford **3al** (78.6 mg, 55%) as a pale-yellow solid. M.p. 164-166 ºC; IR (KBr, cm^{-1}): 2973, 1724, 1513, 1430, 1381, 1294, 1186, 867, 754; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.29 (d, J = 8.5 Hz, 4H), 7.21 (d, J = 8.5 Hz, 4H), 5.45 (d, J = 9.6 Hz, 2H), 4.39 (dd, J = 9.5, 0.95 Hz, 2H), 4.40 (s, 2H), 2.20 (d, J = 0.9 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 171.53, 170.10, 151.53, 141.58, 130.03, 129.18, 126.37, 78.96, 58.03, 41.24, 11.99; MS (ESI): *m/z* 473.1 $[M+H]^+$; HRMS (DART) *m/z* calcd for $C_{25}H_{21}O_6N_4$ $[M+H]^+$ 473.1467, found 473.1455.



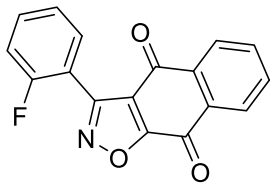
5,5'-(1,4-Phenylene)bis(3-methyl-3a*H*-pyrrolo[3,4-*d*]isoxazole-4,6(5*H*,6a*H*)-dione) (3am): Following the same procedure used for **3a** with $Cu(NO_3)_2{\cdot}3H_2O$ (289.8 mg, 1.2 mmol) 1,1'-(1,4-phenylene)bis(1*H*-pyrrole-2,5-dione) **2m** (80.5 mg, 0.3 mmol) and 2-oxobutanoic acid **1a** (91.9 mg, 0.9 mmol) in dioxane (3.0 mL) for 10 h. The reaction mixture was purified by column chromatography on silica gel (eluted with petroleum ether/ethyl acetate = 1:1) to afford **3am** (67.5 mg, 59%) as a pale-yellow solid. M.p. 164-166 ºC; IR (KBr, cm^{-1}): 2977, 1712, 1463, 1412, 1214, 853; ^{1}H NMR (500 MHz, d_6-Acetone): δ 7.53 (s, 4H), 5.58 (d, J = 9.6 Hz, 2H), 4.76 (dd, J = 9.5, 1.0 Hz, 2H), 2.14 (d, J = 1.0 Hz, 6H); ^{13}C NMR (125 MHz, d_6-Acetone): δ 173.13, 171.58, 152.62, 132.99, 128.18, 80.65, 59.33, 11.75; MS (EI) *m/z* (%): 382 (25) $[M]^+$, 160 (30), 55 (100); HRMS (DART) *m/z* calcd for $C_{18}H_{15}O_6N_4$ $[M+H]^+$ 383.0986, found 383.0986.



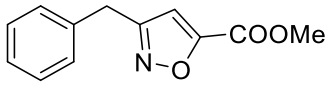
3-Methylnaphtho[2,3-*d*]isoxazole-4,9-dione (3an):[18] Following the same procedure used for **3a** with $Cu(NO_3)_2 \cdot 3H_2O$ (145.0 mg, 0.6 mmol), naphthalene-1,4-dione **2n** (94.8 mg, 0.6 mmol) and 2-oxobutanoic acid **1a** (30.6 mg, 0.30 mmol), in dioxane (1.5 mL) for 8 h. The reaction mixture was purified by column chromatography on silica gel (eluted with petroleum ether/ethyl acetate = 2:1) to afford **3an** (27.5 mg, 43%) as a pale yellow solid. M.p. 176-178 °C; IR (KBr, cm^{-1}): 2927, 1680, 1591, 1428, 1342, 1253, 1201, 1161, 1053, 923, 719; ^1H NMR (500 MHz, $CDCl_3$): δ 8.26-8.21 (m, 2H), 7.86-7.80 (m, 2H), 2.69 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 179.85, 173.38, 165.22, 158.70, 135.23, 134.48, 133.49, 132.54, 127.67, 127.36, 120.85, 10.98; MS (EI): *m/z* (%) 213 (100) $[M]^+$, 104 (90), 76 (50).



3-Methyl-5-phenyl-5,6a-dihydroisothiazolo[5,4-*d*]isoxazol-6(3a*H*)-one 4,4-dioxide (3ao): Following the same procedure used for **3a** with $Cu(NO_3)_2 \cdot 3H_2O$ (145.0 mg, 0.6 mmol), 2-phenylisothiazol-3(2*H*)-one-1,1-dioxide **2o** (125.5 mg, 0.6 mmol) and 2-oxobutanoic acid **1a** (30.6 mg, 0.30 mmol) in dioxane (1.5 mL) for 8 h. The reaction mixture was purified by column chromatography on silica gel (eluted with petroleum ether/ethyl acetate = 2:1) to afford **3ao** (36.3 mg, 45%) as a white solid. M.p. 175-177 °C; IR (KBr, cm^{-1}): 2972, 1746, 1492, 1354, 1321, 1227, 1156, 1029, 990, 885; ^1H NMR (500 MHz, $CDCl_3$): δ 7.54-7.53 (m, 3H), 7.38-7.36 (m, 2H), 5.75 (d, J = 10.4 Hz, 1H), 5.23 (d, J = 10.4 Hz, 1H), 2.36 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.84, 149.06, 130.90, 130.22, 128.70, 128.09, 80.95, 72.03, 12.87; MS (ESI): *m/z* 267.0 $[M+H]^+$; HRMS (DART) *m/z* calcd for $C_{11}H_{11}O_4N_2S$ $[M+H]^+$ 267.0434, found 267.0434.

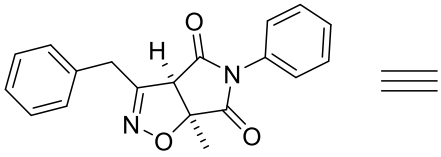


3-(2-Fluorophenyl)naphtho[2,3-*d*]isoxazole-4,9-dione (3ap):[19]
Following the same procedure used for **3a** with $Cu(NO_3)_2 \cdot 3H_2O$ (145.0 mg, 0.6 mmol), naphthalene-1,4-dione **2n** (94.8 mg, 0.6 mmol), 3-(2-fluorophenyl)-2-oxo- propanoic acid **1p** (54.7 mg, 0.3 mmol) and KI (49.8 mg, 0.3 mmol) in dioxane (1.5 mL) for 8 h. The reaction mixture was purified by column chromatography on silica gel (eluted with petroleum ether/ethyl acetate = 10:1) to afford **3ap** (40.1 mg, 46%) as a yellow solid. M.p. 189-190 °C; ^1H NMR (500 MHz, $CDCl_3$): δ 8.32-8.25 (m, 1H), 8.25-8.16 (m, 1H), 7.88-7.78 (m, 2H), 7.70 (td, J = 7.3, 1.8 Hz, 1H), 7.64-7.54 (m, 1H), 7.38-7.23 (m, 2H); ^{19}F NMR (470 MHz, $CDCl_3$): δ -111.22 (dt, J = 11.6, 6.1 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 178.19, 173.33, 165.65, 160.67 (d, $^1J_{C\text{-}F}$ = 251.3 Hz), 156.48, 135.41, 134.48, 133.70, 133.19 (d, $^3J_{C\text{-}F}$ = 8.8 Hz), 132.14, 131.28 (d, $^4J_{C\text{-}F}$ =1.3 Hz), 127.60 (d, $^3J_{C\text{-}F}$ = 8.8 Hz), 124.51 (d, $^4J_{C\text{-}F}$ = 3.8 Hz), 120.72, 116.34 (d, $^2J_{C\text{-}F}$ = 21.3 Hz), 114.78 (d, $^2J_{C\text{-}F}$ = 13.8 Hz).

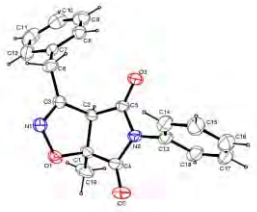


Methyl 3-benzylisoxazole-5-carboxylate (**3s**): Following the same procedure used for **3a** with $Cu(NO_3)_2 \cdot 3H_2O$ (145.0 mg, 0.6 mmol), methyl propiolate (100.8 mg, 1.2 mmol) and 2-oxo-4-phenylbutanoic acid **1i** (53.4 mg, 0.3 mmol) in dioxane (1.5 mL) for 9 h. The reaction mixture was purified by column chromatography on silica gel (eluted with petroleum ether/ethyl acetate = 20:1) to afford **3s** (25.1 mg, 39%) as a white solid. M.p. 45-47 ºC; IR (KBr, cm^{-1}): 1735, 1465, 1420, 1286, 1225, 1080, 995, 710; ^1H NMR (500 MHz, $CDCl_3$): δ 7.34-7.31 (m, 2H), 7.28-7.22 (m, 3H), 6.70 (s, 1H), 4.07 (s, 2H), 3.93 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 163.92, 160.25, 157.34, 136.54, 129.06, 128.91, 127.33, 109.67, 52.92, 32.46; MS (ESI): m/z 218.0 $[M+H]^+$; HRMS (DART) m/z calcd for $C_{12}H_{12}O_3N$ $[M+H]^+$ 218.0812, found 218.0812.

4. X-ray Crystallographic Data for Compounds 3n and 3an

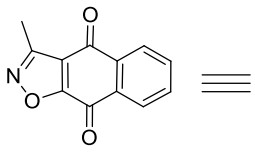


3n

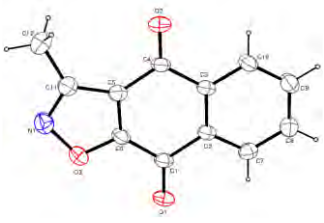


X-ray structure of **3n**

Crystallographic data for **3n**: $C_{19}H_{16}N_2O_3$, M = 320.21, monoclinic, P 21/c, a = 5.556 (3) Å, b = 25.565 (13) Å, c = 11.983 (5) Å, β = 104.38 (2)º, V = 1648.7 (14) $Å^3$, Z = 4, Crystal size: 0.23 × 0.15 × 0.13 mm, T = 295 K, ρ_{calcd} = 1.290 g.cm^{-3}, R_1 = 0.0528 (I>4σ(I)), wR_2 = 0.1734 (all data), GOF = 1.053, reflections collected/unique: 10338 / 3845 (Rint = 0.0274), Data: 2276, restraints: 0, parameters: 234. The crystallographic data for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication (CCDC 1913835). The data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.



3an



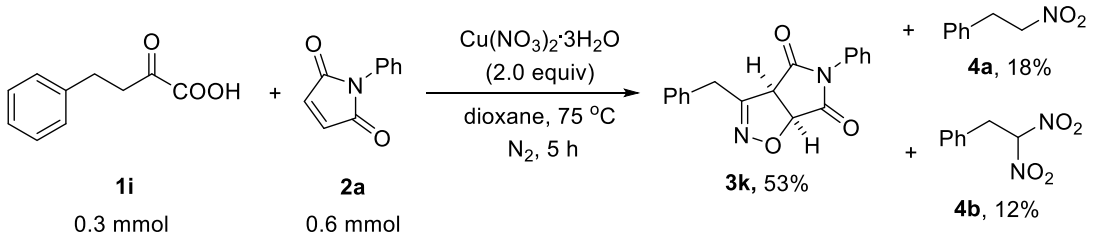
X-ray structure of **3an**

Crystallographic data for **3an**: $C_{12}H_7NO_3$, M = 213.19, monoclinic, P21, a = 5.611 (5) Å, b = 6.369 (5) Å, c = 13.868 (5) Å, β = 96..958 (5)o, V = 491.9 (6) Å3, Z = 2, Crystal size: 0.25 × 0.15 × 0.12 mm, T = 295 K, ρ_{calcd} = 1.439 g.cm^{-3}, R_1 = 0.036 (I>4σ(I)), wR2 = 0.0956 (all data), GOF = 1.050, reflections collected/unique: 2938 / 1972 (Rint = 0.0224), Data: 1792, restraints: 0, parameters: 145. The crystallographic

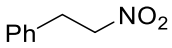
data for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication (CCDC 1985053). The data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

5. Mechanistic Studies

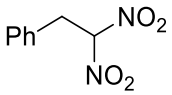
5.1 Possible Intermediates Investigation



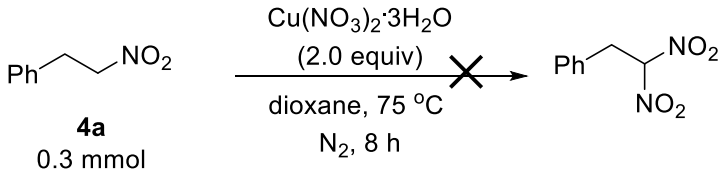
To a 15 mL oven-dried test tube containing $Cu(NO_3)_2 \cdot 3H_2O$ (145.0 mg, 0.6 mmol), 1-phenyl-1*H*-pyrrole-2,5-dione **2a** (103.9 mg, 0.6 mmol), 2-oxo-4-phenylbutanoic acid **1i** (53.4 mg, 0.3 mmol), was added 1.5 mL dioxane. After purged with nitrogen, the mixture was stirred at 75 °C for 5 h. The reaction mixture was cooled down to room temperature, and purified by flash column chromatography on silica gel to afford **4a** (8.0 mg, 18%) as light yellow liquid, **4b** (6.7 mg, 12%) as yellow liquid and to afford **3k** (48.7 mg, 53%) as a white solid.



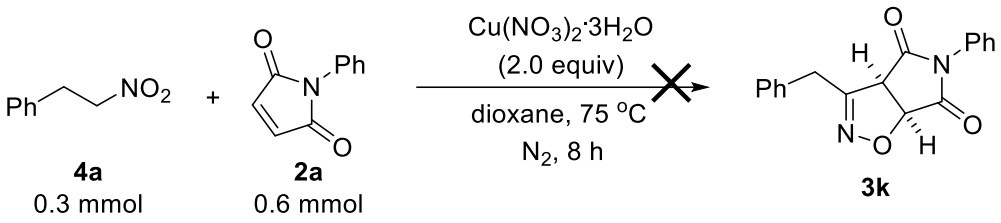
Compound **4a:**[20] ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.38-7.35 (m, 2H), 7.32-7.29 (m, 1H), 7.25-7.23 (m, 2H), 4.64 (t, J = 7.5 Hz, 2H), 3.35 (t, J = 7.5 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 135.76, 129.08, 128.68, 127.55, 76.38, 33.55.



Compound **4b**:[21] ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.42-7.37 (m, 3H), 7.27-7.25 (m, 2H), 6.37 (t, J = 7.5 Hz, 1H), 3.84 (d, J = 7.5 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 130.10, 129.53, 129.10, 128.87, 112.34, 37.13; IR (KBr, cm^{-1}): 1574, 1327, 745, 693; MS (EI) *m/z* (%): *m/z* 196 (20) $[M]^+$, 103 (100), 91 (80).



To a 15 mL oven-dried test tube containing $Cu(NO_3)_2 \cdot 3H_2O$ (145.0 mg, 0.6 mmol), (2-nitroethyl)benzene **4a** (45.3 mg, 0.3 mmol), was added 1.5 mL dioxane after purged with nitrogen. The mixture was stirred at 75 °C for 8 h. No reaction occurred.

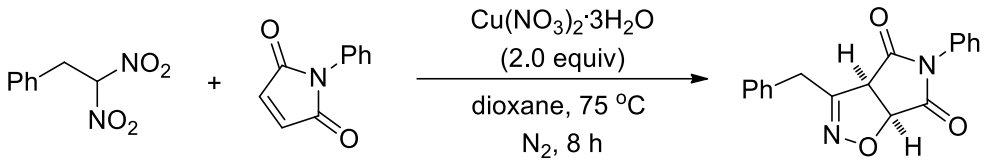


4a
0.3 mmol

2a
0.6 mmol

3k

To a 15 mL oven-dried test tube containing $Cu(NO_3)_2{\cdot}3H_2O$ (145.0 mg, 0.6 mmol), 1-phenyl-1*H*-pyrrole-2,5-dione **2a** (103.9 mg, 0.6 mmol), (2-nitroethyl)benzene **4a** (45.3 mg, 0.3 mmol), was added 1.5 mL dioxane after purged with nitrogen. The mixture was stirred at 75 °C for 8 h. No product **3k** was isolated.

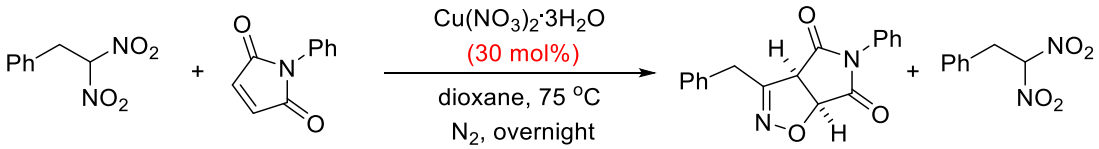


4b
0.3 mmol

2a
0.6 mmol

3k, 86%

To a 15 mL oven-dried test tube containing $Cu(NO_3)_2{\cdot}3H_2O$ (145.0 mg, 0.6 mmol), 1-phenyl-1*H*-pyrrole-2,5-dione **2a** (103.9 mg, 0.6 mmol), (2,2-dinitroethyl)benzene **4b** (58.0 mg, 0.3 mmol), was added 1.5 mL dioxane. After purged with nitrogen, the mixture was stirred at 75 °C for 8 h. The reaction mixture was cooled down to room temperature, and purified by flash column chromatography on silica gel to afford **3k** (77.6 mg, 86%) as a white solid.



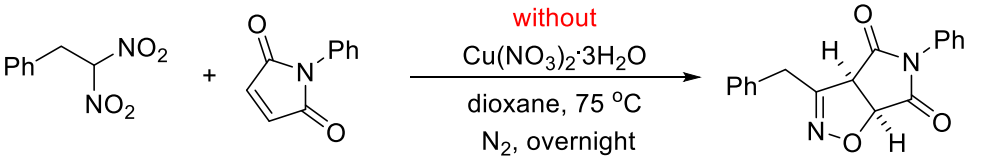
4b
0.3 mmol

2a
0.6 mmol

3k, 68%

4b, 23%
(recovered)

To a 15 mL oven-dried test tube containing $Cu(NO_3)_2{\cdot}3H_2O$ (21.7 mg, 30 mmol%), 1-phenyl-1*H*-pyrrole-2,5-dione **2a** (103.9 mg, 0.6 mmol), (2,2-dinitroethyl)benzene **3b** (58.0 mg, 0.3 mmol), was added 1.5 mL dioxane after purged with nitrogen. The mixture was stirred at 75 °C for overnight. The reaction mixture was cooled down to room temperature, and purified by flash column chromatography on silica gel to afford **3k** (62.1 mg, 68%) as a white solid and **4b** (13.5 mg, 23%) was recovered as yellow liquid.

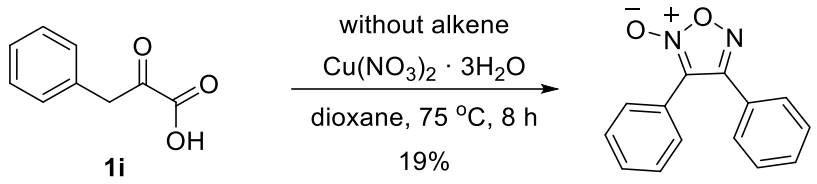


4b
0.3 mmol

2a
0.6 mmol

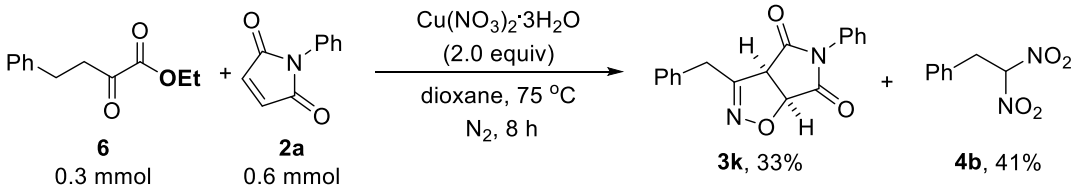
3k, not observed

To a 15 mL oven-dried test tube containing 1-phenyl-1*H*-pyrrole-2,5-dione **2a** (103.9 mg, 0.6 mmol), (2,2-dinitroethyl)benzene **4b** (58.0 mg, 0.3 mmol), was added 1.5 mL dioxane after purged with nitrogen. The mixture was stirred at 75 °C for overnight. Compound **3k** was not observed.

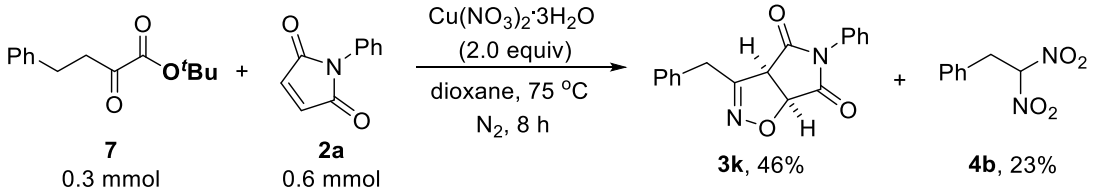


To a 20 mL oven-dried microwave tube containing $Cu(NO_3)_2 \cdot 3H_2O$ (145.0 mg, 0.6 mmol) and 2-oxo-3-phenyl-propanoic acid (49.3 mg, 0.3 mmol) was added 1.5 mL dioxane and purged with nitrogen three times. The mixture was then stirred at 75 °C for 8 h as monitored by TLC. Upon completion, the reaction mixture was cooled down to room temperature, and purified by flash column chromatography on silica gel (eluted with petroleum ether/ethyl acetate = 100 : 1) to afford 2-oxido-3,4-diphenyl-1,2,5-oxadiazol-2-ium **5** (13.8 mg, 19%) as a white solid.[22] M.p. 110-112 ° C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.56-7.51 (m, 5H), 7.49-7.43 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 156.21, 130.97, 130.53, 129.01, 128.94, 128.68, 128.28, 126.66, 122.87, 114.28; MS (ESI): *m/z* 238.9 $[M+H]^+$.

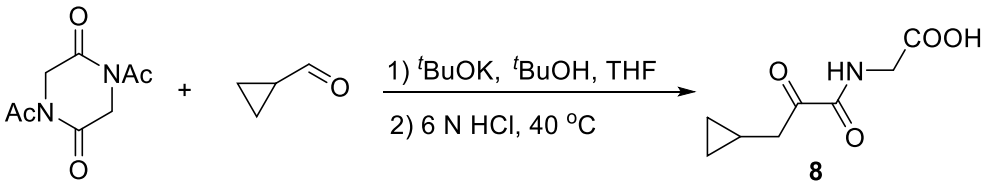
5.2 α-Keto Carboxylic Acid Derivatives Investigation



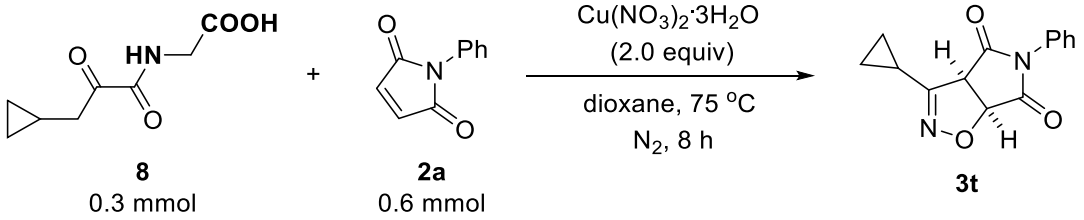
To a 15 mL oven-dried test tube containing $Cu(NO_3)_2 \cdot 3H_2O$ (145.0 mg, 0.6 mmol), 1-phenyl-1*H*-pyrrole-2,5-dione **2a** (103.9 mg, 0.6 mmol), ethyl 2-oxo-4-phenyl-butanoate **6** (61.8 mg, 0.3 mmol), was added 1.5 mL dioxane after purged with nitrogen. The mixture was stirred at 75 °C for 8 h. The reaction mixture was cooled down to room temperature, and purified by flash column chromatography on silica gel to afford **3k** (30.3 mg, 33%) as a white solid and **4b** (24.0 mg, 41%) as yellow liquid.



To a 15 mL oven-dried test tube containing $Cu(NO_3)_2 \cdot 3H_2O$ (145.0 mg, 0.6 mmol), 1-phenyl-1*H*-pyrrole-2,5-dione **2a** (103.9 mg, 0.6 mmol), *tert*-butyl 2-oxo-4-phenyl-butanoate **7** (70.5 mg, 0.3 mmol), was added 1.5 mL dioxane after purged with nitrogen. The mixture was stirred at 75 °C for 8 h. The reaction mixture was cooled down to room temperature, and purified by flash column chromatography on silica gel to afford **3k** (42.1 mg, 46%) as a white solid and **4b** (13.6 mg, 23%) as yellow liquid.

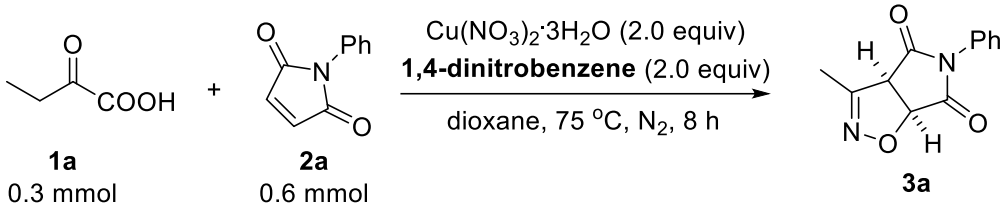


1,4-Diacetyl-piperazine-2,5-dione (990.0 mg, 5 mmol) was dissolved in dry THF (5 mL) under N_2 atmosphere. Cyclopropanecarbaldehyde (354.5 mg, 5 mmol) were added to this solution. Potassium *tert*-butoxide (673.3 mg, 6 mmol) in a *tert*-butanol (5-10 mL) was added dropwise to this solution over 15 min at room temperature. The reaction mixture was stirred for 3 h, then a saturated aqueous solution of NH_4Cl (10 mL) was added to quench the reaction. The aqueous layer was extracted with dichloromethane (3×10 mL) and the combined organic extracts were washed with water and brine (10 mL), dried over anhydrous Na_2SO_4, filtered and dried in vacuum. The residue was recrystallized from hot dichloromethane/hexane to give a solid. Part of the solid (3.0 mmol) was dissolved in 6 M aqueous HCl (10 mL) and heated to 40 °C for 4 h. The reaction was then cooled to room temperature and extracted with ethyl acetate (3×10 mL). The combined organic phase was washed with water and brine (10 mL), The organic phase was dried over anhydrous sodium sulfate, and concentrated in vacuo. The residue was recrystallized from hot ethyl acetate/hexane to afford **8** (293 mg, 53%) as a white solid. IR (KBr, cm^{-1}): 3292, 1731, 1666, 1530, 1426, 1337, 1251, 1134, 950, 690; M.p. 87-89 °C; ^1H NMR (500 MHz, $CDCl_3$): δ 8.19 (s, br, 1H), 7.52 (s, br, 1H), 4.17 (d, J = 5.8 Hz, 2H), 2.84 (d, J = 6.9 Hz, 2H), 1.09-1.01 (m, 1H), 0.61-0.57 (m, 2H), 0.2-0.17 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 197.58, 173.31, 160.46, 41.77, 40.79, 5.37, 4.30. MS (ESI): *m/z* 208.1 $[M+Na]^+$; HRMS (ESI) *m/z* calcd for $C_8H_{11}O_4NNa$ 208.0580 $[M+Na]^+$, found 208.0578.



To a 15 mL oven-dried test tube containing $Cu(NO_3)_2·3H_2O$ (145.0 mg, 0.6 mmol), 1-phenyl-1*H*-pyrrole-2,5-dione **2a** (103.9 mg, 0.6 mmol), 2-(3-cyclopropyl-2-oxopropanamido)acetic acid **8** (47.1 mg, 0.3 mmol), was added 1.5 mL dioxane after purged with nitrogen. The mixture was stirred at 75 °C for 8 h. The reaction mixture was cooled down to room temperature, and purified by flash column chromatography on silica gel to afford **3t** (25.0 mg, 33%) as a white solid. M.p. 150-152 °C; IR (KBr, cm^{-1}): 2963, 1720, 1498, 1385, 1190, 876, 742, 689, 615; ^1H NMR (500 MHz, $CDCl_3$): δ 7.53-7.50 (m, 2H), 7.47-7.44 (m, 1H), 7.31-7.28 (m, 2H), 5.48 (d, J = 9.5 Hz, 1H), 4.50 (d, J = 9.5 Hz, 1H), 1.86-1.81 (m, 1H), 1.12-1.02 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 171.58, 170.17, 157.00, 130.86, 129.38, 129.23, 126.16, 79.19, 57.36, 8.50, 7.80, 7.45; MS (ESI): *m/z* 257.1 $[M+H]^+$; HRMS (ESI) *m/z* calcd for $C_{14}H_{13}O_3N_2$ $[M+H]^+$ 257.0921, found 257.0919.

5.3 Radical Inhititors



To a 15 mL oven-dried test tube containing $Cu(NO_3)_2 \cdot 3H_2O$ (145.0 mg, 0.6 mmol), 1-phenyl-1*H*-pyrrole-2,5-dione **2a** (103.9 mg, 0.6 mmol), 2-oxobutanoic acid **1a** (32.4 mg, 0.3 mmol), and 1,4-dinitrobenzene (100.8 mg, 0.6 mmol) in dioxane (1.5 mL) for 8 h. the reaction mixture was cooled down to room temperature and purified by flash column chromatography on silica gel to afford **3a** (53.8 mg, 73%) as a pale-yellow solid.

