

Supporting Information

"Free of base" sulfa-Michael addition for novel o-carboranyl-DL-cysteine synthesis.

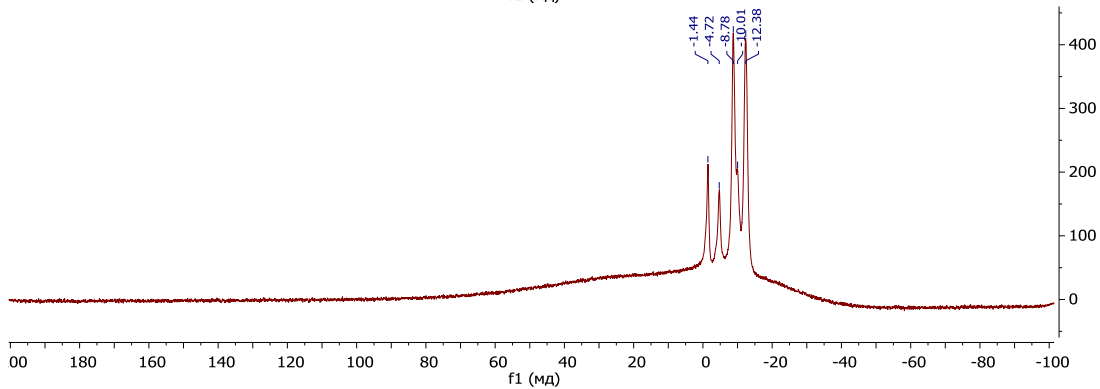
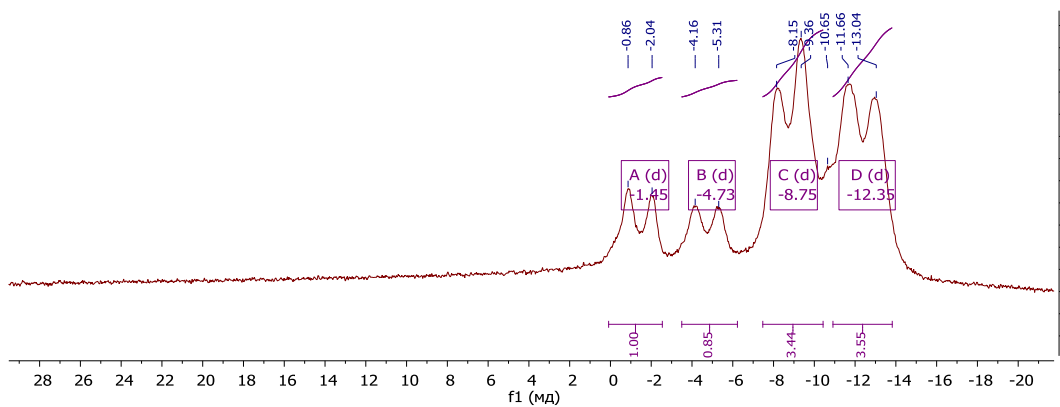
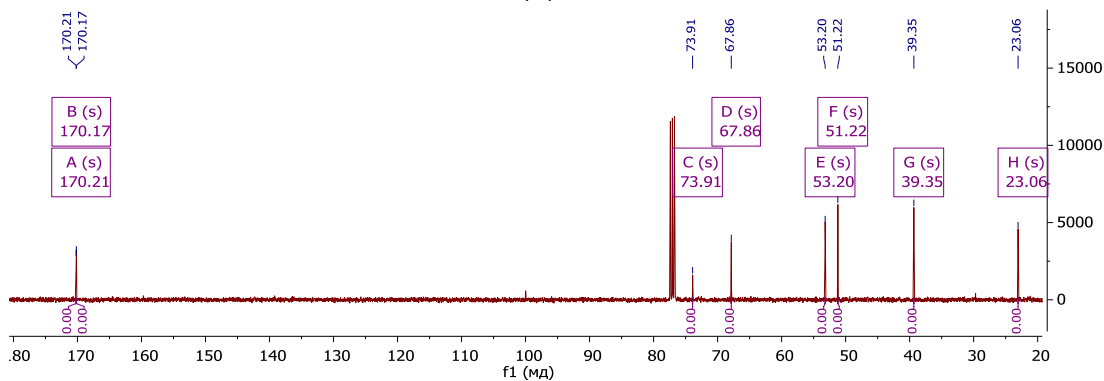
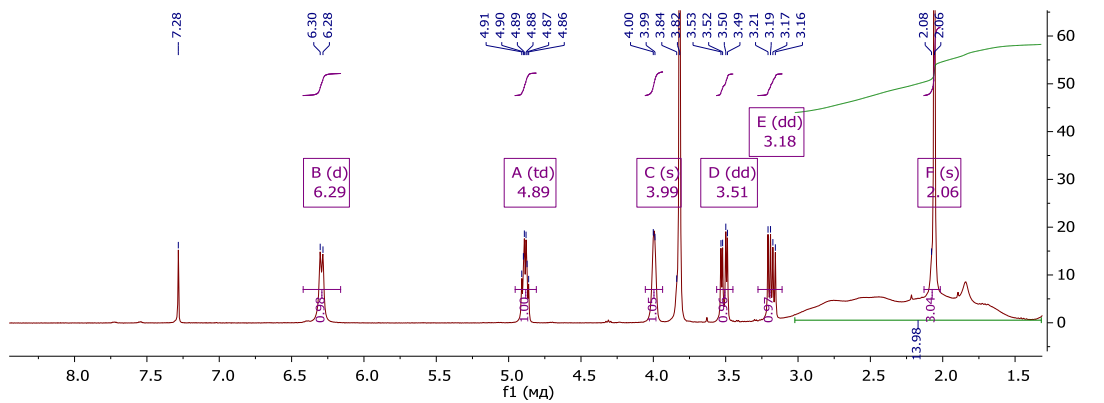
Materials and Methods

[1-S-1,2-C₂B₁₀H₁₁](Me₃NH) (**7**) was prepared according to the literature procedure [1]. Methyl 2-acetamidoacrylate (Sigma Aldrich Chemie GmbH) was used without purification. ²H₂O was received from Carl Roth GmbH. Reactions proceeding were monitored via thin-layer chromatograms (Merck F254 silica gel on aluminum plates). Boron compounds were visualized with PdCl₂ stain solution, which upon heating gave dark brown spots. Purifications were carried out using column chromatography with Silica gel 60 0.060-0.200 mm (Acros Organics). ¹H, ¹³C and ¹¹B NMR spectra were recorded at 400.13, 100.61 and 128.38 MHz, respectively, on a BRUKER-Avance-400 spectrometer. Tetramethylsilane and BF₃·Et₂O were used as standards for ¹H, ¹³C NMR, and ¹¹B NMR respectively. All chemical shifts are reported in ppm (δ) relative to external standards. IR spectra were recorded on IR Prestige-21 (SHIMADZU) instrument. High resolution mass spectra (HRMS) were measured on a Bruker micrOTOF II instrument using electrospray ionization (ESI), mass range from *m/z* 50 to *m/z* 3000; external or internal calibration was done with ESI Tuning Mix, Agilent.

