Electronic supplementary materials *Mendeleev Commun.*, 2022, **32**, 537–539

Synthesis and crystal structures of novel glycoluril carboxylic acids conglomerates

Vladimir V. Baranov, Tatyana N. Vol'khina, Natalya G. Kolotyrkina and Angelina N. Kravchenko

General

All reagents including KOCN, urea, 1,3-dimethylurea, glyoxal (aqueous 40%), HCl (aqueous 36.5%), (*R*,*S*)-Val, (*R*,*S*)-*nor*-Val were obtained from commercial sources and used without additional purification. Melting points were determined in a GALLENKAMP instrument (Sanyo). The IR spectra were recorded on a Bruker "Alpha" spectrometer in the range 400 – 4000 cm^{-1} (resolution 2 cm^{-1}). ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AM-300 spectrometer (300 and 75 MHz, respectively) in DMSO-d_6 with TMS as internal standard. High resolution mass spectra were recorded on a Bruker MicroTOF II instrument in positive ion mode (capillary voltage 4500 V) using electrospray ionization (ESI) and methanol as a solvent.

Synthesis of racemate 1a and 5-isopropylimidazolidine-2,4-dione (4a)

Hydrochloric acid (0.3 ml, 36% aq.) was added to a suspension of *rac*-3-methyl-2-ureidobutanoic acid **3a** (1.60 g, 0.01 mol) and 4,5-dihydroxyimidazolidin-2-one **2a** (1.18 g, 0.01 mol) in a mixture of H_2O (10 ml) and $Pr^{i}OH$ (10 ml). The mixture was refluxed for 2 h, cooled and left for 48 h, the solid **1a** was filtered off. The crystals of hydantoin **4a** were isolated from the filtrate and crystallized from H_2O. The crystals **1a** were obtained by crystallization from MeOH.

1a: Colorless crystals, yield 16% (0.39 g), mp 261-263 °C (MeOH). IR (KBr) ν = 3396, 3276, 3081, 1746, 1722, 1662, 1490, 1456, 1388, 1349, 1295, 1266, 1247, 1206, 1174, 1133, 1116, 999, 977, 924, 908, 885, 861, 817, 777, 761, 713, 626, 531 cm^{-1}. ^{1}H NMR: (300 MHz, DMSO-

d_6) δ 0.91 (d, 3H, ^3J = 6.8 Hz, Me), 0.93 (d, 3H, ^3J = 6.9 Hz, Me), 2.11 – 2.20 (m, 1H, CH), 3.92 (d, 1H, ^3J = 9.6 Hz, CH), 5.28 (d, 1H, ^3J = 8.3 Hz, CH), 5.52 (d, 1H, ^3J = 8.4 Hz, CH), 7.31 (s, 1H, NH), 7.39 (s, 1H, NH), 7.54 (s, 1H, NH), 12.20 – 13.30 (br.s, 1H, COOH). ^{13}C NMR: (75 MHz, DMSO-d_6) δ 19.64, 19.84 (Me), 27.75, 61.01, 62.68, 67.19 (CH), 159.43, 161.28 (C=O), 172.14 (COOH). HRMS (ESI): *m/z* calcd for $C_9H_{14}N_4O_4$+H^+: 243.1088; found: 243.1088; calcd for $C_9H_{14}N_4O_4$+Na^+: 265.0907; found: 265.0906.

4a: Colorless needle crystals, yield 78% (1.11 g), mp 145 – 146 °C (H_2O:Pr^iOH (1:1)), ^{1}H NMR: (300 MHz, DMSO-d_6) δ 0.80 (d, 3H, ^3J = 6.8 Hz, Me), 0.94 (d, 3H, ^3J = 7.0 Hz, Me), 1.91 – 2.09 (m, 1H, CH(Pr^i)), 3.91 (dd, 1H, ^3J = 3.5 Hz, ^3J = 1.4 Hz, CH), 7.90 (s, 1H, NH), 10.52 – 10.68 (br.s, 1H, NH). These spectral data are similar to ^{1}H NMR: (400 MHz, DMSO-d_6) obtained from "Integrated Spectral Data Base System of Organic Compounds" data were obtained from the National Institute of Advanced Industrial Science and Technology (Japan). Spectrum ID: WHSP43568 for compound (CAS RN: 16935-34-5).

Synthesis of racemate 1b and 5-propylimidazolidine-2,4-dione (4b)

Hydrochloric acid (0.3 ml, 35% aq.) was added to a suspension of *rac*-2-ureidopentanoic acid **3b** (1.60 g, 0.01 mol) and DHI **2b+2'b** (1.46 g, 0.01 mol) in a mixture of H_2O (10 ml) and Pr^iOH (10 ml). The mixture was refluxed for 2 h, cooled and left for 48 h. Crystals of hydantoin **4b** were filtered off The filtrate was lefted for 48 h at room temperature, the formed precipitate **1b** was filtered. The solid **1b** was recrystallized from H_2O:Pr^iOH (1:1).

1b: Colorless crystals, yield 7% (0.19 g), mp 240-242 °C. IR (KBr) ν = 3369, 1710, 1649, 1502, 1467, 1413, 1397, 1371, 1314, 1259, 1228, 1190, 1171, 1100, 1083, 1038, 986, 940, 890, 865, 810, 787, 762, 733, 697, 671, 637, 620, 579, 553 cm^{-1}. ^{1}H NMR: (300 MHz, DMSO-d_6) δ 0.90 (t, 3H, ^3J = 7.3 Hz, Me), 1.22 – 1.42 (m, 2H, CH_2), 1.83 – 2.03 (m, 2H, CH_2), 2.67 (s, 3H, Me), 2.77 (s, 3H, Me), 4.03 (dd, 1H, ^2J = 10.0 Hz, ^3J = 5.2 Hz, CH), 5.14 (s, 2H, CH-CH), 7.77 (s, 1H, NH), 12.55 – 13.80 (br.s, 1H, COOH). ^{13}C NMR: (75 MHz, DMSO-d_6) δ 13.63, 27.86, 29.82 (Me), 19.34, 30.22 (CH_2), 55.99, 66.17, 72.14 (CH), 158.36, 160.03 (C=O), 173.02 (COOH). HRMS (ESI): *m/z* calcd for $C_{11}H_{18}N_4O_4$+H^+: 271.1401; found: 271.1398; calcd for $C_{11}H_{18}N_4O_4$+Na^+: 293.1220; found: 293.1216.

4b: Colorless needle crystals, yield 71% (1.01 g), mp 137 – 138 °C (H_2O:Pr^iOH (1:1)), ^{1}H NMR: (300 MHz, DMSO-d_6) δ 0.89 (t, 3H, ^3J = 7.3 Hz, Me), 1.28 – 1.40 (m, 2H, CH_2), 1.42 – 1.57 (m, 1H, CH_2), 1.59 – 1.70 (m, 1H, CH_2), 3.96 – 4.03 (m, 1H, CH), 7.97 (s, 1H, NH), 10.60 (s, 1H, NH). The spectral data are similar to ^{1}H NMR: (408 K, 300 MHz, DMSO-d_6) obtained from Enamine Ltd. Spectrum ID: Z104495354 for compound (CAS RN: 18227-41-3).

Synthesis of 4,5-dihydroxy-1,3-dimethylimidazolidin-2-ones (2b+2'b)

A solution of KOH in H_2O (1 M) was added to a solution of 1,3-dimethylurea (13.2 g, 0.15 mol) in 40% aqueous glyoxal (17.2 ml, 0.15 mol) at pH 11. The mixture was stirred at 50–55 °C for 5 h and evaporated to dryness. The resulting solid was triturated with acetone. The mixture **2b** (*trans*-isomer) **+ 2'b** (*cis*-isomer) (ratio 15:1) was filtered off and dried in air.