6. References

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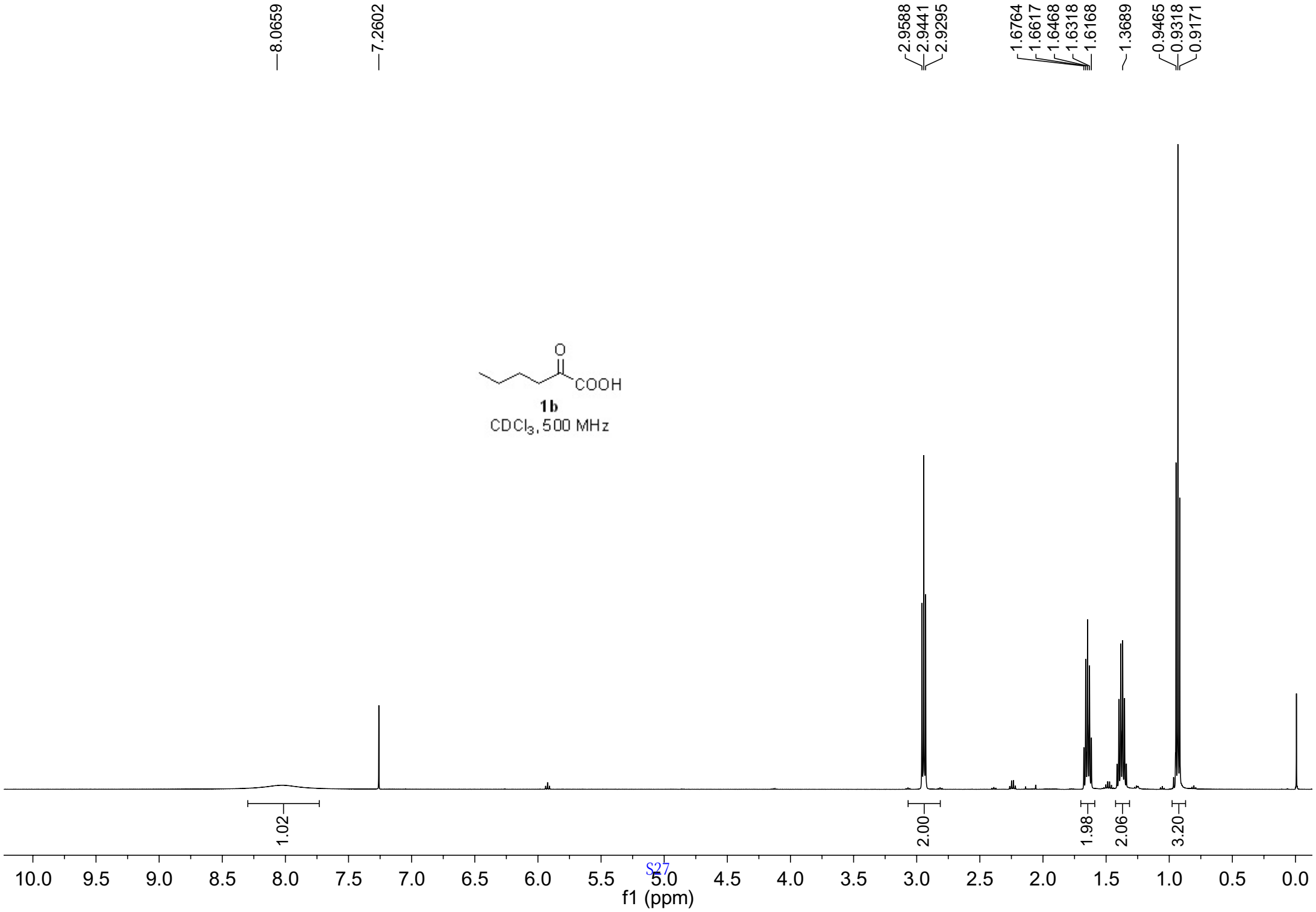
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1.6318
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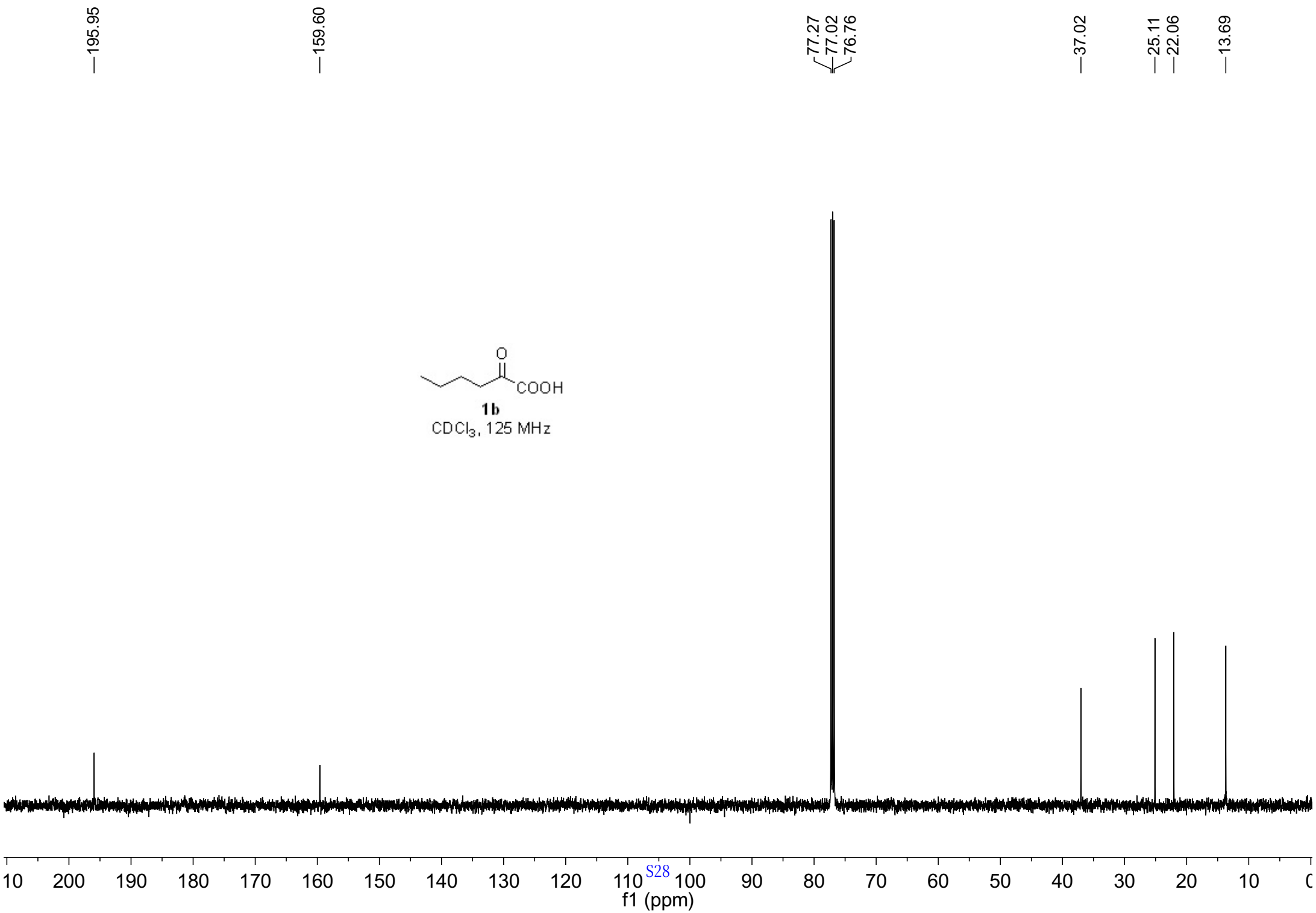
1.3689
0.9465
0.9318
0.9171
O
COOH
1b
CDCl3, 500 MHz
1.02
2.00
1.98
2.06
3.20
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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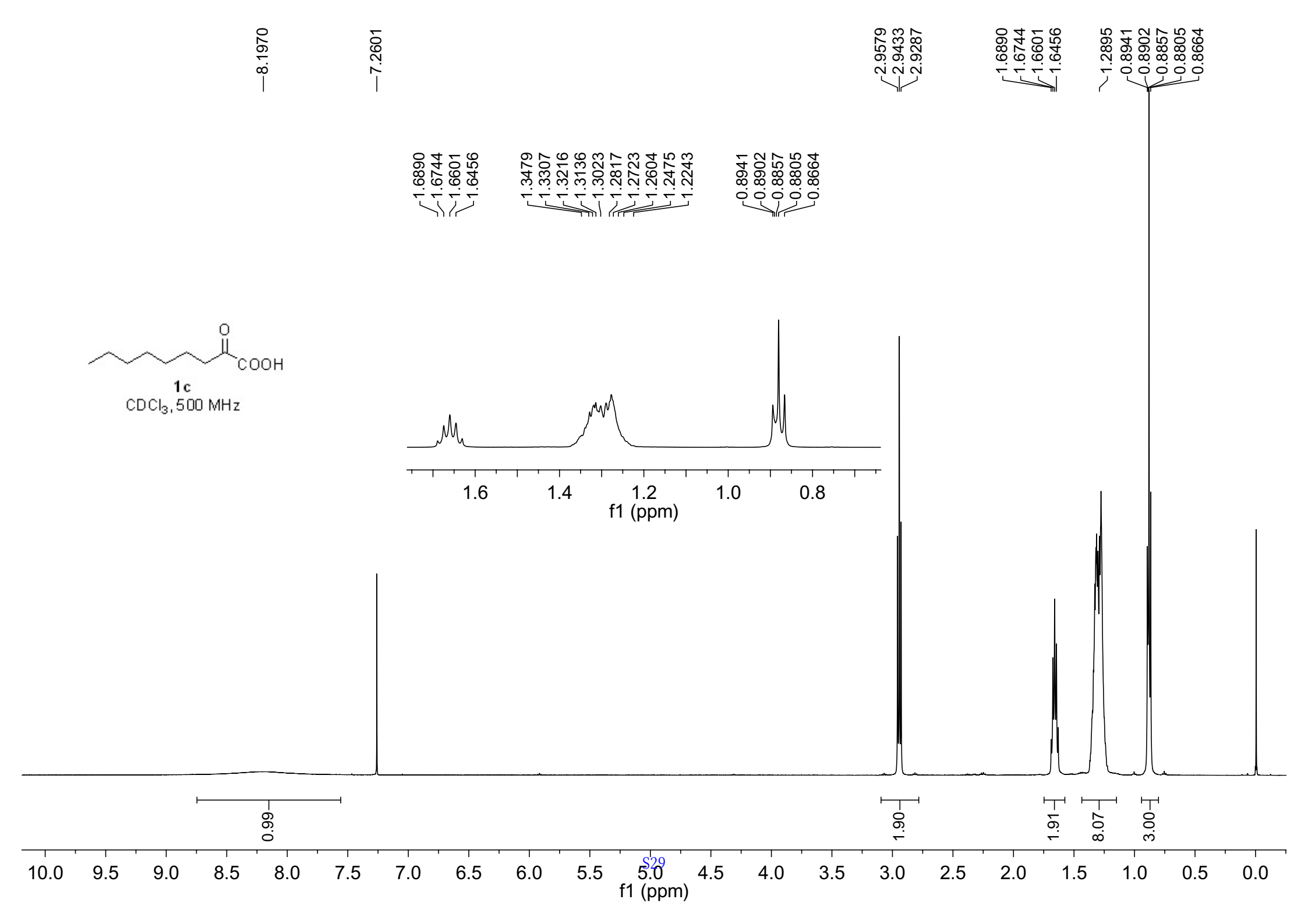
77.27
77.02
76.76
37.02
25.11
22.06
13.69
O
COOH
1b
CDCl3, 125 MHz
10
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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0.8857
0.8805
0.8664
1.3479
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1.3216
1.3136
1.3023
1.2817
1.2723
1.2604
1.2475
1.2243
O
COOH
1c
CDCl3, 500 MHz
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1.4
1.2
1.0
0.8
f1 (ppm)
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1.90
1.91
8.07
3.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
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3.5
3.0
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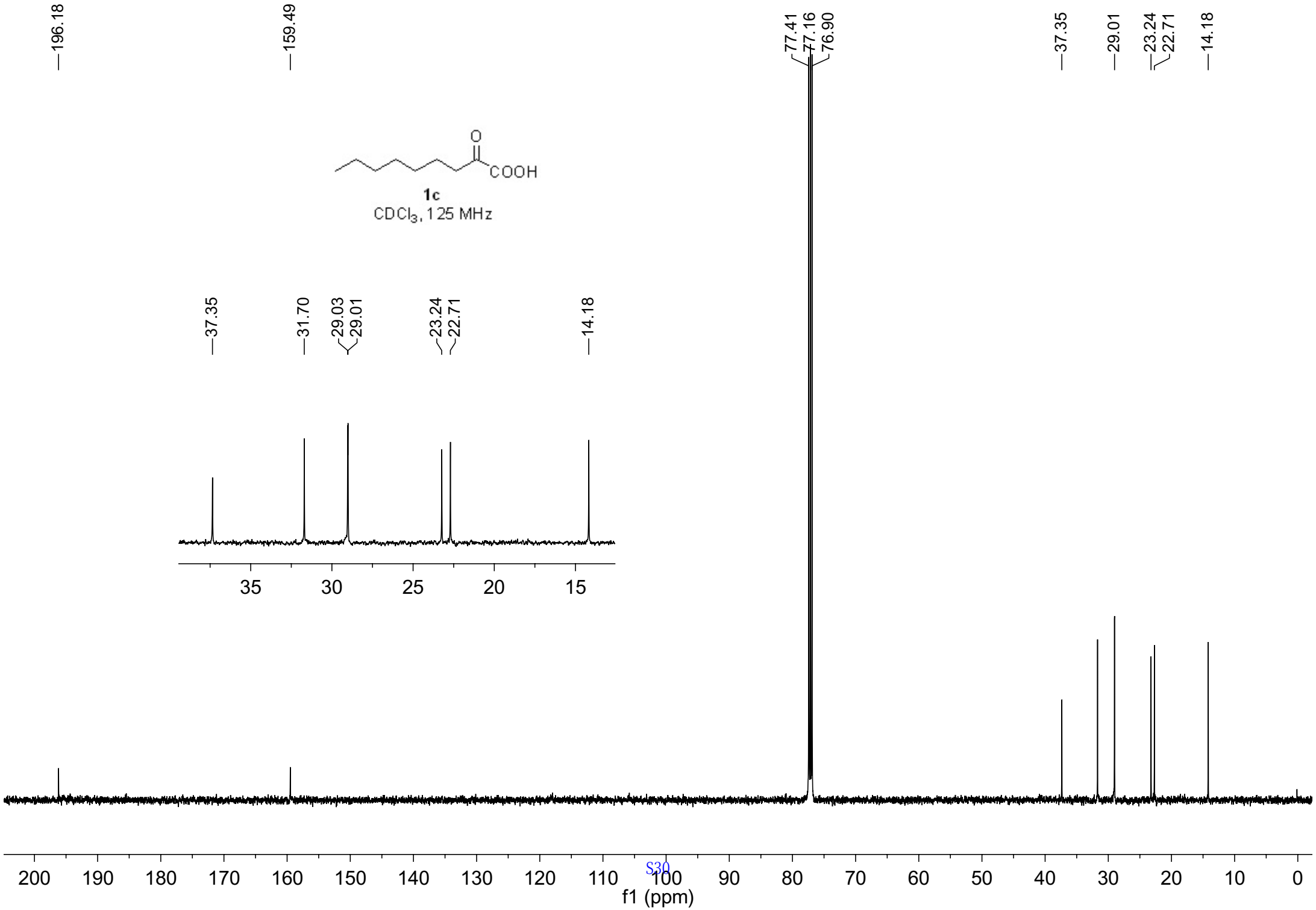
f1 (ppm)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1c
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37.35
31.70
29.03
29.01
23.24
22.71
14.18
35
30
25
20
15
200
190
180
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50
40
30
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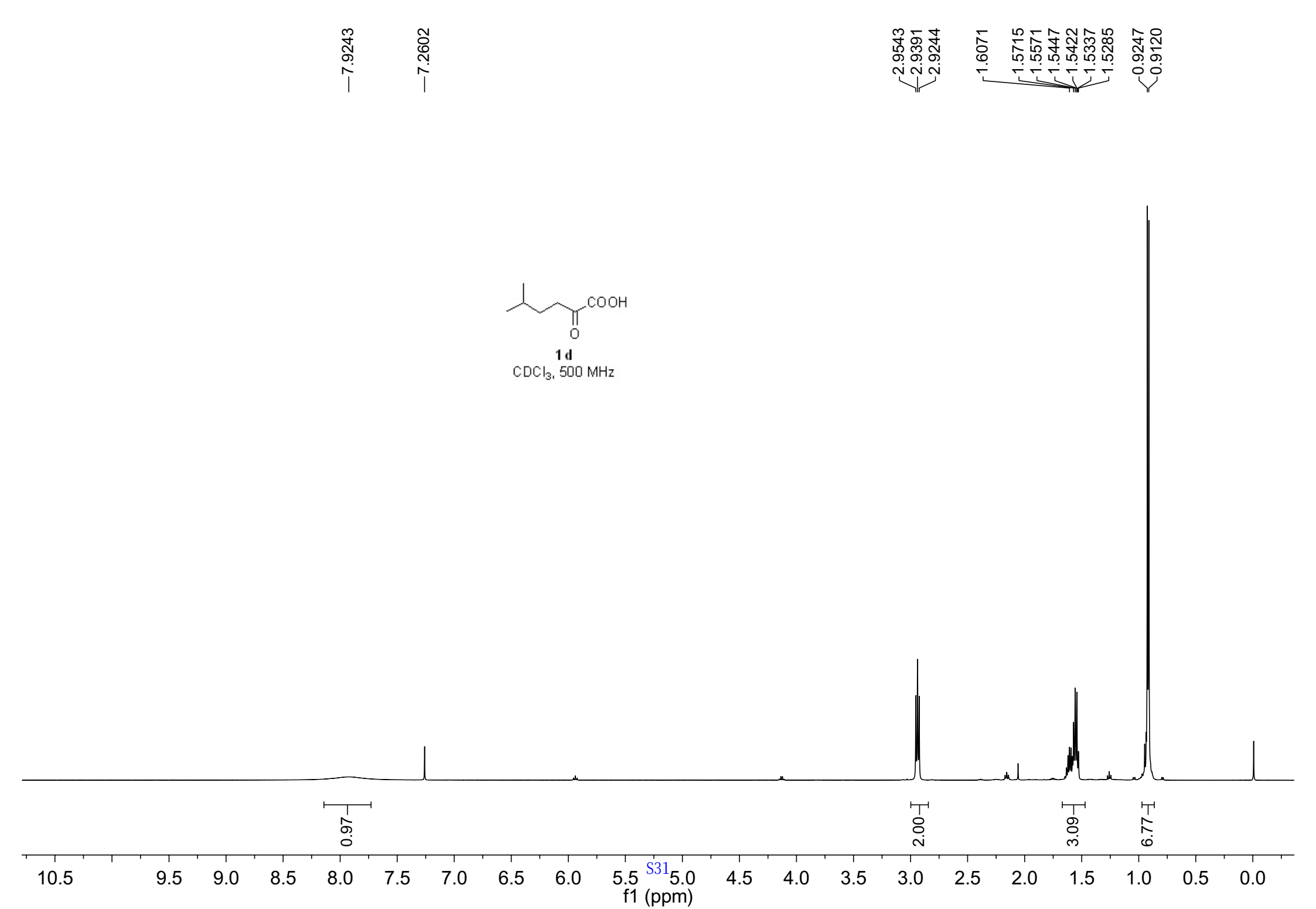
10
0
f1 (ppm)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O
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CDCl3, 500 MHz
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10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
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2.0
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1.0
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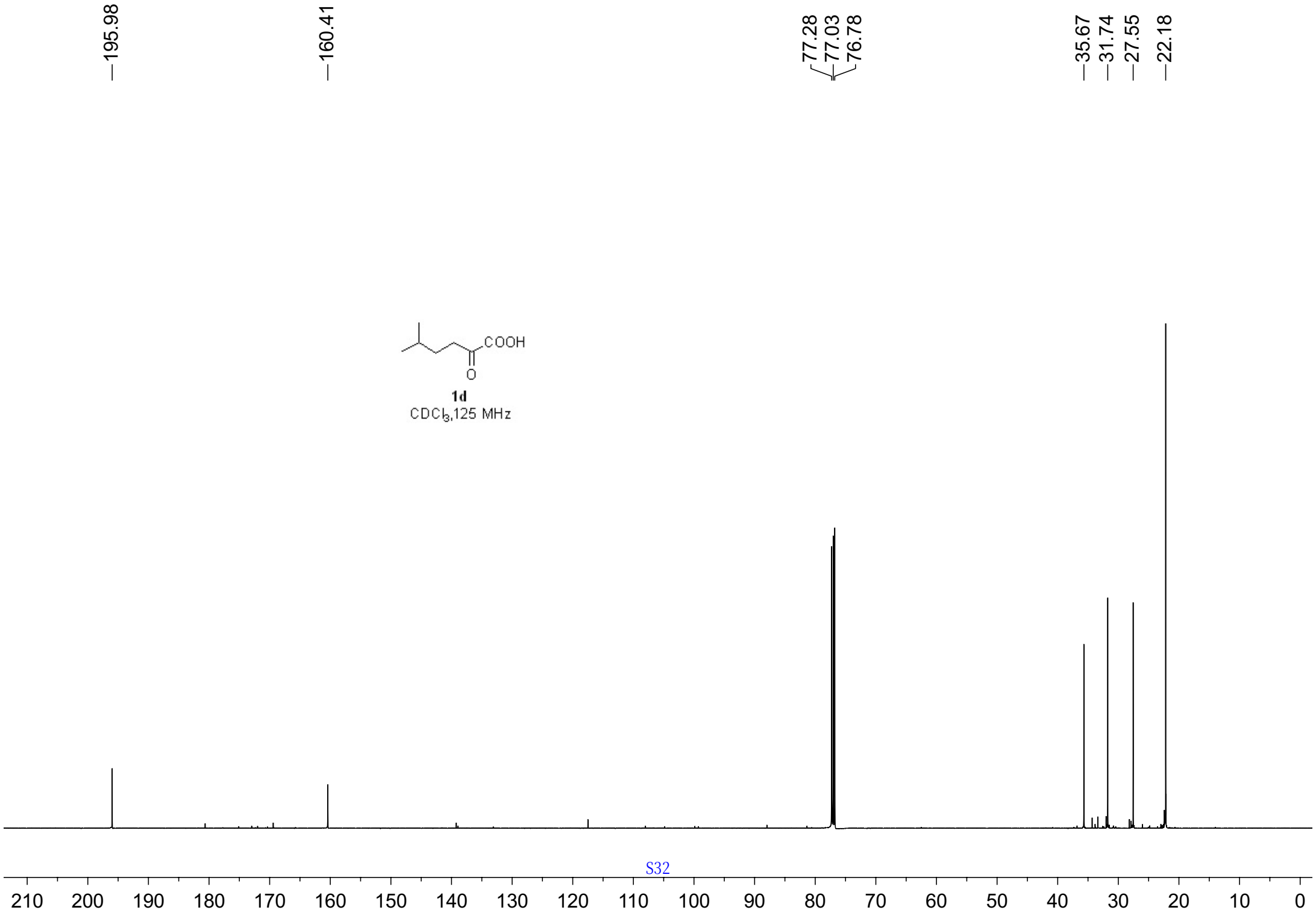
0.0
f1 (ppm)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10
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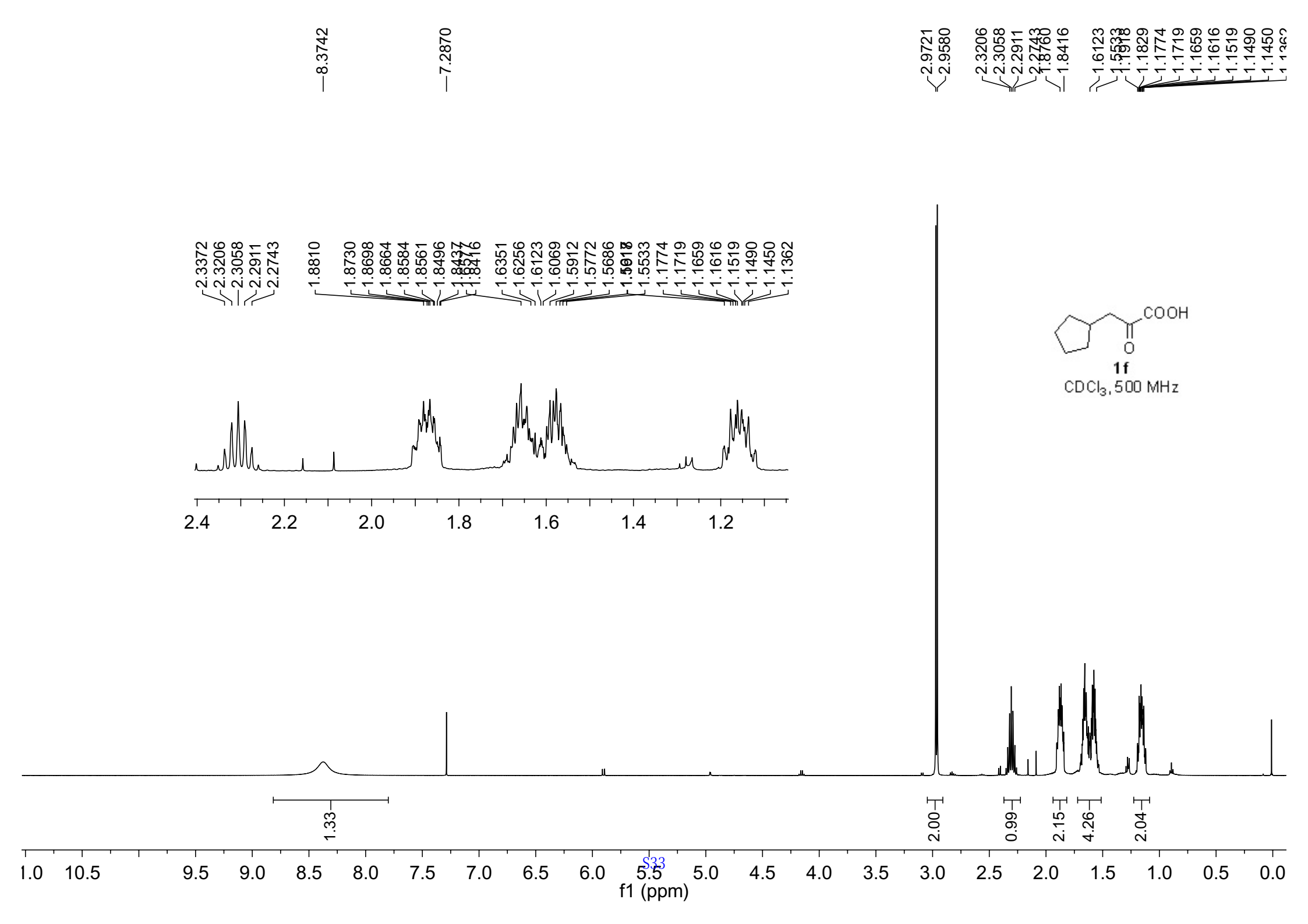
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2.2911
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O
1f
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1.4
1.2
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0.99
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9.5
9.0
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8.0
7.5
7.0
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6.0
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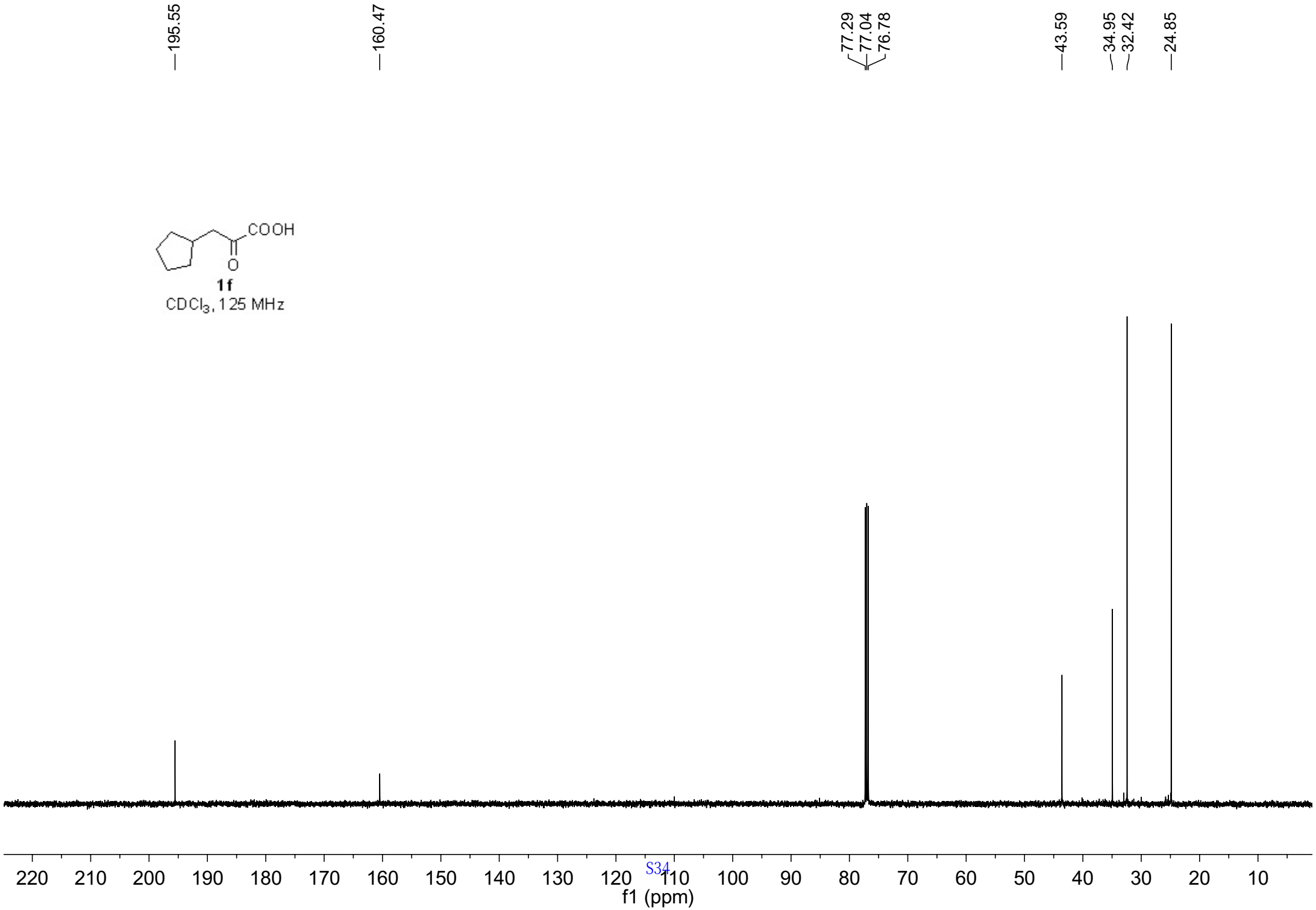
f1 (ppm)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COOH
O
1f
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220
210
200
190
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140
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100
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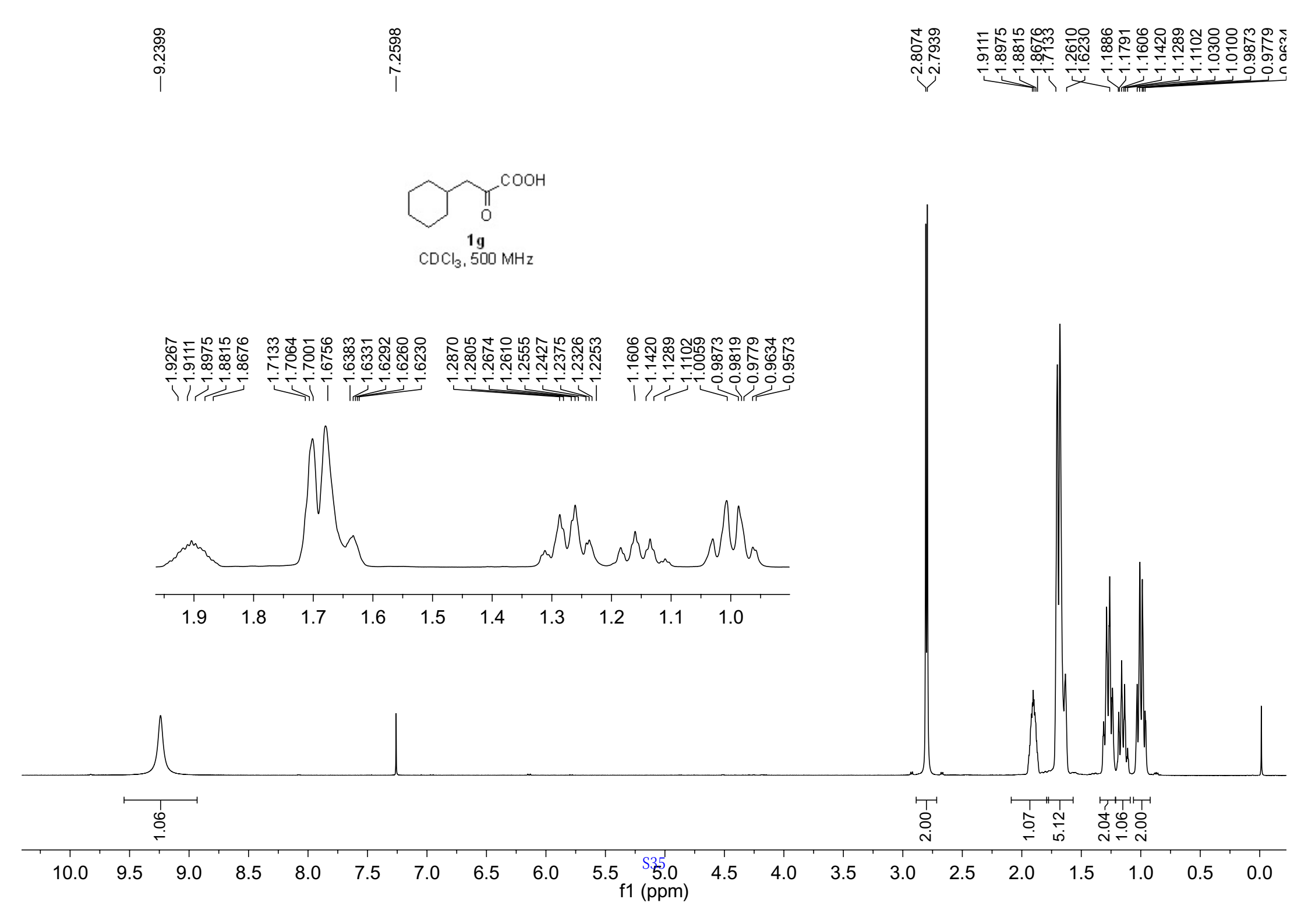
f1 (ppm)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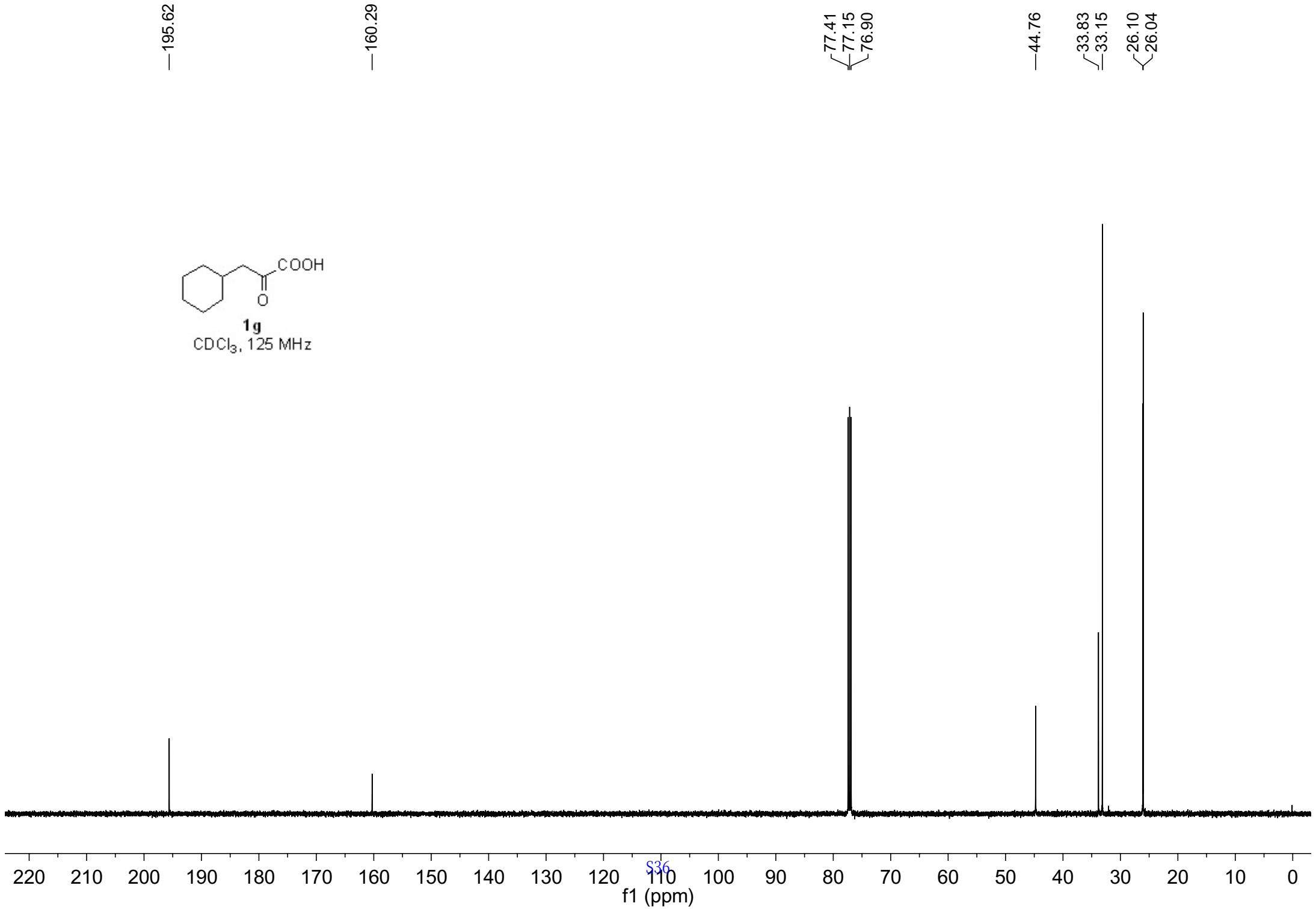
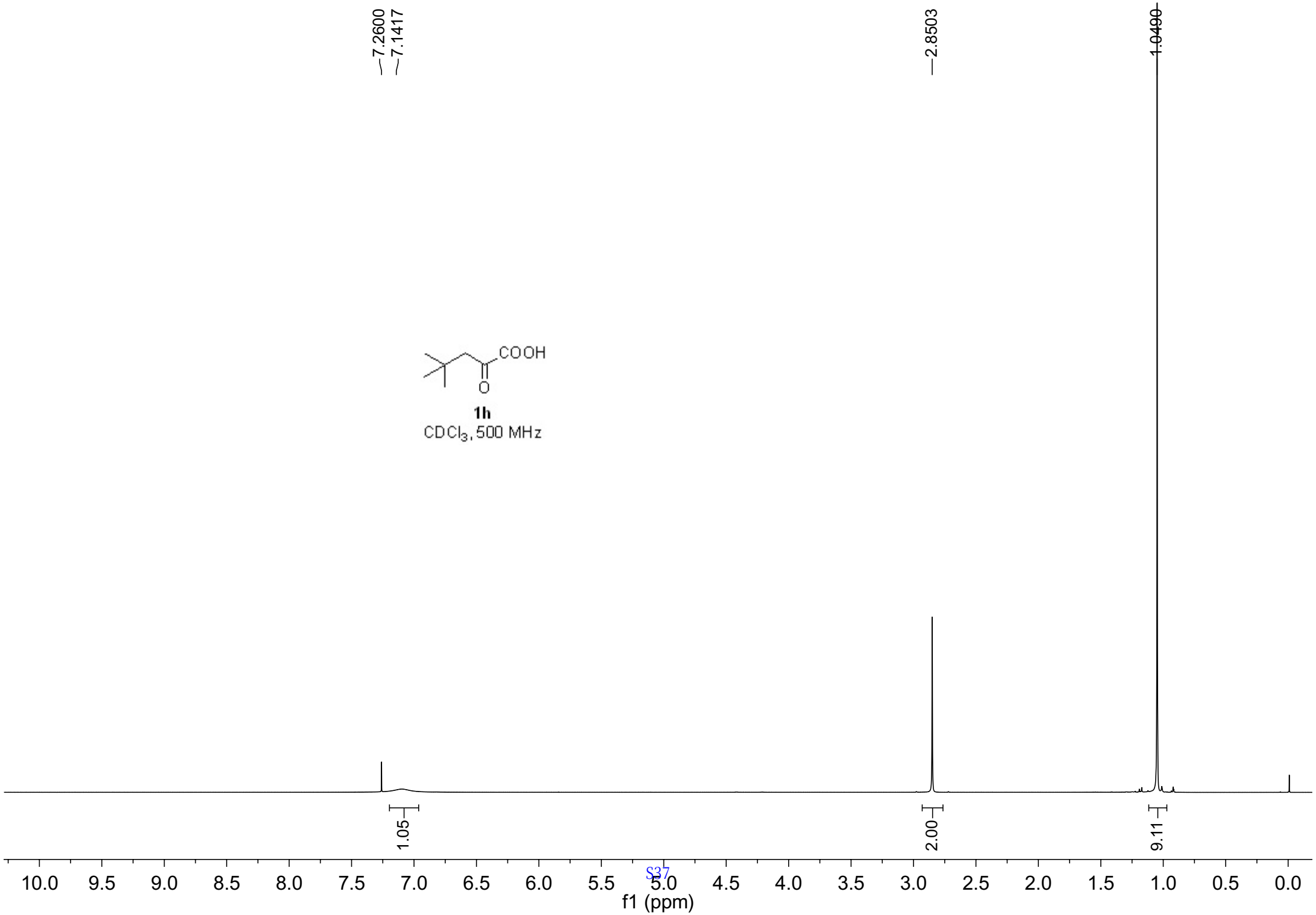
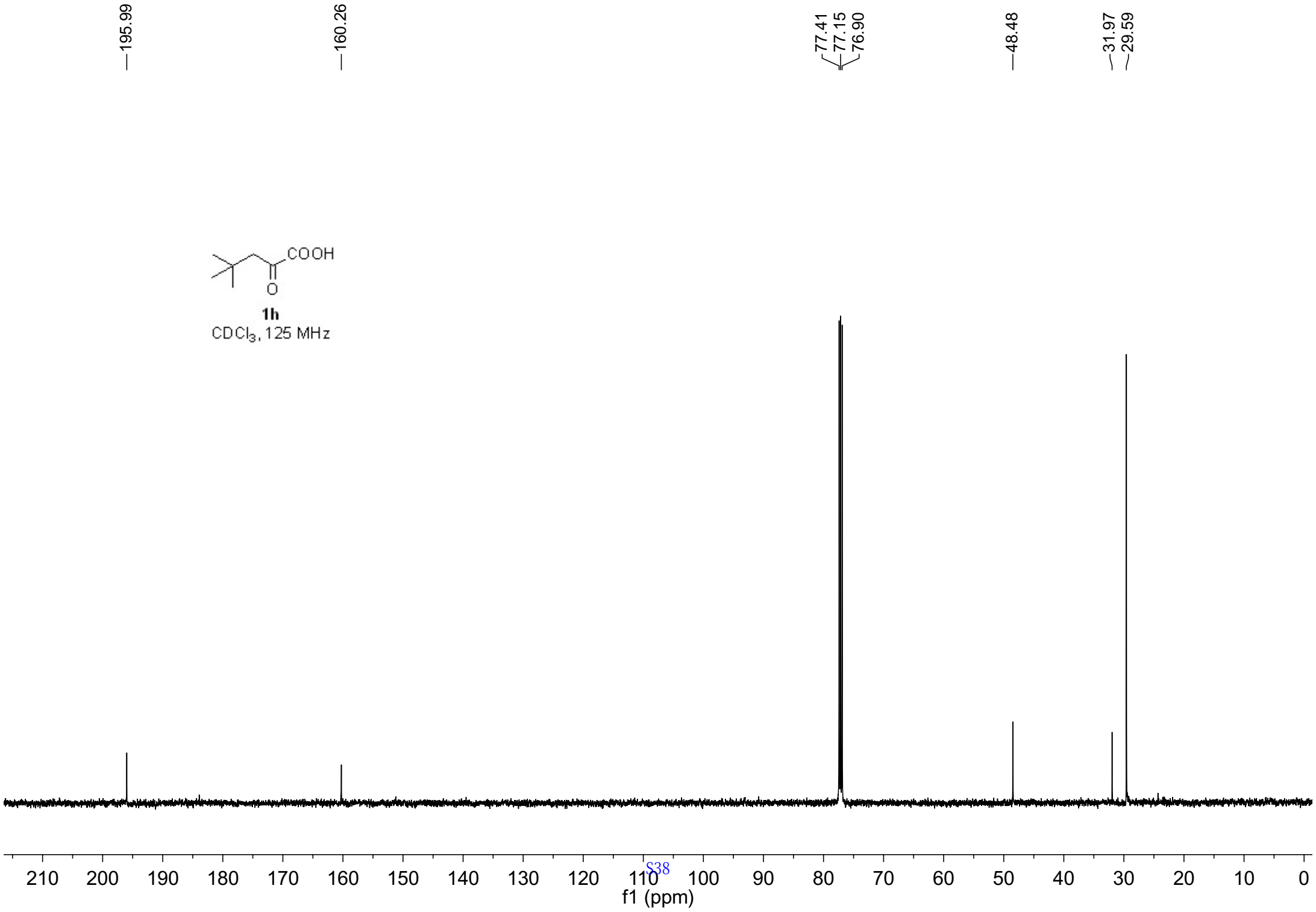
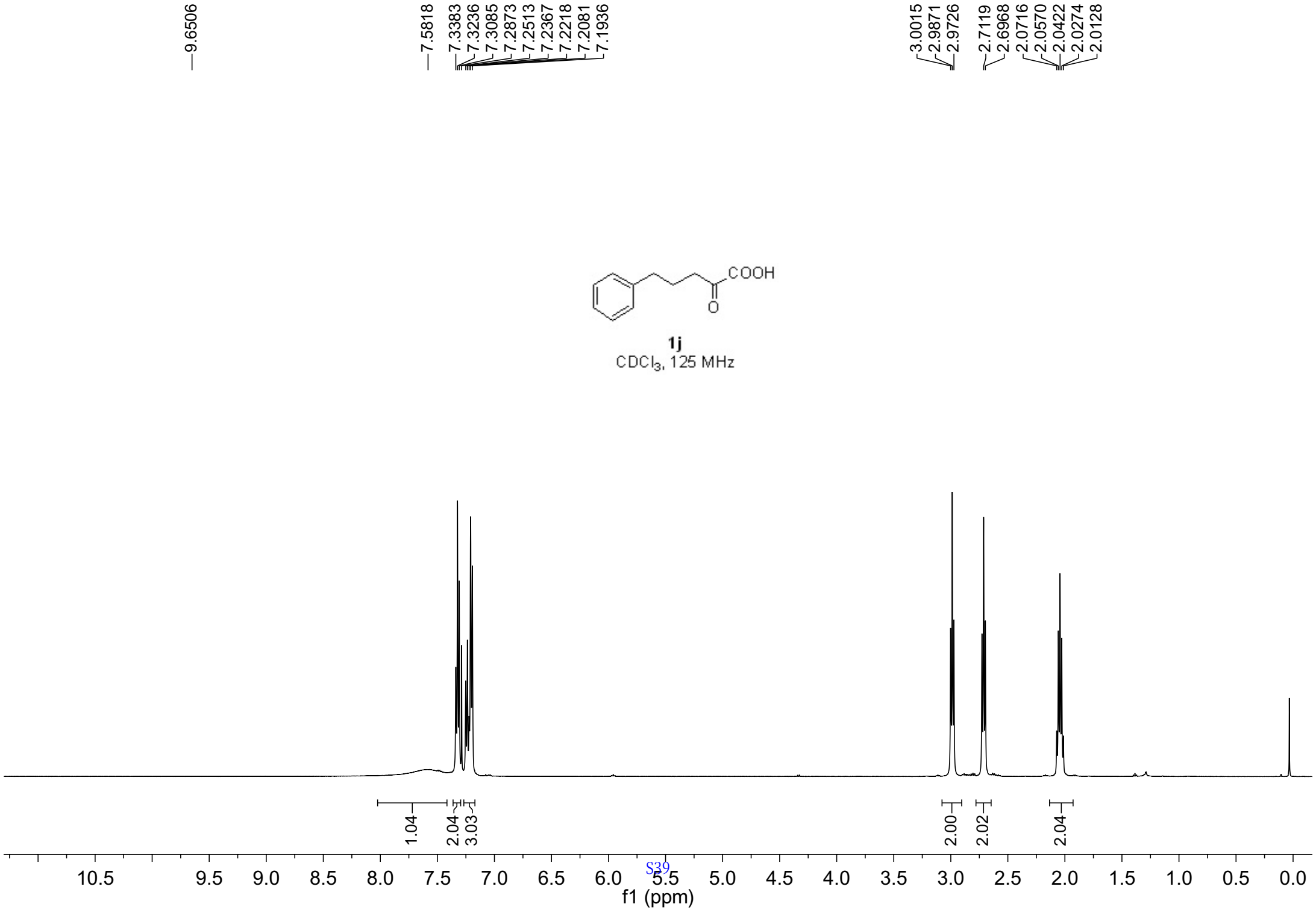
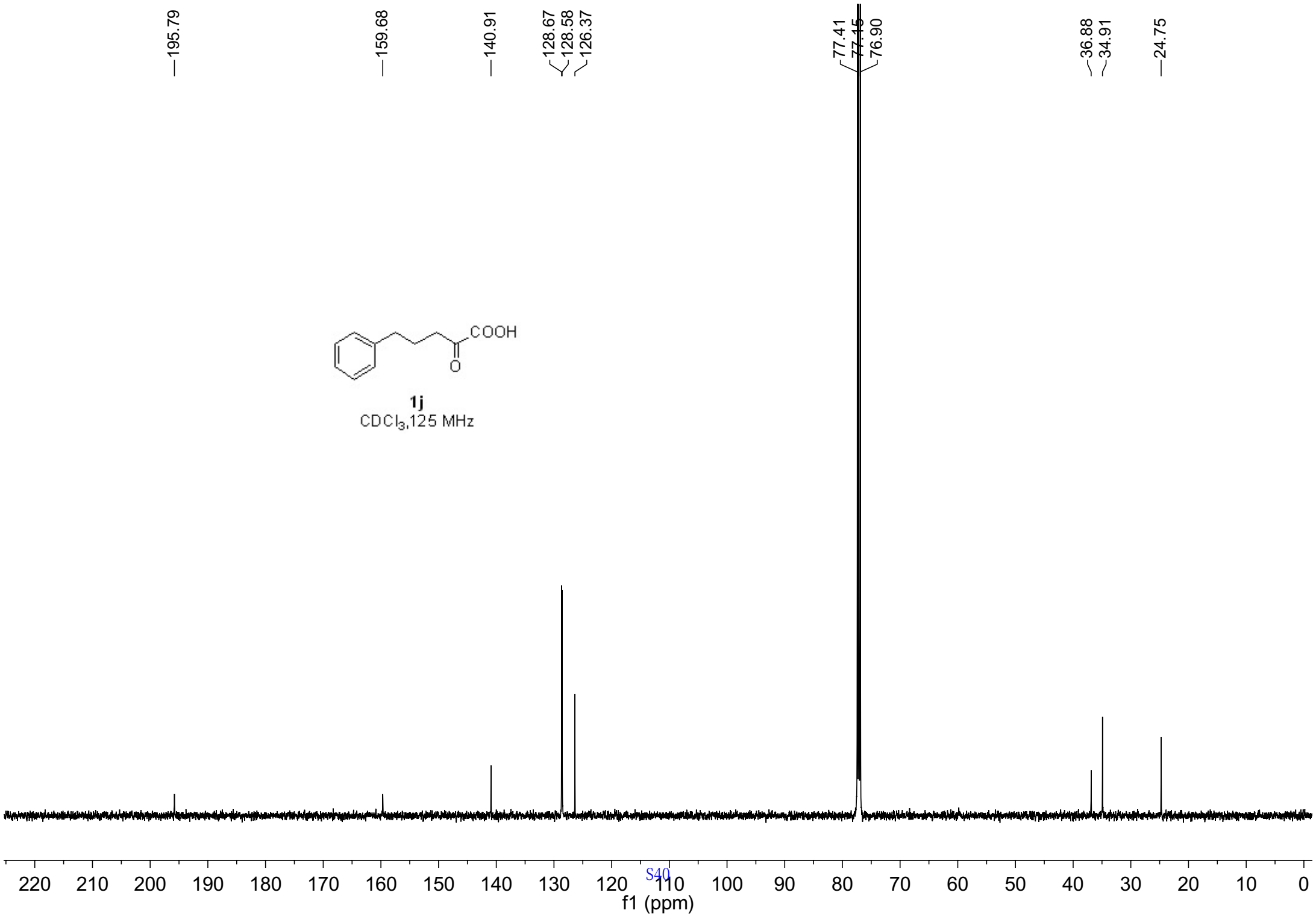
1.1102
1.0300
1.0100
0.9873
0.9779
COOH
O
1g
CDCl3, 500 MHz
1.9267
1.9111
1.8975
1.8815
1.8676
1.7133
1.7064
1.7001
1.6756
1.6383
1.6331
1.6292
1.6260
1.6230
1.2870
1.2805
1.2674
1.2610
1.2555
1.2427
1.2375
1.2326
1.2253
1.1606
1.1420
1.1289
1.1102
1.0059
0.9873
0.9819
0.9779
0.9634
0.9573
1.9 1.8 1.7 1.6 1.5 1.4 1.3 1.2 1.1 1.0
1.06
2.00
1.07
5.12
2.04
1.06
2.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

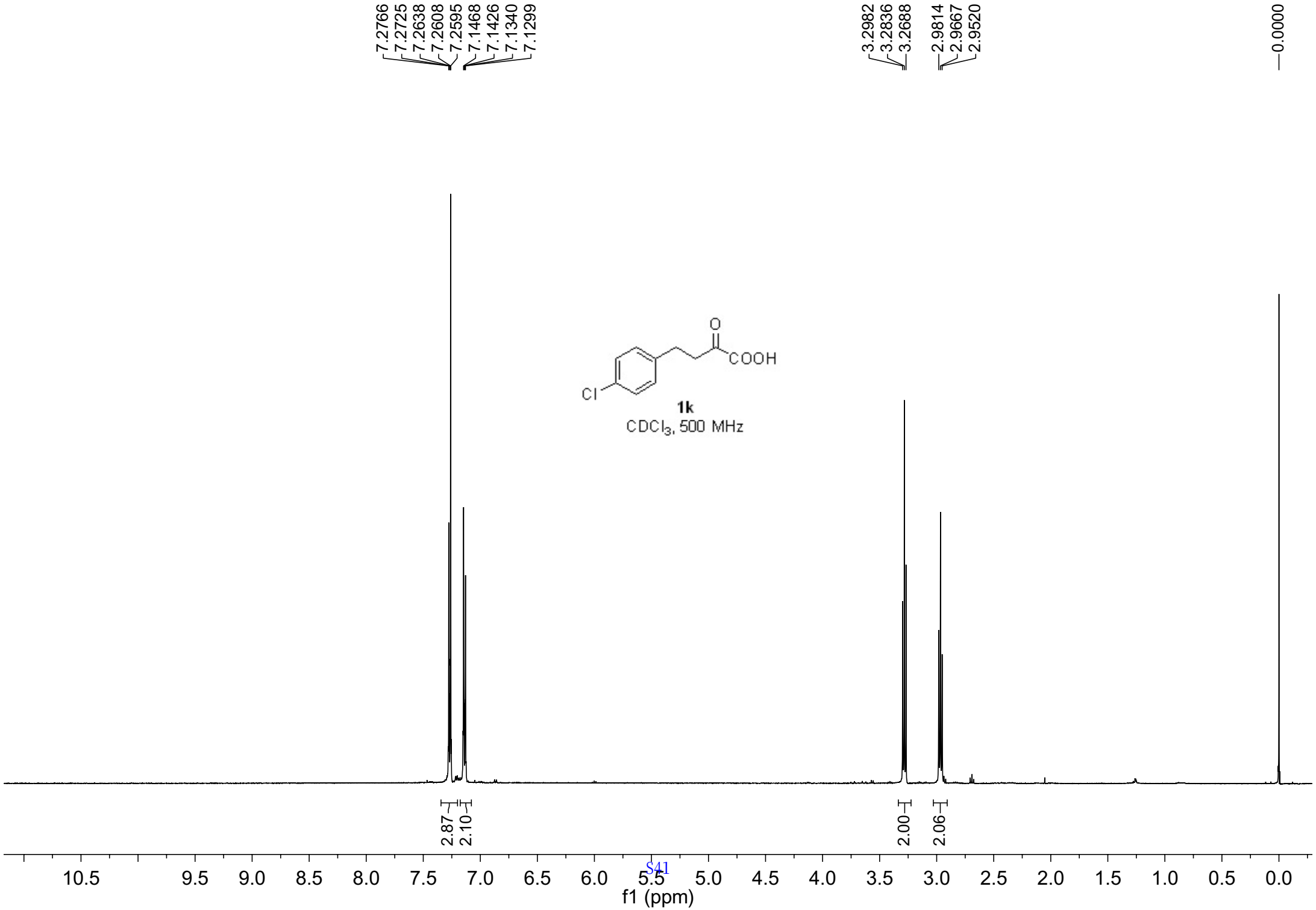

195.62
160.29
77.41
77.15
76.90
44.76
33.83
33.15
26.10
26.04
COOH
O
1g
CDCl3, 125 MHz
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

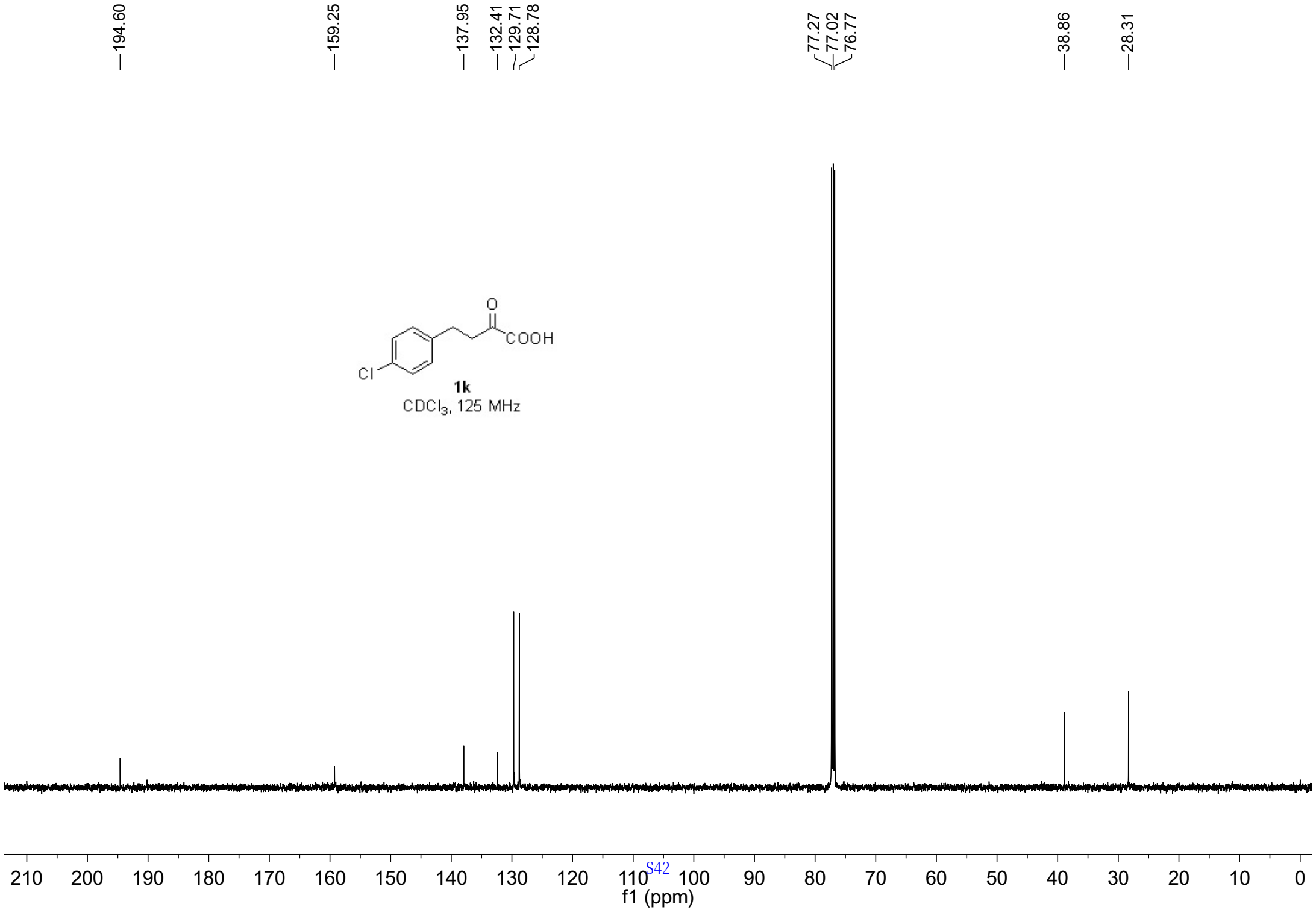

7.2600
7.1417
2.8503
1.0490
COOH
O
1h
CDCl3, 500 MHz
1.05
2.00
9.11
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

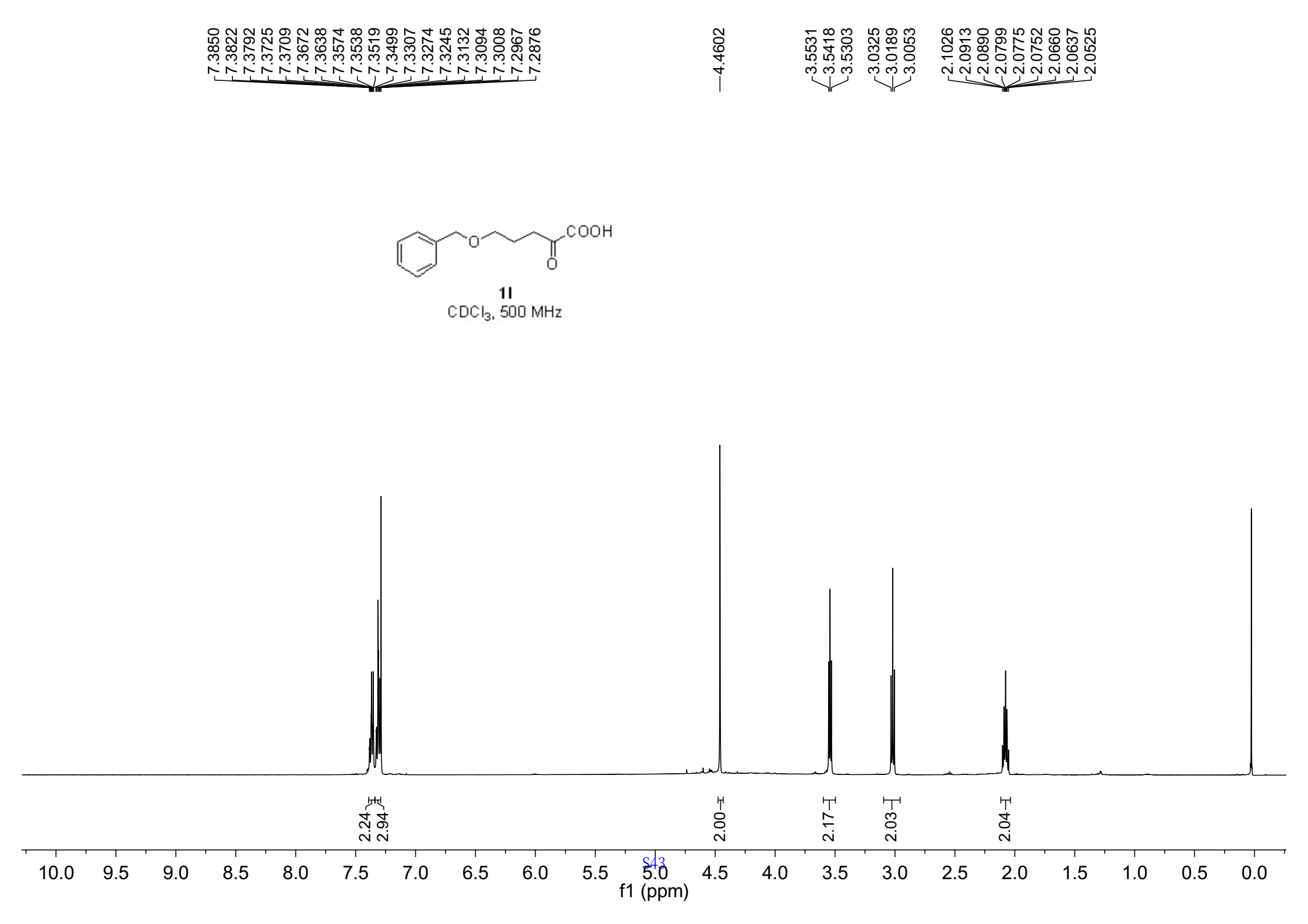

195.99
160.26
77.41
77.15
76.90
48.48
31.97
29.59
COOH
O
1h
CDCl3, 125 MHz
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

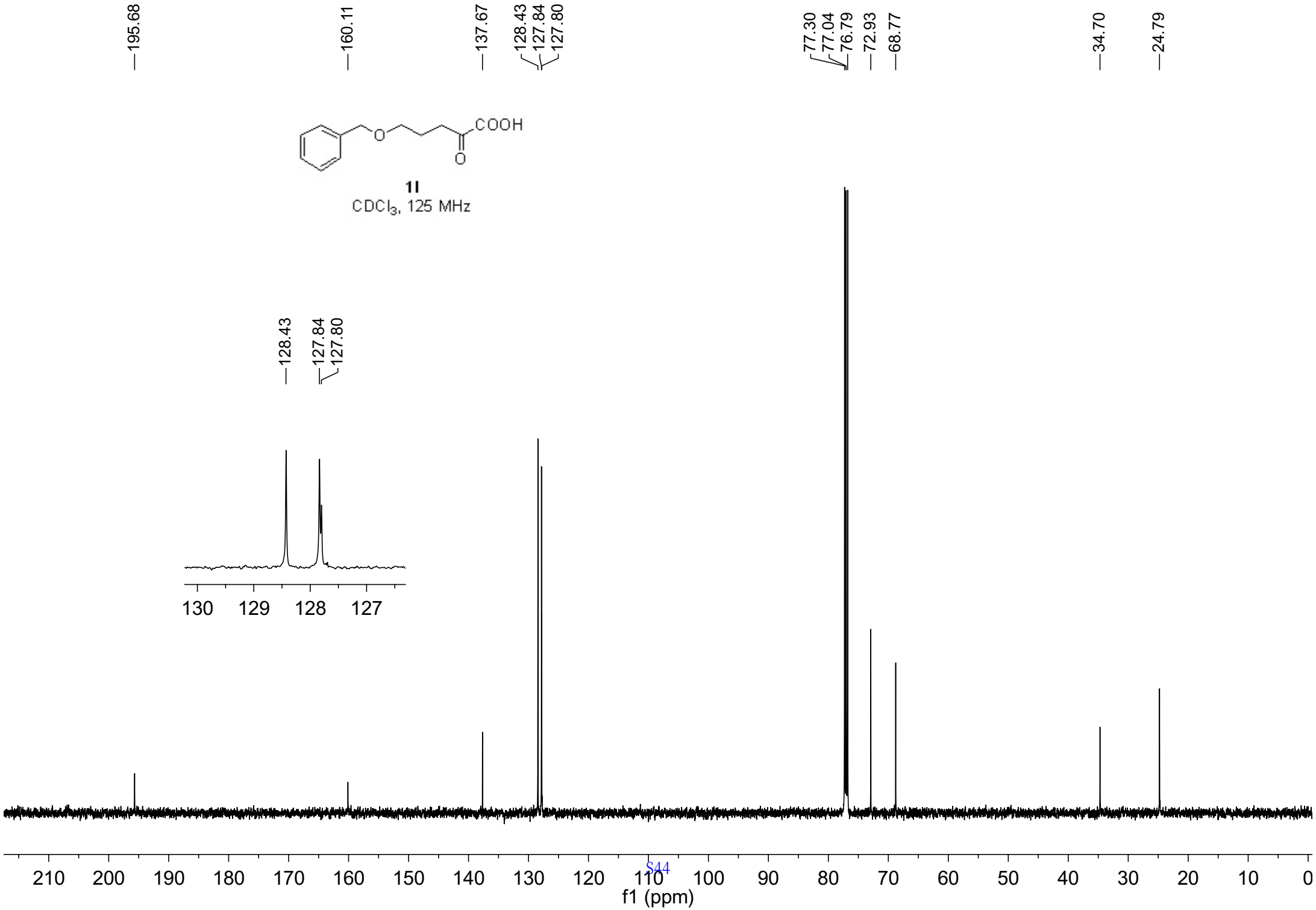

9.6506
7.5818
7.3383
7.3236
7.3085
7.2873
7.2513
7.2367
7.2218
7.2081
7.1936
3.0015
2.9871
2.9726
2.7119
2.6968
2.0716
2.0570
2.0422
2.0274
2.0128
COOH
O
1j
CDCl3, 125 MHz
1.04
2.04
3.03
2.00
2.02
2.04
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

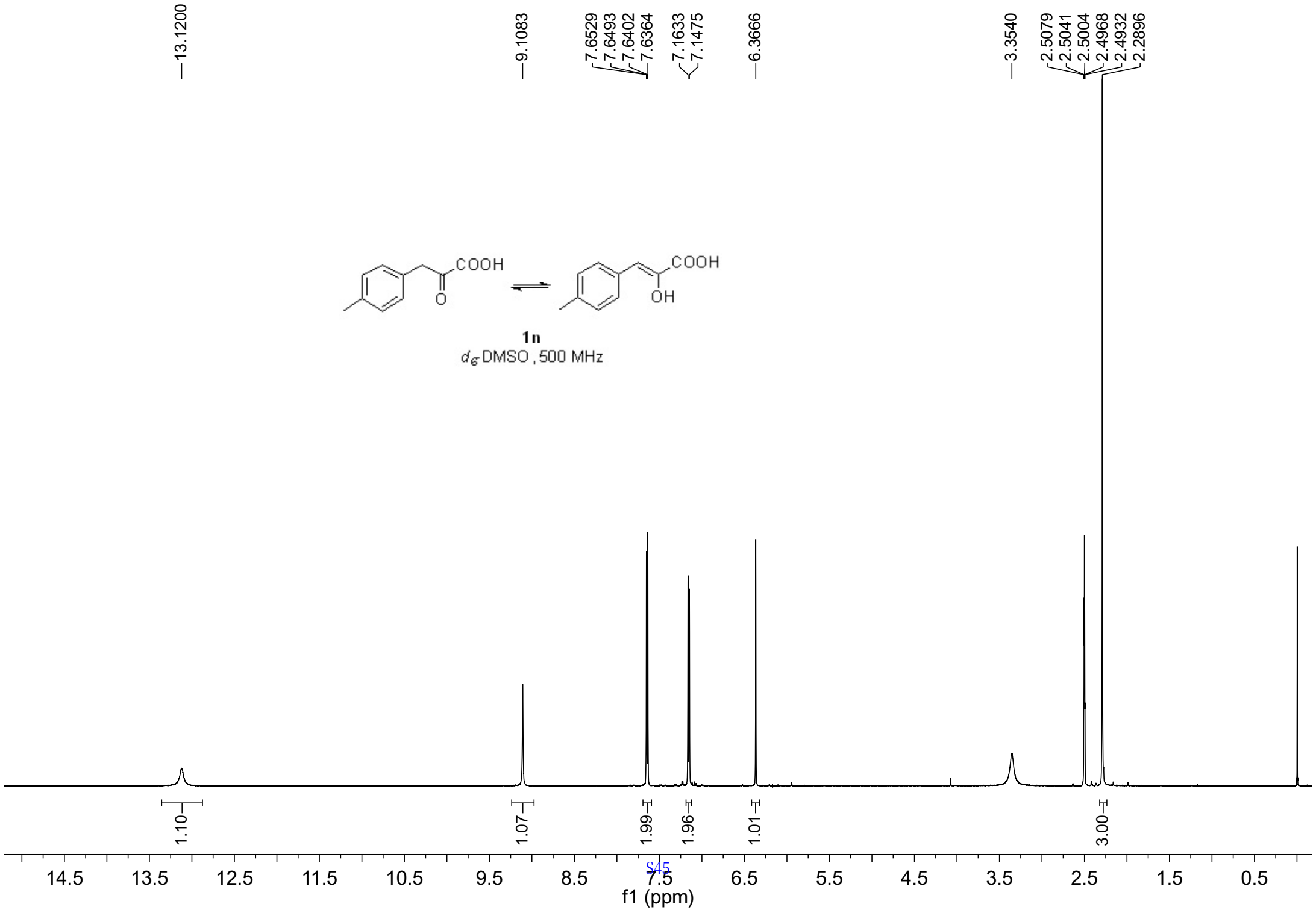

195.79
159.68
140.91
128.67
128.58
126.37
77.41
77.15
76.90
36.88
34.91
24.75
COOH
O
1j
CDCl3,125 MHz
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

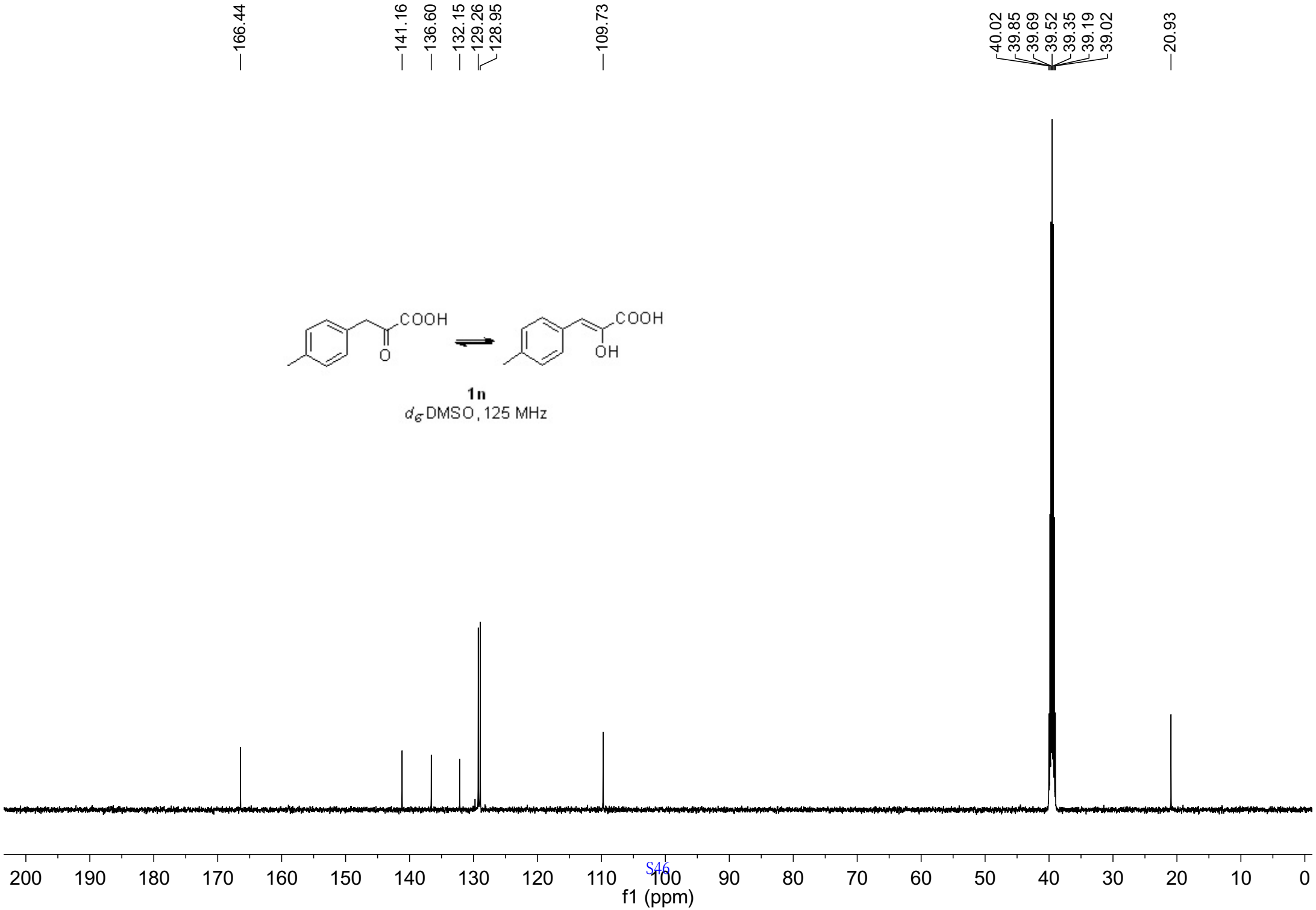

7.2766
7.2725
7.2638
7.2608
7.2595
7.1468
7.1426
7.1340
7.1299
3.2982
3.2836
3.2688
2.9814
2.9667
2.9520
0.0000
O
COOH
Cl
1k
CDCl3, 500 MHz
2.87
2.10
2.00
2.06
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

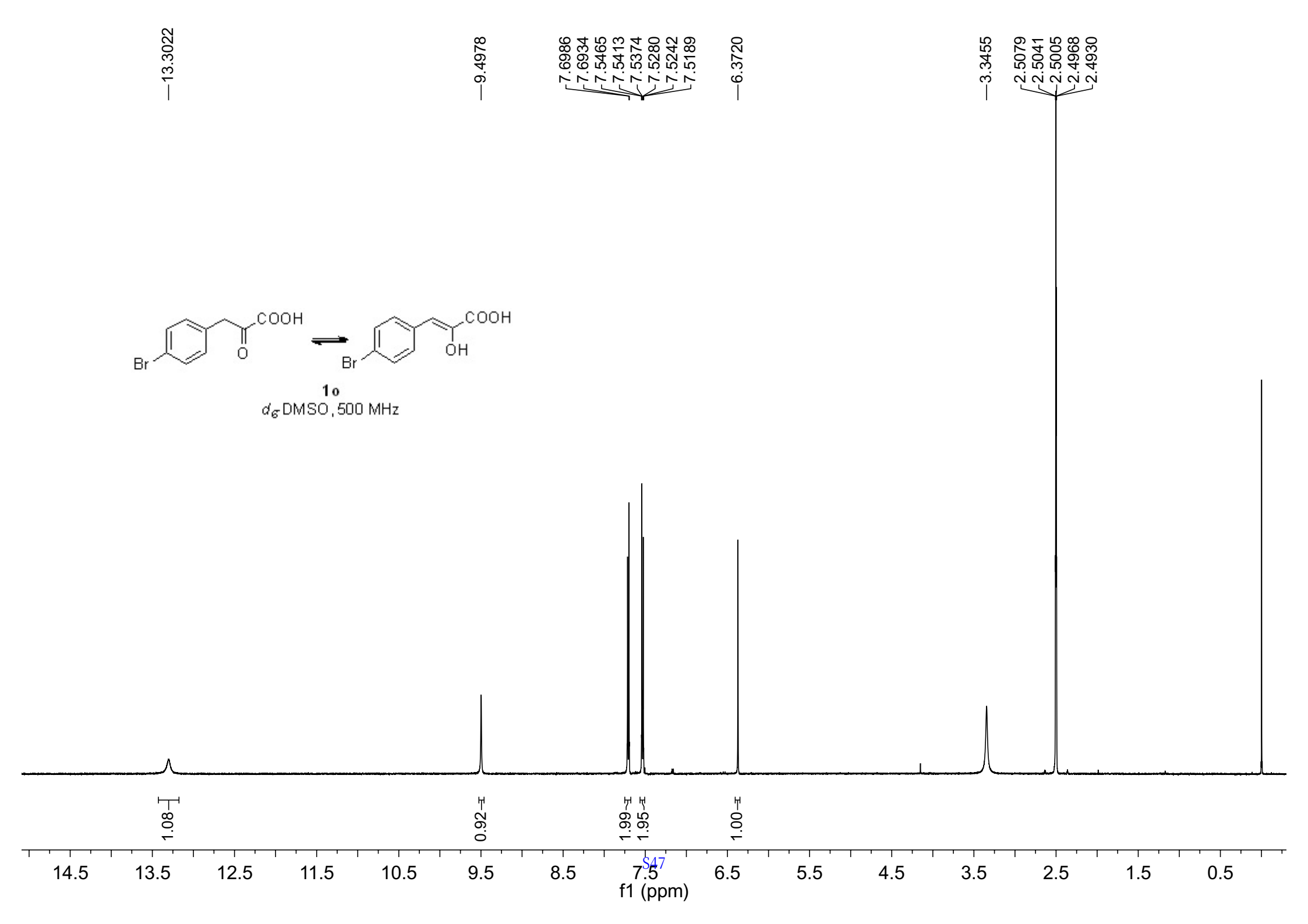

194.60
159.25
137.95
132.41
129.71
128.78
77.27
77.02
76.77
38.86
28.31
O
COOH
Cl
1k
CDCl3, 125 MHz
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

