Supporting Information

Annulated carbamates are precursors for the ring-contraction of the adamantane framework

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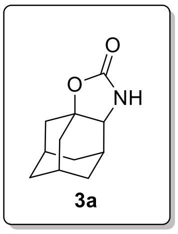
1. General information

NMR spectra were recorded on 400 or 600 MHz machine at RT (25 °C) unless otherwise stated. ^{1}H-NMR chemical shifts are given in ppm relative to Me_4Si with the solvent resonance used as the internal standard ($CDCl_3$ $\delta = 7.26$ ppm). ^{13}C-NMR (60, 101 or 150 MHz) chemical shifts are given in ppm relative to Me_4Si with the solvent resonance used as the internal standard ($CDCl_3 = 77.16$ ppm). IR spectra were recorded using an ATR sampler and are reported in wave numbers (cm^{-1}). Melting points (m.p.) were measured in open capillary tubes and are uncorrected. All reactions involving air sensitive compounds were carried out under dry and inert atmosphere (N_2 or argon) by means of an inert gas/vacuum double manifold line and standard Schlenk techniques. High resolution mass spectra were recorded with Brucker Micro TOF LC.

2. Experimental procedures

2.1 Preparation and characterization of starting materials **3-4**.

2.1.1 Compound 3a

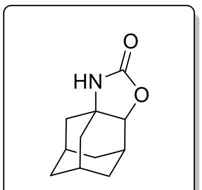

3a

^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 1.57-1.87 (m, 7H), 1.99-2.02 (m, 1H), 2.06-2.16 (m, 3H), 2.27 (m, 2H), 3.65 (m, 1H), 5.71 (bs, 1H)

^{13}C NMR (101 MHz, $CDCl_3$): δ/ppm = 29.1 (CH_2), 29.2 (CH), 31.1 (CH), 31.2 (CH), 36.3 (CH_2), 36.4 (CH_2), 37.2 (CH_2), 40.1 (CH_2), 64.1 (CH), 80.6 (C), 161.4 (C).

Compound **3a** was prepared in two steps from adamantan-1-ol according to the procedure described in Hrdina, R.; Larrosa, M.; Logemann, C. *J. Org. Chem.* **2017**, *82*, 4891−4899.

2.1.2 Compound 3b

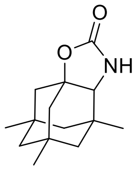

3b

^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 1.57-1.77 (m, 5H), 1.86-1.96 (m, 5H), 2.05 (m, 1H), 2.13 (m, 1H), 2.43 (m, 1H), 4.13 (d, *J*= 4 Hz, 1H), 5.48 (bs, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ/ppm = 27.9 (CH), 29.6 (CH_2), 29.7 (CH), 30.3 (CH), 36.0 (CH_2), 36.4 (CH_2), 39.5 (CH_2), 39.7 (CH_2), 56.7 (C), 85.5 (CH), 161.1 (C).

Compound **3b** was prepared in two steps from adamantan-2-ol according to the procedure described in Hrdina, R.; Larrosa, M.; Logemann, C. *J. Org. Chem.* **2017**, *82*, 4891−4899.

2.1.3 Compound 3c



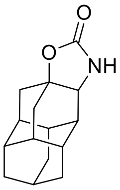
3c

^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 0.90 (s, 3H), 0.92 (s, 3H), 0.94 (s, 3H), 0.98-1.02 (m, 1H), 1.08-1.19 (m, 3H), 1.20-1.27 (m, 1H), 1.36-1.40 (m, 1H), 1.43-1.48 (m, 1H), 1.68-1.77 (m, 3H), 3.19 (m, 1H), 5.76 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ/ppm = 25.6 (CH_3), 29.0 (CH_3), 29.3 (CH_3), 33.1 (C), 34.9 (C), 35.7 (C), 42.7 (CH_2), 42.8 (CH_2), 45.3 (CH_2), 50.2 (CH_2), 50.8 (CH_2), 67.8 (CH), 82.7 (C), 161.6 (C).

Compound **3c** was prepared in two steps from 3,5,7-trimethyl-adamantan-1-ol according to the procedure described in Zonker, B.; Becker, J.; Hrdina, R. *Org. Biomol. Chem.* **2021**, *19*, 4027-4031.

2.1.4 Compound 3d



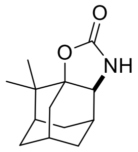
3d

^{1}H NMR (600 MHz, $CDCl_3$): δ/ppm = 1.59 (m, 1H), 1.68-1.71 (m, 1H), 1.77-1.83 (m, 8H), 1.86-1.88 (m, 1H), 1.94 (m, 1H), 1.98-2.01 (m, 2H), 2.04-2.07 (m, 1H), 2.10 (m, 1H), 2.14-2.19 (m, 2H), 3.6 (m, 1H), 5.01 (bs, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ/ppm = 25.9 (CH), 30.6 (CH), 35.9 (CH_2), 36.7 (CH), 36.8 (CH_2), 37.1 (CH), 37.3 (CH_2), 37.5 (CH_2), 38.3 (CH), 40.1 (CH), 40.2 (CH_2), 40.3 (CH), 65.1 (CH), 80.7 (C), 161.1 (C).

Compound **3d** was prepared in two steps from diamantan-ol according to the procedure described in Zonker, B.; Becker, J.; Hrdina, R. *Org. Biomol. Chem.* **2021**, *19*, 4027-4031.

2.1.5 Compound 3e



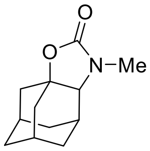
3e

^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 1.15 (s, 3H), 1.18 (s, 3H), 1.44-1.54 (m, 2H), 1.6-1.65 (m, 1H), 1.81-1.86 (m, 1H), 1.96-2.05 (m, 4H), 2.11-2.14 (m, 1H), 2.24-2.26 (m, 1H), 4.09-4.11 (m, 1H), 5.76 (bs, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ/ppm = 22.7 (CH_3), 22.8 (CH_3), 29.4 (CH), 30.7 (CH_2), 31.9 (CH), 32.1 (CH_2), 32.2 (CH_2), 33.1 (CH_2), 39.7 (C), 41.3 (CH), 58.7 (CH), 85.1 (C), 161.5 (C).

Compound **3e** was prepared in 5 steps from noradamantane-3-carboxylic acid according to the procedure described in Zonker, B.; Becker, J.; Hrdina, R. *Org. Biomol. Chem.* **2021**, *19*, 4027-4031.

2.1.6 Compound 4aa



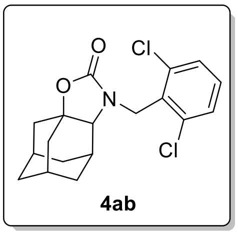
4aa

^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 1.62-1.78 (m, 6H), 1.83-1.86 (m, 1H), 1.96-2.04 (m, 2H), 2.07-2.11 (m, 2H), 2.28 (m, 2H), 2.78 (s, 3H), 3.28 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ/ppm = 29.2 (CH_3), 29.3 (CH), 29.4 (CH_2), 30.3 (C), 31.2 (CH_2), 36.1 (CH), 36.3 (CH_2), 37.8 (CH_2), 40.0 (CH_2), 68.2 (CH), 77.9 (C), 160.6 (C).

Compound **4aa** was prepared from **3a** according to the procedure described in Zonker, B.; Becker, J.; Hrdina, R. *Org. Biomol. Chem.* **2021**, *19*, 4027-4031.

2.1.7 Compound 4ab



4ab

Starting material **3a** (740 mg, 3.84 mmol) was dissolved in THF (8 mL) and the solution was cooled to -15 °C. MeLi (1.6 M solution in Et_2O) 2.4 mL was added dropwise and the reaction mixture was allowed to reach r.t. and stirred for additional 20 minutes. Then 2,6-dichlorobenzyl bromide (1365 mg, 1.5 equiv.) was added to the reaction mixture and the reaction mixture was heated at 50 °C for additional 16 hours. The reaction was quenched with water and the product was extracted using Et_2O. Combined organic fractions were dried over $MgSO_4$ and the product **4ab** was purified by column chromatography on silica gel using hexane: EtOAc 10:1 as a mobile phase. The compound **4ab** was obtained as a crystalline solid (1.02 g) in 76% yield.

m.p. (cryst. from $CDCl_3$): 156 °C.

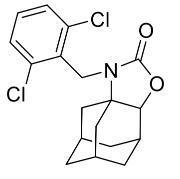
^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 0.87-0.90 (m, 1H), 1.14-1.17 (m, 1H), 1.55 (m, 2H), 1.64-1.74 (m, 3H), 1.94-1.96 (m, 3H), 2.04-2.08 (m, 2H), 2.19 (m, 1H,), 3.45 (m, 1H), 4.52 (d, *J*= 12 Hz, 1H), 5.02 (d, *J*=12 Hz, 1H), 7.16-7.20. (m, 1H), 7.29-7.31 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$): δ/ppm = 29.1 (CH), 29.3 (CH_2), 30.7 (CH), 31.1 (CH), 36.1 (CH_2), 36.6 (CH_2), 38.0 (CH_2), 39.9 (CH_2), 44.0 (CH_2), 68.5 (CH), 77.5 (C), 128.7 (2CH), 129.8 (CH), 132.3 (2C), 136.7 (C), 159.7 (C).

IR (neat): $\tilde{\nu}$ /cm^{-1} = 3086, 3072, 2927, 2868 1749, 1728, 1577, 1560, 1433, 1402, 1433, 1402, 1327, 1306, 1296, 1223, 1205, 1153, 1103. 1088, 1036, 985, 957, 935, 897, 835, 781, 769, 677,611, 575, 517, 411.

HRMS: m/z = 352.0871 ([M+H]$^+$; calculated for $C_{18}H_{20}Cl_2NO_2^+$ m/z = 352.0866).

2.1.8 Compound 4bb



4bb

Starting material **3b** (370 mg, 1.92 mmol) was dissolved in THF (4 mL) and the solution was cooled to -15 °C. MeLi (1.6 M solution in Et_2O) 1.2 mL was added dropwise and the reaction mixture was allowed to reach r.t. and stirred for 20 minutes. Then 2,6-dichloro-benzyl bromide (682 mg, 1.5 equiv.) was added to the reaction mixture and the reaction mixture was heated at 50 °C for additional 16 hours. Th reaction was quenched with water and the product was extracted using Et_2O. Combined organic fractions were dried over $MgSO_4$, concentrated *in vacuo* and the product was purified by column chromatography on silica gel using hexane: EtOAc 10:1 as a mobile phase. The compound **4bb** was obtained as a pale yellow solid (581 mg) in 85% yield.

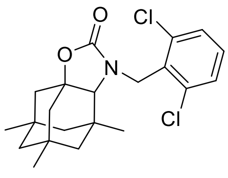
^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 1.16-1.19 (m, 1H), 1.53-1.79 (m, 7H), 1.86-1.93 (m, 2H), 2.07-2.09 (m, 1H), 2.19-2.23 (m, 1H), 2.36-2.39 (m, 1H), 3.95-3.96 (m, 1H,), 4.51 (d, *J*= 12 Hz, 1H), 4.88 (d, *J*= 12 Hz, 1H),7.16-7.20 (m, 1H), 7.29-7.31 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$): δ/ppm = 27.8 (CH), 29.6 (CH), 29.9 (CH_2), 30.1 (CH), 35.45 (CH_2), 36.0 (CH_2), 36.1 (CH_2), 38.4 (CH_2), 40.7 ($2CH_2$), 59.5 (C), 83.3 (CH), 128.7 (2CH),129.7 (CH), 133.0 (C), 136.6 (C), 158.9 (C).

IR (neat): $\tilde{\nu}$ /cm^{-1} = 3070, 2945, 2925, 2854, 1755, 1562, 1598, 1459, 1435, 1358, 1333, 1259, 1260, 1228, 1182, 1149, 1109, 1074, 1026, 1016, 993, 933, 904, 866, 812, 768, 737, 687, 626, 575, 519, 467, 415

HRMS: m/z = 352.0871 ([M+H]$^+$; calculated for $C_{18}H_{20}Cl_2NO_2^+$ m/z = 352.0866).

2.1.9 Compound 4cb



4cb

Starting material **3c** (235 mg, 1.0 mmol) was dissolved in THF (2 mL) and the solution was cooled to -15 °C. MeLi (1.6 M solution in Et_2O) 0.7 mL was added dropwise and the reaction mixture was allowed to reach r.t. and stirred for 20 minutes. Then 2,6-dichloro-benzyl bromide (355 mg, 1.5 equiv.) was added to the reaction mixture and the reaction mixture was heated at

50 °C for additional 16 hours. Th reaction was quenched with water and the product was extracted using Et2O. Combined organic fractions were dried over $MgSO_4$, concentrated *in vacuo* and the product was purified by column chromatography on silica gel using hexane: EtOAc 10:1 as a mobile phase. The compound **4cb** was obtained as a crystalline solid (272 mg) in 69% yield.

m.p. (cryst. from Et_2O): 133.2 °C

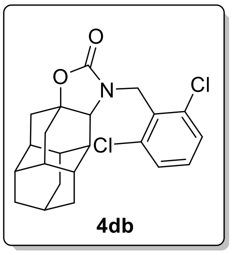
^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 0.82 (s, 3H), 0.89 (s, 3H), 0.93 (s, 4H), 1.01-1.09 (m, 2H), 1.16-1.19 (m, 1H), 1.26-1.32 (m, 2H), 1.36-1.4 (m, 1H), 1.60-1.66 (m, 1H), 1.70-1.72 (m, 1H), 1.84-1.87 (m, 1H), 3.10 (m, 1H), 4.64 (d, *J*=14Hz, 1H), 4.93 (d, *J*=14Hz, 1H), 7.15 (m, 1H), 7.3 (d, *J*=8 Hz, 2H).

^{13}C NMR (101 MHz, $CDCl_3$): δ/ppm = 26.5 (CH_3), 29.0 (CH_3), 29.1 (CH_3), 32.9 (C), 34.9 (C), 36.2 (C), 43.8 (CH_2), 43.9 (CH_2), 45.2 (CH_2), 45.7 (CH_2), 50.0 (CH_2), 52.6 (CH_2), 72.35 (CH), 79.6 (C), 129.0 (CH), 129.2 (2CH),132.8 (2C), 136.0 (C), 160.5 (C).

IR (neat): $\tilde{\nu}$ /cm^{-1} = 3062, 2952, 2908, 2837, 1755, 1562, 1471, 1439, 1410, 1391, 1344, 1298, 1257, 1207, 1193, 1155, 1109, 1086, 1038, 1018, 997, 962, 914, 895, 854, 829, 775, 721, 706, 667, 636, 607, 561, 530, 501, 463.

HRMS: m/z = 394.1334 ($[M+H]^+$; calculated for $C_{21}H_{26}Cl_2NO_2^+$ m/z = 394.1336).

2.1.10 Compound 4db


4db

Starting material **3d** (235 mg, 1.0 mmol) was dissolved in THF (2 mL) and the solution was cooled to -15 °C. MeLi (1.6 M solution in Et_2O) 0.7 mL was added dropwise and the reaction mixture was allowed to reach r.t. and stirred for 20 minutes. Then 2,6-dichloro-benzyl bromide (355 mg, 1.5 equiv.) was added to the reaction mixture and the reaction mixture was heated at 50 °C for additional 16 hours. Th reaction was quenched with water and the product was extracted using Et_2O. Combined organic fractions were dried over $MgSO_4$, concentrated *in vacuo* and the product was purified by column chromatography on silica gel using hexane: EtOAc 10:1 as a mobile phase. The compound **4db** was obtained as a crystalline solid (260 mg) in 64% yield.
m.p. (cryst. from Et_2O): 210.7 °C.

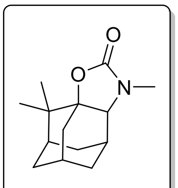
^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 0.96 (m, 1H), 1.09-1.13 (m, 1H), 1.46-1.49 (m, 1H), 1.61-1.75 (m, 9H), 1.81 (m, 1H), 1.90-2.09 (m, 4H), 3.38 (m, 1H), 4.53 (d, *J*= 4 Hz, 1H), 5.00 (d, *J*= 4 Hz, 1H), 7.17-7.21 (m, 1H), 7.30 (s, 1H), 7.32 (s, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ/ppm = 25.6 (CH), 31.1 (2CH), 36.0 (CH_2), 36.5 (CH), 36.6 (CH_2), 37.2 (CH), 37.3 (CH_2), 38.0 (CH), 38.3 (CH_2), 39.9 (CH), 39.92(CH_2) 43.9 (CH_2), 69.3 (CH), 128.7 (CH), 129.8 (2CH), 132.5 (C), 136.9 (2C), 159.8 (C).

IR (neat): $\tilde{\nu}$ /cm^{-1} = 3087, 2956, 2908, 2870, 2779, 2684, 2648, 1751, 1581, 1562, 1543, 1460, 1435, 1388, 1334, 1302, 1137, 1190, 1159, 1088, 1070, 1011, 962, 941, 897, 831, 816, 785, 773, 762, 692, 658, 580, 546, 496.

HRMS: m/z = 426.1000 ($[M+Na]^+$; calculated for $C_{22}H_{23}Cl_2NO_2Na^+$ m/z = 426.0998).

2.1.11 Compound 4ea



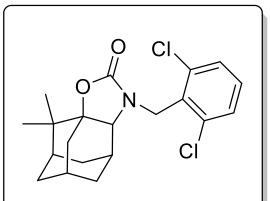
4ea

^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 1.13 (s, 3H), 1.18 (s, 3H), 1.46-1.50 (m, 1H), 1.54-1.59 (m, 1H), 1.65-1.71 (m, 2H), 1.83-1.87 (m, 1H), 1.99-2.04 (m, 3H,), 2.11-2.14 (m, 1H), 2.16-2.25 (m, 1H), 2.77 (s, 3H), 3.7-3.71 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ/ppm = 22.6 (CH_3), 22.8 (CH_3), 29.4 (CH), 29.5 (CH_3), 31.0 (CH), 31.1 (CH_2), 32.1 (CH_2), 32.8 (CH_2), 33.1 (CH_2), 39.6 (C), 41.5 (CH), 63.0 (CH), 86.2 (C), 160.6 (C).

Compound **4ea** was prepared from **3e** according to the procedure described in Zonker, B.; Becker, J.; Hrdina, R. *Org. Biomol. Chem.* **2021**, *19*, 4027-4031.

2.1.12 Compound 4eb



4eb

Starting material **3e** (110 mg, 0.5 mmol) was dissolved in THF (1 mL) and the solution was cooled to -15 °C. MeLi (1.6 M solution in Et_2O) 0.35 mL was added dropwise and the reaction mixture was allowed to reach r.t. and stirred for 20 minutes. Then 2,6-dichloro-benzyl bromide (177 mg, 1.5 equiv.) was added to the reaction mixture and the reaction mixture was heated at 50 °C for additional 16 hours. Th reaction was quenched with water and the product was extracted using Et_2O. Combined organic fractions were dried over $MgSO_4$, concentrated *in vacuo* and the product was purified by column chromatography on silica gel using hexane:

EtOAc 10:1 as a mobile phase. The compound was obtained as a crystalline solid (120 mg) in 63% yield.

m.p. (cryst. from EtOAc): 210 - 211 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 0.79-0.84 (m, 1H), 1.07-1.23 (m, 7H), 1.32-1.36 (m, 1H), 1.46-1.57 (m, 2H), 1.87-1.95 (m, 5H), 2.08-2.11 (m, 1H), 3.86 (m, 1H), 4.5 (d, J=16 Hz, 1H), 5.02 (d, J=12 Hz, 1H), 7.16-7.26 (m, 1H), 7.29-7.31 (m, 2H).

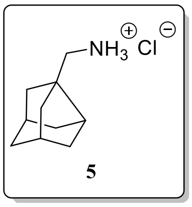
^{13}C NMR (101 MHz, $CDCl_3$): δ/ppm = 22.6 (CH_3), 22.9 (CH_3), 29.3 (CH), 30.9 (CH_2), 31.8 (CH), 32.0 (CH_2), 33.0 (CH_2), 33.3 (CH_2), 39.4 (C), 41.0 (CH), 44.2 (CH_2), 63.5 (CH), 81.8 (C), 128.7 (CH), 129.8 (2CH), 132.3 (C), 136.7 (2C), 159.8 (C).

IR (neat): $\tilde{\nu}$ /cm^{-1} = 2999, 2924, 2887, 2868, 1749, 1562, 1537, 1475, 1435, 1404, 1319, 1292, 1211, 1146, 1103, 1090, 1032, 974, 964, 945, 920, 903, 866, 837, 831, 781, 764, 733, 673, 663, 528, 480, 455, 430.

HRMS: m/z = 380.1181 ($[M+H]^+$; calculated for $C_{20}H_{24}Cl_2NO_2^+$ m/z = 380.1106).

2.2 Preparation and characterisation of compounds **5-26**

2.2.1 Compound 5



5

Starting material **3a** (100 mg, 0.5 mmol) was dissolved in dry 1,2,4-trichlorobenzene (8 mL) and 150 mg (2 equiv.) of freshly distilled anhydrous triflic acid was added to the solution at r.t. The reaction mixture was heated for 4 hours at 120 °C under inert atmosphere. Then the reaction mixture was cooled to -78 °C, it solidified, and $LiAlH_4$ (38 mg, 1 mmol) was added on the top. Then dry THF 2 mL was added at -78 °C and the reaction was let to warm up to r.t. and stirred at r.t. for 3h. The reaction was quenched with sat. solution of Na_2CO_3, product, resulting amine, was extracted with Et_2O. Combined organic fractions were dried over $MgSO_4$ and Et_2O with THF was evaporated under *vacuo*. To the solution of product, free amine, in 1,2,4-trichlorobenzene was added HCl in Et_2O and the resulting hydrochloric salt was filtered off. The product was purified by crystallisation from EtOAc and obtained as colourless crystalline solid (65 mg) in 69% yield.
Please, note that if triflic acid is not anhydrous or the solvent is contaminated with water then the yield drops dramatically.

m.p. (cryst. from EtOAc): 212.4 - 213.1 °C.

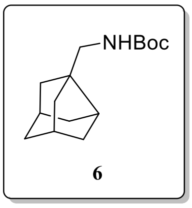
^{1}H NMR (400 MHz, CD_3OD): δ/ppm = 1.65-1.82 (m, 10H), 2.18 (m, 1H), 2.29 (m, 2H), 3.08 (bs, 2H).

^{13}C NMR (101 MHz, CD_3OD): δ/ppm = 35.8 (CH_2), 39.0 (CH), 43.2 (CH), 43.6 (CH), 44.6 (CH_2), 47.7 ($2CH_2$), 48.2 ($2CH_2$), 48.8 (C).

IR (neat): $\tilde{\nu}$ /cm^{-1} = 3535, 2947, 2916, 2488, 1653, 1616, 1506, 1464, 1388,1304, 1252, 1099, 982, 931, 862, 789, 584.

HRMS: m/z = 152.1434 ([M]$^+$; calculated for $C_{10}H_{18}N^+$ m/z = 152.1434).

2.2.2 Compound 6



6

To the solution of **5** (as free amine R-NH_2) (140 mg, 0.93 mmol) and *N*,*N*-dimethylamino pyridine (6 mg) in dichloromethane (2 mL) was added Boc-anhydride (218 mg, 1 mmol) and the reaction mixture was stirred for 16 hours. The reaction was quenched with brine and the product was extracted using Et_2O. Combined organic fractions were concentrated *in vacuo* and the product was purified using column chromatography on silica-gel using hexane: Et_2O 2:1 as a mobile phase. The compound **6** was obtained as a colourless crystalline solid (150mg) in 60% yield.

m.p. (cryst. from pentane): 67.5 - 68.7 °C.

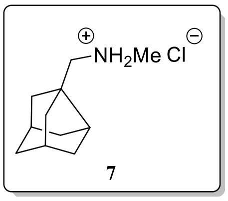
^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 1.42 (s, 9H), 1.52-1.68 (m, 10H), 2.02 (m, 1H), 2. 19 (m, 2H), 3.21 (d, *J*= 8 Hz, 2H), 4.57 (bs, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ/ppm = 28.5 ($3CH_3$), 35.4 (CH_2), 37.5 (2CH), 41.4 (CH), 44.1 (CH_2), 47.0 ($2CH_2$), 47.8 ($2CH_2$), 49.5 (C), 80.0 (C), 156.5 (C).

IR (neat): $\tilde{\nu}$ /cm^{-1} = 3340, 2920, 2862, 1684, 1533, 1479, 1454, 1387, 1361, 1290, 1271, 1250, 1163, 1120, 1097, 1078, 1039, 1082, 982, 893, 866, 843, 781, 766, 658, 461, 434.

HRMS: m/z = 252.1961 ($[M+H]^+$ calculated for $C_{15}H_{26}NO_2^+$ m/z = 252.1958).

2.2.3 Compound 7



Starting material **4aa** (207 mg, 1 mmol) was dissolved in dry 1,2,4-trichlorobenzene (4 mL) and (300 mg, 2 equiv.) of freshly distilled anhydrous triflic acid was added to the solution at r.t. The reaction mixture was heated for 4 hours at 140 °C under inert atmosphere. Then the reaction mixture was cooled to -78 °C, it solidified, and $LiAlH_4$ (76 mg, 2 mmol) was added on the top. Then dry THF (2 mL) was added at -78 °C and the reaction was let to warm up to r.t. and stirred at r.t. for 3h. The reaction was quenched with sat. solution of Na_2CO_3, product, resulting amine, was extracted with Et_2O. Combined organic fractions were dried over $MgSO_4$ and then Et_2O with THF was evaporated under *vacuo*. To the solution of amine in 1,2,4-trichlorobenzene was added HCl in Et_2O and the resulting hydrochloric salt was filtered off. The product was purified by crystallisation from EtOAc and obtained as colourless crystalline solid (140 mg) in 70% yield.

Please, note that if triflic acid is not anhydrous or the solvent is contaminated with water then the yield drops dramatically.

m.p. (cryst. from EtOAc): not measurable, sublimation of the sample occurred at 230 °C.

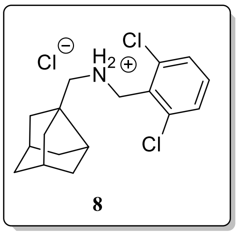
^{1}H NMR (400 MHz, CD_3OD): δ/ppm = 1.65-1.86 (m, 10H), 2.22 (m, 1H), 2.31 (m, 2H), 2.77 (s, 3H), 3.18 (bs, 2H).

^{13}C NMR (101 MHz, CD_3OD): δ/ppm = 35.0 (CH), 35.7 (CH_2), 38.9 (CH_3), 43.6 (CH), 44.5 ($2CH_2$), 47.7 (CH_2), 48.5 (C), 58.6 ($2CH_2$).

IR (neat): $\tilde{\nu}$ /cm^{-1} = 2918, 2862, 2846, 2762, 2438, 1591, 1468, 1460, 1431, 1398, 1338, 1302, 1154, 1134, 1117, 1101, 1024, 1016, 997, 941, 916, 862, 779, 671, 646, 523.

HRMS: m/z = 166.1589 ([M]$^+$; calculated for $C_{11}H_{20}N^+$ m/z = 166.1591).

2.2.4 Compound 8



8

Starting material **4ab** (700 mg, 2 mmol) was dissolved in dry 1,2,4-trichlorobenzene (8 mL) and 600 mg (2 equiv.) of freshly distilled anhydrous triflic acid was added to the solution at r.t. The reaction mixture was heated for 16 hours at 150 °C under inert atmosphere. Then the reaction mixture was cooled to -78 °C, solidified, and $LiAlH_4$ (152 mg, 4 mmol) was added on the surface. Then dry THF (4 mL) was added at -78 °C and the reaction was let to warm up to r.t. and stirred at r.t. for 3h. The reaction was quenched with sat. solution of Na_2CO_3, product, resulting amine, was extracted with Et_2O. Combined organic fractions were dried over $MgSO_4$ and Et_2O with THF was evaporated under *vacuo*. To the solution of amine in 1,2,4-trichlorobenzene was added HCl in Et_2O and the resulting hydrochloric salt was filtered off. The product was purified by crystallisation from EtOAc and obtained as colourless crystalline solid (596 mg) in 84% yield. *Please, note that if triflic acid is not anhydrous or the solvent is contaminated with water then the yield drops dramatically.*
m.p. (cryst. from EtOAc): 197 - 198 °C.

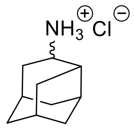
^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 1.50-1.73 (m, 10H), 1.96-1.99 (m, 1H), 2.19 (m, 2H), 2.65 (m, 2H),4.13 (m, 2H), 7.10-7.14 (m, 1H), 7.28-7.30 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$): δ/ppm = 35.5 (CH_2), 37.7 (2CH), 42.3 (CH), 44.0 ($2CH_2$), 47.5 ($2CH_2$), 49.2 (CH_2), 49.5 (C), 56.6 (CH_2), 128.5 (2CH), 128.8 (CH), 136.1 (2C), 136.3 (C).

IR (neat): $\tilde{\nu}$ /cm^{-1} = 2925, 2862, 2802, 1581, 1457, 1410, 1329, 1200, 1147, 1084, 910, 825, 770, 723, 615.

HRMS: m/z = 310.1122 ([M]$^+$; calculated for $C_{17}H_{22}Cl_2N^+$ m/z = 310.1124).

2.2.5 Compound 9



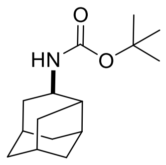
9

Starting material **3b** (318 mg, 1.65 mmol) was dissolved in dry 1,2,4-trichlorobenzene (13 mL) and 495 mg (2 equiv.) of freshly distilled anhydrous triflic acid was added to the solution at r.t. The reaction mixture was heated for 4 hours at 120 °C under inert atmosphere. Then the reaction mixture was cooled to -78 °C, it solidified, and $LiAlH_4$ (125 mg, 3.3 mmol) was added on the surface. Then dry THF (2 mL) was added at -78 °C and the reaction was let to warm up to r.t. and stirred at r.t. for 3h. The reaction was quenched with sat. solution of Na_2CO_3, product, resulting amine, was extracted with Et_2O. Combined organic fractions were dried over $MgSO_4$ and Et_2O with THF was evaporated under *vacuo*. To the solution of amine in 1,2,4-trichlorobenzene was added HCl in Et_2O and the resulting hydrochloric salt was filtered off. The product **9** (1 to 1 mixture of diastereomers) was purified by crystallisation from EtOAc and obtained as colourless crystalline solid (278 mg) in 90% yield. *Please, note that if triflic acid is not anhydrous or the solvent is contaminated with water then the yield drops dramatically. Following NMR spectra were recorded for the 1:1 mixture of diastereomers. The compound was transformed to Boc-protected derivative* ***10****, which was separated into individual isomers.*

^{1}H NMR (400 MHz, CD_3OD): δ/ppm = 1.42-1.53 (m, 6H), 1.56-173 (m, 6H), 1.75-1.80 (m, 2H), 1.84-1.99 (m, 4H), 2.01-2.11 (m, 2H), 2.16-2.42 (m, 6H), 2.48-2.55 (m, 2H), 3.46-3.51 (m, 1H), 3.62-3.65 (m, 1H).

^{13}C NMR (101 MHz, CD_3OD): δ/ppm = 28.4 (CH), 29.6 (CH), 32.1 (CH_2), 32.2 (CH_2), 32.5 (CH_2), 32.9 (CH_2), 33.6 (CH_2), 34.1 (CH_2), 36.1 (CH), 36.2 (CH), 36.3 (CH), 36.6 (CH), 38.1 (CH_2), 39.2 (CH), 39.3 (CH), 39.8 (CH_2), 40.3 (CH_2), 42.2 (CH_2), 49.5 (CH), 50.8 (CH).

2.2.6 Compound 10-l1



10-l1

To the solution of free amine of **9** (151 mg, 1.0 mmol) and *N*,*N*-dimethylamino pyridine (6 mg) in dichloromethane (2 mL) was added Boc-anhydride (240 mg, 1.1 mmol) and the reaction mixture was stirred for 16 hours. The reaction was quenched with brine and the product was extracted using Et_2O. Combined organic fractions were concentrated *in vacuo* and the product was purified using column chromatography on silica-gel using hexane:Et_2O 2:1 as a mobile phase. The compound **10** was obtained as a colourless 1:1 mixture of two isomers **10-I1** and **10-I2** (105 mg) in 42% combined yield.

Isomer **10-I1** crystallises preferentially out of the hexane solution and was recrystallised in pentane.

m.p. (cryst. from pentane): 106.7 - 107.3 °C.

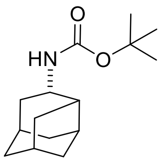
^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 1.15-1.21 (m, 1H), 1.26-1.33 (m, 2H), 1.37-1.42 (m, 2H), 1.45 (m, 9H), 1.49-1.56 (m, 1H), 1.58-1.65 (m, 2H), 1.73-1.83 (m, 1H), 2.00-2.06 (m, 1H), 2.15-2.41 (m, 4H), 3.80-3.90 (m, 1H), 4.40-4.50 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ/ppm = 28.6 ($3CH_3$), 28.8 (CH), 31.9 (CH_2), 32.5 (CH_2), 34.7 (CH), 35.5 (CH), 35.6 (CH_2), 39.8 (CH), 40.0 (CH_2), 41.6 (CH_2), 46.7 (CH), 77.4 (C), 152.1 (C) hardly visible.

IR (neat): $\tilde{\nu}$ /cm^{-1} = 3338, 2978, 2916, 2866, 2846, 2486, 1674, 1520, 1456, 1410, 1365, 1350, 1308, 1252, 1165, 1090, 1039, 1016, 999, 960, 930, 895, 870,829, 804, 793, 762, 737, 619, 577, 461, 426.

HRMS: m/z = 274.1781 ($[M+Na]^+$; calculated for $C_{15}H_{25}NO_2Na^+$ m/z = 274.1778).

Compound 10-12



10-I2

m.p. (cryst. from pentane): 106.7 - 107.3 °C.

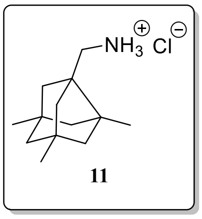
^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 1.30-1.40 (m, 4H), 1.46-1.56 (m, 4H), 1.60-1.68 (m, 3H), 1.75-1.83 (m, 4H), 1.94-2.03 (m, 2H), 2.12-2.24 (m, 3H), 2.36-2.47 (m, 2H),3.86-3.92 (m, 1H), 4.66-4.75 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ/ppm = 27.7 (CH), 28.6 ($3CH_3$), 31.6 (CH_2), 32.2 (CH_2), 34.7 (CH), 35.2 (CH), 37.1 (CH_2), 39.5 (CH), 39.7 (CH_2), 42.6 (CH_2), 48.7 (CH), 79.1 (C), 155.1 (C) hardly visible.

IR (neat): $\tilde{\nu}$ /cm^{-1} = 3456, 3259, 2924, 2866, 2844, 2251, 1693, 1525, 1495, 1473, 1452, 1363, 1352, 1302, 1248, 1163, 1063, 1028, 1014, 997, 978, 908, 872, 850, 818, 779, 729, 649, 586, 567, 461, 440.

HRMS: m/z = 274.1781 ($[M+Na]^+$; calculated for $C_{15}H_{25}NO_2Na^+$ m/z = 274.1778).

2.2.7 Compound 11



Starting material **3c** (117 mg, 0.5 mmol) was dissolved in dry 1,2,4-trichlorobenzene (4 mL) and (150 mg, 2 equiv.) of freshly distilled anhydrous triflic acid was added to the solution at r.t. The reaction mixture was heated for 4 hours at 120 °C under inert atmosphere. Then the reaction mixture was cooled to -78 °C, it solidified, and $LiAlH_4$ (38 mg, 1.0 mmol) was added on the surface. Then dry THF (2 mL) was added at -78 °C and the reaction was let to warm up to r.t. and stirred at r.t. for 3h. The reaction was quenched with sat. solution of Na_2CO_3, product, resulting amine, was extracted with Et_2O. Combined organic fractions were dried over $MgSO_4$ and Et_2O with THF was evaporated under *vacuo*. To the solution of amine in 1,2,4-trichlorobenzene was added HCl in Et_2O and the resulting hydrochloric salt was filtered off. The product was purified by crystallisation from EtOAc and obtained as colourless crystalline solid (90 mg) in 78% yield. *Please, note that if triflic acid is not anhydrous or the solvent is contaminated with water then the yield drops dramatically.*

m.p. (cryst. from EtOAc): 285.4 - 286.3 °C.

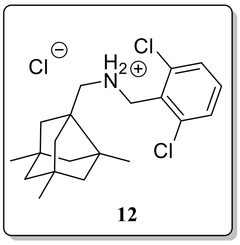
^{1}H NMR (400 MHz, CD_3OD): δ/ppm = 1.03 (s, 6H), 1.05 (s, 3H), 1.38-1.47 (m, 10H), 2.96 (s, 2H).

^{13}C NMR (101 MHz, CD_3OD): δ/ppm = 21.5 (CH_3), 24.9 ($2CH_3$), 40.9 (2C), 47.6 (CH_2), 48.9 (CH_2), 49.7 (C), 50.1 (C), 53.6 ($2CH_2$), 57.9 ($2CH_2$).

IR (neat): $\tilde{\nu}$ /cm^{-1} = 3010, 2943, 2918, 2891, 2662, 2850, 2713, 2609, 2038, 1618, 1604, 1502, 1454, 1390, 1371, 1348, 1286, 1234, 1215, 1149, 1117, 1080, 1022, 968, 708, 638, 579, 525.

HRMS: m/z = 194.1902 ($[M]^+$; calculated for $C_{13}H_{24}N^+$ m/z = 194.1904).

2.2.8 Compound 12



Starting material **4cb** (200 mg, 0.5 mmol) was dissolved in dry 1,2,4-trichlorobenzene (2 mL) and 150 mg (2 equiv.) of freshly distilled anhydrous triflic acid was added to the solution at r.t. The reaction mixture was heated for 16 hours at 150 °C under inert atmosphere. Then the reaction mixture was cooled to -78 °C, it solidified, and $LiAlH_4$ (38 mg,1 mmol) was added on the surface. Then dry THF (2 mL) was added at -78 °C and the reaction was let to warm up to r.t. and stirred at r.t. for 3h. The reaction was quenched with sat. solution of Na_2CO_3, product, resulting amine, was extracted with Et_2O. Combined organic fractions were dried over $MgSO_4$ and Et_2O with THF was evaporated under *vacuo*. To the solution of amine in 1,2,4-trichlorobenzene was added HCl in Et_2O and the resulting hydrochloric salt was filtered off. The product **12** was purified by crystallisation from EtOAc and obtained as colourless crystalline solid (120 mg) in 62% yield. *Please, note that if triflic acid is not anhydrous or the solvent is contaminated with water then the yield drops dramatically.*

m.p. (cryst. from EtOAc): 285.4 - 286.3 °C.

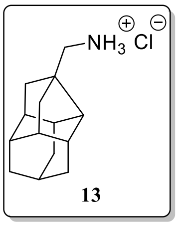
^{1}H NMR (400 MHz, CD_3Cl_3): δ/ppm = 0.84 (s, 3H), 0.92 (s, 6H), 1.22-1.42 (m, 8H), 1.75-1.78 (m, 2H), 2.81 (br s, 2H), 4.64 (m, 2H), 7.31-7.35 (m, 1H), 7.4-7.42 (m, 2H), 9.19 (br s, 2H).

^{13}C NMR (101 MHz, CD_3Cl_3): δ/ppm = 21.3 (CH_3), 24.5 ($2CH_3$), 40.2 (C), 46.5 ($2CH_2$), 47.7 ($2CH_2$), 48.8 (2C), 48.9 (C), 52.7 ($2CH_2$), 56.8 (CH_2), 127.2 (2C), 129.1 (2CH), 131.9 (CH), 137.4 (C).

IR (neat): $\tilde{\nu}$ /cm^{-1} = 3379, 3298, 3226, 3098, 2951, 2937, 2924, 2902, 2864, 2837, 2733, 2584, 1620, 1577, 1562, 1452, 1439, 1408, 1371, 1209, 1169, 1093, 1030, 1005, 968, 949, 922, 789, 764, 719, 661, 634, 546.

HRMS: m/z = 352.1593 ($[M]^+$; calculated for $C_{20}H_{28}Cl_2N^+$ m/z =352.1594).

2.2.9 Compound 13



13

Starting material **3d** (120 mg, 0.5 mmol) was dissolved in dry 1,2,4-trichlorobenzene (4 mL) and (150 mg, 2 equiv.) of freshly distilled anhydrous triflic acid was added to the solution at r.t. The reaction mixture was heated for 4 hours at 120 °C under inert atmosphere. Then the reaction mixture was cooled to -78 °C, solidified, and $LiAlH_4$ (38 mg, 1.0 mmol) was added on the surface. Then dry THF (2 mL) was added at -78 °C and the reaction was let to warm up to r.t. and stirred at r.t. for 3h. The reaction was quenched with sat. solution of Na_2CO_3, product, resulting amine, was extracted with Et_2O. Combined organic fractions were dried over $MgSO_4$ and Et_2O with THF was evaporated under vacuo. To the solution of amine in 1,2,4-trichlorobenzene was added HCl in Et_2O and the resulting hydrochloric salt was filtered off. The product **13** was purified by crystallisation from EtOAc and obtained as colourless crystalline solid (80 mg) in 67% yield. *Please, note that if triflic acid is not anhydrous or the solvent is contaminated with water then the yield drops dramatically.*

m.p. (cryst. from EtOAc): 182.8 - 183.7 °C

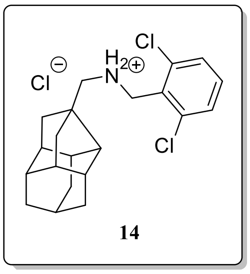
^{1}H NMR (400 MHz, CD_3OD): δ/ppm = 1.61-1.69 (m, 4H), 1.76 (m, 2H), 1.83-1.87 (m, 4H), 1.93-1.96 (m, 5H), 2.03 (m, 2H), 3.04 (m, 2H).

^{13}C NMR (101 MHz, CD_3OD): δ/ppm = 26.1 (CH), 34.3 ($2CH_2$), 35.6 (CH_2), 36.4 (2CH), 43.0 (2CH), 46.1 (CH_2), 46.8 (2CH), 48.0 ($2CH_2$), 50.5 (C).

IR (neat): $\tilde{\nu}$ /cm^{-1} = 3159, 3120, 2908, 2848, 1610, 1504, 1441, 1248, 1225, 1200, 1169,1024, 982, 849, 762, 633, 580, 517.

HRMS: m/z = 204.1747 ($[M]^+$; calculated for $C_{14}H_{22}N^+$ m/z = 204.1747).

2.2.10 Compound 14



14

Starting material **4db** (100 mg, 0.25 mmol) was dissolved in dry 1,2,4-trichlorobenzene (1 mL) and (75 mg, 2 equiv.) of freshly distilled anhydrous triflic acid was added to the solution at r.t. The reaction mixture was heated for 16 hours at 150 °C under inert atmosphere. Then the reaction mixture was cooled to -78 °C, it solidified, and $LiAlH_4$ (19 mg, 0.5 mmol) was added on the surface. Then dry THF (1 mL) was added at -78 °C and the reaction was let to warm up to r.t. and stirred at r.t. for 3h. The reaction was quenched with sat. solution of Na_2CO_3, product, resulting amine, was extracted with Et_2O. Combined organic fractions were dried over $MgSO_4$ and Et_2O with THF was evaporated under *vacuo*. To the solution of amine in 1,2,4-trichlorobenzene was added HCl in Et_2O and the resulting hydrochloric salt was filtered off. The product **14** was purified by crystallisation from EtOAc and obtained as colourless crystalline solid (45 mg) in 45% yield. *Please, note that if triflic acid is not anhydrous or the solvent is contaminated with water then the yield drops dramatically.*

m.p. (cryst. from EtOAc): 182.8 - 183.7 °C

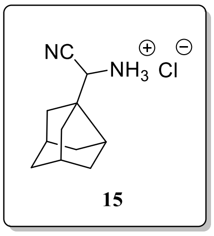
^{1}H NMR (400 MHz, CD_3Cl_3): δ/ppm = 1.63-1.96 (m, 19H), 2.94 (m, 2H), 4.65 (m, 2H), 7.30-7.34 (m, 1H), 7.40-7.42 (m, 2H).

^{13}C NMR (101 MHz, CD_3Cl_3): δ/ppm = 24.6 (CH), 33.3 (CH_2), 34.6 ($2CH_2$), 34.9 (CH), 41.5 (CH), 45.5 (2CH), 45.8 (CH_2), 46.3 ($2CH_2$), 46.5 (2CH), 49.1 (C), 53.3 (CH_2), 127.3 (2C), 129.1 (2CH), 131.8 (CH), 137.4 (C).

IR (neat): $\tilde{\nu}$ /cm^{-1} = 3390, 3062, 2902, 2844, 2642, 2559, 2515, 2387, 1579, 1562, 1452, 1435, 1338, 1302, 1209, 1173, 1092, 1028, 1012, 962, 843, 789, 762, 731, 619, 544.

HRMS: m/z = 362.1438 ($[M]^+$; calculated for $C_{21}H_{26}Cl_2N^+$ m/z = 362.1437).

2.2.11 Compound 15



Starting material **3a** (100 mg, 0.5 mmol) was dissolved in dry 1,2,4-trichlorobenzene (8 mL) and 150 mg (2 equiv.) of freshly distilled anhydrous triflic acid was added to the solution at r.t. The reaction mixture was heated for 4 hours at 120 °C under inert atmosphere. Then the reaction mixture was cooled to -78 °C, it solidified, and TMSCN (250 µL, 2 mmol), DMF (0.2 mL) and Et_3N (0.2 mL) were added to the reaction mixture. The reaction mixture was let to warm up to r.t. and stirred at r.t. for 16h. The reaction was quenched with sat. solution of Na_2CO_3, the product, resulting amine, was extracted with Et_2O. Combined organic fractions were dried over $MgSO_4$ and Et_2O was evaporated under *vacuo*. To the solution of amine in 1,2,4-trichlorobenzene was added HCl in Et_2O and the solvent from the resulting hydrochloric salt solution was evaporated under *vacuo* at elevated temperature. The product **15** was purified by crystallisation from EtOAc and obtained as colourless crystalline solid (82 mg) in 77% yield. *Please, note that if triflic acid is not anhydrous or the solvent is contaminated with water then the yield drops dramatically.*

m.p. (cryst. from EtOAc): 212.3 - 213.1 °C.

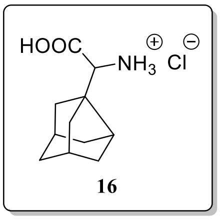
^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 1.61-1.85 (m, 13H), 2.26 (m, 1H), 2.31 (m, 2H), 3.72 (s, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ/ppm = 35.2 ($2CH_2$), 37.5 (CH), 41.6 (CH), 43.8 (CH_2), 44.9 (CH_2), 46.0 ($2CH_2$), 50.5 (CH), 52.5 (C), 121.7 (C).

IR (neat): $\tilde{\nu}$ /cm^{-1} = 3386, 3321, 3195, 3195, 2935, 2866,2669, 2580, 2225, 1716, 1660, 1481, 1458, 1369, 1336, 1306, 1242, 1215, 1130, 1093, 1078, 1063, 962, 947, 908, 862, 843, 781, 708, 638, 588, 523, 420.

HRMS: m/z = 177.1389 ($[M]^+$ calculated for $C_{11}H_{17}N_2^+$ m/z = 177.1386).

2.2.12 Compound 16



16

Starting material **15** (80 mg, 0.38 mmol) was dissolved in concentrated hydrochloric acid (2 mL) and stirred at 100 °C for 36 hours. Then the solution was neutralised using sodium hydroxide and the water was evaporated under *vacuo*. Then the compound was extracted with methanol and converted using HCl/Et_2O to hydrochloric salt. The compound **16** was obtained as colourless solid (71 mg) in 79% yield.

m.p. (cryst. from MeOH): 293.5 - 294.3 °C

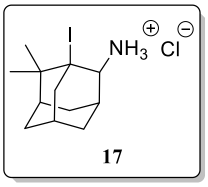
^{1}H NMR (400 MHz, CD_3OD): δ/ppm = 1.57-1.88 (m, 10H), 2.27 (m, 2H), 2.58-2.61 (m, 1H), 4.05 (s, 1H).

^{13}C NMR (101 MHz, CD_3OD): δ/ppm = 35.7 (CH_2), 38.3 (CH), 38.7 (CH), 43.2 (CH), 44.3 (CH_2), 44.4 (CH_2), 46.3 (CH_2), 46.7 (CH_2), 50.9 (C), 60.2 (CH), 170.0 (C).

IR (neat): $\tilde{\nu}$ /cm^{-1} = 3465, 3311 3167, 2914, 2866, 2848, 2667, 2542, 2359, 2189, 1712, 1595, 1576,1520, 1458, 1402, 1336, 1100, 1269, 1250, 1178, 1165, 1092, 1030, 985, 955, 837, 779, 640, 563, 532, 513.

HRMS: m/z = 196.1331 ($[M]^+$; calculated for $C_{11}H_{18}NO_2^+$ m/z = 196.1333).

2.2.13 Compound 17



17

Starting material **3e** (663 mg, 3 mmol) was dissolved in anhydrous dichloromethane (3 mL) in sealed tube and 2 equiv. of KI (6 mmol, 996 mg) were added to the solution. To the resulting suspension TfOH (1050 mg, 0.617 mL, 4 equiv.) was added and the tube was quickly closed. The reaction mixture was heated to 40 °C and stirred at this temperature for 16 hours. Then the reaction mixture was cooled to 0 °C and poured in cold sodium carbonate water solution and Et_2O. The compound was extracted as a free base with cold Et_2O, dried over $MgSO_4$ and transformed into hydrochloric salt using cold HCl in Et_2O and filtered off as product **17** (450 mg, 44% yield). *Please note that all transformations with free amine of* ***17*** *must be performed at low temperatures.*

m.p. (cryst. from EtOAc): 207.5 – 208.9 °C

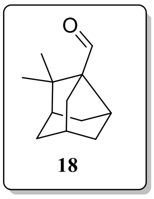
^{1}H NMR (400 MHz, CD_3OD): δ/ppm = 1.30 (s, 3H), 1.39 (s, 3H), 1.68-1.94 (m, 6H), 2.25-2.34 (m, 3H), 2.73-2.78 (m, 1H), 2.92-2.98 (m, 1H), 4.21-4.22 (m, 1H).

^{13}C NMR (101 MHz, CD_3OD): δ/ppm = 28.8 (CH_3), 29.4 (CH_3), 30.8 (CH_2), 32.9 (CH_2), 33.2 (CH_2), 33.9 (CH), 36.1 (CH), 40.1 (CH), 42.4 (CH_2), 45.9 (C), 60.8 (CH), 66.7 (C).

IR (neat): $\tilde{\nu}$ /cm^{-1} = 3178, 3057, 2989, 2910, 2864, 2725, 2629, 2559, 1948, 1587, 1522, 1485, 1466, 1367, 1315, 1232, 1130, 1030, 1001, 985, 945, 922, 870, 822, 802, 727, 669, 602, 526, 492, 420.

HRMS: m/z = 306.0714 ([M]$^+$; calculated for $C_{12}H_{21}IN^+$ m/z = 306.0714).

2.2.14 Compound 18



18

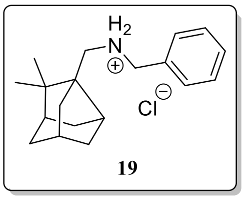
Starting material **17** (156 mg, 0.5 mmol) was placed in 1,4-dioxane (2 mL) and K_2CO_3 (5 equiv.) was added, followed by 4 mL of water. The reaction was heated for 80 °C for 1h and then the product was extracted with diethylether. Diethylether phase was washed with HCl/water solution to remove the side product, then it was washed with water and then the organic fraction was dried over $MgSO_4$. The product **18** was concentrated *in vacuo* and obtained as colourless non-crystalline solid (53 mg) in 60% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 1.03 (s, 3H), 1.18 (s, 3H), 1.40-1.50 (m, 3H), 1.65 (m, 3H), 1.87-1.91 (m, 1H), 2.14-2.25 (m, 3H), 2.73-2.76 (m, 1H), 9.83 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ/ppm = 22.7 (CH_3), 27.2 (CH_3), 32.0 (CH_2), 36.1 (CH), 36.9 (CH_2), 40.2 (CH_2), 44.4 (CH_2), 47.5 (C), 47.7 (CH), 65.3 (CH), 77.4 (C), 205.88 (CH).

Analytical data of compound **18** are in agreement with the reported in publication Zonker, B.; Becker, J.; Hrdina, R. *Org. Biomol. Chem.* **2021**, *19*, 4027-4031.

2.2.15 Compound 19



19

Starting material **18** (40 mg, 0.22 mmol) was mixed with benzylamine (25 mg, 0.22 mmol, 1 equiv.) and stirred in anhydrous dichloromethane (1 mL) with anhydrous $MgSO_4$ (120 mg) at r.t. for 24 hours. Then the solution was filtered concentrated *in vacuo*, dissolved in THF 1 mL

and dropwise added to $LiAlH_4$ suspension and stirred at r.t. for additional 3 hours. Then the reaction was quenched with water and the product was extracted using Et_2O. Combined organic fractions were dried over $MgSO_4$ and the product was concentrated *in vacuo*. Then followed the addition of HCl in Et_2O and the product as hydrochloric salt was filtered off. Compound x was obtained as colourless solid (55 mg) in 82% yield.
m.p. (cryst. from EtOAc): sublimation of the sample at 200 °C

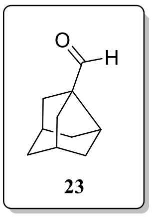
^{1}H NMR (400 MHz, CD_3Cl_3): δ/ppm = 0.71 (s, 3H), 1.03 (s, 3H), 1.25-1.31 (m, 1H), 1.37-1.40 (m, 1H), 1.53-1.68 (m, 5H), 1.81-1.85 (m, 1H), 2.00-2.12 (m, 3H), 2.20 (m, 1H), 2.31-2.34 (m, 1H), 2.70-2.85 (m, 2H), 7.37-7.44 (m, 3H), 7.69-7.71 (m, 2H), 9.31 (bs, 2H)

^{13}C NMR (101 MHz, CD_3Cl_3): δ/ppm = 22.0 (CH_3), 26.7 (CH_3), 32.0 (CH_2), 36.9 (CH), 38.7 (CH_2), 40.2 (CH_2), 42.8 (CH), 44.8 (CH_2), 46.6 (C), 47.5 (CH), 48.9 (CH_2), 51.4 (C), 51.8 (CH_2), 129.4 (CH), 129.5 (CH), 130.6 (CH), 130.7 (C).

IR (neat): $\tilde{\nu}$ /cm^{-1} = 3338, 3037, 2918, 2856, 2777, 2655, 2453, 1655, 1460, 1441, 1419, 1369, 1277, 1211, 1117, 1103, 1080, 1016, 976, 941, 930, 800, 748, 696, 584, 505, 482, 418.

HRMS: m/z = 270.2221 ($[M]^+$; calculated for $C_{19}H_{28}N^+$ m/z = 270.2216).

2.2.16 Compound 23



23

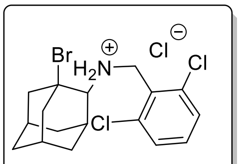
Starting material 1-iodo-2-amino adamantane hydrochloride (100 mg, 0.32 mmol) was placed in 1,4-dioxane 2 mL and K_2CO_3 (250 mg, 5 equiv.) was added, followed by 4 mL of water. The reaction was heated for 80 °C for 1h and then the product was extracted with diethylether. Diethylether phase was washed with HCl/water solution to remove the side product, then it was washed with water and then the organic fraction was dried over $MgSO_4$. The product **23** was concentrated *in vacuo* and obtained as colourless noncrystalline solid (20 mg) in 42% yield.
*Please, note, compound **23** is volatile.*

^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 1.61-1.76 (m, 8H), 2.01-2.04 (m, 2H), 2.36 (m, 2H), 2.57-2.6 (m, 1H), 9,73 (s, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ/ppm = 35.4 ($2CH_2$), 37.5 (2CH), 42.1 (CH), 43.7 ($2CH_2$), 43.7 ($2CH_2$), 60.4 (C), 205.4 (COH).

