Electronic supplementary materials *Mendeleev Commun.*, 2019, **29**, 94–95

A first synthesis of 8- and 8,10-substituted barbiturils and their thio analogues

Vladimir V. Baranov, Aleksandra B. Ivanova, Natal'ya G. Kolotyrkina and Angelina N. Kravchenko

Compounds **3a**,**c-e**, *Method 2 (general procedure).* Paraformaldehyde (0.25 g) and hydrochloric acid (1 ml, 35%) were added to a solution of urea **1a** or thiourea **1d-f** (4.2 mmol) in H_2O (20 ml). The mixture was refluxed with stirring for 2 h, then cooled to 65 °C. Barbituric acid (1.16 g, 4.2 mmol) was added, and this was stirred at 65 °C for 12 h and cooled. The precipitate of productss **3a**,**c-e** was filtered off and dried.

8,10-Dimethyl-9-thioxo-2,4,8,10-tetraazaspiro[5.5]undecane-1,3,5-trione **3c**, white powder, yield 75% (method 1), 75% (method 2), sublimation temperature 300–302 °C. ^{1}H NMR, δ: 3.22 (s, 6 H, 2Me), 3.69 (s, 4 H, 2CH_2), 11.36 (s, 2 H, 2NH). ^{13}C NMR, δ: 42.24 (Me); 49.26 (C); 52.67 (CH_2); 150.13 (C^3=O); 169.34 (C^1=O + C^5=O); 180.39 (C=S). HRMS, m/z: 257.0703 $[M+H]^+$ (calc. for: $C_9H_{13}N_4O_3S^+$, 257.0703).

8,10-Diethyl-9-thioxo-2,4,8,10-tetraazaspiro[5.5]undecane-1,3,5-trione **3d**, light yellow powder, yield 24% (method 1), 22% (method 2), mp 295–297 °C. ^{1}H NMR, δ: 1.07 (t, 6 H, ^3J = 6.9 Hz, 2Me), 3.66 (s, 4 H, C^7H_2 + $C^{11}H_2$), 3.81(q, 4 H, ^3J = 6.8 Hz, 2$\underline{CH_2}$-Me), 11.34 (s, 2 H, 2NH). ^{13}C NMR, 11.94 (Me); 48.29 (C); 48.39 ($\underline{CH_2}$-Me), 49.94 (CH_2), 150.19 (C^3=O); 169.25 (C^1=O + C^5=O); 177.66 (C=S). HRMS, m/z: 285.1017 $[M+H]^+$ (calc. for: $C_{11}H_{17}N_4O_3S^+$, 285.1016).

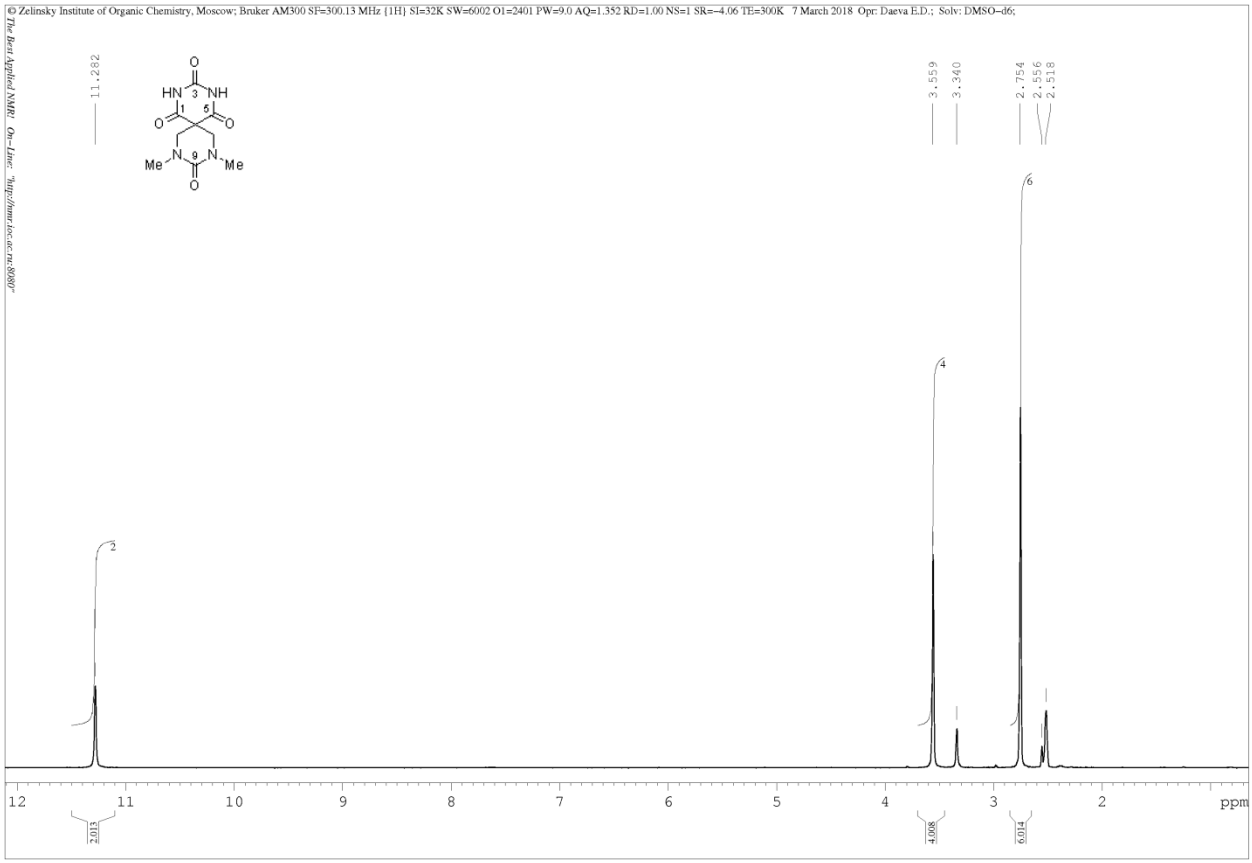
8-Ethyl-10-methyl-9-thioxo-2,4,8,10-tetraazaspiro[5.5]undecane-1,3,5-trione **3e**, white powder, yield 15% (method 1), 27% (method 2), mp >305 °C. ^{1}H NMR, δ: 1.05 (t, 3 H, ^3J = 7.0 Hz, Me), 3.24 (s, 3 H, Me), 3.66 (s, 2 H, CH_2), 3.69 (s, 2 H, CH_2), 3.79 (q, 2 H, ^3J = 6.9 Hz, $\underline{CH_2}$-Me), 11.34 (s, 2 H, 2NH). ^{13}C NMR, δ: 12.09, 42.19 (Me); 48.93 (C); 48.39 ($\underline{CH_2}$-Me), 50.76, 50.98 (CH_2), 150.14 (C^3=O); 169.29 (C^1=O + C^5=O); 179.07 (C=S). HRMS, m/z: 271.0864 $[M+H]^+$ (calc. for: $C_{10}H_{15}N_4O_3S^+$, 271.0859).

8,10-Dimethyl-3-thioxo-2,4,8,10-tetraazaspiro[5.5]undecane-1,5,9-trione **3f**, light yellow powder, yield 33% (method 1), mp 248–250 °C. ^{1}H NMR, δ: 2.76 (s, 6 H, 2Me), 3.55 (s, 4 H, 2CH_2), 12.36 (s, 2 H, 2NH). ^{13}C NMR, δ: 35.22 (Me); 50.31 (C); 51.69 (CH_2); 156.04 (C^9=O); 167.75 (C^1=O + C^5=O); 179.04 (C=S). HRMS, m/z: 257.0713 $[M+H]^+$ (calc. for: $C_9H_{13}N_4O_3S^+$, 257.0703).

8,10-Diethyl-3-thioxo-2,4,8,10-tetraazaspiro[5.5]undecane-1,5,9-trione **3g**, light yellow powder, yield 22% (method 1), mp 268–270 °C. ^{1}H NMR, δ: 0.98 (t, 6 H, ^3J = 7.0 Hz, 2Me), 3.22 (q, 4 H, ^3J = 7.0 Hz, 2$\underline{CH_2}$-Me), 3.55 (s, 4 H, 2CH_2), 12.37 (s, 2 H, 2NH). ^{13}C NMR, δ: 12.68 (Me); 41.67 ($\underline{CH_2}$-Me), 49.05 (CH_2), 49.91 (C); 154.48 (C^9=O); 167.69 (C^1=O + C^5=O); 179.07 (C=S). HRMS, m/z: 285.1017 $[M+H]^+$ (calc. for: $C_{11}H_{17}N_4O_3S^+$, 285.1016).

