

A Route to (Het)arene-Annulated Pyrrolo[1,2-d][1,4]diazepines via the Expanded Intramolecular Paal-Knorr Reaction: Nitro Group and Furan Ring as Equivalents of Amino Group and 1,4-Diketone

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1. X-ray data

Experimental. Single crystals of C₂₇H₂₆N₂O₂ [CCDC 1921628] were obtained from mixture of ethyl acetate/petroleum ether. The crystal was kept at 293(2) K during data collection. The X-ray diffraction data for compound 1921628 was obtained on an Xcalibur R automated diffractometer with a CCD detector [MoK α radiation, 293(2) K, ω -scanning with a step of 1°] according to standard procedure.^[1] A correction for absorption by the crystal was applied empirically using SCALE3 ABSPACK algorithm.^[2] The structures were solved by the direct method and refined against F2 by the fullmatrix least-squares method in anisotropic approximation for all non-hydrogen atoms. The positions of hydrogen atoms were refined according to the riding model in isotropic approximation with dependent thermal parameters. All calculations were performed using SHELX97 software package.^[2]

Table S1 Crystal data and structure refinement for 1921628.

Identification code	1921628
Empirical formula	C ₂₇ H ₂₆ N ₂ O ₂
Formula weight	410.50
Temperature/K	293(2)
Crystal system	monoclinic
Space group	P2 ₁ /n
a/ \AA	10.4256(14)
b/ \AA	12.6372(14)
c/ \AA	16.616(2)
$\alpha/^\circ$	90
$\beta/^\circ$	96.095(12)
$\gamma/^\circ$	90
Volume/ \AA^3	2176.8(5)
Z	4
$\rho_{\text{calc}}/\text{cm}^3$	1.253
μ/mm^{-1}	0.079
F(000)	872.0
Crystal size/mm ³	0.4 × 0.3 × 0.2
Radiation	Mo K α ($\lambda = 0.71073$)
2 Θ range for data collection/°	6.448 to 58.878
Index ranges	-13 ≤ h ≤ 14, -16 ≤ k ≤ 17, -20 ≤ l ≤ 21
Reflections collected	20611
Independent reflections	5390 [$R_{\text{int}} = 0.0338$, $R_{\text{sigma}} = 0.0260$]
Data/restraints/parameters	5390/0/285
Goodness-of-fit on F ²	1.034
Final R indexes [I>=2 σ (I)]	$R_1 = 0.0649$, $wR_2 = 0.1833$
Final R indexes [all data]	$R_1 = 0.0822$, $wR_2 = 0.1970$
Largest diff. peak/hole / e \AA^{-3}	0.33/-0.58

Table S2 Fractional Atomic Coordinates ($\times 10^4$) and Equivalent Isotropic Displacement Parameters ($\text{\AA}^2 \times 10^3$) for 1921628. U_{eq} is defined as 1/3 of the trace of the orthogonalised U_{IJ} tensor.

Atom	x	y	z	U(eq)
N(7)	4421.7(15)	7259.0(11)	1534.0(9)	39.5(3)
C(10)	4766.5(17)	9155.7(13)	1901.6(11)	39.1(4)
N(3)	4116.0(15)	8102.4(11)	3054.0(9)	40.8(4)
C(15)	5555.4(16)	10091.6(12)	1664.4(10)	35.4(4)
C(8)	5234.2(17)	8131.3(13)	1588.4(10)	37.6(4)
C(9)	3173.5(17)	7276.6(13)	1792.8(11)	39.5(4)
C(21)	4440.2(18)	7750.5(14)	3823.9(11)	41.9(4)
O(22)	5113.2(18)	8286.3(12)	4325.8(9)	64.6(5)
C(26)	4156.0(18)	5818.3(14)	3526.3(11)	42.3(4)
C(1)	3021.6(17)	7687.5(13)	2556.6(11)	39.9(4)
C(25)	4022.2(16)	6672.5(13)	4036.5(10)	37.1(4)
C(20)	5138.6(18)	10654.4(14)	971.1(11)	42.6(4)
C(5)	5050(2)	6400.1(14)	1232.9(11)	44.1(4)
C(11)	1810.0(19)	7697.6(15)	2828.0(13)	49.6(5)
C(27)	3861(2)	4813.7(15)	3765.9(12)	48.1(5)
C(30)	3583.4(19)	6497.2(15)	4781.7(11)	44.8(4)
C(16)	6695.8(18)	10408.7(16)	2102.8(12)	48.2(5)
C(6)	6358(2)	7827.6(15)	1313.2(12)	47.8(5)
C(29)	3275(2)	5488.3(16)	5013.0(12)	49.0(5)
C(18)	6960(2)	11805.6(15)	1165.9(12)	49.4(5)
C(19)	5835(2)	11501.9(15)	720.0(12)	49.8(5)
C(2)	4694(2)	9100.8(15)	2817.8(12)	52.1(5)
C(14)	2107(2)	6904.7(15)	1306.1(13)	50.6(5)
C(17)	7386.2(19)	11262.0(17)	1856.9(13)	51.7(5)
C(28)	3417.0(19)	4647.0(15)	4509.3(13)	48.9(5)
C(4)	6238(2)	6748.3(16)	1090.0(13)	52.6(5)
C(23)	4462(2)	5323.4(15)	1148.4(13)	54.8(5)
C(13)	903(2)	6904.3(17)	1596.9(16)	60.3(6)
C(12)	762(2)	7287.5(17)	2353.1(16)	59.2(6)
C(24)	5444(3)	4450.2(19)	1175.4(19)	75.9(7)
O(31)	6385(4)	10217(4)	4753(3)	169.8(14)

Table S3 Anisotropic Displacement Parameters ($\text{\AA}^2 \times 10^3$) for 1921628. The Anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U_{11} + 2hka^{*}b^{*}U_{12} + \dots]$.

Atom	U ₁₁	U ₂₂	U ₃₃	U ₂₃	U ₁₃	U ₁₂
N(7)	52.2(9)	32.3(7)	34.4(7)	-2.1(5)	6.8(6)	-3.4(6)
C(10)	45.1(9)	31.2(8)	42.0(9)	1.2(7)	9.5(7)	-2.1(7)
N(3)	54.4(9)	33.5(7)	36.0(7)	-1.3(6)	11.7(6)	-7.4(6)
C(15)	40.8(9)	27.5(7)	39.1(8)	-1.6(6)	9.5(6)	0.3(6)
C(8)	49.0(9)	32.2(8)	31.7(8)	2.3(6)	4.7(6)	-3.8(7)
C(9)	47.2(9)	29.6(8)	41.3(9)	4.8(7)	3.1(7)	-2.9(7)
C(21)	56.5(11)	33.9(8)	36.6(9)	-6.3(7)	11.3(7)	-4.0(7)
O(22)	100.0(12)	49.7(8)	43.1(8)	-9.3(6)	2.4(7)	-24.4(8)
C(26)	52.9(10)	39.1(9)	34.9(9)	-4.3(7)	4.7(7)	2.2(7)
C(1)	48.1(10)	30.5(8)	41.7(9)	6.5(7)	7.8(7)	-0.9(7)
C(25)	42.4(9)	34.9(8)	33.9(8)	-1.6(6)	4.0(6)	-0.7(7)
C(20)	48.3(10)	39.4(9)	39.5(9)	0.9(7)	1.7(7)	-4.6(7)
C(5)	64.8(12)	33.9(8)	34.4(9)	-1.7(7)	8.8(7)	1.4(8)
C(11)	52.7(11)	40.0(10)	58.6(12)	14.3(8)	17.7(9)	3.6(8)
C(27)	59.3(11)	35.5(9)	48.2(10)	-5.5(8)	-0.1(8)	1.5(8)
C(30)	55.2(11)	44.1(10)	36.3(9)	-3.9(7)	10.2(7)	-0.7(8)
C(16)	45.1(10)	52.4(11)	46.3(10)	9.1(8)	0.7(8)	-0.9(8)
C(6)	54.9(11)	40.1(9)	50.7(11)	2.4(8)	15.7(8)	-2.5(8)
C(29)	54.3(11)	50.8(11)	43.4(10)	6.3(8)	11.4(8)	-3.3(9)
C(18)	56.5(11)	37.2(9)	57.9(12)	-3.4(8)	22.0(9)	-9.8(8)
C(19)	65.7(12)	39.8(9)	45.0(10)	8.7(8)	10.5(8)	-1.7(9)
C(2)	78.8(14)	35.8(9)	45.5(10)	-3.4(8)	24.5(9)	-14.0(9)
C(14)	60.1(12)	36.9(9)	52.4(11)	5.4(8)	-5.4(9)	-6.9(8)
C(17)	41.0(10)	55.6(12)	58.8(12)	-6.2(9)	7.5(8)	-11.4(8)
C(28)	50.6(10)	38.1(9)	56.9(11)	6.0(8)	1.2(8)	-4.2(8)
C(4)	64.8(13)	43.1(10)	52.9(11)	-2.8(9)	20.7(9)	5.6(9)
C(23)	75.5(14)	37.6(10)	51.5(11)	-8.2(8)	8.5(10)	-4.9(9)
C(13)	48.7(11)	43.9(11)	84.8(16)	17.6(11)	-9.2(10)	-7.9(9)
C(12)	46.9(11)	47.0(11)	85.2(16)	24.0(11)	13.5(10)	1.6(9)
C(24)	97.3(19)	38.8(11)	94.5(19)	-2.0(12)	24.1(15)	0.7(12)
O(31)	177(3)	141(3)	191(4)	-26(3)	21(3)	-46(3)

Table S4 Bond Lengths for 1921628.

Atom	Atom	Length/Å	Atom	Atom	Length/ Å
N(7)	C(8)	1.387(2)	C(26)	C(25)	1.389(2)
N(7)	C(5)	1.388(2)	C(1)	C(11)	1.386(3)
N(7)	C(9)	1.413(2)	C(25)	C(30)	1.383(2)
C(10)	C(8)	1.496(2)	C(20)	C(19)	1.383(3)
C(10)	C(15)	1.516(2)	C(5)	C(4)	1.359(3)
C(10)	C(2)	1.534(3)	C(5)	C(23)	1.493(3)
N(3)	C(21)	1.363(2)	C(11)	C(12)	1.379(3)
N(3)	C(1)	1.435(2)	C(27)	C(28)	1.381(3)
N(3)	C(2)	1.469(2)	C(30)	C(29)	1.379(3)
C(15)	C(20)	1.384(2)	C(16)	C(17)	1.382(3)
C(15)	C(16)	1.386(3)	C(6)	C(4)	1.416(3)
C(8)	C(6)	1.357(3)	C(29)	C(28)	1.371(3)
C(9)	C(14)	1.386(3)	C(18)	C(17)	1.371(3)
C(9)	C(1)	1.396(3)	C(18)	C(19)	1.373(3)
C(21)	O(22)	1.234(2)	C(14)	C(13)	1.392(3)
C(21)	C(25)	1.484(2)	C(23)	C(24)	1.502(3)
C(26)	C(27)	1.375(3)	C(13)	C(12)	1.369(4)

Table S5 Bond Angles for 1921628.

Atom	Atom	Atom	Angle/[°]	Atom	Atom	Atom	Angle/[°]
C(8)	N(7)	C(5)	109.68(15)	C(9)	C(1)	N(3)	119.97(16)
C(8)	N(7)	C(9)	122.90(14)	C(30)	C(25)	C(26)	119.10(16)
C(5)	N(7)	C(9)	127.35(15)	C(30)	C(25)	C(21)	119.58(15)
C(8)	C(10)	C(15)	112.25(13)	C(26)	C(25)	C(21)	121.13(15)
C(8)	C(10)	C(2)	110.99(14)	C(19)	C(20)	C(15)	121.36(17)
C(15)	C(10)	C(2)	112.24(14)	C(4)	C(5)	N(7)	106.46(16)
C(21)	N(3)	C(1)	121.62(14)	C(4)	C(5)	C(23)	130.61(18)
C(21)	N(3)	C(2)	117.59(15)	N(7)	C(5)	C(23)	122.85(18)
C(1)	N(3)	C(2)	118.90(15)	C(12)	C(11)	C(1)	120.3(2)
C(20)	C(15)	C(16)	117.70(16)	C(26)	C(27)	C(28)	120.43(17)
C(20)	C(15)	C(10)	119.08(15)	C(29)	C(30)	C(25)	120.44(17)
C(16)	C(15)	C(10)	123.21(16)	C(17)	C(16)	C(15)	120.99(18)
C(6)	C(8)	N(7)	107.23(15)	C(8)	C(6)	C(4)	107.78(17)
C(6)	C(8)	C(10)	133.37(16)	C(28)	C(29)	C(30)	120.21(18)
N(7)	C(8)	C(10)	119.40(15)	C(17)	C(18)	C(19)	119.61(17)
C(14)	C(9)	C(1)	119.69(18)	C(18)	C(19)	C(20)	119.95(18)
C(14)	C(9)	N(7)	121.65(17)	N(3)	C(2)	C(10)	111.64(15)
C(1)	C(9)	N(7)	118.66(16)	C(9)	C(14)	C(13)	119.6(2)
O(22)	C(21)	N(3)	121.48(16)	C(18)	C(17)	C(16)	120.38(19)
O(22)	C(21)	C(25)	120.20(16)	C(29)	C(28)	C(27)	119.75(18)
N(3)	C(21)	C(25)	118.24(15)	C(5)	C(4)	C(6)	108.84(17)
C(27)	C(26)	C(25)	120.06(17)	C(5)	C(23)	C(24)	113.3(2)
C(11)	C(1)	C(9)	119.65(18)	C(12)	C(13)	C(14)	120.5(2)
C(11)	C(1)	N(3)	120.38(17)	C(13)	C(12)	C(11)	120.12(19)

Table S6 Hydrogen Atom Coordinates ($\text{\AA} \times 10^4$) and Isotropic Displacement Parameters ($\text{\AA}^2 \times 10^3$) for 1921628.

Atom	x	y	z	U(eq)
H(10)	3884.17	9260.59	1646.64	47
H(26)	4445.51	5925.82	3022.23	51
H(20)	4374.22	10458.64	667.81	51
H(11)	1703.09	7982.25	3332.66	60
H(27)	3960.94	4242.88	3424.82	58
H(30)	3495.71	7063.23	5129.34	54
H(16)	7000.97	10041.93	2569.39	58
H(6)	7077.73	8252.69	1277.58	57
H(29)	2969.26	5378.6	5512.16	59
H(18)	7429.19	12376.7	1000.09	59
H(19)	5542.38	11865.85	249.67	60
H(2A)	5555.91	9165.94	3097.11	62
H(2B)	4183.87	9689.15	2981.8	62
H(14)	2194.89	6656.76	787.88	61
H(17)	8144.48	11468.52	2161.94	62
H(28)	3215.31	3966.48	4667.8	59
H(4)	6868.88	6343.61	879.86	63
H(23A)	3916.76	5285.27	638.69	66
H(23B)	3919.19	5215.64	1580.33	66
H(13)	189.9	6641.66	1275.17	72
H(12)	-42.7	7271.26	2546.86	71
H(24A)	6083.55	4619.49	820.68	114
H(24B)	5024.66	3799.4	1004.45	114
H(24C)	5850.14	4373.65	1718.33	114
H(31A)	5970.77	9813.2	4407.99	255
H(31B)	6033.67	10204.88	5191.59	255

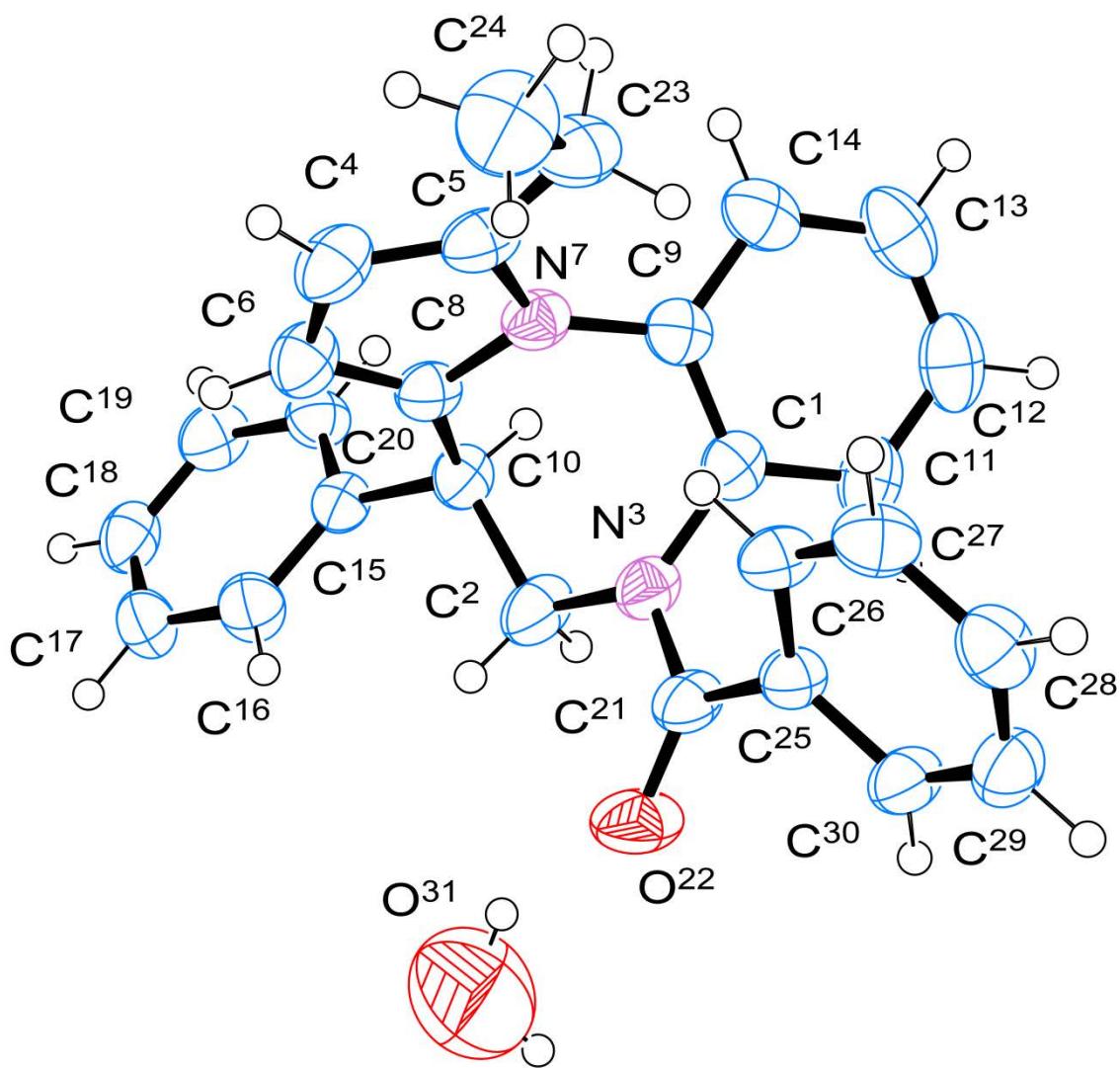


Figure S1. Structure of the (10-Ethyl-7-phenyl-6,7-dihydro-5*H*-benzo[*b*]pyrrolo[1,2-*d*][1,4]diazepin-5-yl)(phenyl)methanone (**8p**·H₂O) according to the X-ray diffraction data; non-hydrogen atoms are shown as thermal vibration ellipsoids with a probability of 50%.

2. Cell lines

A549 is lung adenocarcinoma cell line, MCF7 is breast cancer cell line, VA13 that origins from normal lung fibroblasts and MCF10A origins from noncancerous mammary gland lesion. MCF7, VA13, and A549 cell lines were maintained in DMEM/F-12 culture medium containing 10% fetal bovine serum, 50u/ml penicillin and 0.05 mg/ml streptomycin at 37 °C in 5% CO₂. MCF10A was maintained in 10A media: DMEM/F-12 containing 5% horse serum, 50u/ml penicillin, 0.05 mg/ml streptomycin, EGF 20 ng/ml, cholera toxin 1 µg/ml, hydrocortisone 0.5 µg/ml. All media and supplements were purchased from Thermo Fisher Scientific, USA. Cell cultures were tested for the absence of mycoplasma.

3. Cytotoxicity assays

The primary assessment of cytotoxicity was evaluated by the method based on mammalian cells expressing fluorescent proteins (Katushka in VA13 and MCF10A cell lines and EGFP in A549 and MCF7 cell lines).^[3] Fluorescent viability assay with A549-EGFP and VA13-Katushka cell lines was done in F-12 culture medium containing 10% fetal bovine serum, 50 u/ml penicillin and 0.05 mg/ml streptomycin. Fluorescent viability assay with MCF7-EGFP and MCF10A-Katushka cell lines was done in F-12 culture medium containing 10% fetal bovine serum, 50u/ml penicillin, 0.05 mg/ml streptomycin and 20% 10A media. 400 A549-EGFP cells, 800 VA13-Katushka cells, 500 MCF7-EGFP cells or 700 MCF10A-Katushka cells per well were plated out in 40 µL of media in 384-well plate and incubated at 37 °C in 5% CO₂ incubator for 24 h. Then 40 µL of water-DMSO solution of tested compound was added to the cells (DMSO concentration in the media was kept below 0.5%) in a such way that effective concentrations of studied compounds were in a range of 50 nM to 100 µM (six dilutions). After incubation for 72 h plate was scanned on Typhoon FLA 9500 and cell lines viability was calculated based on fluorescence intensity.

The cytotoxicity verification of tested compounds was assessed using the MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) assay^[4] with some modifications. 2500 cells per well for MCF7, A549 cell lines, 3000 for MCF10A or 4000 cells per well for VA13 cell line were plated out in 140 µL of DMEM containing 10% FBS in 96-well plate and incubated at 37 °C in 5% CO₂ incubator for 24 h. Then 10 µL of water-DMSO solution of tested compound was added to the cells (DMSO concentration in the media was kept below 1%) in a such way that effective concentrations of studied compounds were in a range of 50 nM to 100 µM (eight dilutions). Doxorubicin (3 nM to 6 µM) was used as a control. After incubation for 72 h 10 µL MTT solution in PBS (5 mg/ml) was added, cells were incubated for 2 h. Medium was removed and 100 µL of DMSO was added. Samples were incubated for 15 min with shaking to completely solubilize formazan. Cell survival was measured spectrophotometrically at 565 nm.

4. Cytotoxicity results

Table S7. Primary assessment of cytotoxicity (CC_{50} , μM) of diazepines **8, 15, 19-21**.

Compound	MCF7	MCF10A	A549	VA13
8a	n.a. ^[a]	n.a.	n.a.	n.a.
8b	n.a.	n.a.	n.a.	80.8
8c	n.a.	n.a.	n.a.	n.a.
8e	n.a.	n.a.	78.3	50.0
8f	20.7	61.1	57.0	59.5
8g	n.d. ^[b]	n.d.	n.d.	n.d.
8h	n.d.	n.d.	n.d.	n.d.
8i	n.a.	n.a.	n.a.	n.a.
8j	n.a.	n.a.	83.2	70.3
8k	n.a.	18.2	10.3	7.5
8l	n.a.	n.a.	n.a.	n.a.
8m	0.8	1	0.7	2.9
8n	n.a.	n.a.	61.5	69.4
8o	16.7	n.a.	18.3	32.1
8p	59.7	n.a.	60.9	68.3
8q	n.d.	n.d.	n.d.	n.d.
15a	n.a.	n.a.	n.a.	n.a.
15b	n.a.	n.a.	68.6	60.2
15c	n.a.	n.a.	n.a.	n.a.
15d	n.a.	n.a.	n.a.	86.8
19	35.7	n.a.	56.3	56.0
20	n.a.	n.a.	60.3	51.7
21	92.2	n.a.	80.4	n.a.

^[a]n.a. – not active. ^[b]n.d. – not determined.

Table S8. Cytotoxicity (CC_{50} , μM) of diazepines **8,19**.

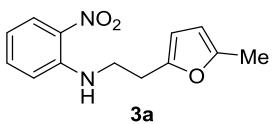
Compound	MCF7	MCF10A	A549	VA13
8f	9±1	21±7	9±1	8±1
8k	13±4	5±2	6±2	21±7
8m	25±3	15±5	19±2	22±1
8o	13±4	n.a. ^[a]	17±4	29±4
8p	16±3	45±4	10±2	34±4
19	20±4	80±18	44±4	47±4
doxorubicin	0.12±0.02	0.08±0.02	0.11±0.01	0.25±0.02

^[a]n.a. – not active.

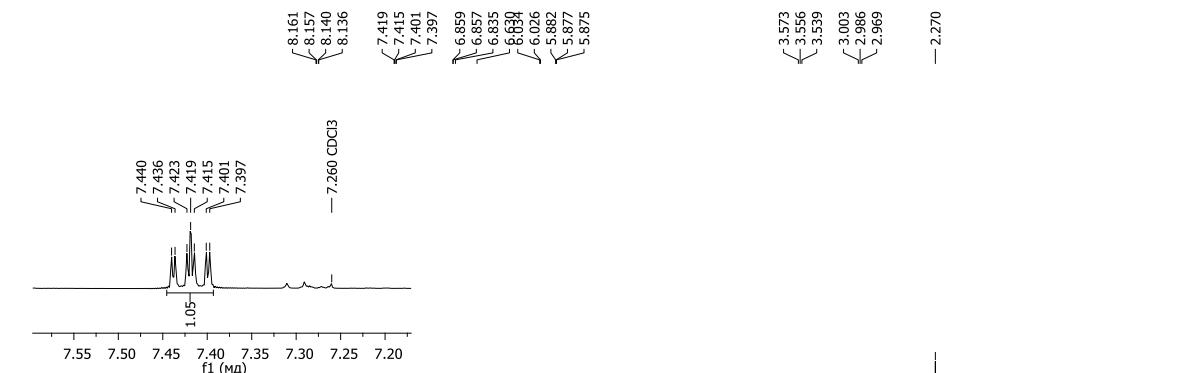
5. References

- 1 *CrysAlisPro, Version 1.171.36.28* (release 01-02-2013 CrysAlis171.NET), Agilent Technologies.
- 2 G. M. Sheldrick, *Acta Crystallogr., Sect. A* **2008**, *64*, 112.
- 3 M.A. Kalinina, D.A. Skvortsov, M.P. Rubtsova, E. S. Komarova, O. A. Dontsova, *Mol. Imaging. Biol.* **2018**, *20*, 368.
- 4 T. Mosmann, *J. Immunol. Methods* **1983**, *65*, 55.

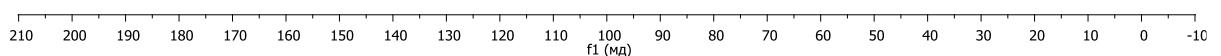
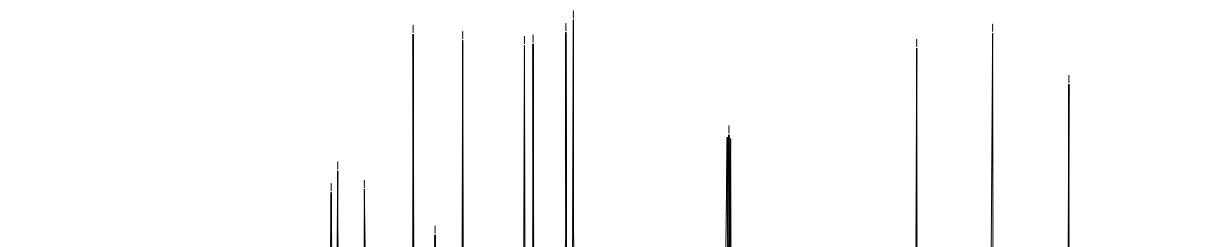
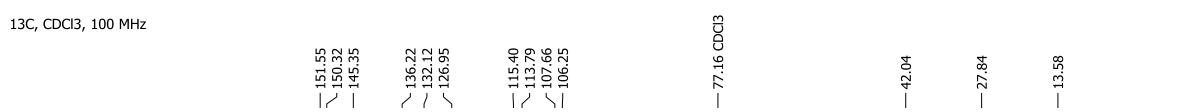
6. Copies of NMR spectra

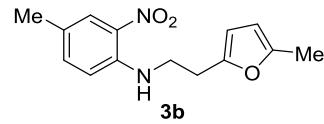


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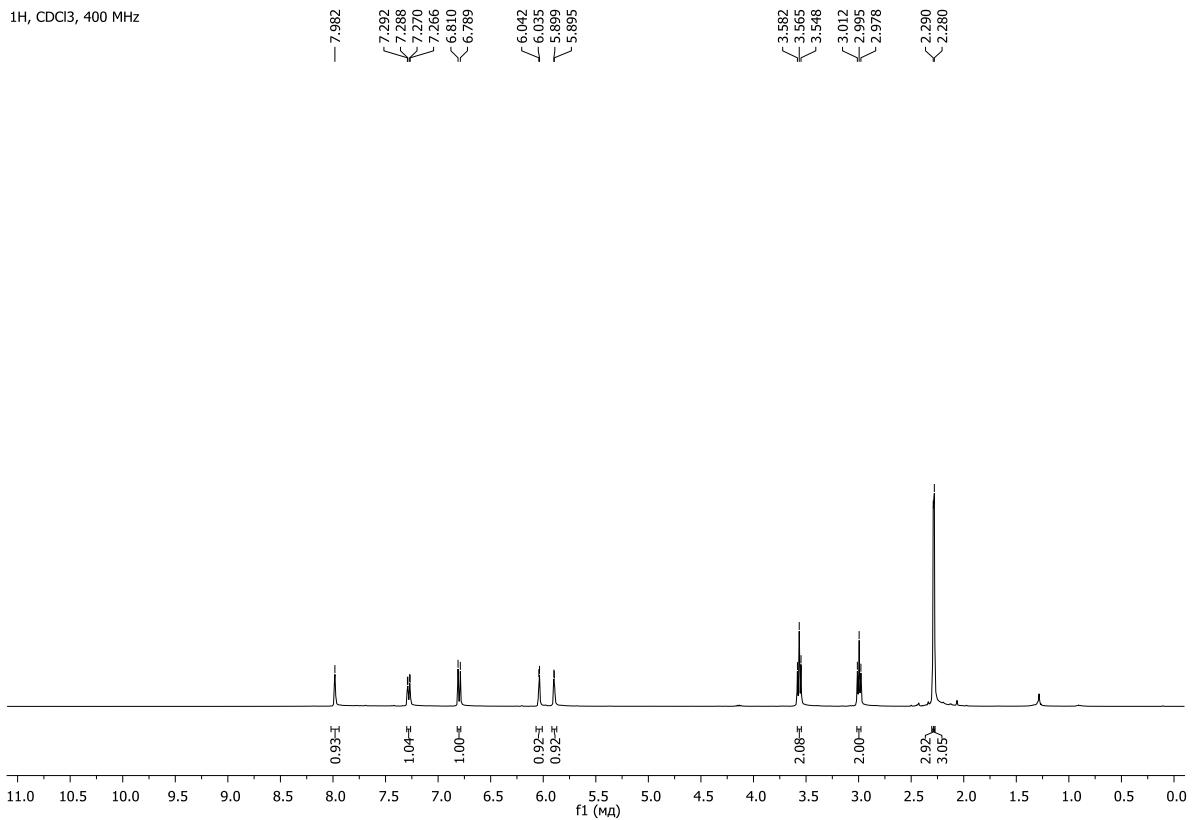


13C, CDCl₃, 100 MHz

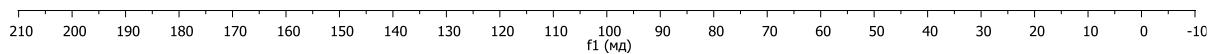
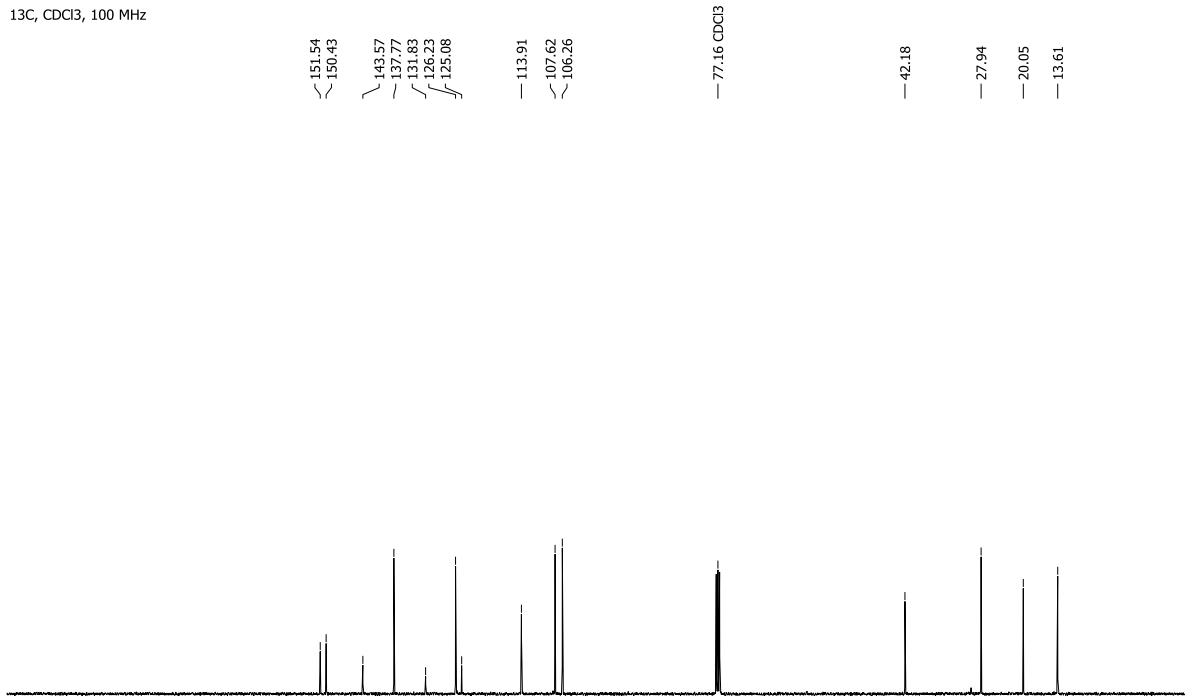


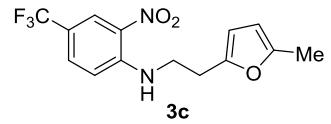


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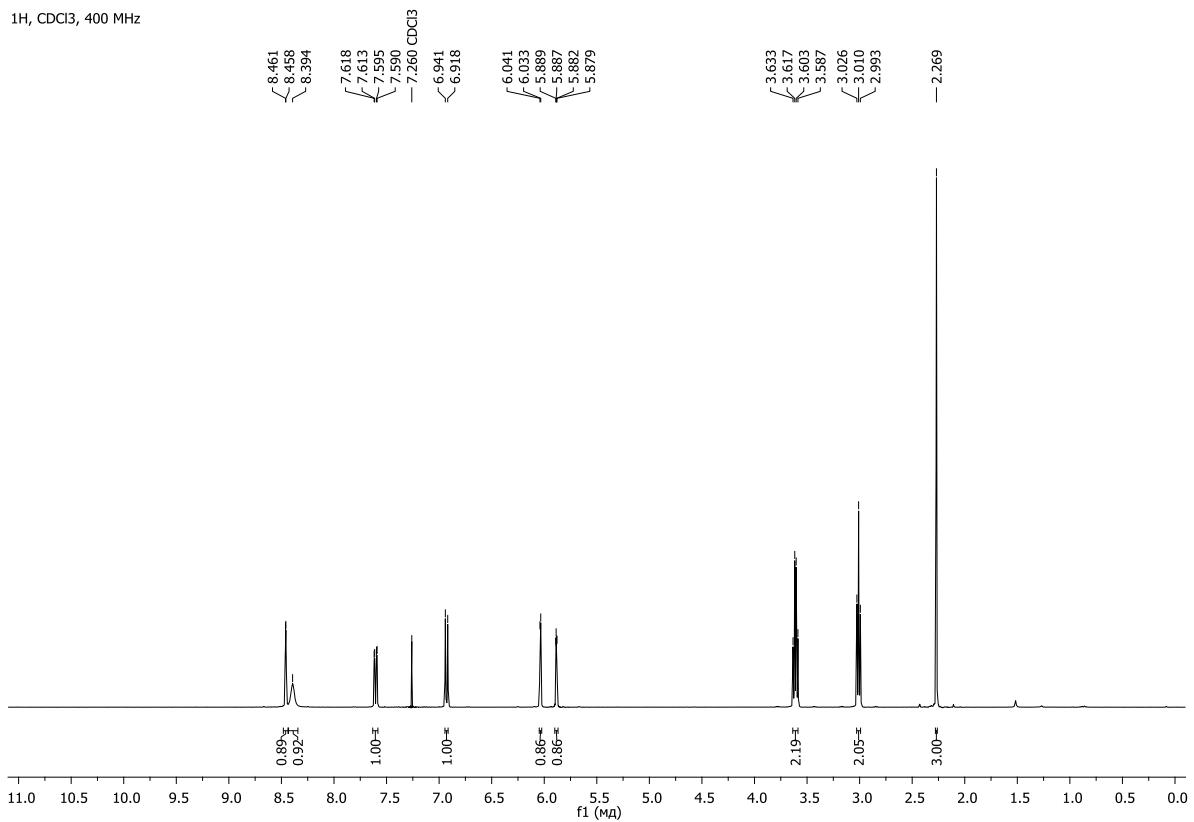


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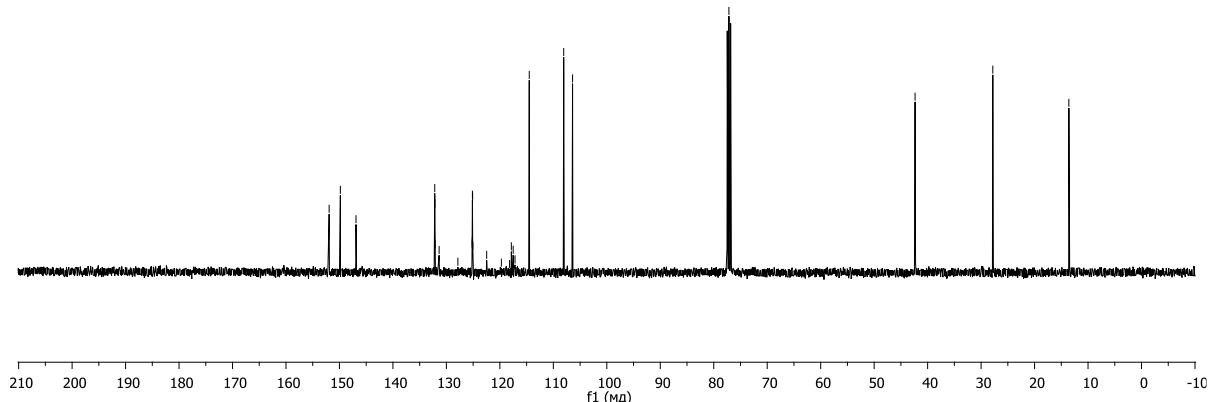
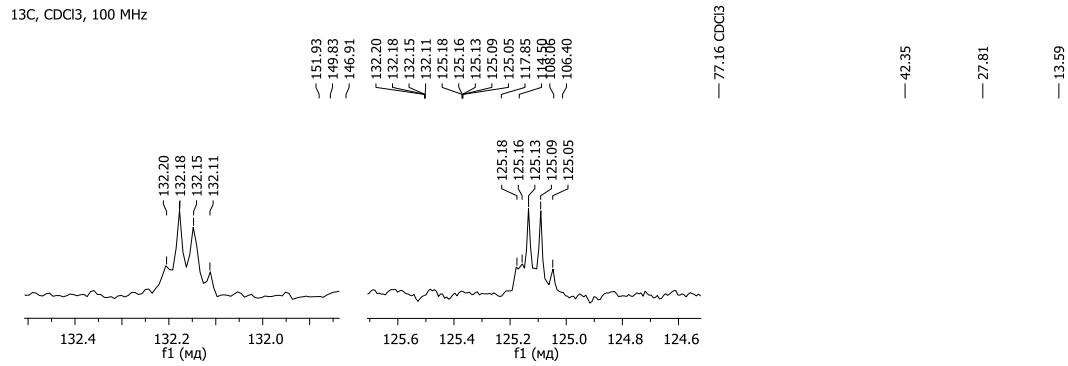


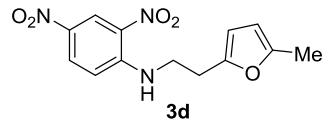


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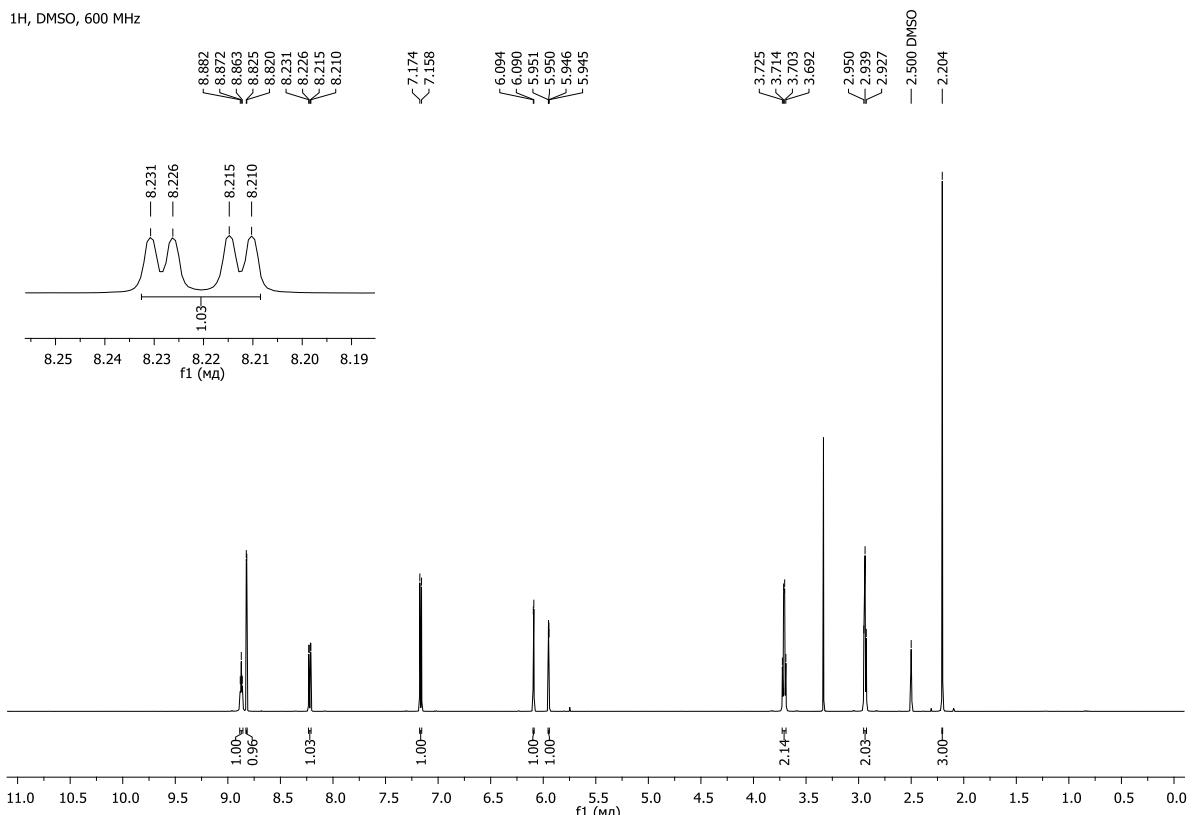


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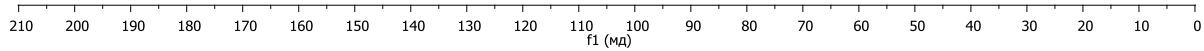
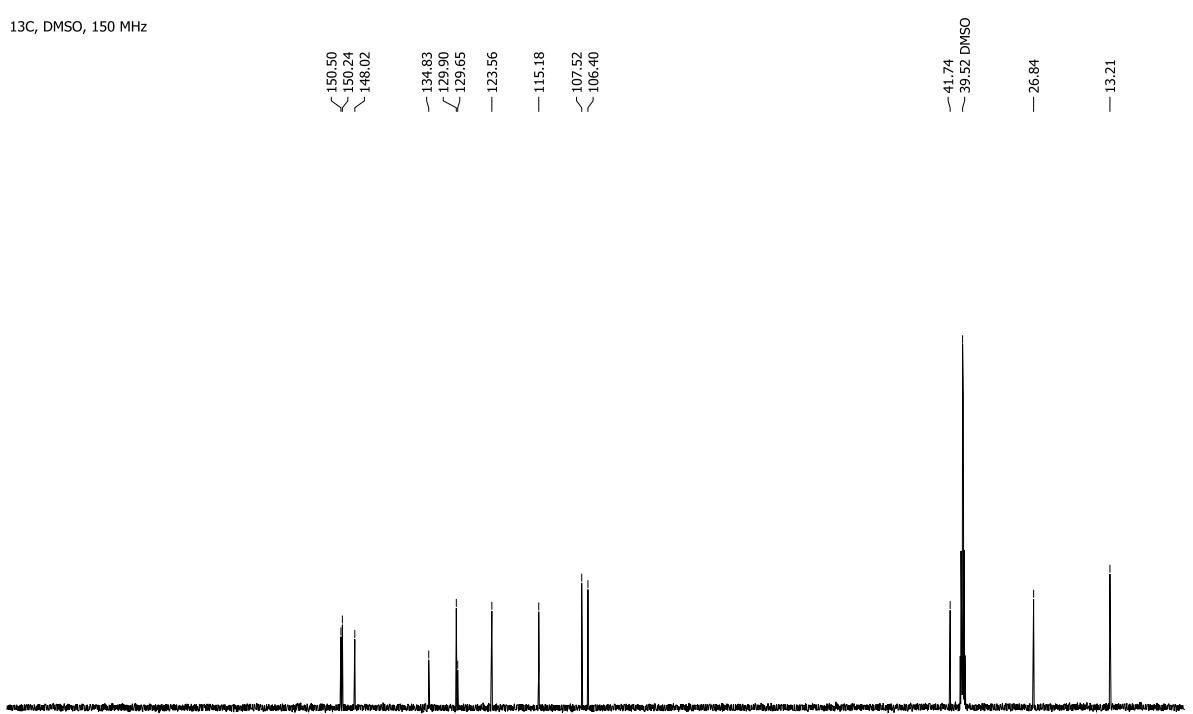


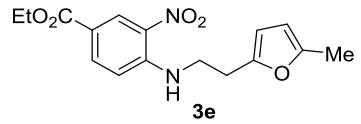


¹H, DMSO, 600 MHz

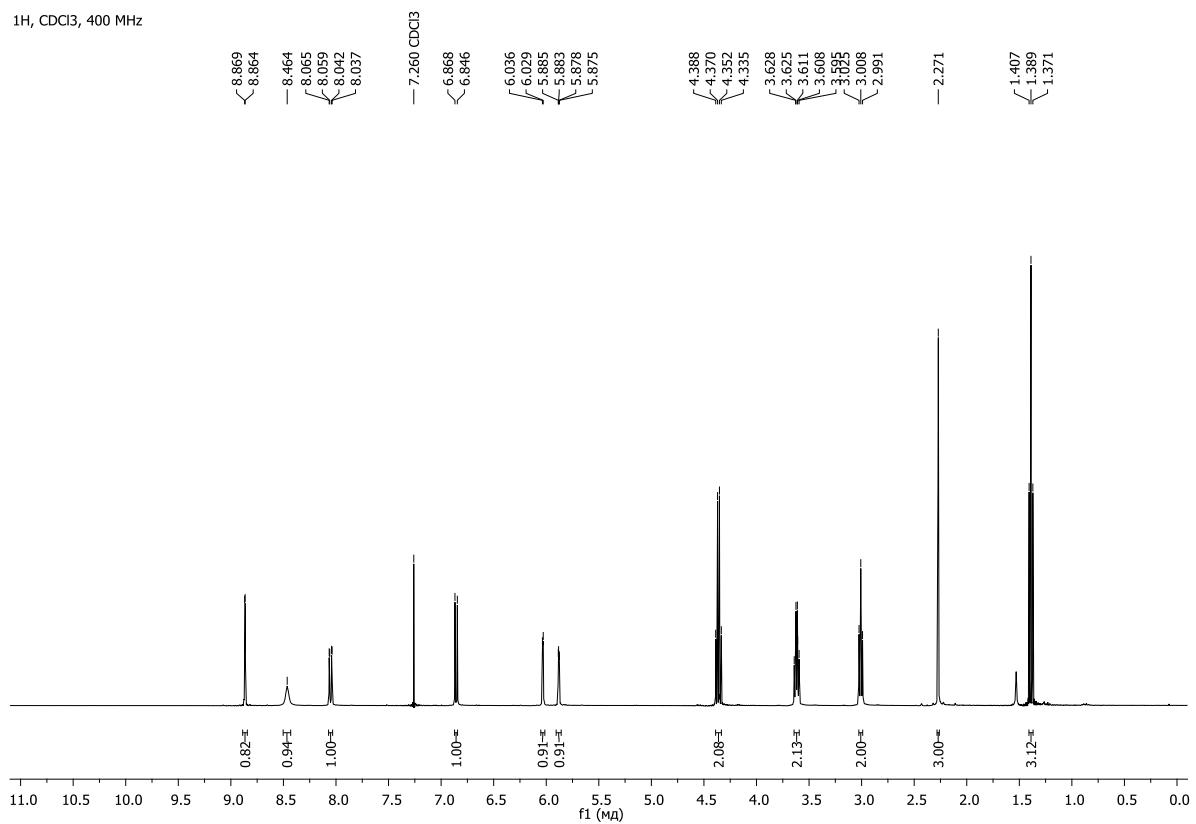


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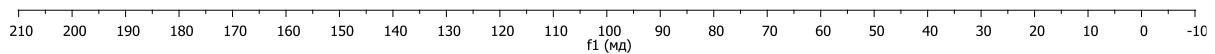
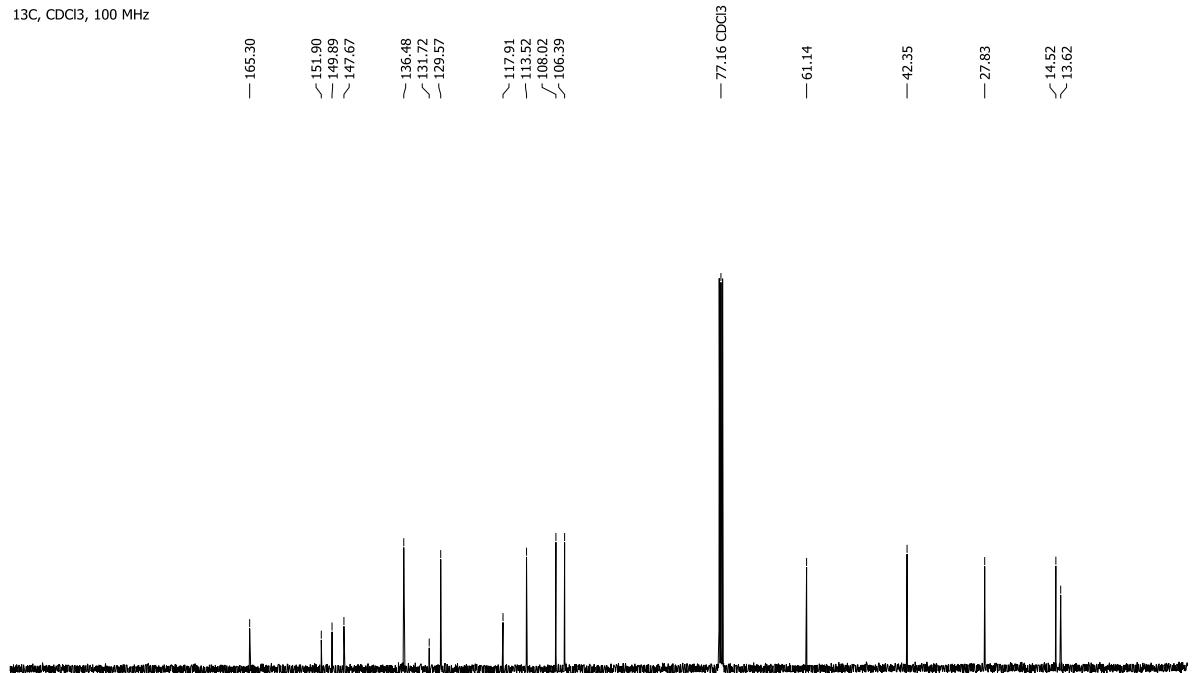


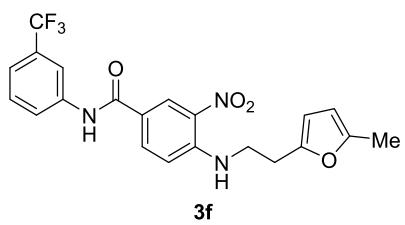


¹H, CDCl₃, 400 MHz

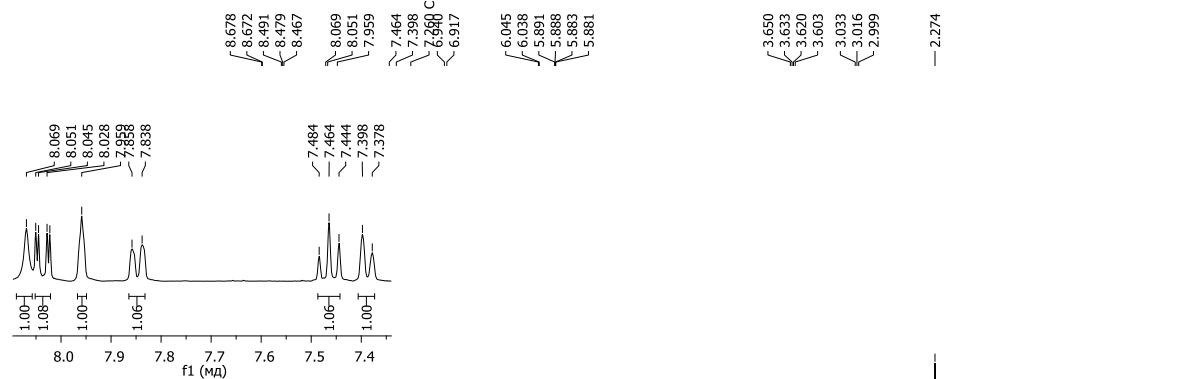


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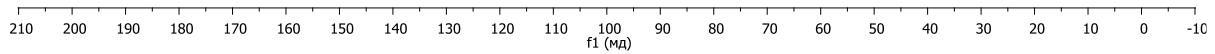
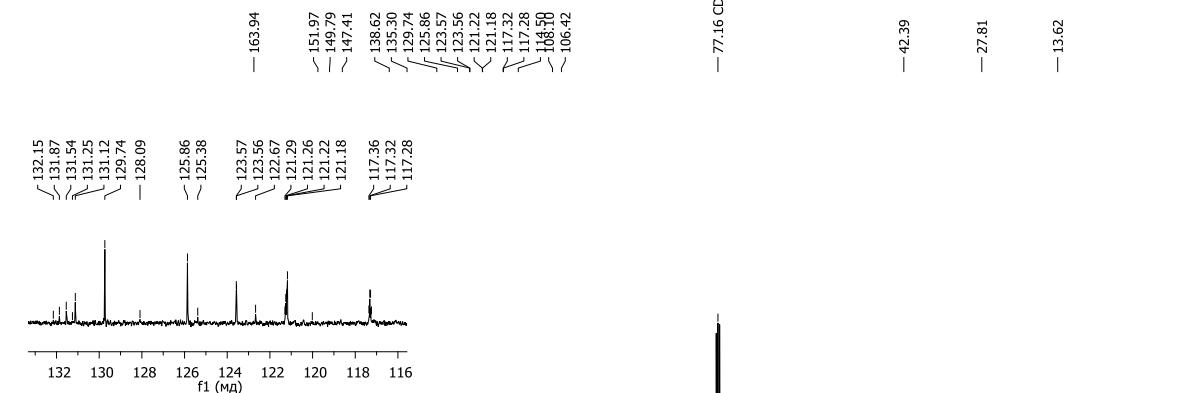