*Synthesis of 1-CH₃O(O)C(CH₃(O)CHN)CHCH₂S-1,2-C₂B₁₀H₁₁ (**8**)*

To a solution of **7** (0.5 g, 2.1 mmol) in toluene (30 ml) methyl 2-acetamidoacrylate (0.3 g, 2.1 mmol) and H₂O (30 ml) were added, resulted system was vigorously stirred under reflux for 24 hours. Then the mixture was cooled to r.t., toluene layer was separated, washed with H₂O (2×20), dried over Na₂SO₄ and evaporated. Product was purified by silica gel column chromatography using Et₂O as eluent and vacuum dried to give light yellow solid. Yield: 0.46 g (68%). ¹H NMR (Chloroform-*d*) δ = 6.29 (d, *J* = 7.7 Hz, 1H, NH), 4.89 (td, *J* = 7.2, 4.5 Hz, 1H, α-CH), 3.99 (broad s, 1H, carb-CH), 3.82 (s, 3H, COOCH₃), 3.51 (dd, *J* = 13.4, 4.6 Hz, 1H, CH₂CH), 3.18 (dd, *J* = 13.4, 6.9 Hz, 1H, CH₂CH), 2.06 (s, 3H, NHCOCH₃), 3.0-1.5 (broad, 10H, BH); ¹¹B NMR (Chloroform-*d*) δ = -1.5 (d, *J* = 150 Hz, 1B), -4.7 (d, *J* = 146 Hz, 1B), -8.8 (d, *J* = 154 Hz, 4B), -12.2 (d, *J* = 162 Hz, 4B); ¹³C NMR (Chloroform-*d*) δ = 170.21, 170.17 (CO), 73.9, 67.9 (C-carb), 53.2 (OCH₃), 51.2 (α-CH), 39.4 (CH₂CH), 23.1 (COCH₃). ESI-MS, *m/z*, C₈H₂₁B₁₀NO₃S calcd. 320.2322, found 320.2322 ([M+H]⁺). IR-FT (ν, cm⁻¹): 3371(NH), 3060 (CH-carb); 2948, 2926, 2852 (broad CH); 2607, 2584, 2557 (BH); 1736, 16177 (CO).

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1. Stogniy, M.Yu.; Erokhina, S.A.; Druzina A.A.; Sivaev I. B.; Bregadze, V.I. Synthesis of novel carboranyl azides and "click" reactions thereof. J. Organomet. Chem. 2019, 904, 121007. <https://doi.org/10.1016/j.jorganchem.2019.121007>

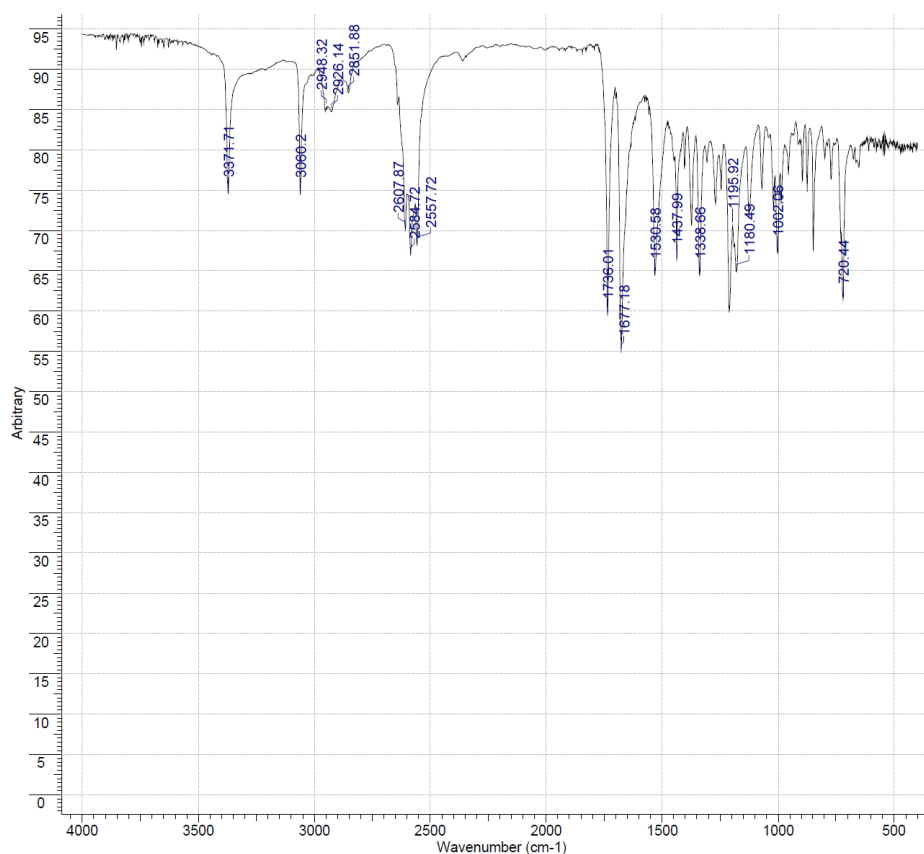
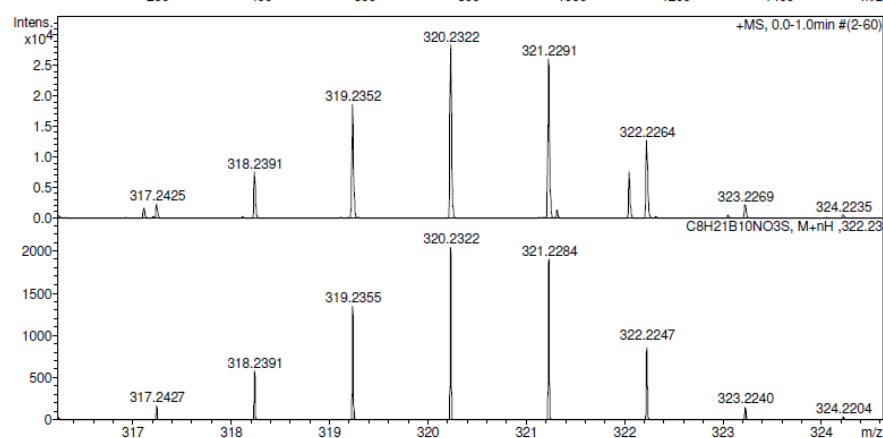
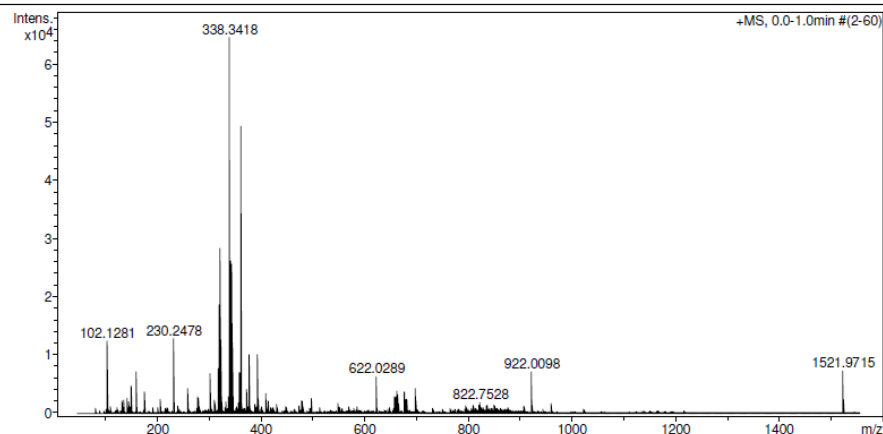


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Comment CH3CN 100 %, dil. 200, calibrant added

