Electronic Supplementary Material (ESI) for RSC Advances.

Electronic Supplementary Information for

Zn-Catalyzed hydrohydrazination of propargylamides with $BocNHNH_2$: a novel entry into 1,2,4-triazine core

Alexey Lukin, Tatiana Vedekhina, Dmitry Tovpeko, Nikolay Zhurilo, and Mikhail Krasavin*

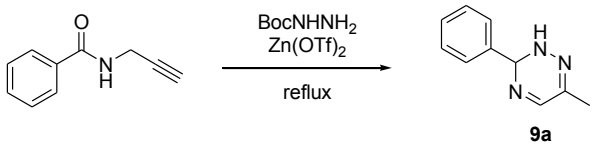
Contents:

General

All reactions were conducted in oven-dried glassware in atmosphere of nitrogen. Melting points were measured with a Buchi B-520 melting point apparatus and were not corrected. Analytical thin-layer chromatography was carried out on Silufol UV-254 silica gel plates using appropriate mixtures of ethyl acetate and hexane. Compounds were visualized with short-wavelength UV light. ^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker MSL-300 spectrometers in DMSO-D6-d_6 using TMS as an internal standard. Mass spectra were recorded using Shimadzu LCMS-2020 system with electron impact (EI) ionization. All and reagents and solvents were obtained from commercial sources and used without purification.

Summary of optimization experiments

- *Screening of solvents*

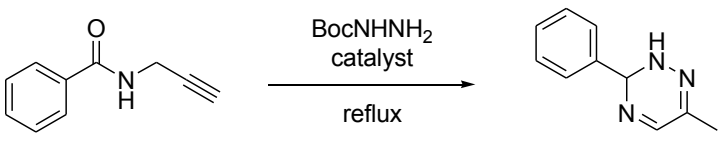


9a

Table S1. Solvent screening results.

Solvent	Starting material present	Reaction time (h)	Formation of **9**
toluene	-	4	+
benzene	-	8	+
MeCN	+	4	-
CH_2Cl_2	+	4	-
THF	+	4	-
DMF	+	4	-
MeOH	+	4	-
Xylene (110 °C)	-	4	+

- *Screening of catalysts*

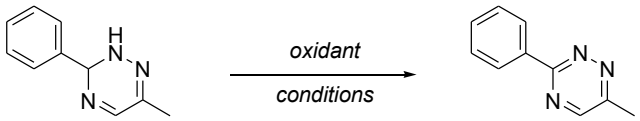


9a

Table S2. Catalyst screening results.

Catalyst	Starting material present	Catalyst mol. %	Reaction time (h)	Formation of **9**
$Zn(OTf)_2$	-	25	4	+
$Cu(OTf)_2$	-	25	8	-
LiOTf	+	25	4	-
$Sc(OTf)_3$	+	25	4	-
$Gd(OTf)_3$	+	25	4	-
$Yb(OTf)_3$	+	25	4	-
$ZnCl_2$	-	100	8	-
$Zn(OTf)_2$	-	25	4	+
none	+	n/a	48	-

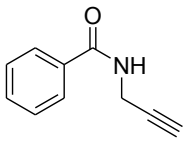
- *Screening of oxidants*



9a **10**

Oxidant	Conditions	Reaction time (h)	**9** present in the reaction mixture	Formation of **10a**	Isolated yield (%)
Air	toluene, reflux	8	+	+	11
MnO_2	CH_2Cl_2, r. t.	12	-	+	32
DDQ	CH_2Cl_2, r. t.	12	-	+	42
$K_3[Fe(CN)_6]$	Benzene/aq. NaOH, r. t.	12	-	+	**77**
$KMnO_4/SiO_2$	CH_2Cl_2, r. t.	0.5	-	+	56
Pd/C	benzene, reflux	3	+	-	0

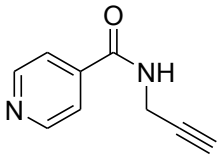
General procedure 1 (exemplified by preparation of benzoic acid propargylamide, 8a)[1]:



To a solution of benzoic acid (5.0 g, 40 mmol) in CH_2Cl_2 (100 mL) *N,N*-carbonyldiimidazole (CDI, 7.13 g, 44 mmol) was added and the mixture was stirred at r. t. for 30 min. Propargylamide (2.42 g, 44 mmol) was added dropwise and the stirring continued for 18 h. The reaction mixture was successively washed with 5% aqueous citric acid (2 x 50 mL) and 10% aqueous K_2CO_3 (2 × 50 mL). The organic phase was dried over anhydrous Na_2SO_4, filtered, concentrated in vacuo and further dried under high vacuum to provide analytically pure **8a** (6.23 g, 39 mmol, 98%) as pale yellow crystals; m. p. 103 – 105 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.90 (s, 1H, NH), 7.86 (d, J = 7.2 Hz, 2H, Ph 2,6-H), 7.59 – 7.41 (m, 3H, Ph 3,4,5-H), 4.06 (dd, J_1 = 5.5 Hz, J_2 = 2.4 Hz, 2H, CH_2), 3.10 (s, 1H, CH).

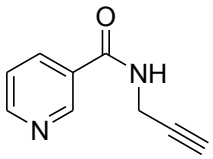
Compounds **8b-q** were prepared in an analogous manner and on approximately the same scale and are all either literature-described or commercially available compounds. Hence only ^{1}H NMR was used as the means to characterize these starting materials.

Isonicotic acid propargylamide (8b)[2]:



Yield 2.7 g (17.0 mmol, 71%); pale-yellow crystals, m.p. 140 – 142 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.27 (s, 1H, NH), 8.73 (d, J = 5.5 Hz, 2H, Py 2,6-H), 7.76 (d, J = 5.5 Hz, 2H, Py 3,5-H), 4.08 (dd, J_1 = 5.2 Hz, J_2 = 2.1 Hz, 2H, CH_2), 3.17 (s, 1H, CH).

Nicotic acid propargylamide (8c)[3]:



Yield 3.11 g (19.0 mmol, 81%); pale-yellow crystals, m.p. 85 – 87 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.15 (s, 1H, NH), 9.00 (d, J = 1.7 Hz, 1H, Py 2-H), 8.71 (dd, J_1 = 4.7 Hz, J_2 = 1.3

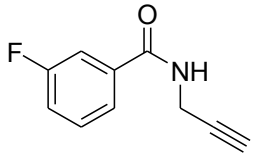
[1] Chachignon, H. *et al. J. Org. Chem*. **2015**, *80*, 5287-5295;

[2] Brik, A. *et al. ChemBioChem* **2003**, *4*, 1246-1248.

[3] Bai, H. *et al. MedChemComm* **2015**, *6*, 418-424.

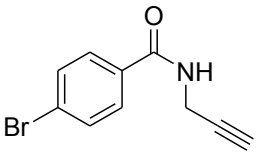
Hz, 1H, Py 6-H), 8.25 – 8.15 (m, 1H, Py 4-H), 7.51 (dd, J_1 = 7.8 Hz, J_2 = 4.8 Hz, 1H, Py 5-H), 4.08 (dd, J_1 = 5.4 Hz, J_2 = 2.4 Hz, 2H, CH_2), 3.16 (t, J = 2.3 Hz, 1H, CH).

3-Fluorobenzoic acid propargylamide (8d)[4]:



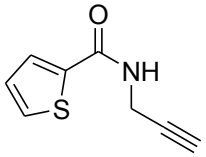
Yield 1.98 g (11.0 mmol, 79%); pale-yellow crystals, m.p. 120 – 122 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.02 (t, J = 5.3 Hz, 1H, NH), 7.67 (d, J = 7.7 Hz, 1H, Ph 6-H), 7.64 – 7.56 (m, 1H, Ph 5-H), 7.49 (td, J_1 = 8.0 Hz, J_2 = 85.9 Hz, 1H, Ph 4-H), 7.36 (td, J_1 = 8.4 Hz, J_2 = 2.3 Hz, 1H, Ph 2-H), 4.02 (dd, J_1 = 5.5 Hz, J_2 = 82.5 Hz, 2H, CH_2), 3.10 (t, J = 2.4 Hz, 1H, CH).

4-Bromobenzoic acid propargylamide (8e)[5]:



Yield 3.90 g (16.0 mmol, 66%), pale-yellow crystals, m.p. 168 – 170 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.02 (t, J = 5.4 Hz, 1H, NH), 7.80 (d, J = 8.5 Hz, 2H Ph 2,6-H), 7.68 (d, J = 8.5 Hz, 2H, Ph 3,5-H), 4.05 (dd, J_1 = 5.5 Hz, J_2 = 2.5 Hz, 2H, CH_2), 3.12 (t, J = 2.4 Hz, 1H, CH).

Thiophene-2-carboxylic acid propargylamide (8f)[6]:



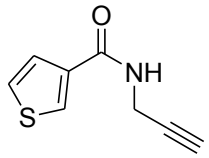
Yield 5.8 g (35.0 mmol, 90%), pale-yellow crystals, m.p. 109 – 111 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.57 (dd, J_1 = 3.7 Hz, J_2 = 0.8 Hz, 1H, Thienyl 3-H), 7.51 (d, J = 5.0 Hz, 1H, Thienyl 5-H), 7.09 (dd, J_1 = 4.9 Hz, J_2 = 3.8 Hz, 1H, Thienyl 4-H), 6.30 (s, 1H, NH), 4.25 (dd, J_1 = 5.1 Hz, J_2 = 2.5 Hz, 2H, CH_2), 2.29 (t, J = 2.5 Hz, 1H, CH).

[4] Guo, P. *et al. Chinese Chem. Lett.* **2013**, *24*, 957-961.

[5] Gao, X.-H. *et al. Synlett* **2016**, *27*, 1110-1115.

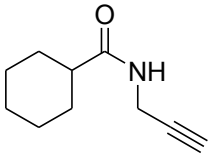
[6] Wang, B. *et al. J. Org. Chem.* **2015**, *80*, 12718-12724.

Thiophene-3-carboxylic acid propargylamide (8g)[7]:



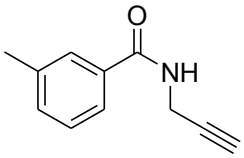
Yield 6.34 g (38.0 mmol, 98%), pale-yellow crystals, m.p. 105 – 107 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.92 (s, 1H), 7.42 (d, J = 5.0 Hz, 1H), 7.36 (dd, J_1 = 4.9 Hz, J_2 = 3.0 Hz, 1H), 6.30 (s, 1H), 4.24 (s, 2H), 2.29 (t, J = 2.4 Hz, 1H).

Cyclohyxanecarboxylic acid propargylamide (8h)[8]:



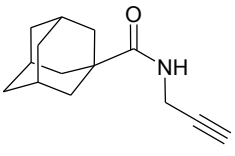
Yield 3.54 g (21.0, 91%), pale-yellow crystals, m.p. 102 – 104 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.76 (s, 1H, NH), 4.05 (dd, J_1 = 5.1 Hz, J_2 = 2.6 Hz, 2H, CH_2), 2.23 (t, J = 2.6 Hz, 1H, CH), 2.11 (tt, J = 11.7, 3.5 Hz, 1H, Cyclohexyl CH), 1.93 – 1.74 (m, 4H, Cyclohexyl), 1.72 – 1.62 (m, 1H, Cyclohexyl), 1.53 – 1.36 (m, 2H, Cyclohexyl), 1.35 – 1.16 (m, 3H, Cyclohexyl).

3-Methylbenzoic acid propargylamide (8i)[9]:



Yield 5.3 g (31.0 mmol, 79%), pale-yellow crystals, m.p. 50 – 52 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43 - 7.20 (3m, 4H, Ph 4 CH), 5.96 (s, 1H, NH), 4.25 (dd, J_1 = 5.2 Hz, J_2 = 2.5 Hz, 2H, CH_2), 2.47 (s, 3H, CH_3), 2.29 (t, J = 2.5 Hz, 1H, CH).

Adamantane-1-carboxylic acid propargylamide (8j)[10]:



[7] CAS 1247507-66-9; UORSY Building Block Library Catalog # BBV-32711101.

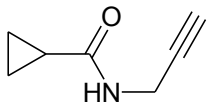
[8] Wang, J. *et al. J. Org. Chem.* **2013**, *78*, 8816-8820.

[9] Gao, X.-H. *et al. Synlett* **2016**, *27*, 1110-1115.

[10] Hashmi, A. S. K. *et al. Org. Lett.* **2004**, *6*, 4391-4394.

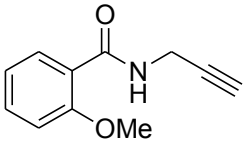
Yield 3.5 g (16.0 mmol, 95%), pale-yellow crystals, m.p. 115 – 117 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.76 (s, 1H, NH), 4.04 (dd, J_1 = 5.0 Hz, J_2 = 2.6 Hz, 2H, CH_2), 2.23 (t, J = 2.6 Hz, 1H, CH), 2.12 – 2.00 (m, 3H, Ad 3,5,7-CH), 1.92 – 1.84 (m, 6H, Ad 2,8,9-CH_2), 1.81 – 1.65 (m, 6H, Ad 4,6,10-CH_2).