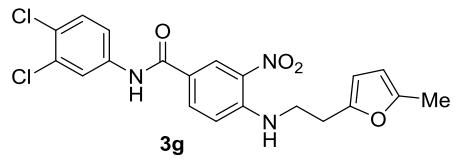


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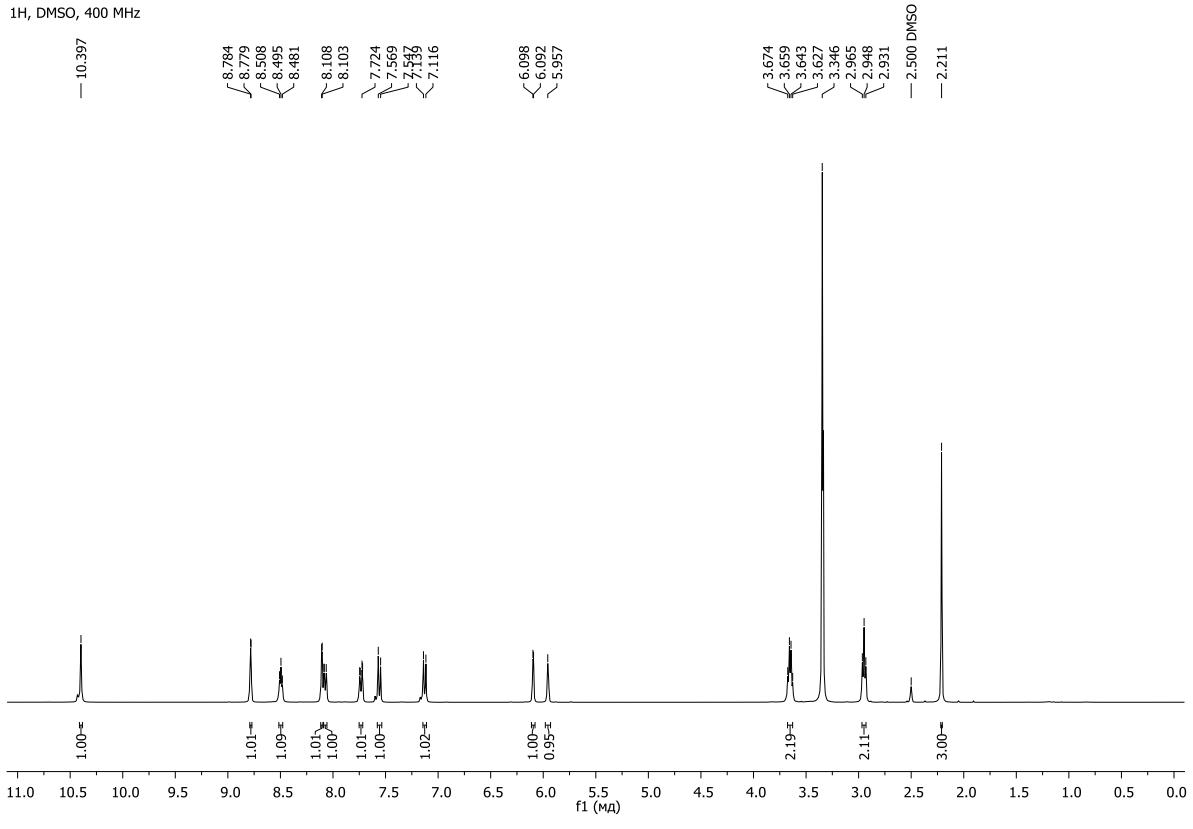


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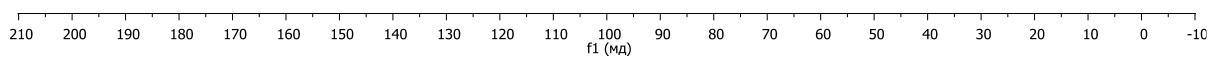
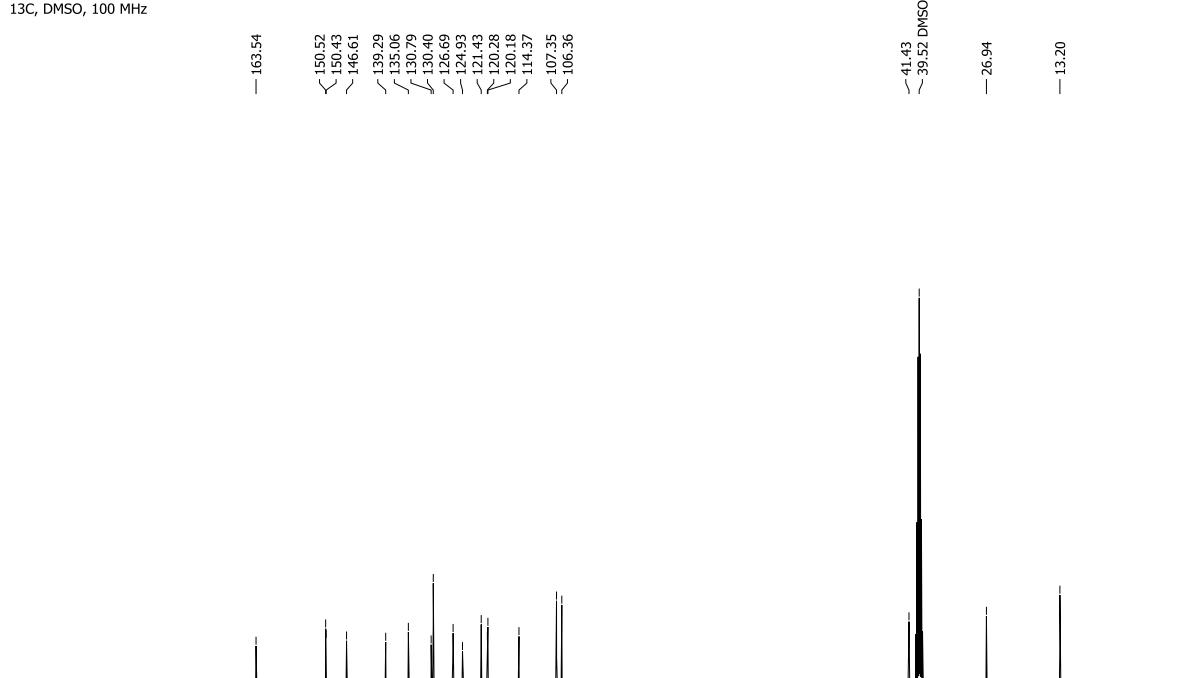


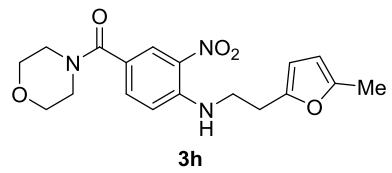


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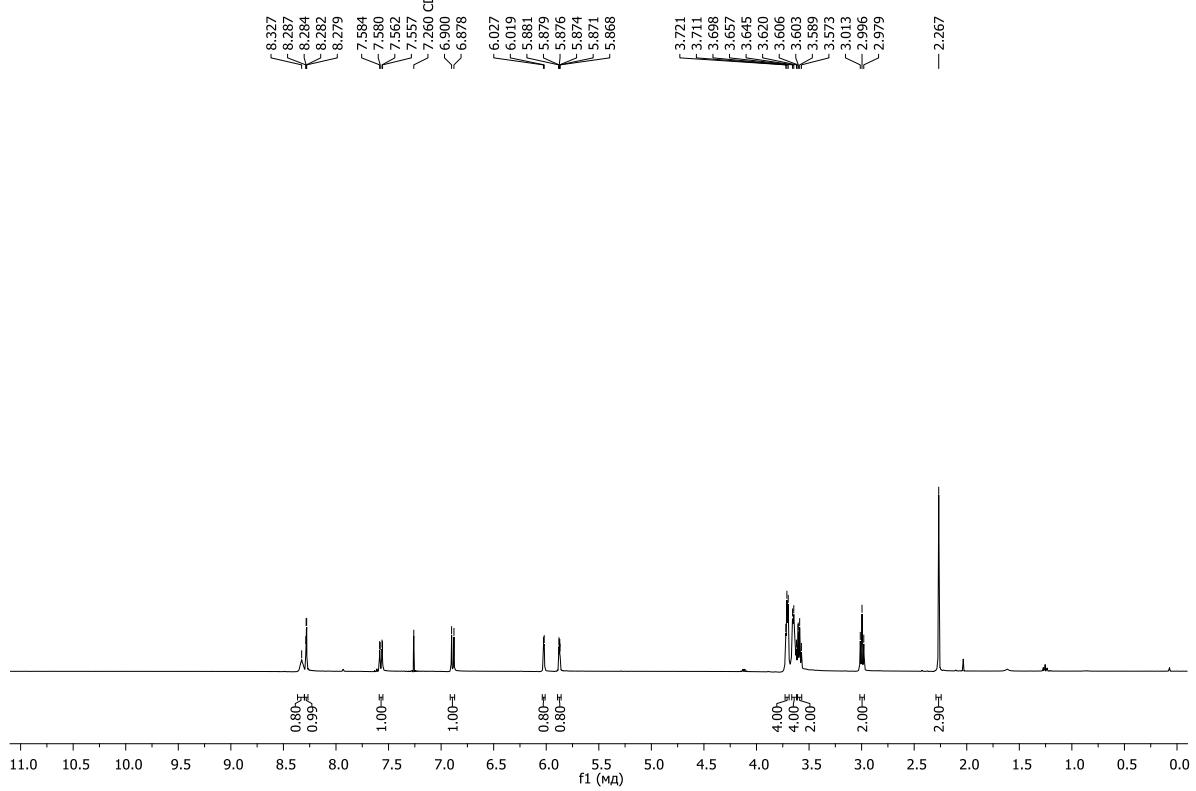


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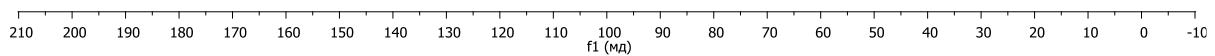
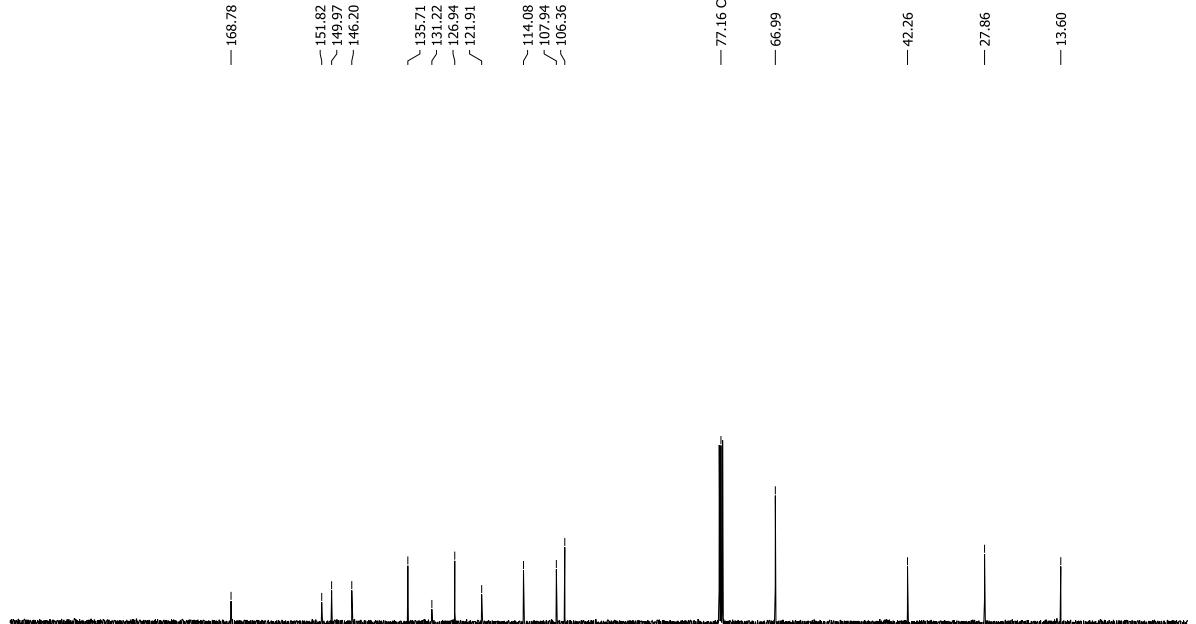


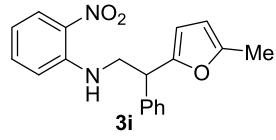


¹H, CDCl₃, 400 MHz

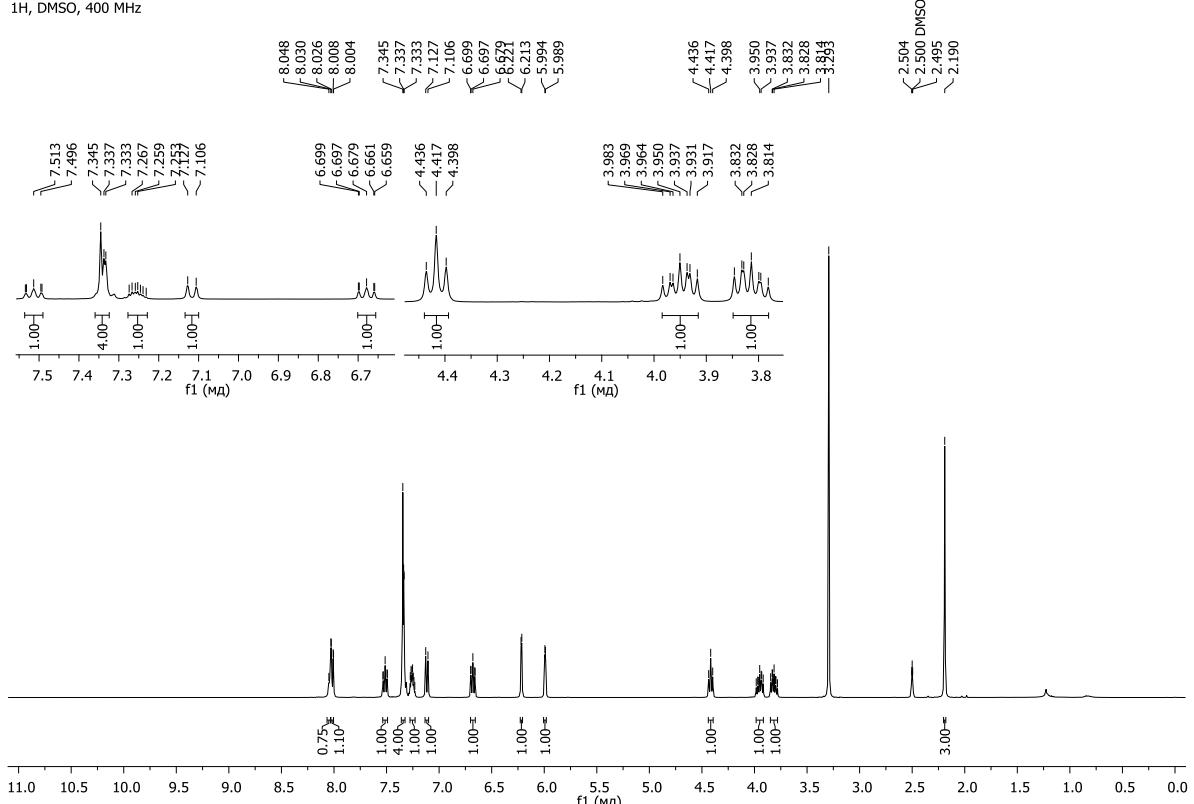


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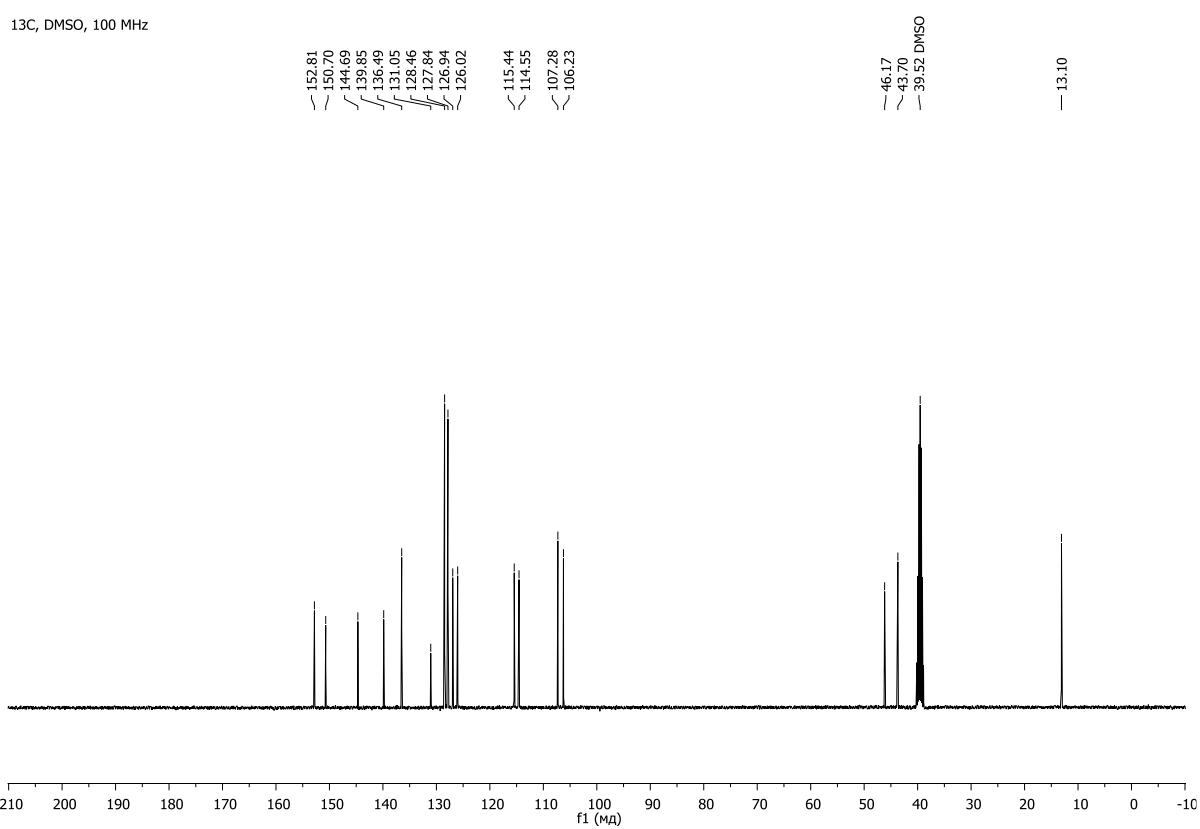


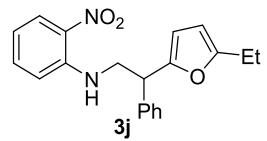


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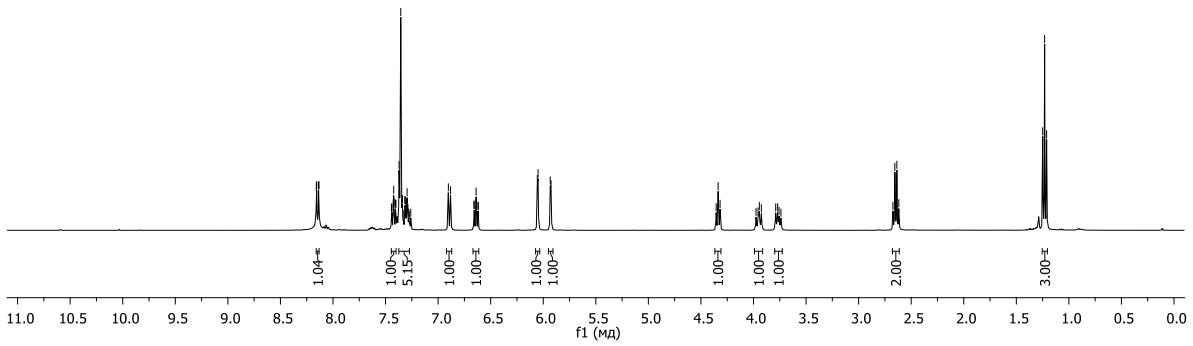
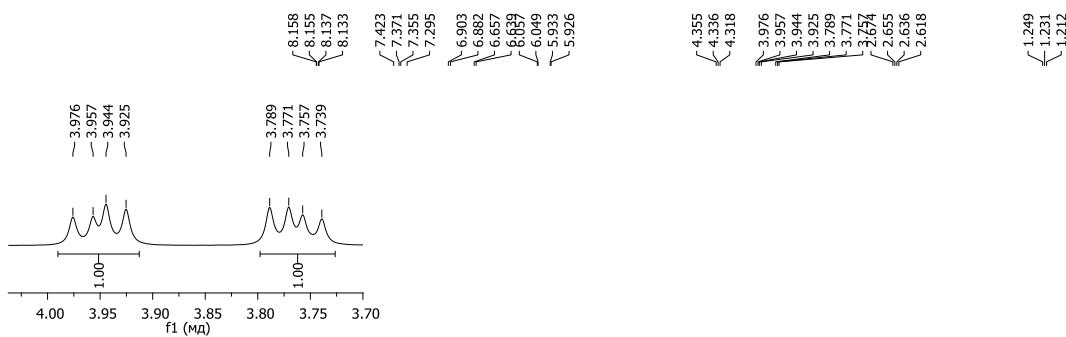


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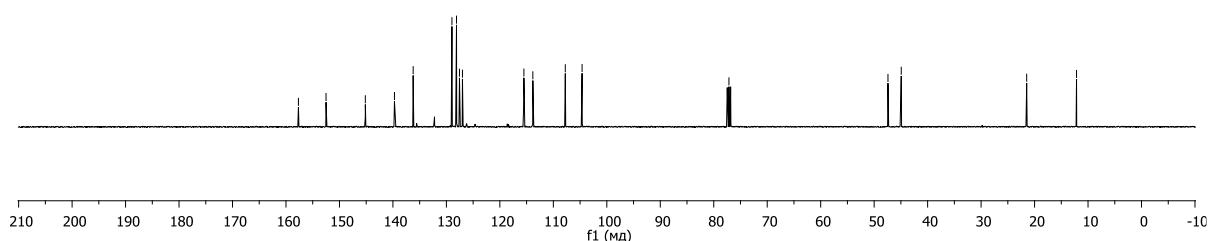




^1H , CDCl_3 , 400 MHz

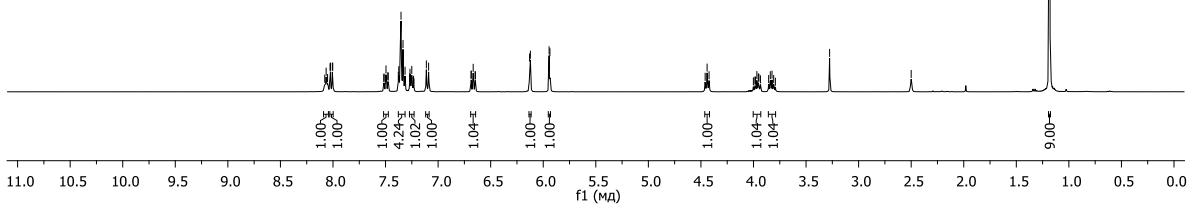
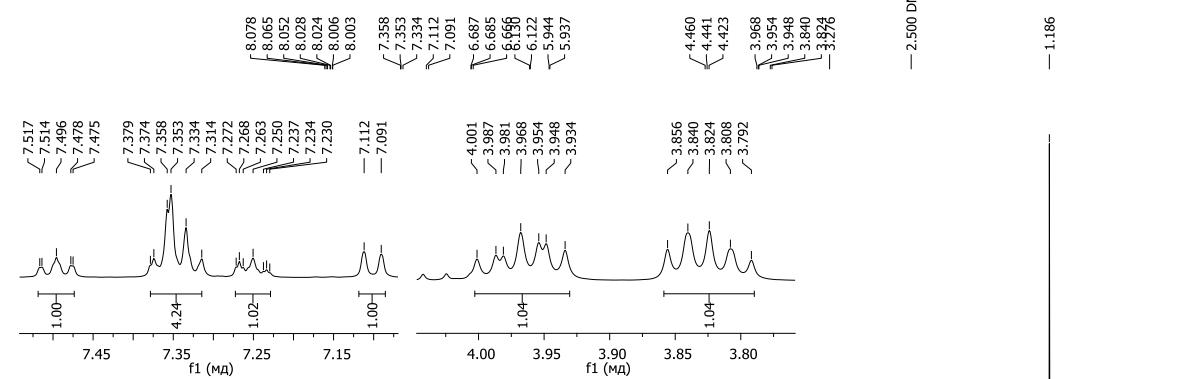


^{13}C , CDCl_3 , 100 MHz

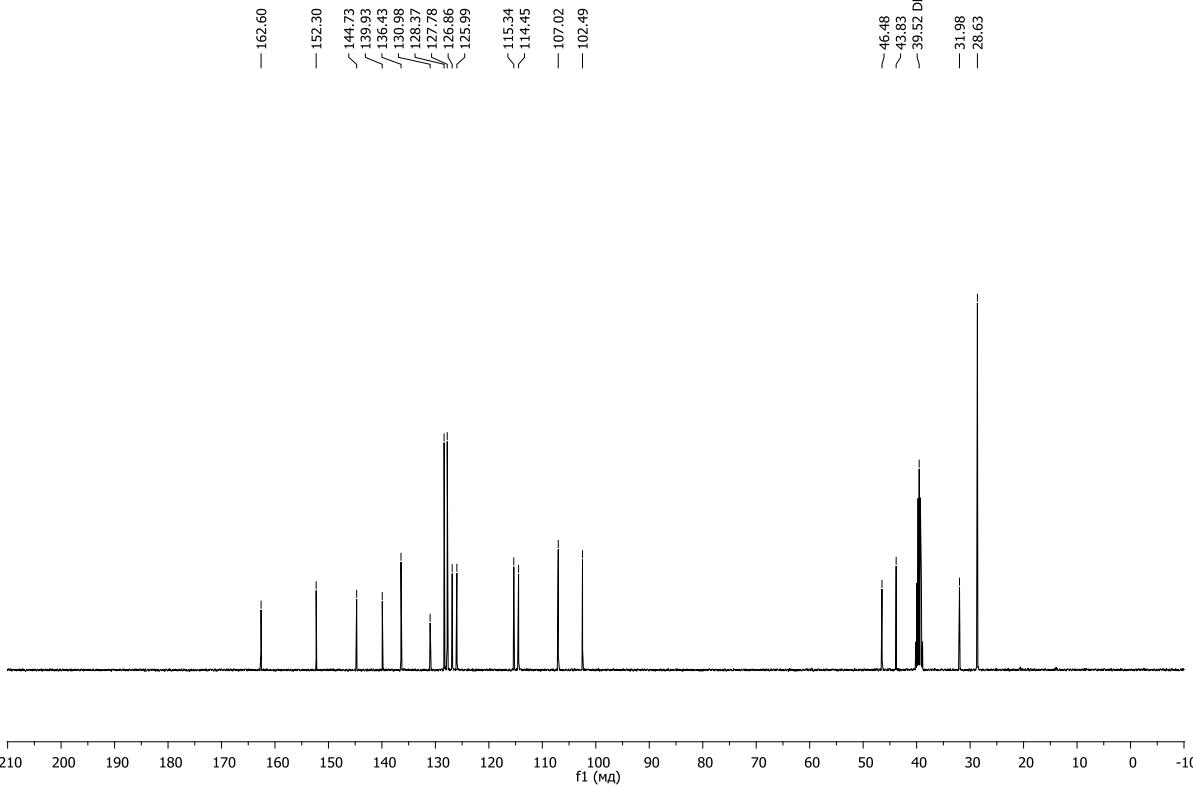


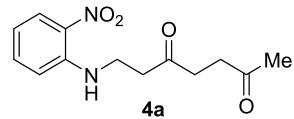


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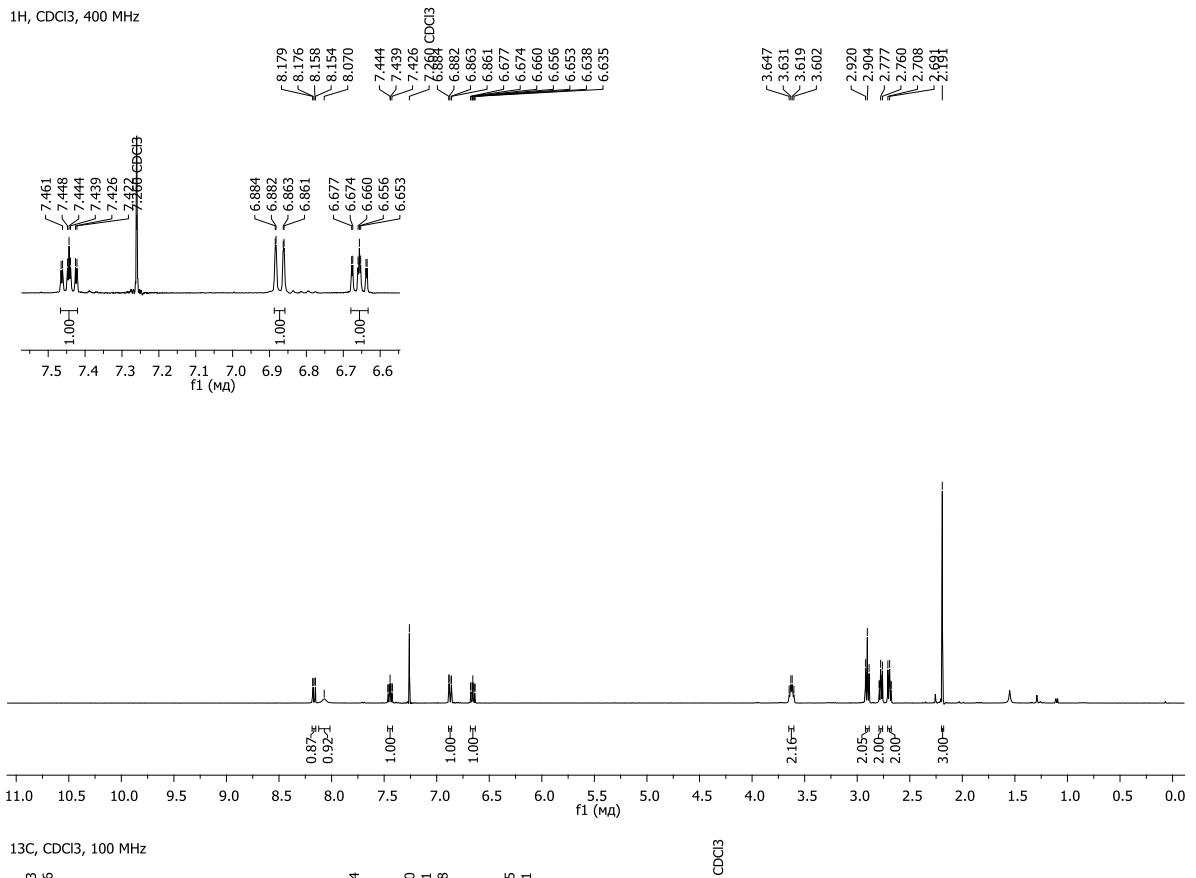


13C, DMSO, 100 MHz

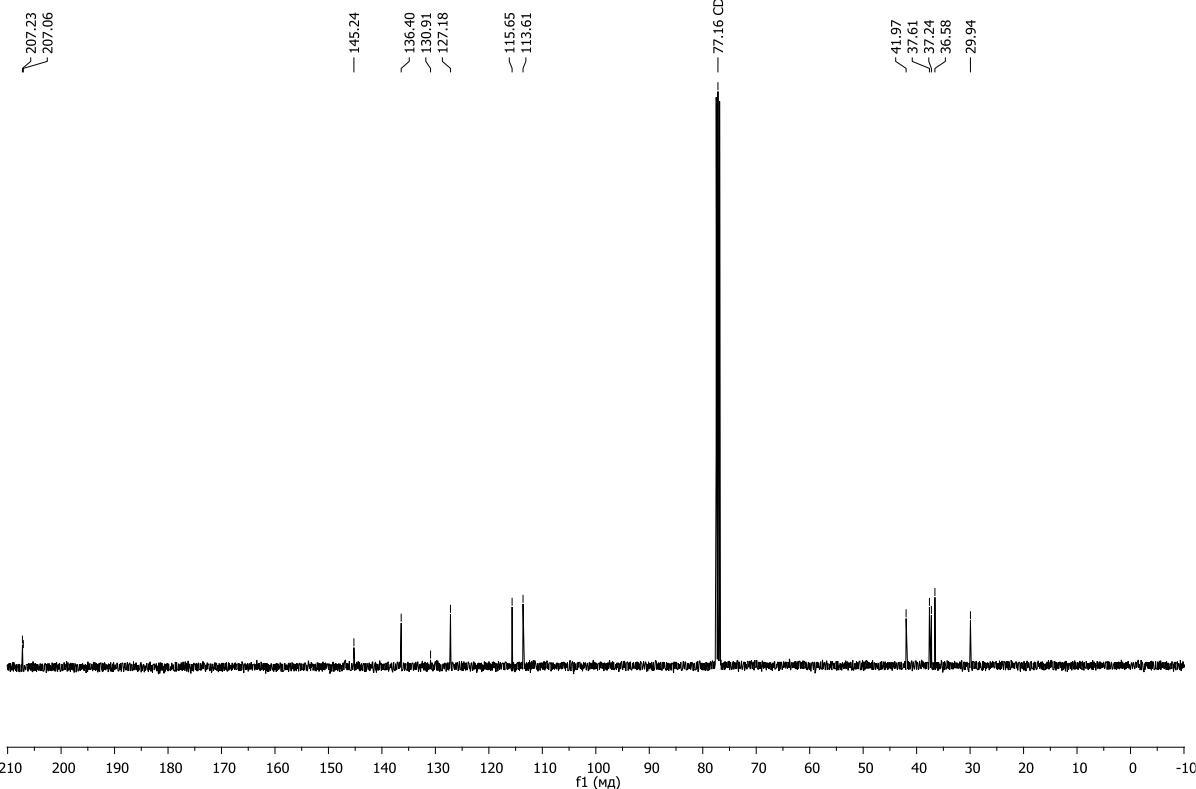


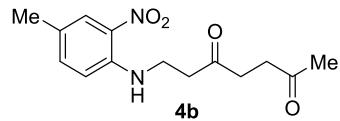


1H, CDCl₃, 400 MHz

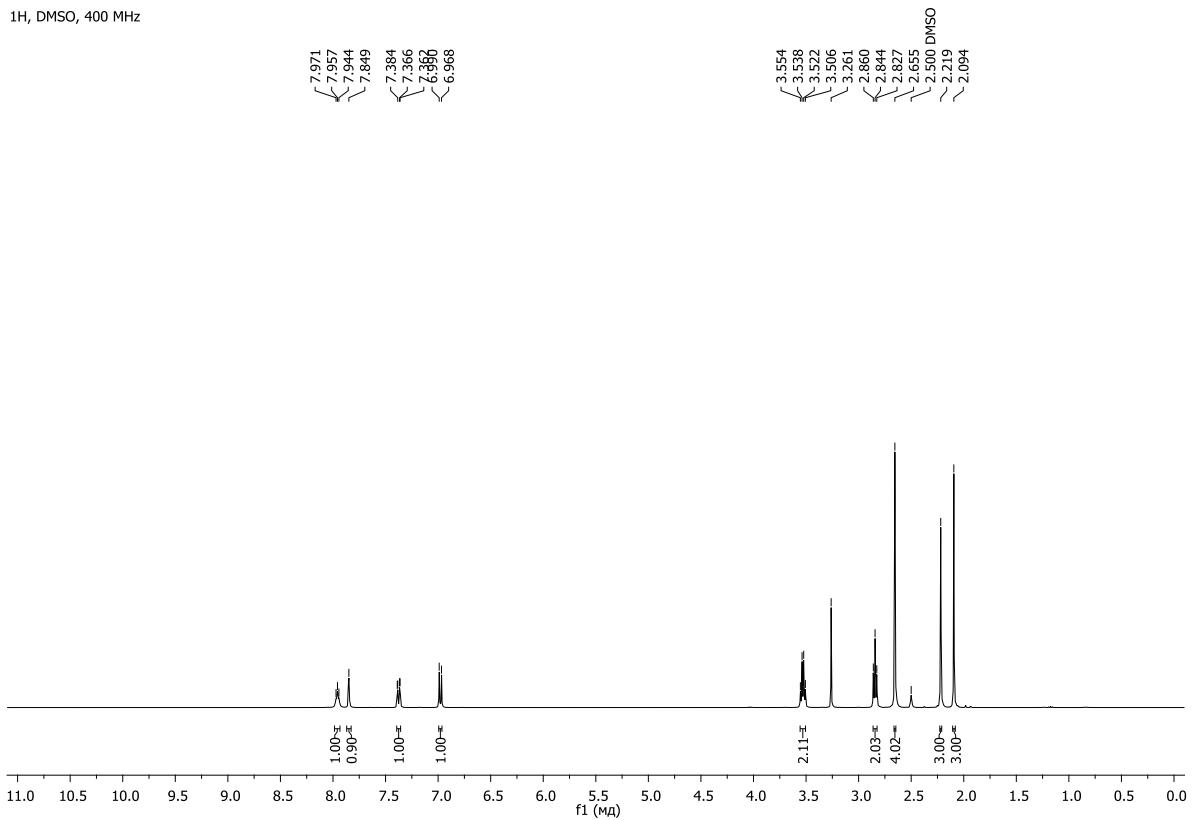


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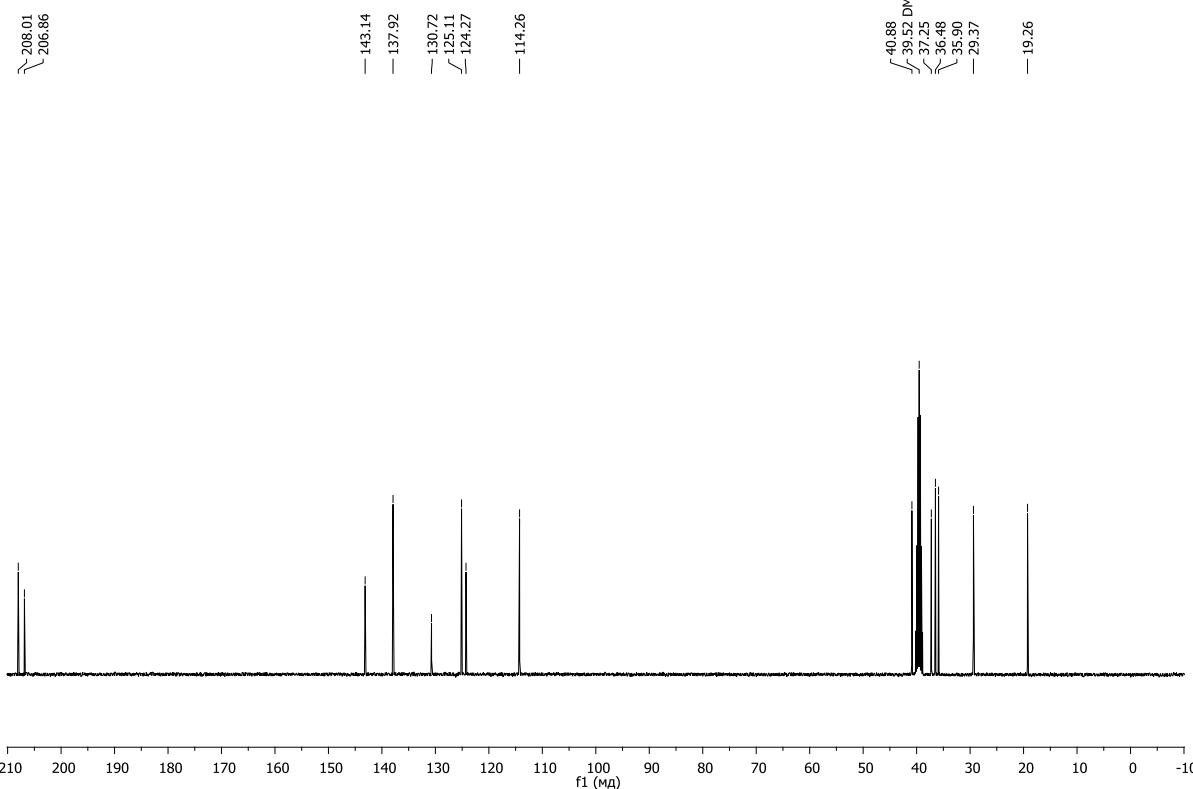


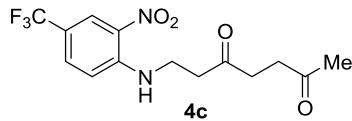


¹H, DMSO, 400 MHz

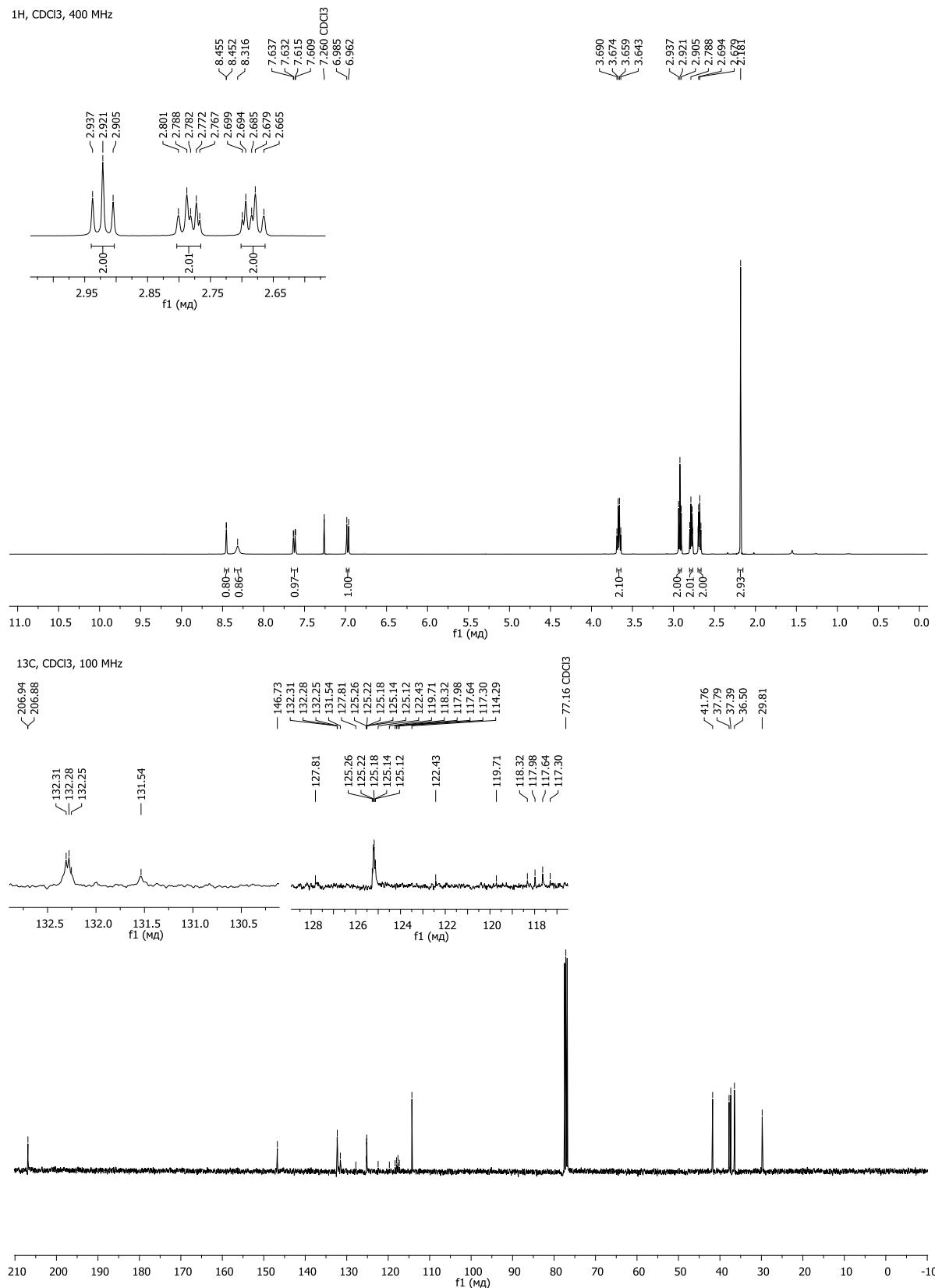


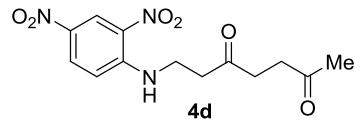
¹³C, DMSO, 100 MHz



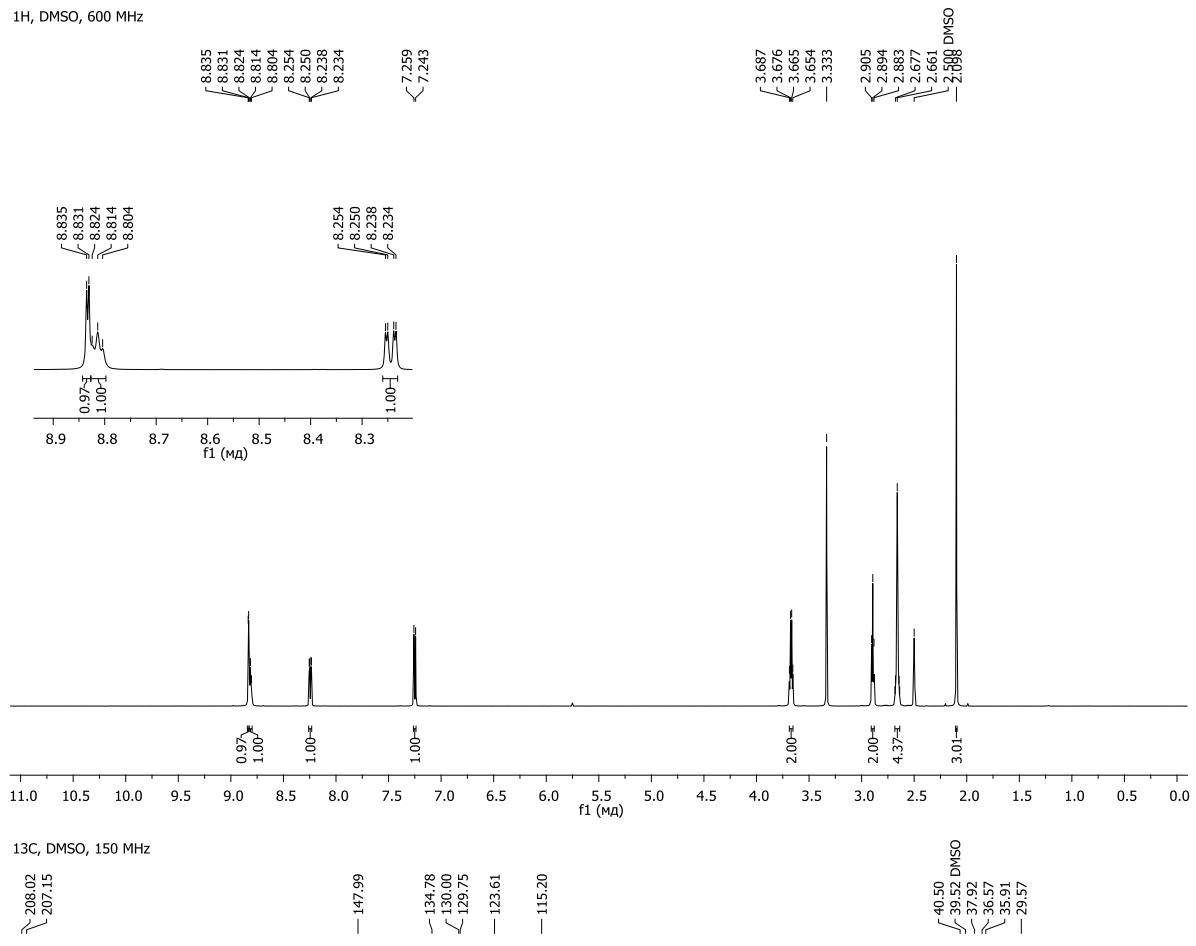


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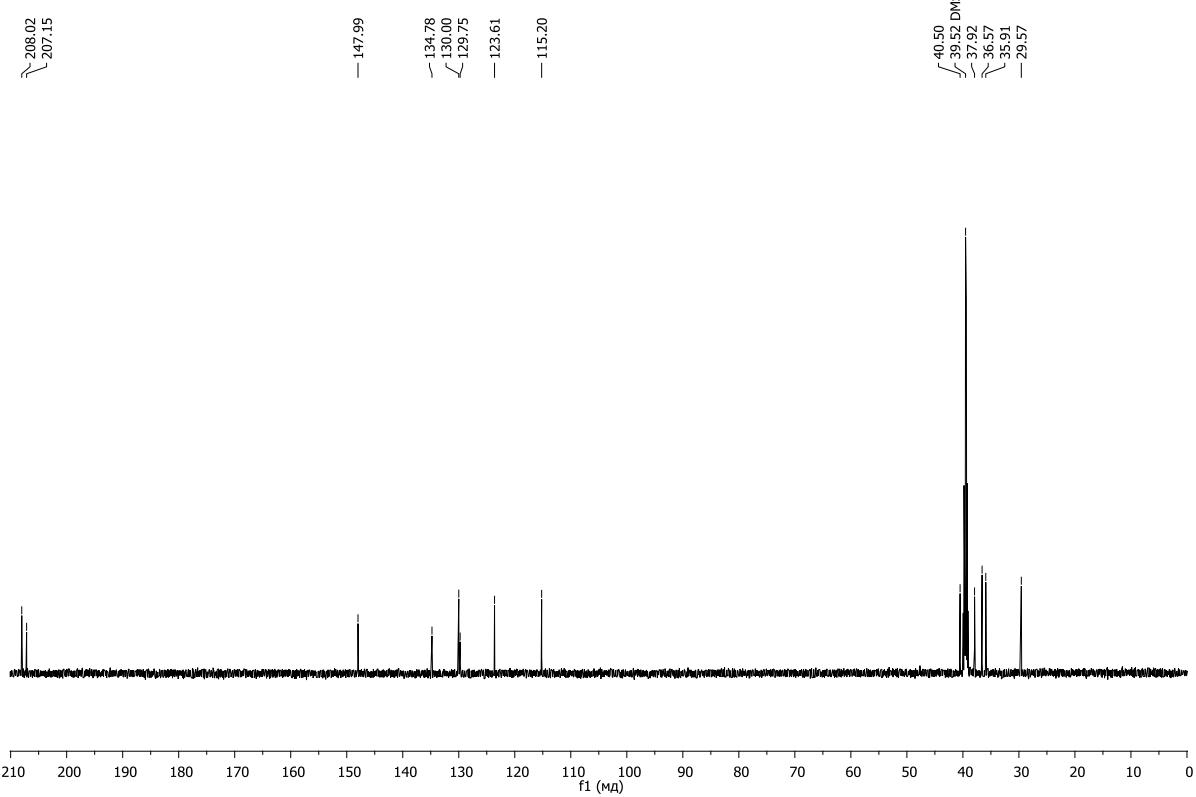


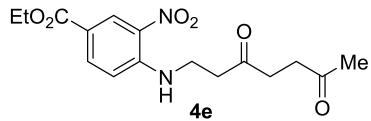


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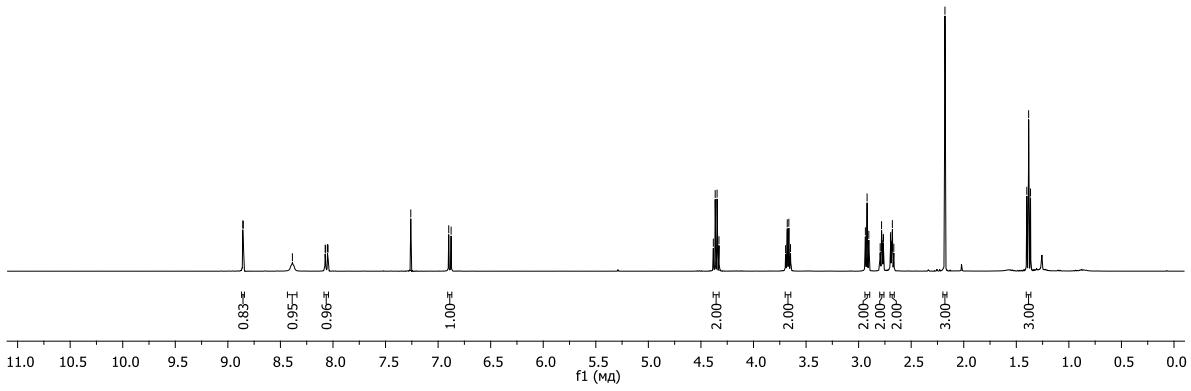
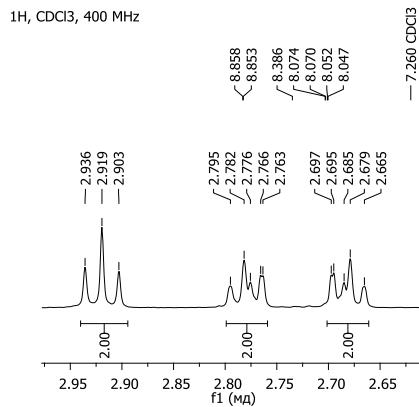


