

Design, synthesis and evaluation of new pyrazino[1',2':1,5]pyrrolo[2,3-*d*]pyrimidines as tacrine-like acetylcholinesterase inhibitors

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Characteristics of synthesized compounds

Methyl 7-(2-bromoethyl)-4-(methylamino)-7H-pyrrolo[2,3-d]pyrimidine-6-carboxylate (3).

Yield 67%, white solid, mp 179-181 °C. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.28 (s, 1H, CH), 8.03 (s, 1H, NH), 7.47 (s, 1H), 4.86 (dd, *J* = 8.3, 5.2 Hz, 2H, CH₂), 3.85 (s, 3H, OCH₃), 3.74 (dd, *J* = 8.3, 5.2 Hz, 2H, CH₂), 2.97 (d, *J* = 5.0 Hz, 3H, CH₃). ¹³C NMR (126 MHz, DMSO-*d*₆) δ 161.5, 158.1, 155.4, 151.8, 123.2, 109.1, 102.6, 52.3, 44.2, 31.6, 27.5. Anal. Calcd. for C₁₁H₁₃BrN₄O₂: C, 42.19; H, 4.18; Br, 25.52; N, 17.89. Found: C, 42.21; H, 4.14; Br, 25.60; N, 17.96.

Methyl 7-(2-bromoethyl)-4-(dimethylamino)-7H-pyrrolo[2,3-d]pyrimidine-6-carboxylate (4).

Yield 75%, white solid, mp 138-140 °C. ¹H NMR (400 MHz, CDCl₃) δ 8.39 (s, 1H, CH), 7.39 (s, 1H, CH), 5.00 (t, *J* = 7.1 Hz, 2H, CH₂), 3.90 (s, 3H, OCH₃), 3.68 (t, *J* = 7.1 Hz, 2H, CH₂), 3.41 (s, 6H, N(CH₃)₂). ¹³C NMR (126 MHz, CDCl₃) δ 161.8, 158.5, 154.2, 153.4, 123.5, 111.9, 102.7, 52.1, 44.5, 39.7, 30.0. Anal. Calcd. for C₁₂H₁₅BrN₄O₂: C, 44.05; H, 4.62; Br, 24.42; N, 17.12. Found: C, 44.09; H, 4.56; Br, 24.35; N, 17.09.

7-Methyl-4-(methylamino)-8,9-dihydropyrazino[1',2':1,5]pyrrolo[2,3-d]pyrimidin-6(7H)-one (5).

Yield 81%, white solid, mp 297-299 °C. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.23 (s, 1H, CH), 7.82 (q, *J* = 5.3 Hz, 1H, NH), 7.14 (s, 1H, CH), 4.32 – 4.17 (m, 2H, CH₂), 3.79 – 3.69 (m, 2H, CH₂), 3.02 (s, 3H, CH₃), 2.97 (d, *J* = 4.6 Hz, 3H, CH₃). ¹³C NMR (101 MHz, DMSO-*d*₆) δ 158.8, 157.4, 153.8, 148.3, 125.1, 103.1, 101.7, 47.3, 38.5, 33.5, 27.0. LCMS [M+H]⁺: 232.0. Anal. Calcd. for C₁₁H₁₃N₅O: C, 57.13; H, 5.67; N, 30.28. Found: C, 57.07; H, 5.71; N, 30.32.

4-(Dimethylamino)-7-methyl-8,9-dihydropyrazino[1',2':1,5]pyrrolo[2,3-d]pyrimidin-6(7H)-one (6).

Yield 87%, white solid, mp 190-191 °C. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.21 (s, 1H, CH), 7.17 (s, 1H, CH), 4.37 – 4.20 (m, 2H, CH₂), 3.84 – 3.65 (m, 2H, CH₂), 3.34 (s, 6H, N(CH₃)₂), 3.03 (s, 3H, CH₃). ¹³C NMR (101 MHz, DMSO-*d*₆) δ 158.8, 157.4, 152.9, 149.7, 124.9, 104.7, 102.6, 47.2, 38.8, 38.5, 33.6. LCMS [M+H]⁺: 246.0. Anal. Calcd. for C₁₂H₁₅N₅O: C, 58.76; H, 6.16; N, 28.55. Found: C, 58.81; H, 6.19; N, 28.59.

Methyl 7-(2-bromoethyl)-4-methoxy-7H-pyrrolo[2,3-d]pyrimidine-6-carboxylate (7).

Yield 75%, white solid, mp 105-107 °C. ¹H NMR (400 MHz, CDCl₃) δ 8.56 (s, 1H), 7.32 (s, 1H), 5.04 (s, 2H), 4.13 (s, 3H), 3.93 (s, 3H), 3.70 (t, *J* = 7.0 Hz, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 164.7, 161.6, 154.0, 153.7, 125.9, 108.0, 104.7, 54.1, 52.2, 44.7, 29.8. Anal. Calcd. for C₁₁H₁₂BrN₃O₃: C, 42.06; H, 3.85; N, 13.38. Found: C, 42.02; H, 3.91; N, 13.33.

4-Methoxy-8,9-dihydropyrazino[1',2':1,5]pyrrolo[2,3-d]pyrimidin-6(7H)-one (8).

Yield 57%, white solid, mp 246-248 °C. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.53 (s, 1H), 8.29 (s, 1H), 7.01 (s, 1H), 4.46 – 4.25 (m, 2H), 4.08 (s, 3H), 3.76 – 3.54 (m, 2H). ¹³C NMR (101 MHz, DMSO-*d*₆) δ 163.5, 159.4, 152.8, 150.5, 128.2, 104.4, 100.2, 53.8. LCMS [M+H]⁺: 219.0. Anal. Calcd. for C₁₀H₁₀N₄O₂: C, 55.04; H, 4.62; N, 25.67. Found: C, 55.11; H, 4.59; N, 25.68.

4-Methoxy-7-methyl-8,9-dihydropyrazino[1',2':1,5]pyrrolo[2,3-d]pyrimidin-6(7H)-one (9).

Yield 63%, white solid, mp 201-203 °C. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.51 (s, 1H), 6.96 (s, 1H), 4.53 – 4.26 (m, 2H), 4.06 (s, 3H), 3.93 – 3.71 (m, 2H), 3.06 (s, 3H). ¹³C NMR (101 MHz, DMSO-*d*₆) δ 163.4, 158.3, 152.7, 150.3, 127.9, 104.6, 100.1, 53.7, 47.1, 38.9, 33.7. LCMS [M+H]⁺: 233.0. Anal. Calcd. for C₁₁H₁₂N₄O₂: C, 56.89; H, 5.21; N, 24.12. Found: C, 56.92; H, 5.18; N, 24.16.

4-Amino-7-methyl-8,9-dihydropyrazino[1',2':1,5]pyrrolo[2,3-d]pyrimidin-6(7H)-one (10). Yield 74%, white solid, mp 301-303 °C. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.14 (s, 1H), 7.28 (s, 2H), 7.17 (s, 1H), 4.25 (t, *J* = 5.7 Hz, 2H), 3.75 (t, *J* = 5.7 Hz, 2H), 3.03 (s, 3H). ¹³C NMR (101 MHz, DMSO-*d*₆) δ 158.9, 158.5, 153.9, 148.9, 125.3, 102.6, 102.3, 47.3, 38.5, 33.6. LCMS [M+H]⁺: 218.0. Anal. Calcd. for C₁₀H₁₁N₅O: C, 55.29; H, 5.10; N, 32.24. Found: C, 55.25; H, 5.15; N, 32.29.

3,7-Dimethyl-8,9-dihydropyrazino[1',2':1,5]pyrrolo[2,3-d]pyrimidine-4,6(3H,7H)-dione (13). Yield 79%, white solid, mp 254-256 °C. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.29 (s, 1H, CH), 6.90 (s, 1H, CH), 4.29 – 4.19 (m, 2H, CH₂), 3.75 – 3.67 (m, 2H, CH₂), 3.42 (s, 3H, CH₃), 2.98 (s, 3H, CH₃). ¹³C NMR (126 MHz, DMSO-*d*₆) δ 158.9, 158.4, 149.4, 146.7, 126.0, 107.9, 104.7, 47.6, 39.4, 34.0, 33.8. LCMS [M+H]⁺: 233.0. Anal. Calcd. for C₁₁H₁₂N₄O₂: C, 56.89; H, 5.21; N, 24.12. Found: C, 56.86; H, 5.25; N, 24.05.

Methyl 7-(2,2-diethoxyethyl)-4-methoxy-7H-pyrrolo[2,3-d]pyrimidine-6-carboxylate (14). Yield 39%, white solid, mp 156-158 °C. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.56 (s, 1H), 7.22 (s, 1H), 4.89 – 4.52 (m, 3H), 4.08 (s, 3H), 3.87 (s, 3H), 3.73 – 3.49 (m, 2H), 3.34 – 3.26 (m, 2H), 0.93 (t, *J* = 7.0 Hz, 6H). ¹³C NMR (101 MHz, DMSO-*d*₆) δ 163.7, 161.0, 153.4, 153.3, 126.9, 106.1, 103.5, 100.3, 62.3, 53.9, 52.1, 45.2, 14.9. Anal. Calcd. for C₁₅H₂₁N₃O₅: C, 55.72; H, 6.55; N, 13.00. Found: C, 55.69; H, 6.59; N, 13.02.

4-Aminopyrazino[1',2':1,5]pyrrolo[2,3-d]pyrimidin-6(7H)-one (15). Yield 55%, white solid, mp >320 °C. ¹H NMR (400 MHz, CDCl₃+CF₃COOH) 10.31 (s, 1H), 9.58 (s, 1H), 8.58 (s, 1H), 8.34 (s, 1H), 8.02 (s, 1H), 7.80 (d, *J* = 5.8 Hz, 1H), 6.95 (s, 1H). ¹³C NMR (126 MHz, CDCl₃+CF₃COOH) δ 159.3, 153.8, 143.6, 141.7, 125.8, 115.5, 106.9, 104.4, 103.7. LCMS [M+H]⁺: 202.0. Anal. Calcd. for C₉H₇N₅O: C, 53.73; H, 3.51; N, 34.81. Found: C, 53.70; H, 3.47; N, 34.85.

Methyl 7-(2,2-diethoxyethyl)-4-(dimethylamino)-7H-pyrrolo[2,3-d]pyrimidine-6-carboxylate (16). Yield 43%, white solid, mp 87-89 °C. ¹H NMR (500 MHz, DMSO-*d*₆) δ 8.25 (s, 1H, CH), 7.40 (s, 1H, CH), 4.71 (t, *J* = 5.5 Hz, 1H), 4.62 (d, *J* = 5.5 Hz, 2H), 3.83 (s, 3H, OCH₃), 3.57 (dq, *J* = 9.7, 7.0 Hz, 2H), 3.44 – 3.11 (m, 8H), 0.94 (t, *J* = 7.0 Hz, 6H, 2CH₃). ¹³C NMR (126 MHz, DMSO-*d*₆) δ 161.7, 157.9, 154.0, 153.4, 124.0, 111.4, 101.9, 100.7, 62.5, 52.1, 45.1, 39.5, 15.5. Anal. Calcd. for C₁₆H₂₄N₄O₄: C, 57.13; H, 7.19; N, 16.16. Found: C, 57.20; H, 7.23; N, 16.12.

4-(Dimethylamino)pyrazino[1',2':1,5]pyrrolo[2,3-d]pyrimidin-6(7H)-one (17). Yield 65%, white solid, mp 305-307 °C. ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.67 (s, 1H, NH), 8.30 (s, 1H, CH), 7.48 (d, *J* = 5.8 Hz, 1H, CH), 7.39 (s, 1H, CH), 6.66 (d, *J* = 5.8 Hz, 1H, CH), 3.39 (s, 6H, N(CH₃)₂). ¹³C NMR (101 MHz, DMSO-*d*₆) δ 158.1, 156.7, 152.6, 145.6, 123.4, 121.6, 114.2, 103.4, 101.9, 38.9. LCMS [M+H]⁺: 230.0. Anal. Calcd. for C₁₁H₁₁N₅O: C, 57.63; H, 4.84; N, 30.55. Found: C, 57.69; H, 4.92; N, 30.49.

4-(Dimethylamino)-7-methylpyrazino[1',2':1,5]pyrrolo[2,3-d]pyrimidin-6(7H)-one (18). Yield 87%, white solid, mp 232-234 °C. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.30 (s, 1H, CH), 7.55 (d, *J* = 6.0 Hz, 1H, CH), 7.37 (s, 1H, CH), 6.89 (d, *J* = 6.0 Hz, 1H, CH), 3.40 (s, 3H, CH₃), 3.39 (s, 6H, N(CH₃)₂). ¹³C NMR (101 MHz, DMSO-*d*₆) δ 157.8, 156.1, 152.5, 145.4, 123.0, 119.1, 103.6, 103.5, 101.6, 39.7, 34.4. LCMS [M+H]⁺: 244.0. Anal. Calcd. for C₁₂H₁₃N₅O: C, 59.25; H, 5.39; N, 28.79. Found: C, 59.32; H, 5.43; N, 28.85.

Methyl 4-chloro-7-(2-oxopropyl)-7H-pyrrolo[2,3-d]pyrimidine-6-carboxylate (19). Yield 76%, white solid, mp 160-161 °C. ¹H NMR (500 MHz, DMSO-*d*₆) δ 8.80 (s, 1H, CH), 7.40 (s, 1H, CH), 5.53

(s, 2H, CH₂), 3.87 (s, 3H, OCH₃), 2.30 (s, 3H, CH₃). ¹³C NMR (126 MHz, DMSO-*d*₆) δ 202.2, 160.9, 154.2, 153.7, 152.4, 129.9, 115.7, 106.6, 53.4, 53.0, 27.4. Anal. Calcd. for C₁₁H₁₀ClN₃O₃: C, 49.36; H, 3.77; N, 15.70. Found: C, 49.39; H, 3.83; N, 15.65.

Methyl 4-(dimethylamino)-7-(2-oxopropyl)-7H-pyrrolo[2,3-*d*]pyrimidine-6-carboxylate (20). Yield 77%, white solid, mp 138-140 °C. ¹H NMR (500 MHz, DMSO-*d*₆) δ 8.20 (s, 1H, CH), 7.43 (s, 1H, CH), 5.36 (s, 2H, CH₂), 3.79 (s, 3H, OCH₃), 3.35 (s, 6H, N(CH₃)₂), 2.22 (s, 3H, CH₃). ¹³C NMR (126 MHz, DMSO-*d*₆) δ 202.7, 161.6, 158.0, 154.1, 153.1, 123.3, 111.3, 102.0, 52.7, 52.1, 39.4, 27.4. Anal. Calcd. for C₁₃H₁₆N₄O₃: C, 56.51; H, 5.84; N, 20.28. Found: C, 56.58; H, 5.89; N, 20.25.

4-(Dimethylamino)-8-methylpyrazino[1',2':1,5]pyrrolo[2,3-*d*]pyrimidin-6(7H)-one (21). Yield 69%, white solid, mp 318-320 °C. ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.65 (s, 1H, NH), 8.26 (s, 1H, CH), 7.31 (s, 1H, CH), 7.30 (s, 1H, CH), 3.38 (s, 6H, N(CH₃)₂), 2.10 (s, 3H, CH₃). ¹³C NMR (101 MHz, DMSO-*d*₆) δ 157.8, 156.8, 152.3, 145.1, 123.2, 122.5, 103.4, 101.3, 100.1, 40.2, 15.7. LCMS [M+H]⁺: 244.0. Anal. Calcd. for C₁₂H₁₃N₅O: C, 59.25; H, 5.39; N, 28.79. Found: C, 59.29; H, 5.44; N, 28.82.

4-(Dimethylamino)-7,8-dimethylpyrazino[1',2':1,5]pyrrolo[2,3-*d*]pyrimidin-6(7H)-one (22). Yield 83%, white solid, mp 208-210 °C. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.23 (s, 1H, CH), 7.39 (s, 1H, CH), 7.22 (s, 1H, CH), 3.38 (s, 3H, CH₃), 3.36 (s, 6H, N(CH₃)₂), 2.27 (s, 3H, CH₃). ¹³C NMR (101 MHz, DMSO-*d*₆) δ 157.7, 156.5, 152.2, 144.7, 125.3, 121.9, 103.3, 101.2, 40.1, 28.9, 16.6. LCMS [M+H]⁺: 258.0. Anal. Calcd. for C₁₃H₁₅N₅O: C, 60.69; H, 5.88; N, 27.22. Found: C, 60.72; H, 5.85; N, 27.26.

Methyl 4-methoxy-7-(2-oxopropyl)-7H-pyrrolo[2,3-*d*]pyrimidine-6-carboxylate (23). Yield 75%, white solid, mp 135-137 °C. ¹H NMR (500 MHz, DMSO-*d*₆) δ 8.55 (s, 1H, CH), 7.28 (s, 1H, CH), 5.46 (s, 2H, CH₂), 4.09 (s, 3H, OCH₃), 3.82 (s, 3H, OCH₃), 2.27 (s, 3H, CH₃). ¹³C NMR (151 MHz, DMSO-*d*₆) δ 202.4, 164.4, 161.3, 154.1, 153.4, 126.6, 106.4, 104.0, 54.5, 53.1, 52.6, 27.4. Anal. Calcd. for C₁₂H₁₃N₃O₄: C, 54.75; H, 4.98; N, 15.96. Found: C, 54.79; H, 4.92; N, 15.91.

4-Methoxy-8-methylpyrazino[1',2':1,5]pyrrolo[2,3-*d*]pyrimidin-6(7H)-one (24). Yield 59%, white solid, mp 297-299 °C. ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.78 (s, 1H, NH), 8.59 (s, 1H, CH), 7.42 (s, 1H, CH), 7.14 (s, 1H, CH), 4.14 (s, 3H, OCH₃), 2.15 (s, 3H, CH₃). ¹³C NMR (101 MHz, CDCl₃+CF₃COOH) δ 163.79, 159.05, 144.35, 142.53, 127.06, 126.51, 105.14, 103.89, 103.19, 60.33, 15.93. LCMS [M+H]⁺: 231.0. Anal. Calcd. for C₁₁H₁₀N₄O₂: C, 57.39; H, 4.38; N, 24.34. Found: C, 57.35; H, 4.41; N, 24.30.

4-Amino-8-methylpyrazino[1',2':1,5]pyrrolo[2,3-*d*]pyrimidin-6(7H)-one (25). Yield 68%, white solid, mp 286-288 °C. ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.75 (s, 1H, NH), 8.21 (s, 1H, CH), 7.60 (s, 2H, NH₂), 7.32 (s, 2H, 2CH), 2.08 (s, 3H, CH₃). ¹³C NMR (101 MHz, DMSO-*d*₆) δ 159.0, 156.9, 153.5, 144.4, 123.0, 103.5, 100.3, 98.7, 15.6. LCMS [M+H]⁺: 216.0. Anal. Calcd. for C₁₀H₉N₅O: C, 55.81; H, 4.22; N, 32.54. Found: C, 55.85; H, 4.19; N, 32.59.

4-Methoxy-7,8-dimethylpyrazino[1',2':1,5]pyrrolo[2,3-*d*]pyrimidin-6(7H)-one (26). Yield 81%, white solid, mp 237-240 °C. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.58 (s, 1H, CH), 7.58 (s, 1H, CH), 7.07 (s, 1H, CH), 4.11 (s, 3H, OCH₃), 3.41 (s, 3H, CH₃), 2.31 (s, 3H, CH₃). ¹³C NMR (101 MHz, DMSO-*d*₆) δ 163.9, 156.3, 152.0, 145.30, 126.20, 125.0, 105.3, 101.4, 96.7, 54.0, 29.2, 16.6. LCMS [M+H]⁺: 245.0. Anal. Calcd. for C₁₂H₁₂N₄O₂: C, 59.01; H, 4.95; N, 22.94. Found: C, 59.06; H, 4.88; N, 22.97.

4-Amino-7,8-dimethylpyrazino[1',2':1,5]pyrrolo[2,3-*d*]pyrimidin-6(7H)-one (27). Yield 67%, white solid, mp >320 °C. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.22 (s, 1H, CH), 7.45 (s, 3H, NH₂, CH),

7.33 (s, 1H, CH), 3.41 (s, 3H, CH₃), 2.30 (s, 3H, CH₃). ¹³C NMR (101 MHz, CDCl₃+CF₃COOH) δ 158.3, 153.6, 142.8, 140.4, 128.2, 125.5, 103.8, 103.3, 102.9, 30.8, 17.5. LCMS [M+H]⁺: 230.0. Anal. Calcd. for C₁₁H₁₁N₅O: C, 57.63; H, 4.84; N, 30.55. Found: C, 57.67; H, 4.80; N, 30.61.

7,8-Dimethyl-4-(methylamino)pyrazino[1',2':1,5]pyrrolo[2,3-d]pyrimidin-6(7H)-one (28). Yield 56%, white solid, mp >320 °C. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.31 (s, 1H, CH), 8.12 (d, *J* = 5.1 Hz, 1H, NH), 7.50 (s, 1H, CH), 7.30 (s, 1H, CH), 3.40 (s, 3H, CH₃), 3.01 (d, *J* = 4.3 Hz, 3H, CH₃), 2.30 (s, 3H, CH₃). ¹³C NMR (101 MHz, DMSO-*d*₆) δ 157.7, 156.6, 153.3, 145.5, 125.3, 122.3, 101.4, 98.1, 97.4, 29.0, 27.1, 16.6. LCMS [M+H]⁺: 244.0. Anal. Calcd. for C₁₂H₁₃N₅O: C, 59.25; H, 5.39; N, 28.79. Found: C, 59.19; H, 5.33; N, 28.82.

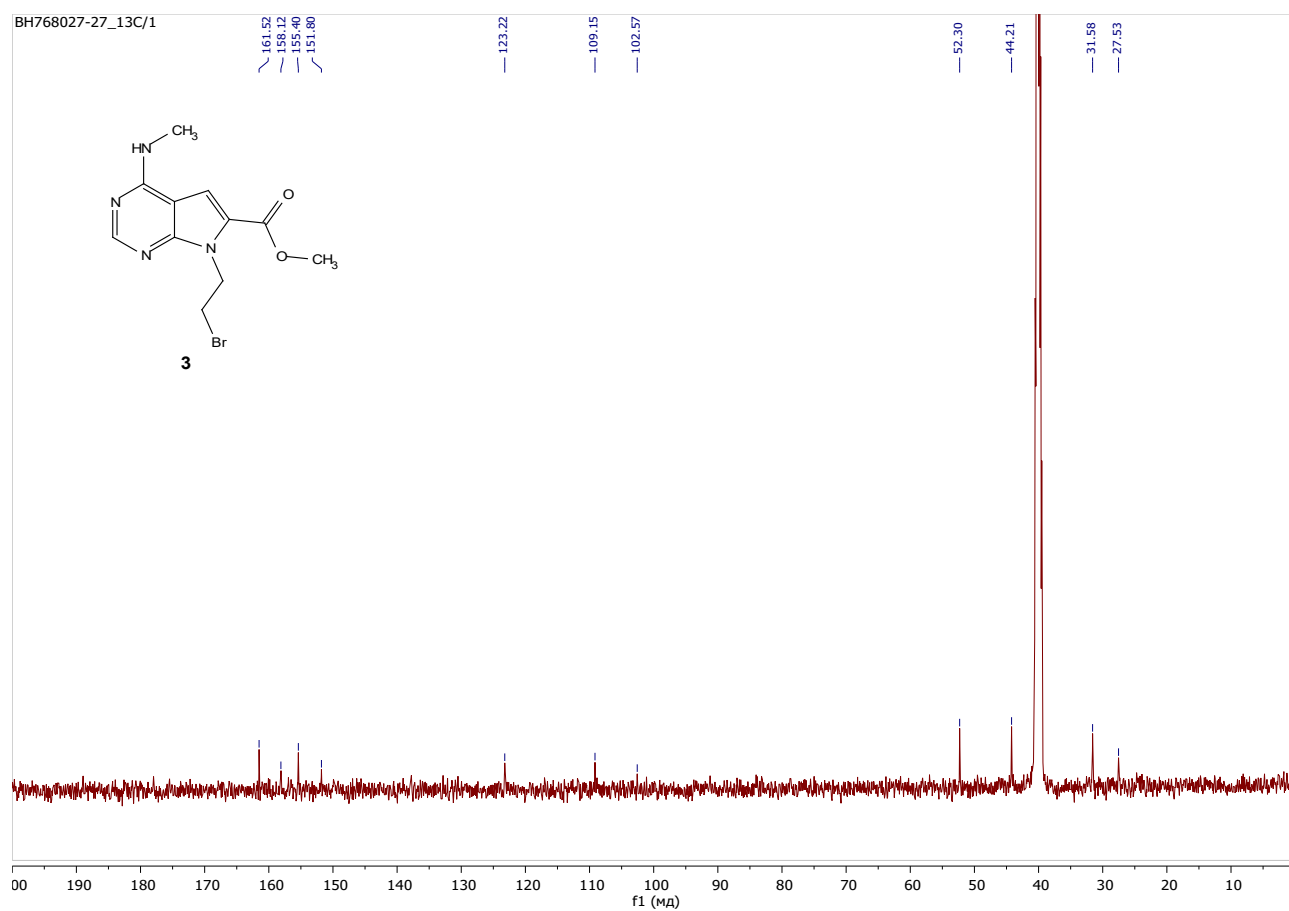
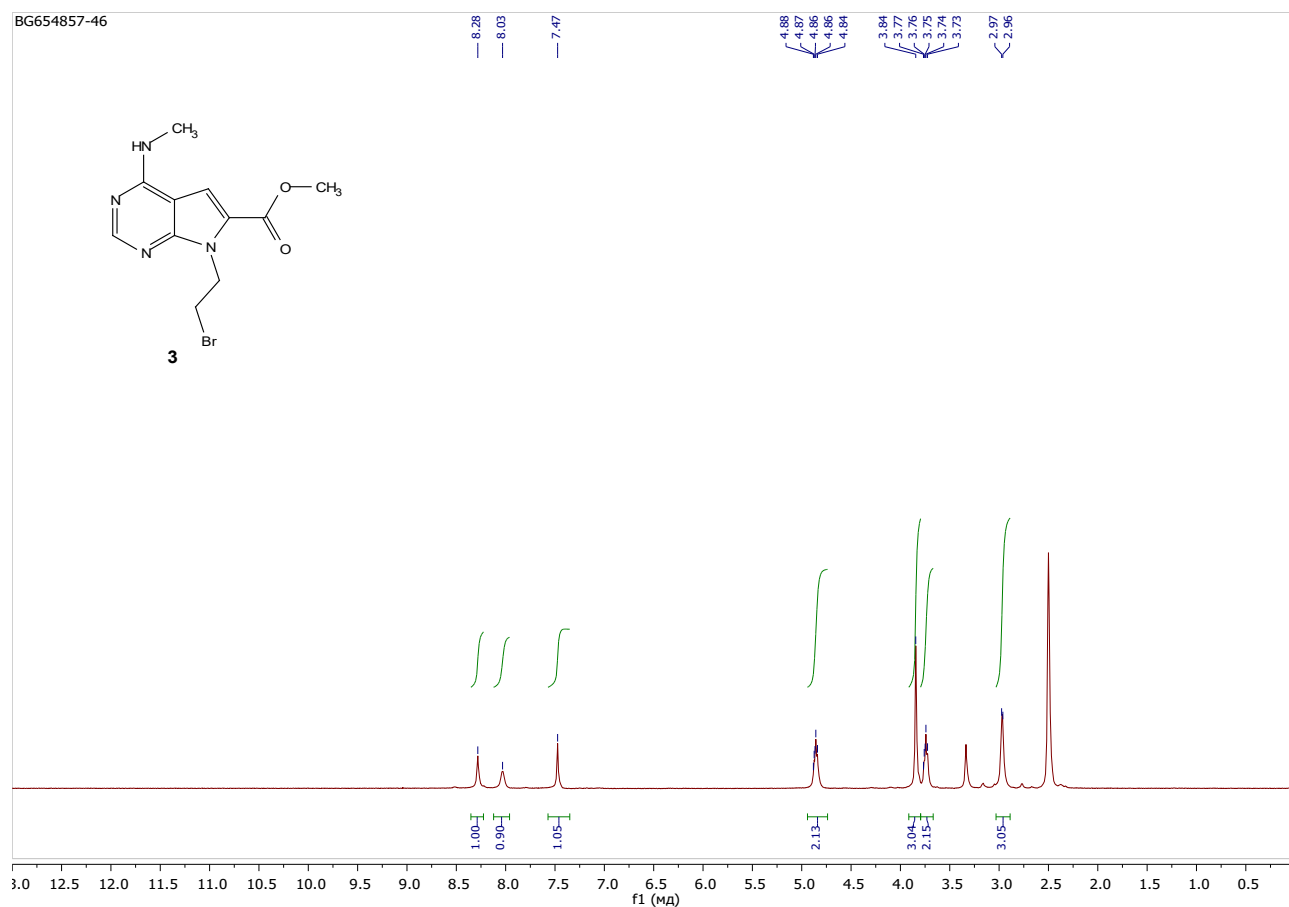
8-(Iodomethyl)-3-methyl-8,9-dihydro-4H-pyrimido[5',4':4,5]pyrrolo[2,1-c][1,4]oxazine-4,6(3H)-dione (30). Yield 84%, white solid, mp 229-231 °C. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.39 (s, 1H, CH), 7.28 (s, 1H, CH), 4.86 (dt, *J* = 8.9, 4.1 Hz, 1H), 4.67 (dd, *J* = 13.1, 3.1 Hz, 1H), 4.05 (dd, *J* = 13.1, 10.1 Hz, 1H), 3.68 – 3.48 (m, 2H, CH₂), 3.44 (s, 3H, CH₃). ¹³C NMR (126 MHz, DMSO-*d*₆) δ 158.2, 158.1, 150.9, 147.4, 119.9, 109.9, 108.7, 76.6, 43.5, 33.9, 4.3. Anal. Calcd. for C₁₁H₁₀IN₃O₃: C, 36.79; H, 2.81; N, 11.70. Found: C, 36.86; H, 2.83; N, 11.75.

3-Methyl-8-methylene-8,9-dihydro-4H-pyrimido[5',4':4,5]pyrrolo[2,1-c][1,4]oxazine-4,6(3H)-dione (31). Yield 75%, white solid, mp 258-260 °C. ¹H NMR (500 MHz, DMSO-*d*₆) δ 8.46 (s, 1H, CH), 7.40 (s, 1H, CH), 5.07 (s, 2H, CH₂), 5.03 (s, 2H, CH₂), 3.48 (s, 3H, CH₃). ¹³C NMR (126 MHz, DMSO-*d*₆) δ 158.2, 155.4, 151.2, 149.1, 147.5, 118.9, 110.6, 99.5, 69.1, 41.6, 33.9. Anal. Calcd. for C₁₁H₉N₃O₃: C, 57.14; H, 3.92; N, 18.17. Found: C, 57.09; H, 3.95; N, 18.11.

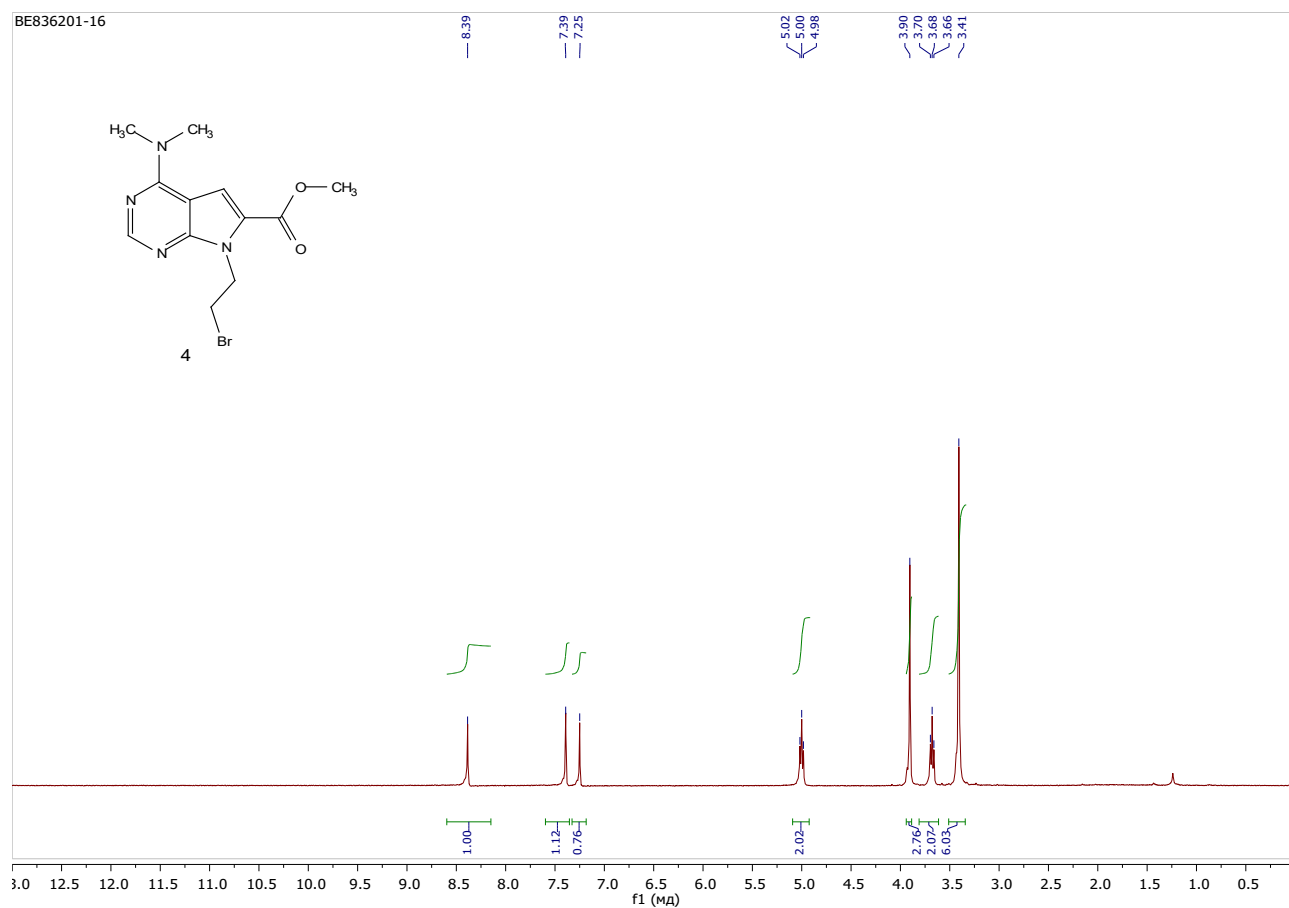
3,8-Dimethylpyrazino[1',2':1,5]pyrrolo[2,3-d]pyrimidine-4,6(3H,7H)-dione (32). Yield 69%, white solid, mp >320 °C. ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.85 (s, 1H, NH), 8.36 (s, 1H, CH), 7.26 (s, 1H, CH), 7.11 (s, 1H, CH), 3.50 (s, 3H, CH₃), 2.09 (s, 3H, CH₃). ¹³C NMR (101 MHz, DMSO-*d*₆) δ 164.0, 161.7, 153.7, 146.7, 130.3, 128.6, 113.9, 106.4, 105.4, 38.7, 21.0. LCMS [M-H]⁺: 231.0. Anal. Calcd. for C₁₁H₁₀N₄O₂: C, 57.39; H, 4.38; N, 24.34. Found: C, 57.45; H, 4.34; N, 24.29.

3,7,8-Trimethylpyrazino[1',2':1,5]pyrrolo[2,3-d]pyrimidine-4,6(3H,7H)-dione (33). Yield 83%, white solid, mp 273-275 °C. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.38 (s, 1H, CH), 7.46 (s, 1H, CH), 7.11 (s, 1H, CH), 3.51 (s, 3H, CH₃), 3.40 (s, 3H, CH₃), 2.30 (s, 3H, CH₃). ¹³C NMR (101 MHz, DMSO-*d*₆) δ 158.3, 156.1, 148.3, 140.9, 127.1, 122.8, 108.7, 101.2, 101.0, 33.4, 29.0, 16.7. LCMS [M+H]⁺: 245.0. Anal. Calcd. for C₁₂H₁₂N₄O₂: C, 59.01; H, 4.95; N, 22.94. Found: C, 59.04; H, 4.99; N, 22.89.