Cyclopropanecarboxylic acid propargylamide (8k)[11]:



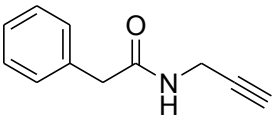
Yield 5.04 g (41.0 mmol, 70%), pale-yellow crystals, m.p. 64 – 66 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.21 (s, 1H, NH), 4.07 (s, 2H, CH_2), 2.24 (t, J = 2.4 Hz, 1H, CH), 1.52 – 1.32 (m, 1H, Cyclopropyl CH), 1.10 – 0.91 (m, 2H, Cyclopropyl CH_2), 0.90 – 0.67 (m, 2H, Cyclopropyl CH_2).

2-Methoxybenzoic acid propargylamide (8l)[12]:



Yield 4.95 g (24.0 mmol, 69%), white crystals, m.p. 40 – 42 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.22 (dd, J_1 = 7.8 Hz, J_2 = 1.8 Hz, 1H, Ph 6-H), 8.10 (s, 1H, NH), 7.52 – 7.40 (m, 1H, Ph 4-H), 7.08 (t, J = 7.5 Hz, 1H, Ph 5-H), 6.98 (d, J = 8.3 Hz, 1H, Ph 3-H), 4.27 (dd, J_1 = 5.1 Hz, J_2 = 2.5 Hz, 2H, CH_2), 3.98 (s, 3H, OCH_3), 2.26 (t, J = 2.5 Hz, 1H, CH).

Phenylacetic acid propargylamide (8m)[13]:



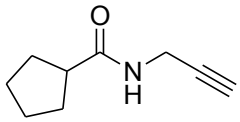
Yield 3.4 g (20.0 mmol, 91%), pale-yellow crystals, m.p. 80 – 82 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42 – 7.24 (m, 5H, Ph), 5.74 (s, 1H, NH), 4.02 (dd, J_1 = 5.3 Hz, J_2 = 2.5 Hz, 2H, CH_2), 3.61 (s, 2H, Ph-CH_2), 2.20 (t, J = 2.5 Hz, 1H, CH).

[11] Weyrauch, J. P. *et al. Chem. Eur. J.* **2010**, *16*, 956-963.

[12] Balaraman, K. *et al. Synthesis* **2010**, 3461-3464.

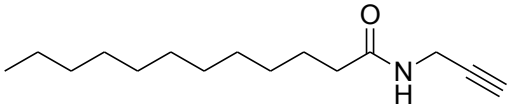
[13] Rajagopal, B. *et al. J. Org. Chem.* **2014**, *79*, 1254-1264.

Cyclopentanecarboxylic acid propargylamide (8n)[14]:



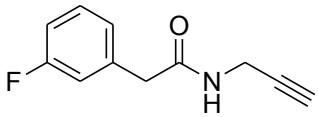
Yield 2.98 g (20.0 mmol, 76%), pale-yellow crystals, m.p. 100 – 102 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.65 (s, 1H, NH), 4.07 (dd, J_1 = 5.0 Hz, J_2 = 2.5 Hz, 2H, CH_2), 2.63 – 2.45 (m, 1H, Cyclopentyl CH), 2.24 (t, J = 2.5 Hz, 1H, CH), 1.95 – 1.47 (2m, 8H, Cyclopentyl 4CH_2).

Lauric acid propargylamide (8o)[15]:



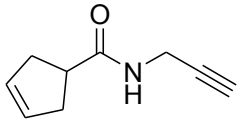
Yield 1.3 g (5.0 mmol, 37%), pale-yellow crystals, m.p. 84 – 86 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.21 (t, J = 5.1 Hz, 1H, NH), 3.82 (dd, J_1 = 5.5 Hz, J_2 = 2.5 Hz, 2H, CH_2), 3.07 (t, J = 2.5 Hz, 1H, CH), 2.05 (t, J = 7.4 Hz, 2H, Undecyl 1-CH_2), 1.54 – 1.40 (m, 2H, Undecyl 2-CH_2), 1.23 (s, 16H, Undecyl 3,4,5,6,7,8,9,10-CH_2), 0.85 (t, J = 6.6 Hz, 3H, Undecyl CH_3).

(3-Fluoro)phenylacetic acid propargylamide (8p)[16]:



Yield 3.54 g (19.0 mmol, 95%), pale-yellow crystals, m.p. 66 – 68 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.39 – 7.28 (m, 1H, Ph 5-H), 7.09 – 6.95 (m, 3H, Ph 2,4,6-H), 5.93 (d, J = 61.0 Hz, 1H, NH), 4.02 (dd, J_1 = 5.2, J_2 = 2.5 Hz, 2H, CH_2), 3.57 (s, 2H, Ph-CH_2), 2.22 (t, J = 2.5 Hz, 1H, CH).

Cyclopent-3-enecarboxylic acid propargylamide (8q)[17]:



[14] Allen, J. G. *et al.* PCT Int. Appl. WO 2007028131 A1; *Chem. Abstr.* **2007**, *146*, 316790.

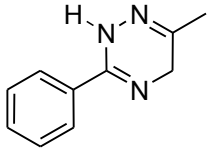
[15] Lindsey, E. A. *et al. Org. Biomol. Chem.* **2012**, *10*, 2552-2561.

[16] CAS 1250077-77-0. UORSY Building Blocks Catalog Number BBV-32710884.

[17] CAS 1342644-38-5. UORSY Building Blocks Catalog Number BBV-39215052.

Yield 3.41 g (19.0 mmol, 72%), off-white crystals, m.p. 105 – 107 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.70 (s, 3H, NH, Cyclopentenyl 1,2-CH), 4.08 (dd, J_1 = 5.2 Hz, J_2 = 2.5 Hz, 2H, CH_2), 3.07 – 2.89 (m, 1H, Cyclopentenyl 4-CH), 2.65 (d, J = 8.0 Hz, 4H, Cyclopentenyl 2CH_2), 2.25 (t, J = 2.5 Hz, 1H, CH).

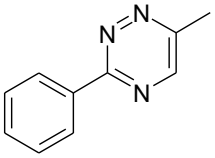
6-Methyl-3-phenyl-2,5-dihydro-1,2,4-triazine (9a).



To a solution of **8a** (1 g, 6.29 mmol) in toluene (40 mL) BocNHNH2 (0.83 g, 6. 29 mmol) and $Zn(OTf)_2$ (0.57 g, 1.57 mmol) were added. The resulting mixture was heated at reflux for 4 h and then cooled down to r. t. It was poured into 10% aqueous K_2CO_3 (100 mL) and extracted with ethyl acetate (3 x 50 mL). The combined organic extracts were dried over anhydrous Na_2SO_4, filtered and concentrated in vacuo. The residue was purified by column chromatography on silica gel using 0→3% gradient of methanol in chloroform to obtain 0.421 g (2.31 mmol, 37%) of the title compound as pale-yellow crystals, m.p. 56-58 °C (decomp.); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.53 – 8.48 (m, 1H, NH), 7.74 – 7.68 (m, 2H, Ph 2,6-H), 7.48 – 7.37 (m, 3H, Ph 3,4,5-H), 3.95 (s, 2H, CH_2), 2.03 (s, 3H, CH_3);^{13}C NMR (75 MHz, $CDCl_3$) δ 154.88 (Dihydrotriazine 3-C), 145.86 (Dihydrotriazine 6-C), 132.72 (Ph 1-C), 130.86 (Ph 4-C), 128.76 (Ph 3,5-C), 126.38 (Ph 2,6-C), 47.58 (Dihydrotriazine CH_2), 20.39 (CH_3). The product is markedly unstable to afford further characterization.

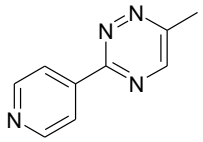
General procedure to obtain compounds 10a-r: The respective propargylamide **8** (1.26 mmol) in dry toluene (15 mL) was treated with $BocNHNH_2$ (**6**, 1.26 mmol) and $Zn(OTf)_2$ (0.32 mmol). The resulting mixture was heated under reflux in the atmosphere of argon for 4 h and then cooled down to r. t. Aqueous solution (10 mL) containing $K_3[Fe(CN)_6]$ (0.62 g, 1.89 mmol) and NaOH (0.13 g, 3.15 mmol) was added. The resulting biphasic mixture was vigorously stirred overnight. The organic phase was separated, dried over anhydrous Na_2SO_4, filtered and concentrated in vacuo. The residue was purified by column chromatography on silica gel using and appropriate gradient of ethyl acetate in hexane as eluent to provide analytically pure 1,2,4-triazines **10** in yields indicated.

6-Methyl-3-phenyl-1,2,4-triazine (10a)



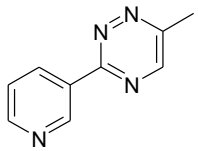
Yield 0.173 g (1.01 mmol, 80%). Pale-yellow crystals, mp = 65 – 67 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.54 (s, 1H, Tr), 8.53 – 8.47 (m, 2H, Ph 2,6-H), 7.59 – 7.49 (m, 3H, Ph 3,4,5-H), 2.76 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 162.13 (Tr 3-C), 156.30 (Tr 6-C), 149.28 (Tr 5-C), 134.84 (Ph 1-C), 131.40 (Ph 4-C), 128.85 (Ph 3,5-C), 127.98 (Ph 2,6-C), 19.41 (CH_3); HRMS (ESI), *m/z* calcd for $C_{10}H_{10}N_3$ [M+H+] 172.0869, found 172.0865.

6-Methyl-3-pyridin-4-yl-1,2,4-triazine (10b)



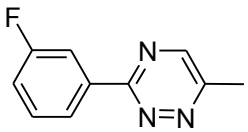
Yield 0.071 g (0.41 mmol, 33%), pale yellow crystals m.p. 112 – 114 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.84 (d, *J* = 5.56 Hz, 2H, Py 2,6-H), 8.63 (s, 1H, Tr), 8.40 (dd, *J* = 4.61, 1.54 Hz, 2H, Py 3,5-H), 2.82 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 160.38 (Tr 3-C), 157.94 (Tr 6-C), 150.24 (Tr 5-C), 149.50 (Py 2,5-C), 142.68 (Py 4-C), 121.78 (Py 3,5-C), 19.59 (CH_3); HRMS (ESI) *m/z* calcd for $C_9H_9N_4$ [M+H$^+$] 173.0821, found 173.0814.

6-Methyl-3-pyridin-3-yl-1,2,4-triazine (10c)



Yield 0.080 g (0.47 mmol, 37%), pale-yellow crystals, m.p. 109 – 111 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 9.73 (s, 1H, Py 2-H), 8.88 (d, *J* = 8.01 Hz, 1H, Py 6-H), 8.81 (d, *J* = 3.94 Hz, 1H, Py4-H), 8.61 (s, 1H, Tr), 7.62 – 7.50 (m, 1H, Py 5-H), 2.81 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 160.34 (Tr 3-C), 157.31 (Tr 6-C), 151.08 (Py 2-C), 149.41 (Py 6-C), 148.64 (Tr 5-C), 136.10 (Py 4-C), 131.17 (Py 3-C), 124.04 (Py 5-C), 19.50 (CH_3); HRMS (ESI) *m/z* calcd for $C_9H_9N_4$ [M+H$^+$] 173.0821, found 173.0824

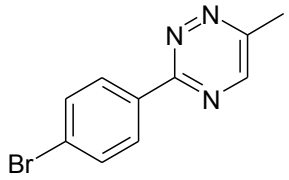
3-(3-Fluorophenyl)-6-methyl-1,2,4-triazine (10d)



Yield 0.09 g (0.48 mmol, 42%), pale-yellow crystals, m.p. 57 – 59 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.56 (s, 1H, Tr), 8.32 (dt, J_1 = 7.87 Hz, J_2 = 1.19 Hz, 1H, Ph 6-H), 8.27 – 8.16 (m, 1H, Ph 2-H), 7.51 (td, J_1 = 8.05 Hz, J_2 =5.79 Hz, 1H, Ph 5-H), 7.27 – 7.20 (m, 1H, Ph 4-H), 2.78 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 163.22 (d, *J* = 245.75 Hz, Ph 3-C), 161.15 (d, *J* = 3.21

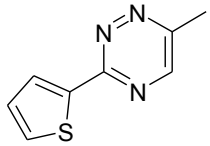
Hz, Tr 3-C), 156.75 (Tr 6-C), 149.30 (Tr 5-C), 137.14 (d, J = 8.09 Hz, Ph 1-C), 130.40 (d, J = 7.99 Hz, Ph 5-C), 123.62 (d, J = 2.99 Hz, Ph6-C), 118.31 (d, J = 21.36 Hz, Ph 4-C), 114.86 (d, J = 23.67 Hz, Ph 2-C), 19.41 (CH_3); HRMS (ESI) *m/z* calcd for $C_{10}H_9FN_3$ [M+H$^+$] 190.0775, found 190.0774.

3-(4-Bromophenyl)-6-methyl-1,2,4-triazine (10e)



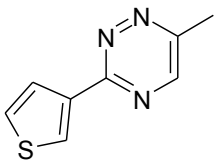
Yield 0.123 g (0.49 mmol, 58%), pale-yellow crystals, m.p. 149 – 151 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.54 (s, 1H, Tr), 8.39 (d, J = 8.59 Hz, 2H, Ph 2,6-H), 7.66 (d, J = 8.56 Hz, 2H, Ph 3,5-H), 2.76 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ161.41 (Tr 3-C), 156.54 (Tr 6-C), 149.28 (Tr 5-C), 133.78 (Ph 1-C), 132.09 (Ph 2,6-C), 129.50 (Ph 3,5-C), 126.30 (Ph 6-C), 19.43 (CH_3); HRMS (ESI) *m/z* calcd for $C_{10}H_9BrN_3$ [M+H$^+$] 249.9974, found 249.9970.

