Supplementary Information

Table of content

1 General information

Reagents, obtained from commercial sources, were used without further purification. Reactions were carried out in 100 ml *Mettler-Toledo* EasyMax™ reactors under atmospheric conditions. Solvents were used as purchased. All products were purified by flash-chromatography (*Interchim* PuriFlash 450) on silica gel (25 µm) using cyclohexane and ethyl acetate as eluents. TLC was performed on silica gel plates 60 F_{254} by *Merck*. NMR spectra were measured on a *Varian* VNMRS 500 or on a *Bruker* Ascend 400 using deuterated solvents with trimethylsilane as internal standard. Chemical shifts δ are given in ppm, coupling constants *J* in Hz. IR spectra were recorded with the FT-IR spectrometer Spectrum One by *Perkin Elmer* using a Germanium-ATR unit and are reported in wave numbers (cm^{-1}). Mass-spectra were obtained with *Waters* GC TOF (EI) and *Bruker* ESI-Q-TOFmicro. Melting points were determined in open glass capillaries on a *Büchi* M-560.

2 Experimental Data

2.1 Syntheses

2.1.1 Guanylations with Iron(III)chloride (General EasyMax-procedure)

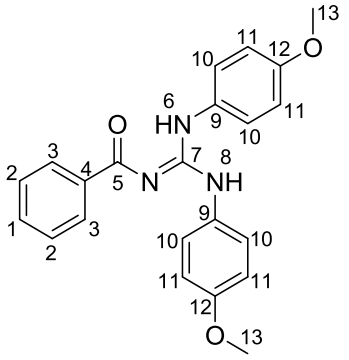
According to a modified procedure from literature.[1] The reactions are done in a 100 ml EasyMax reactor, equipped with reflux cooler, magnetic stirrer bar and temperature sensor. To a solution of thiourea (5 mmol) in 30 ml acetonitrile, triethylamine (20 mmol, 2.02 g, 2.77 ml, 4 eq) and the particular amine (5 mmol, 1 eq) are added with stirring at 300 rpm. The reaction mixture is cooled down to 0°C (reactor temperature (T_R)) in 10 minutes. Then iron(III)chloride (5 mmol, 1 eq) is added. After another 10 minutes, the temperature is raised to 40°C (T_R) in 30 min. Progress of the reaction is monitored by TLC (CHx-EtOAc). With complete conversion, the reaction mixture is transferred into a 250 ml round-bottom flask. Activated carbon is added and the mixture is stirred in a water bath at 70°C for 5 min. The suspension is filtered through a pad of Celite and is washed with dichloromethane. The filtrate is then concentrated in vacuo and the brownish solution is treated with diethyl ether precipitating triethylamine hydrochloride. The suspension is filtered through a G4-frit and is washed subsequently with diethyl ether and tetrahydrofurane. The filtrate is dried in vacuo. Further purification is done by flash chromatography on silica gel with Cyclohexane - Ethyl acetate gradient.

2.1.2 Guanylations with Iron(III)chloride (General procedure)

According to a modified procedure from literature.[1] The reaction is done in a 100 ml 2-neck round bottom flask, equipped with reflux cooler and a magnetic stirrer bar. To a solution of thiourea (5 mmol) in 30 ml acetonitrile, triethylamine (20 mmol, 2.02 g, 2.77 ml, 4 eq) and the particular amine (5 mmol, 1 eq) are added. The reaction mixture is cooled in an ice-bath to about 0°C. Then iron(III)chloride (5 mmol, 1 eq) is added and mixture is vigorously stirred. After approx. 10 minutes, the temperature is raised to 45°C (oil bath). Progress of the reaction is monitored by TLC (CHx-EtOAc). With complete conversion, work-up and purification procedure are done according to section 2.1.1.

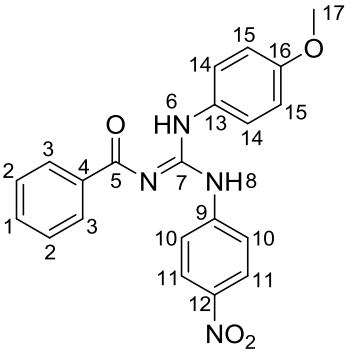
2.1.3 Guanidines

(E)-N-(N,N'-bis(4-methoxyphenyl)carbamimidoyl)benzamide (3)



3 is prepared according to the general EasyMax procedure. Purification is done by flash chromatography on silica gel (cyclohexane-ethyl acetate 4:1) to give the product (1.423 g, 3.79 mmol, 76%) as a beige solid. R_f (cyclohexane-ethyl acetate 1:1) = 0.41; F_P: 127.4-128.2°C (Lit. 128 °C)[2]; ^{1}H-NMR (500 MHz, $CDCl_3$, ppm): δ 3.83 (s, 6H, H-13), 6.87-7.02 (m, 4H, H-11), 7.31-7.36 (m, 4H, H-10), 7.37-7.42 (m, 2H, H-2), 7.45 (tt, ^3J = 6.6 Hz, ^4J = 1.4 Hz, 1H, H-1), 8.13-8.24 (m, 2H, H-3); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 55.5 (C-13), 114.6 (C-11), 126.3 (C-10), 127.9 (C-2), 129.2 (C-3), 131.2 (C-1), 138.4 (C-12), 157.7 (C-7), 178.1 (C-5); IR (cm^{-1}): 3376, 3342, 3074, 2963, 2808, 1599, 1565, 1508, 1460, 1374, 1351, 1300, 1240, 1204, 1181, 1106, 1034, 1010, 906, 888, 830, 819, 752, 716, 684; HRMS (EI): calculated for $C_{22}H_{21}N_3O_3$ $[M]^+$: 375.1583, found: 375.1571.

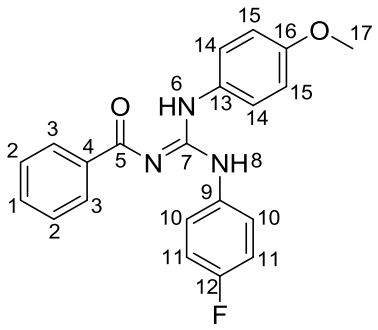
(E)-N-(N'-(4-methoxyphenyl)-N-(4-nitrophenyl)carbamimidoyl)benzamide (5a)



5a is prepared according to the general EasyMax procedure. Purification is done by flash chromatography on silica gel (cyclohexane-ethyl acetate 7:3 > 6:4 > 1:1) to give the product (0.81 g, 2.07 mmol, 41%) as fine, yellow needles. R_f (cyclohexane-ethyl acetate 1:1) = 0.71; F_P: 168.6-168.9°C; ^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ 3.85 (s, 3H, H-17), 6.94-7.04 (m, 2H, H-15), 7.33 (d, ^3J = 8.3 Hz, 2H, H-14), 7.46 (t, ^3J = 7.4 Hz, 2H, H-2), 7.51-7.73 (m, 3H, H-1, H-10), 8.06-8.28 (m, 4H, H-3, H-11); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 55.7 (C-17), 115.6 (C-15), 119.2 (Ar-C), 121.6 (C-10), 123.1 (C-14), 125.0 (C-3), 125.2 (Ar-C), 127.2 (Ar-C), 128.5 (C-2), 129.1 (C-11), 129.4 (Ar-C), 132.3 (Ar-C), 143.5 (Ar-C); IR (cm^{-1}): 3456, 3369, 3016, 2970, 1738, 1625, 1607, 1592, 1561, 1538 1508, 1490, 1420, 1365, 1350, 1336, 1298, 1246, 1217,

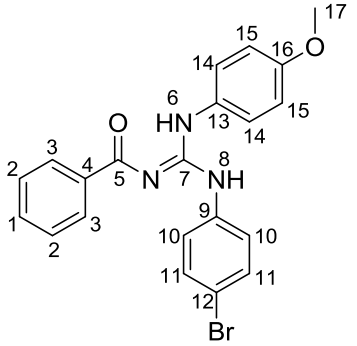
1199, 1112, 1028, 975, 856, 846, 748, 710, 685; HRMS (EI): calculated for $C_{21}H_{18}N_4O_4$ $[M]^+$: 390.1328, found: 390.1324.

(E)-N-(N-(4-fluorophenyl)-N'-(4-methoxyphenyl)carbamimidoyl)benzamide (5b)



5b is prepared according to the general EasyMax procedure. Purification is done by flash chromatography on silica gel (cyclohexane-ethyl acetate 100:0 > 9:1 > 7:3) to give the product (1.17 g, 3.22 mmol, 64%) as a white solid. R_f (cyclohexane-ethyl acetate 1:1) = 0.55; F_P: 137.7-137.9°C; ^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ 3.83 (s, 3H, H-17), 6.96 (d, ^3J = 8.5 Hz, 2H, H-15), 7.08 (t, ^3J = 8.4 Hz, 2H, H-11), 7.31 (d, ^3J = 8.5 Hz, 2H, H-14), 7.36-7.57 (m, 5H, H-1, H-2, H-10), 8.17 (d, ^3J = 7.4, 2H, H-3); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 55.6 (C-17), 115.1 (C-15), 115.8 (d, ^2J (C,F) = 22.8 Hz, C-11), 125.8 (C-10), 127.2 (C-14), 128.0 (C-2), 128.4 (C-13), 129.3 (C-3), 131.5 (C-1), 132.9 (C-9), 138.3 (C-4), 157.5 (C-7), 158.6 (C-16), 160.4 (d, ^1J (C,F) = 245.4 Hz, C-12), 178.3 (C-5); IR (cm^{-1}): 3368, 3072, 2970, 2839, 1737, 1611, 1581, 1566, 1537, 1505, 1445, 1416, 1352, 1292, 1246, 1211, 1198, 1171, 1105, 1030, 979, 908, 886, 829, 797, 746, 713, 685; HRMS (ESI): calculated for $C_{21}H_{19}FN_3O_2$ $[M+H]^+$: 364.1456, found: 364.1463.

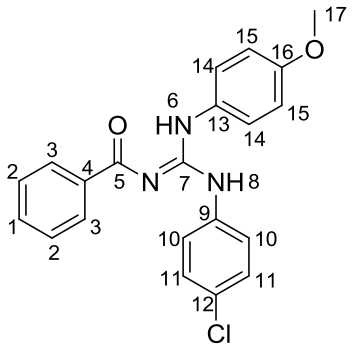
(E)-N-(N-(4-bromophenyl)-N'-(4-methoxyphenyl)carbamimidoyl)benzamide (5c)



5c is prepared according to the general EasyMax procedure. Purification is done by flash chromatography on silica gel (cyclohexane-ethyl acetate 100:0 > 9:1 > 7:3 > 3:2) to give the product (1.509 g, 3.56 mmol, 71%) as an off-white solid. R_f (cyclohexane-ethyl acetate 1:1) = 0.79; F_P: 136.1-136.2°C; ^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ 3.83 (s, 3H, H-17), 6.96 (d, ^3J = 8.5 Hz, 2H, H-15), 7.29 (d, ^3J = 8.3 Hz, 2H, H-14), 7.34-7.58 (m, 7H, H-1, H-2, H-10, H-11), 8.18 (d, ^3J = 7.6 Hz, 2H, H-3); ^{13}C-NMR (100 MHz, $CDCl_3$, ppm): δ 55.6 (C-17), 115.3 (C-15), 118.1 (C-9), 124.9 (C-10), 127.4 (C-14), 128.1 (C-2), 129.3 (C-3), 131.6 (C-1), 132.1 (C-11), 136.3 (C-4), 138.2 (C-12), 157.1 (C-7), 158.8 (C-16), 178.4 (C-5); IR (cm^{-1}):

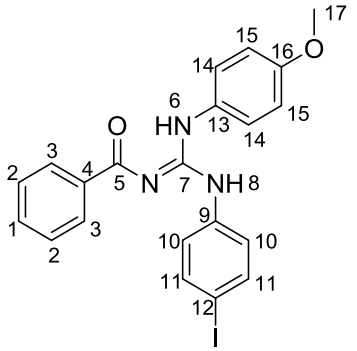
3455, 3347, 3016, 2970, 1738, 1603, 1578, 1558, 1536, 1509, 1489, 1430, 1406, 1352, 1285, 1239, 1216, 1207, 1075, 1032, 1009, 911, 878, 828, 755, 713, 686; HRMS (ESI): calculated for $C_{21}H_{19}BrN_3O_2$ $[M+H]^+$: 424.0655, found: 424.0657.

(E)-N-(N-(4-chlorophenyl)-N'-(4-methoxyphenyl)carbamimidoyl)benzamide (5d)



5d is prepared according to the general EasyMax procedure. Purification is done by flash chromatography on silica gel (cyclohexane-ethyl acetate 100:0 > 9:1 > 7:3 > 3:2) to give the product (1.11 g, 2.92 mmol, 59%) as a beige solid. R_f (cyclohexane-ethyl acetate 2:1) = 0.35; F_P: 128.0-128.1°C; ^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ 3.84 (s, 3H, H-17), 6.97 (d, ^3J = 8.6 Hz, 2H, H-15), 7.27-7.38 (m, 4H, H-11, H-14), 7.38-7.59 (m, 5H, H-1, H-2, H-10), 8.18 (d, ^3J = 7.5 Hz, 2H, H-3); ^{13}C-NMR (100 MHz, $CDCl_3$, ppm): δ 55.7 (C-17), 115.3 (C-15), 124.6 (C-10), 127.4 (C-14), 128.1 (C-2), 129.1 (C-11), 129.4 (C-3), 131.6 (C-1), 135.8 (C-4), 138.2 (C-12), 157.2 (C-7), 158.8 (C-16), 178.4 (C-5); IR (cm^{-1}): 3347, 2970, 1737, 1606, 1581, 1560, 1536, 1508, 1492, 1444, 1430, 1407, 1385, 1352, 1287, 1242, 1208, 1191, 1170, 1091, 1032, 912, 879, 830, 809, 752, 713; HRMS (ESI): calculated for $C_{21}H_{19}ClN_3O_2$ $[M+H]^+$: 380.1160, found: 380.1160.

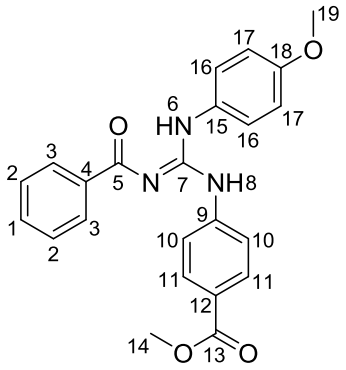
(E)-N-(N-(4-iodophenyl)-N'-(4-methoxyphenyl)carbamimidoyl)benzamide (5e)



5e is prepared according to the general EasyMax procedure. Purification is done by flash chromatography on silica gel (cyclohexane-ethyl acetate 100:0 > 9:1 > 7:3) to give the product (1.6 g, 3.39 mmol, 68%) as a white solid. R_f (cyclohexane-ethyl acetate 2:1) = 0.37; F_P: 143.8-144°C; ^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ 3.84 (s, 3H, H-17), 6.97 (d, ^3J = 8.7 Hz, 2H, H-15), 7.20-7.36 (m, 4H, H-10, H-14), 7.42 (t, ^3J = 7.4 Hz, 2H, H-2), 7.46-7.53 (m, 1H, H-1), 7.67 (d, ^3J = 8.6 Hz, 2H, H-11), 8.19 (d, ^3J = 7.3 Hz, 2H, H-3); ^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ 55.7 (C-17), 88.7 (C-12), 115.3 (C-15), 125.0 (C-10), 127.5 (C-14),

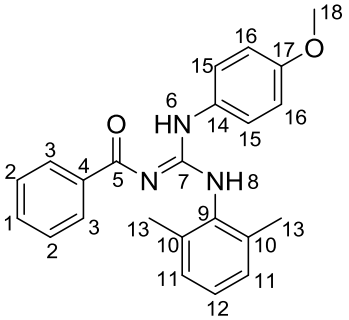
128.1 (C-2), 129.4 (C-3), 131.6 (C-1), 137.1 (C-9), 138.0 (C-11), 138.2 (C-4), 157.1 (C-7), 158.8 (C-16), 178.4 (C-5); IR (cm^{-1}): 3345, 2970, 1737, 1603, 1576, 1557, 1533, 1508, 1486, 1445, 1429, 1403, 1383, 1351, 1282, 1264, 1242, 1207, 1192, 1170, 1117, 1066, 1032, 1006, 912, 877, 836, 827, 810, 756, 713, 685; HRMS (ESI): calculated for $C_{21}H_{19}IN_3O_2$ $[M+H]^+$: 472.0516, found: 472.0522.

(E)-methyl 4-(3-benzoyl-2-(4-methoxyphenyl)guanidino)benzoate (5f)



5f is prepared according to the general EasyMax procedure. Purification is done by flash chromatography on silica gel (cyclohexane-ethyl acetate 100:0 > 9:1 > 1:1) to give the product (1.21 g, 2.99 mmol, 60%) as a white solid. R_f (cyclohexane-ethyl acetate 1:1) = 0.79; F_P: 135.7-136.0°C; ^{1}H-NMR (400 MHz, DMSO-d_6, ppm): δ 3.61-3.95 (m, 6H, H-14, H-19), 6.82- 7.06 (m, 2H, H-17), 7.30-7.60 (m, 5H, H-1, H-2, H-16), 7.61-8.14 (m, 6H, H-10, H-11, H-3), 9.46 (s, NH), 9.78 (s, NH), 10.12 (s, NH), 11.38 (s, NH); ^{13}C-NMR-DEPT135 (100 MHz, DMSO-d_6, ppm) δ 51.7 (C-14), 55.0 (C-15), 114.3 (C-17), 122.0 (C-10), 125.7 (C-16), 127.9 (C-2), 128.5 (C-3), 129.5 (C-11), 131.2 (C-1); IR (cm^{-1}): 3381, 3365, 3015, 2970, 2948, 1723, 1677, 1611, 1582, 1564, 1531, 1508, 1437, 1415, 1349, 1279, 1241, 1201, 1181, 1107, 1032, 977, 909, 883, 842, 824, 763, 743, 712, 701, 687; HRMS (ESI): calculated for $C_{23}H_{22}N_3O_4$ $[M+H]^+$: 404.1605, found: 404.1623.

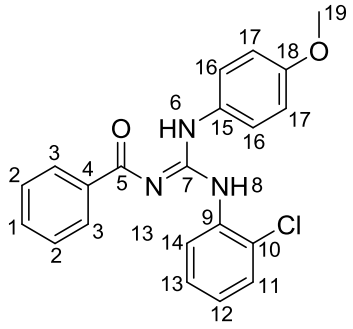
(E)-N-(N-(2,6-dimethylphenyl)-N'-(4-methoxyphenyl)carbamimidoyl)benzamide (5g)



5g is prepared according to the general EasyMax procedure. Purification is done by flash chromatography on silica gel (cyclohexane-ethyl acetate 100:0 > 9:1 > 8:2) to give the product (0.93 g, 2.49 mmol, 50%) as a white solid. R_f (cyclohexane-ethyl acetate 2:1) = 0.42; F_P: 181.5-181.6°C; ^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ 2.38 (s, 6H, H-13), 3.83 (s, 3H, H-18), 6.00 (s, 1H, NH), 6.90 (d, ^3J = 8.5 Hz, 2H, H-

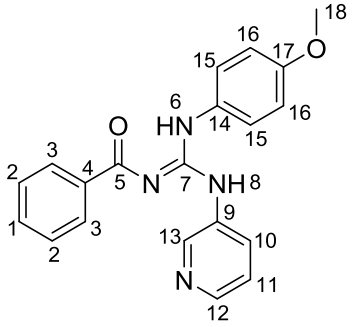
16), 7.10-7.23 (m, 3H, H-11, H-12), 7.29- 7.50 (m, 5H, H-1, H-2, H,15), 8.17-8.24 (m, 2H, H-3), 11.98 (s, 1H, NH); ^{13}C-NMR-APT (125 MHz, $CDCl_3$, ppm) δ 18.5 (C-13), 55.7 (C-18), 113.9 (C-16), 125.2 (C-15), 128.0 (C-2), 128.6 (C-12), 129.2 (C-11), 129.4 (C-3), 130.3 (C-14), 131.4 (C-1), 132.9 (C-9), 136.7 (C-10), 138.5 (C-4), 157.1 (C-17), 158.0 (C-7), 178.4 (C-5); IR (cm^{-1}): 3370, 3185, 3076, 3023, 2970, 1738, 1599, 1567, 1523, 1507, 1439, 1380, 1373, 1347, 1296, 1247, 1214, 1177, 1139, 1104, 1026, 906, 885, 776, 750, 720 683; HRMS (ESI): calculated for $C_{23}H_{24}N_3O_2$ $[M+H]^+$: 374.1863, found: 374.1883.