Analytical data for compound **23** are in agreement with the reported in publication Zonker, B.; Becker, J.; Hrdina, R. *Org. Biomol. Chem.* **2021**, *19*, 4027-4031.

2.2.17 Compound 24



24

Starting material **4ab** (175 mg, 0.5 mmol) was dissolved in anhydrous 1,2,4-trichlorobenzene (2 mL) in sealed tube and 3 equiv. of KBr (1.5 mmol, 178 mg) were added to the solution. Then the suspension was cooled down and solidified, then TfOH (300 mg, 176 µL, 4 equiv.) was added and the tube was closed before the HBr gas started to evolve. The reaction mixture was heated to 150 °C and stirred at this temperature for 16 hours. Then the reaction mixture was cooled to 0 °C and poured in cold sodium carbonate water solution and Et_2O. The compound was extracted as a free base with cold Et_2O, dried over $MgSO_4$ and concentrated at low r.t. Followed short pad chromatography on silica gel using hexane: EtOAc (4:1) as a mobile phase. The compound was concentrated *in vacuo* at r.t. and using HCl in ether transformed into hydrochloric salt and filtered off as product **24** (188 mg) in 88% yield.

m.p. (cryst. from EtOAc): 184.6 - 185.1 °C

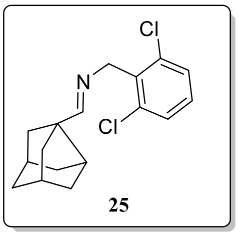
^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 1.66-1.80 (m, 5H), 1.98-2.25 (m, 5H), 2.46-2.49 (m, 1H), 2.74-2.88 (m, 2H), 3.04 (m, 2H), 4.56 (m, 1H), 4.91 (m, 1H,), 7.35-7.39 (m, 1H),7.43-7.45 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$): δ/ppm = 29.3 (CH_2), 31.7 (CH), 31.9 (CH), 32.4 (CH), 35.3 (CH_2), 36.2 (CH_2), 42.9 (CH_2), 44.8 (CH_2), 49.6 (C), 67.3 (CH), 129.3 (CH), 137.1 (2CH), 129.3 (2C), 137.1 (1C).

IR (neat): $\tilde{\nu}$ /cm^{-1} = 3323, 3163, 2912, 2852, 2627, 2312, 1711,1579, 1562, 1464, 1435, 1342, 1194, 1146, 1119, 1093, 1032, 1022, 987, 939, 841, 825, 769, 721, 687, 638, 613, 509, 484, 428.

HRMS: m/z = 388.0227 ($[M]^+$; calculated for $C_{17}H_{21}BrCl_2N^+$ m/z = 388.0229).

2.2.18 Compound 25



25

Starting material, free amine, **24** (88 mg, 0.23 mmol) was dissolved in anhydrous THF (2 mL) and 1.6 M (MeLi in THF) 142 µL was added dropwise to the solution at -78 °C. The reaction mixture was allowed to reach r.t., stirred for additional 20 minutes and then concentrated *in vacuo*. The compound was characterised without further purification.

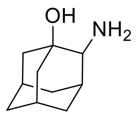
^{1}H NMR (400 MHz, THF-*d_8*): δ/ppm = 1.57-1.62 (m, 6H), 1.75-1.78 (m, 2H), 1.92-1.94 (m, 2H), 2.21 (m, 2H), 2.34-2.37 (m, 1H), 4.81-4.82 (m, 2H), 7.21-7.25 (m, 1H), 7.34-7.36 (m, 2H), 7.85 (m, 1H).

^{13}C NMR (101 MHz, THF-*d_8*): δ/ppm = 35.3 (CH_2), 37.6 (2CH), 42.9 (CH), 43.6 ($2CH_2$), 46.3 ($2CH_2$), 54.4 (C), 59.1 (CH_2), 128.3 (2CH), 129.2 (CH), 135.4 (2C), 136.9 (C), 170.4 (CH).

IR (neat): $\tilde{\nu}$ /cm^{-1} = 3431, 2924, 2864, 1653, 1562, 1437,1369, 1304, 1242, 1084, 1020, 773, 764б 746, 687, 656, 580, 525, 492, 434.

HRMS: m/z = 308.0965 ($[M+H]^+$; calculated for $C_{17}H_{20}Cl_2N^+$ m/z = 308.0968).

2.2.19 Compound 26



26

Starting material **3a** 0.8 g was dissolved in 30 mL of 5M KOH/water solution and stirred at 100 °C for 24 hours. Then the reaction mixture was cooled to r.t. and the product **26** was extracted with chloroform (3 times 50 mL). Combined organic phases were dried over $MgSO_4$ and the solvent was evaporated *in vacuo*. Product **26** was obtained as colourless solid (0.6 g) in 87% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 1.41-1.48 (m, 2H), 2.27 (m, 2H), 1.56-1.68 (m, 4H), 1.70-1.86 (m, 5H), 1.94 (m, 1H), 2.04 (m, 1H), 2.12 (m, 1H), 2,76 (bs, 1H).

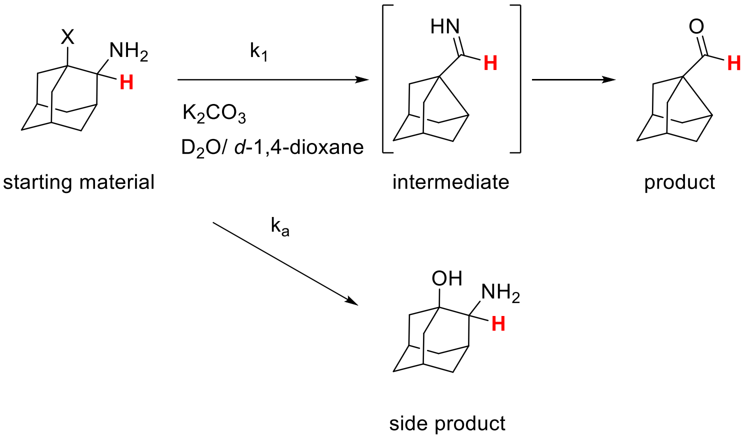
^{13}C NMR (101 MHz, CD_3OD): δ/ppm = 29.6 (CH), 30.1 (CH_2), 30.8 (CH), 36.6 (CH_2), 37.2 (CH), 37.4 (CH_2), 39.0 (CH_2), 44.3 (CH_2), 60.4 (CH), 69.1 (C).

For the first synthesis of **26** see: Curran, W. V.; Angier, R. B.; *Chem. Comm.* **1967**, 563.

3. Kinetic studies

Preacquisition delayed experiments were measured with Varian Inova 400 MHz instrument equipped with an ASW4NUC probe. Experiments were carried out at various temperatures (25, 40, 50, 60, 70, 80 °C) and accurate values (25.2, 40.6, 51.7, 61.7, 72.7, 83.6 with ± 0.30 °C error)[1]were obtained by temperature calibrating experiments with 80% glycol in DMSO-*d*6. Low quality of spectra was caused by many factors and technical limitations of the spectrometer. Experiments were carried out in a mixture of two deuterated solvents (dioxane-*d*8 1:4 D_2O), with highly diluted reactant and high ionic strength due to presence of inorganic salts (KCl, K_2CO_3). These conditions correspond to experimental conditions used during synthesis. Shimming was done in the presence of similar NMR tube with the same solvent ionic strength therefore the homogeneity of the magnetic field could not be ideal. Standard shimming procedure could not be used because of its time demands and the fast kinetics of the measured reaction at higher temperatures. All data were processed with MestRenova 12.0.3 and integral values were obtained by stacked spectra automatization. Combination of lower signal to noise ratio and processing automatization burdened integral with some error. Data were processed in term of time (experiments in the NMR spectrometer were started after some delay) ,values of integrals (to avoid negative concentration because of "integral values of noise") and values of integrals were substituted and normalized by starting concentration. Chemical shifts change their values with temperature and pH of the solution. Labels are with the same chemical shifts across all tables for simplification. Usual chemical shifts from highest to lowest: product (8.9 ppm), intermediate product (7.0 ppm), starting material (2.25 ppm), side product (2.0 ppm) (marked red in Scheme 1).

Scheme 1 Simplified model for kinetic studies



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[1] http://chem.ch.huji.ac.il/nmr/software/thermometer.html

KIN-25-Iodo

Derivative: X=Iodo   Concentration: 53 mᴍ   Base: 5 eqiv.   Temperature: 25 °C

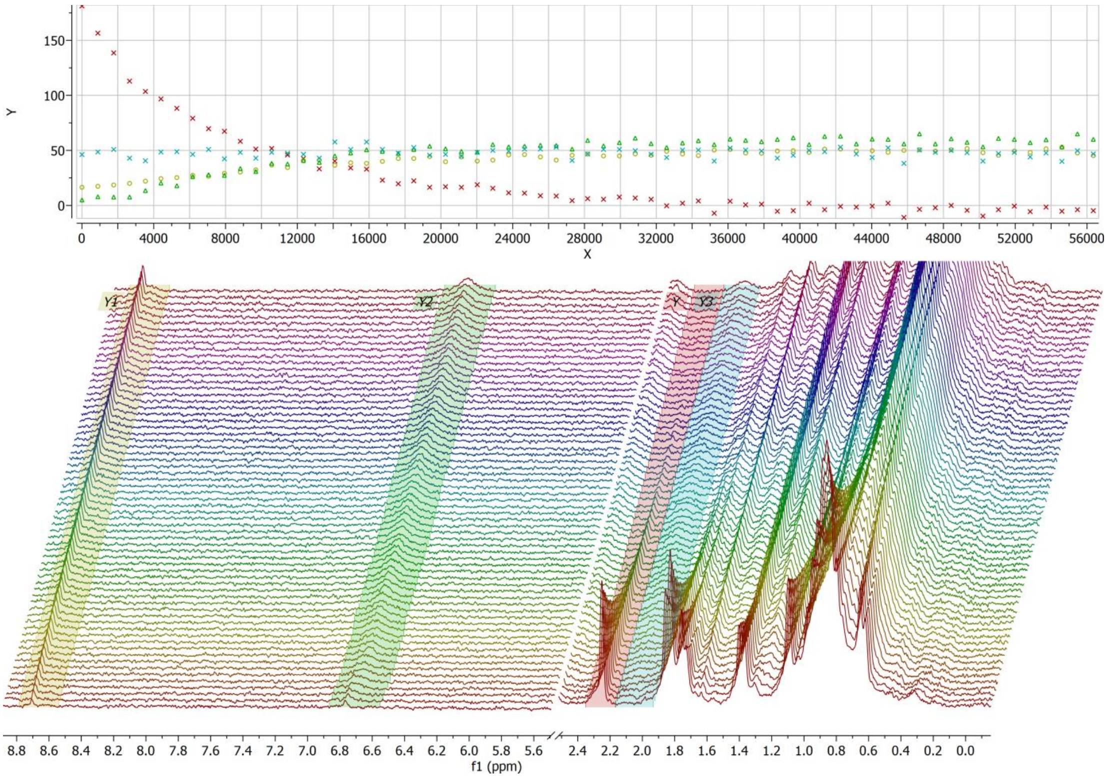


Fig. 1 Mestrenova - Iodo 25 °C

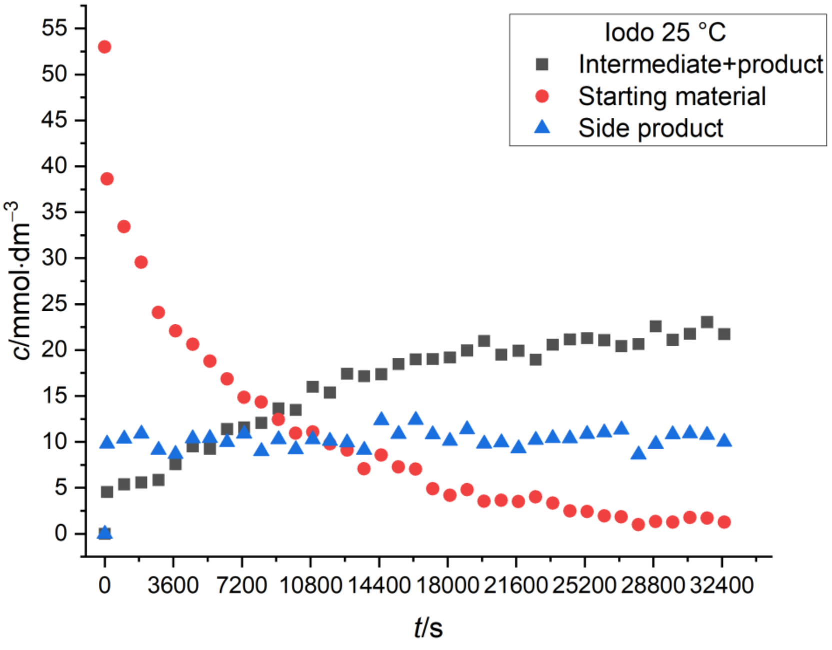


Fig. 2 Processed graph – Iodo 25 °C

Table 1 Raw data – integral values – Iodo 25 °C

Time/s	25 °C				
	product (8.92 ppm)	intermediate product (7.00 ppm)	product + intermediate product	starting material (2.25 ppm)	side product (1.99 ppm)
0	16.3	5.0	21.3	181.1	46.0
900	17.2	8.0	25.2	156.6	48.6
1800	18.4	7.8	26.2	138.5	51.0
2700	19.9	7.5	27.5	112.9	42.8
3600	22.0	13.6	35.5	103.4	40.6
4500	24.4	20.2	44.6	96.7	48.6
5400	25.3	17.9	43.2	88.1	48.8
6300	27.2	26.2	53.4	79.1	46.8
7200	26.3	27.9	54.2	69.6	51.0
8100	29.2	27.4	56.6	67.2	42.2
9000	30.3	33.6	63.9	58.3	48.1
9900	32.3	30.8	63.2	51.3	43.0
10800	36.7	38.2	74.9	51.9	48.2
11700	34.5	37.5	72.0	45.8	47.4
12600	40.7	40.9	81.6	42.7	46.5
13500	41.2	39.2	80.4	33.2	42.7
14400	36.4	45.0	81.4	40.2	57.9
15300	38.9	47.7	86.6	34.2	51.0
16200	38.3	50.6	88.9	32.9	58.0
17100	40.0	49.1	89.1	23.0	50.8
18000	42.7	47.2	89.9	19.7	47.4
18900	42.6	50.9	93.5	22.4	53.3
19800	44.5	53.8	98.3	16.6	46.0
20700	39.8	51.5	91.3	17.1	46.5
21600	44.2	49.1	93.4	16.4	43.6
22500	40.4	48.4	88.8	18.8	47.9
23400	41.2	55.2	96.4	15.6	48.8
24300	46.0	53.2	99.2	11.7	48.7
25200	46.0	53.8	99.8	11.3	50.9
26100	44.2	54.6	98.8	9.1	51.7
27000	41.2	54.5	95.7	8.6	53.1
27900	45.6	51.2	96.7	4.6	40.4
28800	46.8	59.1	105.8	6.2	45.7
29700	44.9	54.0	98.9	5.9	50.8
30600	45.0	57.0	102.0	8.3	51.3
31500	46.9	61.1	108.0	7.9	50.4

32400	45.7	56.2	101.9	6.0	46.9
33300	49.0	52.6	101.6	1.1	43.5
34200	46.7	56.8	103.6	2.8	51.0
35100	45.3	58.7	104.0	4.8	50.9
36000	50.4	55.3	105.7	-5.9	40.8
36900	50.9	60.4	111.3	2.2	52.5
37800	47.7	59.0	106.7	2.8	50.6
38700	47.4	58.0	105.4	4.2	49.7
39600	49.3	60.0	109.4	-2.3	43.1
40500	49.5	61.4	111.0	-1.3	45.6
41400	48.2	55.4	103.6	1.5	50.4
42300	51.2	62.7	113.9	-1.8	49.3
43200	51.1	63.1	114.2	0.9	53.3
44100	49.4	55.9	105.4	0.9	47.1
45000	49.6	60.3	109.8	0.0	43.6
45900	48.1	60.0	108.1	3.5	52.9
46800	49.9	55.9	105.8	-7.6	38.0
47700	50.6	65.1	115.7	0.6	48.4
48600	49.5	55.8	105.3	-0.2	47.5
49500	50.7	60.5	111.2	2.3	48.7
50400	51.9	57.3	109.1	-2.4	47.1
51300	47.8	53.2	101.0	-5.6	38.9
52200	45.6	60.8	106.4	0.6	46.3
53100	49.5	60.0	109.4	3.4	47.3
54000	48.3	57.1	105.4	-5.3	44.2
54900	51.5	59.7	111.1	-1.5	48.6
55800	52.9	53.2	106.1	-5.5	40.5
56700	47.6	65.0	112.6	-4.4	50.2
57600	45.3	60.0	105.4	-3.3	47.1

Table 2 Processed data – Iodo 25 °C

Processed data - concentration normalization

Time/s	25 °C				
	product (8.92 ppm)/mM	intermediate product (7.00 ppm)/mM	product + intermediate product/mM	starting material (2.25 ppm)/mM	side product (1.99 ppm)/mM
120	3.5	1.1	4.6	38.6	9.8
1020	3.7	1.7	5.4	33.4	10.4
1920	3.9	1.7	5.6	29.6	10.9
2820	4.2	1.6	5.9	24.1	9.1
3720	4.7	2.9	7.6	22.1	8.7
4620	5.2	4.3	9.5	20.6	10.4
5520	5.4	3.8	9.2	18.8	10.4
6420	5.8	5.6	11.4	16.9	10.0
7320	5.6	5.9	11.6	14.9	10.9
8220	6.2	5.8	12.1	14.3	9.0
9120	6.5	7.2	13.6	12.4	10.3
10020	6.9	6.6	13.5	10.9	9.2
10920	7.8	8.1	16.0	11.1	10.3
11820	7.4	8.0	15.4	9.8	10.1
12720	8.7	8.7	17.4	9.1	9.9
13620	8.8	8.4	17.1	7.1	9.1
14520	7.8	9.6	17.4	8.6	12.3
15420	8.3	10.2	18.5	7.3	10.9
16320	8.2	10.8	19.0	7.0	12.4
17220	8.5	10.5	19.0	4.9	10.8
18120	9.1	10.1	19.2	4.2	10.1
19020	9.1	10.9	19.9	4.8	11.4
19920	9.5	11.5	21.0	3.5	9.8
20820	8.5	11.0	19.5	3.6	9.9
21720	9.4	10.5	19.9	3.5	9.3
22620	8.6	10.3	18.9	4.0	10.2
23520	8.8	11.8	20.6	3.3	10.4
24420	9.8	11.3	21.2	2.5	10.4
25320	9.8	11.5	21.3	2.4	10.9
26220	9.4	11.6	21.1	1.9	11.0
27120	8.8	11.6	20.4	1.8	11.3
28020	9.7	10.9	20.6	1.0	8.6
28920	10.0	12.6	22.6	1.3	9.8
29820	9.6	11.5	21.1	1.3	10.8
30720	9.6	12.2	21.8	1.8	10.9
31620	10.0	13.0	23.0	1.7	10.7

32520	9.7	12.0	21.7	1.3	10.0
0	0.0	0.0	0.0	53.0	0.0

* Correction: + 2 minutes, slope + 0.0

KIN-40-Iodo

Derivative: X= Iodo   Concentration: 53 mM   Base: 5 eqiv.   Temperature: 40 °C

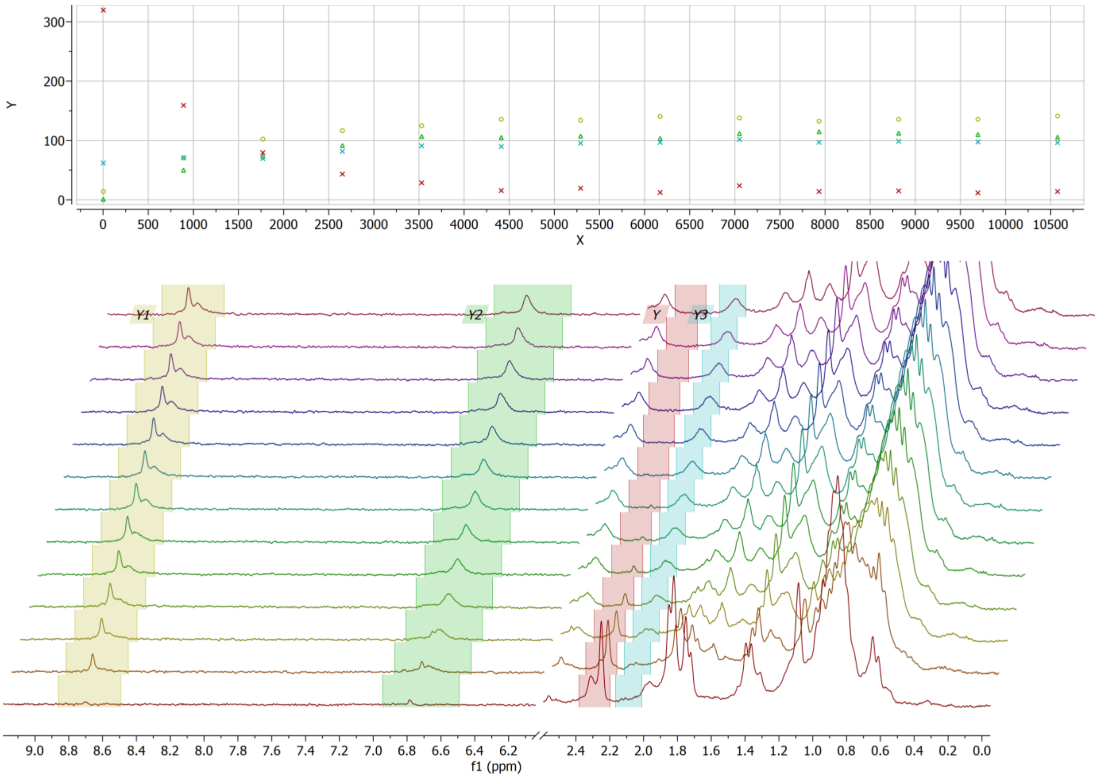


Fig. 3 Mestrenova - Iodo 40 °C

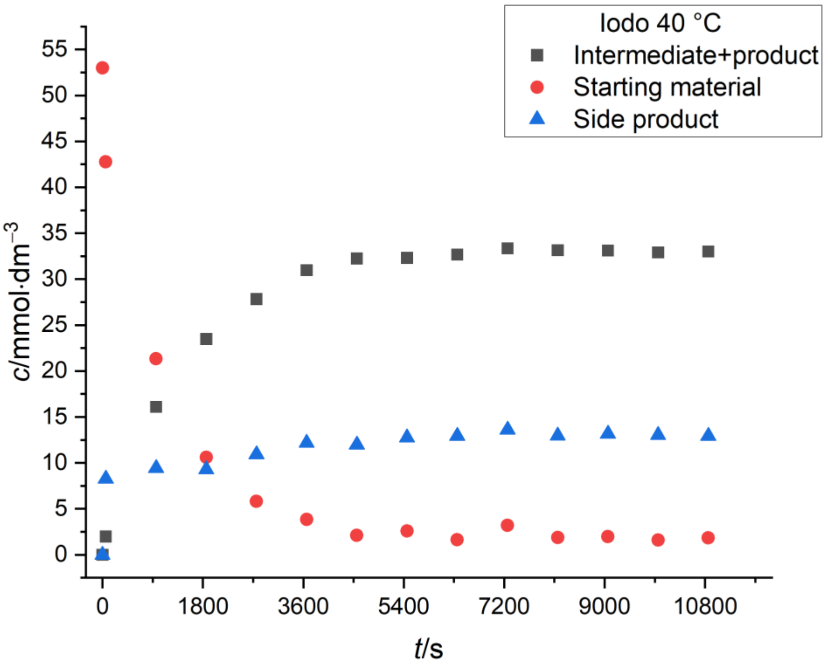


Fig. 4 Processed graph – Iodo 40 °C

Table 3 Raw data – integral values – Iodo 40 °C

Time/s	product (8.92 ppm)	intermediate product (7.00 ppm)	product + intermediate product	starting material (2.25 ppm)	side product (1.99 ppm)
	40 °C				
0	13.9	0.9	14.8	319.4	61.8
900	70.4	49.8	120.2	159.4	70.5
1800	102.3	73.2	175.4	79.3	69.4
2700	116.8	91.2	207.9	43.5	81.7
3600	124.7	106.7	231.4	28.7	91.1
4500	135.7	105.3	241.0	15.8	89.6
5400	134.0	107.4	241.4	19.3	95.4
6300	140.6	103.5	244.1	12.3	96.6
7200	137.6	111.6	249.2	24.0	101.8
8100	132.5	115.1	247.7	13.9	96.9
9000	135.4	112.0	247.4	14.8	98.3
9900	135.8	110.1	245.9	11.8	97.3
10800	141.1	105.6	246.7	13.8	96.5

Table 4 Processed data – Iodo 40 °C

Processed data - concentration normalization

Time/s	40 °C				
	product (8.92 ppm)/mM	intermediate product (7.00 ppm)/mM	product + intermediate product/mM	starting material (2.25 ppm)/mM	side product (1.99 ppm)/mM
60	1.9	0.1	2.0	42.8	8.3
960	9.4	6.7	16.1	21.3	9.4
1860	13.7	9.8	23.5	10.6	9.3
2760	15.6	12.2	27.8	5.8	10.9
3660	16.7	14.3	31.0	3.8	12.2
4560	18.2	14.1	32.3	2.1	12.0
5460	17.9	14.4	32.3	2.6	12.8
6360	18.8	13.9	32.7	1.6	12.9
7260	18.4	14.9	33.4	3.2	13.6
8160	17.7	15.4	33.1	1.9	13.0
9060	18.1	15.0	33.1	2.0	13.2
9960	18.2	14.7	32.9	1.6	13.0
10860	18.9	14.1	33.0	1.9	12.9
0	0.0	0.0	0.0	53.0	0.0

* Correction: + 1 minute, slope + 0.0

KIN-50-Iodo

Derivative: X= Iodo   Concentration: 53 mᴍ   Base: 5 eqiv.   Temperature: 50 °C

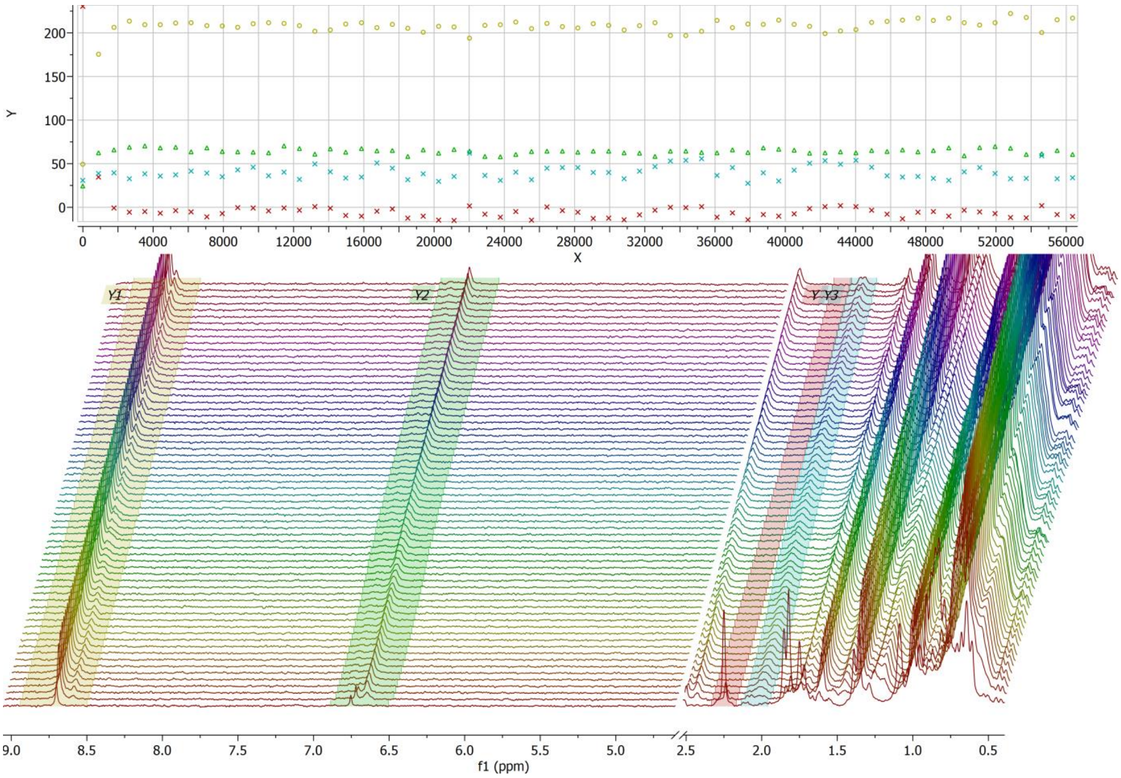


Fig. 5 Mestrenova - Iodo 50 °C

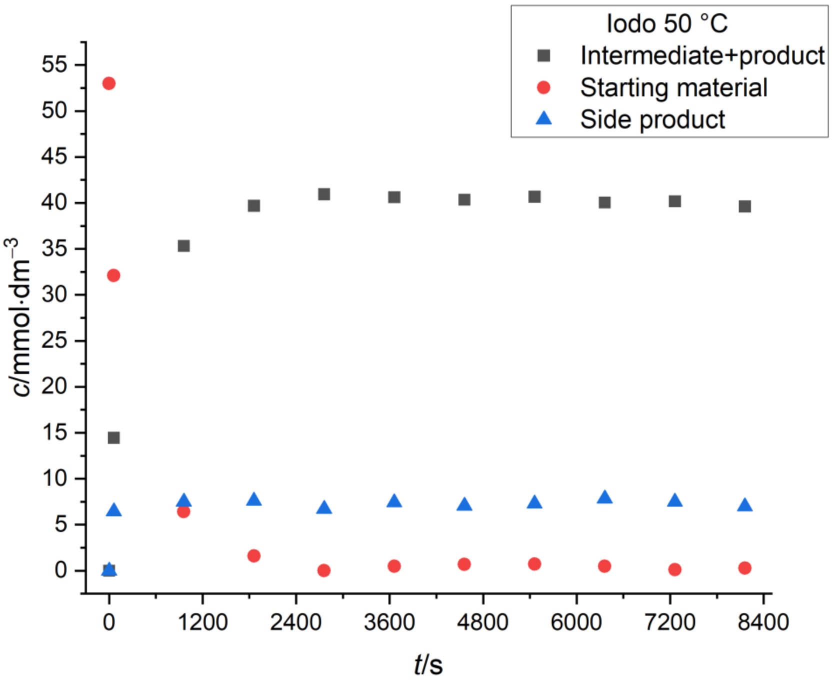


Fig. 6 Processed graph – Iodo 50 °C

Table 5 Raw data – integral values – Iodo 50 °C

	50 °C				
Time/s	product (8.92 ppm)	intermediate product (7.00 ppm)	product + intermediate product	starting material (2.25 ppm)	side product (1.99 ppm)
0	49.3	24.5	73.7	232.7	30.8
900	175.5	62.6	238.0	30.4	38.9
1800	206.4	66.0	272.4	-7.4	39.7
2700	213.4	68.9	282.3	-20.0	32.9
3600	209.3	70.5	279.7	-16.1	38.6
4500	209.5	68.2	277.7	-14.5	35.6
5400	211.3	68.8	280.1	-14.2	37.4
6300	211.5	63.7	275.2	-16.2	41.5
7200	208.3	68.0	276.3	-19.1	39.1
8100	207.8	64.0	271.8	-17.7	34.9
9000	206.4	63.7	270.1	-8.5	42.9
9900	210.7	63.3	274.0	-8.5	45.9
10800	211.7	62.6	274.3	-22.0	36.0
11700	210.8	70.4	281.2	-10.0	40.3
12600	208.2	67.5	275.7	-18.6	31.8
13500	201.7	60.9	262.6	-11.4	49.7
14400	203.4	67.2	270.5	-13.6	40.6
15300	210.3	63.4	273.7	-13.3	33.3
16200	211.6	67.6	279.2	-17.2	34.5
17100	205.9	64.7	270.6	-11.2	50.7
18000	209.9	65.3	275.2	-8.9	44.7
18900	205.3	58.2	263.6	-21.0	31.5
19800	200.9	66.1	267.0	-15.9	38.6
20700	207.5	62.0	269.5	-22.2	29.8
21600	206.8	66.2	273.0	-17.5	35.3
22500	194.0	64.4	258.4	-3.9	62.3
23400	208.8	58.6	267.3	-21.6	36.7
24300	209.3	57.9	267.1	-19.7	30.9
25200	212.3	60.8	273.2	-11.7	40.2
26100	204.9	64.1	269.0	-23.5	31.5
27000	211.0	64.4	275.4	-5.6	44.7
27900	207.2	64.3	271.5	-4.4	45.6
28800	205.6	63.2	268.7	-8.8	45.5
29700	210.4	64.5	274.9	-13.3	39.8
30600	208.8	64.3	273.1	-13.6	40.0
31500	203.3	62.4	265.7	-16.7	32.7

32400	208.3	62.1	270.4	-10.7	41.4
33300	211.7	58.4	270.1	-4.7	46.7
34200	196.9	64.3	261.3	-2.0	53.0
35100	197.1	64.3	261.3	-1.7	53.7
36000	201.7	62.7	264.5	-1.6	55.6
36900	214.3	62.6	276.9	-13.6	36.7
37800	206.1	65.7	271.9	-7.7	45.7
38700	210.2	63.0	273.2	-16.3	27.4
39600	209.7	68.2	277.8	-7.0	39.6
40500	214.5	66.5	281.0	-11.0	30.1
41400	209.8	65.6	275.4	-6.1	42.7
42300	207.4	62.0	269.4	0.9	50.4
43200	199.3	62.5	261.8	6.7	53.5
44100	202.2	63.7	265.9	6.4	49.2
45000	203.9	62.5	266.4	4.6	53.9
45900	212.1	65.0	277.1	-1.5	45.8
46800	213.0	63.9	276.9	-6.8	36.1
47700	214.7	66.0	280.8	-11.7	34.5
48600	217.0	63.6	280.6	-3.6	35.4
49500	214.3	65.2	279.5	-7.8	33.2
50400	217.1	68.1	285.1	-12.0	31.0
51300	211.5	59.2	270.7	-2.1	40.7
52200	209.0	68.4	277.4	-0.4	45.5
53100	211.5	69.8	281.3	-4.5	38.7
54000	222.2	67.9	290.2	-10.0	32.9
54900	217.6	60.4	278.0	-11.2	33.0
55800	200.5	61.3	261.8	8.5	59.3
56700	215.1	65.2	280.4	-6.0	32.8
57600	217.0	60.4	277.5	-9.2	33.9

Table 6 Processed data –Iodo 50 °C

Processed data - concentration normalization

Time/s	50 °C product (8.92 ppm)/mM	intermediate product (7.00 ppm)/mM	product + intermediate product/mM	starting material (2.25 ppm)/mM	side product (1.99 ppm)/mM
60	8.8	5.6	14.4	32.1	6.5
960	24.8	10.5	35.3	6.4	7.5
1860	28.8	10.9	39.7	1.6	7.6
2760	29.7	11.3	40.9	0.0	6.7
3660	29.1	11.5	40.6	0.5	7.4
4560	29.2	11.2	40.4	0.7	7.1
5460	29.4	11.3	40.7	0.7	7.3
6360	29.4	10.6	40.0	0.5	7.8
7260	29.0	11.2	40.2	0.1	7.5
8160	28.9	10.7	39.6	0.3	7.0
0	0.0	0.0	0.0	53.0	0.0

* Correction: + 1 minutes, slope + 20.0

KIN-80-Iodo

Derivative: X= Iodo   Concentration: 53 mM   Base: 5 eqiv.   Temperature: 80 °C

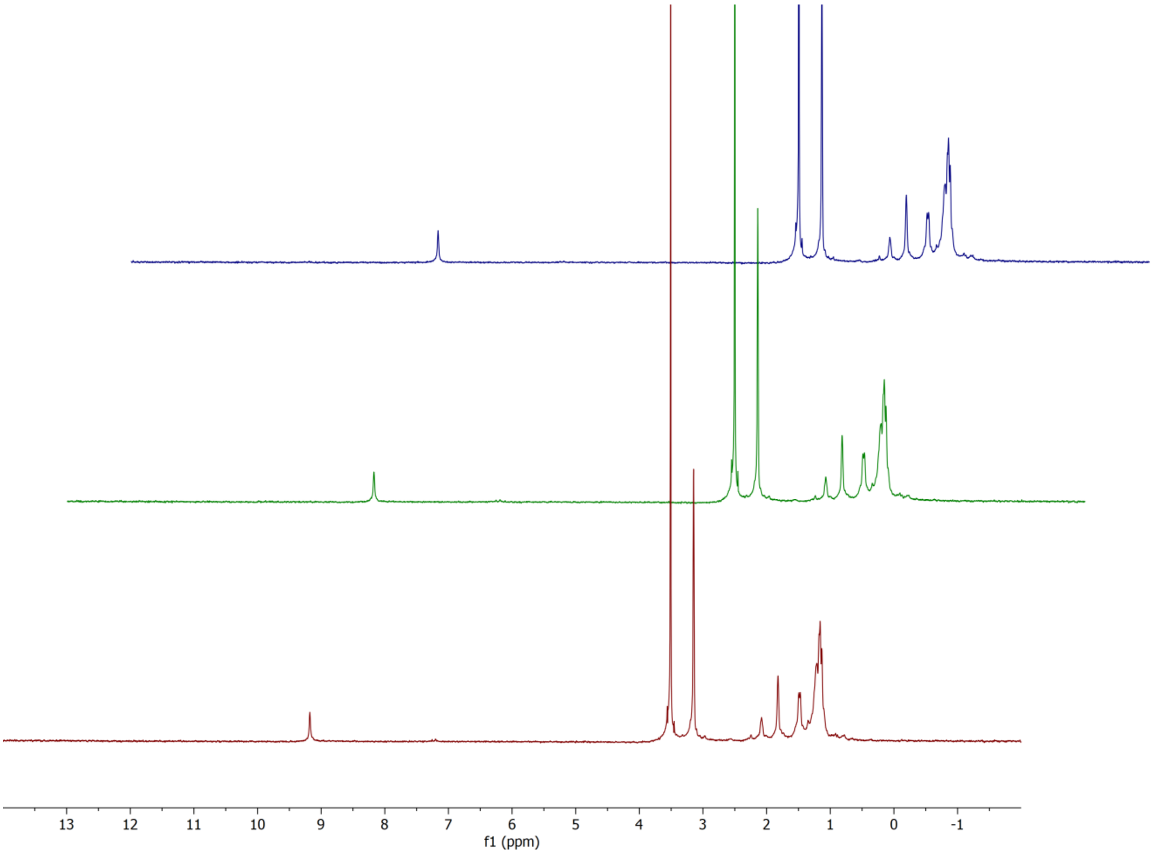


Fig. 7 Mestrenova - Iodo 80 °C

KIN-40-Bromo

Derivative: X= Bromo Concentration: 53 mM Base: 5 eqiv. Temperature: 40 °C

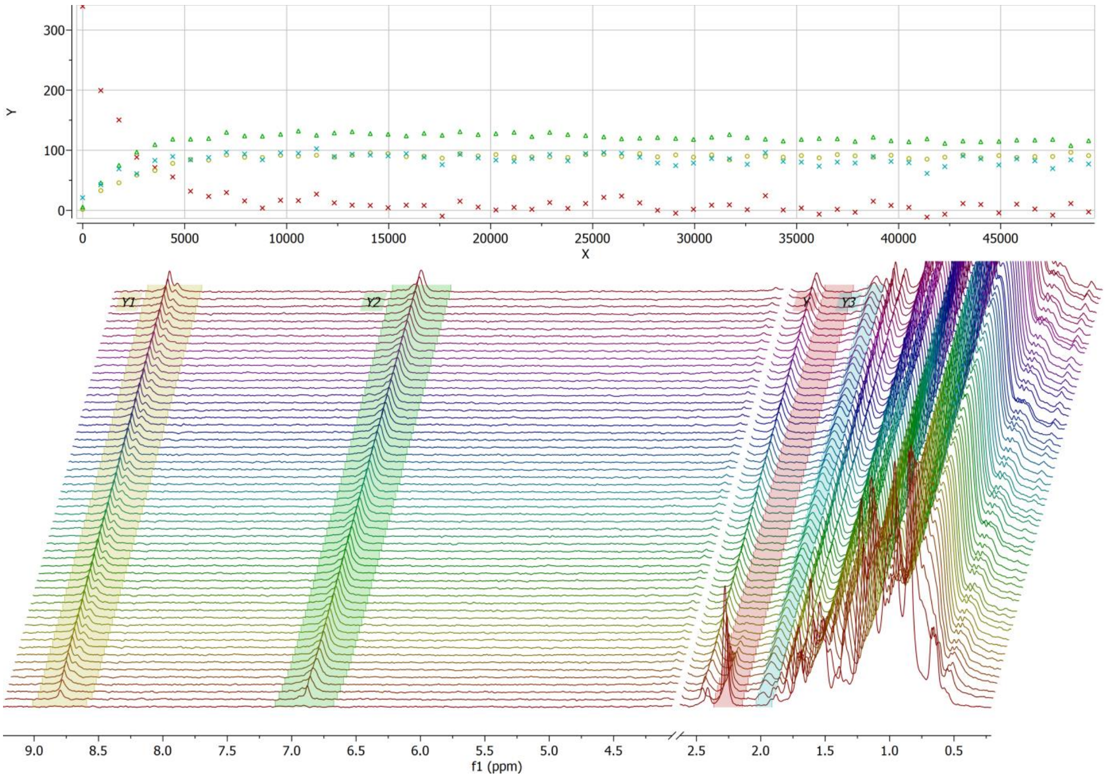


Fig. 8 Mestrenova - Bromo 40 °C

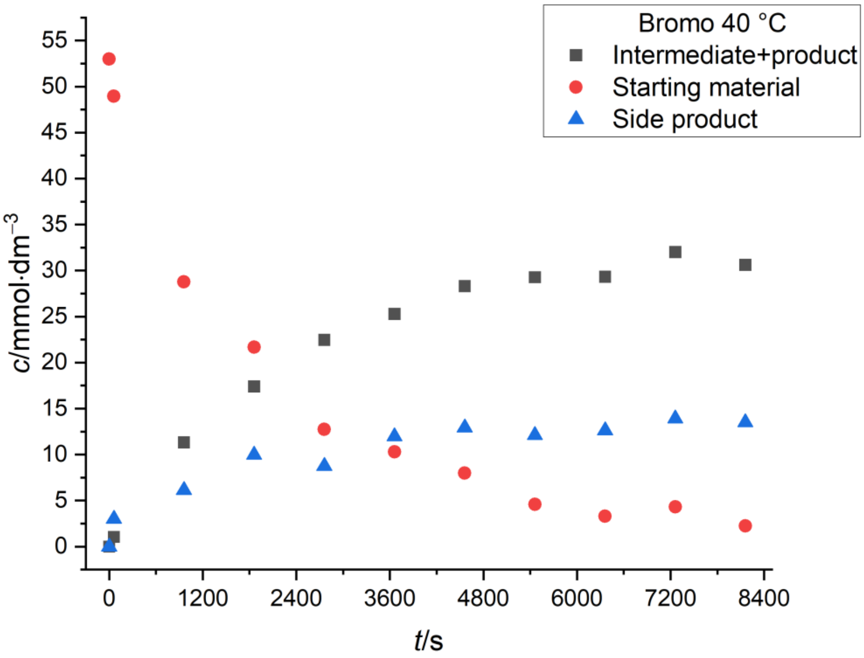


Fig. 9 Processed graph – Bromo 40 °C

Table 7 Raw data – integral values – Bromo 40 °C

Time/s	40 °C				
	product (8.92 ppm)	intermediate product (7.00 ppm)	product + intermediate product	starting material (2.25 ppm)	side product (1.99 ppm)
0	1.6	5.7	7.3	339.5	20.9
900	32.7	45.9	78.6	199.5	42.6
1800	45.7	75.1	120.8	150.3	69.2
2700	58.7	97.1	155.8	88.4	60.8
3600	66.2	109.2	175.5	71.3	83.0
4500	77.9	118.5	196.4	55.4	89.6
5400	84.4	118.7	203.1	31.7	84.1
6300	83.7	119.8	203.4	22.9	87.6
7200	92.0	130.1	222.1	29.9	96.5
8100	88.5	123.9	212.4	15.6	93.8
9000	87.7	123.2	210.9	3.6	84.1
9900	91.5	126.6	218.1	16.9	95.3
10800	89.8	132.1	222.0	16.4	95.0
11700	91.7	124.9	216.6	27.0	102.2
12600	88.6	128.6	217.2	12.3	89.4
13500	91.5	131.0	222.5	8.8	93.3
14400	95.6	127.8	223.4	8.1	92.1
15300	94.4	126.6	221.0	4.6	90.7
16200	89.5	124.0	213.5	8.9	94.5
17100	90.0	128.1	218.1	7.9	88.6
18000	87.0	125.2	212.2	-9.5	76.2
18900	94.6	130.9	225.4	14.9	93.1
19800	90.7	126.2	216.9	5.5	87.1
20700	92.9	128.0	220.9	0.3	83.3
21600	88.4	129.8	218.1	5.2	81.6
22500	88.7	123.0	211.6	1.8	86.5
23400	88.8	129.8	218.6	13.2	92.9
24300	87.7	126.0	213.7	3.2	82.5
25200	92.8	124.6	217.4	11.6	94.4
26100	93.1	122.3	215.4	21.5	95.8
27000	89.4	119.3	208.7	24.0	95.0
27900	94.5	120.1	214.7	12.4	88.5
28800	88.7	121.3	210.0	0.2	78.7
29700	92.3	119.5	211.8	-4.9	74.5
30600	88.6	118.1	206.8	1.5	78.9
31500	92.2	121.8	214.0	8.9	86.3

32400	84.2	126.3	210.4	9.1	85.8
33300	89.9	121.1	211.0	1.0	76.5
34200	89.2	118.5	207.7	24.1	96.0
35100	88.2	115.2	203.4	0.5	81.2
36000	90.8	117.8	208.7	4.0	80.1
36900	87.1	119.4	206.5	-6.6	73.3
37800	92.5	119.0	211.5	1.9	80.6
38700	90.6	115.1	205.7	-3.4	78.6
39600	88.3	121.7	209.9	15.2	89.5
40500	91.7	115.6	207.3	8.4	81.3
41400	86.3	114.4	200.7	4.8	79.0
42300	84.9	118.8	203.7	-11.3	61.4
43200	88.3	111.8	200.1	-6.3	72.8
44100	92.0	115.2	207.2	11.4	90.7
45000	87.5	114.3	201.8	9.8	85.9
45900	91.3	114.8	206.1	-4.4	75.3
46800	87.7	117.1	204.8	10.3	85.9
47700	89.2	116.8	206.0	2.0	82.2
48600	89.5	118.2	207.7	-8.2	69.4
49500	96.5	107.9	204.4	11.4	84.0
50400	91.1	115.7	206.8	-2.6	76.9

Table 8 Processed data – Bromo 40 °C

Processed data - concentration normalization

Time/s	40 °C product (8.92 ppm)/mM	intermediate product (7.00 ppm)/mM	product + intermediate product/mM	starting material (2.25 ppm)/mM	side product (1.99 ppm)/mM
60	0.2	0.8	1.0	48.9	3.0
960	4.7	6.6	11.3	28.8	6.1
1860	6.6	10.8	17.4	21.7	10.0
2760	8.5	14.0	22.5	12.7	8.8
3660	9.5	15.7	25.3	10.3	12.0
4560	11.2	17.1	28.3	8.0	12.9
5460	12.2	17.1	29.3	4.6	12.1
6360	12.1	17.3	29.3	3.3	12.6
7260	13.3	18.8	32.0	4.3	13.9
8160	12.8	17.9	30.6	2.2	13.5
0	0.0	0.0	0.0	53.0	0.0

* Correction: + 1 minute, slope + 0.0

KIN-50-Bromo

Derivative: X= Bromo Concentration: 53 mᴍ Base: 5 eqiv. Temperature: 50 °C

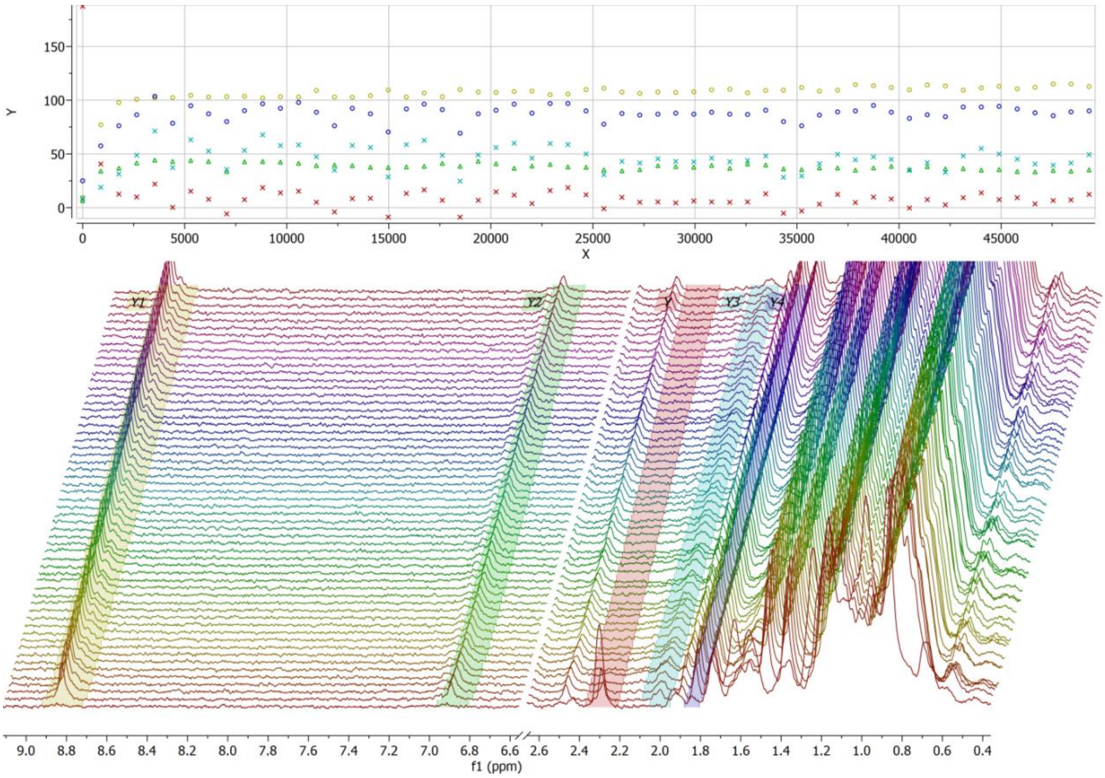


Fig. 10 Mestrenova - Bromo 50 °C

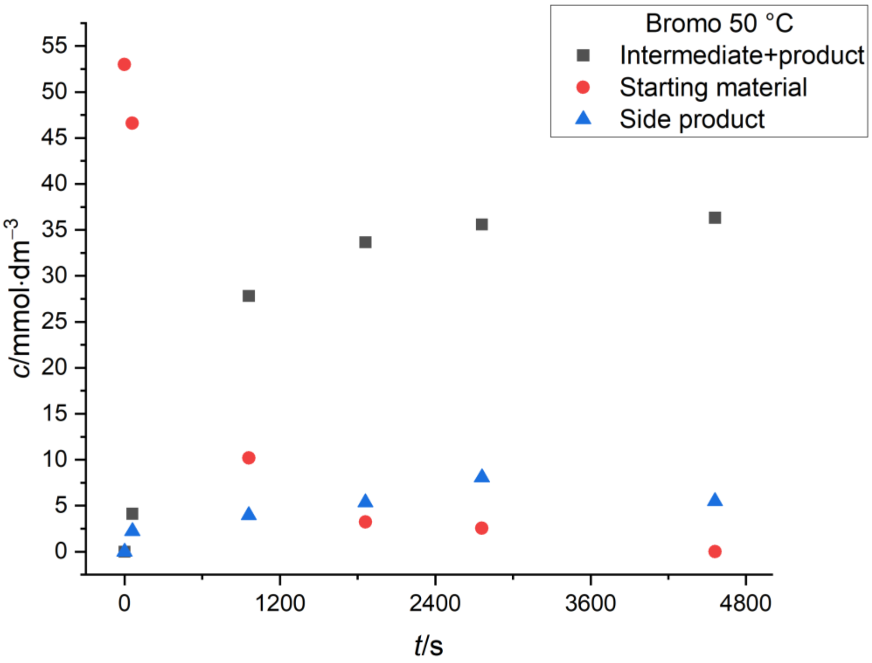


Fig. 11 Processed graph – Bromo 50 °C

Table 9 Raw data – integral values – Bromo 50 °C

	50 °C				
Time/s	product (8.92 ppm)	intermediate product (7.00 ppm)	product + intermediate product	starting material (2.25 ppm)	side product (1.99 ppm)
0	9.2	6.4	15.6	187.5	8.6
900	77.1	34.1	111.2	40.6	15.5
1800	98.0	36.7	134.7	12.5	21.1
2700	100.9	41.6	142.5	9.8	32.0
3600	102.0	44.3	146.3	22.0	46.6
4500	102.5	43.0	145.4	-0.5	21.7
5400	104.5	43.8	148.3	15.8	40.1
6300	103.0	42.9	146.0	7.7	32.9
7200	103.4	33.8	137.2	-6.1	20.9
8100	103.5	42.7	146.2	21.4	33.5
9000	102.2	43.0	145.1	31.8	43.2
9900	103.3	42.5	145.8	20.2	35.9
10800	103.1	41.2	144.3	23.8	36.7
11700	109.2	39.1	148.3	14.6	27.4
12600	103.2	39.7	142.9	-0.7	21.3
13500	102.7	39.1	141.8	21.5	35.6
14400	104.2	37.6	141.8	15.6	35.6
15300	109.2	37.2	146.4	-12.0	17.6
16200	103.0	37.8	140.7	14.2	38.0
17100	106.5	38.6	145.1	17.6	39.7
18000	103.2	41.2	144.4	7.6	32.5
18900	109.8	38.6	148.5	-9.0	13.7
19800	107.7	43.3	151.0	8.5	32.1
20700	107.3	40.8	148.1	16.3	36.2
21600	108.2	36.7	144.9	12.2	39.3
22500	108.4	38.8	147.2	3.8	30.1
23400	105.2	40.4	145.5	18.1	39.7
24300	105.8	37.9	143.7	19.8	38.4
25200	109.9	37.7	147.6	12.5	33.5
26100	111.2	35.3	146.5	0.3	19.0
27000	107.5	34.2	141.7	12.4	27.7
27900	106.2	35.5	141.7	7.0	26.1
28800	107.5	39.0	146.5	6.1	29.4
29700	107.1	38.3	145.4	6.4	28.4
30600	108.0	37.6	145.6	6.6	28.2
31500	109.6	39.5	149.2	7.2	30.1

