Supporting information

Pyrimido[5,4-*e*]azolo[1,5-*a*]pyrimidines and pyrimido[4,5-*e*][1,2,4]triazolo [5,1-*c*][1,2,4]triazines: one-pot multi-component synthesis and cytotoxic activity

Eva V. Bersneva,[a] Konstantin V. Savateev,*[a] Pavel A. Slepukhin,[b] Vsevolod V. Melekhin,[a,c] Maria D. Tohtueva,[a] Vladimir L. Rusinov[a,b]

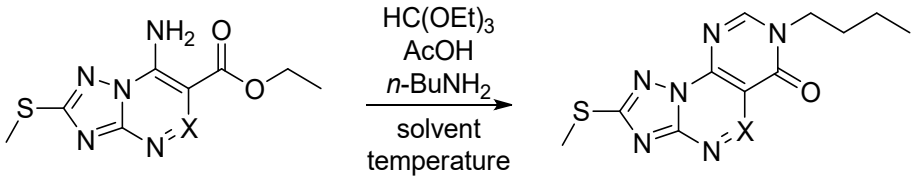
[a]Ural Federal University named after the First President of Russia B.N. Eltsin, Mira st. 19, Yekaterinburg, 620002, Russian Federation

[b]Institute of Organic Synthesis of the Ural Branch of the Russian Academy of Science, Sofii Kovalevskoy st. 22, Yekaterinburg, 620137, Russian Federation

[c]Department of Medical Biology and Genetics, Ural State Medical University, Yekaterinburg, Russian Federation

Contents

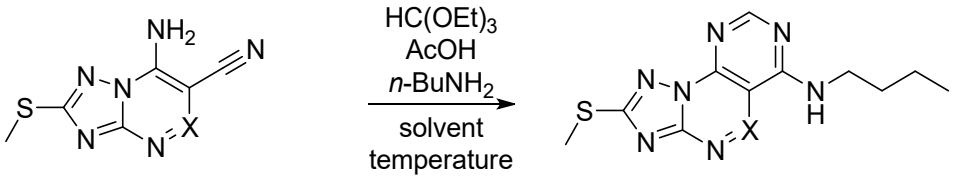
Optimization of reaction conditions for conversion of amino-ethoxycarbonyl-azoloazines to pyrimidoazoloazines



№	X	AcOH, equiv.	$HC(OEt)_3$, equiv.	n-$BuNH_2$, equiv.	Solvent	Conditions	T, °C	Time, h	Yield, %
1	N	3	3	3	$PhCH_3$	Round-bottom flask	reflux	8	79
2	N	3	3	3	1,4-Dioxane	Round-bottom flask	reflux	8	69
3	N	3	3	3	CH_3CN	Round-bottom flask	reflux	8	19
4	N	3	3	3	$PhCH_3$	Autoclave	140	8	80
5	N	3	3	3	$PhCH_3$	Round-bottom flask	reflux	15	80
6	N	3	3	3	$PhCH_3$	Round-bottom flask	reflux	4	53
7	N	3	3	1	$PhCH_3$	Round-bottom flask	reflux	8	47
8	N	3	50	1	-	Round-bottom flask	reflux	8	0
9	N	1	3	1	$PhCH_3$	Round-bottom flask	reflux	8	45
10	N	3	3	3	$PhCH_3$	Round-bottom flask	reflux	8	0[b]
11	N	3	3	3	$PhCH_3$	Round-bottom flask	reflux	8	0[d]
12	CH	3	3	3	$PhCH_3$	Round-bottom flask	reflux	8	0
13	CH	3	3	3	$PhCH_3$	Autoclave	120	8	20
14	CH	3	3	3	$PhCH_3$	Autoclave	140	8	35
15	CH	3	3	3	CH_3CN	Autoclave	120	8	0
16	CH	3	3	3	1,4-Dioxane	Autoclave	160	8	57
17	CH	3	3	3	1,4-Dioxane	Autoclave	160	16	86
18	CH	3	3	1	1,4-Dioxane	Autoclave	160	8	0
19	CH	3	3	3	1,4-Dioxane	Autoclave	160	8	0[b]
20	CH	3	3	3	1,4-Dioxane	Autoclave	160	8	0[c]

[a] – all reactions were carried out with 1 mmol of the starting heterocycle; [b] - $MeC(OEt)_3$ instead of $HC(OEt)_3$; [c] - $ZnCl_2$ instead of AcOH; [d] - $PhC(OEt)_3$ instead of $HC(OEt)_3$

Optimization of reaction conditions for conversion of amino-cyano-azoloazines to pyrimidoazoloazines



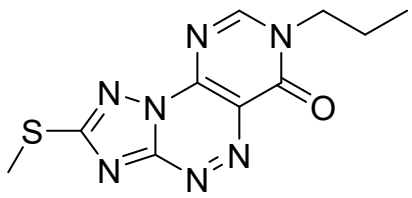
№	X	AcOH, equiv.	$HC(OEt)_3$, equiv.	n-$BuNH_2$, equiv.	Solvent	Conditions	T, °C	Time, h	Yield, %
1	N	3	3	3	$PhCH_3$	Round-bottom flask	reflux	8	96
2	N	3	3	1	$PhCH_3$	Round-bottom flask	reflux	8	81
3	N	3	3	3	1,4-Dioxane	Round-bottom flask	reflux	8	78
4	N	3	3	3	$PhCH_3$	Round-bottom flask	reflux	3	85
5	N	3	3	1	1,4-Dioxane	Round-bottom flask	reflux	8	71
6	N	3	3	1	$PhCH_3$	Autoclave	140	8	83
7	N	3	3	3	$PhCH_3$	Autoclave	160	12	0[b]
8	N	-	-	-	Formamide	Round-bottom flask	reflux	8	0[c]
9	CH	3	3	3	$PhCH_3$	Round-bottom flask	reflux	8	14
10	CH	3	3	3	1,4-Dioxane	Autoclave	160	8	60
11	CH	3	3	3	$PhCH_3$	Autoclave	140	8	75
12	CH	3	3	3	$PhCH_3$	Autoclave	140	12	87
13	CH	3	3	1	$PhCH_3$	Autoclave	140	8	31
14	CH	3	3	3	$PhCH_3$	Autoclave	160	12	0[b]

[a] – all reactions were carried out with 1 mmol of the starting heterocycle; [b] - $PhC(OEt)_3$ instead of $HC(OEt)_3$; [c] – conditions according to ref. 18

Materials and Methods. Commercial reagents were obtained from Sigma-Aldrich, Acros Organics, Macklin, or Alfa Aesar and used without any preprocessing. All workup and purification procedures were carried out using analytical-grade solvents. One-dimensional ^{1}H, ^{13}C, ^{15}N NMR spectra were acquired on a Bruker DRX-400 instrument (400, 101, 400 MHz, respectively) or a Bruker Avance NEO 600 instrument (600, 151, 600 MHz, respectively), equipped with a Prodigy broadband gradient cryoprobe, utilizing DMSO-d_6 and $CDCl_3$ as a solvents. Chemical shifts are expressed in δ (parts per million, ppm) values, and coupling constants are expressed in herts (Hz). The following abbreviations are used for the multiplicity of NMR signals: br., broaded; s, singlet; d, doublet; t, triplet; and m, multiplet. IR spectra were recorded on a Bruker α spectrometer equipped with a ZnSe ATR accessory. Elemental analysis was performed on a PerkinElmer PE 2400 elemental analyzer. Mass spectra were recorded with a Shimadzu GCMS-QP 2010 "Ultra" (Kyoto, Japan) mass spectrometer using the electron impact (EI) ionization technique (40-200 °C, 70 eV). Electrospray mass spectra (HRMS) were recorded in positive ionization mode using qTOF Bruker maXis Impact HD instrument. Melting points were determined on a Stuart SMP-3 (Staffordshire, UK) and are uncorrected. The monitoring of the reaction progress was performed using TLC on Silufol UV254 plates. The XRD analyses were carried out using equipment of the Center for Joint Use "Spectroscopy and Analysis of Organic Compounds" at the Postovsky Institute of Organic Synthesis of the Russian Academy of Sciences (Ural Branch). The experiment was accomplished on the automated X-ray diffractometer «Xcalibur 3» with CCD detector on the standard procedure (MoKα-irradiation, graphite monochromator, ω-scans with 1° step). For the XRD analyses the empirical absorption correction was applied. The solution and refinement of the structures were accomplished with using Olex2 program package.41 The structures were solved by method of the intrinsic phases in ShelXT program and refined by ShelXL by full-matrix least-squared method for non-hydrogen atoms. The H-atoms at the C-H bonds were placed in the calculated positions, H-atoms of the N-H bonds were solved by direct method and were refined independently in the isotropic approximation. Deposition Numbers CCDC 2401392 (for **23d**), contain the supplementary crystallographic data for this paper. These data are provided free of charge by the joint Cambridge Crystallographic Data Centre and Fachinformationszentrum Karlsruhe http://www.ccdc.cam.ac.uk/structures.

General method for the synthesis of pyrimido[4,5-*e*][1,2,4]triazolo[5,1-*c*][1,2,4]triazin-6(7*H*)-one 19a-h.

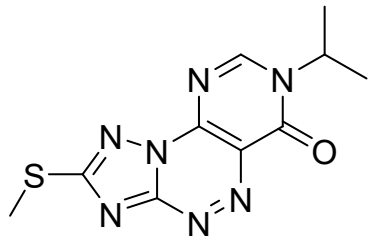
Triethylortoformate (0.498 mL, 0.003 mol, 3 equiv.), appropriate amine (0.003 mol, 3 equiv.) and AcOH (0.172 mL, 0.003 mol, 3 equiv.) were added consequently to a suspension of 4-amino-3-ethoxycarbonyl-7-methylsulfanyl[1,2,4]triazolo[5,1-*c*][1,2,4]triazine **17a** (0.254 g, 0.001 mol) in toluene (7 mL). The resulting mixture was refluxed for 8 hours, cooled to RT, filtered, and solids were washed with Et_2O (5 mL). Another crop of product could be obtained from the mother liquor. The mother liquor was concentrated at reduced pressure, the residue was treated with Et_2O (10 mL), filtered, and solids were washed with Et_2O (5 mL).



7-Propyl-2-(methylthio)pyrimido[4,5-*e*][1,2,4]triazolo[5,1-*c*][1,2,4]triazin-6(7*H*)-one (19a).

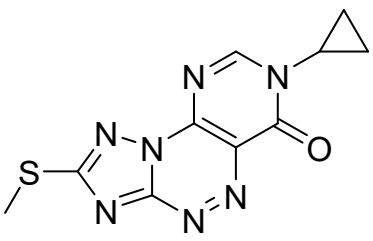
Light brown powder (166 mg, 60% yield). R_f (AcOEt) = 0.7. M.p. = 195 °C. ^{1}H NMR (400 MHz, DMSO-d_6), δ, ppm. (*J*, Hz): 9.02 (s, C8H, H); 4.13 (t, *J* = 7.4 Hz, CH_2, 2H); 2.80 (s, S-CH_3, 3H); 1.80–1.90 (m, CH_2, 2H); 1.01 (t, *J* = 7.4 Hz, CH_3, 3H). ^{13}C NMR (100 MHz, DMSO-d_6), δ, ppm.: 170.5, 157.82, 157.78, 157.3, 140.2, 129.2, 48.8, 21.6, 13.6, 10.6. IR, ν, cm^{-1}: 3054, 2966, 2935, 2877, 2839, 1705, 1607, 1577, 1530, 1469, 1438, 1413, 1380, 1359, 1340, 1306, 1277, 12643, 1231, 1202, 1115, 1094, 1038, 1007, 984, 969, 901, 847, 801, 738, 708, 683, 655, 589, 566, 554, 524, 510. MS (EI, 70 eV), m/z: Calcd for: $C_{10}H_{11}N_7OS$, 277; found $C_{10}H_{11}N_7OS$, 277. Anal. Calcd. For $C_{10}H_{11}N_7OS$: C, 43.31; H, 4.00; N, 35.36; found: C, 43.33; H, 3.92; N, 35.45

7-Isopropyl-2-(methylthio)pyrimido[4,5-*e*][1,2,4]triazolo[5,1-*c*][1,2,4]triazin-6(7*H*)-one (19b).



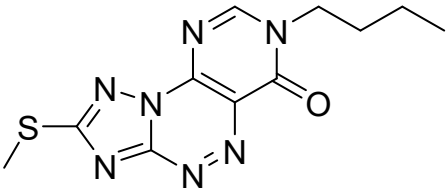
Light brown powder (149 mg, 54% yield). R_f (AcOEt) = 0.7. M.p. = 203 °C. ^{1}H NMR (400 MHz, DMSO-d_6), δ, ppm. (*J*, Hz): 9.08 (s, C8H, H); 5.04–5.10 (m, NCH, H); 2.78 (s, S-CH_3, 3H); 1.52 (d, *J* = 6.8 Hz, 2CH_3, 6H). ^{13}C NMR (100 MHz, DMSO-d_6), δ, ppm.: 170.5, 157.8, 157.1, 155.9, 139.7, 129.0, 48.7, 21.0, 13.6. IR, ν, cm^{-1}: 3065, 2981, 2964, 2939, 1772, 1708, 1581, 1529, 1469, 1422, 1413, 1376, 1350, 1339, 1315, 1280, 1247, 1193, 1177, 1128, 1115, 1094, 997, 971, 881, 831, 799, 752, 729, 706, 679, 638, 623, 592, 558, 544, 506. MS (EI, 70 eV), m/z: Calcd for: $C_{10}H_{11}N_7OS$, 277; found $C_{10}H_{11}N_7OS$, 277. Anal. Calcd. For $C_{10}H_{11}N_7OS$: C, 43.31; H, 4.00; N, 35.36; found: C, 43.25; H, 3.96; N, 35.29

7-Cyclopropyl-2-(methylthio)pyrimido[4,5-*e*][1,2,4]triazolo[5,1-*c*][1,2,4]triazin-6(7*H*)-one (19c).



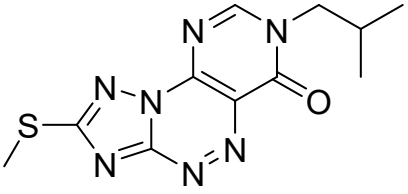
Light brown powder (247 mg, 90% yield). R_f (AcOEt) = 0.7. M.p. = 221 °C. ^{1}H NMR (400 MHz, DMSO-d_6), δ, ppm. (*J*, Hz): 8.88 (s, C8H, H); 3.40–3.46 (m, NCH, H); 2.80 (s, S-CH_3, 3H); 1.12–1.20 (m, 2CH_2, 4H). ^{13}C NMR (100 MHz, DMSO-d_6), δ, ppm.: 170.6, 158.2, 158.1, 157.8, 139.8, 128.8, 30.6, 13.6, 6.0. IR, ν, cm^{-1}: 3194, 3149, 3081, 1717, 1659, 1599, 1570, 1552, 1538, 1503, 1467, 1455, 1426, 1366, 1340, 1304, 1273, 1264, 1228, 1192, 1164, 1124, 1103, 1072, 1033, 1003, 977, 967, 939, 873, 833, 822, 800, 781, 728, 708, 681, 659, 589, 571, 547, 517. MS (EI, 70 eV), m/z: Calcd for: $C_{10}H_9N_7OS$, 275; found $C_{10}H_9N_7OS$, 275. Anal. Calcd. For $C_{10}H_9N_7OS$: C, 43.63; H, 3.30; N, 35.62; found: C, 43.57; H, 3.20; N, 35.66

7-Butyl-2-(methylthio)pyrimido[4,5-*e*][1,2,4]triazolo[5,1-*c*][1,2,4]triazin-6(7*H*)-one (19d).



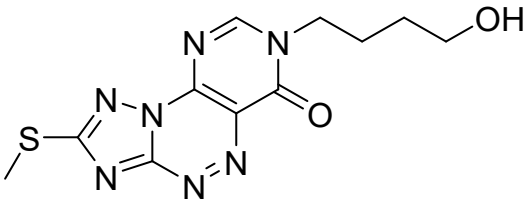
Light brown powder (233 mg, 80% yield). R_f (AcOEt) = 0.7. M.p. = 216 °C. ^{1}H NMR (400 MHz, DMSO-d_6), δ, ppm. (*J*, Hz): 9.02 (s, C8H, H); 4.16 (t, *J* = 7.4 Hz, NCH_2, 2H); 2.8 (s, S-CH_3, 3H); 1.76–1.83 (2H, m, CH_2); 1.39–1.48 (m, CH_2, 2H); 1.00 (t, *J* = 7.4 Hz, CH_3, 3H). ^{13}C NMR (100 MHz, DMSO-d_6), δ, ppm.: 171.0, 158.31, 158.25, 157.8, 140.7, 129.6, 47.6, 30.9, 19.6, 14.1, 14.0. IR, ν, cm^{-1}:3063, 3013, 2958, 2934, 2872, 1717, 1574, 1526, 1469, 1433, 1409, 1382, 1369, 1351, 1337, 1308, 1284, 1258, 1217, 1192, 1170, 1119, 1101, 1018, 998, 990, 934, 802, 736, 705, 692, 653, 587, 554, 504. MS (EI, 70 eV), m/z: Calcd for: $C_{11}H_{13}N_7OS$, 291; found $C_{11}H_{13}N_7OS$, 291. Anal. Calcd. For $C_{11}H_{13}N_7OS$: C, 45.35; H, 4.50; N, 33.65; found: C, 45.35; H, 4.53; N, 35.81

7-Isobutyl-2-(methylthio)pyrimido[4,5-*e*][1,2,4]triazolo[5,1-*c*][1,2,4]triazin-6(7*H*)-one (19e).



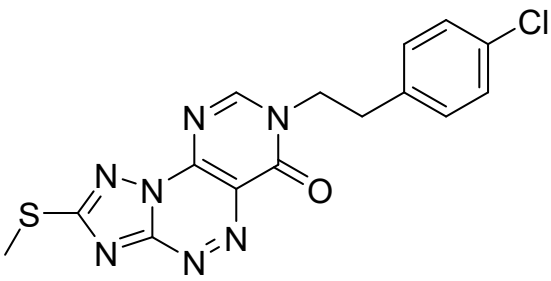
Light brown powder (201 mg, 69% yield). R_f (AcOEt) = 0.7. M.p. = 215 °C. ^{1}H NMR (400 MHz, DMSO-d_6), δ, ppm. (*J*, Hz): 8.99 (s, C8H, H); 3.99 (d, *J* = 7.4 Hz, CH_2, 2H); 2.80 (s, S-CH_3, 3H); 2.18–2.25 (m, CH, H); 1.00 (d, *J* = 6.7 Hz, 2CH_3, 6H). ^{13}C NMR (100 MHz, DMSO-d_6), δ, ppm.: 170.5, 157.8 (2C), 157.4, 140.2, 129.2, 53.8 27.3, 19.4, 13.6. IR, ν, cm^{-1}: 3066, 2957, 2927, 2875, 1697, 1679, 1530, 1472, 1424, 1405, 1378, 1351, 1337, 1319, 1311, 1274, 1225, 1198, 1112, 1098, 1008, 988, 966, 916, 899, 820, 800, 754, 737, 705, 682, 661, 590, 563, 522. MS (EI, 70 eV), m/z: Calcd for: $C_{11}H_{13}N_7OS$, 291; found $C_{11}H_{13}N_7OS$, 291. Anal. Calcd. For $C_{11}H_{13}N_7OS$: C, 45.35; H, 4.50; N, 33.65; found: C, 45.42; H, 4.38; N, 35.61

7-(4-Hydroxybutyl)-2-(methylthio)pyrimido[4,5-*e*][1,2,4]triazolo[5,1-*c*][1,2,4]triazin-6(7*H*)-one (19g).



Light brown powder (34 mg, 11% yield). R_f (AcOEt) = 0.7. M.p. = 223 °C. ^{1}H NMR (400 MHz, DMSO-d_6), δ, ppm. (*J*, Hz): 9.03 (s, C8H, H); 4.32 (s, OH, H); 4.18 (t, *J* = 7.2 Hz, NCH_2, 2H); 3.48 (t, *J* = 6.2 Hz, OCH_2, 2H); 2.80 (s, S-CH_3, 3H); 1.82–1.90 (m, CH_2, 2H); 1.50–1.57 (m, CH_2, 2H). ^{13}C NMR (100 MHz, DMSO-d_6), δ, ppm.: 170.5, 157.9, 157.8, 157.3, 140.3, 129.2, 60.2, 47.4, 29.3, 25.3, 13.7. IR, ν, cm^{-1}: 3487, 1694, 1654, 1630, 1584, 1536, 1470, 1377, 1353, 1338, 1311, 1280, 1211, 1180, 1138, 1085, 1056, 1022, 988, 909, 803, 770, 728, 709, 651, 593, 515. MS (EI, 70 eV), m/z: Calcd for: $C_{11}H_{13}N_7O_2S$, 307; found $C_{11}H_{13}N_7O_2S$, 307. Anal. Calcd. For $C_{11}H_{13}N_7O_2S$: C, 42.99; H, 4.26; N, 31.90; found: C, 43.05; H, 4.39; N, 32.00. HRMS (ESI, Q-TOF), m/z: $[M+H]^+$ Calculated for $C_{11}H_{13}N_7O_2S^+$ 308.0924. Found 308.0927

7-(4-Chlorophenethyl)-2-(methylthio)pyrimido[4,5-*e*][1,2,4]triazolo[5,1-*c*][1,2,4]triazin-6(7*H*)-one (19h).

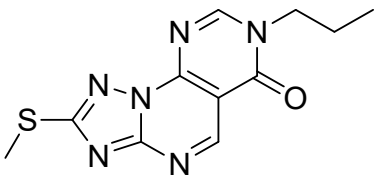


Light brown powder (227 mg, 61% yield). R_f (AcOEt) = 0.7. M.p. = 265 °C. ^{1}H NMR (400 MHz, DMSO-d_6), δ, ppm. (*J*, Hz): 8.79 (s, C8H, H); 7.31 (s, 4CH, 4H); 4.38 (t, *J* = 7.4 Hz, NCH_2, 2H); 3.12 (t, *J* = 7.4 Hz, CH_2, 2H); 2.79 (s, S-CH_3, 3H). ^{13}C NMR (100 MHz, DMSO-d_6), δ, ppm.: 170.6, 157.9, 157.5, 157.2, 140.1, 136.3, 131.4, 130.9, 129.0, 128.5, 48.3, 33.2, 13.6. IR, ν, cm^{-1}: 3044, 2937, 1703, 1574, 1523, 1490, 1469, 1456, 1406, 1378, 1362, 1338, 1301, 1271, 1255, 1213, 1186, 1131, 1113, 1088, 1041, 1006, 979, 863, 842, 819, 800, 743, 707, 657, 590, 563, 551, 519. MS (EI, 70 eV), m/z: Calcd for: $C_{15}H_{12}Cl^{35}N_7OS$, 373; found $C_{15}H_{12}Cl^{35}N_7OS$, 373. Anal. Calcd. For $C_{15}H_{12}ClN_7OS$: C, 48.19; H, 3.24; N, 26.23; found: C, 48.10; H, 3.11; N, 26.35

General method for the synthesis of 7-propyl-2-(methylthio)pyrimido[5,4-*e*][1,2,4]triazolo[1,5-*a*]pyrimidin-6(7*H*)-one 20a-e, 20h.

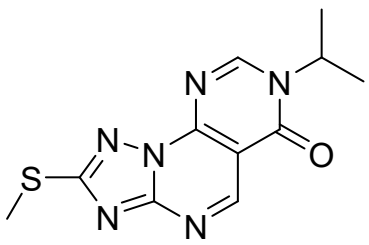
Triethylortoformate (0.498 mL, 0.003 mol, 3 equiv.), appropriate amine (0.003 mol, 3 equiv.) and AcOH (0.172 mL, 0.003 mol, 3 equiv.) were added consequently to a suspension of 7-amino-6-ethoxycarbonyl-2-(methylthio)[1,2,4]triazolo[1,5-*a*]pyrimidine **18a** (0.253 g, 0.001 mol) in 1,4-dioxane (7 mL). The resulting mixture was heated in autoclave at 160 °C for 15-20 hours until disappearance of the starting material by TLC analysis. The resulting mixture was cooled to RT, filtered, and solids were washed with Et_2O (5 mL). Another crop of product could be obtained from the mother liquor. The mother liquor was concentrated at reduced pressure, the residue was treated with Et_2O (10 mL), filtered, and solids were washed with Et_2O (5 mL).

7-Propyl-2-(methylthio)pyrimido[5,4-*e*][1,2,4]triazolo[1,5-*a*]pyrimidin-6(7*H*)-one (20a).



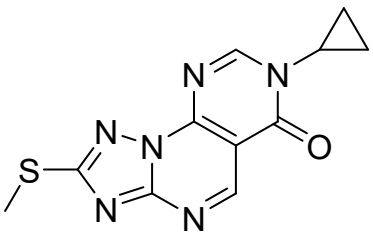
White powder (229 mg, 83% yield). R_f (AcOEt) = 0.4. M.p. = 231-232 °C. ^{1}H NMR (400 MHz, DMSO-d_6), δ, ppm. (*J*, Hz): 9.26 (s, C5H, H); 8.97 (s, C8H, H); 4.06 (t, *J* = 7.4 Hz, NCH_2, 2H); 2.72 (s, S-CH_3, 3H); 1.77–1.83 (m, CH_2, 2H); 0.98 (t, *J* = 7.4 Hz, CH_3, 3H). ^{13}C NMR (100 MHz, DMSO-d_6), δ, ppm.: 168.2, 158.5, 157.5, 157.4, 153.9, 149.2, 104.8, 48.4, 21.7, 13.4, 10.6. IR, ν, cm^{-1}: 3040, 3007, 2959, 2937, 2868, 2817, 1691, 1600, 1556, 1502, 1440, 1421, 1388, 1371, 1357, 1349, 1333, 1311, 1294, 1276, 1252, 1225, 1183, 1120, 1098, 1085, 1050, 999, 980, 967, 951, 888, 875, 833, 798, 784, 753, 738, 709, 688, 648, 624, 616, 569, 557, 545, 511. MS (EI, 70 eV), m/z: Calcd for: $C_{11}H_{12}N_6OS$, 276; found $C_{11}H_{12}N_6OS$, 276. Anal. Calcd. For $C_{11}H_{12}N_6OS$: C, 47.81; H, 4.38; N, 30.41; found: C, 47.81; H, 4.23; N, 30.33

7-Isopropyl-2-(methylthio)pyrimido[5,4-*e*][1,2,4]triazolo[1,5-*a*]pyrimidin-6(7*H*)-one (20b).



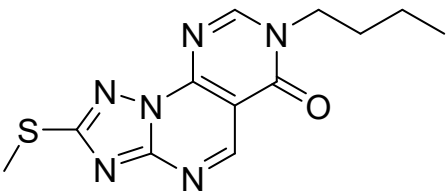
White powder (94 mg, 34% yield). R_f (AcOEt) = 0.45. M.p. = 257-258 °C. ^{1}H NMR (400 MHz, DMSO-d_6), δ, ppm. (*J*, Hz): 9.26 (s, C5H, H); 9.00 (s, C8H, H); 4.99–5.06 (m, NCH, H); 2.72 (s, S-CH_3, 3H); 1.53 (d, *J* = 7.2 Hz, 2CH_3, 6H). ^{13}C NMR (100 MHz, DMSO-d_6), δ, ppm.: 168.1, 158.2, 157.4, 155.5, 154.1, 148.8, 104.7, 48.1, 21.0, 13.4. IR, ν, cm^{-1}: 3048, 2981, 1694, 1655, 1602, 1555, 1501, 1454, 1417, 1395, 1369, 1349, 1309, 1292, 1277, 1251, 1235, 1222, 1189, 1136, 1118, 1112, 1080, 1033, 996, 978, 969, 953, 939, 931, 909, 901, 884, 826, 795, 756, 737, 688, 667, 640, 568, 555, 539, 527, 513. MS (EI, 70 eV), m/z: Calcd for: $C_{11}H_{12}N_6OS$, 276; found $C_{11}H_{12}N_6OS$, 276. Anal. Calcd. For $C_{11}H_{12}N_6OS$: C, 47.81; H, 4.38; N, 30.41; found: C, 47.69; H, 4.20; N, 30.35

7-Cyclopropyl-2-(methylthio)pyrimido[5,4-*e*][1,2,4]triazolo[1,5-*a*]pyrimidin-6(7*H*)-one (20c).



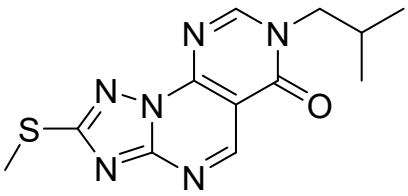
White powder (170 mg, 62% yield). R_f (AcOEt) = 0.35. M.p. = 229-230 °C. ^{1}H NMR (400 MHz, DMSO-d_6), δ, ppm. (*J*, Hz): 9.25 (s, C5H, H); 8.82 (s, C8H, H); 3.33–3.39 (m, NCH, H); 2.71 (s, S-CH_3, 3H); 1.12–1.17 (m, CH_2, 2H); 1.06–1.10 (m, CH_2, 2H). ^{13}C NMR (100 MHz, DMSO-d_6), δ, ppm.: 168.3, 159.4, 157.7, 157.4, 153.8, 148.8, 104.4, 30.2, 13.4, 5.8. IR, ν, cm^{-1}: 3084, 3053, 2932, 1699, 1592, 1550, 1495, 1426, 1397, 1371, 1360, 1340, 1316, 1287, 1275, 1249, 1209, 1175, 1101, 1070, 1052, 1004, 993, 976, 969, 955, 939, 876, 838, 815, 795, 770, 754, 738, 710, 688, 675, 662, 563, 545. MS (EI, 70 eV), m/z: Calcd for: $C_{11}H_{10}N_6OS$, 274; found $C_{11}H_{10}N_6OS$, 274. Anal. Calcd. For $C_{11}H_{10}N_6OS$: C, 48.17; H, 3.67; N, 30.64; found: C, 48.15; H, 3.67; N, 30.59

7-Butyl-2-(methylthio)pyrimido[5,4-*e*][1,2,4]triazolo[1,5-*a*]pyrimidin-6(7*H*)-one (20d).



White powder (249 mg, 86% yield). R_f (AcOEt) = 0.45. M.p. = 190-191 °C. ^{1}H NMR (400 MHz, DMSO-d_6), δ, ppm. (*J*, Hz): 9.26 (s, C5H, H); 8.97 (s, C8H, H); 4.08 (t, *J* = 7.2 Hz, NCH_2, 2H); 2.72 (s, S-CH_3, 3H); 1.71–1.78 (m, CH_2, 2H); 1.35–1.45 (m, CH_2, 2H); 0.98 (t, *J* = 7.4 Hz, CH_3, 3H). ^{13}C NMR (100 MHz, DMSO-d_6), δ, ppm.: 168.2, 158.4, 157.5, 157.4, 153.9, 149.2, 104.8, 46.7, 30.4, 19.1, 13.5, 13.4. IR, ν, cm^{-1}: 3055, 2960, 2929, 2872, 2855, 1963, 1691, 1605, 1556, 1502, 1427, 1390, 1369, 1343, 1295, 1277, 1257, 1233, 1181, 1124, 1097, 1062, 1054, 1019, 987, 973, 949, 883, 837, 820, 797, 762, 749, 710, 689, 650, 623, 611, 592, 571, 549, 522, 515, 506. MS (EI, 70 eV), m/z: Calcd for: $C_{12}H_{14}N_6OS$, 290; found $C_{12}H_{14}N_6OS$, 290. Anal. Calcd. For $C_{12}H_{14}N_6OS$: C, 49.64; H, 4.86; N, 28.95; found: C, 49.69; H, 4.90; N, 29.09

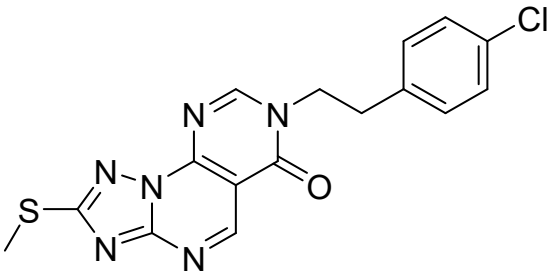
7-Isobutyl-2-(methylthio)pyrimido[5,4-*e*][1,2,4]triazolo[1,5-*a*]pyrimidin-6(7*H*)-one (20e).



White powder (235 mg, 81% yield). R_f (AcOEt) = 0.55. M.p. = 227-228 °C. ^{1}H NMR (400 MHz, DMSO-d_6), δ, ppm. (*J*, Hz): 9.26 (s, C5H, H); 8.94 (s, C8H, H); 3.92 (d, *J* = 7.4 Hz, NCH_2, 2H); 2.72 (s, S-CH_3, 3H); 2.13–2.19 (m, $CH_2C\underline{H}$, H); 0.97 (d, *J* = 6.7 Hz, $2CH_3$, 6H). ^{13}C NMR (150 MHz, DMSO-d_6), δ, ppm.: 168.2, 158.7, 157.6, 157.5, 154.0, 149.2, 104.9, 53.4, 27.4, 19.4, 13.4. IR, ν, cm^{-1}: 3039, 2979, 2957, 2928, 1967, 1693, 1655, 1601, 1558, 1502, 1474, 1455, 1443, 1434, 1425, 1388, 1374, 1363, 1350, 1334, 1296, 1278, 1254, 1229, 1188, 1168, 1121, 1101, 1063, 1052, 1016, 992, 972, 951, 934, 884, 819, 794, 773, 748, 704, 688, 668, 653, 617, 603, 580, 565, 550, 541, 533, 513, 503. MS (EI, 70 eV), m/z: Calcd for:

$C_{12}H_{14}N_6OS$, 290; found $C_{12}H_{14}N_6OS$, 290. Anal. Calcd. For $C_{12}H_{14}N_6OS$: C, 49.64; H, 4.86; N, 28.95; found: C, 49.70; H, 4.92; N, 29.00

7-(4-Chlorophenethyl)-2-(methylthio)pyrimido[5,4-*e*][1,2,4]triazolo[1,5-*a*]pyrimidin-6(7*H*)-one (20h).

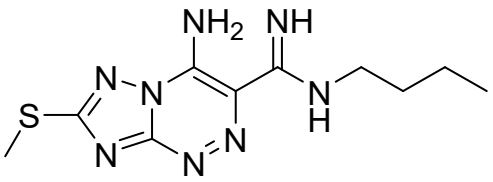


White powder (201 mg, 54% yield). R_f (AcOEt) = 0.50. M.p. = 271 °C. ^{1}H NMR (600 MHz, DMSO-d_6), δ, ppm. (*J*, Hz): 9.30 (s, C5H, H); 8.72 (s, C8H, H); 7.35 (d, *J* = 8.4 Hz, 2CH, 2H); 7.28 (d, *J* = 8.4 Hz, 2CH, 2H); 4.29 (t, *J* = 7.2 Hz, NCH_2, 2H); 3.05 (t, *J* = 7.2 Hz, CH_2, 2H); 2.69 (s, S-CH_3, 3H). ^{13}C NMR (150 MHz, DMSO-d_6), δ, ppm.: 168.3, 158.4, 157.5, 157.3, 154.0, 149.2, 136.4, 131.4, 130.9, 128.6, 104.8, 48.0, 33.3, 13.4. IR, ν, cm^{-1}: 3304, 3236, 3199, 3079, 3057, 3026, 2980, 2949, 2929, 2905, 2870, 2843, 2804, 1695, 1606, 1558, 1504, 1426, 1408, 1385, 1367, 1345, 1304, 1282, 1253, 1229, 1142, 1091, 1063, 1015, 988, 861, 832, 812, 797, 748, 715, 654, 613, 588, 552, 536, 517. MS (EI, 70 eV), m/z: Calcd for: $C_{16}H_{13}Cl^{35}N_6OS$, 372, $C_{16}H_{13}Cl^{37}N_6OS$, 374; found $C_{16}H_{13}Cl^{35}N_6OS$, 372, $C_{16}H_{13}Cl^{37}N_6OS$, 374. Anal. Calcd. For $C_{16}H_{13}ClN_6OS$: C, 51.55; H, 3.51; N, 22.54; found: C, 51.74; H, 3.69; N, 22.44. HRMS (ESI, Q-TOF), m/z: $[M+H]^+$ Calculated for $C_{16}H_{14}ClN_6OS^+$ 373.0633. Found 373.0635

General method for the synthesis of *N*-butyl[1,2,4]triazoloazinecarboximidamide 21d, 22d.

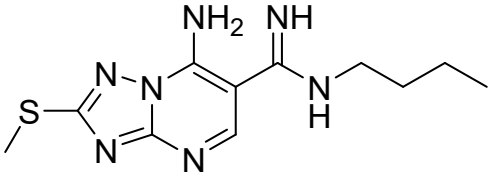
n-Butylamine (0.300 mL, 0.003 mol, 3 equiv.) and AcOH (0.172 mL, 0.003 mol, 3 equiv.) were added consequently to a suspension of appropriate cyano[1,2,4]triazoloazine **17b/18b** (0.001 mol) in toluene (7 mL). The resulting mixture was heated at 140 °C in autoclave for 8 hours, cooled to RT, filtered, and solids were washed with Et_2O (5 mL).

4-Amino-*N*-butyl-7-(methylthio)-[1,2,4]triazolo[5,1-*c*][1,2,4]triazine-3-carboximidamide (21d)



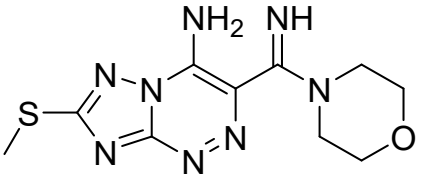
Pink powder (252 mg, 90% yield). R_f (AcOEt) = 0.35. M.p. = 196 °C. ^{1}H NMR (400 MHz, DMSO-d_6), δ, ppm. (*J*, Hz): 11.20 (s, NH, H); 9.77 (br.s, NH, H); 7.82 (br.s, NH_2, 2H); 3.41 (t, *J* = 7.4 Hz, NCH_2, 2H); 2.62 (s, S-CH_3, 3H); 1.58–1.63 (m, CH_2, 2H); 1.35–1.42 (m, CH_2, 2H); 0.91 (t, *J* = 7.4 Hz, CH_3, 3H). ^{13}C NMR (100 MHz, DMSO-d_6), δ, ppm.: 165.0, 158.9, 156.2, 143.8, 120.8, 41.4, 30.0, 19.5, 13.6, 13.4. IR, ν, cm^{-1}: 2958, 2926, 2890, 2885, 2833, 2812, 1663, 1623, 1558, 1505, 1444, 1415, 1388, 1285, 1248, 1200, 1171, 1045, 967, 938, 883, 821, 763, 738, 687, 651, 630, 605, 545, 531, 523, 512. MS (EI, 70 eV), m/z: Calcd for: $C_{10}H_{16}N_8S$, 280; found $C_{10}H_{16}N_8S$, 280. Anal. Calcd. For $C_{10}H_{16}N_8S$: C, 42.84; H, 5.75; N, 39.97; found: C, 42.88; H, 5.75; N, 40.01

7-Amino-*N*-butyl-2-(methylthio)-[1,2,4]triazolo[1,5-*a*]pyrimidine-6-carboximidamide (22d).



The crude product was recrystallized from EtOH. Beige powder (128 mg, 46% yield). R_f (AcOEt) = 0.1. M.p. = 204 °C. ^{1}H NMR (600 MHz, DMSO-d_6), δ, ppm. (*J*, Hz): 11.69 (s, NH, H); 8.60 (s, C5H, H); 8.17 (s, NH_2, 2H); 7.32 (s, NH, H); 4.34 (t, *J* = 5.2 Hz, OH, H); 3.41–3.47 (m, NCH_2, 2H); 3.31 (q, *J* = 7.2 Hz, OCH_2, 2H); 2.59 (s, S-CH_3, 3H); 1.57–1.64 (m, CH_2, 2H); 1.36–1.46 (m, CH_2, 2H); 1.05 (t, *J* = 7.2 Hz, $OCH_2C\underline{H_3}$, 3H); 0.93 (t, *J* = 7.4 Hz, CH_3, 3H). ^{13}C NMR (150 MHz, DMSO-d_6), δ, ppm.: 163.7, 159.2, 156.2, 152.2, 150.1, 91.4, 56.0, 41.8, 30.3, 19.7, 18.6, 13.6, 13.3. IR, ν, cm^{-1}: 3316, 3133, 2956, 2930, 2866, 2818, 1692, 1632, 1554, 1519, 1469, 1437, 1396, 1320, 1263, 1230, 1176, 1127, 1092, 1052, 993, 969, 951, 885, 839, 822, 767, 715, 688, 650, 603, 564, 514. MS (EI, 70 eV), m/z: Calcd for: $C_{11}H_{17}N_7SxEtOH$, 279; found $C_{11}H_{17}N_7S$, 279. Anal. Calcd. For $C_{11}H_{17}N_7SxC_2H_6O$: C, 47.98; H, 7.12; N, 30.13; found: C, 48.01; H, 7.06; N, 30.19. HRMS (ESI, Q-TOF), m/z: $[M+H]^+$ Calculated for $C_{11}H_{18}N_7S^+$ 280.1339. Found 280.1343

3-(Imino(morpholino)methyl)-7-(methylthio)-[1,2,4]triazolo[5,1-*c*][1,2,4]triazin-4-amine (21m). Morpholine (0.095 mL, 0.0011 mol, 1.1 equiv.) was added to a suspension of 4-amino-3-cyano-2-metylthio[1,2,4]triazolo[5,1-*c*][1,2,4]triazine **17b** (0.207 g, 0.001 mol) in MeCN (7 mL). The resulting mixture was refluxed for 4 hours, cooled to RT, filtered, and solids were washed with Et_2O (5 mL).



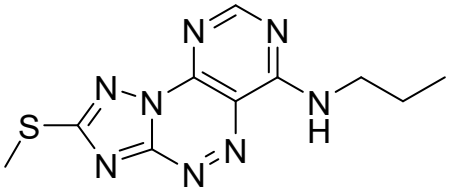
Green powder (252 mg, 86% yield). R_f (AcOEt) = 0.6. Mp = 295 °C. ^{1}H NMR (600 MHz, DMSO-d_6), δ, ppm. (*J*, Hz): 8.43 (br.s, 3NH, 3H); 3.71 (t, *J* = 4.5 Hz, $2CH_2$, 4H); 3.56 (t, *J* = 4.5 Hz, $2CH_2$, 4H); 2.61 (s, S-CH_3, 3H). ^{13}C NMR (150 MHz, DMSO-d_6), δ, ppm.: 165.0, 160.6, 156.,7 141.7, 128.5, 65.6, 47.4, 13.4. IR, ν, cm^{-1}: 3288, 3042, 2976, 2911, 2866, 1683, 1662, 1621, 1594, 1516, 1484, 1446, 1423, 1407, 1373, 1337, 1303, 1290, 1269, 1243, 1204, 1170, 1144, 1119, 1069, 1028, 1013, 941, 874, 845, 798, 752, 739, 688, 671, 656, 635, 613, 577, 557, 526, 507. MS (EI, 70 eV), m/z: Calcd for: $C_{10}H_{14}N_8OS$, 294; found $C_{10}H_{14}N_8OS$, 294. Anal. Calcd. For $C_{10}H_{14}N_8OS$: C, 40.81; H, 4.79; N, 38.07; found: C, 40.88; H, 4.80; N, 38.03

General method for the synthesis of pyrimido[4,5-*e*][1,2,4]triazolo[5,1-*c*] [1,2,4]triazin-6-amines 23a-n.

Triethylortoformate (0.498 mL, 0.003 mol, 3 equiv.), appropriate amine (0.001 mol, 1 equiv.) and AcOH (0.172 mL, 0.003 mol, 3 equiv.) were added consequently to a suspension of 4-amino-3-cyano-7-methylsulfanyl[1,2,4]triazolo[5,1-*c*][1,2,4]triazine **18b** (0.207 g, 0.001 mol) in toluene (7 mL). The resulting mixture was refluxed for 8 hours, cooled to RT, filtered, and solids

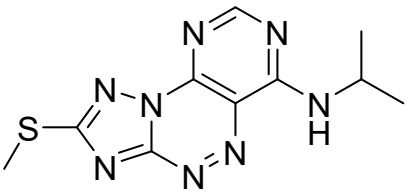
were washed with Et_2O (5 mL). Another crop of product could be obtained from the mother liquor. The mother liquor was concentrated at reduced pressure, the residue was treated with Et_2O (10 mL), filtered, and solids were washed with Et_2O (5 mL).

2-(Methylthio)-*N*-propylpyrimido[4,5-*e*][1,2,4]triazolo[5,1-*c*][1,2,4]triazin-6-amine (23a).



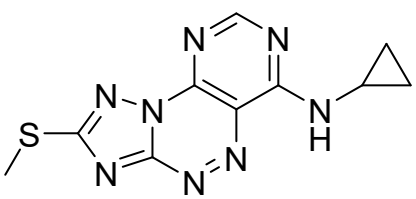
Yellow powder (259 mg, 94% yield). R_f (AcOEt) = 0.7. M.p. = 240 °C. ^{1}H NMR (400 MHz, DMSO-d_6), δ, ppm. (*J*, Hz): 10.26 (s, NH, H); 8.62 (s, C8H, H); 3.66 (t, *J* = 7.3 Hz, NCH_2, 2H); 2.79 (s, S-CH_3, 3H); 1.71–1.81 (m, CH_2, 2H); 1.01 (t, *J* = 7.4 Hz, CH_3, 3H). ^{13}C NMR (100 MHz, DMSO-d_6), δ, ppm.: 168.8, 162.8, 159.0, 157.7, 139.8, 123.3, 42.60, 21.7, 13.6, 11.2. IR, ν, cm^{-1}: 2358, 3207, 3154, 3128, 3113, 3001, 2952, 2929, 2895, 2863, 2838, 1610, 1572, 1533, 1464, 1439, 1413, 1392, 1364, 1328, 1308, 1275, 1186, 1128, 1098, 1087, 1073, 1013, 984, 969, 930, 913, 884, 864, 801, 785, 773, 749, 729, 705, 649, 588, 574, 552, 513. MS (EI, 70 eV), m/z: Calcd for: $C_{10}H_{12}N_8S$, 276; found $C_{10}H_{12}N_8S$, 276. Anal. Calcd. For $C_{10}H_{12}N_8S$: C, 43.47; H, 4.38; N, 40.55; found: C, 43.44; H, 4.40; N, 40.59

***N*-Isopropyl-2-(methylthio)pyrimido[4,5-*e*][1,2,4]triazolo[5,1-*c*][1,2,4]triazin-6-amine (23b).**



Yellow powder (248 mg, 90% yield). R_f (AcOEt) = 0.7. M.p. = 220 °C. ^{1}H NMR (400 MHz, DMSO-d_6), δ, ppm. (*J*, Hz): 10.02 (s, NH, H); 8.61 (s, C8H, H); 4.73 (br.s, NCH, H); 2.79 (s, S-CH_3, 3H); 1.37 (d, *J* = 6.6 Hz, $2CH_3$, 6H). ^{13}C NMR (100 MHz, DMSO-d_6), δ, ppm.: 168.8, 162.8, 158.0, 157.7, 139.9, 123.2, 43.1, 21.5, 13.5. IR, ν, cm^{-1}: 3237, 3218, 3200, 3186, 3174, 3142, 3046, 2973, 2927, 1607, 11576, 1527, 1455, 1413, 1391, 1362, 1313, 1291, 1281, 1271, 1241, 1198, 1178, 1155, 1123, 1093, 1014, 976, 957, 930, 897, 878, 838, 801, 794, 965, 745, 734, 703, 667, 595, 580, 531, 524, 506. MS (EI, 70 eV), m/z: Calcd for: $C_{10}H_{12}N_8S$, 276; found $C_{10}H_{12}N_8S$, 276. Anal. Calcd. For $C_{10}H_{12}N_8S$: C, 43.47; H, 4.38; N, 40.55; found: C, 43.55; H, 4.35; N, 40.55

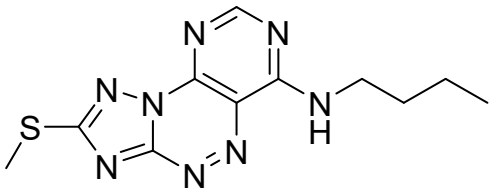
***N*-Cyclopropyl-2-(methylthio)pyrimido[4,5-*e*][1,2,4]triazolo[5,1-*c*][1,2,4]triazin-6-amine (23c).**



Yellow powder (155 mg, 93% yield). R_f (AcOEt) = 0.7. M.p. = 260 °C. ^{1}H NMR (400 MHz, DMSO-d_6), δ, ppm. (*J*, Hz): 10.20 (s, NH, H); 8.68 (s, C8H, H); 3.43 (s, NCH, H); 2.79 (s, S-CH_3, 3H); 0.86–0.90 (m, CH_2, 2H), 0.94–0.98 (m, CH_2, 2H). ^{13}C NMR (100 MHz, DMSO-d_6), δ, ppm.: 168.9, 162.8, 160.1, 157.6, 139.7, 123.3, 25.0, 13.6, 5.9. IR, ν, cm^{-1}:3295, 1600, 1575, 1533, 1509, 1478, 1396, 1366, 1332, 1310, 1277, 1201, 1185, 1131, 1106, 1059, 102, 989, 971, 934, 901, 888, 8435, 820, 802, 751, 737, 703, 692, 633, 611, 587, 577,

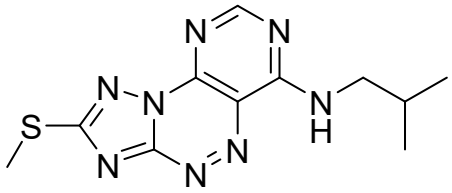
557, 543, 527, 508. MS (EI, 70 eV), m/z: Calcd for: $C_{10}H_{10}N_8S$, 274; found $C_{10}H_{10}N_8S$, 274. Anal. Calcd. For $C_{10}H_{10}N_8S$: C, 43.79; H, 3.67; N, 40.85; found: C, 43.88; H, 3.70; N, 40.88

***N*-Butyl-2-(methylthio)pyrimido[4,5-*e*][1,2,4]triazolo[5,1-*c*][1,2,4]triazin-6-amine (23d).**



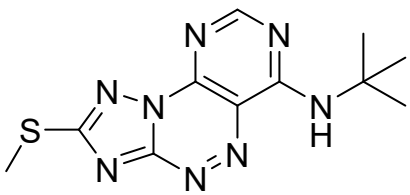
Yellow powder (278 mg, 96% yield). R_f (AcOEt) = 0.7. M.p. = 216 °C. ^{1}H NMR (400 MHz, DMSO-d_6), δ, ppm. (*J*, Hz): 10.24 (s, NH, H); 8.62 (s, C8H, H); 3.69 (t, *J* = 7.3 Hz, NCH_2, 2H); 2.78 (s, S-CH_3, 3H); 1.69–1.74 (m, CH_2, 2H); 1.40–1.46 (m, CH_2, 2H); 0.98 (t, *J* = 7.4 Hz, CH_3, 3H). ^{13}C NMR (100 MHz, DMSO-d_6), δ, ppm.: 168.9, 162.9, 159.0, 157.7, 139.9, 123.4, 40.6, 30.5, 19.6, 13.7, 13.6. IR, ν, cm^{-1}: 3202, 3164, 3142, 3083, 3062, 2967, 2928, 2868, 2854, 1513, 1572, 1535, 1468, 1438, 1411, 1389, 1361, 1330, 1307, 1273, 1248, 1183, 1099, 999, 982, 969, 886, 800, 783, 739, 705, 667, 622, 587, 555, 515. MS (EI, 70 eV), m/z: Calcd for: $C_{11}H_{14}N_8S$, 290; found $C_{11}H_{14}N_8S$, 290. Anal. Calcd. For $C_{11}H_{14}N_8S$: C, 45.50; H, 4.86; N, 38.59; found: C, 45.60; H, 4.76; N, 38.63

***N*-Isobutyl-2-(methylthio)pyrimido[4,5-*e*][1,2,4]triazolo[5,1-*c*][1,2,4]triazin-6-amine (23e).**



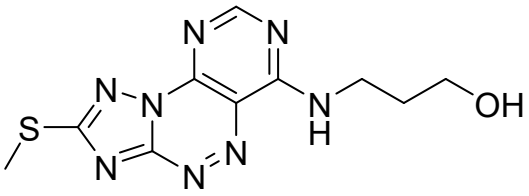
Yellow powder (281 mg, 97% yield). R_f (AcOEt) = 0.7. M.p. = 211 °C. ^{1}H NMR (400 MHz, DMSO-d_6), δ, ppm. (*J*, Hz): 10.27 (s, NH, H); 8.60 (s, C8H, H); 3.53 (d, *J* = 7.2 Hz, NCH_2, 2H); 2.79 (s, S-CH_3, 3H); 2.12–2.18 (m, CH, H); 1.00 (d, *J* = 6.7 Hz, 2CH_3, 6H). ^{13}C NMR (100 MHz, DMSO-d_6), δ, ppm.: 168.8, 162.7, 159.1, 157.7, 139.9, 123.4, 48.2, 27.7, 20.1, 13.6. IR, ν, cm^{-1}: 3228, 3159, 3143, 3082, 3036, 3007, 2955, 2867, 2794, 1988, 1606, 1572, 1532, 1470, 1440, 1413, 1392, 1380, 1361, 1328, 1309, 1277, 1187, 1173, 1130, 1098, 1066, 979, 919, 883, 820, 800, 787, 749, 728, 705, 677, 640, 621, 607, 587, 562, 532, 513. MS (EI, 70 eV), m/z: Calcd for: $C_{11}H_{14}N_8S$, 290; found $C_{11}H_{14}N_8S$, 290. Anal. Calcd. For $C_{11}H_{14}N_8S$: C, 45.50; H, 4.86; N, 38.59; found: C, 45.55; H, 4.86; N, 38.50

***N*-(*Tert*-butyl)-2-(methylthio)pyrimido[4,5-*e*][1,2,4]triazolo[5,1-*c*][1,2,4]triazin-6-amine (23f).**



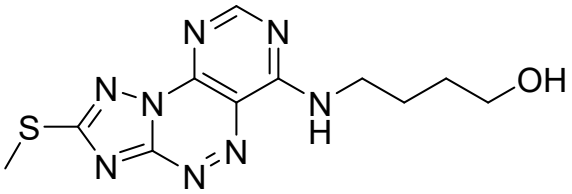
Yellow powder (119 mg, 41% yield). R_f (AcOEt) = 0.7. M.p. = 118 °C. ^{1}H NMR (400 MHz, DMSO-d_6), δ, ppm. (*J*, Hz): 8.99 (s, NH, H); 8.67 (s, C8H, H); 2.79 (s, S-CH_3, 3H); 1.65 (s, 3CH_3, 9H). ^{13}C NMR (100 MHz, DMSO-d_6), δ, ppm.: 169.0, 162.0, 158.7, 157.7, 139.7, 123.3, 53.9, 28.3, 13.6. IR, ν, cm^{-1}: 3559, 3484, 3446, 4468, 3272, 3197, 3139, 3122, 3070, 2978, 2965, 2993, 2823, 2015, 1627, 1597, 1569, 1532, 1452, 1398, 1325, 1283, 1209, 1189, 1145, 1114, 1014, 988, 967, 929, 885, 8557, 805, 795, 774, 714, 627, 589, 567, 557, 522, 504. MS (EI, 70 eV), m/z: Calcd for: $C_{11}H_{14}N_8S$, 290; found $C_{11}H_{14}N_8S$, 290. Anal. Calcd. For $C_{11}H_{14}N_8S$: C, 45.50; H, 4.86; N, 38.59; found: C, 45.48; H, 4.83; N, 38.66

3-((2-(Methylthio)pyrimido[4,5-*e*][1,2,4]triazolo[5,1-*c*][1,2,4]triazin-6-yl)amino)propan-1-ol (23g).



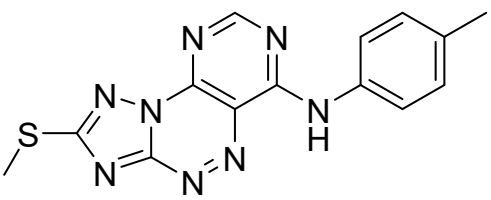
Yellow powder (210 mg, 72% yield). R_f (AcOEt) = 0.7. M.p. = 211 °C. ^{1}H NMR (400 MHz, DMSO-d_6), δ, ppm. (*J*, Hz): 10.13 (d, *J* = 6.4 Hz, NH, H); 8.65 (s, C8H, H); 3.77 (dt, J_1 = 7.6 Hz, J_2 = 6.4 Hz, NCH_2, 2H); 3.56 (t, *J* = 6.1 Hz, OCH_2, 2H); 2.78 (s, S-CH_3, 3H); 1.86–1.91 (m, CH_2, 2H). ^{13}C NMR (150 MHz, DMSO-d_6), δ, ppm.: 168.9, 162.9, 159.0, 157.7, 139.8, 123.4, 58.6, 38.7, 31.5, 13.6. IR, ν, cm^{-1}: 3214, 3125, 2938, 2882, 1610, 1572, 1536, 1468, 1440, 1414, 1392, 1365, 1328, 1308, 1276, 1184, 1113, 1095, 1076, 1030, 1018, 969, 919, 886, 851, 802, 786, 731, 707, 667, 648, 590, 556, 525, 505. MS (EI, 70 eV), m/z: Calcd for: $C_{10}H_{12}N_8OS$, 292; found $C_{10}H_{12}N_8OS$, 292. Anal. Calcd. For $C_{10}H_{12}N_8OS$: C, 41.09; H, 4.14; N, 38.33; found: C, 41.02; H, 4.13; N, 38.40

4-((2-(Methylthio)pyrimido[4,5-*e*][1,2,4]triazolo[5,1-*c*][1,2,4]triazin-6-yl)amino)butan-1-ol (23h).



The crude product was recrystallized from EtOH. Yellow powder (199 mg, 65% yield). R_f (AcOEt) = 0.7. M.p. = 203 °C. ^{1}H NMR (600 MHz, DMSO-d_6), δ, ppm. (*J*, Hz): 10.23 (br.s, NH, H); 8.69 (s, C8H, H); 4.45 (t, *J* = 4.8 Hz, OH, H); 3.67 (t, *J* = 6.6 Hz, $NHC\underline{H}_2$, 2H); 3.44 (dt, J_1 = 6.6 Hz, J_2 = 4.8 Hz OCH_2, 2H); 2.76 (s, S-CH_3, 3H); 1.70–1.75 (m, CH_2, 2H); 1.49–1.54 (m, CH_2, 2H). ^{13}C NMR (150 MHz, DMSO-d_6), δ, ppm.: 168.9, 162.9, 159.0, 157.8, 139.9, 123.4, 60.4, 40.9, 29.8, 25.3, 13.6. IR, ν, cm^{-1}: 4308, 3348, 3271, 3168, 2960, 2942, 2907, 2862, 2829, 1675, 1622, 1575, 1532, 1501, 1470, 1449, 1416, 1388, 1369, 1324, 1308, 1275, 1197, 1184, 1173, 1136, 1116, 1091, 1073, 1055, 988, 973, 943, 903, 873, 836, 819, 804, 766, 729, 705, 691, 663, 646, 626, 612, 587, 558, 536, 512. MS (EI, 70 eV), m/z: Calcd for: $C_{11}H_{14}N_8OS$, 306; found $C_{11}H_{14}N_8OS$, 306. Anal. Calcd. For $C_{11}H_{14}N_8OS$: C, 43.13; H, 4.61; N, 36.58; found: C, 43.02; H, 4.66; N, 36.49

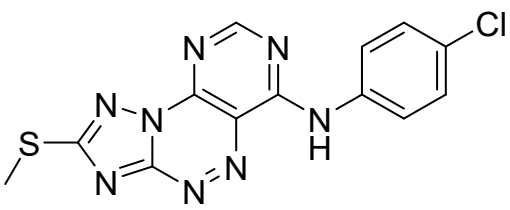
2-(Methylthio)-*N*-(*p*-tolyl)pyrimido[4,5-*e*][1,2,4]triazolo[5,1-*c*][1,2,4]triazin-6-amine (23i).



Orange powder (301mg, 93% yield). R_f (AcOEt) = 0.7. M.p. = 279 °C. ^{1}H NMR (400 MHz, DMSO-d_6), δ, ppm. (*J*, Hz): 11.67 (s, NH, H); 8.75 (s, C8H, H); 7.83 (d, *J* = 8.0 Hz, 2CH, 2H); 7.23 (d, *J* = 8.0 Hz, 2CH, 2H); 2.80 (s, S-CH_3, 3H); 2.37 (s, CH_3, 3H). ^{13}C NMR (100 MHz, DMSO-d_6), δ, ppm.: 169.1, 162.5, 157.6, 157.32, 157.28, 139.8, 134.73, 134.65, 128.9, 123.3, 20.4, 13.5. IR, ν, cm^{-1}:3280, 3262, 1618, 1583, 1565, 15344, 1510, 1425, 1407, 1386, 1358, 1326, 1282, 1214, 1184, 1112, 1018, 990, 981, 940, 906, 817, 801, 773, 736, 703, 663, 638, 582,

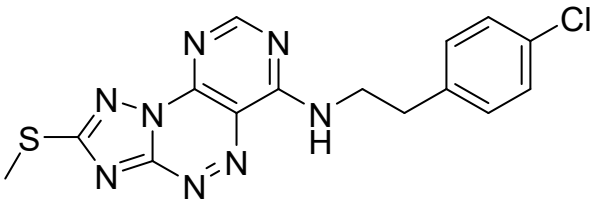
558, 529, 517, 507, 501. MS (EI, 70 eV), m/z: Calcd for: $C_{14}H_{12}N_8S$, 324; found $C_{14}H_{12}N_8S$, 324. Anal. Calcd. For $C_{14}H_{12}N_8S$: C, 51.84; H, 3.73; N, 34.55; found: C, 51.88; H, 3.60; N, 34.69

***N*-(4-Chlorophenyl)-2-(methylthio)pyrimido[4,5-*e*][1,2,4]triazolo[5,1-*c*][1,2,4]triazin-6-amine (23j).**



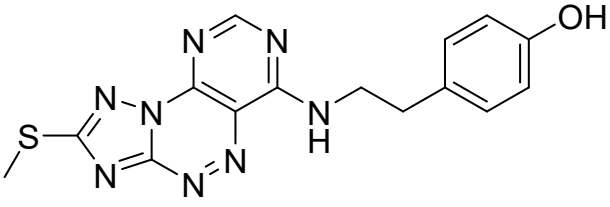
Yellow powder (169 mg, 49% yield). R_f (AcOEt) = 0.7. M.p. = 300 °C. ^{1}H NMR (400 MHz, DMSO-d_6), δ, ppm. (*J*, Hz): 11.84 (s, NH, H); 8.81 (s, C8H, H); 8.06 (d, *J* = 8.8 Hz, 2CH, 2H); 7.42 (d, *J* = 8.8 Hz, 2CH, 2H); 2.82 (s, S-CH_3, 3H). ^{13}C NMR (100 MHz, DMSO-d_6), δ, ppm.: 169.2, 162.4, 157.5, 157.4, 139.8, 136.2, 129.2, 128.4, 124.8, 123.1, 13.5. IR, ν, cm^{-1}: 3237, 3079, 2985, 2350, 2242, 1899, 1730, 1650, 1608, 1575, 1558, 1535, 1509, 1485, 1426, 1401, 1385, 1323, 1279, 1212, 1184, 1143, 1112, 1089, 1008, 985, 962, 908, 829, 800, 731, 712, 701, 671, 653, 585, 579, 554, 523, 507. MS (EI, 70 eV), m/z: Calcd for: $C_{13}H_9ClN_8SCl$, 344; found $C_{13}H_9ClN_8S$, 344. Anal. Calcd. For $C_{13}H_9ClN_8S$: C, 45.29; H, 2.63; N, 32.50; found: C, 45.39; H, 2.40; N, 32.56

***N*-(4-Chlorophenethyl)-2-(methylthio)pyrimido[4,5-*e*][1,2,4]triazolo[5,1-*c*][1,2,4]triazin-6-amine (23k).**



The crude product was recrystallized from EtOH. Yellow powder (223 mg, 60% yield). R_f (AcOEt) = 0.7. M.p. = 284 °C. ^{1}H NMR (600 MHz, DMSO-d_6), δ, ppm. (*J*, Hz): 10.26 (t, *J* = 6.0 Hz, NH, H); 8.70 (s, C8H, H); 7.30–7.34 (m, 4CH, 4H); 3.89 (dt, J_1 = 7.2 Hz, J_2 = 6.0 Hz, NCH_2, 2H); 3.02 (t, *J* = 7.2 Hz, CH_2, 2H); 2.76 (s, S-CH_3, 3H). ^{13}C NMR (150 MHz, DMSO-d_6), δ, ppm.: 168.9, 162.9, 159.1, 157.8, 139.9, 137.9, 130.9, 130.7, 128.3, 123.3, 42.1, 33.5, 13.6. IR, ν, cm^{-1}:3366, 1613, 1570, 1537, 1515, 1491, 1470, 1454, 1432, 1412, 1386, 1365, 1356, 1340, 1326, 1274, 1174, 1143, 1109, 1089, 1068, 1027, 1011, 975, 887, 847, 845, 815, 801, 718, 705, 629, 586, 551, 524. MS (EI, 70 eV), m/z: Calcd for: $C_{15}H_{13}ClN_8S$, 372; found $C_{15}H_{13}ClN_8S$, 372. Anal. Calcd. For $C_{15}H_{13}ClN_8S$: C, 48.32; H, 3.51; N, 30.05; found: C, 48.25; H, 3.41; N, 29.89

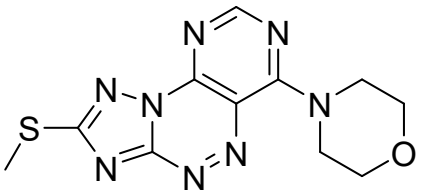
4-(2-((2-(Methylthio)pyrimido[4,5-*e*][1,2,4]triazolo[5,1-*c*][1,2,4]triazin-6-yl)amino)ethyl)phenol (23l).



The crude product was recrystallized from EtOH. Yellow powder (160 mg, 45% yield). R_f (AcOEt) = 0.7. M.p. = 280 °C. ^{1}H NMR (600 MHz, DMSO-d_6), δ, ppm. (*J*, Hz): 10.23 (t, *J* = 6.0 Hz, NH, H); 9.20 (s, OH, H); 8.70 (s, CH,

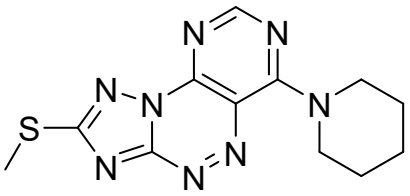
H); 7.06 (d, J = 8.4 Hz, 2CH, 2H); 6.69 (d, J = 8.4 Hz, 2CH, 2H); 3.83 (dt, J_1 = 7.8 Hz, J_2 = 6.0 Hz, CH_2, 2H); 2.90 (t, J = 7.8 Hz, CH_2, 2H); 2.75 (s, S-CH_3, 3H). ^{13}C NMR (150 MHz, DMSO-d_6), δ, ppm.: 168.9, 162.9, 159.0, 157.8, 155.8, 139.9, 129.6, 128.8, 123.4, 115.2, 42.7, 33.5, 13.6. IR, ν, cm^{-1}: 3250, 2149 3017, 2936, 2860, 1714, 1611, 1578, 1537, 1513, 1453, 1411, 1390, 1363, 1328, 1311, 1276, 1183, 1171, 1146, 1111, 1100, 1074, 1023, 987, 970, 890, 851, 828, 802, 725, 705, 677, 639, 588, 564, 550, 514. MS (EI, 70 eV), m/z: Calcd for: $C_{15}H_{14}N_8OS$, 354; found $C_{15}H_{14}N_8OS$, 354. Anal. Calcd. For $C_{15}H_{14}N_8OS$: C, 50.84; H, 3.98; N, 31.62; found: C, 50.86; H, 4.03; N, 31.59

4-(2-(Methylthio)pyrimido[4,5-*e*][1,2,4]triazolo[5,1-*c*][1,2,4]triazin-6-yl)morpholine (23m).



The crude product was recrystallized from EtOH. Orange powder (283 mg, 93% yield). R_f (AcOEt) = 0.65. M.p. = 221 °C. ^{1}H NMR (600 MHz, DMSO-d_6), δ, ppm. (J, Hz): 8.71 (s, CH, H); 4.87 (br.s, CH_2, 2H); 4.27 (br.s, CH_2, 2H); 3.85 (t, J = 4.9 Hz, 2CH_2, 4H); 2.65 (s, S-CH_3, 3H). ^{13}C NMR (150 MHz, DMSO-d_6), δ, ppm.: 166.1, 160.5, 157.2, 156.2, 142.1, 125.2, 66.3, 50.8, 46.7, 14.8. IR, ν, cm^{-1}: 2967, 2938, 2908, 2860, 1746, 1721, 1648, 1582, 1538, 1473, 1434, 1402, 1366, 1339, 1291, 1268, 1241, 1180, 1135, 1116, 1100, 1059, 1013, 983, 926, 903, 858, 813, 800, 751, 729, 690, 670, 648, 635, 600, 587, 541, 524. MS (EI, 70 eV), m/z: Calcd for: $C_{11}H_{12}N_8OS$, 304; found $C_{11}H_{12}N_8OS$, 304. Anal. Calcd. For $C_{11}H_{12}N_8OS$: C, 43.41; H, 3.97; N, 36.82; found: C, 43.33; H, 3.95; N, 36.80

2-(Methylthio)-6-(piperidin-1-yl)pyrimido[4,5-*e*][1,2,4]triazolo[5,1-*c*][1,2,4]triazine (23n).



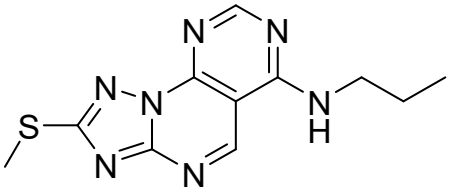
The crude product was recrystallized from *i*-PrOH. Orange powder (200 mg, 66% yield). R_f (AcOEt) = 0.6. M.p. = 206 °C. ^{1}H NMR (400 MHz, DMSO-d_6), δ, ppm. (J, Hz): 8.63 (s, CH, H); 4.75 (br.s, CH_2, 2H); 4.23 (br.s, CH_2, 2H); 2.75 (s, S-CH_3, 3H); 1.79 (br.s, 3CH_2, 6H). ^{13}C NMR (150 MHz, DMSO-d_6), δ, ppm.: 168.8, 160.5, 156.7, 156.3, 141.6, 125.6, 51.1, 48.0, 26.6, 26.1, 23.8, 13.6. IR, ν, cm^{-1}: 2940, 2929, 2887, 2860, 2842, 1582, 1549, 1520, 1447, 1404, 1377, 1358, 1342, 1330, 1305, 1281, 1266, 1236, 1173, 1161, 1088, 1064, 1037, 1017, 974, 956, 898, 848, 796, 772, 705, 669, 652, 633, 611, 585, 575, 557, 536, 512. MS (EI, 70 eV), m/z: Calcd for: $C_{12}H_{14}N_8S$, 302; found $C_{12}H_{14}N_8S$, 302. Anal. Calcd. For $C_{12}H_{14}N_8S$: C, 47.67; H, 4.67; N, 37.06; found: C, 47.51; H, 4.80; N, 36.95. HRMS (ESI, Q-TOF), m/z: $[M+H]^+$ Calculated for $C_{12}H_{15}N_8S^+$ 303.1135. Found 303.1137

General method for the synthesis of pyrimido[5,4-*e*][1,2,4]triazolo[1,5-a]pyrimidin-6-amines 24a-h, 24j, 24l

Triethylortoformate (0.498 mL, 0.003 mol, 3 equiv.), appropriate amine (0.003 mol, 3 equiv.) and AcOH (0.172 mL, 0.003 mol, 3 equiv.) were added consequently to a suspension of 7-

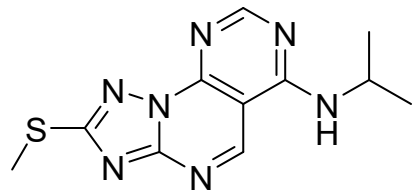
amino-6-cyano-2-(methylthio)[1,2,4]triazolo[1,5-*a*]pyrimidine **18a** (0.206 g, 0.001 mol) in toluene (7 mL). The resulting mixture was heated in autoclave at 140 °C for 12 hours, cooled to RT, filtered, and solids were washed with Et_2O (5 mL). Another crop of product could be obtained from the mother liquor. The mother liquor was concentrated at reduced pressure, the residue was treated with Et_2O (10 mL), filtered, and solids were washed with Et_2O (5 mL).

2-(Methylthio)-*N*-propylpyrimido[5,4-*e*][1,2,4]triazolo[1,5-*a*]pyrimidin-6-amine (24a).



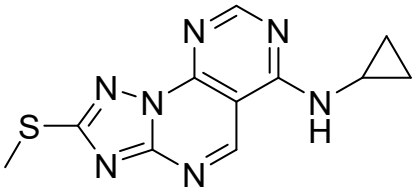
Pale yellow powder (165 mg, 66% yield). R_f (AcOEt) = 0.4. M.p. = 282-283 °C. ^{1}H NMR (400 MHz, DMSO-d_6), δ, ppm. (*J*, Hz): 9.54 (s, C5H, H); 9.21 (s, NH, H); 8.69 (s, C8H, H); 3.56 (dt, J_1 = 7.4 Hz, J_2 = 6.5 Hz, NCH_2, 2H); 2.68 (s, S-CH_3, 3H); 1.63–1.72 (m, CH_2, 2H); 0.96 (t, *J* = 7.4 Hz, CH_3, 3H). ^{13}C NMR (100 MHz, DMSO-d_6), δ, ppm.: 166.6, 161.9, 159.3, 156.5, 152.8, 149.3, 98.4, 42.8, 21.7, 13.4, 11.4. IR, ν, cm^{-1}: 3265, 3251, 3178, 3164, 3109, 2956, 1900, 1593, 1568, 1514, 1452, 1436, 1405, 1385, 1344, 1326, 1285, 1245, 1170, 1110, 1074, 1011, 983, 970, 924, 910, 890, 848, 798, 777, 755, 738, 696, 665, 586, 548, 510. MS (EI, 70 eV), m/z: Calcd for: $C_{11}H_{13}N_7S$, 275; found $C_{11}H_{13}N_7S$, 275. Anal. Calcd. For $C_{11}H_{13}N_7S$: C, 47.98; H, 4.76; N, 35.61; found: C, 48.05; H, 4.90; N, 35.44

***N*-Isopropyl-2-(methylthio)pyrimido[5,4-*e*][1,2,4]triazolo[1,5-*a*]pyrimidin-6-amine (24b).**



Pale yellow powder (148 mg, 54% yield). R_f (AcOEt) = 0.3. M.p. = 248-249 °C. ^{1}H NMR (400 MHz, DMSO-d_6), δ, ppm. (*J*, Hz): 9.60 (s, C5H, H); 8.89 (d, *J* = 7.5 Hz, NH, H); 8.70 (s, C8H, H); 4.53–4.61 (m, NHC<u>H</u>, H); 2.68 (s, S-CH_3, 3H); 1.30 (d, *J* = 6.6 Hz, $2CH_3$, 6H). ^{13}C NMR (100 MHz, DMSO-d_6), δ, ppm.: 166.6, 161.9, 158.5, 156.6, 153.0, 149.5, 98.3, 43.1, 21.8, 13.4. IR, ν, cm^{-1}: 2525, 2486, 2451, 2205, 2170, 2971, 2932, 2350, 1592, 1571, 1518, 1462, 1414, 1384, 1349, 1329, 1301, 1285, 1253, 1161, 1014, 983, 920, 896, 839, 800, 756, 693, 581, 546, 534, 512. MS (EI, 70 eV), m/z: Calcd for: $C_{11}H_{13}N_7S$, 275; found $C_{11}H_{13}N_7S$, 275. Anal. Calcd. For $C_{11}H_{13}N_7S$: C, 47.98; H, 4.76; N, 35.61; found: C, 47.99; H, 4.71; N, 35.58

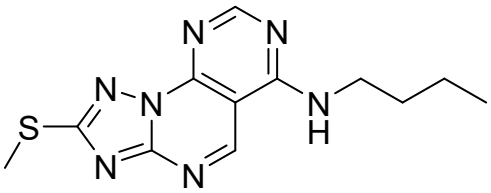
***N*-Cyclopropyl-2-(methylthio)pyrimido[5,4-*e*][1,2,4]triazolo[1,5-*a*]pyrimidin-6-amine (24c).**



Pale yellow powder (136 mg, 50% yield). R_f (AcOEt) = 0.2. M.p. = 255-258 °C. ^{1}H NMR (400 MHz, DMSO-d_6), δ, ppm. (*J*, Hz): 9.50 (s, C5H, H); 9.15 (br.s, NH, H); 8.75 (s, C8H, H); 3.12–3.17 (m, NHC<u>H</u>, H); 2.68 (s, S-CH_3, 3H); 0.86–0.90 (m, CH_2, 2H); 0.70–0.74 (m, CH_2, 2H). ^{13}C NMR (100 MHz, DMSO-d_6), δ, ppm.: 166.6, 161.9, 160.6, 156.5, 153.0, 149.2, 98.5, 24.7, 13.4, 6.1. IR, ν, cm^{-1}: 3441, 3409, 3377, 3278, 3163, 3012, 1595, 1572, 1519, 1506, 1455, 1409,

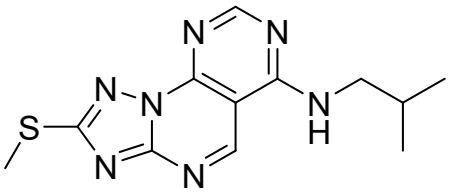
1353, 1332, 1284, 1251, 1127, 1025, 984, 961, 944, 928, 894, 831, 819, 799, 745, 704, 690, 623, 576, 552, 533, 516. MS (EI, 70 eV), m/z: Calcd for: $C_{11}H_{11}N_7S$, 273; found $C_{11}H_{11}N_7S$, 273. Anal. Calcd. For $C_{11}H_{11}N_7S$: C, 48.34; H, 4.06; N, 35.87; found: C, 48.45; H, 3.95; N, 35.84

***N*-Butyl-2-(methylthio)pyrimido[5,4-*e*][1,2,4]triazolo[1,5-*a*]pyrimidin-6-amine (24d).**



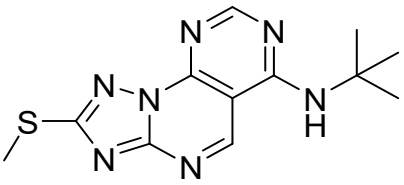
Pale yellow powder (209 mg, 72% yield). R_f (AcOEt) = 0.6. M.p. = 257-258 °C. ^{1}H NMR (400 MHz, DMSO-d_6), δ, ppm. (*J*, Hz): 9.53 (s, C5H, H); 9.19 (s, NH, H); 8.69 (s, C8H, H); 3.57–3.61 (m, NCH_2, 2H); 2.68 (s, S-CH_3, 3H); 1.61–1.66 (m, CH_2, 2H); 1.37–1.42 (m, CH_2, 2H); 0.93 (t, *J* = 7.4 Hz, CH_3, 3H). ^{13}C NMR (100 MHz, DMSO-d_6), δ, ppm.: 166.6, 161.9, 159.3, 156.6, 152.8, 149.4, 98.4, 40.7, 30.5, 19.6, 13.7, 13.4. IR, ν, cm^{-1}: 3280, 3269, 3198, 3169, 3139, 3110, 2958, 2933, 2871, 2859, 2342, 1595, 1571, 1523, 1451, 1406, 1387, 1375, 1357, 1343, 1320, 1285, 1247, 1169, 1113, 1072, 1054, 1002, 972, 920, 891, 799, 778, 756, 743, 729, 707, 691, 656, 584, 557, 546, 527, 511. MS (EI, 70 eV), m/z: Calcd for: $C_{12}H_{15}N_7S$, 289; found $C_{12}H_{15}N_7S$, 289. Anal. Calcd. For $C_{12}H_{15}N_7S$: C, 49.81; H, 5.23; N, 33.88; found: C, 49.81; H, 5.24; N, 33.75.

***N*-Isobutyl-2-(methylthio)pyrimido[5,4-*e*][1,2,4]triazolo[1,5-*a*]pyrimidin-6-amine (24e).**



Pale yellow powder (196 mg, 68% yield). R_f (AcOEt) = 0.5. M.p. = 277-278 °C. ^{1}H NMR (400 MHz, DMSO-d_6), δ, ppm. (*J*, Hz): 9.57 (s, C5H, H); 9.21 (s, NH, H); 8.67 (s, C8H, H); 3.42 (d, *J* = 7.0 Hz, NCH_2, 2H); 2.68 (s, S-CH_3, 3H); 1.97–2.07 (m, CH, H); 0.96 (d, *J* = 6.7 Hz, 2CH_3, 6H). ^{13}C NMR (100 MHz, DMSO-d_6), δ, ppm.: 166.6, 161.9, 159.6, 156.6, 152.9, 149.4, 98.5, 48.4, 27.6, 20.2, 13.4. IR, ν, cm^{-1}: 3284, 3173, 2958, 2928, 2869, 1592, 1569, 1521, 1451, 1436, 1404, 1385, 1354, 1343, 1323, 1285, 1246, 1171, 1112, 1065, 971, 902, 889, 876, 816, 799, 756, 738, 705, 647, 585, 560, 545, 516. MS (EI, 70 eV), m/z: Calcd for: $C_{12}H_{15}N_7S$, 289; found $C_{12}H_{15}N_7S$, 289. Anal. Calcd. For $C_{12}H_{15}N_7S$: C, 49.81; H, 5.23; N, 33.88; found: C, 49.90; H, 5.09; N, 33.71

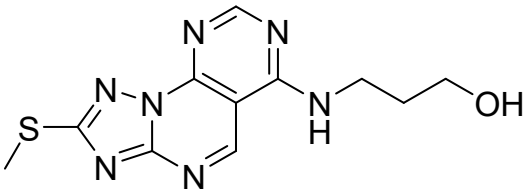
***N*-(*Tert*-butyl)-2-(methylthio)pyrimido[5,4-*e*][1,2,4]triazolo[1,5-*a*]pyrimidin-6-amine (24f).**



The crude product was recrystallized from *iso*-propanol. Pale yellow crystals (58 mg, 20% yield). R_f (AcOEt) = 0.5. M.p. = 255-256 °C. ^{1}H NMR (600 MHz, DMSO-d_6), δ, ppm. (*J*, Hz): 9.69 (s, C5H, H); 8.65 (s, C8H, H); 8.26 (s, NH, H); 2.71 (s, S-CH_3, 3H); 1.58 (s, 3CH_3, 9H). ^{13}C NMR (150 MHz, DMSO-d_6), δ, ppm.: 166.6, 161.0, 159.3, 156.5, 153.7, 149.5, 98.9, 53.8, 28.4, 13.4. IR, ν, cm^{-1}: 3327, 3290, 3083, 2962, 2931, 2221, 1655, 1584, 1568, 1517, 1476, 1458, 1434, 1409, 1349, 1288, 1243, 1200, 1136, 1114, 1011, 988, 967, 948, 899, 803, 768, 708, 675, 641, 579, 551, 534. MS (EI, 70 eV), m/z: Calcd for: $C_{12}H_{15}N_7S$,

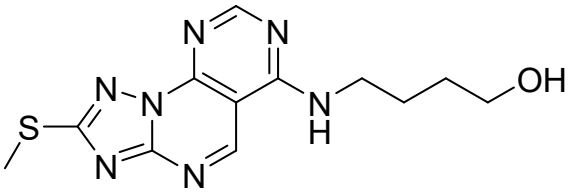
289; found $C_{12}H_{15}N_7S$, 289. Anal. Calcd. For $C_{12}H_{15}N_7S$: C, 49.81; H, 5.23; N, 33.88; found: C, 49.91; H, 5.25; N, 33.88

3-((2-(Methylthio)pyrimido[5,4-*e*][1,2,4]triazolo[1,5-*a*]pyrimidin-6-yl)amino)propan-1-ol (24g).



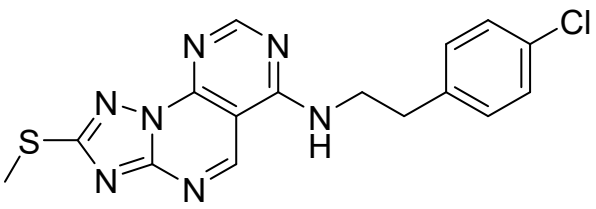
The crude product was recrystallized from EtOH. Pale yellow powder (125 mg, 43% yield). R_f (AcOEt) = 0.4. M.p. = 246-247 °C. ^{1}H NMR (600 MHz, DMSO-d_6), δ, ppm. (*J*, Hz): 9.52 (s, C5H, H); 9.20 (t, J = 6.0 Hz, NH, H); 8.68 (s, C8H, H); 4.57 (t, J = 5.4 Hz, OH, H); 3.65 (dt, J_1 = 7.8 Hz, J_2 = 6.0 Hz, NCH_2, 2H); 3.52 (dt, J_1 = 6.6 Hz, J_2 = 5.4 Hz, OCH_2, 2H); 2.68 (s, S-CH_3, 3H); 1.79–1.84 (m, CH_2, 2H). ^{13}C NMR (150 MHz, DMSO-d_6), δ, ppm.: 166.6, 162.0, 159.4, 156.6, 152.9, 149.4, 98.6, 58.4, 38.5, 31.7, 13.4. IR, ν, cm^{-1}: 3442, 3369, 3336, 3238, 3195, 3164, 3116, 2990, 2951, 2915, 2870, 2772, 2744, 2675, 2652, 1651, 1594, 1570, 1518, 1455, 1405, 1341, 1285, 1252, 1191, 1154, 1122, 1094, 1070, 1020, 969, 944, 894, 854, 800, 759, 726, 702, 624, 575, 559, 519. MS (EI, 70 eV), m/z: Calcd for: $C_{11}H_{13}N_7OS$, 291; found $C_{11}H_{13}N_7OS$, 291. Anal. Calcd. For $C_{11}H_{13}N_7OS$: C, 45.35; H, 4.50; N, 33.66; found: C, 45.47; H, 4.36; N, 33.80

4-((2-(Methylthio)pyrimido[5,4-*e*][1,2,4]triazolo[1,5-*a*]pyrimidin-6-yl)amino)butan-1-ol (24h).



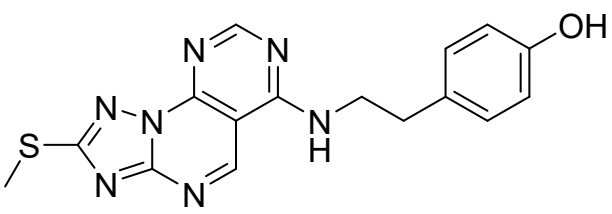
The crude product was recrystallized from EtOH. Pale yellow powder (195 mg, 64% yield). R_f (AcOEt) = 0.1. M.p. = 201-202 °C. ^{1}H NMR (600 MHz, DMSO-d_6), δ, ppm. (*J*, Hz): 9.52 (s, C5H, H); 9.21 (t, J = 6.0 Hz, NH, H); 8.68 (s, C8H, H); 4.46 (t, J = 4.8 Hz, OH, H); 3.59 (dt, J_1 = 7.2 Hz, J_2 = 6.4 Hz, NCH_2, 2H), 3.45 (dt, J_1 = 7.6 Hz, J_2 = 6.0 Hz, OCH_2, 2H); 2.68 (s, S-CH_3, 3H); 1.68–1.72 (m, CH_2, 2H); 1.51–1.56 (m, CH_2, 2H). ^{13}C NMR (150 MHz, DMSO-d_6), δ, ppm.: 166.6, 162.0, 159.4, 156.6, 152.9, 149.4, 98.5, 60.4, 41.0, 29.9, 25.2, 13.4. IR, ν, cm^{-1}: 3402, 3312, 3229, 3132, 3104, 3009, 2943, 2883, 1584, 1467, 1516, 1480, 1452, 1410, 1372, 1349, 1333, 1280, 1249, 1227, 1160, 1121, 1090, 1062 1027, 999, 985, 962, 939, 903, 879, 826, 801, 756, 722, 701, 668, 632, 577, 559, 522, 511. MS (EI, 70 eV), m/z: Calcd for: $C_{12}H_{15}N_7OS$, 305; found $C_{12}H_{15}N_7OS$, 305. Anal. Calcd. For $C_{12}H_{15}N_7OS$: C, 47.20; H, 4.95; N, 32.11; found: C, 47.11; H, 5.06; N, 32.00. HRMS (ESI, Q-TOF), m/z: $[M+H]^+$ Calculated for $C_{12}H_{16}N_7OS^+$ 306.1132. Found 306.1132

***N*-(4-Chlorophenethyl)-2-(methylthio)pyrimido[5,4-*e*][1,2,4]triazolo[1,5-a]pyrimidin-6-amine (24k).**



Pale yellow powder (274 mg, 74% yield). R_f (AcOEt) = 0.3. M.p. = 283-294 °C. ^{1}H NMR (400 MHz, DMSO-d_6), δ, ppm. (*J*, Hz): 9.49 (s, C5H, H); 9.26 (t, *J* = 5.7 Hz, NH, H); 8.65 (s, C8H, H); 7.29 (s, 4CH, 4H); 3.83 (dt, J_1 = 6.8 Hz, J_2 = 5.7 Hz, NCH_2, 2H); 2.98 (t, *J* = 7.4 Hz, CH_2,2H); 2.71 (s, S-CH_3, 3H). ^{13}C NMR (100 MHz, DMSO-d_6), δ, ppm.: 166.6, 161.9, 159.3, 156.6, 155.8, 152.7, 149.3, 129.6, 128.9, 115.2, 98.5, 42.9, 33.6, 13.4. IR, ν, cm^{-1}: 3314, 3293, 3269, 3253, 3196, 3106, 3019, 2940, 2906, 2871, 1901, 1589, 1572, 1522, 1488, 1454, 1436, 1404, 1388, 1355, 1322, 1285, 1248, 1202, 1139, 1116, 1092, 1063, 1015, 984, 971, 894, 841, 812, 799, 777, 755, 733, 717, 706, 662, 598, 553, 518. MS (EI, 70 eV), m/z: Calcd for: $C_{16}H_{14}Cl^{35}N_7S$, 371; found $C_{16}H_{14}Cl^{35}N_7S$, 371. Anal. Calcd. For $C_{16}H_{14}ClN_7S$: C, 51.68; H, 3.79; N, 26.37; found: C, 51.77; H, 3.74; N, 26.19

4-(2-((2-(Methylthio)pyrimido[5,4-*e*][1,2,4]triazolo[1,5-*a*]pyrimidin-6-yl)amino)ethyl)phenol (24l).

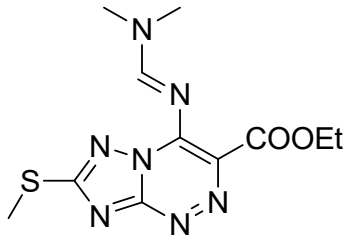


Orange powder (109 mg, 31% yield). R_f (AcOEt) = 0.6. M.p. = 229-230 °C. ^{1}H NMR (400 MHz, DMSO-d_6), δ, ppm. (*J*, Hz): 9.50 (s, C5H, H); 9.25 (t, *J* = 6.4 Hz, NH, H); 8.98 (s, OH, H); 8.65 (s, C8H, H); 7.03 (d, *J* = 8.4 Hz, 2CH, 2H); 6.66 (d, *J* = 8.4 Hz, 2CH, 2H); 3.86 (dt, J_1 = 8.0 Hz, J_2 = 6.4 Hz, NCH_2, 2H); 2.86 (t, *J* = 8.0 Hz, CH_2, 2H); 2.71 (s, S-CH_3, 3H). ^{13}C NMR (100 MHz, DMSO-d_6), δ, ppm.: 166.5, 161.5, 159.2, 156.3, 152.4, 149.1, 137.7, 130.7, 130.2, 127.9, 98.2, 41.9, 33.4, 13.1. IR, ν, cm^{-1}: 1570, 1513, 1444, 1407, 1335, 1278, 1259, 1225, 1147, 1114, 1075, 978, 898, 854, 828, 801, 726, 704, 580, 553, 507. MS (EI, 70 eV), m/z: Calcd for: $C_{16}H_{15}N_7OS$, 353; found $C_{16}H_{15}N_7OS$, 353. Anal. Calcd. For $C_{16}H_{15}N_7OS$: C, 54.38; H, 4.28; N, 27.74; found: C, 54.44; H, 4.39; N, 27.71

General method for the synthesis of *N′*-([1,2,4]triazoloazinyl)-*N*,*N*-dimethylformimidamide 27a, 27b, 28a, 28b.

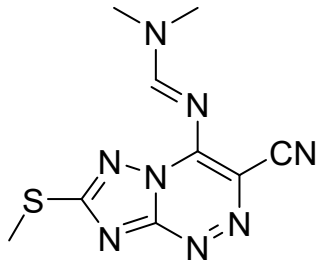
DMF-DMA (0.200 mL, 0.0015 mol, 1.5 equiv.) was added to a suspension of appropriate [1,2,4]triazoloazine **17a/17b/18a/18b** (0.001 mol) in 1,4-dioxane (7 mL). The resulting mixture was refluxed for 3 hours, cooled to RT, filtered, and solids were washed with Et_2O (5 mL).

Ethyl 4-(((dimethylamino)methylene)amino)-7-(methylthio)-[1,2,4]triazolo[5,1-*c*][1,2,4]triazine-3-carboxylate (27a).



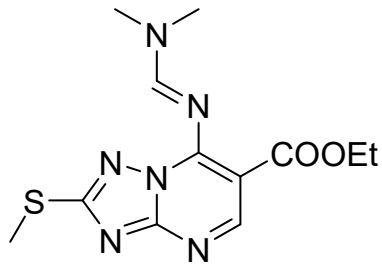
Light brown powder (269 mg, 87% yield). R_f (AcOEt) = 0.5. M.p. = 167 °C. ^{1}H NMR (400 MHz, DMSO-d_6), δ, ppm. (*J*, Hz): 9.10 (s, CH, H); 4.38 (q, *J* = 7.1 Hz, CH_2, 2H); 3.35 (s, CH_3, 3H); 3.24 (s, CH_3, 3H); 2.71 (s, S-CH_3, 3H); 1.39 (t, J = 7.1 Hz, CH_3, 3H). ^{13}C NMR (100 MHz, DMSO-d_6), δ, ppm.: 169.1, 164.0, 160.2, 157.6, 141.0, 132.3, 61.3, 41.4, 34.9, 14.1, 13.5. IR, ν, cm^{-1}: 2994, 2978, 2956, 2929, 1703, 1642, 1621, 1548, 1514, 1369, 1437, 1400, 1364, 1345, 1326, 1314, 1294, 1201, 1143, 1102, 1056, 1008, 968, 862, 847, 792, 755, 723, 706, 680, 637, 600, 589, 566, 538, 519, 503. MS (EI, 70 eV), m/z: Calcd for: $C_{11}H_{15}N_7O_2S$, 309; found $C_{11}H_{15}N_7O_2S$, 309. Anal. Calcd. For $C_{11}H_{15}N_7O_2S$: C, 42.71; H, 4.89; N, 31.69; found: C, 42.75; H, 4.89; N, 31.78

***N*'-(3-Cyano-7-(methylthio)-[1,2,4]triazolo[5,1-*c*][1,2,4]triazin-4-yl)-*N*,*N*-dimethylformimidamide (27b).**



Green powder (231 mg, 88% yield). R_f (AcOEt) = 0.6. M.p. = 222 °C. ^{1}H NMR (400 MHz, DMSO-d_6), δ, ppm. (*J*, Hz): 9.59 (s, CH, H); 3.44 (s, CH_3, 3H); 3.34 (s, CH_3, 3H); 2.74 (s, S-CH_3, 3H). ^{13}C NMR (100 MHz, DMSO-d_6), δ, ppm.: 169.6, 161.1, 157.4, 142.9, 119.2, 115.6, 42.2, 35.3, 13.5. IR, ν, cm^{-1}: 3202, 3164, 3142, 3083, 3062, 2967, 2928, 2868, 2854, 1513, 1572, 1535, 1468, 1438, 1411, 1389, 1361, 1330, 1307, 1273, 1248, 1183, 1099, 999, 982, 969, 886, 800, 783, 739, 705, 667, 622, 587, 555, 515. MS (EI, 70 eV), m/z: Calcd for: $C_9H_{10}N_8S$, 262; found $C_9H_{10}N_8S$, 262. Anal. Calcd. For $C_9H_{10}N_8S$: C, 41.21; H, 3.84; N, 42.72; found: C, 41.17; H, 3.88; N, 42.70

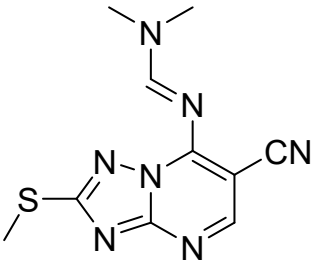
Ethyl 7-(((dimethylamino)methylene)amino)-2-(methylthio)-[1,2,4]triazolo[1,5-*a*]pyrimidine-6-carboxylate (28a).



Pale yellow powder (293 mg, 95% yield). R_f (AcOEt) = 0.45. M.p. = 135 °C. ^{1}H NMR (400 MHz, DMSO-d_6), δ, ppm. (*J*, Hz): 8.83 (s, CH, H); 8.45 (s, C5H, H); 4.24 (q, *J* = 7.1 Hz, CH_2, 2H); 3.23 (s, CH_3, 3H); 3.15 (s, CH_3, 3H); 2.62 (s, S-CH_3, 3H); 1.28 (t, *J* = 7.1 Hz, CH_3, 3H). ^{13}C NMR (100 MHz, DMSO-d_6), δ, ppm.: 166.8, 164.5, 159.1, 157.4, 156.4, 152.2, 102.3, 60.6, 40.6, 34.6, 14.0, 13.3. IR, ν, cm^{-1}: 2994, 2976, 2929, 2900, 2873, 1718, 1704, 1632, 1571, 15337, 1521, 1472, 1416, 1393, 1368, 1333, 1315, 1110, 1092, 1025, 991, 981, 955, 876, 864, 782, 711, 695, 682, 652, 624, 612, 592, 574, 539, 522. MS (EI, 70 eV), m/z: Calcd for: $C_{12}H_{16}N_6O_2S$, 308; found

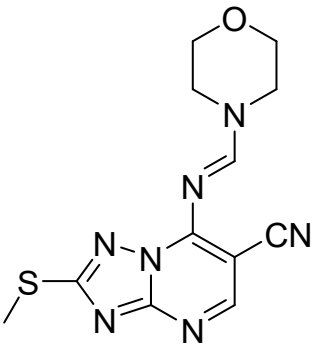
$C_{12}H_{16}N_6O_2S$, 308. Anal. Calcd. For $C_{12}H_{16}N_6O_2S$: C, 46.74; H, 5.23; N, 27.25; found: C, 46.85; H, 5.11; N, 27.13

***N*'-(6-Cyano-2-(methylthio)-[1,2,4]triazolo[1,5-*a*]pyrimidin-7-yl)-*N*,*N*-dimethylformimidamide (28b).**



Pale yellow powder (217 mg, 83% yield). R_f (AcOEt) = 0.55. M.p. = 241 °C. ^{1}H NMR (400 MHz, DMSO-d_6), δ, ppm. (*J*, Hz): 9.39 (s, CH, H); 8.66 (s, C5H, H); 3.33 (s, CH_3, 3H); 3.23 (s, CH_3, 3H); 2.65 (s, S-CH_3, 3H). ^{13}C NMR (100 MHz, DMSO-d_6), δ, ppm.: 167.4, 159.9, 157.5, 156.5, 151.1, 115.8, 87.3, 41.4, 34.6, 13.1. IR, ν, cm^{-1}: 2218, 1625, 1576, 1537, 1503, 1470, 1435, 1391, 1364, 1335, 1283, 1252, 1215, 1130, 1108, 985, 958, 916, 859, 809, 762, 736, 712, 684, 605, 554, 521. MS (EI, 70 eV), m/z: Calcd for: $C_{10}H_{11}N_7S$, 261; found $C_{10}H_{11}N_7S$, 261. Anal. Calcd. For $C_{10}H_{11}N_7S$: C, 45.96; H, 4.24; N, 37.52; found: C, 46.03; H, 4.23; N, 37.66

2-(Methylthio)-7-((morpholinomethylene)amino)-[1,2,4]triazolo[1,5-*a*]pyrimidine-6-carbonitrile (29).

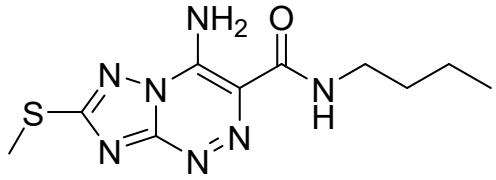


Morpholine (0.130 mL, 0.0015 mol, 1.5 equiv.) was added to a suspension of *N*'-(6-cyano-2-(methylthio)-[1,2,4]triazolo[1,5-*a*]pyrimidin-7-yl)-*N,N*-dimethylformimidamide **28b** (0.261 g, 0.001 mol) in MeCN (7 mL). The resulting mixture was refluxed for 7 hours, cooled to RT, filtered, and solids were washed with Et_2O (5 mL).

White powder (203 mg, 67% yield). R_f (AcOEt) = 0.7. M.p. = 216 °C. ^{1}H NMR (600 MHz, DMSO-d_6), δ, ppm. (*J*, Hz): 9.53 (s, CH, H); 8.72 (s, C5H, H); 3.90 (t, *J* = 5.1 Hz, CH_2, 2H); 3.78 (t, *J* = 5.1 Hz, 3CH_2, 6H); 2.65 (s, S-CH_3, 3H). ^{13}C NMR (100 MHz, DMSO-d_6), δ, ppm.: 167.7, 158.9, 157.7, 156.8, 151.3, 116.0, 87.7, 66.4, 65.4, 50.7, 43.6, 13.3. IR, ν, cm^{-1}: 3018, 3008, 2990, 2928, 2871, 2226, 1605, 1582, 1543, 1520, 1456, 1445, 1431, 1398, 1351, 1317, 1302, 1290, 1267, 1258, 1243, 1176, 1110, 1067, 1021, 992, 976, 969, 952, 931, 902, 861, 819, 791, 768, 738, 709, 688, 672, 638, 619, 594, 572, 550, 529, 518. MS (EI, 70 eV), m/z: Calcd for: $C_{12}H_{13}N_7OS$, 303; found $C_{12}H_{13}N_7OS$, 303. Anal. Calcd. For $C_{12}H_{13}N_7OS$: C, 47.51; H, 4.32; N, 32.32; found: C, 47.65; H, 4.25; N, 32.40

4-Amino-*N*-butyl-7-(methylthio)-[1,2,4]triazolo[5,1-*c*][1,2,4]triazine-3-carboxamide (30d).

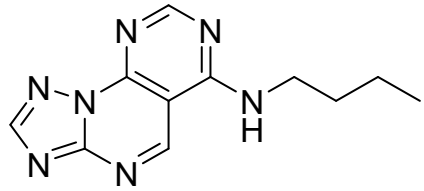
n-Butylamine (0.300 mL, 0.003 mol, 3 equiv.) and AcOH (0.172 mL, 0.003 mol, 3 equiv.) were added consequently to a suspension of 2-methylthio-3-ethoxycarbonyl-4-amino[1,2,4]triazolo[5,1-*c*][1,2,4]triazine **17a** (0.001 mol) in toluene (7 mL). The resulting mixture was heated at 140 °C in autoclave for 8 hours, cooled to RT, filtered, and solids were washed with Et_2O (5 mL).



White powder (225 mg, 80% yield). R_f (AcOEt) = 0.1. M.p. = 203 °C. ^{1}H NMR (600 MHz, DMSO-d_6), δ, ppm. (*J*, Hz): 9.96 (br.s, NH ,H); 9.45 (br.s, NH_2, H); 8.82 (br.s, NH_2, H); 3.45 (t, *J* = 7.4 Hz, NCH_2, 2H); 2.63 (s, S-CH_3, 3H); 1.60–1.65 (m, CH_2, 2H); 1.35–1.41 (m, CH_2, 2H); 0.92 (t, *J* = 7.4 Hz, CH_3, 3H). ^{13}C NMR (100 MHz, DMSO-d_6), δ, ppm.: 166.1, 159.6, 158.8, 149.6, 123.1, 41.2, 29.8, 19.4, 13.6, 13.4. IR, ν, cm^{-1}: 3390, 3200, 2986, 2932, 2851, 2719, 1700, 1640, 1546, 1465, 1441, 1409, 13390, 1372, 1347, 1325, 1295, 1269, 1241, 1178, 1164, 1083, 1003, 970, 913, 853, 788, 776, 758, 708, 687, 669, 643, 616, 576, 554. MS (EI, 70 eV), m/z: Calcd for: $C_{10}H_{15}N_7OS$, 281; found $C_{10}H_{15}N_7OS$, 281. Anal. Calcd. For $C_{10}H_{15}N_7OS$: C, 42.69; H, 5.37; N, 34.85; found: C, 42.77; H, 5.40; N, 34.69

General method for the synthesis of pyrimido[5,4-*e*][1,2,4]triazolo[1,5-*a*]pyrimidin-6-amines 36-39.

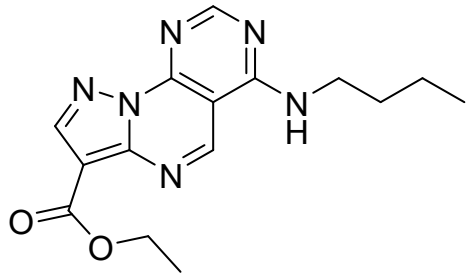
Triethylortoformate (0.498 mL, 0.003 mol, 3 equiv.), *n*-butylamine (0.300 mL, 0.003 mol, 3 equiv.) and AcOH (0.172 mL, 0.003 mol, 3 equiv.) were added consequently to a suspension of appropriate 7-amino-6-cyano[1,2,4]triazolo[1,5-*a*]pyrimidine **32-35** (0.001 mol) in toluene (7 mL). The resulting mixture was heated in autoclave at 140 °C for 12 hours, cooled to RT, filtered, and solids were washed with Et_2O (5 mL). Another crop of product could be obtained from the mother liquor. The mother liquor was concentrated at reduced pressure, the residue was treated with Et_2O (10 mL), filtered, and solids were washed with Et_2O (5 mL).



***N*-butylpyrimido[5,4-*e*][1,2,4]triazolo[1,5-*a*]pyrimidin-6-amine (36).**

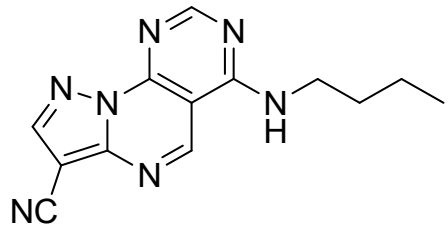
Yellow powder (192 mg, 79% yield). R_f (AcOEt) = 0.6. M.p. = 235 °C. ^{1}H NMR (400 MHz, DMSO-d_6), δ, ppm. (*J*, Hz): 9.59 (s, C5H, H); 9.19 (s, NH, H); 8.71 (s, C2H, H); 8.65 (s, C8H, H); 3.58 (t, *J* = 7.1 Hz, NCH_2, 2H); 1.60–1.67 (m, CH_2, 2H); 1.34–1.43 (m, CH_2, 2H); 0.92 (t, *J* = 7.4 Hz, CH_3, 3H). ^{13}C NMR (100 MHz, DMSO-d_6), δ, ppm.: 161.9, 159.4, 155.9, 155.1, 153.0, 150.5, 98.7, 40.8, 30.5, 19.6, 13.7. IR, ν, cm^{-1}: 3308, 3258, 3174, 3162, 3103, 2955, 2936, 2872, 1603, 1592, 1574, 1525, 1515, 1457, 1442, 1420, 1496, 1356, 1315, 1260, 1249, 1229, 1183, 1171, 1115, 1099, 1067, 1006, 946, 926, 892, 801, 748, 726, 704, 685, 667, 650, 603, 576, 560, 542, 518, 507. MS (EI, 70 eV), m/z: Calcd for: $C_{11}H_{13}N_7$, 243; found $C_{11}H_{13}N_7$, 243. Anal. Calcd. For $C_{11}H_{13}N_7$: C, 54.31; H, 5.39; N, 40.30; found: C, 54.33; H, 5.45; N, 40.39

Ethyl 4-(butylamino)pyrazolo[1,5-*a*]pyrimido[5,4-*e*]pyrimidine-7-carboxylate (37).



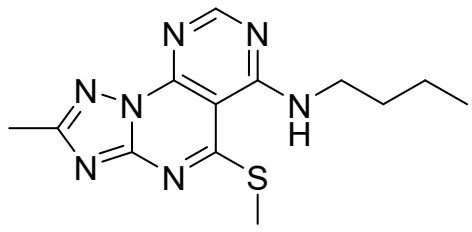
White powder (165 mg, 77% yield). R_f (AcOEt) = 0.6. M.p. > 300 °C. ^{1}H NMR (400 MHz, DMSO-d_6), δ, ppm. (*J*, Hz): 9.45 (s, C5H, H); 9.04 (br.s, NH, H); 8.70 (s, C2H, H); 8.55 (s, C8H, H); 4.32 (dt, J_1 = 6.8 Hz, J_2 = 8.0 Hz, NCH_2, 2H); 3.60 (q, *J* = 7.2 Hz, OCH_2, 2H); 1.64–1.68 (m, CH_2, 2H); 1.38–1.42 (m, CH_2, 2H); 1.34 (t, *J* = 7.1 Hz, CH_3, 3H); 0.94 (t, *J* = 7.2 Hz, CH_3, 3H). ^{13}C NMR (100 MHz, DMSO-d_6), δ, ppm.: 161.7, 161.3, 159.1, 150.1, 149.9, 147.8, 146.2, 104.5, 98.2, 59.5, 40.6, 30.4, 19.4, 14.1, 13.4. IR, ν, cm^{-1}: 3289, 3181, 3146, 3001, 2958, 2932, 2866, 1711, 1595, 1573, 1553, 1486, 1451, 1434, 1400, 1379, 1354, 1254, 1222, 1180, 1126, 1103, 1022, 985, 945, 917, 890, 835, 799, 772, 742, 703, 673, 633, 610, 549, 538, 508. MS (EI, 70 eV), m/z: Calcd for: $C_{15}H_{18}N_6O_2$, 314; found $C_{15}H_{18}N_6O_2$, 314. Anal. Calcd. For $C_{15}H_{18}N_6O_2$: C, 57.31; H, 5.77; N, 26.74; found: C, 57.40; H, 5.66; N, 26.89

3-Butyl-4-imino-3,4-dihydropyrazolo[1,5-*a*]pyrimido[5,4-*e*]pyrimidine-7-carbonitrile (38).



The crude product was recrystallized from EtOH. Yellow powder (200 mg, 75% yield). R_f (AcOEt) = 0.6. M.p. = 252 °C. ^{1}H NMR (600 MHz, DMSO-d_6), δ, ppm. (*J*, Hz): 9.48 (s, C5H, H); 9.23 (t, *J* = 5.4 Hz, NH, H); 8.78 (s, C2H, H); 8.72 (s, C8H, H); 3.58 (t, *J* = 7.2 Hz, NCH_2, 2H); 1.62–1.66 (m, CH_2, 2H); 1.36–1.43 (m, CH_2, 2H); 0.93 (t, *J* = 7.2 Hz, CH_3, 3H). ^{13}C NMR (150 MHz, DMSO-d_6), δ, ppm.: 162.2, 159.3, 151.2 (2C), 150.4, 146.8, 113.2, 99.0, 84.0, 40.8, 30.5, 19.6, 13.7. IR, ν, cm^{-1}: 3372, 3328, 3292, 2958, 2939, 2873, 2241, 1605, 1594, 1572, 1470, 1452, 1429, 1395, 1357, 1336, 1312, 1254, 1236, 1187, 1155, 1109, 1071, 1009, 992, 946, 917, 904, 889, 799, 738, 707, 683, 662, 637, 630, 600, 555, 539, 513. MS (EI, 70 eV), m/z: Calcd for: $C_{13}H_{13}N_7$, 267; found $C_{13}H_{13}N_7$, 267. Anal. Calcd. For $C_{13}H_{13}N_7$: C, 58.42; H, 4.90; N, 36.68; found: C, 58.51; H, 4.80; N, 36.66

***N*-Butyl-2-methyl-5-(methylthio)pyrimido[5,4-*e*][1,2,4]triazolo[1,5-*a*]pyrimidin-6-amine (39).**

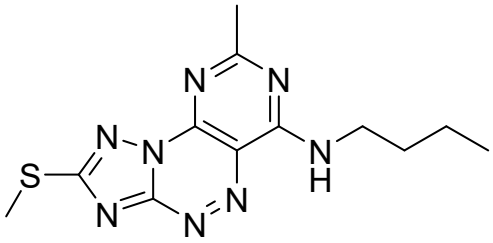


White powder (167 mg, 55% yield). R_f (AcOEt) = 0.5. M.p. = 223 °C. ^{1}H NMR (400 MHz, DMSO-d_6), δ, ppm. (*J*, Hz): 8.62 (s, C8H, H); 7.75 (br.s, NH, H); 3.64 (t, *J* = 6.8 Hz, NCH_2, 2H); 2.75 (s, S-CH_3, 3H); 2.45 (s, CH_3, 3H); 1.61–1.68 (m, CH_2, 2H); 1.37–1.46 (m, CH_2, 2H); 0.94 (t, *J* = 7.2 Hz, CH_3, 3H). ^{13}C NMR (100 MHz, DMSO-d_6), δ, ppm.: 164.5, 164.0, 160.1, 158.6, 154.2, 149.8, 97.4, 41.5, 30.3, 19.6, 14.7, 14.1, 13.7. IR, ν, cm^{-1}: 3385, 3005, 2957, 2925,

2891, 2870, 2834, 1592, 1556, 1498, 1454, 1402, 1369, 1458, 1328, 1267, 1249, 1233, 1181, 1113, 1073, 1037, 1016, 994, 978, 963, 892, 848, 803, 765, 752, 736, 715, 691, 670, 660, 650, 631, 616, 602, 577, 538. MS (EI, 70 eV), m/z: Calcd for: $C_{13}H_{17}N_7S$, 303; found $C_{13}H_{17}N_7S$, 303. Anal. Calcd. For $C_{13}H_{17}N_7S$: C, 51.47; H, 5.65; N, 32.32; found: C, 51.56; H, 5.72; N, 32.27

_N_-Butyl-8-methyl-2-(methylthio)pyrimido[4,5-*e*][1,2,4]triazolo[5,1-*c*][1,2,4]triazin-6-amine (40).

Triethylortoacetate (0.549 mL, 0.003 mol, 3 equiv.), *n*-butylamine (0.300 mL, 0.003 mol, 3 equiv.) and AcOH (0.172 mL, 0.003 mol, 3 equiv.) were added consequently to a suspension of 4-amino-3-cyano-7-methylsulfanyl[1,2,4]triazolo[5,1-c][1,2,4]triazine **18b** (0.207 g, 0.001 mol) in toluene (7 mL). The resulting mixture was heated in autoclave at 140 °C for 12 hours, cooled to RT, filtered, and solids were washed with Et_2O (5 mL). Another crop of product could be obtained from the mother liquor. The mother liquor was concentrated at reduced pressure, the residue was treated with Et_2O (10 mL), filtered, and solids were washed with Et_2O (5 mL).



Brown powder (67 mg, 22% yield). R_f (AcOEt) = 0.65. M.p. = 259 °C. ^{1}H NMR (400 MHz, DMSO-d_6), δ, ppm. (*J*, Hz): 10.04 (s, NH, H); 3.68 (br.s, NCH_2, 2H); 2.78 (s, S-CH_3, 3H); 2.62 (s, CH_3, 3H); 1.67–1.74 (m, CH_2, 2H); 1.38–1.48 (m, CH_2, 2H); 0.99 (t, *J* = 7.4 Hz, CH_3, 3H). ^{13}C NMR (100 MHz, DMSO-d_6), δ, ppm.: 173.4, 168.7, 158.7, 157.7, 139.9, 122.1, 40.4, 30.5, 27.2, 19.5, 13.6, 13.6. IR, ν, cm^{-1}: 3269, 3252, 3158, 2958, 2930, 2872, 2819, 1688, 1614, 1580, 1530, 1484, 1468, 1441, 1375, 1338, 1294, 1276 1211, 1184, 1140, 1113, 1089, 1030, 990, 936, 921, 859, 839, 815, 800, 766, 741, 718, 703, 669, 642, 626, 570, 541, 524, 514. MS (EI, 70 eV), m/z: Calcd for: $C_{12}H_{16}N_8S$, 304; found $C_{12}H_{16}N_8S$, 304. Anal. Calcd. For $C_{12}H_{16}N_8S$: C, 47.35; H, 5.30; N, 36.81; found: C, 47.26; H, 5.34; N, 36.96

Alternative method for the synthesis of _N_-butyl-2-(methylthio)pyrimido[1,2,4]triazoloazin-6-amines 23d, 24d from aminocyano[1,2,4]triazoloazines 17b, 18b.

Triethylortoformate (0.498 mL, 0.003 mol, 3 equiv.) and *n*-butylamine (0.300 mL, 0.003 mol, 3 equiv.) were added consequently to a suspension of appropriate aminocyano[1,2,4]triazoloazine **17b, 18b** (0.001 mol) in toluene (7 mL). The resulting mixture was heated at 140 °C in autoclave for 8 hours, cooled to RT, filtered, and solids were washed with Et_2O (5 mL). Another crop of products could be obtained from the mother liquor. The mother liquor was concentrated at reduced pressure, the residue was treated with Et_2O (10 mL), filtered, and solids were washed with Et_2O (5 mL).

Alternative method for the synthesis of *N*-butyl-2-(methylthio)pyrimido[1,2,4]triazolo-azin-6-amines 23d, 24d from *N*'-(cyano-(methylthio)-[1,2,4]triazoloazinyl)-*N,N*-dimethylformimidamides 27b, 28b.

n-Butylamine (0.300 mL, 0.003 mol, 3 equiv.) was added to a suspension of appropriate *N*'-(cyano-(methylthio)-[1,2,4]triazoloazinyl)-*N,N*-dimethylformimidamide **27b, 28b** (0.001 mol) in MeCN (7 mL). The resulting mixture was refluxed for 8 hours, cooled to RT, filtered, and solids were washed with Et_2O (5 mL).

Alternative method for the synthesis of *N*-butyl-2-(methylthio)pyrimido[1,2,4]triazoloazin-6-amines 23d, 24d from amino-*N*-butyl-(methylthio)-[1,2,4]triazoloazinecarboximidamides 21d, 22d

A mixture of appropriate amino-*N*-butyl-(methylthio)-[1,2,4]triazoloazinecarboximidamide **21d, 22d** (0.001 mol) and triethylortoformate (5 mL) was heated at reflux for 8 hours, cooled to RT, filtered, and solids were washed with Et_2O (5 mL).

Alternative method for the synthesis of 7-butyl-2-(methylthio)pyrimido[5,4-e][1,2,4]triazolo[1,5-*a*]pyrimidin-6(7H)-one 20d from 2-methylthio-6-ethoxycarbonyl-7-amino-[1,2,4]triazolo[1,5-a]pyrimidine 18a.

Triethylortoformate (0.498 mL, 0.003 mol, 3 equiv.) and *n*-butylamine (0.300 mL, 0.003 mol, 3 equiv.) were added consequently to a suspension of 2-methylthio-6-ethoxycarbonyl-7-amino-[1,2,4]triazolo[1,5-*a*]pyrimidine **18a** (0.253 g, 0.001 mol) in toluene (7 mL). The resulting mixture was heated at 140 °C in autoclave for 8 hours, cooled to RT, filtered, and solids were washed with Et_2O (5 mL).

Alternative method for the synthesis of 4-(2-(methylthio)pyrimido[4,5-e][1,2,4]triazolo[5,1-*c*][1,2,4]triazin-6-yl)morpholine 23m from *N*'-(6-cyano-2-(methylthio)-[1,2,4]triazolo[5,1-*c*][1,2,4]triazin-6-yl)-N,N-dimethylformimidamide 27b.

Morpholine (0.260 mL, 0.003 mol, 3 equiv.) was added to a suspension of *N*'-(6-cyano-2-(methylthio)-[1,2,4]triazolo[5,1-*c*][1,2,4]triazin-6-yl)-*N,N*-dimethylformimidamide **27b** (0.001 mol) in MeCN (7 mL). The resulting mixture was refluxed for 8 hours, cooled to RT, filtered, and solids were washed with Et_2O (5 mL).

Alternative method for the synthesis of 4-(2-(methylthio)pyrimido[4,5-e][1,2,4]triazolo[5,1-*c*][1,2,4]triazin-6-yl)morpholine 23m from 3-(imino(morpholino)methyl)-7-(methylthio)-[1,2,4]triazolo[5,1-*c*][1,2,4]triazin-4-amine 21m.

A mixture of 3-(imino(morpholino)methyl)-7-(methylthio)-[1,2,4]triazolo[5,1-*c*][1,2,4]triazin-4-amine **21m** (0.001 mol), triethylortoformate (5 mL), and AcOH (5 mL) was heated at reflux for 6 hours, cooled to RT, filtered, and solids were washed with Et_2O (5 mL). Another crop of products could be obtained from the mother liquor. The mother liquor was concentrated at

reduced pressure, the residue was treated with Et_2O (10 mL), filtered, and solids were washed with Et_2O (5 mL).

Table 1. X-ray data for compound **23d**.

Parameter	Compound **23d**
Empirical formula	$C_{11}H_{14}N_8S$
Formula weight	290.36
T/K	295(2)
Crystal system	orthorhombic
Space group	Pbca
a/Å	13.0522(13)
b/Å	7.5876(12)
c/Å	28.440(4)
α/°	90
β/°	90
γ/°	90
V/Å^3	2816.5(6)
Z	8
ρ_{calc}g/cm^3	1.370
μ/mm^{-1}	0.234
F(000)	1216.0
Crystal size/mm^3	0.48 × 0.17 × 0.06
Radiation	Mo Kα (λ = 0.71073)
Index ranges	$-9 \leq h \leq 17$, $-10 \leq k \leq 10$, $-39 \leq l \leq 18$
2Θ range for data collection/°	5.72 to 61
Reflections collected	11951
Independent reflections	3957 [R_{int} = 0.0785, R_{sigma} = 0.0890]
Data/restraints/parameters	3957/0/184
Goodness-of-fit on F^2	0.999
Final R indexes [I>=2σ (I)]	R_1 = 0.0828, wR_2 = 0.2002
Final R indexes [all data]	R_1 = 0.1891, wR_2 = 0.2670
Largest diff. peak/hole / e Å^{-3}	0.28/-0.29

Cell Culture

Experiments were carried out on cultured human glioblastoma cells (A172, ATCC CRL 1620), human lung carinoma (A549, ATCC CCL 185), human liver carcinoma (HepG2, ATCC HB 8065), human embryo kidney cells (HEK-293, ATCC CRL 1573) obtained from a shared research facility, the "Vertebrate Cell Culture Collection" (Institute of Cytology RAS, St. Petersburg, Russia). The cells were cultured using DMEM/F-12 medium containing 10% fetal bovine serum (FBS) at 37°C, 5% CO_2 and 98% humidity. Subculturing using 0.25% trypsin solution was performed when the culture reached ≥ 90% confluency. DMEM/F-12, FBS and Trypsin were purchased from Biolot Ltd., St. Petersburg, Russia.

***In vitro* cytotoxicity assay**

The compounds were dissolved in DMSO. The solutions were diluted with DMEM/F-12 culture medium with 10 % FBS to the studied concentrations: 8–1024; 2–256; 1–128 μM. In all cases, the concentration of DMSO in the final solution did not exceed 1%. Cisplatin (1134357, U. S. Pharmacopeia, USA) was used as a comparison compound.

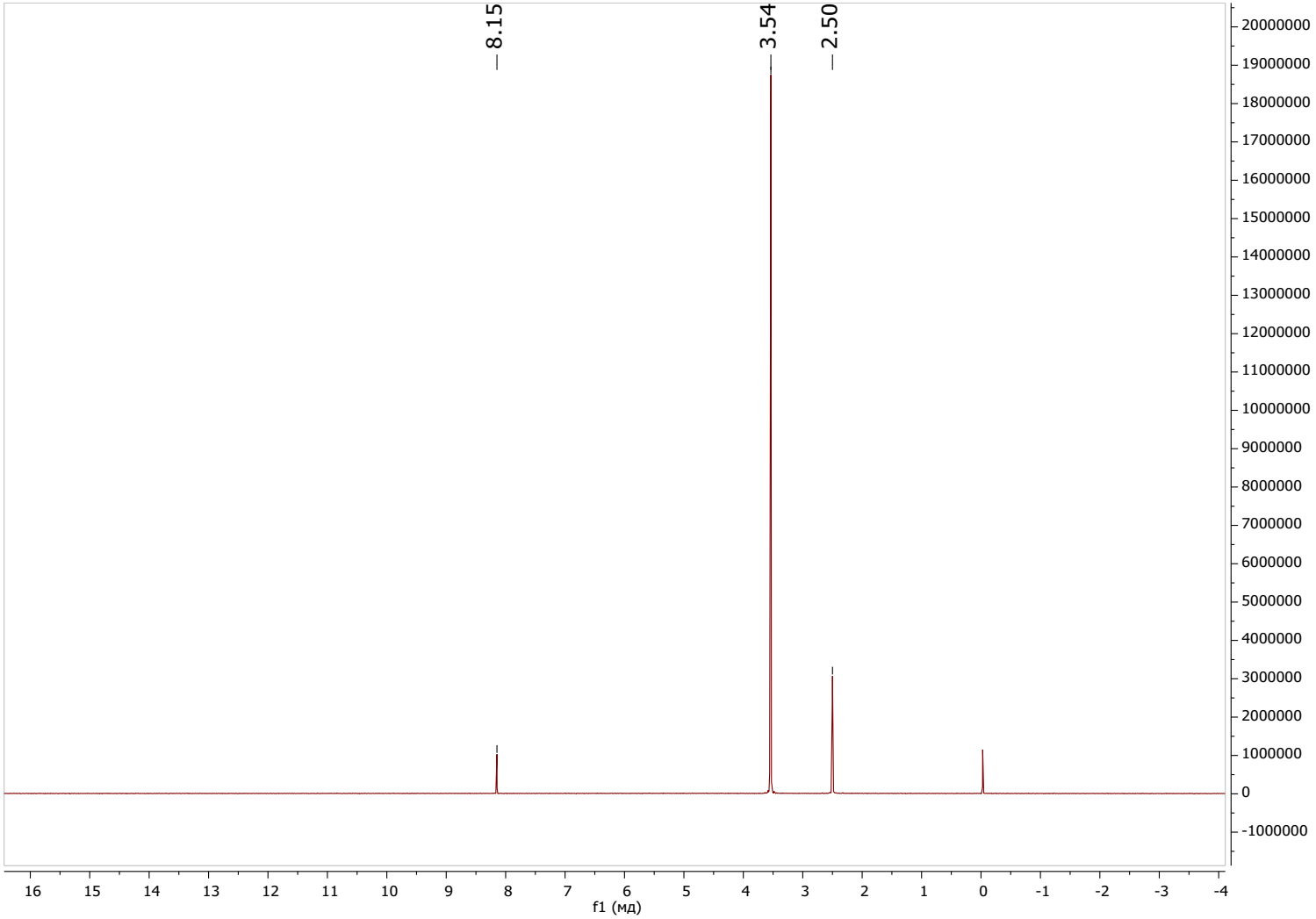
Cells were seeded in 96-well plates at a concentration of 4×10^3 cells per well. After 24 h, test compounds were added to the wells in a given concentration range. Then, the cells were incubated for 72 h, after which a solution of MTT (3-(4,5-dimethyl-2-thiazolyl)-2,5-diphenyl-2Htetrazolium bromide) (Dia-m, Russia) was added to the cultures at 20 μL (5 mg/mL) per well. After 2 h, the medium was removed from the wells and 200 μL of a mixture of DMSO and propanol-2, 1:1, was added. Optical density was measured on a plate spectrophotometer (Victor Nivo™, PerkinElmer, USA) at a wavelength of 570 nm.

