Supplementary Material (ESI) for Chemical Communications

Novel Chiral Derivatizing Isothiocyanate-Based Agent for the Enantiomeric Excess Determination of Amines

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Electronic Supplementary Information

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I. General information

All reactions were performed under an Argon atmosphere. The following solvent was distilled from the indicated drying agent: CH_2Cl_2 (CaH_2). $CDCl_3$ was used as purchased from Aldrich. All commercially available reagents were used without further purification. Analytical thin-layer chromatography (TLC) was performed on glass-backed silica gel plates. Visualization of the developed chromatogram was performed using UV absorbance and a vanillin solution. Flash column chromatography was performed with silica gel (40-63 μm) according to a standard technique. Nuclear magnetic resonance spectra (^1H, ^{13}C and ^{19}F) were recorded on a 400 MHz spectrometer equipped with a BBI or a DUAL probe. Chemical shifts for ^1H and ^{13}C spectra are recorded in parts per million using the residual chloroform as internal standard (^1H, δ = 7.26 ppm; ^{13}C, δ = 77.16 ppm). Multiplicities are indicated by s (singlet), bs (broad singlet), d (doublet), t (triplet), q (quadruplet), qt (quintuplet) and m (multiplet). Coupling constants, *J*, are reported in Hertz. Infrared spectra were recorded on a FT-IR spectrometer equipped with KRS-5 (ThI/ThBr) lenses and are reported in reciprocal centimetres (cm^{-1}). The melting point was measured with an SMP3 Melting Point Apparatus Stuart Scientific (Bibby).

II. General procedure for the preparation of 1,1,1-trifluoro-N-((1S,2S)-2-isothiocyanatocyclohexyl)methanesulfonamide 2

1. Synthesis of (4S,5S)-4,5-tetramethylenimidazolidine-2-thione[a]

1.13g of (1S, 2S)-cyclohexyldiamine (9.91 mmol) are first dissolved in 4 mL of a 1/1 mixture of water/ethanol. The carbon disulfide in then added slowly drop wise to the homogeneous solution. The reaction mixture is then heated at 80°C for 1h and 100 μL of 5N aqueous HCl is then added, and the resulting mixture is heated at reflux for overnight. The reaction mixture is then cooled to room temperature, the solid is filtrated, washed with cold ethanol, and dried under vacuum to afford 1.02g of a white solid (68%).

[a] See also : a) S. G. Davis, A. A. Mortlock, *Tetrahedron* **1993**, ***49***, 4419.; b) O. P. Kleidernigg, K. Posch, W. Lindner, *J. Chromatogr. A* **1996**, ***33***, 729.; and reference 14.

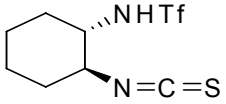
2. Synthesis of 1,1,1-trifluoro-N-((1S,2S)-2-isothiocyanatocyclohexyl) methane sulfonamide 2

Under an Argon atmosphere 200 mg of (4S,5S)-4,5-tetramethylenimidazolidine-2-thione is dissolved in 4 mL of anhydrous DCM. The homogeneous solution is then cooled to 0°C, 535 µL of triethylamine (2 eq., 2.69 mmol) followed with 441 µL of trifluoromethanesulfonic anhydride (1 eq., 1.35 mmol), dissolved in 1 mL of dry ether, are added successively dropwise. The reaction mixture is then stirred at 0°C for 3h, and at room temperature for overnight. 4 mL of saturated aqueous solution of sodium hydrogenocarbonate are then added, and the aqueous phase extracted trice with DCM (3*4mL). The organic phase are recovered, washed with brine, dried over Na_2SO_4, and concentrated under vacuum. The crude residue is then purified by flash chromatography (cyclohexane/ethyl acetate 95/5) to yield after recristallization in hexane 275 mg of a yellow solid (75 %).

3. Generale procedure for the thiourea formation and *ee* determination.

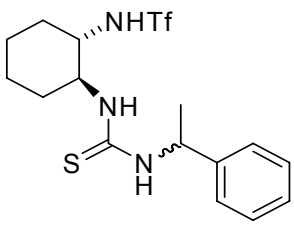
To a 9 ml $CDCl_3$ solution containing (1.05 equiv) of the chiral isothiocyanate **2** is added the racemic mixture of the amine of interest or the amine to be analyzed (1 equiv). The reaction mixture is then stirred for 2h at room temperature. After completion of the reaction, monitored by TLC analysis, the crude medium is then, without any work-up procedure, directly analyzed by ^{19}F NMR spectroscopy for the *ee* determination. The reaction can be eventually performed in cheaper CH_2Cl_2. In this case, after completion of the reaction, the solvent is simply evaporated and the residue dissolved in $CDCl_3$ for quick analysis by ^{19}F NMR spectroscopy. Usual flash column chromatography on silica gel afforded analytically pure inseparable mixtures of thiourea diastereoisomers.

III. Characterization data of 2 and diastereoisomeric mixture for all thioureas



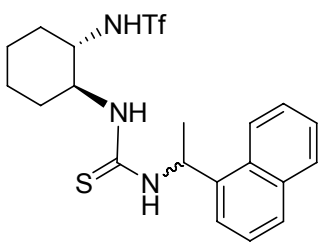
1, 1, 1-trifluoro-N-((1S, 2S)-2-isothiocyanatocyclohexyl) methane sulfonamide 2

TLC (SiO_2), R_f: 0.60 (cyclohexane/ethyl acetate : 70/30); ^1H NMR (400 MHz, $CDCl_3$): 3.63-3.43 (m, 2H), 2.29-1.25 (m, 9H); ^{13}C NMR (100.62 MHz, $CDCl_3$) : 133.77, 123.06, 116.70, 60.61-59.19, 33.33-32.78, 30.58, 27.31, 24.31-23.69; ^{19}F NMR (376.59 MHz, $CDCl_3$): -78.142 (s, 3F); IR ν (cm^{-1}) : 1188, 1378, 1450, 2861, 2964, 3293; MS (EI) M-1: 287; Specific rotation $[\alpha]^{20}_D$ + 58.5 (c = 0.5, CH_2Cl_2); MP: 86°C.



1, 1, 1-trifluoro-N-((1S, 2S)-2-(3-(1-phenylethyl)thioureido)cyclohexyl) methane sulfonamide 4a

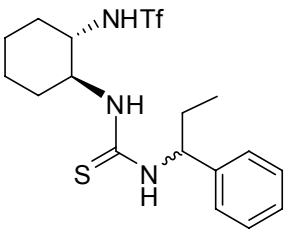
1/1 mixture of diastereoisomers: colourless oil; Yield: 100%; TLC (SiO_2), R_f: 0.50 (cyclohexane/ethyl acetate : 70/30); ^1H NMR (400 MHz, $CDCl_3$): 7.36-7.19 (m,5H), 6.46(m,1H), 5.45-5.26 (s,1H), 4.35-4,21(m,2H), 3,09-2.78 (m,1H), 2,09-1.91 (m,2H), 1,65-1.05(m,10H), 0.82-0.84(m,1H); ^{13}C NMR (100.62 MHz, $CDCl_3$): 181.8, 179.6, 140.5, 127.1, 124.7, 120.3, 117.1, 61.0, 60.0, 57.3, 56.3, 55.5, 52.9, 33.3, 32.9, 31.5, 30.8, 29.2, 28.7, 25.9, 23.5-23.1, 17.2; ^{19}F NMR (376.59 MHz, $CDCl_3$): -77.964 (s, 3F), -78.248 (s, 3F); IR ν (cm^{-1}) : 908, 1187, 1227, 1368, 1536, 2932, 3056, 3372; MS (ESI) M+1: 410.1



1, 1, 1-trifluoro-N-((1S, 2S)-2-(3-(1-(naphthalen-1-yl)ethyl)thioureido)cyclohexyl) methane sulfonamide 4b

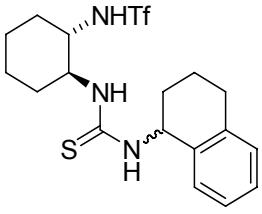
1/1 mixture of diastereoisomers. Colourless oil; Yield: 100%; TLC

(SiO_2), R_f: 0.55 (cyclohexane/ethyl acetate : 70/30); ^{1}H NMR (400 MHz, $CDCl_3$): 7.97-7.32 (m, 10H), 6.77(s, 1H), 4.30-4.16(s, 1H), 2.97(s, 1H), 2.02-1.95 (m, 1H), 1.75-1.72 (m, 1H), 1.59-0.87(m, 14H); ^{13}C NMR (100.62 MHz, $CDCl_3$): 180.8, 180.0, 133.0, 128.2-127.8, 126.1-125.8, 125.2-124.6, 122.3-121.9, 120.4-120.3, 117.2-117.1, 60.9, 60.1, 56.0, 55.2, 49.5-49.3, 42.4, 33.2-32.8, 31.2, 30.7, 29.2, 28.7, 25.9, 23.5-23.1 ; ^{19}F NMR (376.59 MHz, $CDCl_3$): -77.964 (s, 3F), -78.282 (s, 3F) ; IR ν (cm^{-1}) : 1147, 1189, 1227, 1371, 1441, 1530, 2856, 2932, 3368 ; MS (ESI) M+1: 460.1.



1, 1, 1-trifluoro-N-((1S,2S)-2-(3-(1-phenylethyl)thioureido)cyclohexyl) methane sulfonamide 4c

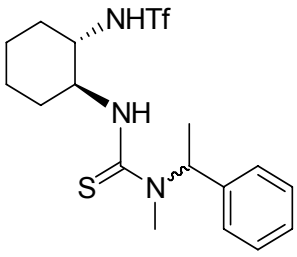
1/1 mixture of diastereoisomers : colourless oil; Yield: 100%; TLC (SiO_2), R_f: 0.45 (cyclohexane/ethyl acetate : 70/30) ^{1} H NMR (400 MHz, $CDCl_3$): 7.34-7.20 (m, 5H) 6.74-6.65 (d, 1H), 5.78-5.13 (s,1H), 4.32-4.18 (m,1H), 3.07-2.88 (m,1H), 2.09-1.1 (m,10H), 0.86-0.80 (t,3H); ^{13}C NMR (100.62 MHz, $CDCl_3$) :181.1, 180.3, 138.9, 128.3, 127.2, 125.5, 120.2, 117.0, 60.4(t, 3C), 59.0, 56.2, 55.4, 33.4, 33.1, 31.2, 30.7, 29.6, 29.1, 25.9, 23.5-23.1, 9.5, 9.3; ^{19}F NMR (376.59 MHz, $CDCl_3$): -77.464 (s, 3F) -77.676 (s, 3F); IR ν (cm^{-1}) : 912, 1190, 1226, 1368, 1536, 2941, 3079, 3368; MS (ESI) M+1: 424.1



1, 1, 1-trifluoro-N-((1S,2S)-2-(3-(1,2,3,4-tetrahydronaphthalen-1-yl) thioureido) cyclohexyl) methane sulfonamide 4d

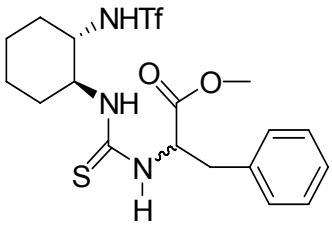
1/1 mixture of diastereoisomers : colourless oil; Yield: 100%; TLC (SiO_2), R_f: 0.50 (cyclohexane/ethyl acetate : 70/30); ^{1}H NMR (400 MHz, $CDCl_3$): 7.22-7.01(m, 5H), 6.2(s, 1H), 5.75(s, 1H), 4.47-4.42(m, 1H), 3.62-3.56(m, 1H), 3.21^{1}H NMR (400 MHz, $CDCl_3$-3.14(m, 1H), 2.76-2.62(m, 2H), 2.11-1.68(m, 9H), 1.48-

0.04(m, 10H) ; ^{13}C NMR (100.62 MHz, $CDCl_3$):182.4, 181.7, 134.3, 129.9-129.4, 127.7-127.4, 121.7-126.1, 123.8-123.3, 122.1, 62.3-61.9, 57.3-56.8, 51.2-50.6, 34.7-34.5, 32.8, 32.1, 30.5, 27.4, 25.-24.5 ; ^{19}F NMR (376.59 MHz, $CDCl_3$): -77.993 (s, 3F) 78.067 (s, 3F) ; IR ν (cm^{-1}) : 916, 1146, 1188, 1227, 1370, 1536, 2860, 2932, 3372 ; MS (ESI) M+1: 436.1



1, 1, 1-trifluoro-N-((1S,2S)-2-(3-methyl-3-(1-phenylethyl)thioureido)cyclohexyl) methane sulfonamide 4e

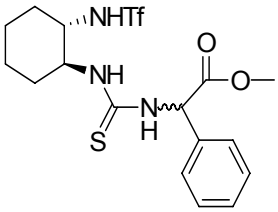
1/1 mixture of diastereoisomers: colourless oil; Yield: 100%; TLC (SiO_2), R_f : 0.45 (cyclohexane/ethyl acetate : 70/30); ^{1}H NMR (400 MHz, $CDCl_3$): 7.29-7.16(m, 5H), 6.68(s, 1H), 5.45-5.43(s, 1H), 4.71-4.66(m, 1H), 3.26-3.18(m, 1H) 2.65(s, 3H), 2.14-2.10(m, 1H), 2.03-1.99(m, 1H), 1.71-1.68(m, 1H), 1.53-1.04(m, 8H); ^{13}C NMR (100.62 MHz, $CDCl_3$):180.8, 180.7, 138.9, 138.6, 127.6, 126.6, 125.9, 120.5-120.4, 117.3-117.2, 61.7, 61.2, 57.6, 57.3, 56.4, 56.1, 33.7-33.4, 31.8-31.7, 30.1-29.9, 28.7, 14.6, 14.1; ^{19}F NMR (376.59 MHz, $CDCl_3$): -77.867 (s, 3F), -78.286 (s, 3F); IR ν (cm^{-1}) : 908, 1187, 1227, 1368, 1536, 2932, 2944, 3056, 3385; MS (ESI) M+1: 424.1



Methyl-3-phenyl-2-(3-((1S, 2S)-2-(trifluoromethylsulfonamido)cyclohexyl)thioureido) Propanoate 4f

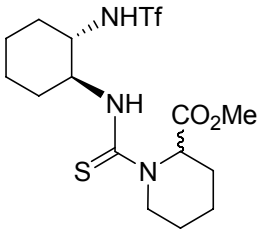
1/1 mixture of diastereoisomers: Colourless oil; Yield: 100%; TLC (SiO_2), R_f: 0.446 (cyclohexane/ethyl acetate : 70/30); ^{1}H NMR (400 MHz, $CDCl_3$): 7.22-7.12 (m, 3H), 7.05-7.02(m, 2H), 6.67-6.64(m, 1H), 6.40-6.38(m, 1H), 3.65-.55 (s, 3H), 3.17-.01(m, 2H), 2.01-1.08(m, 12H); ^{13}C NMR (100.62 MHz, $CDCl_3$): 181.9, 172.7, 171.7, 134.8-134-6, 128.3, 127.7-127.6, 126.2-126.1, 120.3, 117.1, 60.7, 57.3-57.2, 53.4-53.2, 37.2-36.9, 33.1, 31.3, 29.2, 25.9, 23.8-23.3, 20.1, 17.1, 13.1; ^{19}F NMR (376.59 MHz, $CDCl_3$): -77.276 (s, 3F) -

78.328 (s, 3F); IR ν (cm^{-1}) : 1147, 1188, 1227, 1373, 1530, 1725, 2861, 2941, 3061, 3359; MS (ESI) M+1: 468.1.



Methyl-2-phenyl-2-(3-((1S, 2S)-2-(trifluoromethylsulfonamido)cyclohexyl)thioureido) acetate 4g

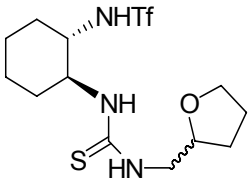
1/1 mixture of diastereoisomers: colourless oil; Yield: 100%; TLC (SiO_2), R_f: 0.405 (cyclohexane/ethyl acetate : 70/30); ^{1}H NMR (400 MHz, $CDCl_3$): 7.29-7.19 (m, 5H), 6.44 (s, 1H), 5.96 (s, 1H), 4.32-4.28 (m, 1H), 3.64-3.61 (s, 3H), 3.19-3.18 (m, 1H), 2.10-1.06 (m, 10H); ^{13}C NMR (100.62 MHz, $CDCl_3$): 202.4, 191.4, 191.3, 155.6, 154.6, 148.6-148.2, 146.8-146.7, 140.8-140.7, 137.6-137.5, 81.3, 80.5, 75.9, 72.6-72.5, 53.6, 51.7-51.6, 49.6, 49.1, 43.9-43.7, 40.6, 37.6, 33.6, 20.5; ^{19}F NMR (376.59 MHz, $CDCl_3$): -78.147 (s, 3F) -78.234 (s, 3F); IR ν (cm^{-1}) : 1147, 1189, 1227, 1371, 1535, 1722, 2856, 2941, 3048, 3368; MS (ESI) M+1: 454.1



Methyl-1-((1S, 2S)-2-(trifluoromethylsulfonamido) cyclohexylcarbamothioyl)piperidine -2- carboxylate 4h

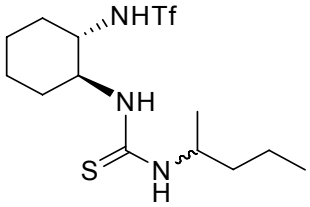
1/1 mixture of diastereoisomers: colourless oil; Yield: 100%; TLC (SiO_2), R_f: 0.432 (cyclohexane/ethyl acetate : 70/30); ^{1}H NMR (400 MHz, $CDCl_3$): 5.71(s, 1H), 4.74-4.70 (m, 1H), 4.61-4.54 (m, 1H), 3.95 (s, 1H), 3.81-3.76 (m, 1H), 3.06-2.95 (m, 1H), 2.51-2.37 (m, 1H), 2.12-2.13 (m, 3H), 1.97-1.94 (m, 1H), 1.79-1.72 (m, 5H), 1.65-1.08 (m, 9H); ^{13}C NMR (100.62 MHz, $CDCl_3$): 180.0, 179.6, 172.7, 172.7, 120.1-120, 117.0-116.9, 58.9, 57.2, 57.1, 55.1, 54.5, 44.1-43.7, 42.5, 33.3, 29.2, 26.8-25.9, 24.0-23.9, 23.5, 21.9-21.8; ^{19}F NMR (376.59 MHz, $CDCl_3$): -77.915 (s, 3F) -78.099 (s, 3F)

IR ν (cm^{-1}) : 922, 1185, 1371, 1499, 1723, 2358, 2856, 2937, 3159; MS (ESI) M+1: 400.1



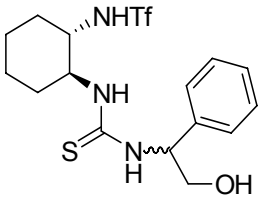
1, 1, 1-trifluoro-N-((1S,2S)-2-(3-((tetrahydrofuran-2-yl)methyl)thioureido)cyclohexyl) methane sulfonamide 4i

1/1 mixture of diastereoisomers: colourless oil; Yield: 100%; TLC (SiO_2), R_f : 0.243 (cyclohexane/ethyl acetate : 70/30); ^{1}H NMR (400 MHz, $CDCl_3$):7.91(s, 1H), 7.2-7.0(s, 1H), 4.3(s, 1H), 3.9-3.7(m, 4H), 3.2(m, 2H), 2.1-1.2(m, 14H); ^{13}C NMR (100.62 MHz, $CDCl_3$):182.6, 182.4, 120.4-120.3, 117.3-117.1, 67.4, 61.2, 47.3, 33.5-33.3, 31.3-31.1, 29.2, 28.7, 25.9, 24.9, 24.7, 23.6, 23.4-23.3; ^{19}F NMR (376.59 MHz, $CDCl_3$): -77.873 (s, 3F) -78.234 (s, 3F); IR ν (cm^{-1}) : 916, 1067, 1186, 1227, 1371, 2936, 3266; MS (ESI) M+1: 390.1



1, 1, 1-trifluoro-N-((1S,2S)-2-(3-pentan-2-ylthioureido)cyclohexyl)methanesulfonamide 4j

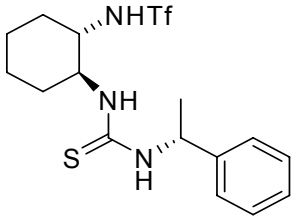
1/1 mixture of diastereoisomers: colourless oil; Yield: 100%; TLC (SiO_2), R_f: 0.514 (cyclohexane/ethyl acetate : 70/30); ^{1}H NMR (400 MHz, $CDCl_3$): 6.15-6.12 (m, 1H), 4.43-4.37 (m, 1H), 3.23-3.18 (m, 1H), 2.93-2.82 (s, 1H), 2.14-1.99 (m, 2H), 1.72-1.70 (m, 2H), 1.51-1.16 (m, 8H), 1.14-1.09 (m, 3H), 0.87-0.83 (m, 3H)**;** ^{13}C NMR (100.62 MHz, $CDCl_3$): 188.3, 162.0, 123.6, 120.4, 117.2, 61.0, 59.7, 55.4, 49.0, 37.8-37.7, 30.7, 29.2, 25.9, 23.6-23.4, 19.5, 19.1 18.1-18.0, 17.3, 12.9**;** ^{19}F NMR (376.47 MHz, $CDCl_3$): -77.633 (s, 3F) -77.653 (s, 3F)**;** IR ν (cm^{-1}) : 1370, 2350, 2856, 2928, 3266, 3382**;** MS (ESI) M+1: 376.1



1, 1, 1-trifluoro-N-((1S, 2S)-2-(3-(2-hydroxy-1-phenylethyl)thioureido)cyclohexyl)methane sulfonamide 4k

1/1 mixture of diastereoisomers: colourless oil; Yield: 100%. TLC (SiO_2), R_f: 0.189 (cyclohexane/ethyl acetate : 70/30). ^{1}H NMR (400 MHz, $CDCl_3$): 7.34-7.19 (m, 5H), 6.98-6.91(s, 1H), 6.30-6.02 (m, 1H), 4.38-4.25 (m, 1H), 3.90-3.77 (m, 2H), 3.17-3.10 (m, 1H), 2.10-1.95 (m, 2H), 1.72-0.77 (m, 10H). ^{13}C NMR (100.62 MHz, $CDCl_3$): 181.9, 180.6, 128.2, 127.2, 125.7, 120.2, 117.0, 65.0, 60.4, 59.7-58.9, 57.4, 55.8, 42.5, 32.9-32.7, 31.3-31.0, 29.2, 28.7 25.9, 23.5-23.3, 17.2; ^{19}F NMR (376.59 MHz, $CDCl_3$): -77.788 (s, 3F) -77.936 (s, 3F); IR ν (cm^{-1}): 1370, 1450, 1539, 2861, 2937, 3057, 3372; MS (ESI) M+1: 426.1

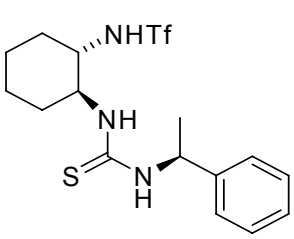
IV. Characterization data of each diastereoisomer for selected thioureas



1, 1, 1-trifluoro-N-((1S, 2S)-2-(3-((R)-1-phenylethyl)thioureido)cyclohexyl) methane sulfonamide

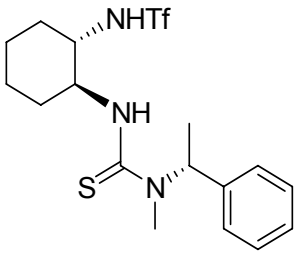
Colourless oil; ^{1}H NMR (400MHz, $CDCl_3$): 7.42-7.24(m, 5H), 6.48(s, 1H), 5.28(s, 1H), 4.63(s, 1H), 4.23(s, 1H), 3.08(m, 1H), 2.07-2.03(s, 1H), 1.73-1.03(m, 10H); ^{13}C NMR (100.62MHz, $CDCl_3$): 181.5, 141.3, 129.4, 128.4, 125.7, 121.4, 118.2, 61.2, 57.3, 53.9, 34.0, 31.8, 24.4, 24.2; ^{19}F NMR (188.295 MHz, $CDCl_3$): -78.274; IR: 908, 1187, 1227, 1368, 1536, 2932, 3056, 3372; MS (ESI) M+1: 410.1

Specific rotation $[\alpha]^{20}_D$ - 52.33 (c = 0.34, CH_2Cl_2)



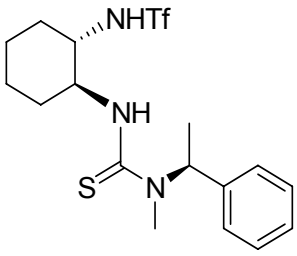
1, 1, 1-trifluoro-N-((1S, 2S)-2-(3-((S)-1-phenylethyl)thioureido)cyclohexyl) methane sulfonamide

Colourless oil; ^{1}H NMR (400MHz, $CDCl_3$):7.36-7.19 (m, 5H), 6.40(s, 1H), 5.38(s, 1H), 4.74(s, 1H), 4.34(s, 1H), 2.95(m, 1H), 2.1-2.06(m, 1H), 1.93-1.91(m, 1H), 1.69-1.09(m, 10H); ^{13}C NMR (100.62MHz, $CDCl_3$): 182.06, 141.68, 129.54, 128.42, 125.83, 121.19,118, 61.99, 56.57, 54.55, 34.32, 32.66, 24.56-24.13; ^{19}F NMR (188.295 MHz, $CDCl_3$): -77.993; IR: 908, 1187, 1227, 1368, 1536, 2932, 3056, 3372; MS (ESI) M+1: 410.1; Specific rotation $[\alpha]^{20}_{D}$ - 16 (c = 0.35, CH_2Cl_2)



1, 1, 1-trifluoro-N-((1S,2S)-2-(3-methyl-3-((R)-1-phenylethyl)thioureido)cyclohexyl) methane sulfonamide

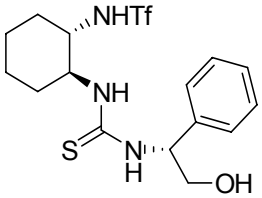
Colourless oil**;** ^{1}H NMR (400MHz, $CDCl_3$): 7.30-7.23 (m, 5H), 6.73(s, 1H), 4.76-4.66 (m, 1H), 3.68-3.63 (m, 1H), 3.26-3.19(m, 1H), 2.87(s, 3H), 2.18-2.13(m, 1H), 2.06-2.03(m, 1H), 1.75(m, 2H), 1.54-1.15(m, 10H)**;** ^{13}C NMR (100.62MHz, $CDCl_3$): 182.0, 139.6, 128.7, 127.7, 127.0, 121.3, 118.1, 62.1, 58.4, 58.3, 34.3, 33.0, 31.1, 29.7, 18.4, 15.7**;** ^{19}F NMR (188.295 MHz, $CDCl_3$): -78.289**;** IR: 908, 1187, 1227, 1368, 1536, 2932, 2944, 3056, 3385**;** MS (ESI) M+1: 424.1; Specific rotation $[\alpha]^{20}_{D}$ - 106.1 (c = 0.34, CH_2Cl_2).



1, 1, 1-trifluoro-N-((1S,2S)-2-(3-methyl-3-((S)-1-phenylethyl)thioureido)cyclohexyl) methane sulfonamide

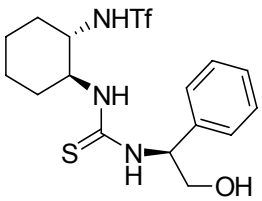
Colourless oil; ^{1}H NMR (400MHz, $CDCl_3$): 7.30-7.19(m, 5H), 6.71(s, 1H), 5.33-5.31(m, 1H), 4.79-4.70(m, 1H), 3.24-3.17(m, 1H),

2.67(s, 1H), 2.17-2.13(m, 1H), 2.05-2.03(m, 1H), 1.75-1.72(m, 2H), 1.56-1.05(m, 10H); ^{13}C NMR (100.62MHz, $CDCl_3$): 182.0, 140.0, 128.7, 127.6, 127.0, 121.45, 118.3, 62.8, 58.6, 57.1, 34.7, 32.9, 24.8-24.5, 15.2; ^{19}F NMR (188.295 MHz, $CDCl_3$): -77.861; IR: 908, 1187, 1227, 1368, 1536, 2932, 2944, 3056, 3385; MS (ESI) M+1: 424.1. Specific rotation $[\alpha]^{20}_D$ + 40 (c = 0.57, CH_2Cl_2).