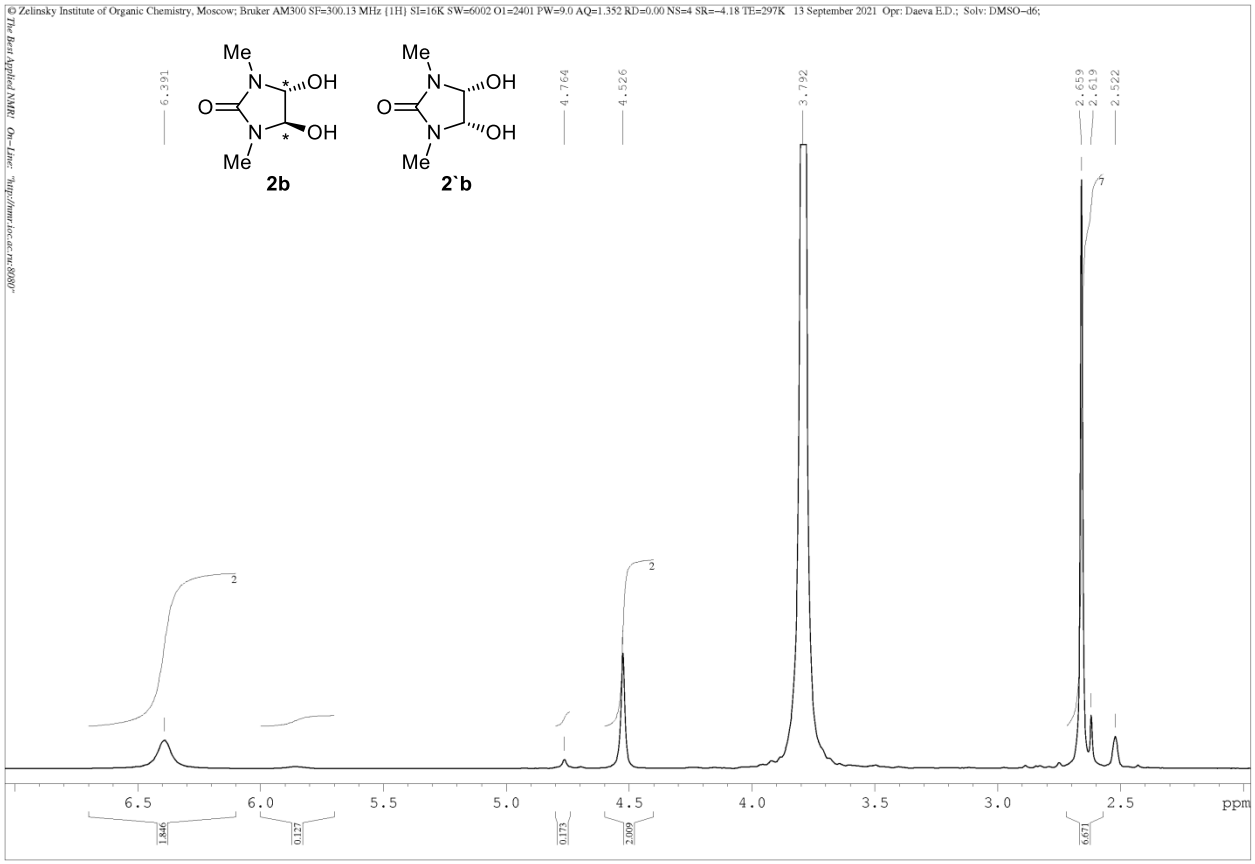
(2b+2'b): Light beige solid, yield 95% (20.80 g), mp 141–143 °C. ^{1}H NMR: (300 MHz, DMSO-d_6) δ 2.62 (s, 6H, Me (**2`b**)), 2.66 (s, 6H, Me (**2b**)), 4.53 (s, 2H, CH-CH (**2b**)), 4.74 (s, 2H, CH-CH (**2`b**)), 5.76 – 5.97 (br.s, 2H, OH (**2`b**)), 6.14 – 6.62 (br.s, 2H, OH (**2b**)). The spectral data are similar to ^{1}H NMR (500 MHz, DMSO-d_6) obtained from John Wiley & Sons, Inc. Spectrum ID: CB3_004186 for compound (CAS RN: 3923-79-3).

General procedure for the synthesis of compounds 3a,b

Potassium cyanate (8.505 g, 0.105 mol) by was added slowly portionwise to a boiling solution (*R,S*)-Val (11.7 g, 0.1 mol) or (*R,S*)-*nor*-Val (11.7 g, 0.1 mol) in water (200 ml) and refluxed for 20 min. The mixture was cooled to 10 °C with the ice bath. Hydrochloric acid (10.6 ml, 35%) was added dropwise to adjust pH to 1. The obtained white powder of product **3a** or **3b** was filtered off and washed with H_2O (10 ml) and dried in air.

3-Methyl-2-ureidobutanoic acid (3a): White powder, yield 91% (14.56 g), mp 175-177 °C. IR (KBr) ν = 3455, 3353, 3297, 1689, 1633, 1575, 1469, 1401, 1309, 1175, 1164, 1136, 1102, 1011, 971, 929, 902, 777, 723, 595, 581, 516 cm^{-1}. ^{1}H NMR: (300 MHz, DMSO-d_6) δ 0.84 (d, 3H, ^3J = 6.8 Hz, Me), 0.88 (d, 3H, ^3J = 6.8 Hz, Me), 1.91 – 2.09 (m, 1H, CH), 4.00 (dd, 1H, ^2J = 8.6 Hz, ^3J = 5.0 Hz, CH), 5.62 (c, 1H, NH), 6.21 (d, 2H, ^3J = 8.7 Hz, NH_2). ^{13}C NMR: (75 MHz, DMSO-d_6) δ 17.68, 19.19 (Me), 30.33, 57.48 (CH), 158.63 (C=O), 174.17 (COOH). HRMS (ESI): *m/z* calcd for $C_6H_{12}N_2O_3$+H^+: 161.0921. Found: 161.0915; calcd for $C_6H_{12}N_2O_3$+Na^+: 183.0740. Found: 183.0740.