Statistical Analysis

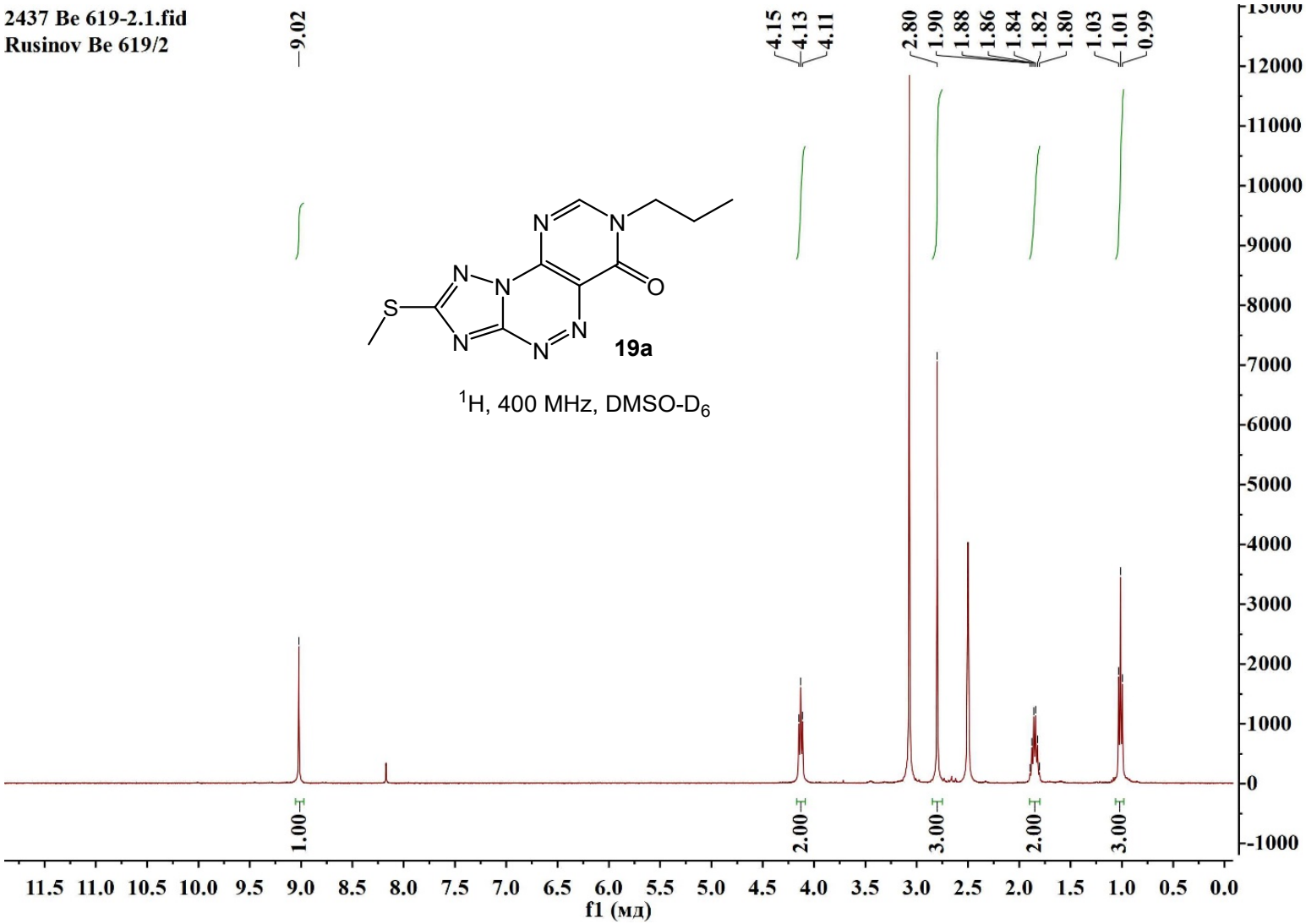
Statistical data processing was carried out in the RStudio program (Version 2023.09.1© 2009-2023 RStudio, PBC) using the R package (version 4.3.2). The cytotoxicity index (IC50) was calculated by plotting dose–response curves using the «drc» package.[1]

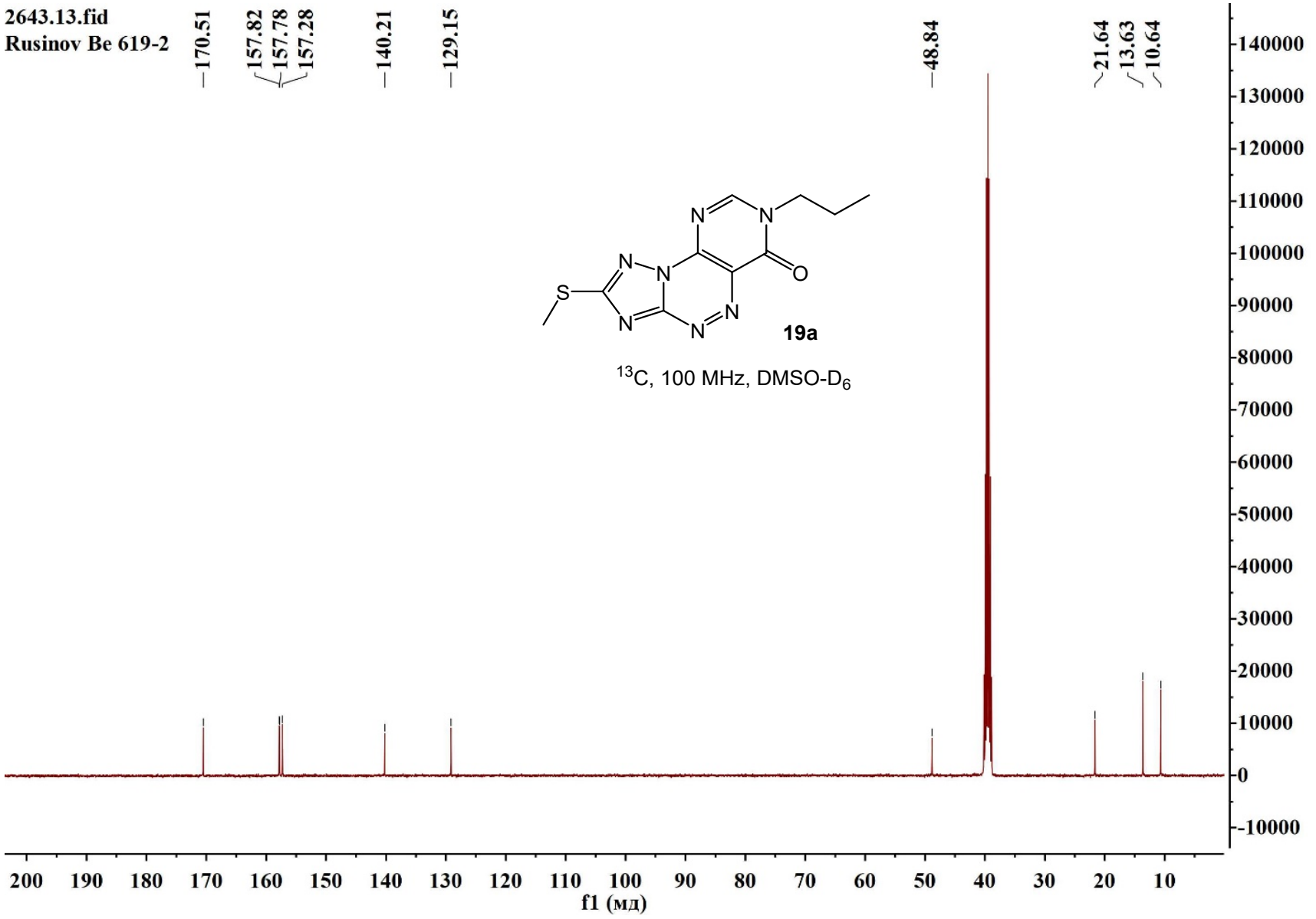
1. C. Ritz, F. Baty, J.C. Streibig, D. Gerhard. Dose-Response Analysis Using R. PLoS One. 10 (2015). https://doi.org/10.1371/journal.pone.0146021.

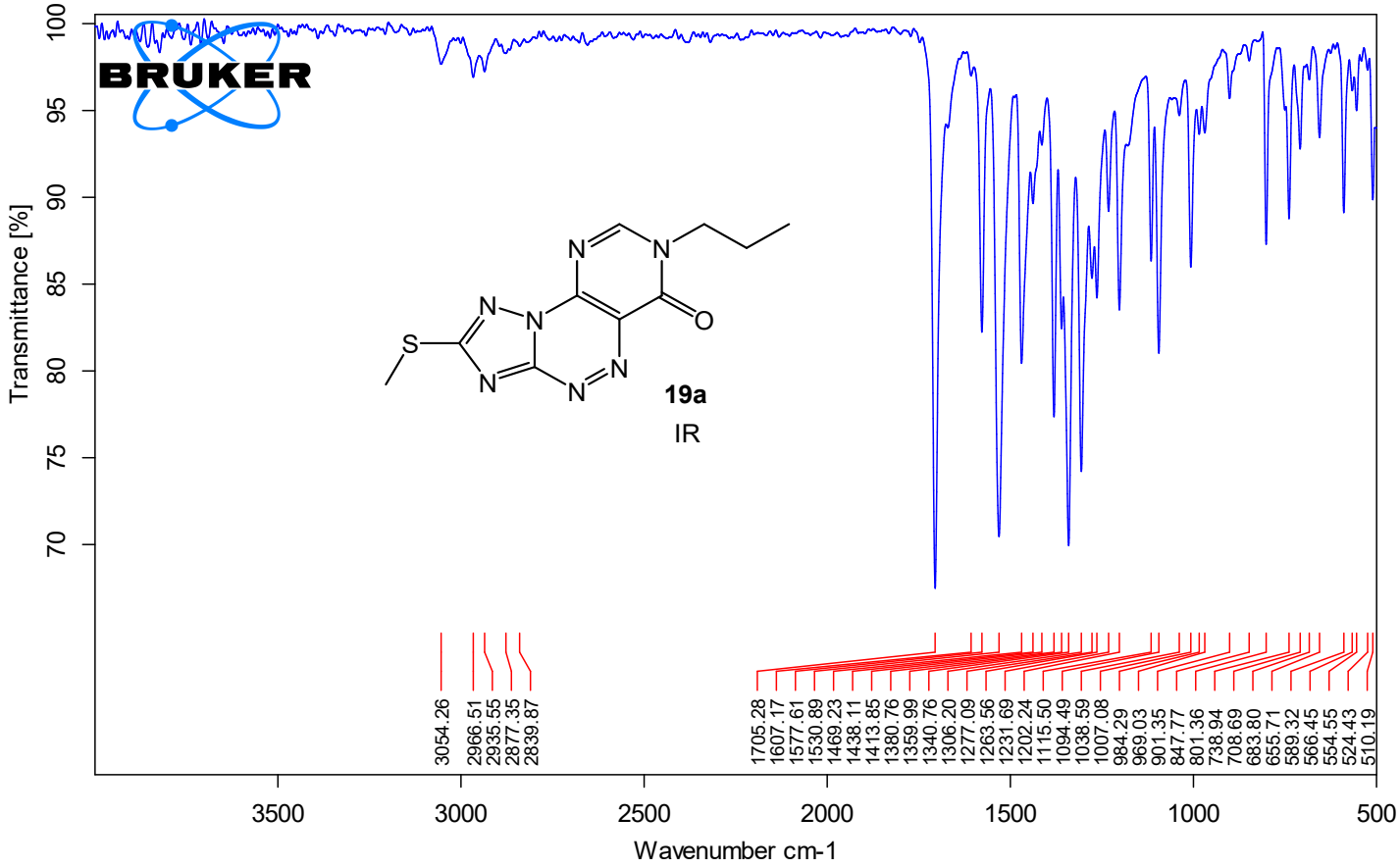
^{1}H NMR, 400 MHz, DMSO-d_6 (blank solvent for spectra recorded at 400 MHz)



7-Propyl-2-(methylthio)pyrimido[4,5-*e*][1,2,4]triazolo[5,1-*c*][1,2,4]triazin-6(7*H*)-one (19a)

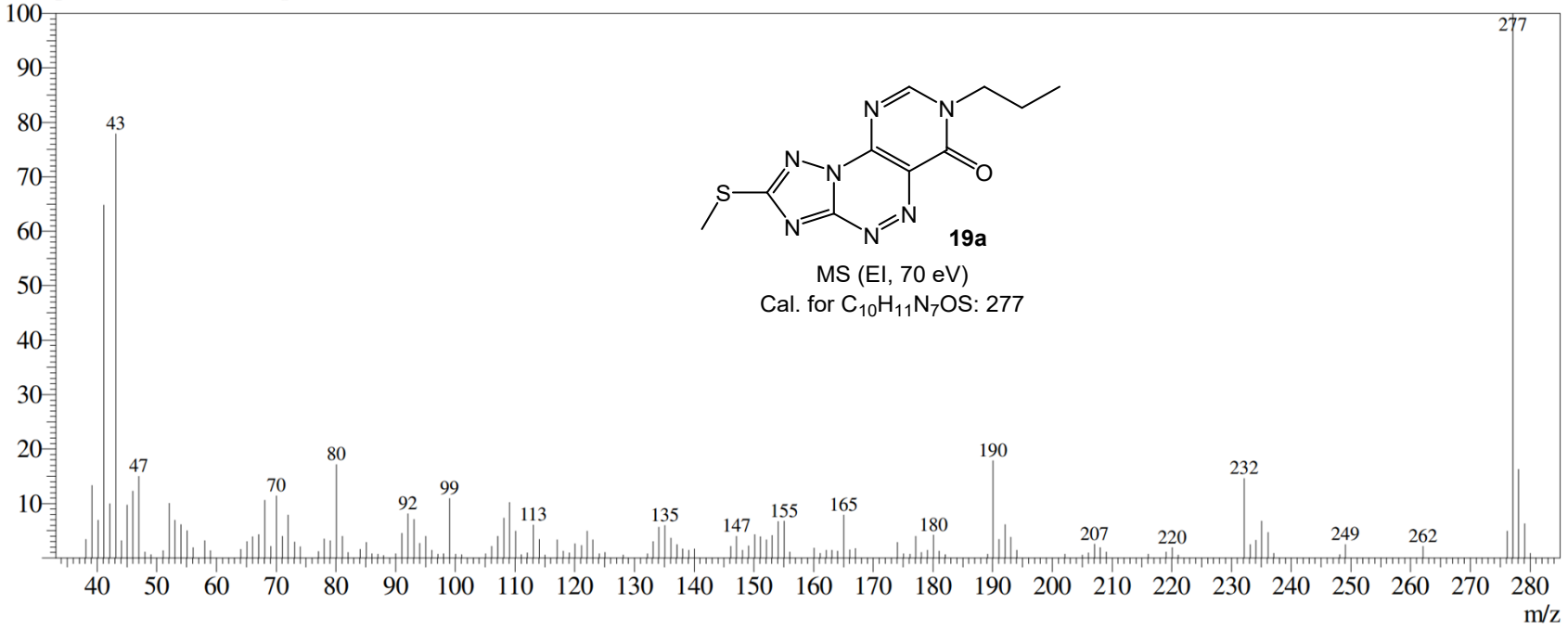



2643.13.fid
Rusinov Be 619-2
170.51
157.82
157.78
157.28
140.21
129.15
48.84
21.64
13.63
10.64
19a
^{13}C, 100 MHz, DMSO-D$_6$
f1 (мд)


BRUKER
Transmittance [%]
100
95
90
85
80
75
70
3500
3000
2500
2000
1500
1000
500
Wavenumber cm-1
19a
IR
3054.26
2966.51
2935.55
2877.35
2839.87
1705.28
1607.17
1577.61
1530.89
1469.23
1438.11
1413.85
1380.76
1359.99
1340.76
1306.20
1277.09
1263.56
1231.69
1202.24
1115.50
1094.49
1038.59
1007.08
984.29
969.03
901.35
847.77
801.36
738.94
708.69
683.80
655.71
589.32
566.45
554.55
524.43
510.19

Page 1/1

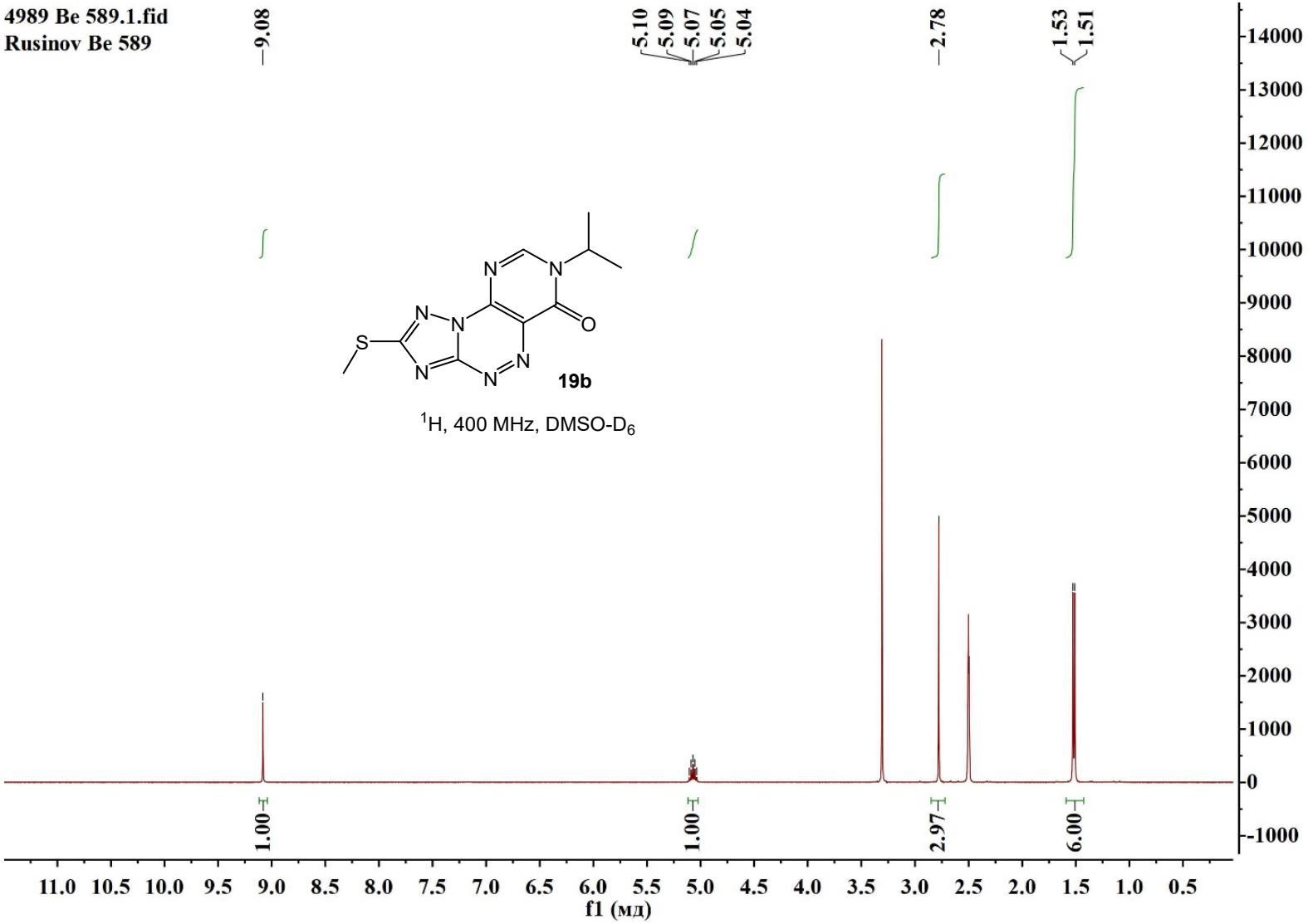
Line#:1 R.Time:2.370(Scan#:909)
MassPeaks:142
RawMode:Single 2.370(909) BasePeak:277(2554332)
Фон.реж.:1.138(416) Group 1 - Event 1

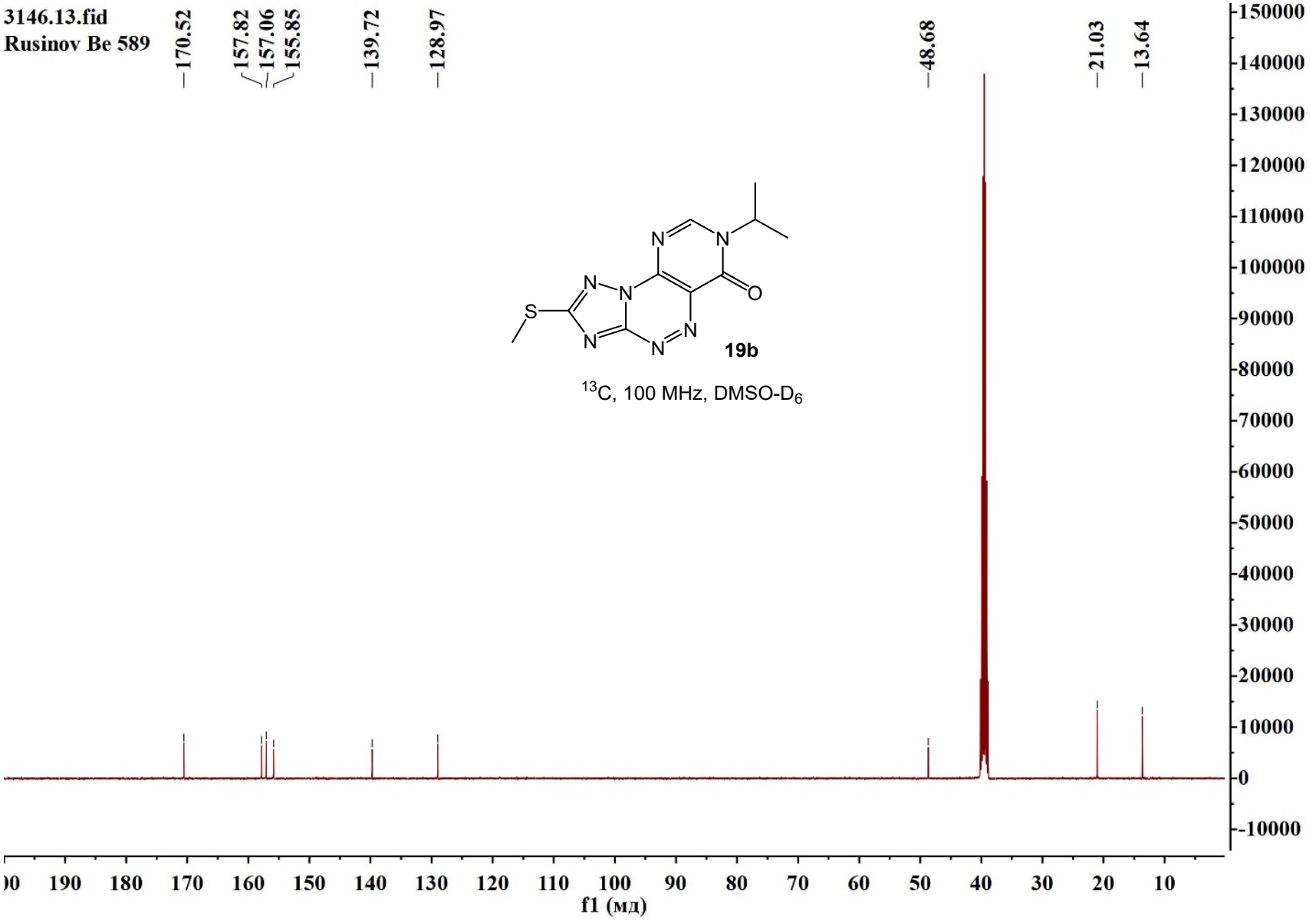


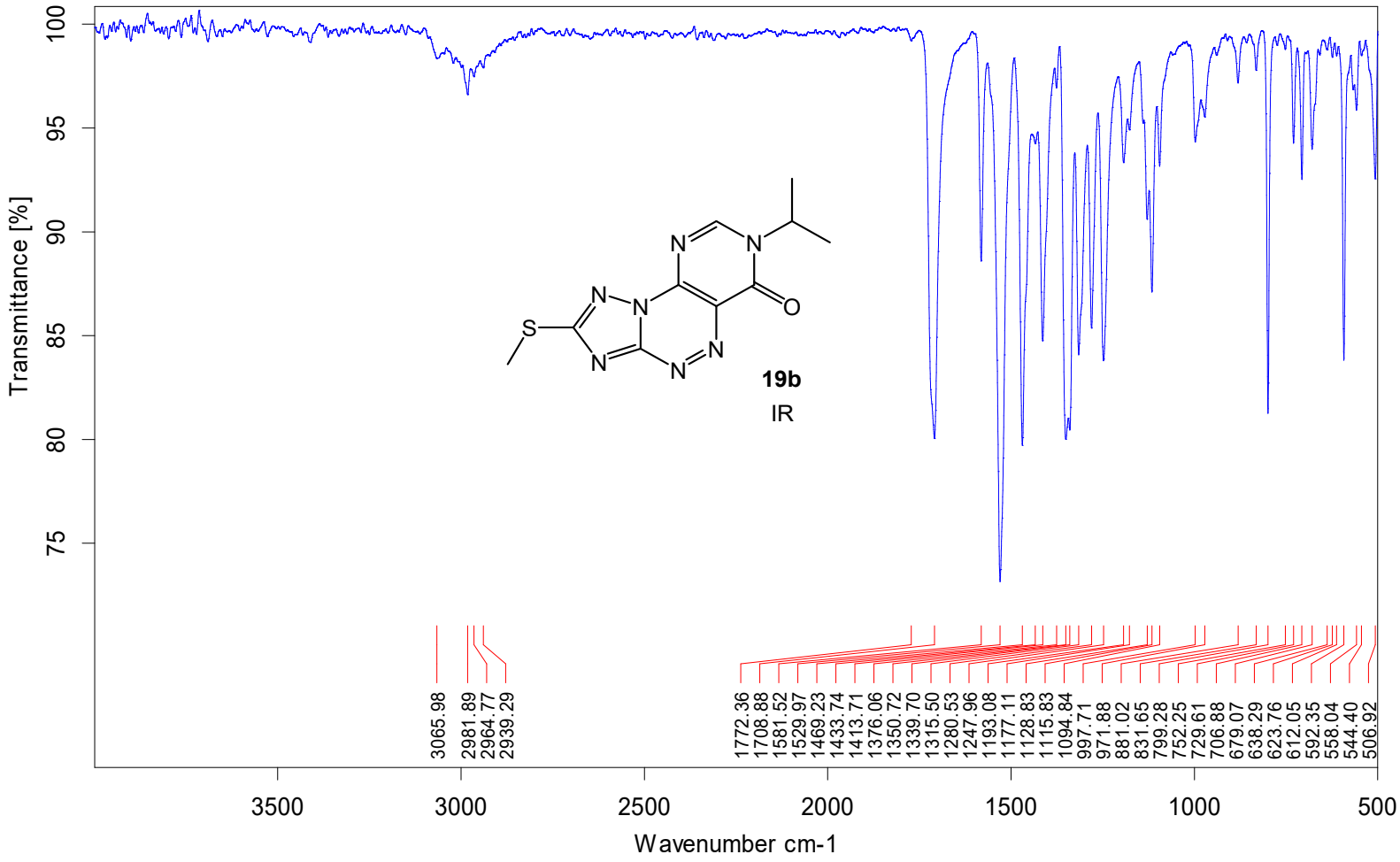
19a

MS (EI, 70 eV)
Cal. for $C_{10}H_{11}N_7OS$: 277

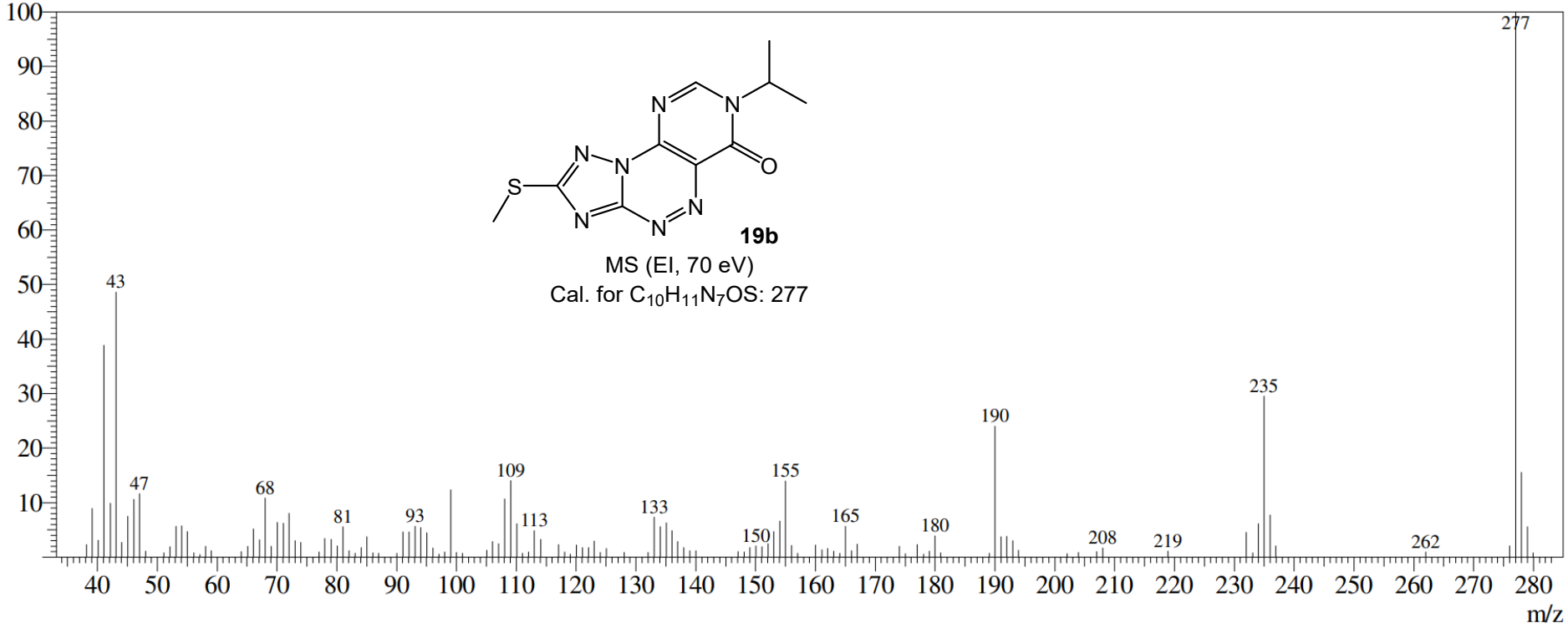
7-Isopropyl-2-(methylthio)pyrimido[4,5-*e*][1,2,4]triazolo[5,1-*c*][1,2,4]triazin-6(7*H*)-one (19b)




3146.13.fid
Rusinov Be 589
170.52
157.82
157.06
155.85
139.72
128.97
48.68
21.03
13.64
19b
13C, 100 MHz, DMSO-D6
f1 (мд)


Transmittance [%]
100
95
90
85
80
75
3500
3000
2500
2000
1500
1000
500
Wavenumber cm-1
3065.98
2981.89
2964.77
2939.29
1772.36
1708.88
1581.52
1529.97
1469.23
1433.74
1413.71
1376.06
1350.72
1339.70
1315.50
1280.53
1247.96
1193.08
1177.11
1128.83
1115.83
1094.84
997.71
971.88
881.02
831.65
799.28
752.25
729.61
706.88
679.07
638.29
623.76
612.05
592.35
558.04
544.40
506.92
19b
IR

Line#:1 R.Time:2.103(Scan#:802)
MassPeaks:132
RawMode:Single 2.103(802) BasePeak:277(6652995)
Фон.реж.:1.215(447) Group 1 - Event 1

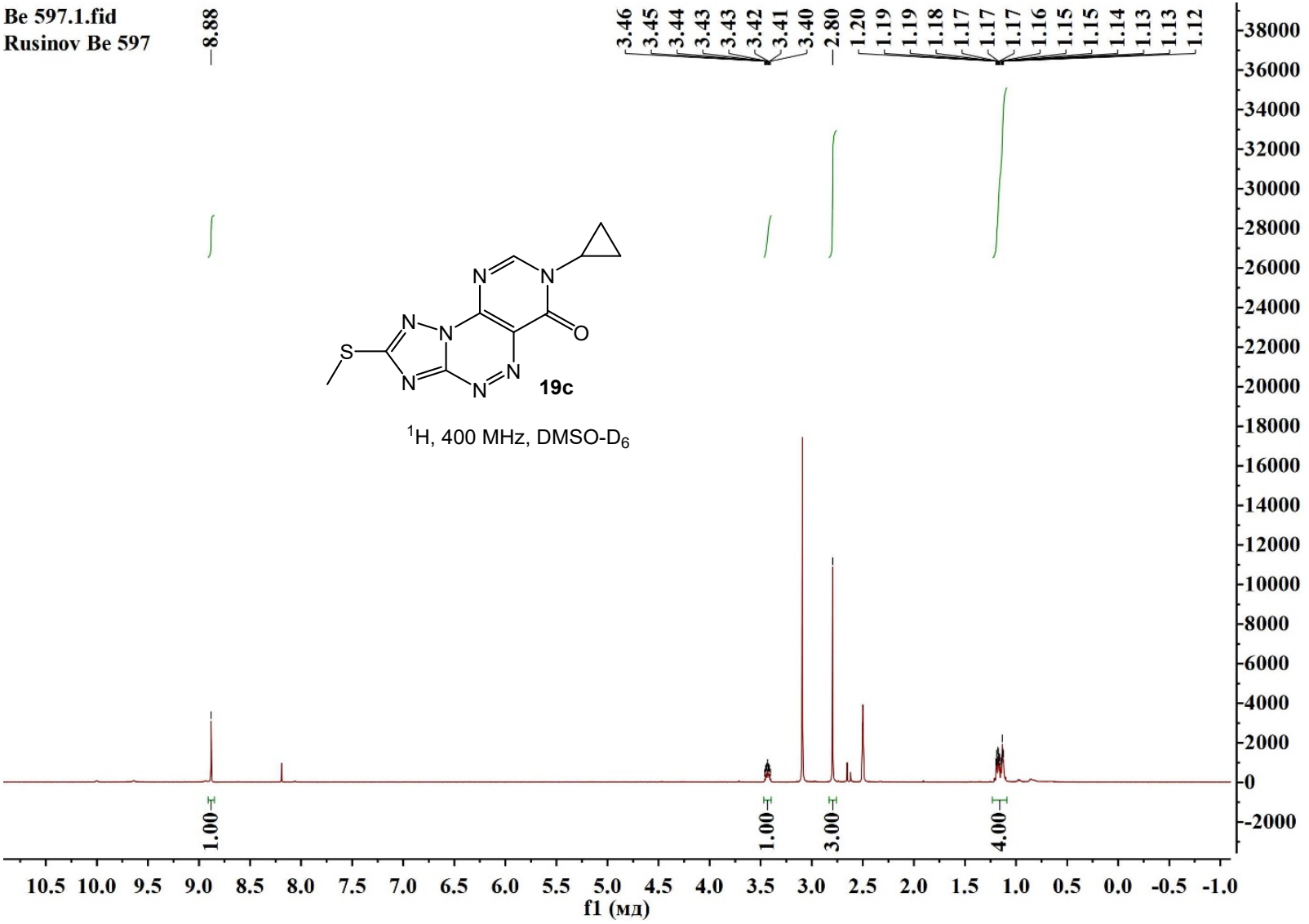


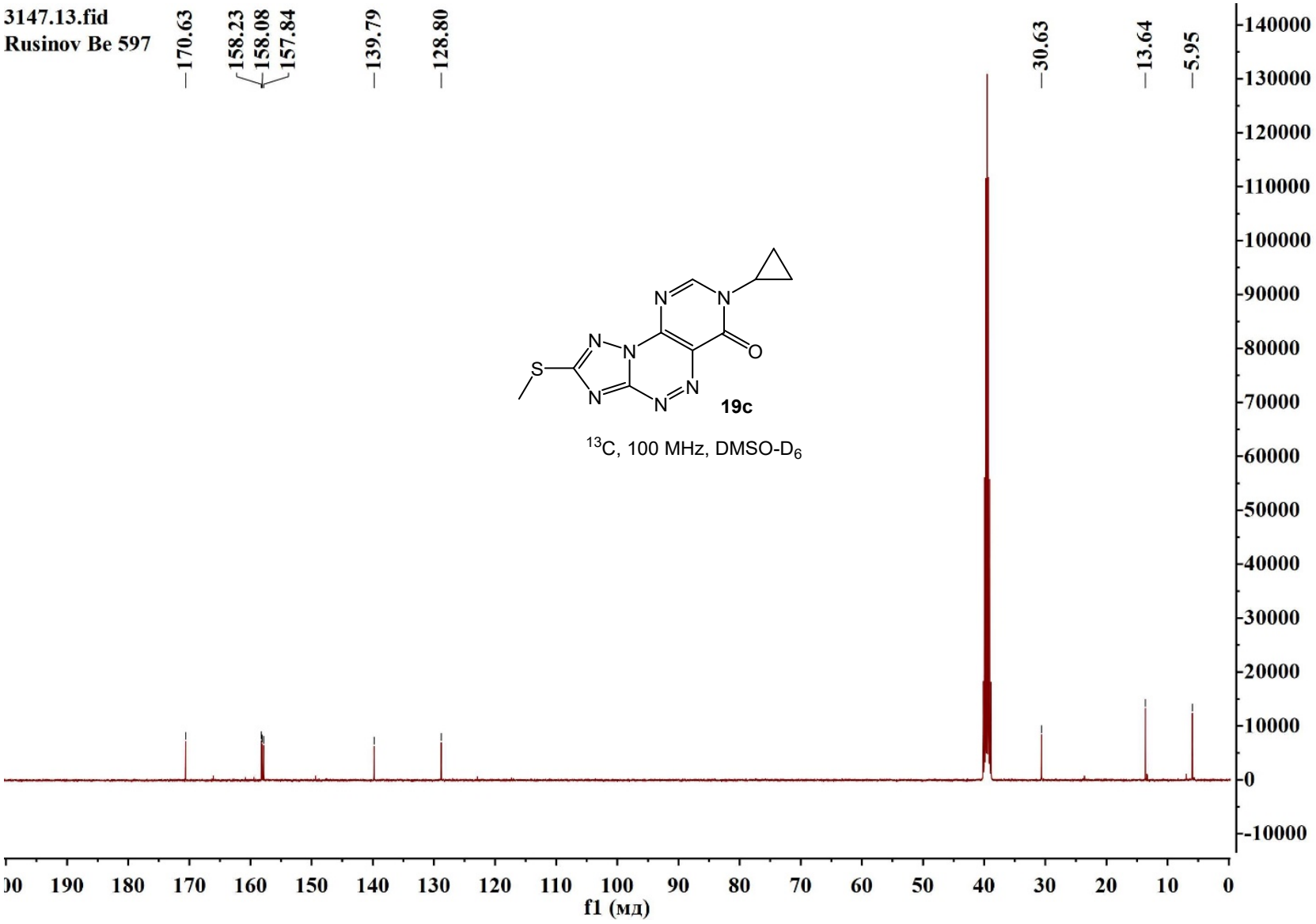
19b

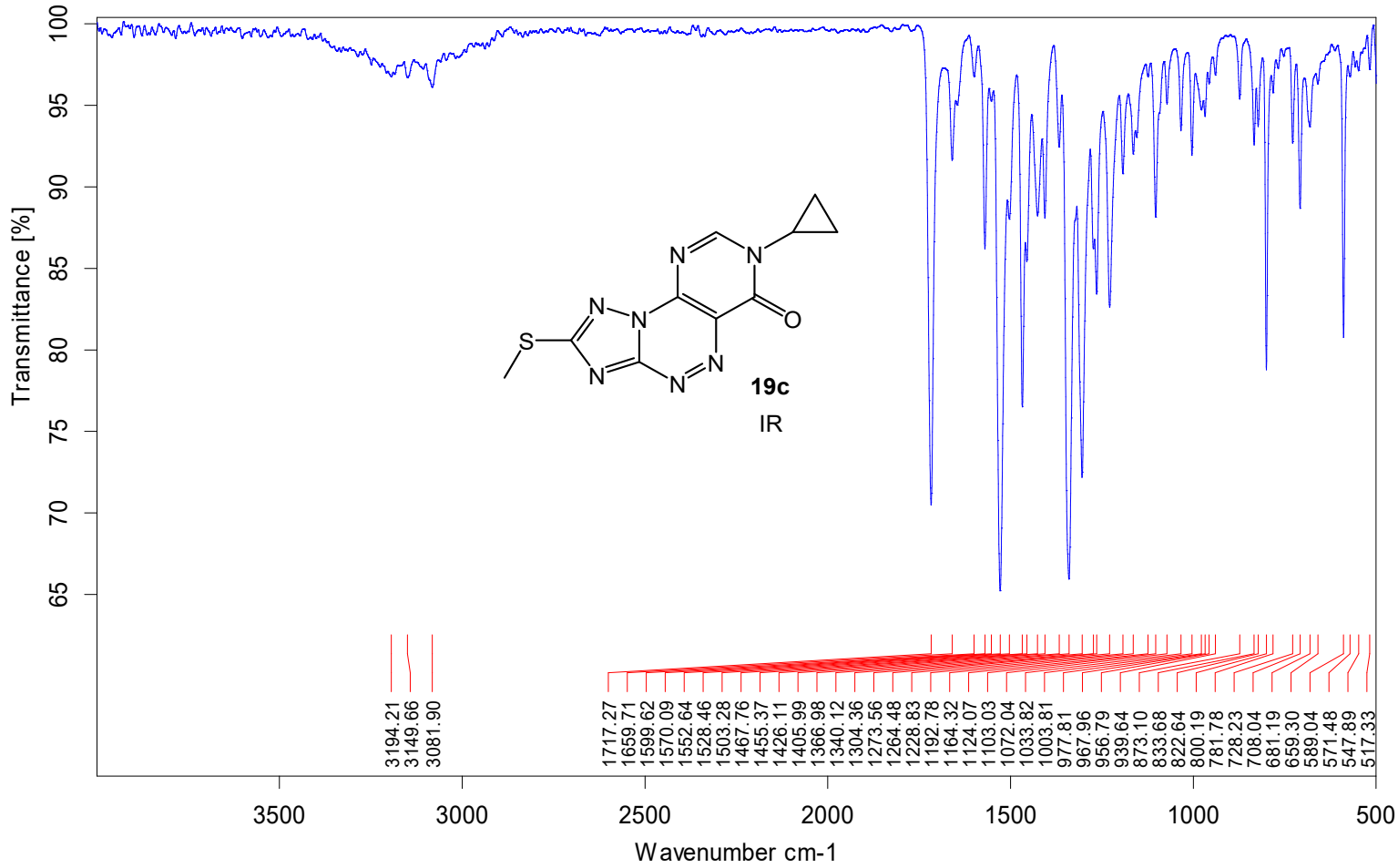
MS (EI, 70 eV)

Cal. for $C_{10}H_{11}N_7OS$: 277

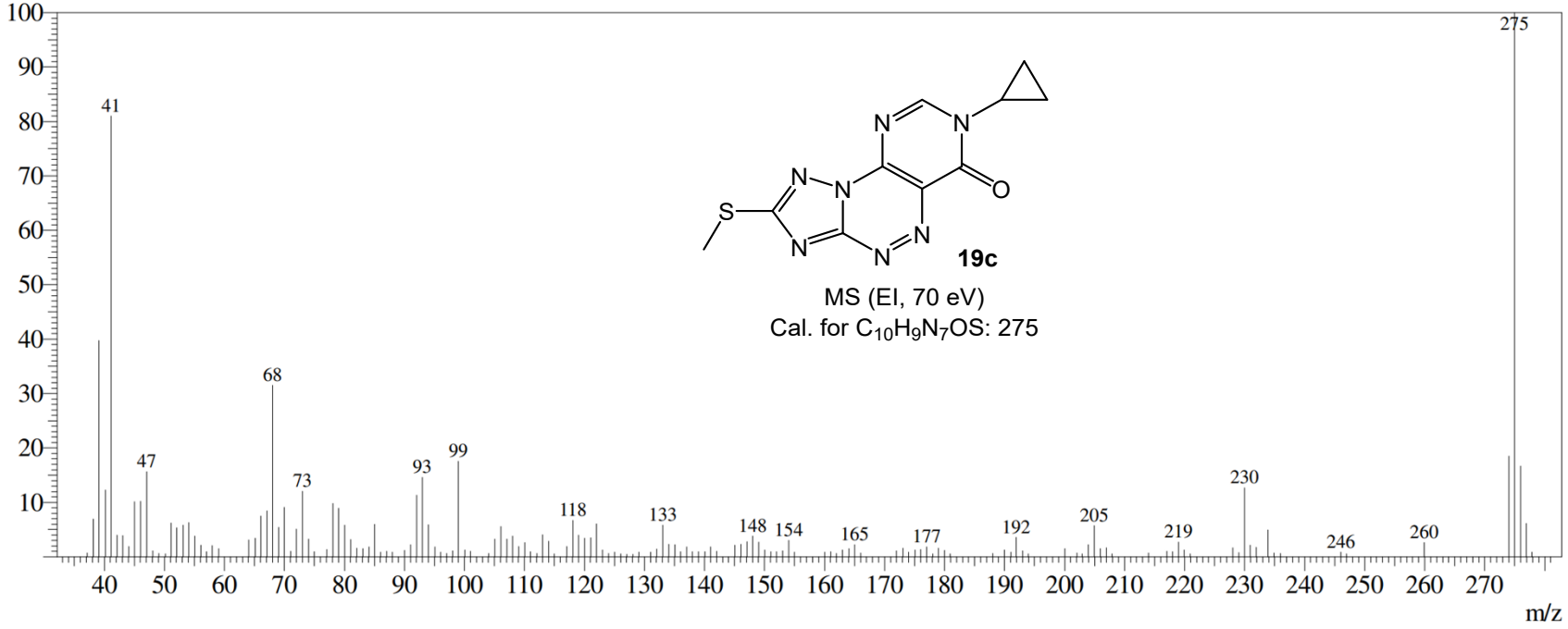
7-Cyclopropyl-2-(methylthio)pyrimido[4,5-*e*][1,2,4]triazolo[5,1-*c*][1,2,4]triazin-6(7*H*)-one (19c)




3147.13.fid
Rusinov Be 597
170.63
158.23
158.08
157.84
139.79
128.80
30.63
13.64
5.95
19c
^{13}C, 100 MHz, DMSO-D$_6$
f1 (мд)


Transmittance [%]
100
95
90
85
80
75
70
65
3500
3000
2500
2000
1500
1000
500
Wavenumber cm-1
3194.21
3149.66
3081.90
1717.27
1659.71
1599.62
1570.09
1552.64
1528.46
1503.28
1467.76
1455.37
1426.11
1405.99
1366.98
1340.12
1304.36
1273.56
1264.48
1228.83
1192.78
1164.32
1124.07
1103.03
1072.04
1033.82
1003.81
977.81
967.96
956.79
939.64
873.10
833.68
822.64
800.19
781.78
728.23
708.04
681.19
659.30
589.04
571.48
547.89
517.33
19c
IR

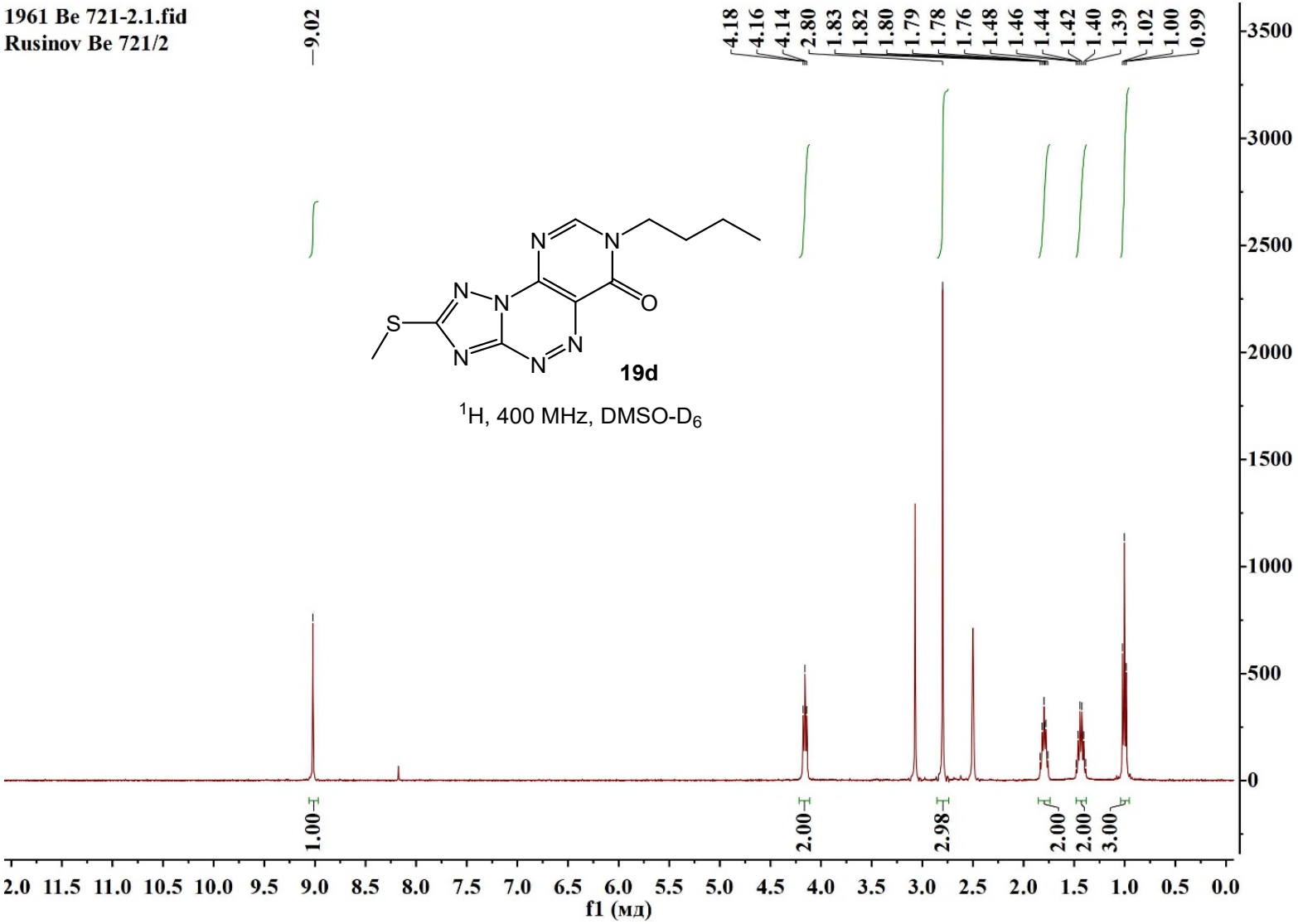
Line#:1 R.Time:2.475(Scan#:951)
MassPeaks:160
RawMode:Single 2.475(951) BasePeak:275(2457363)
Фон.реж.:0.922(330) Group 1 - Event 1

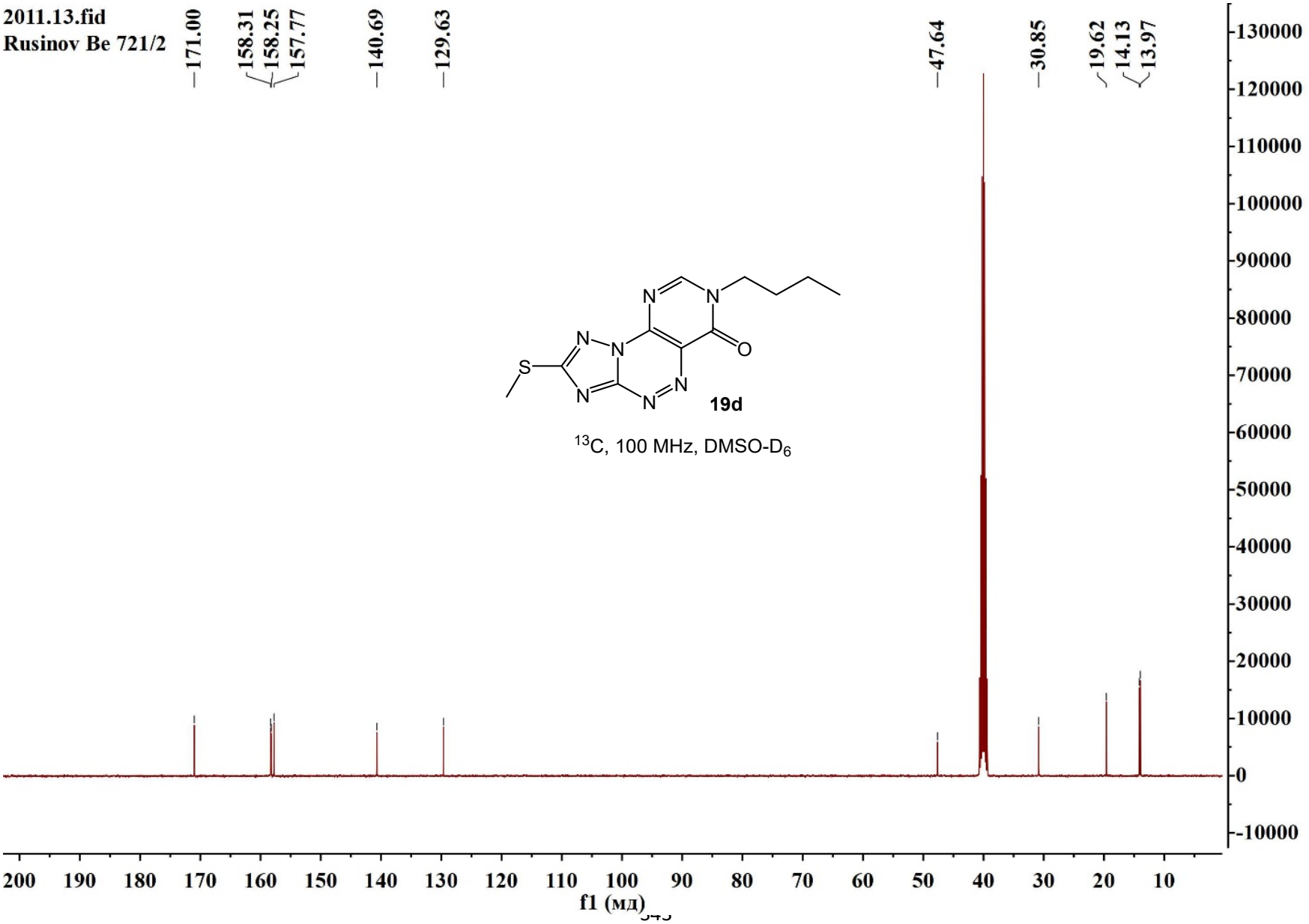


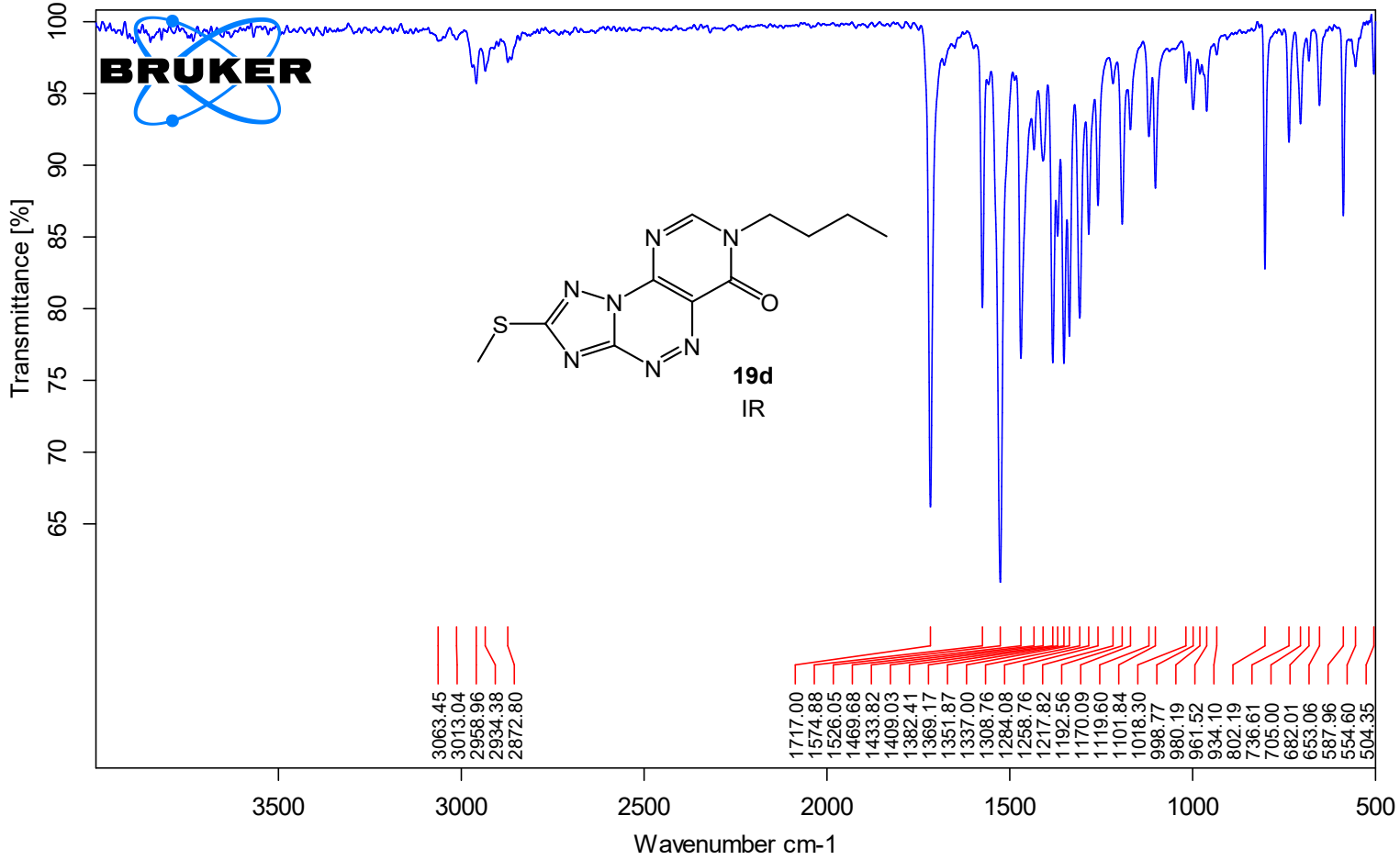
19c

MS (EI, 70 eV)
Cal. for $C_{10}H_9N_7OS$: 275

7-Butyl-2-(methylthio)pyrimido[4,5-*e*][1,2,4]triazolo[5,1-*c*][1,2,4]triazin-6(7*H*)-one (19d)

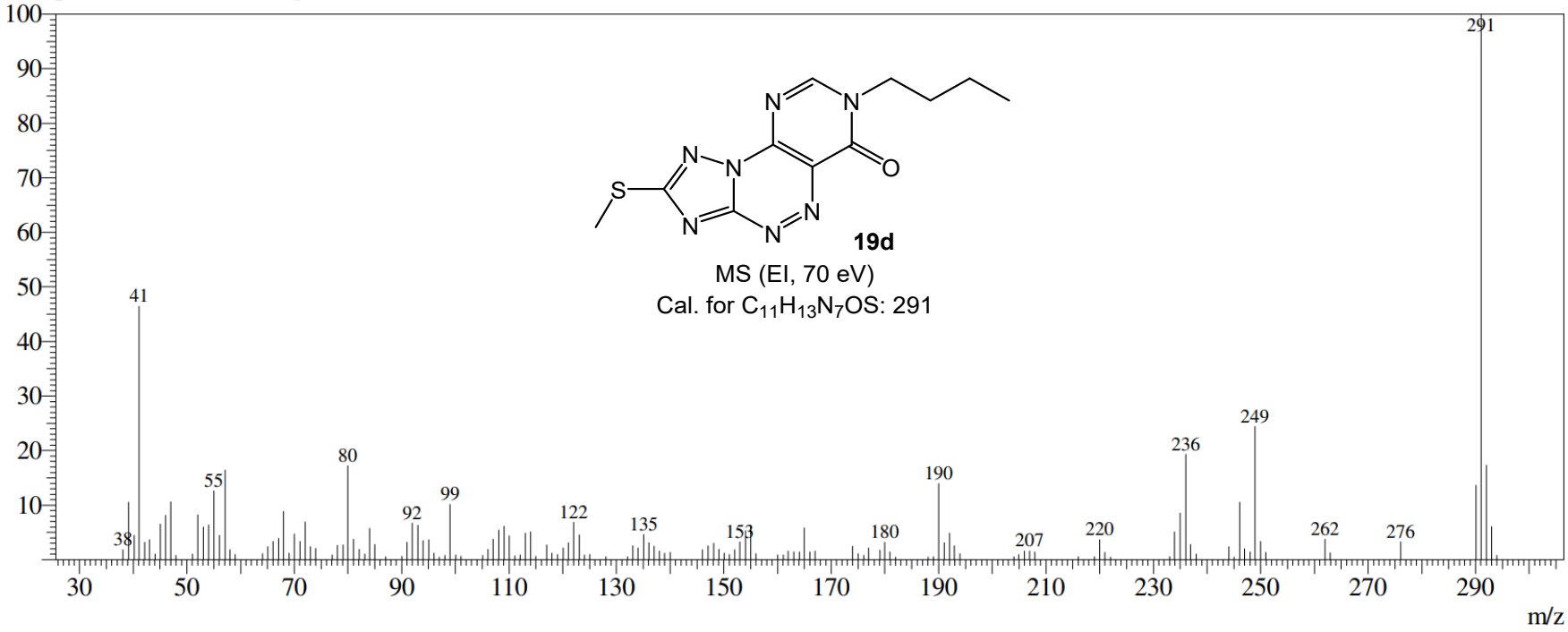



2011.13.fid
Rusinov Be 721/2
171.00
158.31
158.25
157.77
140.69
129.63
47.64
30.85
19.62
14.13
13.97
19d
13C, 100 MHz, DMSO-D6
f1 (мд)


BRUKER
Transmittance [%]
100
95
90
85
80
75
70
65
3063.45
3013.04
2958.96
2934.38
2872.80
1717.00
1574.88
1526.05
1469.68
1433.82
1409.03
1382.41
1369.17
1351.87
1337.00
1308.76
1284.08
1258.76
1217.82
1192.56
1170.09
1119.60
1101.84
1018.30
998.77
980.19
961.52
934.10
802.19
736.61
705.00
682.01
653.06
587.96
554.60
504.35
3500
3000
2500
2000
1500
1000
500
Wavenumber cm-1
19d
IR

Page 1/1

Line#:1 R.Time:4.677(Scan#:1832)
MassPeaks:149
RawMode:Single 4.678(1832) BasePeak:291(4338712)
Фон.реж.:2.640(1017) Group 1 - Event 1

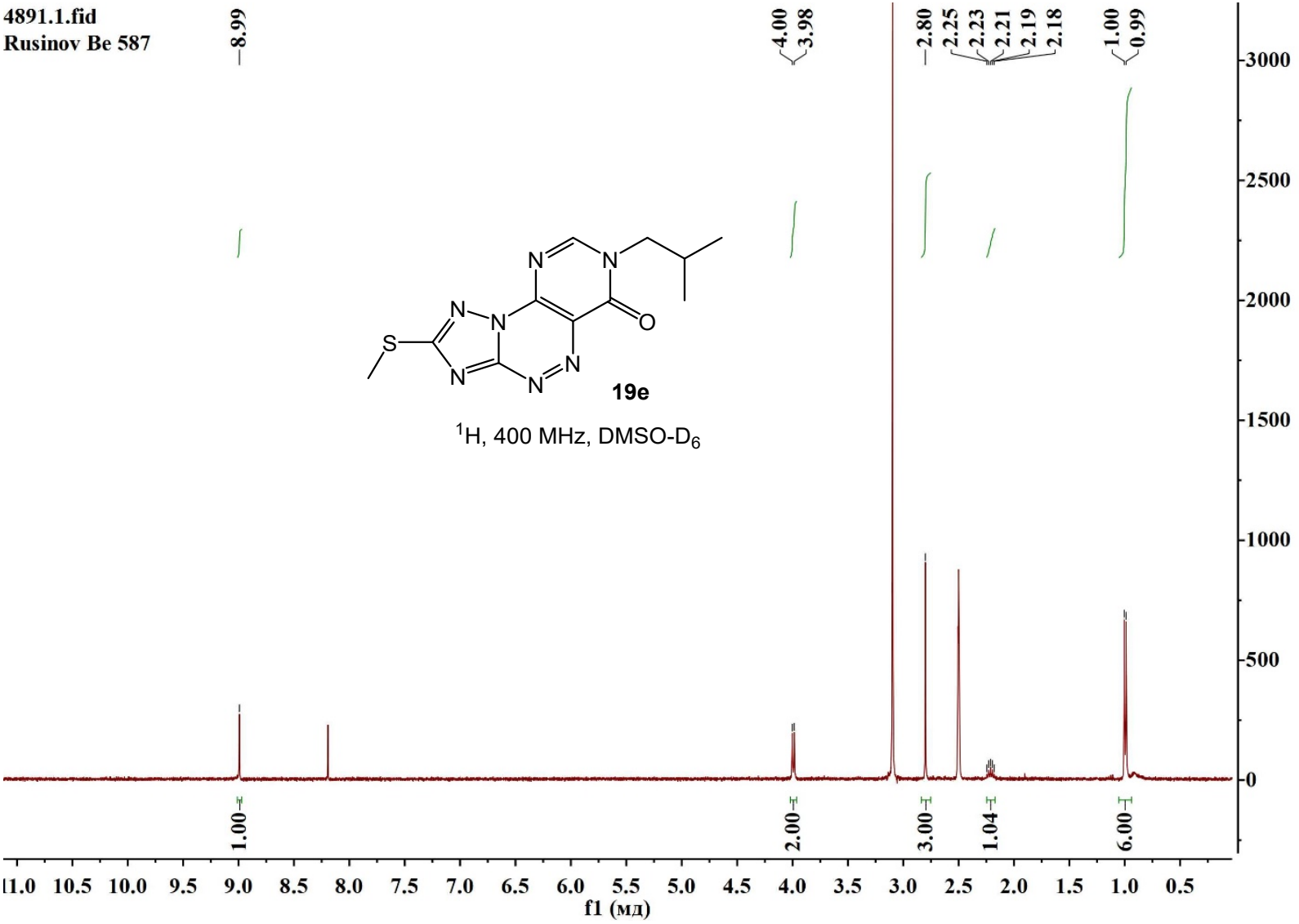


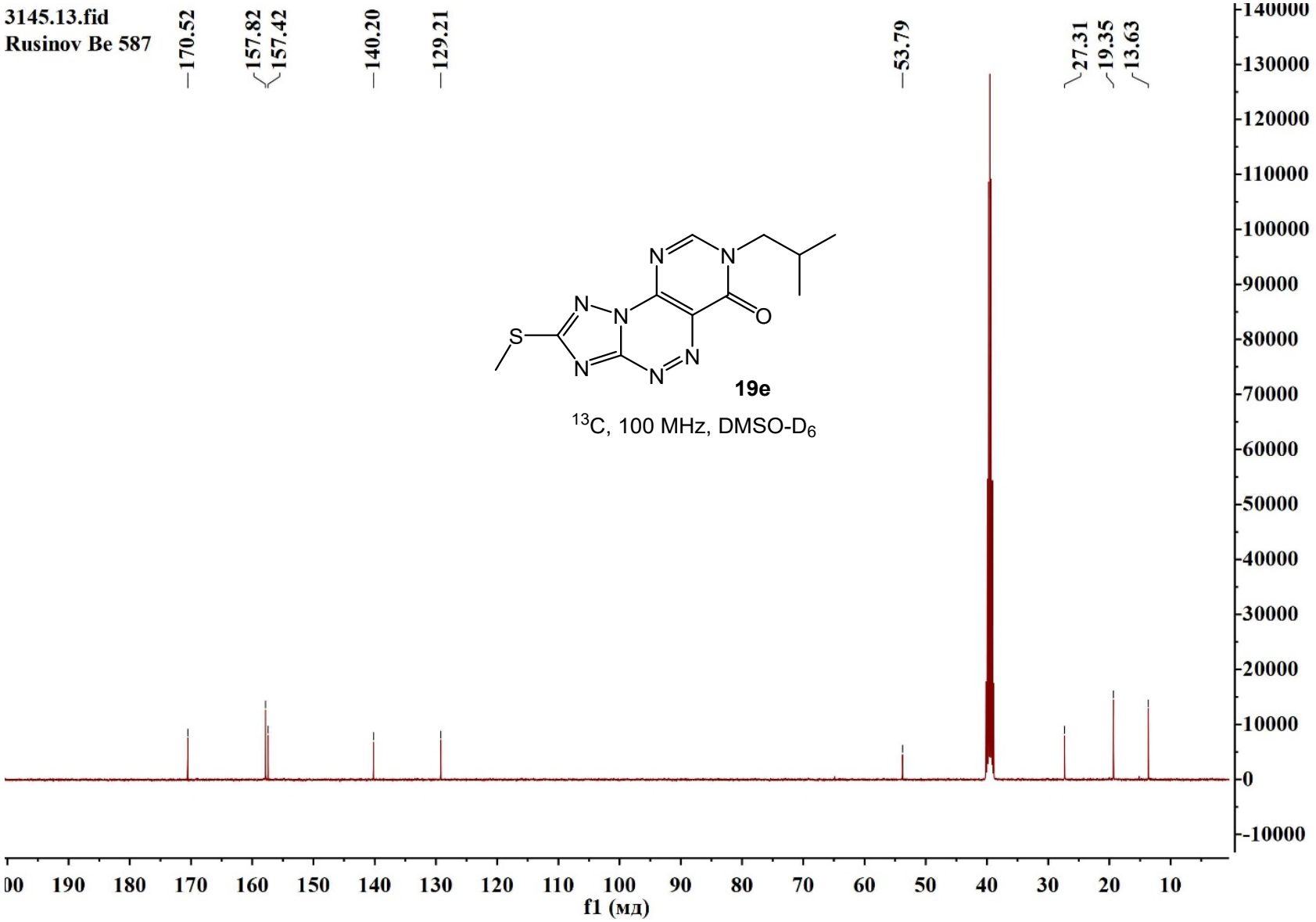
19d

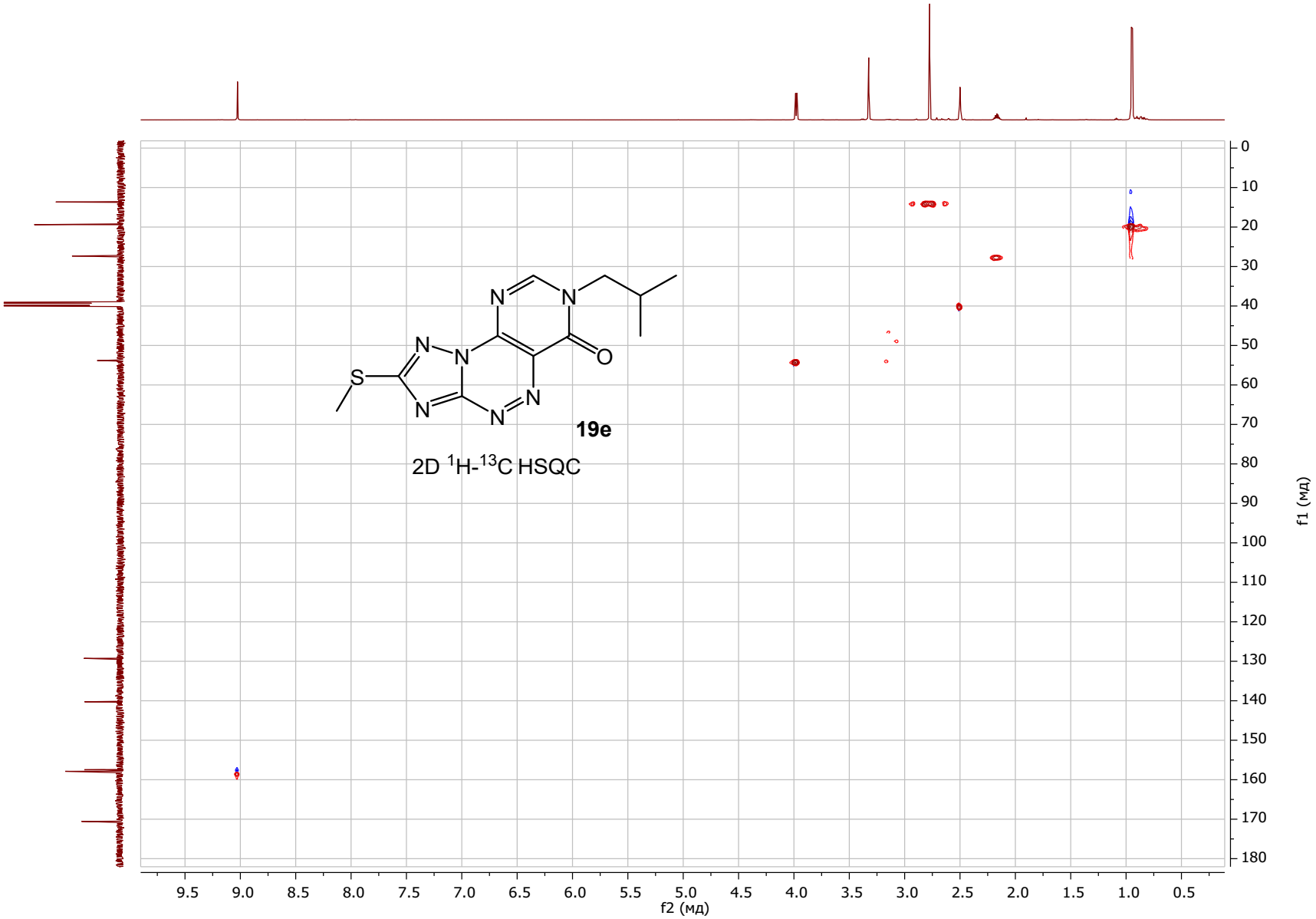
MS (EI, 70 eV)

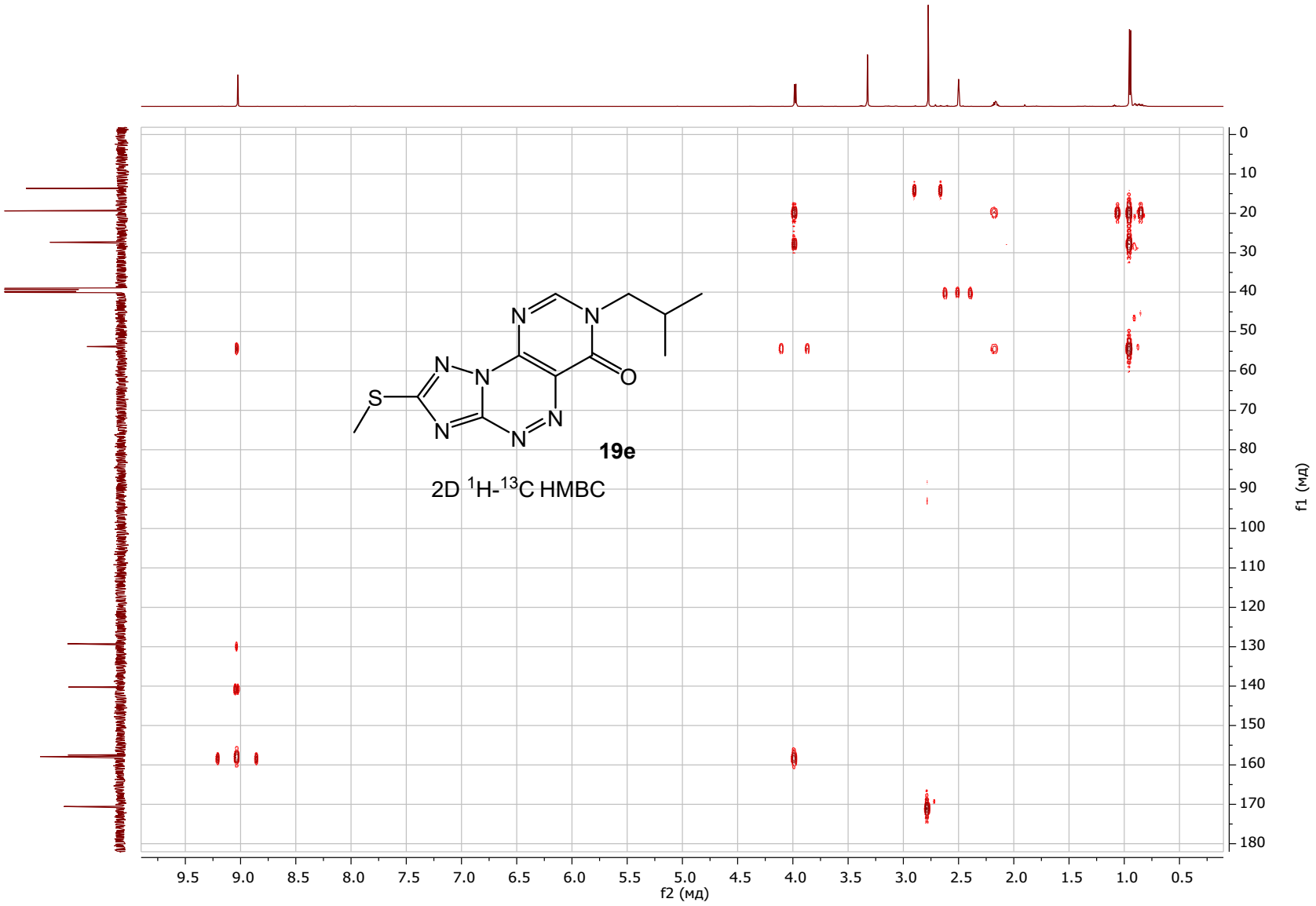
Cal. for $C_{11}H_{13}N_7OS$: 291

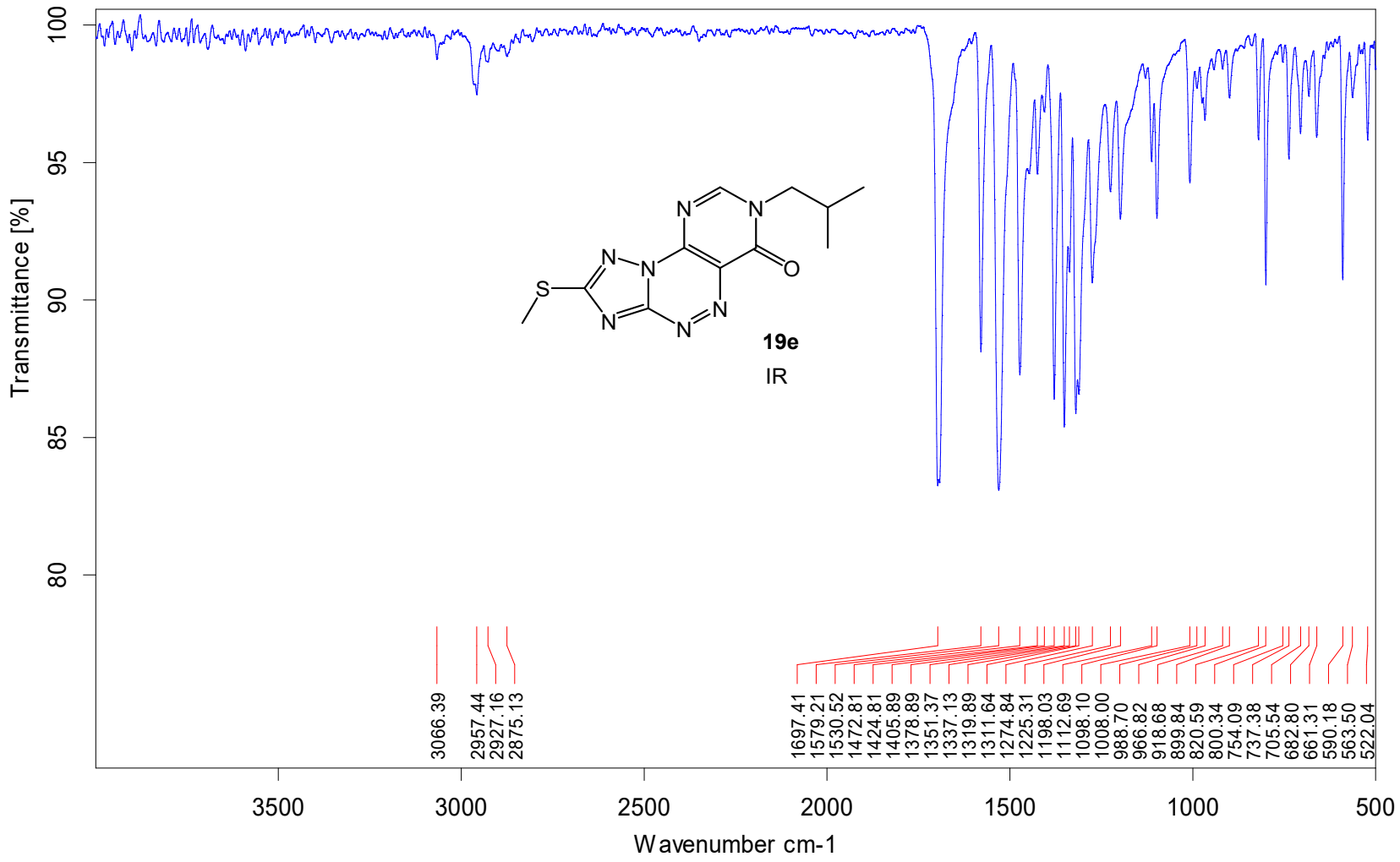
7-Isobutyl-2-(methylthio)pyrimido[4,5-*e*][1,2,4]triazolo[5,1-*c*][1,2,4]triazin-6(7*H*)-one (19e)



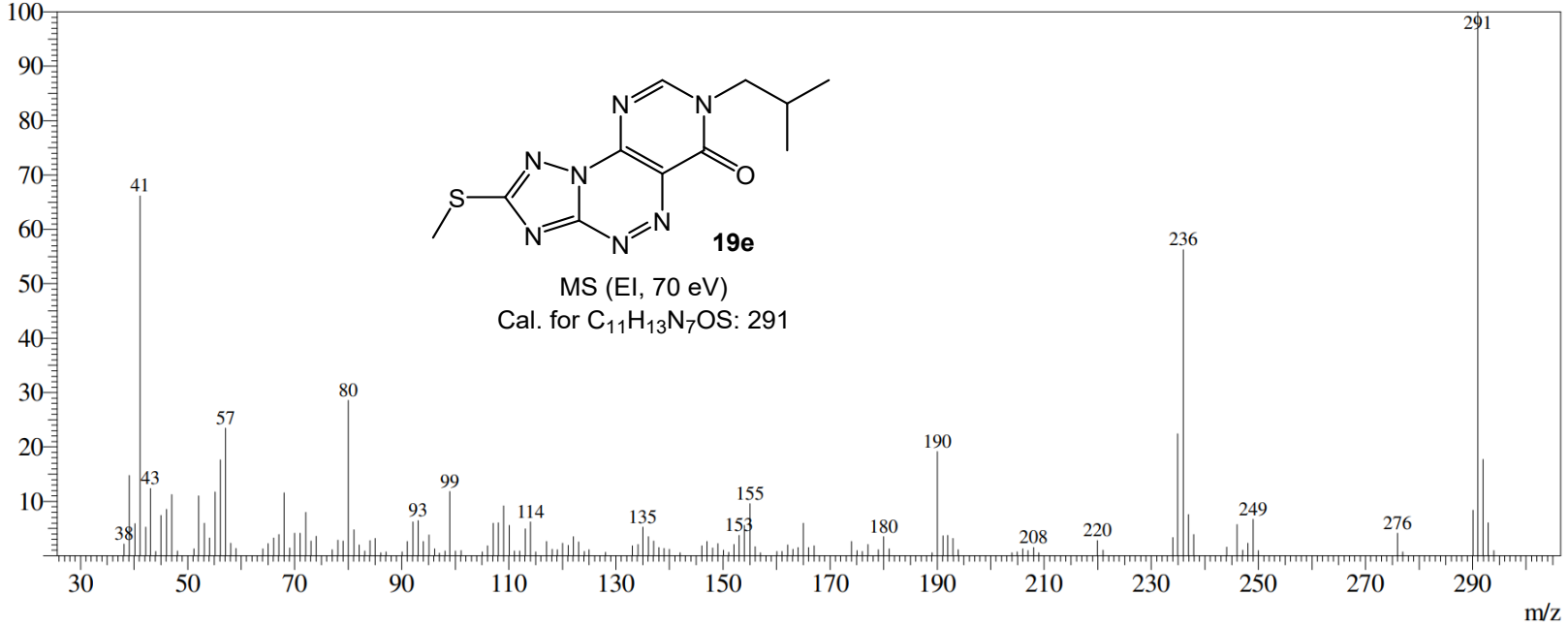

3145.13.fid
Rusinov Be 587
170.52
157.82
157.42
140.20
129.21
53.79
27.31
19.35
13.63
19e
13C, 100 MHz, DMSO-D6
f1 (мд)


19e
2D ^{1}H-^{13}C HSQC
f2 (мд)
f1 (мд)

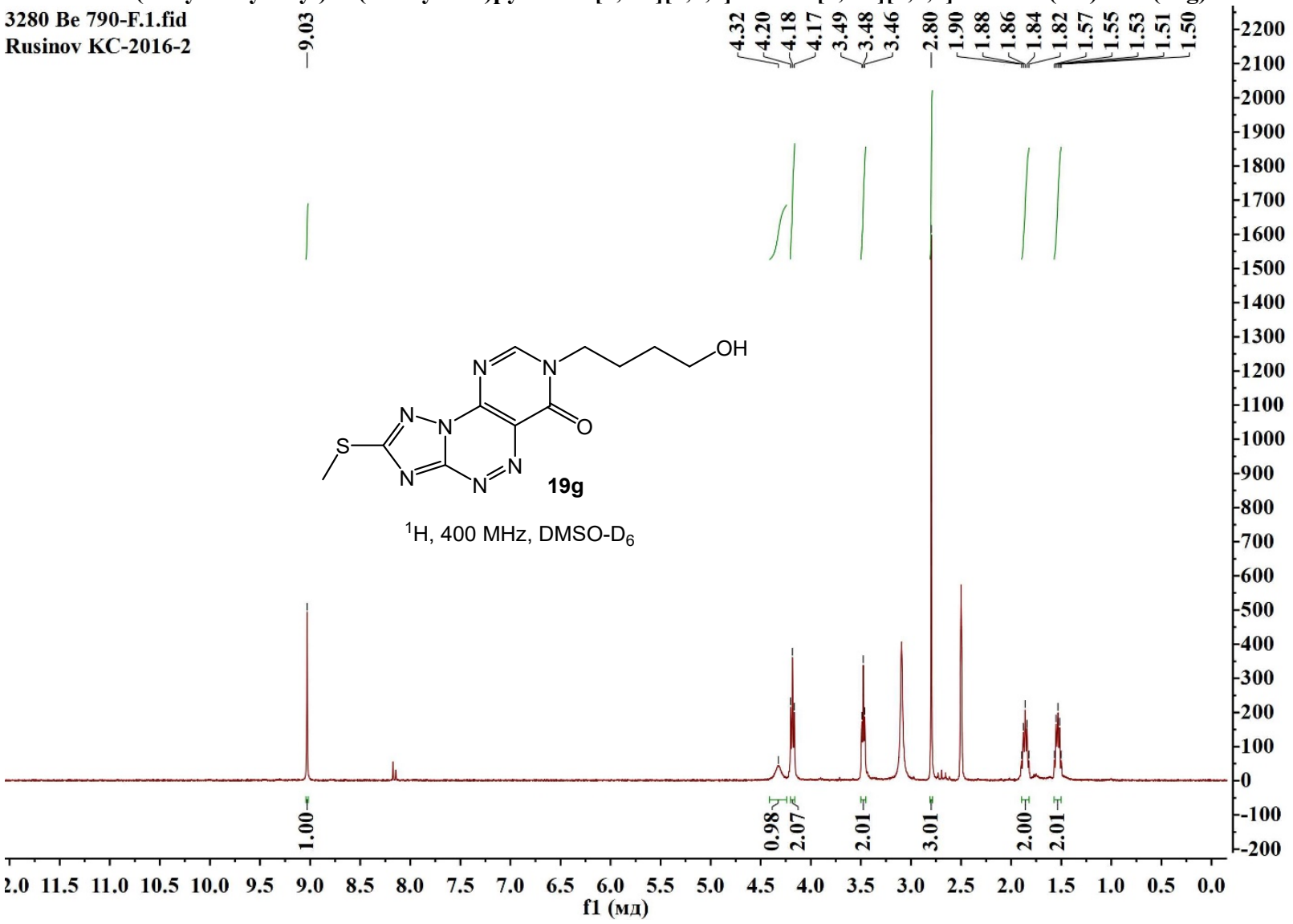

19e
2D ^{1}H-^{13}C HMBC
f2 (мд)
f1 (мд)

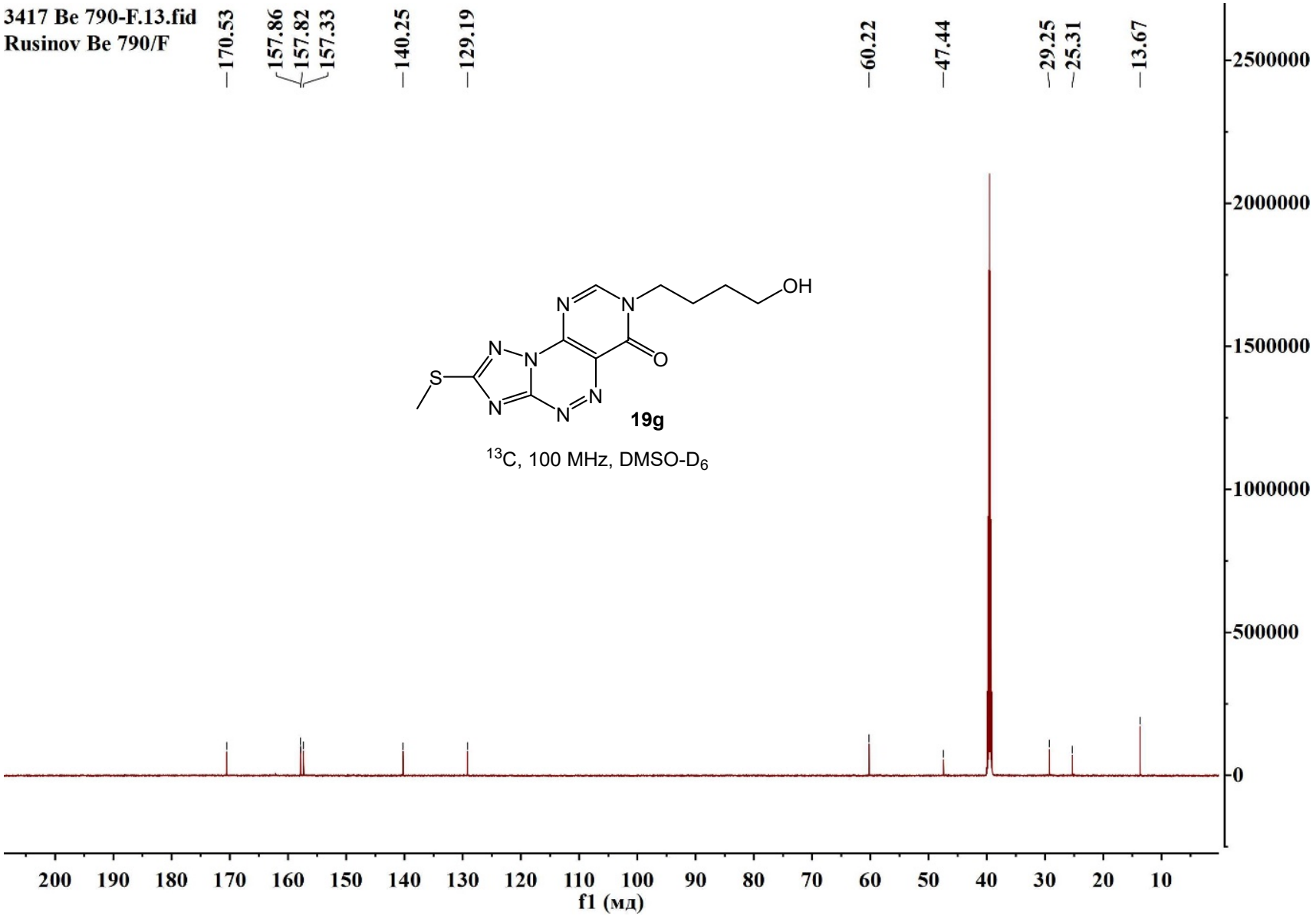

Transmittance [%]
100
95
90
85
80
3500
3000
2500
2000
1500
1000
500
Wavenumber cm-1
19e
IR
3066.39
2957.44
2927.16
2875.13
1697.41
1579.21
1530.52
1472.81
1424.81
1405.89
1378.89
1351.37
1337.13
1319.89
1311.64
1274.84
1225.31
1198.03
1112.69
1098.10
1008.00
988.70
966.82
918.68
899.84
820.59
800.34
754.09
737.38
705.54
682.80
661.31
590.18
563.50
522.04

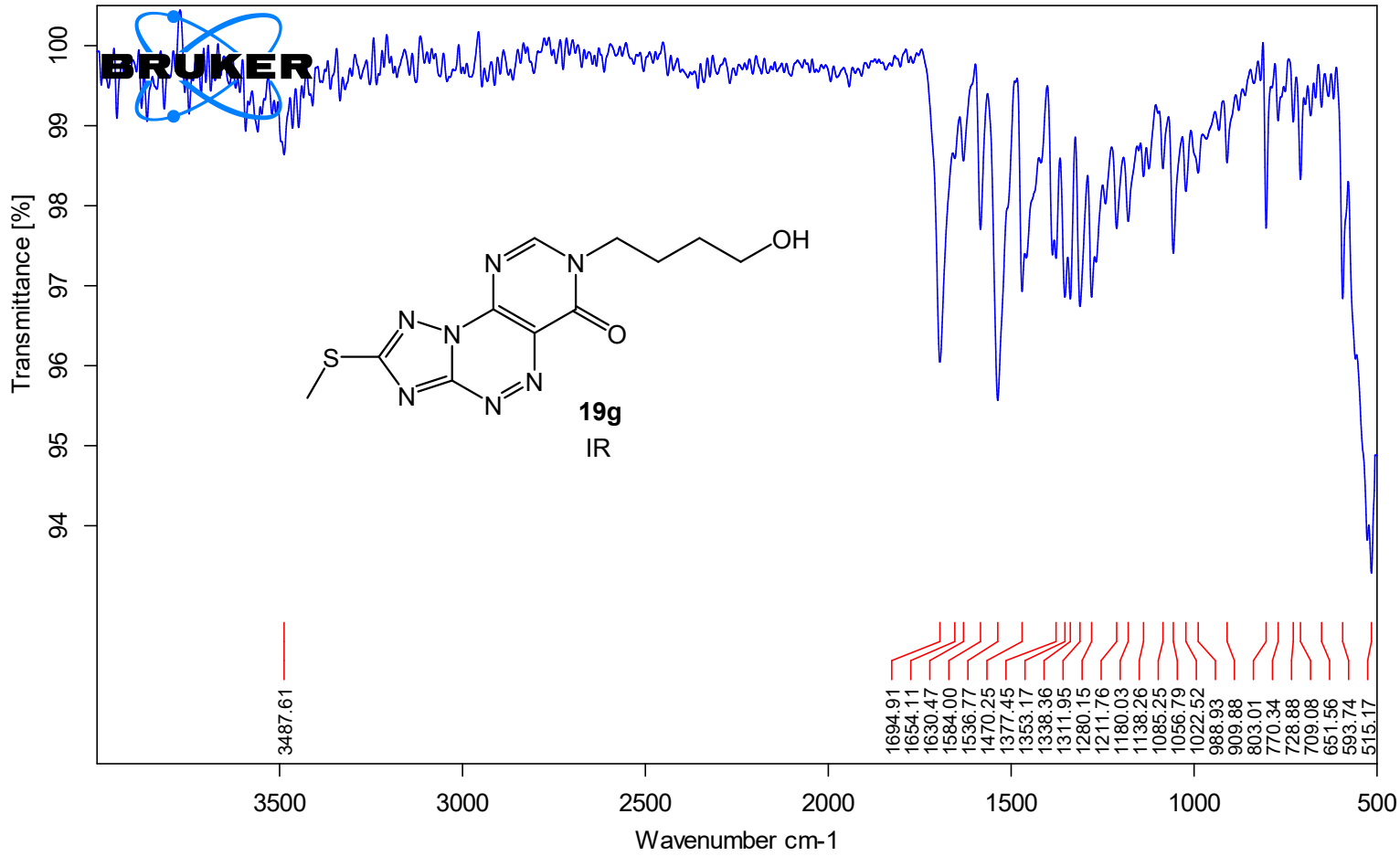
Line#:1 R.Time:3.200(Scan#:1241)
MassPeaks:143
RawMode:Single 3.200(1241) BasePeak:291(3917519)
Фон.реж.:2.408(924) Group 1 - Event 1



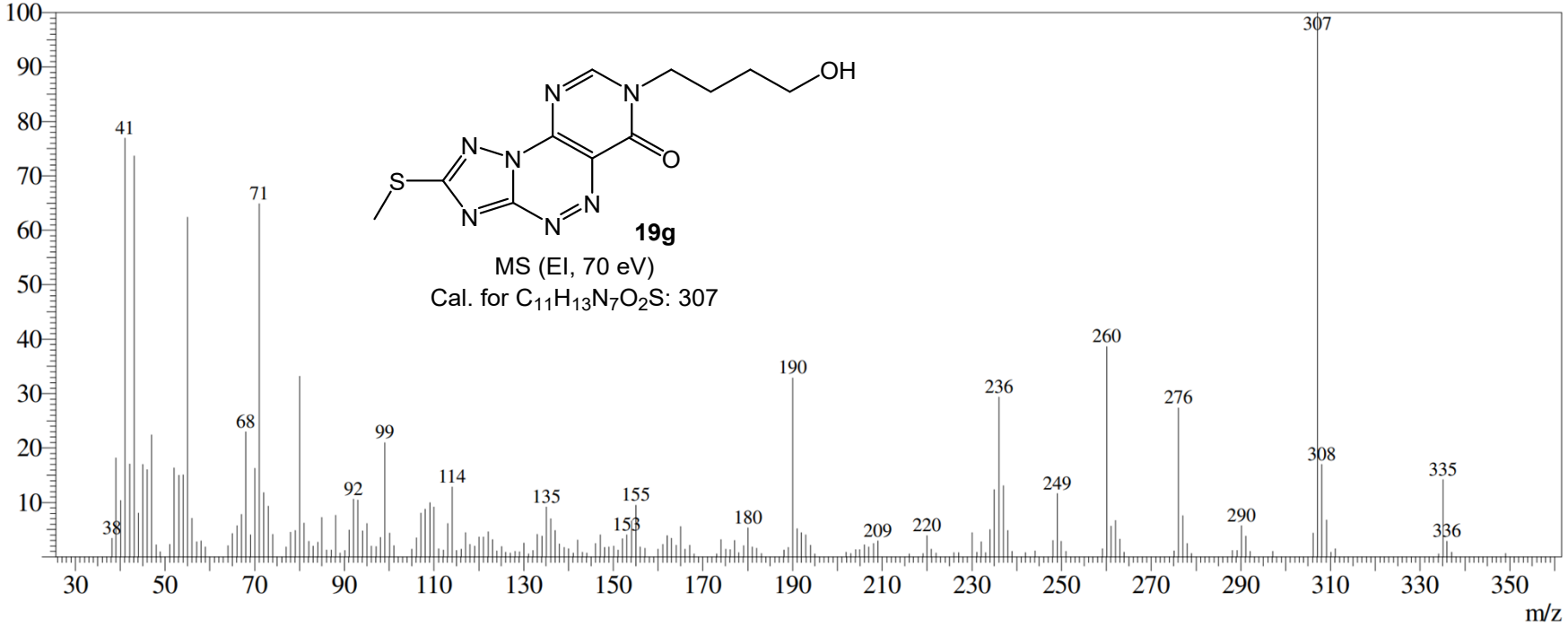
7-(4-Hydroxybutyl)-2-(methylthio)pyrimido[4,5-*e*][1,2,4]triazolo[5,1-*c*][1,2,4]triazin-6(7*H*)-one (19g)




3417 Be 790-F.13.fid
Rusinov Be 790/F
170.53
157.86
157.82
157.33
140.25
129.19
60.22
47.44
29.25
25.31
13.67
OH
N
N
N
N
N
N
N
O
S
19g
13C, 100 MHz, DMSO-D6
2500000
2000000
1500000
1000000
500000
0
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (мд)

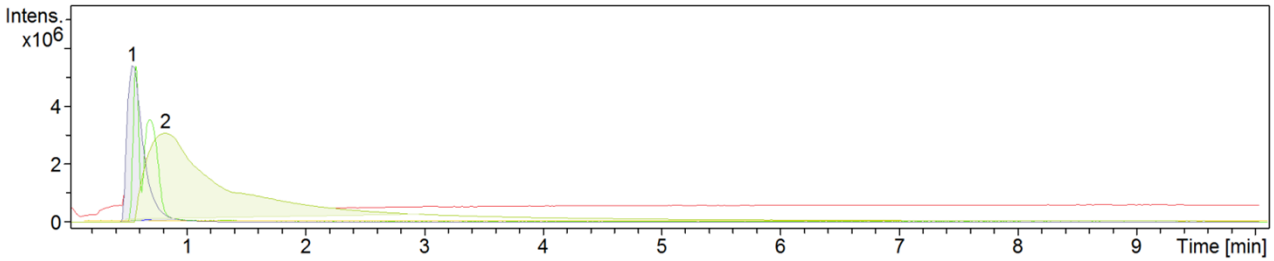

BRUKER
Transmittance [%]
100
99
98
97
96
95
94
OH
N
N
N
N
N
N
S
O
19g
IR
3487.61
1694.91
1654.11
1630.47
1584.00
1536.77
1470.25
1377.45
1353.17
1338.36
1311.95
1280.15
1211.76
1180.03
1138.26
1085.25
1056.79
1022.52
988.93
909.88
803.01
770.34
728.88
709.08
651.56
593.74
515.17
3500
3000
2500
2000
1500
1000
500
Wavenumber cm-1

Line#:1 R.Time:4.698(Scan#:1840)
MassPeaks:196
RawMode:Single 4.697(1840) BasePeak:307(959331)
Фон.реж.:2.845(1099) Group 1 - Event 1



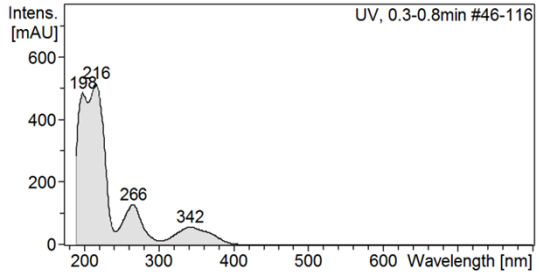
Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	2.0 Bar
Focus	Active	Set Capillary	4500 V	Set Dry Heater	200 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	8.0 l/min
Scan End	1400 m/z	Set Charging Voltage	2000 V	Set Divert Valve	Waste
		Set Corona	0 nA	Set APCI Heater	0 °C

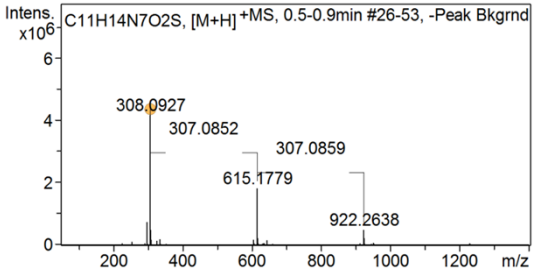


#	RT [min]	Area	Int. Type	I	S/N	Chromatogram	Max. m/z	FWHM [min]
1	0.5	50059508	Manual	5377082	27792.5	EIC 308.0917±0.01 +All MS	308.0927	
2	0.8	124236288	Manual	3057557	1373.1	EIC 79.0213±0.01 +All MS	79.0212	

Cmpd 1, 0.5 min

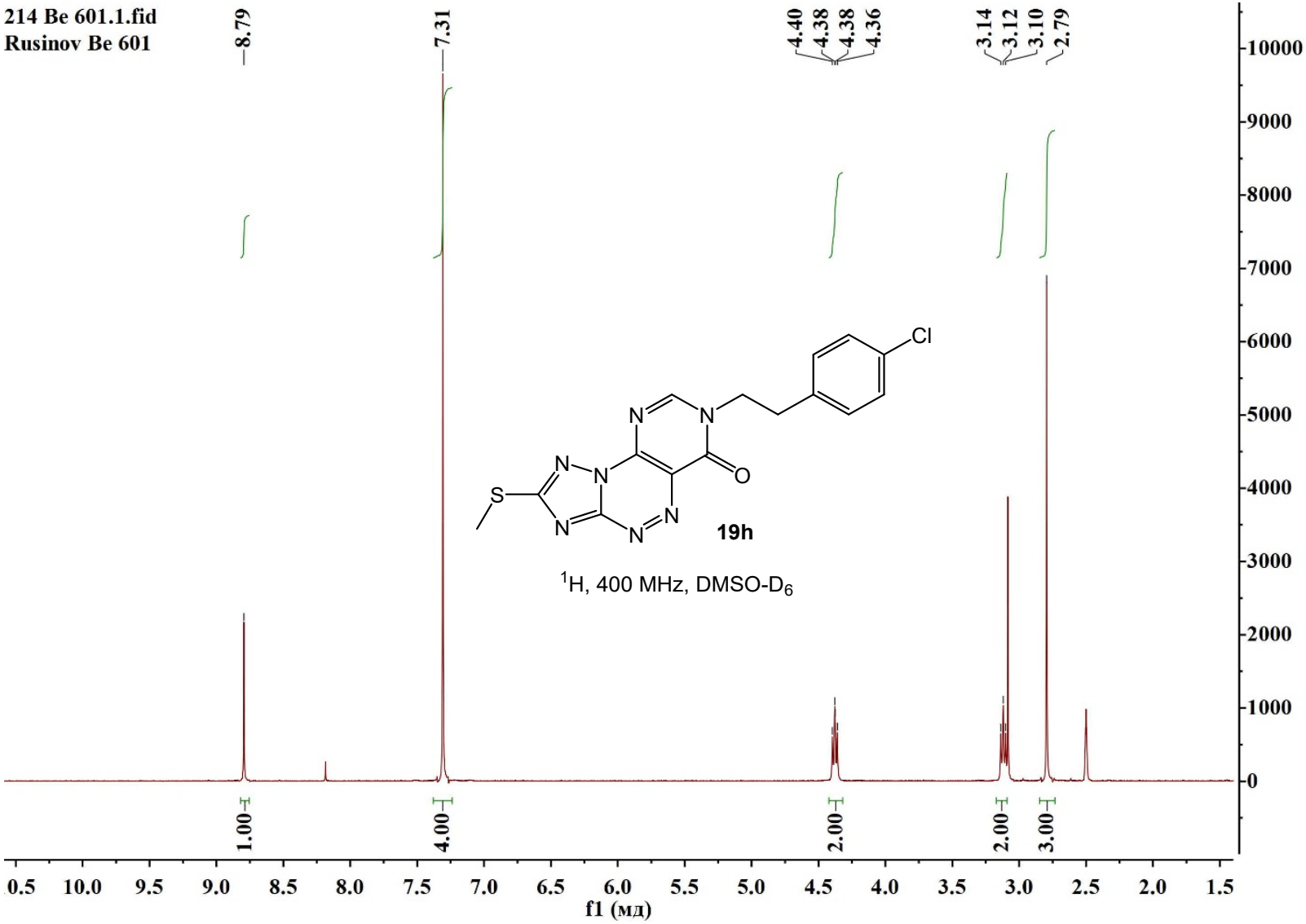


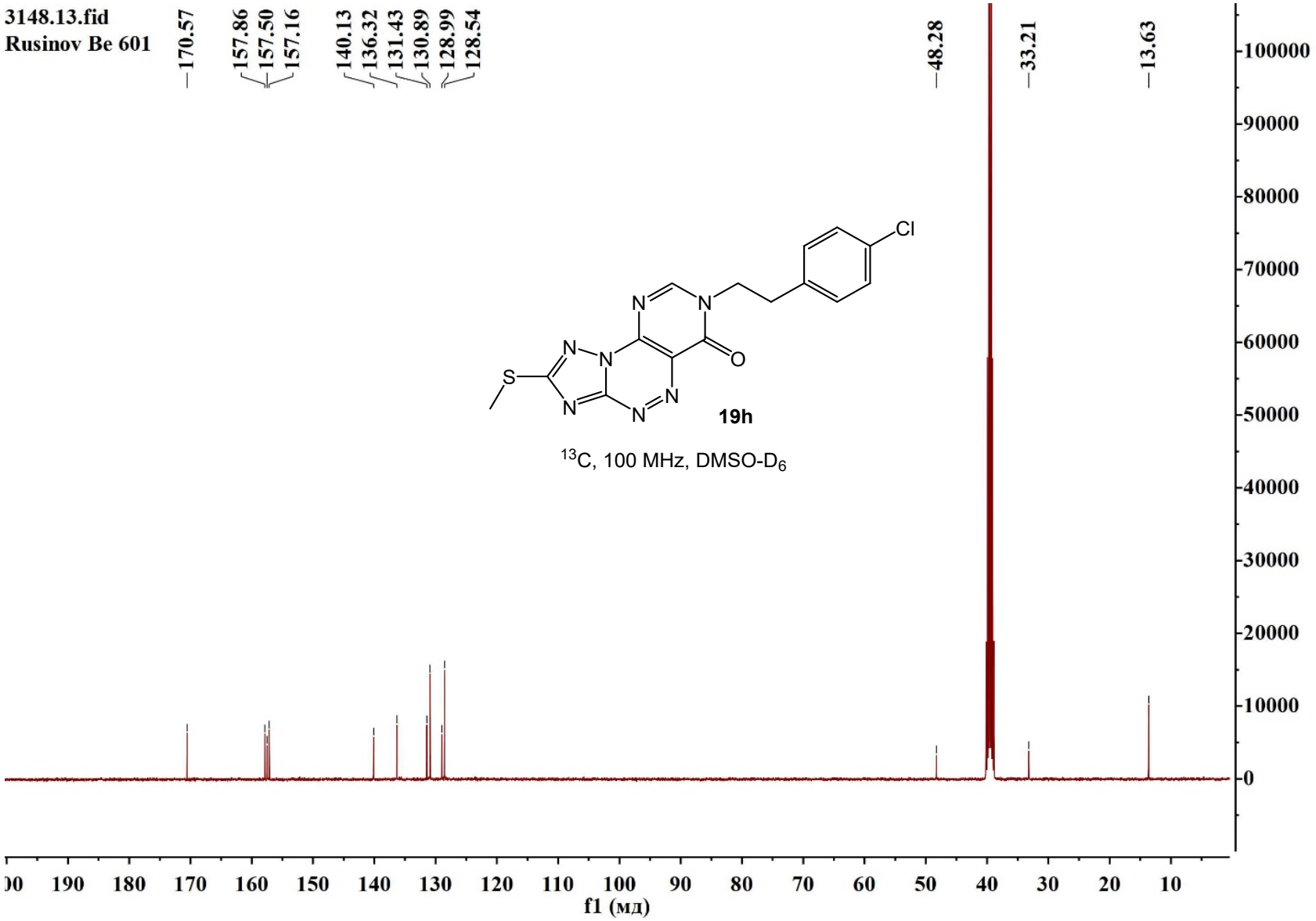
#	Wavelength	Intensity
0	198	483.6
1	216	515.2
2	266	130.0
3	342	58.0

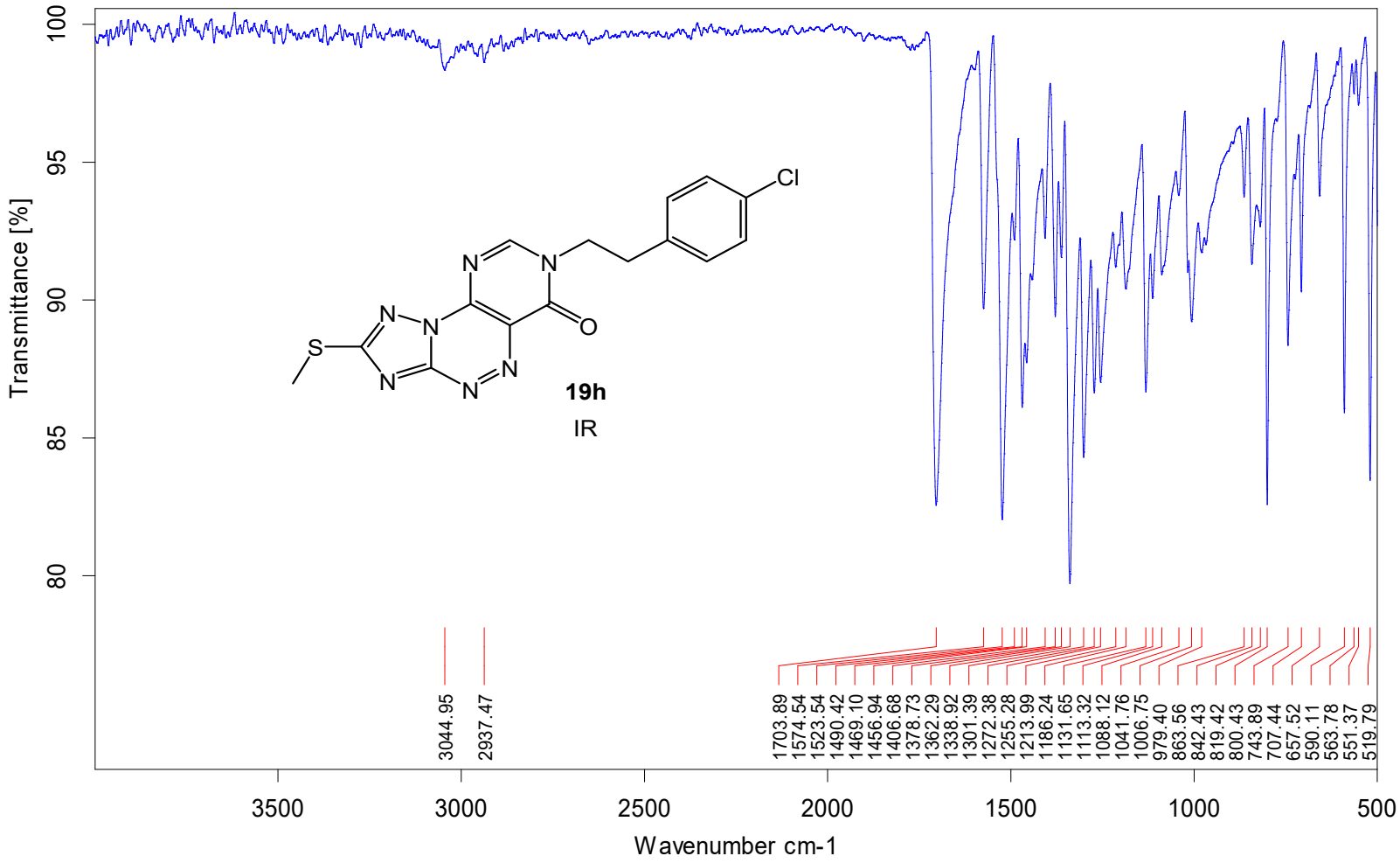


#	m/z	Res.	S/N	I	I %	FWHM
1	298.1082	28982	308252256.0	724348	17.5	0.0103
2	308.0927	35513	1765091712.0	4147707	100.0	0.0087
3	309.0949	24499	205099328.0	481953	11.6	0.0126
4	310.0899	18703	72333192.0	169972	4.1	0.0166
5	336.0871	22548	78992440.0	185621	4.5	0.0149
6	615.1779	39722	777050432.0	1825955	44.0	0.0155
7	616.1796	28876	205588656.0	483103	11.6	0.0213
8	617.1762	22376	90307312.0	212209	5.1	0.0276
9	922.2638	38041	202804592.0	476561	11.5	0.0242
10	923.2655	29853	88222328.0	207310	5.0	0.0309

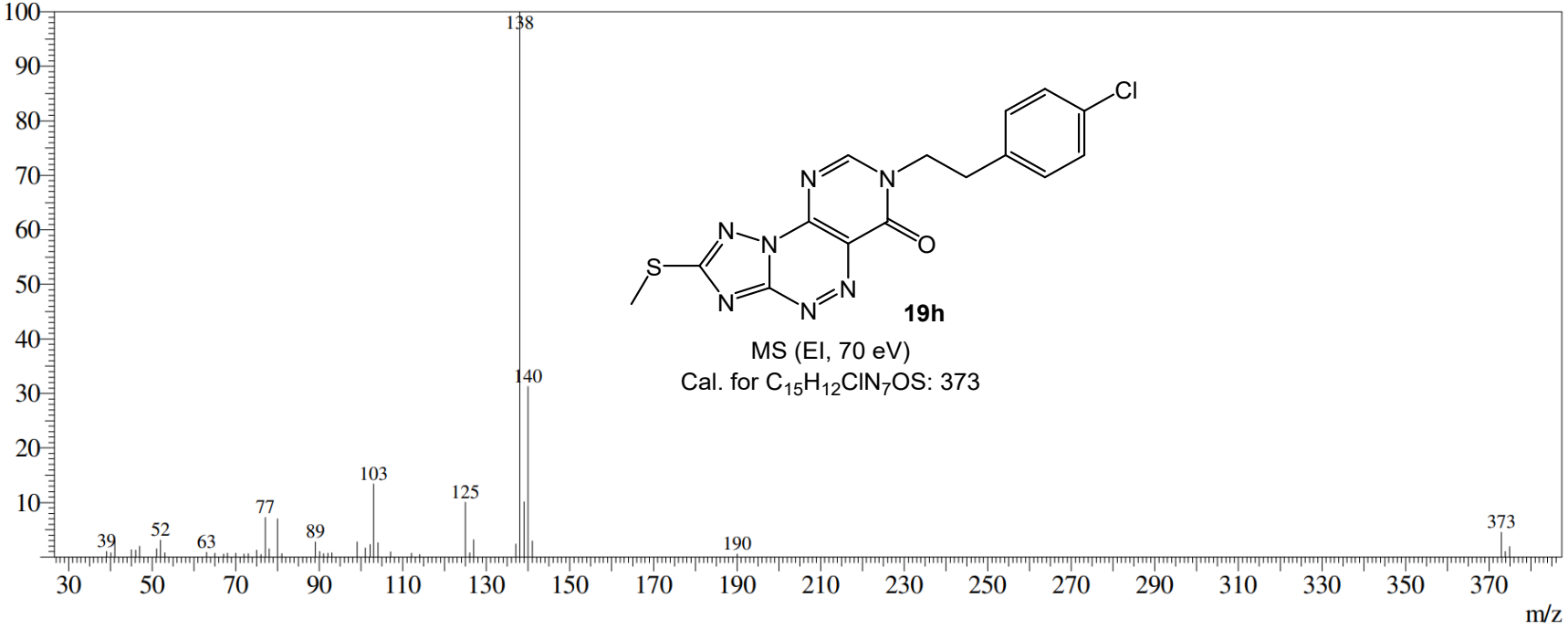
7-(4-Chlorophenethyl)-2-(methylthio)pyrimido[4,5-*e*][1,2,4]triazolo[5,1-*c*][1,2,4]triazin-6(7*H*)-one (19h)



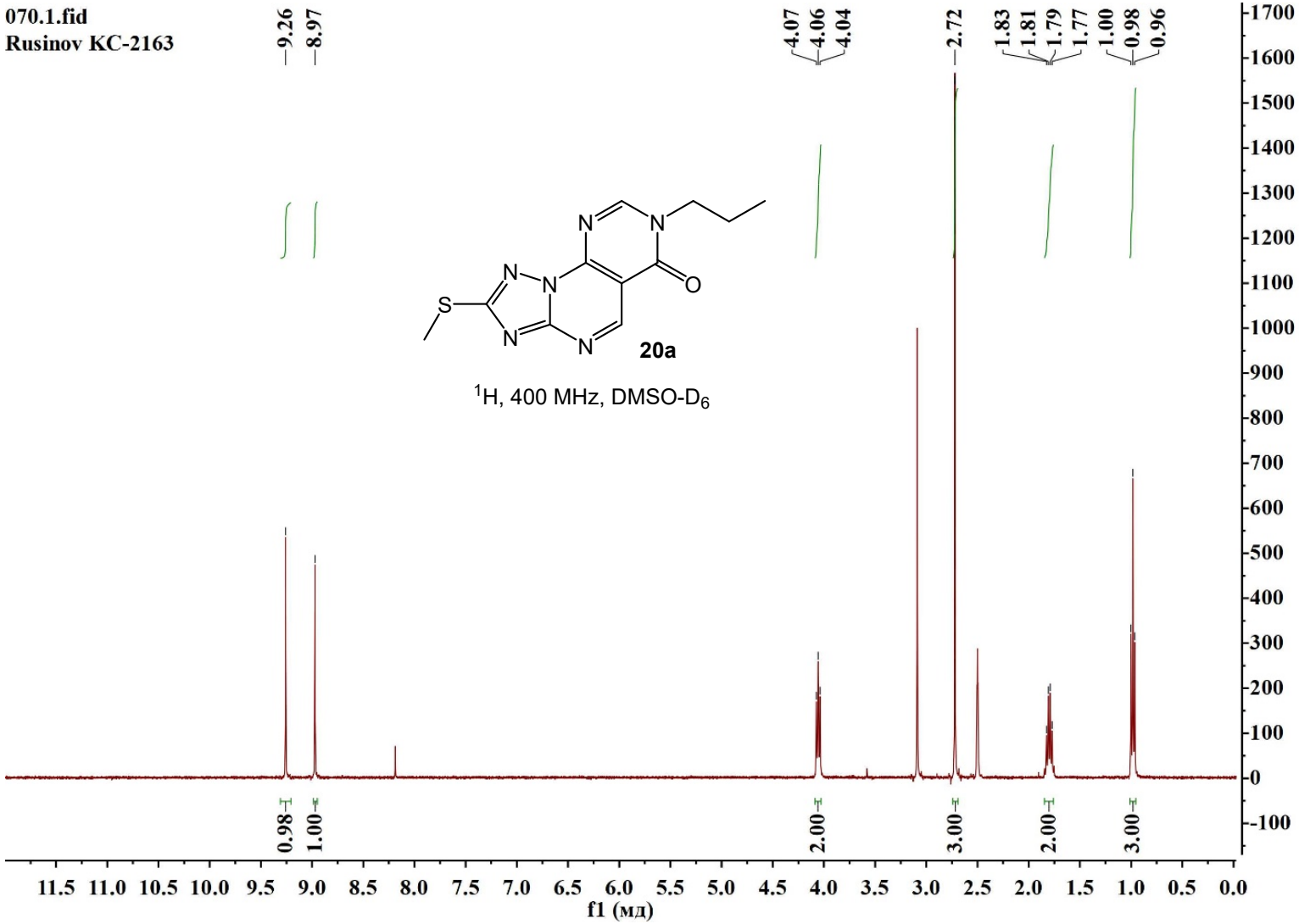

3148.13.fid
Rusinov Be 601
170.57
157.86
157.50
157.16
140.13
136.32
131.43
130.89
128.99
128.54
48.28
33.21
13.63
Cl
N
N
N
N
N
N
S
O
19h
13C, 100 MHz, DMSO-D6
100000
90000
80000
70000
60000
50000
40000
30000
20000
10000
0
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (мд)