¹³C, DMSO, 150 MHz

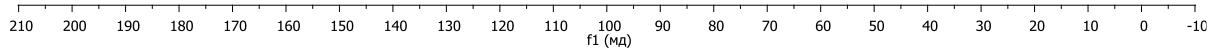
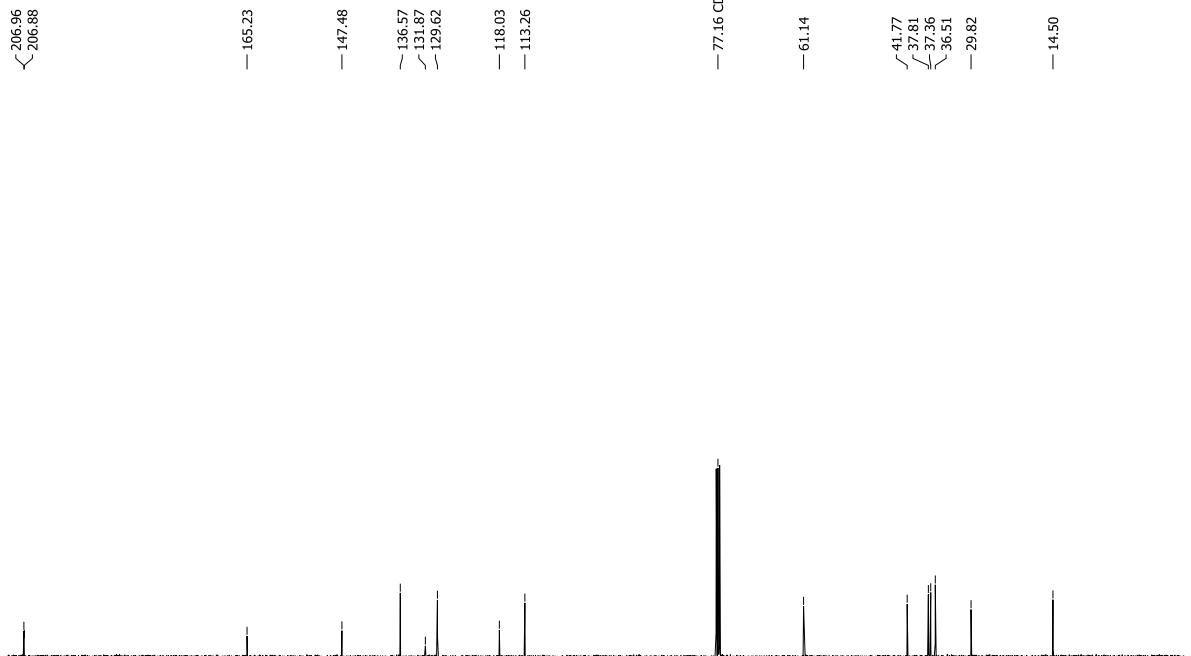


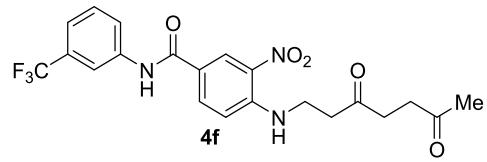


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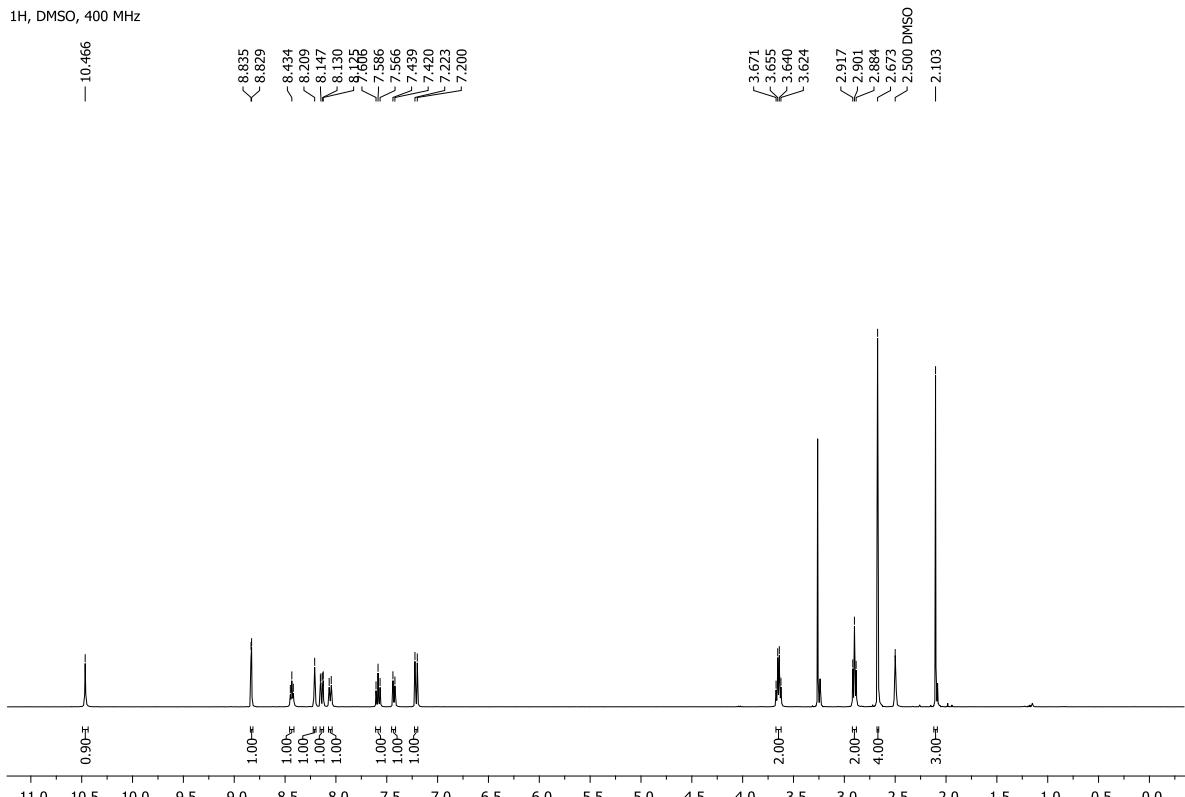


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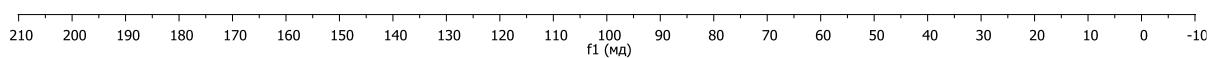
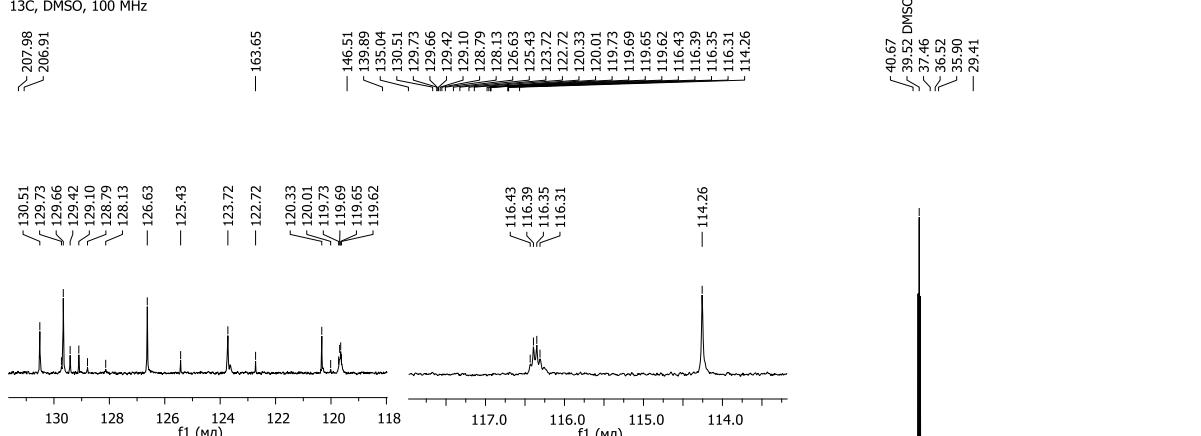


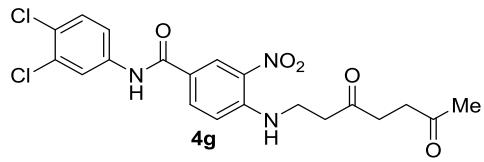


¹H, DMSO, 400 MHz

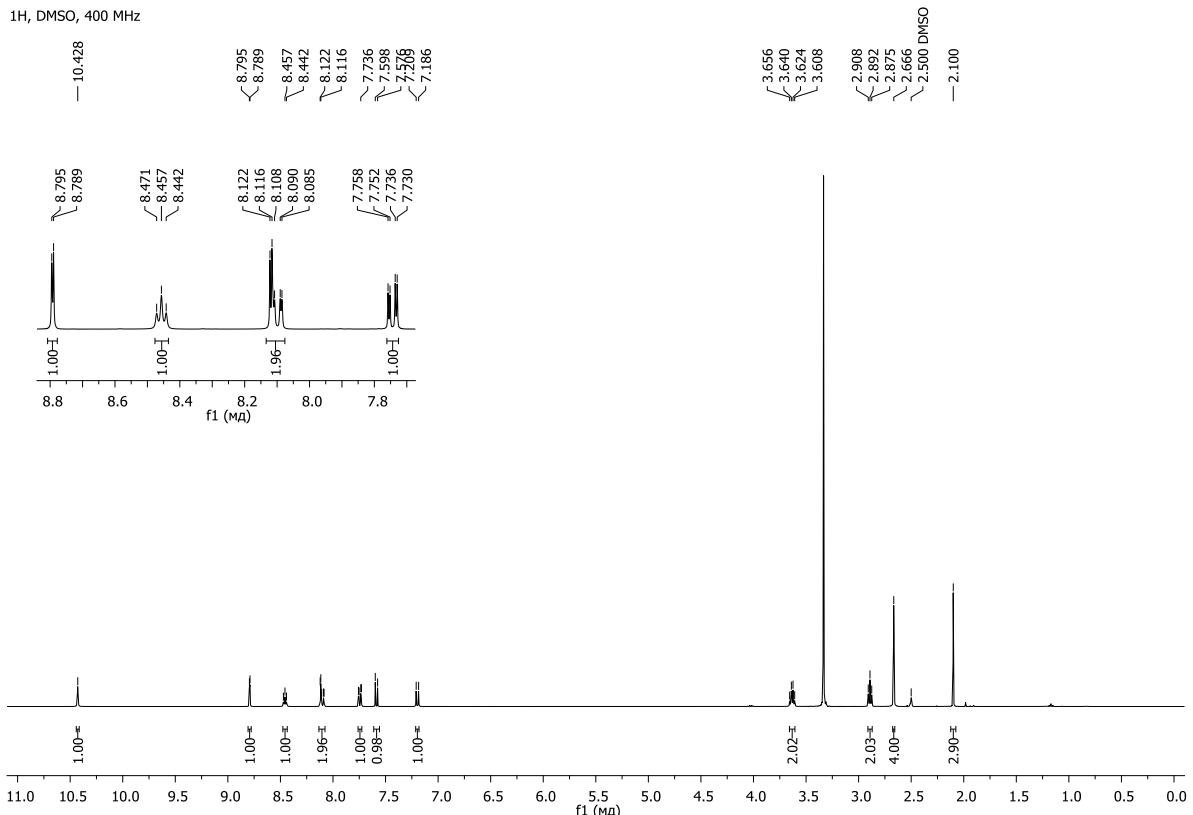


¹³C, DMSO, 100 MHz

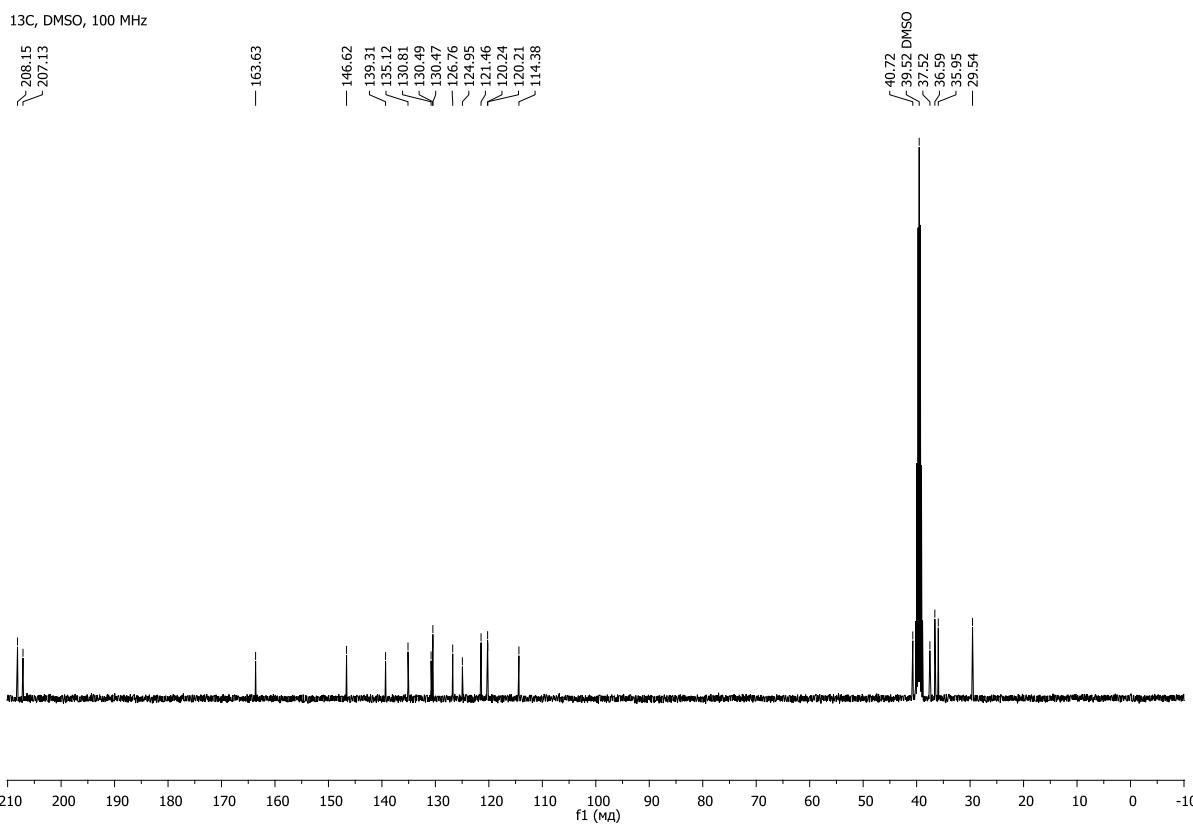


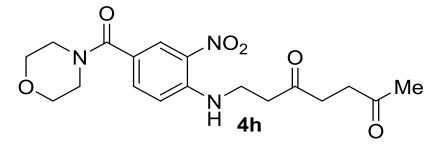


1H, DMSO, 400 MHz

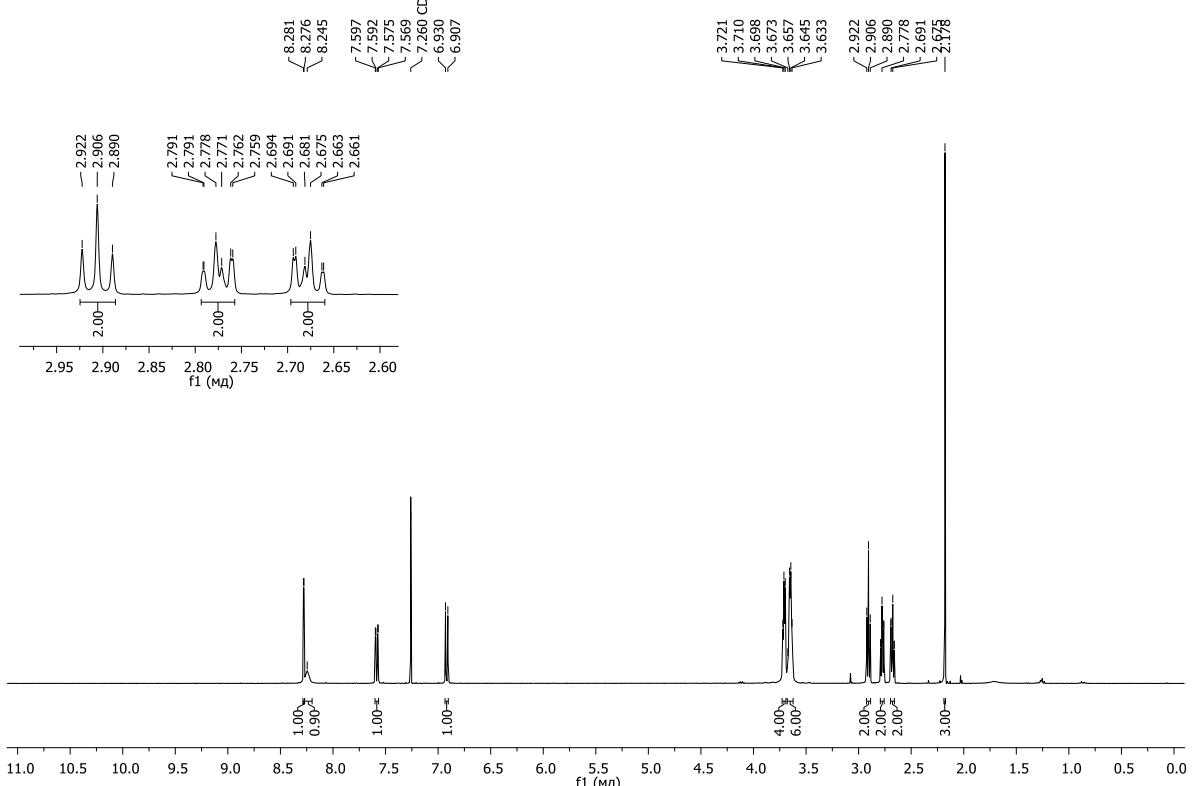


13C, DMSO, 100 MHz

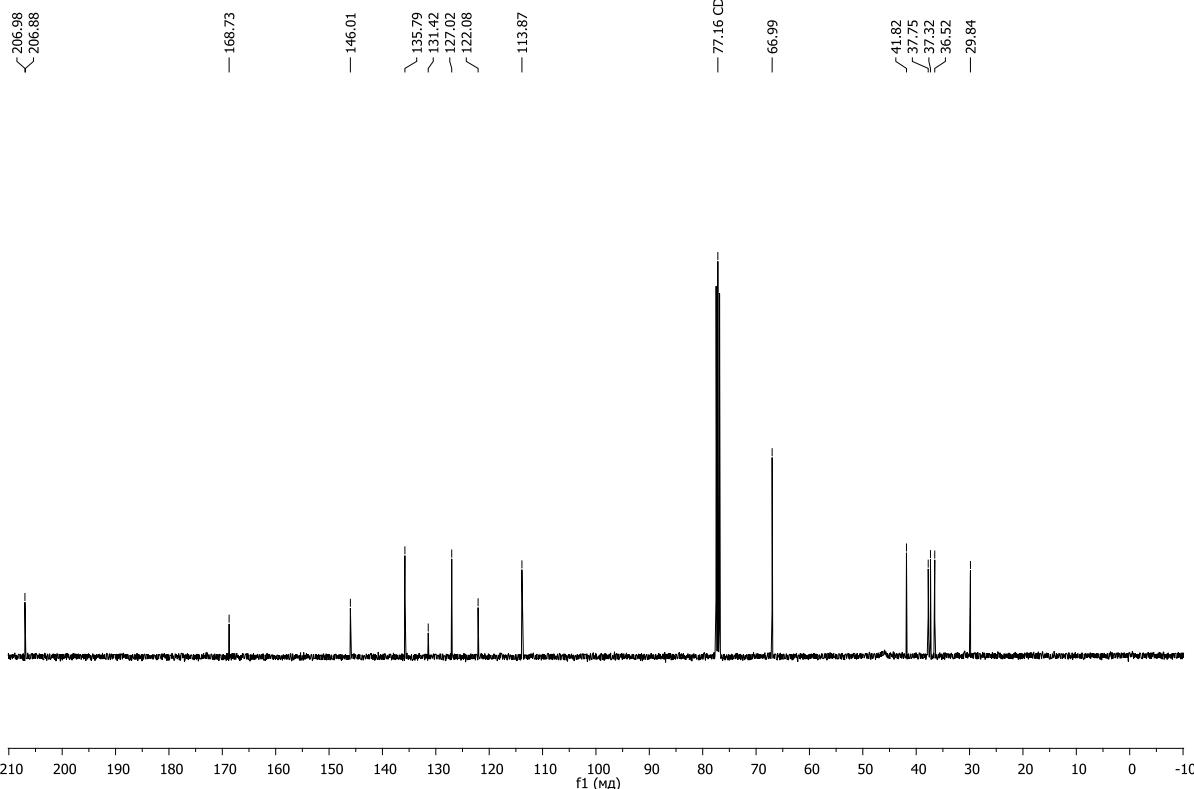


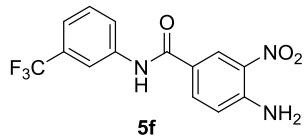


¹H, CDCl₃, 400 MHz

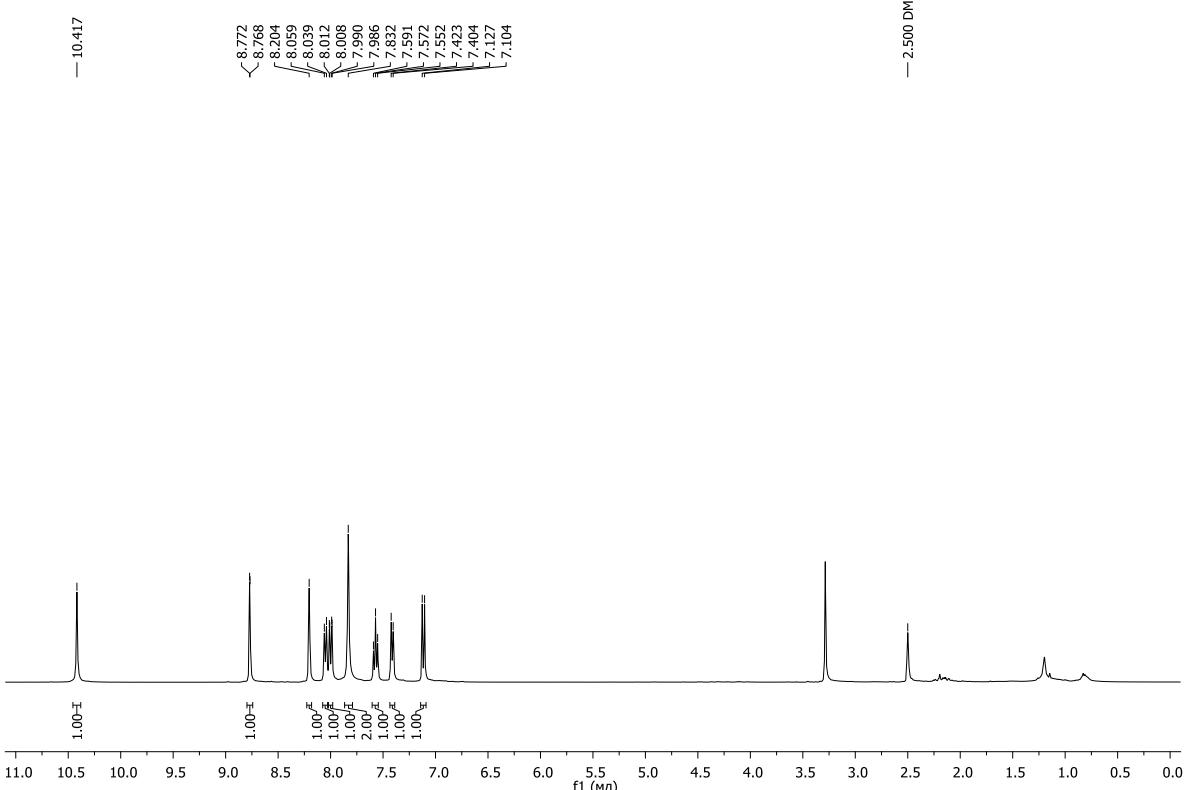


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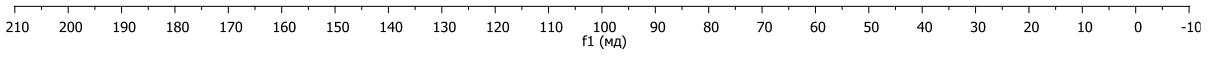
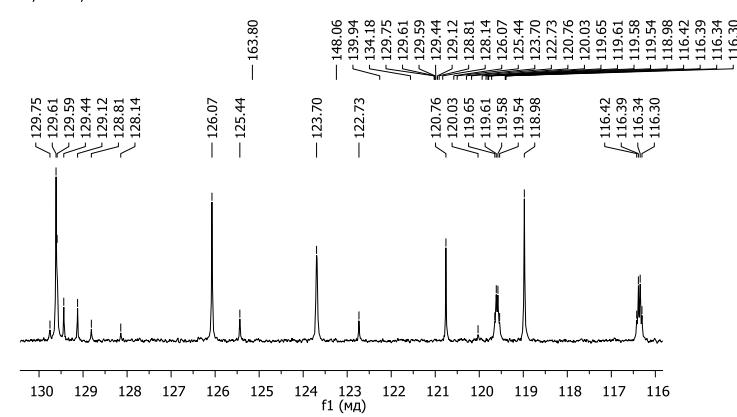


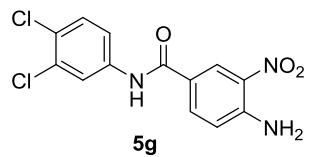


1H, DMSO, 400 MHz

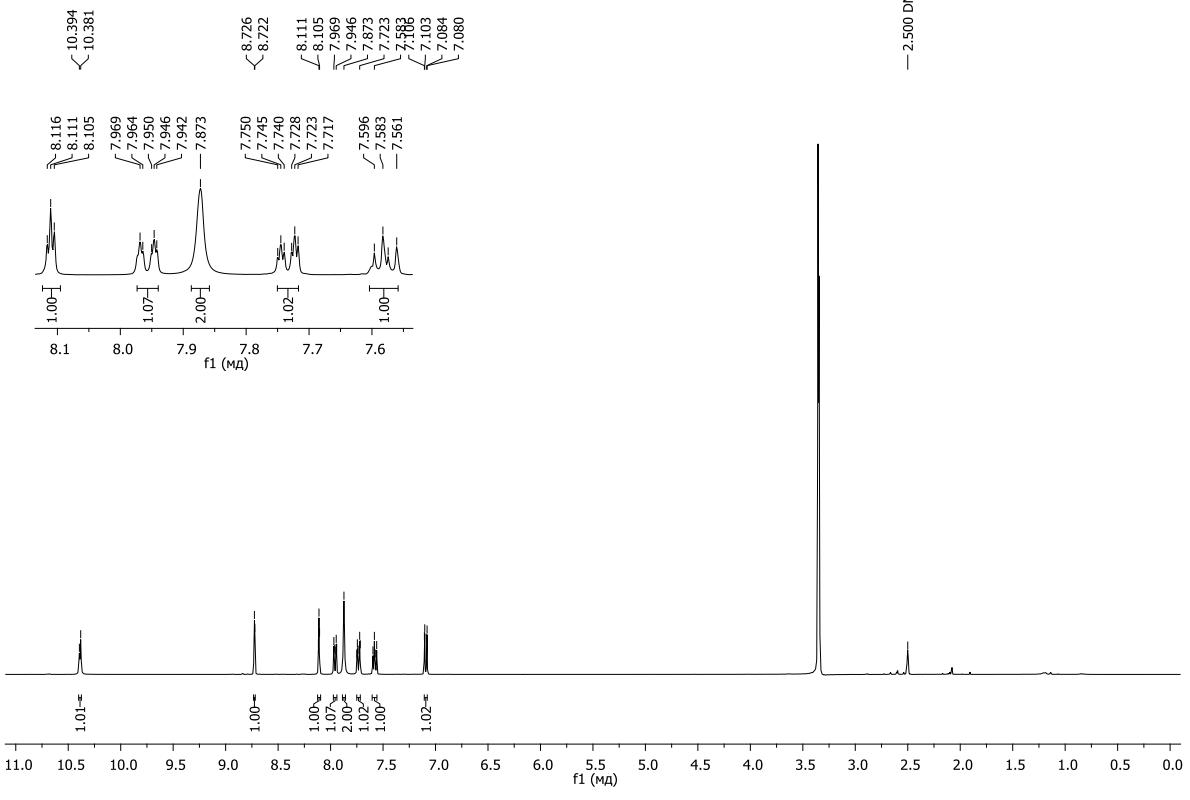


13C, DMSO, 100 MHz

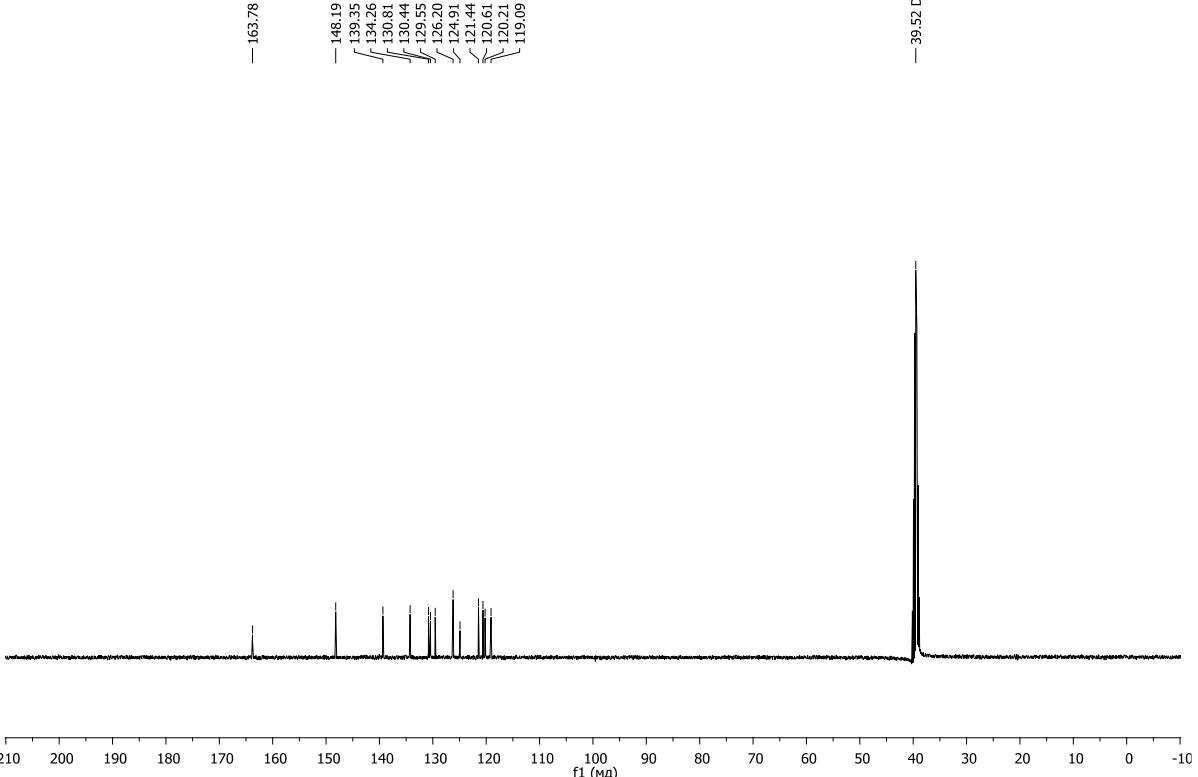


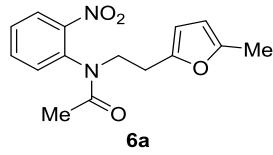


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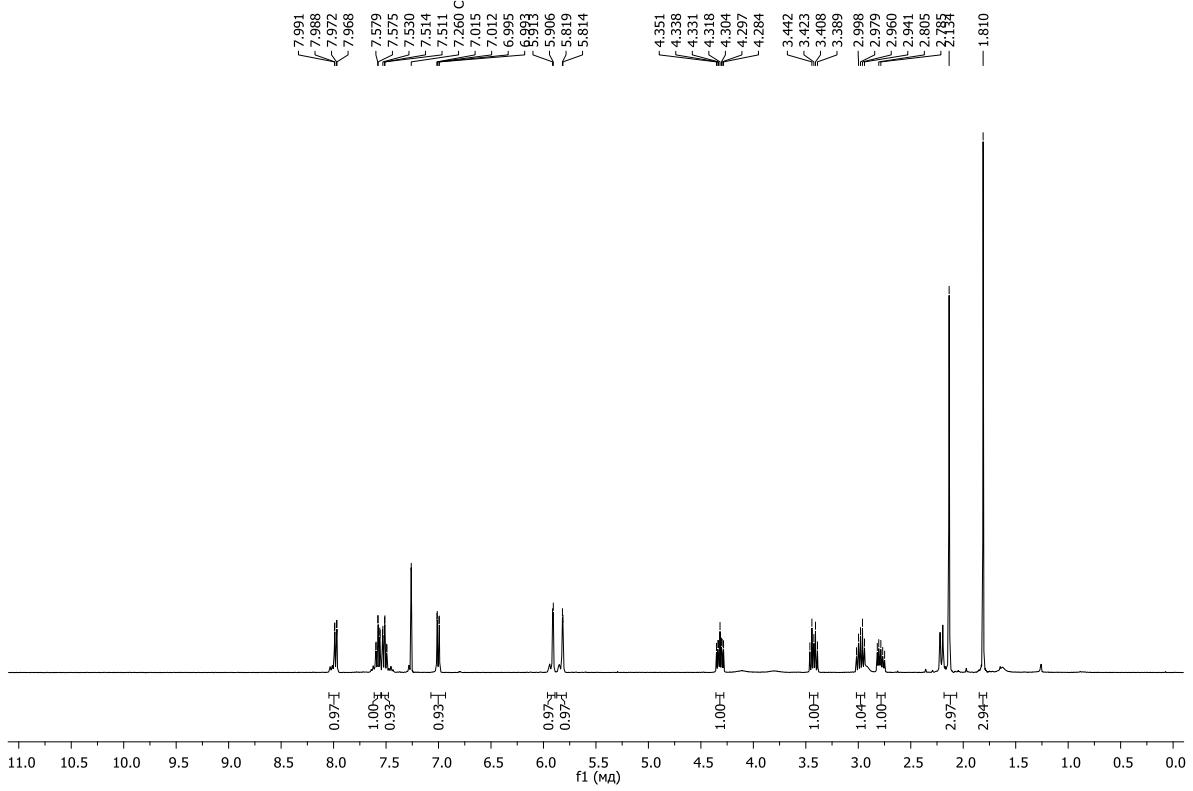


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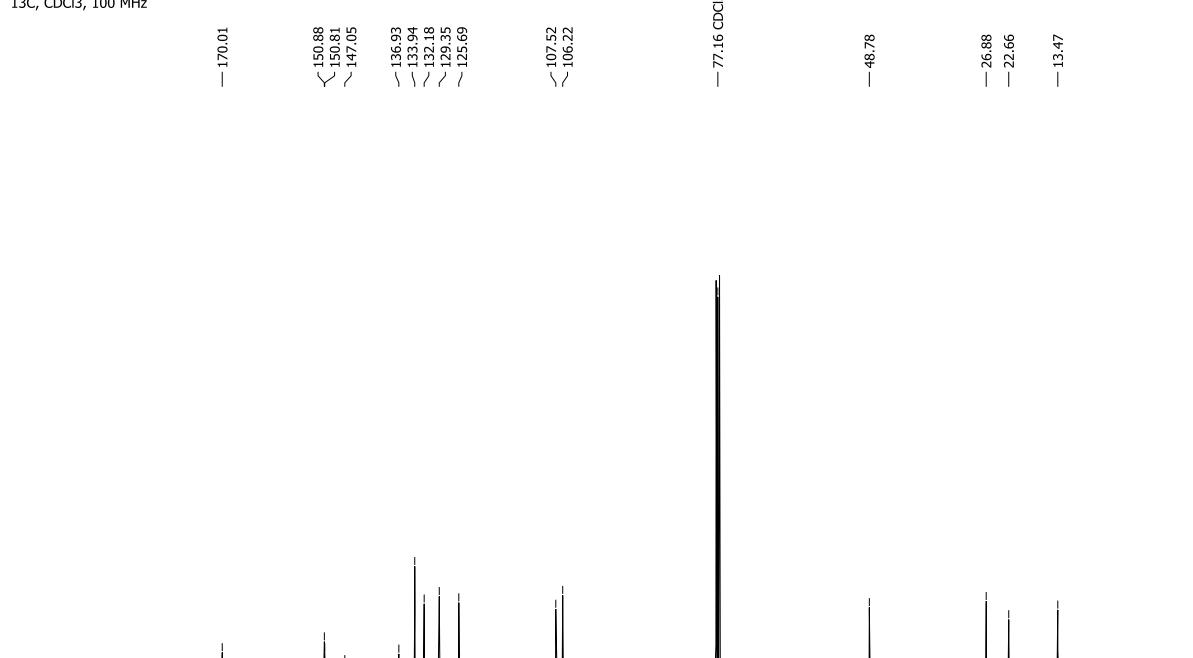


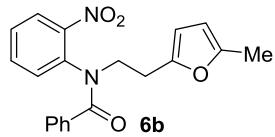


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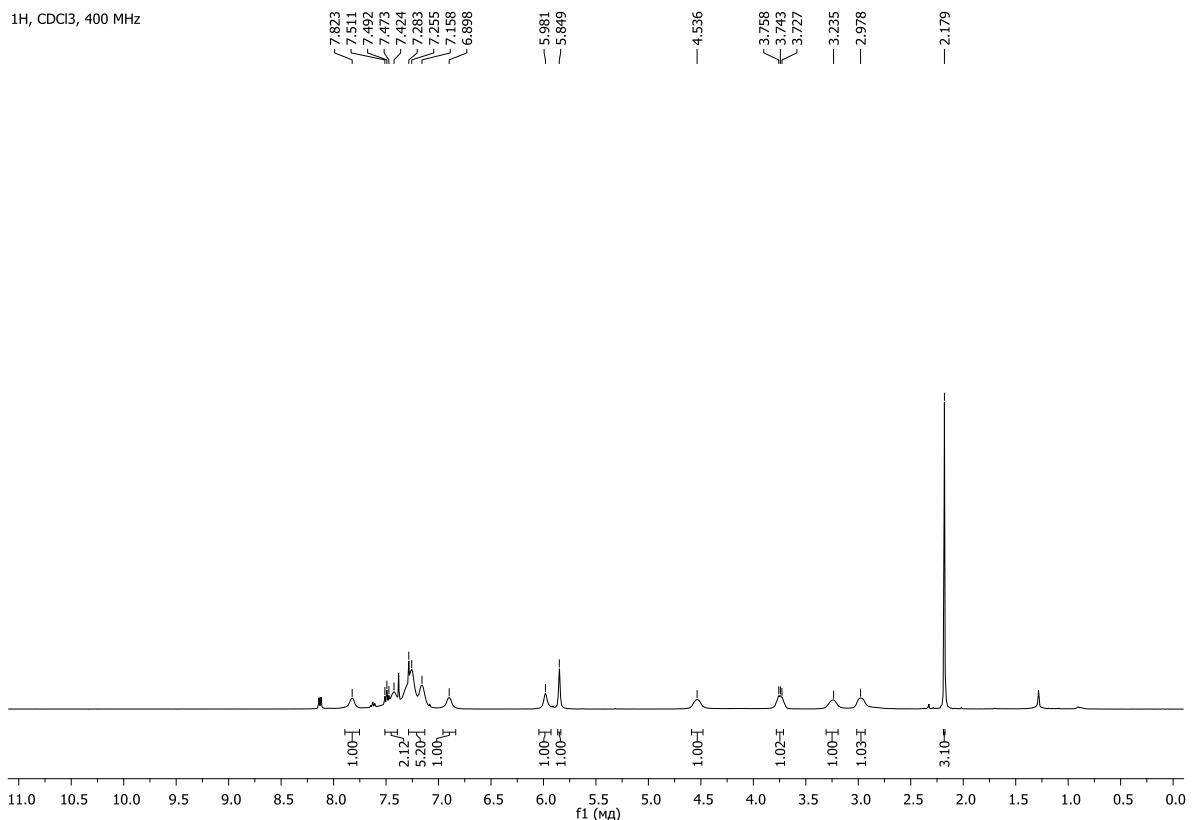


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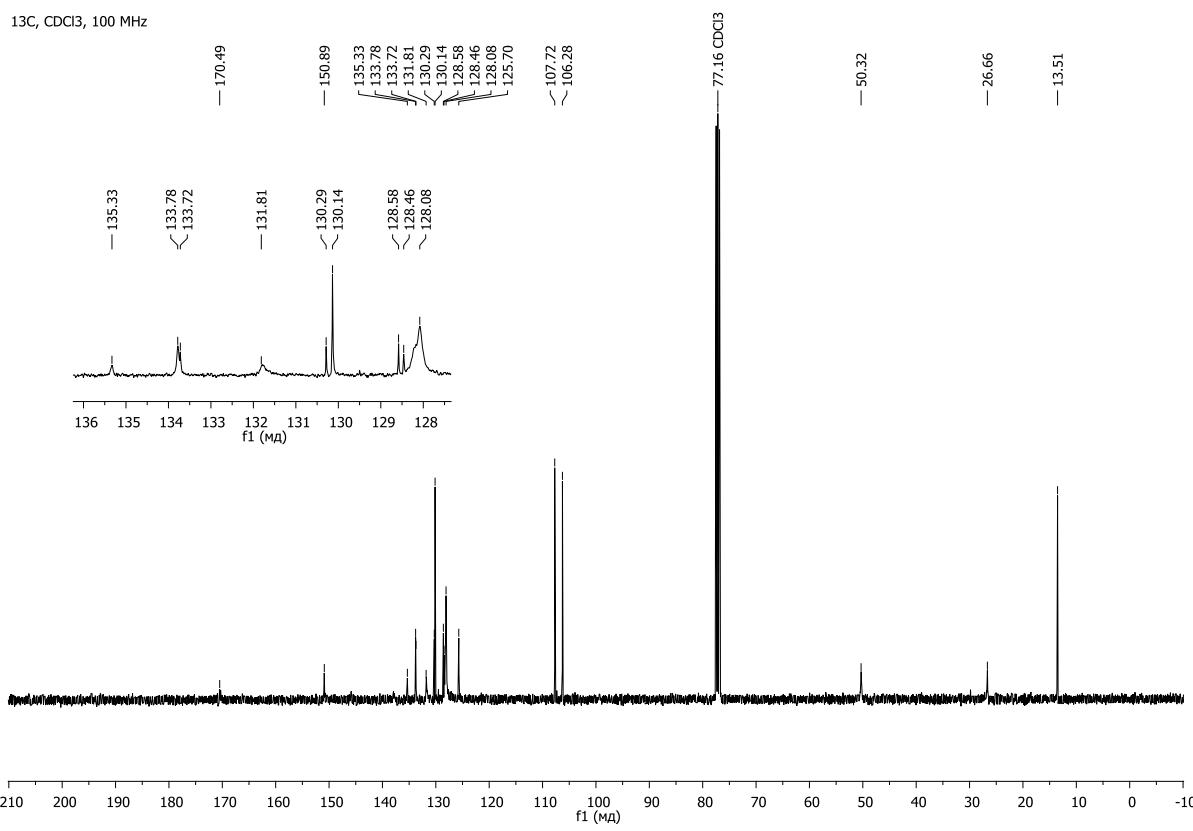


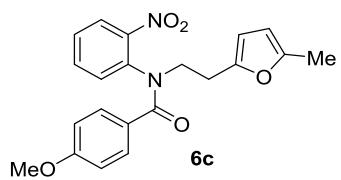


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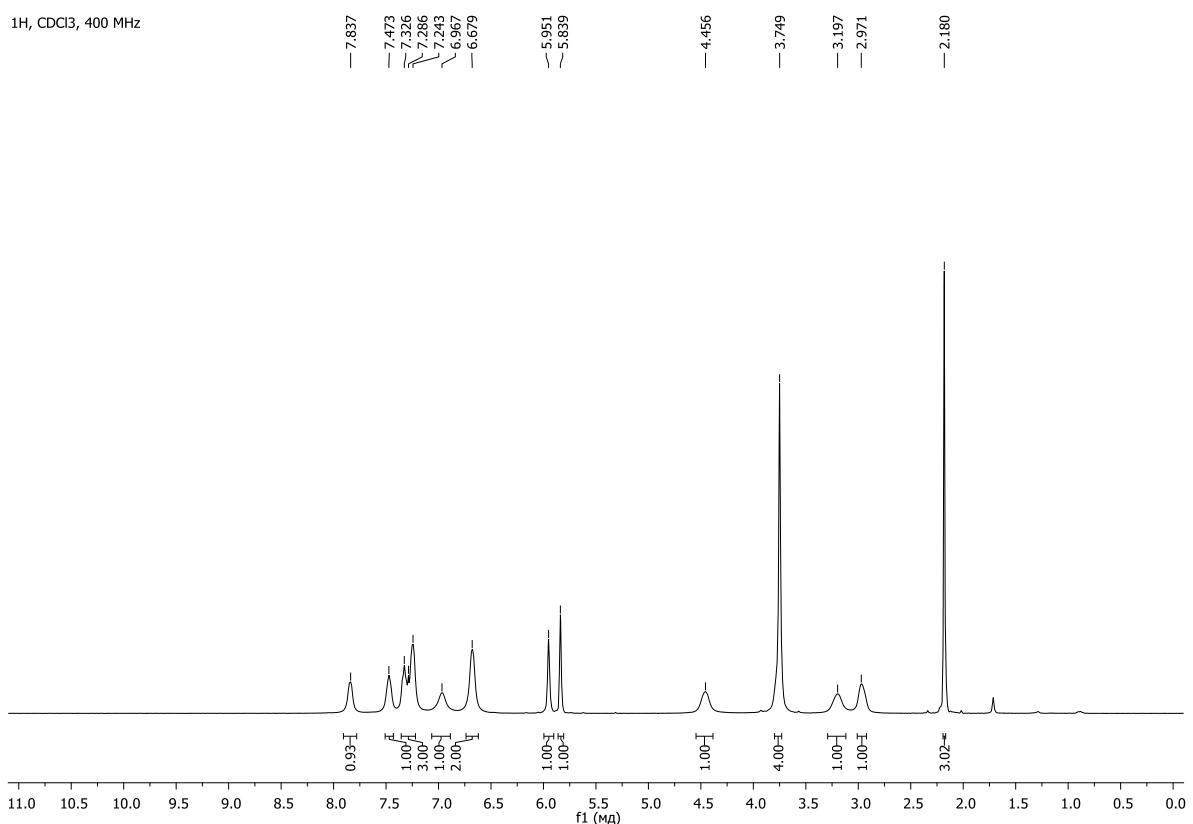