6-Methyl-3-thiophen-2-yl-1,2,4-triazine (10f)



Yield 0.051 g (0.28 mmol, 23%), pale-yellow crystals, m.p. 112 – 114 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.46 (s, 1H, tr), 8.15 (dd, J_1 = 3.71 Hz, J_2 = 1.07 Hz, 1H, Thienyl 3-H), 7.57 (dd, J_1 = 4.99 Hz, J_2 = 1.07 Hz, 1H, Thienyl 5-H), 7.21 (dd, J_1 = 4.93 Hz, J_2 = 3.79 Hz, 1H, Thienyl 4-H), 2.74 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 159.61 (Tr 6-C), 155.62 (Tr 3-C), 149.31 (Tr 5-C), 139.47 (Thienyl 2-C), 130.80 (Thienyl 3-C), 129.90 (Thienyl 5-C), 128.50 (Thienyl 4-C), 19.35 (CH_3); HRMS (ESI) *m/z* calcd for $C_8H_8N_3S$ [M+H$^+$] 178.0433, found 178.0427.

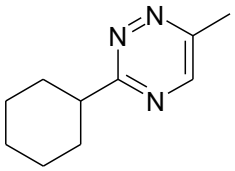
6-Methyl-3-thiophen-3-yl-1,2,4-triazine (10g)



Yield 0.131 g (0.74 mmol, 61%), pale-yellow crystals, m.p. 83 – 85 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.50 (s, 1H, Tr), 8.42 (dd, J_1 = 3.07 Hz, J_2 =1.19 Hz, 1H, Thienyl 2-H), 8.00 (dd, J_1 =5.09 Hz, J_2 =1.19 Hz, 1H, Thienyl 5-H), 7.45 (dd, J_1 = 5.09 Hz, J_2 =3.08 Hz, 1H, Thienyl 4-H), 2.74 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ159.60 (Tr 3-C), 155.74 (Tr 6-C), 149.34 (Tr 5-

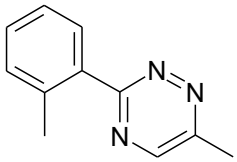
C), 138.30 (Thienyl 2-C), 128.59 (Thienyl 5-C), 127.00 (Thienyl 4-C), 126.64 (Thienyl 3-C), 19.43 (CH_3); HRMS (ESI) *m/z* calcd for $C_8H_8N_3S$ [M+H$^+$] 178.0433, found 178.0427.

3-Cyclohexyl-6-methyl-1,2,4-triazine (10h)



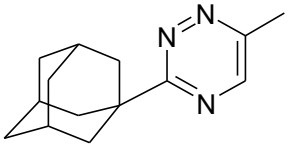
Yield 0.133 g (0.73 mmol, 61%), pale-yellow crystals, m.p. 63 – 65 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.43 (s, 1H, Tr), 3.09 (tt, J_1 = 11.76 Hz, J_2 = 3.46 Hz, 1H, Cyclohexyl CH), 2.69 (s, 3H, CH_3), 2.11 - 1.97 (m, 2H, Cyclohexyl CH_2), 1.95 – 1.83 (m, 2H, Cyclohexyl CH_2), 1.57 - 1.23 (m, 2H, Cyclohexyl CH_2), 1.56 – 1.24 (m, 4H, Cyclohexyl CH_2); ^{13}C NMR (75 MHz, $CDCl_3$): δ 171.01 (Tr 3-C), 155.98 (Tr 6-C), 149.24 (Tr 5-C), 45.11 (Cyclohexyl 1-C), 31.61 (Cyclohexyl 2,6-C), 26.10 (Cyclohexyl 3,5-C), 25.85 (Cyclohexyl 4-C), 19.25 (CH_3); HRMS (ESI) *m/z* calcd for $C_{10}H_{16}N_3$ [M+H$^+$] 178.1338, found 178.1333.

6-Methyl-3-(2-methylphenyl)-1,2,4-triazine (10i)



Yield 0.104 g (0.55 mmol, 47%), yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.58 (s, 1H, Tr), 7.95 – 7.85 (m, 1H, Ph 6-H), 7.45 – 7.31 (m, 3H, Ph 3,4,5-H), 2.77 (s, 3H, Tr-CH_3), 2.59 (s, 3H, Ph-CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 165.03 (Tr 3-C), 155.60 (Tr 6-C), 148.81 (Tr 5-C), 137.84 (Ph 2-C), 135.01 (Ph 6-C), 131.51 (Ph 1-C), 130.66 (Ph 3-C), 130.17 (Ph 4-C), 126.10 (Ph 5-C), 21.24 (Ph-CH_3), 19.37 (Tr-CH_3); HRMS (ESI) *m/z* calcd for $C_{11}H_{12}N_3$ [M+H$^+$] 186.1025, found 186.1022.

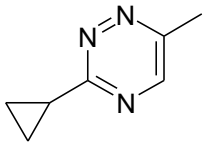
3-Adamantyl-6-methyl-1,2,4-triazine (10j)



Yield 0.131 g (0.57 mmol, 62%), pale-yellow crystals, m.p. 92 – 94 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.43 (s, 1H, Tr), 2.68 (s, 3H, CH_3), 2.13 (s, 9H, Ad 2,8,9-CH, 3,5,7-CH_2), 1.81 (s, 6H, Ad 4,6,10-CH_2); ^{13}C NMR (75 MHz, $CDCl_3$): δ172.82 (Tr 3-C), 155.58 (Tr 6-C), 149.01 (Tr 5-

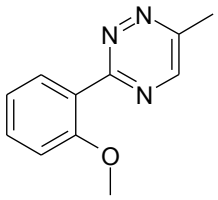
C), 40.89 (Ad 2,8,9-C), 39.91 (Ad 1-C), 36.61 (Ad 4,6,10-C), 28.44 (Ad 3,5,7-C), 19.26 (CH_3); HRMS (ESI) *m/z* calcd for $C_{14}H_{20}N_3$ [M+H$^+$] 230.1651, found 230.1647.

3-Cyclopropyl-6-methyl-1,2,4-triazine (10k)



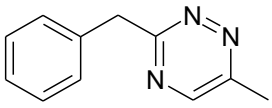
Yield 0.072 g (0.52 mmol, 32%), yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.30 (s, 1H, Tr), 2.64 (s, 3H, CH_3), 2.50 – 2.38 (m, 1H, Cyclopropyl CH), 1.19 – 1.12 (m, 4H, Cyclopropyl 2CH_2); ^{13}CNMR (75 MHz, $CDCl_3$): δ 168.95 (Tr 3-C), 155.39 (Tr 6-C), 149.15 (Tr 5-C), 19.12 (CH_3), 16.00 (Cyclopropyl 1-C), 10.73 (Cyclopropyl 2,3-C); HRMS (ESI) *m/z* calcd for $C_7H_{10}N_3$ [M+H$^+$] 136.0869, found 136.0864.

3-(2-Methoxyphenyl)-6-methyl-1,2,4-triazine (10l)



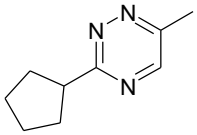
Yield 0.073 g (0.35 mmol, 35%), amorphous solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.59 (s, 1H, Tr), 7.79 (dd, J_1 = 7.60 Hz, J_2 = 1.78 Hz, 1H, Ph 6-H), 7.53 – 7.45 (m, 1H, Ph 3-H), 7.15 – 7.05 (m, 2H, Ph 4,5-H), 3.88 (s, 3H, OCH_3), 2.77 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.62 (Ph 2-C), 157.91 (Tr 3-C), 155.77 (Tr 6-C), 148.76 (Tr 5-C), 131.83 (Ph 6-C), 131.81 (Ph 4-C), 125.35 (Ph 1-C), 120.82 (Ph 5-C), 111.96 (Ph 3-C), 56.03 (OCH_3), 19.44 (CH_3); HRMS (ESI) *m/z* calcd for $C_{11}H_{12}N_3O$ [M+H$^+$] 202.0974, found 202.0982.

3-Benzyl-6-methyl-1,2,4-triazine (10m)



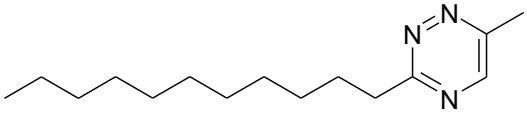
Yield 0.083 g (0.43 mmol, 37%), yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.40 (s, 1H, Tr), 7.42 – 7.18 (m, 5H, Ph), 4.42 (s, 2H, CH_2), 4.42 (s, 2H), 2.66 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 166.83 (Tr 3-C), 156.26 (Tr 6-C), 149.66 (Tr 5-C), 137.36 (Ph 1-C), 129.19 (Ph 3,5-C), 128.65 (Ph 2,6-C), 126.88 (Ph 4-C), 43.25 (CH_2), 19.24 (CH_3); HRMS (ESI) *m/z* calcd for $C_{11}H_{12}N_3$ [M+H$^+$] 186.1025, found 186.1032.

3-Cyclopentyl-6-methyl-1,2,4-triazine (10n)



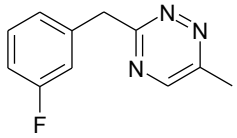
Yield 0.092 g (0.55 mmol, 42%), yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.43 (s, 1H, Tr), 3.63 – 3.49 (m, 1H, Cyclopentyl CH), 2.69 (s, 3H, CH_3), 2.23 – 1.69 (3m, 8H, Cyclopentyl 4CH_2); ^{13}C NMR (75 MHz, $CDCl_3$): δ 171.20 (Tr 3-C), 155.88 (Tr 6-C), 149.38 (Tr 5-C), 46.33 (Cyclopentyl 1-C), 32.92 (Cyclopentyl 2,5-C), 26.09 (Cyclopentyl 3,4-C), 19.26 (CH_3); HRMS (ESI) *m/z* calcd for $C_9H_{14}N_3$ [M+H$^+$] 164.1182, found 164.1184.

6-Methyl-3-undecyl-1,2,4-triazine (10o)



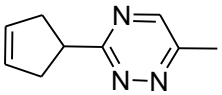
Yield 0.062 g (0.35 mmol, 29%), pale-yellow crystals, m.p, 59 – 61 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.43 (s, 1H, Tr), 3.15 – 3.02 (m, 2H, Undecyl 1-CH_2), 2.69 (s, 3H, Tr-CH_3), 1.91 – 1.78 (m, 2H, Undecyl 2-CH_2), 1.56 – 1.17 (m, 16H, Undecyl 3,4,5,6,7,8,9,10-CH_2), 0.91 – 0.85 (m, 3H, Undecyl CH_3); ^{13}C NMR (75 MHz, DMSO) δ 168.24 (Tr 3-C), 155.88 (Tr 6-C), 149.26 (Tr 5-C), 36.83 (Undecyl 1-C), 31.91 (Undecyl 9-C), 29.61 (Undecyl 7-C), 29.50 (Undecyl 3-C), 29.38 (Undecyl 4-C), 29.34 (Undecyl 5,7-C), 29.26 (Undecyl 6-C), 28.52 (Undecyl 6-C), 22.69 (Undecyl 10-C), 19.25 (Tr CH_3), 14.12 (Undecyl CH_3); HRMS (ESI) *m/z* calcd for $C_{15}H_{28}N_3$ [M+H$^+$] 250.2277, found 250.2289.