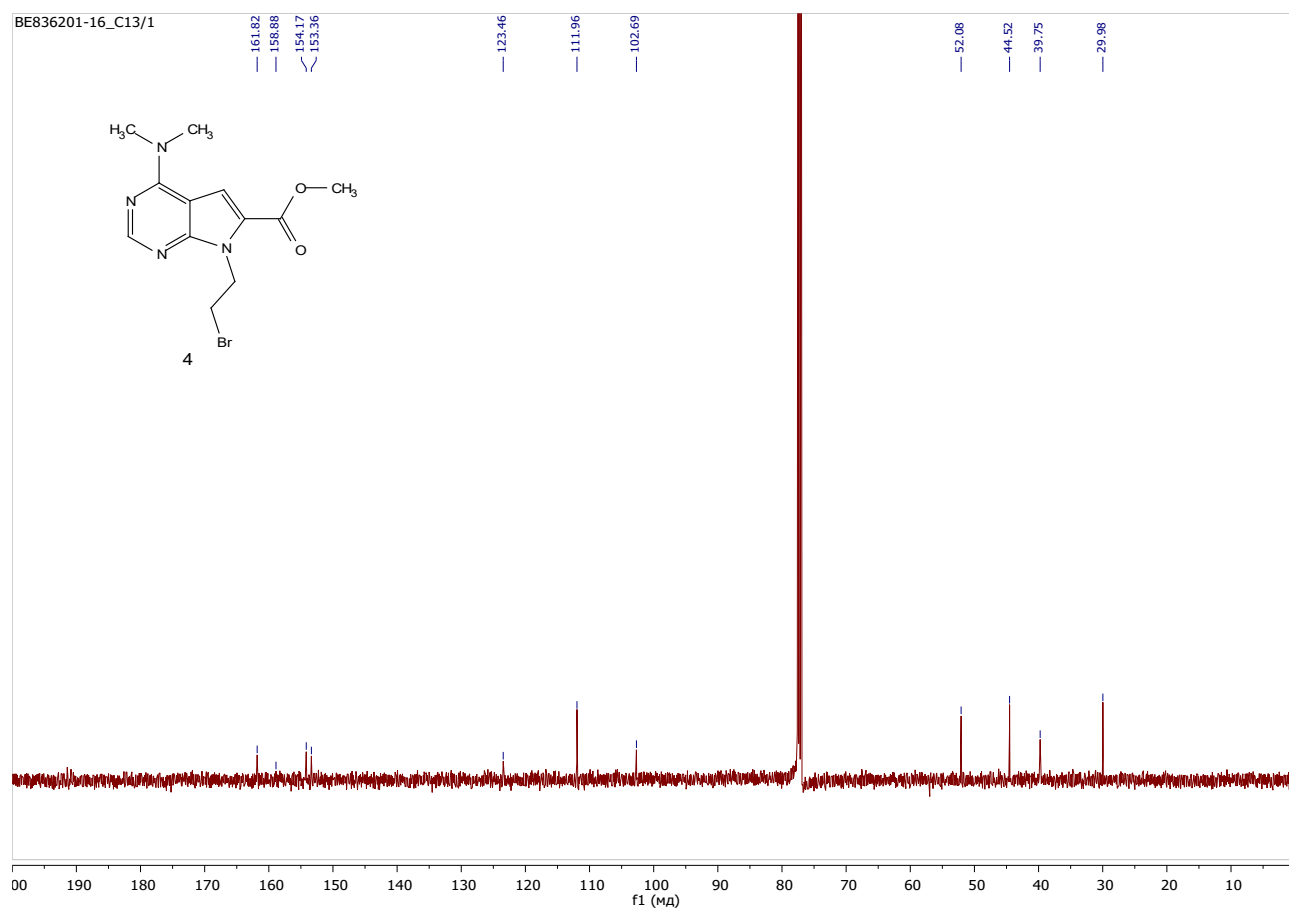
¹H and ¹³C NMR spectra of synthesized compounds

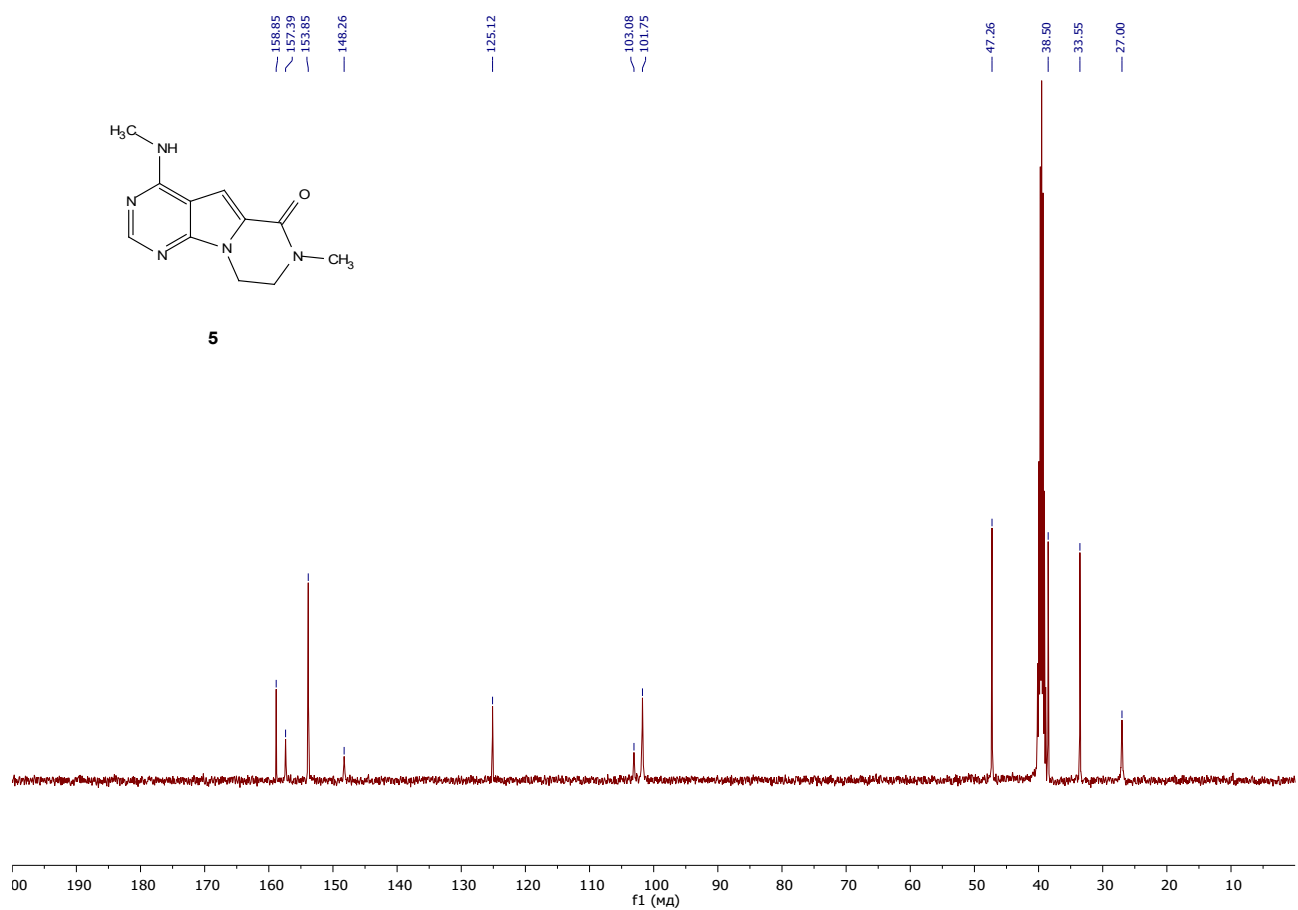
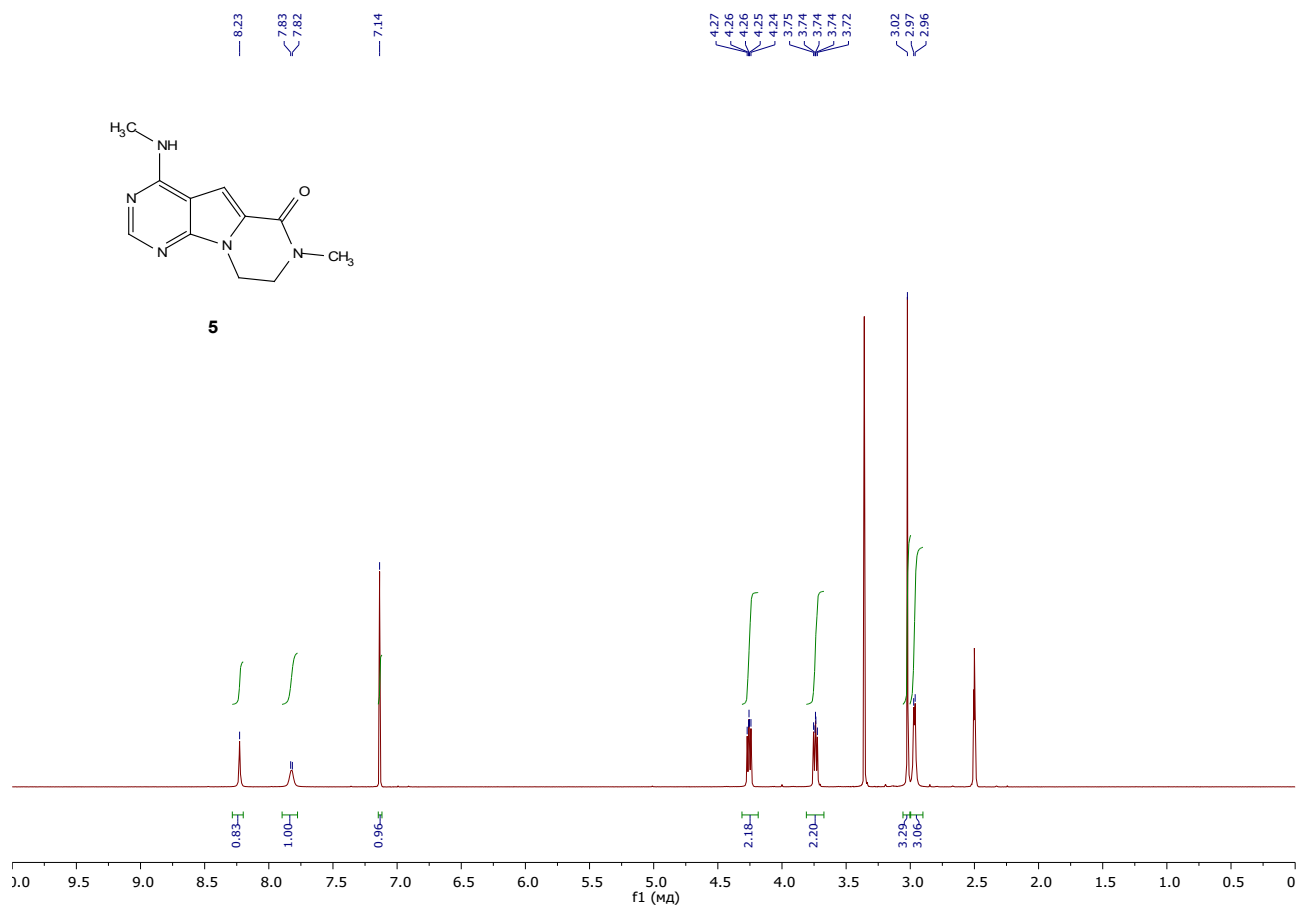


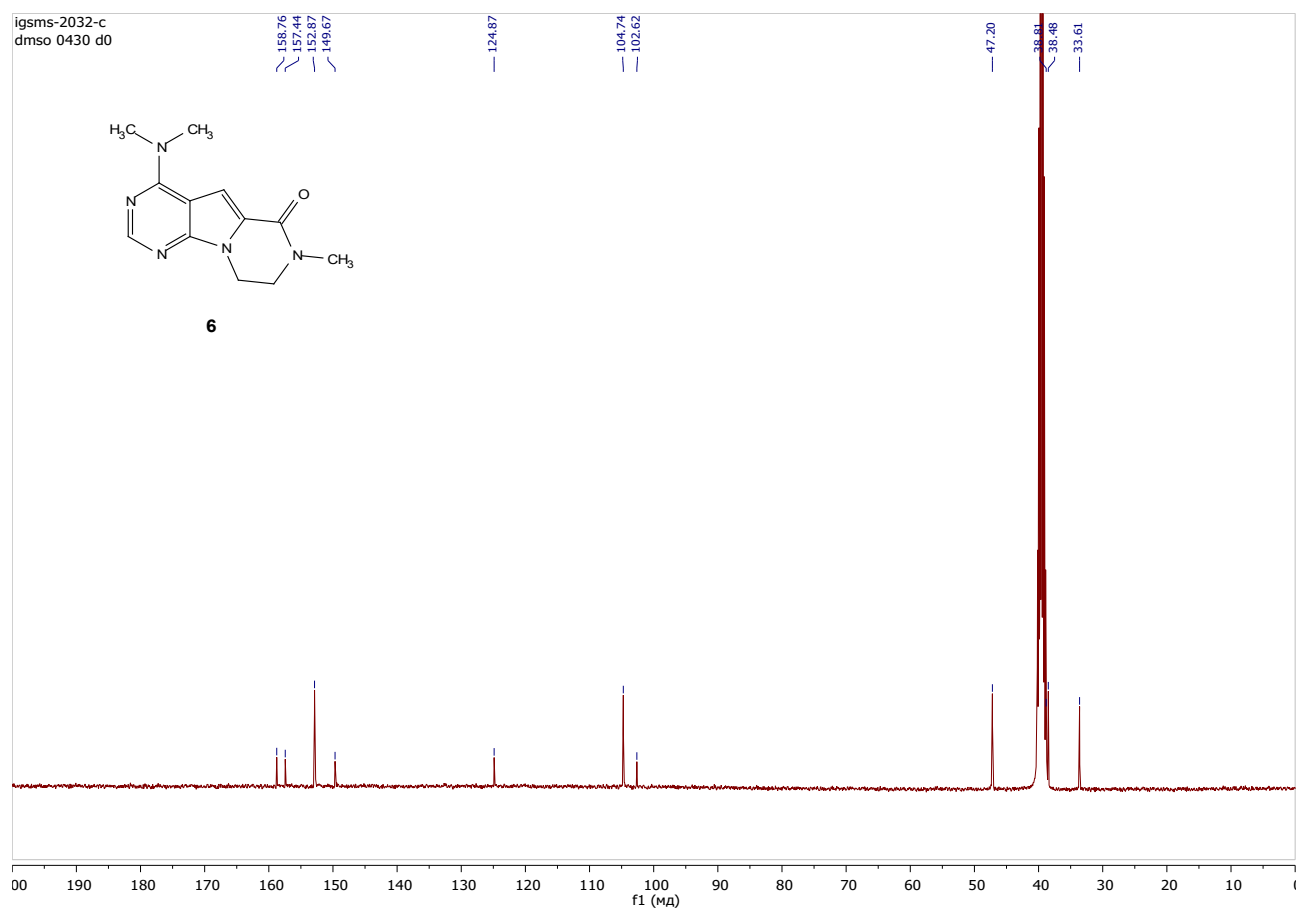
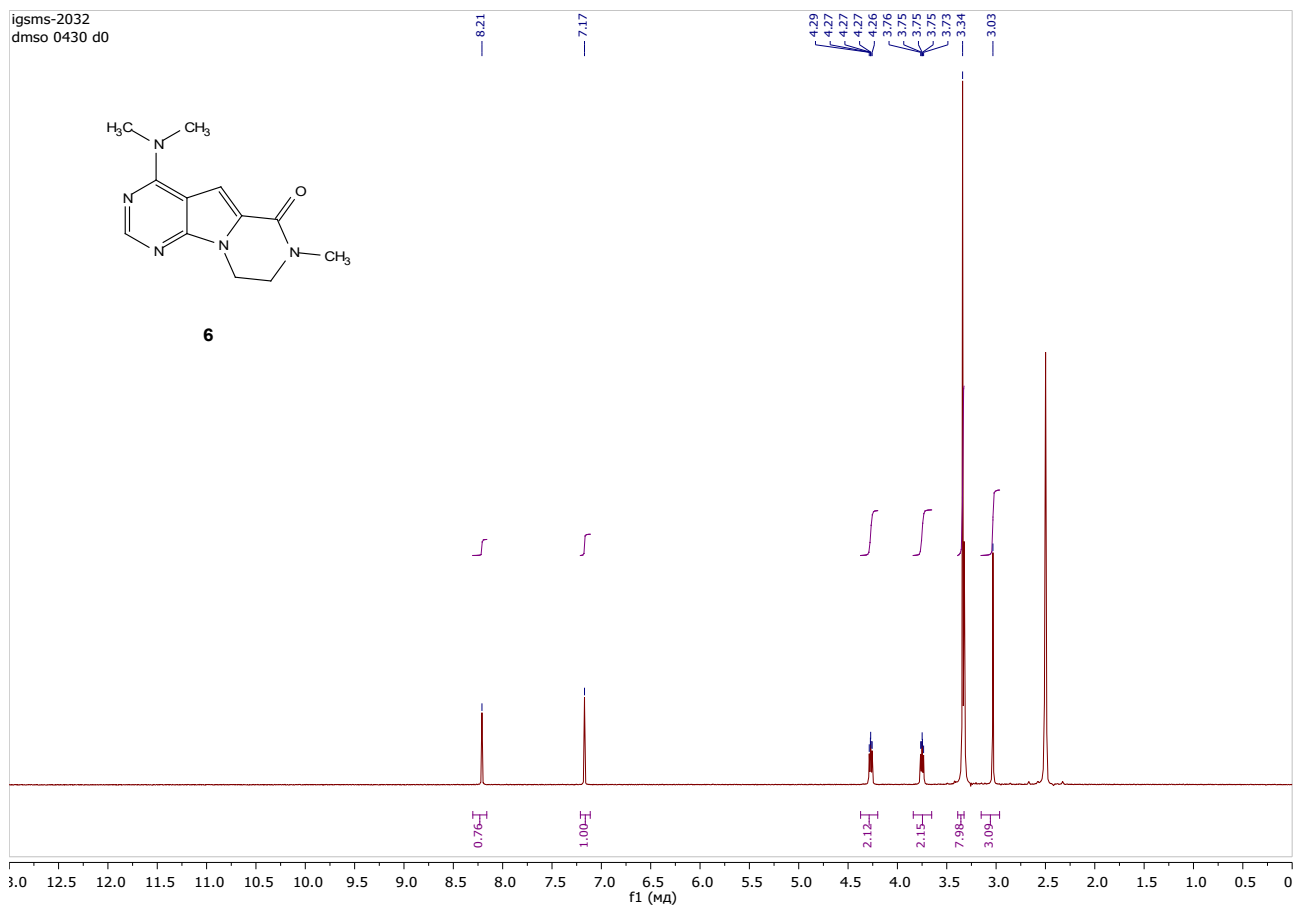
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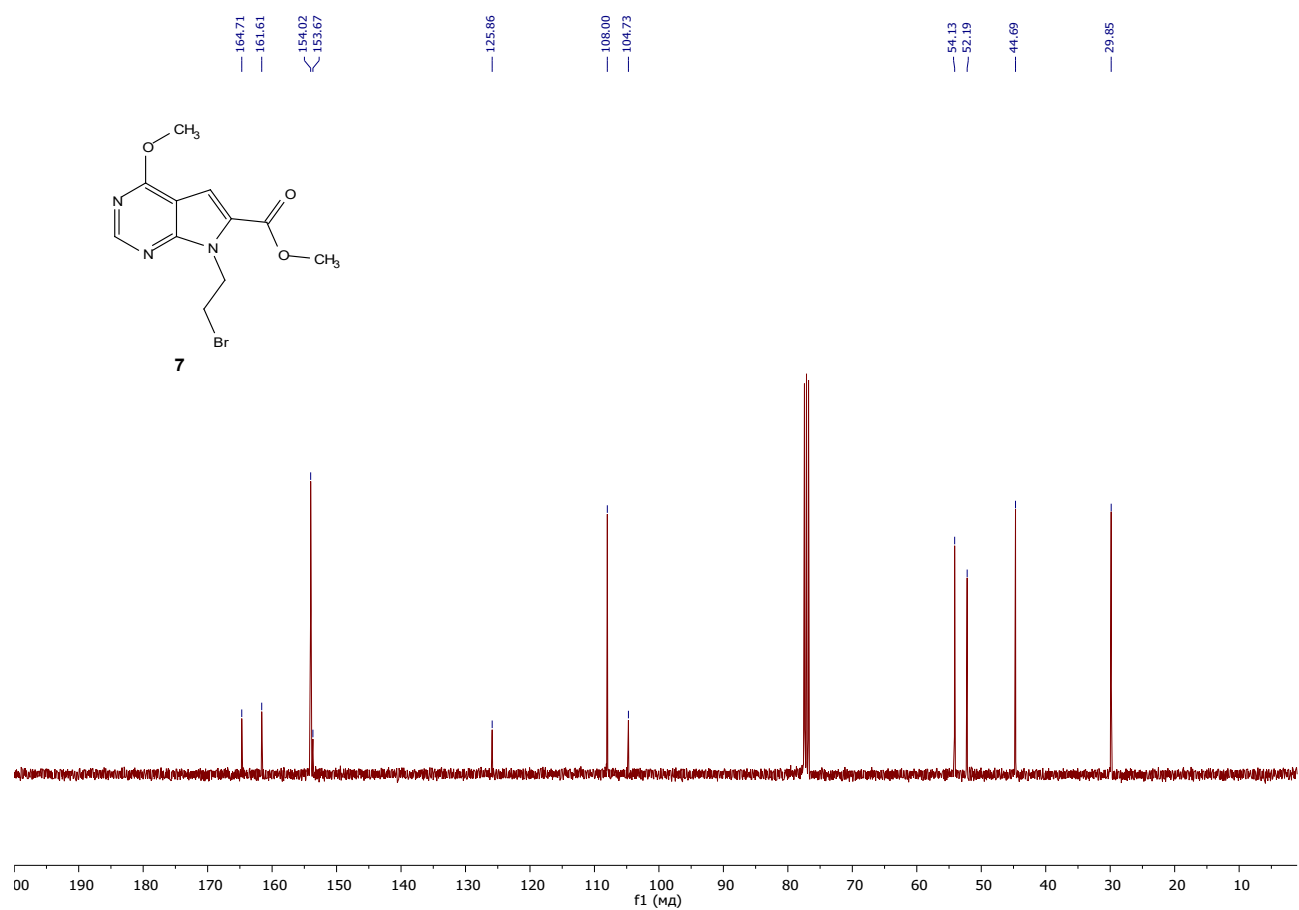
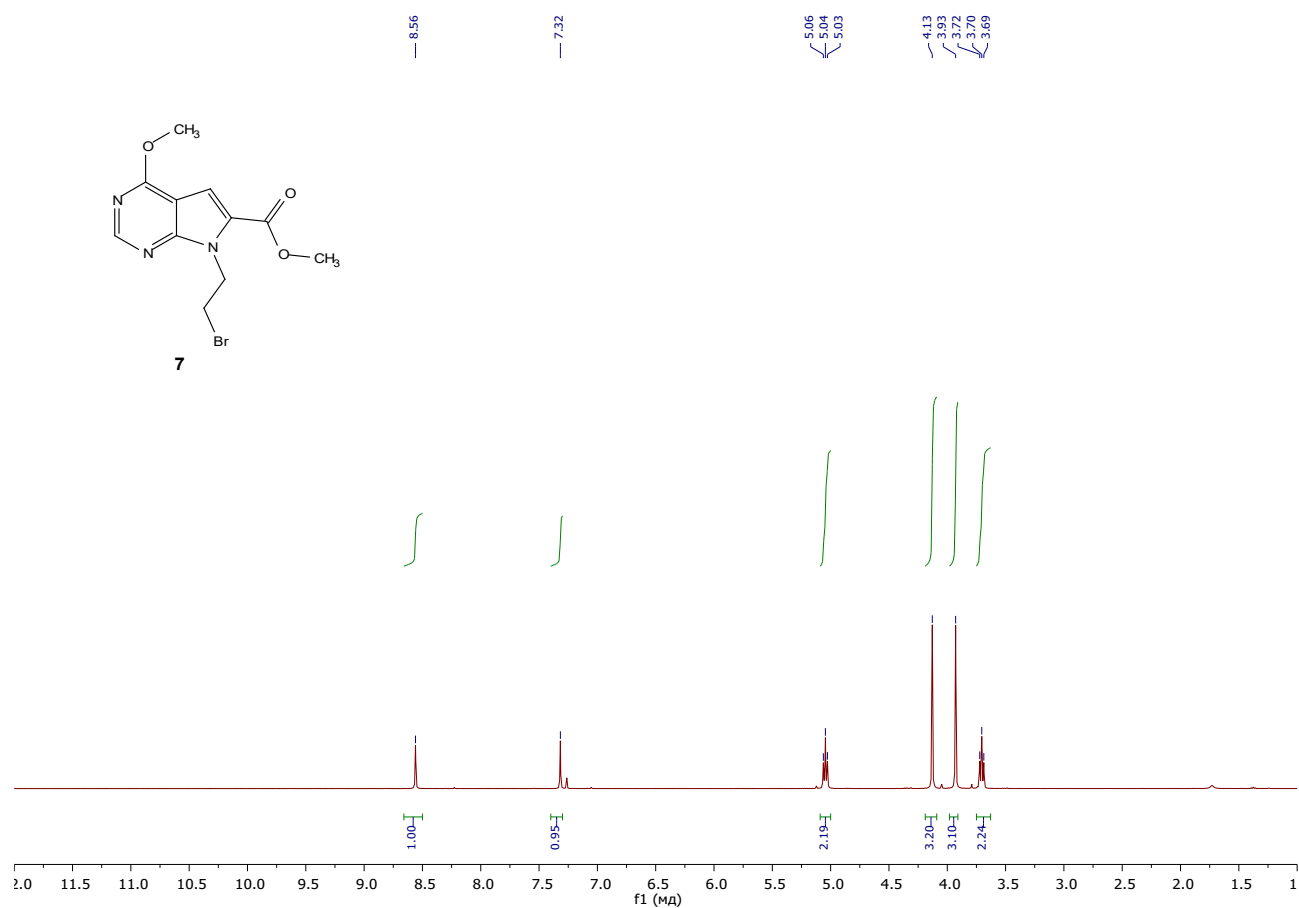


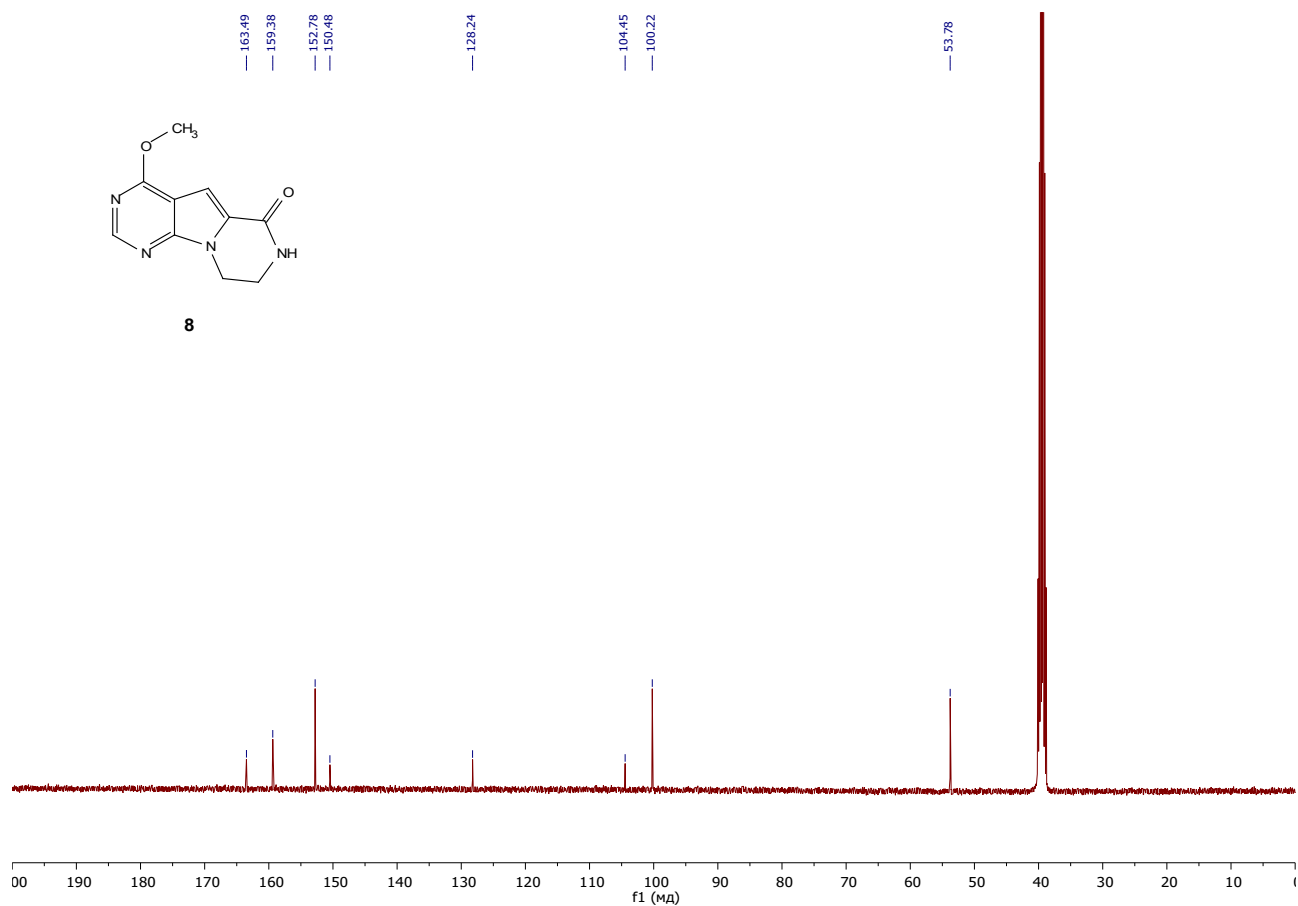
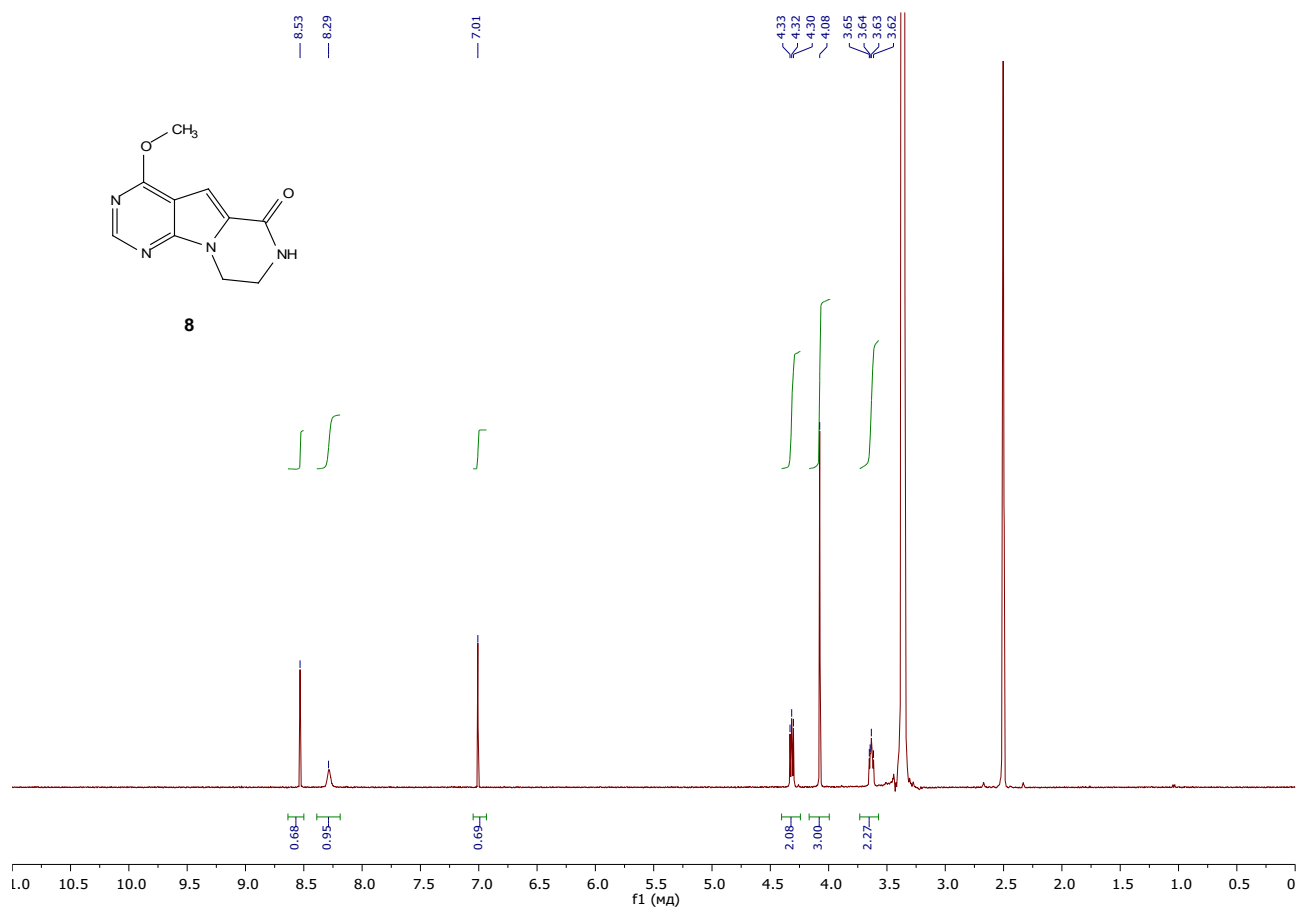
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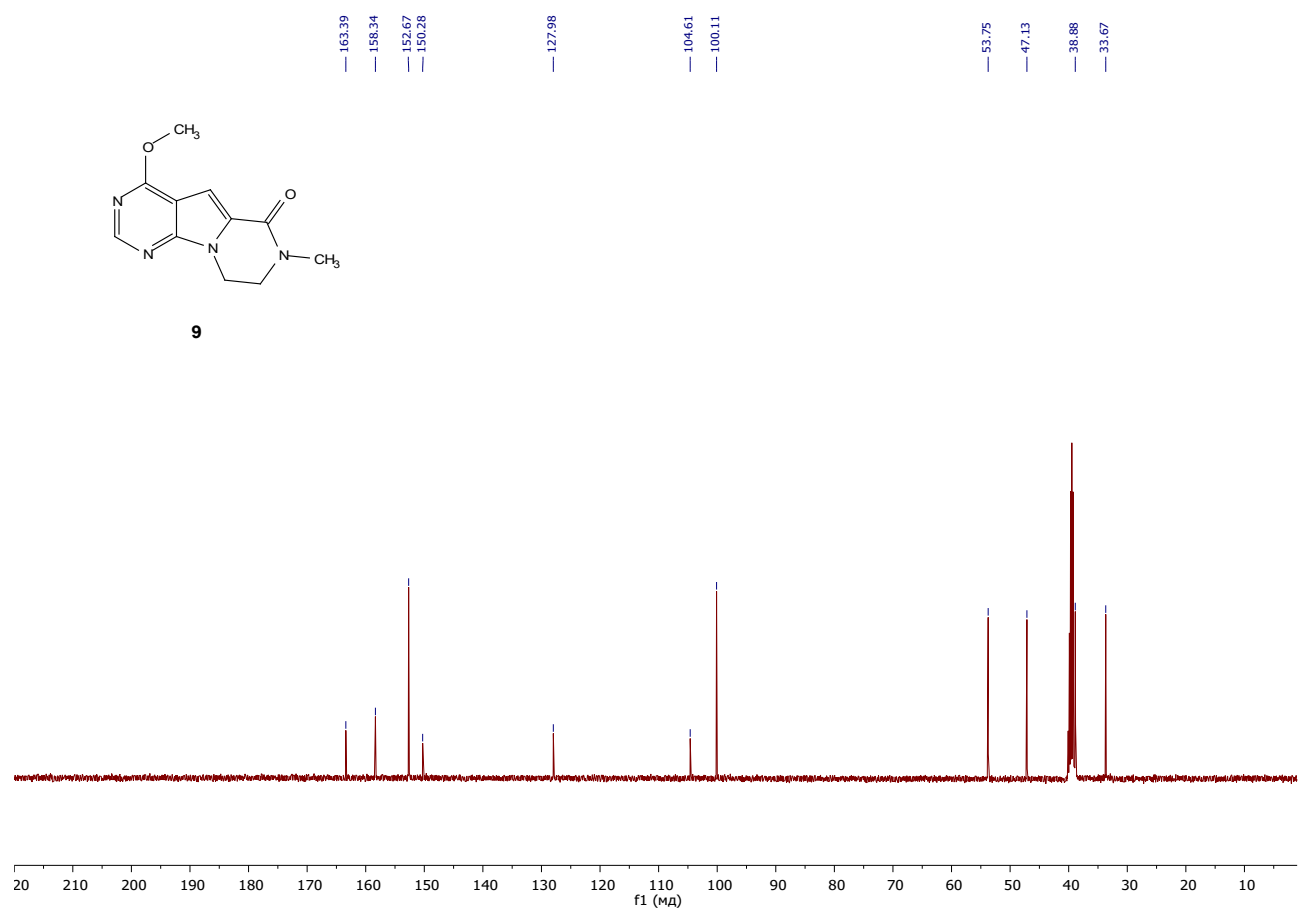
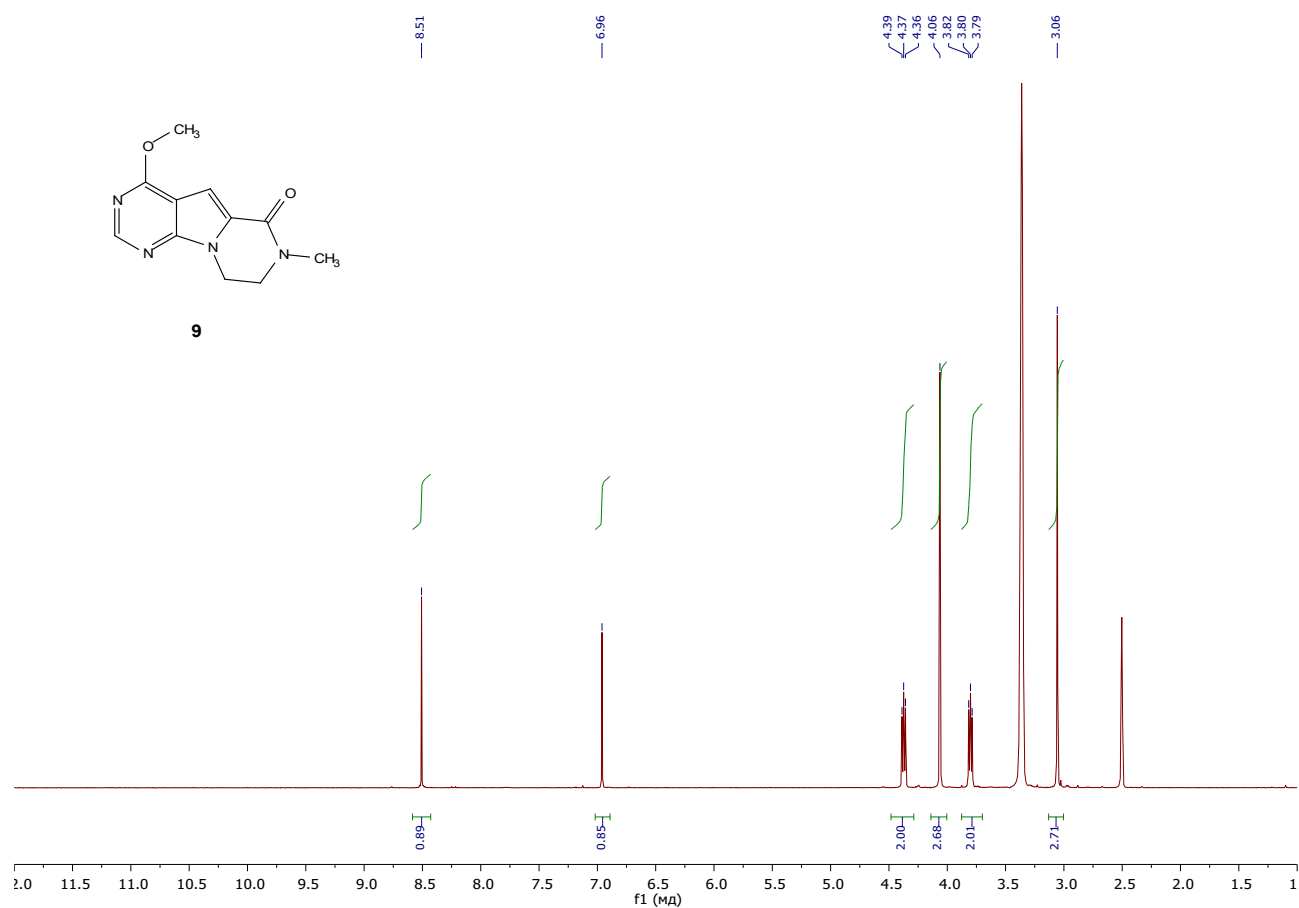