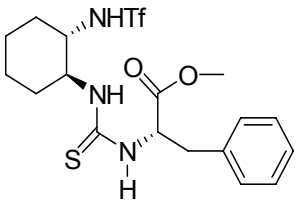
1, 1, 1-trifluoro-N-((1S, 2S)-2-(3-((R)-2-hydroxy-1-phenylethyl)thioureido)cyclohexyl)methane sulfonamide

Colourless oil; ^1H NMR (400MHz, $CDCl_3$): 7.65 (s, 1H), 7.30-7.19 (m, 5H), 6.39 (m, 1H), 4.33-4.29 (m, 1H), 3.86-3.51, (m, 5H), 1H), 3.17-3.11(m, 2H), 2.07-1.91 (m, 4H), 1.67-1.11 (m, 10H); ^{13}C NMR (100.62MHz, $CDCl_3$): 183.0, 129.1, 128.3, 126.7, 121.1, 118.0, 66.0, 60.6, 60.4, 56.9, 33.9, 32.3, 29.7, 24.5, 24.3; ^{19}F NMR (188.295 MHz, $CDCl_3$): -77.792; IR: 1370, 1450, 1539, 2861, 2937, 3057, 3372; MS (ESI) M+1: 426.1. Specific rotation $[\alpha]^{20}_D$ + -24.5 (c = 0.4, CH_2Cl_2).



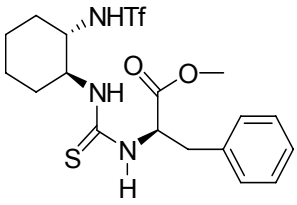
1, 1, 1-trifluoro-N-((1S, 2S)-2-(3-((S)-2-hydroxy-1-phenylethyl)thioureido)cyclohexyl)methane sulfonamide

Colourless oil; ^1H NMR (400MHz, $CDCl_3$): 7.62 (s, 1H), 7.33-7.23 (m, 5H), 5.85(s, 1H), 5.13 (s, 1H), 4.19 (s, 1H), 3.78-3.46 (m, 3H), 3.17-3.09 (m, 1H), 2.05-2.01 (m, 1H), 1.64-0.66 (m, 10H); ^{13}C NMR (100.62MHz, $CDCl_3$): 171.5, 129.2, 128.7, 128.6, 128.5, 126.7, 121.2, 118.1, 66.0, 60.8; 60.0, 57.7; 57.6, 33.8, 32.0, 29.7, 27.0, 24.5, 14.2; ^{19}F NMR (188.295 MHz, $CDCl_3$): -77.929; IR: 1370, 1450, 1539, 2861, 2937, 3057, 3372; MS (ESI) M+1: 426.1; Specific rotation $[\alpha]^{20}_D$ - 15.9 (c = 0.26, CH_2Cl_2).



(S)-Methyl-3-phenyl-2-(3-((1S, 2S)-2-(trifluoromethylsulfonamido)cyclohexyl)thioureido)Propanoate

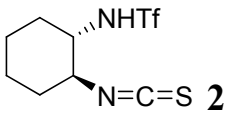
Colourless oil; ^{1}H NMR (400MHz, $CDCl_3$): 7.35-7.34 (m, 1H), 7.32-7.24 (m, 5H), 6.54 (s, 1H), 5.98 (s, 1H), 4.35-4.28 (m, 1H), 4.06-4.00 (m, 1H), 3.61 (s, 3H), 3.22-3.17 (m, 1H), 2.13-2.07 (m, 1H), 1.97 (s, 1H), 1.93-1.91 (m, 1H), 1.69-1.12 (m, 10H); ^{13}C NMR (100.62MHz, $CDCl_3$): 183.0, 172.0, 139.3, 129.3, 129.0, 128.1, 127.4, 124.5, 121.3, 118.2, 115.0, 62.1, 61.0, 60.7, 58.5, 56.3, 53.0, 34.2, 24.5; 24.3, 21.1, 18.2, 14.13; ^{19}F NMR (188.295 MHz, $CDCl_3$): -78.324; IR: 1147, 1189, 1227, 1371, 1535, 1722, 2856, 2941, 3048, 3368; MS (ESI) M+1: 454.1; Specific rotation $[\alpha]^{20}_{D}$ - 89.8 (c = 0.19, CH_2Cl_2).



(R)-Methyl-3-phenyl-2-(3-((1S, 2S)-2-(trifluoromethylsulfonamido)cyclohexyl)thioureido)Propanoate

Colourless oil; ^{1}H NMR (400MHz, $CDCl_3$): 7.33-7.28(m, 5H), 7.10-7.07 (m, 1H), 6.01 (s, 1H), 5.89 (s, 1H), 4.39-4.31 (m, 1H), 3.66 (s, 3H), 3.20-3.15 (m, 1H), 2.13-2.10 (m, 1H), 1.98-1.94 (m, 1H), 1.71-1.08 (m, 10H); ^{13}C NMR (100.62MHz, $CDCl_3$): 183.3, 171.7, 135.3, 129.1, 127.3, 121.3, 118.1, 61.8, 61.0, 60.6, 56.3, 53.1, 34.3, 32.2, 29.7, 26.9, 24.4; 24.3, 21.0, 14.1. ^{19}F NMR (188.295 MHz, $CDCl_3$): -78.269; IR: 1147, 1189, 1227, 1371, 1535, 1722, 2856, 2941, 3048, 3368. MS (ESI) M+1: 454.1; Specific rotation $[\alpha]^{20}_{D}$ + 28.0 (c = 0.35, CH_2Cl_2).

V. ^{1}H, ^{13}C and ^{19}F NMR spectra for 2 and for diastereoisomeric mixture of all thioureas



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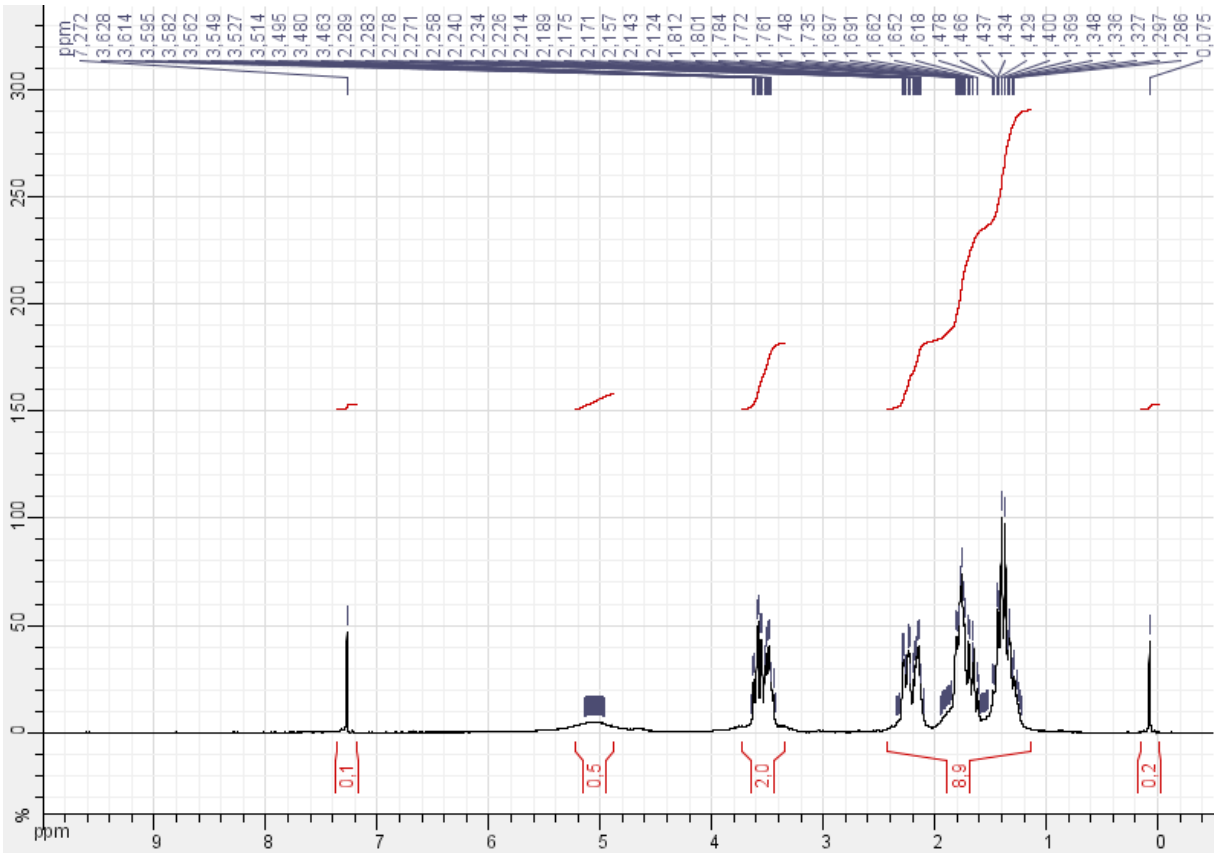

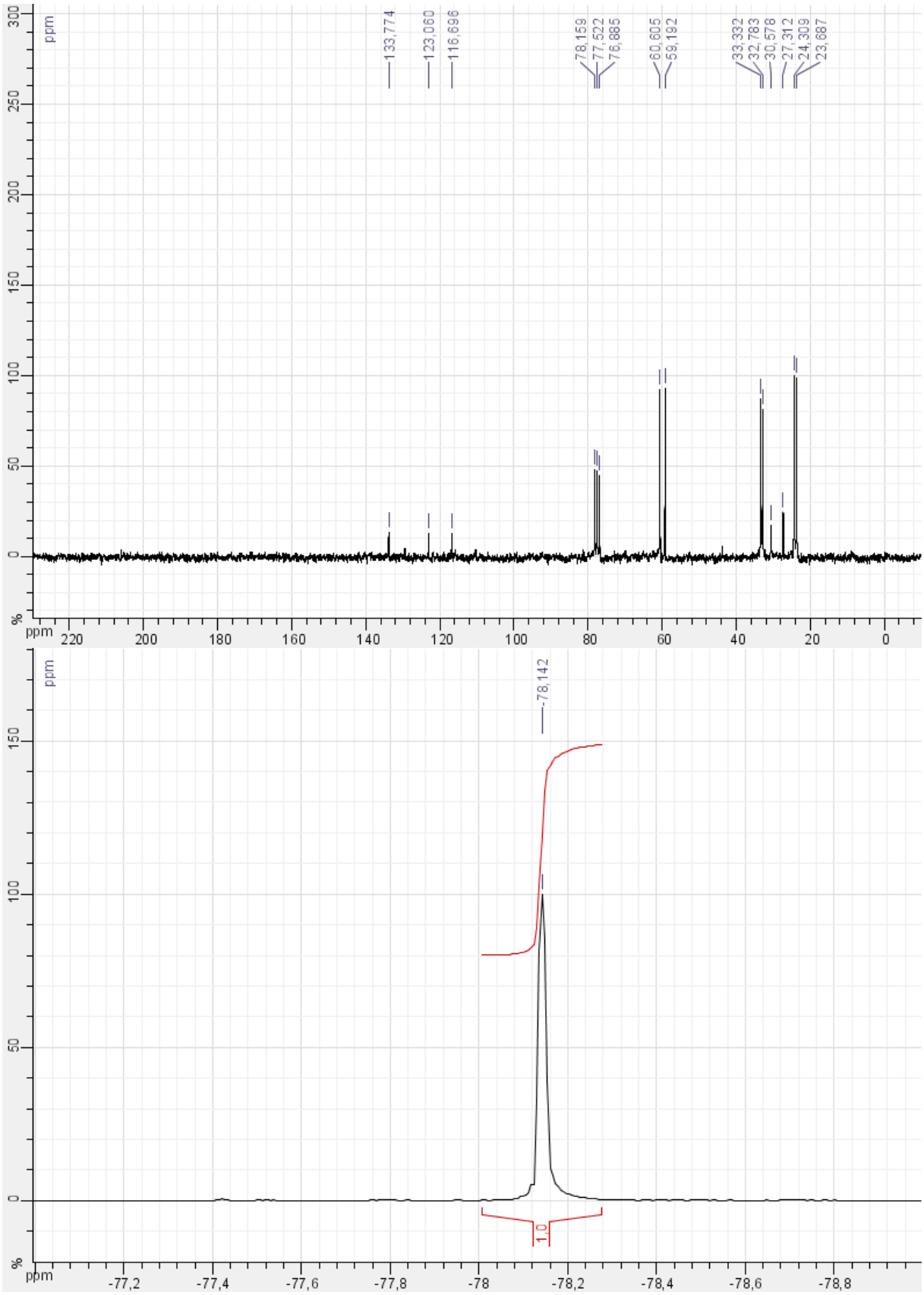

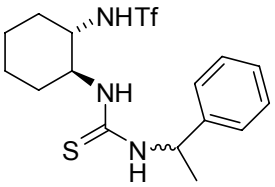
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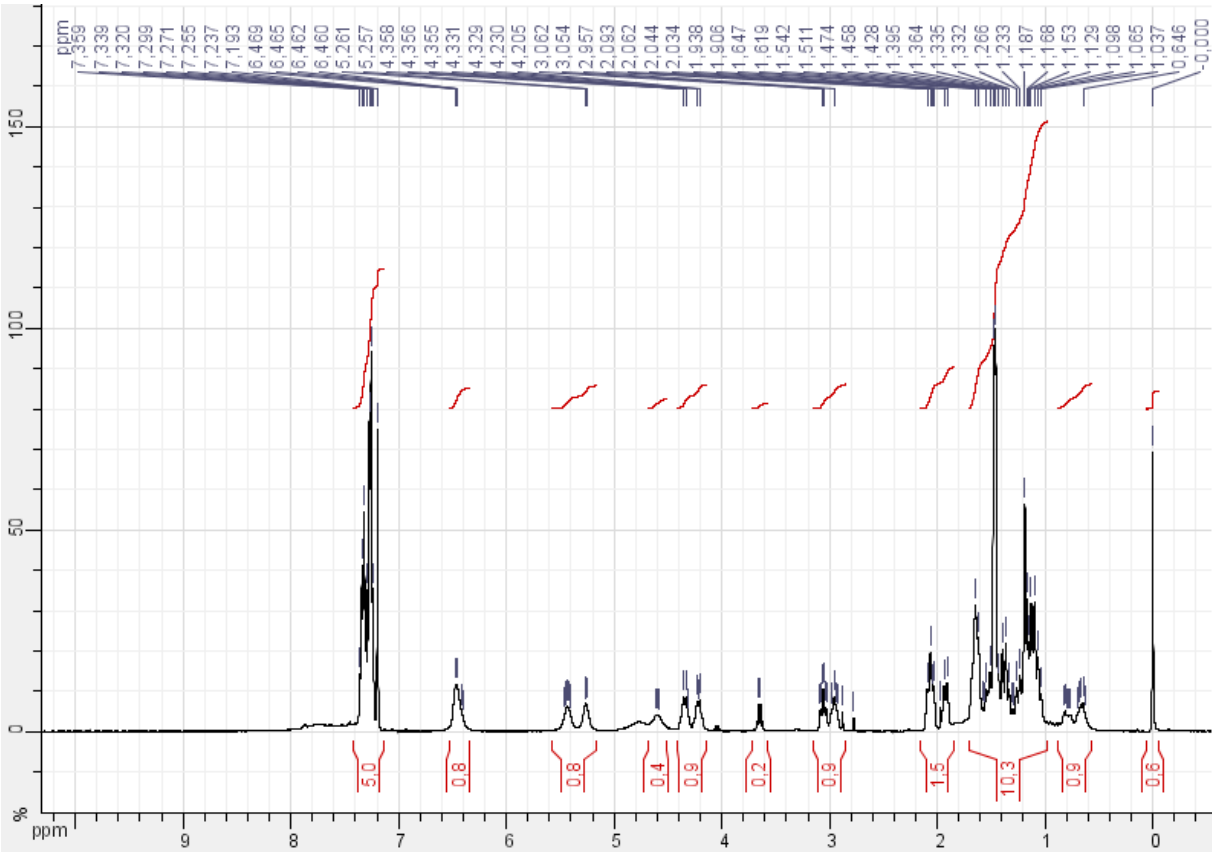
4a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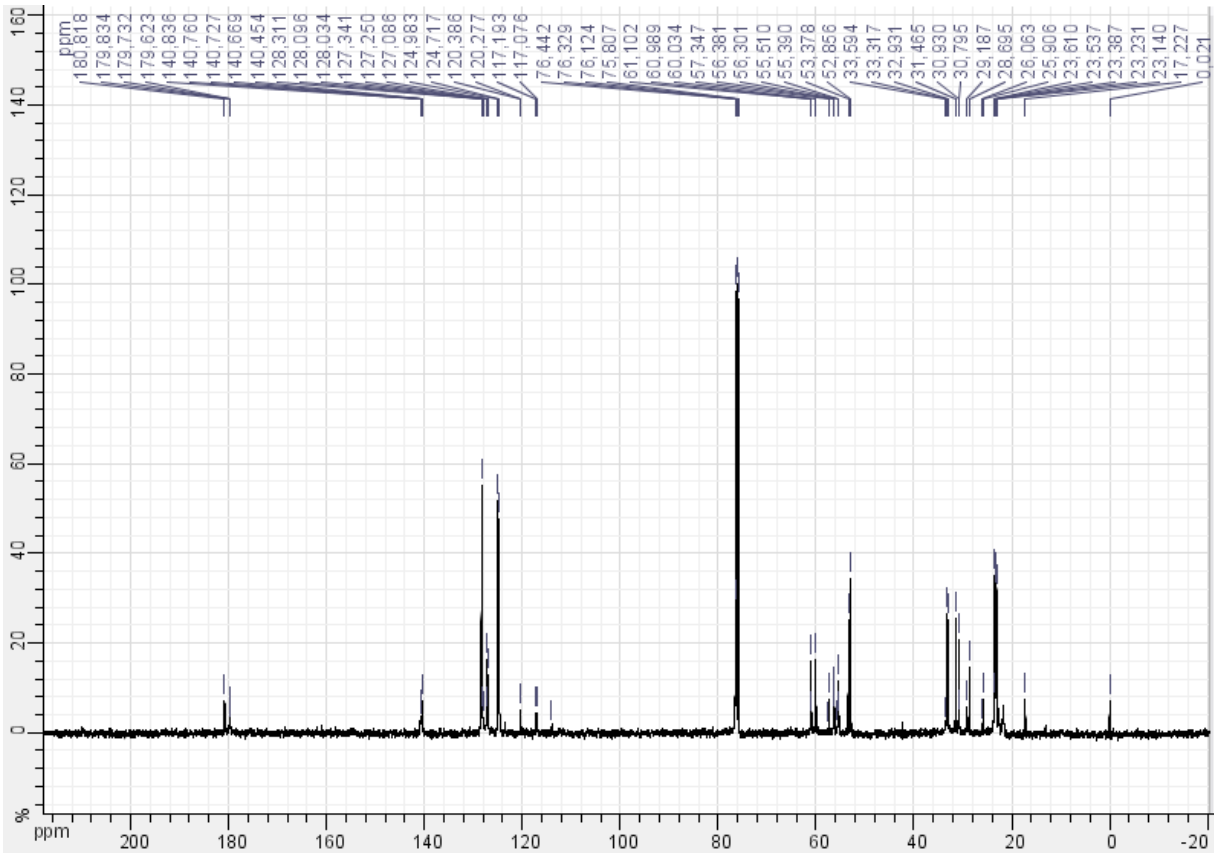
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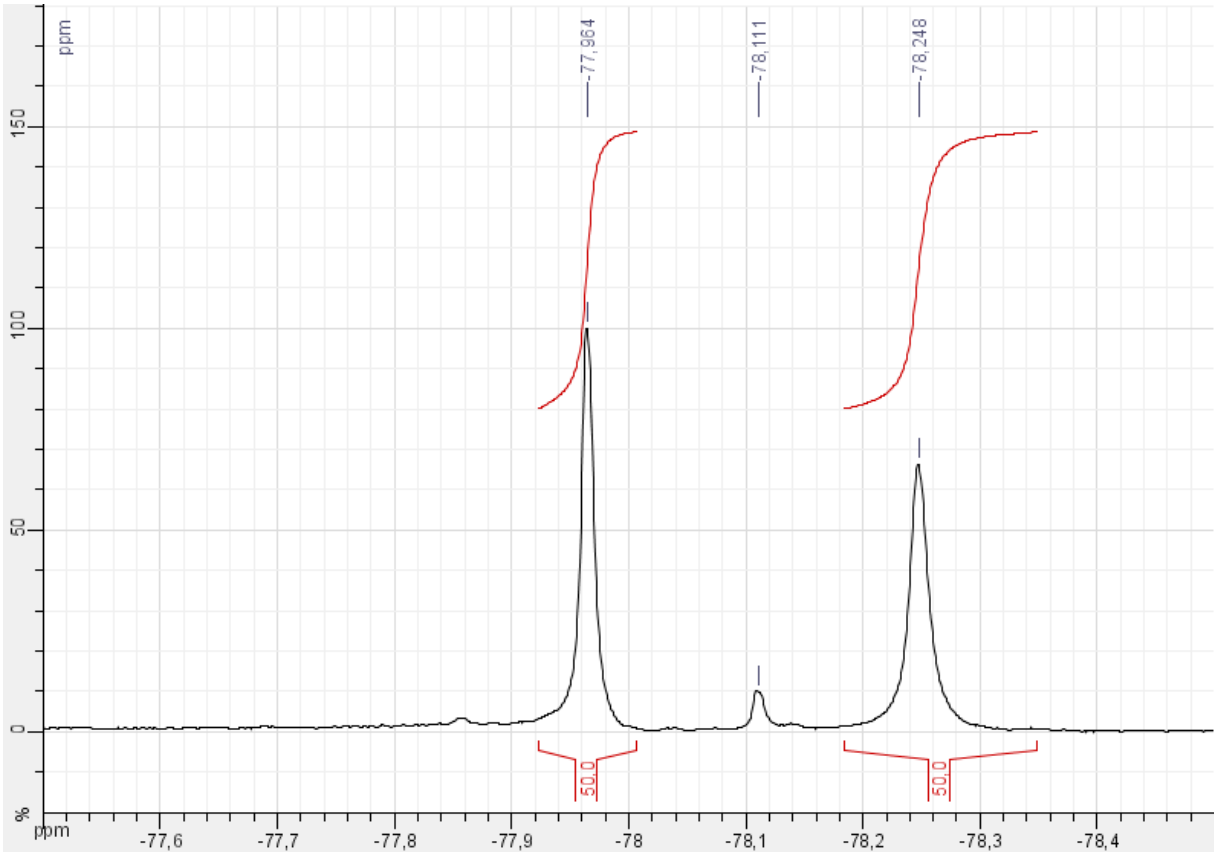
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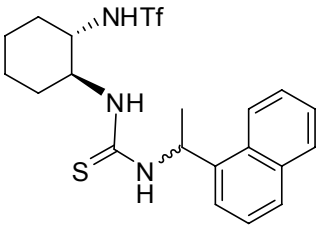
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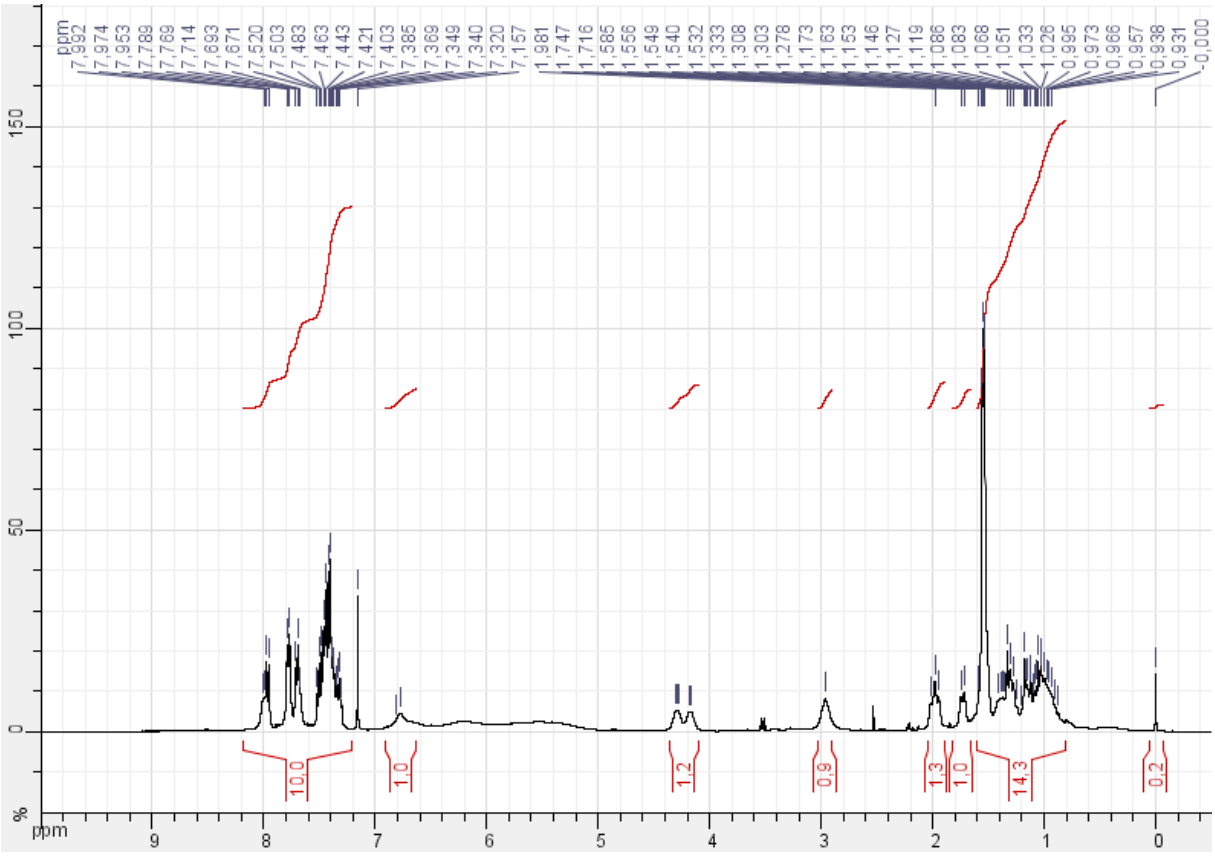
4b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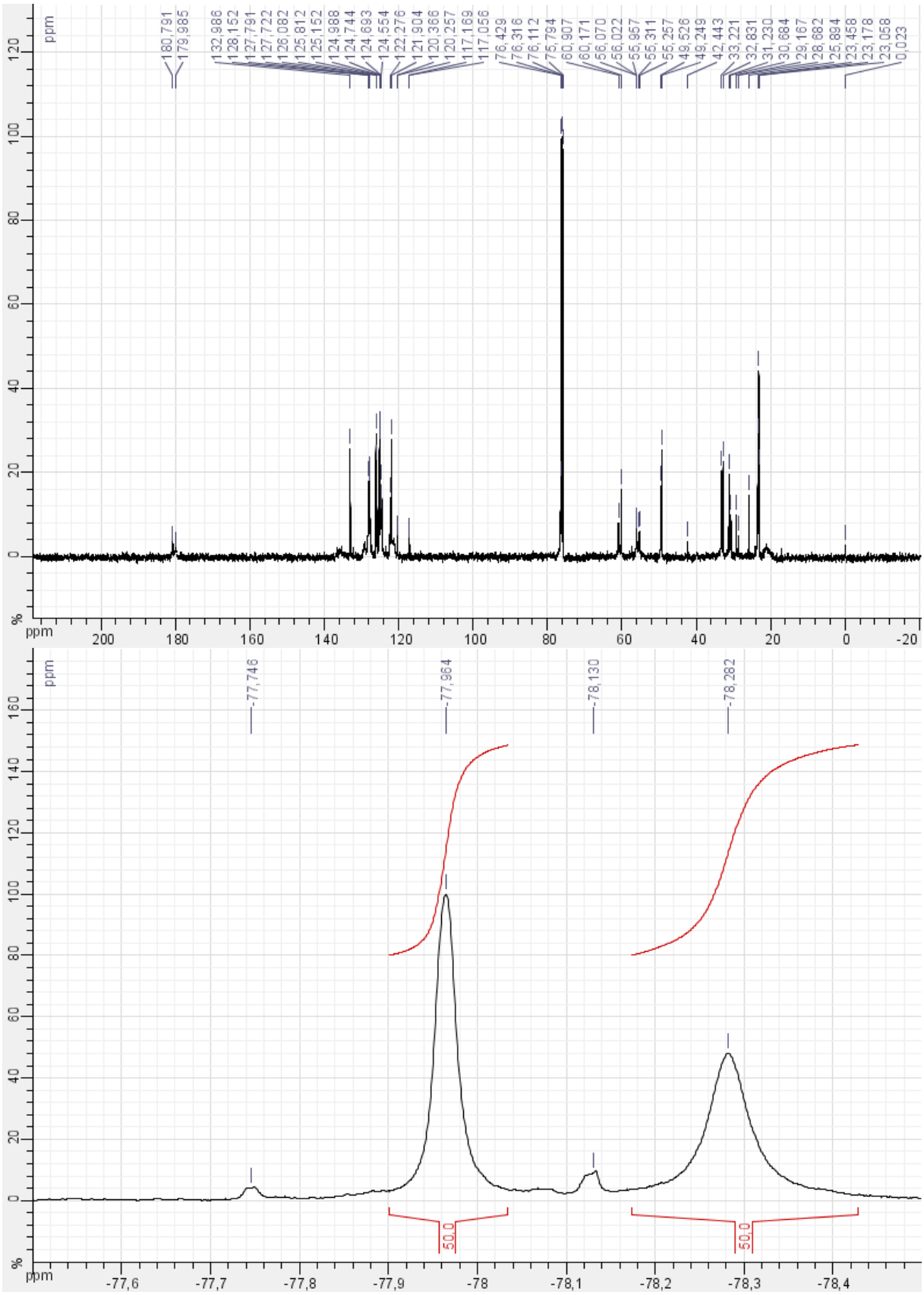
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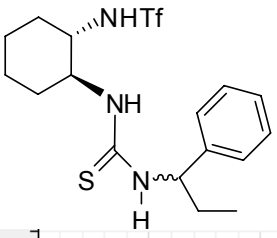
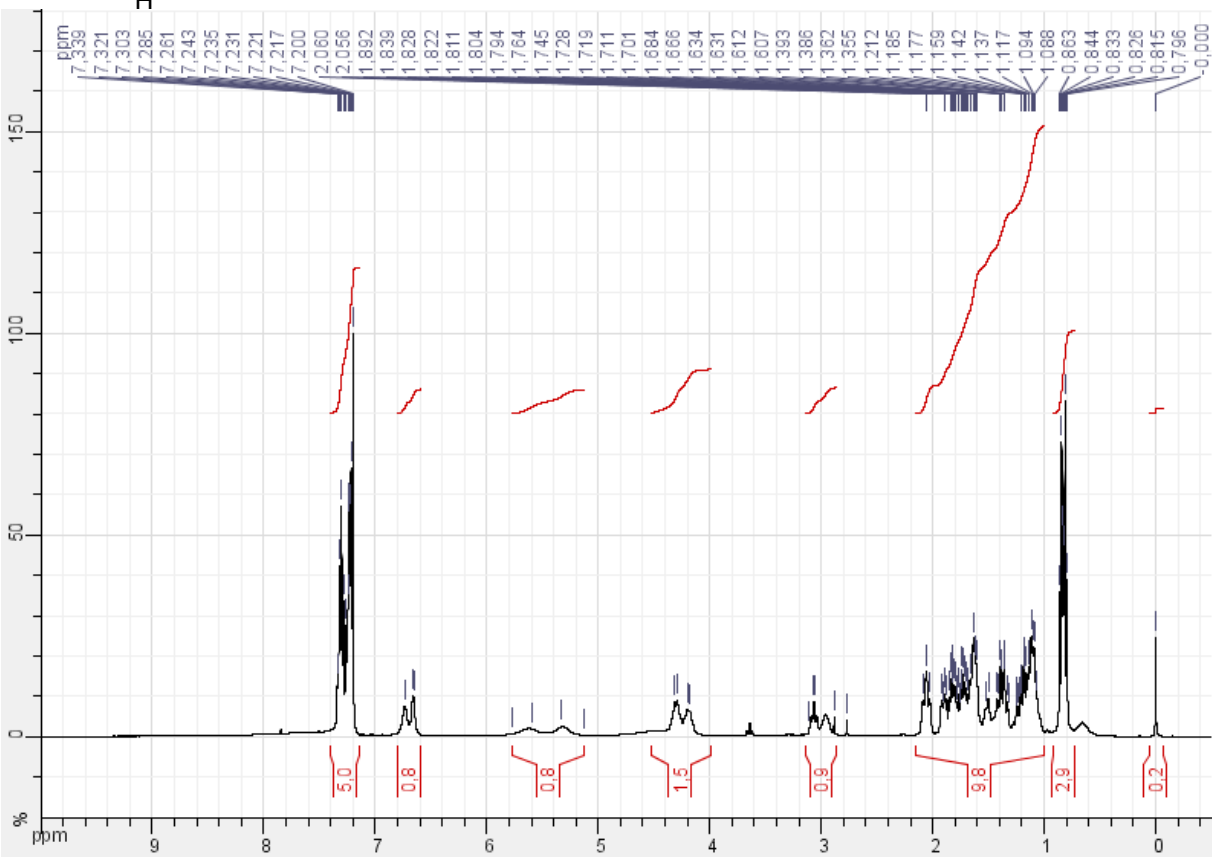
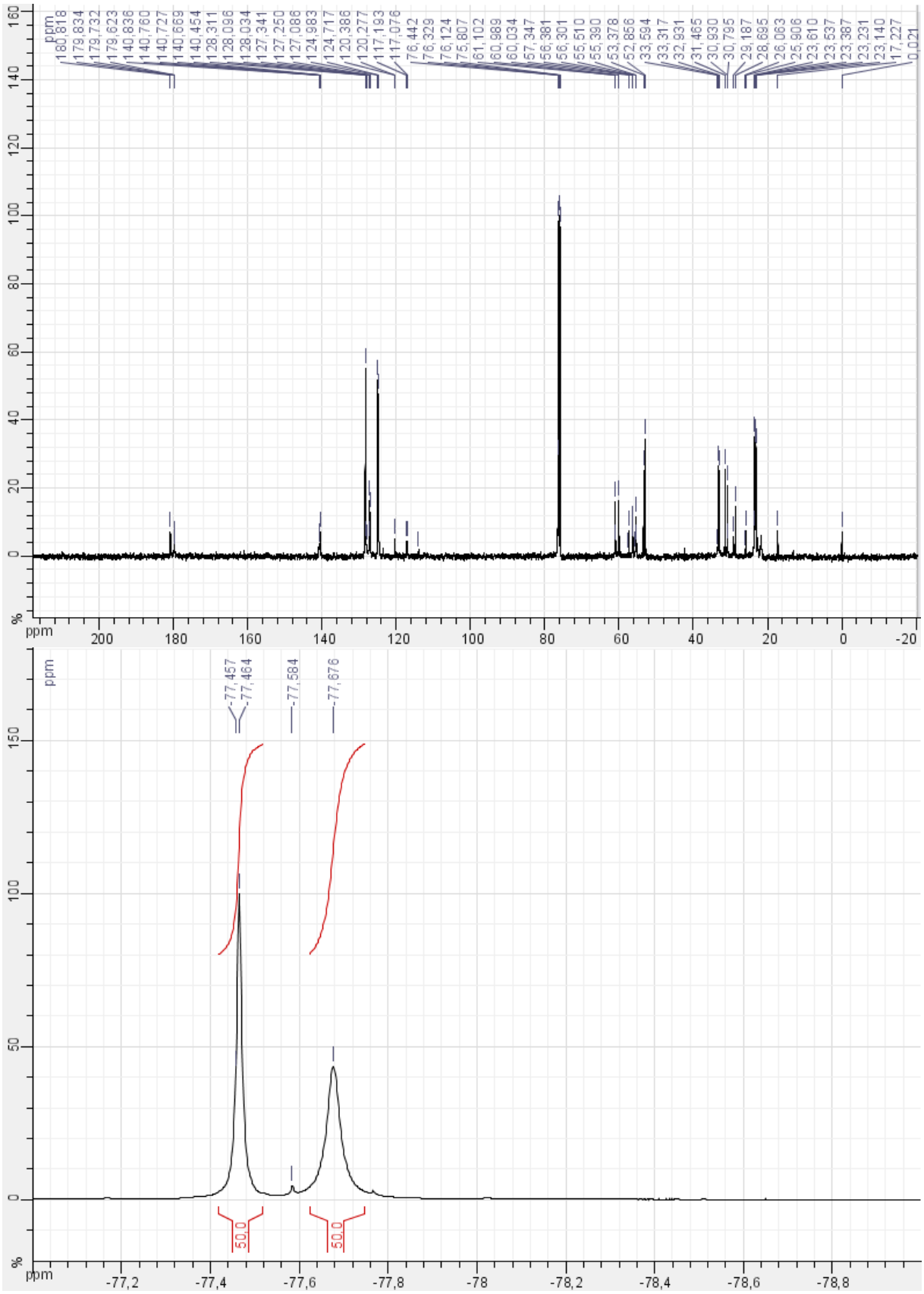