3-(3-Fluorobenzyl)-6-methyl-1,2,4-triazine (10p)



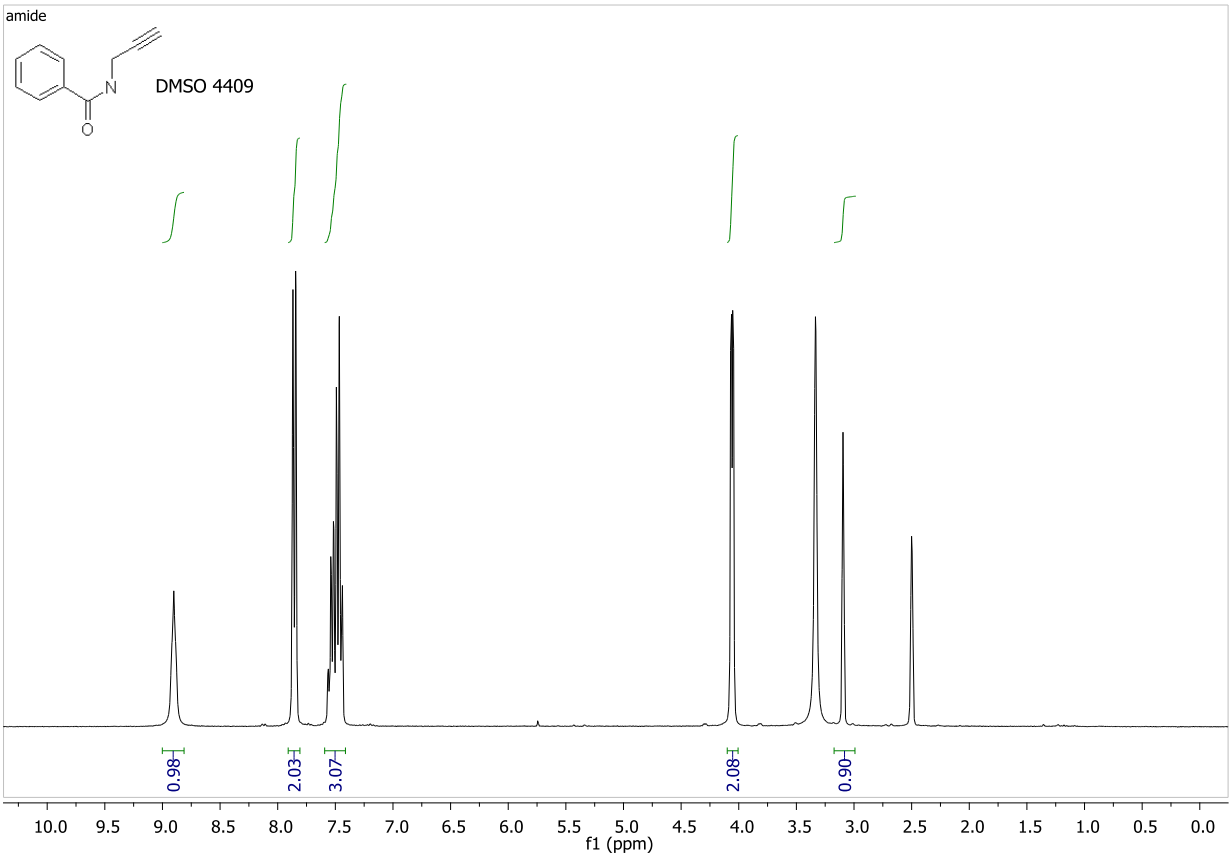
Yield 0.092 g (0.44 mmol, 42%), yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.40 (s, 1H, Tr), 7.28 – 7.19 (m, 1H, Ph 6-H), 7.12 (d, *J* = 7.68 Hz, 1H, Ph 2-H), 7.09 – 7.03 (m, 1H, Ph 5-H), 6.94 – 6.85 (m, 1H, Ph 4-H), 4.38 (s, 2H, CH_2), 2.65 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.29 (Tr 3-C), 162.83 (d, *J* = 246.07 Hz, Ph 3-C), 156.48 (Tr 6-C), 149.68 (Tr 5-C), 139.64 (d, *J* = 7.58 Hz, Ph 1-C), 130.07 (d, *J* = 8.32 Hz, Ph 5-C), 124.87 (d, *J* = 2.86 Hz, Ph 6-C), 116.14 (d, *J* = 21.61 Hz, Ph 2-C), 113.83 (d, *J* = 21 Hz, Ph 4-C), 42.87 (d, *J* = 1.53 Hz, CH_2), 19.25 (CH_3); HRMS (ESI) *m/z* calcd for $C_{11}H_{11}FN_3$ [M+H$^+$] 204.0931, found 204.0942.

3-Cyclopent-3-enyl-6-methyl-1,2,4-triazine (10q)

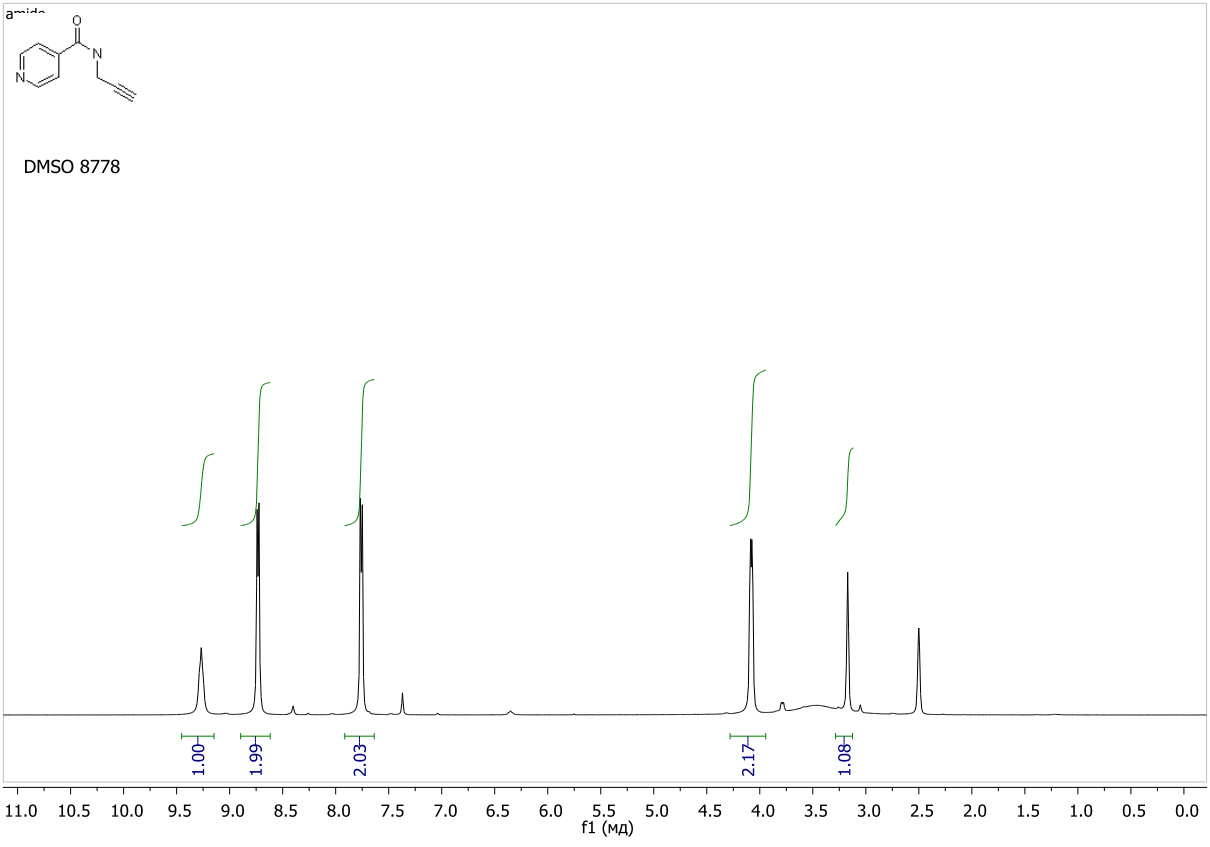


Yield 0.091 g (0.56 mmol, 42%), yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.42 (s, 1H, Tr), 5.74 (s, 2H, Cyclopentenyl 1,2-CH), 4.10 – 3.88 (m, 1H, Cyclopentenyl 4-CH), 2.97 – 2.69 (m, 4H, Cyclopentenyl $2CH_2$), 2.66 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.97 (Tr 3-C), 156.03 (Tr 6-C), 149.53 (Tr 5-C), 129.29 (Cyclopentenyl 1,2-C), 43.56 (Cyclopentenyl 4-C), 39.05 (Cyclopentenyl 3,5-C), 19.24 (CH_3); HRMS (ESI) *m/z* calcd for $C_9H_{12}N_3$ [$M+H^+$] 162.1025, found 162.1032.