(E)-N-(N-(2-chlorophenyl)-N'-(4-methoxyphenyl)carbamimidoyl)benzamide (5h)



5h is prepared according to the general EasyMax procedure. Purification is done by flash chromatography on silica gel (cyclohexane-ethyl acetate 100:0 > 9:1 > 7:2) to give the product (1.44 g, 3.78 mmol, 76%) as an off-white solid. R_f (cyclohexane-ethyl acetate 1:1) = 0.54; F_P: 124.3-124.6°C; ^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ 3.85 (s, 3H, H-19), 7.00 (d, ^3J = 8.3 Hz, 2H, H-17), 7.08 (t, ^3J = 7.8 Hz, 1H, H-12), 7.31-7.61 (m, 7H, H-1, H-2, H-11, H-13, H.16), 8.22 (s, 2H, H-3), 8.44 (s, 1H, H-14); ^{13}C-NMR-DEPT135 (100 MHz, $CDCl_3$, ppm) δ 55.6 (C-19), 115.3 (C-17), 124.8 (C-14), 125.0 (C-12), 127.3 (C-11), 127.8 (C-16), 128.1 (C-2), 129.1 (C-13), 129.3 (C-3), 131.5 (C-1); IR (cm^{-1}): 3367, 3002, 2970, 1738, 1619, 1598, 1578, 1561, 1535, 1508, 1443, 1378, 1355, 1298, 1243, 1201, 1169, 1106, 1057, 1029, 982, 910, 879, 838, 731, 742, 706; HRMS (ESI): calculated for $C_{21}H_{19}ClN_3O_2$ $[M+H]^+$: 360.1160, found: 360.1159.

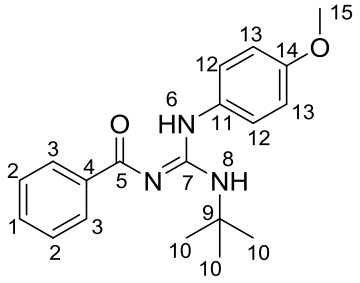
(E)-N-(N'-(4-methoxyphenyl)-N-(pyridin-3-yl)carbamimidoyl)benzamide (7)



7 is prepared according to the general EasyMax procedure. Purification is done by flash chromatography on silica gel (cyclohexane-ethyl acetate 4:1 > 2:3 > 1:4) to give the product (0.87 g, 2.5 mmol, 50%) as a white solid. R_f (cyclohexane-ethyl acetate 1:3) = 0.26; F_P: 153.2°C; ^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ 3.84 (s, 3H, H-18), 6.99 (d, ^3J = 8.4 Hz, 2H, H-16), 7.22-7.37 (m, 3H, H-11, H-15), 7.37-7.57 (m, 3H, H-1, H-2),

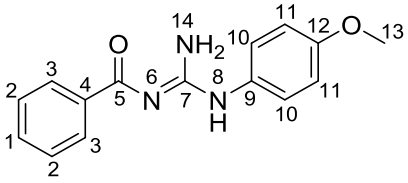
8.01 (d, ^3J = 8.8 Hz, 1H, H-10), 8.10-8.24 (m, 2H, H-3), 8.39 (d, ^3J = 4.3 Hz, 2H, H-12), 8.61 (s, 1H, H-13); ^{13}C-NMR (100 MHz, $CDCl_3$, ppm): δ 55.7 (C-18), 115.5 (C-16), 123.5 (C-11), 127.8 (C-15), 128.2 (C-2), 129.3 (C-3), 130.5 (C-10), 131.8 (C-1), 134.3 (C-9), 138.0 (C-4), 144.2 (C-13), 145.9 (C-12), 157.4 (C-7), 159.2 (C-17), 178.6 (C-5); IR (cm^{-1}): 2970, 1738, 1618, 1600, 1561, 1538, 1513, 1475, 1441, 1397, 1346, 1265, 1243, 1216, 1186, 1031, 981, 914, 839, 807, 750, 716, 688; HRMS (ESI): calculated for $C_{20}H_{19}N_4O_2$ $[M+H]^+$: 347.1503, found: 347.1503.

(E)-N-(N-(tert-butyl)-N'-(4-methoxyphenyl)carbamimidoyl)benzamide (10a)



10a is prepared according to the general EasyMax procedure. Purification is done by flash chromatography on silica gel (cyclohexane-ethyl acetate 100:0 > 9:1 > 7:3) to give the product (1.16 g, 3.56 mmol, 71%) as a white solid. R_f (cyclohexane-ethyl acetate 2:1) = 0.42; F_P: 119.1-119.2°C; ^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ 1.49 (s, 9H, H-10), 3.82 (s, 3H, H-15), 4.68 (s, 1H, H-8), 6.89-6.98 (m, 2H, H-13), 7.12-7.21 (m, 2H, H-12), 7.37-7.51 (m, 3H, H-1, H-2), 8.22-8.30 (m, 2H, H-3); ^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ 29.8 (C-10), 52.4 (C-9), 55.6 (C-15), 115.3 (C-13), 127.5 (C-12), 127.9 (C-2), 128.9 (C-11), 129.1 (C-3), 131.0 (C-1), 139.1 (C-4), 158.5 (C-14), 158.9 (C-7), 177.1 (C-5); IR (cm^{-1}): 3412, 289, 2970, 1738, 1595, 1570, 1511, 1448, 1358, 1294, 1247, 1227, 1216, 1107, 1026, 916, 894, 853, 821, 758, 749, 710, 692; HRMS (EI): calculated for $C_{19}H_{23}N_3O_2$ $[M]^+$: 325.1790, found: 325.1797.

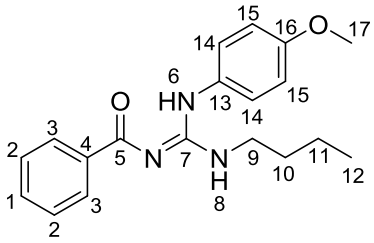
N-(N-(4-methoxyphenyl)carbamimidoyl)benzamide (10b)



10b is prepared according to the general EasyMax procedure, using hexamethyldisilazane (8.07 g, 10.6 ml, 50 mmol, 10 eq) as NH_3-surrogate. Purification is done by flash chromatography on silica gel (cyclohexane-ethyl acetate 8:2 > 1:1) to give the product (0.55 g, 2.03 mmol, 41%) as a white solid. R_f (cyclohexane-ethyl acetate 1:1) = 0.18; F_P: 136.3-136.9 °C (Lit.: 136-137°C)[3]; ^{1}H-NMR (500 MHz, DMSO-d_6, ppm): δ 3.76 (s, 3H, H-13), 6.90-7.01 (m, 2H, H-11), 7.35-7.44 (m, 4H, H-2, H-10), 7.44-7.49 (m, 1H, H-1), 8.05-8.12 (m, 2H, H-3), 9.29 (s, 2H, H-14); ^{13}C-NMR (125 MHz, DMSO-d_6, ppm): δ 55.3 (C-13), 114.2 (C-11), 124.5 (C-10), 127.8 (C-2), 128.6 (C-3), 130.6 (C-9), 130.8 (C-1), 138.8 (C-4), 156.2 (C-12), 159.8 (C-7), 176.0 (C-5); IR (cm^{-1}): 3465, 3070, 3000, 2970, 1738, 1639, 1596, 1558, 1512, 1442, 1354, 1298, 1250,

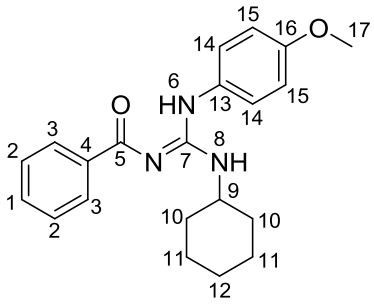
1205, 1181, 1106, 1087, 1028, 910, 862, 826, 815, 756, 716, 685; HRMS (ESI): calculated for $C_{15}H_{16}N_3O_2$ $[M+H]^+$: 270.1237, found: 270.1234.

(E)-N-(N-butyl-N'-(4-methoxyphenyl)carbamimidoyl)benzamide (10c)



10c is prepared according to the general EasyMax procedure. Purification is done by flash chromatography on silica gel (cyclohexane-ethyl acetate 100:0 > 4:1 > 7:3) to give the product (0.55 g, 2.03 mmol, 41%) as a white solid. R_f (cyclohexane-ethyl acetate 1:3) = 0.69; F_P: 107.9-108.3°C; ^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ 0.94 (t, ^3J = 7.3 Hz, 3H, H-12), 1.36 (h, ^3J = 7.3 Hz, 2H, H-11), 1.56 (p, ^3J = 7.2 Hz, 2H, H-10), 3.52 (q, ^3J = 6.6 Hz, 2H, H-9), 3.81 (s, 3H, H-17), 4.76 (s, 1H, H-8), 6.89-6.98 (m, 2H, H-15), 7.18 (d, ^3J = 8.3, 2H, H-14), 7.36-7.50 (m, 3H, H-1, H-2), 8.27 (d, ^3J = 7.0 Hz, 2H, H-9), 11.83 (s, 1H, H-6); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 13.9 (C-12), 20.1 (C-11), 32.0 (C-10), 41.2 (C-9), 55.6 (C-17), 115.3 (C-15), 127.7 (C-14), 127.9 (C-2), 128.5 (C-13), 129.2 (C-3), 131.1 (C-1), 138.9 (C-4), 158.6 (C-16), 159.5 (C-7), 177.5 (C-5); IR (cm^{-1}): 3373, 3175, 2958, 1737, 1601, 1568, 1446, 1355, 1300, 1245, 1204, 1178, 1145, 1027, 893, 856, 816, 751, 712, 686; HRMS (ESI): calculated for $C_{19}H_{24}N_3O_2$ $[M+H]^+$: 326.1863, found: 326.1861.

(E)-N-(N'-cyclohexyl-N-(4-methoxyphenyl)carbamimidoyl)benzamide (10d)



10d is prepared according to the general EasyMax procedure. Purification is done by flash chromatography on silica gel (cyclohexane-ethyl acetate 100:0 > 4:1 > 7:3) to give the product (0.55 g, 2.03 mmol, 41%) as a white solid. R_f (cyclohexane-ethyl acetate 1:3) = 0.75; F_P: 131.5-131.9 (Lit.: 129-131°C)[4] ^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ 1.07-1.25 (m, 3H, H-11, H-12), 1.44 (dtd, ^2J = 16.7 Hz, ^3J = 11.8 Hz, ^3J = 5.9 Hz, 2H, H-11), 1.56-1.76 (m, 3H, H-10, H-12), 1.98-2.09 (m, 2H, H-10), 3.81 (m, 3H, H-17), 4.13 (s, 1H, H-9), 4.65 (s, 1H, H-8), 6.89-6.98 (m, 2H, H-15), 7.18 (d, ^3J = 8.3 Hz, 2H, H-14), 7.34-7.51 (m, 3H, H-1, H-2), 8.22-8.29 (m, 2H, H-3), 11.86 (s, 1H, H-6); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 24.9 (C-11), 25.6 (C-12), 33.3 (C-10), 50.1 (C-9), 55.6 (C-17), 115.2 (C-15), 127.5 (C-14), 127.9 (C-2), 128.6 (C-13), 129.1 (C-3), 131.0 (C-1), 138.9 (C-4), 158.5 (C-16), 158.6 (C-7), 177.5 (C-5); IR (cm^{-1}): 3367, 2933, 2845, 1738, 1597,

1567, 1512, 1444, 1405, 1358, 1346, 1246, 1204, 1180, 1136, 1066, 1028, 909, 892, 860, 824, 748, 713, 687; HRMS (ESI): calculated for $C_{21}H_{26}N_3O_2$ $[M+H]^+$: 352.2020, found: 352.2023.

2.2 Calorimetric Measurements

2.2.1 Heat of reaction

In a 50 ml EasyMax®-Reactor, equipped with reflux cooler with drying tube, magnetic stirrer bar, temperature sensor and a calibration heater, thiourea (5 mmol, 1.432 g) **1** is mixed with 30 ml Acetonitrile while stirring (300 prm). Triethylamine (20 mmol, 2.024 g, 2.77 ml, 4 Eq) is added and the mixture is cooled down to 0°C (Reator temperature (T_R)) in 10 min. When the temperature remains constant, two to three calibration steps are done. Therefore the calibration heater is switched on for 15 min at 100% power. After the temperature (T_R) remains constantly at 0°C again, the surface integral of reactor temperature (T_R) minus jacket temperature (T_J) is determined and the calibration steps is repeated. If the deviation of surface integrals of the calibration steps is less than 4 %, the reaction step follows. The metal salt (5 mmol, 1 Eq) is added at 0°C into the reaction vessel. The heat flow is recorded and the surface integral can be determined after the temperature has reached a constant level again. The three following calibration steps are done in the same manner as described before.

2.2.2 Heat of solution

The determination of the solvation heat is done according to the procedure described in 2.2.1 merely with 30 ml acetonitrile and the metal salt (5 mmol), added at 0°C (T_R).

2.2.3 Calculations

Calculations of the amount of heat released by the reaction Q_r with the EasyMax®-System are based on the measureable amounts of heat Q_f (amount of heat between reactor and reactor jacket) and Q_C (amount of heat released by Calibration heater). Accordingly, Q_f is proportional to surface integral of the temperature difference between reaction vessel and reactor jacket T_R-T_J multiplied by proportionality factor *UA* with *U* being the heat exchange coefficient and heat exchange area *A*.

$$Q_f = UA \cdot \int (T_R - T_J)_r \, dt = Q_r \quad (1)$$

Proportionality factor *UA* is determined by the calibration steps done before and after the reaction. The defined amount of heat Q_C, released by the calibration heater is calculated by its electric voltage *U*, its resistance *R* and the time *t* that it is switched on.

$$Q_c = \frac{U^2}{R} \cdot t \quad (2)$$

During the calibration step no other reaction occurs in the reaction vessel, thus the amount of heat is completely dissipated by the reactor jacket. Proportionality factor *UA* is then calculated by:

$$UA = \frac{Q_c}{\int (T_R - T_J)_c \, dt} \quad (3)$$

With the heat capacity C_p assumed to be constant throughout the complete experiment, the heat of reaction Q_r approximately matches Q_f as defined in equation (1). Correlation of Q_r with moles of the metal salt being used leads to enthalpy ΔH_r (4).

$$\Delta H_r = -\frac{Q_r}{n_{MetX_n}} \quad (4)$$

2.2.4 Results

The surface integrals of calorimetric measurements are summarized in Table 1 with C being the calibration steps and R being the reaction step.

Table 1 Surface integrals of calibration and reaction steps

Integral	$FeCl_3$ R	$FeCl_3$ Sol	$InCl_3$ R	$InCl_3$ Sol	$ZnCl_2$ R	$ZnCl_2$ Sol	$Bi(NO_3)_3$ R	$Bi(NO_3)_3$ Sol
C 1 [K*s]	4773,9	5762,0	5944,5	5844,6	5718,7	5722,7	5701,9	5832,9
C 2 [K*s]	4784,9	5728,0	5930,3,	5833,7	5707,8	5726,4	5774,4	5818,3
C 3 [K*s]	4844,2	5861,8	6086,6	6013,0	5683,2	5782,4	5991,5	5887,3
C 4 [K*s]	4865,3	5864,8	6033,0	6032,1	5741,0	5835,4	5919,3	5835,8
C 5 [K*s]	4819,0	5868,0	6069,8	6030,9	5709,0	5766,5	5876,7	5854,8
R [K*s]	3317,2	545,1	1308,7	476,7	563,17	319,6	850,7	-436,1

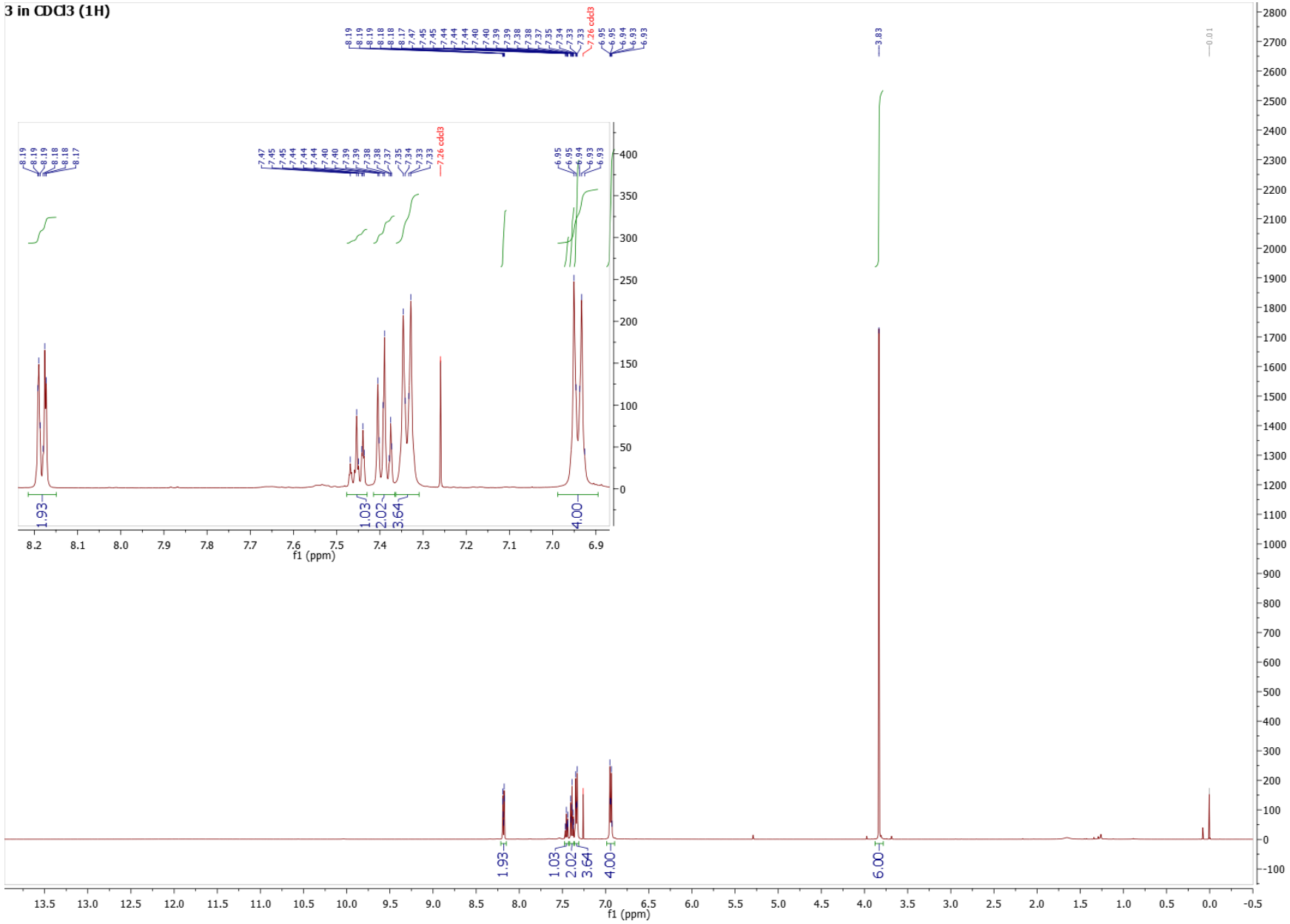
Accordingly, table 2 shows the calculated, molar heat of solution and heat of reaction for each thiophile. The values are referred to 5 mmol metal salt. Heat of reaction had to be done in 60 ml acetonitrile, due to the high viscosity observed at 0°C (T_R) in 30 ml acetonitrile and the resulting heat accumulation in the reaction mixture. On account of the twofold amount of solvent, the measured value for iron(III)chloride was then multiplied by factor 2.