4c

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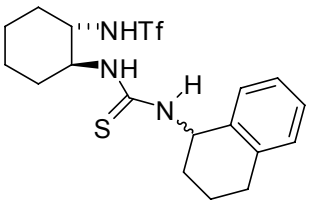
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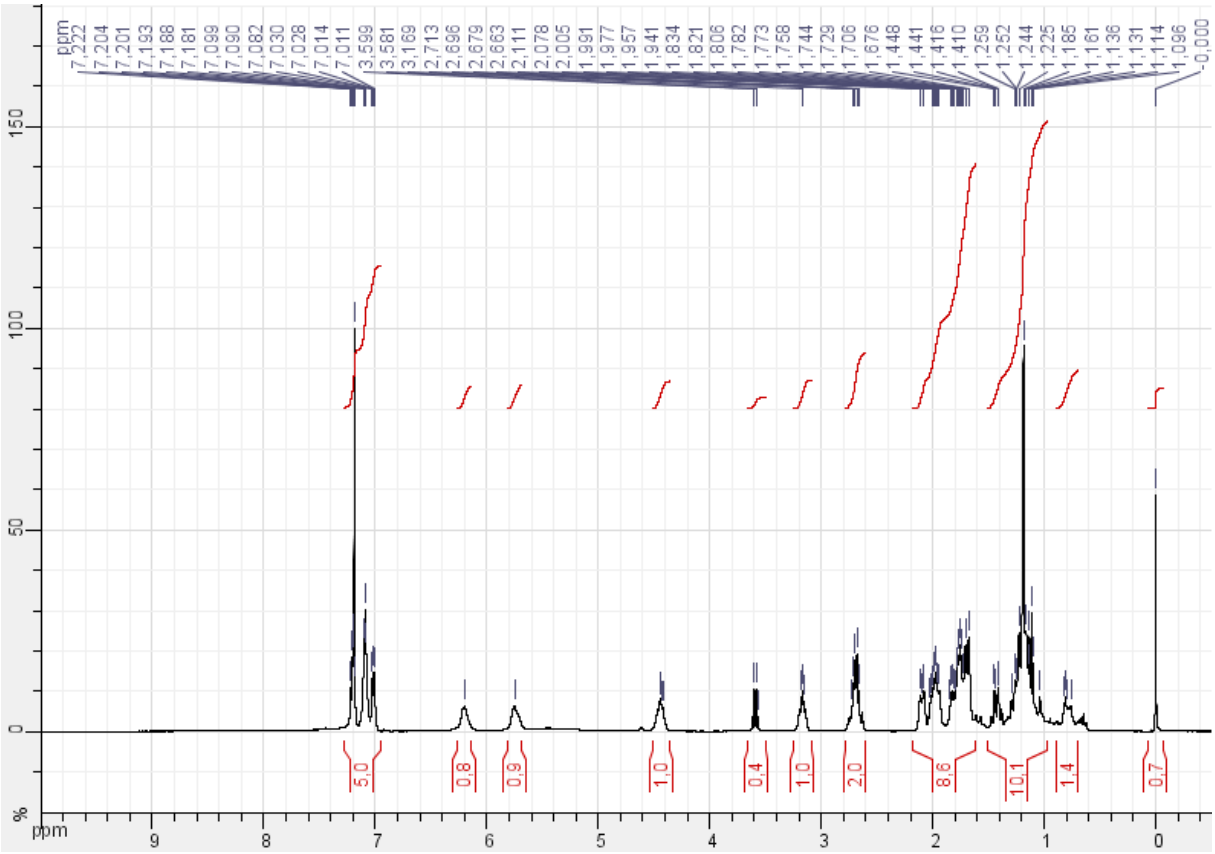
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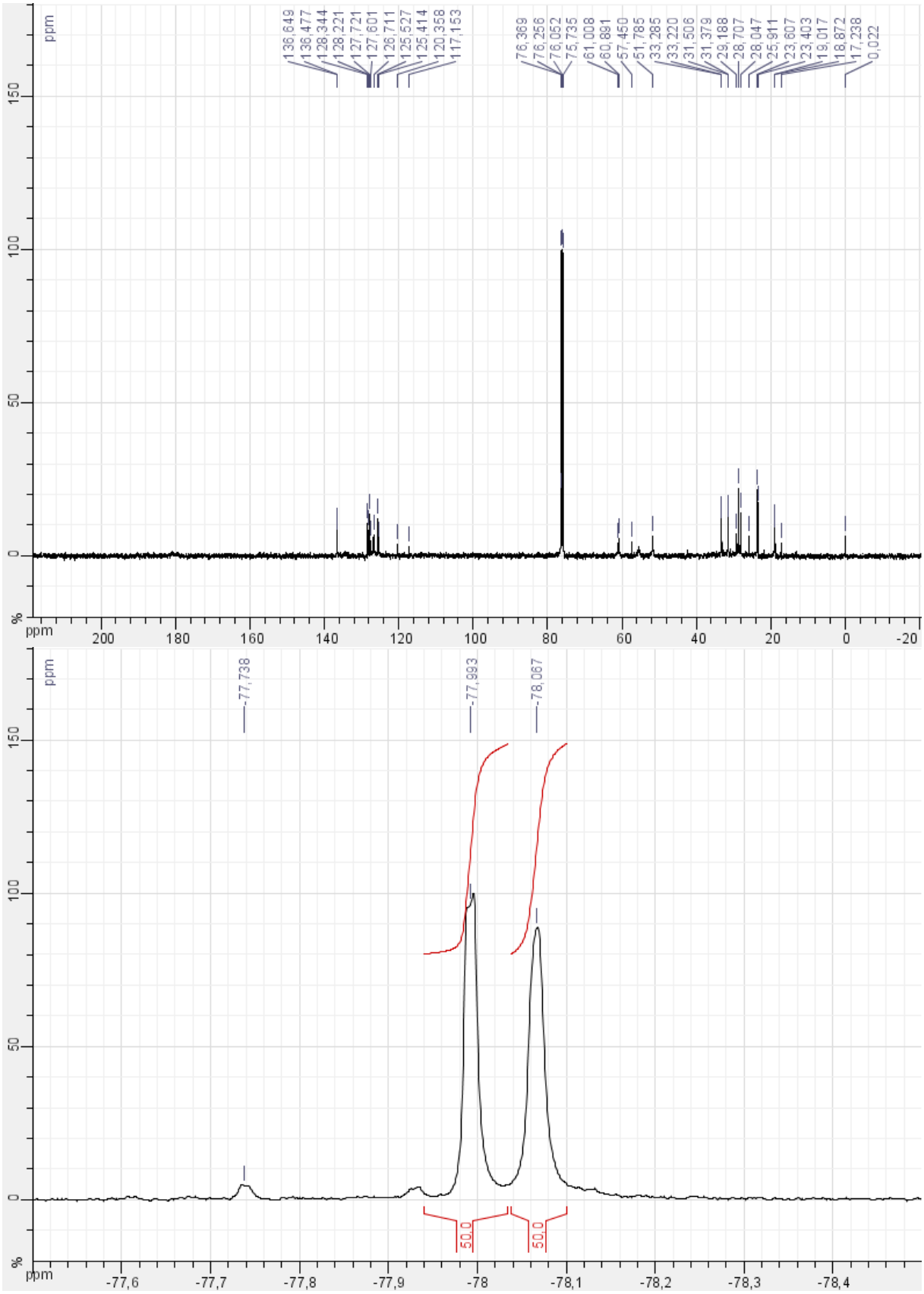
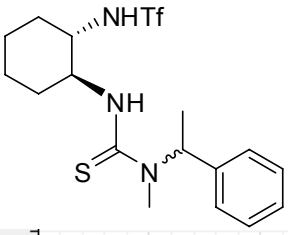
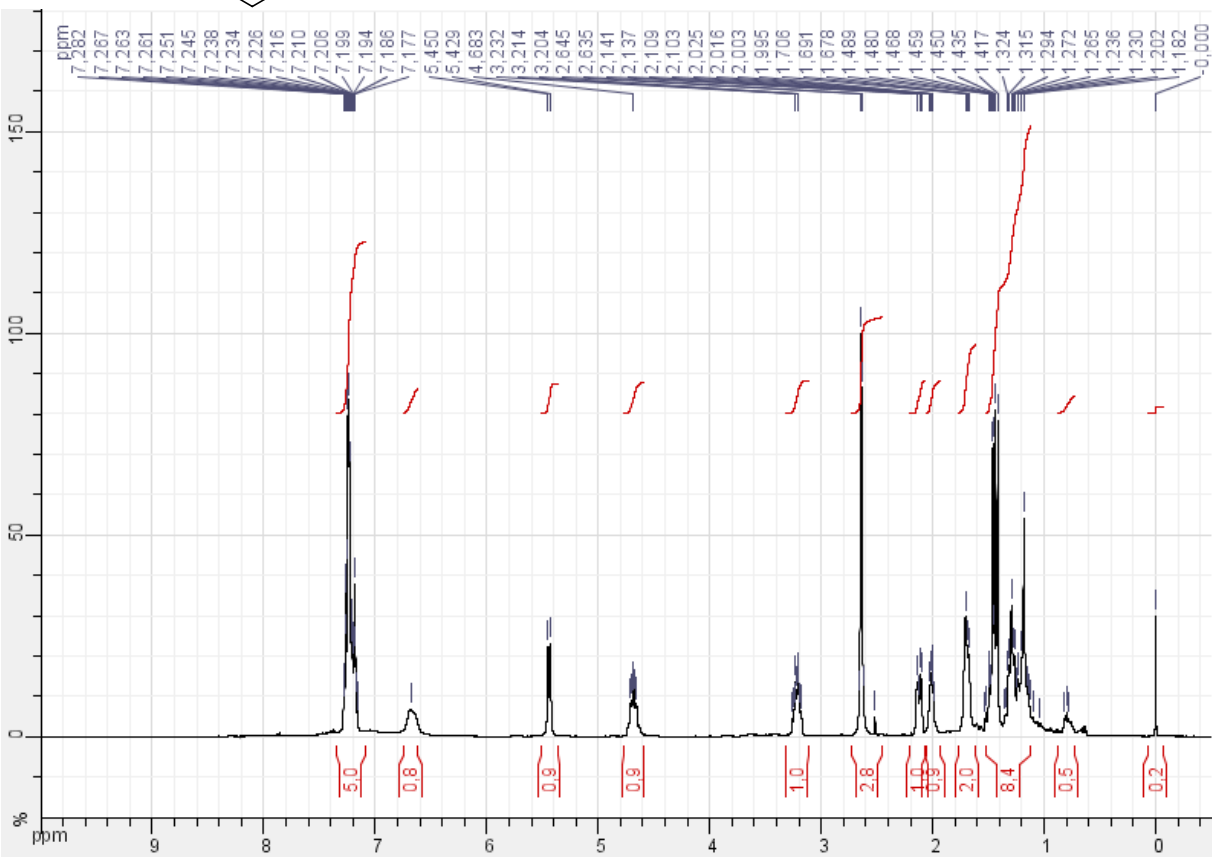
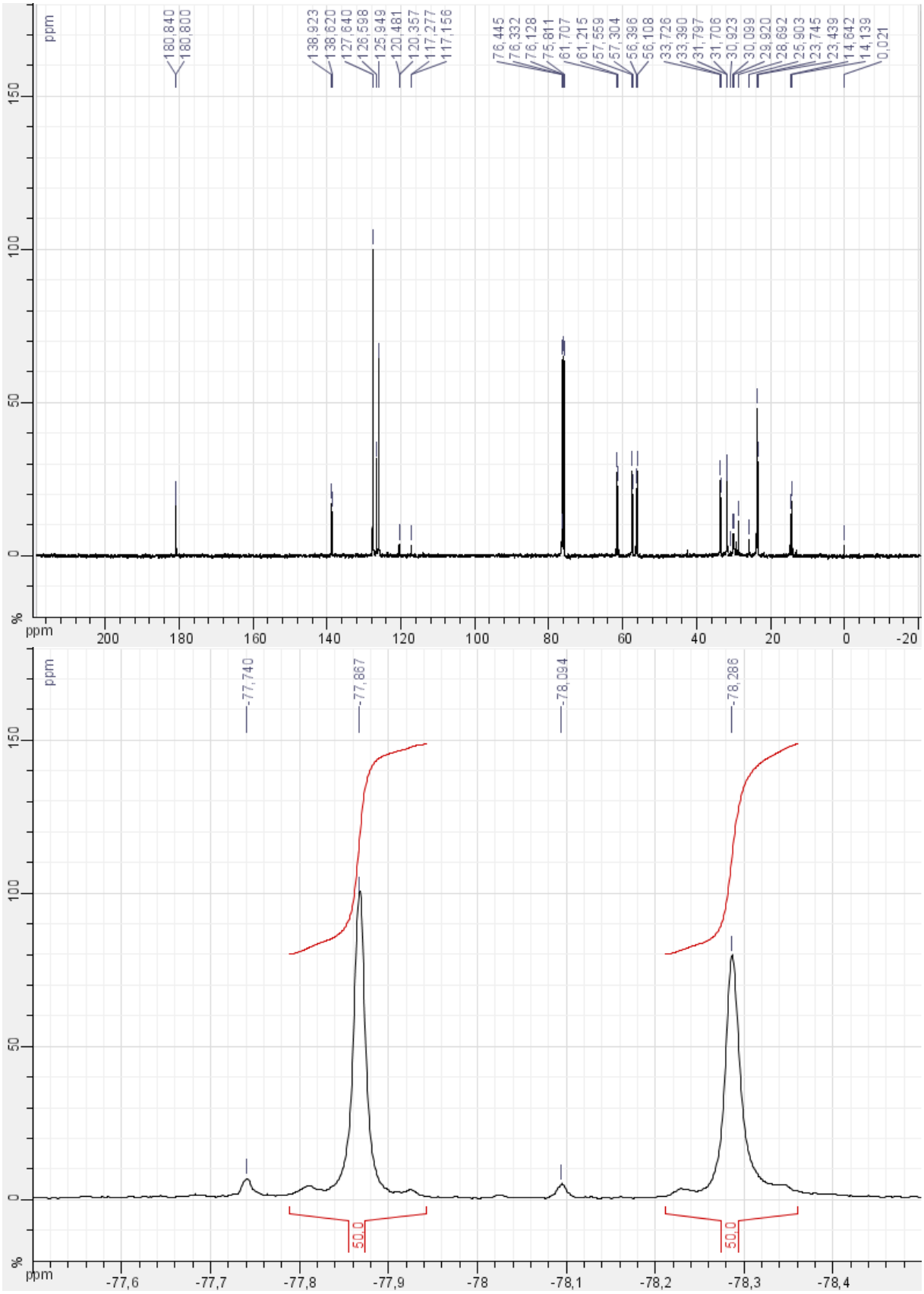
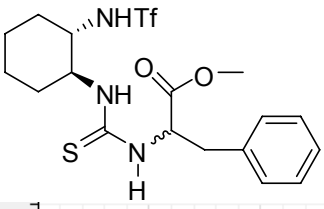

ppm
136,649
136,477
128,344
128,221
127,721
127,601
126,711
125,527
125,414
120,358
117,153
76,369
76,256
76,052
75,735
61,008
60,891
57,450
51,785
33,285
33,220
31,506
31,379
29,188
28,707
28,047
25,911
23,607
23,403
19,017
18,872
17,238
0,022
%
150
100
50
0
200
180
160
140
120
100
80
60
40
20
0
-20
-77,738
-77,993
-78,067
50,0
50,0
-77,6
-77,7
-77,8
-77,9
-78
-78,1
-78,2
-78,3
-78,4


NHTf
NH
S
N

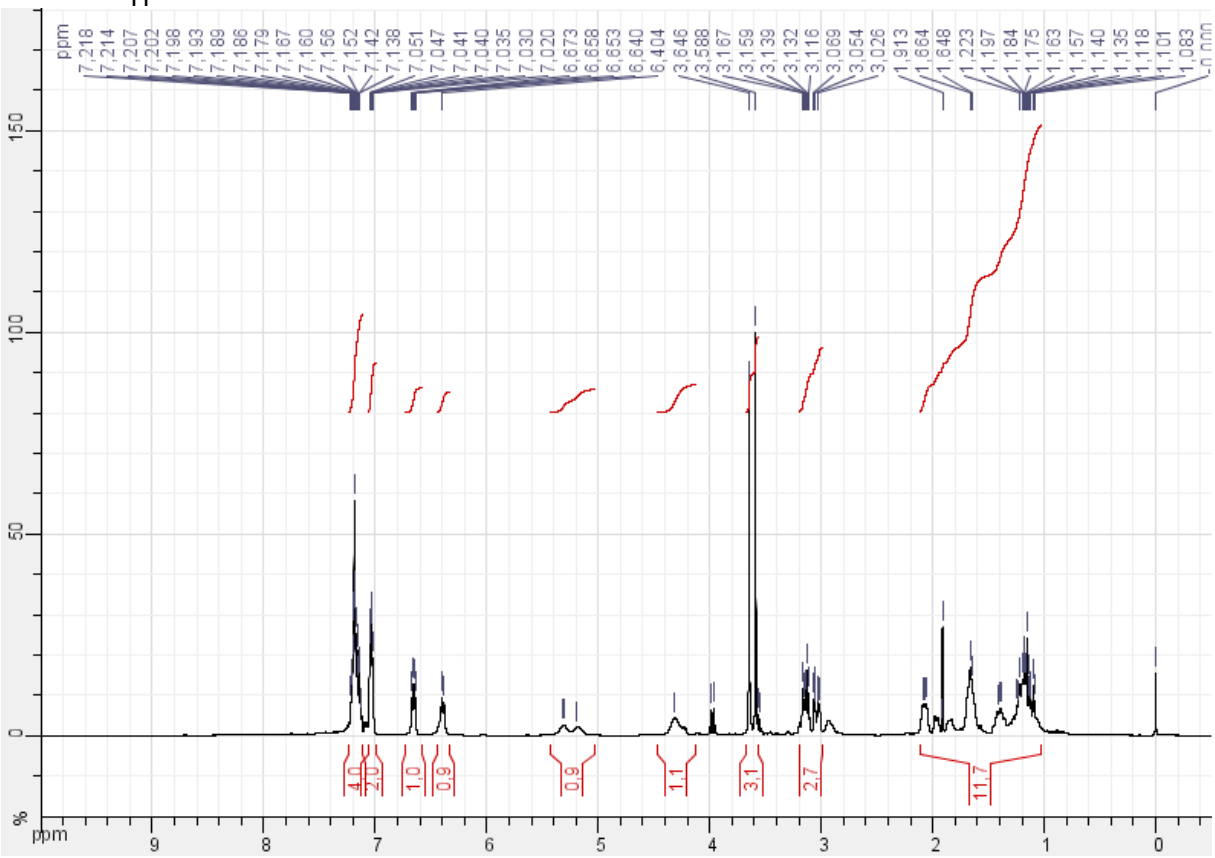
4e

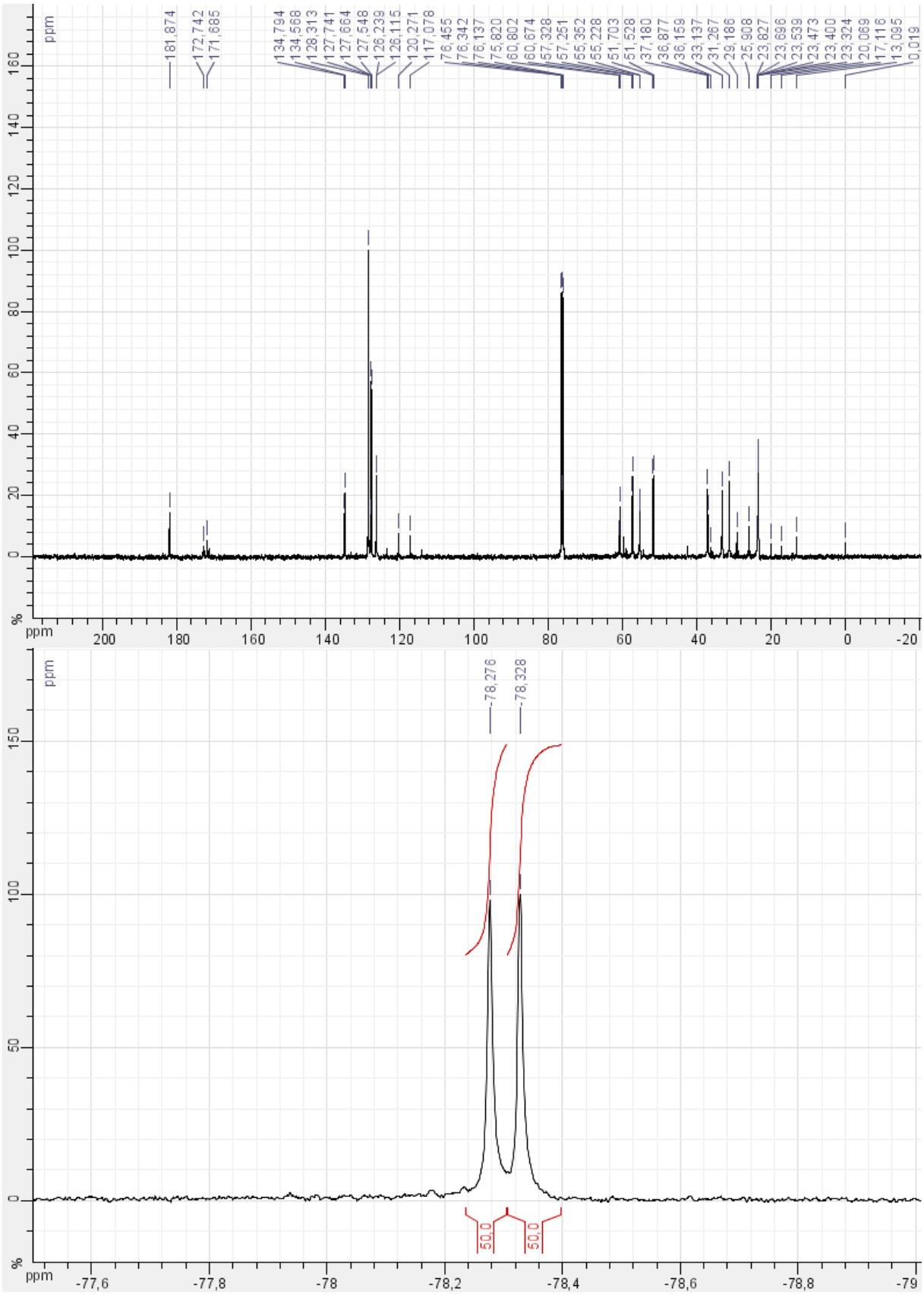

ppm
7,282
7,267
7,263
7,261
7,251
7,245
7,238
7,234
7,226
7,216
7,210
7,206
7,199
7,194
7,186
7,177
5,450
5,429
4,683
3,232
3,214
3,204
2,645
2,635
2,141
2,137
2,109
2,103
2,025
2,016
2,003
1,995
1,706
1,691
1,678
1,489
1,480
1,468
1,459
1,450
1,435
1,417
1,324
1,315
1,294
1,272
1,265
1,236
1,230
1,202
1,182
0,000
150
100
50
0
%
ppm
9
8
7
6
5
4
3
2
1
0
5,0
0,8
0,9
0,9
1,0
2,8
1,0
0,9
2,0
8,4
0,5
0,2