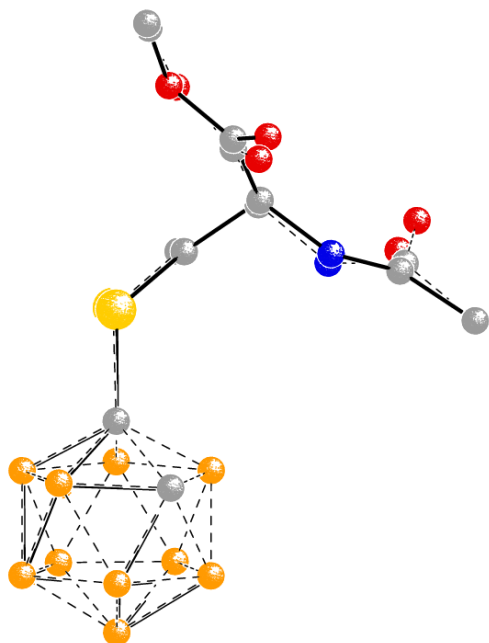
Operator BDAL@DE
Instrument maXis 43

Acquisition Parameter

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Scan End	1550 m/z	Set Collision Cell RF	300.0 Vpp	Set Divert Valve	Source



Crystallographic data:



Crystals of **8** ($\text{C}_8\text{H}_{21}\text{B}_{10}\text{NO}_3\text{S}$, $M = 319.42$) are triclinic, space group P-1, at 120K: $a = 7.6513(5)$, $b = 10.5669(7)$, $c = 11.5392(7)$, $\alpha = 68.378(1)^\circ$, $\beta = 85.686(1)^\circ$, $\gamma = 72.663(1)^\circ$, $V = 827.27(9) \text{ \AA}^3$, $Z = 2$ ($Z' = 1$), $d_{\text{calc}} = 1.282 \text{ g}\cdot\text{cm}^{-3}$, $F(000) = 332$. Intensities of 11058 reflections were measured with a Bruker SMART APEX 2 Duo CCD diffractometer [$\lambda(\text{MoK}\alpha) = 0.71072 \text{ \AA}$, ω -scans, $2\theta < 60^\circ$] and 4824 independent reflections [$R_{\text{int}} = 0.0324$] were used in further refinement. The structure was solved by the direct method and refined by the full-matrix least-squares technique against F^2 in the anisotropic-isotropic approximation. The hydrogen atoms were found in the difference Fourier synthesis and refined in the isotropic approximation within the riding model. For **8**, the refinement converged to $wR_2 = 0.1167$ and $\text{GOF} = 0.781$ for all independent reflections ($R_1 = 0.0371$ was calculated for 3661 observed reflections with $I > 2\sigma(I)$). All calculations were performed using SHELX2018 [2]. The CCDC 2034871 contains the supplementary crystallographic data for **8**. These data can be obtained free of charge via <http://www.ccdc.cam.ac.uk/conts/retrieving.html> (or from the CCDC, 12 Union Road, Cambridge, CB21EZ, UK; or deposit@ccdc.cam.ac.uk).

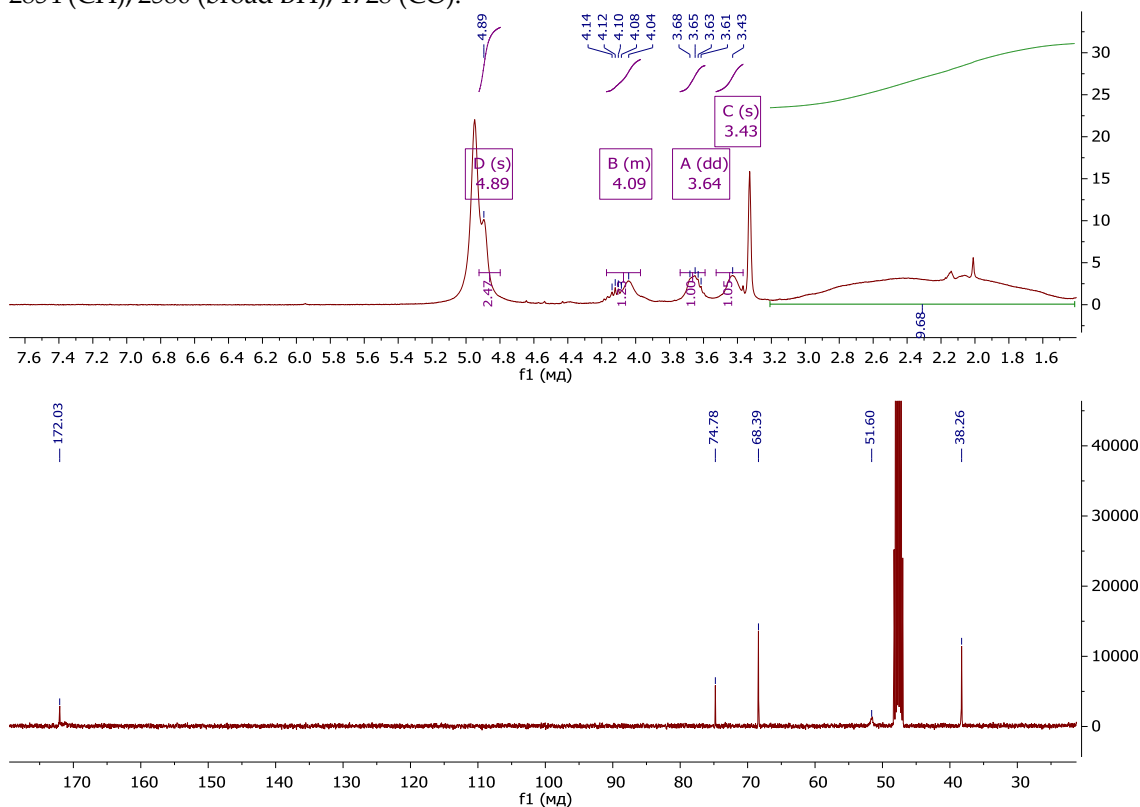
Computational details: All calculations were done in the Gaussian09 program (rev. D01) [3]. The geometry optimization procedures were performed using standard criteria on displacements and forces. The DFT optimization were performed using the PBE0 functional [4] and the 6-311++G(d,p) basis set (ultrafine integration grids were used). The non-specific solvation was modelled using the self-consistent reaction field approach (PCM model, $\epsilon=72$). The influence of specific solvation on the geometry of **8** was