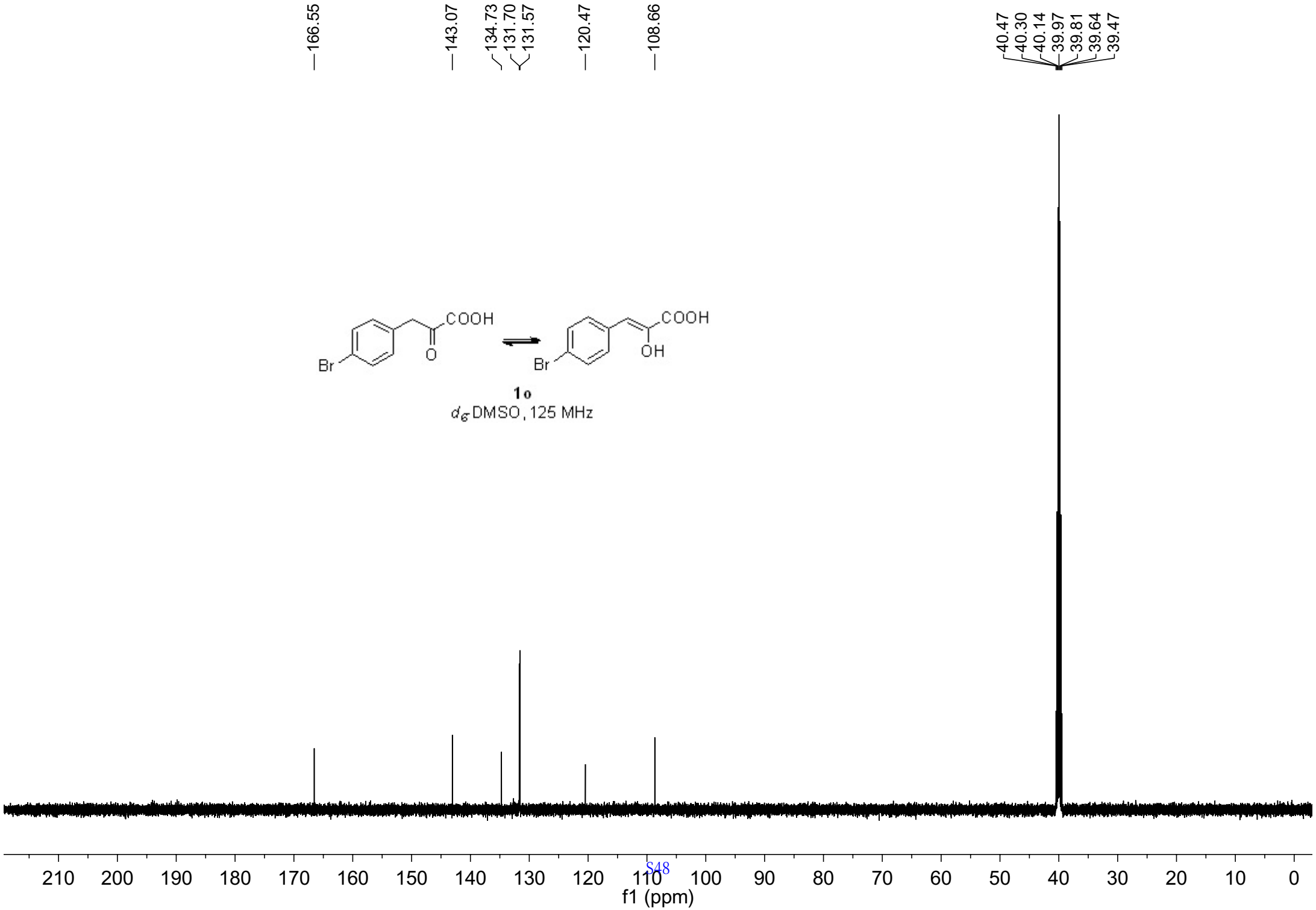

7.3850
7.3822
7.3792
7.3725
7.3709
7.3672
7.3638
7.3574
7.3538
7.3519
7.3499
7.3307
7.3274
7.3245
7.3132
7.3094
7.3008
7.2967
7.2876
4.4602
3.5531
3.5418
3.5303
3.0325
3.0189
3.0053
2.1026
2.0913
2.0890
2.0799
2.0775
2.0752
2.0660
2.0637
2.0525
COOH
O
O
1l
CDCl3, 500 MHz
2.24
2.94
2.00
2.17
2.03
2.04
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

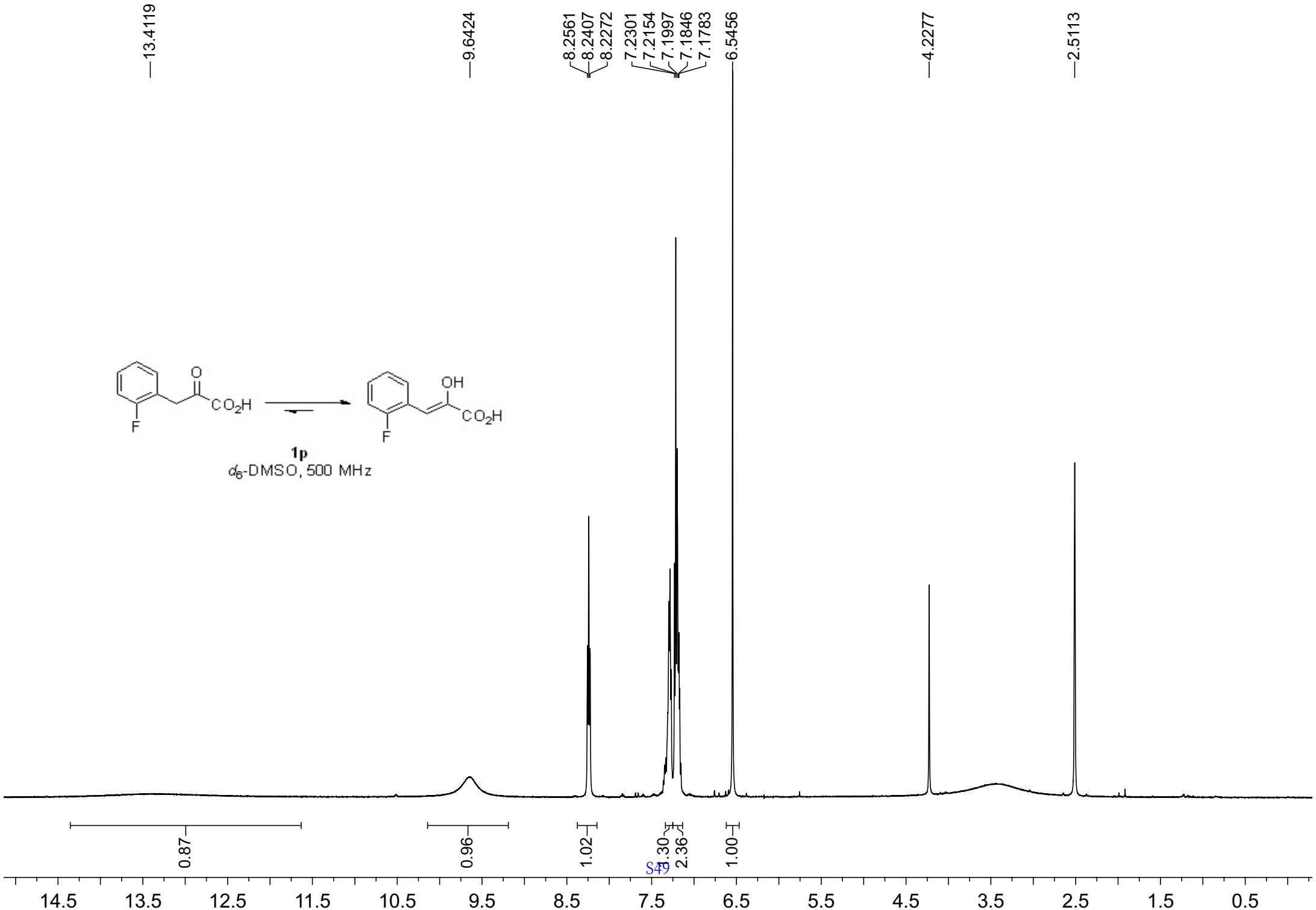

195.68
160.11
137.67
128.43
127.84
127.80
77.30
77.04
76.79
72.93
68.77
34.70
24.79
COOH
O
O
1l
CDCl3, 125 MHz
128.43
127.84
127.80
130
129
128
127
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

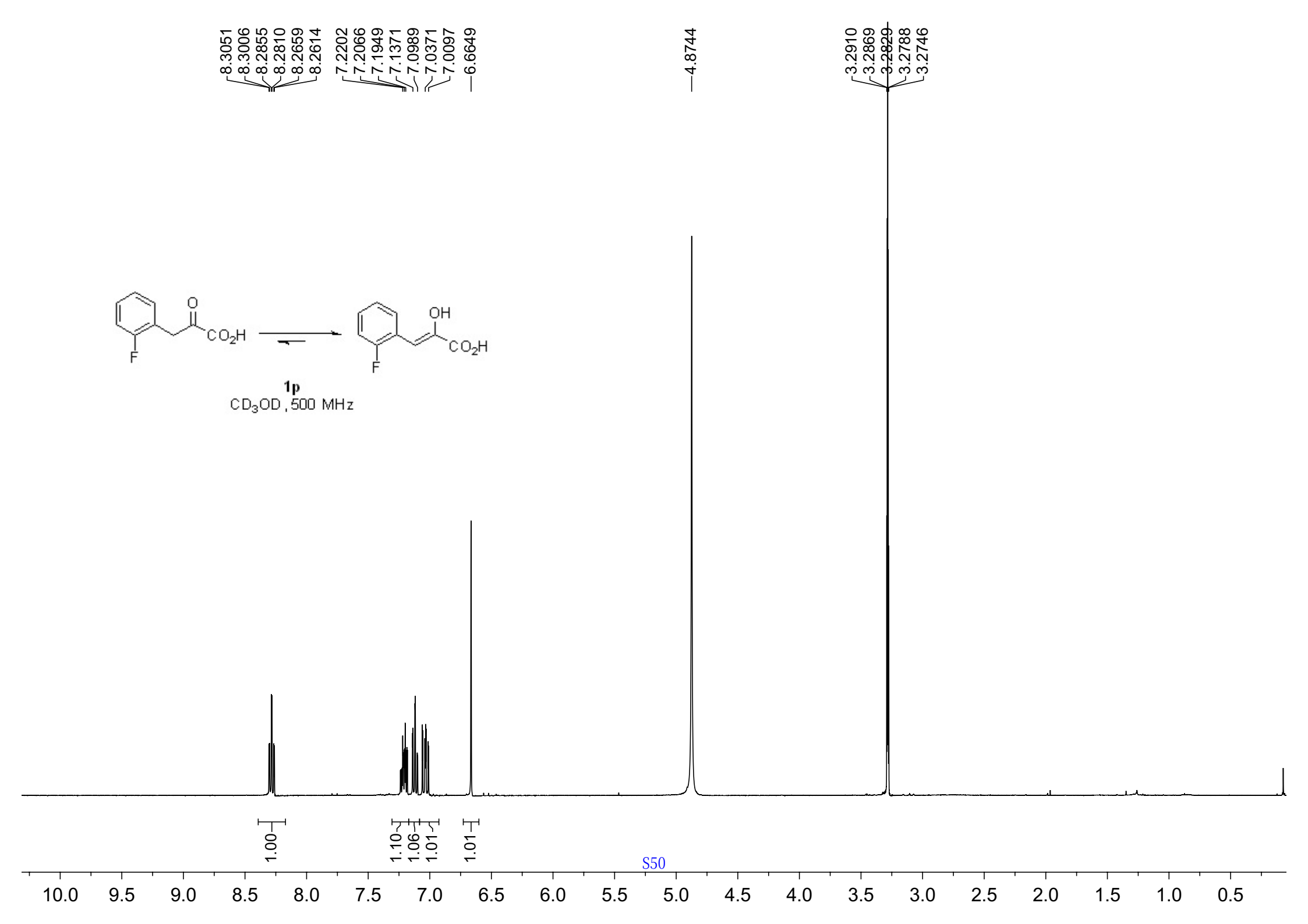

13.1200
9.1083
7.6529
7.6493
7.6402
7.6364
7.1633
7.1475
6.3666
3.3540
2.5079
2.5041
2.5004
2.4968
2.4932
2.2896
COOH
O
COOH
OH
1n
d_6-DMSO, 500 MHz
1.10
1.07
1.99
1.96
1.01
3.00
14.5
13.5
12.5
11.5
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
f1 (ppm)

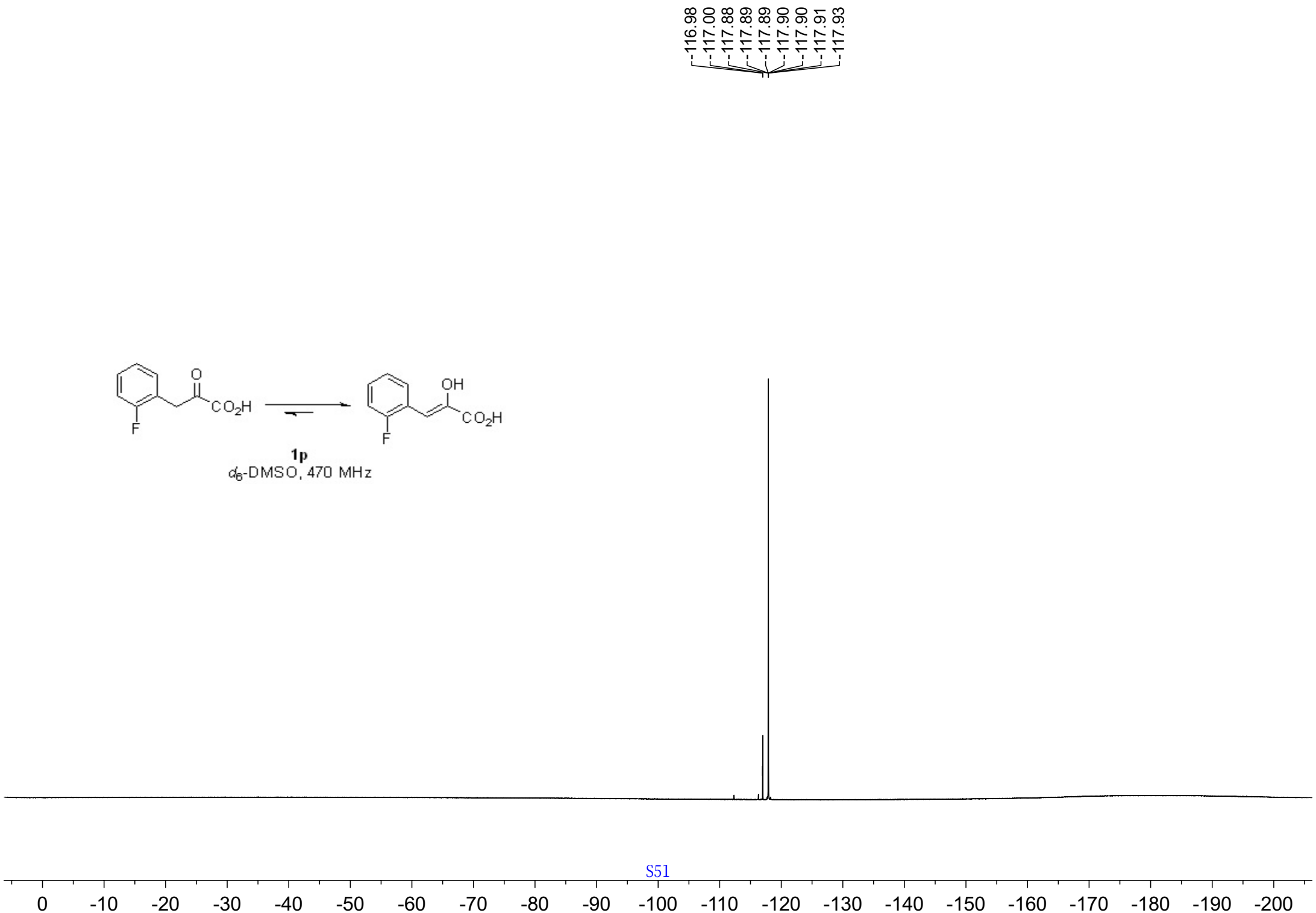

166.44
141.16
136.60
132.15
129.26
128.95
109.73
40.02
39.85
39.69
39.52
39.35
39.19
39.02
20.93
COOH
O
COOH
OH
1n
d_6-DMSO, 125 MHz
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

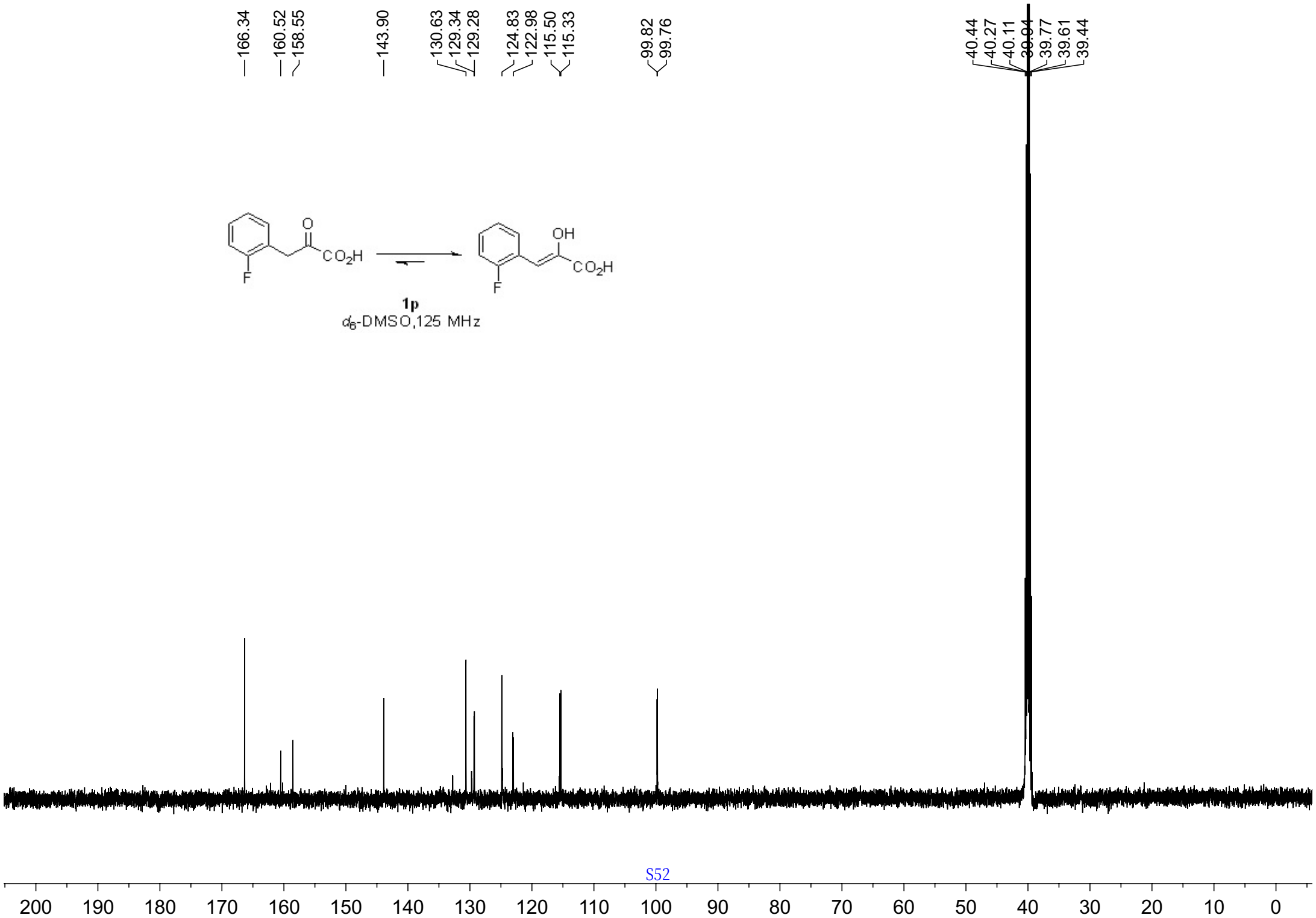

13.3022
9.4978
7.6986
7.6934
7.5465
7.5413
7.5374
7.5280
7.5242
7.5189
6.3720
3.3455
2.5079
2.5041
2.5005
2.4968
2.4930
COOH
O
Br
COOH
OH
Br
1o
d_6-DMSO, 500 MHz
1.08
0.92
1.99
1.95
1.00
14.5
13.5
12.5
11.5
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
f1 (ppm)

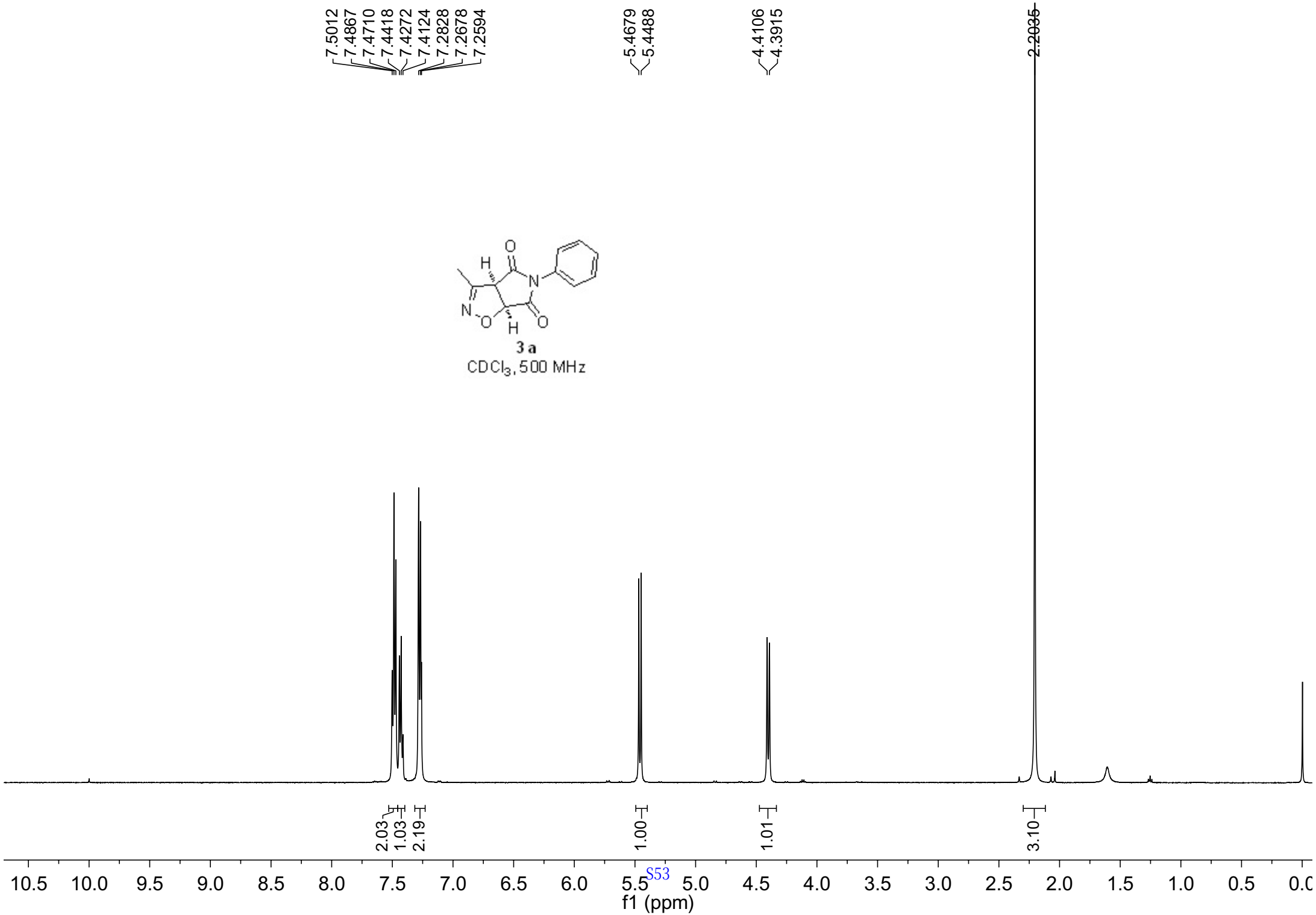

166.55
143.07
134.73
131.70
131.57
120.47
108.66
40.47
40.30
40.14
39.97
39.81
39.64
39.47
COOH
O
Br
COOH
OH
Br
1o
d_6-DMSO, 125 MHz
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

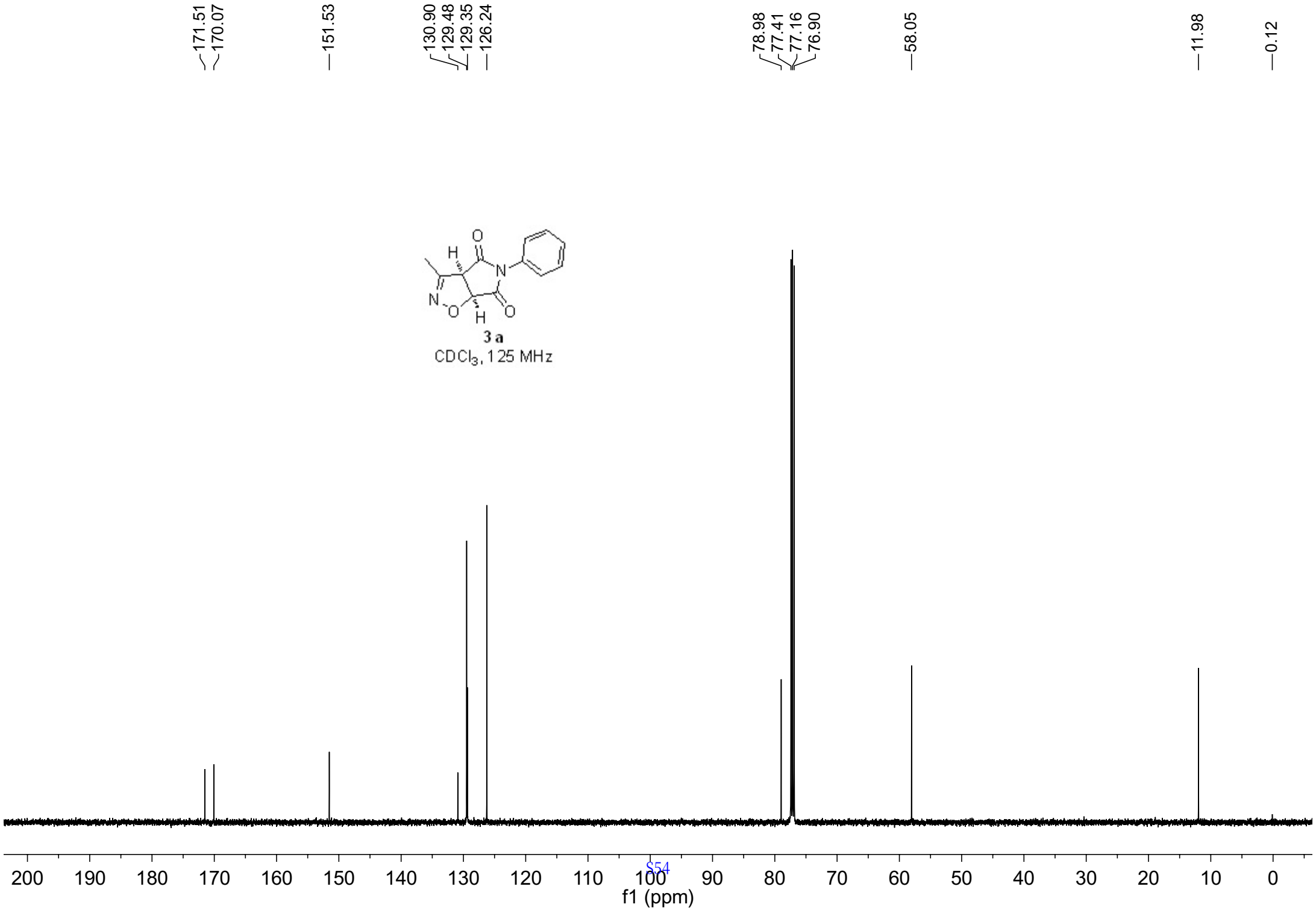

13.4119
9.6424
8.2561
8.2407
8.2272
7.2301
7.2154
7.1997
7.1846
7.1783
6.5456
4.2277
2.5113
O
CO2H
F
OH
CO2H
F
1p
d6-DMSO, 500 MHz
0.87
0.96
1.02
2.30
2.36
1.00
14.5
13.5
12.5
11.5
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5

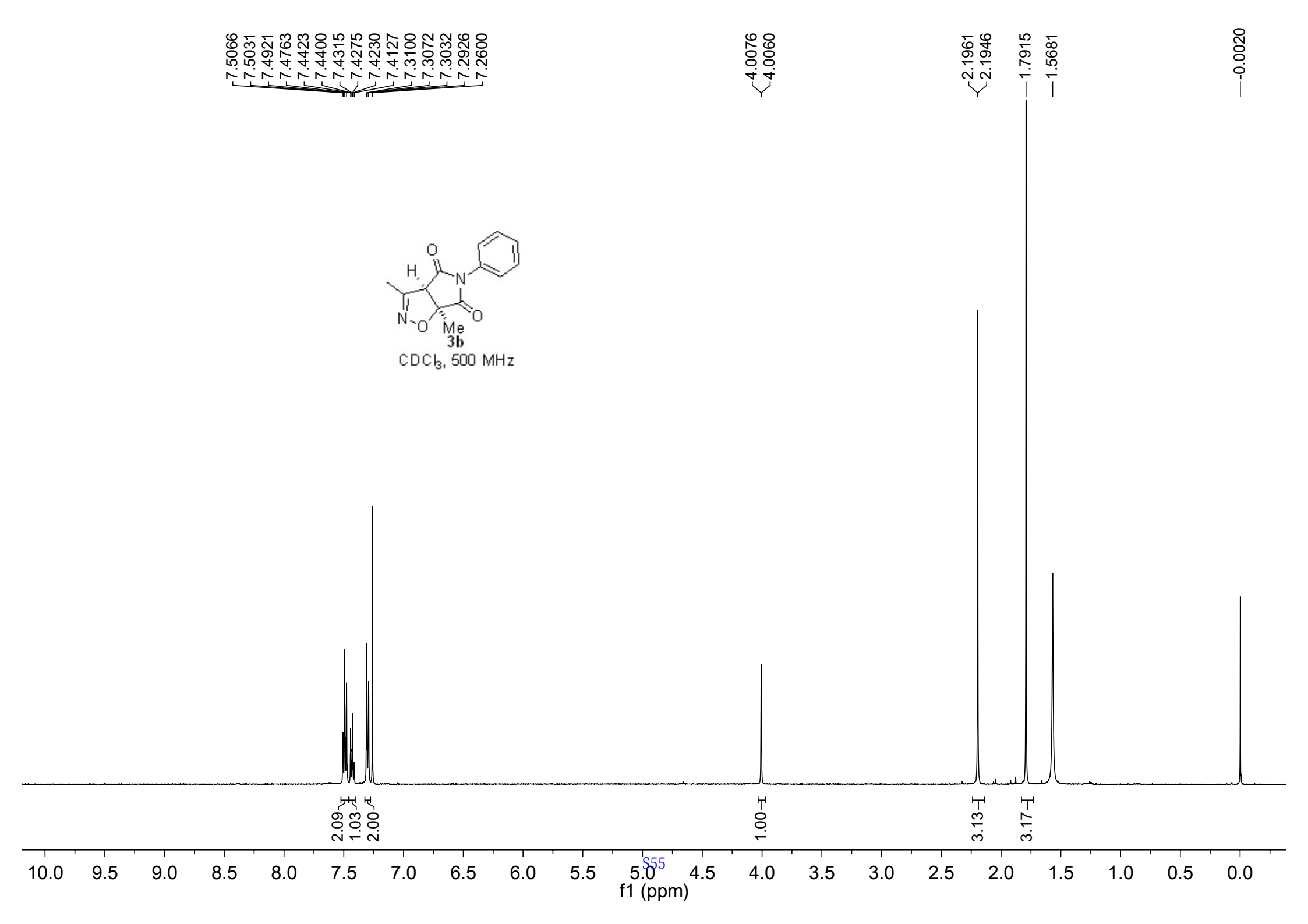

8.3051
8.3006
8.2855
8.2810
8.2659
8.2614
7.2202
7.2066
7.1949
7.1371
7.0989
7.0371
7.0097
6.6649
4.8744
3.2910
3.2869
3.2829
3.2788
3.2746
O
CO2H
F
OH
CO2H
F
1p
CD3OD, 500 MHz
1.00
1.10
1.06
1.01
1.01
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5

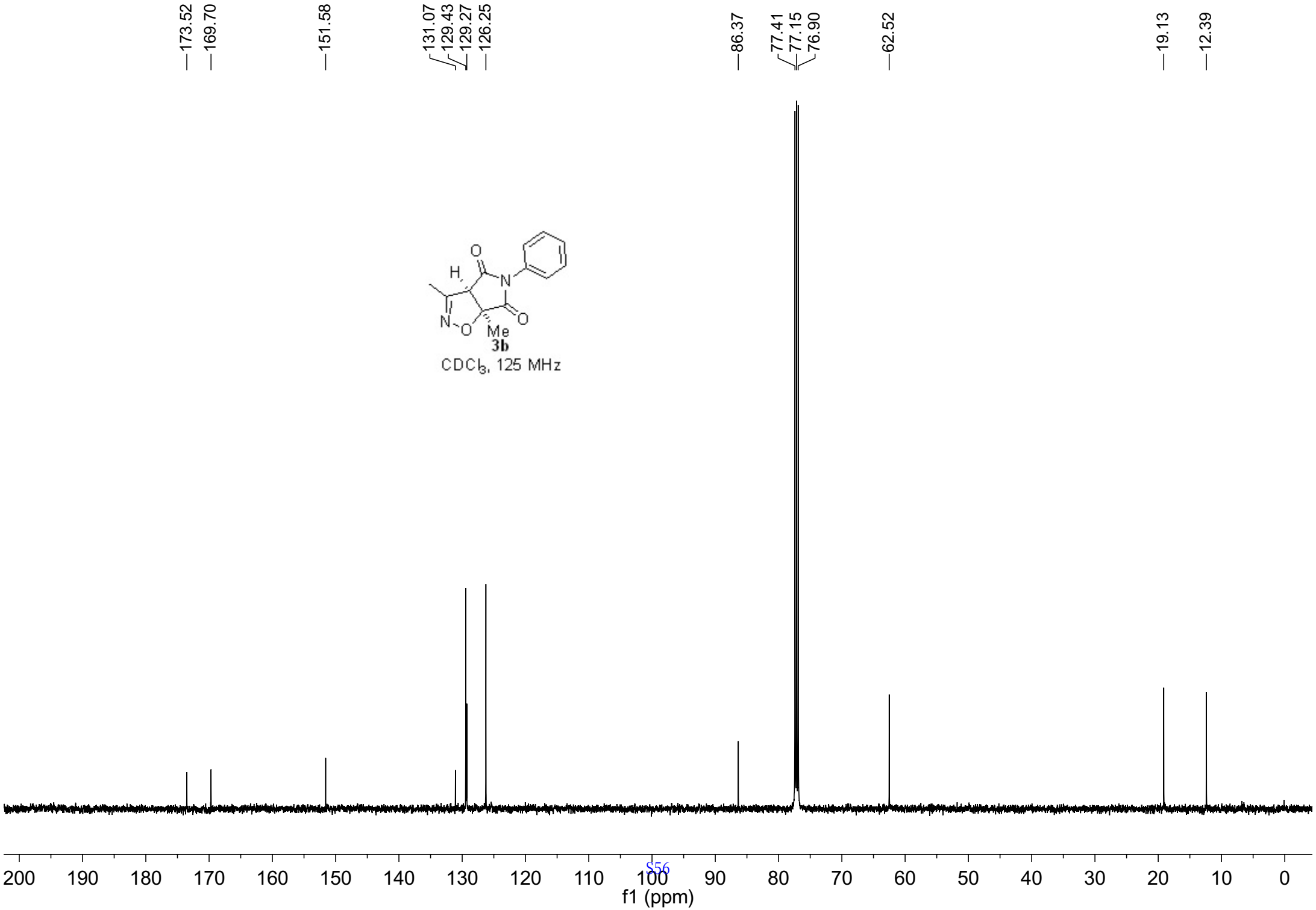

116.98
117.00
117.88
117.89
117.89
117.90
117.90
117.91
117.93
O
CO2H
F
OH
CO2H
F
1p
d6-DMSO, 470 MHz
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200

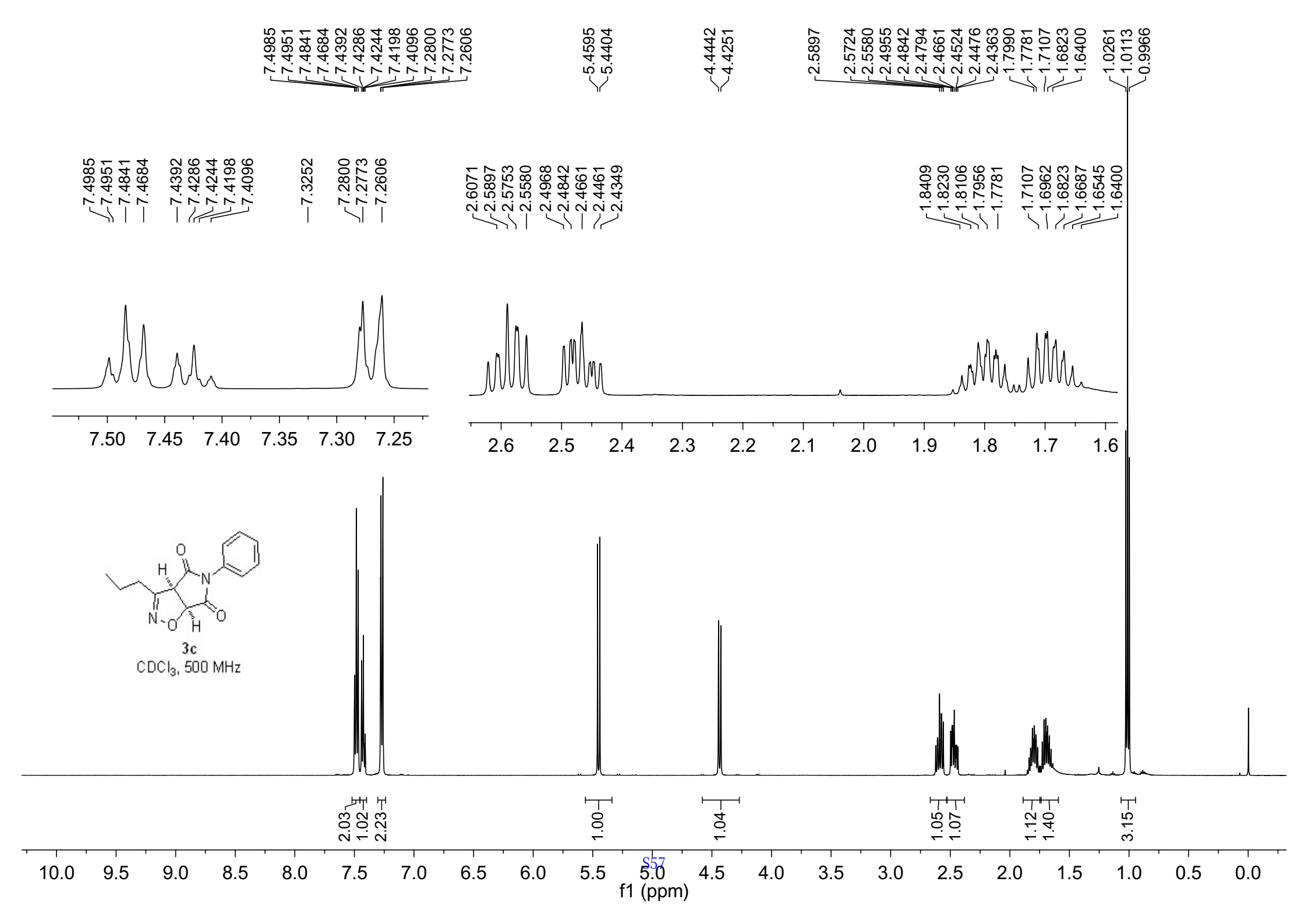

166.34
160.52
158.55
143.90
130.63
129.34
129.28
124.83
122.98
115.50
115.33
99.82
99.76
40.44
40.27
40.11
39.94
39.77
39.61
39.44
O
CO2H
F
OH
CO2H
F
1p
d6-DMSO,125 MHz
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

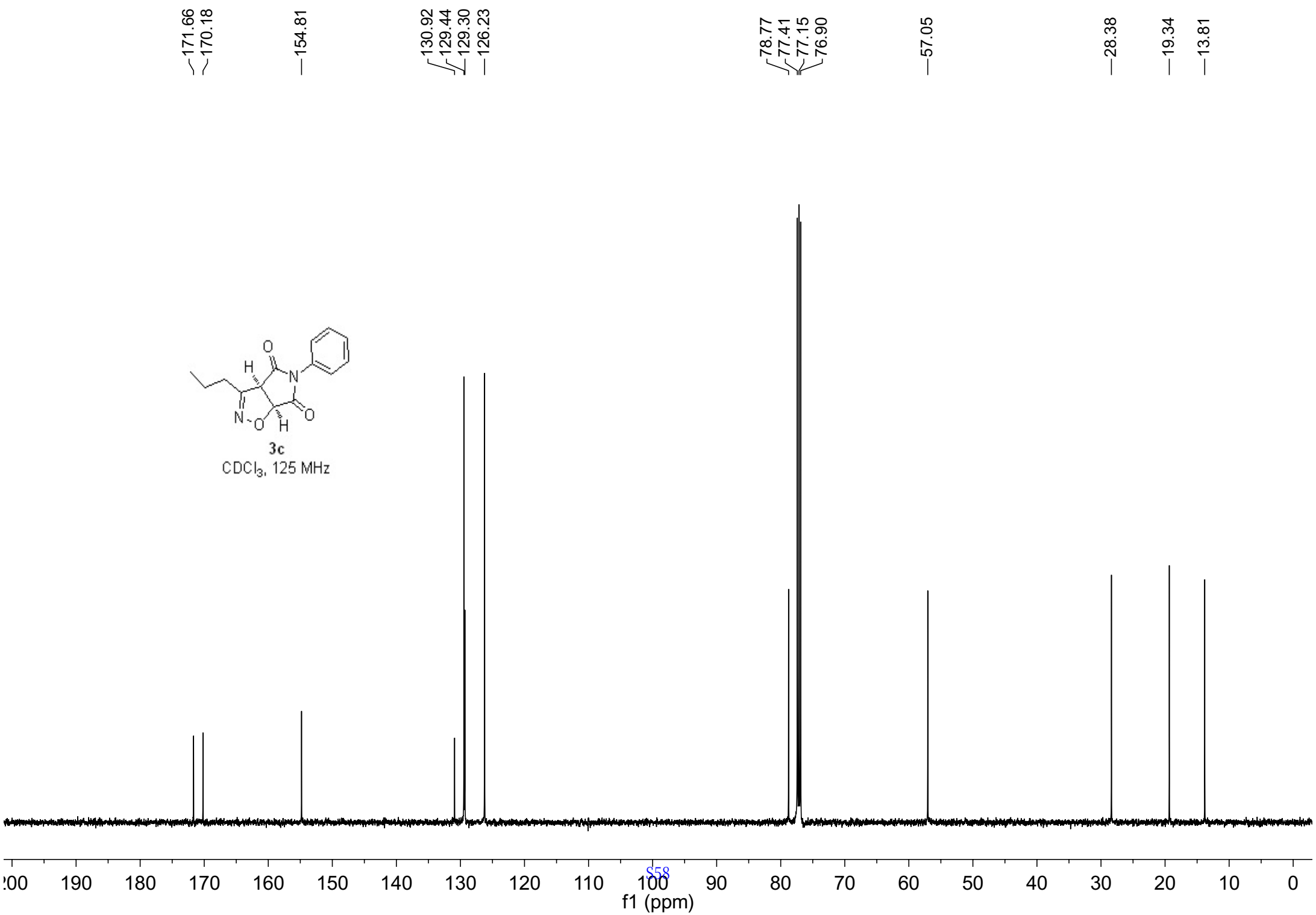

7.5012
7.4867
7.4710
7.4418
7.4272
7.4124
7.2828
7.2678
7.2594
5.4679
5.4488
4.4106
4.3915
2.2035
3a
CDCl3, 500 MHz
2.03
1.03
2.19
1.00
1.01
3.10
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

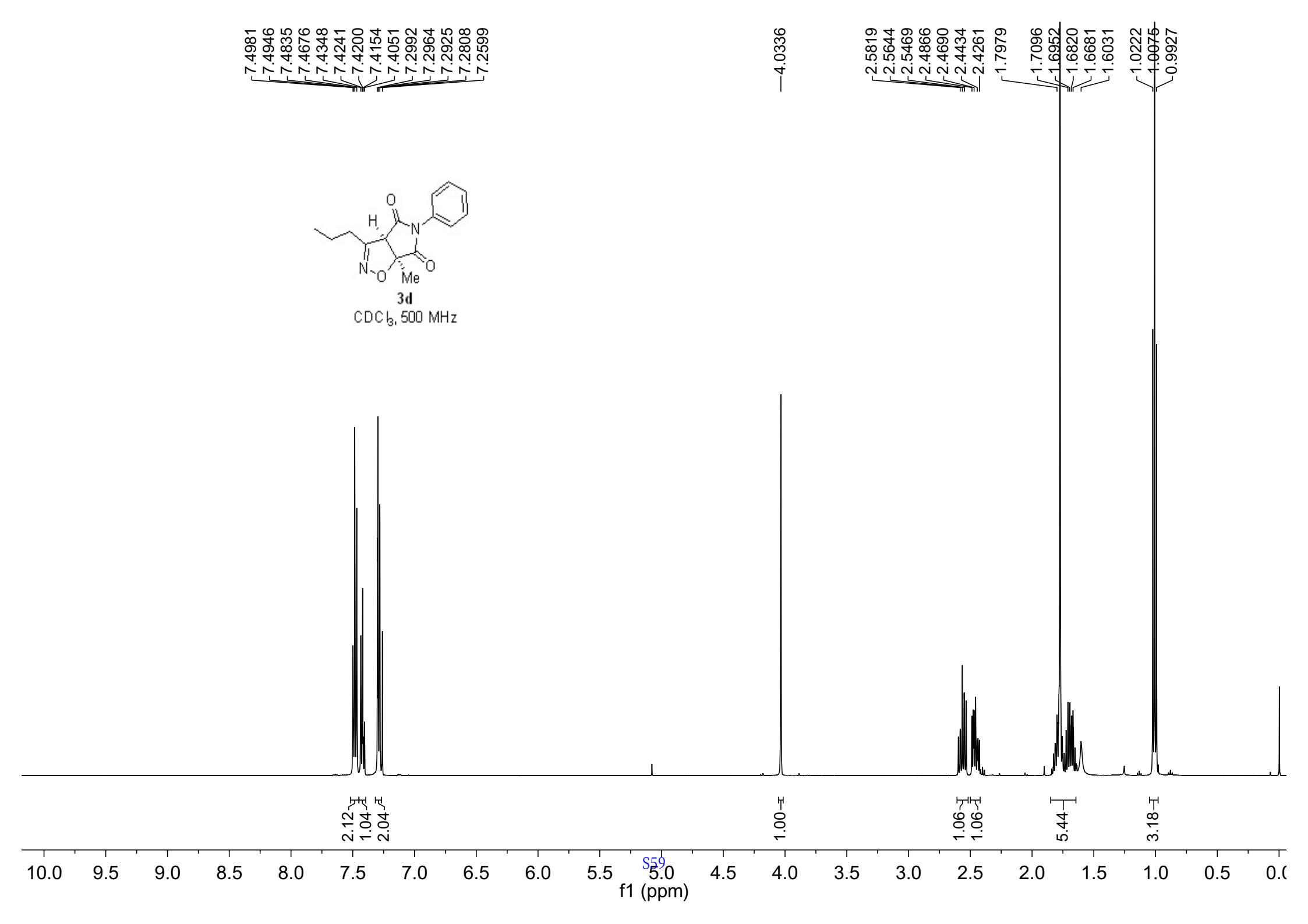

171.51
170.07
151.53
130.90
129.48
129.35
126.24
78.98
77.41
77.16
76.90
58.05
11.98
0.12
3 a
CDCl3, 125 MHz
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

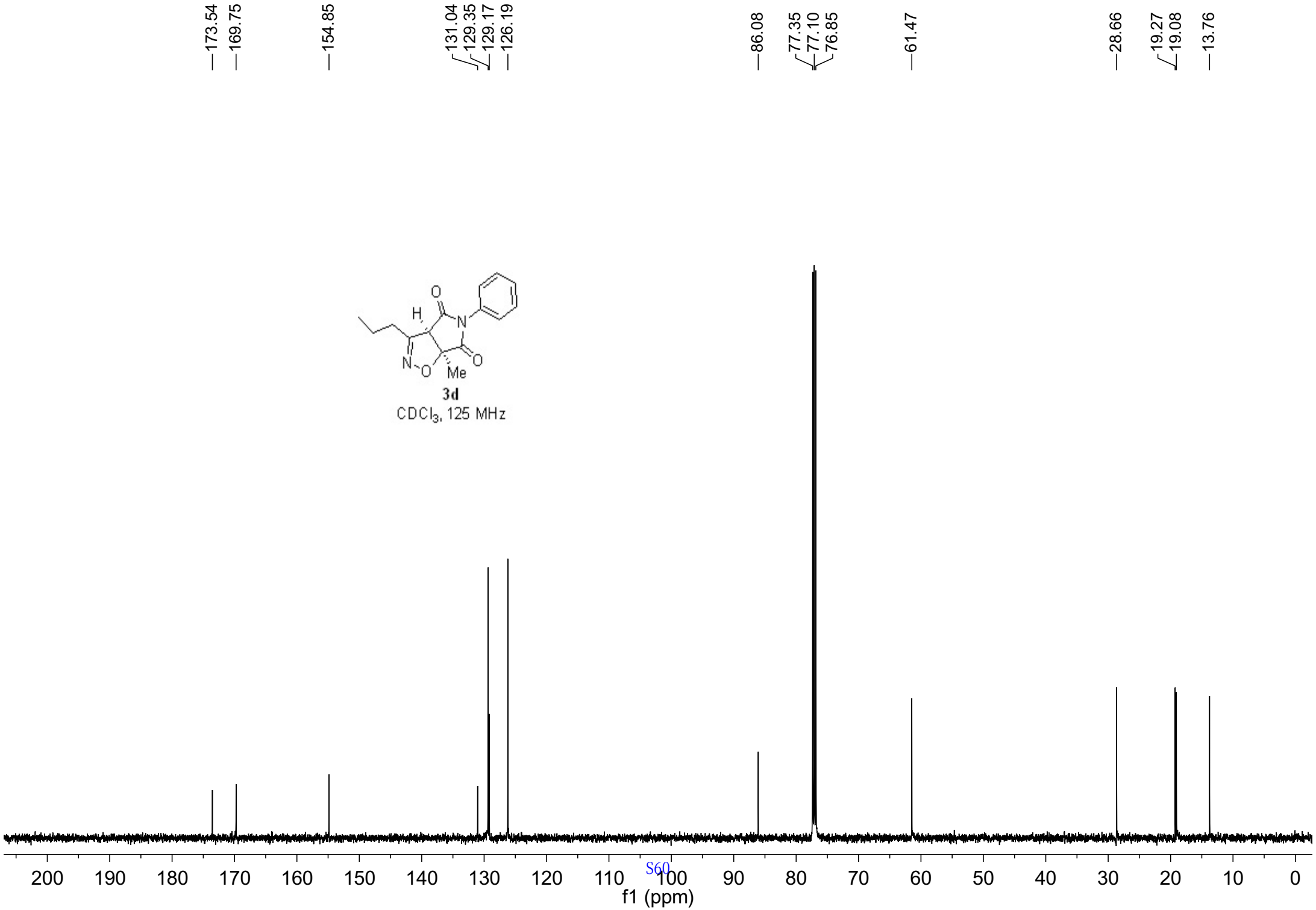

7.5066
7.5031
7.4921
7.4763
7.4423
7.4400
7.4315
7.4275
7.4230
7.4127
7.3100
7.3072
7.3032
7.2926
7.2600
4.0076
4.0060
2.1961
2.1946
1.7915
1.5681
-0.0020
3b
CDCl3, 500 MHz
2.09
1.03
2.00
1.00
3.13
3.17
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