¹³C, CDCl₃, 100 MHz

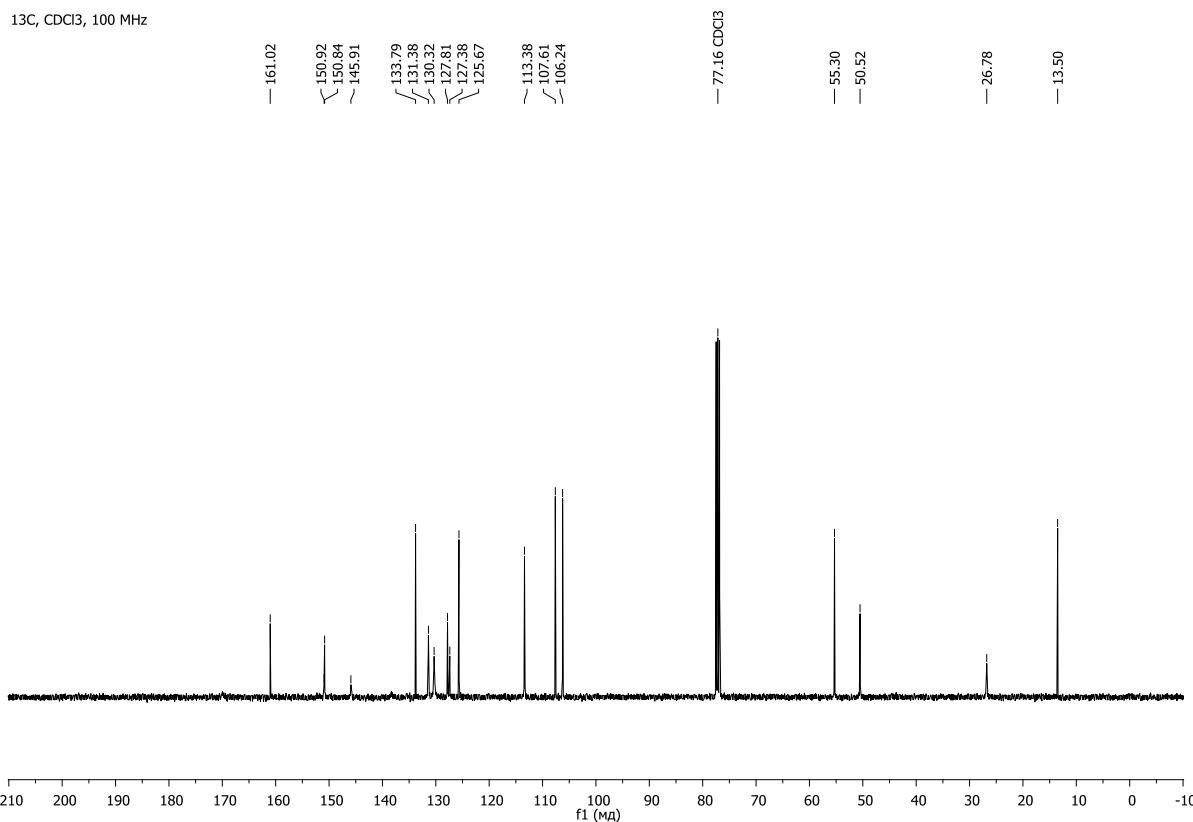


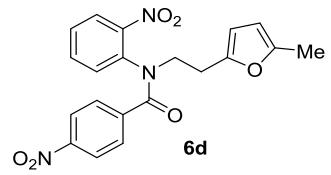


¹H, CDCl₃, 400 MHz

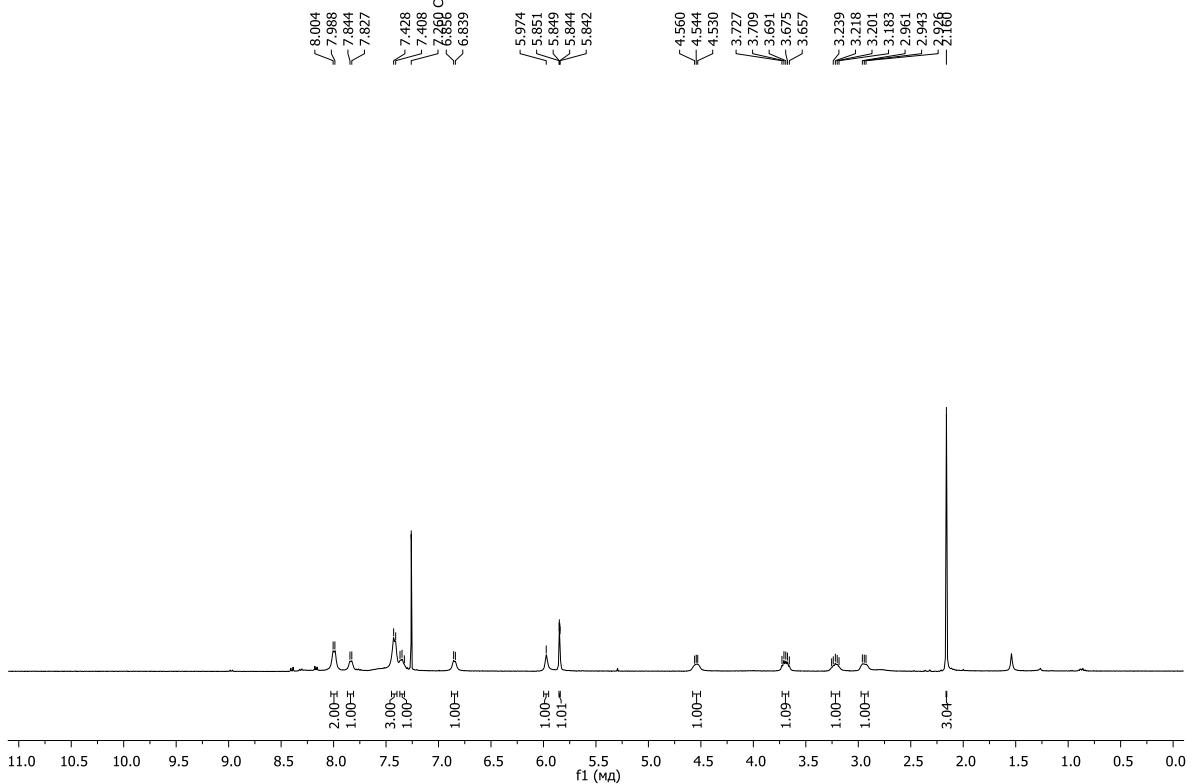


¹³C, CDCl₃, 100 MHz

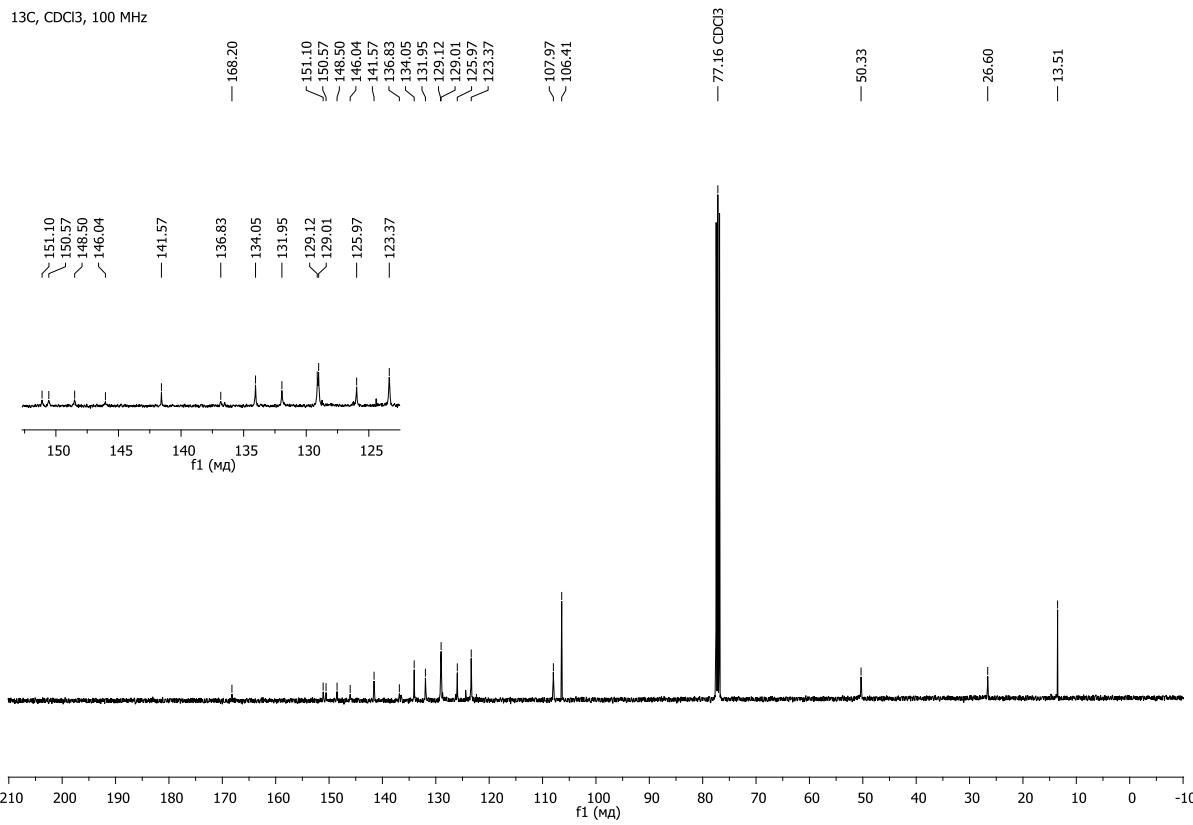


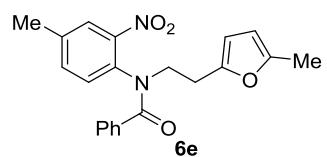


1H, CDCl₃, 400 MHz

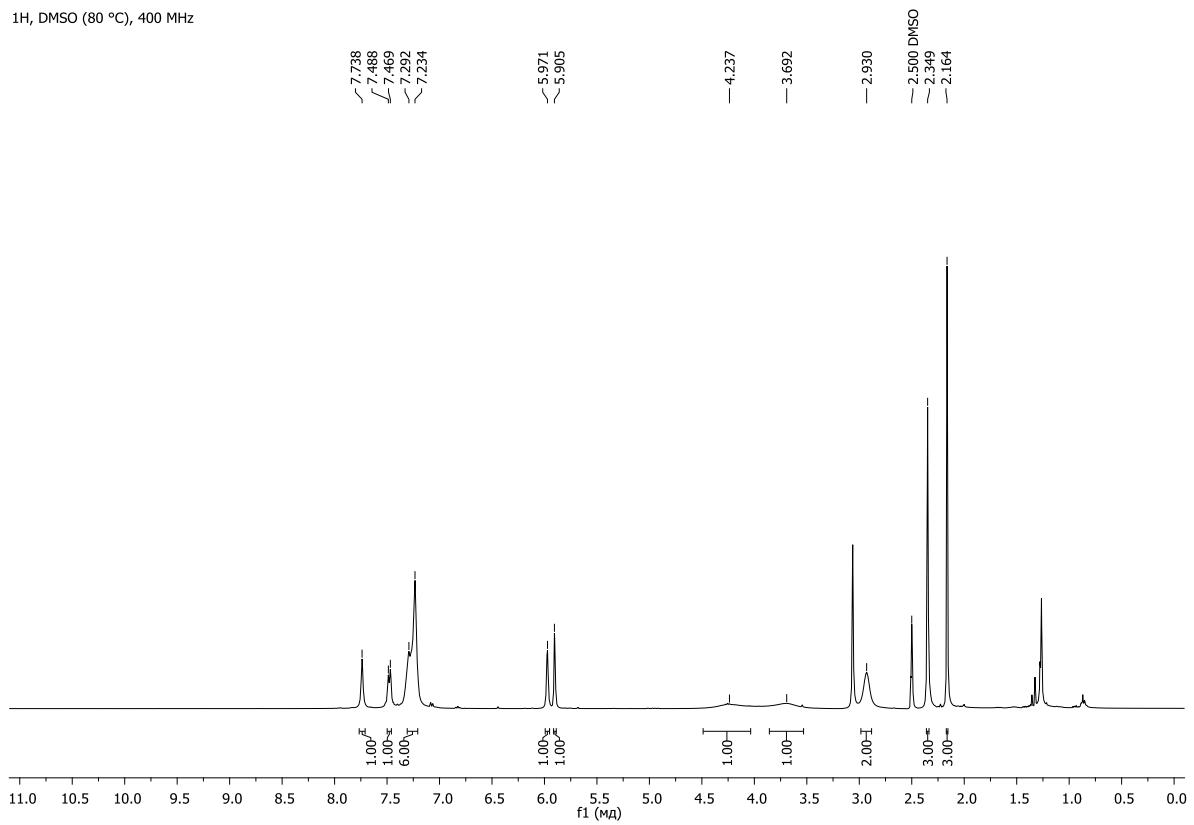


13C, CDCl₃, 100 MHz

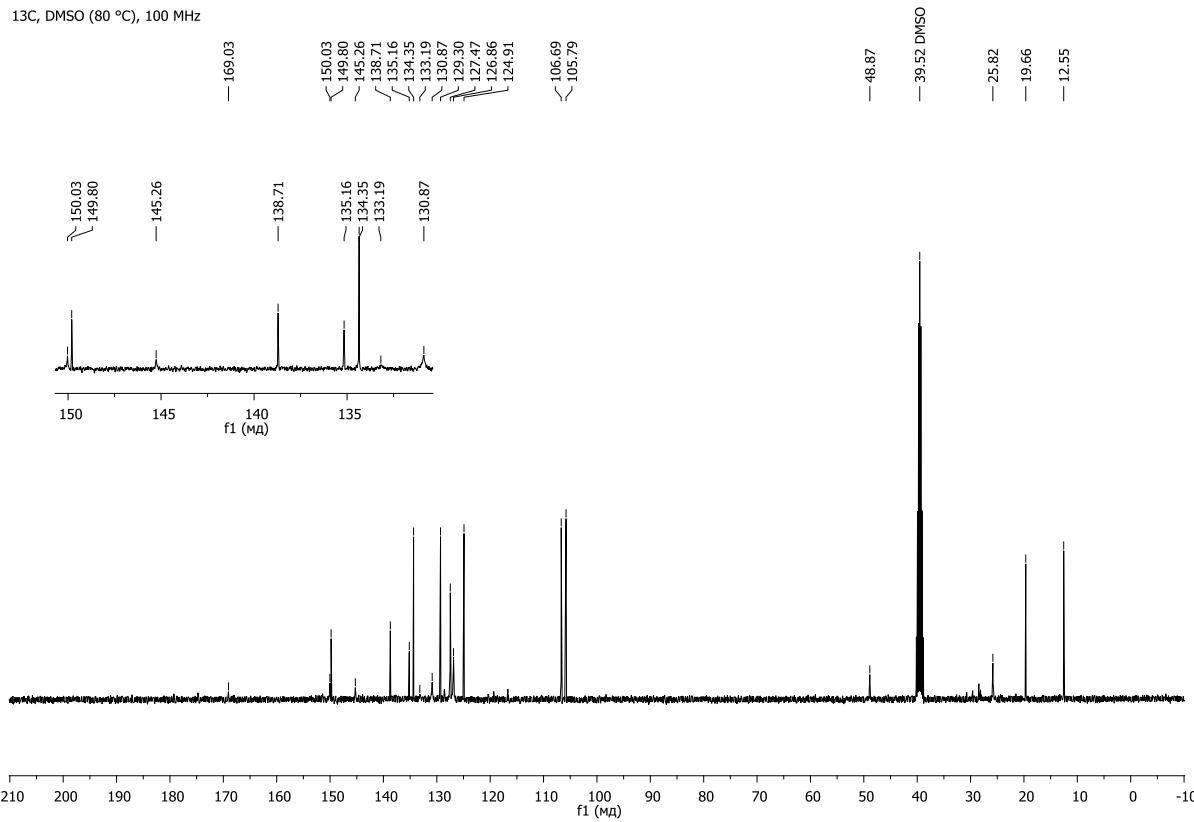


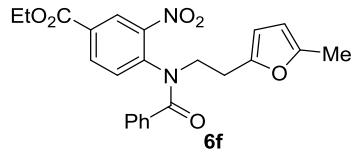


¹H, DMSO (80 °C), 400 MHz

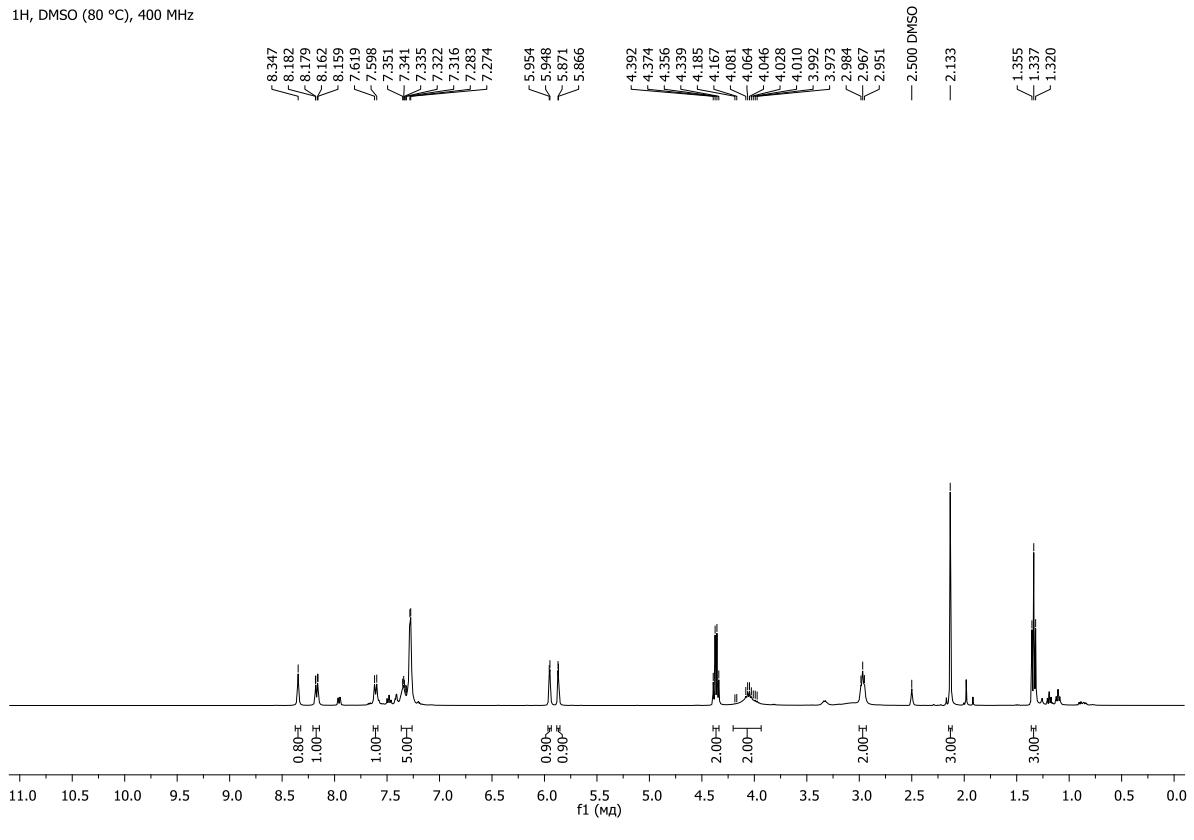


¹³C, DMSO (80 °C), 100 MHz

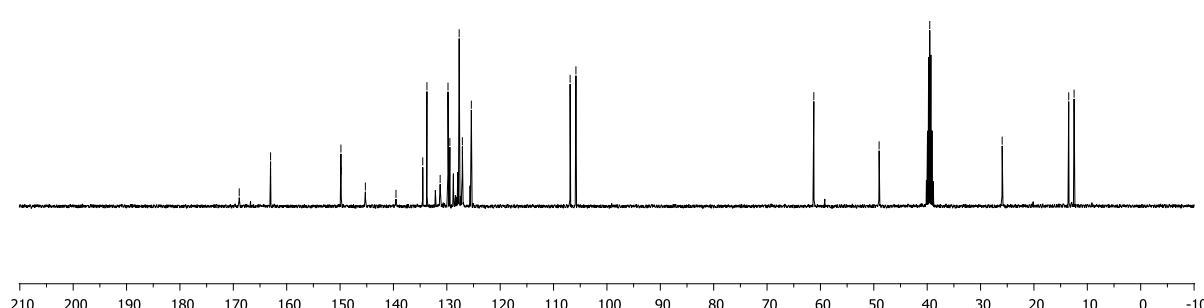
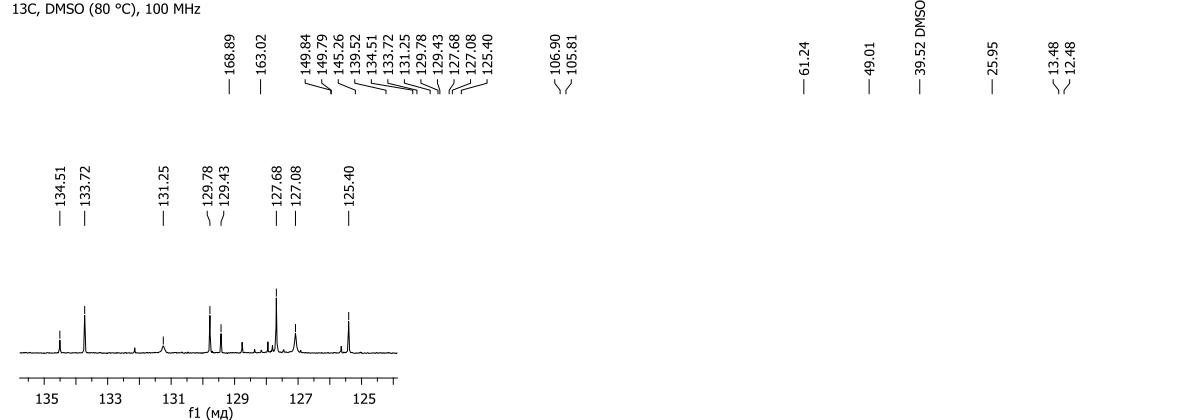


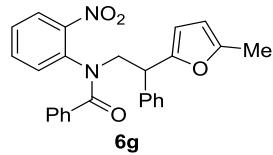


¹H, DMSO (80 °C), 400 MHz

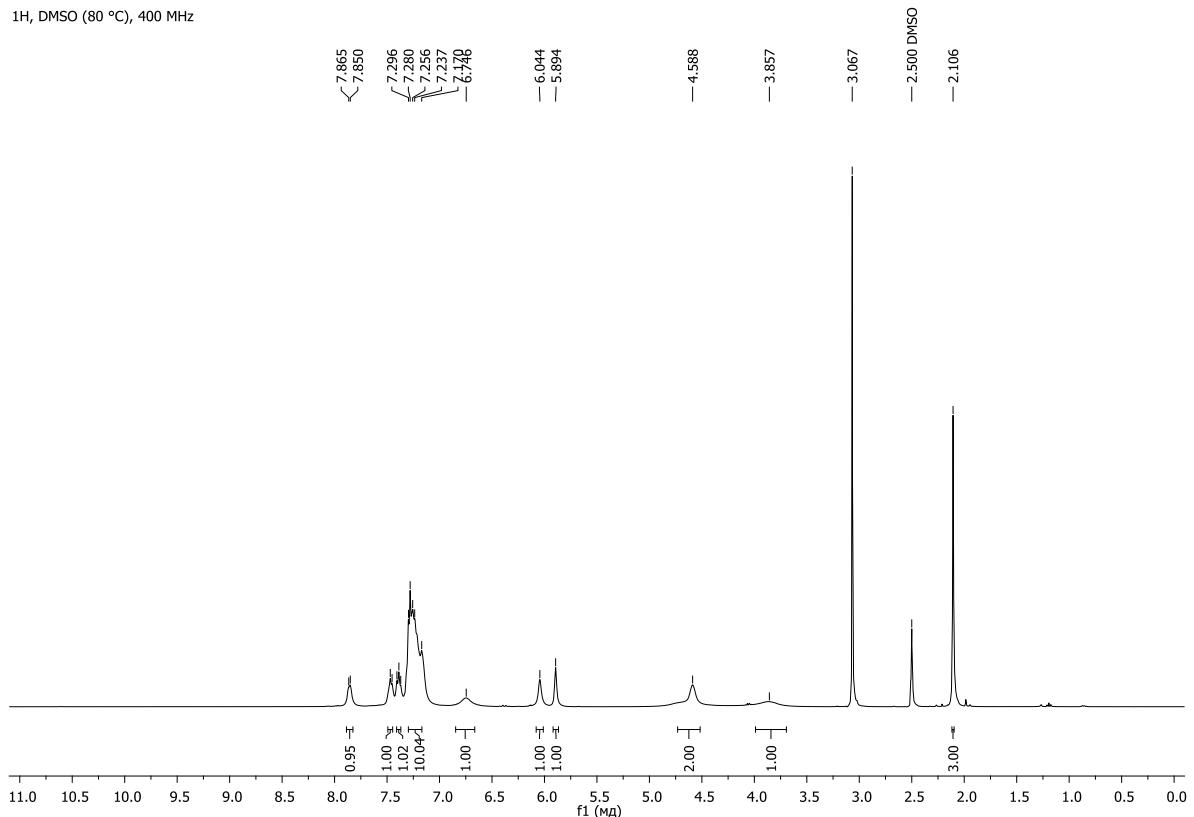


¹³C, DMSO (80 °C), 100 MHz

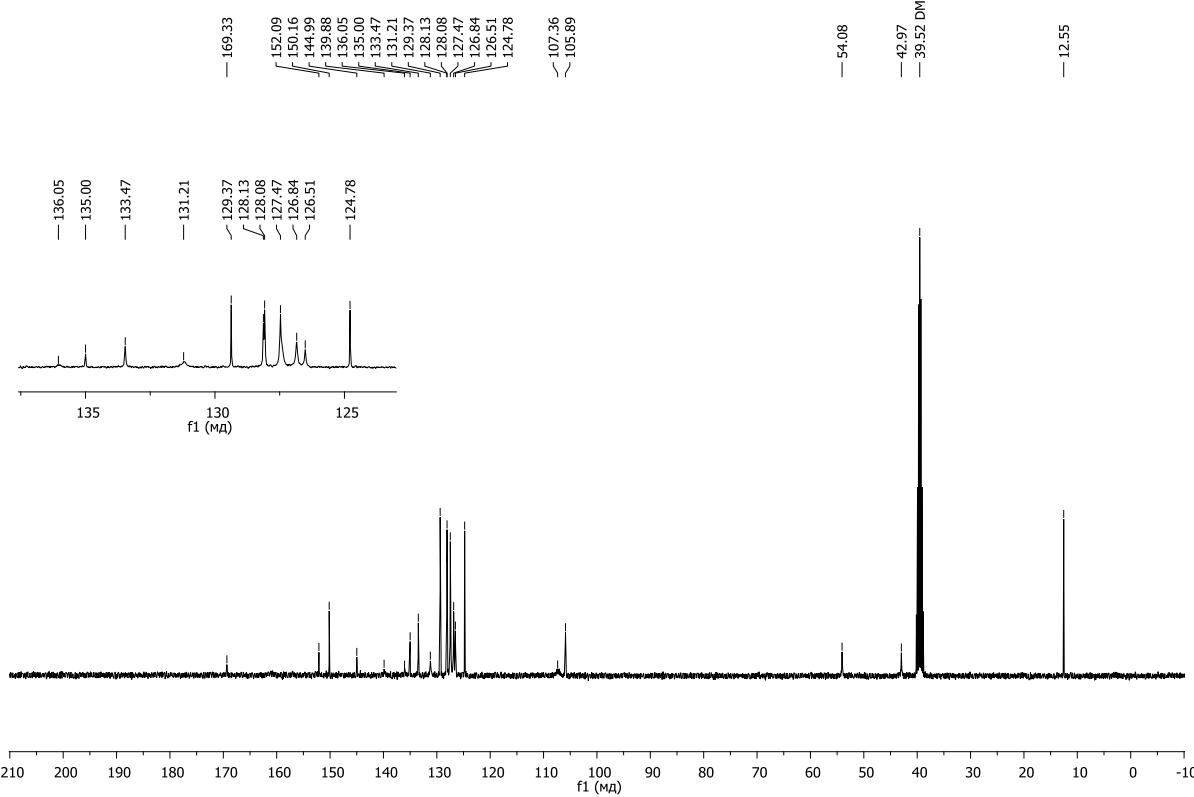


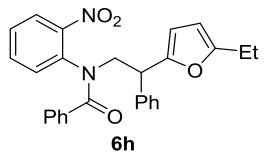


¹H, DMSO (80 °C), 400 MHz

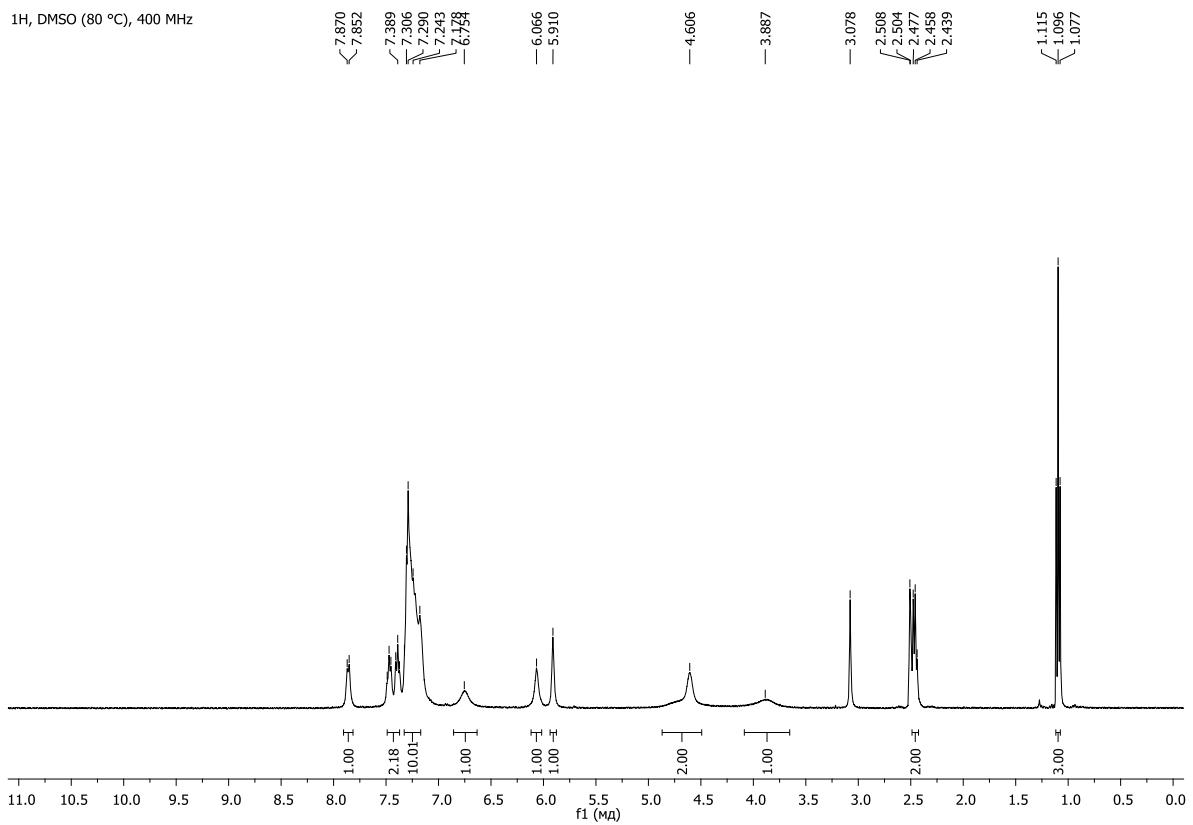


¹³C, DMSO (80 °C), 100 MHz

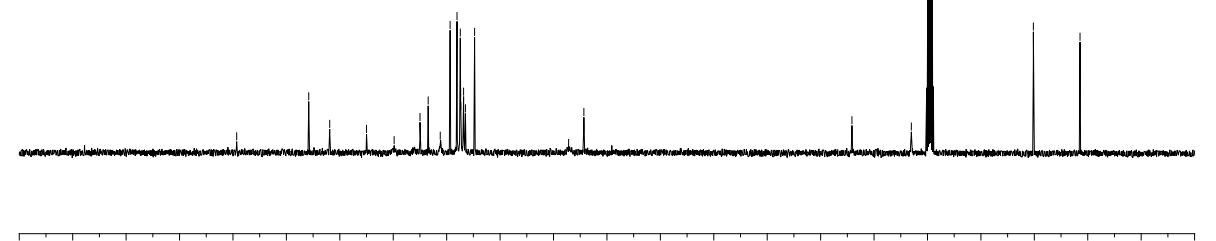
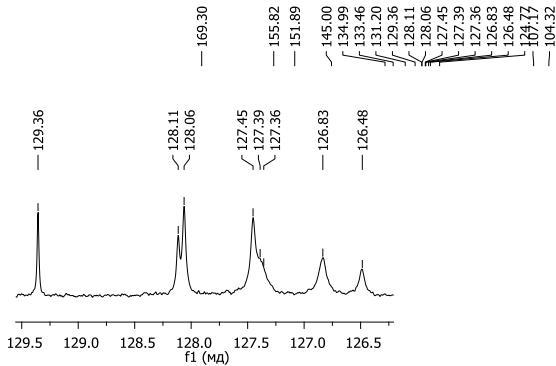


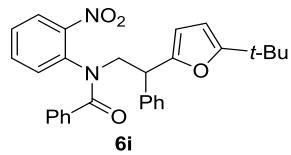


¹H, DMSO (80 °C), 400 MHz

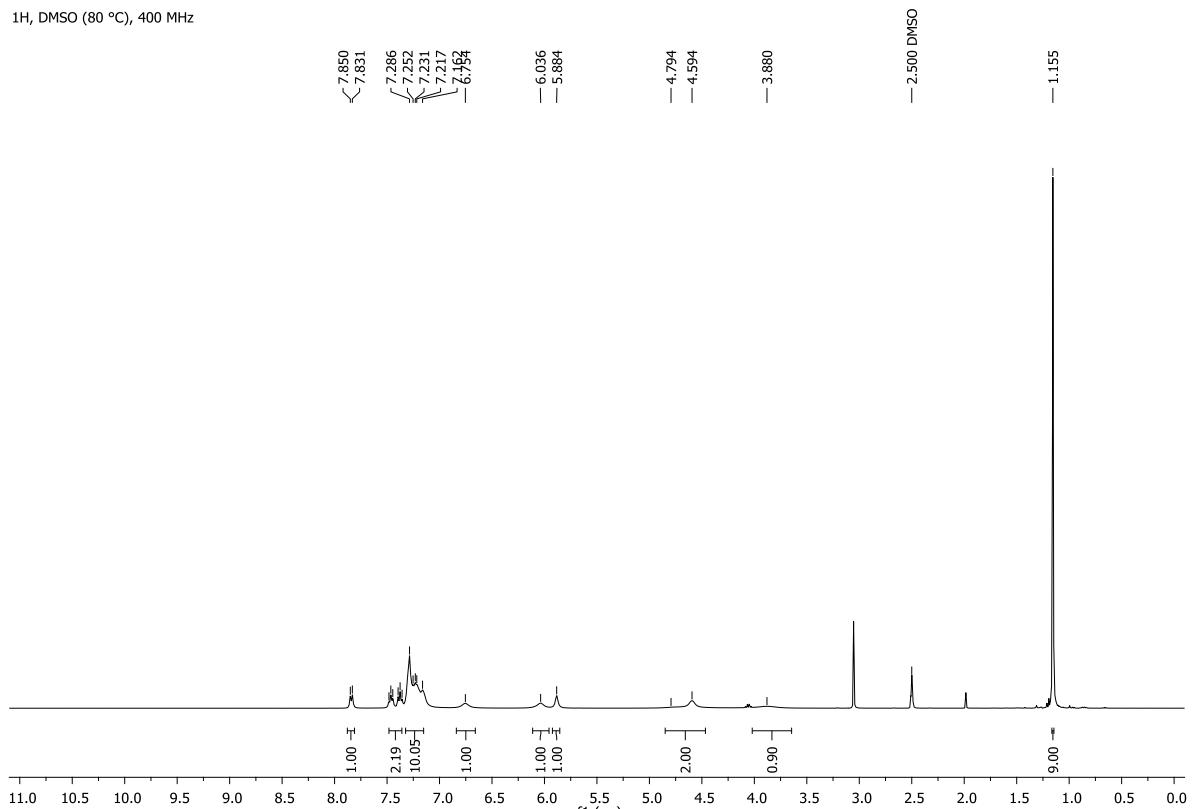


¹³C, DMSO (80 °C), 100 MHz

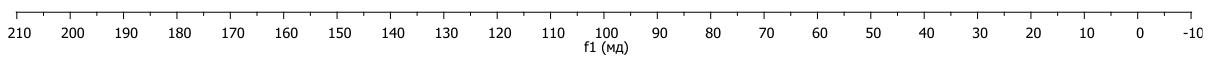
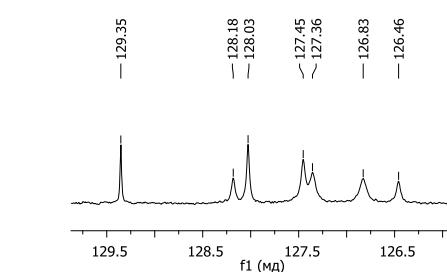
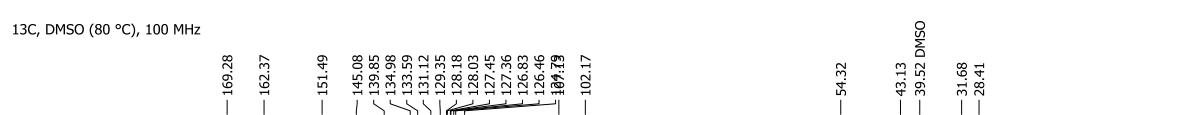


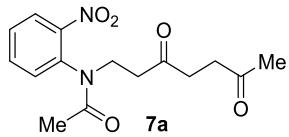


¹H, DMSO (80 °C), 400 MHz

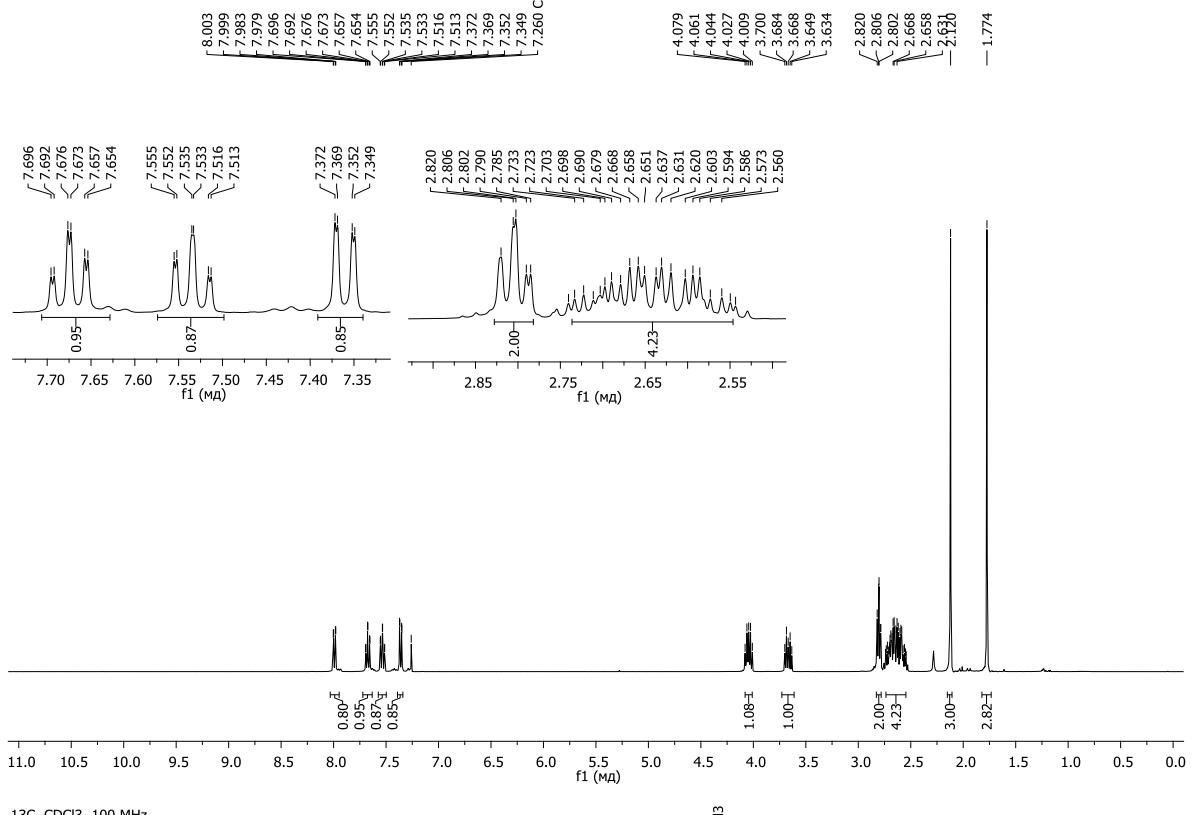


¹³C, DMSO (80 °C), 100 MHz

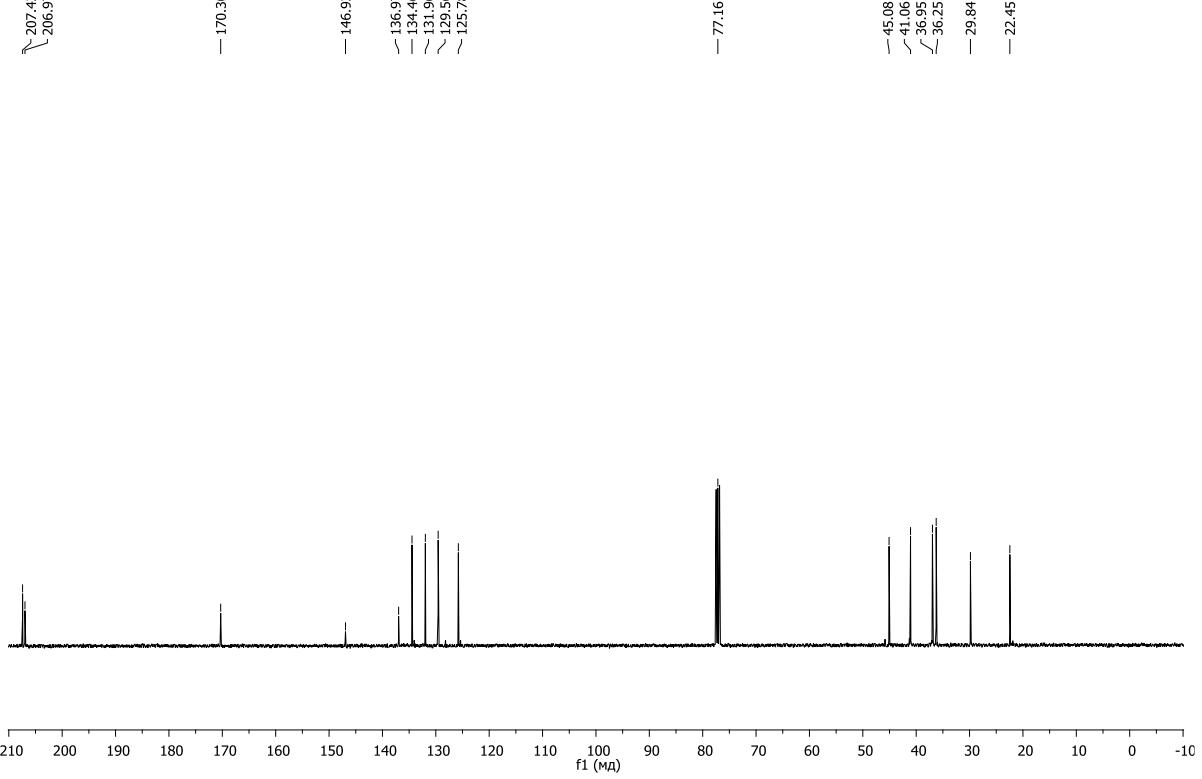


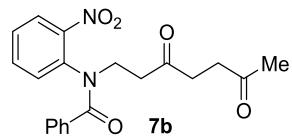


¹H, CDCl₃, 400 MHz

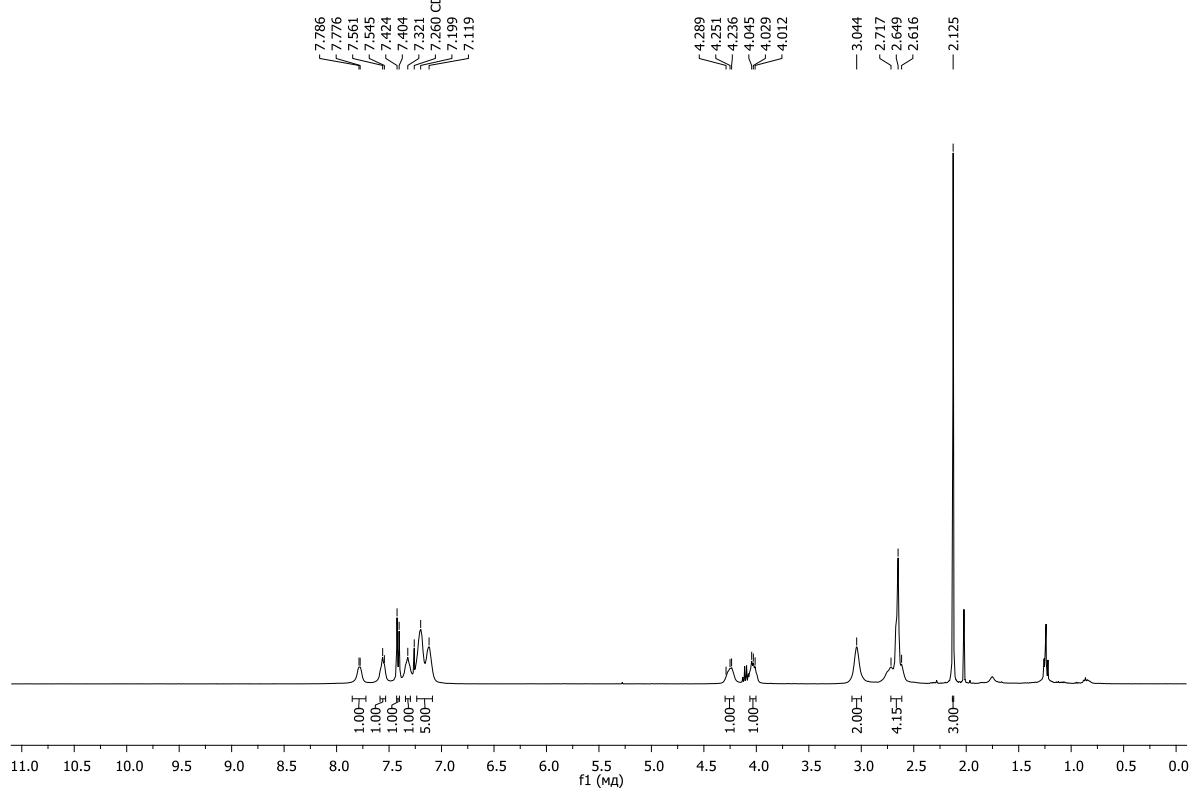


¹³C, CDCl₃, 100 MHz

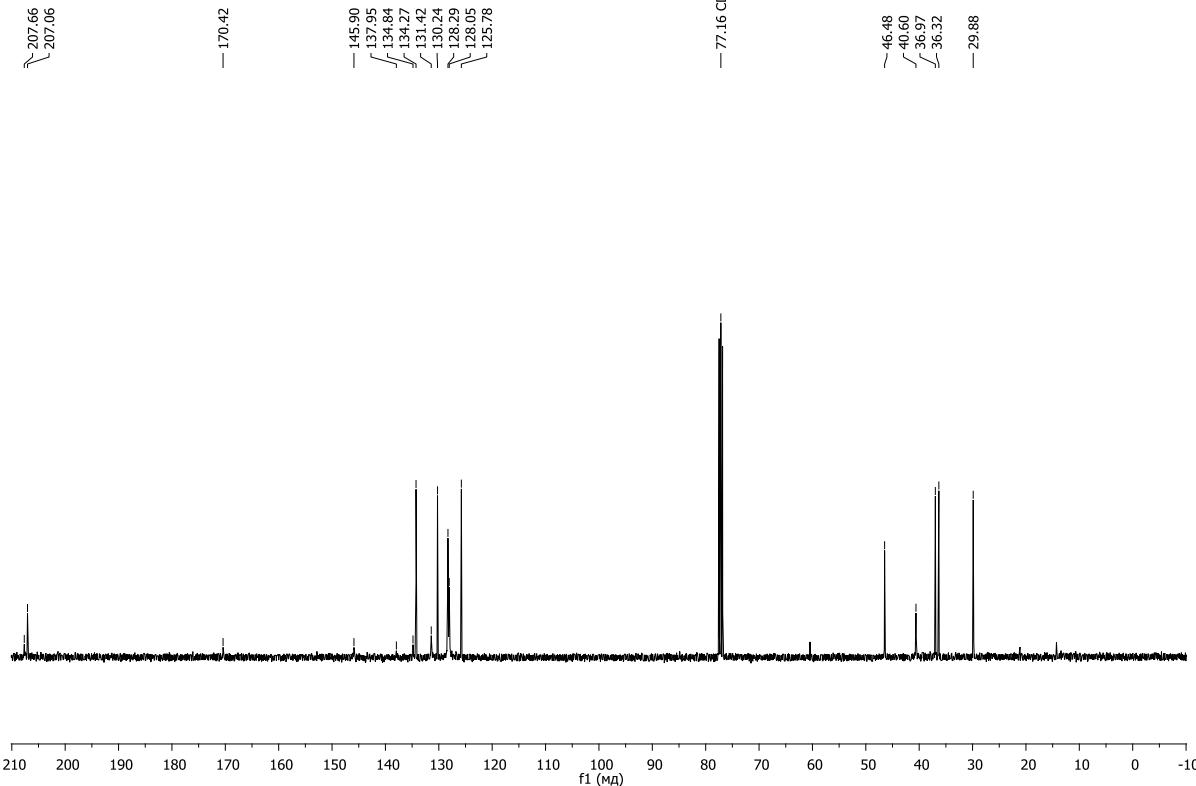


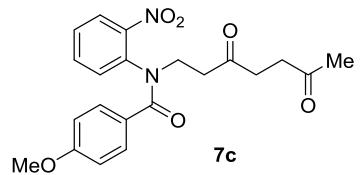


1H, CDCl₃, 400 MHz

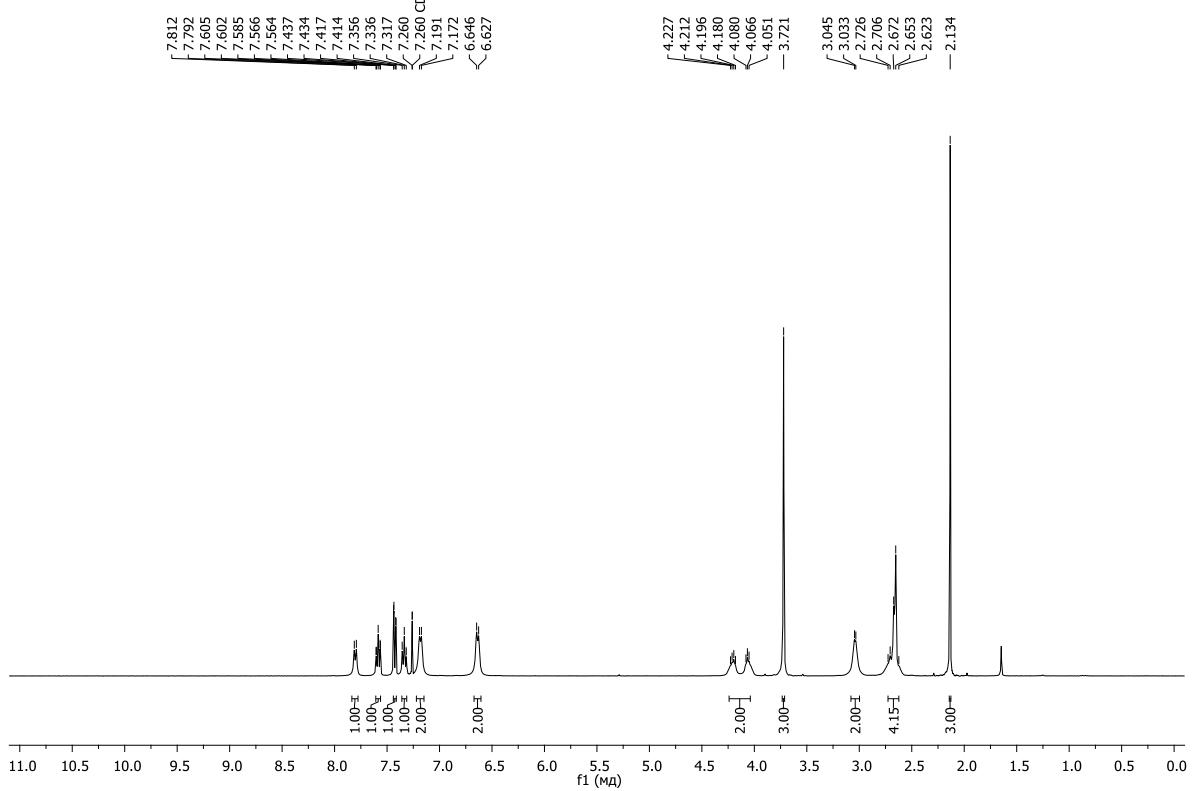


13C, CDCl₃, 100 MHz

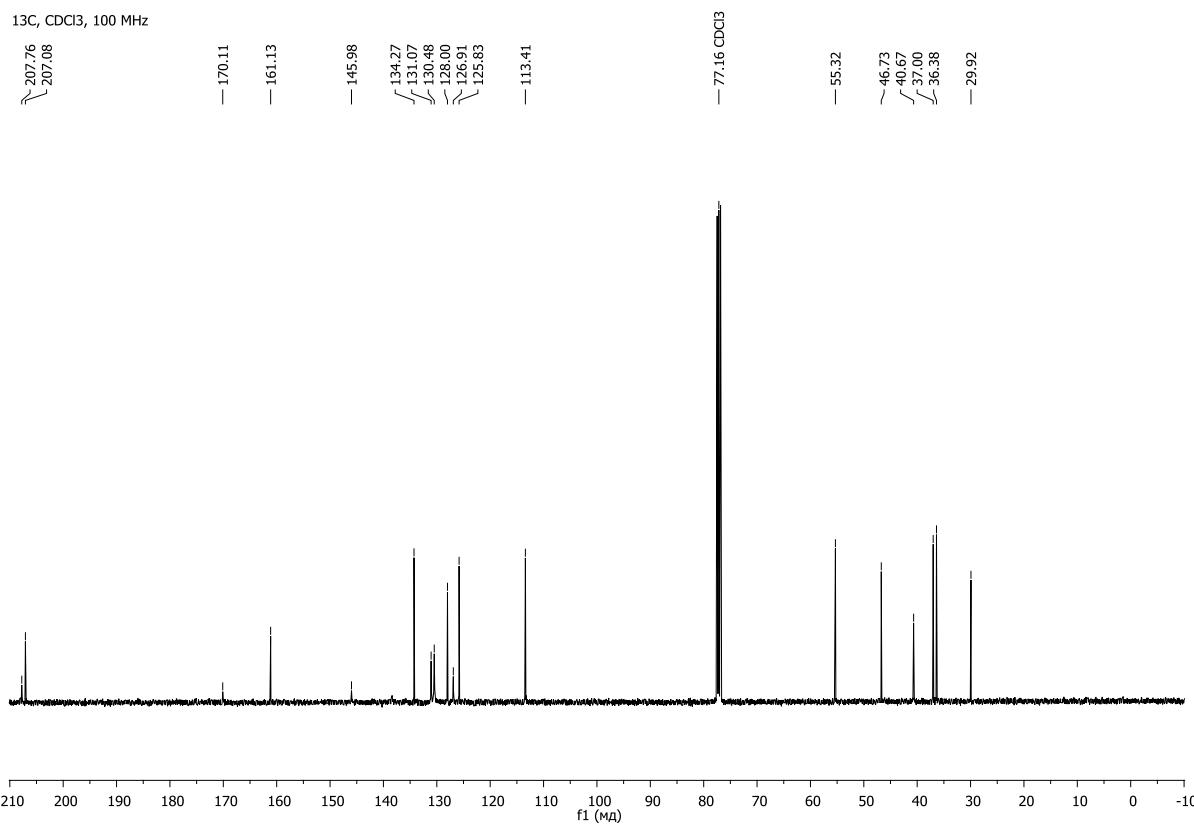


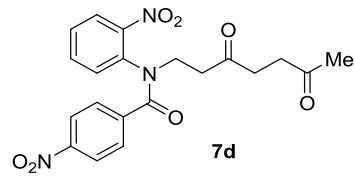


¹H, CDCl₃, 400 MHz

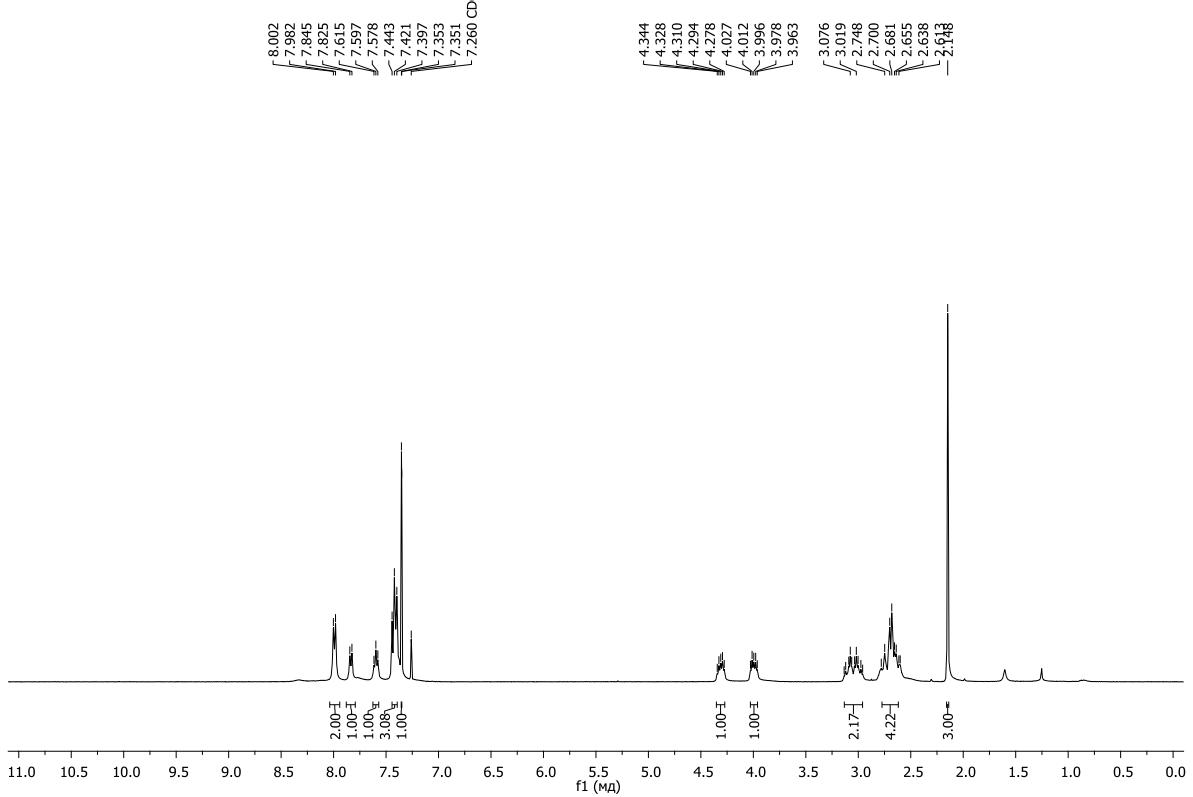


¹³C, CDCl₃, 100 MHz

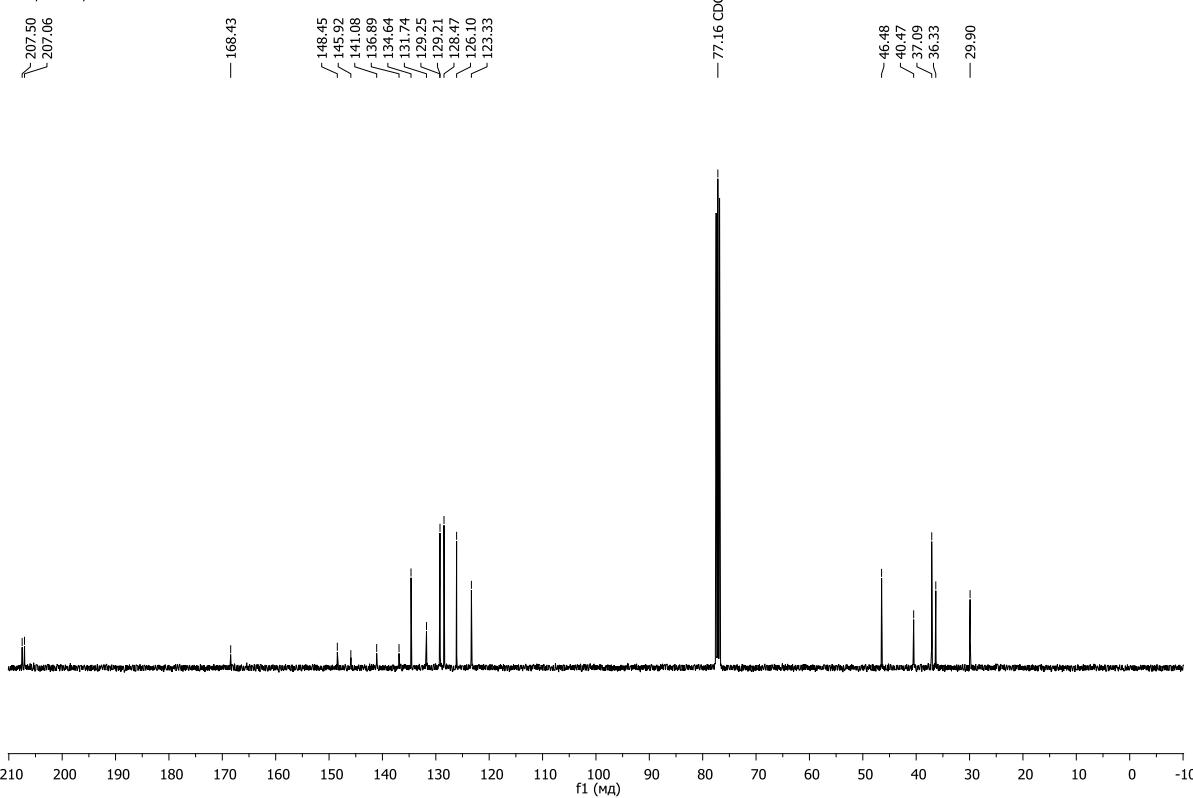


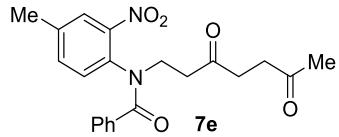


¹H, CDCl₃, 400 MHz

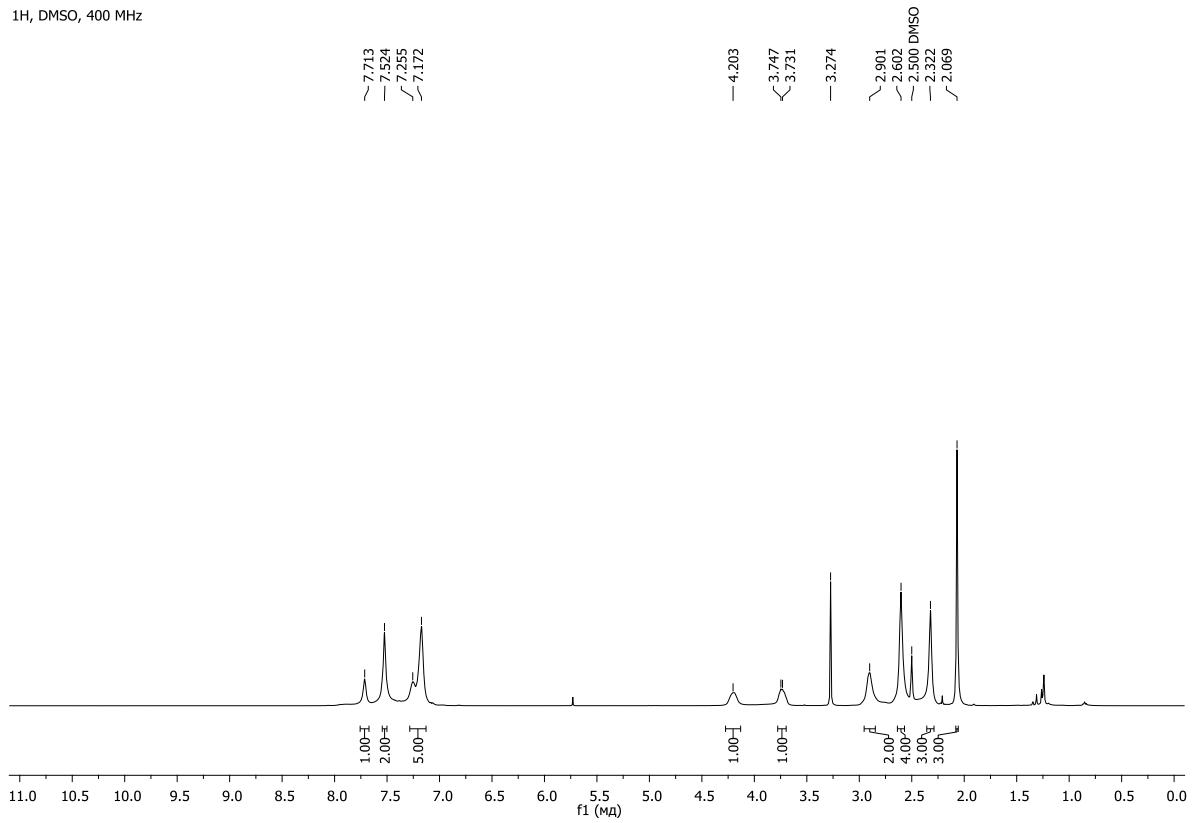


¹³C, CDCl₃, 100 MHz

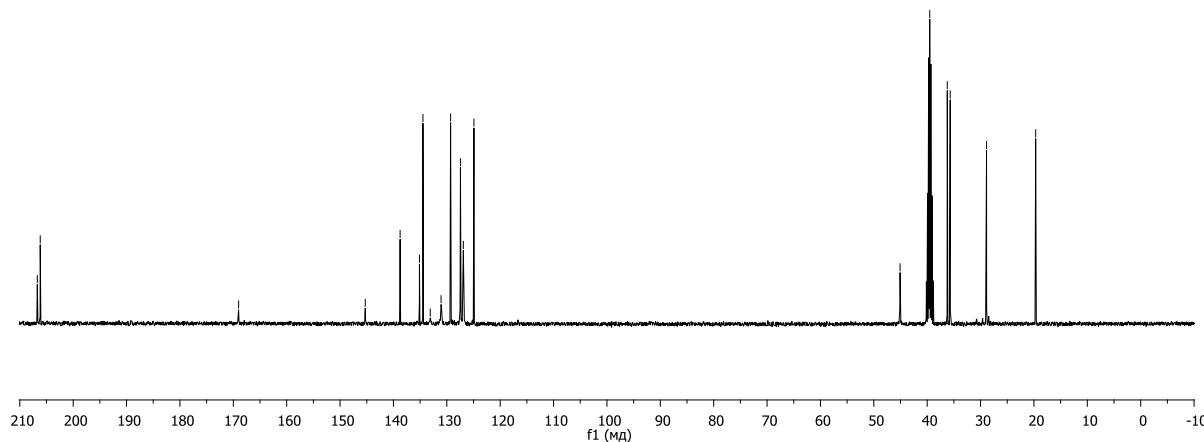
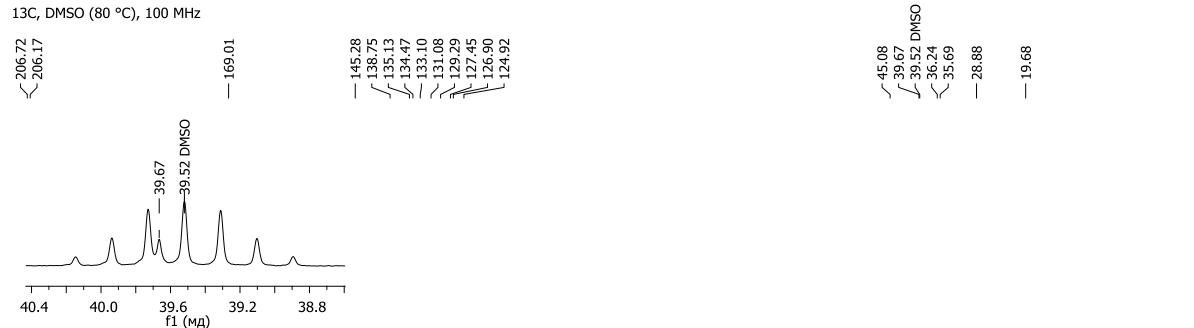


