Supporting Information

Ti (IV)-catalyzed cascade synthesis of tetrahydrofuro[3,2-d]oxazole from arene-1,4-diones

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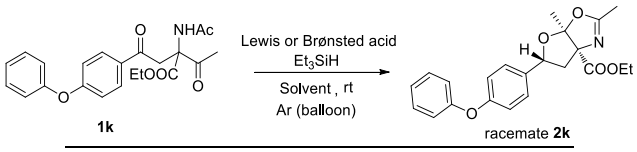
General Information

Equipment: Melting points were determined on Yanaco MP-*J*3 microscope melting point apparatus. ^{1}H and ^{13}C NMR spectra were recorded on Varian-300, Mercury-400 and Mercury-500 spectrometer. Chemical shifts are referenced to the residual solvent peak and reported in ppm (δ scale) and all coupling constant (J) values are given in Hz. The following multiplicity abbreviations are used: (s) singlet, (d) doublet, (t) triplet, (q) quartet, (m) multiplet, and (br) broad. Infrared spectra were measured on Thermo FT-IR Nicolet 5700 spectrometer (microscope transmission). ESI-HRMS data were measured on Thermo Exactive Orbitrap plus spectrometer. Circular Dichroism spectra were measured on JASCO LC-CD spectrometer.

Solvents and chemicals: All solvents were dried before use. All the reagents were obtained from Adamas-beta and other commercial suppliers and used without further purification.

Table 1. The Heterocyclization of 1k with other Catalysts[a]



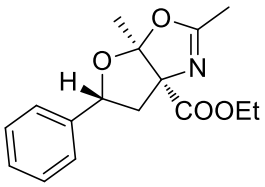
1k racemate **2k**

entry	catalyst	solvent	yield[b](%)
1	$AlCl_3$	CH_2Cl_2	NR[c]
2	$FeCl_2$	CH_2Cl_2	NR
3	$ZnCl_2$	CH_2Cl_2	NR
4	$SnCl_4$	CH_2Cl_2	NR
5	$SnCl_2$	CH_2Cl_2	NR
6	BF_3	CH_2Cl_2	NR
7	$MgCl_2$	CH_2Cl_2	NR
8	CF_3COOH	CH_2Cl_2	NR
9	H_2SO_4	CH_2Cl_2	NR

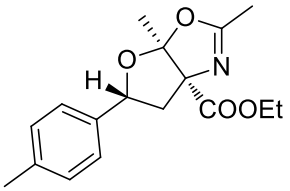
[a]All reactions were performed at room temperature under an argon atmosphere for 4 h with 0.5 mmol of **1k**, 3.8 equiv of Lewis or Brønsted acid, and 1.1 equiv of Et_3SiH in 5.0 mL of CH_2Cl_2. [b]Isolated yields. [c]No reaction.

Experimental Procedures and Characterization Data

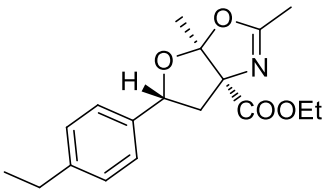
General procedure: the synthesis of tetrahydrofuro[3,2-d]oxazole **2k**: To a magnetically stirred solution of **1k** (0.5 mmol) in dry dichloromethane (5 mL) was added Et_3SiH (0.09 mL, 0.55 mmol) under an atmosphere of argon. $TiCl_4$ (0.21 mL, 1.91 mmol) was then added with a syringe to the reaction mixture cooled with an ice bath. The contents were stirred at r.t. for 4h. The solution was poured slowly into ice water and the aqueous phase was extracted with dichloromethane. The organic layers were combined, washed with brine, dried over Na_2SO_4. After filtration and concentration under reduced pressure, the residue was purified by flash column chromatography to afford the desired product **2k**.



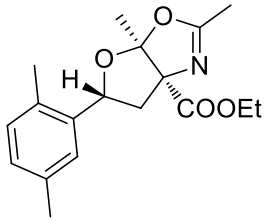
(3aS*, 5R*, 6aS*)-Ethyl 2,3a-dimethyl-5-phenyl-3a,5,6,6a-tetrahydrofuro[3,2-d]oxazole-6a-carboxylate 2a. Colorless oil. The title compound was prepared according to the general procedure and purified by silica gel column chromatography eluted with 20% ethyl acetate in petroleum ether. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.36 (m, 4H), 7.32 (m, 1H), 4.95 (dd, J_1 = 11.5 Hz, J_2 = 4.5 Hz, 1H), 4.29 (m, 2H), 2.73 (t, J = 12.3, 1H), 2.49 (dd, J_1 = 13.0 Hz, J_2 = 4.5 Hz, 1H), 2.14 (s, 3H), 1.67 (s, 3H), 1.32 (t, J = 7.0 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.2, 167.0, 138.4, 128.4, 128.2, 126.1, 117.3, 84.9, 79.8, 62.0, 44.7, 20.7, 14.3, 14.1; IR (NEAT): ν 3065, 2981, 1735, 1658, 1501, 1299, 1094 cm^{-1}; ESI-HRMS m/z calcd for $C_{16}H_{20}O_4N$ ($M+H^+$): 290.1387, found: 290.1387.



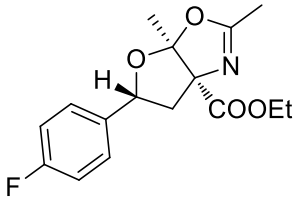
(3aS*, 5R*, 6aS*)-Ethyl 2,3a-dimethyl-5-(p-tolyl)-3a,5,6,6a-tetrahydrofuro[3,2-d]oxazole-6a-carboxylate 2b. Colorless oil. The title compound was prepared according to the general procedure and purified by silica gel column chromatography eluted with 20% ethyl acetate in petroleum ether. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.26 (d, J = 8.0 Hz, 2H), 7.16 (d, J = 8.0 Hz, 2H), 4.92 (dd, J_1 = 11.0 Hz, J_2 = 4.0 Hz, 1H), 4.28 (m, 2H), 2.73 (t, J = 12.3 Hz, 1H), 2.47 (dd, J_1 = 13.0 Hz, J_2 = 4.5 Hz, 1H), 2.34 (s, 3H), 2.14 (s, 3H), 1.66 (s, 3H), 1.32 (t, J = 7.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.2, 166.9, 138.0, 135.3, 129.1, 126.1, 117.3, 84.9, 79.8, 61.9, 44.6, 21.1, 20.7, 14.3, 14.1; IR (NEAT): ν 2984, 1734, 1660, 1515, 1298, 1094 cm^{-1}; ESI-HRMS m/z calcd for $C_{17}H_{22}O_4N$ ($M+H^+$): 304.1543, found: 304.1548.



(3aS*, 5R*, 6aS*)-Ethyl 5-(4-ethylphenyl)-2,3a-dimethyl-3a,5,6,6a-tetrahydrofuro[3,2-d] oxazole-6a-carboxylate 2c. Colorless oil. The title compound was prepared according to the general procedure and purified by silica gel column chromatography eluted with 20% ethyl acetate in petroleum ether. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.29 (d, J = 8.0 Hz, 2H), 7.19 (d, J = 8.0 Hz, 2H), 4.93 (dd, J_1 = 11.2 Hz, J_2 = 4.0 Hz, 1H), 4.29 (m, 2H), 2.75 (t, J = 12.2 Hz, 1H), 2.64 (q, J = 7.6 Hz, 2H), 2.48 (dd, J_1 = 12.8 Hz, J_2 = 4.0 Hz), 2.14 (s, 3H), 1.66 (s, 3H), 1.32 (t, J = 7.0 Hz, 3H), 1.23 (t, J = 7.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.2, 167.0, 144.4, 135.5, 128.0, 126.3, 117.4, 84.9, 79.9, 62.0, 44.5, 28.5, 20.7, 15.5, 14.4, 14.1. IR (NEAT): ν 2967, 1736, 1670, 1289, 1099 cm^{-1}; ESI-HRMS m/z calcd for $C_{18}H_{24}O_4N$ ($M+H^+$): 318.16998, found: 318.17053.

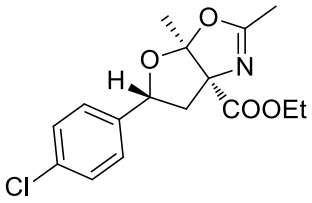


(3aS*, 5R*, 6aS*)-Ethyl 5-(2,5-dimethylphenyl)-2,3a-dimethyl-3a,5,6,6a-tetrahydrofuro [3,2-d]oxazole-6a-carboxylate 2d. Colorless oil. The title compound was prepared according to the general procedure and purified by silica gel column chromatography eluted with 20% ethyl acetate in petroleum ether. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.27 (s, 1H), 7.02 (m, 2H), 5.08 (dd, J_1 = 11.2 Hz, J_2 = 4.4 Hz, 1H), 4.29 (m, 2H), 2.66 (t, J = 12.0 Hz, 1H), 2.49 (dd, J_1 = 12.8 Hz, J_2 = 4.4 Hz, 1H), 2.33 (s, 3H), 2.27 (s, 3H), 2.15 (s, 3H), 1.70 (s, 3H), 1.32 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.3, 166.9, 136.1, 135.7, 131.8, 130.3, 128.5, 125.7, 117.1, 85.0, 61.9, 43.2, 21.0, 20.7, 18.6, 14.4, 14.1. IR (NEAT): ν 2985, 1736, 1671, 1295, 1264, 1099 cm^{-1}; ESI-HRMS m/z calcd for $C_{18}H_{24}O_4N$ ($M+H^+$): 318.16998, found: 318.16986.

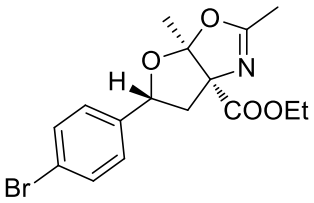


(3aS*, 5R*, 6aS*)-Ethyl 5-(4-fluorophenyl)-2,3a-dimethyl-3a,5,6,6a-tetrahydrofuro[3,2-d] oxazole-6a-carboxylate 2e. Colorless oil. The title compound was prepared according to the general procedure and purified by silica gel column chromatography eluted with 20% ethyl acetate in petroleum ether. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34 (m, 2H), 7.03 (t, J = 8.8 Hz, 2H), 4.93 (dd, J_1 = 11.2 Hz, J_2 = 4.4 Hz, 1H), 4.31 (m, 2H), 2.70 (t, J = 12.0 Hz, 1H), 2.48 (dd, J_1 = 12.8 Hz, J_2 = 4.4 Hz, 1H), 2.14 (s, 3H), 1.66 (s, 3H), 1.33 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.0, 167.0, 162.5 (J = 245 Hz), 134.1 (J = 3 Hz), 127.8 (J = 8 Hz), 117.2, 115.3 (J = 21 Hz), 84.9, 79.2, 62.0, 44.7, 20.6, 14.3, 14.1; IR (NEAT): ν 3128, 2988, 1737, 1652, 1512, 1223, 1096

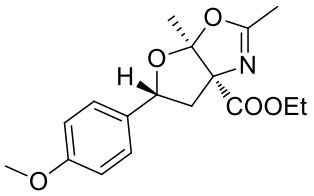
cm^{-1}; ESI-HRMS m/z calcd for $C_{16}H_{19}O_4NF$ ($M+H^+$): 308.12926, found: 308.12866.



(3aS*, 5R*, 6aS*)-Ethyl 5-(4-chlorophenyl)-2,3a-dimethyl-3a,5,6,6a-tetrahydrofuro[3,2-d] oxazole-6a-carboxylate 2f. Pale yellow oil. The title compound was prepared according to the general procedure and purified by silica gel column chromatography eluted with 20% ethyl acetate in petroleum ether. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30 (m, 4H), 4.92 (dd, J_1 = 11.2 Hz, J_2 = 4.4 Hz, 1H), 4.29 (m, 2H), 2.67 (t, J = 12.2 Hz, 1H), 2.50 (dd, J_1 = 12.8 Hz, J_2 = 4.4 Hz, 1H), 2.14 (s, 3H), 1.67 (s, 3H), 1.32 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.0, 167.1, 137.0, 133.9, 128.6, 127.4, 117.4, 84.8, 79.1, 62.1, 44.6, 20.6, 14.3, 14.1; IR (NEAT): ν 2986, 1735, 1665, 1494, 1295, 1091 cm^{-1}; ESI-HRMS m/z calcd for $C_{16}H_{19}O_4NCl$ ($M+H^+$): 324.09971, found: 324.09964.

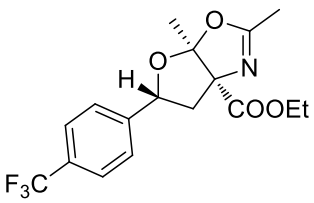


(3aS*, 5R*, 6aS*)-Ethyl 5-(4-bromophenyl)-2,3a-dimethyl-3a,5,6,6a-tetrahydrofuro[3,2-d] oxazole-6a-carboxylate 2g. Pale yellow oil. The title compound was prepared according to the general procedure and purified by silica gel column chromatography eluted with 20% ethyl acetate in petroleum ether. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.48 (d, J = 8.0 Hz, 2H), 7.23 (d, J = 8.0 Hz, 2H), 4.89 (m, 1H), 4.27 (m, 2H), 2.66 (t, J = 12.0 Hz, 1H), 2.48 (dd, J_1 = 12.5 Hz, J_2 = 3.5 Hz, 1H), 2.13 (s, 3H), 1.65 (s, 3H), 1.32 (t, J = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.0, 167.1, 137.6, 131.6, 127.8, 122.1, 117.4, 84.9, 79.2, 62.1, 44.7, 20.7, 14.4, 14.2; IR (NEAT): ν 2981, 1732, 1658, 1491, 1219, 1089 cm^{-1}; ESI-HRMS m/z calcd for $C_{16}H_{19}O_4NBr$ ($M+H^+$): 368.0492, found: 368.0487.

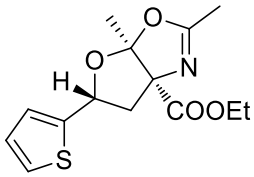


(3aS*, 5R*, 6aS*)-Ethyl 5-(4-methoxyphenyl)-2,3a-dimethyl-3a,5,6,6a-tetrahydrofuro[3,2-d] oxazole-6a-carboxylate 2h. Pale yellow oil. The title compound was prepared according to the general procedure and purified by silica gel column chromatography eluted with 20% ethyl acetate in petroleum ether. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30 (d, J = 8.4 Hz, 2H), 6.89 (d, J = 8.4 Hz, 2H), 4.91 (dd, J_1 = 11.2 Hz, J_2 = 4.4 Hz, 1H), 4.29 (m, 2H), 3.81 (s, 3H), 2.74 (t, J = 12.0 Hz, 1H), 2.47 (dd, J_1 = 12.8 Hz, J_2 = 4.0 Hz, 1H), 2.16 (s, 3H), 1.66 (s, 3H), 1.33 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.2, 167.3, 159.7, 130.1, 127.7, 117.5, 113.9, 84.7, 79.8, 62.1, 55.3,

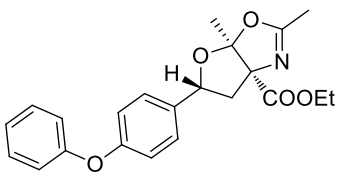
44.5, 20.7, 14.4, 14.2; IR (NEAT): ν 2987, 1733, 1670, 1516, 1298, 1099 cm^{-1}; ESI-HRMS m/z calcd for $C_{17}H_{22}O_5N$ ($M+H^+$): 320.14925, found: 320.14908.



(3aS*,5R*,6aS*)-Ethyl 2,3a-dimethyl-5-(4-(trifluoromethyl)phenyl)-3a,5,6,6a-tetrahydrofuro [3,2-d]oxazole-6a-carboxylate 2i. Pale yellow oil. The title compound was prepared according to the general procedure and purified by silica gel column chromatography eluted with 25% ethyl acetate in petroleum ether. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.63 (d, J = 8.4 Hz, 2H), 7.48 (d, J = 8.4 Hz, 2H), 5.01 (dd, J_1 = 11.2 Hz, J_2 = 4.4 Hz, 1H), 4.30 (m, 2H), 2.69 (t, J = 12.0 Hz, 1H), 2.58 (dd, J_1 = 12.8 Hz, J_2 = 4.4 Hz, 1H), 2.18 (s, 3H), 1.69 (s, 3H), 1.33 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.5, 168.1, 142.4, 130.5 (J = 32 Hz), 126.3, 125.5 (J = 4 Hz), 124.0 (J = 270 Hz), 118.1, 84.4, 79.3, 62.4, 44.6, 20.6, 14.4, 14.2; IR (NEAT): ν 2988, 1738, 1669, 1327, 1298, 1127 cm^{-1}; ESI-HRMS m/z calcd for $C_{17}H_{19}O_4NF_3$ ($M+H^+$): 358.1261, found: 358.1254.

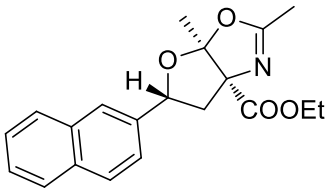


(3aS*, 5R*, 6aS*)-Ethyl 2,3a-dimethyl-5-(thiophen-2-yl)-3a,5,6,6a-tetrahydrofuro[3,2-d] oxazole-6a-carboxylate 2j. Pale yellow oil. The title compound was prepared according to the general procedure and purified by silica gel column chromatography eluted with 20% ethyl acetate in petroleum ether. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31 (d, J = 5.2 Hz, 1H), 7.08 (d, J = 2.8 Hz, 1H), 6.98 (t, J = 4.2 Hz, 1H), 5.19 (dd, J_1 = 11.2 Hz, J_2 = 4.4 Hz, 1H), 4.28 (m, 2H), 2.90 (t, J = 12.0 Hz, 1H), 2.55 (dd, J_1 = 12.8 Hz, J_2 = 4.4 Hz, 1H), 2.14 (s, 3H), 1.66 (s, 3H), 1.33 (t, J = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.9, 167.1, 141.0, 126.6, 125.8, 125.7, 117.0, 84.8, 75.7, 62.0, 44.5, 20.7, 14.3, 14.1; IR (NEAT): ν 3106, 2985, 1733, 1665, 1504, 1297, 1095 cm^{-1}; ESI-HRMS m/z calcd for $C_{14}H_{18}O_4NS$ ($M+H^+$): 296.09511, found: 296.09491.

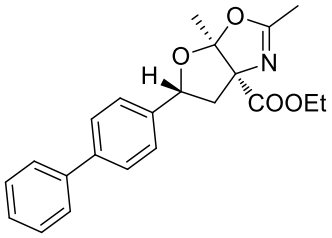


(3aS*, 5R*, 6aS*)-Ethyl 2,3a-dimethyl-5-(4-phenoxyphenyl)-3a,5,6,6a-tetrahydrofuro[3,2-d] oxazole-6a-carboxylate 2k. Colorless oil. The title compound was prepared according to the general procedure and purified by silica gel column chromatography eluted with 20% ethyl acetate in petroleum ether. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.33 (m, 4H), 7.11 (t, J = 7.2 Hz, 1H), 6.99 (m, 4H), 4.93 (dd, J_1 = 11.5 Hz, J_2 = 4.5 Hz, 1H), 4.33 (m, 1H), 4.26 (m, 1H), 2.74 (t, J = 12.0 Hz, 1H), 2.49 (dd, J_1 = 13.0 Hz, J_2 = 4.5 Hz, 1H), 2.15 (s, 3H), 1.66 (s, 3H), 1.33 (t, J = 7.2 Hz, 3H); ^{13}C

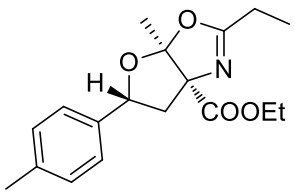
NMR (125 MHz, $CDCl_3$): δ 170.2, 167.1, 157.3, 157.0, 133.0, 129.7, 127.8, 123.4, 119.0, 118.8, 117.4, 84.9, 79.6, 62.1, 44.6, 20.7, 14.4, 14.2; IR (NEAT): ν 3039, 2987, 1734, 1670, 1509, 1489, 1241, 1098 cm^{-1}; ESI-HRMS m/z calcd for $C_{22}H_{24}O_5N$ ($M+H^+$): 382.1649, found: 382.1659.



(3aS*, 5R*, 6aS*)-Ethyl 2,3a-dimethyl-5-(naphthalen-2-yl)-3a,5,6,6a-tetrahydrofuro[3,2-d] oxazole-6a-carboxylate 2l. Pale yellow oil. The title compound was prepared according to the general procedure and purified by silica gel column chromatography eluted with 20% ethyl acetate in petroleum ether. ^1H NMR (300 MHz, $CDCl_3$): δ 7.84 (m, 4H), 7.46 (m, 3H), 5.12 (dd, J_1 = 11.4 Hz, J_2 = 3.9 Hz, 1H), 4.29 (m, 2H), 2.82 (t, J = 12.2 Hz, 1H), 2.56 (dd, J_1 = 12.9 Hz, J_2 = 4.2 Hz, 1H), 2.16 (s, 3H), 1.71 (s, 3H), 1.32 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.2, 167.1, 135.8, 133.3, 133.1, 128.4, 128.0, 127.7, 126.2, 126.1, 125.2, 123.8, 117.6, 85.0, 80.1, 62.1, 44.7, 20.8, 14.4, 14.2; IR (NEAT): ν 3058, 2977, 1730, 1676, 1509, 1295, 1092 cm^{-1}; ESI-HRMS m/z calcd for $C_{20}H_{22}O_4N$ ($M+H^+$): 340.1543, found: 340.1559.

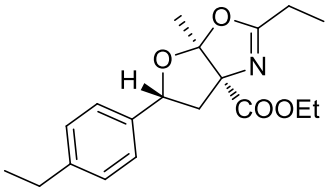


(3aS*, 5R*, 6aS*)-Ethyl 5-([1,1'-biphenyl]-4-yl)-2,3a-dimethyl-3a,5,6,6a-tetrahydrofuro [3,2-d]oxazole-6a-carboxylate 2m. Colorless oil. The title compound was prepared according to the general procedure and purified by silica gel column chromatography eluted with 20% ethyl acetate in petroleum ether. ^1H NMR (300 MHz, $CDCl_3$): δ 7.58 (m, 4H), 7.43 (m, 4H), 7.34 (t, J = 7.2 Hz, 1H), 5.01 (dd, J_1 = 11.1 Hz, J_2 = 4.2 Hz, 1H), 4.29 (m, 2H), 2.79 (t, J = 12.2 Hz, 1H), 2.54 (dd, J_1 = 12.9 Hz, J_2 = 4.5 Hz, 1H), 2.15 (s, 3H), 1.69 (s, 3H), 1.33 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.1, 167.2, 141.3, 140.7, 137.3, 128.8, 127.4, 127.3, 127.1, 126.6, 117.5, 84.9, 79.7, 62.1, 44.6, 20.7, 14.4, 14.2; IR (NEAT): ν 2986, 1734, 1670, 1384, 1288, 1098 cm^{-1}; ESI-HRMS m/z calcd for $C_{22}H_{24}O_4N$ ($M+H^+$): 366.1700, found: 366.1696.

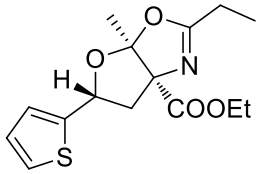


(3aS*,5R*,6aS*)-Ethyl 2-ethyl-3a-methyl-5-(p-tolyl)-3a,5,6,6a-tetrahydrofuro[3,2-d]oxazole-6a-carboxylate 2n. Pale yellow oil. The title compound was prepared according to the general procedure and purified by silica gel column chromatography eluted with 20% ethyl acetate in petroleum ether. ^1H NMR (300 MHz, $CDCl_3$): δ 7.27 (d, J = 7.8 Hz, 2H), 7.18 (d, J = 7.8 Hz, 2H),

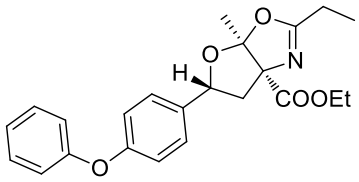
4.91 (dd, J_1 = 11.1 Hz, J_2 = 3.6 Hz, 1H), 4.27 (m, 2H), 2.75 (t, J = 12.1 Hz, 1H), 2.48 (m, 3H), 2.36 (s, 3H), 1.67 (s, 3H), 1.31 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 171.2, 170.2, 138.0, 135.4, 129.1, 126.2, 117.1, 84.7, 79.9, 61.9, 44.5, 21.9, 21.1, 20.7, 14.1, 10.2; IR (NEAT): ν 2987, 1737, 1648, 1502, 1284, 1134, 1088 cm^{-1}; ESI-HRMS m/z calcd for $C_{18}H_{24}O_4N$ ($M+H^+$): 318.1700, found:318.1704.



(3aS*, 5R*, 6aS*)-Ethyl 2-ethyl-5-(4-ethylphenyl)-3a-methyl-3a,5,6,6a-tetrahydrofuro[3,2-d] oxazole-6a-carboxylate 2o. Colorless oil. The title compound was prepared according to the general procedure and purified by silica gel column chromatography eluted with 20% ethyl acetate in petroleum ether. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.29 (d, J = 7.8 Hz, 2H), 7.19 (d, J = 7.8 Hz, 2H), 4.91 (dd, J_1 = 11.4 Hz, J_2 = 4.2 Hz, 1H), 4.31 (m, 1H), 4.23 (m, 1H), 2.76 (t, J = 12.3 Hz, 1H), 2.64 (q, J = 7.6 Hz, 2H), 2.49 (dd, J_1 = 12.6 Hz, J_2 = 4.2 Hz, 1H), 2.44 (q, J = 7.6 Hz, 2H), 1.66 (s, 3H), 1.31 (t, J = 7.2 Hz, 3H), 1.28 (t, J = 7.8 Hz, 3H), 1.22 (t, J = 7.8 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 171.1, 170.3, 144.4, 135.6, 127.9, 126.2, 117.0, 84.7, 79.8, 61.9, 44.4, 28.5, 21.8, 20.7, 15.5, 14.1, 10.2; IR (NEAT): ν 2971, 1737, 1665, 1297, 1265, 1230, 1098 cm^{-1}; ESI-HRMS m/z calcd for $C_{19}H_{26}O_4N$ ($M+H^+$): 332.18563, found:332.18585.

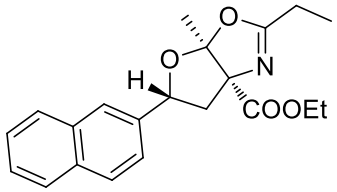


(3aS*, 5R*, 6aS*)-Ethyl 2-ethyl-3a-methyl-5-(thiophen-2-yl)-3a,5,6,6a-tetrahydrofuro[3,2-d] oxazole-6a-carboxylate 2p. Colorless oil. The title compound was prepared according to the general procedure and purified by silica gel column chromatography eluted with 20% ethyl acetate in petroleum ether. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31 (d, J = 5.2 Hz, 1H), 7.07 (m, 1H), 6.98 (t, J = 3.6 Hz, 1H), 5.16 (dd, J_1 = 11.2 Hz, J_2 = 4.0 Hz, 1H), 4.27 (m, 2H), 2.90 (t, J = 12.2 Hz, 1H), 2.57 (dd, J_1 = 12.8 Hz, J_2 = 4.4 Hz, 1H), 2.44 (q, J = 7.5 Hz, 2H), 1.63 (s, 3H), 1.30 (m, 6H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 171.3, 169.9, 141.1, 126.7, 125.8, 125.7, 116.8, 84.6, 75.8, 62.0, 44.4, 21.8, 20.7, 14.1, 10.2; IR (NEAT): ν 2985, 1737, 1665, 1298, 1265, 1098 cm^{-1}; ESI-HRMS m/z calcd for $C_{15}H_{20}O_4NS$ ($M+H^+$): 310.11076, found: 310.11035.