8,10-Dimethyl-3,9-dithioxo-2,4,8,10-tetraazaspiro[5.5]undecane-1,5-dione **3h**, beige powder, yield 18% (method 1), mp 228–230 °C. ^{1}H NMR, δ: 3.23 (s, 6 H, 2Me), 3.69 (s, 4 H, 2CH_2), 12.44 (s, 2 H, 2NH). ^{13}C NMR, δ: 42.29 (Me); 49.97 (C); 52.47 (CH_2); 167.31 (C=O), 179.02 (C=S). HRMS, m/z: 273.0475 $[M+H]^+$ (calc. for: $C_9H_{13}N_4O_2S_2^+$, 273.0474).

8-Methyl-3,9-dithioxo-2,4,8,10-tetraazaspiro[5.5]undecane-1,5-dione **3i**, white powder, yield 69% (method 1), mp 262–264 °C. ^{1}H NMR, δ: 3.23 (s, 3 H, Me), 3.38 (s, 2 H, CH_2), 3.68 (s, 2 H, CH_2), 8.20 (s, 1 H, $N^{10}H$), 12.41 (s, 2 H, $N^{2}H$+$N^{4}H$). ^{13}C NMR, δ: 40.86 (Me); 48.45 (C); 45.58 (CH_2), 50.97 (CH_2); 167.26 (C^{1}=O + C^{5}=O); 177.23 (C^{9}=S), 179.03 (C^{3}=S). HRMS, m/z: 259.0312 $[M+H]^+$ (calc. for: $C_8H_{11}N_4O_2S_2^+$, 259.0318).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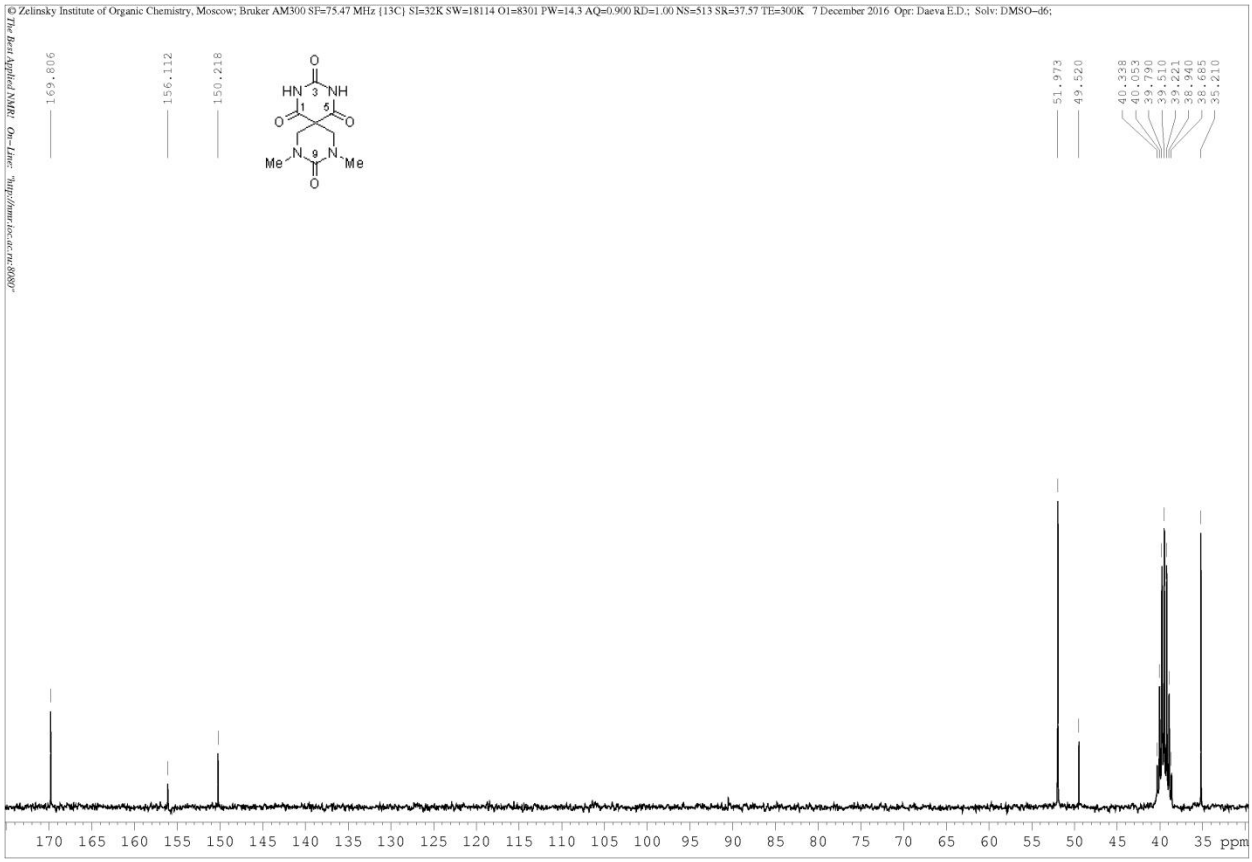
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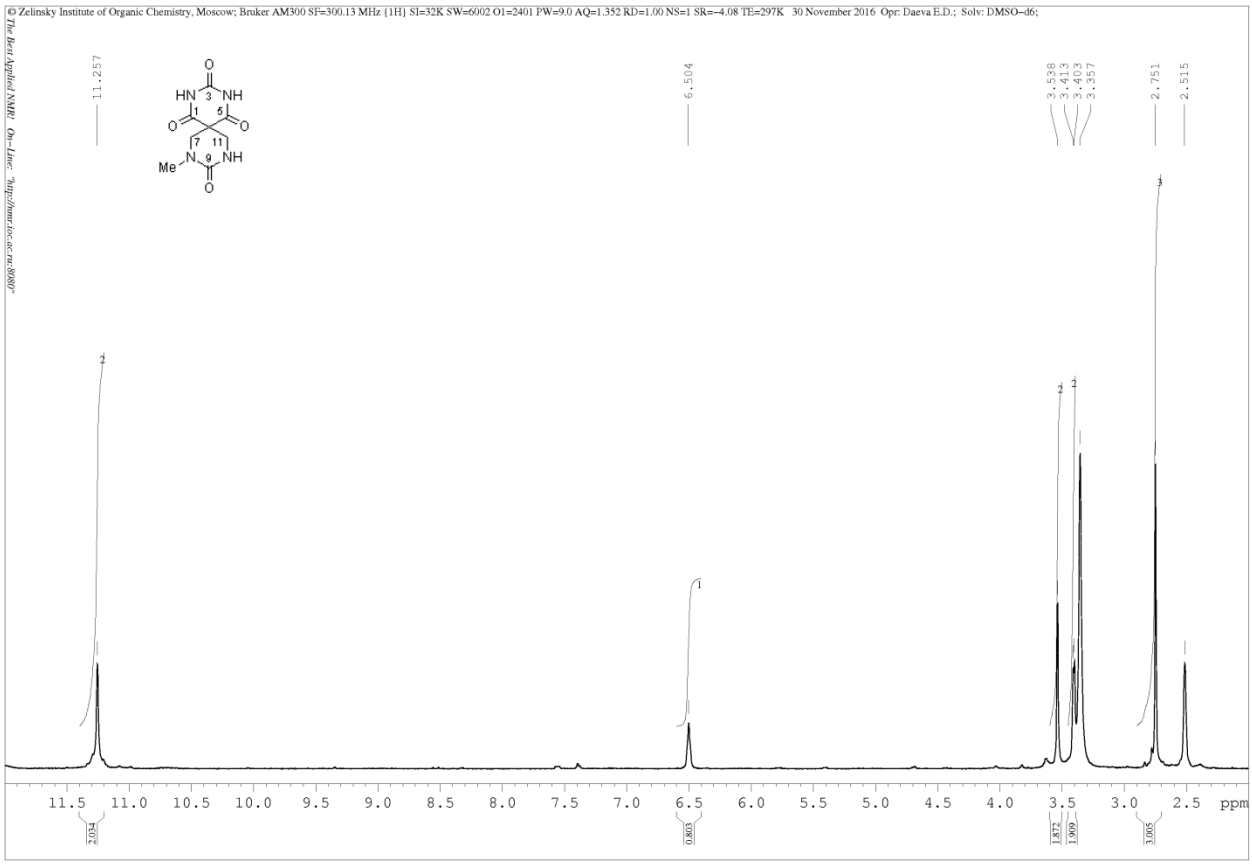