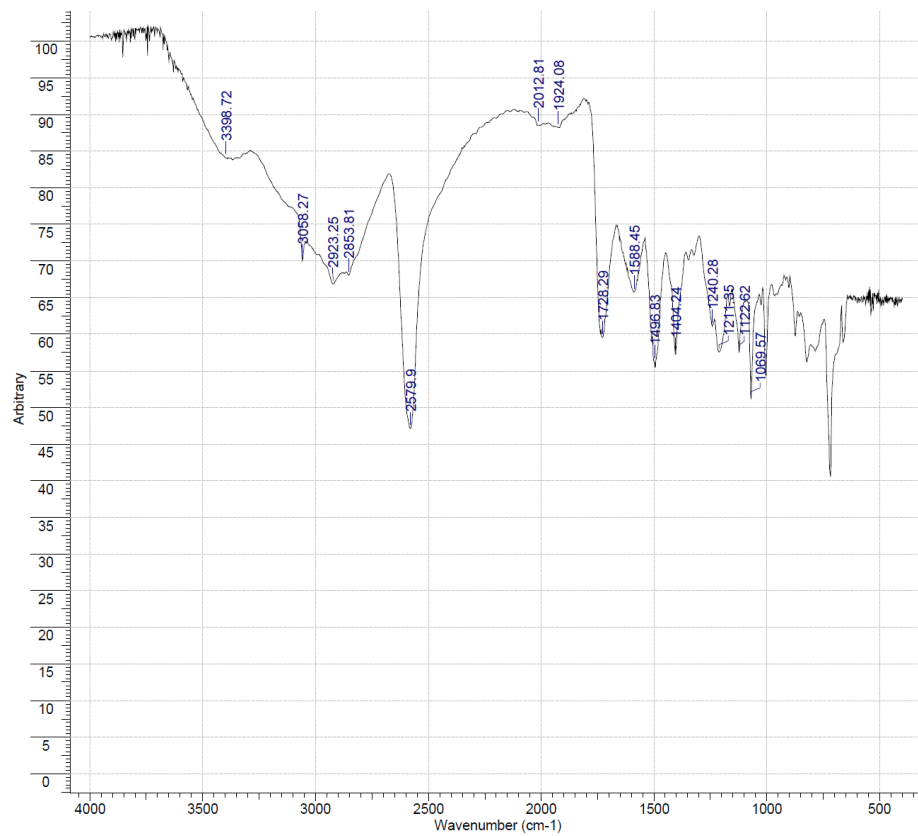
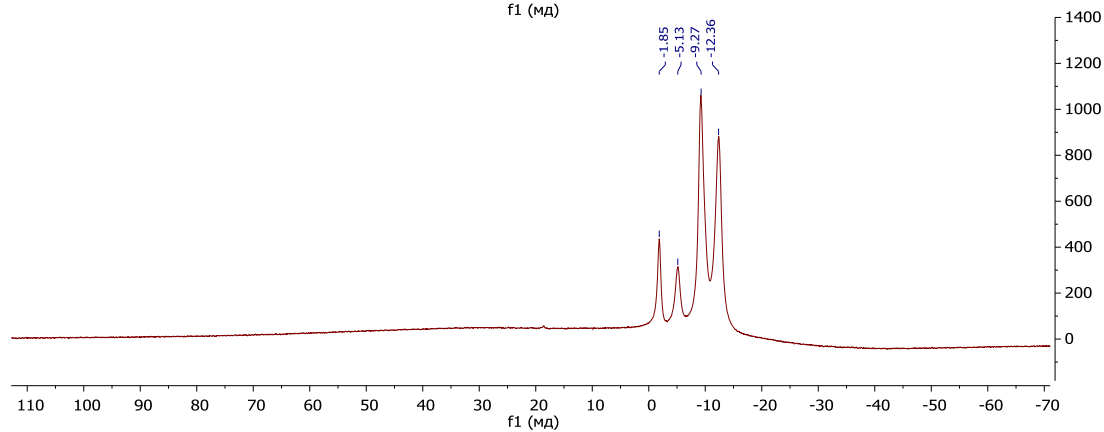
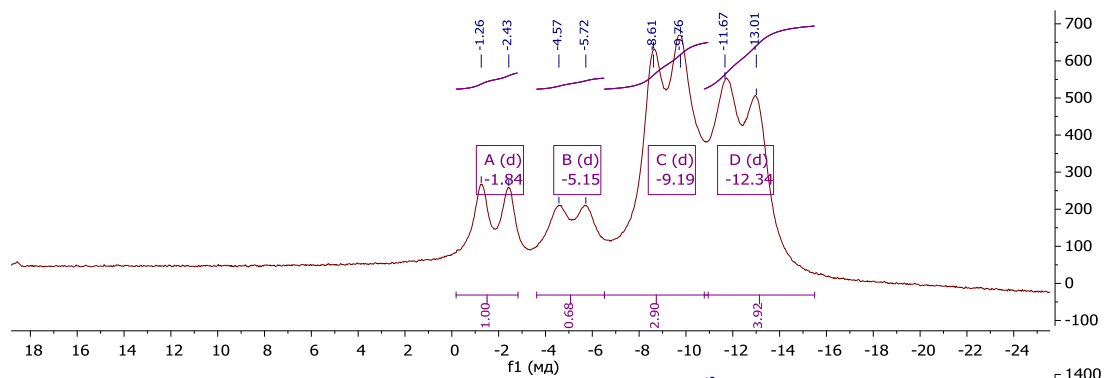
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- Sheldrick G. M. Crystal structure refinement with SHELXL. *Acta Cryst.* **2015**, C71, 3-8.
 - Gaussian 09, Revision D.01, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, G. A. Petersson, H. Nakatsuji, X. Li, M. Caricato, A. Marenich, J. Bloino, B. G. Janesko, R. Gomperts, B. Mennucci, H. P. Hratchian, J. V. Ortiz, A. F. Izmaylov, J. L. Sonnenberg, D. Williams-Young, F. Ding, F. Lipparini, F. Egidi, J. Goings, B. Peng, A. Petrone, T. Henderson, D. Ranasinghe, V. G. Zakrzewski, J. Gao, N. Rega, G. Zheng, W. Liang, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, K. Throssell, J. A. Montgomery, Jr., J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, T. Keith, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, J. M. Millam, M. Klene, C. Adamo, R. Cammi, J. W. Ochterski, R. L. Martin, K. Morokuma, O. Farkas, J. B. Foresman, and D. J. Fox, Gaussian, Inc., Wallingford CT, **2016**.
 - (a) Perdew J.; Ernzerhof M.; Burke K. *J. Chem. Phys.* **1996**, *105*, 9982-9985.
(b) Carlo A.; Barone V. *J. Chem. Phys.* **1999**, *110*, 6158-6170.

accounted for by the optimization of a central molecule in clusters; two models were used: 1) the trimer of molecules from crystal of **8** with fixed coordinates and normalized X-H bond lengths for lateral molecules and 2) the shell of molecules from crystal of **8** with fixed coordinates and normalized X-H bond lengths. The QTAIM surface integrals for the trimer were calculated using the AIMAll program [5]. The shell in the second model was generated using the criteria of at least one geometrical contact (within the sum of van der Waals radii plus 5 Å) between surrounding molecules and the central molecule. The shell was described by the ONIOM approach (PBE0/6-311++G(d,p):PBE0/3-21G) and only the internal layer (the central molecule) was optimized. The Hessian calculations for all optimized structures revealed their correspondence to energy minimums.

Synthesis of 1-HOOC(NH₂)CHCH₂S-1,2-C₂B₁₀H₁₁×HCl (9**)**

Water (2 ml) and concentrated HCl (10 ml) were added to a solution of **8** (0.1 g, 0.3 mmol) in glacial acetic acid (10 ml). The resulted mixture was heated at 70°C for 40 h., cooled to r.t. and evaporated. The residue was suspended in 5 ml of water, formed solid was filtered, washed with water (2×5 ml) and vacuum dried to give **9**. Light yellow solid (0.093 mg, 70%). ¹H NMR (Methanol-*d*₄) δ = 4.89 (s, 1H, carb-CH), 4.09 (m, 1H, α-CH), 3.64 (m, 1H, CH₂CH), 3.43 (m, 1H, CH₂CH), 3.0-1.5 (broad, 10H, BH); ¹¹B NMR (Methanol-*d*₄) δ = -1.8 (d, *J* = 151 Hz, 1B), -5.1 (d, *J* = 148 Hz, 1B), -9.2 (d, *J* = 148 Hz, 4B), -12.3 (d, *J* = 172 Hz, 4B). ¹³C NMR (Methanol-*d*₄) δ 172.0 (COOH), 74.8, 68.4 (C-carb), 51.60 (α-CH), 38.3 (CH₂CH). ESI-MS, *m/z*, C₅H₁₇B₁₀NO₂S calcd. 264.2059, found 264.2061. IR-FT (ν, cm⁻¹): 3399 (broad NH⁺), 3058 (CH - carb); 2923, 2854 (CH); 2580 (broad BH), 1728 (CO).