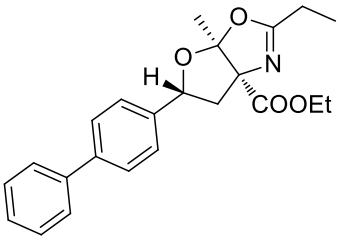


(3aS*, 5R*, 6aS*)-Ethyl 2-ethyl-3a-methyl-5-(4-phenoxyphenyl)-3a,5,6,6a-tetrahydrofuro [3,2-d]oxazole-6a-carboxylate 2q. Colorless oil. The title compound was prepared according to

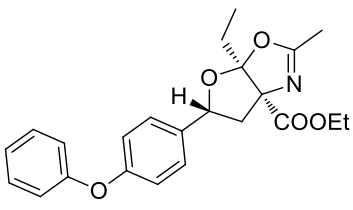
the general procedure and purified by silica gel column chromatography eluted with 20% ethyl acetate in petroleum ether. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.33 (m, 4H), 7.10 (t, J = 7.4 Hz, 1H), 7.00 (m, 4H), 4.91 (dd, J_1 = 11.4 Hz, J_2 = 3.9 Hz, 1H), 4.29 (m, 2H), 2.75 (t, J = 12.2 Hz, 1H), 2.48 (m, 3H), 1.66 (s, 3H), 1.30 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 171.3, 170.2, 157.3, 157.0, 133.1, 129.7, 127.8, 123.4, 118.9, 118.8, 117.1, 84.7, 79.6, 62.0, 44.5, 21.9, 20.7, 14.1, 10.2; IR (NEAT): ν 2982, 1734, 1656, 1589, 1490, 1239, 1087 cm^{-1}; ESI-HRMS m/z calcd for $C_{23}H_{26}O_5N$ ($M+H^+$): 396.1805, found: 396.1795.



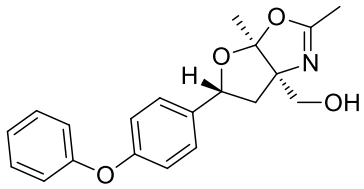
(3aS*, 5R*, 6aS*)-Ethyl 2-ethyl-3a-methyl-5-(naphthalen-2-yl)-3a,5,6,6a-tetrahydrofuro [3,2-d]oxazole-6a-carboxylate 2r. Pale yellow oil. The title compound was prepared according to the general procedure and purified by silica gel column chromatography eluted with 20% ethyl acetate in petroleum ether. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.85 (m, 4H), 7.48 (m, 3H), 5.11 (dd, J_1 = 11.1 Hz, J_2 = 4.2 Hz, 1H), 4.30 (m, 2H), 2.84 (t, J = 12.0 Hz, 1H), 2.59 (dd, J_1 = 12.9 Hz, J_2 = 4.5 Hz, 1H), 2.48 (q, J = 7.5 Hz, 2H), 1.72 (s, 3H), 1.32 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 171.2, 170.3, 135.9, 133.2, 133.1, 128.4, 127.9, 127.7, 126.2, 126.1, 125.2, 123.8, 117.2, 84.9, 80.0, 62.0, 44.6, 21.9, 20.8, 14.1, 10.3; IR (NEAT): ν 2983, 1736, 1660, 1508, 1297, 1095 cm^{-1}; ESI-HRMS m/z calcd for $C_{21}H_{24}O_4N$ ($M+H^+$): 354.1700, found: 354.1707.



(3aS*, 5R*, 6aS*)-Ethyl 5-([1,1'-biphenyl]-4-yl)-2-ethyl-3a-methyl-3a,5,6,6a-tetrahydrofuro [3,2-d]oxazole-6a-carboxylate 2s. Pale yellow oil. The title compound was prepared according to the general procedure and purified by silica gel column chromatography eluted with 20% ethyl acetate in petroleum ether. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.59 (m, 4H), 7.44 (m, 4H), 7.34 (m, 1H), 4.99 (dd, J_1 = 11.1 Hz, J_2 = 4.5 Hz, 1H), 4.28 (m, 2H), 2.80 (t, J = 12.2 Hz, 1H), 2.56 (dd, J_1 = 13.2 Hz, J_2 = 4.5 Hz, 1H), 2.47 (q, J = 7.6 Hz, 2H), 1.69 (s, 3H), 1.31 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 171.1, 170.2, 141.1, 140.6, 137.4, 128.7, 127.3, 127.2, 127.0, 126.5, 117.1, 84.7, 79.6, 61.9, 44.4, 21.8, 20.7, 14.1, 10.2; IR (NEAT): ν 3031, 2979, 1735, 1659, 1489, 1223, 1089 cm^{-1}; ESI-HRMS m/z calcd for $C_{23}H_{26}O_4N$ ($M+H^+$): 380.1856, found: 380.1846.

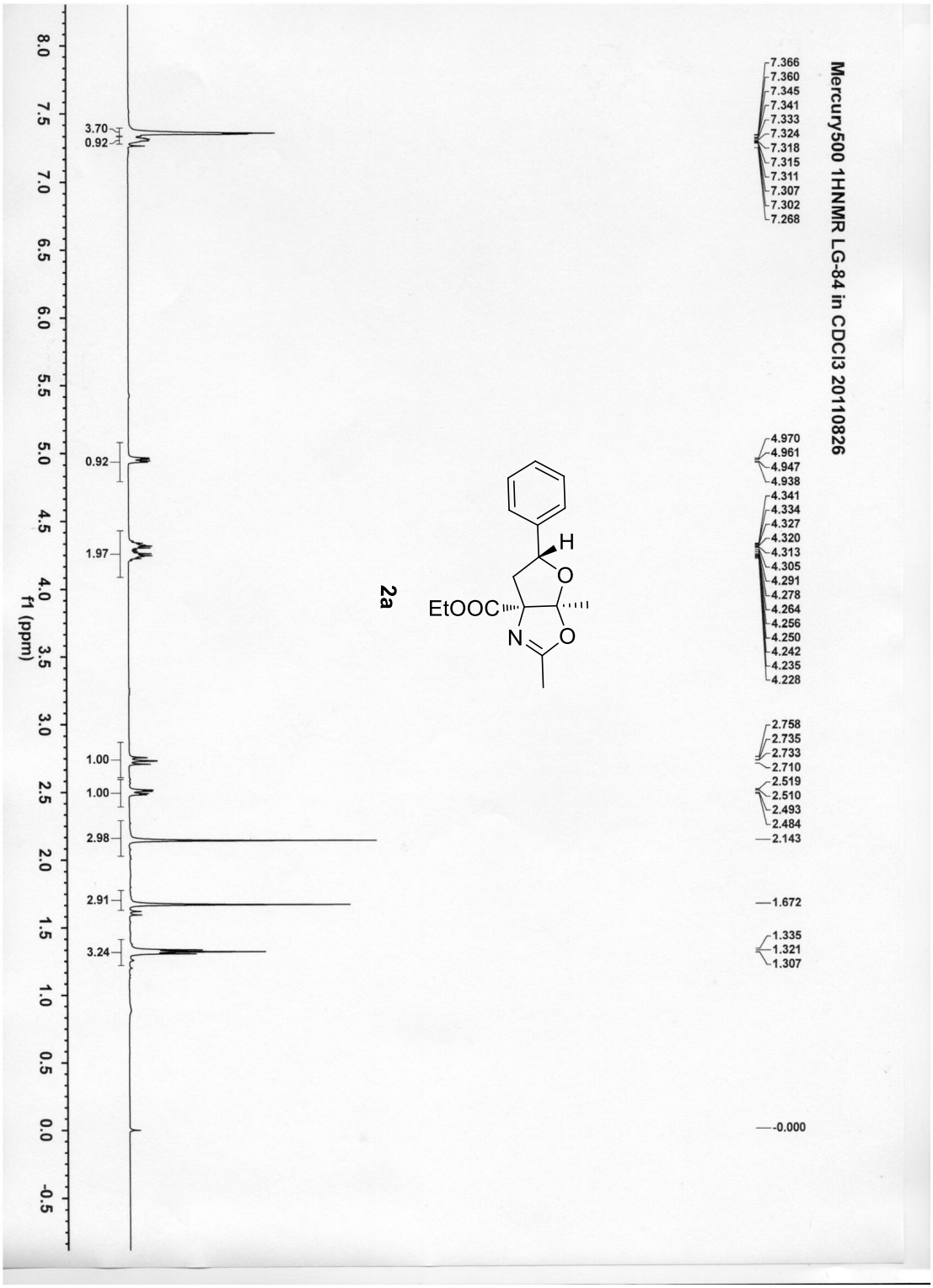


(3aS*, 5R*, 6aS*)-Ethyl 3a-ethyl-2-methyl-5-(4-phenoxyphenyl)-3a,5,6,6a-tetrahydrofuro [3,2-d]oxazole-6a-carboxylate 2t. Colorless oil. The title compound was prepared according to the general procedure and purified by silica gel column chromatography eluted with 20% ethyl acetate in petroleum ether. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34 (m, 4H), 7.10 (t, J = 7.2 Hz, 1H), 7.00 (m, 4H), 4.94 (dd, J_1 = 11.2 Hz, J_2 = 3.6 Hz, 1H), 4.28 (m, 2H), 2.67 (t, J = 12.2 Hz, 1H), 2.50 (dd, J_1 = 13.2 Hz, J_2 =4.0 Hz, 1H), 2.15 (s, 3H), 1.98 (q, J = 7.2 Hz, 2H), 1.32 (t, J = 7.0 Hz, 3H), 1.06 (t, J = 7.4 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 170.2, 167.2, 157.2, 157.0, 133.3, 129.7, 127.7, 123.4, 119.3, 118.9, 118.7, 84.5, 79.3, 62.0, 44.9, 27.4, 14.4, 14.1, 7.7; IR (NEAT): ν 2983, 1734, 1669, 1489, 1289, 1242, 1091 cm^{-1}; ESI-HRMS m/z calcd for $C_{23}H_{26}O_5N$ ($M+H^+$): 396.18055, found: 396.18079.



((3aS*, 5R*, 6aR*)-2,3a-Dimethyl-5-(4-phenoxyphenyl)-3a,5,6,6a-tetrahydrofuro[3,2-d] oxazol-6a-yl)methanol 6. To a solution of **2k** (0.4 mmol) in EtOH (4 mL) was added K_2HPO_4 (2.76 mmol) buffer and $NaBH_4$ (1.2 mmol), then stirred for 12 h at room temperature. The solution was poured slowly into a mixture of saturated aq. NH_4Cl and EtOAc. The aqueous phase was extracted with EtOAc. The combined organic layers were washed with brine, dried over Na_2SO_4, filtered and concentrated. The residue was purified by silica gel column chromatography eluted with 4% methanol in dichloromethane to afford compound **6** in 92% yield as white solid. Mp: 133-135°C. ^{1}H NMR (500 MHz, DMSO): δ 7.36 (m, 4H), 7.12 (t, J = 7.5 Hz, 1H), 6.97 (m, 4H), 4.91 (t, J = 5.5 Hz, 1H), 4.80 (dd, J_1 = 11.0 Hz, J_2 = 4.5 Hz, 1H), 3.58 (d, J = 5.5 Hz, 2H), 2.13 (dd, J_1 = 12.5 Hz, J_2 = 4.5 Hz, 1H), 1.96 (m, 4H), 1.62 (s, 3H); ^{13}C NMR (125 MHz, DMSO): δ 163.3, 156.7, 156.2, 135.0, 130.1, 128.0, 123.5, 118.6, 118.5, 116.3, 81.8, 77.5, 62.4, 42.7, 19.9, 14.0; IR (NEAT): ν 3241, 2982, 2928, 1660, 1592, 1492, 1284, 1248, 1180, 1073 cm^{-1}; ESI-HRMS m/z calcd for $C_{20}H_{22}O_4N$ ($M+H^+$): 340.1543, found: 340.1528.

1H and 13C NMR Spectra


Mercury500 1HNMR LG-84 in CDCl3 20110826
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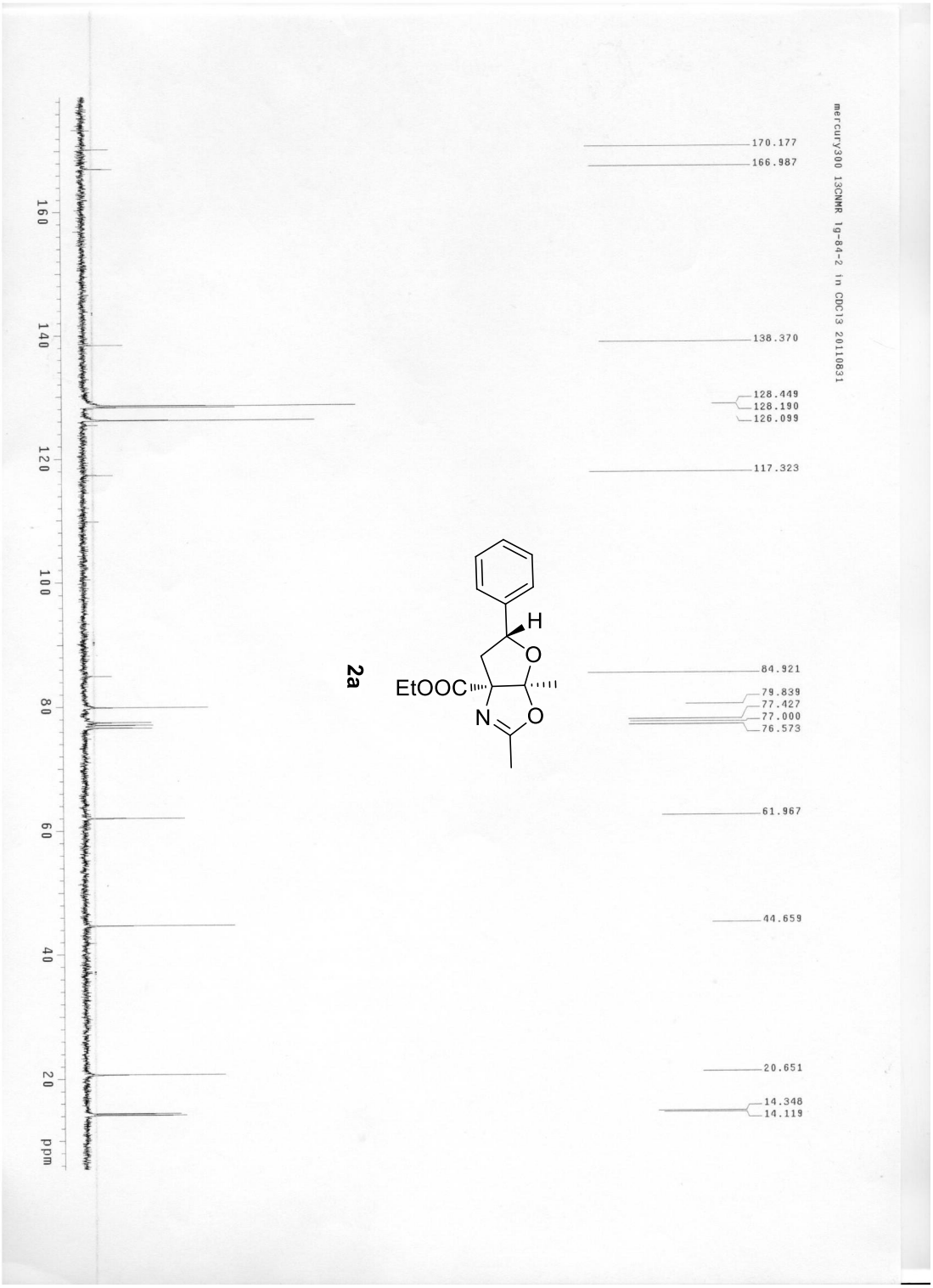
7.345
7.341
7.333
7.324
7.318
7.315
7.311
7.307
7.302
7.268
4.970
4.961
4.947
4.938
4.341
4.334
4.327
4.320
4.313
4.305
4.291
4.278
4.264
4.256
4.250
4.242
4.235
4.228
2.758
2.735
2.733
2.710
2.519
2.510
2.493
2.484
2.143
1.672
1.335
1.321
1.307
0.000
3.70
0.92
0.92
1.97
1.00
1.00
2.98
2.91
3.24
f1 (ppm)
2a
EtOOC
H
O
N
O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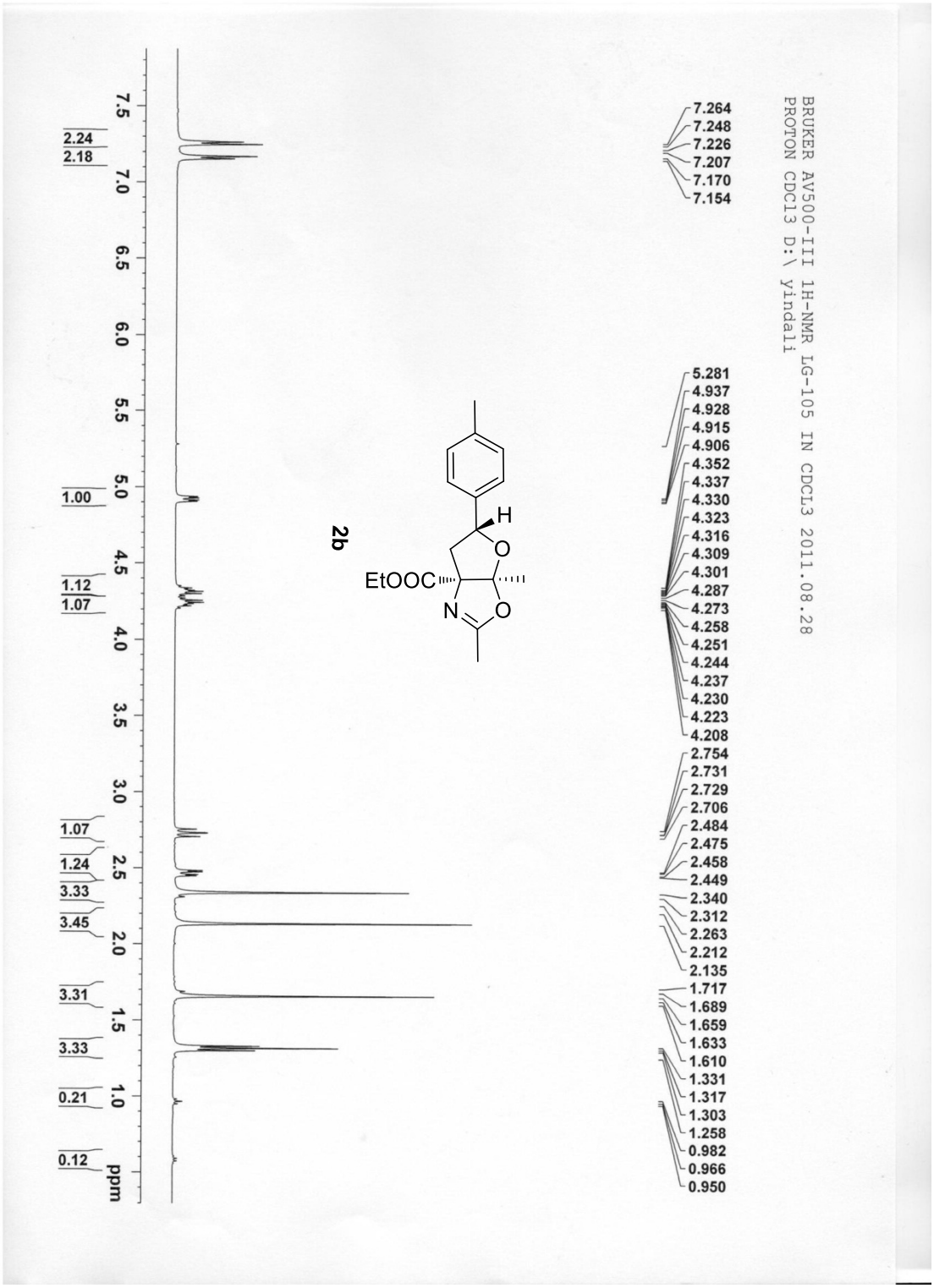
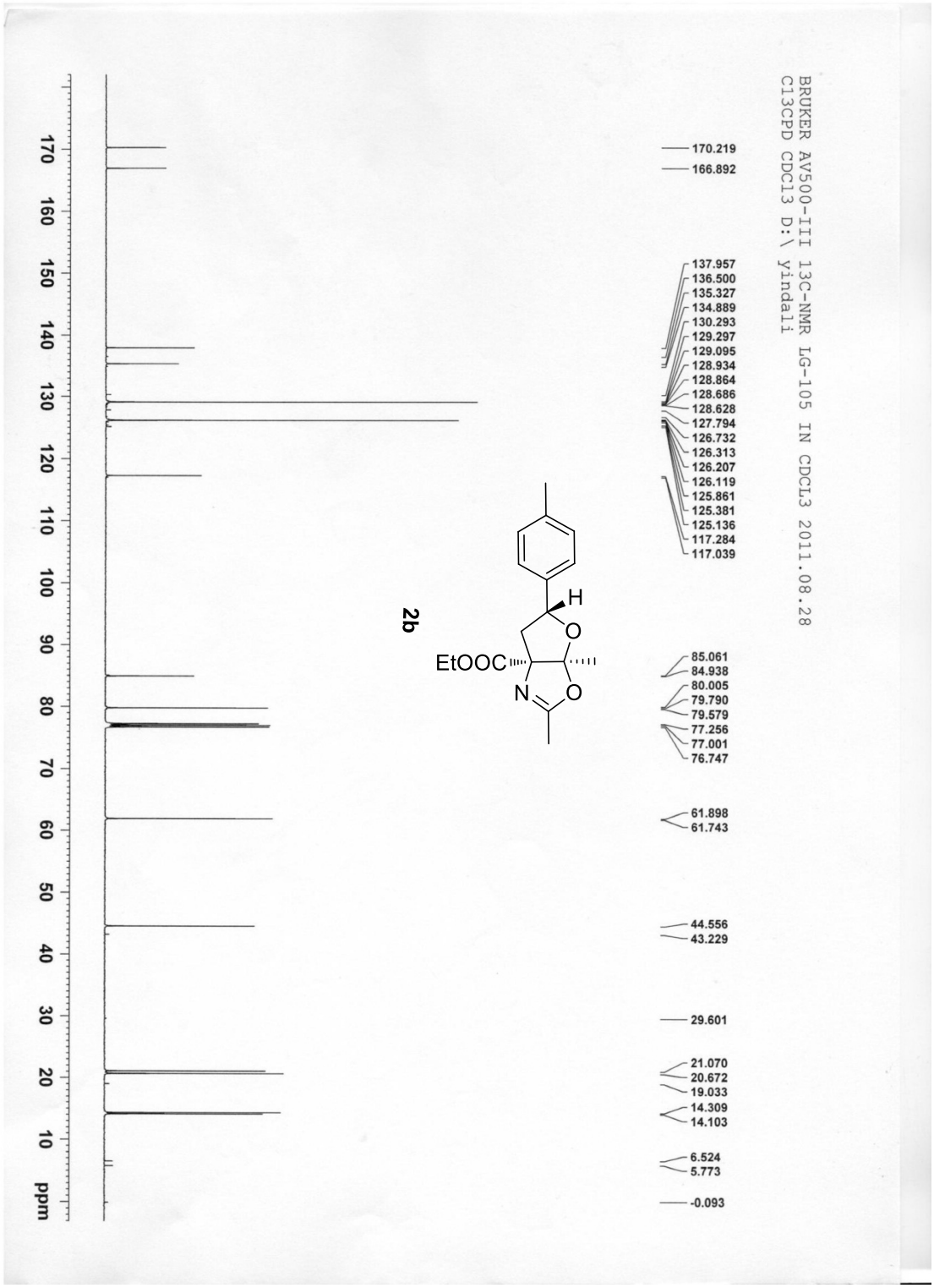
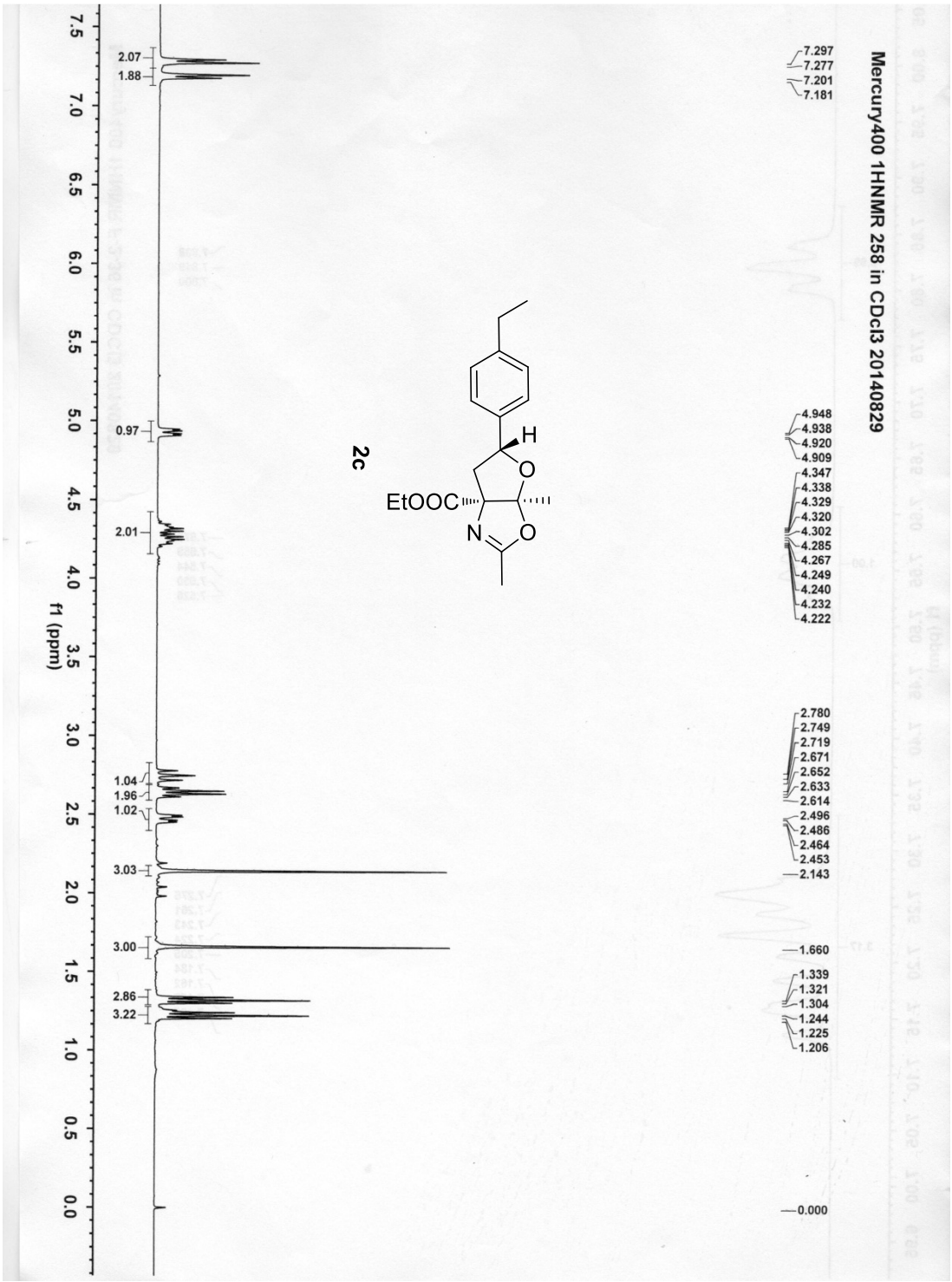
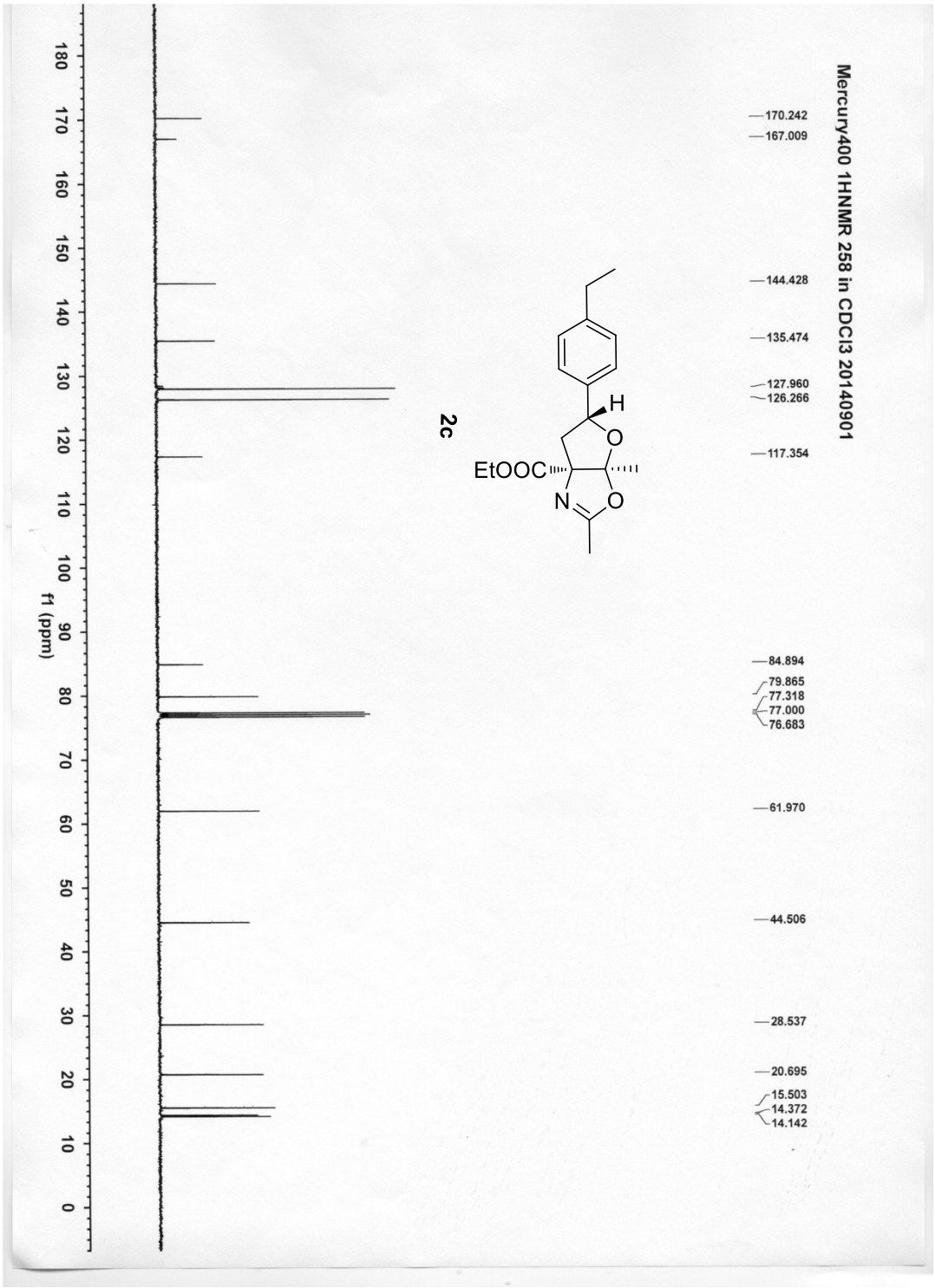
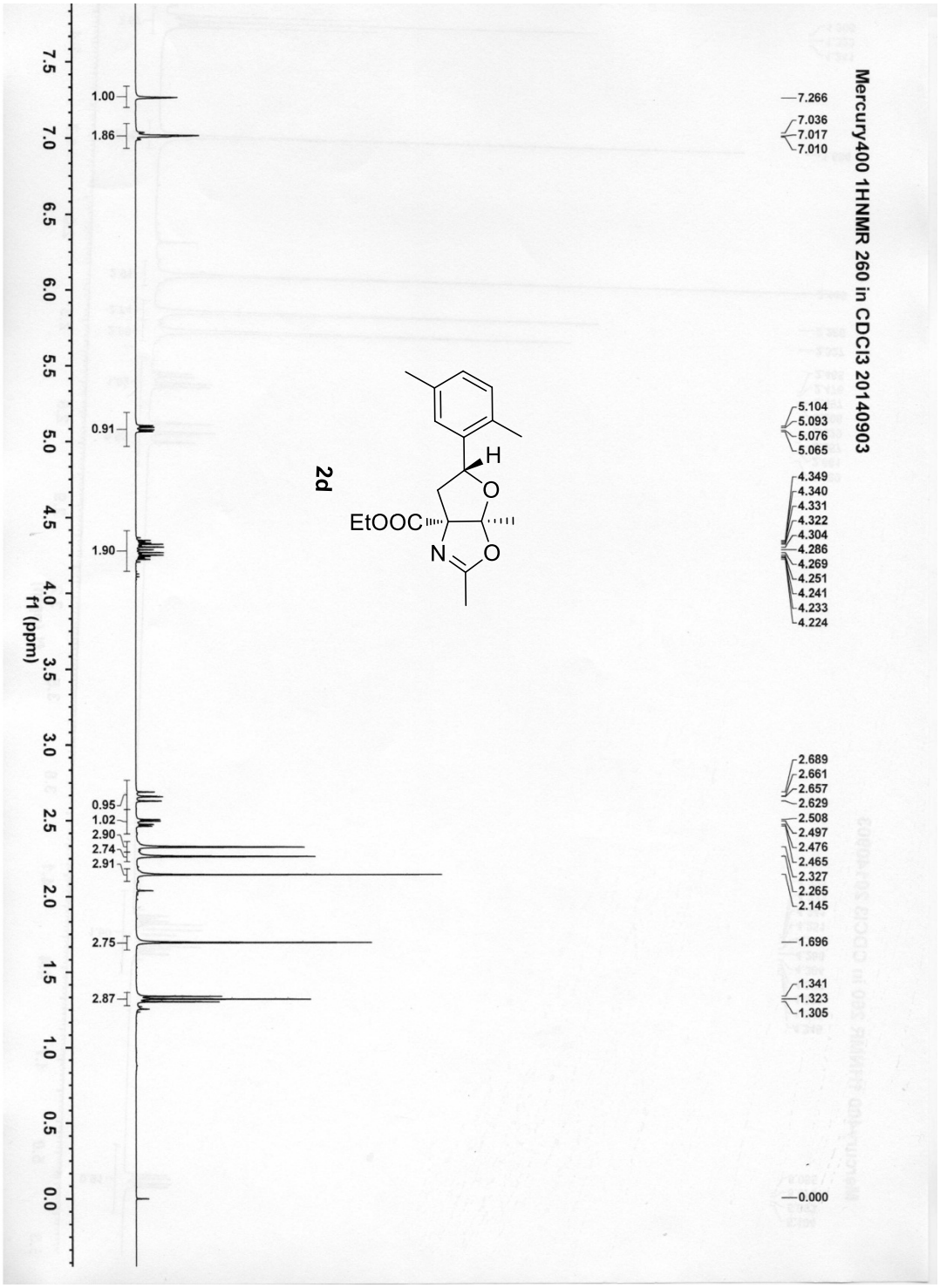
166.987
138.370
128.449
128.190
126.099
117.323
84.921
79.839
77.427
77.000
76.573
61.967
44.659
20.651
14.348
14.119
160
140
120
100
80
60
40
20
ppm
2a
EtOOC
H
O
N
O