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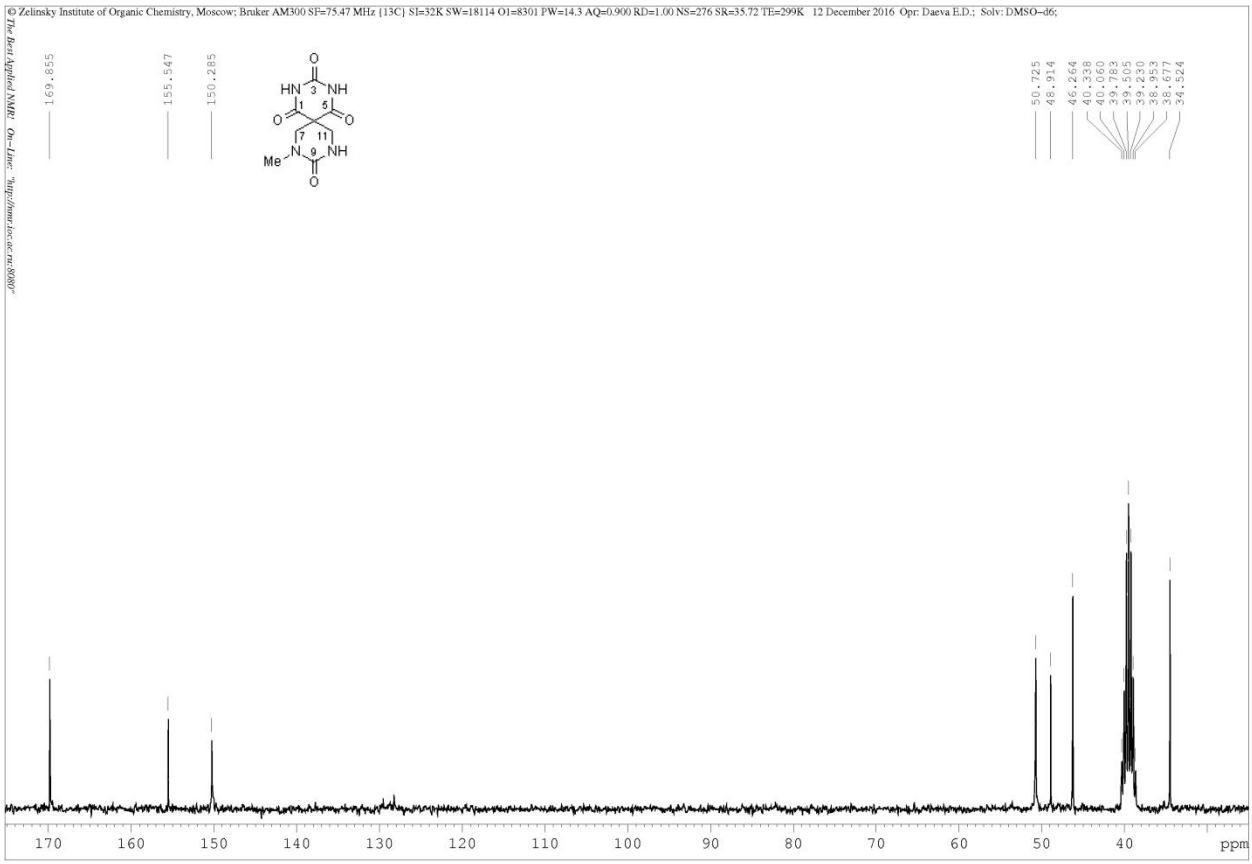
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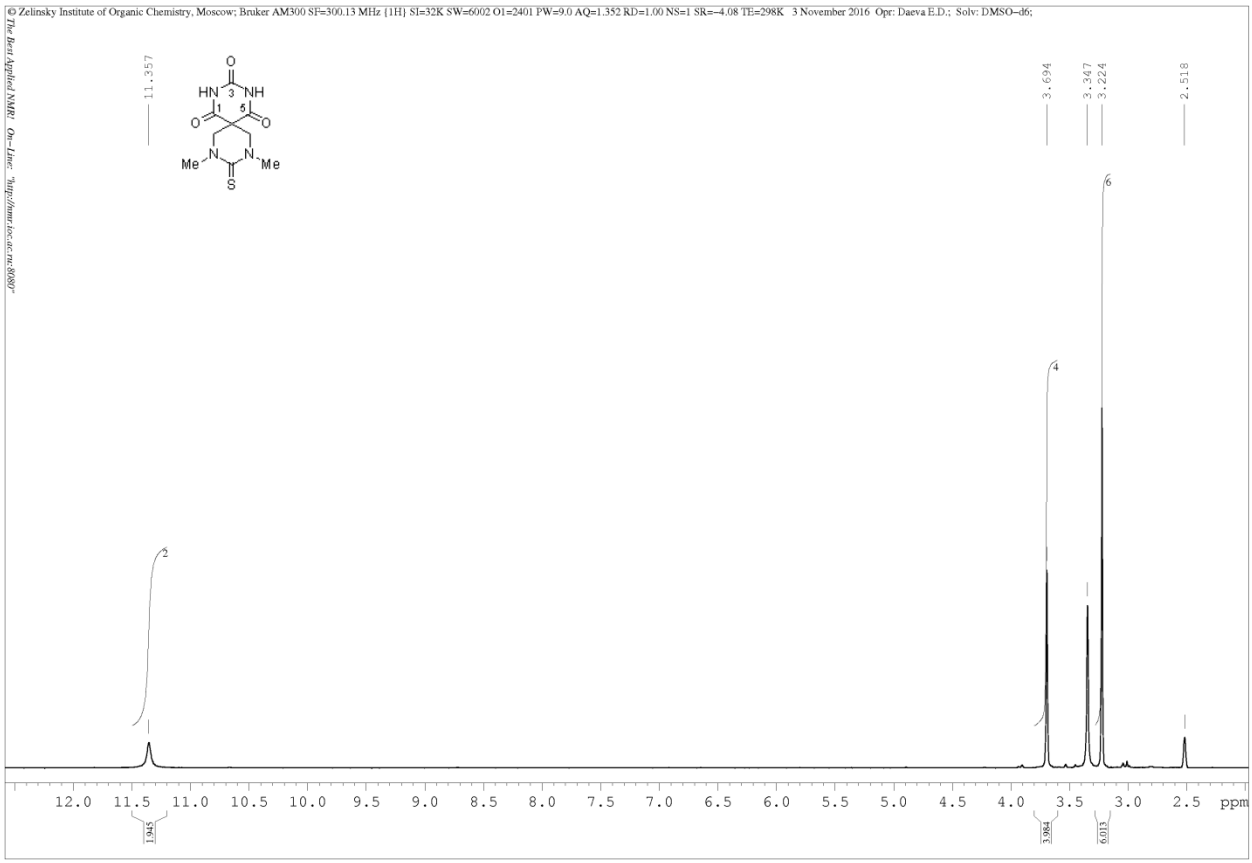
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3.347
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2.518
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NH
O
Me
N
S
12.0
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11.0
10.5
10.0
9.5
9.0
8.5
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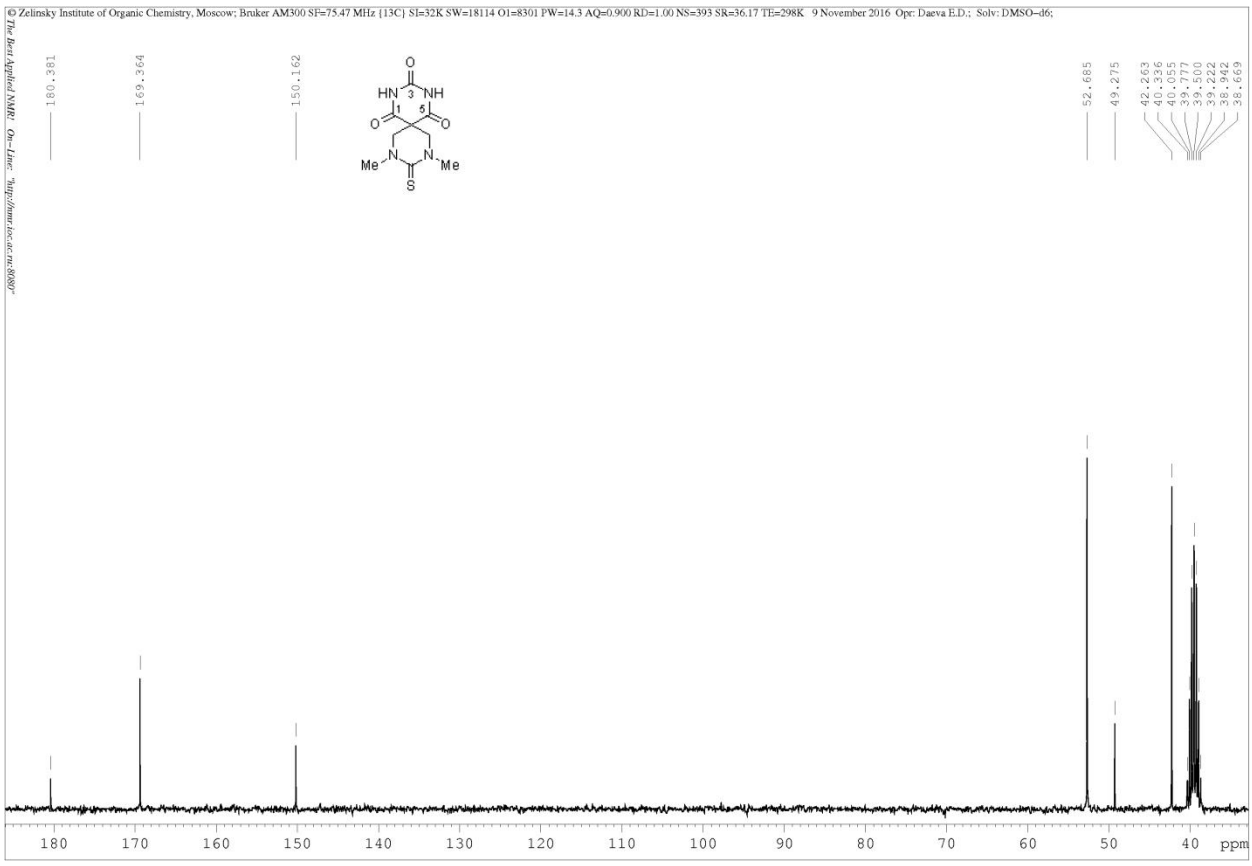