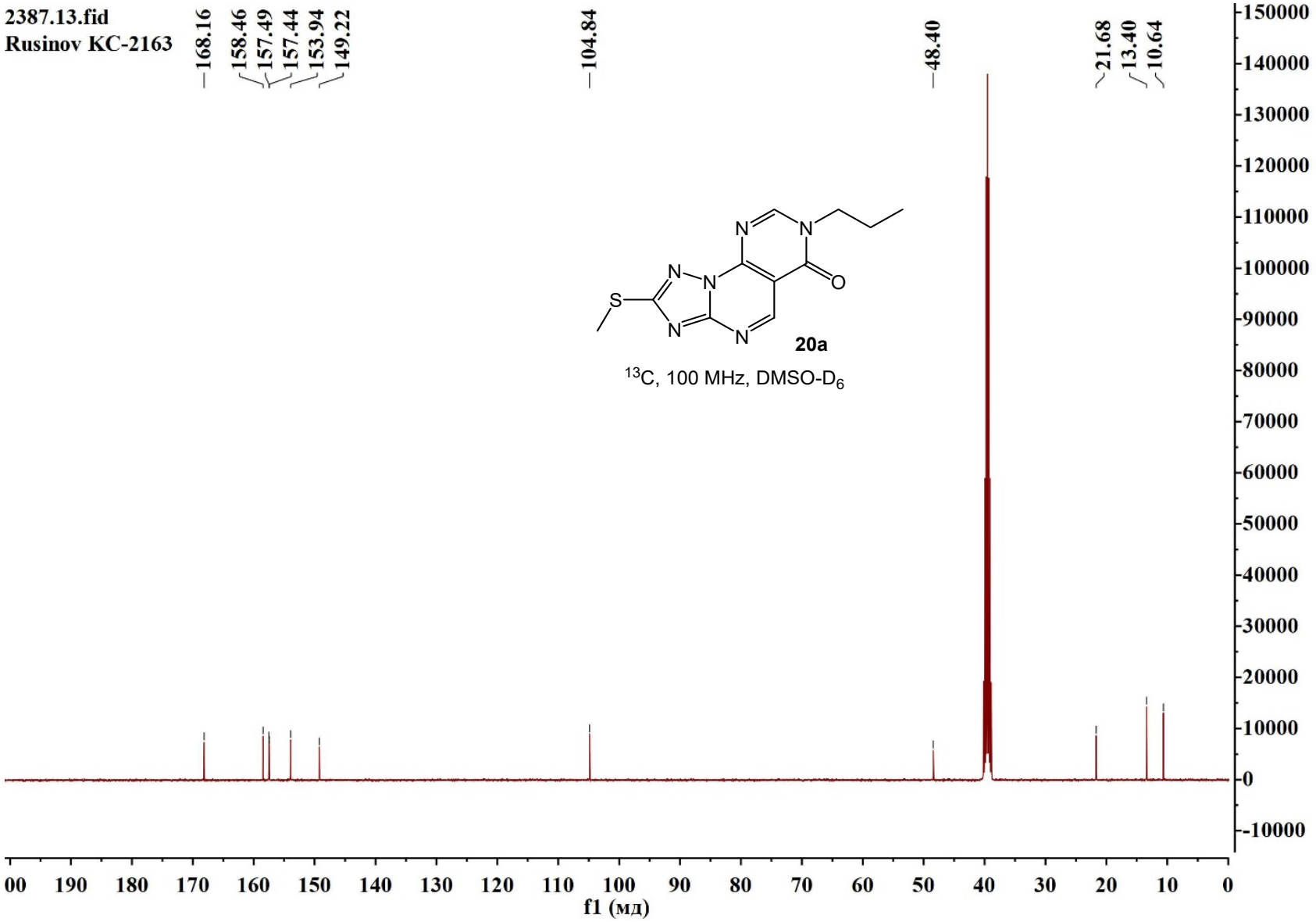

Transmittance [%]
100
95
90
85
80
Cl
N
N
N
N
N
N
S
O
19h
IR
3044.95
2937.47
1703.89
1574.54
1523.54
1490.42
1469.10
1456.94
1406.68
1378.73
1362.29
1338.92
1301.39
1272.38
1255.28
1213.99
1186.24
1131.65
1113.32
1088.12
1041.76
1006.75
979.40
863.56
842.43
819.42
800.43
743.89
707.44
657.52
590.11
563.78
551.37
519.79
3500
3000
2500
2000
1500
1000
500
Wavenumber cm-1

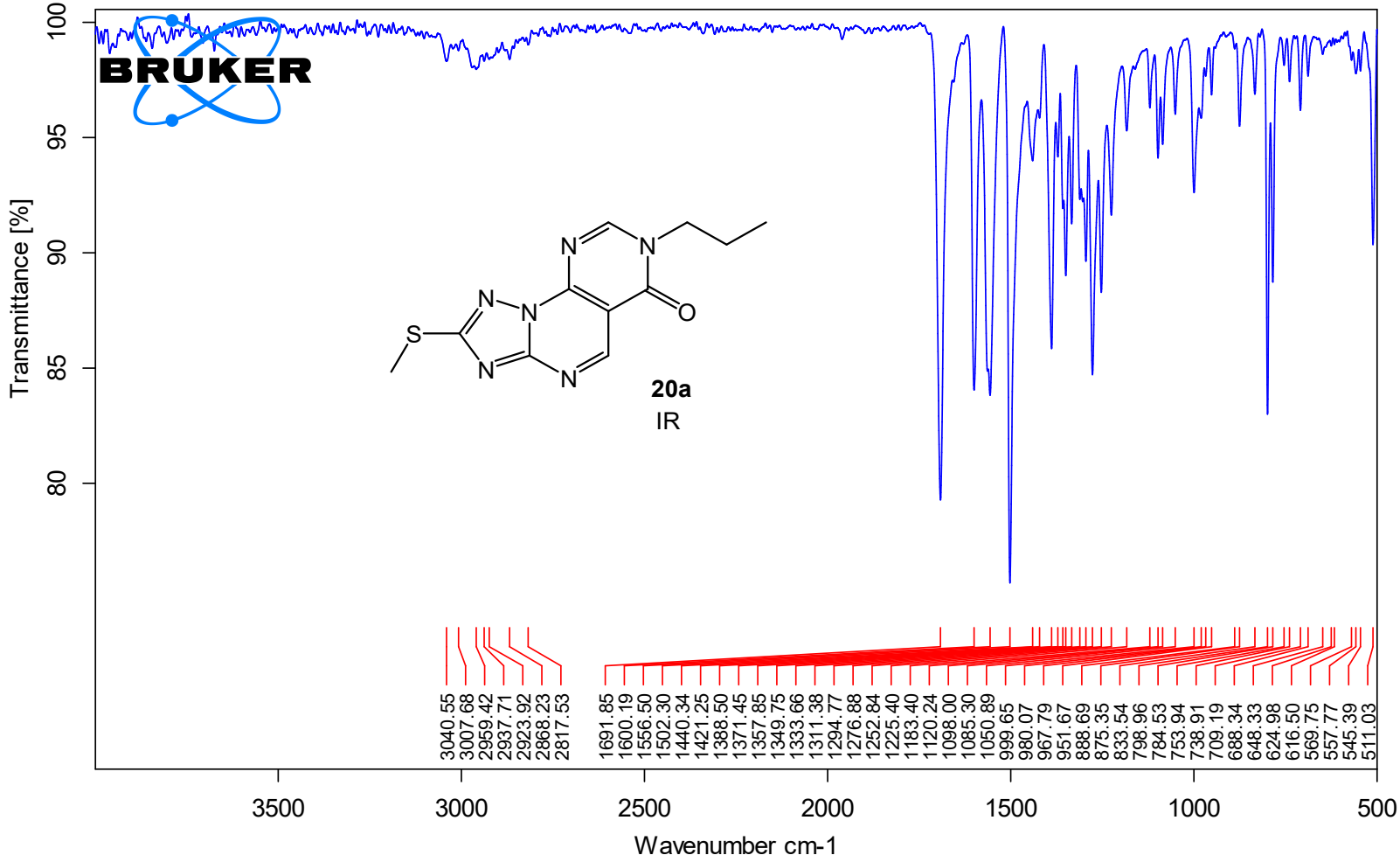
Line#:1 R.Time:2.765(Scan#:1067)
MassPeaks:47
RawMode:Single 2.765(1067) BasePeak:138(6910195)
Фон.реж.:1.363(506) Group 1 - Event 1



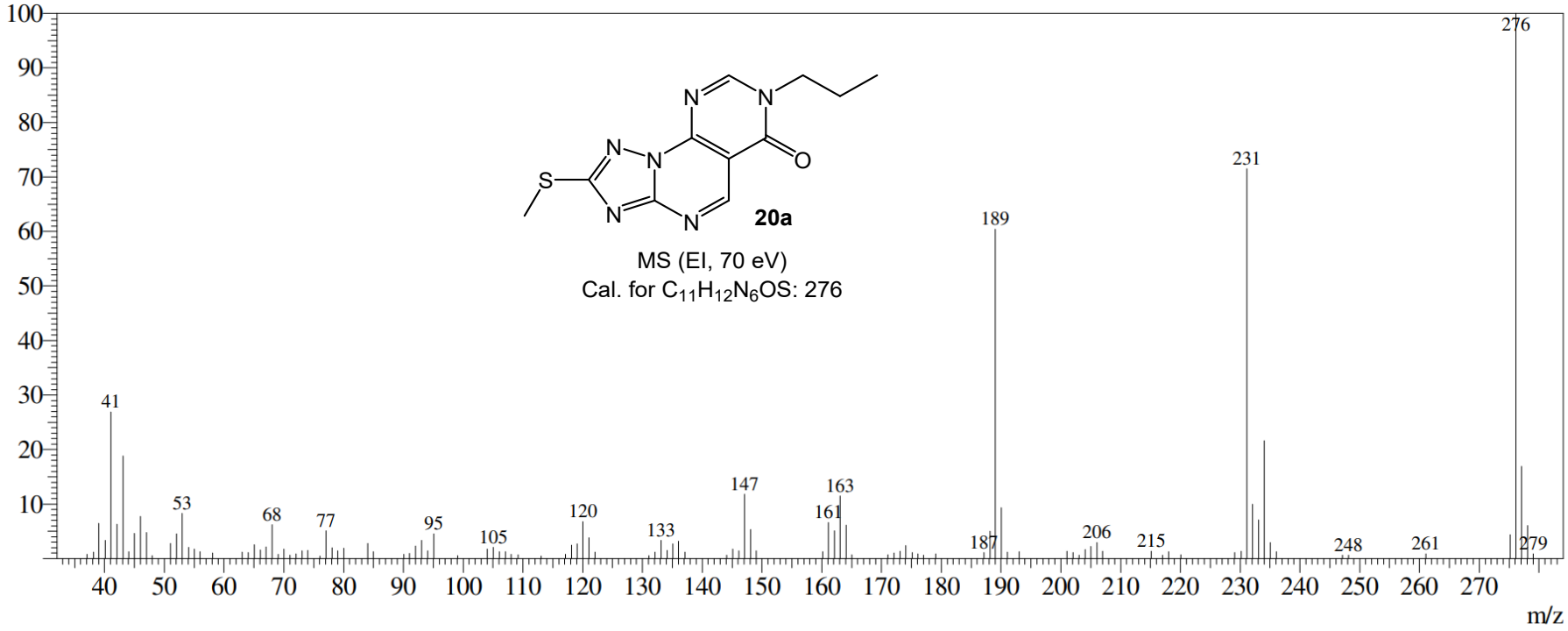
7-Propyl-2-(methylthio)pyrimido[4,5-*e*][1,2,4]triazolo[5,1-*c*][1,5-a]pyrimidin-6(7*H*)-one (20a)



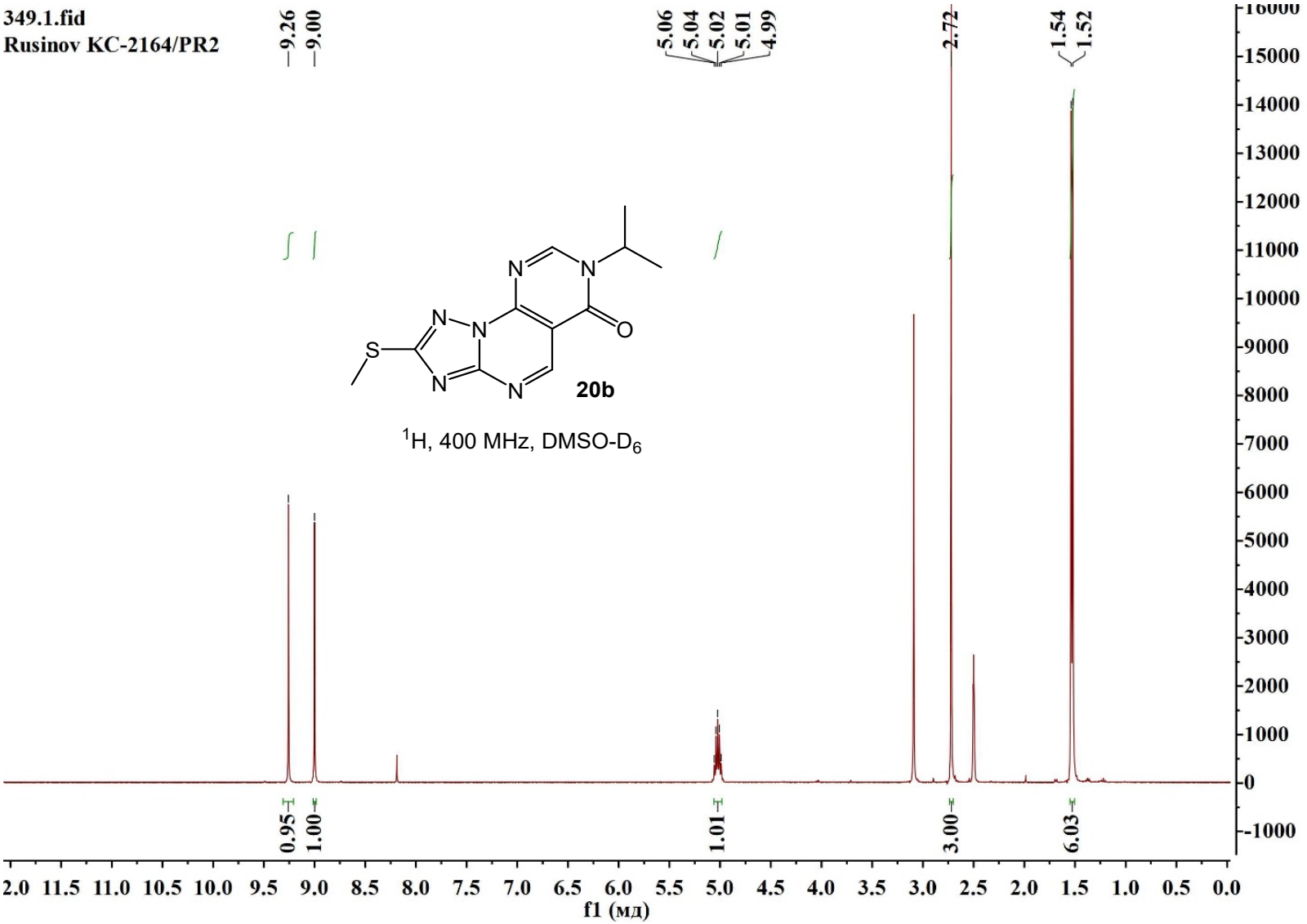

2387.13.fid
Rusinov KC-2163
168.16
158.46
157.49
157.44
153.94
149.22
104.84
48.40
21.68
13.40
10.64
20a
13C, 100 MHz, DMSO-D6
f1 (мд)

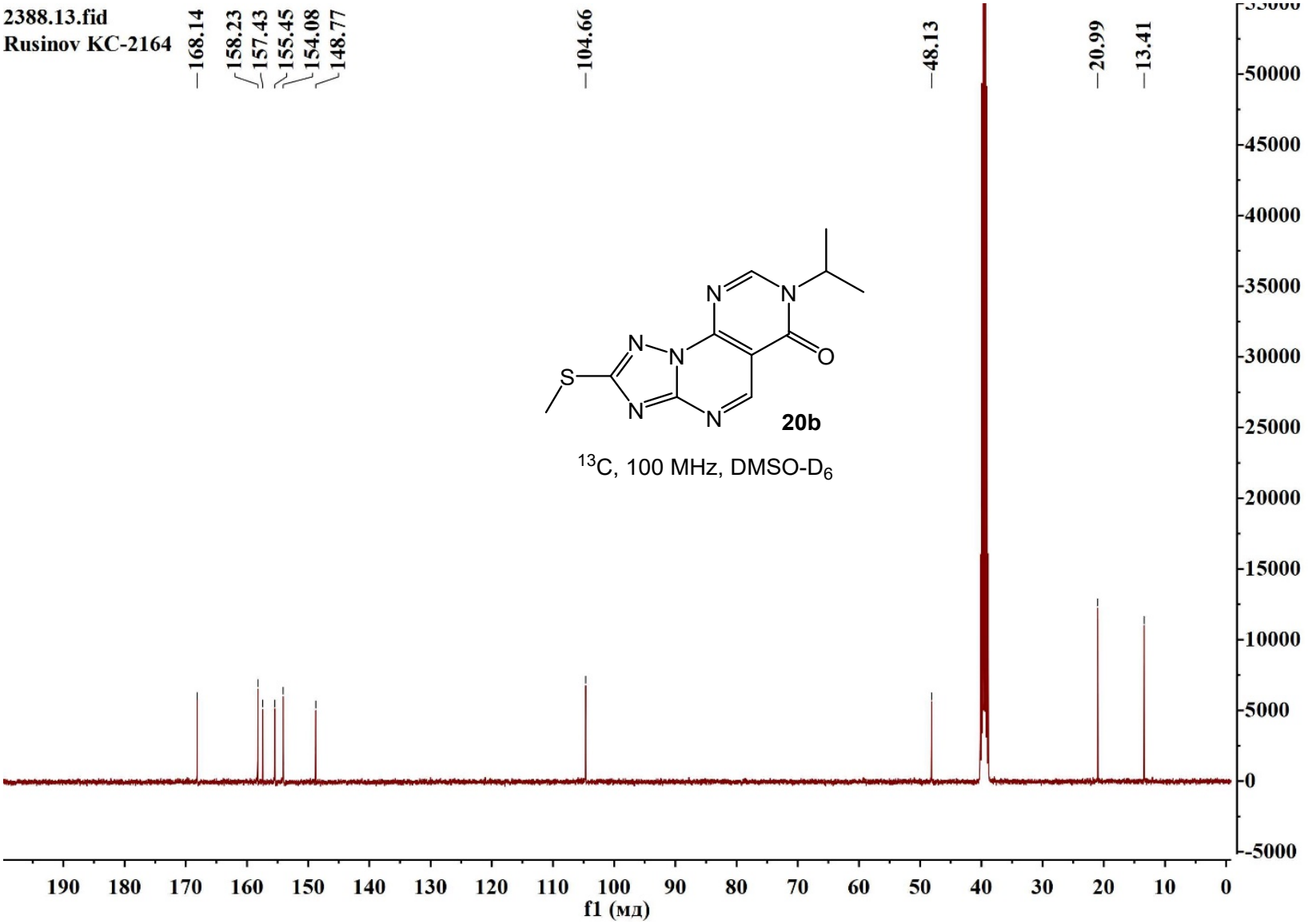

BRUKER
Transmittance [%]
100
95
90
85
80
3040.55
3007.68
2959.42
2937.71
2923.92
2868.23
2817.53
1691.85
1600.19
1556.50
1502.30
1440.34
1421.25
1388.50
1371.45
1357.85
1349.75
1333.66
1311.38
1294.77
1276.88
1252.84
1225.40
1183.40
1120.24
1098.00
1085.30
1050.89
999.65
980.07
967.79
951.67
888.69
875.35
833.54
798.96
784.53
753.94
738.91
709.19
688.34
648.33
624.98
616.50
569.75
557.77
545.39
511.03
3500
3000
2500
2000
1500
1000
500
Wavenumber cm-1
20a
IR

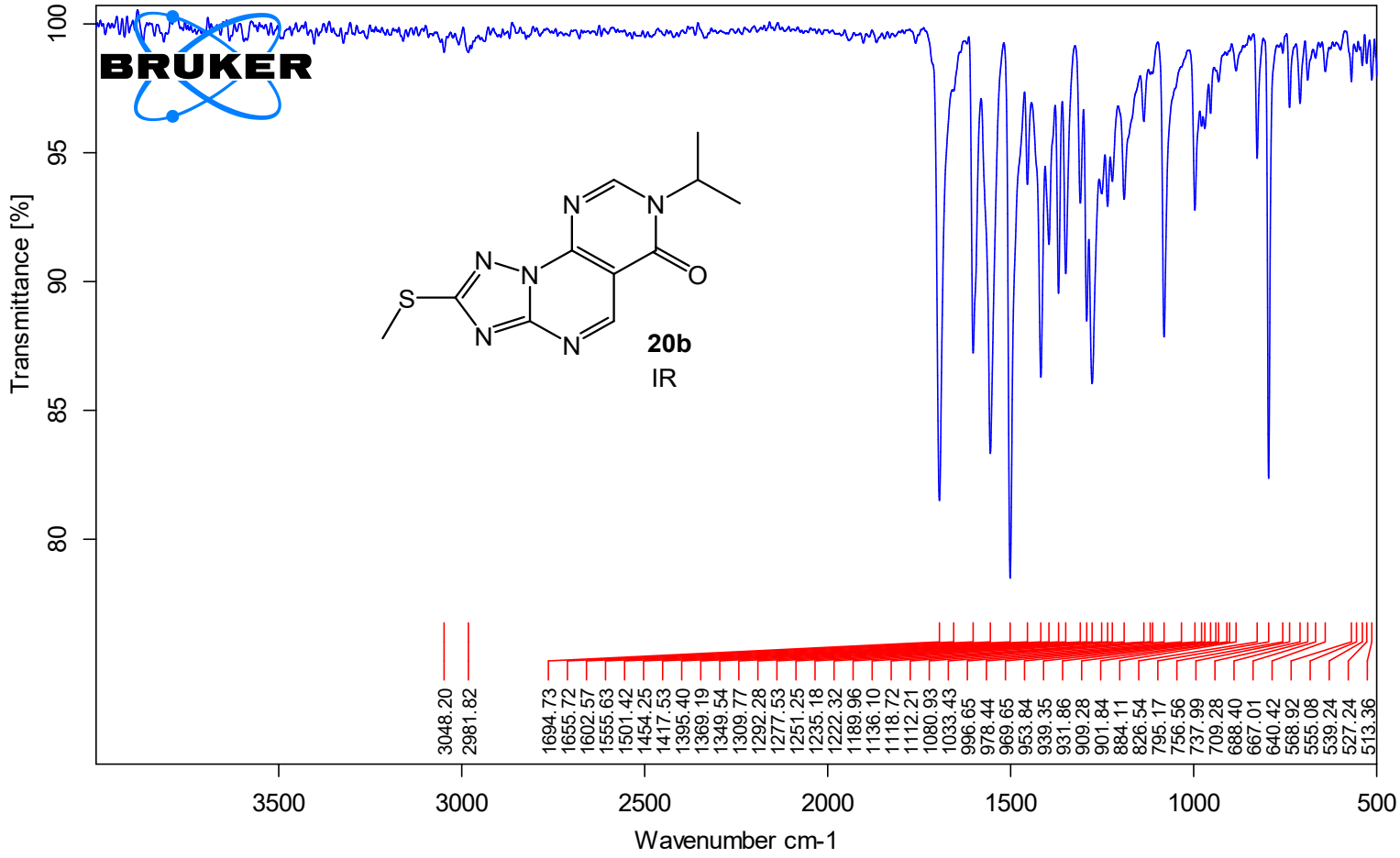
Line#:1 R.Time:2.265(Scan#:867)
MassPeaks:118
RawMode:Single 2.265(867) BasePeak:276(4987212)
Фон.реж.:0.990(357) Group 1 - Event 1



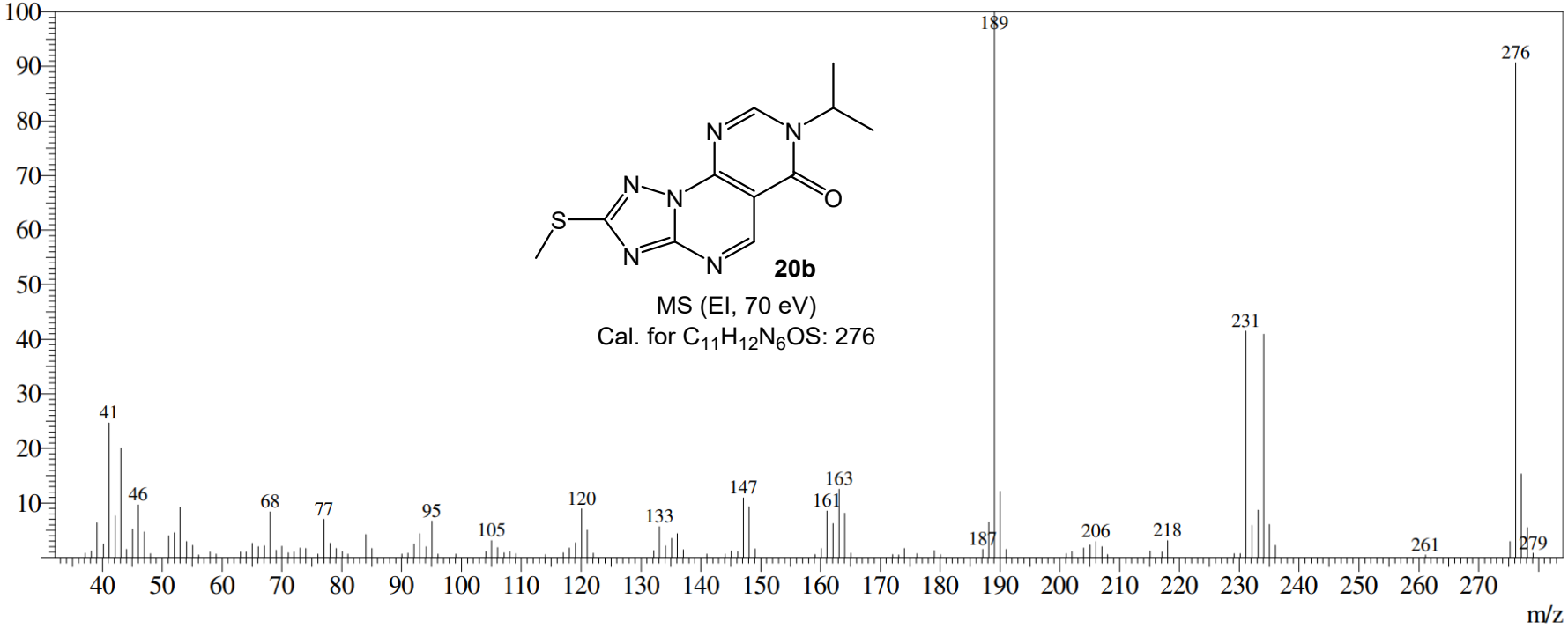
7-Isopropyl-2-(methylthio)pyrimido[5,4-*e*][1,2,4]triazolo[5,1-*c*][1,5-a]pyrimidin-6(7*H*)-one (20b)



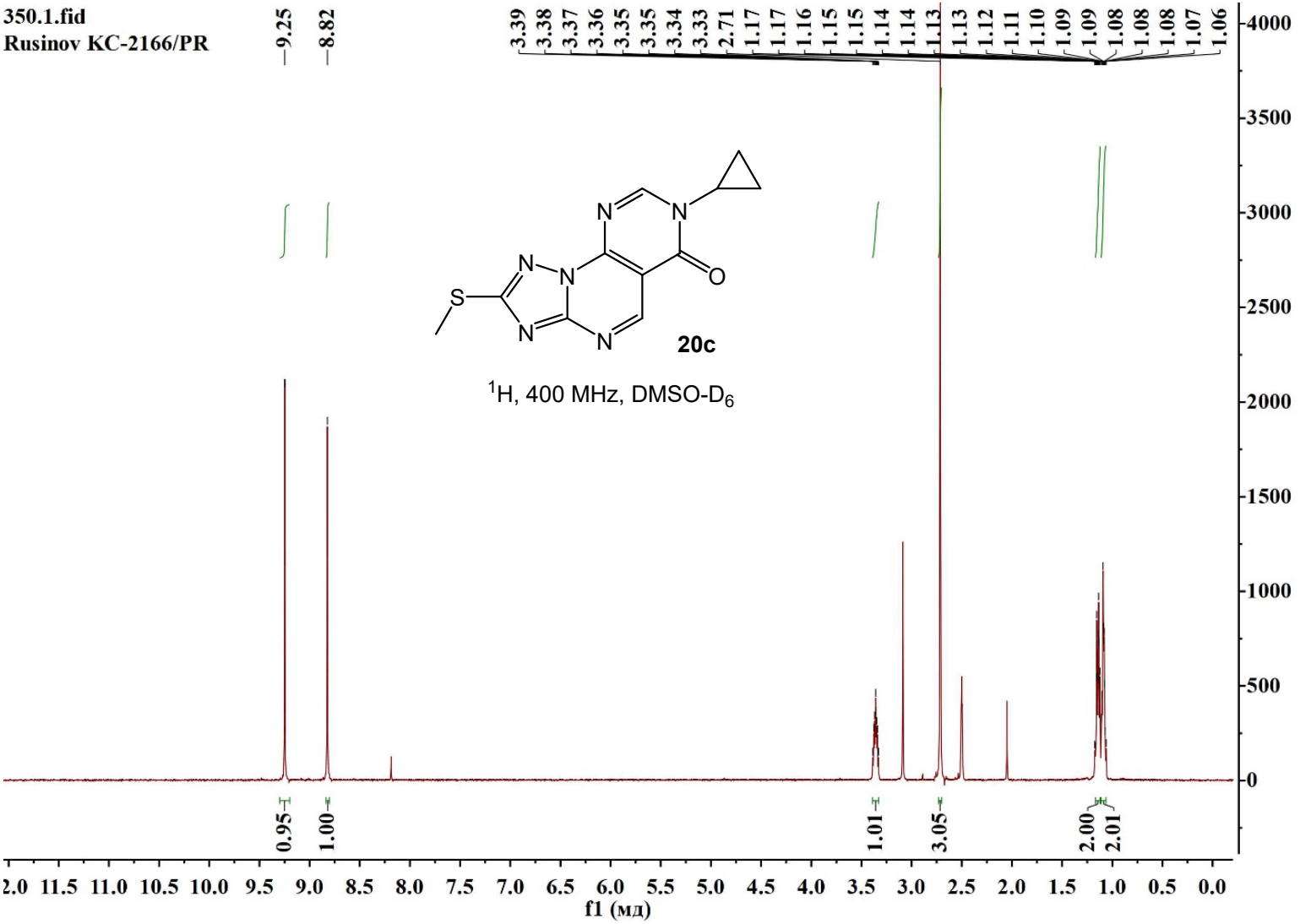

2388.13.fid
Rusinov KC-2164
168.14
158.23
157.43
155.45
154.08
148.77
104.66
48.13
20.99
13.41
20b
13C, 100 MHz, DMSO-D6
f1 (мд)

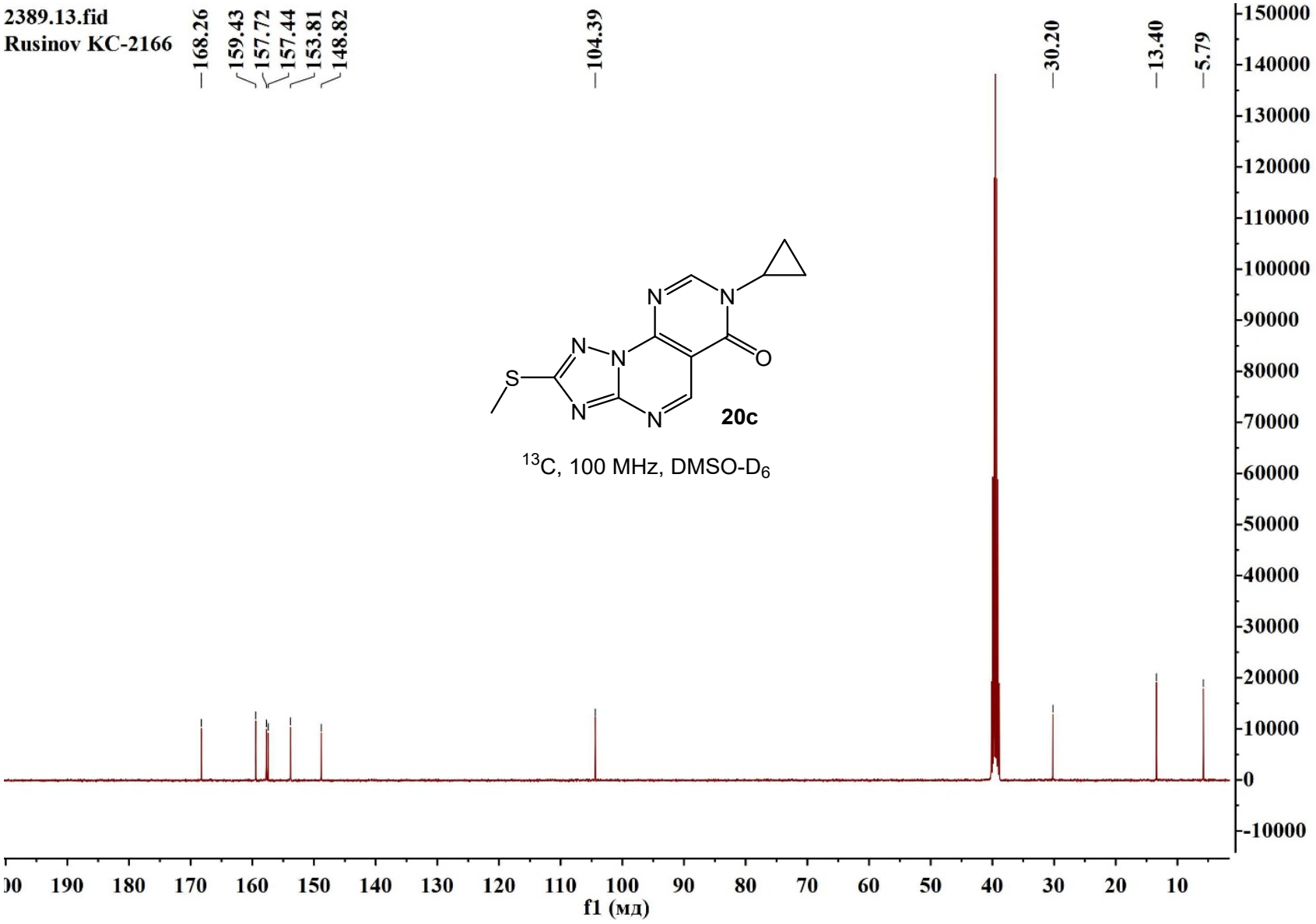

BRUKER
Transmittance [%]
100
95
90
85
80
3500
3000
2500
2000
1500
1000
500
Wavenumber cm-1
20b
IR
3048.20
2981.82
1694.73
1655.72
1602.57
1555.63
1501.42
1454.25
1417.53
1395.40
1369.19
1349.54
1309.77
1292.28
1277.53
1251.25
1235.18
1222.32
1189.96
1136.10
1118.72
1112.21
1080.93
1033.43
996.65
978.44
969.65
953.84
939.35
931.86
909.28
901.84
884.11
826.54
795.17
756.56
737.99
709.28
688.40
667.01
640.42
568.92
555.08
539.24
527.24
513.36

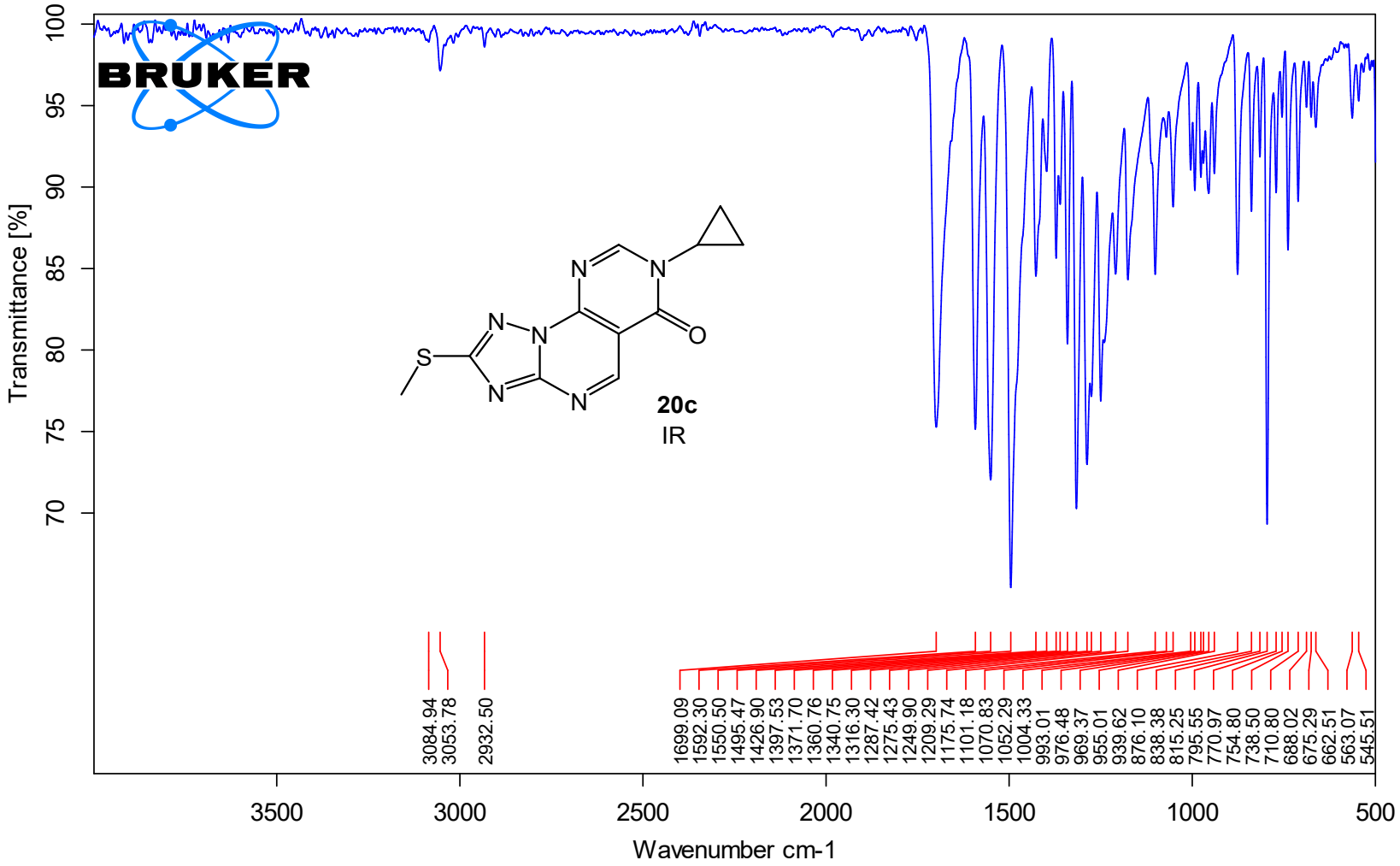
Line#:1 R.Time:2.143(Scan#:818)
MassPeaks:116
RawMode:Single 2.143(818) BasePeak:189(4904083)
Фон.реж.:0.828(292) Group 1 - Event 1



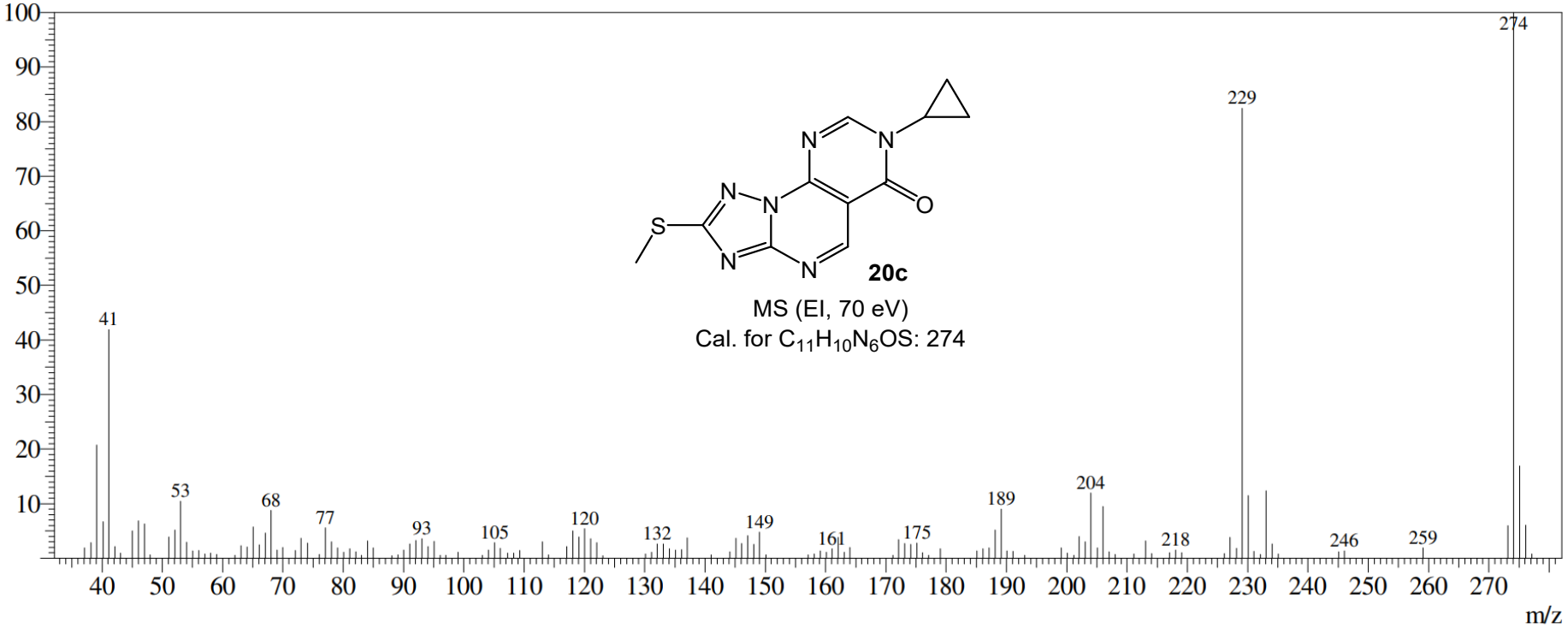
7-Cyclopropyl-2-(methylthio)pyrimido[5,4-*e*][1,2,4]triazolo[1,5-*a*]pyrimidin-6(7*H*)-one (20c)




2389.13.fid
Rusinov KC-2166
168.26
159.43
157.72
157.44
153.81
148.82
104.39
30.20
13.40
5.79
20c
^{13}C, 100 MHz, DMSO-D$_6$
f1 (мд)


BRUKER
Transmittance [%]
100
95
90
85
80
75
70
3500
3000
2500
2000
1500
1000
500
Wavenumber cm-1
20c
IR
3084.94
3053.78
2932.50
1699.09
1592.30
1550.50
1495.47
1426.90
1397.53
1371.70
1360.76
1340.75
1316.30
1287.42
1275.43
1249.90
1209.29
1175.74
1101.18
1070.83
1052.29
1004.33
993.01
976.48
969.37
955.01
939.62
876.10
838.38
815.25
795.55
770.97
754.80
738.50
710.80
688.02
675.29
662.51
563.07
545.51

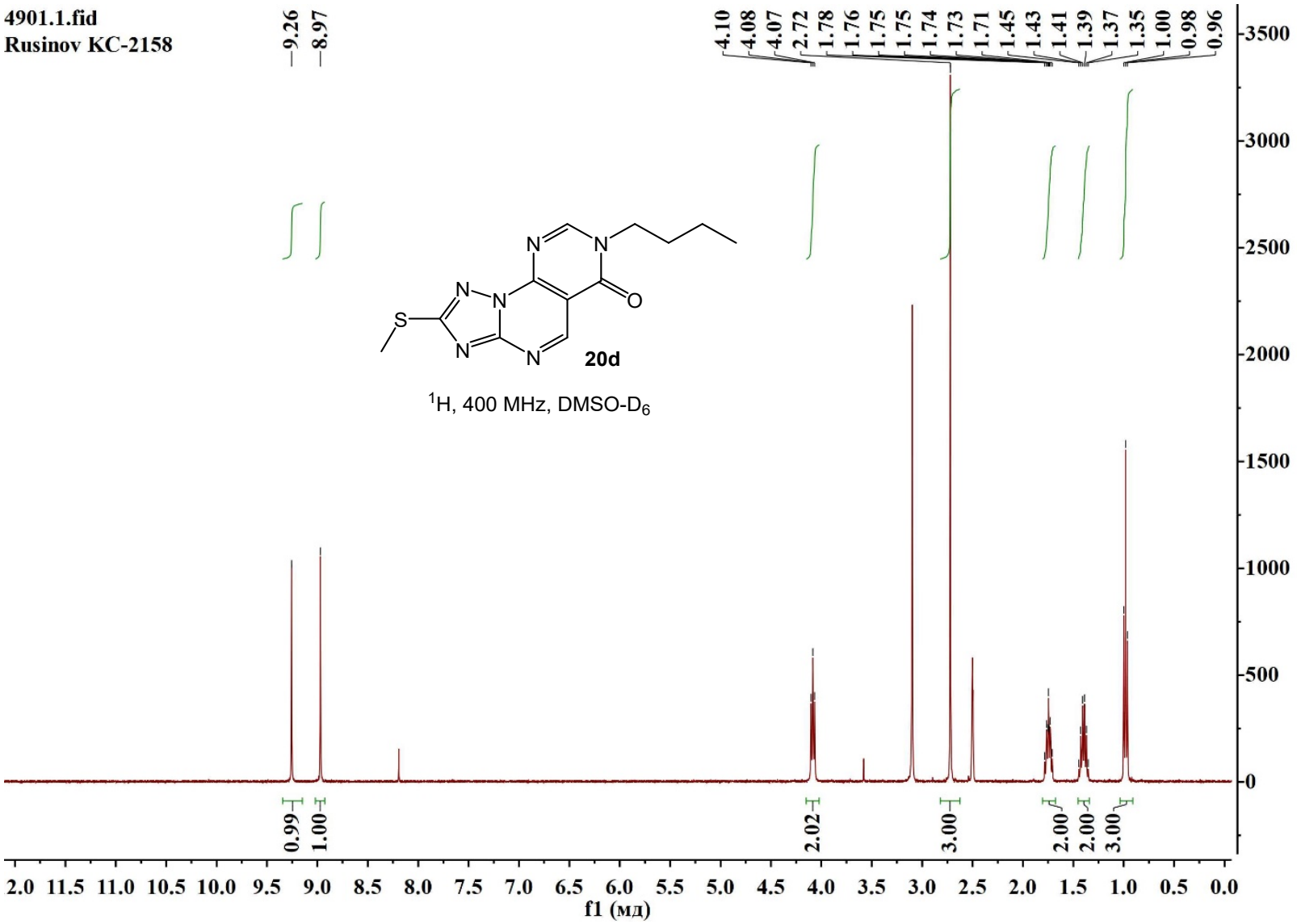
Line#:1 R.Time:2.560(Scan#:985)
MassPeaks:143
RawMode:Single 2.560(985) BasePeak:274(5699415)
Фон.реж.:1.718(648) Group 1 - Event 1

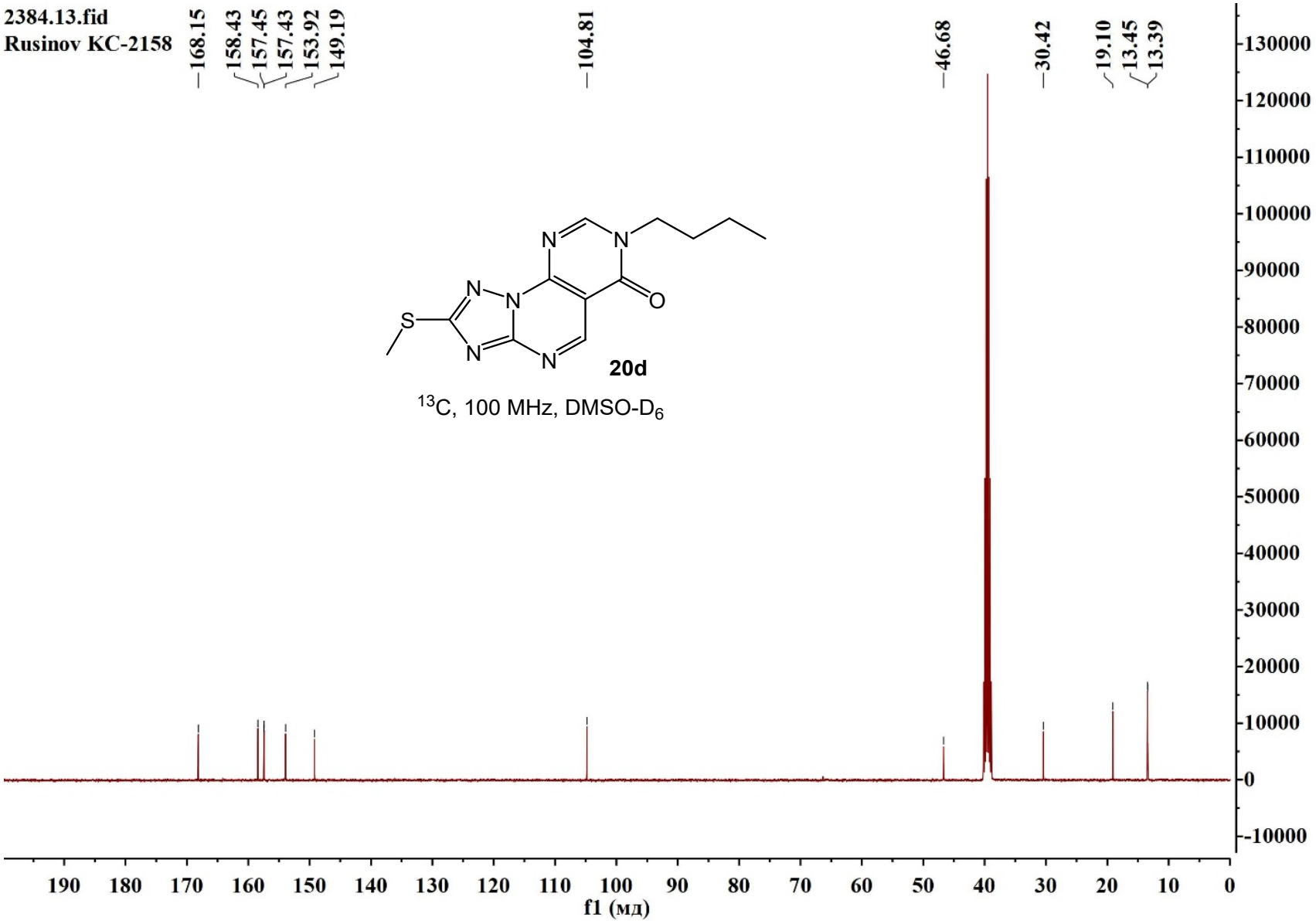


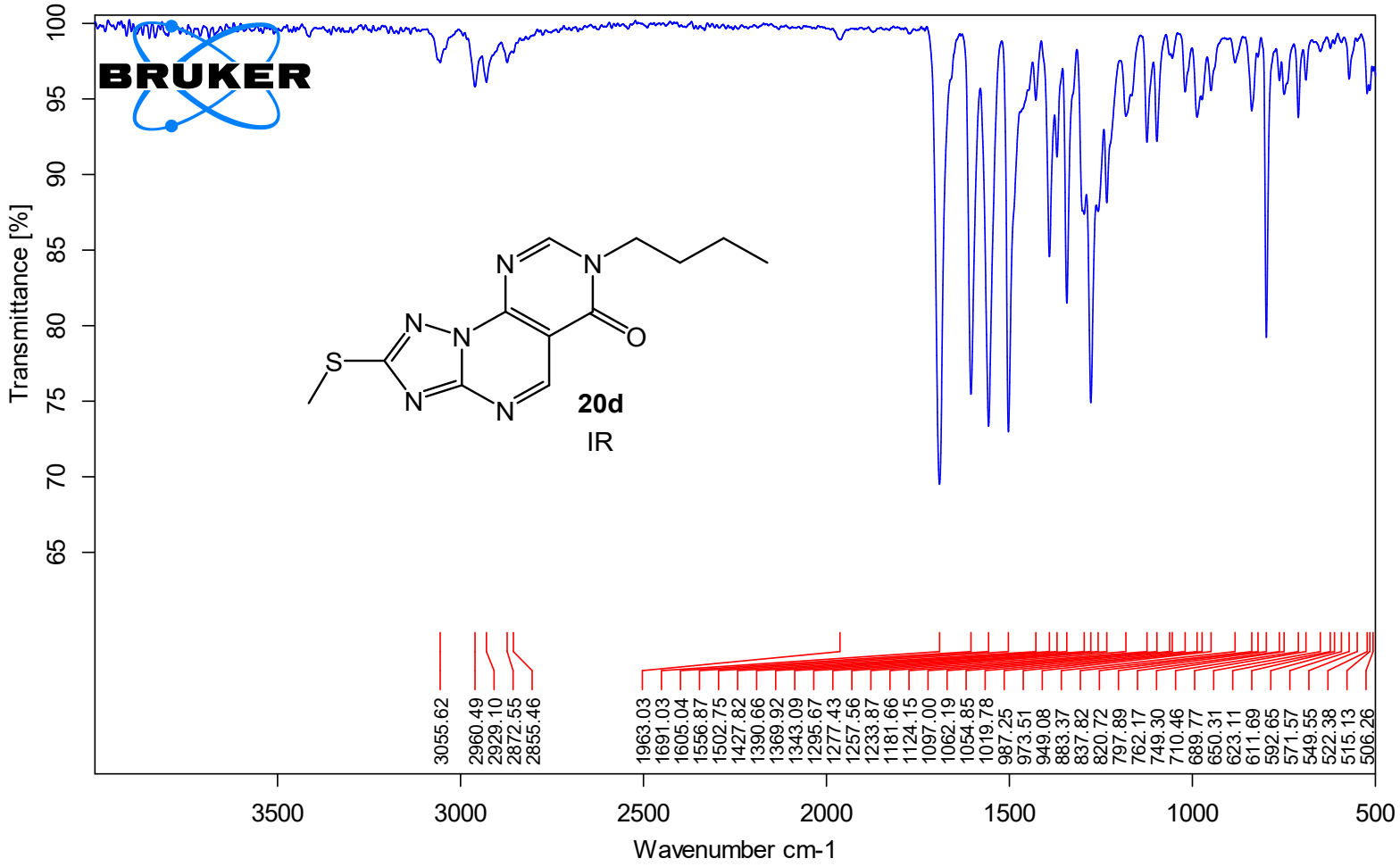
20c

MS (EI, 70 eV)
Cal. for $C_{11}H_{10}N_6OS$: 274

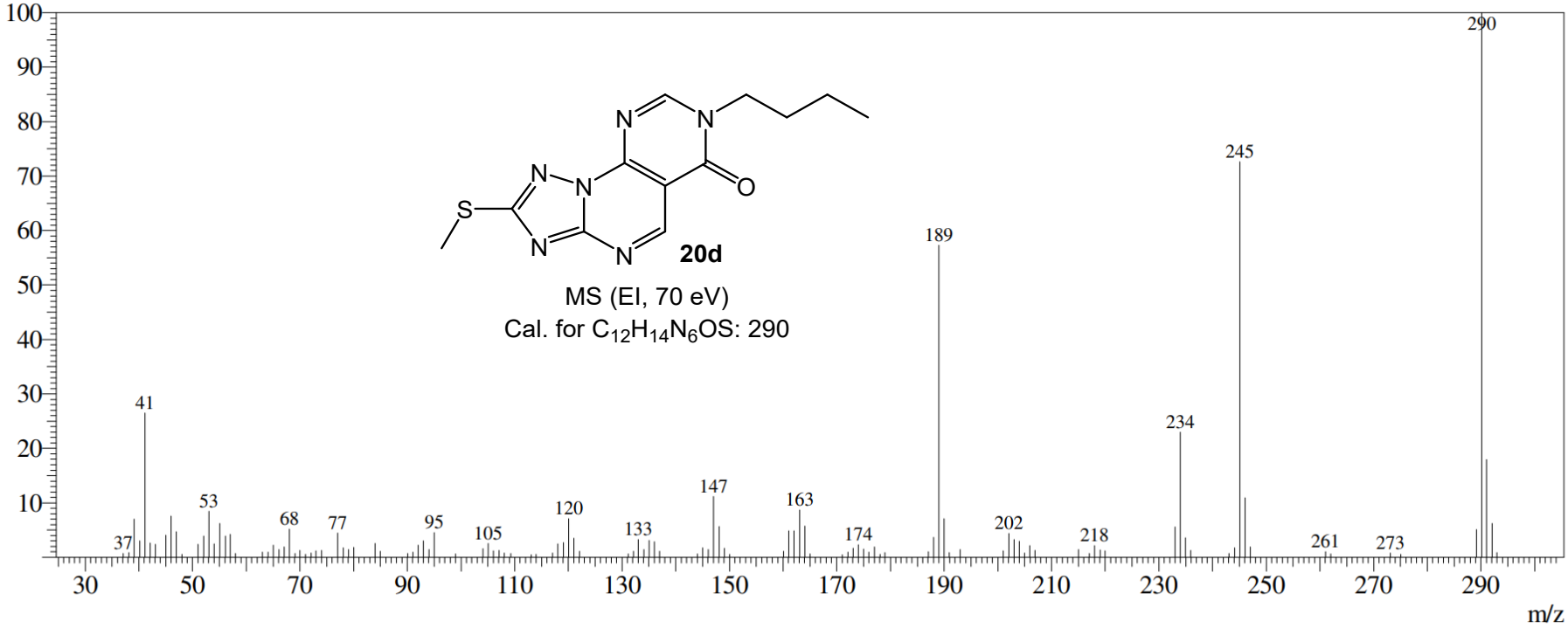
7-Butyl-2-(methylthio)pyrimido[5,4-*e*][1,2,4]triazolo[1,5-*a*]pyrimidin-6(7*H*)-one (20d)



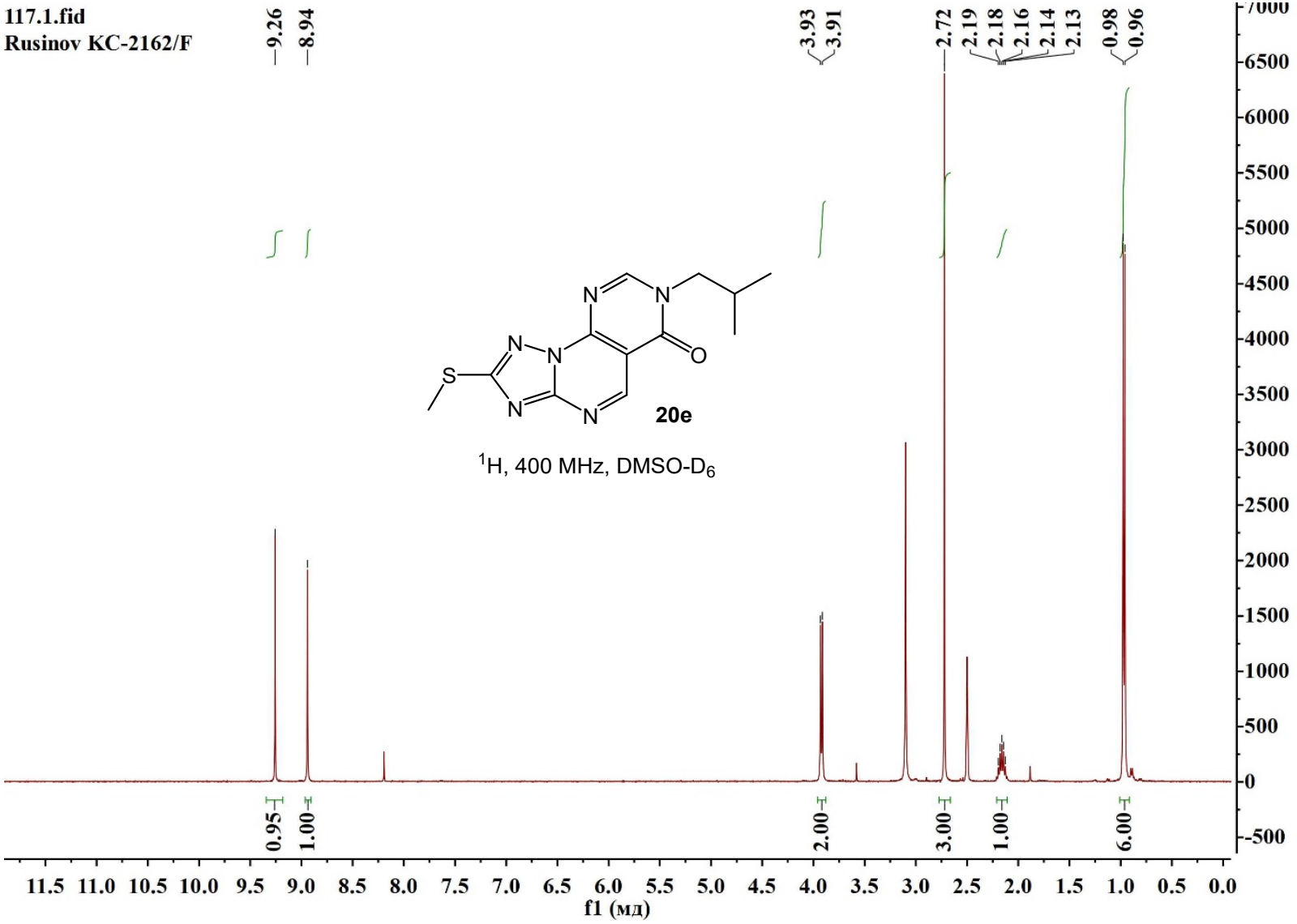

2384.13.fid
Rusinov KC-2158
168.15
158.43
157.45
157.43
153.92
149.19
104.81
46.68
30.42
19.10
13.45
13.39
20d
13C, 100 MHz, DMSO-D6
f1 (мд)

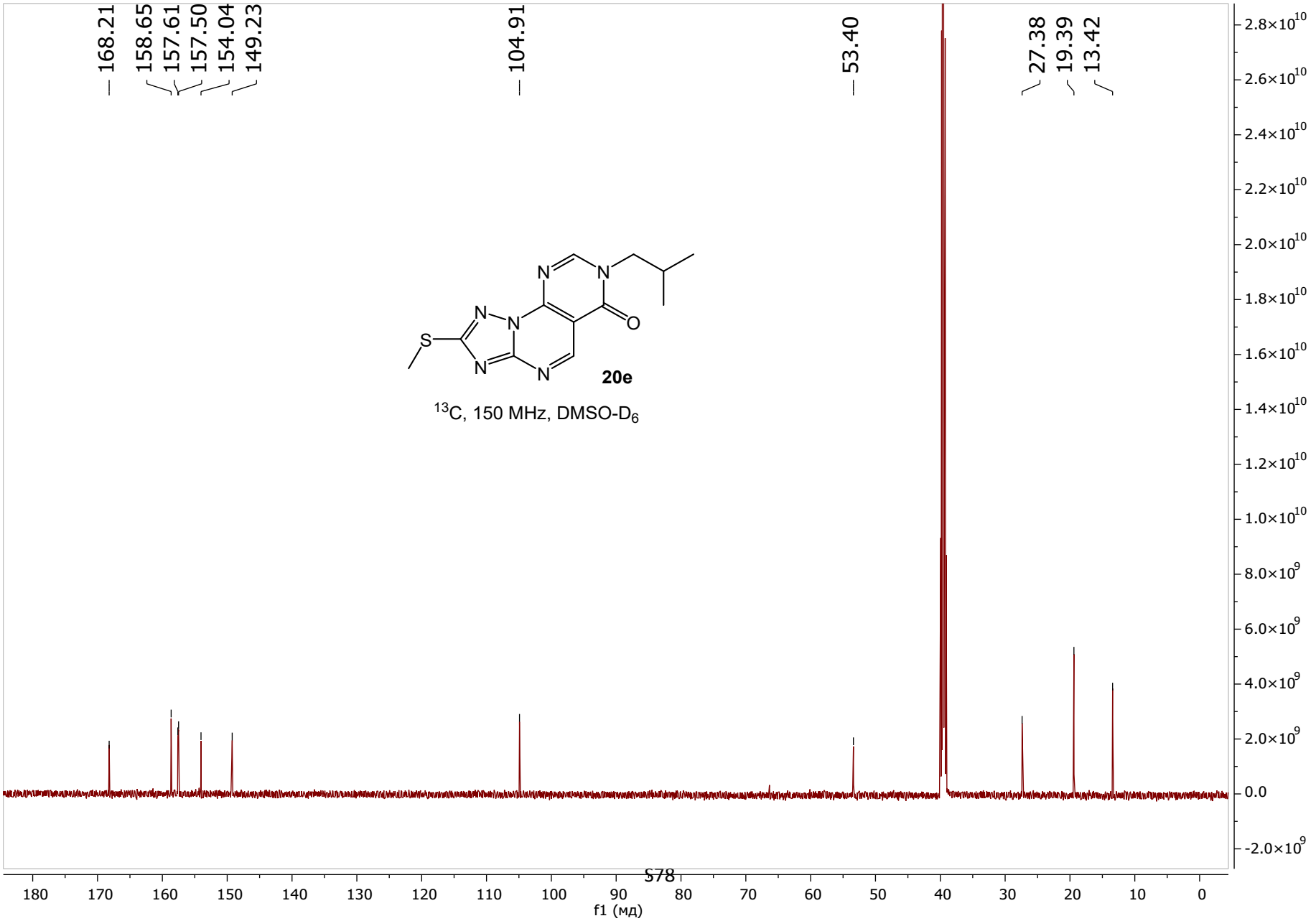

BRUKER
Transmittance [%]
100
95
90
85
80
75
70
65
N
N
N
N
N
S
O
20d
IR
3055.62
2960.49
2929.10
2872.55
2855.46
1963.03
1691.03
1605.04
1556.87
1502.75
1427.82
1390.66
1369.92
1343.09
1295.67
1277.43
1257.56
1233.87
1181.66
1124.15
1097.00
1062.19
1054.85
1019.78
987.25
973.51
949.08
883.37
837.82
820.72
797.89
762.17
749.30
710.46
689.77
650.31
623.11
611.69
592.65
571.57
549.55
522.38
515.13
506.26
3500
3000
2500
2000
1500
1000
500
Wavenumber cm-1

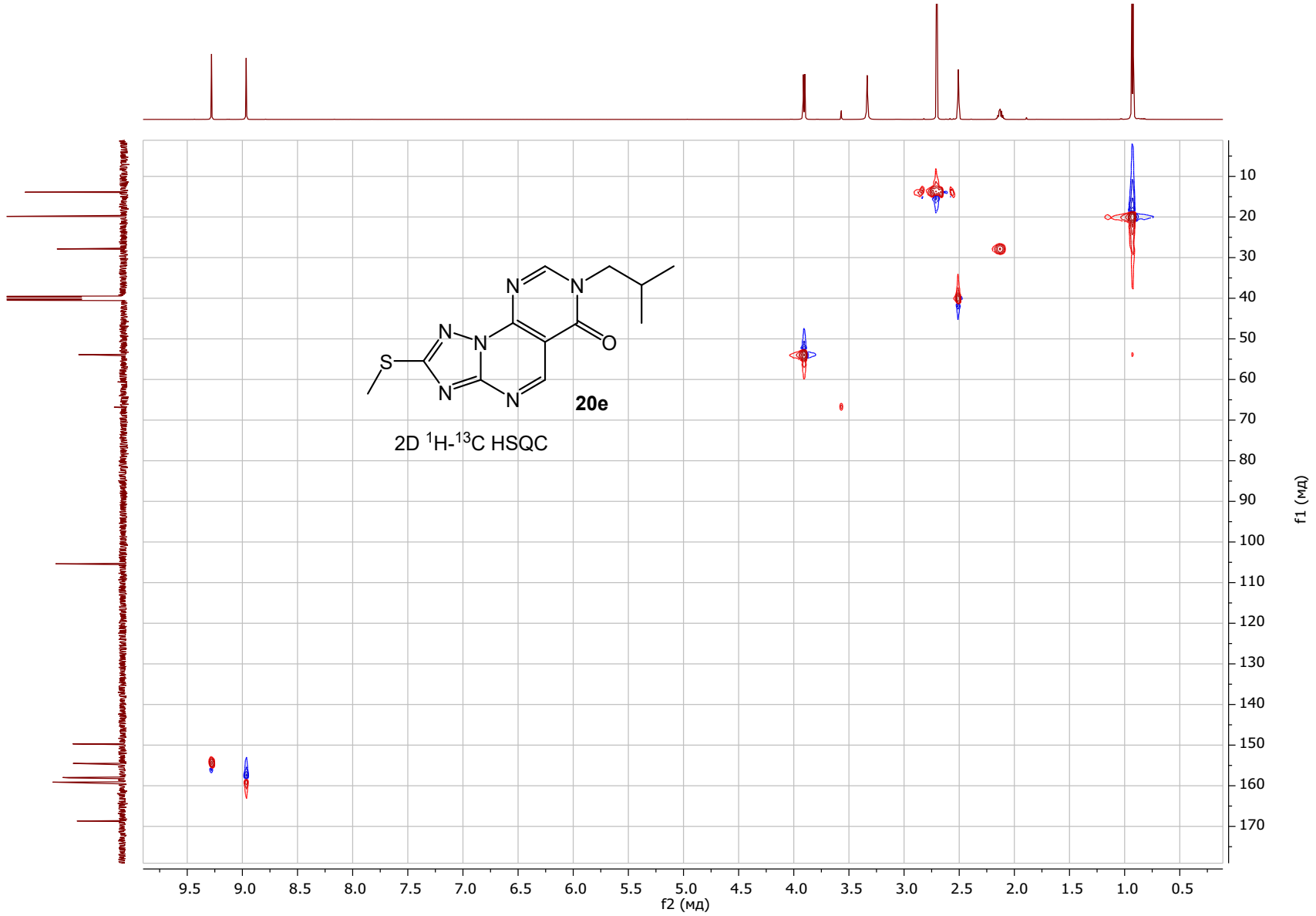
Line#:1 R.Time:3.190(Scan#:1237)
MassPeaks:123
RawMode:Single 3.190(1237) BasePeak:290(3244138)
Фон.реж.:1.410(525) Group 1 - Event 1

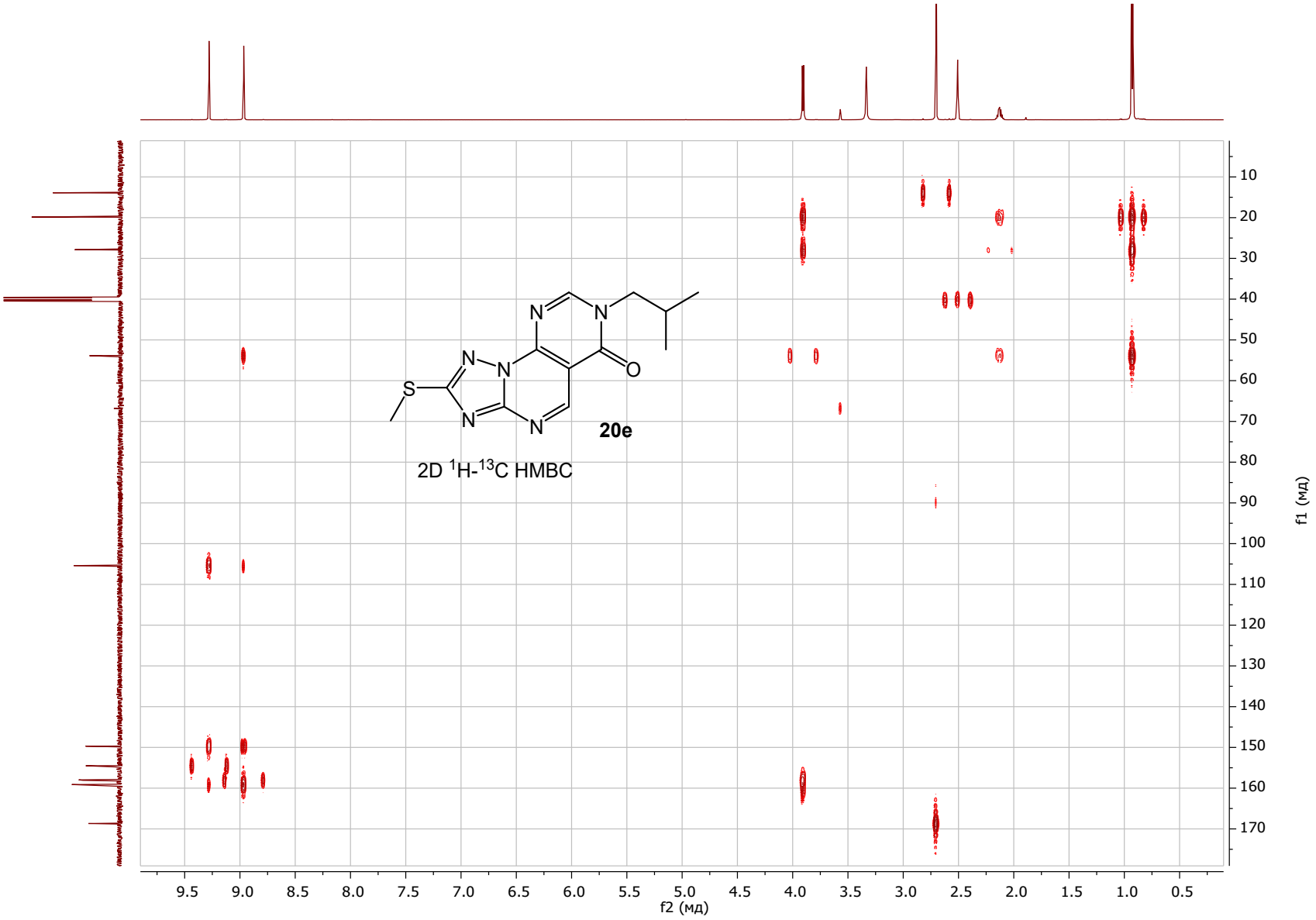


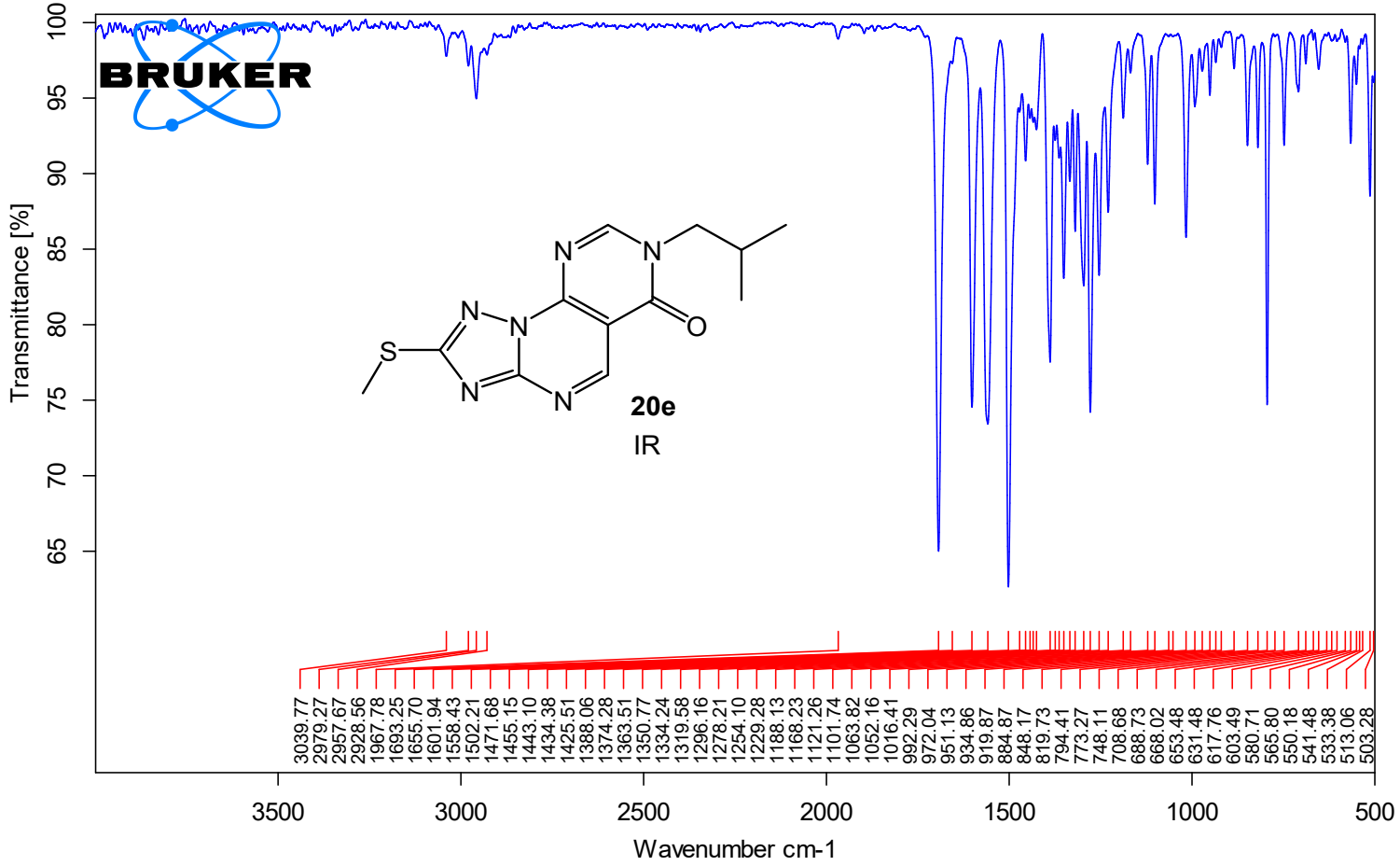
7-Isobutyl-2-(methylthio)pyrimido[5,4-*e*][1,2,4]triazolo[1,5-*a*]pyrimidin-6(7*H*)-one (20e)



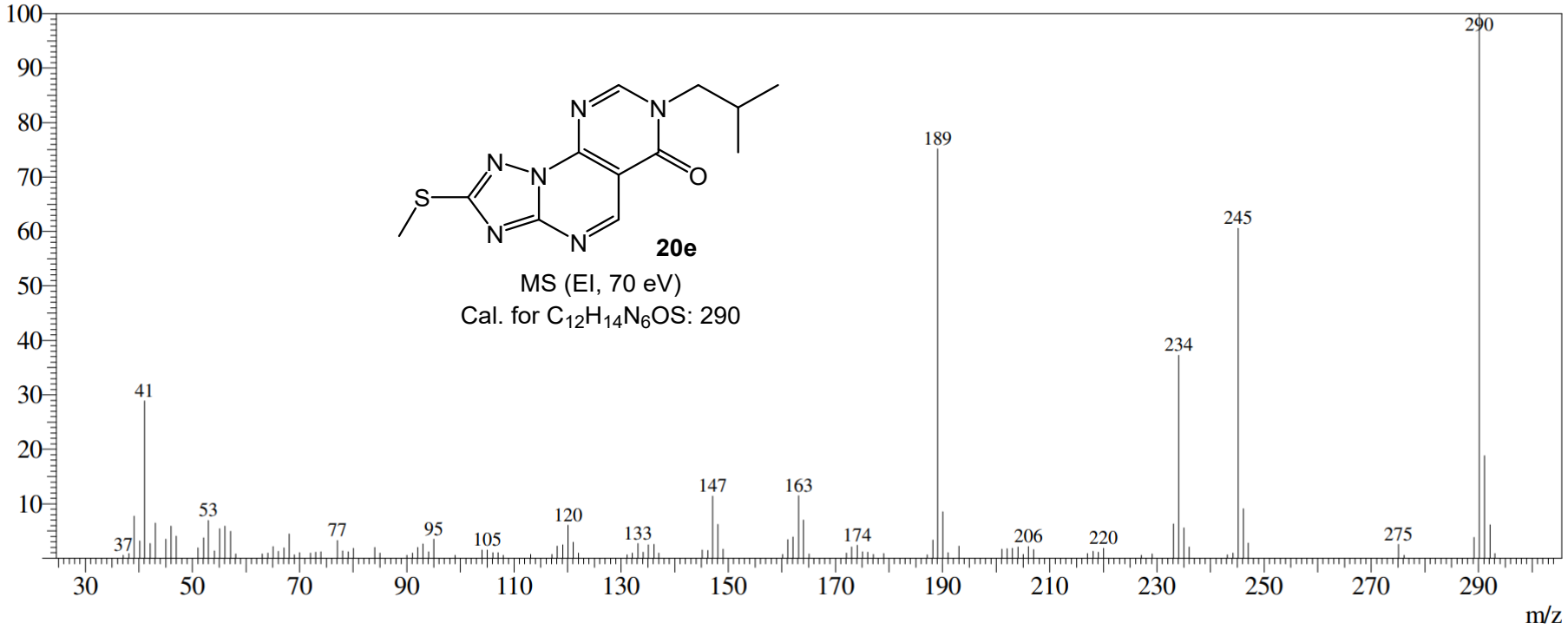

168.21
158.65
157.61
157.50
154.04
149.23
104.91
53.40
27.38
19.39
13.42
20e
13C, 150 MHz, DMSO-D6
f1 (мд)


20e
2D ^{1}H-^{13}C HSQC
f2 (мд)
f1 (мд)

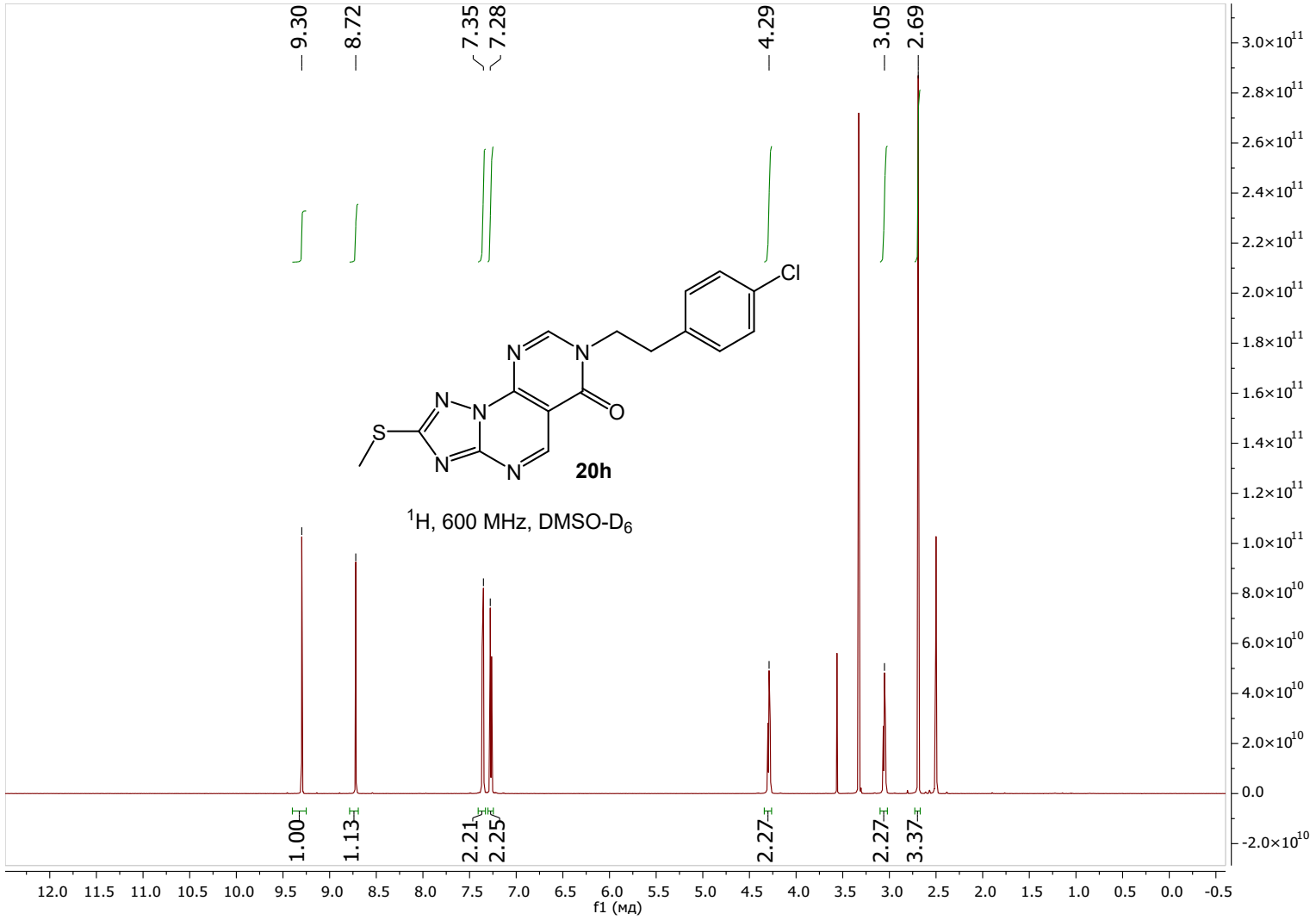

N
N
N
N
S
O
20e
2D ^{1}H-^{13}C HMBC
f2 (мд)
f1 (мд)

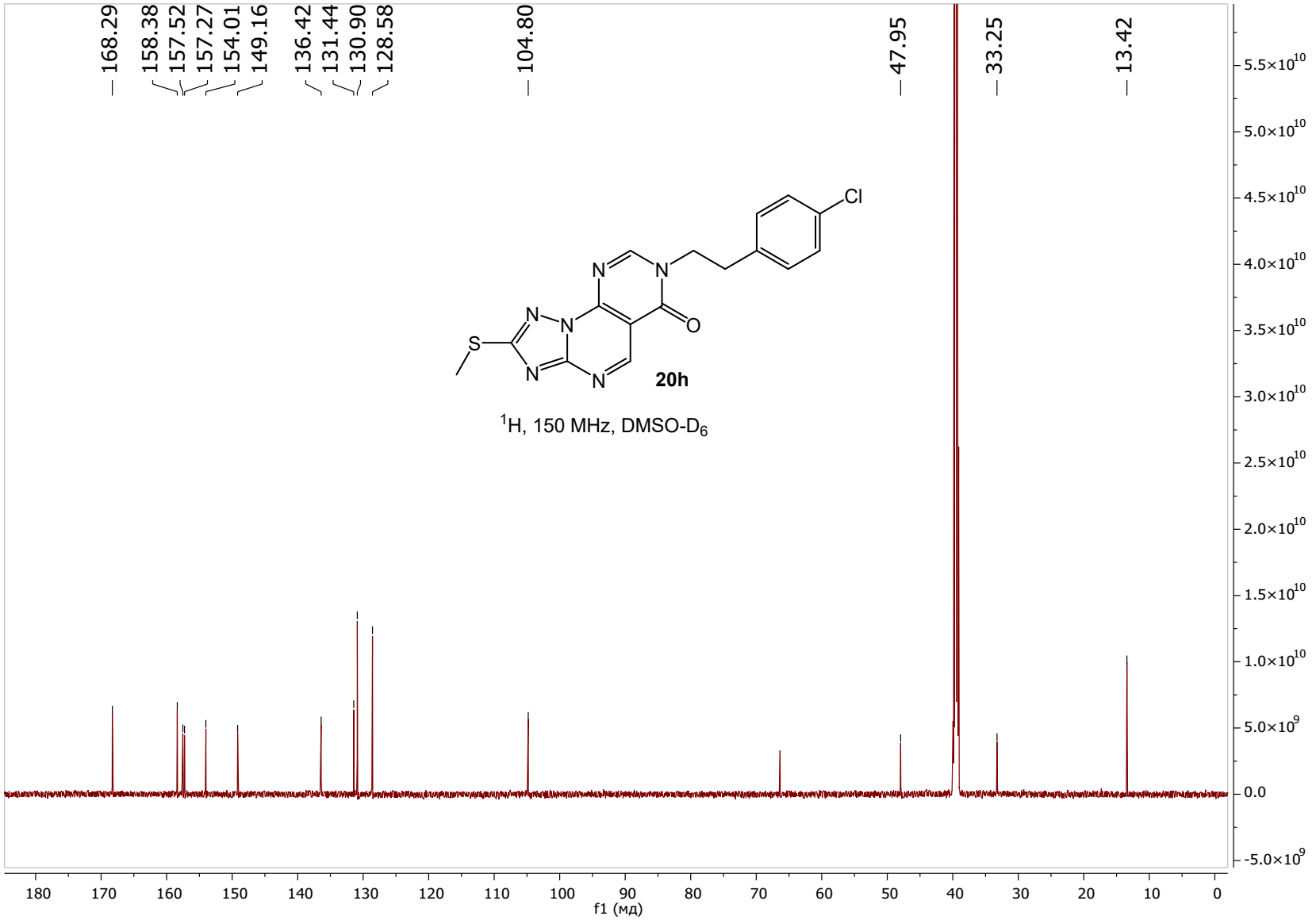

BRUKER
Transmittance [%]
100
95
90
85
80
75
70
65
3039.77
2979.27
2957.67
2928.56
1967.78
1693.25
1655.70
1601.94
1558.43
1502.21
1471.68
1455.15
1443.10
1434.38
1425.51
1388.06
1374.28
1363.51
1350.77
1334.24
1319.58
1296.16
1278.21
1254.10
1229.28
1188.13
1168.23
1121.26
1101.74
1063.82
1052.16
1016.41
992.29
972.04
951.13
934.86
919.87
884.87
848.17
819.73
794.41
773.27
748.11
708.68
688.73
668.02
653.48
631.48
617.76
603.49
580.71
565.80
550.18
541.48
533.38
513.06
503.28
3500
3000
2500
2000
1500
1000
500
Wavenumber cm-1
N
N
N
N
N
N
S
O
20e
IR

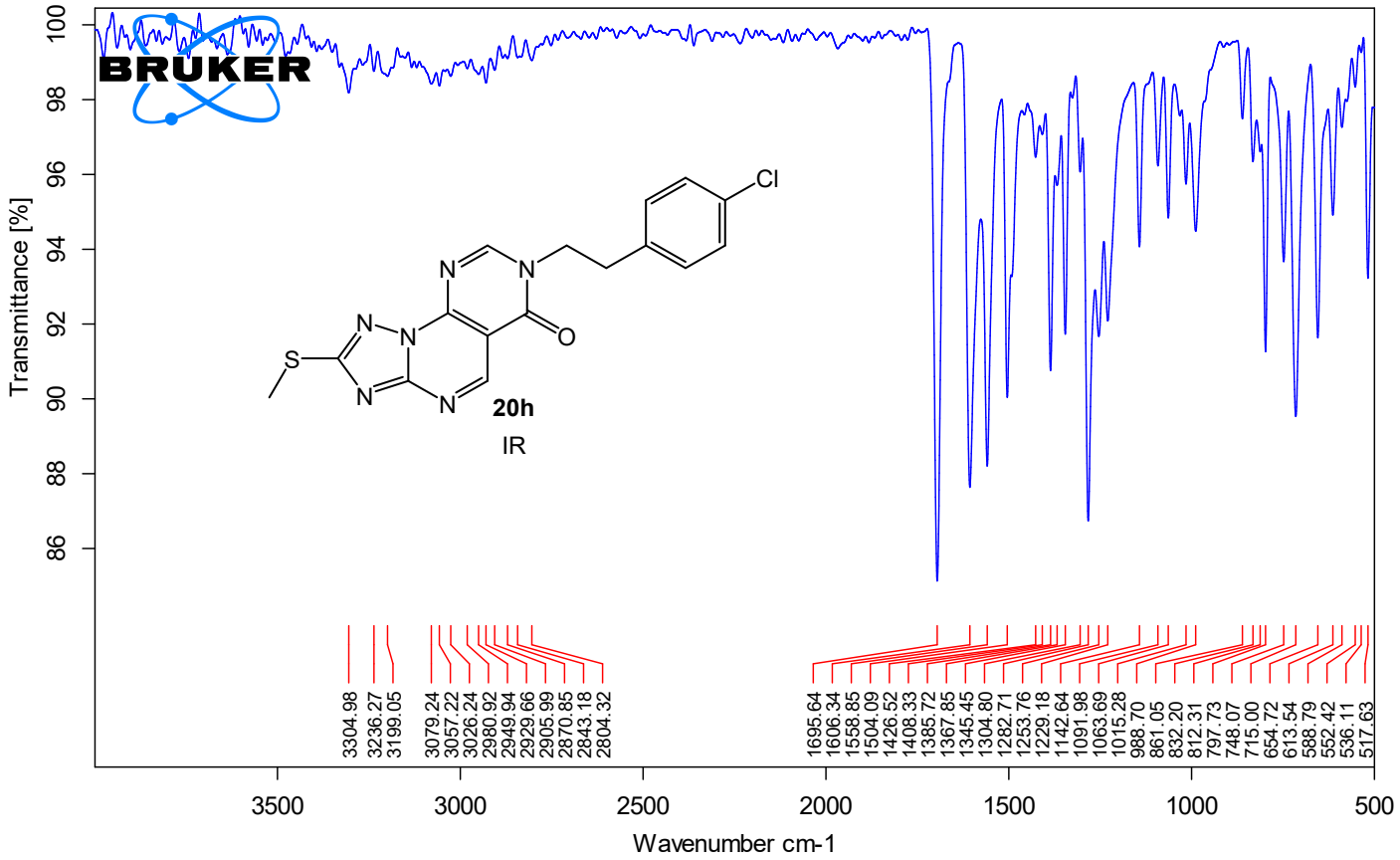
Line#:1 R.Time:2.510(Scan#:965)
MassPeaks:114
RawMode:Single 2.510(965) BasePeak:290(3749511)
Фон.реж.:2.132(814) Group 1 - Event 1



7-(4-Chlorophenethyl)-2-(methylthio)pyrimido[5,4-*e*][1,2,4]triazolo[1,5-*a*]pyrimidin-6(7*H*)-one (20h)

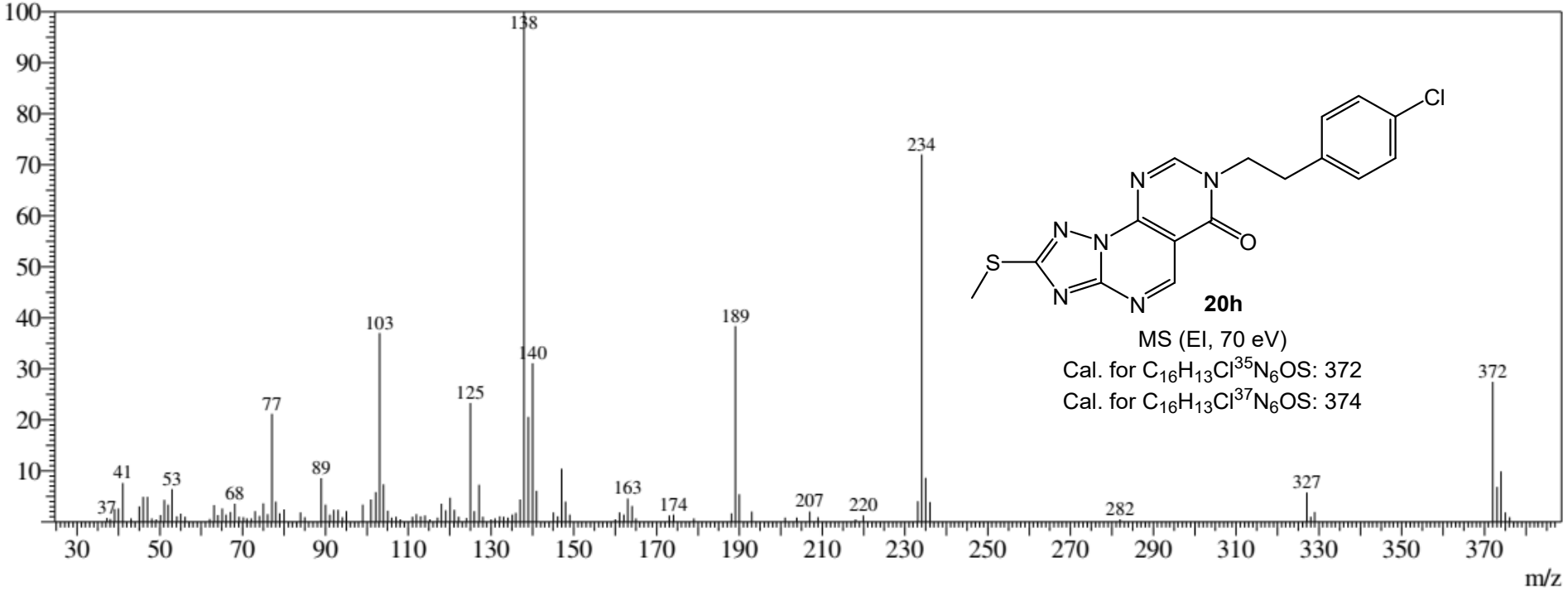



168.29
158.38
157.52
157.27
154.01
149.16
136.42
131.44
130.90
128.58
104.80
47.95
33.25
13.42
Cl
N
N
N
N
N
N
S
O
20h
1H, 150 MHz, DMSO-D6
5.5×10^10
5.0×10^10
4.5×10^10
4.0×10^10
3.5×10^10
3.0×10^10
2.5×10^10
2.0×10^10
1.5×10^10
1.0×10^10
5.0×10^9
0.0
-5.0×10^9
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (мд)


BRUKER
Transmittance [%]
100
98
96
94
92
90
88
86
Cl
N
N
N
N
S
N
N
O
20h
IR
3304.98
3236.27
3199.05
3079.24
3057.22
3026.24
2980.92
2949.94
2929.66
2905.99
2870.85
2843.18
2804.32
1695.64
1606.34
1558.85
1504.09
1426.52
1408.33
1385.72
1367.85
1345.45
1304.80
1282.71
1253.76
1229.18
1142.64
1091.98
1063.69
1015.28
988.70
861.05
832.20
812.31
797.73
748.07
715.00
654.72
613.54
588.79
552.42
536.11
517.63
3500
3000
2500
2000
1500
1000
500
Wavenumber cm-1

Page 1/1

Line#:2 R.Time:39.008(Scan#:8763)
MassPeaks:120
RawMode:Averaged 39.004-39.013(8762-8764) BasePeak:138(73238)
Фон.реж.:Calc. from Peak Group 1 - Event 1



20h

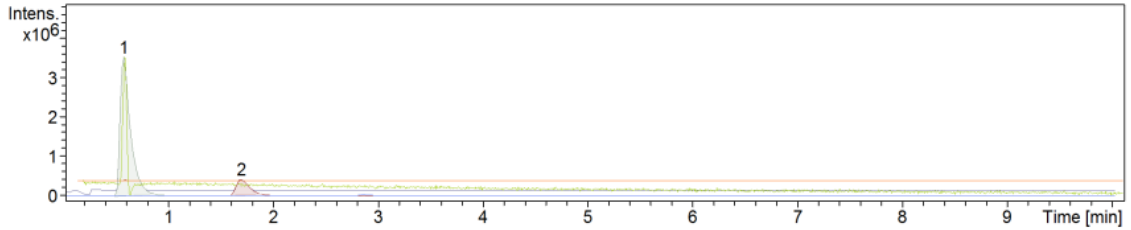
MS (EI, 70 eV)

Cal. for $C_{16}H_{13}Cl^{35}N_6OS$: 372

Cal. for $C_{16}H_{13}Cl^{37}N_6OS$: 374

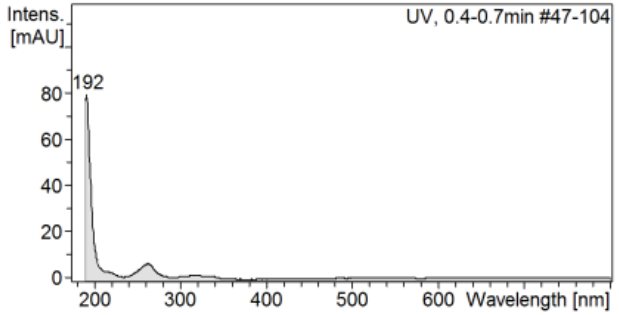
Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	2.0 Bar
Focus	Active	Set Capillary	4500 V	Set Dry Heater	200 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	8.0 l/min
Scan End	1400 m/z	Set Charging Voltage	2000 V	Set Divert Valve	Waste
		Set Corona	0 nA	Set APCI Heater	0 °C

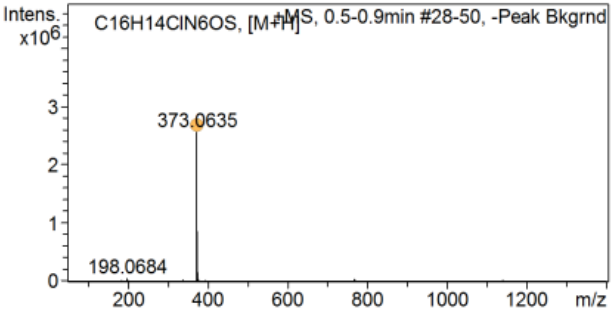


#	RT [min]	Area	Int. Type	I	S/N	Chromatogram	Max. m/z	FWHM [min]
1	0.6	23898960	Manual	3486000	30496.8	EIC 373.0619±0.005 +All MS	373.0635	
2	1.7	3216180	Manual	410657	93.8	EIC 321.0905±0.005 +All MS	321.0919	

Cmpd 1, 0.6 min

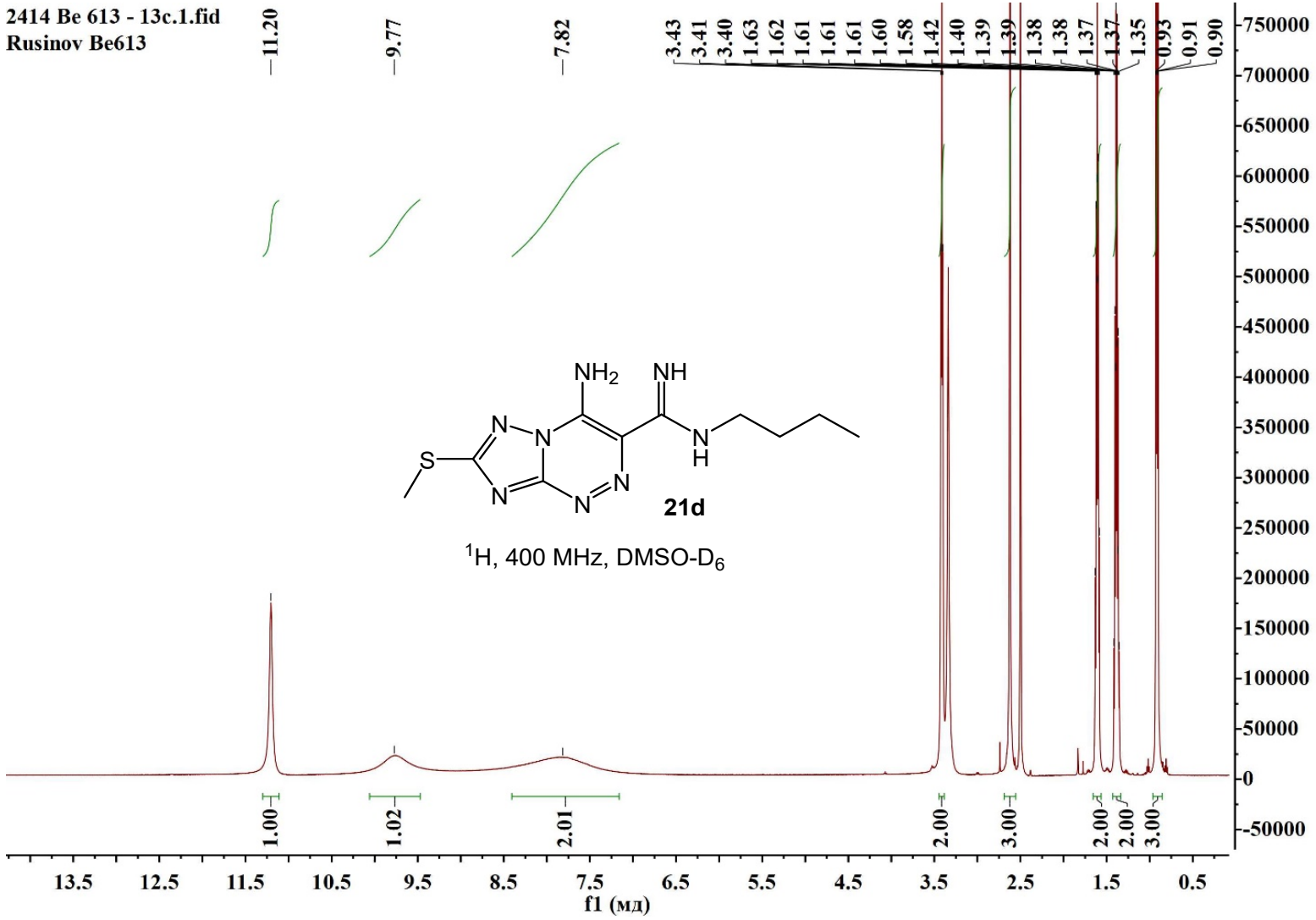


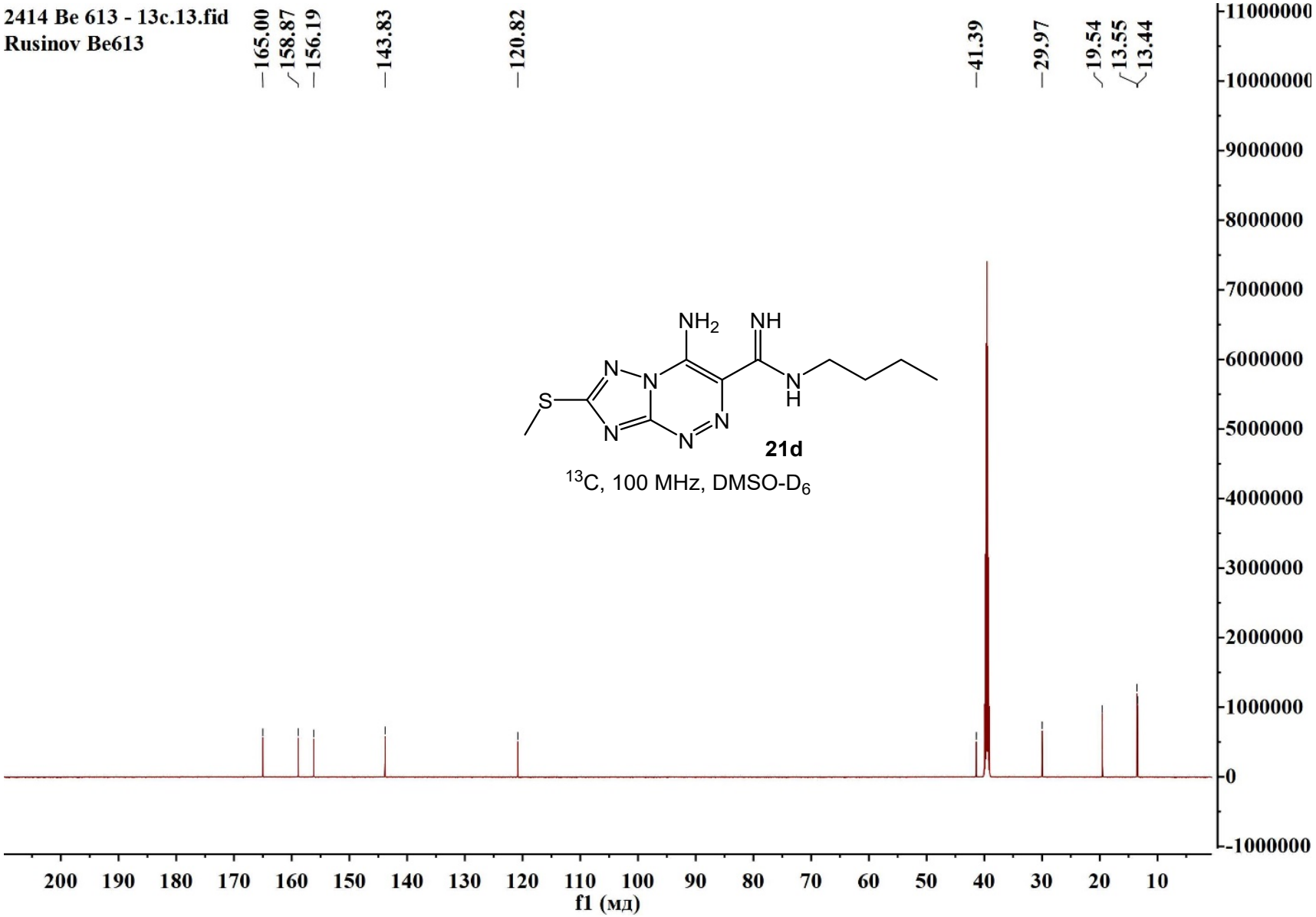
#	Wavelength	Intensity
0	192	79.3

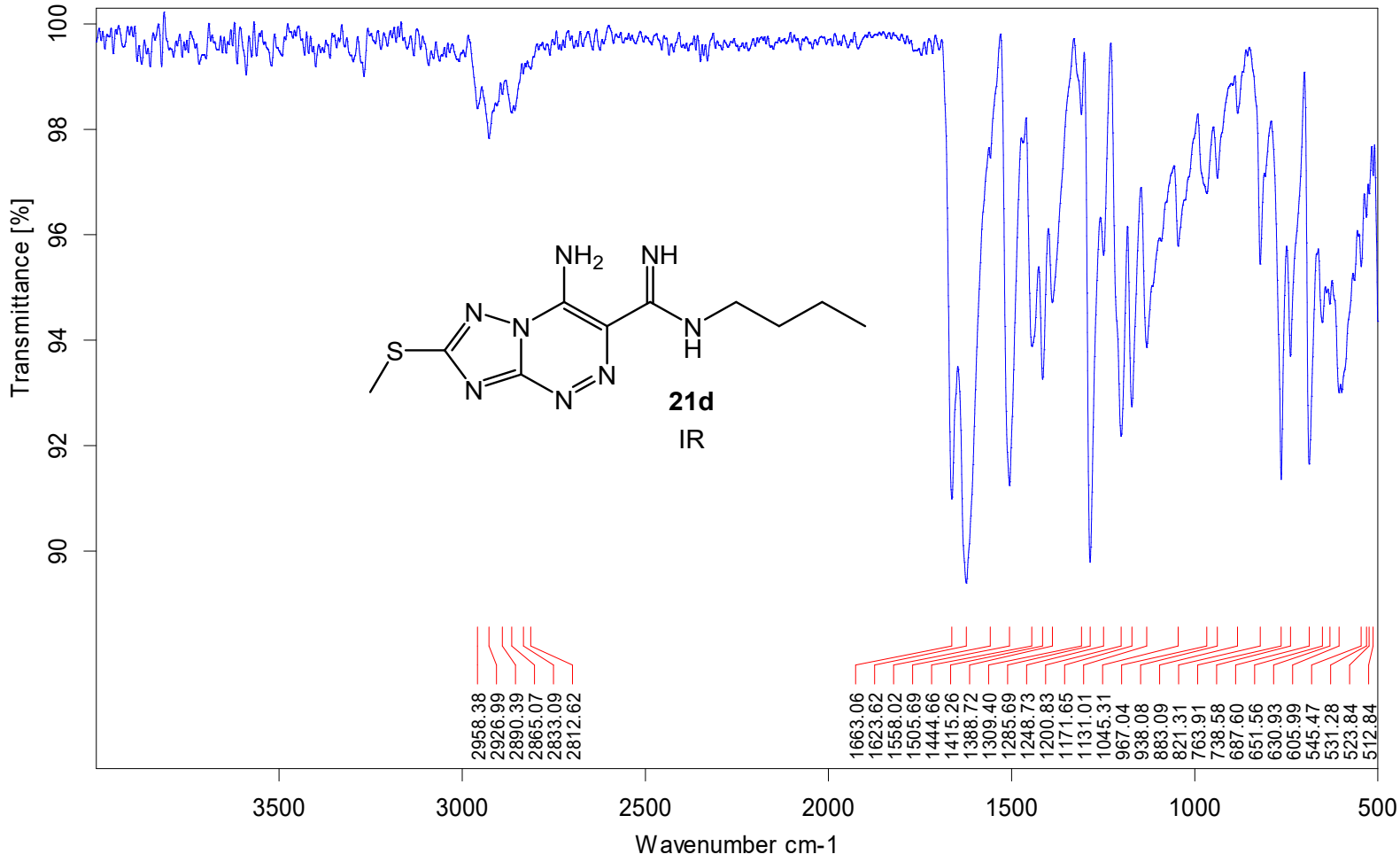


#	m/z	Res.	S/N	I	I %	FWHM
1	198.0684	18519	22574452.0	55113	2.2	0.0107
2	339.1022	18707	10730792.0	26198	1.0	0.0181
3	373.0635	34093	1043798656.0	2548337	100.0	0.0109
4	374.0661	24225	176225632.0	430238	16.9	0.0154
5	375.0608	28133	353640320.0	863380	33.9	0.0133
6	376.0630	20786	63788436.0	155733	6.1	0.0181
7	377.0589	16404	16307131.0	39812	1.6	0.0230
8	767.1038	21648	15030682.0	36696	1.4	0.0354
9	769.1009	20089	11844270.0	28917	1.1	0.0383
10	1141.1643	21698	10243735.0	25009	1.0	0.0526

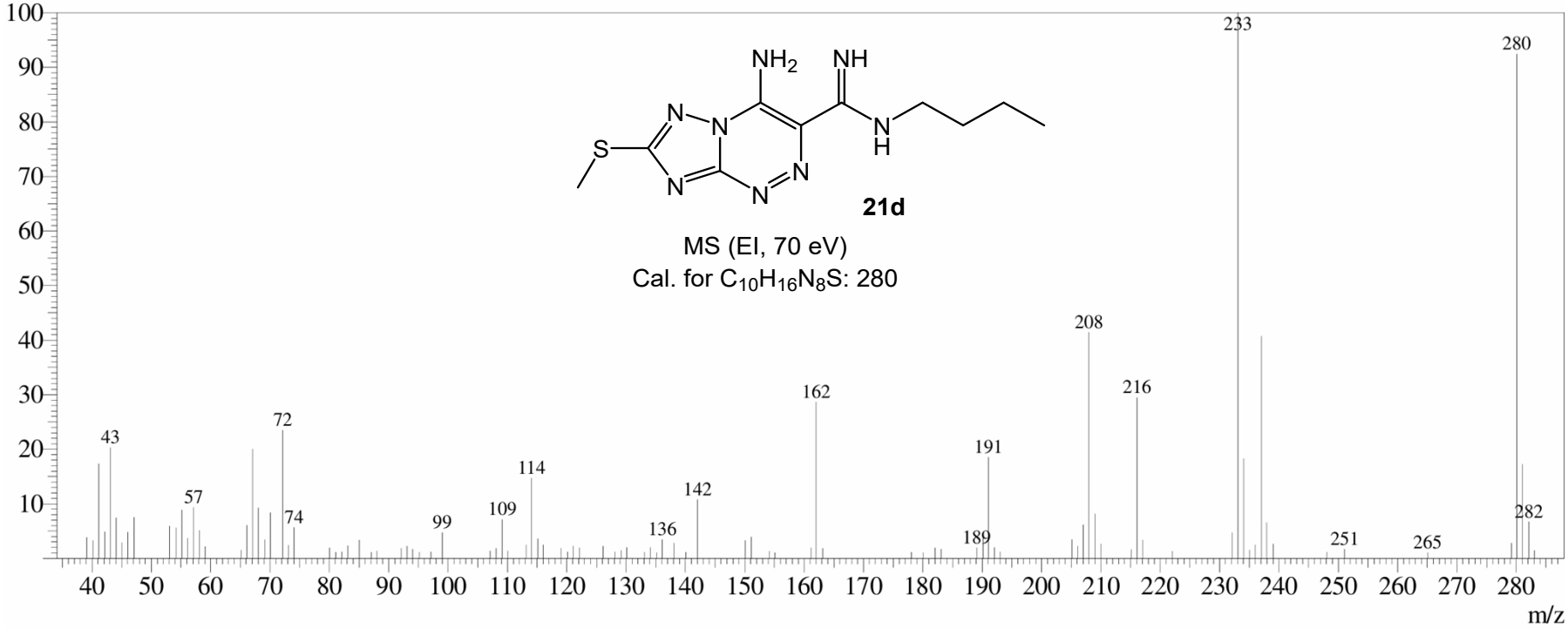
4-Amino-*N*-butyl-7-(methylthio)-[1,2,4]triazolo[5,1-*c*][1,2,4]triazine-3-carboximidamide (21d).



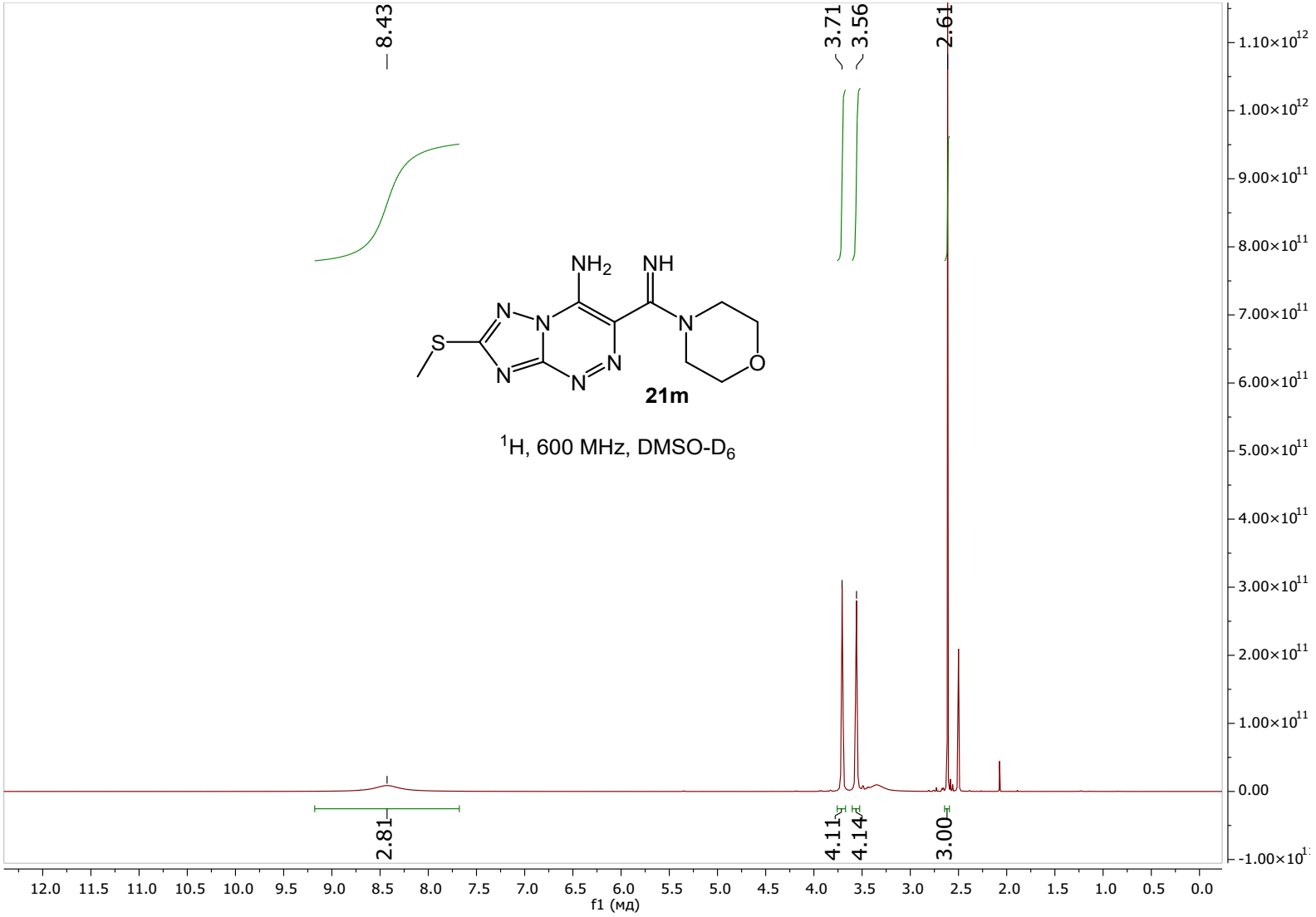

2414 Be 613 - 13c.13.fid
Rusinov Be613
165.00
158.87
156.19
143.83
120.82
41.39
29.97
19.54
13.55
13.44
NH2
NH
N
N
S
N
N
N
N
H
21d
13C, 100 MHz, DMSO-D6
11000000
10000000
9000000
8000000
7000000
6000000
5000000
4000000
3000000
2000000
1000000
0
-1000000
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (мд)

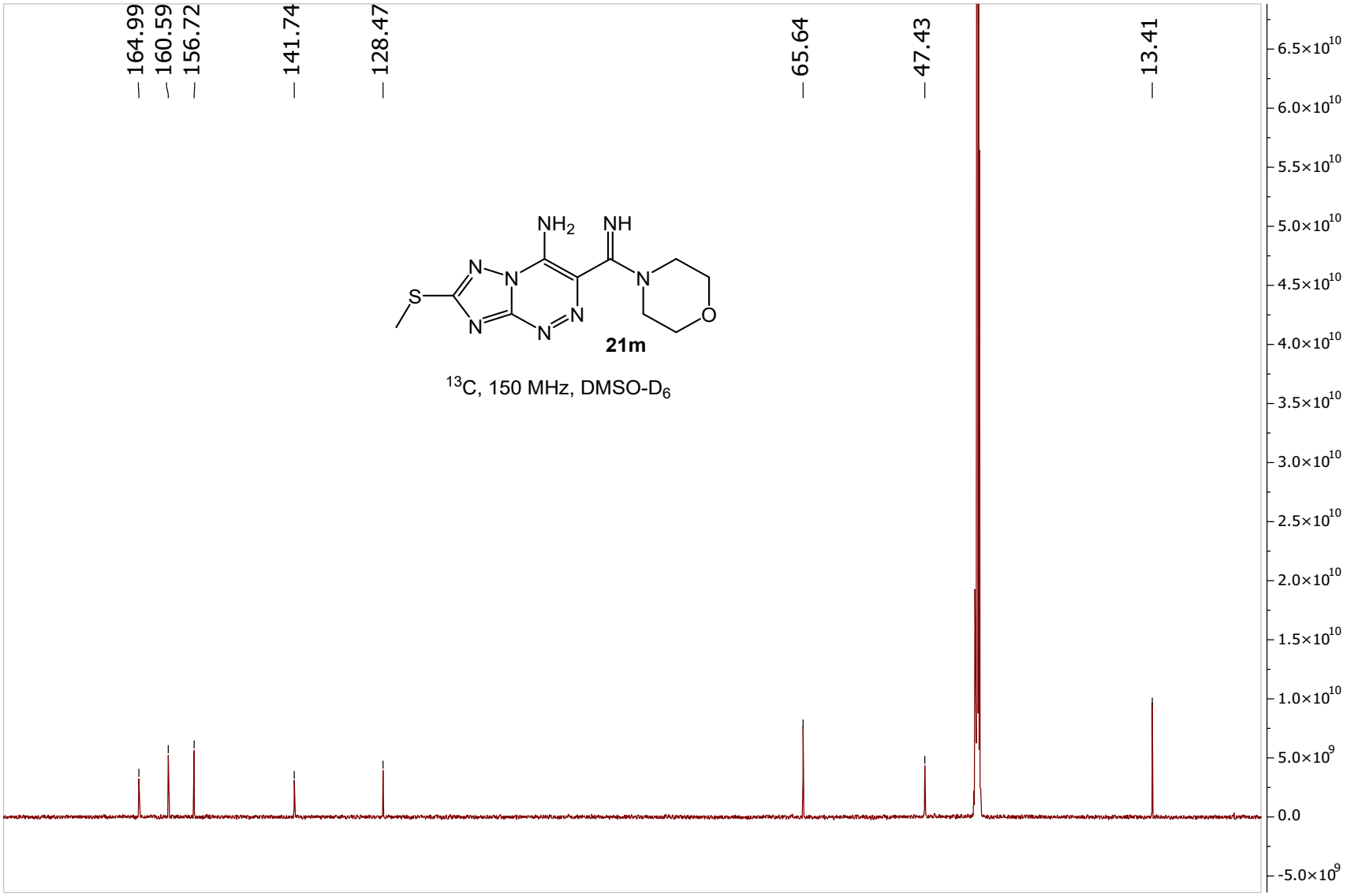

Transmittance [%]
100
98
96
94
92
90
3500
3000
2500
2000
1500
1000
500
Wavenumber cm-1
NH2
NH
N
N
N
N
N
S
N
H
21d
IR
2958.38
2926.99
2890.39
2865.07
2833.09
2812.62
1663.06
1623.62
1558.02
1505.69
1444.66
1415.26
1388.72
1309.40
1285.69
1248.73
1200.83
1171.65
1131.01
1045.31
967.04
938.08
883.09
821.31
763.91
738.58
687.60
651.56
630.93
605.99
545.47
531.28
523.84
512.84

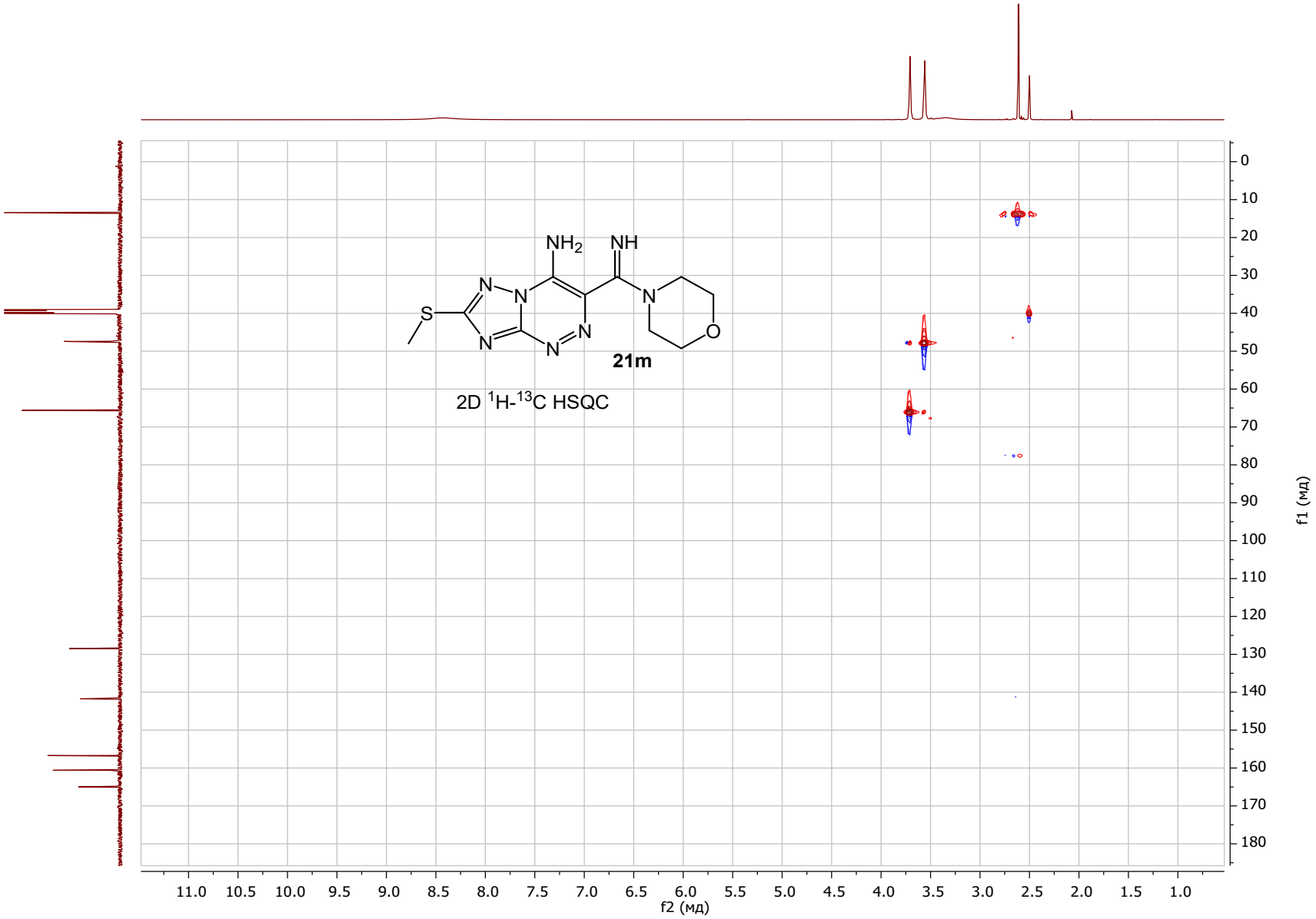
Line#:1 R.Time:2.655(Scan#:1023)
MassPeaks:103
RawMode:Single 2.655(1023) BasePeak:233(489344)
Фон.реж.:2.283(874) Group 1 - Event 1

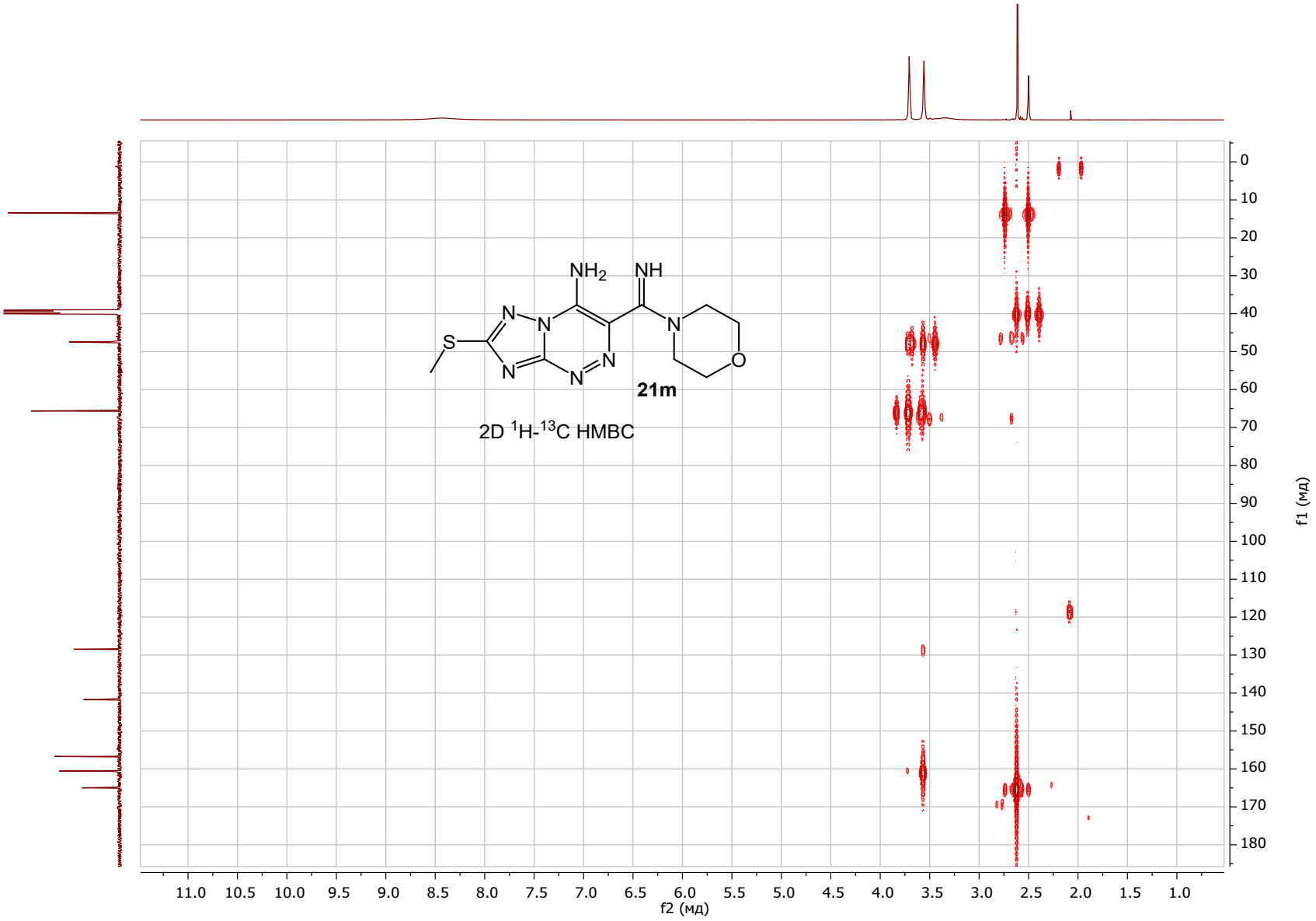


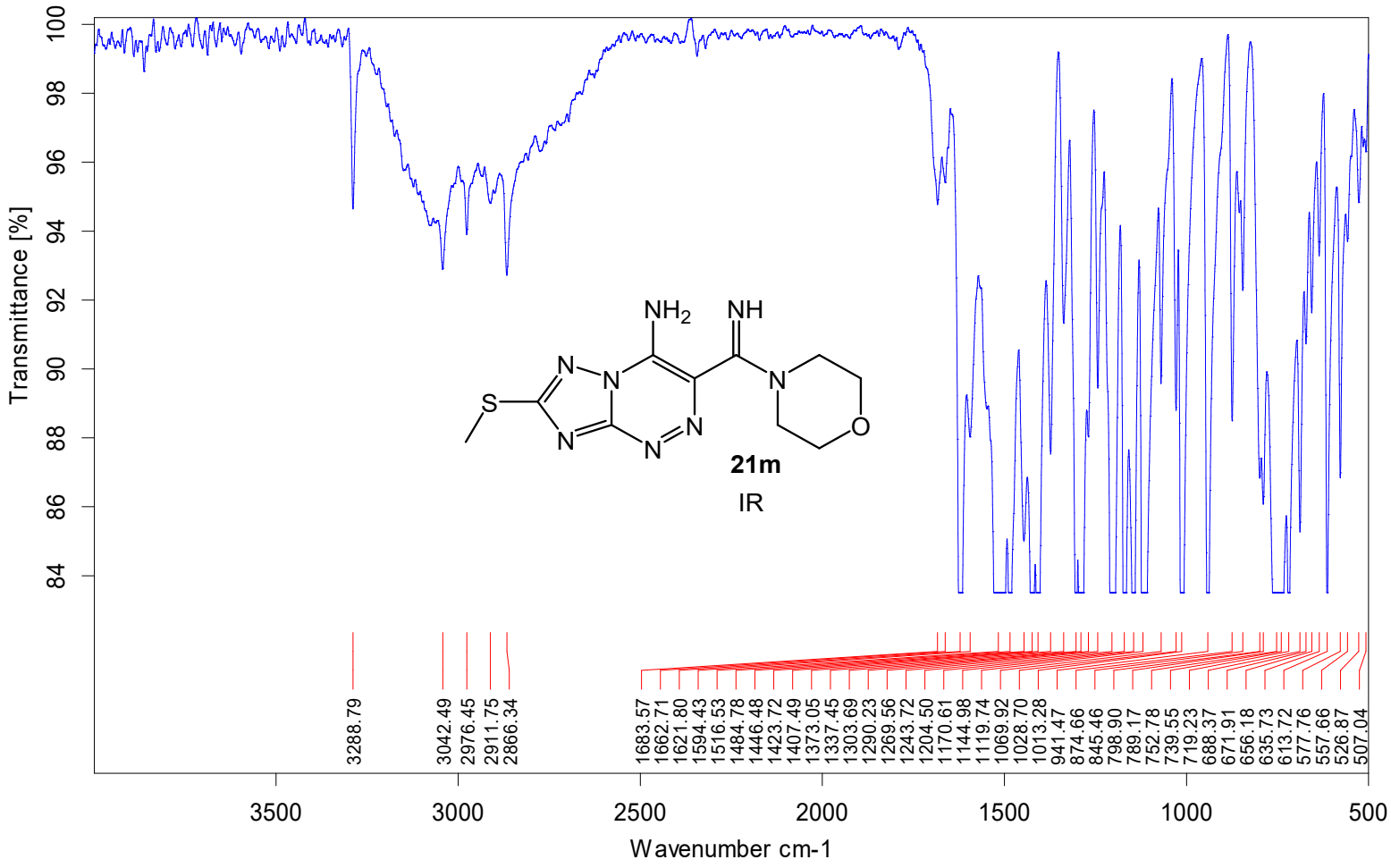
3-(Imino(morpholino)methyl)-7-(methylthio)-[1,2,4]triazolo[5,1-*c*][1,2,4]triazin-4-amine (21m).