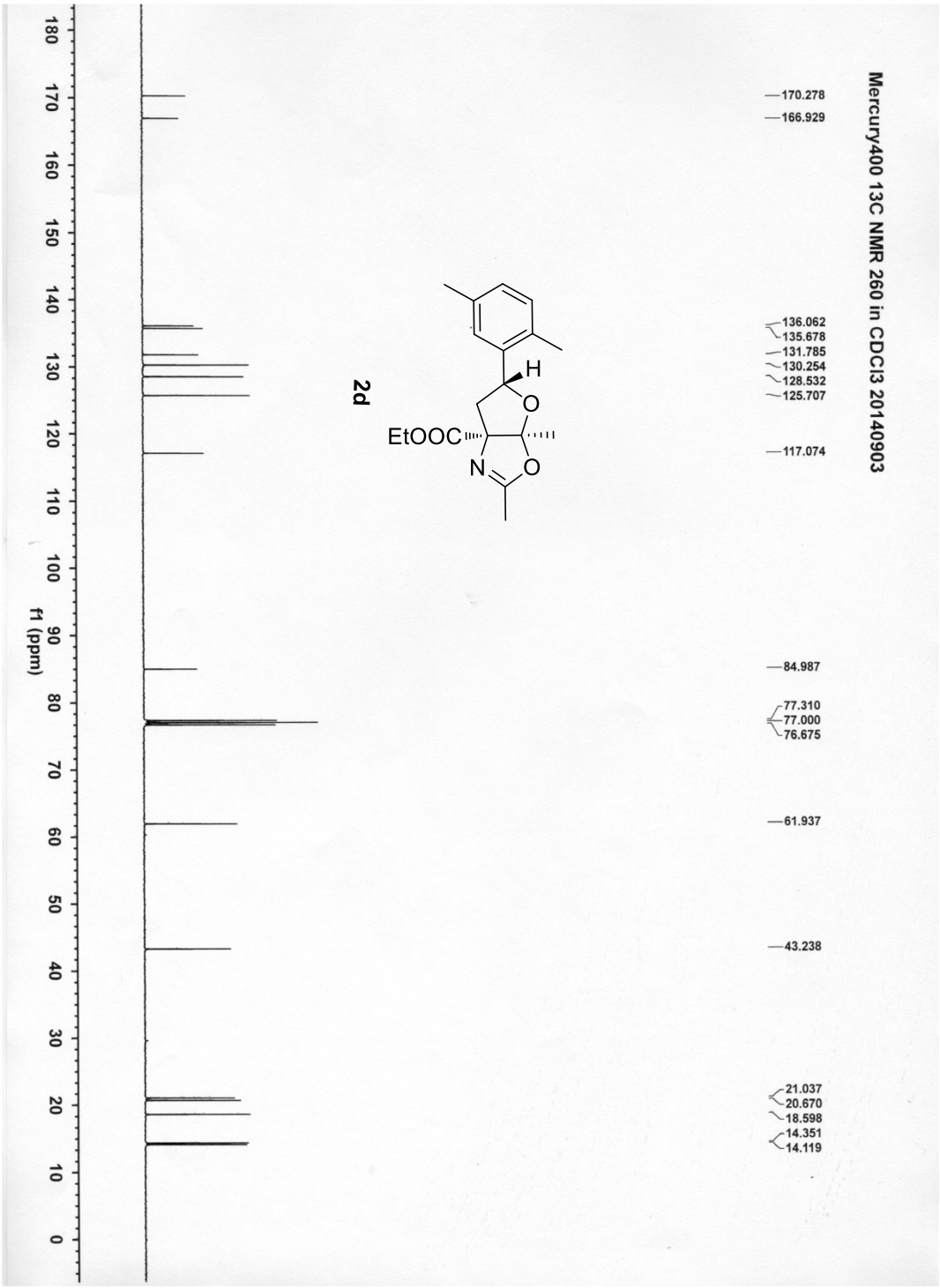

BRUKER AV500-III 1H-NMR LG-105 IN CDCL3 2011.08.28
PROTON CDCl3 D:\ yindali
7.264
7.248
7.226
7.207
7.170
7.154
5.281
4.937
4.928
4.915
4.906
4.352
4.337
4.330
4.323
4.316
4.309
4.301
4.287
4.273
4.258
4.251
4.244
4.237
4.230
4.223
4.208
2.754
2.731
2.729
2.706
2.484
2.475
2.458
2.449
2.340
2.312
2.263
2.212
2.135
1.717
1.689
1.659
1.633
1.610
1.331
1.317
1.303
1.258
0.982
0.966
0.950
2b
EtOOC
H
O
N
O
2.24
2.18
1.00
1.12
1.07
1.07
1.24
3.33
3.45
3.31
3.33
0.21
0.12
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
ppm

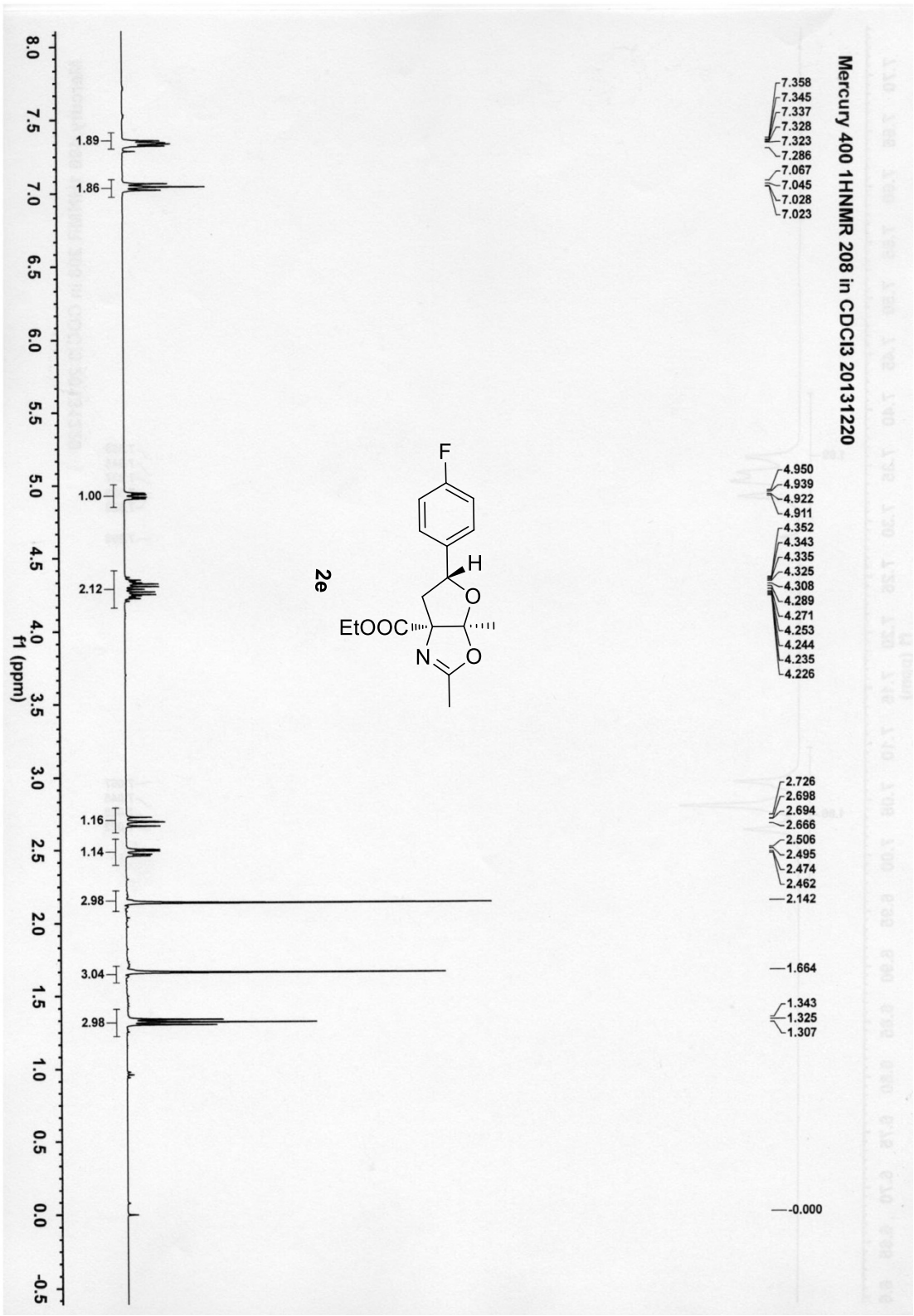

BRUKER AV500-III 13C-NMR LG-105 IN CDCL3 2011.08.28
C13CPD CDC13 D:\ yindali
170.219
166.892
137.957
136.500
135.327
134.889
130.293
129.297
129.095
128.934
128.864
128.686
128.628
127.794
126.732
126.313
126.207
126.119
125.861
125.381
125.136
117.284
117.039
85.061
84.938
80.005
79.790
79.579
77.256
77.001
76.747
61.898
61.743
44.556
43.229
29.601
21.070
20.672
19.033
14.309
14.103
6.524
5.773
-0.093
2b
EtOOC
H
O
N
O
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

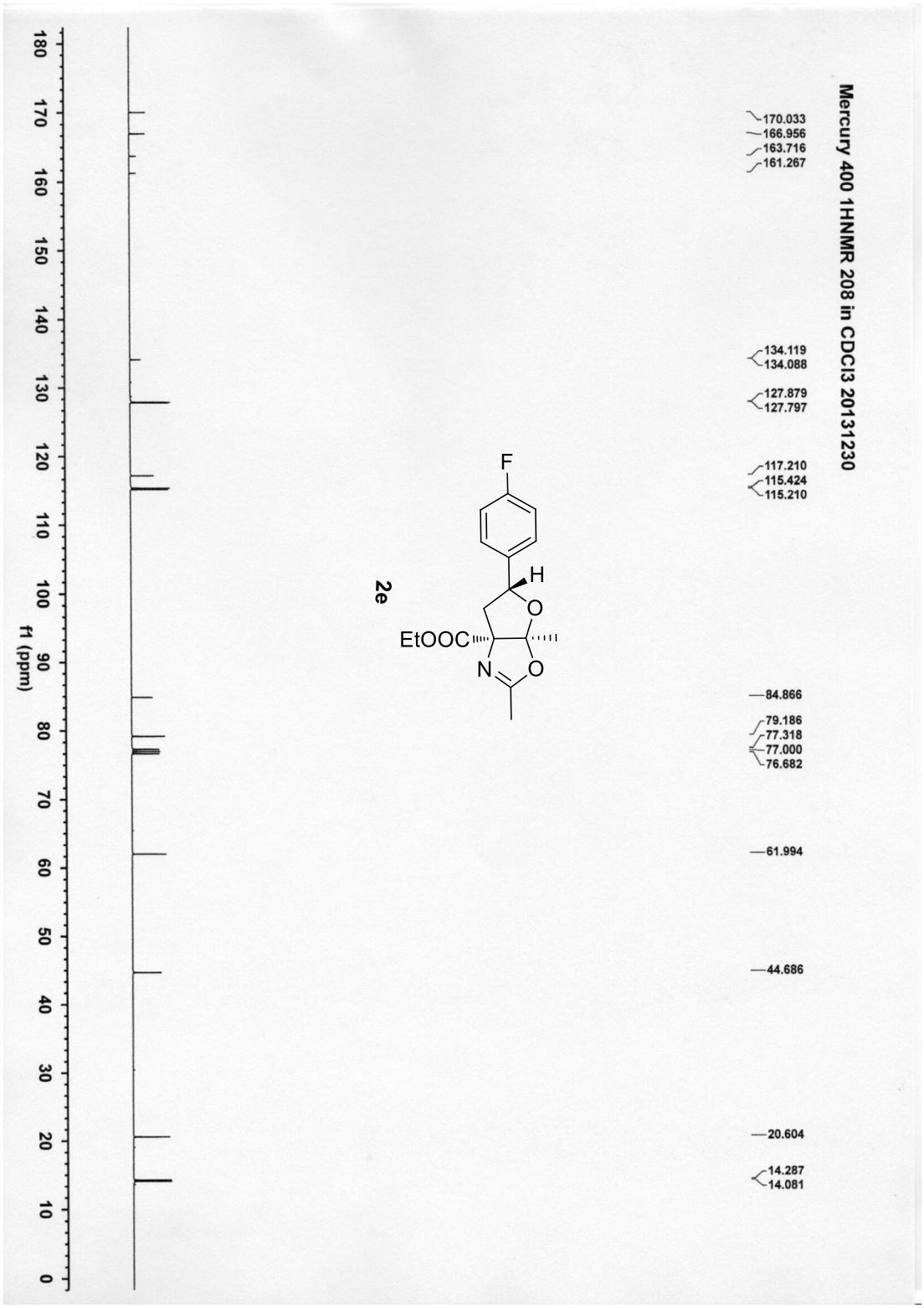

Mercury400 1HNMR 258 in CDcl3 20140829
2c
EtOOC
H
O
N
O
f1 (ppm)
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
2.07
1.88
0.97
2.01
1.04
1.96
1.02
3.03
3.00
2.86
3.22
7.297
7.277
7.201
7.181
4.948
4.938
4.920
4.909
4.347
4.338
4.329
4.320
4.302
4.285
4.267
4.249
4.240
4.232
4.222
2.780
2.749
2.719
2.671
2.652
2.633
2.614
2.496
2.486
2.464
2.453
2.143
1.660
1.339
1.321
1.304
1.244
1.225
1.206
0.000

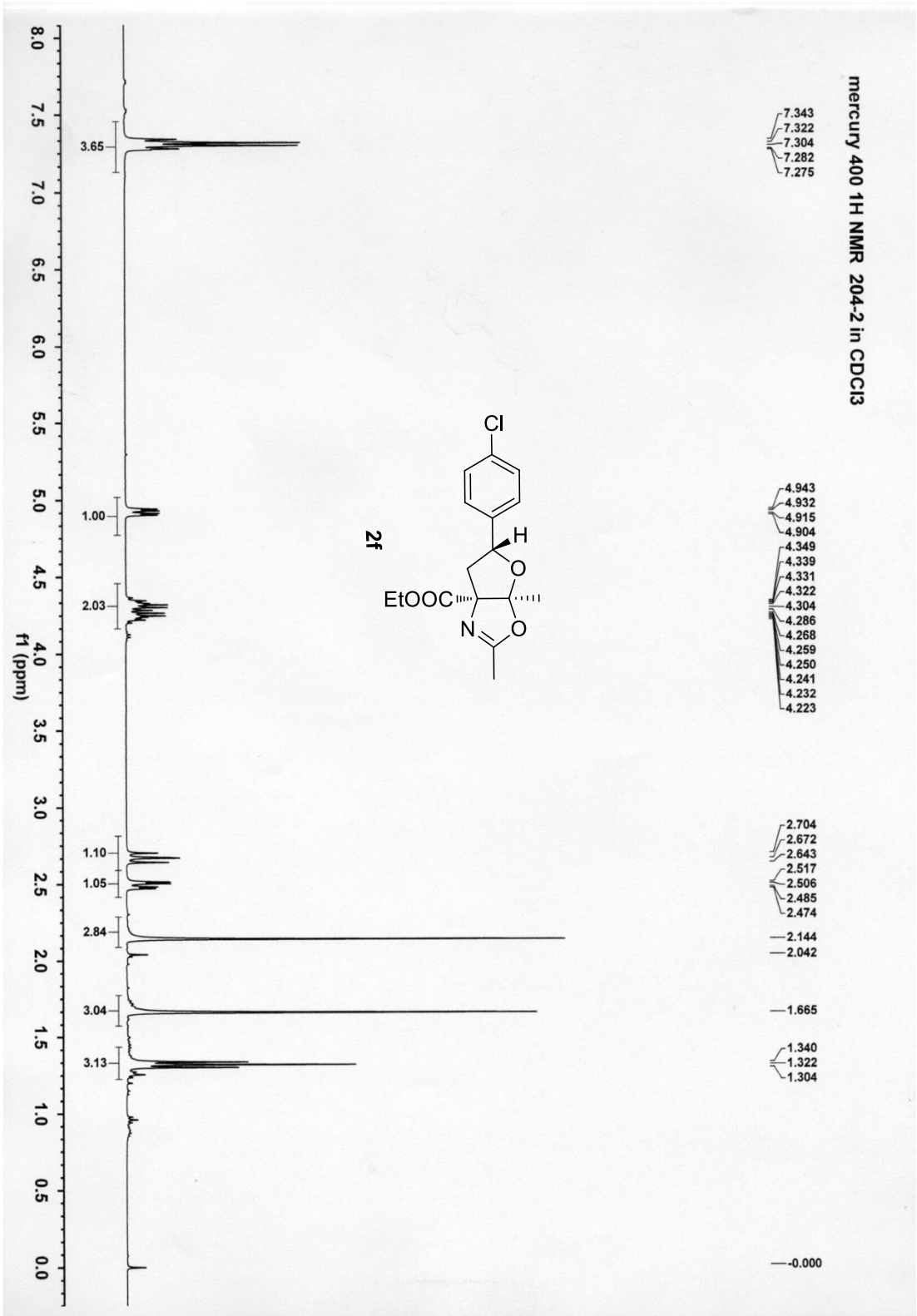

Mercury400 1HNMR 258 in CDCl3 20140901
170.242
167.009
144.428
135.474
127.960
126.266
117.354
84.894
79.865
77.318
77.000
76.683
61.970
44.506
28.537
20.695
15.503
14.372
14.142
2c
EtOOC
H
O
N
O
f1 (ppm)
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