32400	110.3	36.8	147.1	5.9	29.1
33300	106.9	40.7	147.6	8.4	29.7
34200	109.1	39.8	148.9	15.6	31.7
35100	109.3	36.1	145.4	-2.7	18.2
36000	111.8	35.6	147.4	1.4	18.9
36900	108.5	37.1	145.6	8.1	27.2
37800	109.5	36.9	146.4	17.5	34.2
38700	114.5	34.9	149.4	10.6	28.5
39600	113.6	36.9	150.5	11.5	31.0
40500	111.7	38.6	150.3	12.3	30.8
41400	109.5	35.5	145.0	3.9	22.9
42300	114.3	38.2	152.5	11.5	27.8
43200	113.2	36.1	149.3	5.6	22.5
44100	109.2	36.4	145.6	12.5	32.0
45000	111.5	34.9	146.4	16.2	37.8
45900	113.0	35.4	148.4	11.5	35.2
46800	110.4	33.7	144.1	12.1	30.7
47700	112.2	33.3	145.5	7.1	25.7
48600	115.1	34.7	149.8	9.0	27.5
49500	115.1	34.1	149.2	8.9	28.8
50400	112.6	35.1	147.7	13.9	33.2

Table 10 Processed data – Bromo 50 °C

Processed data - concentration normalization

Time/s	50 °C				
	product (8.92 ppm)/mM	intermediate product (7.00 ppm)/mM	product + intermediate product/mM	starting material (2.25 ppm)/mM	side product (1.99 ppm)/mM
60	2.4	1.7	4.1	46.6	2.2
960	19.2	8.6	27.8	10.2	4.0
1860	24.4	9.2	33.6	3.2	5.4
2760	25.1	10.4	35.6	2.6	8.1
3660					
4560	25.5	10.8	36.3	0.0	5.5
0	0.0	0.0	0.0	53.0	0.0

* Correction: + 1 minutes, slope + 0.5

KIN-80-Bromo

Derivative: X= Bromo   Concentration: 53 mM   Base: 5 eqiv.   Temperature: 80 °C

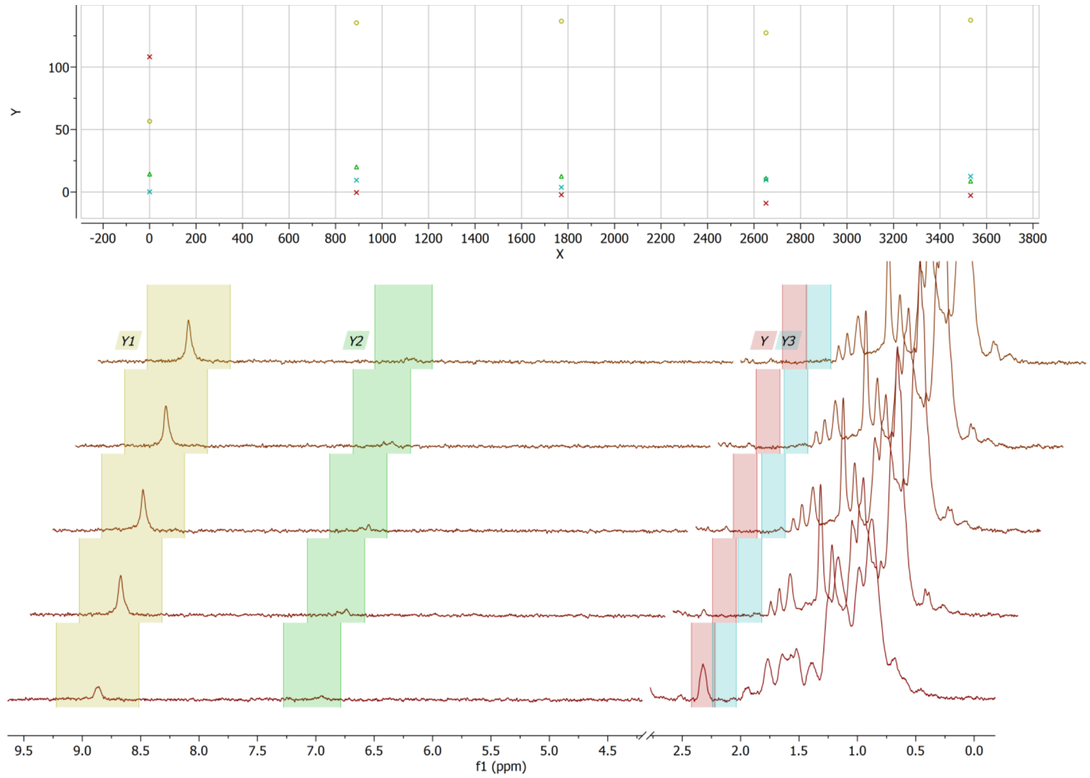


Fig. 12 Mestrenova - Chloro 80 °C

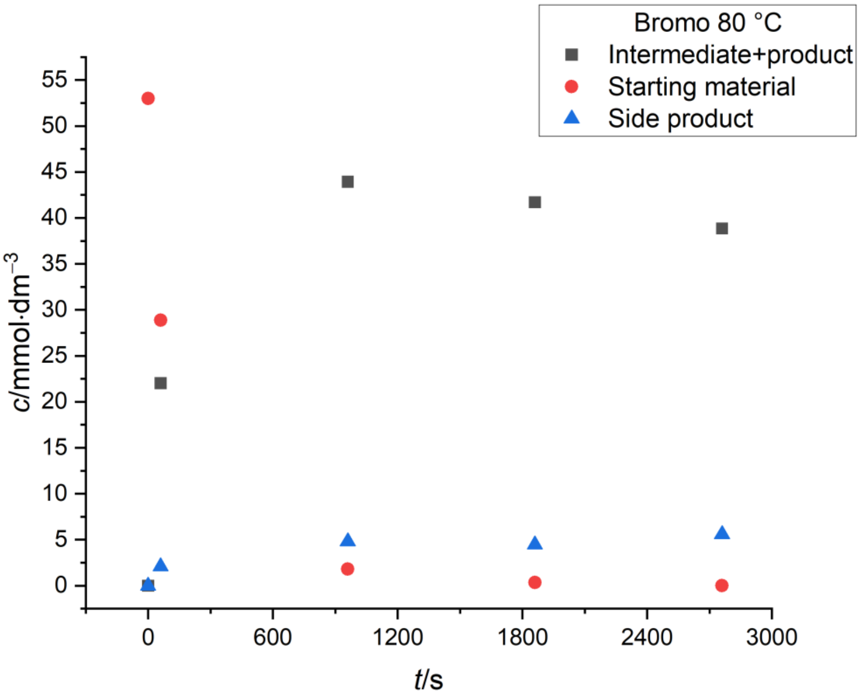


Fig. 13 Processed graph – Bromo 80 °C

Table 11 Raw data – integral values – Bromo 80 °C

Time/s	80 °C				
	product (8.92 ppm)	intermediate product (7.00 ppm)	product + intermediate product	starting material (2.25 ppm)	side product (1.99 ppm)
0	59.1	15.6	74.6	108.3	1.9
900	142.5	19.1	161.6	0.8	12.7
1800	141.1	11.7	152.8	-5.0	11.3
2700	132.0	9.5	141.4	-6.4	15.9
3600	141.0	6.8	147.8	-1.3	16.6

Table 12 Processed data – Bromo 80 °C

Processed data - concentration normalization

Time/s	80 °C				
	product (8.92 ppm)/mM	intermediate product (7.00 ppm)/mM	product + intermediate product/mM	starting material (2.25 ppm)/mM	side product (1.99 ppm)/mM
60	16.5	5.5	22.0	28.9	2.1
960	37.5	6.4	43.9	1.8	4.8
1860	37.1	4.6	41.7	0.3	4.5
2760	34.9	4.0	38.8	0.0	5.6
0	0.0	0.0	0.0	53.0	0.0

* Correction: + 1 minute, slope + 6.4

KIN-40-Chloro

Derivative: X= Chloro Concentration: 53 mM Base: 5 eqiv. Temperature: 40 °C

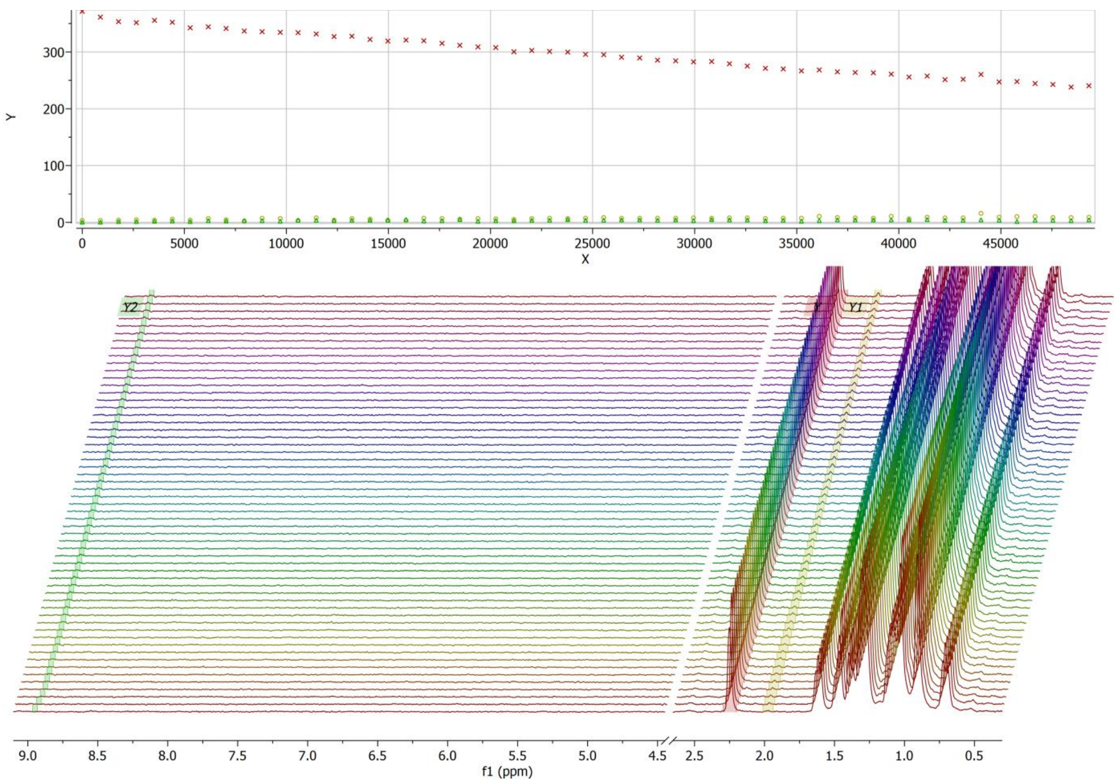


Fig. 14 Mestrenova - Chloro 40 °C

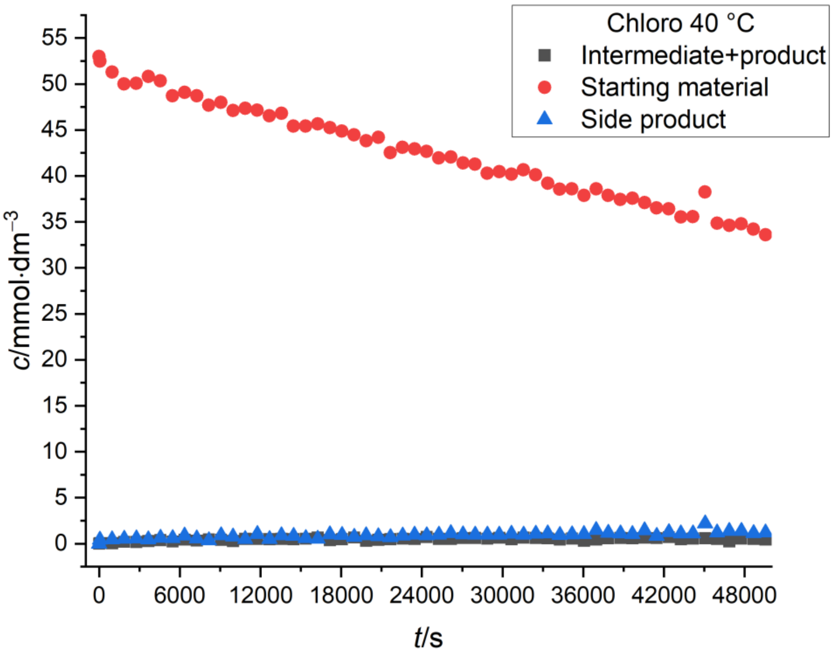


Fig. 15 Processed graph – Chloro 40 °C

Table 13 Raw data – integral values – Chloro 40 °C

Time/s	40 °C				
	product (8.92 ppm)	intermediate product (7.00 ppm)	product + intermediate product	starting material (2.25 ppm)	side product (1.99 ppm)
0	0.5	0.0	0.5	379.7	3.2
900	0.4	0.0	0.4	371.0	3.2
1800	1.4	0.0	1.4	361.6	3.8
2700	1.4	0.0	1.4	362.2	4.0
3600	2.1	0.0	2.1	367.6	3.4
4500	2.9	0.0	2.9	364.2	4.5
5400	1.7	0.0	1.7	352.3	4.3
6300	3.1	0.0	3.1	355.2	6.2
7200	2.5	0.0	2.5	352.3	4.1
8100	3.4	0.0	3.4	345.1	2.7
9000	3.0	0.0	3.0	347.1	6.6
9900	2.1	0.0	2.1	340.7	5.6
10800	3.8	0.0	3.8	342.6	3.6
11700	3.6	0.0	3.6	341.0	7.6
12600	3.5	0.0	3.5	336.6	3.5
13500	3.7	0.0	3.7	338.6	6.5
14400	3.6	0.0	3.6	328.5	5.9
15300	4.0	0.0	4.0	328.5	4.3
16200	4.7	0.0	4.7	330.2	3.7
17100	2.8	0.0	2.8	327.3	7.3
18000	3.5	0.0	3.5	324.6	6.8
18900	4.9	0.0	4.9	321.6	5.3
19800	2.2	0.0	2.2	317.1	6.5
20700	3.1	0.0	3.1	319.7	5.8
21600	3.5	0.0	3.5	307.6	5.1
22500	3.9	0.0	3.9	311.9	6.4
23400	3.6	0.0	3.6	310.6	7.1
24300	5.3	0.0	5.3	308.7	6.5
25200	3.8	0.0	3.8	303.6	7.0
26100	3.7	0.0	3.7	304.2	8.2
27000	4.4	0.0	4.4	299.5	7.2
27900	4.5	0.0	4.5	298.5	7.2
28800	3.9	0.0	3.9	291.4	7.1
29700	4.6	0.0	4.6	292.8	7.1
30600	3.5	0.0	3.5	290.7	7.9
31500	4.7	0.0	4.7	294.0	7.1

32400	4.5	0.0	4.5	290.2	7.8
33300	4.2	0.0	4.2	283.5	8.0
34200	3.2	0.0	3.2	278.8	6.8
35100	4.0	0.0	4.0	279.1	7.2
36000	2.1	0.0	2.1	274.1	7.4
36900	3.2	0.0	3.2	279.2	10.6
37800	4.1	0.0	4.1	273.9	8.5
38700	4.5	0.0	4.5	270.9	8.0
39600	4.2	0.0	4.2	271.9	7.4
40500	4.6	0.0	4.6	268.3	10.5
41400	4.3	0.0	4.3	264.1	6.0
42300	5.1	0.0	5.1	263.4	8.9
43200	3.6	0.0	3.6	257.2	8.0
44100	4.1	0.0	4.1	257.2	8.0
45000	4.3	0.0	4.3	276.8	16.0
45900	3.8	0.0	3.8	252.2	8.7
46800	1.8	0.0	1.8	250.4	10.0
47700	4.1	0.0	4.1	251.6	10.0
48600	3.8	0.0	3.8	247.5	8.3
49500	3.1	0.0	3.1	243.0	8.7
50400	4.1	0.0	4.1	246.7	9.0

Table 14 Processed data – Chloro 40 °C

Processed data - concentration normalization

Time/s	40 °C				
	product (8.92 ppm)/mM	intermediate product (7.00 ppm)/mM	product + intermediate product/mM	starting material (2.25 ppm)/mM	side product (1.99 ppm)/mM
60	0.1	0.0	0.1	52.5	0.4
960	0.0	0.0	0.0	51.3	0.4
1860	0.2	0.0	0.2	50.0	0.5
2760	0.2	0.0	0.2	50.1	0.6
3660	0.3	0.0	0.3	50.8	0.5
4560	0.4	0.0	0.4	50.4	0.6
5460	0.2	0.0	0.2	48.7	0.6
6360	0.4	0.0	0.4	49.1	0.9
7260	0.3	0.0	0.3	48.7	0.6
8160	0.5	0.0	0.5	47.7	0.4
9060	0.4	0.0	0.4	48.0	0.9
9960	0.3	0.0	0.3	47.1	0.8
10860	0.5	0.0	0.5	47.4	0.5
11760	0.5	0.0	0.5	47.1	1.1
12660	0.5	0.0	0.5	46.5	0.5
13560	0.5	0.0	0.5	46.8	0.9
14460	0.5	0.0	0.5	45.4	0.8
15360	0.5	0.0	0.5	45.4	0.6
16260	0.7	0.0	0.7	45.6	0.5
17160	0.4	0.0	0.4	45.2	1.0
18060	0.5	0.0	0.5	44.9	0.9
18960	0.7	0.0	0.7	44.5	0.7
19860	0.3	0.0	0.3	43.8	0.9
20760	0.4	0.0	0.4	44.2	0.8
21660	0.5	0.0	0.5	42.5	0.7
22560	0.5	0.0	0.5	43.1	0.9
23460	0.5	0.0	0.5	42.9	1.0
24360	0.7	0.0	0.7	42.7	0.9
25260	0.5	0.0	0.5	42.0	1.0
26160	0.5	0.0	0.5	42.0	1.1
27060	0.6	0.0	0.6	41.4	1.0
27960	0.6	0.0	0.6	41.3	1.0
28860	0.5	0.0	0.5	40.3	1.0

29760	0.6	0.0	0.6	40.5	1.0
30660	0.5	0.0	0.5	40.2	1.1
31560	0.7	0.0	0.7	40.6	1.0
32460	0.6	0.0	0.6	40.1	1.1
33360	0.6	0.0	0.6	39.2	1.1
34260	0.4	0.0	0.4	38.5	0.9
35160	0.5	0.0	0.5	38.6	1.0
36060	0.3	0.0	0.3	37.9	1.0
36960	0.4	0.0	0.4	38.6	1.5
37860	0.6	0.0	0.6	37.9	1.2
38760	0.6	0.0	0.6	37.4	1.1
39660	0.6	0.0	0.6	37.6	1.0
40560	0.6	0.0	0.6	37.1	1.5
41460	0.6	0.0	0.6	36.5	0.8
42360	0.7	0.0	0.7	36.4	1.2
43260	0.5	0.0	0.5	35.5	1.1
44160	0.6	0.0	0.6	35.6	1.1
45060	0.6	0.0	0.6	38.3	2.2
45960	0.5	0.0	0.5	34.9	1.2
46860	0.2	0.0	0.2	34.6	1.4
47760	0.6	0.0	0.6	34.8	1.4
48660	0.5	0.0	0.5	34.2	1.1
49560	0.4	0.0	0.4	33.6	1.2
0	0.0	0.0	0.0	53.0	0.0

* Correction: + 1 minute, slope + 0.0

KIN-60-Chloro

Derivative: X= Chloro   Concentration: 53 mᴍ   Base: 5 eqiv.   Temperature: 60 °C

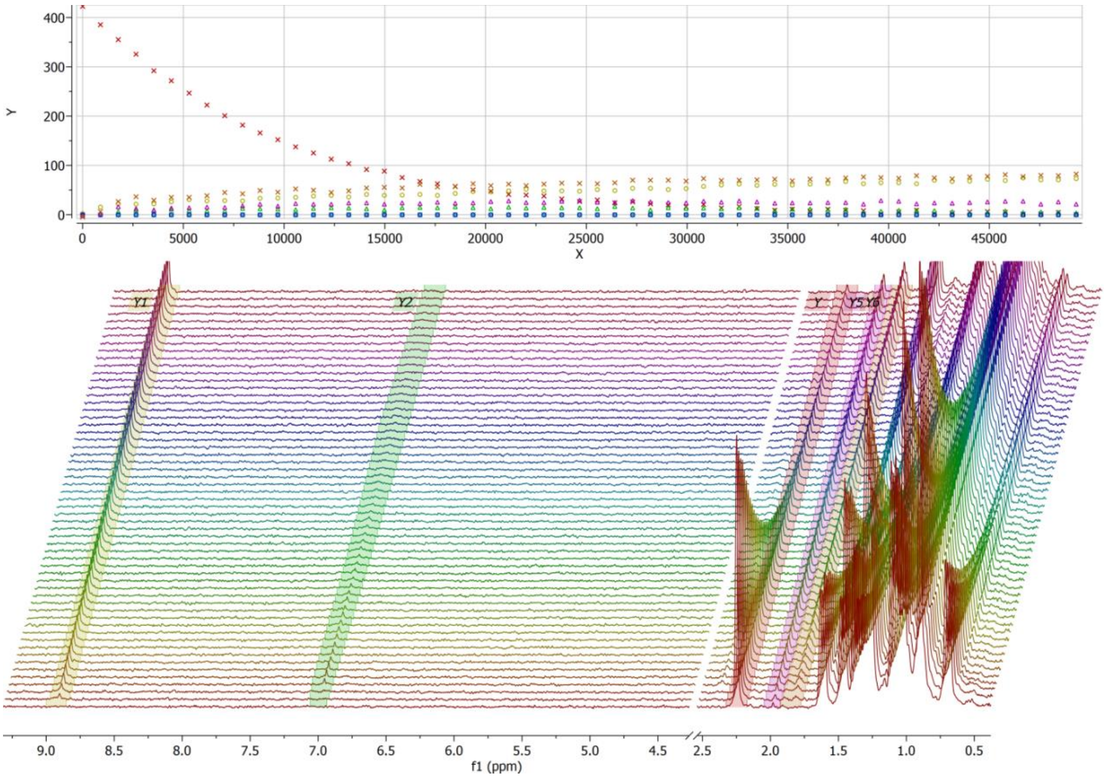


Fig. 16 Mestrenova - Chloro 60 °C

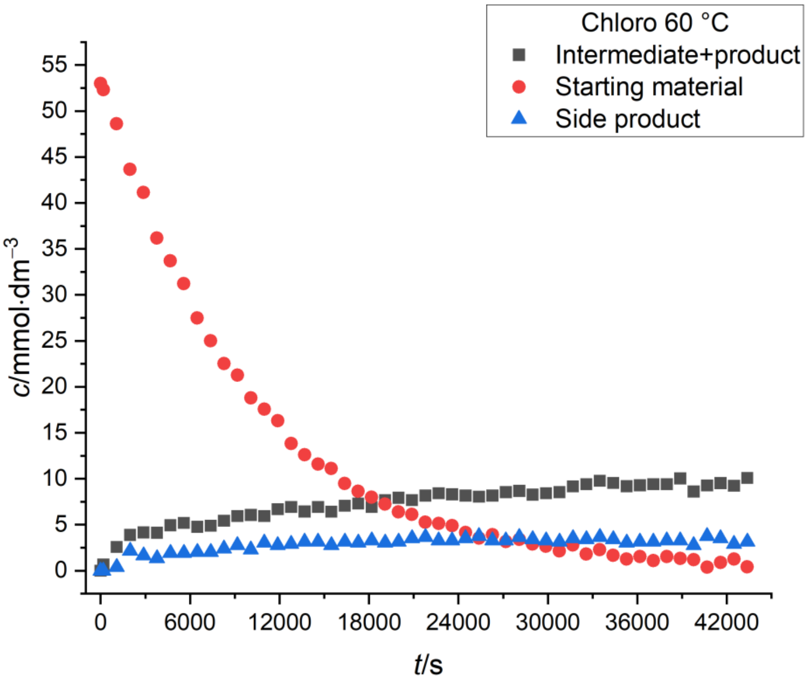


Fig. 17 Processed graph – Chloro 60 °C

Table 15 Raw data – integral values – Chloro 60 °C

Time/s	60 °C				
	product (8.92 ppm)	intermediate product (7.00 ppm)	product + intermediate product	starting material (2.25 ppm)	side product (1.99 ppm)
0	2.2	0.4	2.6	420.0	-1.4
900	16.0	1.9	17.9	390.0	1.8
1800	22.0	6.5	28.5	350.0	16.0
2700	21.0	9.7	30.7	330.0	12.0
3600	22.0	8.4	30.4	290.0	9.4
4500	26.0	11.0	37.0	270.0	14.0
5400	31.0	8.0	39.0	250.0	14.0
6300	28.0	7.6	35.6	220.0	15.0
7200	29.0	7.6	36.6	200.0	15.0
8100	28.0	13.0	41.0	180.0	18.0
9000	33.0	12.0	45.0	170.0	21.0
9900	34.0	12.0	46.0	150.0	17.0
10800	35.0	10.0	45.0	140.0	23.0
11700	38.0	13.0	51.0	130.0	21.0
12600	39.0	14.0	53.0	110.0	22.0
13500	36.0	13.0	49.0	100.0	24.0
14400	41.0	12.0	53.0	92.0	24.0
15300	39.0	9.9	48.9	88.0	21.0
16200	40.0	14.0	54.0	75.0	24.0
17100	41.0	15.0	56.0	68.0	23.0
18000	39.0	14.0	53.0	63.0	25.0
18900	43.0	16.0	59.0	57.0	23.0
19800	47.0	14.0	61.0	50.0	24.0
20700	47.0	12.0	59.0	48.0	27.0
21600	48.0	15.0	63.0	41.0	28.0
22500	52.0	13.0	65.0	40.0	25.0
23400	49.0	15.0	64.0	38.0	25.0
24300	49.0	14.0	63.0	32.0	27.0
25200	48.0	14.0	62.0	27.0	29.0
26100	51.0	12.0	63.0	30.0	25.0
27000	49.0	17.0	66.0	24.0	25.0
27900	53.0	14.0	67.0	26.0	28.0
28800	54.0	9.8	63.8	22.0	26.0
29700	51.0	14.0	65.0	20.0	25.0
30600	53.0	13.0	66.0	16.0	24.0
31500	58.0	13.0	71.0	21.0	27.0

32400	60.0	13.0	73.0	13.0	26.0
33300	62.0	14.0	76.0	17.0	28.0
34200	60.0	14.0	74.0	12.0	26.0
35100	62.0	9.2	71.2	8.7	23.0
36000	60.0	12.0	72.0	11.0	24.0
36900	62.0	11.0	73.0	7.3	24.0
37800	63.0	10.0	73.0	11.0	25.0
38700	67.0	11.0	78.0	9.2	25.0
39600	63.0	3.5	66.5	8.3	21.0
40500	65.0	6.9	71.9	1.6	29.0
41400	65.0	8.9	73.9	5.8	27.0
42300	63.0	8.6	71.6	8.7	22.0
43200	70.0	8.4	78.4	1.8	24.0
44100	67.0	6.2	73.2	3.2	24.0
45000	68.0	3.3	71.3	5.8	25.0
45900	72.0	5.0	77.0	6.1	26.0
46800	69.0	7.6	76.6	5.1	27.0
47700	75.0	4.6	79.6	1.3	27.0
48600	71.0	5.3	76.3	1.5	22.0
49500	70.0	5.2	75.2	4.4	26.0
50400	73.0	3.6	76.6	0.3	21.0

Table 16 Processed data – Chloro 60 °C

	Processed data - concentration normalization				
	60 °C				
Time/s	product (8.92 ppm)/mM	intermediate product (7.00 ppm)/mM	product + intermediate product/mM	starting material (2.25 ppm)/mM	side product (1.99 ppm)/mM
180	0.4	0.2	0.7	52.3	0.0
1080	2.2	0.4	2.6	48.6	0.4
1980	2.9	1.0	3.9	43.6	2.2
2880	2.8	1.4	4.2	41.2	1.7
3780	2.9	1.2	4.1	36.2	1.3
4680	3.4	1.5	4.9	33.7	1.9
5580	4.0	1.2	5.2	31.2	1.9
6480	3.7	1.1	4.8	27.5	2.0
7380	3.8	1.1	4.9	25.0	2.0
8280	3.7	1.8	5.4	22.5	2.4
9180	4.3	1.7	5.9	21.3	2.8
10080	4.4	1.7	6.1	18.8	2.3
10980	4.5	1.4	5.9	17.6	3.0
11880	4.9	1.8	6.7	16.3	2.8
12780	5.0	1.9	6.9	13.8	2.9
13680	4.6	1.8	6.4	12.6	3.2
14580	5.3	1.7	6.9	11.6	3.2
15480	5.0	1.4	6.4	11.1	2.8
16380	5.1	1.9	7.1	9.5	3.2
17280	5.3	2.0	7.3	8.6	3.0
18180	5.0	1.9	6.9	8.0	3.3
19080	5.5	2.2	7.7	7.3	3.0
19980	6.0	1.9	7.9	6.4	3.2
20880	6.0	1.7	7.7	6.1	3.5
21780	6.1	2.0	8.2	5.3	3.7
22680	6.6	1.8	8.4	5.1	3.3
23580	6.3	2.0	8.3	4.9	3.3
24480	6.3	1.9	8.2	4.1	3.5
25380	6.1	1.9	8.0	3.5	3.8
26280	6.5	1.7	8.2	3.9	3.3
27180	6.3	2.3	8.5	3.2	3.3
28080	6.8	1.9	8.7	3.4	3.7
28980	6.9	1.4	8.3	2.9	3.4

29880	6.5	1.9	8.4	2.7	3.3
30780	6.8	1.8	8.5	2.2	3.2
31680	7.4	1.8	9.2	2.8	3.5
32580	7.6	1.8	9.4	1.8	3.4
33480	7.9	1.9	9.8	2.3	3.7
34380	7.6	1.9	9.5	1.7	3.4
35280	7.9	1.3	9.2	1.3	3.0
36180	7.6	1.7	9.3	1.5	3.2
37080	7.9	1.5	9.4	1.1	3.2
37980	8.0	1.4	9.4	1.5	3.3
38880	8.5	1.5	10.0	1.3	3.3
39780	8.0	0.6	8.6	1.2	2.8
40680	8.2	1.0	9.3	0.4	3.8
41580	8.2	1.3	9.5	0.9	3.5
42480	8.0	1.2	9.2	1.3	2.9
43380	8.9	1.2	10.1	0.4	3.2
0	0.0	0.0	0.0	53.0	0.0

* Correction: + 3 minutes, slope + 1.4

KIN-70-Chloro

Derivative: X= Chloro Concentration: 53 mM Base: 5 eqiv. Temperature: 70 °C

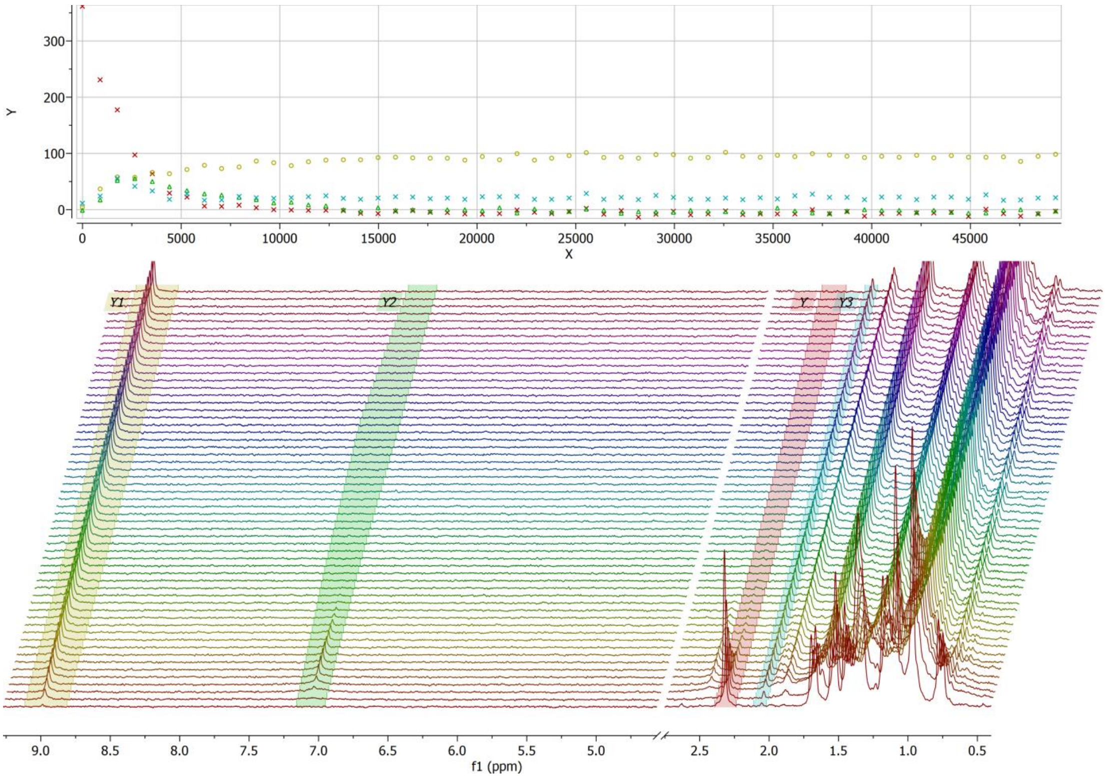


Fig. 18 Mestrenova - Chloro 70 °C

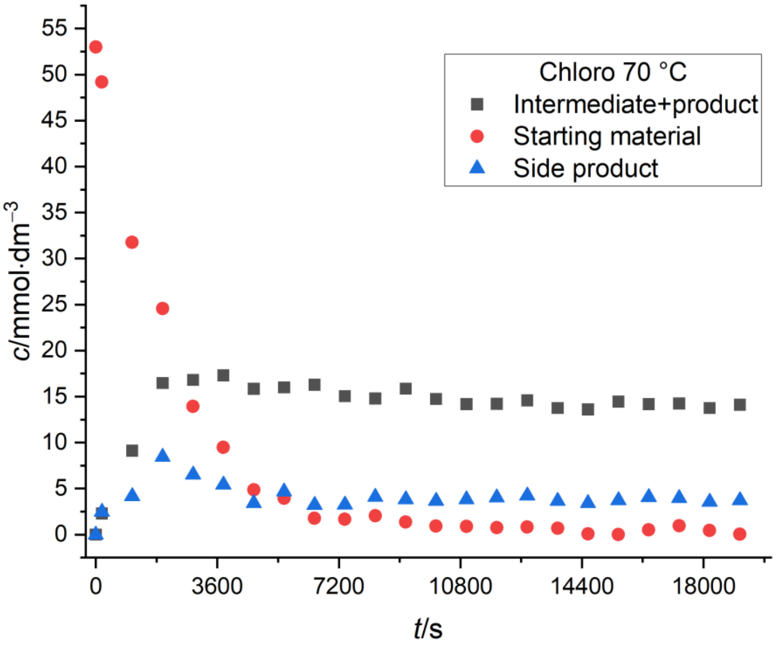


Fig. 19 Processed graph – Chloro 70 °C

Table 17 Raw data – integral values – Chloro 70 °C

Time/s	70 °C				
	product (8.92 ppm)	intermediate product (7.00 ppm)	product + intermediate product	starting material (2.25 ppm)	side product (1.99 ppm)
0	3.7	-0.9	2.8	361.7	11.4
900	36.9	17.1	54.0	231.0	23.9
1800	58.3	50.9	109.2	177.1	56.1
2700	57.8	53.9	111.7	97.3	41.6
3600	66.2	49.2	115.3	63.8	33.5
4500	64.0	40.4	104.4	29.3	18.4
5400	71.2	34.3	105.5	22.3	28.0
6300	79.0	28.7	107.7	6.1	16.9
7200	73.1	25.4	98.5	5.4	17.1
8100	76.2	20.3	96.5	8.0	23.5
9000	86.1	18.4	104.5	3.1	21.6
9900	83.3	12.8	96.1	-0.2	20.1
10800	78.3	13.6	91.9	-0.5	21.4
11700	85.0	7.2	92.2	-1.5	23.0
12600	88.0	6.9	95.0	-1.0	24.5
13500	88.7	0.1	88.8	-2.0	20.2
14400	88.8	-1.2	87.6	-6.7	18.4
15300	92.6	1.4	94.0	-7.2	20.8
16200	93.3	-1.3	92.0	-3.4	23.2
17100	92.0	0.4	92.4	-0.1	22.6
18000	91.4	-2.7	88.7	-4.0	19.5
18900	91.5	-0.1	91.4	-6.9	20.6
19800	88.1	0.8	88.9	-10.5	18.5
20700	94.2	-2.1	92.1	-8.2	23.3
21600	88.7	1.2	89.8	-4.2	22.9
22500	99.5	-5.7	93.7	-3.2	23.5
23400	88.3	1.1	89.3	-7.9	18.6
24300	91.6	-3.5	88.1	-6.3	18.6
25200	96.2	-2.7	93.4	-2.7	20.7
26100	101.5	-0.5	101.0	4.2	28.9
27000	92.6	-0.6	92.1	-8.7	18.4
27900	93.0	-2.1	90.9	-1.5	21.7
28800	91.7	-1.9	89.8	-10.0	17.6
29700	97.7	-1.6	96.2	-5.0	25.4
30600	97.7	0.7	98.3	-1.6	21.8
31500	91.5	-2.3	89.2	-8.3	18.6

32400	92.8	3.0	95.8	-7.9	18.7
33300	102.2	-0.6	101.6	-3.3	20.8
34200	95.2	-0.6	94.6	-5.6	17.7
35100	93.2	-2.3	90.9	-7.4	21.1
36000	97.0	-1.5	95.5	-5.4	19.2
36900	94.7	-5.2	89.5	-6.7	24.6
37800	99.7	-6.5	93.2	-0.1	27.8
38700	97.4	-5.6	91.8	-6.1	21.6
39600	95.0	-1.6	93.4	-4.4	22.0
40500	92.6	-0.5	92.1	-6.4	17.8
41400	95.1	-2.2	92.9	-8.0	22.4
42300	93.4	-1.7	91.7	-6.6	22.2
43200	96.8	-4.6	92.2	-5.6	18.1
44100	92.1	-0.8	91.3	-4.6	22.5
45000	96.1	-4.8	91.3	-3.1	22.2
45900	93.0	-6.1	86.9	-13.1	18.1
46800	93.0	-5.9	87.1	-0.8	26.4
47700	94.0	-1.0	92.9	-5.2	16.7
48600	85.6	1.2	86.8	-9.6	17.2
49500	95.1	-5.1	90.0	-7.5	20.4
50400	98.4	-2.1	96.3	-2.7	21.3

Table 18 Processed data – Chloro 70 °C

Processed data - concentration normalization

Time/s	70 °C product (8.92 ppm)/mM	intermediate product (7.00 ppm)/mM	product + intermediate product/mM	starting material (2.25 ppm)/mM	side product (1.99 ppm)/mM
180	1.5	0.8	2.3	49.2	2.5
1080	5.9	3.2	9.1	31.8	4.2
1980	8.7	7.7	16.5	24.6	8.4
2880	8.7	8.1	16.8	13.9	6.5
3780	9.8	7.5	17.3	9.5	5.4
4680	9.5	6.3	15.8	4.9	3.4
5580	10.5	5.5	16.0	3.9	4.7
6480	11.5	4.8	16.3	1.8	3.2
7380	10.7	4.3	15.0	1.7	3.2
8280	11.1	3.7	14.8	2.0	4.1
9180	12.4	3.4	15.9	1.4	3.8
10080	12.1	2.7	14.7	0.9	3.6
10980	11.4	2.8	14.2	0.9	3.8
11880	12.3	1.9	14.2	0.8	4.0
12780	12.7	1.9	14.6	0.8	4.2
13680	12.8	1.0	13.8	0.7	3.7
14580	12.8	0.8	13.6	0.1	3.4
15480	13.3	1.1	14.4	0.0	3.7
16380	13.4	0.8	14.2	0.5	4.1
17280	13.2	1.0	14.2	0.9	4.0
18180	13.2	0.6	13.7	0.4	3.6
19080	13.2	0.9	14.1	0.0	3.7
0	0.0	0.0	0.0	53.0	0.0

* Correction: + 3 minutes, slope + 7.2

KIN-80-Chloro

Derivative: X= Chloro Concentration: 53 mM Base: 5 eqiv. Temperature: 80 °C

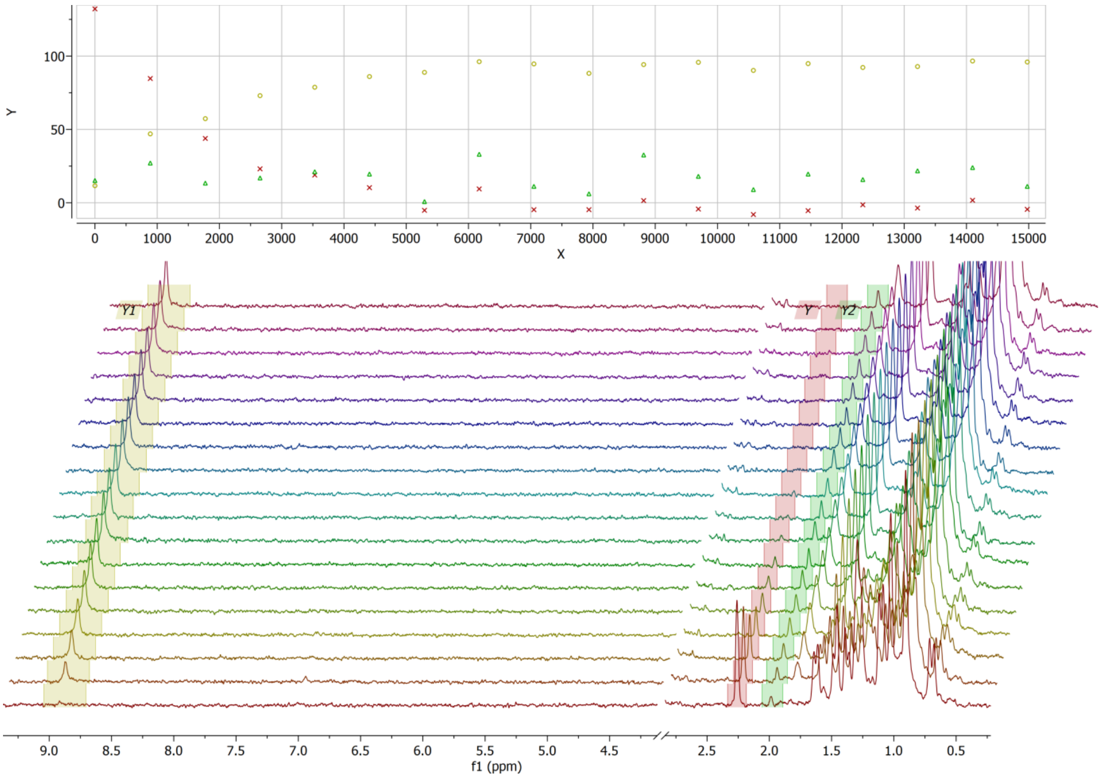


Fig. 20 Mestrenova – Chloro 80 °C

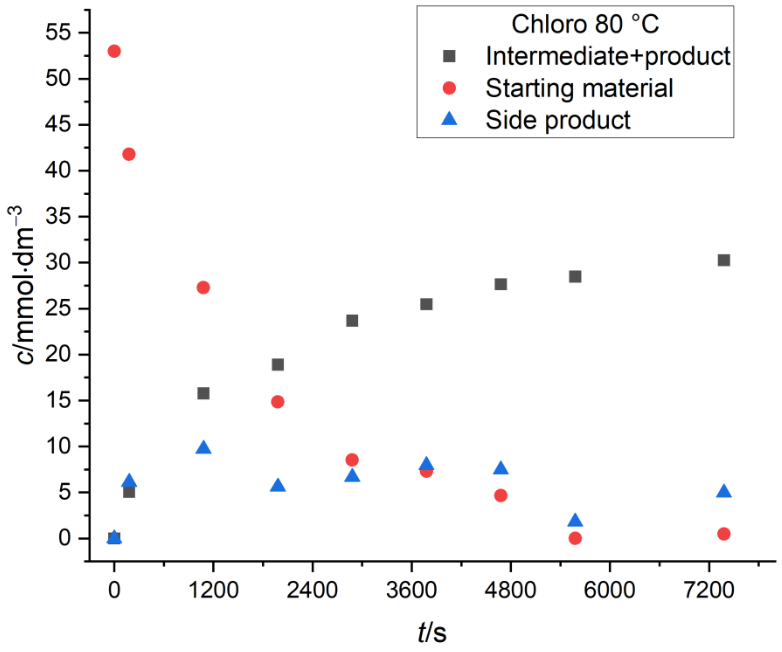


Fig. 21 Processed graph – Chloro 80 °C

Table 19 Raw data – integral values – Chloro 80 °C

Time/s	80 °C				
	product (8.92 ppm)	intermediate product (7.00 ppm)	product + intermediate product	starting material (2.25 ppm)	side product (1.99 ppm)
0	11.6	0.0	11.6	132.7	15.1
900	46.9	0.0	46.9	84.8	27.0
1800	57.2	0.0	57.2	43.9	13.5
2700	73.0	0.0	73.0	23.0	16.9
3600	78.8	0.0	78.8	18.9	21.2
4500	86.0	0.0	86.0	10.2	19.6
5400	88.8	0.0	88.8	-5.1	0.9
6300	96.3	0.0	96.3	9.4	33.0
7200	94.6	0.0	94.6	-3.5	11.3
8100	88.1	0.0	88.1	-8.2	6.1
9000	94.1	0.0	94.1	2.1	32.7
9900	95.7	0.0	95.7	-7.4	17.9
10800	90.1	0.0	90.1	-8.7	9.0
11700	94.7	0.0	94.7	-3.3	19.6
12600	92.3	0.0	92.3	-1.0	15.7
13500	92.8	0.0	92.8	-2.0	21.8
14400	96.7	0.0	96.7	-0.4	24.0
15300	96.0	0.0	96.0	-3.9	11.3

Table 20 Processed data – Chloro 80 °C

Processed data - concentration normalization					
	80 °C				
Time/s	product (8.92 ppm)	intermediate product (7.00 ppm)	product + intermediate product	starting material (2.25 ppm)	side product (1.99 ppm)
180	5.1	0.0	5.1	41.8	6.1
1080	15.8	0.0	15.8	27.3	9.7
1980	18.9	0.0	18.9	14.9	5.6
2880	23.7	0.0	23.7	8.5	6.7
3780	25.5	0.0	25.5	7.3	8.0
4680	27.6	0.0	27.6	4.7	7.5
5580	28.5	0.0	28.5	0.0	1.8
6480					
7380	30.3	0.0	30.3	0.5	5.0
0	0.0	0.0	0.0	53.0	0.0

* Correction: + 3 minutes, slope + 5.1

KIN-80-Chloro 2xC

Derivative: X= Chloro Concentration: 106 mM Base: 5 eqiv. Temperature: 80 °C

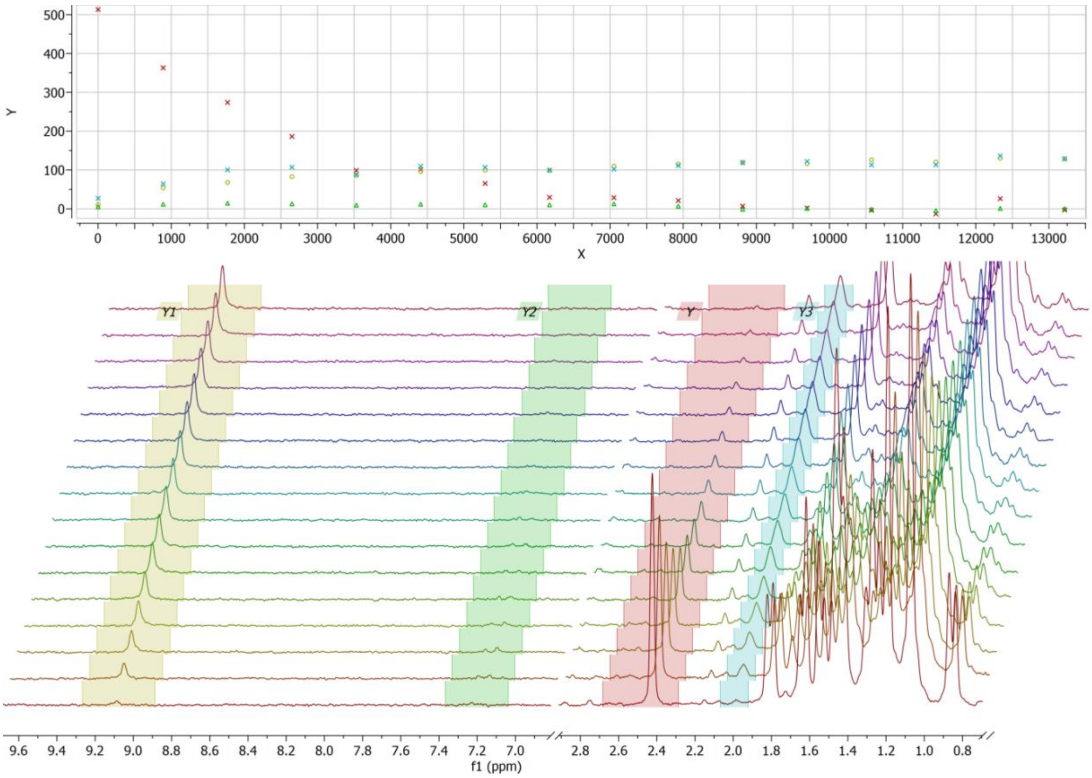


Fig. 22 Mestrenova – Chloro 80 °C – 2x higher concentration of starting material

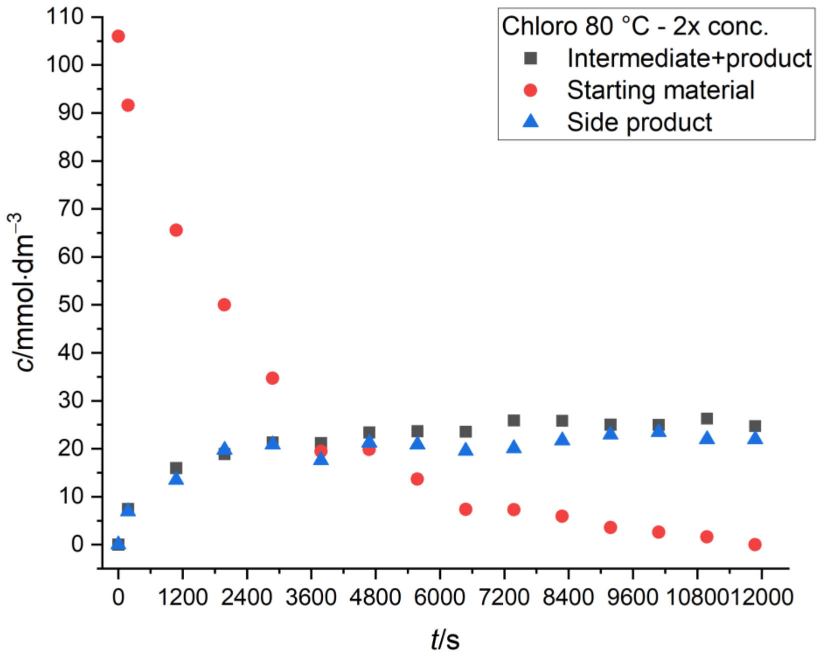


Fig. 23 Processed graph – Chloro 80 °C – 2x higher concentration of starting material

Table 21 Raw data – integral values – Chloro 80 °C – 2x higher concentration of starting material

	80 °C - 2.0x c				
Time/s	product (8.92 ppm)	intermediate product (7.00 ppm)	product + intermediate product	starting material (2.25 ppm)	side product (1.99 ppm)
0.00	11.5	4.9	16.4	513.1	26.9
900.00	53.6	11.9	65.5	363.4	64.3
1800.00	67.9	14.4	82.3	273.9	100.5
2700.00	83.1	12.9	96.1	186.1	106.8
3600.00	86.1	9.3	95.4	98.6	88.0
4500.00	96.0	12.2	108.2	101.1	109.1
5400.00	99.5	10.1	109.6	65.4	106.8
6300.00	98.9	10.2	109.1	29.2	99.1
7200.00	109.5	13.0	122.5	28.7	102.3
8100.00	115.0	7.1	122.1	20.8	111.6
9000.00	119.1	-1.7	117.4	7.3	118.6
9900.00	116.4	0.7	117.2	2.0	121.7
10800.00	126.4	-1.6	124.8	-3.7	113.2
11700.00	120.4	-4.6	115.8	-13.1	112.9
12600.00	130.2	0.8	130.9	25.8	136.3
13500.00	128.3	0.2	128.5	-2.7	128.5

Table 22 Processed data – Chloro 80 °C – 2x higher concentration of starting material

	80 °C - 2.0x c				
Time/s	product (8.92 ppm)/mM	intermediate product (7.00 ppm)/mM	product + intermediate product/mM	starting material (2.25 ppm)/mM	side product (1.99 ppm)/mM
180.00	4.3	3.1	7.4	91.6	7.0
1080.00	11.6	4.4	16.0	65.6	13.5
1980.00	14.1	4.8	18.9	50.0	19.8
2880.00	16.8	4.5	21.3	34.7	20.9
3780.00	17.3	3.9	21.2	19.4	17.6
4680.00	19.0	4.4	23.4	19.9	21.3
5580.00	19.6	4.0	23.6	13.7	20.9
6480.00	19.5	4.1	23.5	7.4	19.5
7380.00	21.3	4.5	25.9	7.3	20.1
8280.00	22.3	3.5	25.8	5.9	21.7
9180.00	23.0	2.0	25.0	3.5	22.9
10080.00	22.6	2.4	25.0	2.6	23.5
10980.00	24.3	2.0	26.3	1.6	22.0
11880.00	23.2	1.5	24.7	0.0	21.9
0.00	0.0	0.0	0.0	106.0	0.0