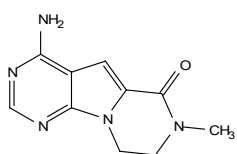




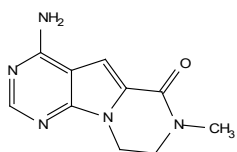
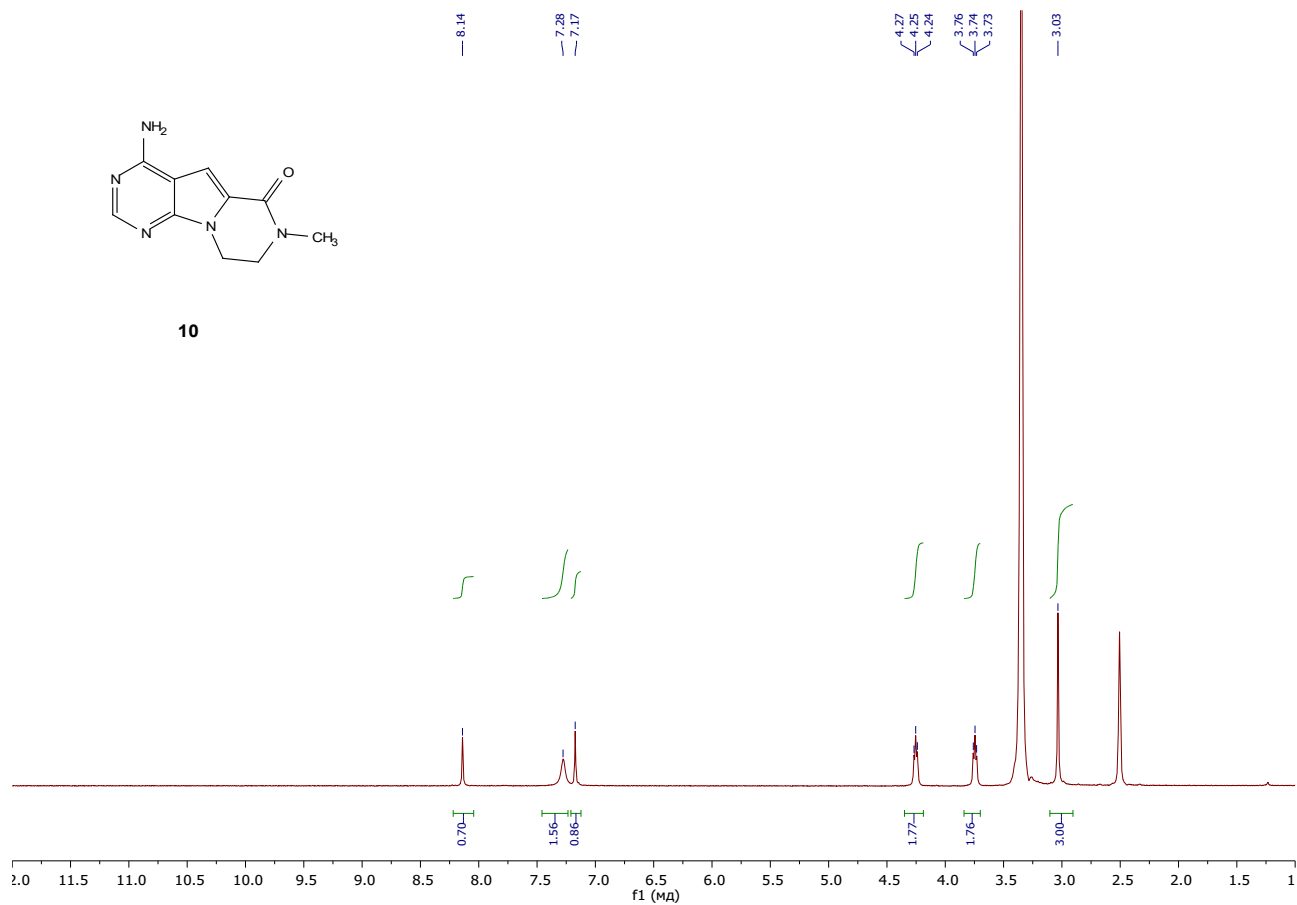




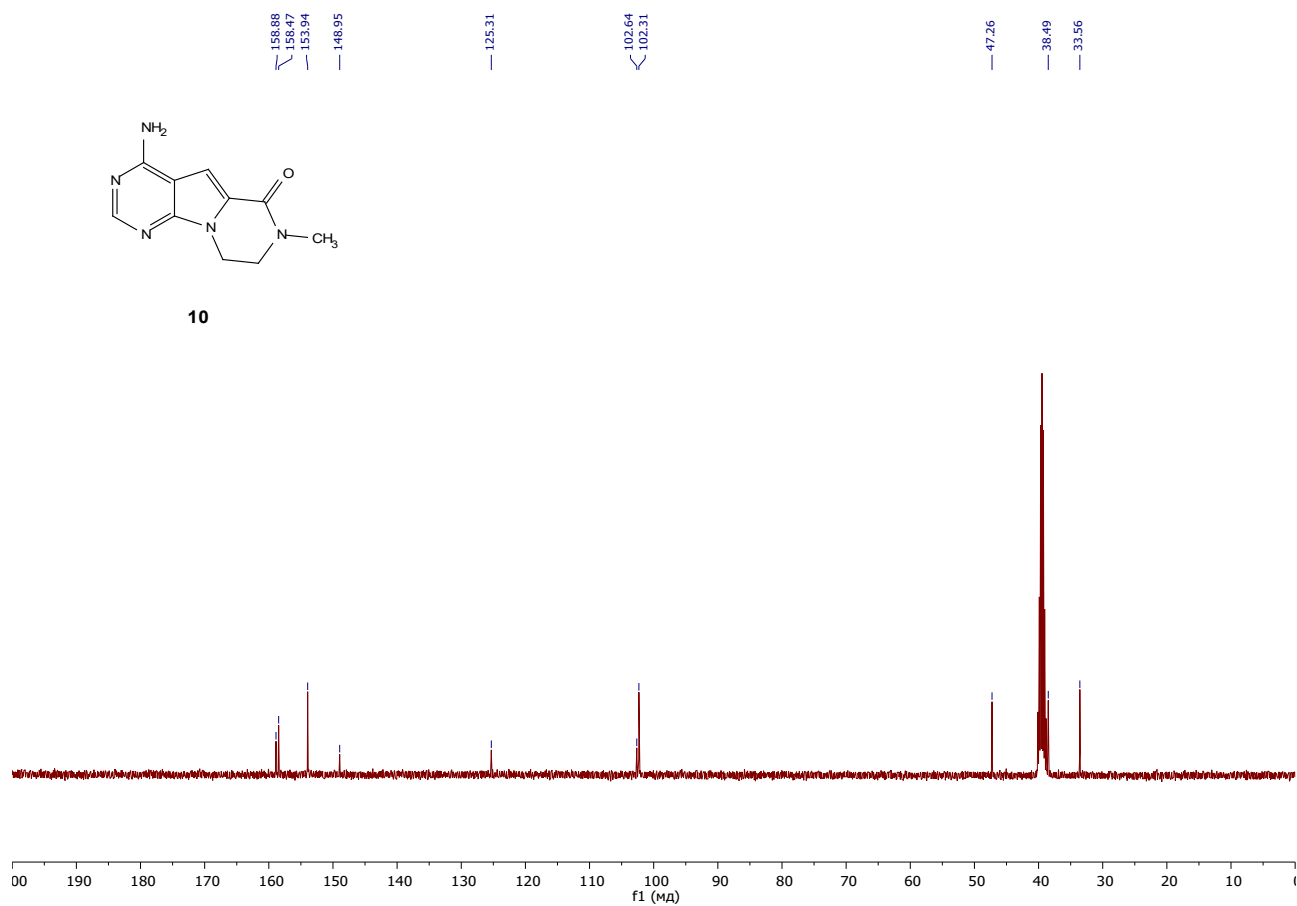


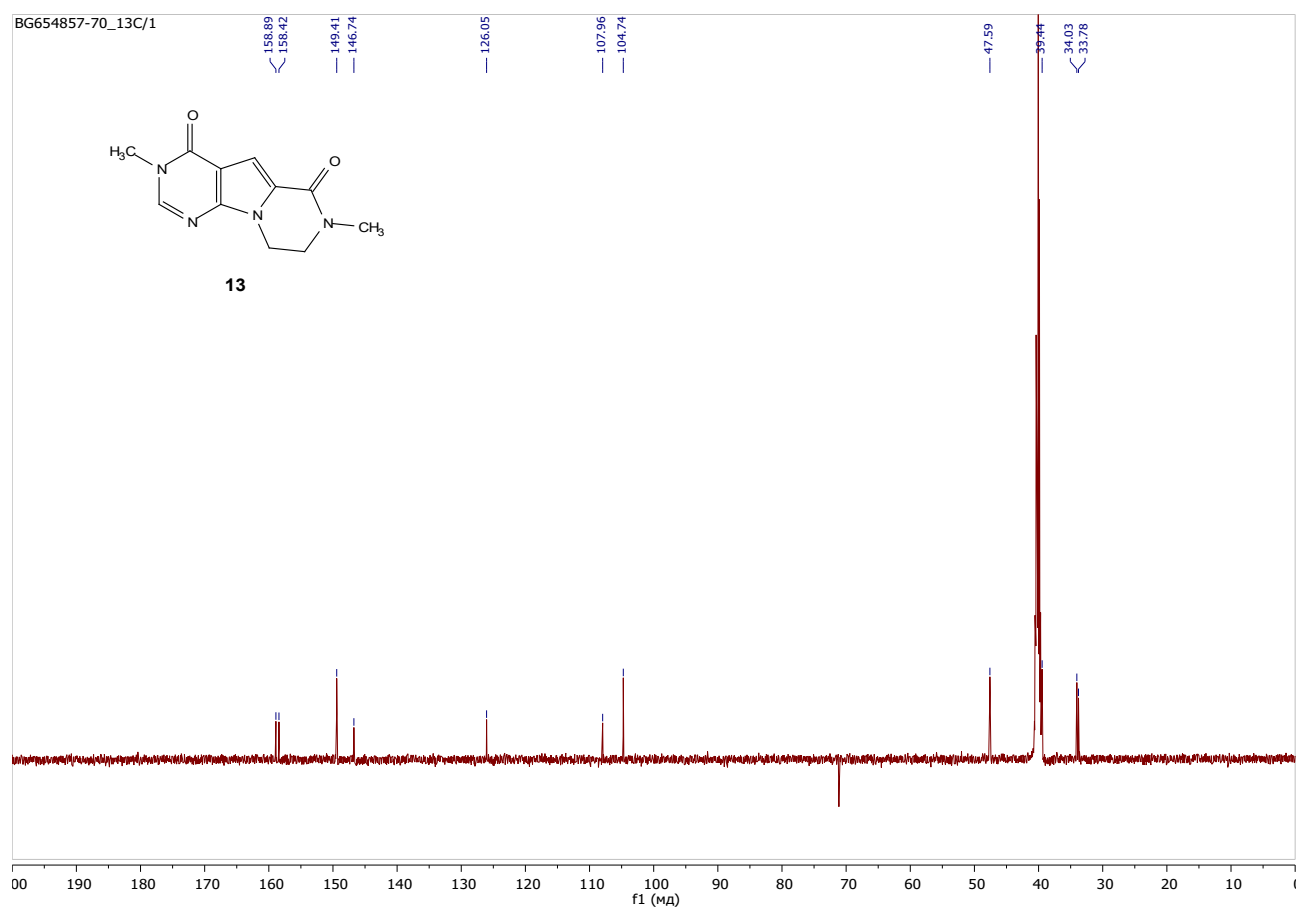
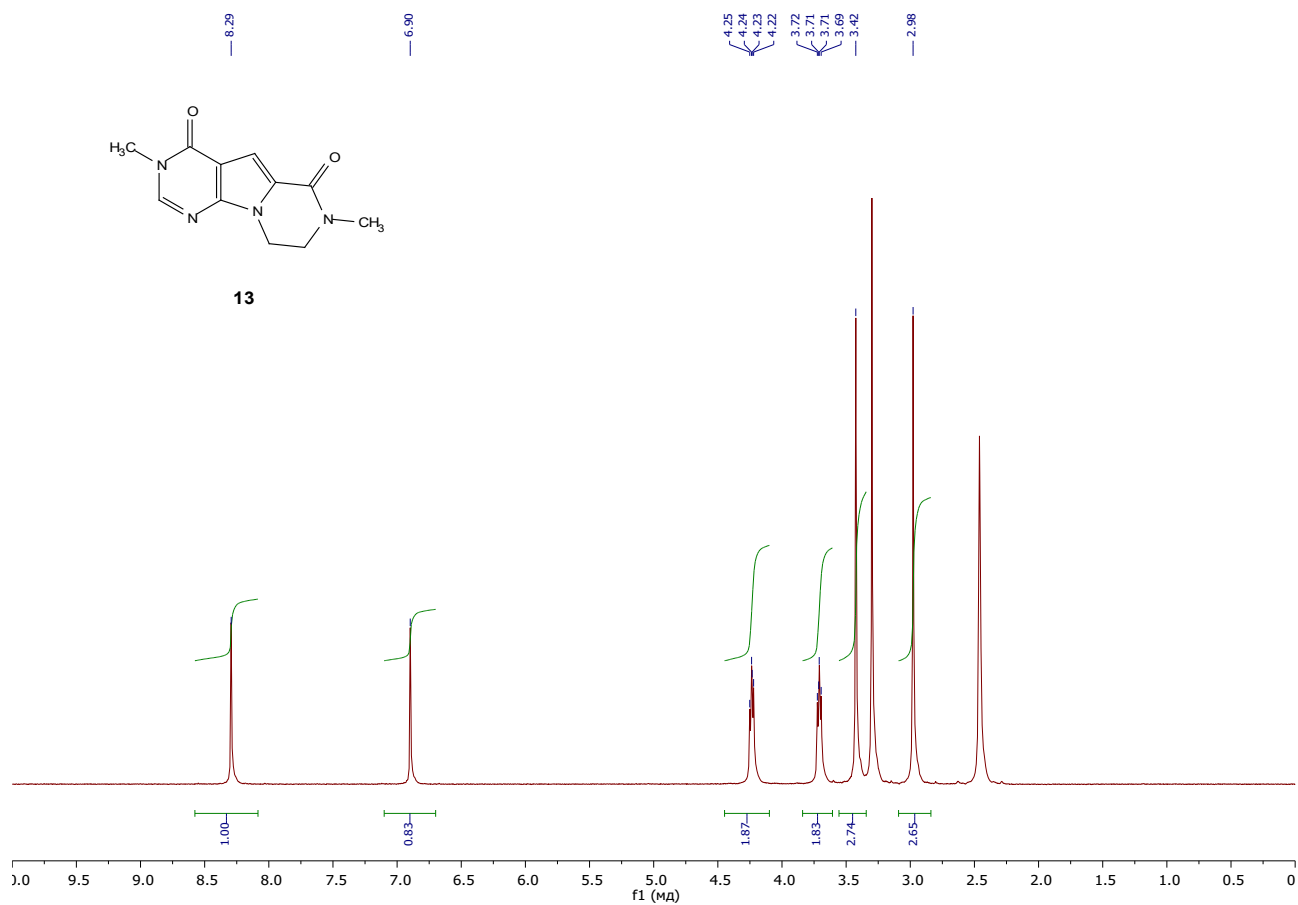


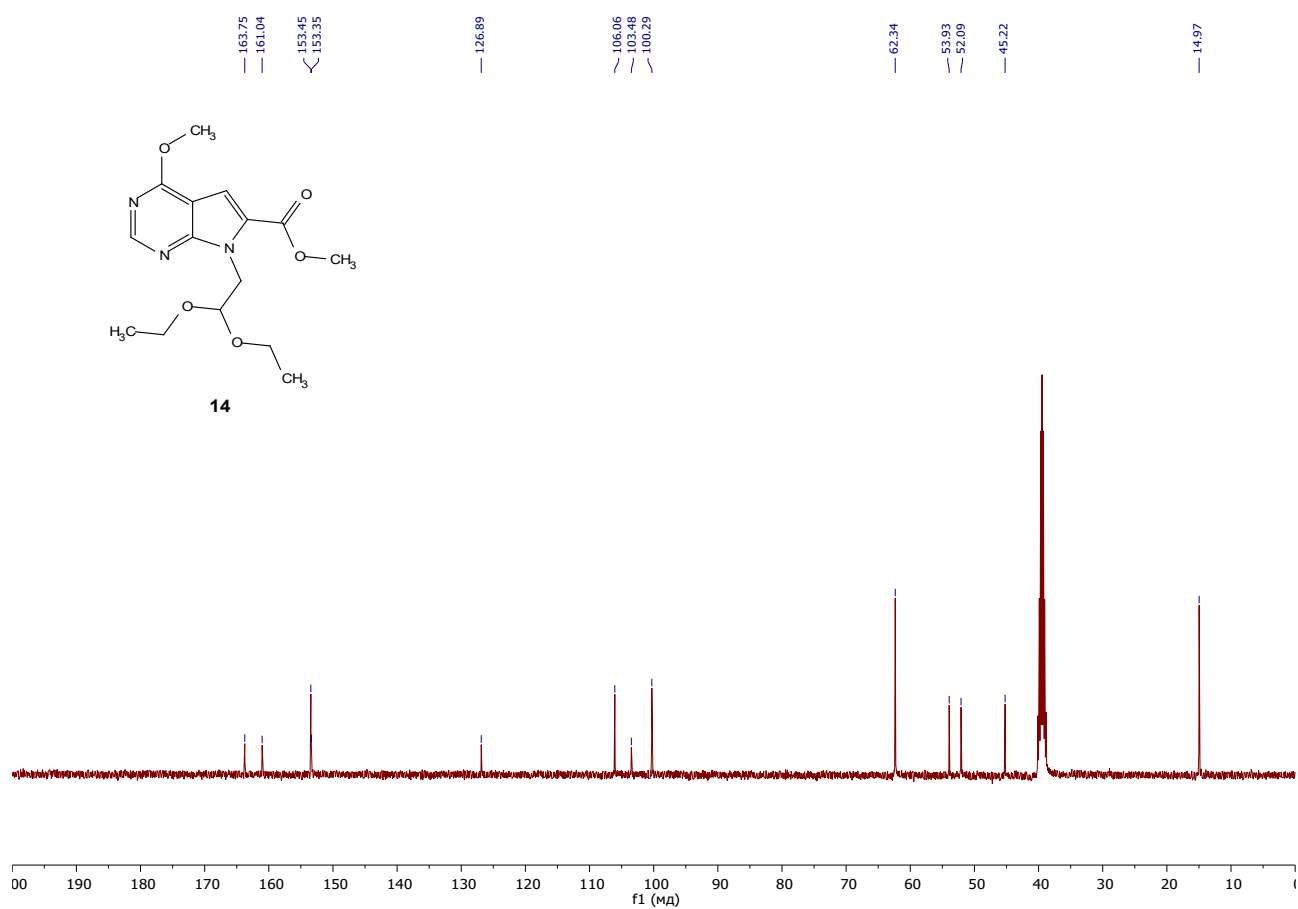
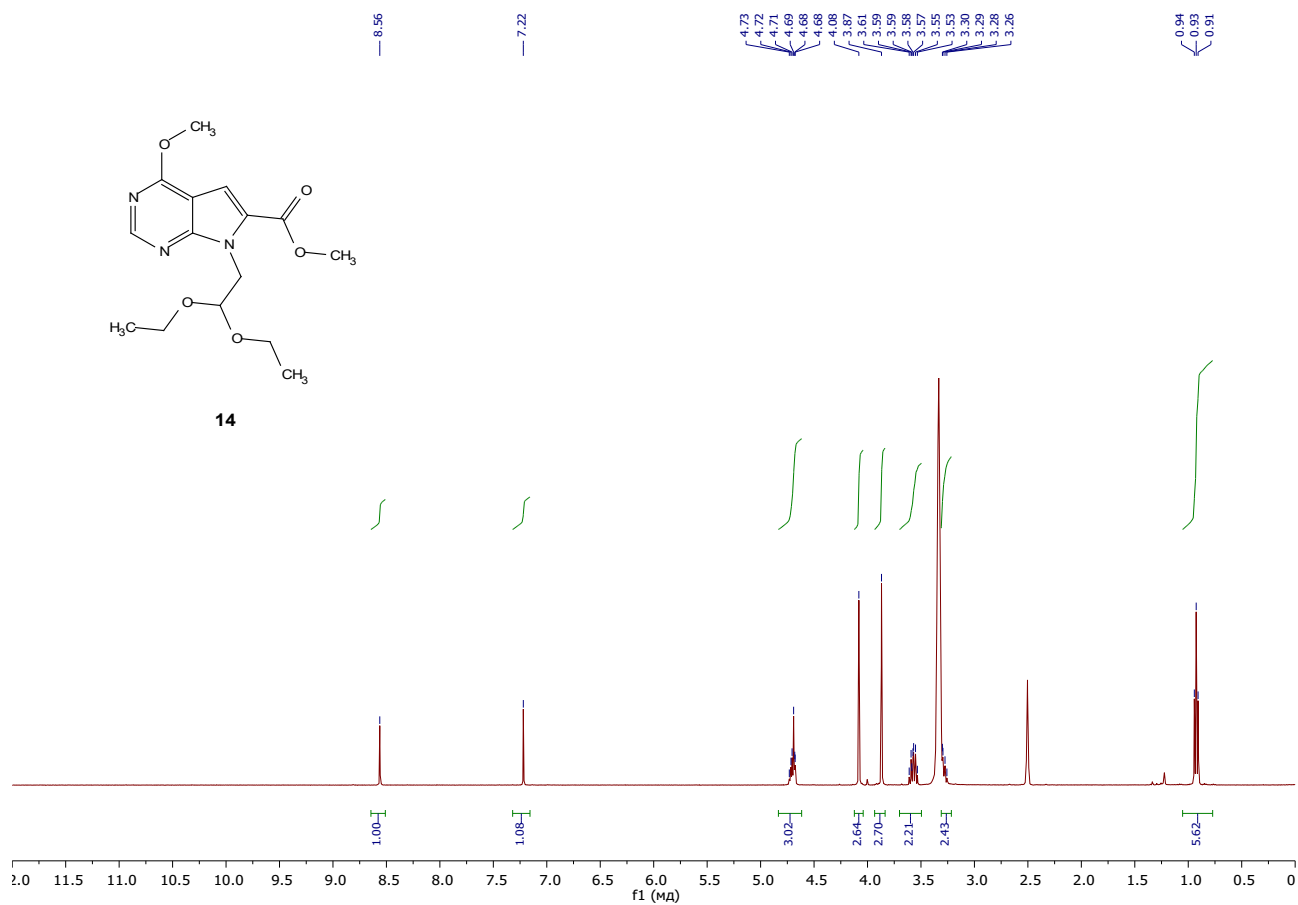
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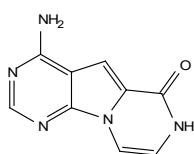


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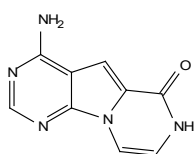
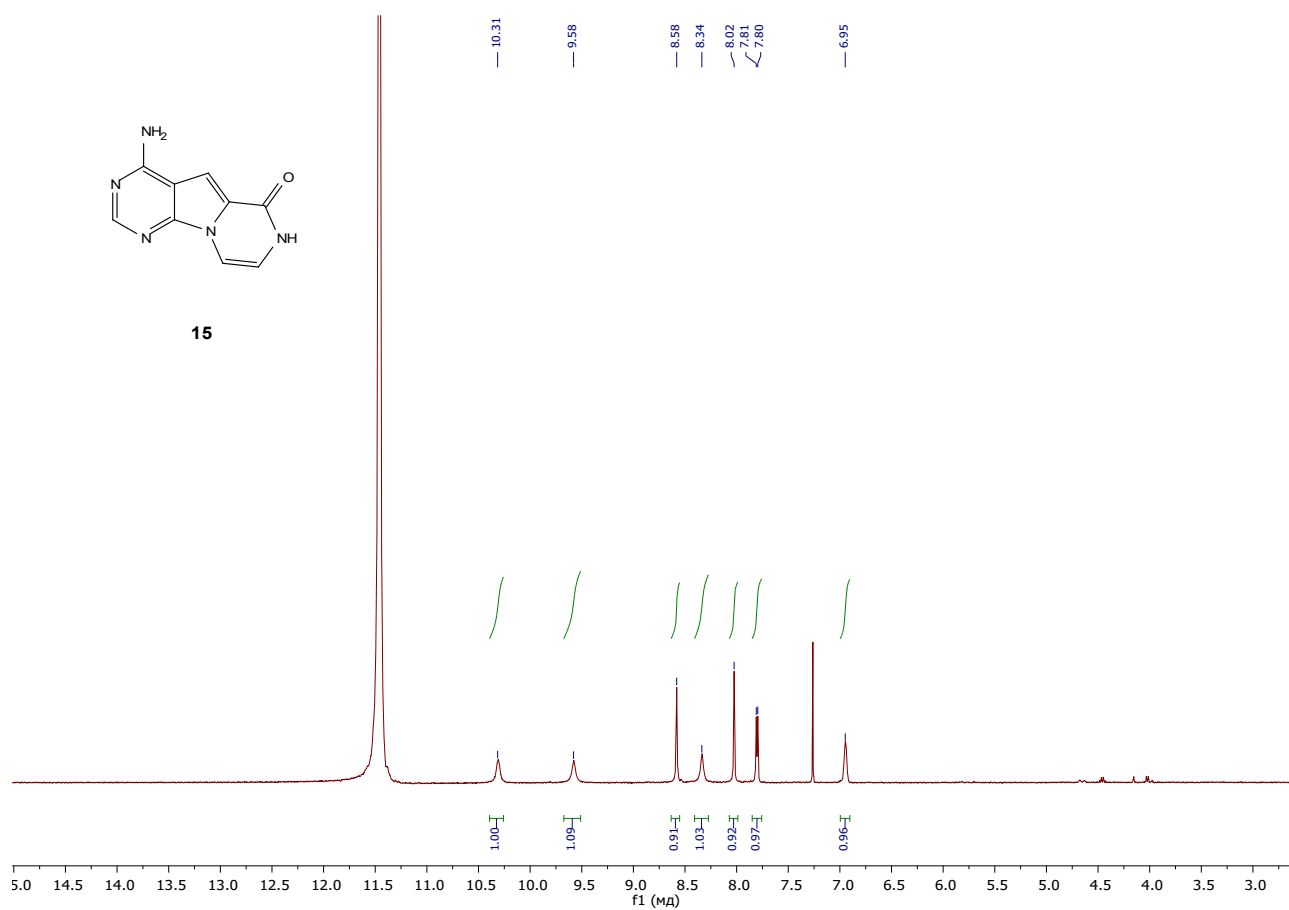




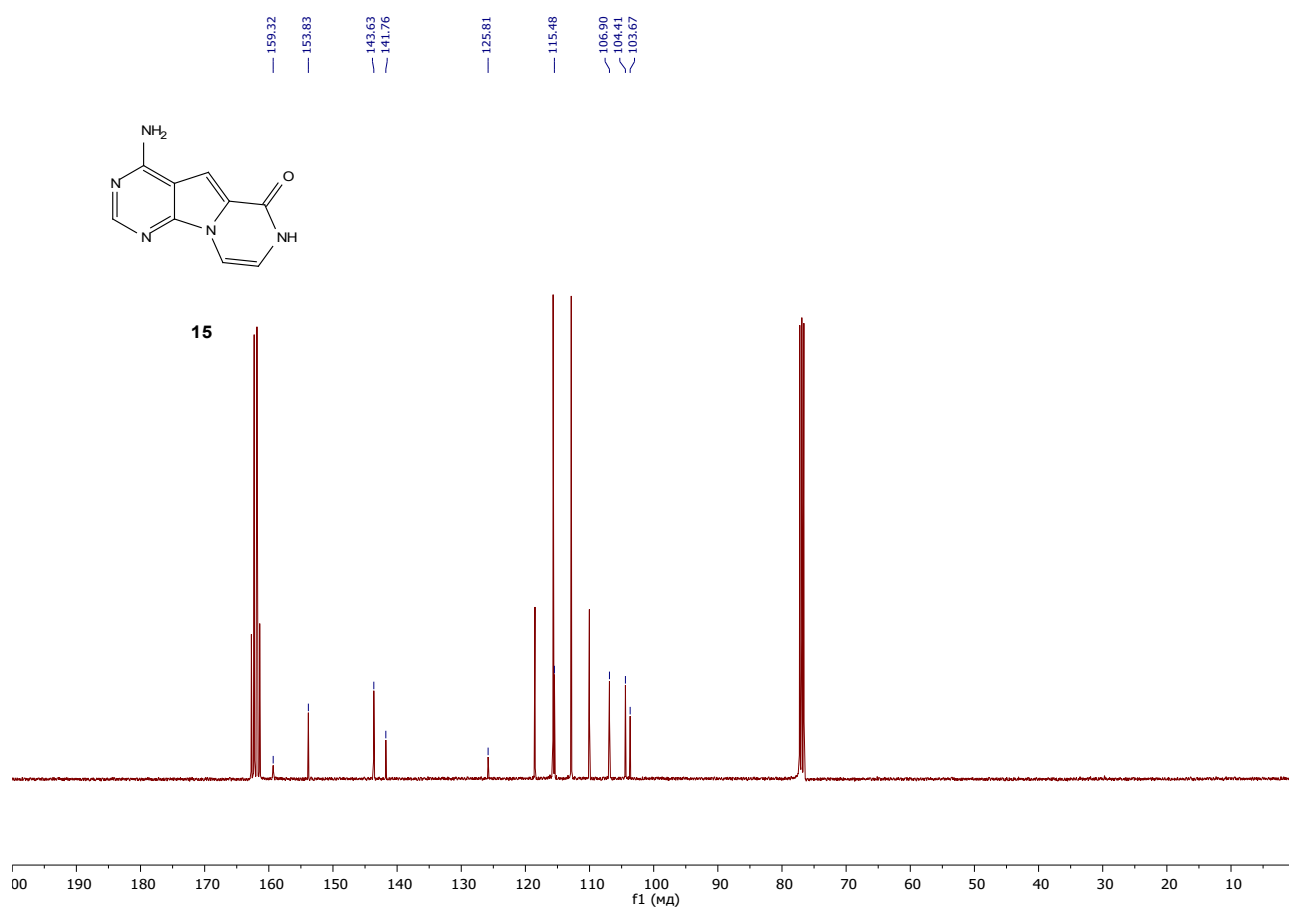


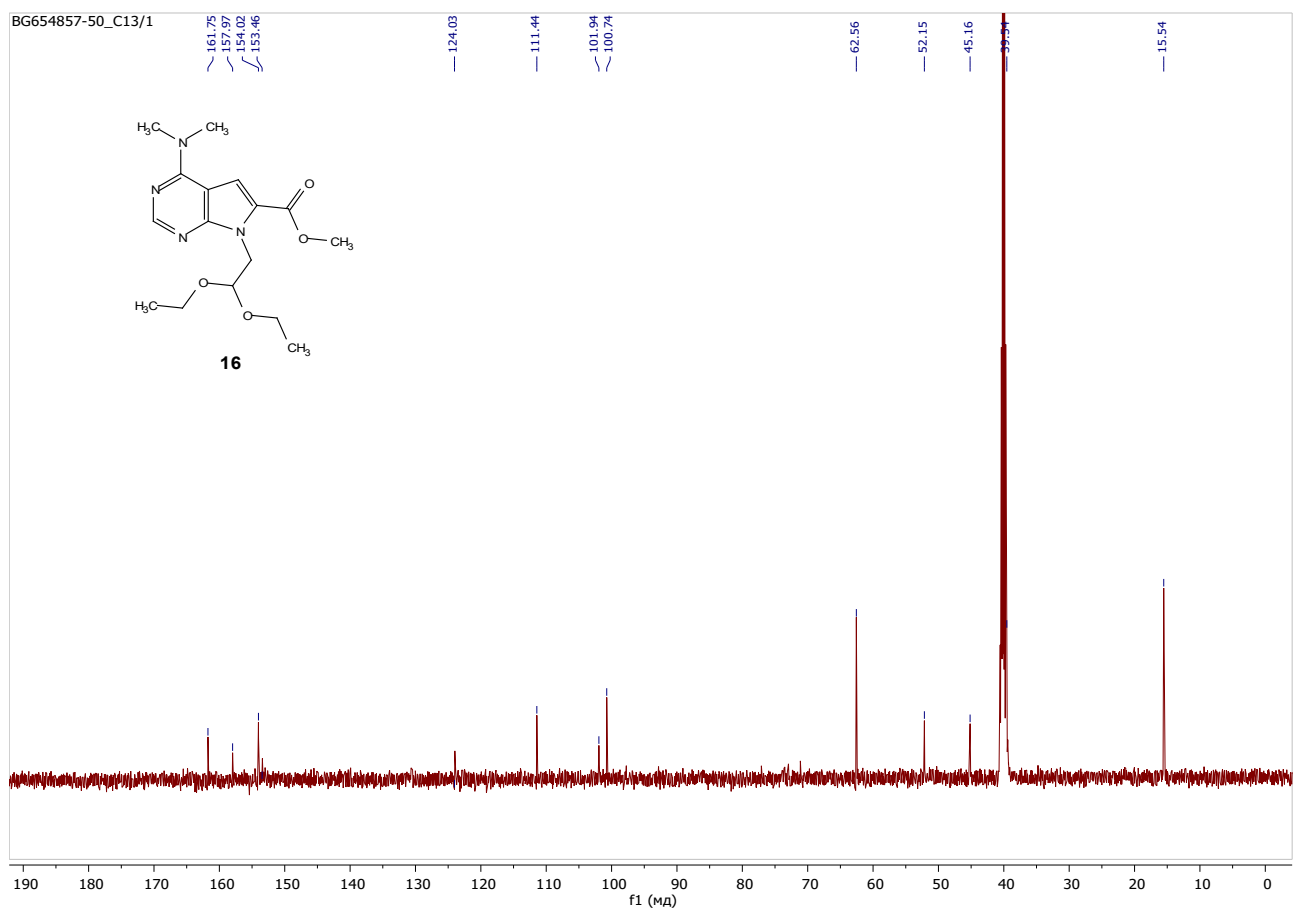
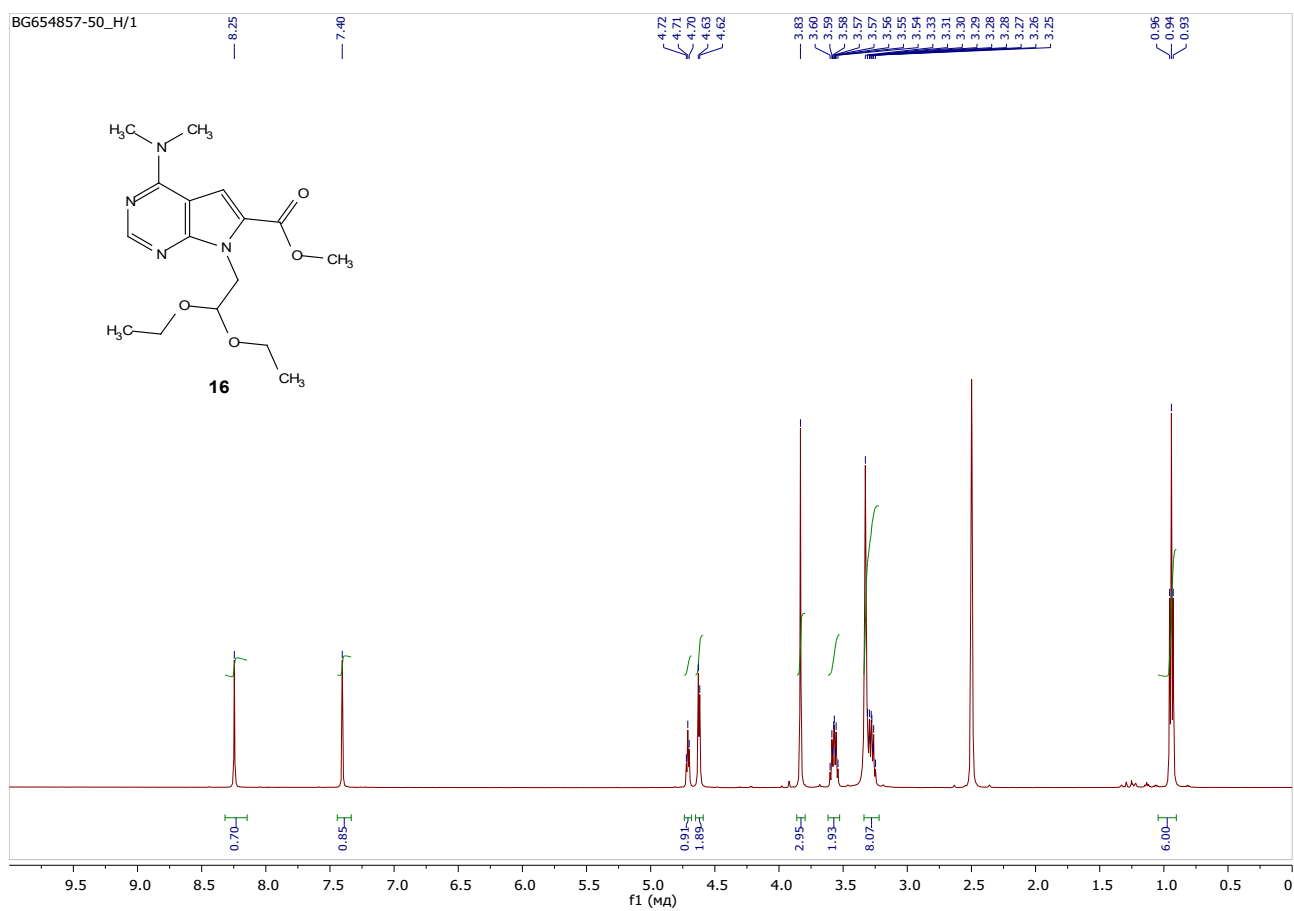