2-Ureidopentanoic acid (3b): White powder, yield 89% (14.24 g), mp 170-172°C. IR (KBr) ν = 3450, 3293, 1694, 1636, 1560, 1468, 1450, 1405, 1382, 1366, 1309, 1293, 1256, 1218, 1165, 1128, 1096, 1056, 996, 921, 838, 779, 747, 726, 677, 619, 572 cm^{-1}. ^{1}H NMR: (300 MHz, DMSO-d_6) δ 0.85 (t, 3H, ^3J = 7.2 Hz, Me), 1.20 – 1.36 (m, 2H, CH_2), 1.43 – 1.65 (m, 2H, CH_2), 3.97 – 4.07 (m, 1H, CH), 5.60 (s, 2H, NH_2), 6.35 (d, 1H, ^3J = 8.0 Hz, NH). ^{13}C NMR: (75 MHz, DMSO-d_6) δ 14.05 (Me), 18.90, 34.42 (CH_2), 52.63 (CH), 159.38 (C=O), 175.52 (COOH). HRMS (EI): *m/z* calcd for $C_6H_{12}N_2O_3$+H^+: 161.0921. Found: 161.0927; calcd for $C_6H_{12}N_2O_3$+Na^+: 183.0740. Found: 183.0752.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© The Best Applied NMR On-Line: "http://nmr.ioc.ac.ru:8080/"
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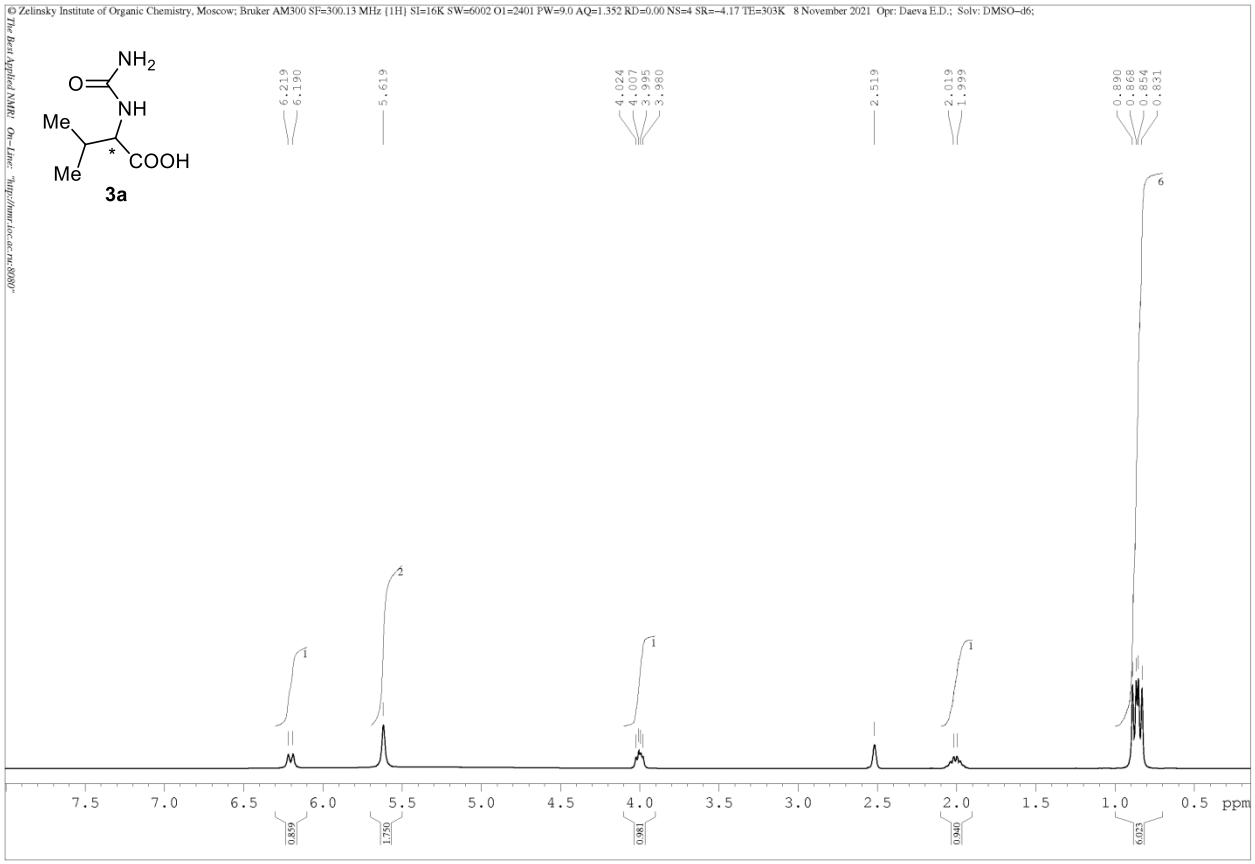
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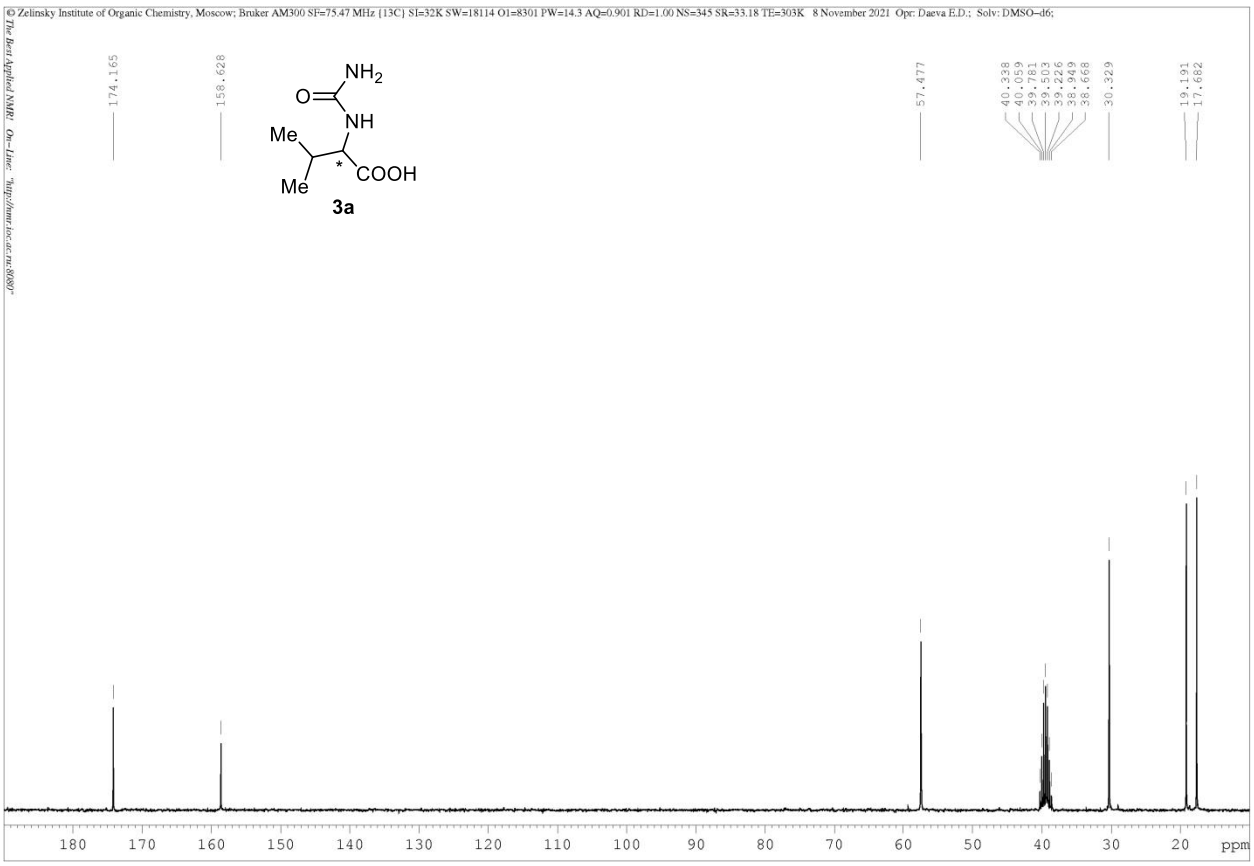