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39.777
39.500
39.222
38.942
38.669
HN
NH
O
O
O
Me
N
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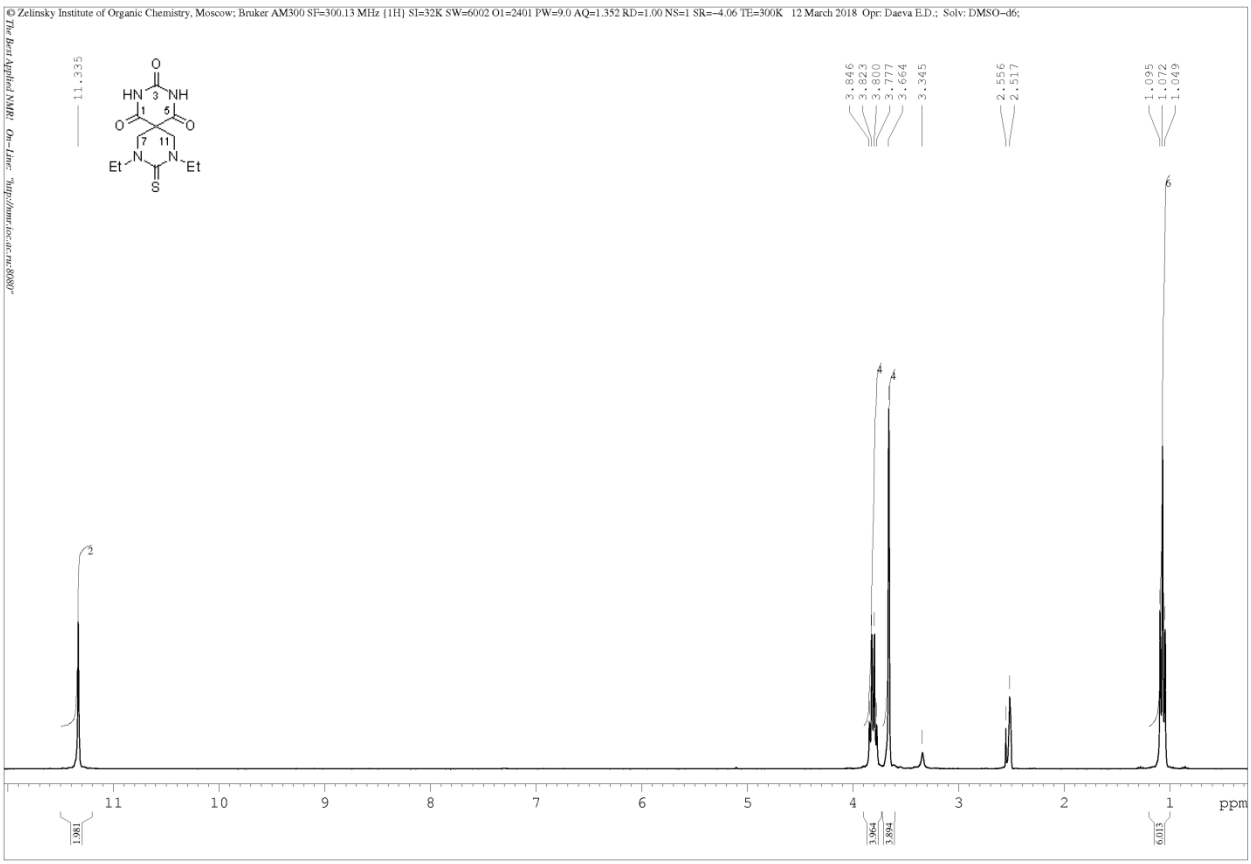
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3.823
3.800
3.777
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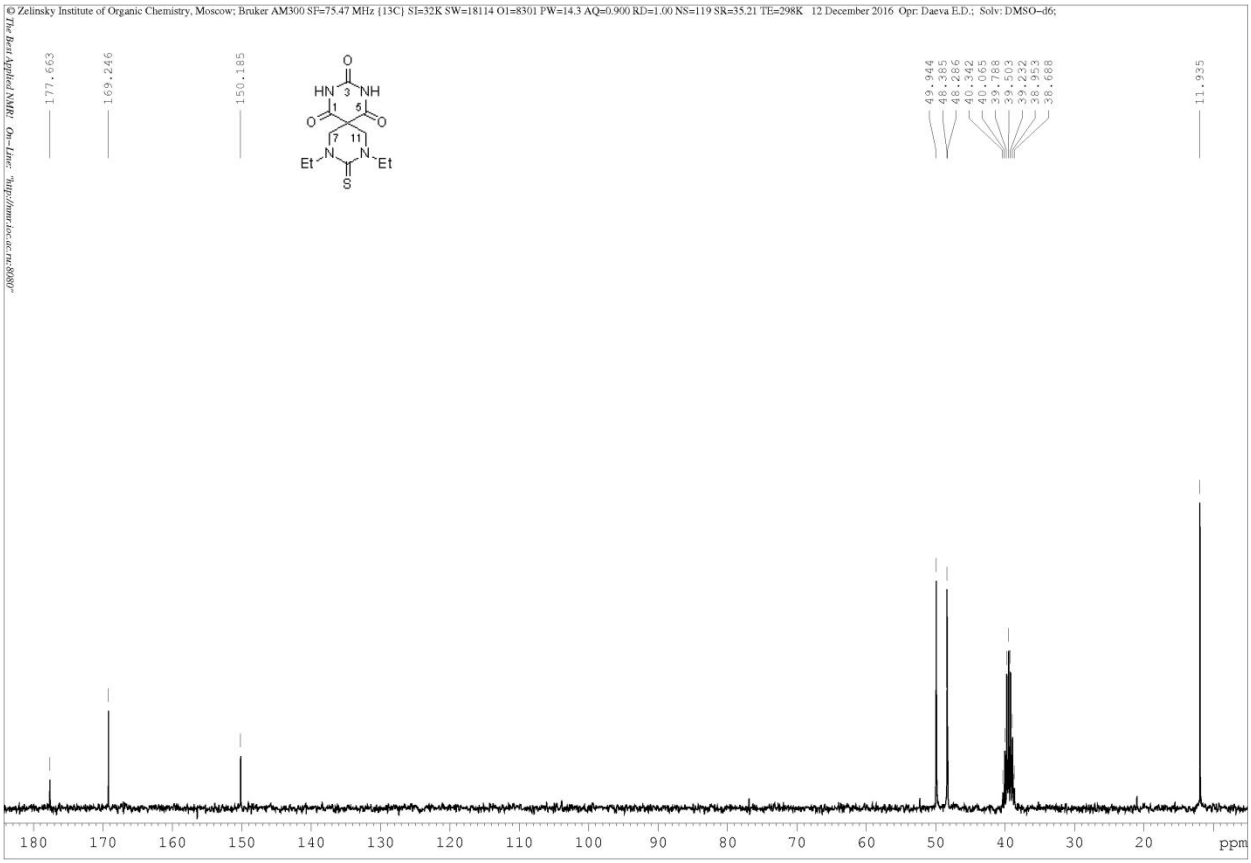
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Et
Et
S
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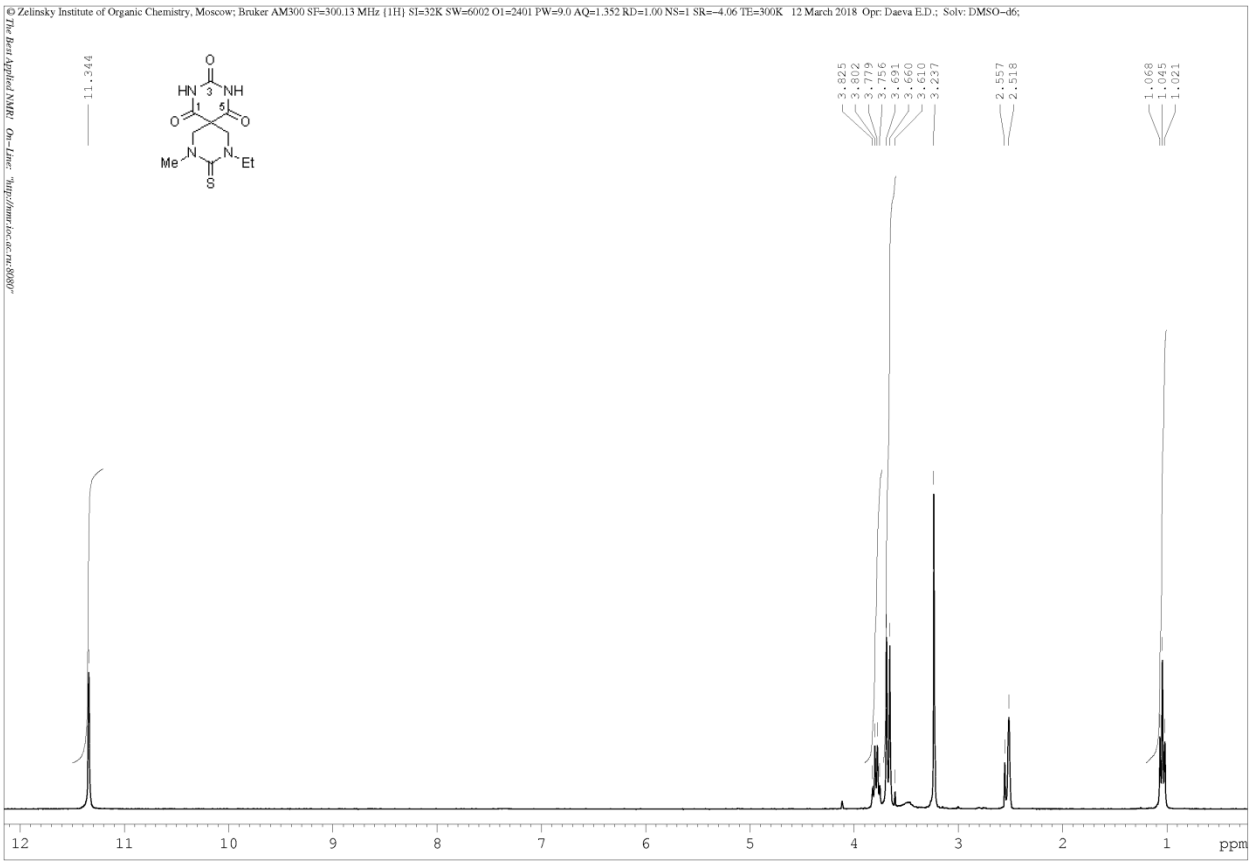