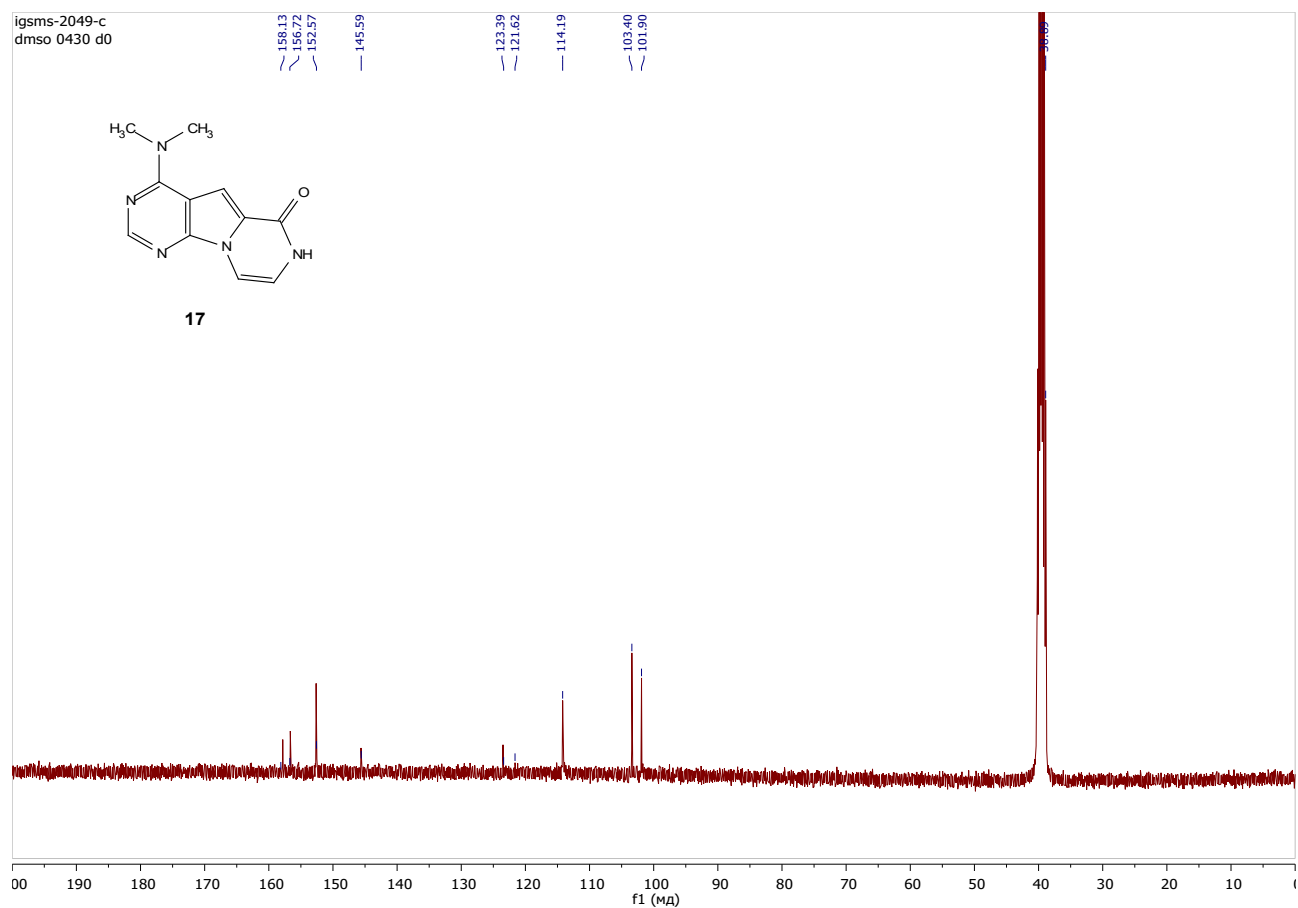
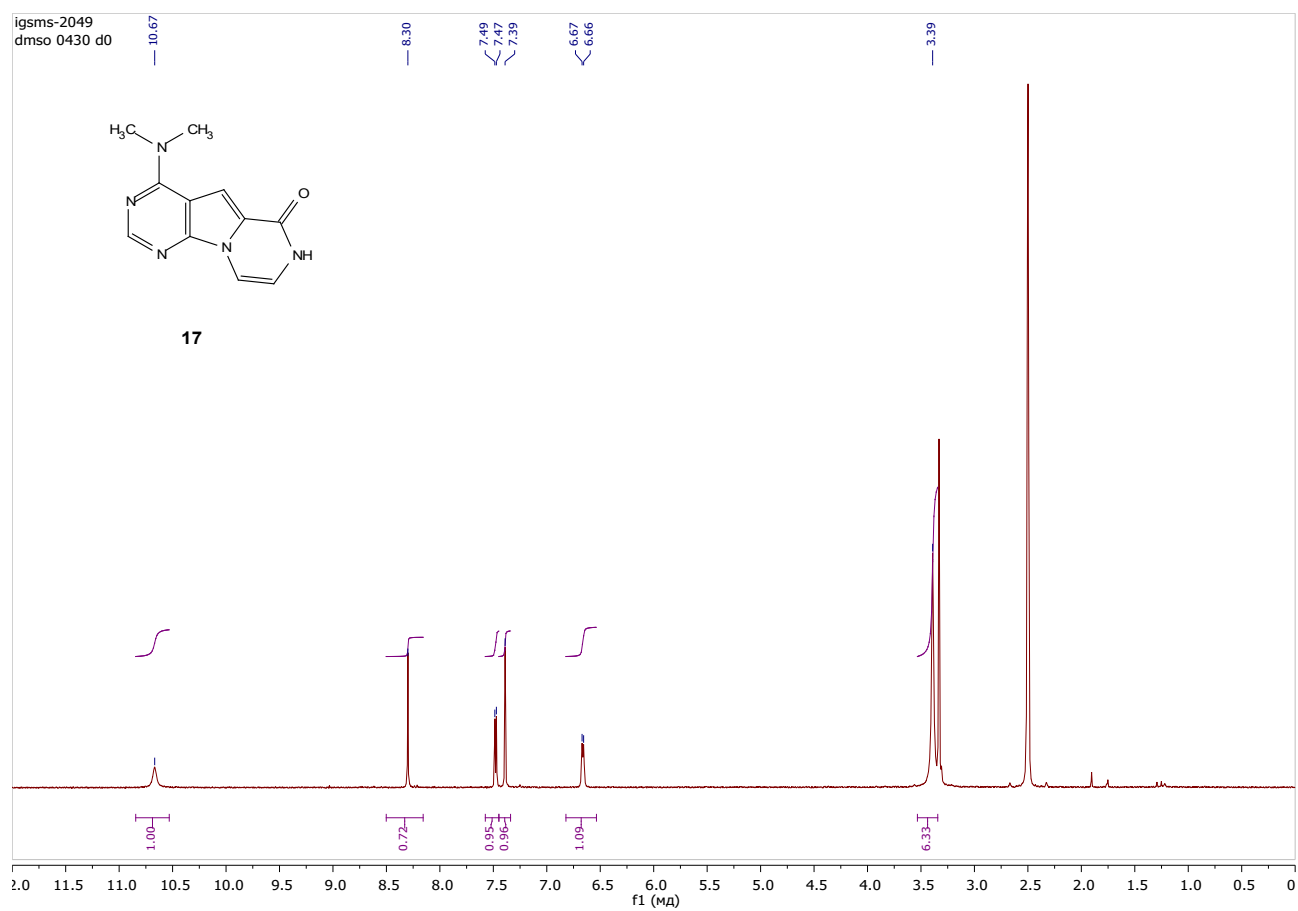
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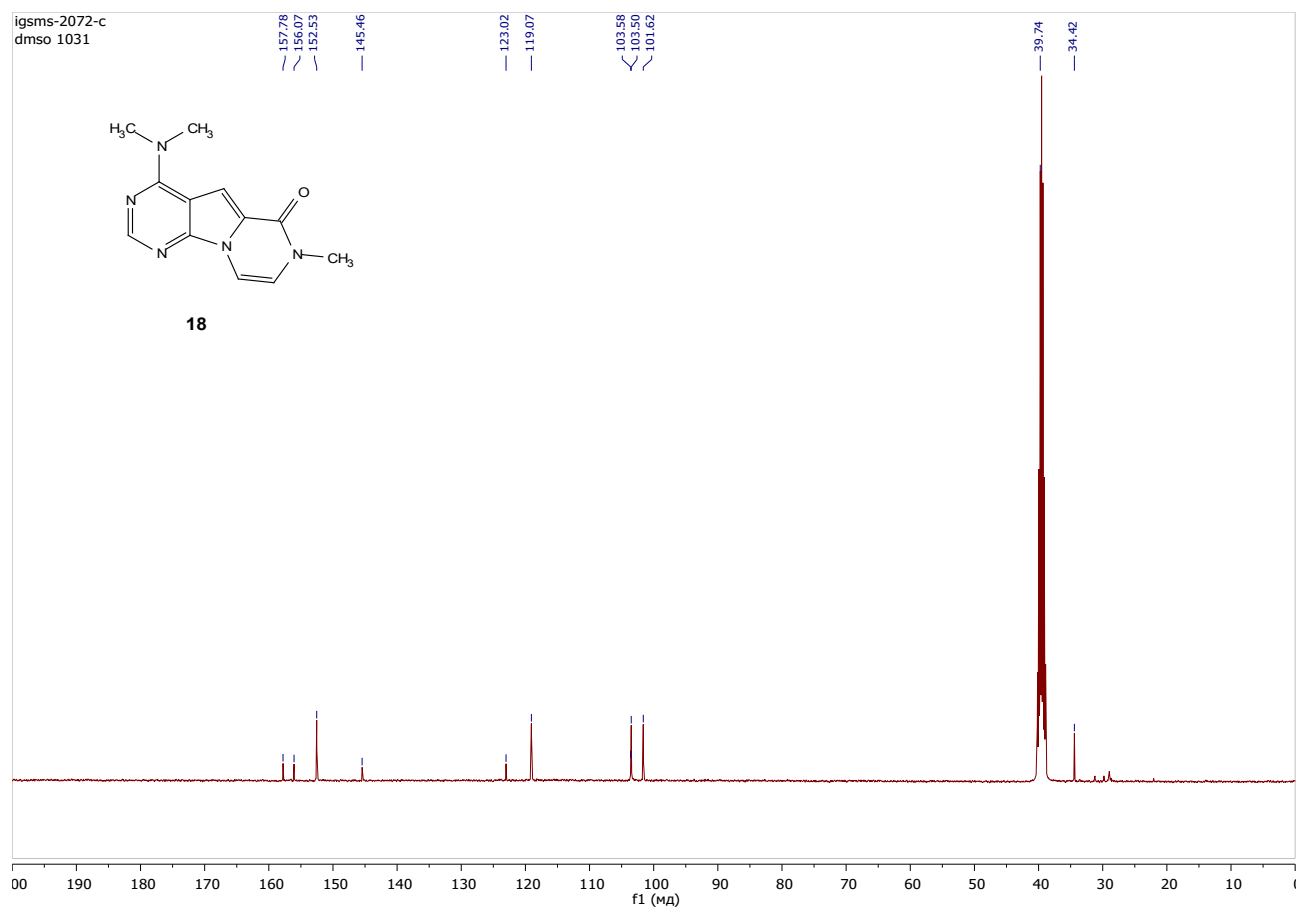
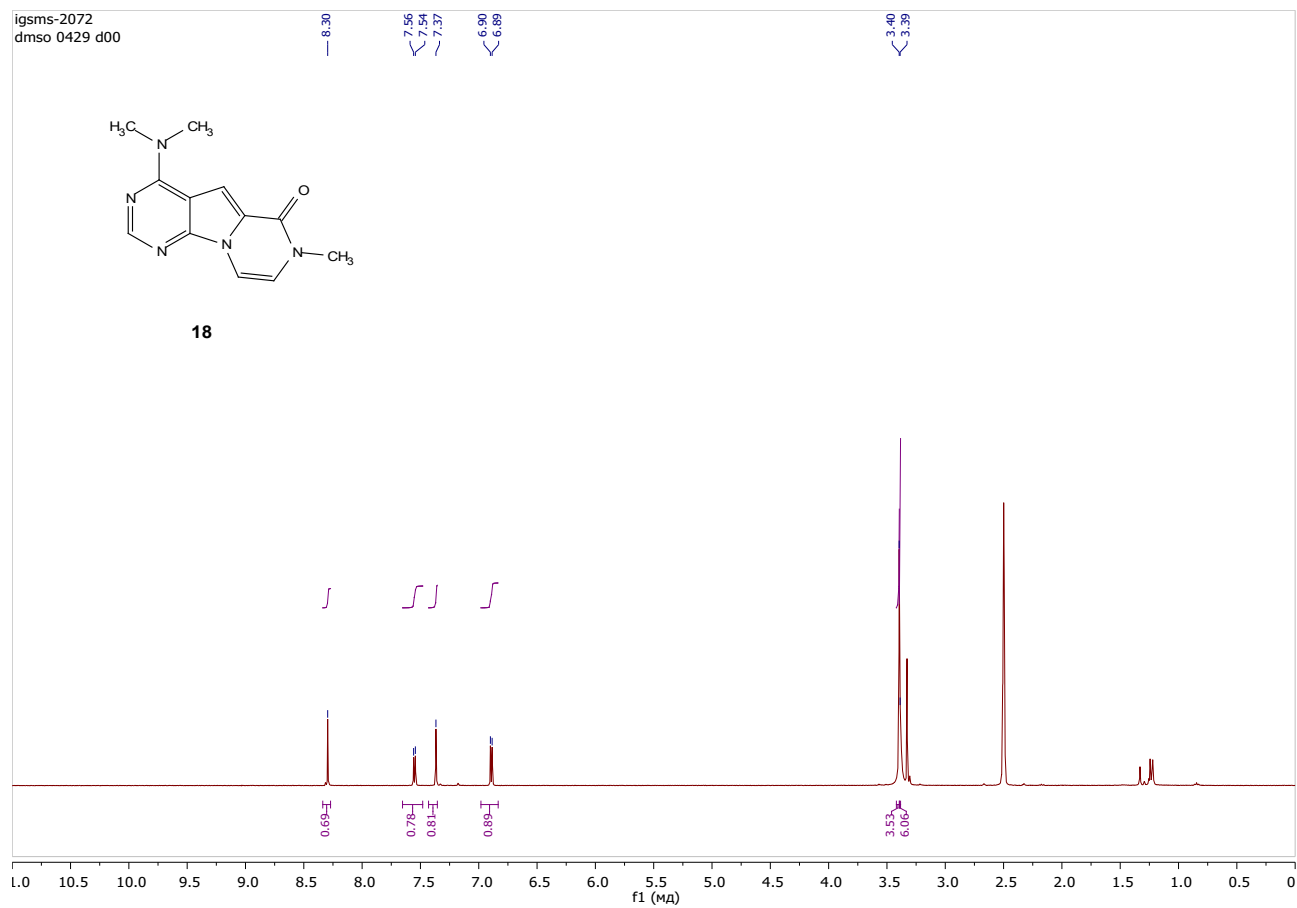


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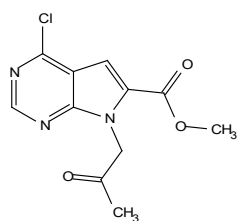




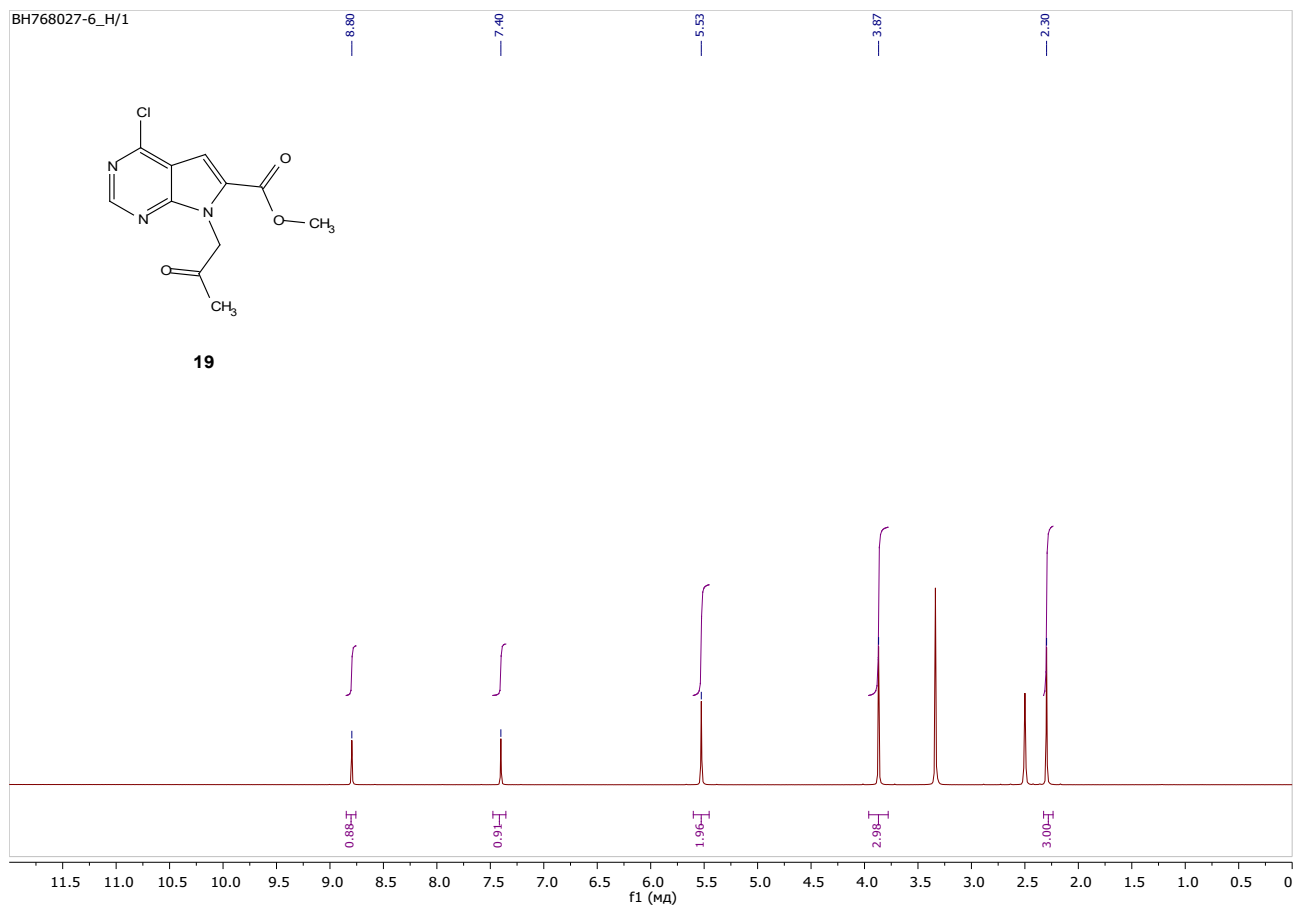




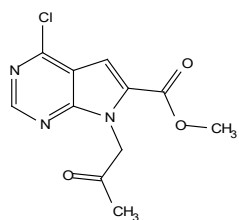
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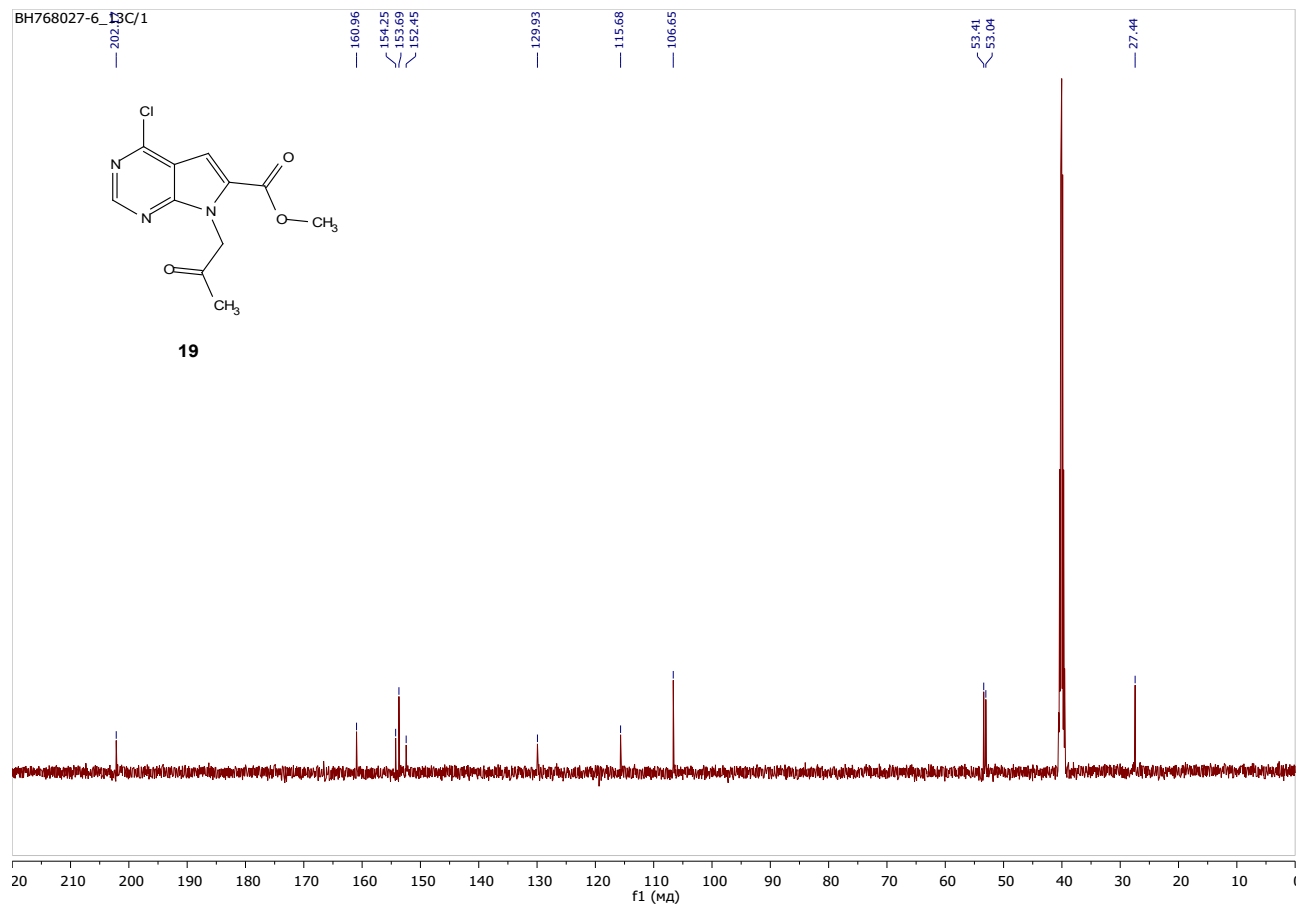
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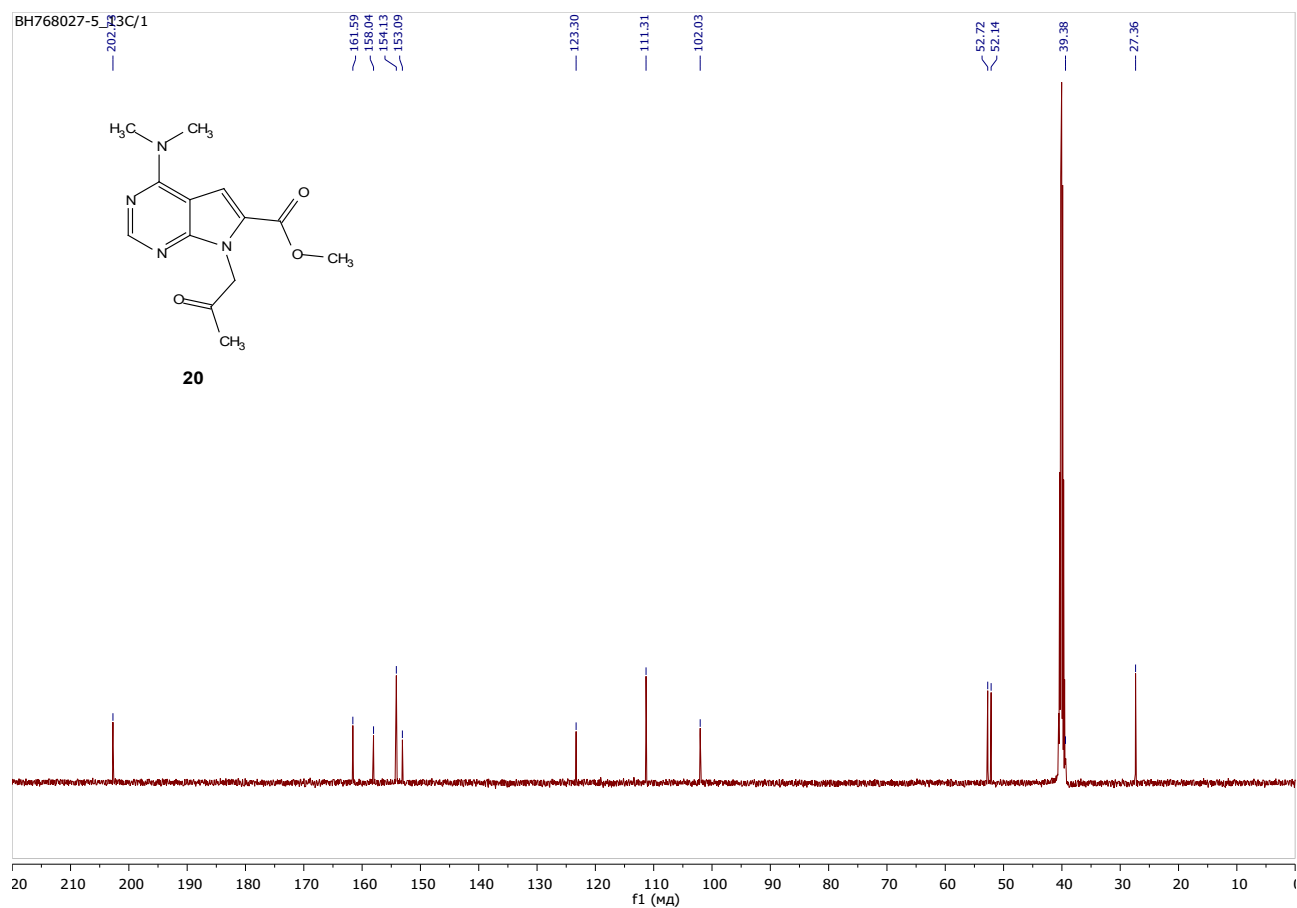
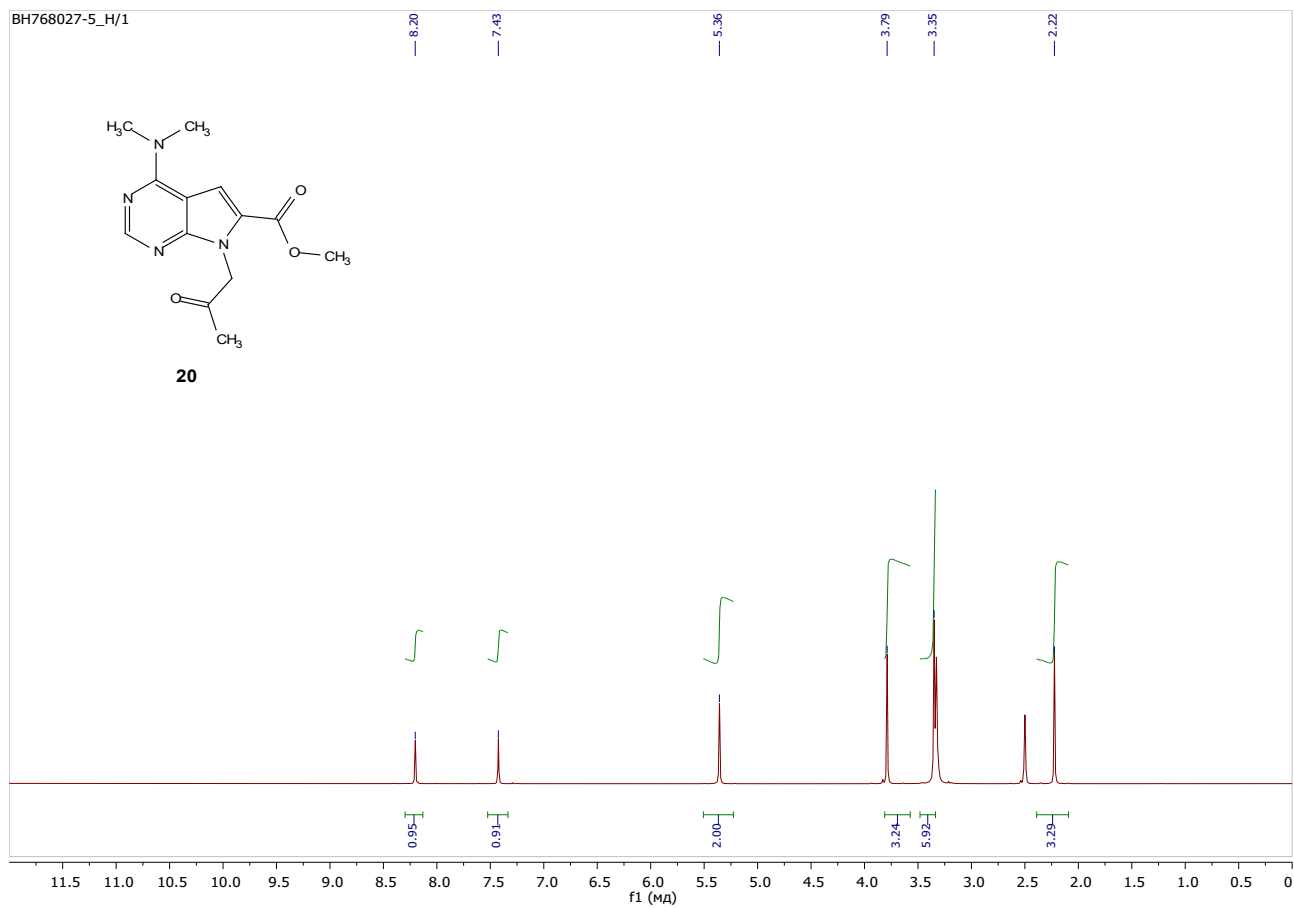