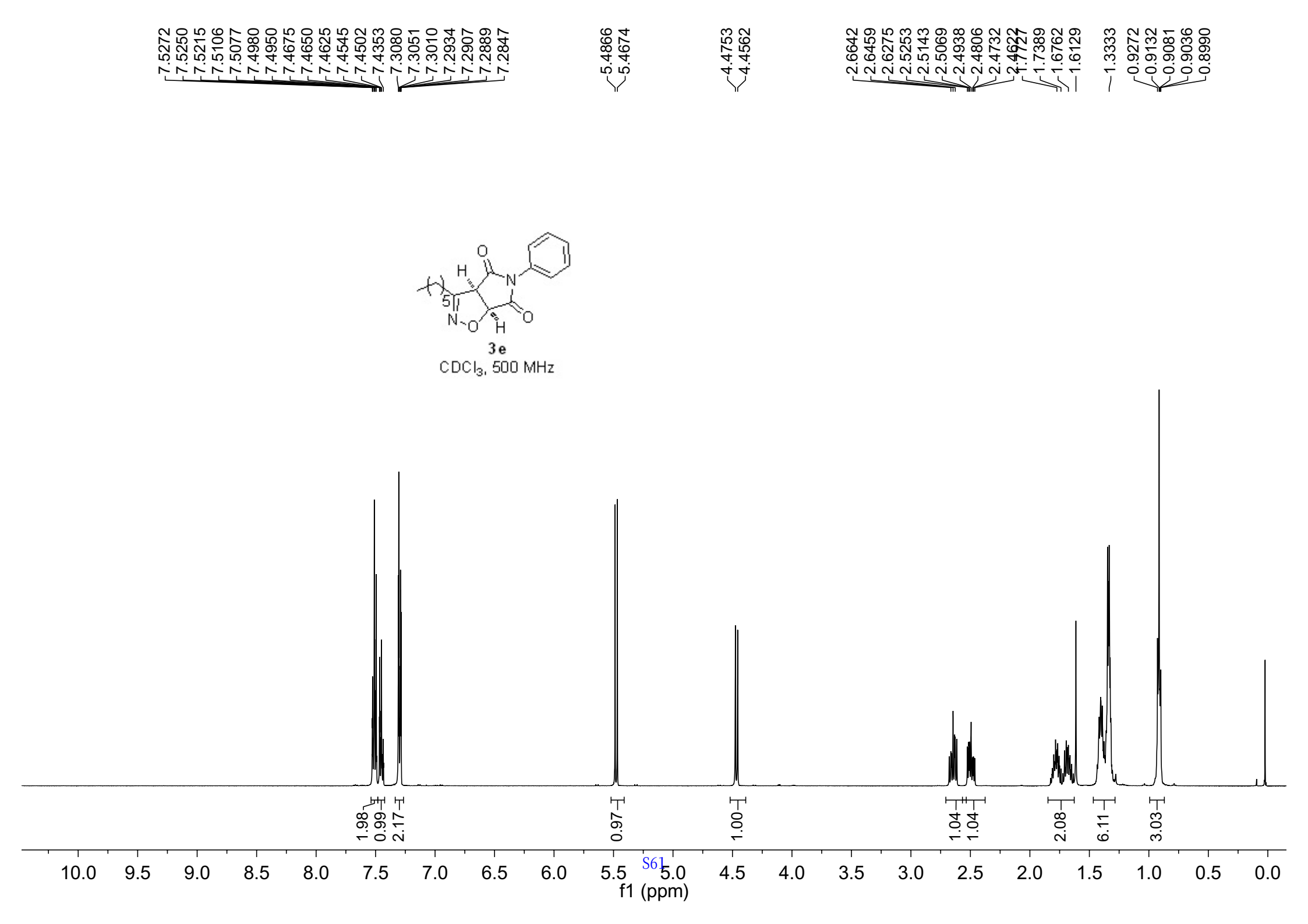

173.52
169.70
151.58
131.07
129.43
129.27
126.25
86.37
77.41
77.15
76.90
62.52
19.13
12.39
O
H
N
N
O
O
Me
3b
CDCl3, 125 MHz
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

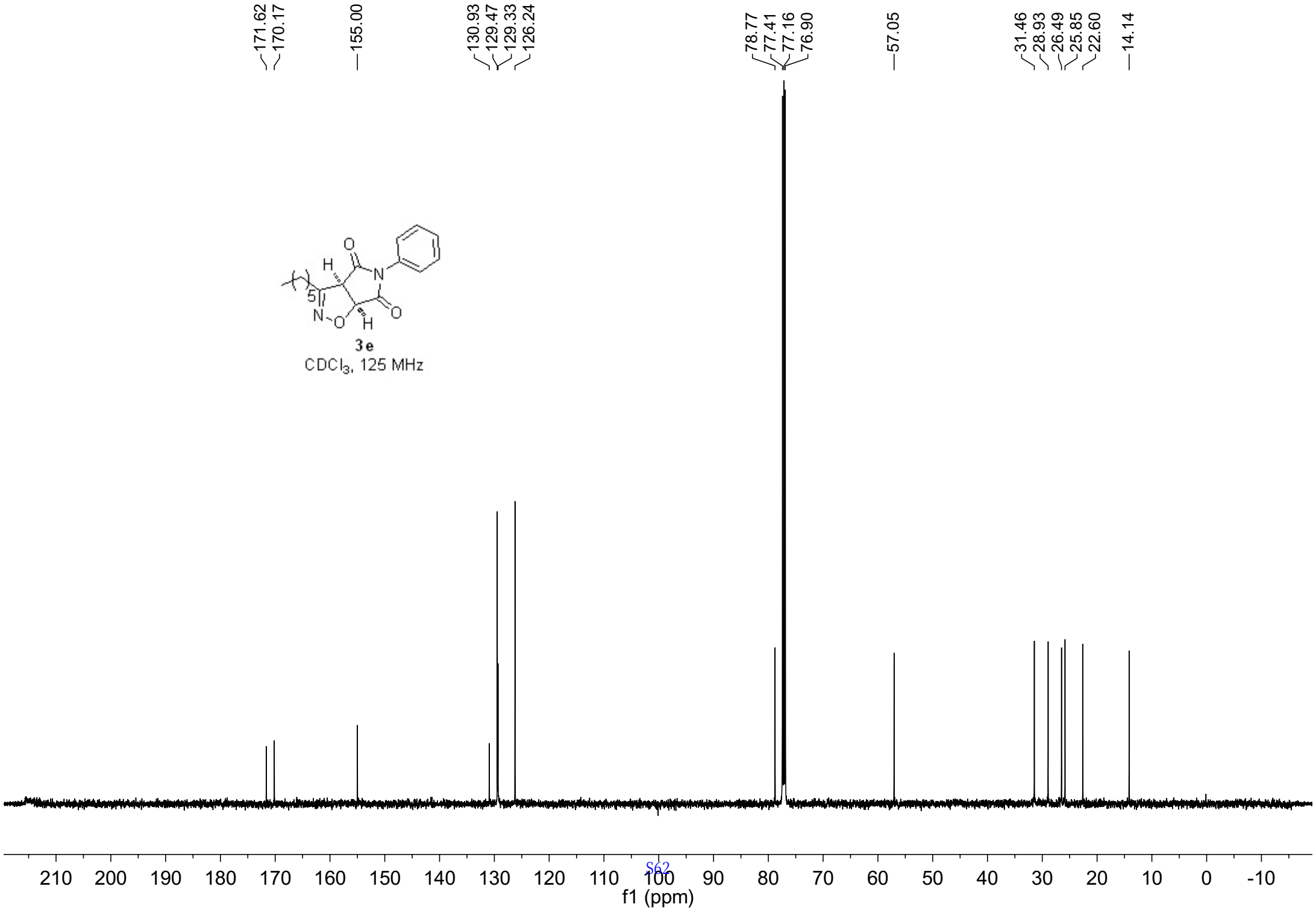

7.4985
7.4951
7.4841
7.4684
7.4392
7.4286
7.4244
7.4198
7.4096
7.2800
7.2773
7.2606
5.4595
5.4404
4.4442
4.4251
2.5897
2.5724
2.5580
2.4955
2.4842
2.4794
2.4661
2.4524
2.4476
2.4363
1.7990
1.7781
1.7107
1.6823
1.6400
1.0261
1.0113
0.9966
7.50 7.45 7.40 7.35 7.30 7.25
2.6 2.5 2.4 2.3 2.2 2.1 2.0 1.9 1.8 1.7 1.6
3c
CDCl3, 500 MHz
2.03
1.02
2.23
1.00
1.04
1.05
1.07
1.12
1.40
3.15
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

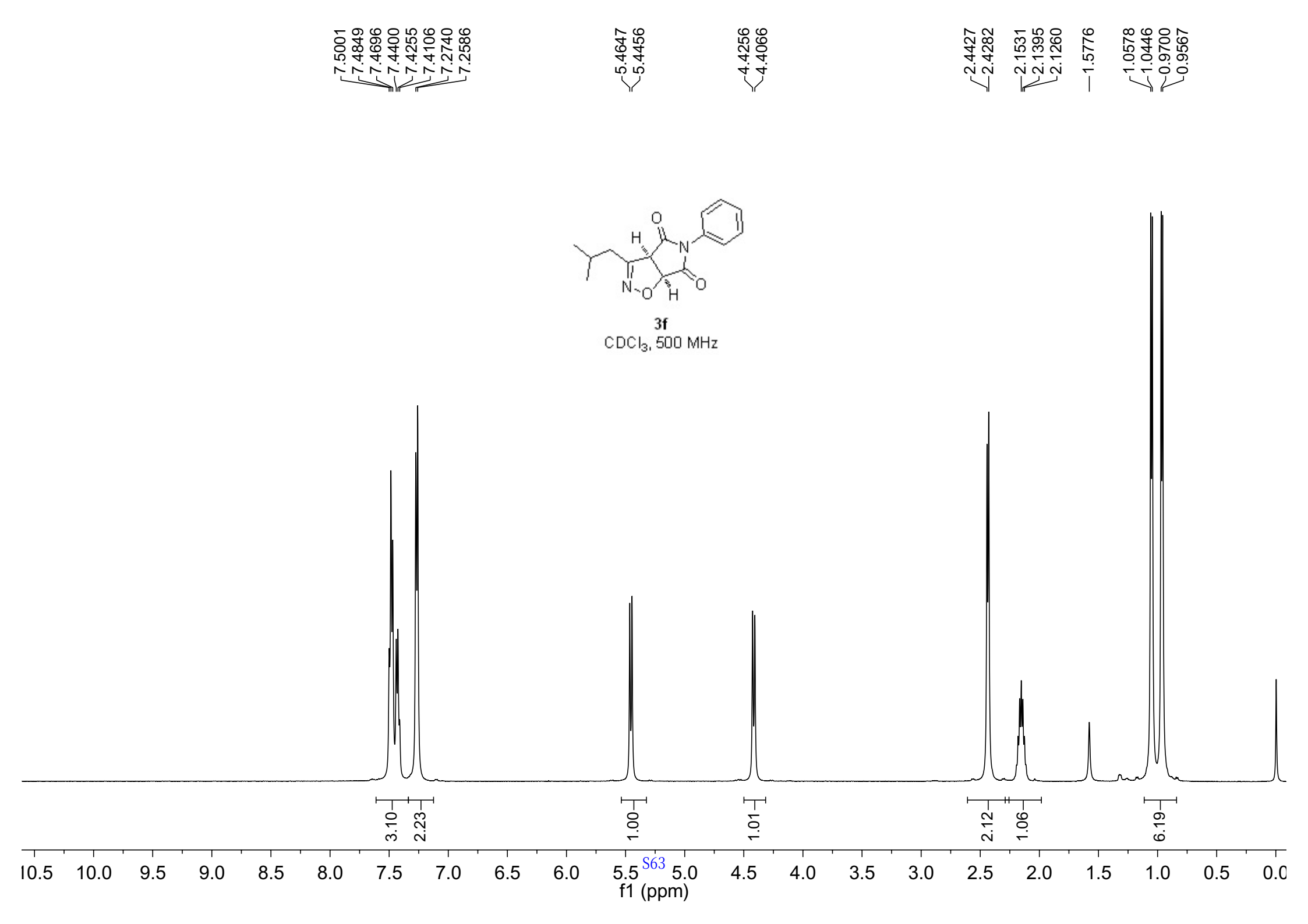

171.66
170.18
154.81
130.92
129.44
129.30
126.23
78.77
77.41
77.15
76.90
57.05
28.38
19.34
13.81
3c
CDCl3, 125 MHz
f1 (ppm)

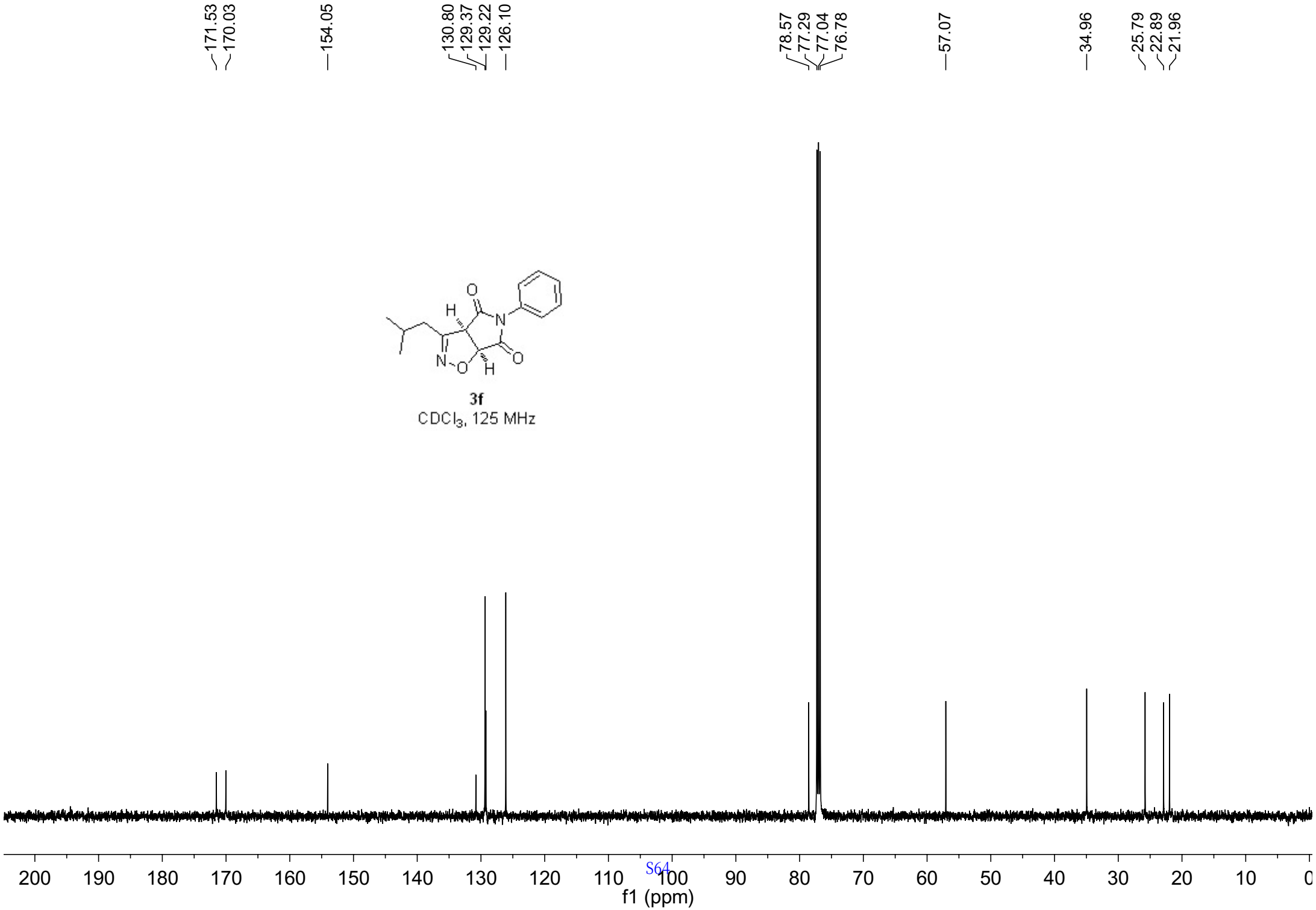

7.4981
7.4946
7.4835
7.4676
7.4348
7.4241
7.4200
7.4154
7.4051
7.2992
7.2964
7.2925
7.2808
7.2599
4.0336
2.5819
2.5644
2.5469
2.4866
2.4690
2.4434
2.4261
1.7979
1.7096
1.6952
1.6820
1.6681
1.6031
1.0222
1.0076
0.9927
3d
CDCl3, 500 MHz
2.12
1.04
2.04
1.00
1.06
1.06
5.44
3.18
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

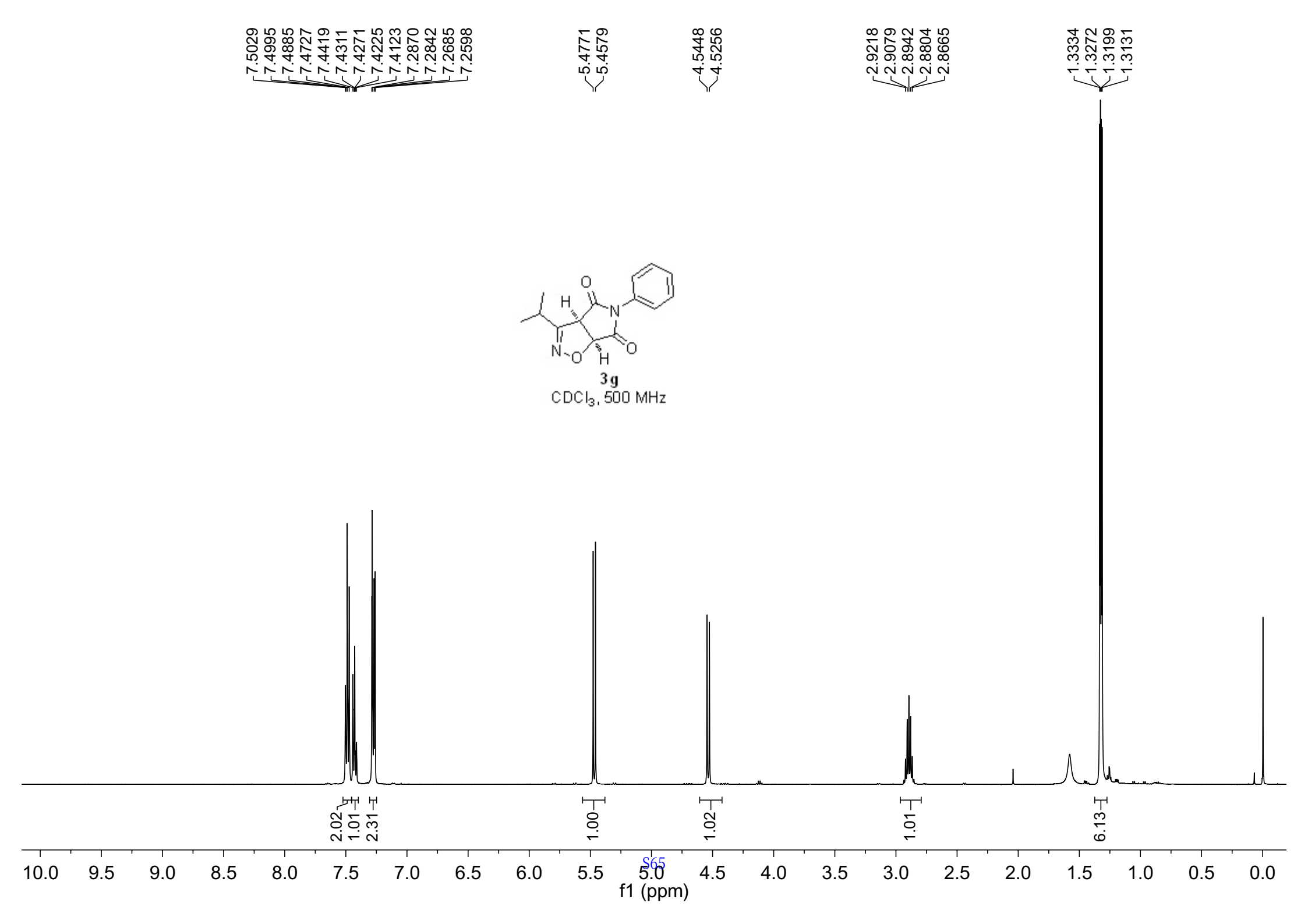

173.54
169.75
154.85
131.04
129.35
129.17
126.19
86.08
77.35
77.10
76.85
61.47
28.66
19.27
19.08
13.76
O
H
N
O
N
O
Me
3d
CDCl3, 125 MHz
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

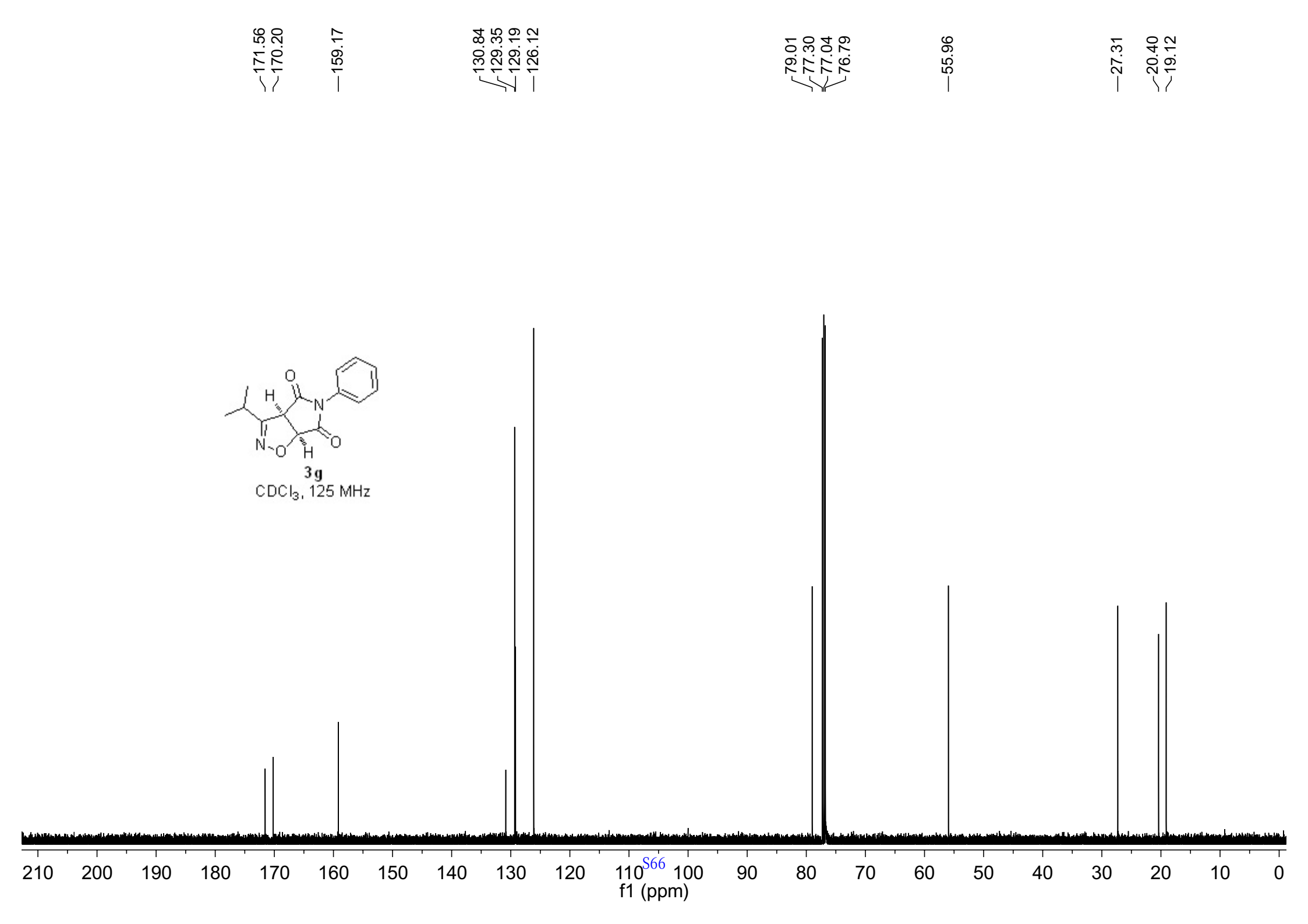

7.5272
7.5250
7.5215
7.5106
7.5077
7.4980
7.4950
7.4675
7.4650
7.4625
7.4545
7.4502
7.4353
7.3080
7.3051
7.3010
7.2934
7.2907
7.2889
7.2847
5.4866
5.4674
4.4753
4.4562
2.6642
2.6459
2.6275
2.5253
2.5143
2.5069
2.4938
2.4806
2.4732
1.7727
1.7389
1.6762
1.6129
1.3333
0.9272
0.9132
0.9081
0.9036
0.8990
3e
CDCl3, 500 MHz
1.98
0.99
2.17
0.97
1.00
1.04
1.04
2.08
6.11
3.03
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

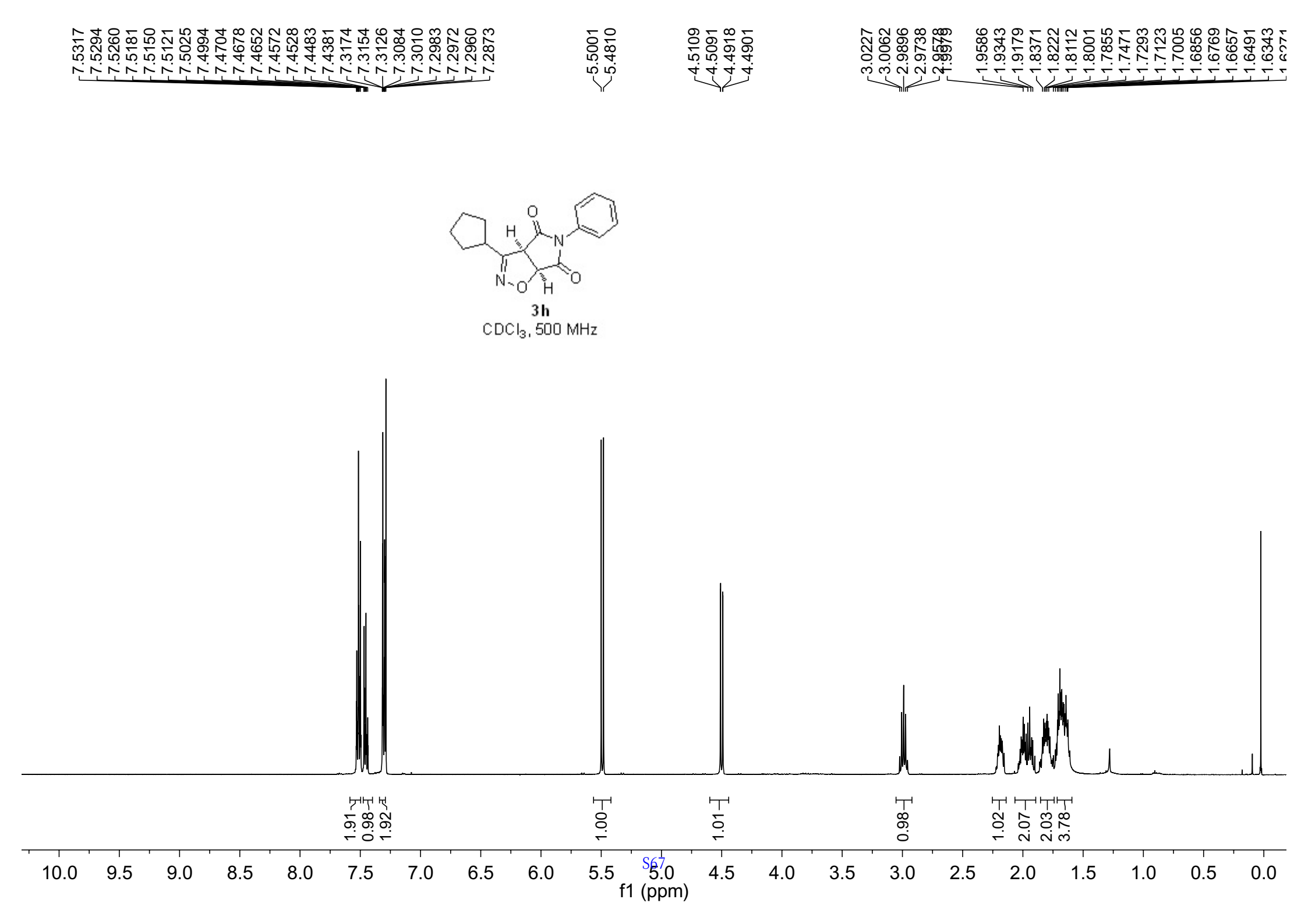

171.62
170.17
155.00
130.93
129.47
129.33
126.24
78.77
77.41
77.16
76.90
57.05
31.46
28.93
26.49
25.85
22.60
14.14
O
H
N
O
5
N
O
H
3e
CDCl3, 125 MHz
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

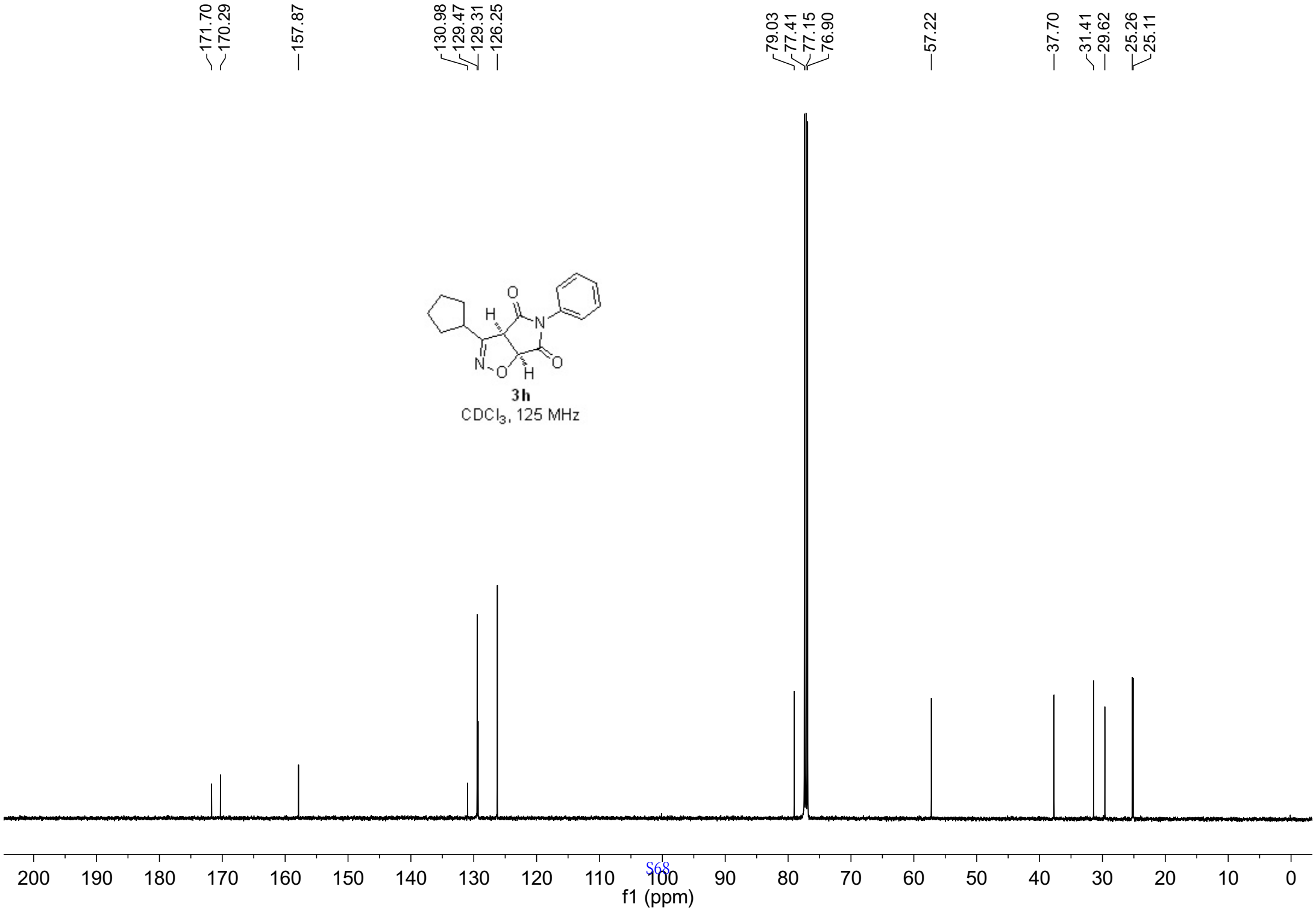

7.5001
7.4849
7.4696
7.4400
7.4255
7.4106
7.2740
7.2586
5.4647
5.4456
4.4256
4.4066
2.4427
2.4282
2.1531
2.1395
2.1260
1.5776
1.0578
1.0446
0.9700
0.9567
O
H
N
O
N
O
H
3f
CDCl3, 500 MHz
3.10
2.23
1.00
1.01
2.12
1.06
6.19
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

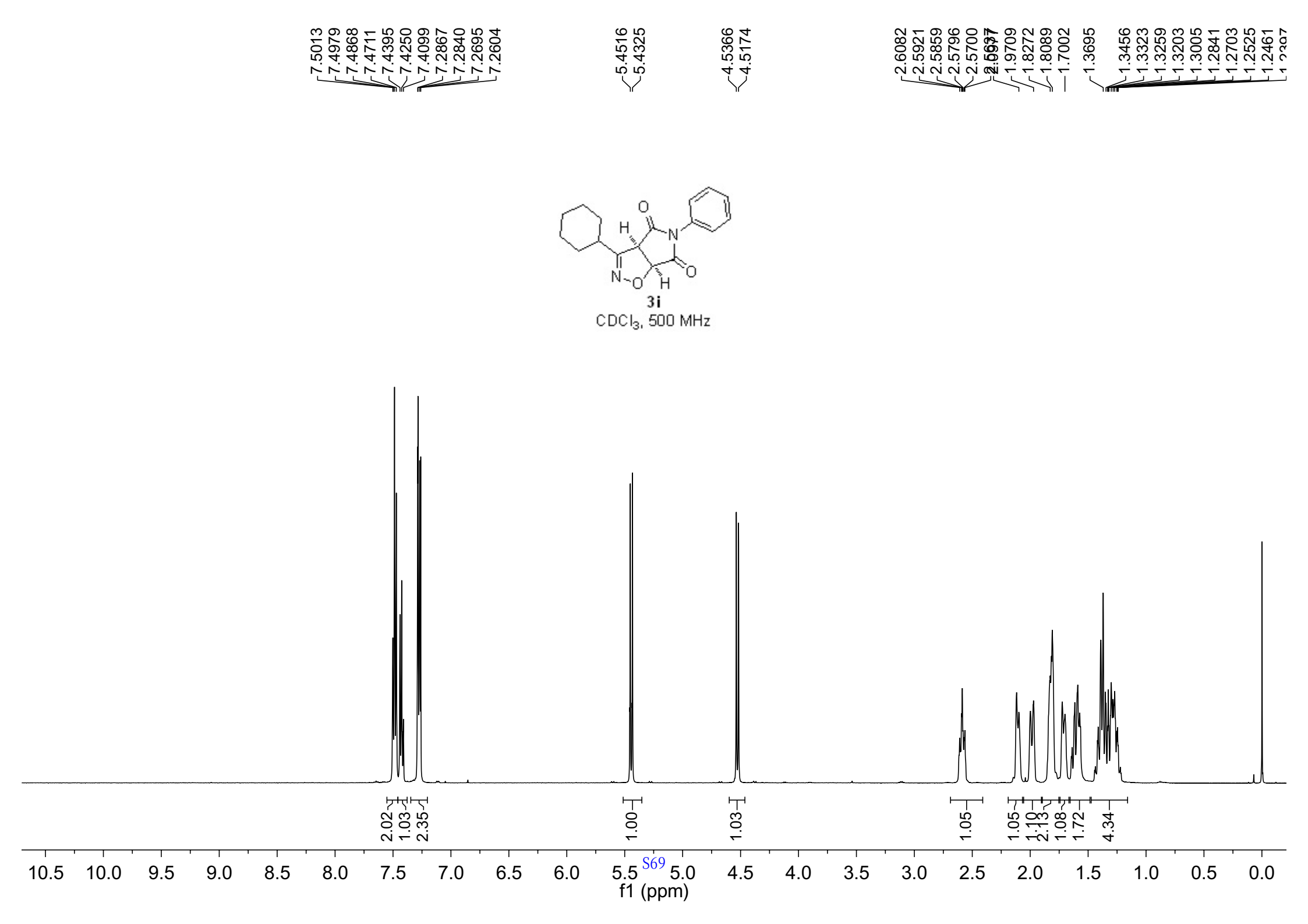

171.53
170.03
154.05
130.80
129.37
129.22
126.10
78.57
77.29
77.04
76.78
57.07
34.96
25.79
22.89
21.96
O
H
N
O
N
O
H
3f
CDCl3, 125 MHz
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

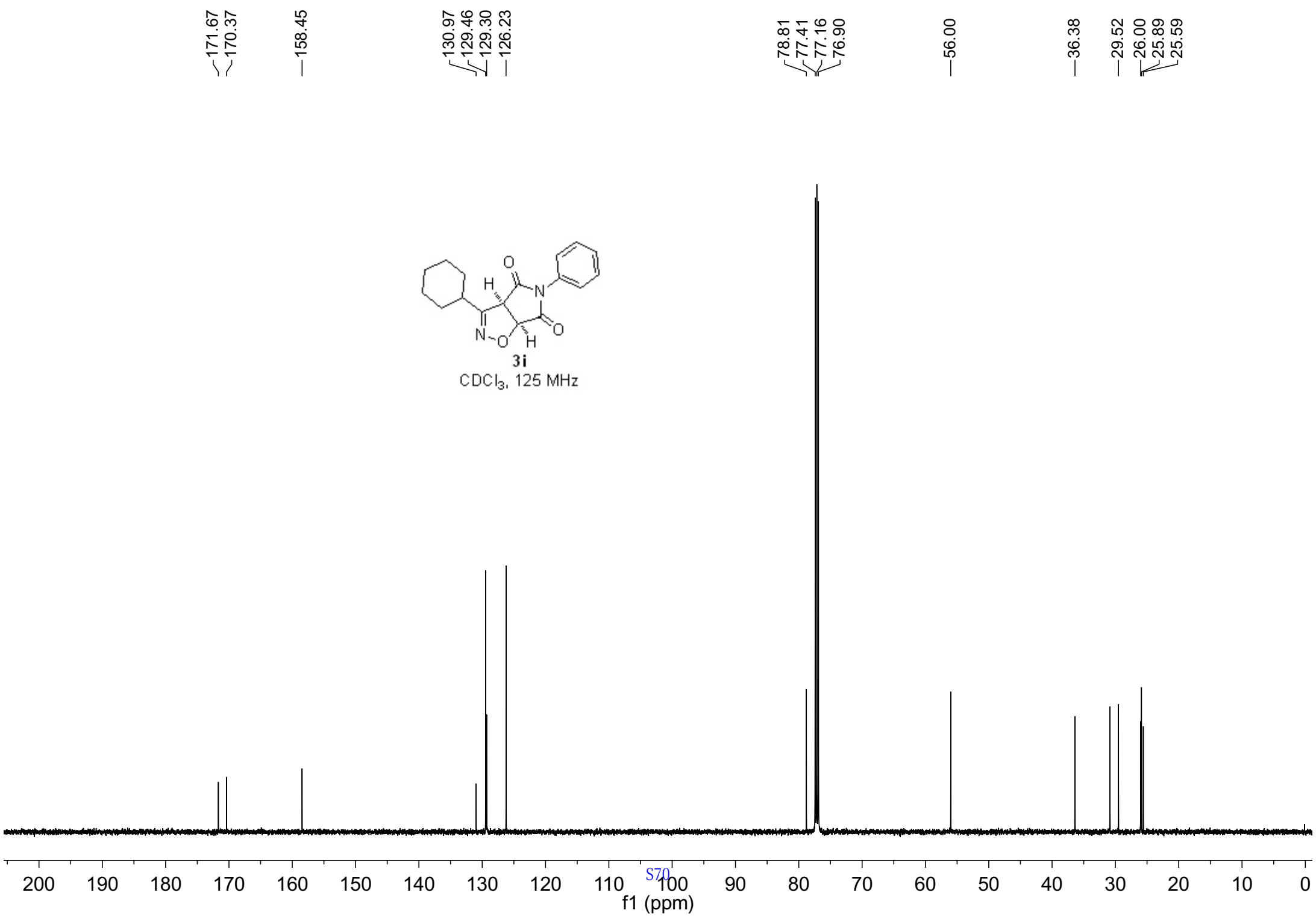

7.5029
7.4995
7.4885
7.4727
7.4419
7.4311
7.4271
7.4225
7.4123
7.2870
7.2842
7.2685
7.2598
5.4771
5.4579
4.5448
4.5256
2.9218
2.9079
2.8942
2.8804
2.8665
1.3334
1.3272
1.3199
1.3131
3g
CDCl3, 500 MHz
2.02
1.01
2.31
1.00
1.02
1.01
6.13
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

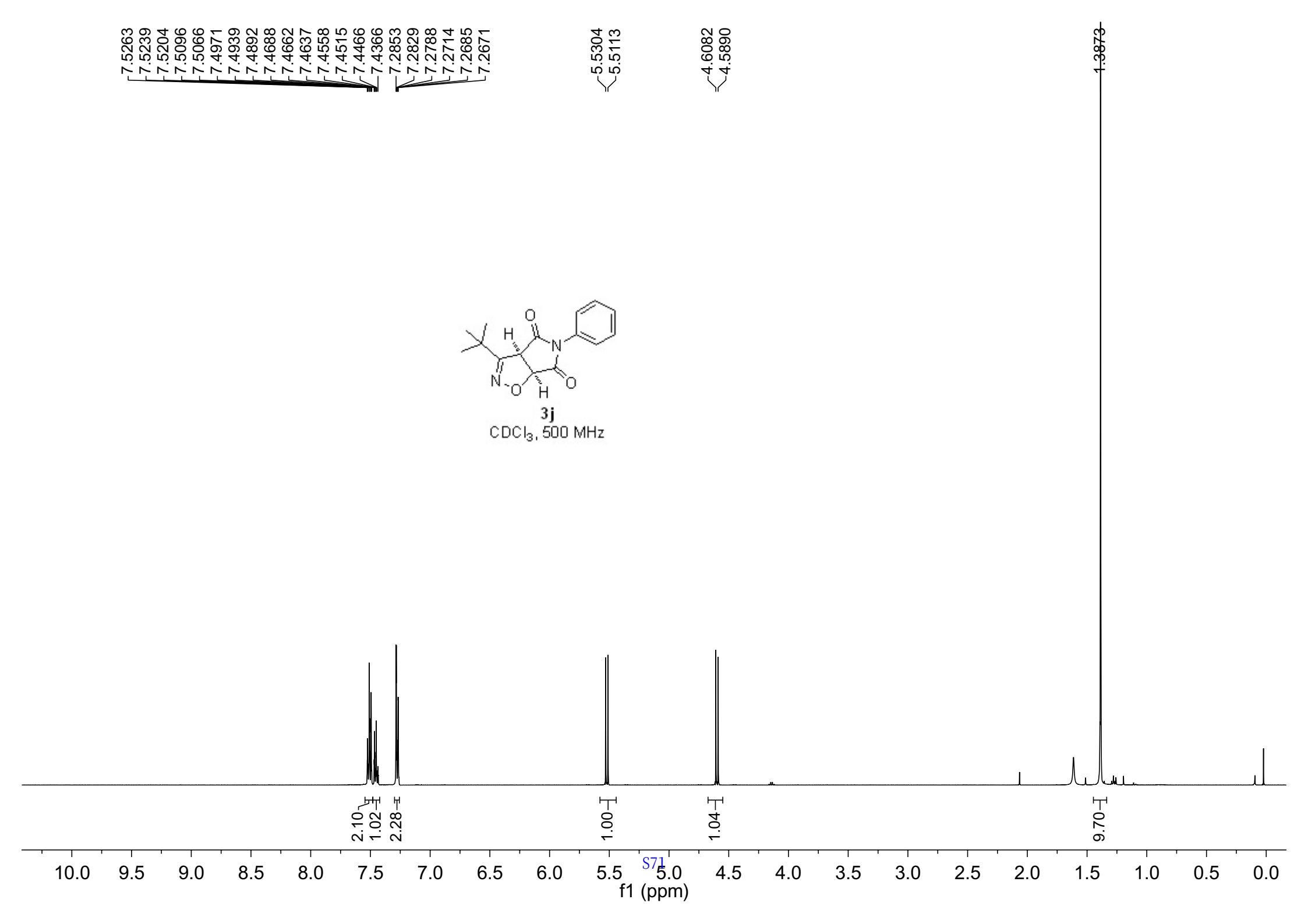

171.56
170.20
159.17
130.84
129.35
129.19
126.12
79.01
77.30
77.04
76.79
55.96
27.31
20.40
19.12
O
H
N
O
N
O
H
3g
CDCl3, 125 MHz
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

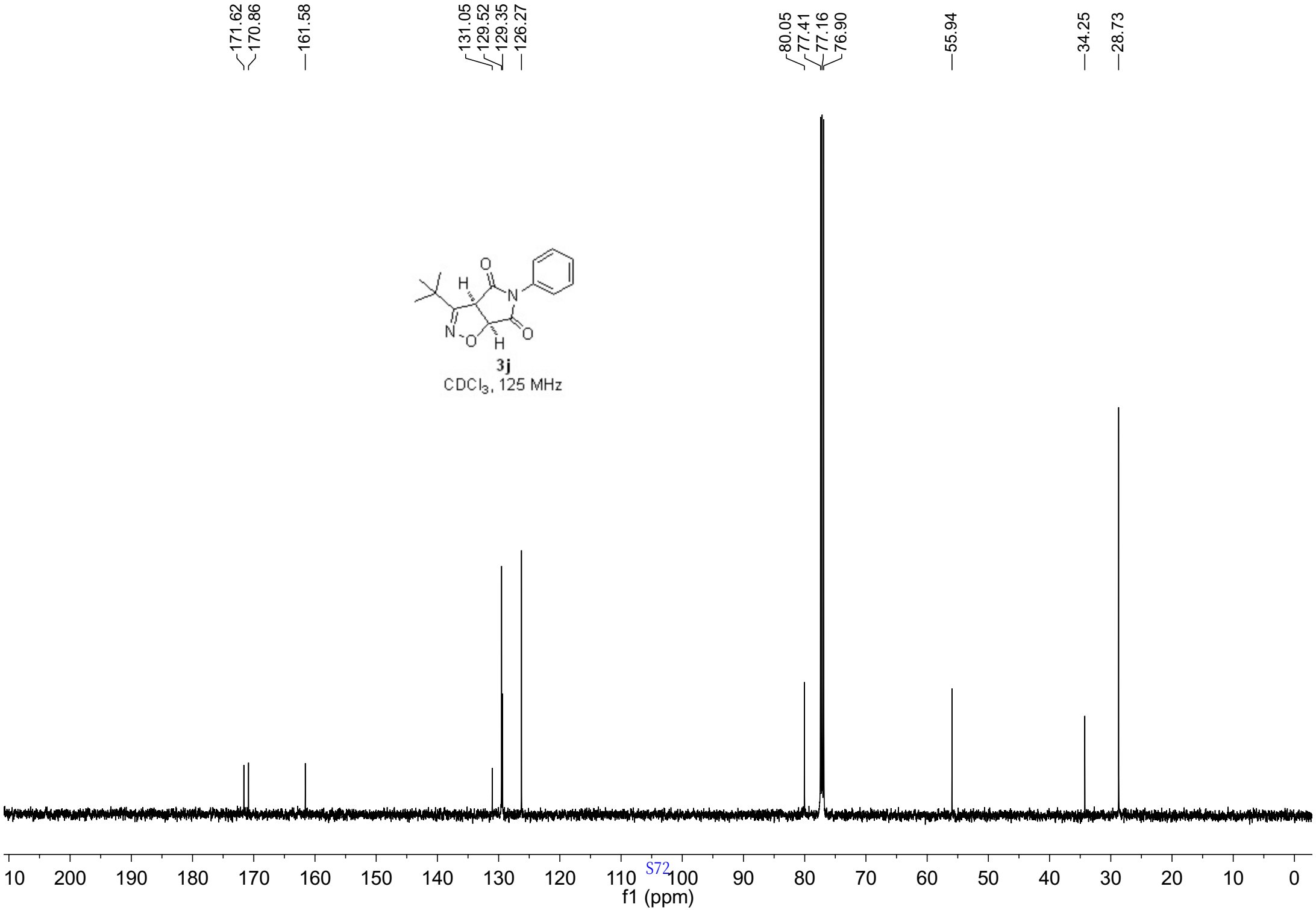

7.5317
7.5294
7.5260
7.5181
7.5150
7.5121
7.5025
7.4994
7.4704
7.4678
7.4652
7.4572
7.4528
7.4483
7.4381
7.3174
7.3154
7.3126
7.3084
7.3010
7.2983
7.2972
7.2960
7.2873
5.5001
5.4810
4.5109
4.5091
4.4918
4.4901
3.0227
3.0062
2.9896
2.9738
1.9586
1.9343
1.9179
1.8371
1.8222
1.8112
1.8001
1.7855
1.7471
1.7293
1.7123
1.7005
1.6856
1.6769
1.6657
1.6491
1.6343
O
H
N
O
N
O
H
3h
CDCl3, 500 MHz
1.91
0.98
1.92
1.00
1.01
0.98
1.02
2.07
2.03
3.78
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

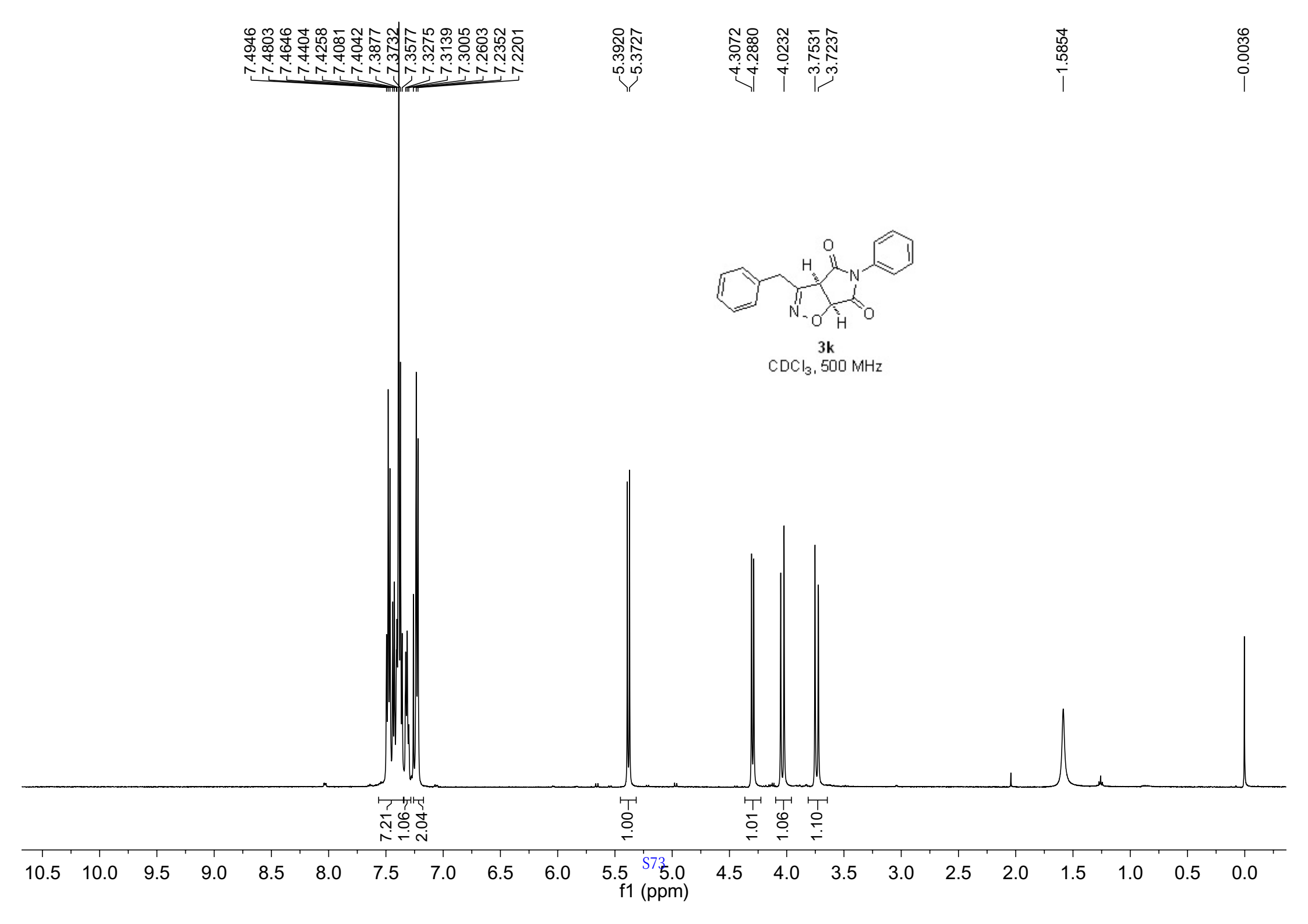

171.70
170.29
157.87
130.98
129.47
129.31
126.25
79.03
77.41
77.15
76.90
57.22
37.70
31.41
29.62
25.26
25.11
O
H
N
O
N
O
H
3h
CDCl3, 125 MHz
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

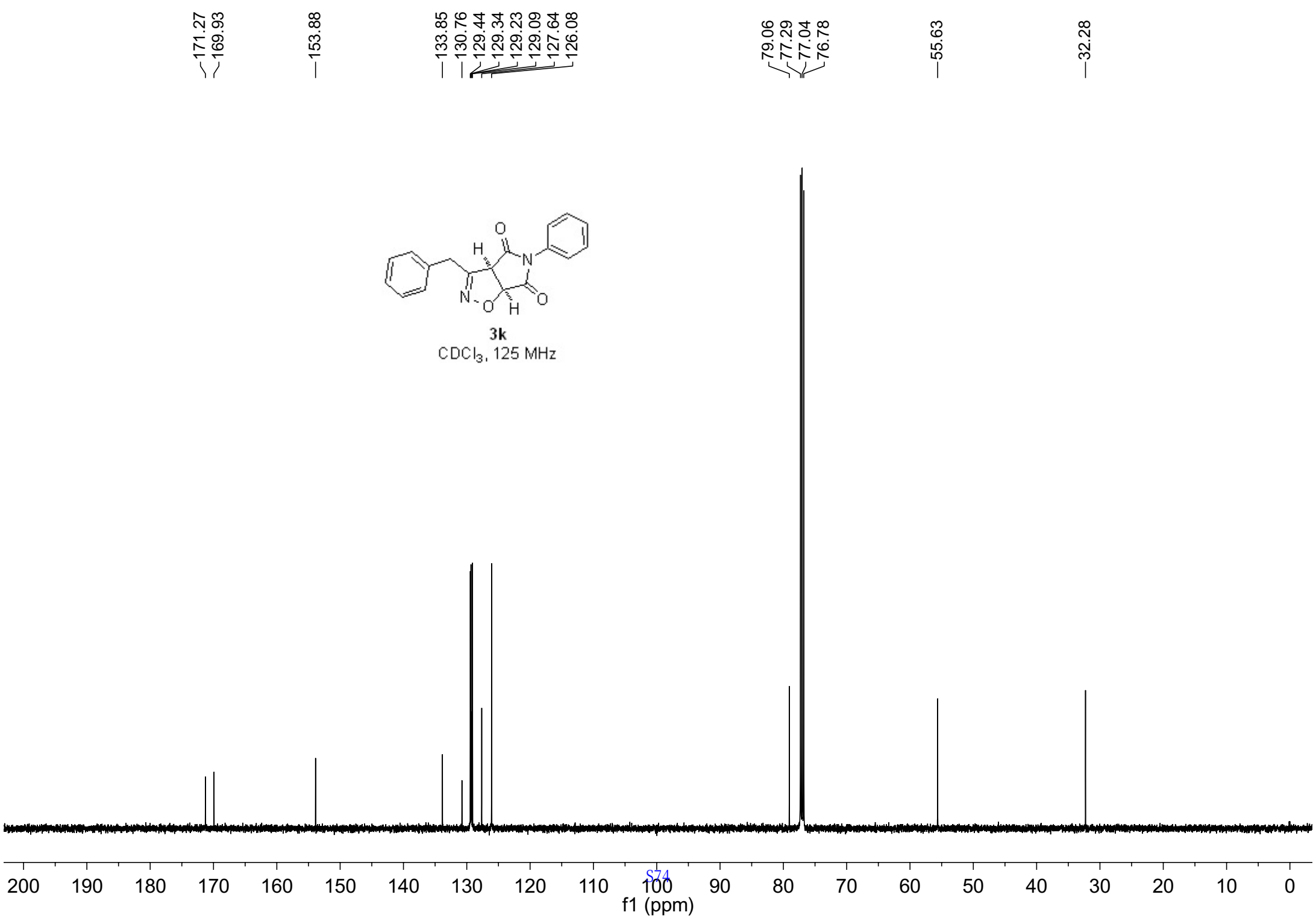

7.5013
7.4979
7.4868
7.4711
7.4395
7.4250
7.4099
7.2867
7.2840
7.2695
7.2604
5.4516
5.4325
4.5366
4.5174
2.6082
2.5921
2.5859
2.5796
2.5700
1.9709
1.8272
1.8089
1.7002
1.3695
1.3456
1.3323
1.3259
1.3203
1.3005
1.2841
1.2703
1.2525
1.2461
O
H
N
O
N
O
H
3i
CDCl3, 500 MHz
2.02
1.03
2.35
1.00
1.03
1.05
1.05
1.10
2.13
1.08
1.72
4.34
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