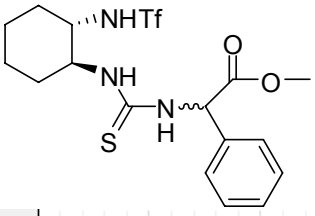

ppm
180,840
180,800
138,923
138,620
127,640
126,598
125,949
120,481
120,357
117,277
117,156
76,445
76,332
76,128
75,811
61,707
61,215
57,559
57,304
56,396
56,108
33,726
33,390
31,797
31,706
30,923
30,099
29,920
28,692
25,903
23,745
23,439
14,642
14,139
0,021
%
150
100
50
0
200
180
160
140
120
100
80
60
40
20
0
-20
-77,740
-77,867
-78,094
-78,286
50,0
50,0
-77,6
-77,7
-77,8
-77,9
-78
-78,1
-78,2
-78,3
-78,4


NHTf
O
O
NH
S
N
H

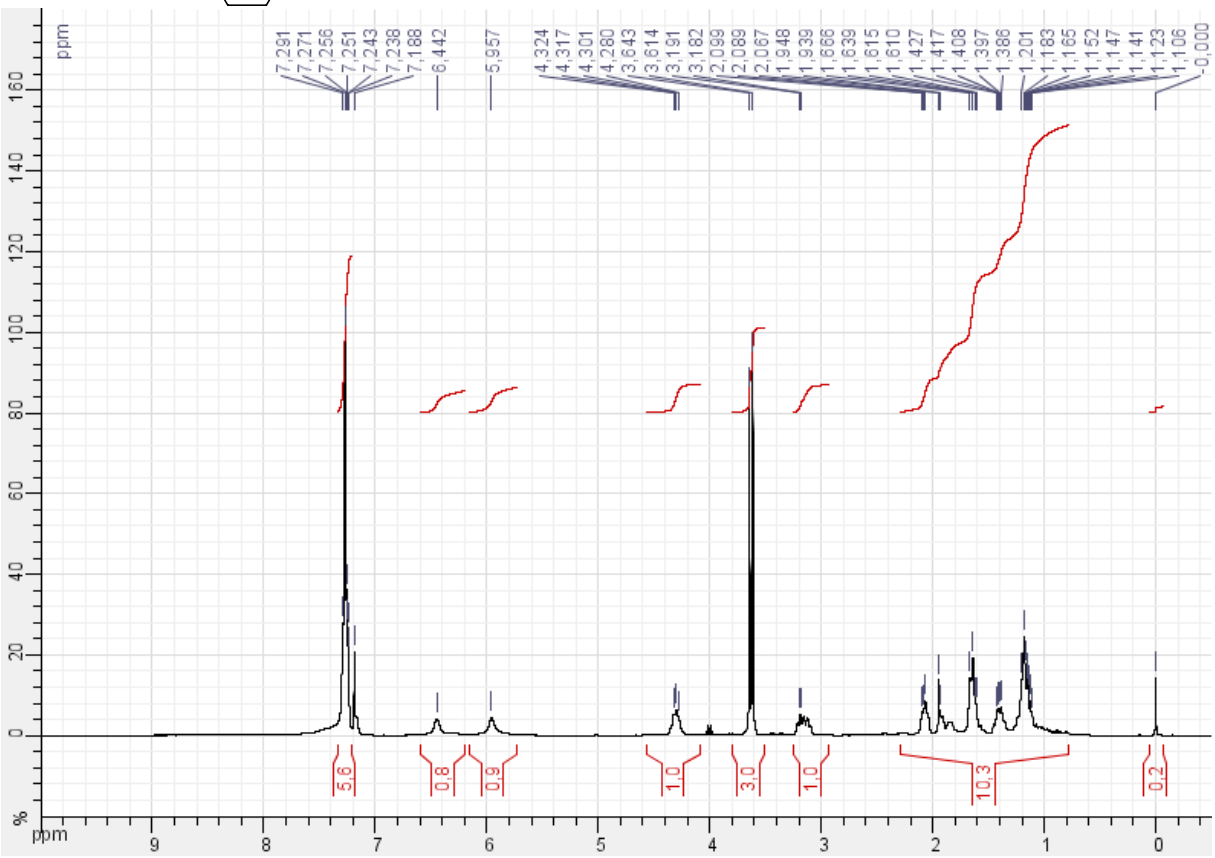
4f

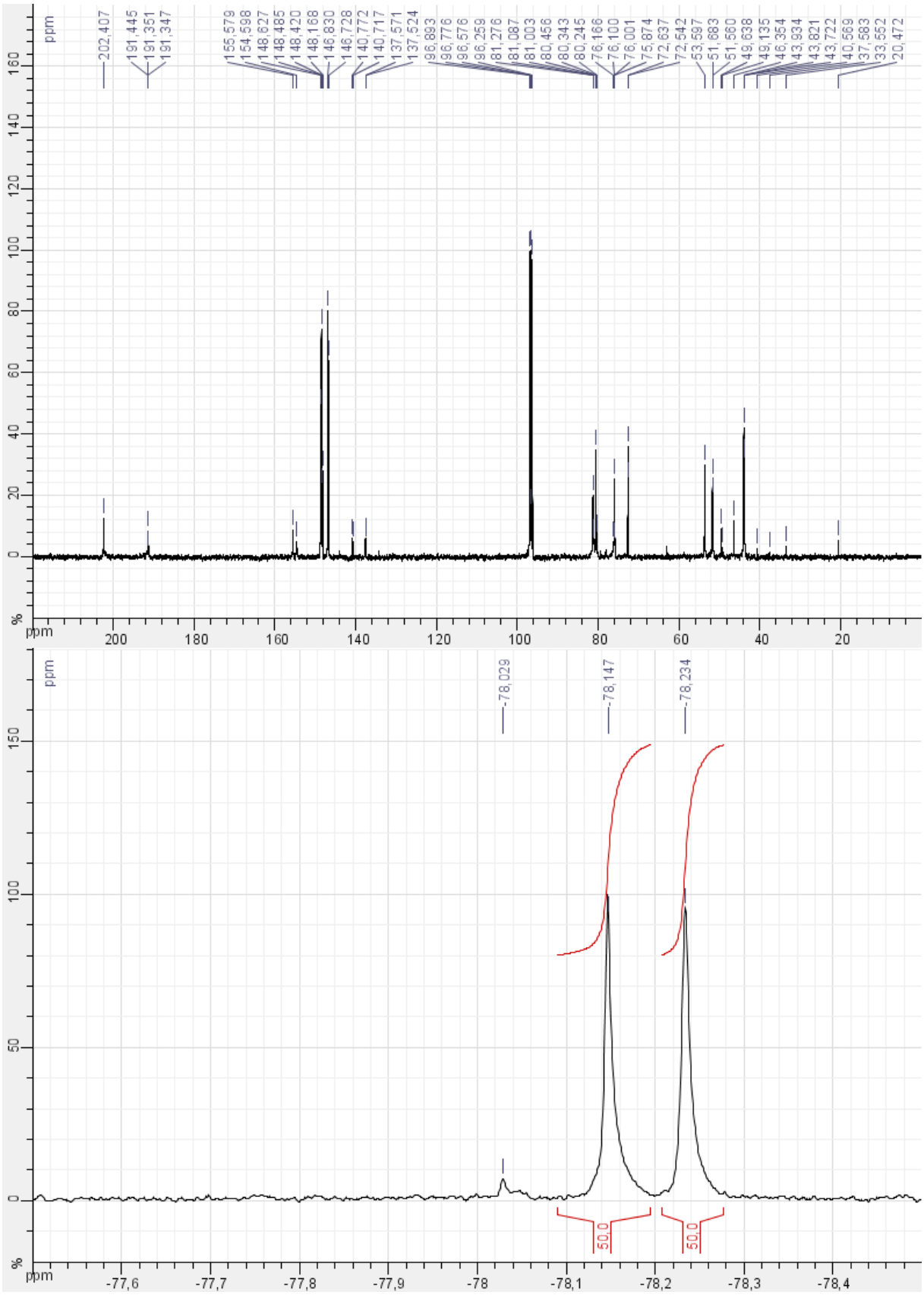

ppm
7.218
7.214
7.207
7.202
7.198
7.193
7.189
7.186
7.179
7.167
7.160
7.156
7.152
7.142
7.138
7.051
7.047
7.041
7.040
7.035
7.030
7.020
6.673
6.658
6.653
6.640
6.404
3.646
3.588
3.167
3.159
3.139
3.132
3.116
3.069
3.054
3.026
1.913
1.664
1.648
1.223
1.197
1.184
1.175
1.163
1.157
1.140
1.135
1.118
1.101
1.083
150
100
50
0
%
4.0
2.0
1.0
0.9
0.9
1.1
3.1
2.7
11.7
ppm
9
8
7
6
5
4
3
2
1
0

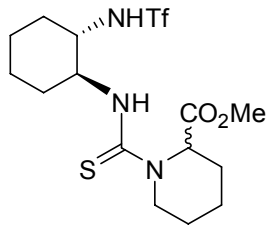

ppm
181,874
172,742
171,685
134,794
134,568
128,313
127,741
127,664
127,548
126,239
126,115
120,271
117,078
76,455
76,342
76,137
75,820
60,802
60,674
57,328
57,251
55,352
55,228
51,703
51,528
37,180
36,877
36,159
33,137
31,267
29,186
25,908
23,827
23,696
23,539
23,473
23,400
23,324
20,069
17,116
13,095
0,019
%
ppm
200
180
160
140
120
100
80
60
40
20
0
-20
ppm
-78,276
-78,328
50,0
50,0
%
ppm
-77,6
-77,8
-78
-78,2
-78,4
-78,6
-78,8
-79



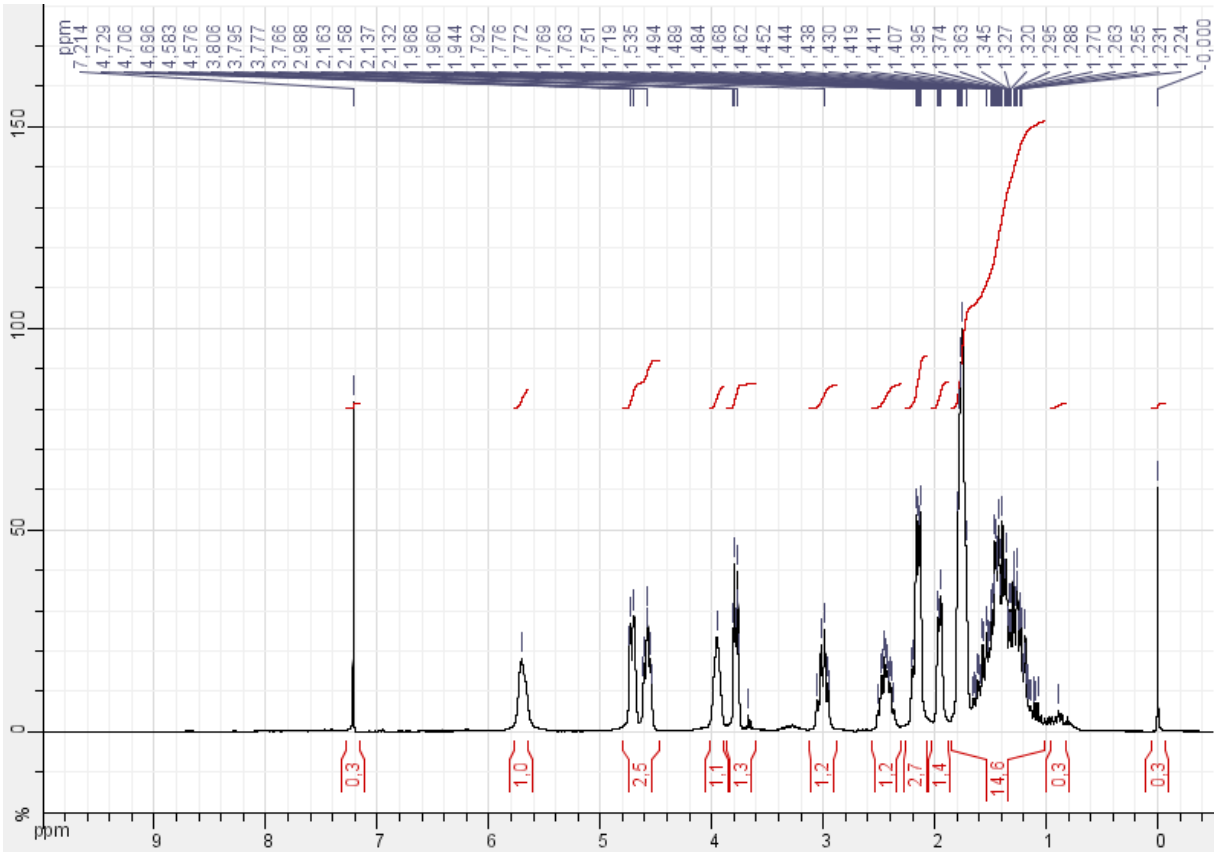
4g

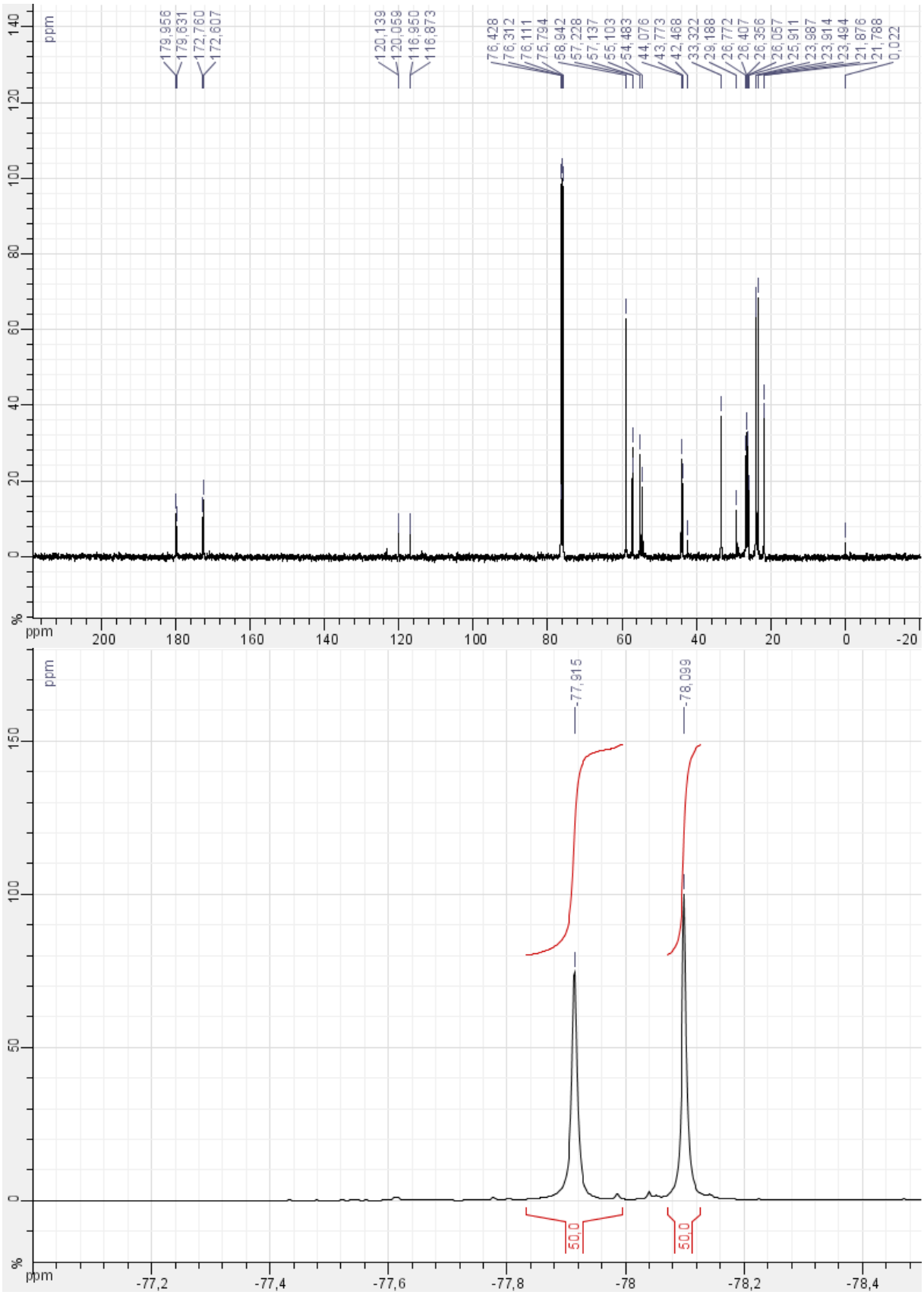


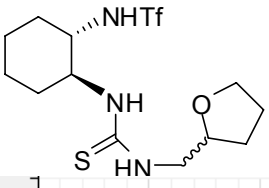

ppm
202,407
191,445
191,351
191,347
155,579
154,598
148,627
148,485
148,420
148,168
146,830
146,728
140,772
140,717
137,571
137,524
96,893
96,776
96,576
96,259
81,276
81,087
81,003
80,456
80,343
80,245
76,166
76,100
76,001
75,874
72,637
72,542
53,597
51,683
51,560
49,638
49,135
46,354
43,934
43,821
43,722
40,569
37,583
33,552
20,472
%
ppm
200
180
160
140
120
100
80
60
40
20
ppm
-78,029
-78,147
-78,234
50,0
50,0
%
ppm
-77,6
-77,7
-77,8
-77,9
-78
-78,1
-78,2
-78,3
-78,4


NHTf
NH
CO2Me
S
N

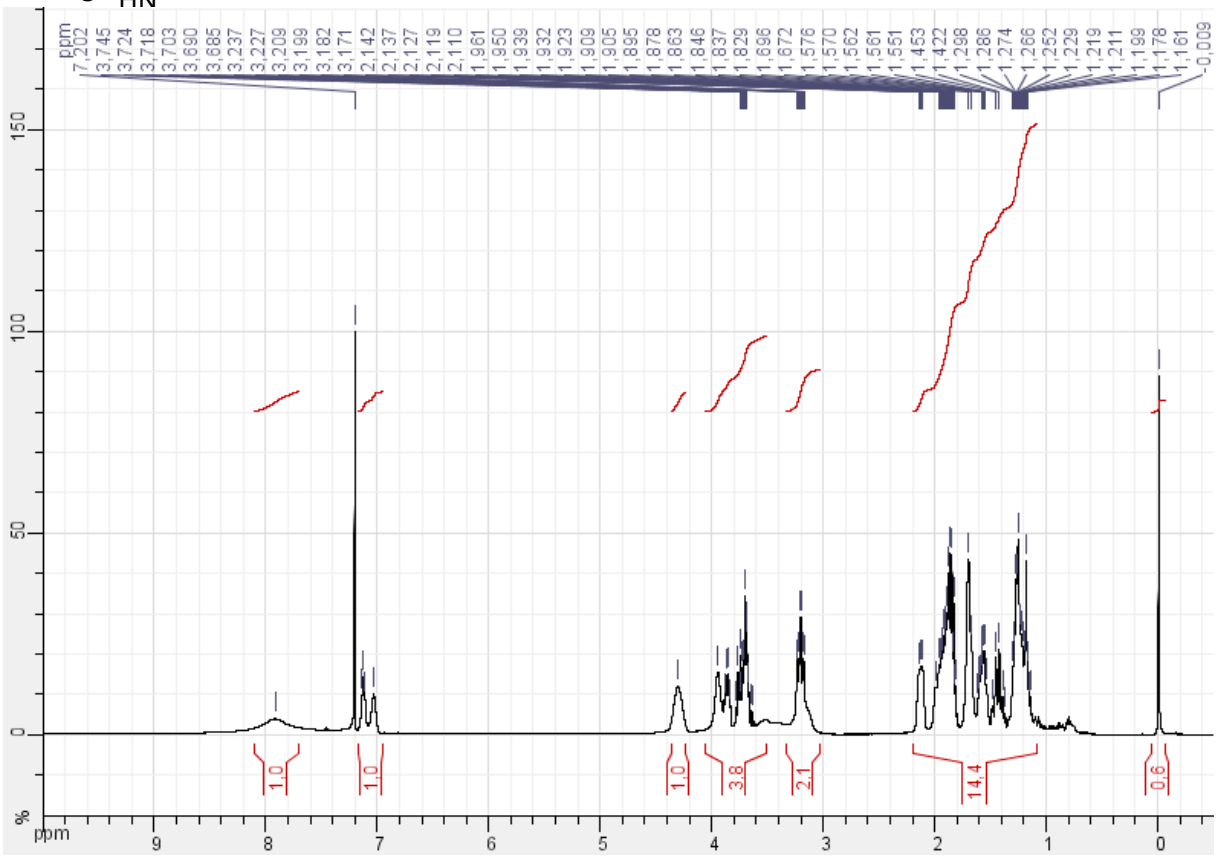
4h

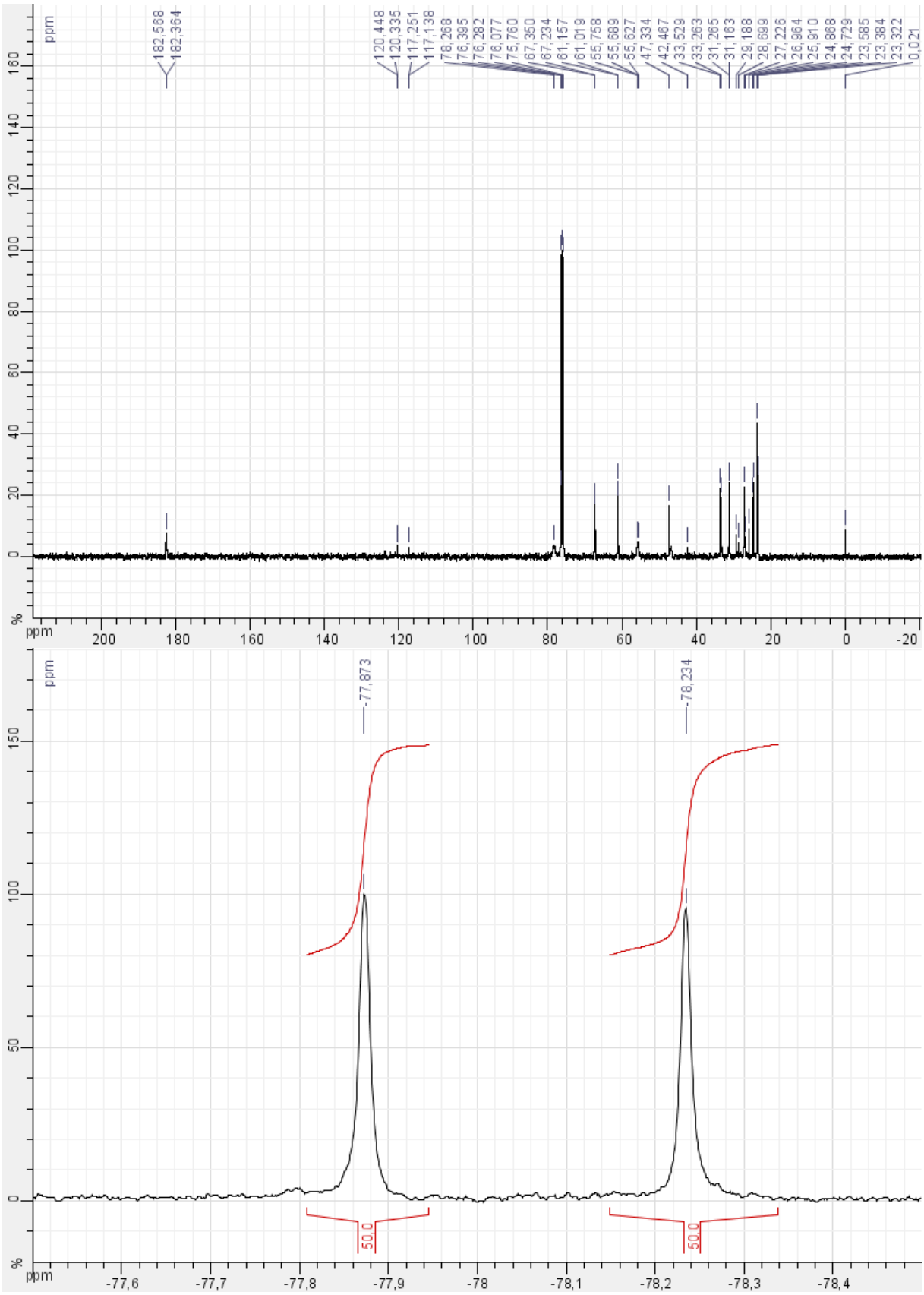

ppm
7,214
4,729
4,706
4,696
4,583
4,576
3,806
3,795
3,777
3,766
2,988
2,163
2,158
2,137
2,132
1,968
1,960
1,944
1,792
1,776
1,772
1,769
1,763
1,751
1,719
1,535
1,494
1,489
1,484
1,468
1,462
1,452
1,444
1,438
1,430
1,419
1,411
1,407
1,395
1,374
1,363
1,345
1,327
1,320
1,295
1,288
1,270
1,263
1,255
1,231
1,224
0,000
150
100
50
0
%
0,3
1,0
2,5
1,1
1,3
1,2
1,2
2,7
1,4
14,6
0,3
0,3
ppm
9
8
7
6
5
4
3
2
1
0