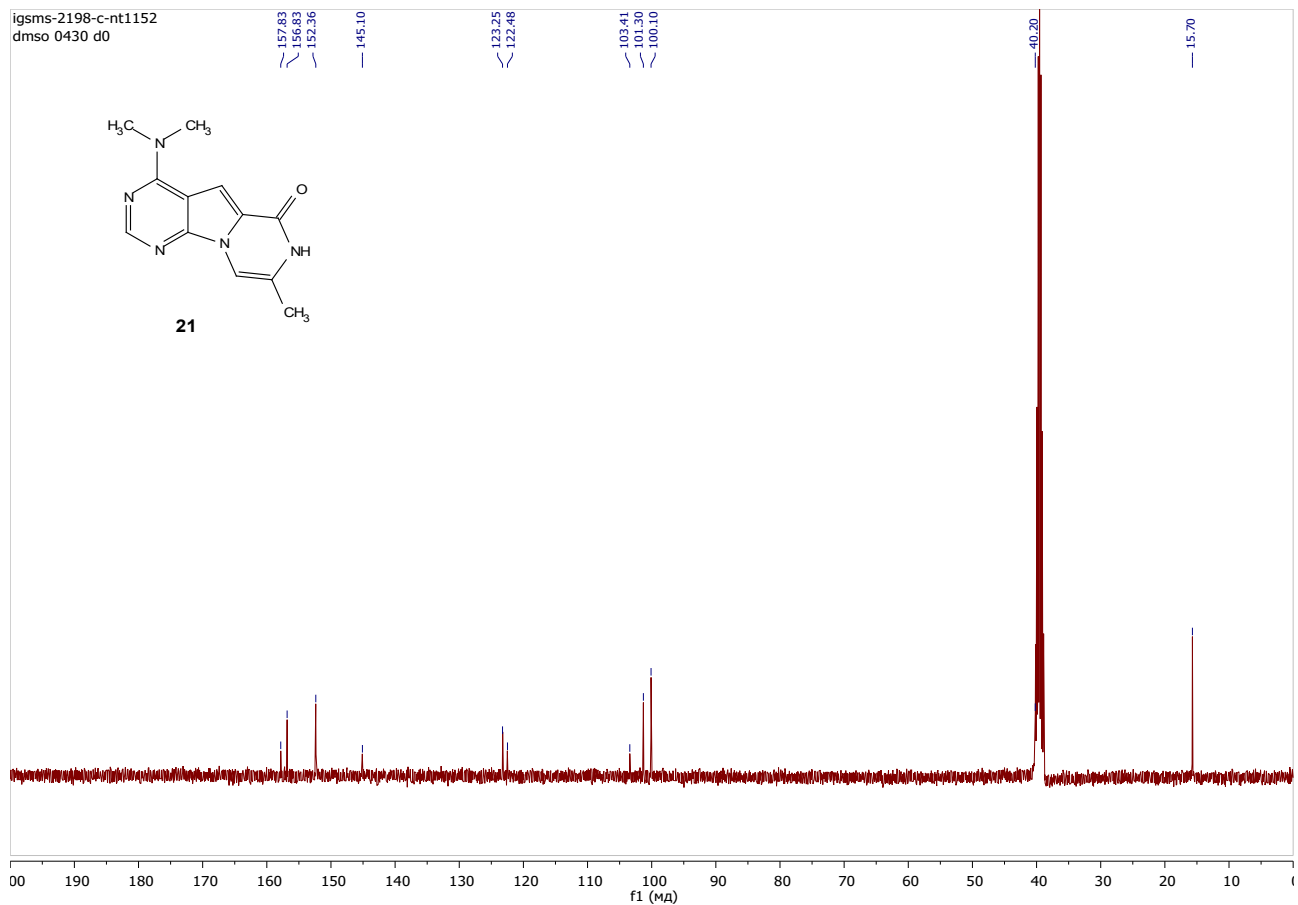
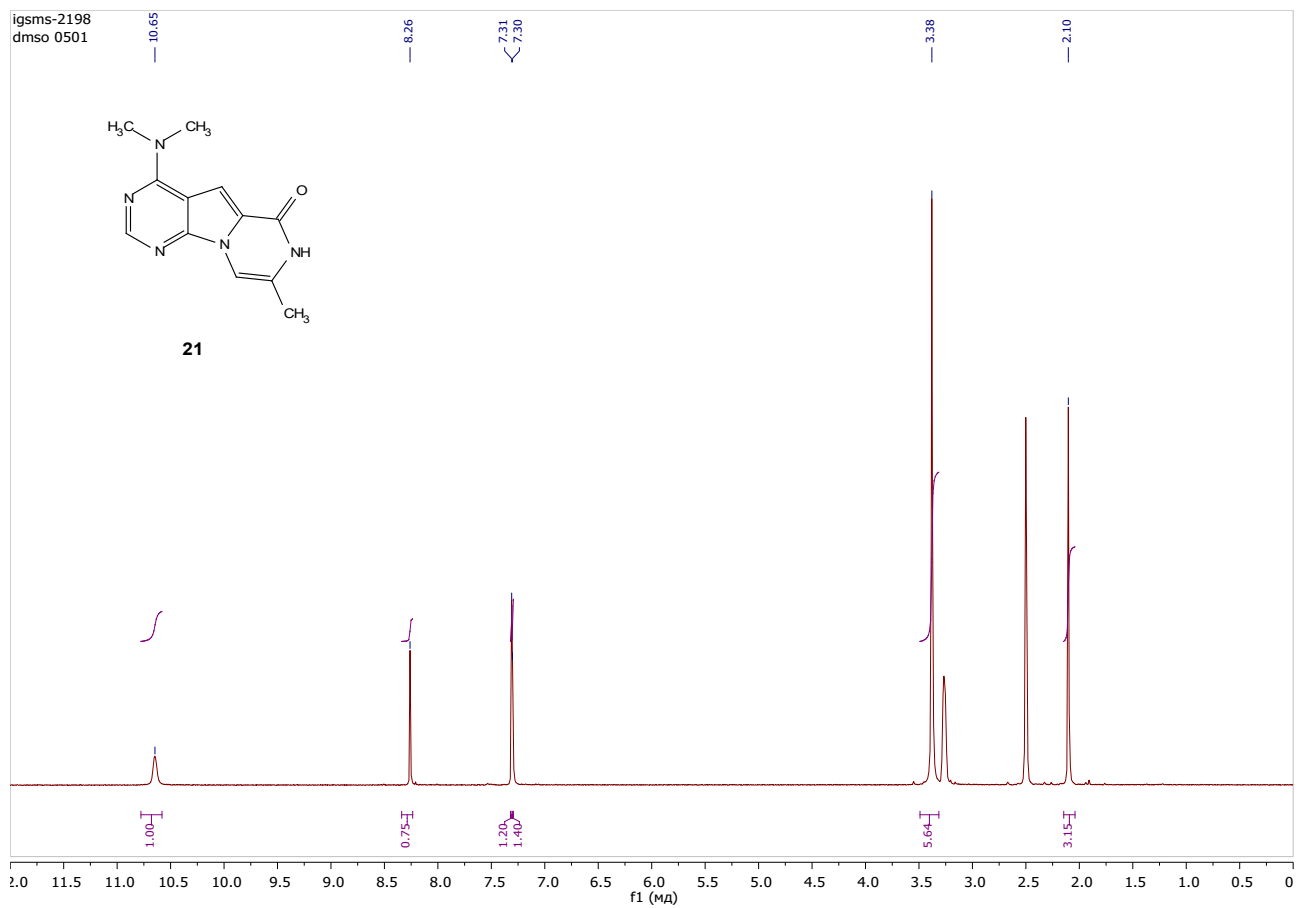
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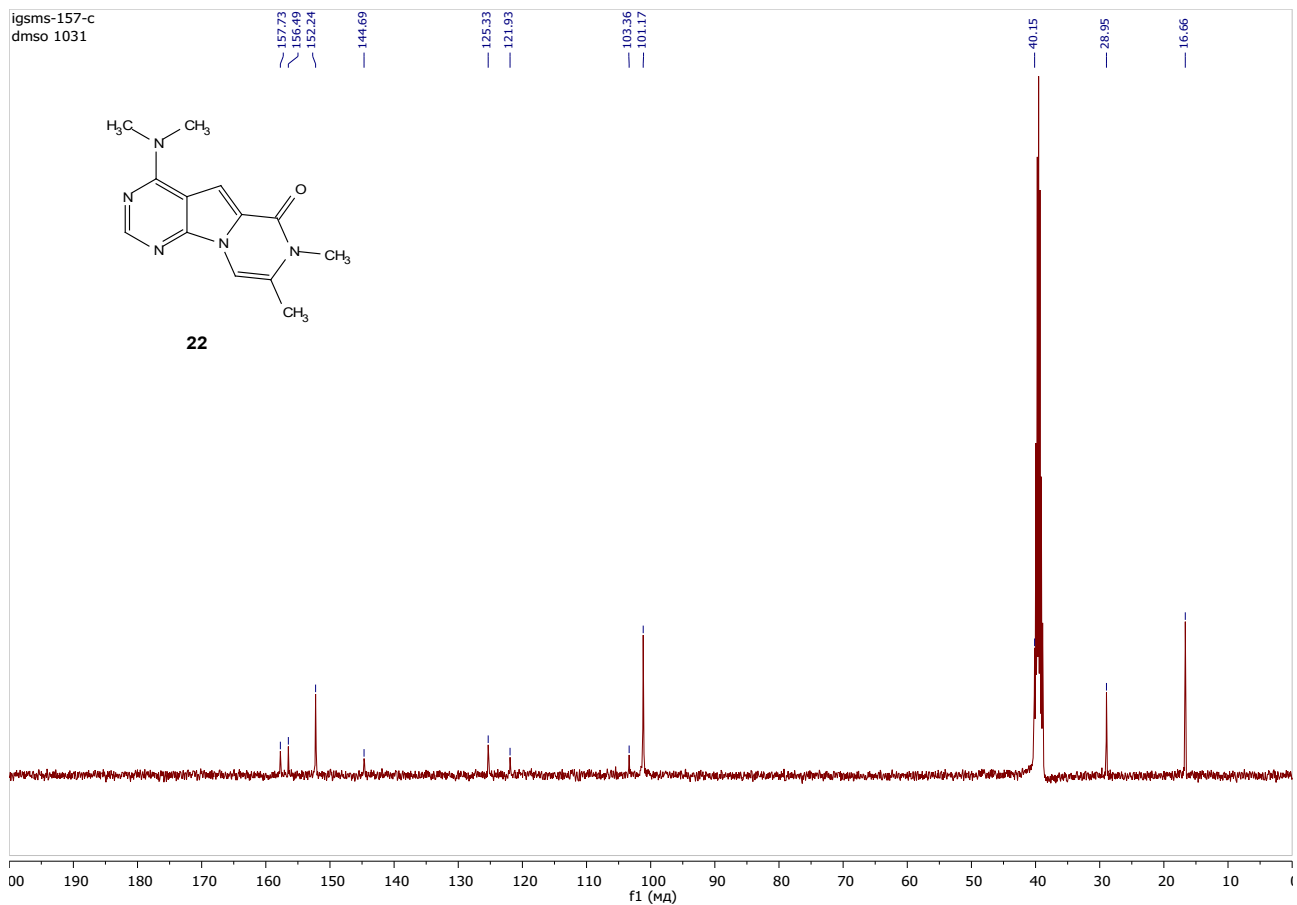
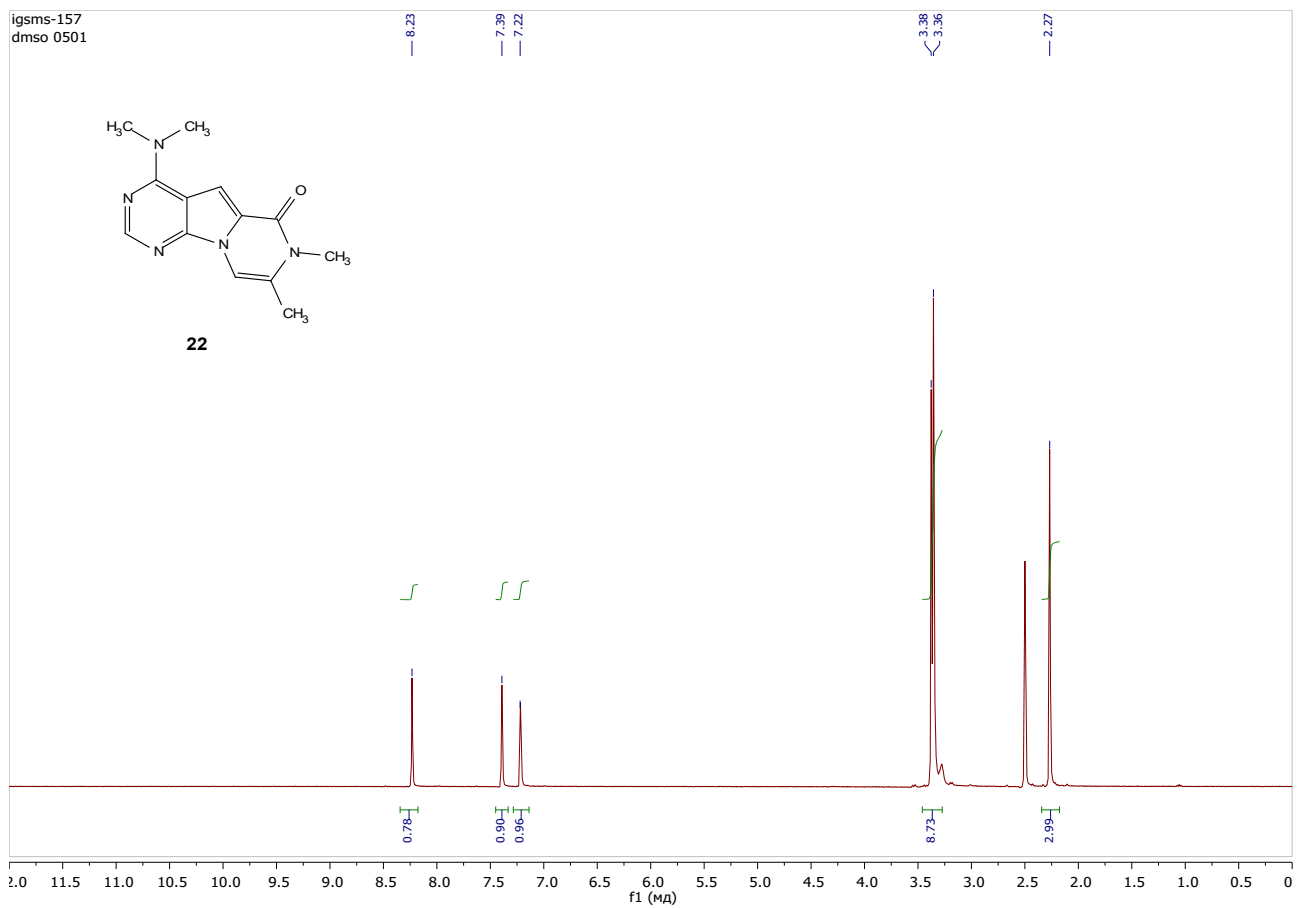


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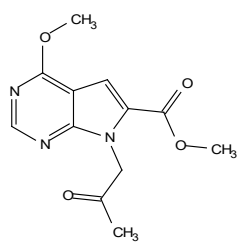
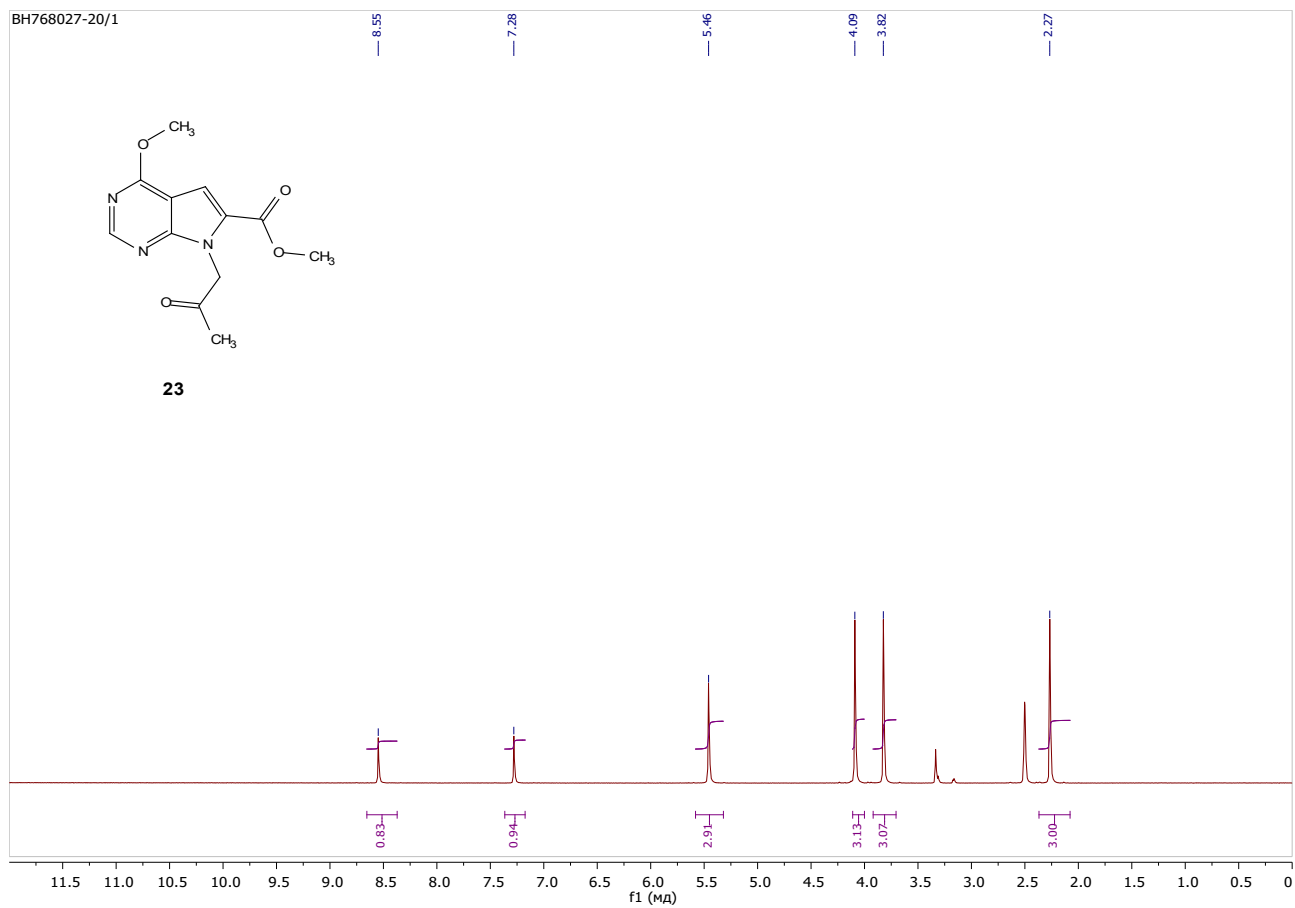




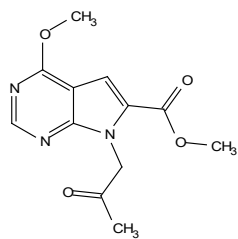
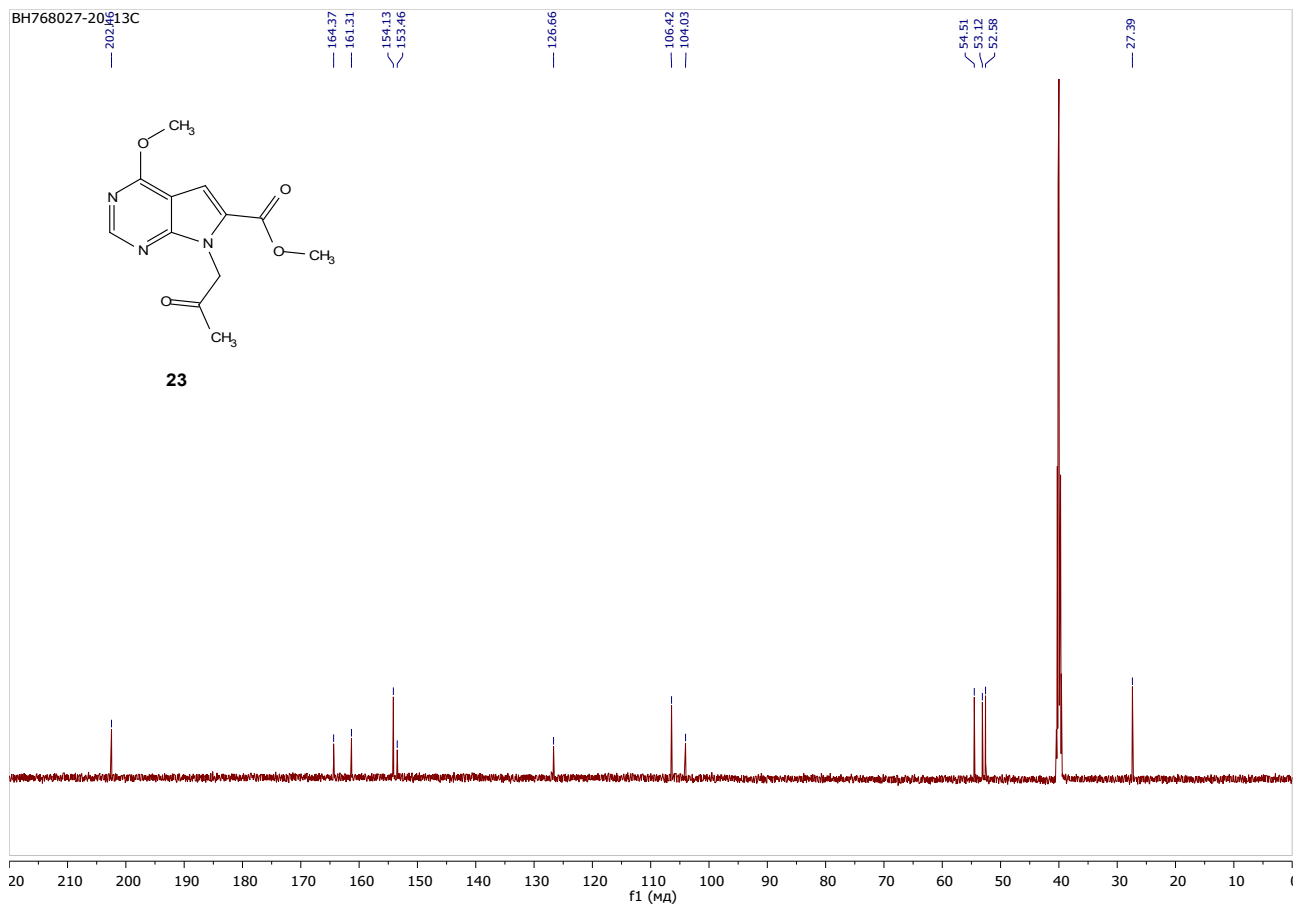


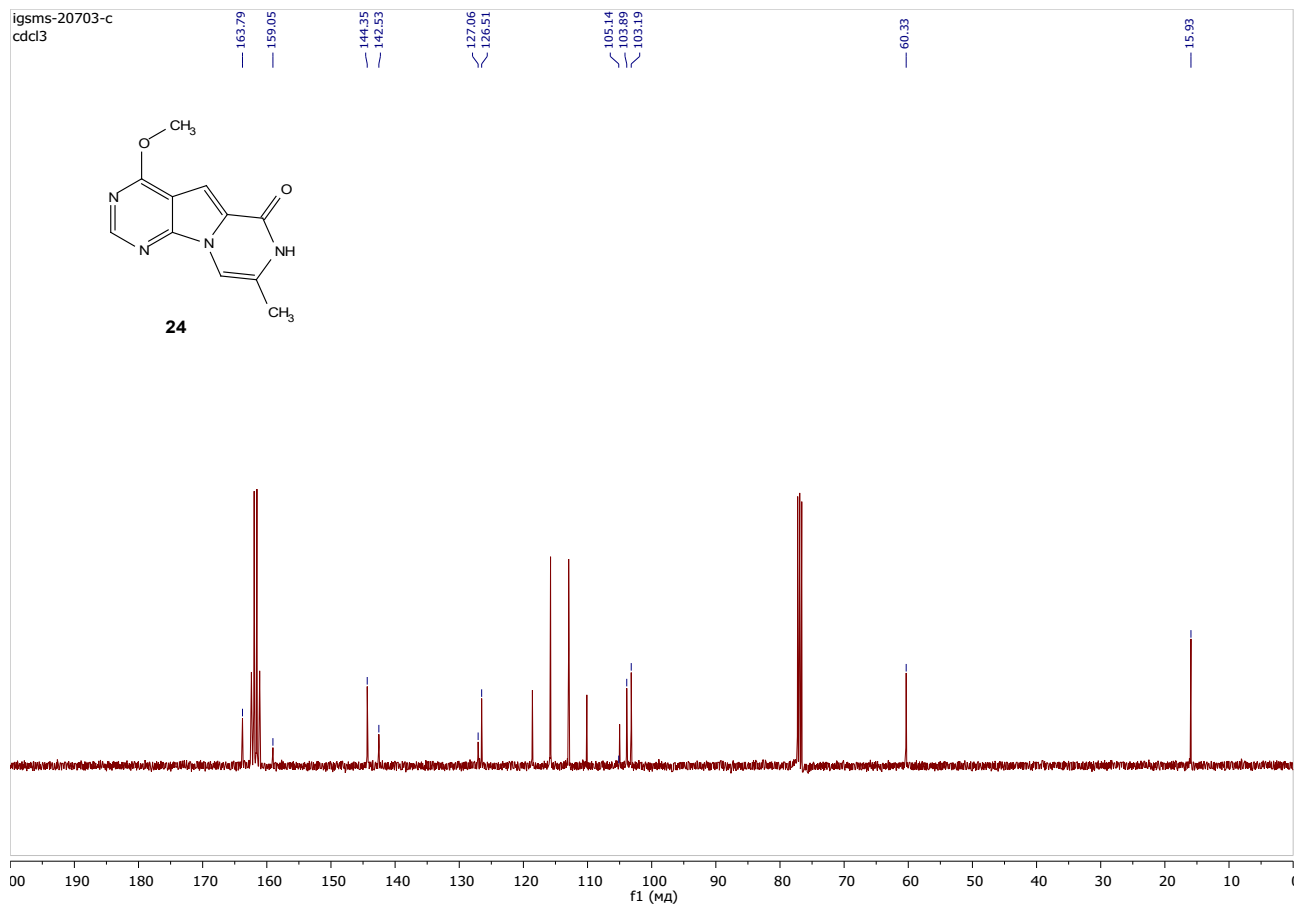
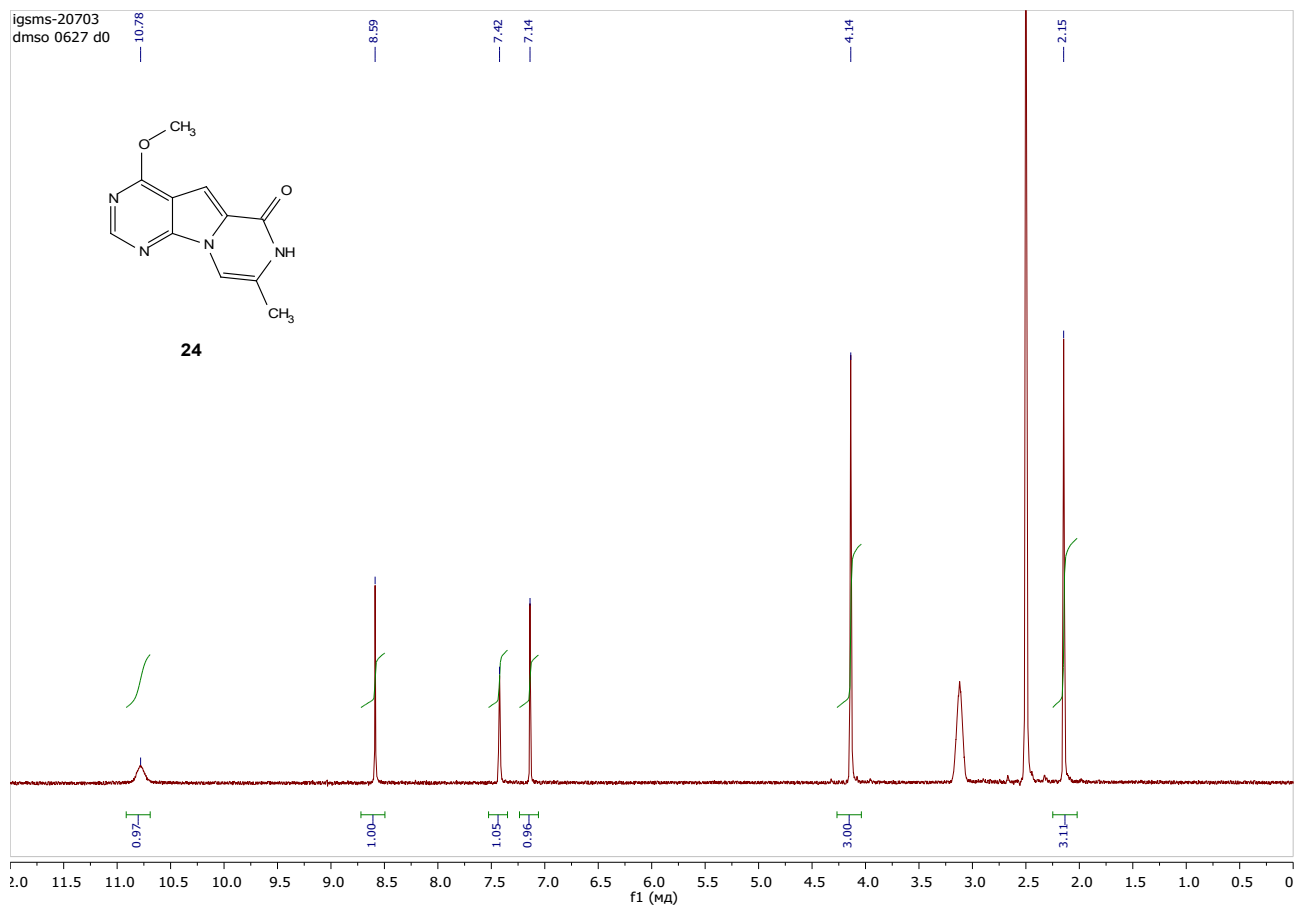


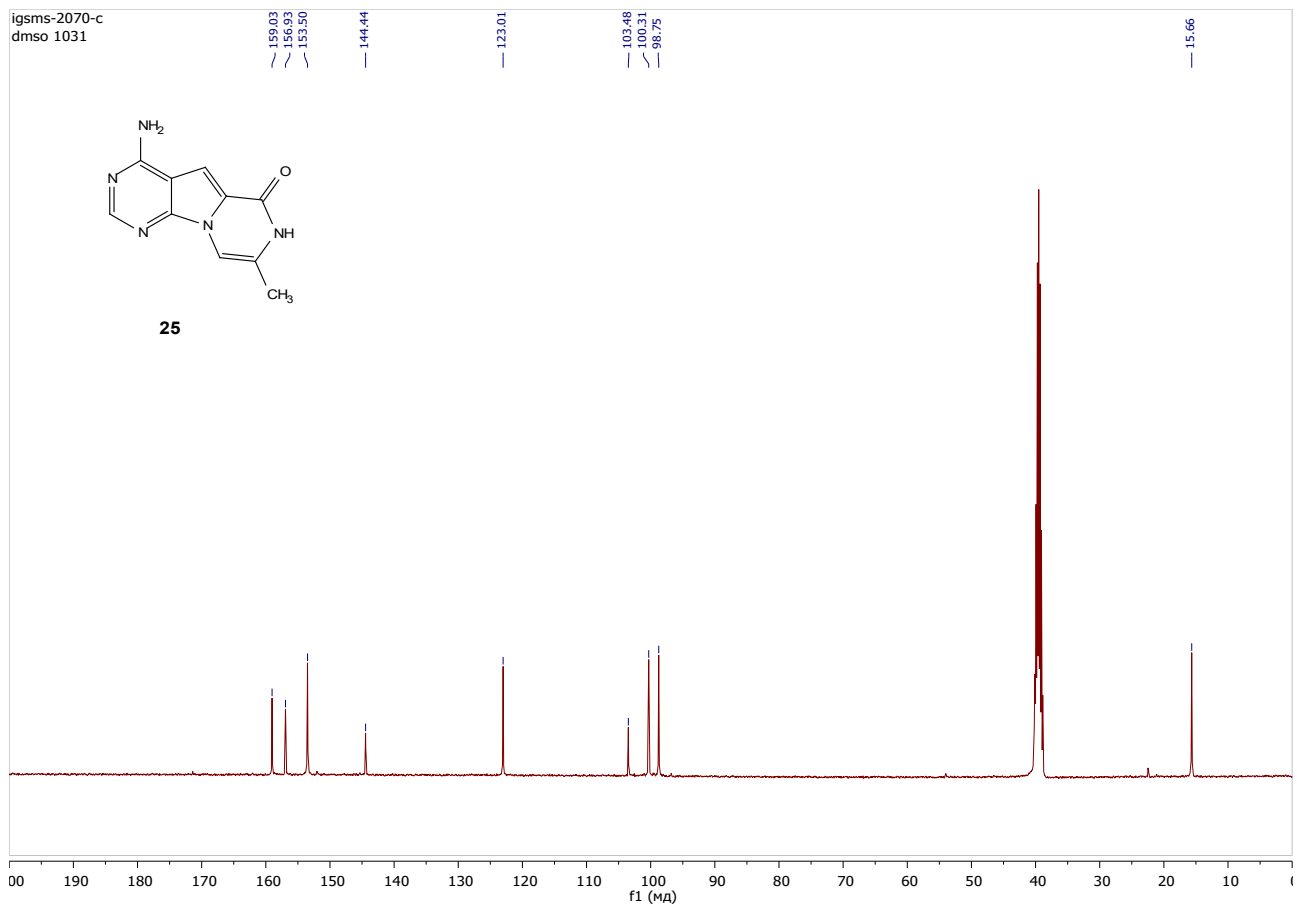
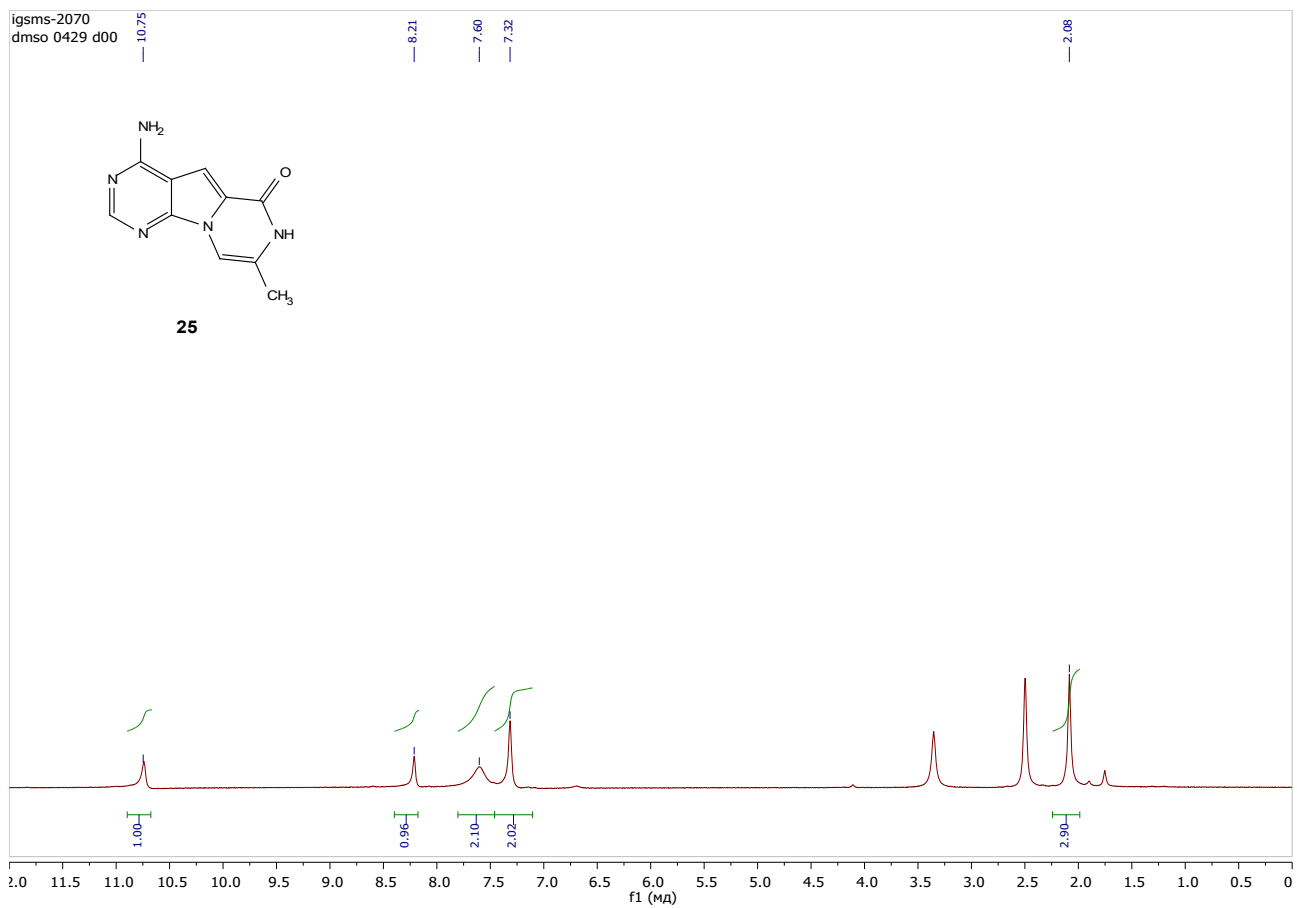
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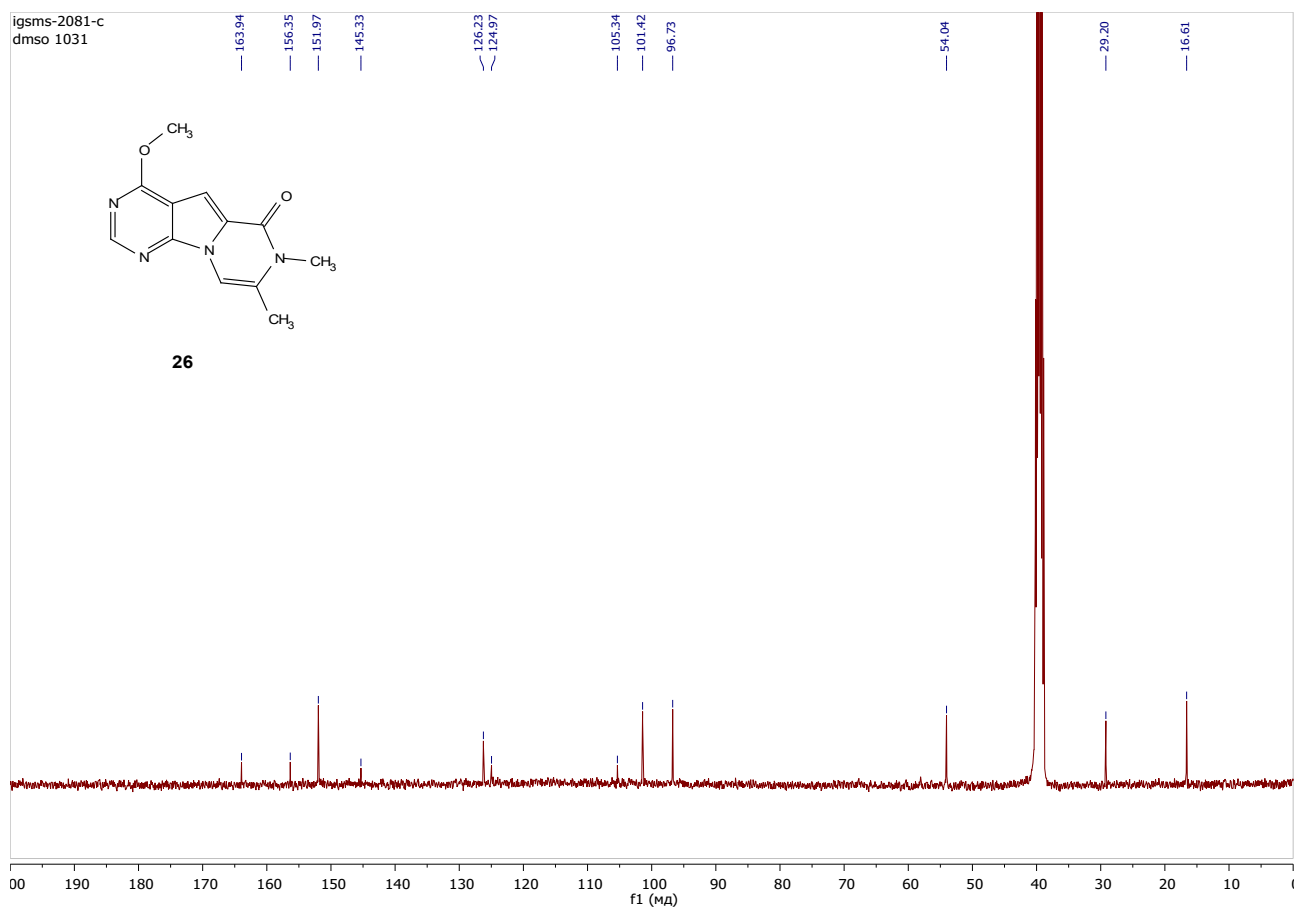
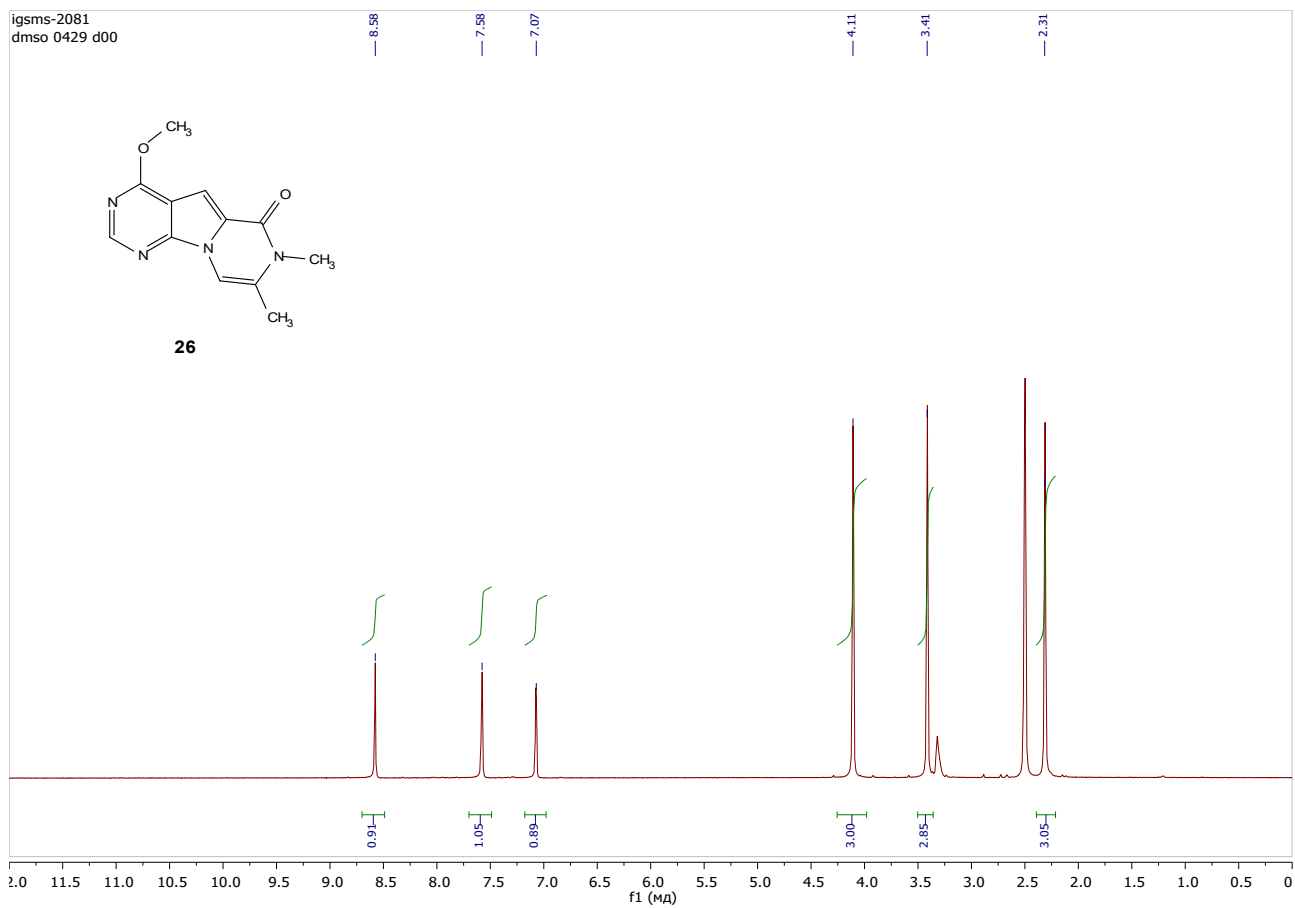
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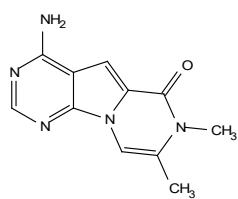
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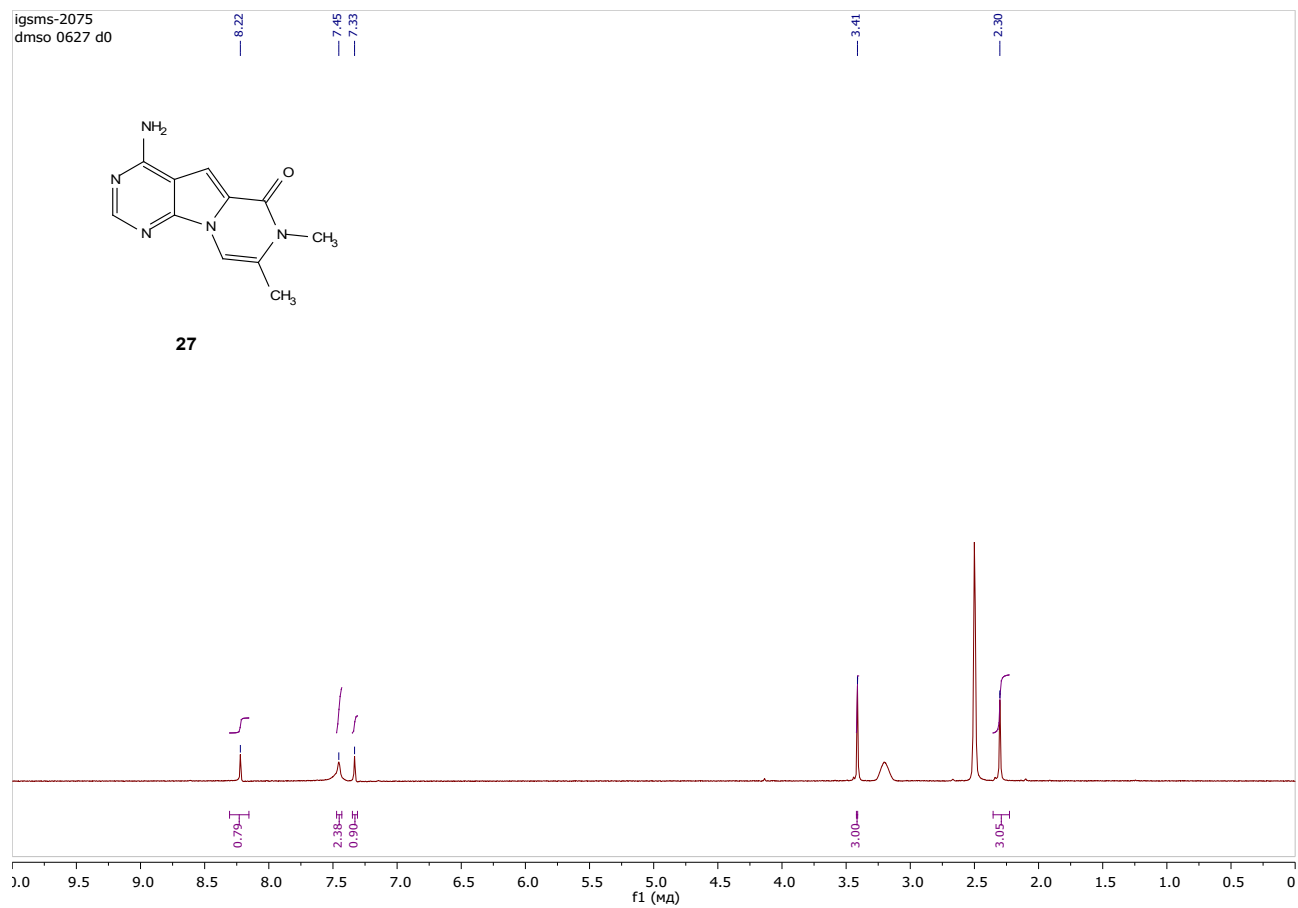