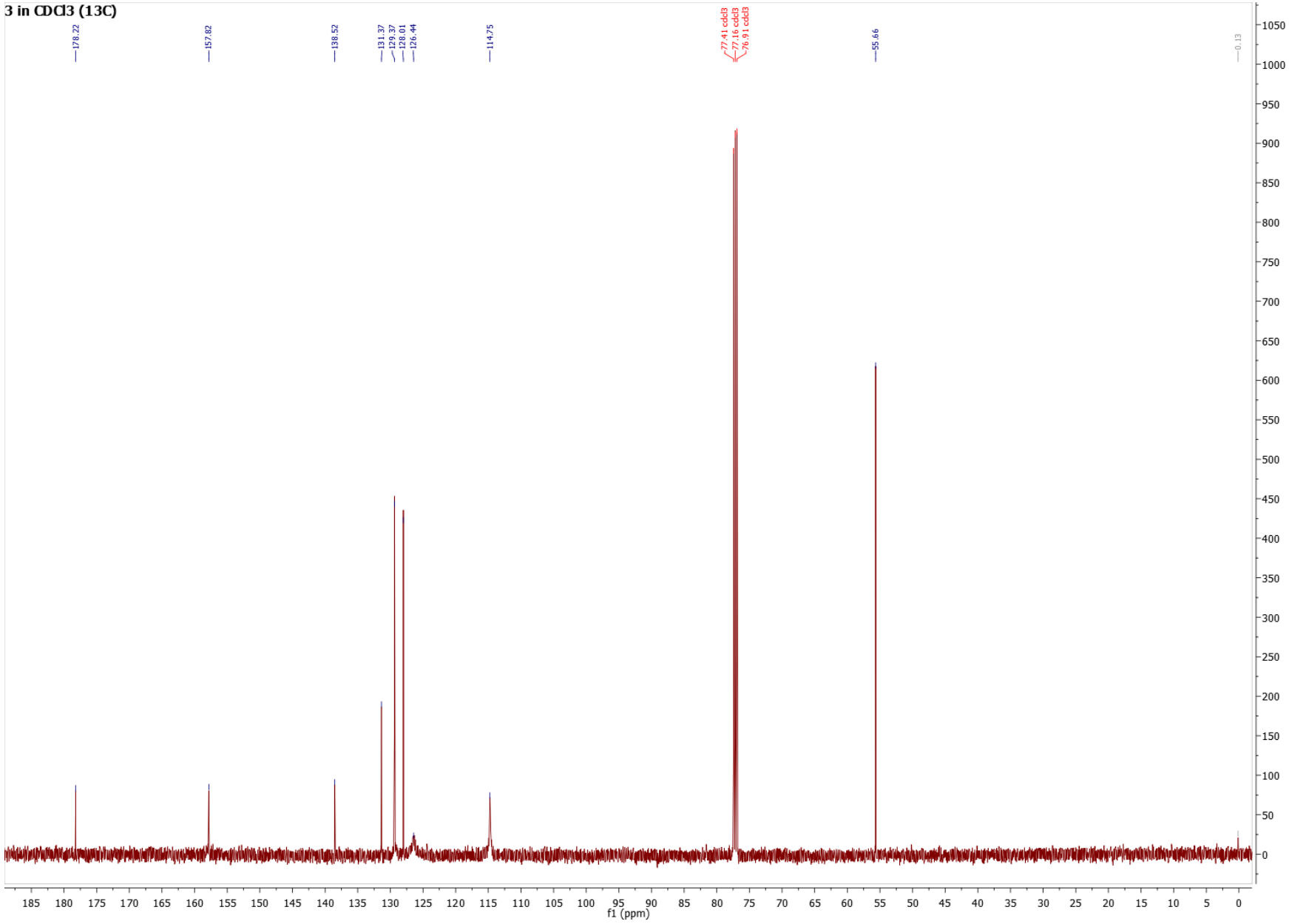
Table 2 Enthalpies of different thiophiles

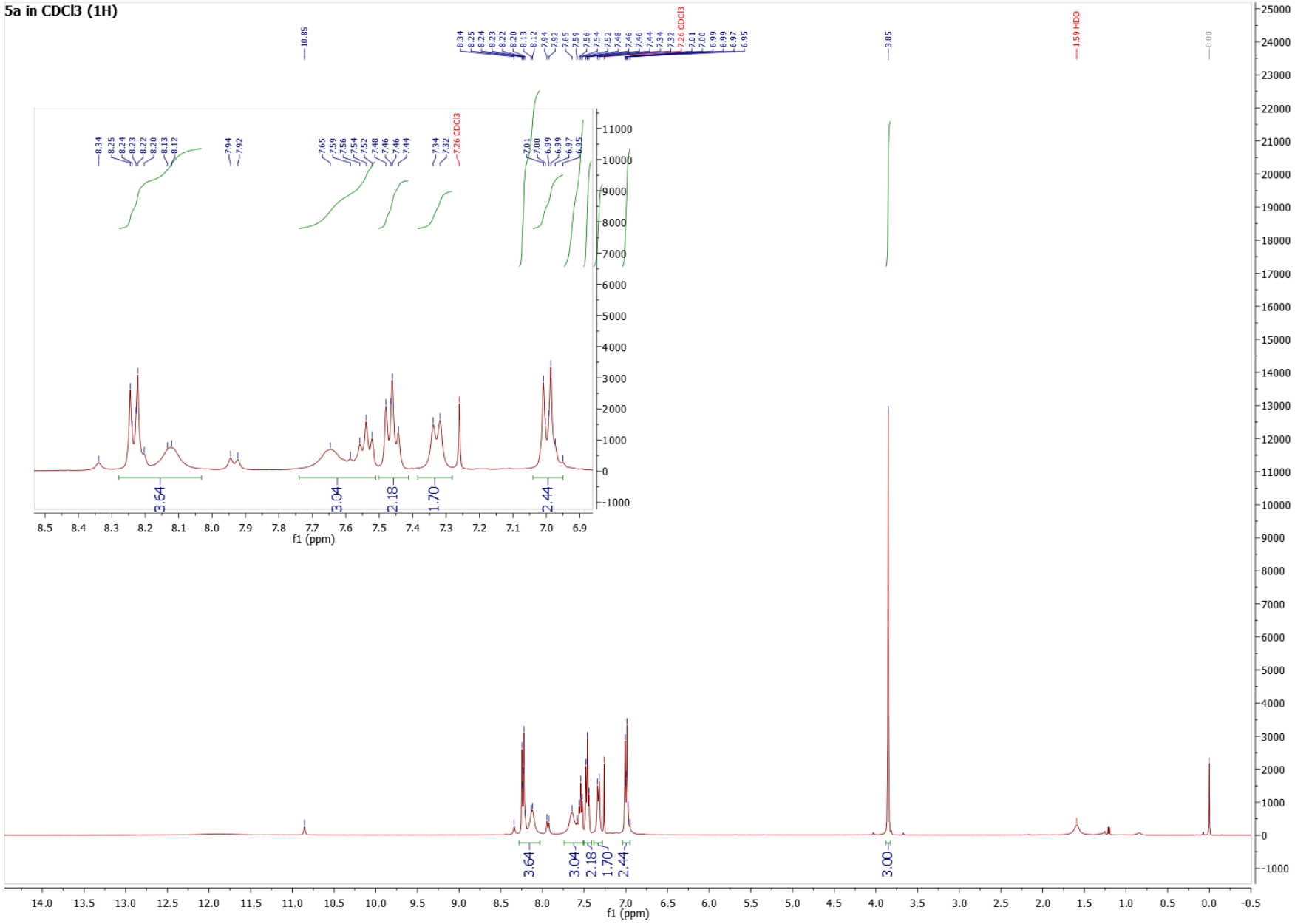
Thiophile	Heat of solution [kJ/mol]	Heat of reaction [kJ/mol]
$Bi(NO_3)_3$	51.6	-100.5
$FeCl_3$	-65.6	-475.9
$InCl_3$	-55.4	-149.9
$ZnCl_2$	-38.3	-68.1

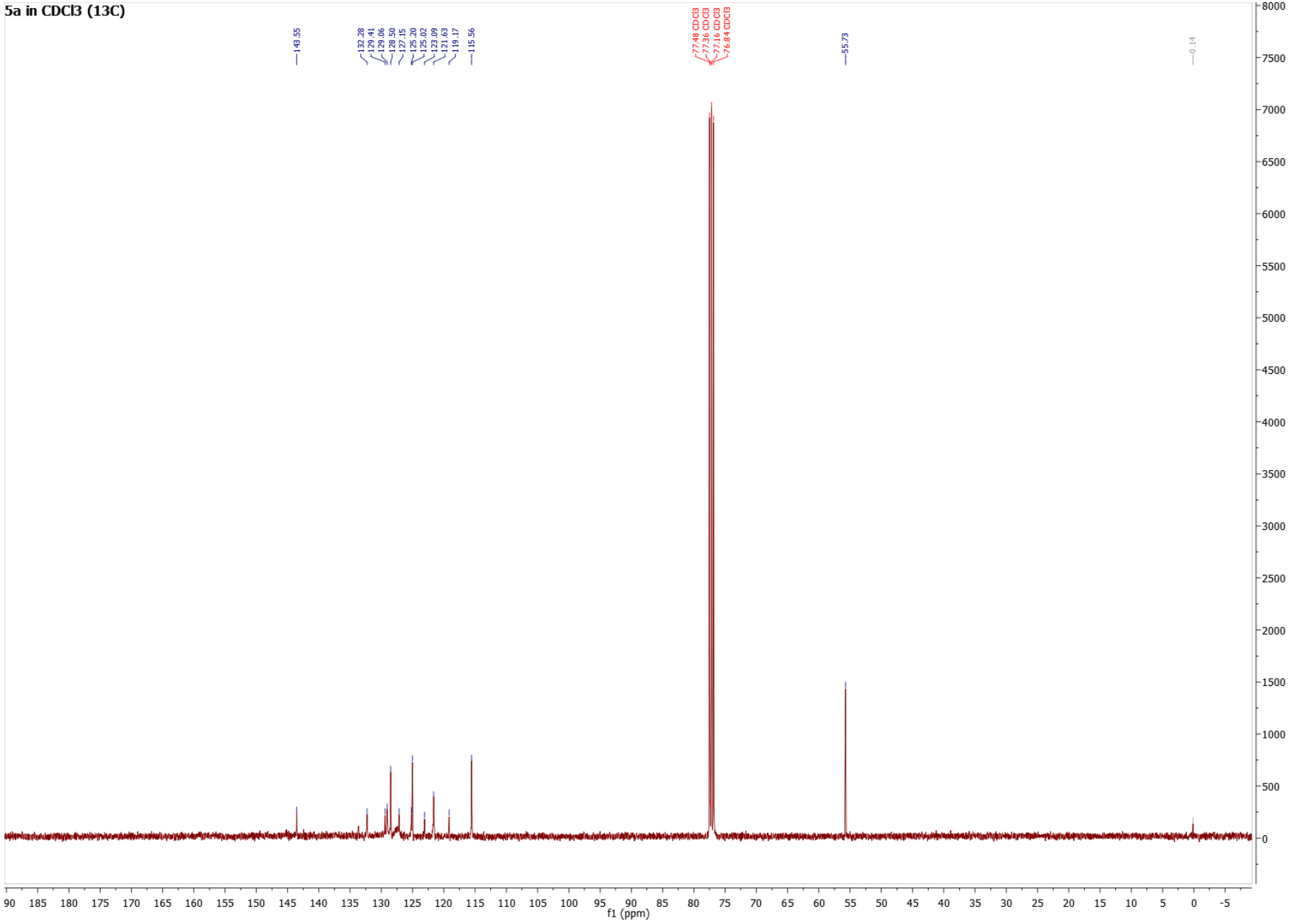
3 Spectra

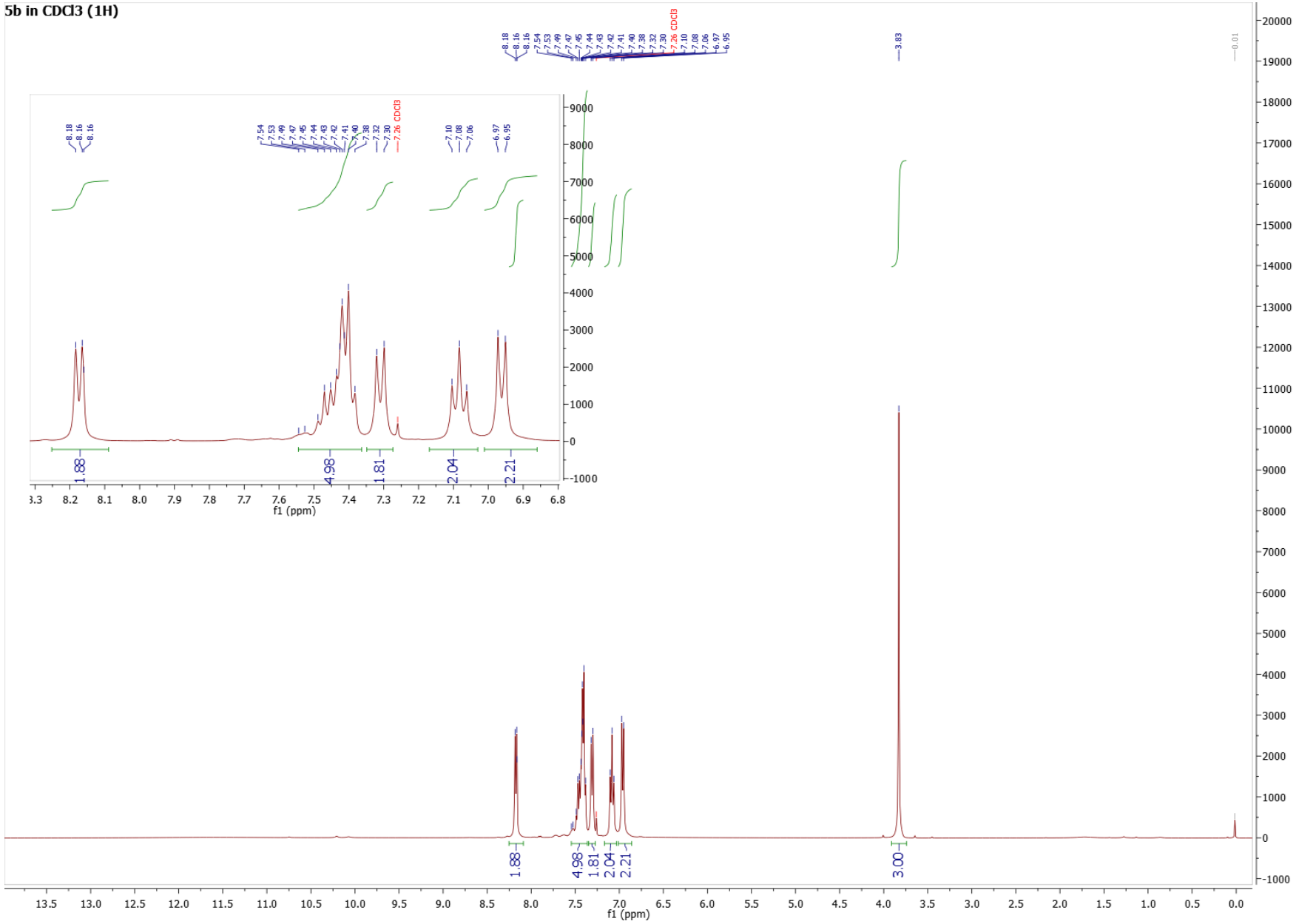
3.1 Guanidines

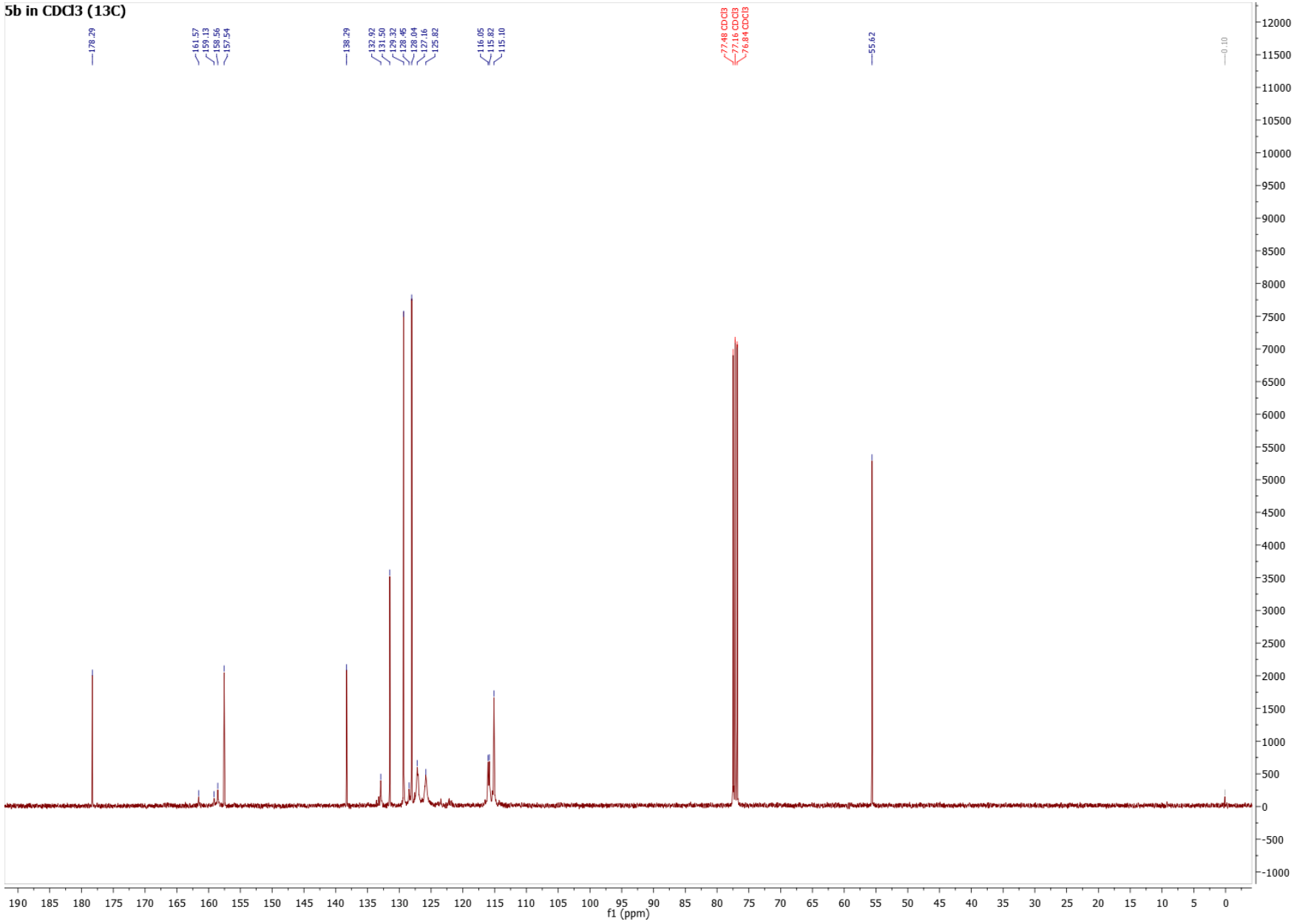

3 in CDCl3 (1H)
7.26 cdcl3
3.83
1.93
1.03
2.02
3.64
4.00
6.00
f1 (ppm)