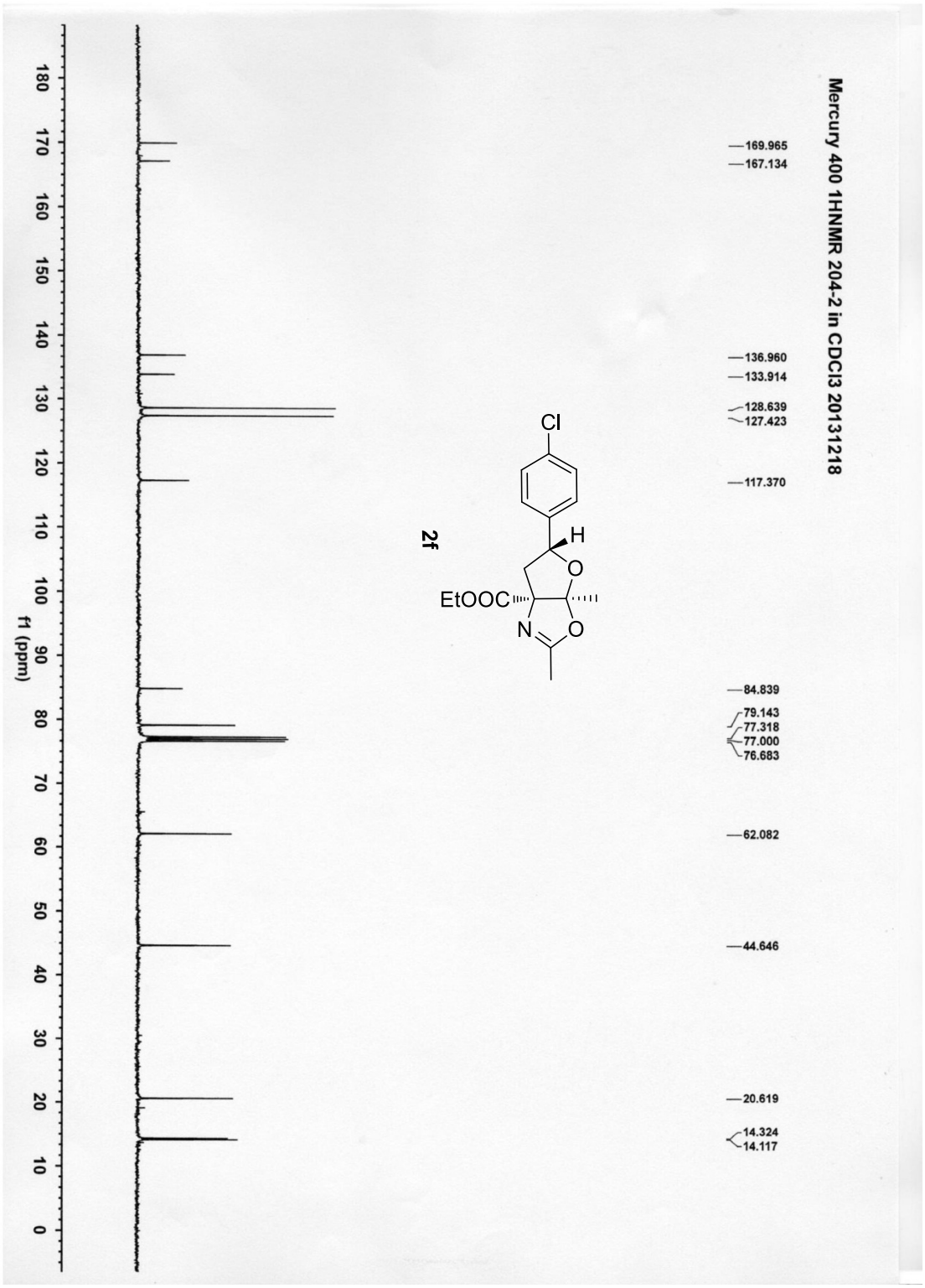

Mercury400 1HNMR 260 in CDCl3 20140903
2d
EtOOC
H
O
N
O
f1 (ppm)
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
1.00
1.86
0.91
1.90
0.95
1.02
2.90
2.74
2.91
2.75
2.87
7.266
7.036
7.017
7.010
5.104
5.093
5.076
5.065
4.349
4.340
4.331
4.322
4.304
4.286
4.269
4.251
4.241
4.233
4.224
2.689
2.661
2.657
2.629
2.508
2.497
2.476
2.465
2.327
2.265
2.145
1.696
1.341
1.323
1.305
0.000

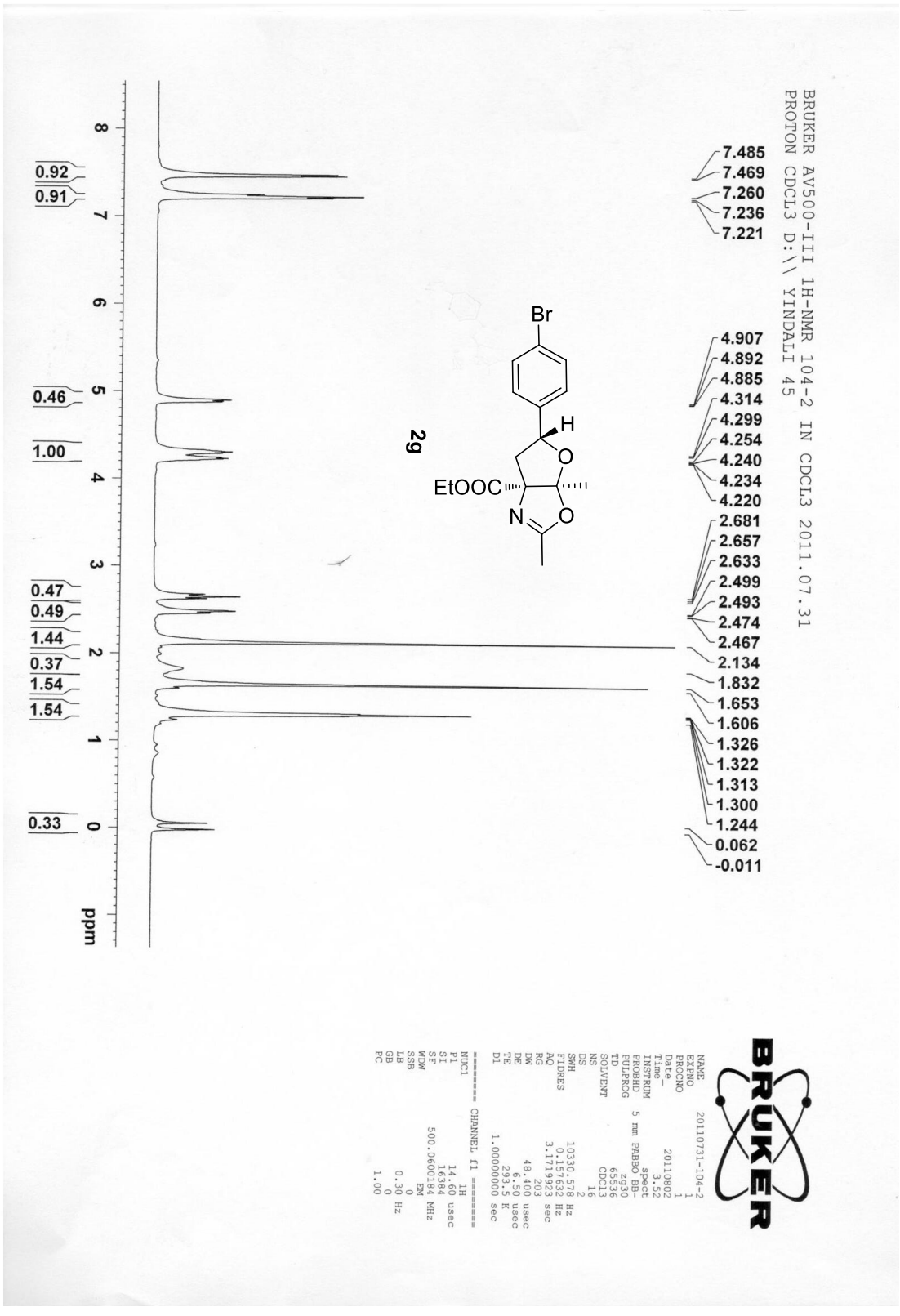

Mercury400 13C NMR 260 in CDCl3 20140903
170.278
166.929
136.062
135.678
131.785
130.254
128.532
125.707
117.074
84.987
77.310
77.000
76.675
61.937
43.238
21.037
20.670
18.598
14.351
14.119
2d
EtOOC
H
O
N
O
f1 (ppm)


Mercury 400 1HNMR 208 in CDCl3 20131220
7.358
7.345
7.337
7.328
7.323
7.286
7.067
7.045
7.028
7.023
4.950
4.939
4.922
4.911
4.352
4.343
4.335
4.325
4.308
4.289
4.271
4.253
4.244
4.235
4.226
2.726
2.698
2.694
2.666
2.506
2.495
2.474
2.462
2.142
1.664
1.343
1.325
1.307
-0.000
1.89
1.86
1.00
2.12
1.16
1.14
2.98
3.04
2.98
F
H
O
EtOOC
N
O
2e
f1 (ppm)


Mercury 400 1HNMR 208 in CDCl3 20131230
170.033
166.956
163.716
161.267
134.119
134.088
127.879
127.797
117.210
115.424
115.210
84.866
79.186
77.318
77.000
76.682
61.994
44.686
20.604
14.287
14.081
F
H
O
EtOOC
N
O
2e
f1 (ppm)
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0


mercury 400 1H NMR 204-2 in CDCl3
2f
Cl
H
O
EtOOC
N
O
f1 (ppm)
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
3.65
1.00
2.03
1.10
1.05
2.84
3.04
3.13
7.343
7.322
7.304
7.282
7.275
4.943
4.932
4.915
4.904
4.349
4.339
4.331
4.322
4.304
4.286
4.268
4.259
4.250
4.241
4.232
4.223
2.704
2.672
2.643
2.517
2.506
2.485
2.474
2.144
2.042
1.665
1.340
1.322
1.304
-0.000


Mercury 400 1HNMR 204-2 in CDCl3 20131218
169.965
167.134
136.960
133.914
128.639
127.423
117.370
84.839
79.143
77.318
77.000
76.683
62.082
44.646
20.619
14.324
14.117
2f
Cl
H
O
EtOOC
N
O
f1 (ppm)
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0


BRUKER AV500-III 1H-NMR 104-2 IN CDCL3 2011.07.31
PROTON CDCL3 D:\\ YINDALI 45
7.485
7.469
7.260
7.236
7.221
4.907
4.892
4.885
4.314
4.299
4.254
4.240
4.234
4.220
2.681
2.657
2.633
2.499
2.493
2.474
2.467
2.134
1.832
1.653
1.606
1.326
1.322
1.313
1.300
1.244
0.062
-0.011
Br
H
O
EtOOC
N
O
2g
0.92
0.91
0.46
1.00
0.47
0.49
1.44
0.37
1.54
1.54
0.33
8
7
6
5
4
3
2
1
0
ppm
BRUKER
NAME 20110731-104-2
EXPNO 1
PROCNO 1
Date_ 20110802
Time_ 3.52
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 10330.578 Hz
FIDRES 0.157632 Hz
AQ 3.1719923 sec
RG 203
DW 48.400 usec
DE 6.50 usec
TE 293.5 K
D1 1.00000000 sec
======== CHANNEL f1 ========
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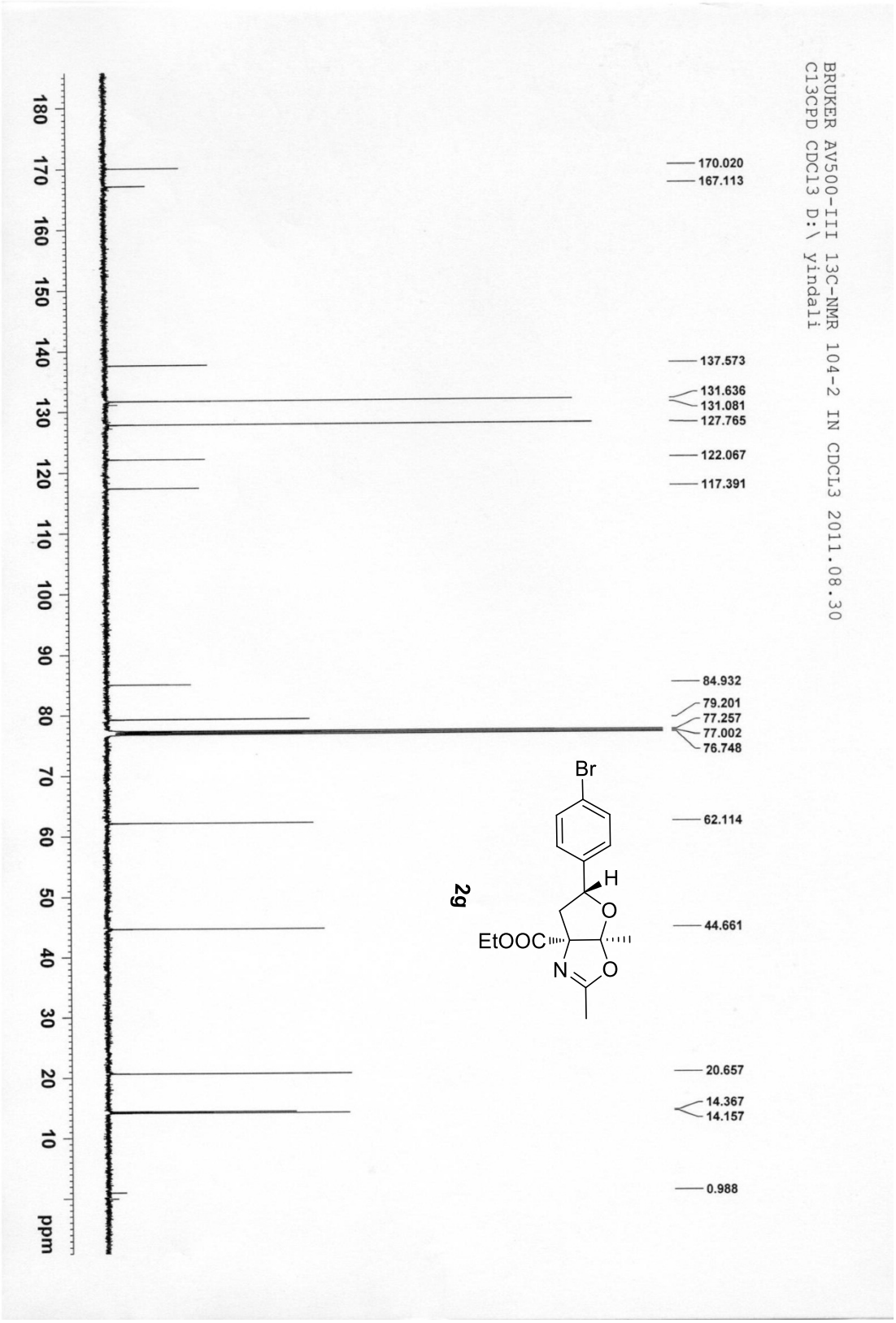
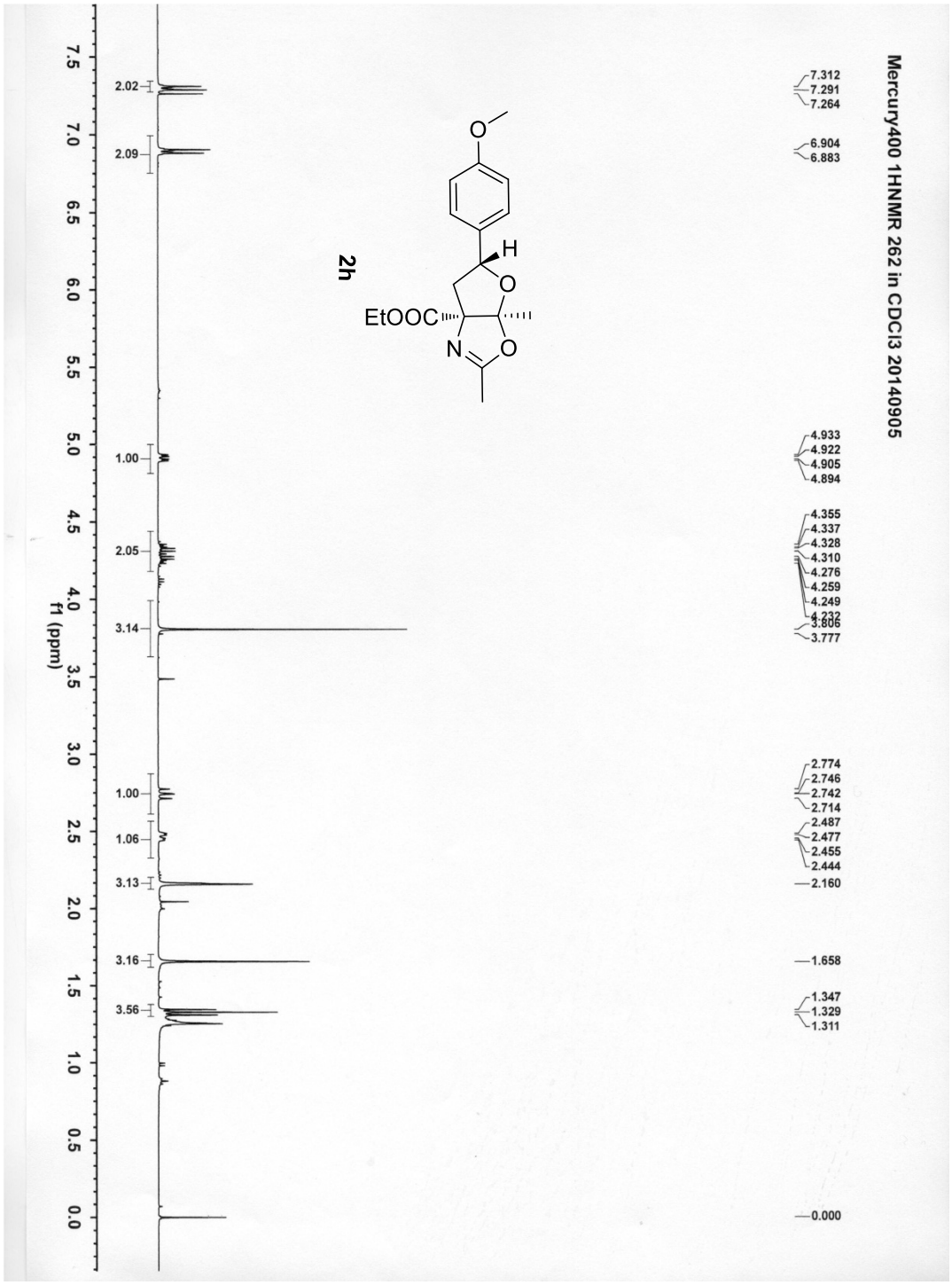
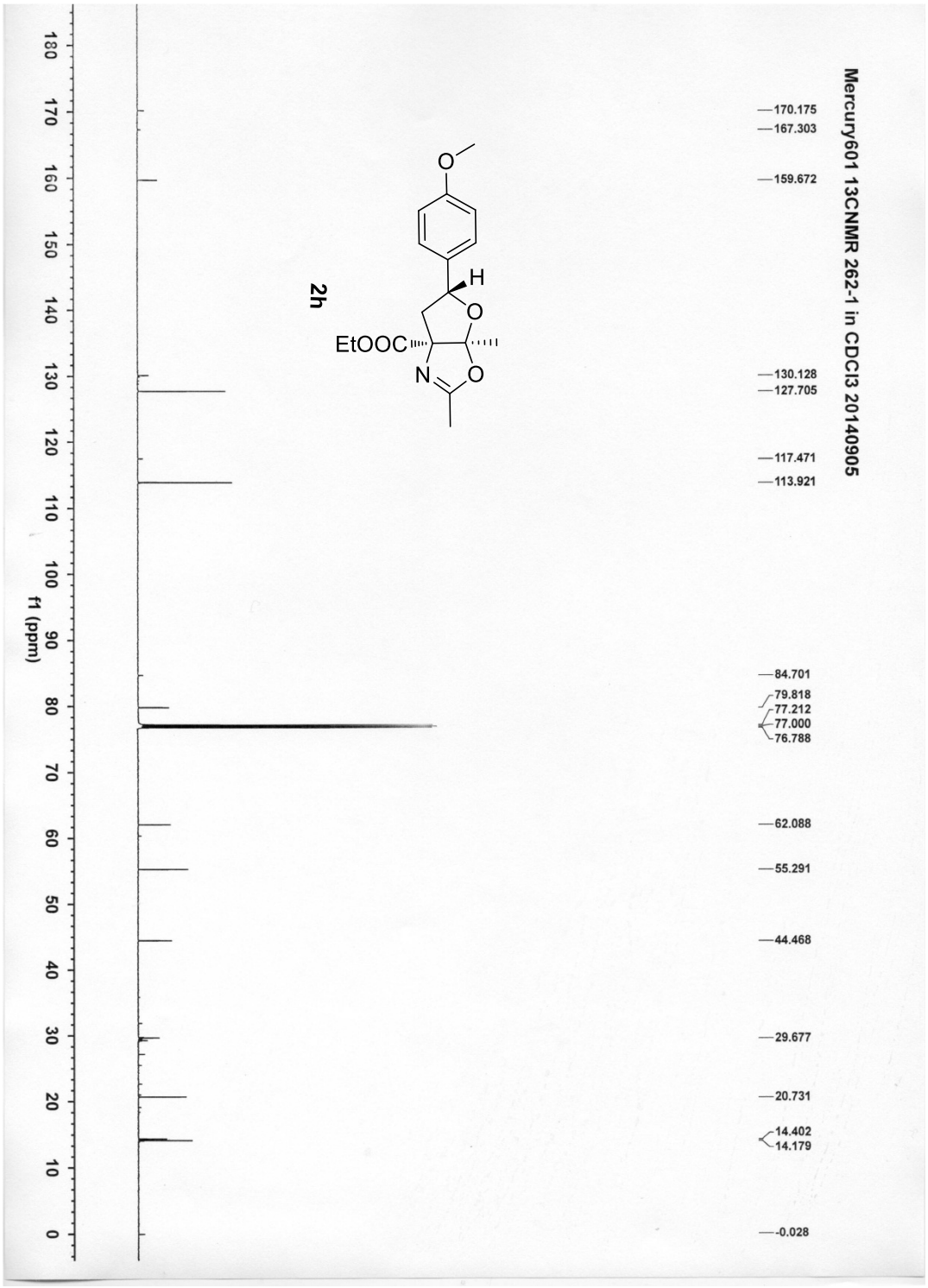
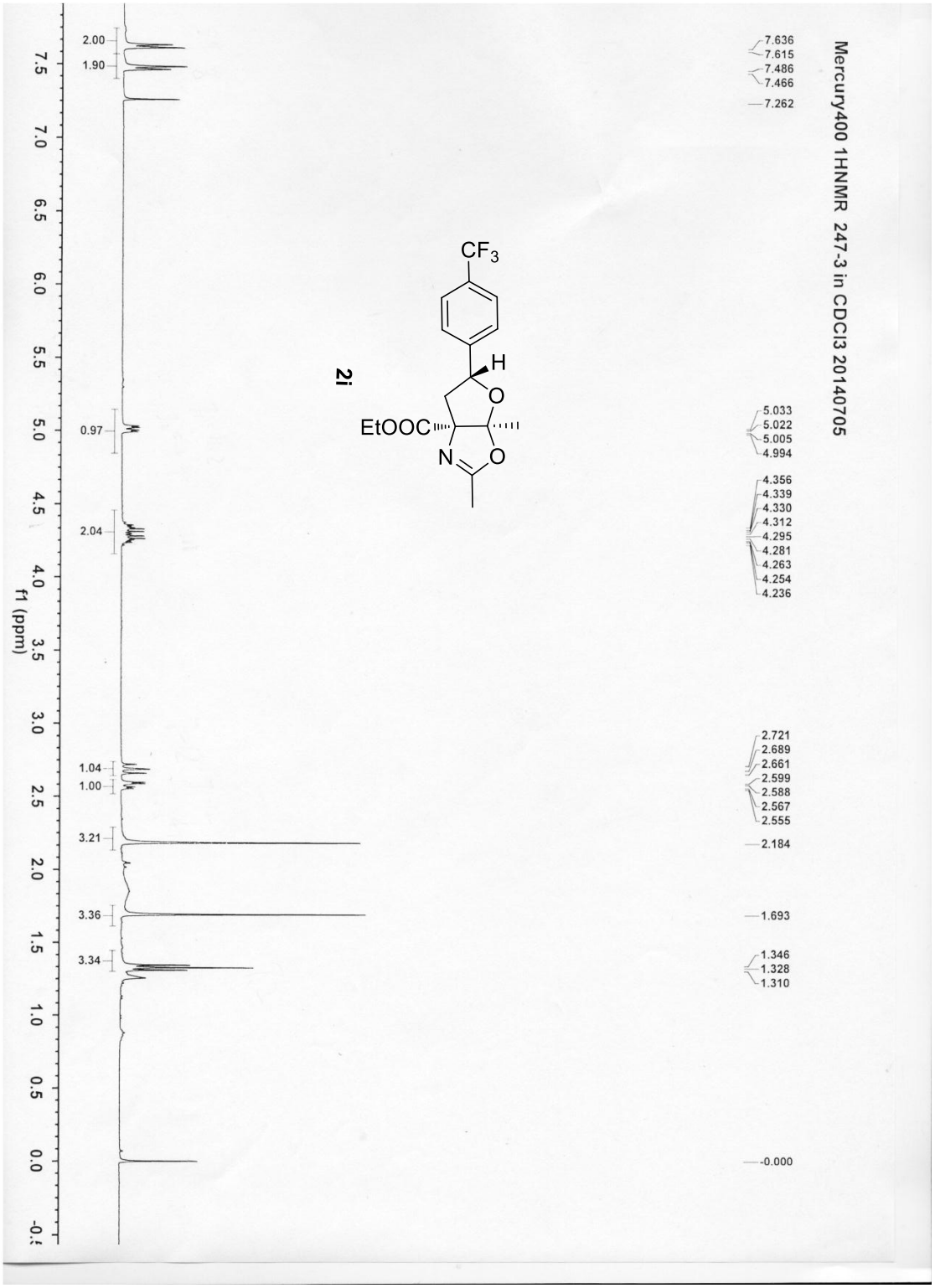
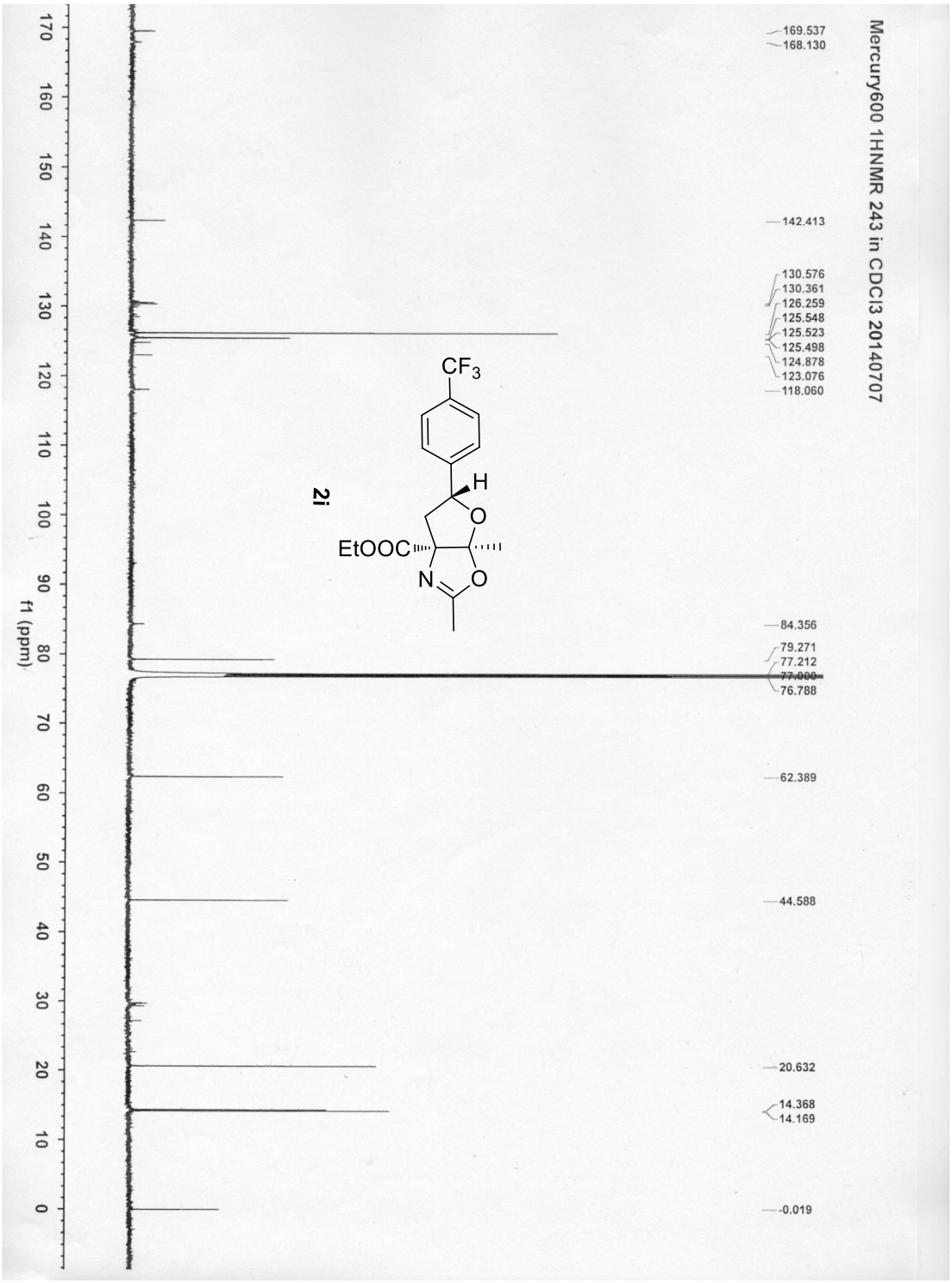
P1 14.60 usec
SI 16384
SF 500.0600184 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