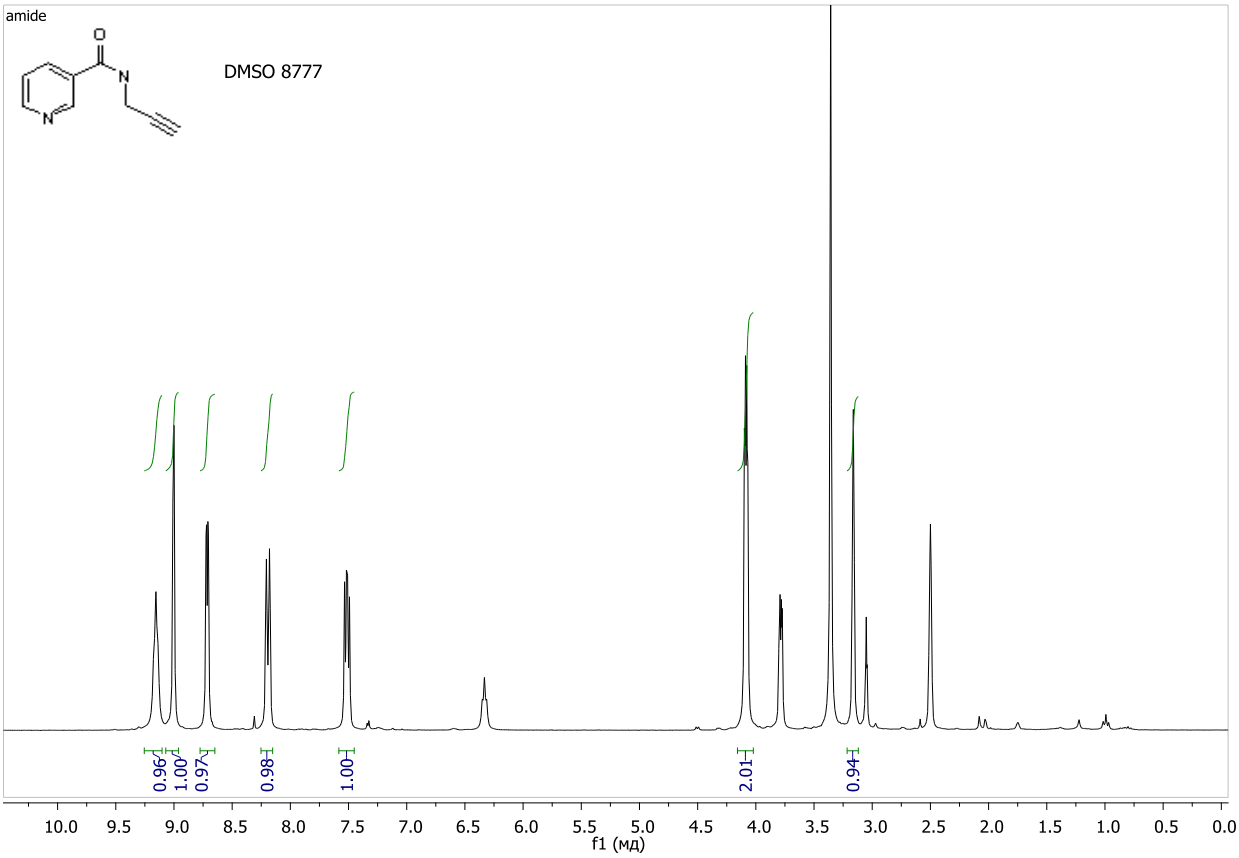
Compound **8a:**



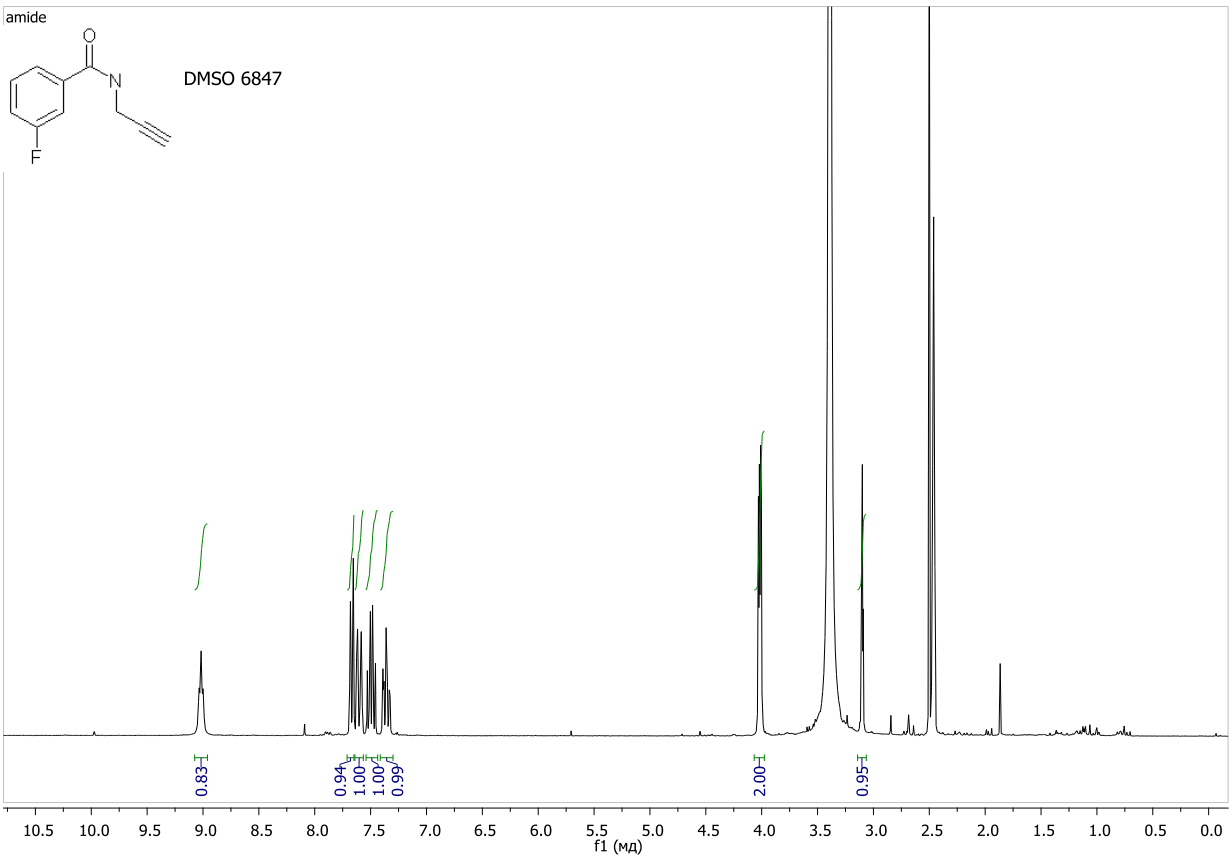
Compound **8b:**



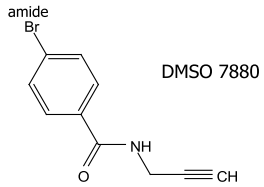
Compound **8c:**

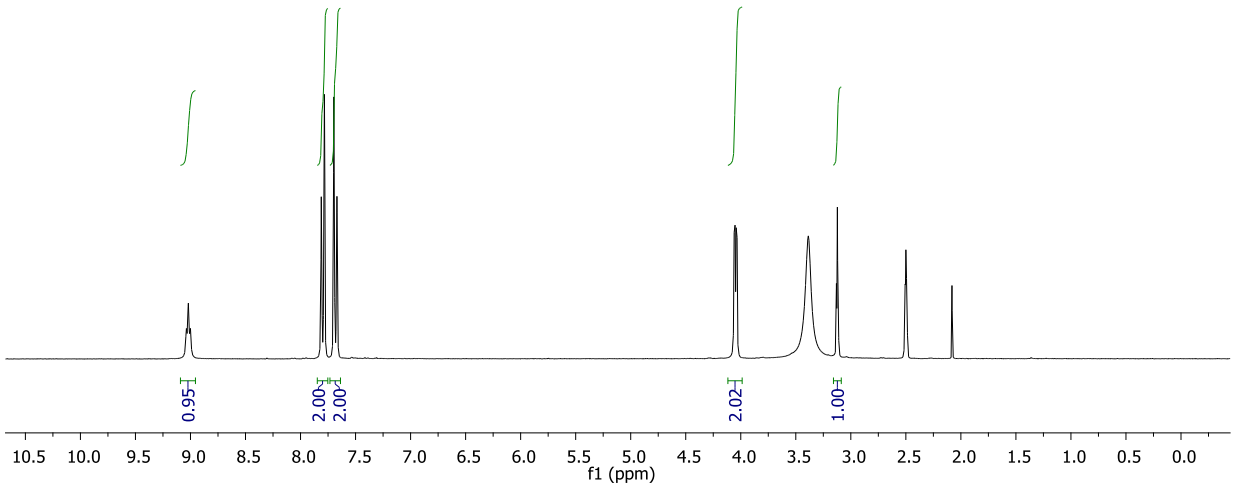


Compound **8d:**

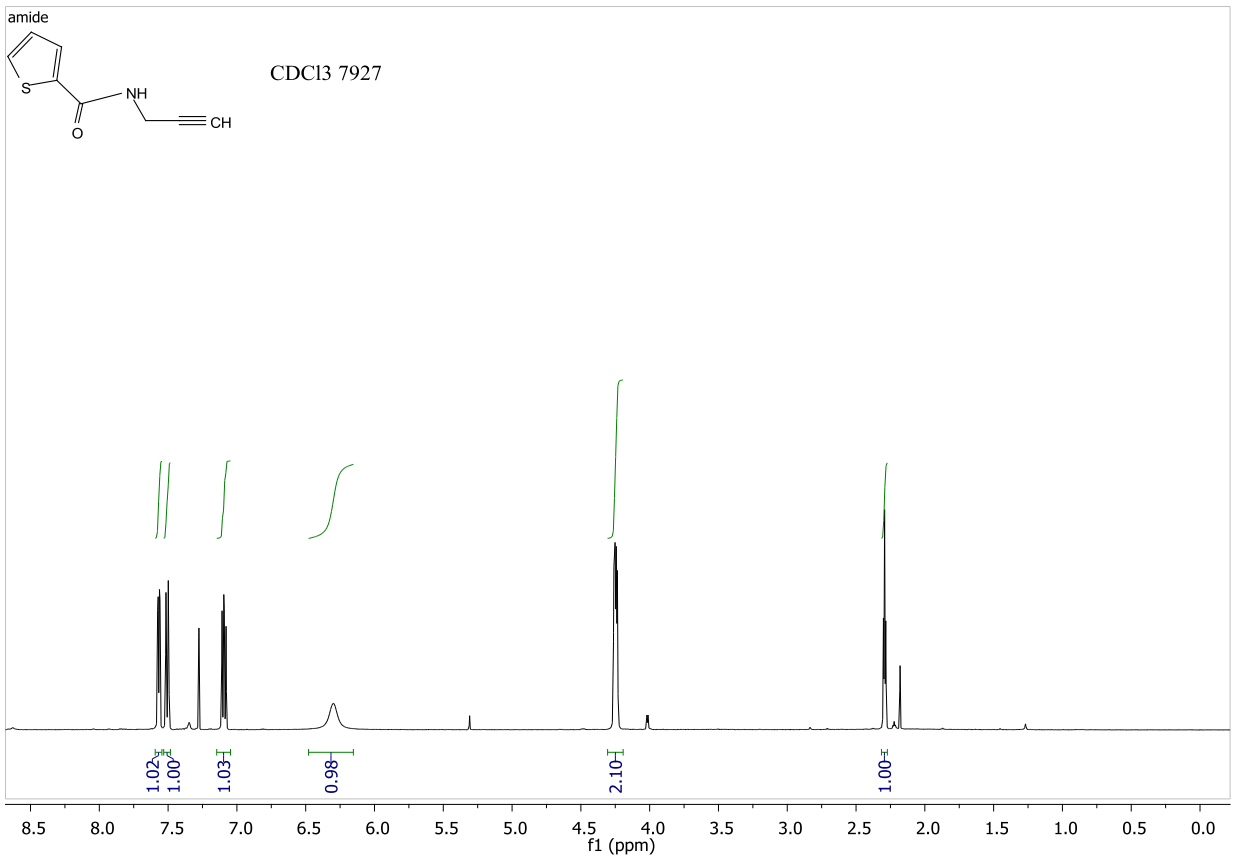


Compound **8e:**