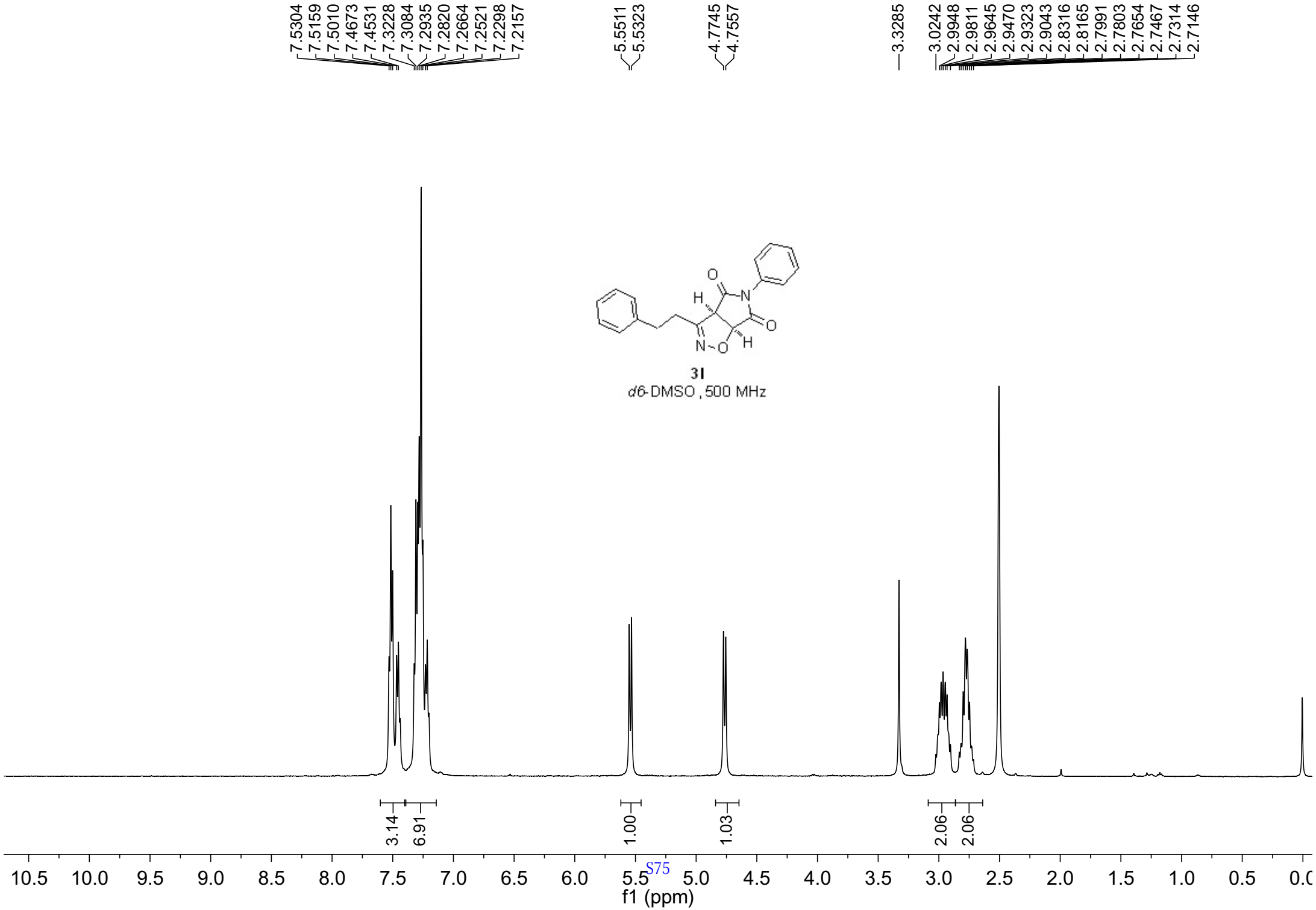

171.67
170.37
158.45
130.97
129.46
129.30
126.23
78.81
77.41
77.16
76.90
56.00
36.38
29.52
26.00
25.89
25.59
O
H
N
O
N
O
H
3i
CDCl3, 125 MHz
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

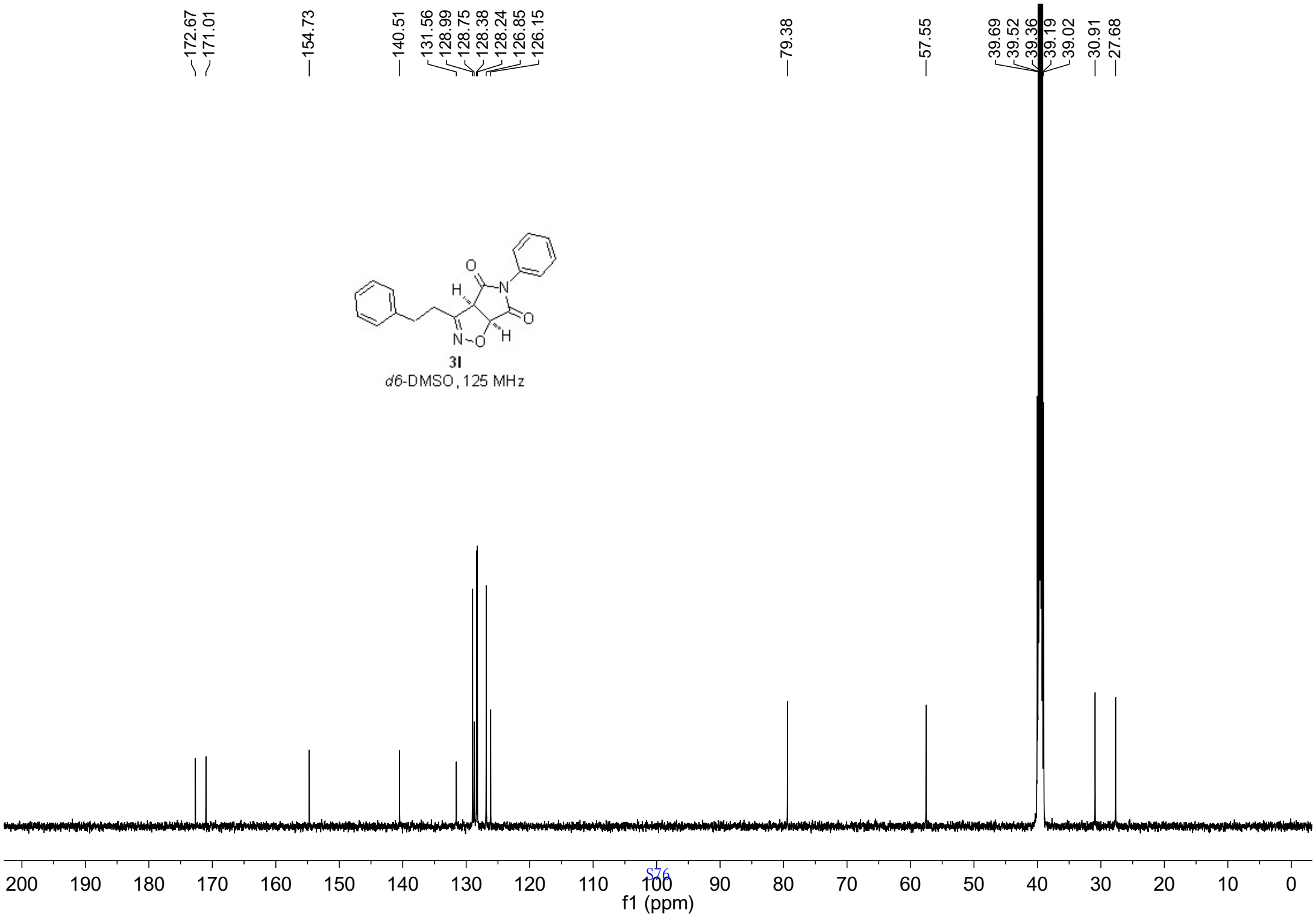

7.5263
7.5239
7.5204
7.5096
7.5066
7.4971
7.4939
7.4892
7.4688
7.4662
7.4637
7.4558
7.4515
7.4466
7.4366
7.2853
7.2829
7.2788
7.2714
7.2685
7.2671
5.5304
5.5113
4.6082
4.5890
1.3873
3j
CDCl3, 500 MHz
2.10
1.02
2.28
1.00
1.04
9.70
f1 (ppm)

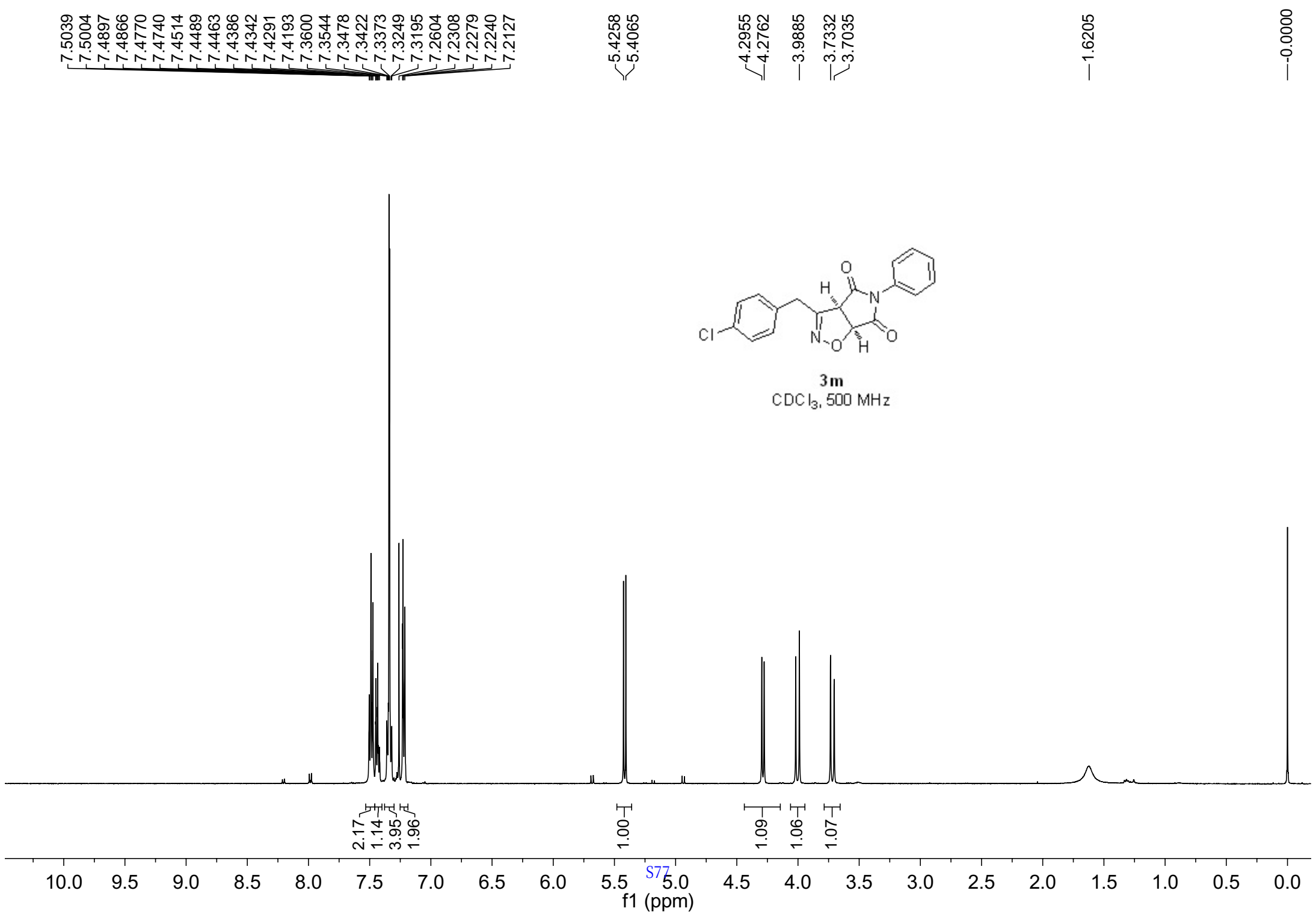

171.62
170.86
161.58
131.05
129.52
129.35
126.27
80.05
77.41
77.16
76.90
55.94
34.25
28.73
3j
CDCl3, 125 MHz
f1 (ppm)

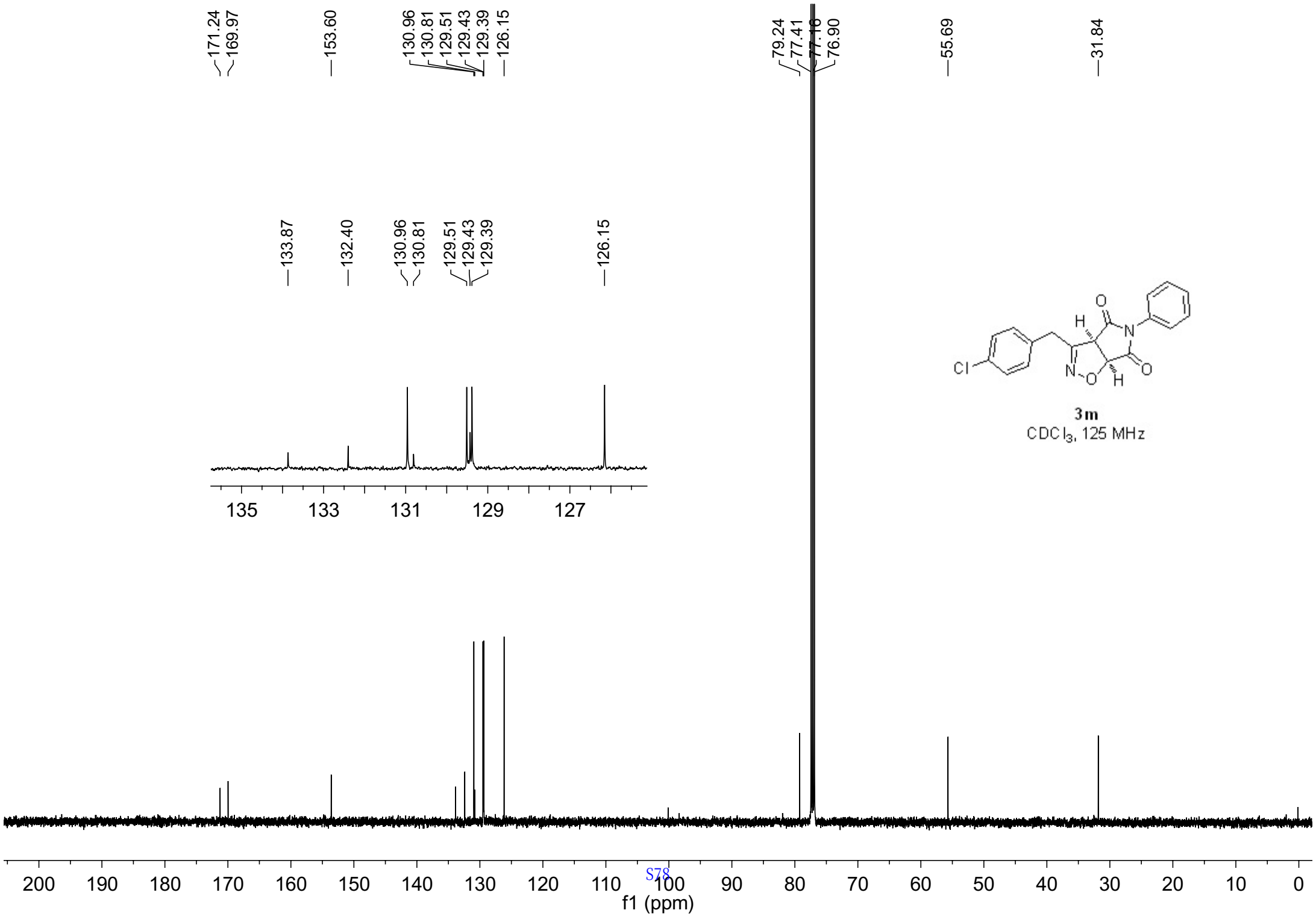

7.4946
7.4803
7.4646
7.4404
7.4258
7.4081
7.4042
7.3877
7.3732
7.3577
7.3275
7.3139
7.3005
7.2603
7.2352
7.2201
5.3920
5.3727
4.3072
4.2880
4.0232
3.7531
3.7237
1.5854
0.0036
O
H
N
N
O
O
H
3k
CDCl3, 500 MHz
7.21
1.06
2.04
1.00
1.01
1.06
1.10
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

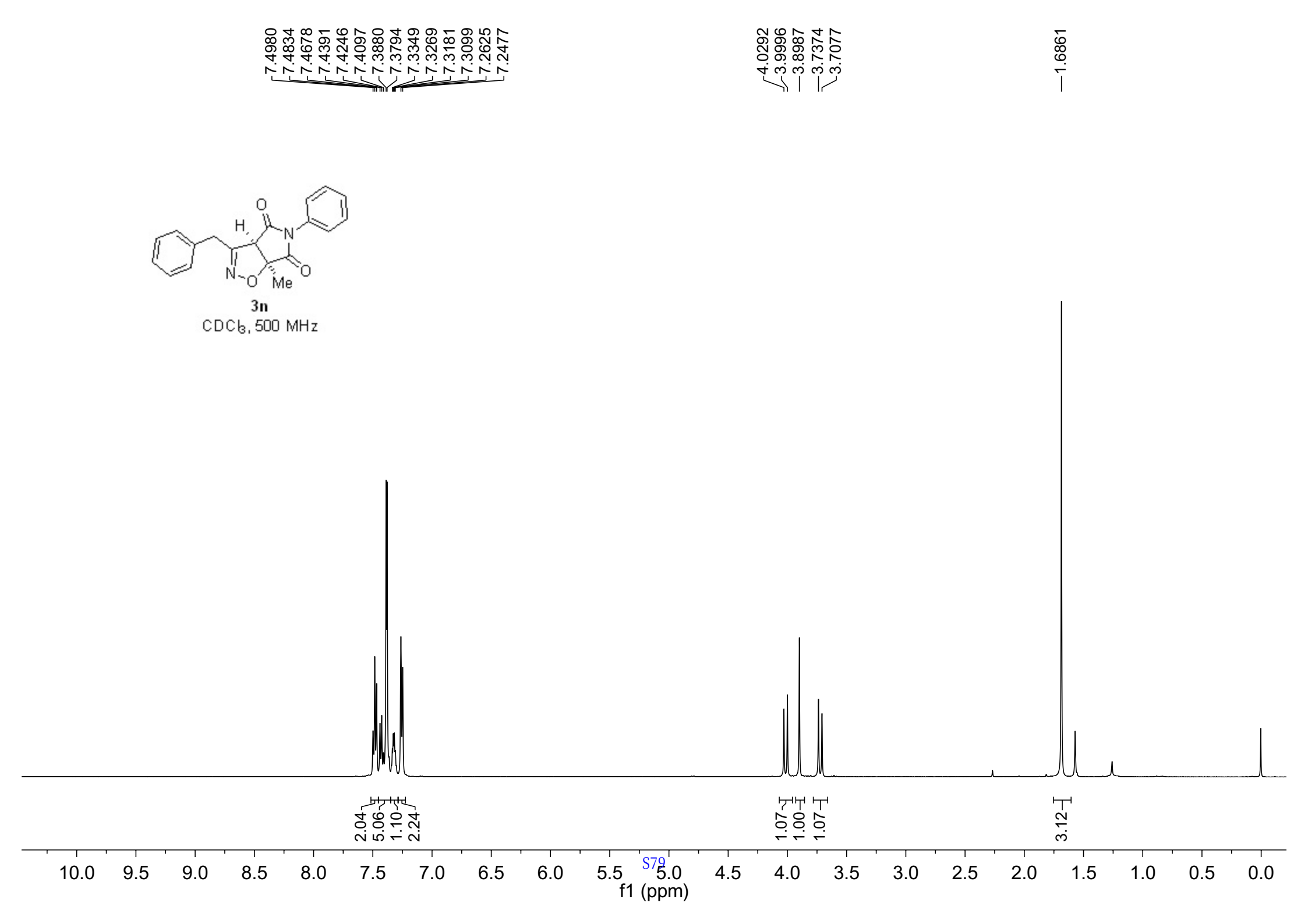

171.27
169.93
153.88
133.85
130.76
129.44
129.34
129.23
129.09
127.64
126.08
79.06
77.29
77.04
76.78
55.63
32.28
O
H
N
O
N
O
H
3k
CDCl3, 125 MHz
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

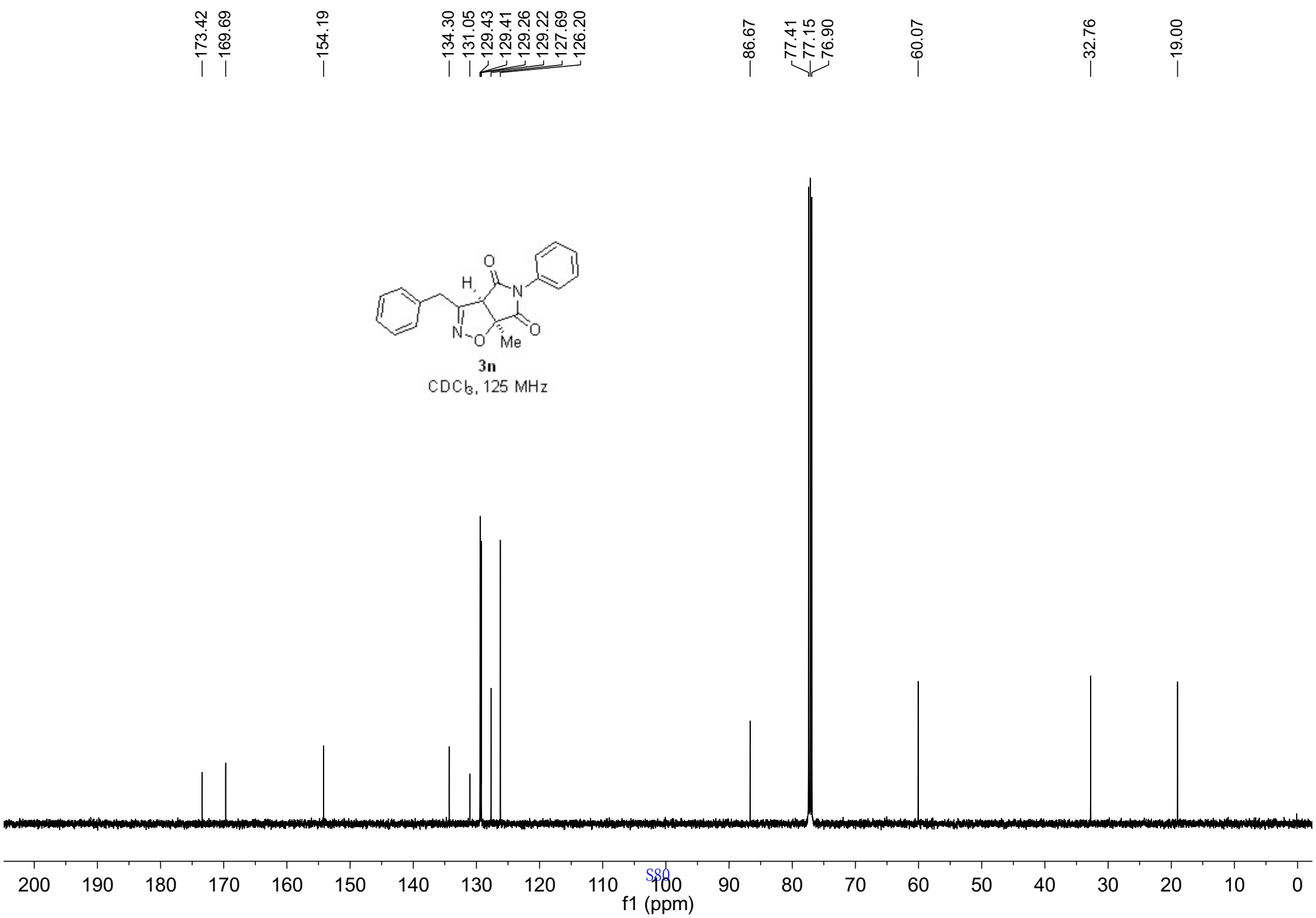

7.5304
7.5159
7.5010
7.4673
7.4531
7.3228
7.3084
7.2935
7.2820
7.2664
7.2521
7.2298
7.2157
5.5511
5.5323
4.7745
4.7557
3.3285
3.0242
2.9948
2.9811
2.9645
2.9470
2.9323
2.9043
2.8316
2.8165
2.7991
2.7803
2.7654
2.7467
2.7314
2.7146
O
N
H
O
N
O
H
3l
d6-DMSO , 500 MHz
3.14
6.91
1.00
1.03
2.06
2.06
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

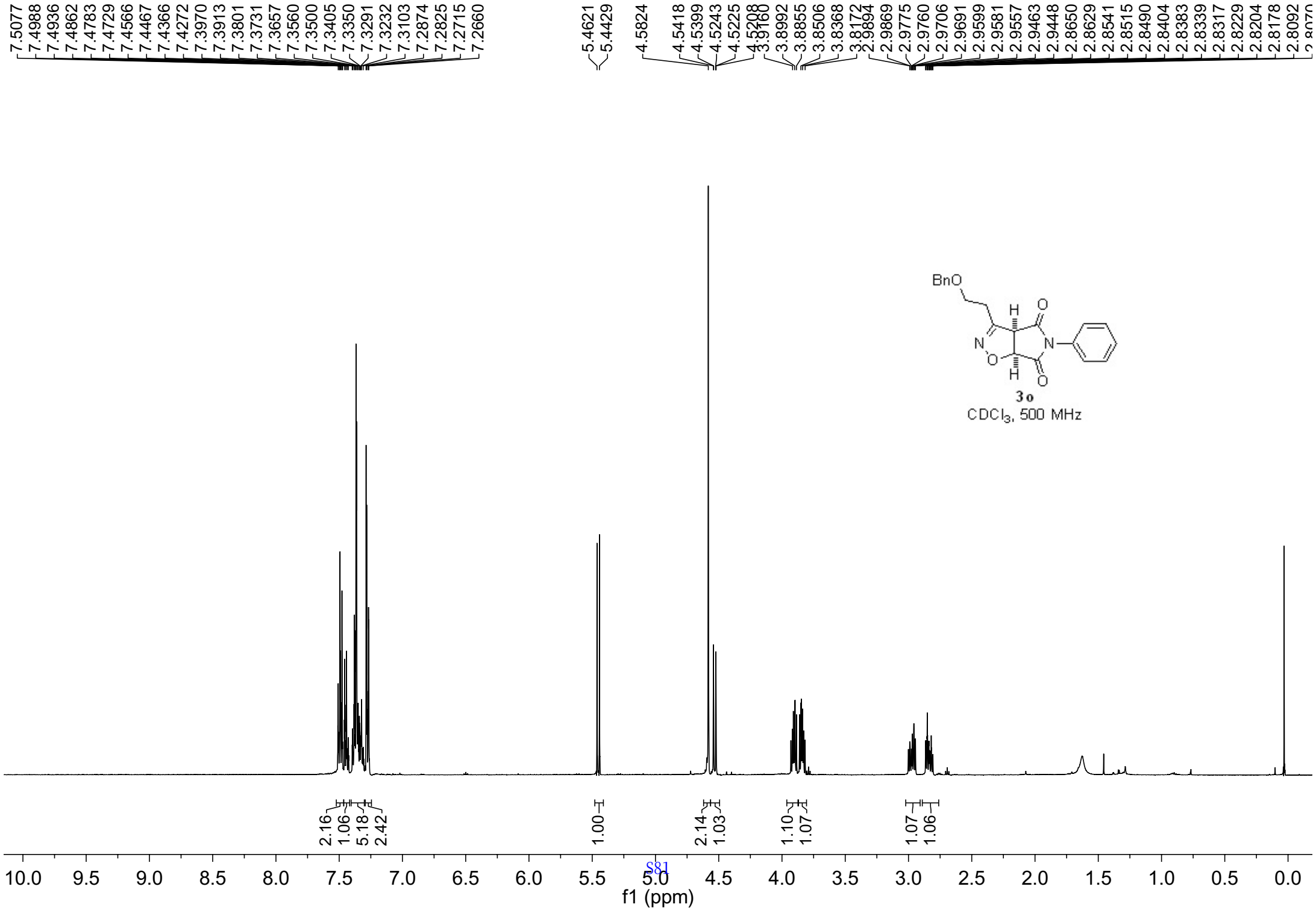

172.67
171.01
154.73
140.51
131.56
128.99
128.75
128.38
128.24
126.85
126.15
79.38
57.55
39.69
39.52
39.36
39.19
39.02
30.91
27.68
O
H
N
O
O
N
O
H
3l
d6-DMSO, 125 MHz
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

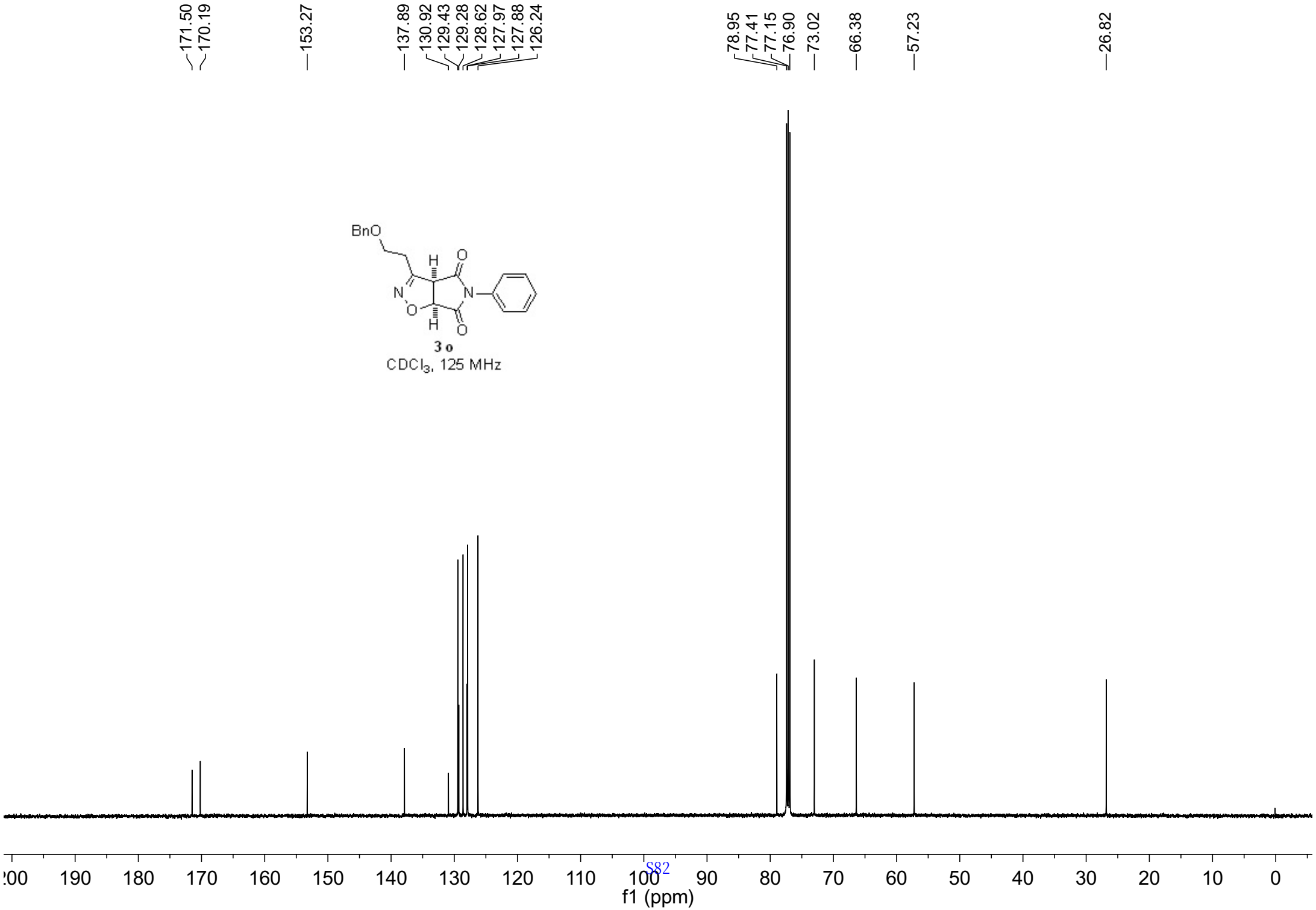

7.5039
7.5004
7.4897
7.4866
7.4770
7.4740
7.4514
7.4489
7.4463
7.4386
7.4342
7.4291
7.4193
7.3600
7.3544
7.3478
7.3422
7.3373
7.3249
7.3195
7.2604
7.2308
7.2279
7.2240
7.2127
5.4258
5.4065
4.2955
4.2762
3.9885
3.7332
3.7035
1.6205
-0.0000
Cl
O
H
N
O
N
O
H
O
3m
CDCl3, 500 MHz
2.17
1.14
3.95
1.96
1.00
1.09
1.06
1.07
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

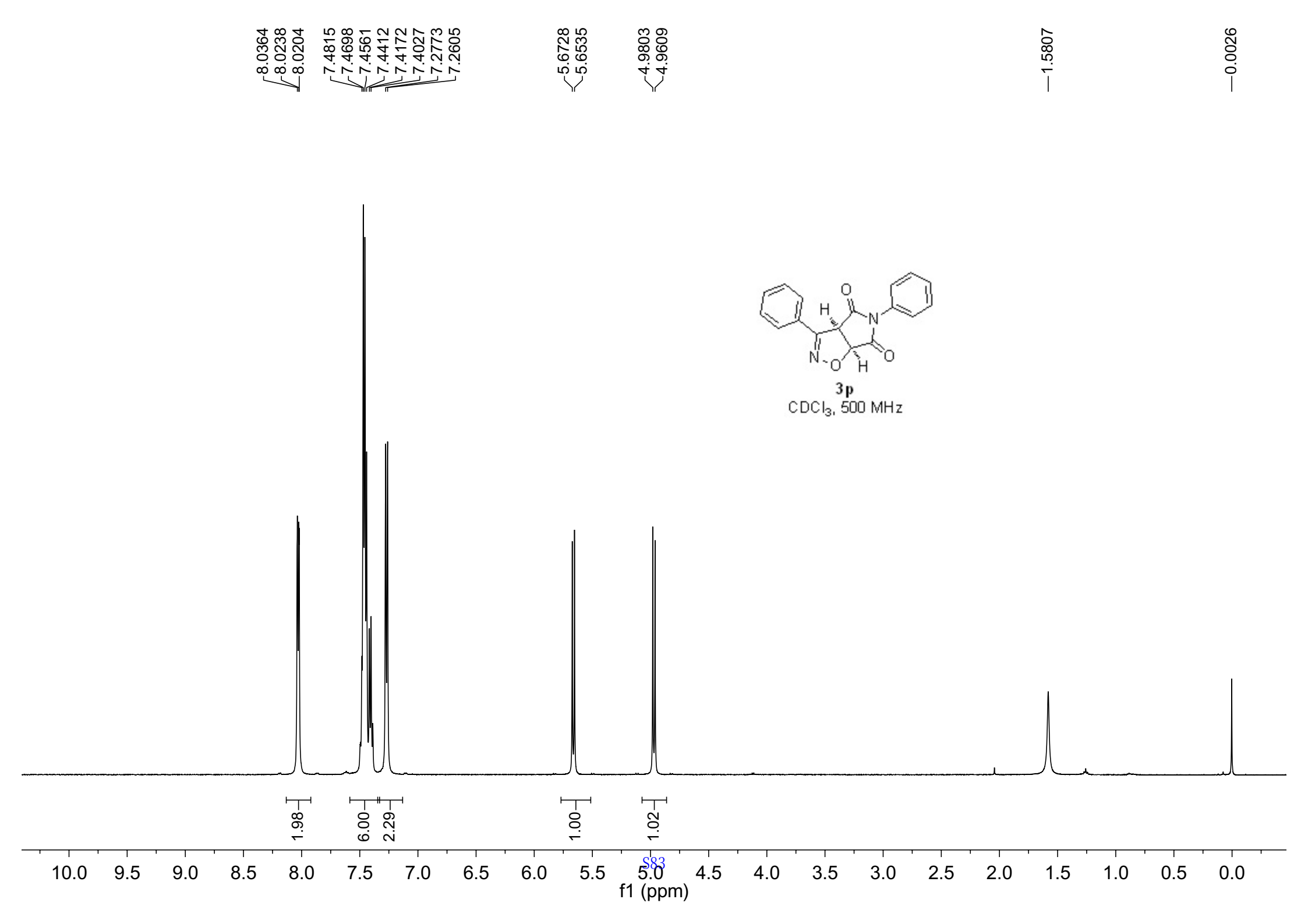

171.24
169.97
153.60
130.96
130.81
129.51
129.43
129.39
126.15
79.24
77.41
77.16
76.90
55.69
31.84
133.87
132.40
130.96
130.81
129.51
129.43
129.39
126.15
135
133
131
129
127
Cl
O
H
N
O
O
N
O
H
3m
CDCl3, 125 MHz
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

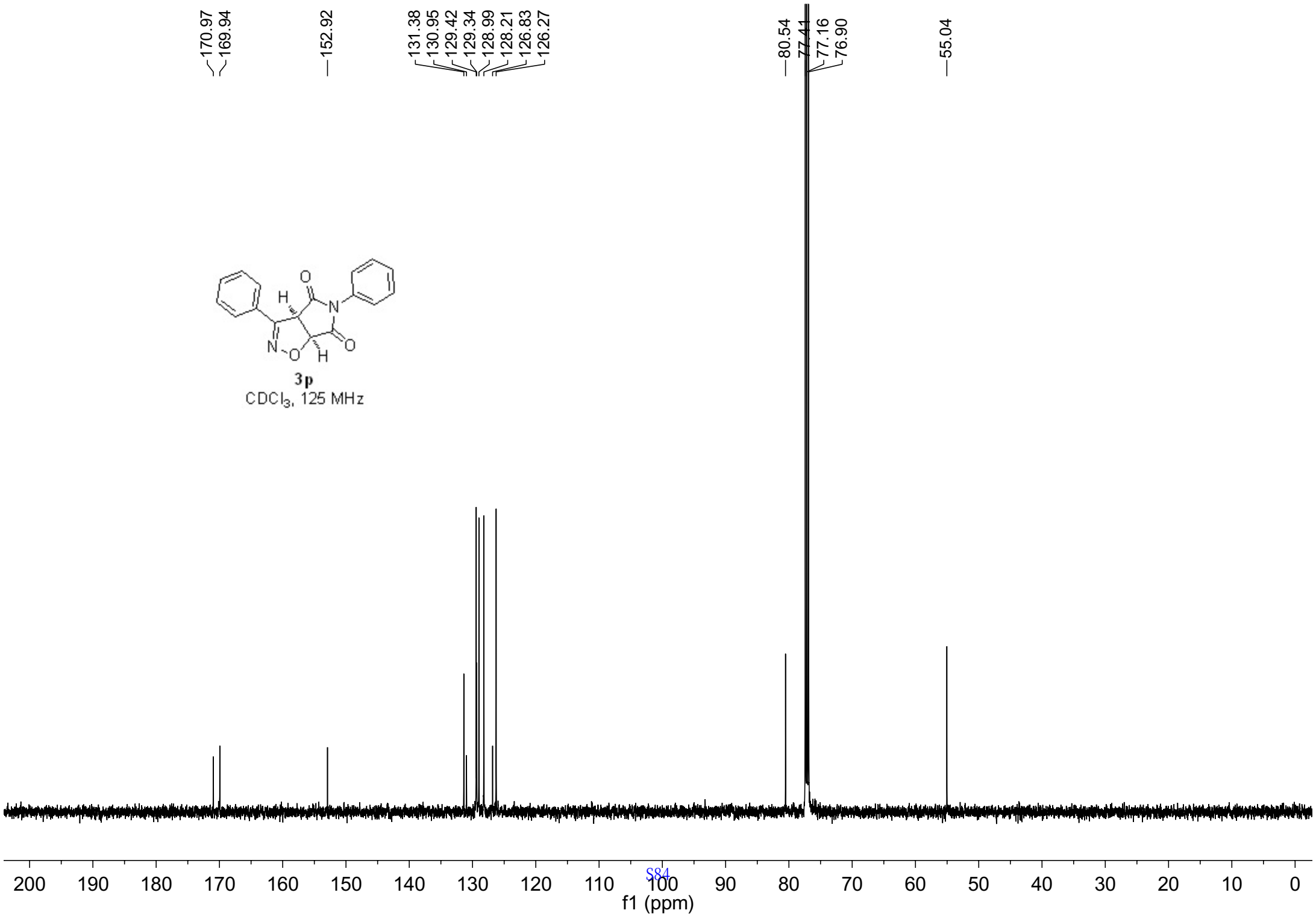

7.4980
7.4834
7.4678
7.4391
7.4246
7.4097
7.3880
7.3794
7.3349
7.3269
7.3181
7.3099
7.2625
7.2477
4.0292
3.9996
3.8987
3.7374
3.7077
1.6861
O
H
N
O
N
O
Me
3n
CDCl3, 500 MHz
2.04
5.06
1.10
2.24
1.07
1.00
1.07
3.12
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

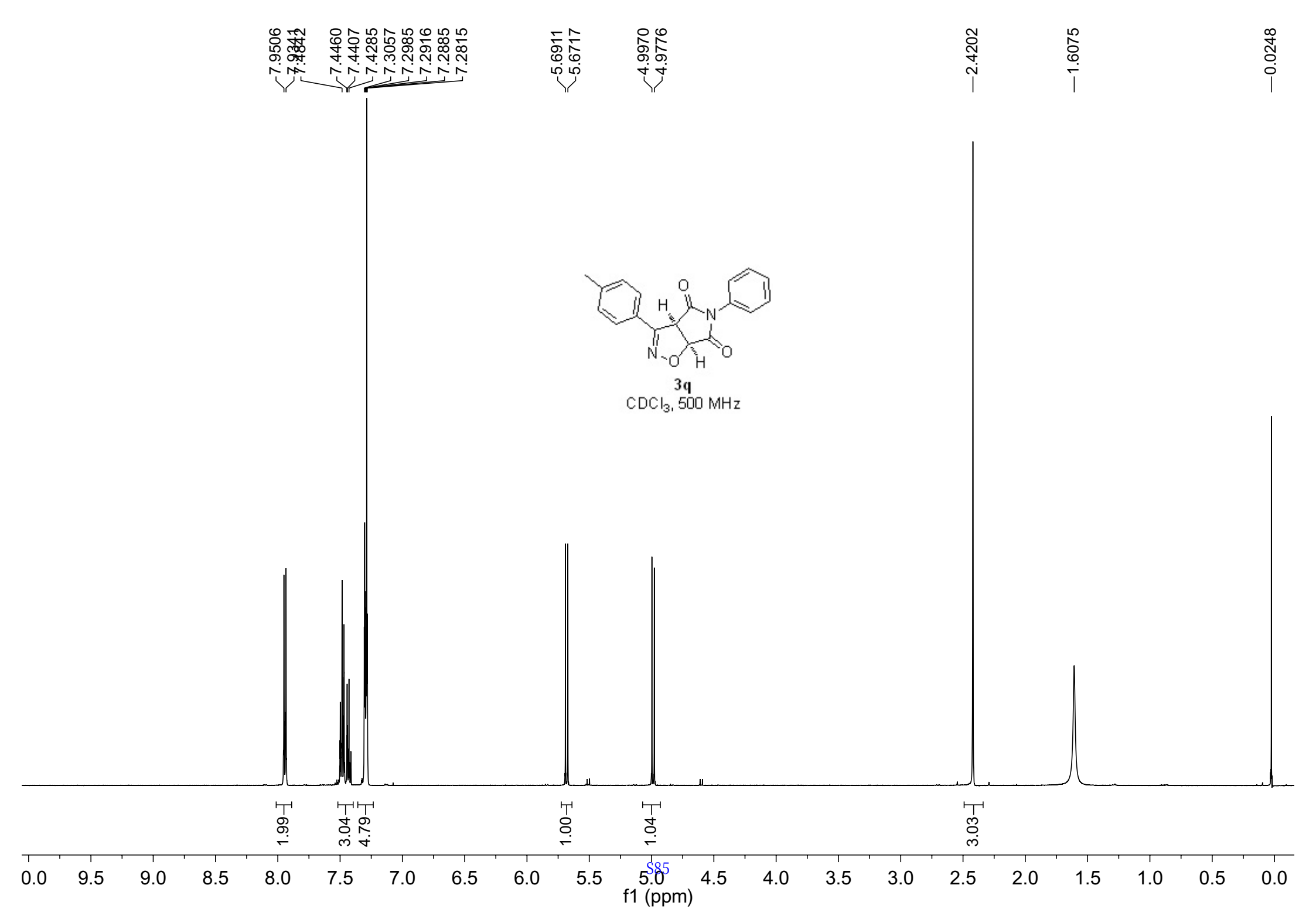

173.42
169.69
154.19
134.30
131.05
129.43
129.41
129.26
129.22
127.69
126.20
86.67
77.41
77.15
76.90
60.07
32.76
19.00
O
H
N
O
N
O
Me
3n
CDCl3, 125 MHz
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

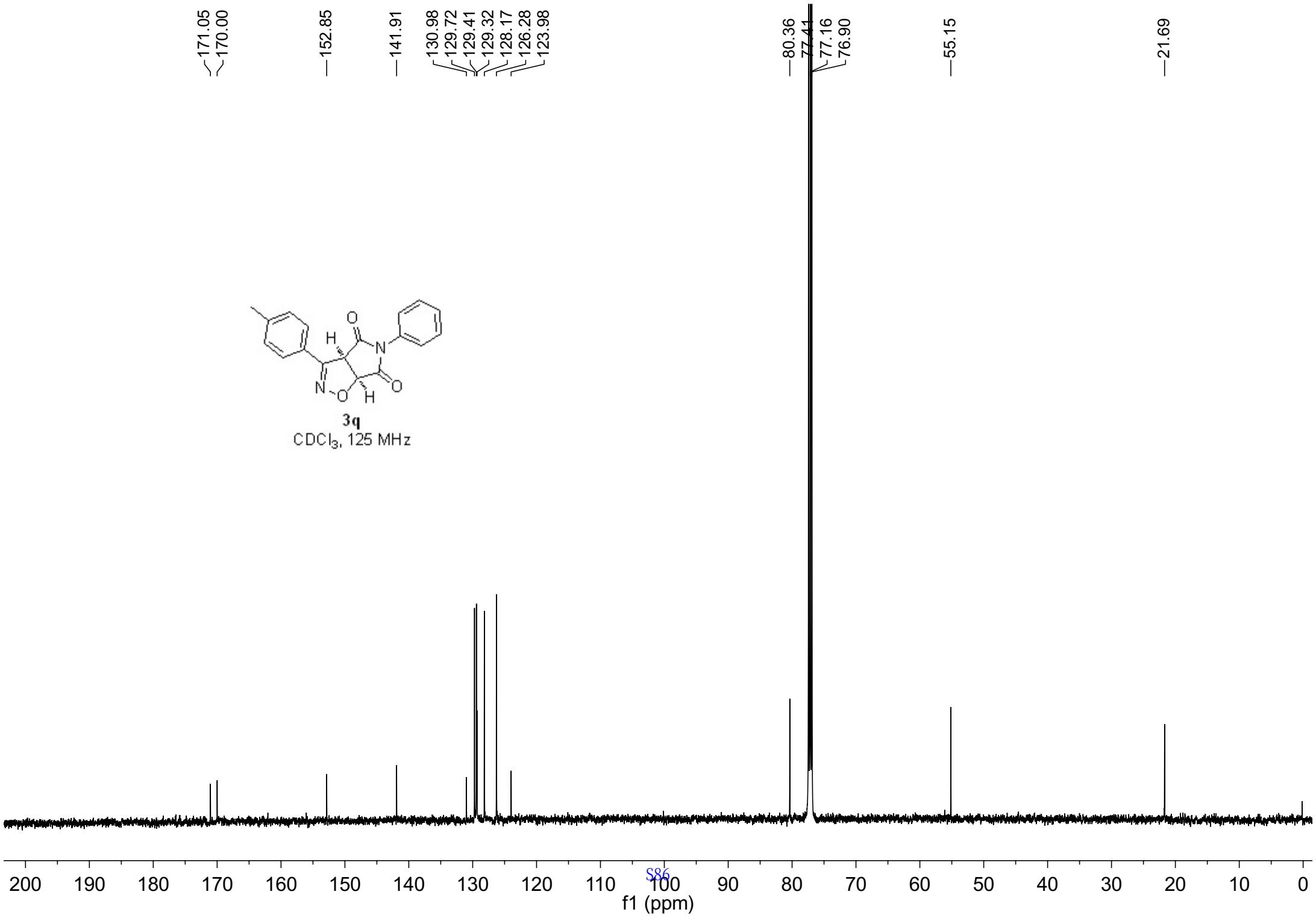

7.5077
7.4988
7.4936
7.4862
7.4783
7.4729
7.4566
7.4467
7.4366
7.4272
7.3970
7.3913
7.3801
7.3731
7.3657
7.3560
7.3500
7.3405
7.3350
7.3291
7.3232
7.3103
7.2874
7.2825
7.2715
7.2660
5.4621
5.4429
4.5824
4.5418
4.5399
4.5243
4.5225
4.5208
3.9160
3.8992
3.8855
3.8506
3.8368
3.8172
2.9894
2.9869
2.9775
2.9760
2.9706
2.9691
2.9599
2.9581
2.9557
2.9463
2.9448
2.8650
2.8629
2.8541
2.8515
2.8490
2.8404
2.8383
2.8339
2.8317
2.8229
2.8204
2.8178
2.8092
BnO
H
O
N
N
O
H
O
3o
CDCl3, 500 MHz
2.16
1.06
5.18
2.42
1.00
2.14
1.03
1.10
1.07
1.07
1.06
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

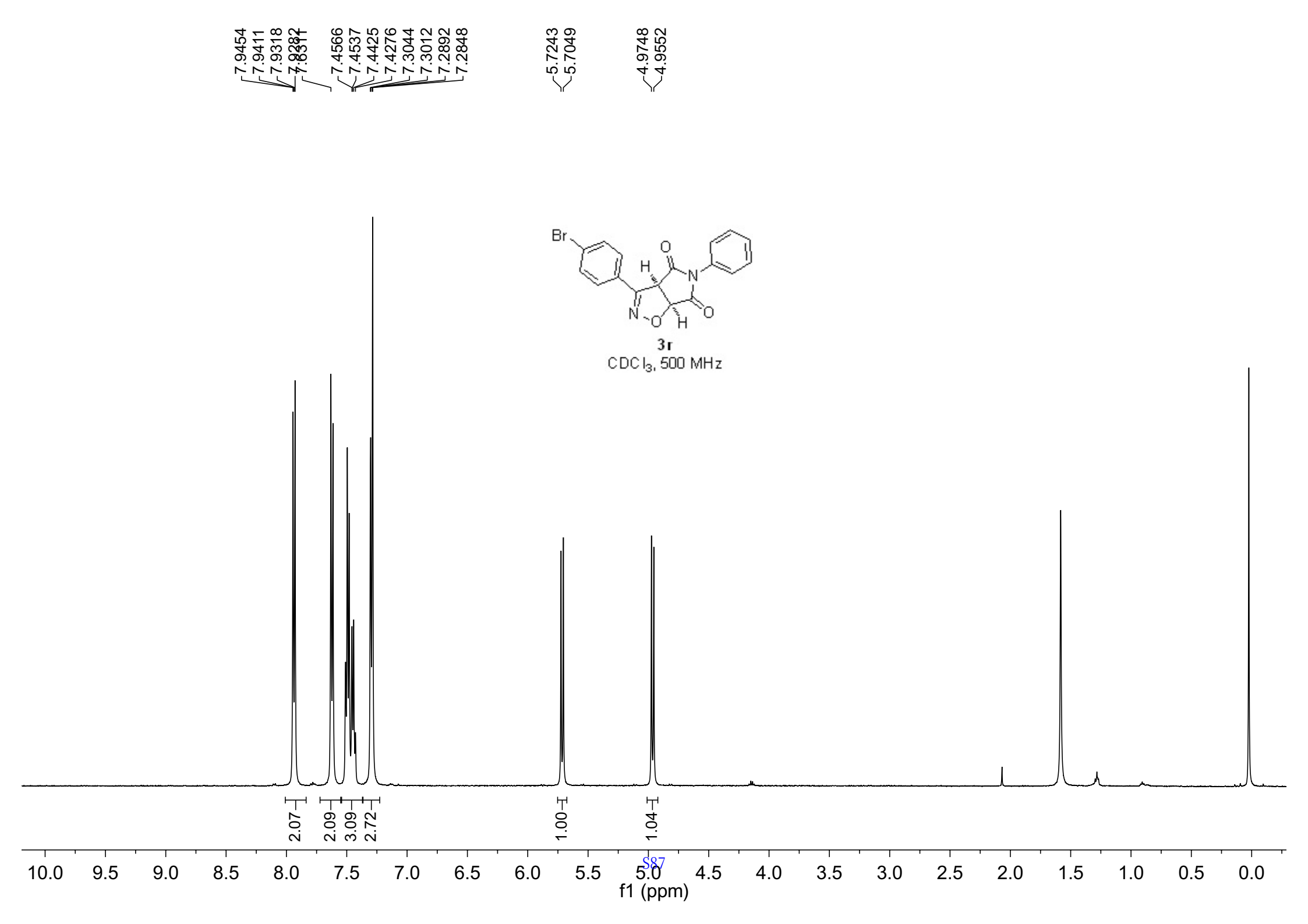

171.50
170.19
153.27
137.89
130.92
129.43
129.28
128.62
127.97
127.88
126.24
78.95
77.41
77.15
76.90
73.02
66.38
57.23
26.82
BnO
O
H
N
N
O
H
O
3 o
CDCl3, 125 MHz
f1 (ppm)