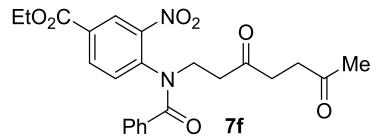


¹H, DMSO, 400 MHz

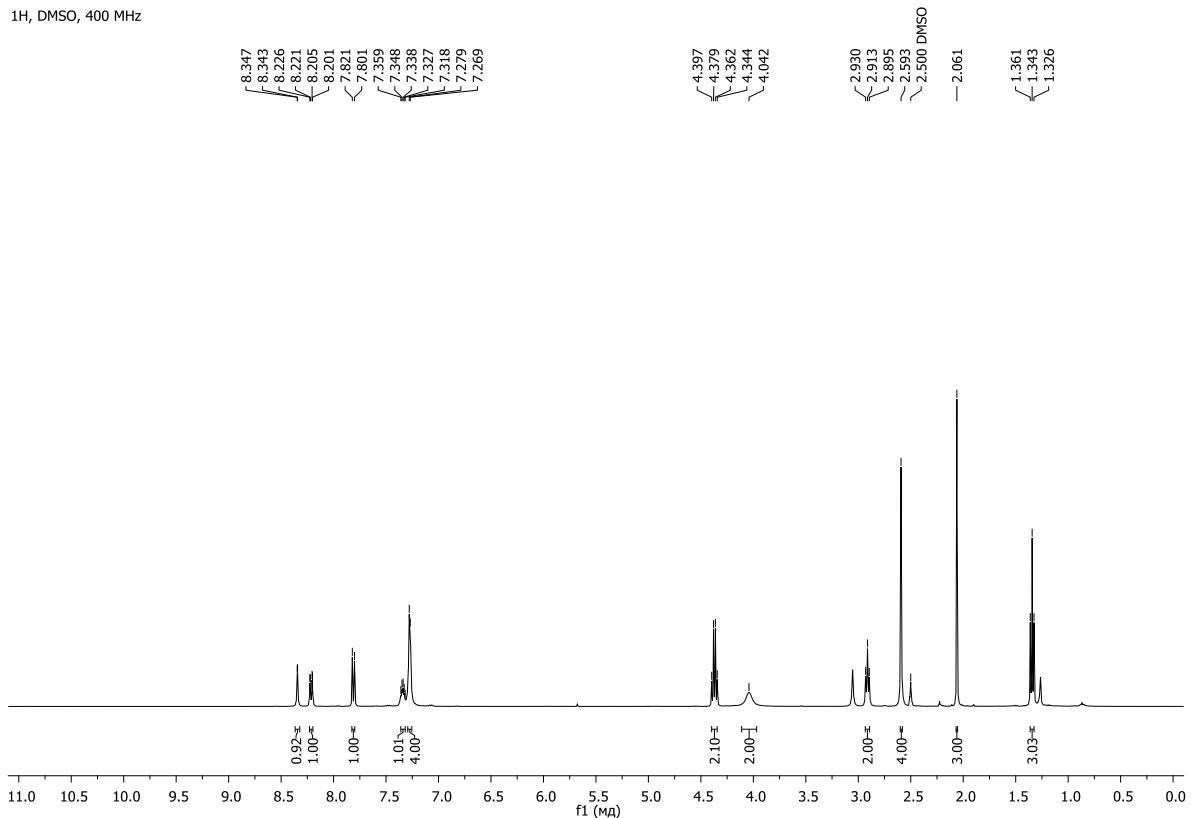


¹³C, DMSO (80 °C), 100 MHz

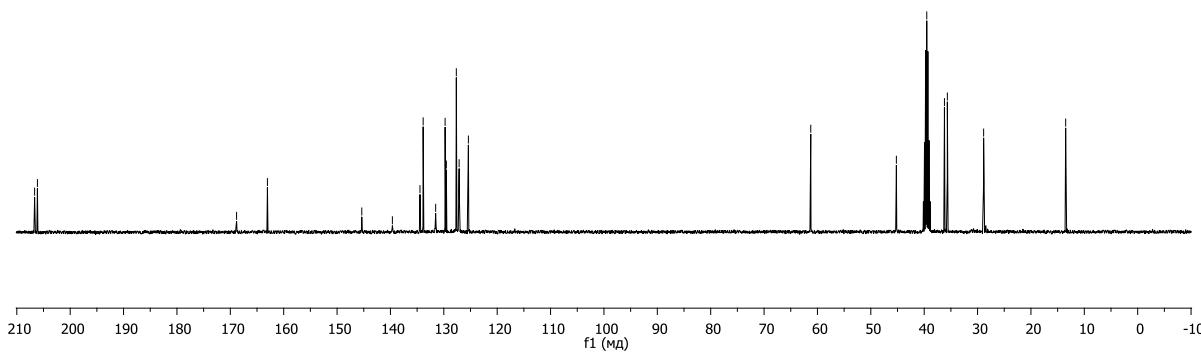
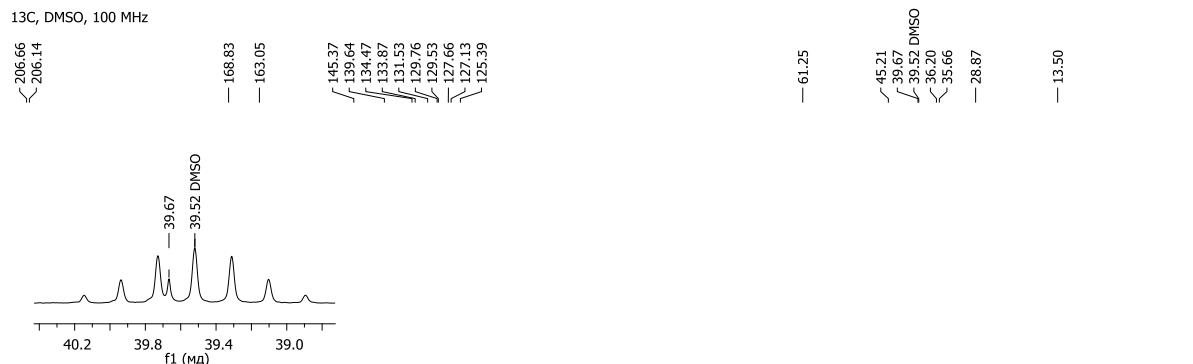


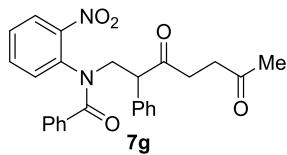


¹H, DMSO, 400 MHz

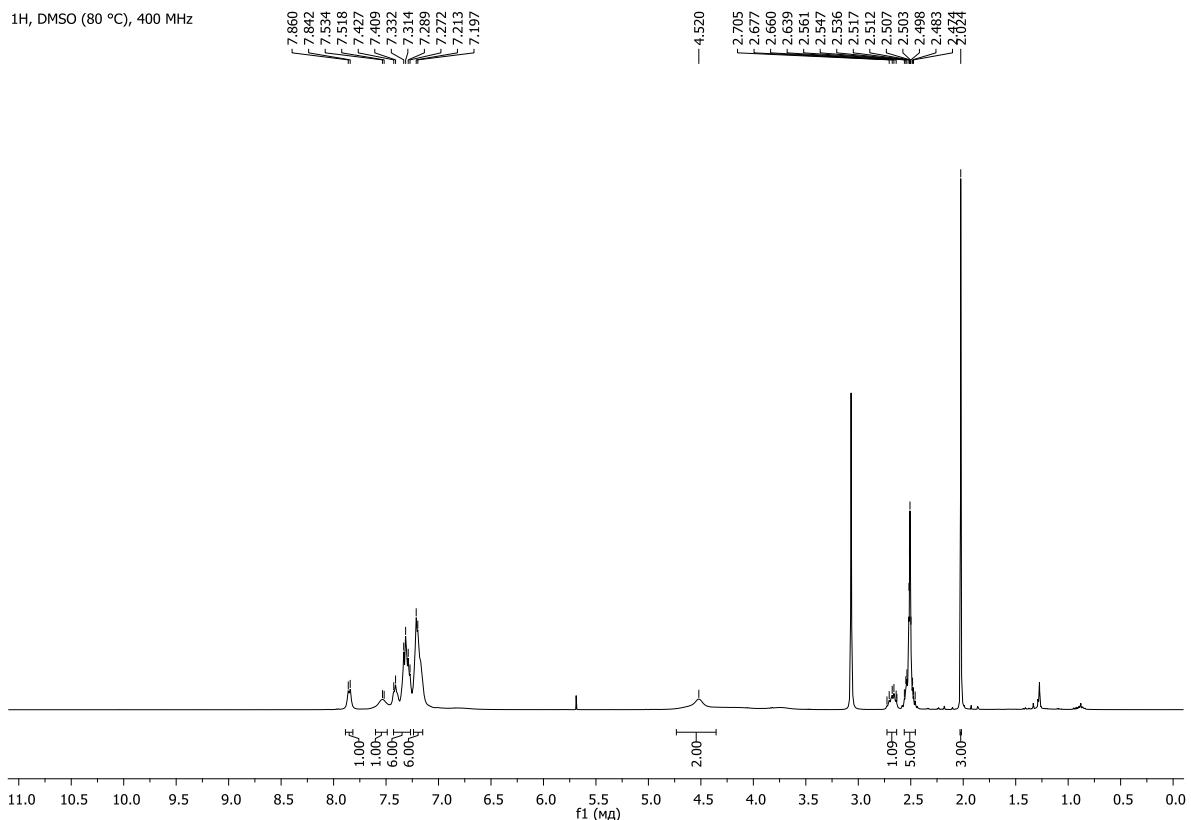


¹³C, DMSO, 100 MHz

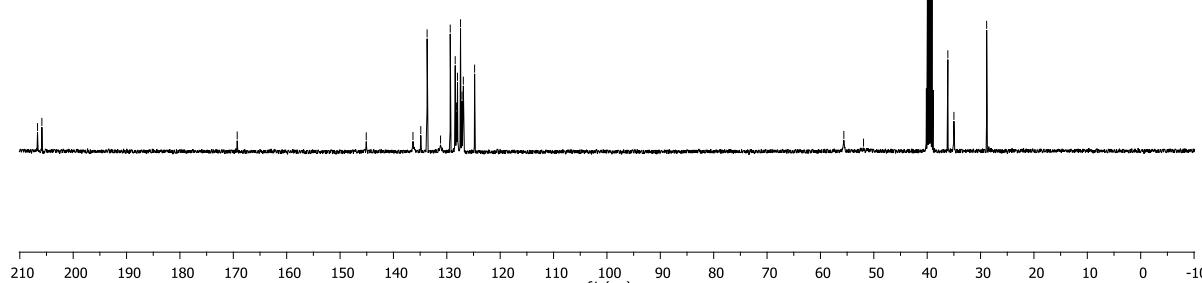
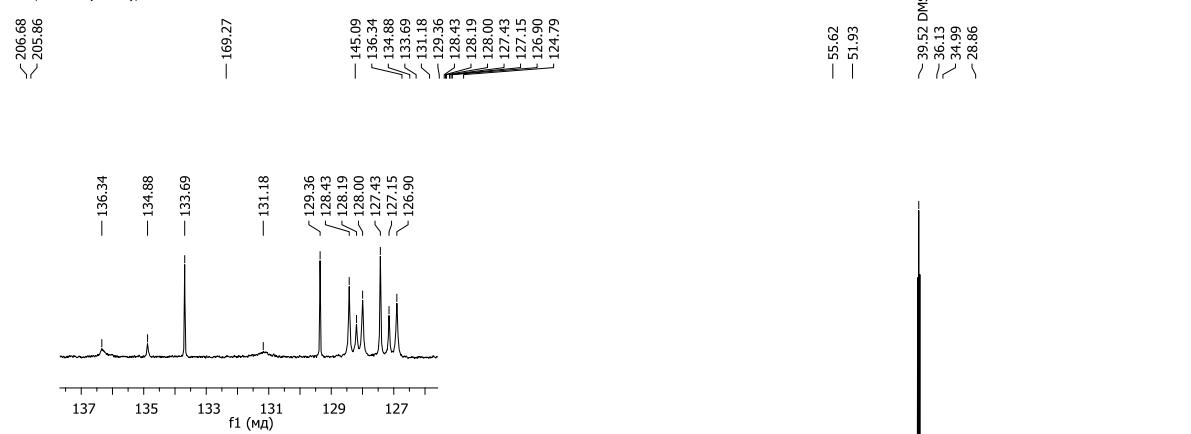


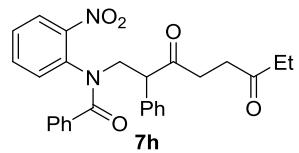


¹H, DMSO (80 °C), 400 MHz

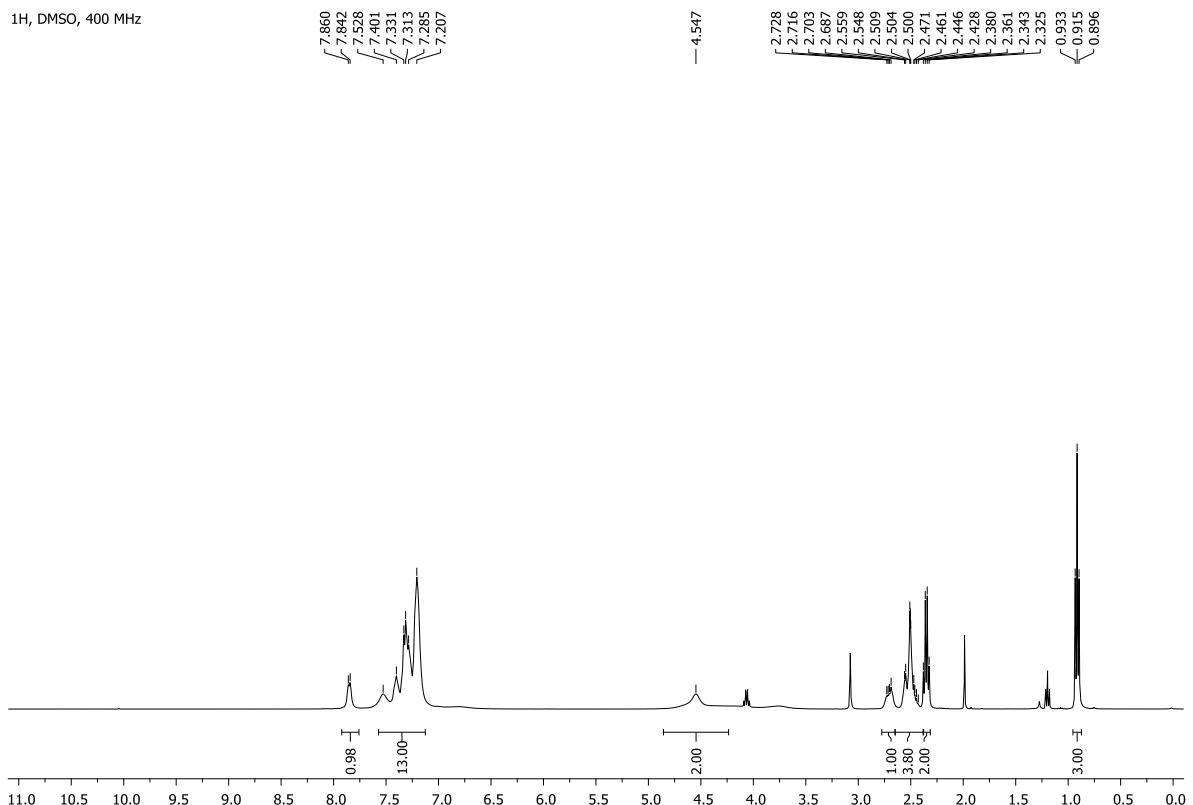


¹³C, DMSO (80 °C), 100 MHz

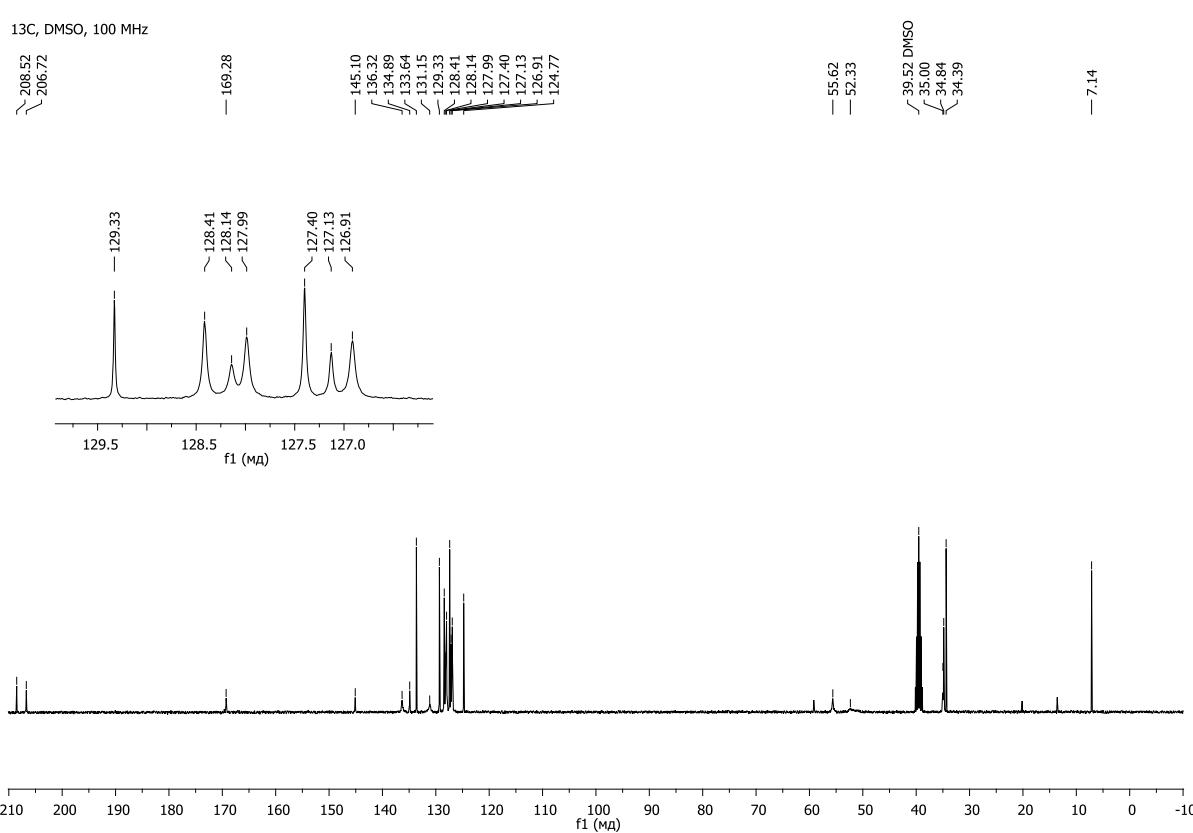


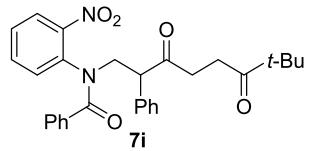


¹H, DMSO, 400 MHz

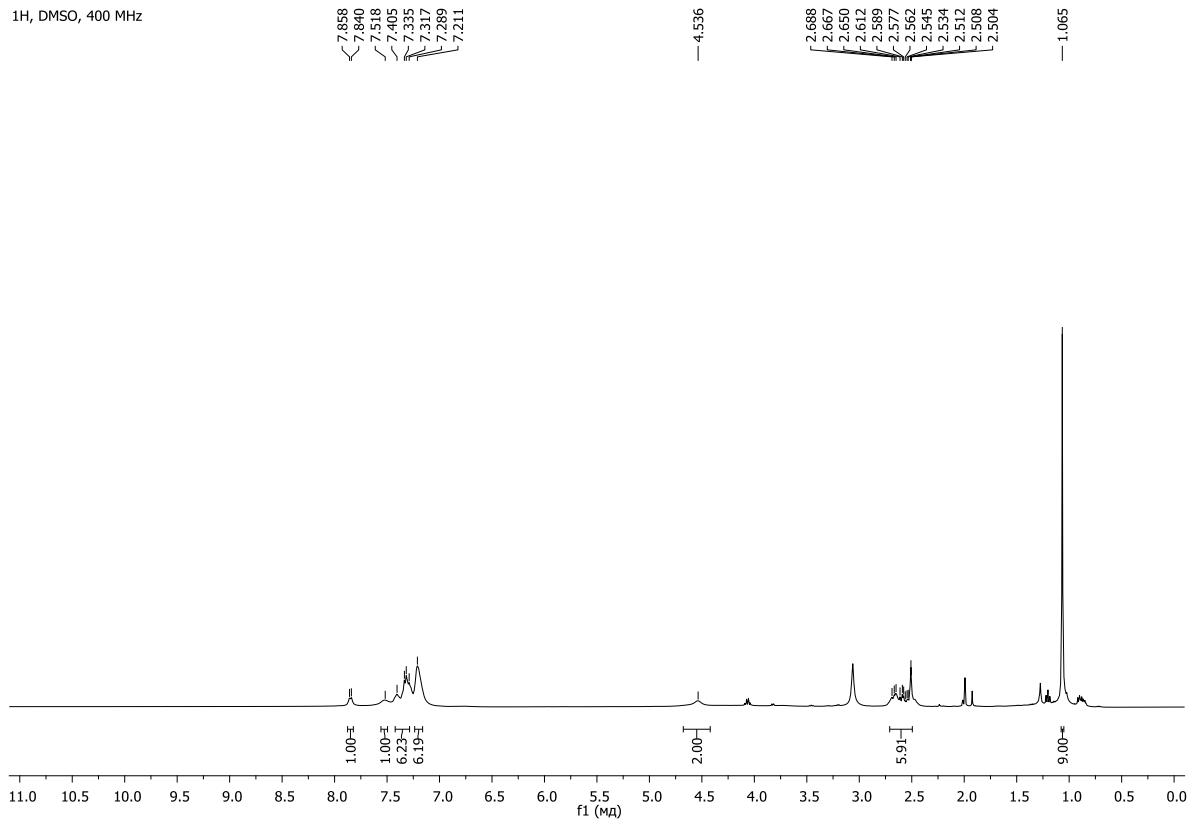


¹³C, DMSO, 100 MHz

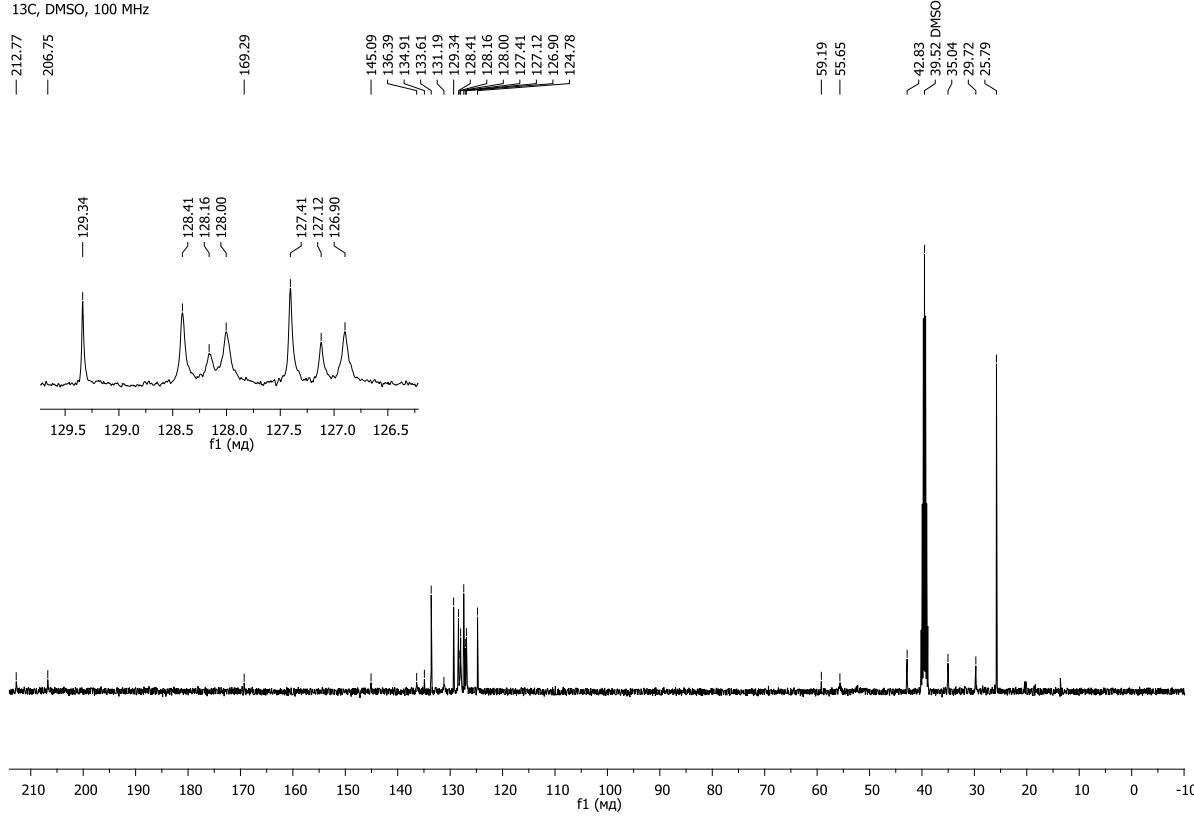


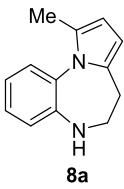


^1H , DMSO, 400 MHz

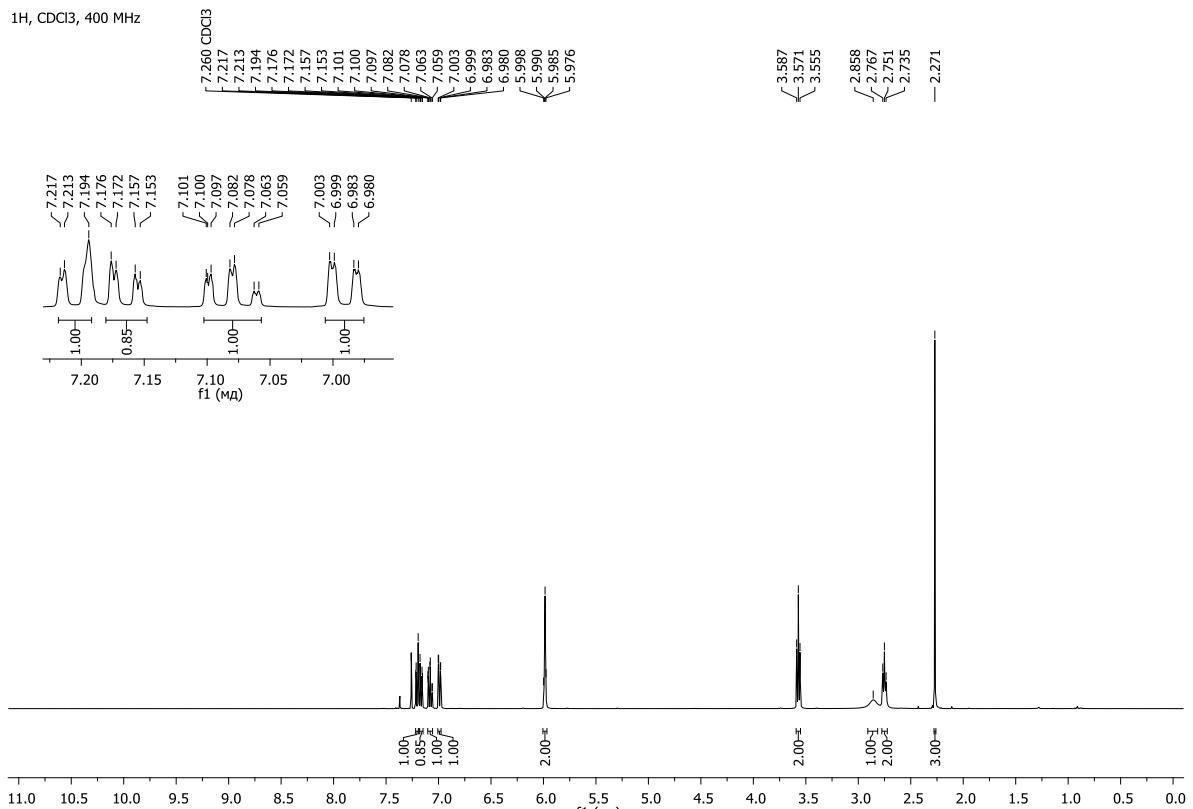


^{13}C , DMSO, 100 MHz

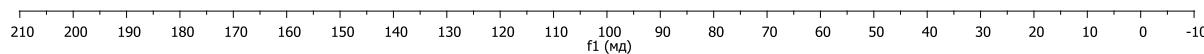
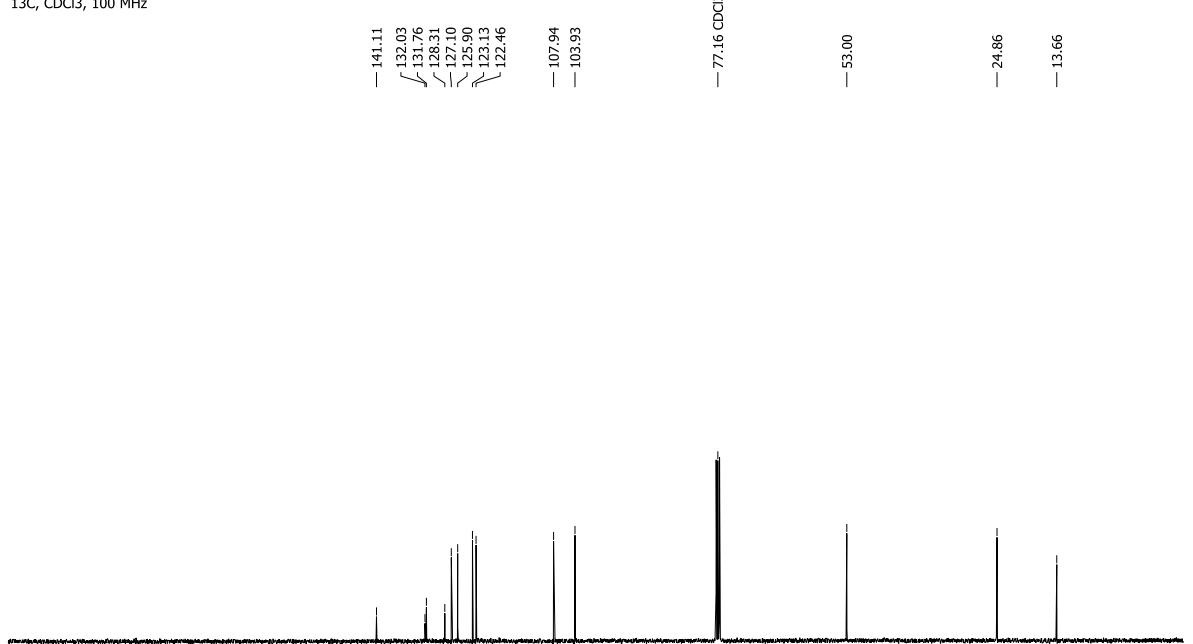


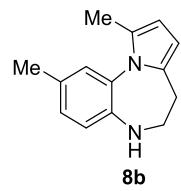


1H, CDCl₃, 400 MHz

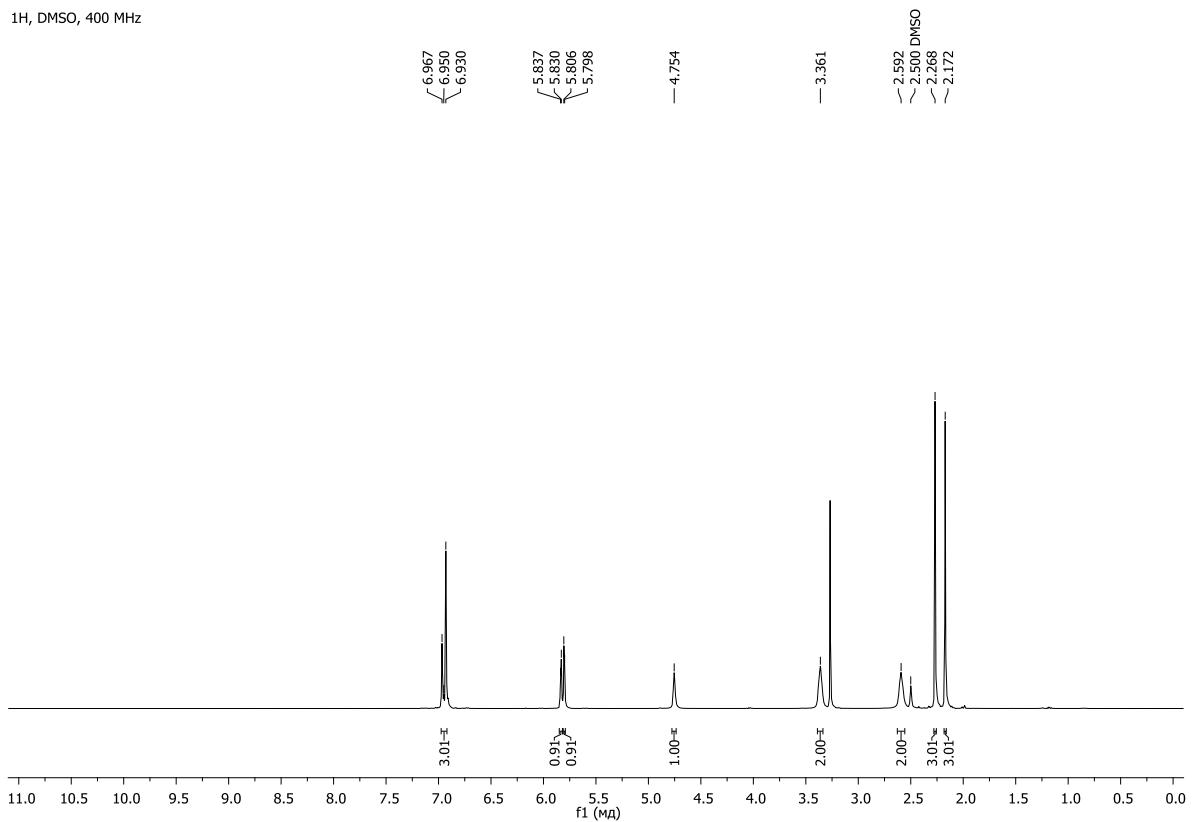


13C, CDCl₃, 100 MHz

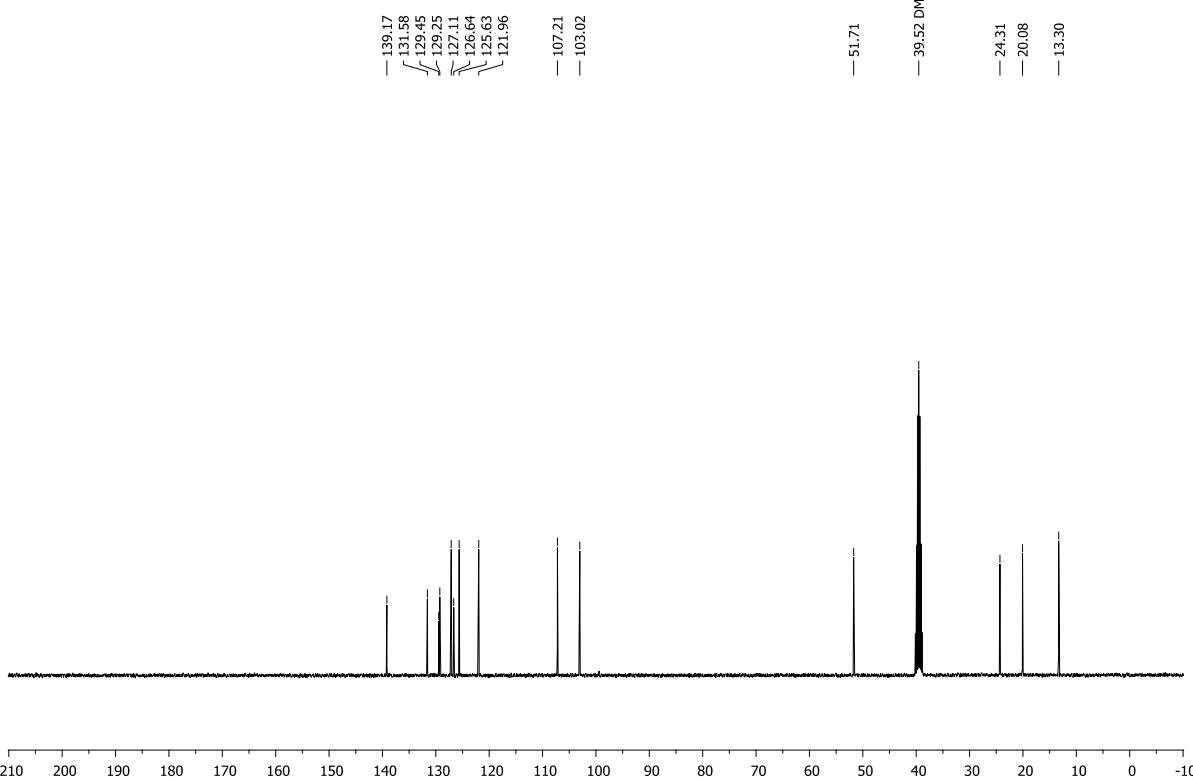


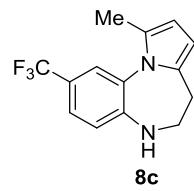


1H, DMSO, 400 MHz

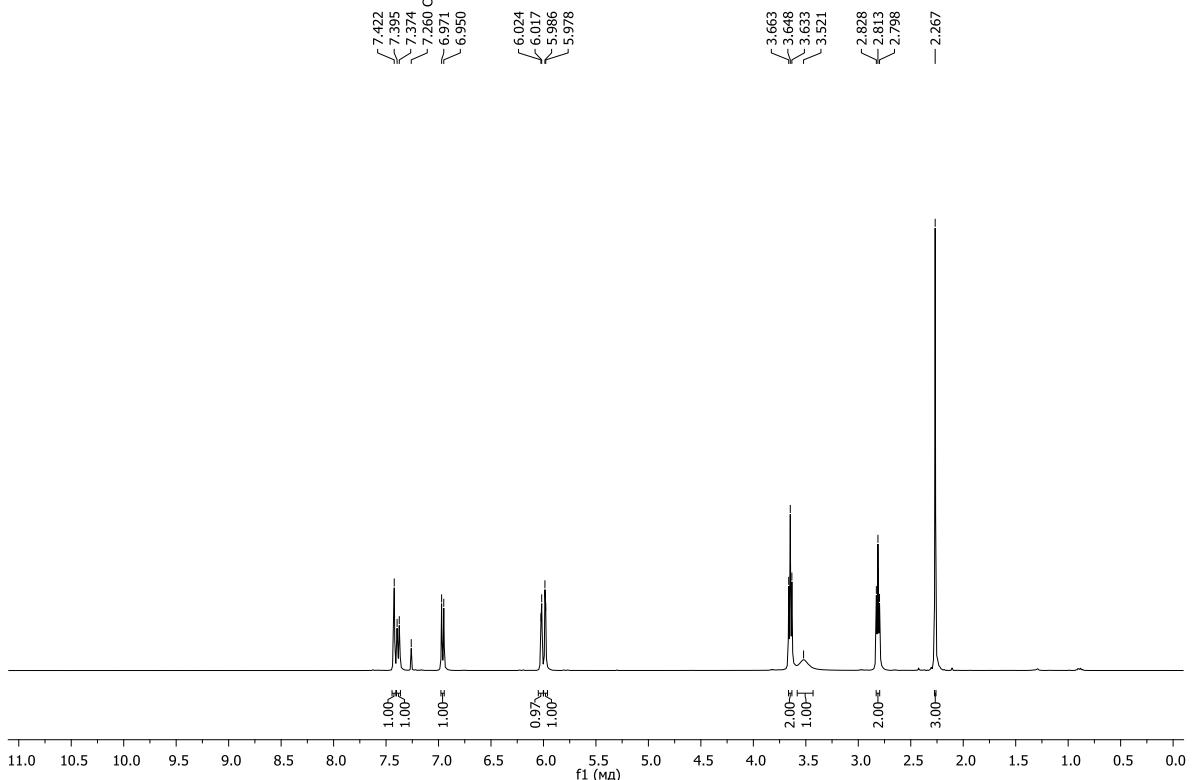


13C, DMSO, 100 MHz

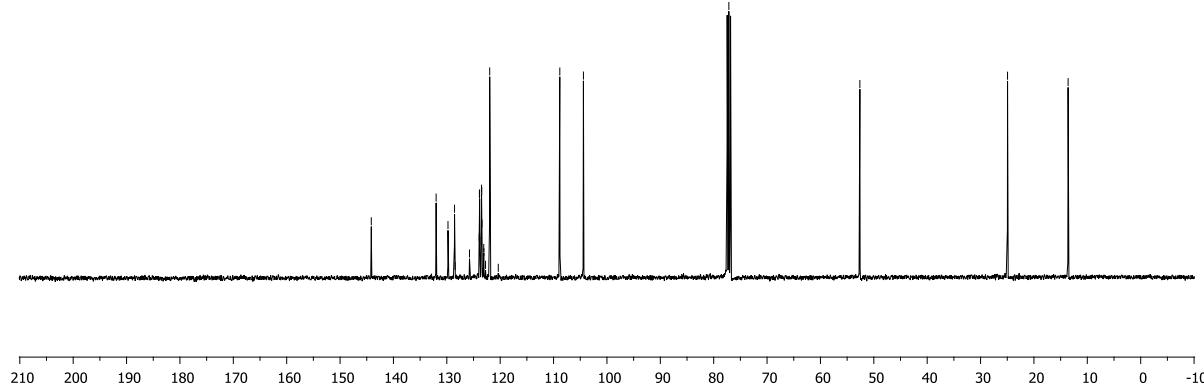
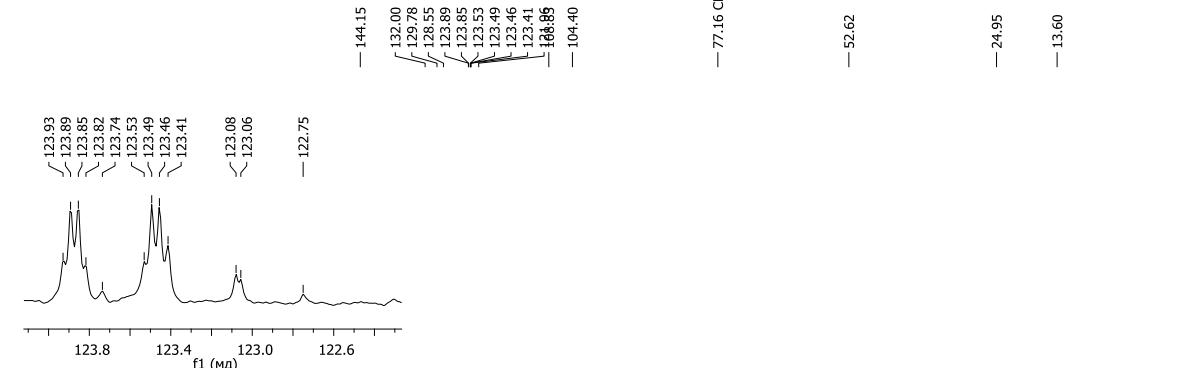


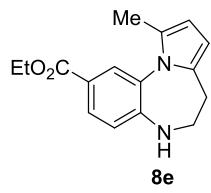


1H, CDCl₃, 400 MHz

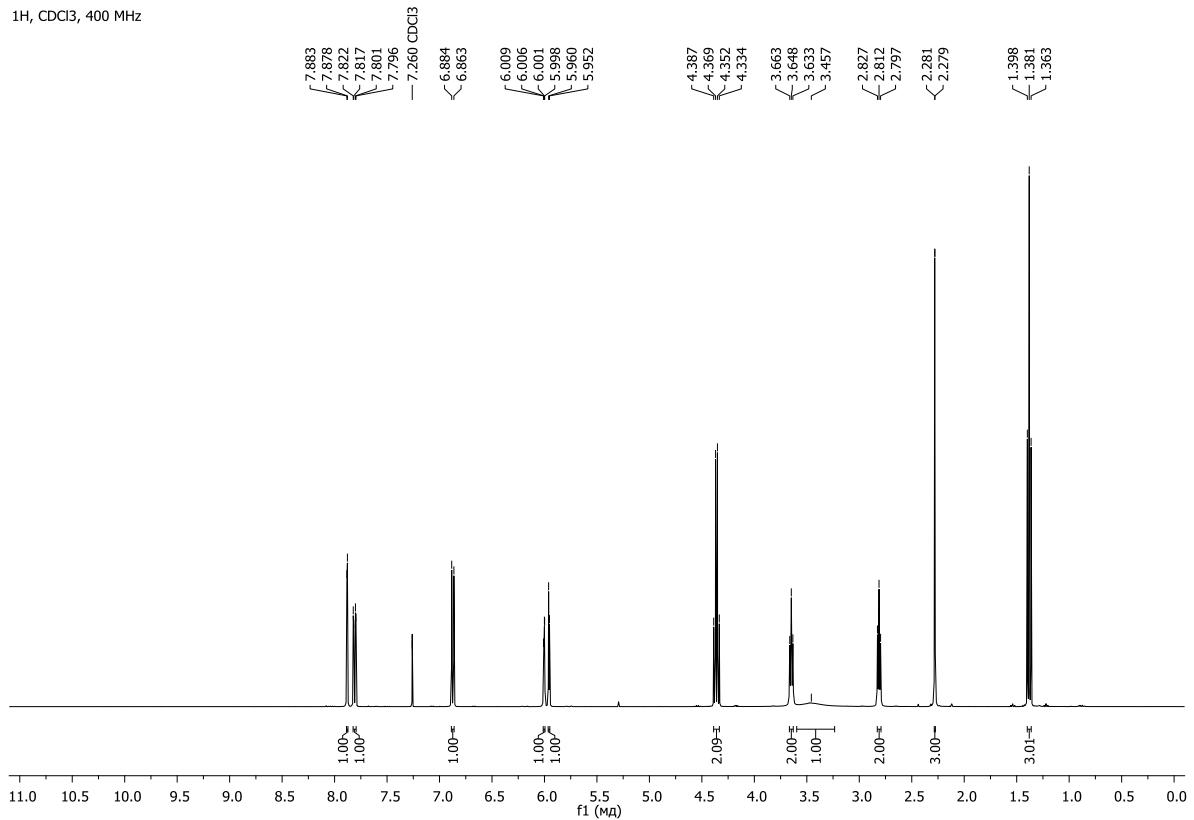


13C, CDCl₃, 100 MHz

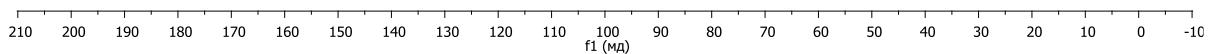
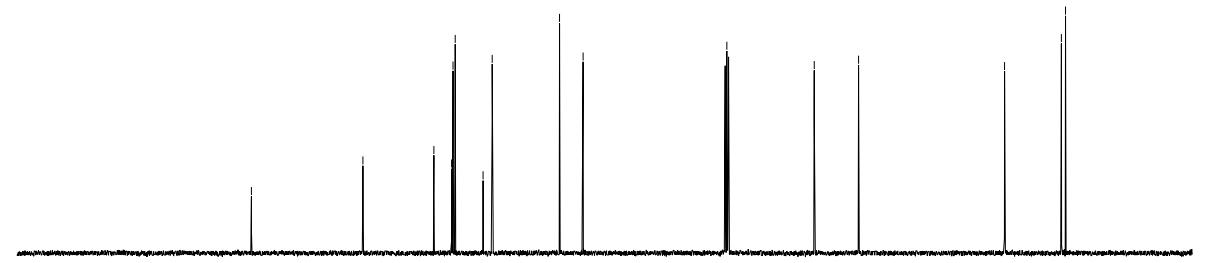
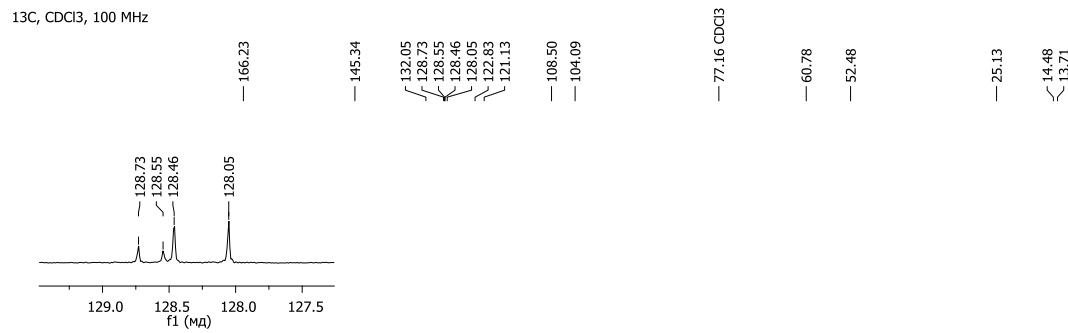