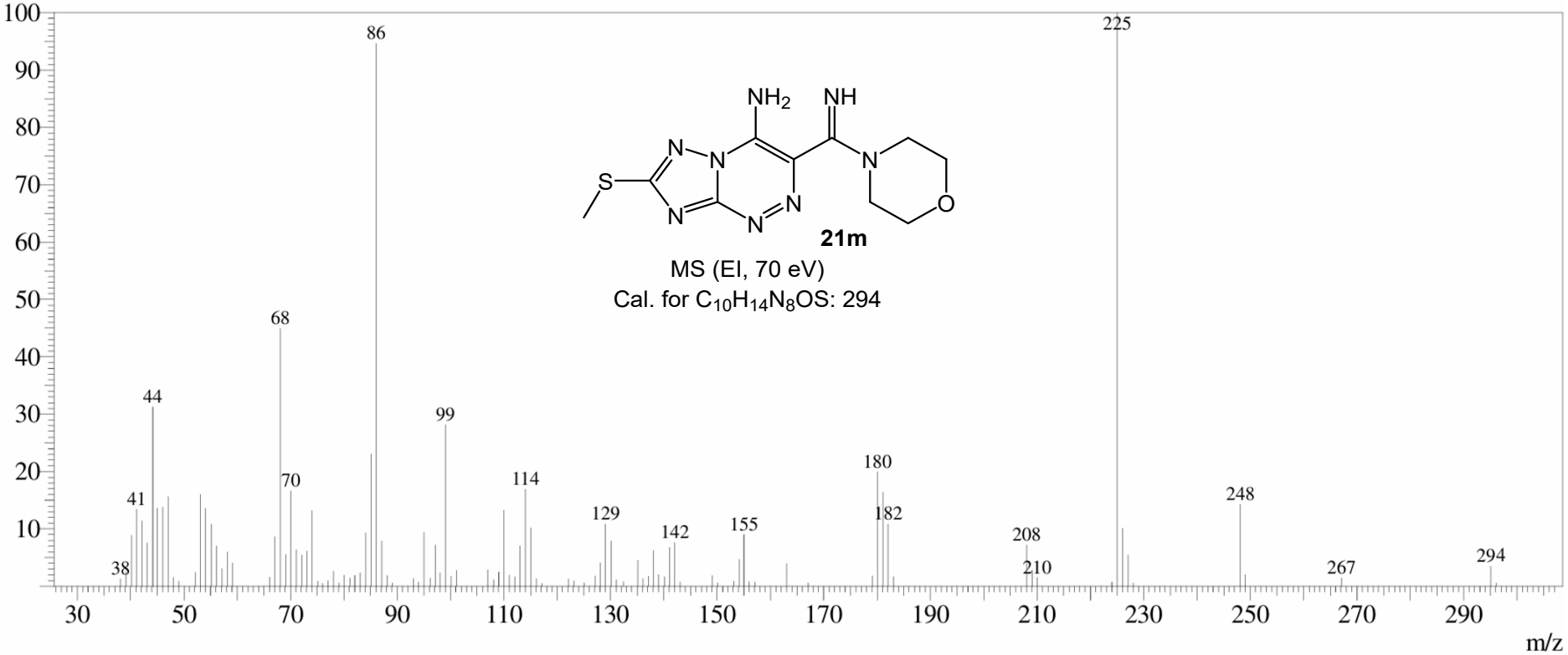

164.99
160.59
156.72
141.74
128.47
65.64
47.43
13.41
NH2
NH
S
N
N
N
N
N
N
O
21m
13C, 150 MHz, DMSO-D6
6.5×10^10
6.0×10^10
5.5×10^10
5.0×10^10
4.5×10^10
4.0×10^10
3.5×10^10
3.0×10^10
2.5×10^10
2.0×10^10
1.5×10^10
1.0×10^10
5.0×10^9
0.0
-5.0×10^9
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (мд)


NH2
NH
N
N
S
N
N
N
N
O
21m
2D 1H-13C HSQC
11.0 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
f2 (мд)
0 10 20 30 40 50 60 70 80 90 100 110 120 130 140 150 160 170 180
f1 (мд)


NH2
NH
N
N
N
N
N
S
N
O
21m
2D 1H-13C HMBC
11.0 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
f2 (мд)
0 10 20 30 40 50 60 70 80 90 100 110 120 130 140 150 160 170 180
f1 (мд)


Transmittance [%]
100
98
96
94
92
90
88
86
84
NH2
NH
N
N
N
N
S
N
O
21m
IR
3288.79
3042.49
2976.45
2911.75
2866.34
1683.57
1662.71
1621.80
1594.43
1516.53
1484.78
1446.48
1423.72
1407.49
1373.05
1337.45
1303.69
1290.23
1269.56
1243.72
1204.50
1170.61
1144.98
1119.74
1069.92
1028.70
1013.28
941.47
874.66
845.46
798.90
789.17
752.78
739.55
719.23
688.37
671.91
656.18
635.73
613.72
577.76
557.66
526.87
507.04
3500
3000
2500
2000
1500
1000
500
Wavenumber cm-1

Line#:1 R.Time:2.237(Scan#:856)
MassPeaks:109
RawMode:Single 2.237(856) BasePeak:225(837487)
Фон.реж.:3.710(1445) Group 1 - Event 1

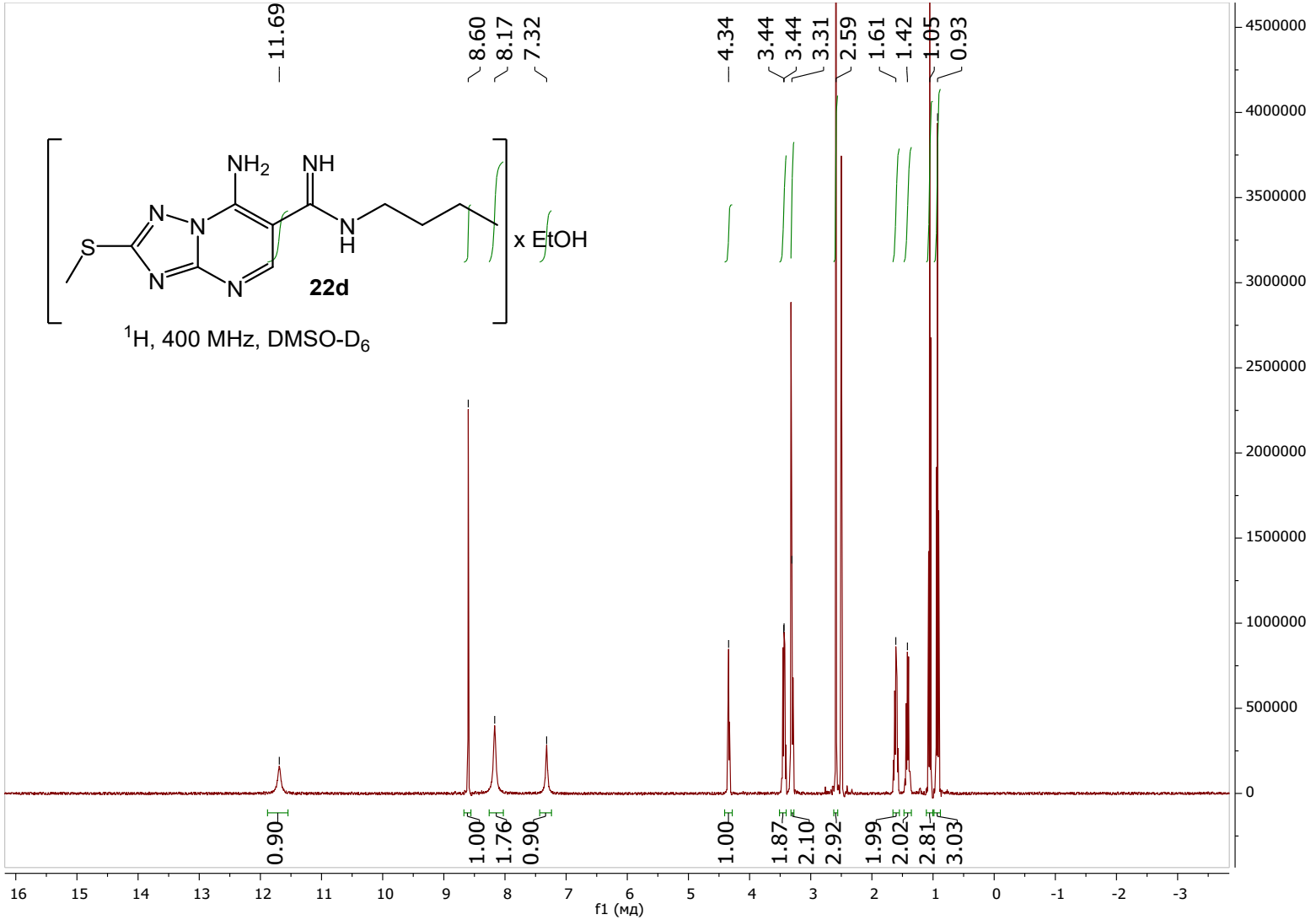


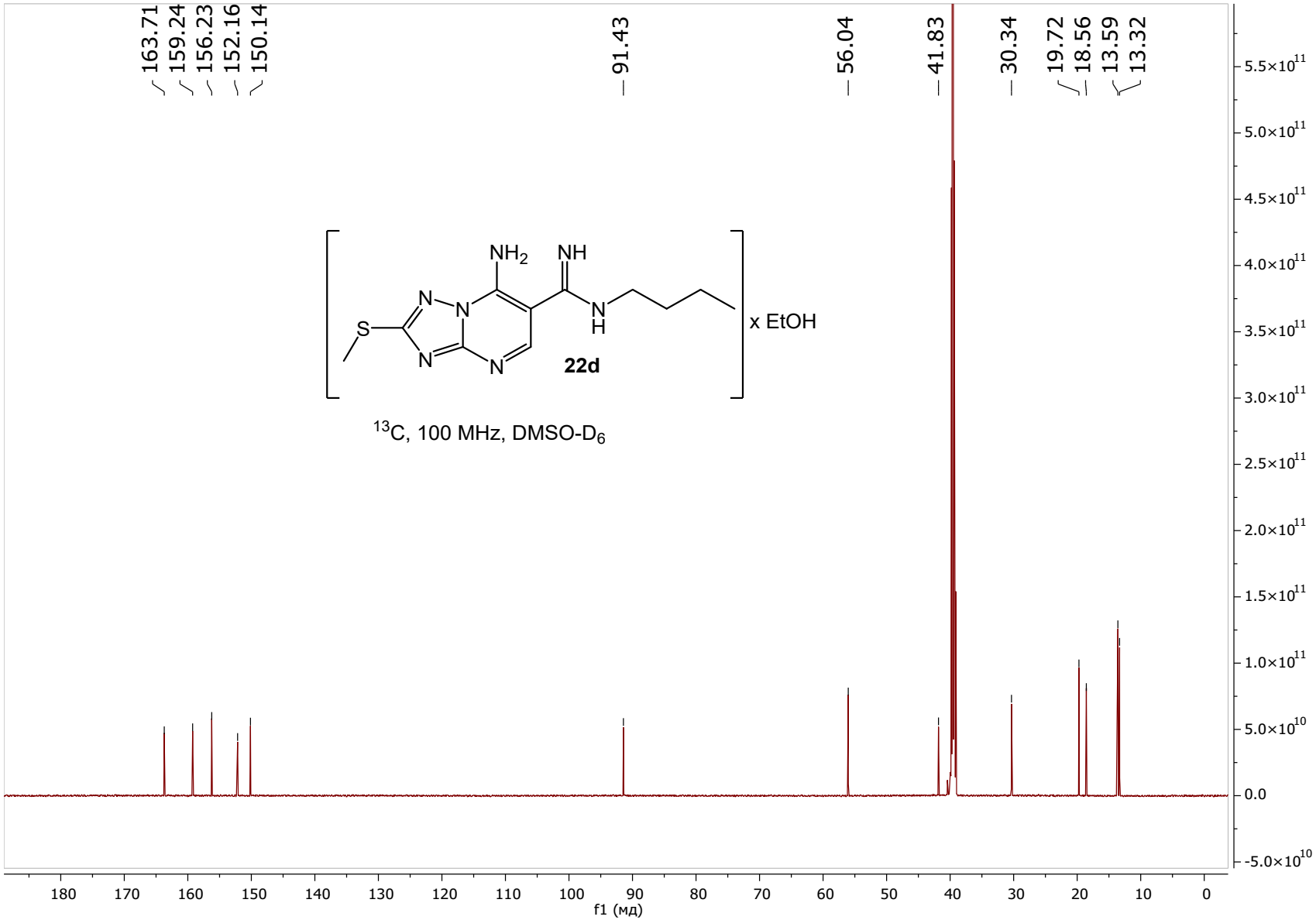
21m

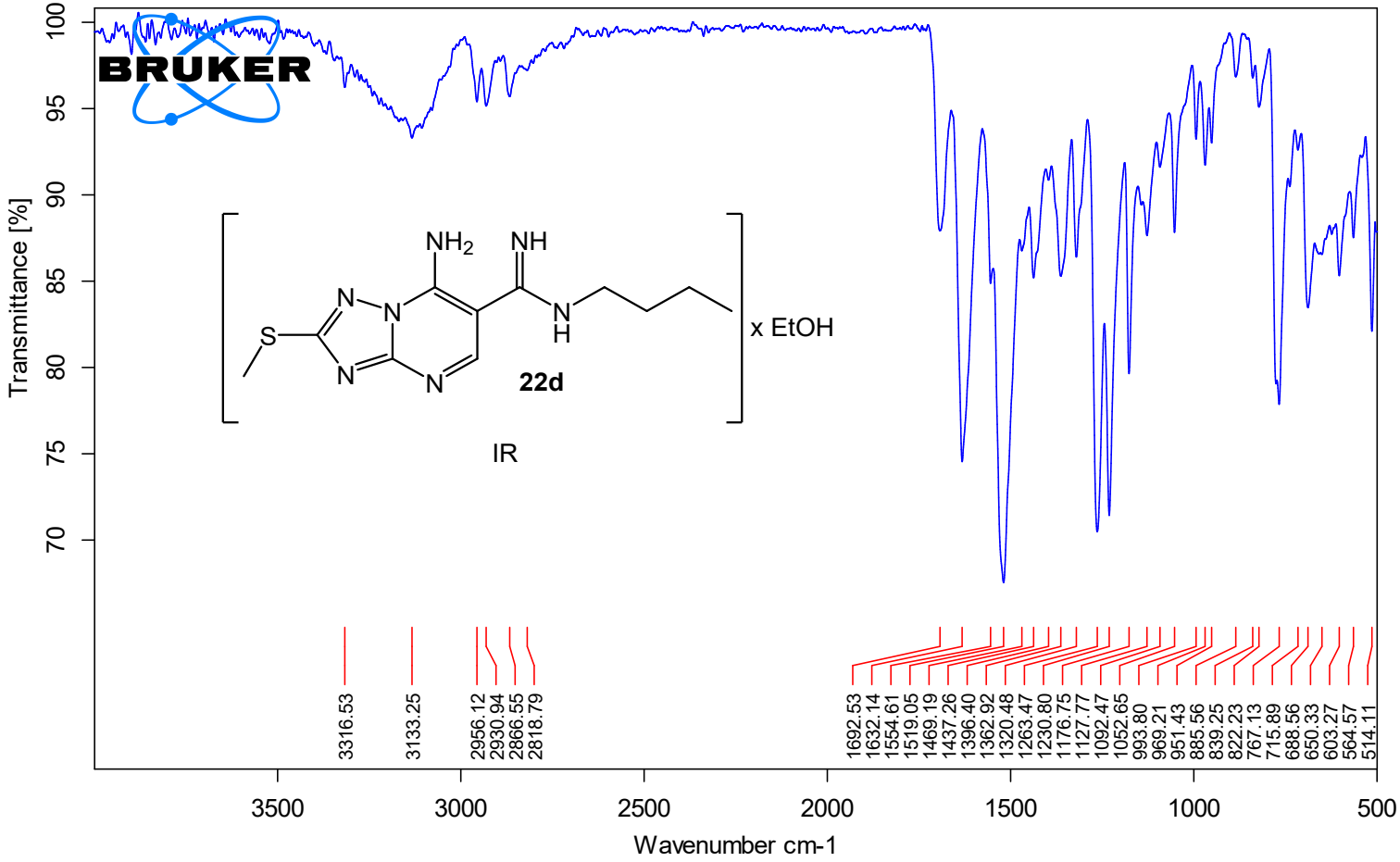
MS (EI, 70 eV)

Cal. for $C_{10}H_{14}N_8OS$: 294

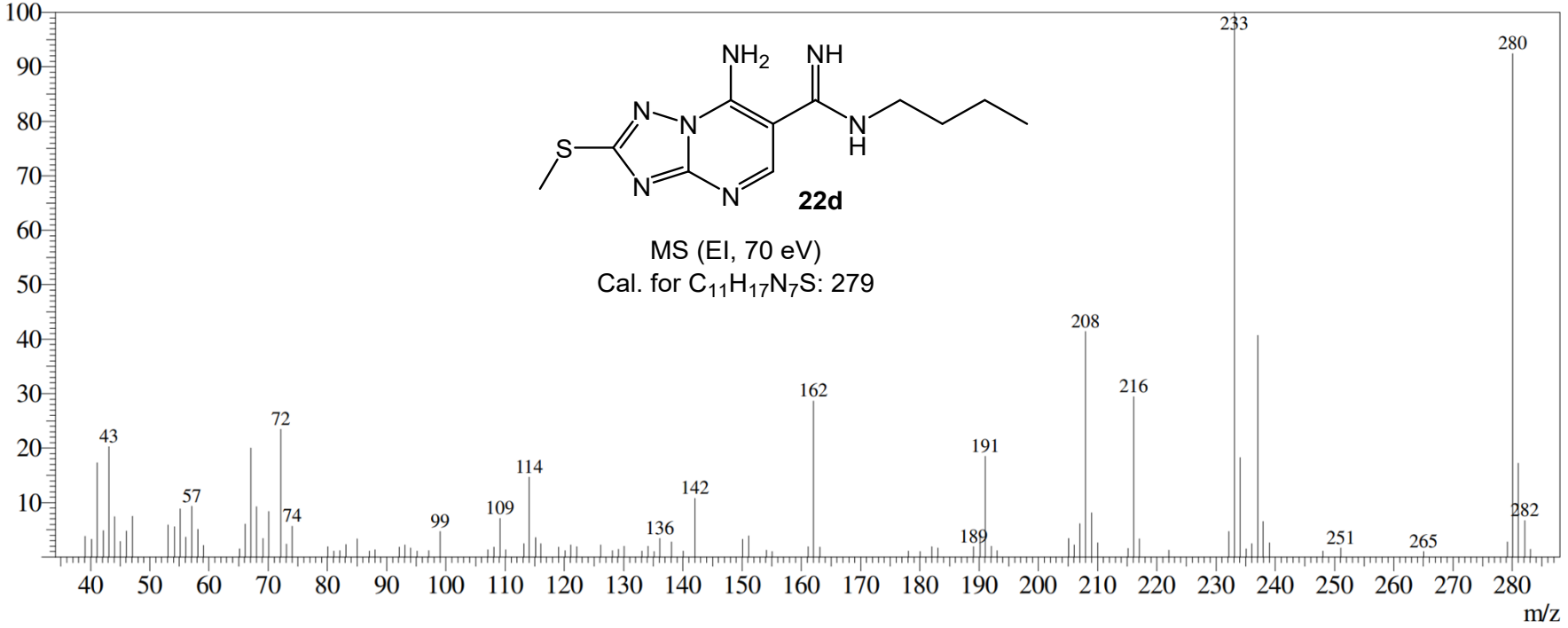
7-Amino-*N*-butyl-2-(methylthio)-[1,2,4]triazolo[1,5-*a*]pyrimidine-6-carboximidamide (22d)




163.71
159.24
156.23
152.16
150.14
91.43
56.04
41.83
30.34
19.72
18.56
13.59
13.32
NH2
NH
N
N
S
N
N
H
N
22d
x EtOH
13C, 100 MHz, DMSO-D6
5.5×10^11
5.0×10^11
4.5×10^11
4.0×10^11
3.5×10^11
3.0×10^11
2.5×10^11
2.0×10^11
1.5×10^11
1.0×10^11
5.0×10^10
0.0
-5.0×10^10
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (мд)

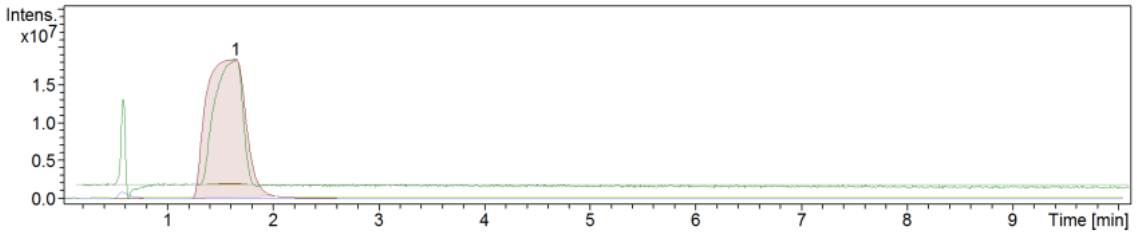

BRUKER
Transmittance [%]
100
95
90
85
80
75
70
NH2
NH
N
N
S
N
N
N
H
x EtOH
22d
IR
3316.53
3133.25
2956.12
2930.94
2866.55
2818.79
1692.53
1632.14
1554.61
1519.05
1469.19
1437.26
1396.40
1362.92
1320.48
1263.47
1230.80
1176.75
1127.77
1092.47
1052.65
993.80
969.21
951.43
885.56
839.25
822.23
767.13
715.89
688.56
650.33
603.27
564.57
514.11
3500
3000
2500
2000
1500
1000
500
Wavenumber cm-1

Line#:1 R.Time:2.655(Scan#:1023)
MassPeaks:103
RawMode:Single 2.655(1023) BasePeak:233(489344)
Фон.реж.:2.283(874) Group 1 - Event 1



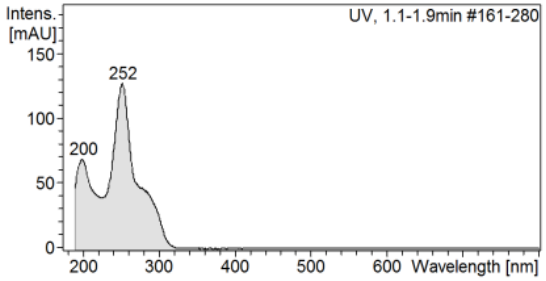
Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.3 Bar
Focus	Active	Set Capillary	3500 V	Set Dry Heater	200 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	4.0 l/min
Scan End	1400 m/z	Set Charging Voltage	2000 V	Set Divert Valve	Source
		Set Corona	0 nA	Set APCI Heater	0 °C

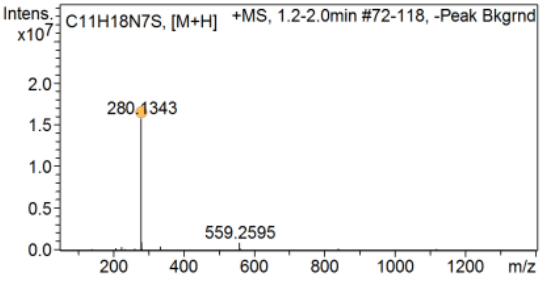


#	RT [min]	Area	Int. Type	I	S/N	Chromatogram	Max. m/z	FWHM [min]
1	1.6	459410560	Manual	18261930	29852.9	EIC 280.1325±0.005 +All MS	280.1343	

Cmpd 1, 1.6 min

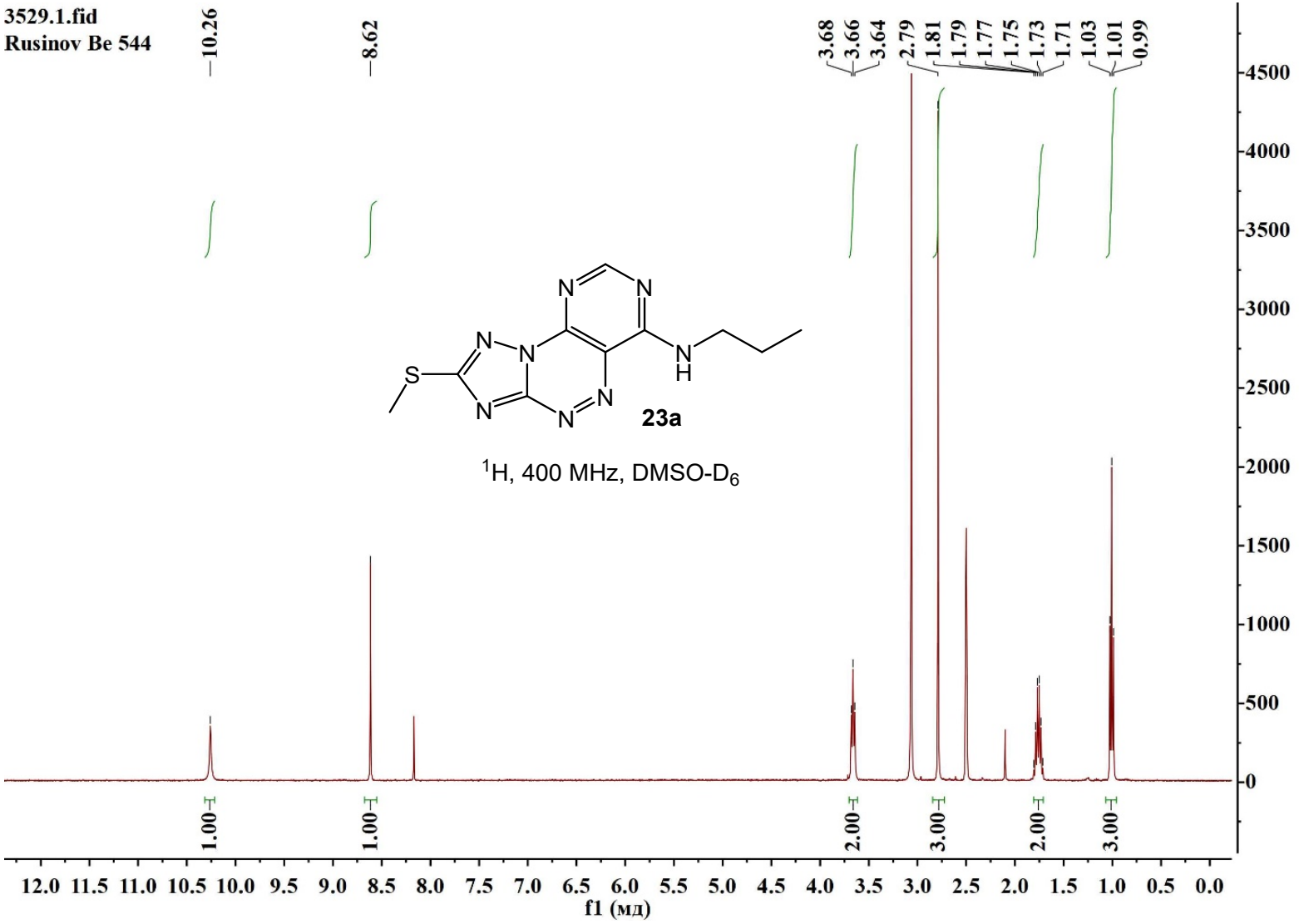


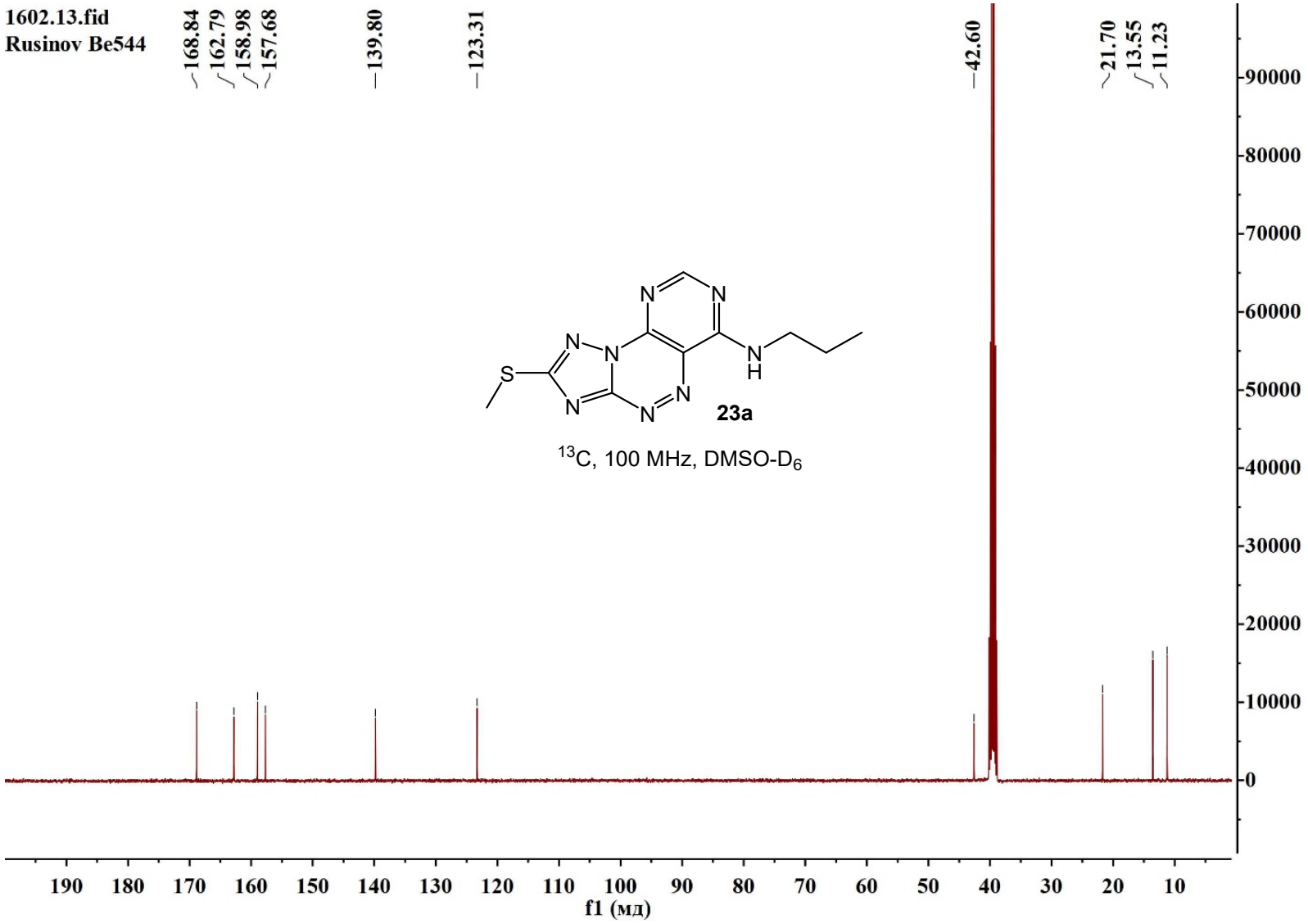
#	Wavelength	Intensity
0	200	68.1
1	252	126.1

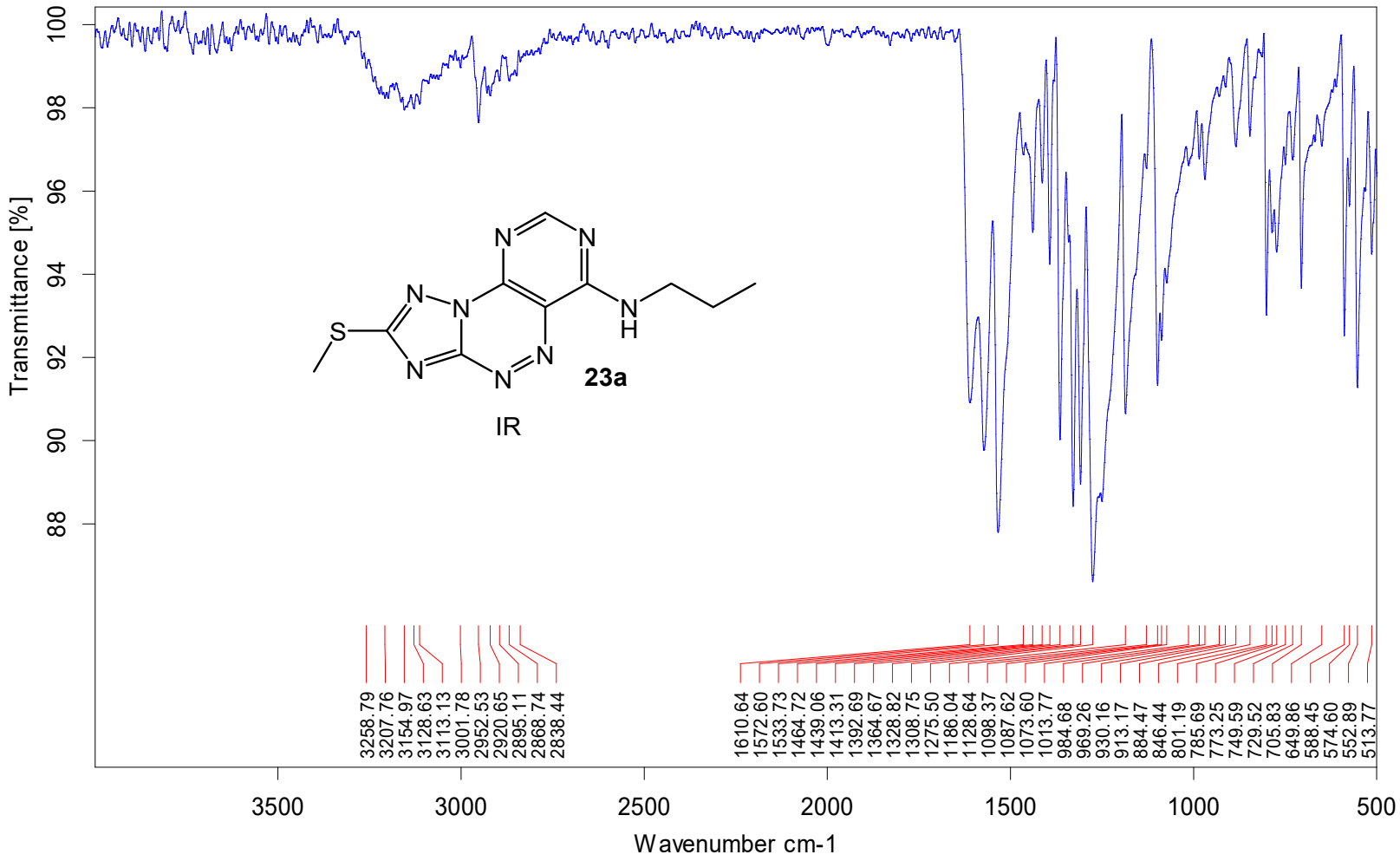


#	m/z	Res.	S/N	I	I %	FWHM
1	207.0445	19824	5890769.0	229479	1.5	0.0104
2	224.0713	21149	9368683.0	364964	2.3	0.0106
3	263.1069	21283	4699401.0	183068	1.2	0.0124
4	280.1343	14500	403645184.0	15724276	100.0	0.0193
5	281.1361	31020	81261704.0	3165606	20.1	0.0091
6	282.1307	25056	24125042.0	939808	6.0	0.0113
7	336.1962	26251	11103424.0	432542	2.8	0.0128
8	559.2595	28702	22831000.0	889397	5.7	0.0195
9	560.2615	21947	6767906.0	263648	1.7	0.0255
10	838.3871	24733	5159190.5	200980	1.3	0.0339

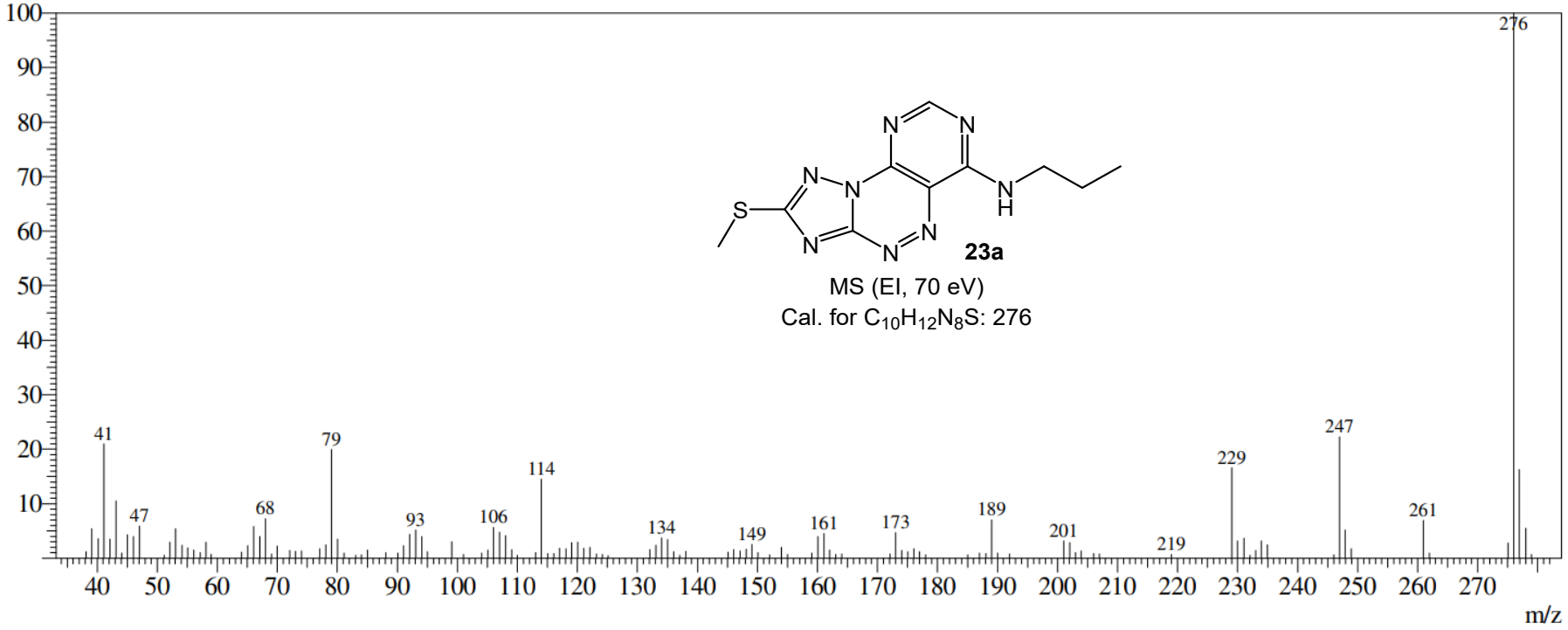
2-(Methylthio)-*N*-propylpyrimido[4,5-*e*][1,2,4]triazolo[5,1-*c*][1,2,4]triazin-6-amine (23a)




1602.13.fid
Rusinov Be544
168.84
162.79
158.98
157.68
139.80
123.31
42.60
21.70
13.55
11.23
90000
80000
70000
60000
50000
40000
30000
20000
10000
0
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (мд)
N
N
N
N
N
S
N
H
23a
13C, 100 MHz, DMSO-D6


Transmittance [%]
100
98
96
94
92
90
88
3500
3000
2500
2000
1500
1000
500
Wavenumber cm-1
N
N
N
N
N
S
N
H
23a
IR
3258.79
3207.76
3154.97
3128.63
3113.13
3001.78
2952.53
2920.65
2895.11
2868.74
2838.44
1610.64
1572.60
1533.73
1464.72
1439.06
1413.31
1392.69
1364.67
1328.82
1308.75
1275.50
1186.04
1128.64
1098.37
1087.62
1073.60
1013.77
984.68
969.26
930.16
913.17
884.47
846.44
801.19
785.69
773.25
749.59
729.52
705.83
649.86
588.45
574.60
552.89
513.77

Line#:1 R.Time:2.855(Scan#:1103)
MassPeaks:126
RawMode:Single 2.855(1103) BasePeak:276(7048154)
Фон.реж.:1.712(646) Group 1 - Event 1

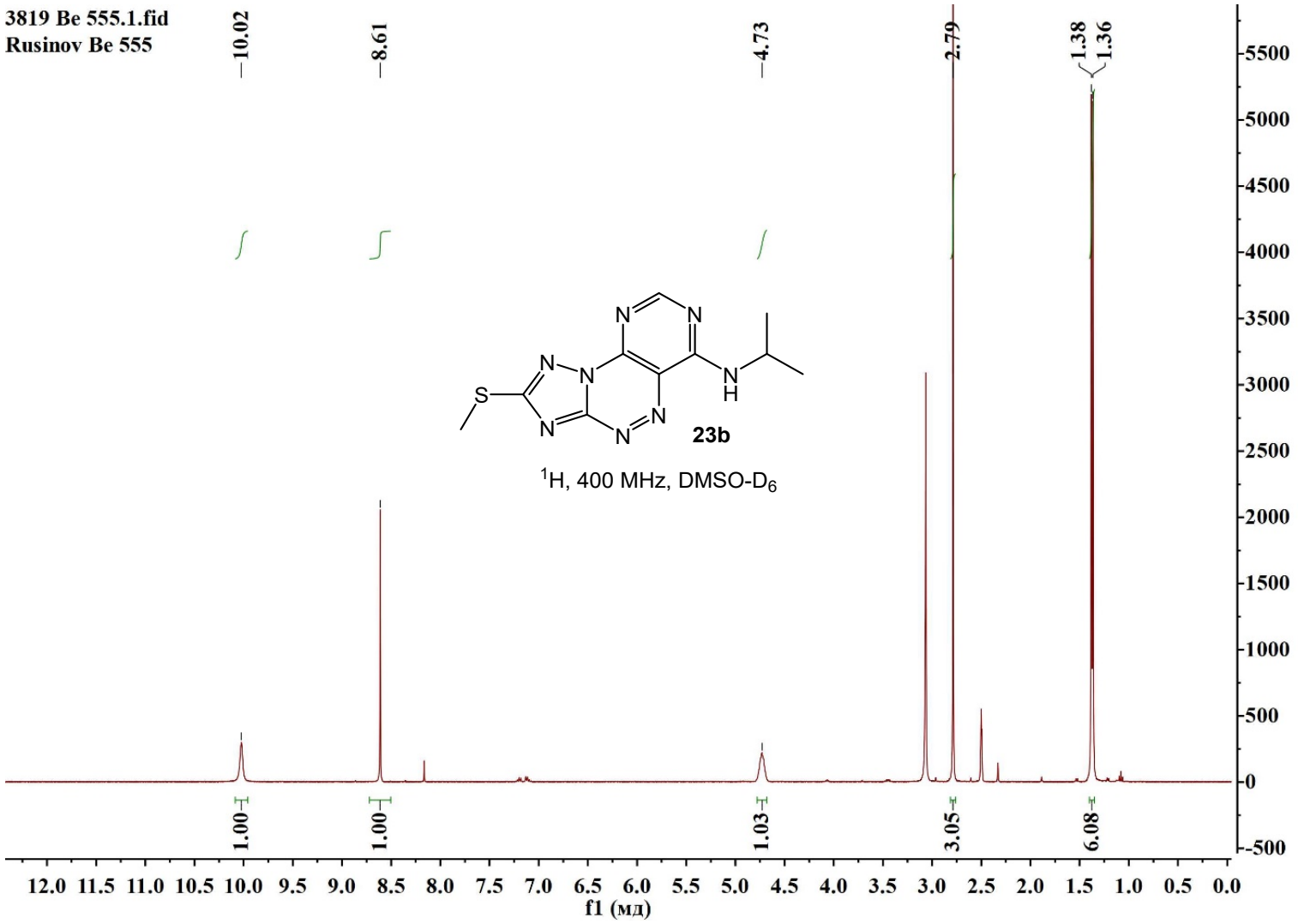


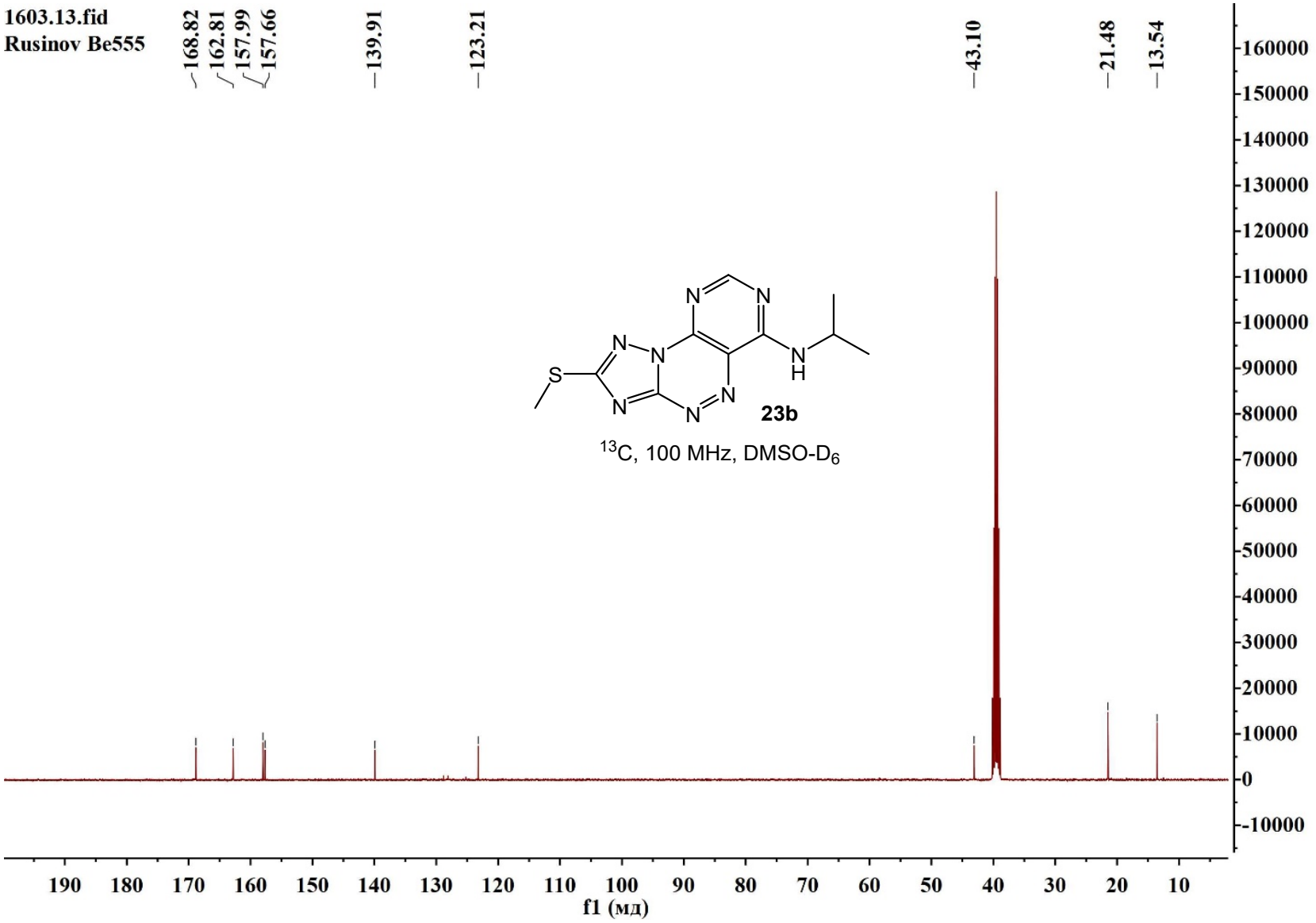
23a

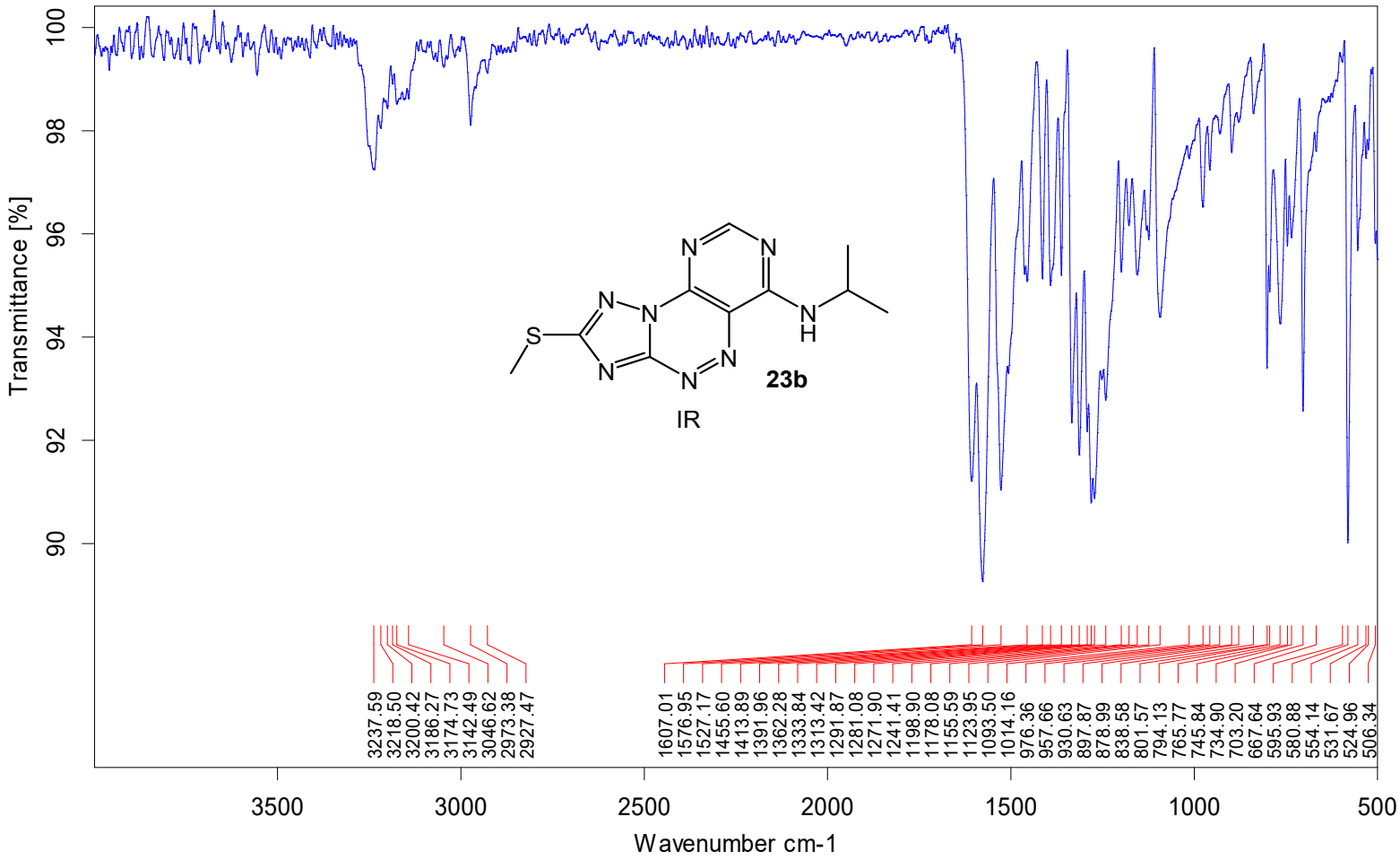
MS (EI, 70 eV)

Cal. for $C_{10}H_{12}N_8S$: 276

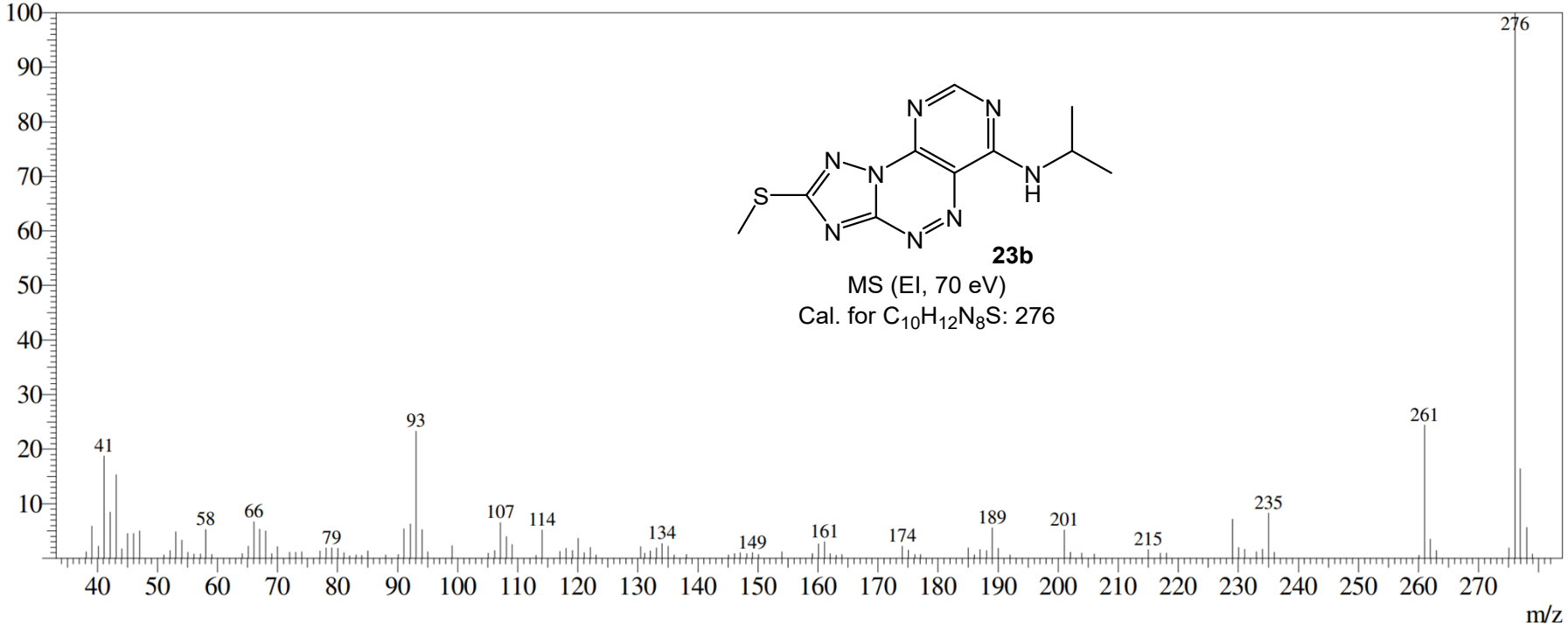
_N_-Isopropyl-2-(methylthio)pyrimido[4,5-_e_][1,2,4]triazolo[5,1-_c_][1,2,4]triazin-6-amine (23b)




1603.13.fid
Rusinov Be555
168.82
162.81
157.99
157.66
139.91
123.21
43.10
21.48
13.54
23b
13C, 100 MHz, DMSO-D6
f1 (мд)


Transmittance [%]
100
98
96
94
92
90
3500
3000
2500
2000
1500
1000
500
Wavenumber cm-1
3237.59
3218.50
3200.42
3186.27
3174.73
3142.49
3046.62
2973.38
2927.47
1607.01
1576.95
1527.17
1455.60
1413.89
1391.96
1362.28
1333.84
1313.42
1291.87
1281.08
1271.90
1241.41
1198.90
1178.08
1155.59
1123.95
1093.50
1014.16
976.36
957.66
930.63
897.87
878.99
838.58
801.57
794.13
765.77
745.84
734.90
703.20
667.64
595.93
580.88
554.14
531.67
524.96
506.34
23b
IR

Line#:1 R.Time:2.465(Scan#:947)
MassPeaks:115
RawMode:Single 2.465(947) BasePeak:276(6765279)
Фон.реж.:0.688(236) Group 1 - Event 1

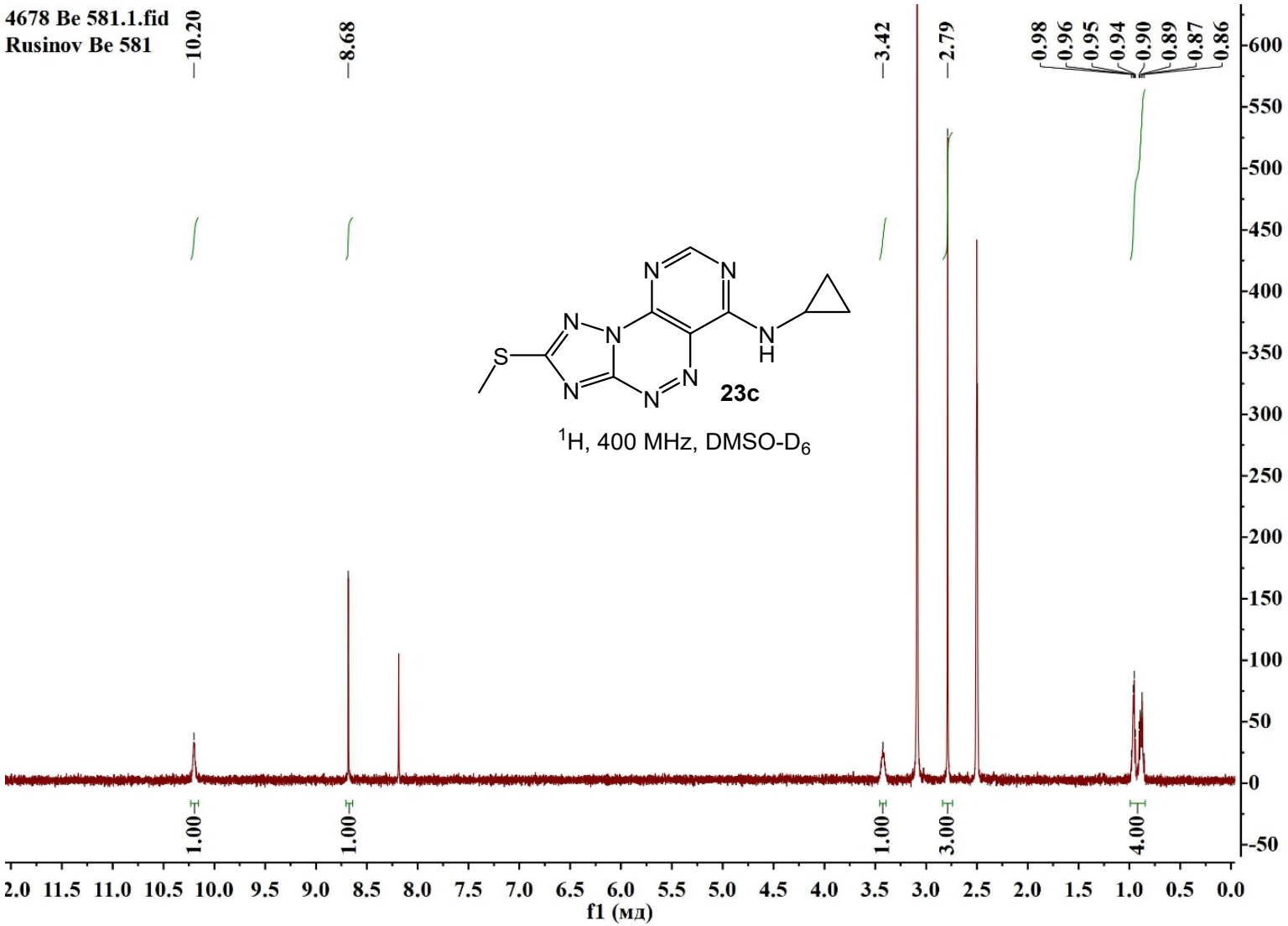


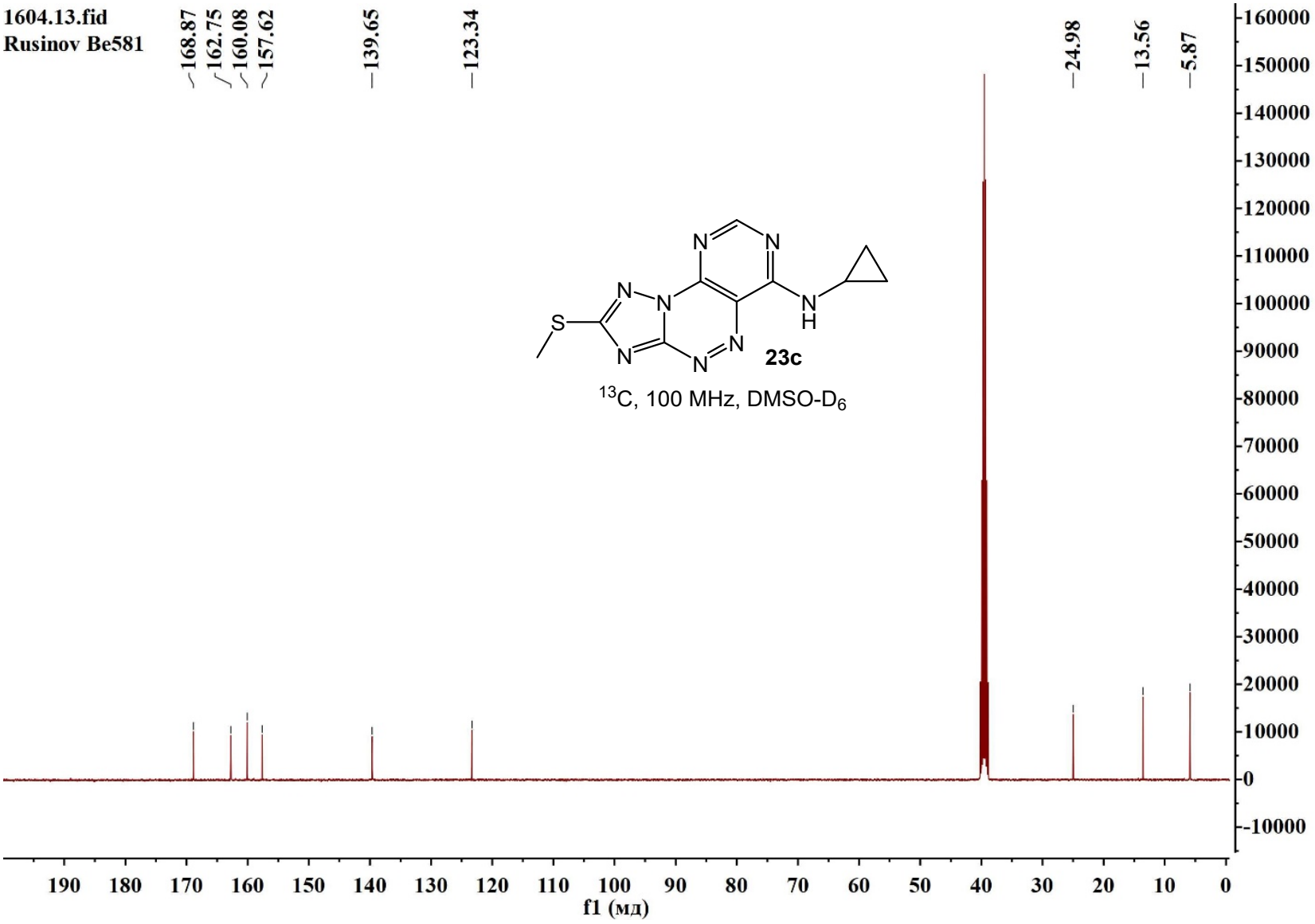
23b

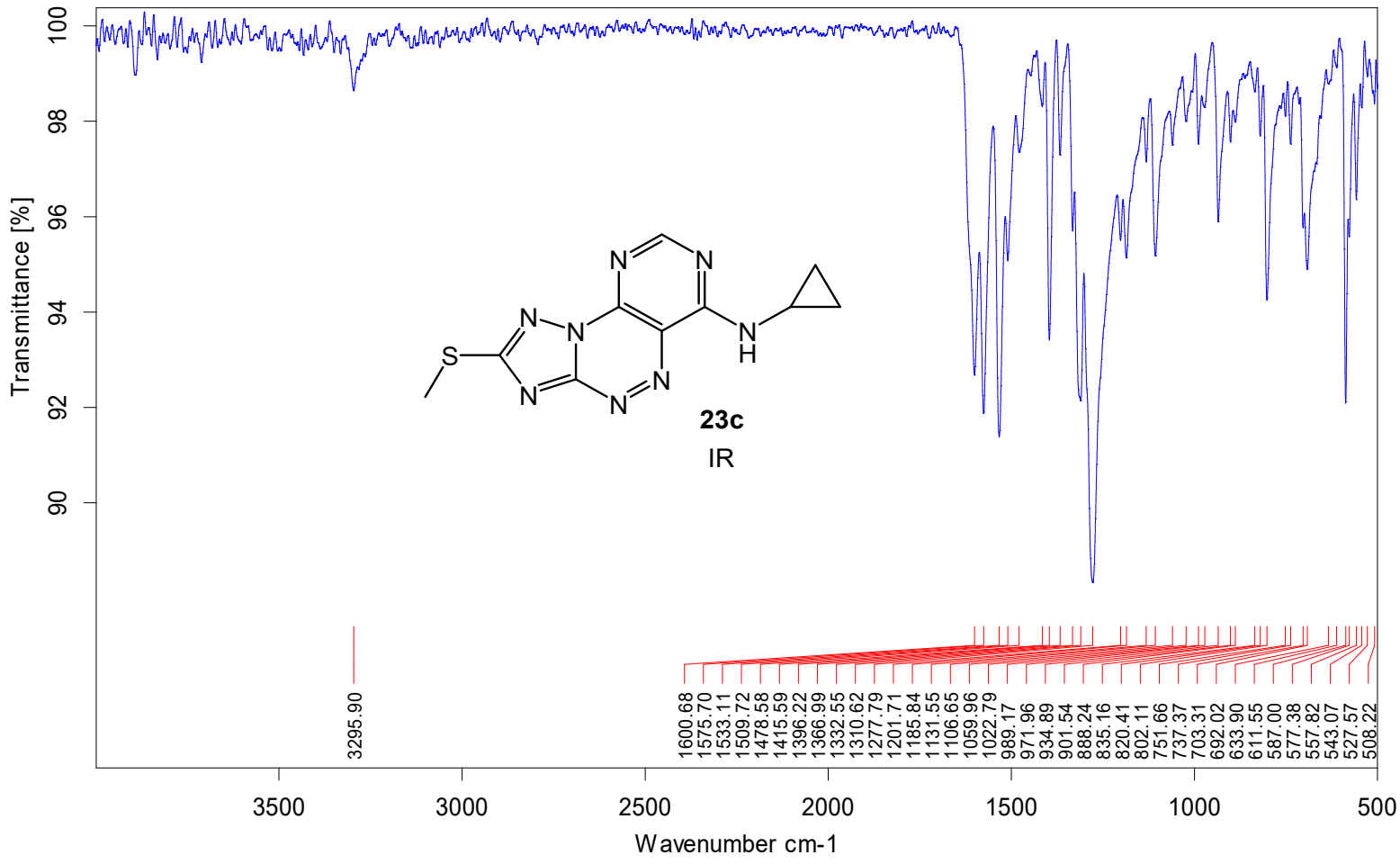
MS (EI, 70 eV)

Cal. for $C_{10}H_{12}N_8S$: 276

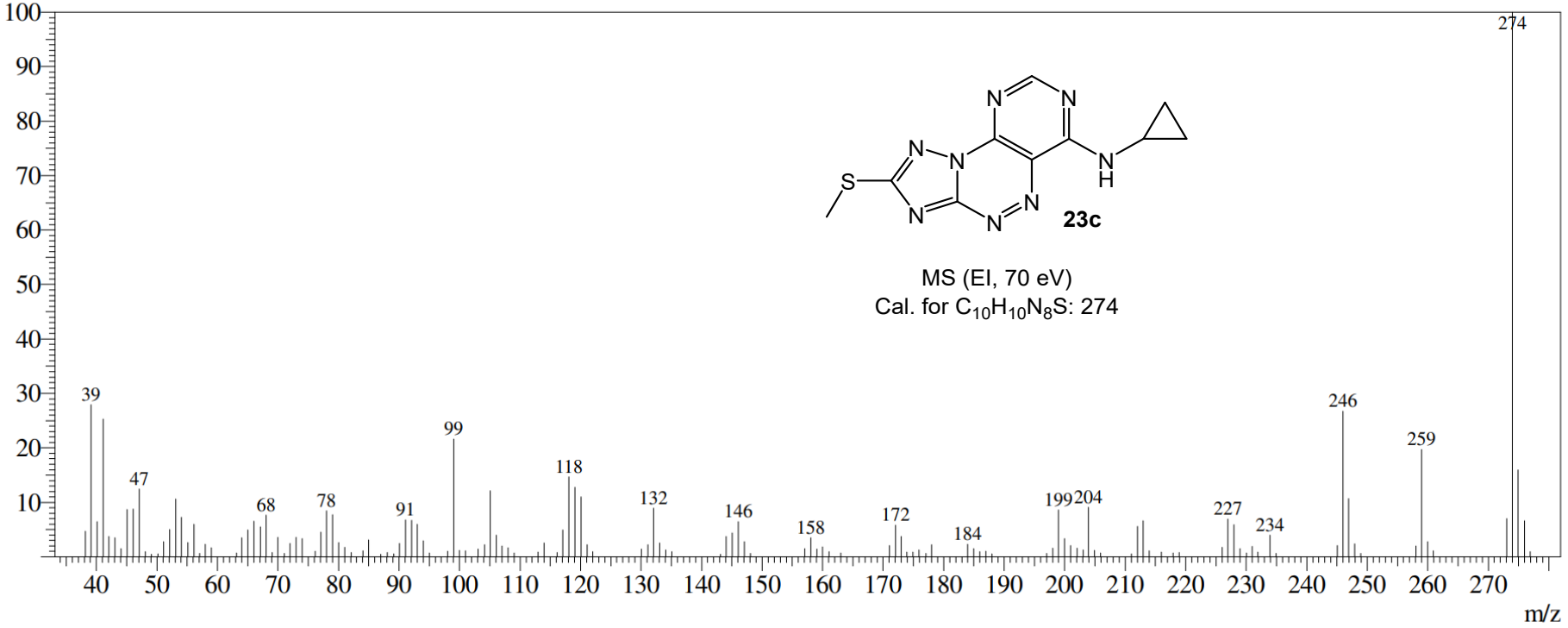
_N_-Cyclopropyl-2-(methylthio)pyrimido[4,5-_e_][1,2,4]triazolo[5,1-_c_][1,2,4]triazin-6-amine (23c)




1604.13.fid
Rusinov Be581
168.87
162.75
160.08
157.62
139.65
123.34
24.98
13.56
5.87
23c
13C, 100 MHz, DMSO-D6
f1 (мд)


Transmittance [%]
100
98
96
94
92
90
3500
3000
2500
2000
1500
1000
500
Wavenumber cm-1
3295.90
1600.68
1575.70
1533.11
1509.72
1478.58
1415.59
1396.22
1366.99
1332.55
1310.62
1277.79
1201.71
1185.84
1131.55
1106.65
1059.96
1022.79
989.17
971.96
934.89
901.54
888.24
835.16
820.41
802.11
751.66
737.37
703.31
692.02
633.90
611.55
587.00
577.38
557.82
543.07
527.57
508.22
N
N
N
N
N
N
S
N
H
23c
IR

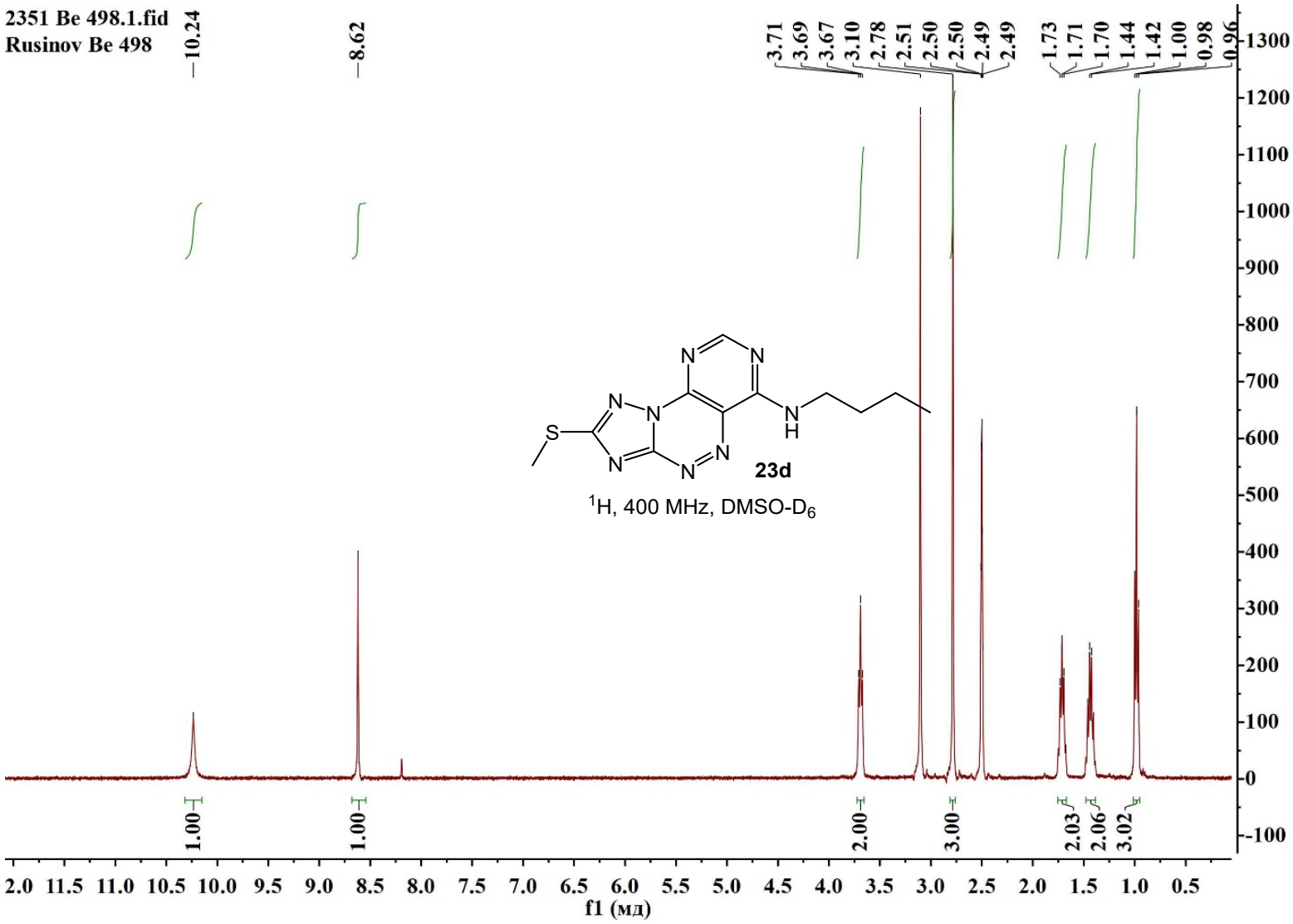
Line#:1 R.Time:1.900(Scan#:721)
MassPeaks:143
RawMode:Single 1.900(721) BasePeak:274(2593917)
Фон.реж.:3.190(1237) Group 1 - Event 1



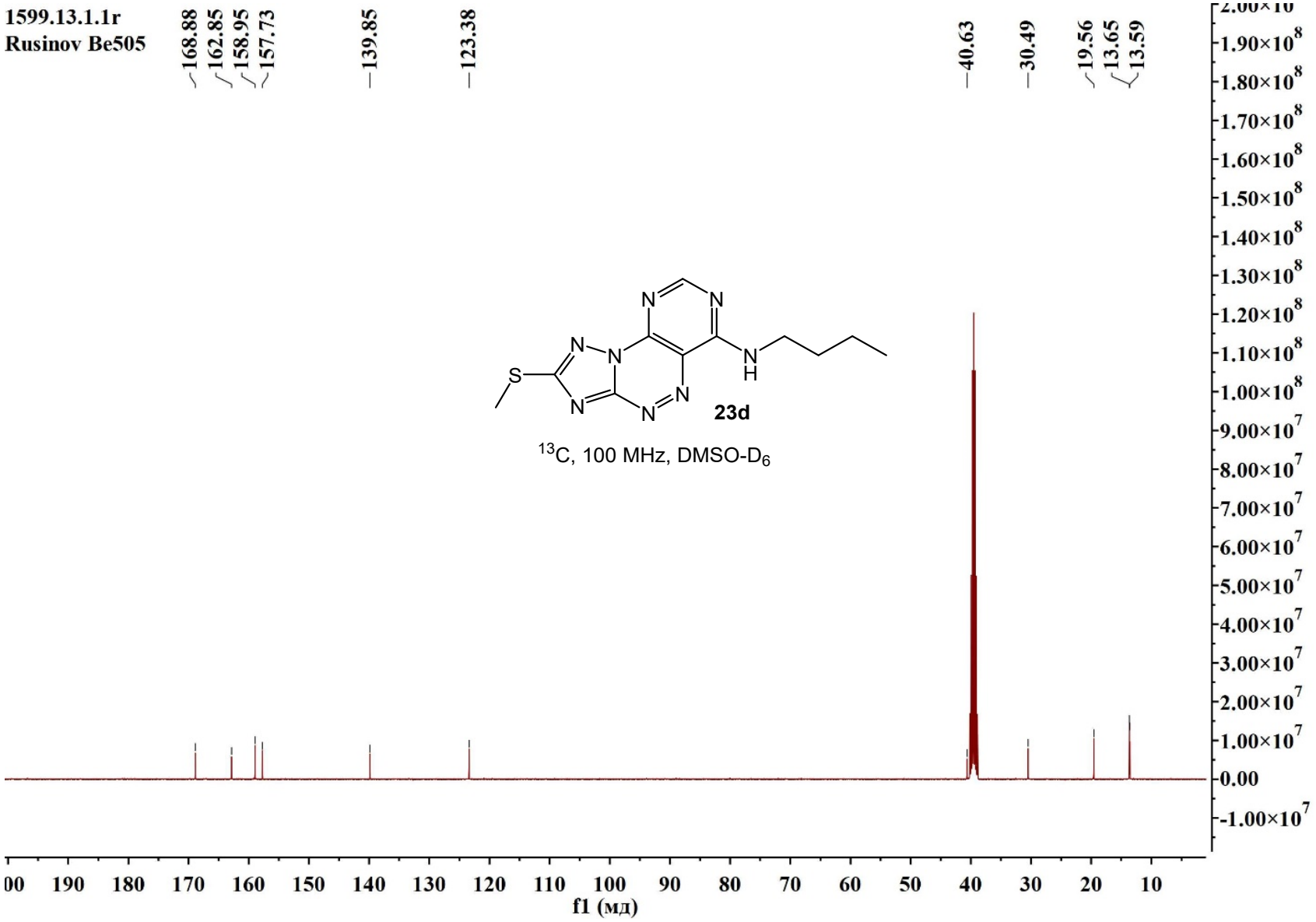
23c

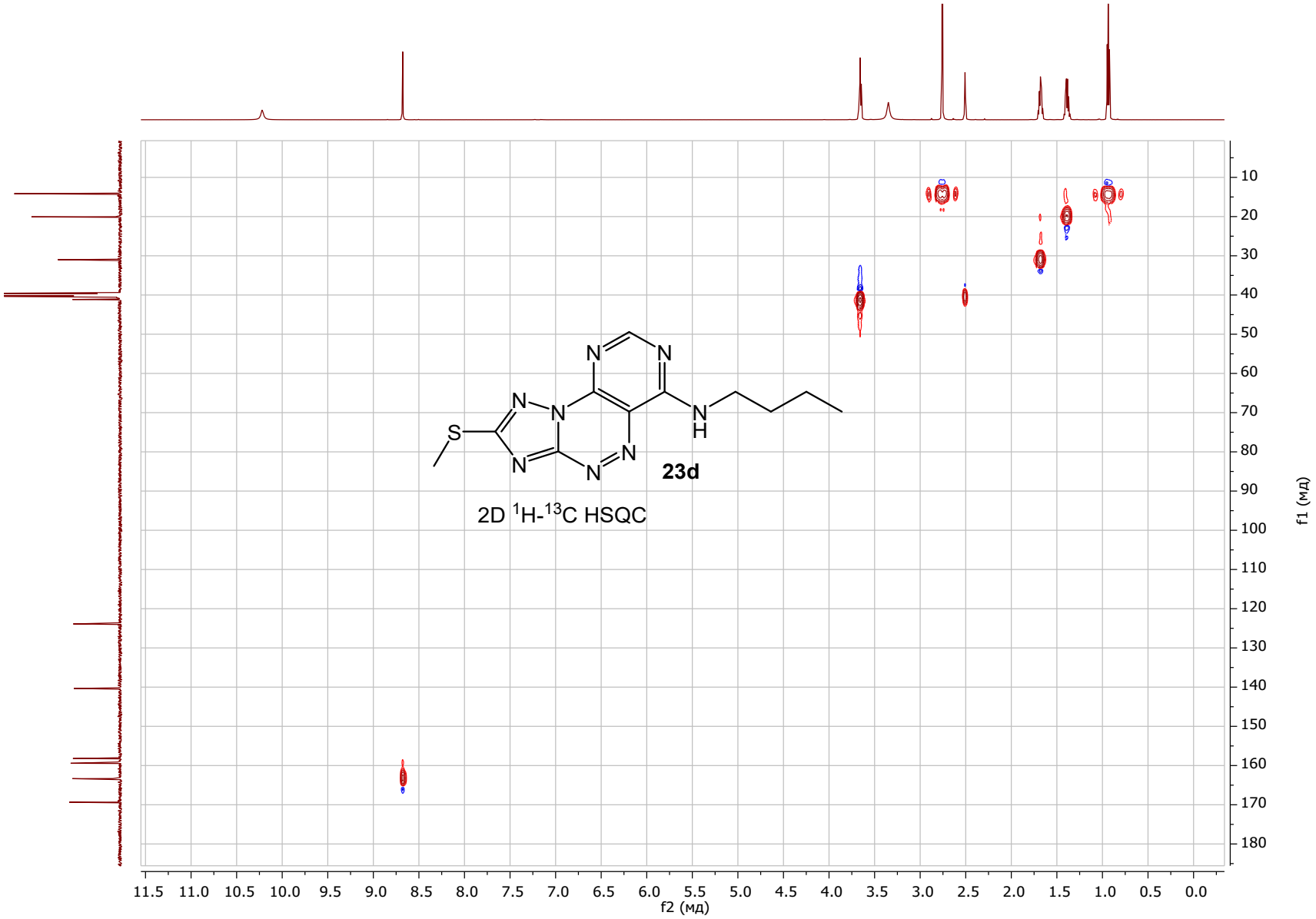
MS (EI, 70 eV)
Cal. for $C_{10}H_{10}N_8S$: 274

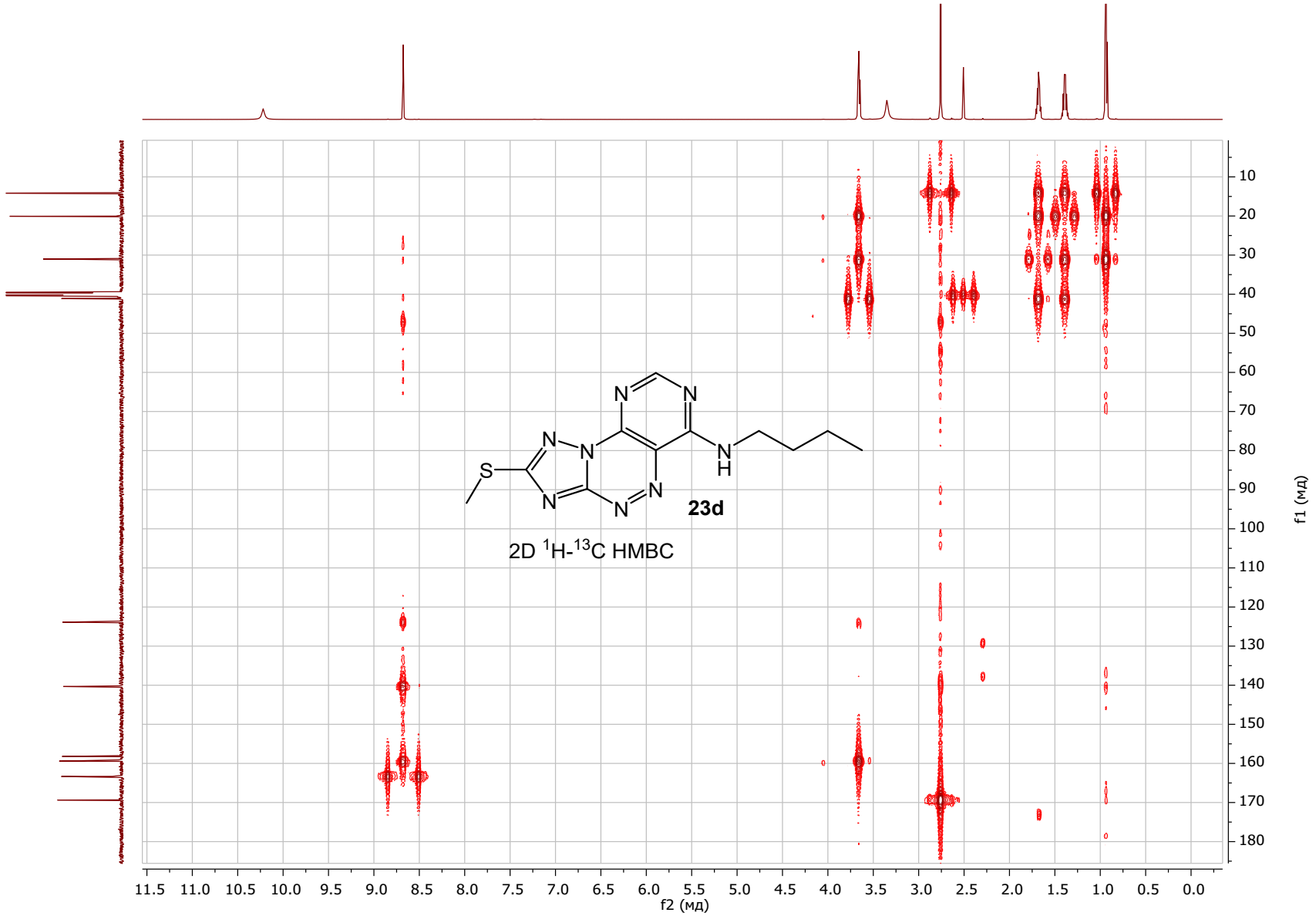
_N_-Butyl-2-(methylthio)pyrimido[4,5-*e*][1,2,4]triazolo[5,1-*c*][1,2,4]triazin-6-amine (23d)

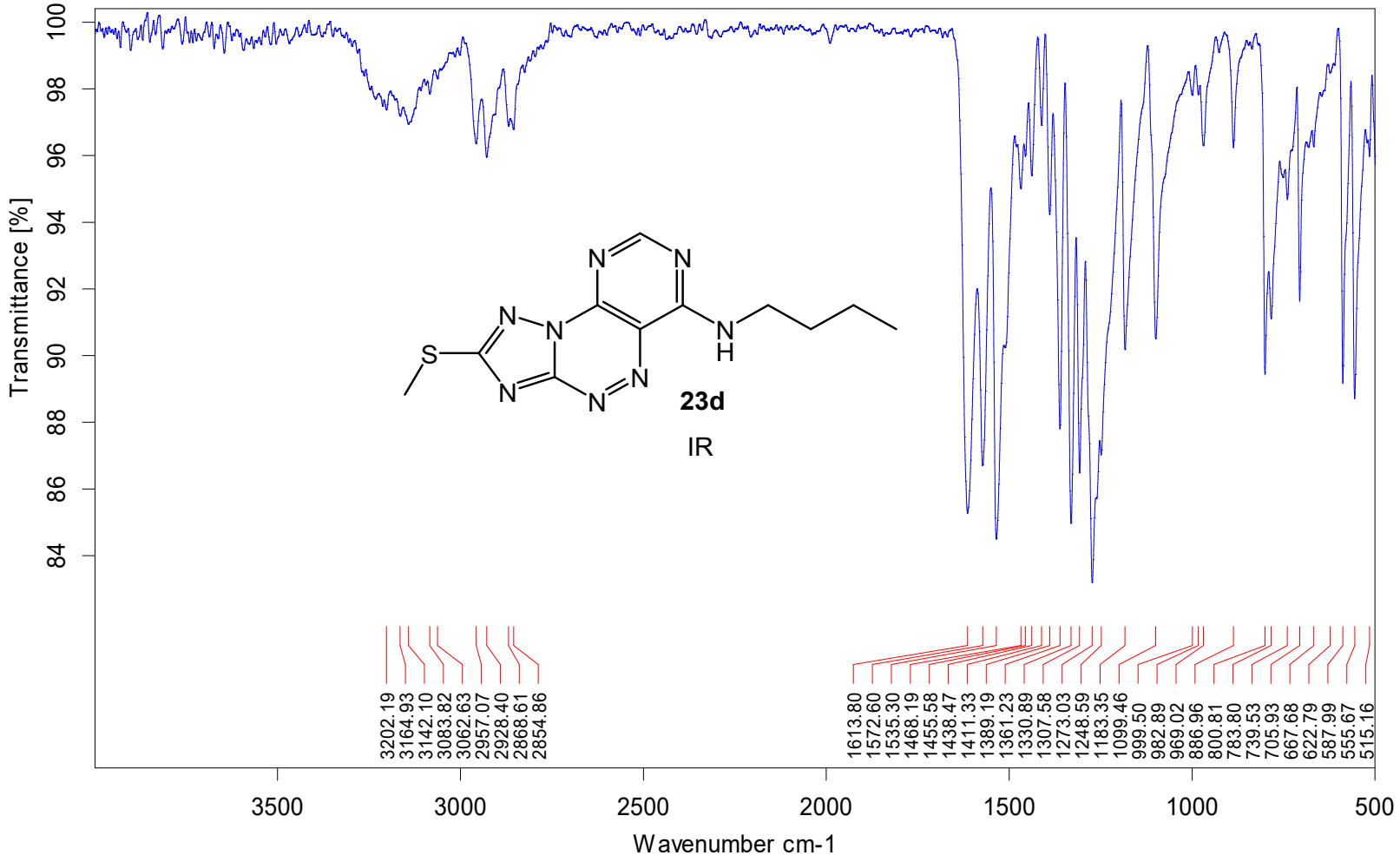


q

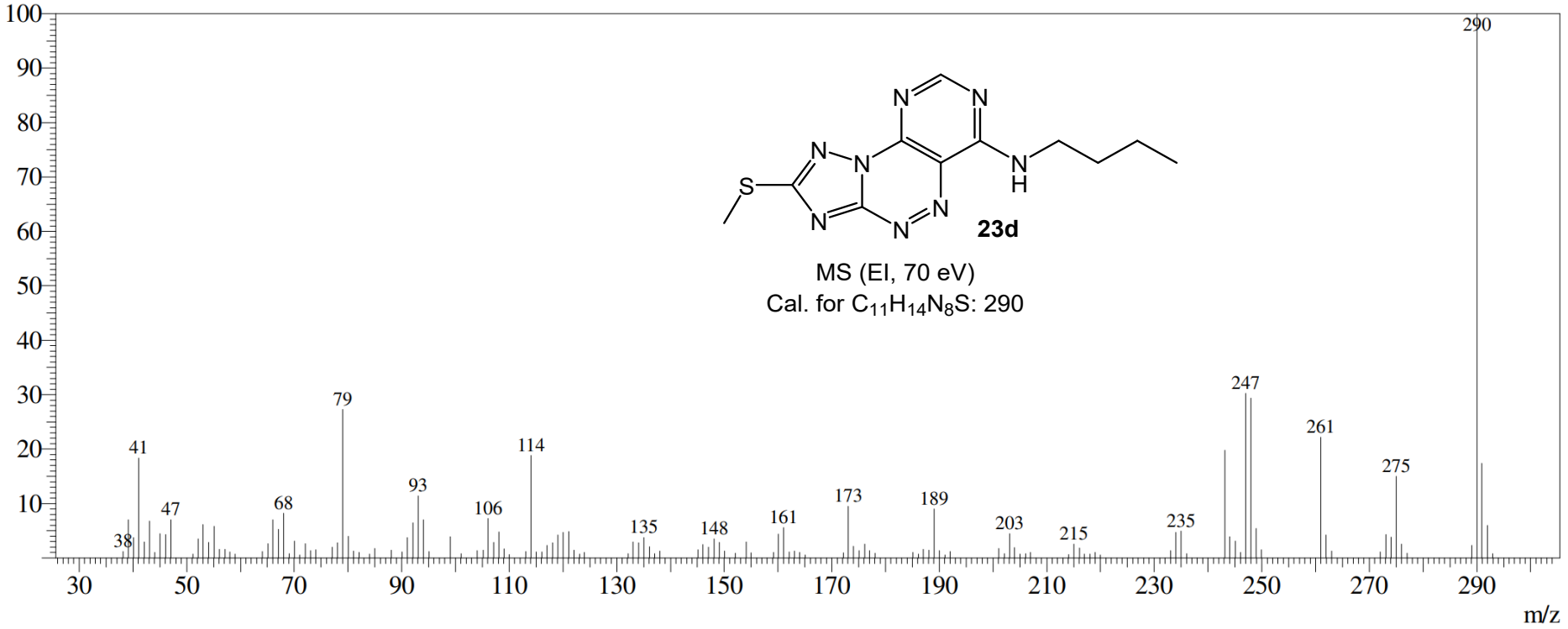

1599.13.1.1r
Rusinov Be505
168.88
162.85
158.95
157.73
139.85
123.38
40.63
30.49
19.56
13.65
13.59
23d
13C, 100 MHz, DMSO-D6
f1 (мд)


23d
2D ^{1}H-^{13}C HSQC
f2 (мд)
f1 (мд)


23d
2D ^{1}H-^{13}C HMBC
f2 (мд)
f1 (мд)


Transmittance [%]
100
98
96
94
92
90
88
86
84
3500
3000
2500
2000
1500
1000
500
Wavenumber cm-1
3202.19
3164.93
3142.10
3083.82
3062.63
2957.07
2928.40
2868.61
2854.86
1613.80
1572.60
1535.30
1468.19
1455.58
1438.47
1411.33
1389.19
1361.23
1330.89
1307.58
1273.03
1248.59
1183.35
1099.46
999.50
982.89
969.02
886.96
800.81
783.80
739.53
705.93
667.68
622.79
587.99
555.67
515.16
N
N
N
N
N
N
N
S
N
H
23d
IR

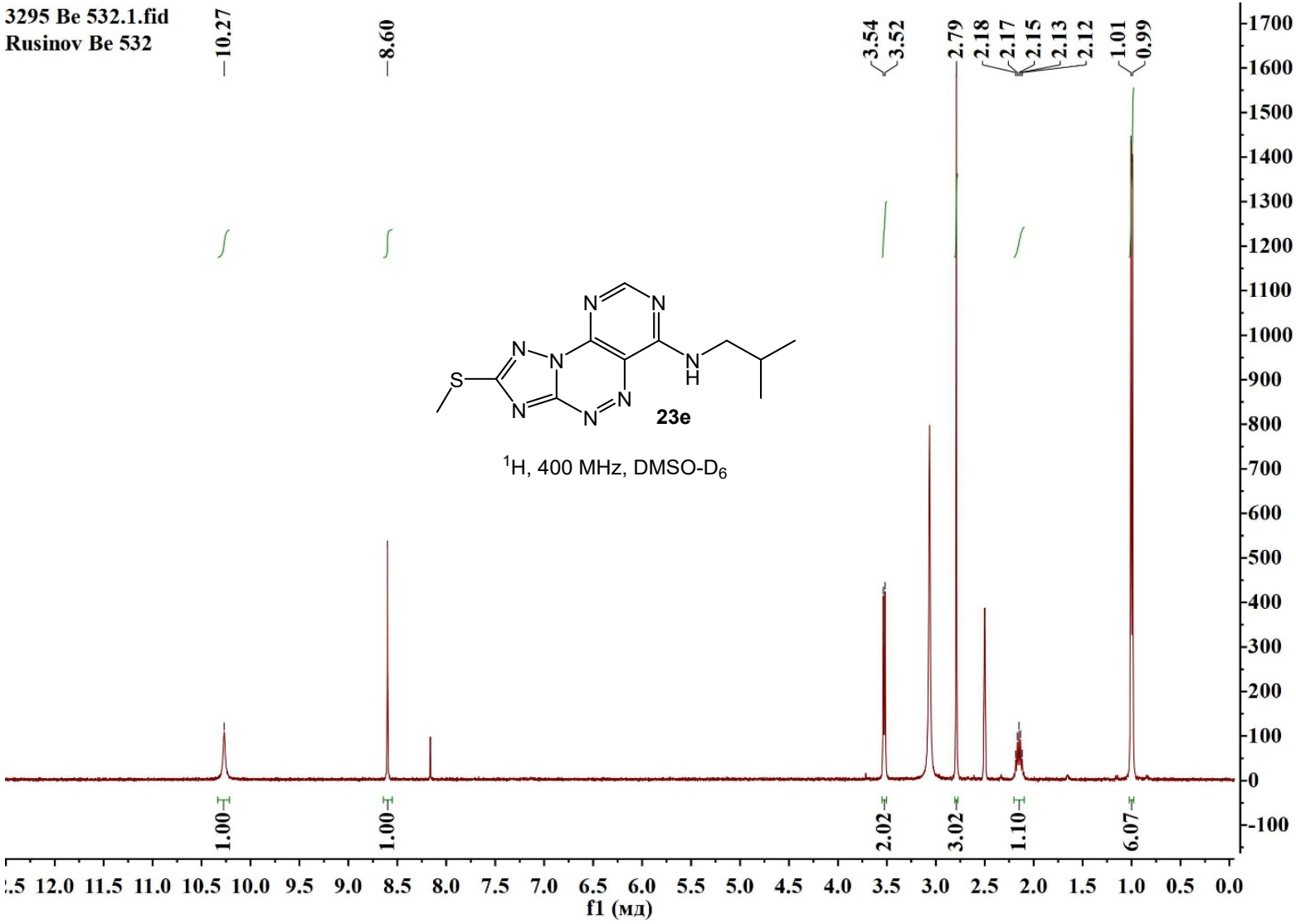
Line#:1 R.Time:2.572(Scan#:990)
MassPeaks:144
RawMode:Single 2.572(990) BasePeak:290(5635427)
Фон.реж.:3.350(1301) Group 1 - Event 1

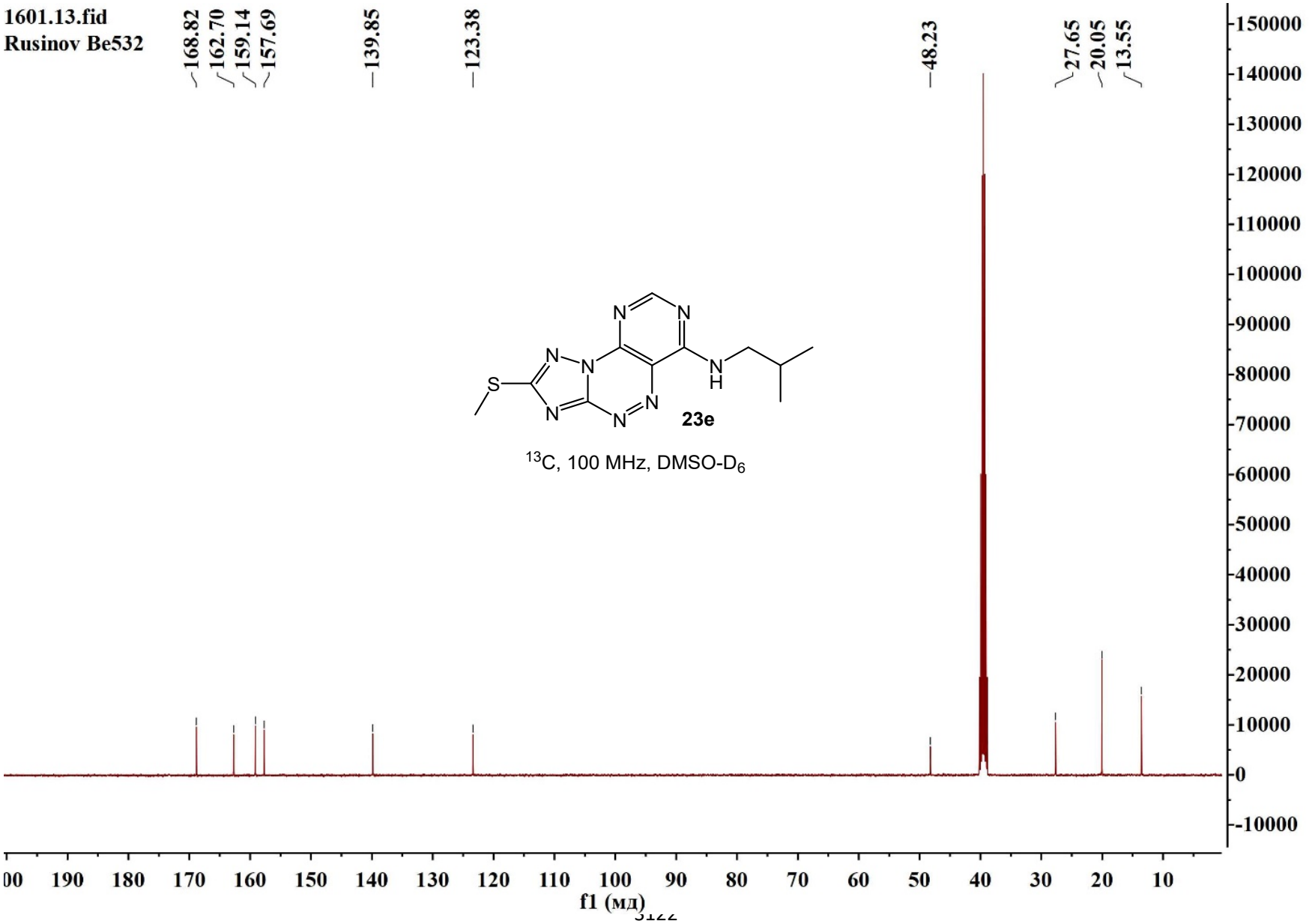


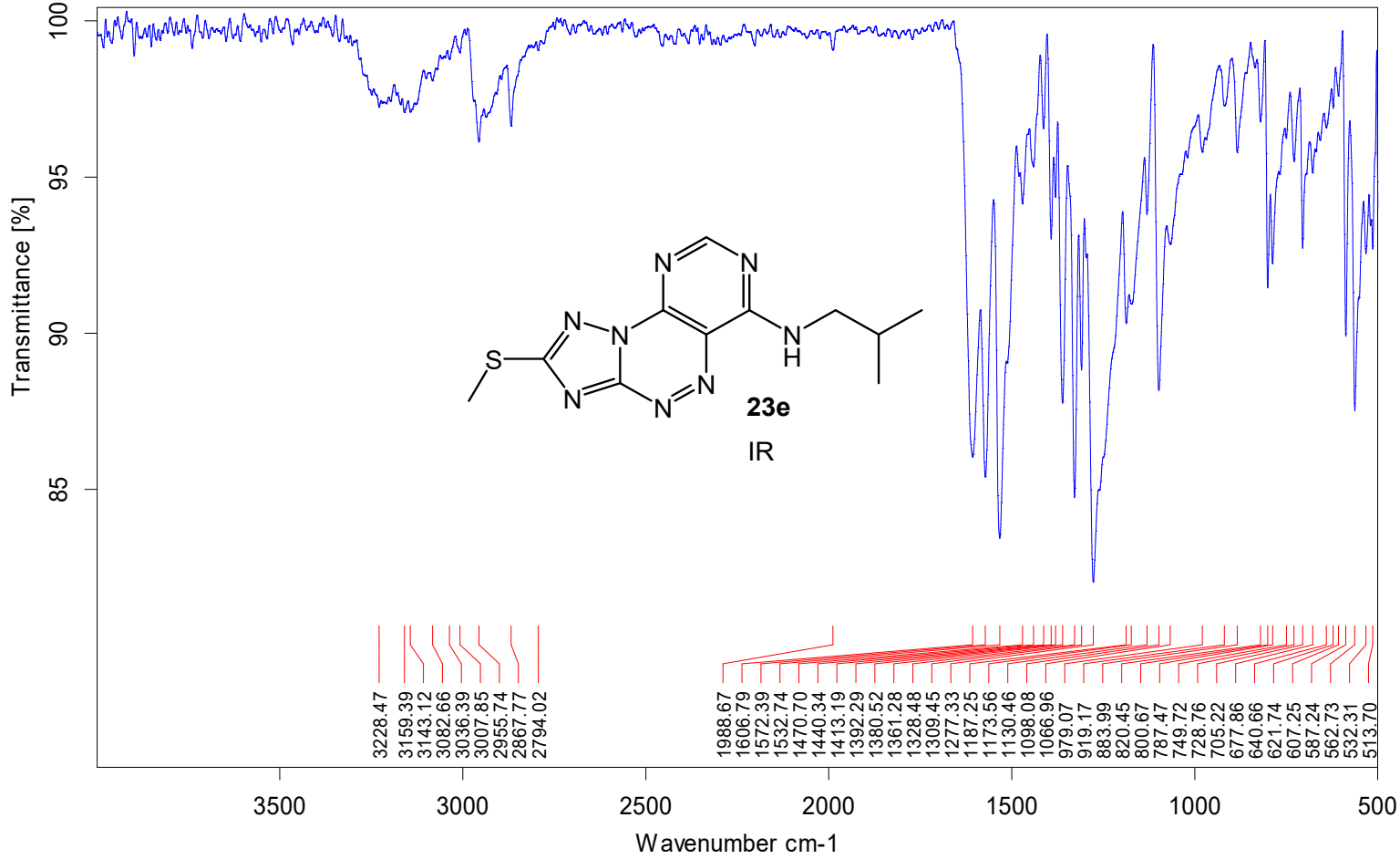
23d

MS (EI, 70 eV)
Cal. for $C_{11}H_{14}N_8S$: 290

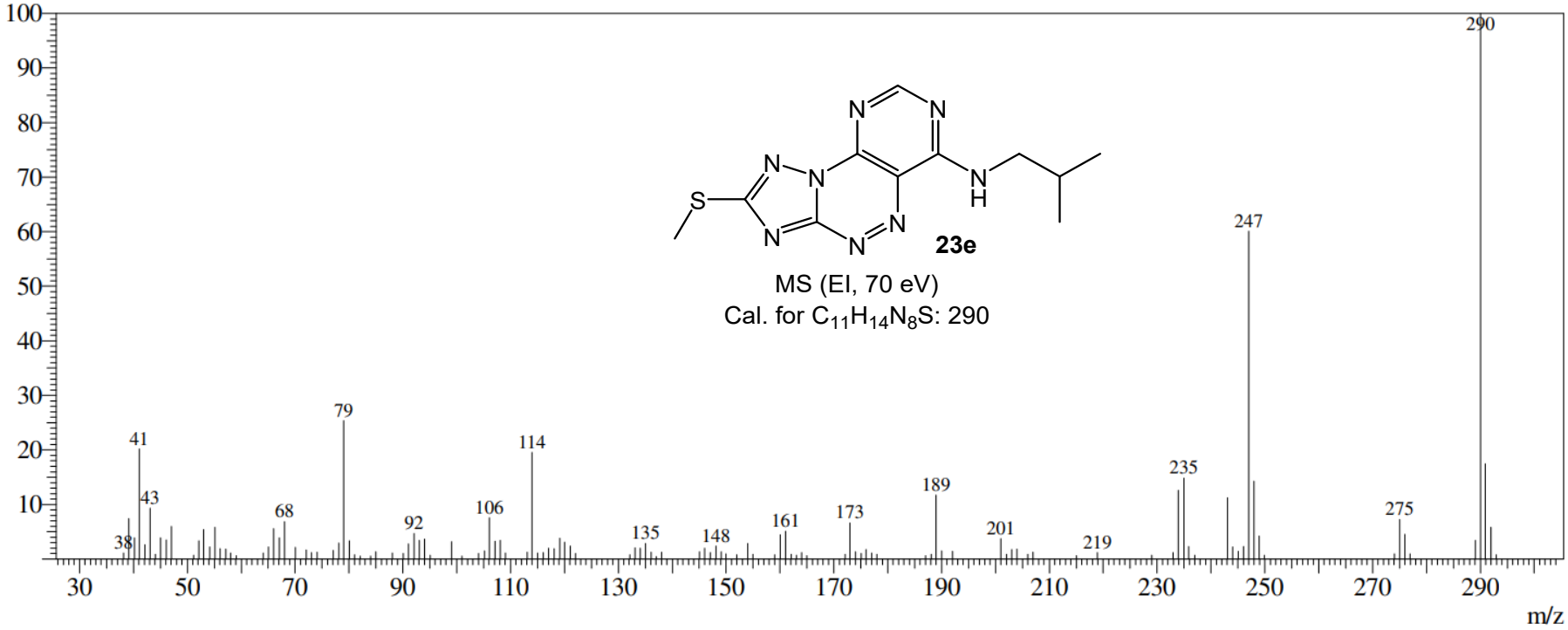
_N_-Isobutyl-2-(methylthio)pyrimido[4,5-_e_][1,2,4]triazolo[5,1-_c_][1,2,4]triazin-6-amine (23e)




1601.13.fid
Rusinov Be532
168.82
162.70
159.14
157.69
139.85
123.38
48.23
27.65
20.05
13.55
150000
140000
130000
120000
110000
100000
90000
80000
70000
60000
50000
40000
30000
20000
10000
0
-10000
00
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (мд)
N
N
N
N
N
N
S
N
H
23e
13C, 100 MHz, DMSO-D6


Transmittance [%]
100
95
90
85
3500
3000
2500
2000
1500
1000
500
Wavenumber cm-1
23e
IR
3228.47
3159.39
3143.12
3082.66
3036.39
3007.85
2955.74
2867.77
2794.02
1988.67
1606.79
1572.39
1532.74
1470.70
1440.34
1413.19
1392.29
1380.52
1361.28
1328.48
1309.45
1277.33
1187.25
1173.56
1130.46
1098.08
1066.96
979.07
919.17
883.99
820.45
800.67
787.47
749.72
728.76
705.22
677.86
640.66
621.74
607.25
587.24
562.73
532.31
513.70

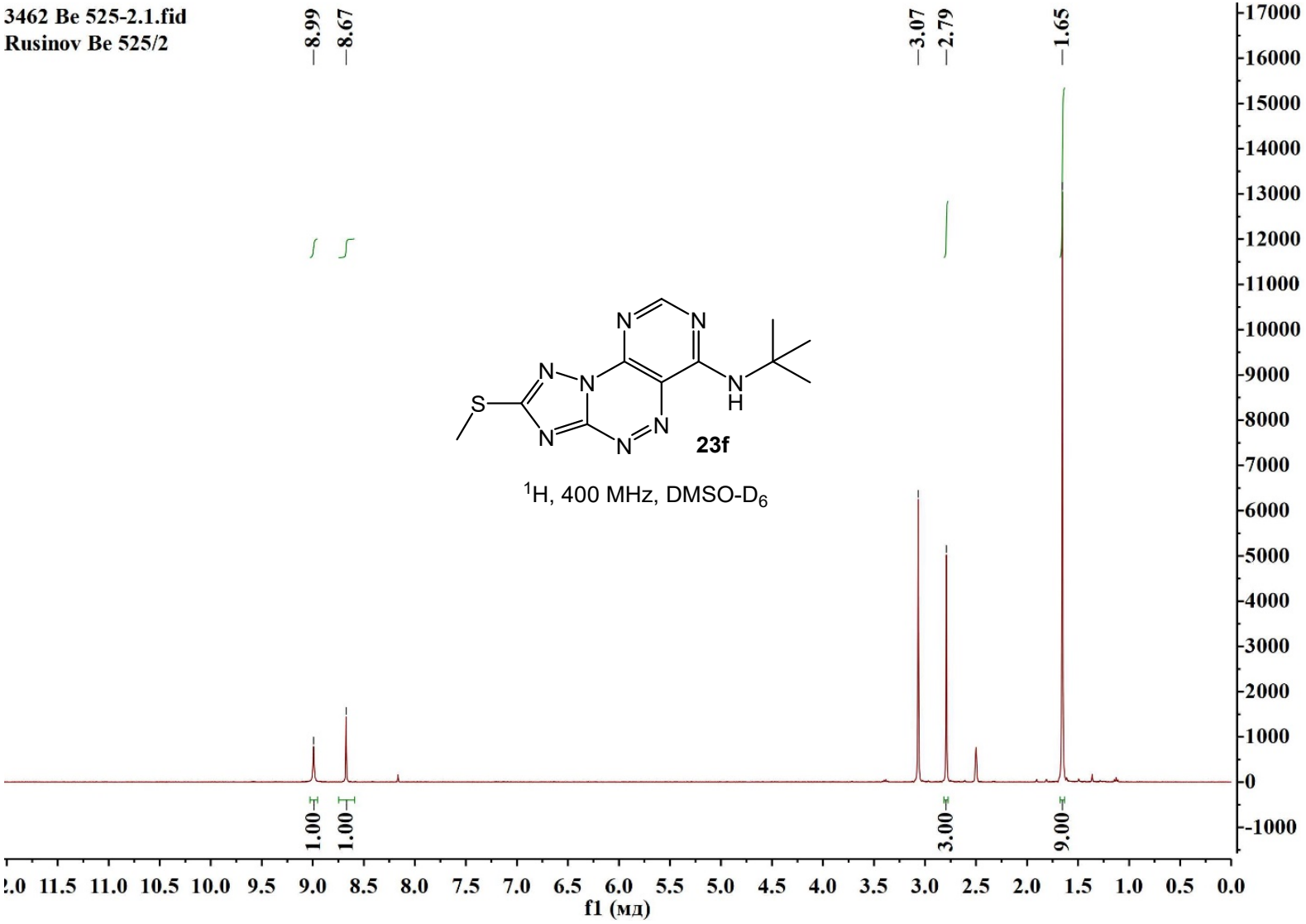
Line#:1 R.Time:1.763(Scan#:666)
MassPeaks:127
RawMode:Single 1.763(666) BasePeak:290(6816659)
Фон.реж.:0.425(131) Group 1 - Event 1