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3.779
3.756
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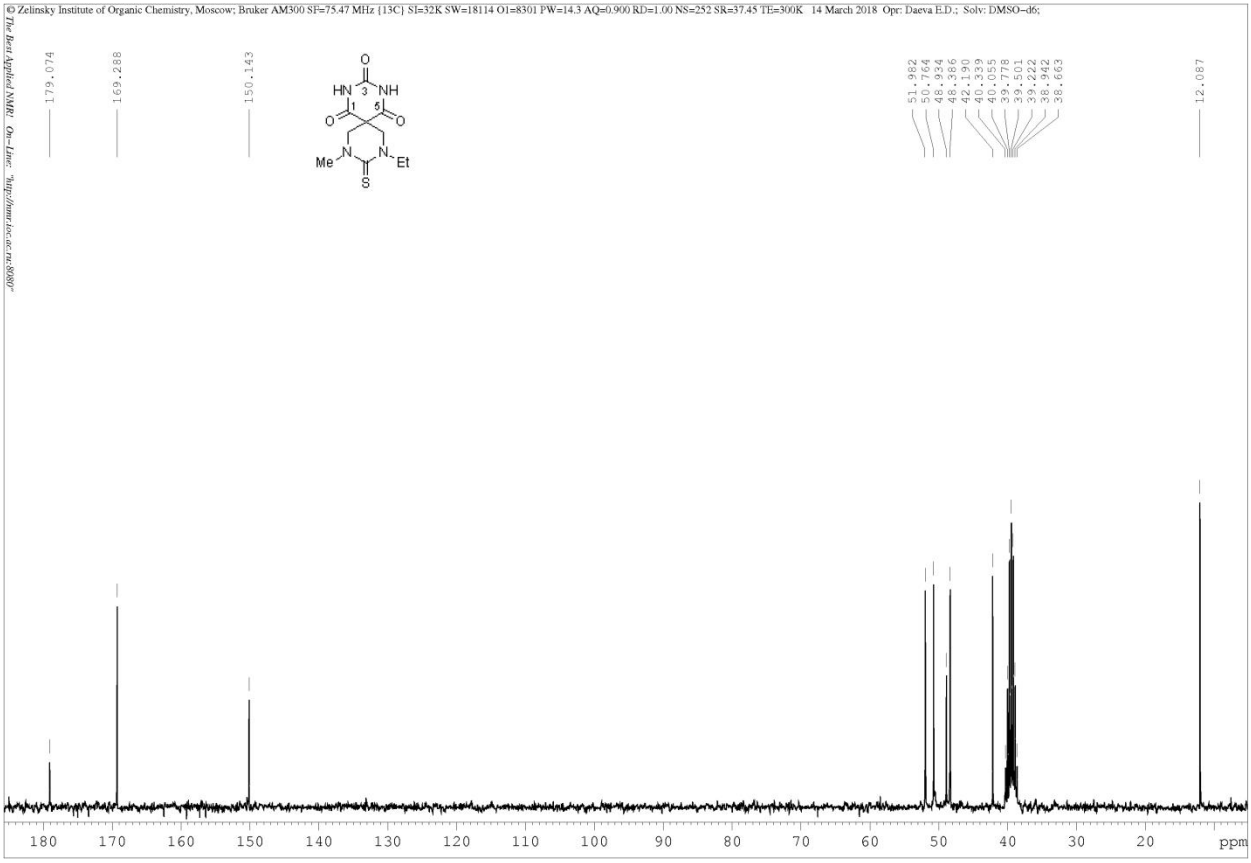
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© The Best Applied NMR: On-Line: "http://nmr.tsc.ac.ru:8080"
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50.764
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48.686
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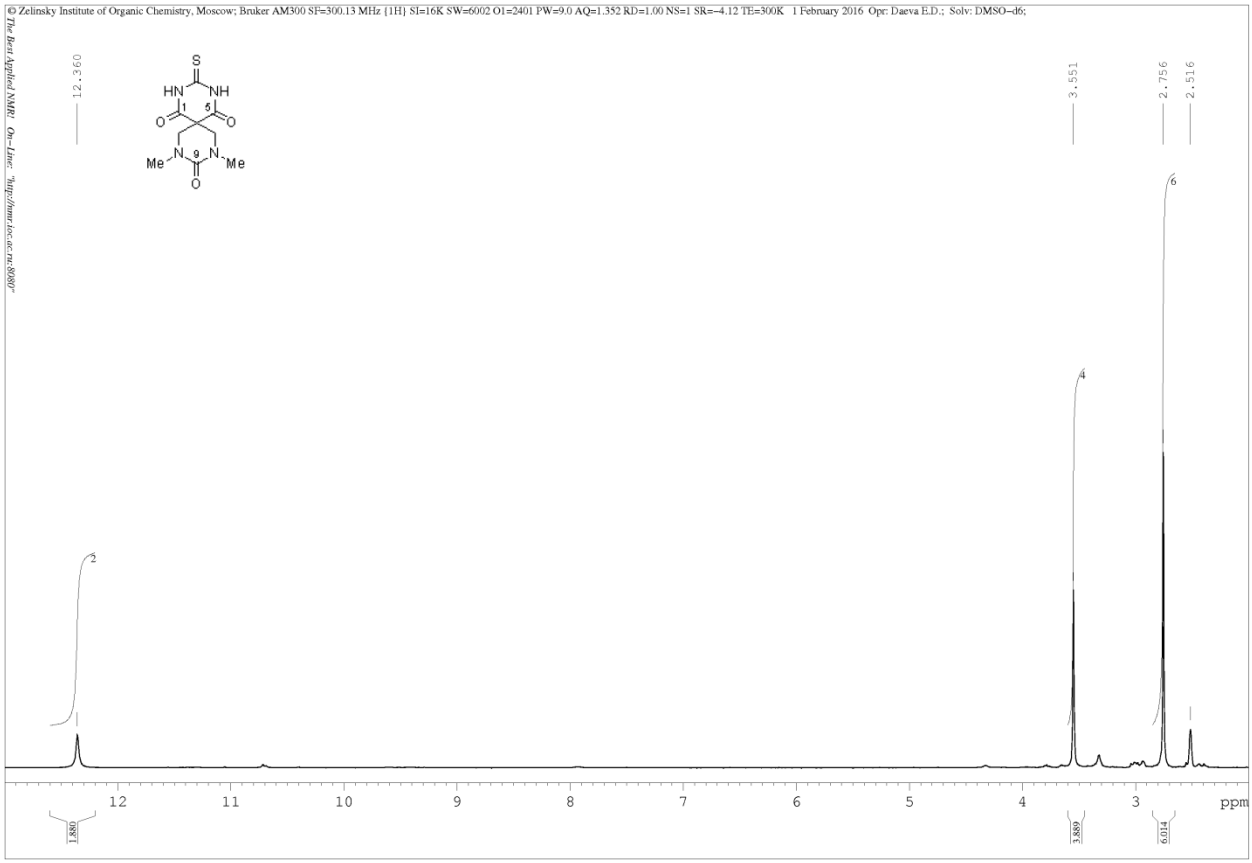