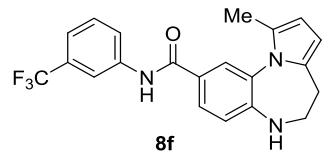


¹H, CDCl₃, 400 MHz

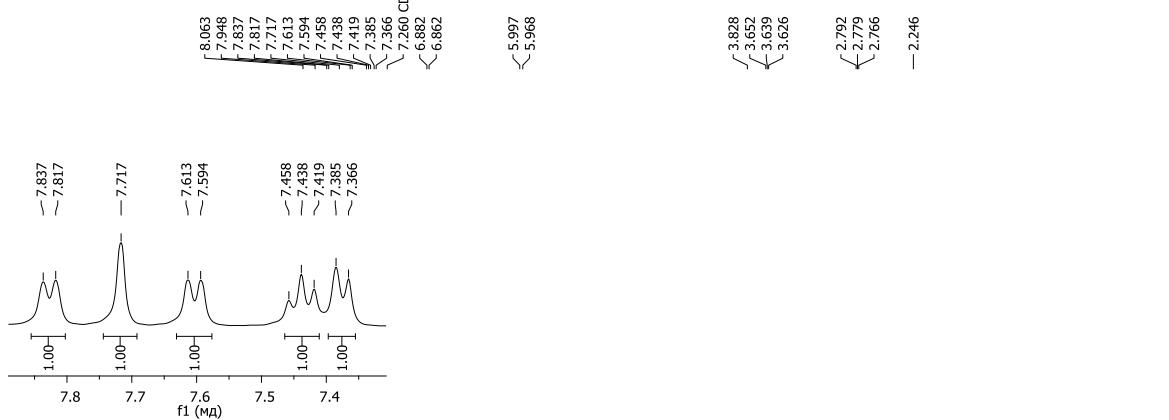


¹³C, CDCl₃, 100 MHz

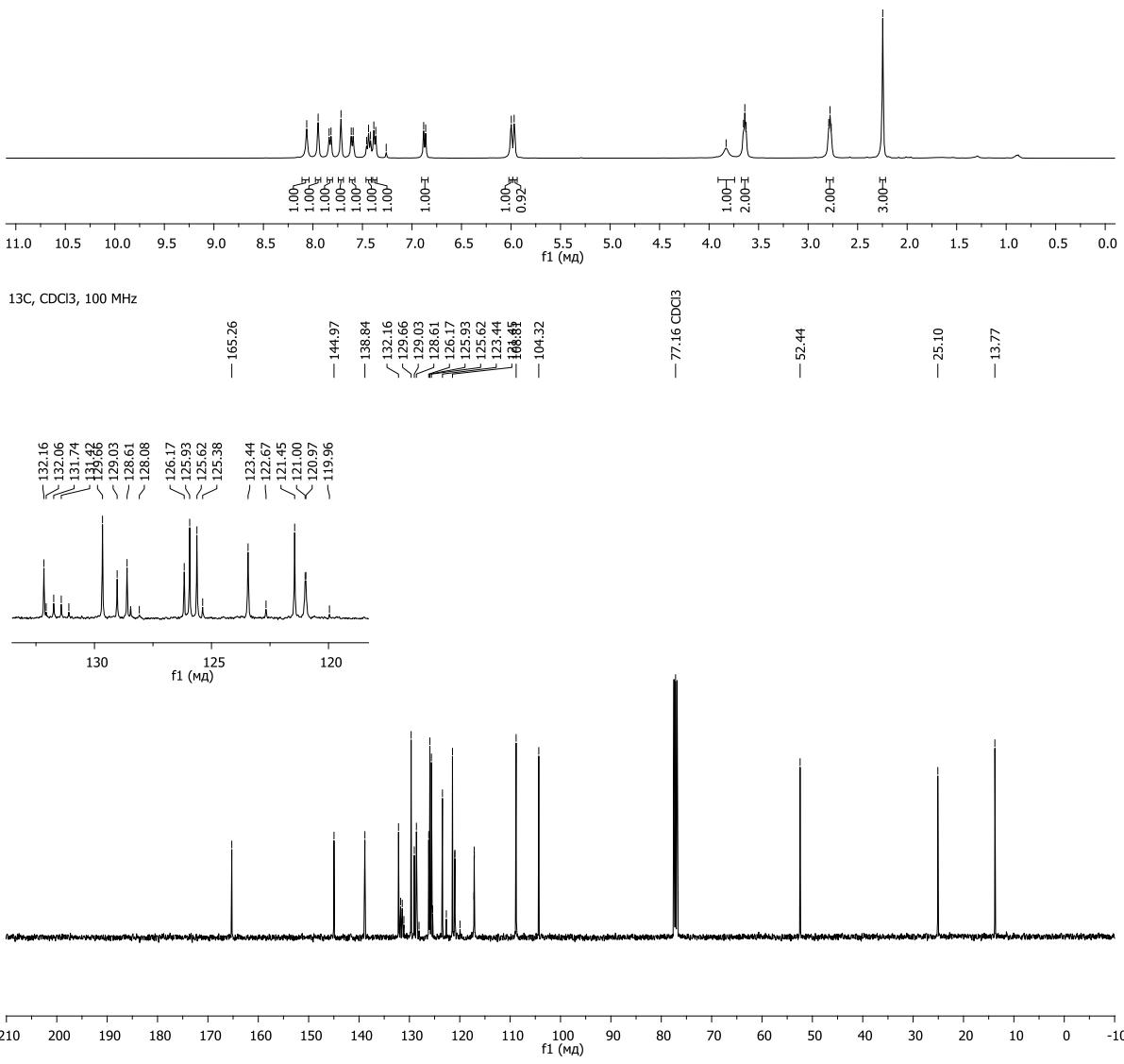


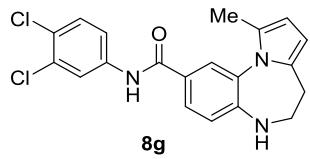


¹H, CDCl₃, 400 MHz



¹³C, CDCl₃, 100 MHz

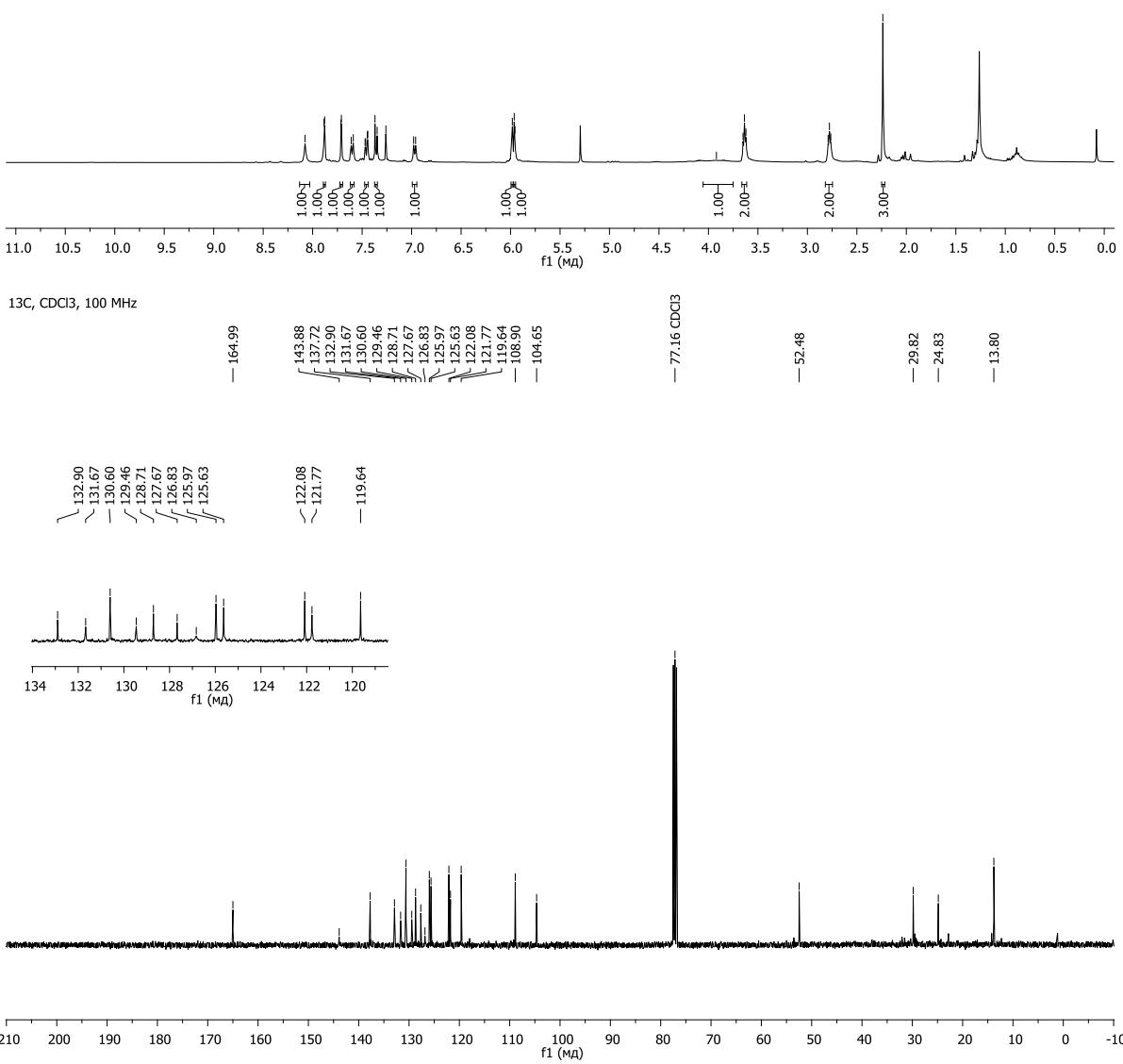


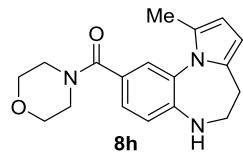


¹H, CDCl₃, 400 MHz

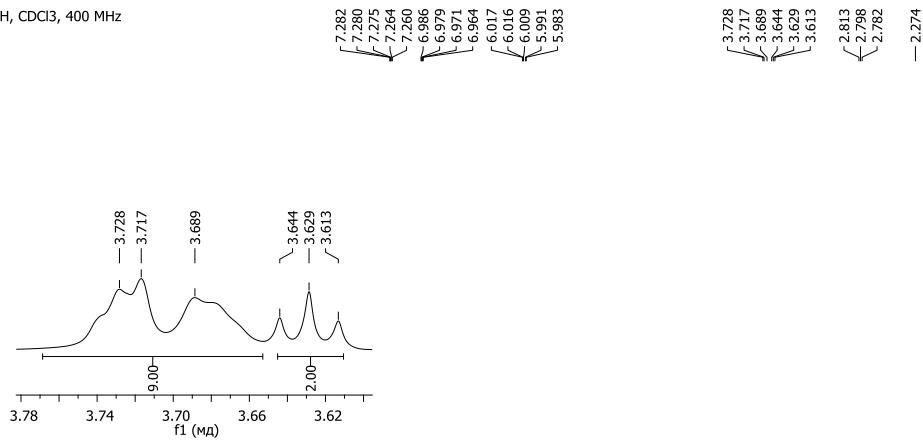


¹³C, CDCl₃, 100 MHz

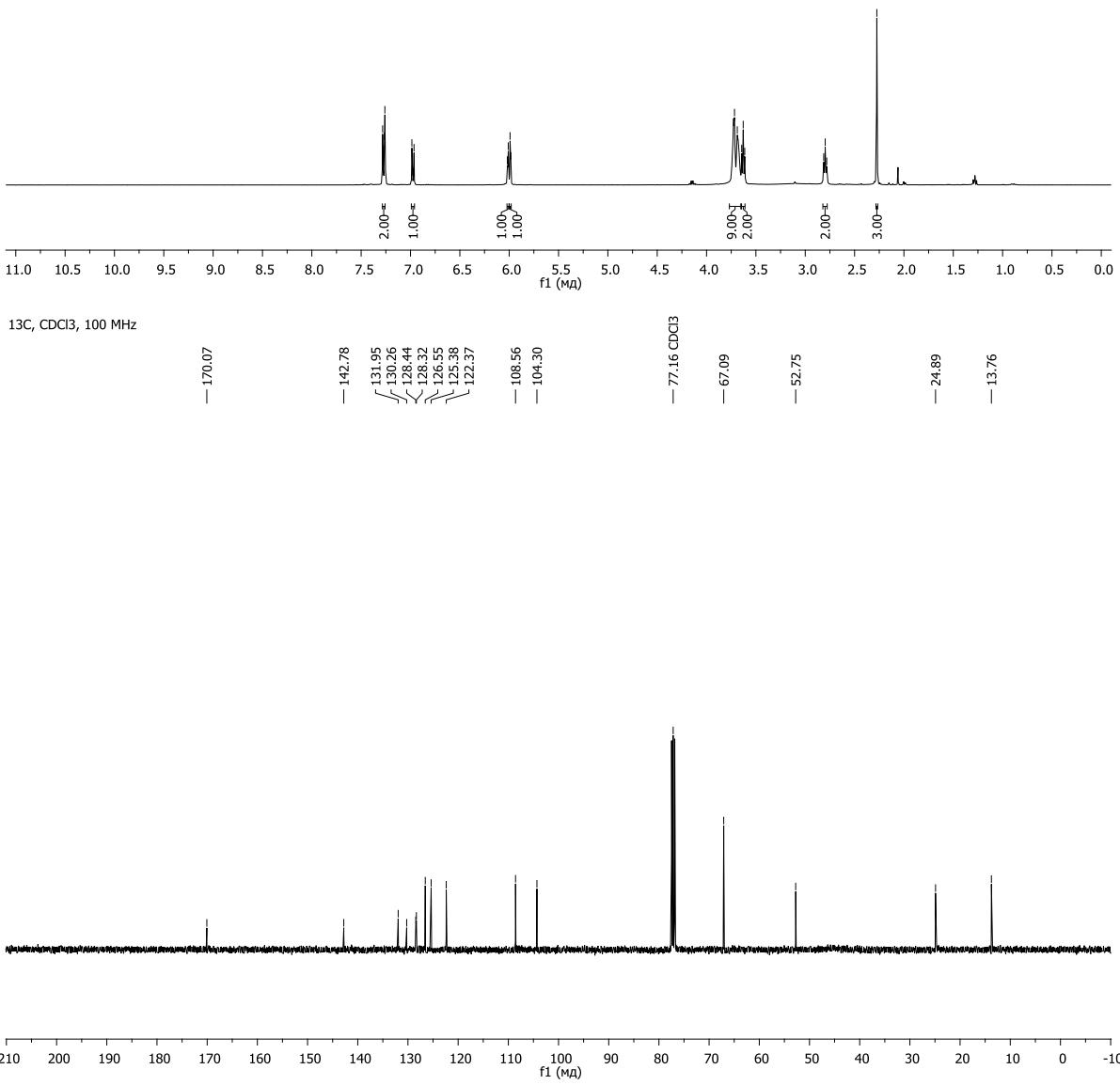


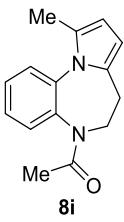


¹H, CDCl₃, 400 MHz

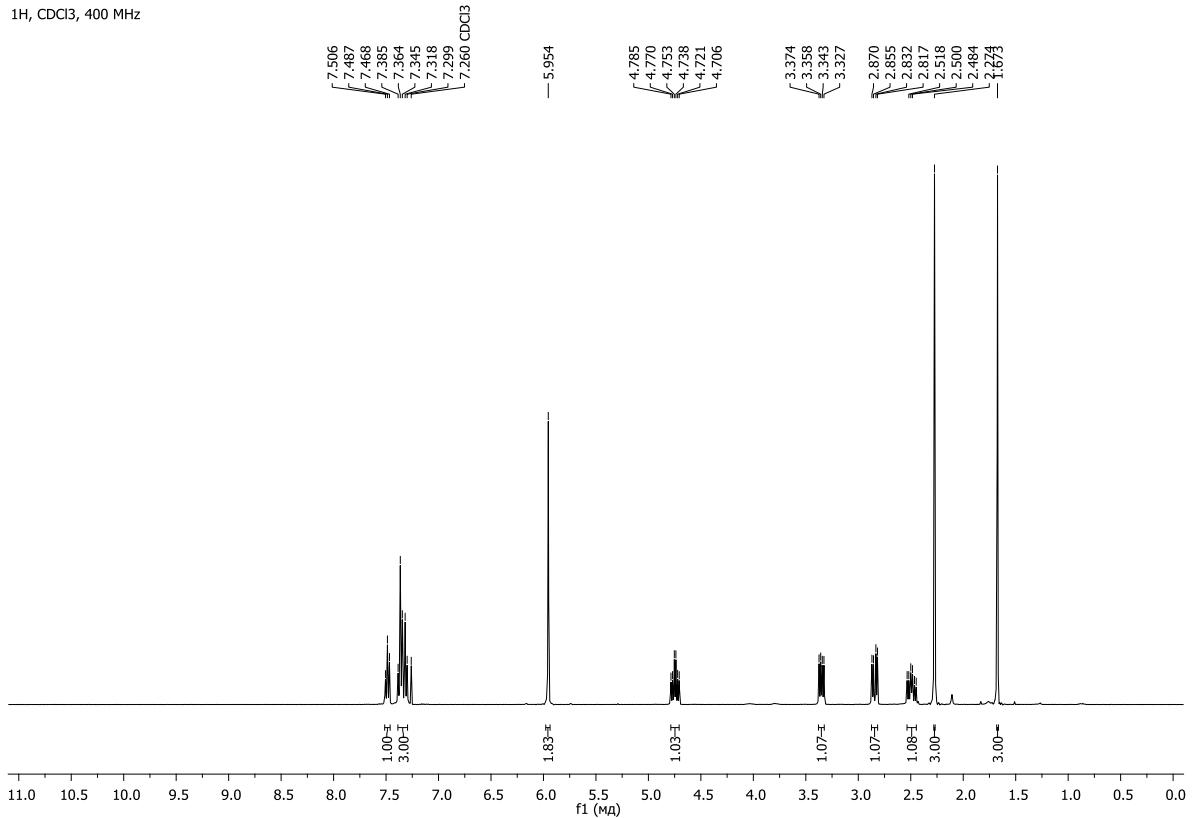


¹³C, CDCl₃, 100 MHz

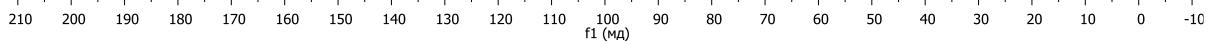
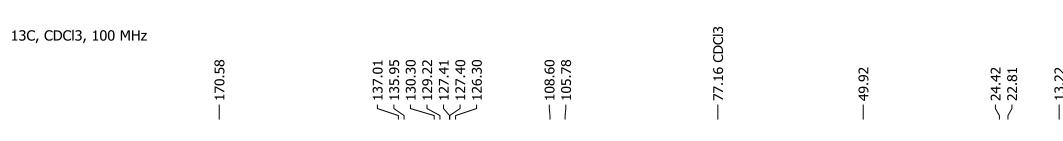


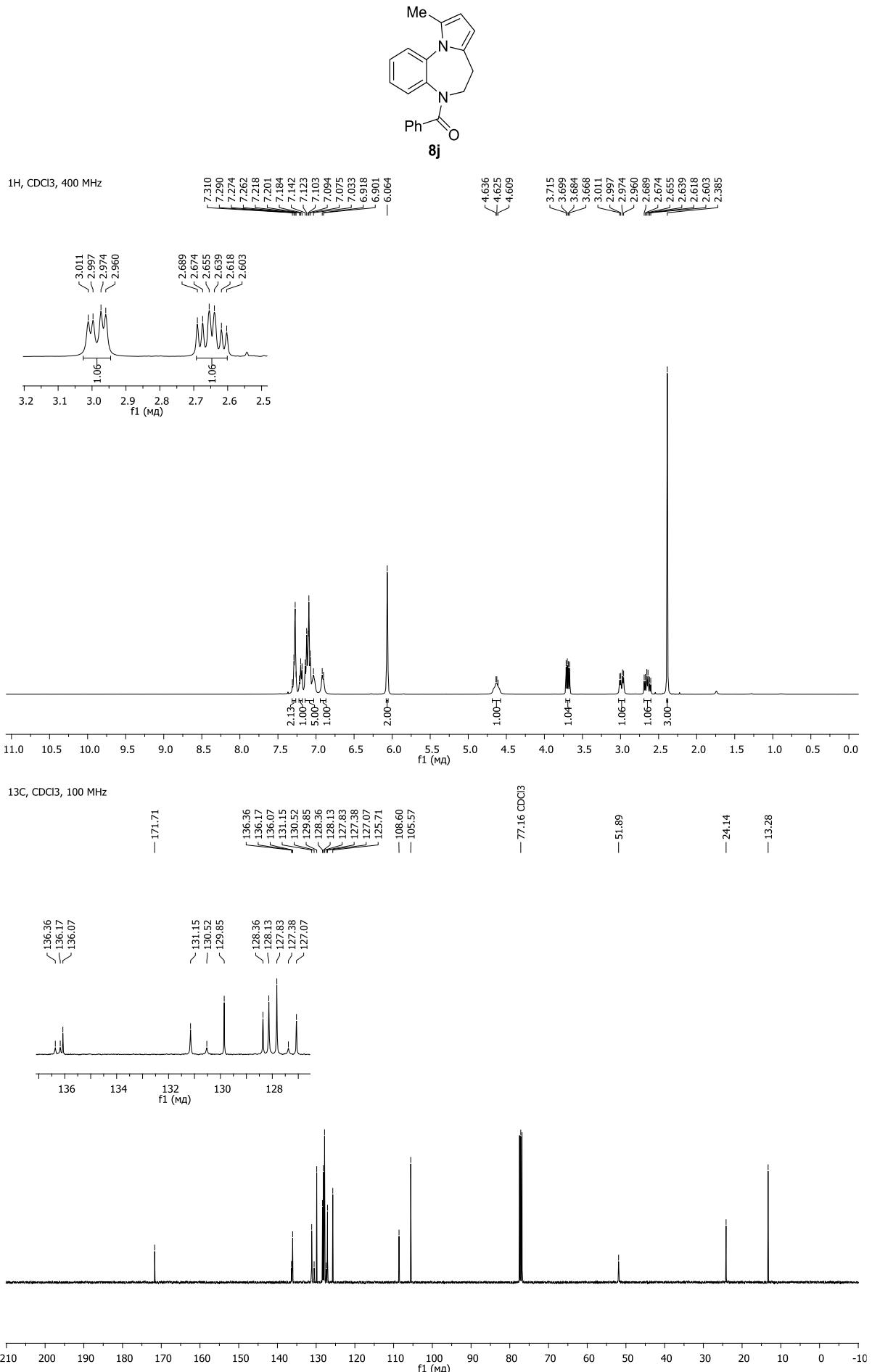


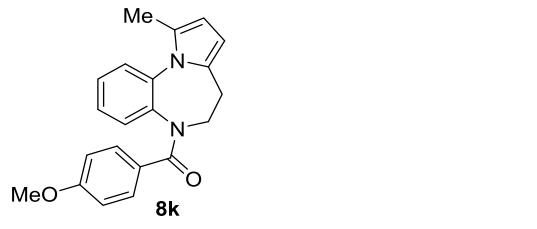
¹H, CDCl₃, 400 MHz



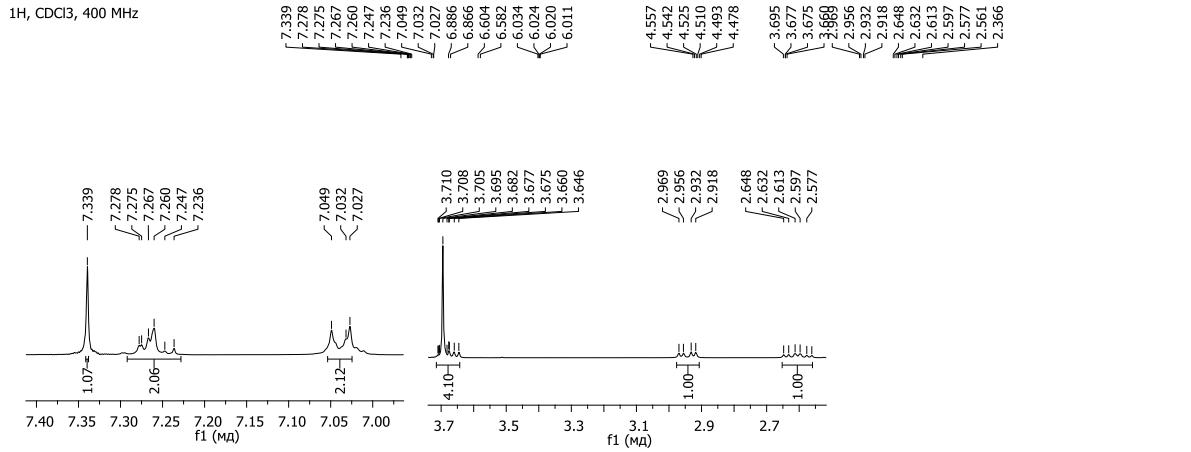
¹³C, CDCl₃, 100 MHz



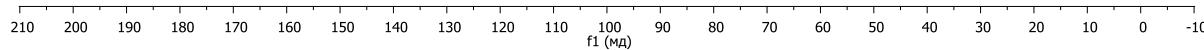
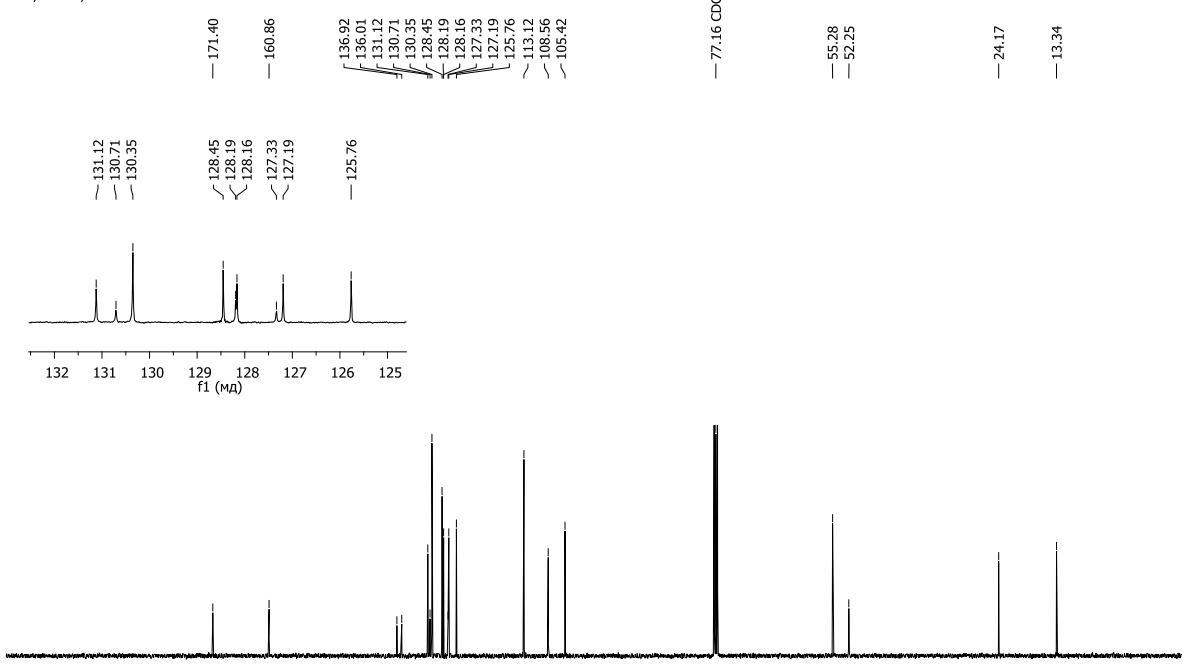


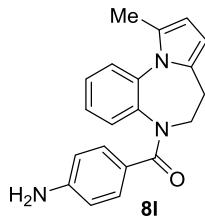


¹H, CDCl₃, 400 MHz

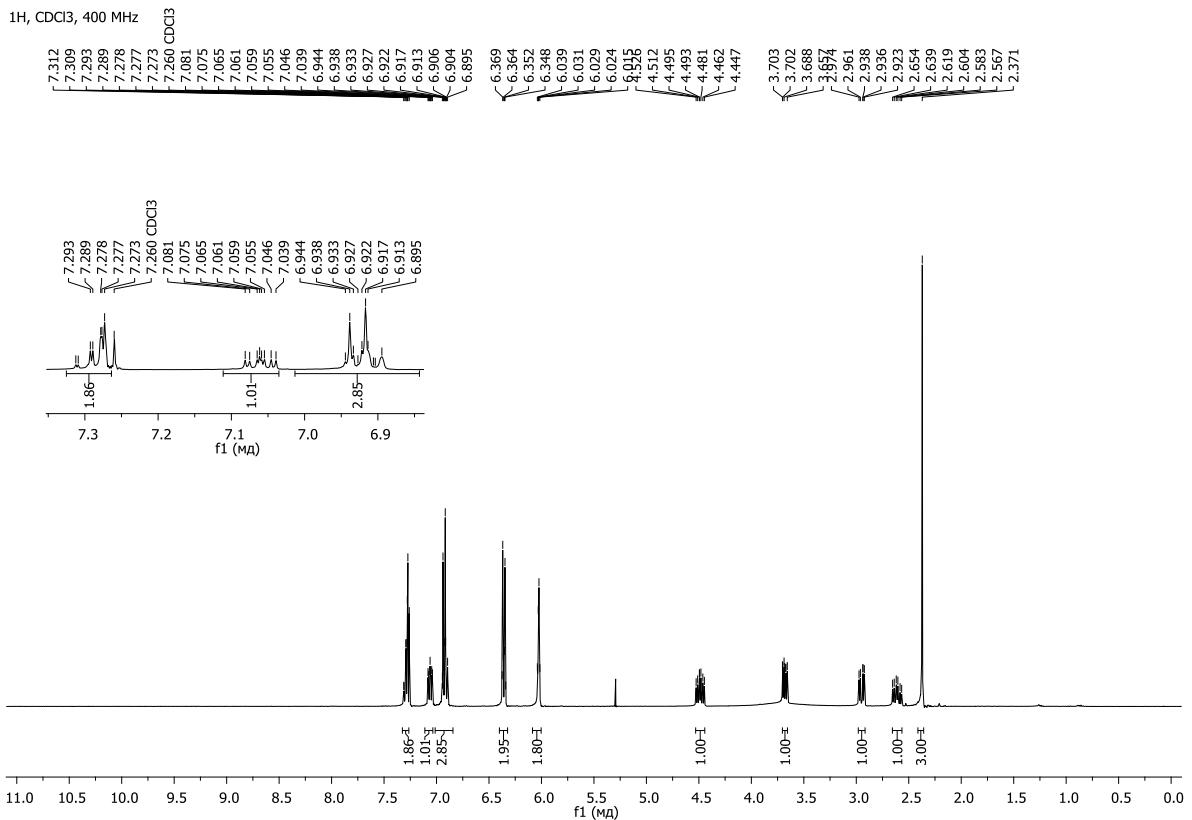


¹³C, CDCl₃, 100 MHz

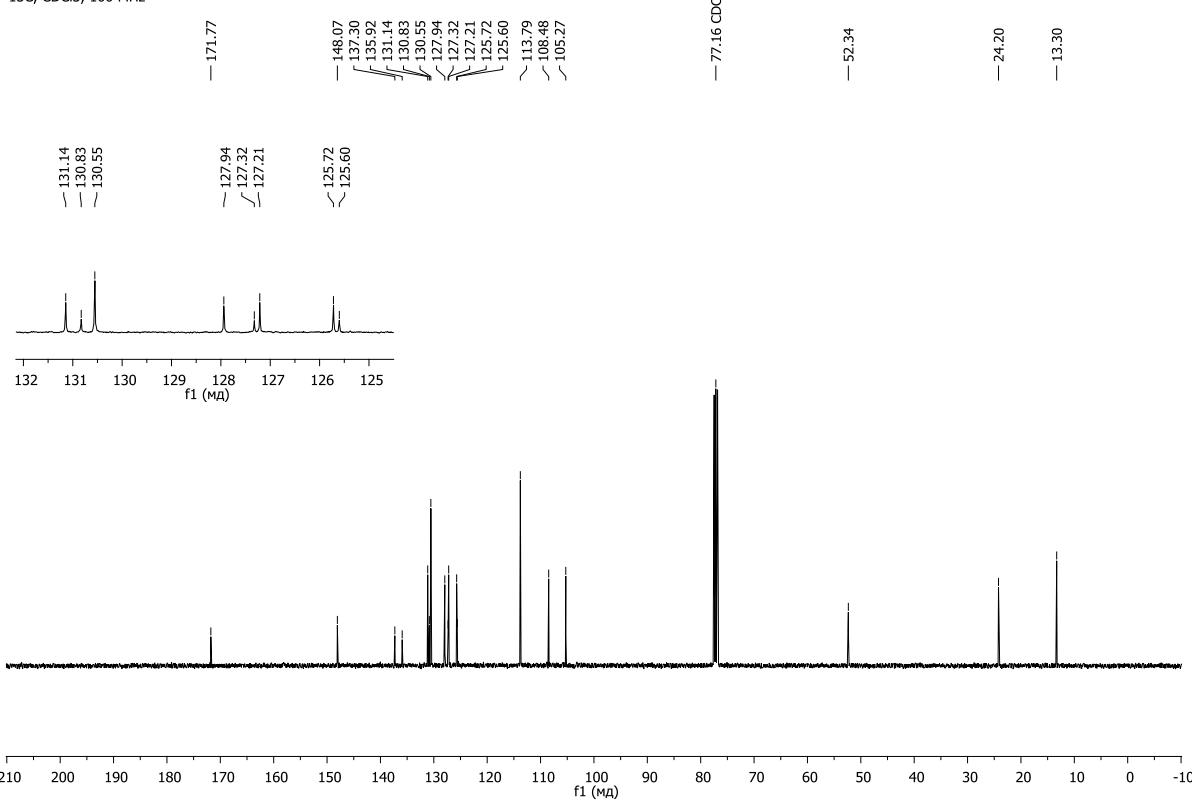


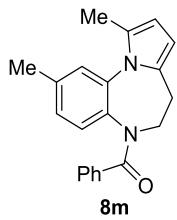


¹H, CDCl₃, 400 MHz

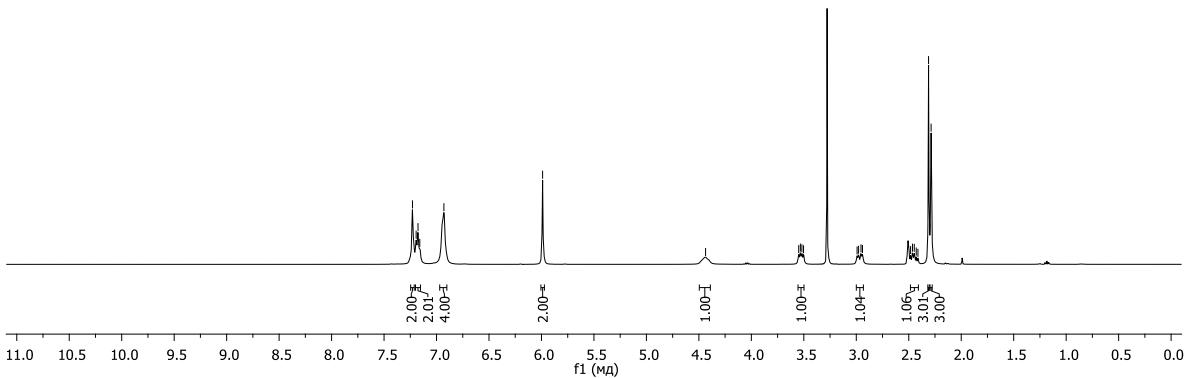
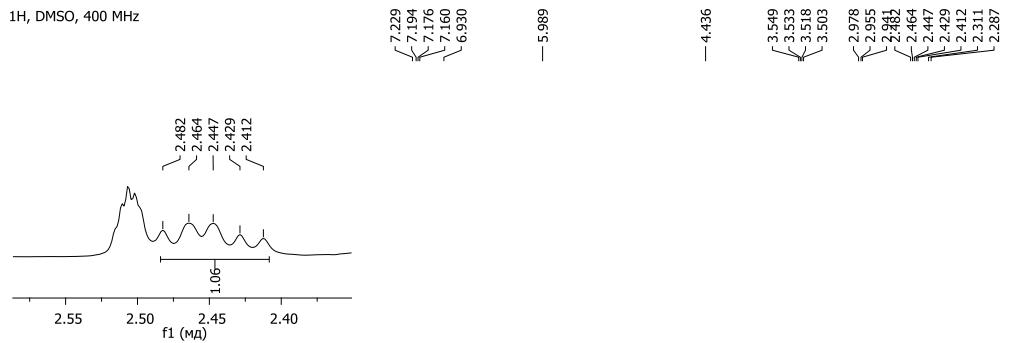


¹³C, CDCl₃, 100 MHz

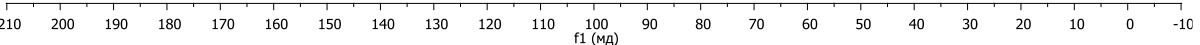
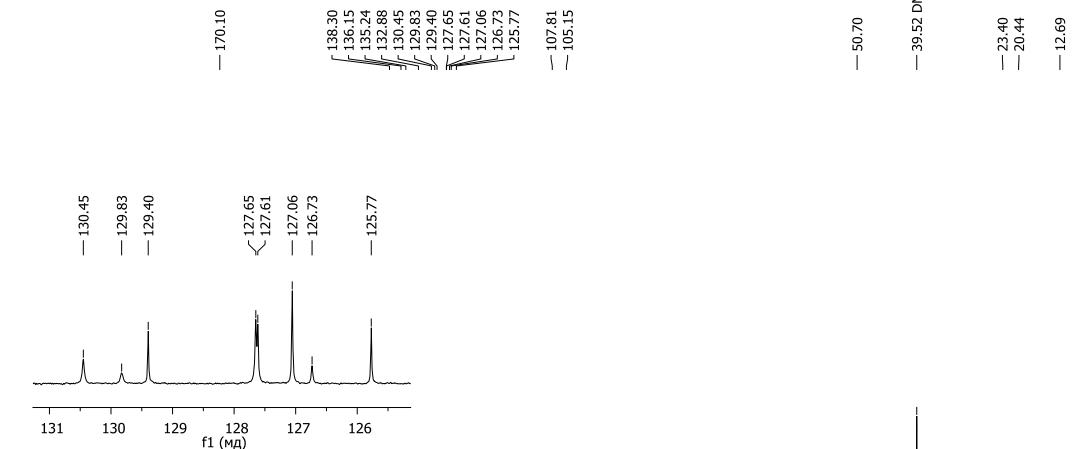


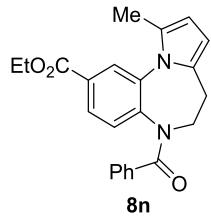


¹H, DMSO, 400 MHz

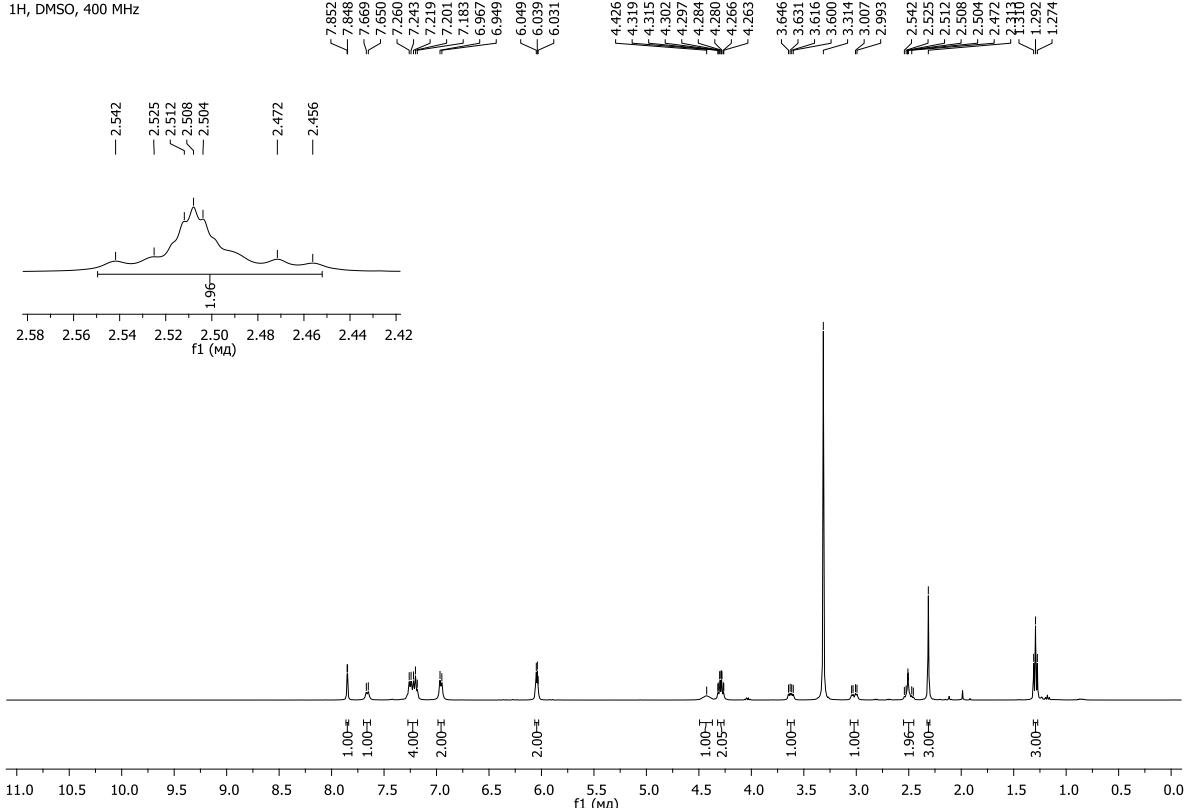


¹³C, DMSO, 100 MHz

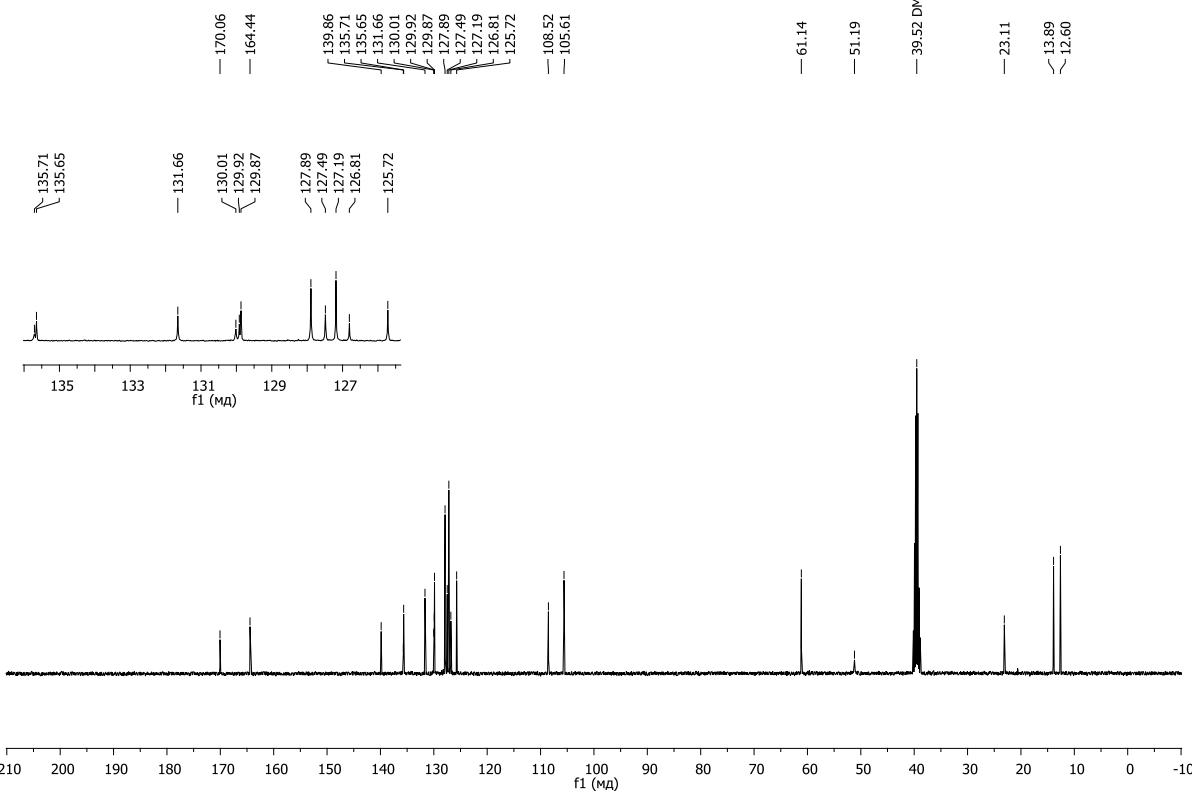


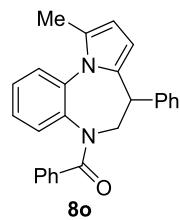


^1H , DMSO, 400 MHz

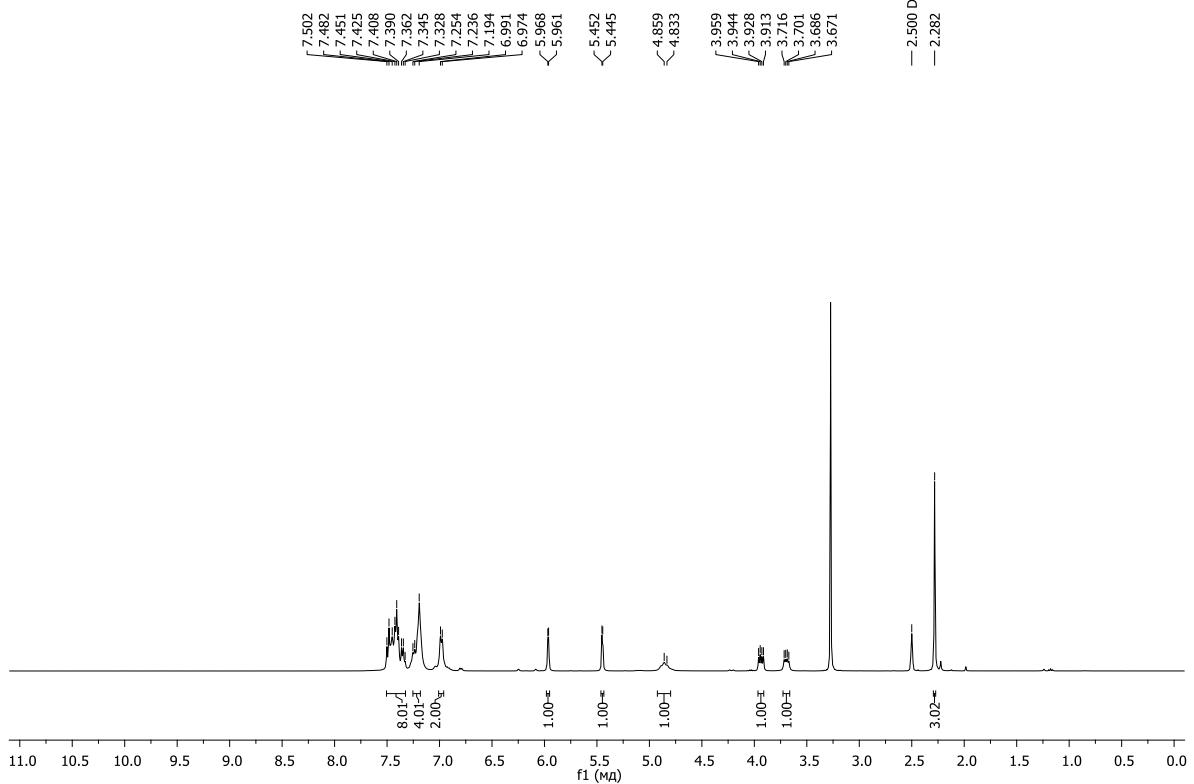


^{13}C , DMSO, 100 MHz

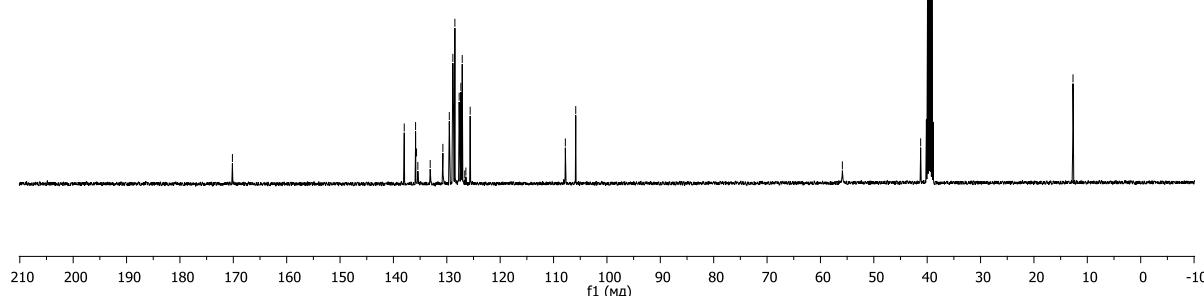
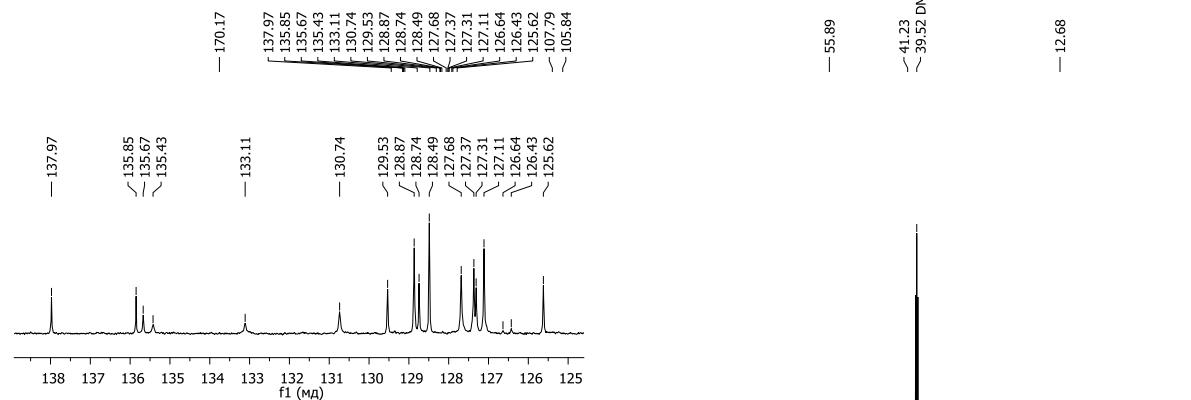