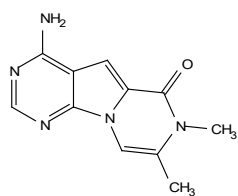
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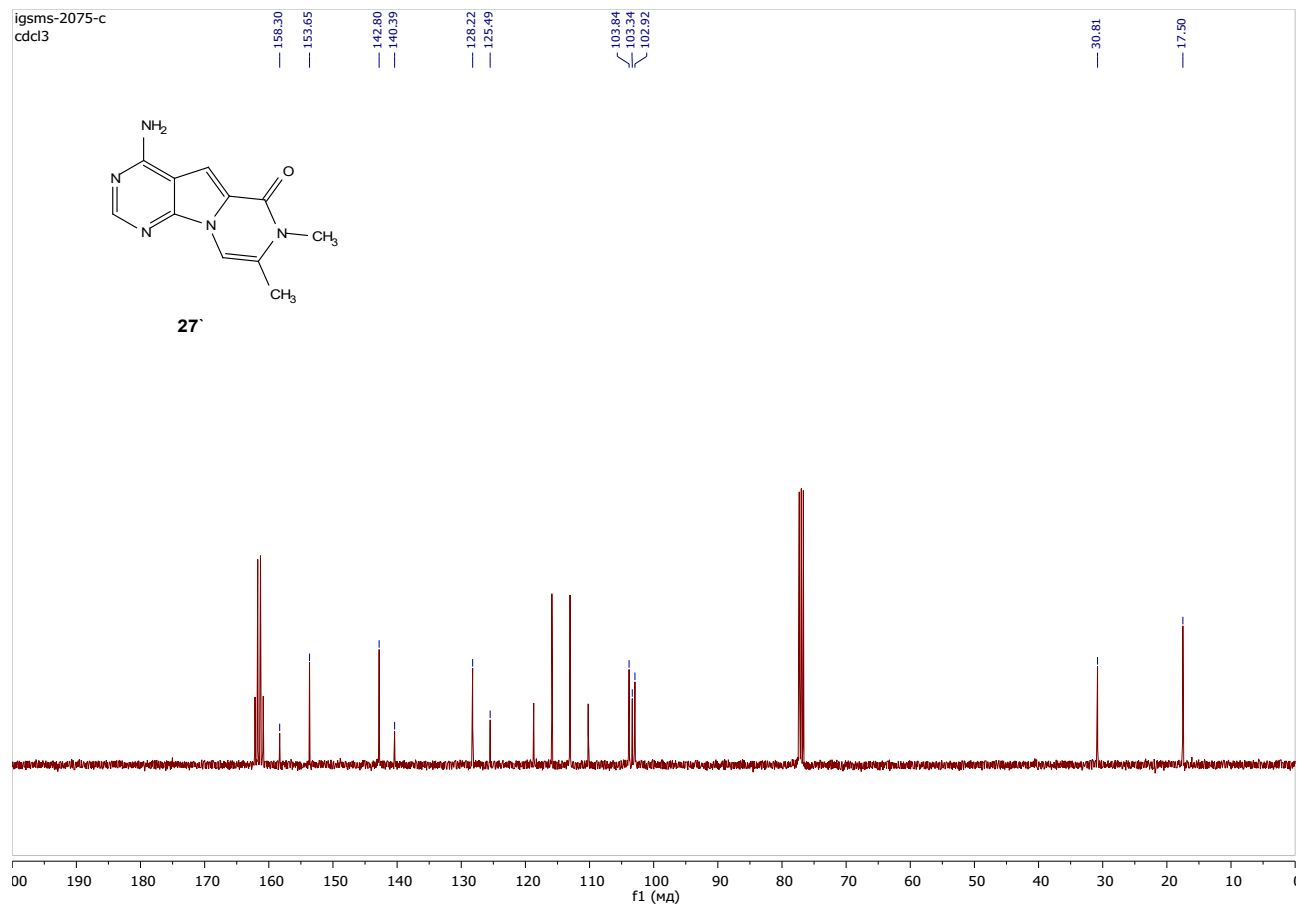
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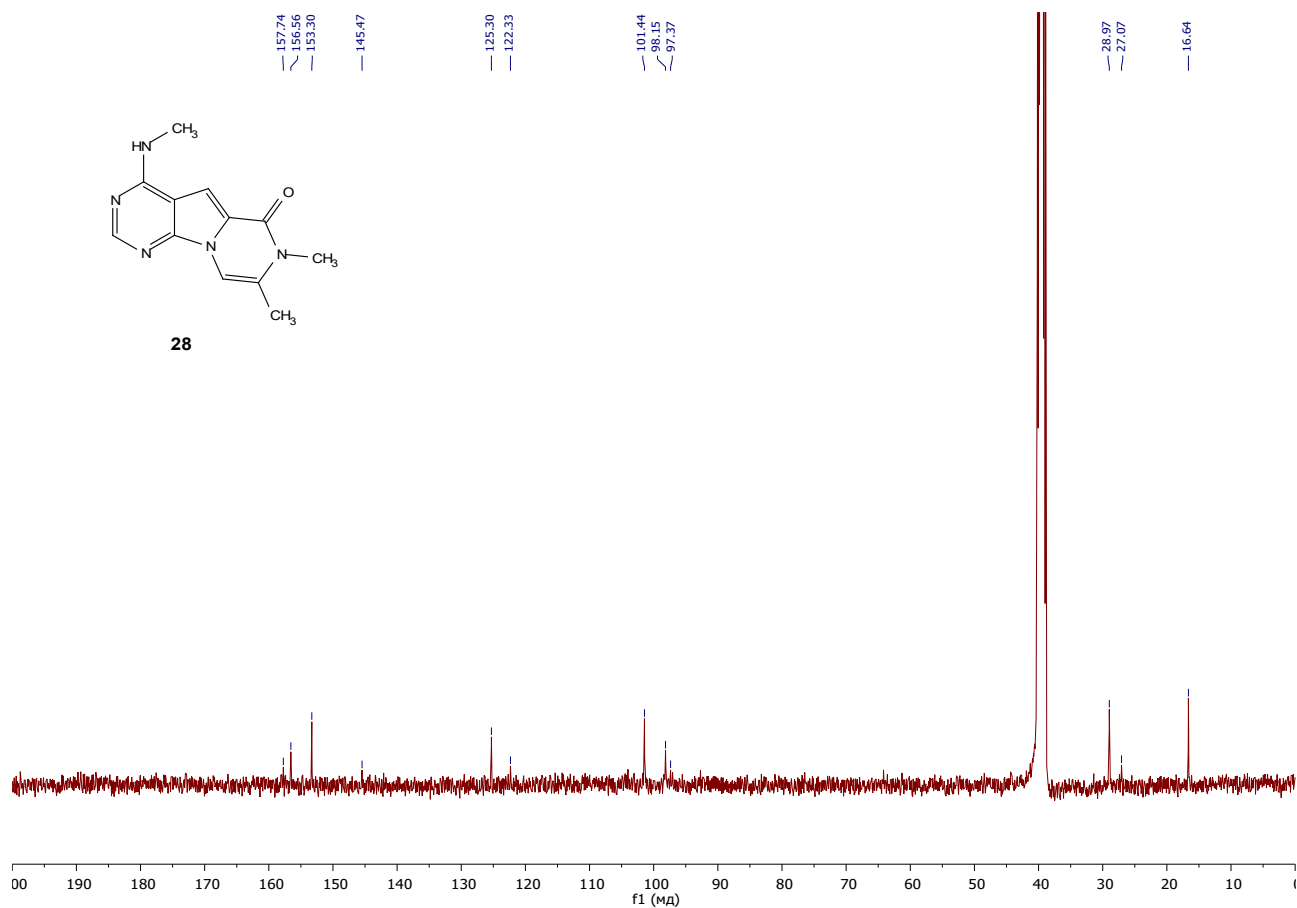
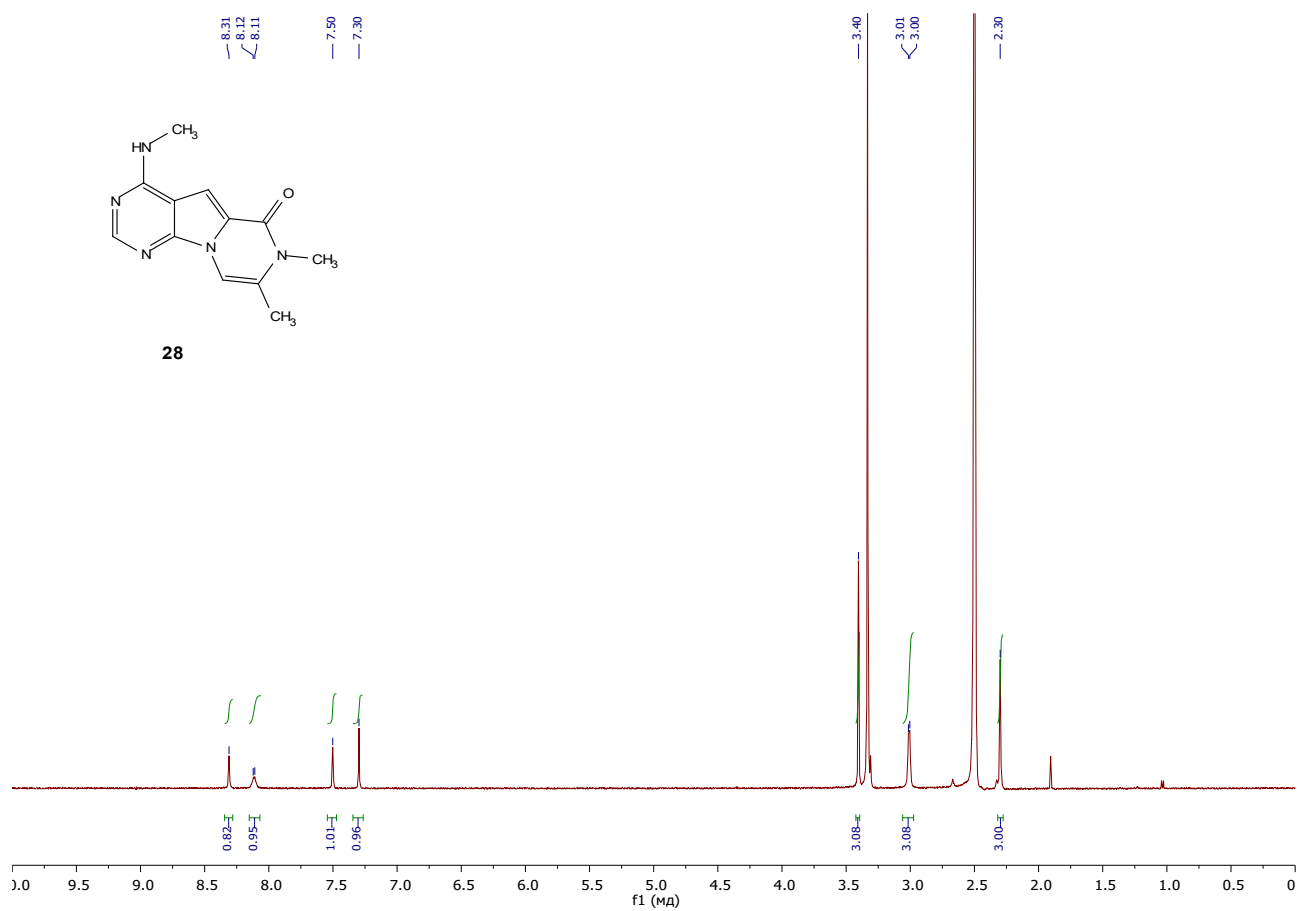


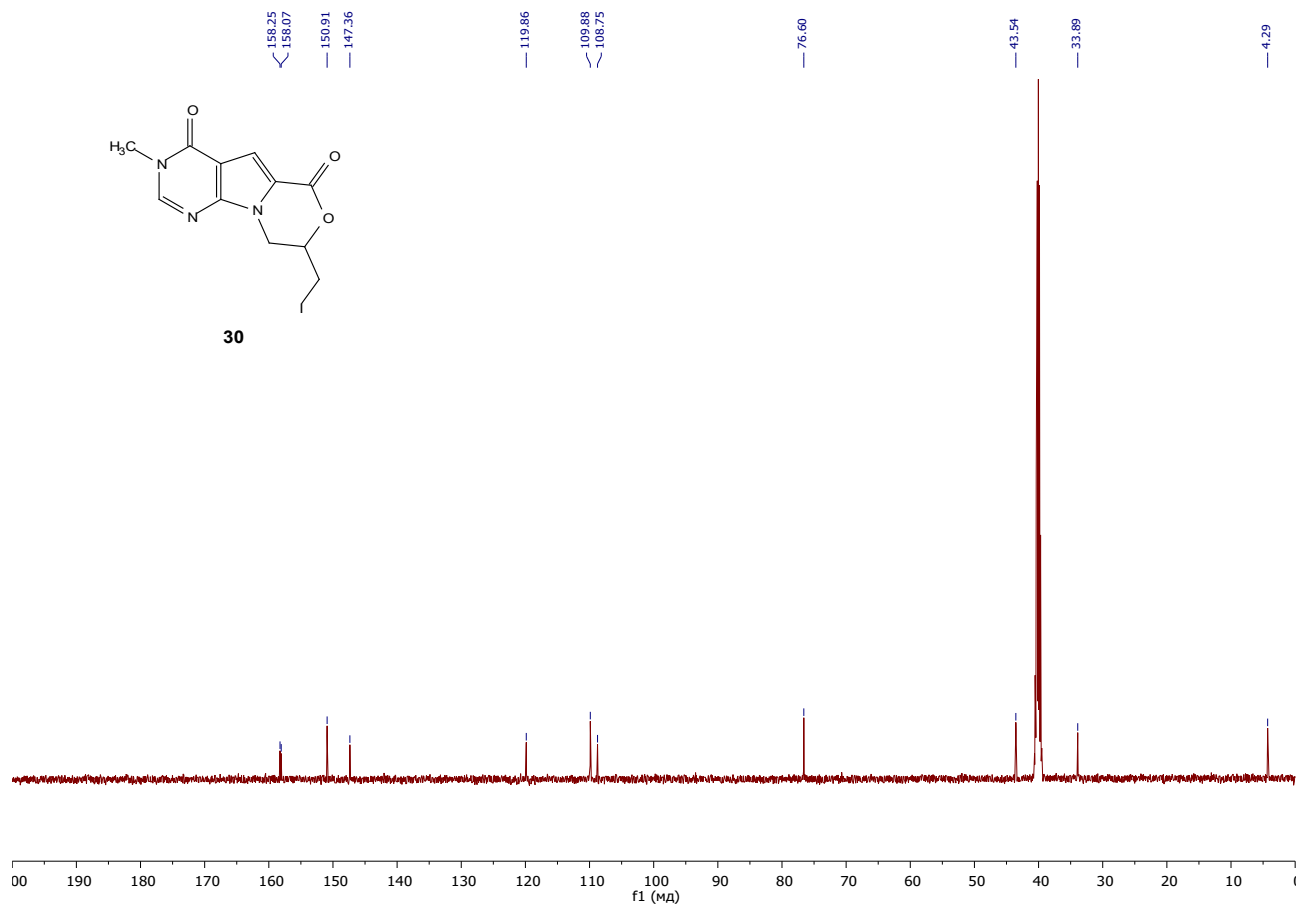
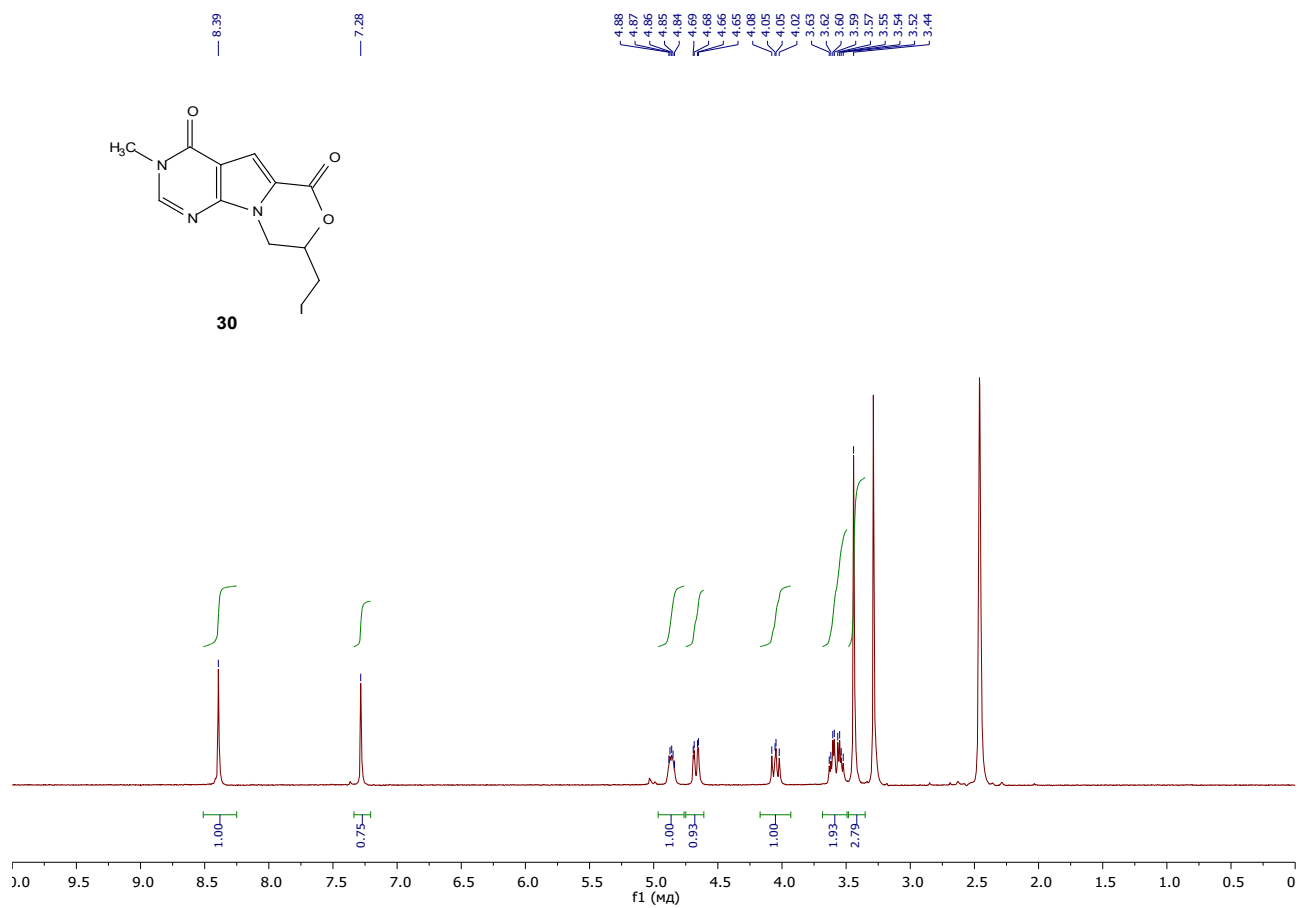
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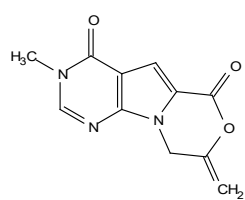


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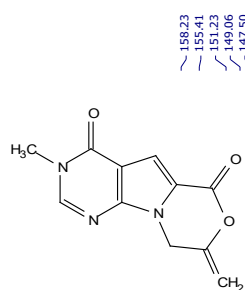
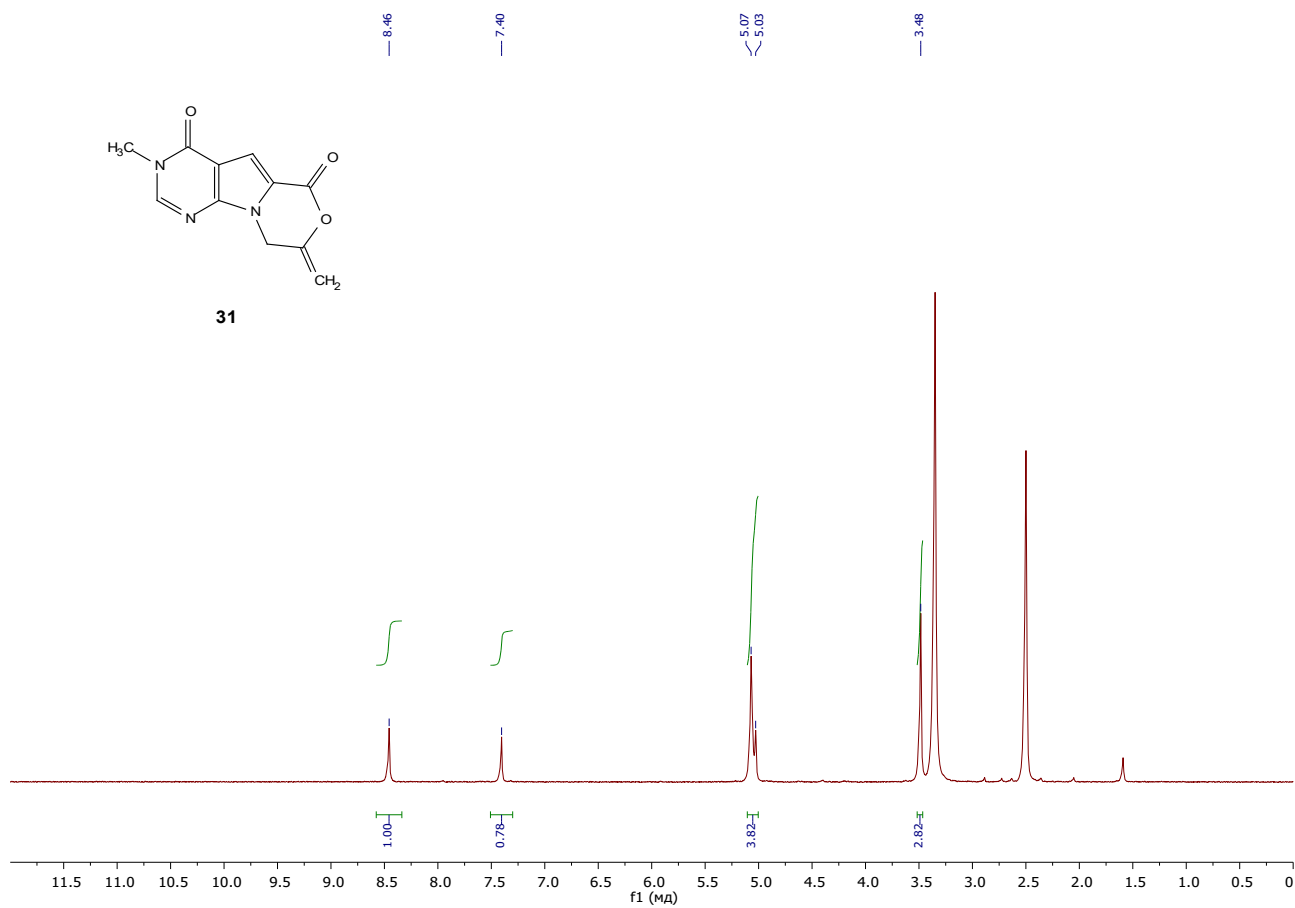