* Correction: + 3 minutes, slope + 13.1

KIN-80-Chloro 3xC

Derivative: X= Chloro Concentration: 159 mM Base: 5 eqiv. Temperature: 80 °C

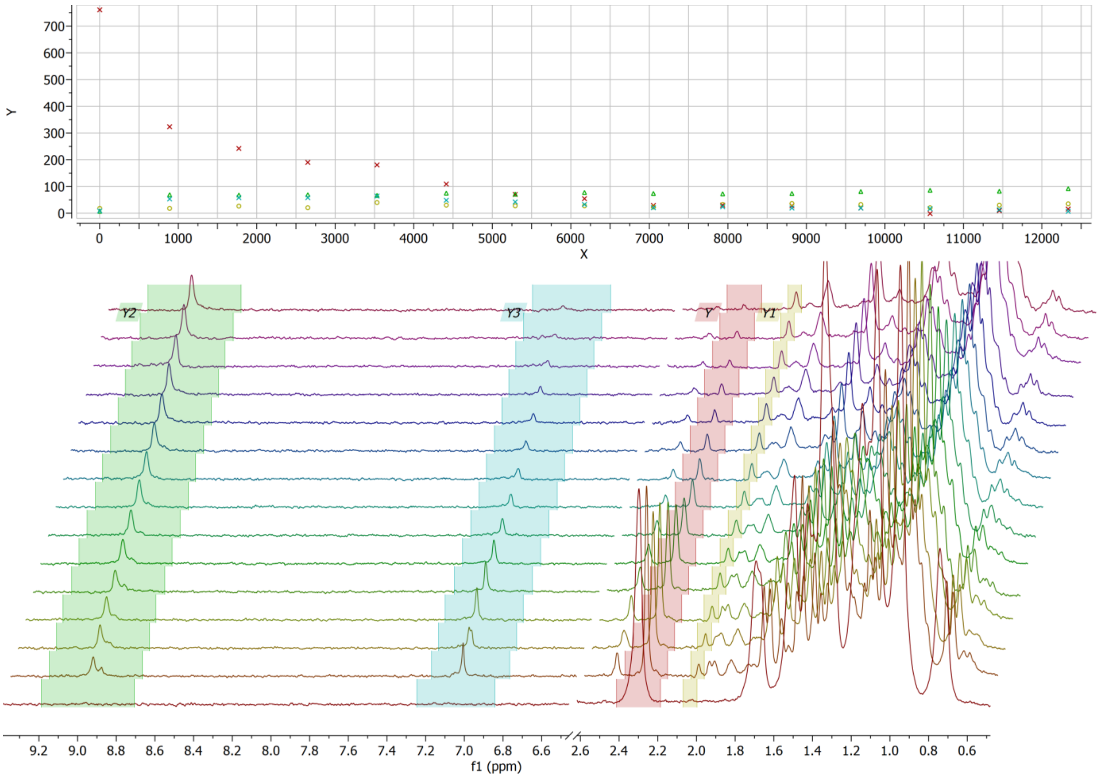


Fig. 24 Mestrenova – Chloro 80 °C – 3x higher concentration of starting material

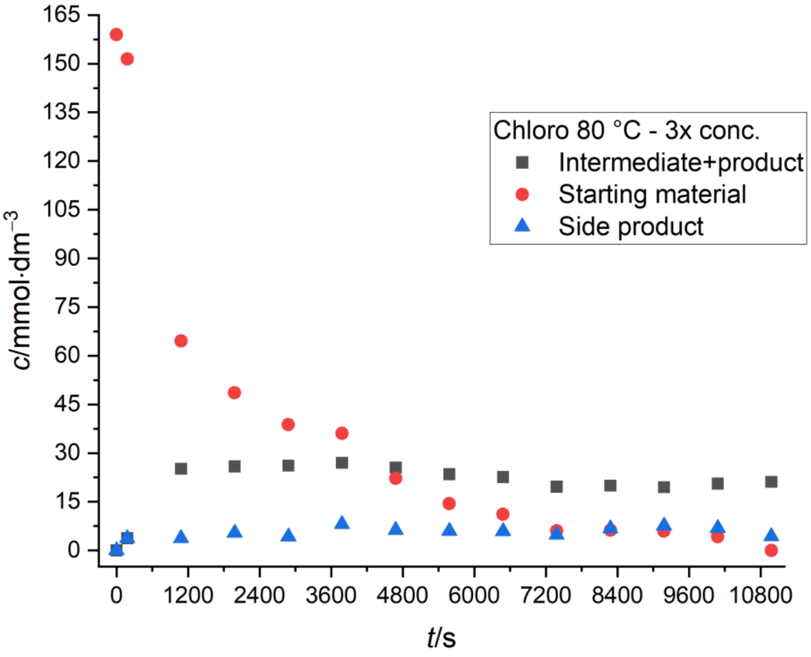


Fig. 25 Processed graph – Chloro 80 °C – 3x higher concentration of starting material

Table 23 Raw data – integral values – Chloro 80 °C – 3x higher concentration of starting material

	80 °C - 3.0x c				
Time/s	product (8.92 ppm)	intermediate product (7.00 ppm)	product + intermediate product	starting material (2.25 ppm)	side product (1.99 ppm)
0.00	7.3	8.7	16.1	749.6	17.4
900.00	69.2	52.9	122.2	318.8	17.6
1800.00	67.3	58.5	125.8	239.8	25.4
2700.00	68.4	58.5	127.0	190.9	19.9
3600.00	66.8	64.5	131.3	177.6	38.9
4500.00	75.2	48.9	124.2	108.6	29.7
5400.00	71.3	42.6	113.9	70.0	28.3
6300.00	77.1	32.4	109.6	53.9	27.9
7200.00	74.0	20.6	94.7	28.6	22.8
8100.00	72.2	24.2	96.4	29.8	32.3
9000.00	74.4	19.6	94.0	28.3	36.7
9900.00	80.8	18.7	99.5	19.4	32.5
10800.00	85.6	16.6	102.2	-1.3	20.5
11700.00	82.2	13.6	95.8	10.1	30.2
12600.00	92.2	7.3	99.5	15.8	34.9

Table 24 Processed data – Chloro 80 °C – 3x higher concentration of starting material

Processed data - concentration normalization

	80 °C - 3.0x c				
Time/s	product (8.92 ppm)/mM	intermediate product (7.00 ppm)/mM	product + intermediate product/mM	starting material (2.25 ppm)/mM	side product (1.99 ppm)/mM
180.00	1.7	2.0	3.8	151.5	3.8
1080.00	14.2	10.9	25.2	64.6	3.8
1980.00	13.8	12.1	25.9	48.6	5.4
2880.00	14.1	12.1	26.1	38.8	4.3
3780.00	13.7	13.3	27.0	36.1	8.1
4680.00	15.4	10.1	25.6	22.2	6.2
5580.00	14.6	8.9	23.5	14.4	6.0
6480.00	15.8	6.8	22.6	11.1	5.9
7380.00	15.2	4.4	19.6	6.0	4.9
8280.00	14.8	5.1	20.0	6.3	6.8
9180.00	15.3	4.2	19.5	6.0	7.7
10080.00	16.6	4.0	20.6	4.2	6.8
10980.00	17.5	3.6	21.1	0.0	4.4
0.00	0.0	0.0	0.0	159.0	0.0

* Correction: + 3 minutes, slope + 1.3

KIN-80-Chloro-50B

Derivative: X= Chloro Concentration: 53 mM Base: 10 eqiv. Temperature: 80 °C

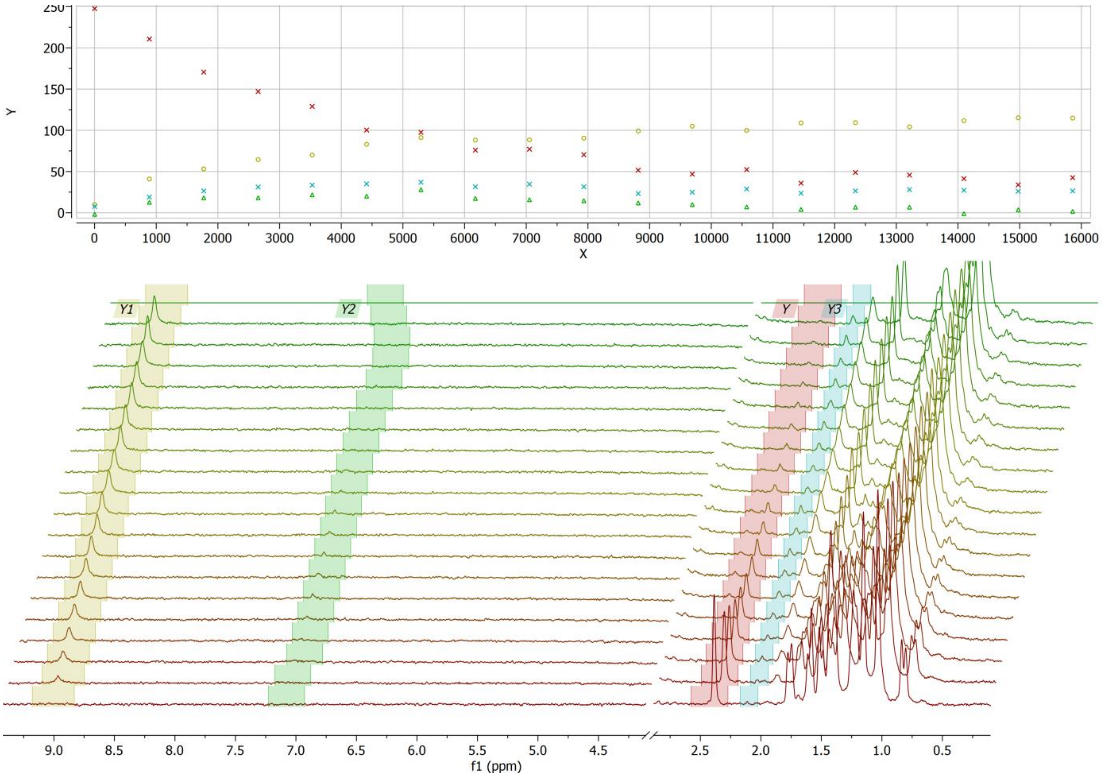


Fig. 26 Mestrenova – Chloro 80 °C – 50 eq. of base

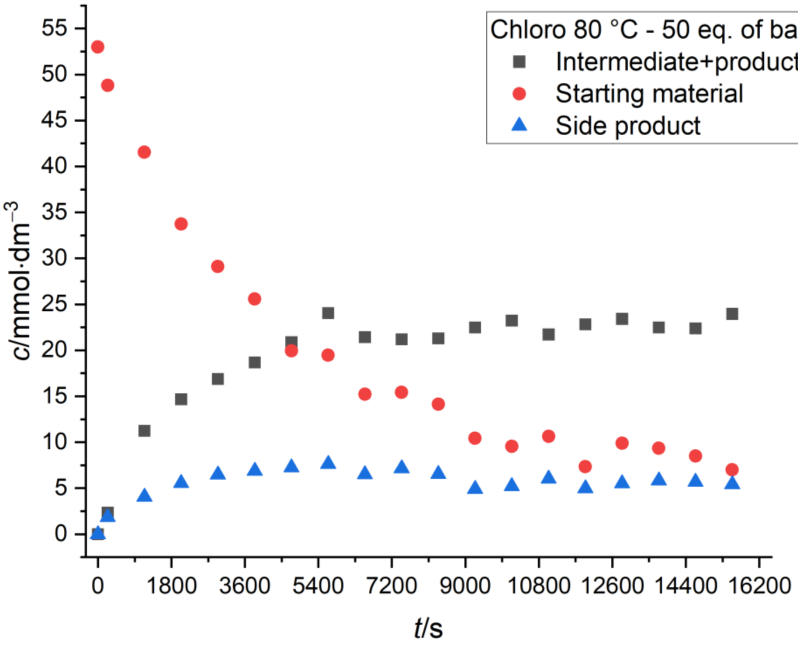


Fig. 27 Processed graph – Chloro 80 °C – 50 eq. of base

Table 25 Raw data – integral values – Chloro 80 °C – 50 eq. of base

Time/s	80 °C 50 B				
	product (8.92 ppm)	intermediate product (7.00 ppm)	product + intermediate product	starting material (2.25 ppm)	side product (1.99 ppm)
0	10.1	-1.9	8.1	247.6	7.7
900	41.0	12.7	53.7	210.5	18.9
1800	53.2	18.0	71.2	170.5	26.5
2700	64.5	18.0	82.5	146.9	31.2
3600	70.2	21.5	91.7	129.0	33.4
4500	82.8	20.1	102.9	100.1	35.1
5400	91.3	27.9	119.1	97.6	37.2
6300	88.2	17.6	105.7	76.0	31.4
7200	88.6	16.0	104.6	77.0	34.6
8100	90.3	14.8	105.1	70.4	31.6
9000	99.2	11.9	111.1	51.5	23.2
9900	105.0	10.0	115.0	46.9	24.8
10800	99.9	7.3	107.2	52.4	28.9
11700	108.8	4.1	112.9	35.7	23.5
12600	109.3	6.6	115.9	48.7	26.4
13500	104.2	7.0	111.1	45.8	27.8
14400	111.7	-1.1	110.6	41.5	27.3
15300	115.3	3.5	118.7	34.0	25.9
16200	114.7	1.8	116.5	42.6	26.2

Table 26 Processed data – Chloro 80 °C – 50 eq. of base

Processed data - concentration normalization					
	80 °C 50 B				
Time/s	product (8.92 ppm)/mM	intermediate product (7.00 ppm)/mM	product + intermediate product/mM	starting material (2.25 ppm)/mM	side product (1.99 ppm)/mM
240	2.3	0.0	2.3	48.8	1.9
1140	8.4	2.9	11.2	41.5	4.1
2040	10.8	3.9	14.7	33.7	5.6
2940	13.0	3.9	16.9	29.1	6.5
3840	14.1	4.6	18.7	25.6	6.9
4740	16.6	4.3	20.9	20.0	7.2
5640	18.2	5.8	24.0	19.5	7.6
6540	17.6	3.8	21.4	15.2	6.5
7440	17.7	3.5	21.2	15.4	7.1
8340	18.0	3.3	21.3	14.1	6.5
9240	19.8	2.7	22.5	10.4	4.9
10140	20.9	2.3	23.2	9.5	5.2
11040	19.9	1.8	21.7	10.6	6.0
11940	21.7	1.2	22.8	7.4	5.0
12840	21.7	1.7	23.4	9.9	5.5
13740	20.7	1.7	22.5	9.3	5.8
14640	22.2	0.2	22.4	8.5	5.7
15540	22.9	1.0	24.0	7.0	5.4
0	0.0	0.0	0.0	53.0	0.0

* Correction: + 4 minutes, slope + 1.9

Evaluation of kinetic data points for solvolysis of 1-halogeno-2-amine adamantanes using kinetic model for parallel reaction.

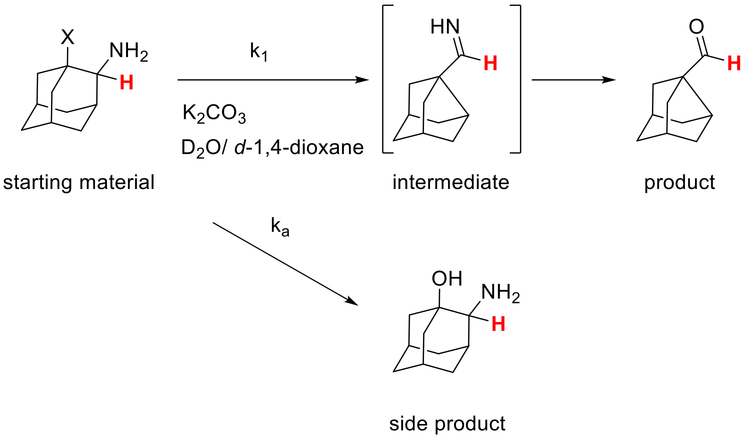


Figure 1 Kinetic model for solvolysis of 1-halogeno-2-amine adamantanes used; X= I, Br and Cl.

1-Halogen 2-amine adamantanes decompose in alkali aqueous solution to form imine as the main product and alcohol as a side product (Fig. 1). The imine product hydrolyses to an aldehyde. Kinetics of formation of the main product was evaluated accordingly to monomolecular model for parallel reaction using Eqs. 1-7. Concentration of product was taken as the sum of conc. of imine plus conc. of aldehyde. Experimental data points and regression curves for 1-iodo-2-amine adamantane solvolysis at 50 °C and the initial concentration of starting material equals to 53 mg/L = $a_0 = [starting\ material] + [product] + [side\ product]$ are exampled in Fig. 2. Calculated apparent rate constants are summarised in Tab. 1 for several temperatures. The chlorine derivative reacted slowly at 60 °C so that its rate constants at 50 °C in Tab. 1 were extrapolated using experimental data measured at 60, 70 and 80 °C and Arrhenius equation.

$$-\frac{d[product]}{dt} = (k_I + k_A)[starting\ material] \tag{1}$$

$$\frac{d[product]}{dt} = k_I[starting\ material] \tag{2}$$

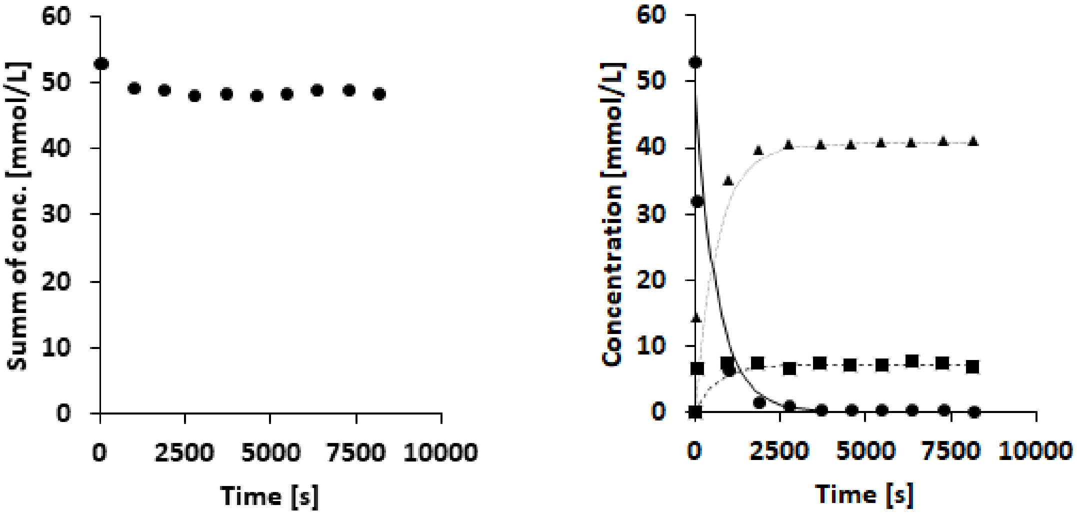
$$\frac{d[side\ product]}{dt} = k_A[starting\ material] \tag{3}$$

$$\sum k = k_I + k_A \tag{4}$$

$$[starting\ material] = a_0 e^{-(\sum k)t} \tag{5}$$

$$[starting\ material] = \frac{k_I a_0}{\sum k}\left(e^{-(\sum k)t} + 1\right) \tag{6}$$

$$[side\ product] = \frac{k_A a_0}{\sum k}\left(e^{-(\sum k)t} + 1\right) \tag{7}$$



a) b)

Figure 2 Kinetic data for solvolysis of 1-iodo-2-amine adamantane at 50 °C: a) Dependence of sum of concentrations $a_0 = [starting\ material] + [product] + [side\ product]$ in time; b) Data points and regression curves of time dependence of concentrations of starting material, product and side product.

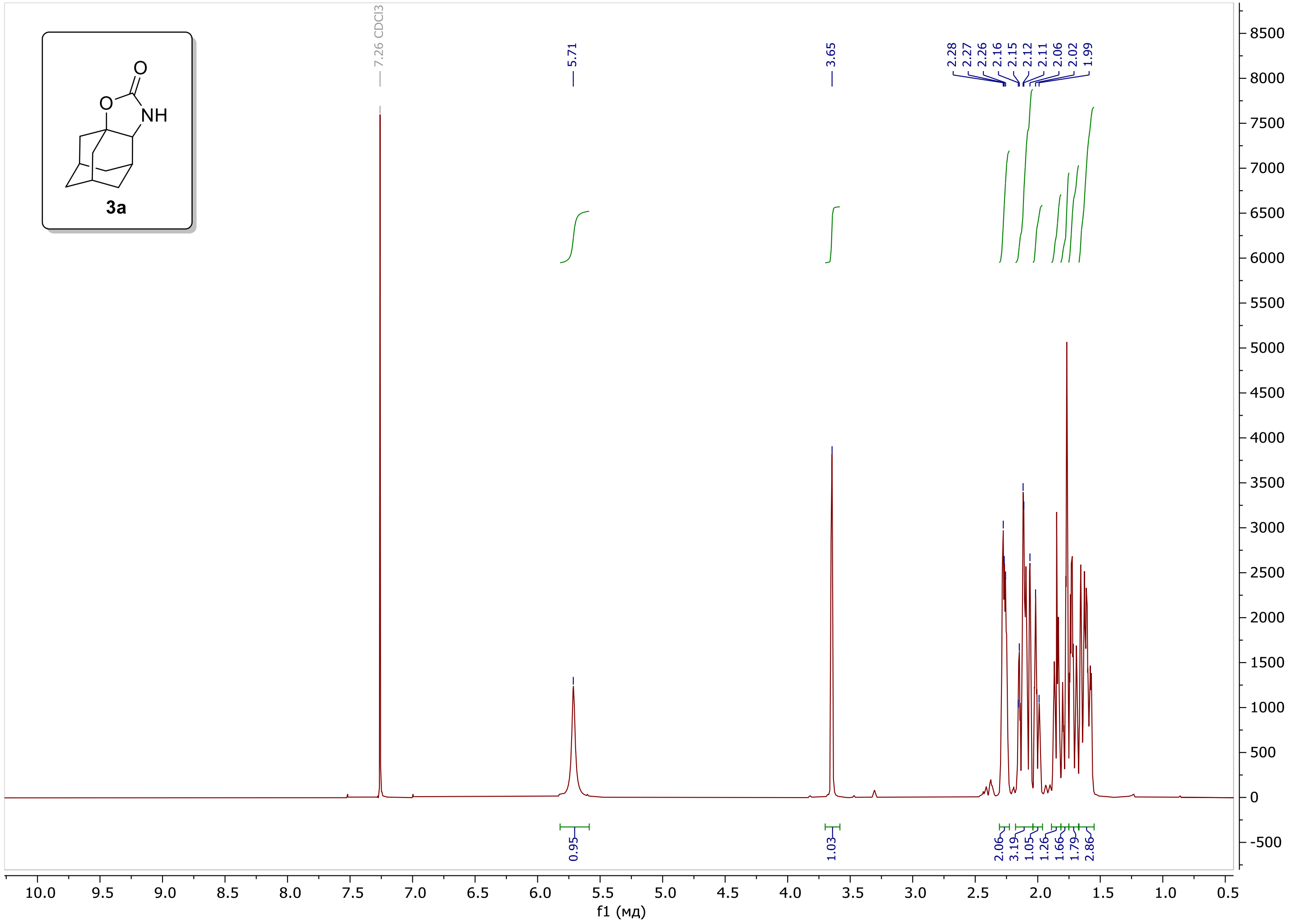
Table 1 Apparent first order kinetic constants of solvolysis of 1-halogeno-2-amino adamantanes.

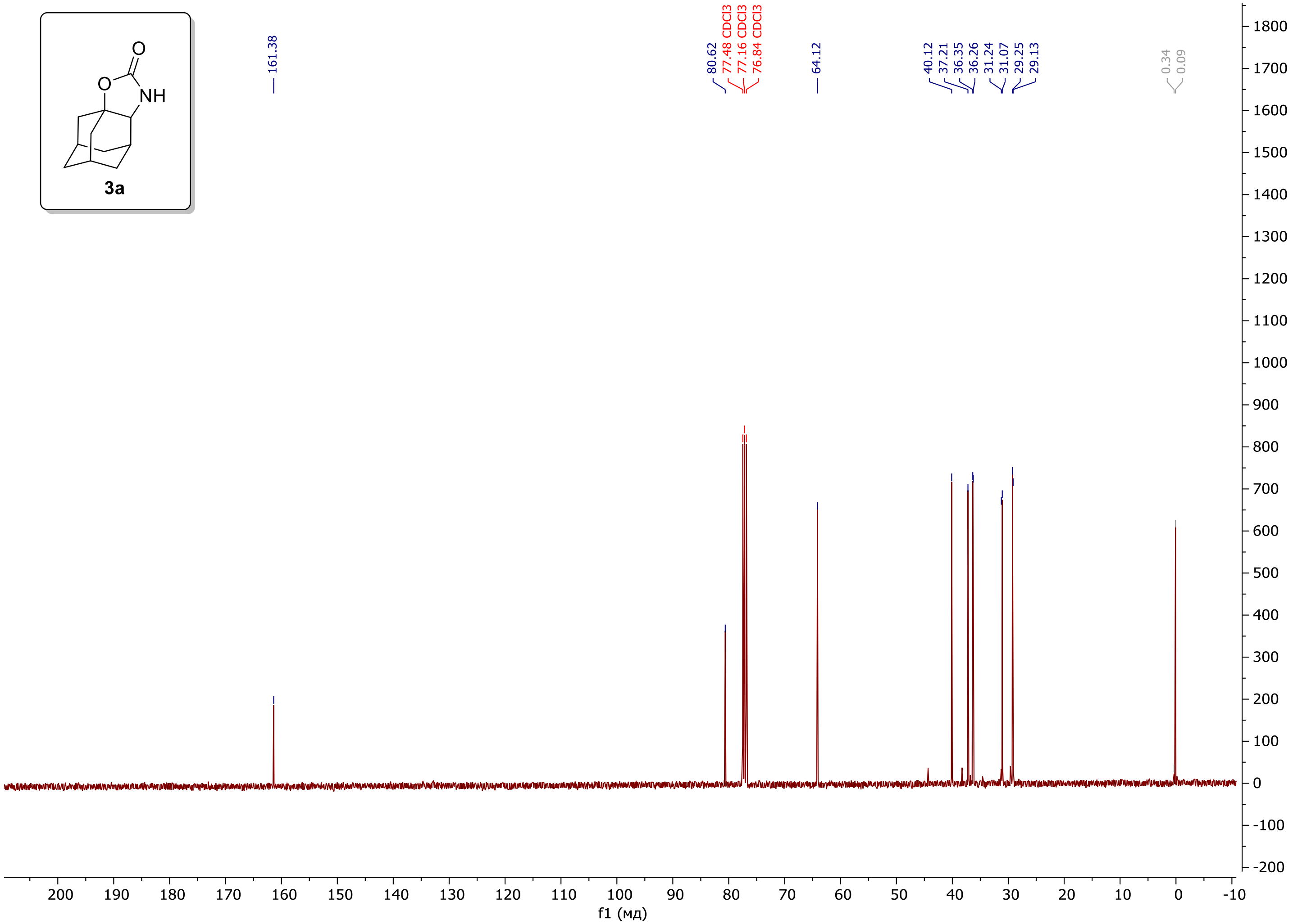
	X = I			X = Br			X = Cl		
Temp.	Σk	k_1	k_A	Σk	k_1	k_A	Σk	k_1	k_A
[°C]		$\times 10^{-5}$ [1/s]			$\times 10^{-5}$ [1/s]			$\times 10^{-5}$ [1/s]	
25	13	8.0	5.0						
40	60	43	17	40	27	13			
50	150	130	23	150	125	21	4.0	3.0	1.0
60							10	7.0	2.0
70							38	31	7.0
80				300	270	30	70	55	15

Apparent first order kinetic constants estimated for solvolysis of 1-halogeno-2-amine adamantanes to the main product at 50 °C are within the range: $k_1 = (130 \pm 20) \times 10^{-5}\ s^{-1}$ for X = I; $k_1 = (125 \pm 20) \times 10^{-5}\ s^{-1}$ for X = Br; and $k_1 = (3 \pm 0.2) \times 10^{-5}\ s^{-1}$ for X = Cl.

4. NMR spectra of compounds **3-26**

Compound 3a




O
O
NH
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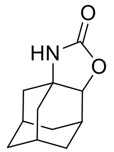
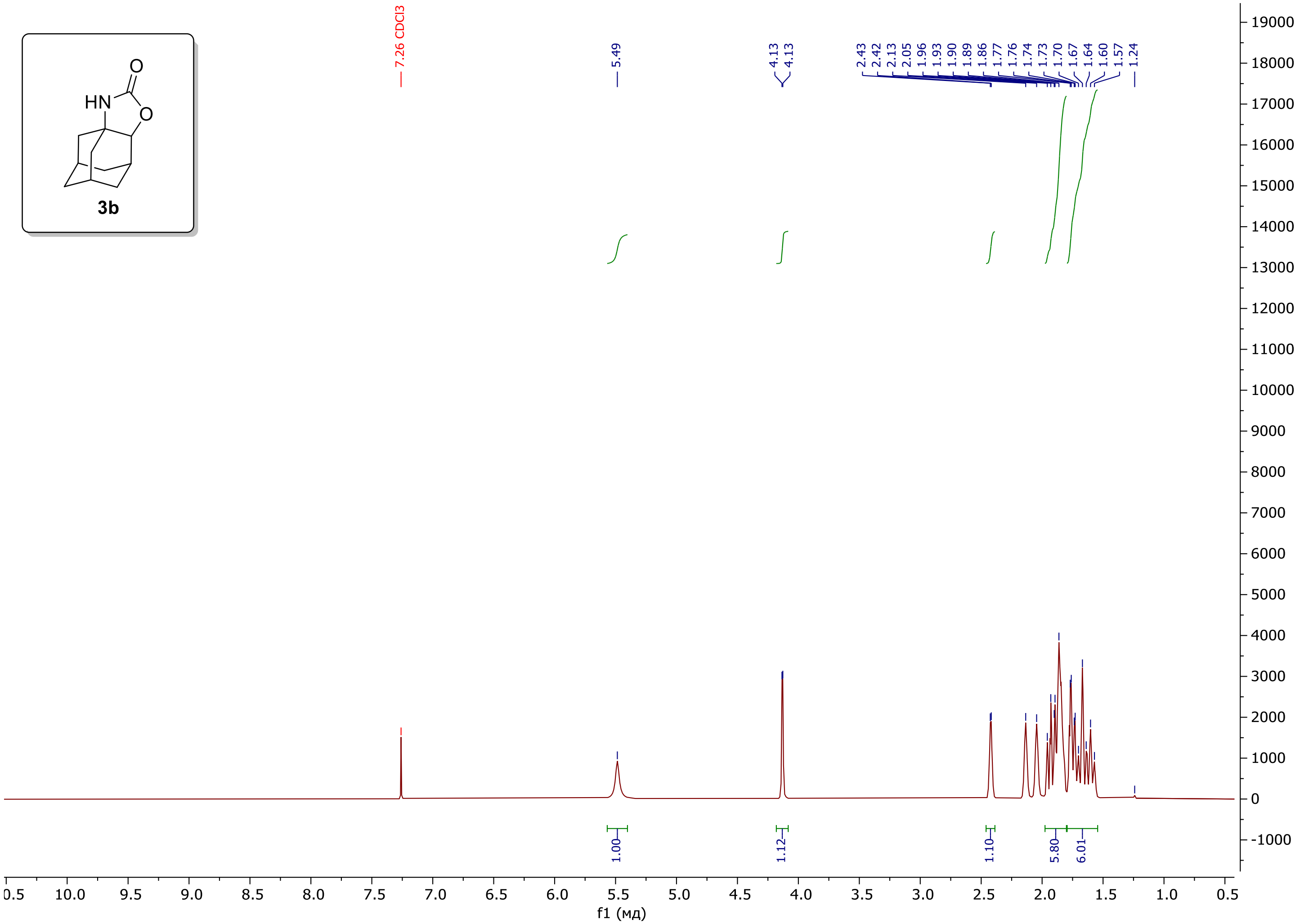
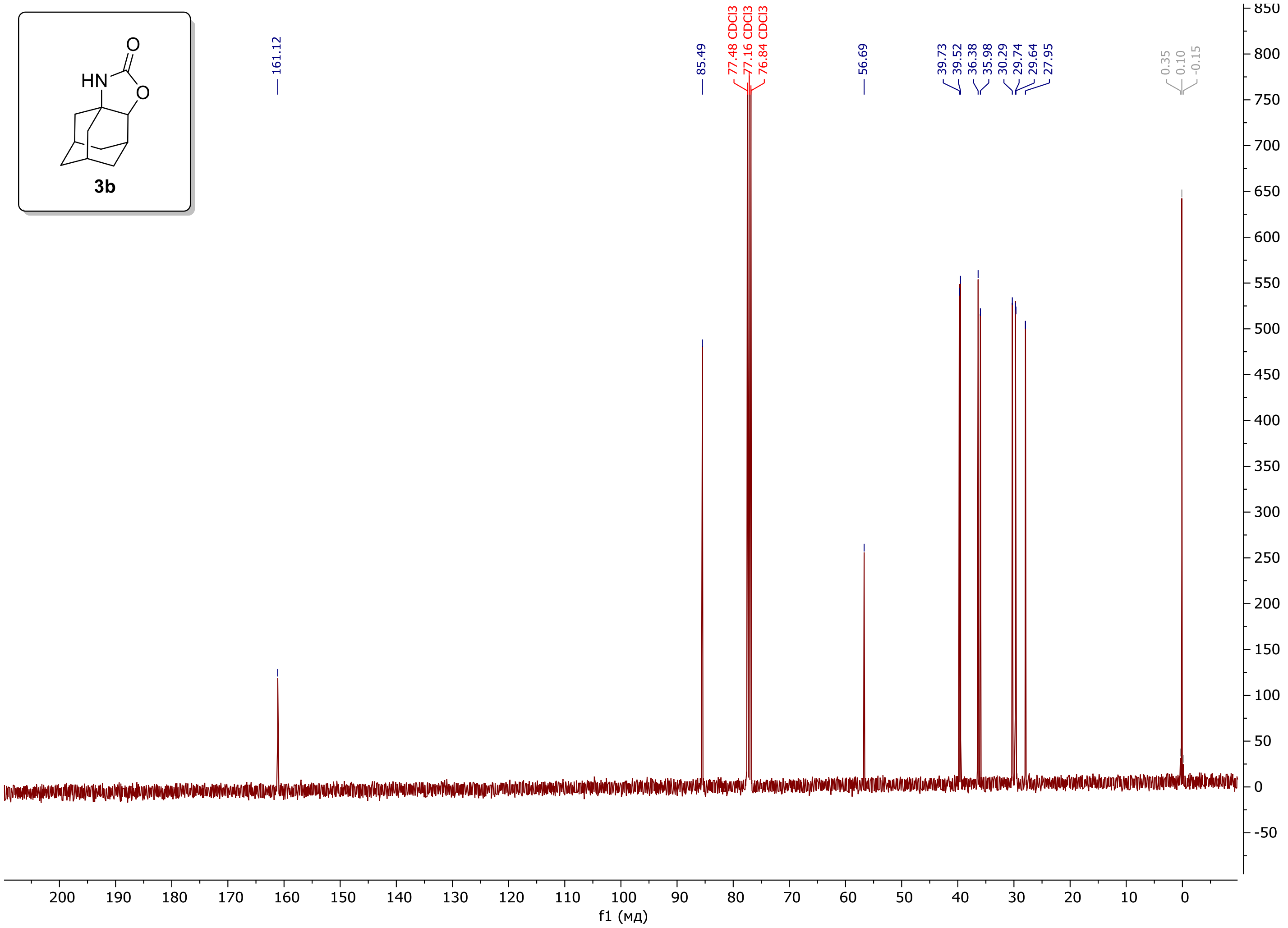
80.62
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
64.12
40.12
37.21
36.35
36.26
31.24
31.07
29.25
29.13
0.34
0.09
1800
1700
1600
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
-200
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (мд)

Compound 3b



3b

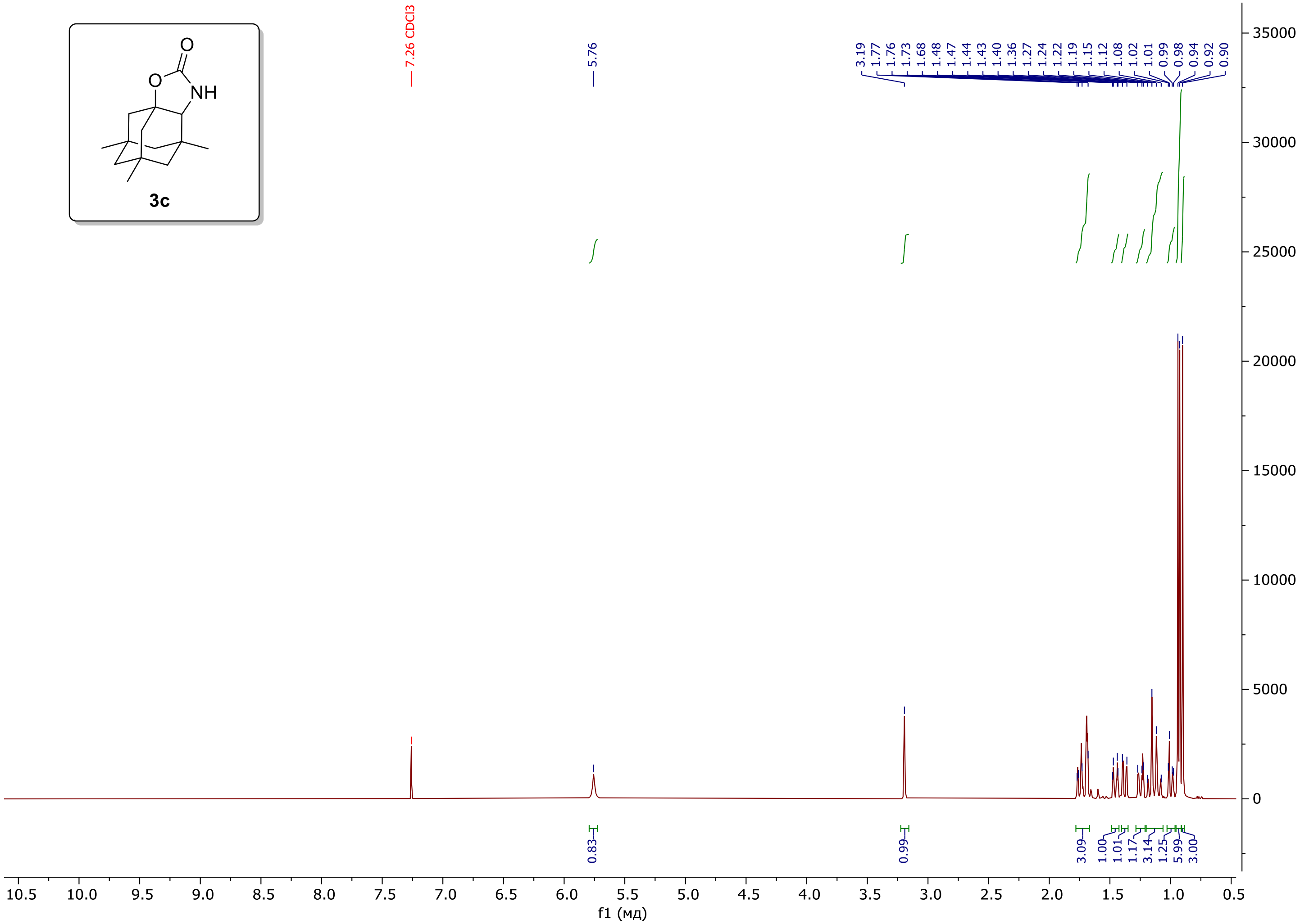


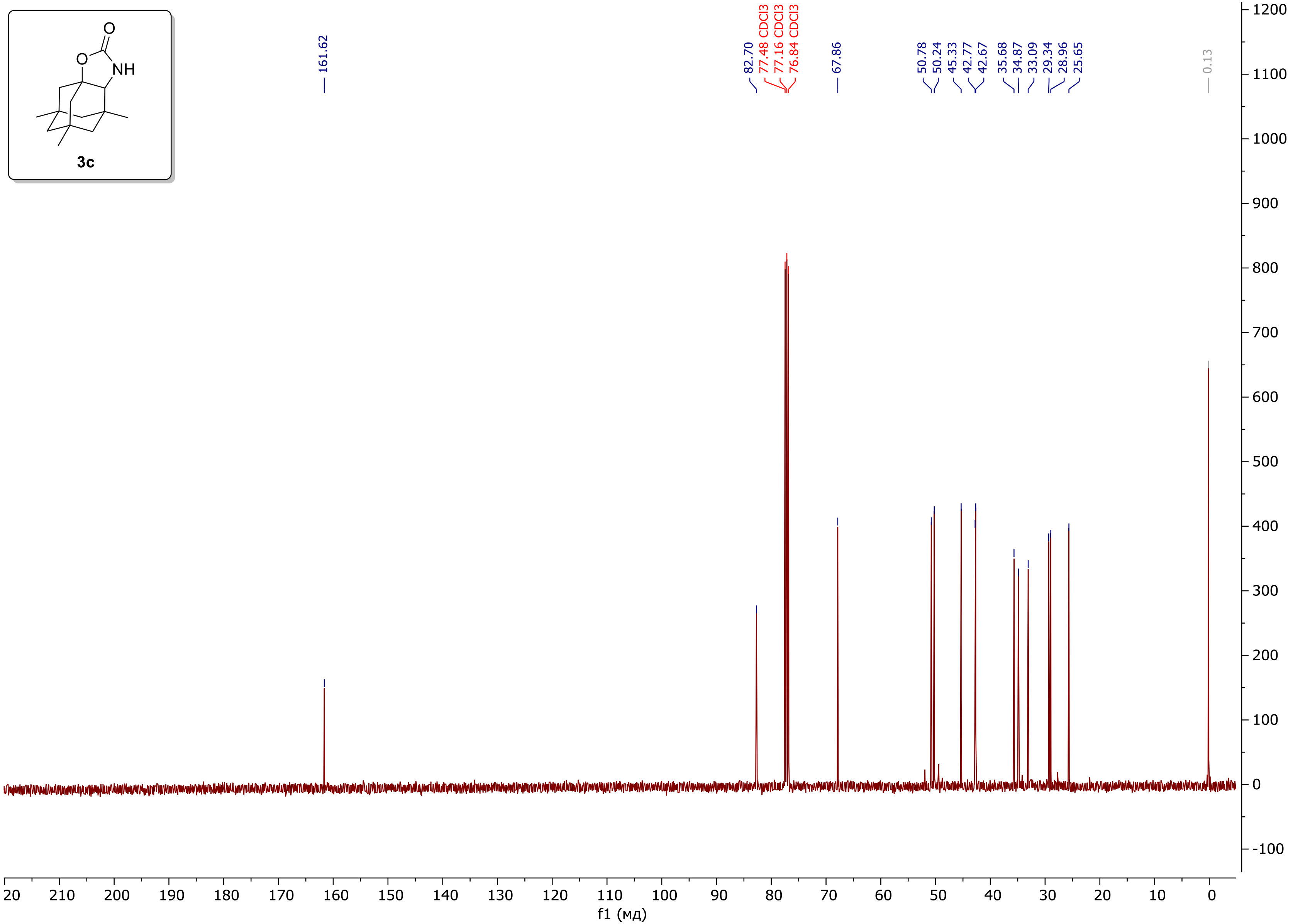


3b
HN
O
O
161.12
85.49
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
56.69
39.73
39.52
36.38
35.98
30.29
29.74
29.64
27.95
0.35
0.10
-0.15
850
800
750
700
650
600
550
500
450
400
350
300
250
200
150
100
50
0
-50
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (мд)

Compound 3c

3c

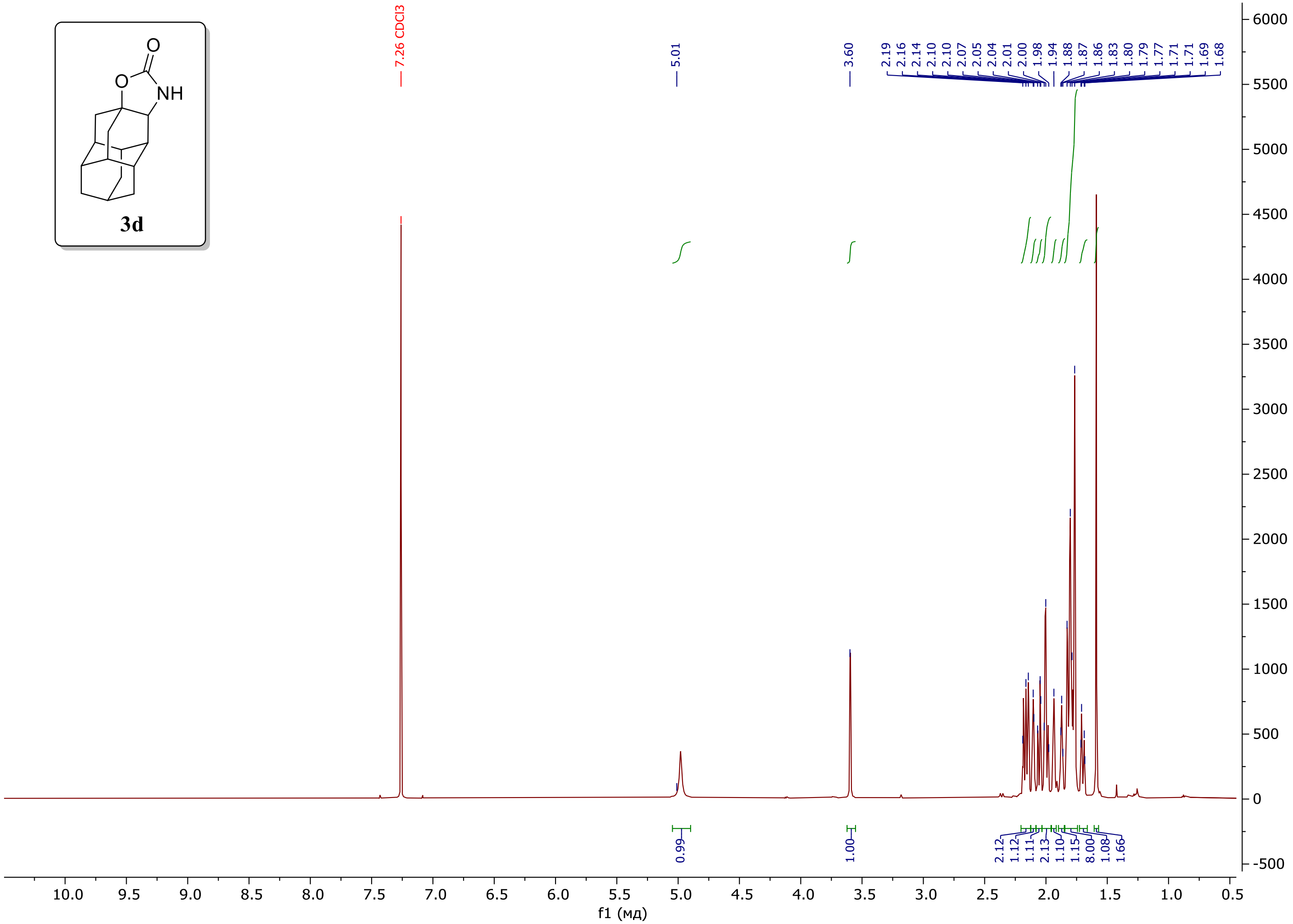


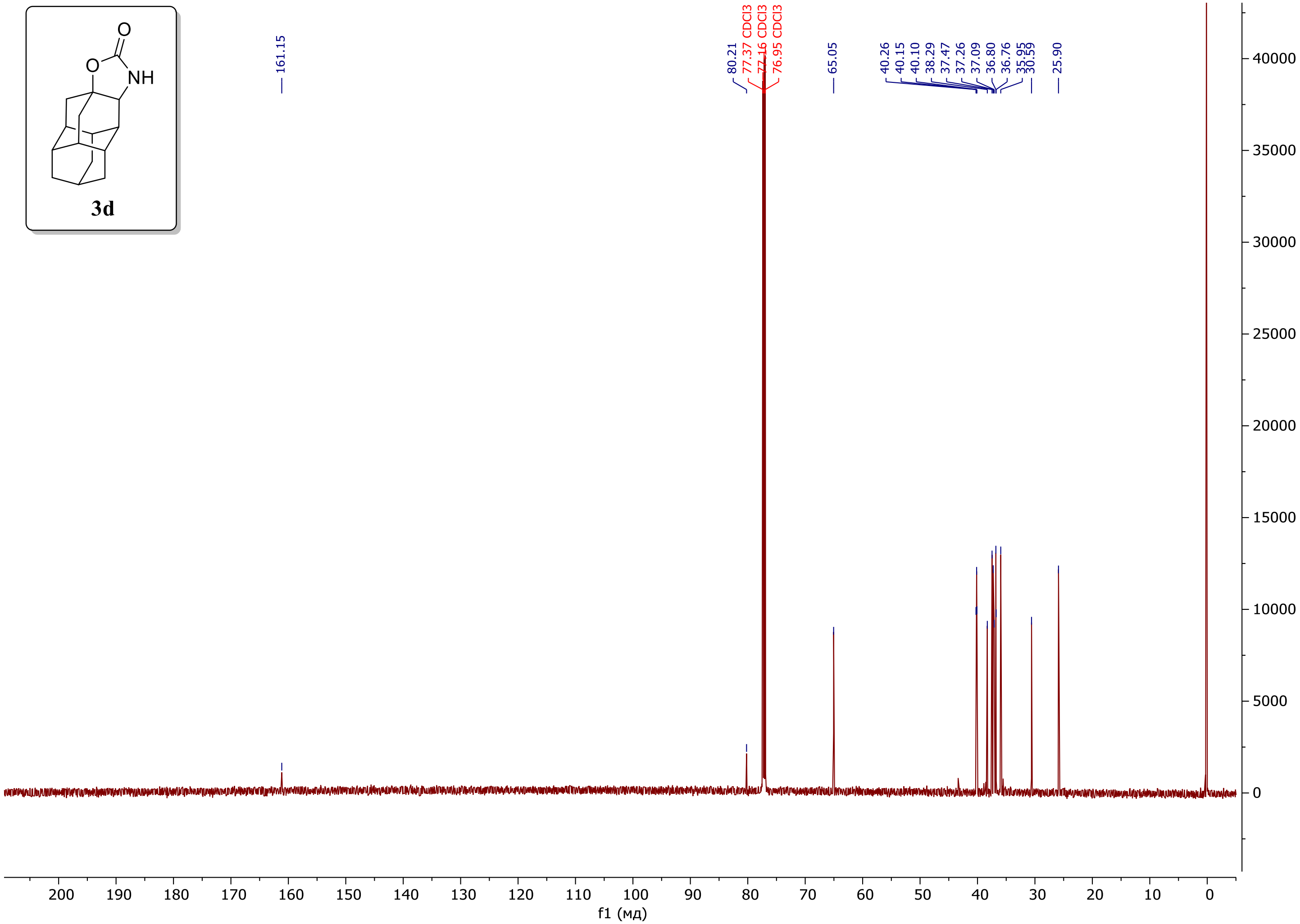


O
O
NH
3c
161.62
82.70
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
67.86
50.78
50.24
45.33
42.77
42.67
35.68
34.87
33.09
29.34
28.96
25.65
0.13
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
20
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (мд)

Compound 3d

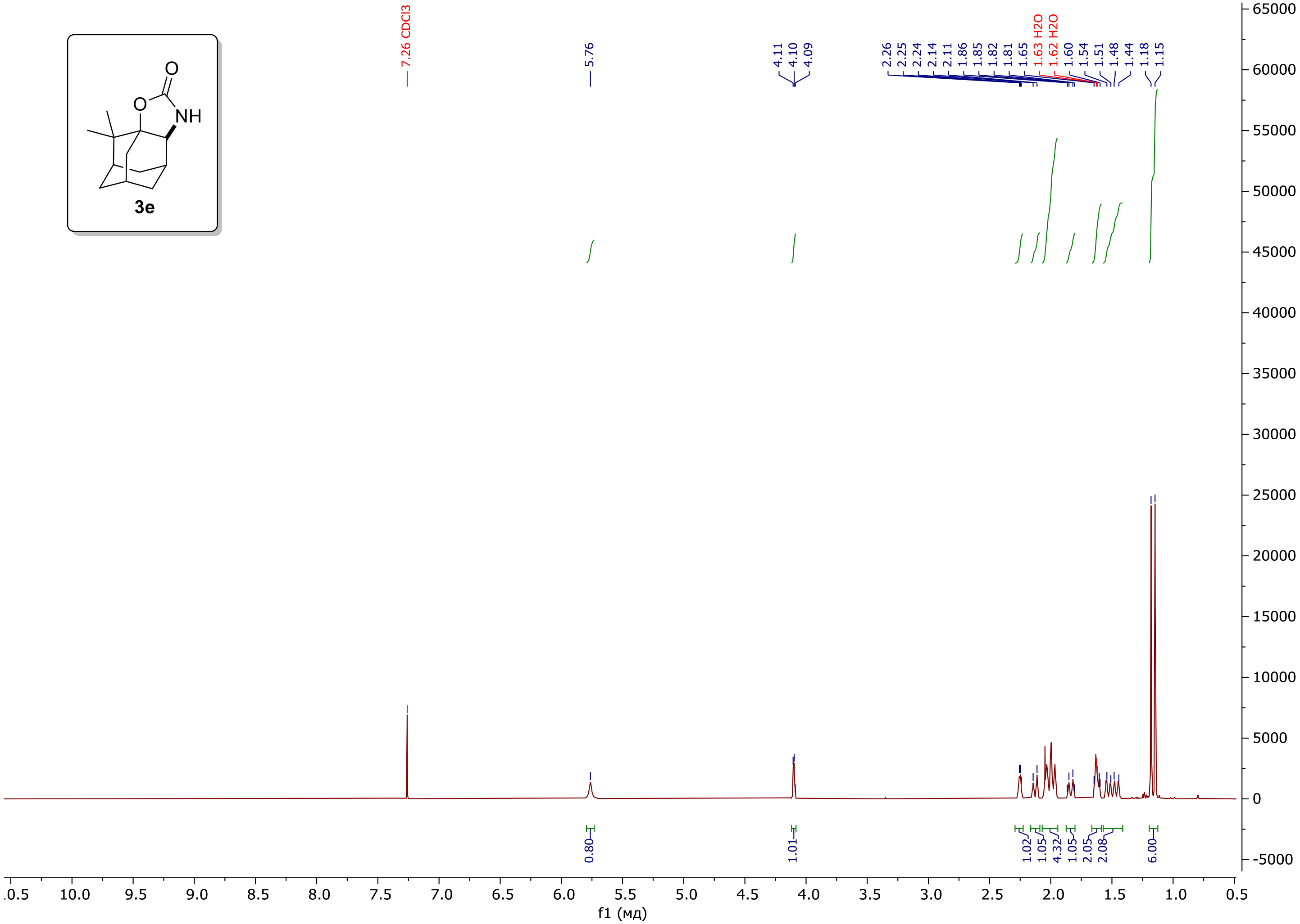
3d




3d
O
O
NH
161.15
80.21
77.37 CDCl3
77.16 CDCl3
76.95 CDCl3
65.05
40.26
40.15
40.10
38.29
37.47
37.26
37.09
36.80
36.76
35.95
30.59
25.90
40000
35000
30000
25000
20000
15000
10000
5000
0
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (мд)