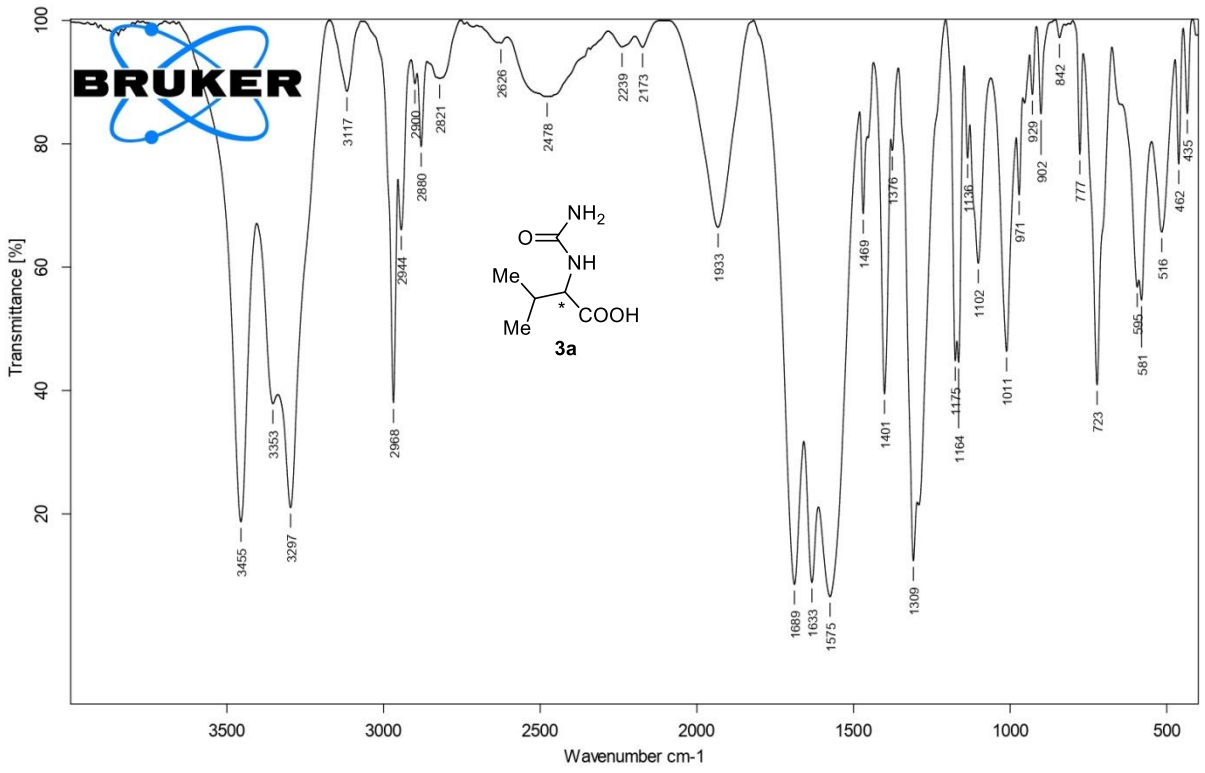

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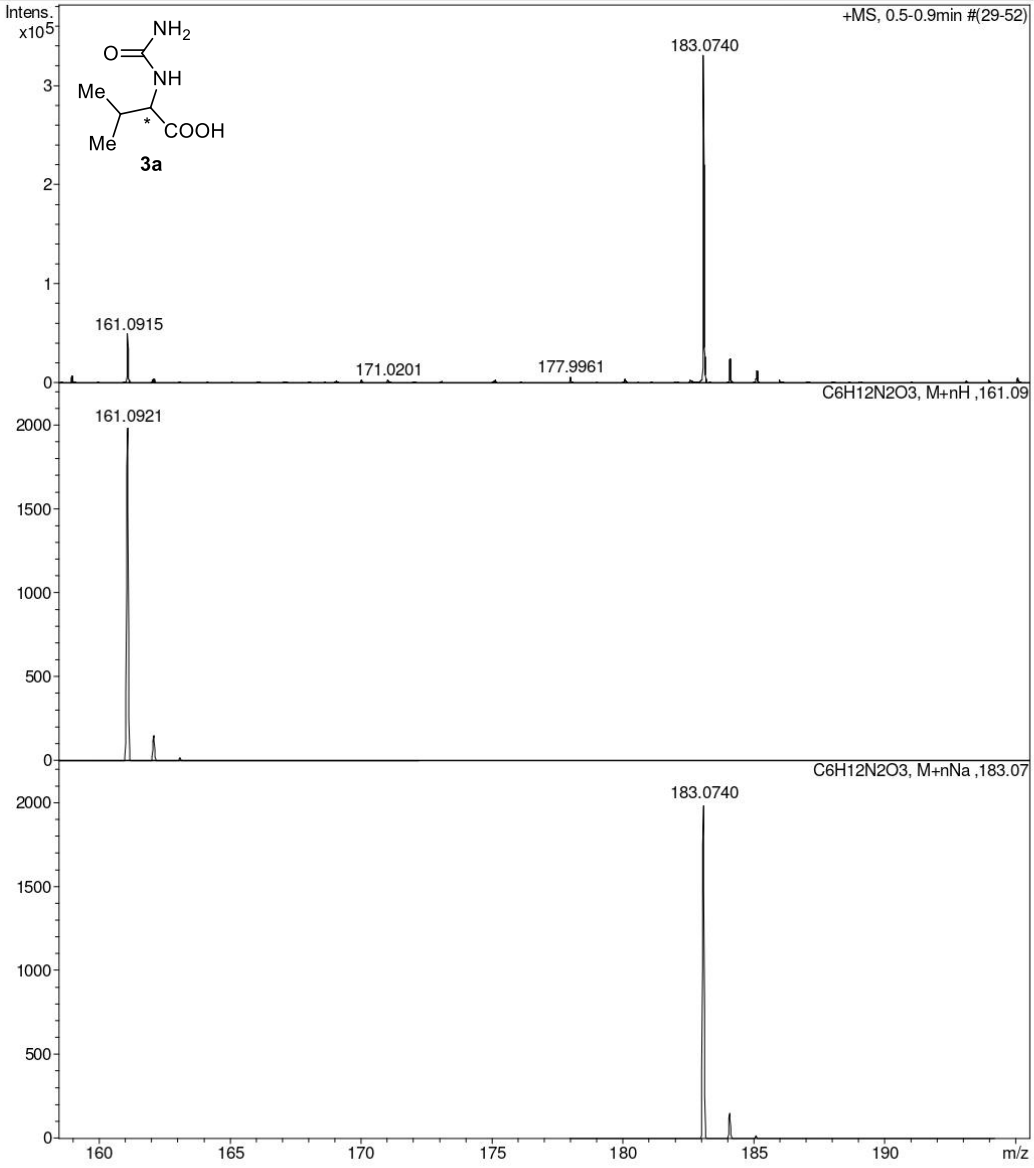