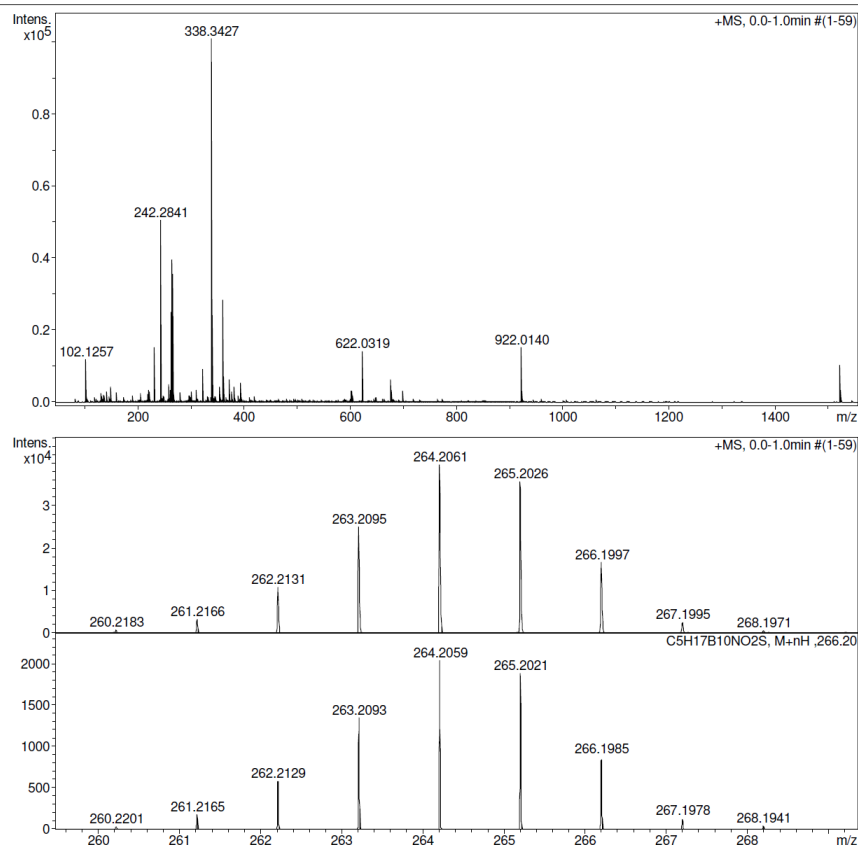


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Operator BDAL@DE
 Instrument maXis 43

Acquisition Parameter

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Scan End	1550 m/z	Set Collision Cell RF	300.0 Vpp	Set Divert Valve	Source



Synthesis of 1-CH₃O(O)C(CH₃(O)CHN)CDCH₂S-1,2-C₂B₁₀H₁₁ (10)

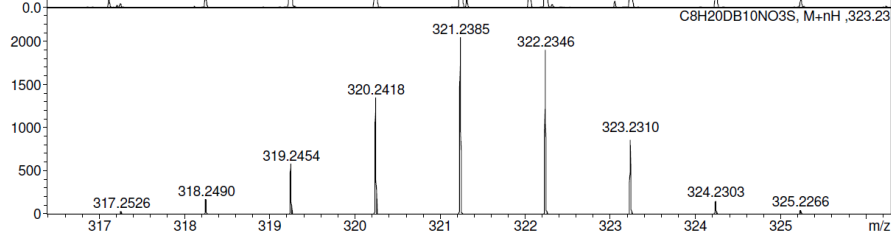
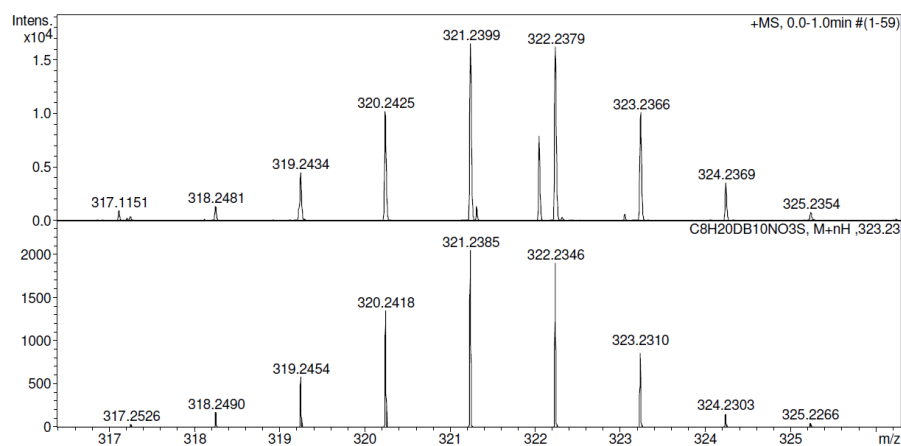
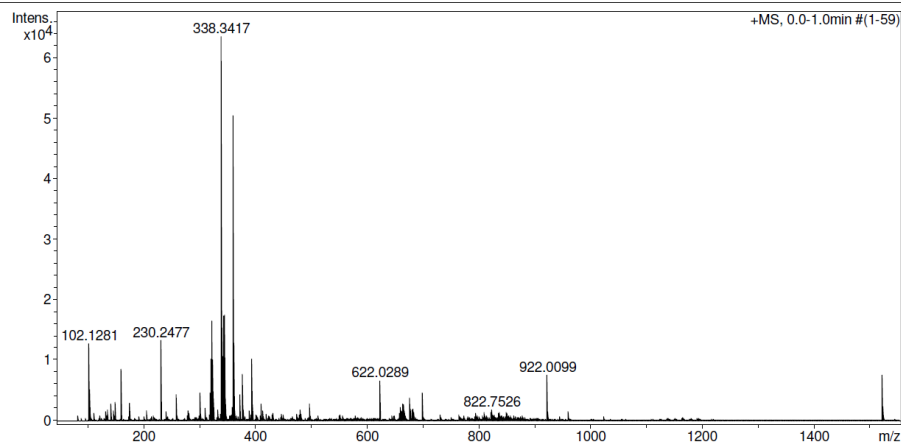
Under argon atmosphere methyl 2-acetamidoacrylate (0.06 g, 0.4 mmol) and ²H₂O (5 ml) were added to a solution of **7** (0.1 g, 0.4 mmol) in toluene (15ml), resulted two-phase system was vigorously stirred under reflux for 30 hours. Purification was held in the same manner as for compound **8**. Light yellow solid (90 mg, 66%). ¹H NMR (Chloroform-*d*) δ = 6.31 (s, 1H, NH), 4.00 (broad s, 1H, CH-carb), 3.82 (s, 3H, COOCH₃), 3.50 (d, *J* = 13.4 Hz, 1H, CH₂CD), 3.17 (d, *J* = 13.4 Hz, 1H, CH₂CD), 2.06 (s, 3H, NHCOCH₃), 3.0-1.5 (broad, 10H, BH); ¹¹B NMR (Chloroform-*d*) δ = -1.5 (d, *J* = 151 Hz, 1B), -4.8 (d, *J* = 150 Hz, 1B), -8.9 (d, *J* = 151 Hz, 4B), -12.4 (d, *J* = 176 Hz, 4B); ¹³C NMR (Chloroform-*d*) δ = 170.23, 170.17 (CO), 73.9, 67.9 (C-carb), 53.2 (OCH₃), 51.0 (t, α-CD), 39.3 (CH₂), 23.1 (COCH₃). ESI-MS, *m/z*, C₈H₂₀DB₁₀NO₃S calcd. 321.2385, found 321.2399. IR-FT (ν, cm⁻¹): 3370 (NH), 3061 (CH - carb); 2953 (CH); 2608, 2586, 2557 (BH), 1733, 1674 (CO).