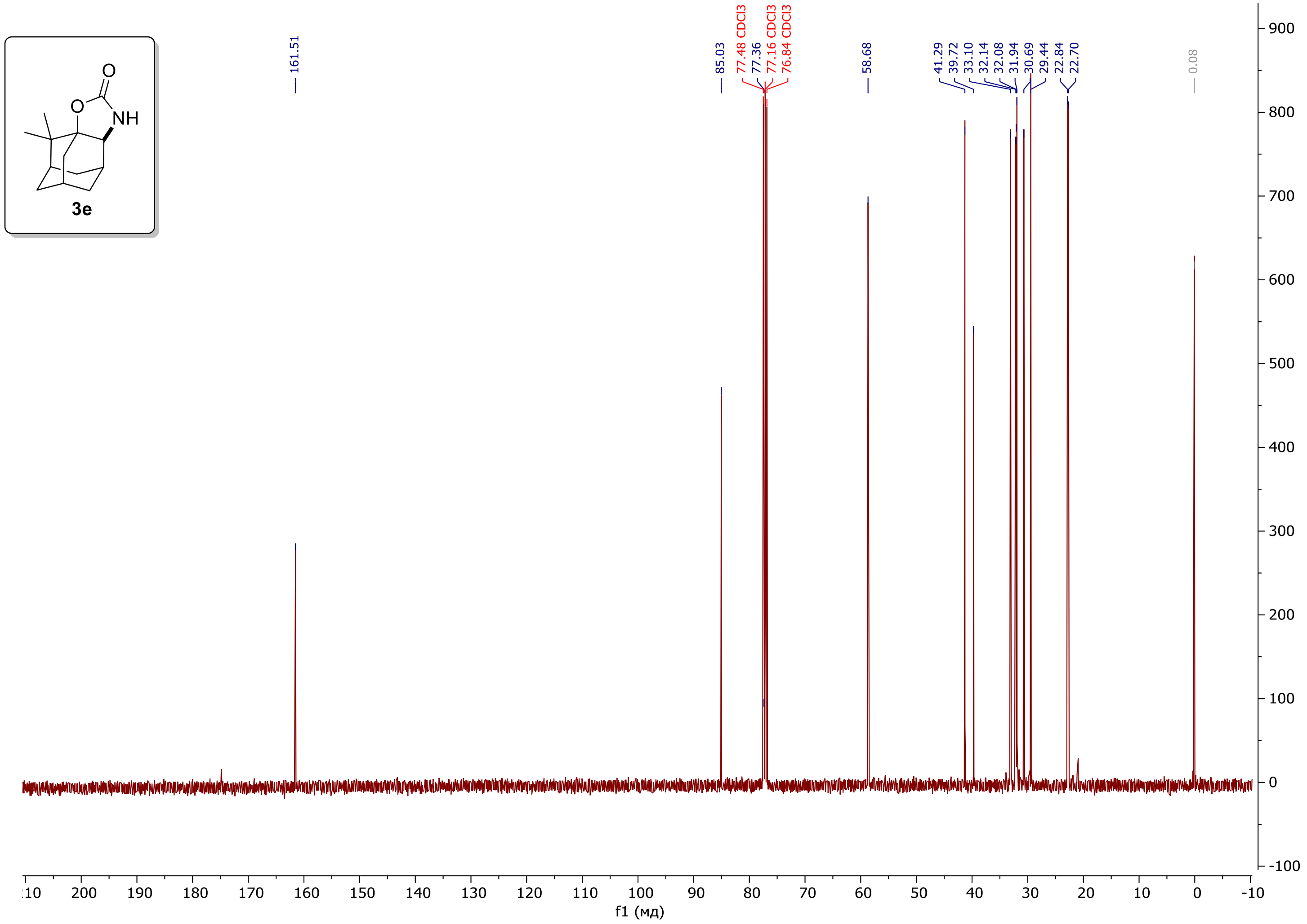
Compound 3e

3e



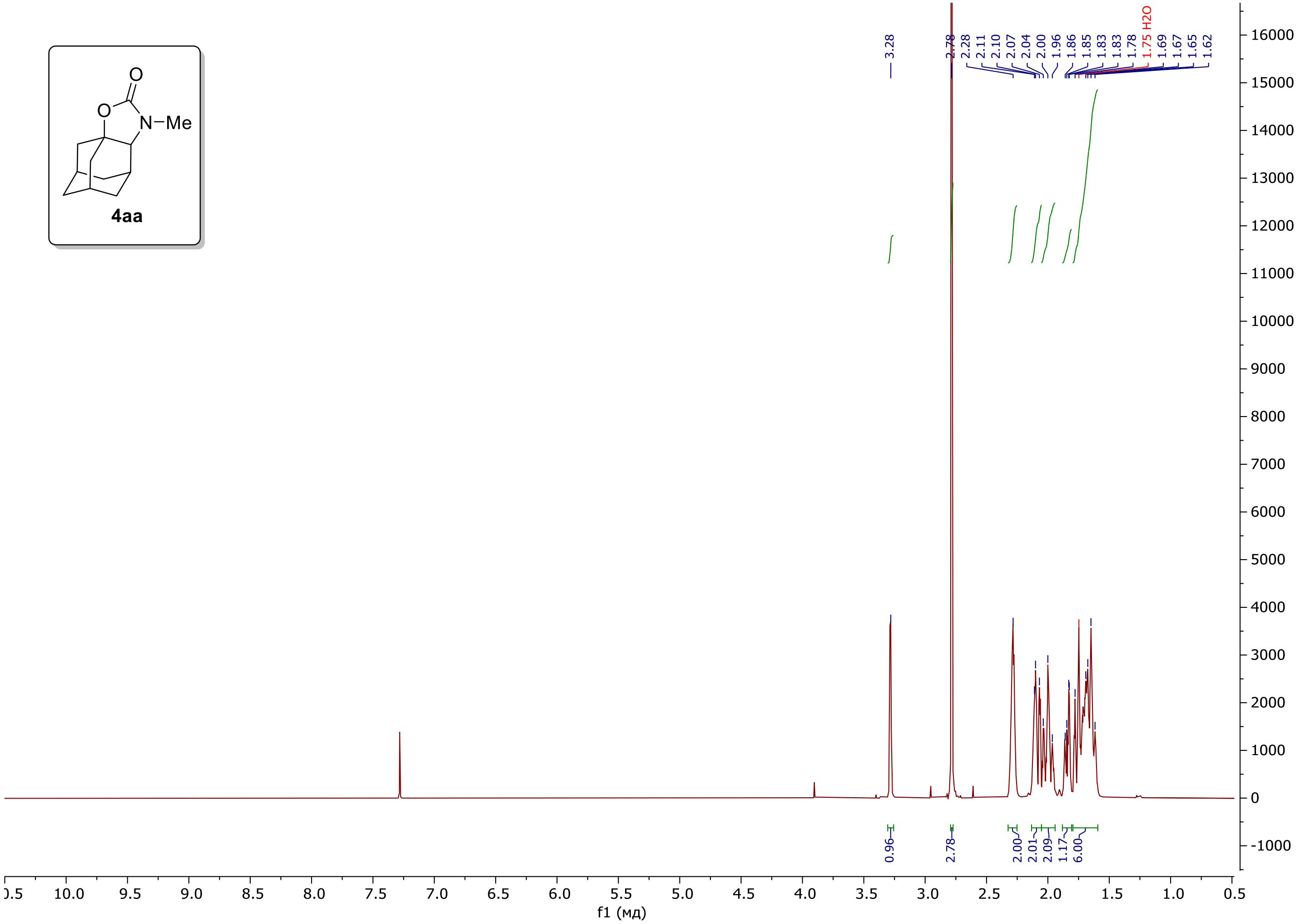
O
O
NH

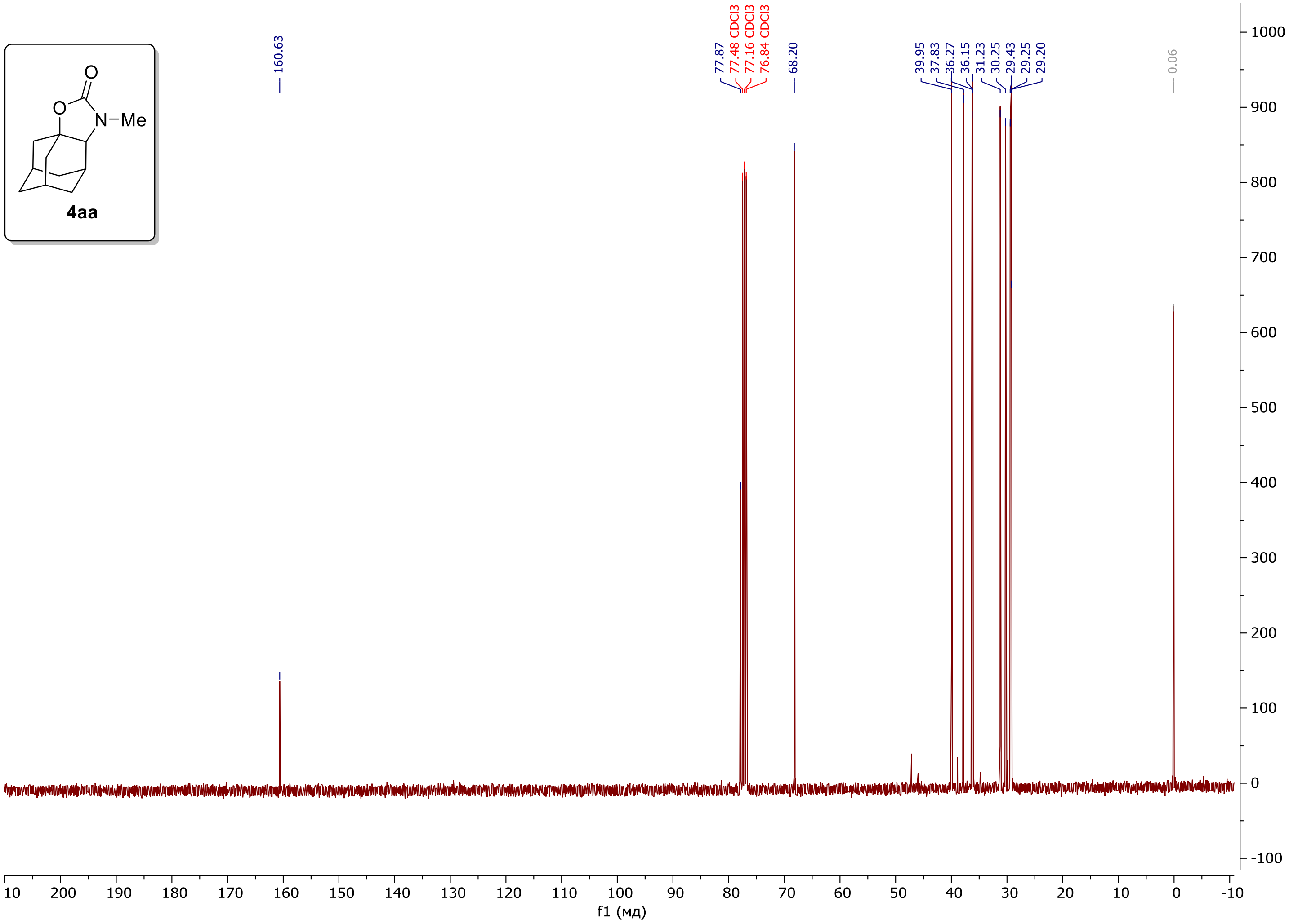
3e


161.51
85.03
77.48 CDCl3
77.36
77.16 CDCl3
76.84 CDCl3
58.68
41.29
39.72
33.10
32.14
32.08
31.94
30.69
29.44
22.84
22.70
0.08
900
800
700
600
500
400
300
200
100
0
-100
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (мд)

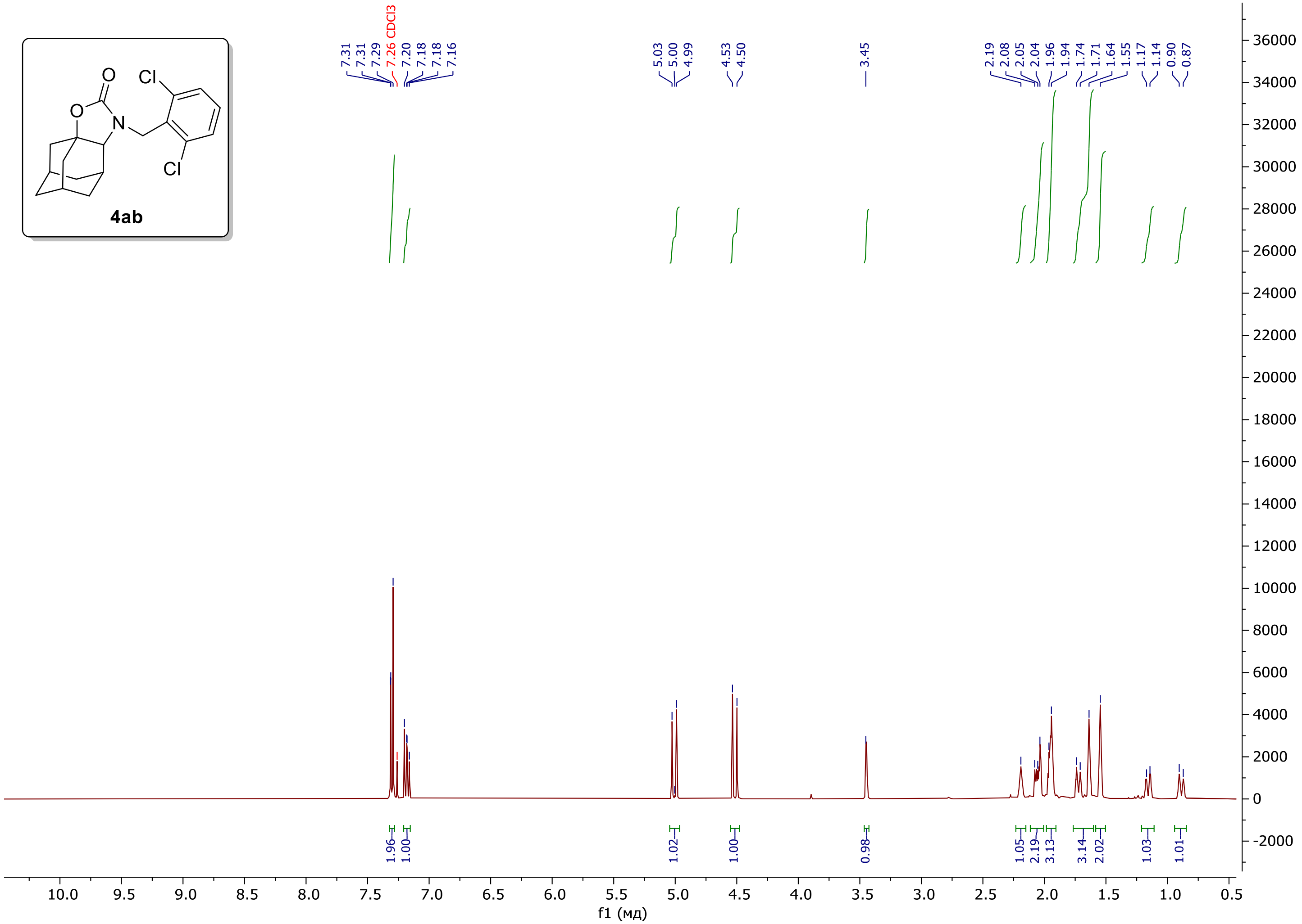
Compound 4aa

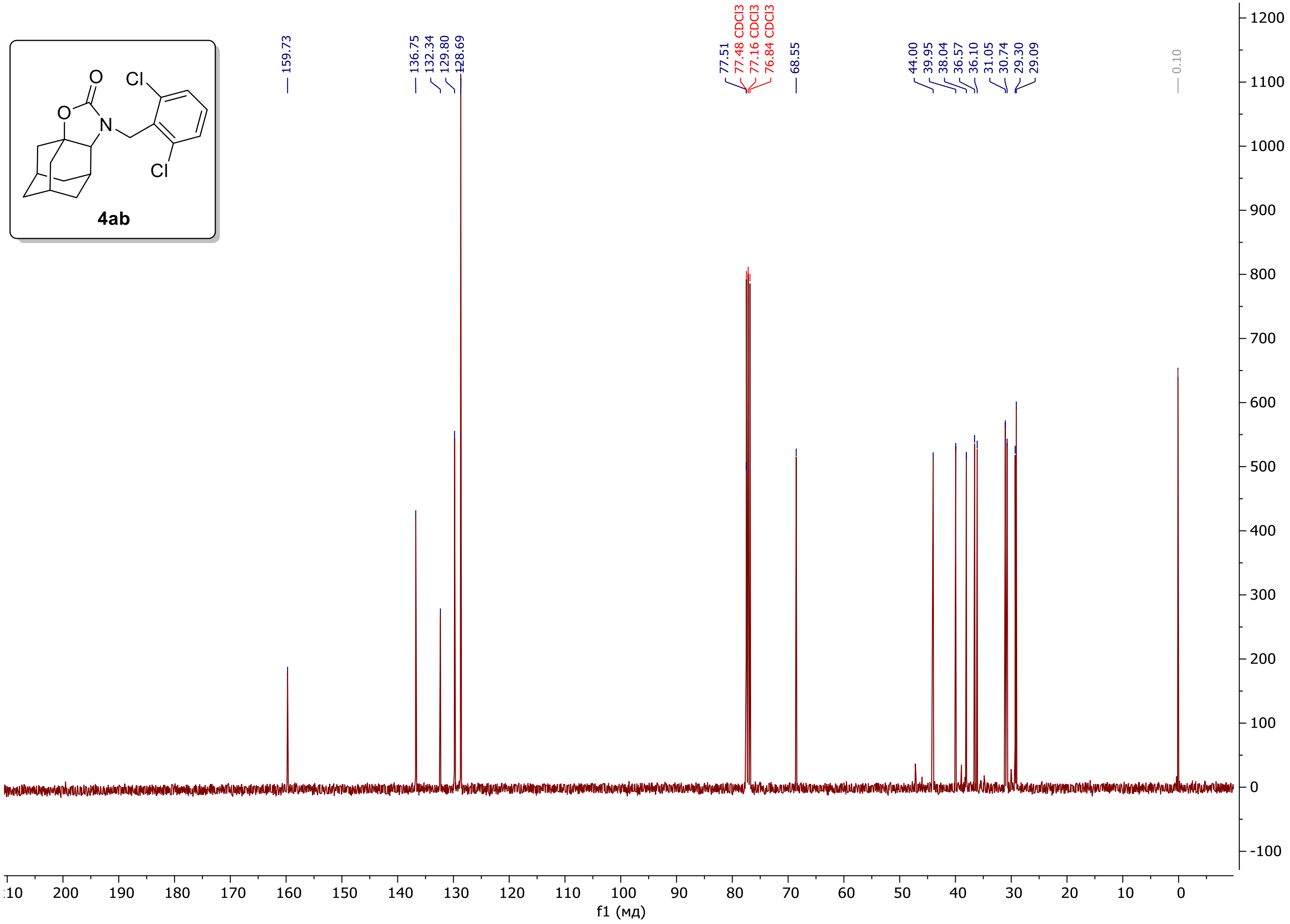
4aa




O
O
N−Me
4aa
160.63
77.87
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
68.20
39.95
37.83
36.27
36.15
31.23
30.25
29.43
29.25
29.20
0.06
1000
900
800
700
600
500
400
300
200
100
0
-100
10
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (мд)

Compound 4ab

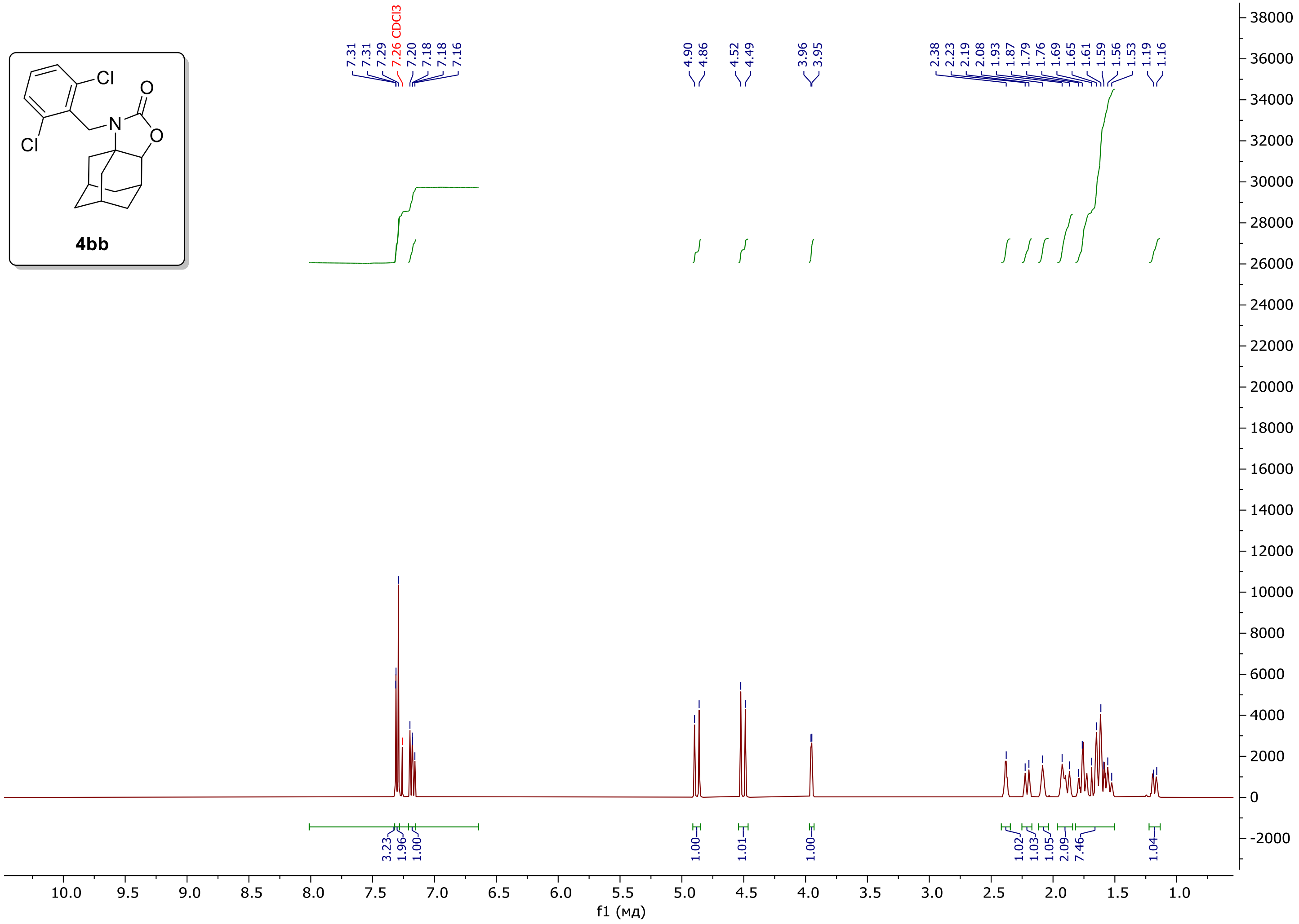


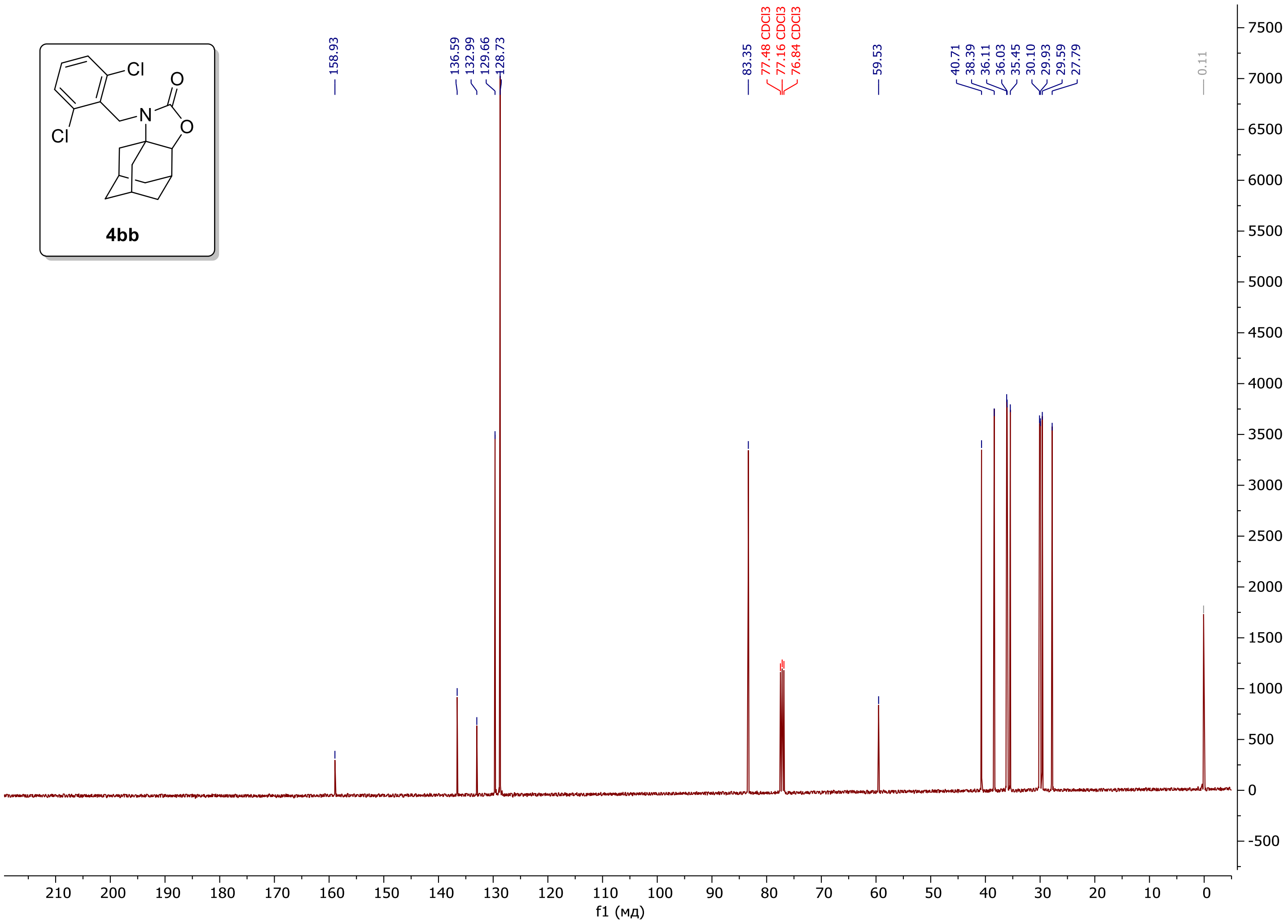

4ab

O
Cl
O
N
Cl
159.73
136.75
132.34
129.80
128.69
77.51
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
68.55
44.00
39.95
38.04
36.57
36.10
31.05
30.74
29.30
29.09
0.10
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (мд)

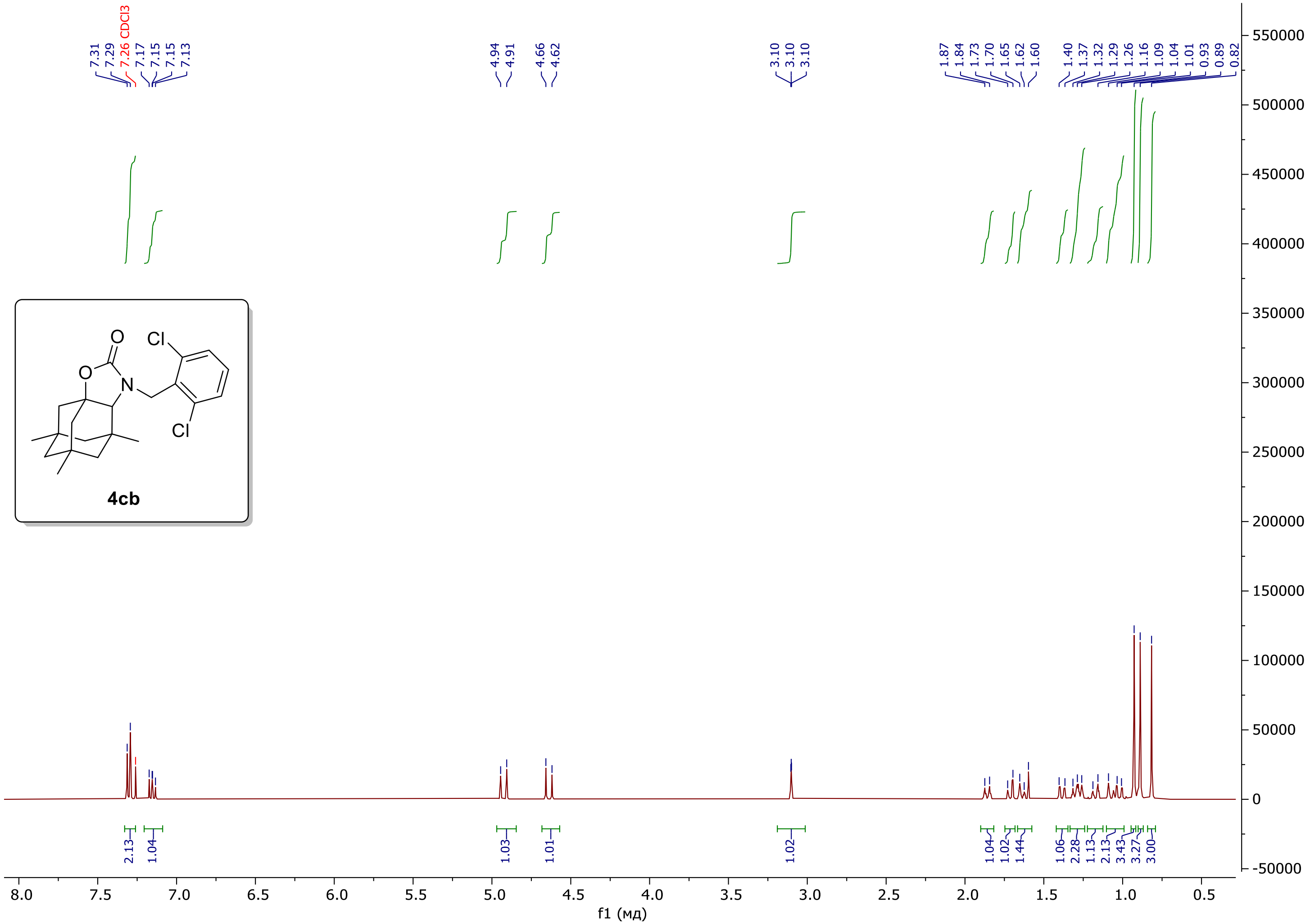
Compound 4bb

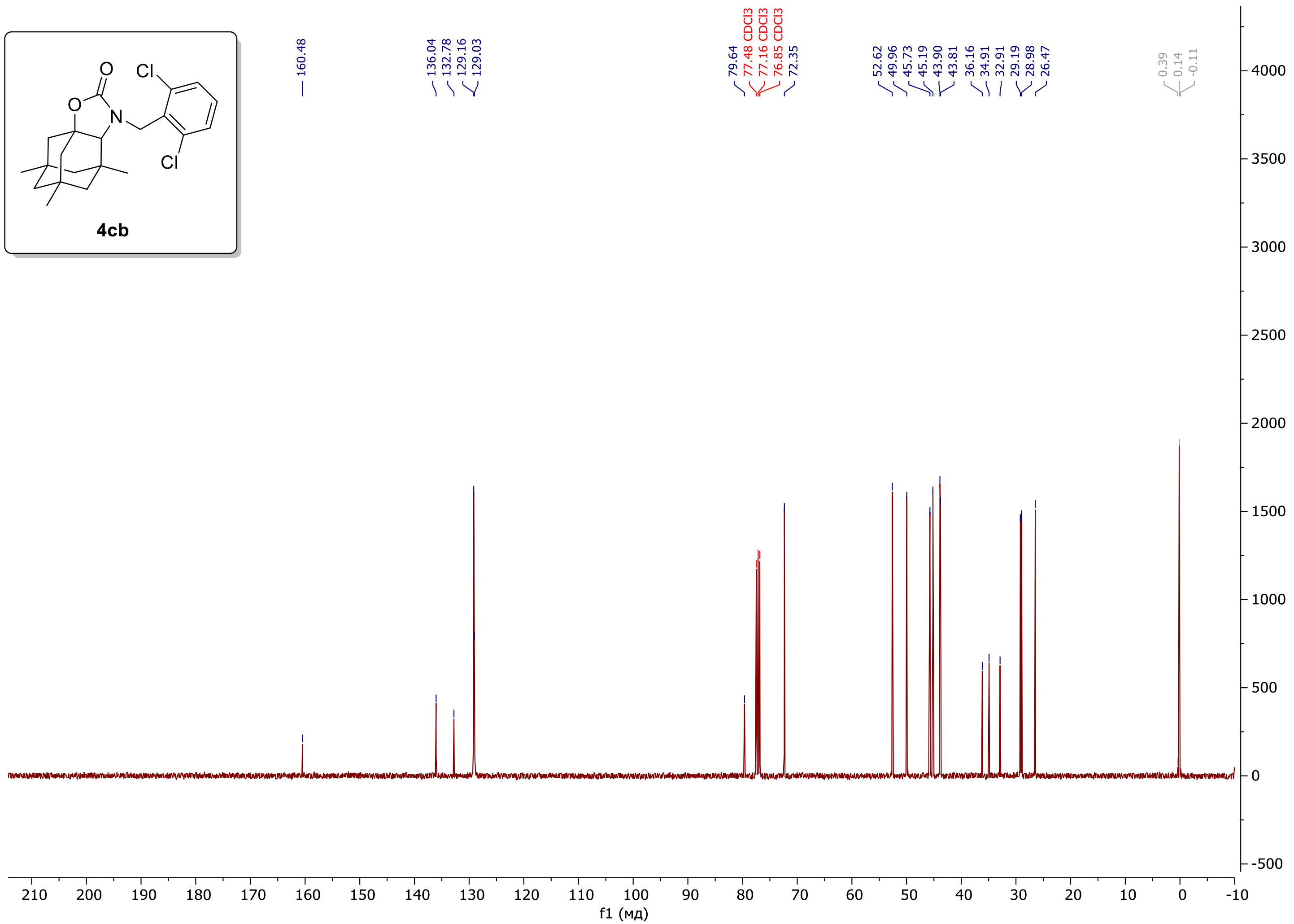
4bb



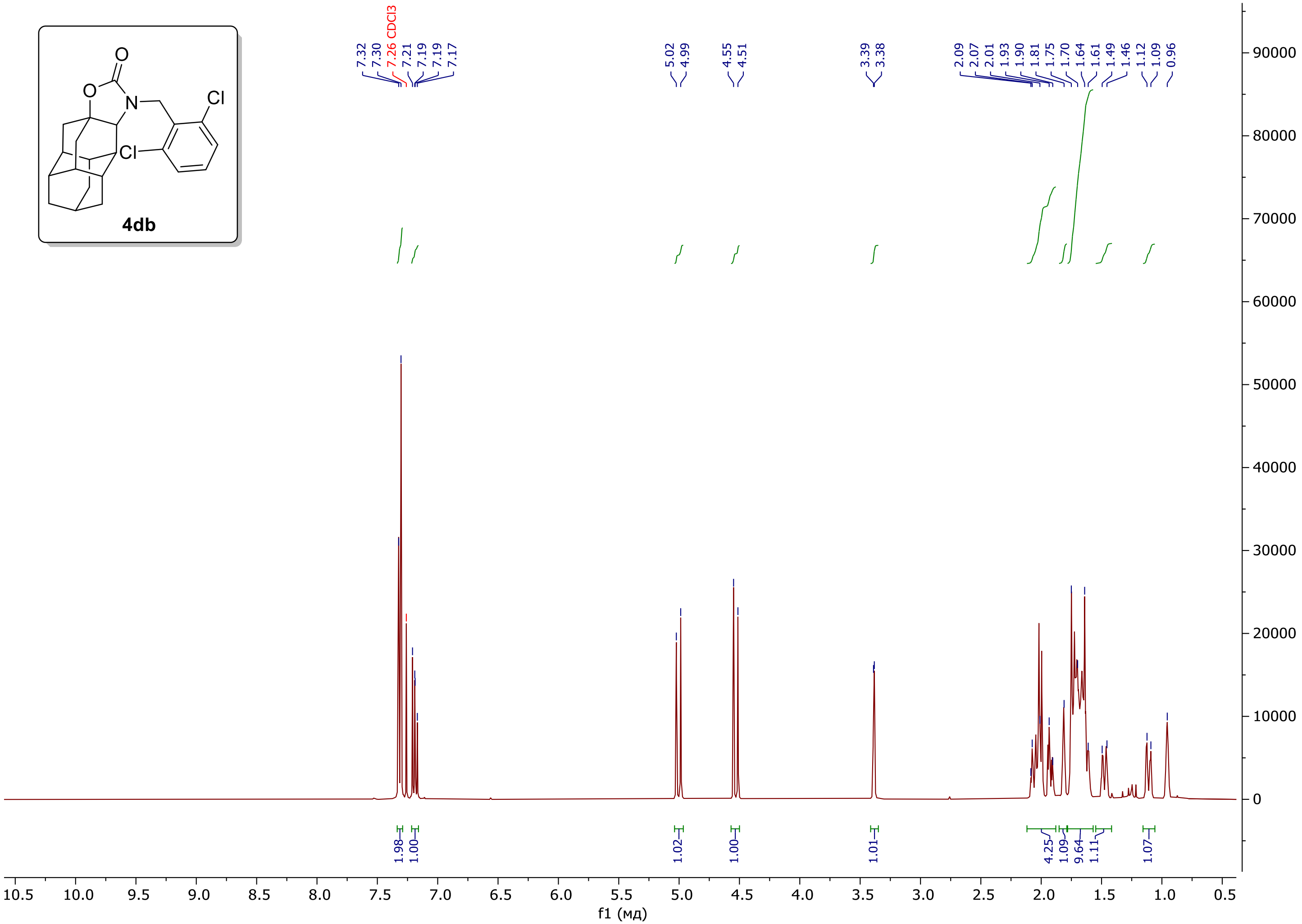

Cl
Cl
N
O
O
4bb
158.93
136.59
132.99
129.66
128.73
83.35
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
59.53
40.71
38.39
36.11
36.03
35.45
30.10
29.93
29.59
27.79
0.11
7500
7000
6500
6000
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
-500
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (мд)

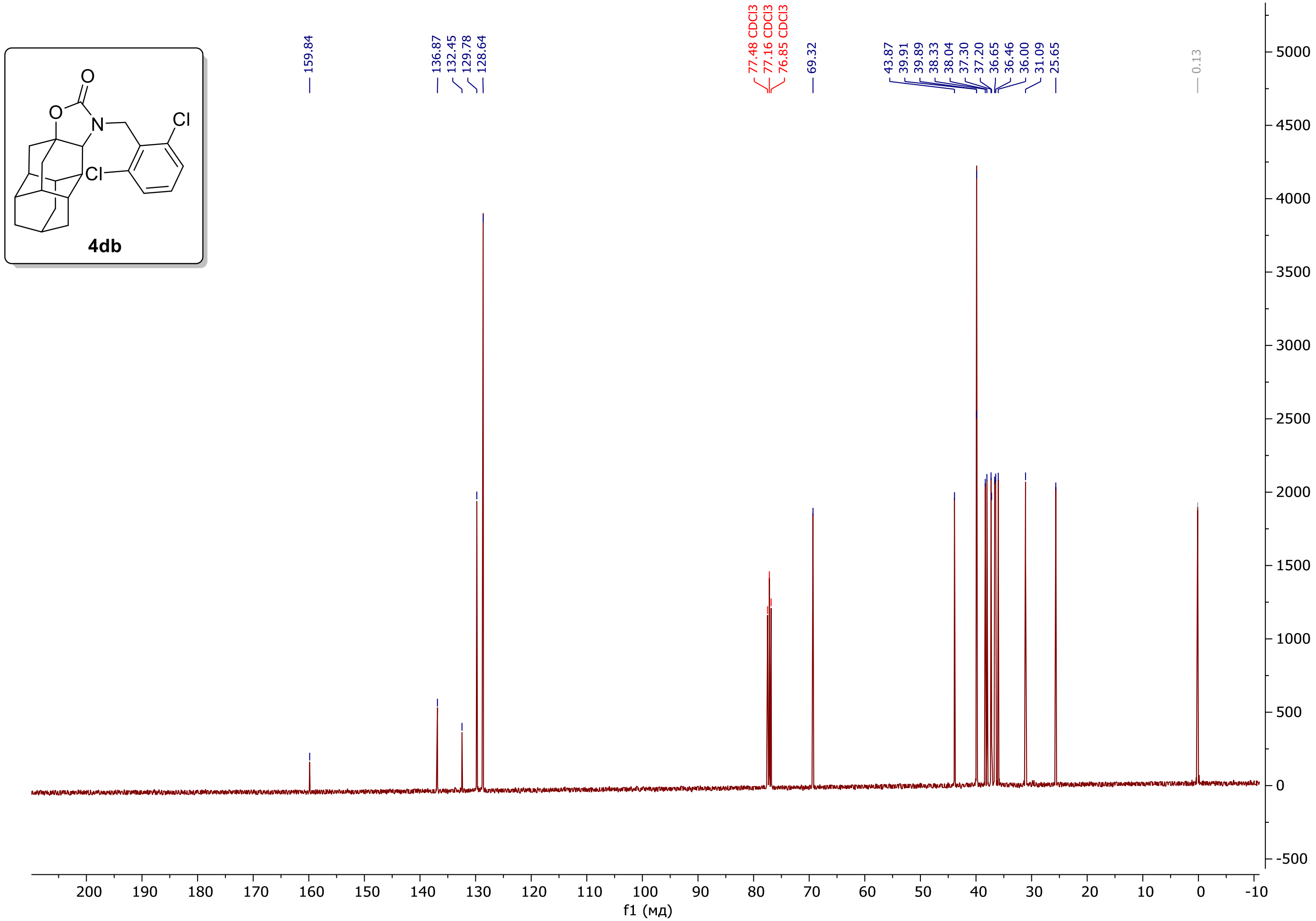
Compound 4cb



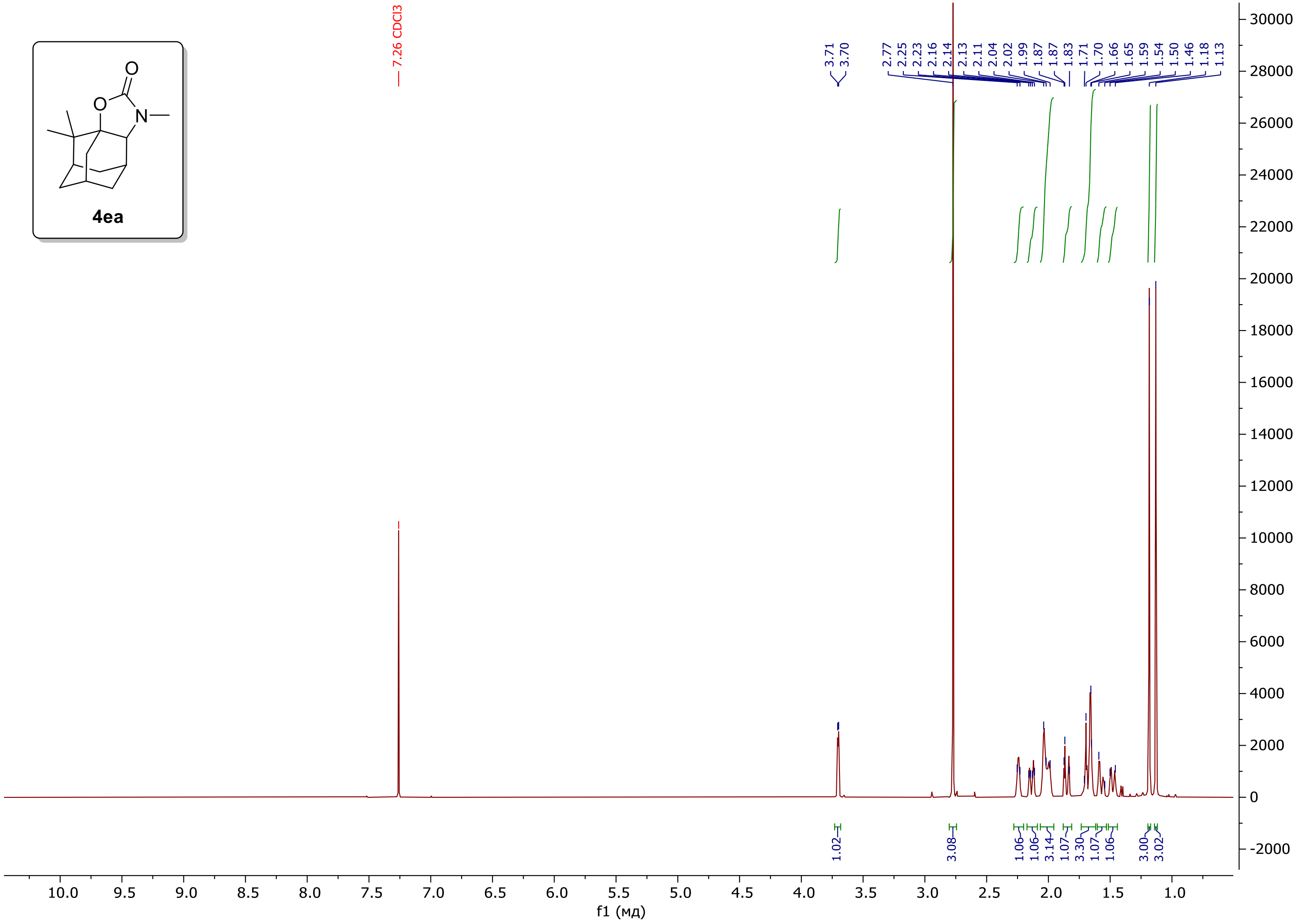

4cb
160.48
136.04
132.78
129.16
129.03
79.64
77.48 CDCl3
77.16 CDCl3
76.85 CDCl3
72.35
52.62
49.96
45.73
45.19
43.90
43.81
36.16
34.91
32.91
29.19
28.98
26.47
0.39
0.14
-0.11
4000
3500
3000
2500
2000
1500
1000
500
0
-500
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (мд)

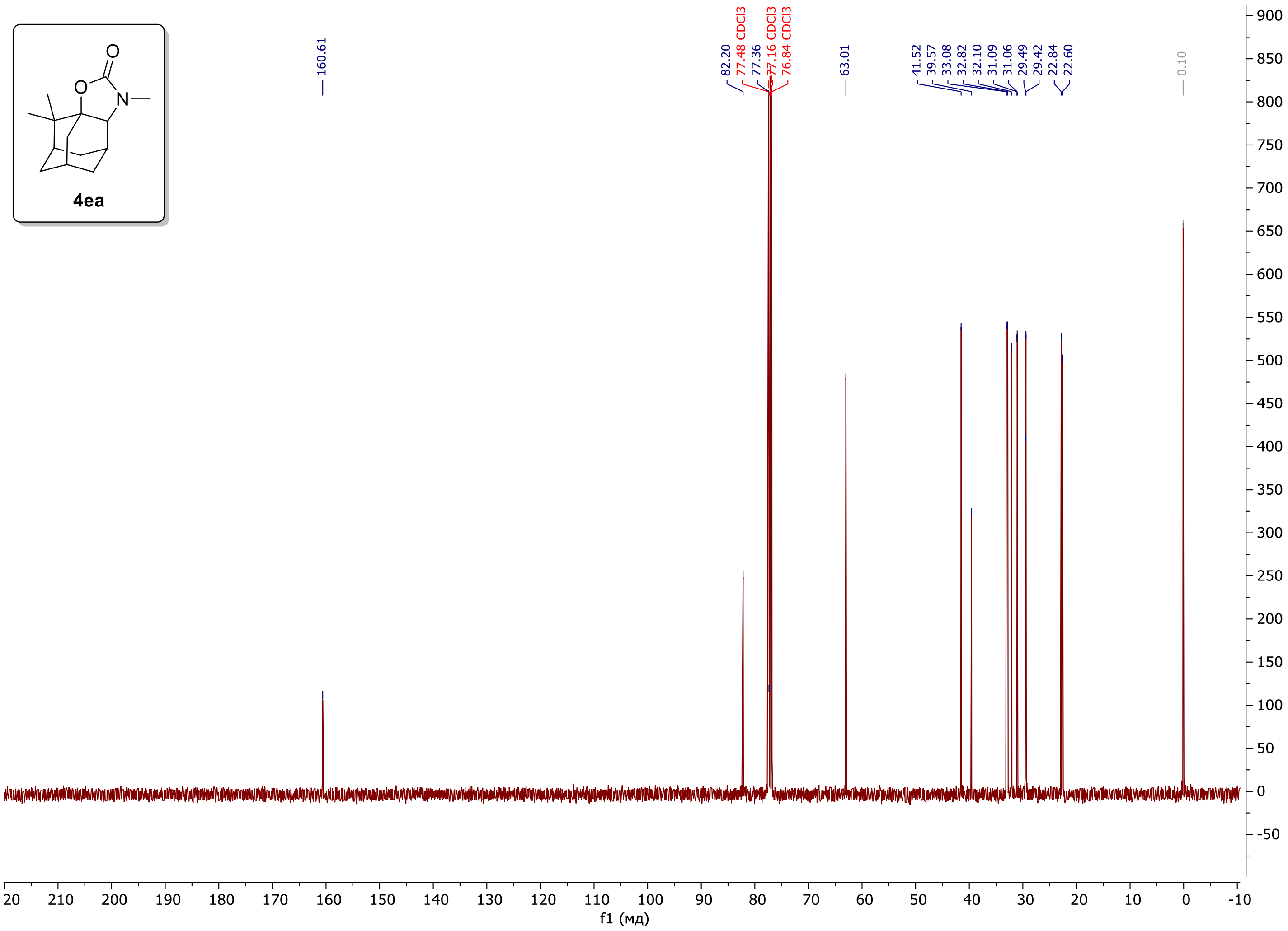
Compound 4db


4db


4db
O
O
N
Cl
Cl
159.84
136.87
132.45
129.78
128.64
77.48 CDCl3
77.16 CDCl3
76.85 CDCl3
69.32
43.87
39.91
39.89
38.33
38.04
37.30
37.20
36.65
36.46
36.00
31.09
25.65
0.13
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
-500
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (мд)

Compound 4ea



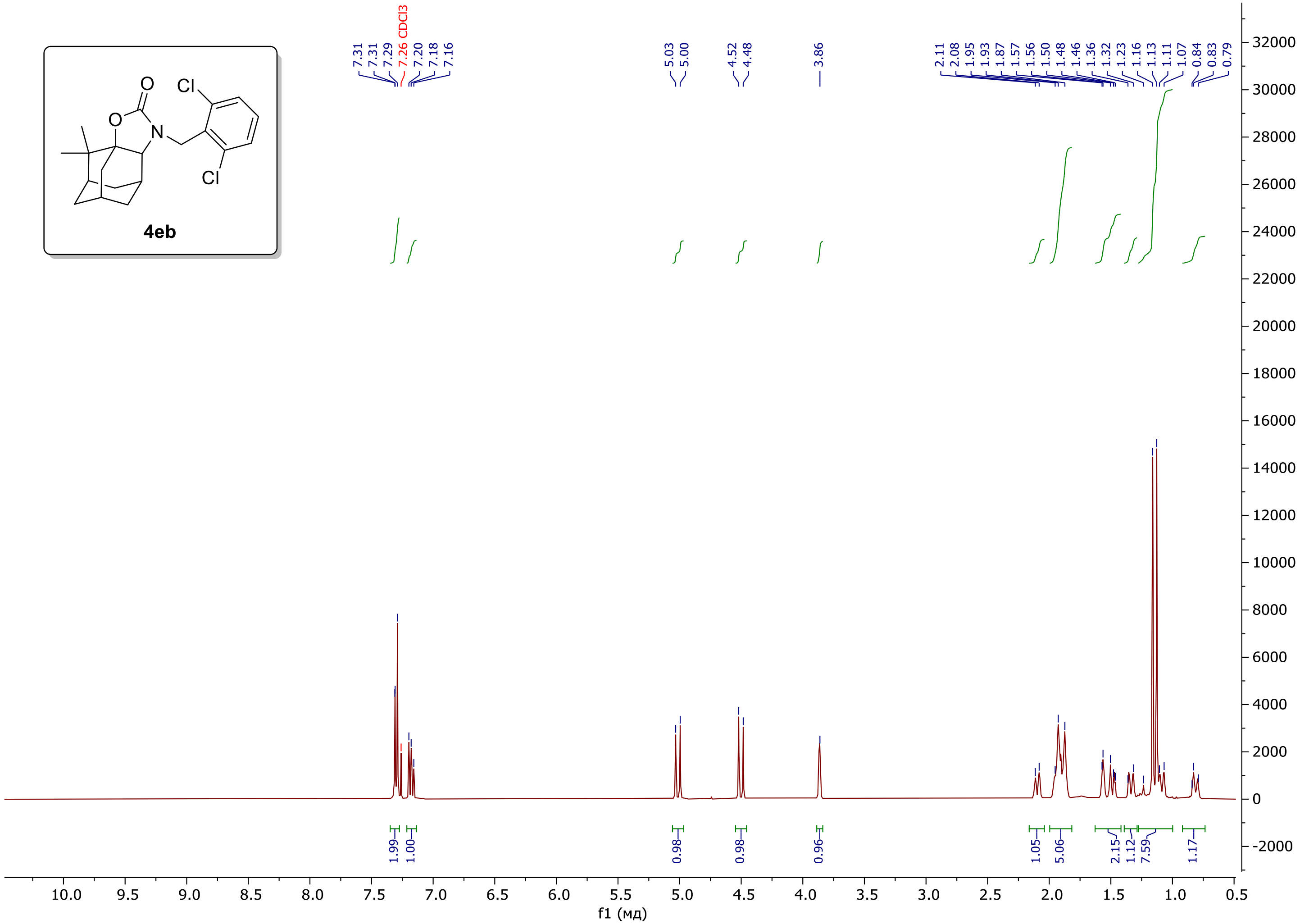


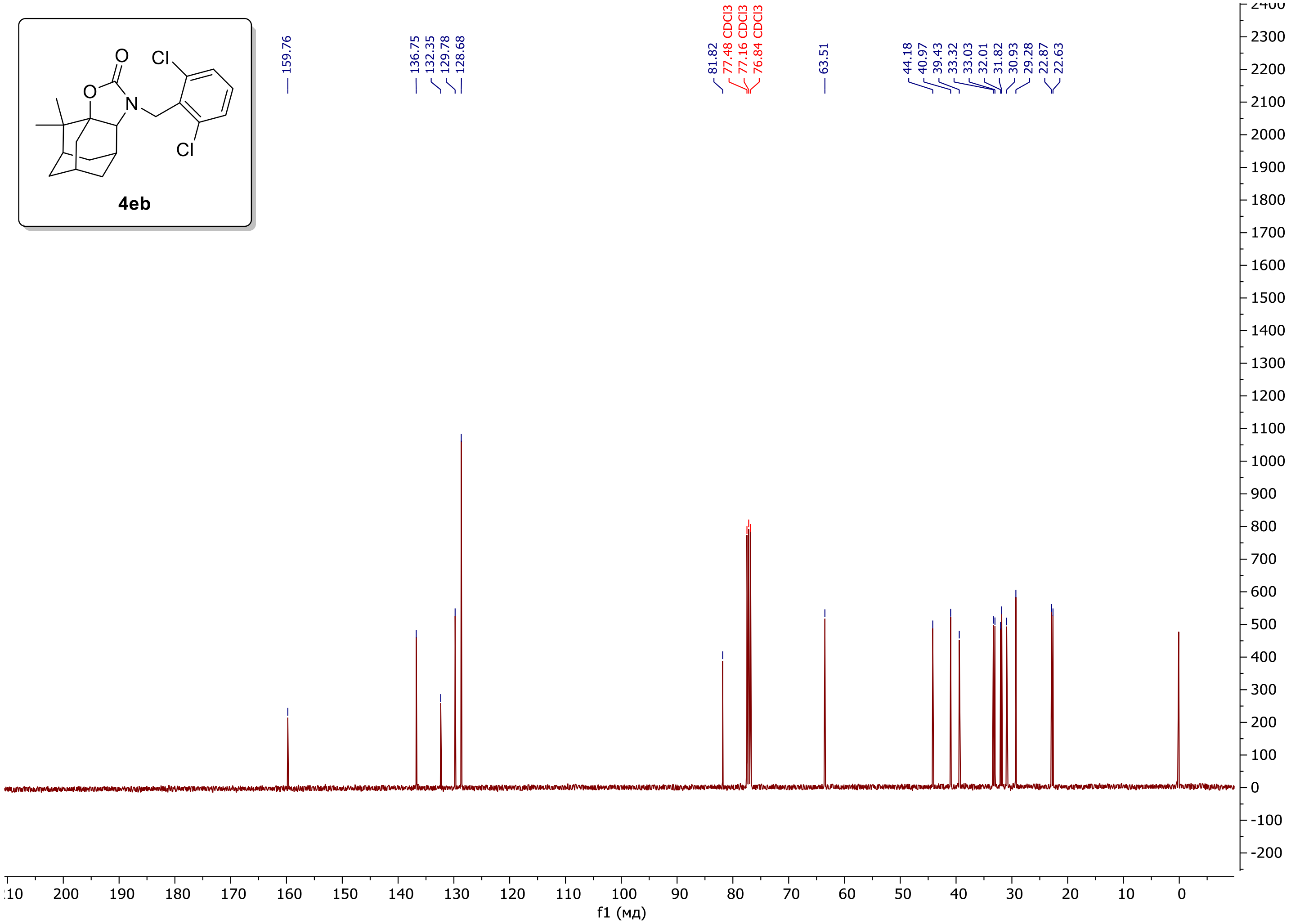
4ea

O
O
N
160.61
82.20
77.48 CDCl3
77.36
77.16 CDCl3
76.84 CDCl3
63.01
41.52
39.57
33.08
32.82
32.10
31.09
31.06
29.49
29.42
22.84
22.60
0.10
900
850
800
750
700
650
600
550
500
450
400
350
300
250
200
150
100
50
0
-50
20
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (мд)