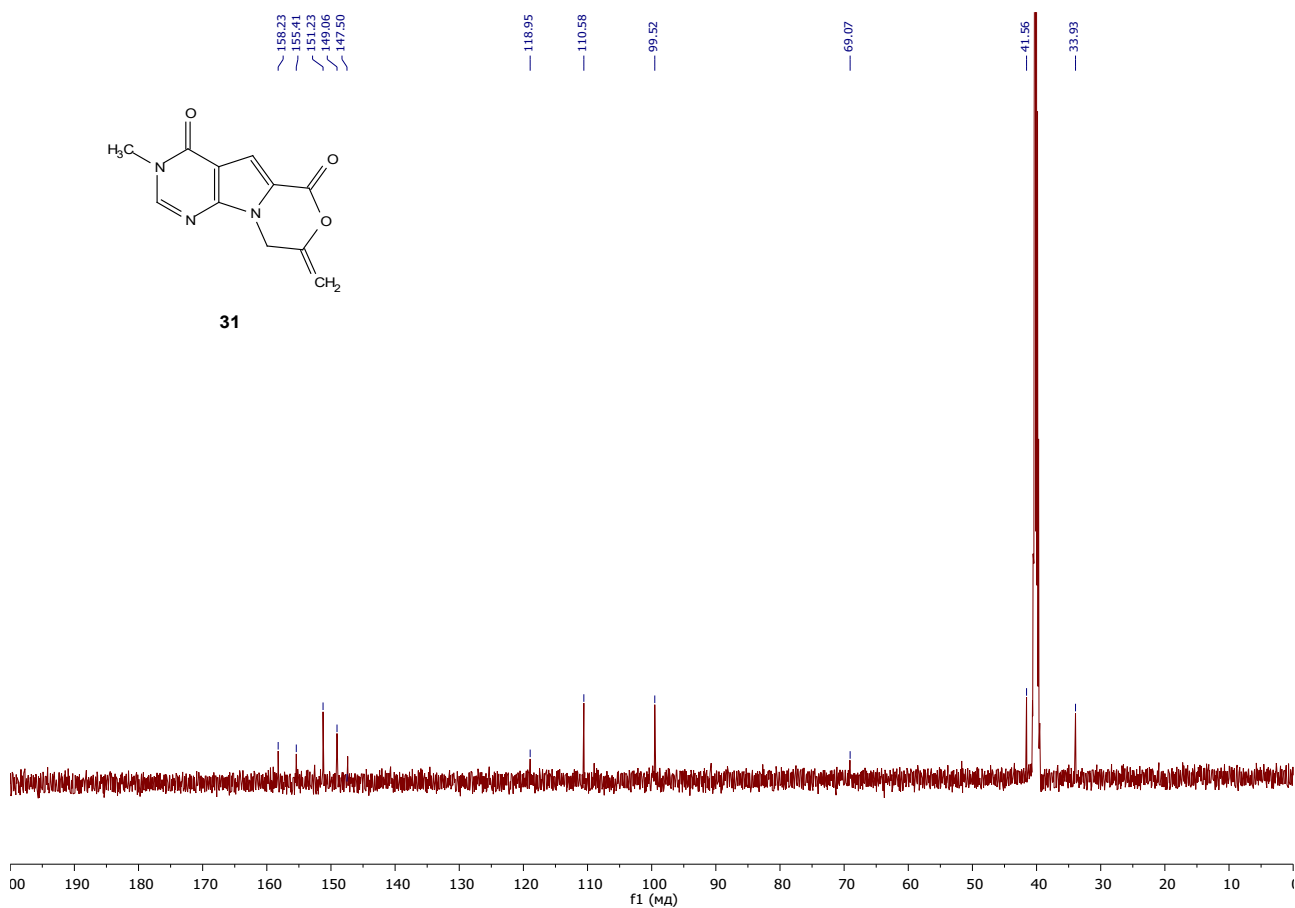


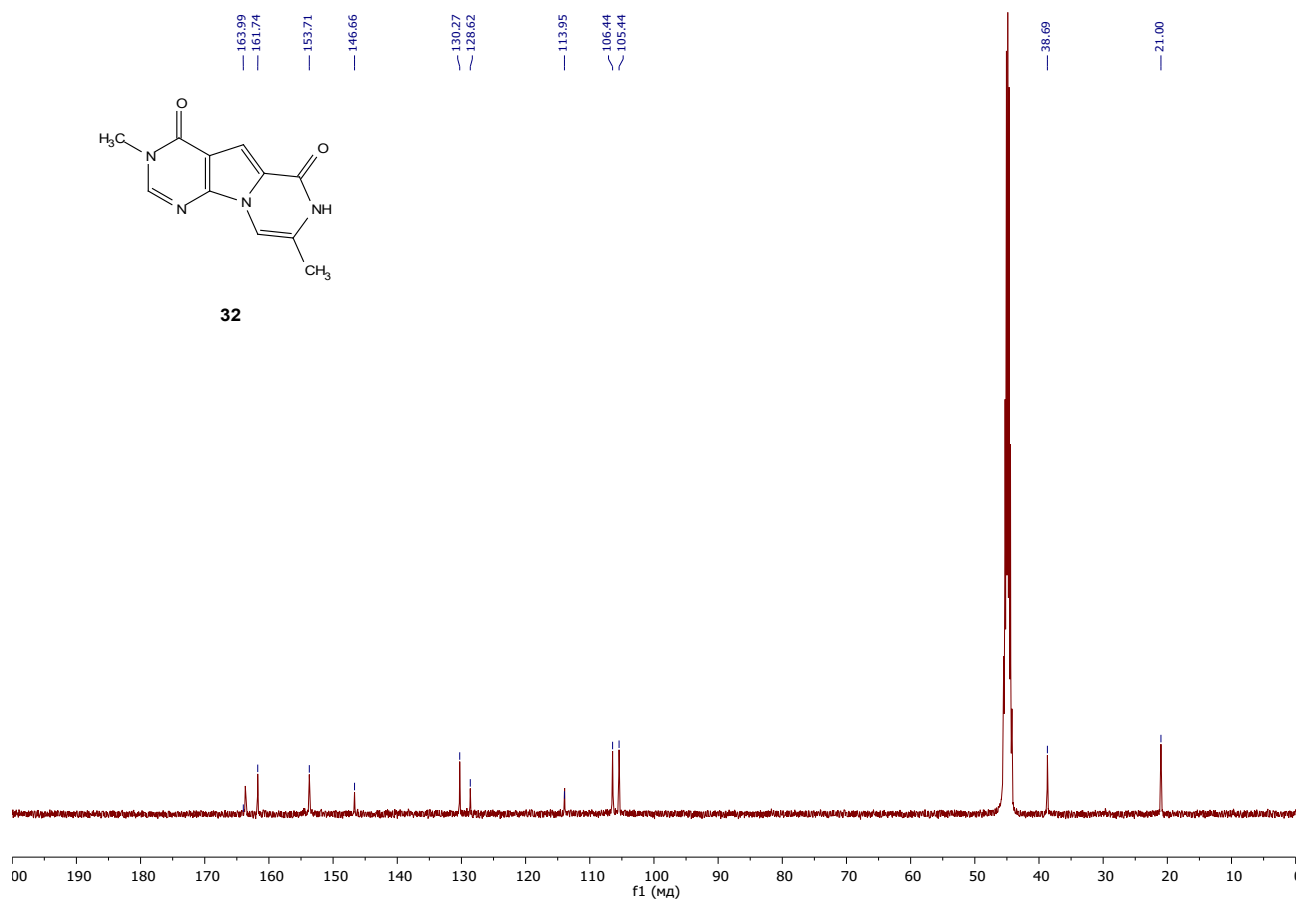
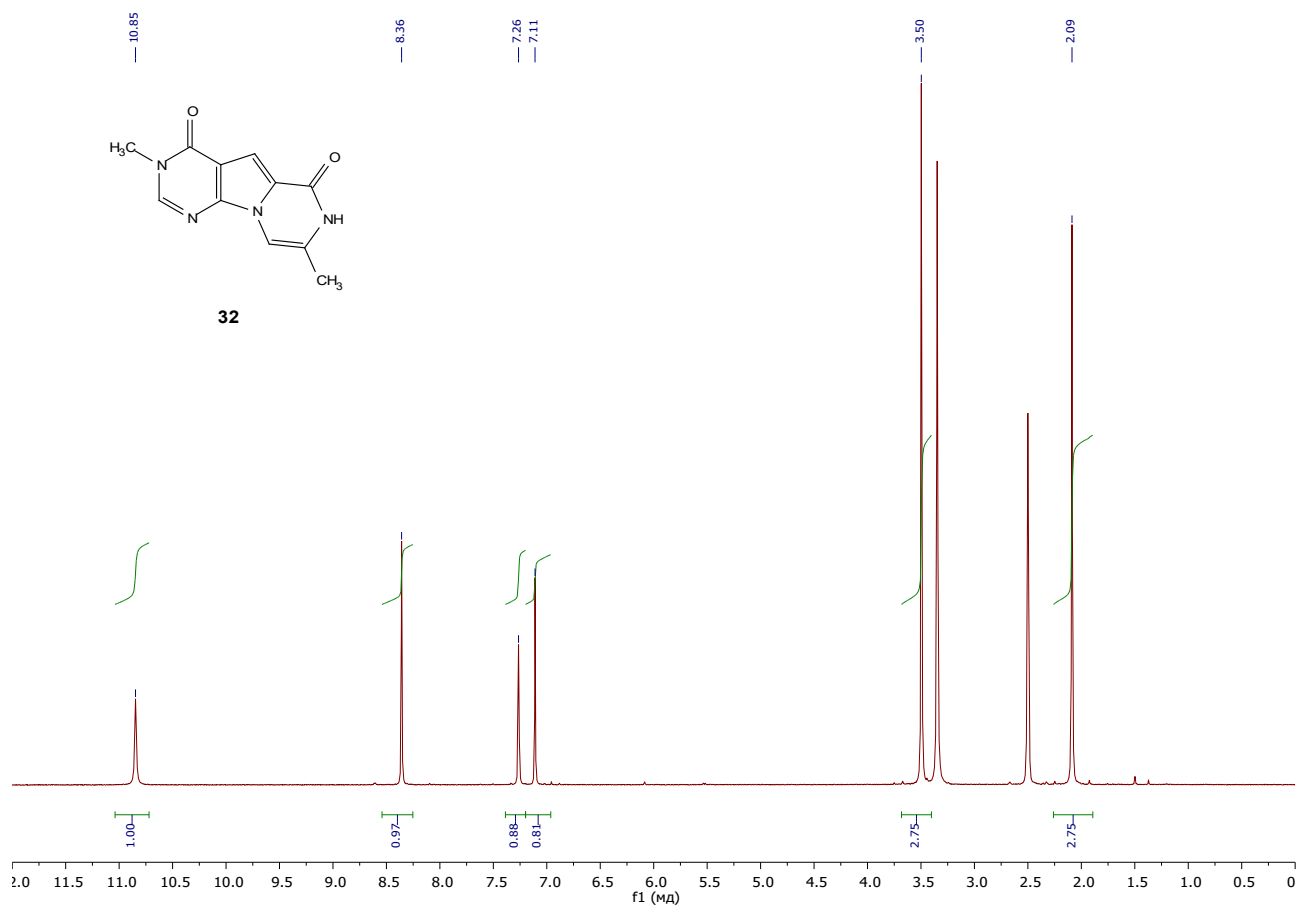


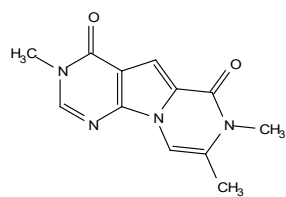
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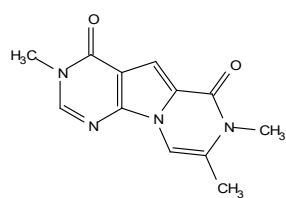
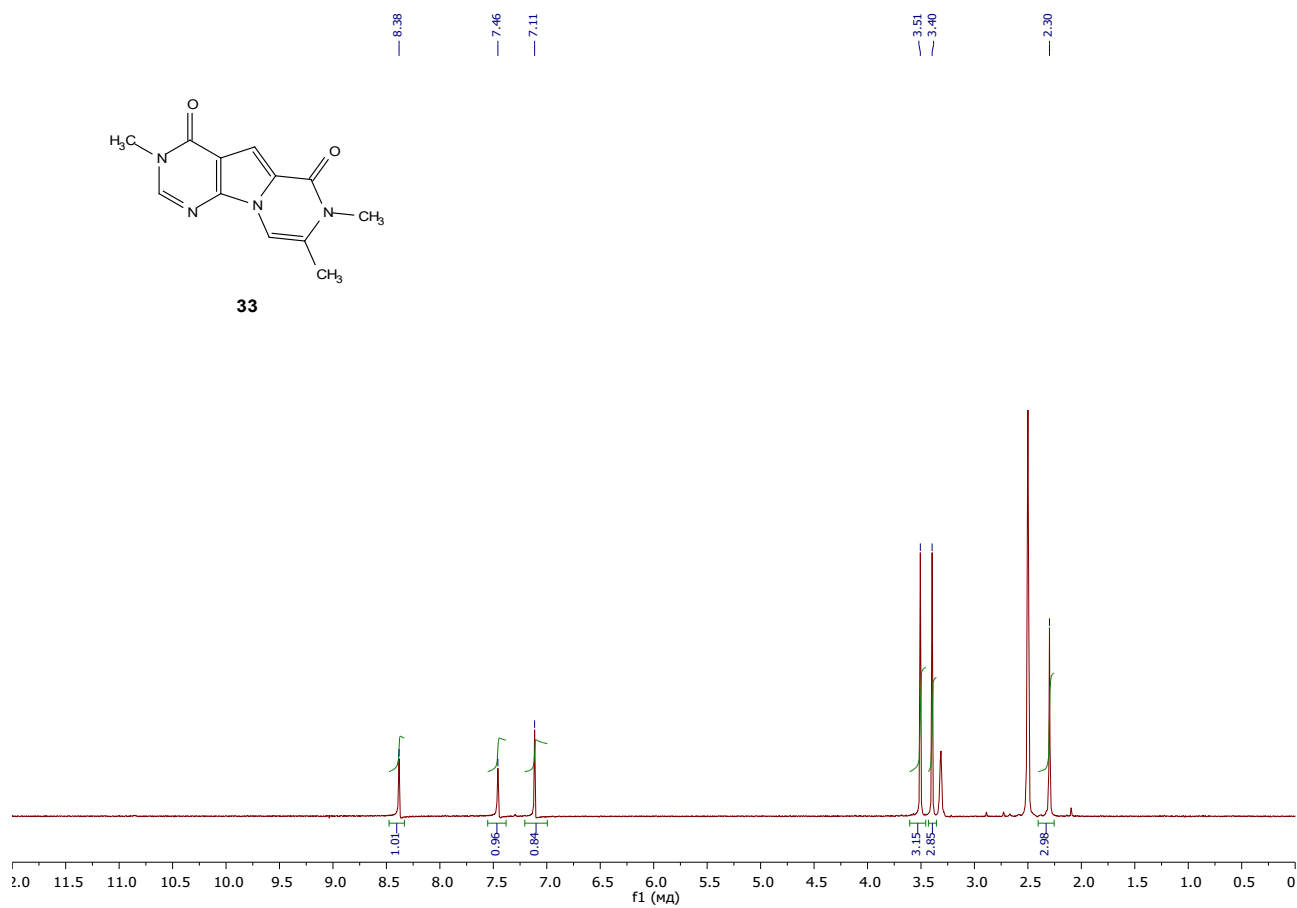
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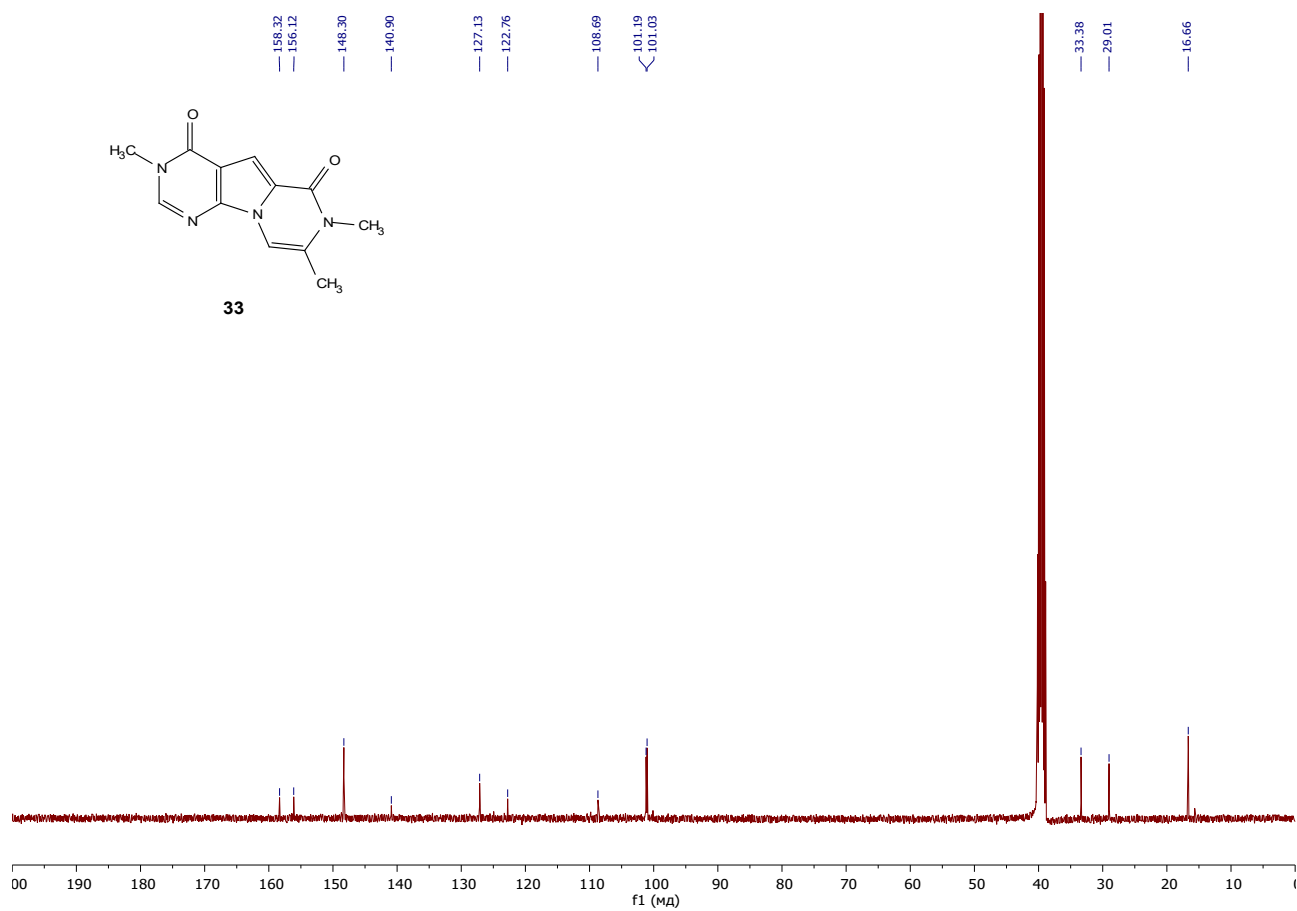




33



33



LCMS spectra of synthesized compounds

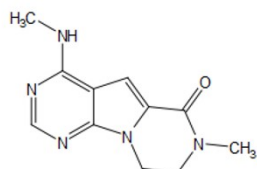
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Sample Name: SOB00087

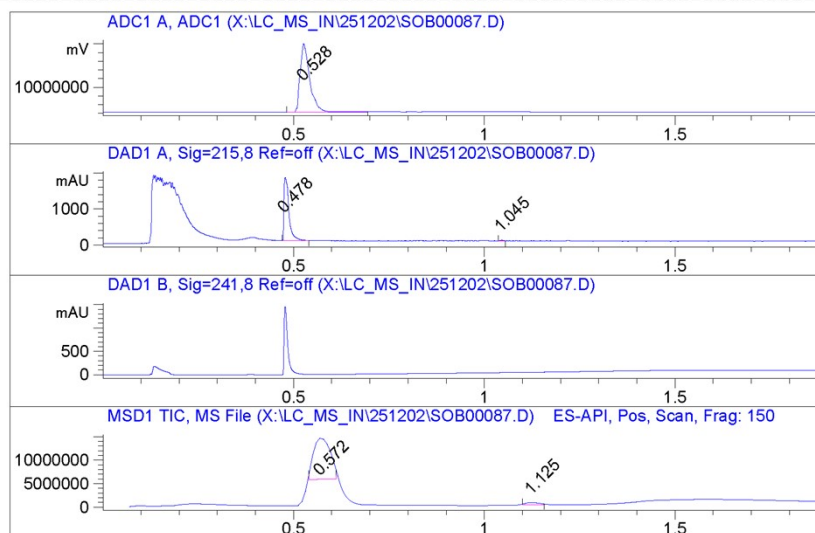
-.o.-Syntez Purity Report -.o.-

System: Agilent 1260 LC/MSD SL
 Detector: Diodearray G1315B (DAD1)
 MassQuad G1956B (MSD1-Pos, MSD2-Neg)

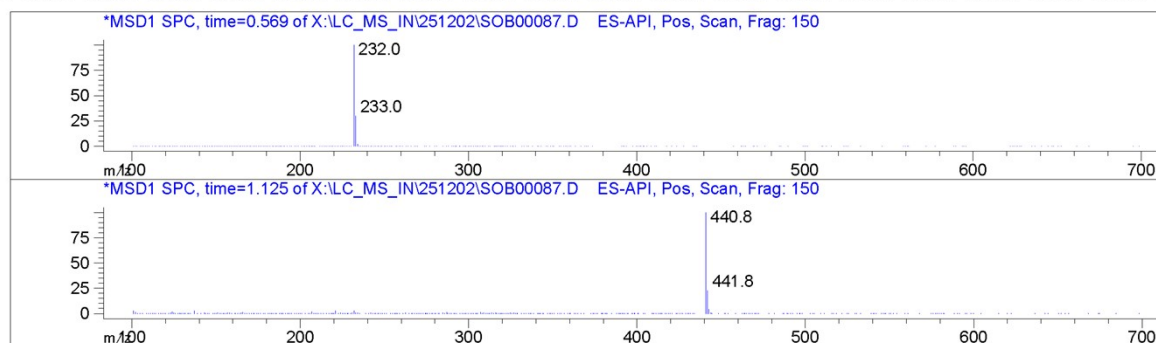
Mobile phase: A-H₂O+0.1% HCOOH; B-MeCN+0.1% HCOOH
 Separation column:
 Rapid Resolution HT Cartige 4.6x30mm,
 1.8-Micron, Zorbax SB C-18



5



Block:



#	Signal	R.Time	Area %
1	ADC1 A, ADC1	0.528	100.000

#	Signal	R.Time	Area %
1	DAD1 A, Sig=215,8 Ref=off	0.478	99.426
2		1.045	0.574

#	Signal	R.Time	Area %
1	MSD1 TIC, MS File	0.572	96.312
2		1.125	3.688

Inj. Data 02.12.2025 Report str-1260 P4-G-09
 * www.lifechemicals.com *

-o.-Syntez Purity Report -o.-

Agilent 1260 LC/MSD

Diodearray G1315B (DAD1A-215nm; DAD1B-241nm)

Mass Quad G6140 (MSD1-Pos, MSD2-Neg)

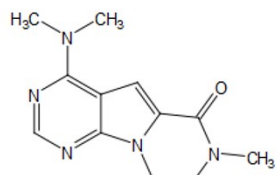
ELSD SOFTA 1400

Mobile Phase:A-H₂O+0.1HCOOH;B-MeCN+0.1HCOOH

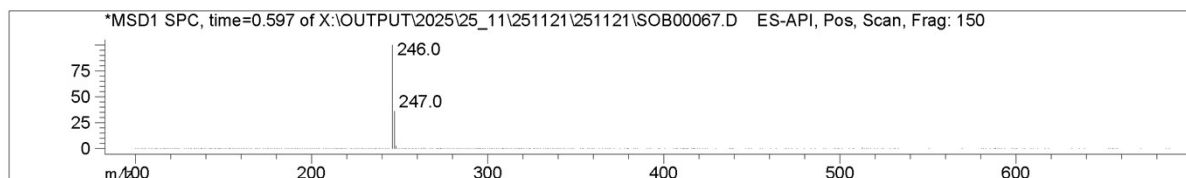
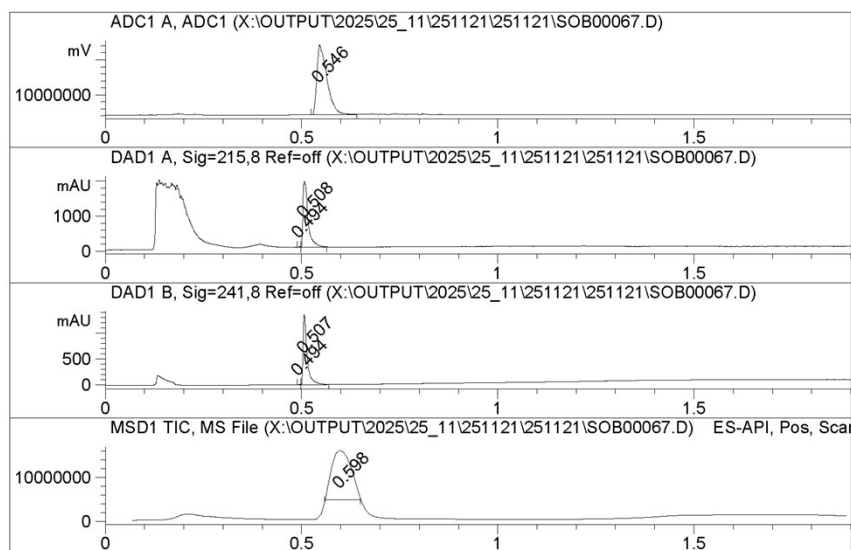
Separation column:

Rapid Resolutionn HT Cartige 4.6x30mm,

1.8-Micron, Zorbax SB-C18



6



#	Signal	R.Time	Area %
1	ADC1 A, ADC1	0.546	100.000

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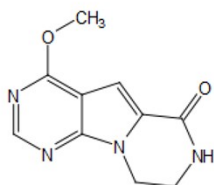
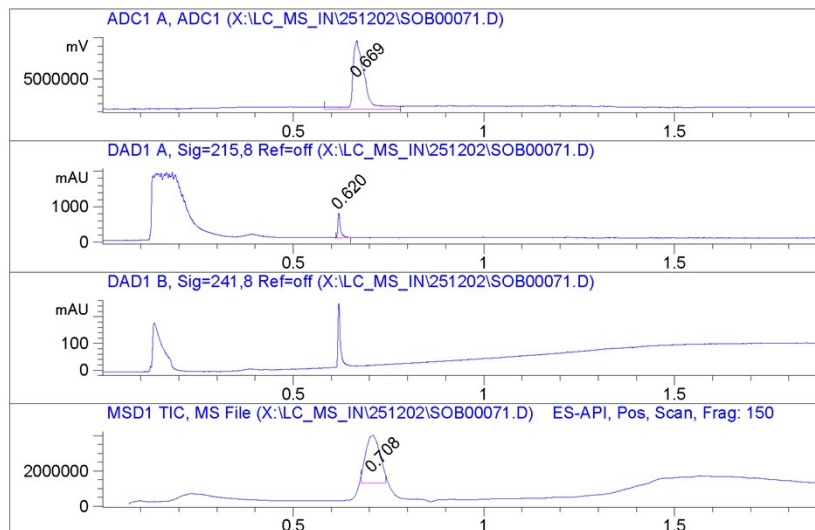
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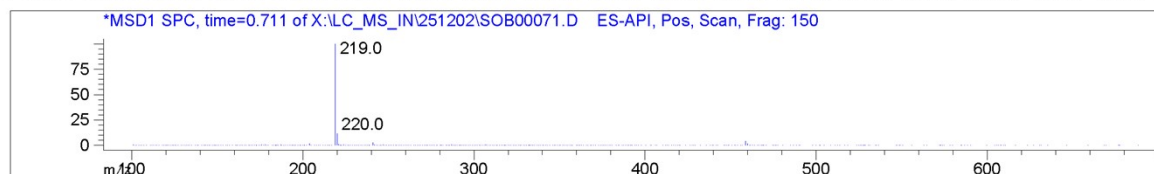
-.o.-Syntez Purity Report -.o.-

System: Agilent 1260 LC/MSD SL
Detector: Diodearray G1315B (DAD1)
MassQuad G1956B (MSD1-Pos, MSD2-Neg)

Mobile phase:A-H₂O+0.1%HCOOH;B-MeCN+0.1%HCOOH
Separation column:
Rapid Resolutionn HT Cartige 4.6x30mm,
1.8-Micron, Zorbax SB C-18

**8**

Block:



#	Signal	R.Time	Area %
1	ADC1 A, ADC1	0.669	100.000

#	Signal	R.Time	Area %
1	DAD1 A, Sig=215,8 Ref=off	0.620	100.000

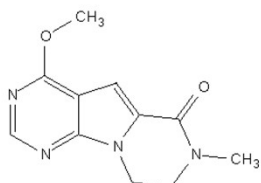
#	Signal	R.Time	Area %
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#	Signal	R.Time	Area %
1	MSD1 TIC, MS File	0.708	100.000

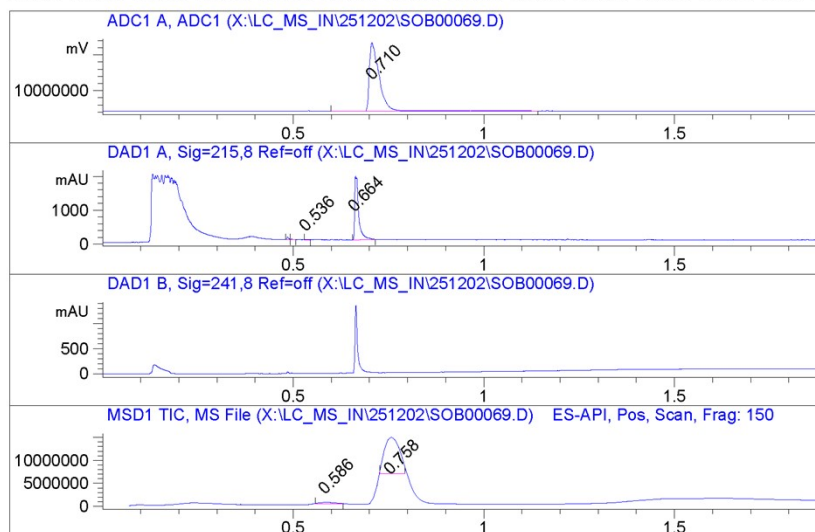
-.o.-Syntez Purity Report -.o.-

System: Agilent 1260 LC/MSD SL
Detector: Diodearray G1315B (DAD1)
MassQuad G1956B (MSD1-Pos, MSD2-Neg)

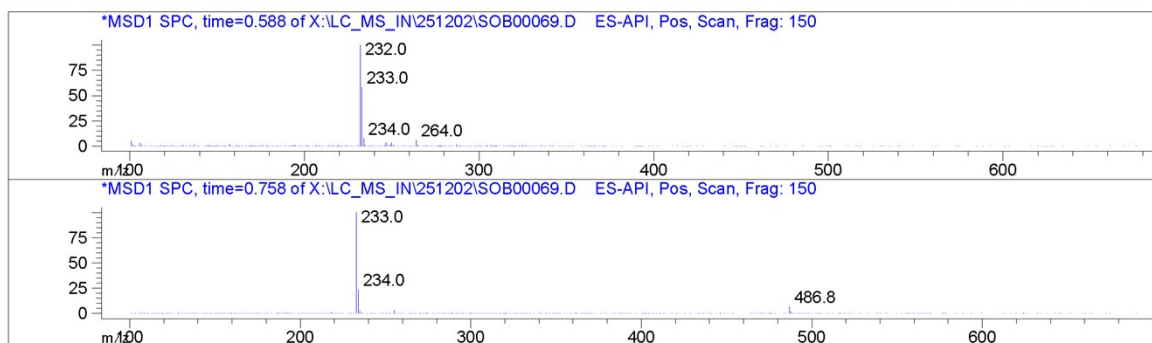
Mobile phase:A-H₂O+0.1%HCOOH;B-MeCN+0.1%HCOOH
Separation column:
Rapid Resolutionn HT Cartige 4.6x30mm,
1.8-Micron, Zorbax SB C-18



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Block:



#	Signal	R.Time	Area %
1	ADC1 A, ADC1	0.710	100.000

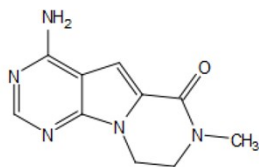
#	Signal	R.Time	Area %
1	DAD1 A, Sig=215,8 Ref=off	0.486	1.880
2		0.496	0.413
3		0.536	0.311
4		0.664	97.396

#	Signal	R.Time	Area %
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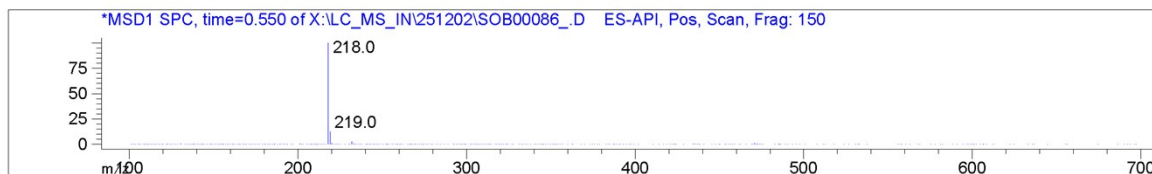
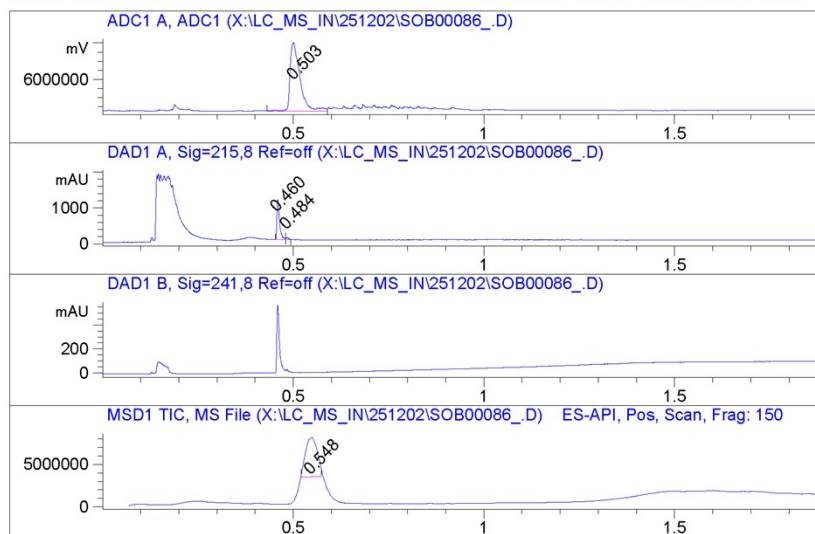
-.o.-Syntez Purity Report -.o.-

System: Agilent 1260 LC/MSD SL
 Detector: Diodearray G1315B (DAD1)
 MassQuad G6140A (MSD1-Pos, MSD2-Neg)

Mobile phase:A-H₂O+0.1%HCOOH;B-MeCN+0.1%HCOOH
 Separation column:
 Rapid Resolutionn HT Cartige 4.6x30mm,
 1.8-Micron, Zorbax SB C-18

**10**

Block:



#	Signal	R.Time	Area %
1	ADC1 A, ADC1	0.503	100.000
#	Signal	R.Time	Area %
1	DAD1 A, Sig=215,8 Ref=off	0.460	96.167
2		0.484	3.833
#	Signal	R.Time	Area %
#	Signal	R.Time	Area %
1	MSD1 TIC, MS File	0.548	100.000

-.o.-Syntez Purity Report -.o.-

Agilent 1260 LC/MSD

Diodearray G1315B (DAD1A-215nm; DAD1B-241nm)

Mass Quad G6140A (MSD1-Pos, MSD2-Neg)

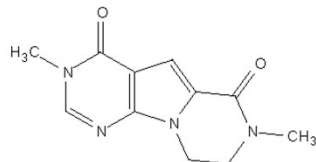
ELSD (ADC1 A, ELSD)

Mobile Phase:A-H₂O+0.1HCOOH;B-MeCN+0.1HCOOH

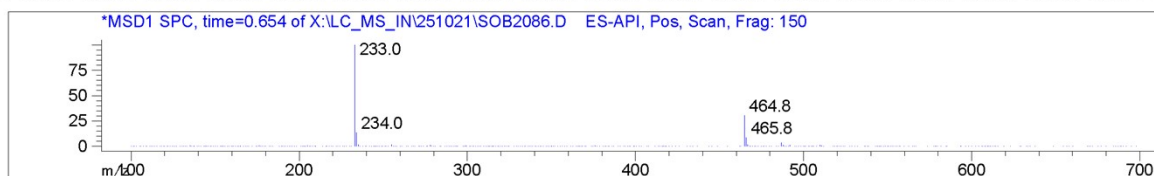
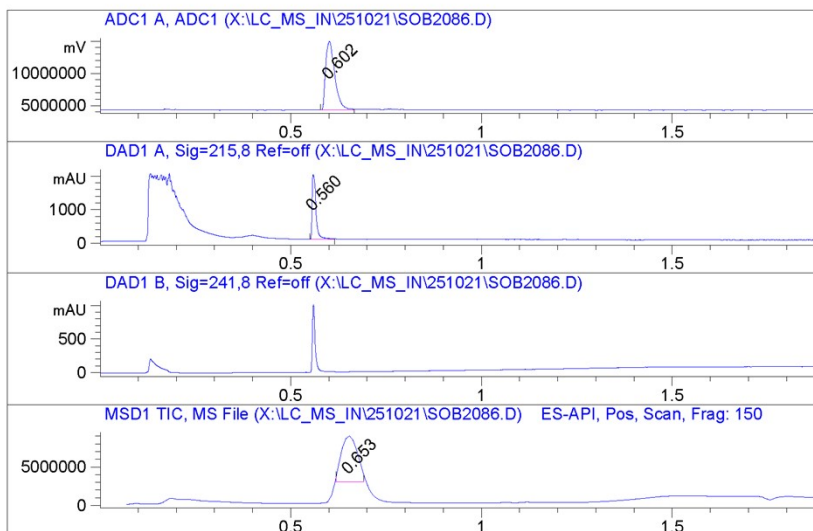
Separation column:

Rapid Resolutionn HT Cartige 4.6x30mm,

1.8-Micron, Zorbax SB-C18



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#	Signal	R.Time	Area %
1	ADC1 A, ADC1	0.602	100.000

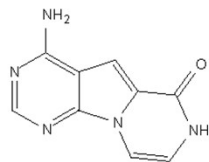
#	Signal	R.Time	Area %
1	DAD1 A, Sig=215,8 Ref=off	0.560	100.000

#	Signal	R.Time	Area %
1	MSD1 TIC, MS File	0.653	100.000

-.o.-Syntez Purity Report -.o.-

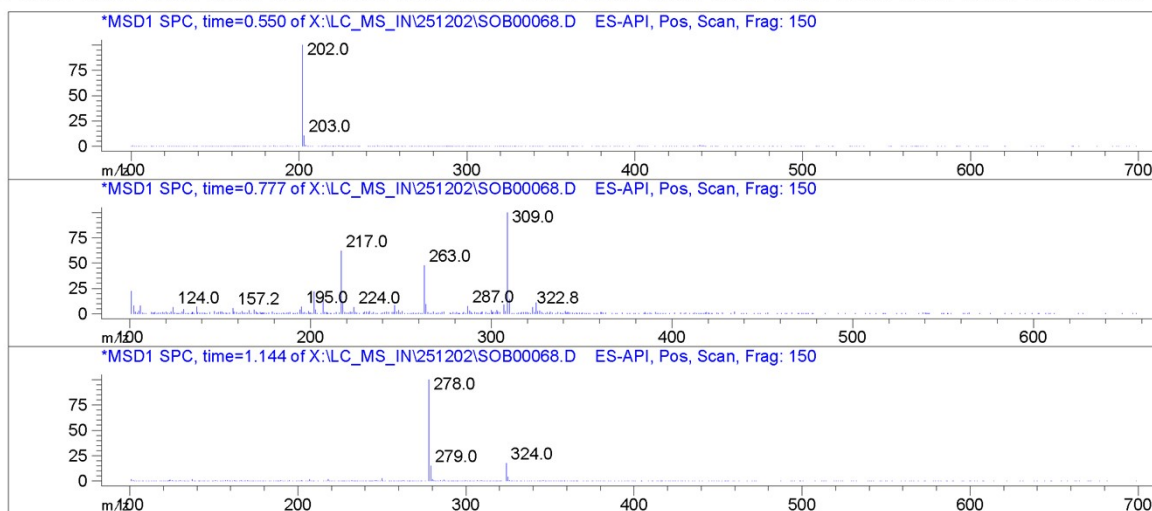
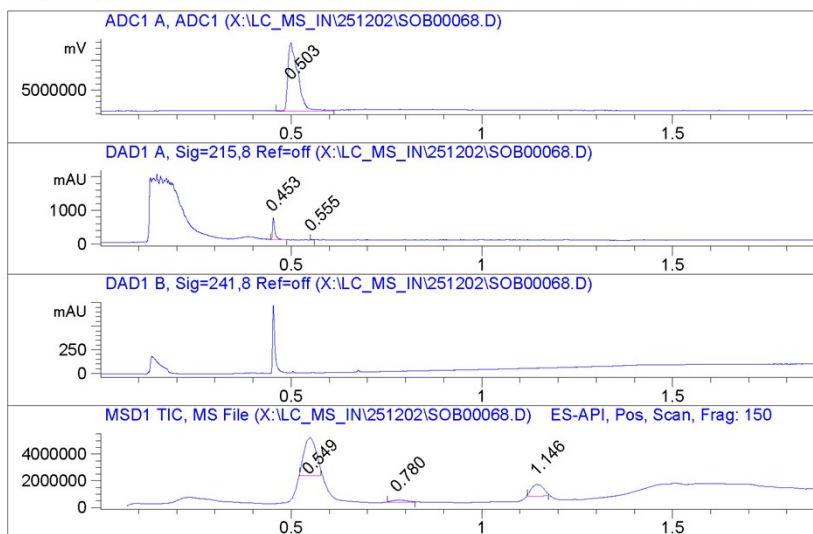
System: Agilent 1260 LC/MSD SL
Detector: Diodearray G1315B (DAD1)
MassQuad G1956B (MSD1-Pos, MSD2-Neg)

Mobile phase: A-H₂O+0.1% HCOOH; B-MeCN+0.1% HCOOH
Separation column:
Rapid Resolution HT Cartige 4.6x30mm,
1.8-Micron, Zorbax SB C-18