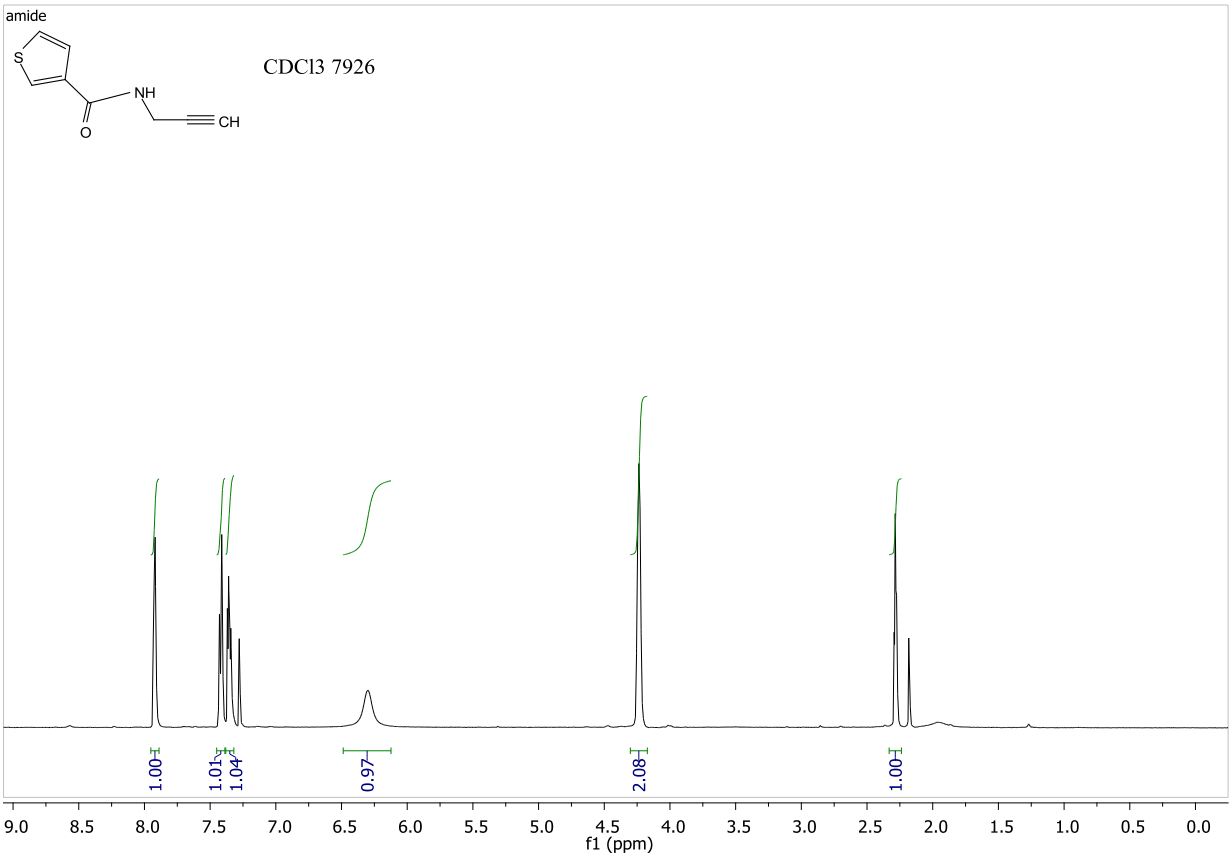




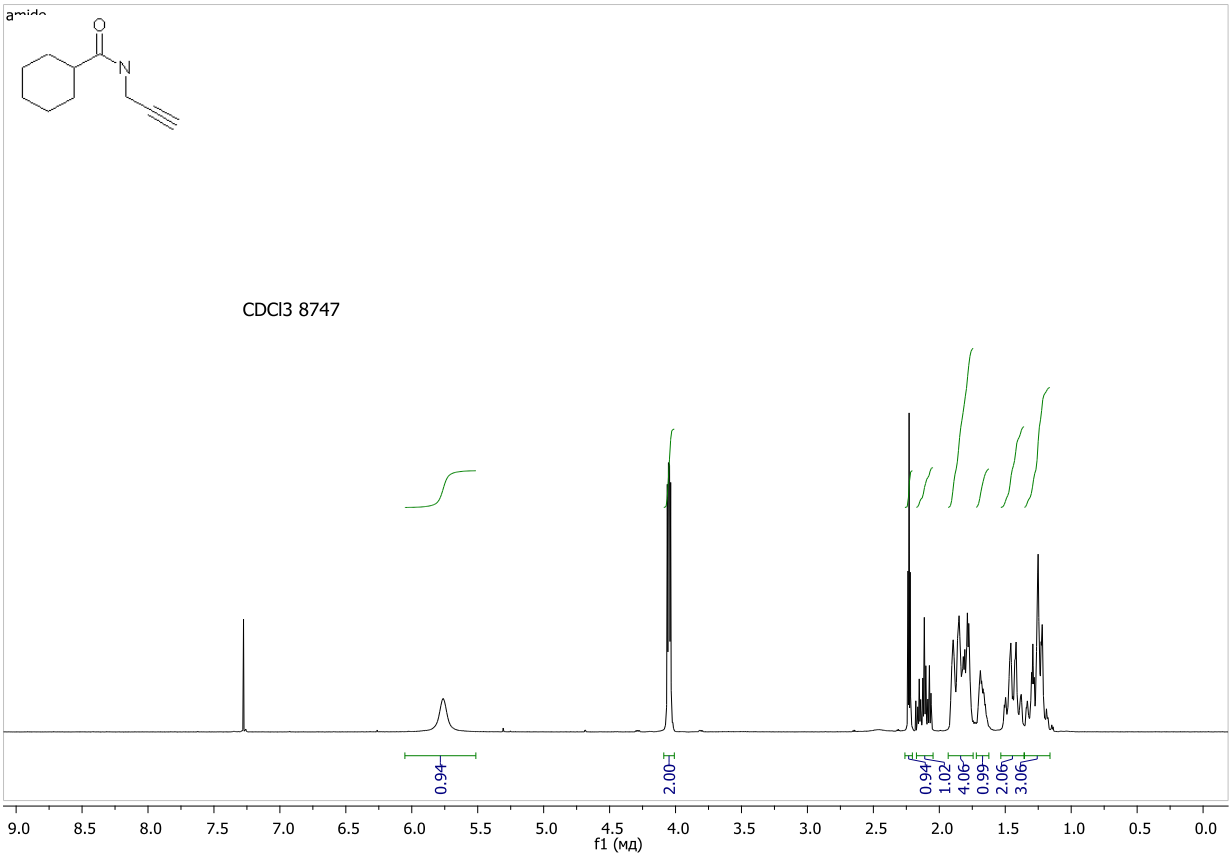
Compound **8f:**



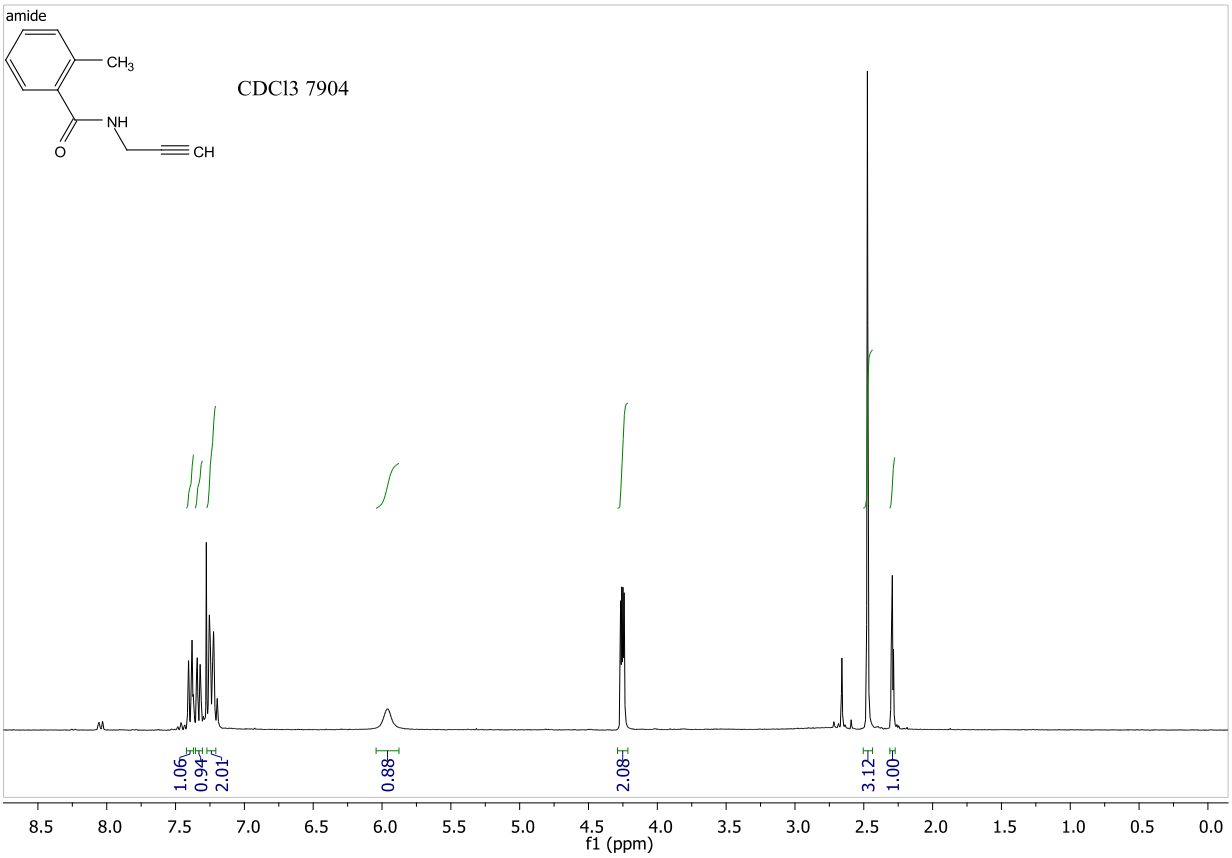
Compound **8g:**



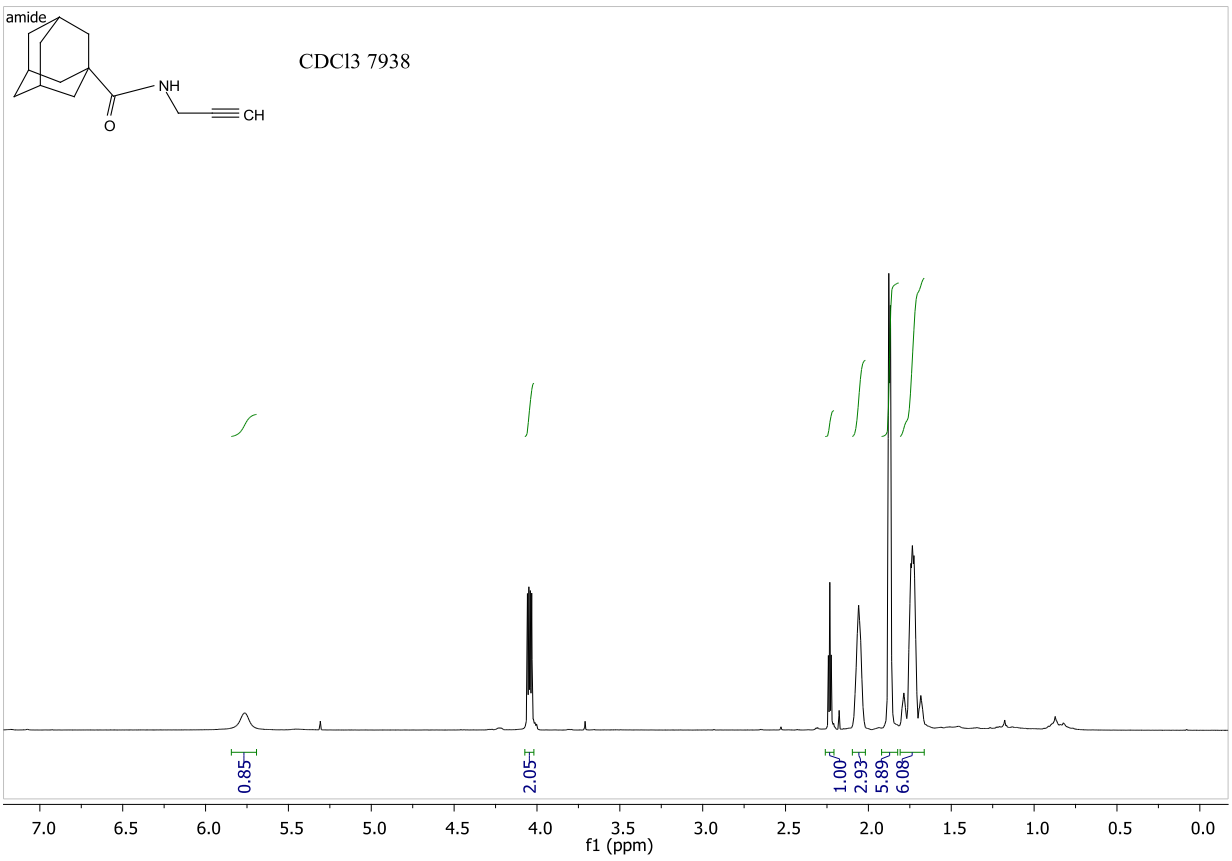
Compound **8h:**



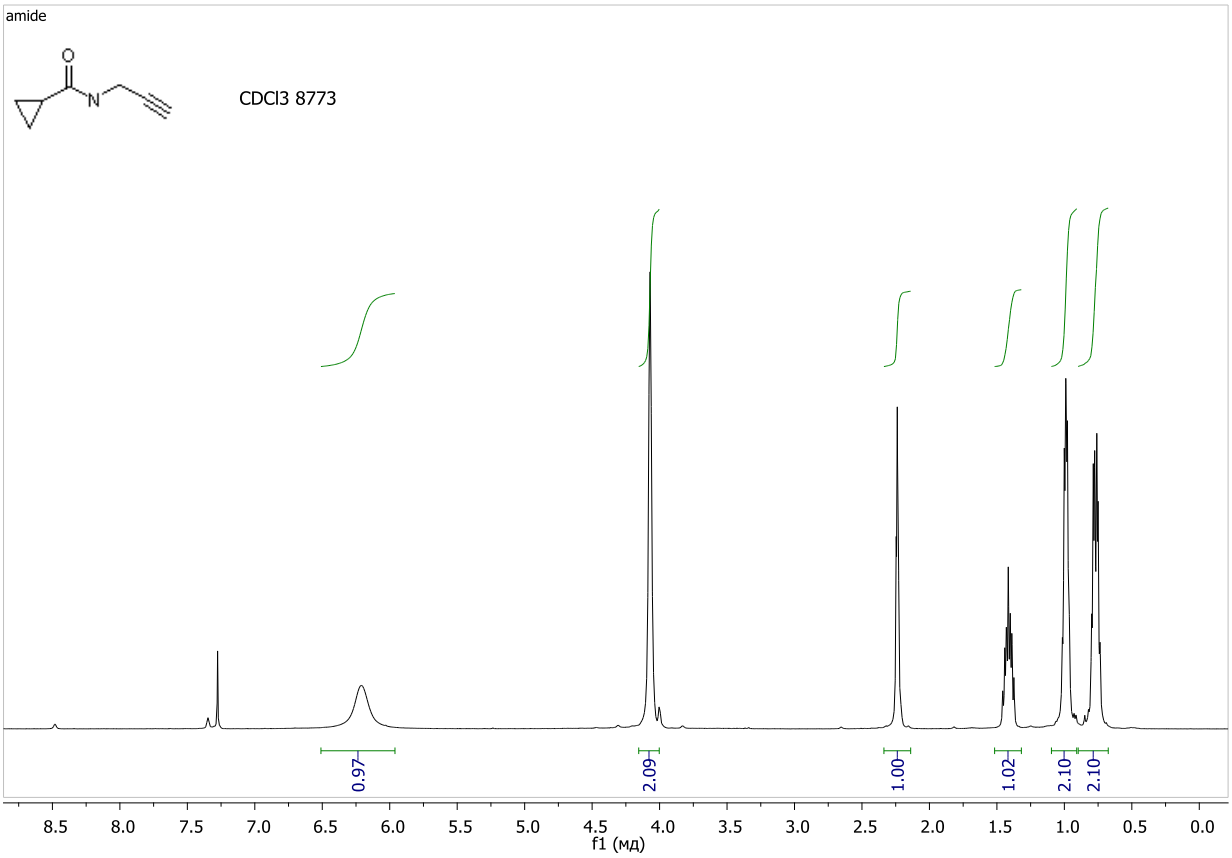
Compound **8i:**