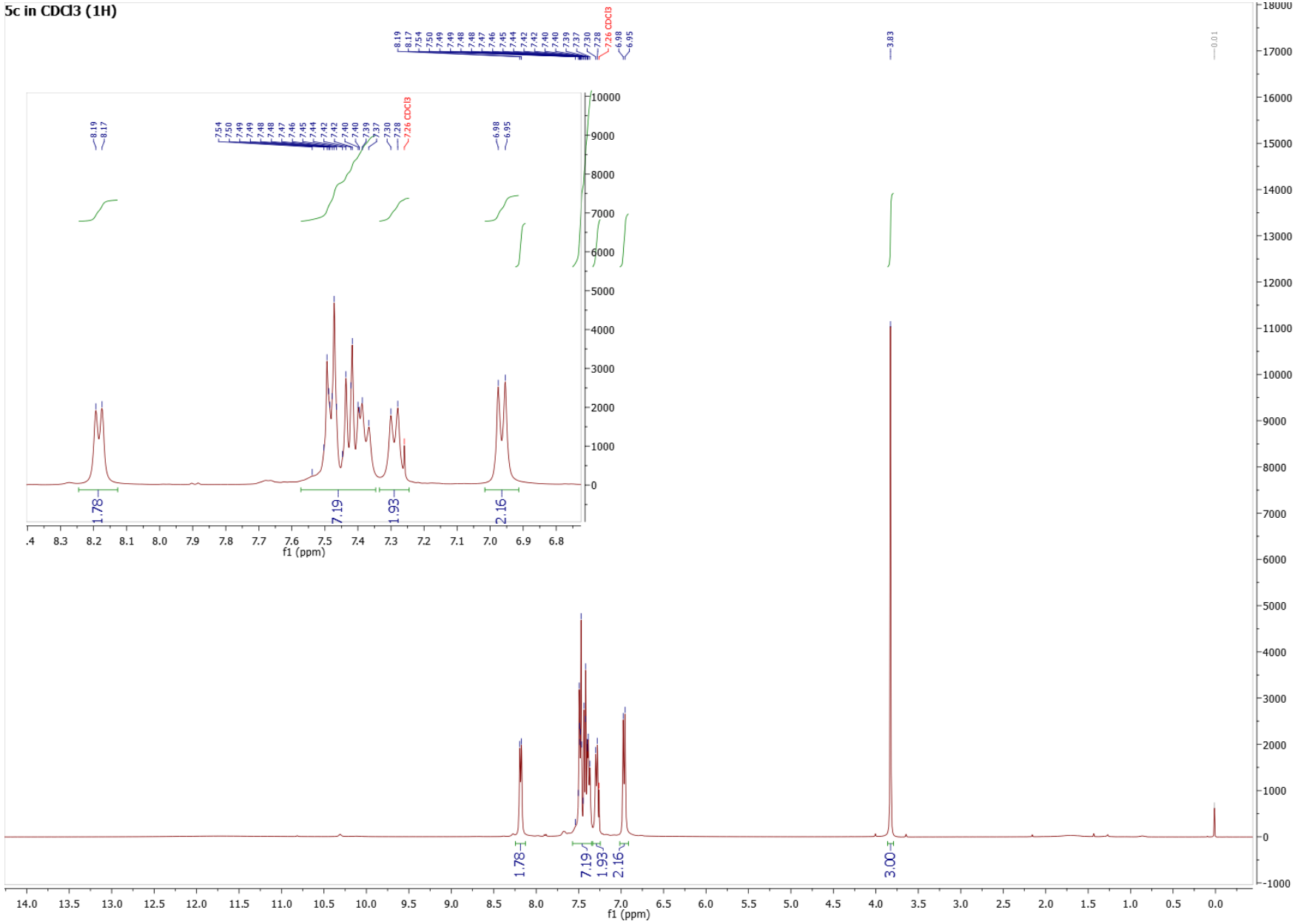

3 in CDCl3 (13C)
178.22
157.82
138.52
131.37
129.37
128.01
126.44
114.75
77.41 cdcl3
77.16 cdcl3
76.91 cdcl3
55.66
f1 (ppm)

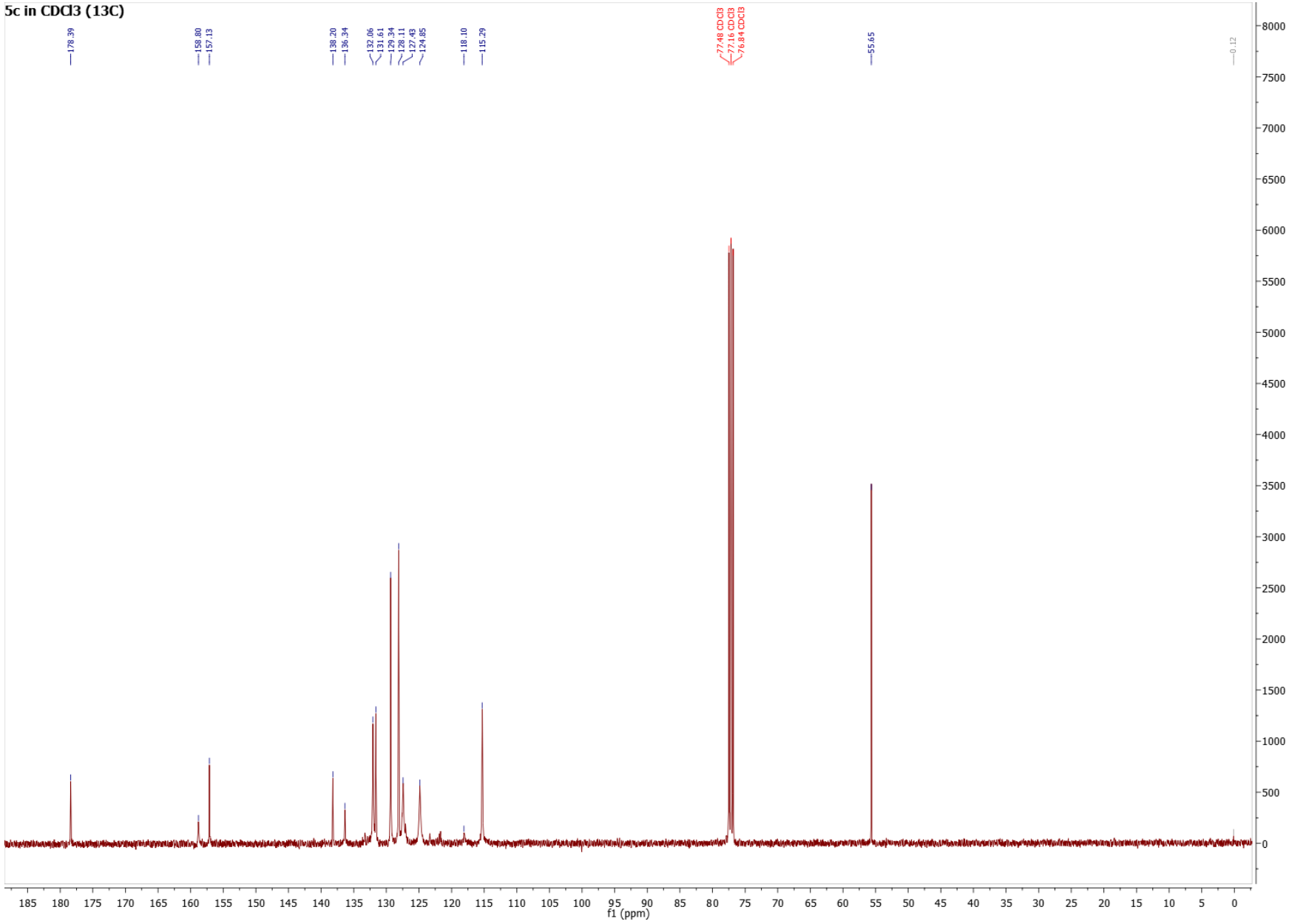

5a in CDCl3 (1H)
10.85
8.34
8.25
8.24
8.23
8.22
8.20
8.13
8.12
7.94
7.92
7.65
7.59
7.56
7.54
7.52
7.48
7.46
7.44
7.34
7.32
7.26 CDCl3
7.01
7.00
6.99
6.99
6.97
6.95
3.85
1.59 HDO
0.00
3.64
3.04
2.18
1.70
2.44
3.00
f1 (ppm)

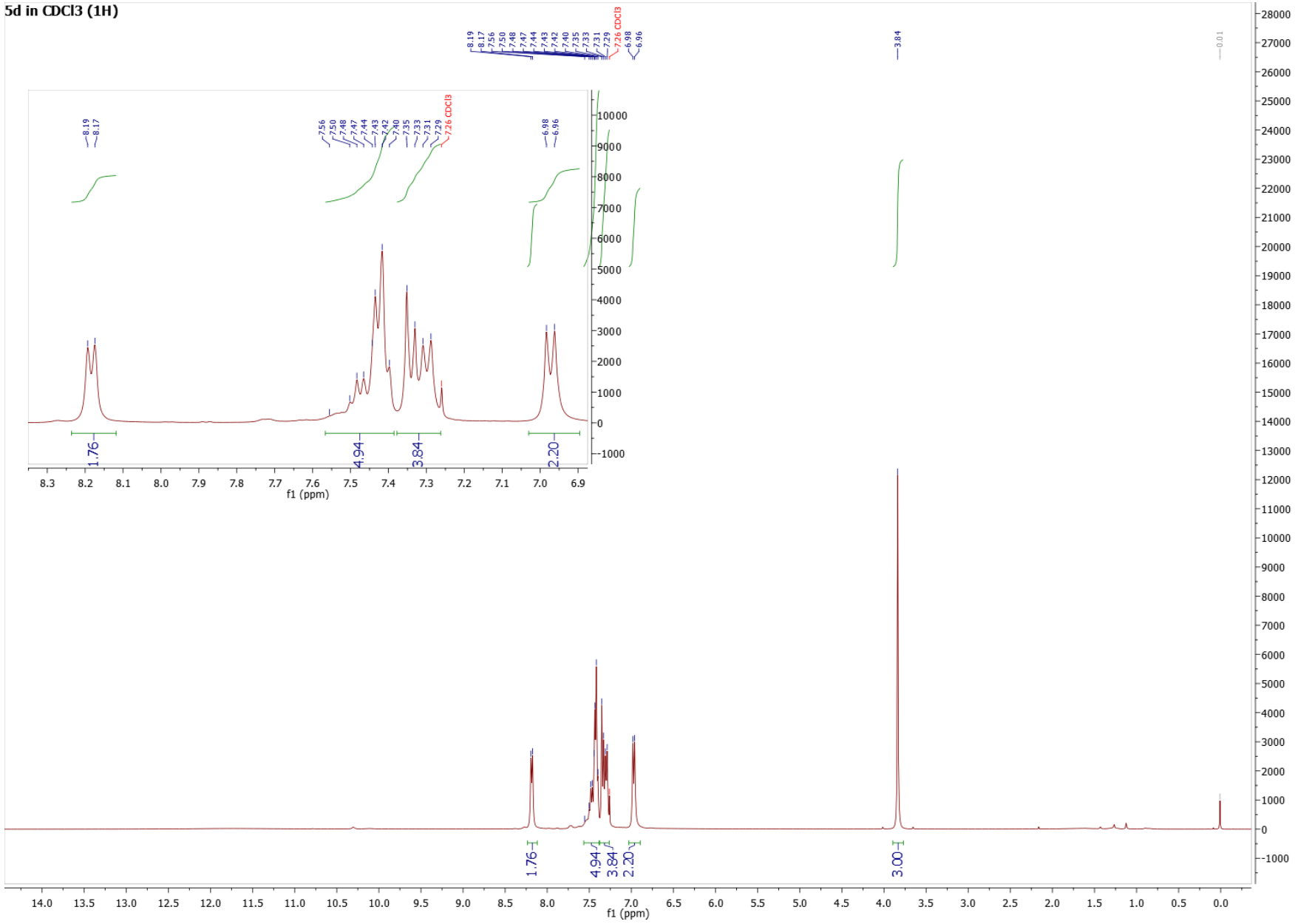

5a in CDCl3 (13C)
143.55
132.28
129.41
129.06
128.50
127.15
125.20
125.02
123.09
121.63
119.17
115.56
77.48 CDCl3
77.36 CDCl3
77.16 CDCl3
76.84 CDCl3
55.73
0.14
f1 (ppm)

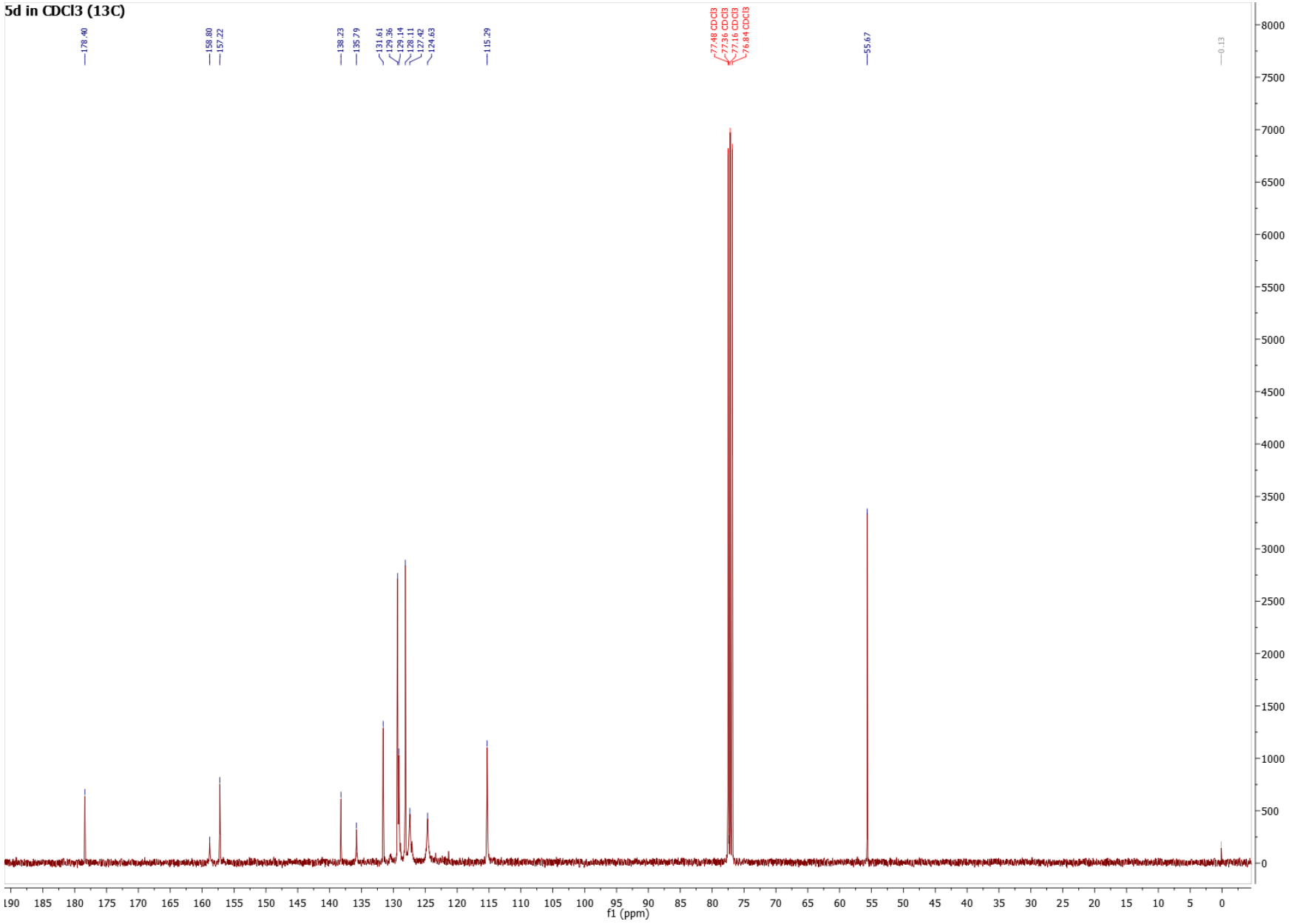

5b in CDCl3 (1H)
f1 (ppm)
1.88
4.98
1.81
2.04
2.21
3.00

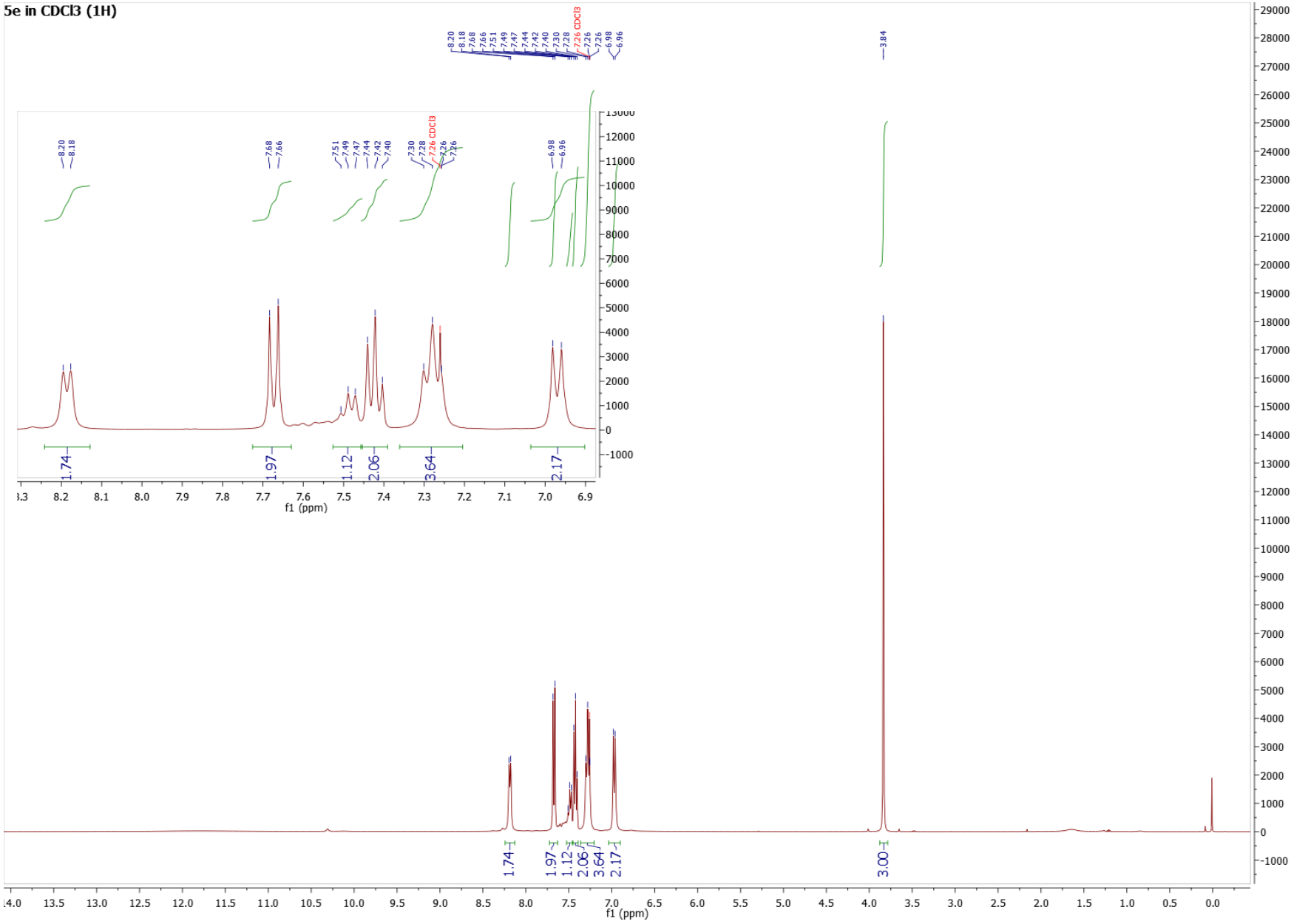

5b in CDCl3 (13C)
178.29
161.57
159.13
158.56
157.54
138.29
132.92
131.50
129.32
128.45
128.04
127.16
125.82
116.05
115.82
115.10
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
55.62
-0.10
f1 (ppm)


5c in CDCl3 (1H)
8.19
8.17
7.54
7.50
7.49
7.49
7.48
7.48
7.47
7.46
7.45
7.44
7.42
7.42
7.40
7.40
7.39
7.37
7.30
7.28
7.26 CDCl3
6.98
6.95
3.83
1.78
7.19
1.93
2.16
3.00
f1 (ppm)