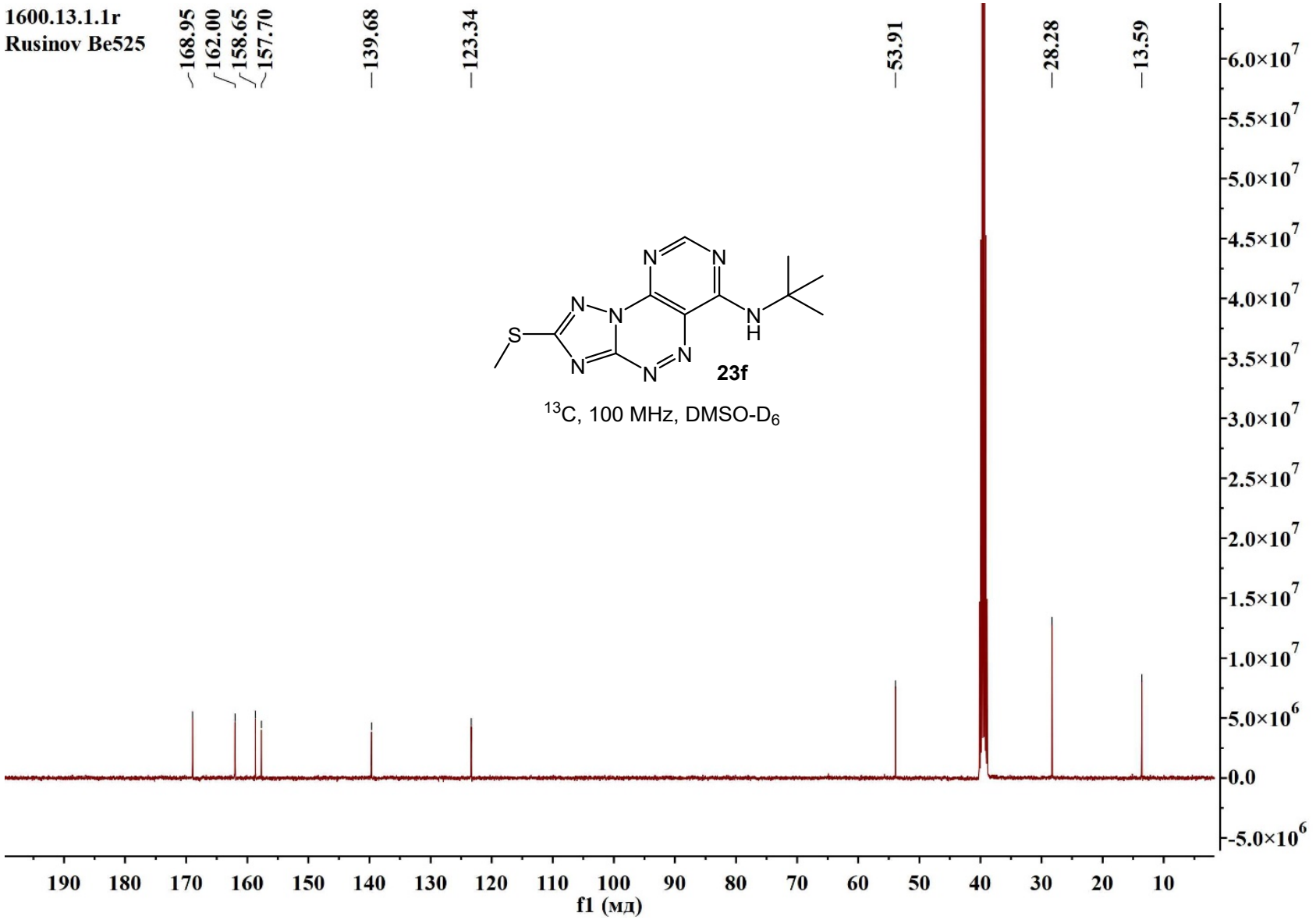


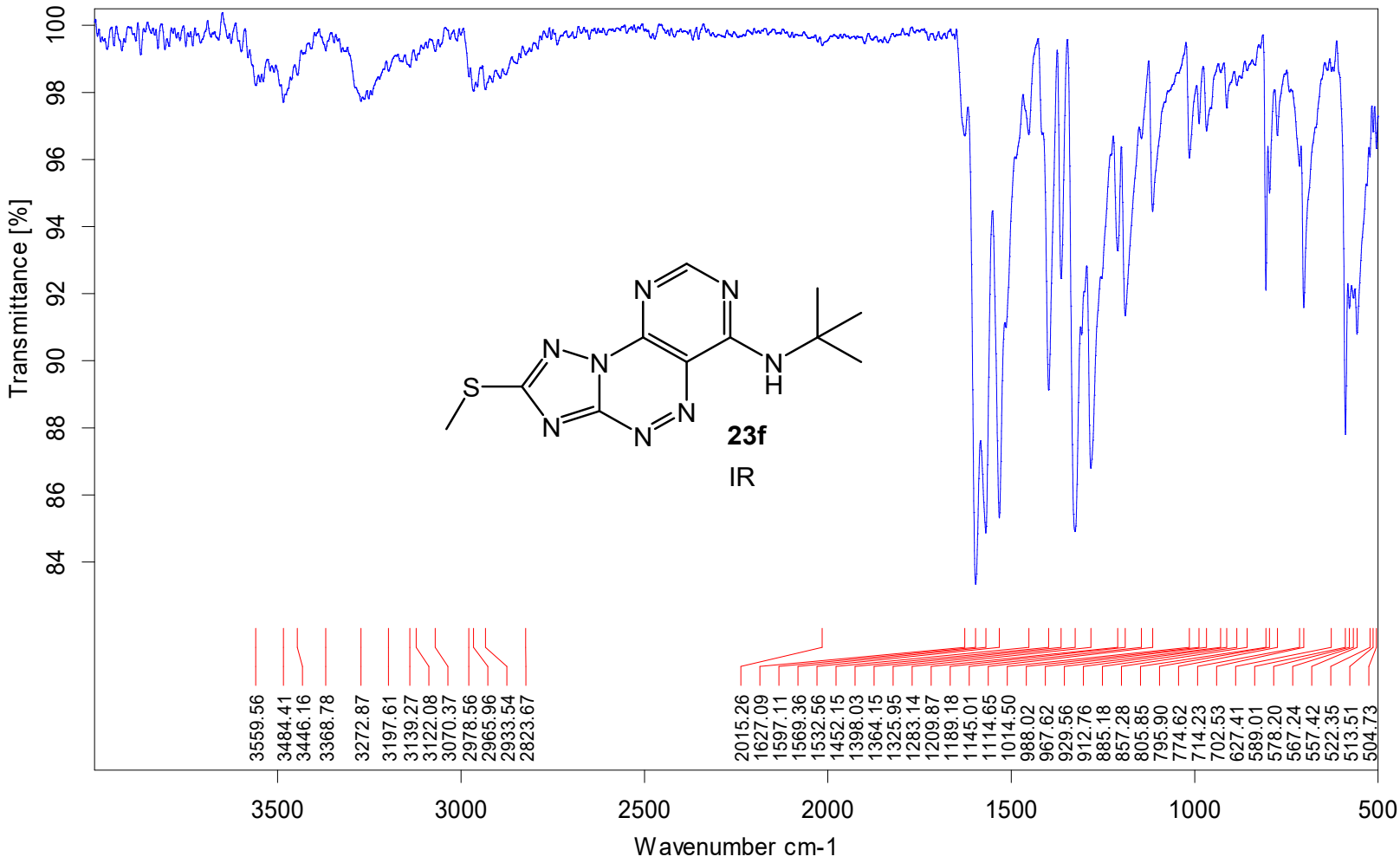
23e

MS (EI, 70 eV)
Cal. for $C_{11}H_{14}N_8S$: 290

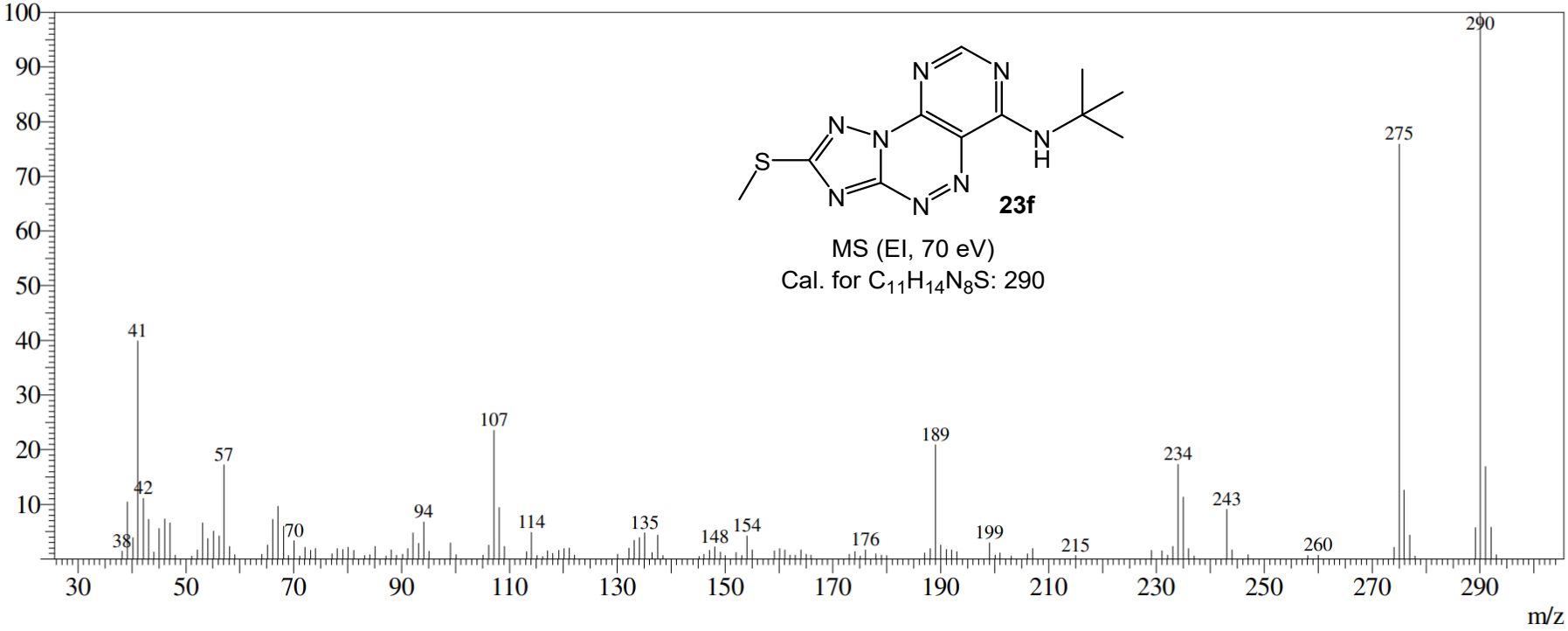
_N_-(_Tert_-butyl)-2-(methylthio)pyrimido[4,5-_e_][1,2,4]triazolo[5,1-_c_][1,2,4]triazin-6-amine (23f)



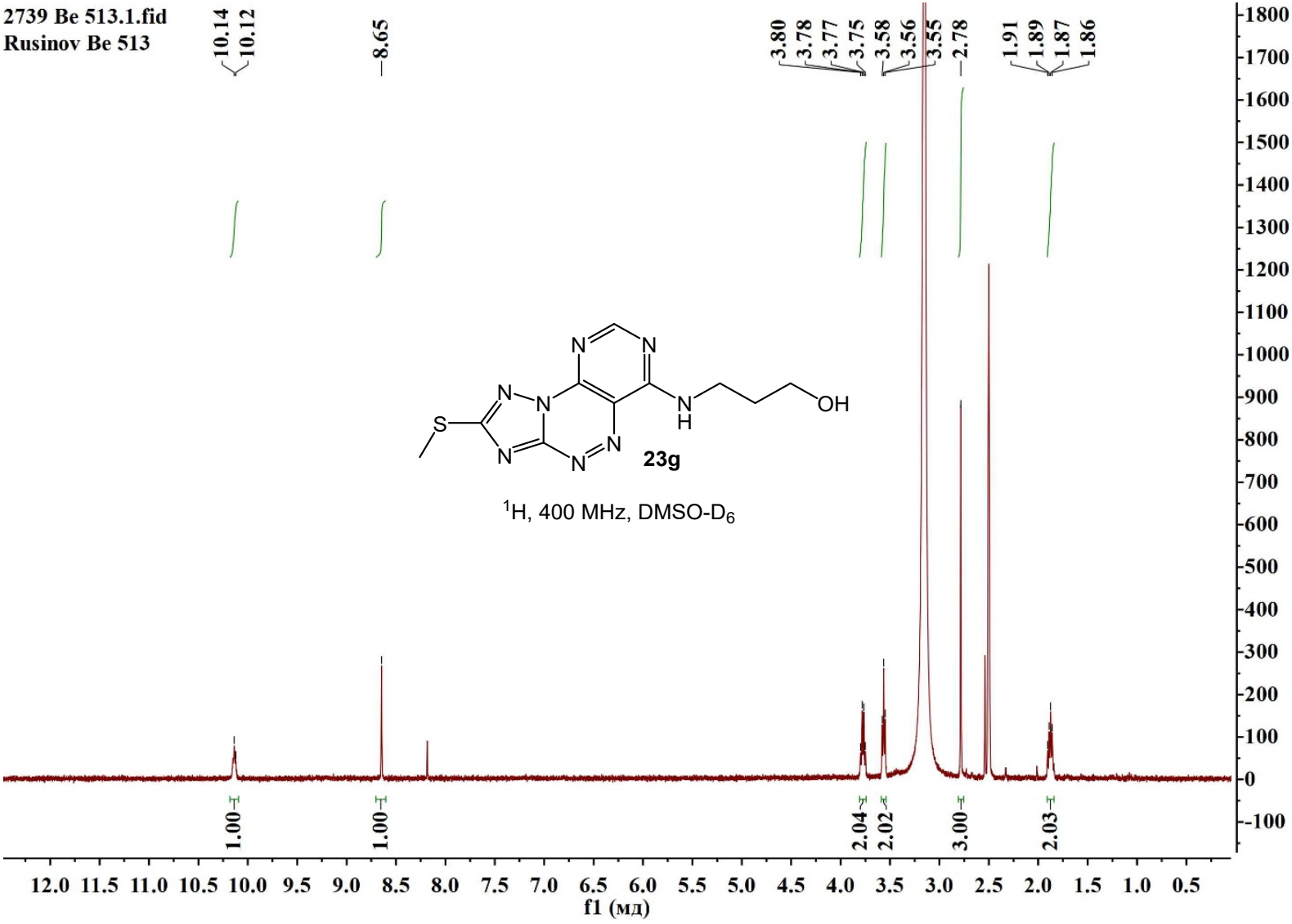

1600.13.1.1r
Rusinov Be525
168.95
162.00
158.65
157.70
139.68
123.34
53.91
28.28
13.59
23f
13C, 100 MHz, DMSO-D6
6.0×10^7
5.5×10^7
5.0×10^7
4.5×10^7
4.0×10^7
3.5×10^7
3.0×10^7
2.5×10^7
2.0×10^7
1.5×10^7
1.0×10^7
5.0×10^6
0.0
-5.0×10^6
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (мд)

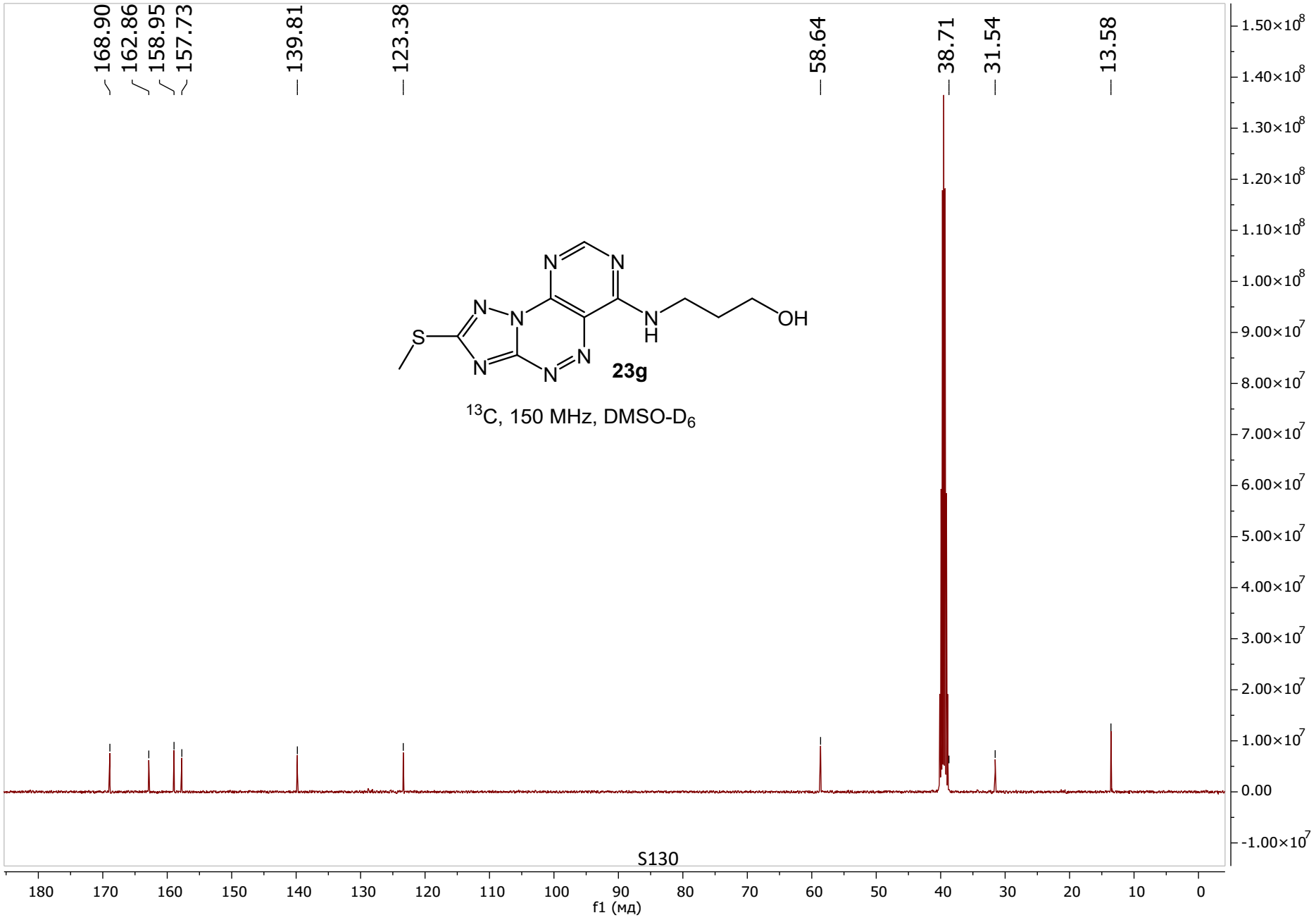

Transmittance [%]
100
98
96
94
92
90
88
86
84
3500
3000
2500
2000
1500
1000
500
Wavenumber cm-1
3559.56
3484.41
3446.16
3368.78
3272.87
3197.61
3139.27
3122.08
3070.37
2978.56
2965.96
2933.54
2823.67
2015.26
1627.09
1597.11
1569.36
1532.56
1452.15
1398.03
1364.15
1325.95
1283.14
1209.87
1189.18
1145.01
1114.65
1014.50
988.02
967.62
929.56
912.76
885.18
857.28
805.85
795.90
774.62
714.23
702.53
627.41
589.01
578.20
567.24
557.42
522.35
513.51
504.73
N
N
N
N
N
N
S
H
23f
IR

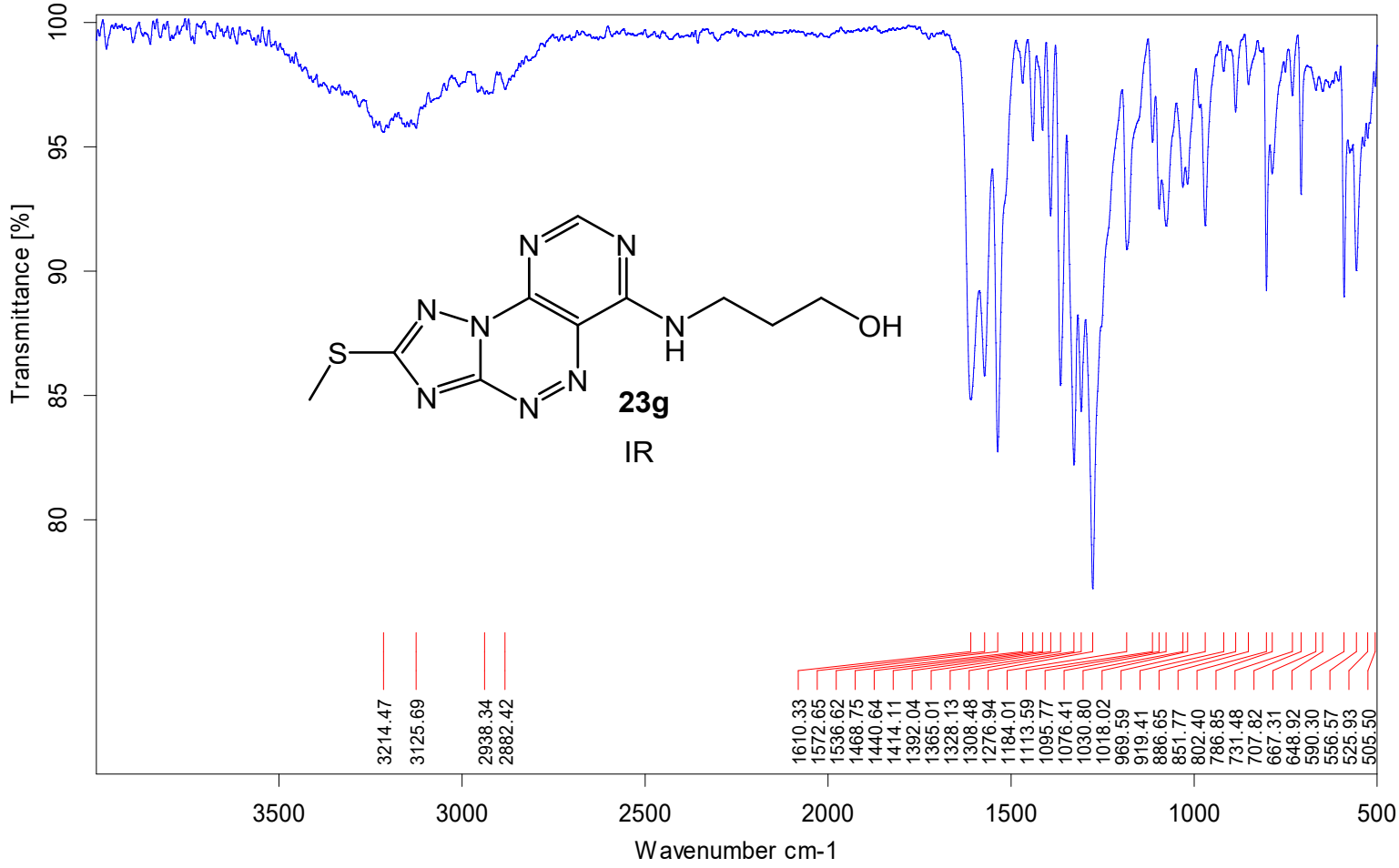
Line#:1 R.Time:1.492(Scan#:558)
MassPeaks:135
RawMode:Single 1.492(558) BasePeak:290(3501298)
Фон.реж.:2.555(983) Group 1 - Event 1



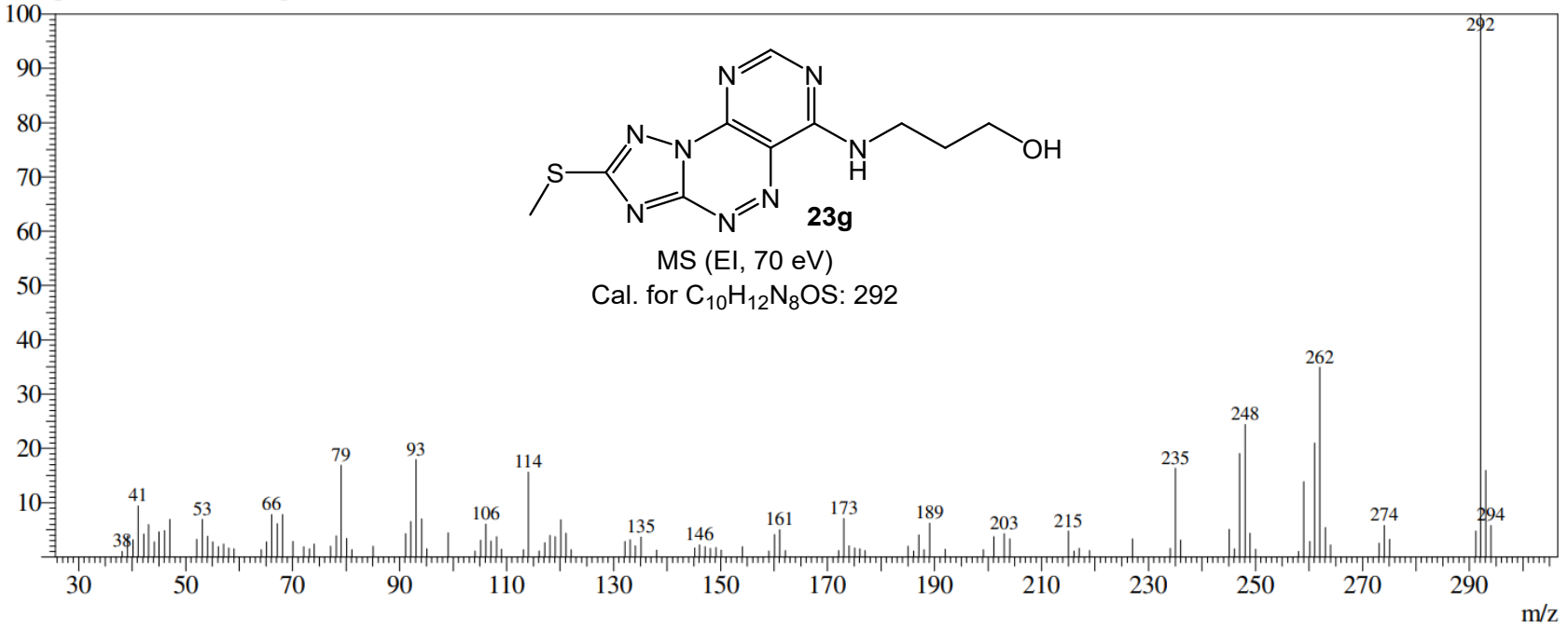
3-((2-(Methylthio)pyrimido[4,5-*e*][1,2,4]triazolo[5,1-*c*][1,2,4]triazin-6-yl)amino)propan-1-ol (23g)



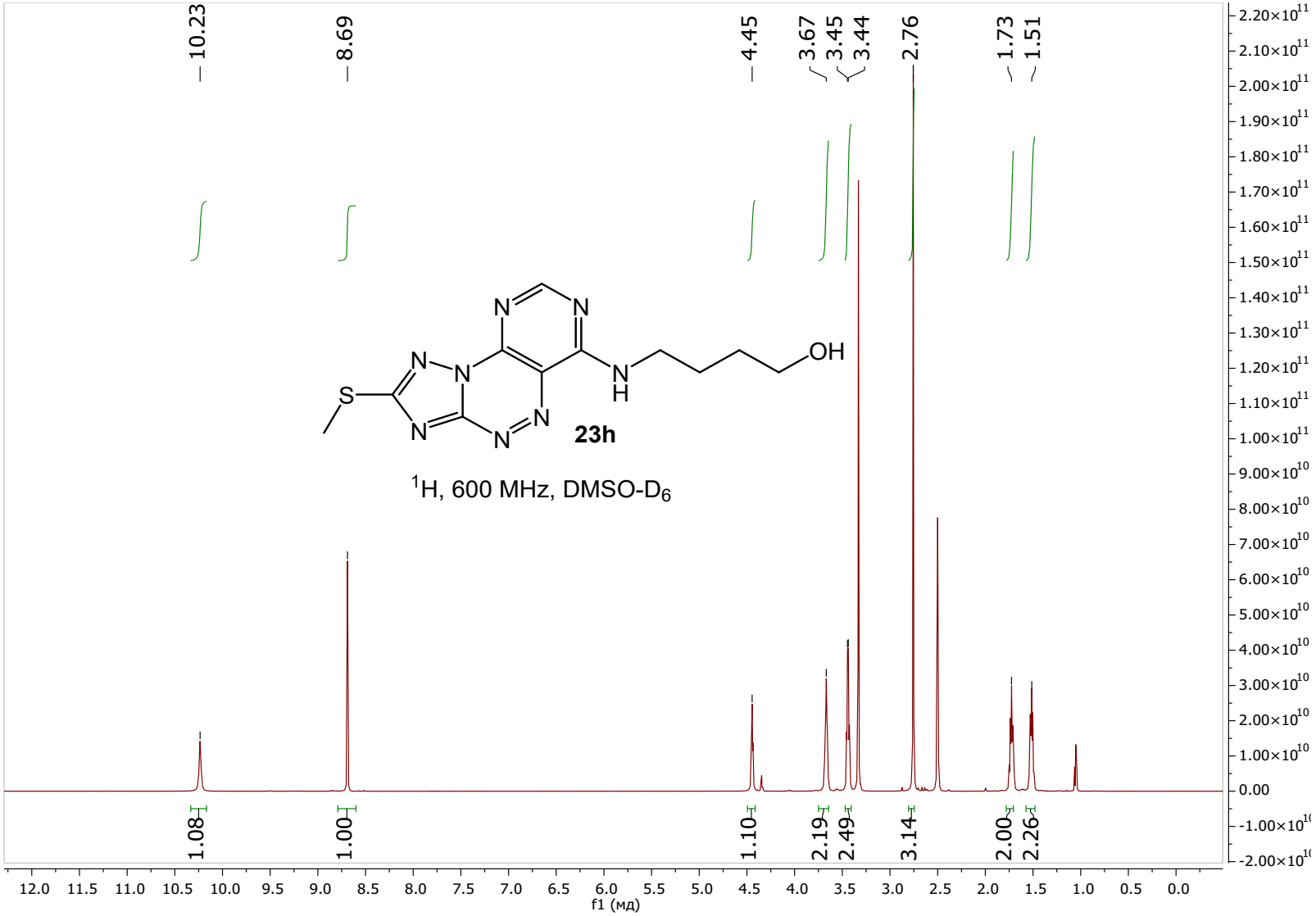

168.90
162.86
158.95
157.73
139.81
123.38
58.64
38.71
31.54
13.58
N
N
N
N
N
N
S
N
H
OH
23g
^{13}C, 150 MHz, DMSO-D$_6$
S130
f1 (мд)

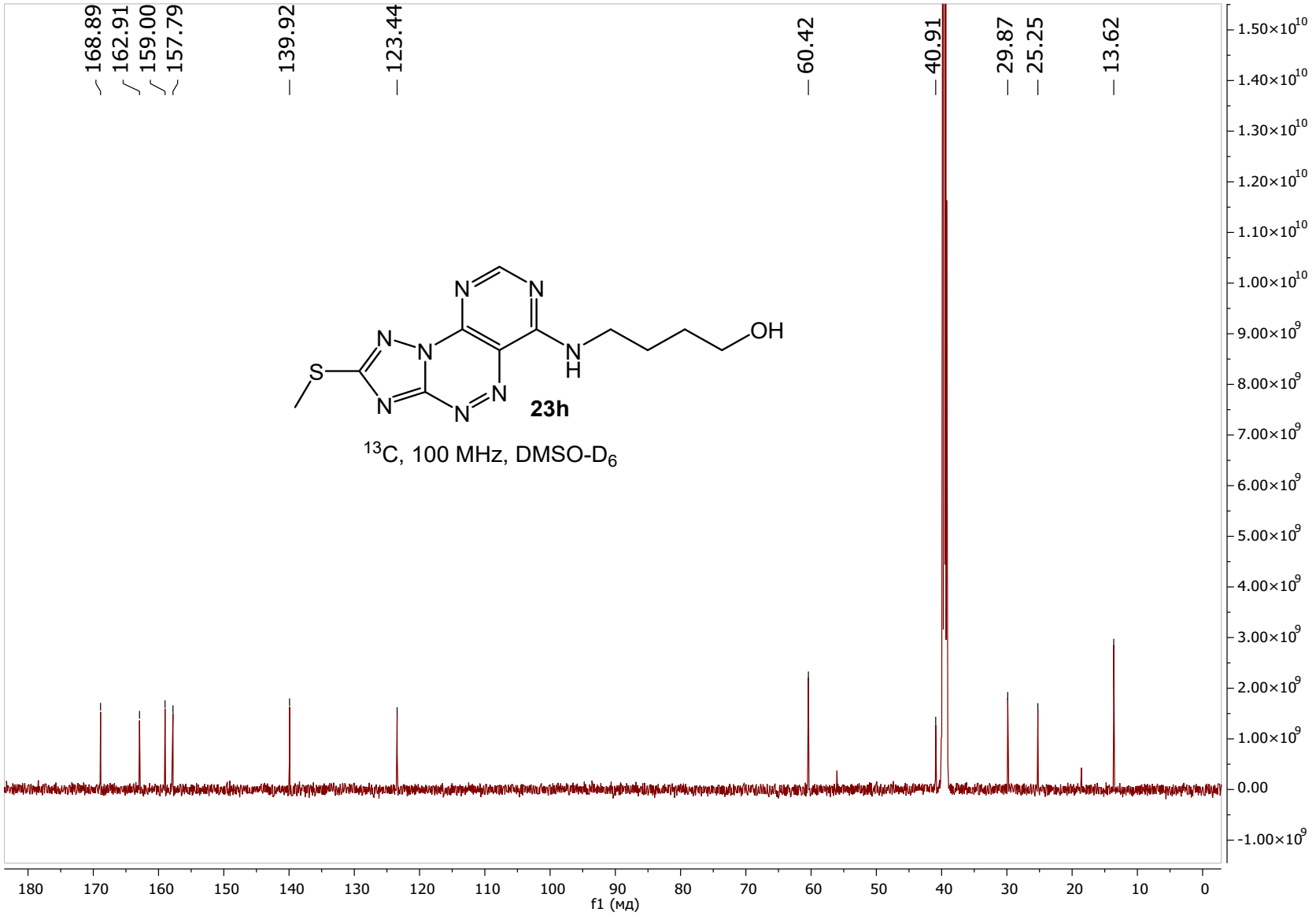

Transmittance [%]
100
95
90
85
80
3500
3000
2500
2000
1500
1000
500
Wavenumber cm-1
23g
IR
3214.47
3125.69
2938.34
2882.42
1610.33
1572.65
1536.62
1468.75
1440.64
1414.11
1392.04
1365.01
1328.13
1308.48
1276.94
1184.01
1113.59
1095.77
1076.41
1030.80
1018.02
969.59
919.41
886.65
851.77
802.40
786.85
731.48
707.82
667.31
648.92
590.30
556.57
525.93
505.50

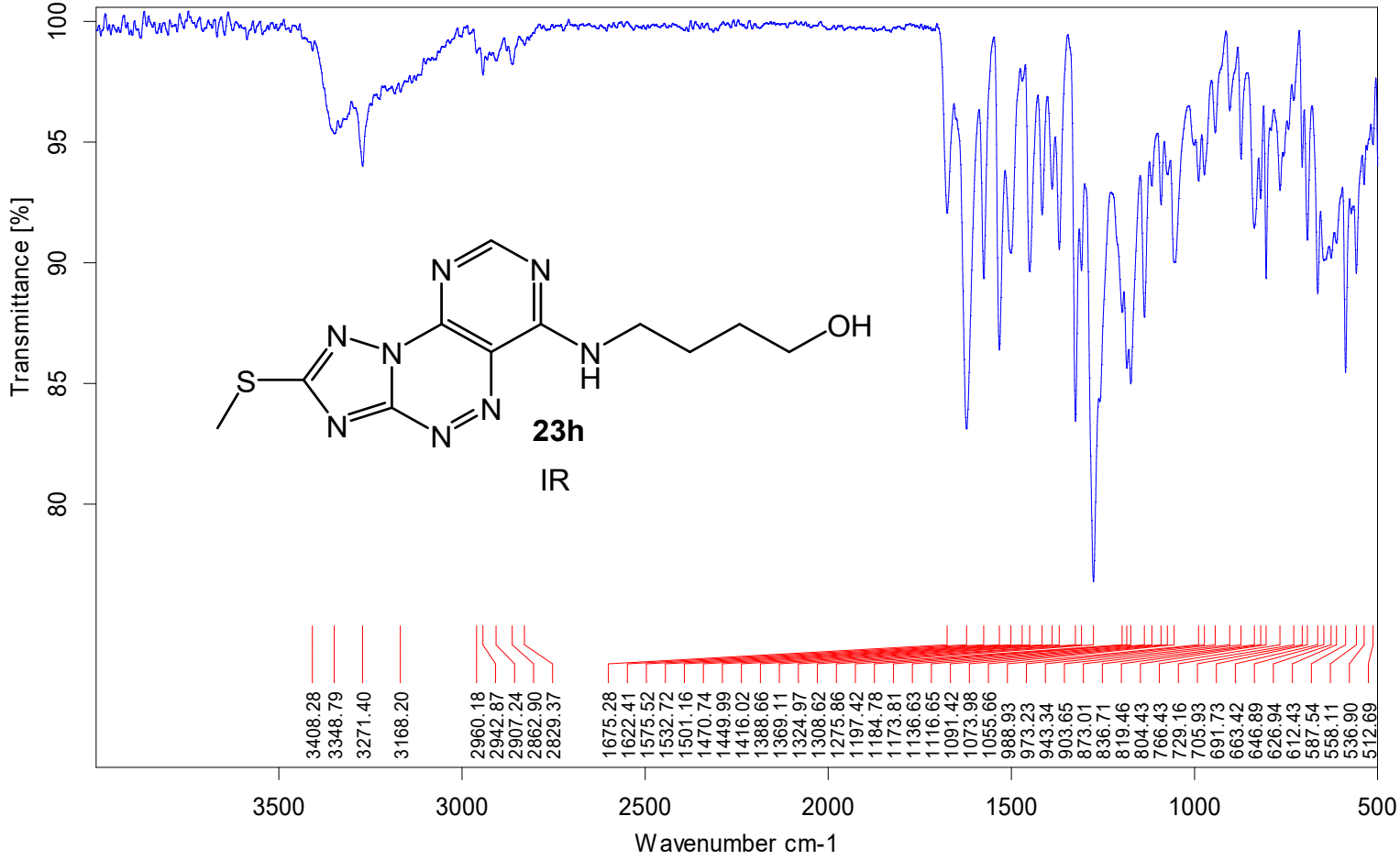
Line#:1 R.Time:2.632(Scan#:1014)
MassPeaks:114
RawMode:Single 2.632(1014) BasePeak:292(4061466)
Фон.реж.:2.380(913) Group 1 - Event 1



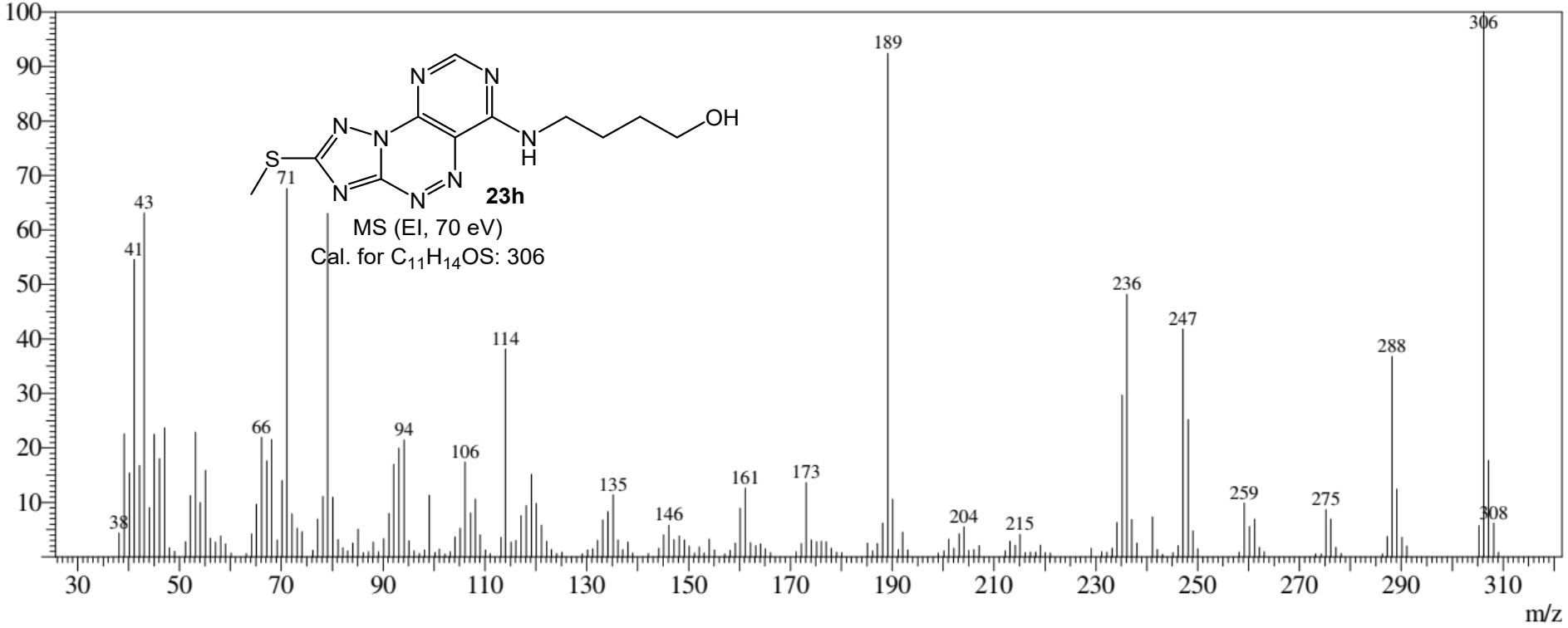
4-((2-(Methylthio)pyrimido[4,5-*e*][1,2,4]triazolo[5,1-*c*][1,2,4]triazin-6-yl)amino)butan-1-ol (23h)



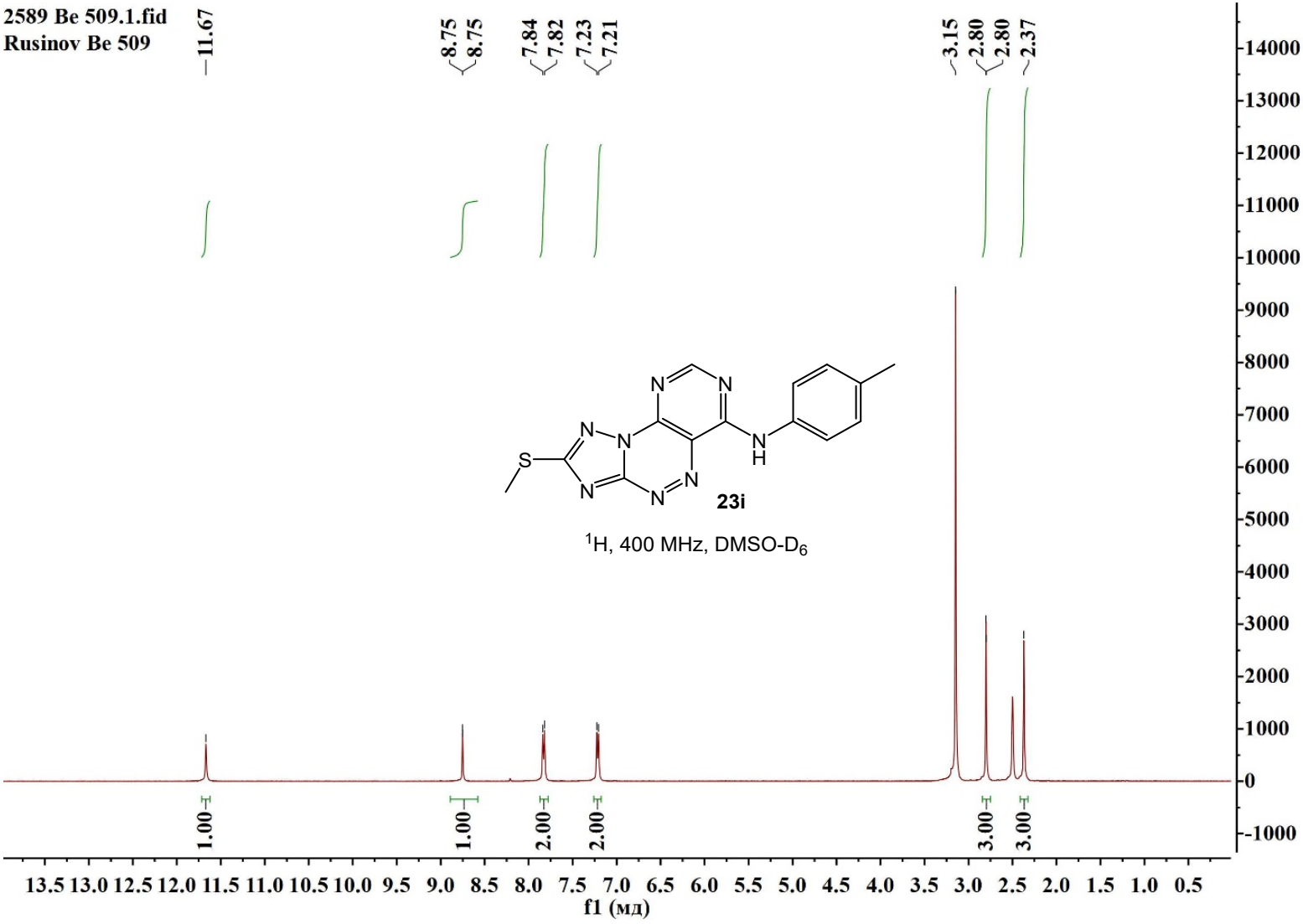

168.89
162.91
159.00
157.79
139.92
123.44
60.42
40.91
29.87
25.25
13.62
N
N
N
N
N
S
N
H
OH
23h
^{13}C, 100 MHz, DMSO-D$_6$
1.50×10^{10}
1.40×10^{10}
1.30×10^{10}
1.20×10^{10}
1.10×10^{10}
1.00×10^{10}
9.00×10^{9}
8.00×10^{9}
7.00×10^{9}
6.00×10^{9}
5.00×10^{9}
4.00×10^{9}
3.00×10^{9}
2.00×10^{9}
1.00×10^{9}
0.00
-1.00×10^{9}
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (мд)

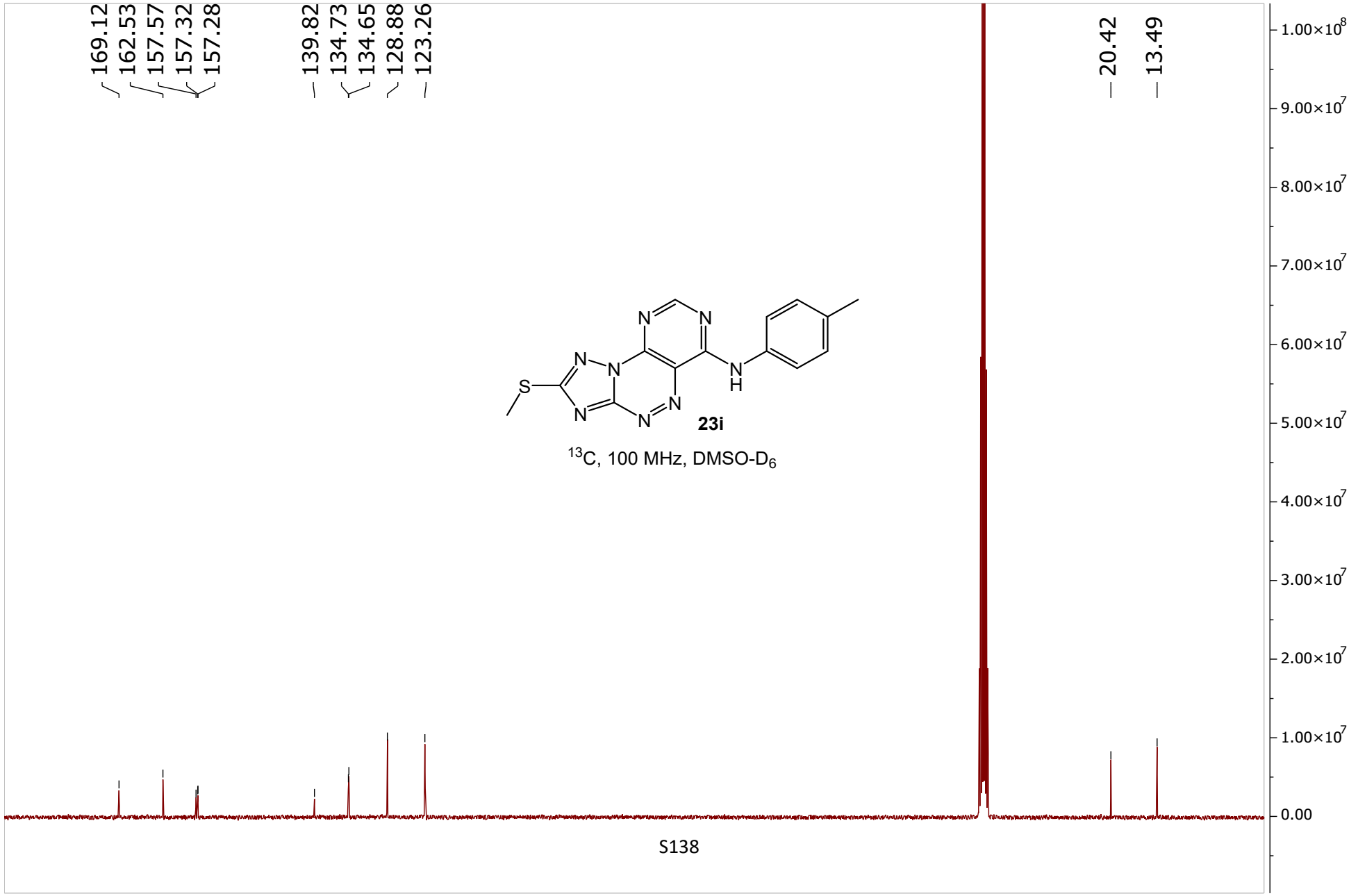

Transmittance [%]
100
95
90
85
80
3500
3000
2500
2000
1500
1000
500
Wavenumber cm-1
N
N
N
N
N
N
S
N
H
OH
23h
IR
3408.28
3348.79
3271.40
3168.20
2960.18
2942.87
2907.24
2862.90
2829.37
1675.28
1622.41
1575.52
1532.72
1501.16
1470.74
1449.99
1416.02
1388.66
1369.11
1324.97
1308.62
1275.86
1197.42
1184.78
1173.81
1136.63
1116.65
1091.42
1073.98
1055.66
988.93
973.23
943.34
903.65
873.01
836.71
819.46
804.43
766.43
729.16
705.93
691.73
663.42
646.89
626.94
612.43
587.54
558.11
536.90
512.69

Line#:1 R.Time:2.368(Scan#:908)
MassPeaks:196
RawMode:Single 2.368(908) BasePeak:306(1534400)
Фон.реж.:2.835(1095) Group 1 - Event 1



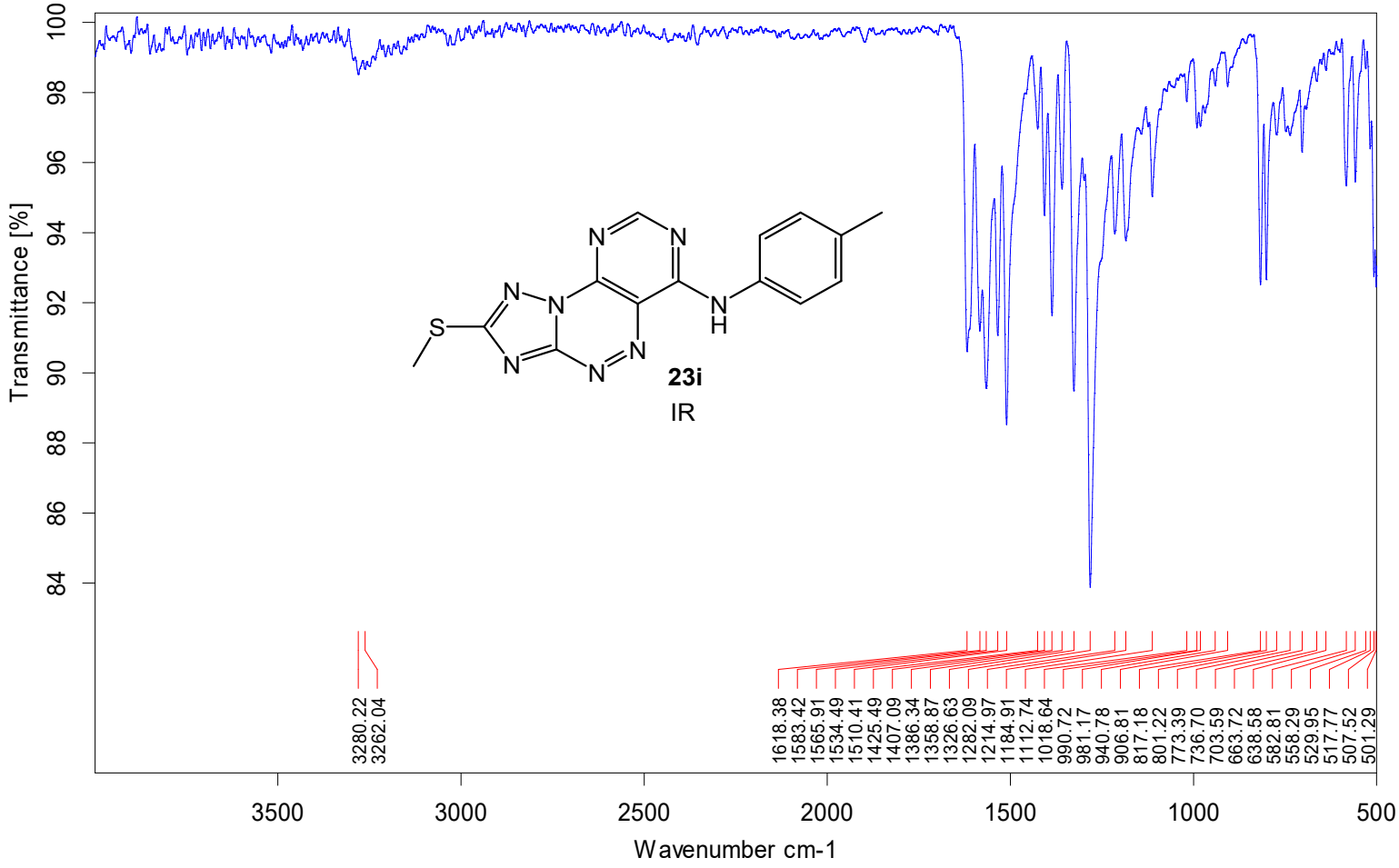
2-(Methylthio)-*N*-(*p*-tolyl)pyrimido[4,5-*e*][1,2,4]triazolo[5,1-*c*][1,2,4]triazin-6-amine (23i)





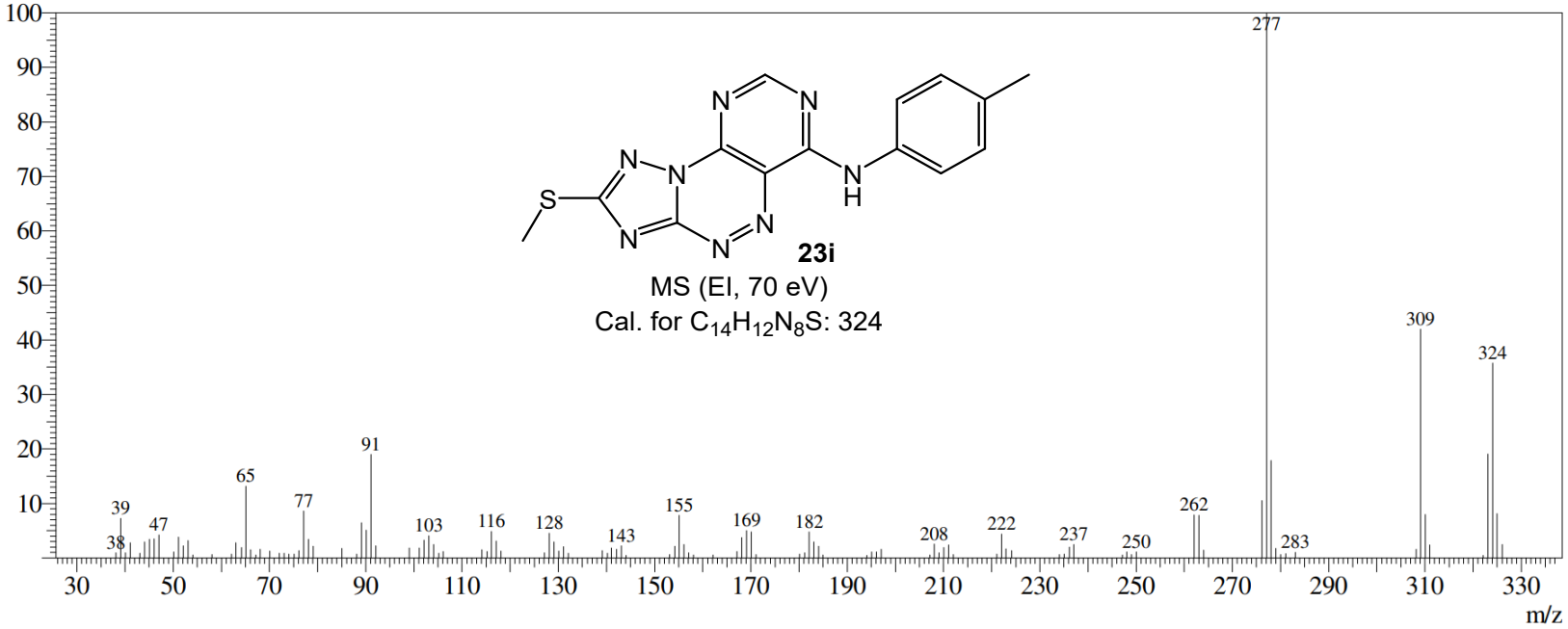
23i

^{13}C, 100 MHz, DMSO-D_6

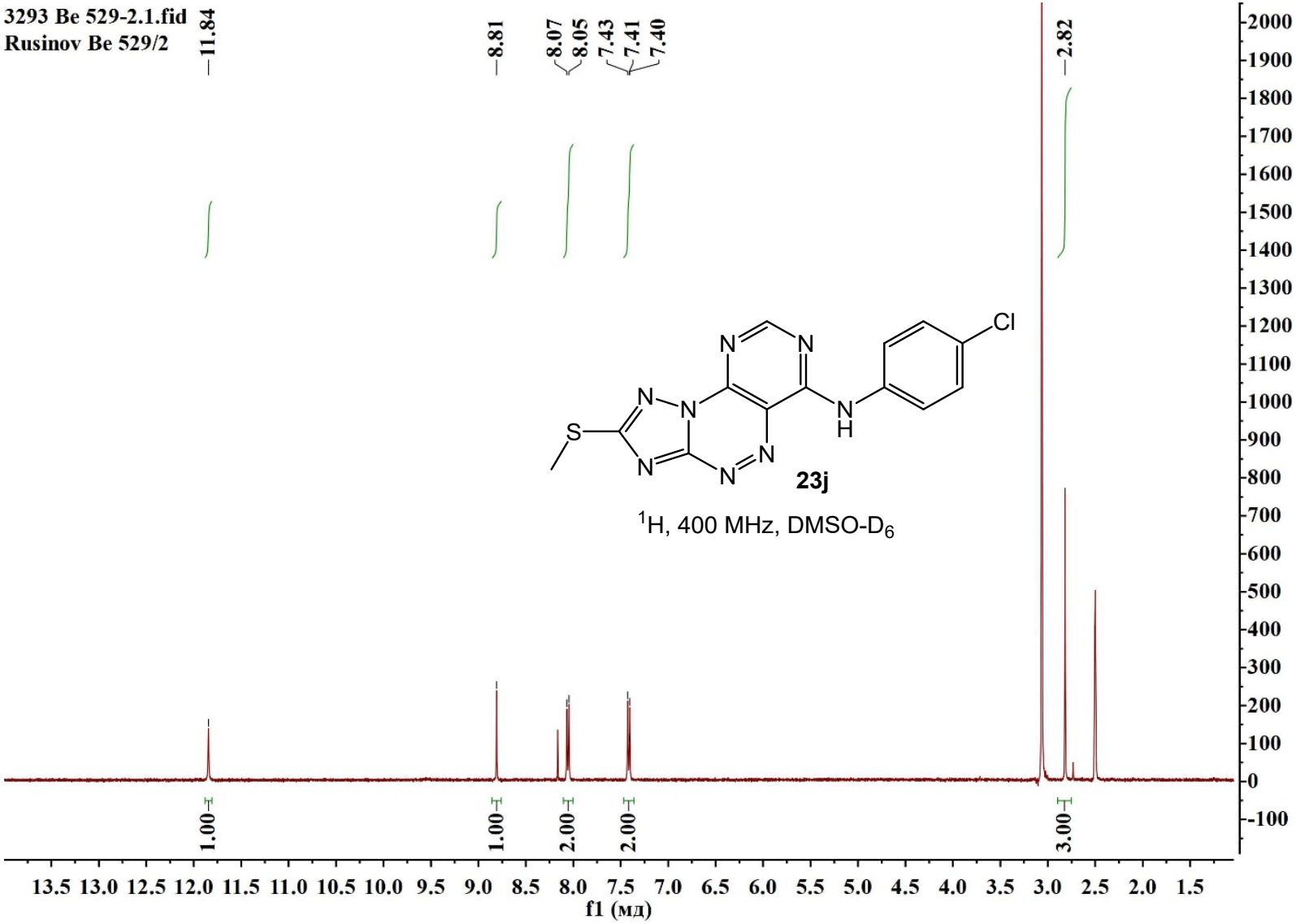

Transmittance [%]
100
98
96
94
92
90
88
86
84
3500
3000
2500
2000
1500
1000
500
Wavenumber cm-1
3280.22
3262.04
1618.38
1583.42
1565.91
1534.49
1510.41
1425.49
1407.09
1386.34
1358.87
1326.63
1282.09
1214.97
1184.91
1112.74
1018.64
990.72
981.17
940.78
906.81
817.18
801.22
773.39
736.70
703.59
663.72
638.58
582.81
558.29
529.95
517.77
507.52
501.29
N
N
N
N
N
N
S
H
23i
IR

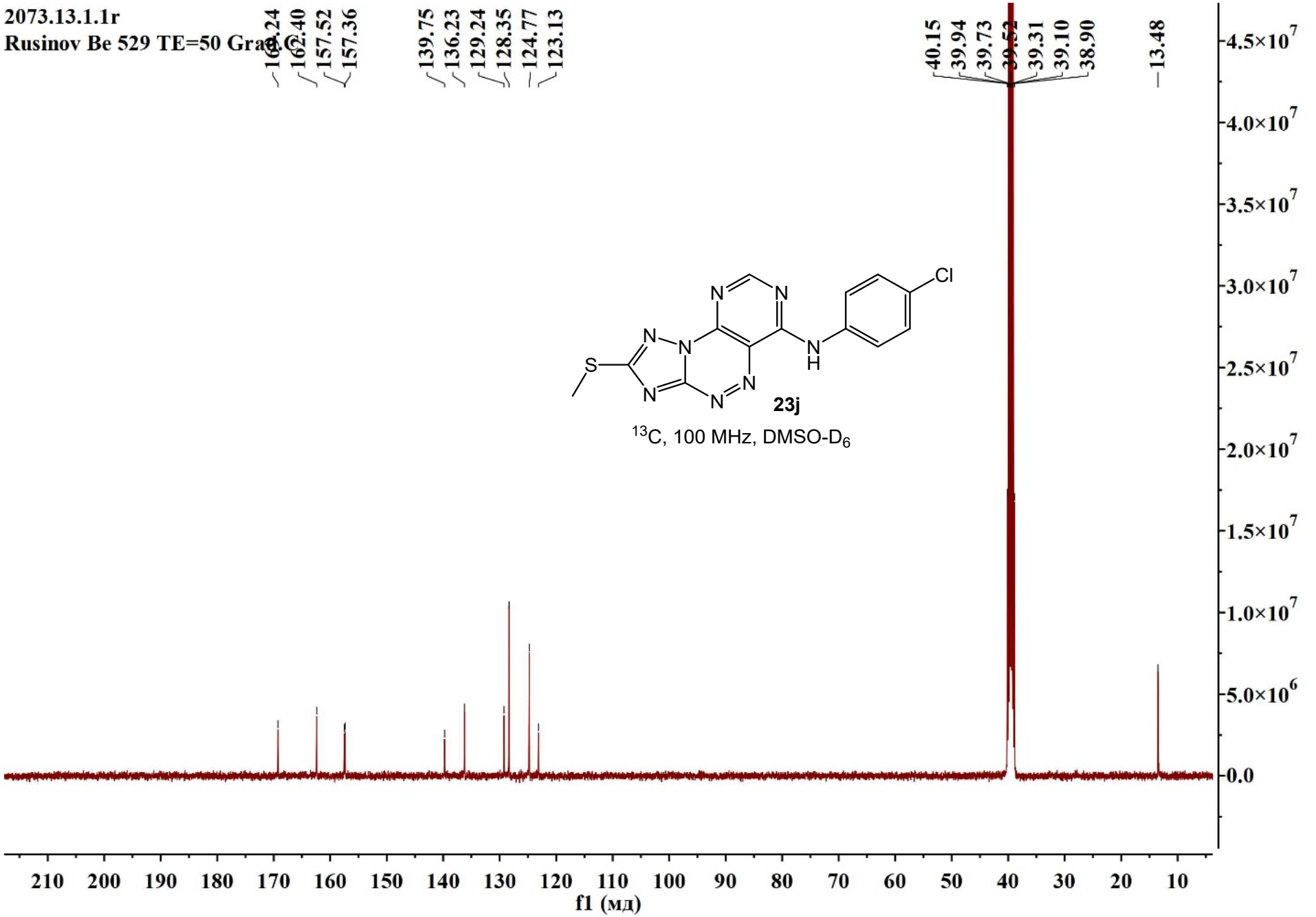
Page 1/1

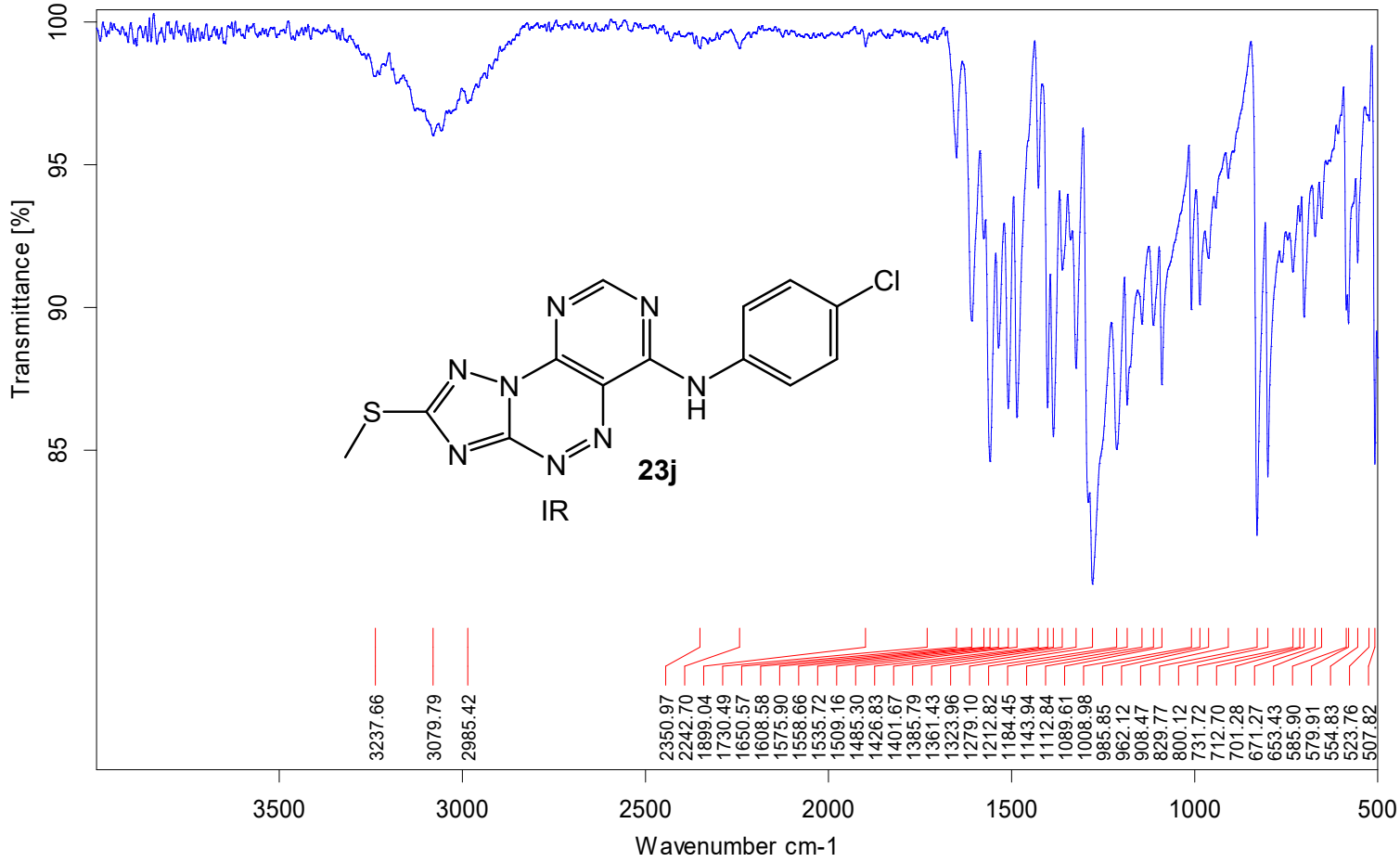
Line#:1 R.Time:2.403(Scan#:922)
MassPeaks:120
RawMode:Single 2.402(922) BasePeak:277(3207225)
Фон.реж.:1.357(504) Group 1 - Event 1



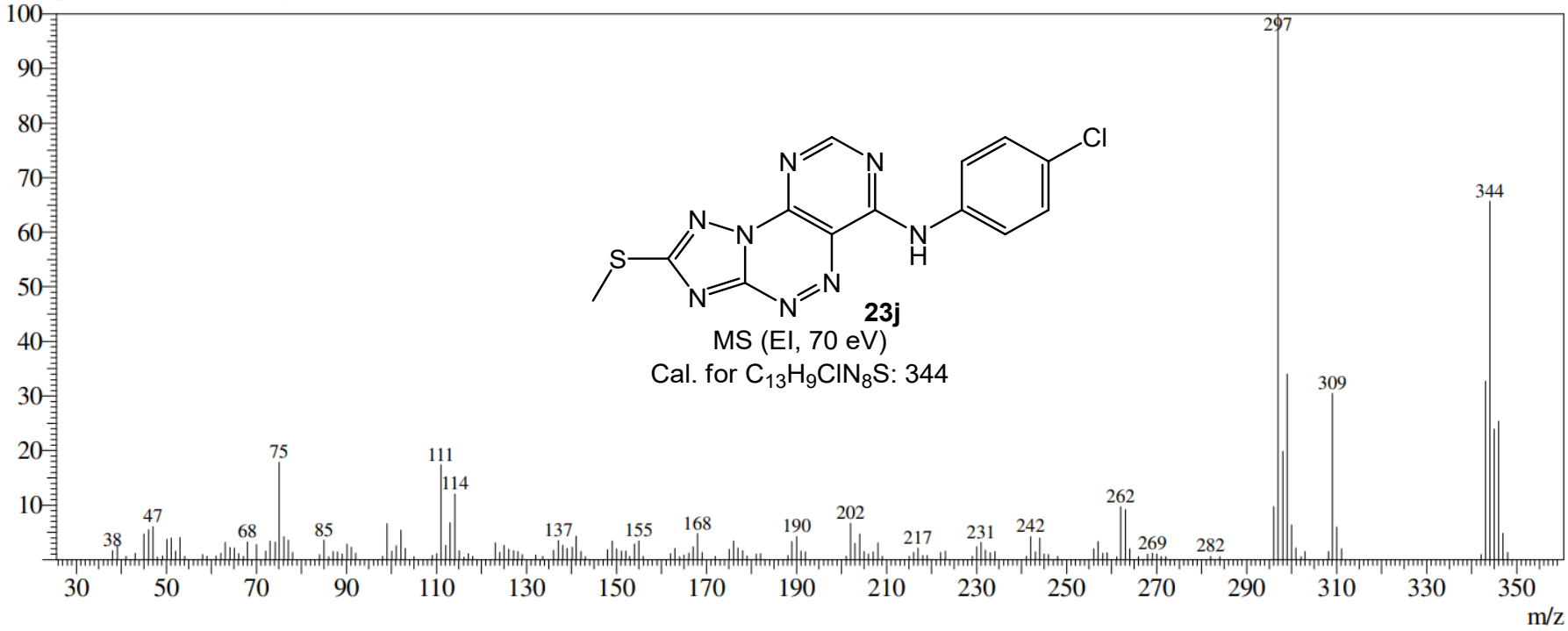
_N_-(4-Chlorophenyl)-2-(methylthio)pyrimido[4,5-*e*][1,2,4]triazolo[5,1-*c*][1,2,4]triazin-6-amine (23j)




2073.13.1.1r
Rusinov Be 529 TE=50 Grad.C
169.24
162.40
157.52
157.36
139.75
136.23
129.24
128.35
124.77
123.13
40.15
39.94
39.73
39.52
39.31
39.10
38.90
13.48
Cl
N
N
N
N
N
N
N
S
H
23j
13C, 100 MHz, DMSO-D6
4.5×10^7
4.0×10^7
3.5×10^7
3.0×10^7
2.5×10^7
2.0×10^7
1.5×10^7
1.0×10^7
5.0×10^6
0.0
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (мд)


Transmittance [%]
100
95
90
85
3500
3000
2500
2000
1500
1000
500
Wavenumber cm-1
Cl
N
N
N
N
N
N
S
N
H
23j
IR
3237.66
3079.79
2985.42
2350.97
2242.70
1899.04
1730.49
1650.57
1608.58
1575.90
1558.66
1535.72
1509.16
1485.30
1426.83
1401.67
1385.79
1361.43
1323.96
1279.10
1212.82
1184.45
1143.94
1112.84
1089.61
1008.98
985.85
962.12
908.47
829.77
800.12
731.72
712.70
701.28
671.27
653.43
585.90
579.91
554.83
523.76
507.82

Line#:1 R.Time:2.830(Scan#:1093)
MassPeaks:169
RawMode:Single 2.830(1093) BasePeak:297(6882499)
Фон.реж.:1.490(557) Group 1 - Event 1

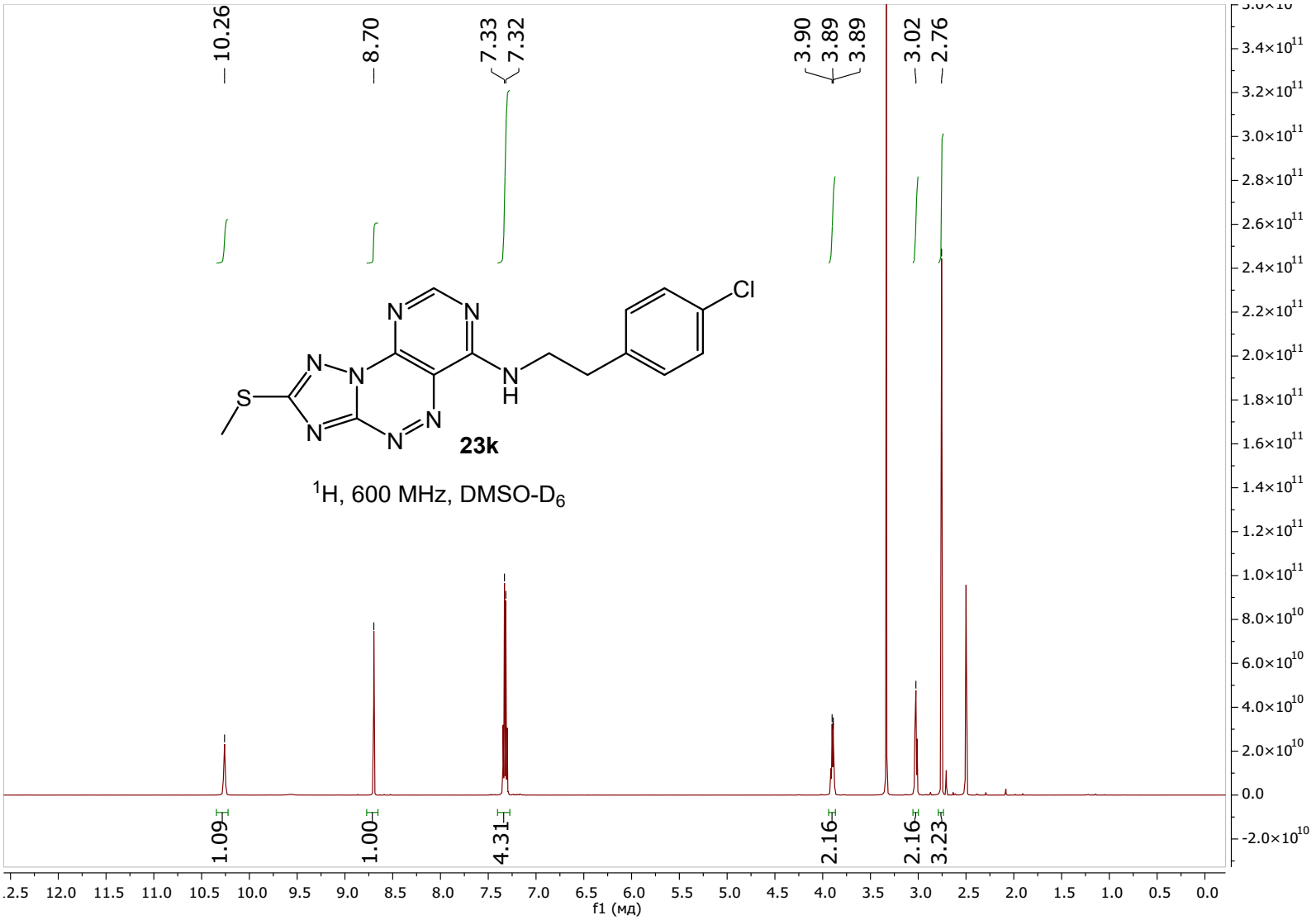


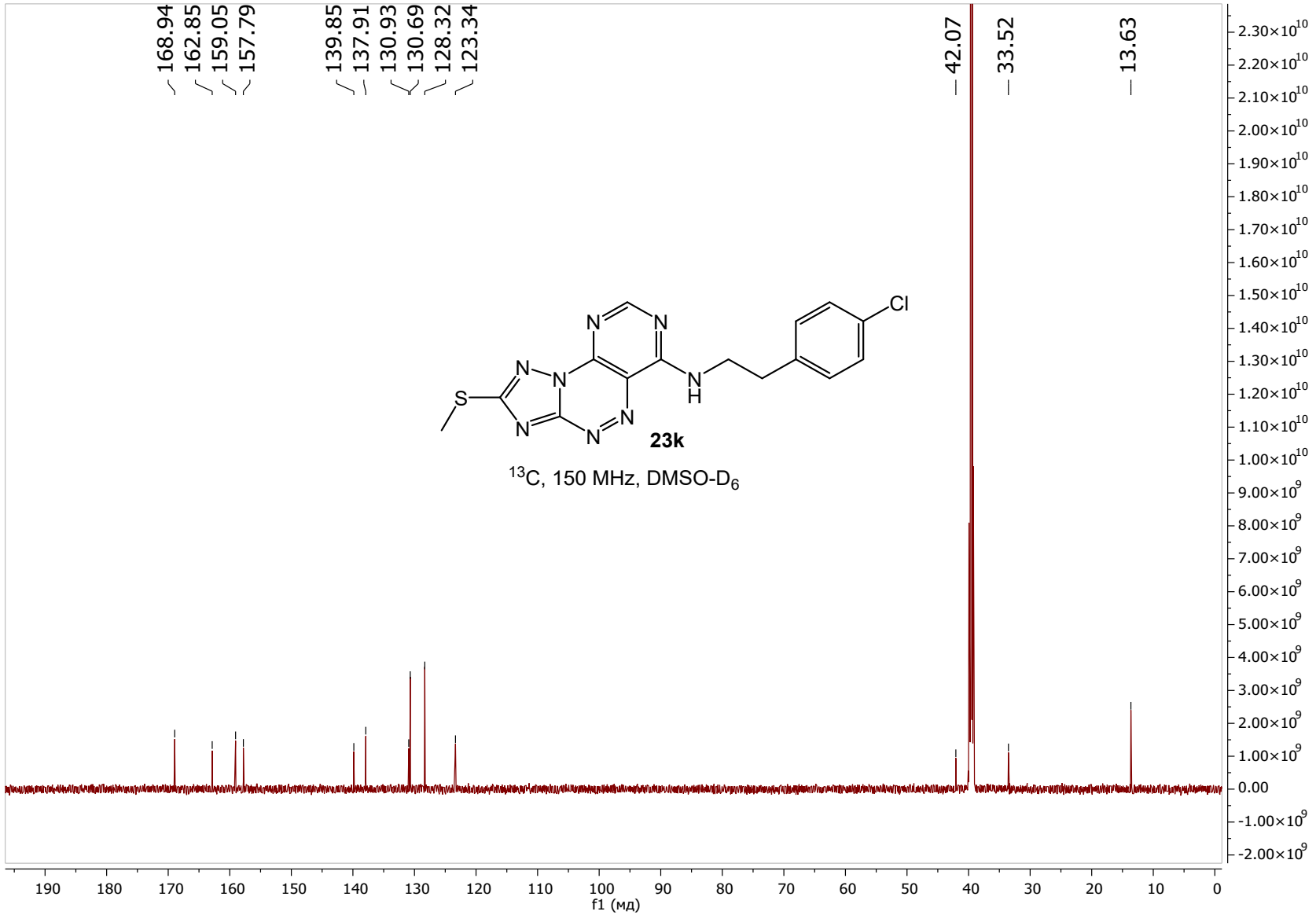
23j

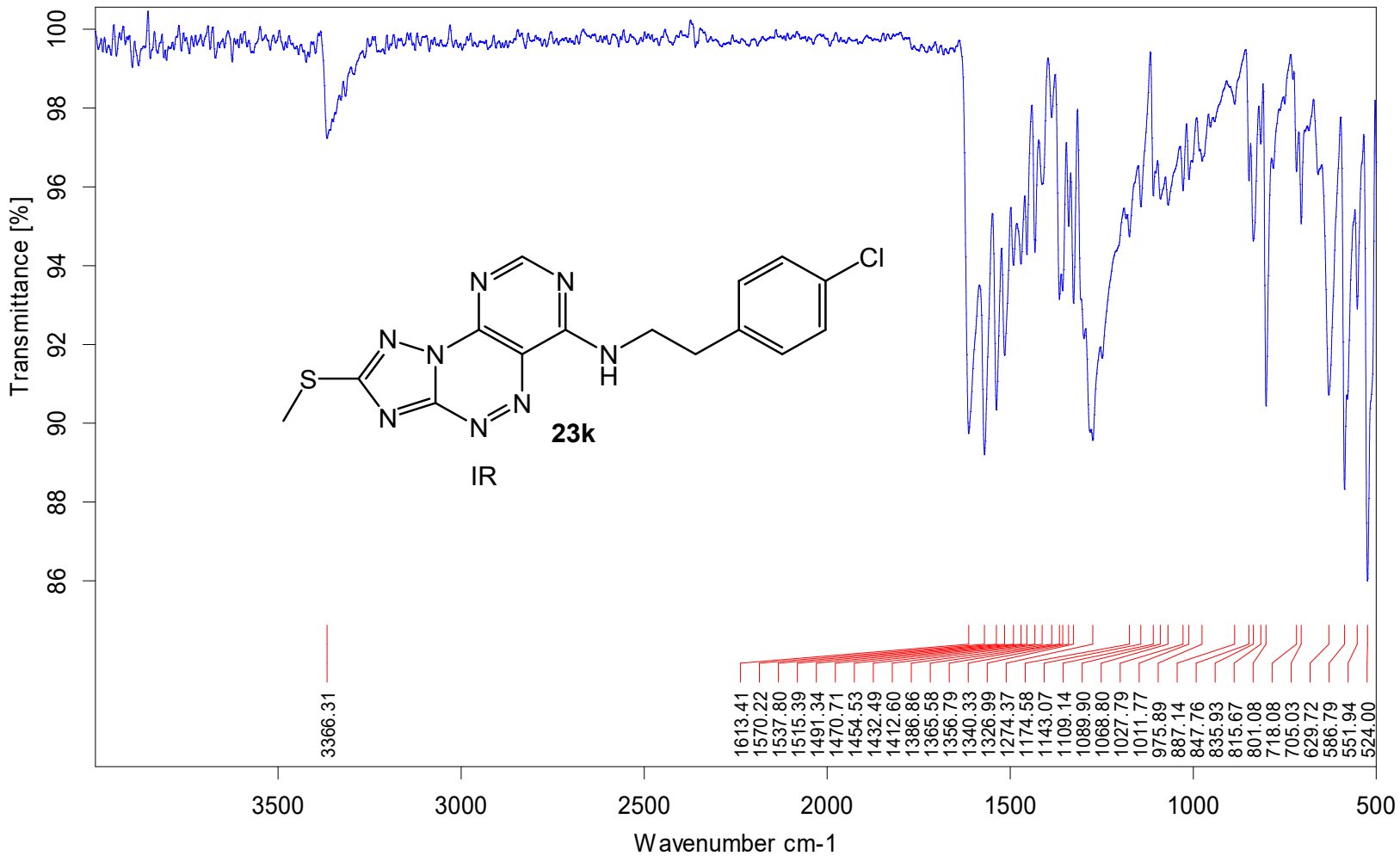
MS (EI, 70 eV)

Cal. for $C_{13}H_9ClN_8S$: 344

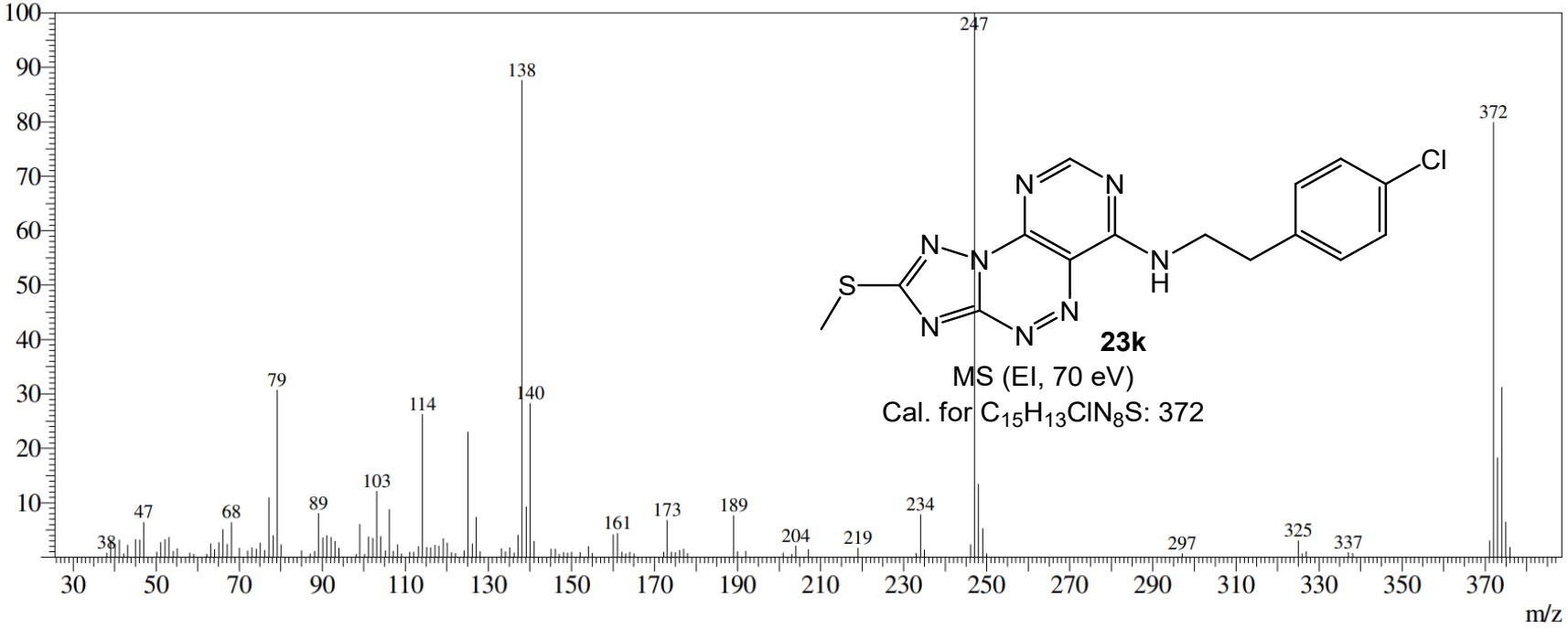
_N_-(4-Chlorophenethyl)-2-(methylthio)pyrimido[4,5-_e_][1,2,4]triazolo[5,1-_c_][1,2,4]triazin-6-amine (23k)



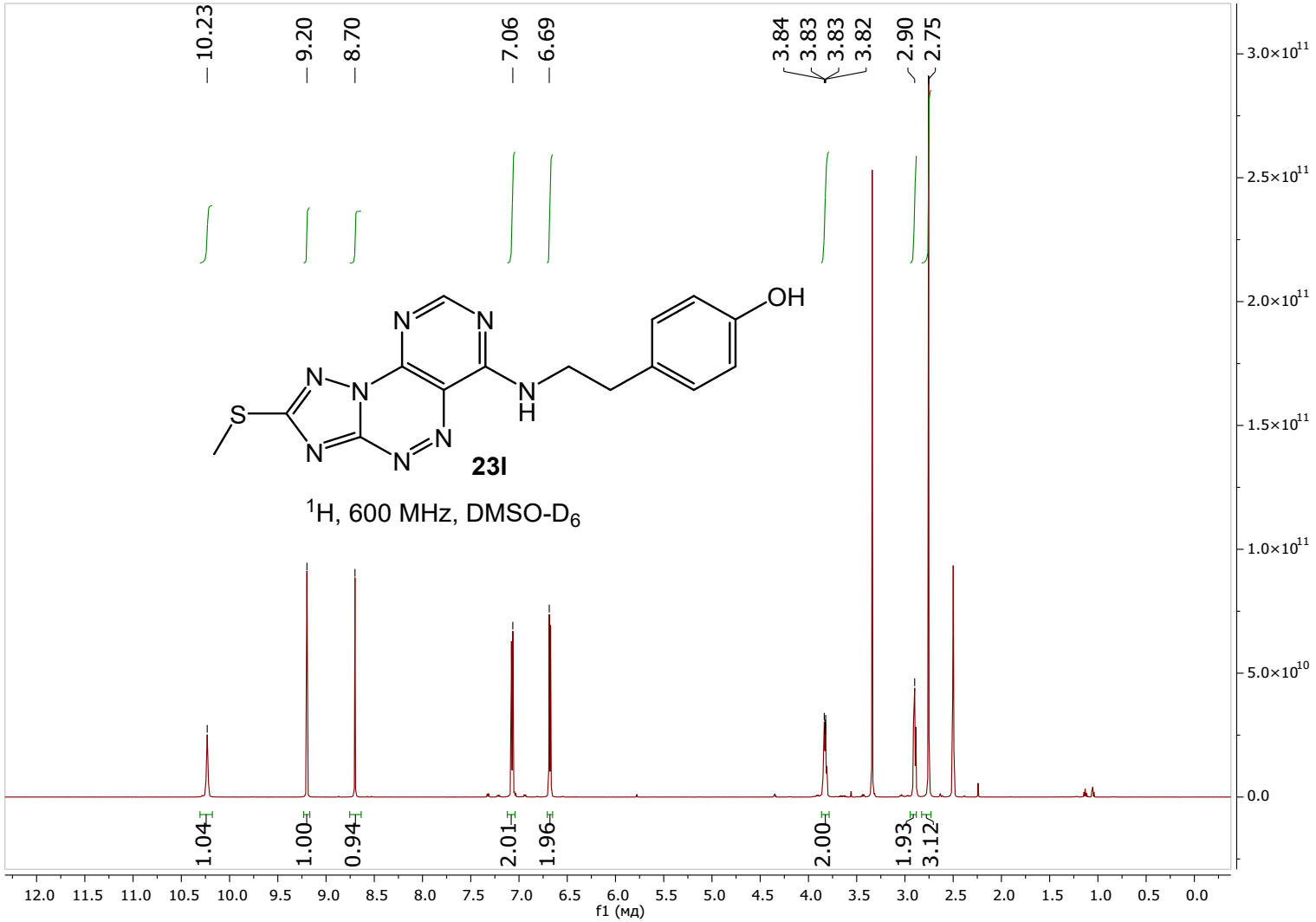

168.94
162.85
159.05
157.79
139.85
137.91
130.93
130.69
128.32
123.34
42.07
33.52
13.63
Cl
N
N
N
N
N
N
S
N
H
23k
^{13}C, 150 MHz, DMSO-D$_6$
f1 (мд)

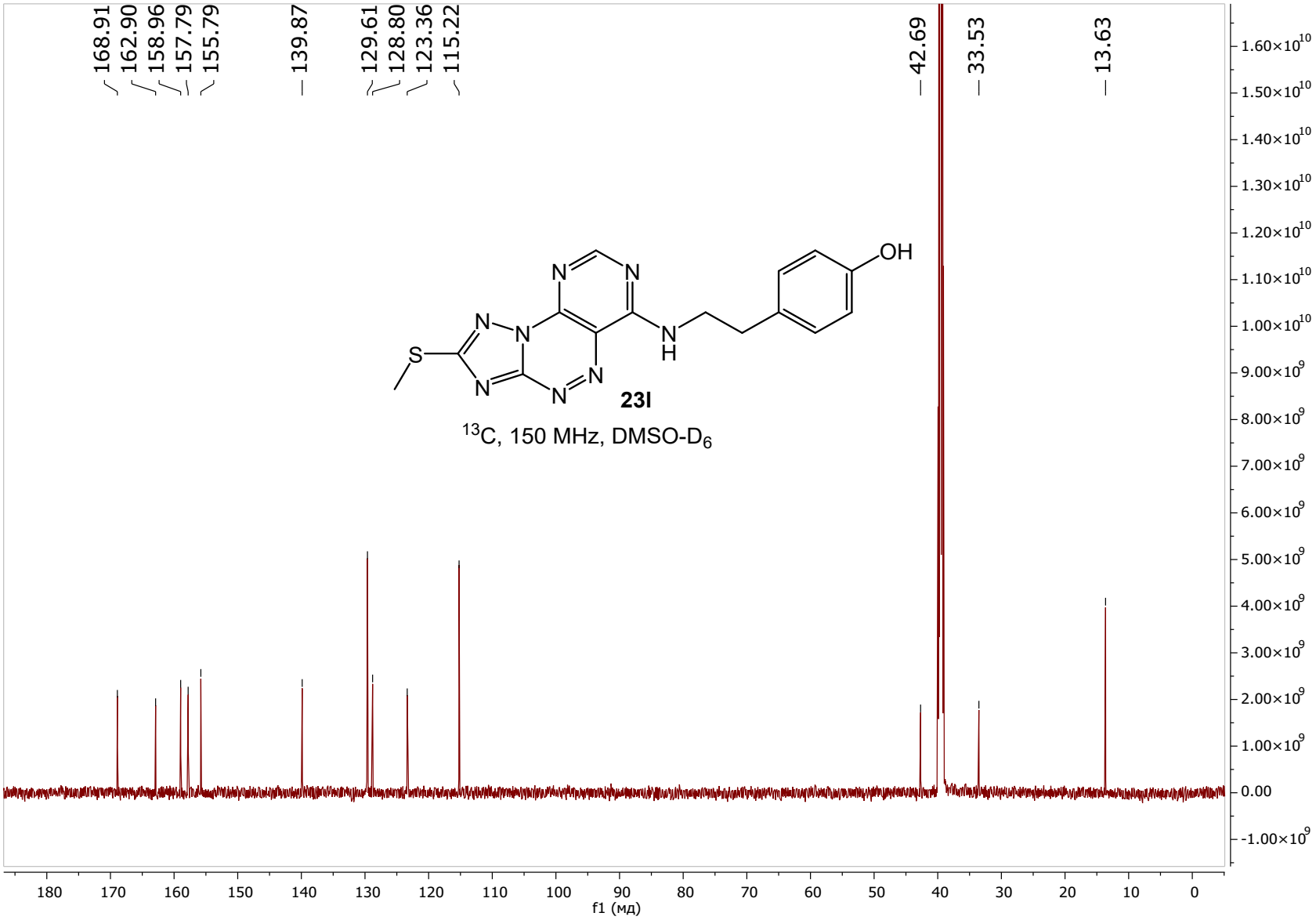

Transmittance [%]
100
98
96
94
92
90
88
86
3500
3000
2500
2000
1500
1000
500
Wavenumber cm-1
Cl
N
N
N
N
N
N
S
N
H
23k
IR
3366.31
1613.41
1570.22
1537.80
1515.39
1491.34
1470.71
1454.53
1432.49
1412.60
1386.86
1365.58
1356.79
1340.33
1326.99
1274.37
1174.58
1143.07
1109.14
1089.90
1068.80
1027.79
1011.77
975.89
887.14
847.76
835.93
815.67
801.08
718.08
705.03
629.72
586.79
551.94
524.00

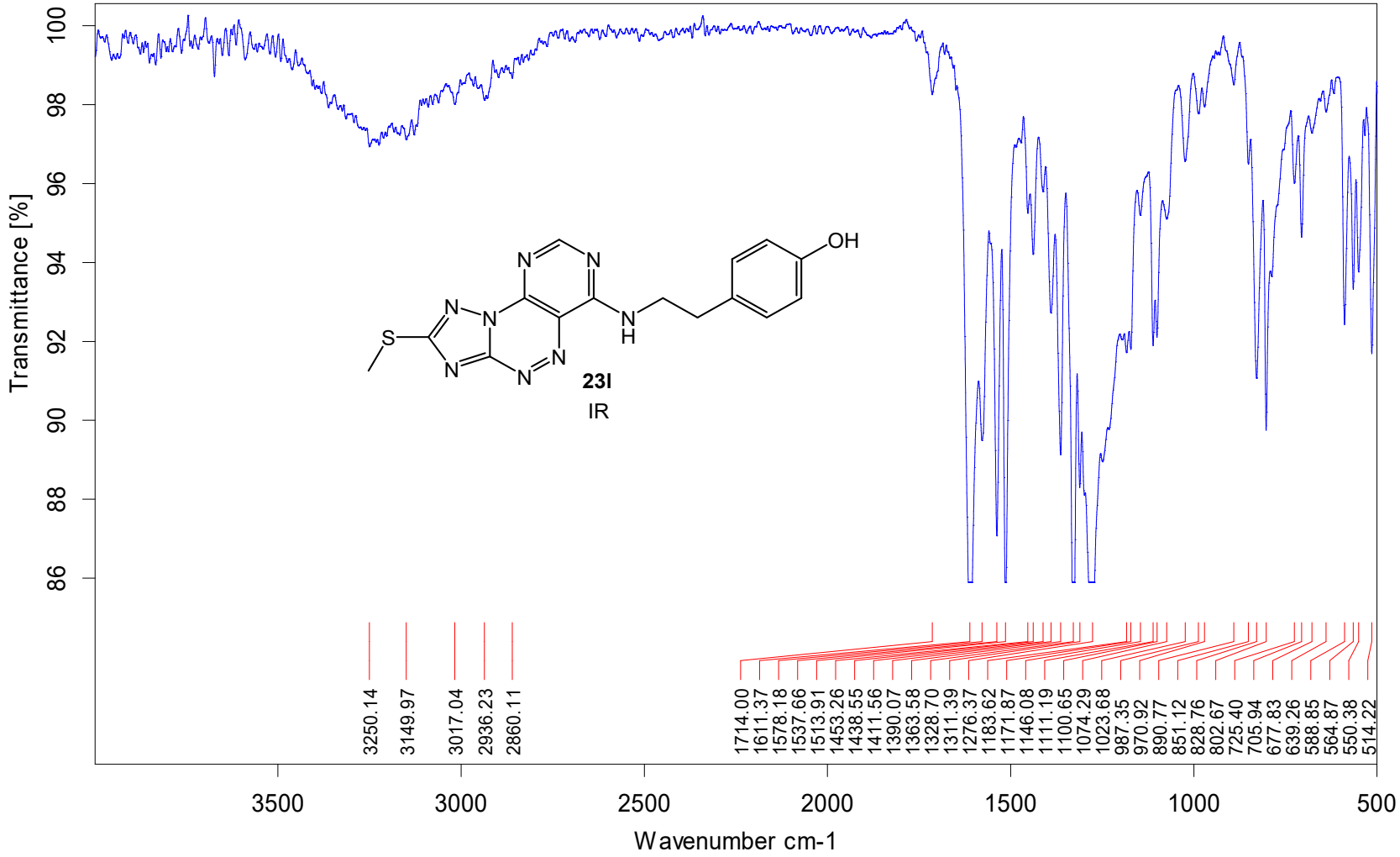
Line#:1 R.Time:3.018(Scan#:1168)
MassPeaks:131
RawMode:Single 3.018(1168) BasePeak:247(7281719)
Фон.реж.:1.130(413) Group 1 - Event 1



4-(2-((2-(Methylthio)pyrimido[4,5-*e*][1,2,4]triazolo[5,1-*c*][1,2,4]triazin-6-yl)amino)ethyl)phenol (23l)

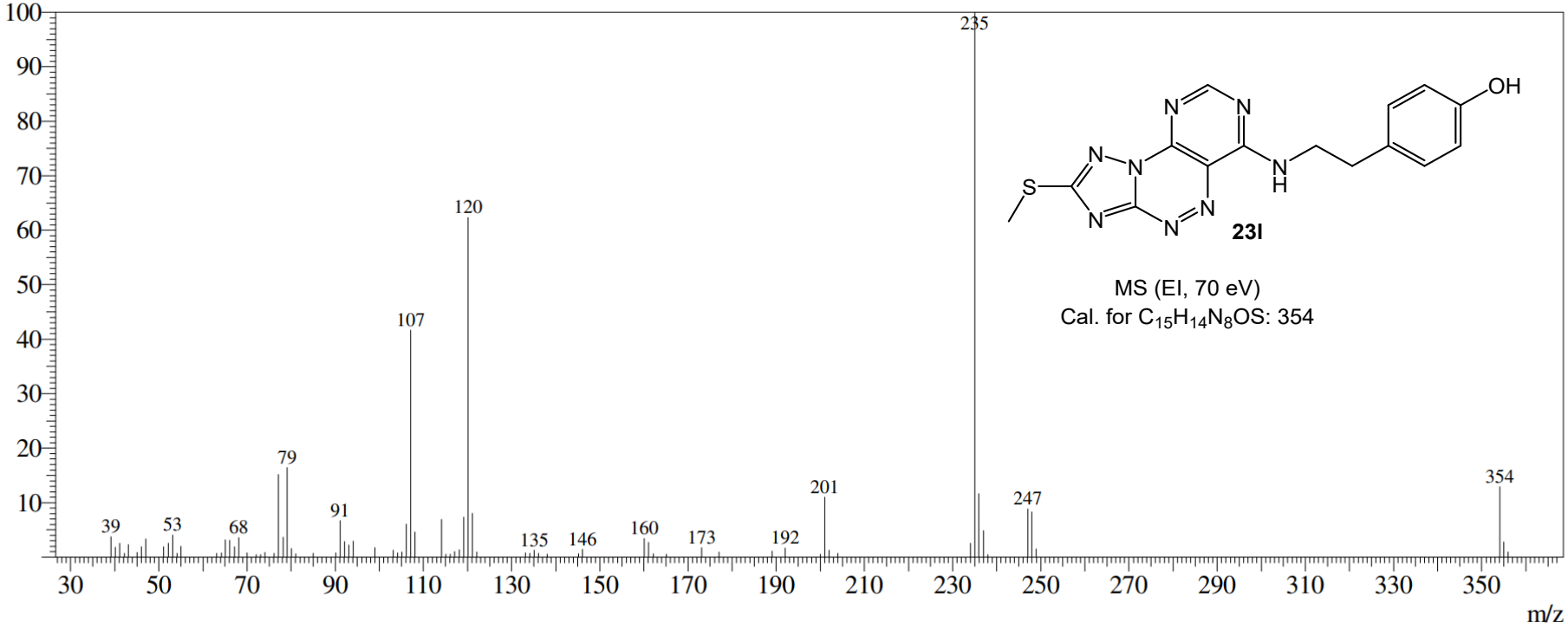



168.91
162.90
158.96
157.79
155.79
139.87
129.61
128.80
123.36
115.22
42.69
33.53
13.63
OH
N
N
N
N
N
N
N
S
H
23l
13C, 150 MHz, DMSO-D6
1.60×10^10
1.50×10^10
1.40×10^10
1.30×10^10
1.20×10^10
1.10×10^10
1.00×10^10
9.00×10^9
8.00×10^9
7.00×10^9
6.00×10^9
5.00×10^9
4.00×10^9
3.00×10^9
2.00×10^9
1.00×10^9
0.00
-1.00×10^9
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (мд)

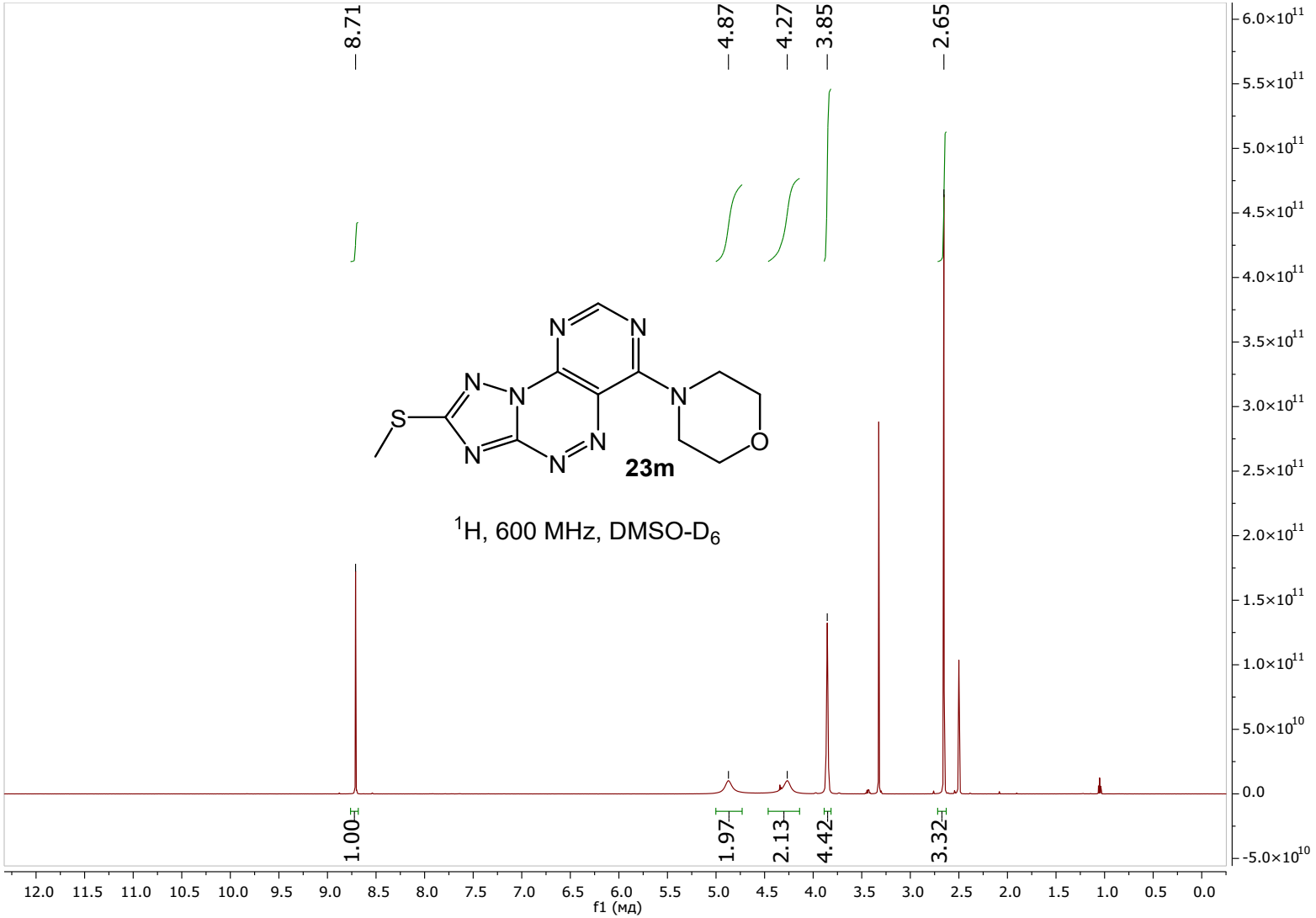

Transmittance [%]
100
98
96
94
92
90
88
86
3500
3000
2500
2000
1500
1000
500
Wavenumber cm-1
OH
N
N
N
N
N
N
S
N
H
23l
IR
3250.14
3149.97
3017.04
2936.23
2860.11
1714.00
1611.37
1578.18
1537.66
1513.91
1453.26
1438.55
1411.56
1390.07
1363.58
1328.70
1311.39
1276.37
1183.62
1171.87
1146.08
1111.19
1100.65
1074.29
1023.68
987.35
970.92
890.77
851.12
828.76
802.67
725.40
705.94
677.83
639.26
588.85
564.87
550.38
514.22

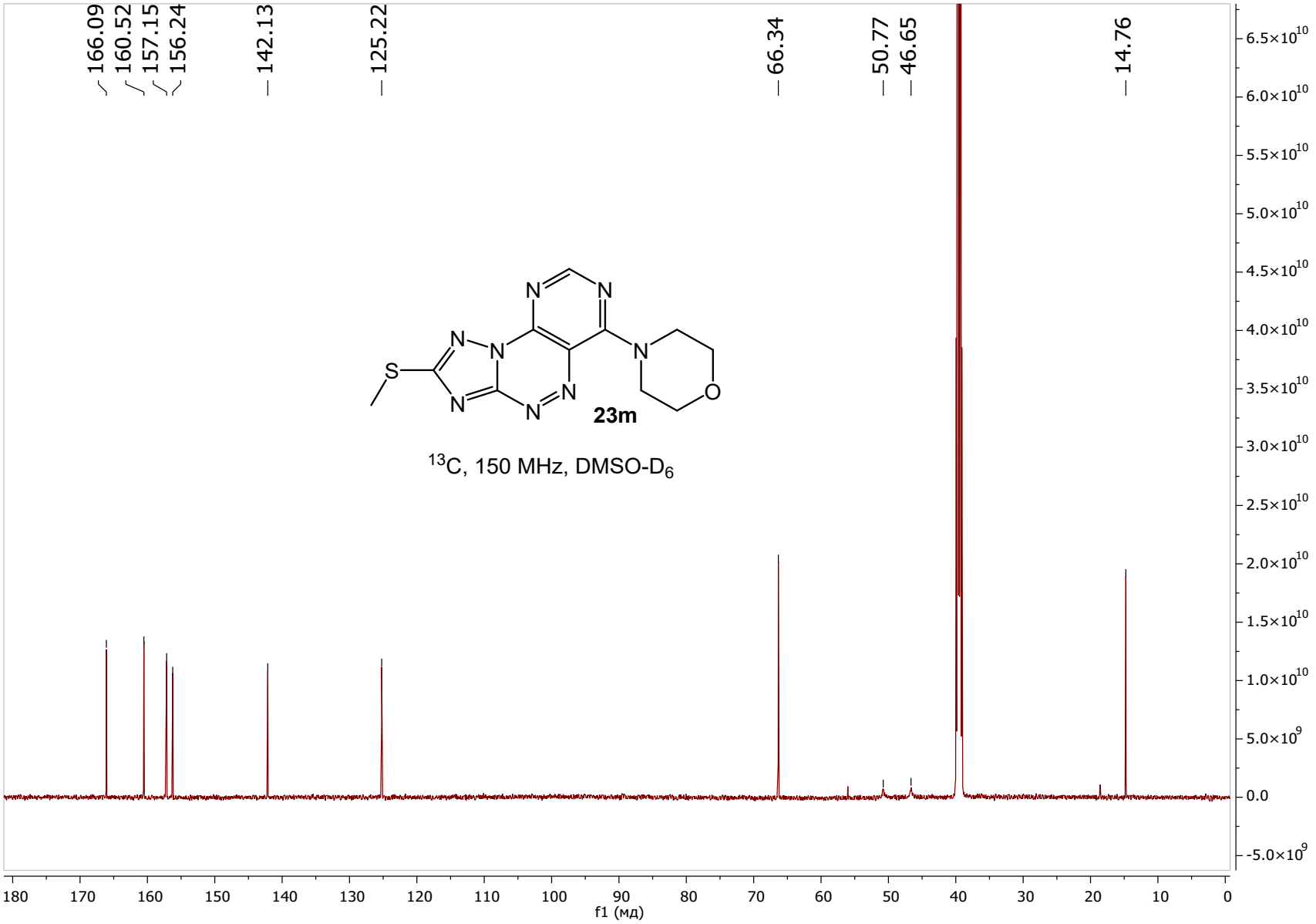
Page 1/1

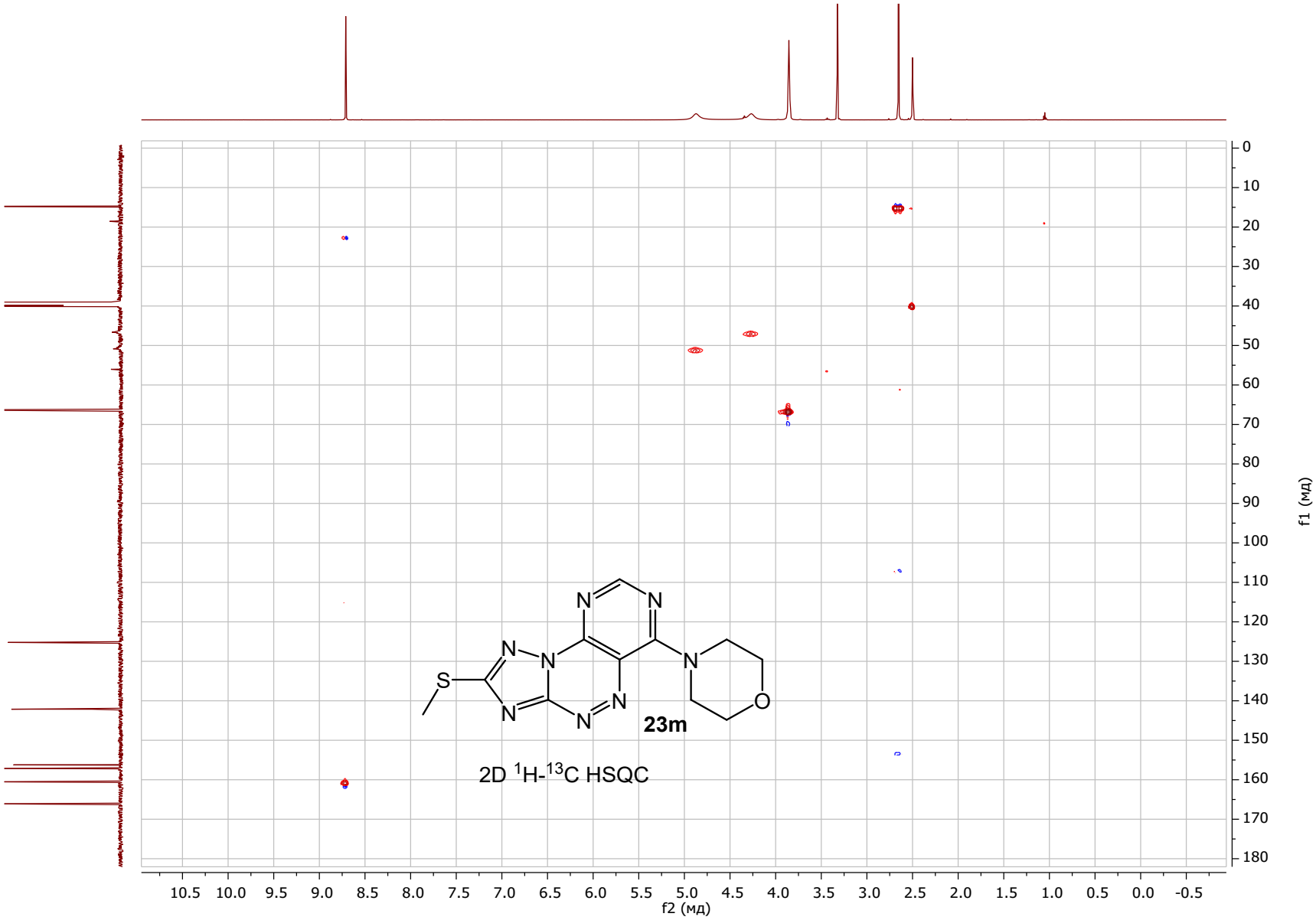
Line#:1 R.Time:3.005(Scan#:1163)
MassPeaks:81
RawMode:Single 3.005(1163) BasePeak:235(3146637)
Фон.реж.:1.423(530) Group 1 - Event 1

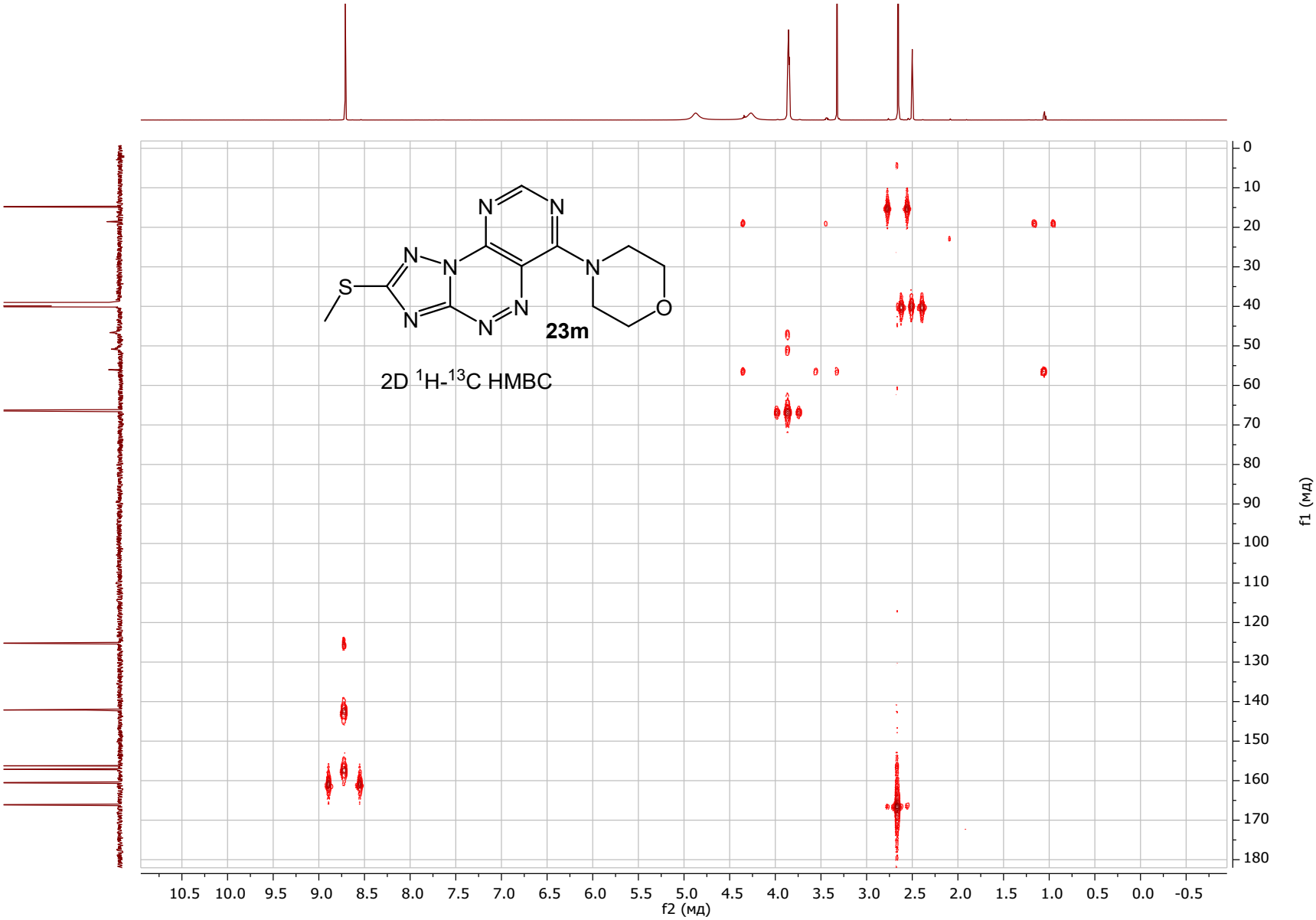


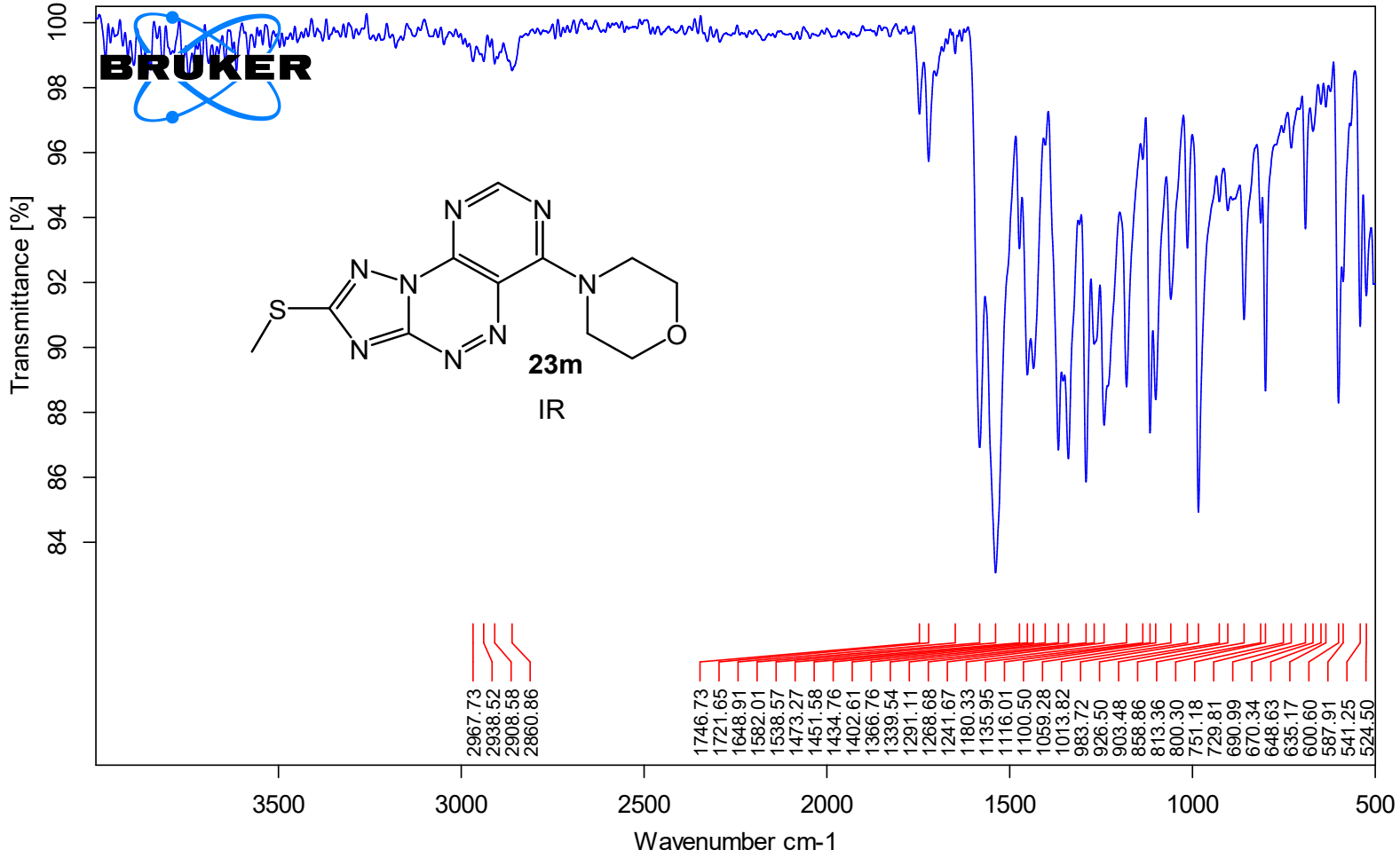
4-(2-(Methylthio)pyrimido[4,5-*e*][1,2,4]triazolo[5,1-*c*][1,2,4]triazin-6-yl)morpholine (23m).