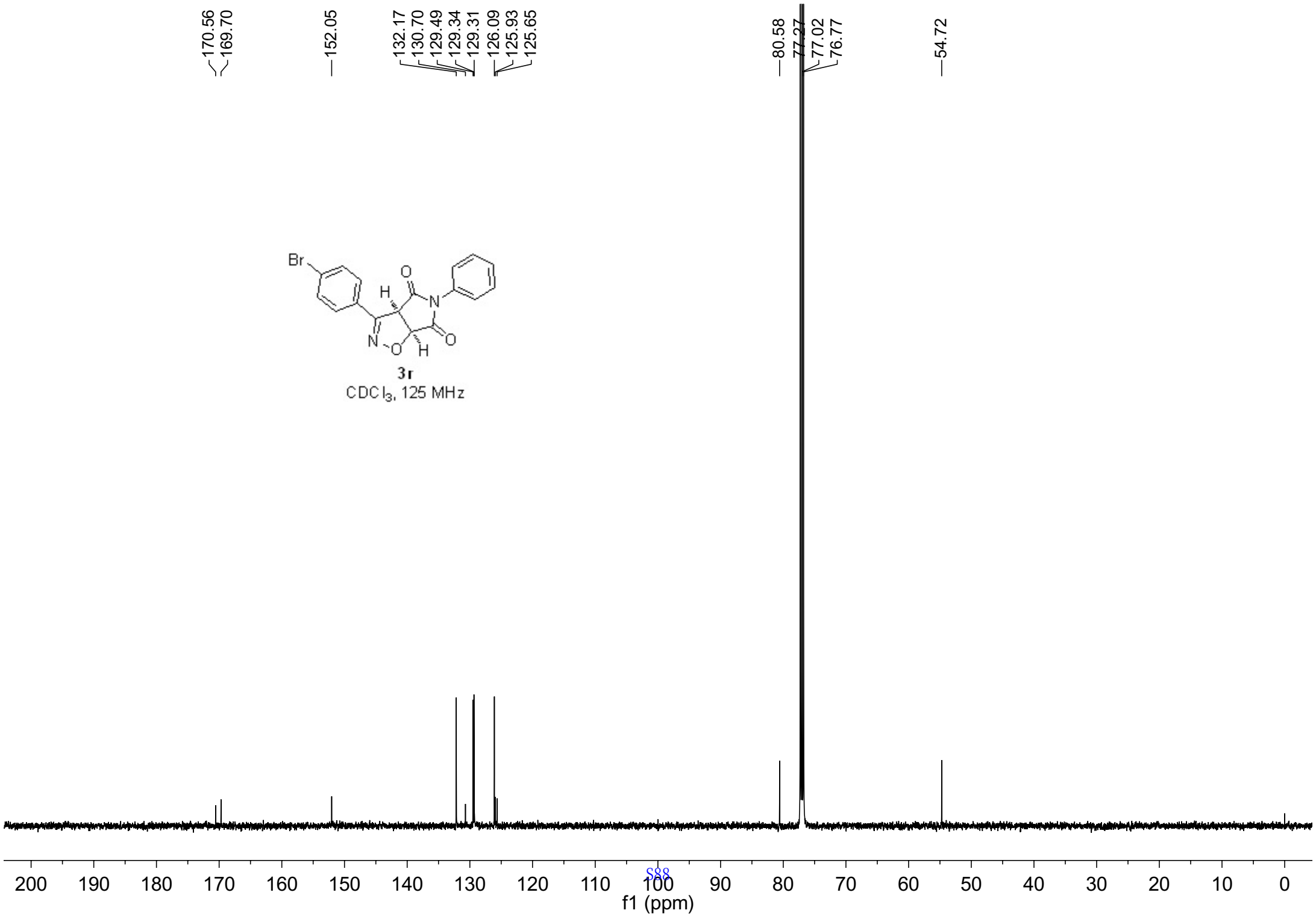

8.0364
8.0238
8.0204
7.4815
7.4698
7.4561
7.4412
7.4172
7.4027
7.2773
7.2605
5.6728
5.6535
4.9803
4.9609
1.5807
0.0026
3p
CDCl3, 500 MHz
1.98
6.00
2.29
1.00
1.02
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

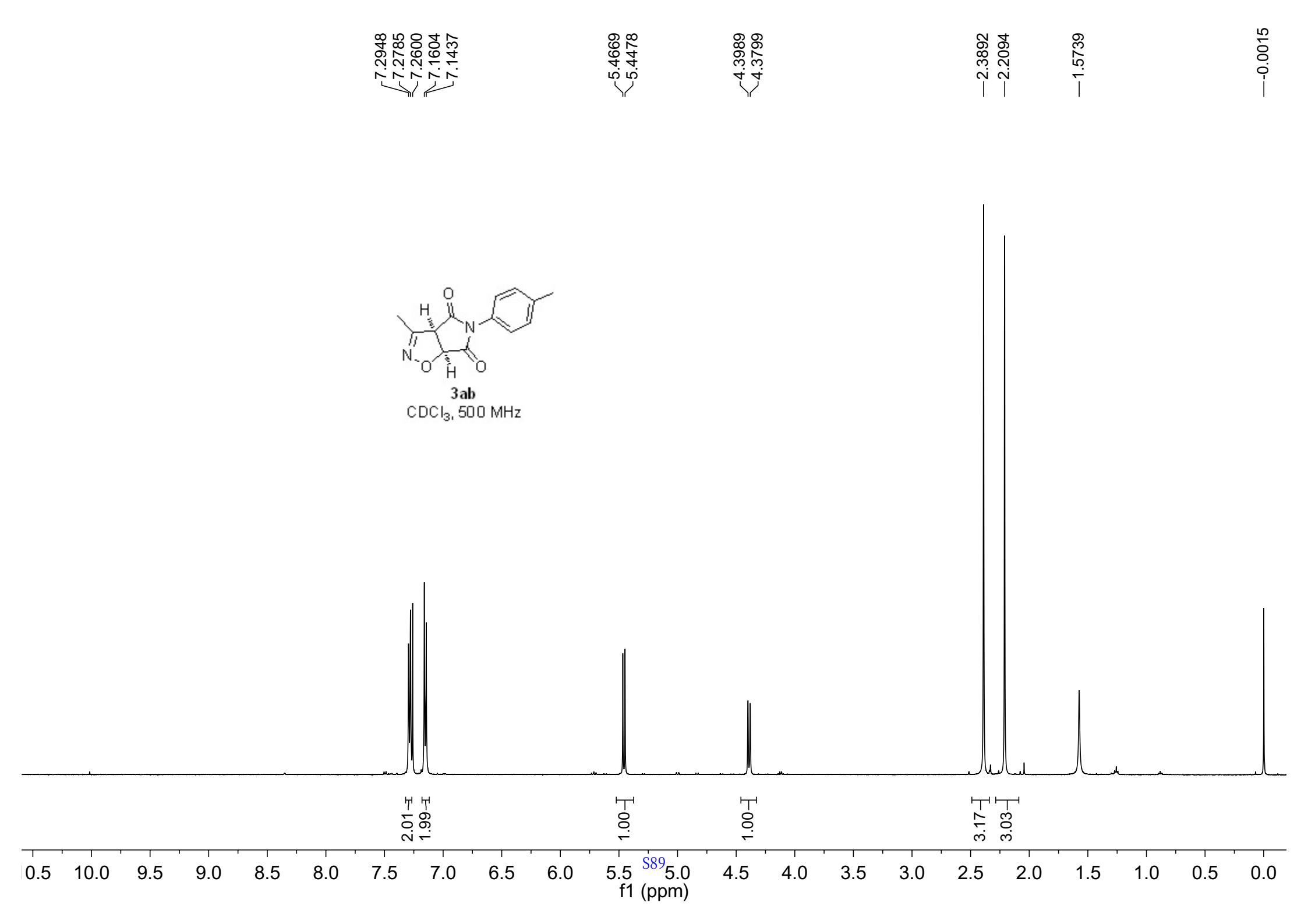

170.97
169.94
152.92
131.38
130.95
129.42
129.34
128.99
128.21
126.83
126.27
80.54
77.41
77.16
76.90
55.04
O
H
N
O
N
O
H
3p
CDCl3, 125 MHz
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

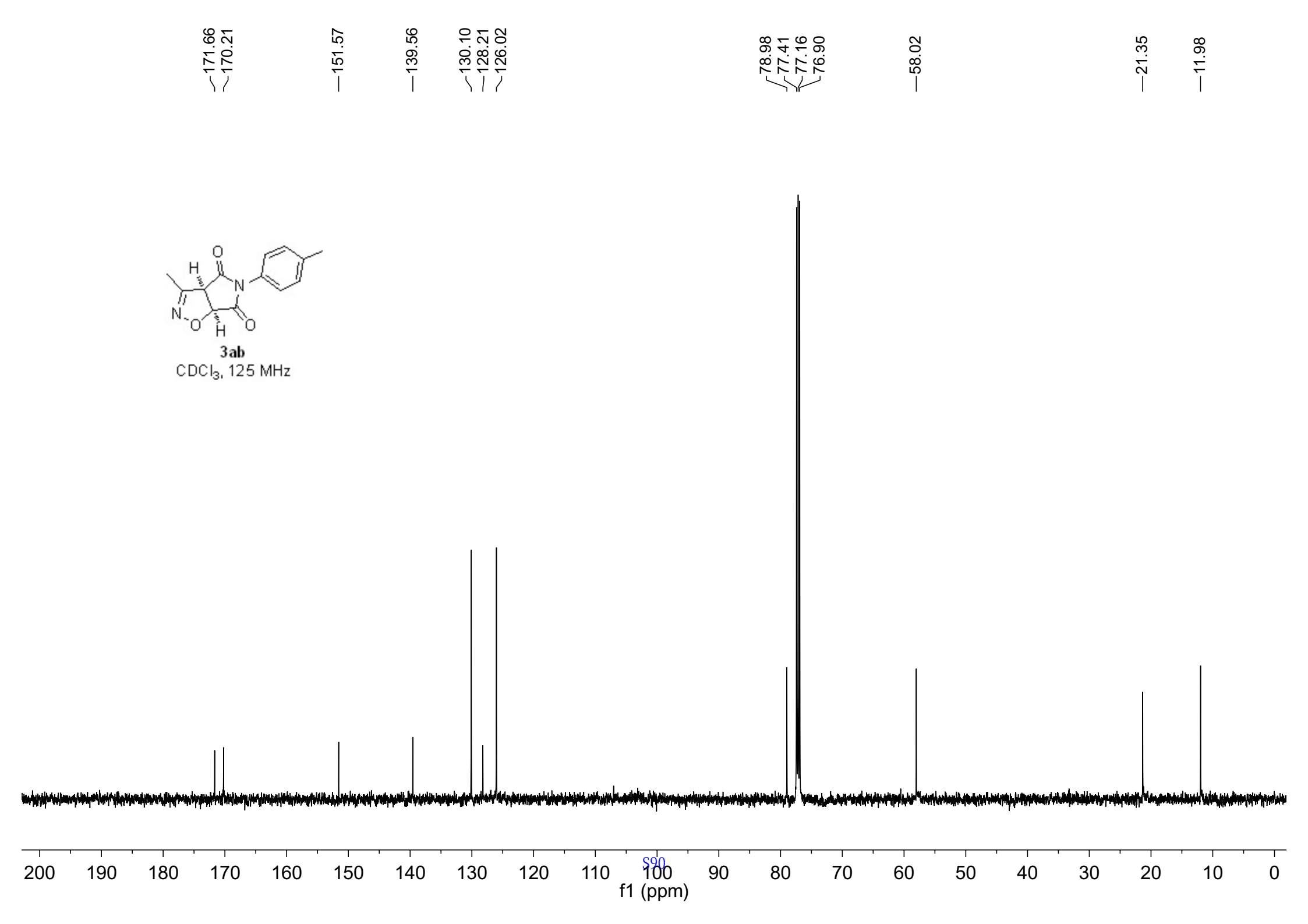

7.9506
7.9341
7.9242
7.4460
7.4407
7.4285
7.3057
7.2985
7.2916
7.2885
7.2815
5.6911
5.6717
4.9970
4.9776
2.4202
1.6075
0.0248
3q
CDCl3, 500 MHz
1.99
3.04
4.79
1.00
1.04
3.03
0.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

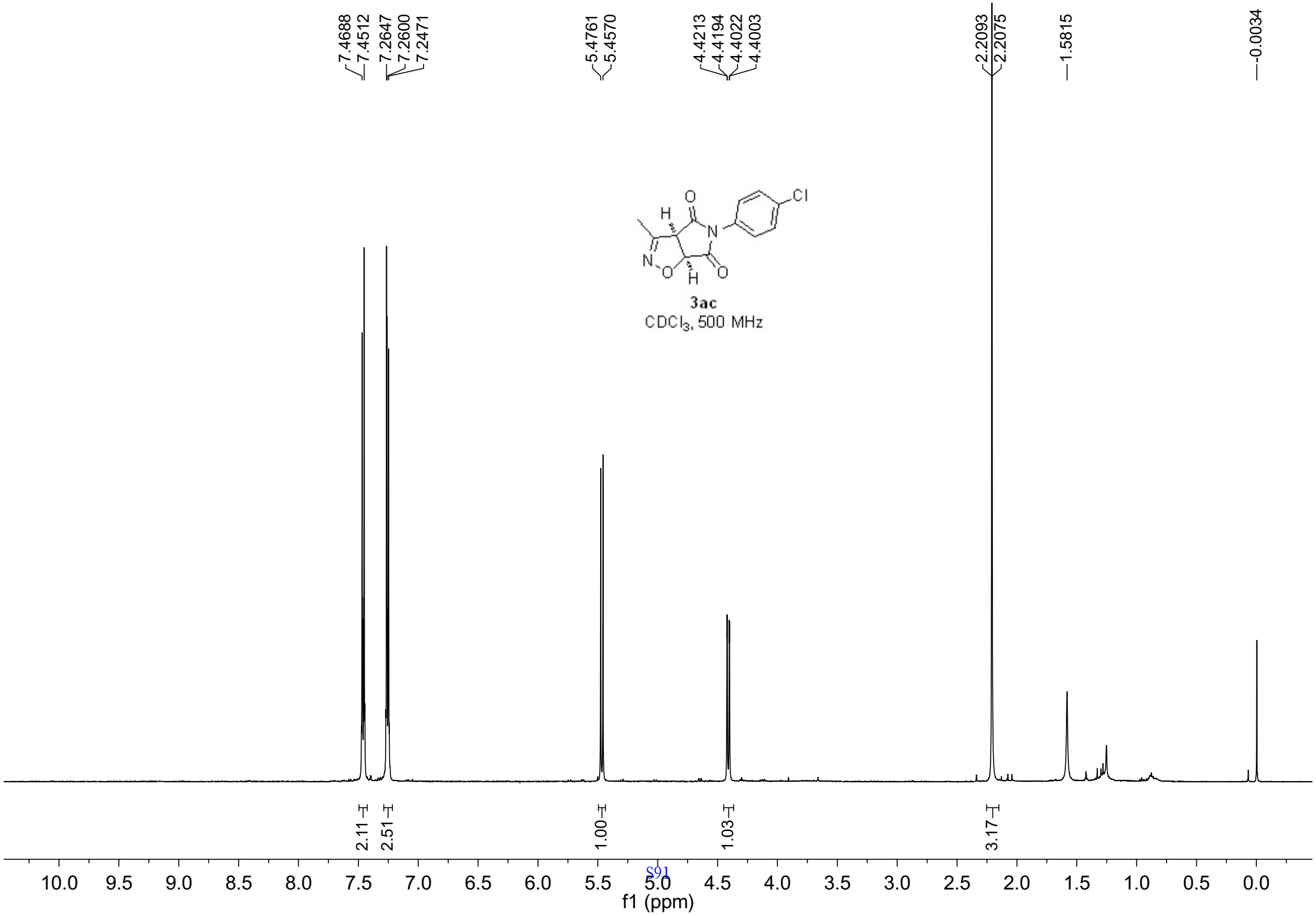

171.05
170.00
152.85
141.91
130.98
129.72
129.41
129.32
128.17
126.28
123.98
80.36
77.41
77.16
76.90
55.15
21.69
3q
CDCl3, 125 MHz
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

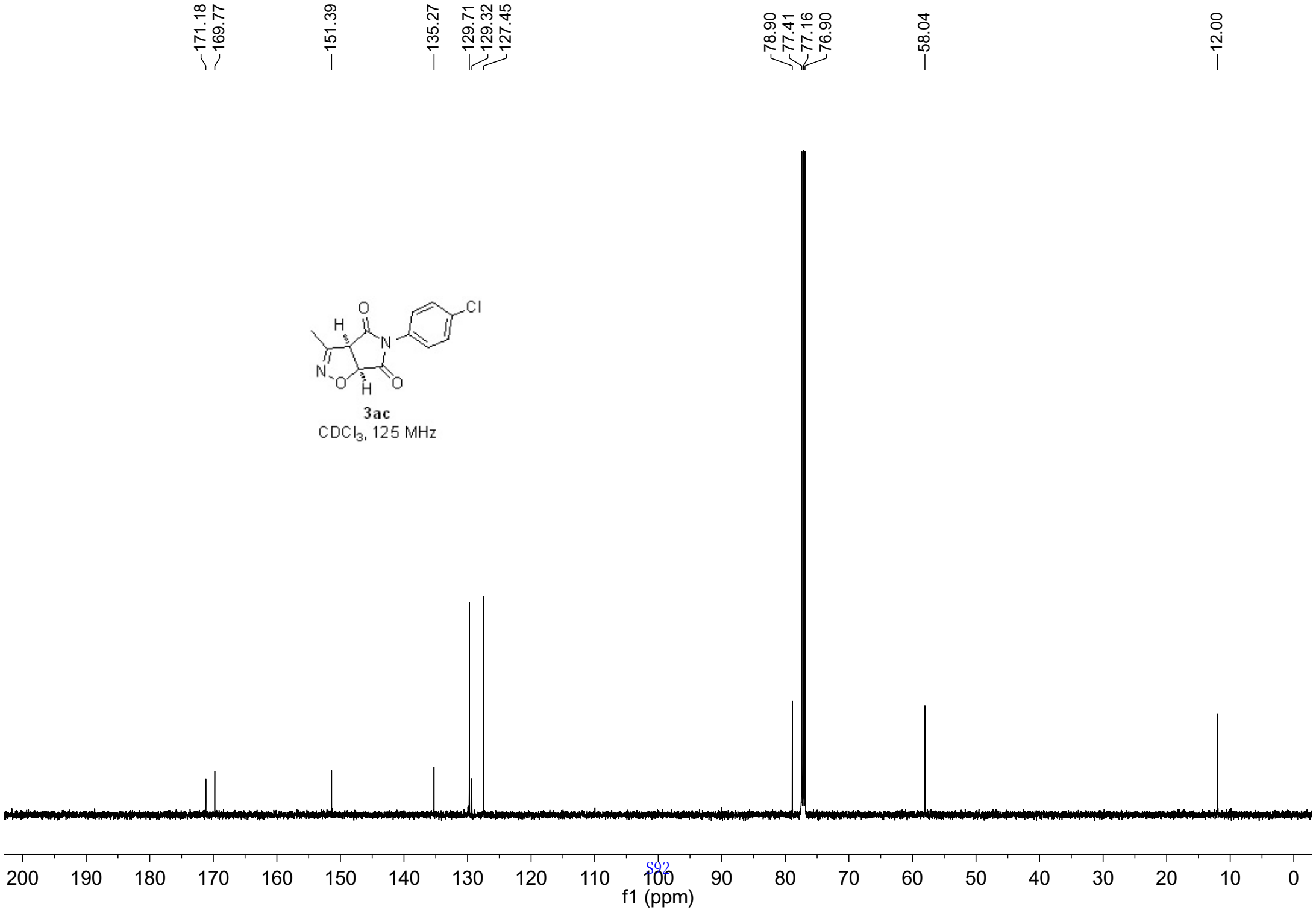

7.9454
7.9411
7.9318
7.8311
7.4566
7.4537
7.4425
7.4276
7.3044
7.3012
7.2892
7.2848
5.7243
5.7049
4.9748
4.9552
Br
O
H
N
O
N
O
H
3r
CDCl3, 500 MHz
2.07
2.09
3.09
2.72
1.00
1.04
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

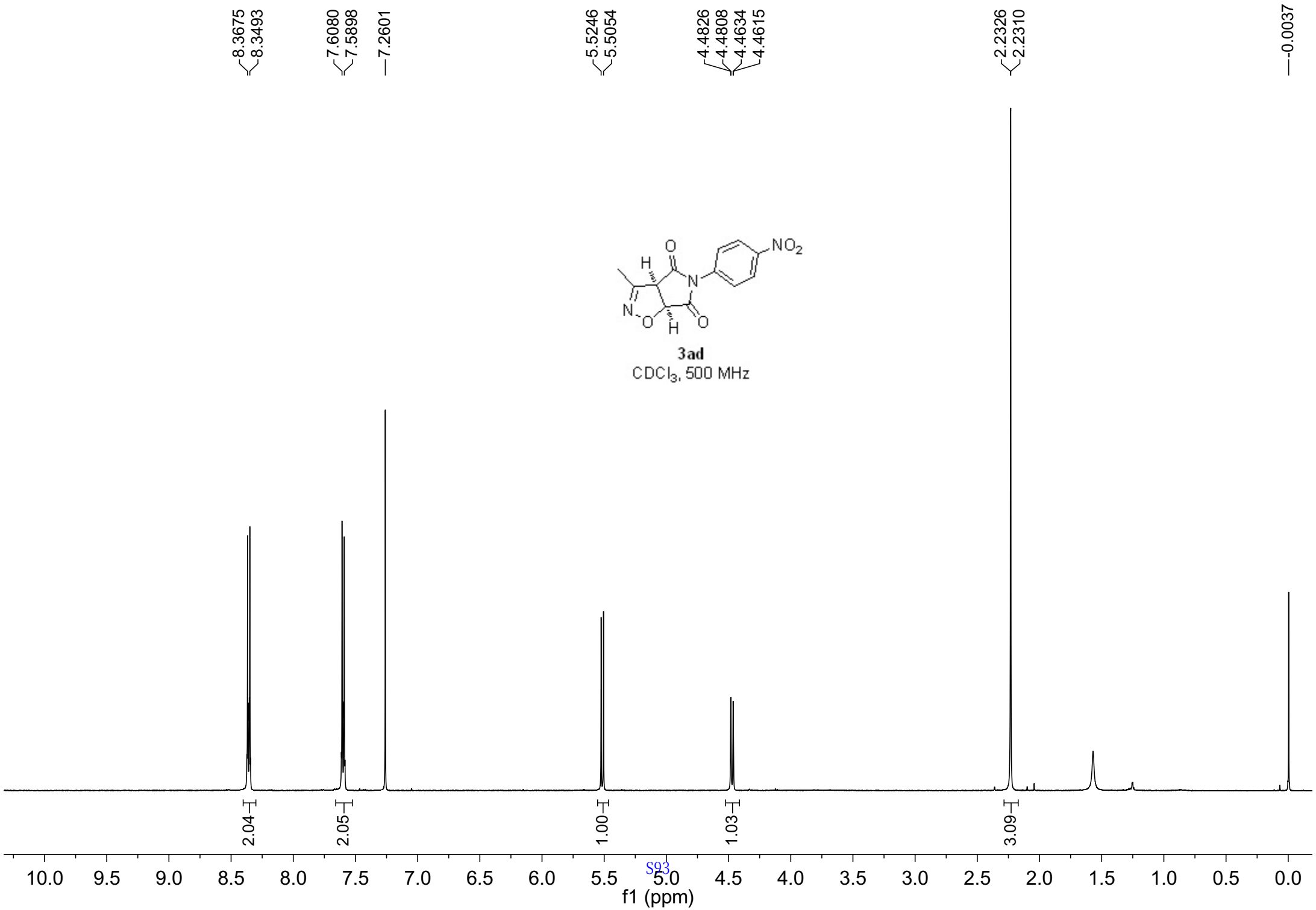

170.56
169.70
152.05
132.17
130.70
129.49
129.34
129.31
126.09
125.93
125.65
80.58
77.27
77.02
76.77
54.72
Br
O
H
N
O
N
O
H
3r
CDCl3, 125 MHz
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

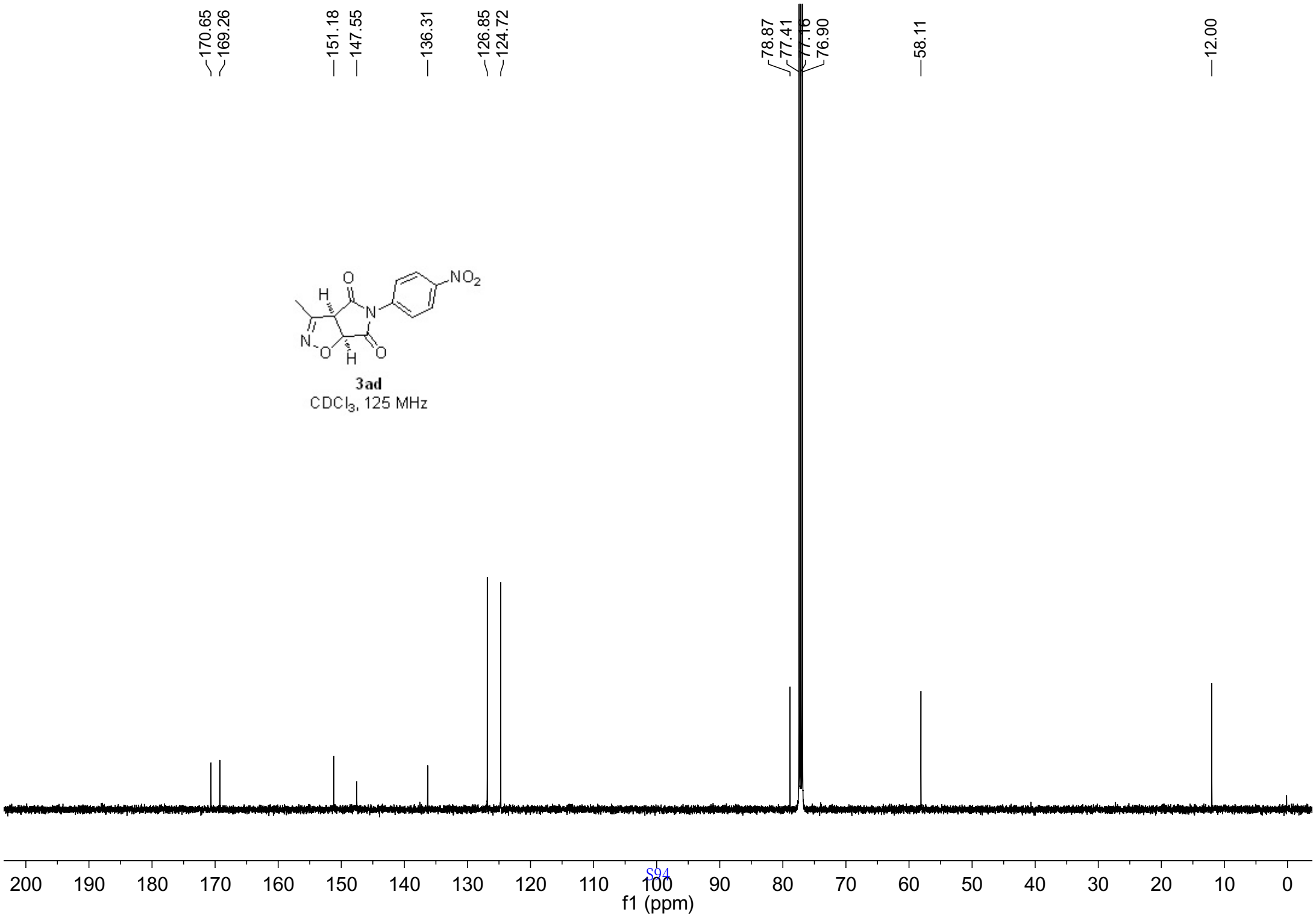

7.2948
7.2785
7.2600
7.1604
7.1437
5.4669
5.4478
4.3989
4.3799
2.3892
2.2094
1.5739
-0.0015
3ab
CDCl3, 500 MHz
2.01
1.99
1.00
1.00
3.17
3.03
f1 (ppm)

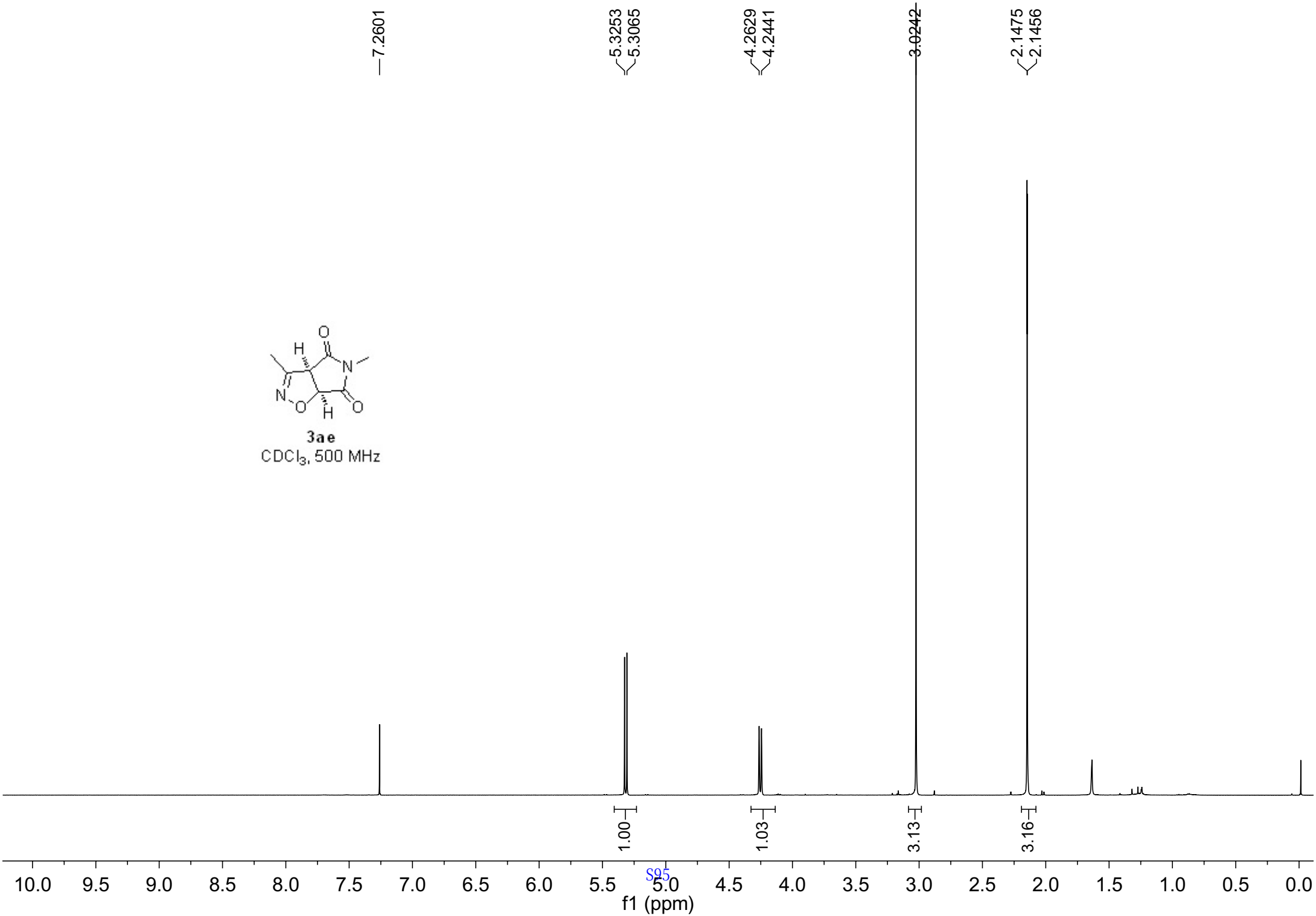

171.66
170.21
151.57
139.56
130.10
128.21
126.02
78.98
77.41
77.16
76.90
58.02
21.35
11.98
3ab
CDCl3, 125 MHz
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

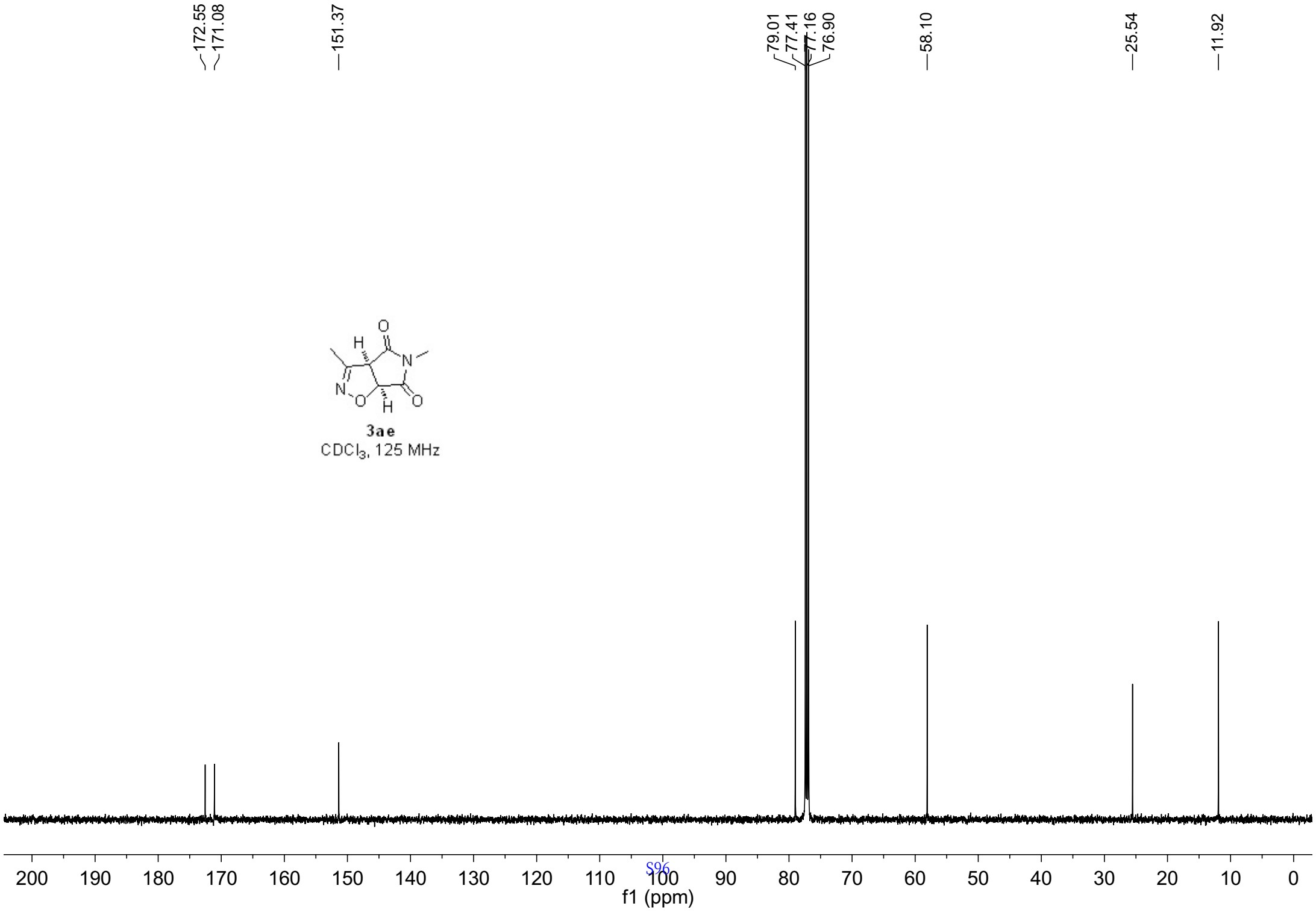

7.4688
7.4512
7.2647
7.2600
7.2471
5.4761
5.4570
4.4213
4.4194
4.4022
4.4003
2.2093
2.2075
1.5815
-0.0034
O
H
N
Cl
N
O
H
O
3ac
CDCl3, 500 MHz
2.11
2.51
1.00
1.03
3.17
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

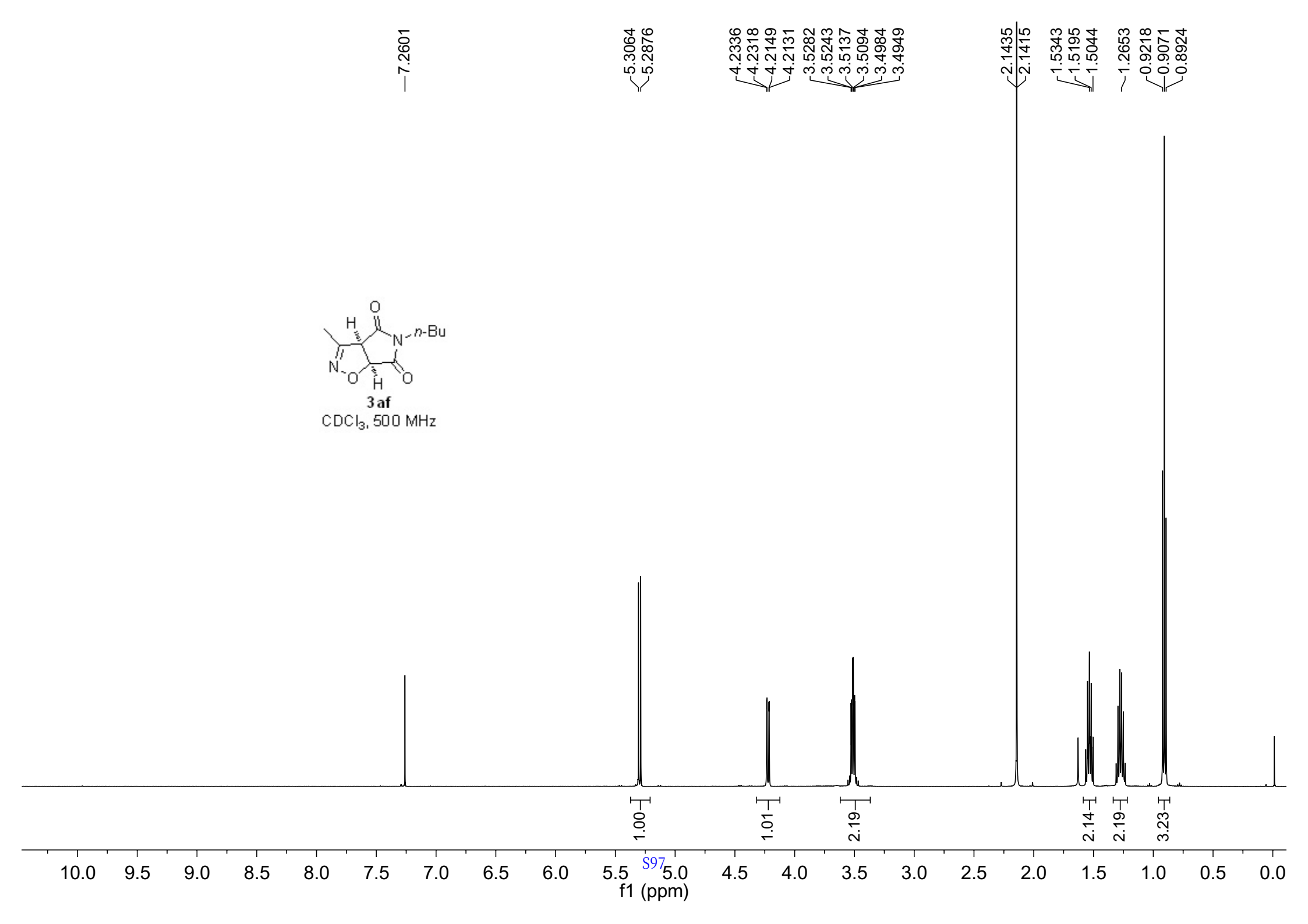

171.18
169.77
151.39
135.27
129.71
129.32
127.45
78.90
77.41
77.16
76.90
58.04
12.00
O
H
N
Cl
N
O
H
O
3ac
CDCl3, 125 MHz
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

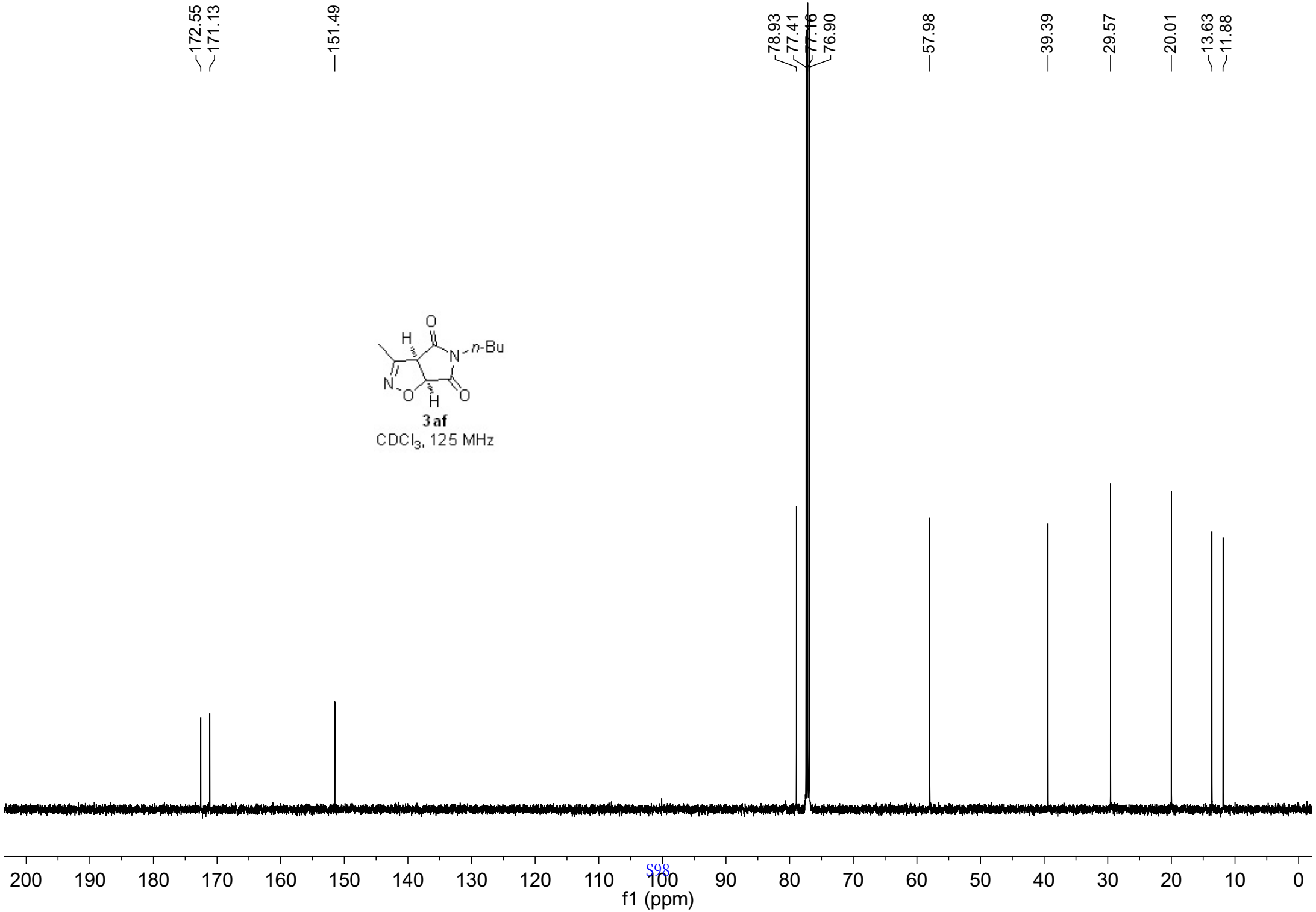

8.3675
8.3493
7.6080
7.5898
7.2601
5.5246
5.5054
4.4826
4.4808
4.4634
4.4615
2.2326
2.2310
-0.0037
O
H
N
O
N
O
NO2
H
O
3ad
CDCl3, 500 MHz
2.04
2.05
1.00
1.03
3.09
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

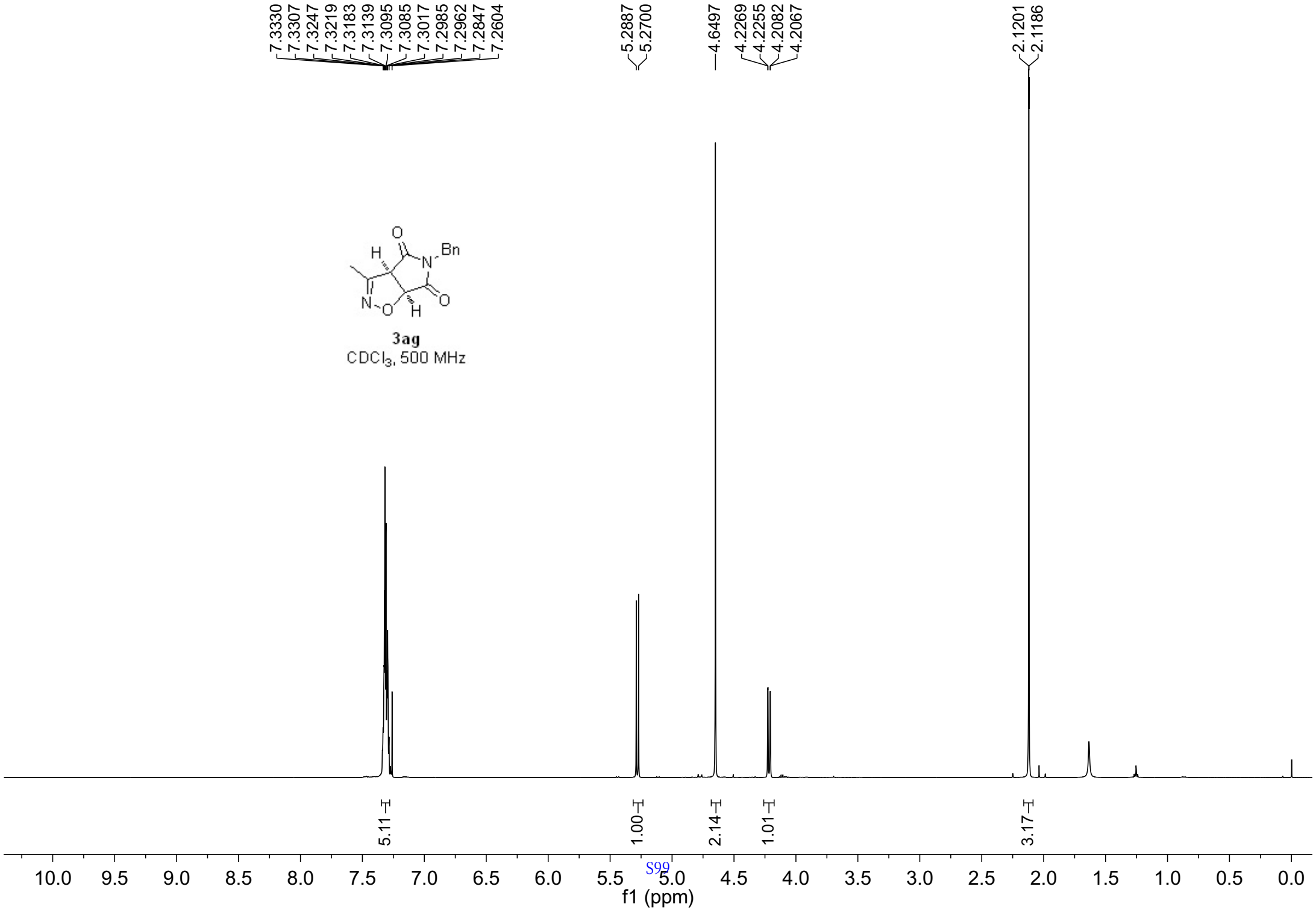

170.65
169.26
151.18
147.55
136.31
126.85
124.72
78.87
77.41
77.16
76.90
58.11
12.00
O
H
N
NO2
N
O
H
O
3ad
CDCl3, 125 MHz
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

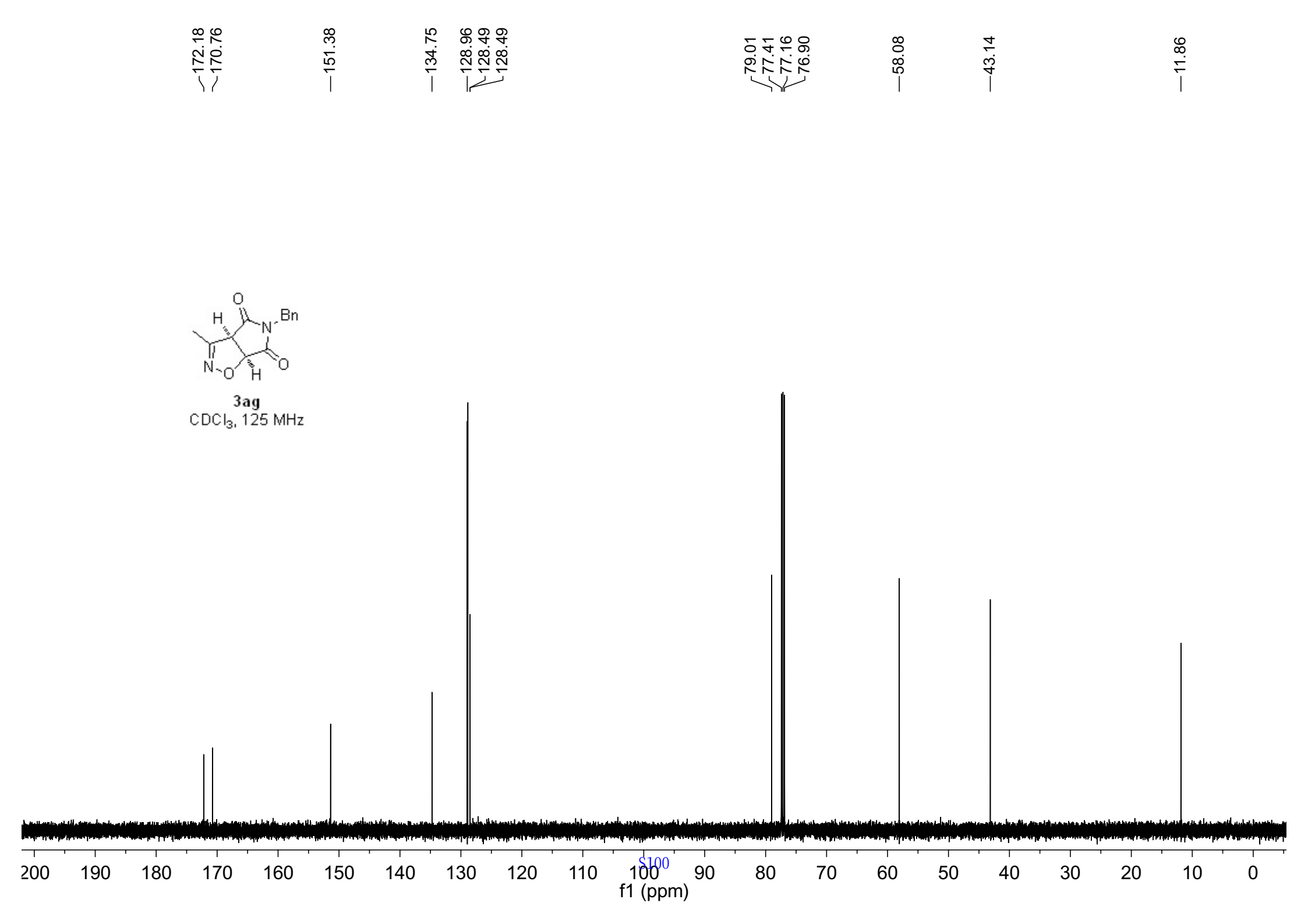

7.2601
5.3253
5.3065
4.2629
4.2441
3.0242
2.1475
2.1456
3ae
CDCl3, 500 MHz
1.00
1.03
3.13
3.16
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

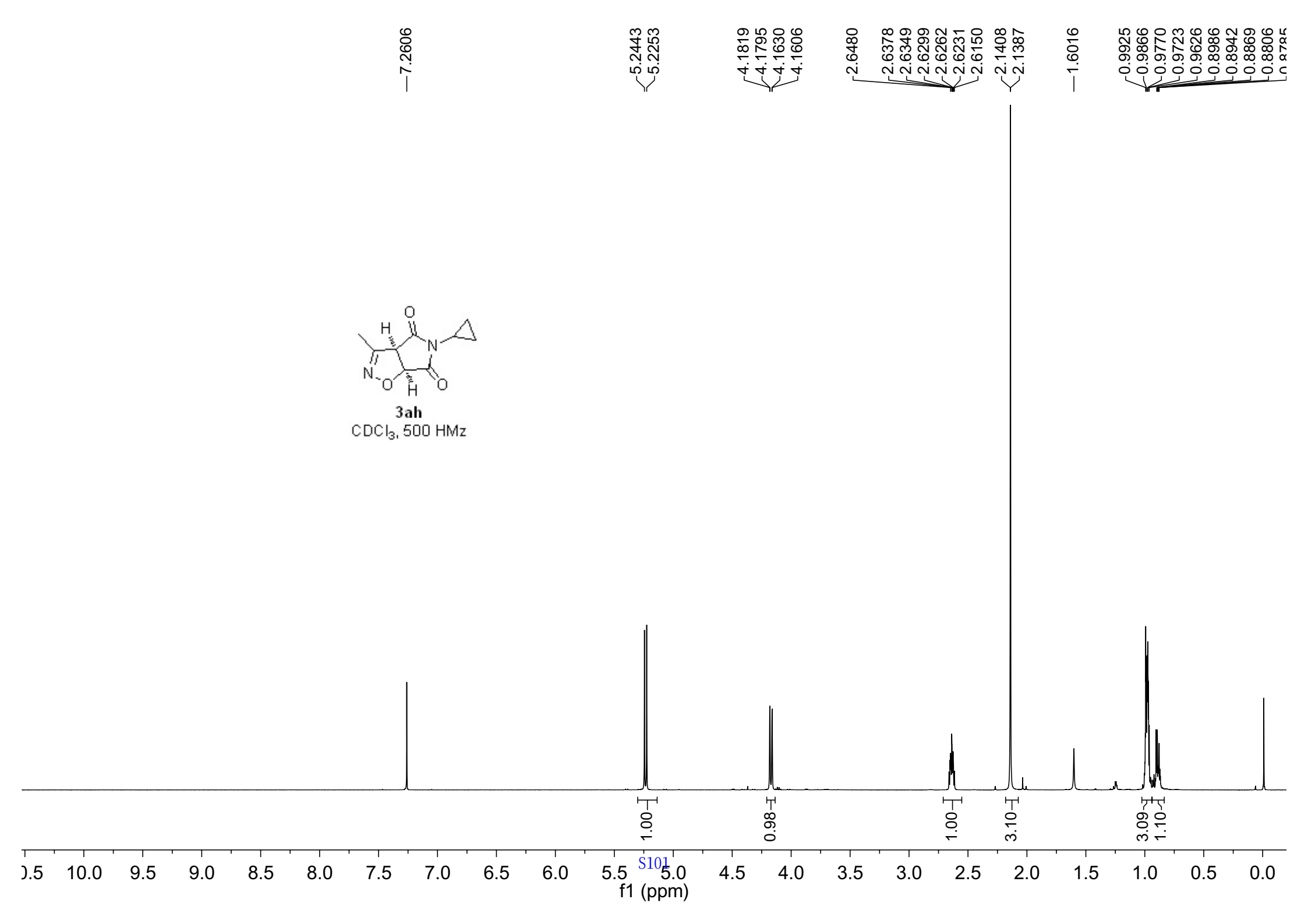

172.55
171.08
151.37
79.01
77.41
77.16
76.90
58.10
25.54
11.92
O
H
N
N
O
H
O
3ae
CDCl3, 125 MHz
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