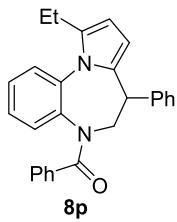


1H, DMSO, 400 MHz

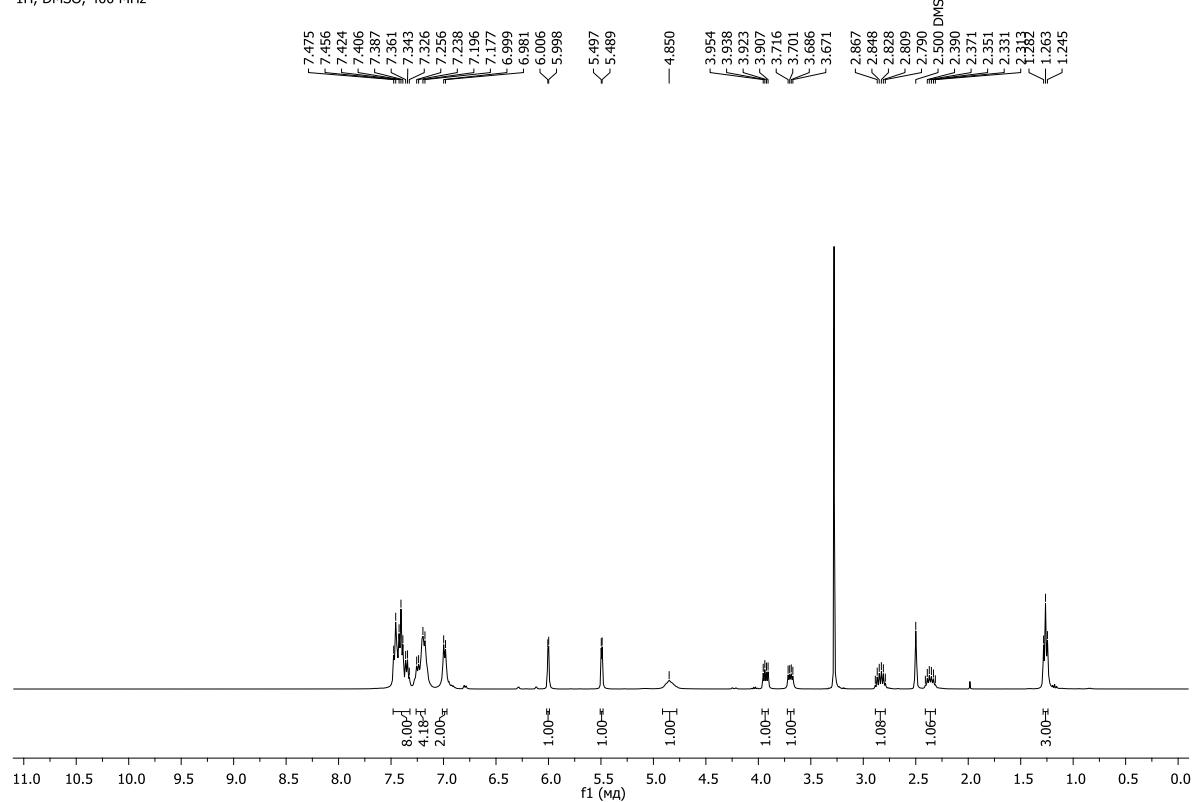


13C, DMSO, 100 MHz

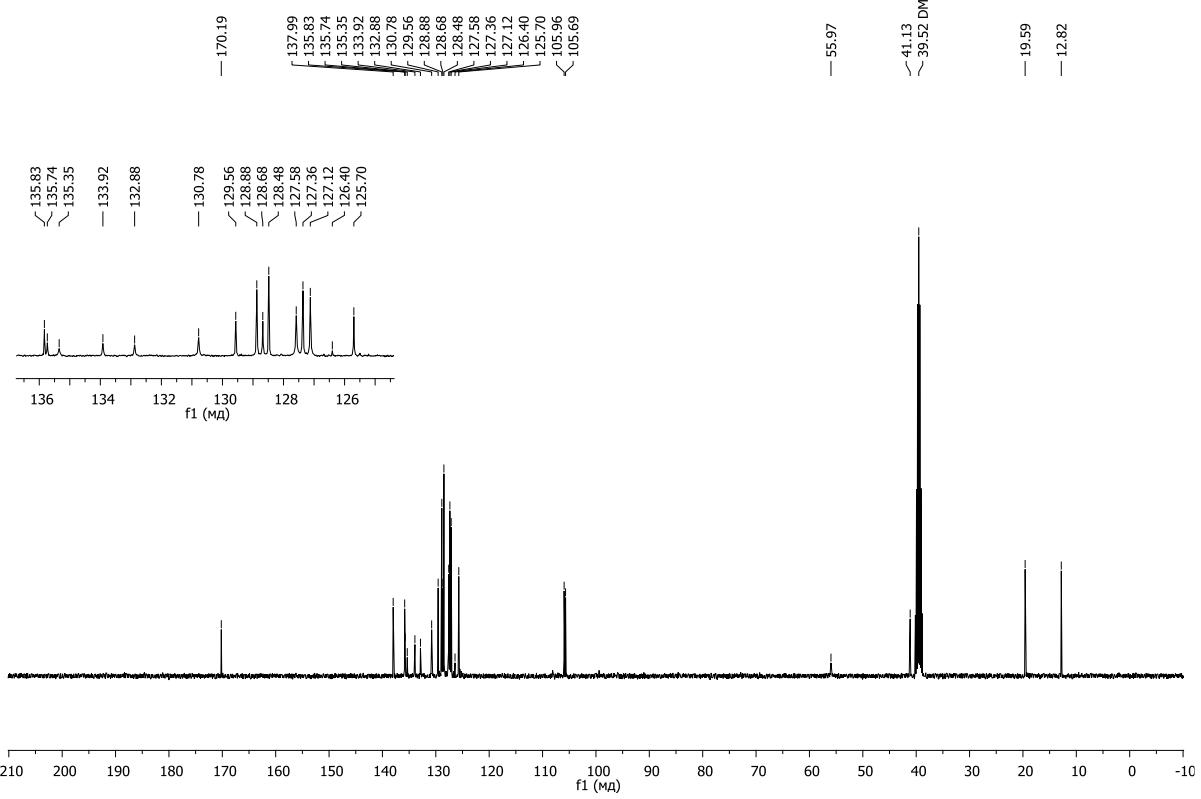


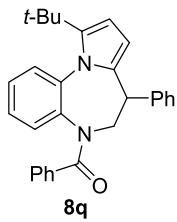


¹H, DMSO, 400 MHz

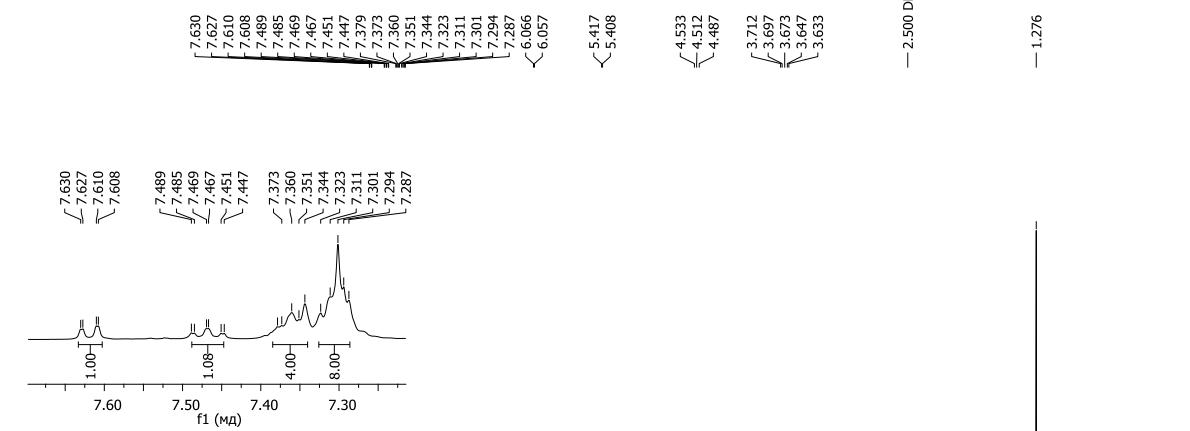


¹³C, DMSO, 100 MHz

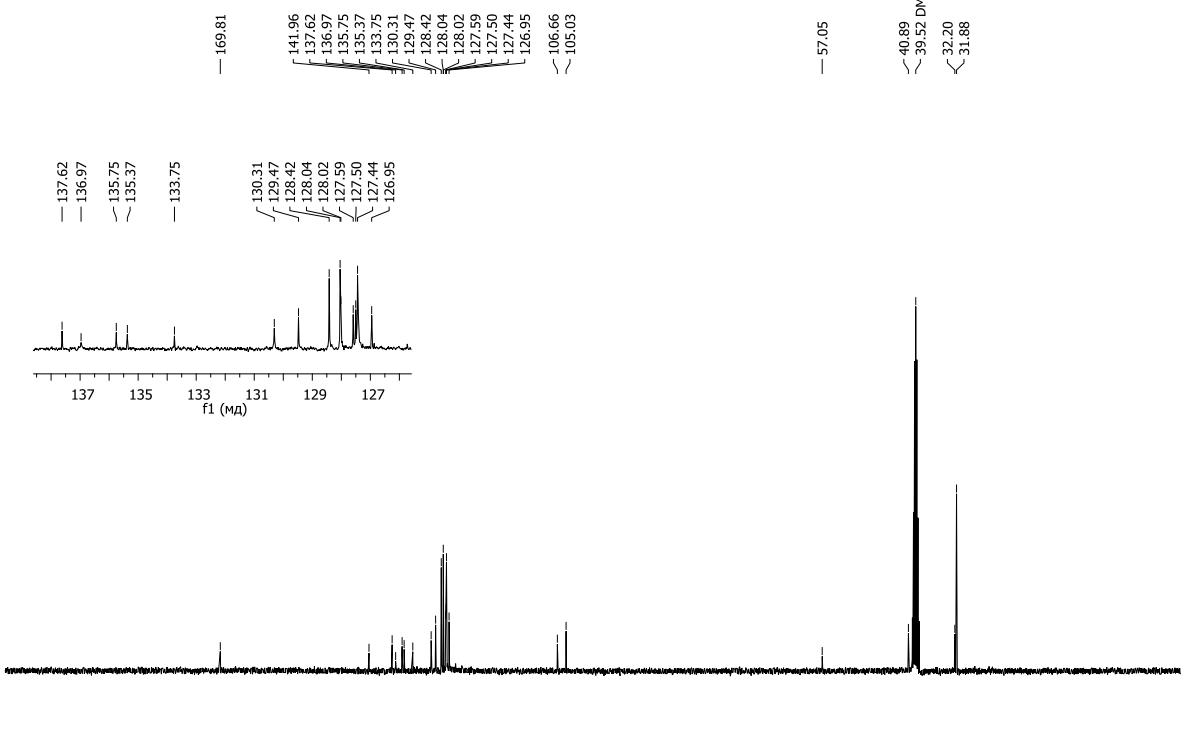


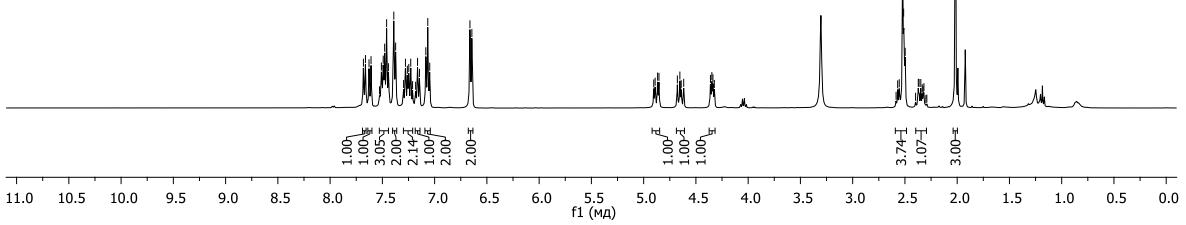
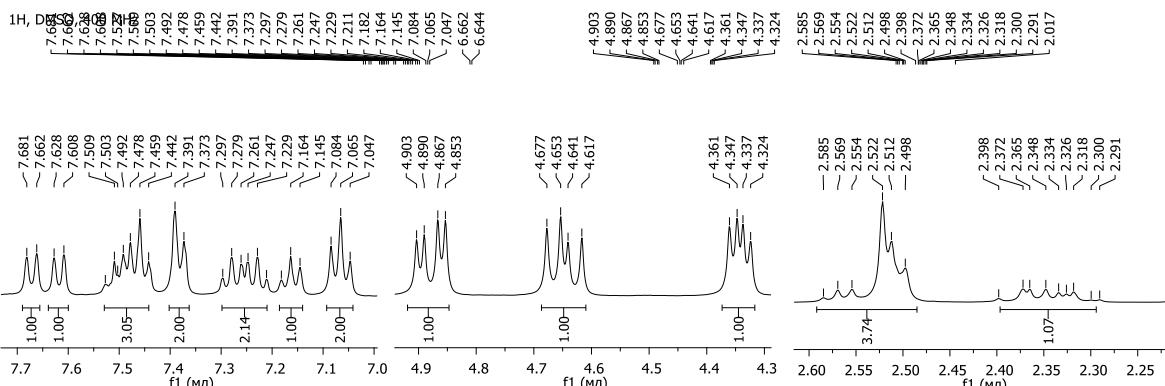
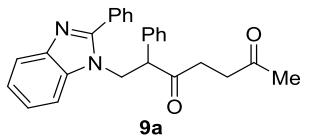


¹H, DMSO, 400 MHz

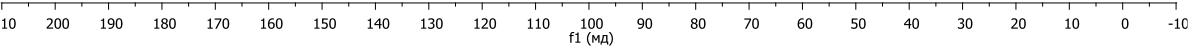
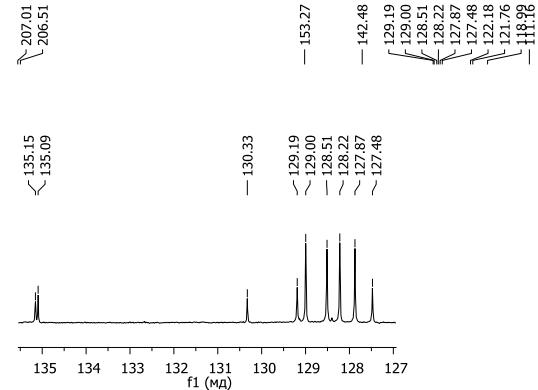


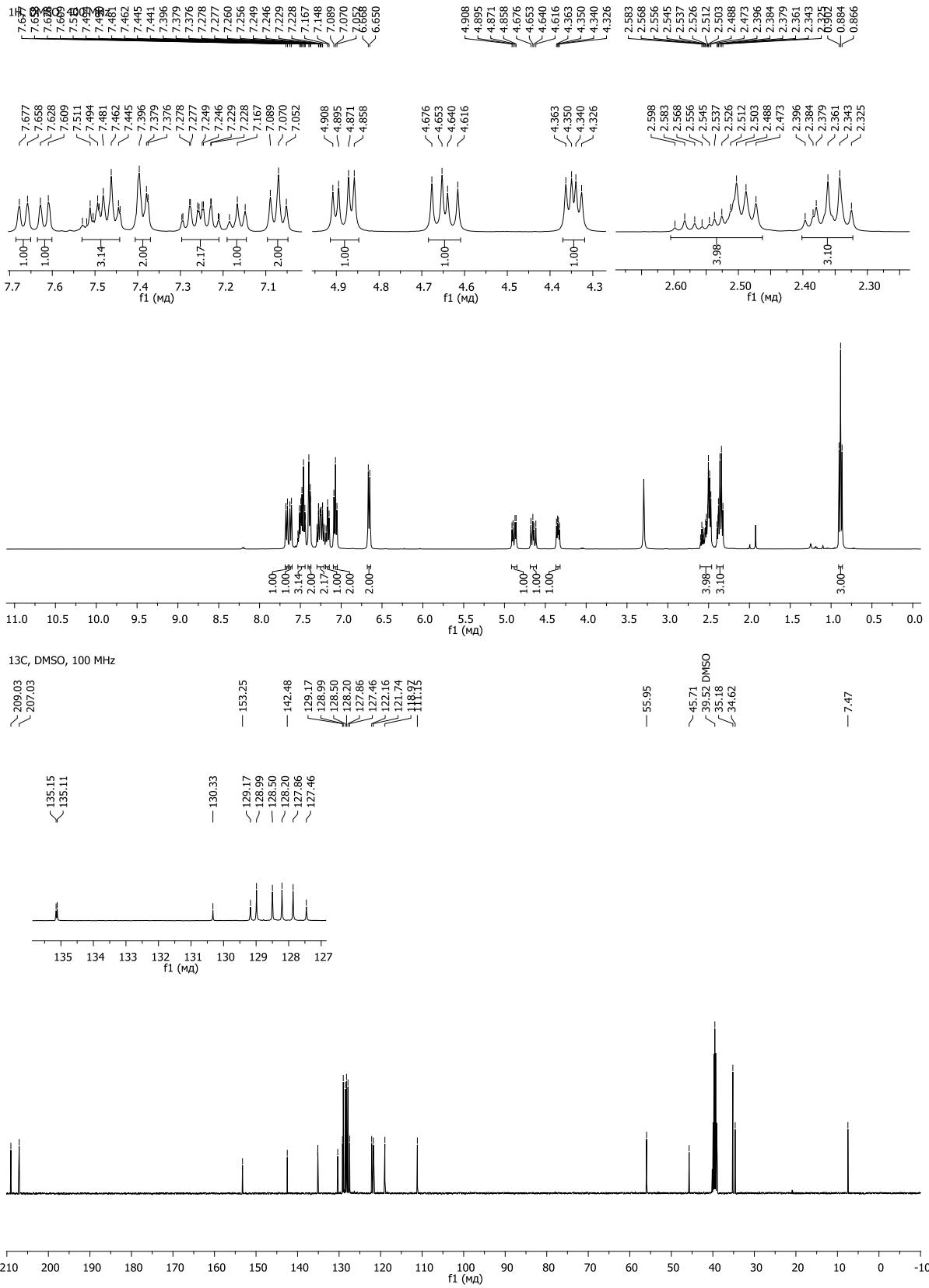
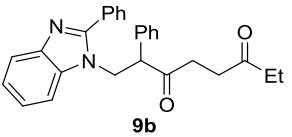
¹³C, DMSO, 100 MHz

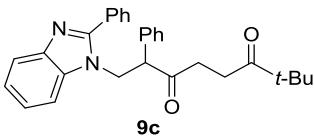




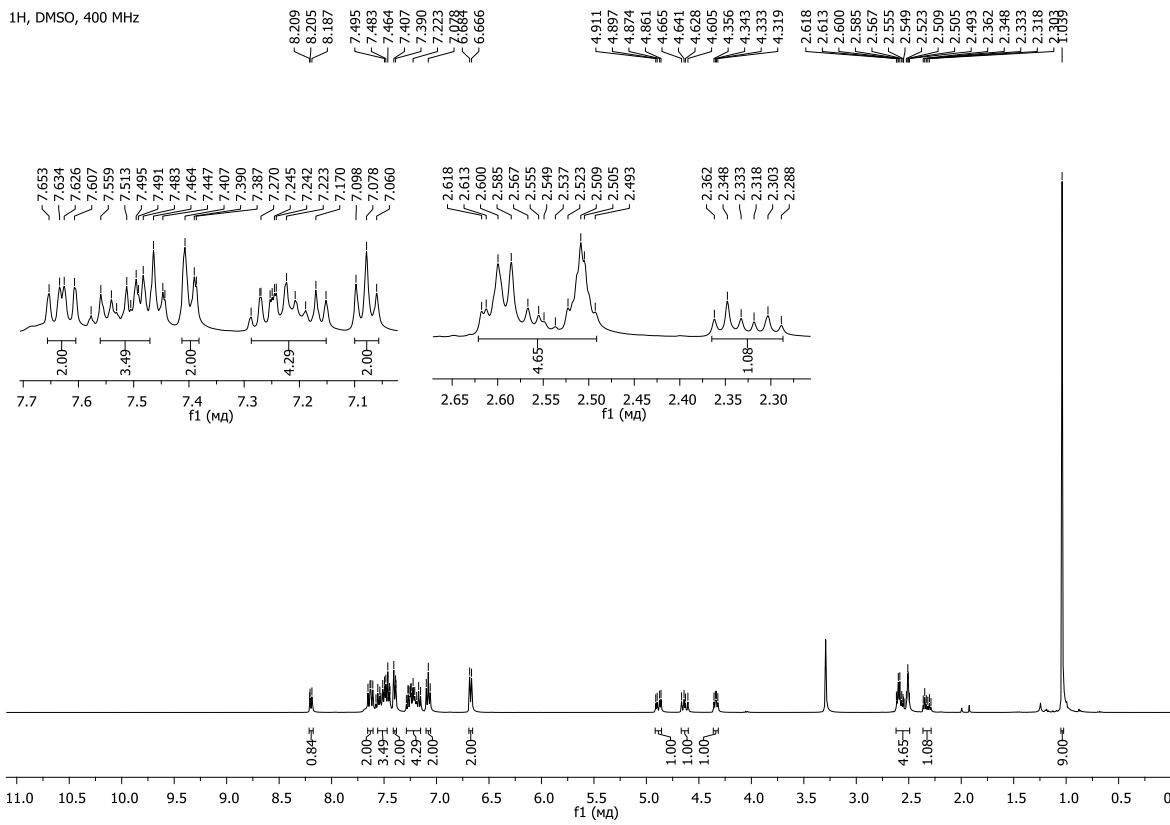
¹³C, DMSO, 100 MHz



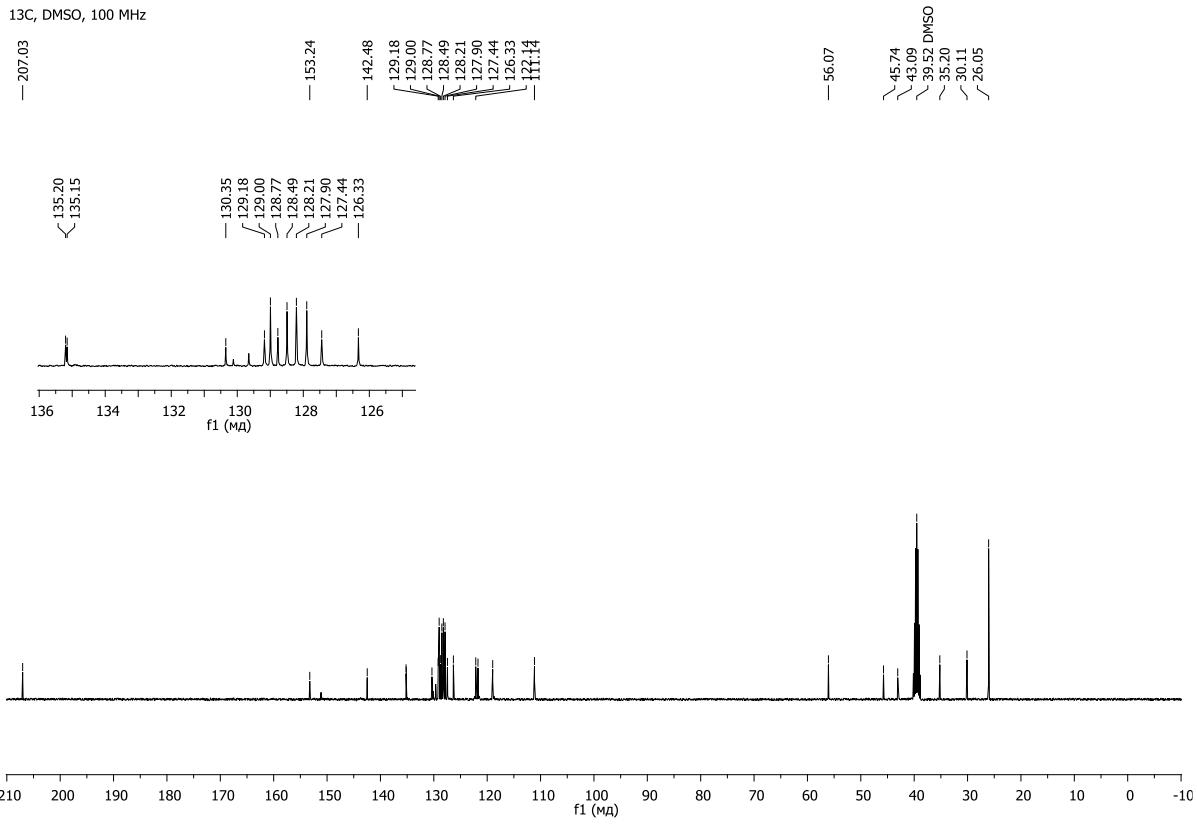


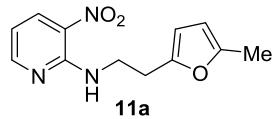


¹H, DMSO, 400 MHz

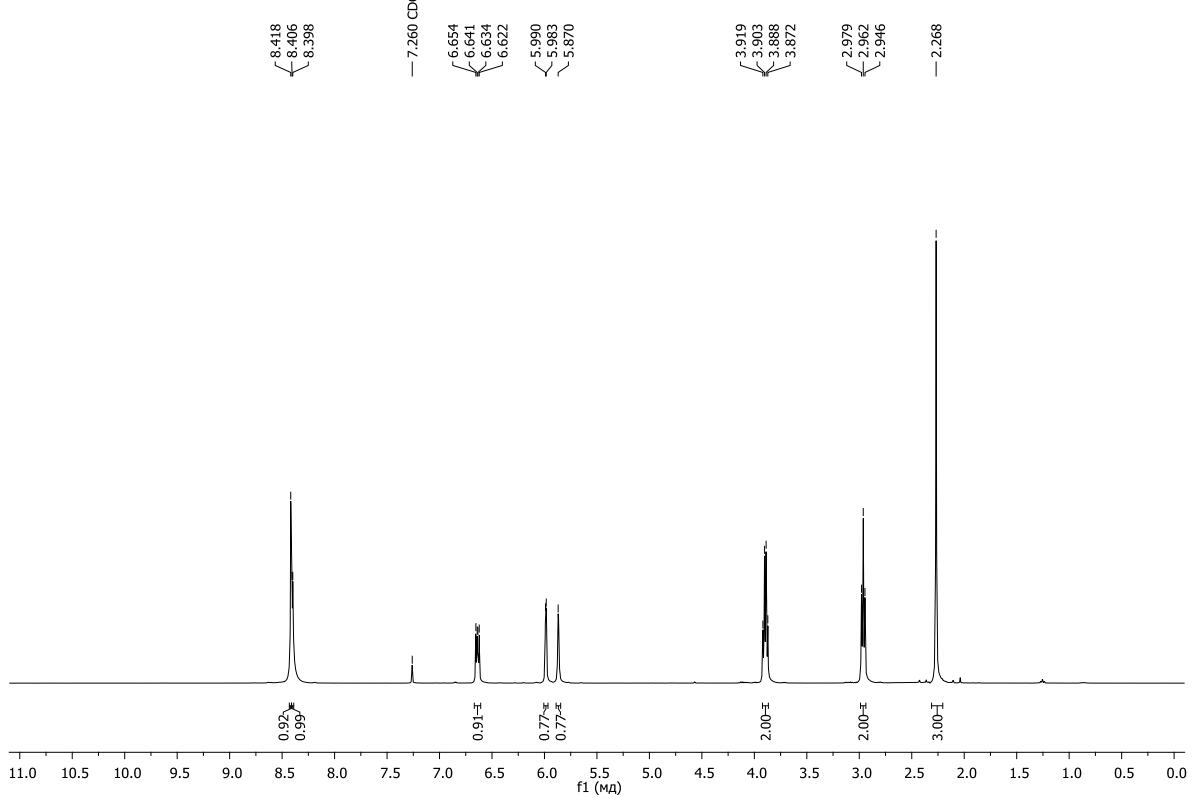


¹³C, DMSO, 100 MHz

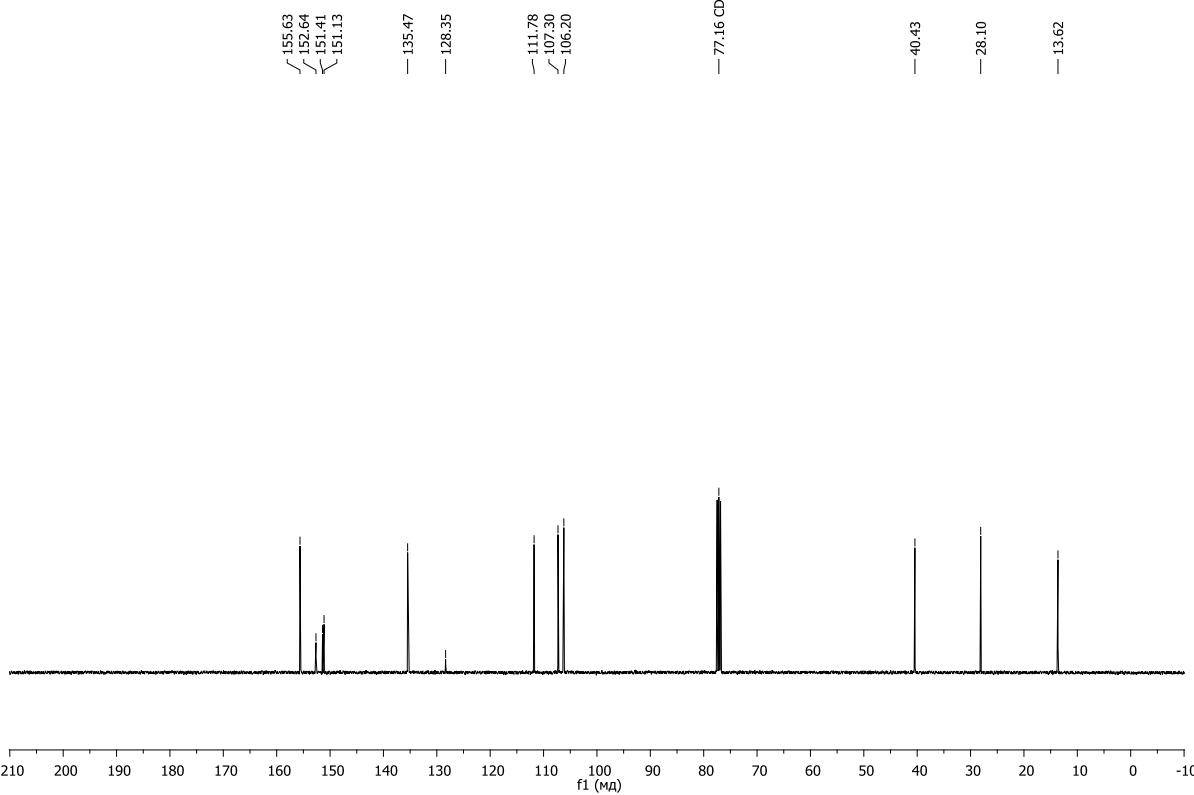


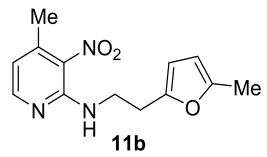


1H, CDCl₃, 400 MHz

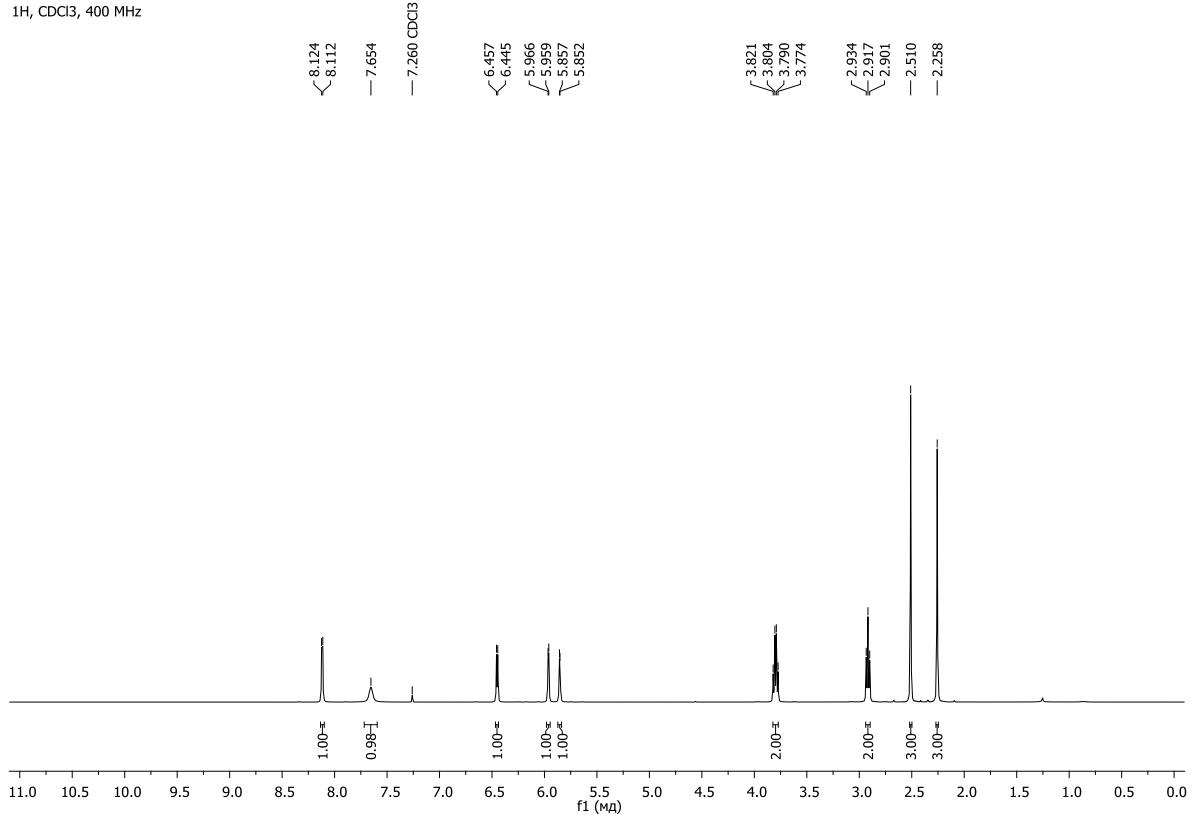


13C, CDCl₃, 100 MHz

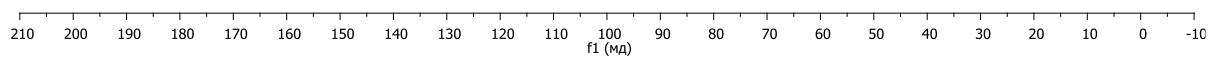
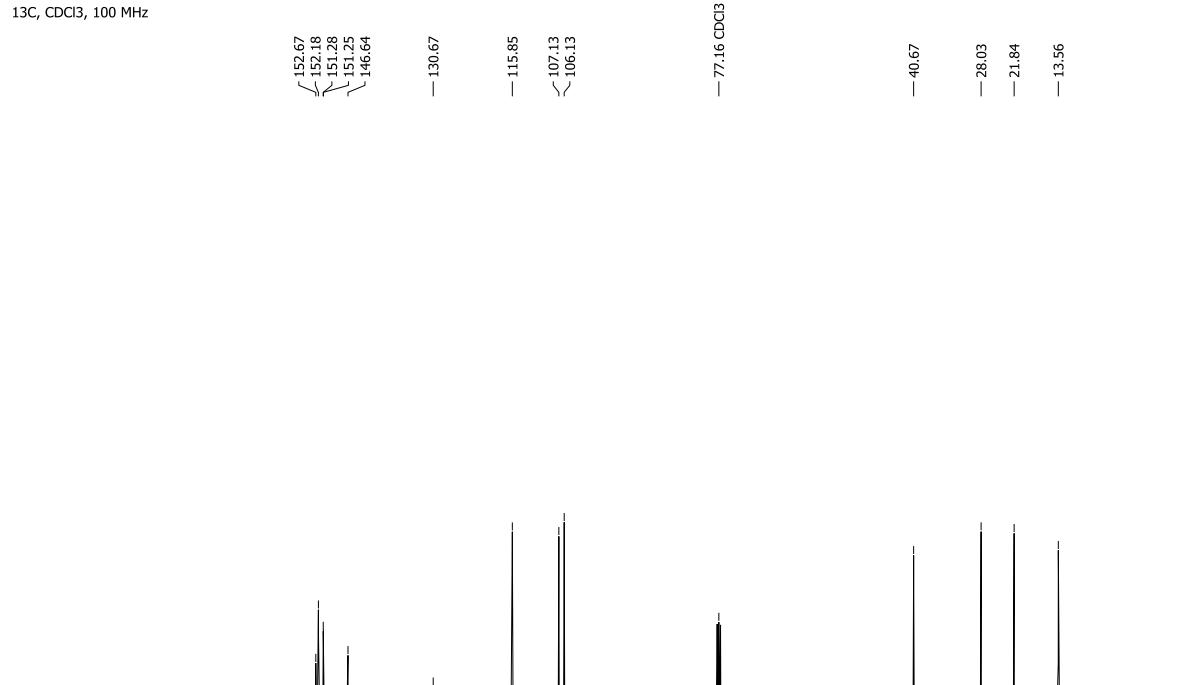


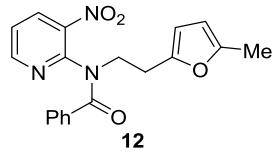


¹H, CDCl₃, 400 MHz

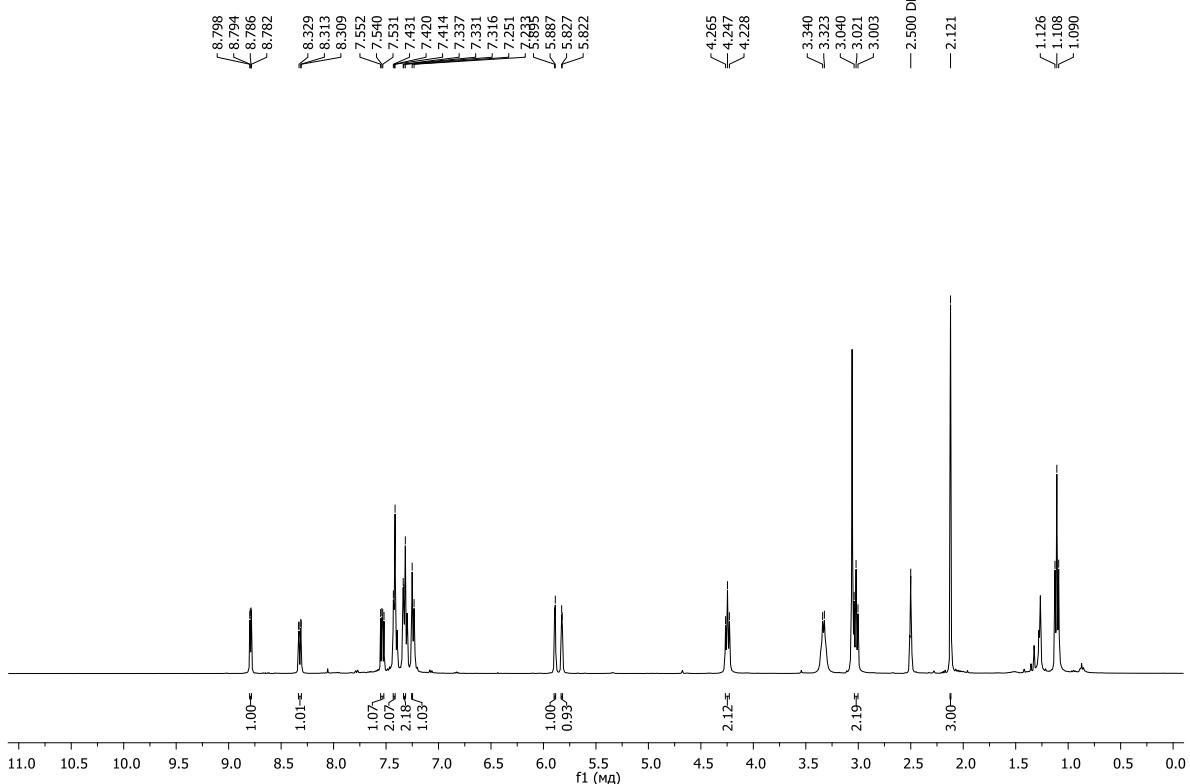


¹³C, CDCl₃, 100 MHz

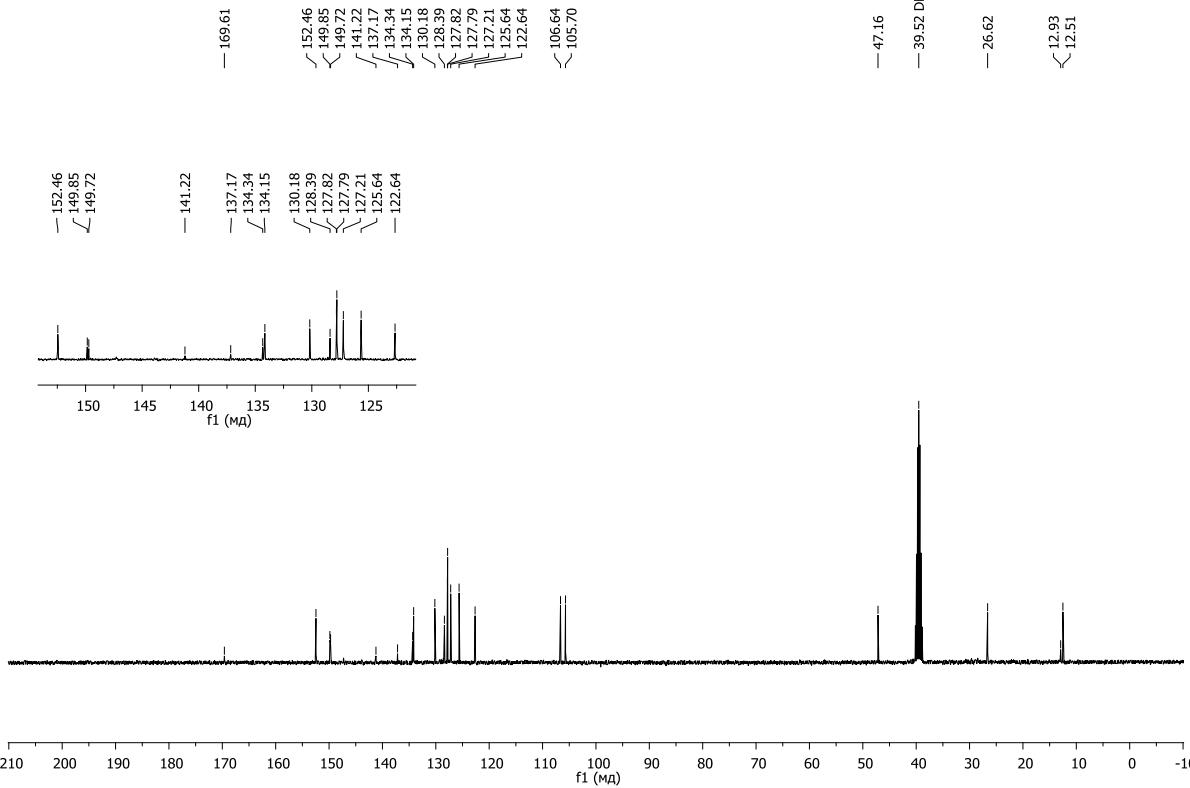


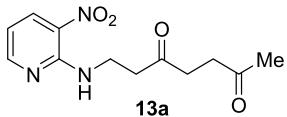


¹H, DMSO (80 °C), 400 MHz

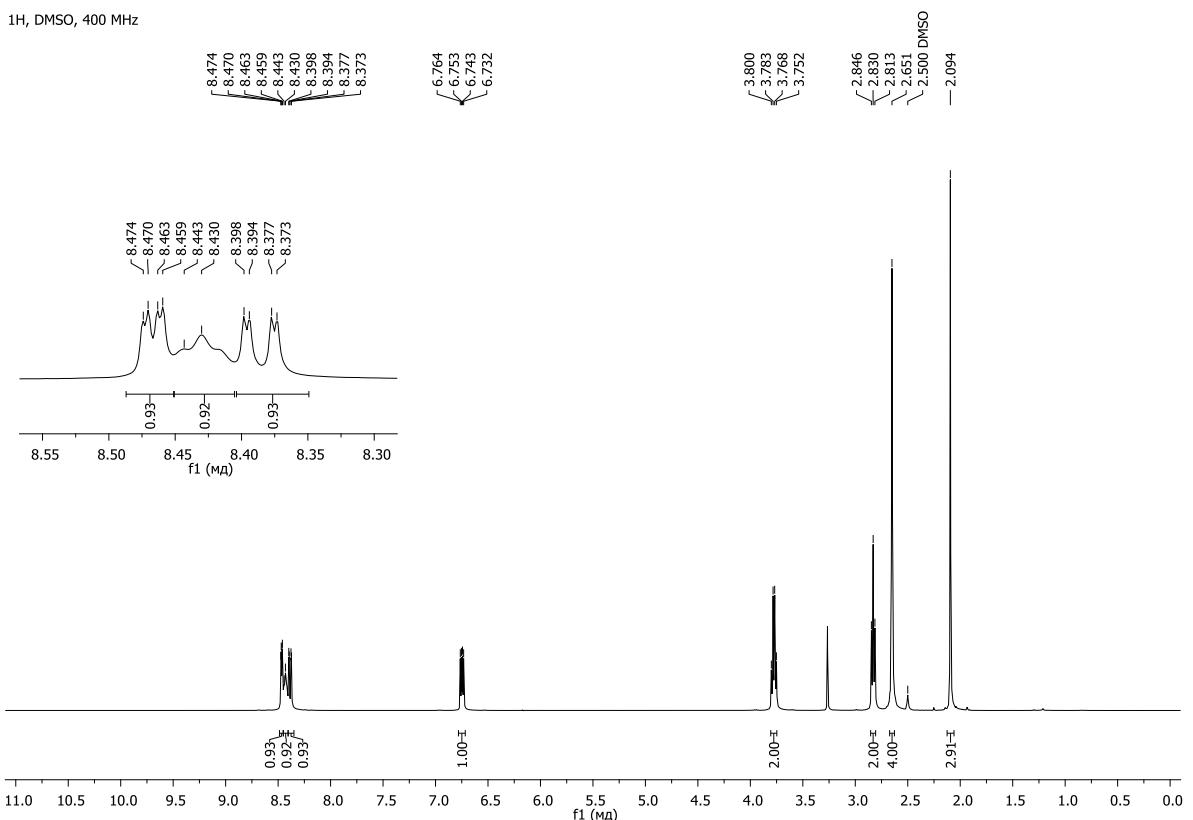


¹³C, DMSO (80 °C), 100 MHz

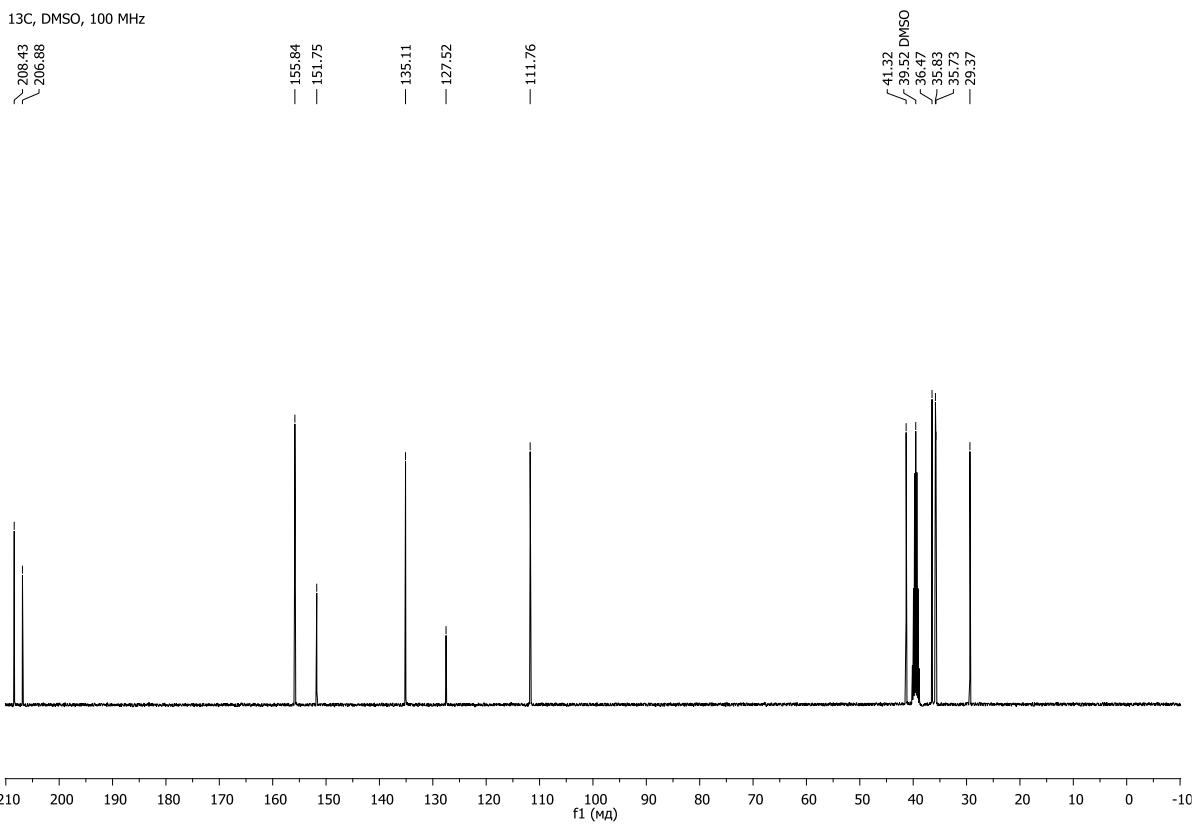


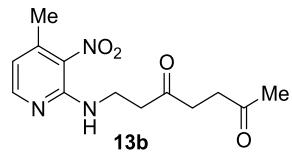


¹H, DMSO, 400 MHz

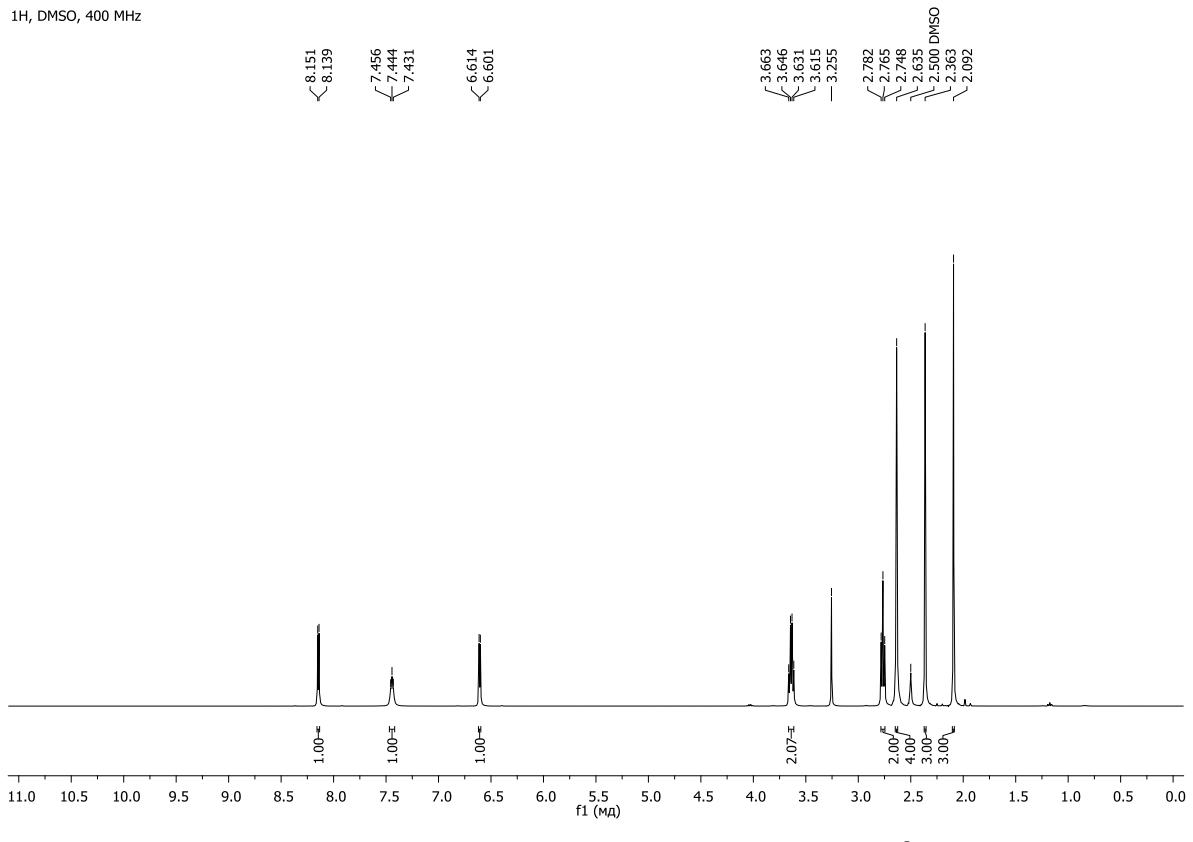


¹³C, DMSO, 100 MHz

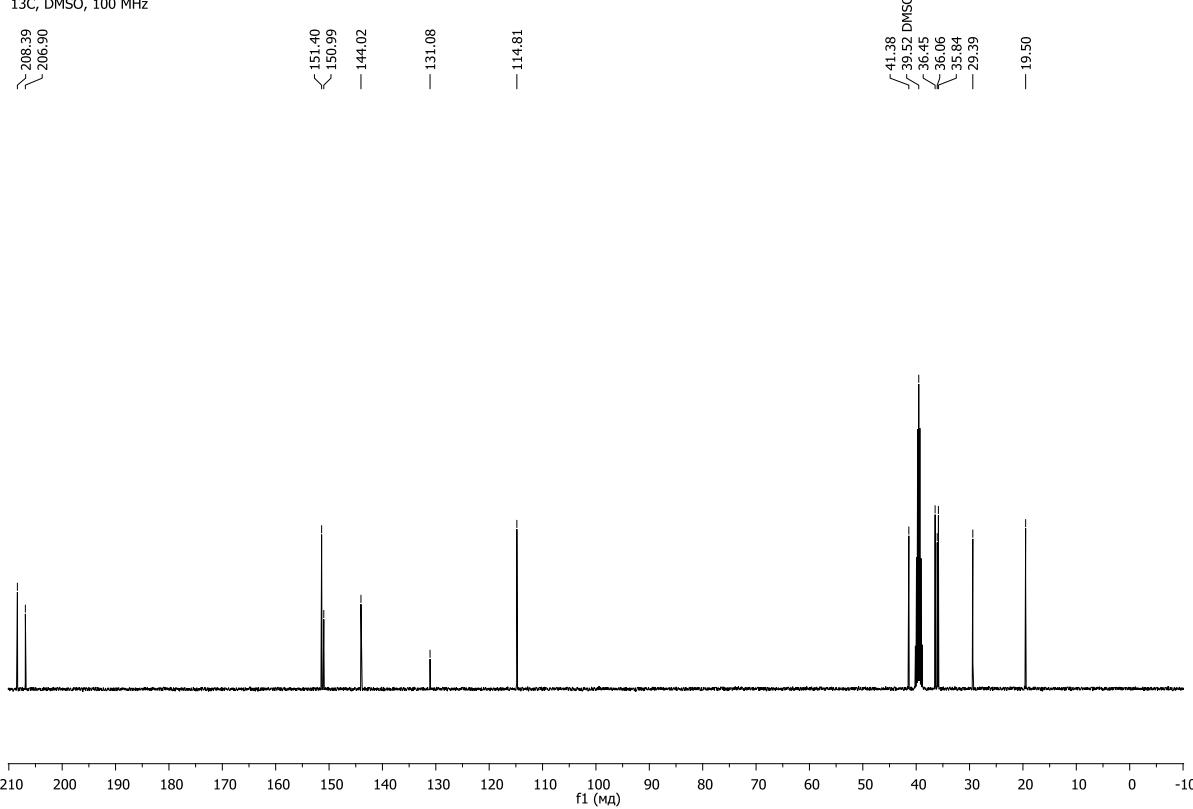


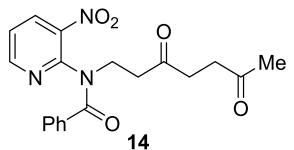


¹H, DMSO, 400 MHz

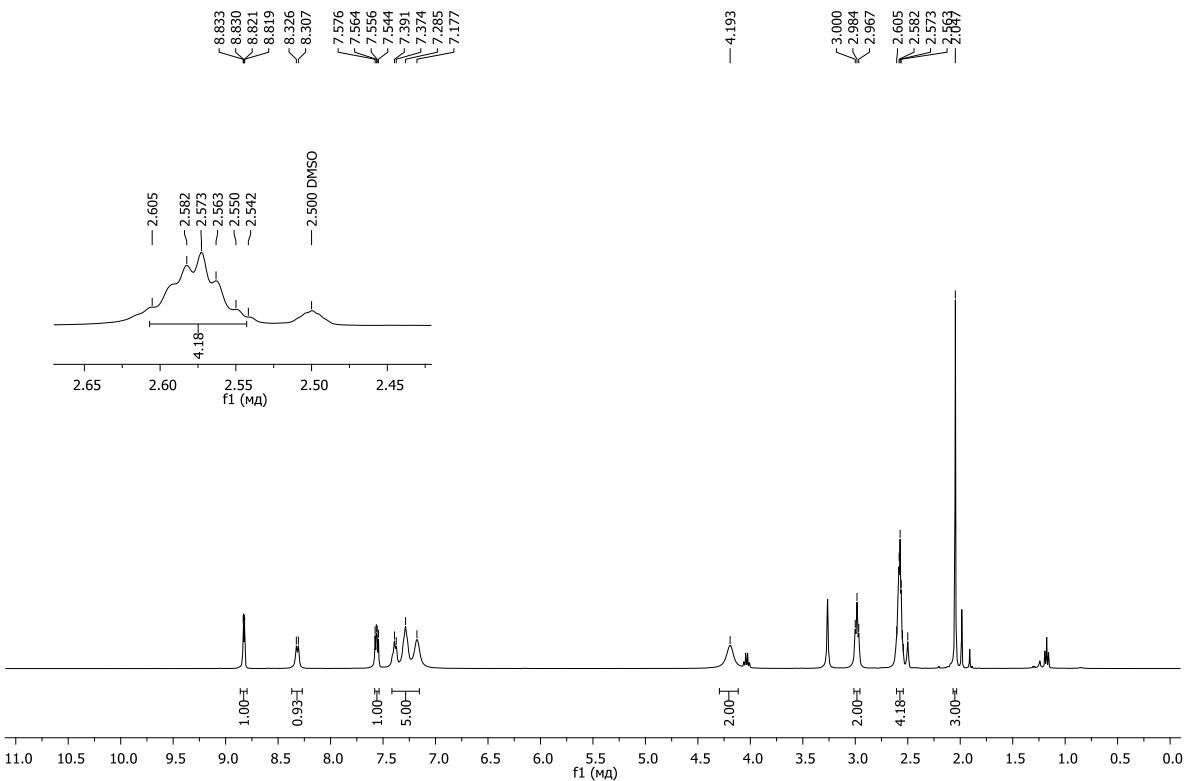


¹³C, DMSO, 100 MHz

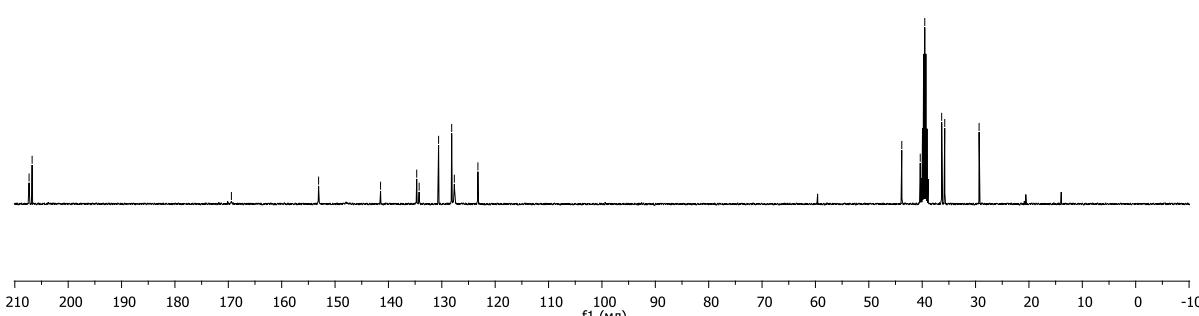
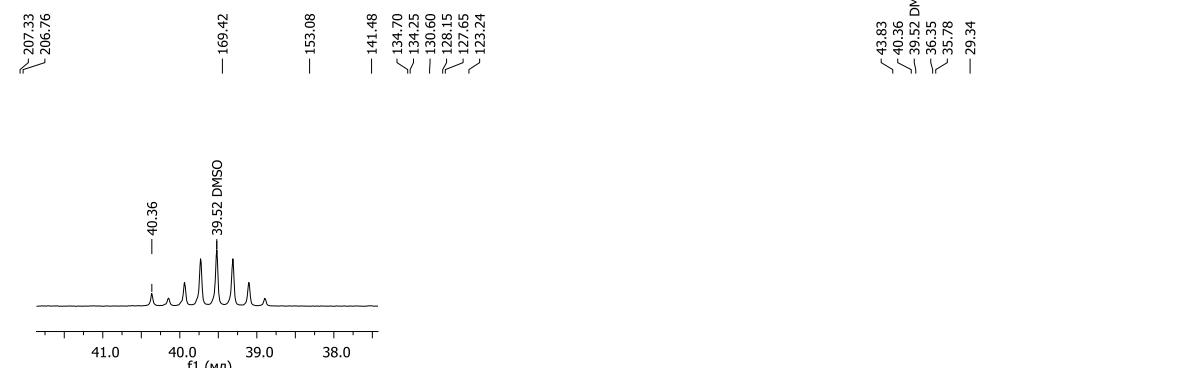