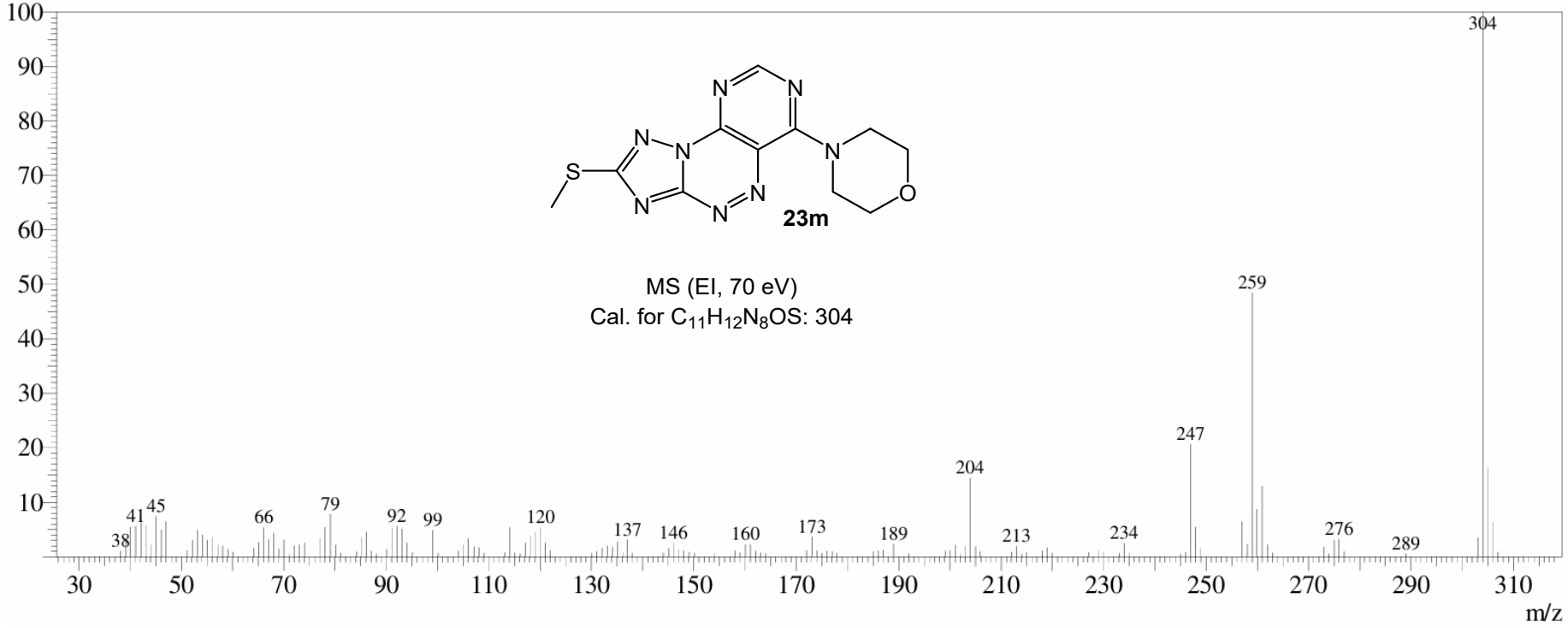

166.09
160.52
157.15
156.24
142.13
125.22
66.34
50.77
46.65
14.76
23m
^{13}C, 150 MHz, DMSO-D$_6$
f1 (мд)


23m
2D ^{1}H-^{13}C HSQC
f2 (мд)
f1 (мд)

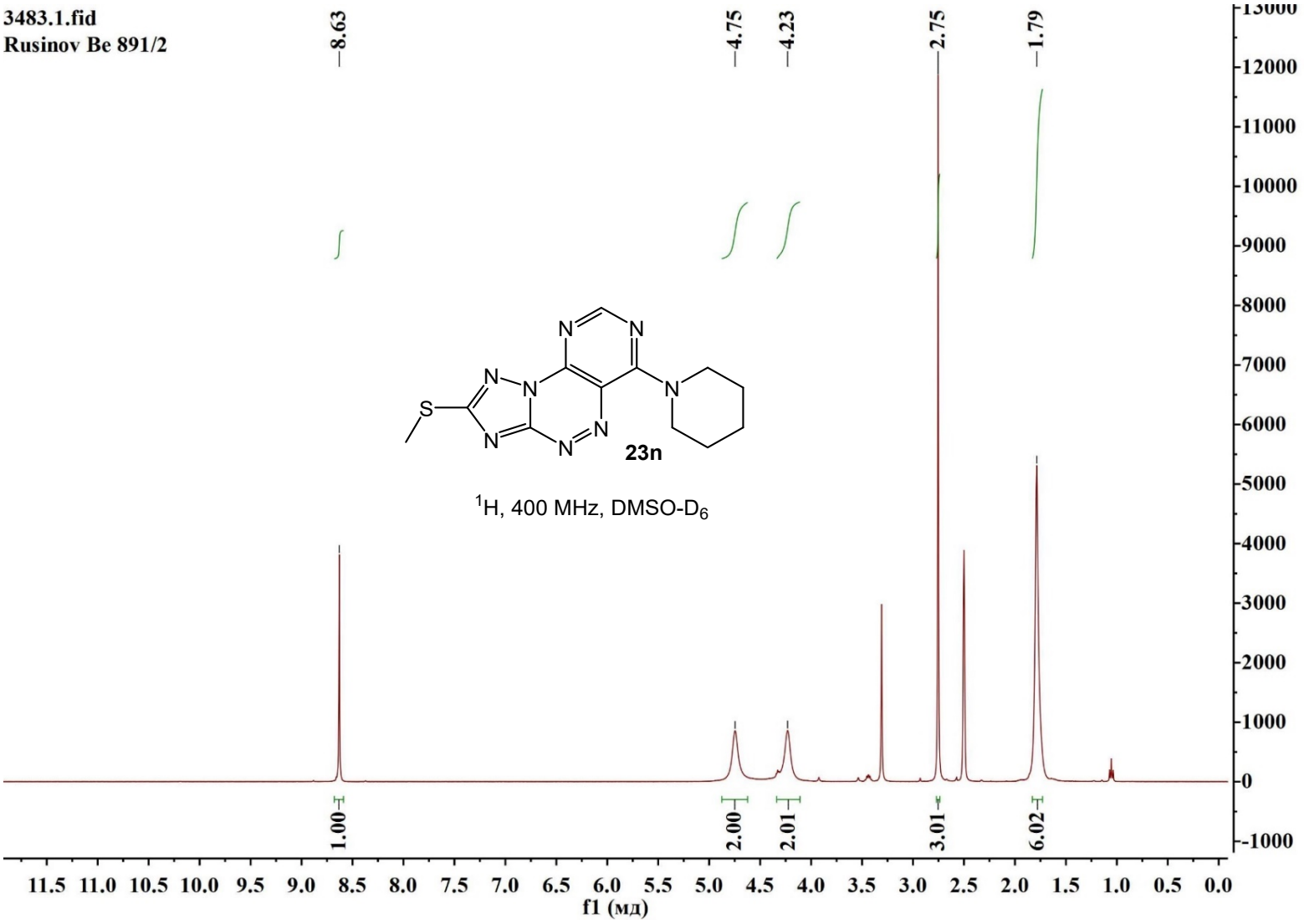

23m
2D ^{1}H-^{13}C HMBC
f2 (мд)
f1 (мд)

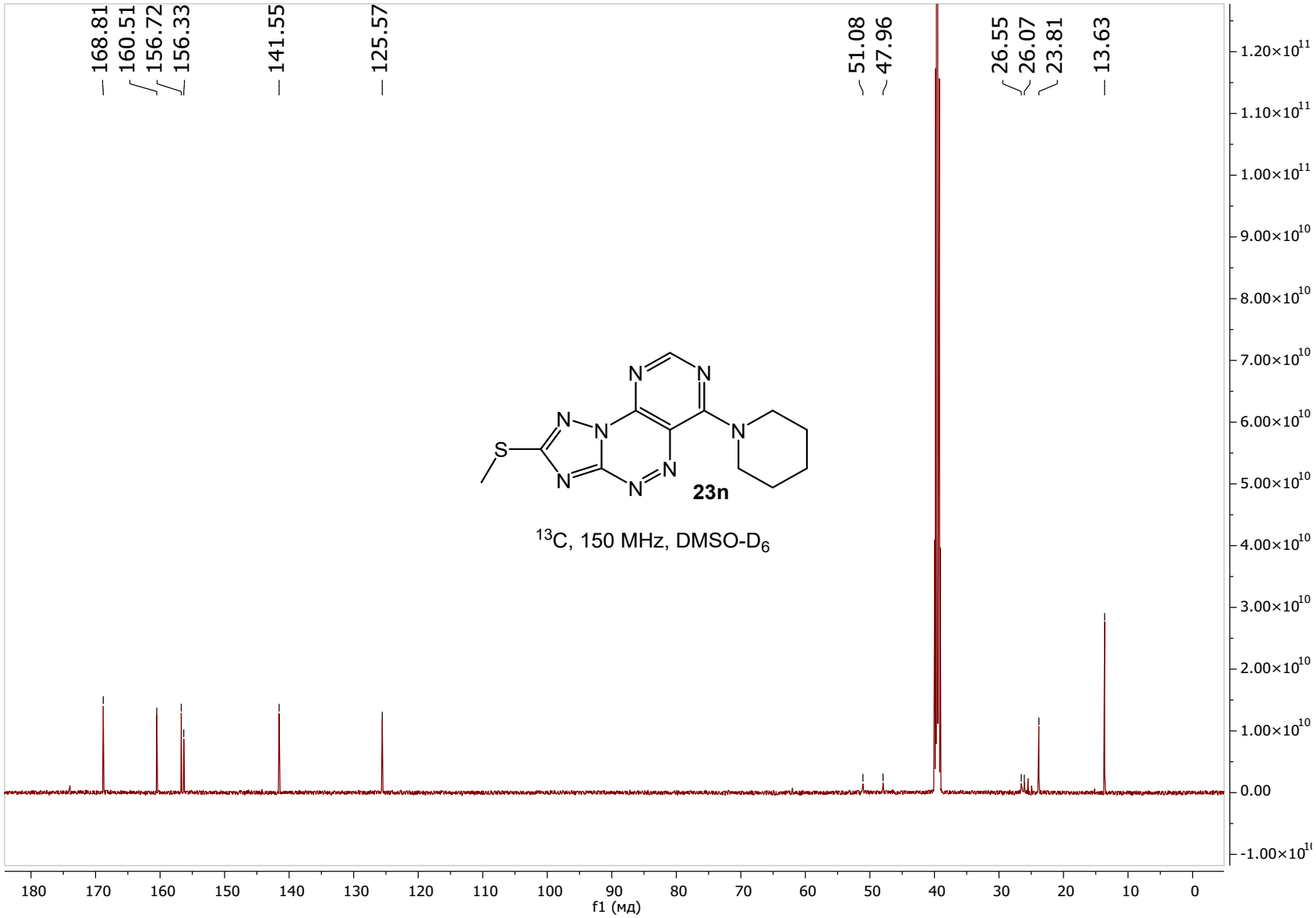

BRUKER
Transmittance [%]
100
98
96
94
92
90
88
86
84
S
N
O
23m
IR
2967.73
2938.52
2908.58
2860.86
1746.73
1721.65
1648.91
1582.01
1538.57
1473.27
1451.58
1434.76
1402.61
1366.76
1339.54
1291.11
1268.68
1241.67
1180.33
1135.95
1116.01
1100.50
1059.28
1013.82
983.72
926.50
903.48
858.86
813.36
800.30
751.18
729.81
690.99
670.34
648.63
635.17
600.60
587.91
541.25
524.50
3500
3000
2500
2000
1500
1000
500
Wavenumber cm-1

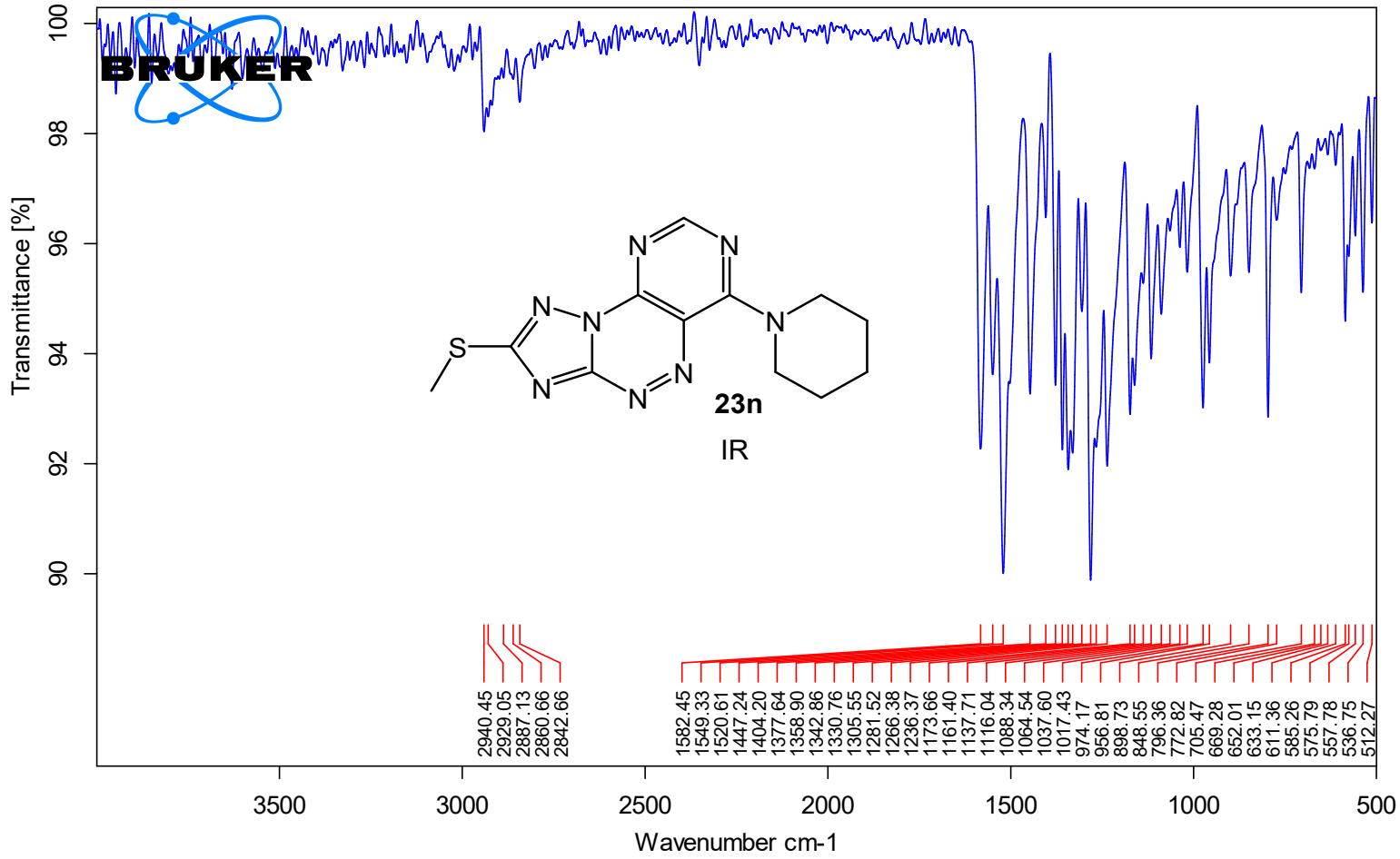
Line#:1 R.Time:1.837(Scan#:696)
MassPeaks:145
RawMode:Single 1.837(696) BasePeak:304(6841278)
Фон.реж.:0.417(128) Group 1 - Event 1



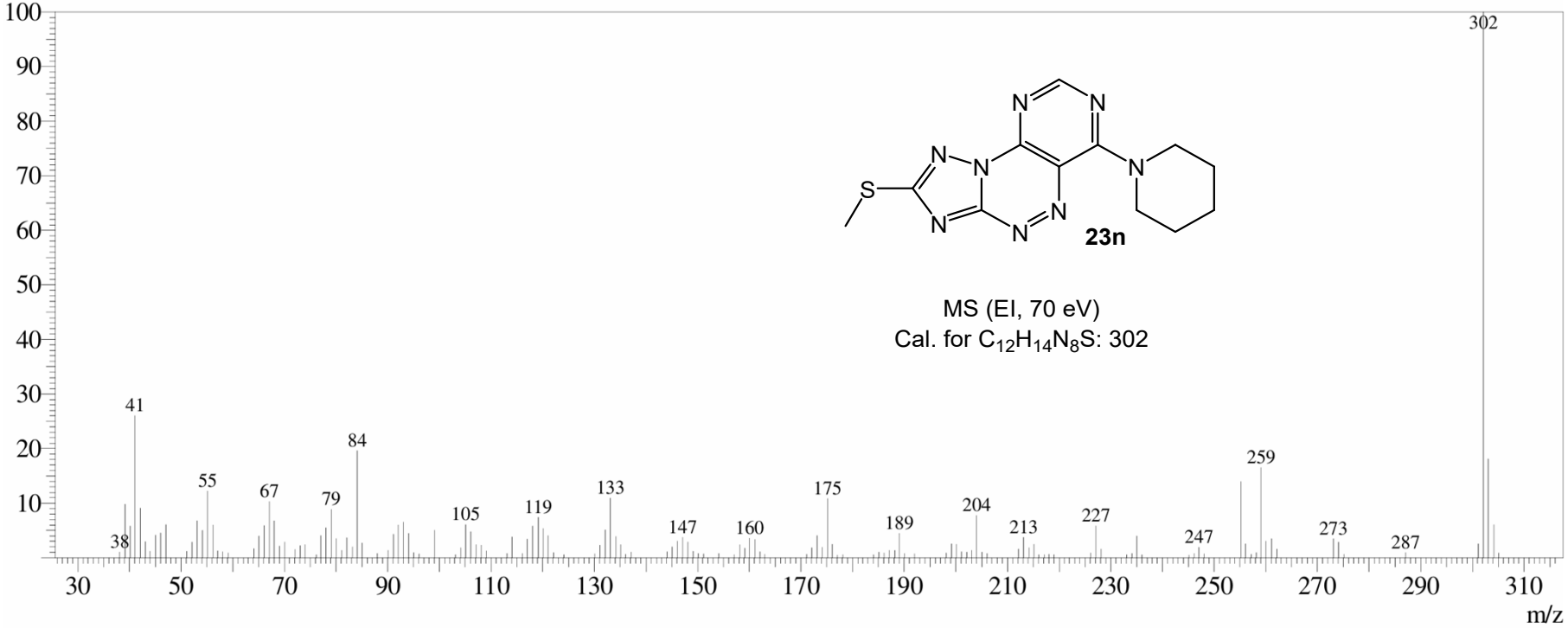
2-(Methylthio)-6-(piperidin-1-yl)pyrimido[4,5-*e*][1,2,4]triazolo[5,1-*c*][1,2,4]triazine (23n).




168.81
160.51
156.72
156.33
141.55
125.57
51.08
47.96
26.55
26.07
23.81
13.63
23n
^{13}C, 150 MHz, DMSO-D$_6$
f1 (мд)


BRUKER
Transmittance [%]
100
98
96
94
92
90
3500
3000
2500
2000
1500
1000
500
Wavenumber cm-1
23n
IR
2940.45
2929.05
2887.13
2860.66
2842.66
1582.45
1549.33
1520.61
1447.24
1404.20
1377.64
1358.90
1342.86
1330.76
1305.55
1281.52
1266.38
1236.37
1173.66
1161.40
1137.71
1116.04
1088.34
1064.54
1037.60
1017.43
974.17
956.81
898.73
848.55
796.36
772.82
705.47
669.28
652.01
633.15
611.36
585.26
575.79
557.78
536.75
512.27

Line#:1 R.Time:1.603(Scan#:602)
MassPeaks:150
RawMode:Single 1.603(602) BasePeak:302(6498882)
Фон.реж.:3.268(1268) Group 1 - Event 1

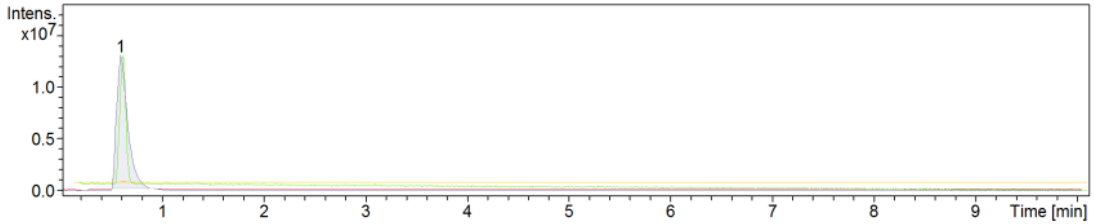


23n

MS (EI, 70 eV)
Cal. for $C_{12}H_{14}N_8S$: 302

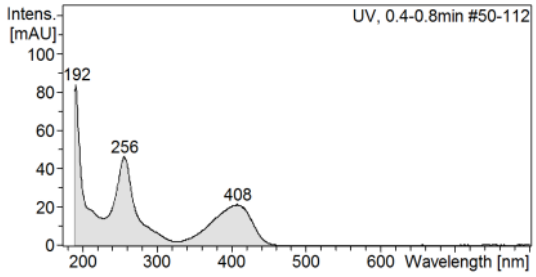
Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	2.0 Bar
Focus	Active	Set Capillary	4500 V	Set Dry Heater	200 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	8.0 l/min
Scan End	1400 m/z	Set Charging Voltage	2000 V	Set Divert Valve	Waste
		Set Corona	0 nA	Set APCI Heater	0 °C

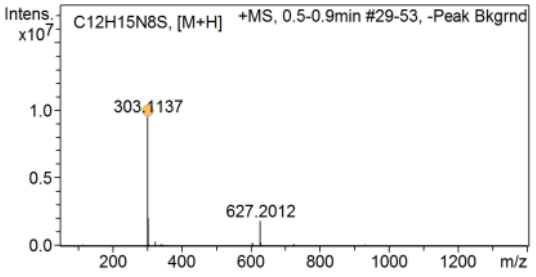


#	RT [min]	Area	Int. Type	I	S/N	Chromatogram	Max. m/z	FWHM [min]
1	0.6	96468096	Manual	12909648	59569.2	EIC 303.1138±0.005 +All MS	303.1137	

Cmpd 1, 0.6 min

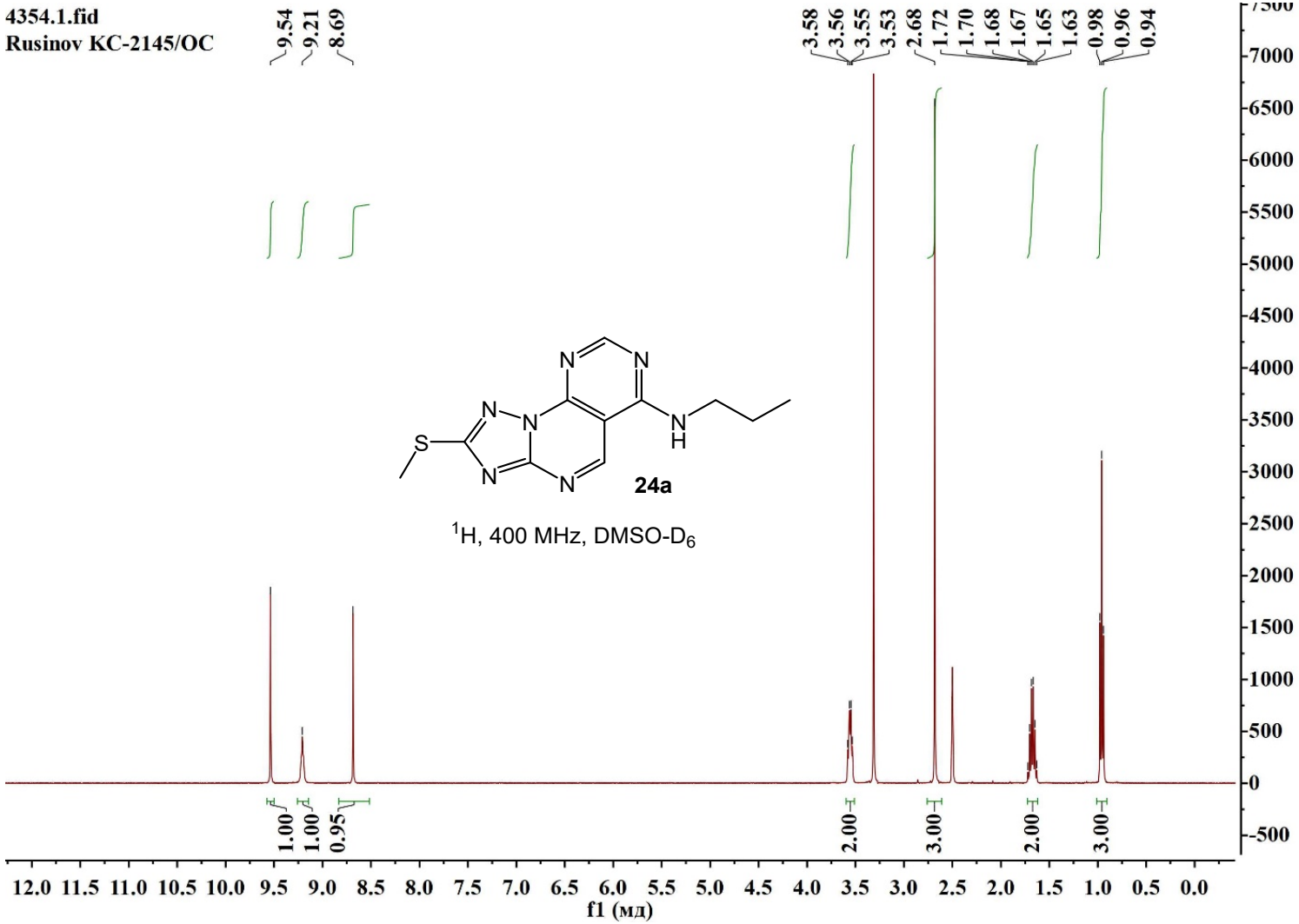


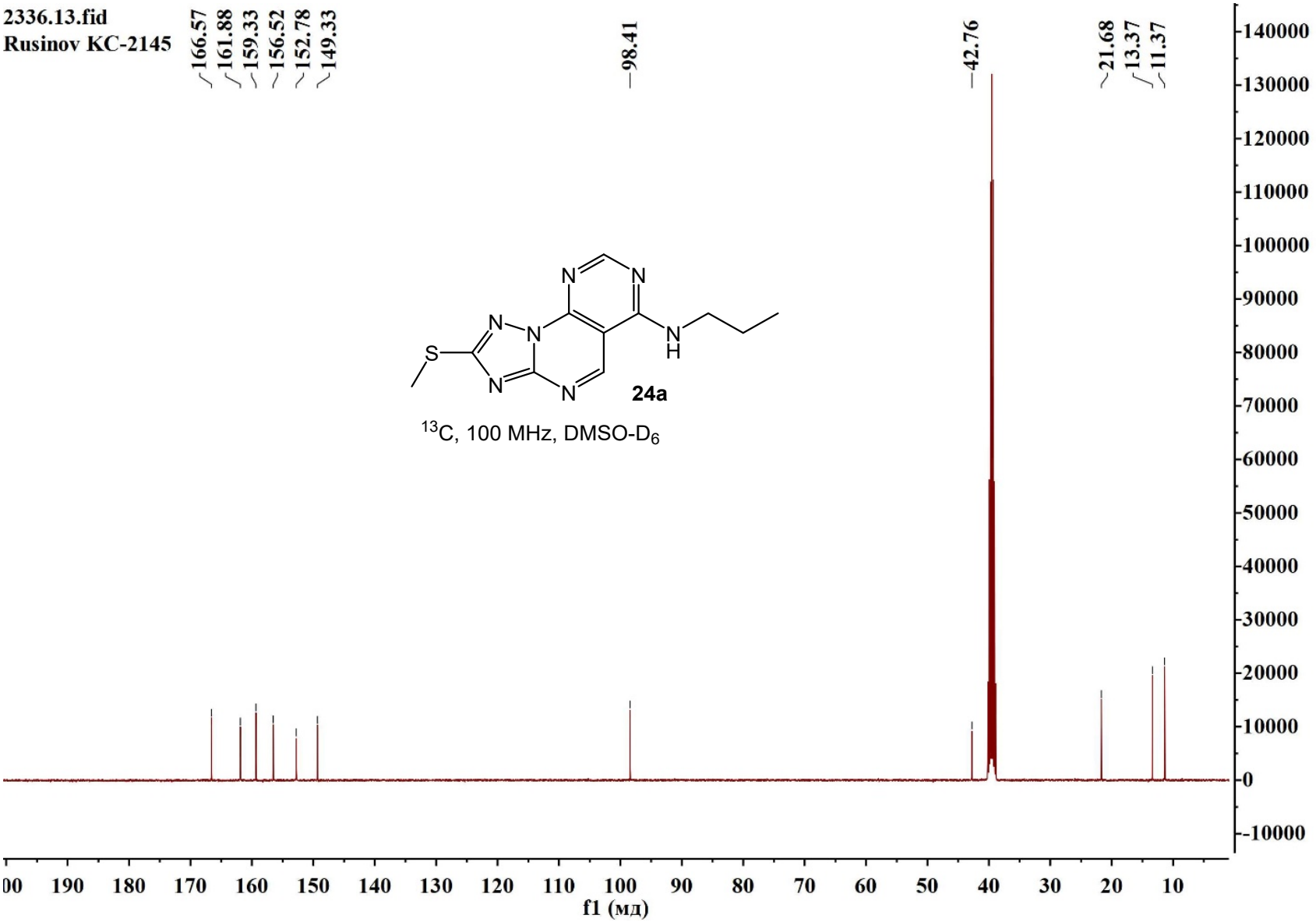
#	Wavelength	Intensity
0	192	83.8
1	256	46.0
2	408	21.3

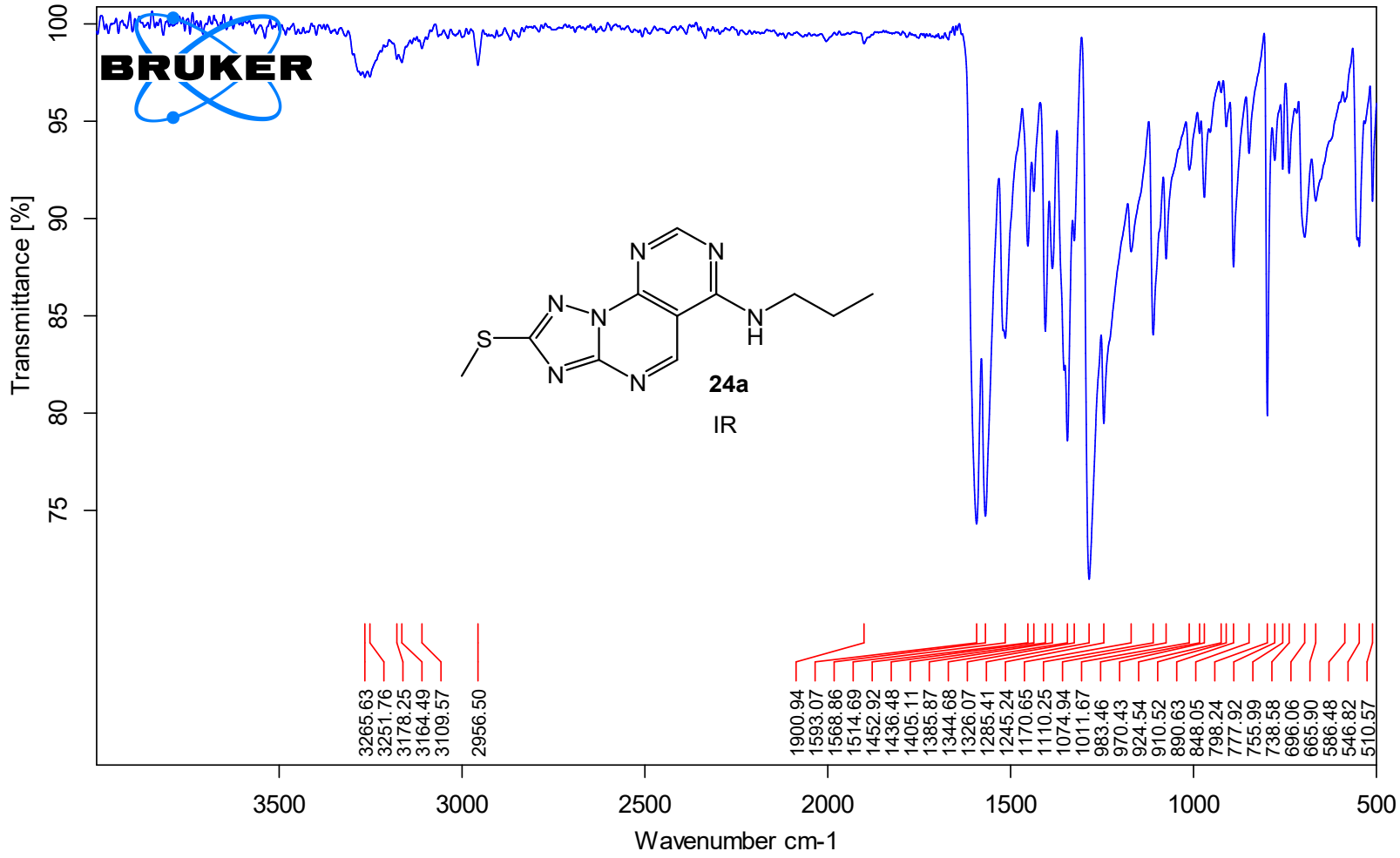


#	m/z	Res.	S/N	I	I %	FWHM
1	303.1137	15899	670977984.0	9483236	100.0	0.0191
2	304.1155	33205	142157408.0	2009175	21.2	0.0092
3	305.1102	25729	40027480.0	565727	6.0	0.0119
4	325.0948	24102	22614914.0	319627	3.4	0.0135
5	341.0687	20234	6738350.5	95236	1.0	0.0169
6	605.2190	25534	16006233.0	226223	2.4	0.0237
7	627.2012	38875	129641488.0	1832282	19.3	0.0161
8	628.2032	30497	39065236.0	552127	5.8	0.0206
9	629.1996	23341	15705074.0	221967	2.3	0.0270
10	724.1348	23010	9027483.0	127590	1.3	0.0315

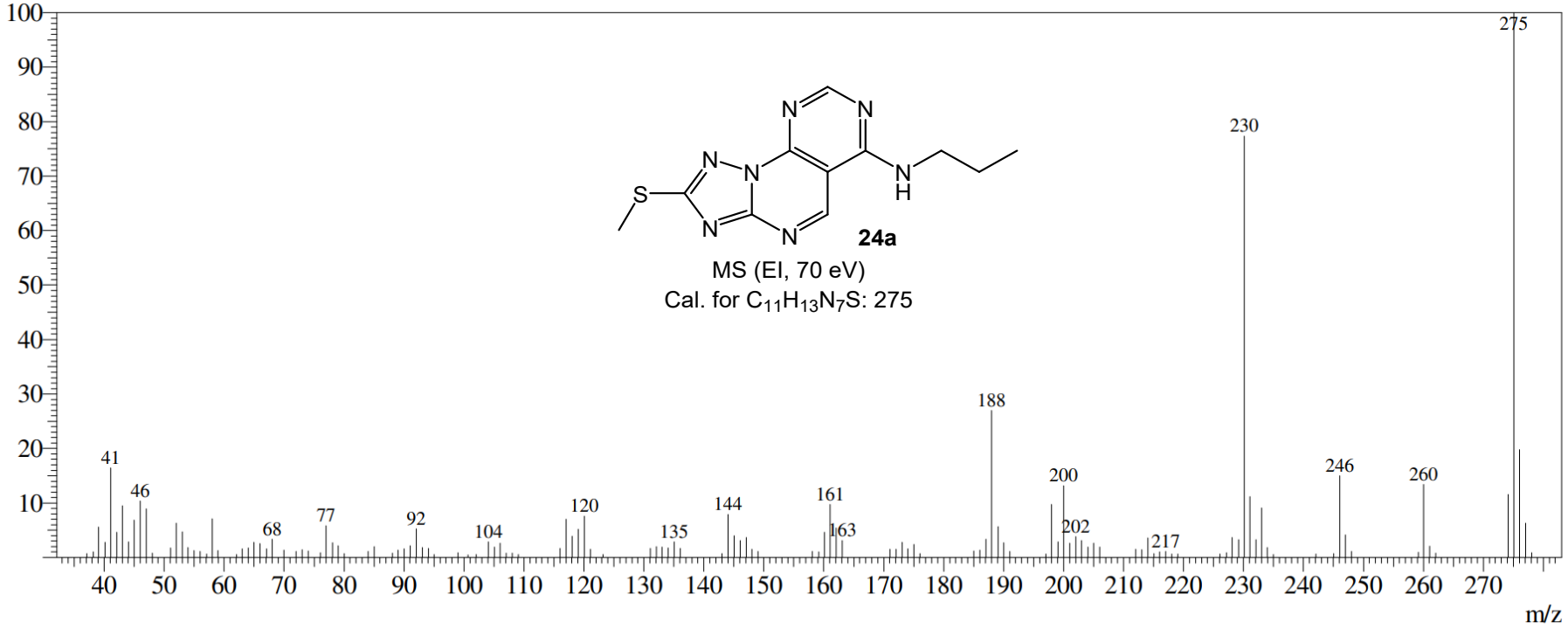
2-(Methylthio)-*N*-propylpyrimido[5,4-*e*][1,2,4]triazolo[1,5-*a*]pyrimidin-6-amine (24a)



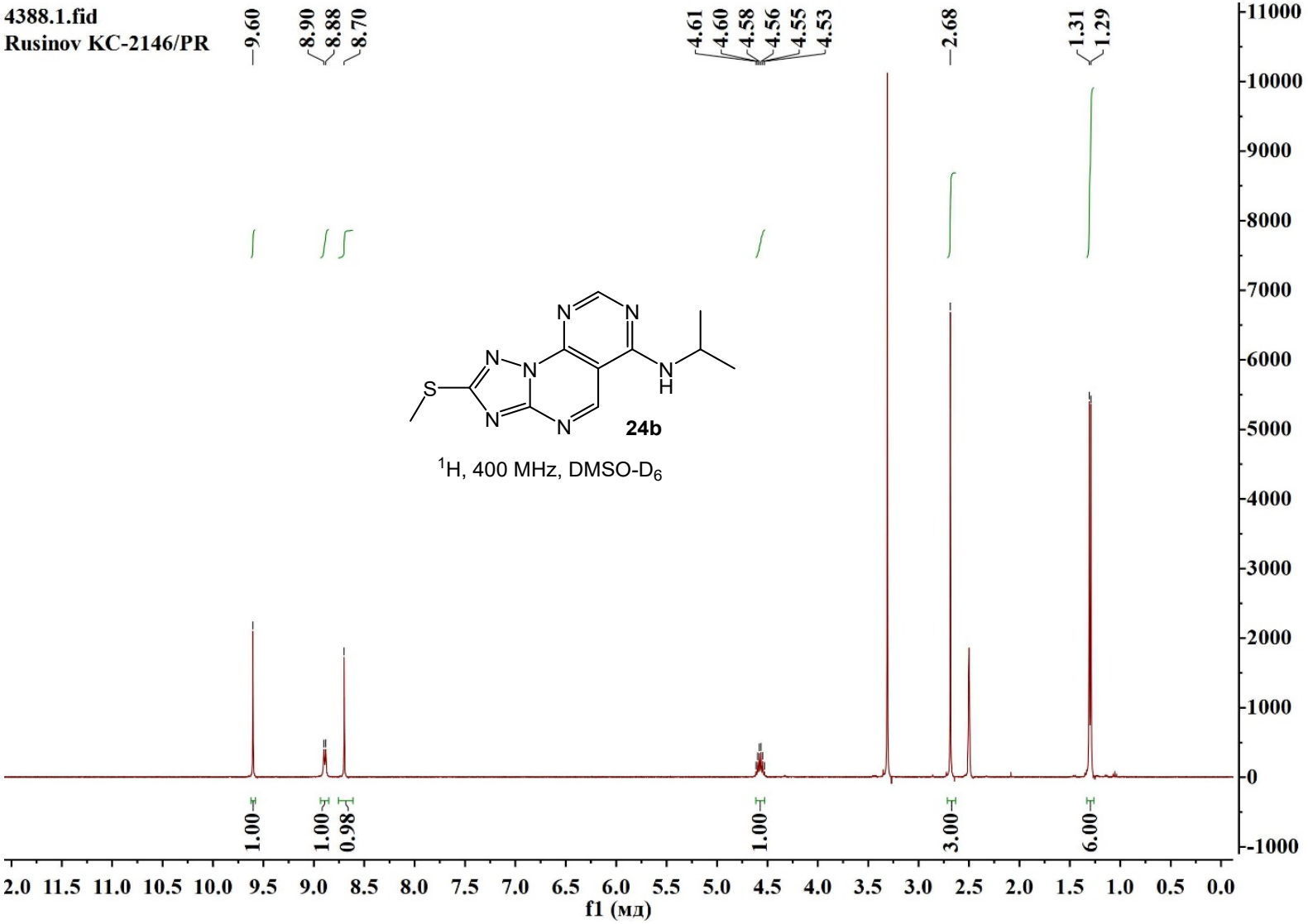

2336.13.fid
Rusinov KC-2145
166.57
161.88
159.33
156.52
152.78
149.33
98.41
42.76
21.68
13.37
11.37
24a
13C, 100 MHz, DMSO-D6
f1 (мд)

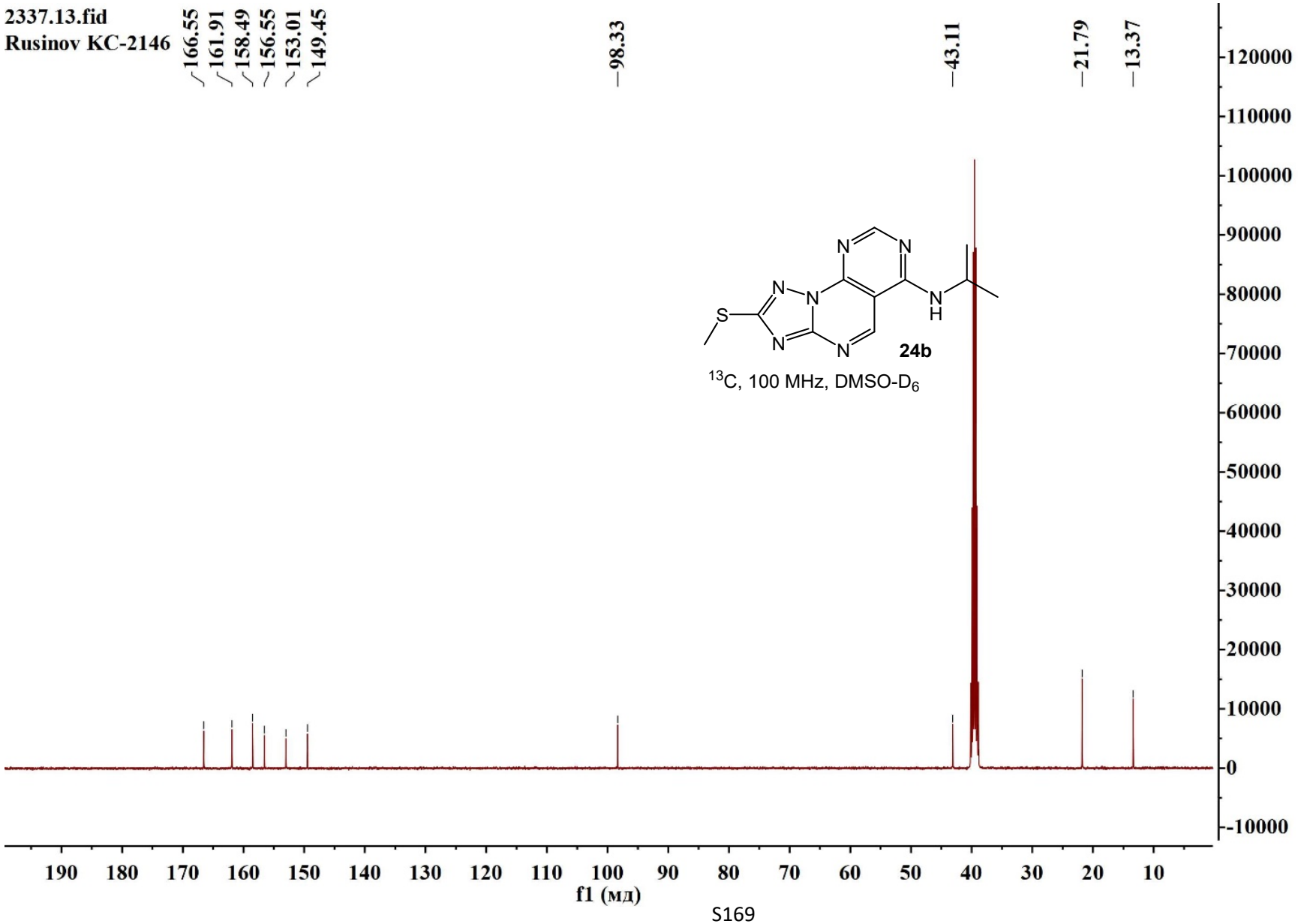

BRUKER
Transmittance [%]
100
95
90
85
80
75
3500
3000
2500
2000
1500
1000
500
Wavenumber cm-1
24a
IR
3265.63
3251.76
3178.25
3164.49
3109.57
2956.50
1900.94
1593.07
1568.86
1514.69
1452.92
1436.48
1405.11
1385.87
1344.68
1326.07
1285.41
1245.24
1170.65
1110.25
1074.94
1011.67
983.46
970.43
924.54
910.52
890.63
848.05
798.24
777.92
755.99
738.58
696.06
665.90
586.48
546.82
510.57

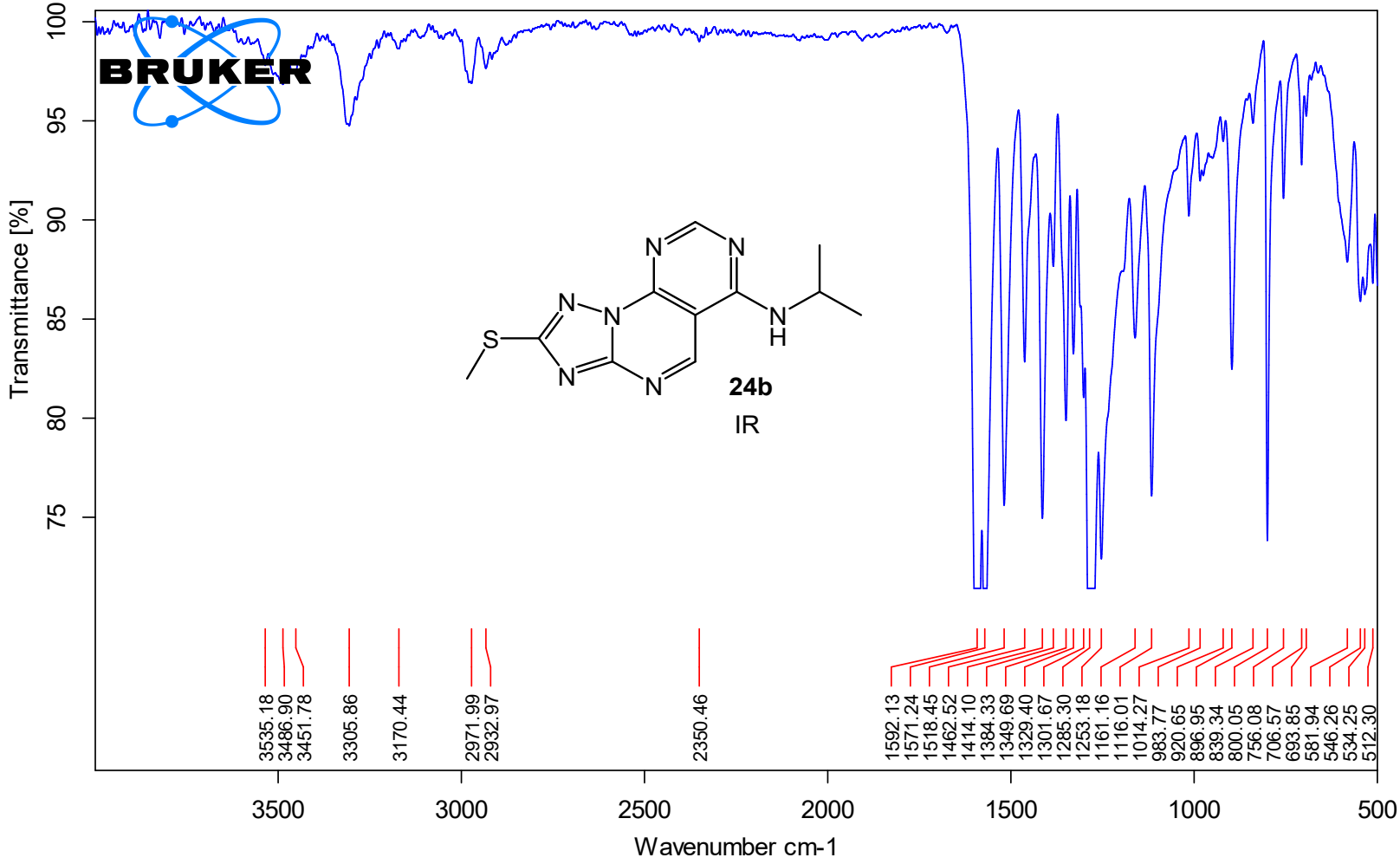
Line#:1 R.Time:2.790(Scan#:1077)
MassPeaks:137
RawMode:Single 2.790(1077) BasePeak:275(4518060)
Фон.реж.:None Group 1 - Event 1



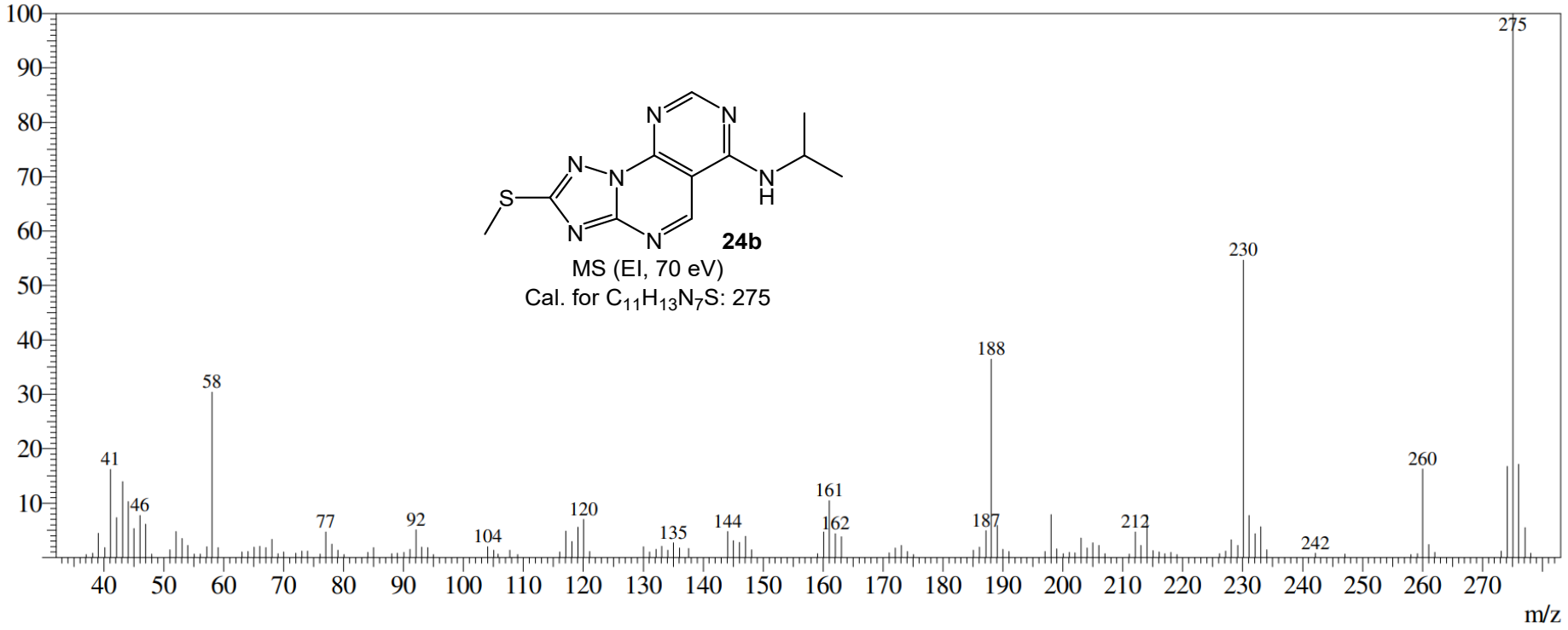
_N_-Isopropyl-2-(methylthio)pyrimido[5,4-_e_][1,2,4]triazolo[1,5-_a_]pyrimidin-6-amine (24b)



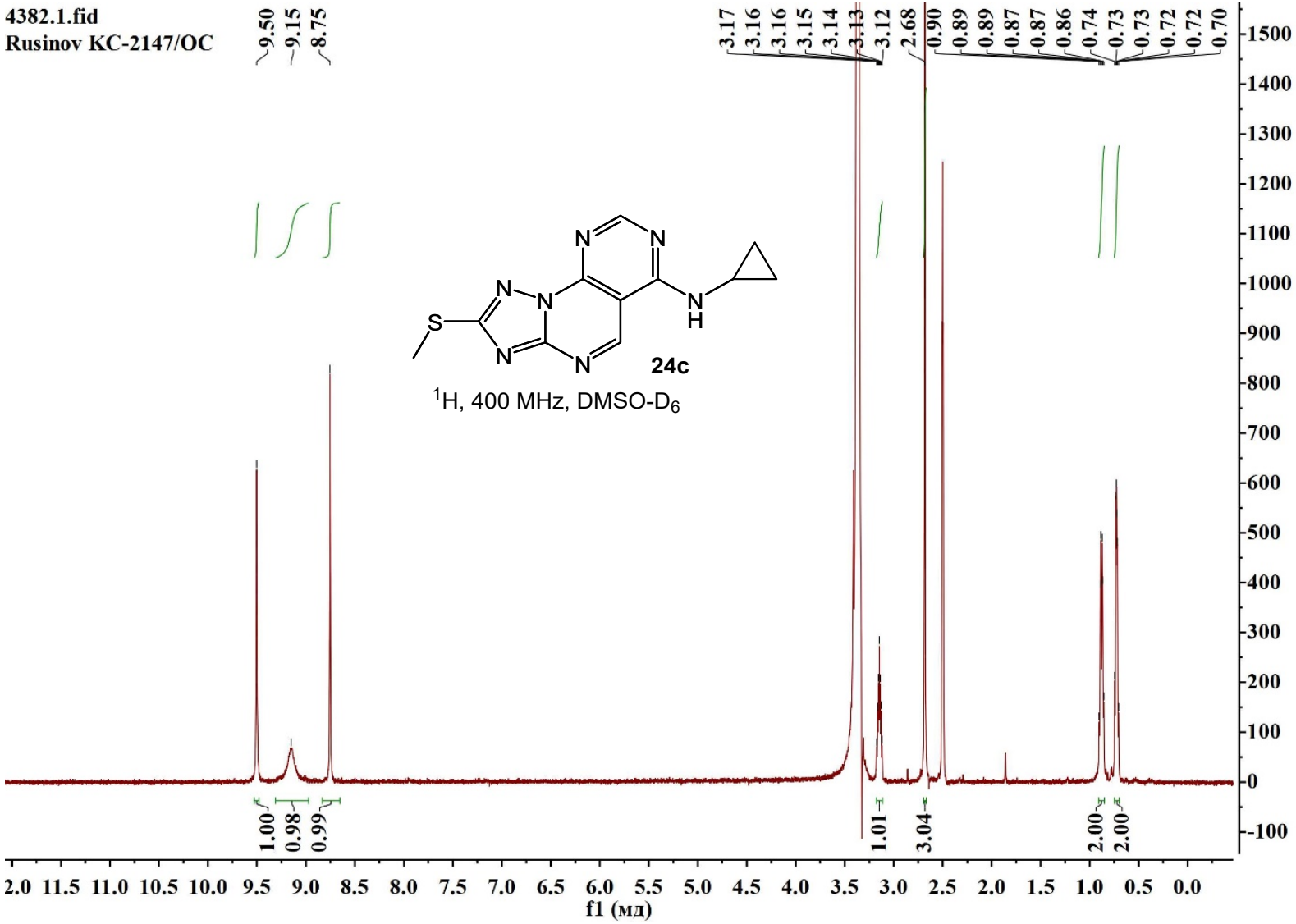

2337.13.fid
Rusinov KC-2146
166.55
161.91
158.49
156.55
153.01
149.45
98.33
43.11
21.79
13.37
24b
13C, 100 MHz, DMSO-D6
f1 (мд)

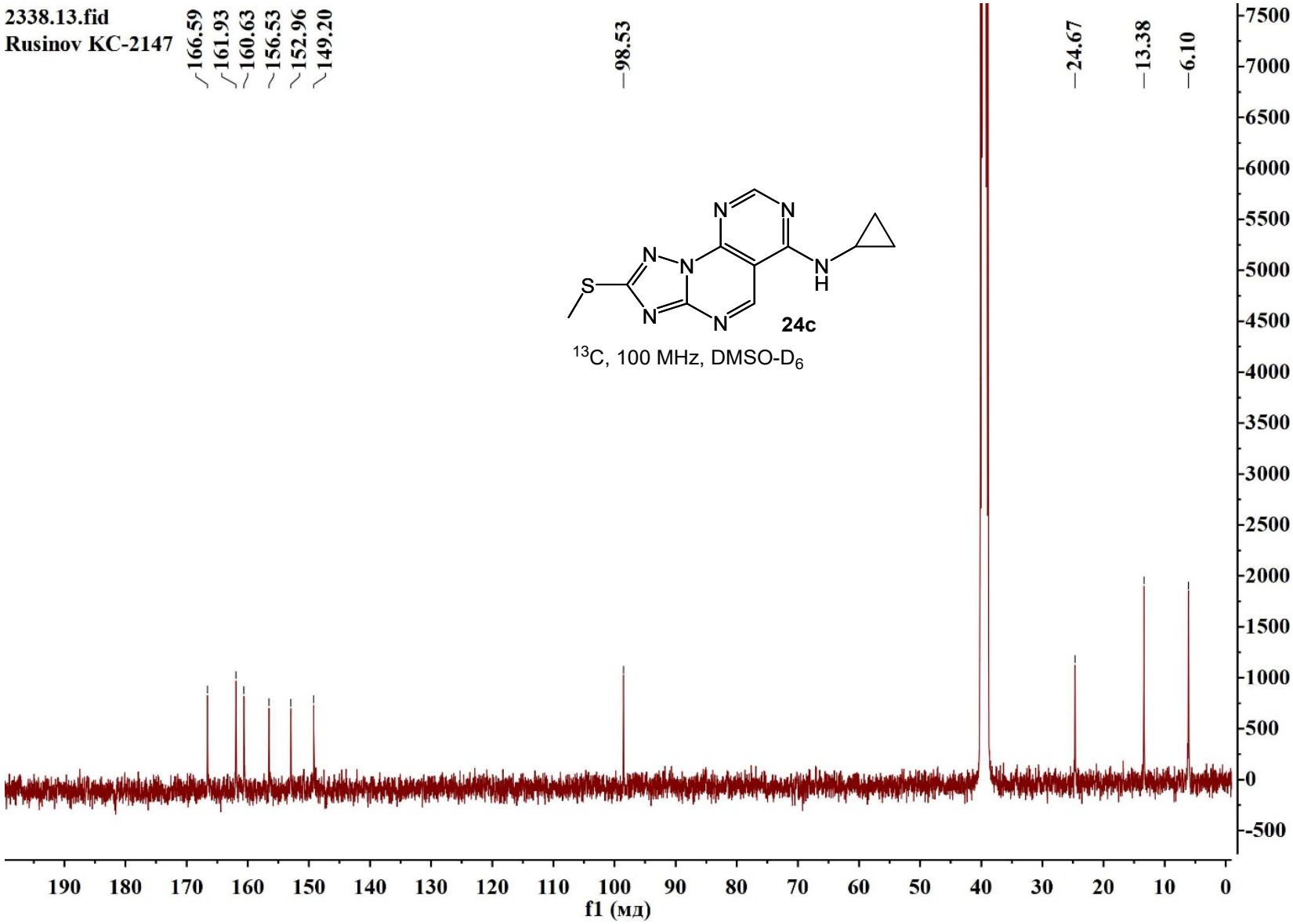

BRUKER
Transmittance [%]
100
95
90
85
80
75
3535.18
3486.90
3451.78
3305.86
3170.44
2971.99
2932.97
2350.46
1592.13
1571.24
1518.45
1462.52
1414.10
1384.33
1349.69
1329.40
1301.67
1285.30
1253.18
1161.16
1116.01
1014.27
983.77
920.65
896.95
839.34
800.05
756.08
706.57
693.85
581.94
546.26
534.25
512.30
3500
3000
2500
2000
1500
1000
500
Wavenumber cm-1
24b
IR

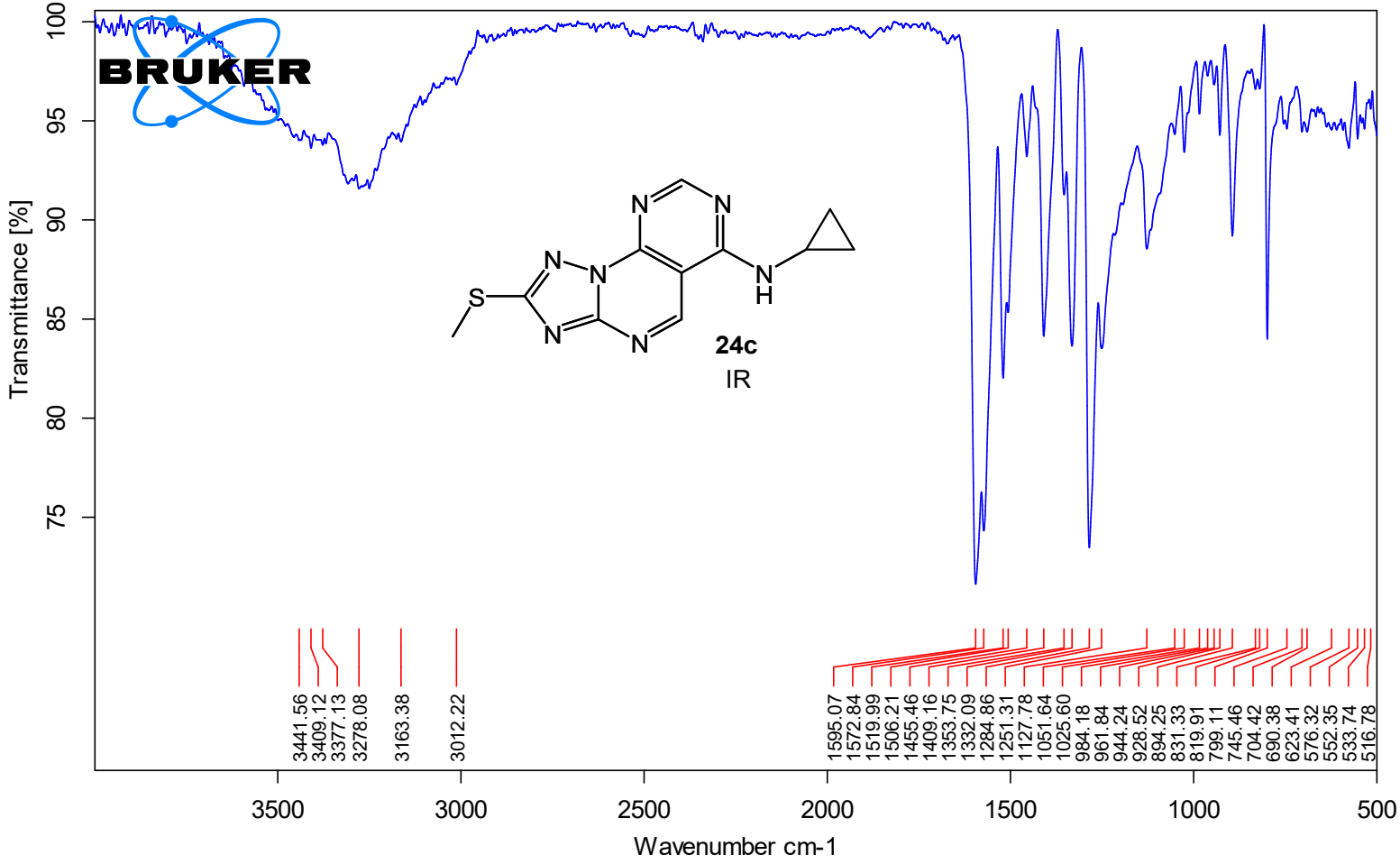
Line#:1 R.Time:2.850(Scan#:1101)
MassPeaks:130
RawMode:Single 2.850(1101) BasePeak:275(4953572)
Фон.реж.:1.373(510) Group 1 - Event 1



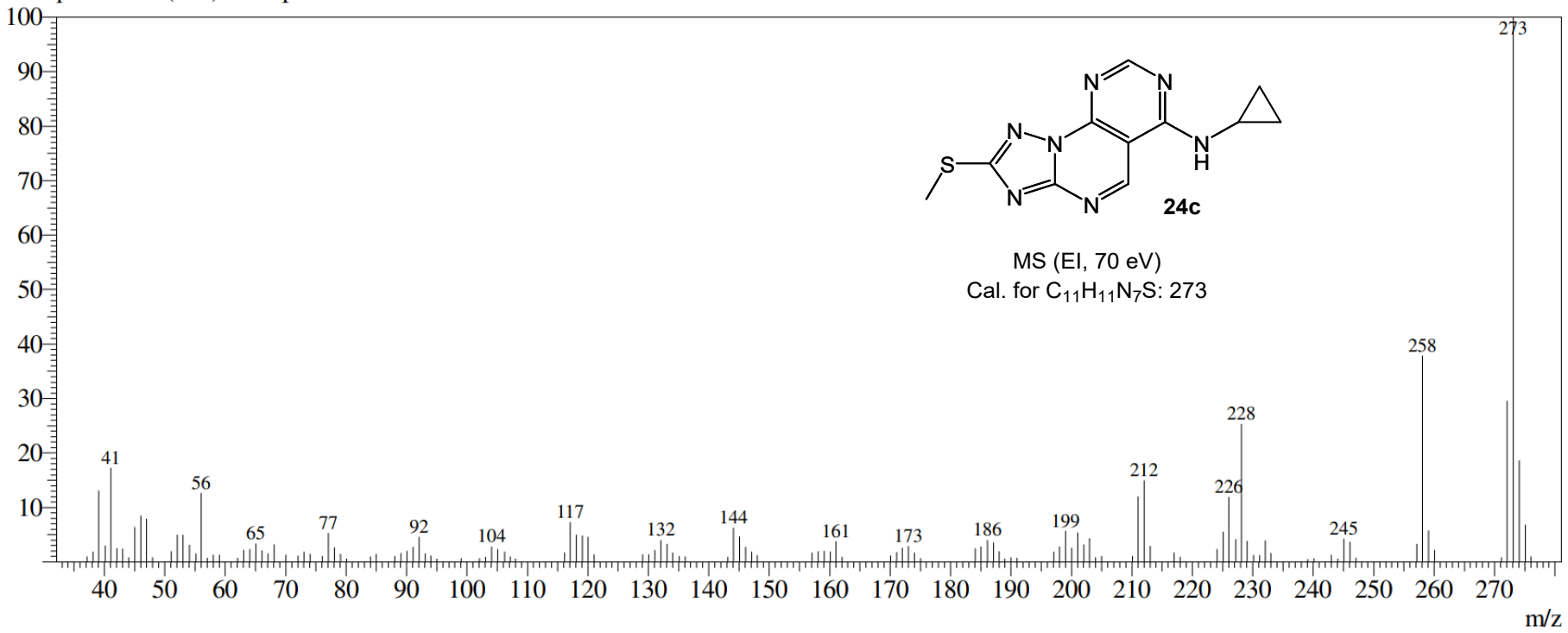
_N_-Cyclopropyl-2-(methylthio)pyrimido[5,4-*e*][1,2,4]triazolo[1,5-*a*]pyrimidin-6-amine (24c)



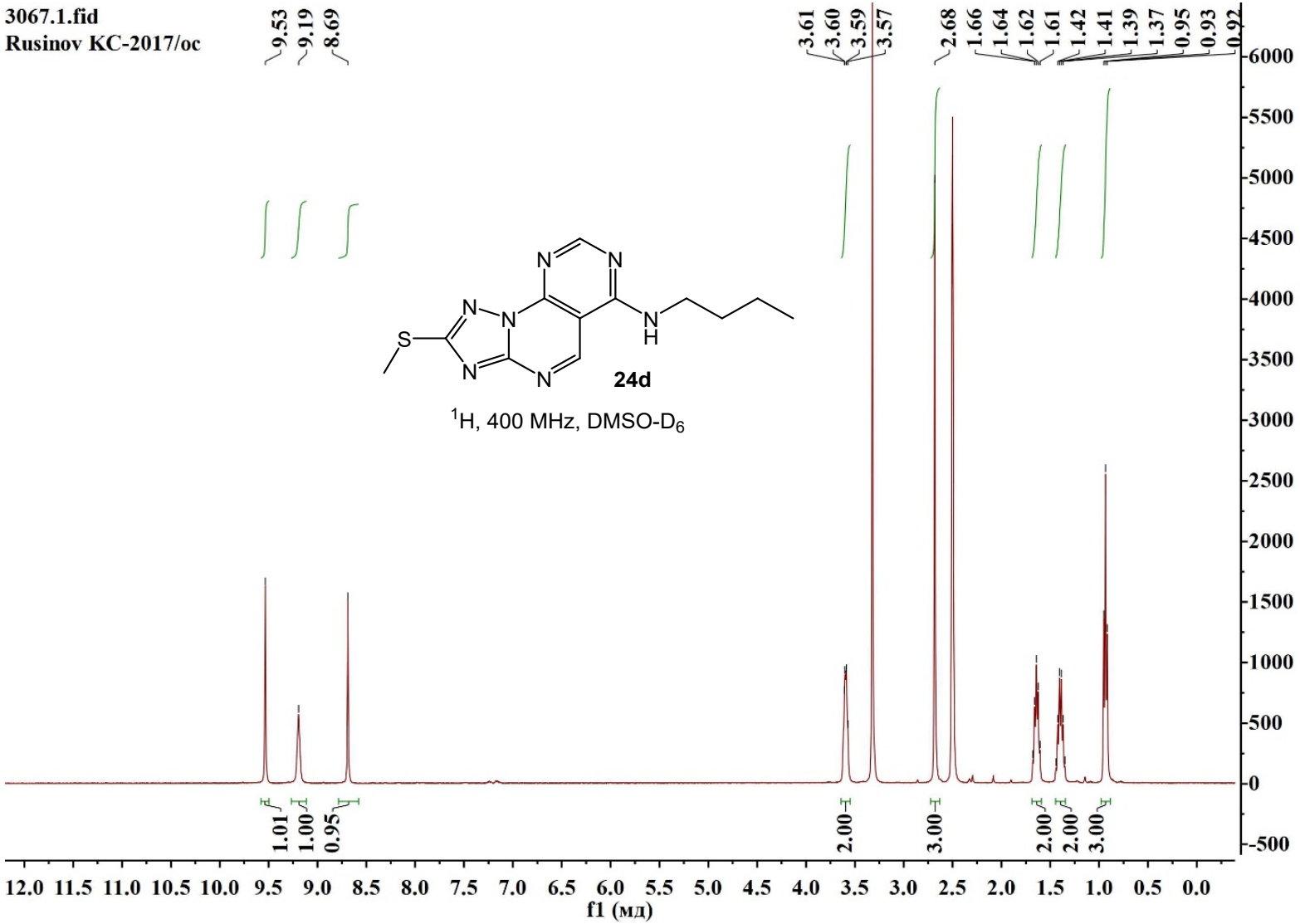

2338.13.fid
Rusinov KC-2147
166.59
161.93
160.63
156.53
152.96
149.20
98.53
24.67
13.38
6.10
24c
13C, 100 MHz, DMSO-D6
f1 (мд)

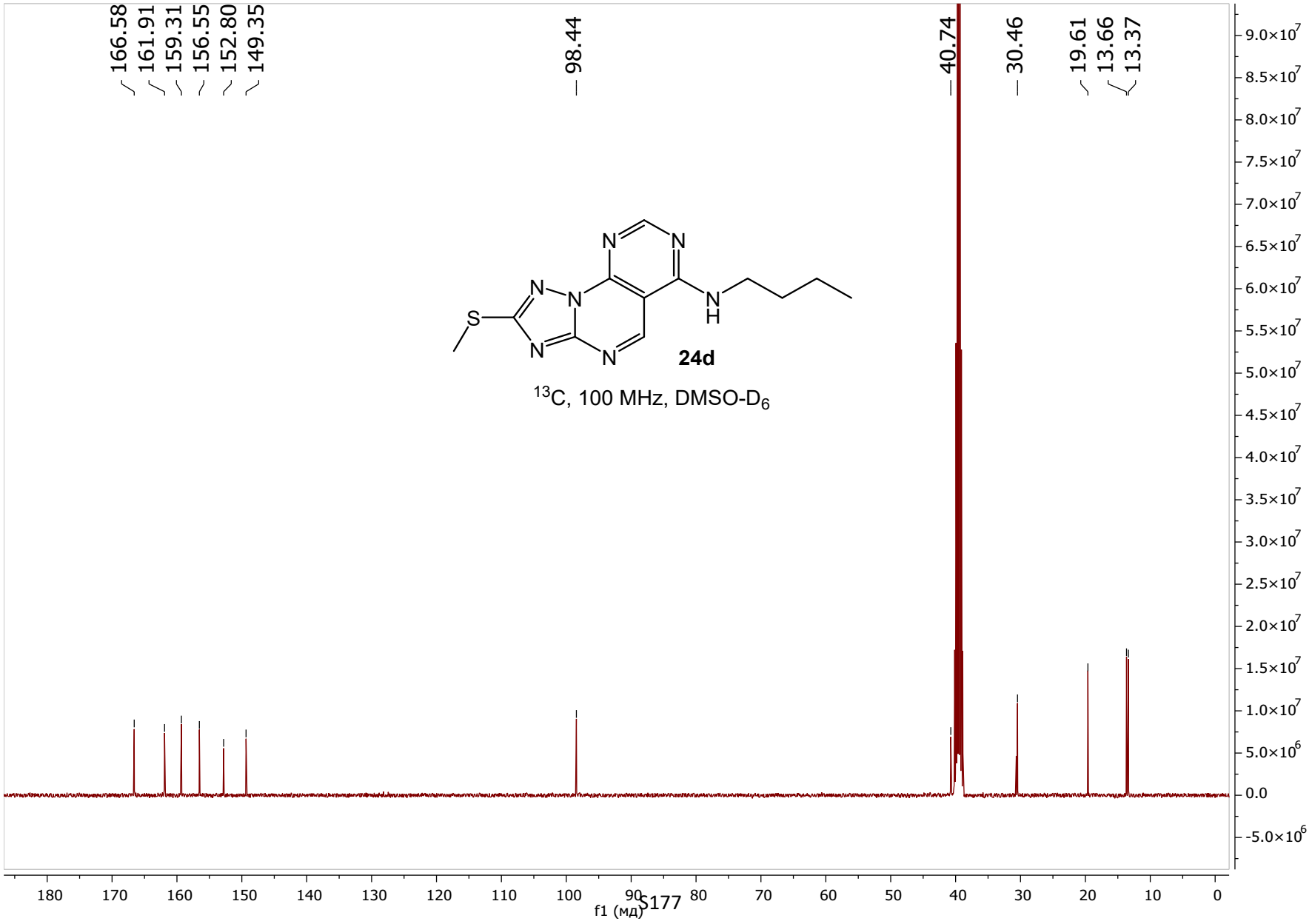

BRUKER
Transmittance [%]
100
95
90
85
80
75
3500
3000
2500
2000
1500
1000
500
Wavenumber cm-1
3441.56
3409.12
3377.13
3278.08
3163.38
3012.22
1595.07
1572.84
1519.99
1506.21
1455.46
1409.16
1353.75
1332.09
1284.86
1251.31
1127.78
1051.64
1025.60
984.18
961.84
944.24
928.52
894.25
831.33
819.91
799.11
745.46
704.42
690.38
623.41
576.32
552.35
533.74
516.78
24c
IR

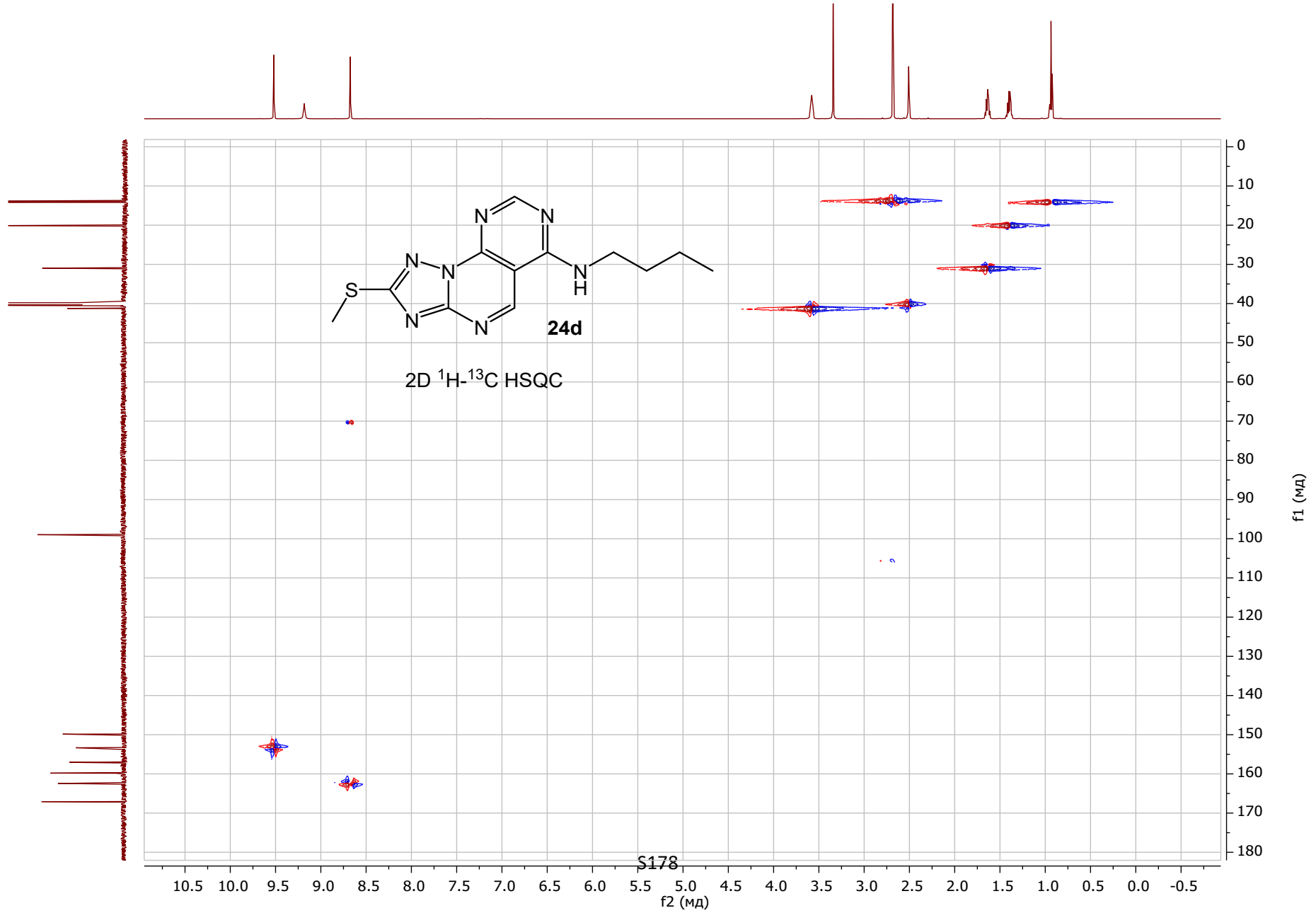
Line#:1 R.Time:2.595(Scan#:999)
MassPeaks:137
RawMode:Single 2.595(999) BasePeak:273(4378085)
Фон.реж.:1.523(570) Group 1 - Event 1

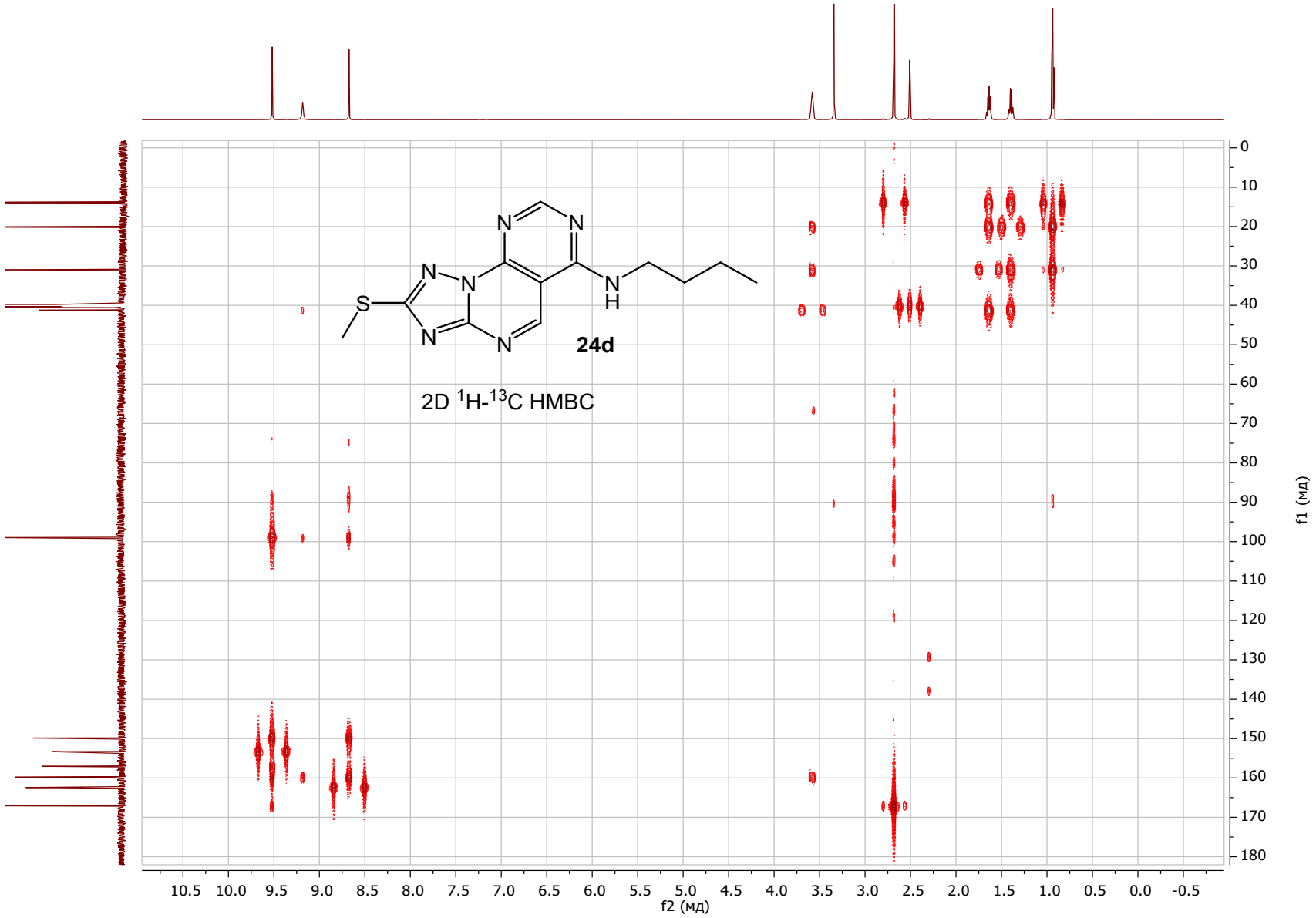


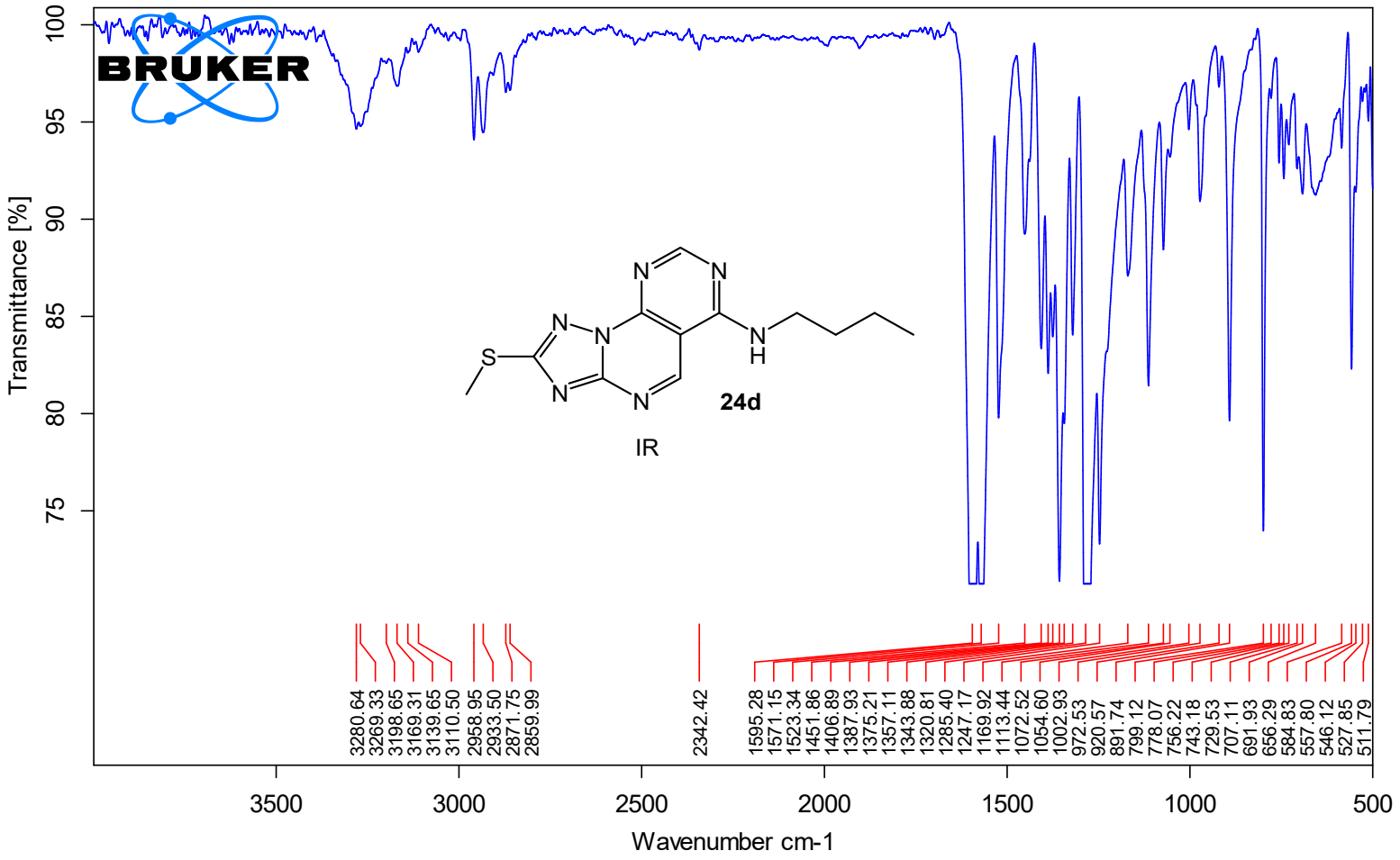
_N_-Butyl-2-(methylthio)pyrimido[5,4-_e_][1,2,4]triazolo[1,5-_a_]pyrimidin-6-amine (24d)



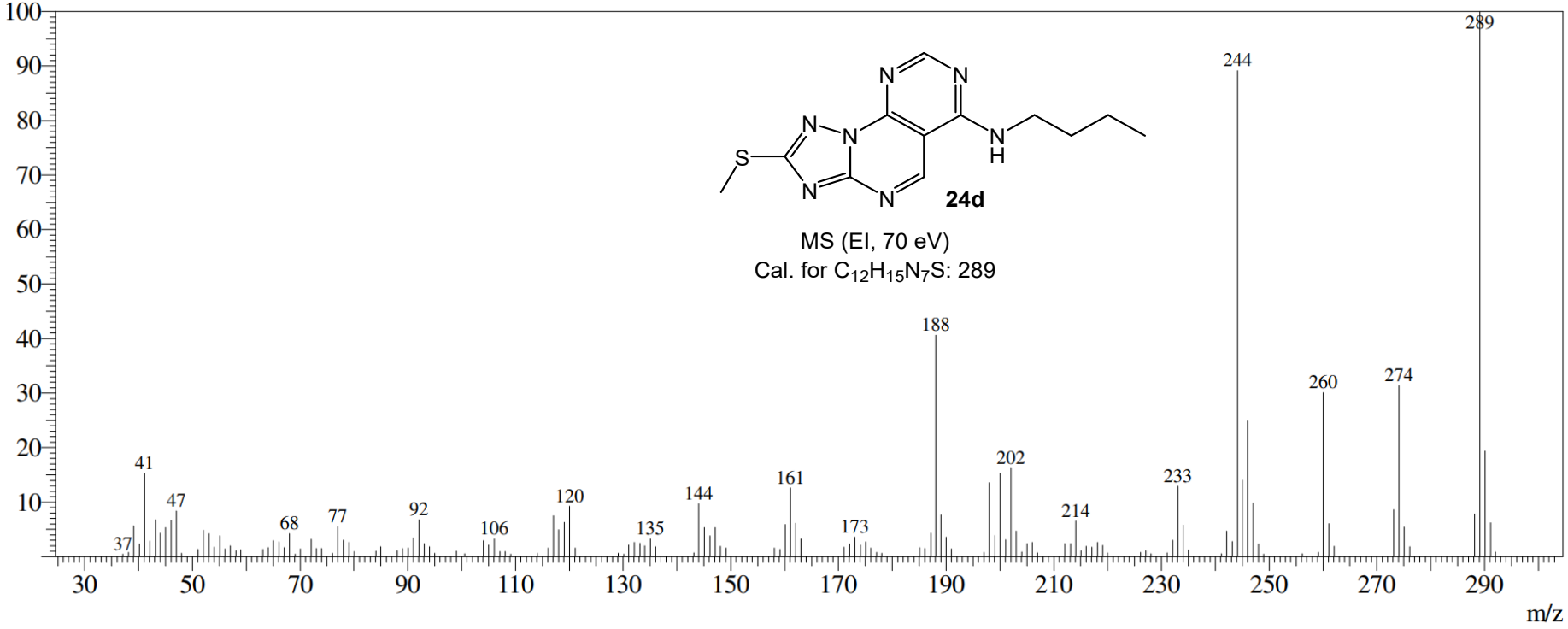

166.58
161.91
159.31
156.55
152.80
149.35
98.44
40.74
30.46
19.61
13.66
13.37
N
N
N
N
N
S
N
H
24d
13C, 100 MHz, DMSO-D6
9.0×10^7
8.5×10^7
8.0×10^7
7.5×10^7
7.0×10^7
6.5×10^7
6.0×10^7
5.5×10^7
5.0×10^7
4.5×10^7
4.0×10^7
3.5×10^7
3.0×10^7
2.5×10^7
2.0×10^7
1.5×10^7
1.0×10^7
5.0×10^6
0.0
-5.0×10^6
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (мд)


24d
2D ^{1}H-^{13}C HSQC
f2 (мд)
f1 (мд)

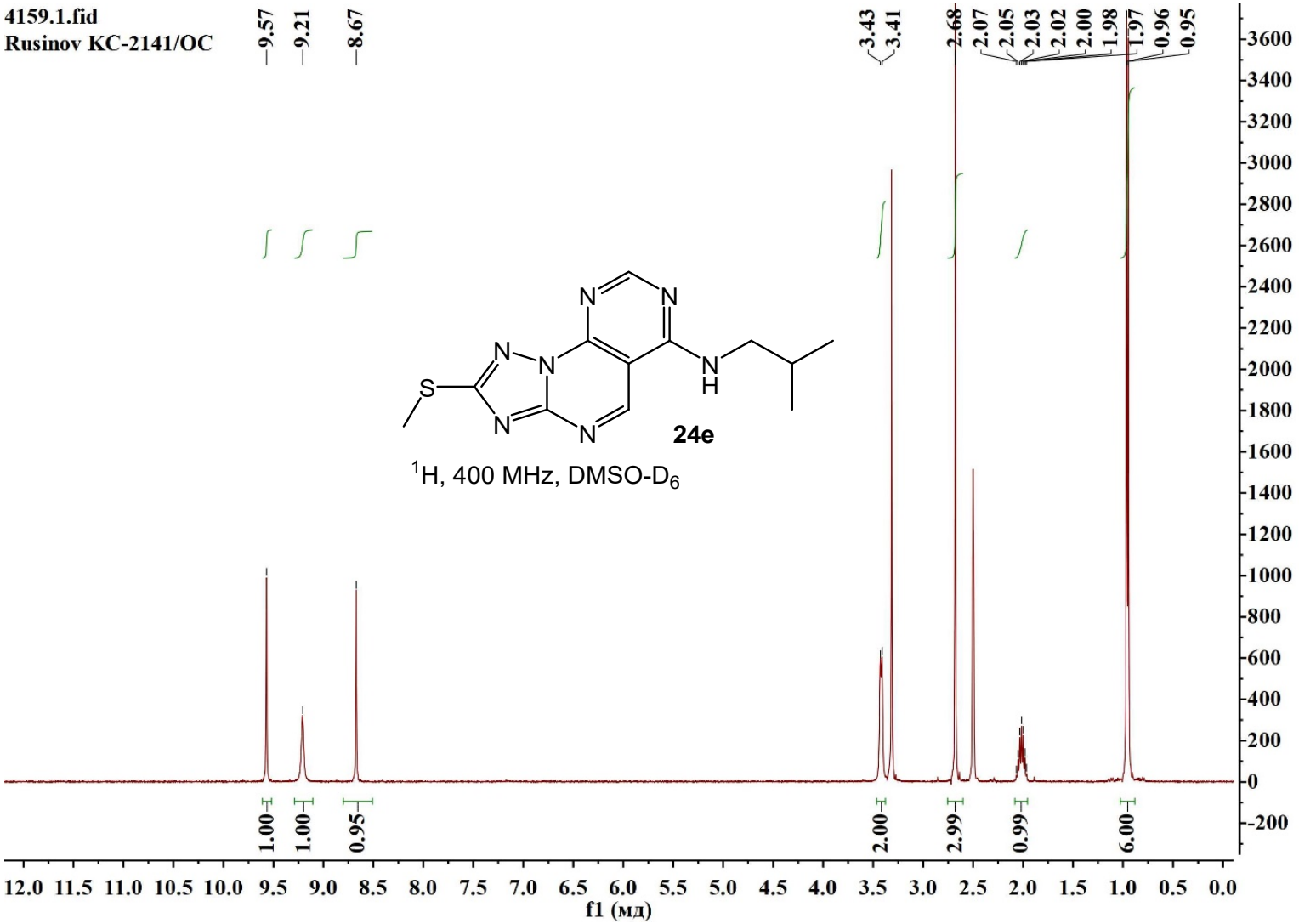

24d
2D ^{1}H-^{13}C HMBC
f2 (мд)
f1 (мд)

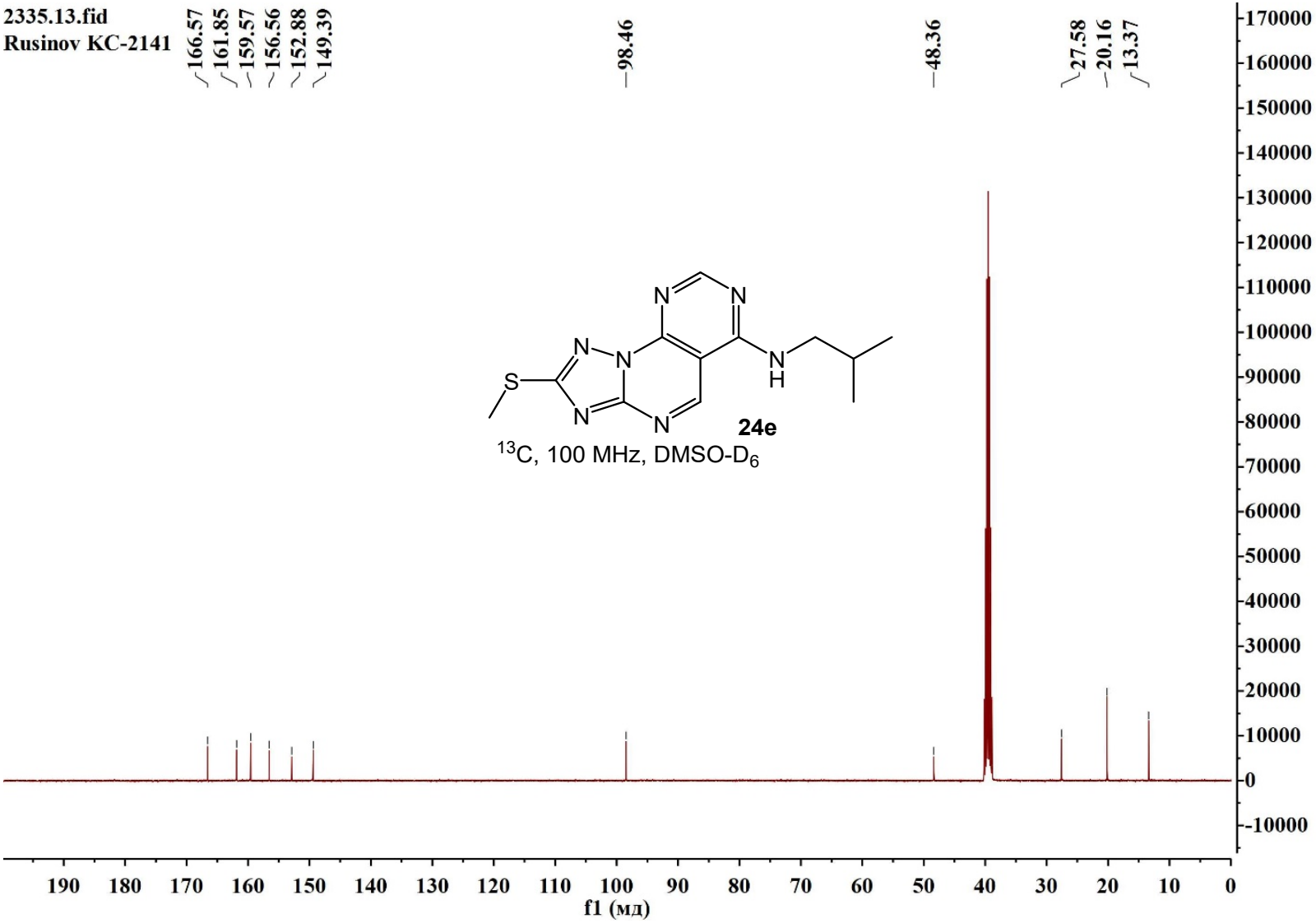

BRUKER
Transmittance [%]
100
95
90
85
80
75
3500
3000
2500
2000
1500
1000
500
Wavenumber cm-1
24d
IR
3280.64
3269.33
3198.65
3169.31
3139.65
3110.50
2958.95
2933.50
2871.75
2859.99
2342.42
1595.28
1571.15
1523.34
1451.86
1406.89
1387.93
1375.21
1357.11
1343.88
1320.81
1285.40
1247.17
1169.92
1113.44
1072.52
1054.60
1002.93
972.53
920.57
891.74
799.12
778.07
756.22
743.18
729.53
707.11
691.93
656.29
584.83
557.80
546.12
527.85
511.79

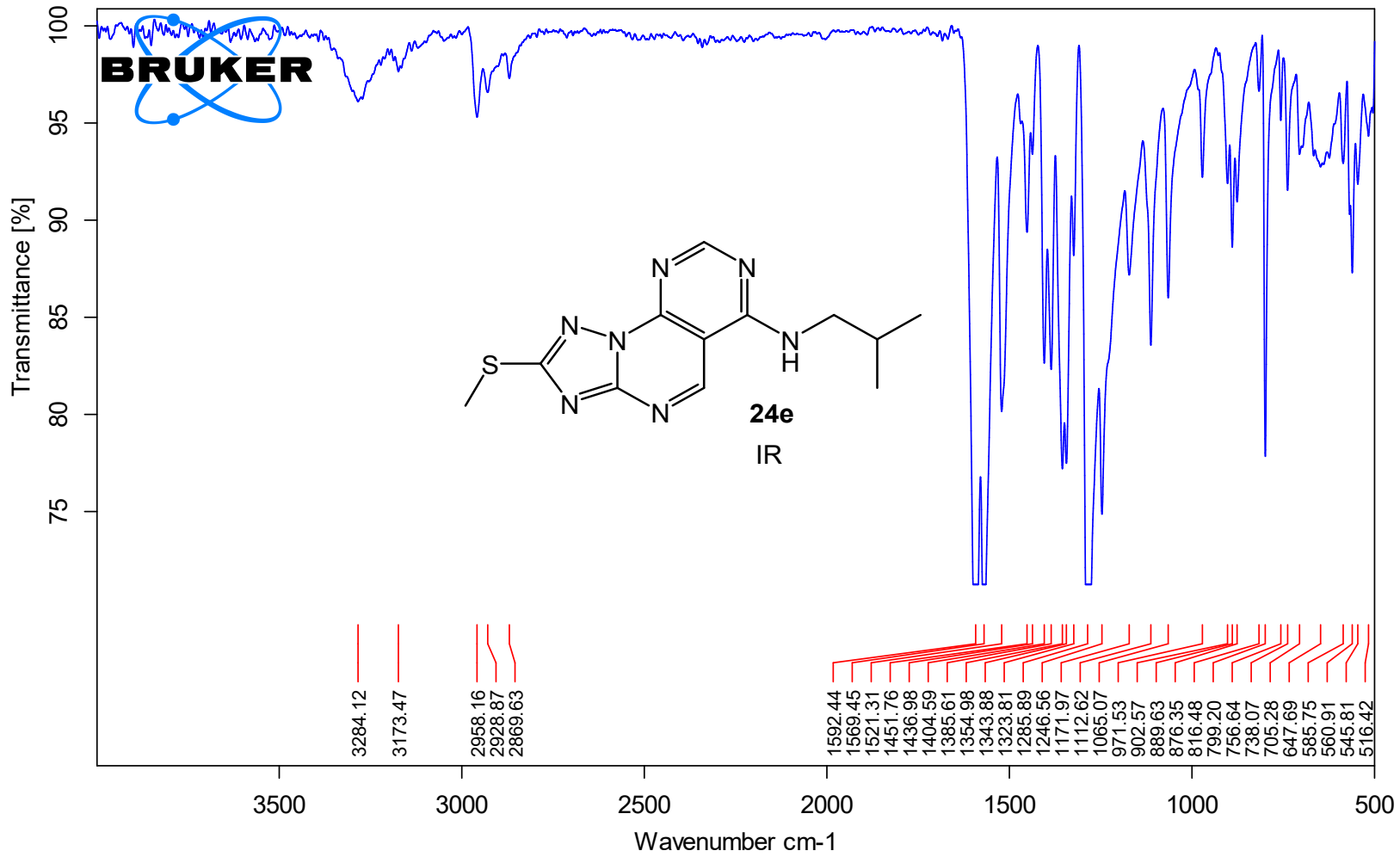
Line#:1 R.Time:2.432(Scan#:934)
MassPeaks:149
RawMode:Single 2.433(934) BasePeak:289(4675417)
Фон.реж.:1.357(504) Group 1 - Event 1



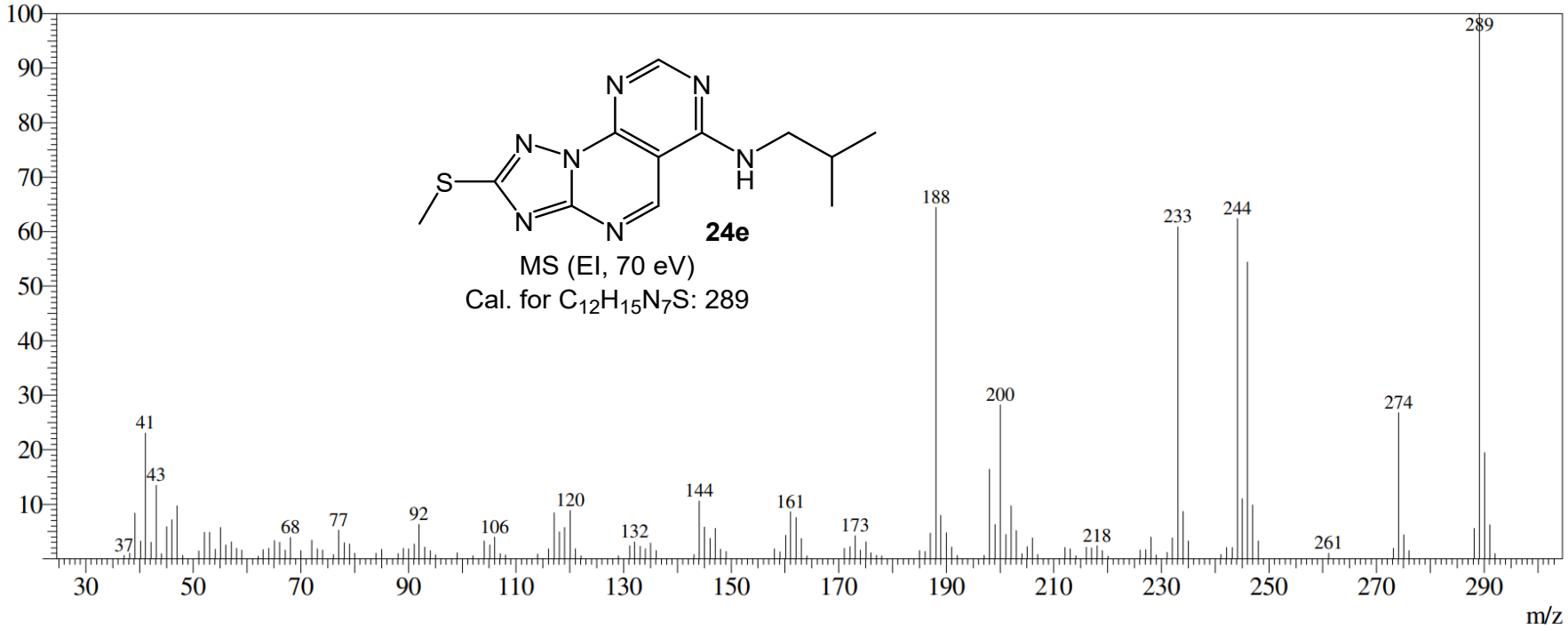
_N_-Isobutyl-2-(methylthio)pyrimido[5,4-_e_][1,2,4]triazolo[1,5-_a_]pyrimidin-6-amine (24e)



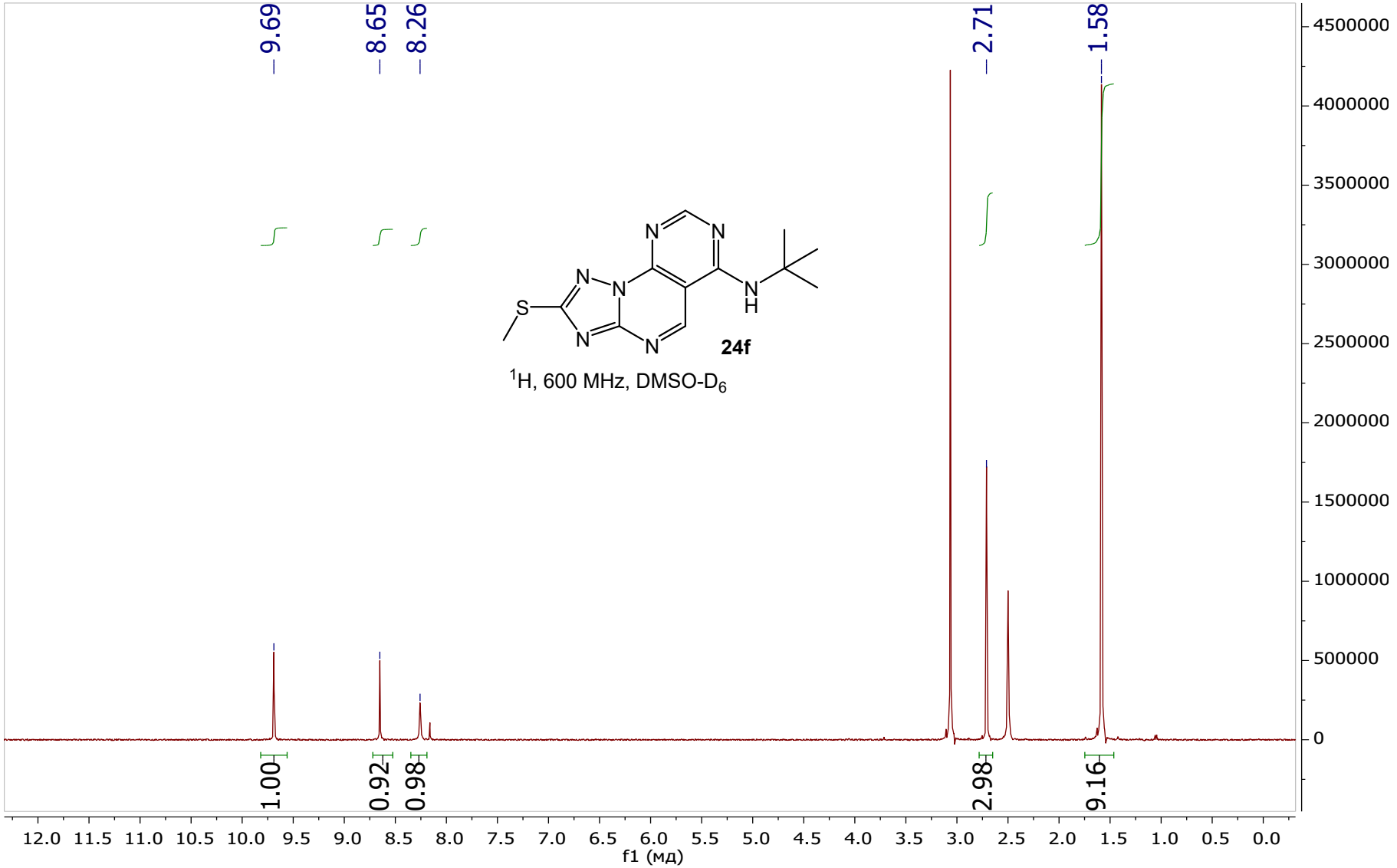

2335.13.fid
Rusinov KC-2141
166.57
161.85
159.57
156.56
152.88
149.39
98.46
48.36
27.58
20.16
13.37
24e
13C, 100 MHz, DMSO-D6
f1 (мд)

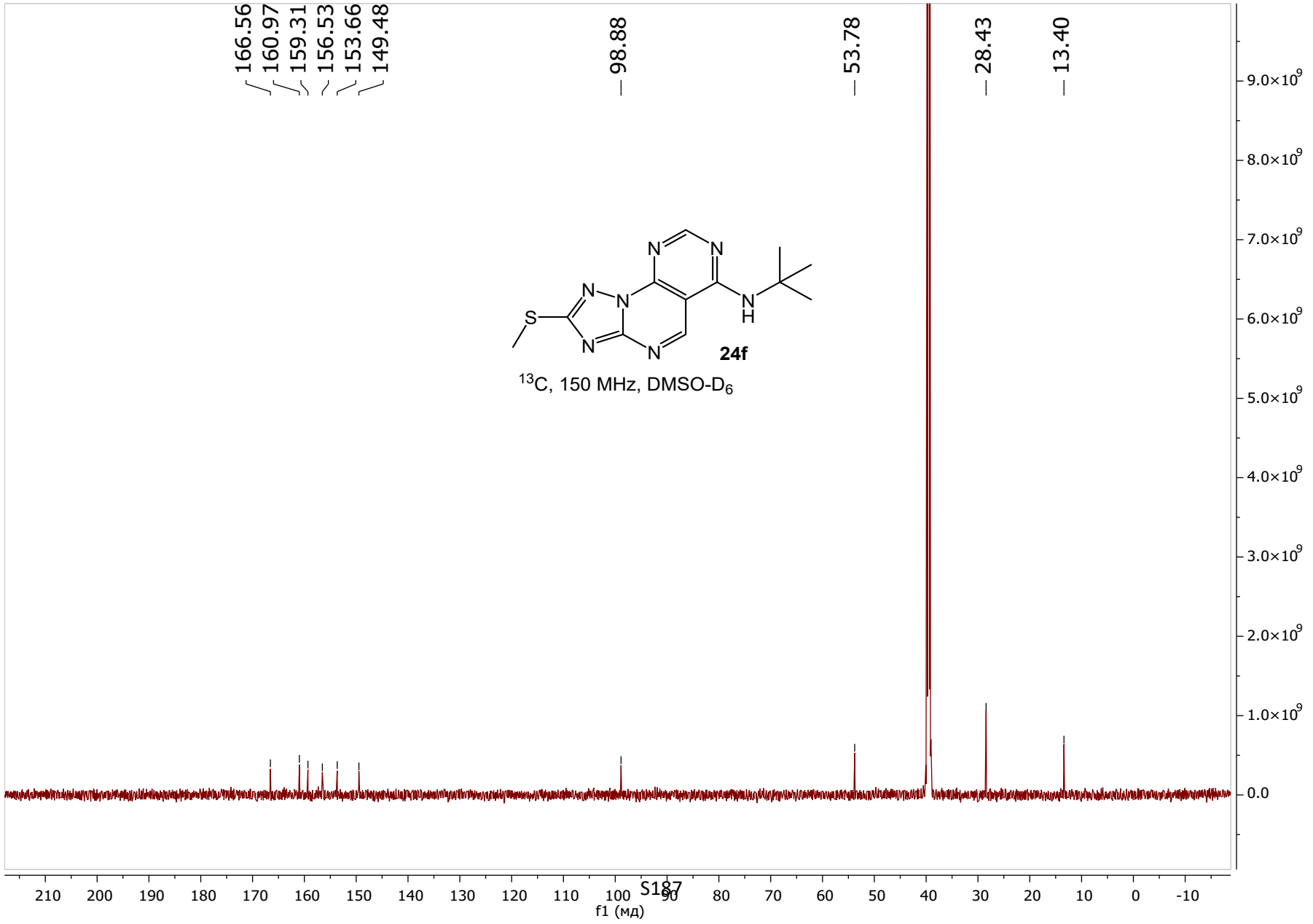

BRUKER
Transmittance [%]
100
95
90
85
80
75
3284.12
3173.47
2958.16
2928.87
2869.63
1592.44
1569.45
1521.31
1451.76
1436.98
1404.59
1385.61
1354.98
1343.88
1323.81
1285.89
1246.56
1171.97
1112.62
1065.07
971.53
902.57
889.63
876.35
816.48
799.20
756.64
738.07
705.28
647.69
585.75
560.91
545.81
516.42
3500
3000
2500
2000
1500
1000
500
Wavenumber cm-1
N
N
N
N
N
S
N
H
24e
IR

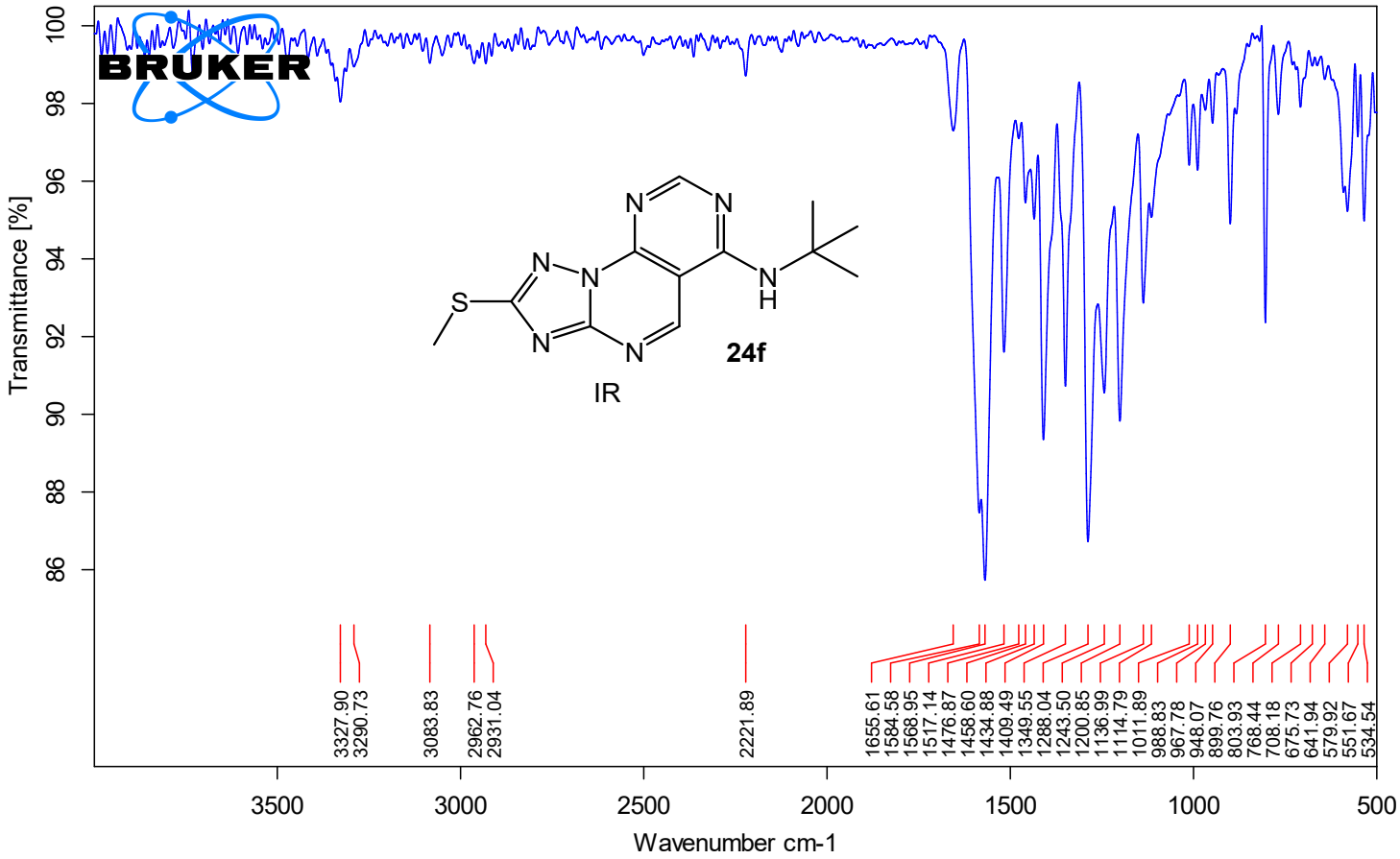
Line#:1 R.Time:2.498(Scan#:960)
MassPeaks:145
RawMode:Single 2.498(960) BasePeak:289(4354368)
Фон.реж.:1.388(516) Group 1 - Event 1



_N_-(_Tert_-butyl)-2-(methylthio)pyrimido[5,4-_e_][1,2,4]triazolo[1,5-_a_]pyrimidin-6-amine (24f)

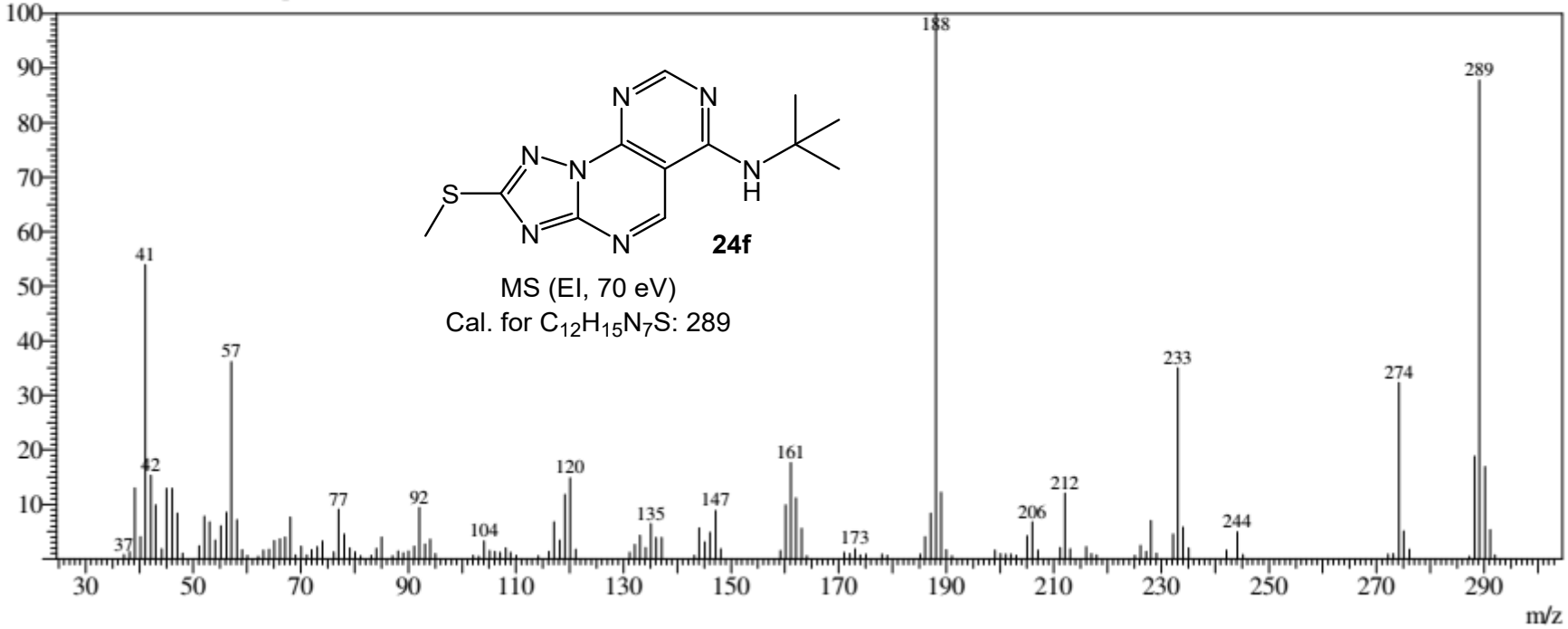



166.56
160.97
159.31
156.53
153.66
149.48
98.88
53.78
28.43
13.40
N
N
N
N
N
S
N
H
24f
^{13}C, 150 MHz, DMSO-D$_6$
9.0×10^9
8.0×10^9
7.0×10^9
6.0×10^9
5.0×10^9
4.0×10^9
3.0×10^9
2.0×10^9
1.0×10^9
0.0
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (мд)


BRUKER
Transmittance [%]
100
98
96
94
92
90
88
86
3500
3000
2500
2000
1500
1000
500
Wavenumber cm-1
3327.90
3290.73
3083.83
2962.76
2931.04
2221.89
1655.61
1584.58
1568.95
1517.14
1476.87
1458.60
1434.88
1409.49
1349.55
1288.04
1243.50
1200.85
1136.99
1114.79
1011.89
988.83
967.78
948.07
899.76
803.93
768.44
708.18
675.73
641.94
579.92
551.67
534.54
N
N
N
N
N
S
N
H
24f
IR

Page 1/1

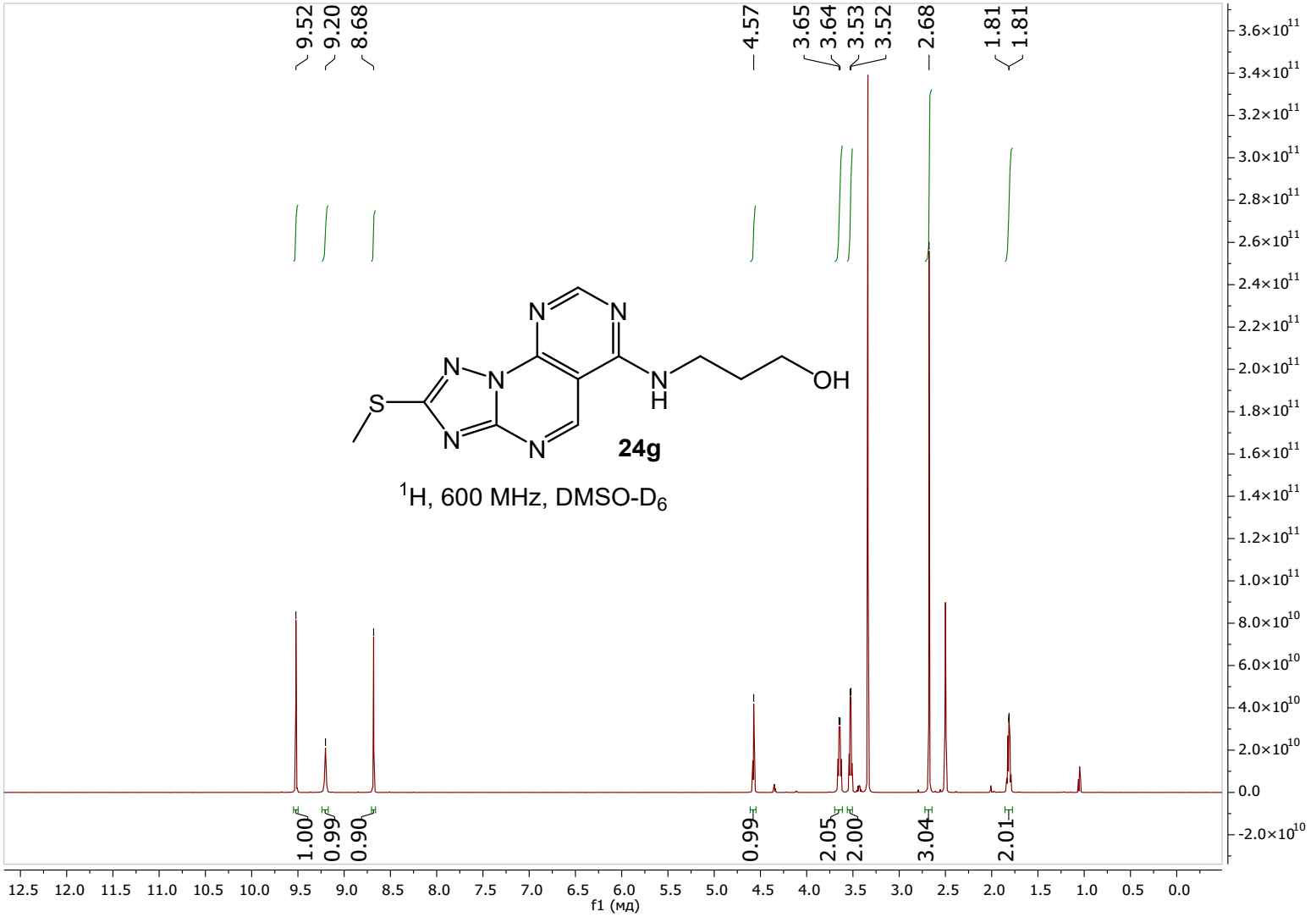
Line#:1 R.Time:2.340(Scan#:897)
MassPeaks:139
RawMode:Single 2.340(897) BasePeak:188(4455877)
Фон.реж.:0.765(267) Group 1 - Event 1

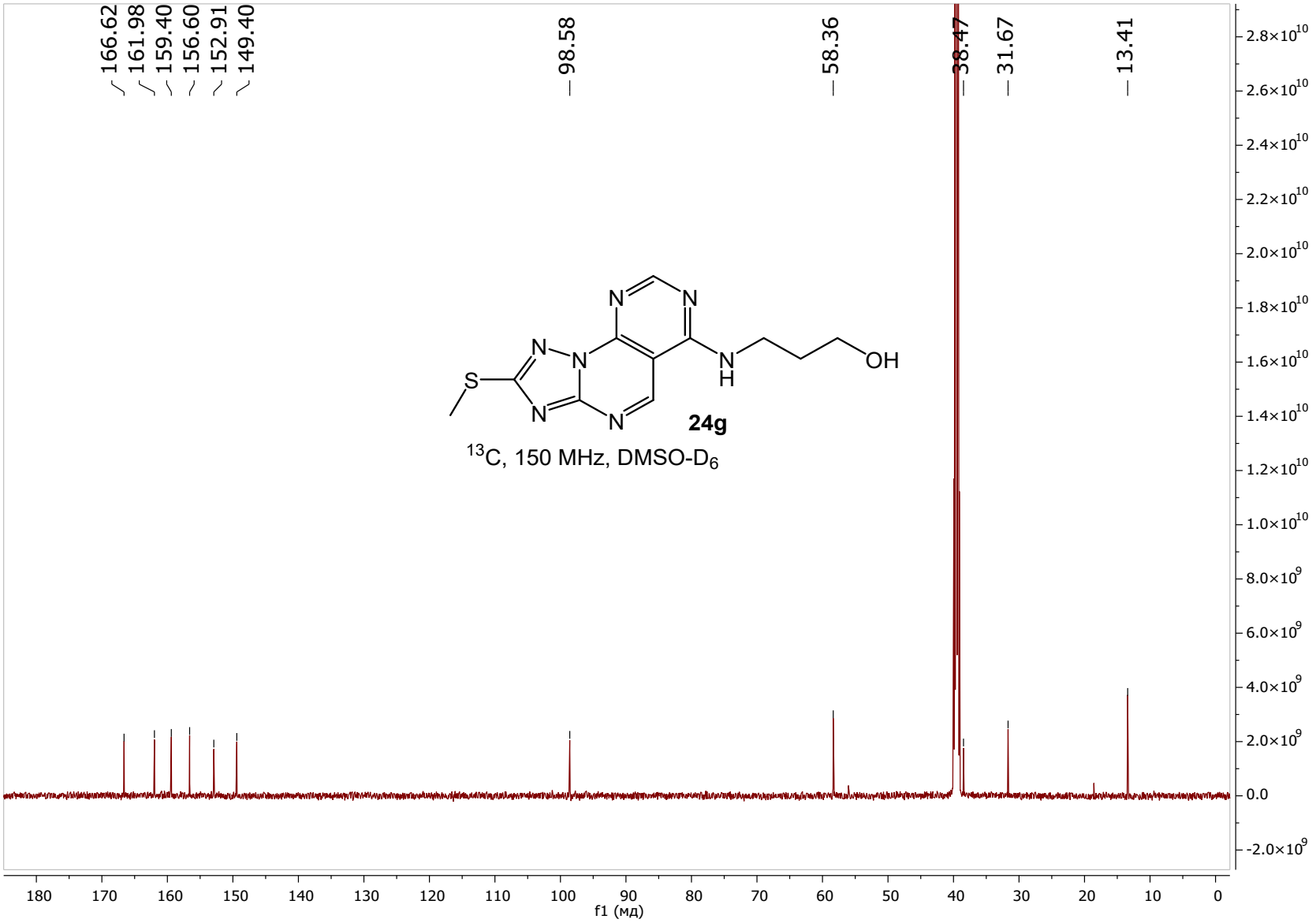


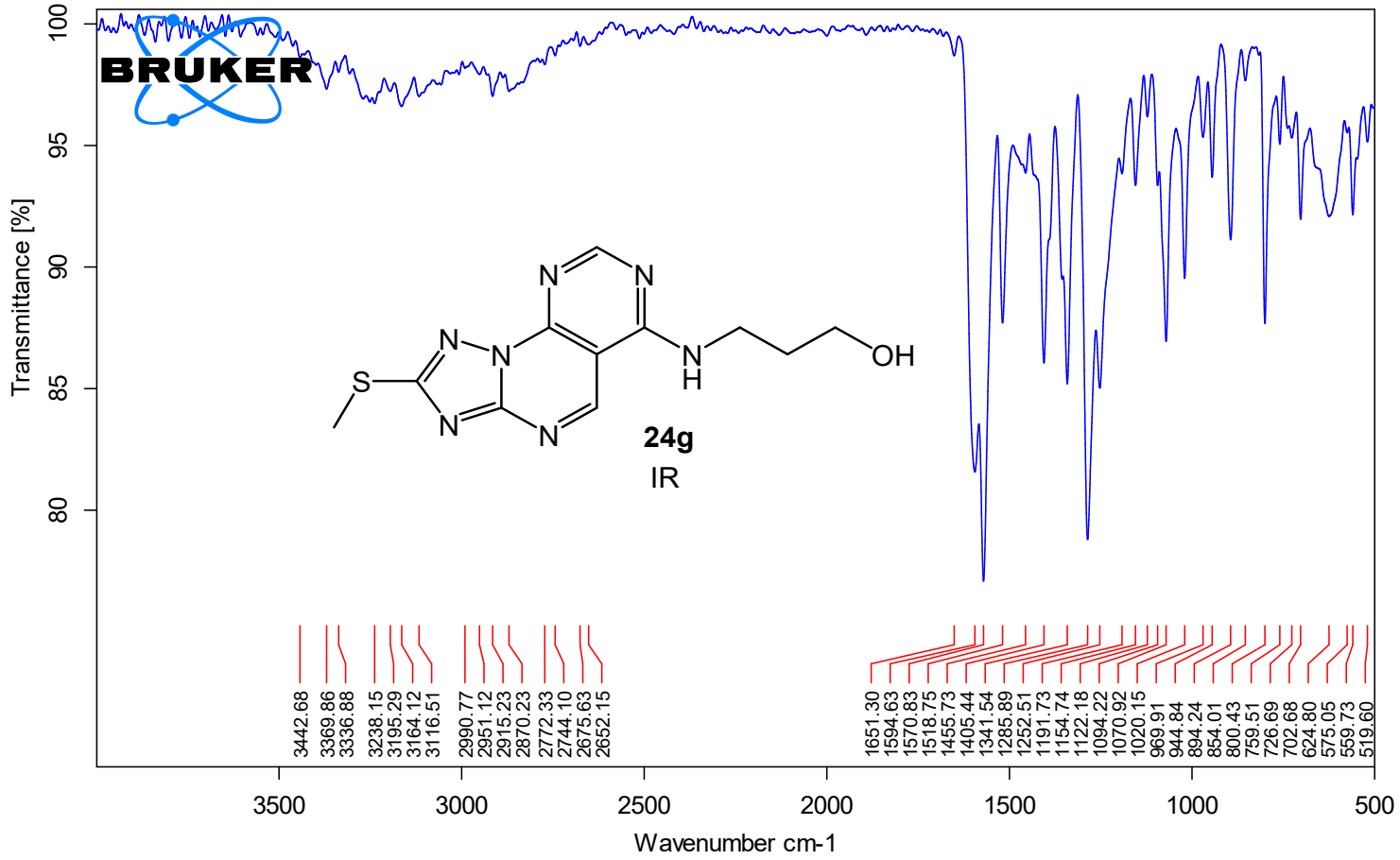
24f

MS (EI, 70 eV)
Cal. for $C_{12}H_{15}N_7S$: 289

3-((2-(Methylthio)pyrimido[5,4-*e*][1,2,4]triazolo[1,5-*a*]pyrimidin-6-yl)amino)propan-1-ol (24g)