Compound 4eb

4eb

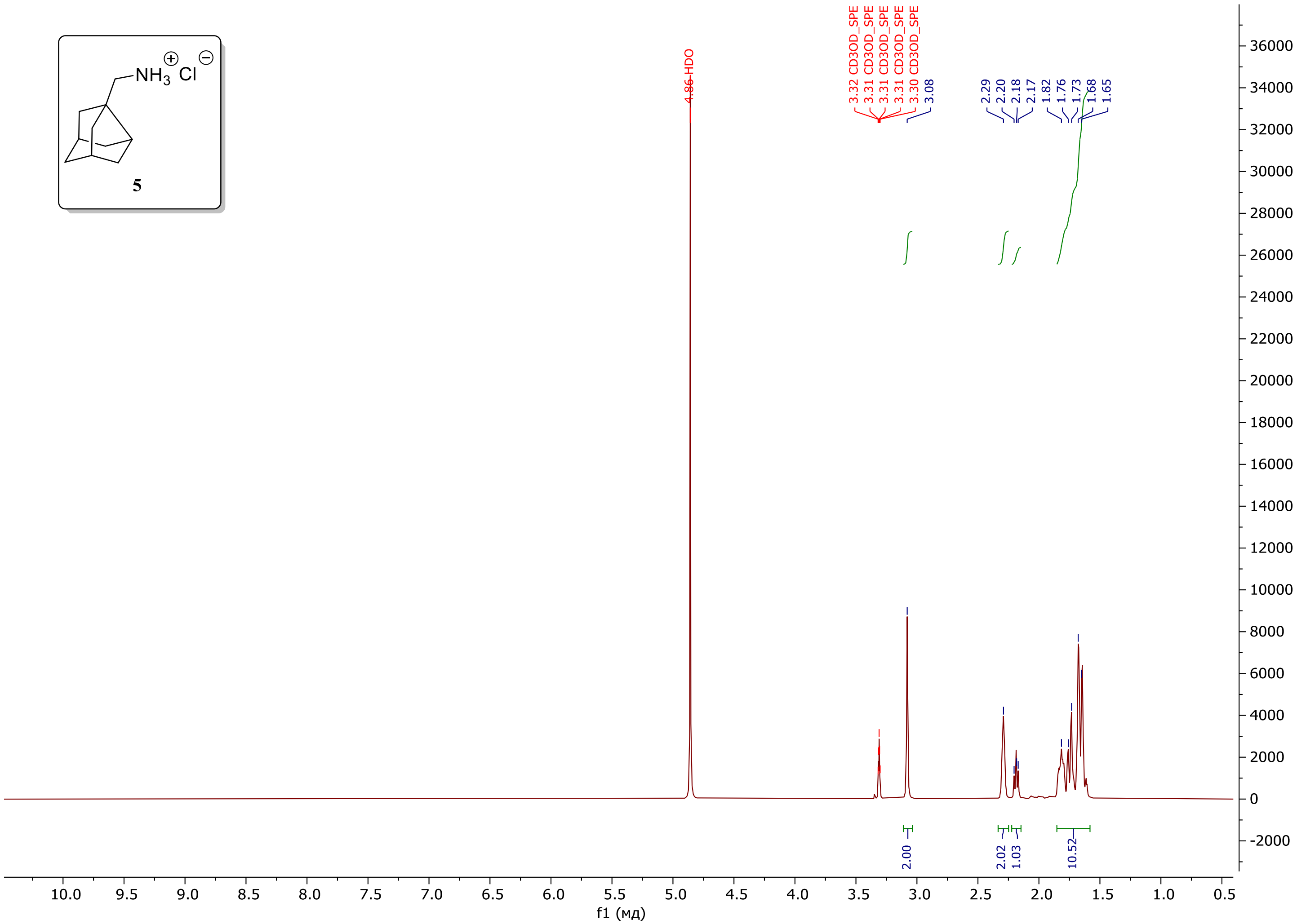



4eb
O
O
N
Cl
Cl
159.76
136.75
132.35
129.78
128.68
81.82
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
63.51
44.18
40.97
39.43
33.32
33.03
32.01
31.82
30.93
29.28
22.87
22.63
2400
2300
2200
2100
2000
1900
1800
1700
1600
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
-200
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (мд)

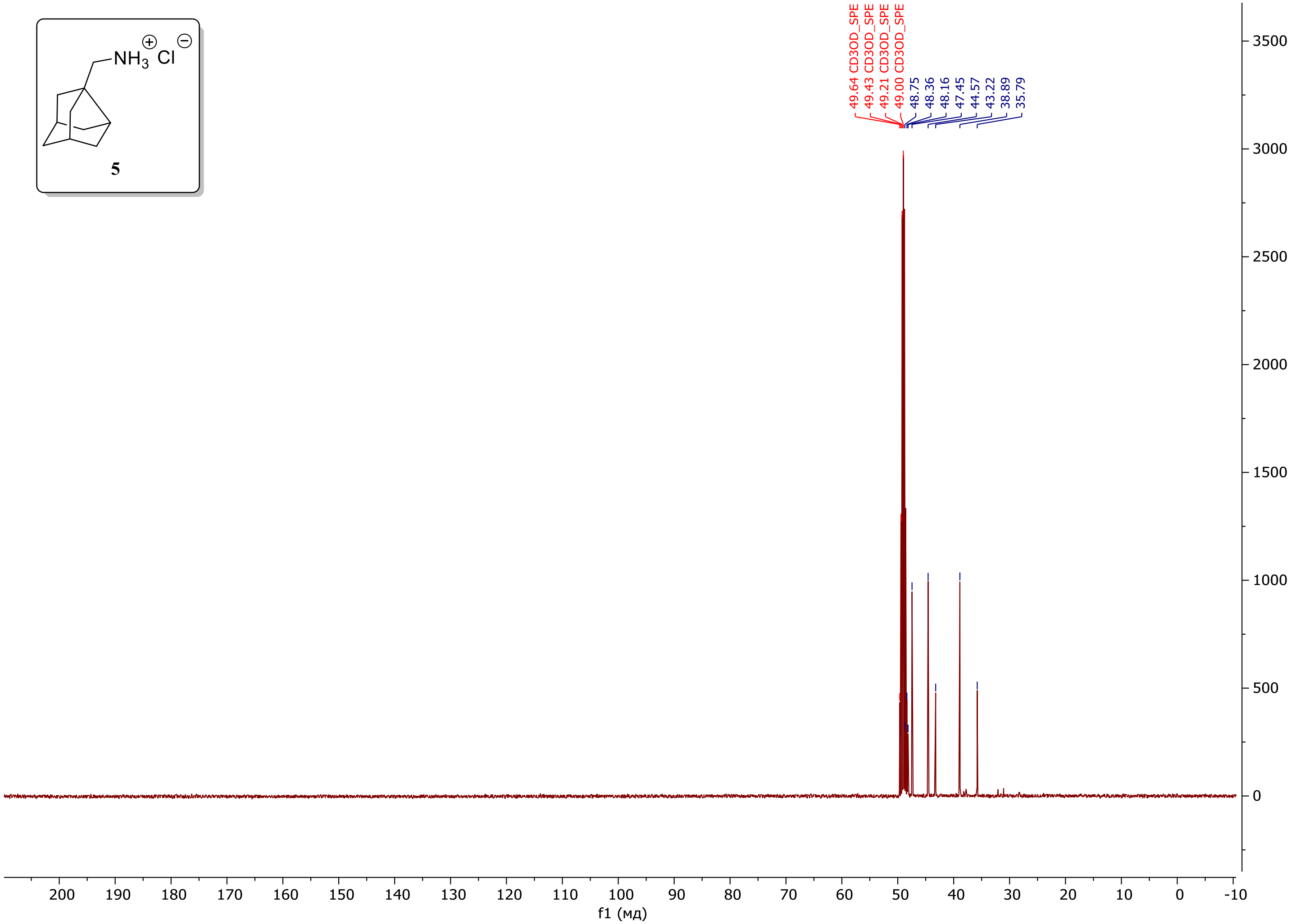
Compound 5

NH3 Cl

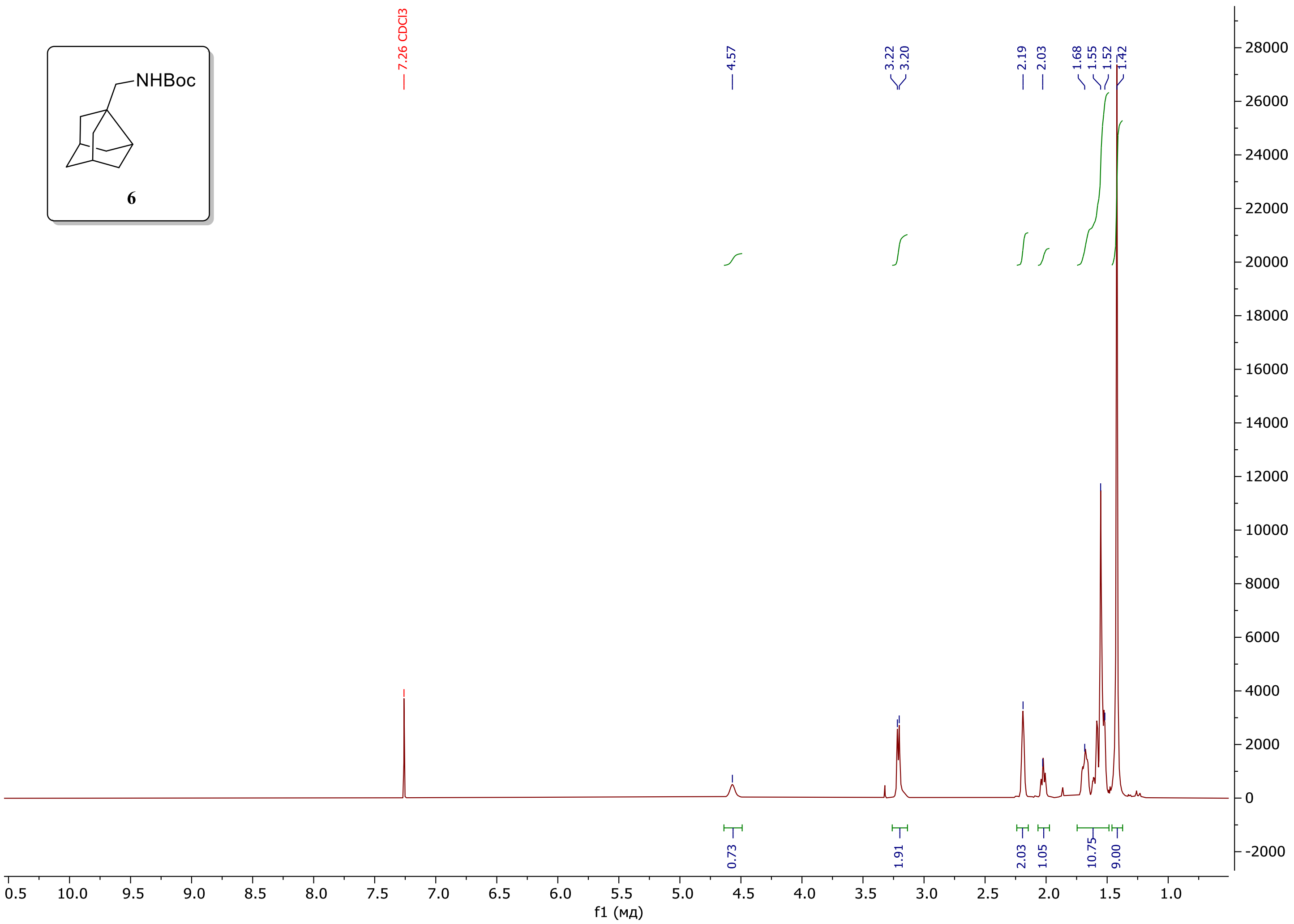
5

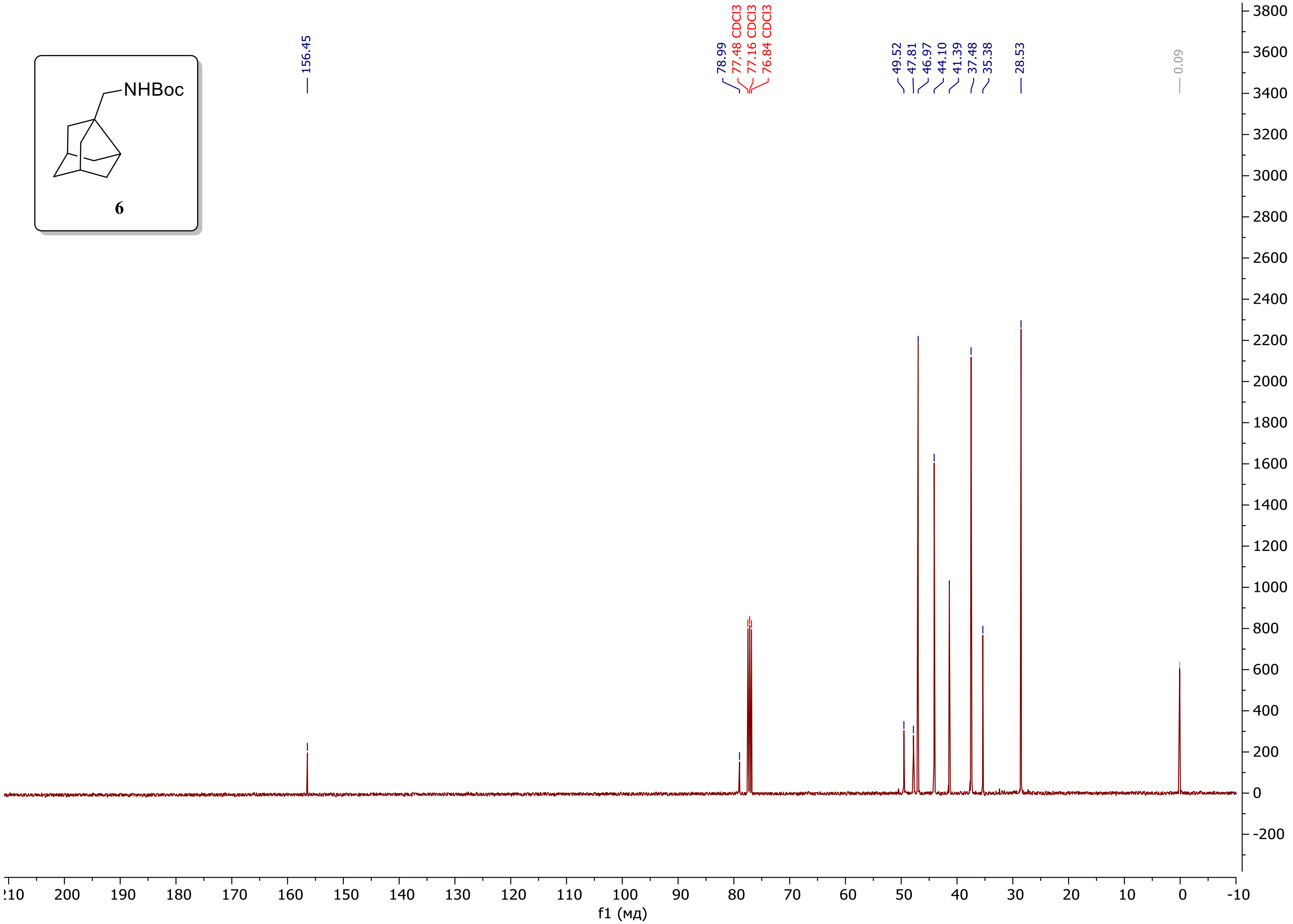


4.86 HDO
3.32 CD3OD_SPE
3.31 CD3OD_SPE
3.31 CD3OD_SPE
3.31 CD3OD_SPE
3.30 CD3OD_SPE
3.08
2.29
2.20
2.18
2.17
1.82
1.76
1.73
1.68
1.65
2.00
2.02
1.03
10.52
f1 (мд)
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
36000
34000
32000
30000
28000
26000
24000
22000
20000
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
-2000


$NH_3^{\oplus}$ $Cl^{\ominus}$
5
49.64 CD3OD_SPE
49.43 CD3OD_SPE
49.21 CD3OD_SPE
49.00 CD3OD_SPE
48.75
48.36
48.16
47.45
44.57
43.22
38.89
35.79
3500
3000
2500
2000
1500
1000
500
0
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (мд)

Compound 6

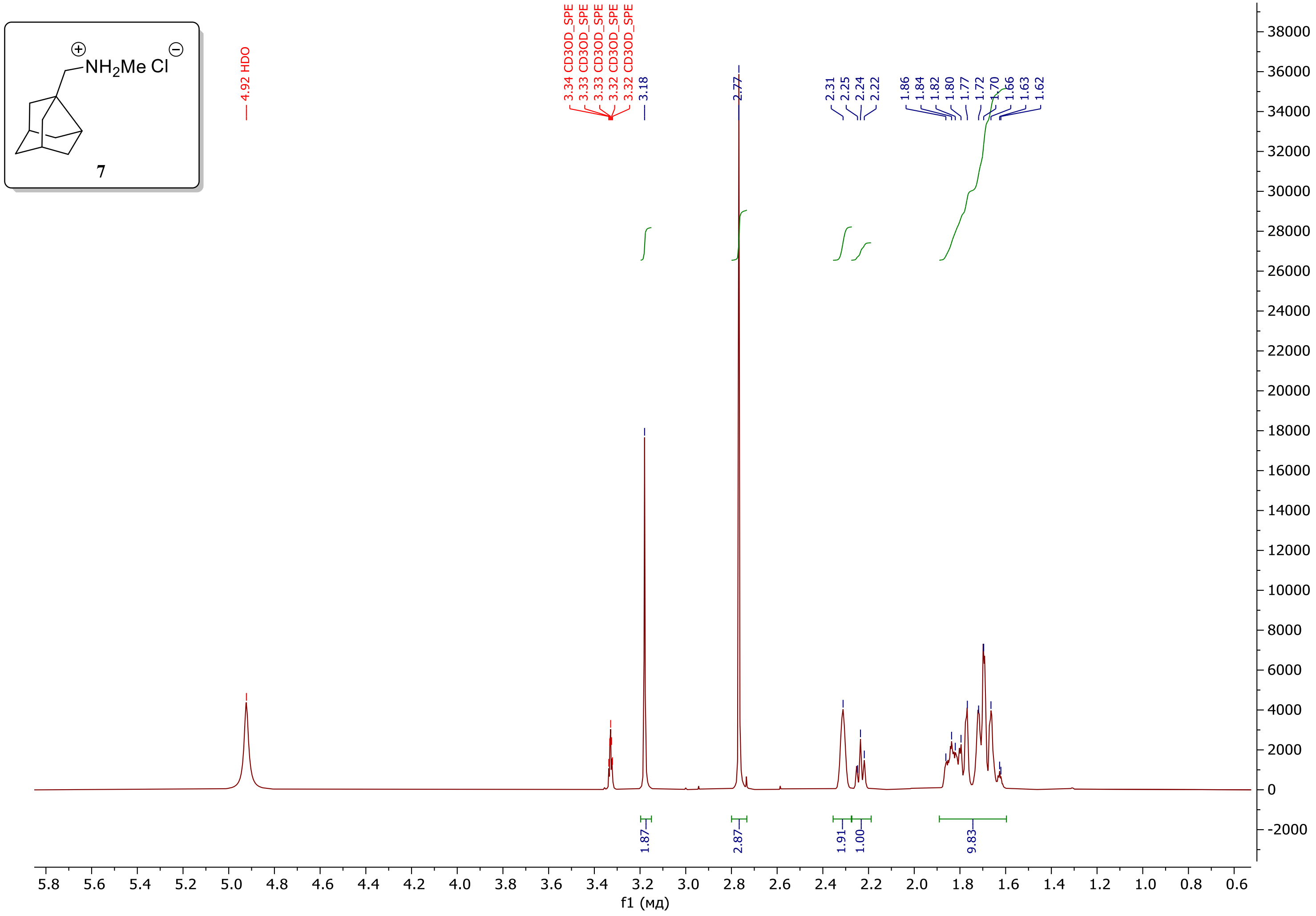

NHBoc
6
7.26 CDCl3
4.57
3.22
3.20
2.19
2.03
1.68
1.55
1.52
1.42
0.73
1.91
2.03
1.05
10.75
9.00
28000
26000
24000
22000
20000
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
-2000
0.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f1 (мд)



6

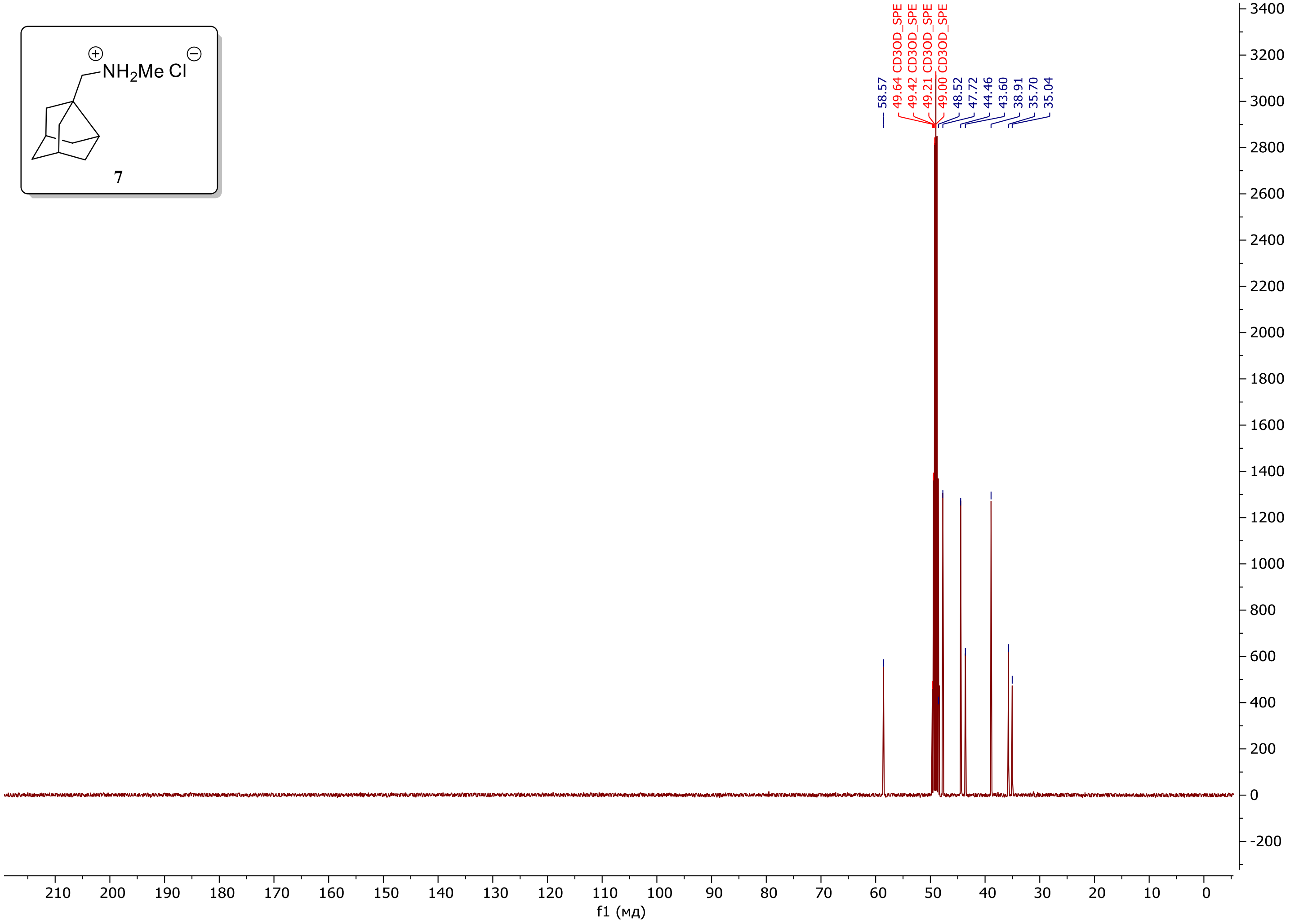
156.45
78.99
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
49.52
47.81
46.97
44.10
41.39
37.48
35.38
28.53
0.09
3800
3600
3400
3200
3000
2800
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
-200
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (мд)

Compound 7

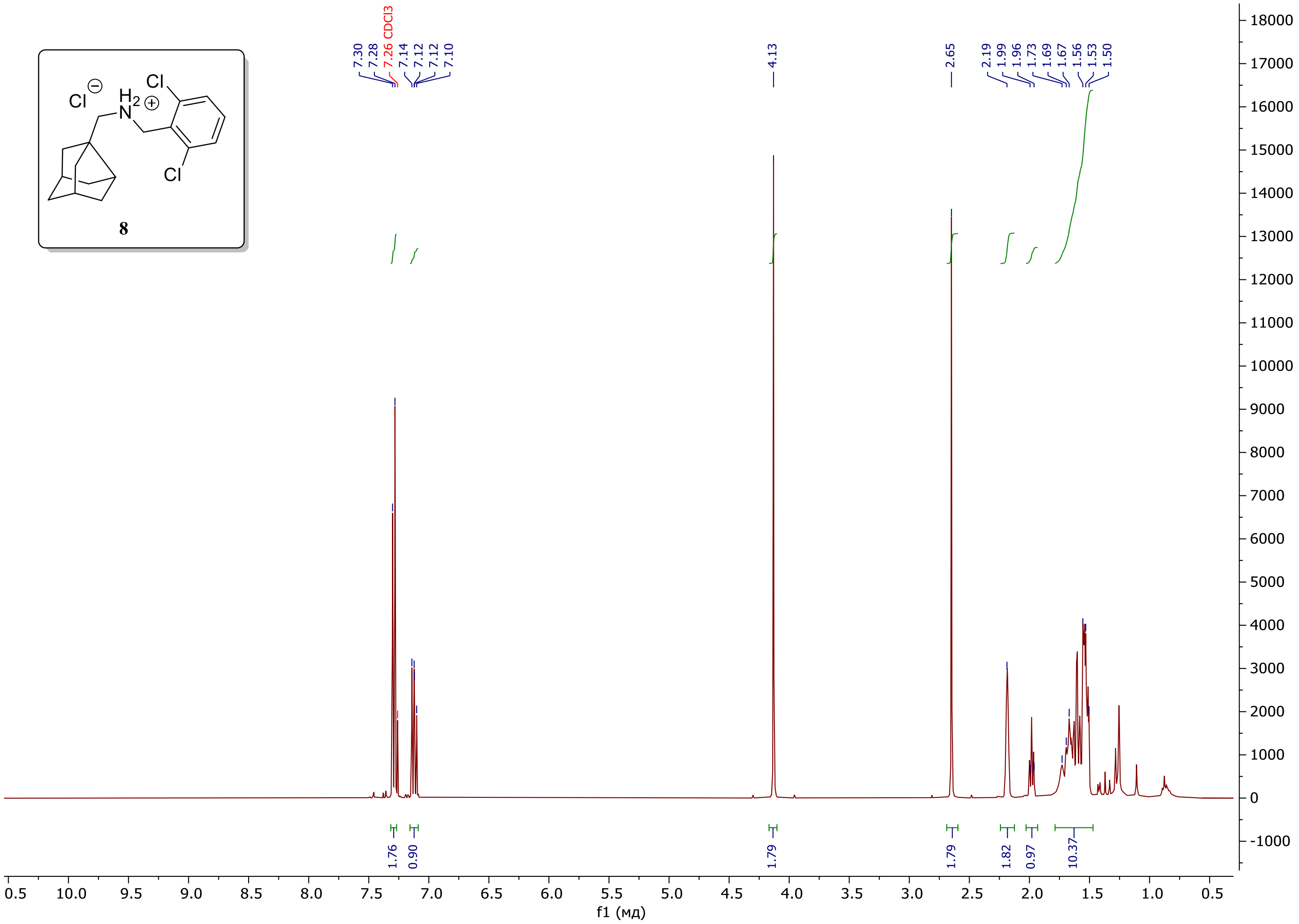

NH2Me Cl
7
4.92 HDO
3.34 CD3OD_SPE
3.33 CD3OD_SPE
3.33 CD3OD_SPE
3.32 CD3OD_SPE
3.32 CD3OD_SPE
3.18
2.77
2.31
2.25
2.24
2.22
1.86
1.84
1.82
1.80
1.77
1.72
1.70
1.66
1.63
1.62
1.87
2.87
1.91
1.00
9.83
38000
36000
34000
32000
30000
28000
26000
24000
22000
20000
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
-2000
5.8
5.6
5.4
5.2
5.0
4.8
4.6
4.4
4.2
4.0
3.8
3.6
3.4
3.2
3.0
2.8
2.6
2.4
2.2
2.0
1.8
1.6
1.4
1.2
1.0
0.8
0.6
f1 (мд)

NH2Me Cl

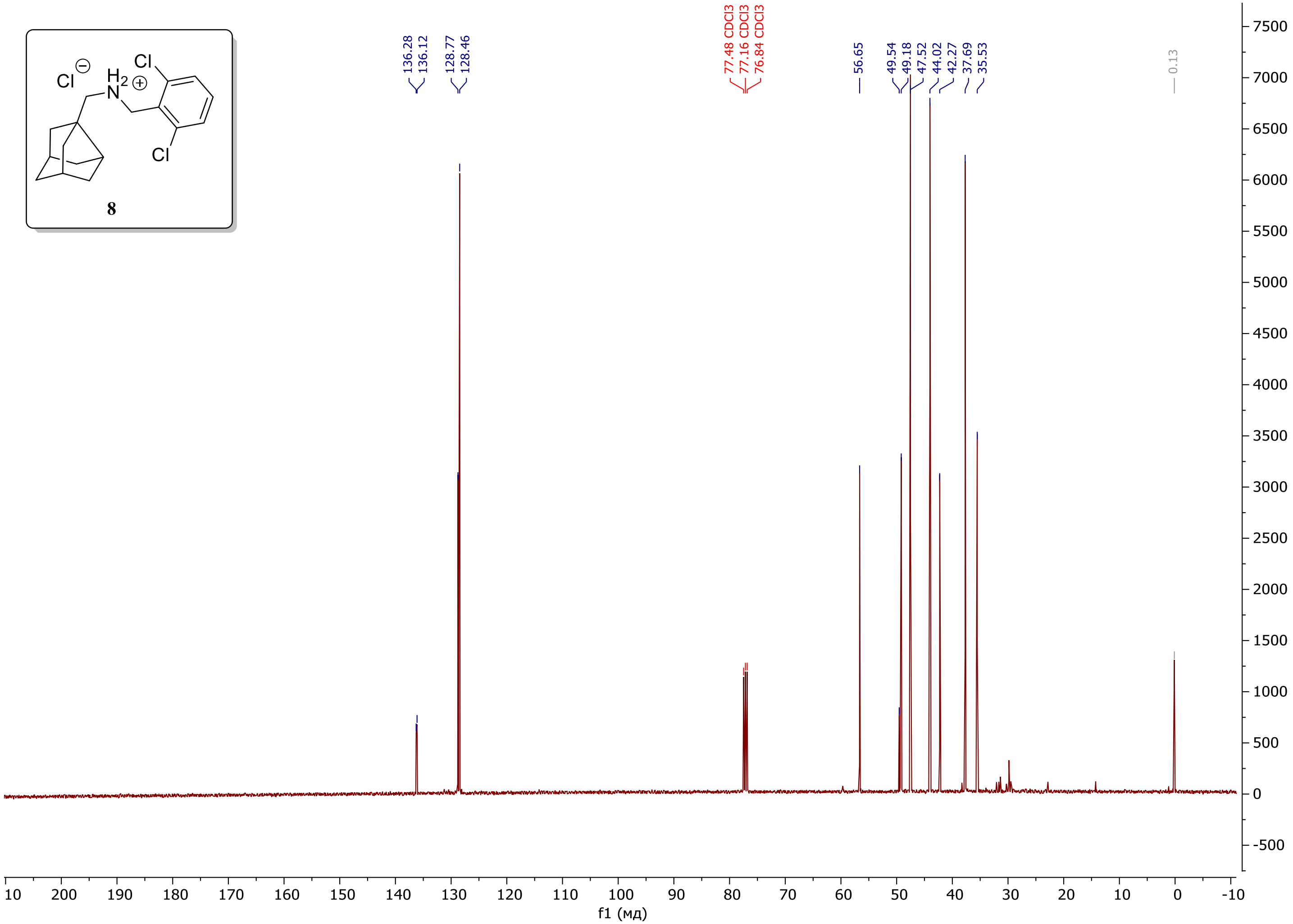
7


58.57
49.64 CD3OD_SPE
49.42 CD3OD_SPE
49.21 CD3OD_SPE
49.00 CD3OD_SPE
48.52
47.72
44.46
43.60
38.91
35.70
35.04
3400
3200
3000
2800
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
-200
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (мд)

Compound 8



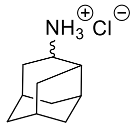
8
7.30
7.28
7.26 CDCl3
7.14
7.12
7.12
7.10
4.13
2.65
2.19
1.99
1.96
1.73
1.69
1.67
1.56
1.53
1.50
1.76
0.90
1.79
1.79
1.82
0.97
10.37
18000
17000
16000
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
0.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (мд)


Cl
H2
N
Cl
Cl

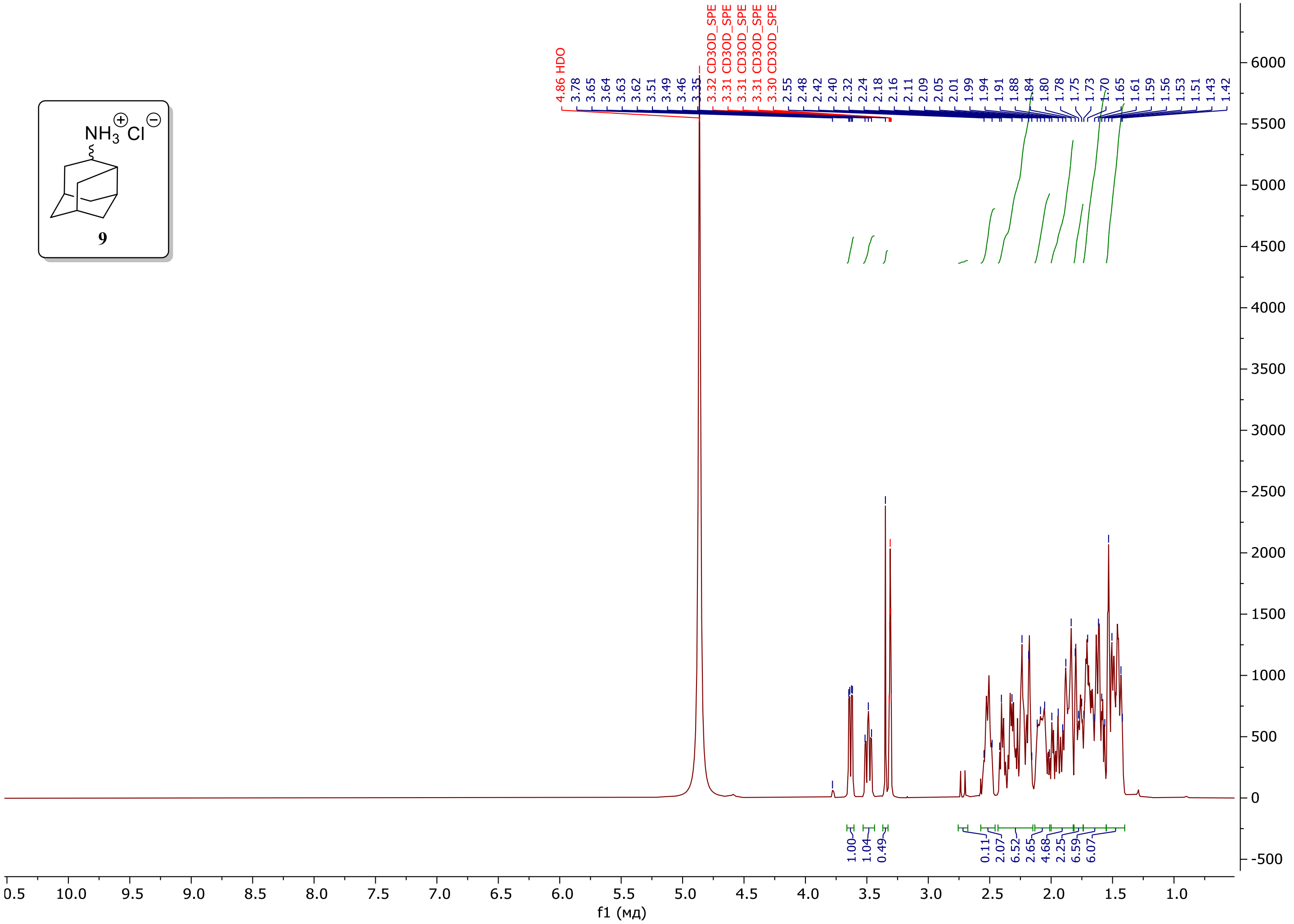
8

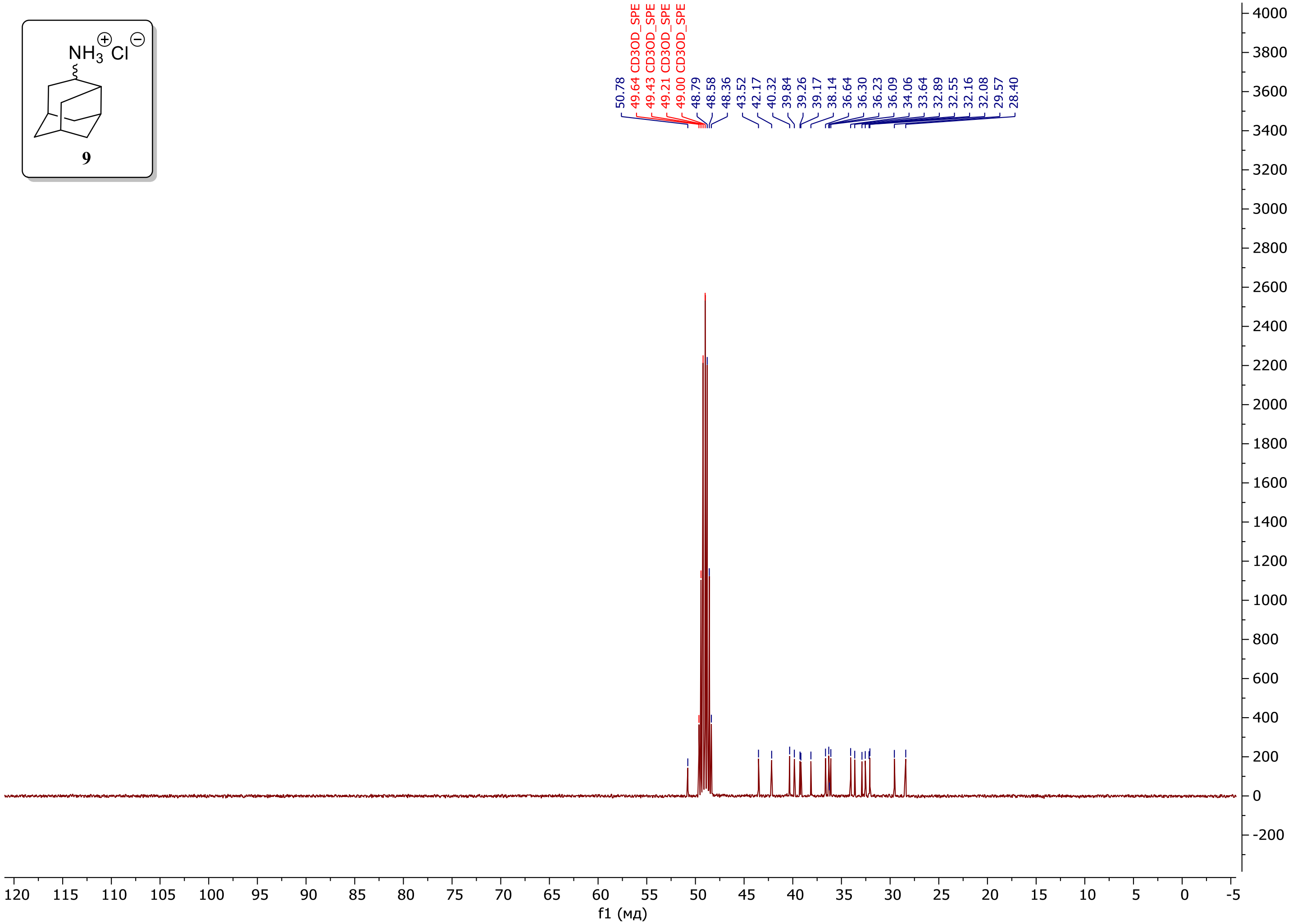
136.28
136.12
128.77
128.46
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
56.65
49.54
49.18
47.52
44.02
42.27
37.69
35.53
0.13
7500
7000
6500
6000
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
-500
10
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (мд)

Compound 9 (both isomers)



9

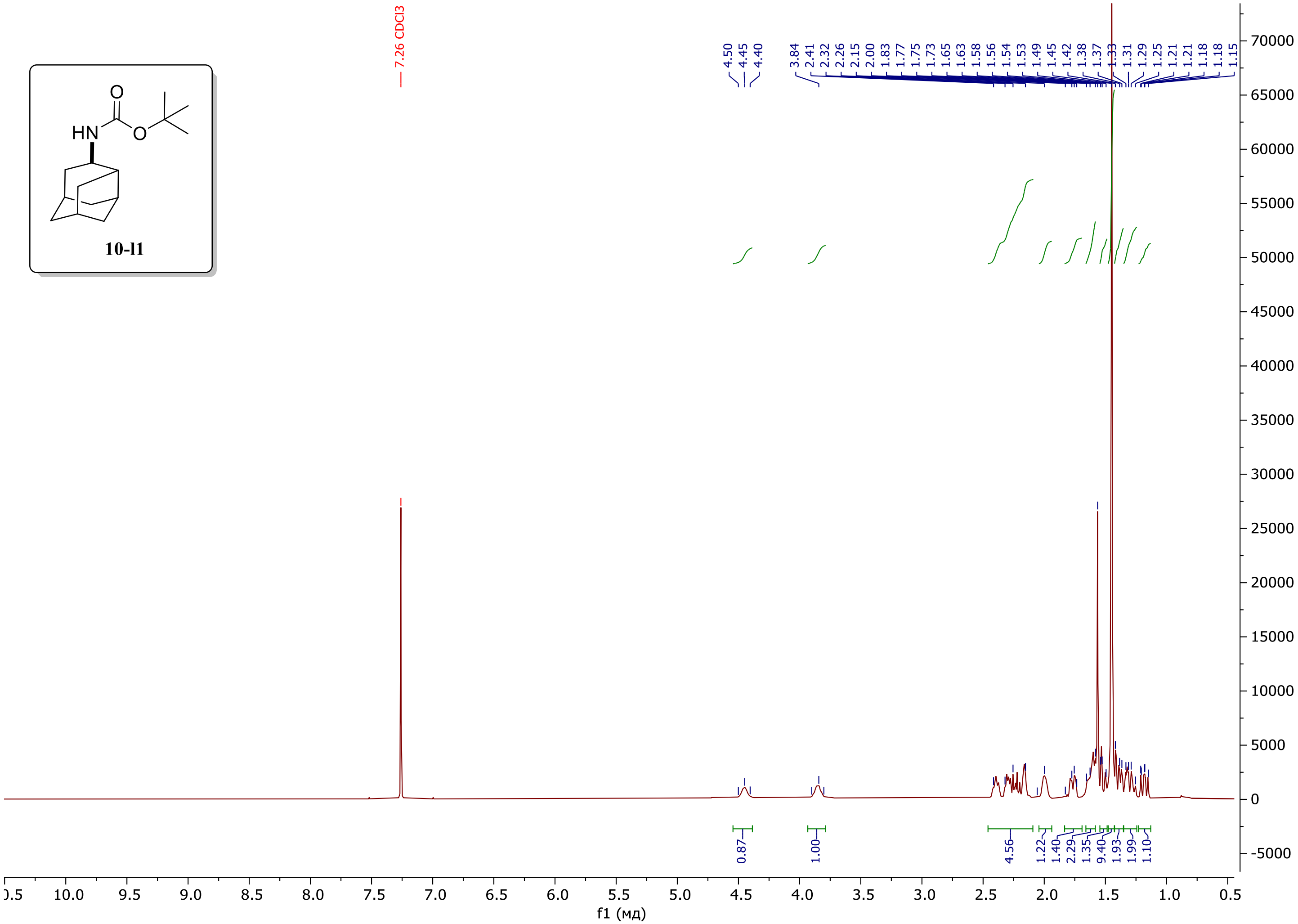



NH3 ⊕ Cl ⊖

9

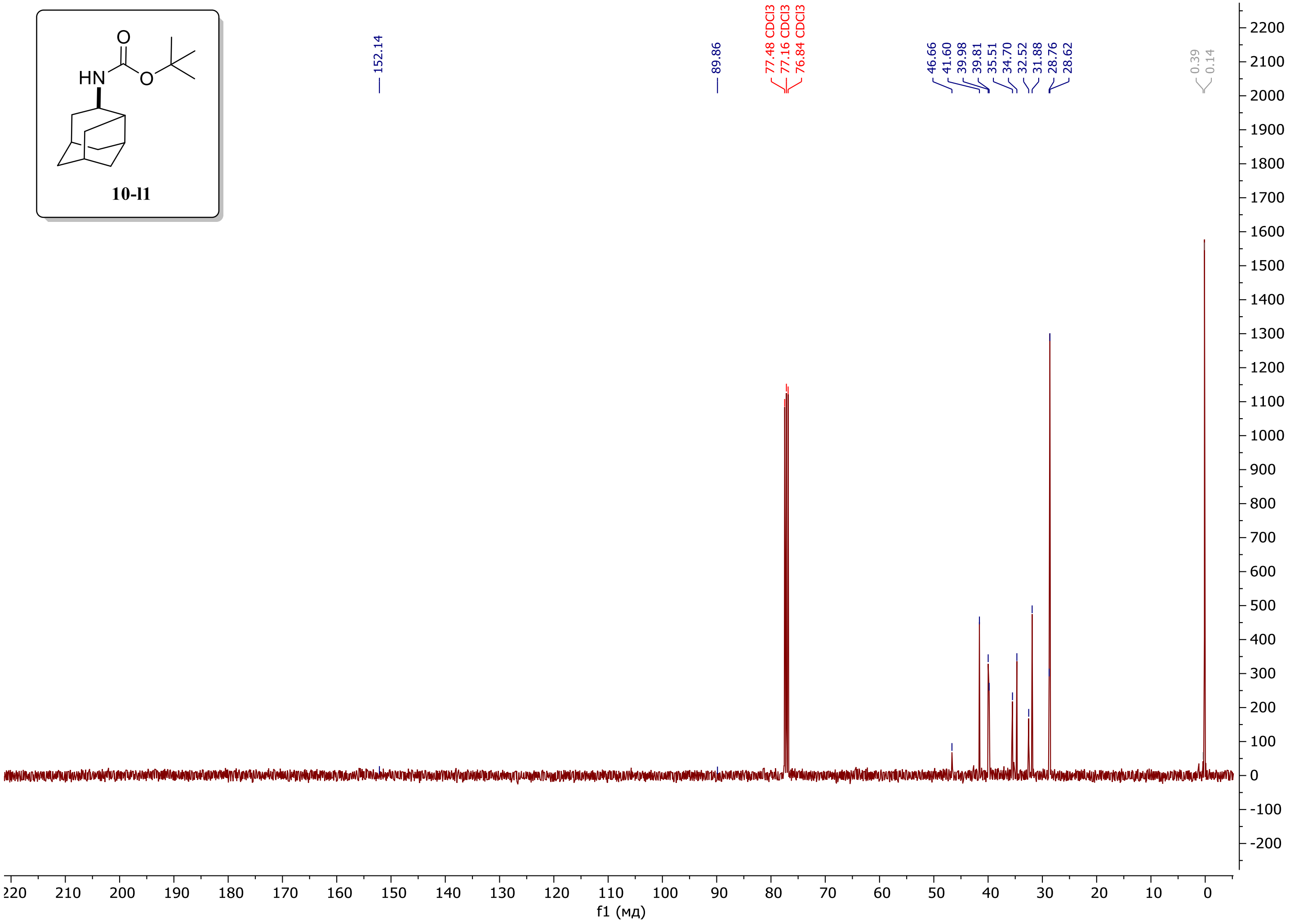
50.78
49.64 CD3OD_SPE
49.43 CD3OD_SPE
49.21 CD3OD_SPE
49.00 CD3OD_SPE
48.79
48.58
48.36
43.52
42.17
40.32
39.84
39.26
39.17
38.14
36.64
36.30
36.23
36.09
34.06
33.64
32.89
32.55
32.16
32.08
29.57
28.40
4000
3800
3600
3400
3200
3000
2800
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
-200
120
115
110
105
100
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
0
-5
f1 (мд)

Compound 10-l1

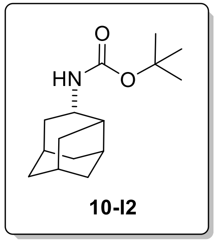


O
HN
O

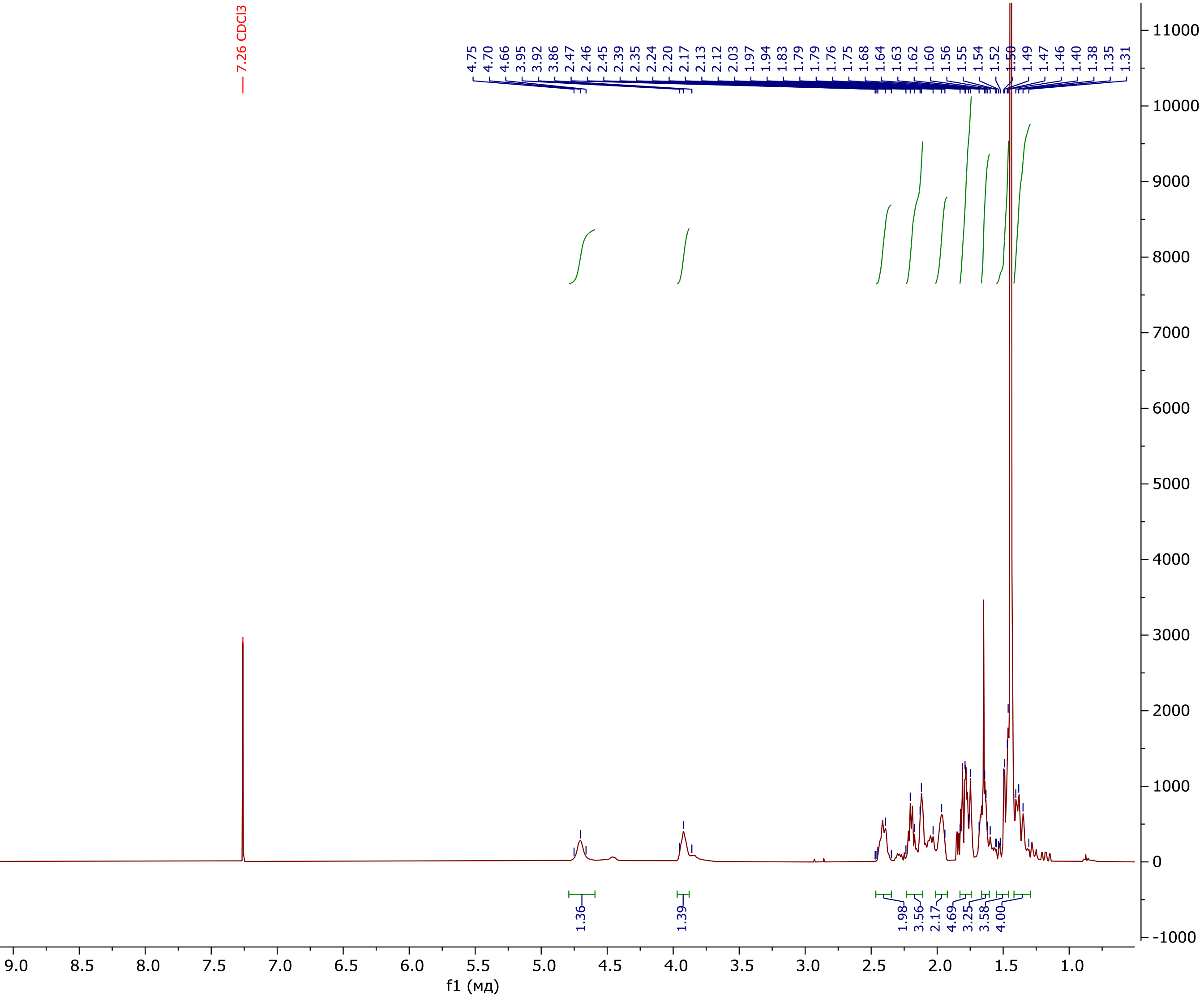
10-l1

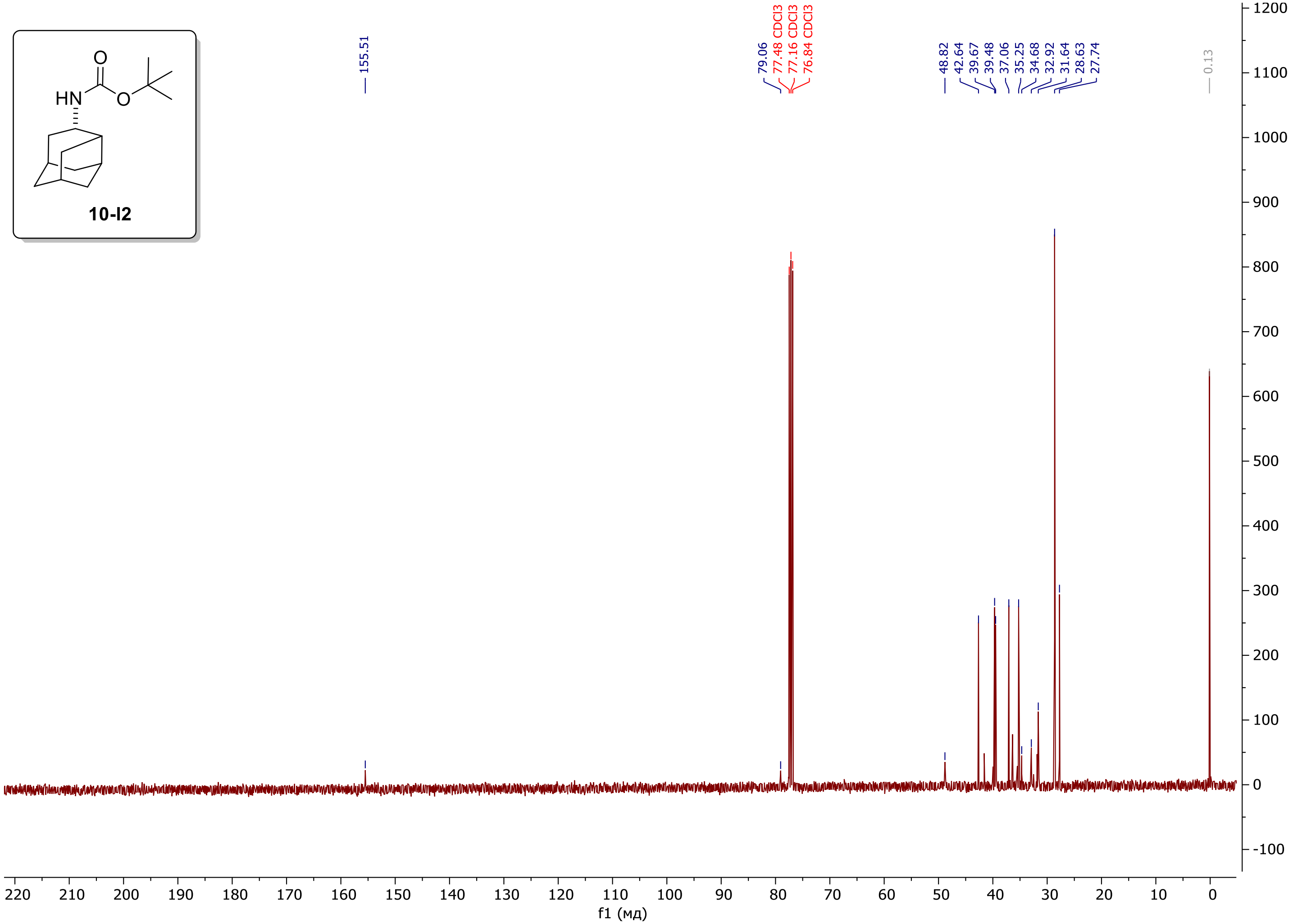

152.14
89.86
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
46.66
41.60
39.98
39.81
35.51
34.70
32.52
31.88
28.76
28.62
0.39
0.14
2200
2100
2000
1900
1800
1700
1600
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
-200
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (мд)