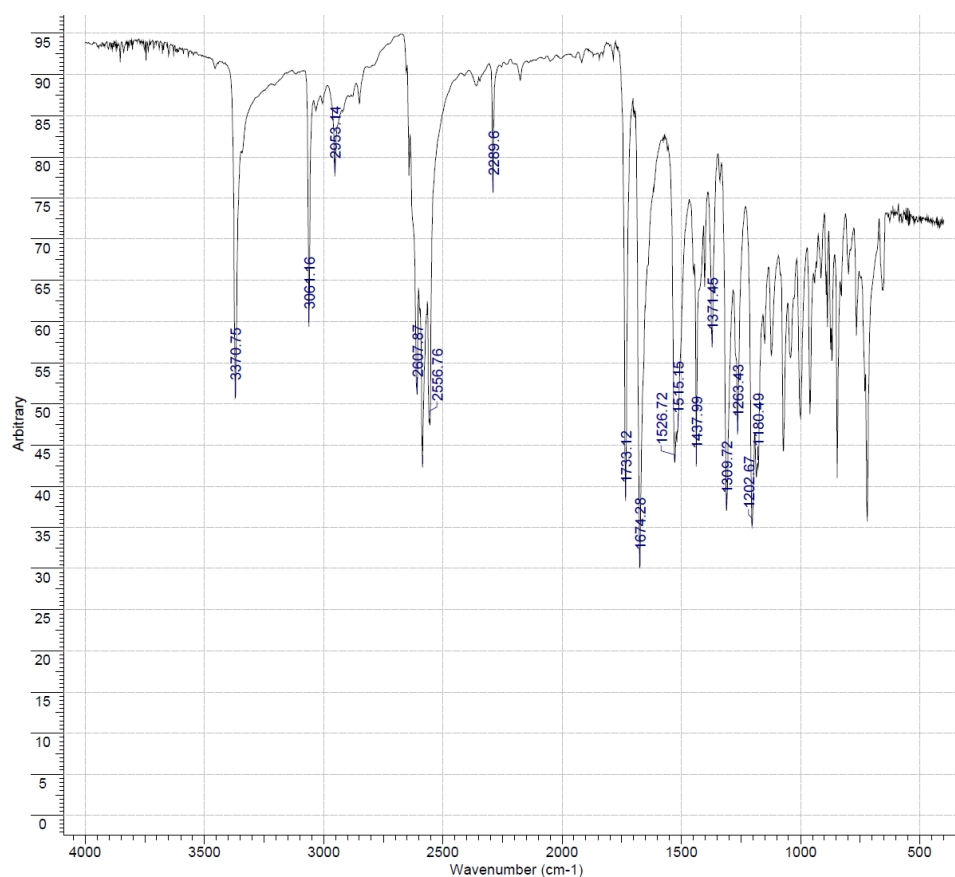
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Comment CH3CN 100 %, dil. 200, calibrant added

Operator BDAL@DE
Instrument maXis 43

Acquisition Parameter

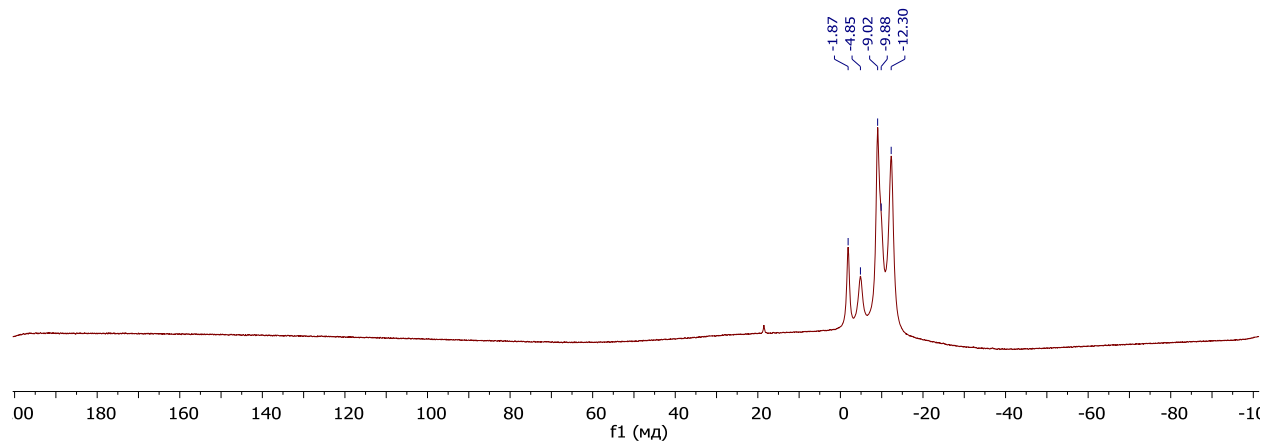
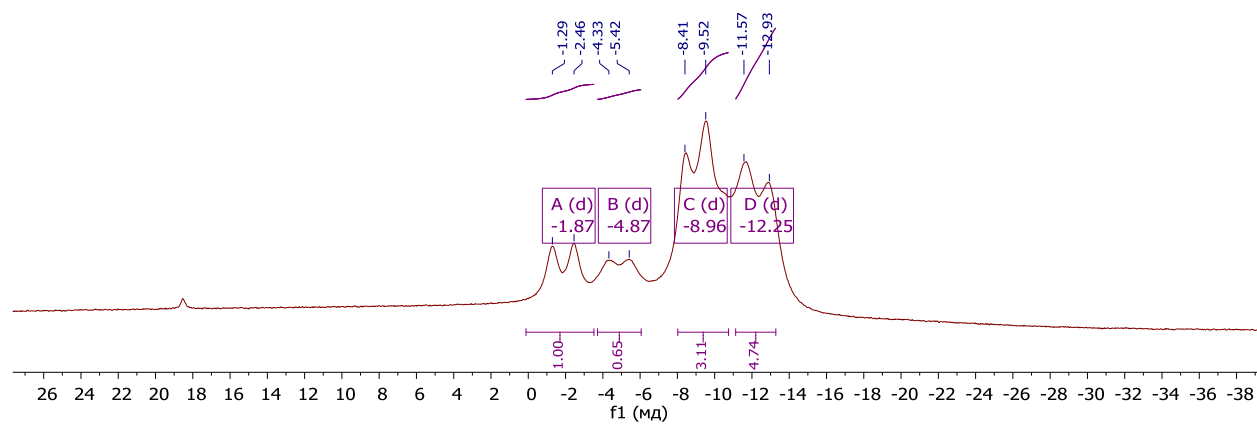
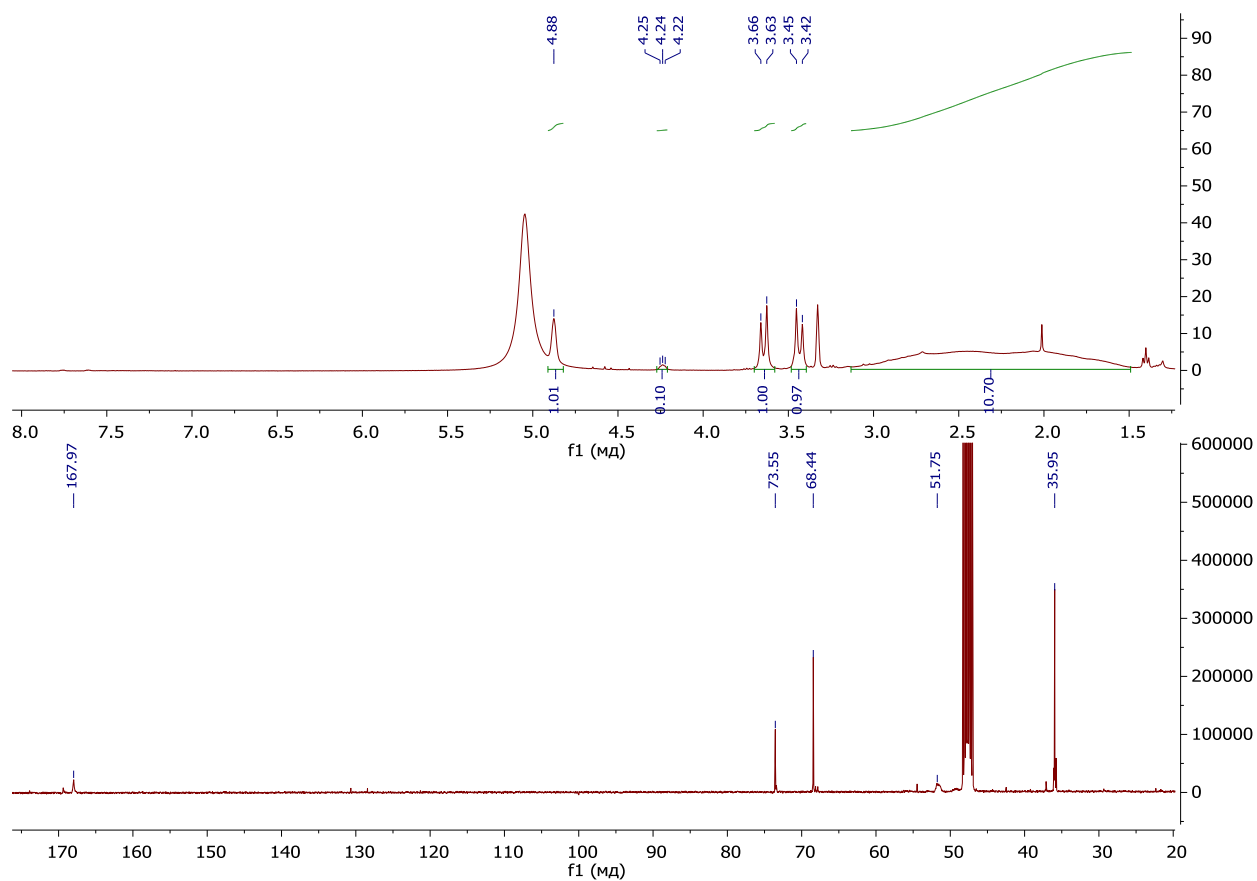
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Scan End	1550 m/z	Set Collision Cell RF	300.0 Vpp	Set Divert Valve	Source