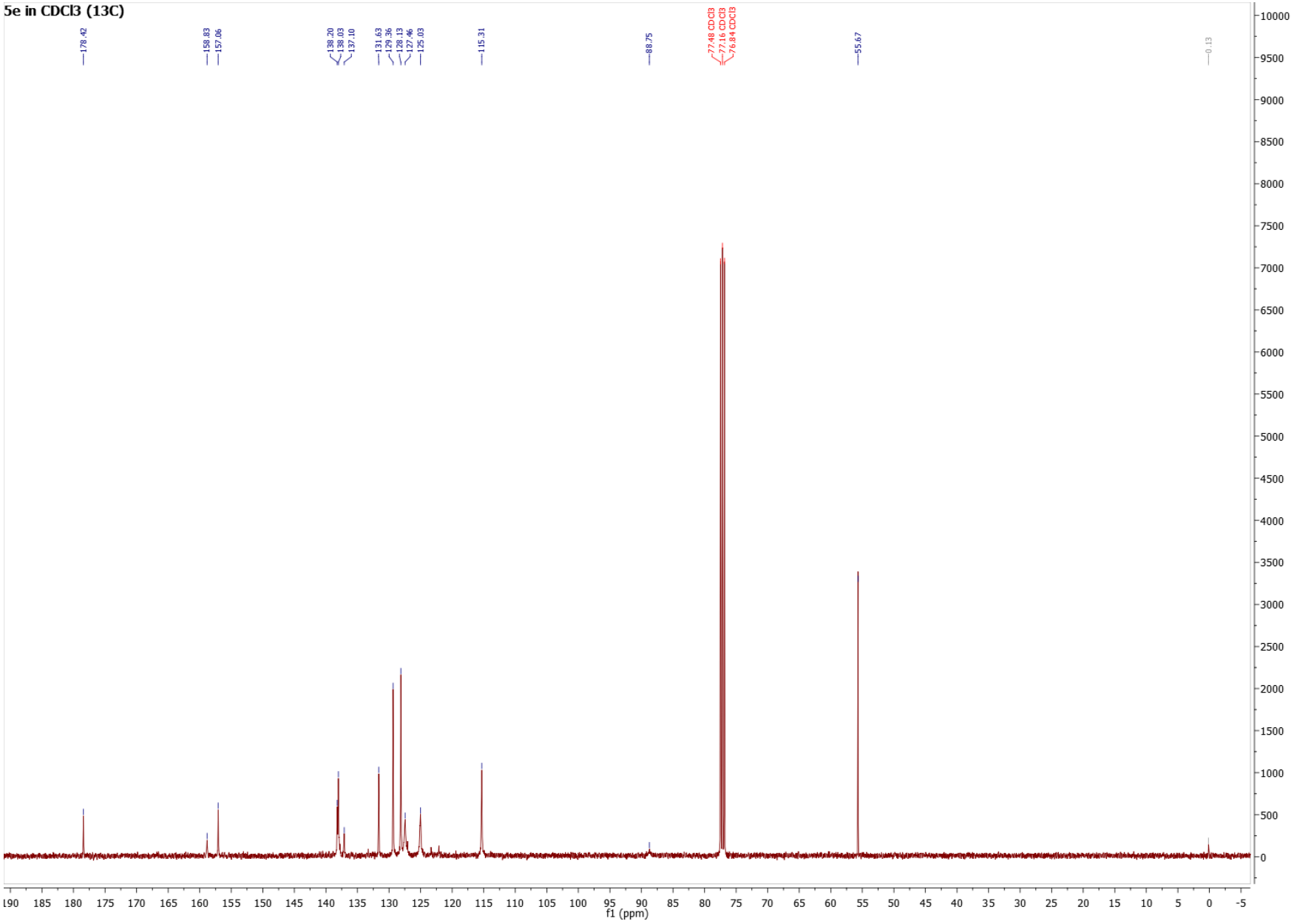

5c in CDCl3 (13C)
178.39
158.80
157.13
138.20
136.34
132.06
131.61
129.34
128.11
127.43
124.85
118.10
115.29
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
55.65
0.12
f1 (ppm)

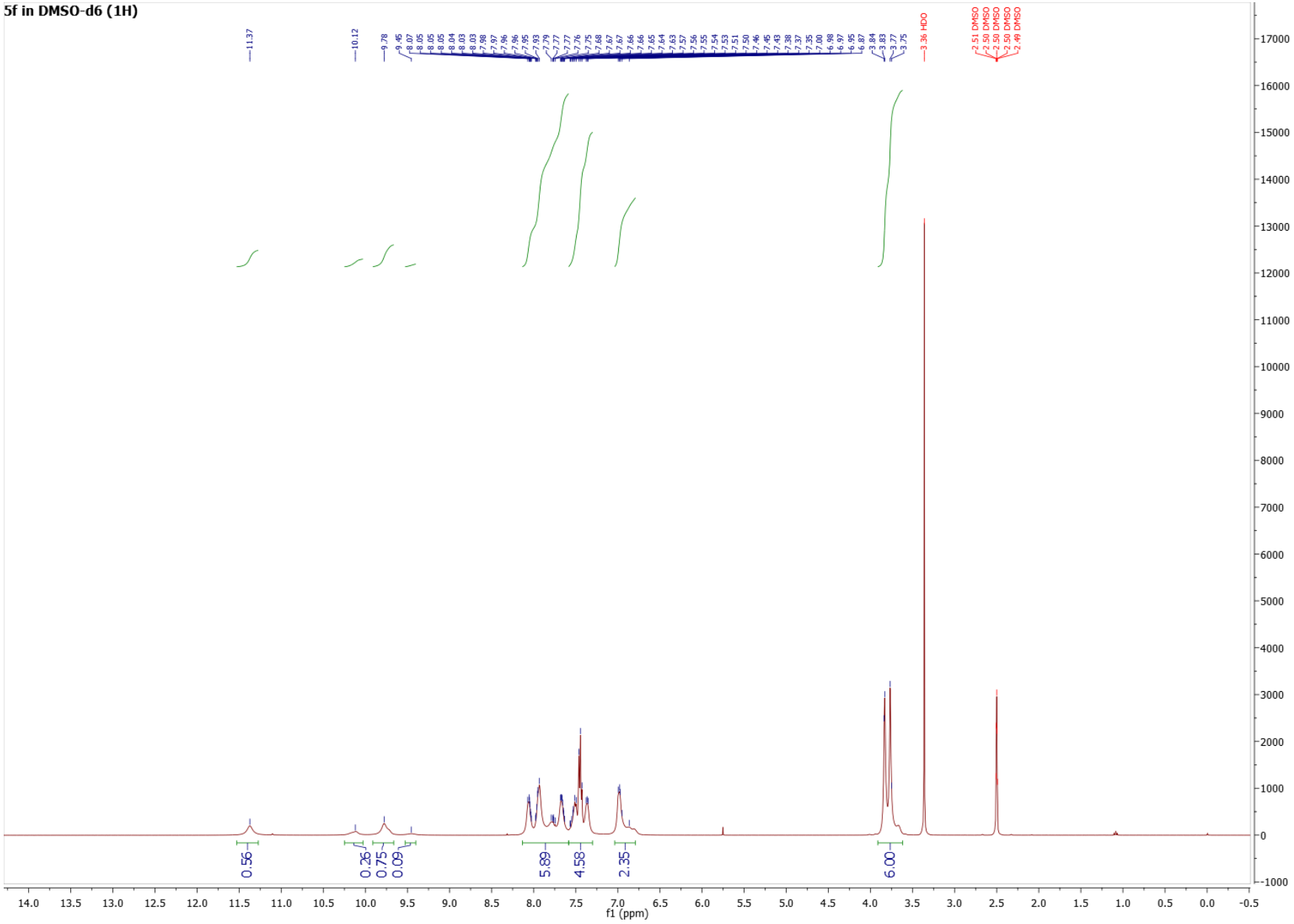

5d in CDCl3 (1H)
8.19
8.17
7.56
7.50
7.48
7.47
7.44
7.43
7.42
7.40
7.35
7.33
7.31
7.29
7.26 CDCl3
6.98
6.96
3.84
1.76
4.94
3.84
2.20
3.00
f1 (ppm)

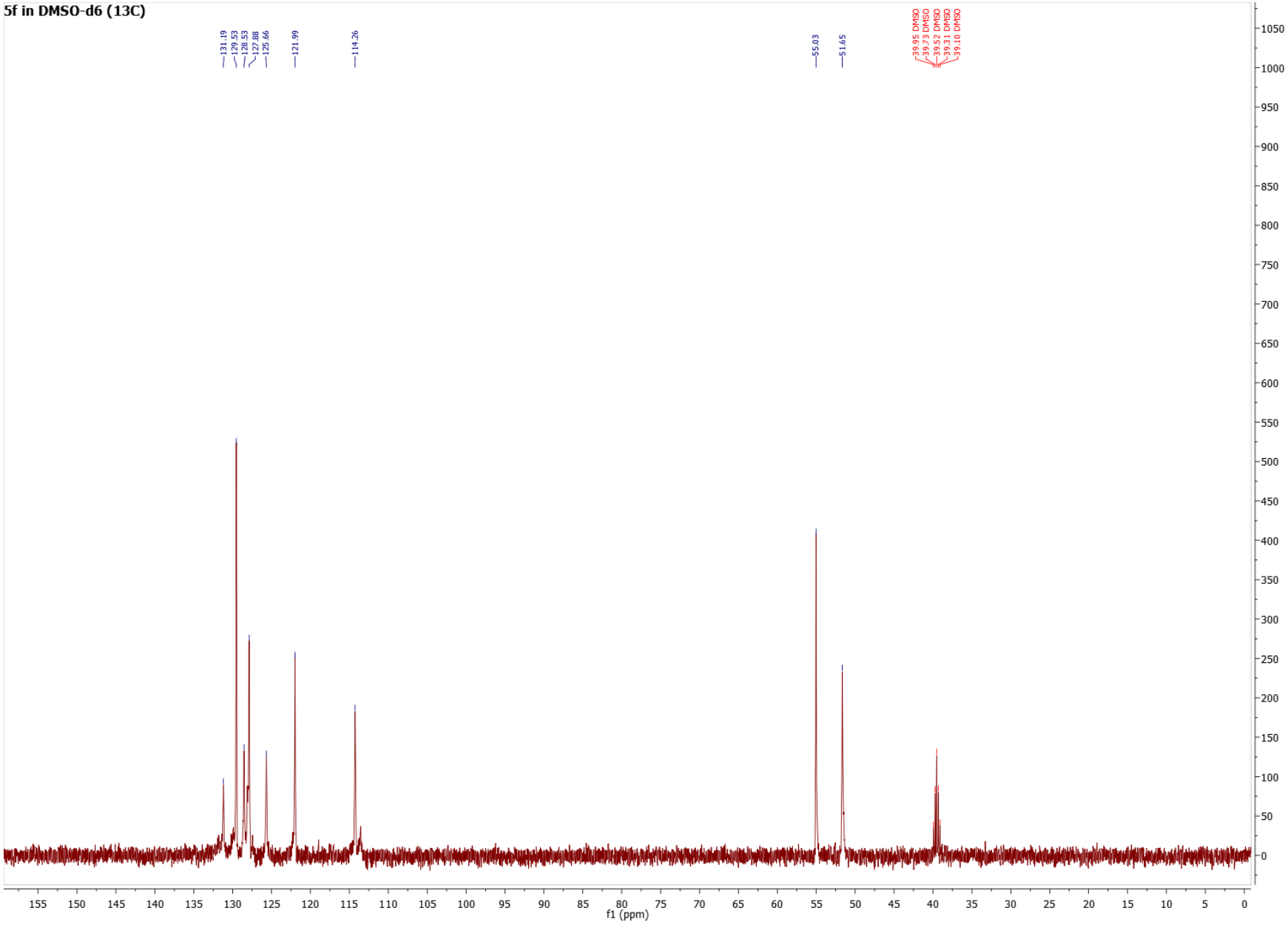

5d in CDCl3 (13C)
178.40
158.80
157.22
138.23
135.79
131.61
129.36
129.14
128.11
127.42
124.63
115.29
77.48 CDCl3
77.36 CDCl3
77.16 CDCl3
76.84 CDCl3
55.67
0.13
f1 (ppm)

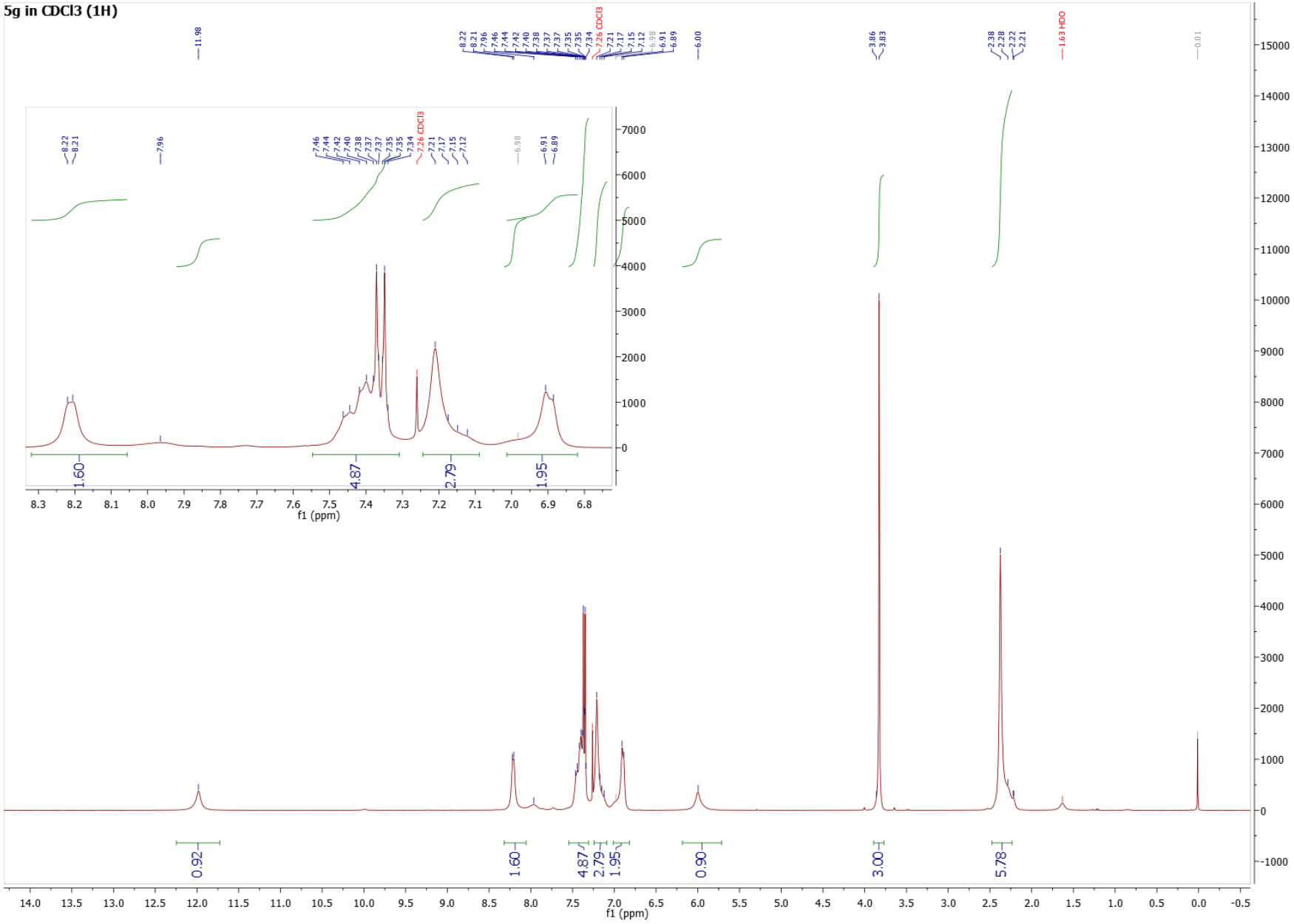


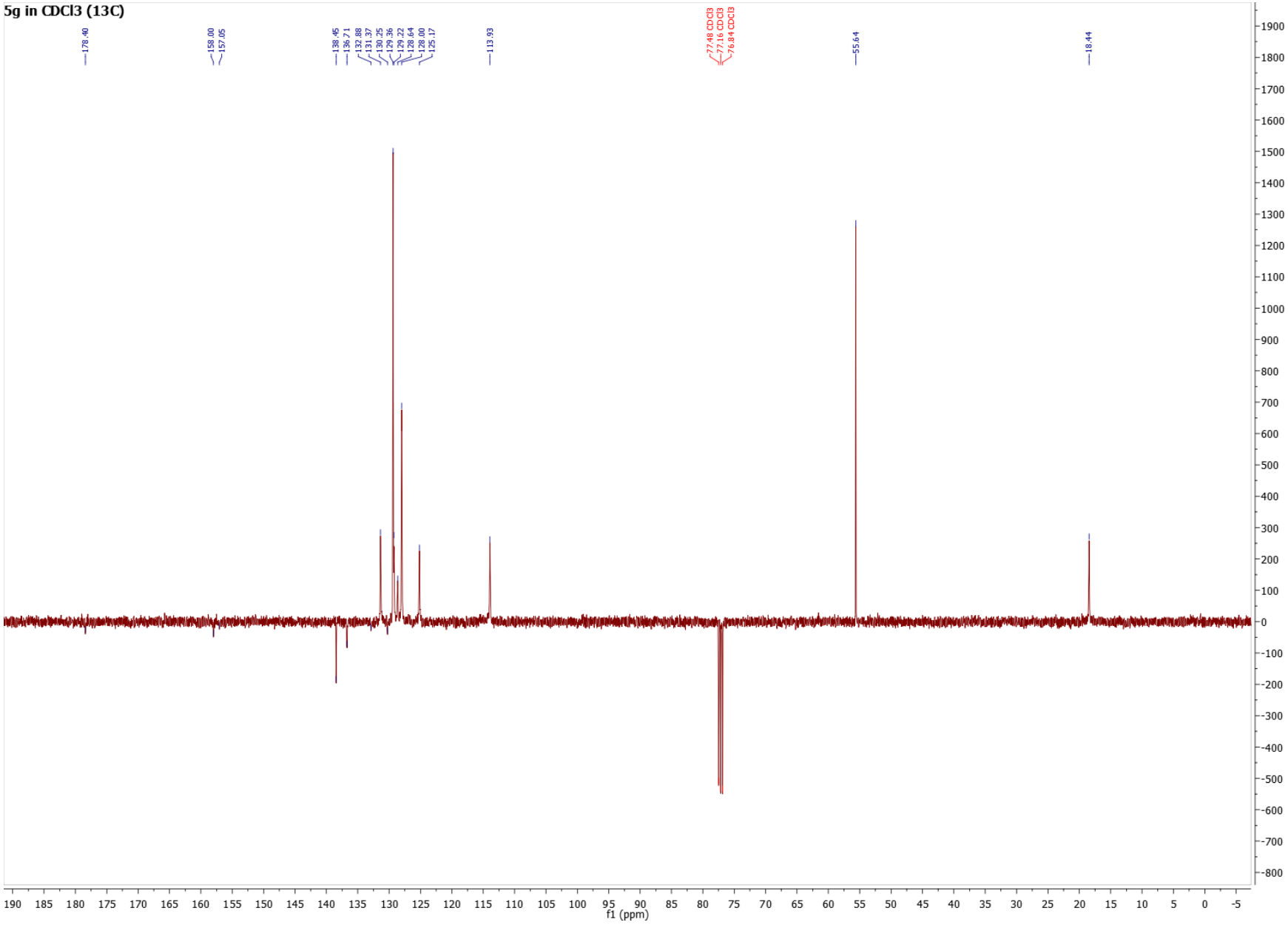
3.1.1.1

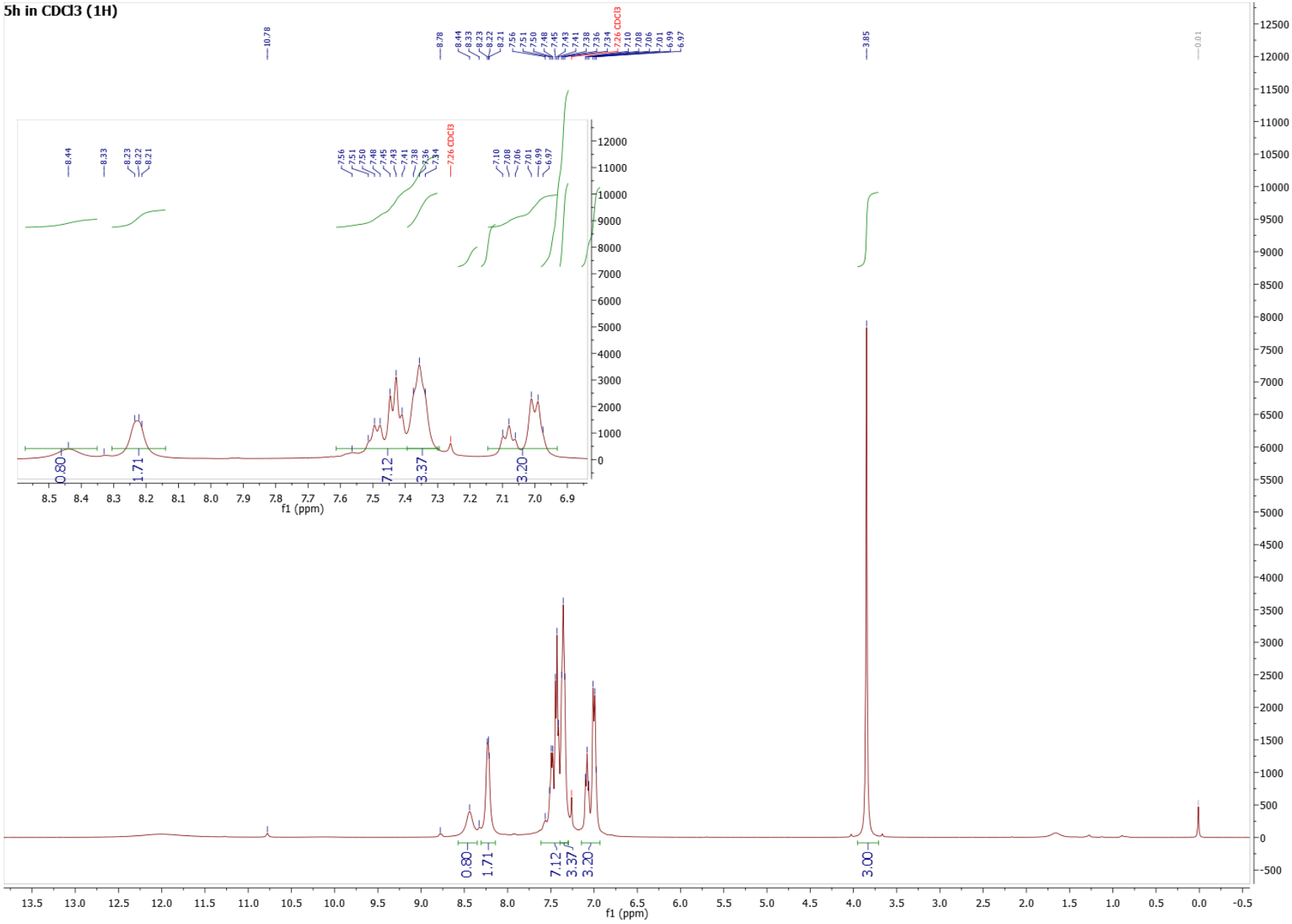

5e in CDCl3 (13C)
178.42
158.83
157.06
138.20
138.03
137.10
131.63
129.36
128.13
127.46
125.03
115.31
88.75
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
55.67
0.13
f1 (ppm)