Compound 10-I2

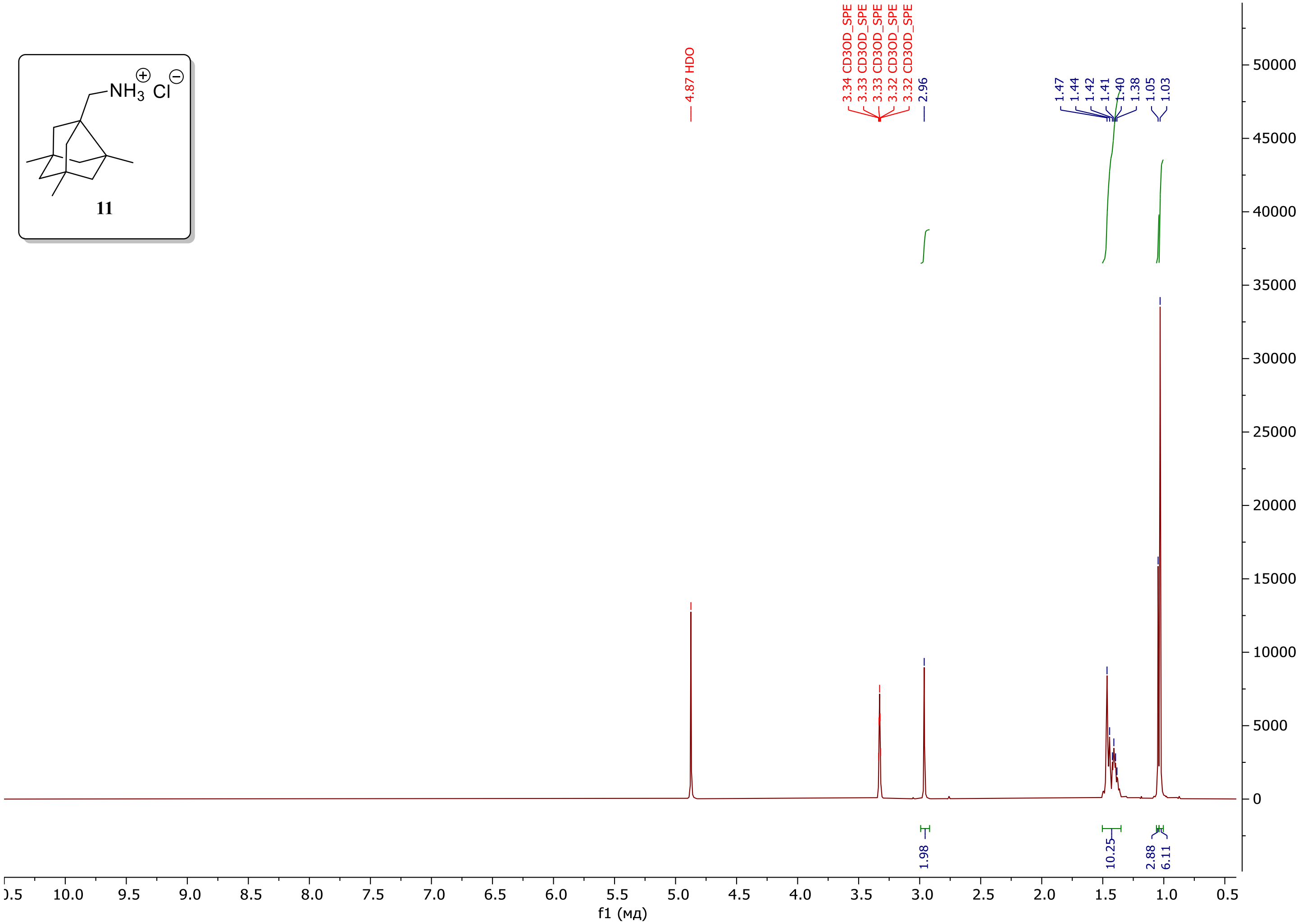


10-I2




10-I2
HN
O
O
155.51
79.06
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
48.82
42.64
39.67
39.48
37.06
35.25
34.68
32.92
31.64
28.63
27.74
0.13
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (мд)

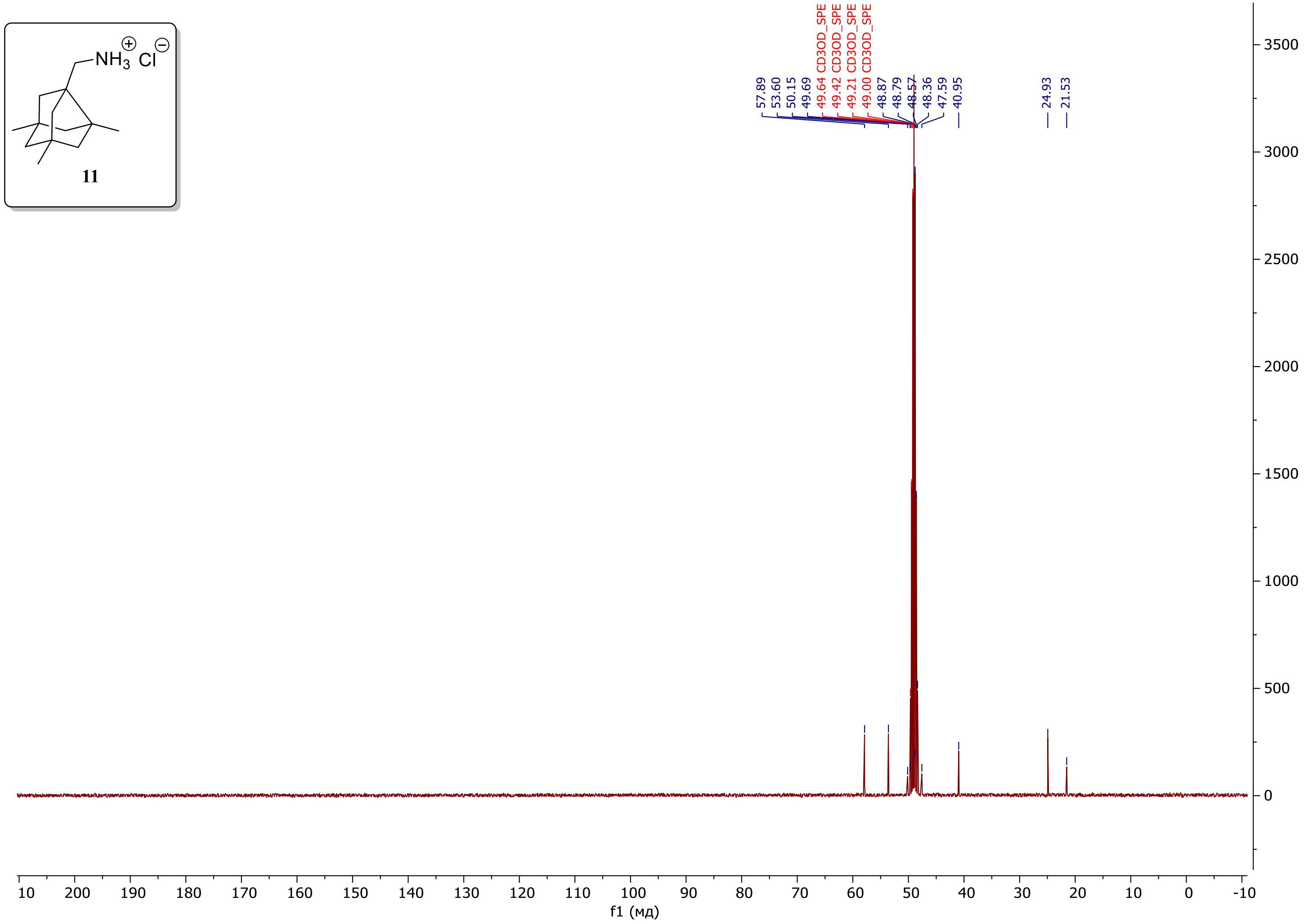
Compound 11



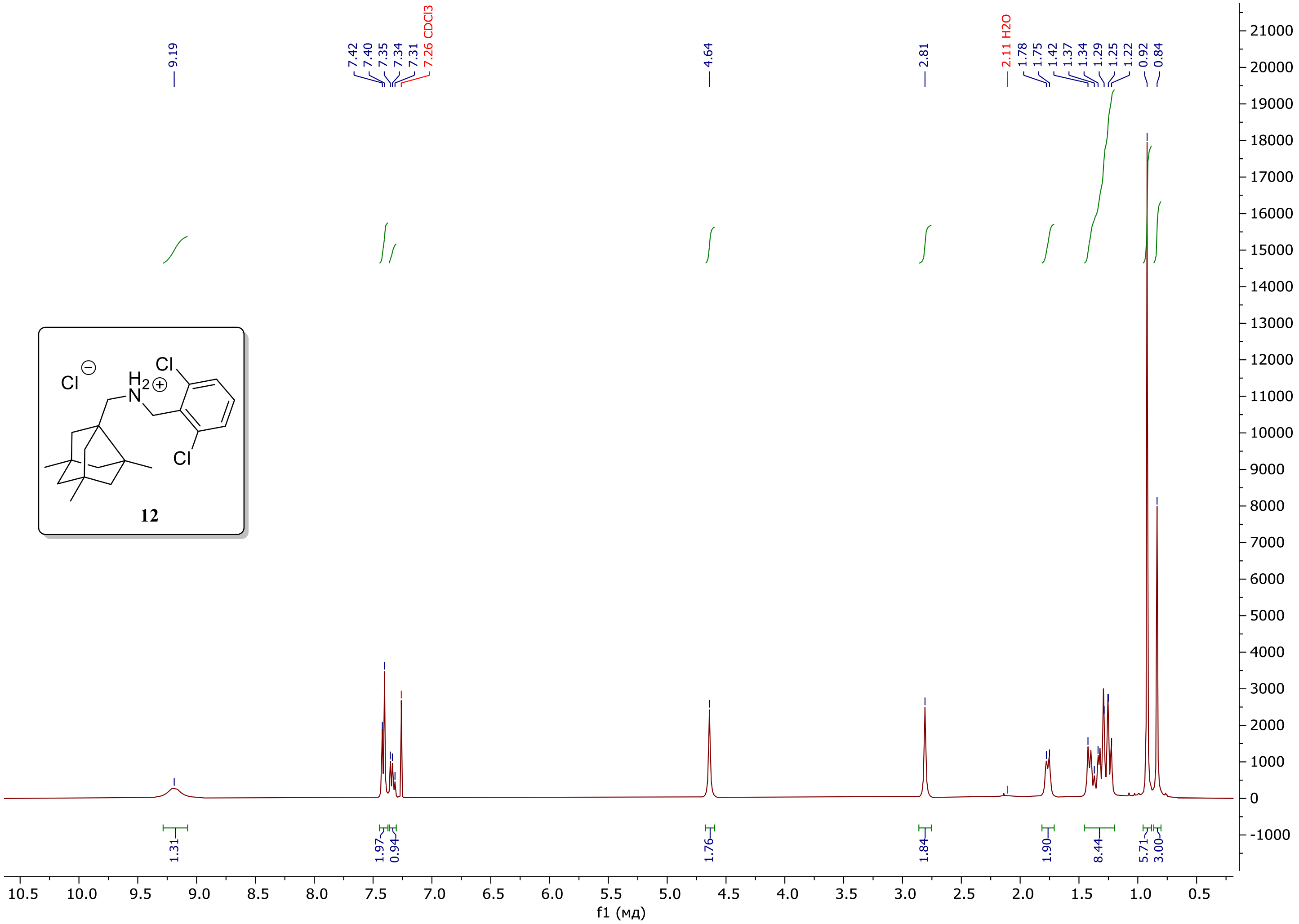
11

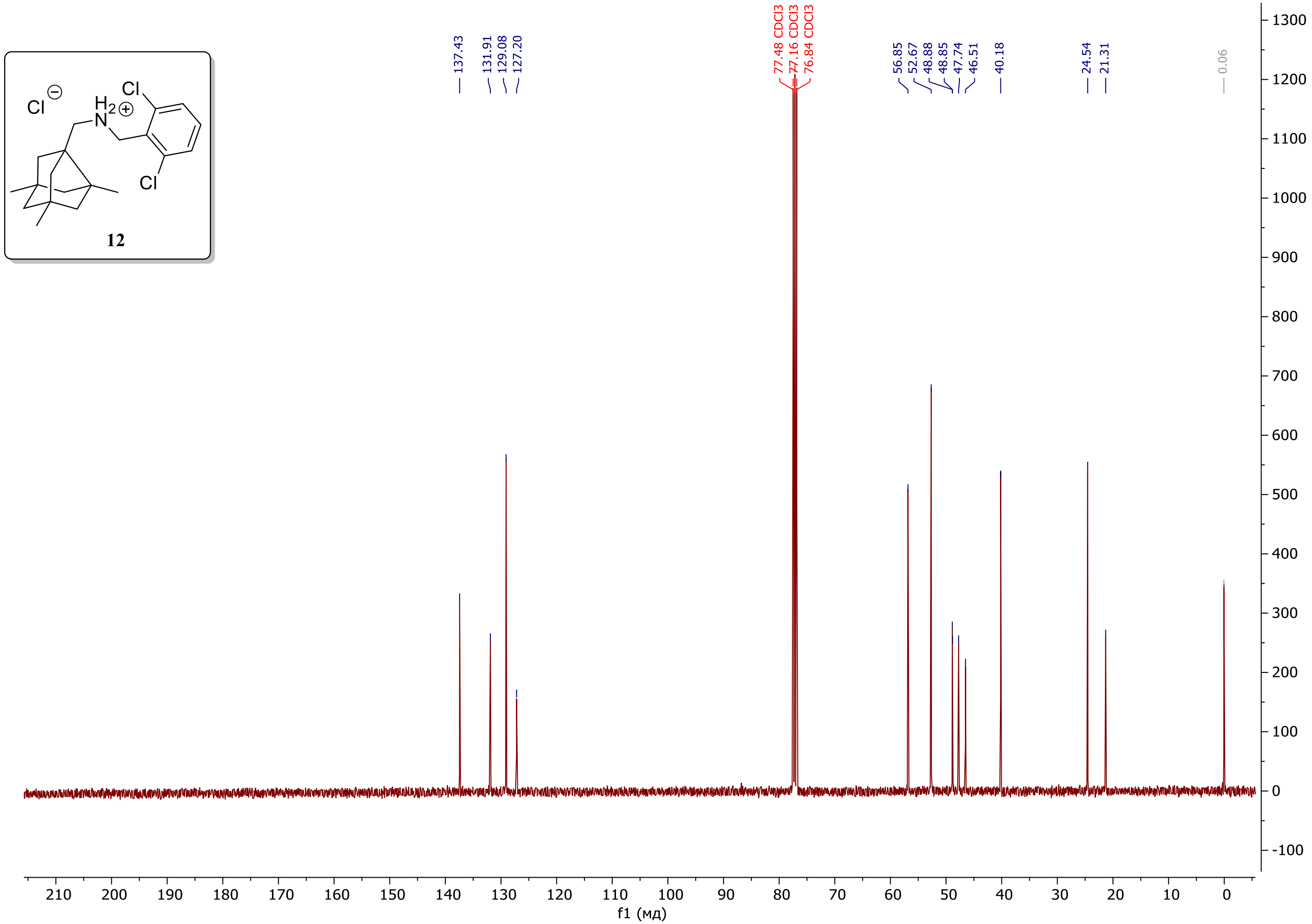
NH3⊕ Cl⊖

11


57.89
53.60
50.15
49.69
49.64 CD3OD_SPE
49.42 CD3OD_SPE
49.21 CD3OD_SPE
49.00 CD3OD_SPE
48.87
48.79
48.57
48.36
47.59
40.95
24.93
21.53
3500
3000
2500
2000
1500
1000
500
0
10
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (мд)

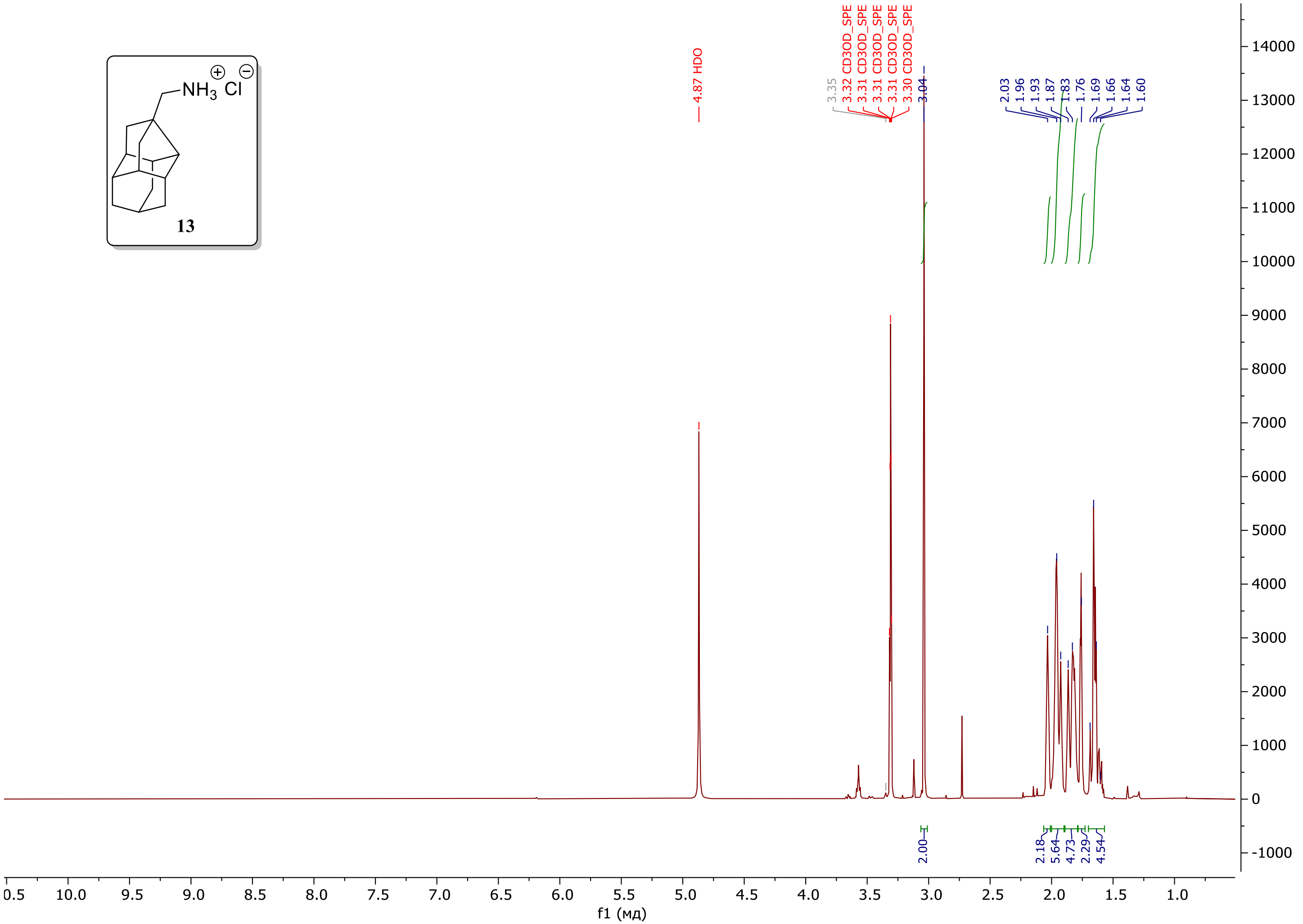
Compound 12


9.19
7.42
7.40
7.35
7.34
7.31
7.26 CDCl3
4.64
2.81
2.11 H2O
1.78
1.75
1.42
1.37
1.34
1.29
1.25
1.22
0.92
0.84
1.31
1.97
0.94
1.76
1.84
1.90
8.44
5.71
3.00
Cl
H2
N
Cl
Cl
12
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (мд)
21000
20000
19000
18000
17000
16000
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000



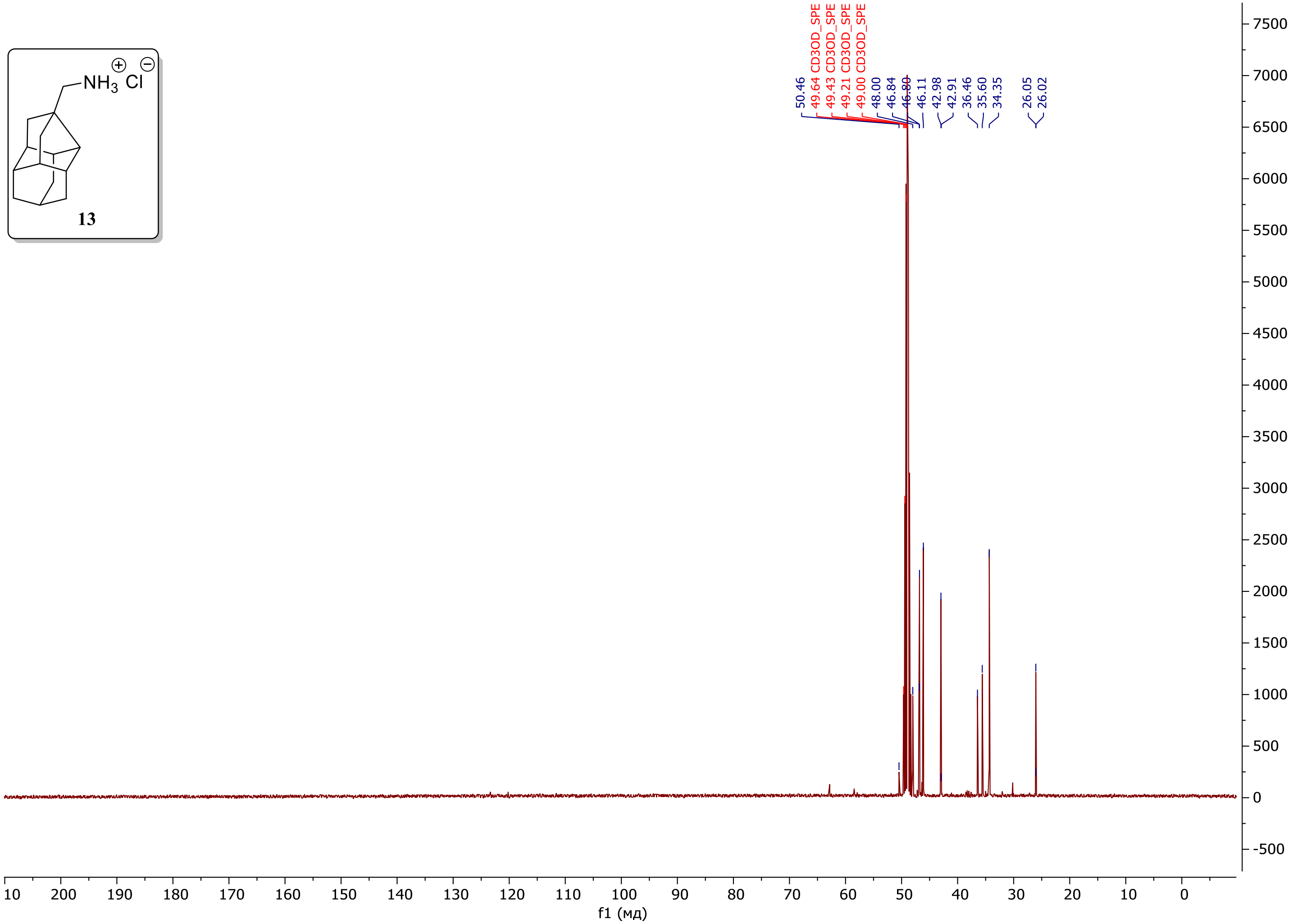
12
Cl⊖
H2⊕
N
Cl
Cl
137.43
131.91
129.08
127.20
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
56.85
52.67
48.88
48.85
47.74
46.51
40.18
24.54
21.31
0.06
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (мд)

Compound 13

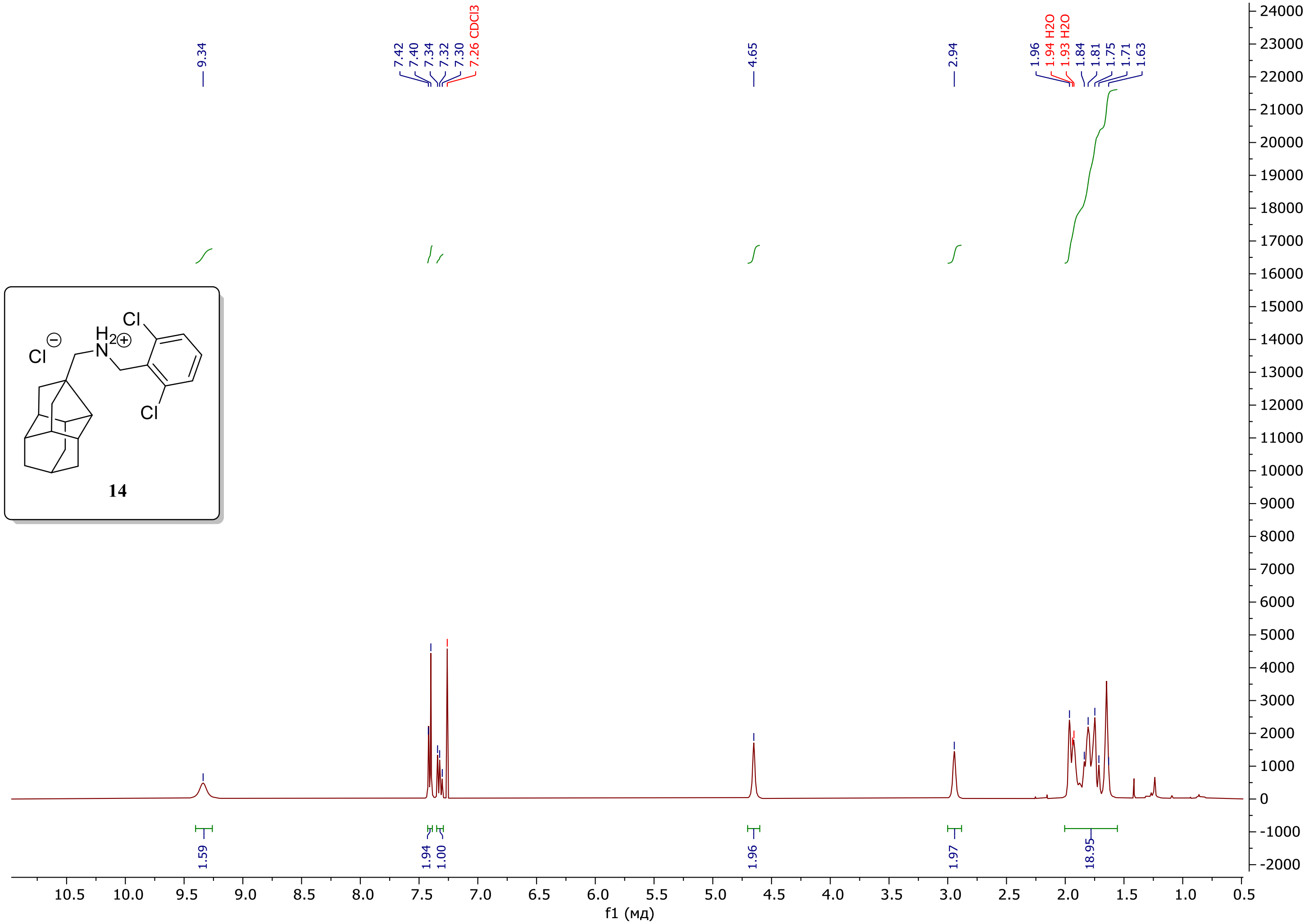

NH3 Cl
13
4.87 HDO
3.35
3.32 CD3OD_SPE
3.31 CD3OD_SPE
3.31 CD3OD_SPE
3.31 CD3OD_SPE
3.30 CD3OD_SPE
3.04
2.03
1.96
1.93
1.87
1.83
1.76
1.69
1.66
1.64
1.60
2.00
2.18
5.64
4.73
2.29
4.54
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
0.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f1 (мд)

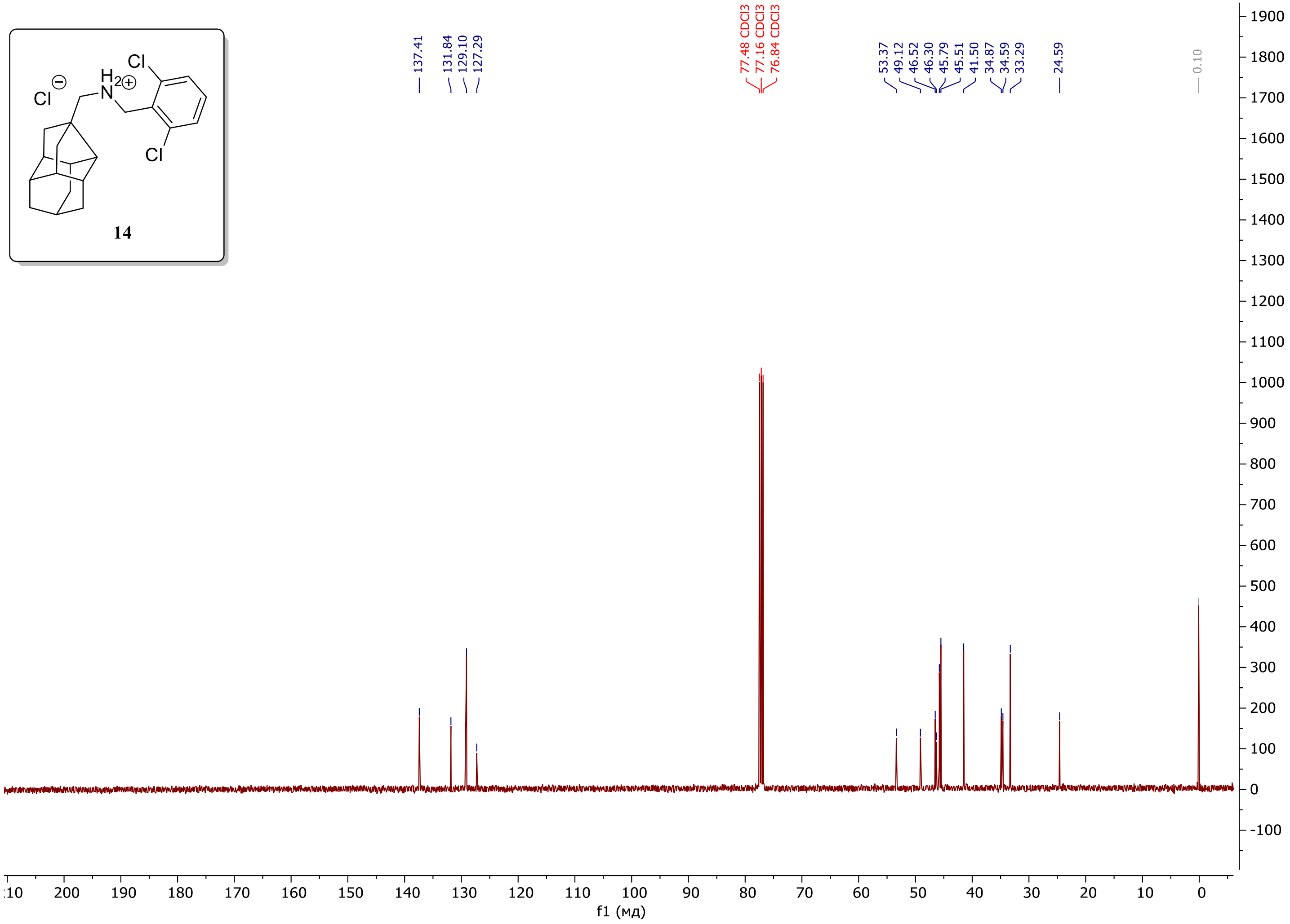
NH3
Cl

13


50.46
49.64 CD3OD_SPE
49.43 CD3OD_SPE
49.21 CD3OD_SPE
49.00 CD3OD_SPE
48.00
46.84
46.80
46.11
42.98
42.91
36.46
35.60
34.35
26.05
26.02
7500
7000
6500
6000
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
-500
10
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (мд)

Compound 14

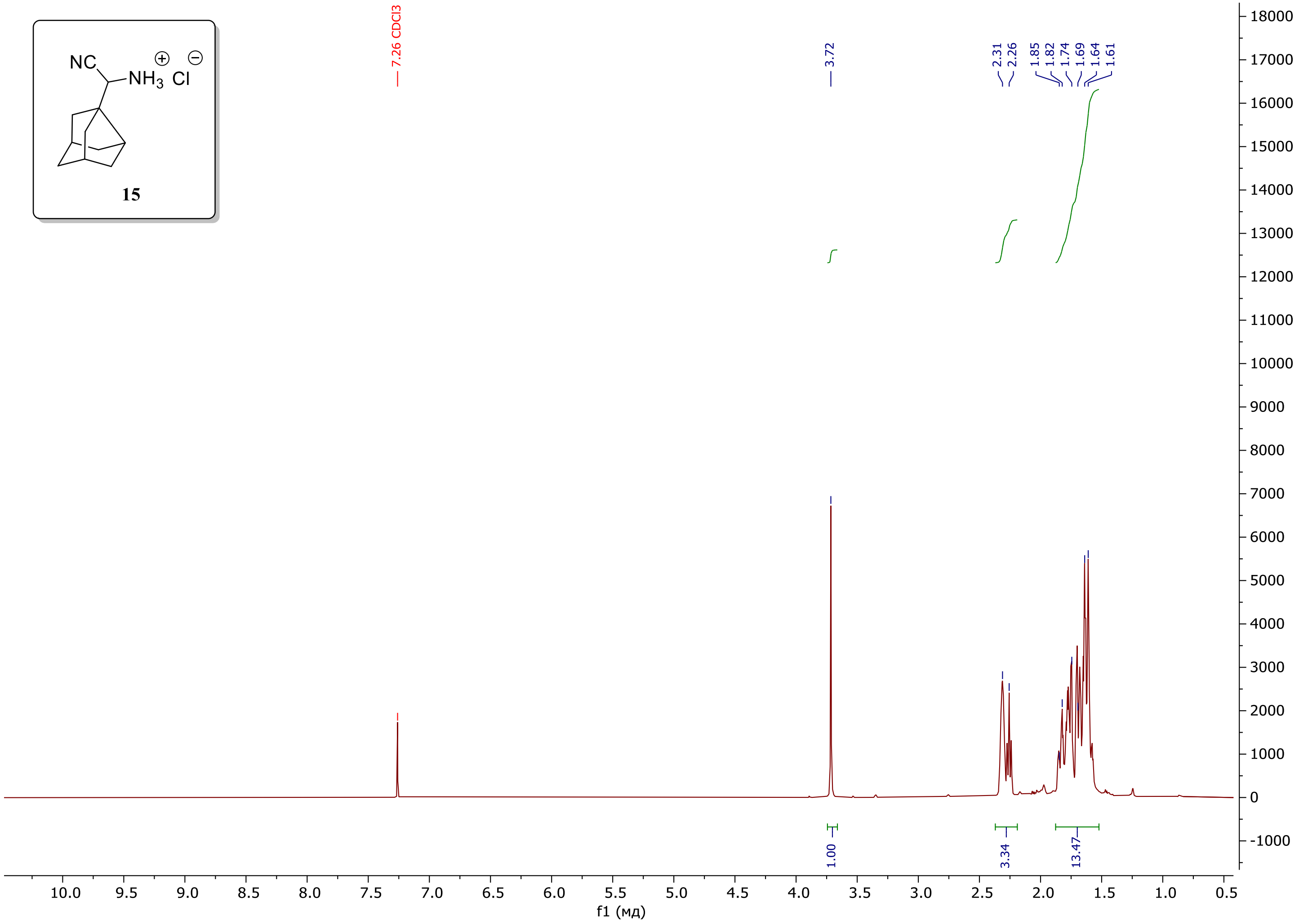

9.34
7.42
7.40
7.34
7.32
7.30
7.26 CDCl3
4.65
2.94
1.96
1.94 H2O
1.93 H2O
1.84
1.81
1.75
1.71
1.63
1.59
1.94
1.00
1.96
1.97
18.95
Cl
H2
N
Cl
Cl
14
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (мд)
24000 23000 22000 21000 20000 19000 18000 17000 16000 15000 14000 13000 12000 11000 10000 9000 8000 7000 6000 5000 4000 3000 2000 1000 0 -1000 -2000

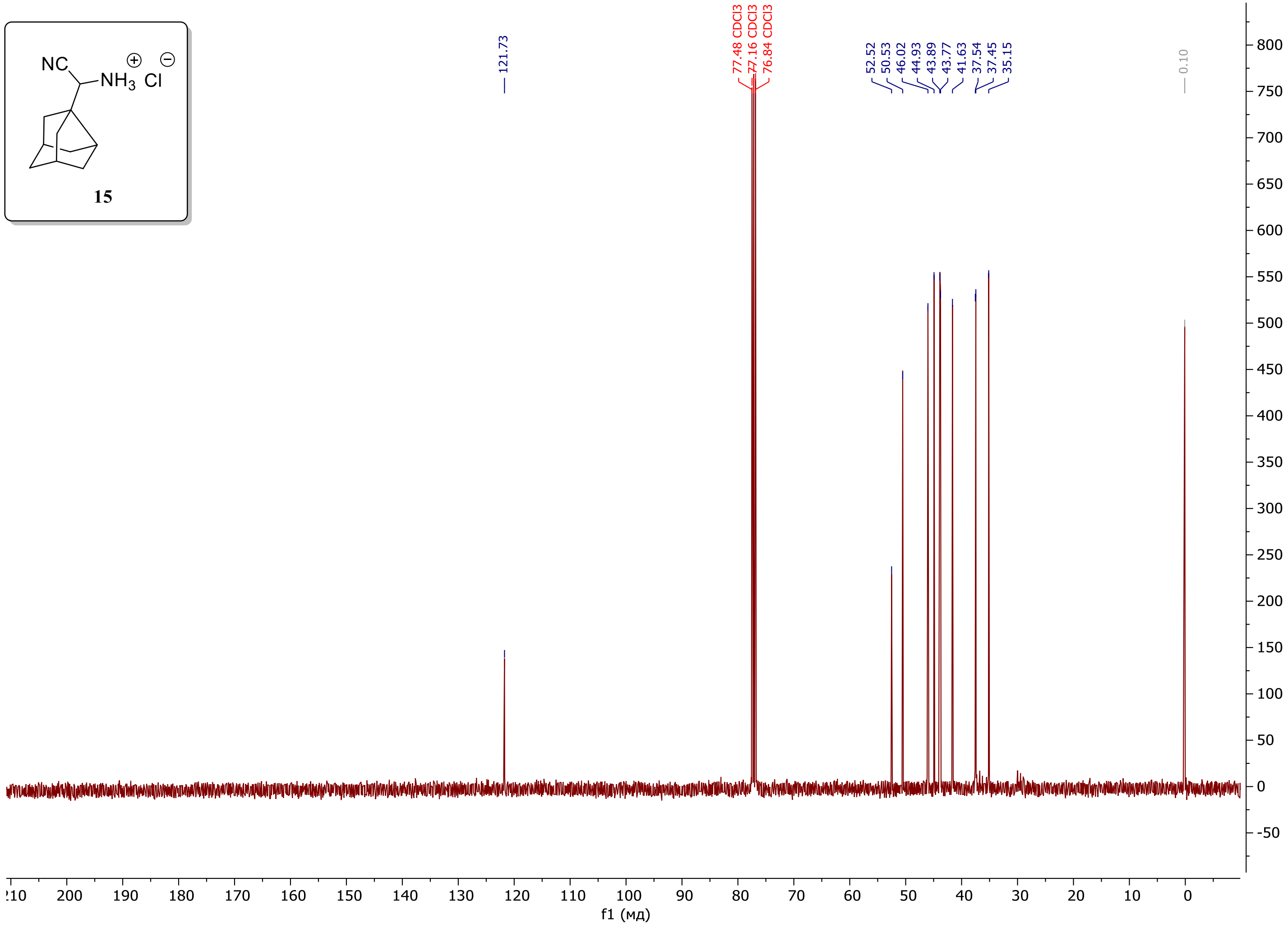

Cl
H2
N
Cl
Cl

14

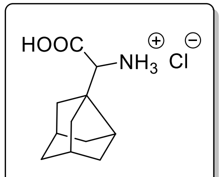
137.41
131.84
129.10
127.29
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
53.37
49.12
46.52
46.30
45.79
45.51
41.50
34.87
34.59
33.29
24.59
0.10
1900
1800
1700
1600
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (мд)

Compound 15

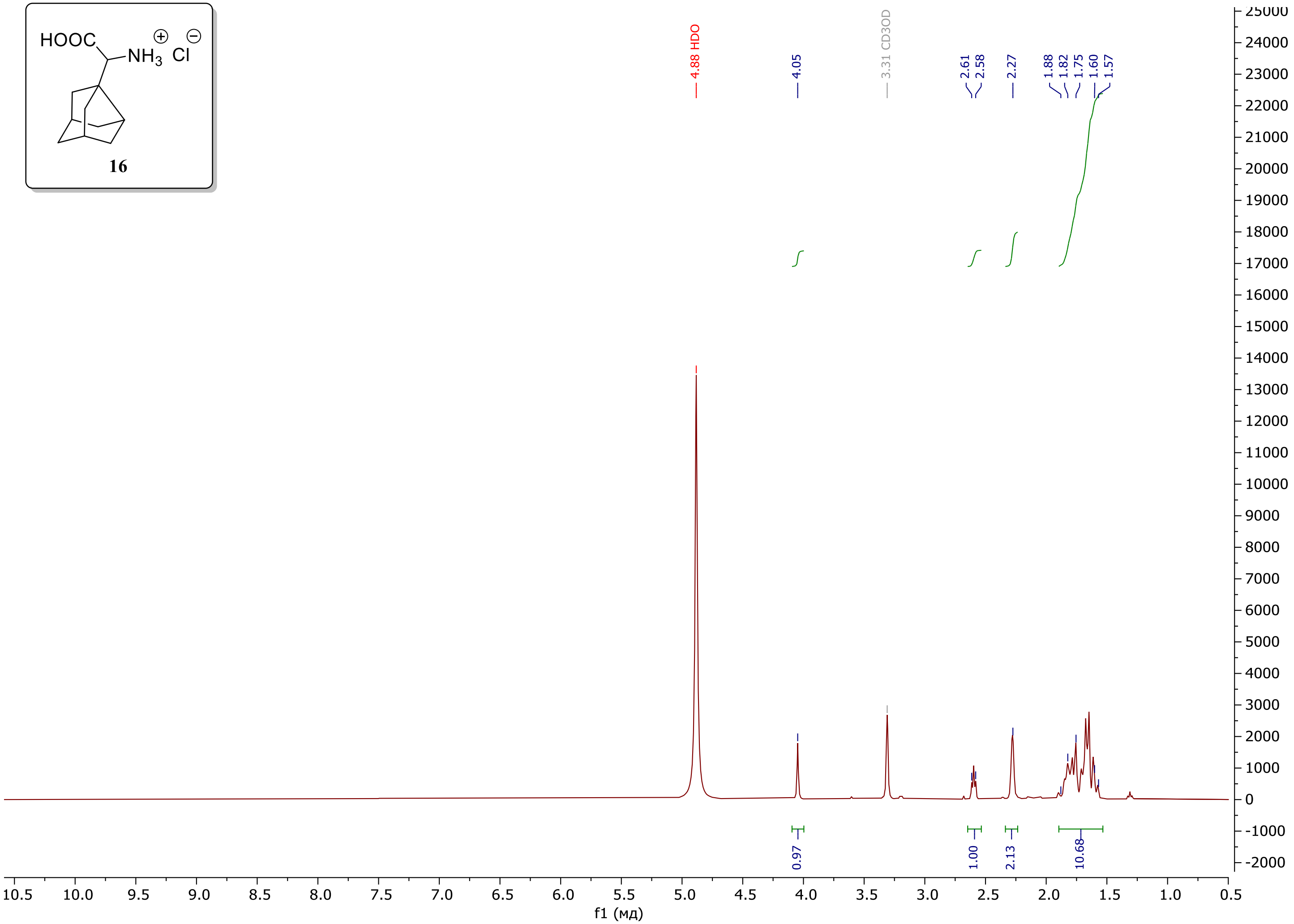

NC
NH3 Cl
15
7.26 CDCl3
3.72
2.31
2.26
1.85
1.82
1.74
1.69
1.64
1.61
1.00
3.34
13.47
18000
17000
16000
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (мд)


NC
NH3 Cl
15
121.73
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
52.52
50.53
46.02
44.93
43.89
43.77
41.63
37.54
37.45
35.15
0.10
f1 (мд)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
800
750
700
650
600
550
500
450
400
350
300
250
200
150
100
50
0
-50

Compound 16

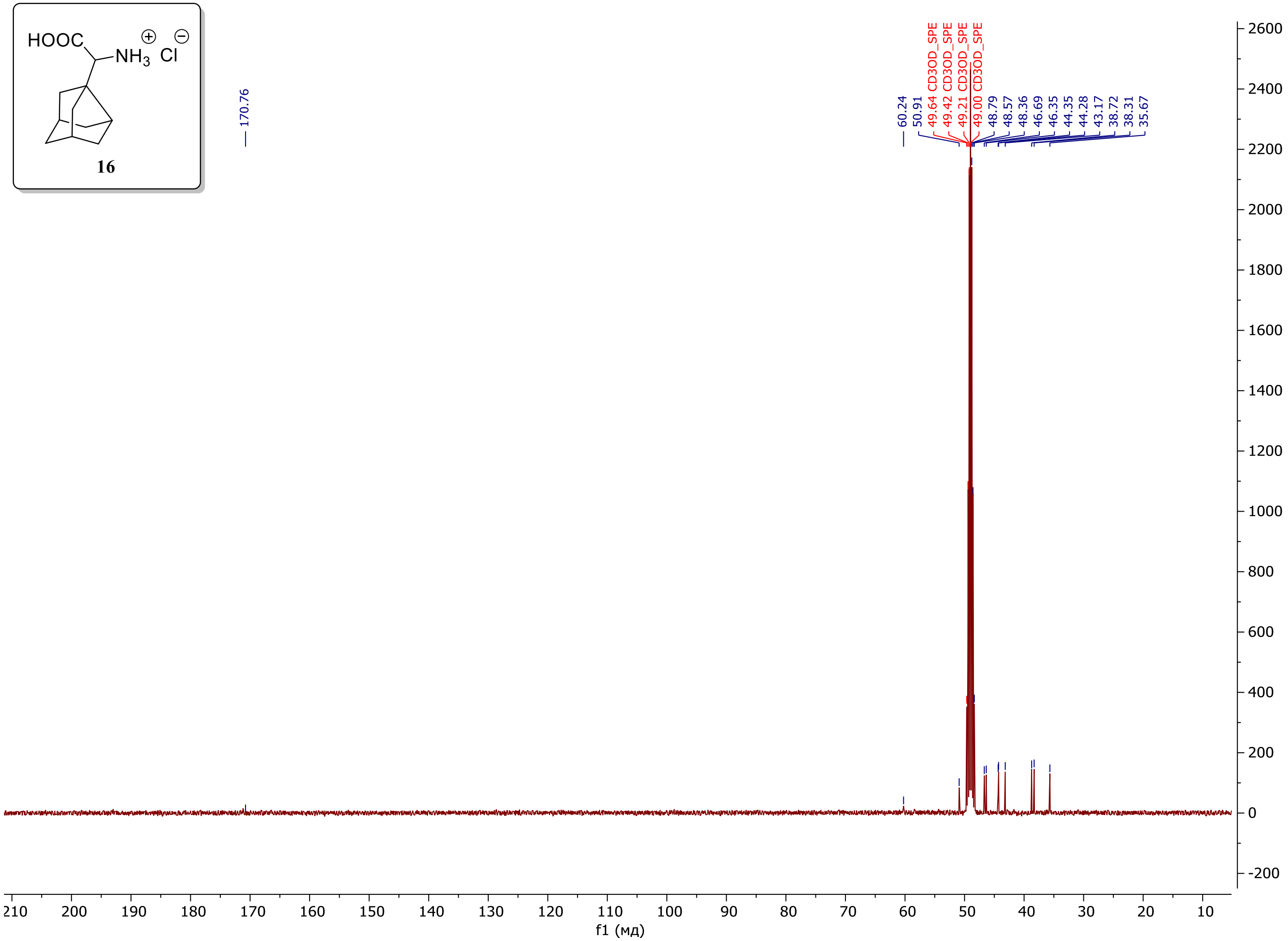


16

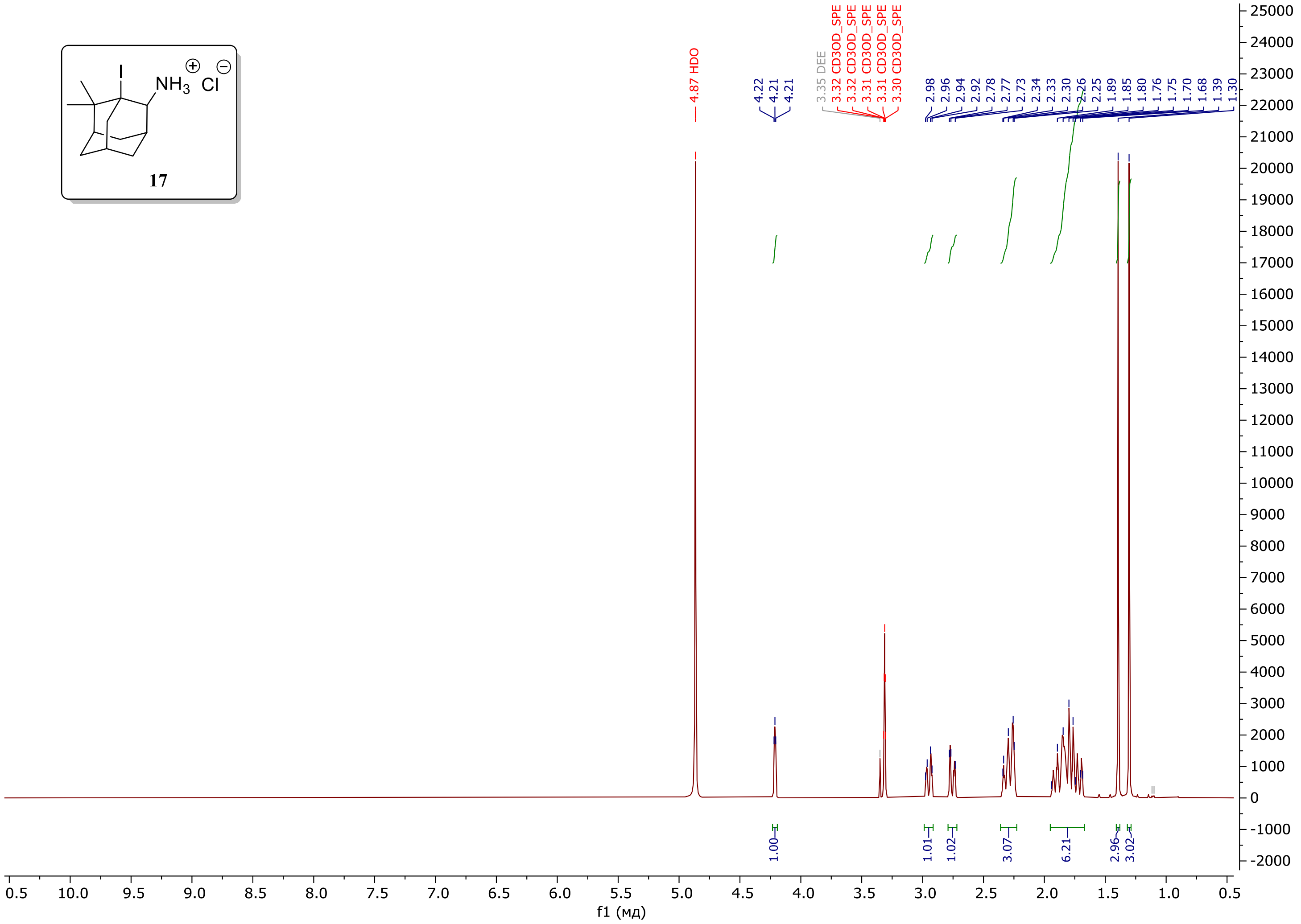


HOOC
NH3
Cl

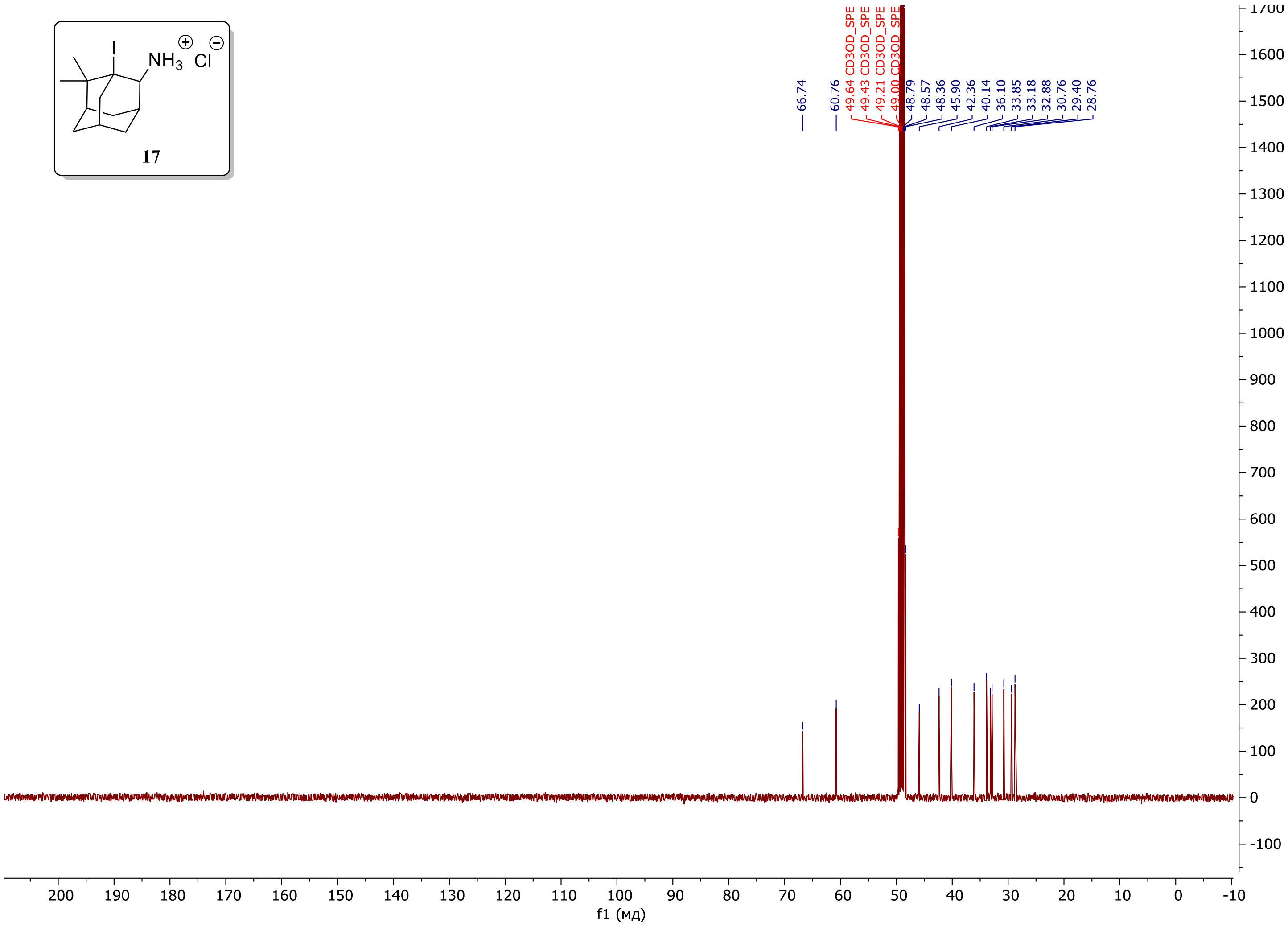
16


170.76
60.24
50.91
49.64 CD3OD_SPE
49.42 CD3OD_SPE
49.21 CD3OD_SPE
49.00 CD3OD_SPE
48.79
48.57
48.36
46.69
46.35
44.35
44.28
43.17
38.72
38.31
35.67
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
-200
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (мд)