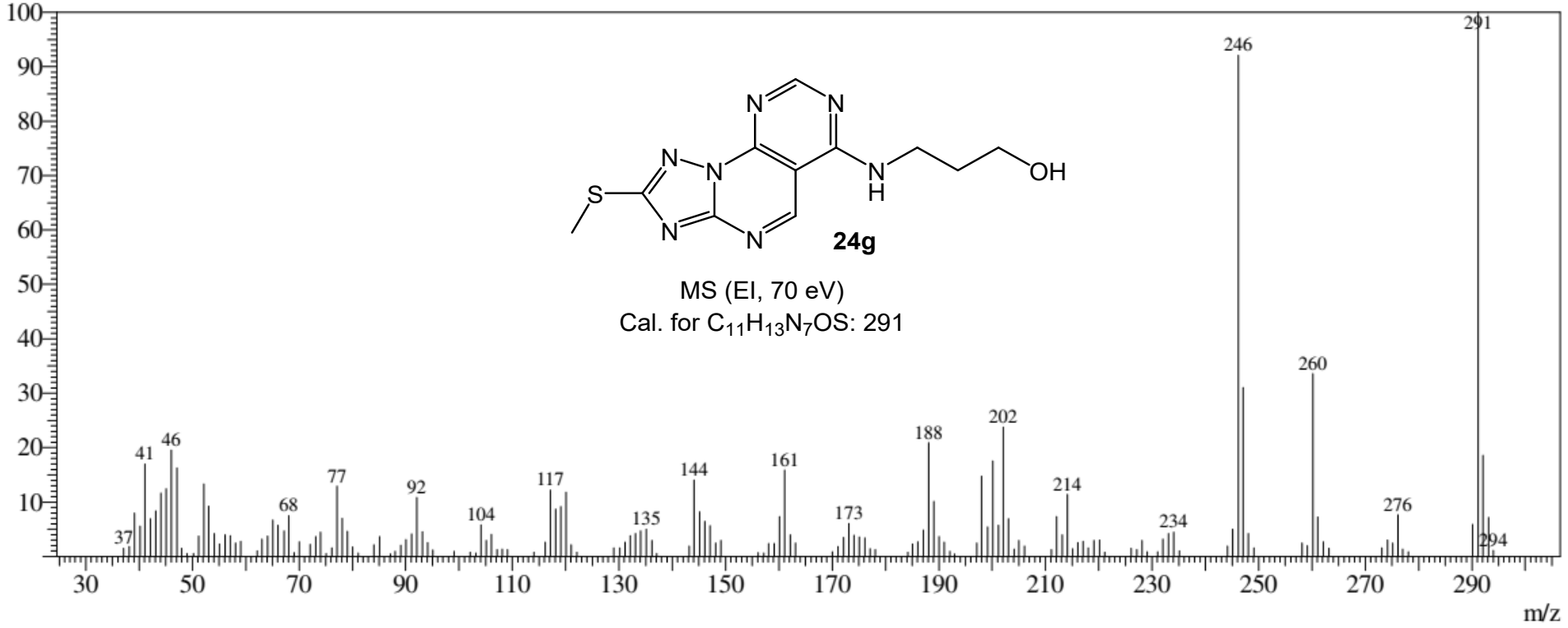



166.62
161.98
159.40
156.60
152.91
149.40
98.58
58.36
39.47
31.67
13.41
N
N
N
N
N
S
N
H
OH
24g
13C, 150 MHz, DMSO-D6
2.8×10^10
2.6×10^10
2.4×10^10
2.2×10^10
2.0×10^10
1.8×10^10
1.6×10^10
1.4×10^10
1.2×10^10
1.0×10^10
8.0×10^9
6.0×10^9
4.0×10^9
2.0×10^9
0.0
-2.0×10^9
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (мд)


BRUKER
Transmittance [%]
100
95
90
85
80
N
N
N
N
N
S
N
H
OH
24g
IR
3442.68
3369.86
3336.88
3238.15
3195.29
3164.12
3116.51
2990.77
2951.12
2915.23
2870.23
2772.33
2744.10
2675.63
2652.15
1651.30
1594.63
1570.83
1518.75
1455.73
1405.44
1341.54
1285.89
1252.51
1191.73
1154.74
1122.18
1094.22
1070.92
1020.15
969.91
944.84
894.24
854.01
800.43
759.51
726.69
702.68
624.80
575.05
559.73
519.60
3500
3000
2500
2000
1500
1000
500
Wavenumber cm-1

Page 1/1

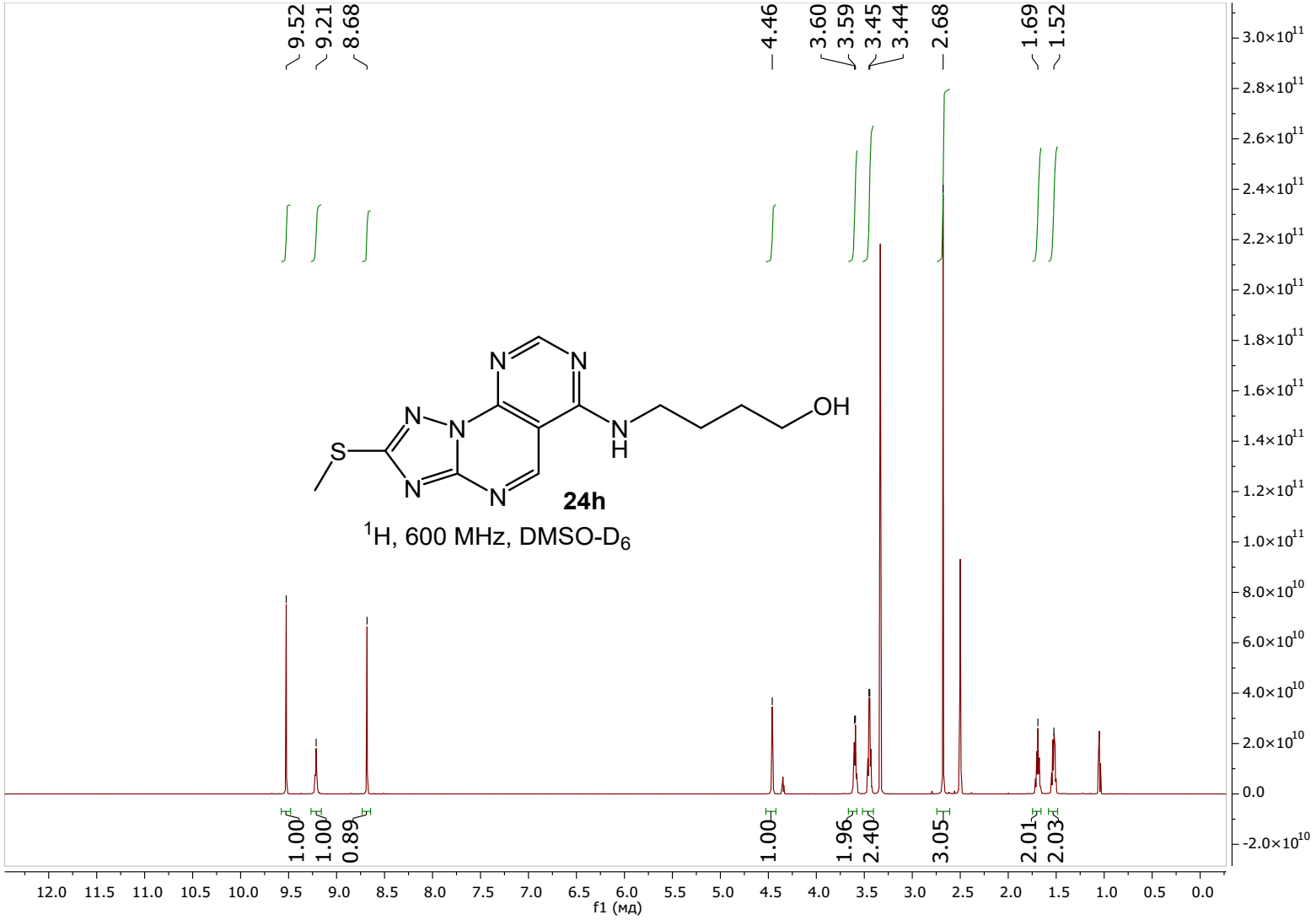
Line#:1 R.Time:3.170(Scan#:1229)
MassPeaks:166
RawMode:Single 3.170(1229) BasePeak:291(623971)
Фон.реж.:2.650(1021) Group 1 - Event 1

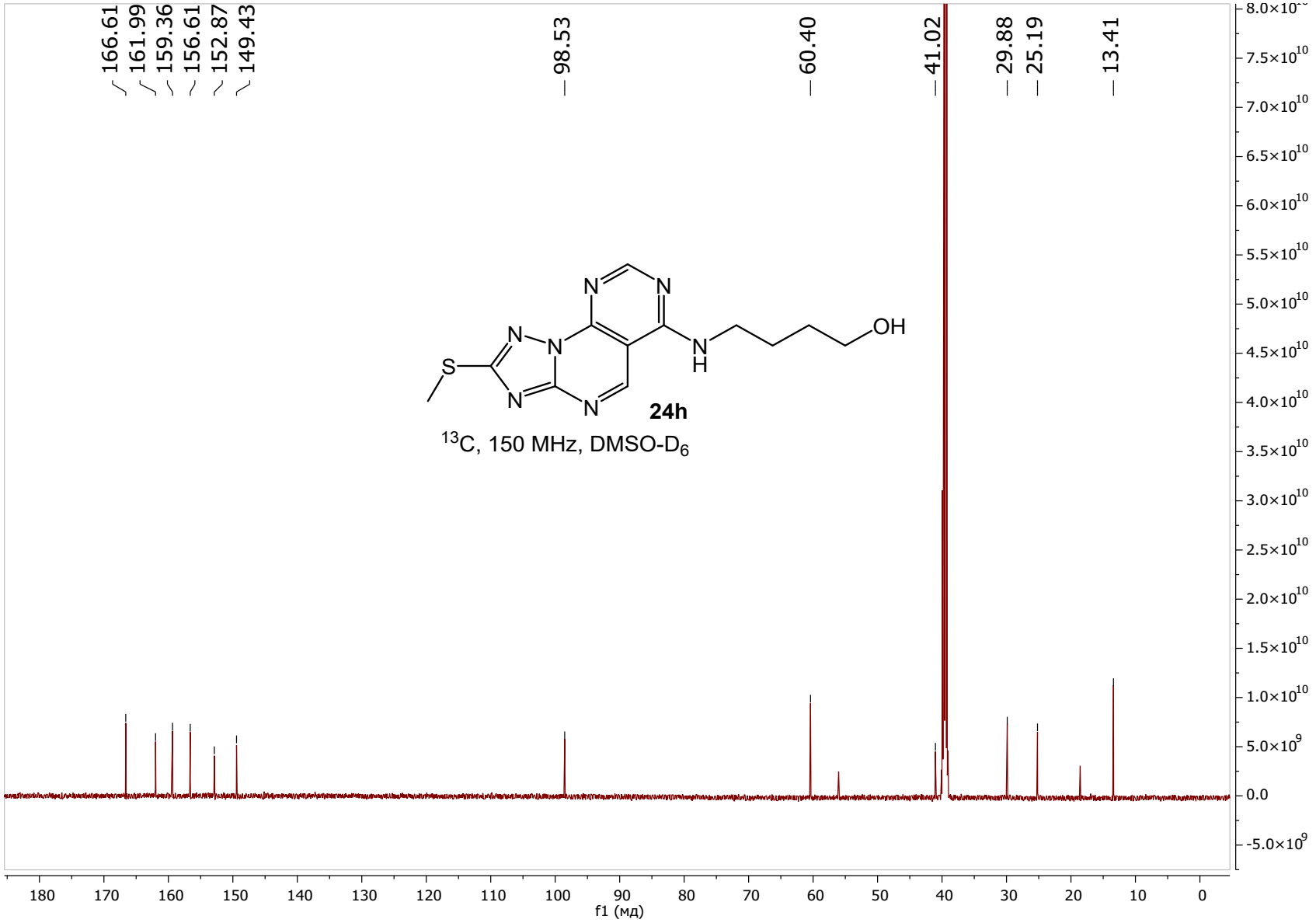


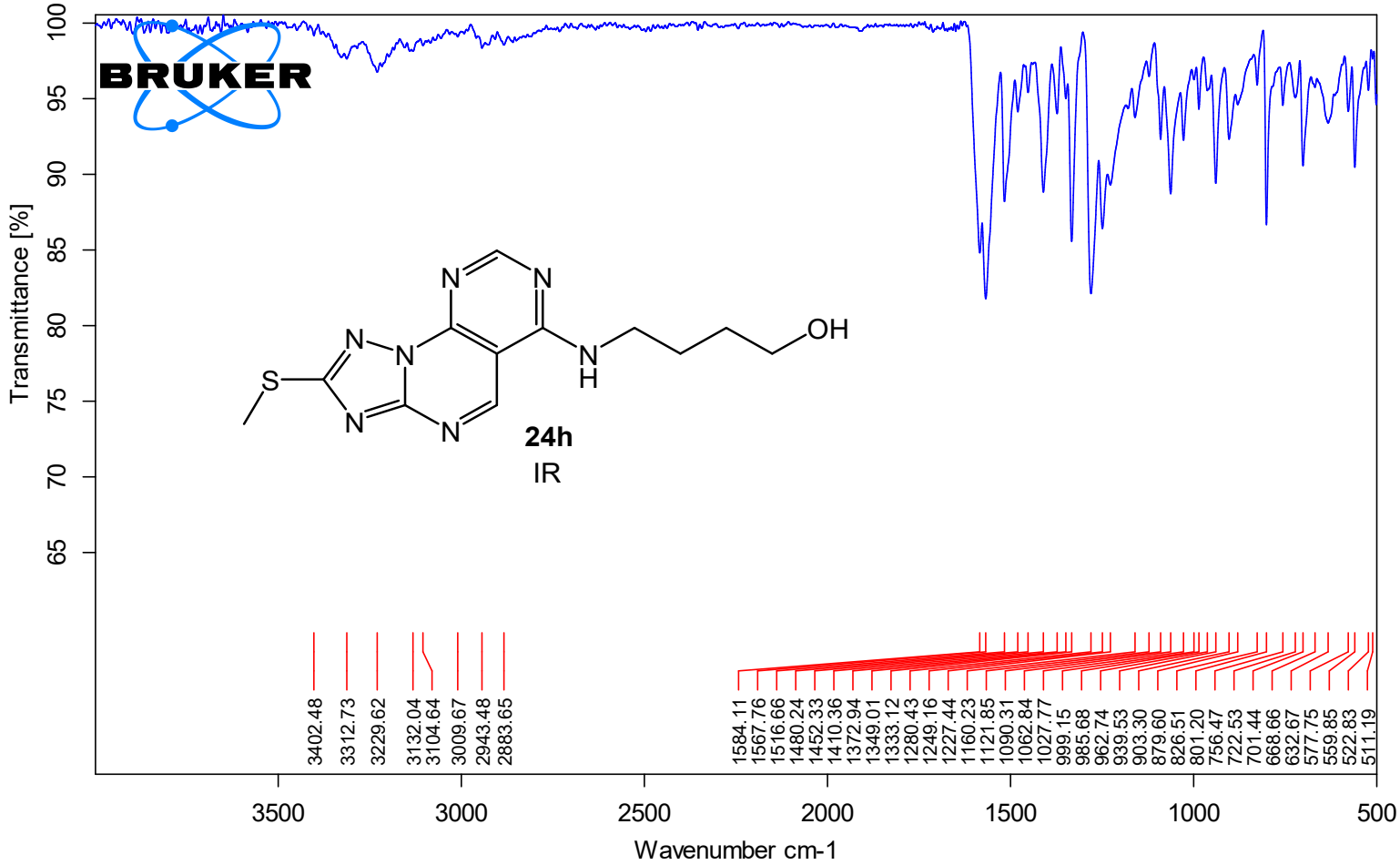
24g

MS (EI, 70 eV)
Cal. for $C_{11}H_{13}N_7OS$: 291

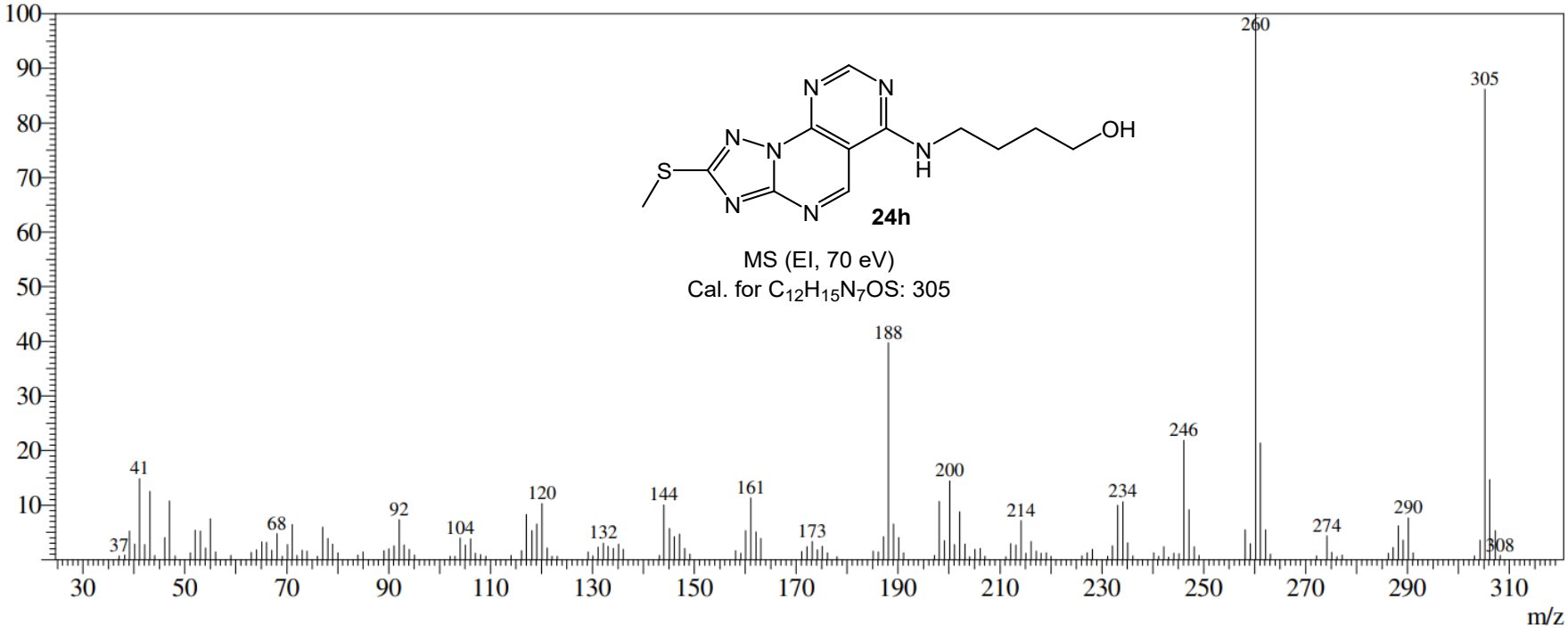
4-((2-(Methylthio)pyrimido[5,4-*e*][1,2,4]triazolo[1,5-*a*]pyrimidin-6-yl)amino)butan-1-ol (24h)




166.61
161.99
159.36
156.61
152.87
149.43
98.53
60.40
41.02
29.88
25.19
13.41
N
N
N
N
N
S
N
H
OH
24h
13C, 150 MHz, DMSO-D6
8.0×10
7.5×10^10
7.0×10^10
6.5×10^10
6.0×10^10
5.5×10^10
5.0×10^10
4.5×10^10
4.0×10^10
3.5×10^10
3.0×10^10
2.5×10^10
2.0×10^10
1.5×10^10
1.0×10^10
5.0×10^9
0.0
-5.0×10^9
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (мд)

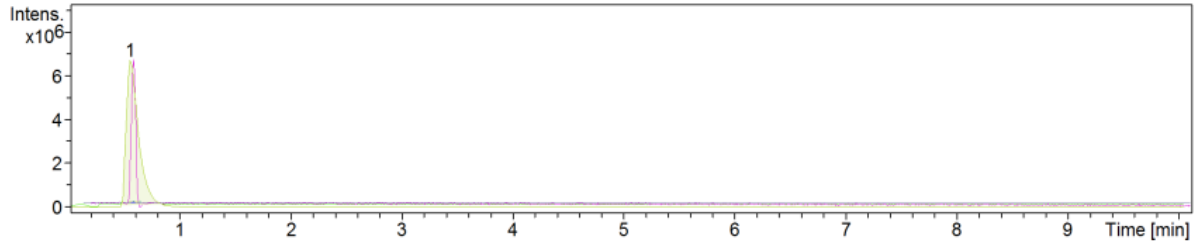

BRUKER
Transmittance [%]
100
95
90
85
80
75
70
65
N
N
N
N
N
N
S
OH
H
24h
IR
3402.48
3312.73
3229.62
3132.04
3104.64
3009.67
2943.48
2883.65
1584.11
1567.76
1516.66
1480.24
1452.33
1410.36
1372.94
1349.01
1333.12
1280.43
1249.16
1227.44
1160.23
1121.85
1090.31
1062.84
1027.77
999.15
985.68
962.74
939.53
903.30
879.60
826.51
801.20
756.47
722.53
701.44
668.66
632.67
577.75
559.85
522.83
511.19
3500
3000
2500
2000
1500
1000
500
Wavenumber cm-1

Line#:1 R.Time:4.960(Scan#:1945)
MassPeaks:159
RawMode:Single 4.960(1945) BasePeak:260(1164210)
Фон.реж.:4.345(1699) Group 1 - Event 1



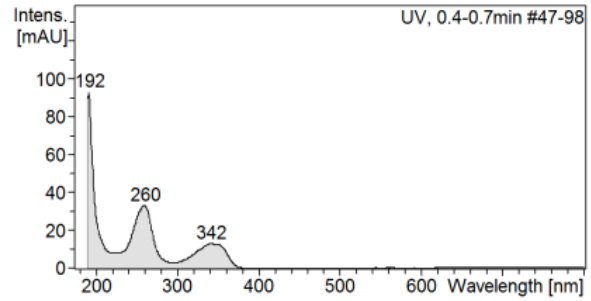
Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.3 Bar
Focus	Active	Set Capillary	3500 V	Set Dry Heater	200 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	4.0 l/min
Scan End	1400 m/z	Set Charging Voltage	2000 V	Set Divert Valve	Source
		Set Corona	0 nA	Set APCI Heater	0 °C

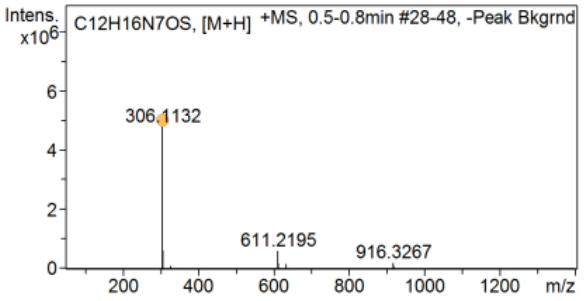


#	RT [min]	Area	Int. Type	I	S/N	Chromatogram	Max. m/z	FWHM [min]
1	0.6	49257304	Manual	6647376	44584.3	EIC 306.1132±0.005 +All MS	306.1132	

Cmpd 1, 0.6 min

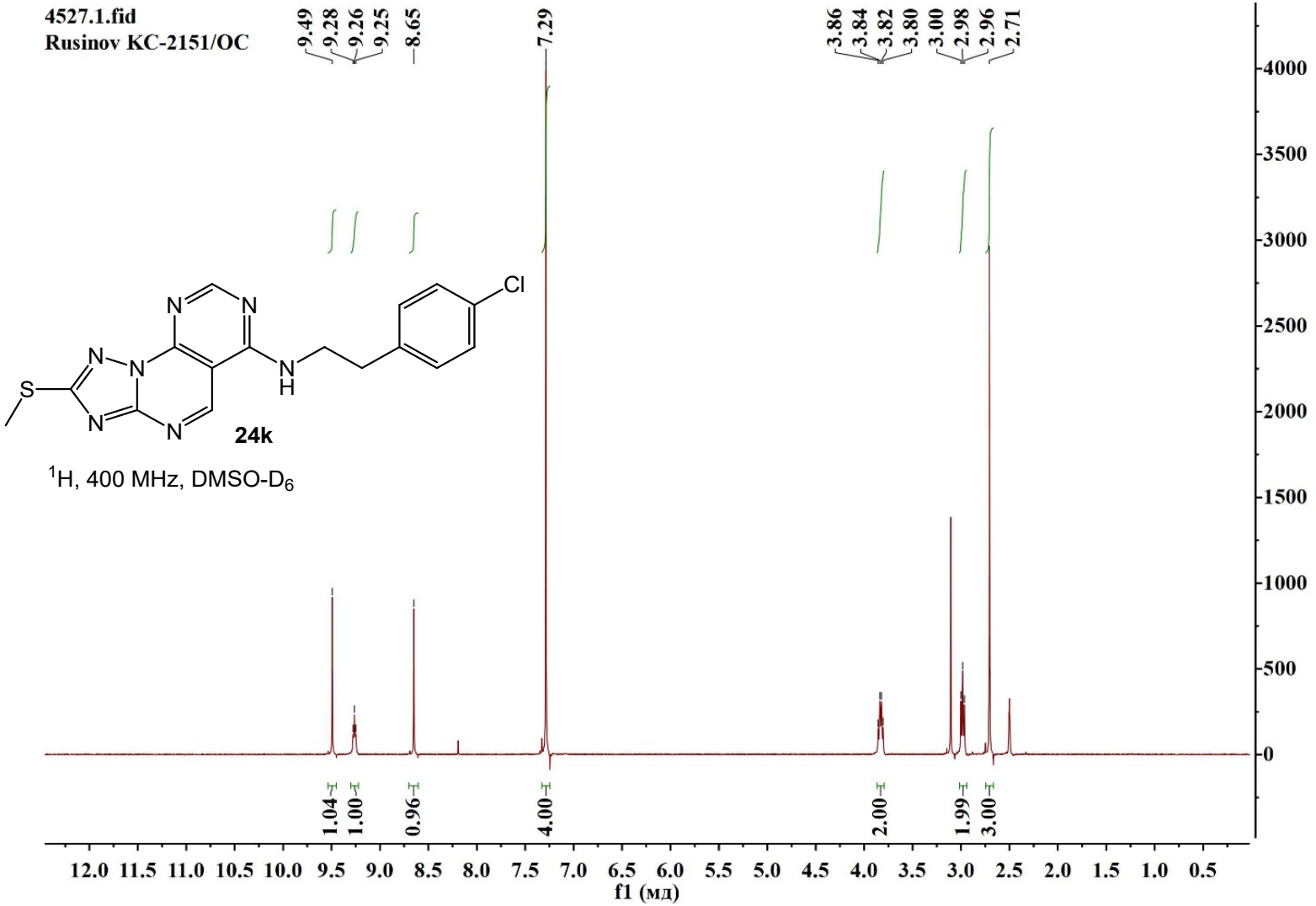


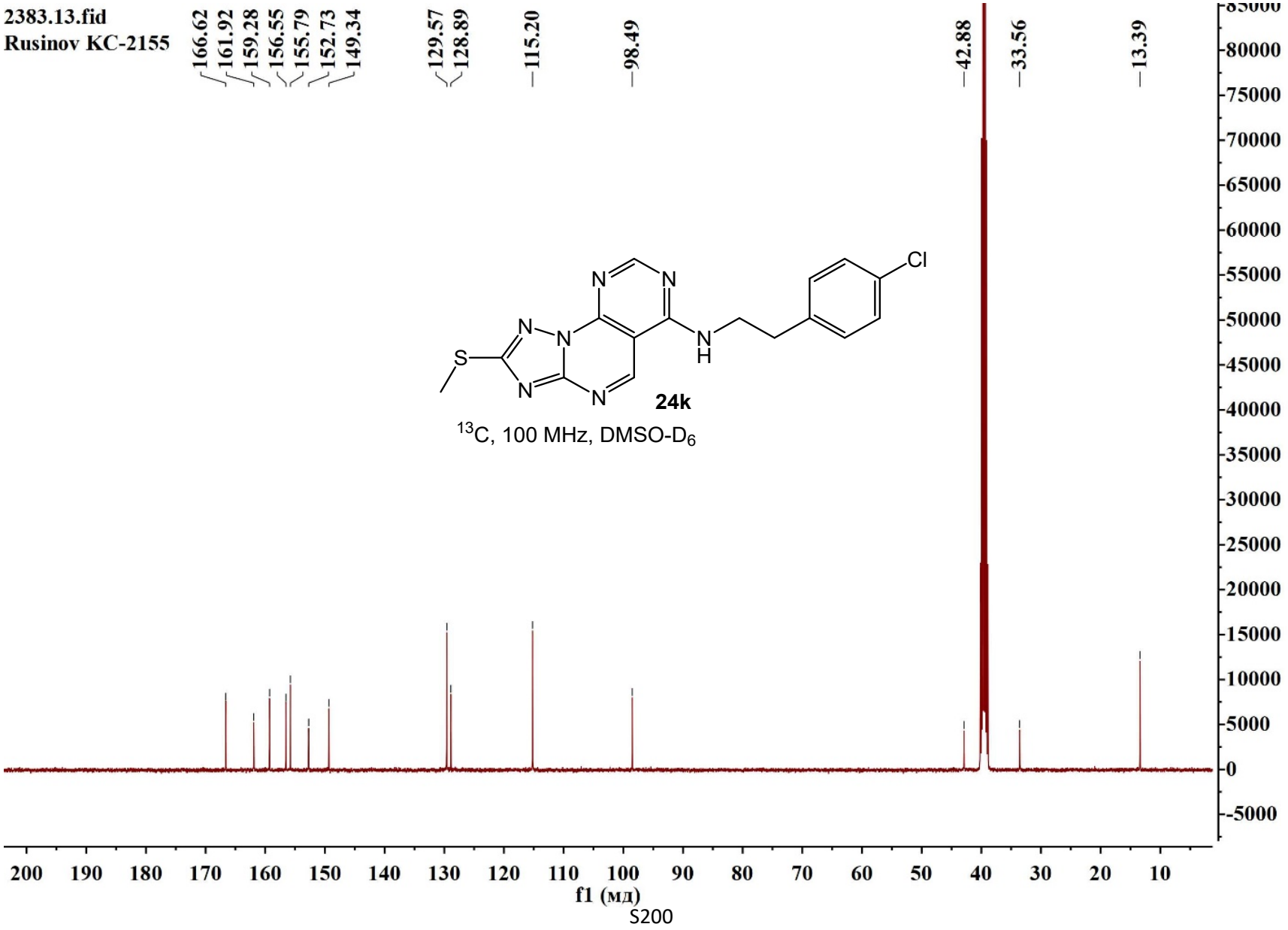
#	Wavelength	Intensity
0	192	92.7
1	260	33.3
2	342	13.1

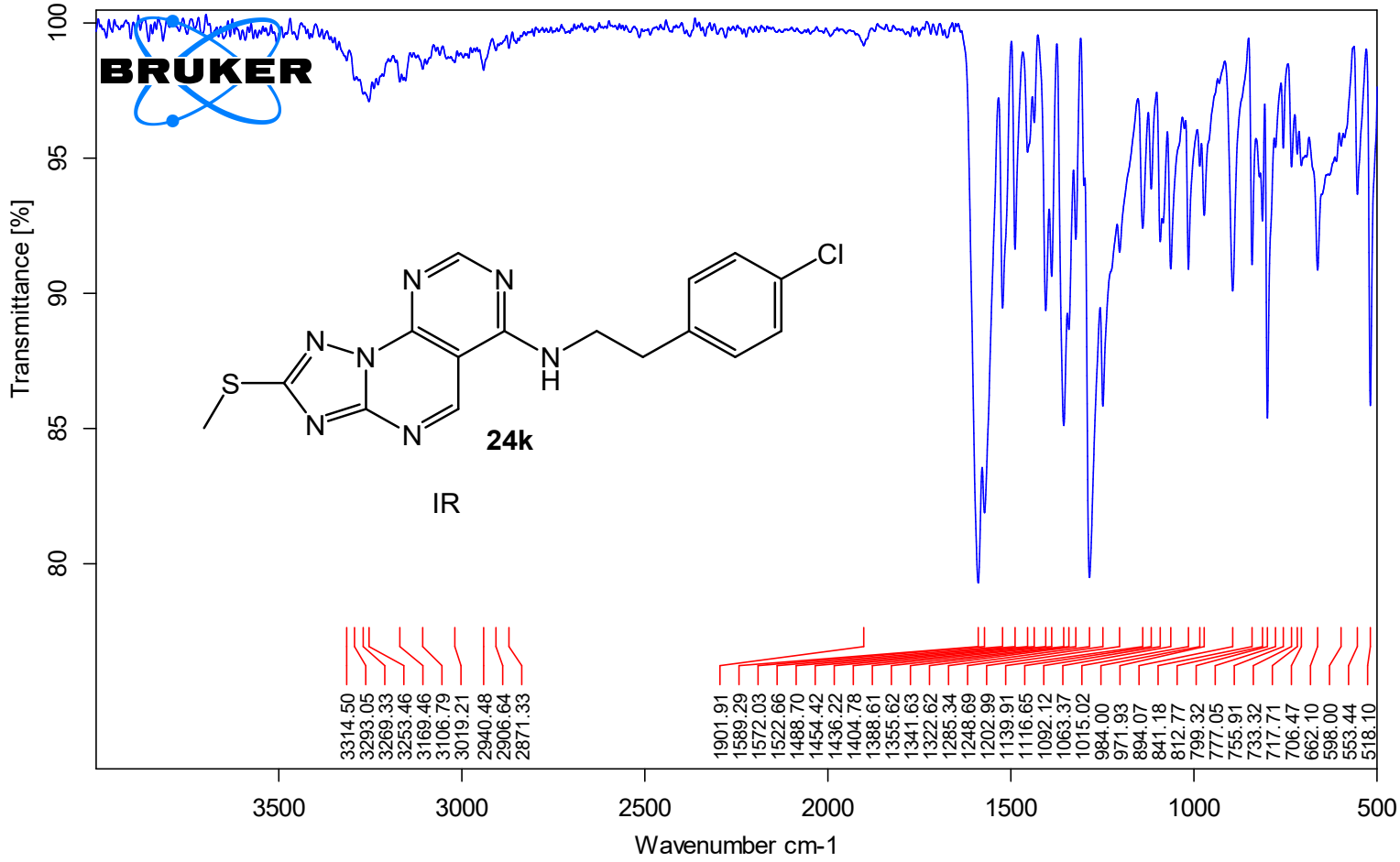


#	m/z	Res.	S/N	I	I %	FWHM
1	306.1132	33974	536240448.0	4758054	100.0	0.0090
2	307.1156	24638	67519376.0	599099	12.6	0.0125
3	308.1104	18780	21182608.0	187953	4.0	0.0164
4	328.0947	20405	9678586.0	85878	1.8	0.0161
5	611.2195	29803	66112336.0	586614	12.3	0.0205
6	612.2216	22944	20257160.0	179742	3.8	0.0267
7	613.2182	19617	8664569.0	76881	1.6	0.0313
8	633.2011	22502	18168052.0	161205	3.4	0.0281
9	916.3267	28494	21172970.0	187867	3.9	0.0322
10	917.3287	24510	10441449.0	92647	1.9	0.0374

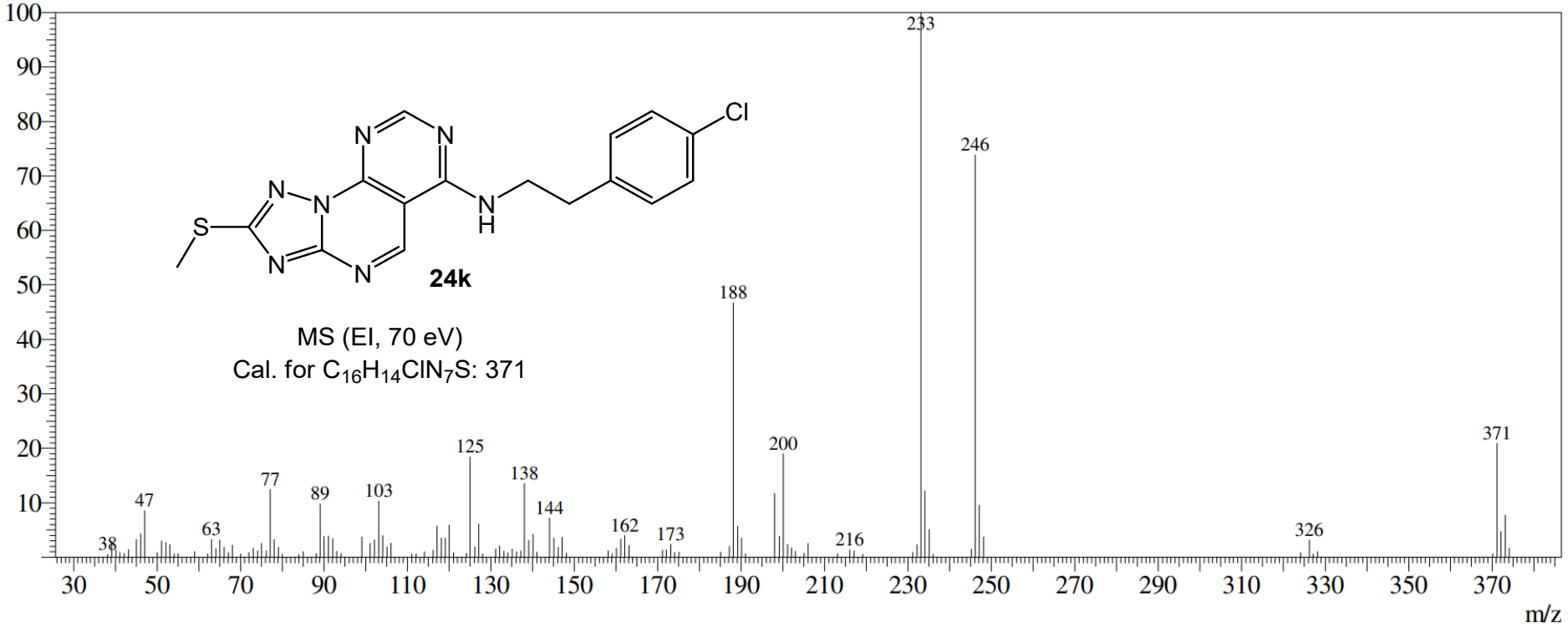
_N_-(4-Chlorophenethyl)-2-(methylthio)pyrimido[5,4-_e_][1,2,4]triazolo[1,5-_a_]pyrimidin-6-amine (24k)



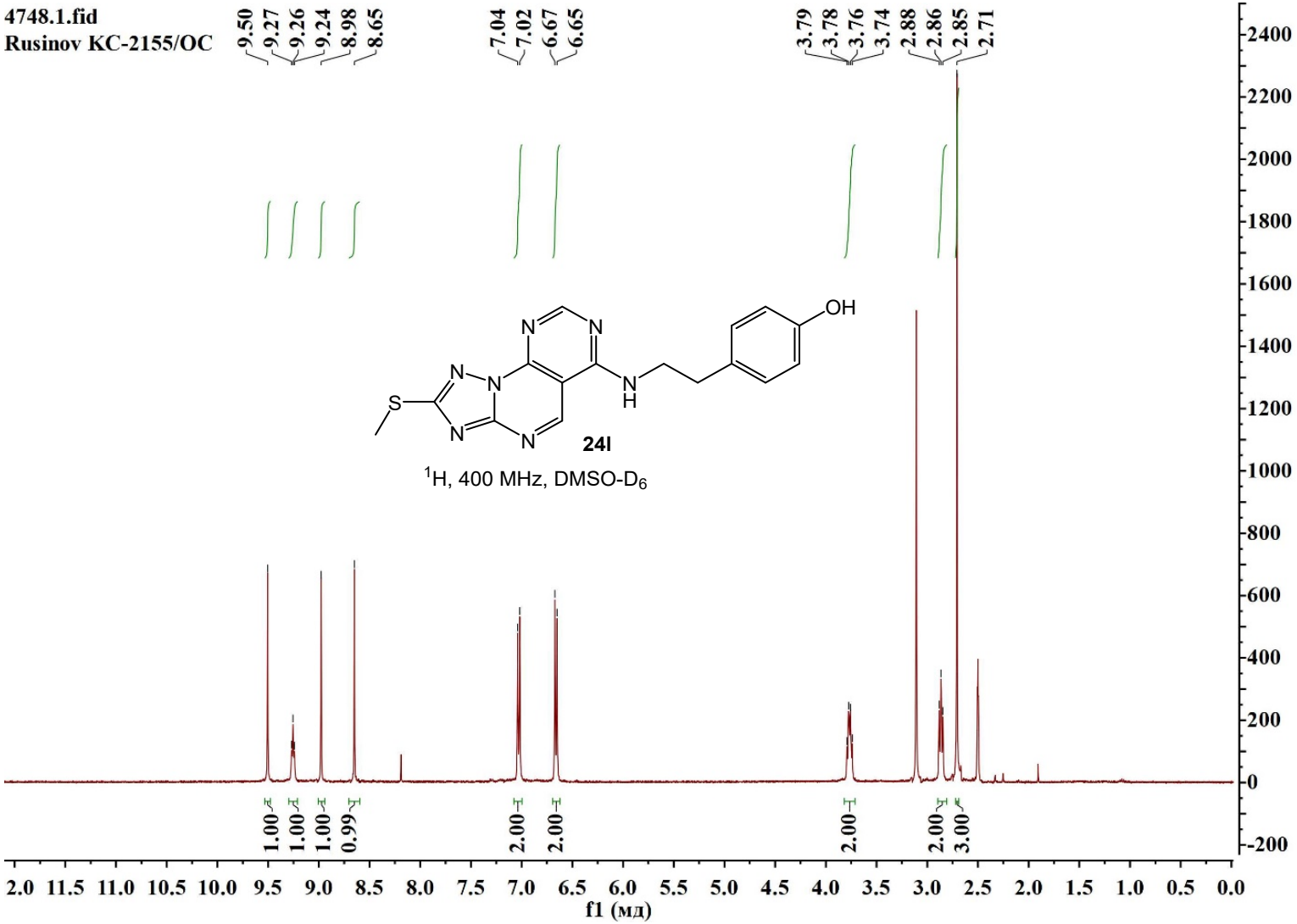

2383.13.fid
Rusinov KC-2155
166.62
161.92
159.28
156.55
155.79
152.73
149.34
129.57
128.89
115.20
98.49
42.88
33.56
13.39
Cl
N
N
N
N
N
N
S
N
H
24k
^{13}C, 100 MHz, DMSO-D$_6$
f1 (мд)

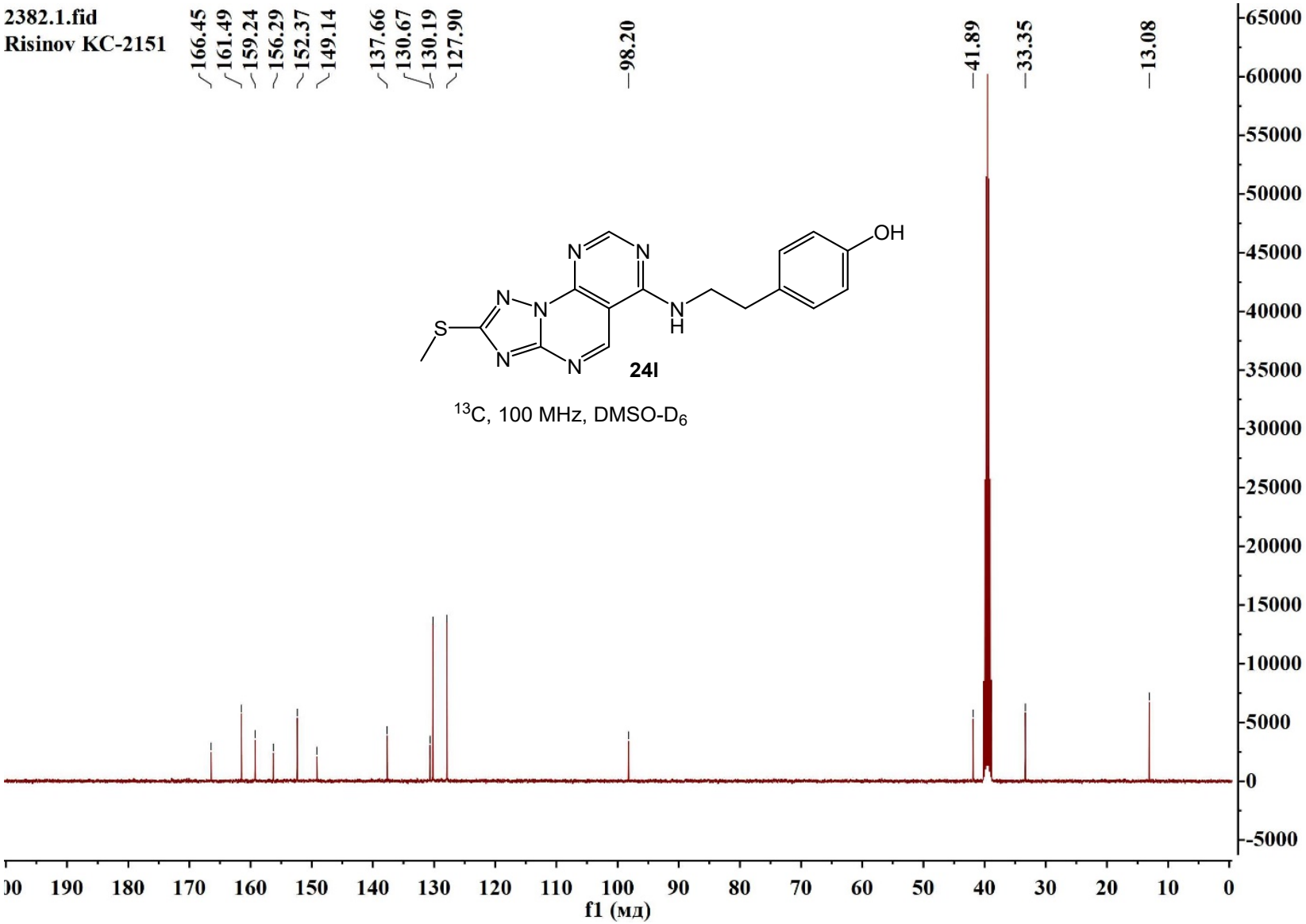

BRUKER
Transmittance [%]
100
95
90
85
80
Cl
N
N
N
N
N
S
H
24k
IR
3314.50
3293.05
3269.33
3253.46
3169.46
3106.79
3019.21
2940.48
2906.64
2871.33
1901.91
1589.29
1572.03
1522.66
1488.70
1454.42
1436.22
1404.78
1388.61
1355.62
1341.63
1322.62
1285.34
1248.69
1202.99
1139.91
1116.65
1092.12
1063.37
1015.02
984.00
971.93
894.07
841.18
812.77
799.32
777.05
755.91
733.32
717.71
706.47
662.10
598.00
553.44
518.10
3500
3000
2500
2000
1500
1000
500
Wavenumber cm-1

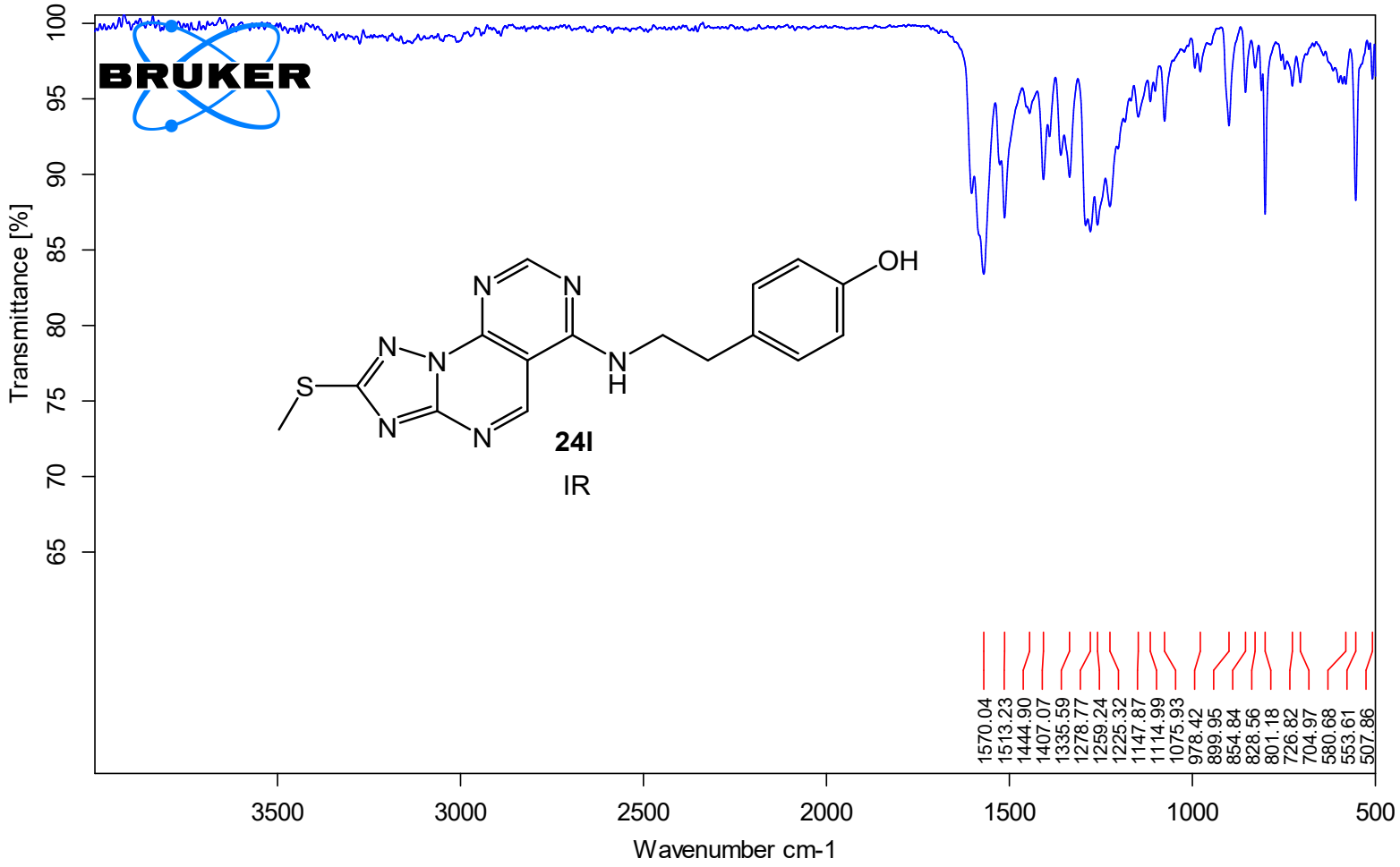
Line#:1 R.Time:3.553(Scan#:1382)
MassPeaks:127
RawMode:Single 3.553(1382) BasePeak:233(3234623)
Фон.реж.:2.507(964) Group 1 - Event 1



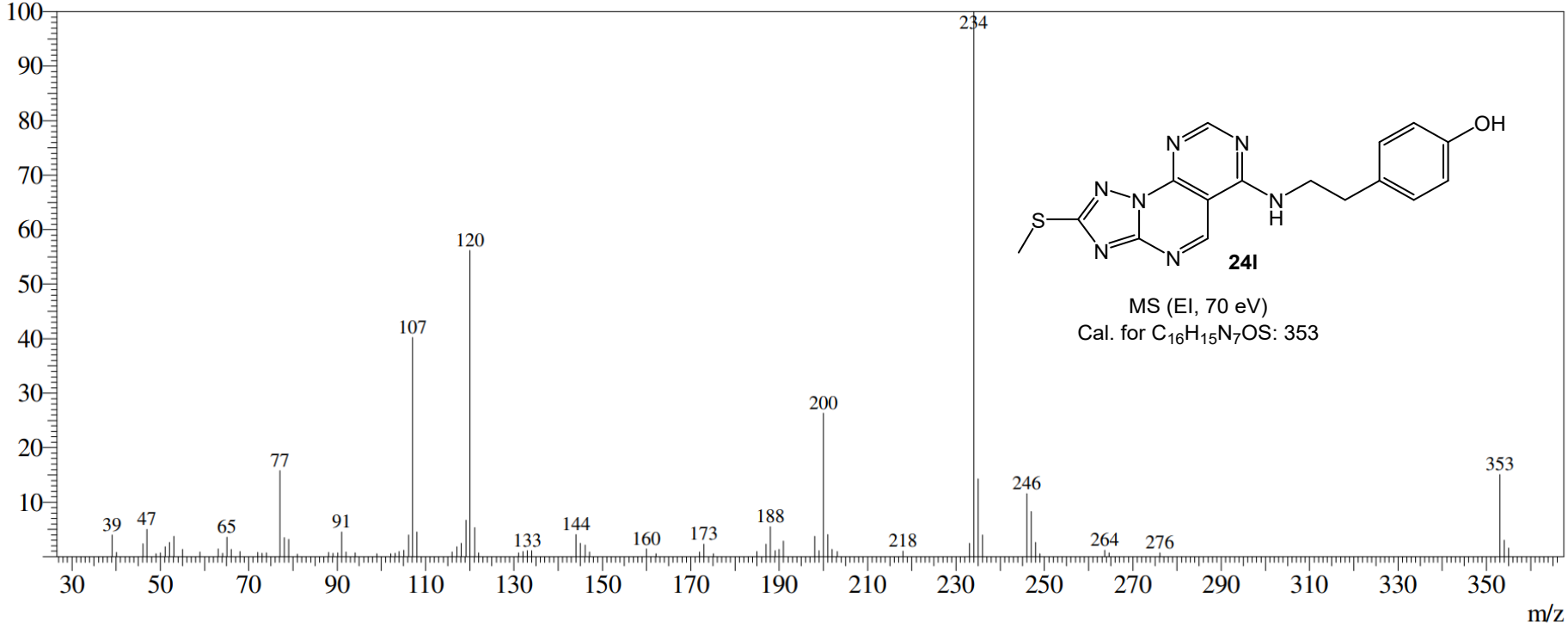
4-(2-((2-(Methylthio)pyrimido[5,4-*e*][1,2,4]triazolo[1,5-*a*]pyrimidin-6-yl)amino)ethyl)phenol (24l)



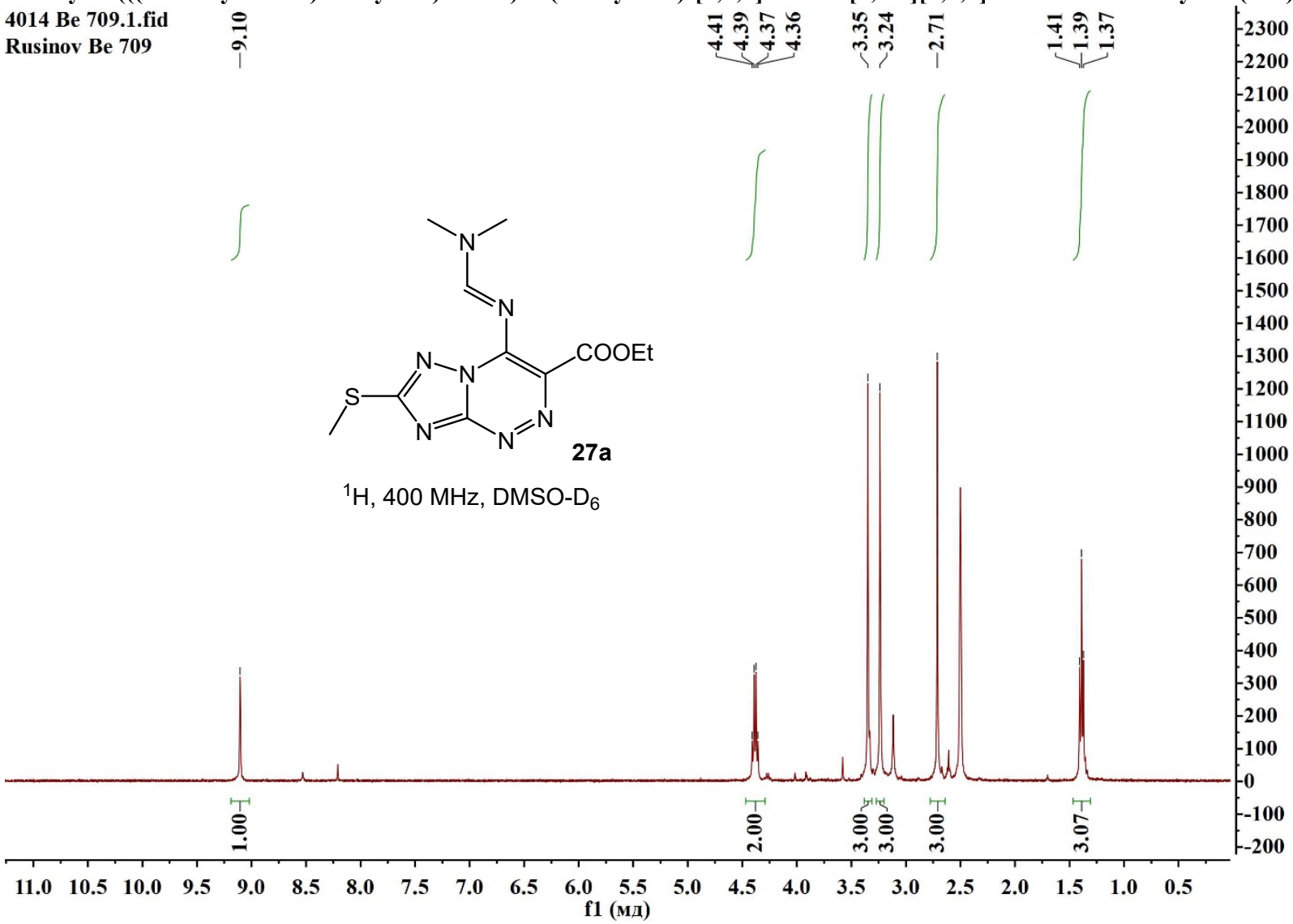

2382.1.fid
Risinov KC-2151
166.45
161.49
159.24
156.29
152.37
149.14
137.66
130.67
130.19
127.90
98.20
41.89
33.35
13.08
OH
N
N
N
N
N
N
S
H
24l
13C, 100 MHz, DMSO-D6
65000
60000
55000
50000
45000
40000
35000
30000
25000
20000
15000
10000
5000
0
-5000
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (мд)

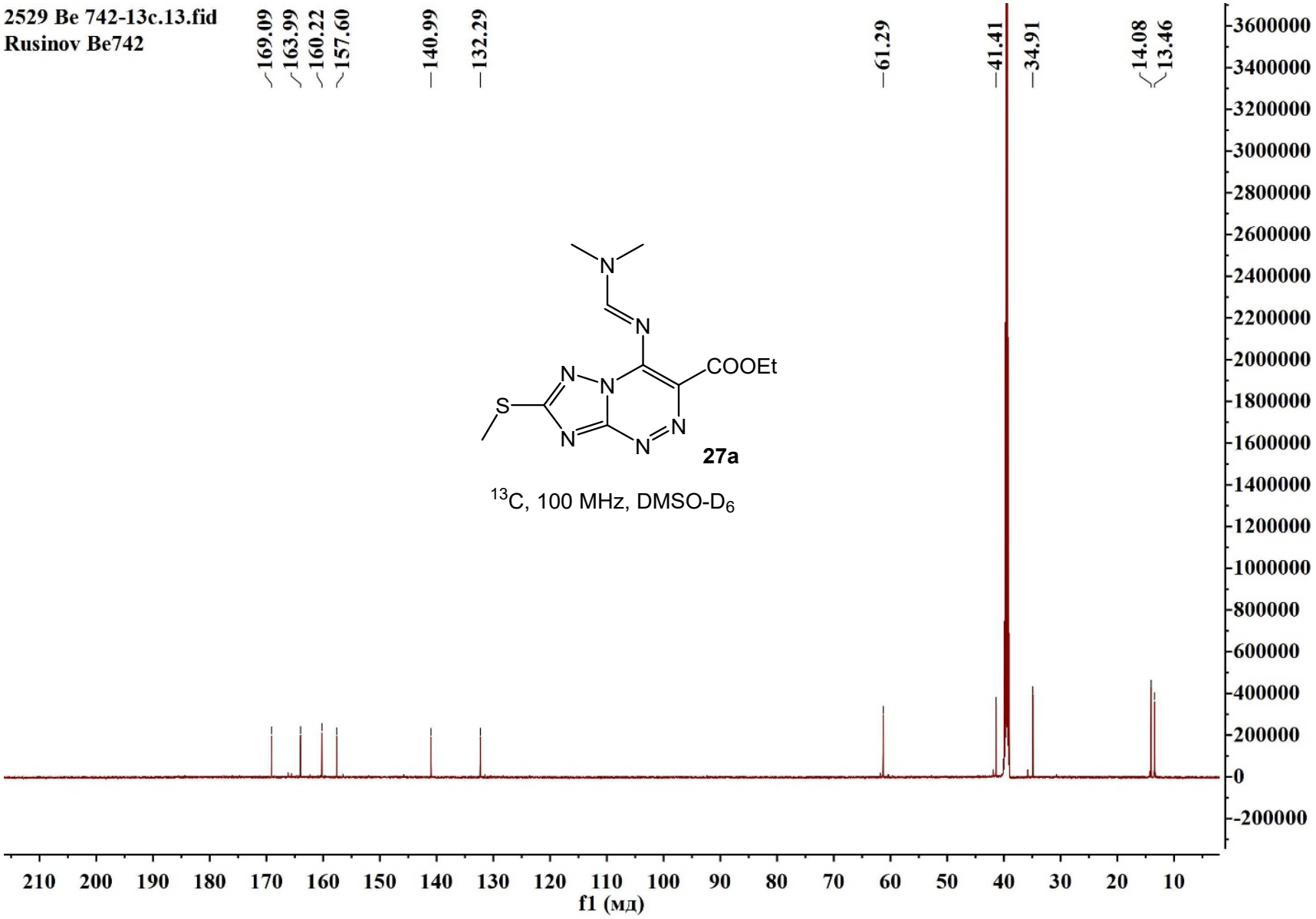

BRUKER
Transmittance [%]
100
95
90
85
80
75
70
65
3500
3000
2500
2000
1500
1000
500
Wavenumber cm-1
OH
N
N
N
N
N
N
S
H
24l
IR
1570.04
1513.23
1444.90
1407.07
1335.59
1278.77
1259.24
1225.32
1147.87
1114.99
1075.93
978.42
899.95
854.84
828.56
801.18
726.82
704.97
580.68
553.61
507.86

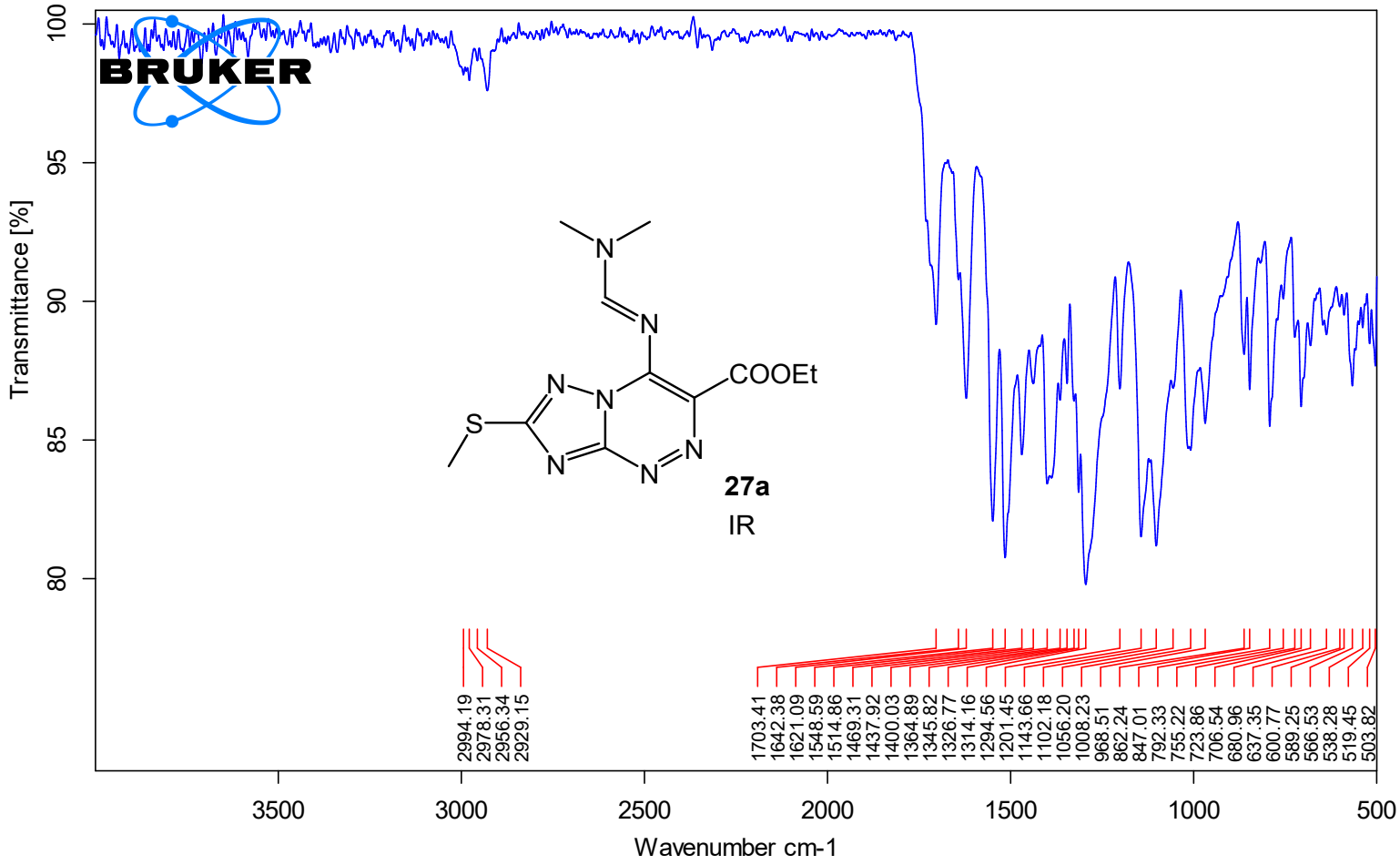
Line#:1 R.Time:3.735(Scan#:1455)
MassPeaks:84
RawMode:Single 3.735(1455) BasePeak:234(170300)
Фон.реж.:3.270(1269) Group 1 - Event 1



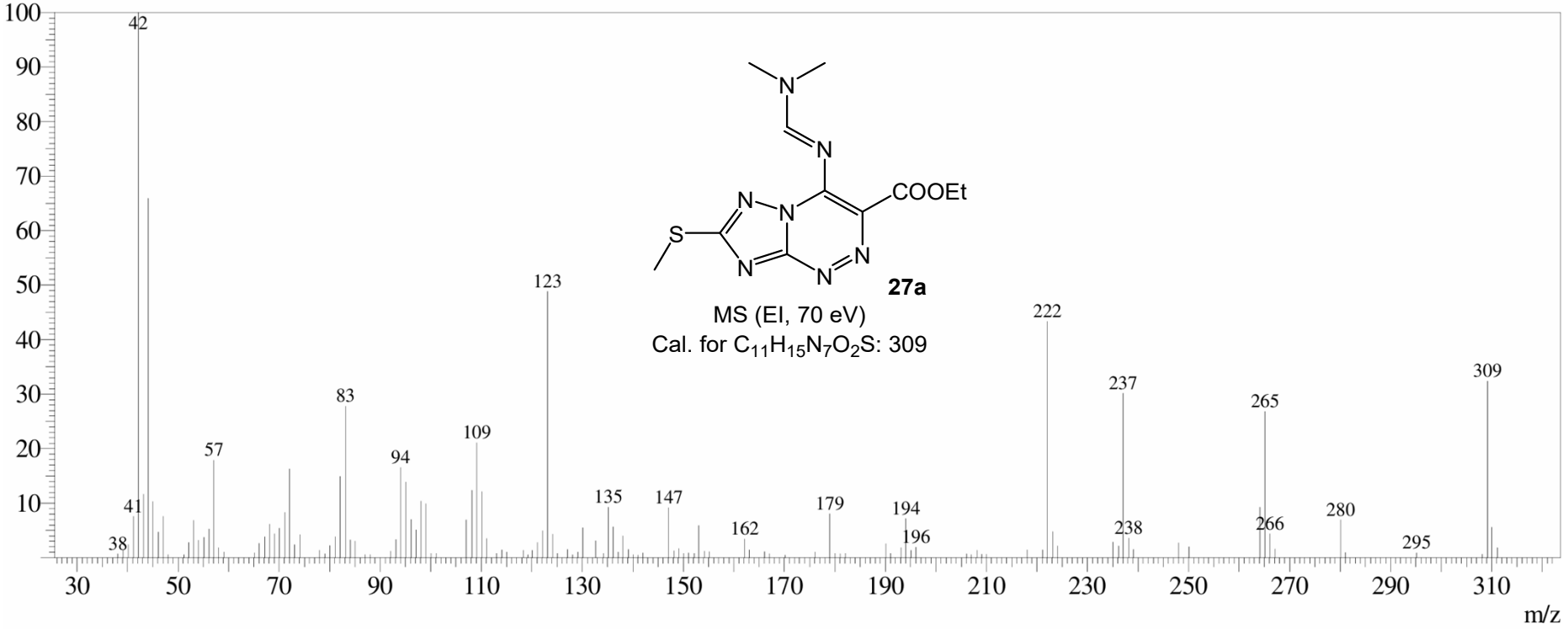
Ethyl 4-(((dimethylamino)methylene)amino)-7-(methylthio)-[1,2,4]triazolo[5,1-*c*][1,2,4]triazine-3-carboxylate (27a)



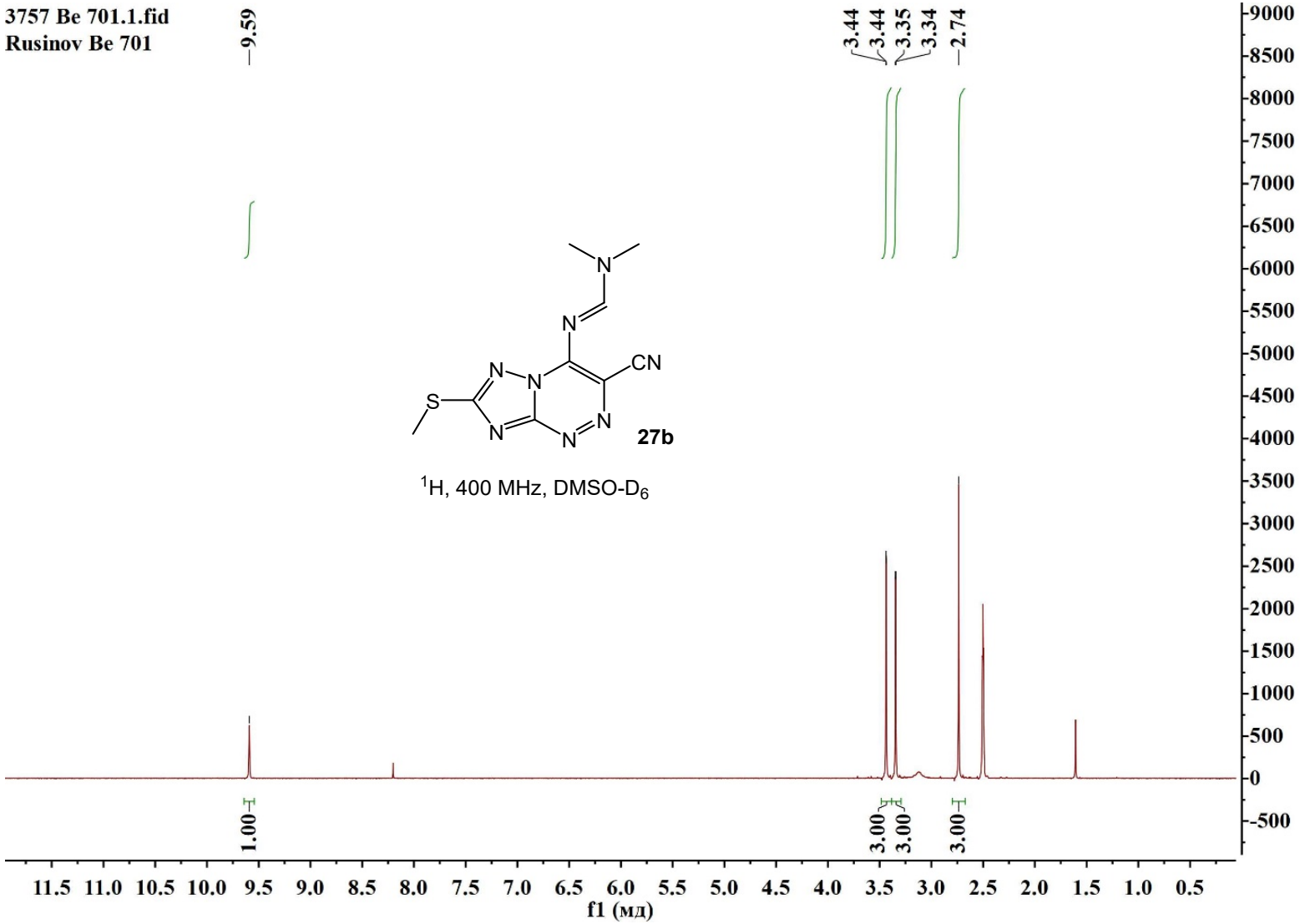

2529 Be 742-13c.13.fid
Rusinov Be742
169.09
163.99
160.22
157.60
140.99
132.29
61.29
41.41
34.91
14.08
13.46
COOEt
27a
13C, 100 MHz, DMSO-D6
f1 (мд)

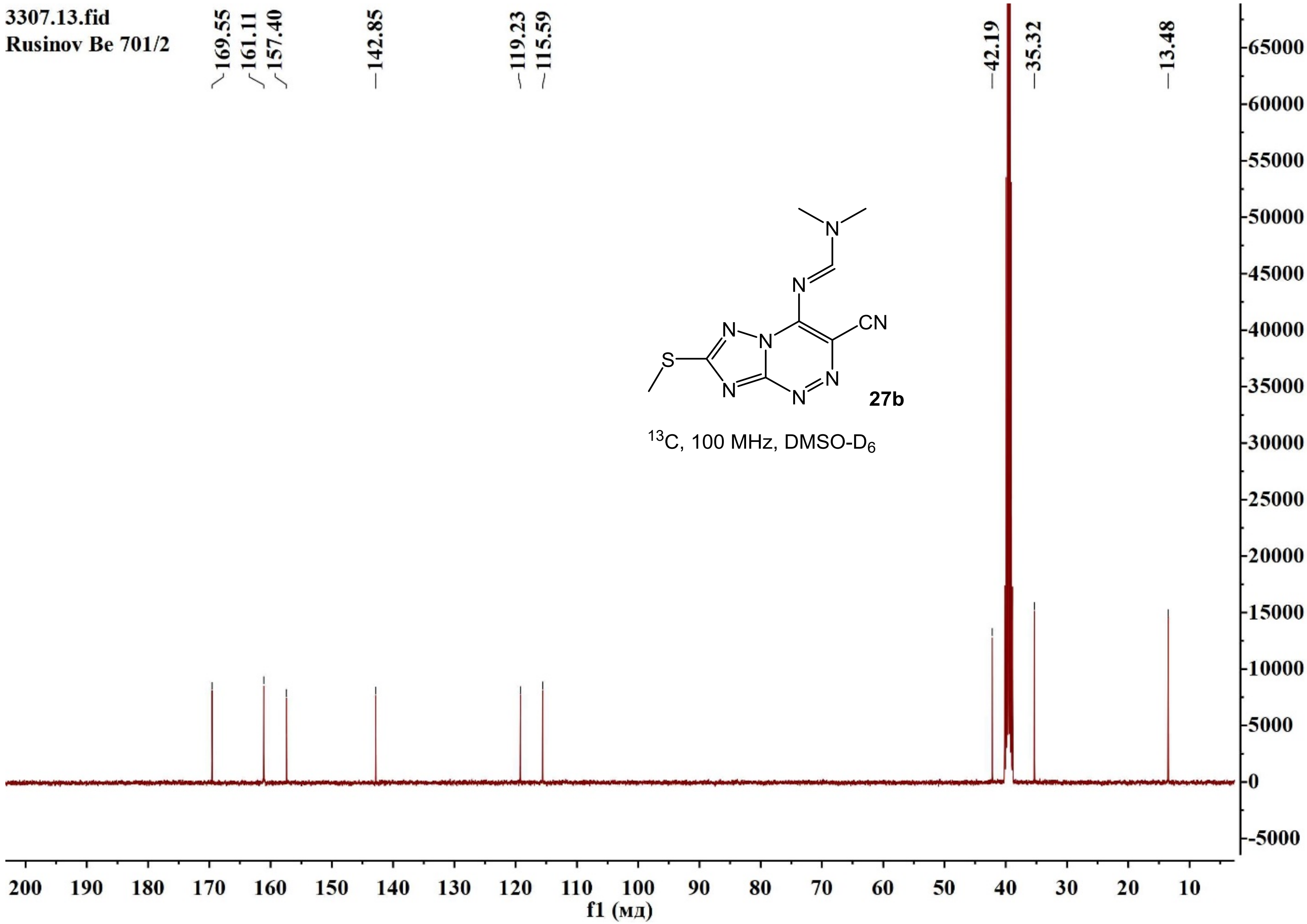

BRUKER
Transmittance [%]
100
95
90
85
80
3500
3000
2500
2000
1500
1000
500
Wavenumber cm-1
COOEt
27a
IR
2994.19
2978.31
2956.34
2929.15
1703.41
1642.38
1621.09
1548.59
1514.86
1469.31
1437.92
1400.03
1364.89
1345.82
1326.77
1314.16
1294.56
1201.45
1143.66
1102.18
1056.20
1008.23
968.51
862.24
847.01
792.33
755.22
723.86
706.54
680.96
637.35
600.77
589.25
566.53
538.28
519.45
503.82

Line#:1 R.Time:2.237(Scan#:856)
MassPeaks:133
RawMode:Single 2.237(856) BasePeak:42(2653108)
Фон.реж.:0.897(320) Group 1 - Event 1

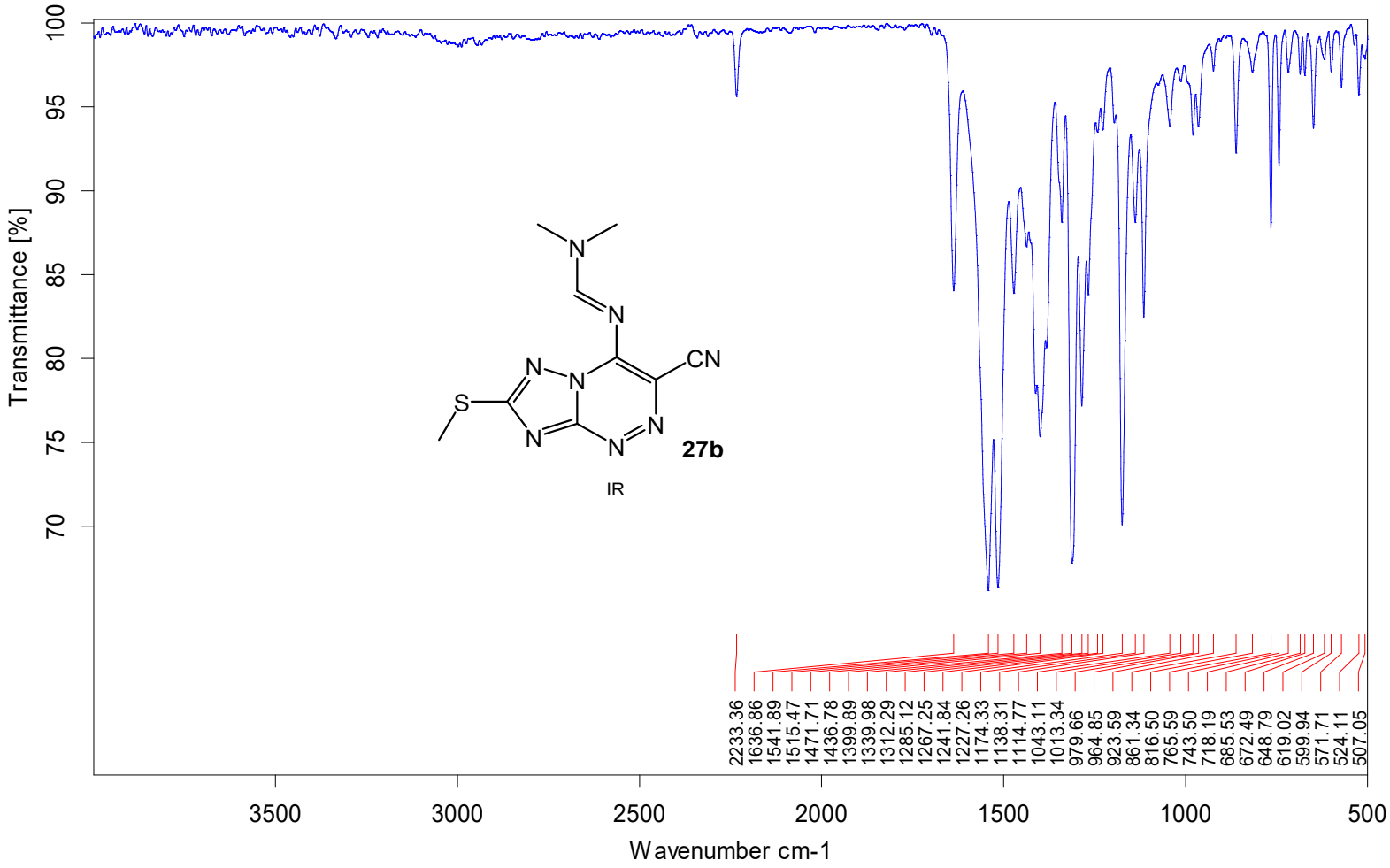


_N′_-(3-cyano-7-(methylthio)-[1,2,4]triazolo[5,1-_c_][1,2,4]triazin-4-yl)-_N,N_-dimethylformimidamide (27b)

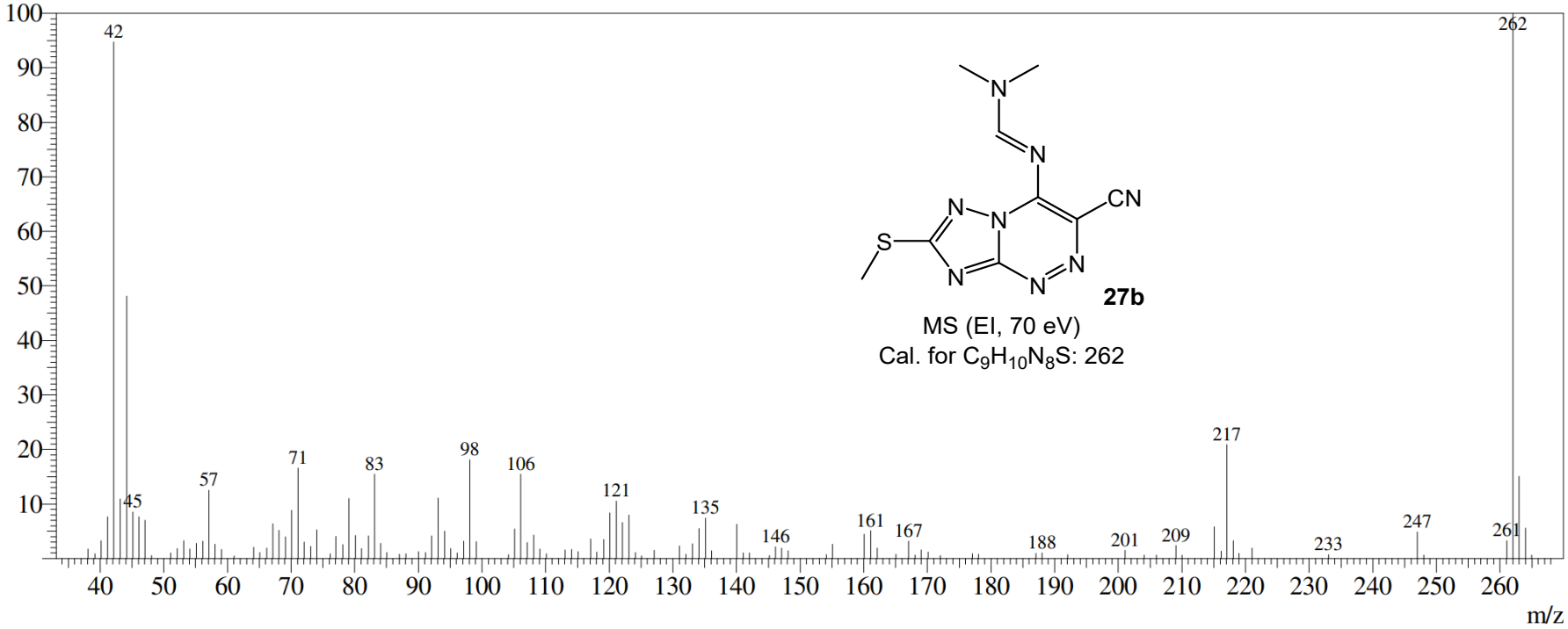




3307.13.fid
Rusinov Be 701/2
169.55
161.11
157.40
142.85
119.23
115.59
42.19
35.32
13.48
27b
^{13}C, 100 MHz, DMSO-D$_6$
65000
60000
55000
50000
45000
40000
35000
30000
25000
20000
15000
10000
5000
0
-5000
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (мд)


Transmittance [%]
100
95
90
85
80
75
70
3500
3000
2500
2000
1500
1000
500
Wavenumber cm-1
27b
IR
2233.36
1636.86
1541.89
1515.47
1471.71
1436.78
1399.89
1339.98
1312.29
1285.12
1267.25
1241.84
1227.26
1174.33
1138.31
1114.77
1043.11
1013.34
979.66
964.85
923.59
861.34
816.50
765.59
743.50
718.19
685.53
672.49
648.79
619.02
599.94
571.71
524.11
507.05

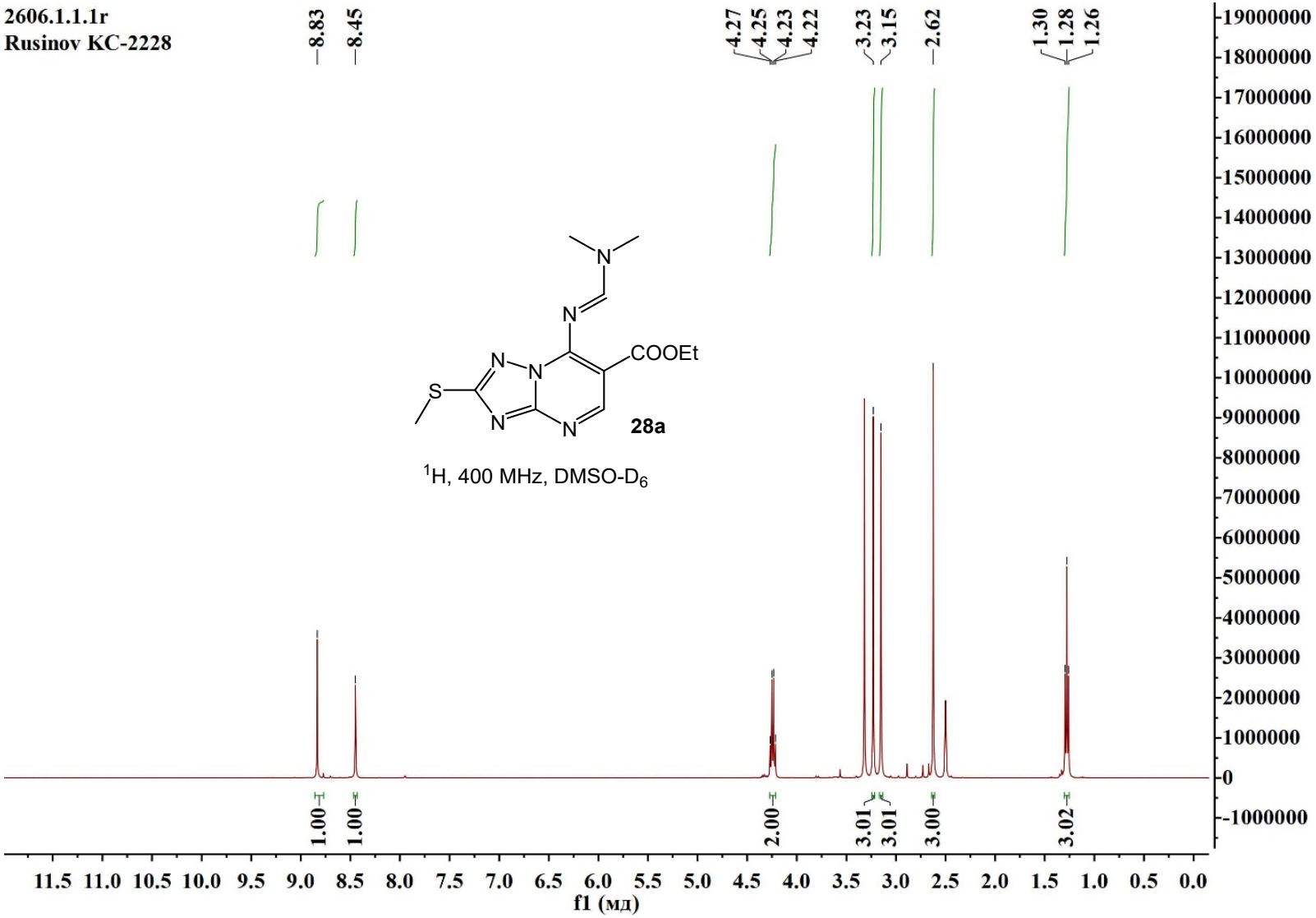
Line#:1 R.Time:4.048(Scan#:1580)
MassPeaks:122
RawMode:Single 4.048(1580) BasePeak:262(5579360)
Фон.реж.:2.755(1063) Group 1 - Event 1

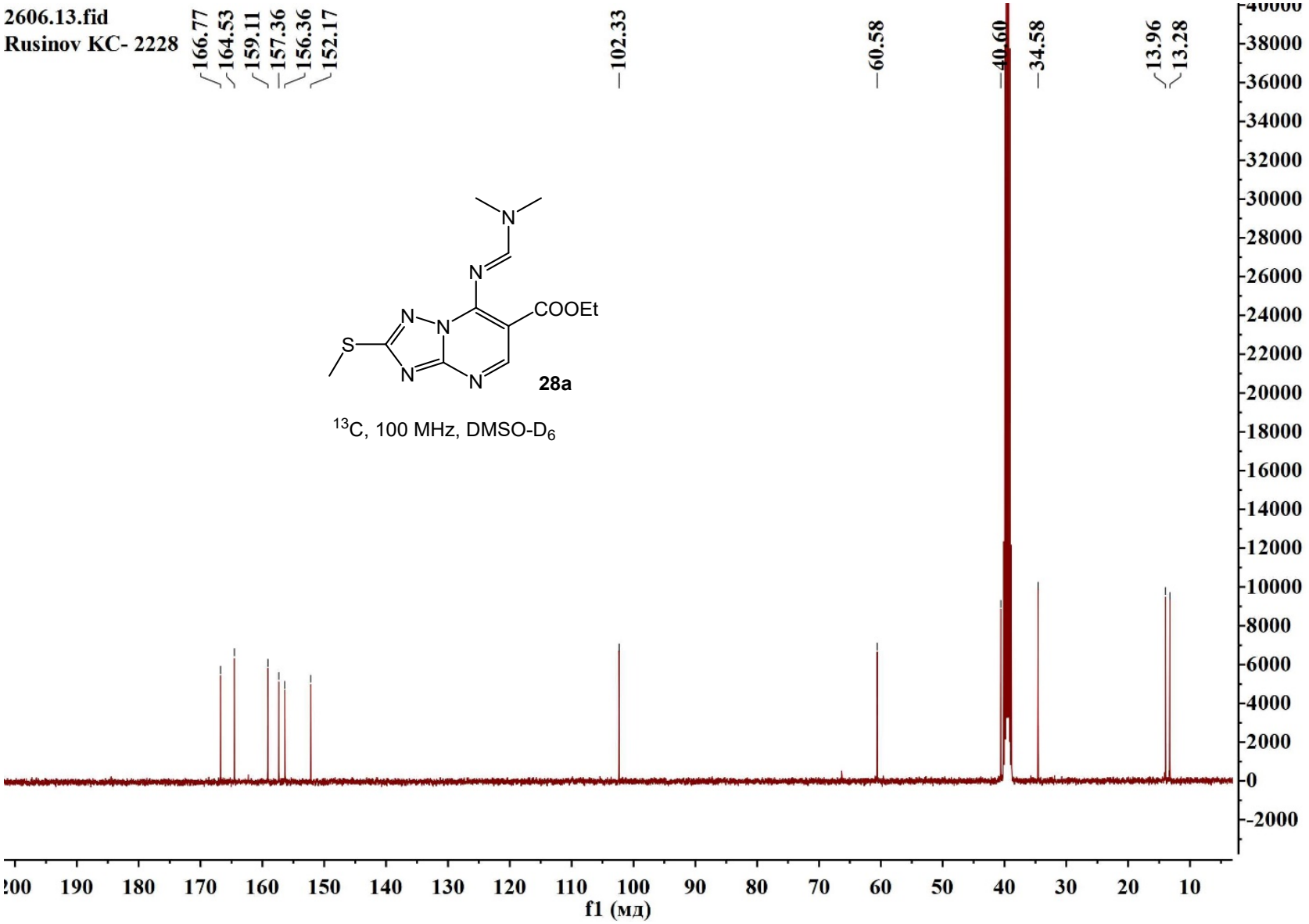


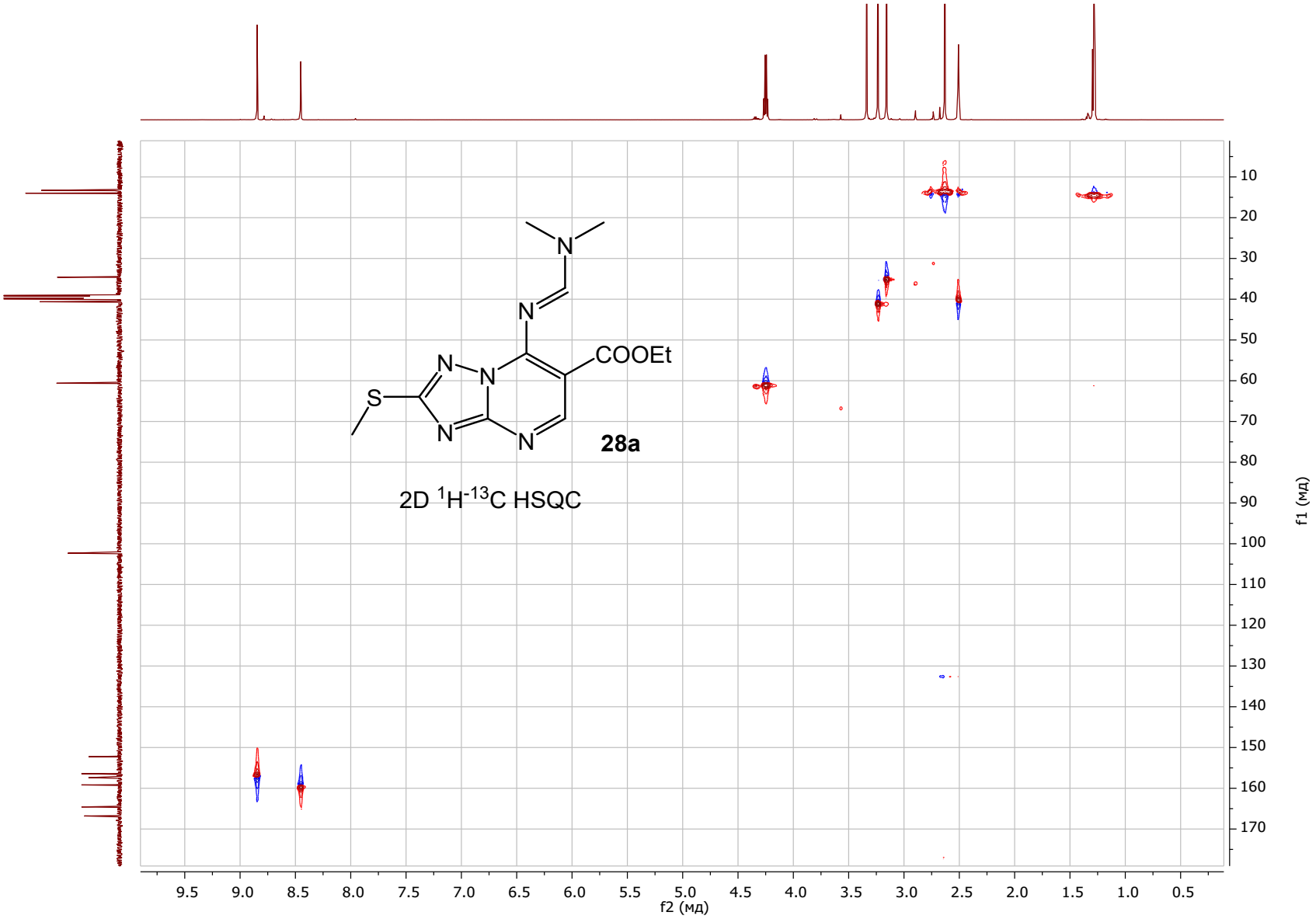
27b

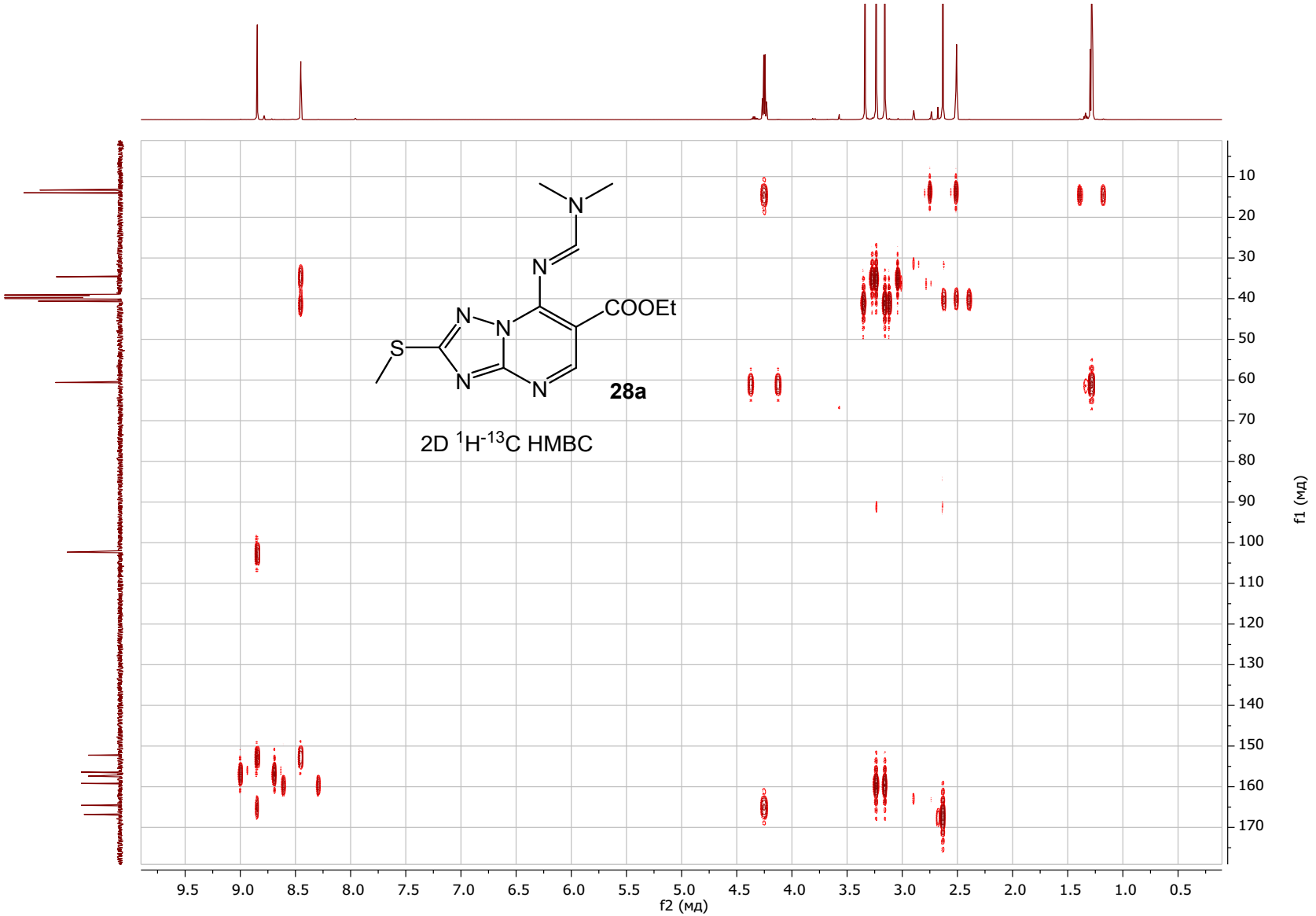
MS (EI, 70 eV)
Cal. for $C_9H_{10}N_8S$: 262

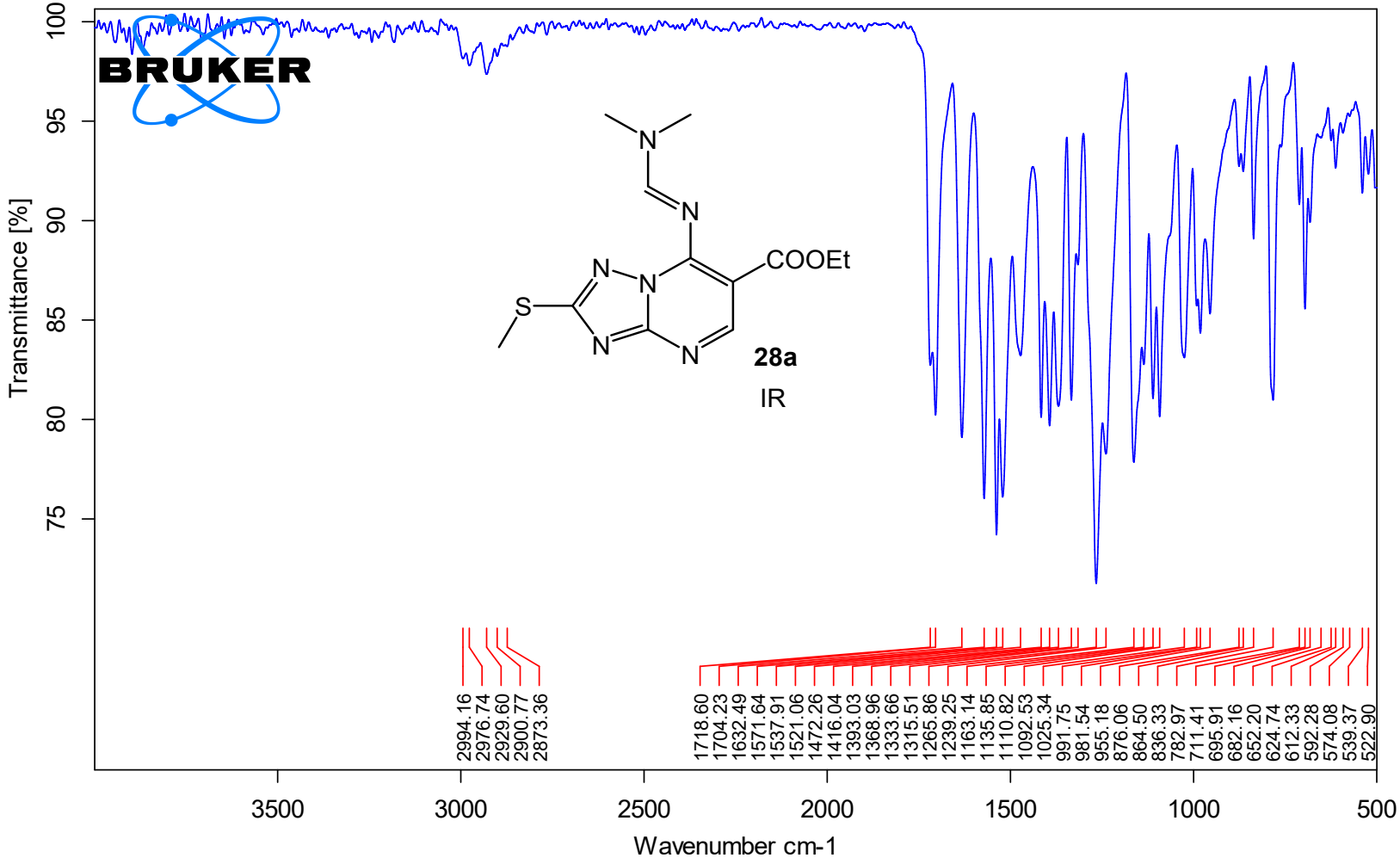
Ethyl 7-(((dimethylamino)methylene)amino)-2-(methylthio)-[1,2,4]triazolo[1,5-*a*]pyrimidine-6-carboxylate (28a)



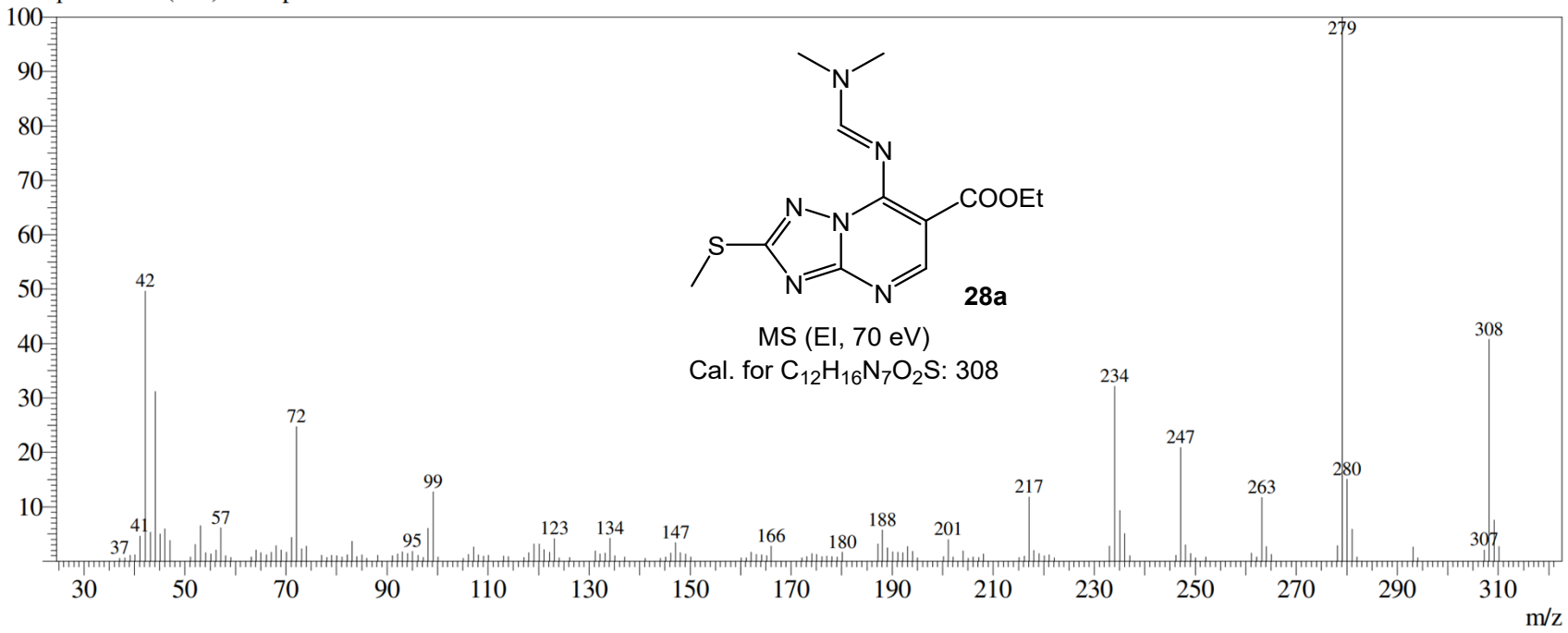

2606.13.fid
Rusinov KC- 2228
166.77
164.53
159.11
157.36
156.36
152.17
102.33
60.58
40.60
34.58
13.96
13.28
COOEt
28a
13C, 100 MHz, DMSO-D6
f1 (мд)


N
N
COOEt
N
N
S
N
N
28a
2D ^{1}H-^{13}C HSQC
f2 (мд)
f1 (мд)

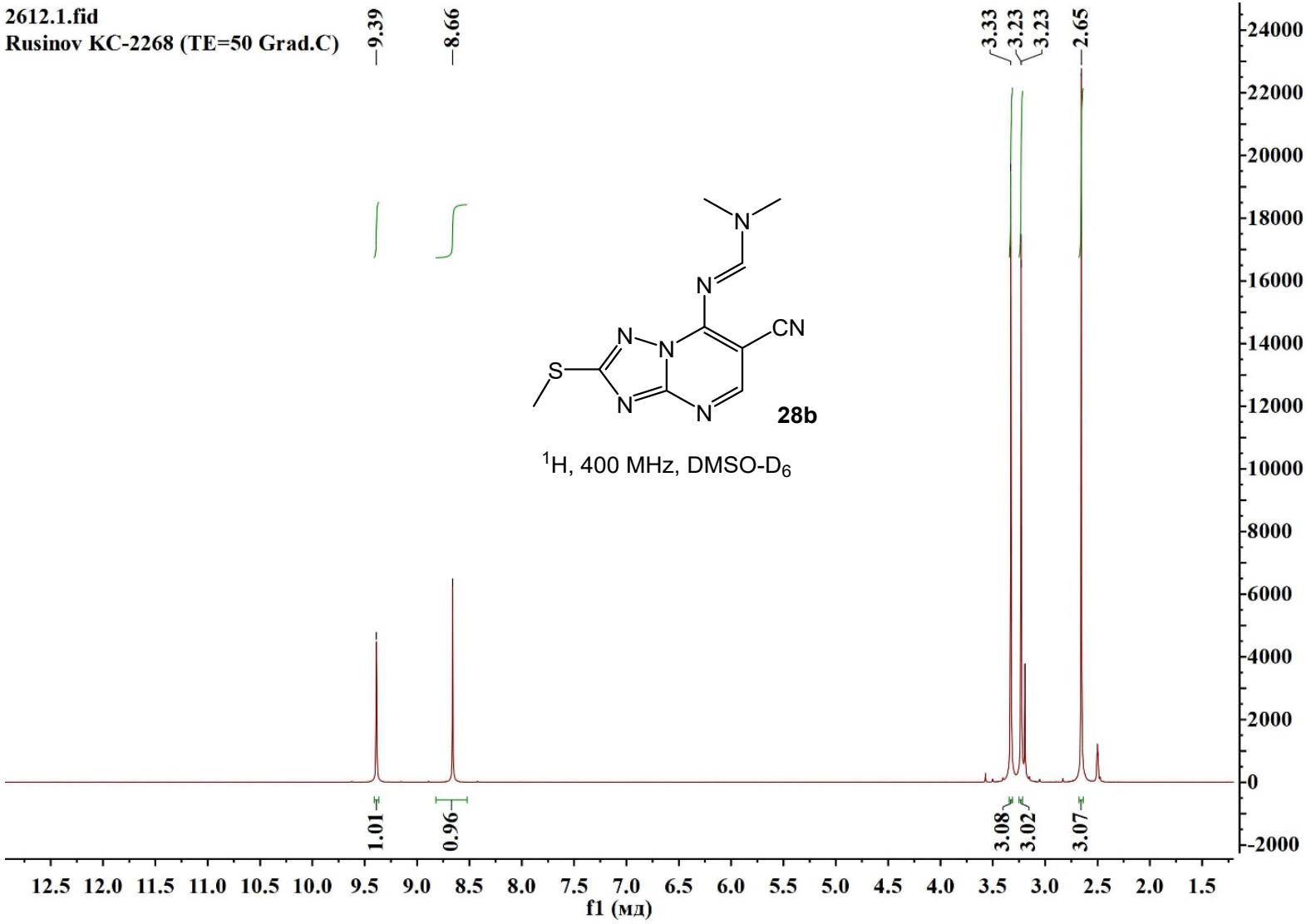

COOEt
28a
2D ^{1}H-^{13}C HMBC
f2 (мд)
f1 (мд)

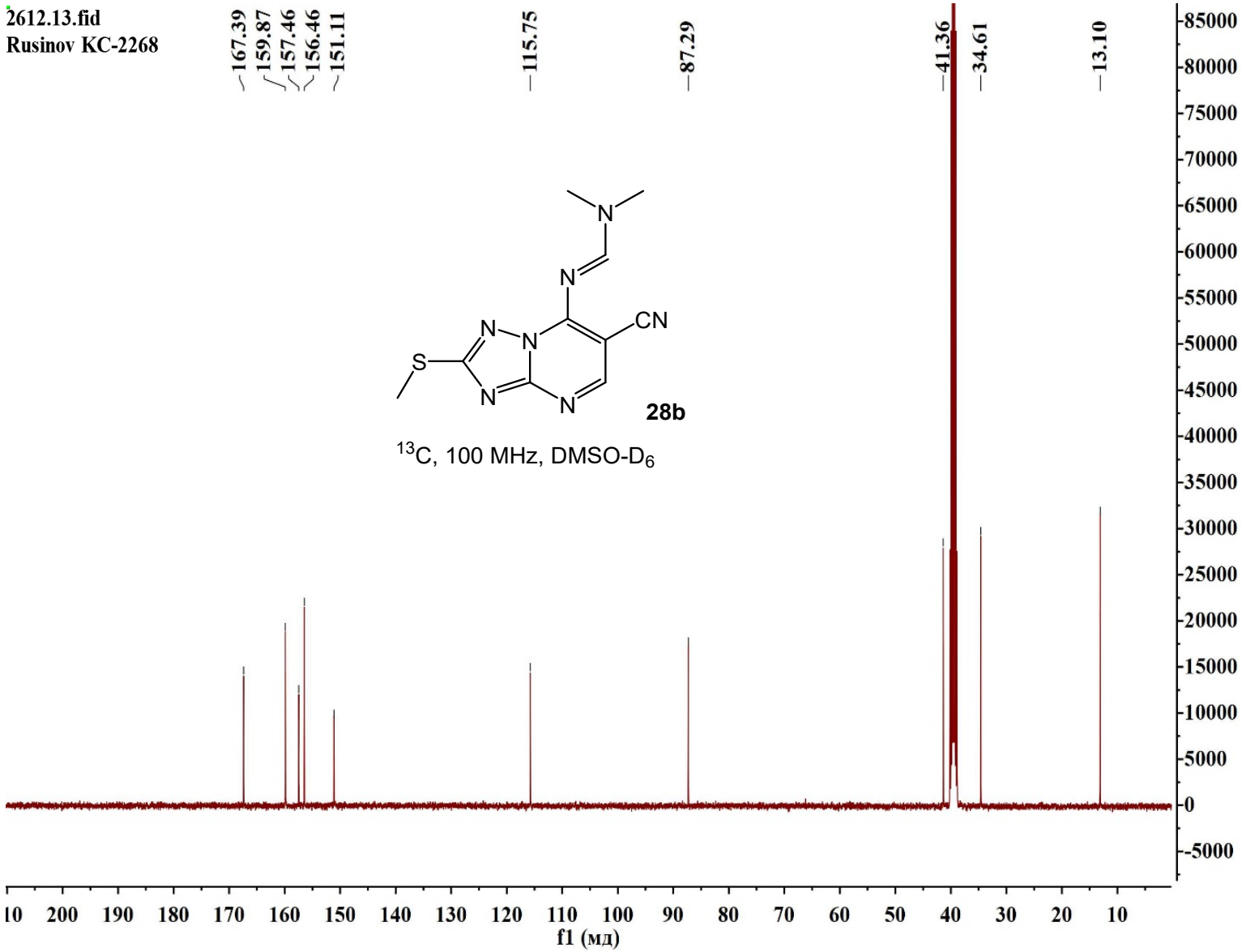

BRUKER
Transmittance [%]
100
95
90
85
80
75
3500
3000
2500
2000
1500
1000
500
Wavenumber cm-1
COOEt
28a
IR
2994.16
2976.74
2929.60
2900.77
2873.36
1718.60
1704.23
1632.49
1571.64
1537.91
1521.06
1472.26
1416.04
1393.03
1368.96
1333.66
1315.51
1265.86
1239.25
1163.14
1135.85
1110.82
1092.53
1025.34
991.75
981.54
955.18
876.06
864.50
836.33
782.97
711.41
695.91
682.16
652.20
624.74
612.33
592.28
574.08
539.37
522.90

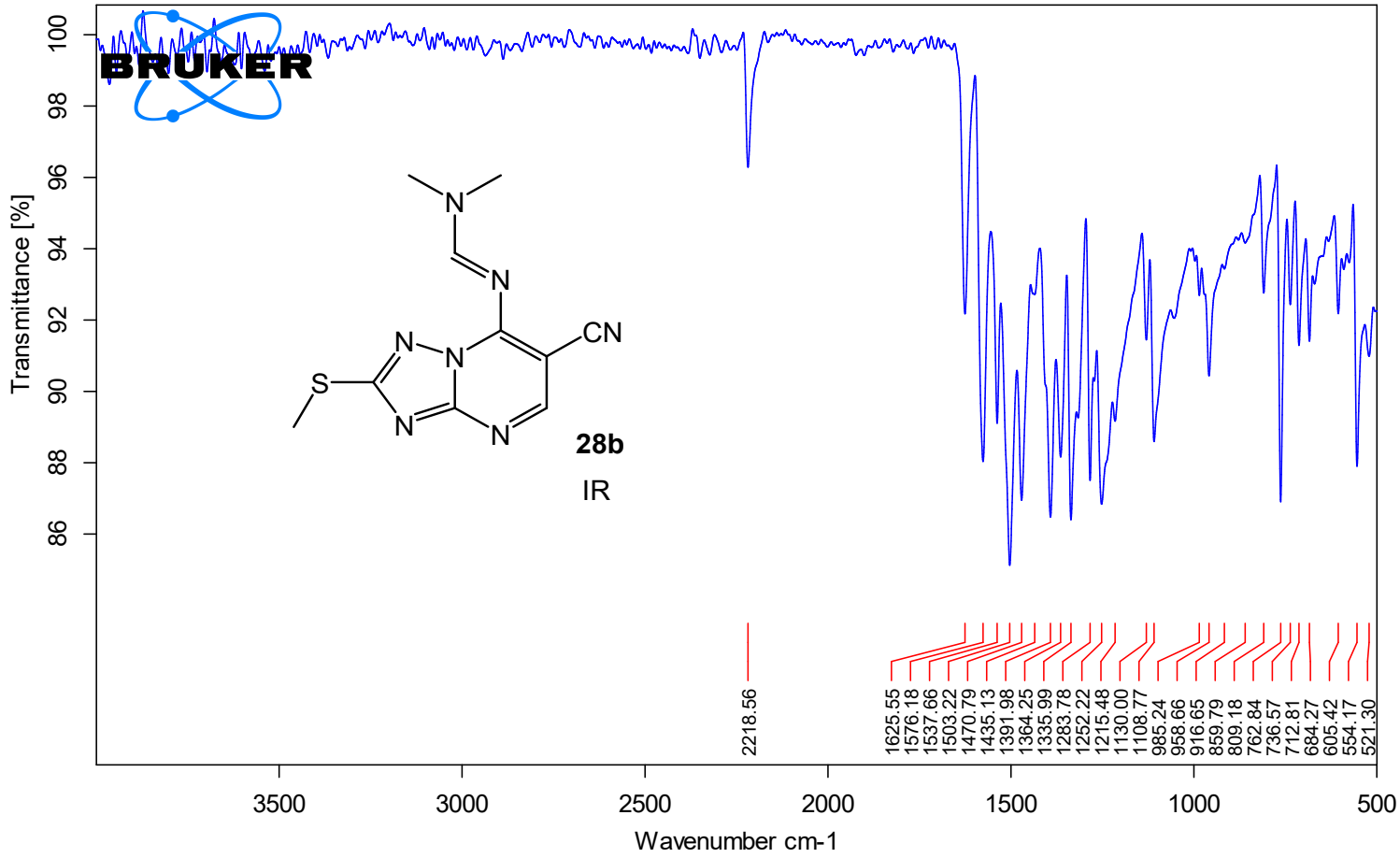
Line#:1 R.Time:2.720(Scan#:1049)
MassPeaks:152
RawMode:Single 2.720(1049) BasePeak:279(6476047)
Фон.реж.:1.670(629) Group 1 - Event 1



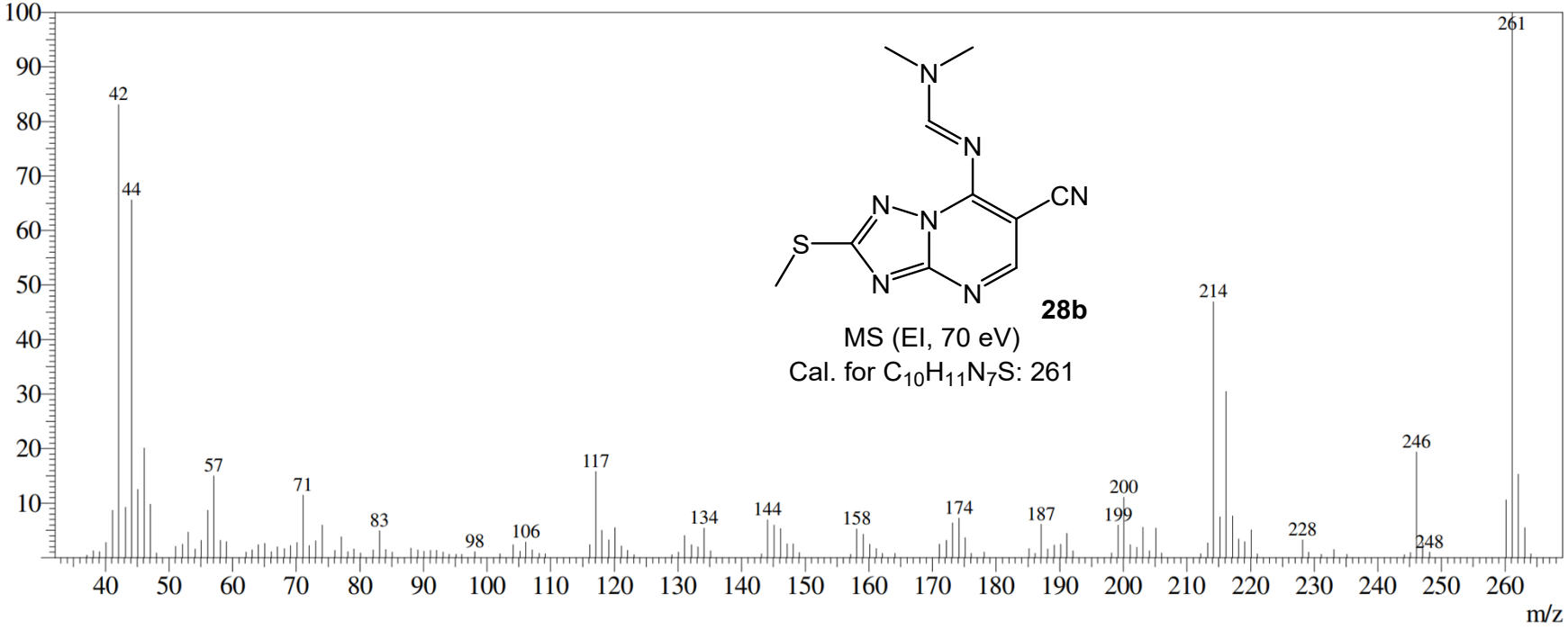
***N'*-(6-cyano-2-(methylthio)-[1,2,4]triazolo[1,5-*a*]pyrimidin-7-yl)-*N*,*N*-dimethylformimidamide (28b)**




2612.13.fid
Rusinov KC-2268
167.39
159.87
157.46
156.46
151.11
115.75
87.29
41.36
34.61
13.10
N
N
CN
N
N
S
N
N
28b
^{13}C, 100 MHz, DMSO-D$_6$
85000
80000
75000
70000
65000
60000
55000
50000
45000
40000
35000
30000
25000
20000
15000
10000
5000
0
-5000
10 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (мд)


BRUKER
Transmittance [%]
100
98
96
94
92
90
88
86
3500
3000
2500
2000
1500
1000
500
Wavenumber cm-1
28b
IR
2218.56
1625.55
1576.18
1537.66
1503.22
1470.79
1435.13
1391.98
1364.25
1335.99
1283.78
1252.22
1215.48
1130.00
1108.77
985.24
958.66
916.65
859.79
809.18
762.84
736.57
712.81
684.27
605.42
554.17
521.30

Line#:1 R.Time:1.995(Scan#:759)
MassPeaks:138
RawMode:Single 1.995(759) BasePeak:261(6989975)
Фон.реж.:0.760(265) Group 1 - Event 1

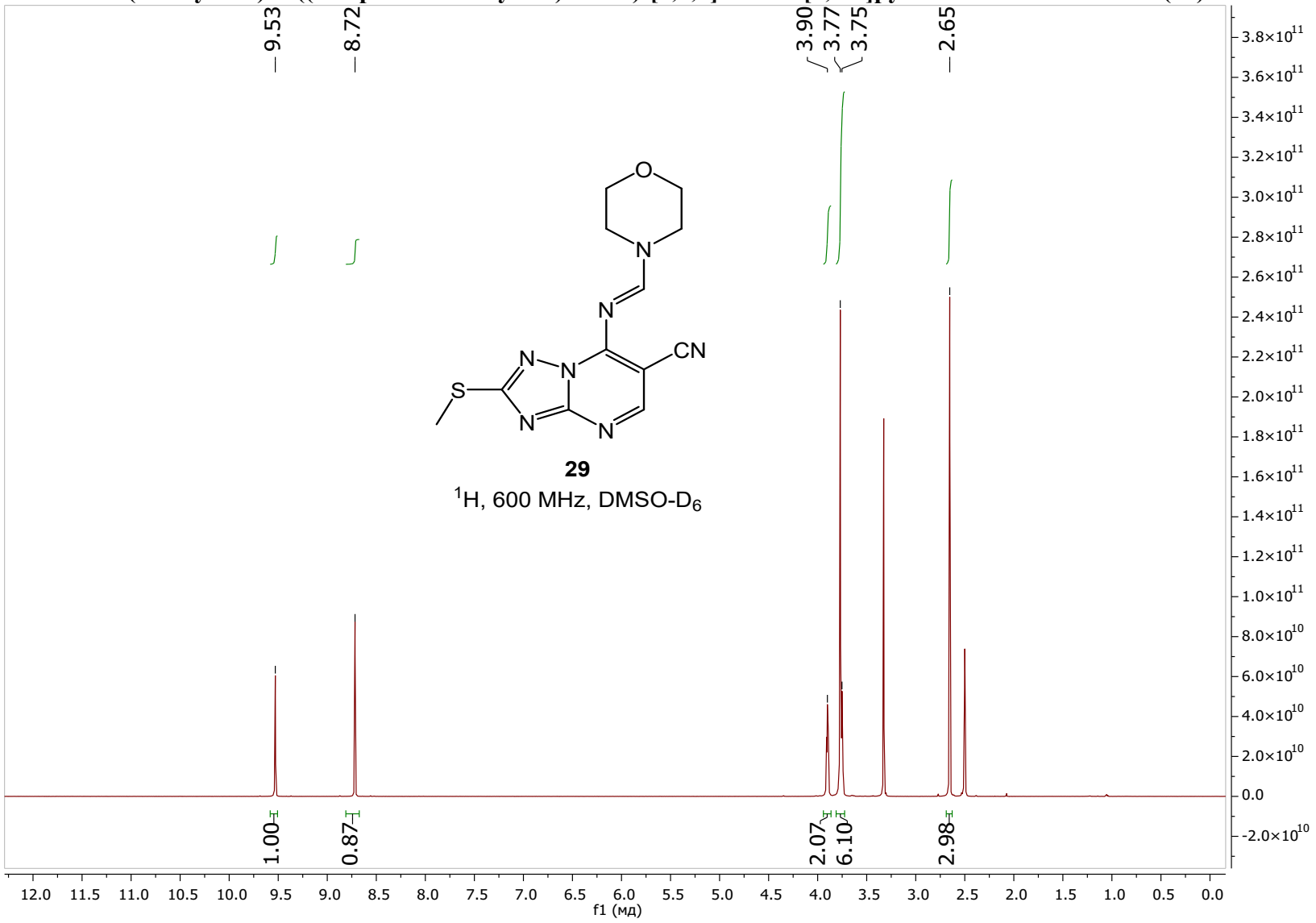


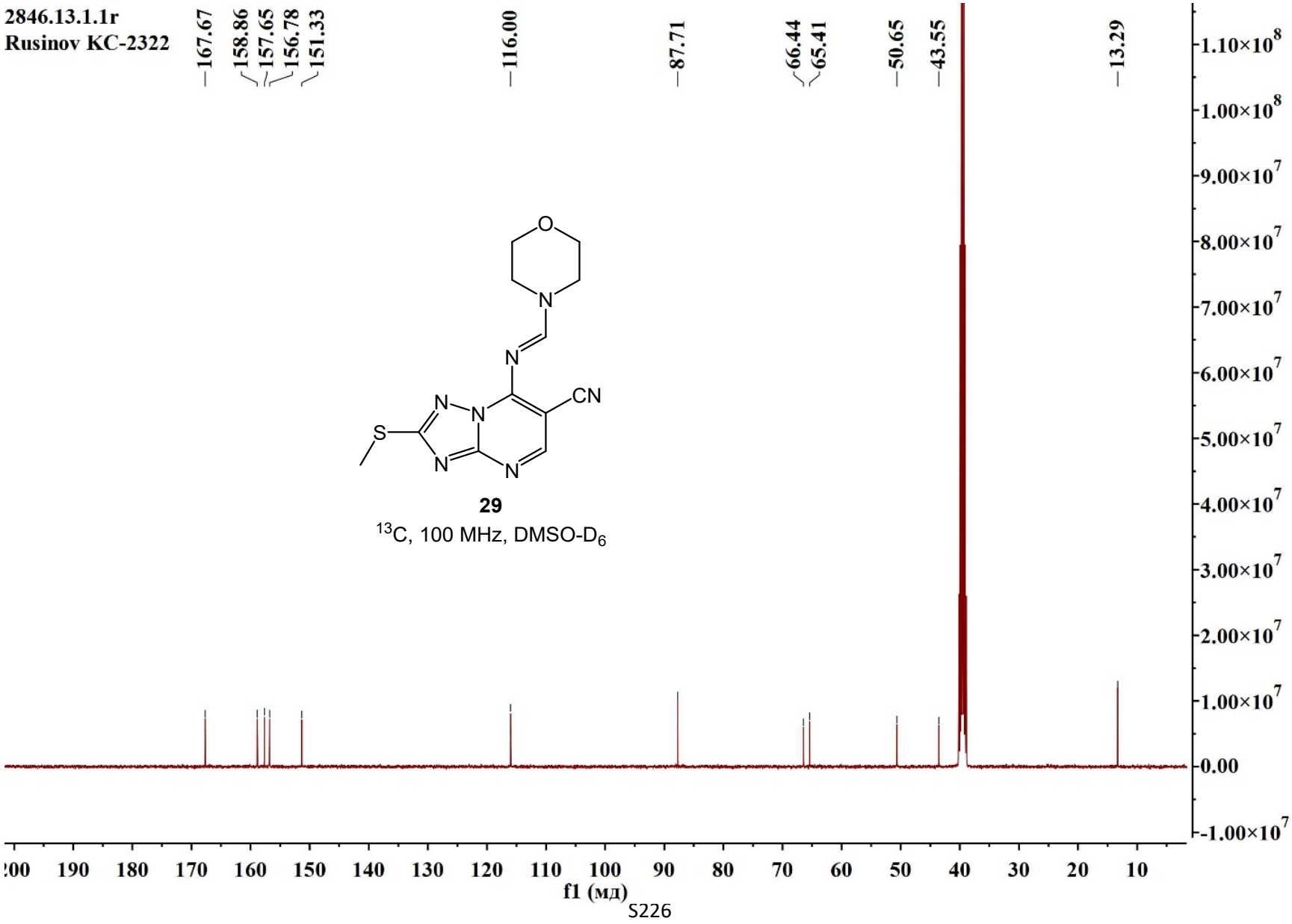
28b

MS (EI, 70 eV)

Cal. for $C_{10}H_{11}N_7S$: 261

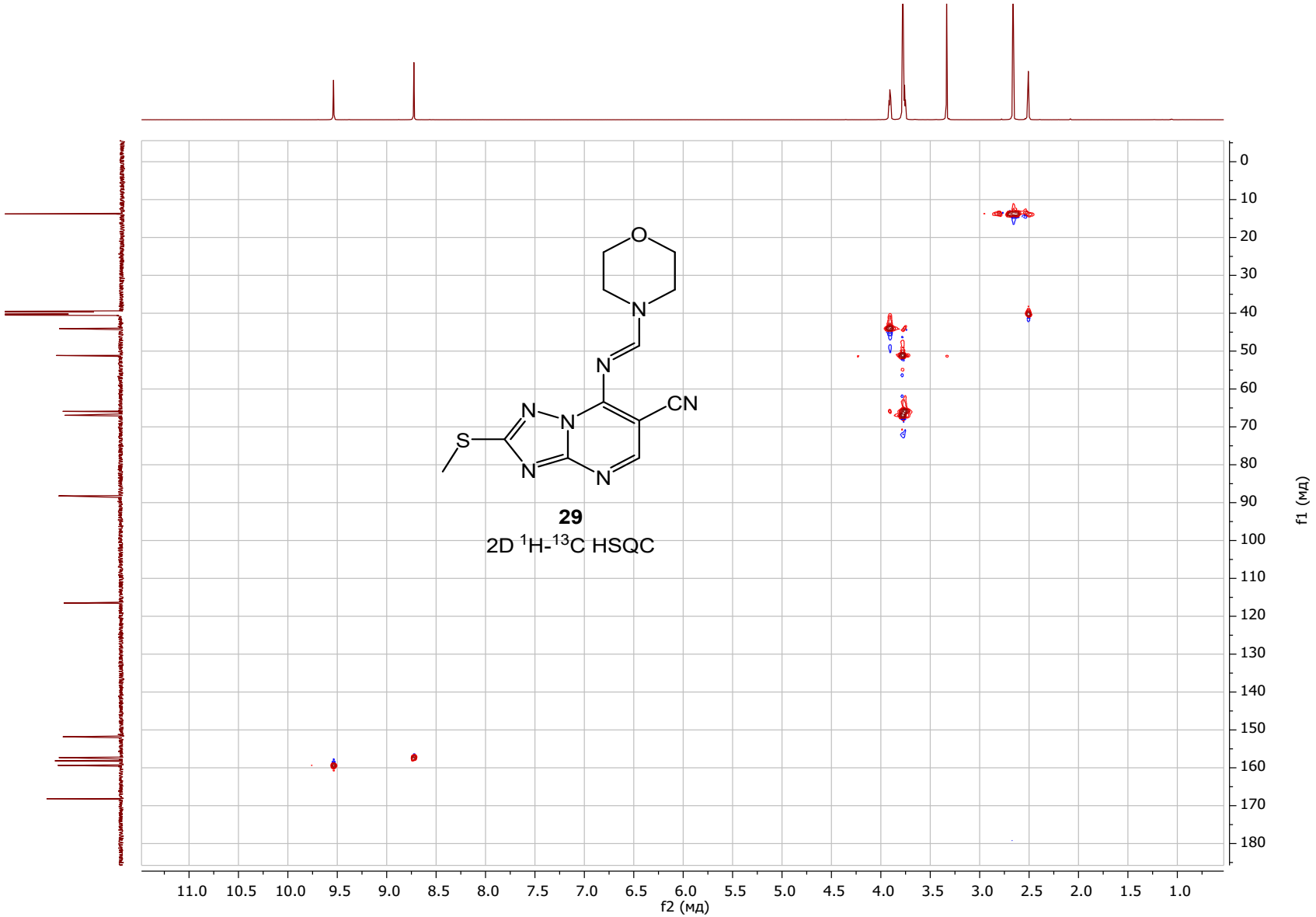
2-(Methylthio)-7-((morpholinomethylene)amino)-[1,2,4]triazolo[1,5-*a*]pyrimidine-6-carbonitrile (29).