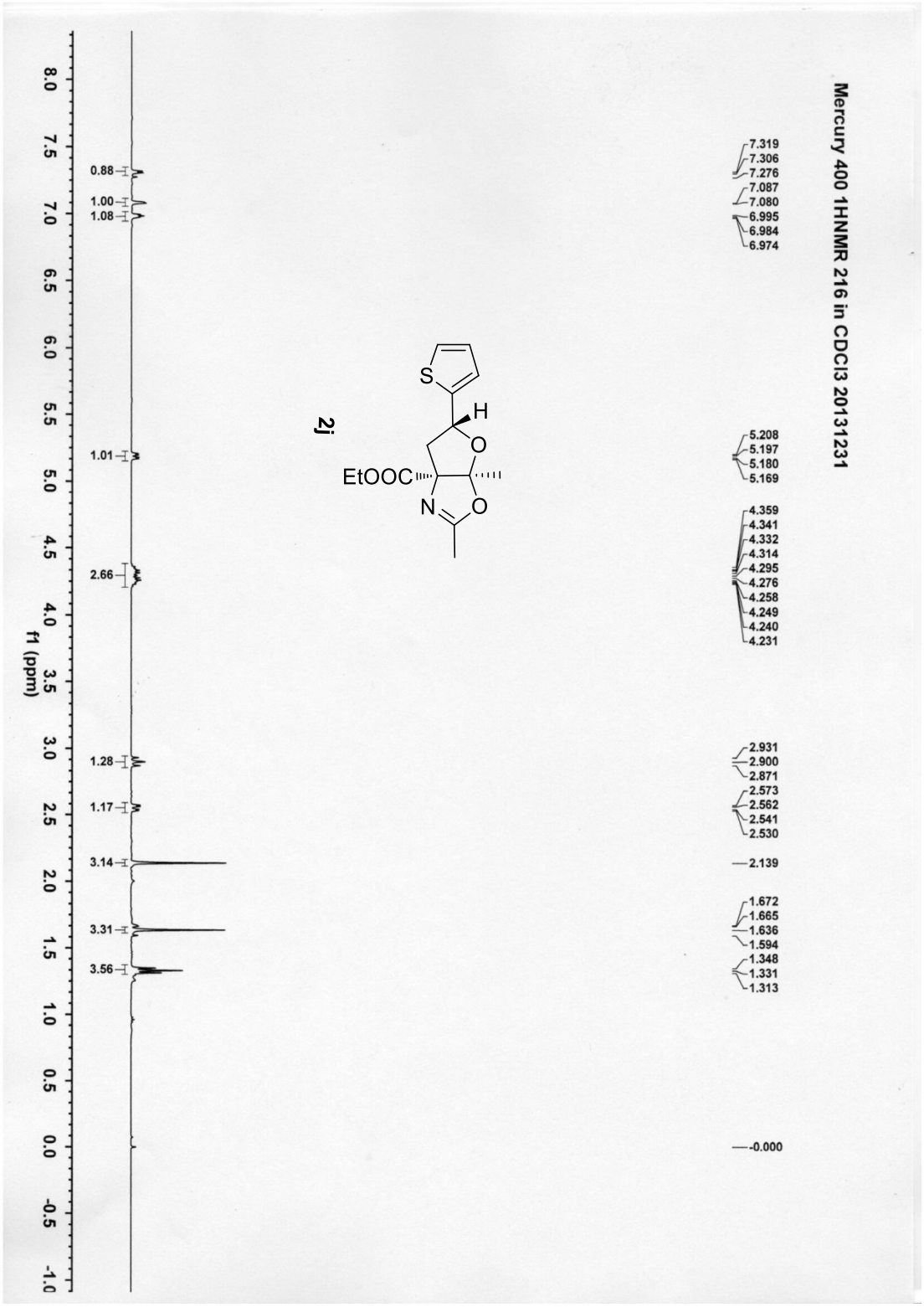

BRUKER AV500-III 13C-NMR 104-2 IN CDCL3 2011.08.30
C13CPD CDC13 D:\ yindali
170.020
167.113
137.573
131.636
131.081
127.765
122.067
117.391
84.932
79.201
77.257
77.002
76.748
62.114
44.661
20.657
14.367
14.157
0.988
ppm
Br
H
O
EtOOC
N
O
2g

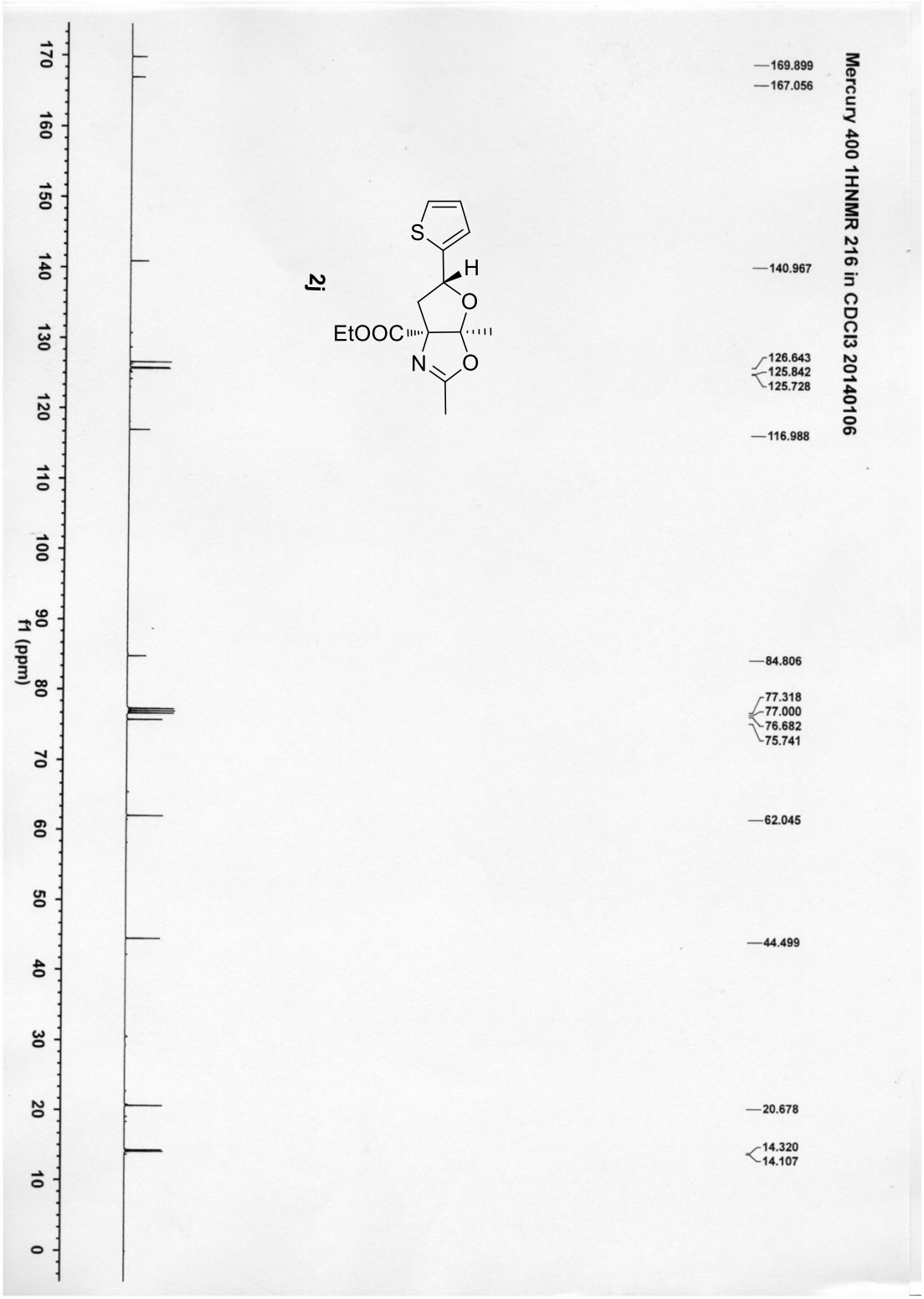

Mercury400 1HNMR 262 in CDCl3 20140905
2h
EtOOC
H
O
N
7.312
7.291
7.264
6.904
6.883
4.933
4.922
4.905
4.894
4.355
4.337
4.328
4.310
4.276
4.259
4.249
3.806
3.777
2.774
2.746
2.742
2.714
2.487
2.477
2.455
2.444
2.160
1.658
1.347
1.329
1.311
0.000
2.02
2.09
1.00
2.05
3.14
1.00
1.06
3.13
3.16
3.56
f1 (ppm)

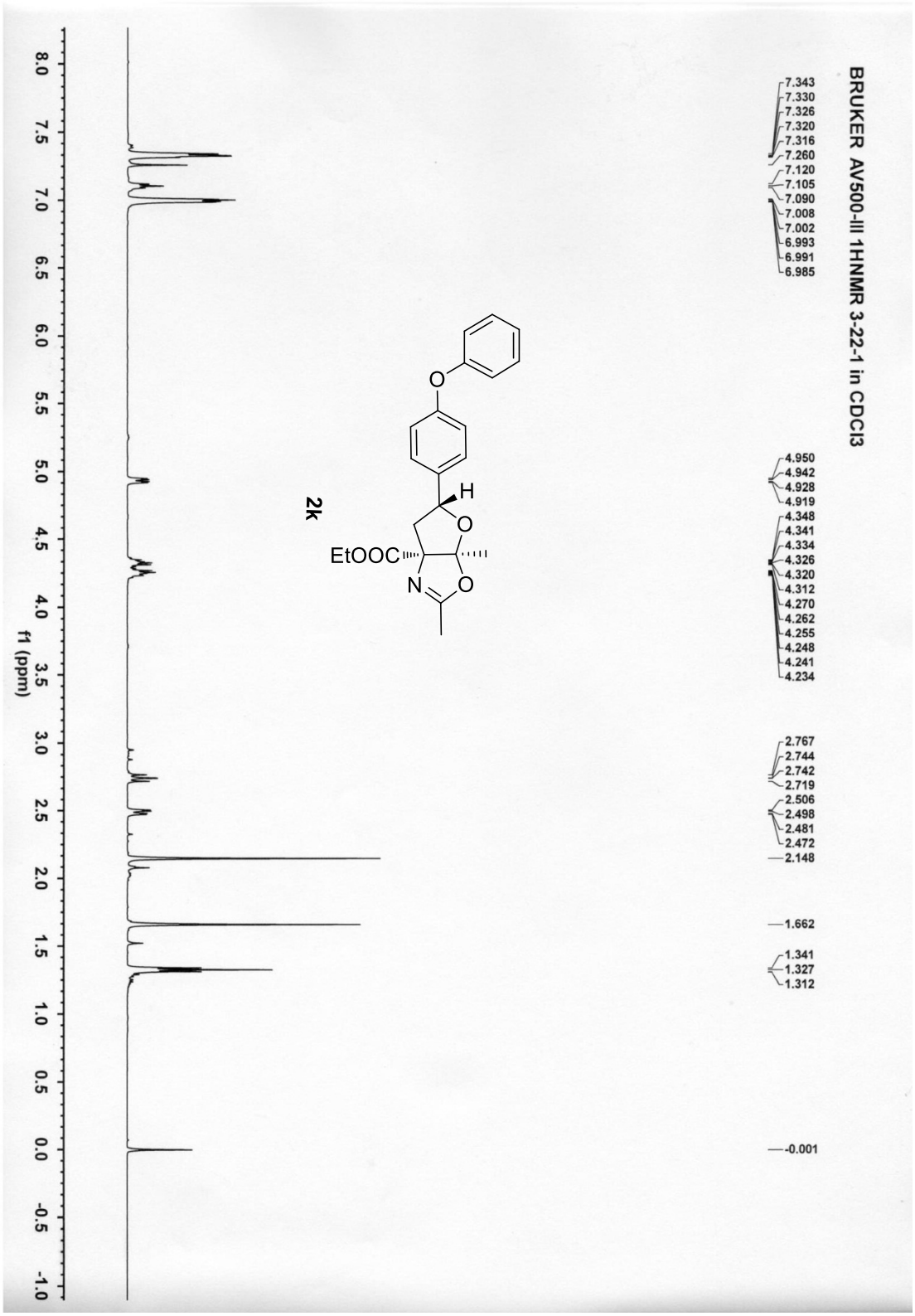

Mercury601 13CNMR 262-1 in CDCl3 20140905
2h
EtOOC
O
H
O
N
O
f1 (ppm)
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
170.175
167.303
159.672
130.128
127.705
117.471
113.921
84.701
79.818
77.212
77.000
76.788
62.088
55.291
44.468
29.677
20.731
14.402
14.179
-0.028

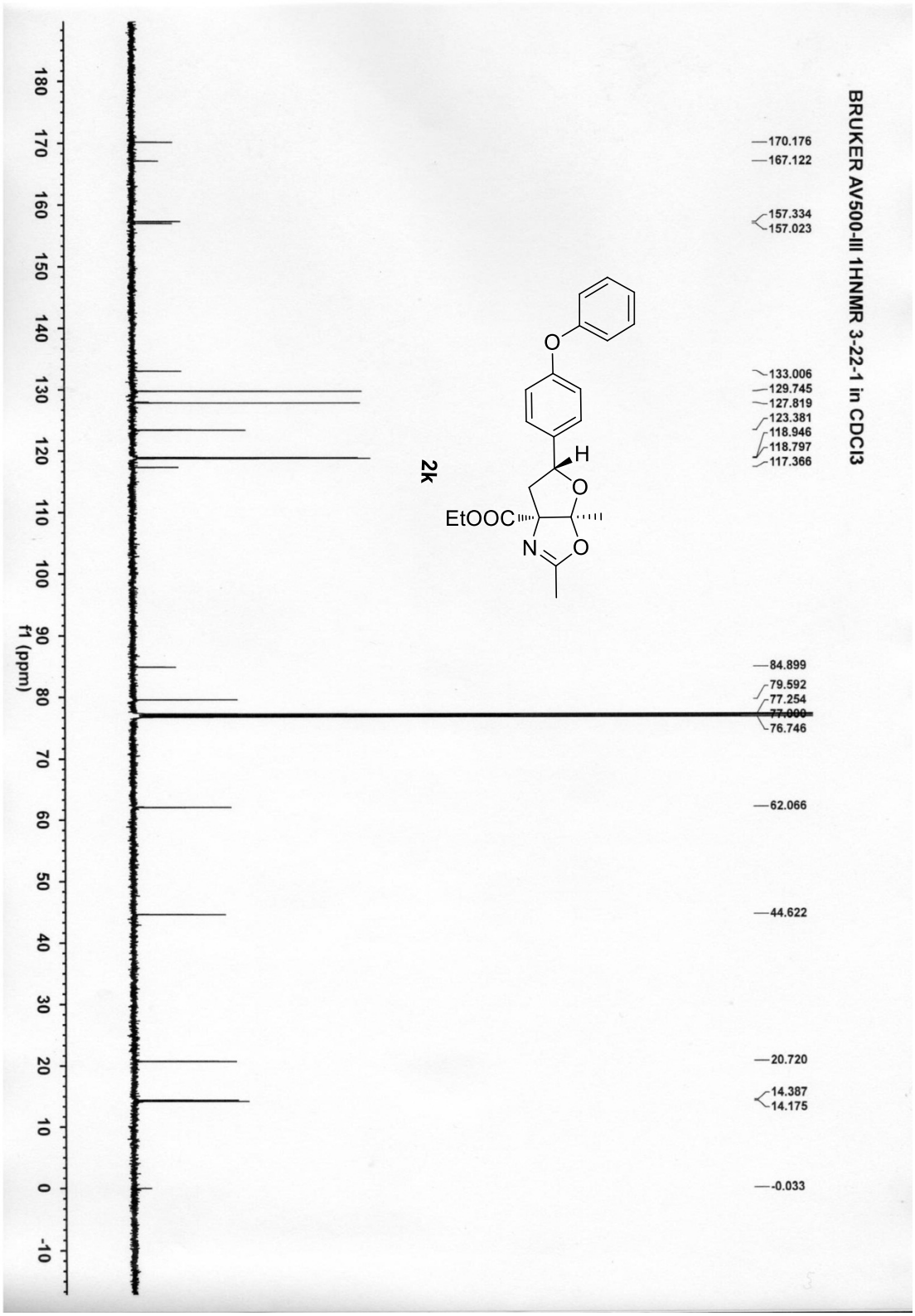

Mercury400 1HNMR 247-3 in CDCl3 20140705
2i
CF3
H
O
EtOOC
N
O
7.636
7.615
7.486
7.466
7.262
5.033
5.022
5.005
4.994
4.356
4.339
4.330
4.312
4.295
4.281
4.263
4.254
4.236
2.721
2.689
2.661
2.599
2.588
2.567
2.555
2.184
1.693
1.346
1.328
1.310
-0.000
2.00
1.90
0.97
2.04
1.04
1.00
3.21
3.36
3.34
f1 (ppm)

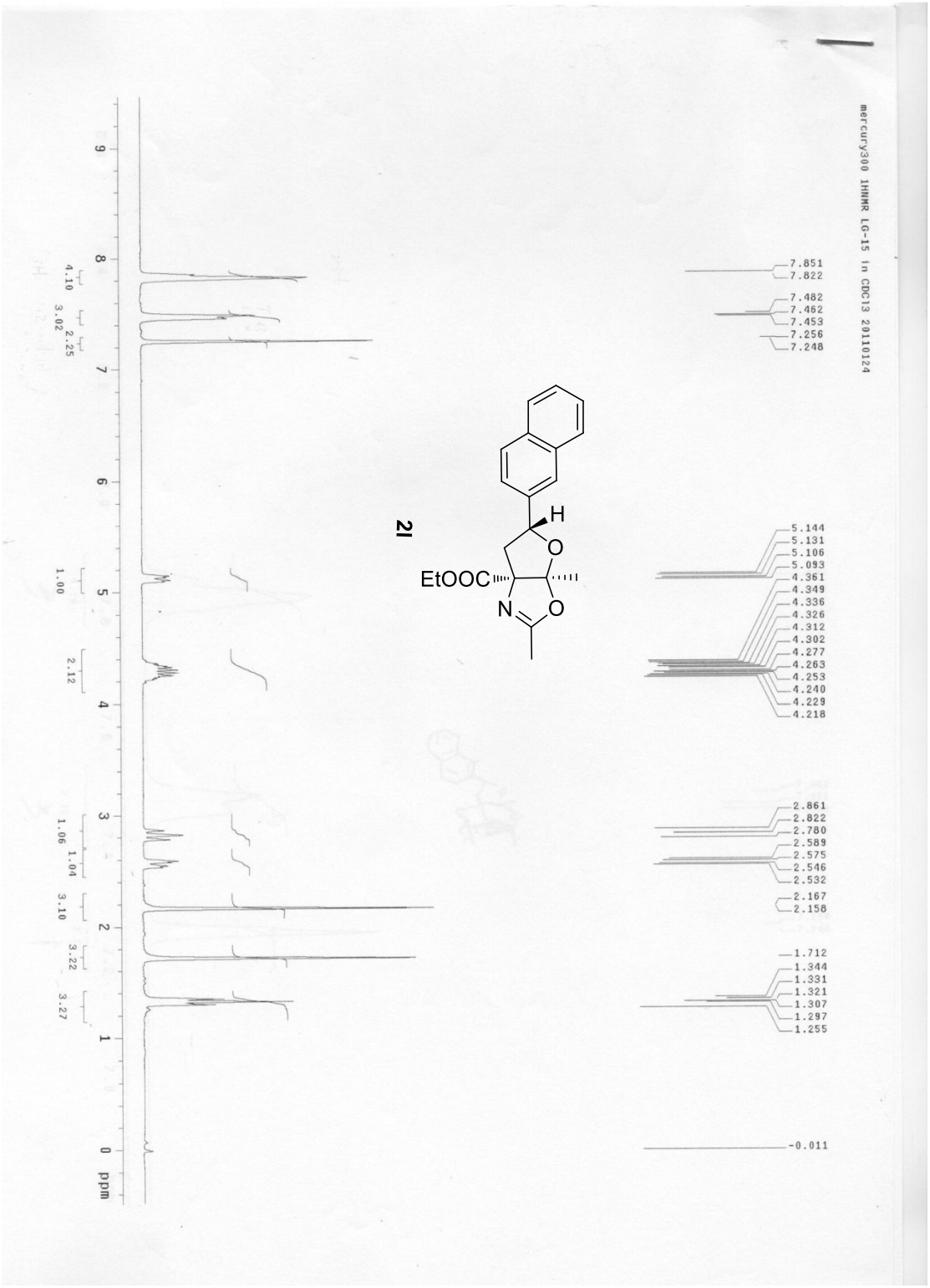

Mercury600 1HNMR 243 in CDCl3 20140707
169.537
168.130
142.413
130.576
130.361
126.259
125.548
125.523
125.498
124.878
123.076
118.060
84.356
79.271
77.212
77.000
76.788
62.389
44.588
20.632
14.368
14.169
-0.019
f1 (ppm)
CF3
H
O
EtOOC
N
O
2i

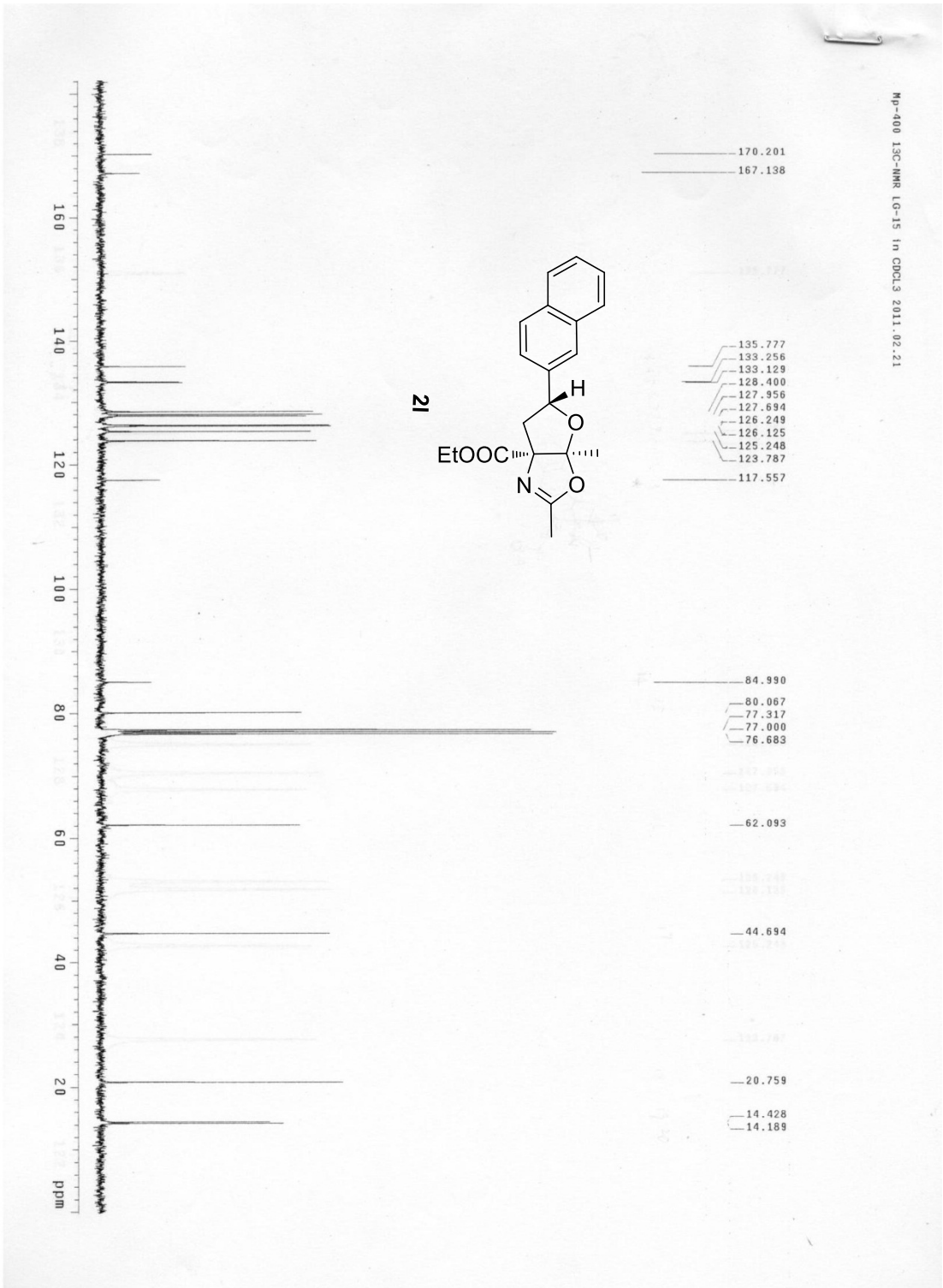

Mercury 400 1HNMR 216 in CDCl3 20131231
2j
EtOOC
S
H
O
N
O
7.319
7.306
7.276
7.087
7.080
6.995
6.984
6.974
5.208
5.197
5.180
5.169
4.359
4.341
4.332
4.314
4.295
4.276
4.258
4.249
4.240
4.231
2.931
2.900
2.871
2.573
2.562
2.541
2.530
2.139
1.672
1.665
1.636
1.594
1.348
1.331
1.313
-0.000
0.88
1.00
1.08
1.01
2.66
1.28
1.17
3.14
3.31
3.56
f1 (ppm)