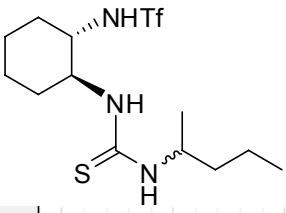

ppm
179,956
179,631
172,760
172,607
120,139
120,059
116,950
116,873
76,428
76,312
76,111
75,794
58,942
57,228
57,137
55,103
54,483
44,076
43,773
42,468
33,322
29,188
26,772
26,407
26,356
26,057
25,911
23,987
23,914
23,494
21,876
21,788
0,022
%
200
180
160
140
120
100
80
60
40
20
0
-20
-77,915
-78,099
50,0
50,0
-77,2
-77,4
-77,6
-77,8
-78
-78,2
-78,4


NHTf
NH
S
HN
O

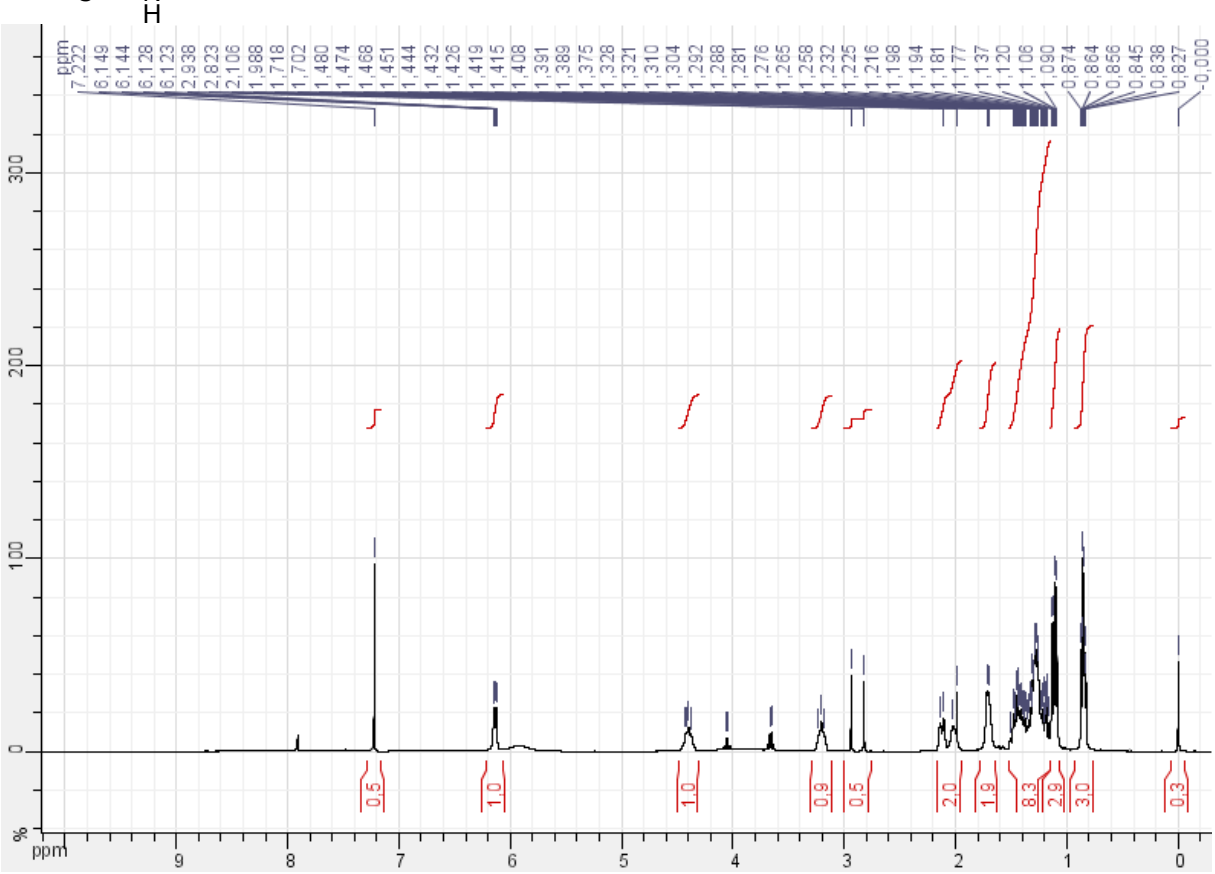
4i

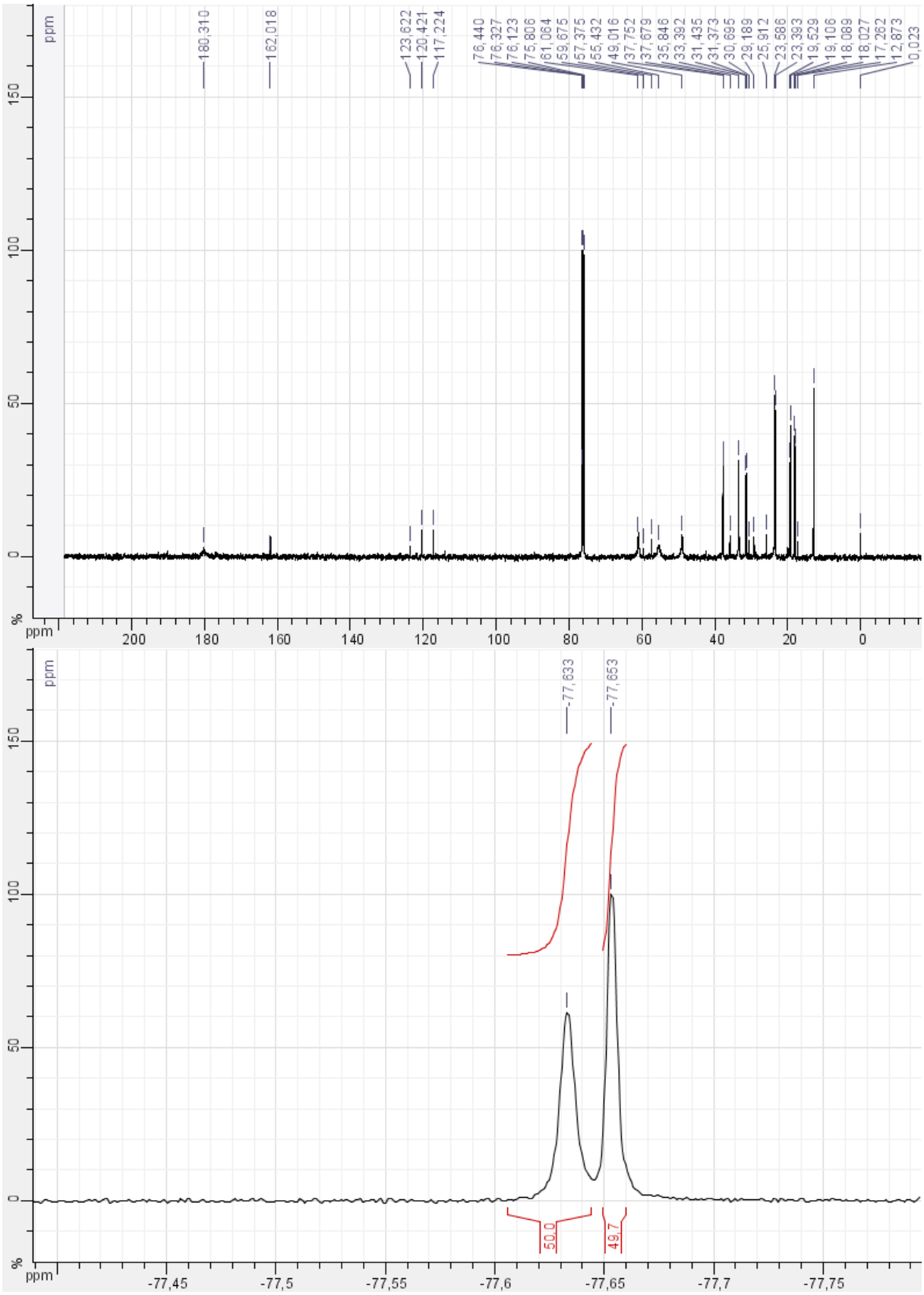

ppm
7,202
3,745
3,724
3,718
3,703
3,690
3,685
3,237
3,227
3,209
3,199
3,182
3,171
2,142
2,137
2,127
2,119
2,110
1,961
1,950
1,939
1,932
1,923
1,909
1,905
1,895
1,878
1,863
1,846
1,837
1,829
1,696
1,672
1,576
1,570
1,562
1,561
1,551
1,453
1,422
1,298
1,286
1,274
1,266
1,252
1,229
1,219
1,211
1,199
1,178
1,161
0,009
150
100
50
0
%
1,0
1,0
1,0
3,8
2,1
14,4
0,6
ppm
9
8
7
6
5
4
3
2
1
0

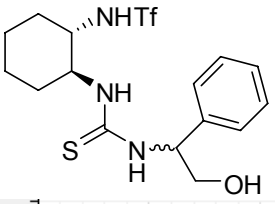

ppm
182,568
182,364
120,448
120,335
117,251
117,138
78,268
76,395
76,282
76,077
75,760
67,350
67,234
61,157
61,019
55,758
55,689
55,627
47,334
42,467
33,529
33,263
31,265
31,163
29,188
28,699
27,226
26,964
25,910
24,868
24,729
23,585
23,384
23,322
0,021
%
ppm
200
180
160
140
120
100
80
60
40
20
0
-20
ppm
-77,873
-78,234
50,0
50,0
%
ppm
-77,6
-77,7
-77,8
-77,9
-78
-78,1
-78,2
-78,3
-78,4


NHTf
NH
S
N
H

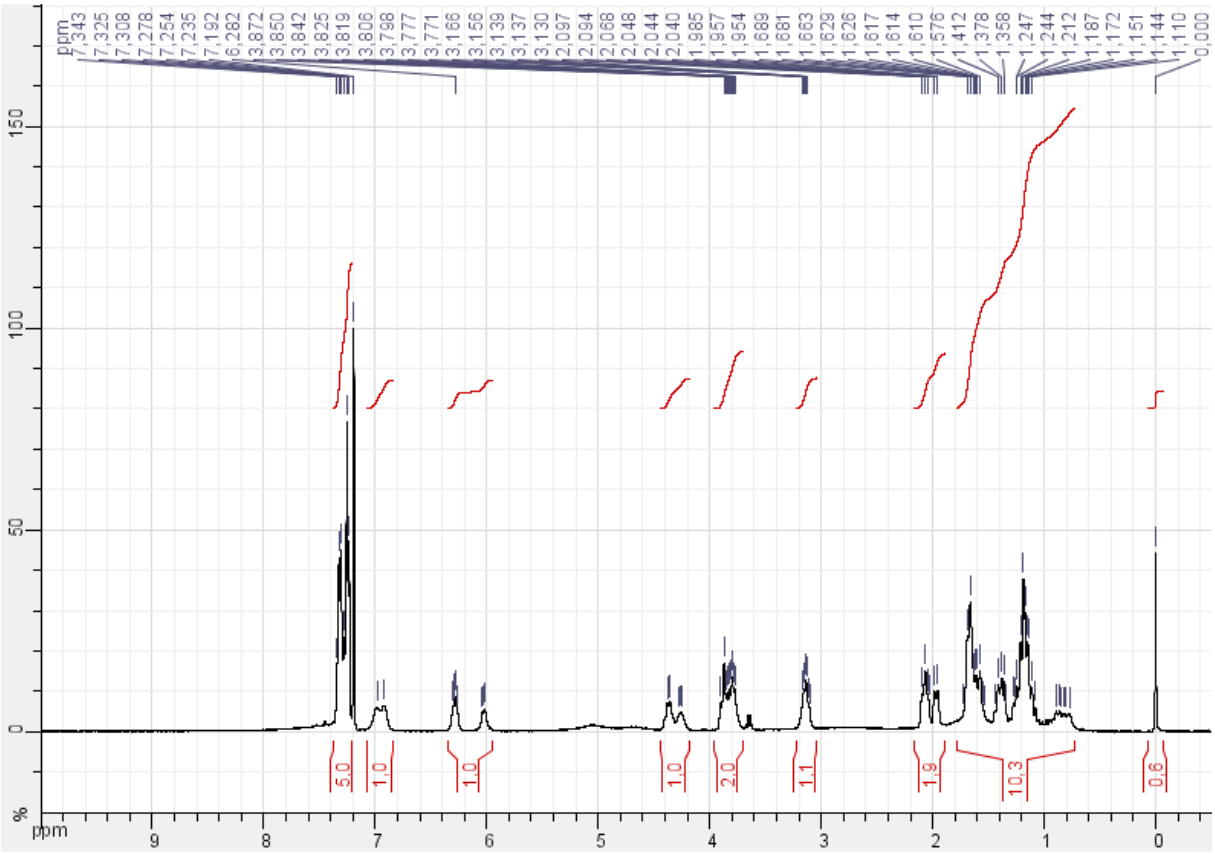
4j

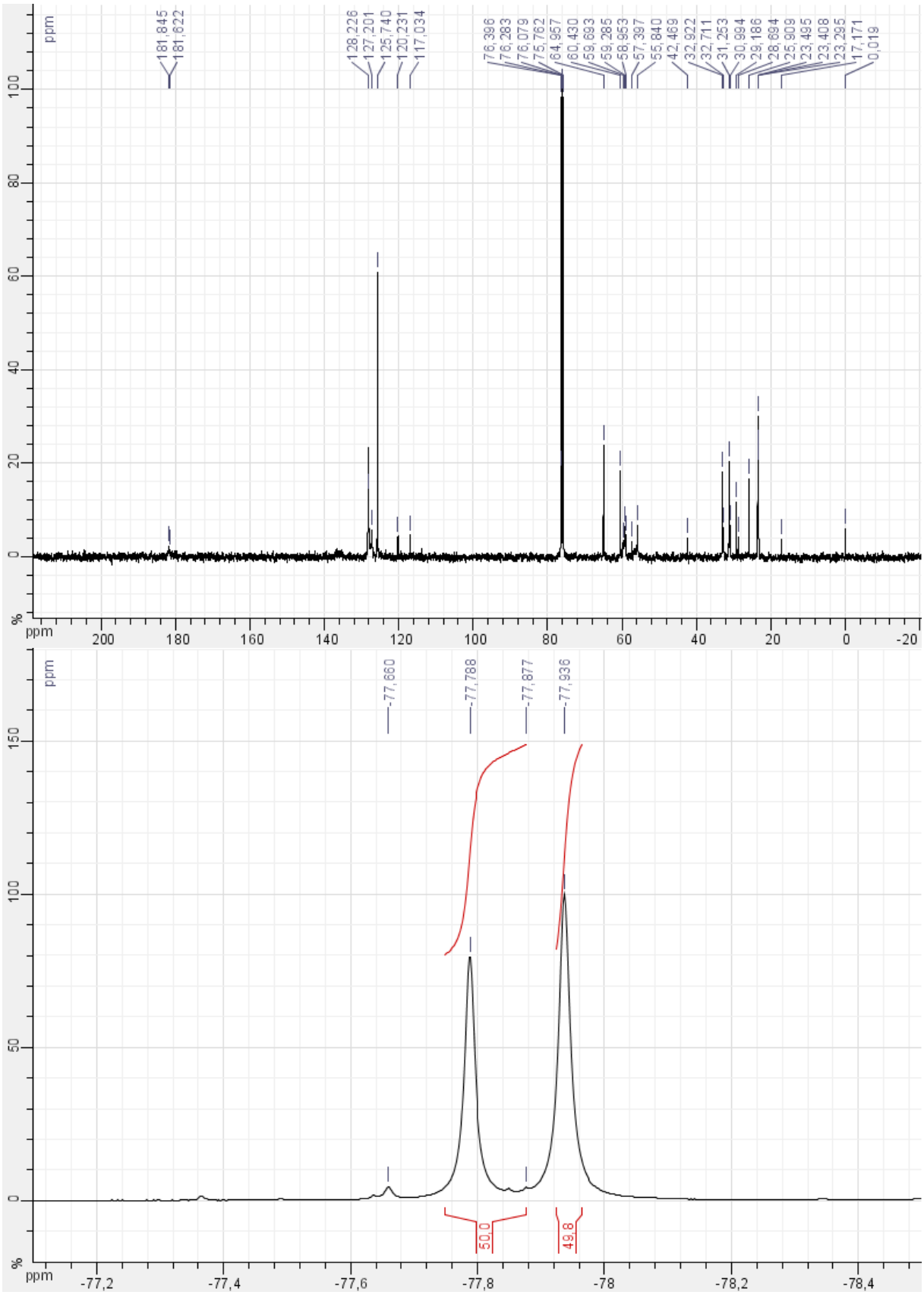

ppm
7,522
6,149
6,144
6,128
6,123
2,938
2,823
2,106
1,988
1,718
1,702
1,480
1,474
1,468
1,451
1,444
1,432
1,426
1,419
1,415
1,408
1,391
1,389
1,375
1,328
1,321
1,310
1,304
1,292
1,288
1,281
1,276
1,265
1,258
1,232
1,225
1,216
1,198
1,194
1,181
1,177
1,137
1,120
1,106
1,090
0,874
0,864
0,856
0,845
0,838
0,827
-0,000
300
200
100
0
%
ppm
9
8
7
6
5
4
3
2
1
0
0,5
1,0
1,0
0,9
0,5
2,0
1,9
8,3
2,9
3,0
0,3


ppm
180,310
162,018
123,622
120,421
117,224
76,440
76,327
76,123
75,806
61,064
59,675
57,375
55,432
49,016
37,752
37,679
35,846
33,392
31,435
31,373
30,695
29,189
25,912
23,586
23,393
19,529
19,106
18,089
18,027
17,262
12,873
0,023
150
100
50
0
%
200
180
160
140
120
100
80
60
40
20
0
-77,633
-77,853
50,0
49,7
-77,45
-77,5
-77,55
-77,6
-77,65
-77,7
-77,75

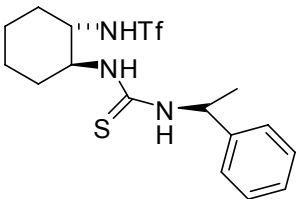

NHTf
NH
S
N
H
OH

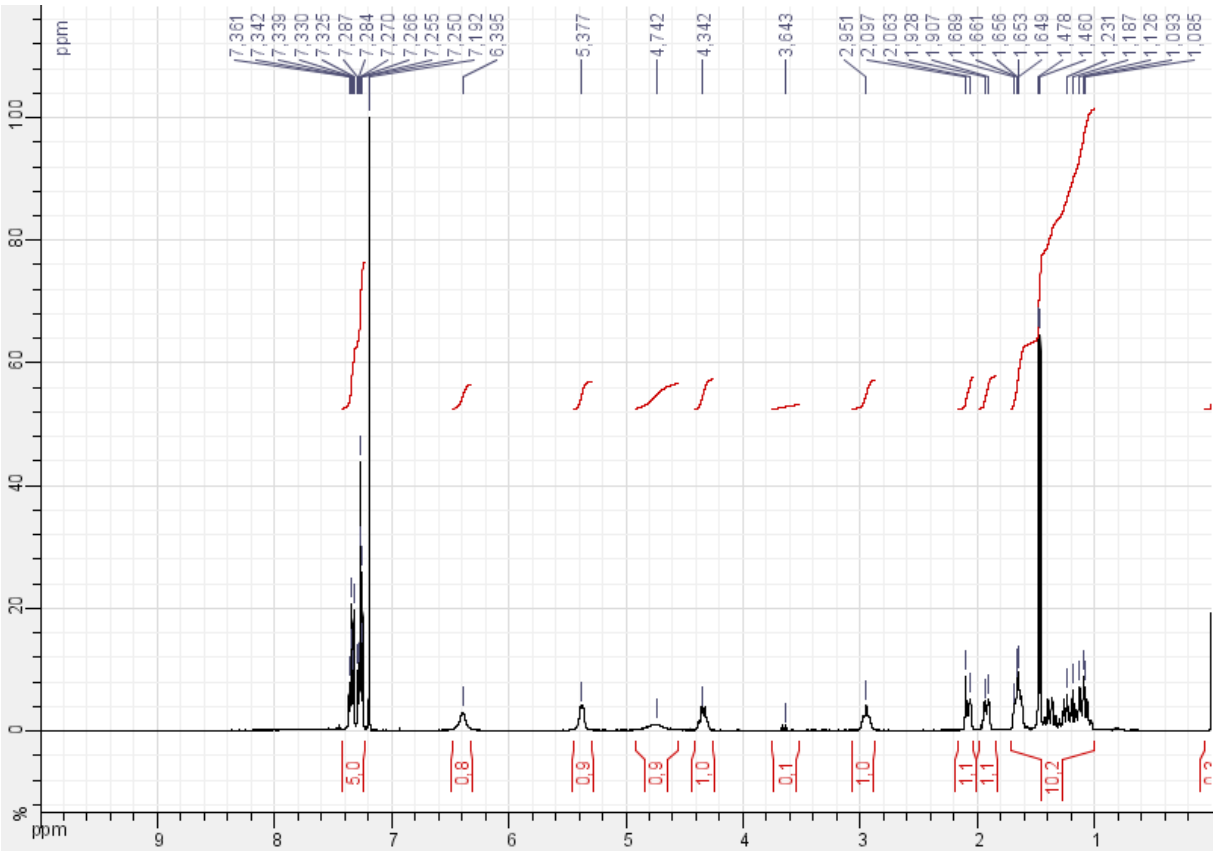
4k

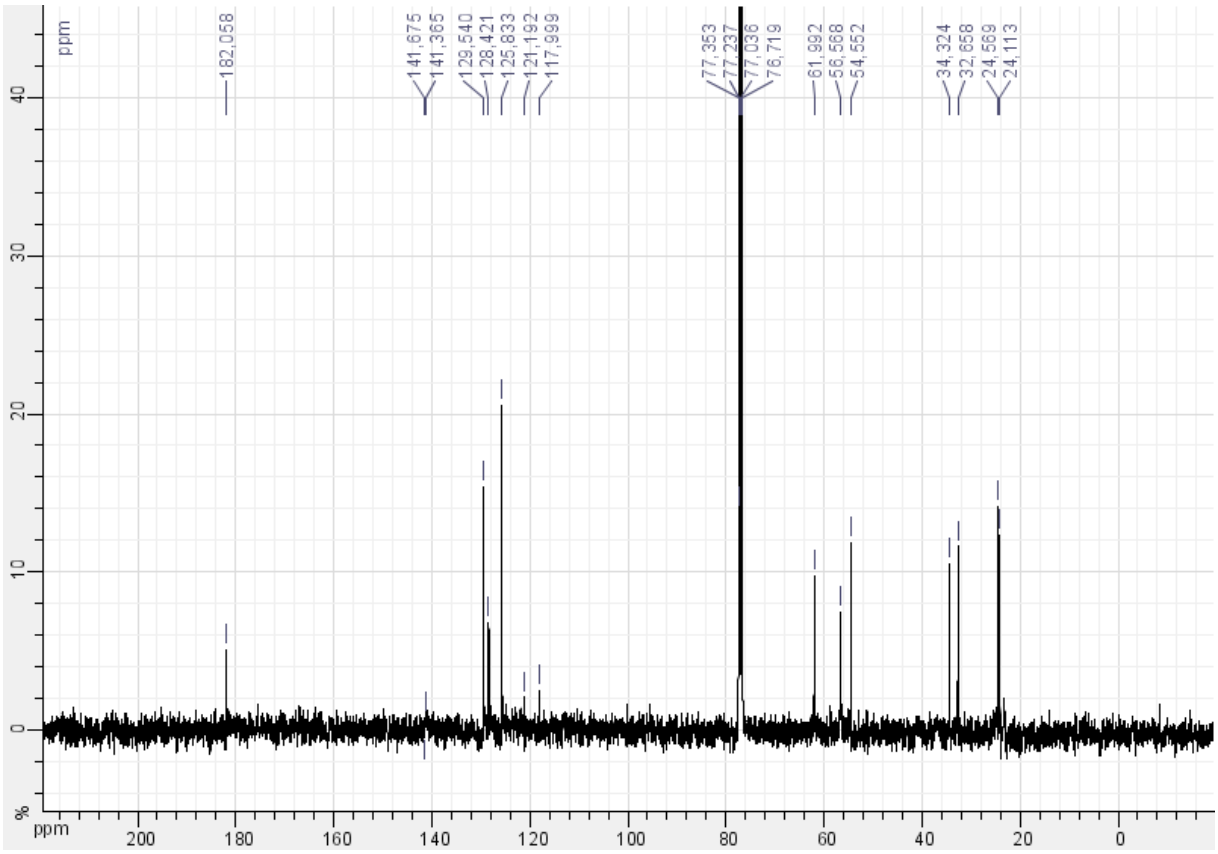

ppm
7,343
7,325
7,308
7,278
7,254
7,235
7,192
6,282
3,872
3,850
3,842
3,825
3,819
3,806
3,798
3,777
3,771
3,166
3,156
3,139
3,137
3,130
2,097
2,094
2,068
2,048
2,044
2,040
1,985
1,957
1,954
1,689
1,681
1,663
1,629
1,626
1,617
1,614
1,610
1,576
1,412
1,378
1,358
1,247
1,244
1,212
1,187
1,172
1,151
1,144
1,110
0,000
150
100
50
0
%
5,0
1,0
1,0
1,0
2,0
1,1
1,9
10,3
0,6
ppm
9
8
7
6
5
4
3
2
1
0

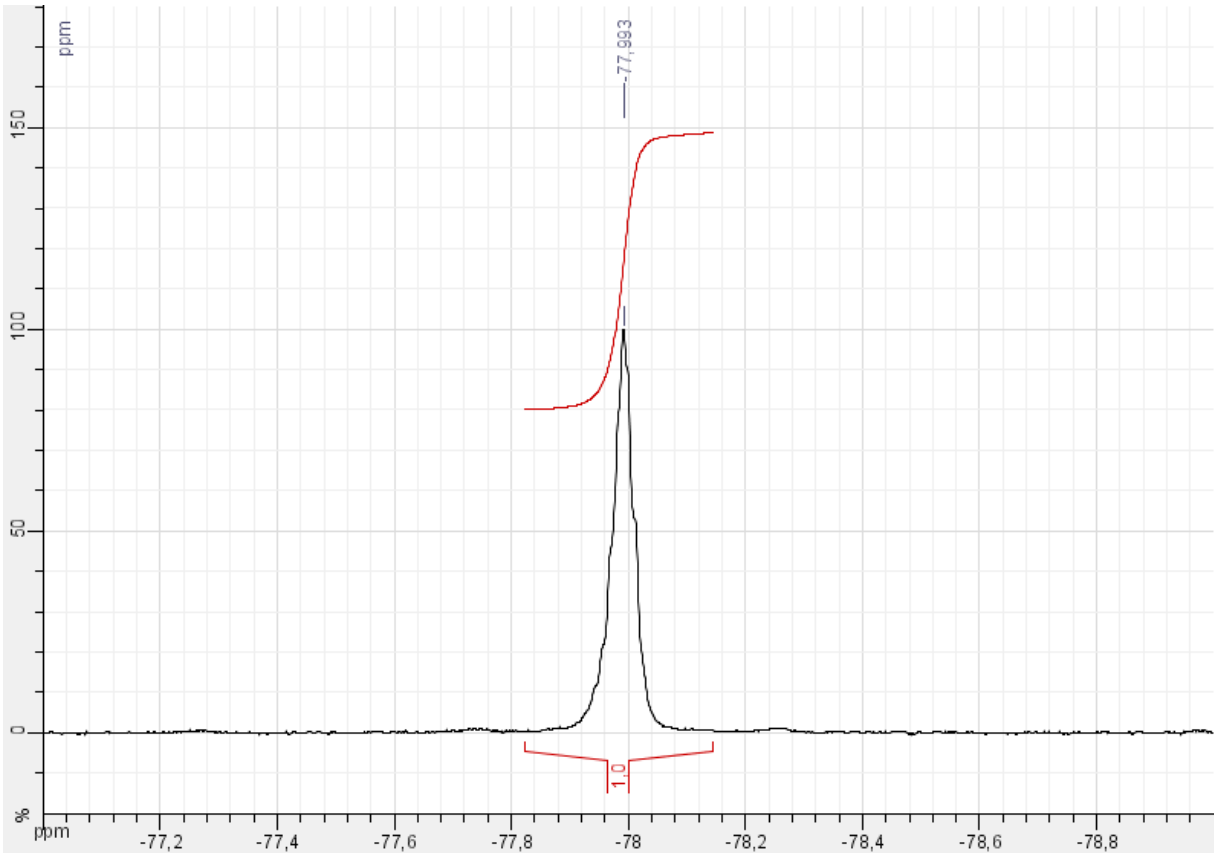

ppm
181,845
181,622
128,226
127,201
125,740
120,231
117,034
76,396
76,283
76,079
75,762
64,957
60,430
59,693
59,285
58,953
57,397
55,840
42,469
32,922
32,711
31,253
30,984
29,186
28,694
25,909
23,495
23,408
23,295
17,171
0,019
%
-77,660
-77,788
-77,877
-77,936
50,0
49,8