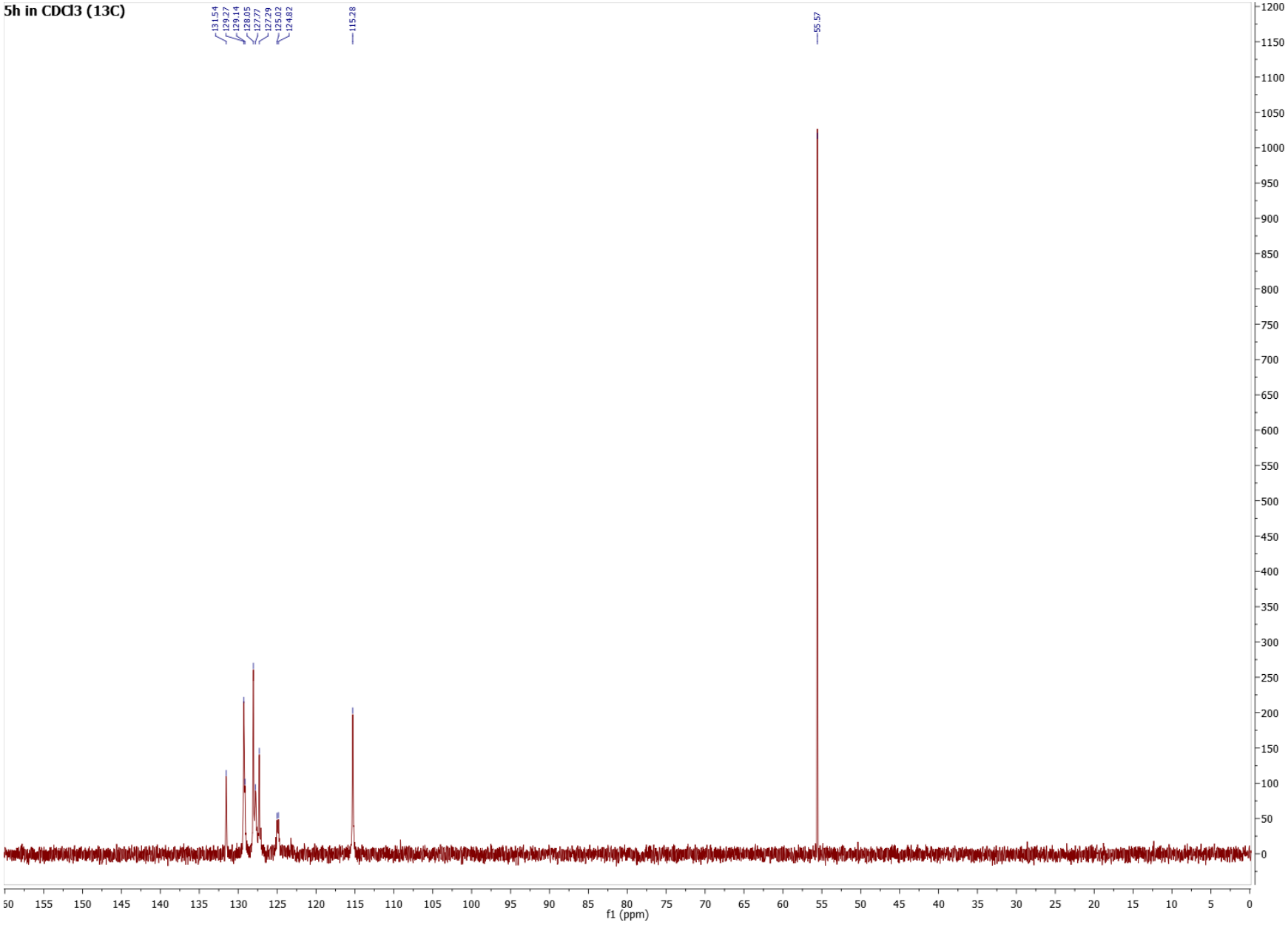

5f in DMSO-d6 (1H)
11.37
10.12
9.78
9.45
8.07
8.05
8.05
8.05
8.04
8.04
8.03
8.03
7.98
7.97
7.96
7.96
7.95
7.93
7.79
7.77
7.77
7.76
7.75
7.68
7.67
7.67
7.66
7.66
7.65
7.64
7.63
7.57
7.56
7.55
7.54
7.53
7.51
7.50
7.46
7.45
7.43
7.38
7.37
7.35
7.00
6.98
6.97
6.95
6.87
3.84
3.83
3.77
3.75
3.36 HDO
2.51 DMSO
2.50 DMSO
2.50 DMSO
2.50 DMSO
2.50 DMSO
2.49 DMSO
0.56
0.26
0.75
0.09
5.89
4.58
2.35
6.00
f1 (ppm)

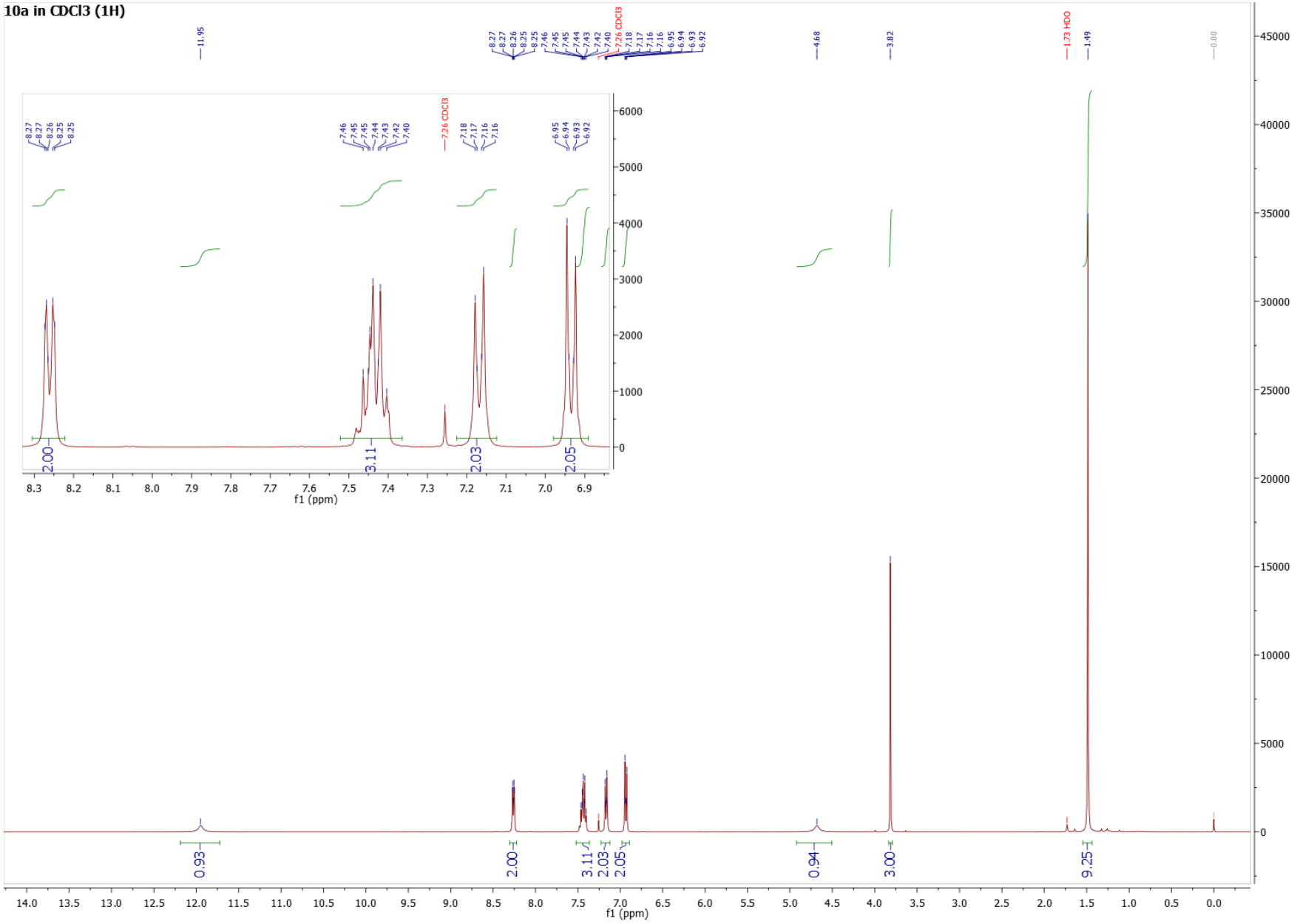

5f in DMSO-d6 (13C)
131.19
129.53
128.53
127.88
125.66
121.99
114.26
55.03
51.65
39.95 DMSO
39.73 DMSO
39.52 DMSO
39.31 DMSO
39.10 DMSO
f1 (ppm)

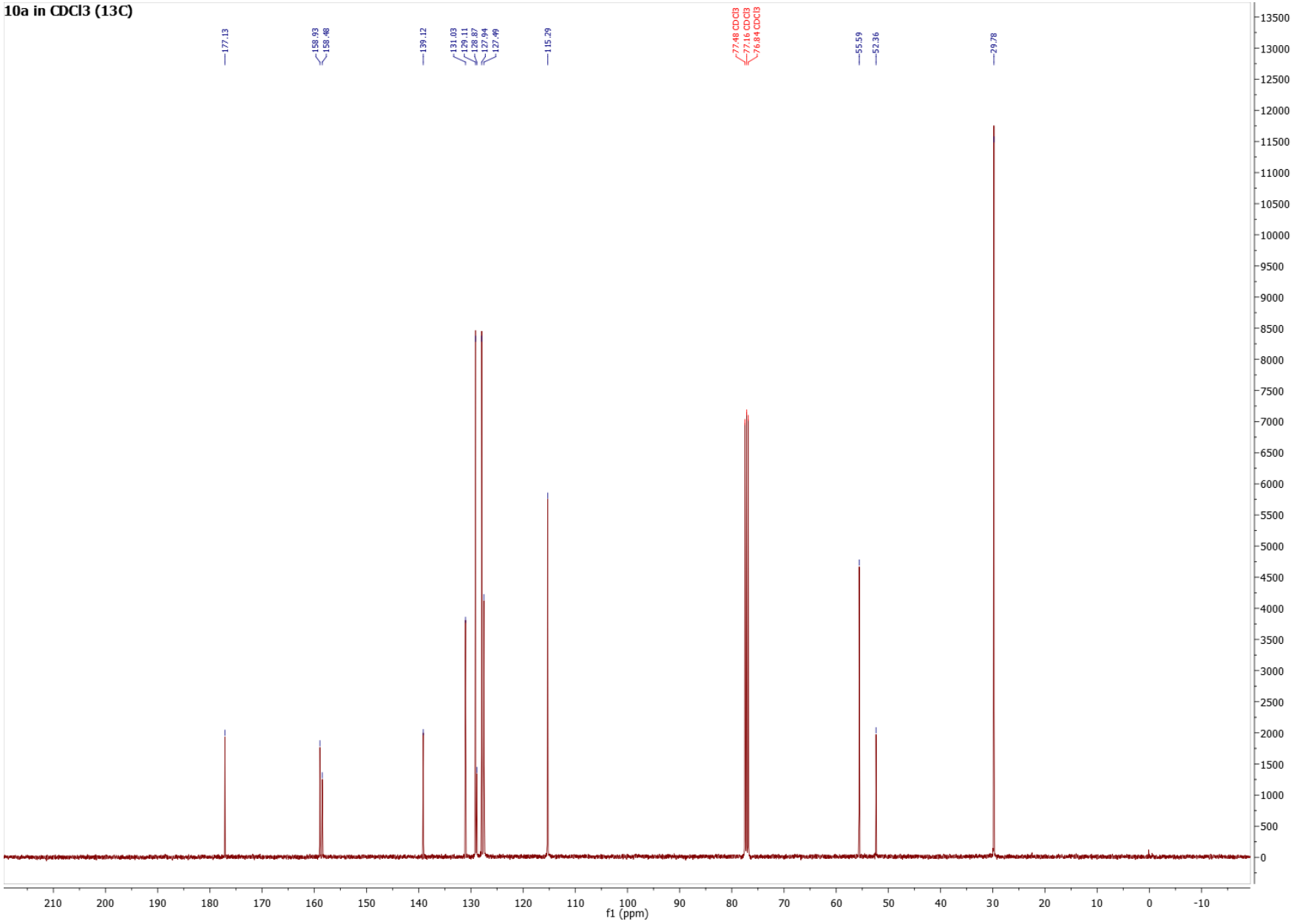

5g in CDCl3 (1H)
f1 (ppm)

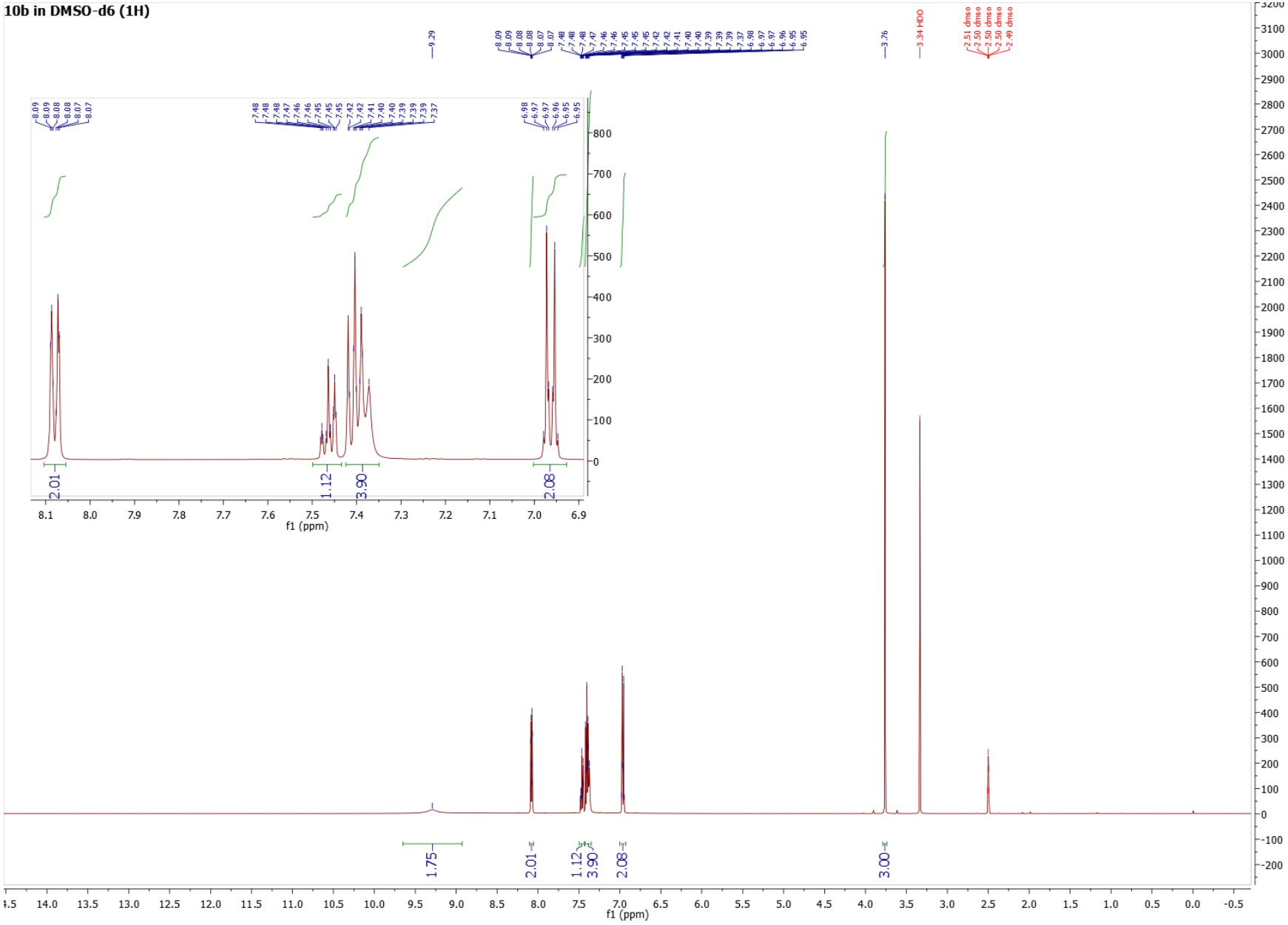

5g in CDCl3 (13C)
178.40
158.00
157.05
138.45
136.71
132.88
131.37
130.25
129.36
129.22
128.64
128.00
125.17
113.93
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
55.64
18.44
f1 (ppm)