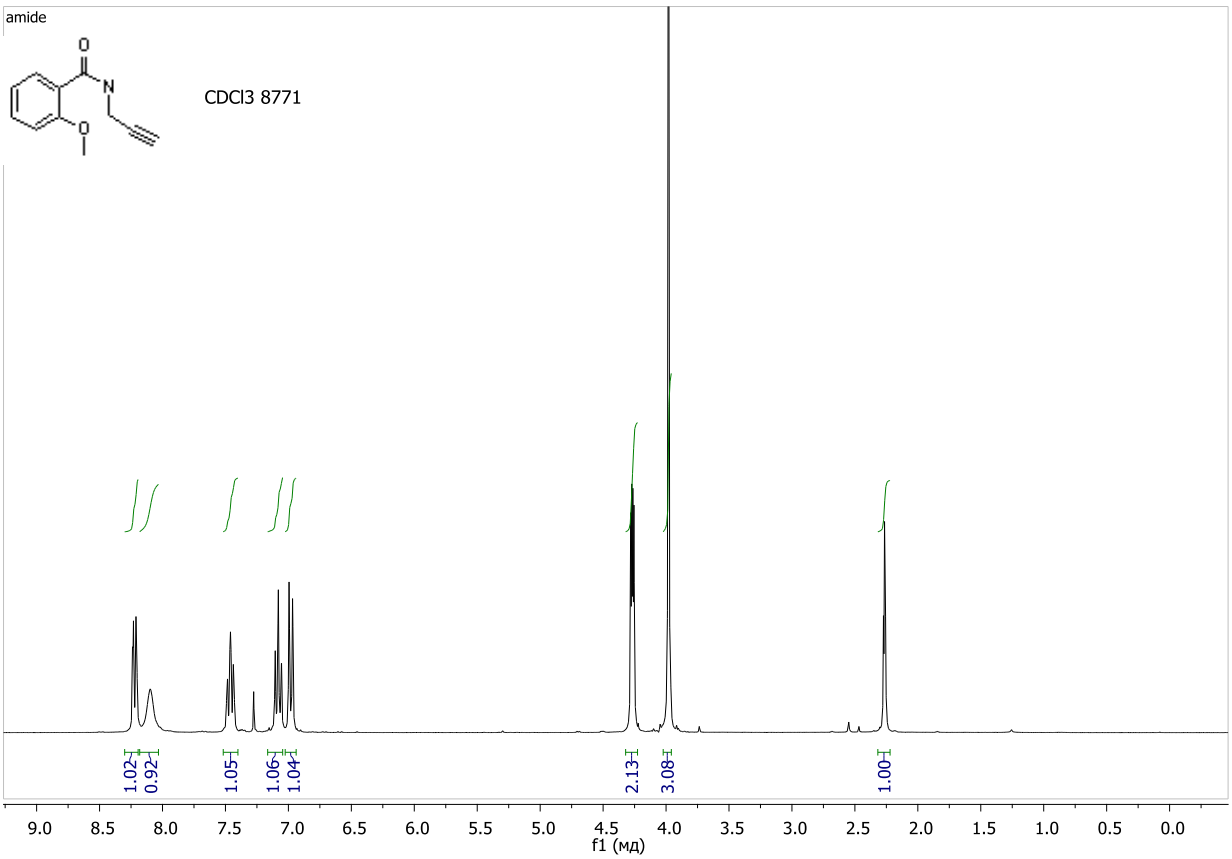
Compound **8j:**



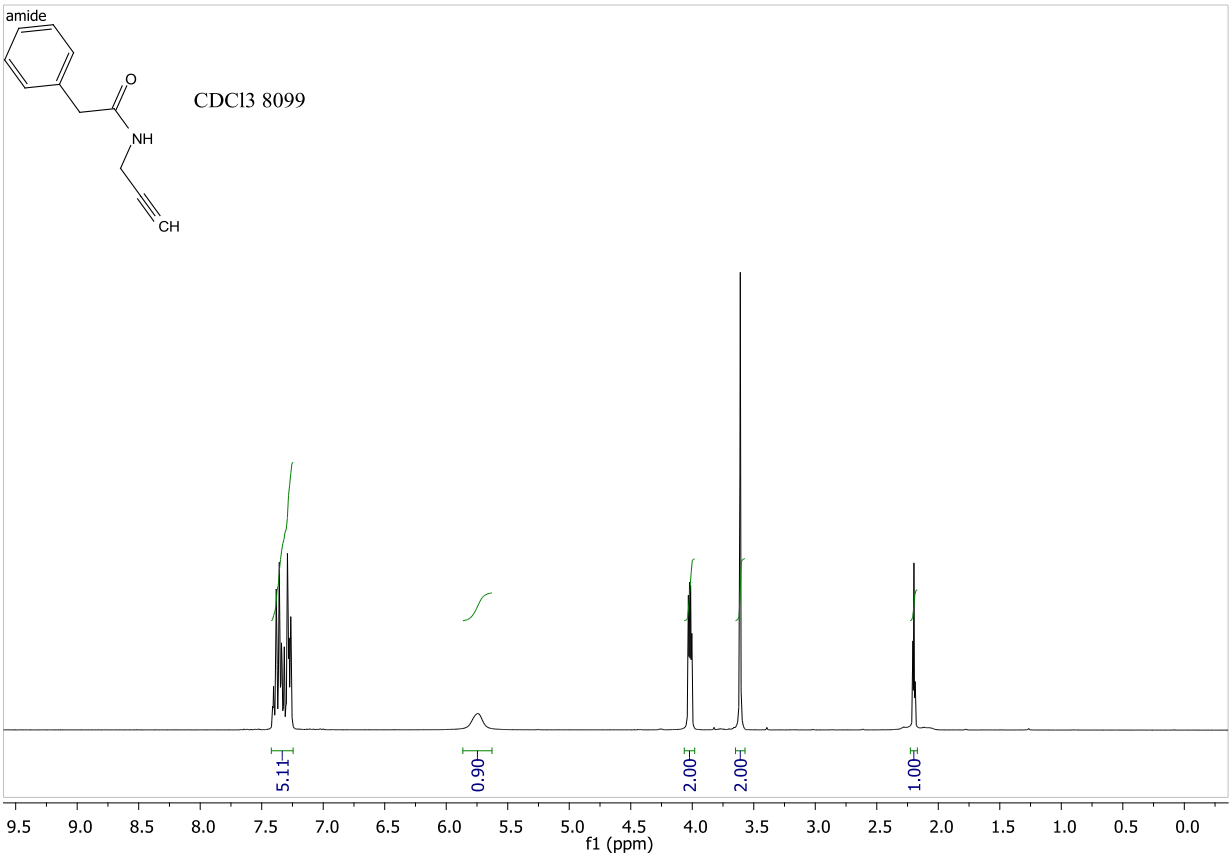
Compound **8k:**



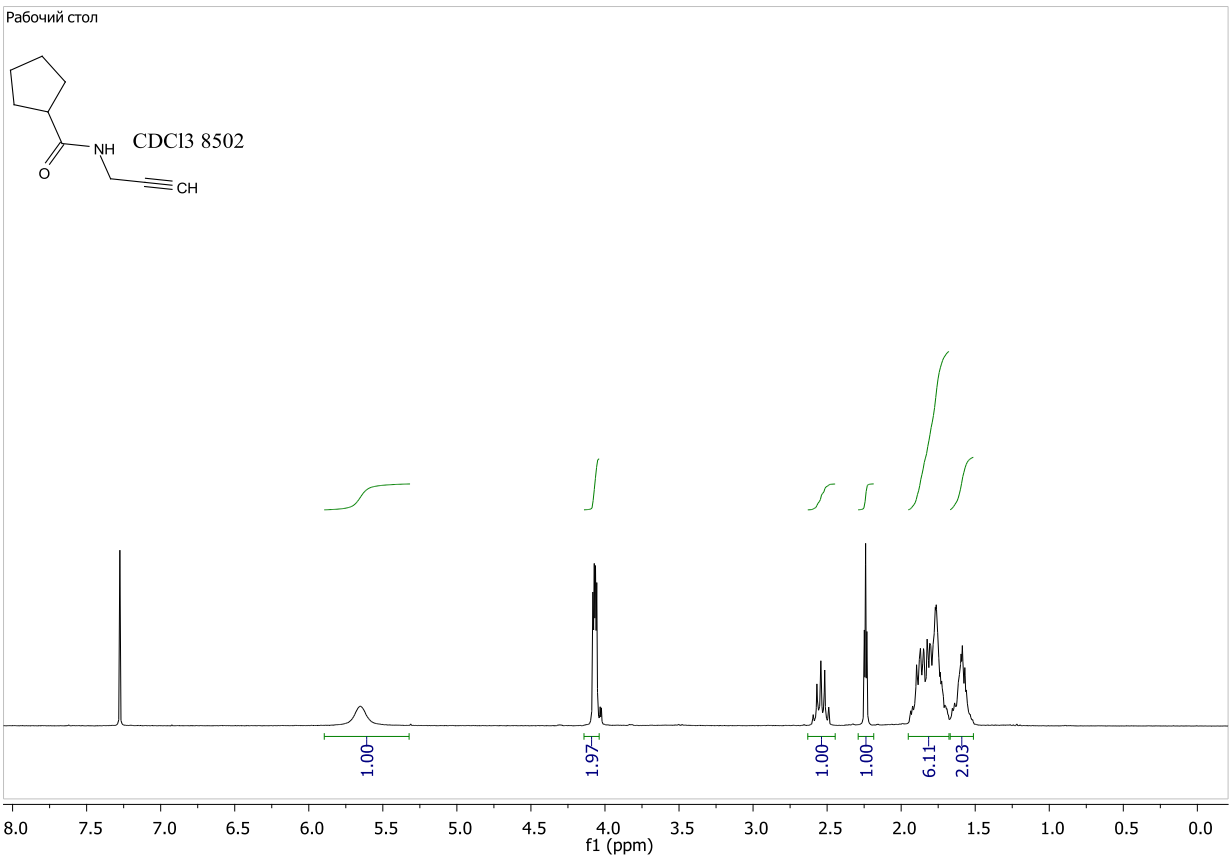
Compound **8l:**



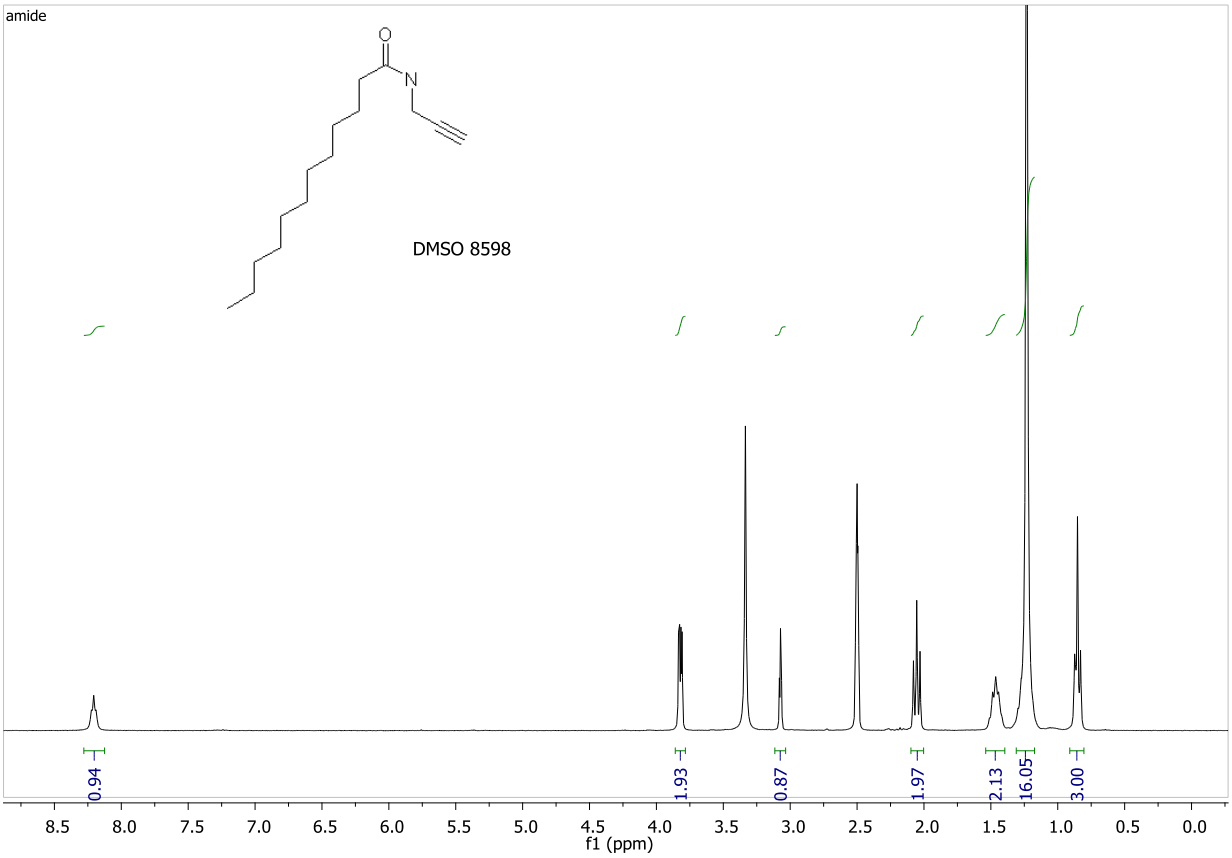
Compound **8m:**



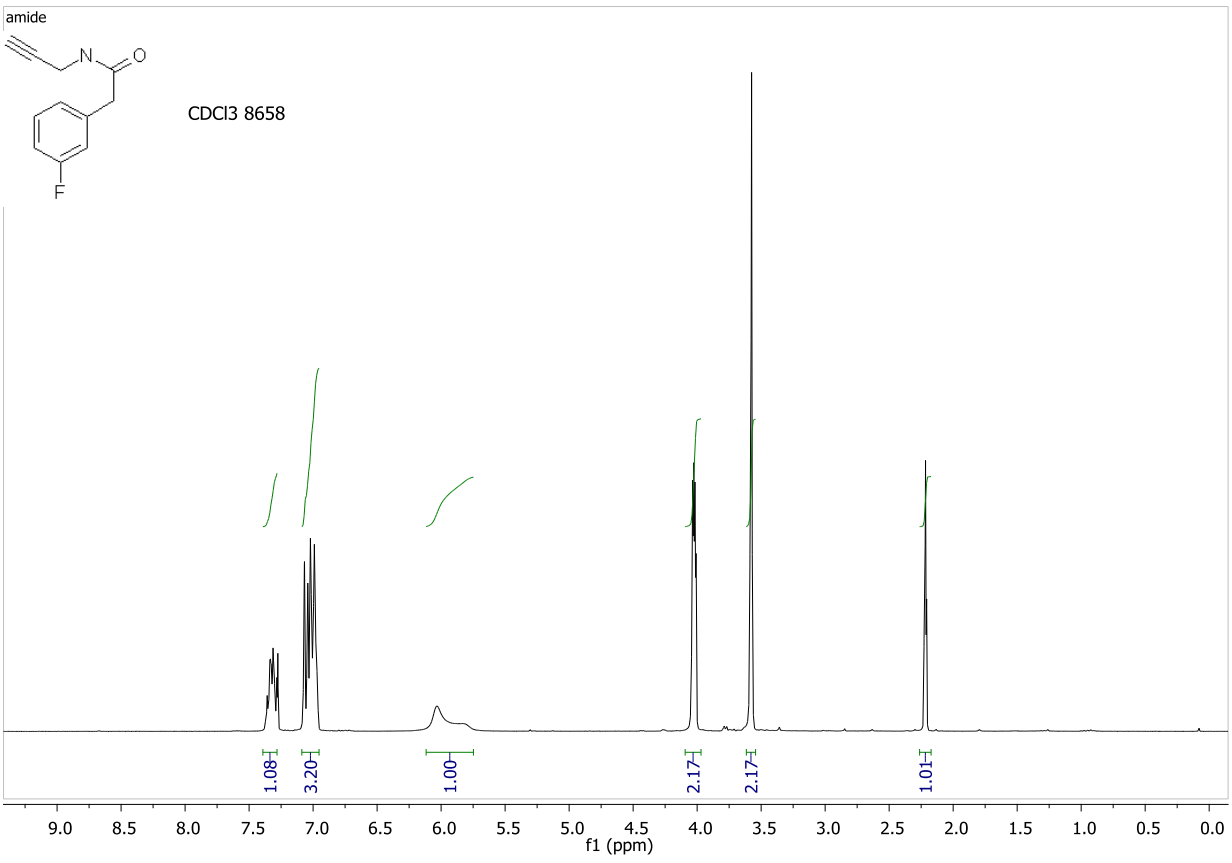
Compound **8n:**