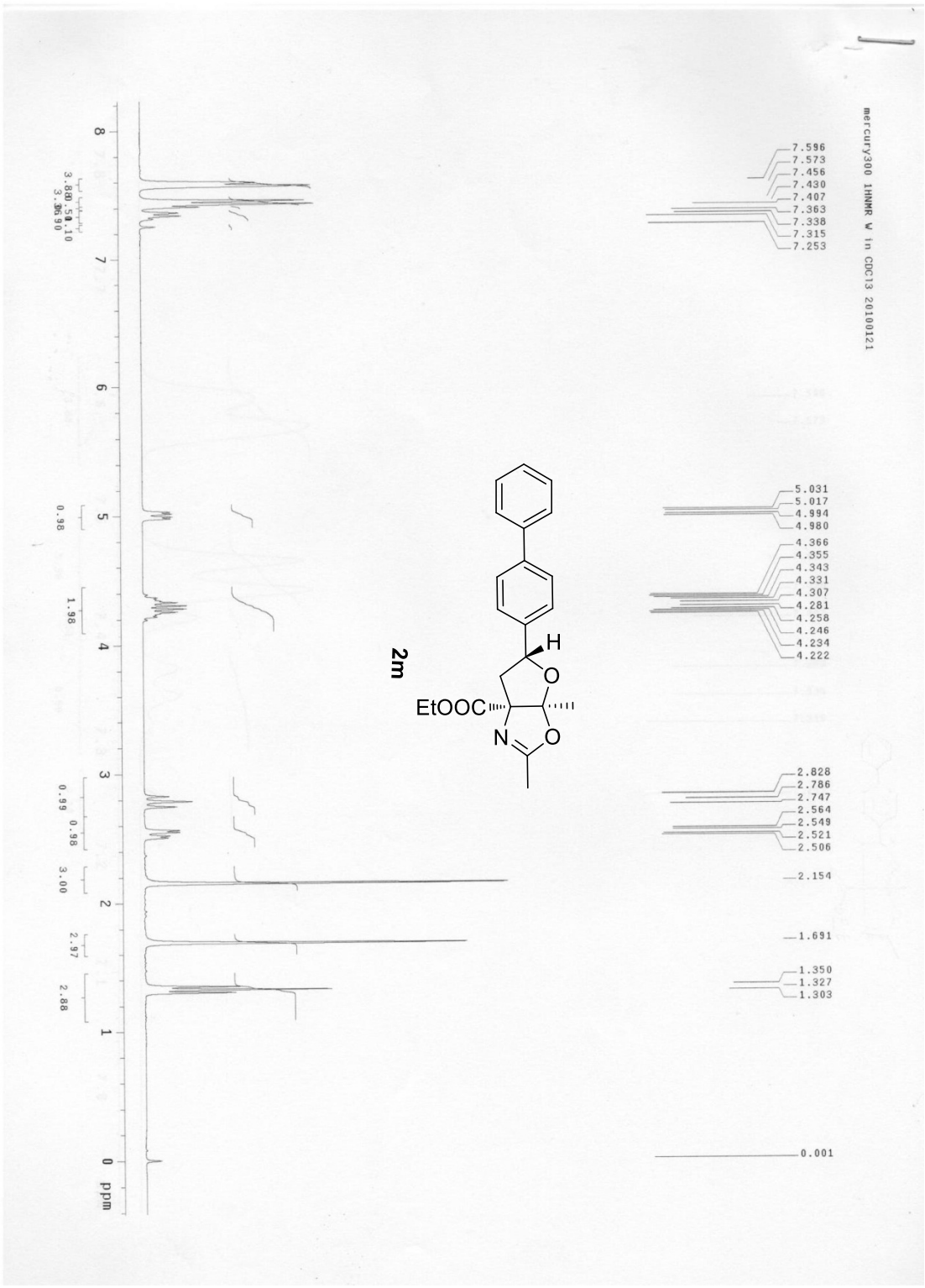

Mercury 400 1HNMR 216 in CDCl3 20140106
—169.899
—167.056
—140.967
—126.643
—125.842
—125.728
—116.988
—84.806
—77.318
—77.000
—76.682
—75.741
—62.045
—44.499
—20.678
—14.320
—14.107
2j
S
H
O
EtOOC
N
O
f1 (ppm)
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0


BRUKER AV500-III 1HNMR 3-22-1 in CDCl3
7.343
7.330
7.326
7.320
7.316
7.260
7.120
7.105
7.090
7.008
7.002
6.993
6.991
6.985
4.950
4.942
4.928
4.919
4.348
4.341
4.334
4.326
4.320
4.312
4.270
4.262
4.255
4.248
4.241
4.234
2.767
2.744
2.742
2.719
2.506
2.498
2.481
2.472
2.148
1.662
1.341
1.327
1.312
-0.001
2k
EtOOC
H
O
N
O
O
f1 (ppm)
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
-0.5
-1.0

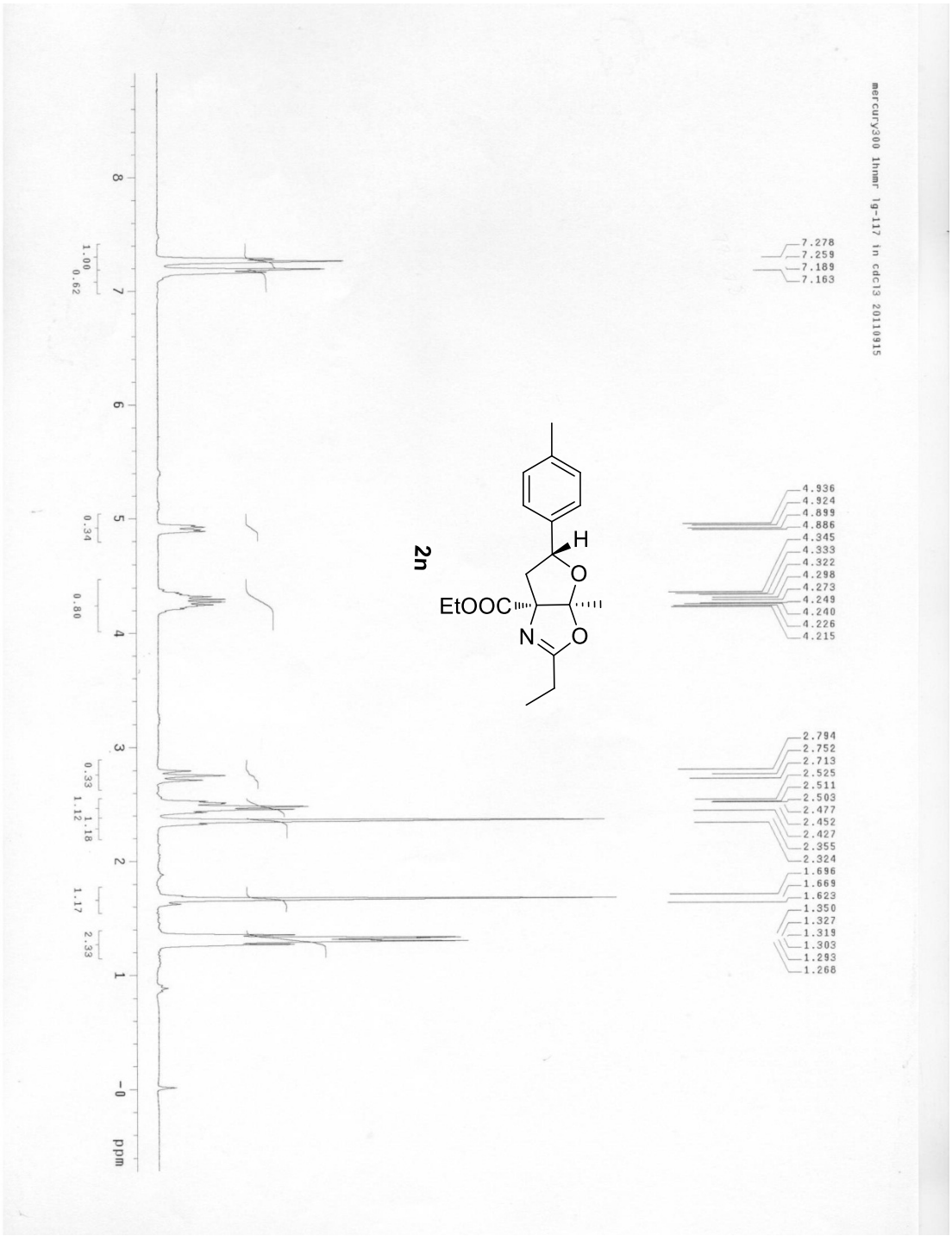

BRUKER AV500-III 1HNMR 3-22-1 in CDCl3
2k
EtOOC
H
O
N
O
O
170.176
167.122
157.334
157.023
133.006
129.745
127.819
123.381
118.946
118.797
117.366
84.899
79.592
77.254
77.000
76.746
62.066
44.622
20.720
14.387
14.175
-0.033
f1 (ppm)

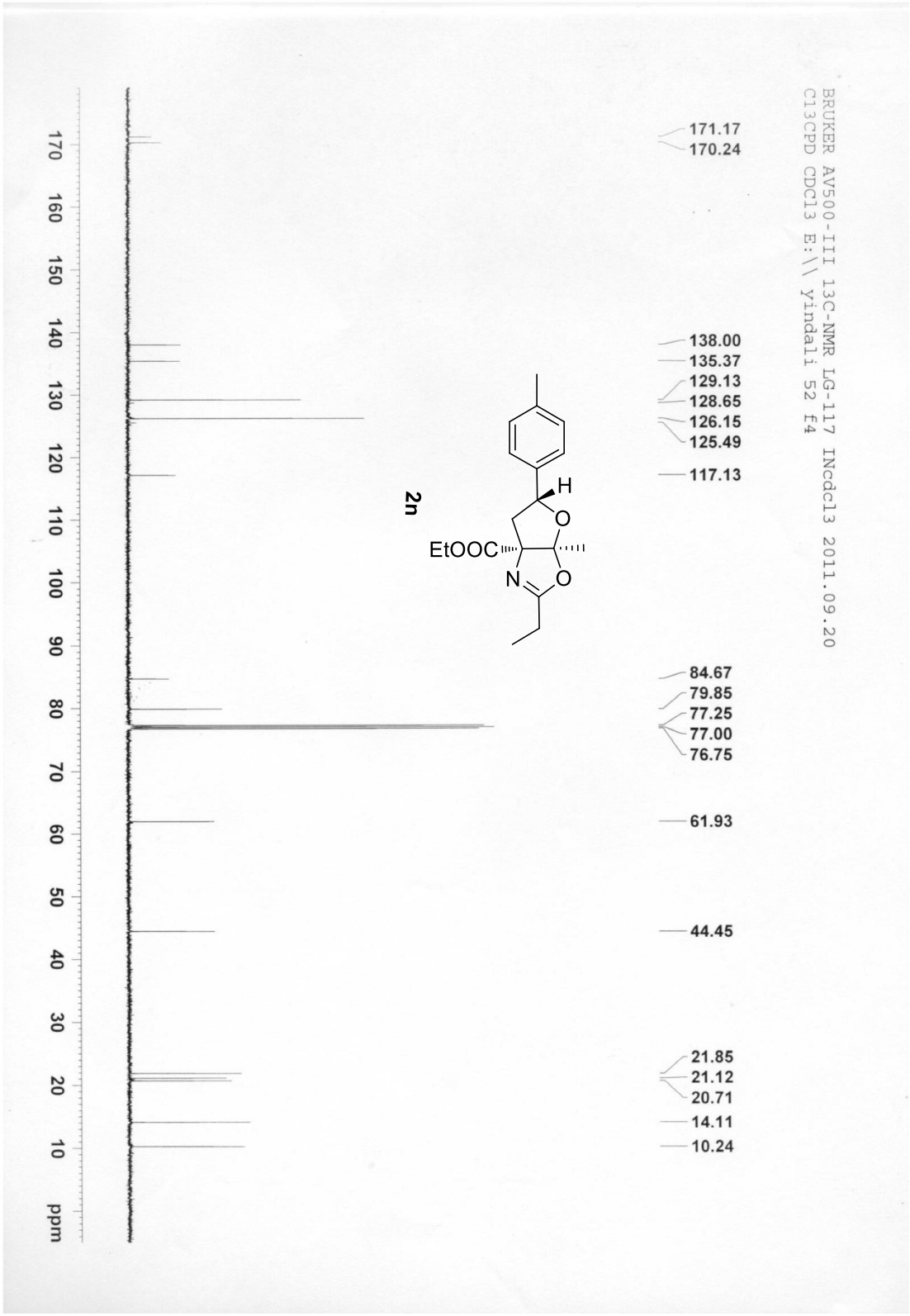

mercury300 1HNMR LG-15 in CDCl3 20110124
7.851
7.822
7.482
7.462
7.453
7.256
7.248
5.144
5.131
5.106
5.093
4.361
4.349
4.336
4.326
4.312
4.302
4.277
4.263
4.253
4.240
4.229
4.218
2.861
2.822
2.780
2.589
2.575
2.546
2.532
2.167
2.158
1.712
1.344
1.331
1.321
1.307
1.297
1.255
-0.011
2l
EtOOC
H
O
N
O
4.10
3.02
2.25
1.00
2.12
1.06
1.04
3.10
3.22
3.27
9
8
7
6
5
4
3
2
1
0
ppm

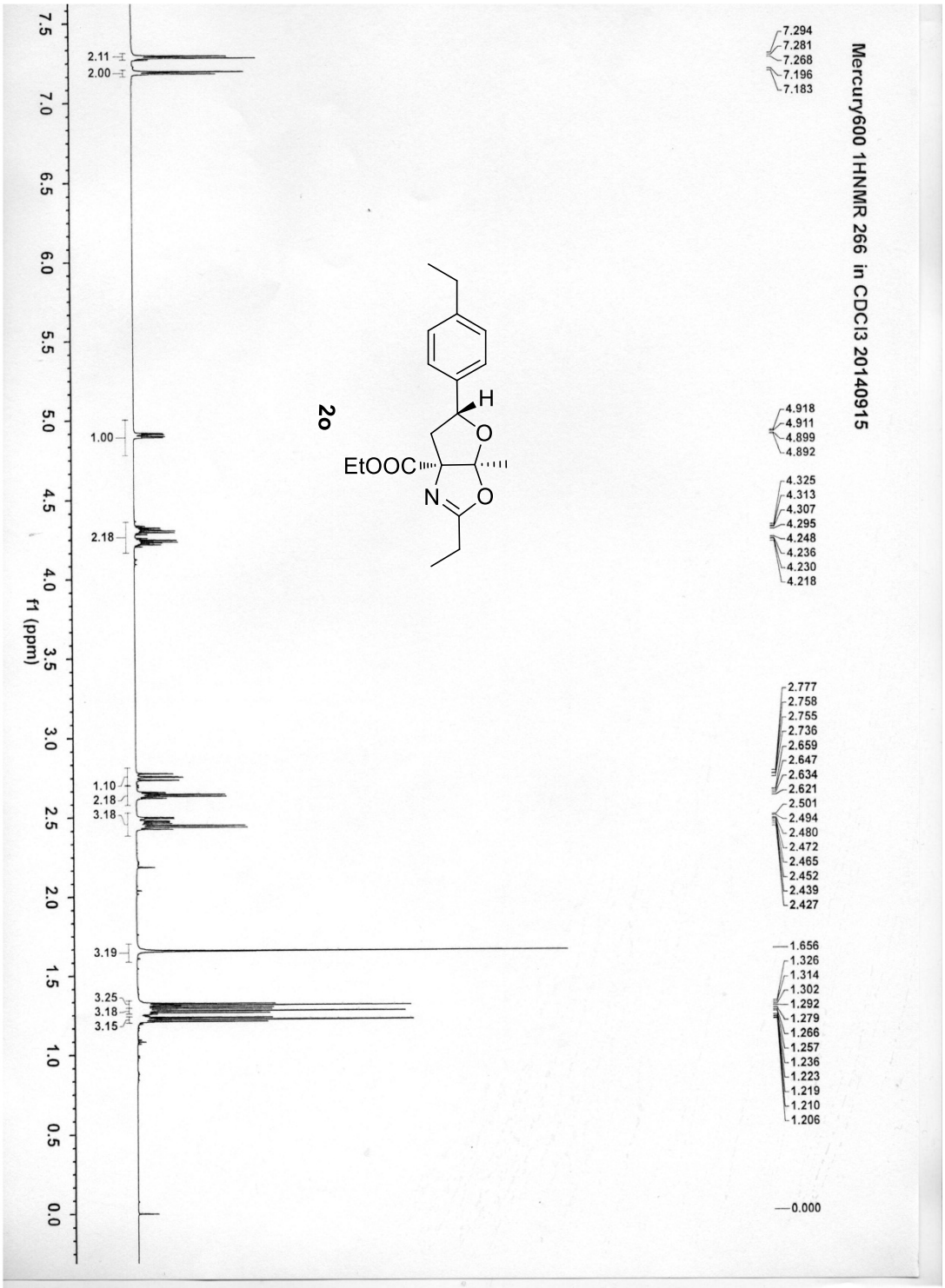

Mp-400 13C-NMR LG-15 in CDCL3 2011.02.21
170.201
167.138
135.777
133.256
133.129
128.400
127.956
127.694
126.249
126.125
125.248
123.787
117.557
84.990
80.067
77.317
77.000
76.683
62.093
44.694
20.759
14.428
14.189
2l
EtOOC
H
O
N
O
160
140
120
100
80
60
40
20
ppm

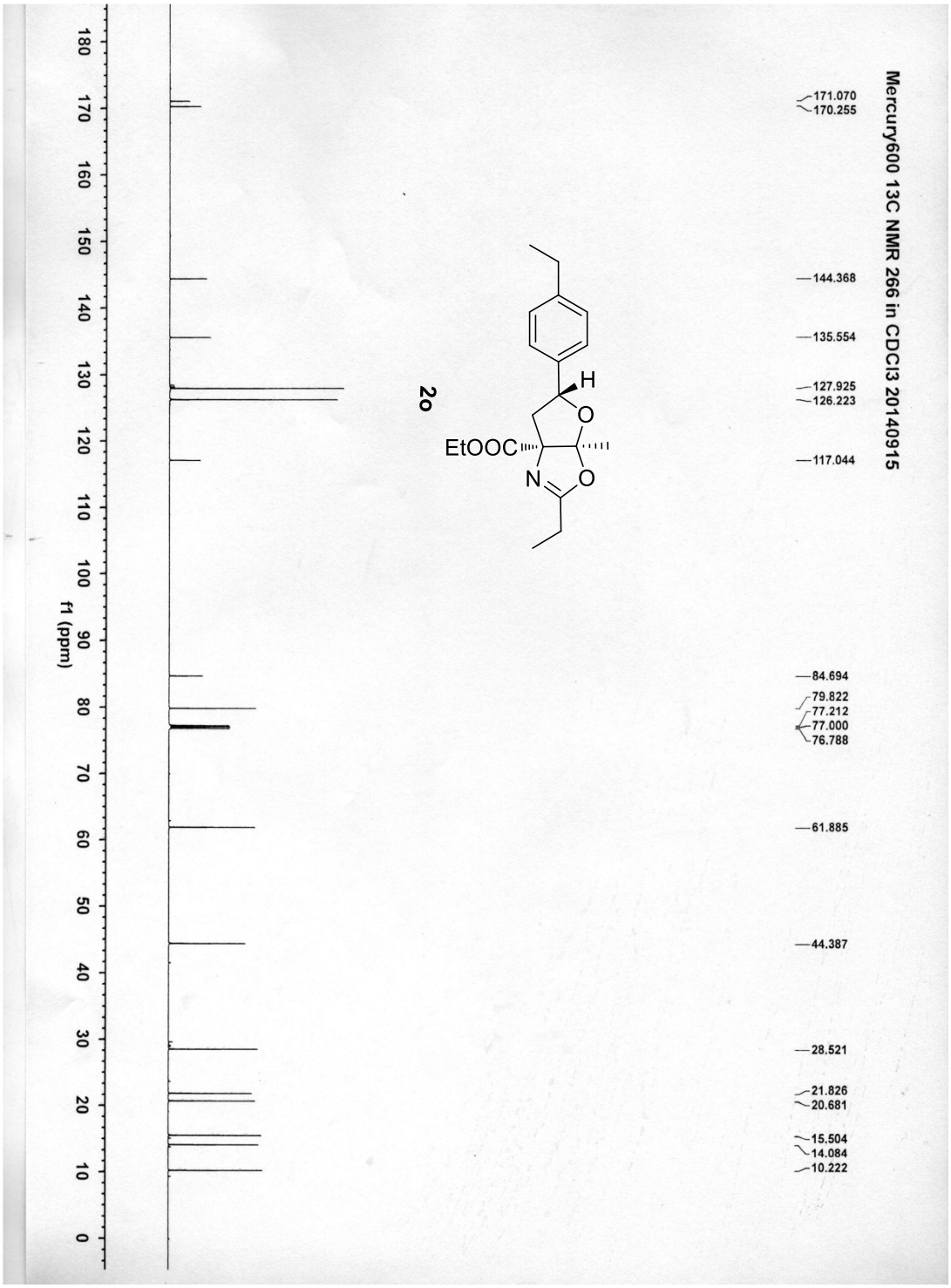

mercury300 1HNMR W in CDCl3 20100121
7.596
7.573
7.456
7.430
7.407
7.363
7.338
7.315
7.253
5.031
5.017
4.994
4.980
4.366
4.355
4.343
4.331
4.307
4.281
4.258
4.246
4.234
4.222
2.828
2.786
2.747
2.564
2.549
2.521
2.506
2.154
1.691
1.350
1.327
1.303
0.001
2m
EtOOC
H
O
N
O
ppm

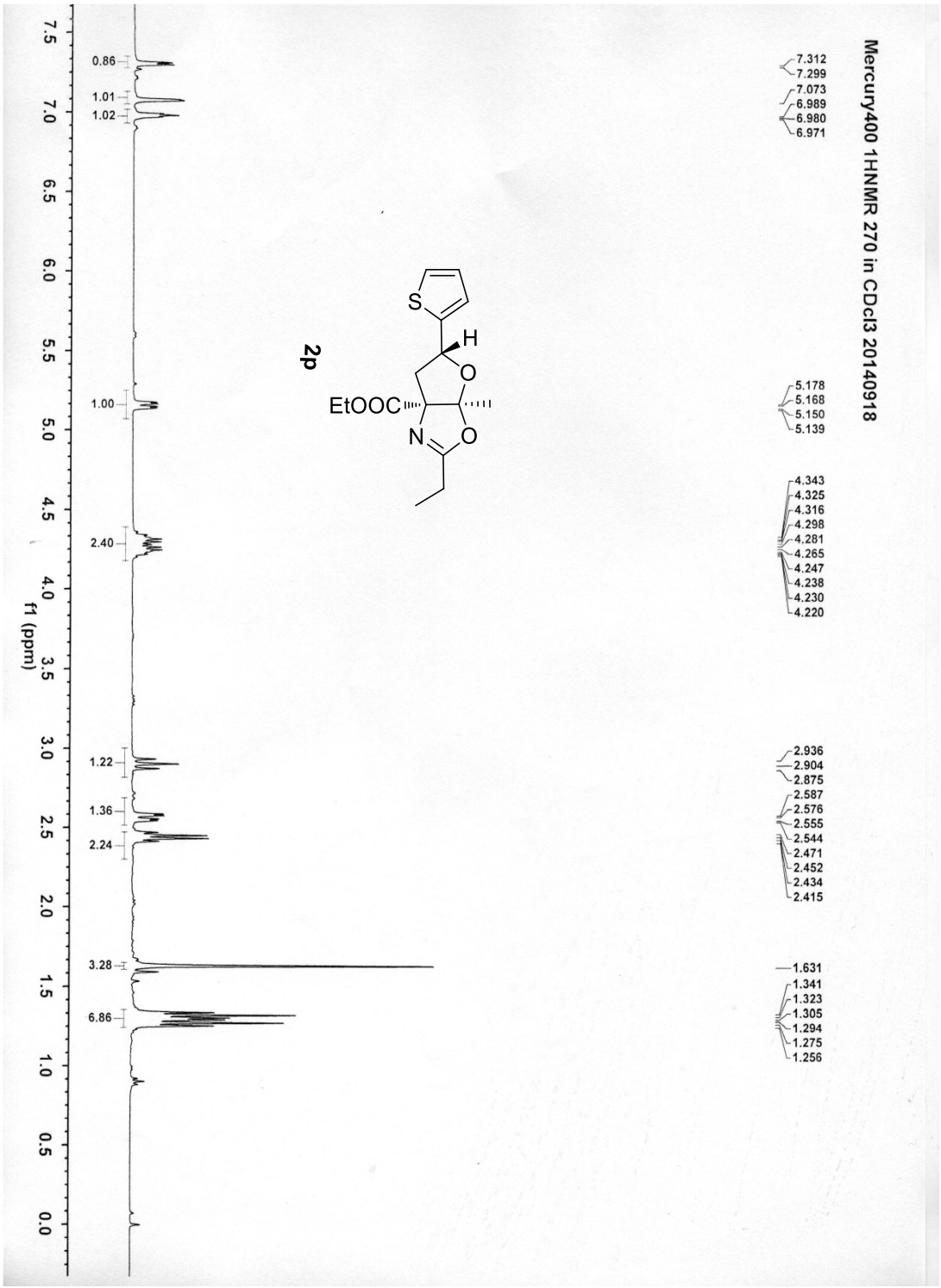

Mp-400 13C-NMR w in CDCl34 2011.02.21
170.145
167.194
141.264
140.689
137.346
128.755
127.369
127.265
127.085
126.637
117.497
84.892
79.730
77.317
77.000
76.683
62.078
44.601
20.726
14.402
14.178
2m
EtOOC
H
O
N
O
160
140
120
100
80
60
40
20
ppm

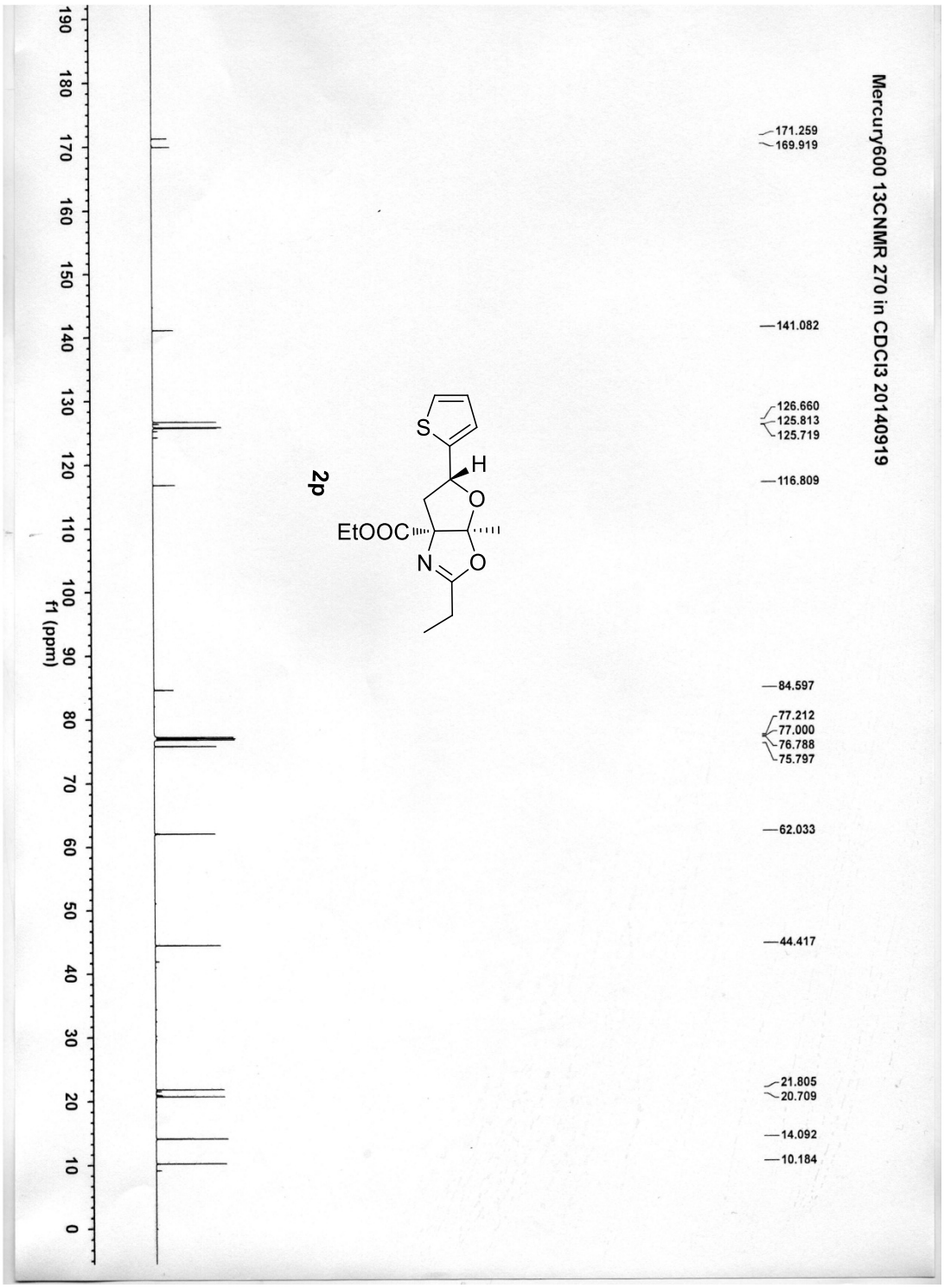

mercury300 1hnmr lg-117 in cdcl3 20110915
7.278
7.259
7.189
7.163
4.936
4.924
4.899
4.886
4.345
4.333
4.322
4.298
4.273
4.249
4.240
4.226
4.215
2.794
2.752
2.713
2.525
2.511
2.503
2.477
2.452
2.427
2.355
2.324
1.696
1.669
1.623
1.350
1.327
1.319
1.303
1.293
1.268
1.00
0.62
0.34
0.80
0.33
1.12
1.18
1.17
2.33
8
7
6
5
4
3
2
1
-0
ppm
2n
H
O
EtOOC
N
O