Synthesis of 1-HOOC(NH₂)CDCH₂S-1,2-C₂B₁₀H₁₁×HCl (11)

Water (2 ml) and concentrated HCl (5 ml) were added to a solution of **10** (0.05 g, 0.16 mmol) in glacial acetic acid (5 ml). The resulted mixture was heated at 70°C for 40 h., cooled to r.t. and evaporated. The residue was suspended in 5 ml of water, formed solid was filtered, washed with water (2 ml) and vacuum dried to yield **11**: 38 mg (81%). ¹H NMR (Methanol-*d*₄) δ = 4.88 (broad s, 1H, CH-carb), 4.27 – 4.20 (α-CH, m, 0,1H), 3.64 (d, *J* = 13.9 Hz, 1H, CH₂CD), 3.44 (d, *J* = 13.9 Hz, 1H, CH₂CD), 3.0-1.5 (broad, 10H, BH). ¹¹B NMR (Methanol-*d*₄) δ = -1.9 (d, *J* = 149 Hz, 1B), -4.9 (d, *J* = 140 Hz, 1B), -9.0 (d, *J* = 143 Hz, 4B), -12.3 (d, *J* = 175 Hz, 4B). ¹³C NMR (Methanol-*d*₄) δ = 168.0 (CO), 73.6 (C-carb), 68.4 (C-carb), 51.8 (α-C), 36.0 (CH₂). ESI-MS, *m/z*, C₅H₁₇B₁₀NO₂S calcd. 265.2122, found 265.2127.

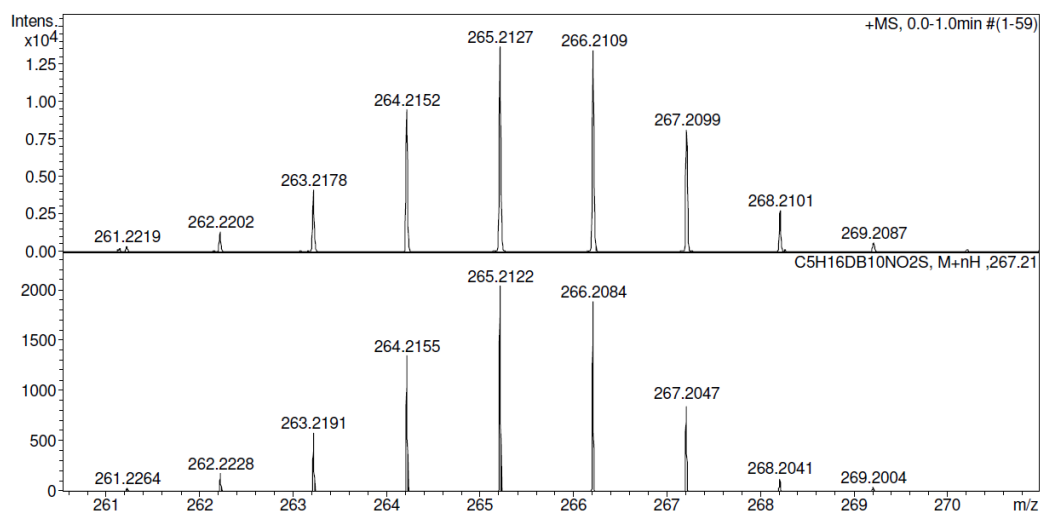
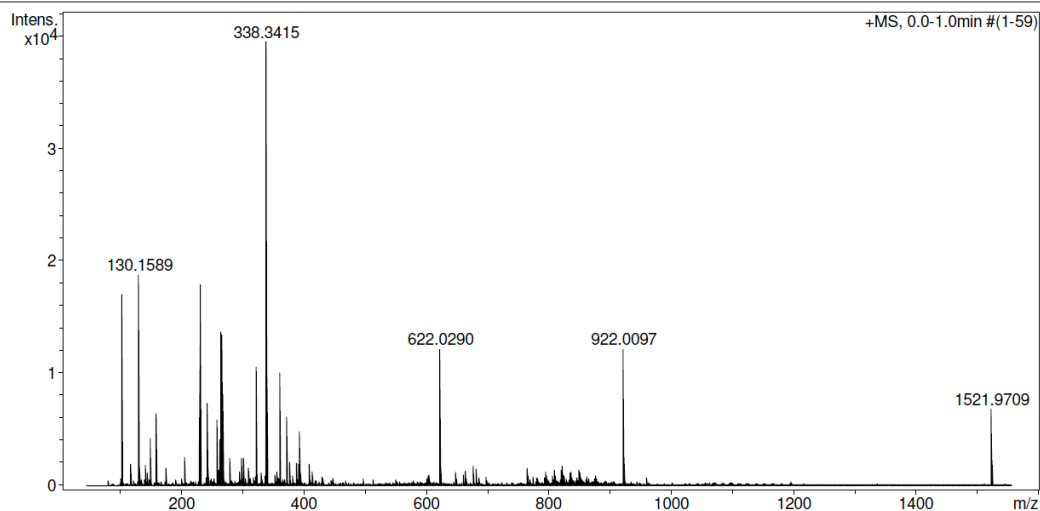