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Block:



#	Signal	R.Time	Area %
1	ADC1 A, ADC1	0.503	100.000

#	Signal	R.Time	Area %
1	DAD1 A, Sig=215,8 Ref=off	0.453	98.963
2		0.555	1.037

-o.-Syntez Purity Report -o.-

Agilent 1260 LC/MSD

Diodearray G1315B (DAD1A-215nm; DAD1B-241nm)

Mass Quad G6140 (MSD1-Pos, MSD2-Neg)

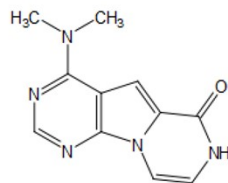
ELSD SOFTA 1400

Mobile Phase:A-H₂O+0.1HCOOH;B-MeCN+0.1HCOOH

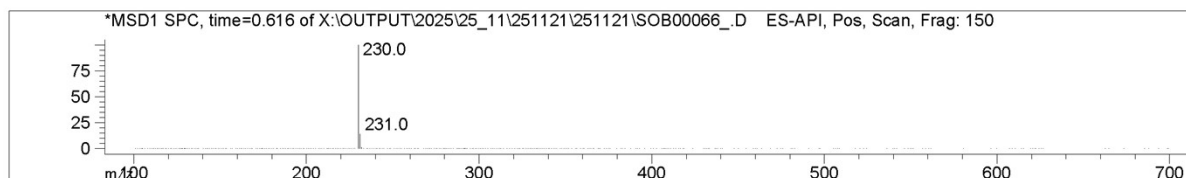
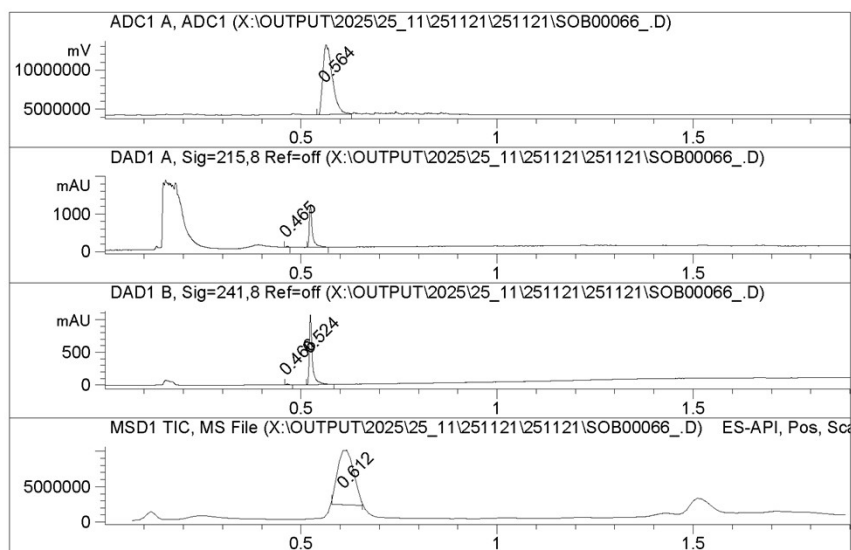
Separation column:

Rapid Resolutionn HT Cartige 4.6x30mm,

1.8-Micron, Zorbax SB-C18



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#	Signal	R.Time	Area %
1	ADC1 A, ADC1	0.564	100.000

#	Signal	R.Time	Area %
1	DAD1 A, Sig=215,8 Ref=off	0.465	1.561
2		0.524	98.439

#	Signal	R.Time	Area %
1	DAD1 B, Sig=241,8 Ref=off	0.466	1.050
2		0.524	98.950

#	Signal	R.Time	Area %
1	MSD1 TIC, MS File	0.612	100.000

-o.-Syntez Purity Report -o.-

Agilent 1260 LC/MSD

Diodearray G1315B (DAD1A-215nm; DAD1B-241nm)

Mass Quad G6140 (MSD1-Pos, MSD2-Neg)

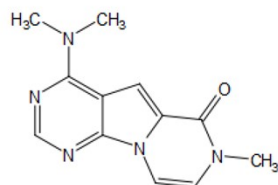
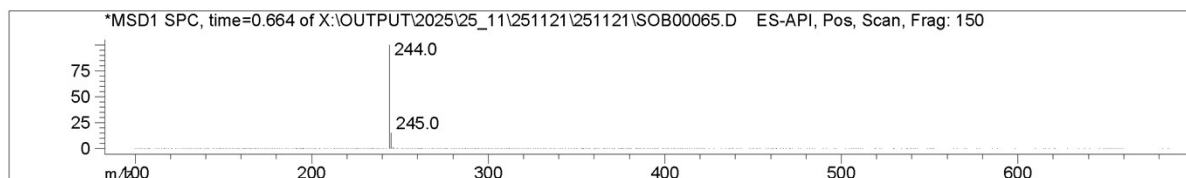
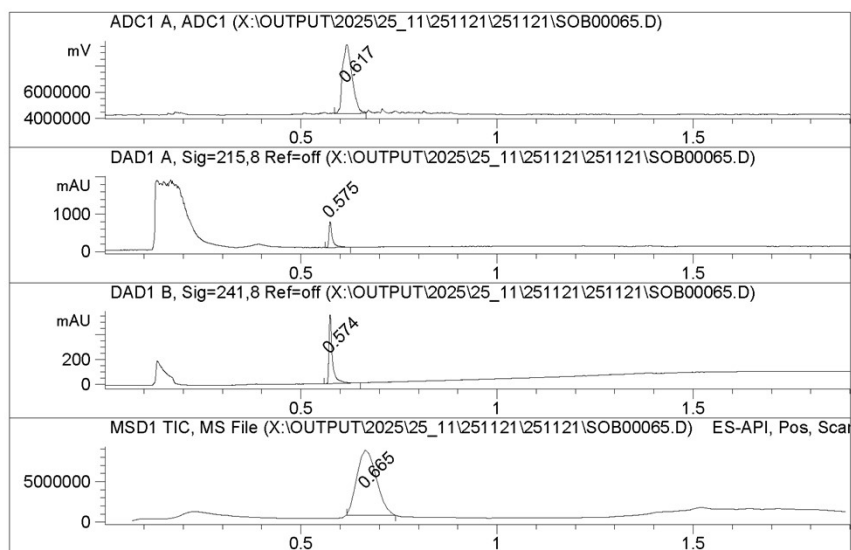
ELSD SOFTA 1400

Mobile Phase:A-H₂O+0.1HCOOH;B-MeCN+0.1HCOOH

Separation column:

Rapid Resolutionn HT Cartige 4.6x30mm,

1.8-Micron, Zorbax SB-C18

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#	Signal	R.Time	Area %
1	ADC1 A, ADC1	0.617	100.000

#	Signal	R.Time	Area %
1	DAD1 A, Sig=215,8 Ref=off	0.575	100.000

#	Signal	R.Time	Area %
1	DAD1 B, Sig=241,8 Ref=off	0.574	100.000

#	Signal	R.Time	Area %
1	MSD1 TIC, MS File	0.665	100.000

-.o.-Syntez Purity Report -.o.-

Agilent 1260 LC/MSD

Diodearray G1315B (DAD1A-215nm; DAD1B-241nm)

Mass Quad G6140A (MSD1-Pos, MSD2-Neg)

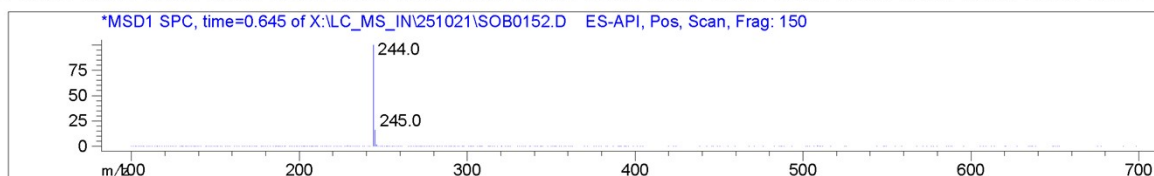
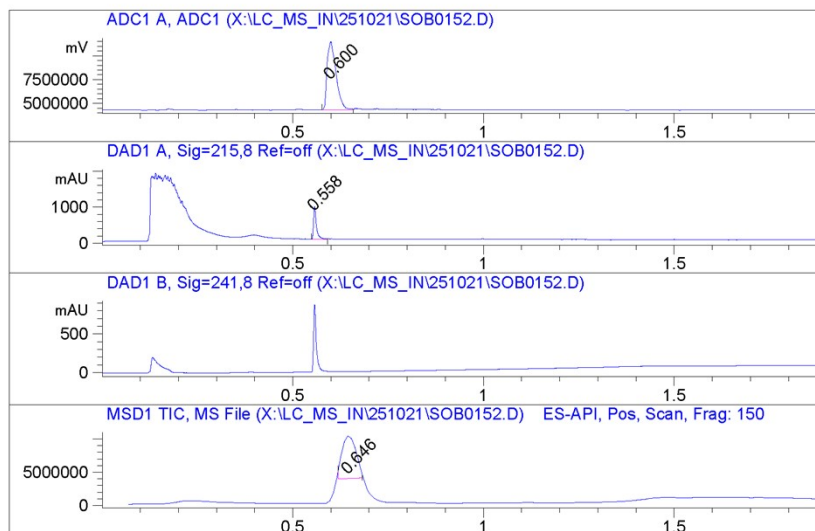
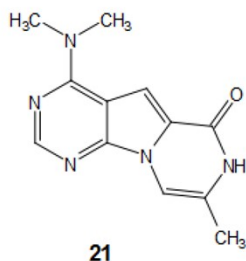
ELSD (ADC1 A, ELSD)

Mobile Phase:A-H₂O+0.1HCOOH;B-MeCN+0.1HCOOH

Separation column:

Rapid Resolutionn HT Cartige 4.6x30mm,

1.8-Micron, Zorbax SB-C18



#	Signal	R.Time	Area %
1	ADC1 A, ADC1	0.600	100.000

#	Signal	R.Time	Area %
1	DAD1 A, Sig=215,8 Ref=off	0.558	100.000

#	Signal	R.Time	Area %
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#	Signal	R.Time	Area %
1	MSD1 TIC, MS File	0.646	100.000

-o.-Syntez Purity Report -o.-

Agilent 1260 LC/MSD

Mobile Phase:A-H₂O+0.1HCOOH;B-MeCN+0.1HCOOH

Diodearray G1315B (DAD1A-215nm; DAD1B-241nm)

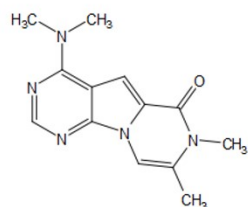
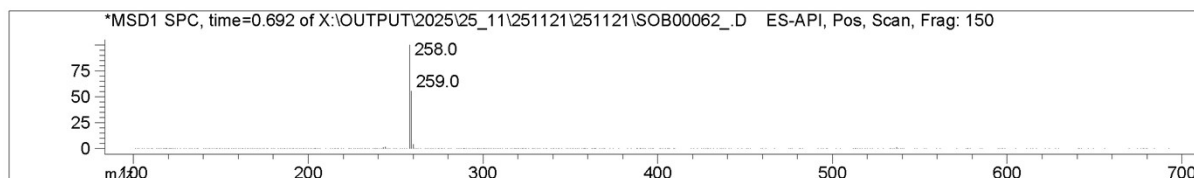
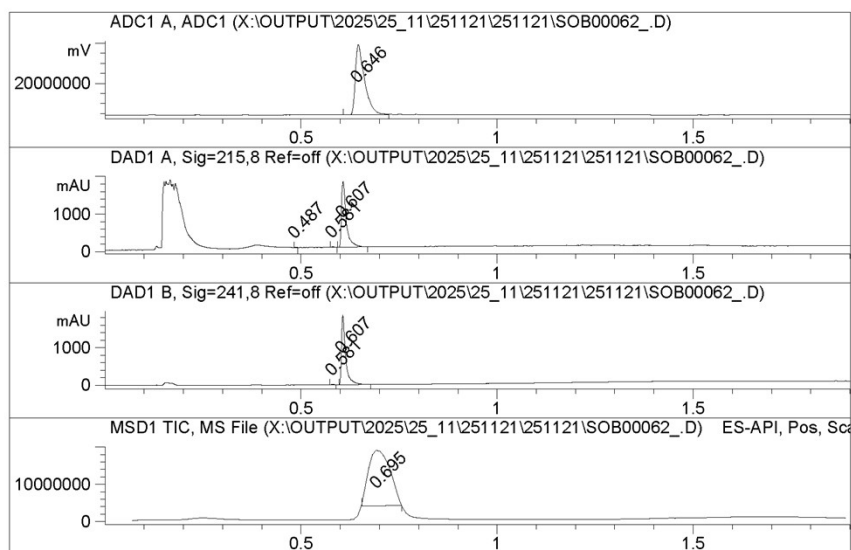
Separation column:

Mass Quad G6140 (MSD1-Pos, MSD2-Neg)

Rapid Resolutionn HT Cartige 4.6x30mm,

ELSD SOFTA 1400

1.8-Micron, Zorbax SB-C18

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#	Signal	R.Time	Area %
1	ADC1 A, ADC1	0.646	100.000

#	Signal	R.Time	Area %
1	DAD1 A, Sig=215,8 Ref=off	0.487	0.280
2		0.581	0.521
3		0.607	99.199

#	Signal	R.Time	Area %
1	DAD1 B, Sig=241,8 Ref=off	0.581	0.414
2		0.607	99.586

#	Signal	R.Time	Area %
1	MSD1 TIC, MS File	0.695	100.000

-o.-Syntez Purity Report -o.-

Agilent 1260 LC/MSD

Diodearray G1315B (DAD1A-215nm; DAD1B-241nm)

Mass Quad G6140 (MSD1-Pos, MSD2-Neg)

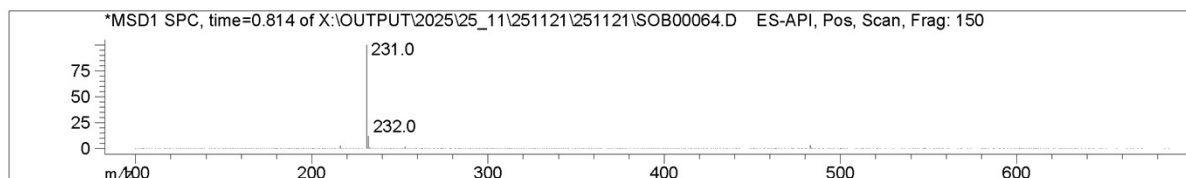
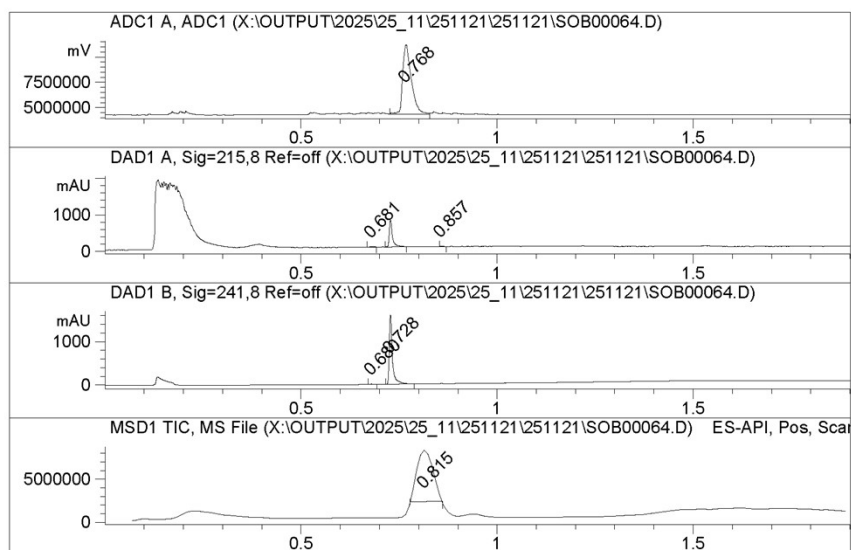
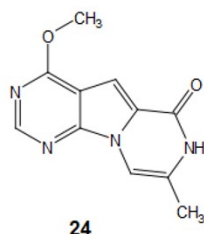
ELSD SOFTA 1400

Mobile Phase:A-H₂O+0.1HCOOH;B-MeCN+0.1HCOOH

Separation column:

Rapid Resolutionn HT Cartige 4.6x30mm,

1.8-Micron, Zorbax SB-C18



#	Signal	R.Time	Area %
1	ADC1 A, ADC1	0.768	100.000

#	Signal	R.Time	Area %
1	DAD1 A, Sig=215,8 Ref=off	0.681	2.306
2		0.728	95.439
3		0.857	2.255

#	Signal	R.Time	Area %
1	DAD1 B, Sig=241,8 Ref=off	0.680	0.348
2		0.728	99.652

#	Signal	R.Time	Area %
1	MSD1 TIC, MS File	0.815	100.000

-o.-Syntez Purity Report -o.-

Agilent 1260 LC/MSD

Diodearray G1315B (DAD1A-215nm; DAD1B-241nm)

Mass Quad G6140 (MSD1-Pos, MSD2-Neg)

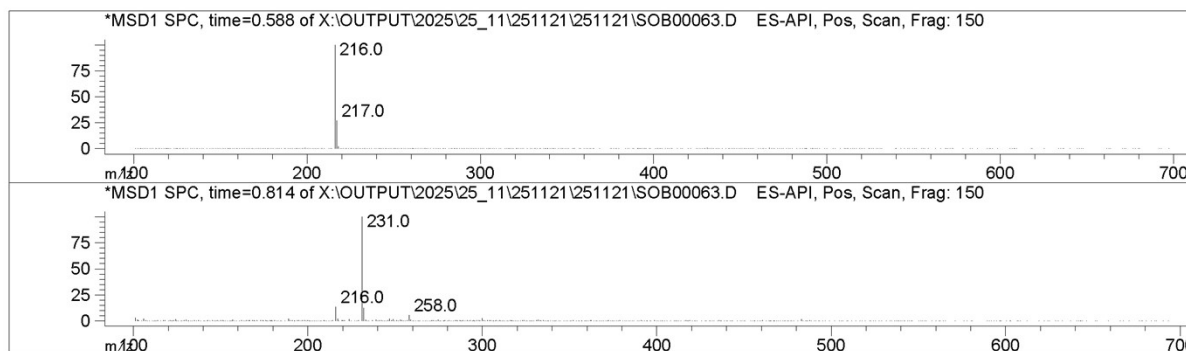
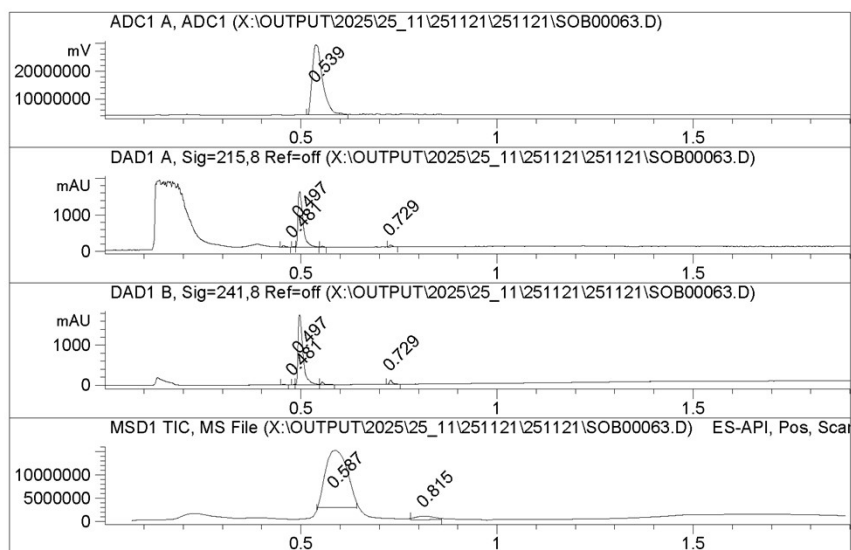
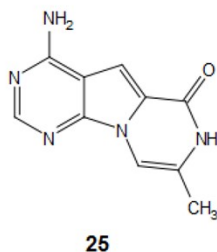
ELSD SOFTA 1400

Mobile Phase:A-H₂O+0.1HCOOH;B-MeCN+0.1HCOOH

Separation column:

Rapid Resolutionn HT Cartige 4.6x30mm,

1.8-Micron, Zorbax SB-C18



#	Signal	R.Time	Area %
1	ADC1 A, ADC1	0.539	100.000

#	Signal	R.Time	Area %
1	DAD1 A, Sig=215,8 Ref=off	0.456	2.204
2		0.481	0.739
3		0.497	94.109
4		0.554	0.964
5		0.729	1.984

#	Signal	R.Time	Area %
1	DAD1 B, Sig=241,8 Ref=off	0.455	0.576
2		0.481	0.374
3		0.497	92.604
4		0.554	2.709
5		0.729	3.736

#	Signal	R.Time	Area %
1	MSD1 TIC, MS File	0.587	94.590
2		0.815	5.410

-.o.-Syntez Purity Report -.o.-

Agilent 1260 LC/MSD

Diodearray G1315B (DAD1A-215nm; DAD1B-241nm)

Mass Quad G6140A (MSD1-Pos, MSD2-Neg)

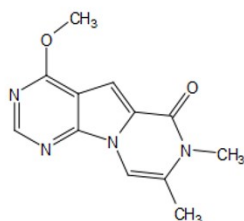
ELSD (ADC1 A, ELSD)

Mobile Phase:A-H₂O+0.1HCOOH;B-MeCN+0.1HCOOH

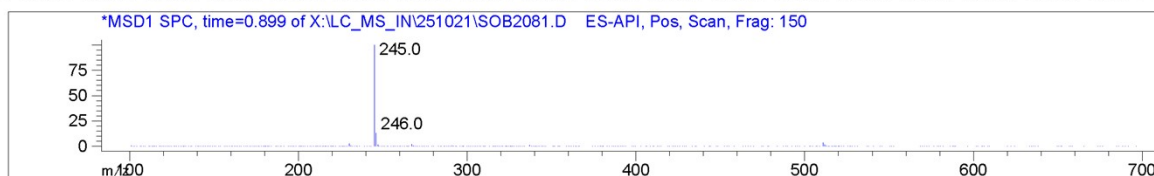
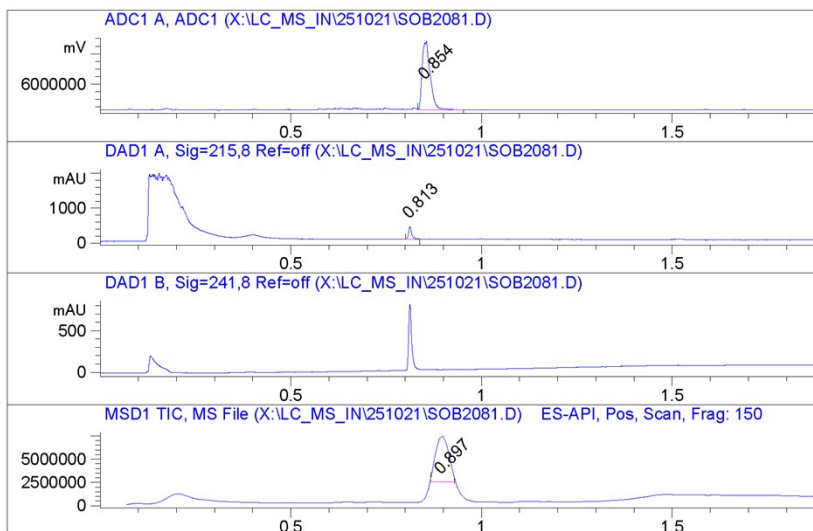
Separation column:

Rapid Resolutionn HT Cartige 4.6x30mm,

1.8-Micron, Zorbax SB-C18



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#	Signal	R.Time	Area %
1	ADC1 A, ADC1	0.854	100.000

#	Signal	R.Time	Area %
1	DAD1 A, Sig=215,8 Ref=off	0.813	100.000

#	Signal	R.Time	Area %
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#	Signal	R.Time	Area %
1	MSD1 TIC, MS File	0.897	100.000

-.o.-Syntez Purity Report -.o.-

Agilent 1260 LC/MSD

Diodearray G1315B (DAD1A-215nm; DAD1B-241nm)

Mass Quad G6140A (MSD1-Pos, MSD2-Neg)

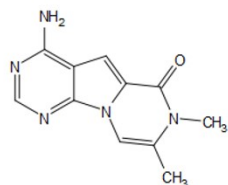
ELSD (ADC1 A, ELSD)

Mobile Phase:A-H₂O+0.1HCOOH;B-MeCN+0.1HCOOH

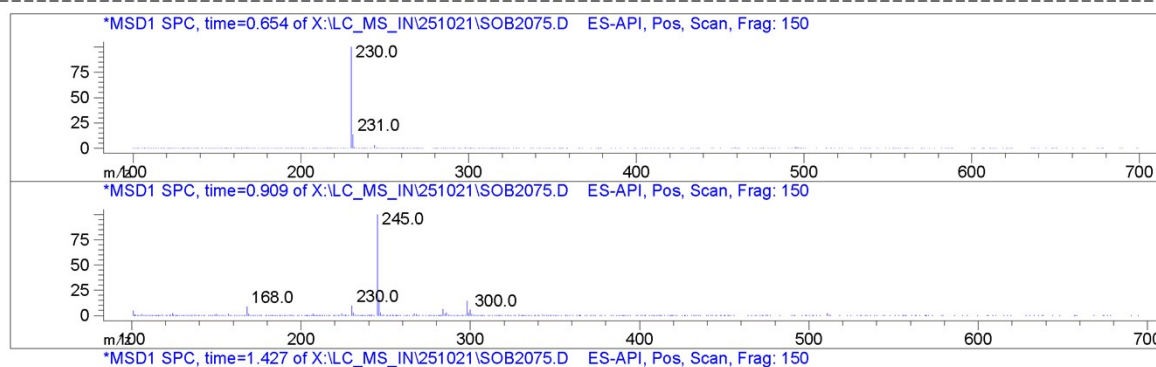
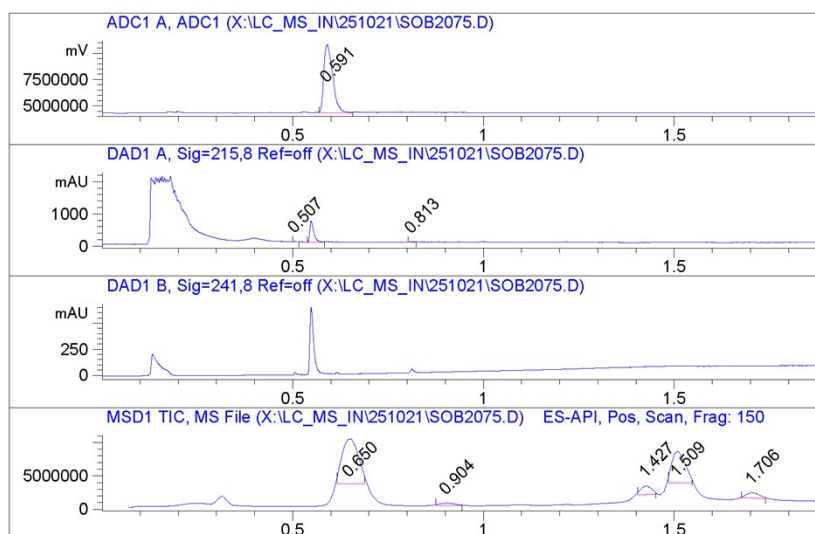
Separation column:

Rapid Resolutionn HT Cartige 4.6x30mm,

1.8-Micron, Zorbax SB-C18



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#	Signal	R.Time	Area %
1	ADC1 A, ADC1	0.591	100.000

#	Signal	R.Time	Area %
1	DAD1 A, Sig=215,8 Ref=off	0.507	1.843
2		0.548	96.139
3		0.813	2.017

#	Signal	R.Time	Area %
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-.o.-Syntez Purity Report -.o.-

Agilent 1260 LC/MSD

Diodearray G1315B (DAD1A-215nm; DAD1B-241nm)

Mass Quad G6140A (MSD1-Pos, MSD2-Neg)

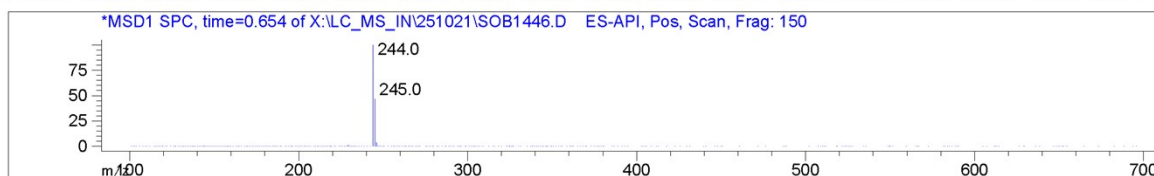
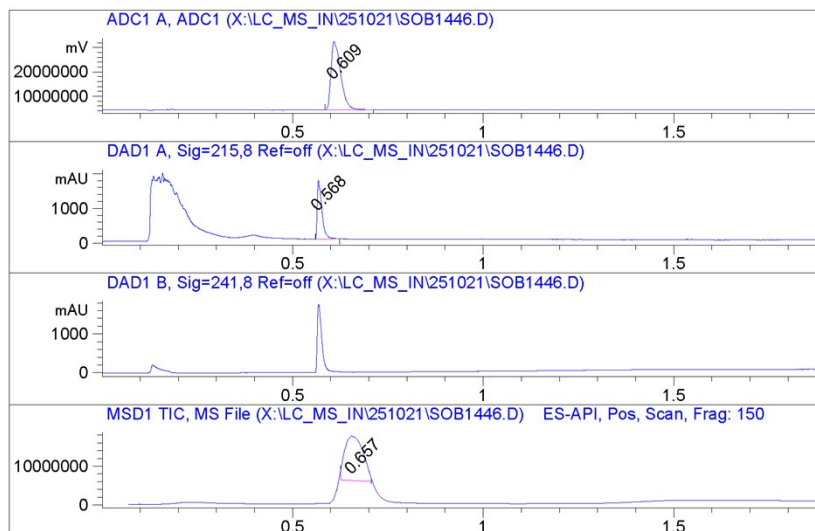
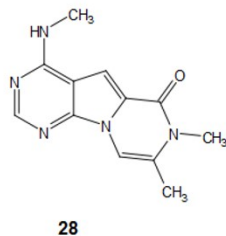
ELSD (ADC1 A, ELSD)

Mobile Phase:A-H₂O+0.1HCOOH;B-MeCN+0.1HCOOH

Separation column:

Rapid Resolutionn HT Cartige 4.6x30mm,

1.8-Micron, Zorbax SB-C18



#	Signal	R.Time	Area %
1	ADC1 A, ADC1	0.609	100.000

#	Signal	R.Time	Area %
1	DAD1 A, Sig=215,8 Ref=off	0.568	100.000

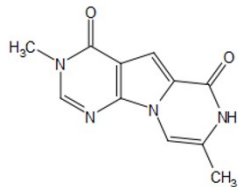
#	Signal	R.Time	Area %
---	--------	--------	--------

#	Signal	R.Time	Area %
1	MSD1 TIC, MS File	0.657	100.000

-.o.-Syntez Purity Report -.o.-

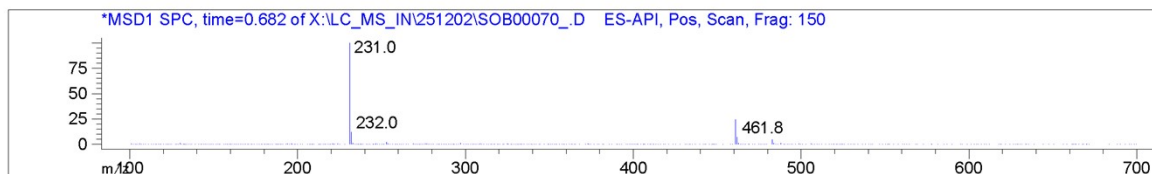
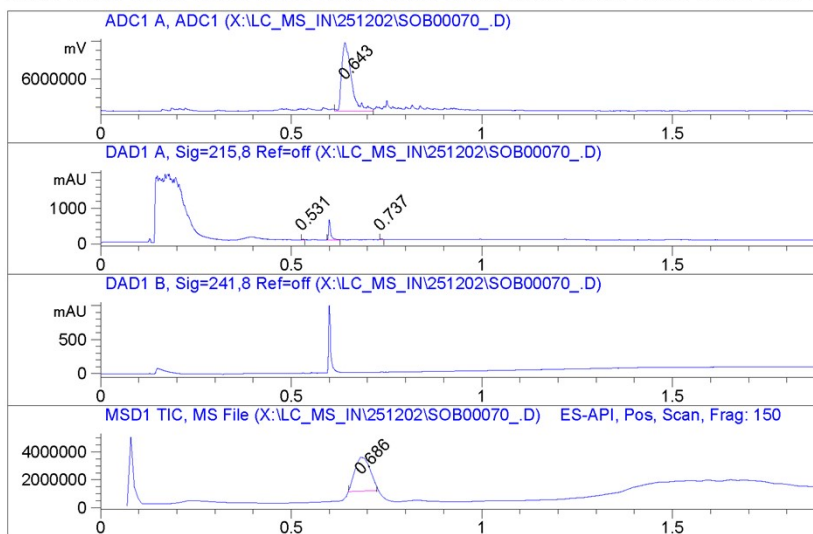
System: Agilent 1260 LC/MSD SL
Detector: Diodearray G1315B (DAD1)
MassQuad G6140A (MSD1-Pos, MSD2-Neg)

Mobile phase:A-H₂O+0.1%HCOOH;B-MeCN+0.1%HCOOH
Separation column:
Rapid Resolutionn HT Cartige 4.6x30mm,
1.8-Micron, Zorbax SB C-18



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Block:



#	Signal	R.Time	Area %
1	ADC1 A, ADC1	0.643	100.000

#	Signal	R.Time	Area %
1	DAD1 A, Sig=215,8 Ref=off	0.531	1.820
2		0.600	95.054
3		0.737	3.126

#	Signal	R.Time	Area %
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#	Signal	R.Time	Area %
1	MSD1 TIC, MS File	0.686	100.000

-.o.-Syntez Purity Report -.o.-

Agilent 1260 LC/MSD

Diodearray G1315B (DAD1A-215nm; DAD1B-241nm)

Mass Quad G6140A (MSD1-Pos, MSD2-Neg)

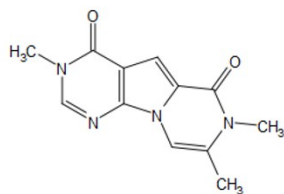
ELSD (ADC1 A, ELSD)

Mobile Phase:A-H₂O+0.1HCOOH;B-MeCN+0.1HCOOH

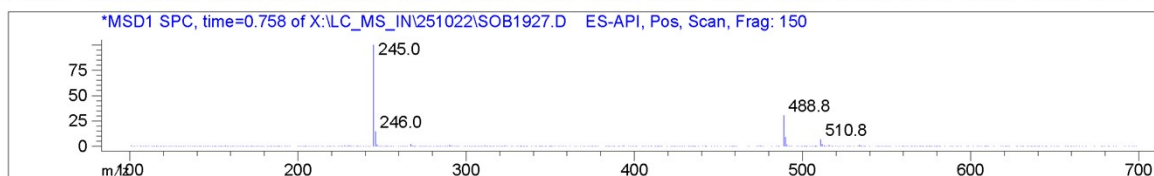
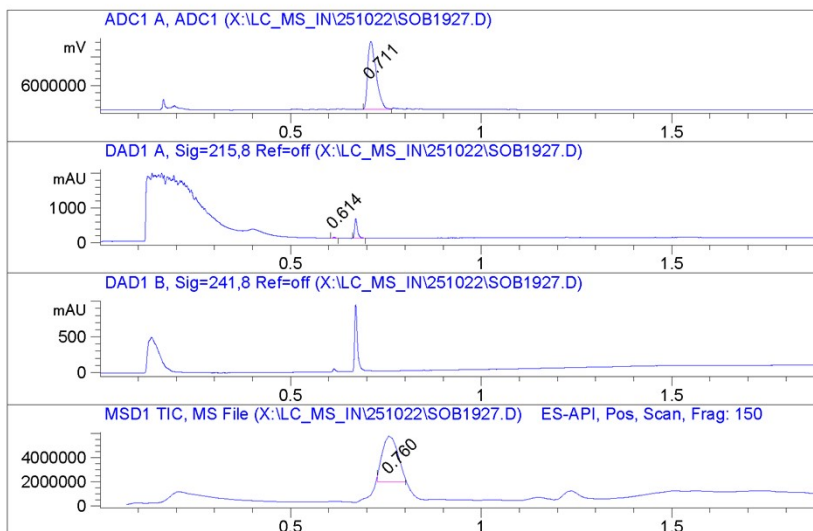
Separation column:

Rapid Resolutionn HT Cartige 4.6x30mm,

1.8-Micron, Zorbax SB-C18



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#	Signal	R.Time	Area %
1	ADC1 A, ADC1	0.711	100.000

#	Signal	R.Time	Area %
1	DAD1 A, Sig=215,8 Ref=off	0.614	4.714
2		0.671	95.286

#	Signal	R.Time	Area %
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#	Signal	R.Time	Area %
1	MSD1 TIC, MS File	0.760	100.000