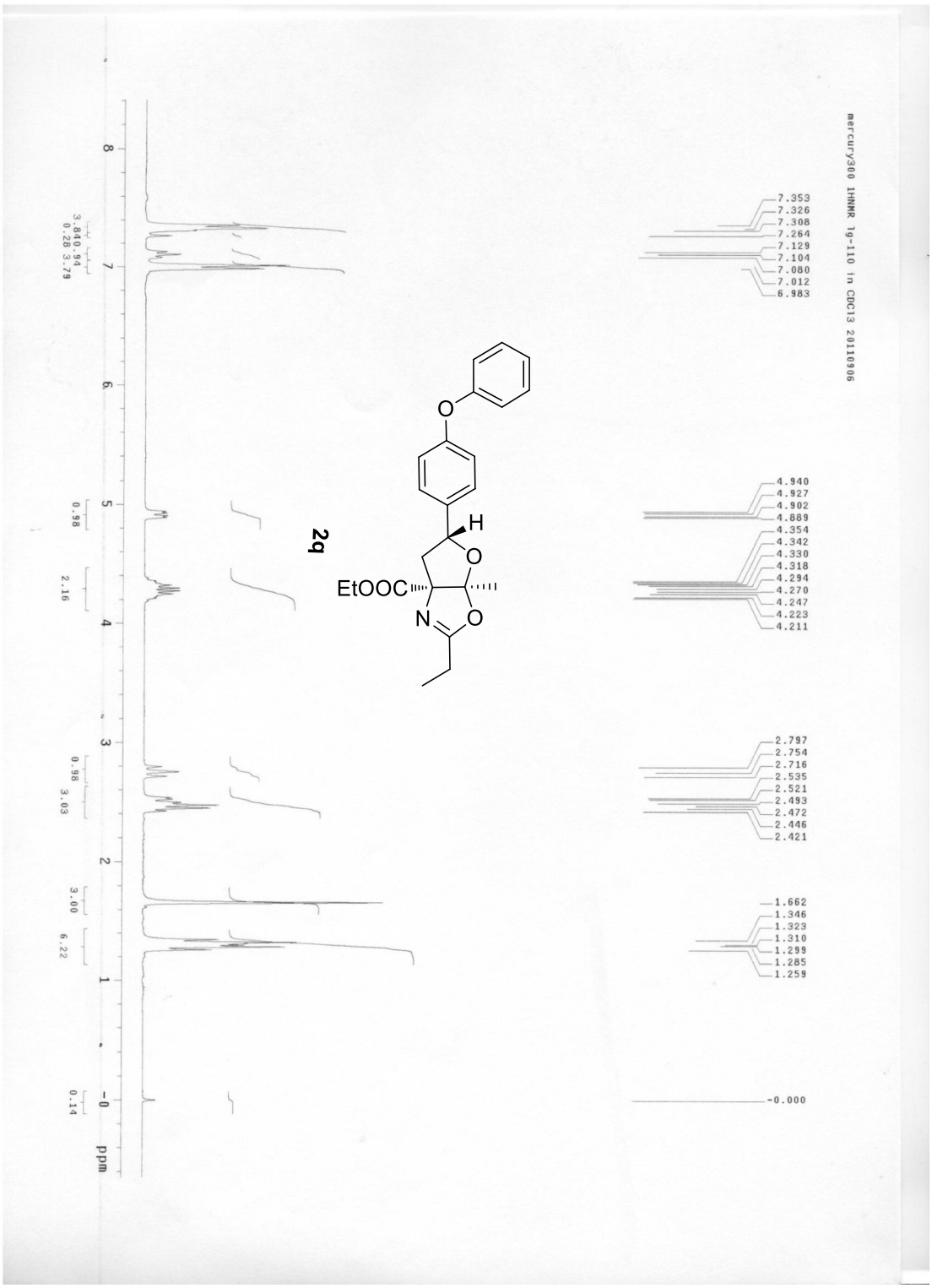

BRUKER AV500-III 13C-NMR LG-117 INcdcl3 2011.09.20
C13CPD CDCl3 E:\\ yindali 52 f4
171.17
170.24
138.00
135.37
129.13
128.65
126.15
125.49
117.13
84.67
79.85
77.25
77.00
76.75
61.93
44.45
21.85
21.12
20.71
14.11
10.24
2n
EtOOC
H
O
N
O
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

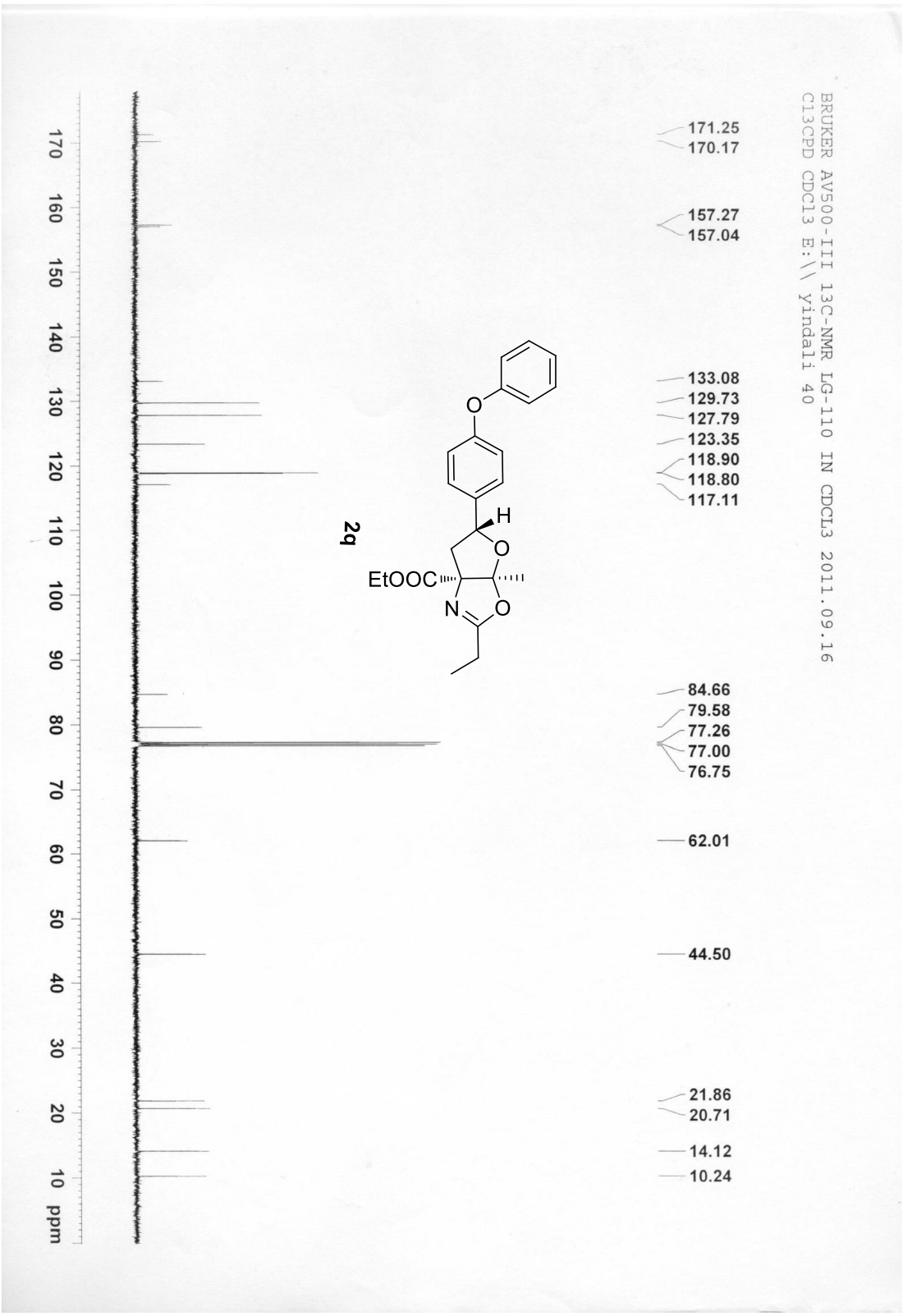

Mercury600 1HNMR 266 in CDCl3 20140915
2o
EtOOC
H
O
N
O
f1 (ppm)
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
2.11
2.00
1.00
2.18
1.10
2.18
3.18
3.19
3.25
3.18
3.15
7.294
7.281
7.268
7.196
7.183
4.918
4.911
4.899
4.892
4.325
4.313
4.307
4.295
4.248
4.236
4.230
4.218
2.777
2.758
2.755
2.736
2.659
2.647
2.634
2.621
2.501
2.494
2.480
2.472
2.465
2.452
2.439
2.427
1.656
1.326
1.314
1.302
1.292
1.279
1.266
1.257
1.236
1.223
1.219
1.210
1.206
0.000

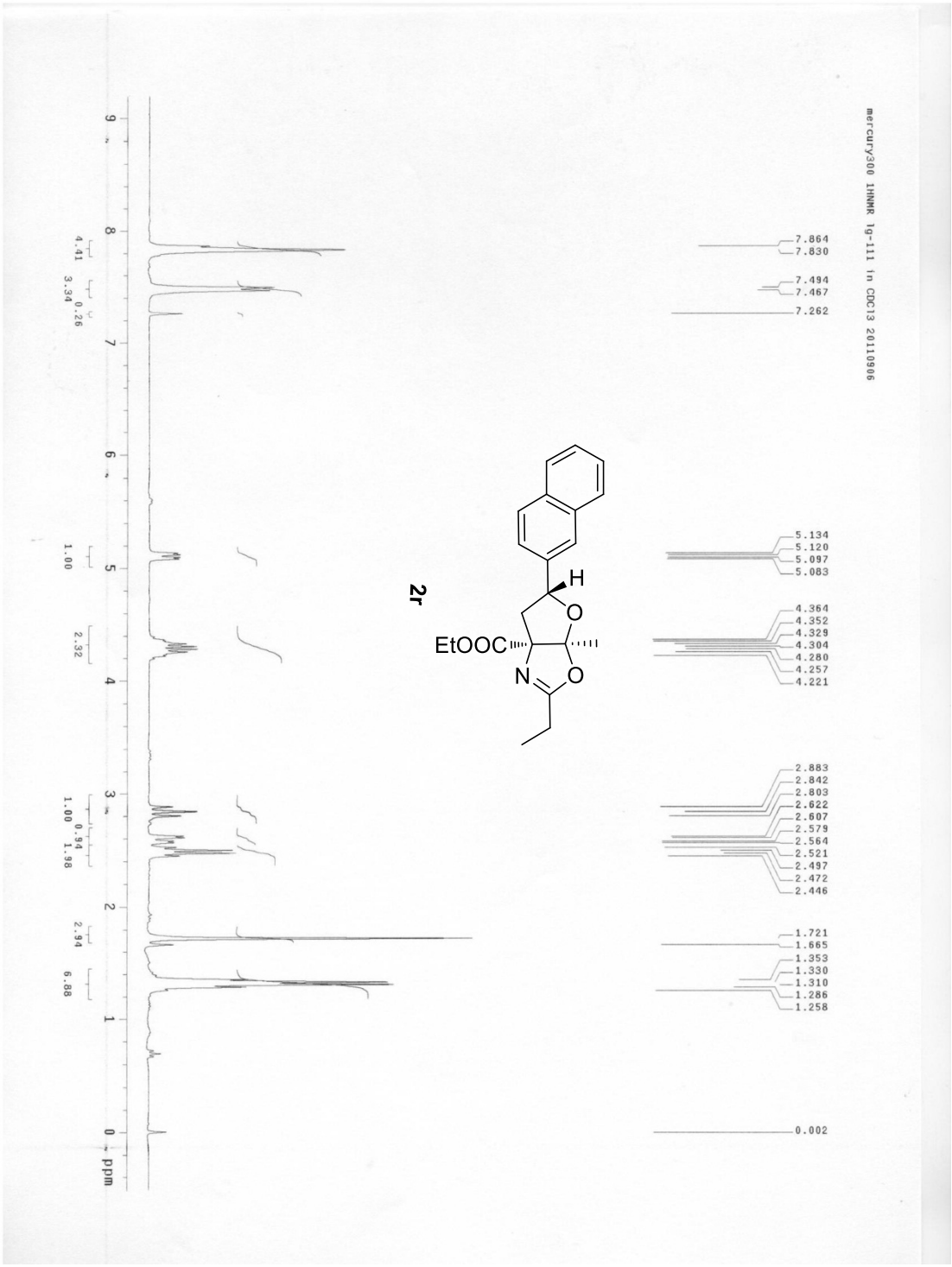

Mercury600 13C NMR 266 in CDCl3 20140915
171.070
170.255
144.368
135.554
127.925
126.223
117.044
84.694
79.822
77.212
77.000
76.788
61.885
44.387
28.521
21.826
20.681
15.504
14.084
10.222
2o
EtOOC
H
O
N
O
f1 (ppm)
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

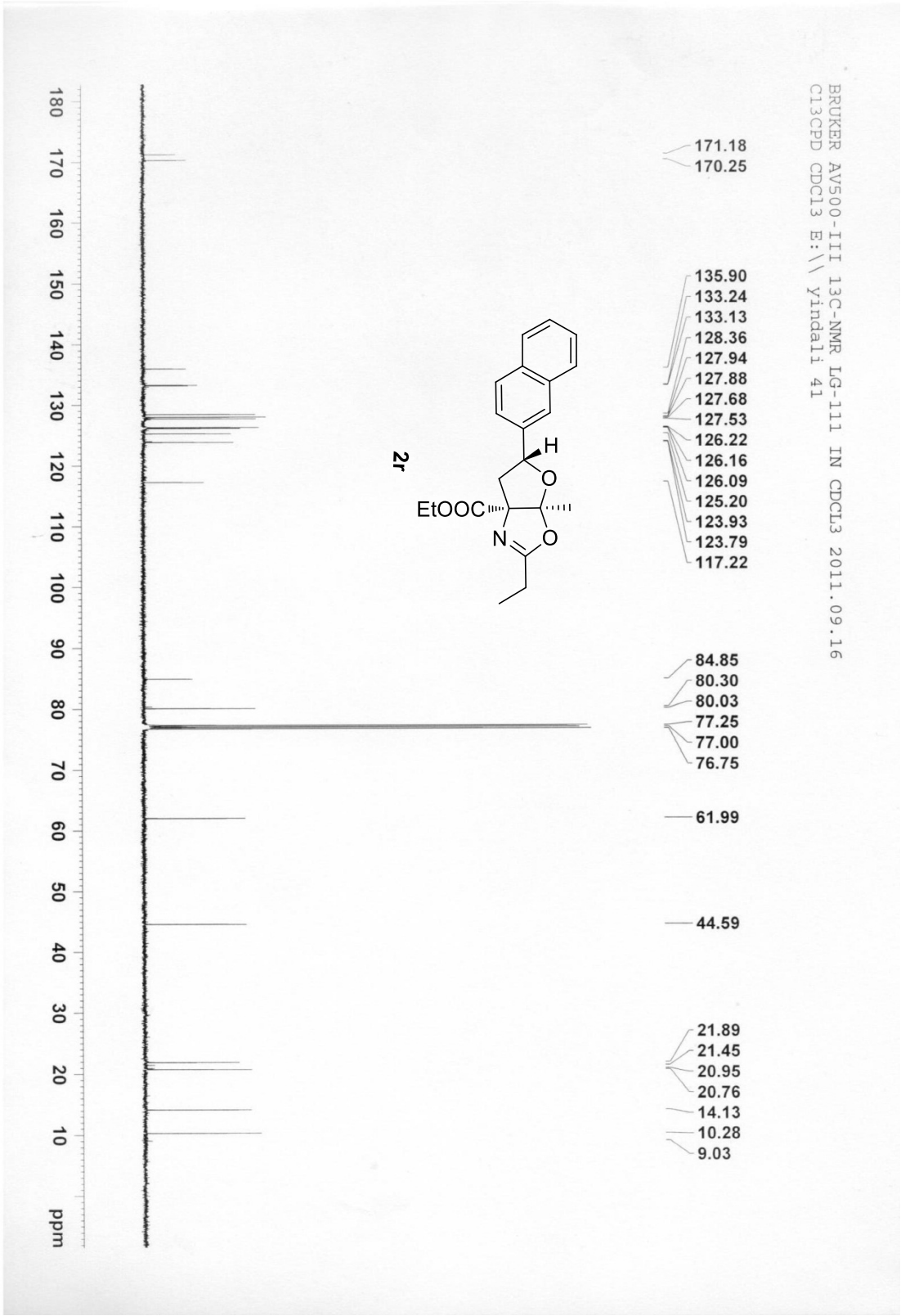

Mercury400 1HNMR 270 in CDcl3 20140918
2p
EtOOC
S
H
O
N
O
f1 (ppm)
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
0.86
1.01
1.02
1.00
2.40
1.22
1.36
2.24
3.28
6.86
7.312
7.299
7.073
6.989
6.980
6.971
5.178
5.168
5.150
5.139
4.343
4.325
4.316
4.298
4.281
4.265
4.247
4.238
4.230
4.220
2.936
2.904
2.875
2.587
2.576
2.555
2.544
2.471
2.452
2.434
2.415
1.631
1.341
1.323
1.305
1.294
1.275
1.256

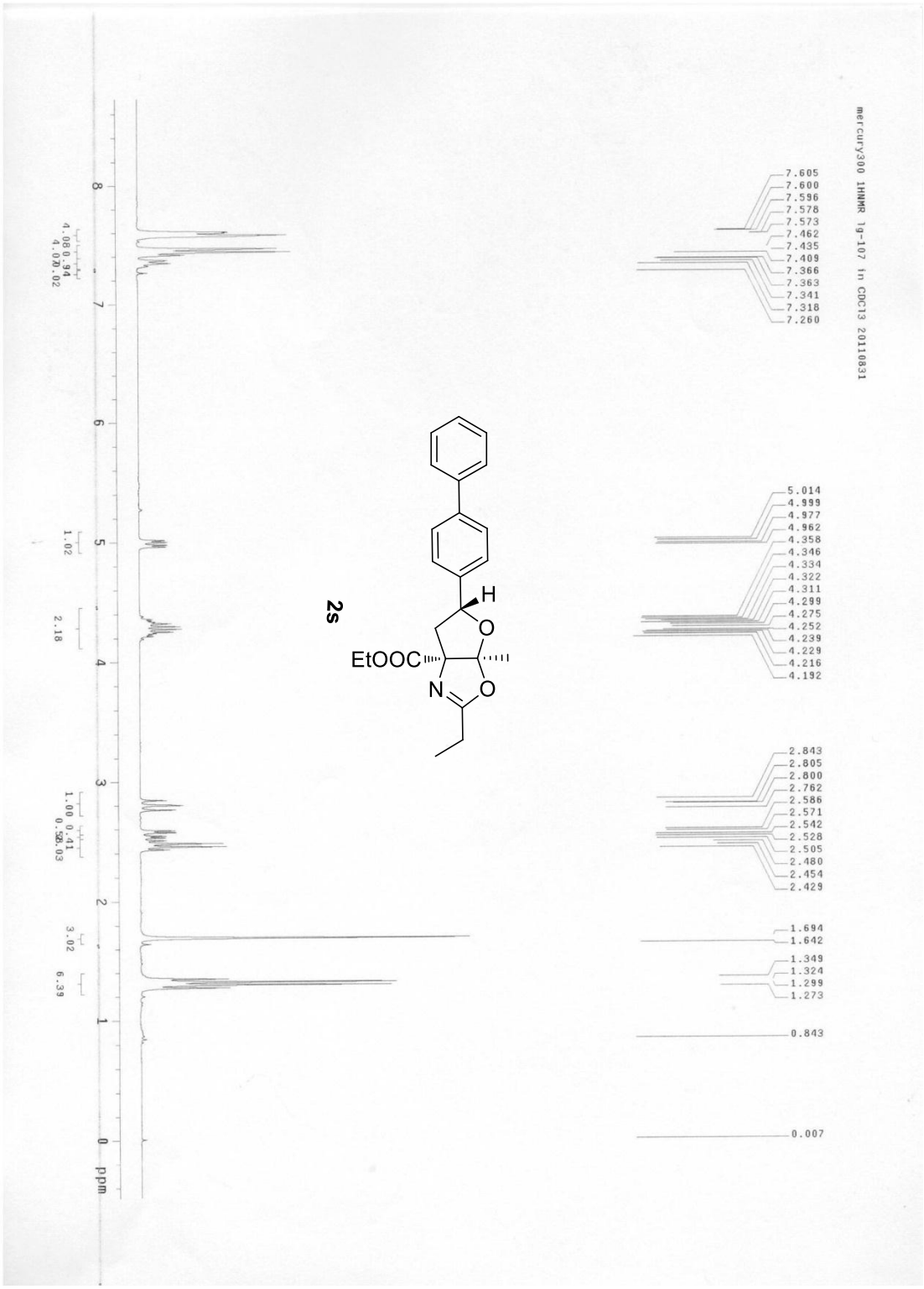

Mercury600 13CNMR 270 in CDCl3 20140919
171.259
169.919
141.082
126.660
125.813
125.719
116.809
84.597
77.212
77.000
76.788
75.797
62.033
44.417
21.805
20.709
14.092
10.184
2p
EtOOC
S
H
O
N
O
f1 (ppm)
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

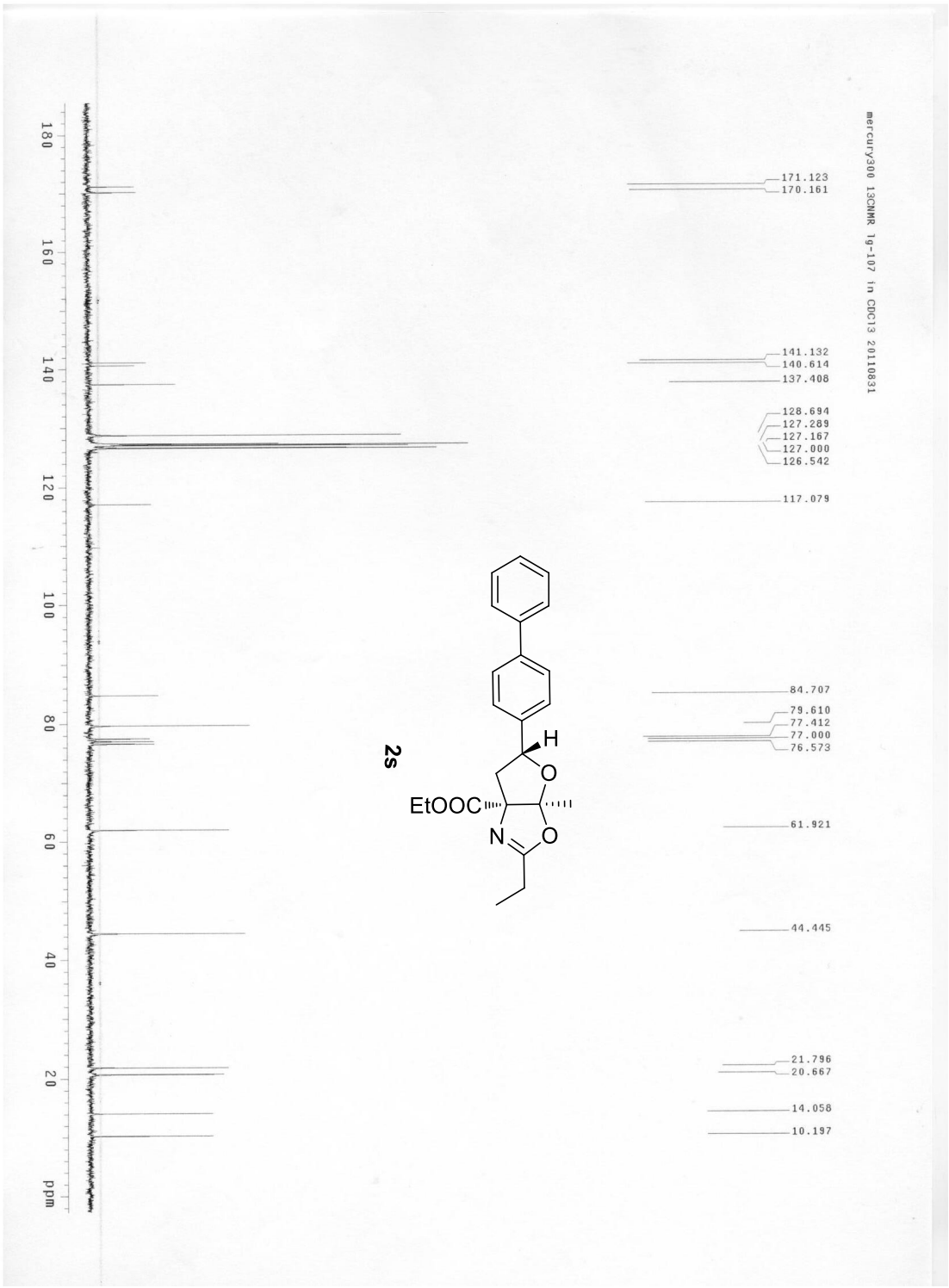

mercury300 1HNMR lg-110 in CDCl3 20110906
7.353
7.326
7.308
7.264
7.129
7.104
7.080
7.012
6.983
4.940
4.927
4.902
4.889
4.354
4.342
4.330
4.318
4.294
4.270
4.247
4.223
4.211
2.797
2.754
2.716
2.535
2.521
2.493
2.472
2.446
2.421
1.662
1.346
1.323
1.310
1.299
1.285
1.259
-0.000
2q
EtOOC
H
O
N
O
O
3.840 9.41
0.28 3.79
0.98
2.16
0.98
3.03
3.00
6.22
0.14
8
7
6
5
4
3
2
1
-0
ppm