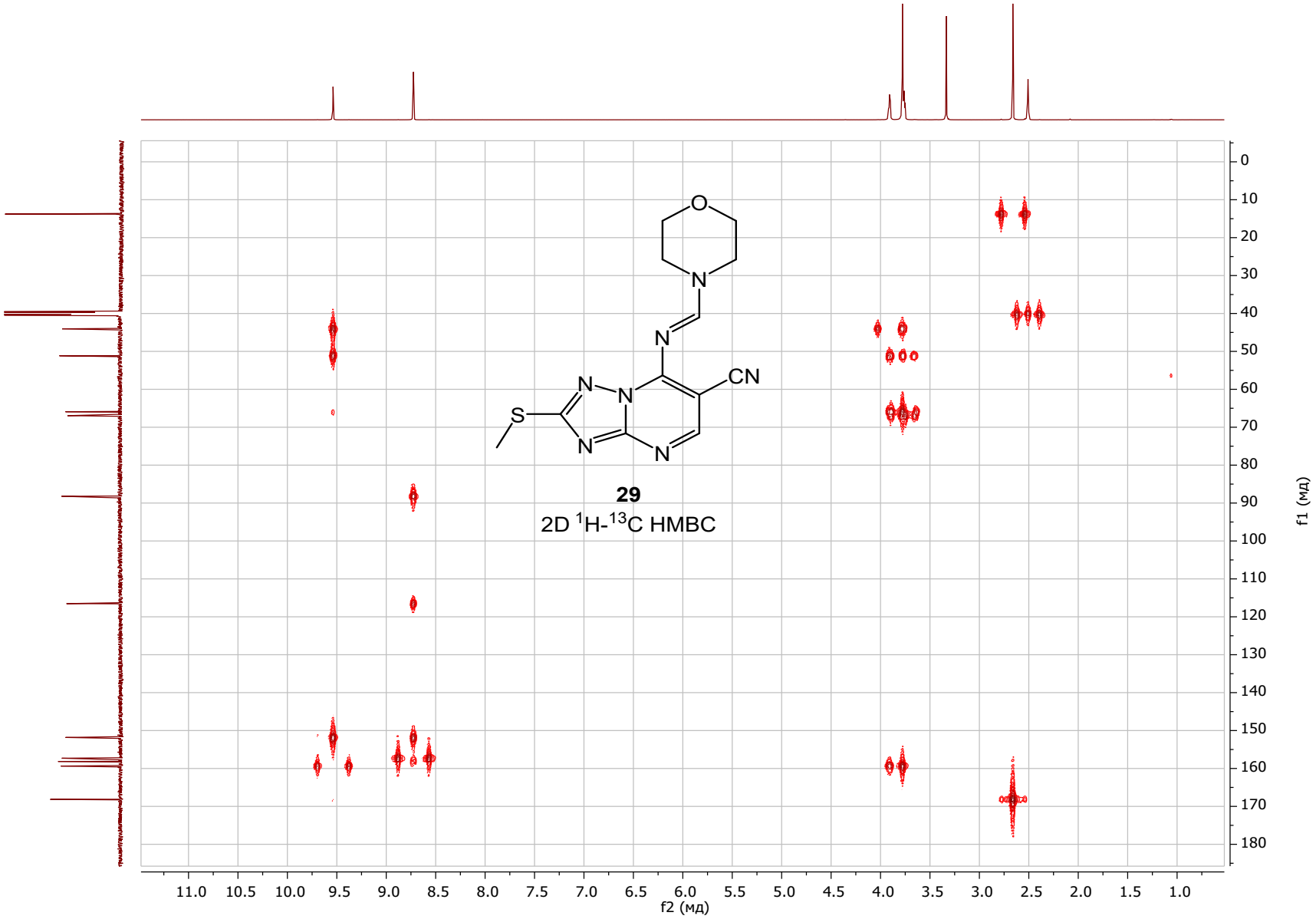


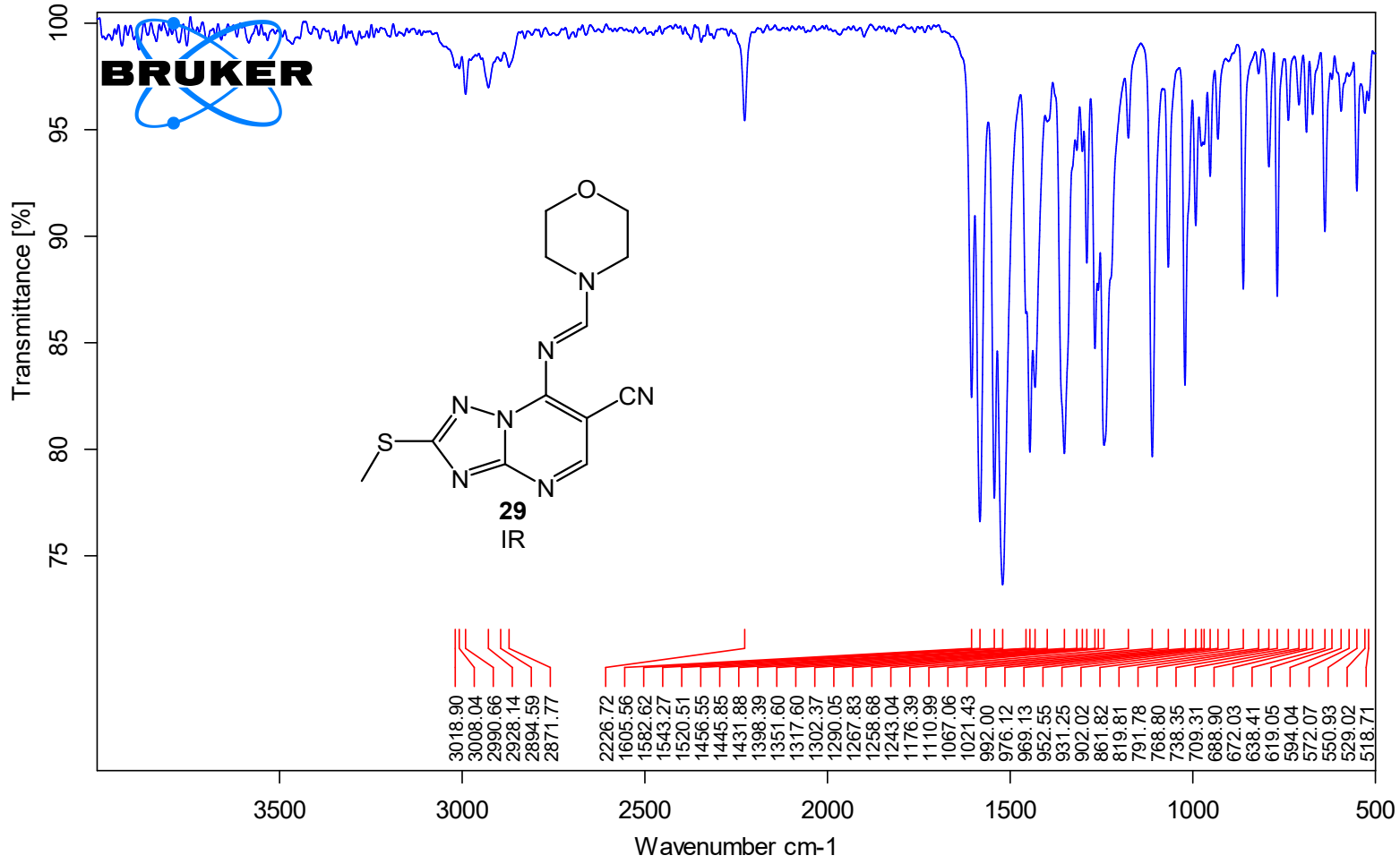


29

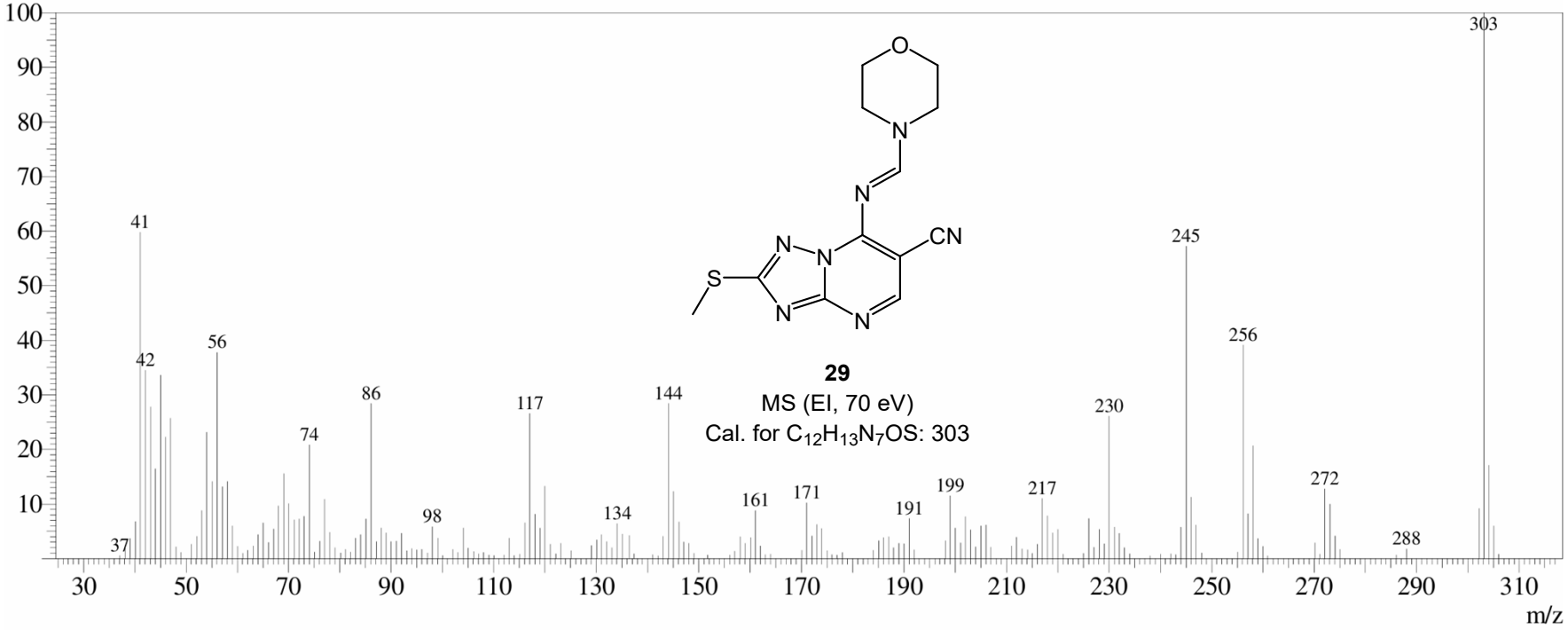
^{13}C, 100 MHz, DMSO-D_6


O
N
N
N
N
N
S
CN
29
2D ^{1}H-^{13}C HSQC
f2 (мд)
f1 (мд)

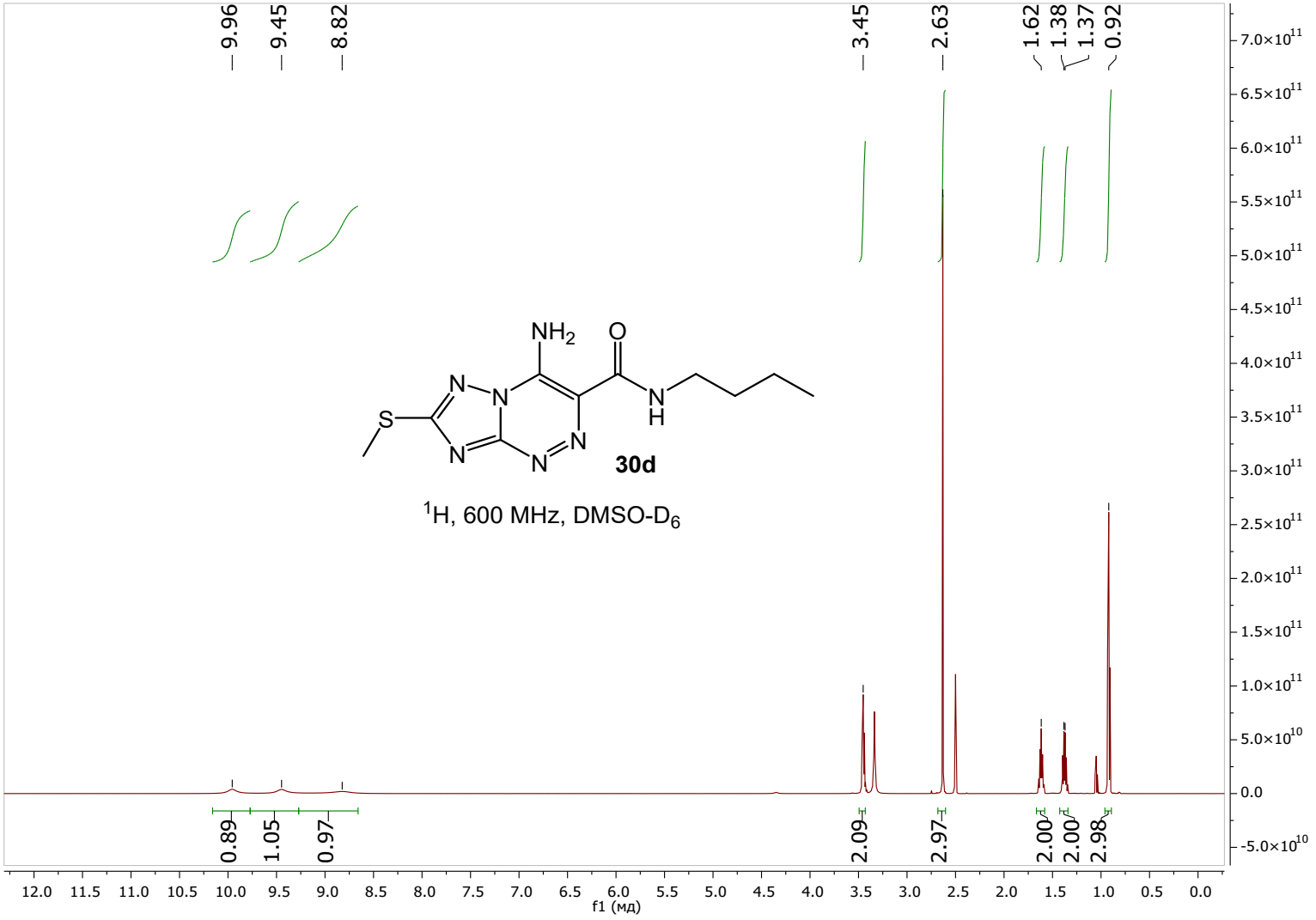

O
N
N
CN
N
N
S
N
N
29
2D ^{1}H-^{13}C HMBC
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0
f2 (мд)
0 10 20 30 40 50 60 70 80 90 100 110 120 130 140 150 160 170 180
f1 (мд)

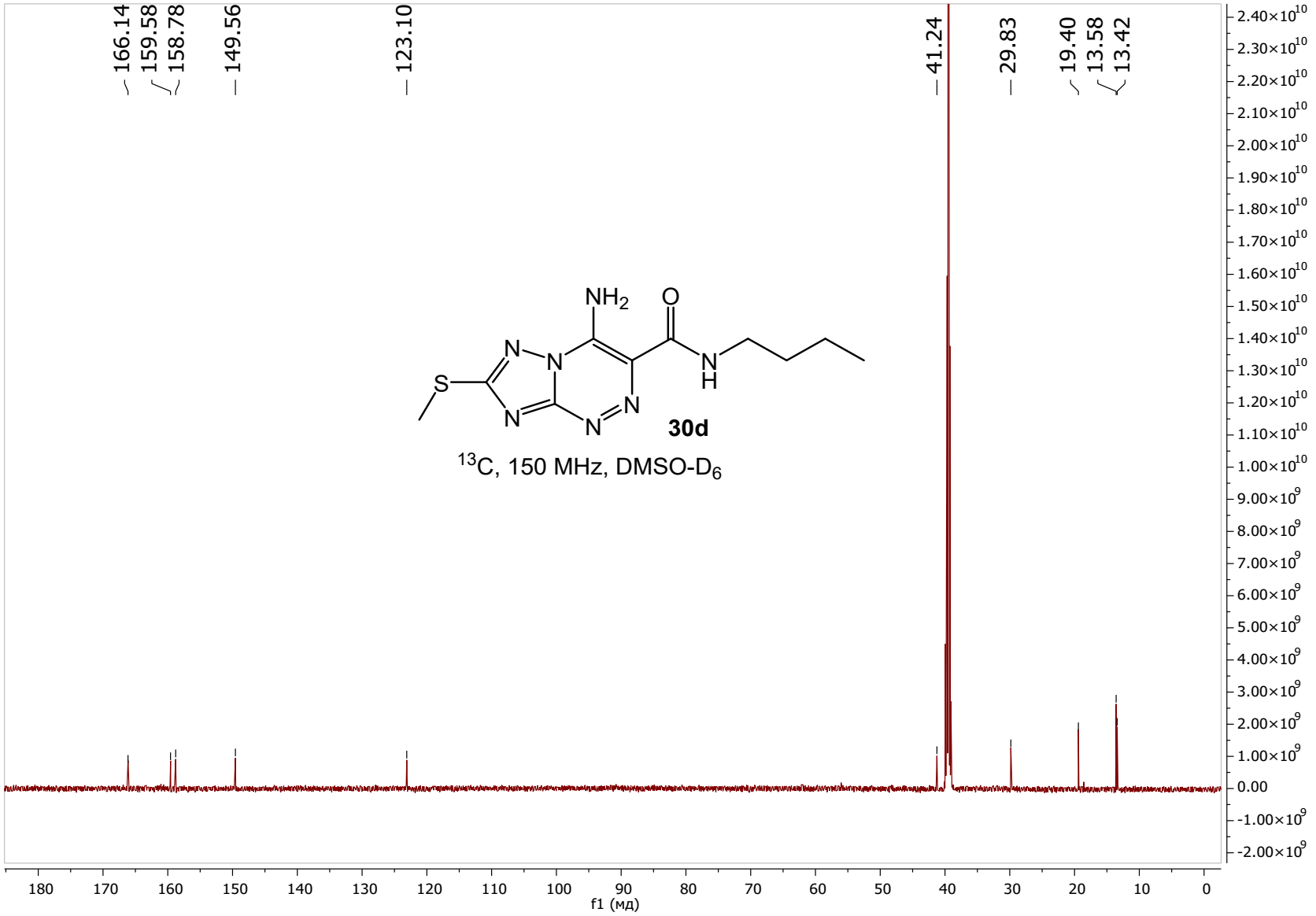

BRUKER
Transmittance [%]
100
95
90
85
80
75
3500
3000
2500
2000
1500
1000
500
Wavenumber cm-1
O
N
N
CN
N
N
S
N
N
29
IR
3018.90
3008.04
2990.66
2928.14
2894.59
2871.77
2226.72
1605.56
1582.62
1543.27
1520.51
1456.55
1445.85
1431.88
1398.39
1351.60
1317.60
1302.37
1290.05
1267.83
1258.68
1243.04
1176.39
1110.99
1067.06
1021.43
992.00
976.12
969.13
952.55
931.25
902.02
861.82
819.81
791.78
768.80
738.35
709.31
688.90
672.03
638.41
619.05
594.04
572.07
550.93
529.02
518.71

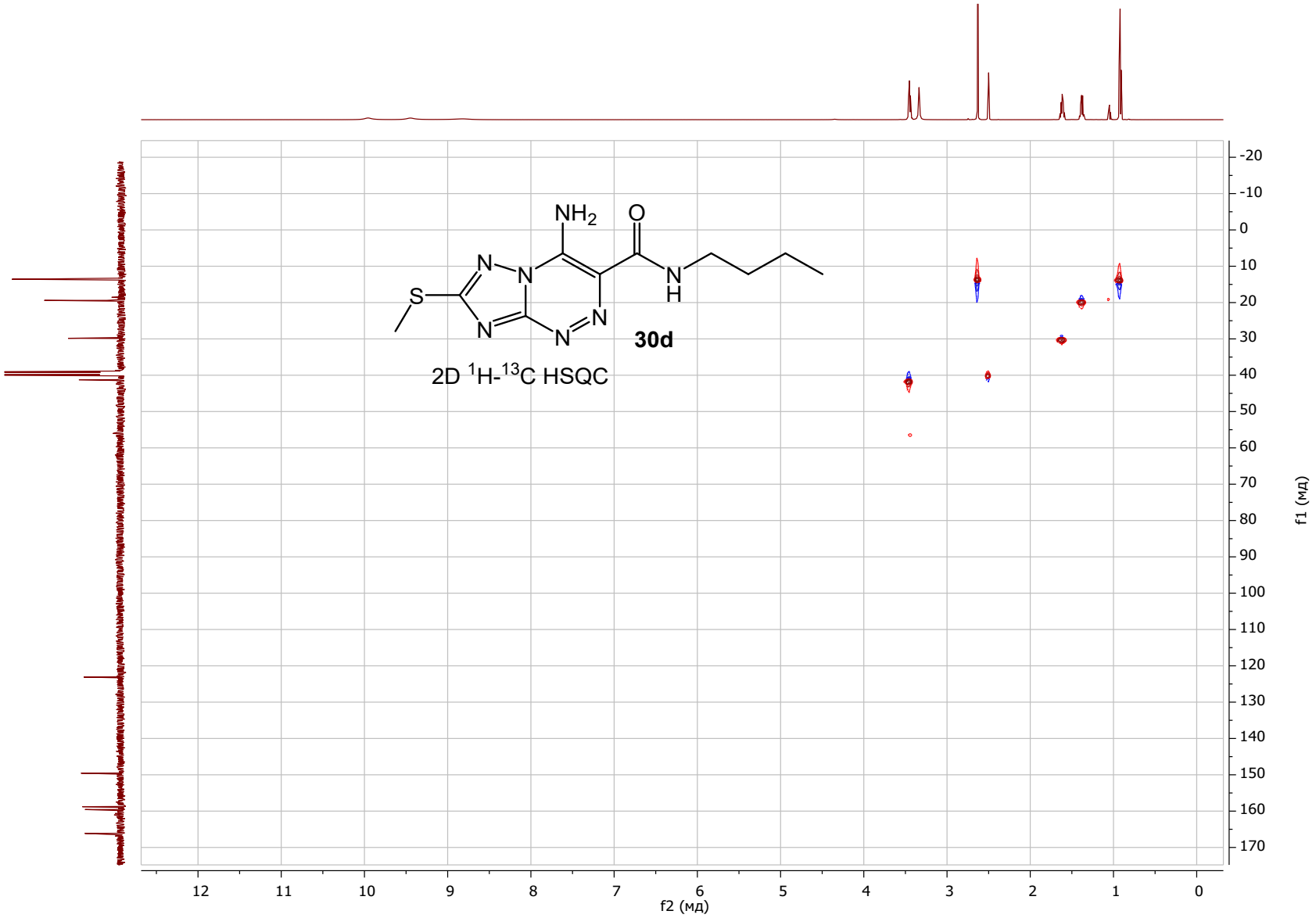
Line#:1 R.Time:2.495(Scan#:959)
MassPeaks:191
RawMode:Single 2.495(959) BasePeak:303(1187910)
Фон.реж.:1.440(537) Group 1 - Event 1

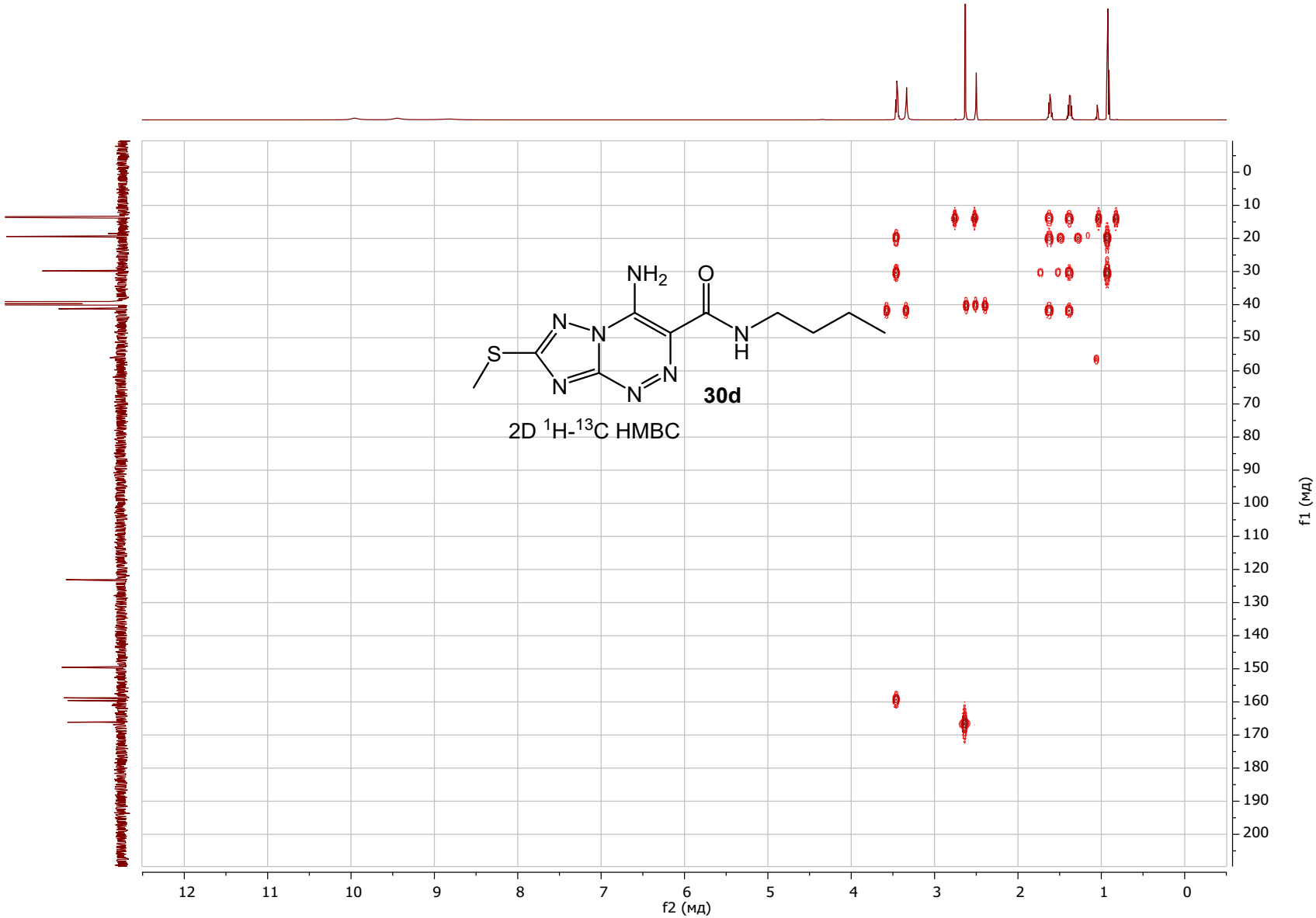


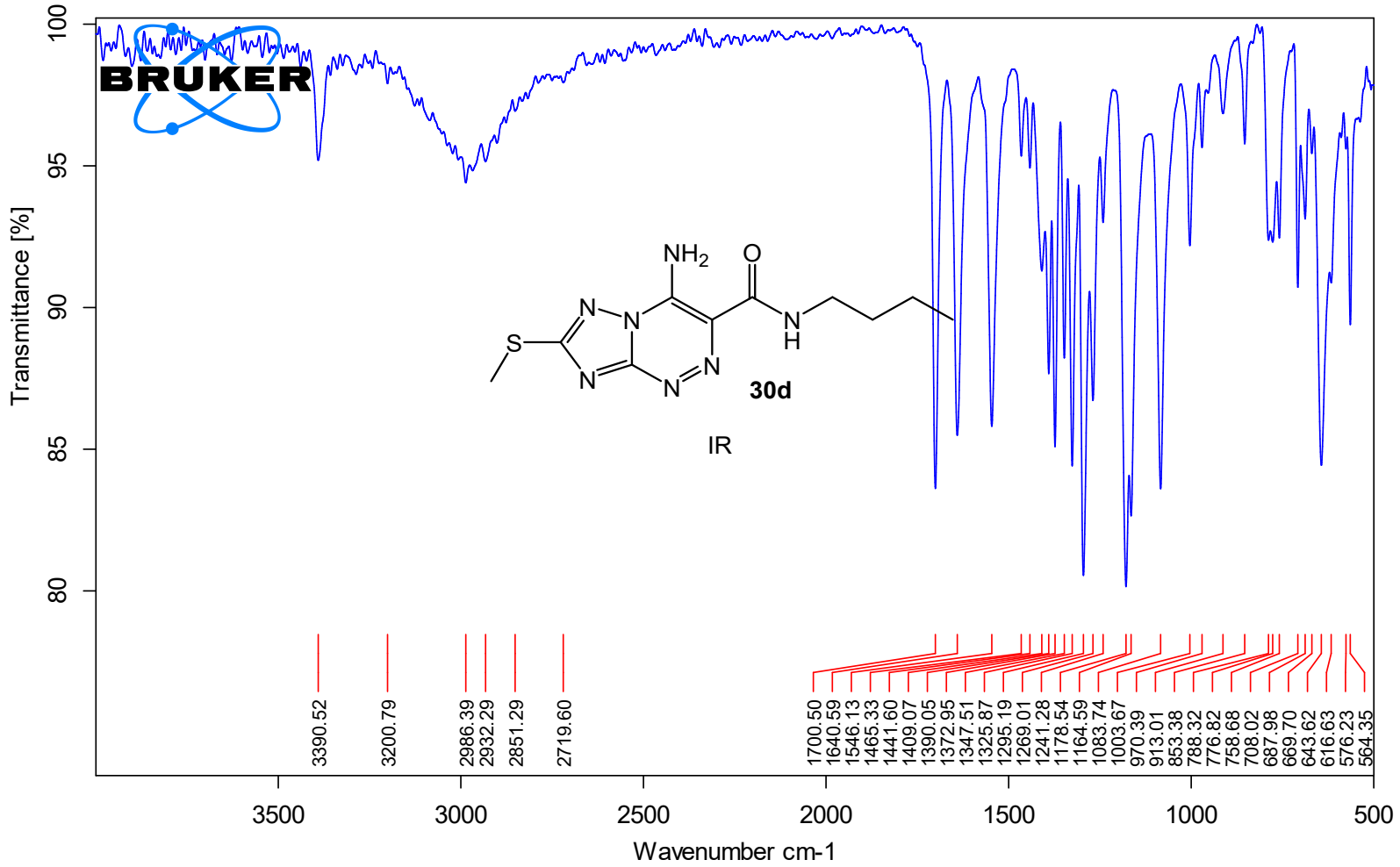
4-Amino-*N*-butyl-7-(methylthio)-[1,2,4]triazolo[5,1-*c*][1,2,4]triazine-3-carboxamide (30d)



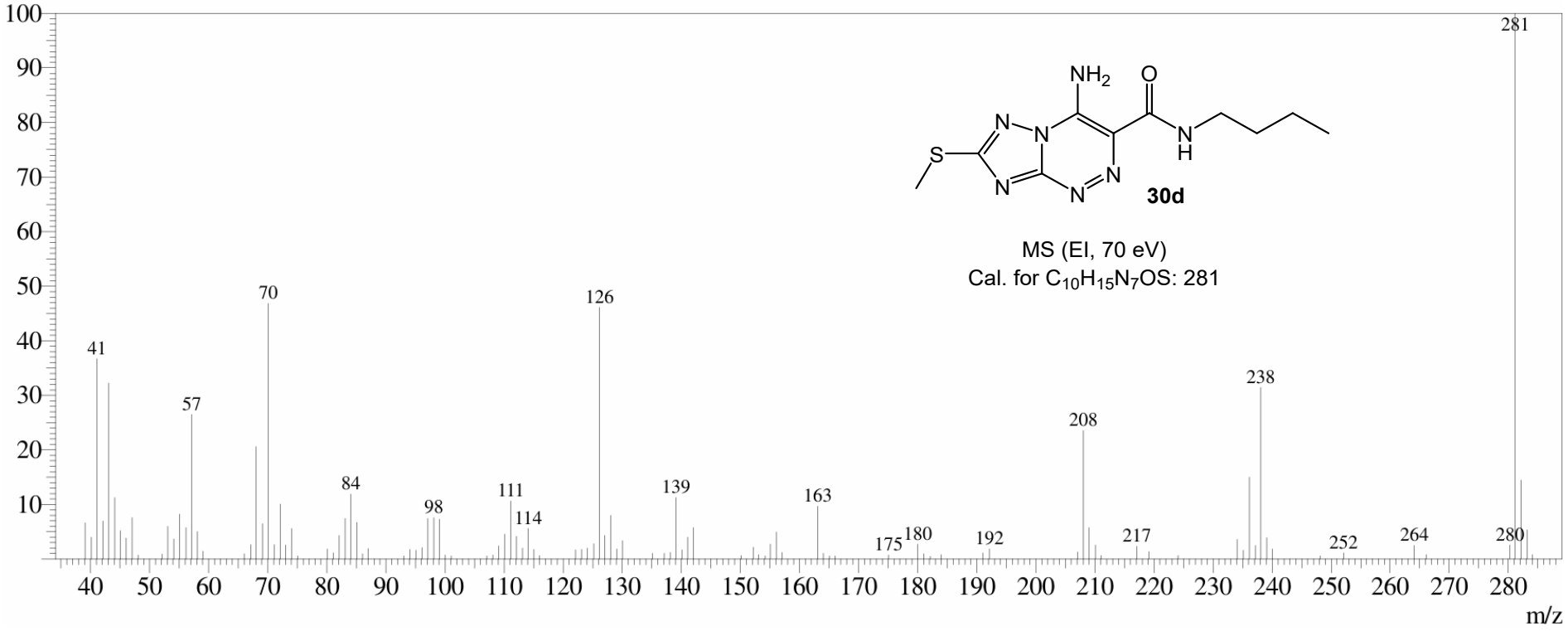

166.14
159.58
158.78
149.56
123.10
41.24
29.83
19.40
13.58
13.42
NH2
O
N
N
S
N
N
N
H
30d
13C, 150 MHz, DMSO-D6
f1 (мд)


NH2
O
N
N
S
N
N
N
H
30d
2D 1H-13C HSQC
f2 (мд)
f1 (мд)

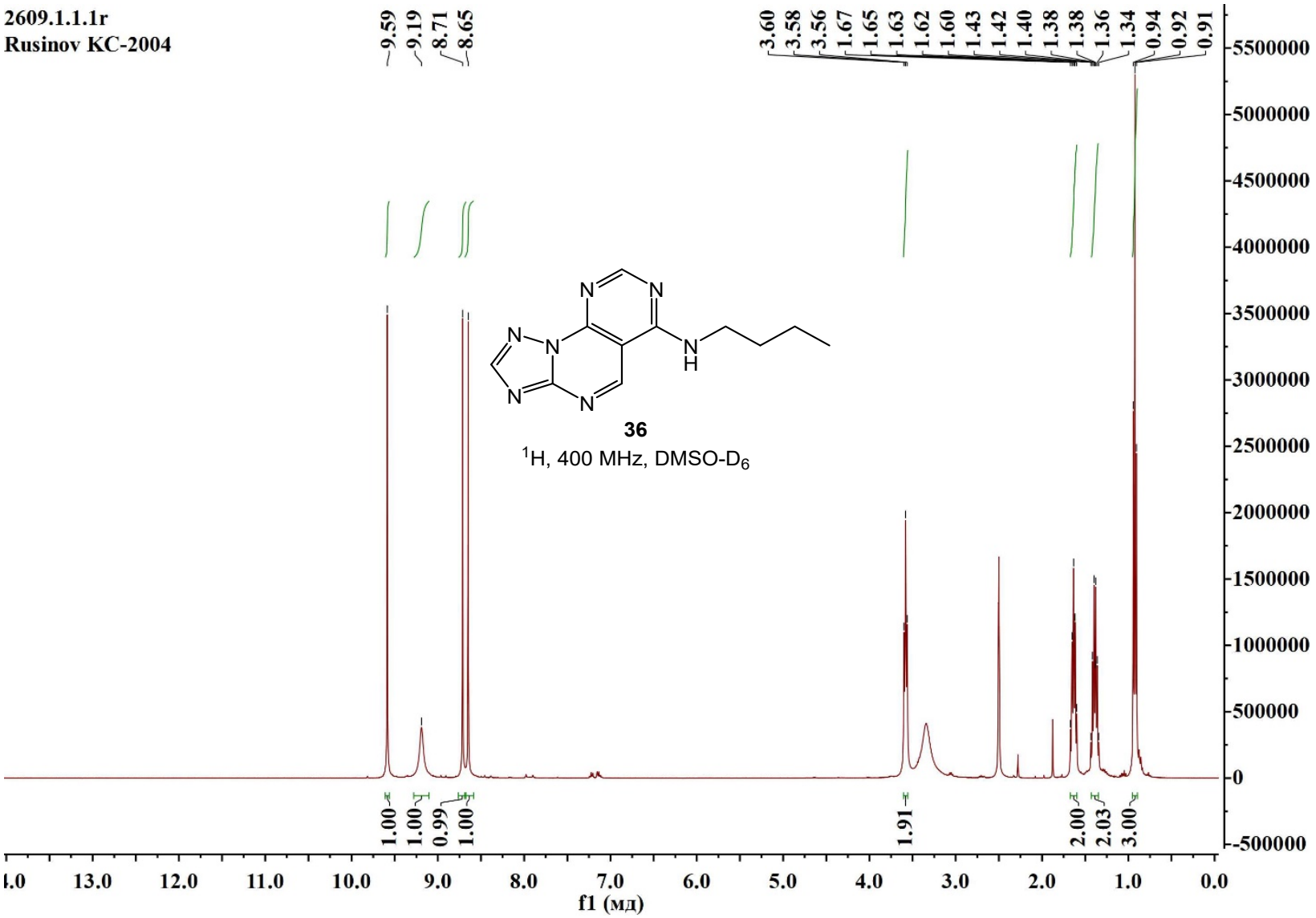

NH2
O
N
N
S
N
N
N
H
30d
2D 1H-13C HMBC
f2 (мд)
f1 (мд)

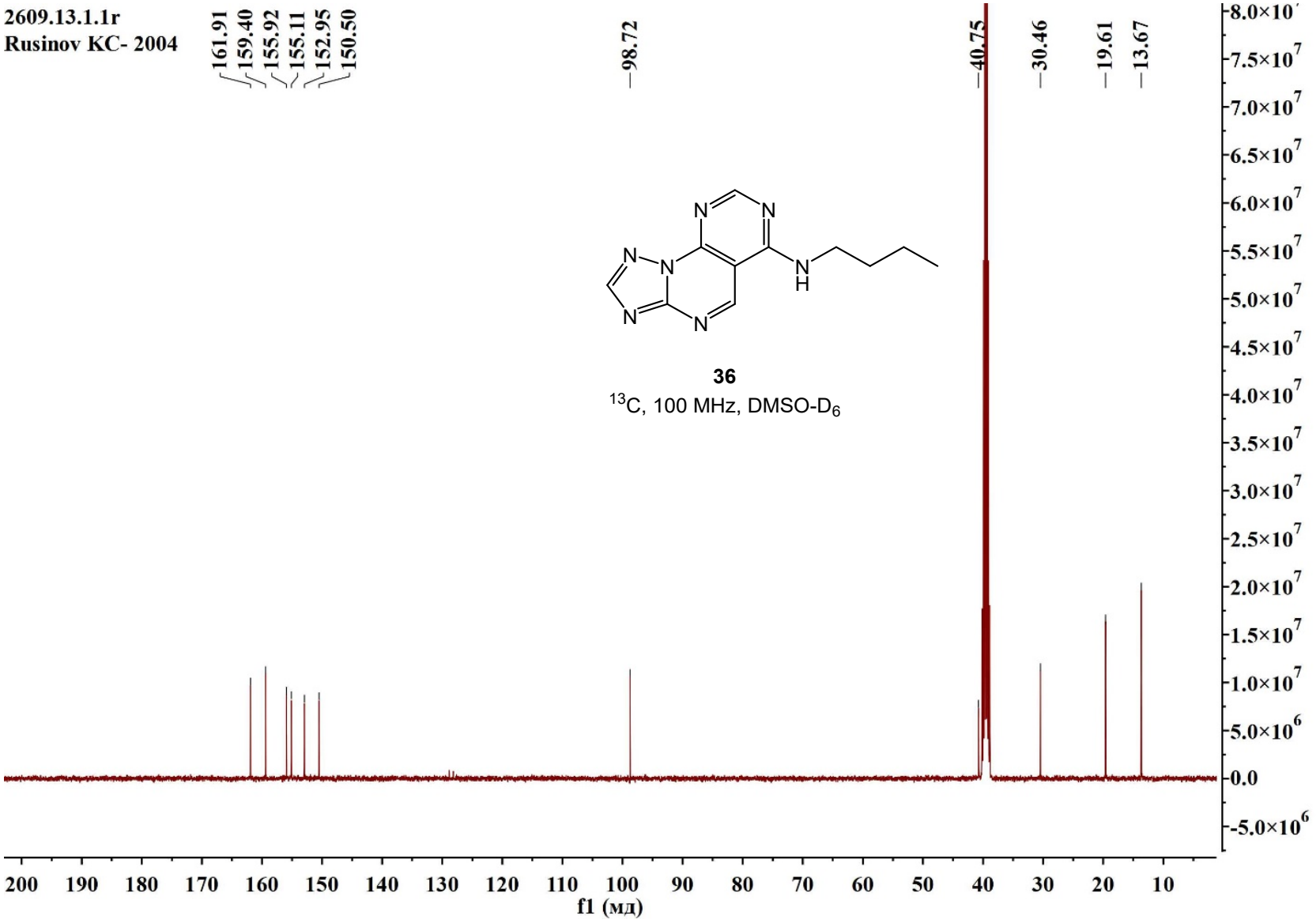

BRUKER
Transmittance [%]
100
95
90
85
80
NH2
O
N
N
S
N
N
N
H
30d
IR
3390.52
3200.79
2986.39
2932.29
2851.29
2719.60
1700.50
1640.59
1546.13
1465.33
1441.60
1409.07
1390.05
1372.95
1347.51
1325.87
1295.19
1269.01
1241.28
1178.54
1164.59
1083.74
1003.67
970.39
913.01
853.38
788.32
776.82
758.68
708.02
687.98
669.70
643.62
616.63
576.23
564.35
3500
3000
2500
2000
1500
1000
500
Wavenumber cm-1

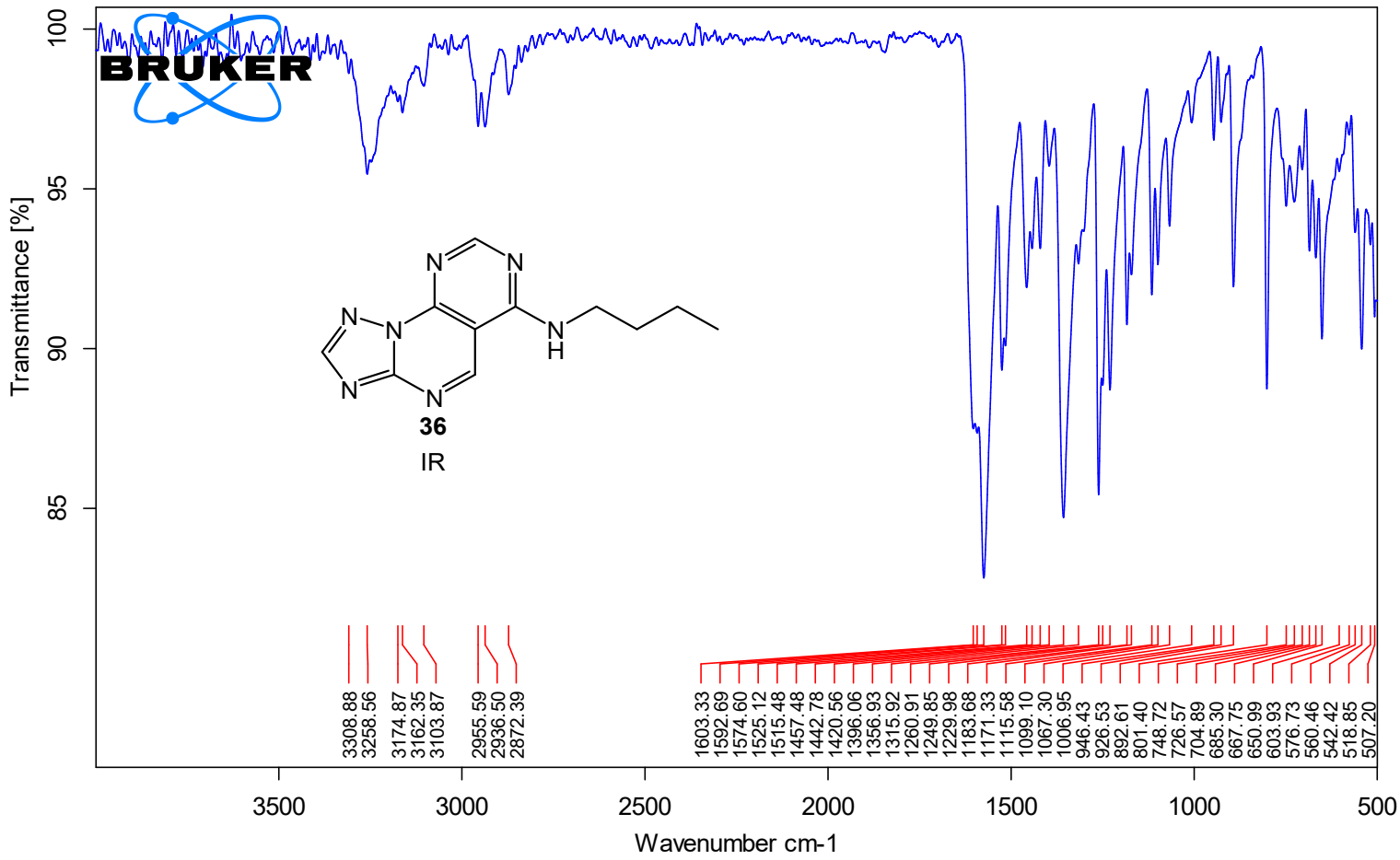
Line#:1 R.Time:3.830(Scan#:1493)
MassPeaks:113
RawMode:Single 3.830(1493) BasePeak:281(3700897)
Фон.реж.:2.060(785) Group 1 - Event 1



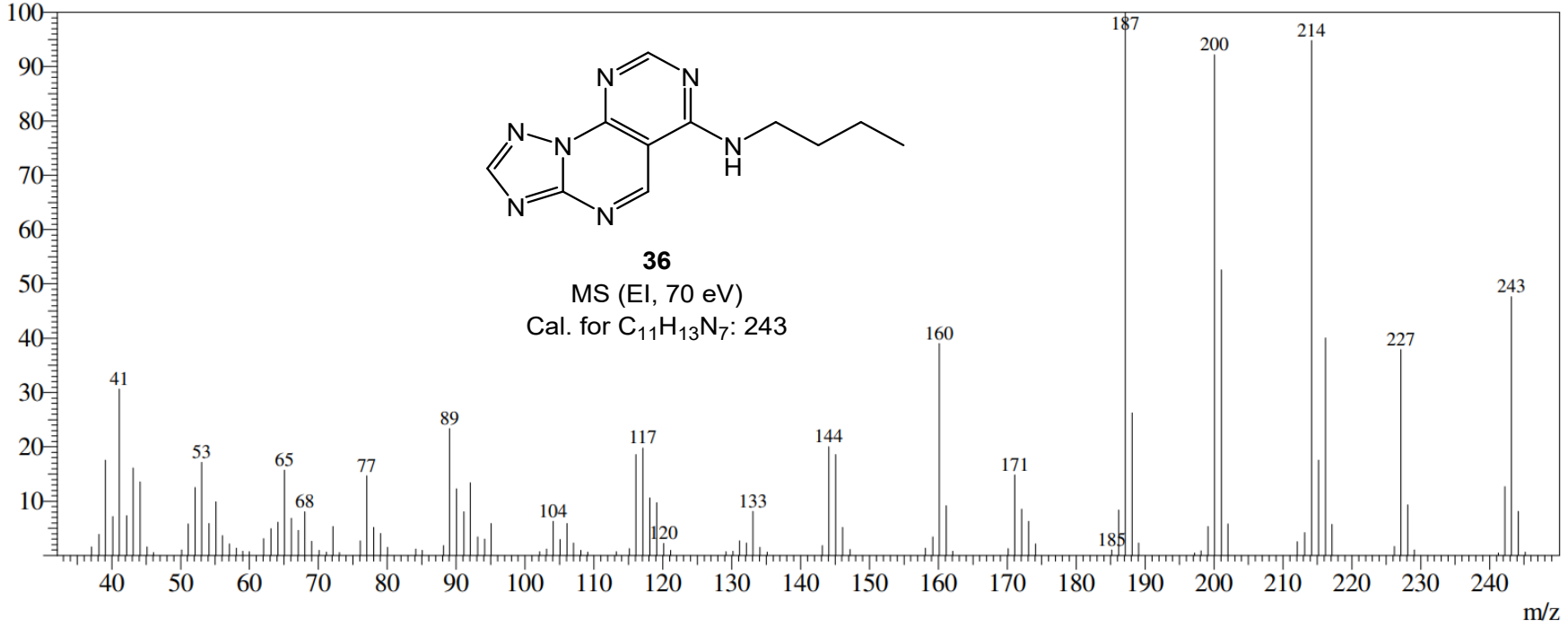
_N_-Butylpyrimido[5,4-_e_][1,2,4]triazolo[1,5-_a_]pyrimidin-6-amine (36).



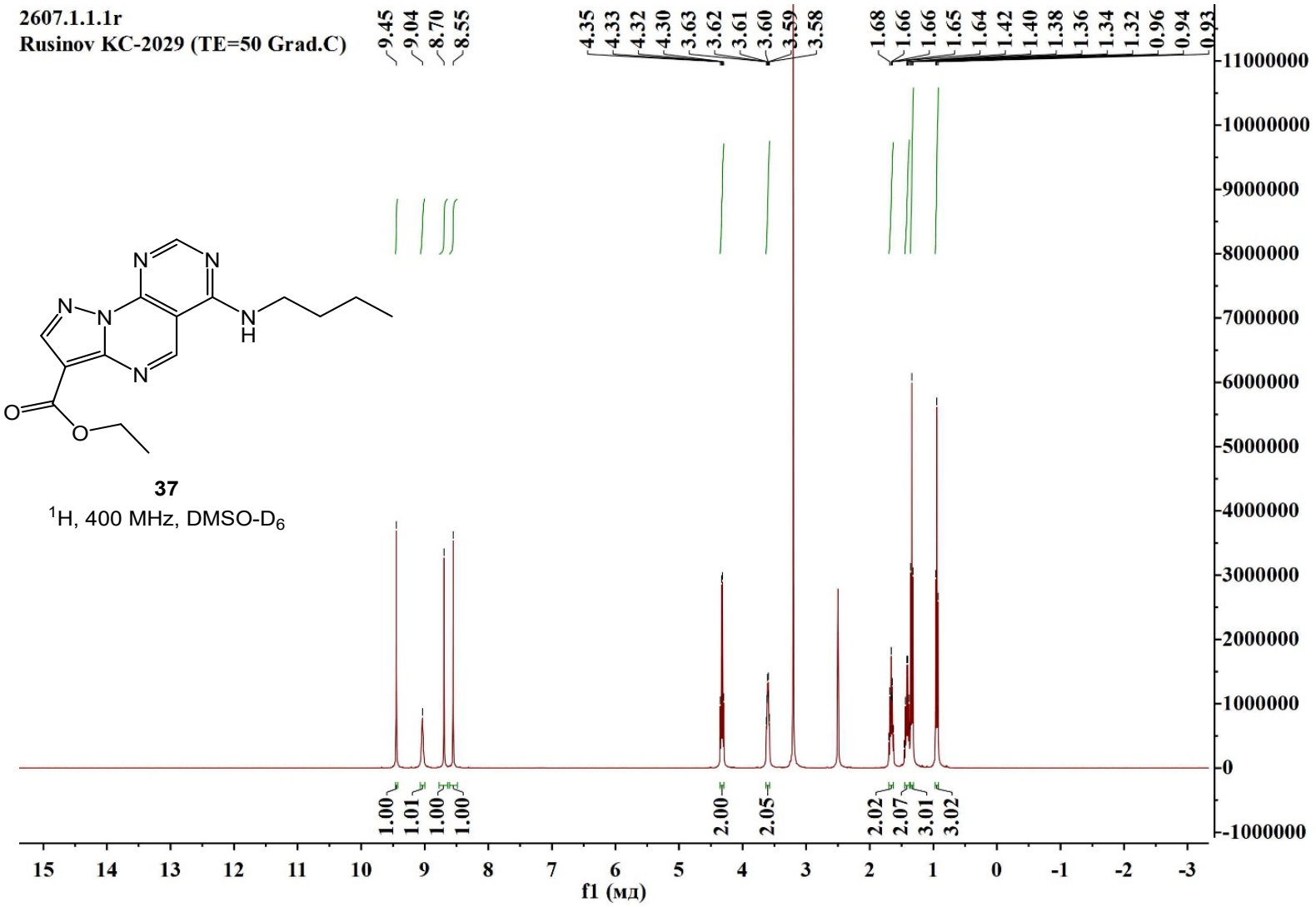

2609.13.1.1r
Rusinov KC- 2004
161.91
159.40
155.92
155.11
152.95
150.50
98.72
40.75
30.46
19.61
13.67
N
N
N
N
N
N
H
36
13C, 100 MHz, DMSO-D6
8.0×10^7
7.5×10^7
7.0×10^7
6.5×10^7
6.0×10^7
5.5×10^7
5.0×10^7
4.5×10^7
4.0×10^7
3.5×10^7
3.0×10^7
2.5×10^7
2.0×10^7
1.5×10^7
1.0×10^7
5.0×10^6
0.0
-5.0×10^6
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (мд)


BRUKER
Transmittance [%]
100
95
90
85
N
N
N
N
N
N
H
36
IR
3308.88
3258.56
3174.87
3162.35
3103.87
2955.59
2936.50
2872.39
1603.33
1592.69
1574.60
1525.12
1515.48
1457.48
1442.78
1420.56
1396.06
1356.93
1315.92
1260.91
1249.85
1229.98
1183.68
1171.33
1115.58
1099.10
1067.30
1006.95
946.43
926.53
892.61
801.40
748.72
726.57
704.89
685.30
667.75
650.99
603.93
576.73
560.46
542.42
518.85
507.20
3500
3000
2500
2000
1500
1000
500
Wavenumber cm-1

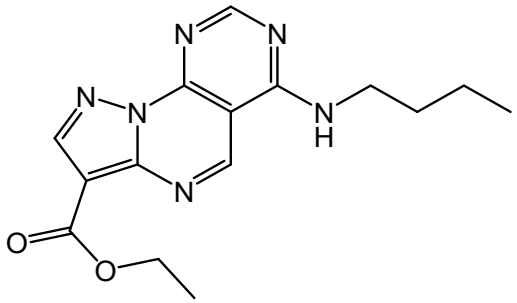
Line#:1 R.Time:1.958(Scan#:744)
MassPeaks:112
RawMode:Single 1.958(744) BasePeak:187(1295014)
Фон.реж.:2.240(857) Group 1 - Event 1



Ethyl 4-(butylamino)pyrazolo[1,5-*a*]pyrimido[5,4-*e*]pyrimidine-7-carboxylate (37).

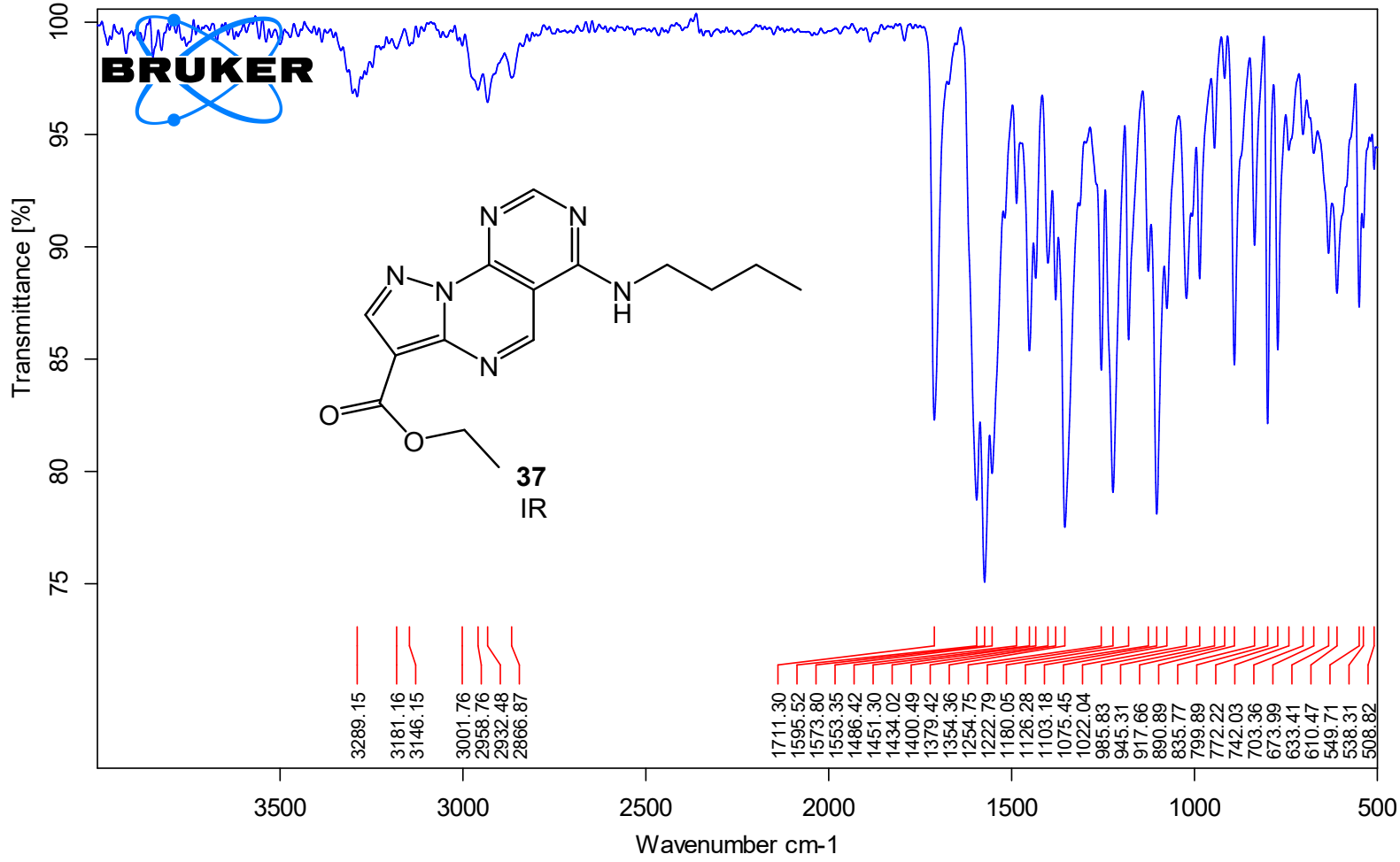


2607.13.1.1r
Rusinov KC-2029

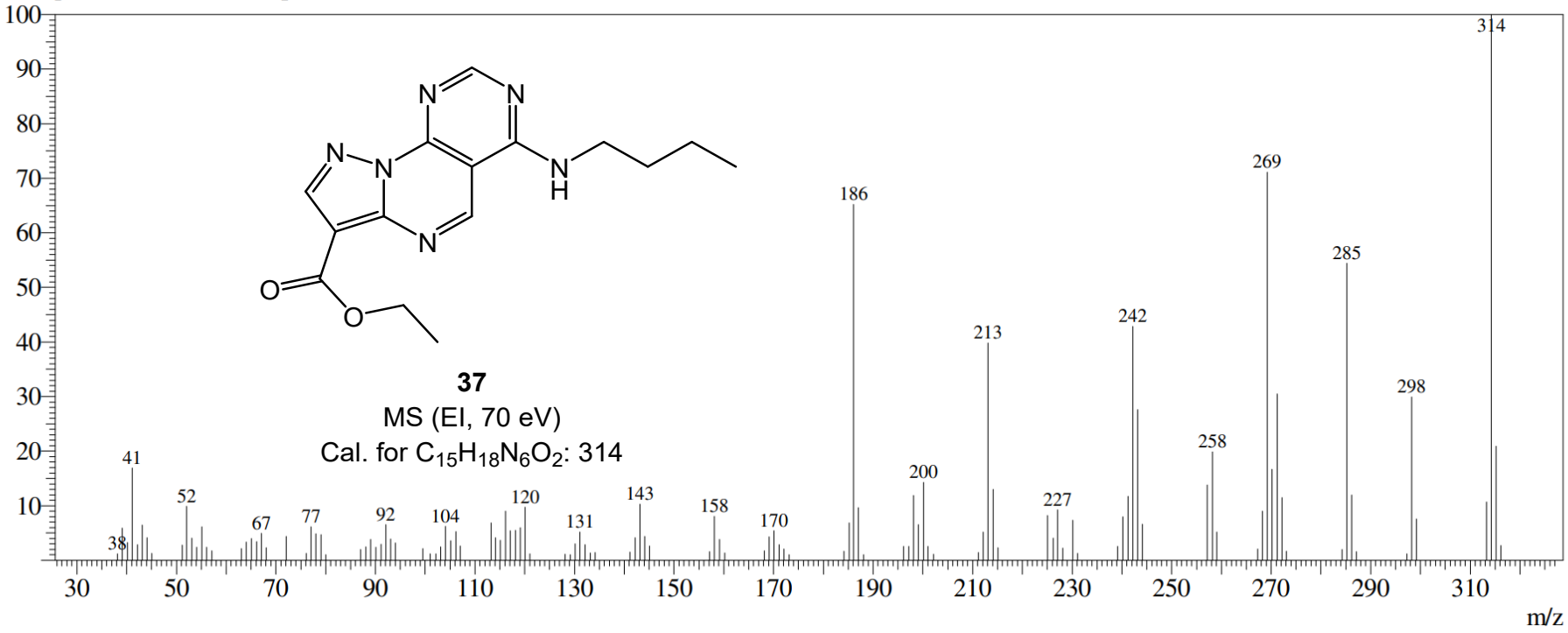


37

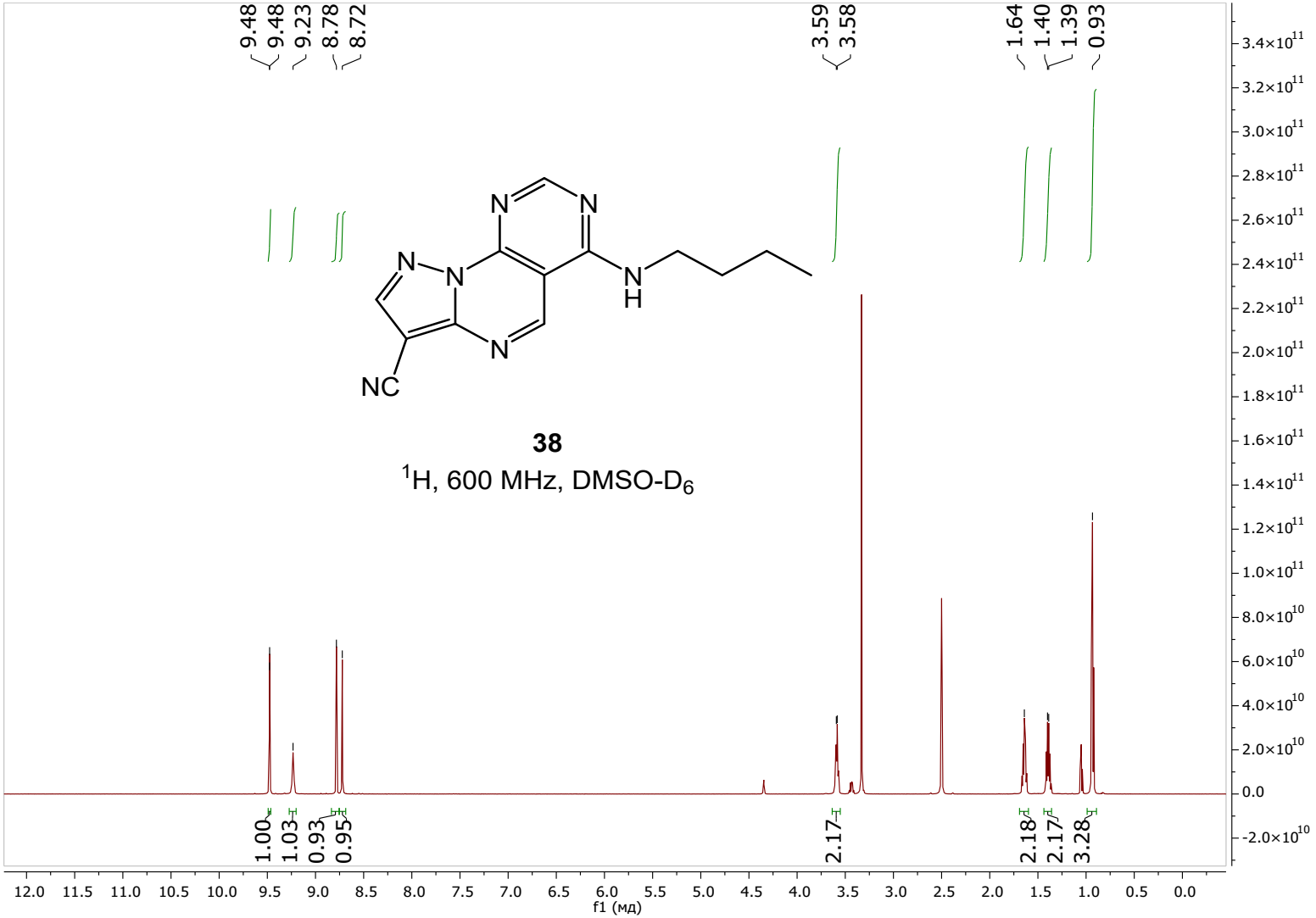
^{13}C, 100 MHz, DMSO-D_6

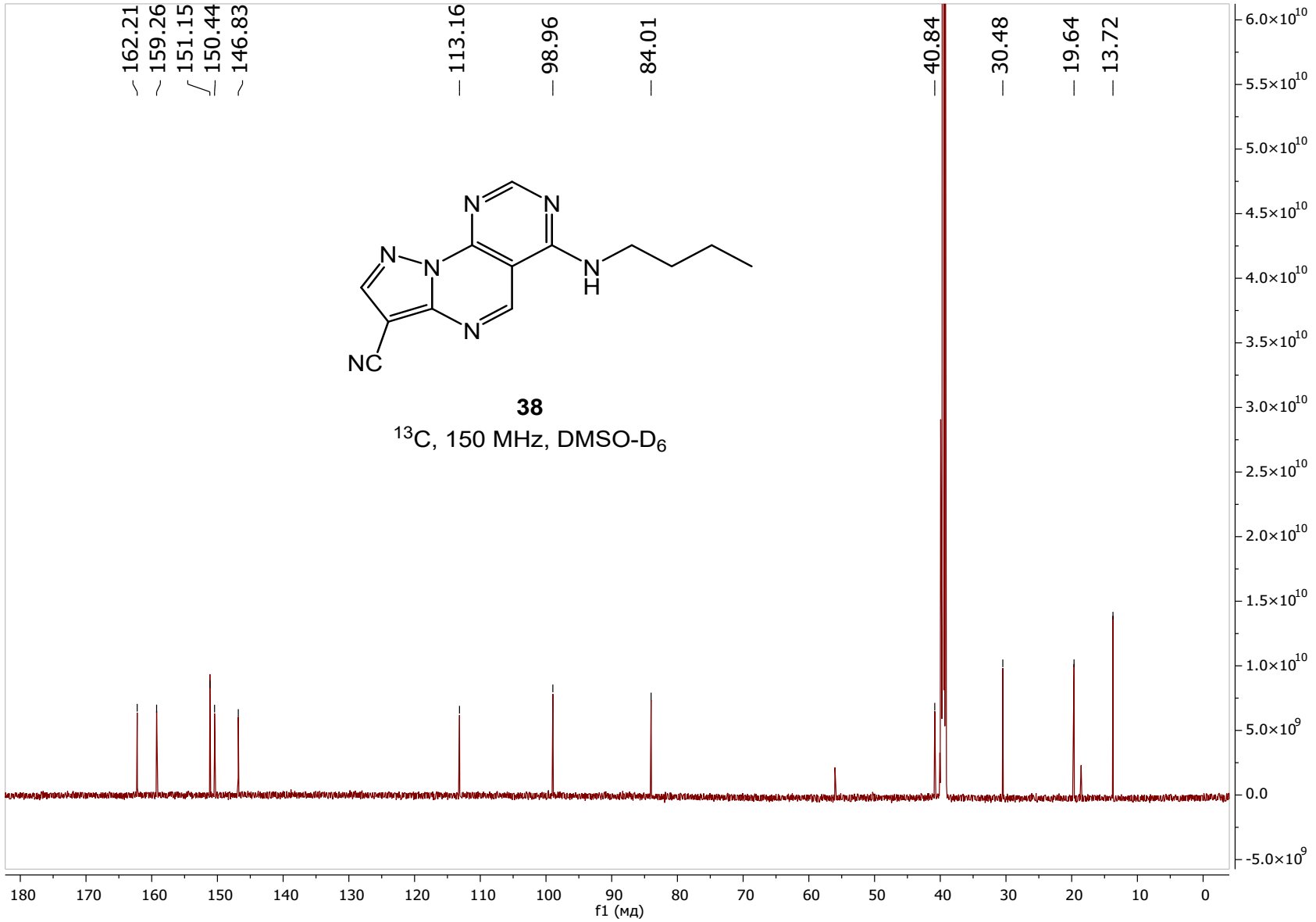

BRUKER
Transmittance [%]
100
95
90
85
80
75
3500
3000
2500
2000
1500
1000
500
Wavenumber cm-1
N
N
N
N
N
H
O
O
37
IR
3289.15
3181.16
3146.15
3001.76
2958.76
2932.48
2866.87
1711.30
1595.52
1573.80
1553.35
1486.42
1451.30
1434.02
1400.49
1379.42
1354.36
1254.75
1222.79
1180.05
1126.28
1103.18
1075.45
1022.04
985.83
945.31
917.66
890.89
835.77
799.89
772.22
742.03
703.36
673.99
633.41
610.47
549.71
538.31
508.82

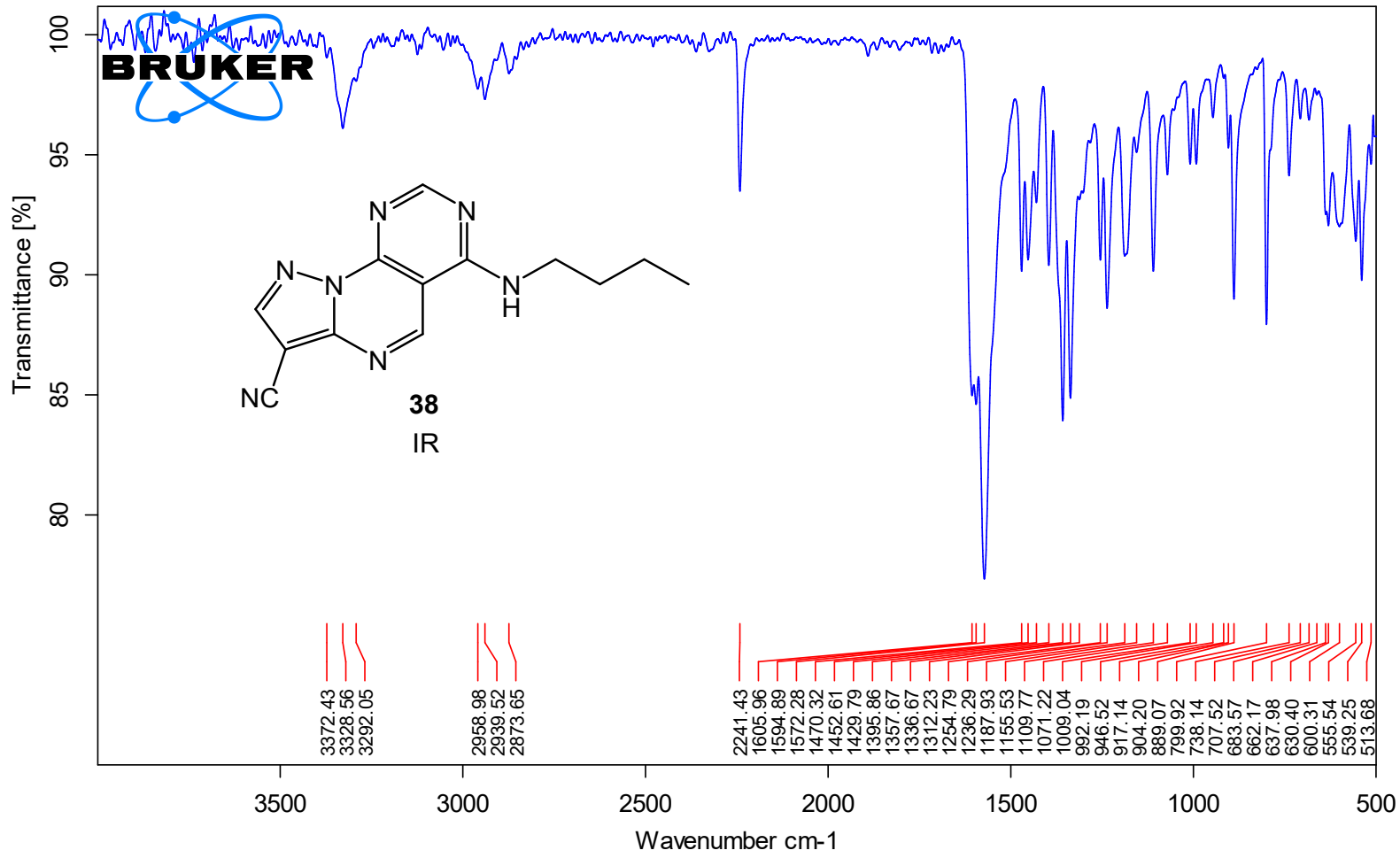
Line#:1 R.Time:3.413(Scan#:1326)
MassPeaks:124
RawMode:Single 3.413(1326) BasePeak:314(6209440)
Фон.реж.:2.408(924) Group 1 - Event 1



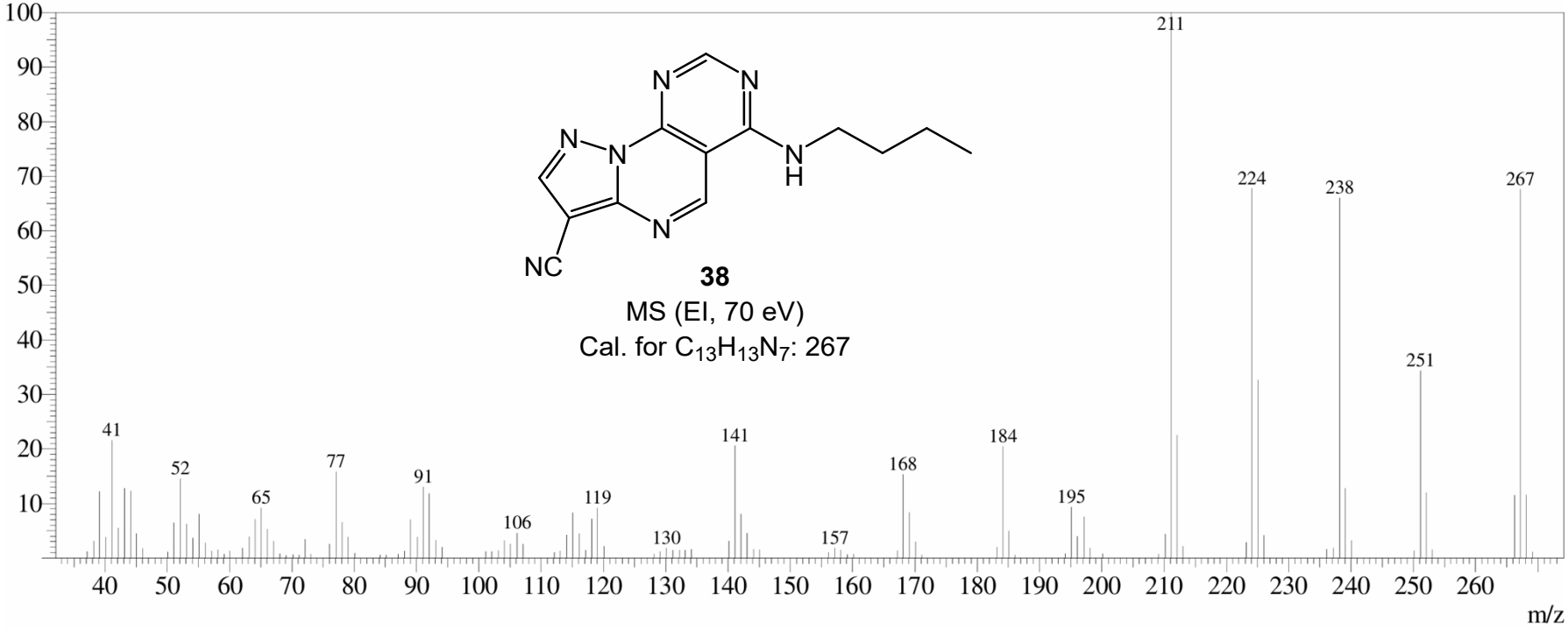
3-Butyl-4-imino-3,4-dihydropyrazolo[1,5-*a*]pyrimido[5,4-*e*]pyrimidine-7-carbonitrile (38).




162.21
159.26
151.15
150.44
146.83
113.16
98.96
84.01
40.84
30.48
19.64
13.72
N
N
N
N
N
H
NC
38
13C, 150 MHz, DMSO-D6
6.0×10^10
5.5×10^10
5.0×10^10
4.5×10^10
4.0×10^10
3.5×10^10
3.0×10^10
2.5×10^10
2.0×10^10
1.5×10^10
1.0×10^10
5.0×10^9
0.0
-5.0×10^9
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (мд)


BRUKER
Transmittance [%]
100
95
90
85
80
N
N
N
N
N
H
NC
38
IR
3372.43
3328.56
3292.05
2958.98
2939.52
2873.65
2241.43
1605.96
1594.89
1572.28
1470.32
1452.61
1429.79
1395.86
1357.67
1336.67
1312.23
1254.79
1236.29
1187.93
1155.53
1109.77
1071.22
1009.04
992.19
946.52
917.14
904.20
889.07
799.92
738.14
707.52
683.57
662.17
637.98
630.40
600.31
555.54
539.25
513.68
3500
3000
2500
2000
1500
1000
500
Wavenumber cm-1

Line#:1 R.Time:2.557(Scan#:984)
MassPeaks:119
RawMode:Single 2.558(984) BasePeak:211(2228250)
Фон.реж.:1.482(554) Group 1 - Event 1

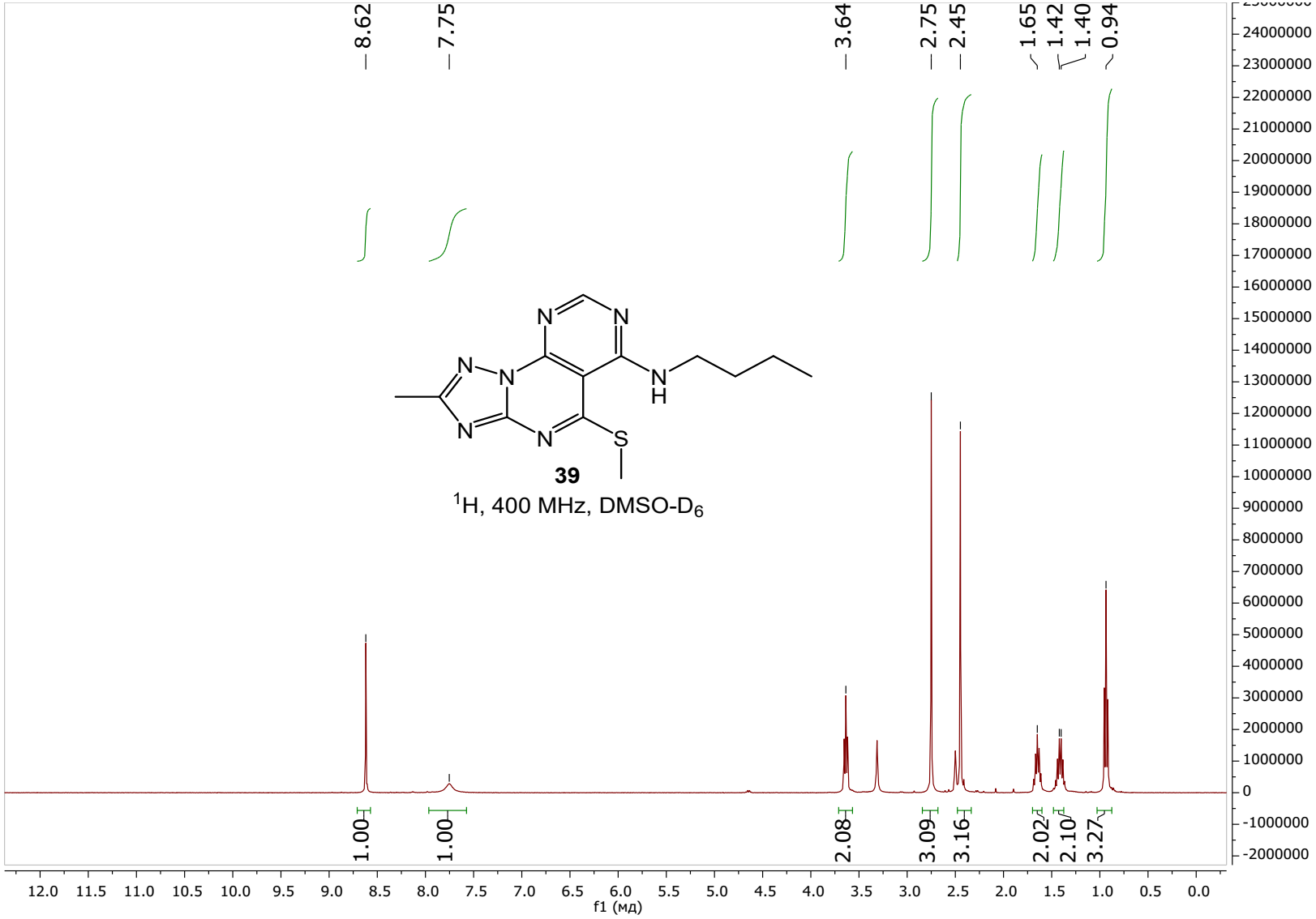


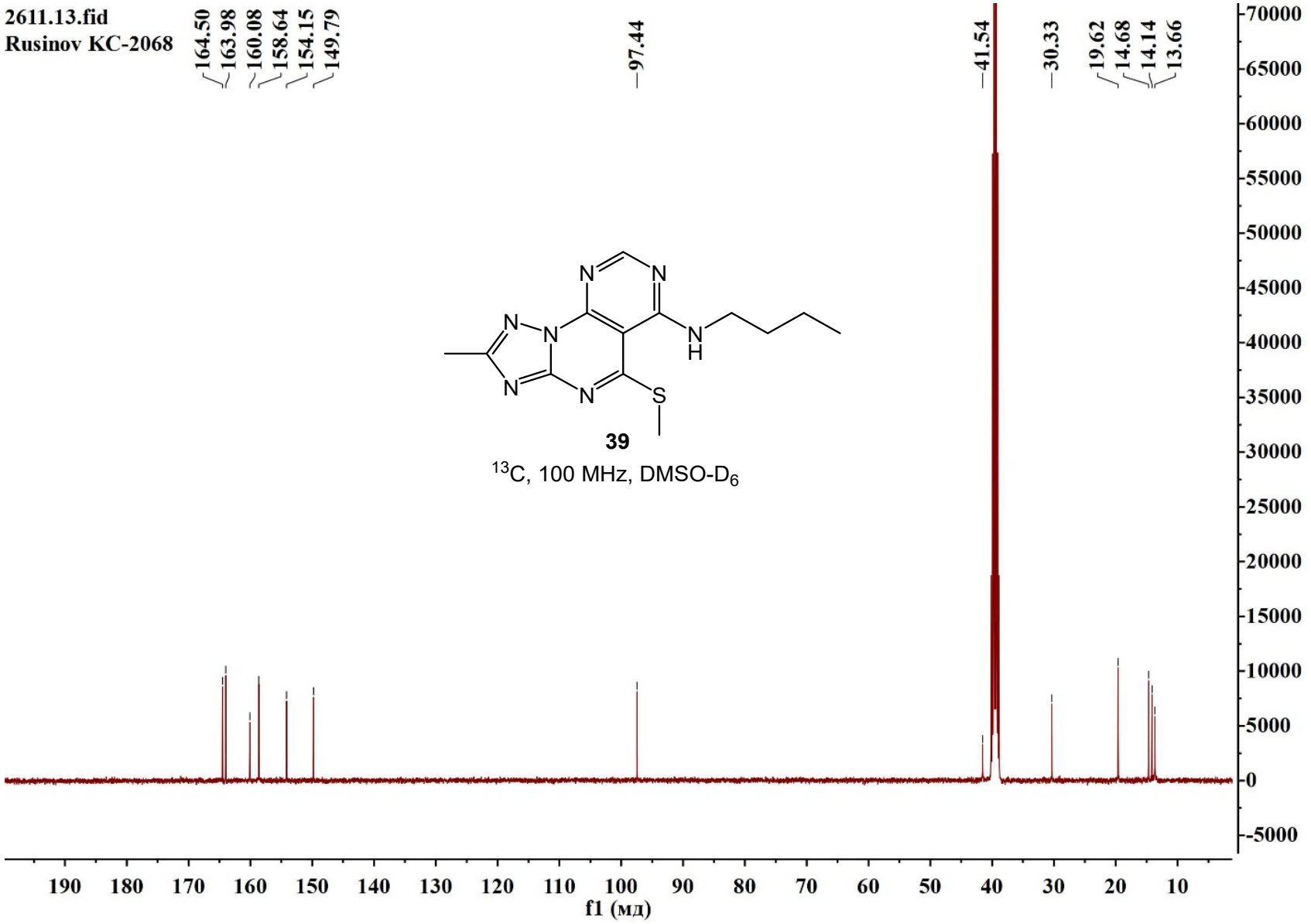
38

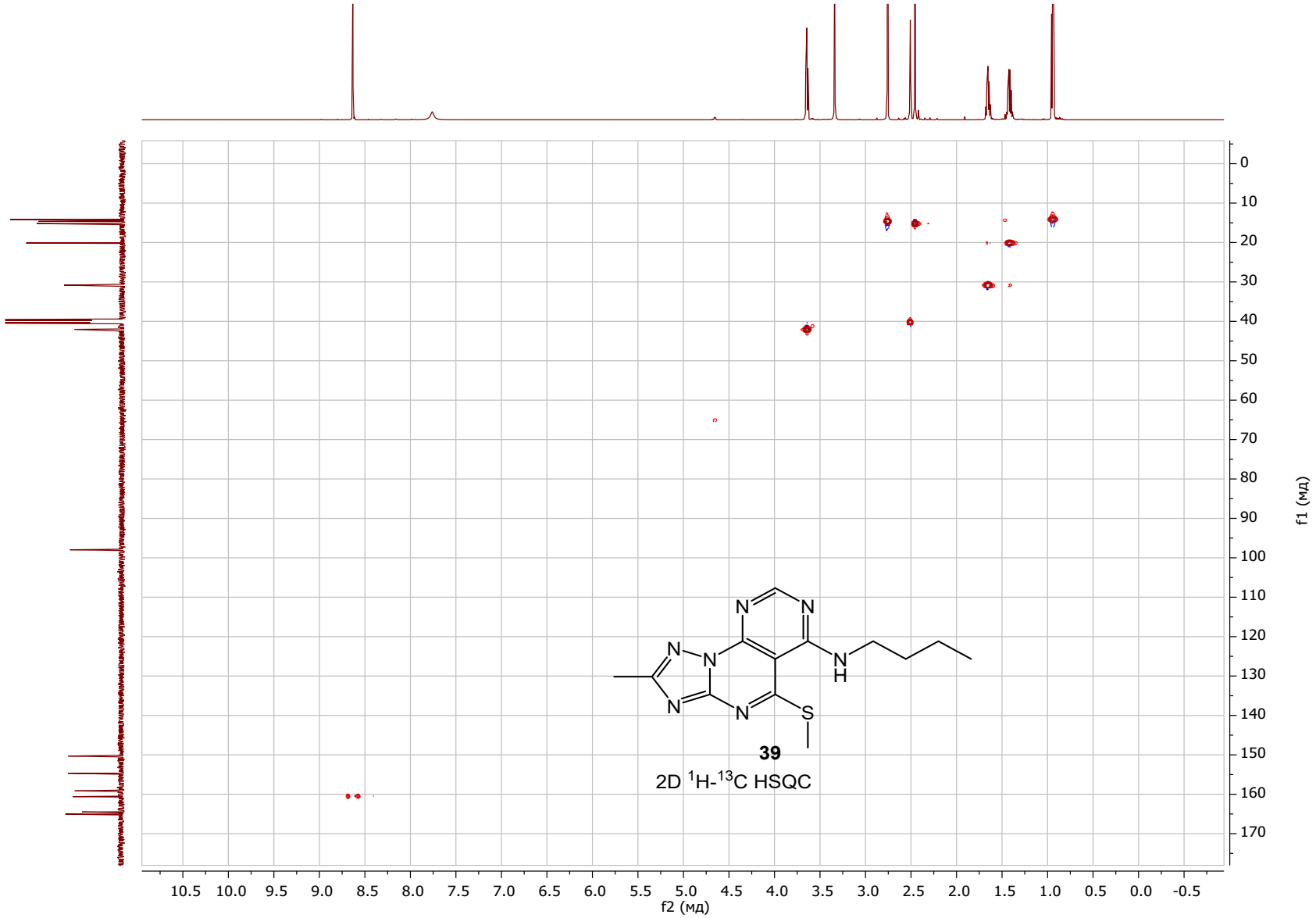
MS (EI, 70 eV)

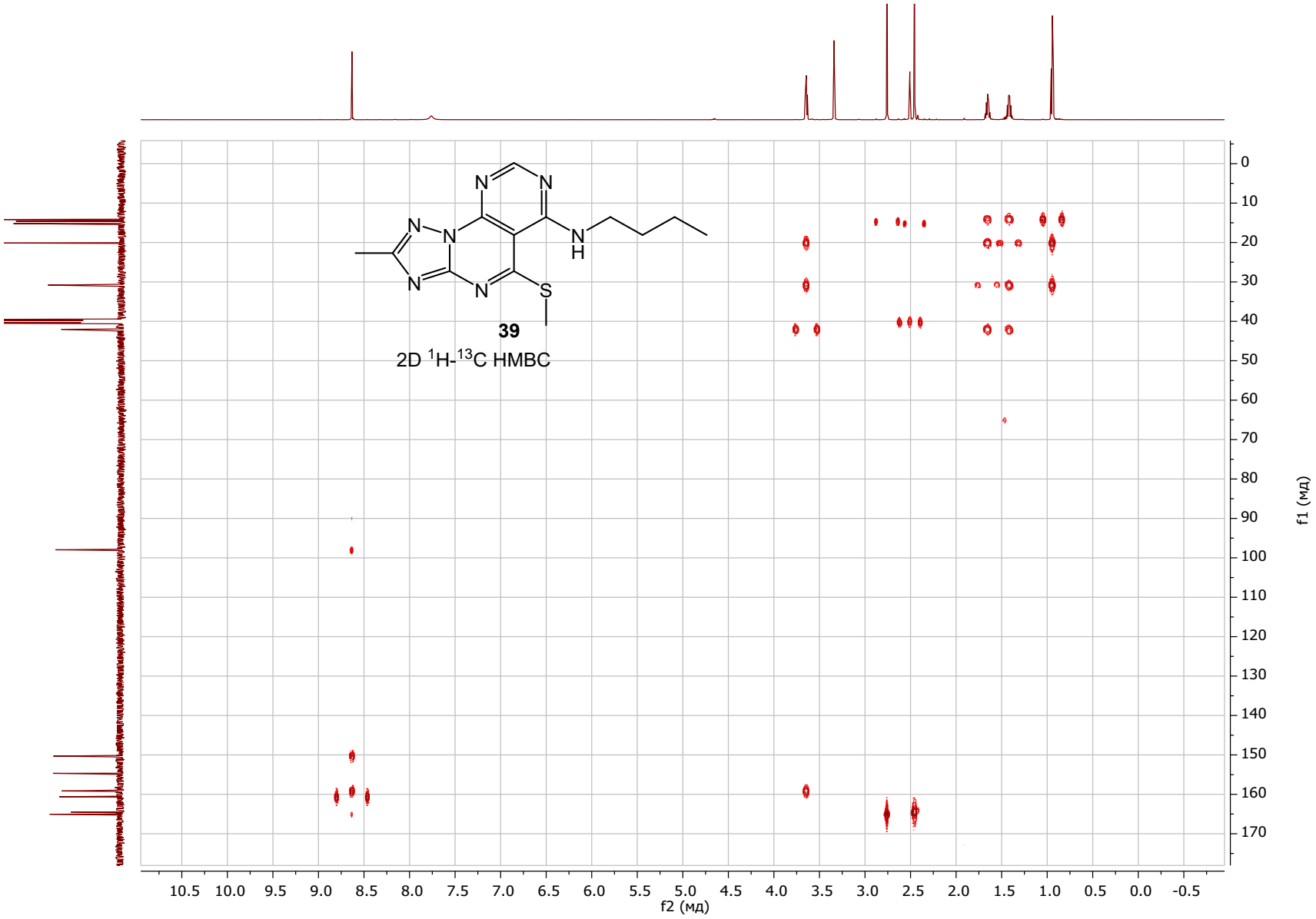
Cal. for $C_{13}H_{13}N_7$: 267

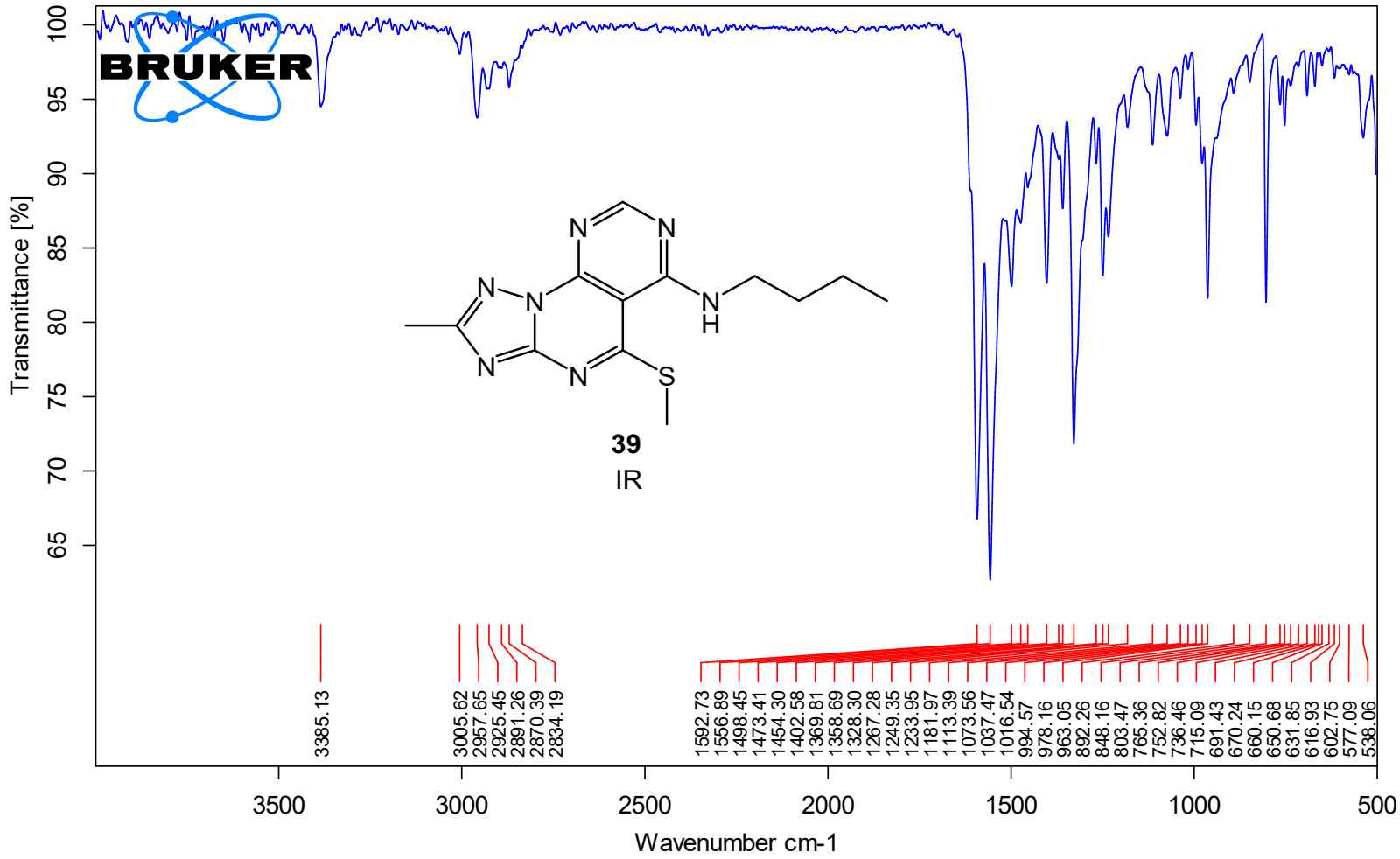
_N_-Butyl-2-methyl-5-(methylthio)pyrimido[5,4-_e_][1,2,4]triazolo[1,5-_a_]pyrimidin-6-amine (39).



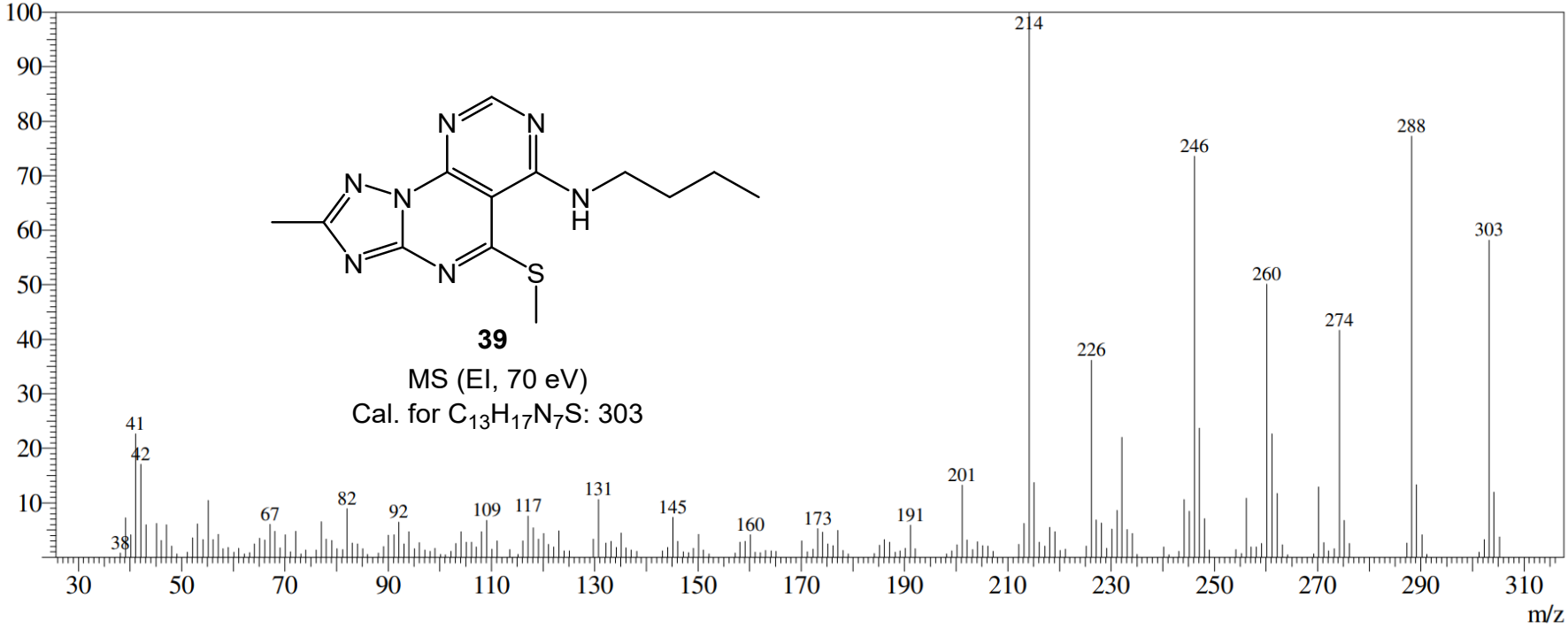

2611.13.fid
Rusinov KC-2068
164.50
163.98
160.08
158.64
154.15
149.79
97.44
41.54
30.33
19.62
14.68
14.14
13.66
N
N
N
N
N
H
N
S
39
13C, 100 MHz, DMSO-D6
70000
65000
60000
55000
50000
45000
40000
35000
30000
25000
20000
15000
10000
5000
0
-5000
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (мд)


f2 (мд)
f1 (мд)
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 0.0 -0.5
0 10 20 30 40 50 60 70 80 90 100 110 120 130 140 150 160 170
N
N
N
N
N
N
H
S
39
2D ^{1}H-^{13}C HSQC


39
2D ^{1}H-^{13}C HMBC
f2 (мд)
f1 (мд)


BRUKER
Transmittance [%]
100
95
90
85
80
75
70
65
N
N
N
N
N
H
N
S
39
IR
3385.13
3005.62
2957.65
2925.45
2891.26
2870.39
2834.19
1592.73
1556.89
1498.45
1473.41
1454.30
1402.58
1369.81
1358.69
1328.30
1267.28
1249.35
1233.95
1181.97
1113.39
1073.56
1037.47
1016.54
994.57
978.16
963.05
892.26
848.16
803.47
765.36
752.82
736.46
715.09
691.43
670.24
660.15
650.68
631.85
616.93
602.75
577.09
538.06
3500
3000
2500
2000
1500
1000
500
Wavenumber cm-1

Line#:1 R.Time:1.138(Scan#:416)
MassPeaks:198
RawMode:Single 1.138(416) BasePeak:214(734807)
Фон.реж.:4.508(1764) Group 1 - Event 1

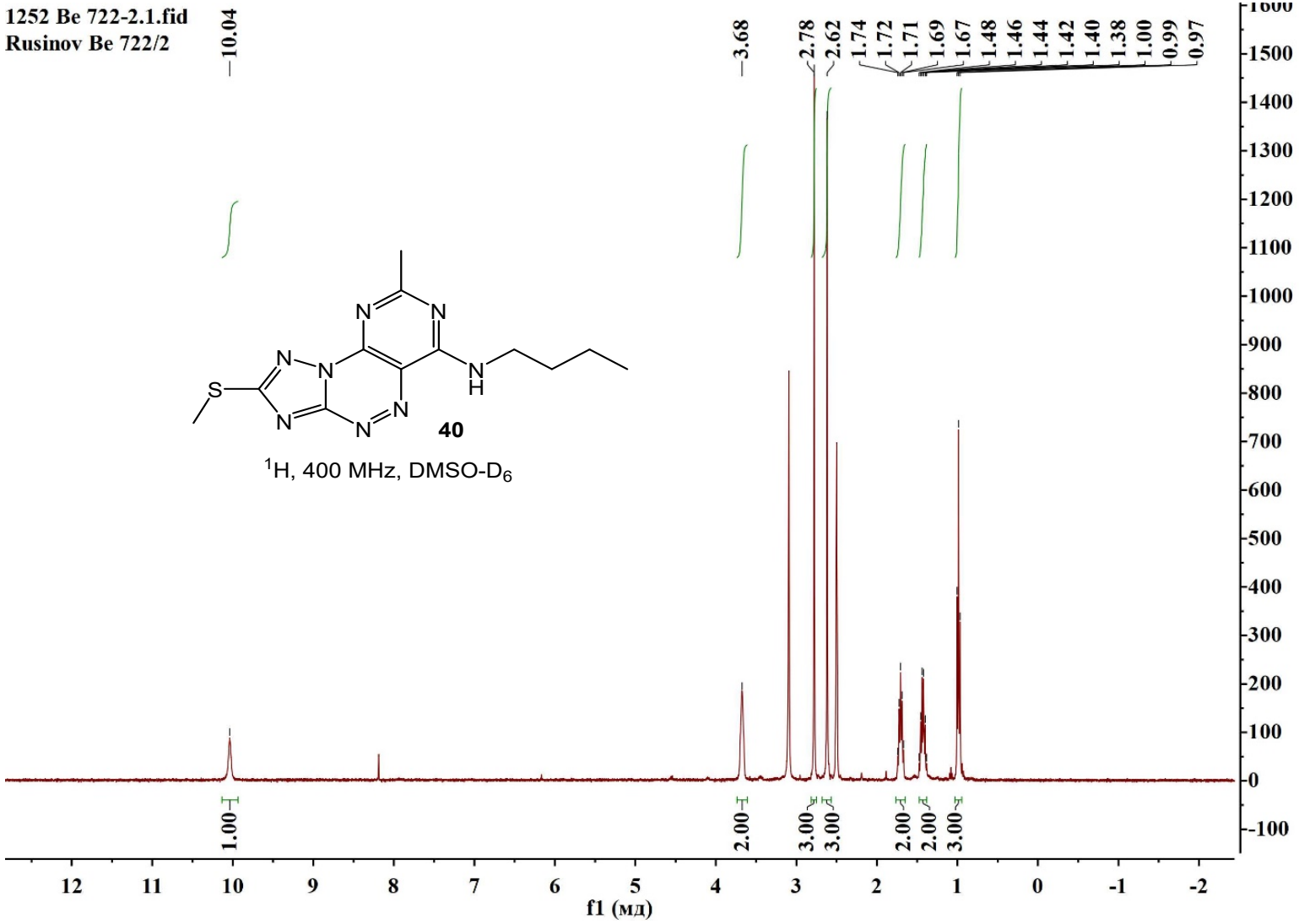


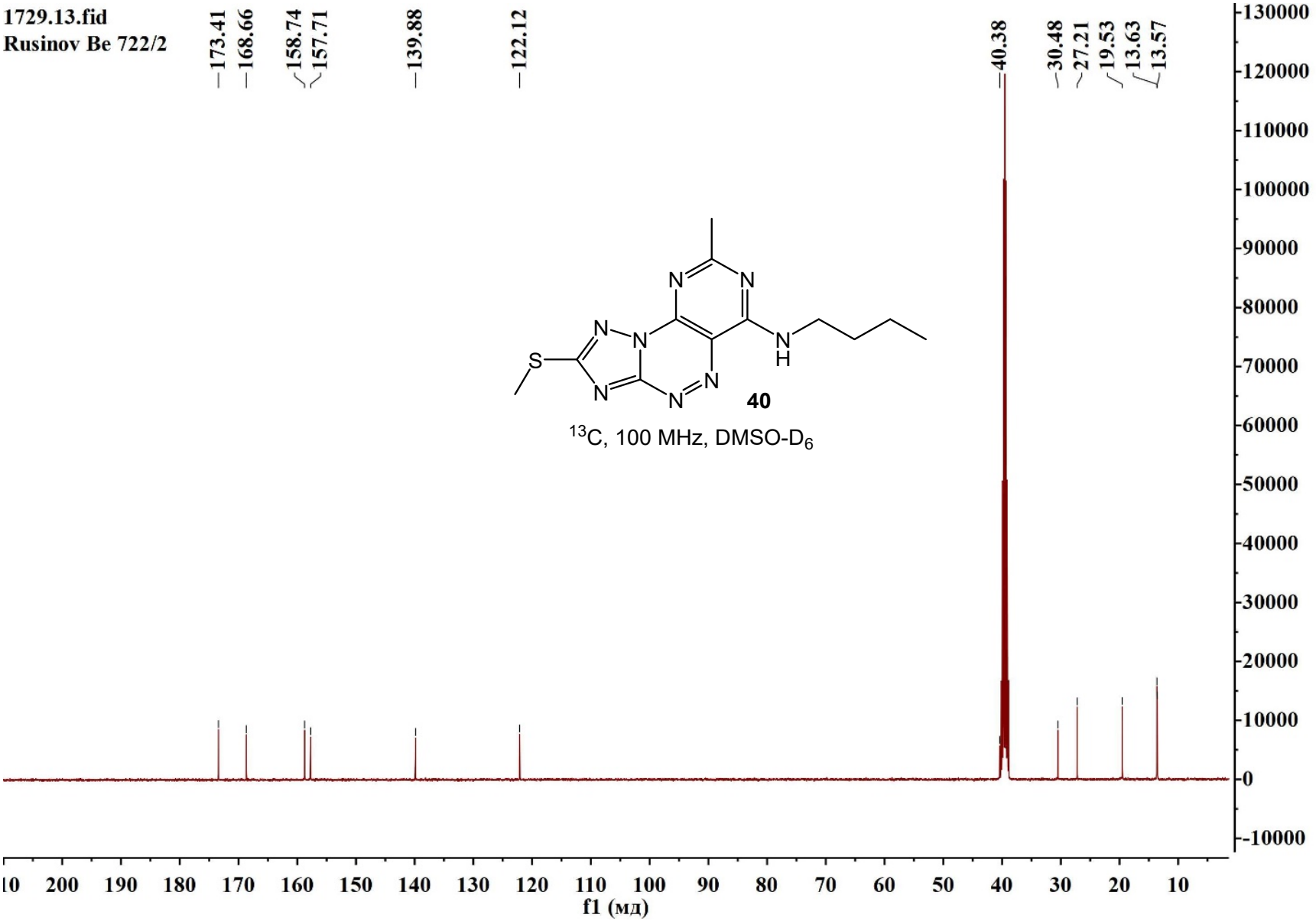
39

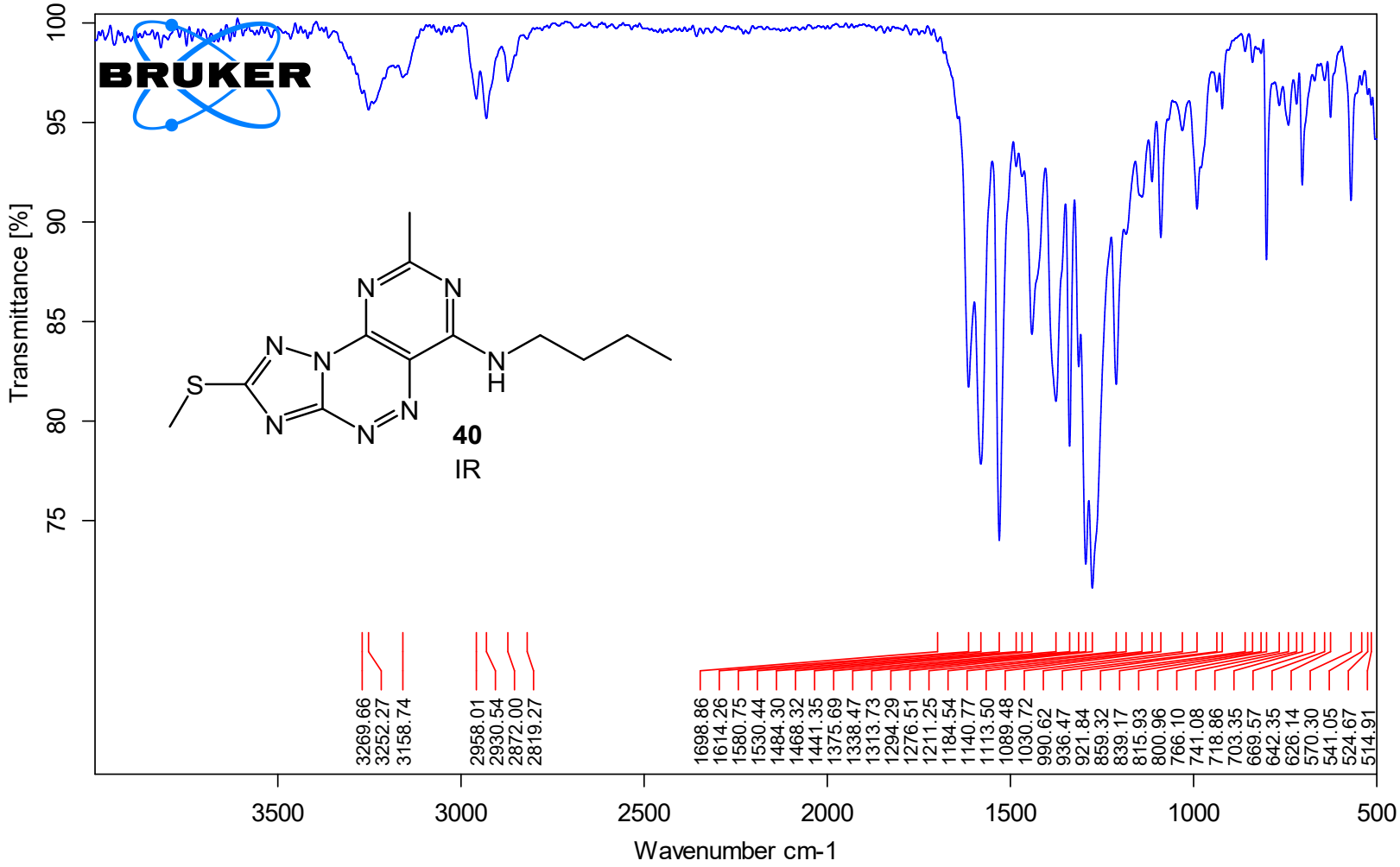
MS (EI, 70 eV)

Cal. for $C_{13}H_{17}N_7S$: 303

_N_-Butyl-8-methyl-2-(methylthio)pyrimido[4,5-_e_][1,2,4]triazolo[5,1-_c_][1,2,4]triazin-6-amine (40).




1729.13.fid
Rusinov Be 722/2
173.41
168.66
158.74
157.71
139.88
122.12
40.38
30.48
27.21
19.53
13.63
13.57
N
N
N
N
N
N
S
H
40
13C, 100 MHz, DMSO-D6
130000
120000
110000
100000
90000
80000
70000
60000
50000
40000
30000
20000
10000
0
-10000
10 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (мд)


BRUKER
Transmittance [%]
100
95
90
85
80
75
3500
3000
2500
2000
1500
1000
500
Wavenumber cm-1
40
IR
3269.66
3252.27
3158.74
2958.01
2930.54
2872.00
2819.27
1698.86
1614.26
1580.75
1530.44
1484.30
1468.32
1441.35
1375.69
1338.47
1313.73
1294.29
1276.51
1211.25
1184.54
1140.77
1113.50
1089.48
1030.72
990.62
936.47
921.84
859.32
839.17
815.93
800.96
766.10
741.08
718.86
703.35
669.57
642.35
626.14
570.30
541.05
524.67
514.91

Line#:1 R.Time:1.825(Scan#:691)
MassPeaks:154
RawMode:Single 1.825(691) BasePeak:304(6102418)
Фон.реж.:0.738(256) Group 1 - Event 1