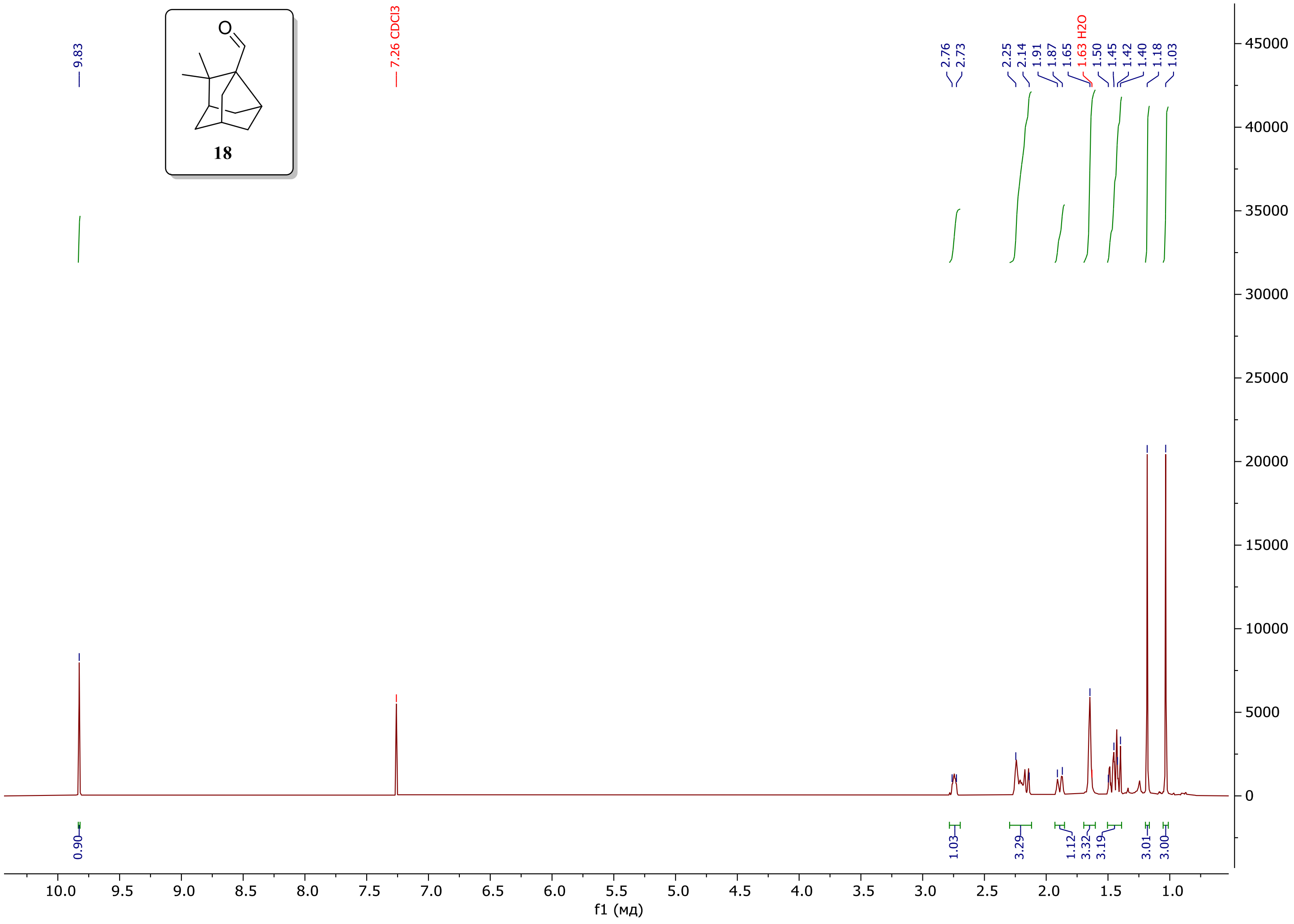
Compound 17



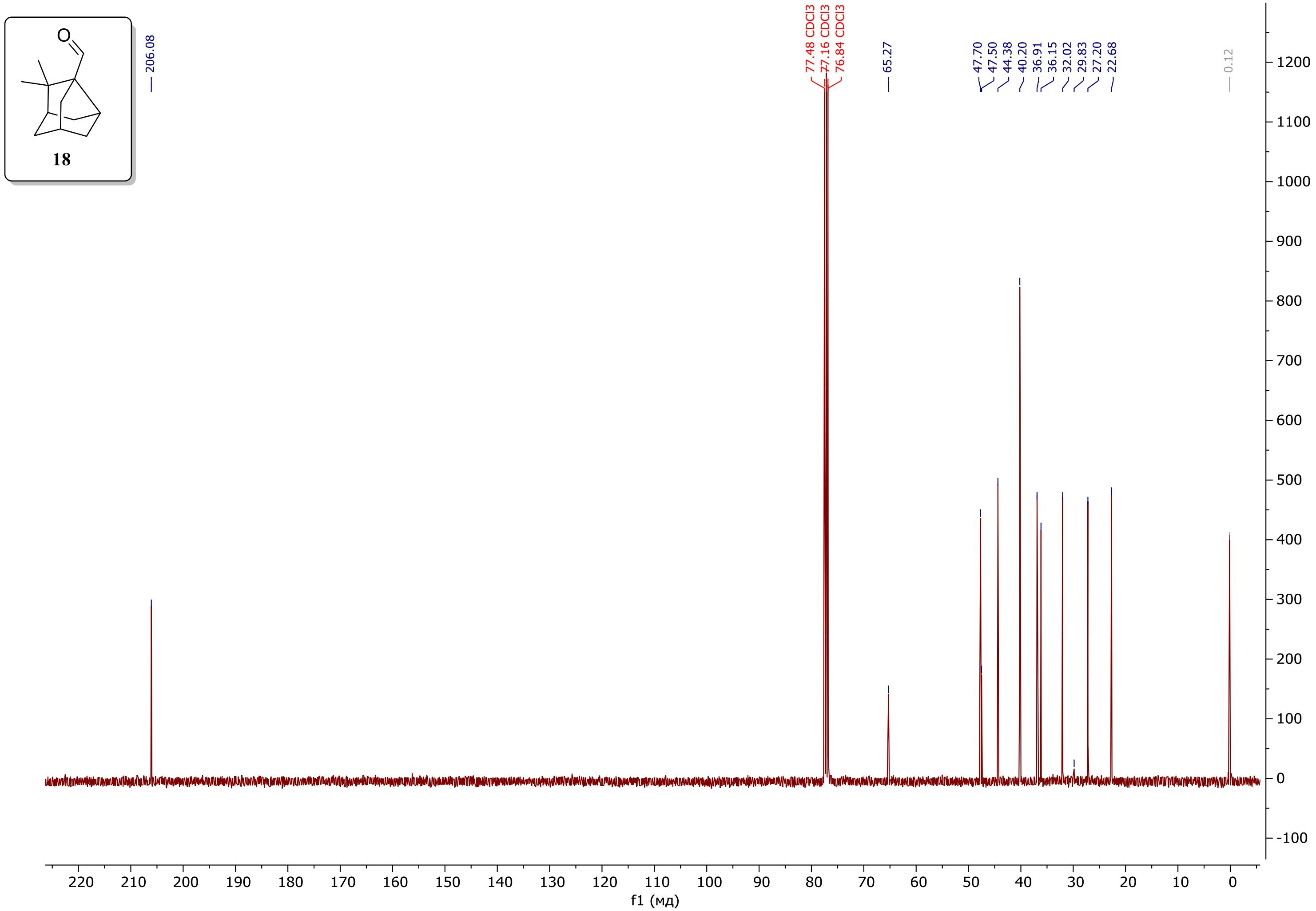
NH3
Cl
I
17
4.87 HDO
4.22
4.21
4.21
3.35 DEE
3.32 CD3OD_SPE
3.32 CD3OD_SPE
3.31 CD3OD_SPE
3.31 CD3OD_SPE
3.30 CD3OD_SPE
2.98
2.96
2.94
2.92
2.78
2.77
2.73
2.34
2.33
2.30
2.26
2.25
1.89
1.85
1.80
1.76
1.75
1.70
1.68
1.39
1.30
1.00
1.01
1.02
3.07
6.21
2.96
3.02
25000
24000
23000
22000
21000
20000
19000
18000
17000
16000
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
-2000
0.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (мд)


I
NH3 ⊕ Cl ⊖
17
66.74
60.76
49.64 CD3OD_SPE
49.43 CD3OD_SPE
49.21 CD3OD_SPE
49.00 CD3OD_SPE
48.79
48.57
48.36
45.90
42.36
40.14
36.10
33.85
33.18
32.88
30.76
29.40
28.76
1700
1600
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (мд)

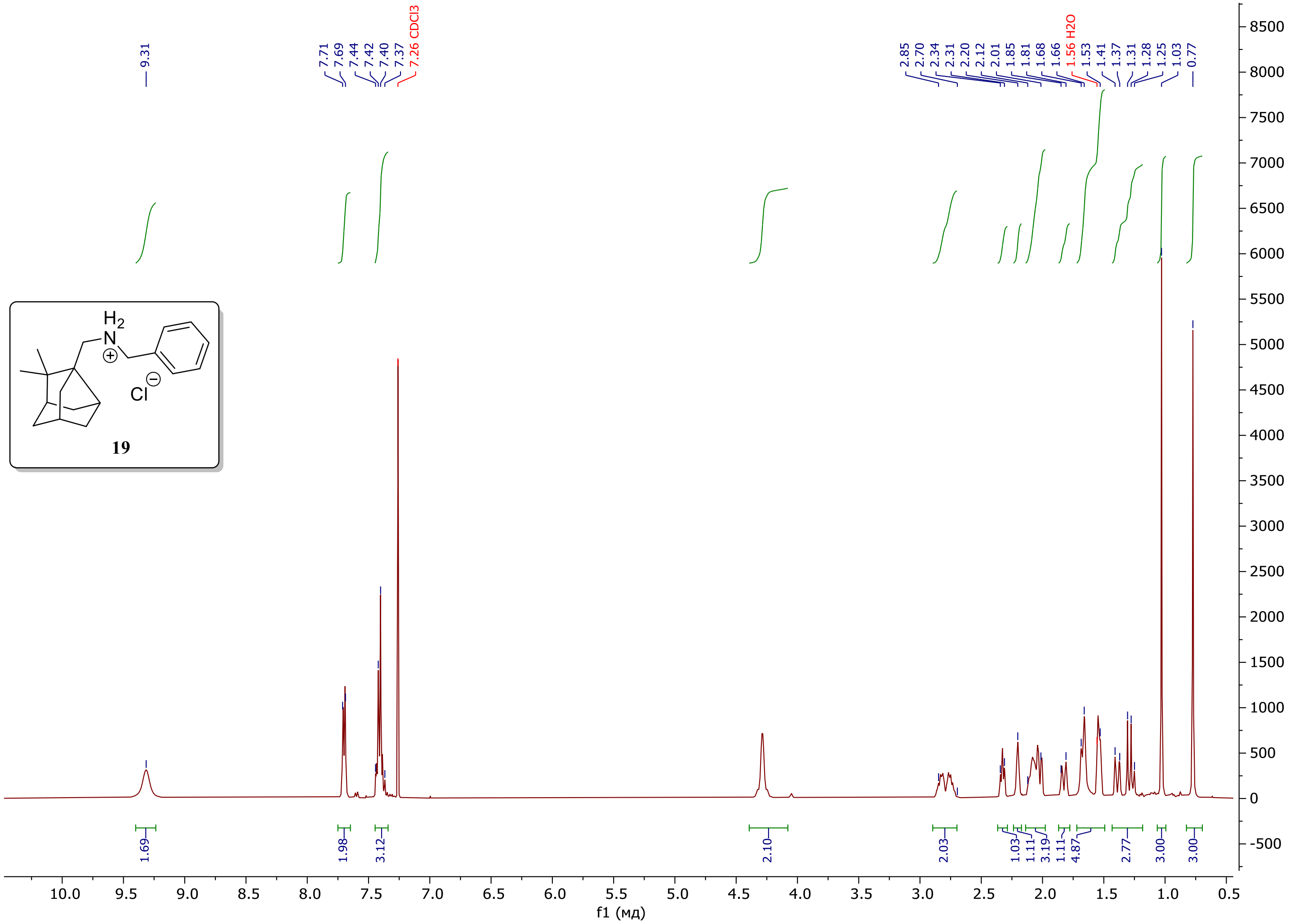
Compound 18

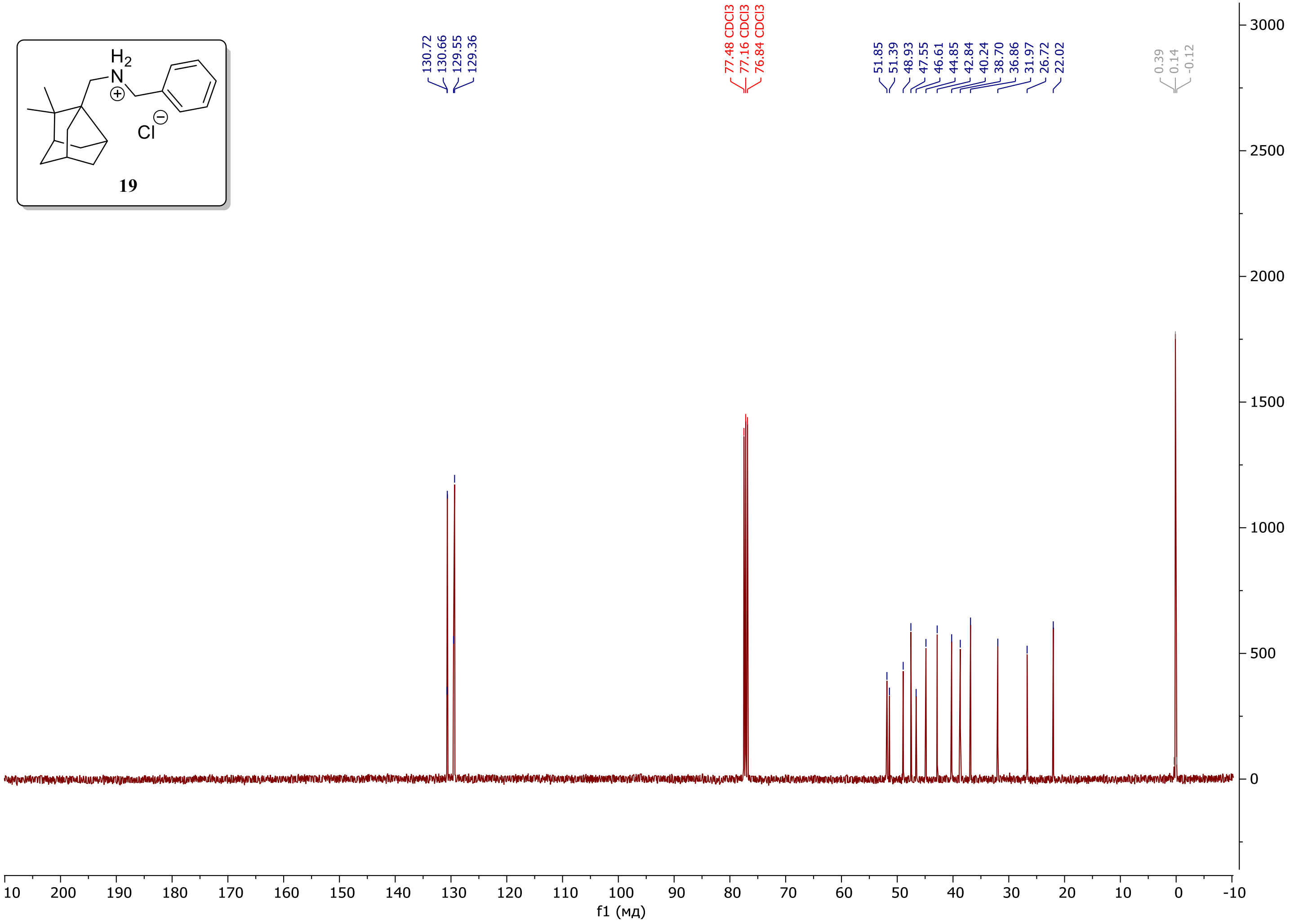


18
9.83
7.26 CDCl3
2.76
2.73
2.25
2.14
1.91
1.87
1.65
1.63 H2O
1.50
1.45
1.42
1.40
1.18
1.03
0.90
1.03
3.29
1.12
3.32
3.19
3.01
3.00
45000
40000
35000
30000
25000
20000
15000
10000
5000
0
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f1 (мд)

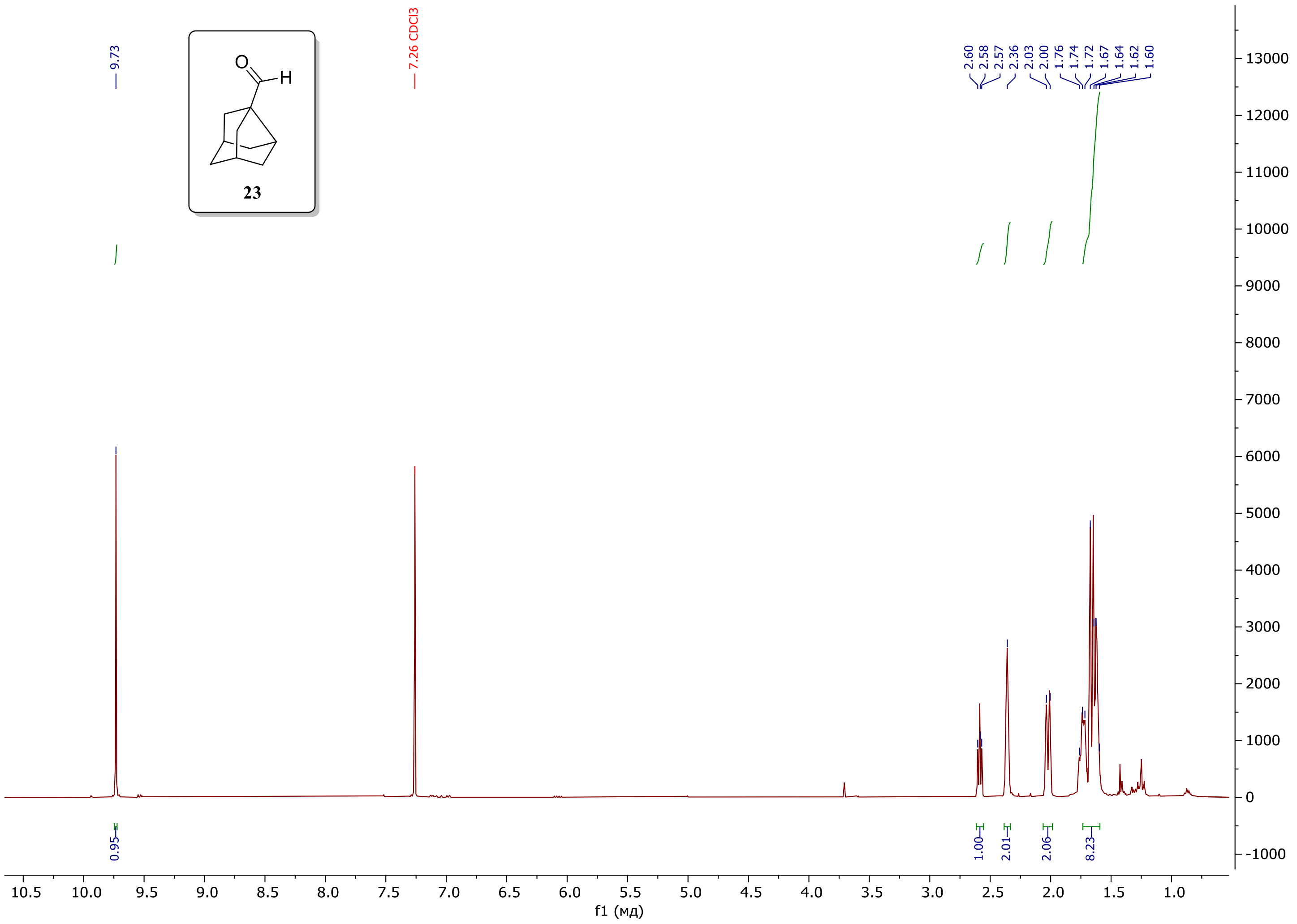

O
18
206.08
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
65.27
47.70
47.50
44.38
40.20
36.91
36.15
32.02
29.83
27.20
22.68
0.12
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (мд)

Compound 19

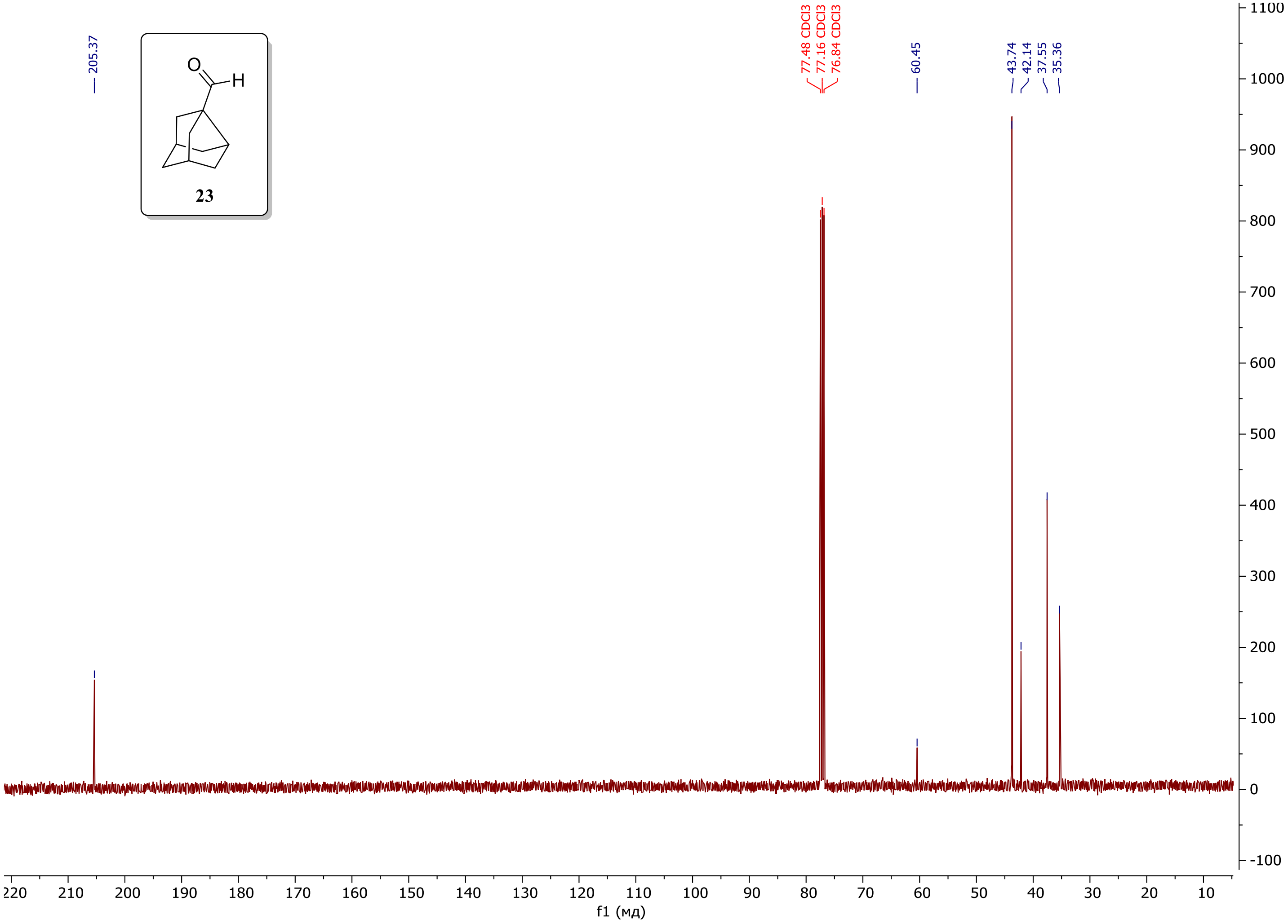

9.31
7.71
7.69
7.44
7.42
7.40
7.37
7.26 CDCl3
2.85
2.70
2.34
2.31
2.20
2.12
2.01
1.85
1.81
1.68
1.66
1.56 H2O
1.53
1.41
1.37
1.31
1.28
1.25
1.03
0.77
H2
N
+
Cl
−
19
1.69
1.98
3.12
2.10
2.03
1.03
1.11
3.19
1.11
4.87
2.77
3.00
3.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (мд)
8500
8000
7500
7000
6500
6000
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
-500


19
Cl
130.72
130.66
129.55
129.36
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
51.85
51.39
48.93
47.55
46.61
44.85
42.84
40.24
38.70
36.86
31.97
26.72
22.02
0.39
0.14
-0.12
3000
2500
2000
1500
1000
500
0
10
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (мд)

Compound 23



O
H
23
9.73
7.26 CDCl3
2.60
2.58
2.57
2.36
2.03
2.00
1.76
1.74
1.72
1.67
1.64
1.62
1.60
0.95
1.00
2.01
2.06
8.23
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f1 (мд)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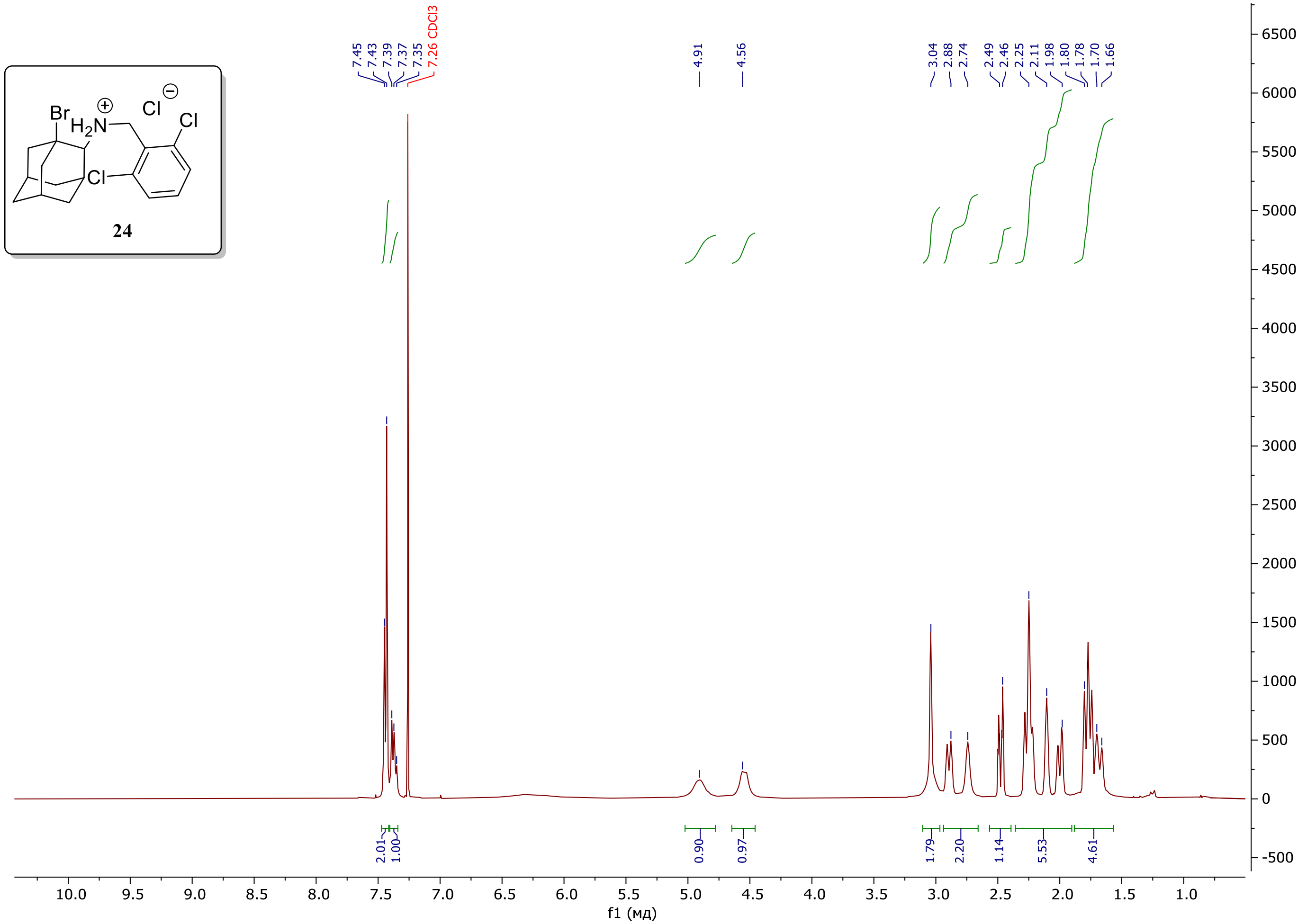
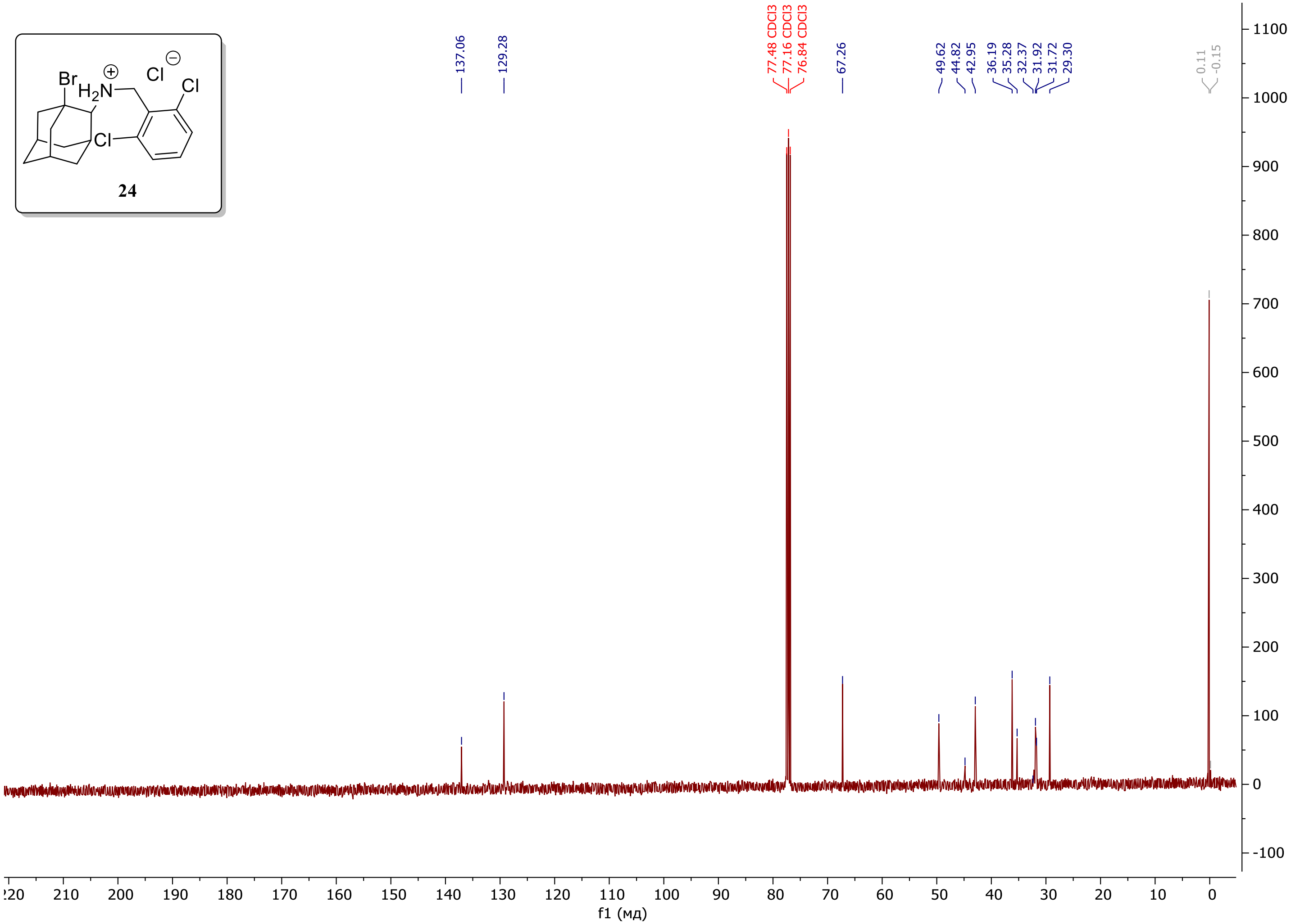
O
H
23
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
60.45
43.74
42.14
37.55
35.36
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (мд)

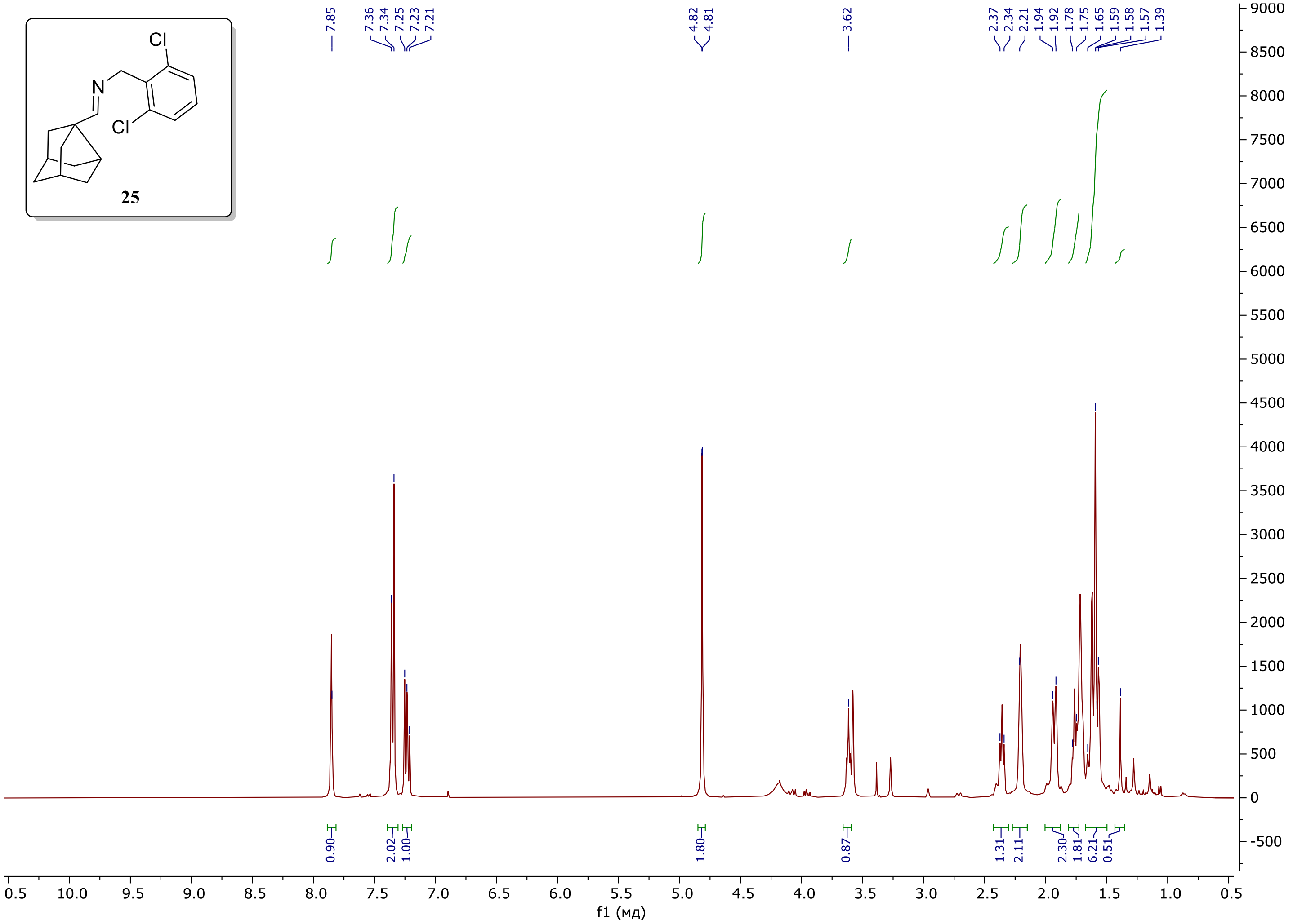
Compound 24



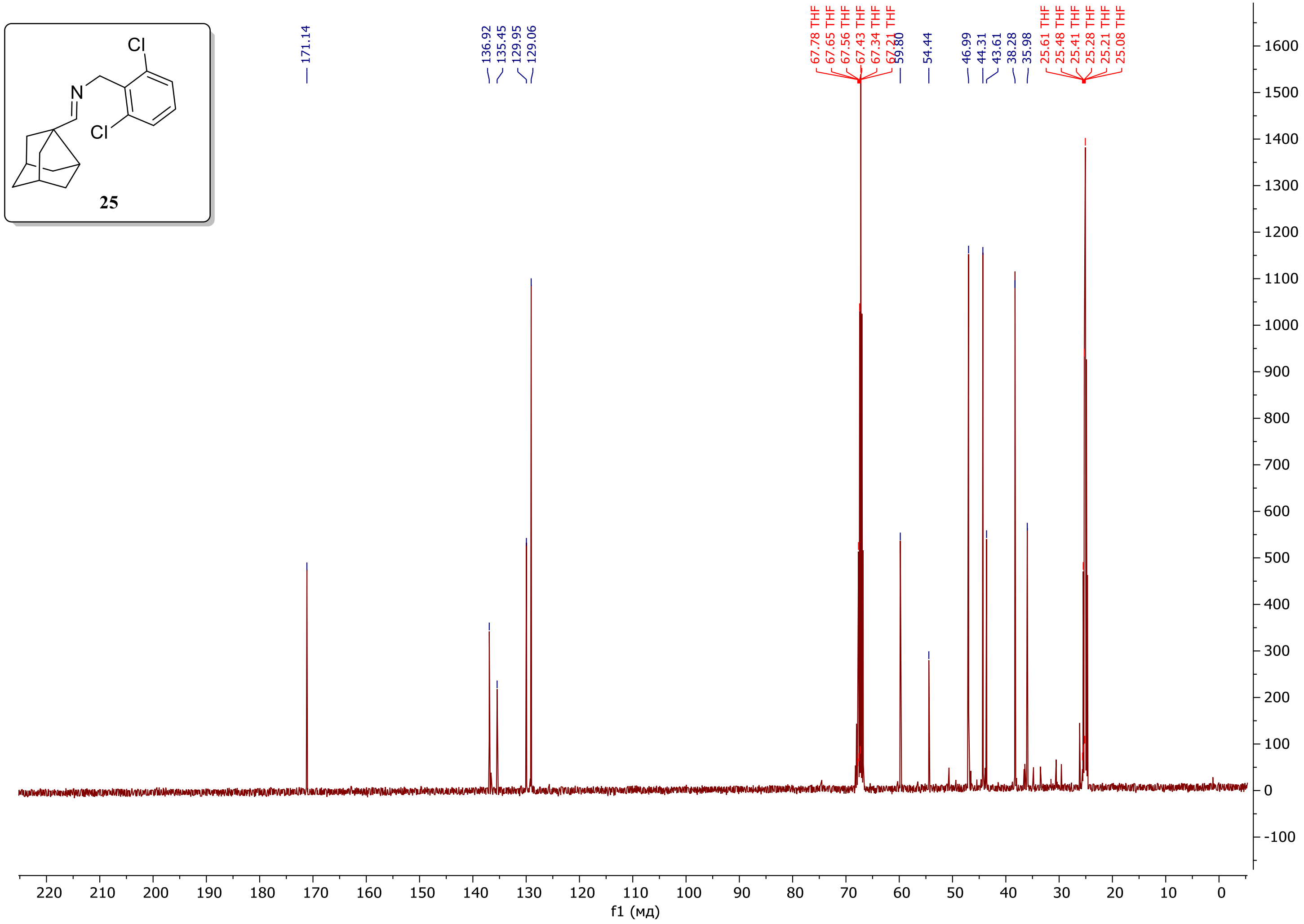
Br
H2N
Cl
Cl
Cl
24
7.45
7.43
7.39
7.37
7.35
7.26 CDCl3
4.91
4.56
3.04
2.88
2.74
2.49
2.46
2.25
2.11
1.98
1.80
1.78
1.70
1.66
2.01
1.00
0.90
0.97
1.79
2.20
1.14
5.53
4.61
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f1 (мд)
6500
6000
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
-500


Br
H2N⊕
Cl⊖
Cl
Cl
24
137.06
129.28
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
67.26
49.62
44.82
42.95
36.19
35.28
32.37
31.92
31.72
29.30
0.11
-0.15
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (мд)

Compound 25



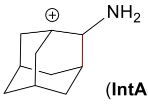
25


Cl
N
Cl
25
171.14
136.92
135.45
129.95
129.06
67.78 THF
67.65 THF
67.56 THF
67.43 THF
67.34 THF
67.21 THF
59.80
54.44
46.99
44.31
43.61
38.28
35.98
25.61 THF
25.48 THF
25.41 THF
25.28 THF
25.21 THF
25.08 THF
1600
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (мд)

5. DFT analyses

Geometric Structures and Electronic energies (Hartree)

IntA$^+$



(**IntA$^+$**)

Temperature 298.150 Kelvin. Pressure 1.00000 Atm.

Zero-point correction= 0.247133 (Hartree/Particle)

Thermal correction to Energy= 0.255753

Thermal correction to Enthalpy= 0.256697

Thermal correction to Gibbs Free Energy= 0.214776

Sum of electronic and zero-point Energies= -445.100782

Sum of electronic and thermal Energies= -445.092162

Sum of electronic and thermal Enthalpies= -445.091218

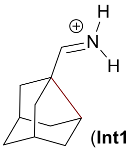
Sum of electronic and thermal Free Energies= -445.133139

Charge = 1 Multiplicity = 1

6	-1.391571000	-0.643739000	-0.368024000
1	-1.490529000	-1.661280000	-0.757837000
6	-0.392324000	0.118170000	-1.120040000
6	-0.534880000	-0.776452000	1.019077000
1	-1.191250000	-1.340963000	1.683494000
6	0.759789000	-1.538576000	0.735696000
1	0.548995000	-2.539163000	0.355486000
1	1.309864000	-1.672441000	1.669059000

6	0.764580000	-0.609641000	-1.621924000
1	1.350241000	-0.048576000	-2.345474000
1	0.533940000	-1.602952000	-1.997781000
6	1.615225000	-0.750017000	-0.258386000
1	2.525659000	-1.286204000	-0.523150000
6	1.915058000	0.659756000	0.254308000
1	2.507881000	0.596704000	1.169482000
1	2.517972000	1.213536000	-0.466846000
6	-0.240693000	1.528370000	-0.843786000
1	-1.169678000	2.043721000	-0.626525000
1	0.373842000	2.061505000	-1.563248000
6	-0.253066000	0.628667000	1.554207000
1	-1.179606000	1.162375000	1.754637000
1	0.280495000	0.548743000	2.503904000
6	0.607711000	1.394046000	0.550723000
1	0.780912000	2.422741000	0.864219000
7	-2.630853000	0.051269000	-0.116647000
1	-3.159360000	-0.391744000	0.624482000
1	-3.222377000	0.071615000	-0.938483000

Int1$^+$



(**Int1$^+$**)

Temperature 298.150 Kelvin. Pressure 1.00000 Atm.

Zero-point correction= 0.248560 (Hartree/Particle)

Thermal correction to Energy= 0.257231

Thermal correction to Enthalpy= 0.258176

Thermal correction to Gibbs Free Energy= 0.214975

Sum of electronic and zero-point Energies= -445.125833

Sum of electronic and thermal Energies= -445.117161

Sum of electronic and thermal Enthalpies= -445.116217

Sum of electronic and thermal Free Energies= -445.159418

Charge = 1 Multiplicity = 1

6	-0.029621000	1.252576000	-1.017267000
1	-0.594320000	2.166201000	-0.826598000
1	0.061286000	1.120741000	-2.093887000
6	-0.695000000	-0.000009000	-0.329523000
6	1.302452000	1.279519000	-0.255140000
1	1.881838000	2.172337000	-0.487205000
6	0.785019000	1.247859000	1.190313000
1	0.225373000	2.157220000	1.416413000
1	1.570477000	1.150329000	1.937597000
6	-0.120611000	0.000005000	1.150889000
1	-0.870823000	0.000005000	1.943840000
6	0.785032000	-1.247841000	1.190329000
1	1.570489000	-1.150292000	1.937612000
1	0.225396000	-2.157204000	1.416441000
6	-0.029608000	-1.252594000	-1.017251000
1	0.061298000	-1.120772000	-2.093872000

1	-0.594298000	-2.166223000	-0.826570000
6	2.116329000	0.000005000	-0.561669000
1	2.424851000	0.000000000	-1.609111000
1	3.030535000	0.000014000	0.034012000
6	1.302465000	-1.279514000	-0.255123000
1	1.881861000	-2.172328000	-0.487176000
6	-2.129598000	-0.000014000	-0.549057000
1	-2.493923000	-0.000032000	-1.573646000
7	-3.040359000	0.000004000	0.364428000
1	-2.792480000	0.000020000	1.346982000
1	-4.026201000	0.000001000	0.135169000

TS

Temperature 298.150 Kelvin. Pressure 1.00000 Atm.

Zero-point correction= 0.246238 (Hartree/Particle)

Thermal correction to Energy= 0.254558

Thermal correction to Enthalpy= 0.255502

Thermal correction to Gibbs Free Energy= 0.214064

Sum of electronic and zero-point Energies= -445.099699

Sum of electronic and thermal Energies= -445.091380

Sum of electronic and thermal Enthalpies= -445.090435

Sum of electronic and thermal Free Energies= -445.131873

Charge = 1 Multiplicity = 1

6	-1.497953000	-0.677923000	-0.289466000

1	-1.594207000	-1.752258000	-0.435512000
6	-0.477408000	-0.063960000	-1.068010000
6	-0.436716000	-0.594761000	1.143224000
1	-1.133044000	-1.049417000	1.845911000
6	0.818000000	-1.417697000	0.922443000
1	0.577398000	-2.460769000	0.711567000
1	1.399948000	-1.416282000	1.847420000
6	0.680208000	-0.871233000	-1.489497000
1	1.187203000	-0.428943000	-2.344810000
1	0.428510000	-1.905863000	-1.708903000
6	1.626335000	-0.798413000	-0.218463000
1	2.528898000	-1.368730000	-0.433607000
6	1.952731000	0.673514000	0.068123000
1	2.592778000	0.742329000	0.949795000
1	2.519768000	1.104682000	-0.758438000
6	-0.257523000	1.384535000	-0.997013000
1	-1.156953000	1.972785000	-0.844563000
1	0.300767000	1.762502000	-1.850160000
6	-0.154780000	0.863667000	1.449125000
1	-1.083712000	1.409427000	1.603602000
1	0.404478000	0.916408000	2.386651000
6	0.664807000	1.470971000	0.310161000
1	0.878940000	2.525405000	0.479991000
7	-2.696220000	0.019688000	-0.004161000
1	-3.425116000	-0.572439000	0.364537000
1	-3.058320000	0.571153000	-0.768119000

6. Crystallographic data collection and refinement details

The X-ray experimental data for **7** (73b-200) and **10I1** (rh82) were acquired on Bruker D8 VENTURE Kappa Duo PHOTON III by IμS micro-focus sealed tube either with MoKα (λ = 0.71073 Å) for 7 or CuKα (λ= 1.54178 Å) for 10i1 radiation at a low temperature. The structures were solved by direct methods (XT39a)[39a] and refined by full matrix least squares based on F2 (SHELXL201839b).[39b] The hydrogen atoms on carbon were fixed into idealized positions (riding model) and assigned temperature factors either Hiso(H) = 1.2 Ueq(pivot atom) or Hiso(H) = 1.5 Ueq (pivot atom) for methyl moiety. The hydrogens on N and O atoms were found on difference Fourier maps and refined under rigid-body assumption.

Crystal data for **7**: C11H20N·Cl·H2O, Mr = 219.74, Monoclinic, P21/c (No 14), a = 16.6281 (13) Å, b = 6.4734 (4) Å, c = 11.5542 (9) Å, β = 103.171 (3)°, V = 1210.98 (15) Å3 , Z = 4, Dx = 1.205 Mg m-3, colourles plate of dimensions 0.50 × 0.44 × 0.04 mm, temperature of the crystal 200K, multi-scan absorption correction (μ = 0.29 mm-1) Tmin = 0.88, Tmax = 0.99; a total of 10958 measured reflections (θmax= 27.5°), from which 2773 were unique (Rint = 0.029) and 2180 observed according to the I > 2σ(I) criterion. The refinement converged (Δ/σmax≤ 0.001) to R = 0.045 for observed reflections and wR(F2) = 0.123, GOF = 1.04 for 128 parameters and all 2773 reflections. The final difference map displayed no peaks of chemical significance (Δρmax = 0.46, Δρmin −0.39 e.Å-3).

The temperature of 200K was chosen for the measurement due to phase transition of the structure at lower temperature. At 120K the crystal exhibits splitting of diffractions accompany with change of lattice symmetry to triclinic one. The structure was solved in P -1 space group with two symmetrically independent molecules in the unit cell. Except smaller displacement parameters, all other geometric parameters (intra- and inter- atomic distances and angles) compares well with high temperature phase, therefore the structure at 120K was included only in the form of cif-file deposited into CSD with ccdc number 2194852.

Crystal data for **10I1**: C15H25NO2, Mr = 251.36, Monoclinic, P21/c (No 14), a = 12.2381 (5) Å, b = 11.7529 (6) Å, c = 10.0683 (4) Å, V = 1398.00 (11) Å3 , Z = 4, Dx = 1.194 Mg m-3, colourles needle of dimensions 0.28 × 0.05 × 0.04 mm, temperature of the sample 120K, multi-scan absorption correction (μ = 0.61 mm-1) Tmin = 0.85, Tmax = 0.97; a total of 31666 measured reflections (θmax= 66.6°), from which 4600 were unique (Rint = 0.034) and 3745 observed according to the I > 2σ(I) criterion. The refinement converged (Δ/σmax≤ 0.004) to R = 0.046 for observed reflections and wR(F2) = 0.109, GOF = 1.05 for 267 parameters and all 4600 reflections. The final difference map displayed no peaks of chemical significance (Δρmax = 0.29, Δρmin −0.21 e.Å-3). The measured crystal was refined as non-merohedral twin with the domains ration 0.67:0.33.The influence of real structure of the crystal of 10i1 on diffraction pattern is not expresed only by twinning but also by disorder by major part of the molecule of 10i1. However the second position is occupied only by 12% of molecules suggesting the idea, that the driving force of disorder is rather the entrophy instead equality of minima of energy for both orientations.

X-ray crystallographic data have been deposited with the Cambridge Crystallographic Data Centre (CCDC) under deposition numbers 2194850 and 2194851 for 7 and 10i1, respectively and can be obtained free of charge from the Centre via its website (www.ccdc.cam.ac.uk/getstructures).

References:

[39a] SHELXT: Sheldrick, G.M. (2015). Acta Cryst. A71, 3-8.

[39] SHELXL: Sheldrick, G.M. (2015). Acta Cryst. C71, 3-8.

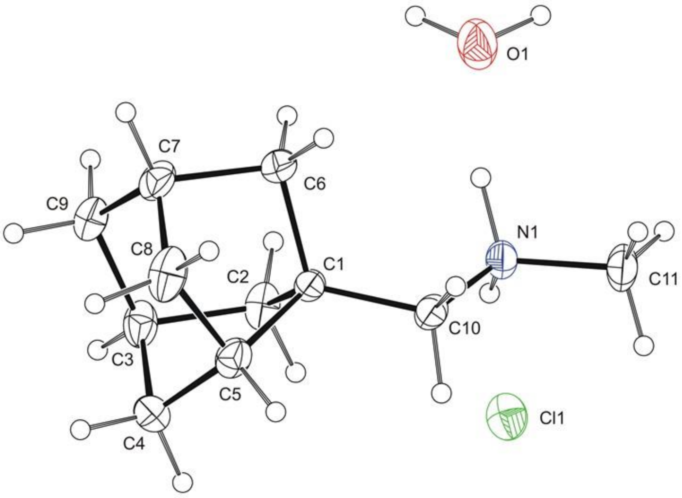


Fig.1 View on the molecule of **7** with atom numbering schema. The displacement ellipsoids are drawn on 30% probability level.

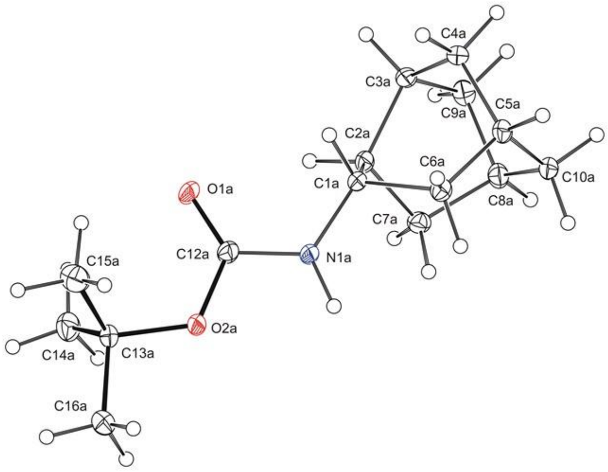


Fig.2 View on the molecule of **10I1** with atom numbering schema. The displacement ellipsoids are drawn on 30% probability level. The second positions of disordered atoms are omitted for clarity.