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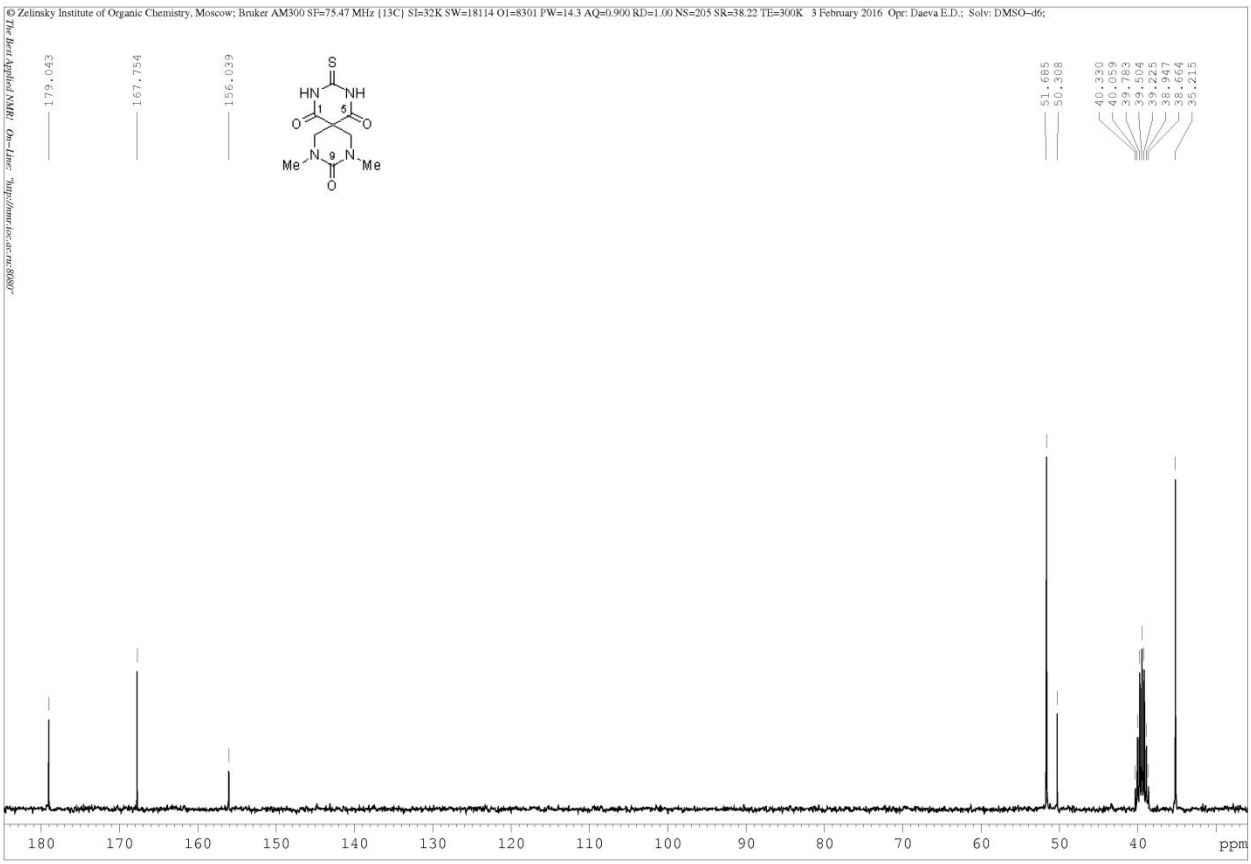
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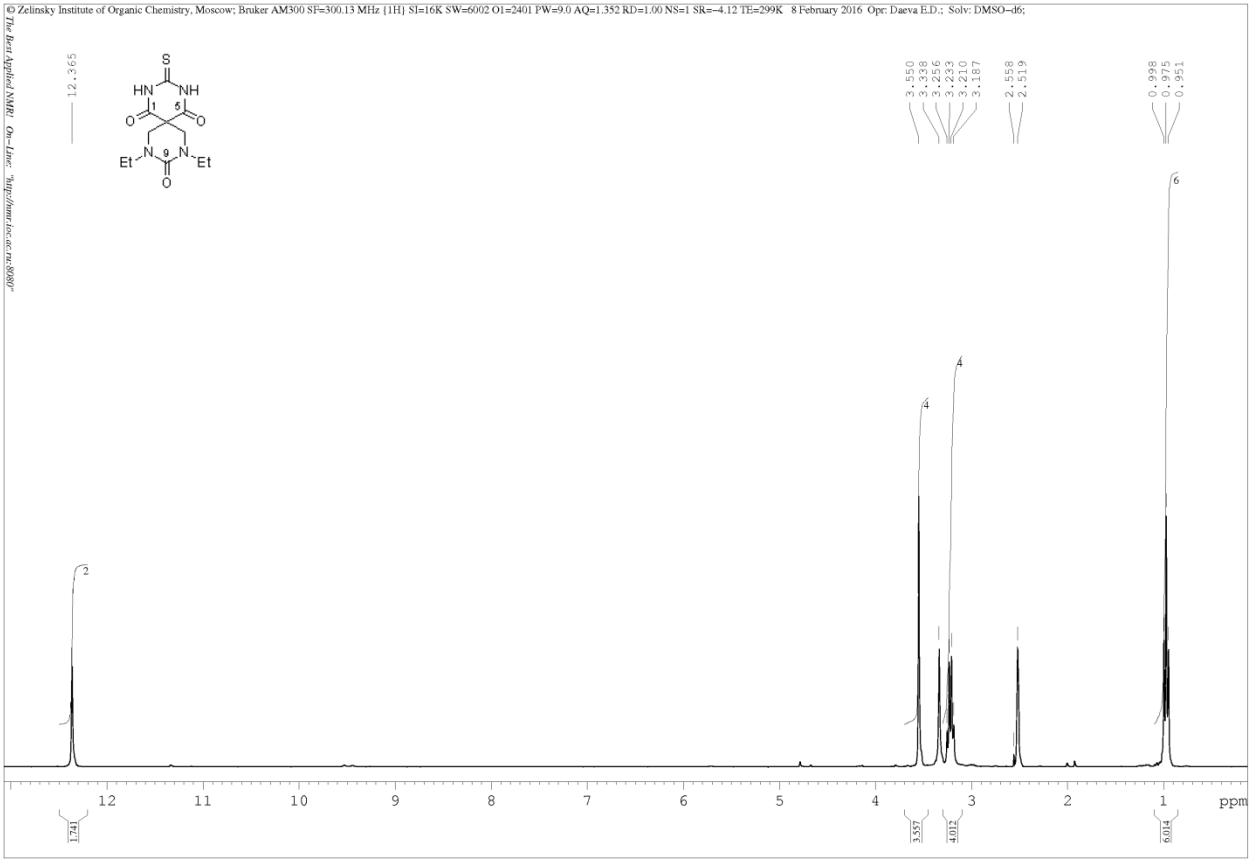
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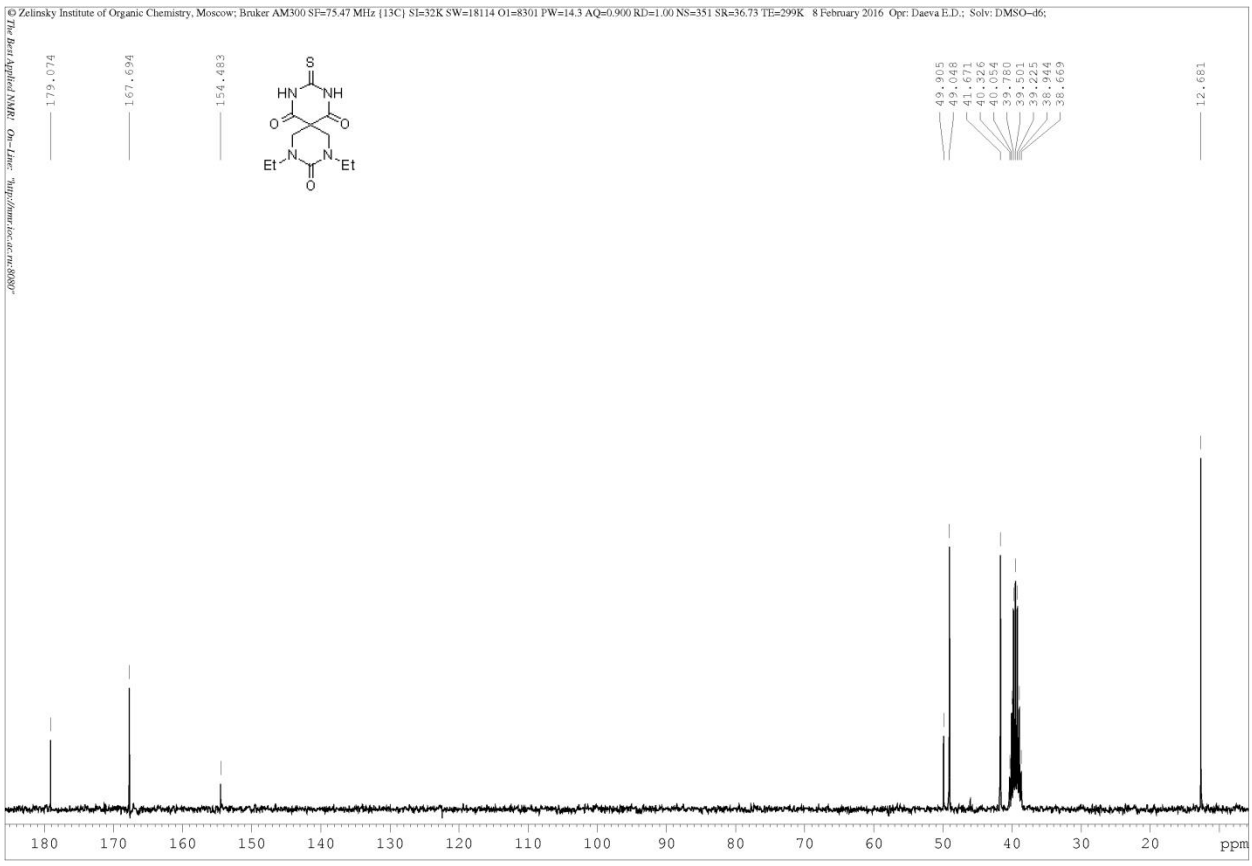
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39.501
39.225
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N
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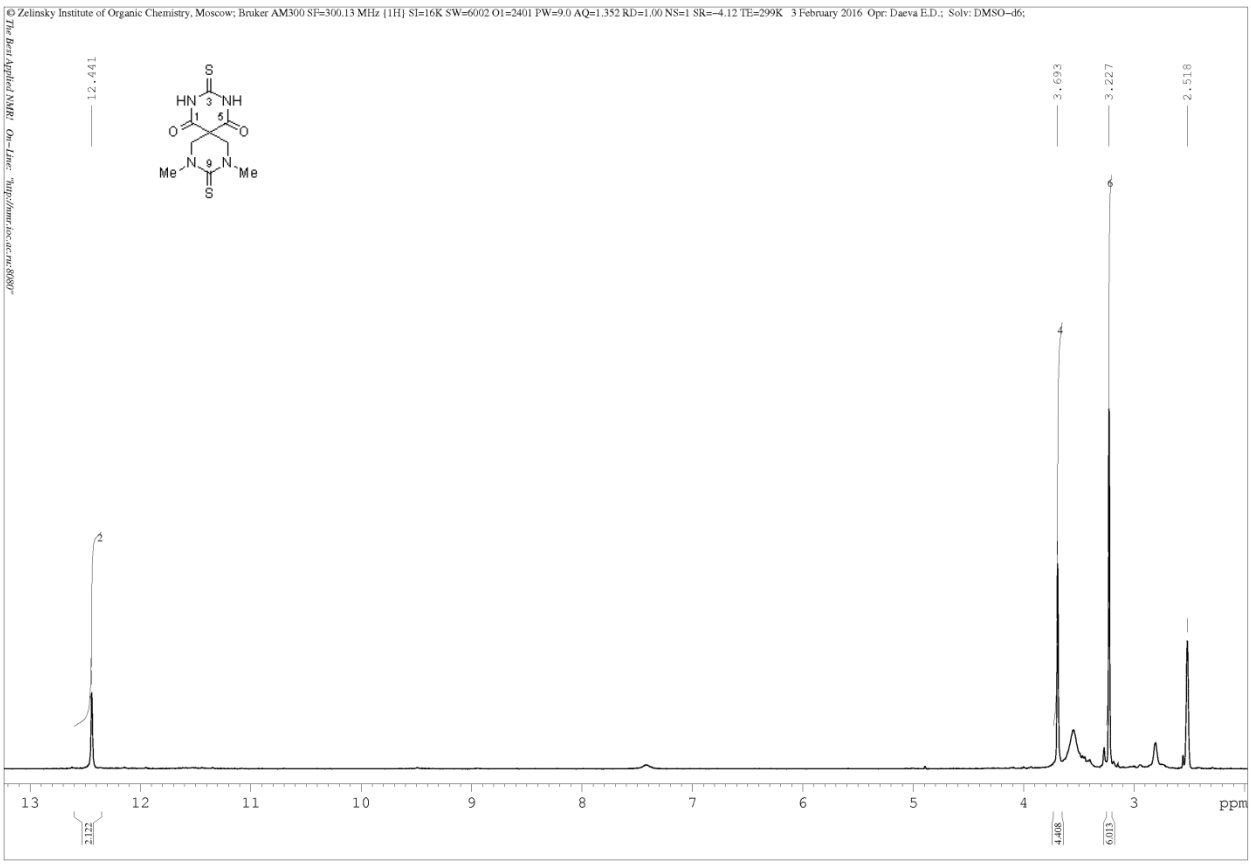