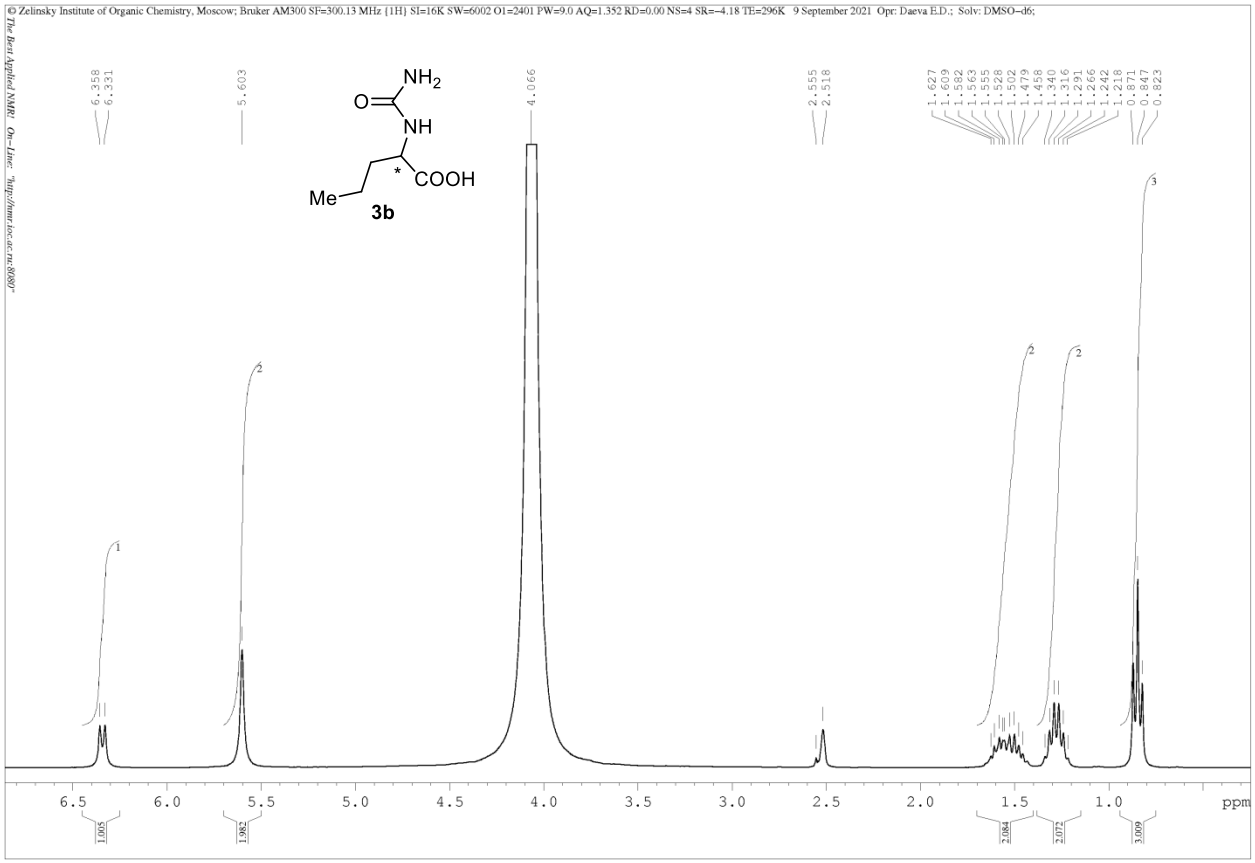
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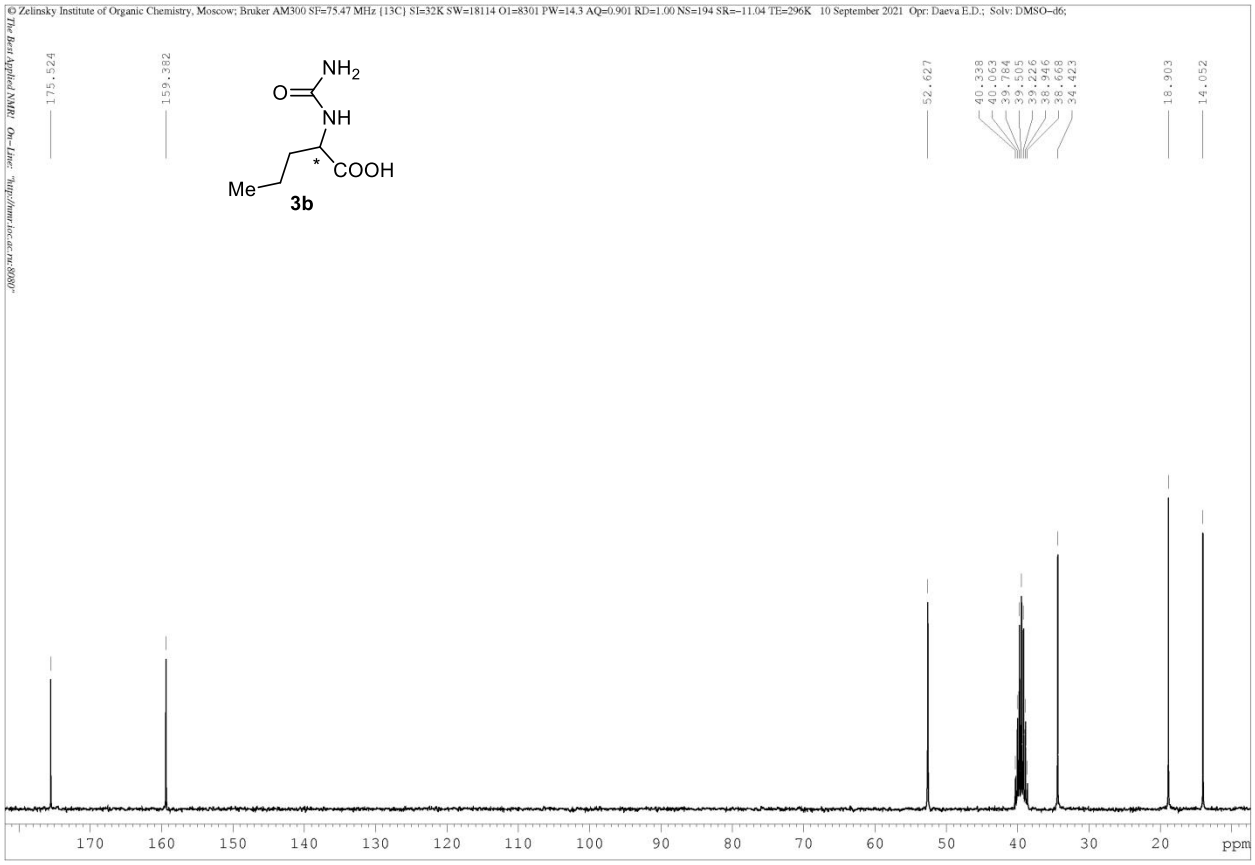
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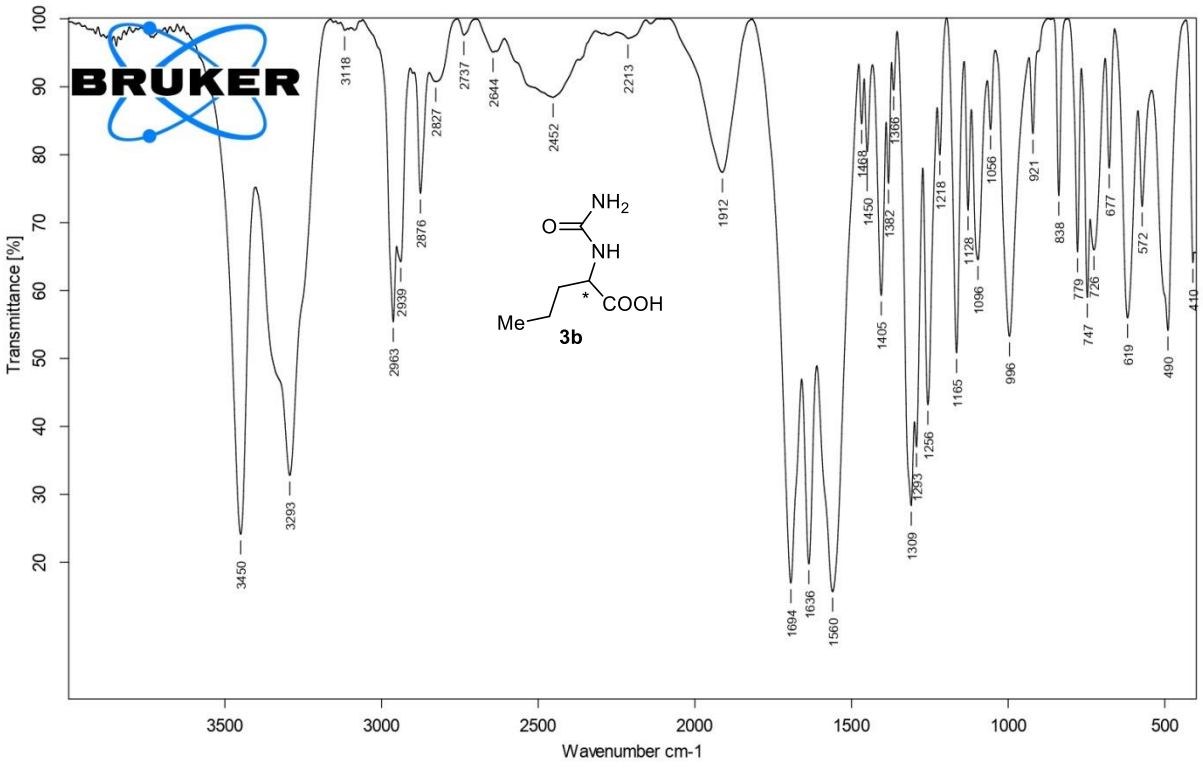

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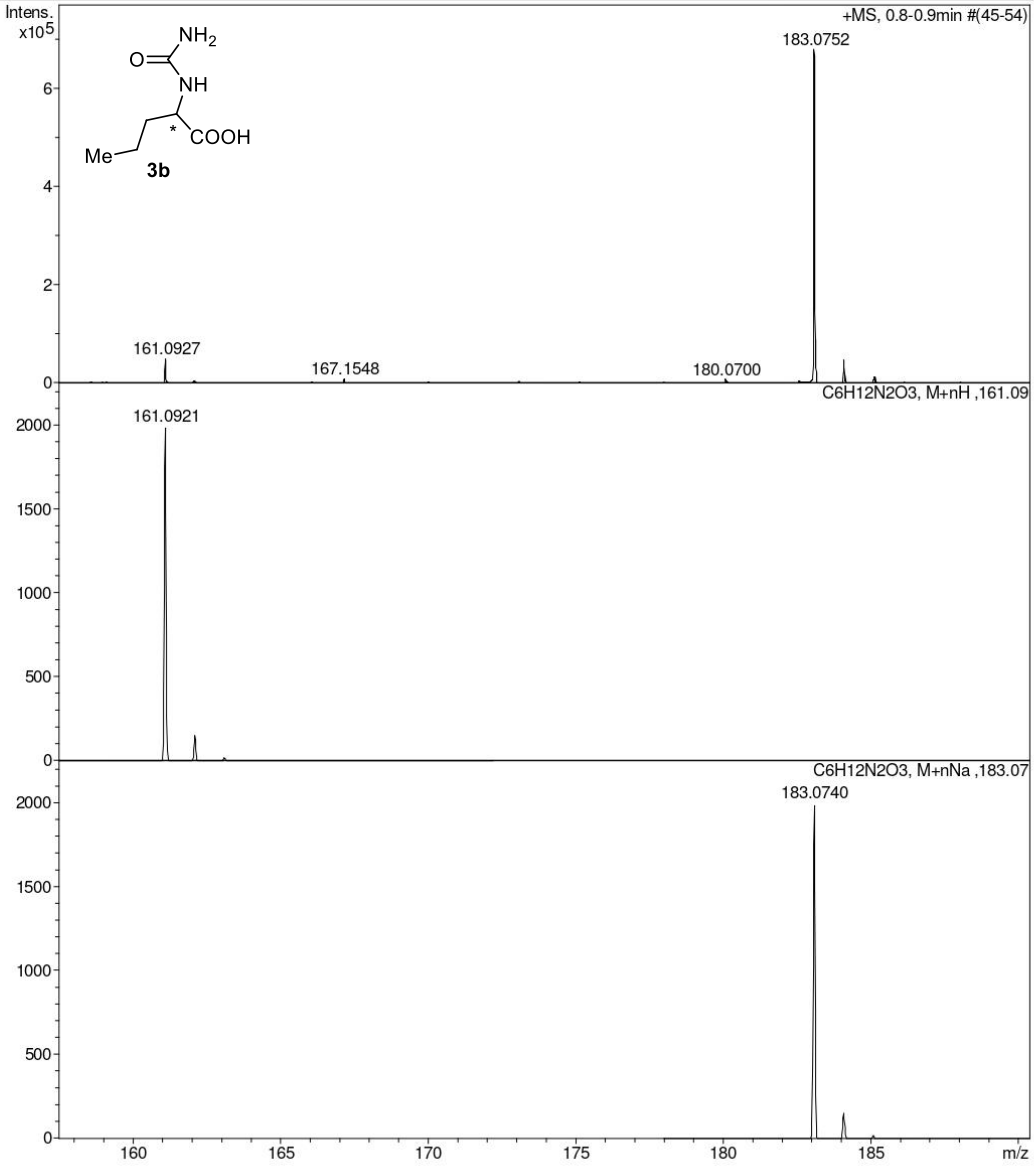