VI. ^{1}H, ^{13}C and ^{19}F NMR spectra of each diastereoisomer for selected thioureas






ppm
182,058
141,675
141,365
129,540
128,421
125,833
121,192
117,999
77,353
77,237
77,036
76,719
61,992
56,568
54,552
34,324
32,658
24,569
24,113
%
ppm
200
180
160
140
120
100
80
60
40
20
0


ppm
-77,993
1,0
%
ppm
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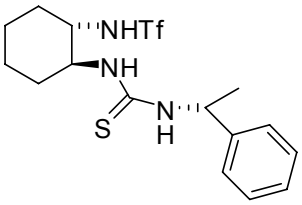
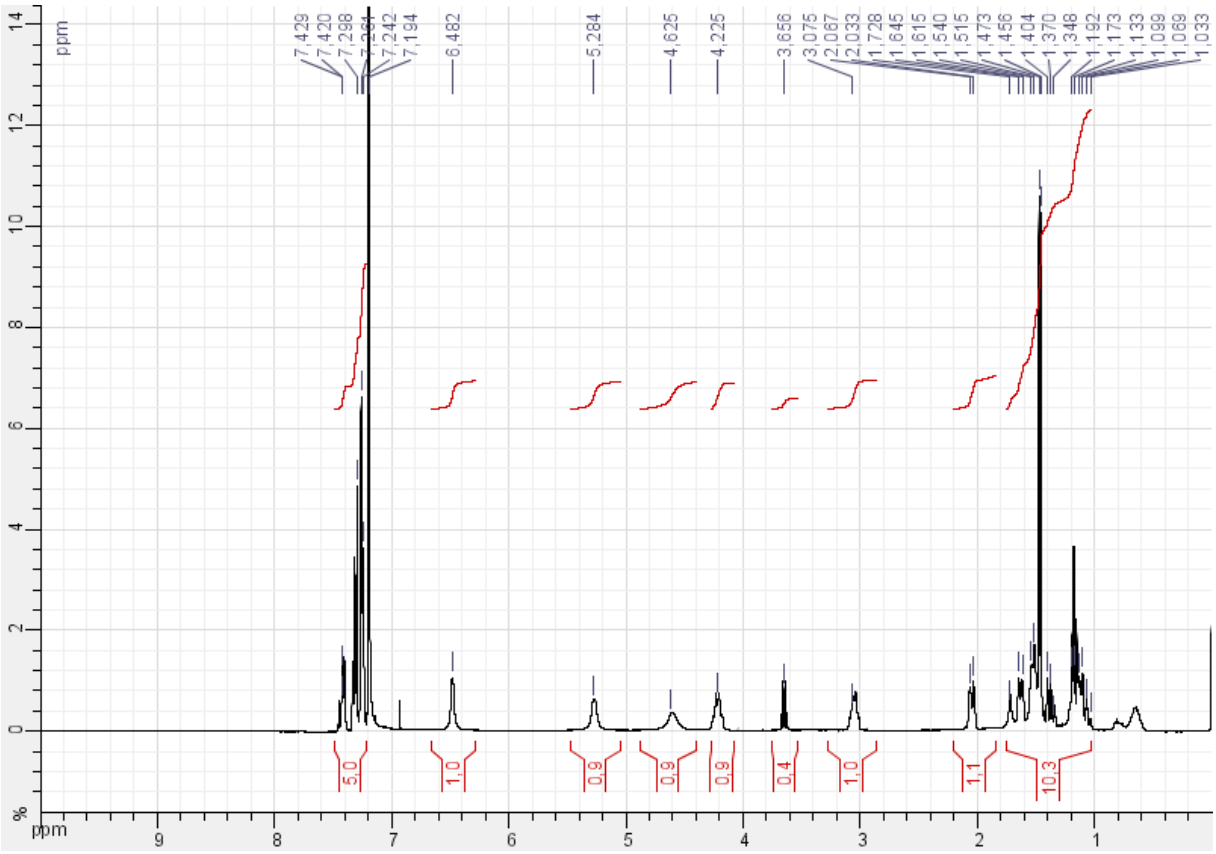
-77,4
-77,6
-77,8
-78
-78,2
-78,4
-78,6
-78,8


NHTf
NH
N
H
S


ppm
7,429
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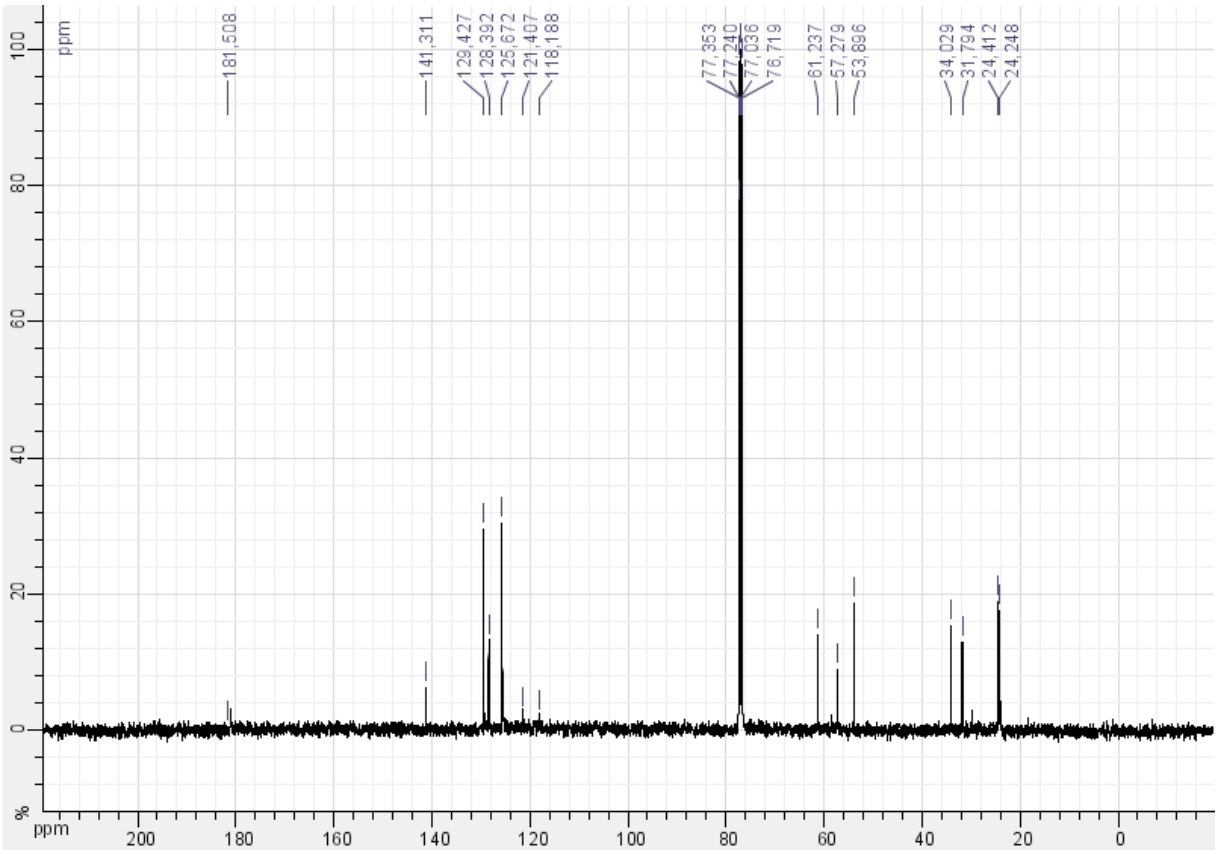
7,261
7,242
7,194
6,482
5,284
4,625
4,225
3,656
3,075
2,067
2,033
1,728
1,645
1,615
1,540
1,515
1,473
1,456
1,404
1,370
1,348
1,192
1,173
1,133
1,099
1,069
1,033
5,0
1,0
0,9
0,9
0,9
0,4
1,0
1,1
10,3
%
ppm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128,392
125,672
121,407
118,188
77,353
77,240
77,036
76,719
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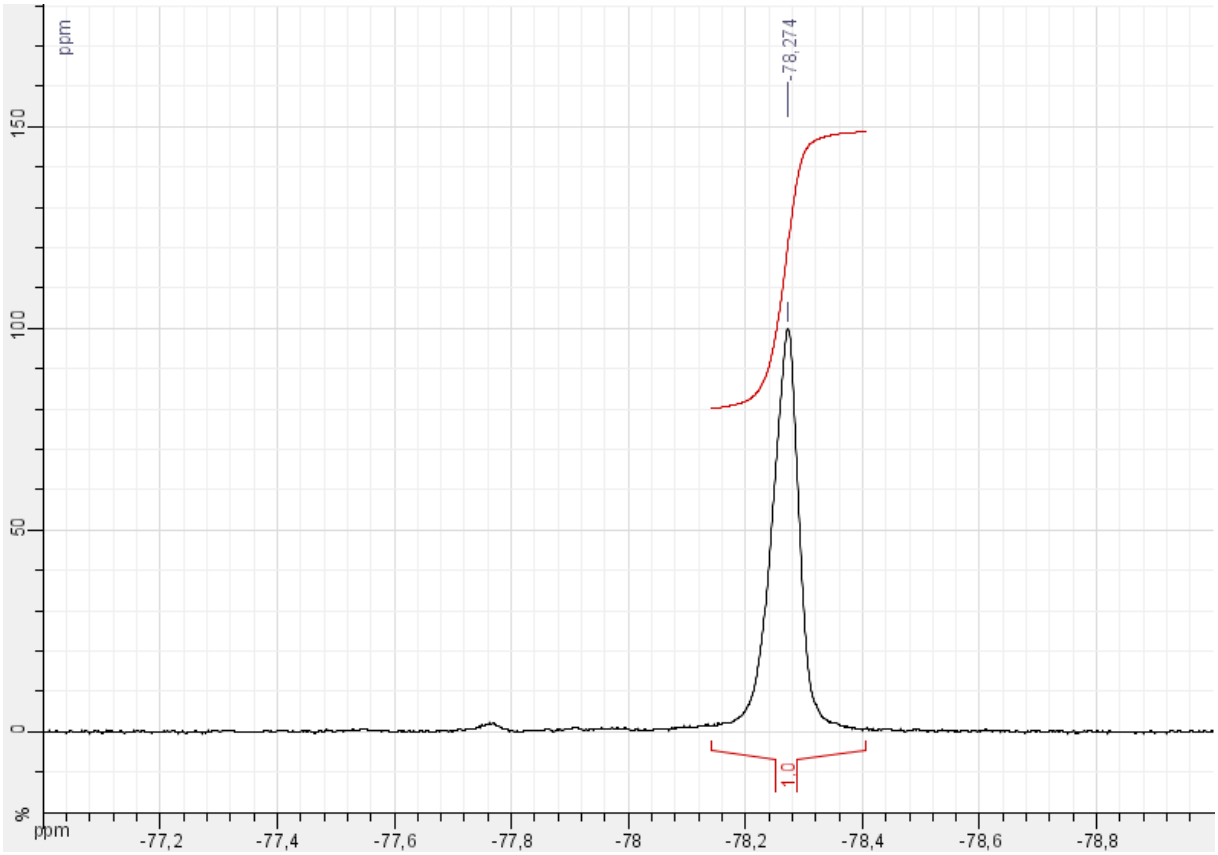
57,279
53,896
34,029
31,794
24,412
24,248
%
ppm
200
180
160
140
120
100
80
60
40
20
0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%
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-77,4
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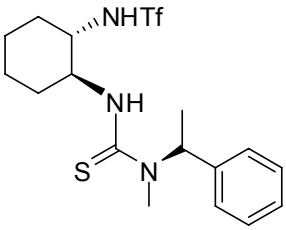
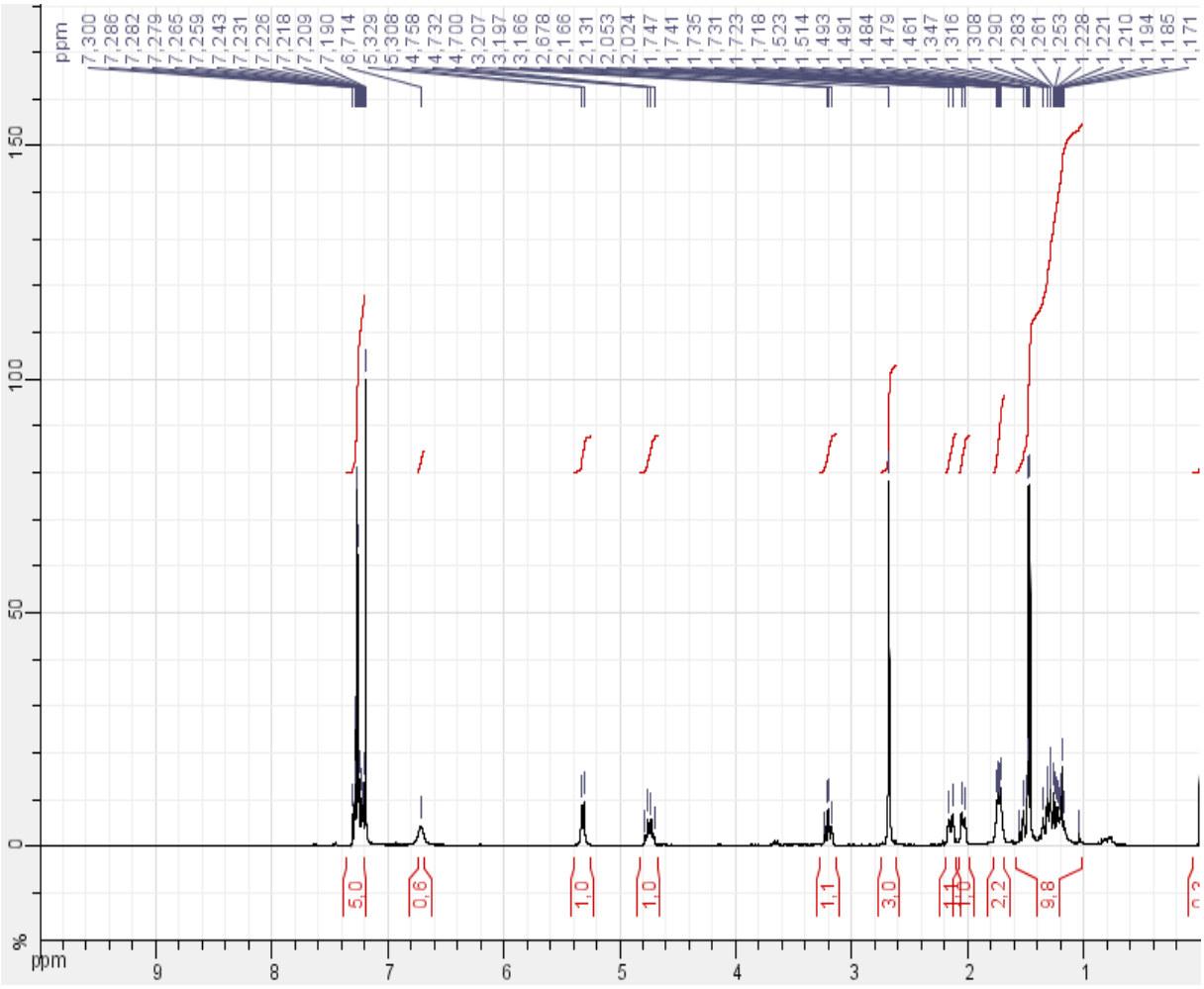
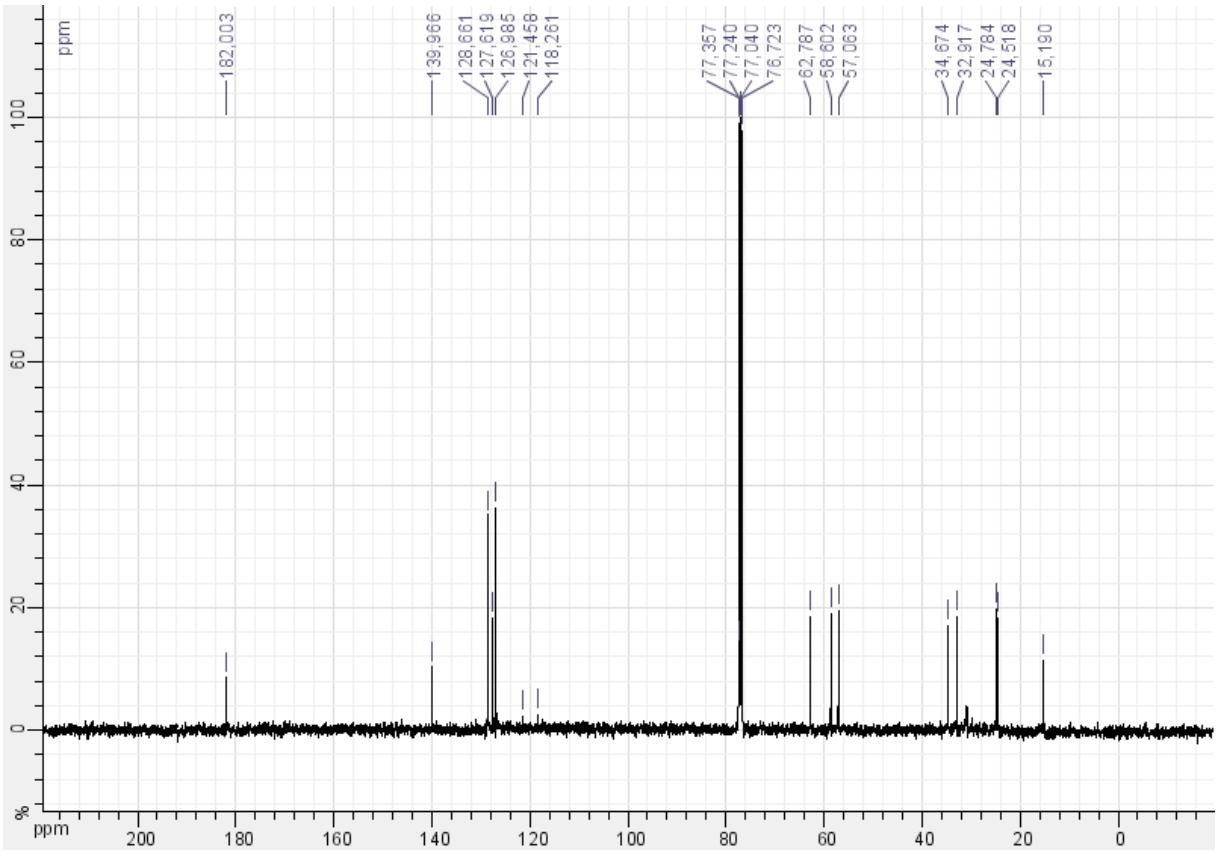
-77,8
-78
-78,2
-78,4
-78,6
-78,8


NHTf
NH
S
N


ppm
7,300
7,286
7,282
7,279
7,265
7,259
7,243
7,231
7,226
7,218
7,209
7,190
6,714
5,329
5,308
4,758
4,732
4,700
3,207
3,197
3,166
2,678
2,166
2,131
2,053
2,024
1,747
1,741
1,735
1,731
1,723
1,718
1,523
1,514
1,493
1,491
1,484
1,479
1,461
1,347
1,316
1,308
1,290
1,283
1,261
1,253
1,228
1,221
1,210
1,194
1,185
1,171
150
100
50
0
%
ppm
9
8
7
6
5
4
3
2
1
5,0
0,6
1,0
1,0
1,1
3,0
1,1
1,0
2,2
9,8


ppm
182,003
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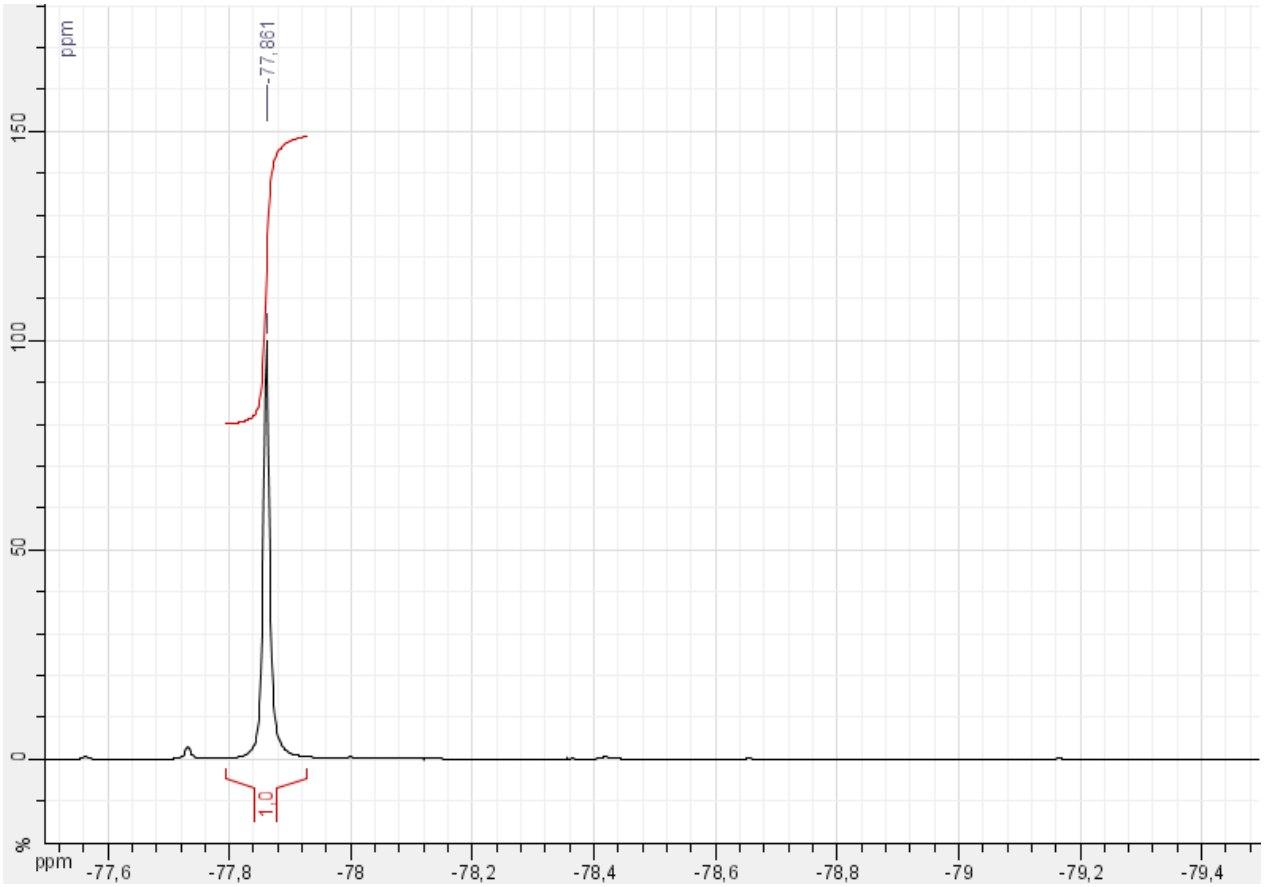
128,661
127,619
126,985
121,458
118,261
77,357
77,240
77,040
76,723
62,787
58,602
57,063
34,674
32,917
24,784
24,518
15,190
%
ppm
200
180
160
140
120
100
80
60
40
20
0


ppm
-77,861
1,0
%
ppm
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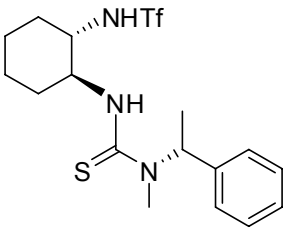
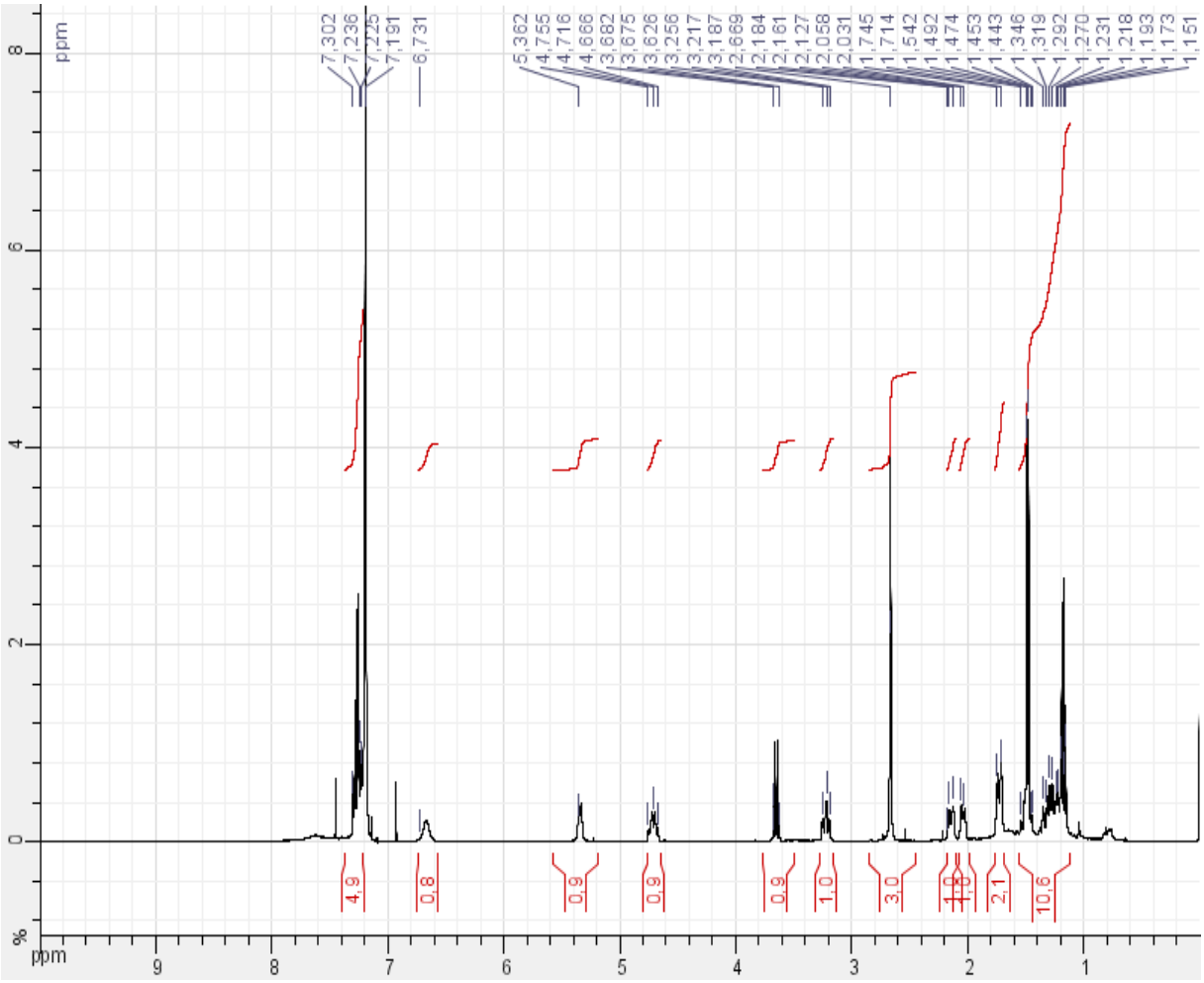
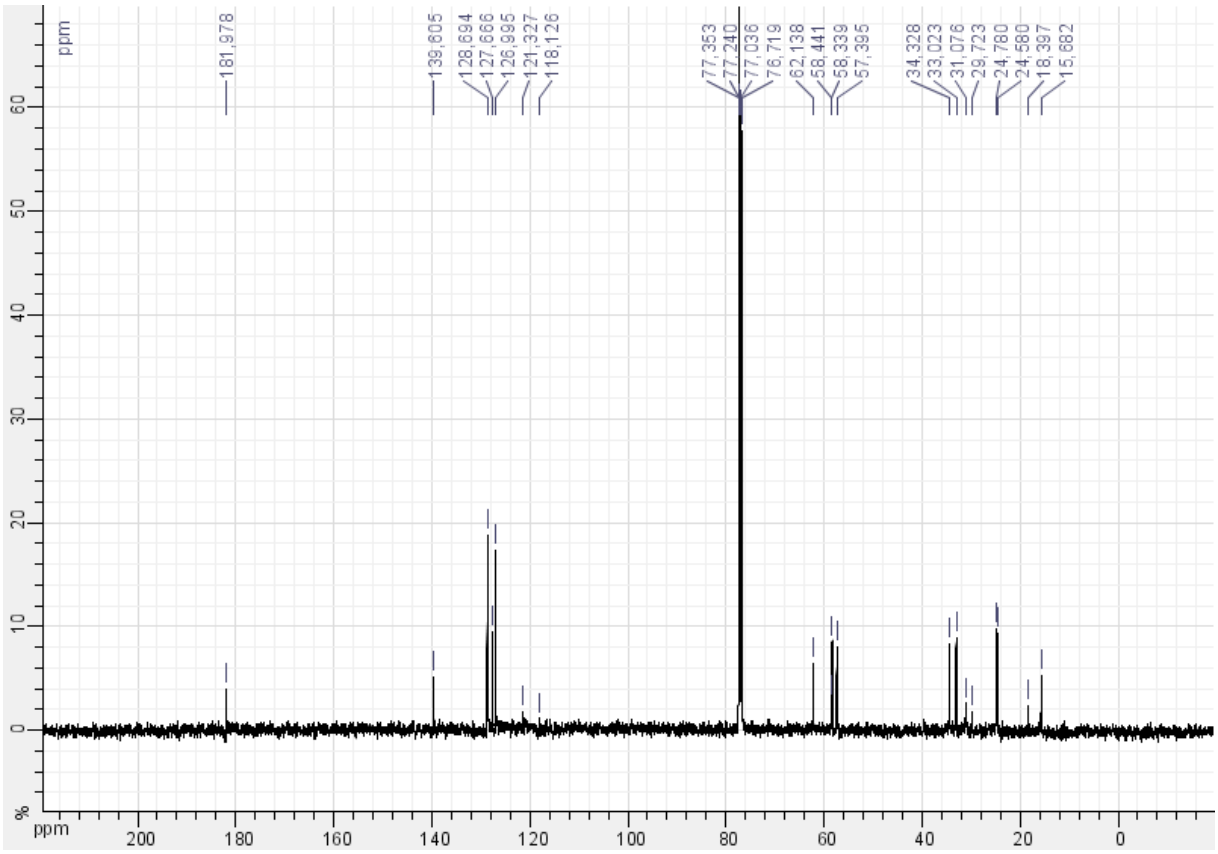
-77,8
-78
-78,2
-78,4
-78,6
-78,8
-79
-79,2
-79,4