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Operator BDAL@DE
 Instrument maXis 43

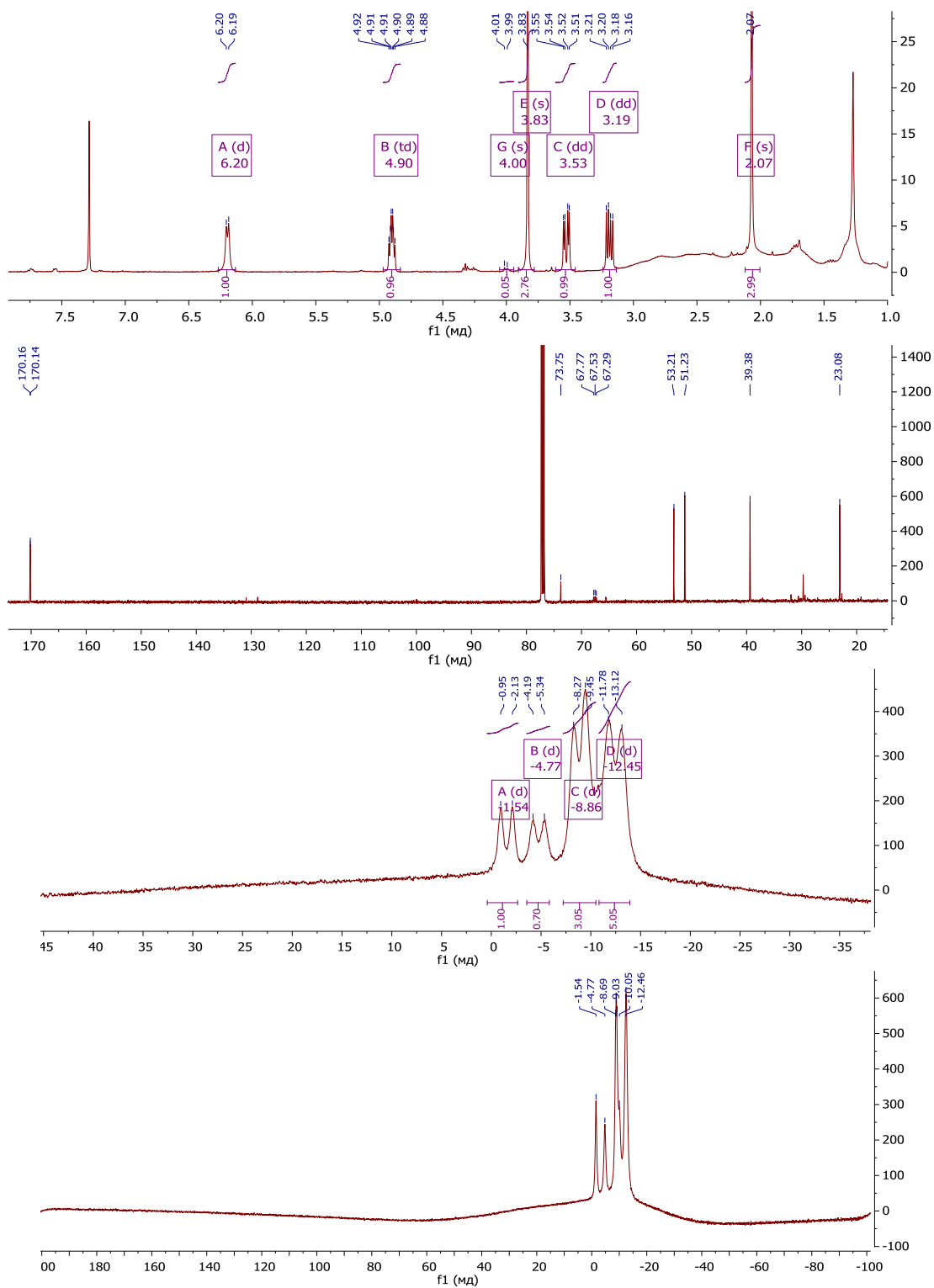
Acquisition Parameter

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Scan End	1550 m/z	Set Collision Cell RF	300.0 Vpp	Set Divert Valve	Source



Synthesis of 1-CH₃O(O)C(CH₃(O)CHN)CHCH₂S-2-D-1,2-C₂B₁₀H₁₀ (12)

Under argon atmosphere methyl 2-acetamidoacrylate (0.06 g, 0.4 mmol), ²H₂O (5 ml) and anhydrous K₂CO₃ (0.055 g, 0.4 mmol) were added to a solution of 7 (0.1 g, 0.4 mmol) in toluene (15ml), resulted system was vigorously stirred under reflux for 10 hours. The purification was held in the same manner as for compound 8. Light yellow solid (13 mg, 10%). ¹H NMR (Chloroform-d) δ = 6.20 (d, J = 7.7 Hz, 1H, NH), 4.90 (td, J = 7.2, 4.7 Hz, 1H, α-CH), 4.00 (undetectable, s, 0H, carb-CD), 3.83 (s, 3H, COOCH₃), 3.53 (dd, J = 13.4, 4.7 Hz, 1H, CH₂CH), 3.19 (dd, J = 13.4, 6.9 Hz, 1H, CH₂CH), 2.07 (s, 3H, NHCOCH₃), 3.0-1.5 (broad, 10H, BH); ¹¹B NMR (Chloroform-d) δ = -1.5 (d, J = 152 Hz, 1B), -4.8 (d, J = 147 Hz, 1B), -8.9 (d, J = 152 Hz, 4B), -12.5 (d, J = 173 Hz, 4B); ¹³C NMR (Chloroform-d) δ = 170.16, 170.14 (CO), 73.8 (CH-carb), 68.5 – 66.8 (t, CD-carb), 53.2 (OCH₃), 51.2 (α-CH), 39.4 (CH₂), 23.1 (COCH₃). ESI-MS, m/z, C₈H₂₀DB₁₀NO₃S calcd. 321.2385, found 321.2384. IR-FT (ν, cm⁻¹): 3372(NH), 2923, 2851 (CH); 2607, 2584, 2557 (BH); 2289 (CD-carb); 1736, 1677 (CO).



Method tune_low_1550.m
Sample Name /CHIZ GB-C4
Comment CH3CN 100 %, dil. 200, calibrant added

Operator BDAL@DE
Instrument maXis 43

Acquisition Parameter

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