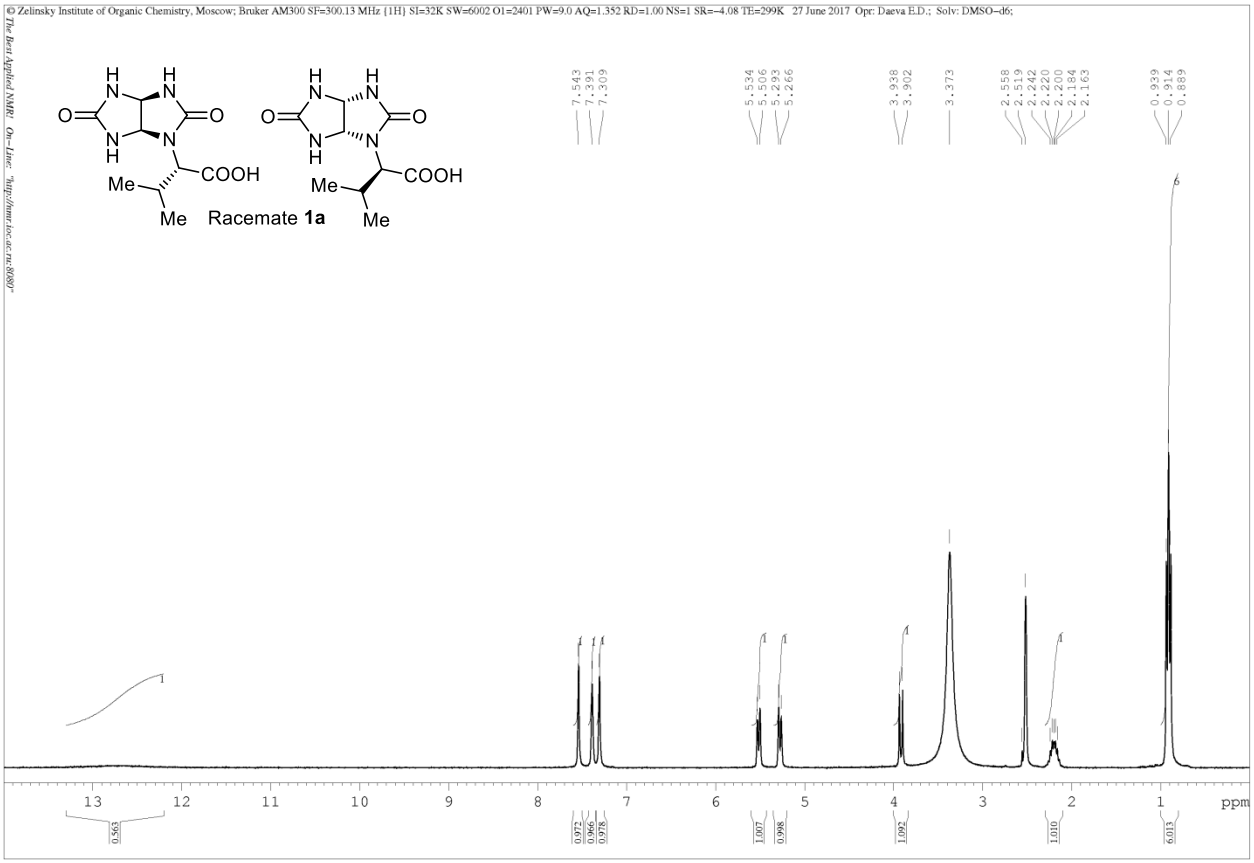
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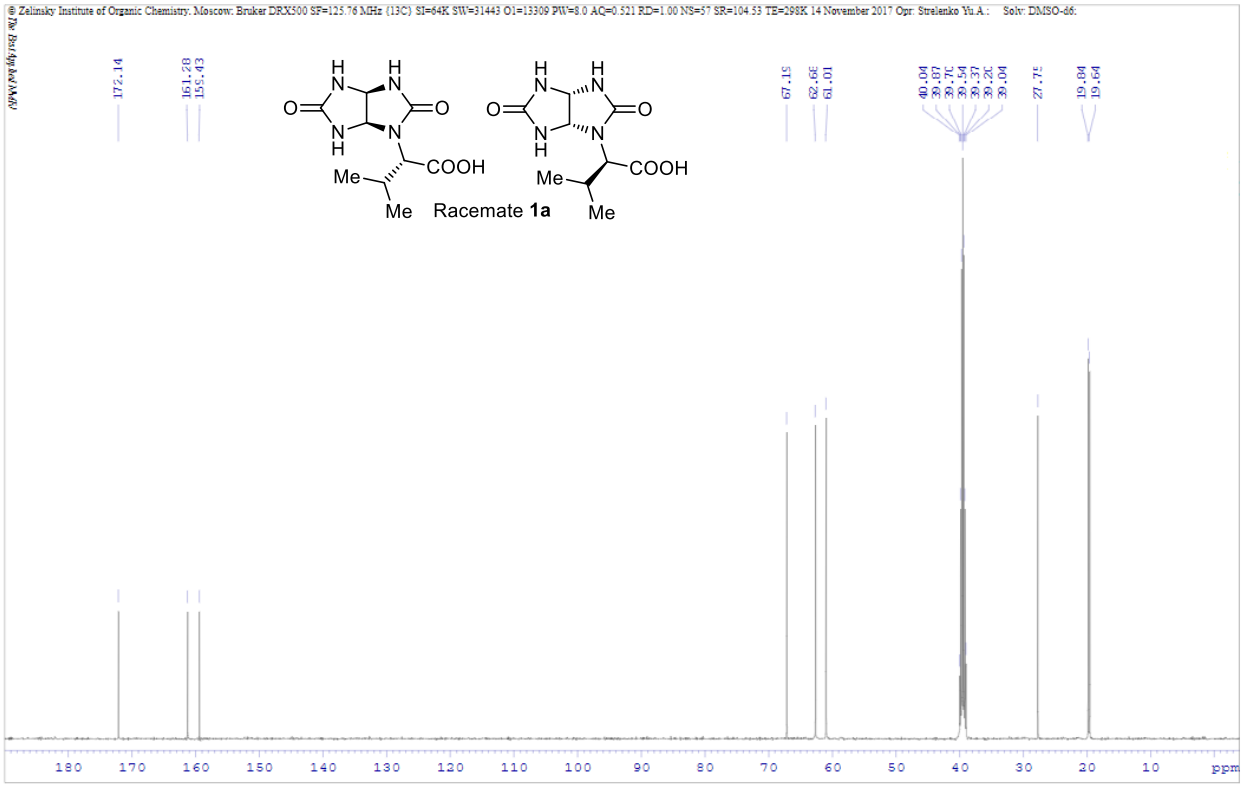
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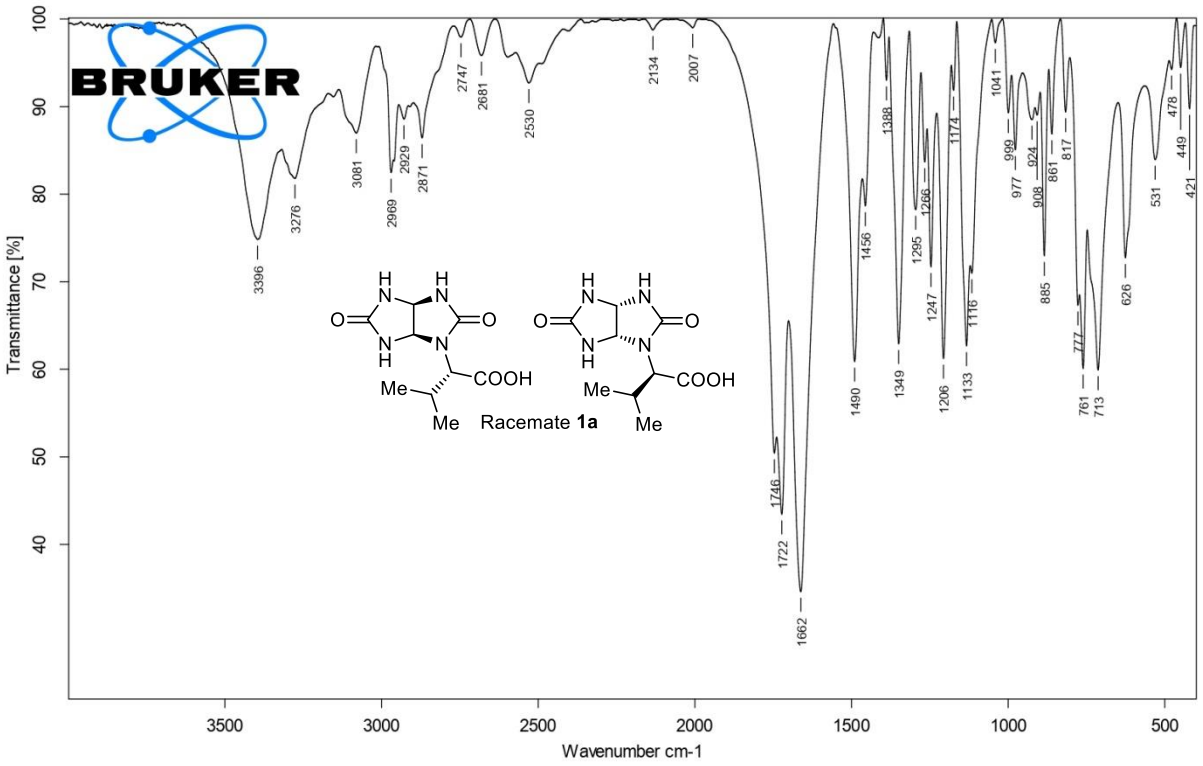