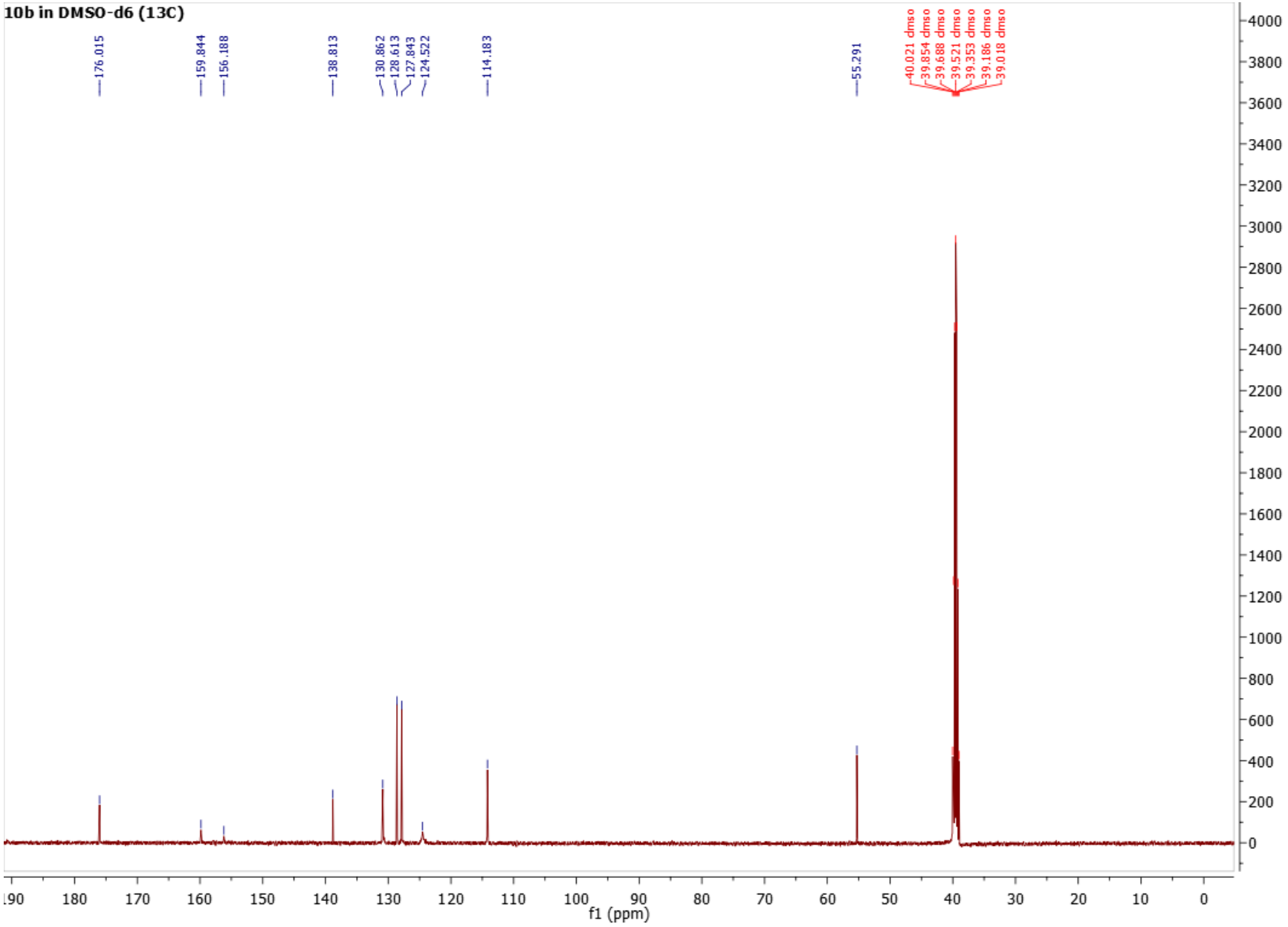

5h in CDCl3 (1H)
f1 (ppm)
0.80
1.71
7.12
3.37
3.20
3.00

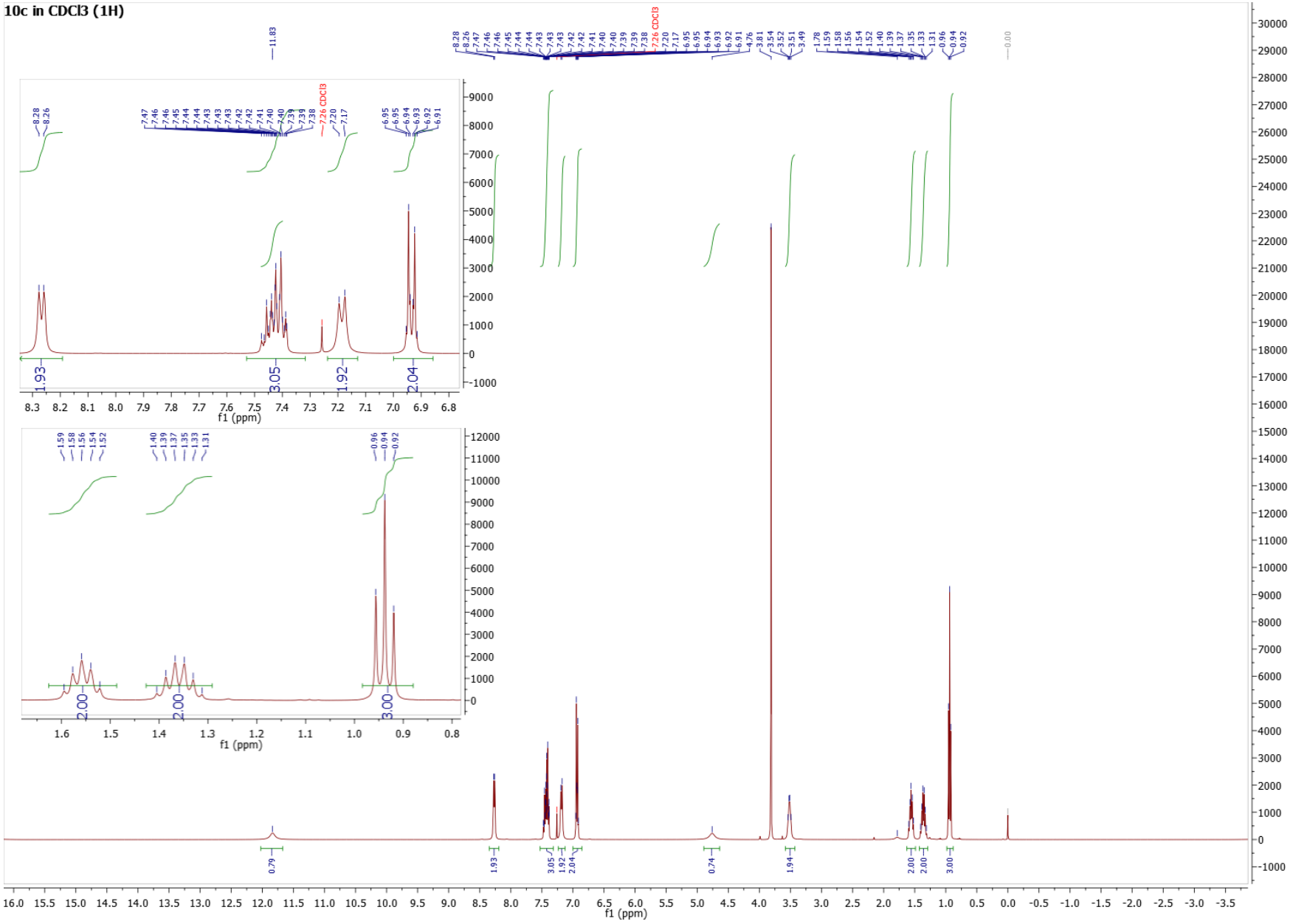

5h in CDCl3 (13C)
131.54
129.27
129.14
128.05
127.77
127.29
125.02
124.82
115.28
55.57
f1 (ppm)

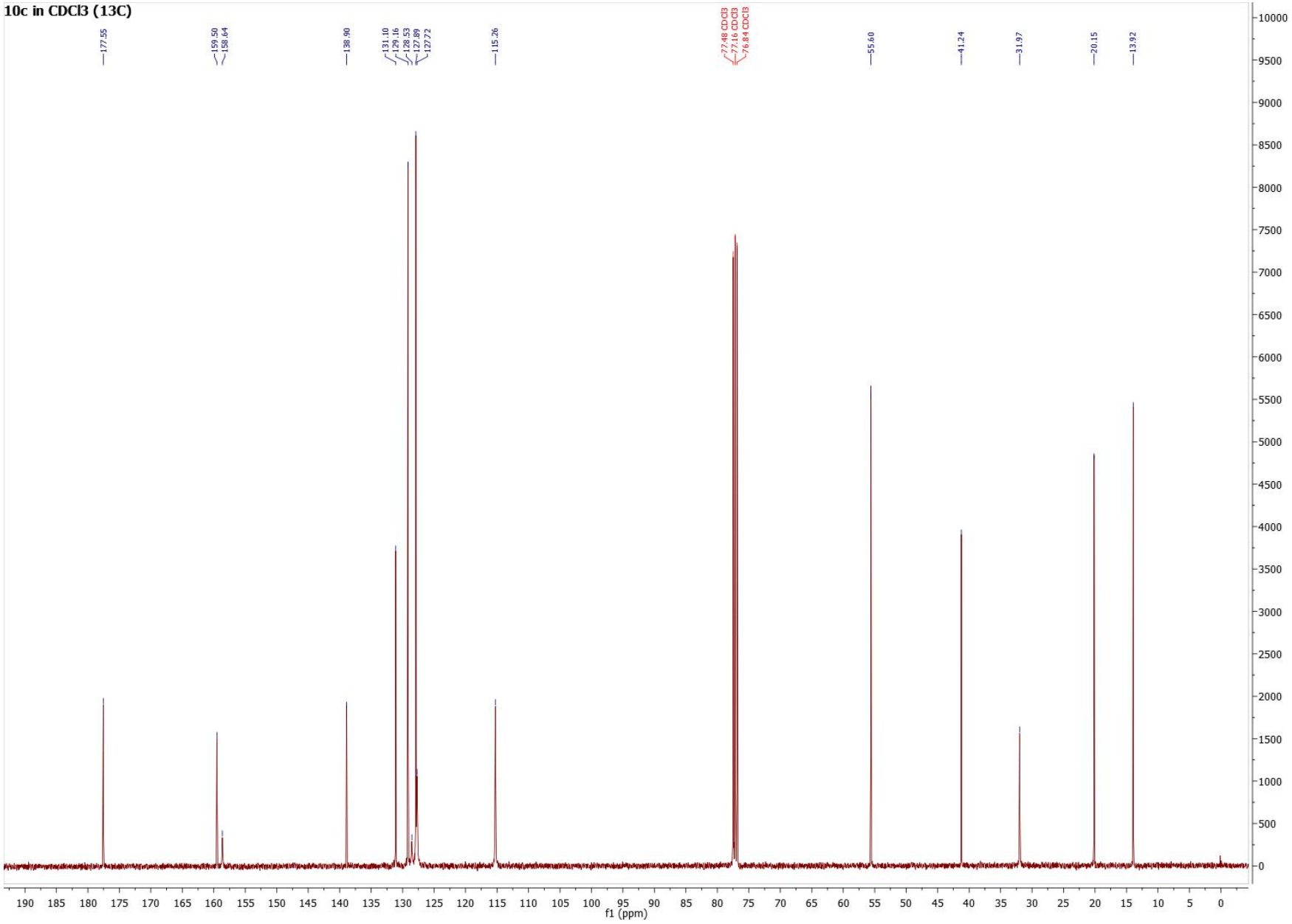

10a in CDCl3 (1H)
11.95
8.27
8.27
8.26
8.25
8.25
7.46
7.45
7.45
7.44
7.43
7.42
7.40
7.26 CDCl3
7.18
7.17
7.16
7.16
6.95
6.94
6.93
6.92
4.68
3.82
1.73 HDO
1.49
0.00
2.00
3.11
2.03
2.05
f1 (ppm)
0.93
2.00
3.11
2.03
2.05
0.94
3.00
9.25
f1 (ppm)

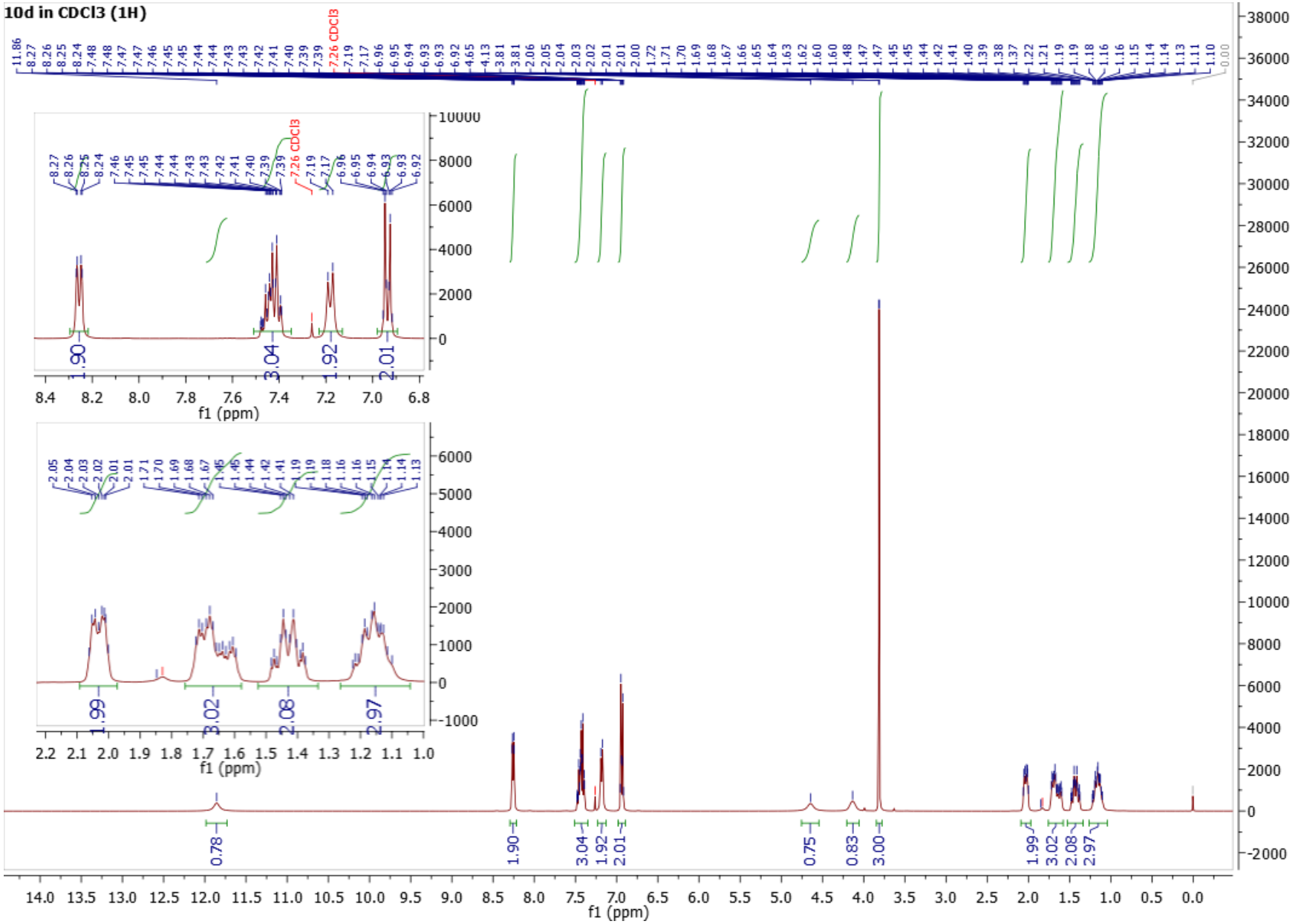

10a in CDCl3 (13C)
177.13
158.93
158.48
139.12
131.03
129.11
128.87
127.94
127.49
115.29
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
55.59
52.36
29.78
f1 (ppm)

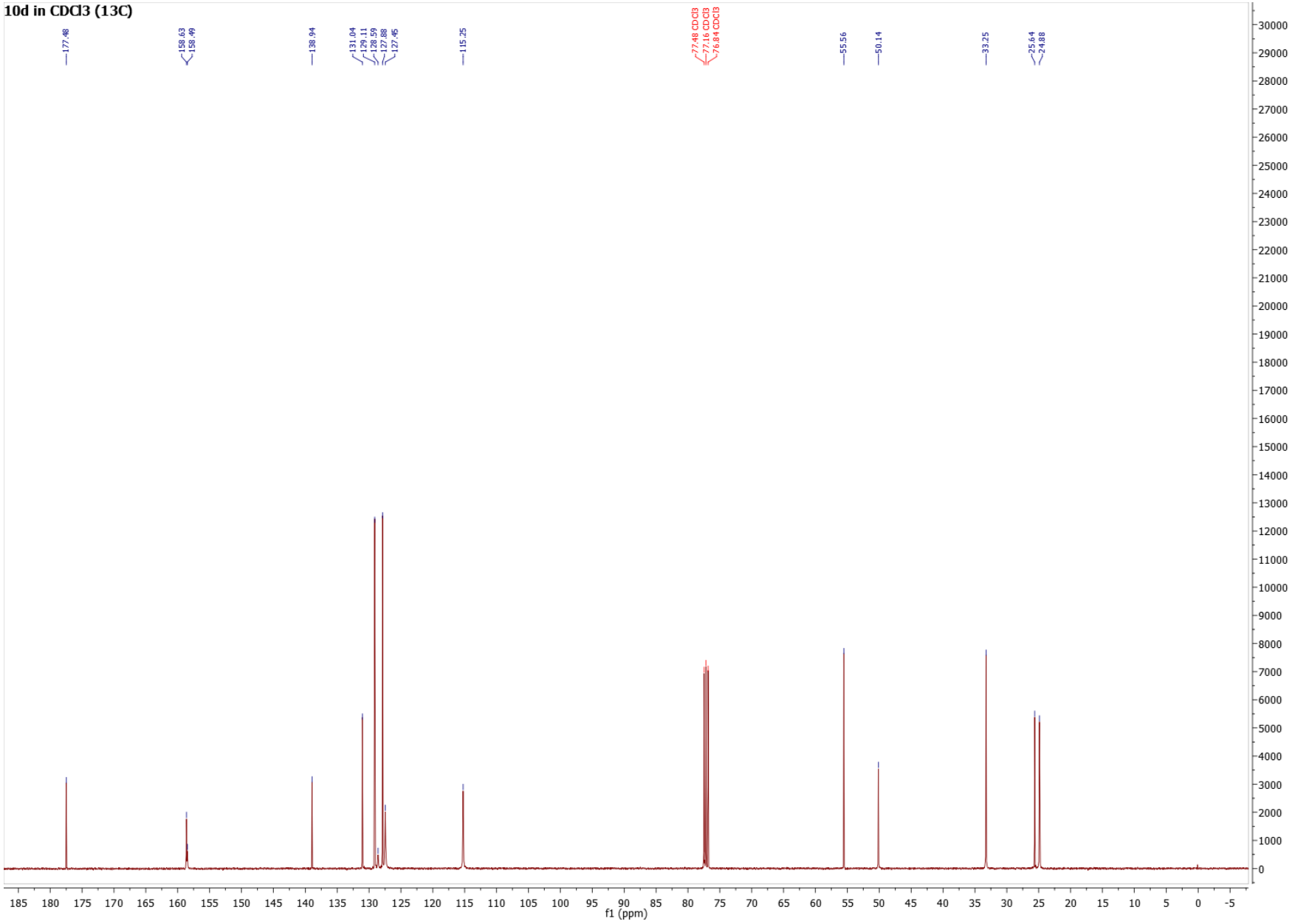

10b in DMSO-d6 (1H)
f1 (ppm)


10b in DMSO-d6 (13C)
176.015
159.844
156.188
138.813
130.862
128.613
127.843
124.522
114.183
55.291
40.021 dmso
39.854 dmso
39.688 dmso
39.521 dmso
39.353 dmso
39.186 dmso
39.018 dmso
f1 (ppm)


10c in CDCl3 (1H)
f1 (ppm)


10c in CDCl3 (13C)
177.55
159.50
158.64
138.90
131.10
129.16
128.53
127.89
127.72
115.26
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
55.60
41.24
31.97
20.15
13.92
f1 (ppm)

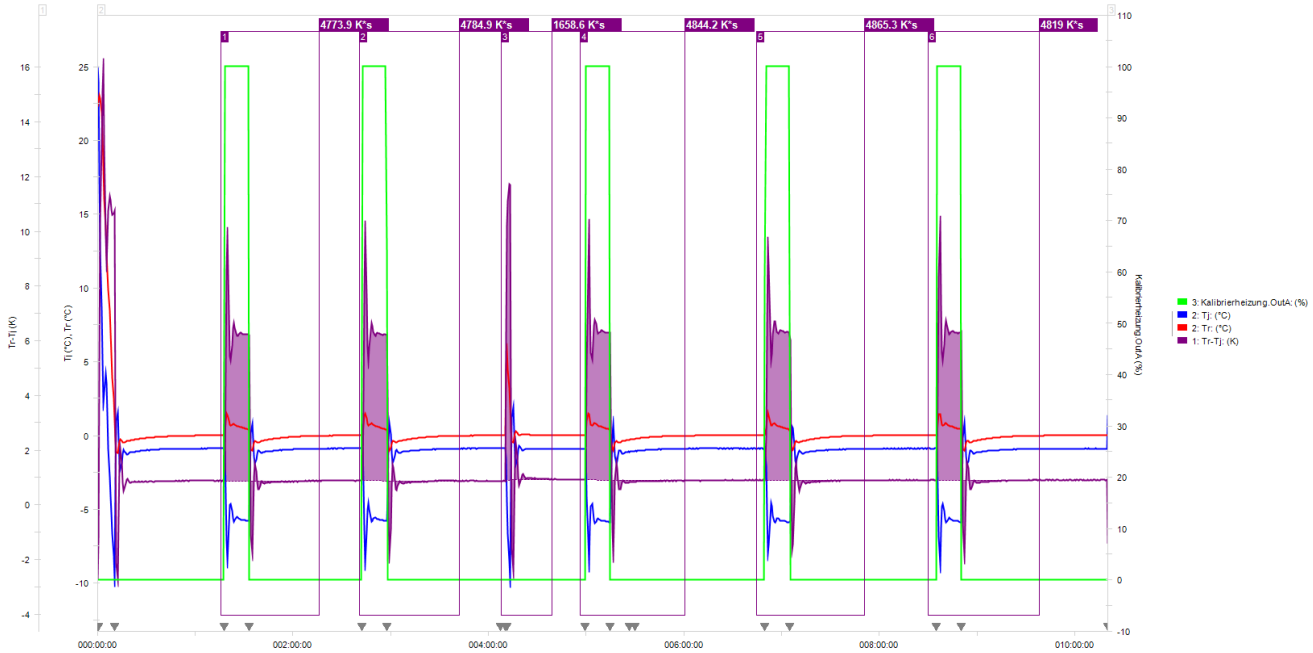

10d in CDCl3 (1H)
7.26 CDCl3
f1 (ppm)
1.90
3.04
1.92
2.01
1.99
3.02
2.08
2.97
0.78
1.90
3.04
1.92
2.01
0.75
0.83
3.00
1.99
3.02
2.08
2.97