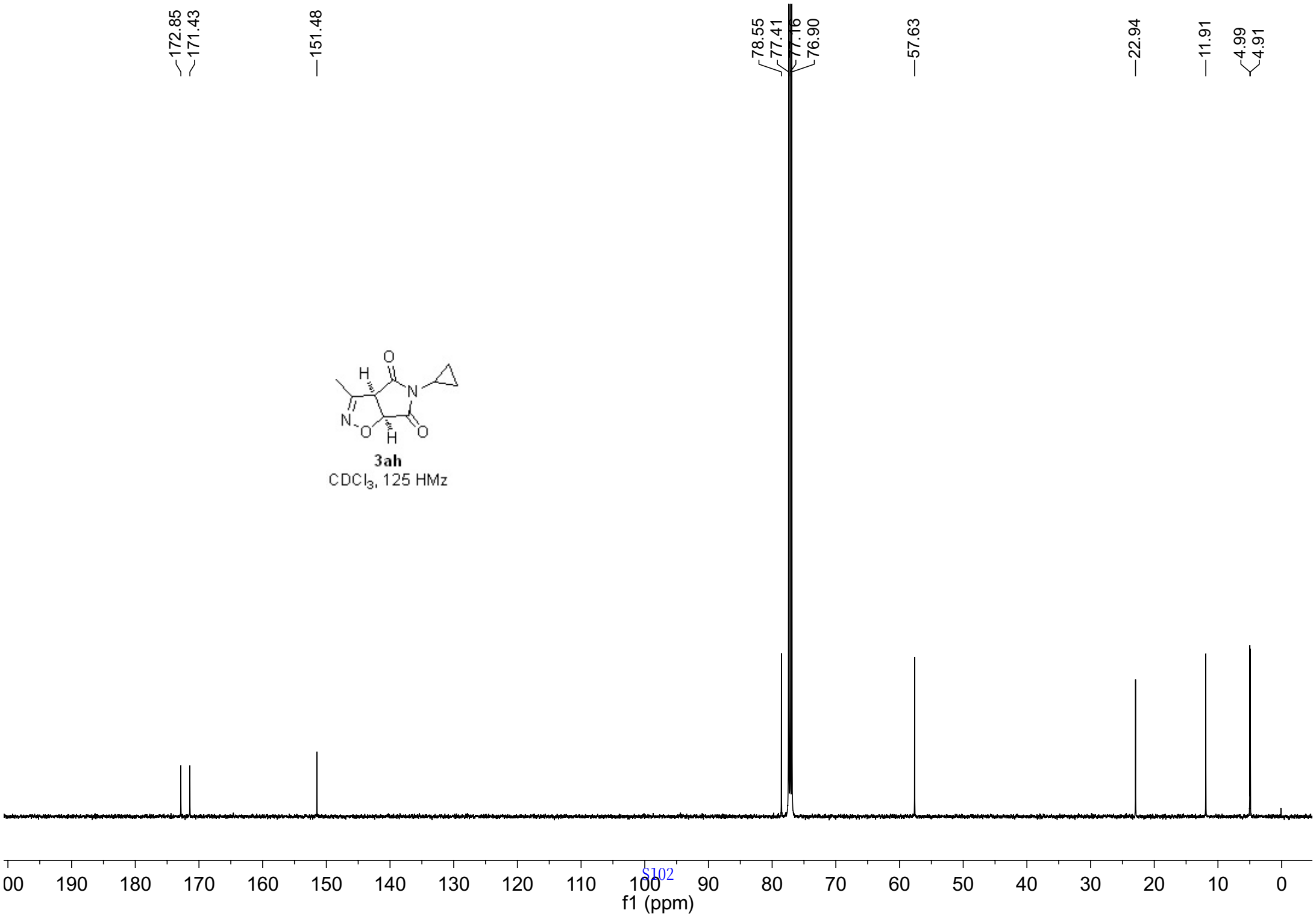

7.2601
5.3064
5.2876
4.2336
4.2318
4.2149
4.2131
3.5282
3.5243
3.5137
3.5094
3.4984
3.4949
2.1435
2.1415
1.5343
1.5195
1.5044
1.2653
0.9218
0.9071
0.8924
n-Bu
3af
CDCl3, 500 MHz
1.00
1.01
2.19
2.14
2.19
3.23
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

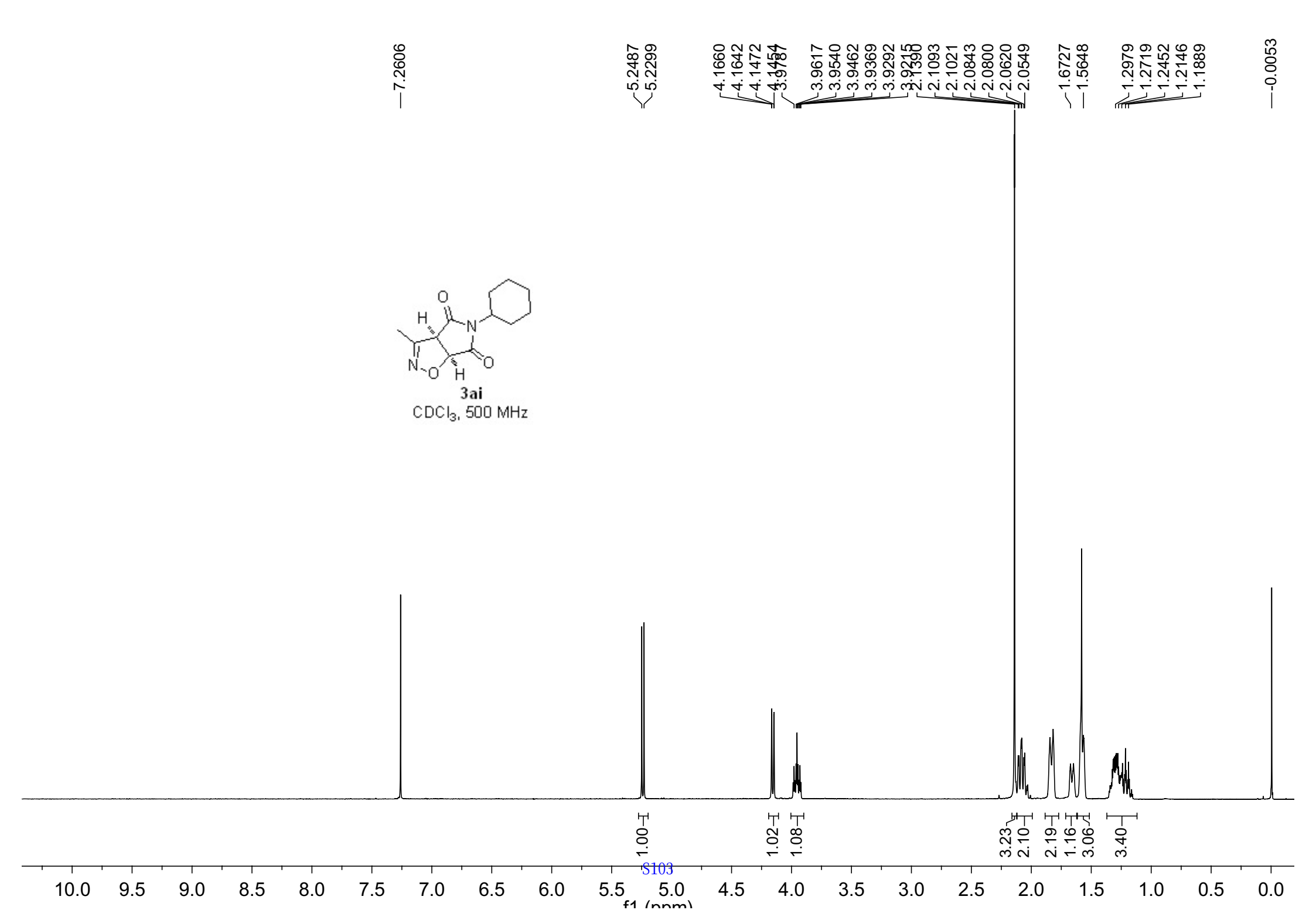

172.55
171.13
151.49
78.93
77.41
77.16
76.90
57.98
39.39
29.57
20.01
13.63
11.88
O
H
N
n-Bu
N
O
O
H
O
3af
CDCl3, 125 MHz
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

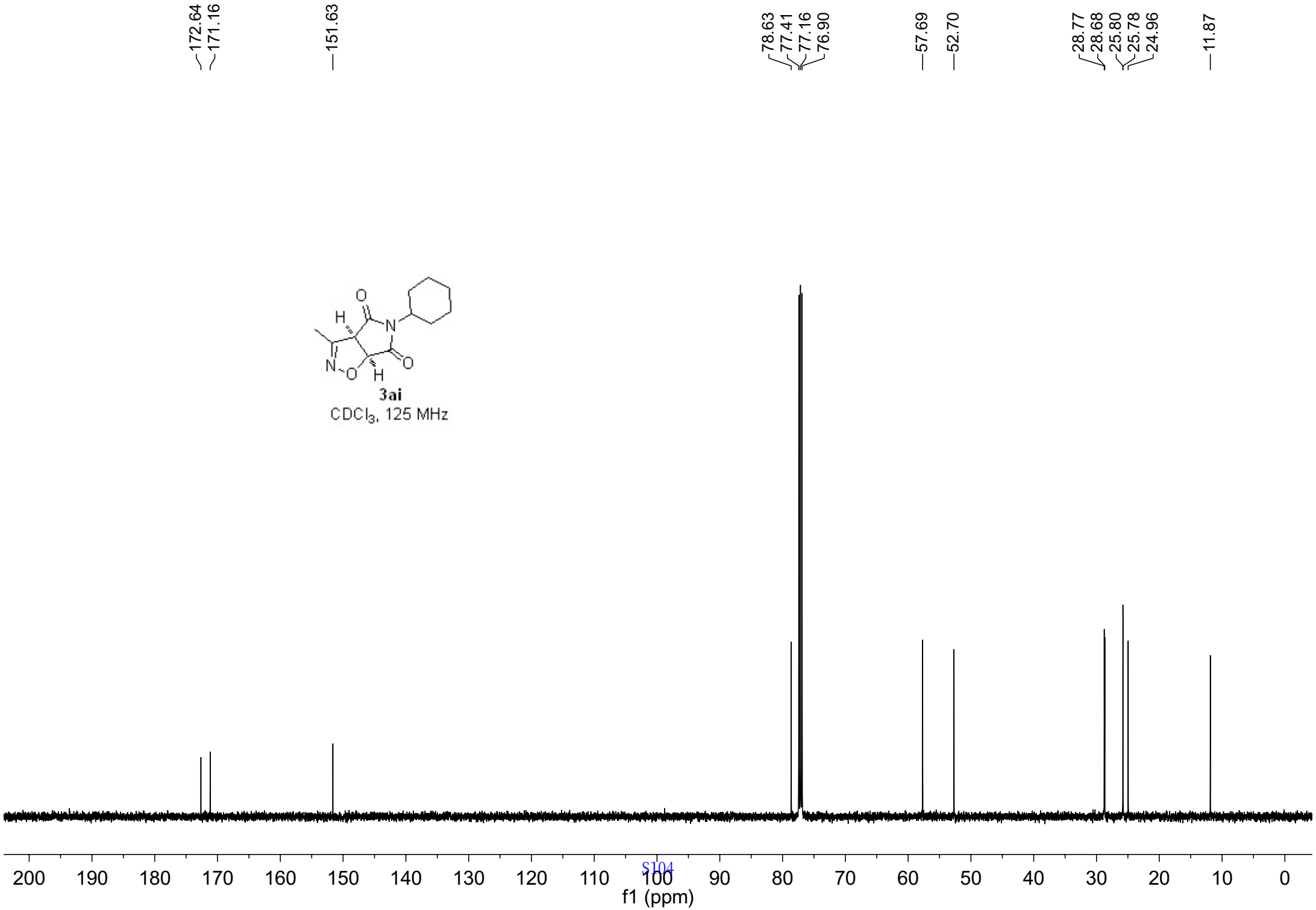

7.3330
7.3307
7.3247
7.3219
7.3183
7.3139
7.3095
7.3085
7.3017
7.2985
7.2962
7.2847
7.2604
5.2887
5.2700
4.6497
4.2269
4.2255
4.2082
4.2067
2.1201
2.1186
O
H
N
Bn
N
O
O
H
3ag
CDCl3, 500 MHz
5.11
1.00
2.14
1.01
3.17
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

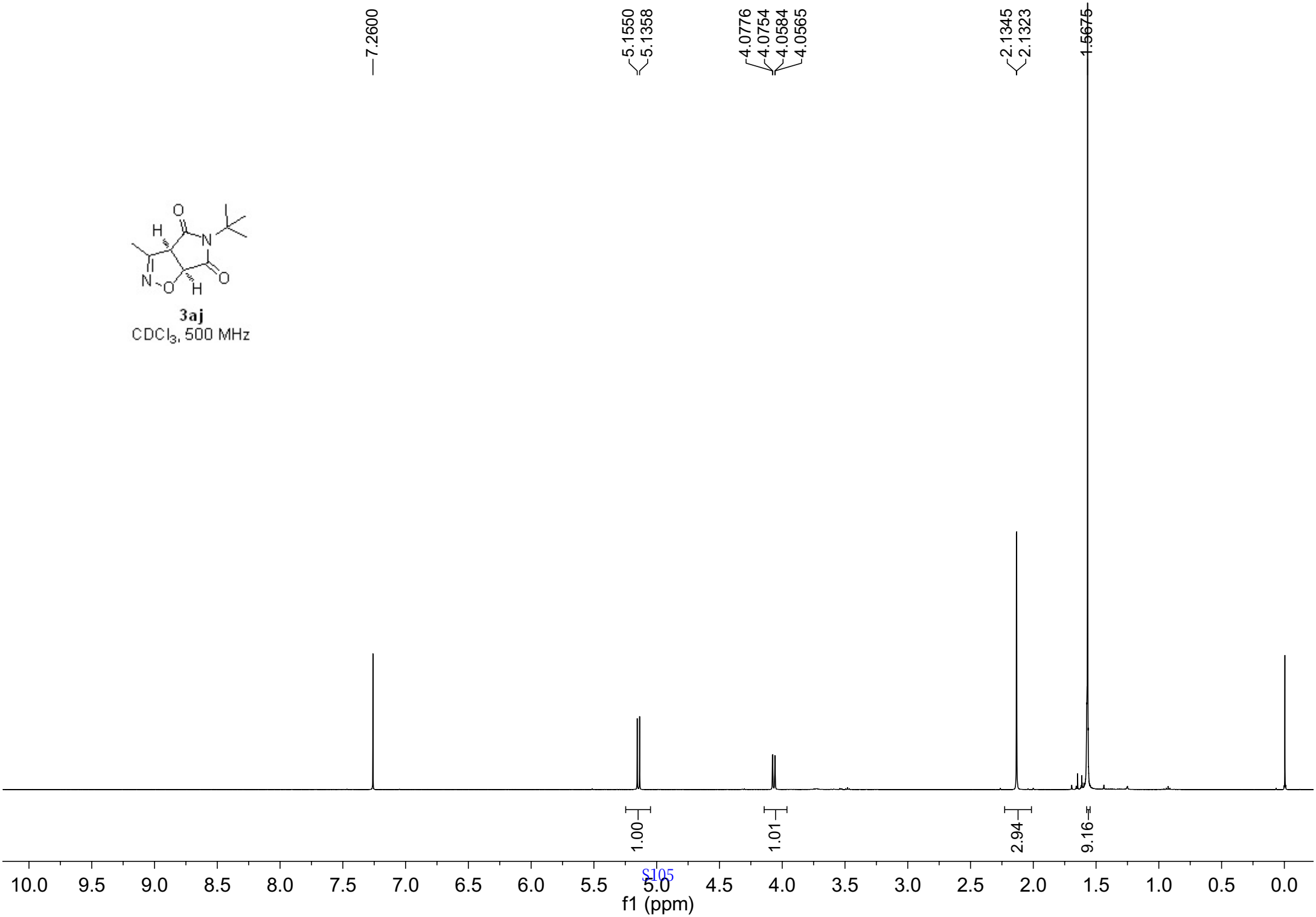

172.18
170.76
151.38
134.75
128.96
128.49
128.49
79.01
77.41
77.16
76.90
58.08
43.14
11.86
O
H
N
Bn
N
O
O
H
3ag
CDCl3, 125 MHz
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

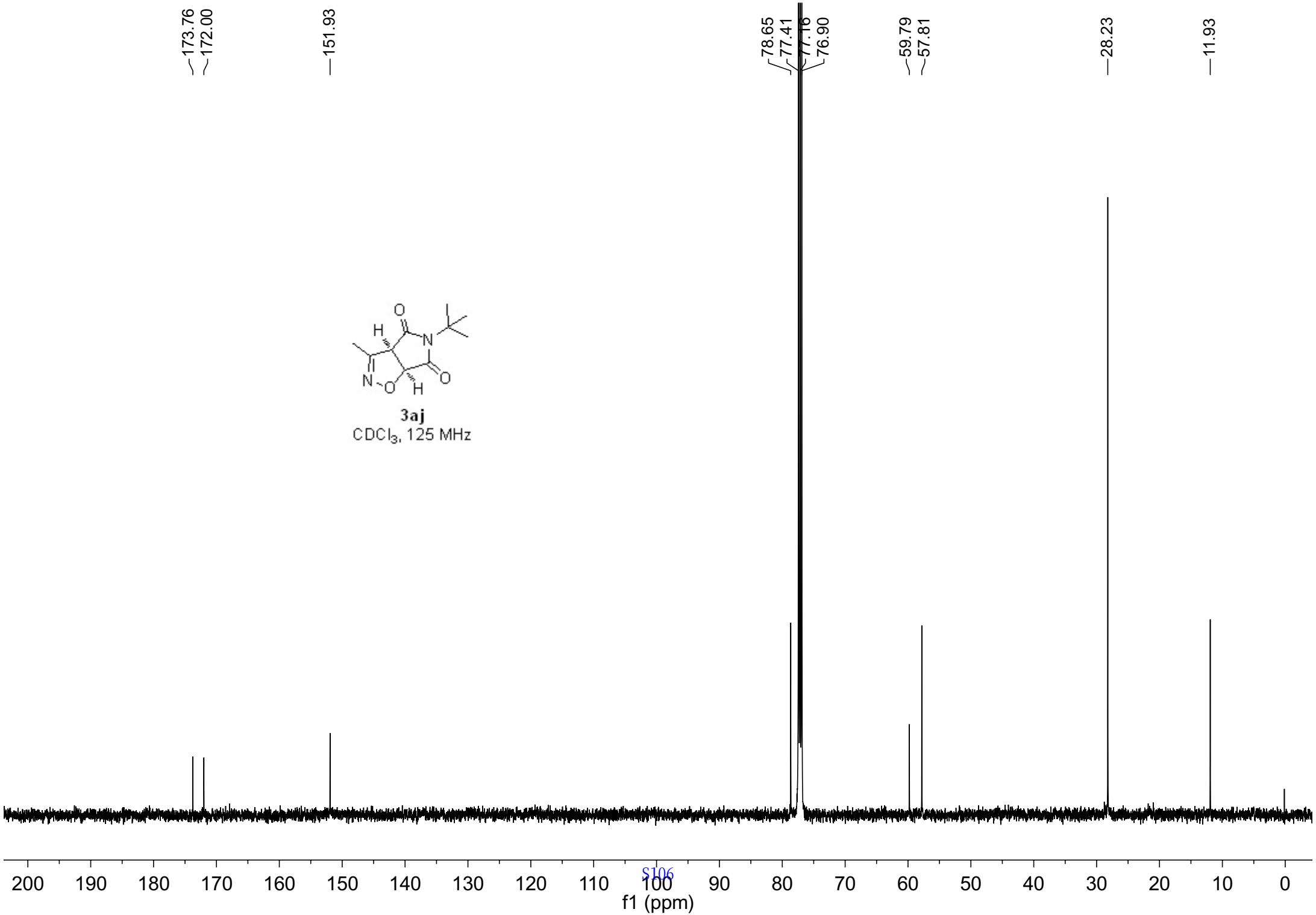

7.2606
5.2443
5.2253
4.1819
4.1795
4.1630
4.1606
2.6480
2.6378
2.6349
2.6299
2.6262
2.6231
2.6150
2.1408
2.1387
1.6016
0.9925
0.9866
0.9770
0.9723
0.9626
0.8986
0.8942
0.8869
0.8806
3ah
CDCl3, 500 HMz
1.00
0.98
1.00
3.10
3.09
1.10
f1 (ppm)

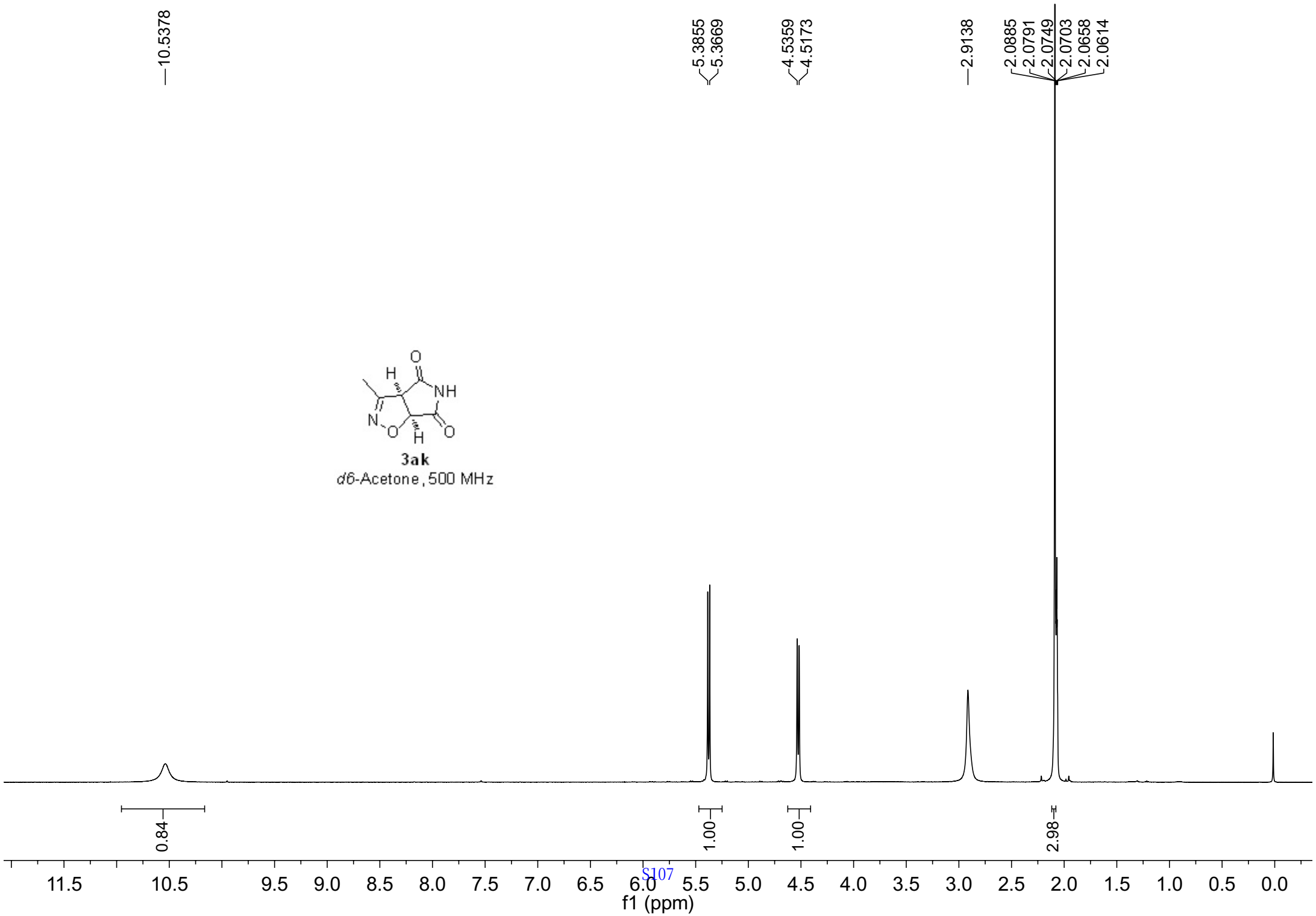

172.85
171.43
151.48
78.55
77.41
77.16
76.90
57.63
22.94
11.91
4.99
4.91
O
H
N
N
O
O
H
O
3ah
CDCl3, 125 HMz
00
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

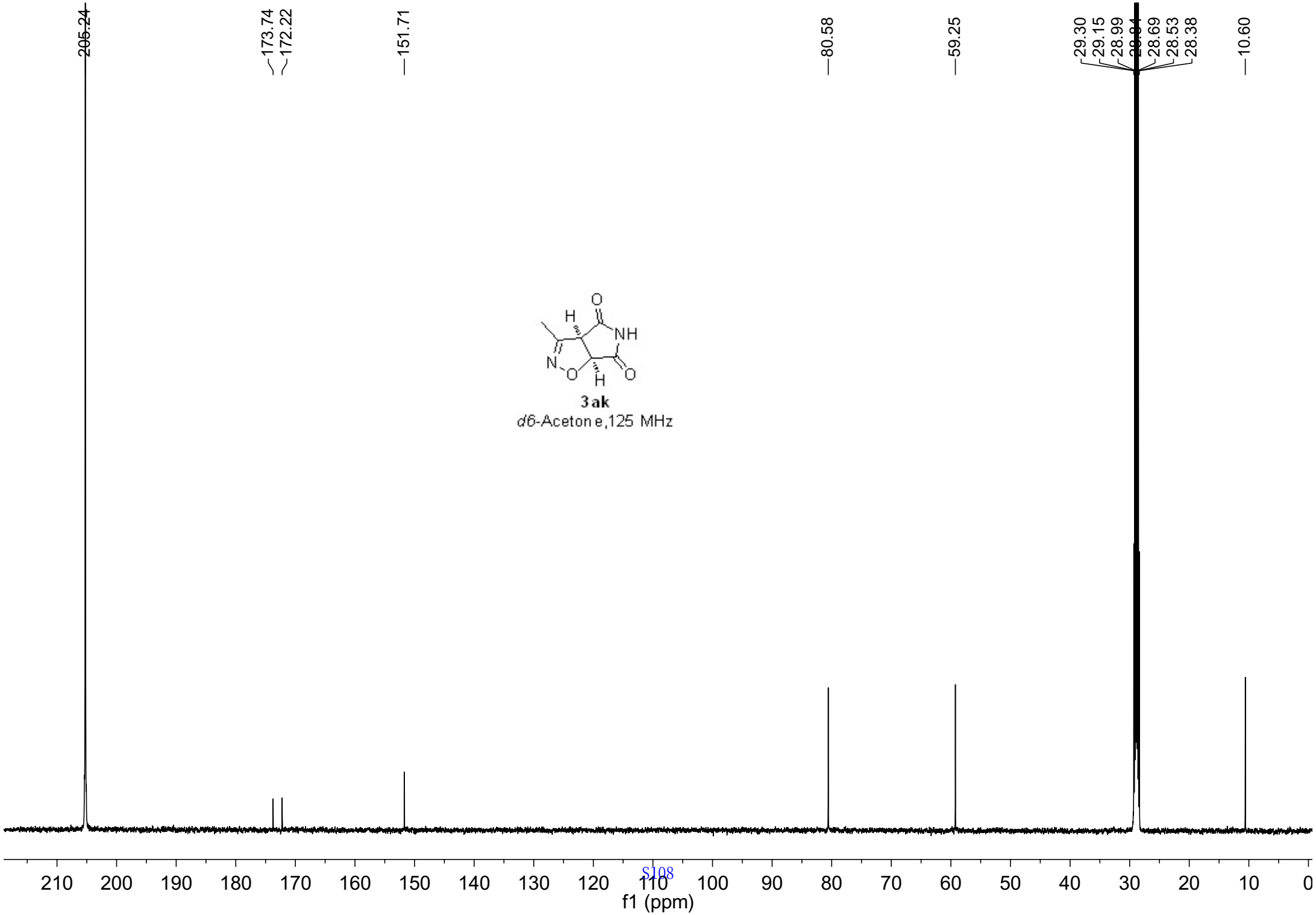

7.2606
5.2487
5.2299
4.1660
4.1642
4.1472
4.1454
3.9787
3.9617
3.9540
3.9462
3.9369
3.9292
3.9215
2.1390
2.1093
2.1021
2.0843
2.0800
2.0620
2.0549
1.6727
1.5648
1.2979
1.2719
1.2452
1.2146
1.1889
-0.0053
3ai
CDCl3, 500 MHz
1.00
1.02
1.08
3.23
2.10
2.19
1.16
3.06
3.40
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

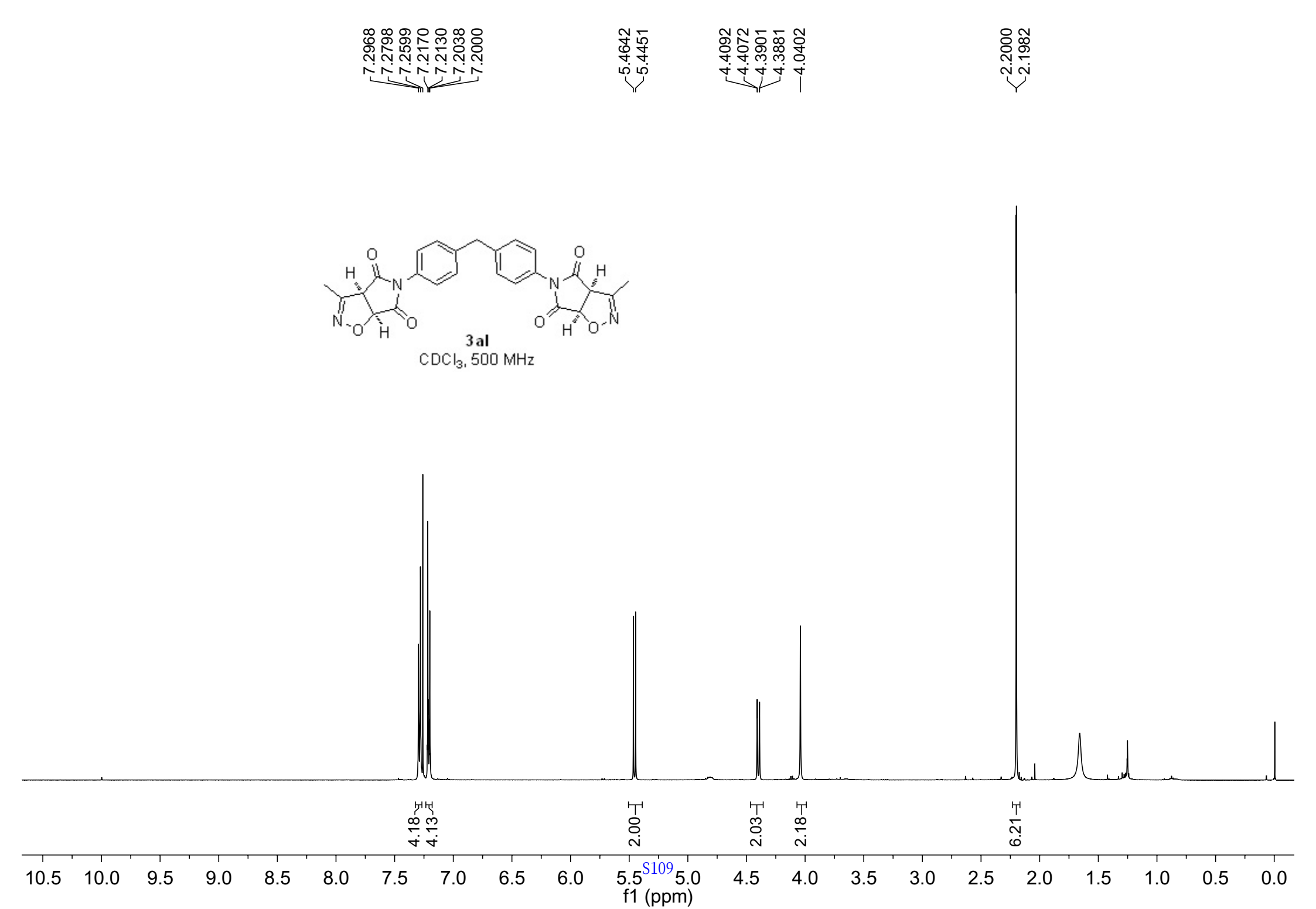

172.64
171.16
151.63
78.63
77.41
77.16
76.90
57.69
52.70
28.77
28.68
25.80
25.78
24.96
11.87
3ai
CDCl3, 125 MHz
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

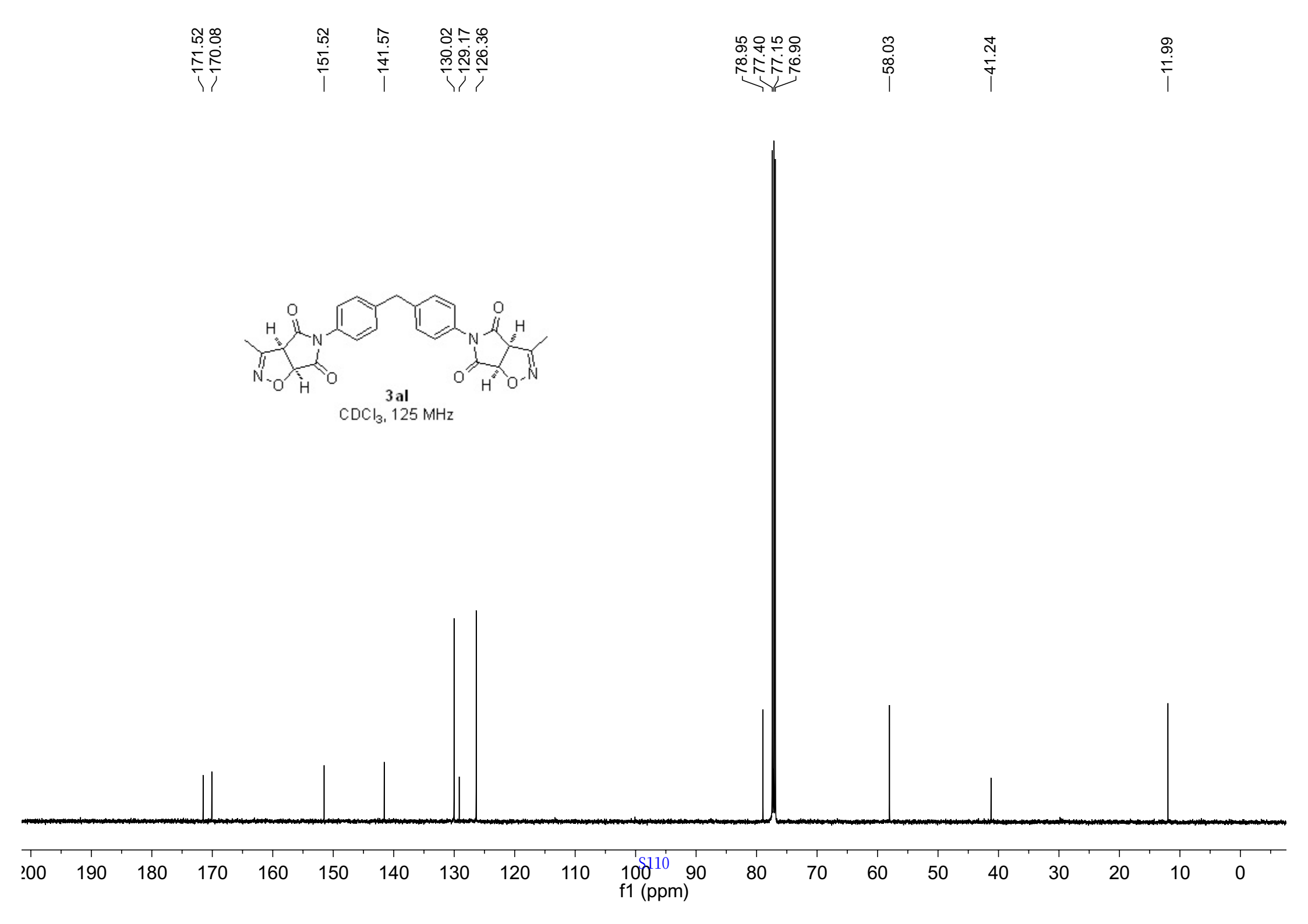

7.2600
5.1550
5.1358
4.0776
4.0754
4.0584
4.0565
2.1345
2.1323
1.5675
3aj
CDCl3, 500 MHz
1.00
1.01
2.94
9.16
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

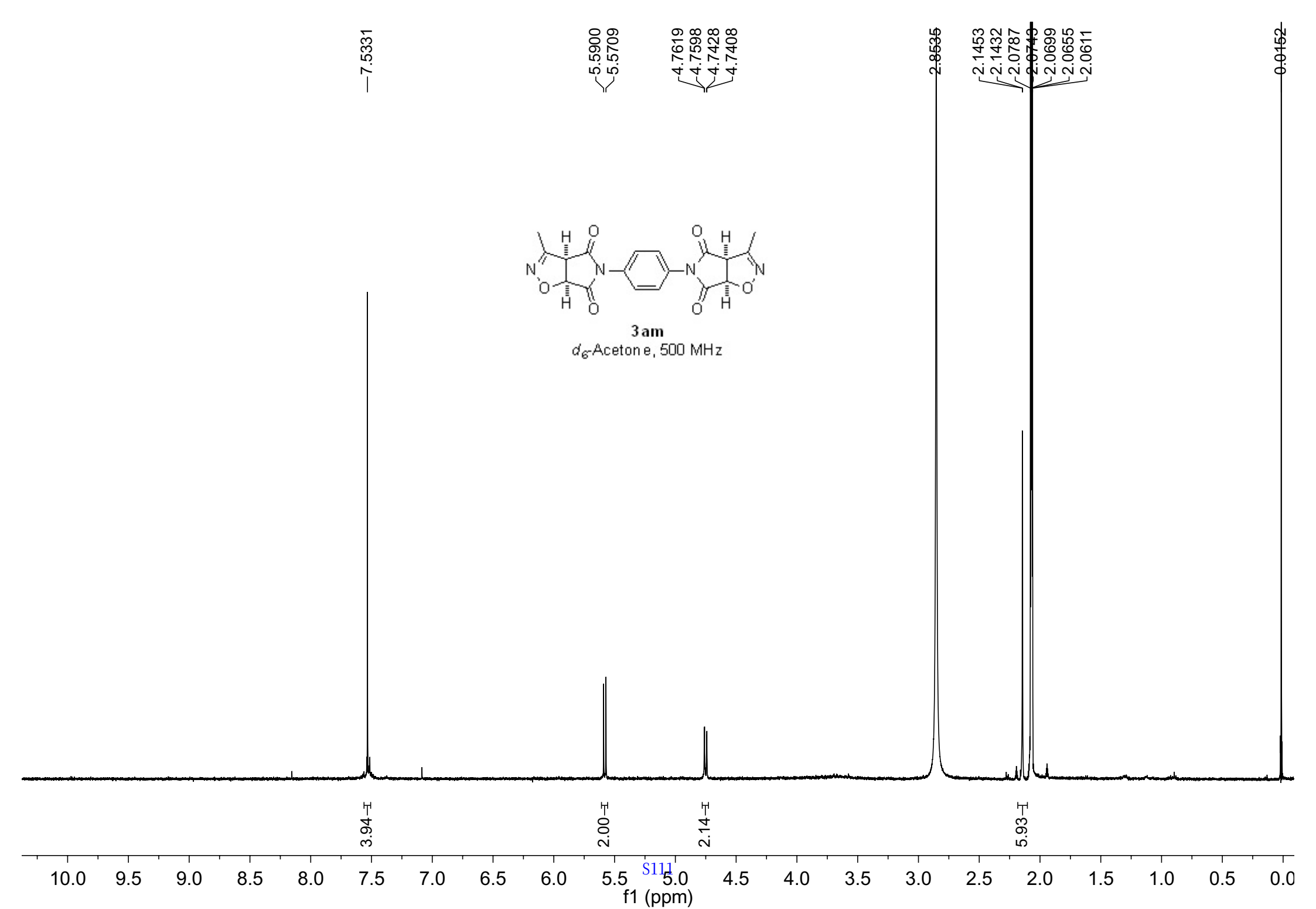

173.76
172.00
151.93
78.65
77.41
77.16
76.90
59.79
57.81
28.23
11.93
O
H
N
O
N
O
H
3aj
CDCl3, 125 MHz
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

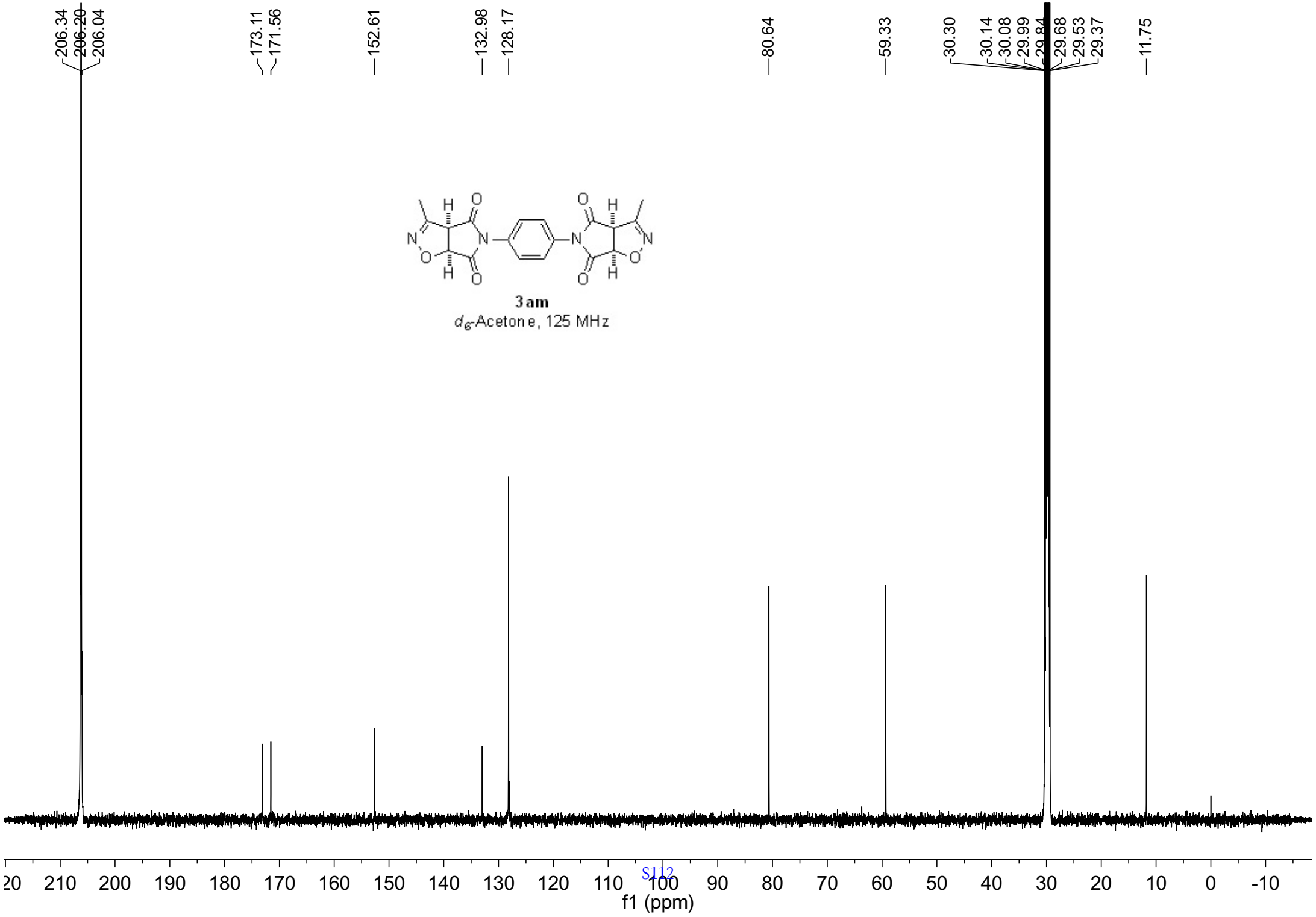

10.5378
5.3855
5.3669
4.5359
4.5173
2.9138
2.0885
2.0791
2.0749
2.0703
2.0658
2.0614
O
H
NH
N
O
H
O
3ak
d6-Acetone, 500 MHz
0.84
1.00
1.00
2.98
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

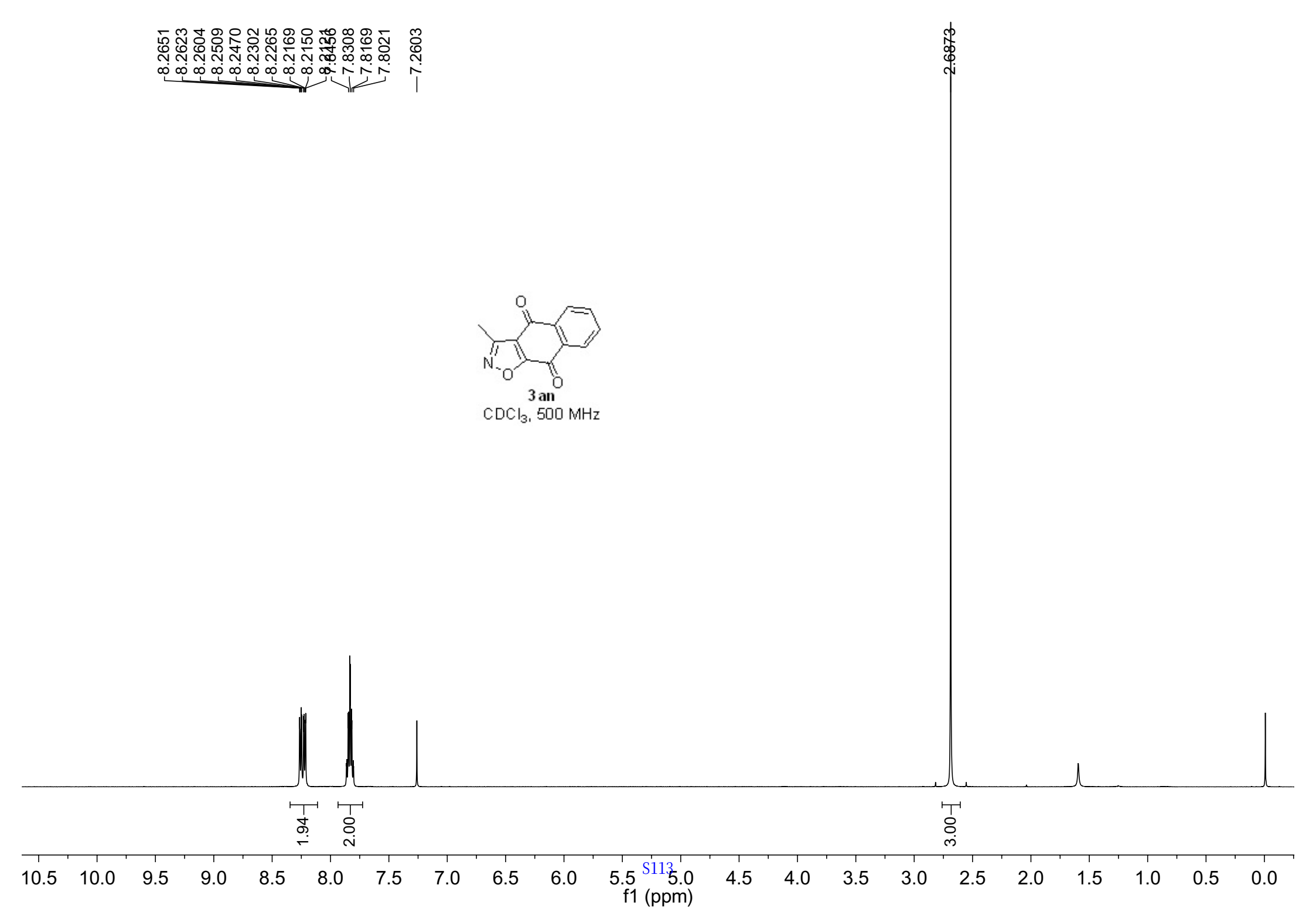

205.24
173.74
172.22
151.71
80.58
59.25
29.30
29.15
28.99
28.69
28.53
28.38
10.60
O
H
NH
N
O
H
O
3ak
d6-Acetone,125 MHz
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

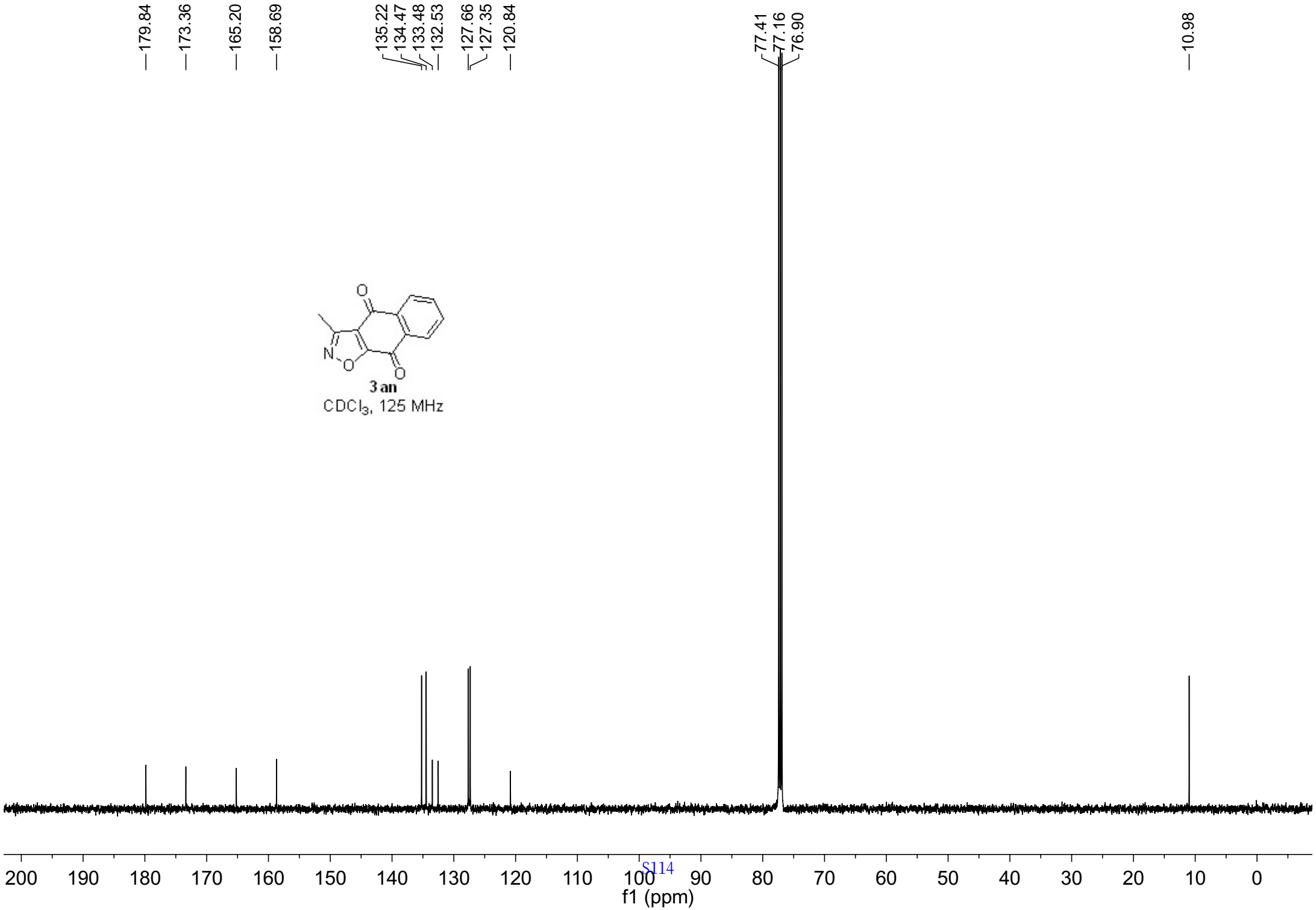

7.2968
7.2798
7.2599
7.2170
7.2130
7.2038
7.2000
5.4642
5.4451
4.4092
4.4072
4.3901
4.3881
4.0402
2.2000
2.1982
3al
CDCl3, 500 MHz
4.18
4.13
2.00
2.03
2.18
6.21
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

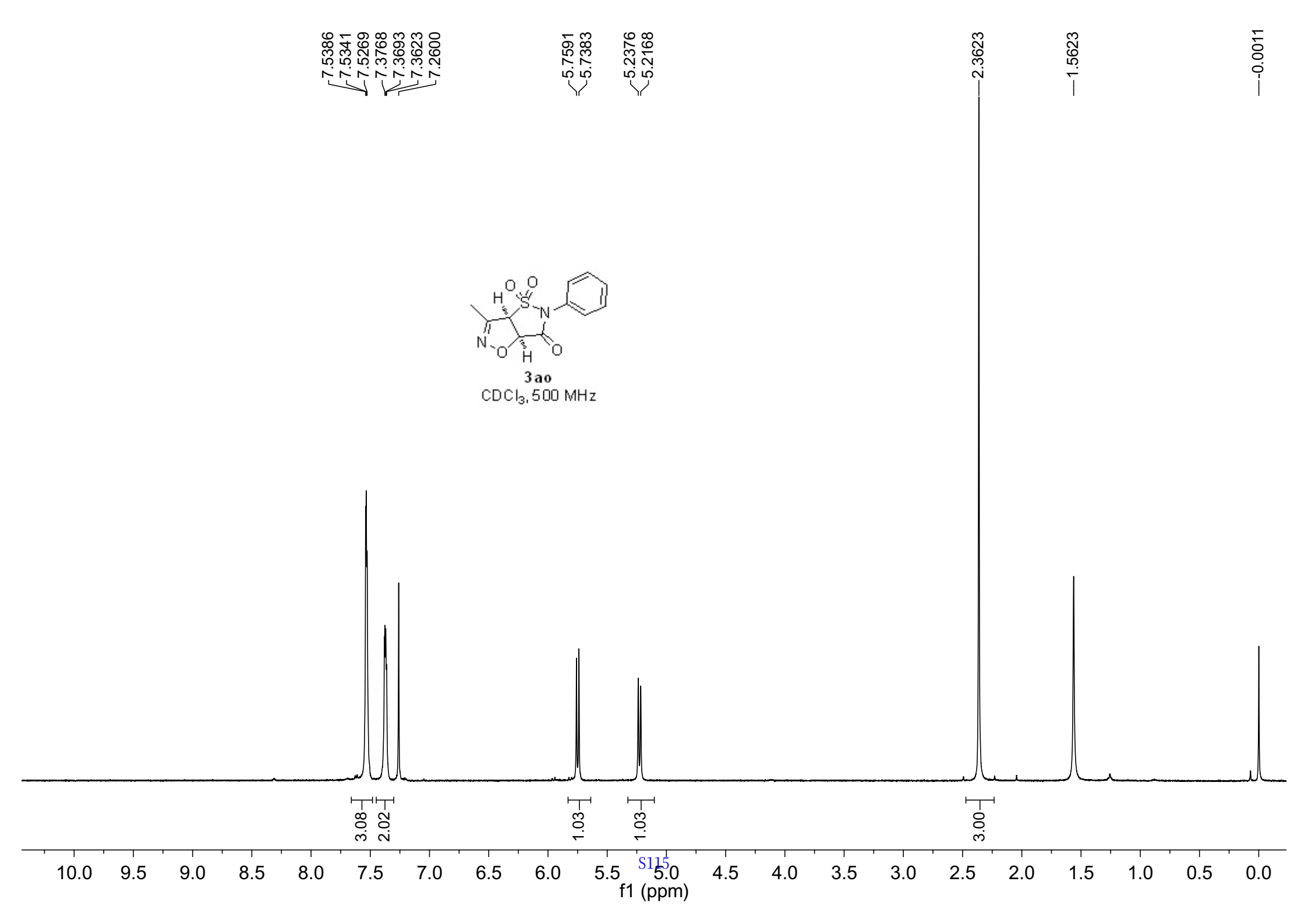

171.52
170.08
151.52
141.57
130.02
129.17
126.36
78.95
77.40
77.15
76.90
58.03
41.24
11.99
3al
CDCl3, 125 MHz
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