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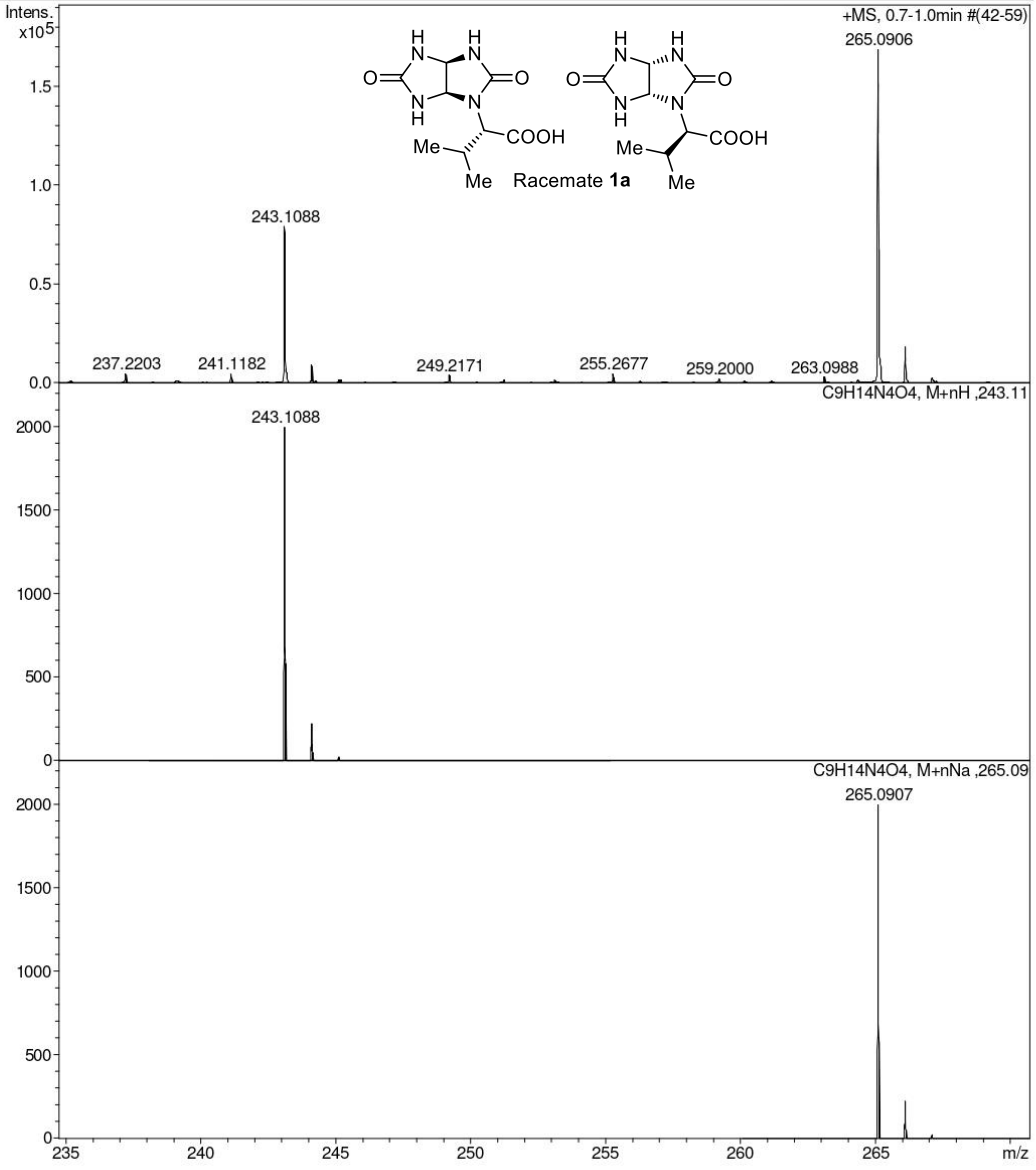