10d in CDCl3 (13C)
177.48
158.63
158.49
138.94
131.04
129.11
128.59
127.88
127.45
115.25
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
55.56
50.14
33.25
25.64
24.88
f1 (ppm)

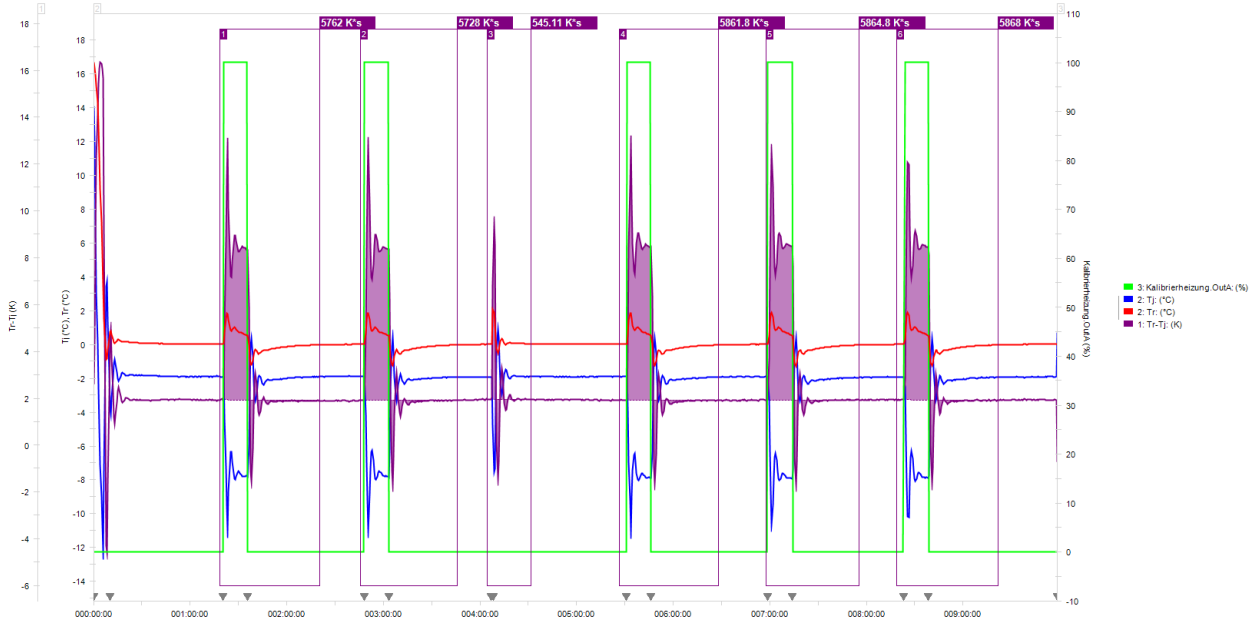
3.2 Calorimetric measurements

3.2.1 Iron(III)chloride

3.2.1.1 Heat of reaction

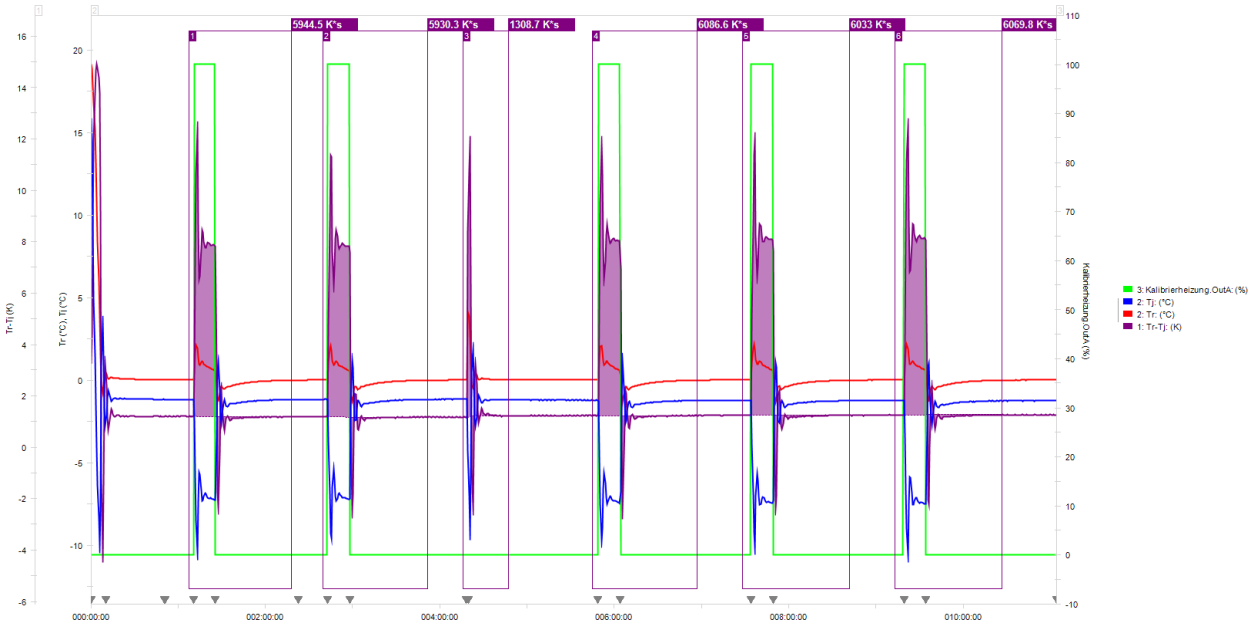


3.2.1.2 Heat of solution

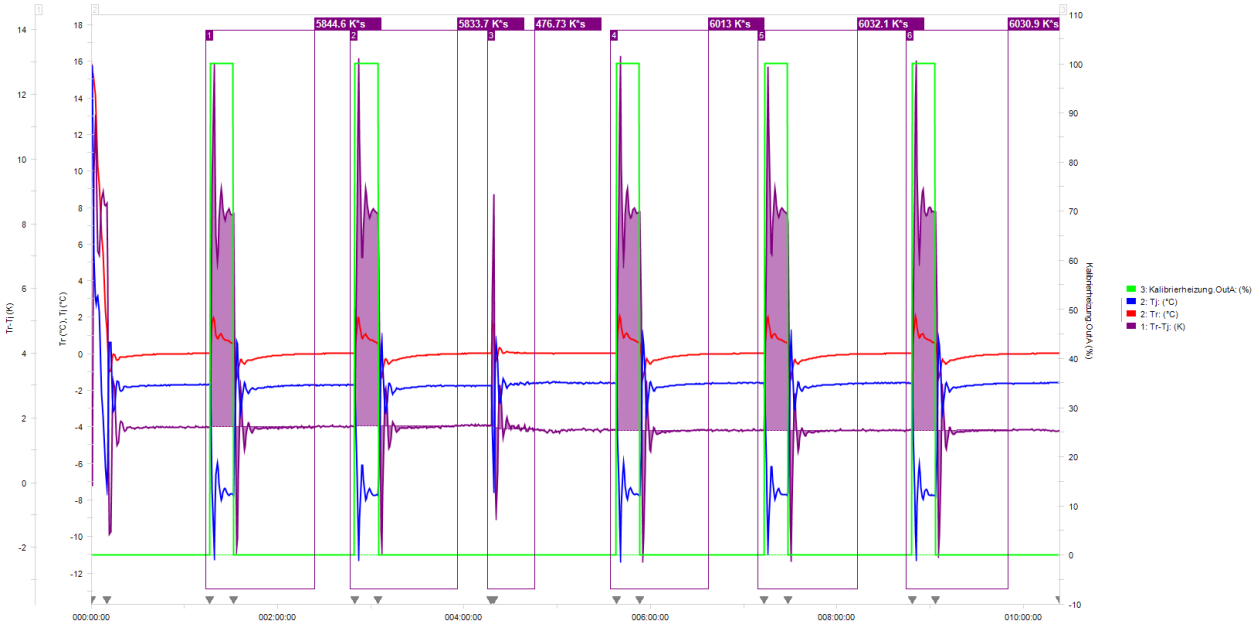


3.2.2 Indium(III)trichloride

3.2.2.1 Heat of reaction

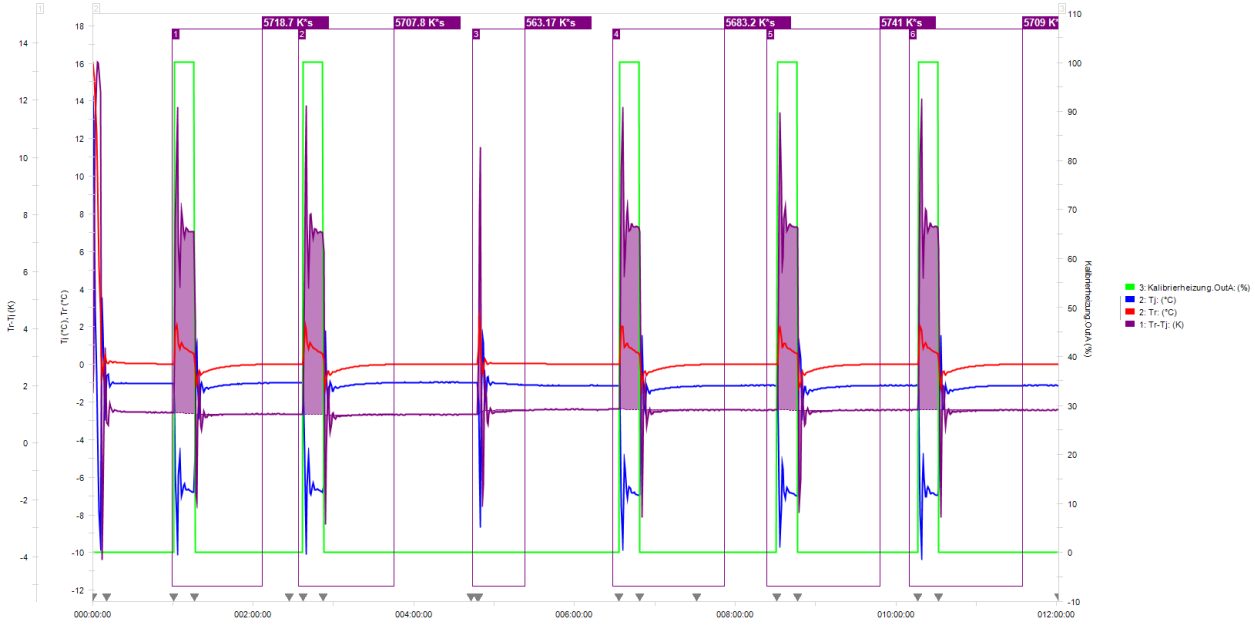


3.2.2.2 Heat of solution

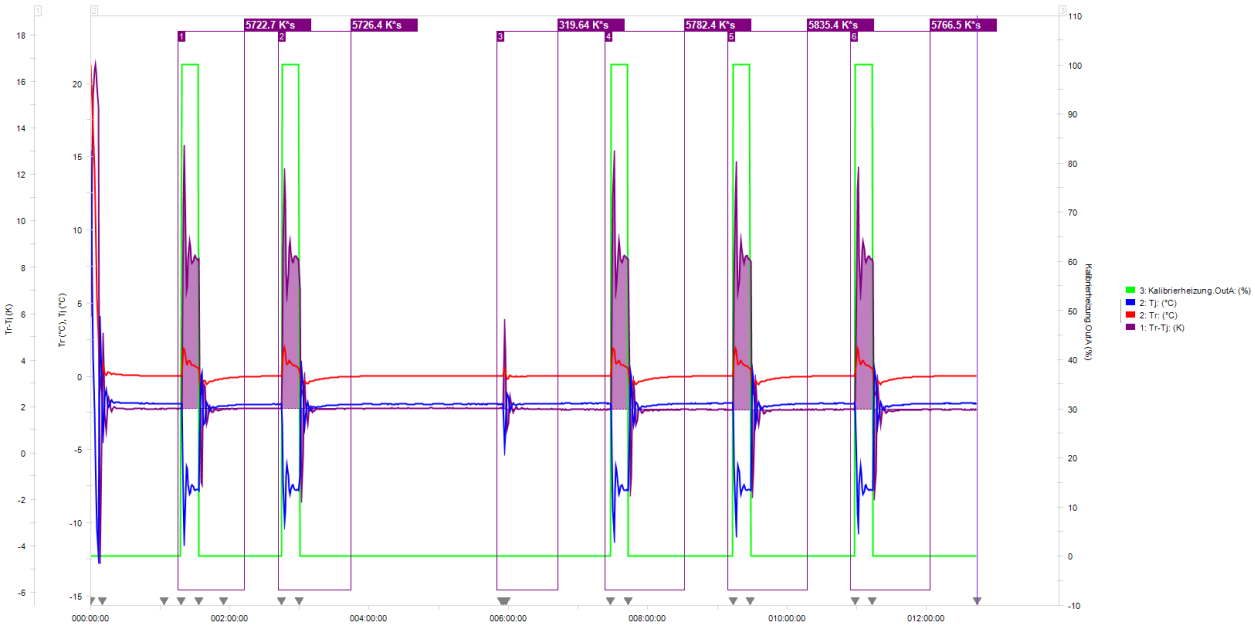


3.2.3 Zinc(II)chloride

3.2.3.1 Heat of reaction

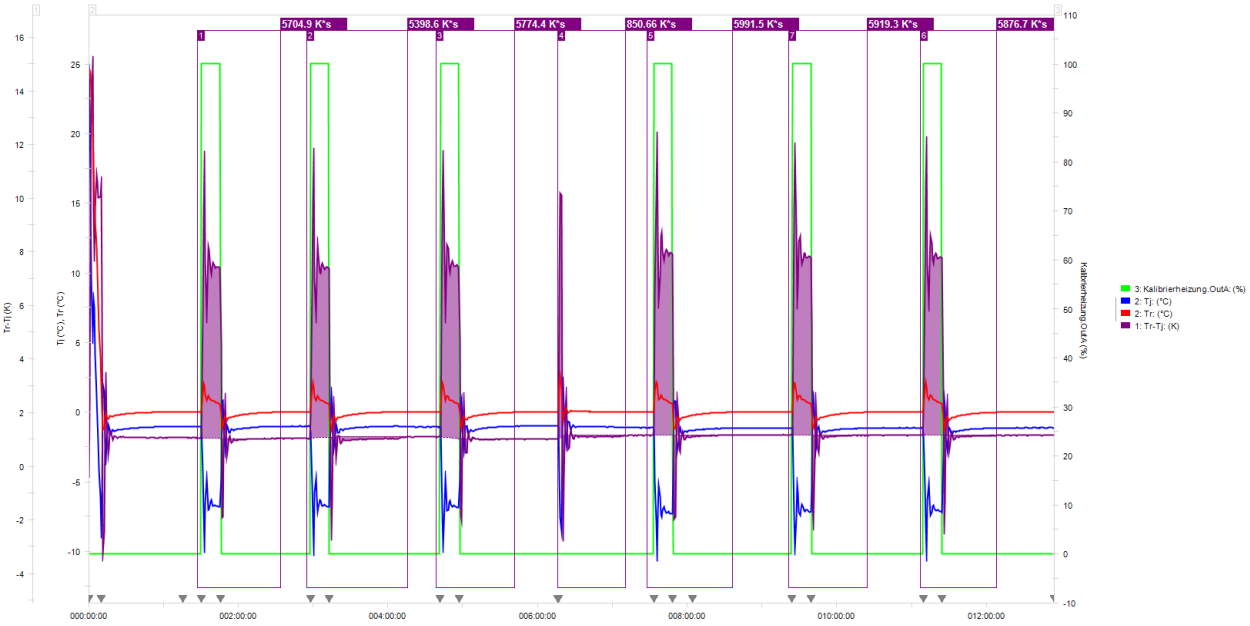


3.2.3.2 Heat of solution

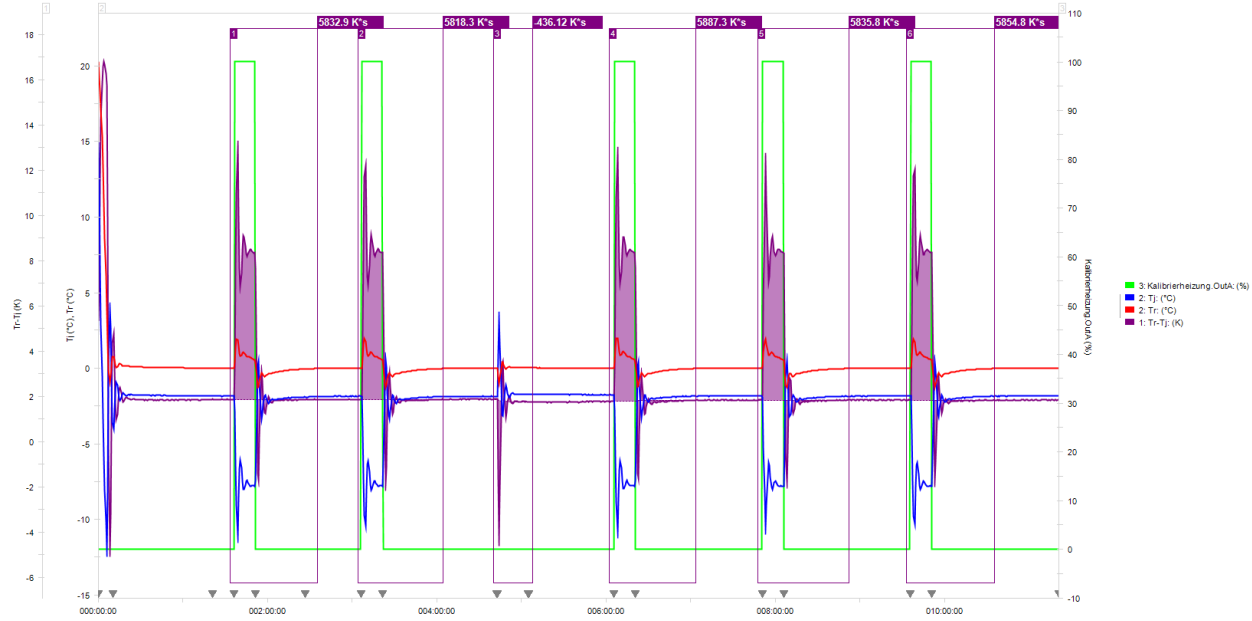


3.2.4 Bismuth(III)nitrate

3.2.4.1 Heat or reaction



3.2.4.2 Heat of solution



4 References

[1] S. Cunha, B. R. de Lima, A. R. de Souza, *Tetrahedron Lett.* **2002**, *43*, 49–52.

[2] T. B. Johnson, L. H. Chernoff, *J. Am. Chem. Soc.* **1912**, *34*, 164–170.

[3] G. Ito, *Chemical & Pharmaceutical Bulletin* **1961**, *9*, 245–248.

[4] S. Cunha, M. B. Costa, H. B. Napolitano, C. Lariucci, I. Vencato, *Tetrahedron* **2001**, *57*, 1671–1675.