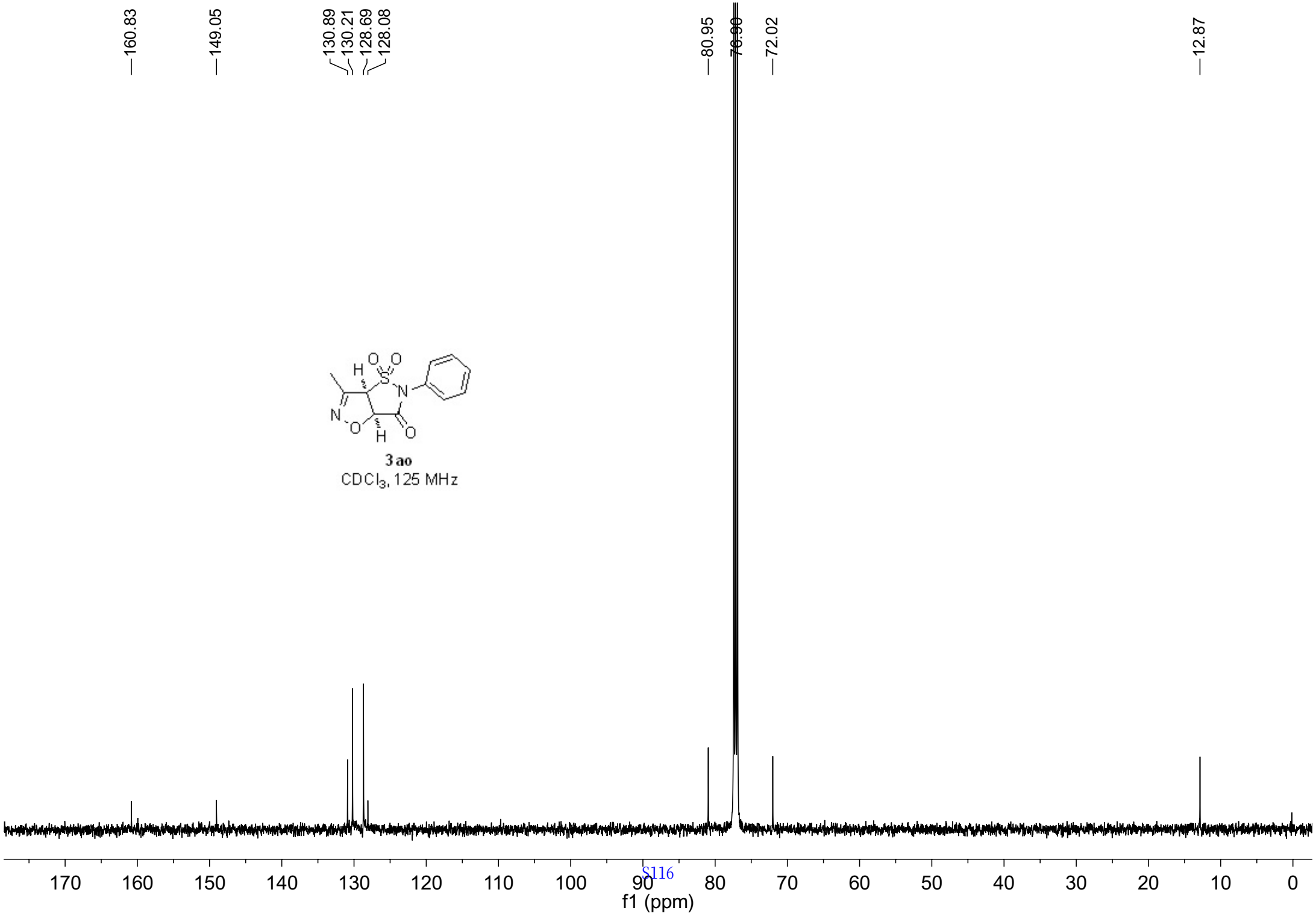

7.5331
5.5900
5.5709
4.7619
4.7598
4.7428
4.7408
2.8535
2.1453
2.1432
2.0787
2.0743
2.0699
2.0655
2.0611
0.0152
3am
d6-Acetone, 500 MHz
3.94
2.00
2.14
5.93
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

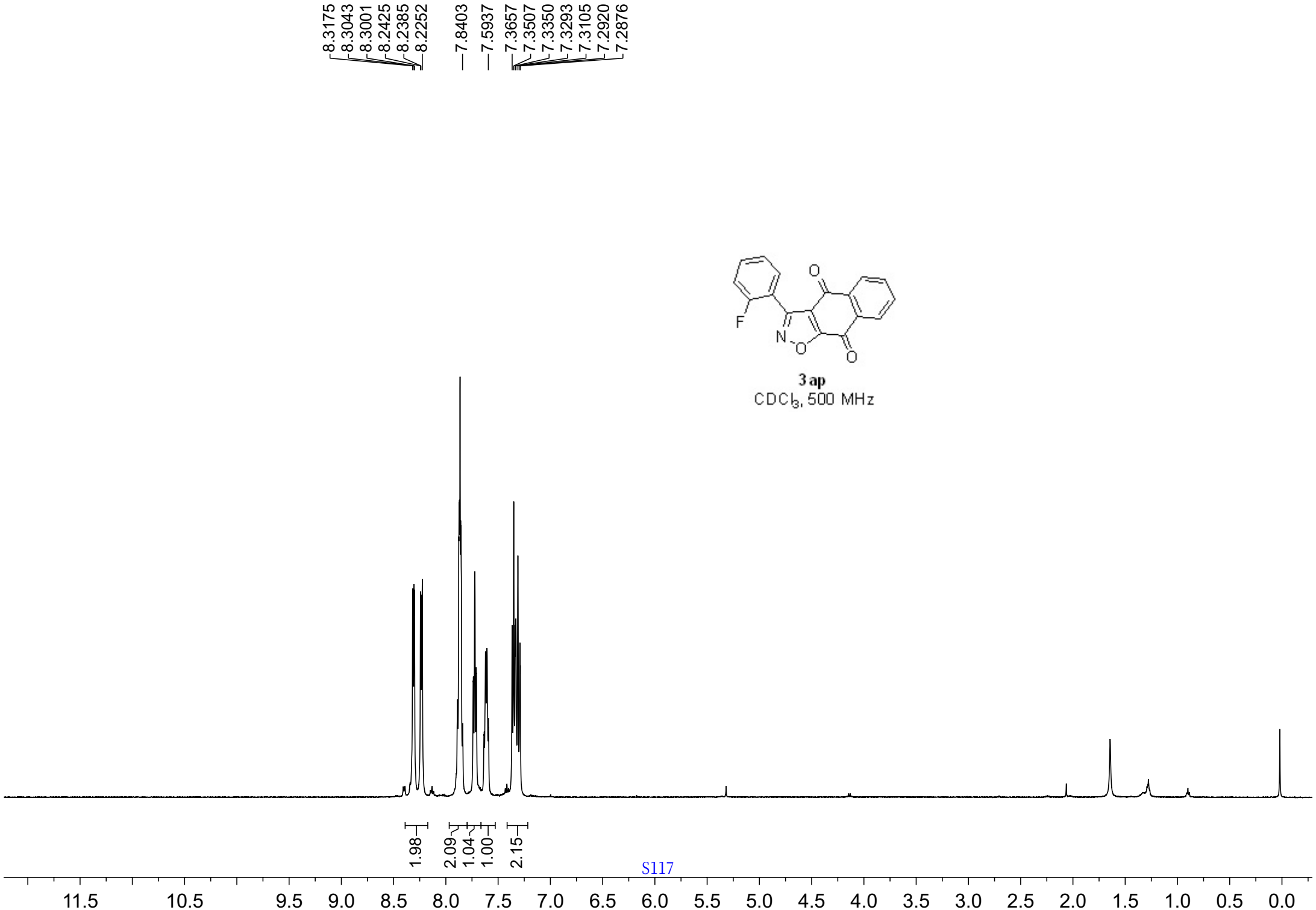

206.34
206.20
206.04
173.11
171.56
152.61
132.98
128.17
80.64
59.33
30.30
30.14
30.08
29.99
29.84
29.68
29.53
29.37
11.75
3am
d_6-Acetone, 125 MHz
f1 (ppm)

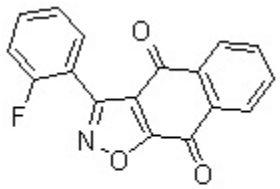

8.2651
8.2623
8.2604
8.2509
8.2470
8.2302
8.2265
8.2169
8.2150
7.8456
7.8308
7.8169
7.8021
7.2603
2.6873
O
N
O
O
3an
CDCl3, 500 MHz
1.94
2.00
3.00
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


179.84
173.36
165.20
158.69
135.22
134.47
133.48
132.53
127.66
127.35
120.84
77.41
77.16
76.90
10.98
O
N
O
O
3an
CDCl3, 125 MHz
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

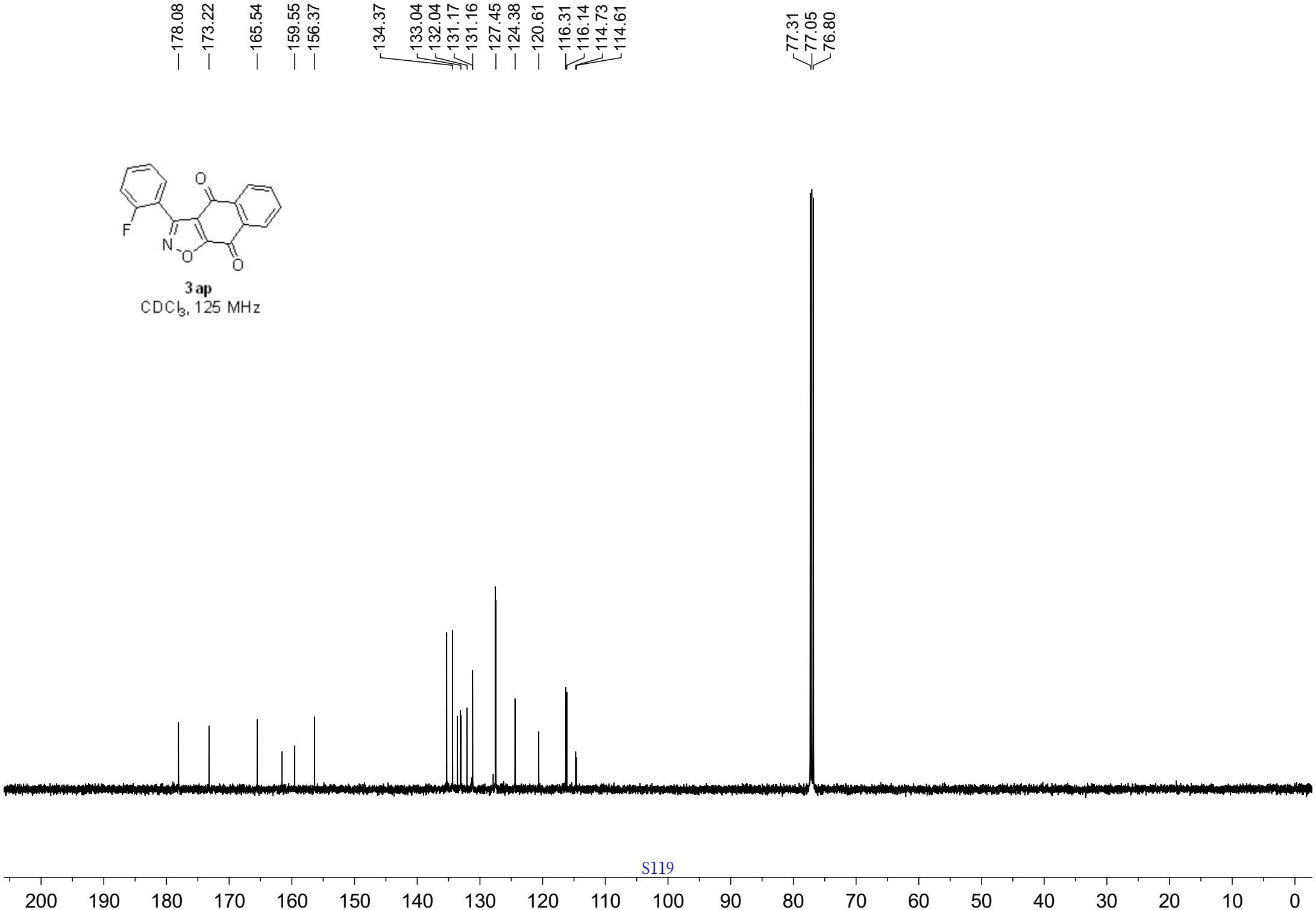

7.5386
7.5341
7.5269
7.3768
7.3693
7.3623
7.2600
5.7591
5.7383
5.2376
5.2168
2.3623
1.5623
-0.0011
3ao
CDCl3, 500 MHz
3.08
2.02
1.03
1.03
3.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

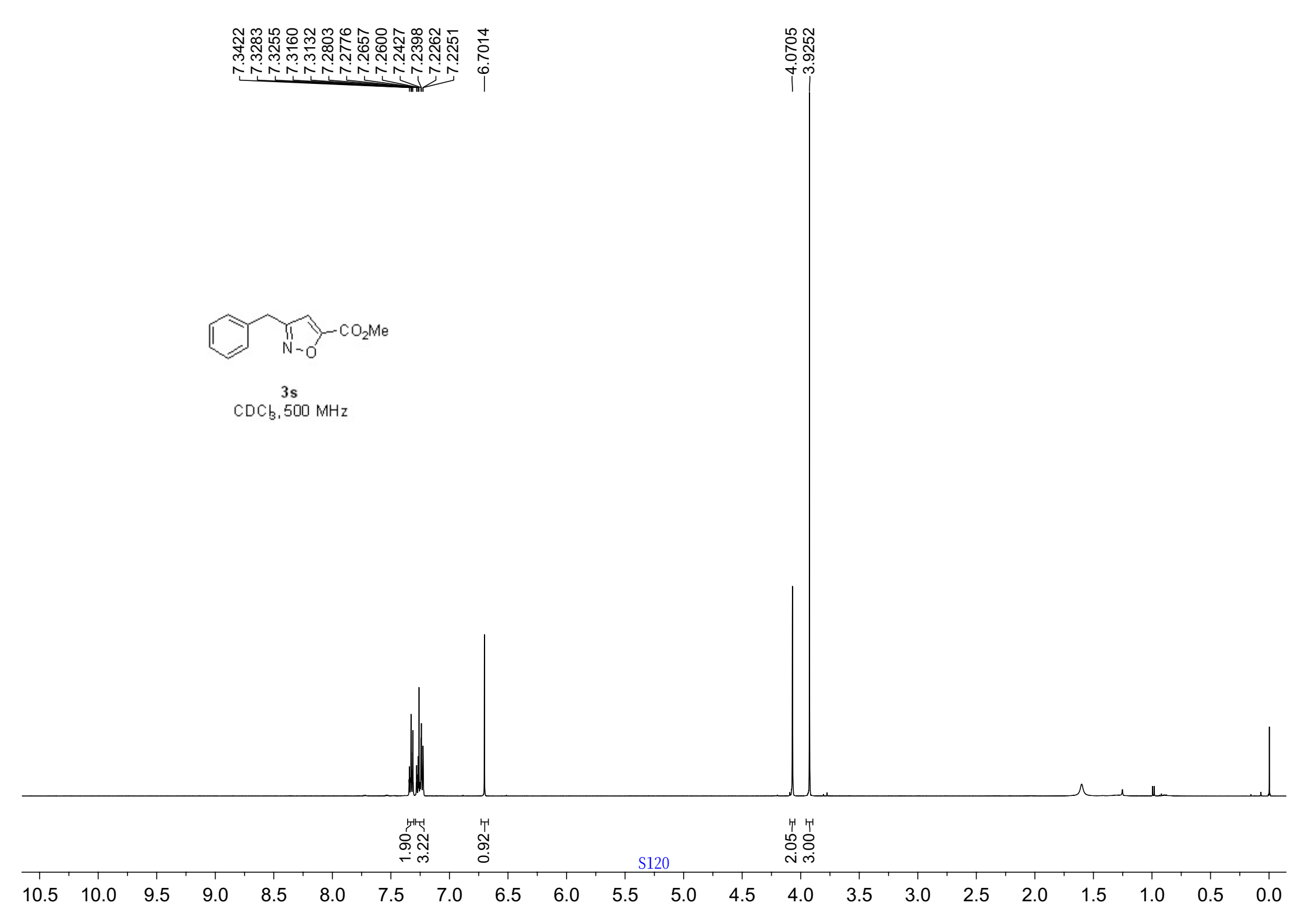

160.83
149.05
130.89
130.21
128.69
128.08
80.95
70.90
72.02
12.87
3ao
CDCl3, 125 MHz
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

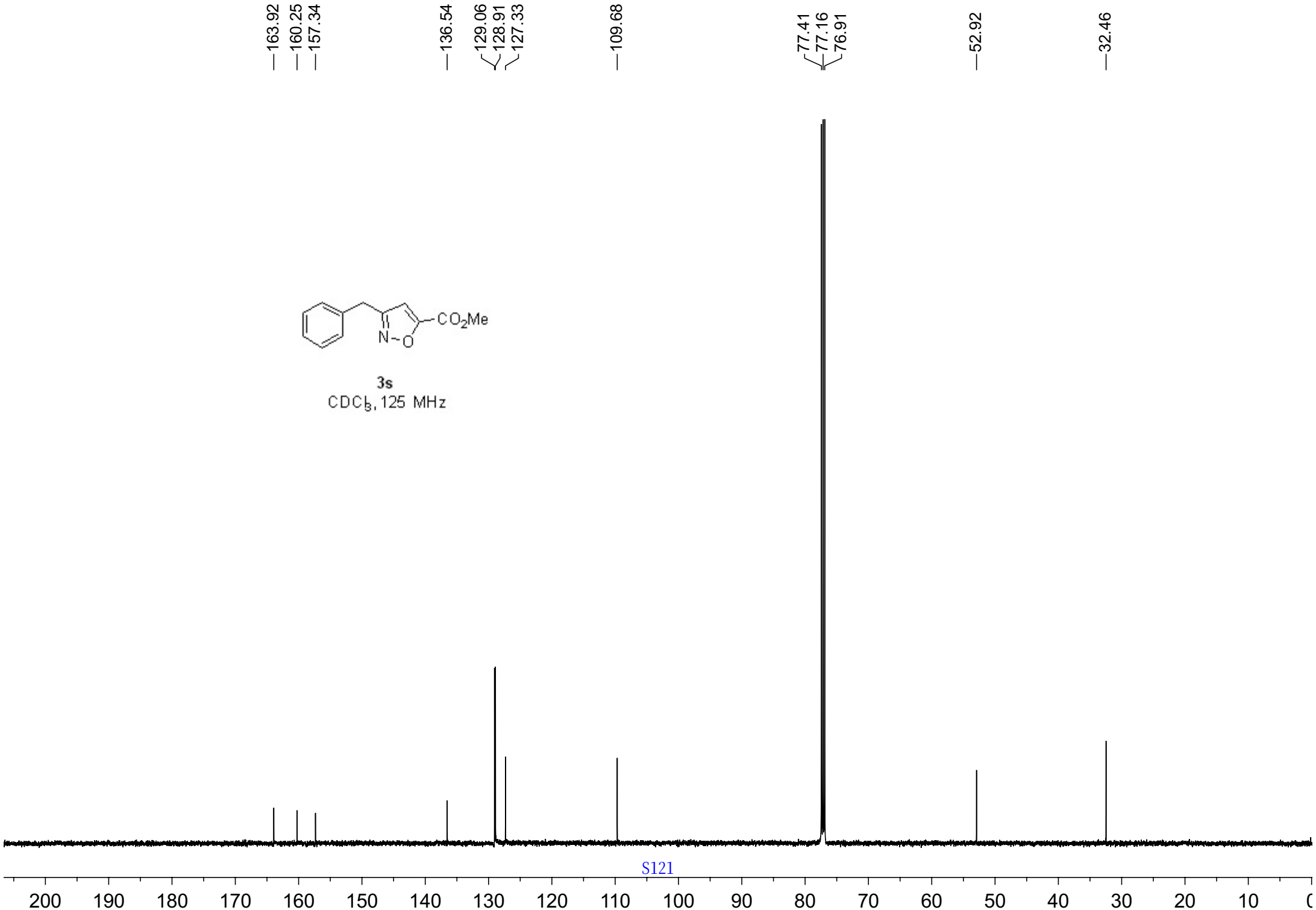

8.3175
8.3043
8.3001
8.2425
8.2385
8.2252
7.8403
7.5937
7.3657
7.3507
7.3350
7.3293
7.3105
7.2920
7.2876
F
N
O
O
O
3ap
CDCl3, 500 MHz
1.98
2.09
1.04
1.00
2.15
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0

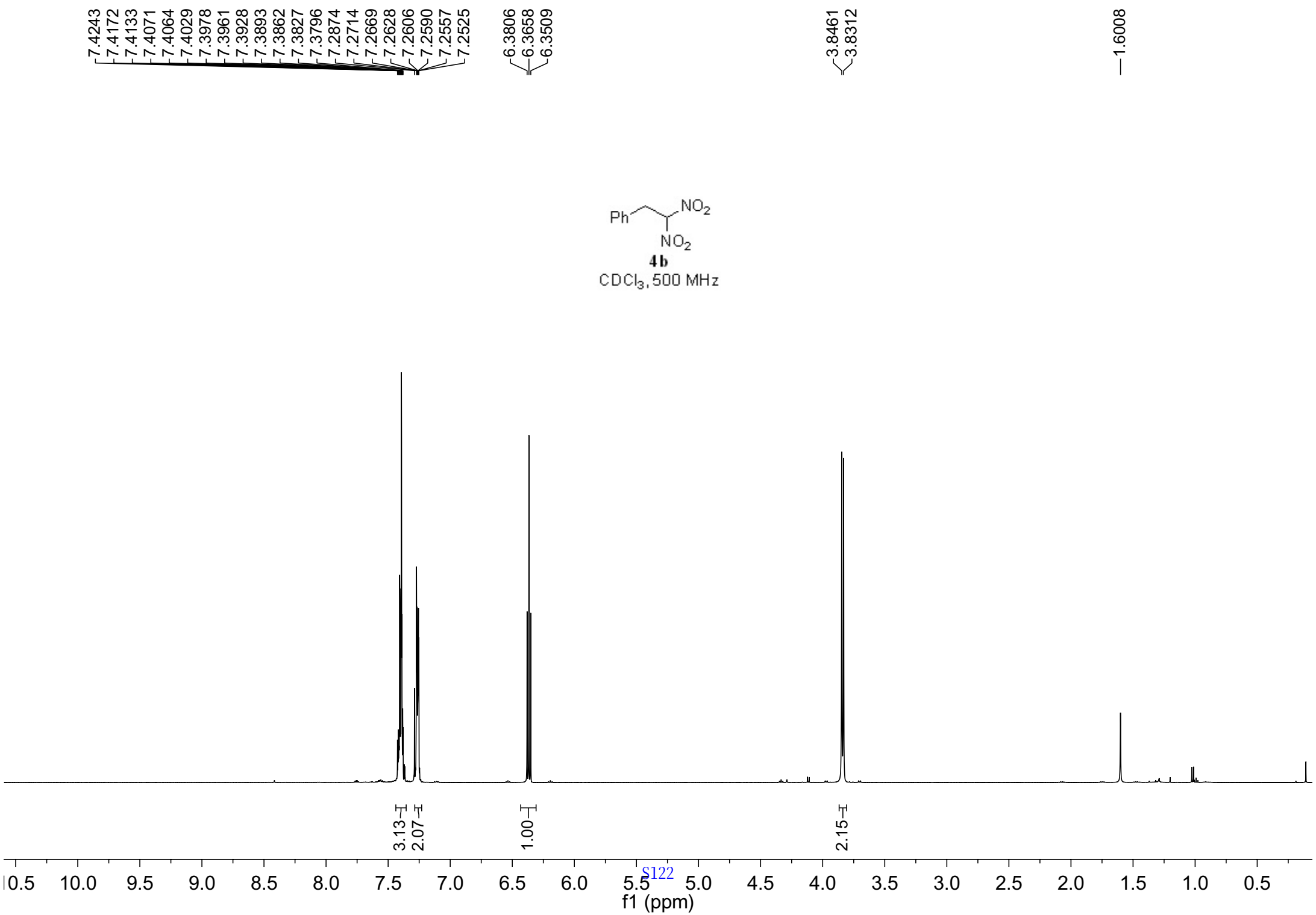


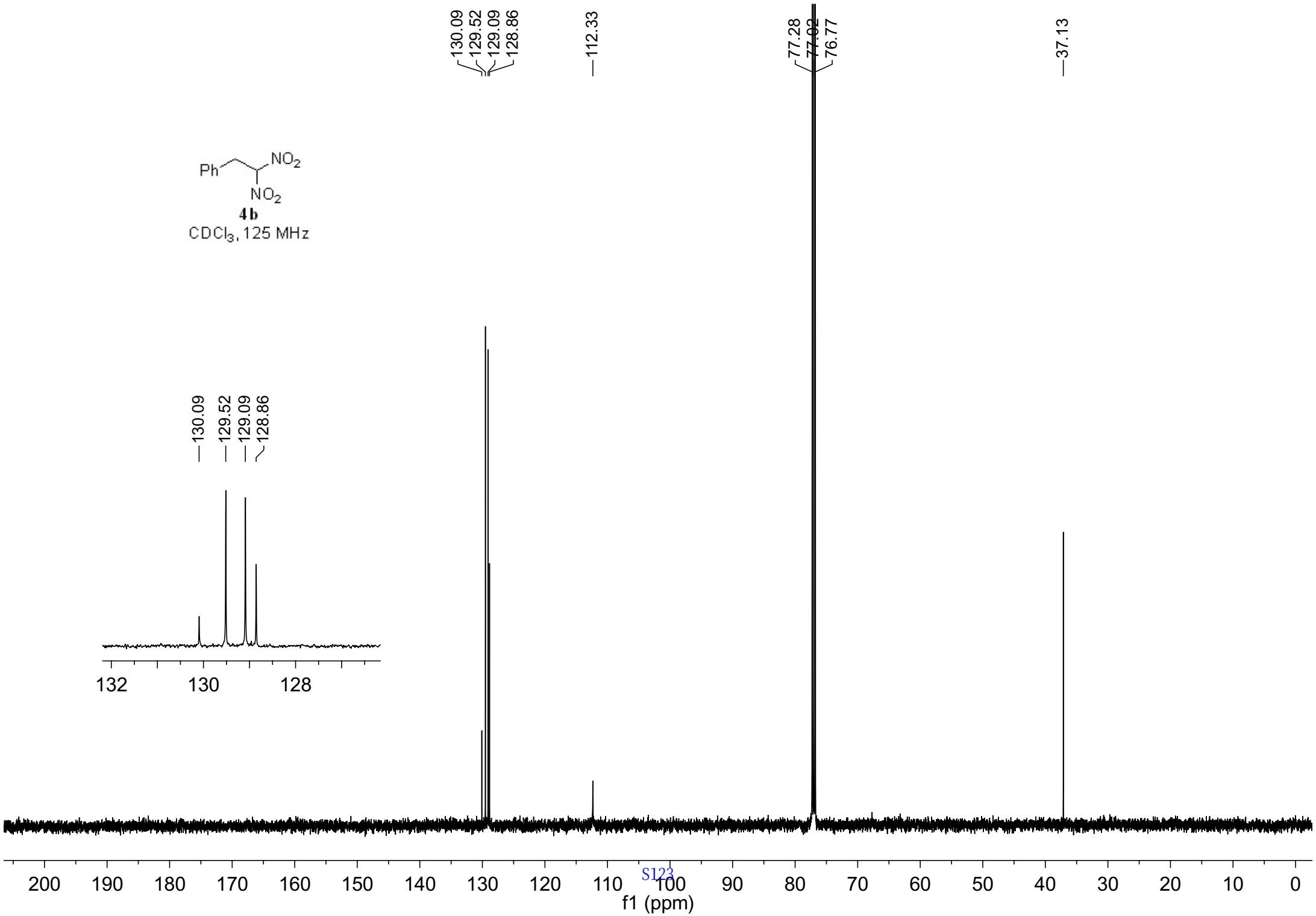
3ap
$CDCl_3$, 470 MHz

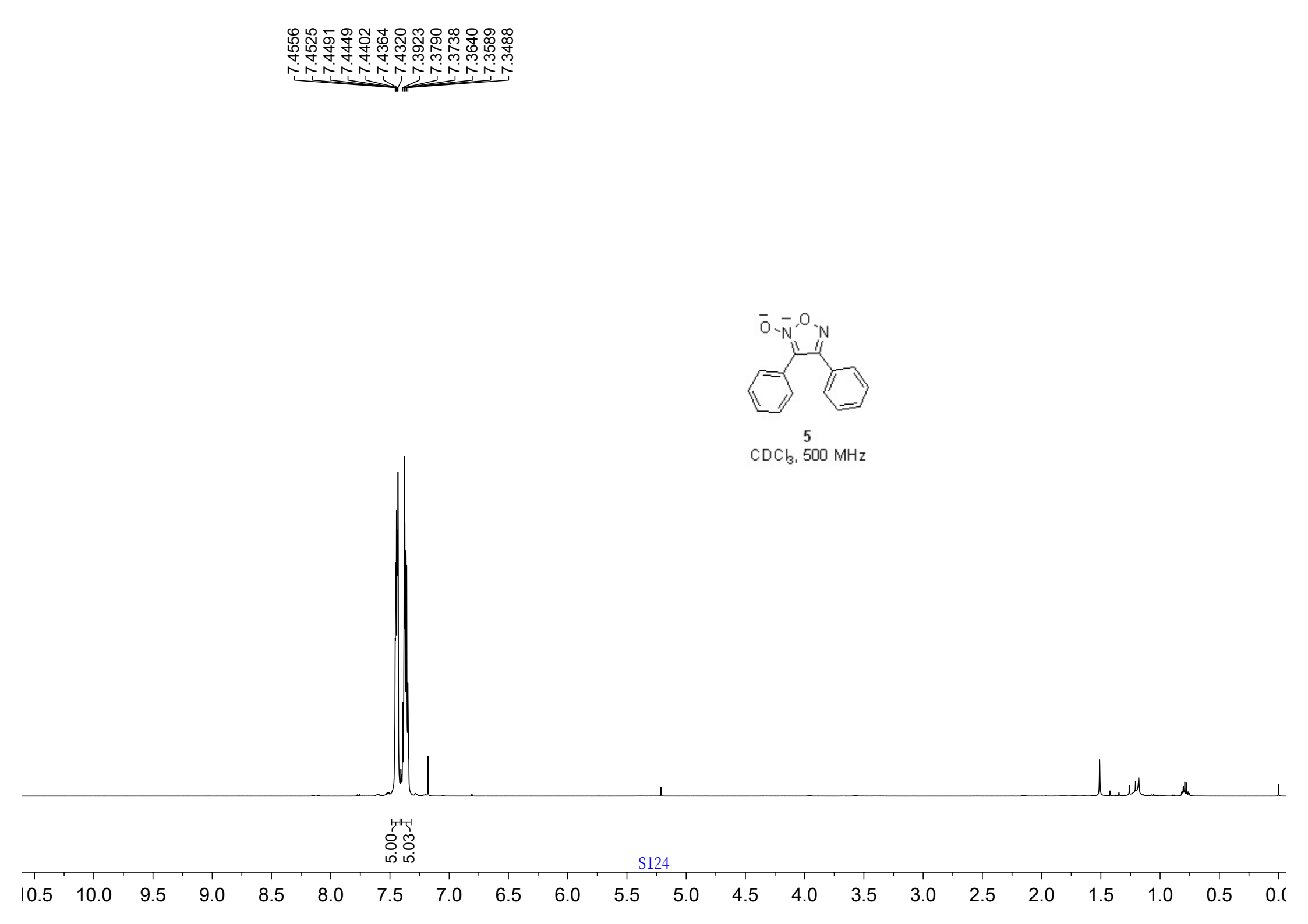

178.08
173.22
165.54
159.55
156.37
134.37
133.04
132.04
131.17
131.16
127.45
124.38
120.61
116.31
116.14
114.73
114.61
77.31
77.05
76.80
O
F
N
O
O
3ap
CDCl3, 125 MHz
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

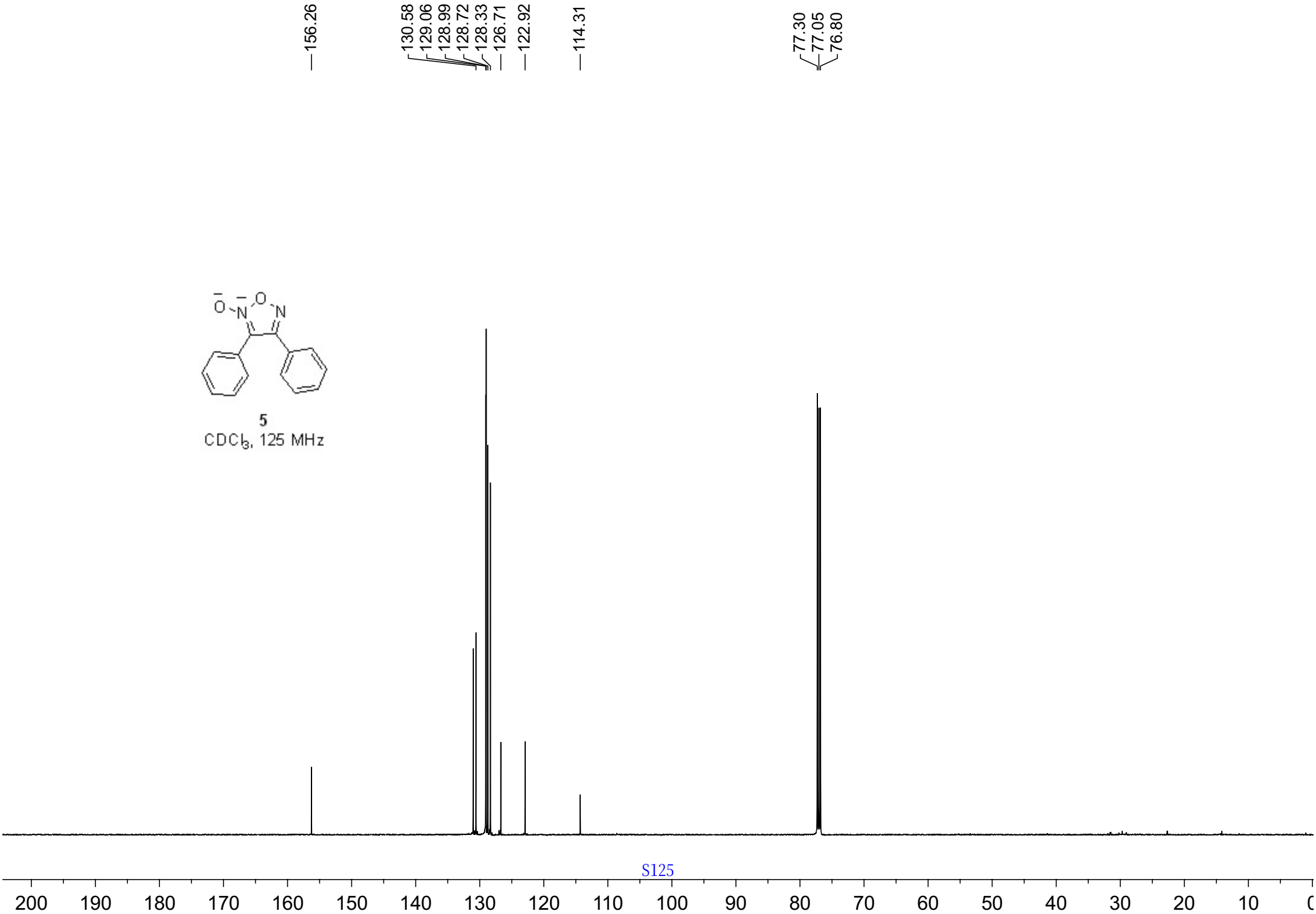

7.3422
7.3283
7.3255
7.3160
7.3132
7.2803
7.2776
7.2657
7.2600
7.2427
7.2398
7.2262
7.2251
6.7014
4.0705
3.9252
CO2Me
N
O
3s
CDCl3, 500 MHz
1.90
3.22
0.92
2.05
3.00
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0

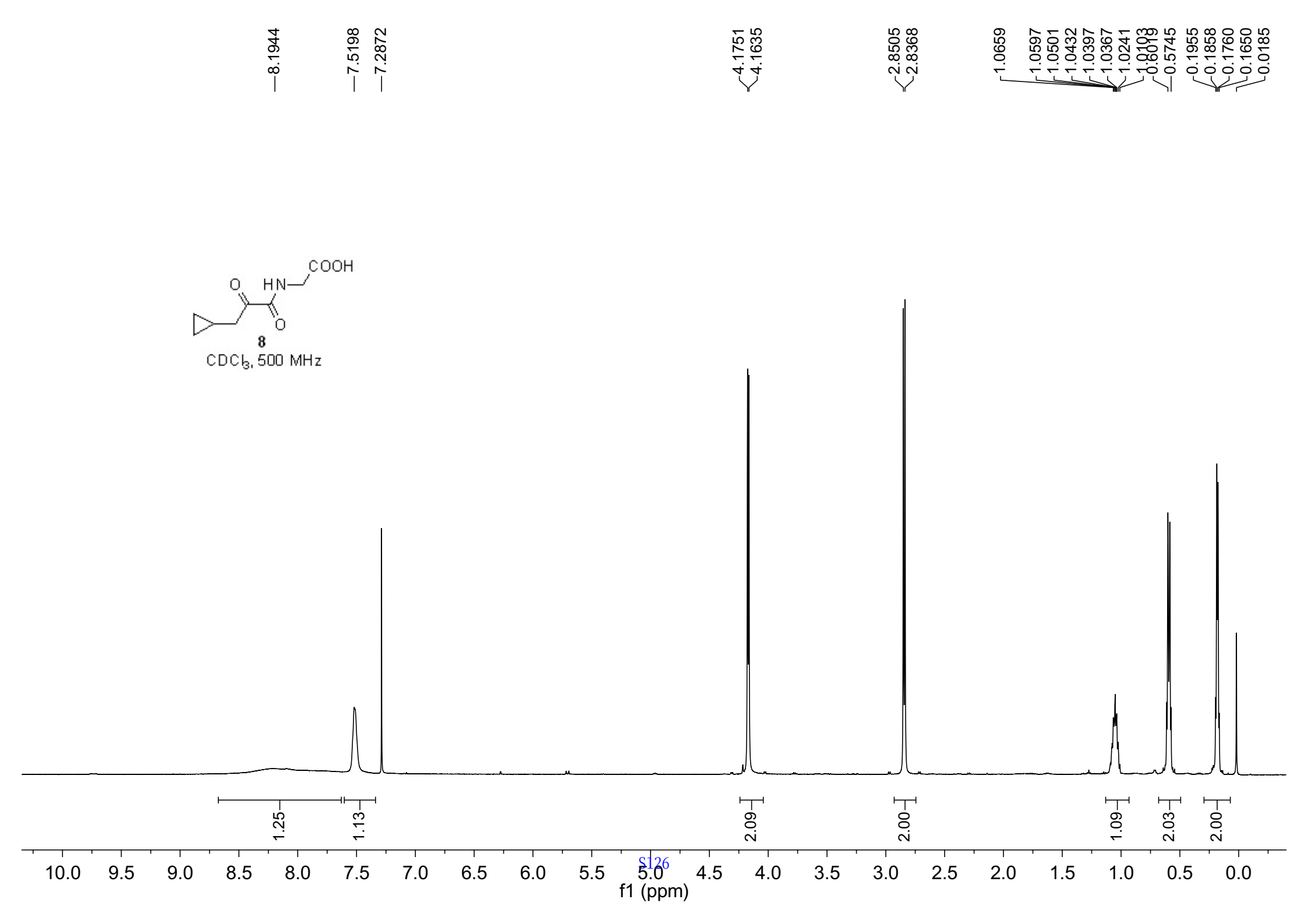

163.92
160.25
157.34
136.54
129.06
128.91
127.33
109.68
77.41
77.16
76.91
52.92
32.46
CO2Me
N
O
3s
CDCl3, 125 MHz
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

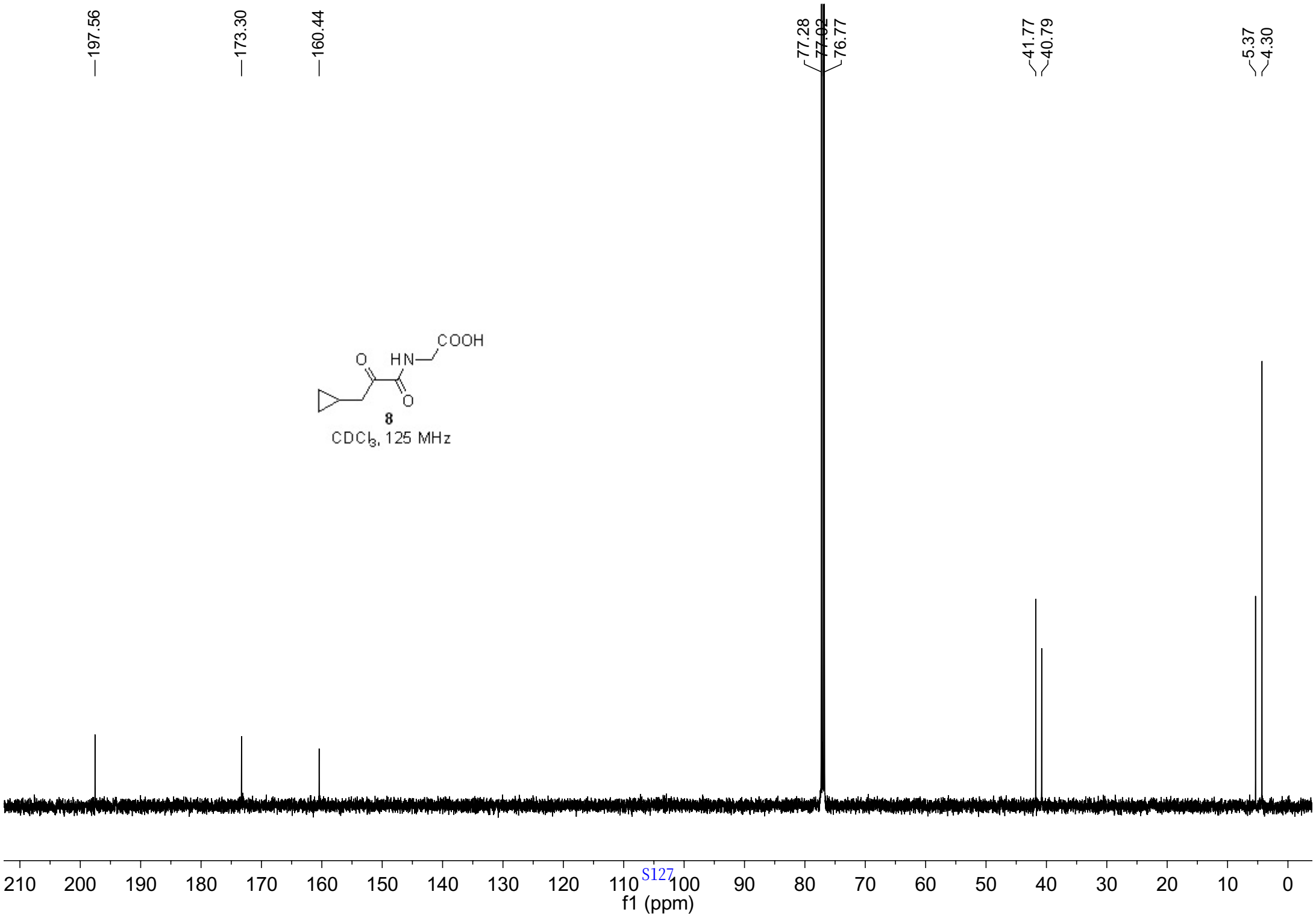

7.4243
7.4172
7.4133
7.4071
7.4064
7.4029
7.3978
7.3961
7.3928
7.3893
7.3862
7.3827
7.3796
7.2874
7.2714
7.2669
7.2628
7.2606
7.2590
7.2557
7.2525
6.3806
6.3658
6.3509
3.8461
3.8312
1.6008
Ph
NO2
NO2
4b
CDCl3, 500 MHz
3.13
2.07
1.00
2.15
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

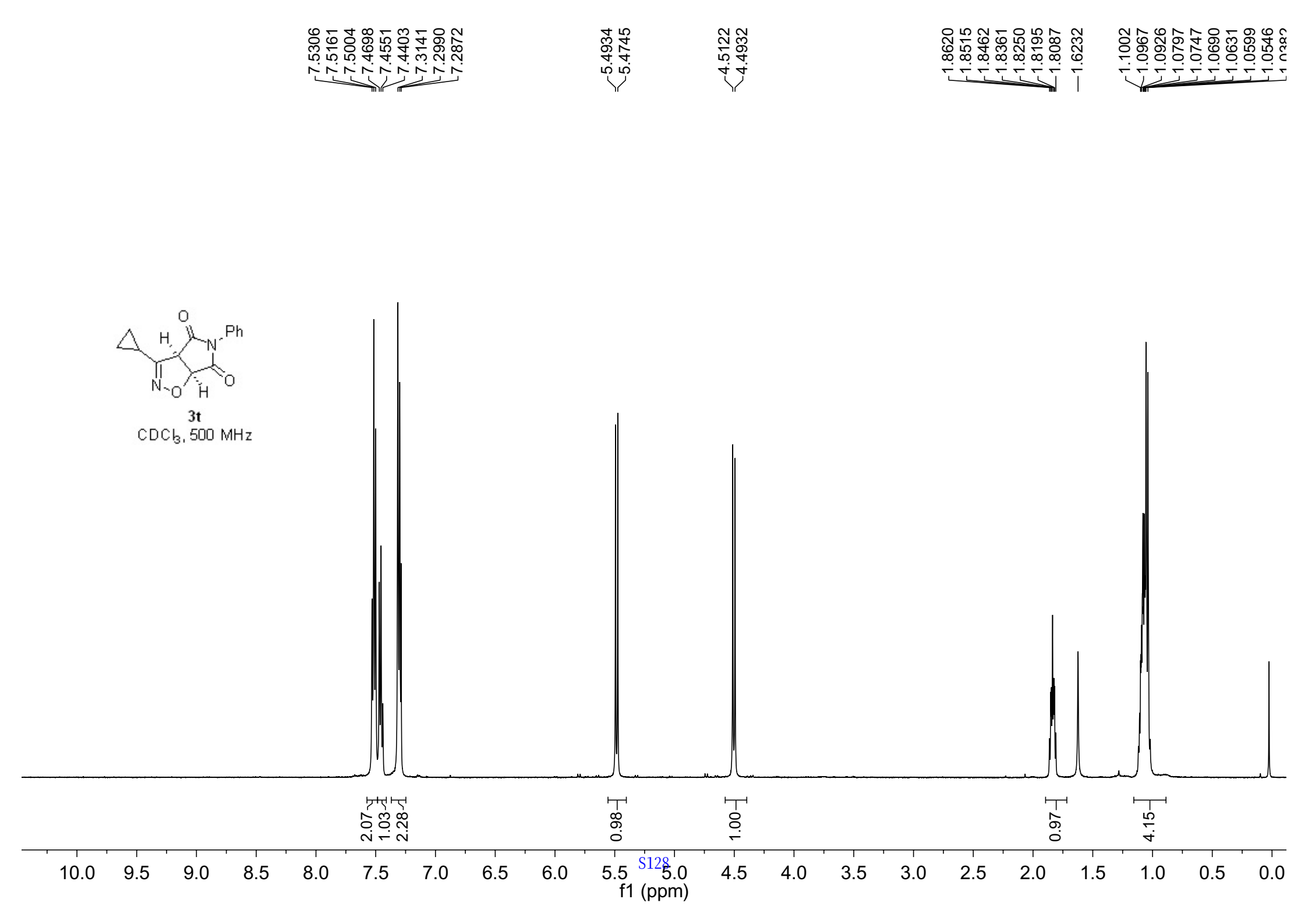

130.09
129.52
129.09
128.86
112.33
77.28
77.02
76.77
37.13
Ph
NO2
NO2
4b
CDCl3, 125 MHz
130.09
129.52
129.09
128.86
132
130
128
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

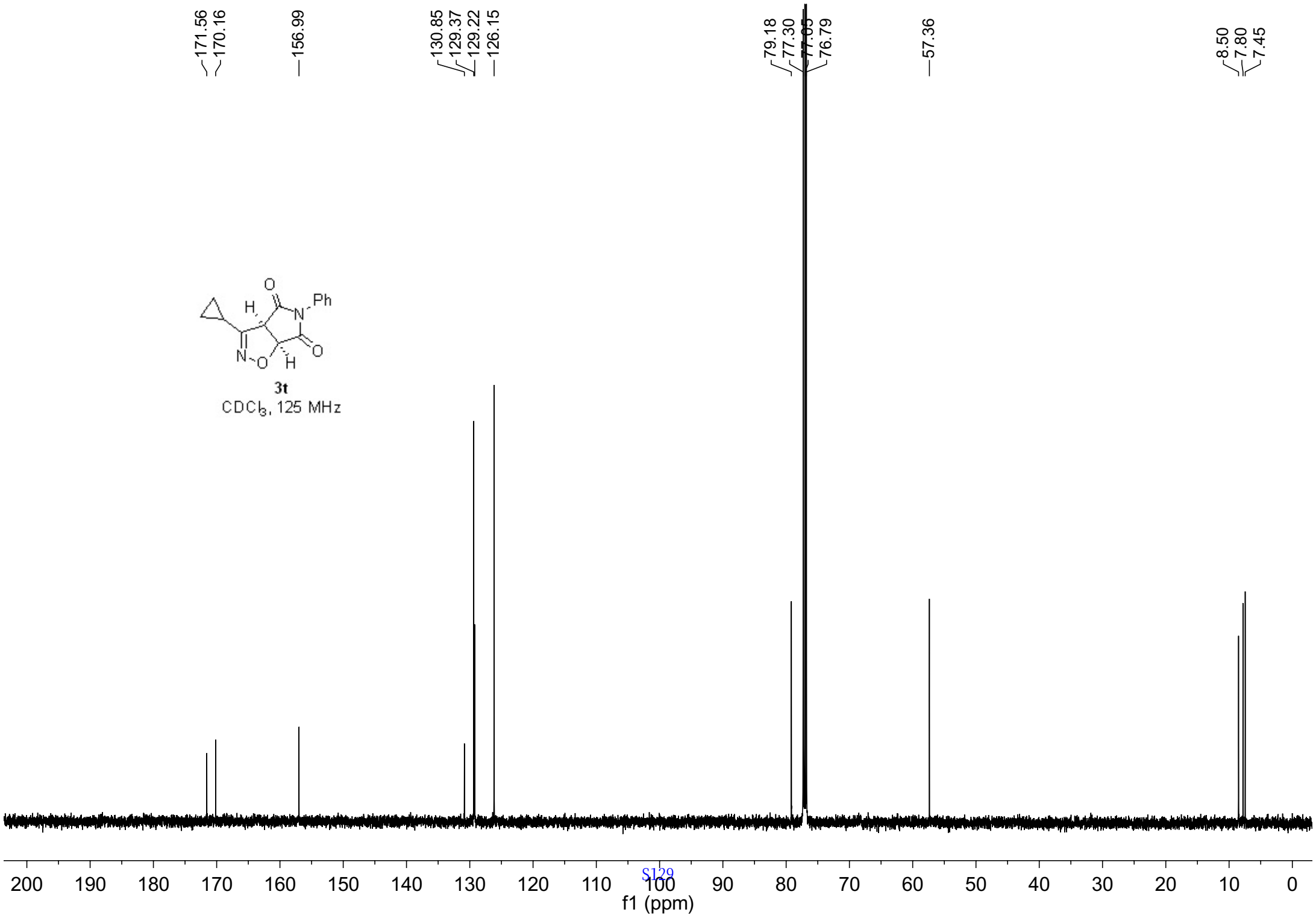

7.4556
7.4525
7.4491
7.4449
7.4402
7.4364
7.4320
7.3923
7.3790
7.3738
7.3640
7.3589
7.3488
5
CDCl3, 500 MHz
5.00
5.03
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0


156.26
130.58
129.06
128.99
128.72
128.33
126.71
122.92
114.31
77.30
77.05
76.80
5
CDCl3, 125 MHz
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0


8.1944
7.5198
7.2872
4.1751
4.1635
2.8505
2.8368
1.0659
1.0597
1.0501
1.0432
1.0397
1.0367
1.0241
1.0103
0.8019
0.5745
0.1955
0.1858
0.1760
0.1650
0.0185
COOH
HN
O
O
8
CDCl3, 500 MHz
1.25
1.13
2.09
2.00
1.09
2.03
2.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


197.56
173.30
160.44
77.28
77.02
76.77
41.77
40.79
5.37
4.30
COOH
HN
O
O
O
8
CDCl3, 125 MHz
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.5306
7.5161
7.5004
7.4698
7.4551
7.4403
7.3141
7.2990
7.2872
5.4934
5.4745
4.5122
4.4932
1.8620
1.8515
1.8462
1.8361
1.8250
1.8195
1.8087
1.6232
1.1002
1.0967
1.0926
1.0797
1.0747
1.0690
1.0631
1.0599
1.0546
O
H
N
Ph
O
N
O
H
3t
CDCl3, 500 MHz
2.07
1.03
2.28
0.98
1.00
0.97
4.15
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


171.56
170.16
156.99
130.85
129.37
129.22
126.15
79.18
77.30
77.05
76.79
57.36
8.50
7.80
7.45
O
H
N
Ph
O
N
O
H
3t
CDCl3, 125 MHz
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)