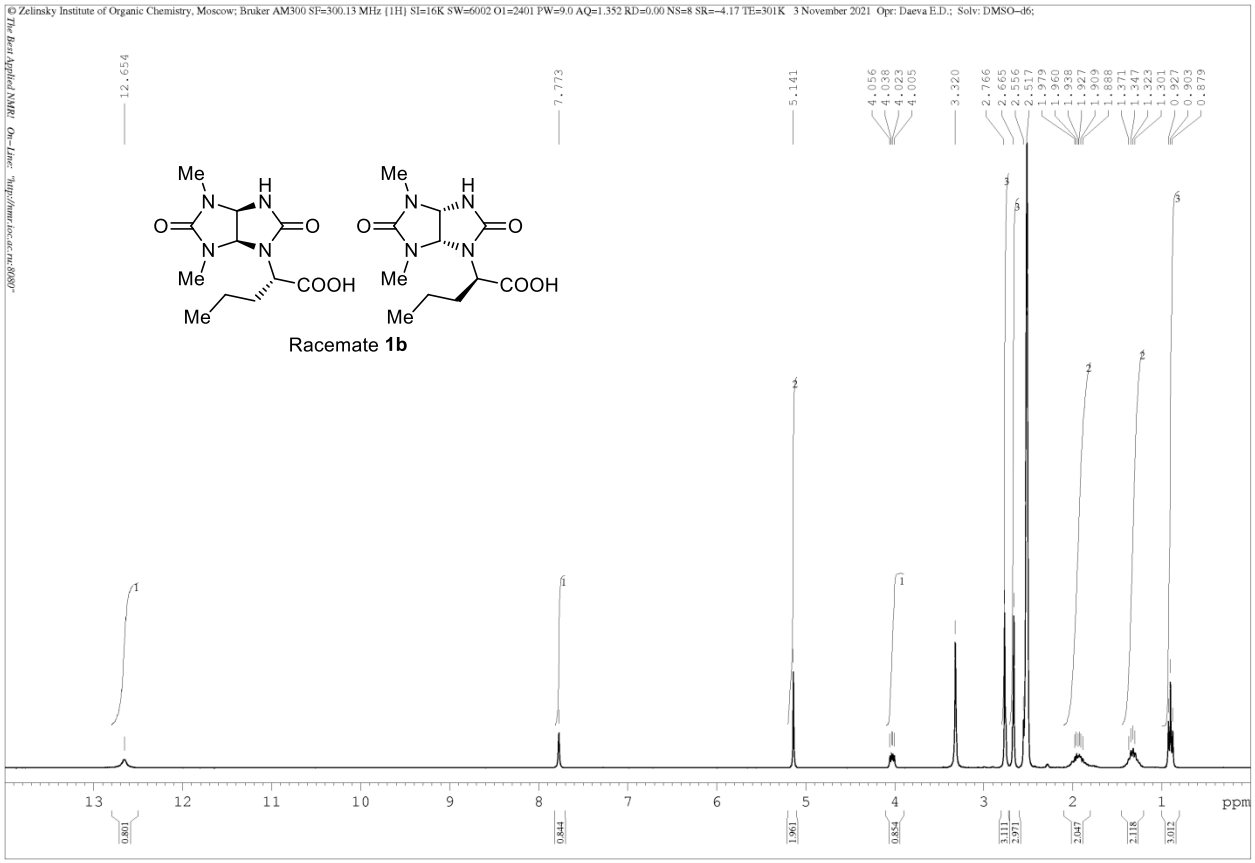
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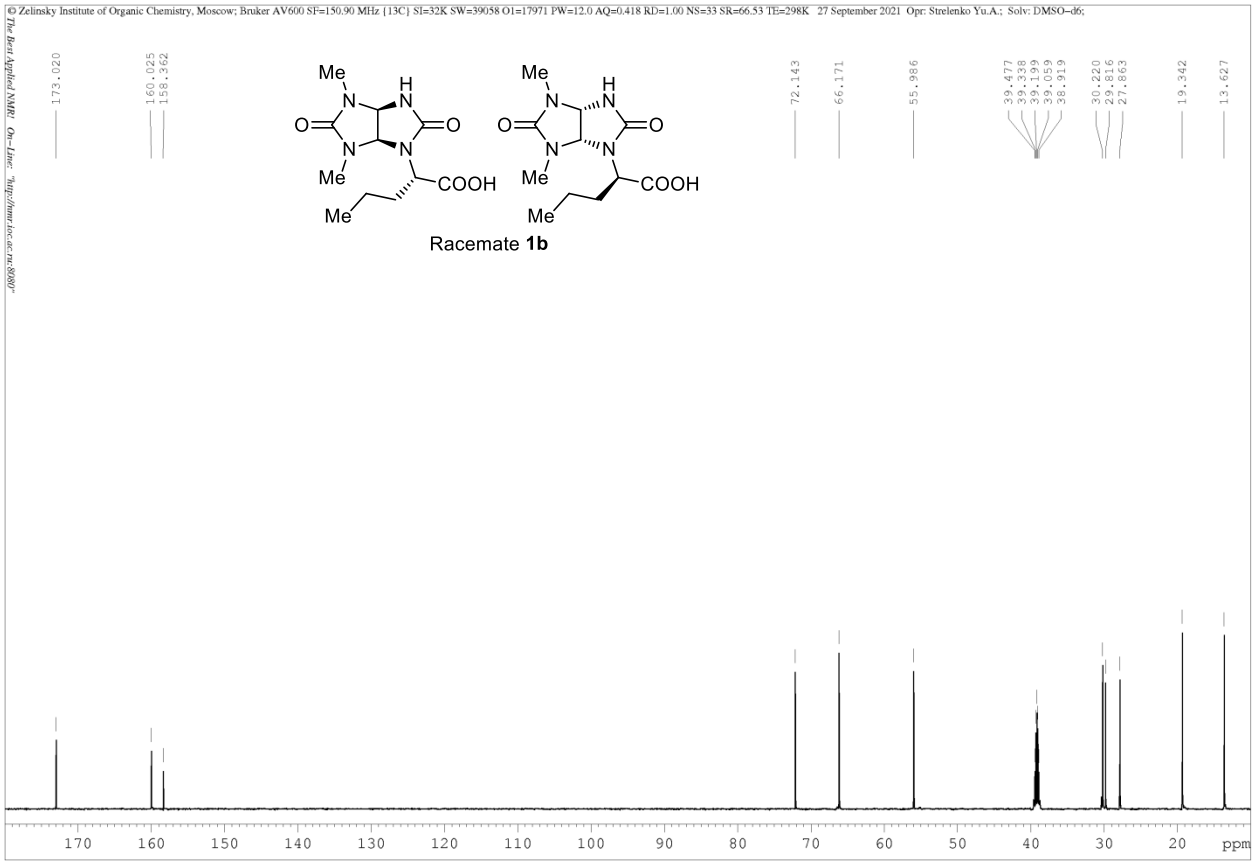
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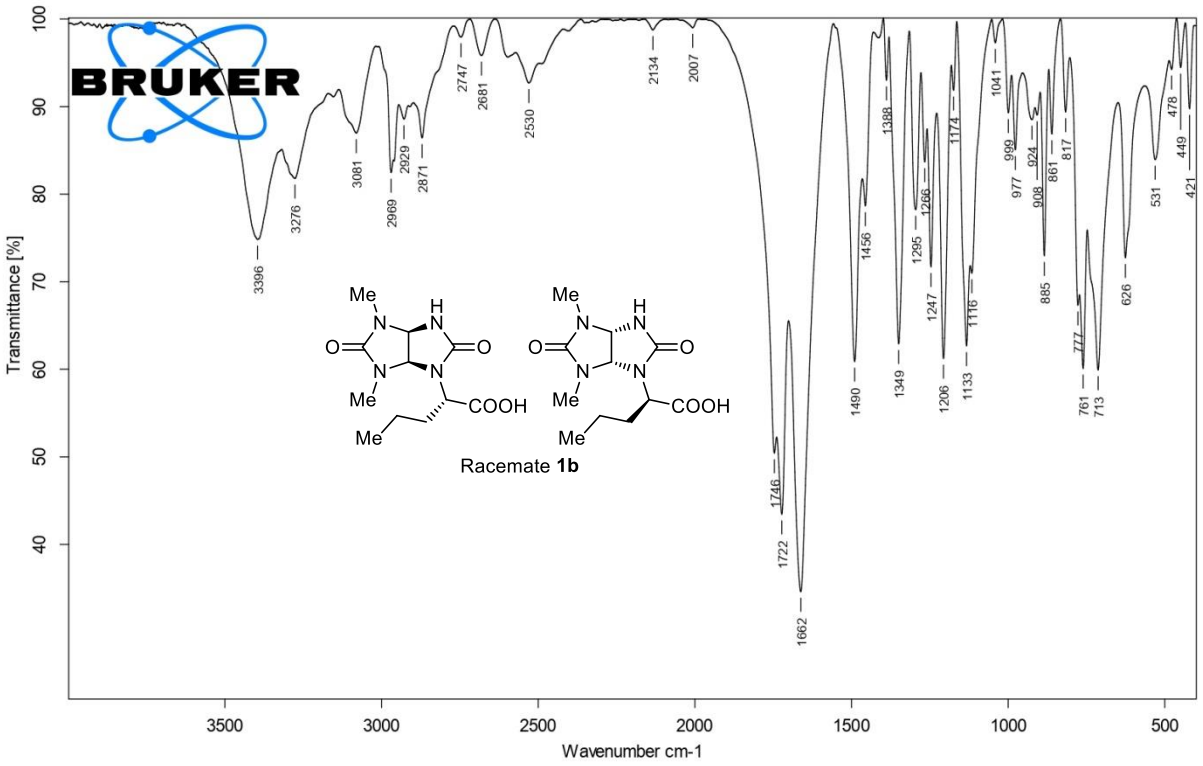

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