NHTf
NH
S
N


ppm
7,302
7,236
7,225
7,191
6,731
5,362
4,755
4,716
4,666
3,682
3,675
3,626
3,256
3,217
3,187
2,669
2,184
2,161
2,127
2,058
2,031
1,745
1,714
1,542
1,492
1,474
1,453
1,443
1,346
1,319
1,292
1,270
1,231
1,218
1,193
1,173
1,151
4,9
0,8
0,9
0,9
0,9
1,0
3,0
1,0
1,0
2,1
10,6
%
ppm


ppm
181,978
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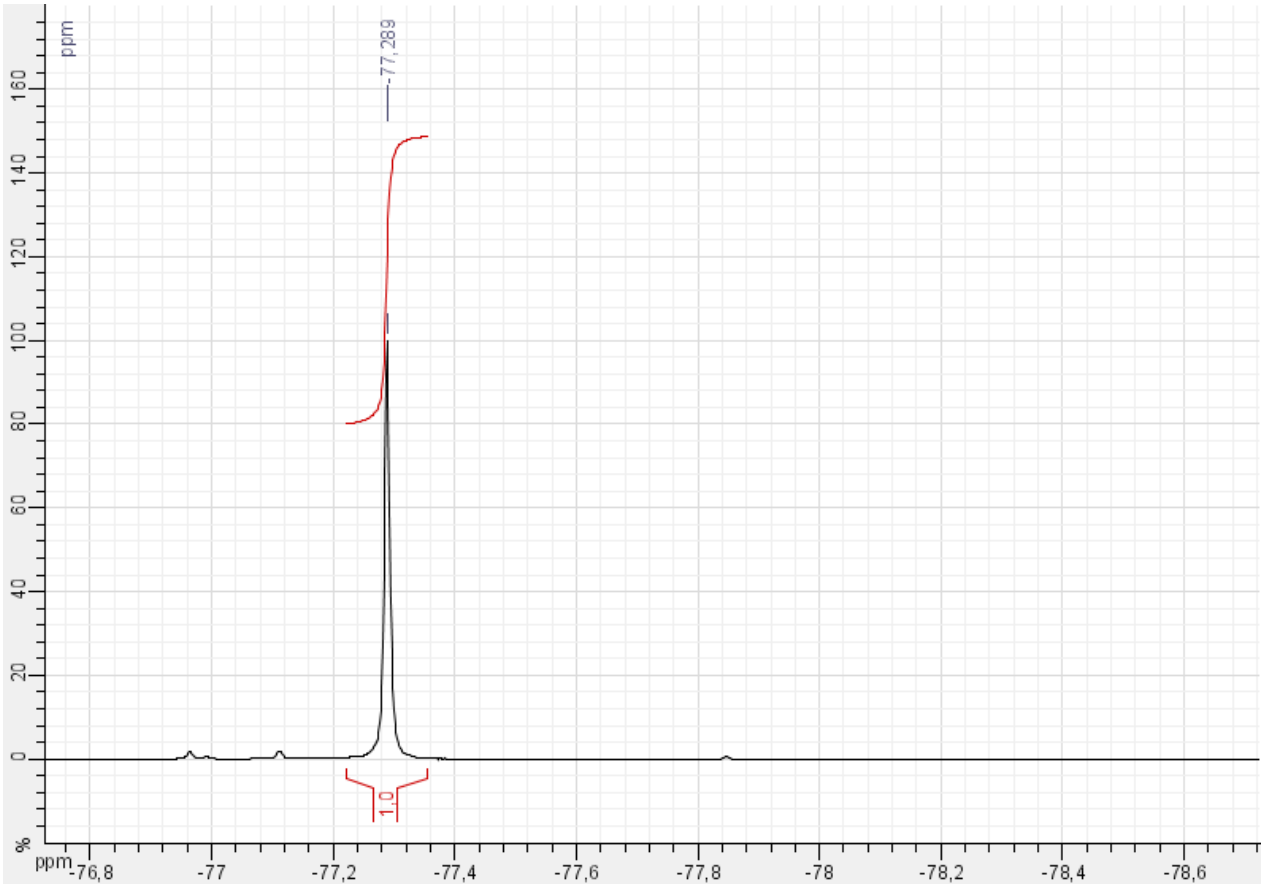
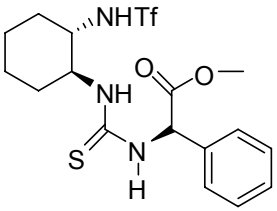
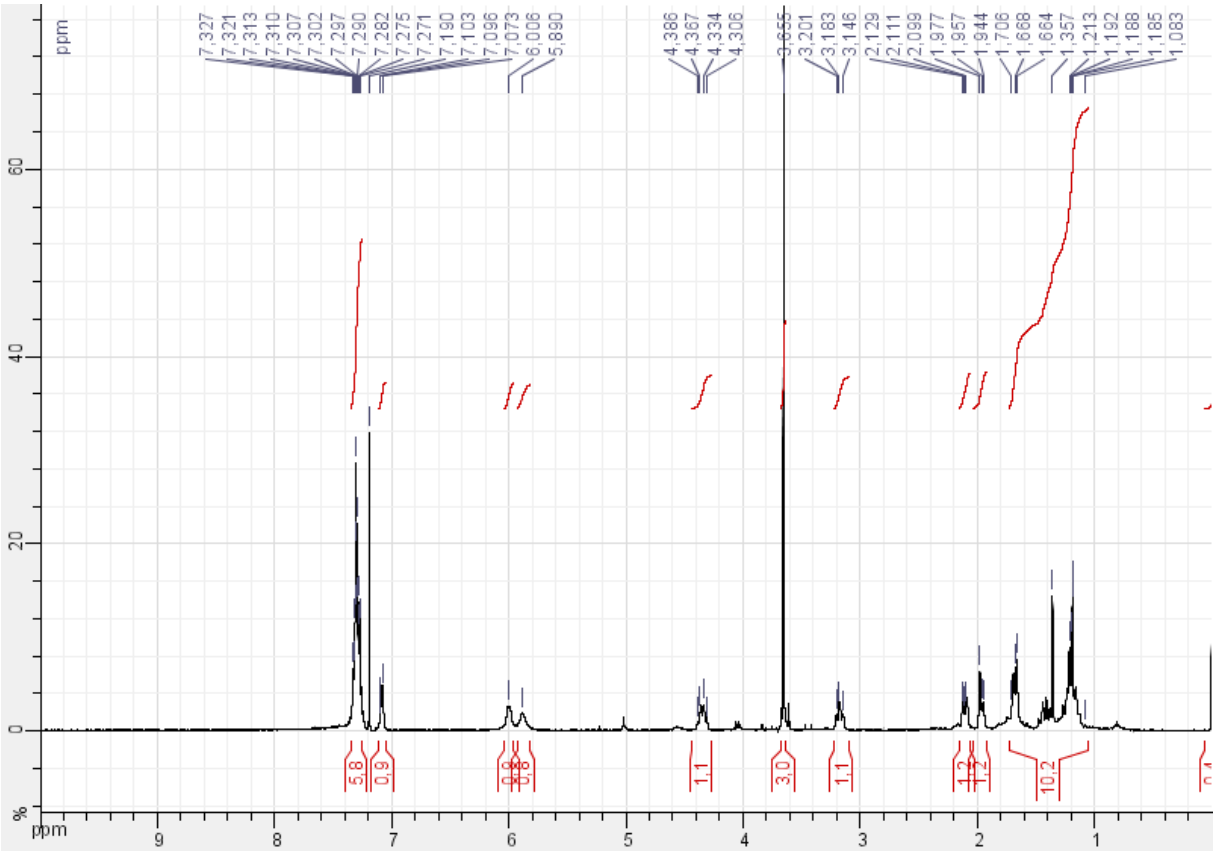
128,694
127,666
126,995
121,327
118,126
77,353
77,240
77,036
76,719
62,138
58,441
58,339
57,395
34,328
33,023
31,076
29,723
24,780
24,580
18,397
15,682
%
ppm
200
180
160
140
120
100
80
60
40
20
0


ppm
-77,289
1,0
%
ppm
-76,8
-77
-77,2
-77,4
-77,6
-77,8
-78
-78,2
-78,4
-78,6


NHTf
O
O
NH
S
N
H


ppm
7,327
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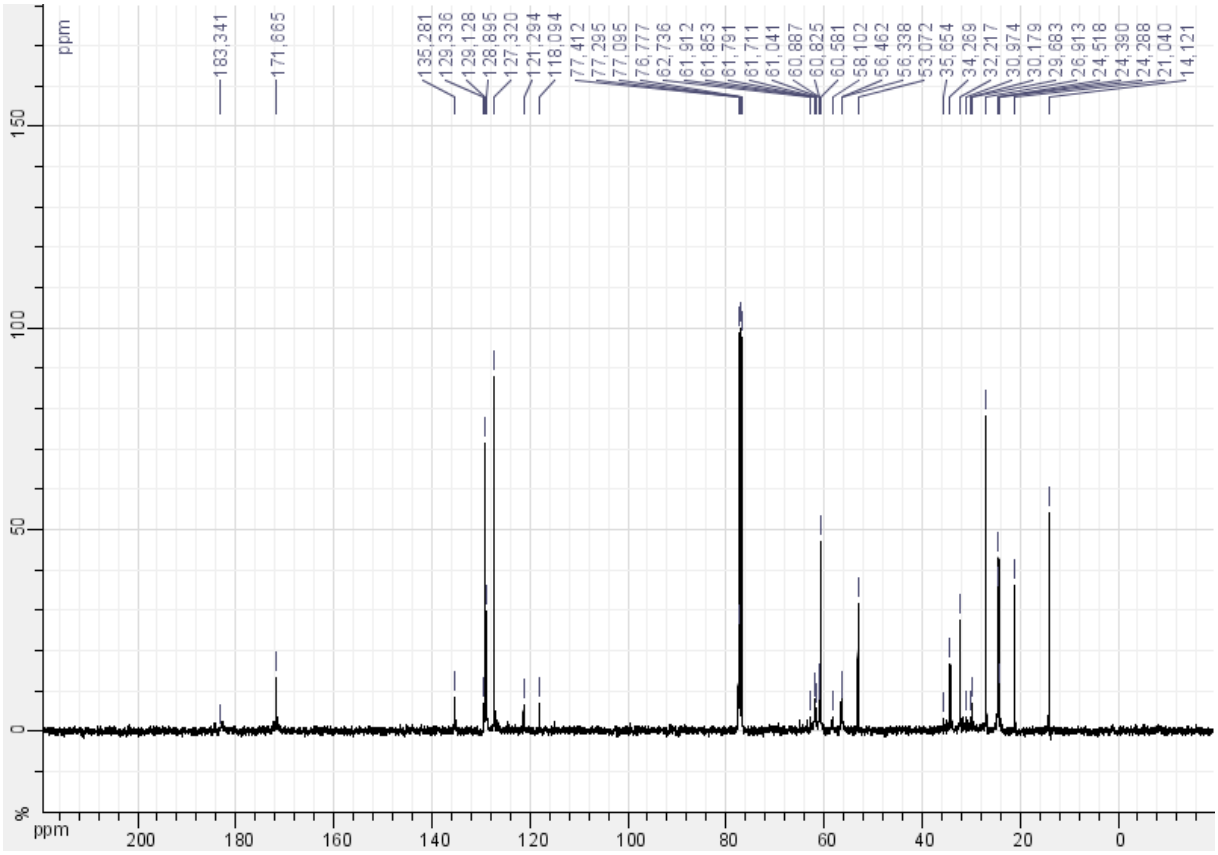
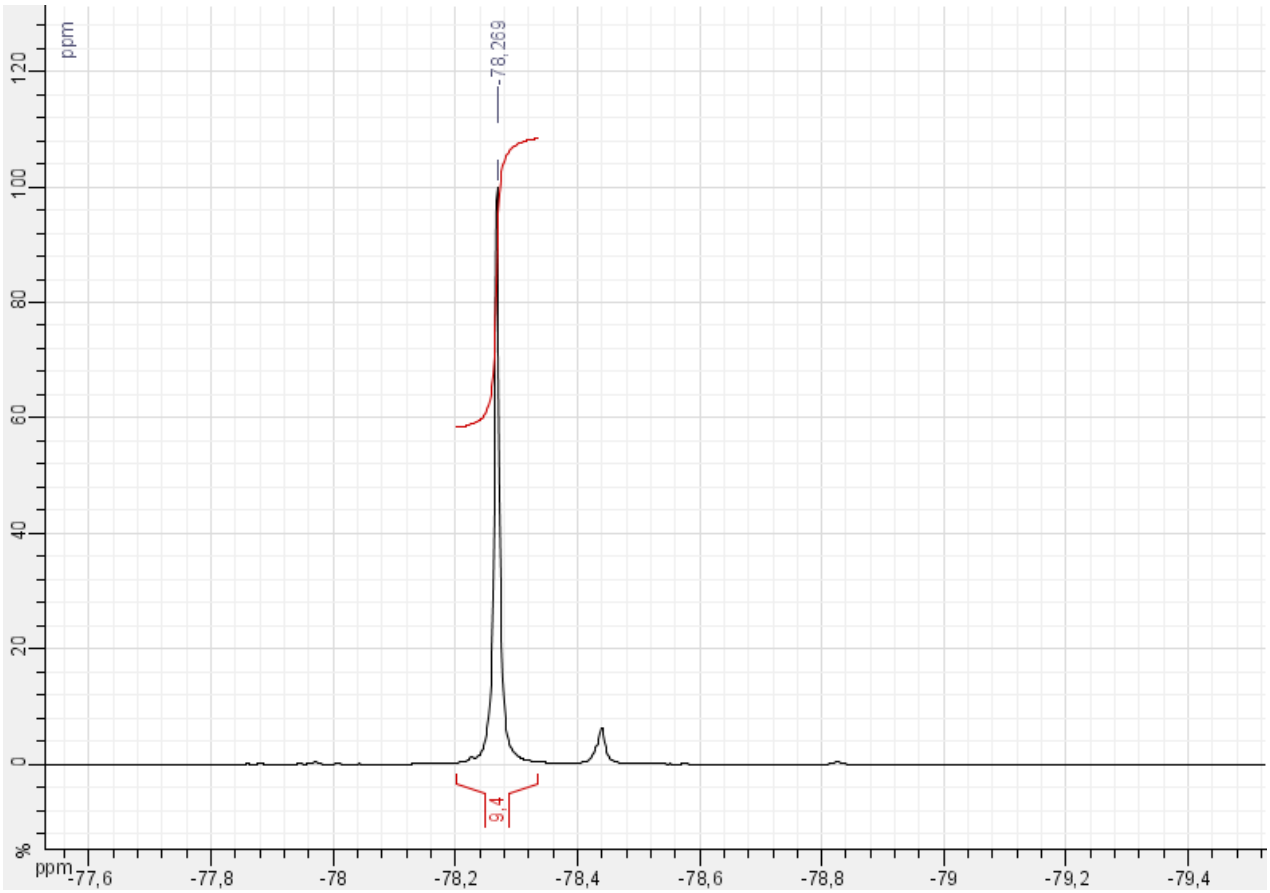
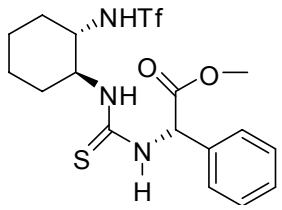
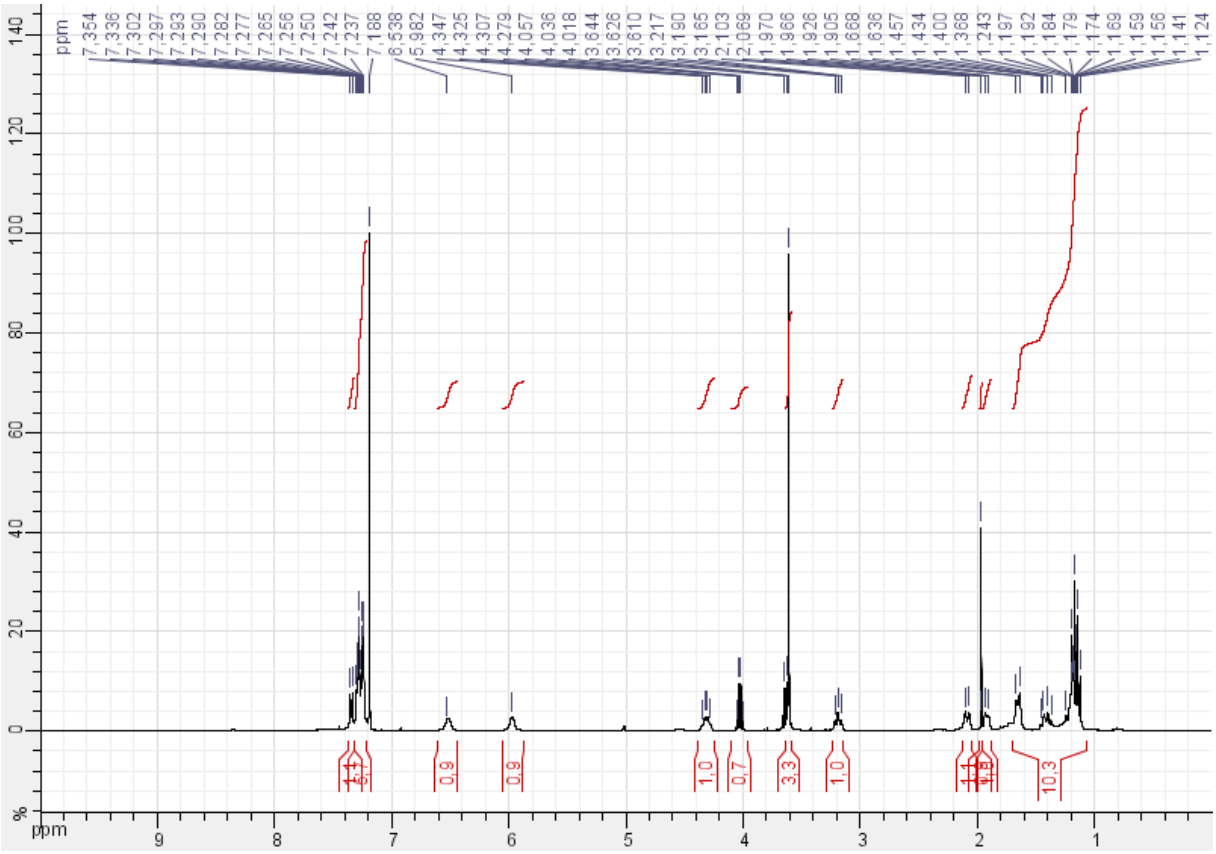
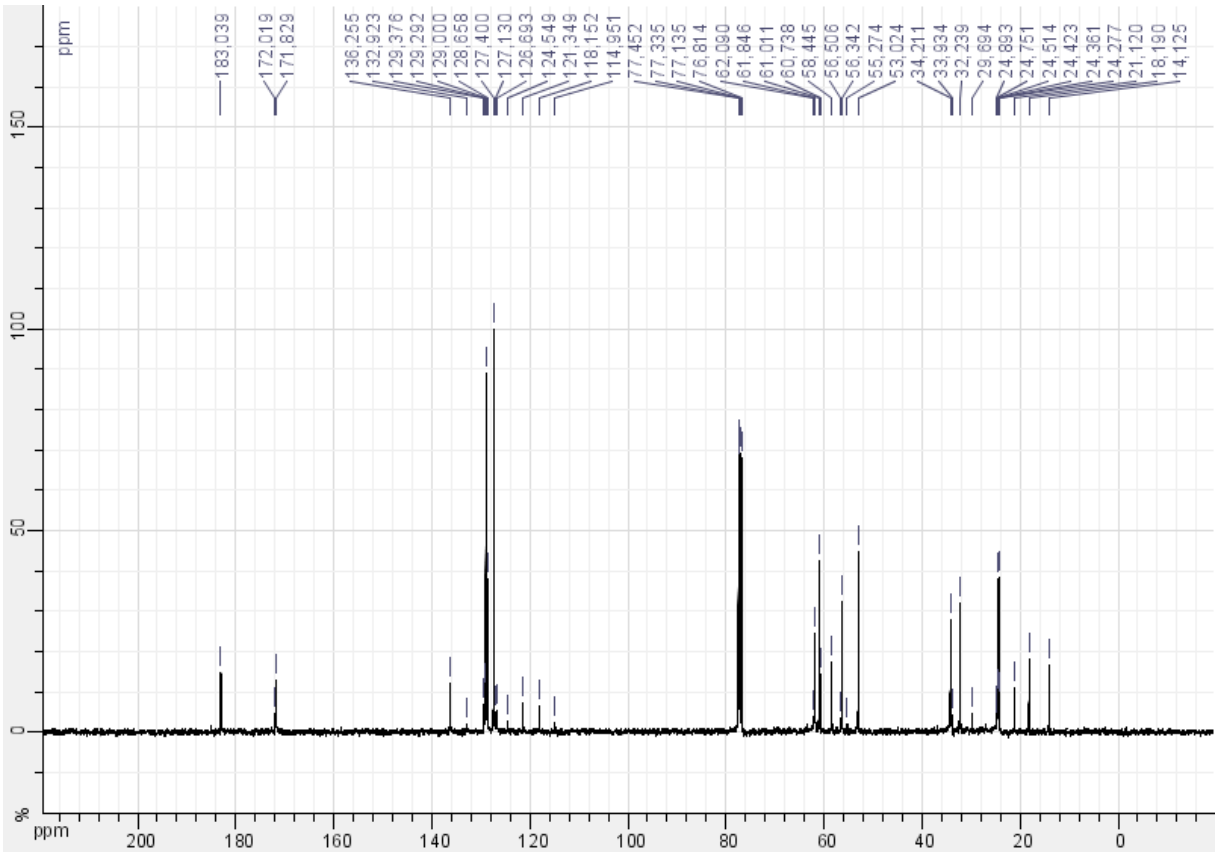
7,313
7,310
7,307
7,302
7,297
7,290
7,282
7,275
7,271
7,190
7,103
7,096
7,073
6,006
5,890
4,386
4,367
4,334
4,306
3,655
3,201
3,183
3,146
2,129
2,111
2,099
1,977
1,957
1,944
1,706
1,668
1,664
1,357
1,213
1,192
1,188
1,185
1,083
60
40
20
0
%
5,8
0,9
0,6
0,6
1,1
3,0
1,1
1,2
1,2
10,2
ppm
9
8
7
6
5
4
3
2
1

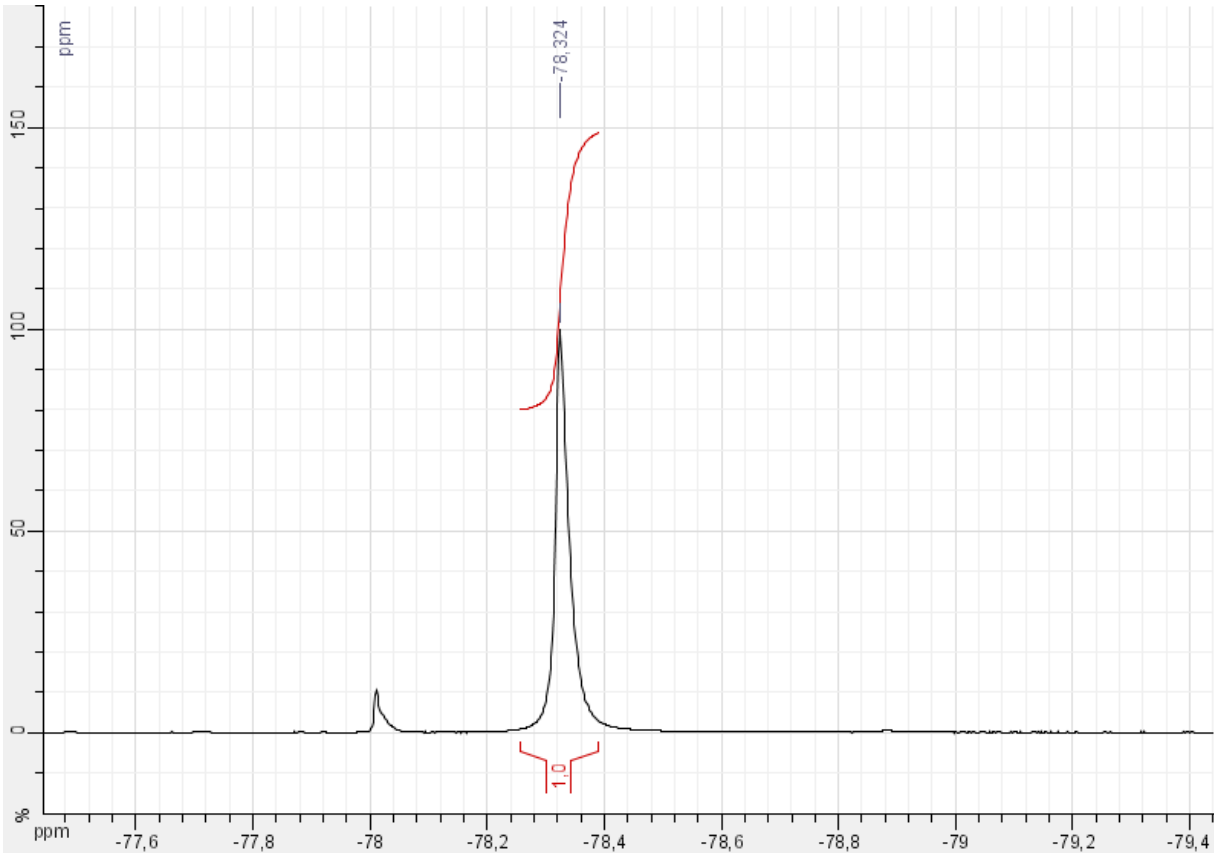

ppm
183,341
171,665
135,281
129,336
129,128
128,895
127,320
121,294
118,094
77,412
77,295
77,095
76,777
62,736
61,912
61,853
61,791
61,711
61,041
60,887
60,825
60,581
58,102
56,462
56,338
53,072
35,654
34,269
32,217
30,974
30,179
29,683
26,913
24,518
24,380
24,288
21,040
14,121
150
100
50
0
%
ppm
200
180
160
140
120
100
80
60
40
20
0