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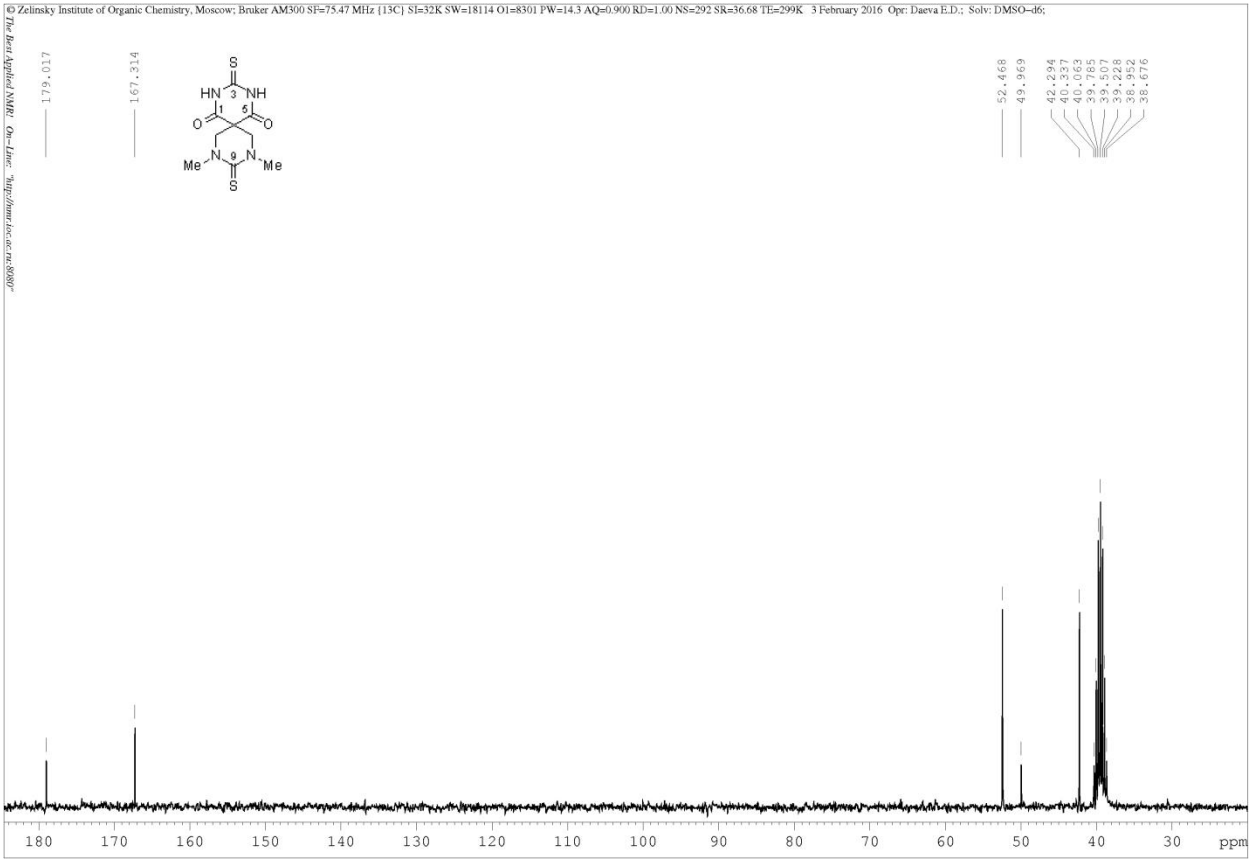
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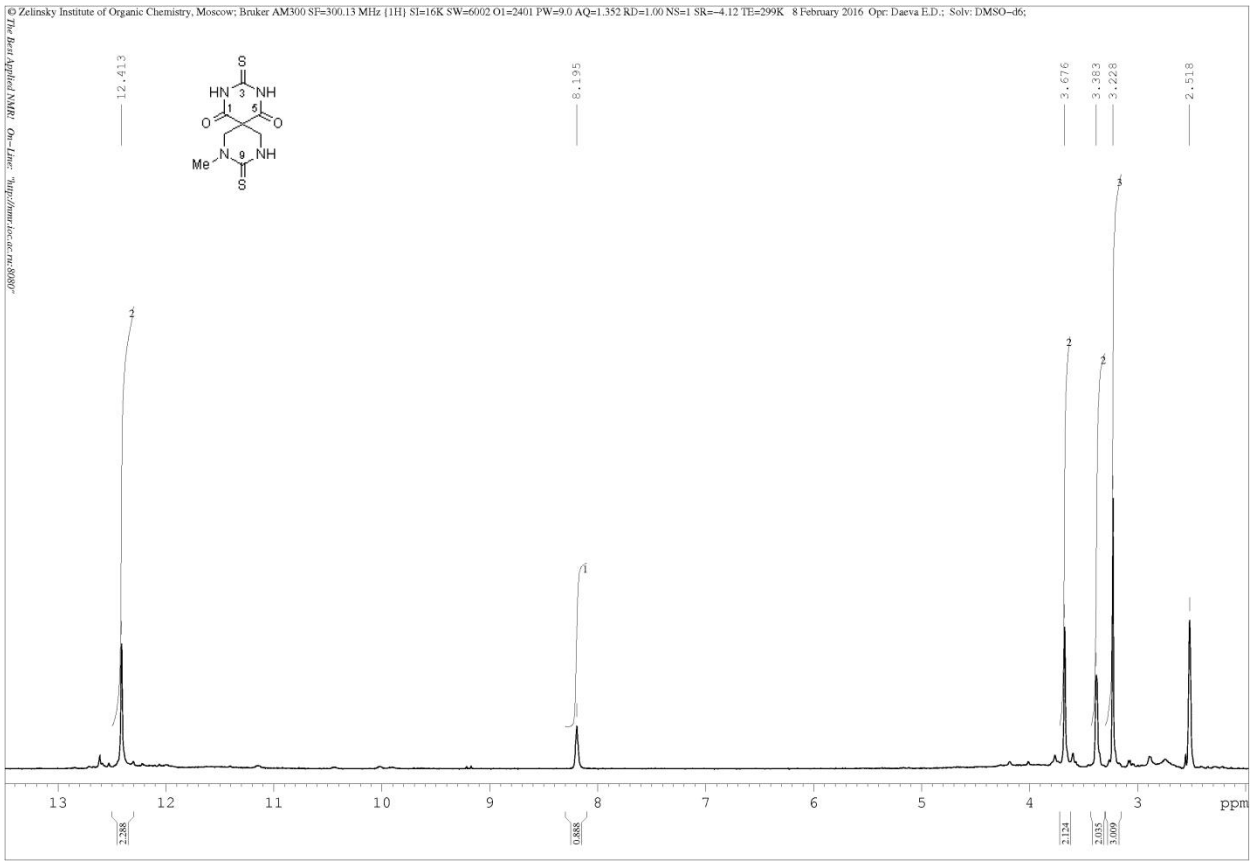
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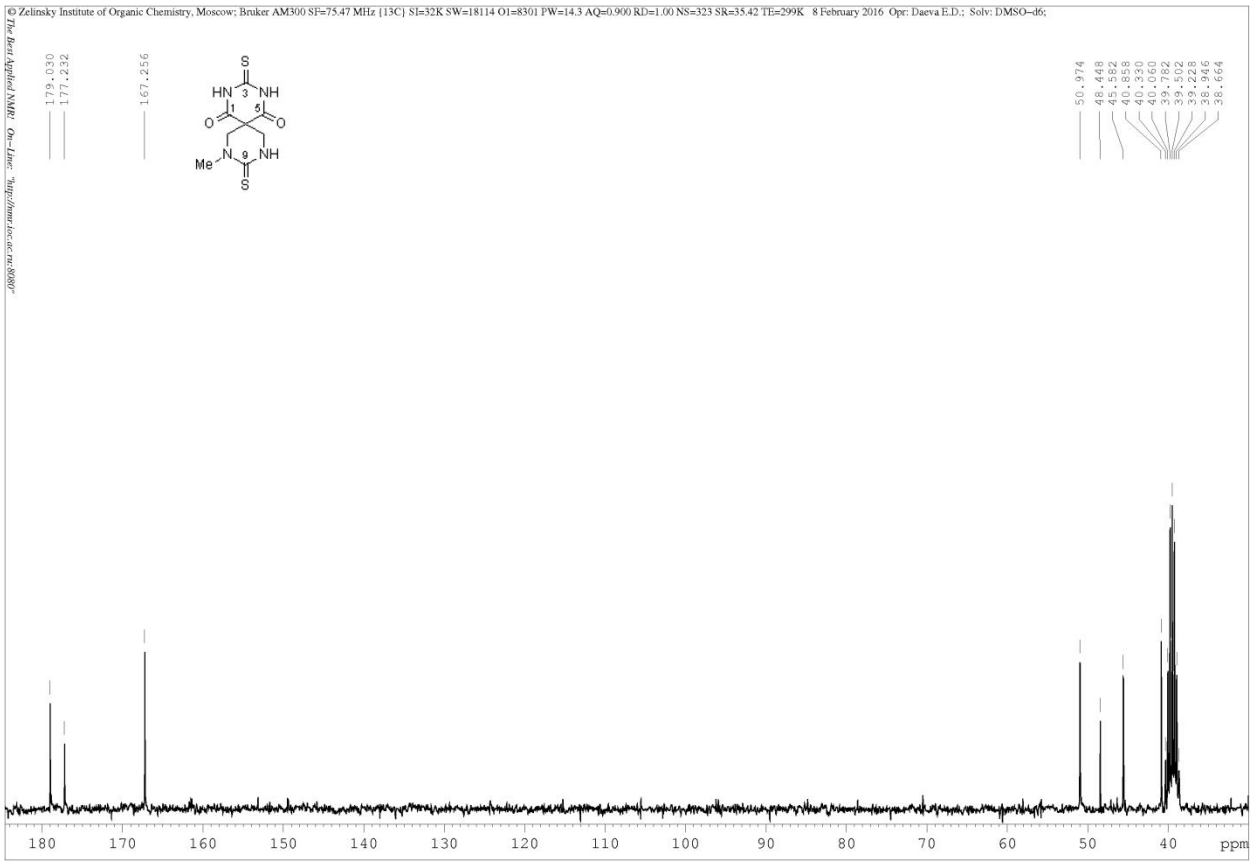
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© The Best Applied NMR: On-Line: "http://nmr.tsc.ac.ru:8080"
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177.232
167.256
50.974
48.448
45.582
40.858
40.330
40.060
39.782
39.502
39.228
38.946
38.664
ppm