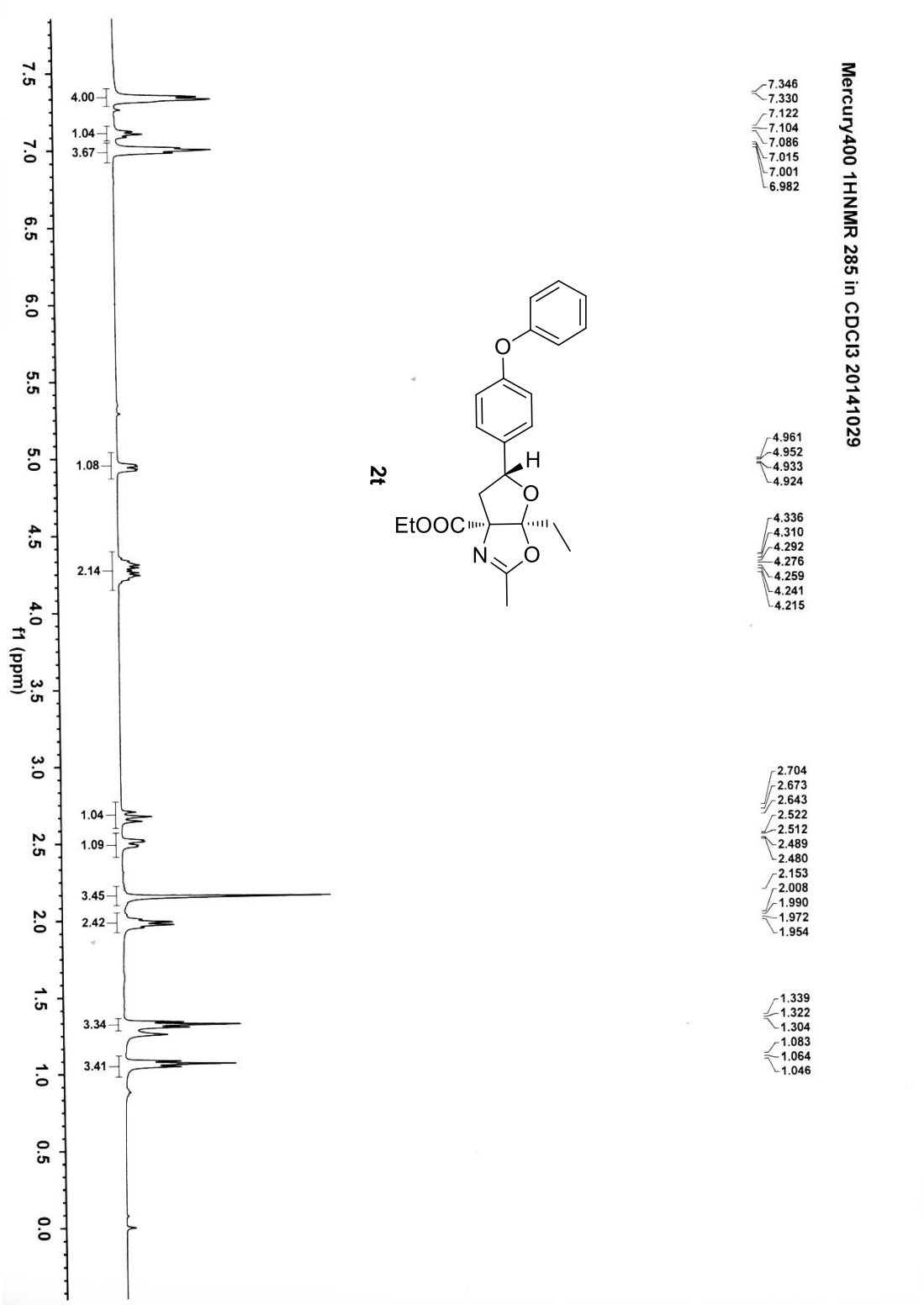

BRUKER AV500-III 13C-NMR LG-110 IN CDCL3 2011.09.16
C13CPD CDCl3 E:\\ yindali 40
171.25
170.17
157.27
157.04
133.08
129.73
127.79
123.35
118.90
118.80
117.11
84.66
79.58
77.26
77.00
76.75
62.01
44.50
21.86
20.71
14.12
10.24
2q
EtOOC
H
O
N
O
O
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

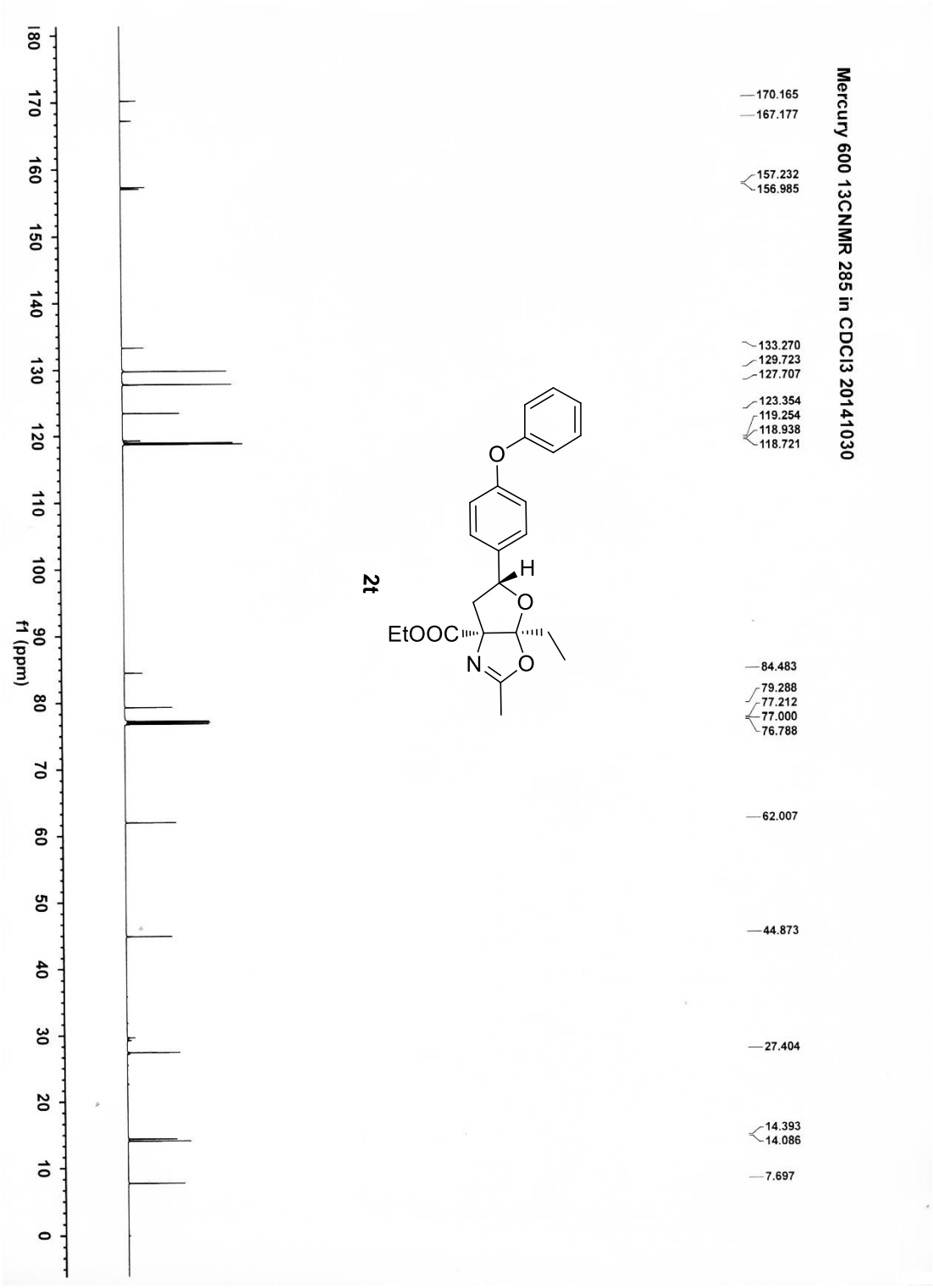

mercury300 1HNMR lg-111 in CDCl3 20110906
7.864
7.830
7.494
7.467
7.262
5.134
5.120
5.097
5.083
4.364
4.352
4.329
4.304
4.280
4.257
4.221
2.883
2.842
2.803
2.622
2.607
2.579
2.564
2.521
2.497
2.472
2.446
1.721
1.665
1.353
1.330
1.310
1.286
1.258
0.002
2r
EtOOC
H
O
N
O
4.41
3.34
0.26
1.00
2.32
1.00
0.94
1.98
2.94
6.88
ppm

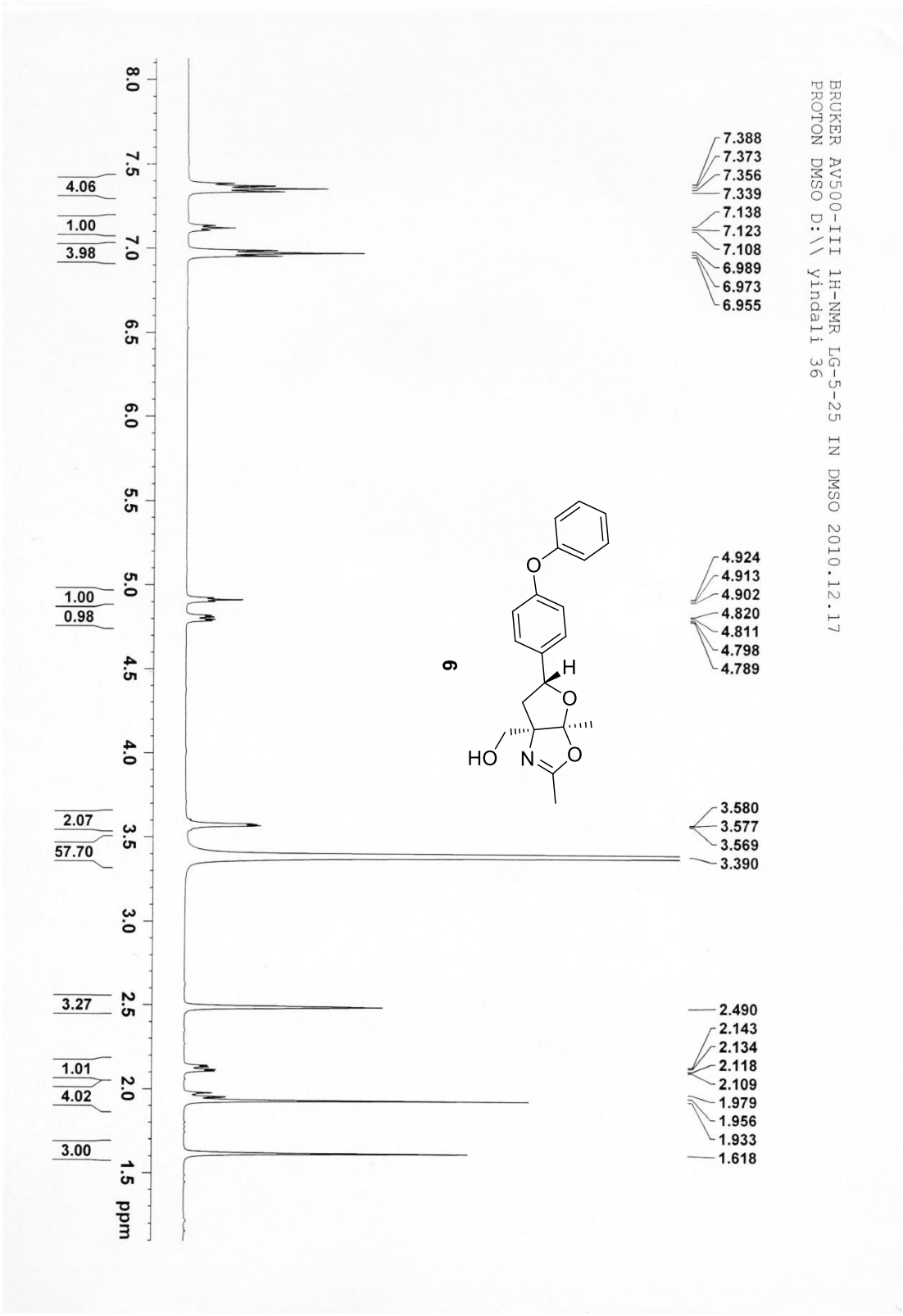

BRUKER AV500-III 13C-NMR LG-111 IN CDCL3 2011.09.16
C13CPD CDCl3 E:\\ yindali 41
171.18
170.25
135.90
133.24
133.13
128.36
127.94
127.88
127.68
127.53
126.22
126.16
126.09
125.20
123.93
123.79
117.22
84.85
80.30
80.03
77.25
77.00
76.75
61.99
44.59
21.89
21.45
20.95
20.76
14.13
10.28
9.03
2r
H
O
EtOOC
N
O
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

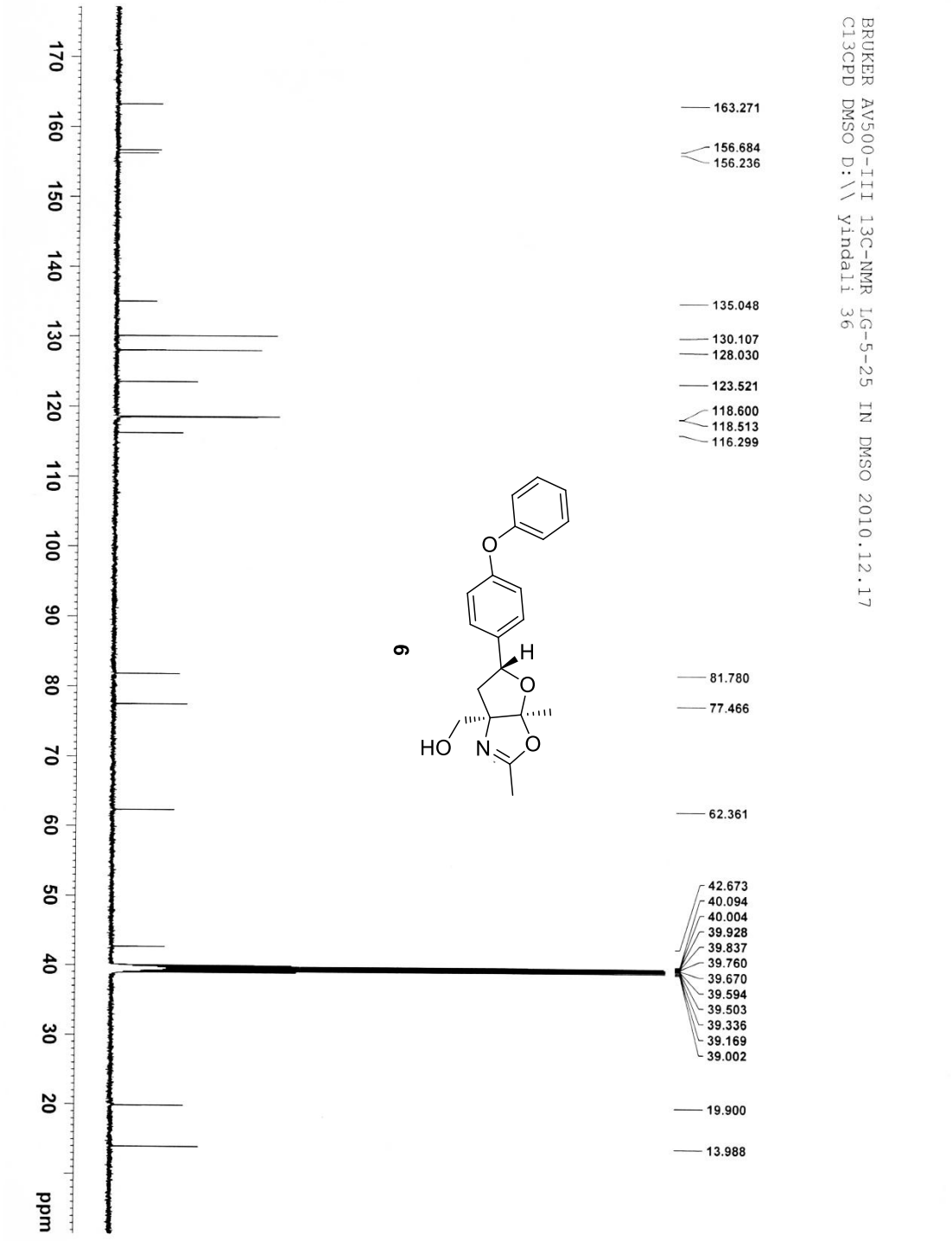

mercury300 1HNMR lg-107 in CDCl3 20110831
7.605
7.600
7.596
7.578
7.573
7.462
7.435
7.409
7.366
7.363
7.341
7.318
7.260
5.014
4.999
4.977
4.962
4.358
4.346
4.334
4.322
4.311
4.299
4.275
4.252
4.239
4.229
4.216
4.192
2.843
2.805
2.800
2.762
2.586
2.571
2.542
2.528
2.505
2.480
2.454
2.429
1.694
1.642
1.349
1.324
1.299
1.273
0.843
0.007
2s
EtOOC
H
O
N
O
ppm


mercury300 13CNMR lg-107 in CDCl3 20110831
171.123
170.161
141.132
140.614
137.408
128.694
127.289
127.167
127.000
126.542
117.079
84.707
79.610
77.412
77.000
76.573
61.921
44.445
21.796
20.667
14.058
10.197
180
160
140
120
100
80
60
40
20
ppm
2s
H
O
EtOOC
N
O


Mercury400 1HNMR 285 in CDCl3 20141029
7.346
7.330
7.122
7.104
7.086
7.015
7.001
6.982
4.961
4.952
4.933
4.924
4.336
4.310
4.292
4.276
4.259
4.241
4.215
2.704
2.673
2.643
2.522
2.512
2.489
2.480
2.153
2.008
1.990
1.972
1.954
1.339
1.322
1.304
1.083
1.064
1.046
4.00
1.04
3.67
1.08
2.14
1.04
1.09
3.45
2.42
3.34
3.41
f1 (ppm)
2t
EtOOC
H
O
N
O
O


Mercury 600 13CNMR 285 in CDCl3 20141030
170.165
167.177
157.232
156.985
133.270
129.723
127.707
123.354
119.254
118.938
118.721
84.483
79.288
77.212
77.000
76.788
62.007
44.873
27.404
14.393
14.086
7.697
2t
EtOOC
H
O
N
O
O
f1 (ppm)
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

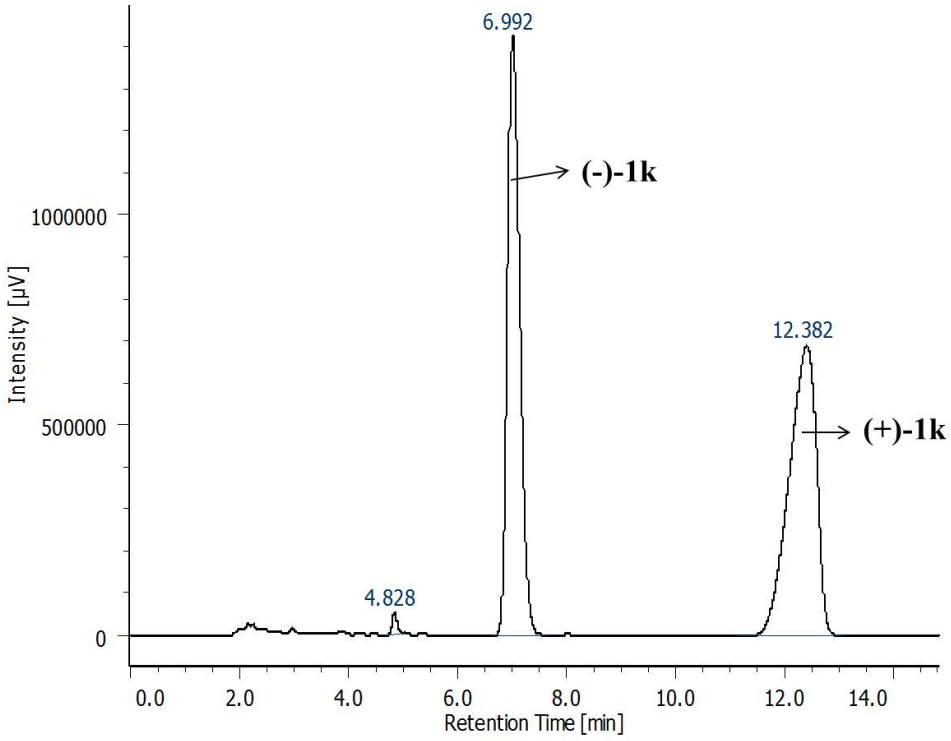

BRUKER AV500-III 1H-NMR LG-5-25 IN DMSO 2010.12.17
PROTON DMSO D:\\ yindali 36
7.388
7.373
7.356
7.339
7.138
7.123
7.108
6.989
6.973
6.955
4.924
4.913
4.902
4.820
4.811
4.798
4.789
3.580
3.577
3.569
3.390
2.490
2.143
2.134
2.118
2.109
1.979
1.956
1.933
1.618
4.06
1.00
3.98
1.00
0.98
2.07
57.70
3.27
1.01
4.02
3.00
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
ppm
6
O
H
O
HO
N
O


BRUKER AV500-III 13C-NMR LG-5-25 IN DMSO 2010.12.17
C13CPD DMSO D:\\ yindali 36
163.271
156.684
156.236
135.048
130.107
128.030
123.521
118.600
118.513
116.299
81.780
77.466
62.361
42.673
40.094
40.004
39.928
39.837
39.760
39.670
39.594
39.503
39.336
39.169
39.002
19.900
13.988
ppm
6
HO
N
O
O
H

Chiral Chromatography Report of Racemate **1k**

Column	:	CHIRALCEL AD-H
Column size	:	0.46 cm I.D. × 25 cm L
Injection	:	10ul
Mobile phase	:	CO_2/MeOH=60/40(V/V)
Flow rate	:	2.0 ml/min
Wave length	:	UV 220 nm
Temperature	:	35 ℃
Sample solution	:	X mg/ml in MeOH
SFC equipment	:	
Sample structure	:	Racemate

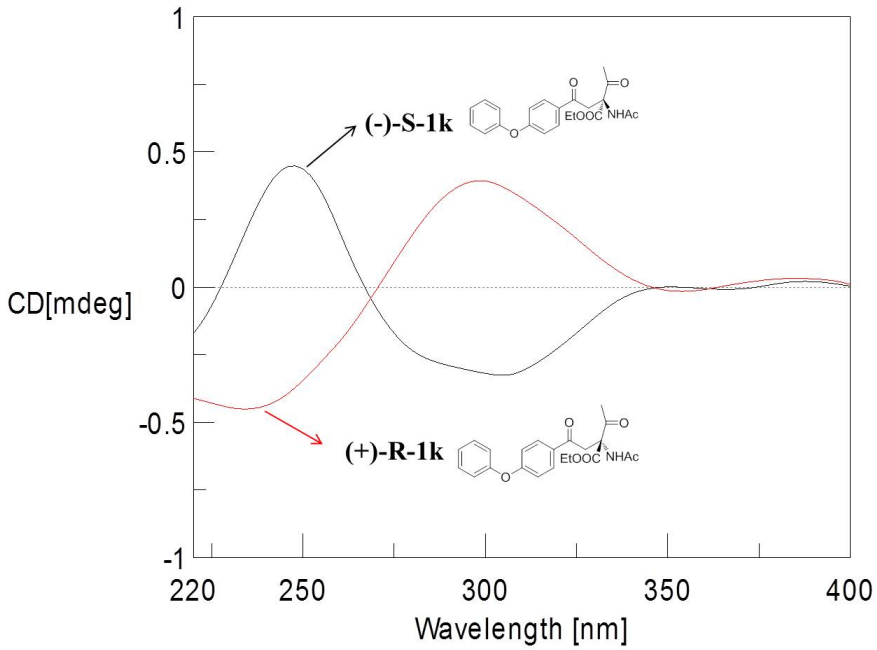
< Chromatogram >



<Column Performance Report>

#	tR	Area	Area%	Height%	NTP	Resolution	Symmetry Factor
1	4.828	304371	0.648	2.319	14378	7.386	1.122
2	6.992	22663876	48.241	65.843	4304	7.832	1.282
3	12.382	24012505	51.111	31.838	2696	N/A	0.753

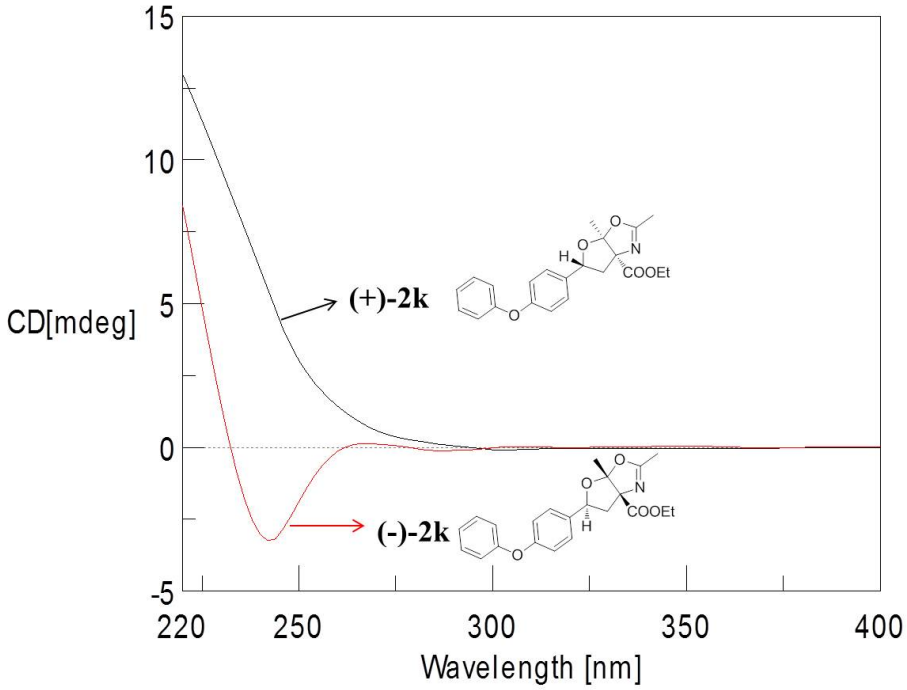
Circular Dichroism Spectra



The absolute configuration was confirmed by circular dichroism spectra according to octant rule.

(-)-1k was given S configuration $[\alpha]_D^{20}$ -3.4 (c = 1.02, $CHCl_3$).

(+)-1k was given R configuration $[\alpha]_D^{20}$ +3.2 (c = 1.16, $CHCl_3$).



The absolute configuration was confirmed by electronic circular dichroism.

(+)-2k was given R, S, S configuration $[\alpha]_D^{20}$ +71.8 (c = 0.95, $CHCl_3$).

(-)-2k was given S, R, R configuration $[\alpha]_D^{20}$ -71.2 (c = 0.80, $CHCl_3$).