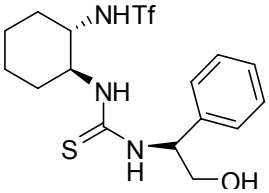

ppm
-78,269
120
100
80
60
40
20
0
%
9,4
ppm
-77,6
-77,8
-78
-78,2
-78,4
-78,6
-78,8
-79
-79,2
-79,4

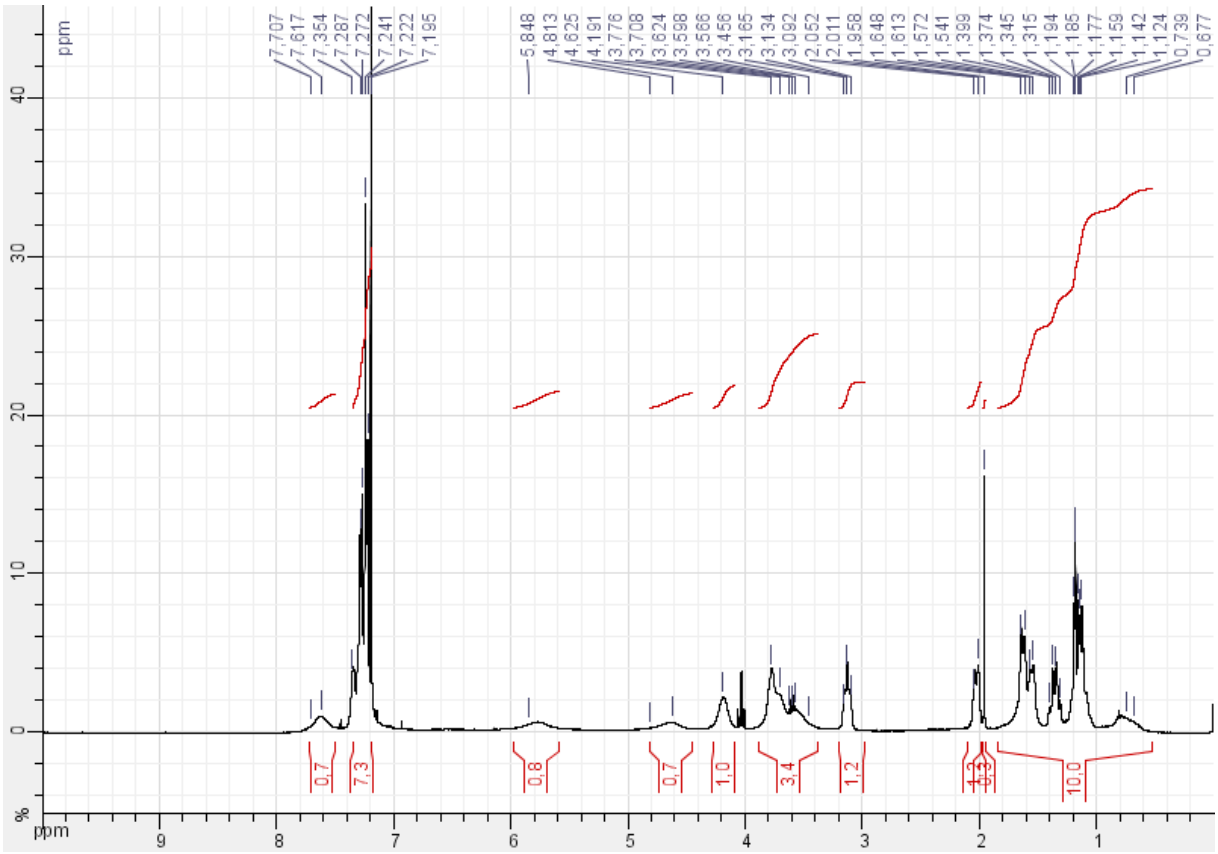


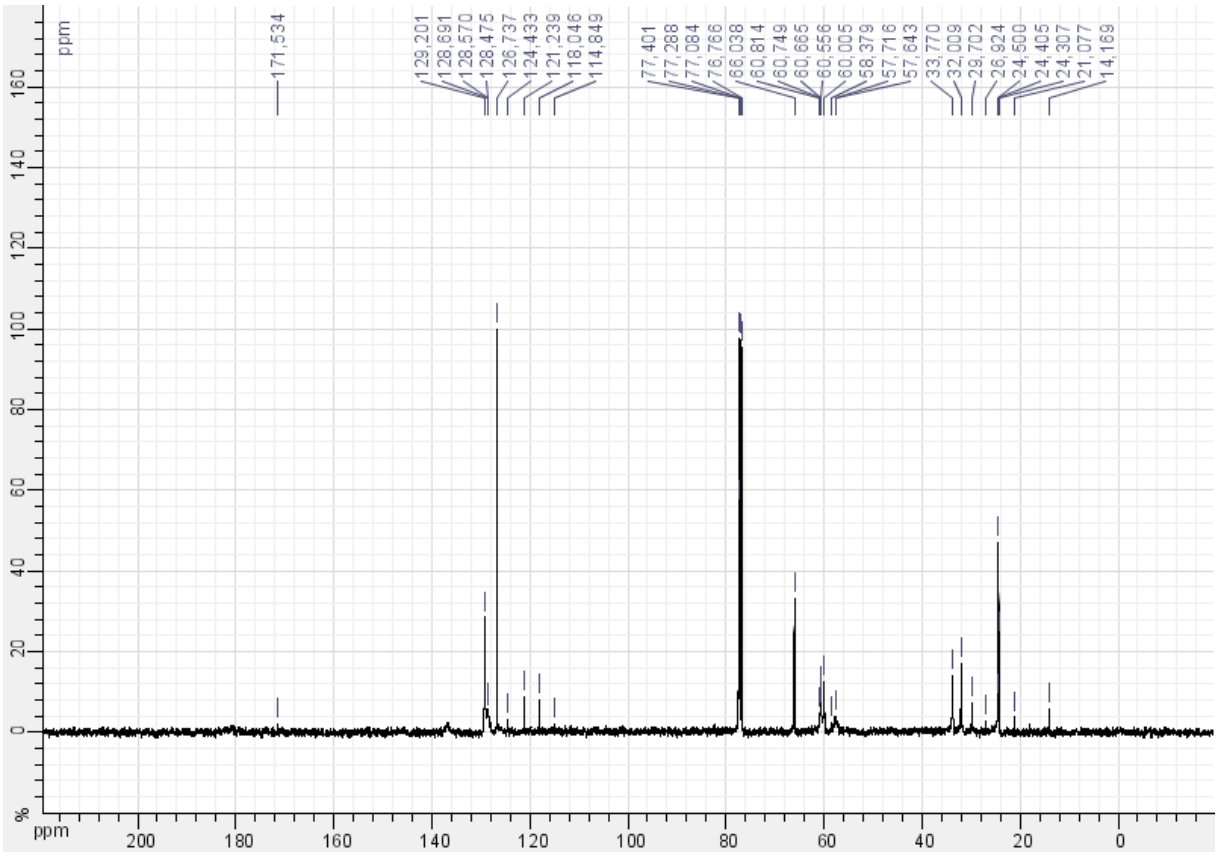


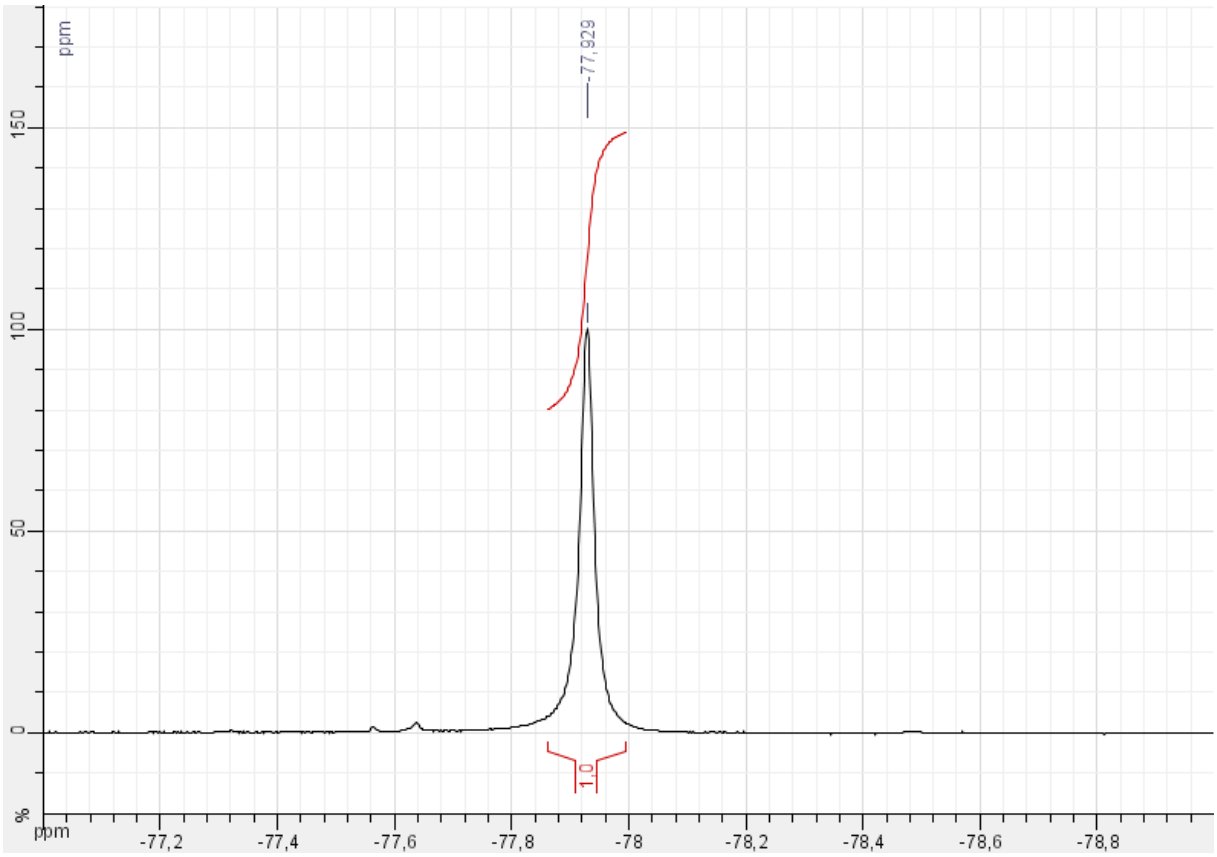

ppm
183,039
172,019
171,829
136,255
132,923
129,376
129,292
129,000
128,658
127,400
127,130
126,693
124,549
121,349
118,152
114,951
77,452
77,335
77,135
76,814
62,080
61,846
61,011
60,738
58,445
56,506
56,342
55,274
53,024
34,211
33,934
32,239
29,694
24,893
24,751
24,514
24,423
24,361
24,277
21,120
18,190
14,125
150
100
50
0
%
ppm
200
180
160
140
120
100
80
60
40
20
0

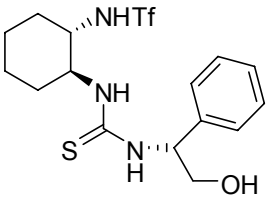

ppm
-78,324
150
100
50
0
%
ppm
-77,6
-77,8
-78
-78,2
-78,4
-78,6
-78,8
-79
-79,2
-79,4
1,0

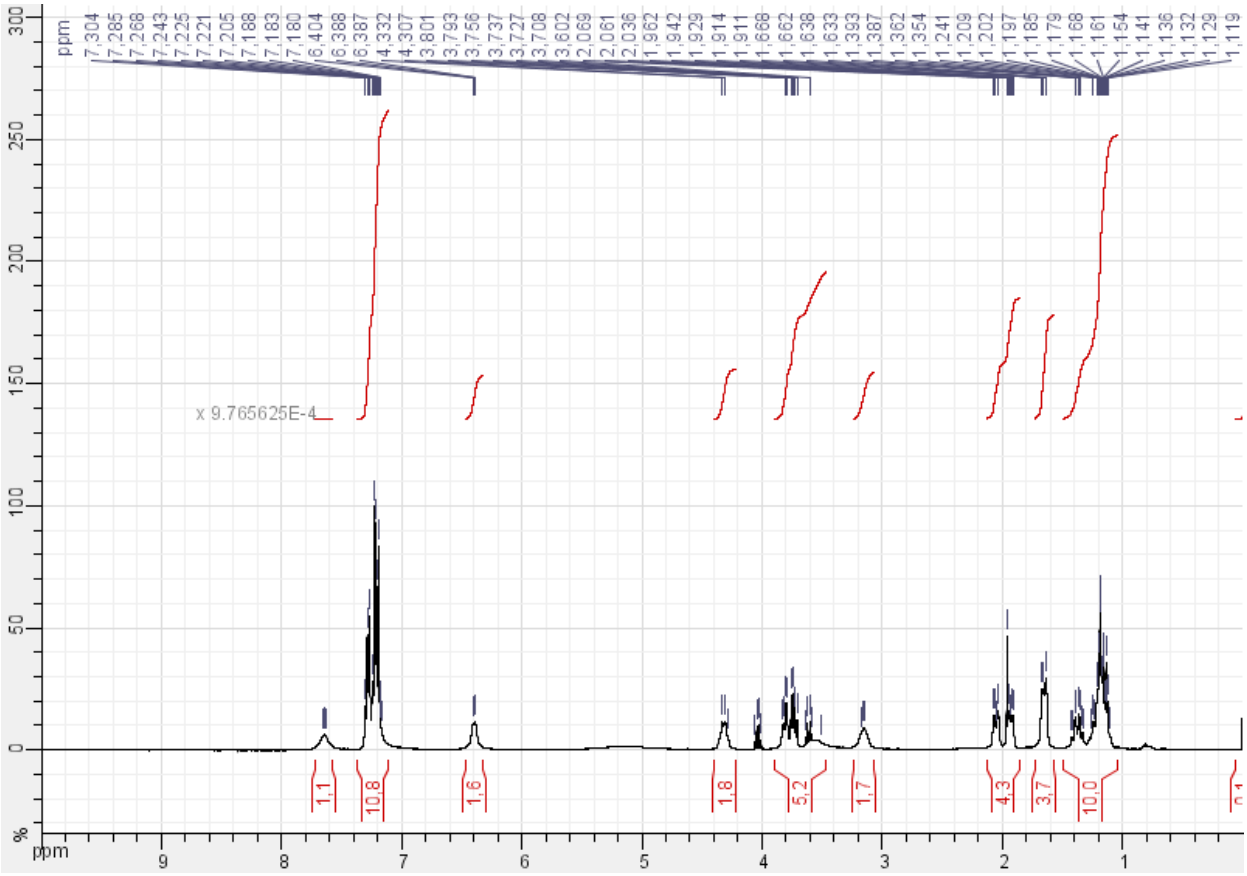

NHTf
NH
S
N
H
OH

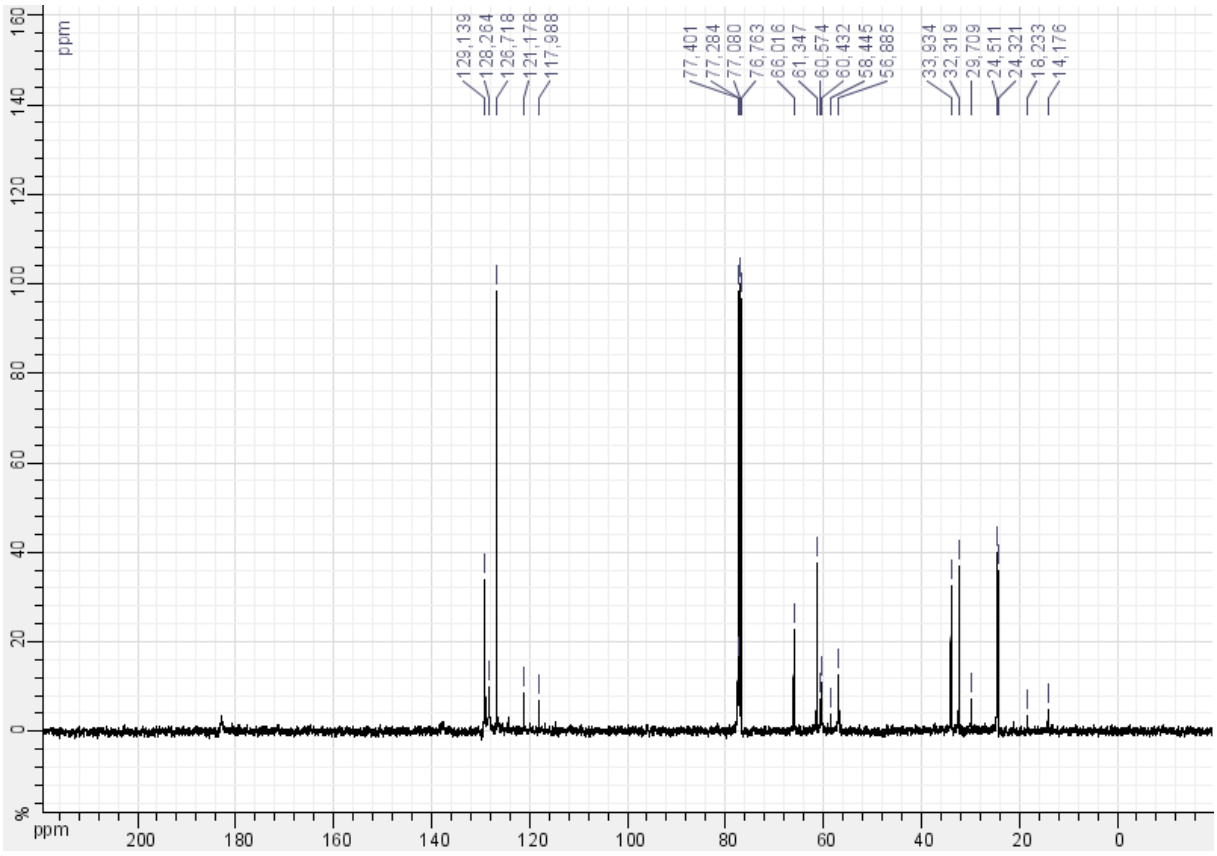

ppm
7,707
7,617
7,354
7,287
7,272
7,241
7,222
7,195
5,848
4,813
4,625
4,191
3,776
3,708
3,624
3,598
3,566
3,456
3,165
3,134
3,092
2,052
2,011
1,958
1,648
1,613
1,572
1,541
1,399
1,374
1,345
1,315
1,194
1,185
1,177
1,159
1,142
1,124
0,739
0,677
0,7
7,3
0,8
0,7
1,0
3,4
1,2
1,3
0,3
10,0
%
ppm

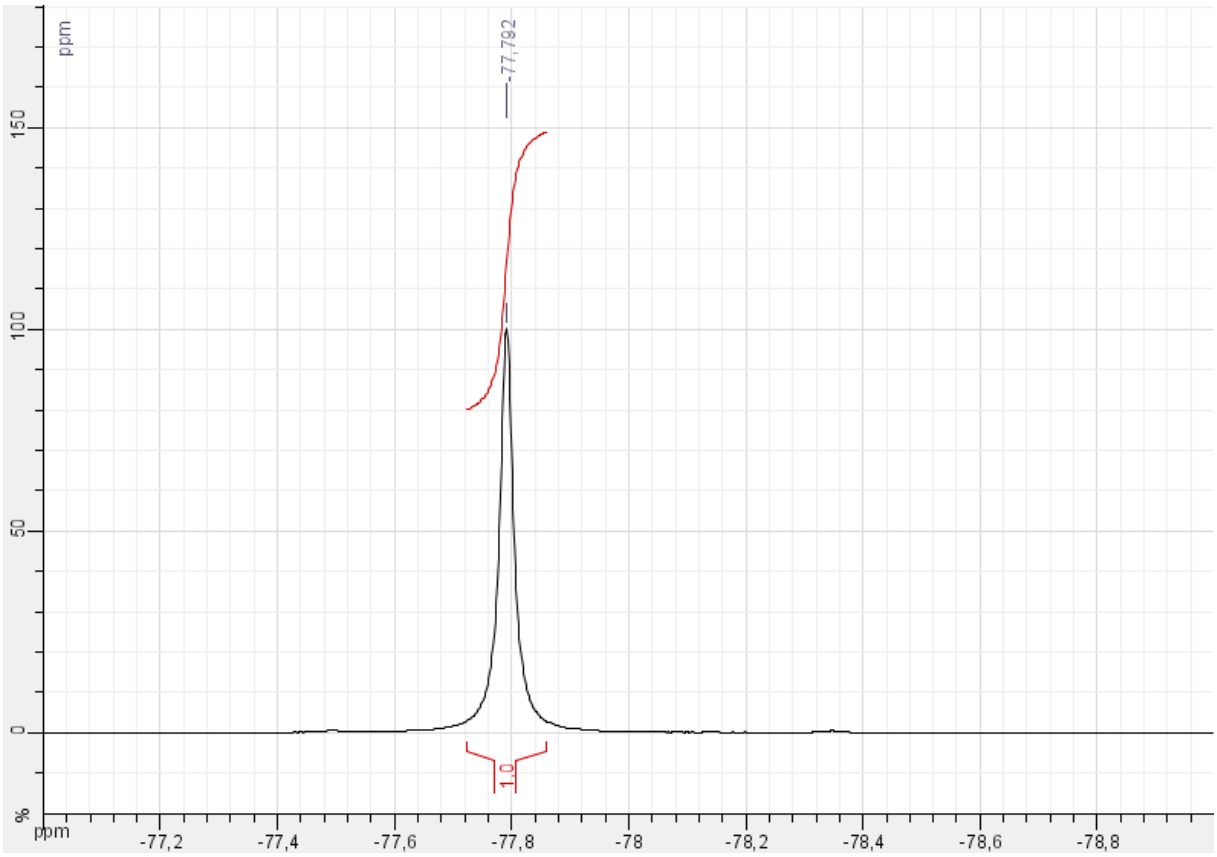

ppm
171,534
129,201
128,691
128,570
128,475
126,737
124,433
121,239
118,046
114,849
77,401
77,288
77,084
76,766
66,038
60,814
60,749
60,665
60,556
60,005
58,379
57,716
57,643
33,770
32,009
29,702
26,924
24,500
24,405
24,307
21,077
14,169
%
ppm
200
180
160
140
120
100
80
60
40
20
0


ppm
-77,929
1,0
%
ppm
-77,2
-77,4
-77,6
-77,8
-78
-78,2
-78,4
-78,6
-78,8


NHTf
NH
S
N
H
OH


ppm
x 9.765625E-4
1,1
10,8
1,6
1,8
5,2
1,7
4,3
3,7
10,0
%
ppm


ppm
129,139
128,264
126,718
121,178
117,988
77,401
77,284
77,080
76,763
66,016
61,347
60,574
60,432
58,445
56,885
33,934
32,319
29,709
24,511
24,321
18,233
14,176
%
ppm
200
180
160
140
120
100
80
60
40
20
0

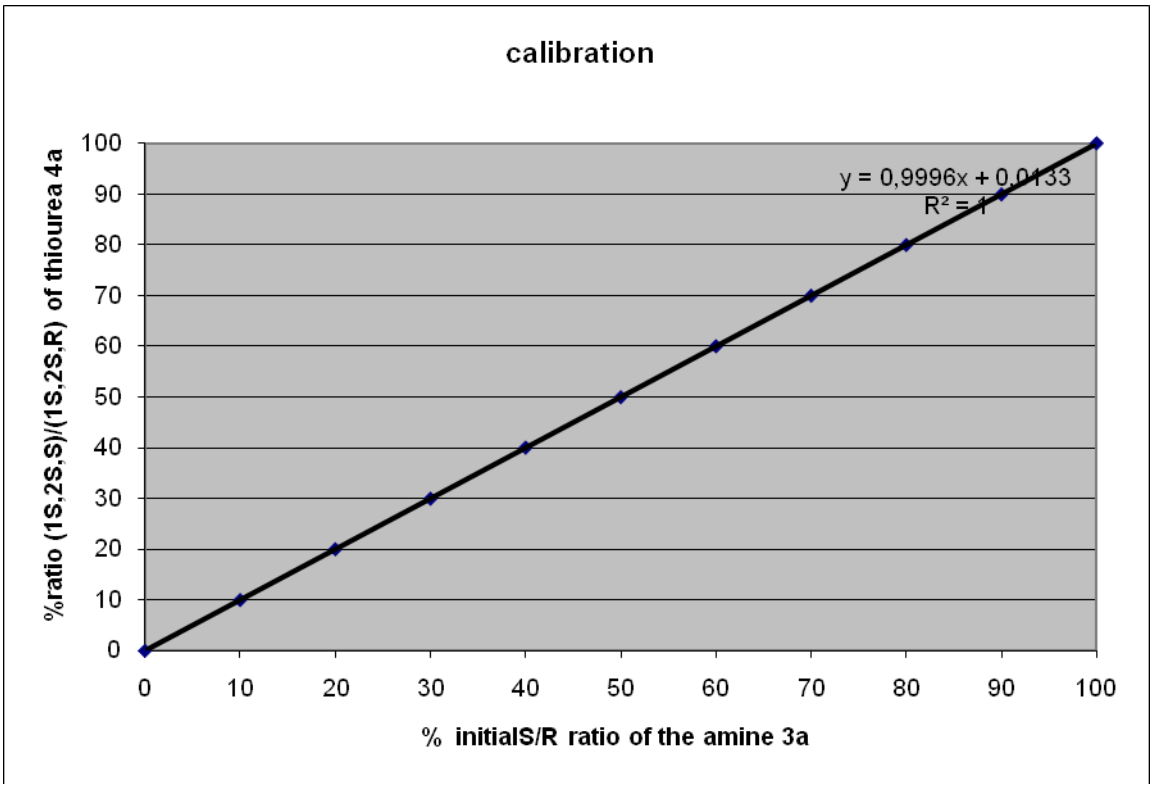

ppm
-77,792
1,0
%
ppm
-77,2
-77,4
-77,6
-77,8
-78
-78,2
-78,4
-78,6
-78,8

VII. Plot of the initial S/R ratio of 3a *vs*. the experimental ratio of thiourea diastereoisomers 4a.

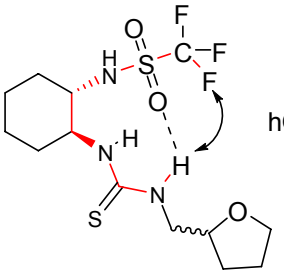
Theoretical[a] **S/R** ratio of amine **3a** used for the thiourea **4a** formation	Experimental [b] (1S,2S,**S**)/(1S,2S,**R**) ratio of thiourea mixture **4a**
0/100	0/100
10/90	10.00/90.00
20/80	20.03/79.97
30/70	29.98/70.02
40/60	40.04/59.96
50/50	49.97/50.03
60/60	60.02/39.98
70/30	69.98/30.02
80/20	79.96/20.04
90/10	89.94/10.06
100/0	100/0

[a] mixtures prepared prior use, by mixing (1S, 2S) and (1R,2R) amine **3a**
[b] ratio determined by quantitative integration by ^{19}F NMR of the (-CF_3) signals of both diastereoisomers **4a**

Plot of the initial S/R ratio of **3a** vs. experimental ratio of thiourea diastereoisomers **4a**.



VIII. Representative hOe effect for compound 4i.



hOe : *heterooverhauser effect*