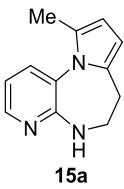


1H, DMSO, 400 MHz

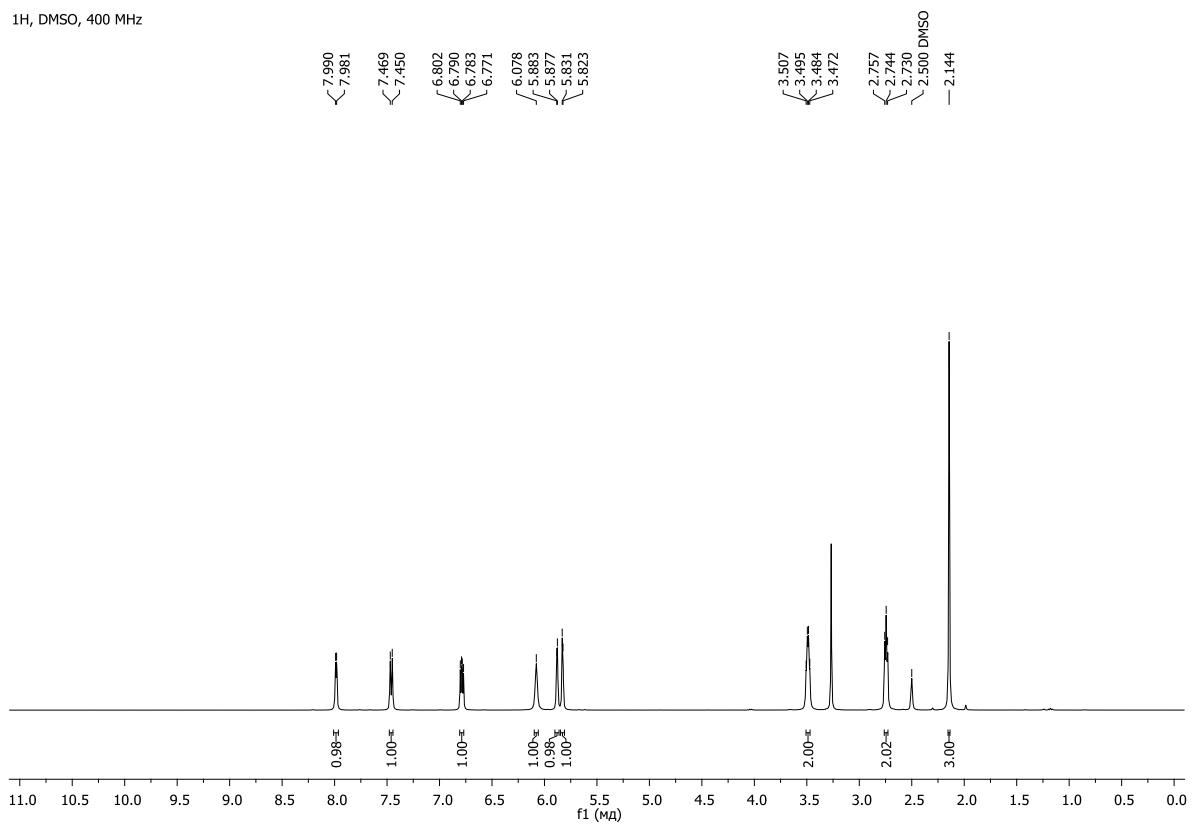


13C, DMSO, 100 MHz

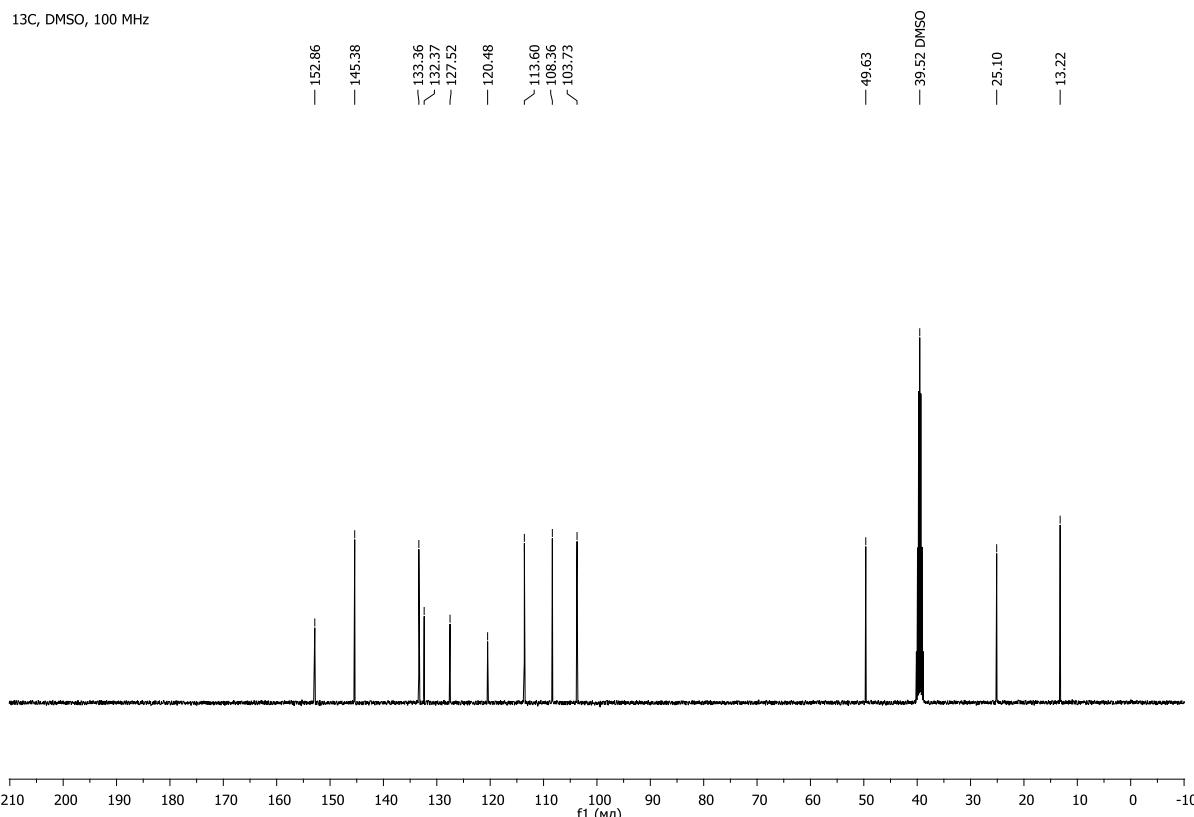


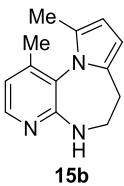


1H, DMSO, 400 MHz

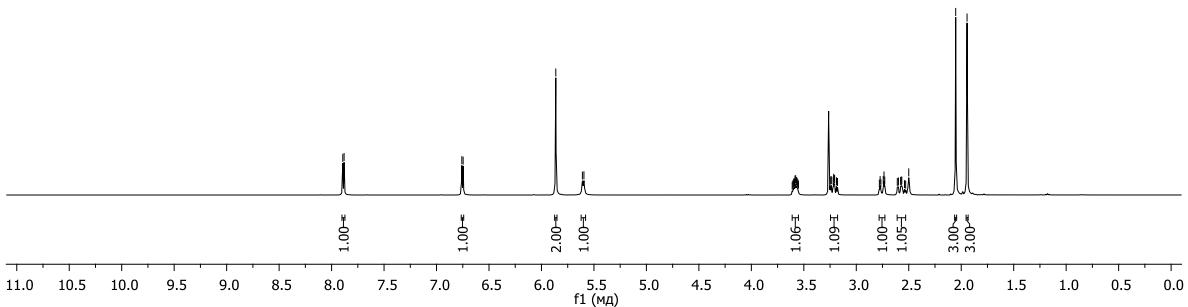
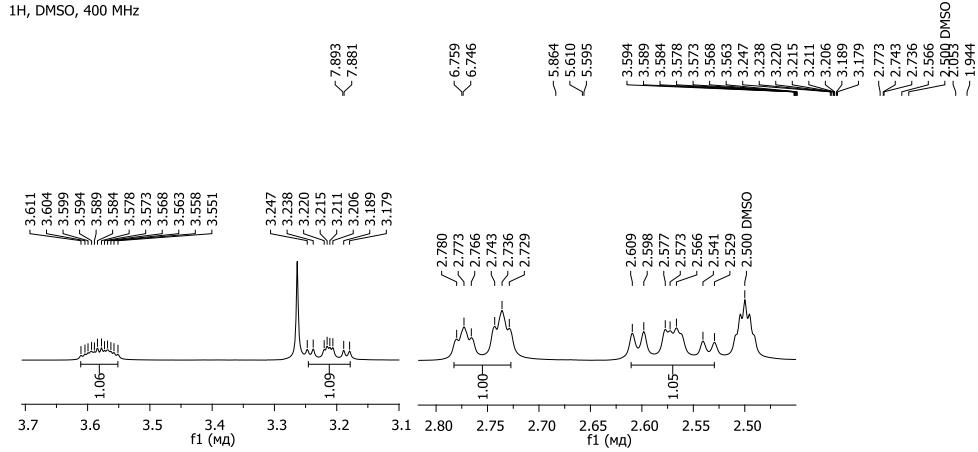


13C, DMSO, 100 MHz

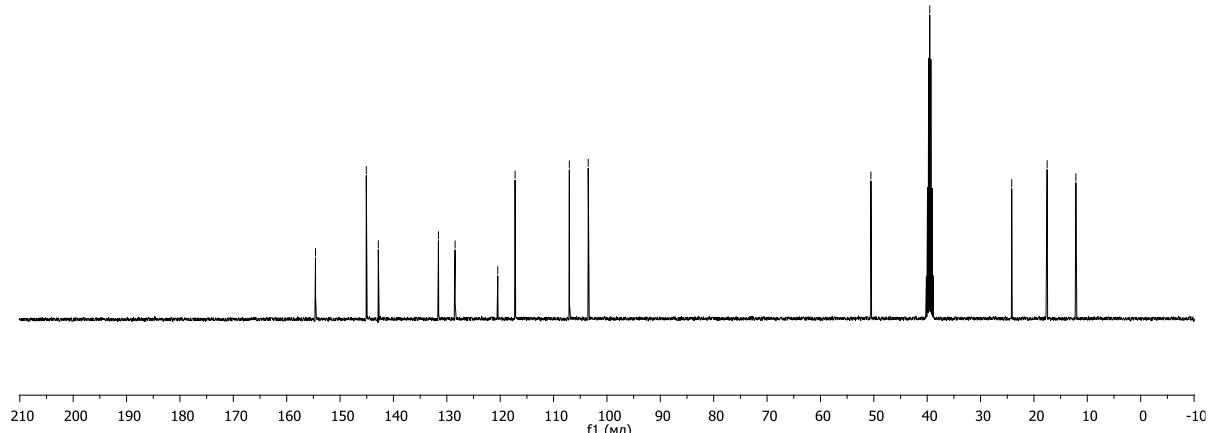


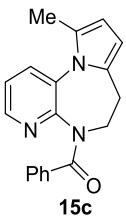


1H, DMSO, 400 MHz

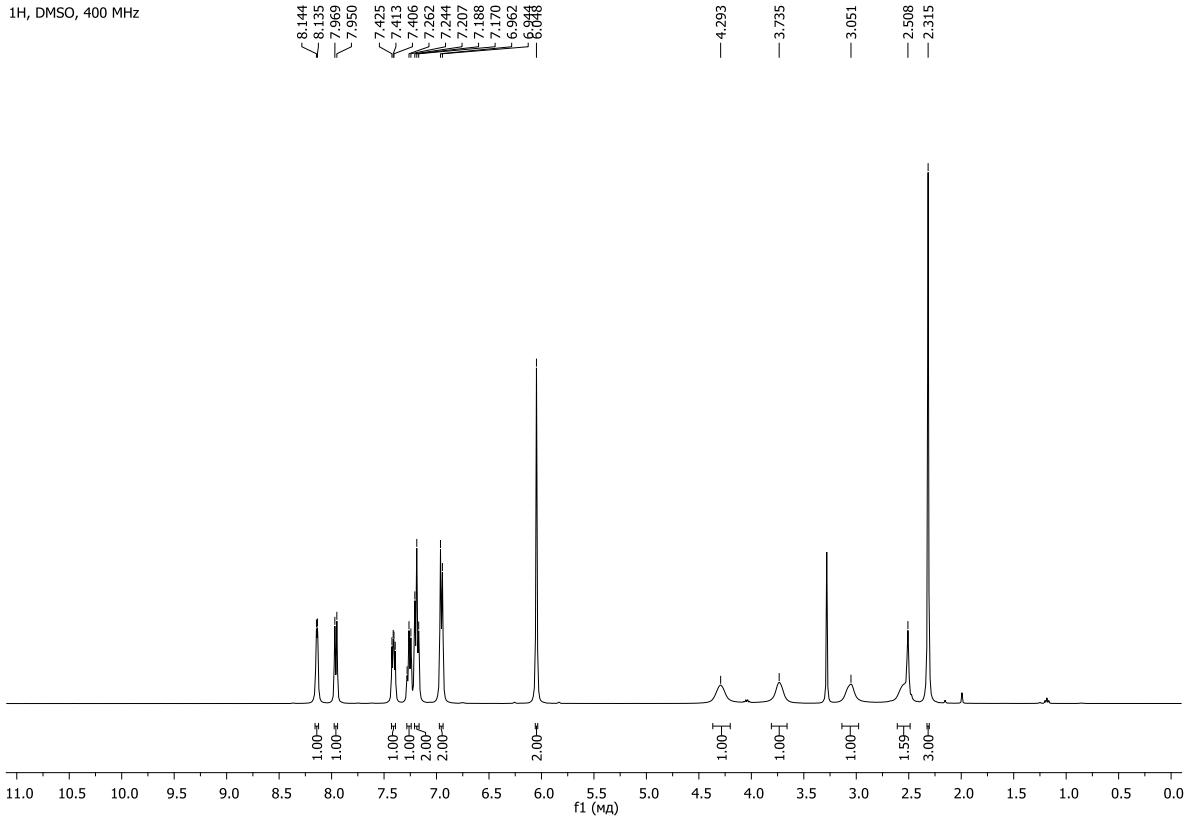


13C, DMSO, 100 MHz

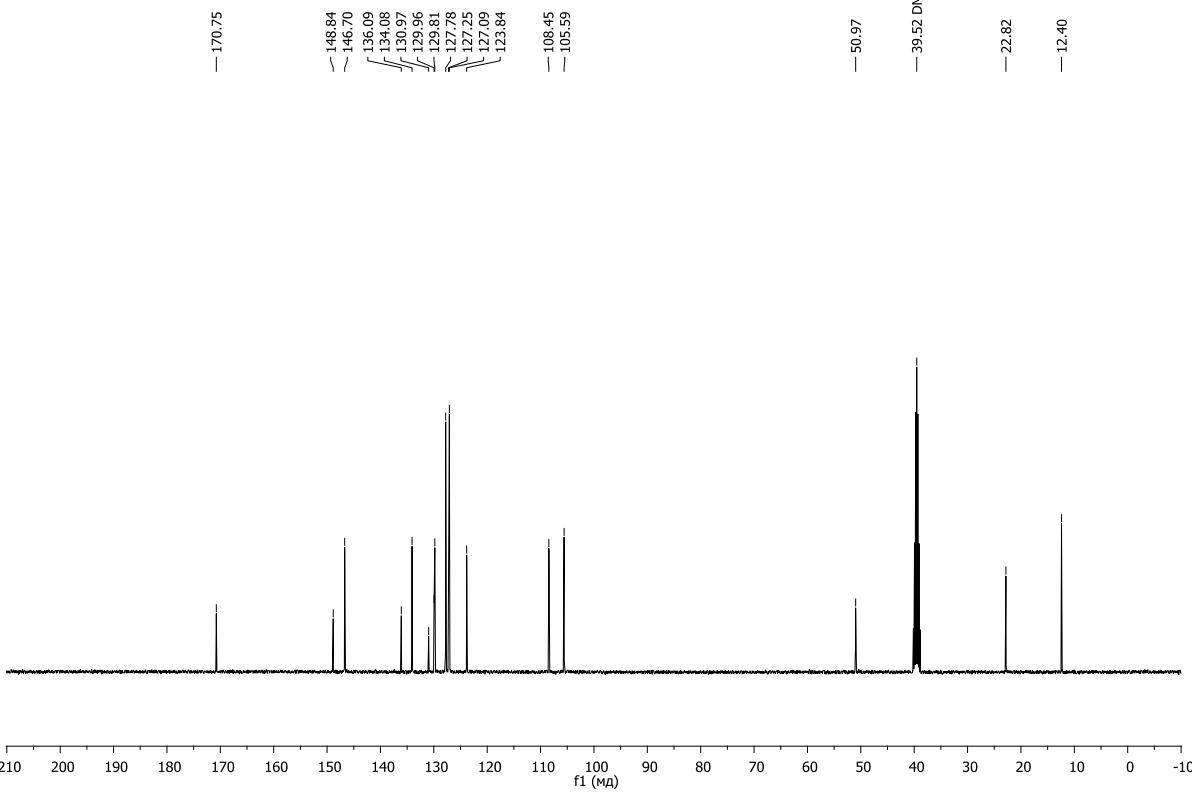


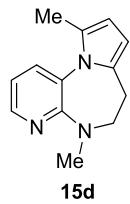


¹H, DMSO, 400 MHz

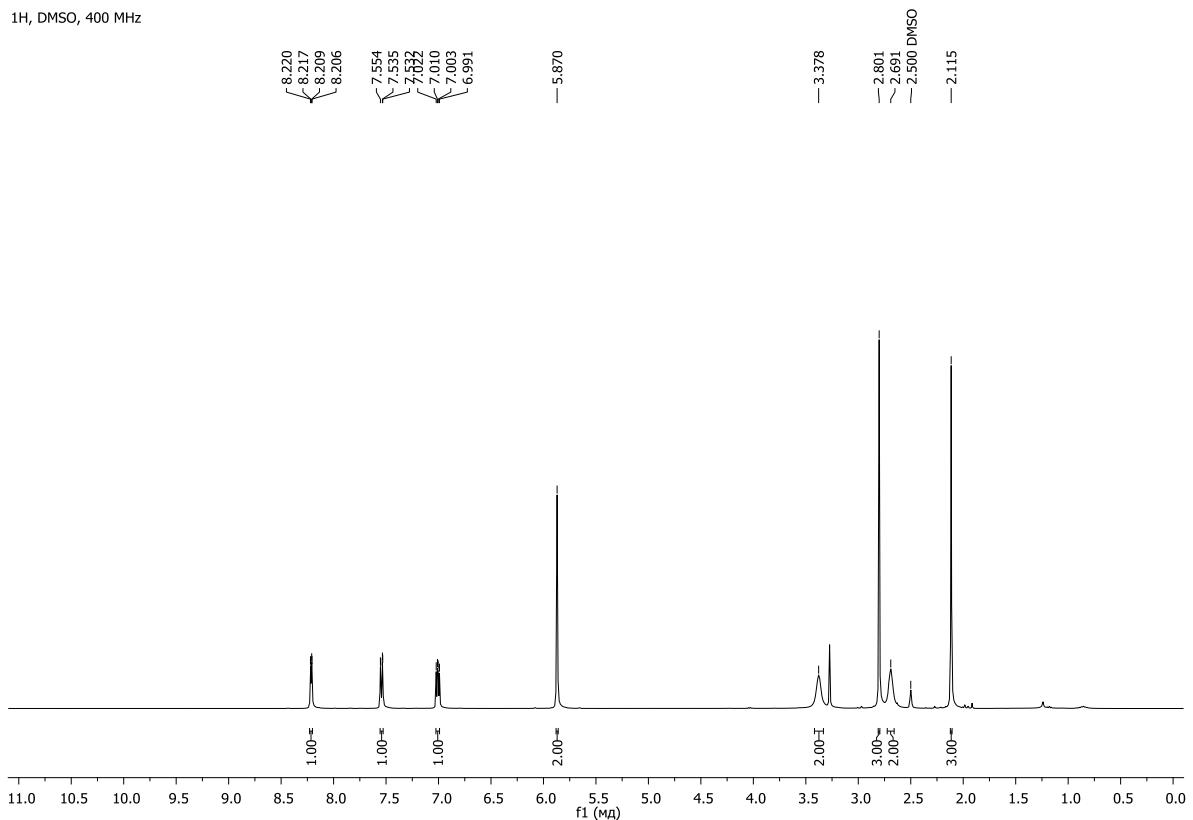


¹³C, DMSO, 100 MHz

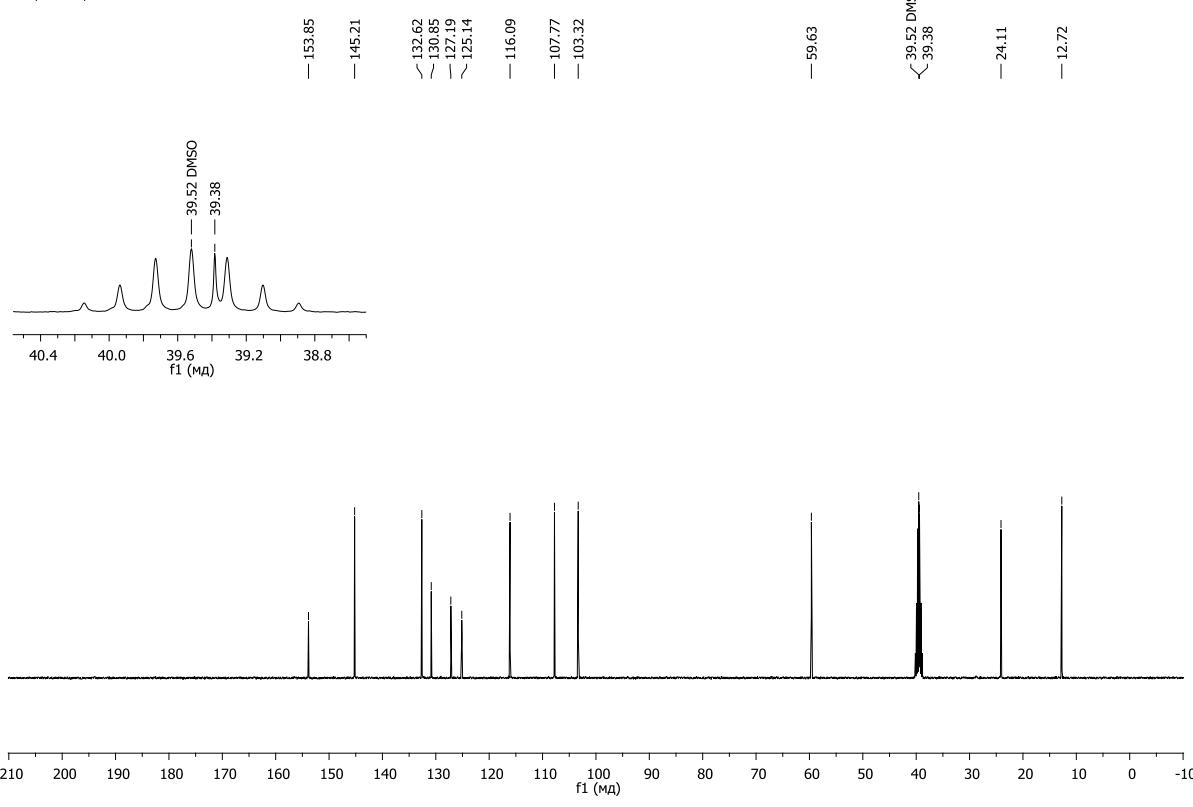


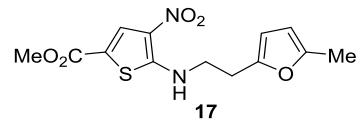


1H, DMSO, 400 MHz

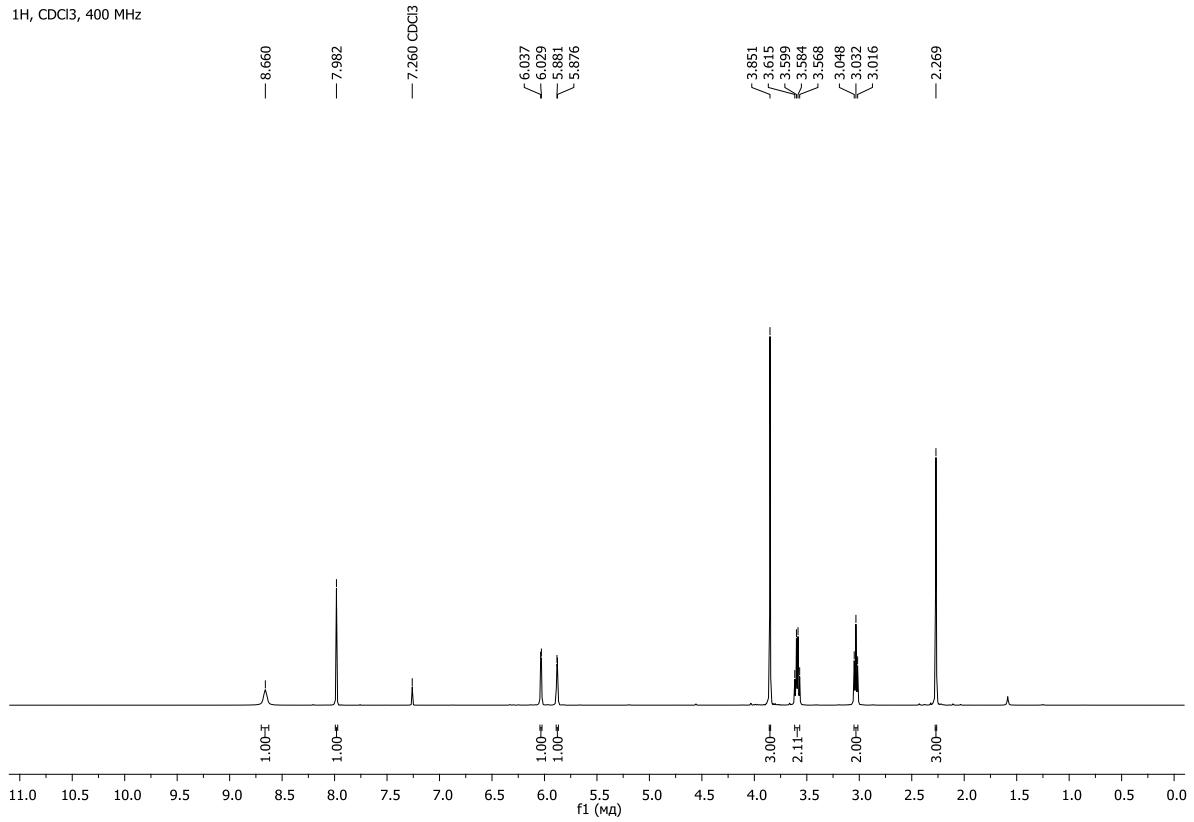


13C, DMSO, 100 MHz

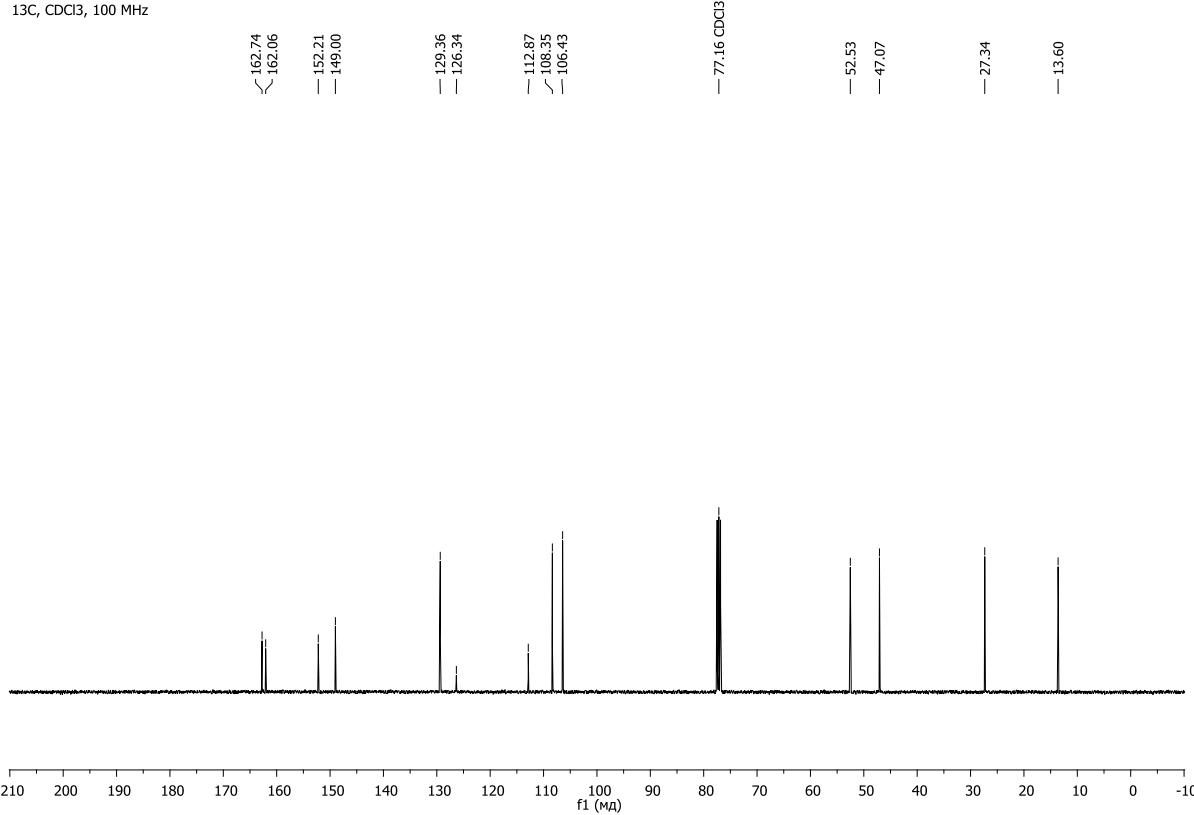


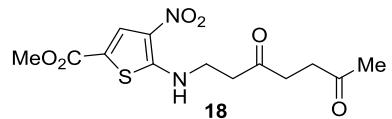


¹H, CDCl₃, 400 MHz

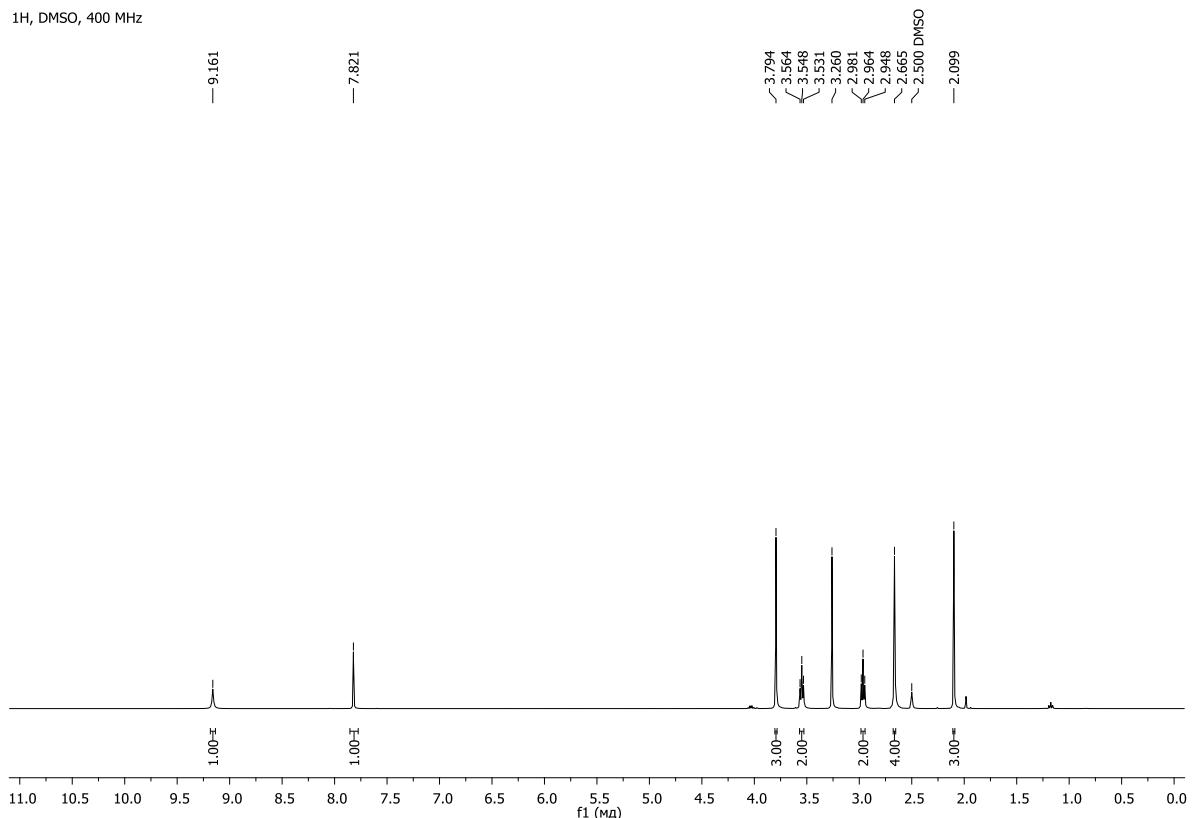


¹³C, CDCl₃, 100 MHz

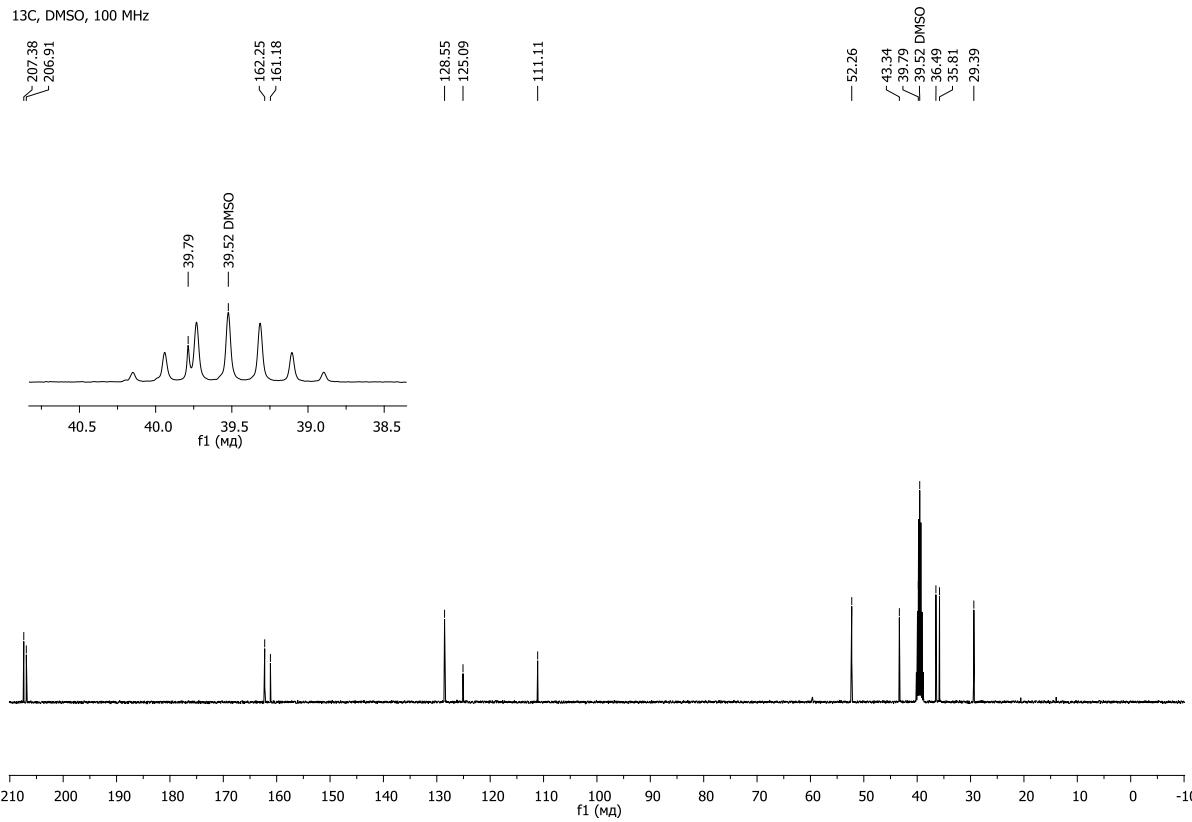


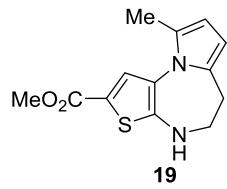


¹H, DMSO, 400 MHz

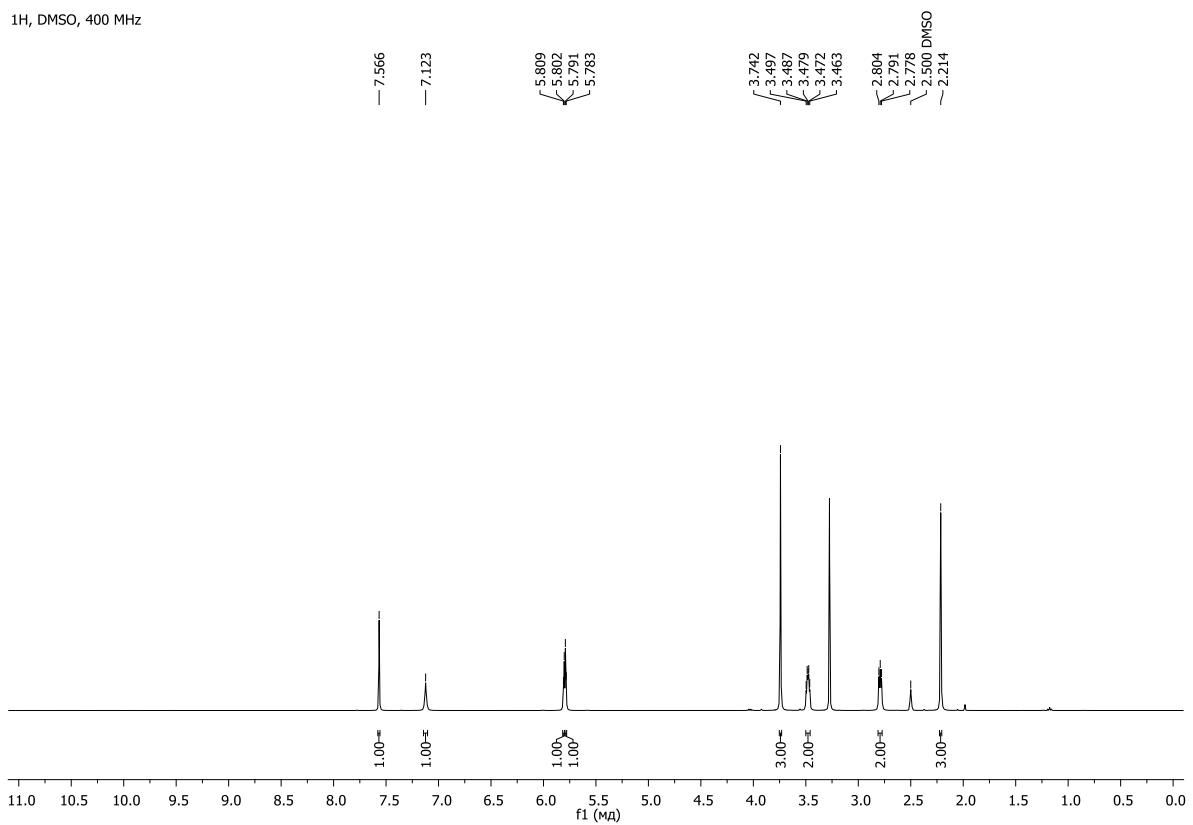


¹³C, DMSO, 100 MHz

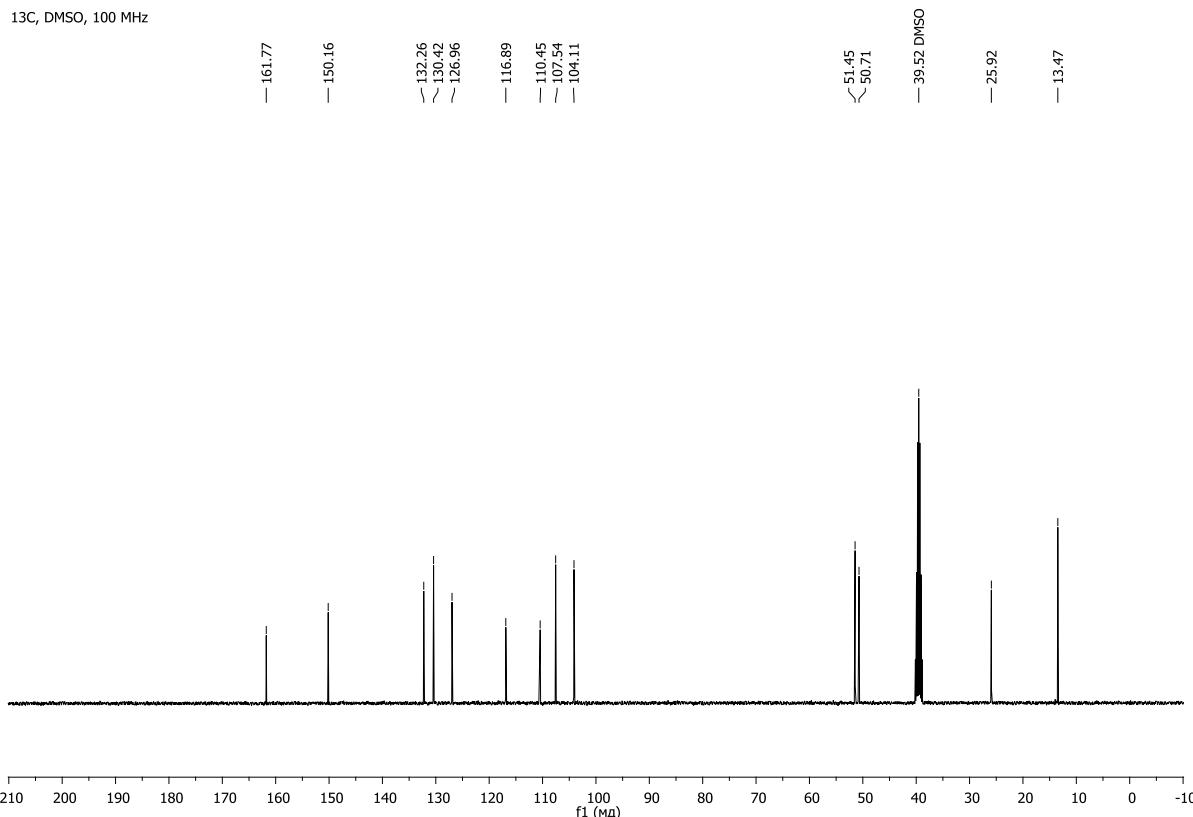


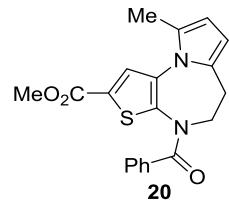


¹H, DMSO, 400 MHz

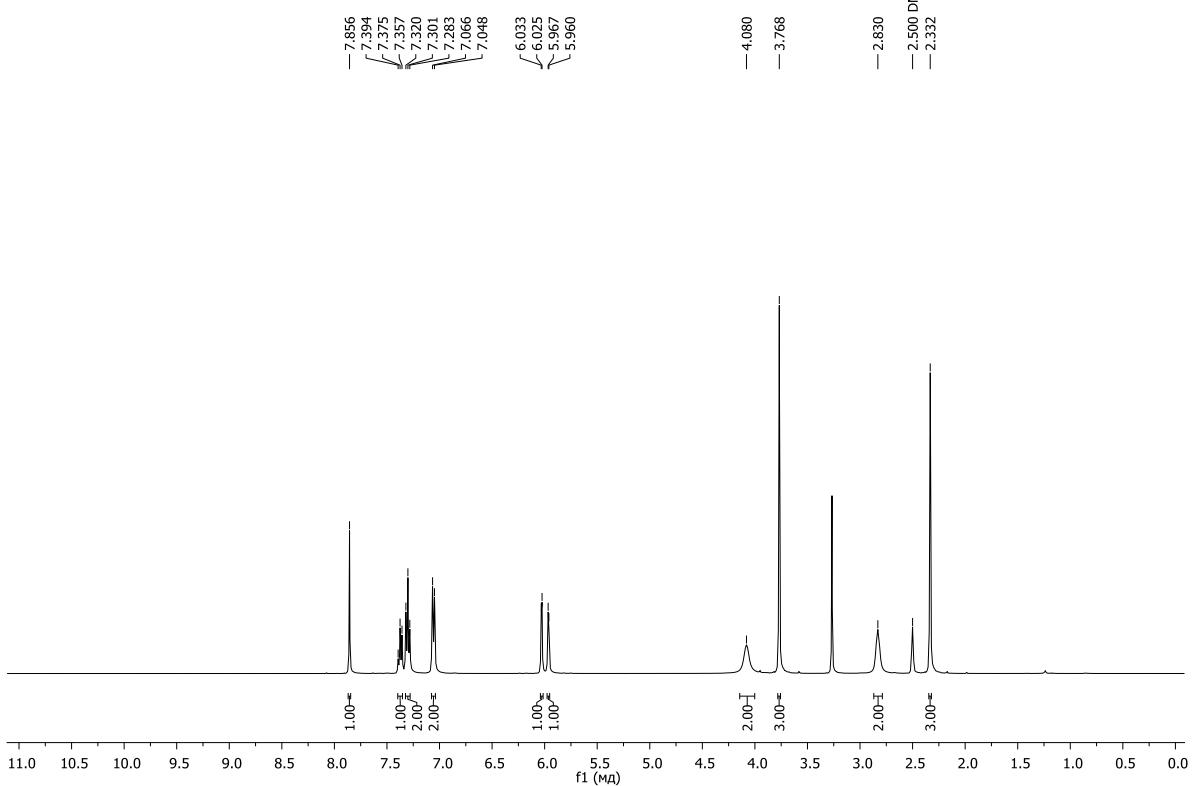


¹³C, DMSO, 100 MHz

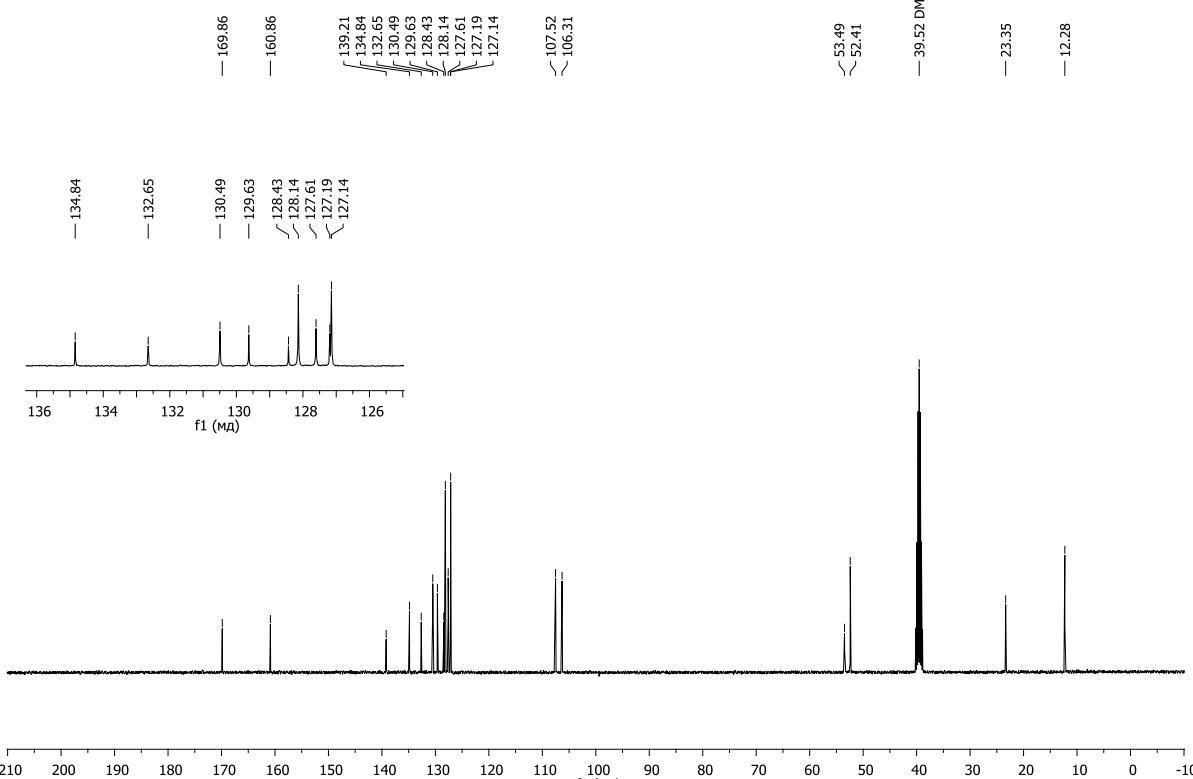


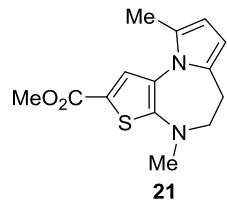


1H, DMSO, 400 MHz

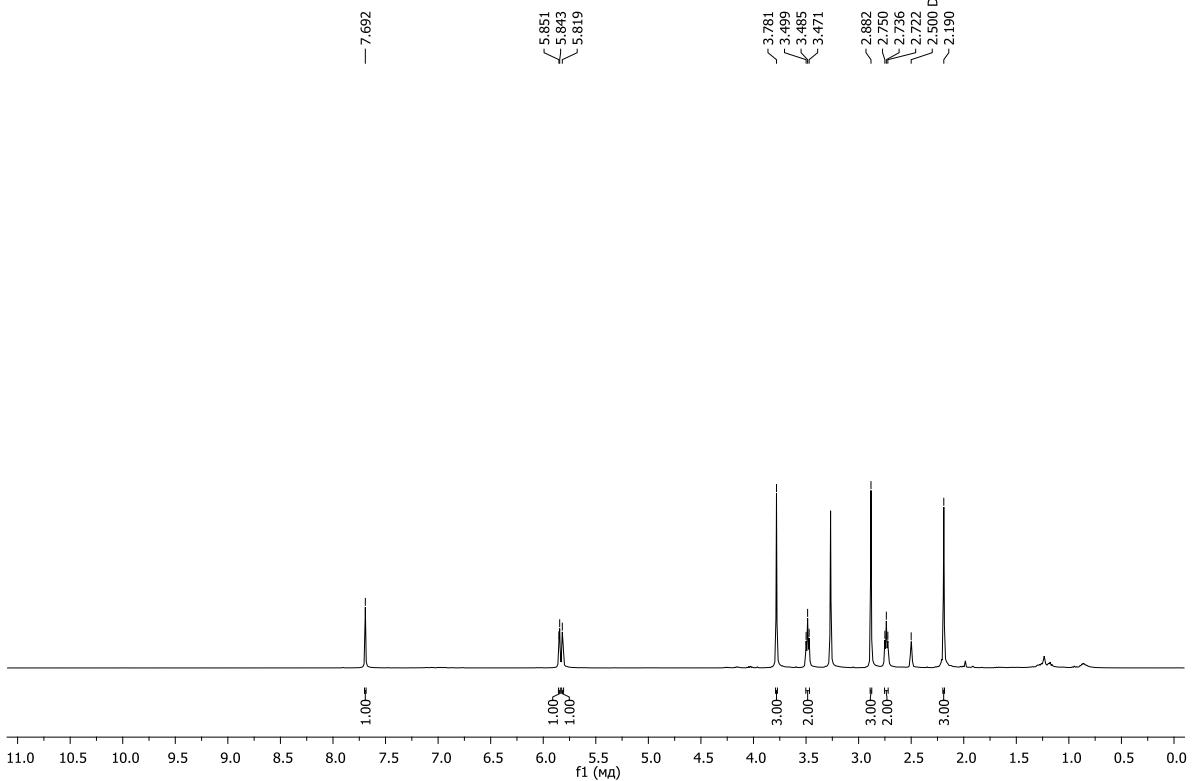


13C, DMSO, 100 MHz





1H, DMSO, 400 MHz



13C, DMSO, 100 MHz