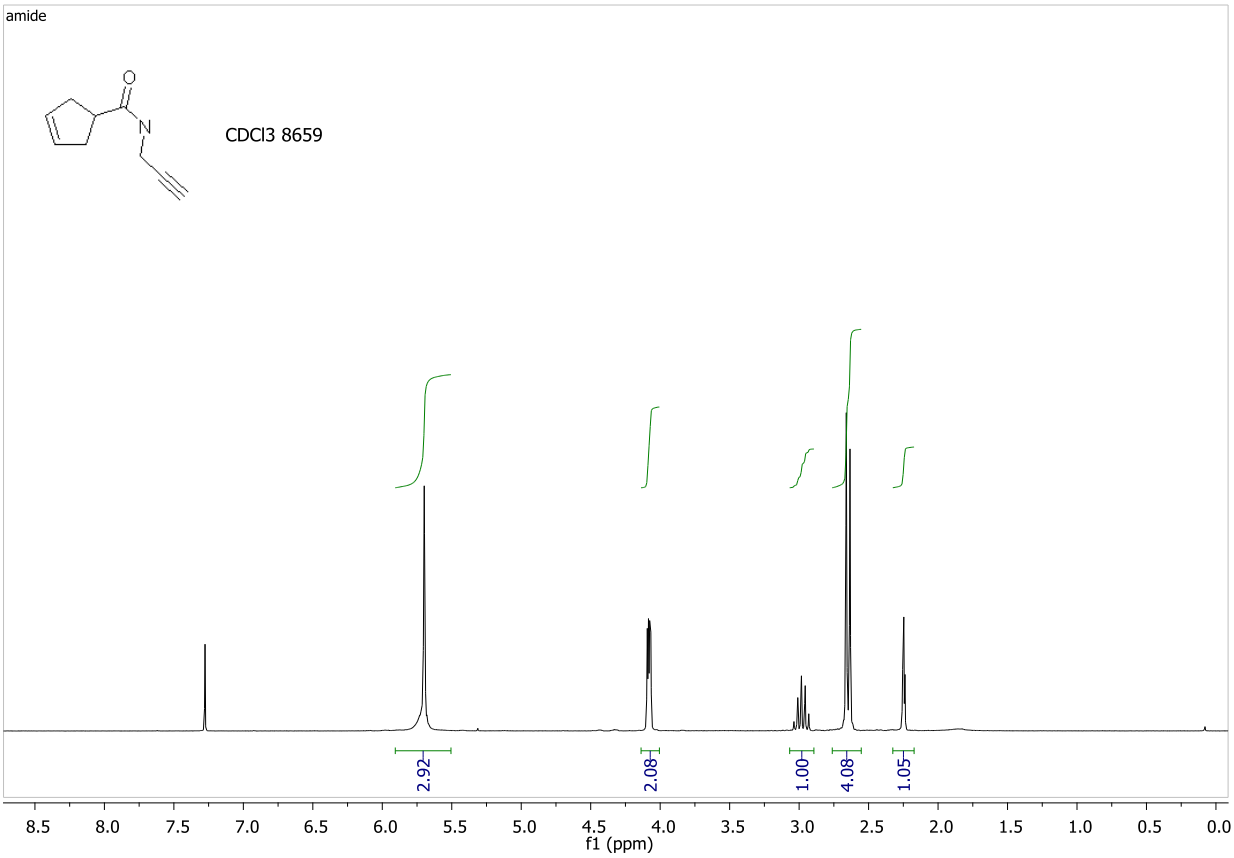
Compound **8o:**



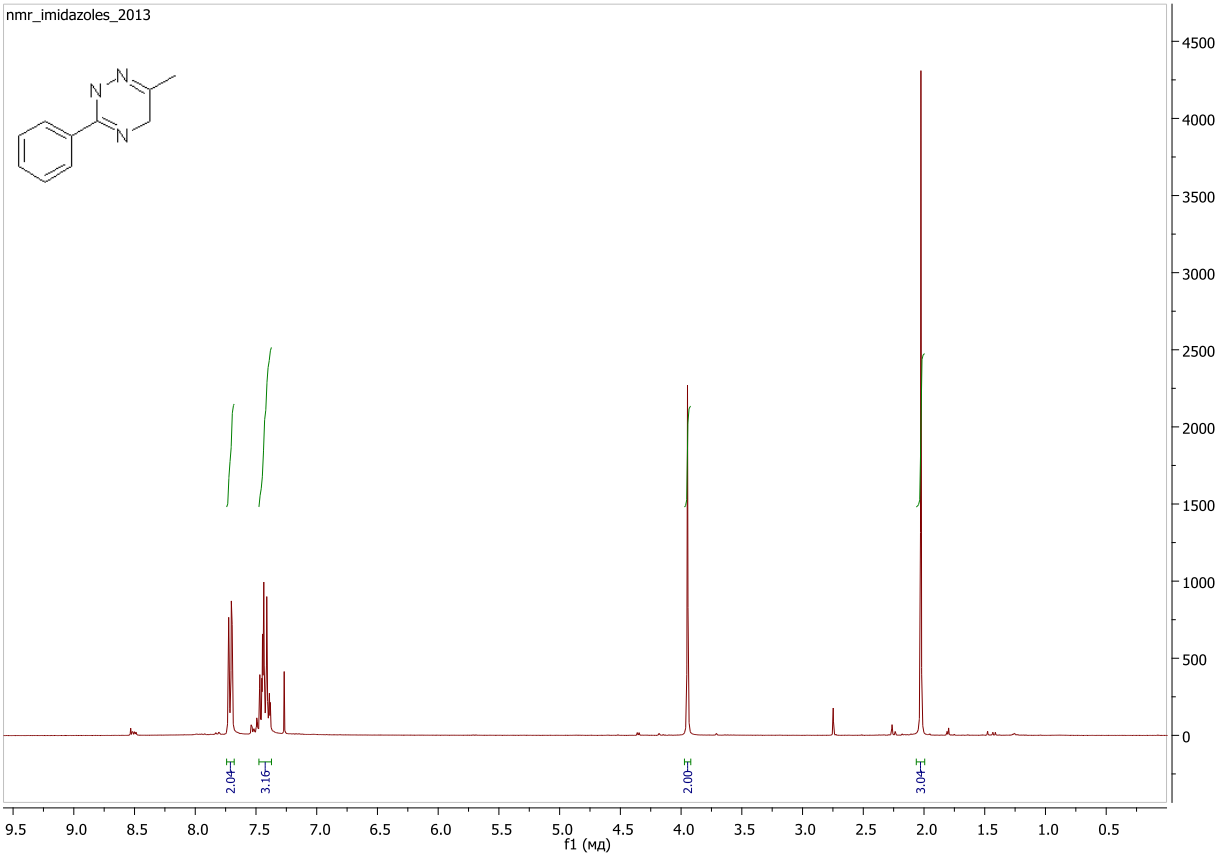
Compound **8p:**

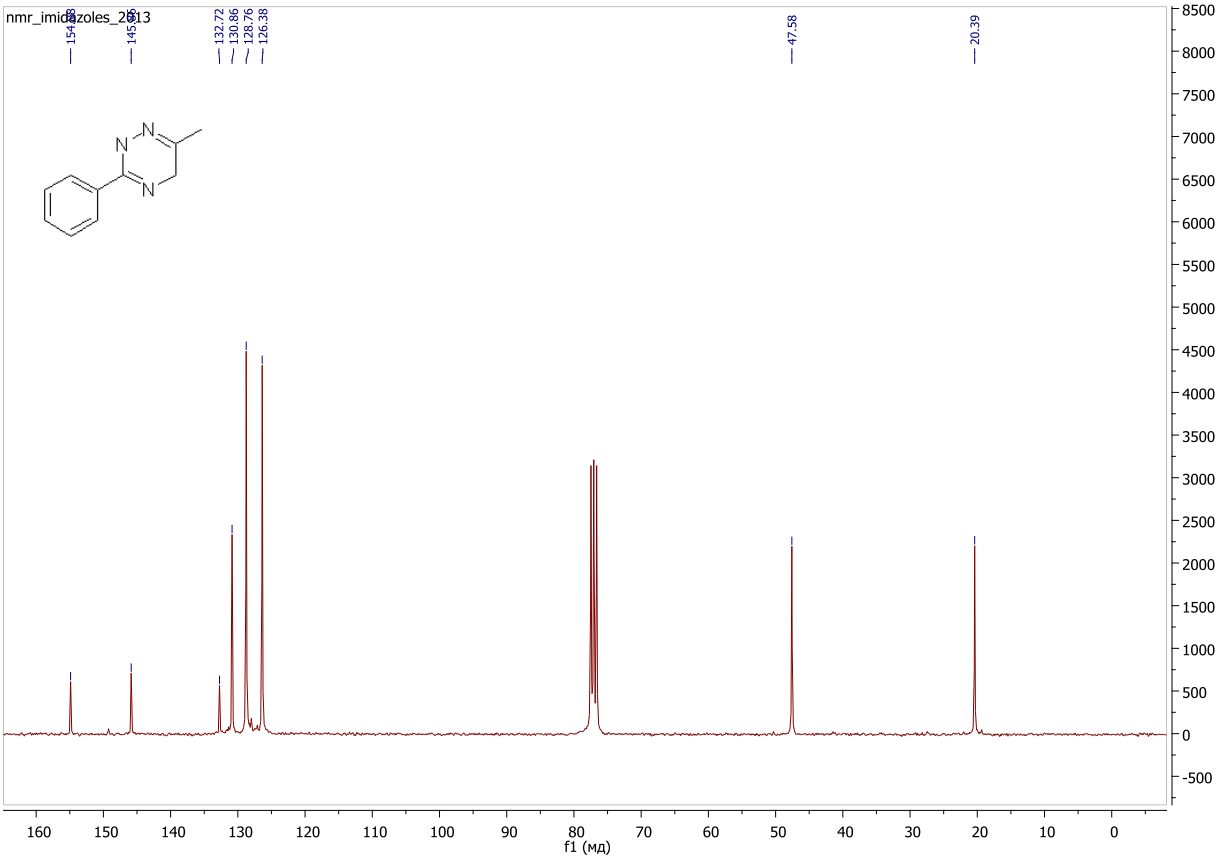


Compound **8q:**

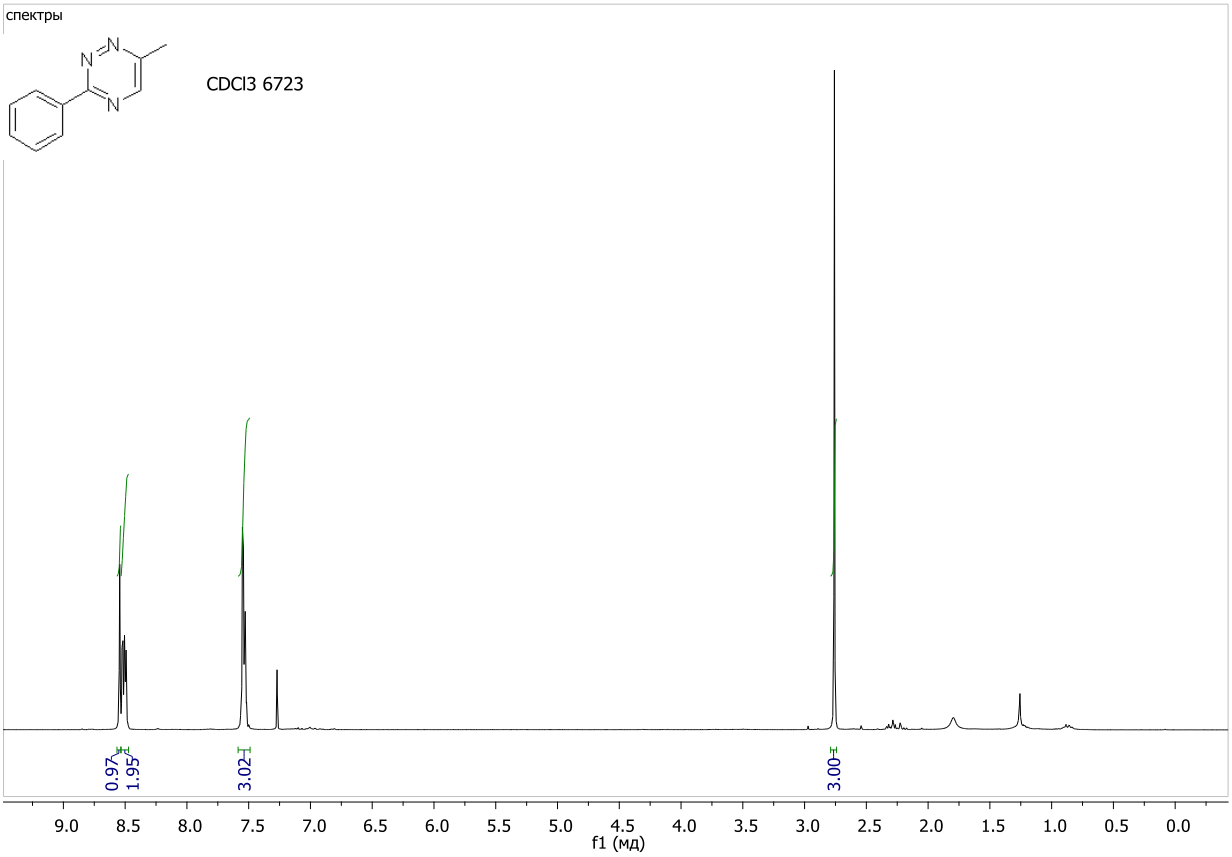

amide
CDCl3 8659
2.92
2.08
1.00
4.08
1.05
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

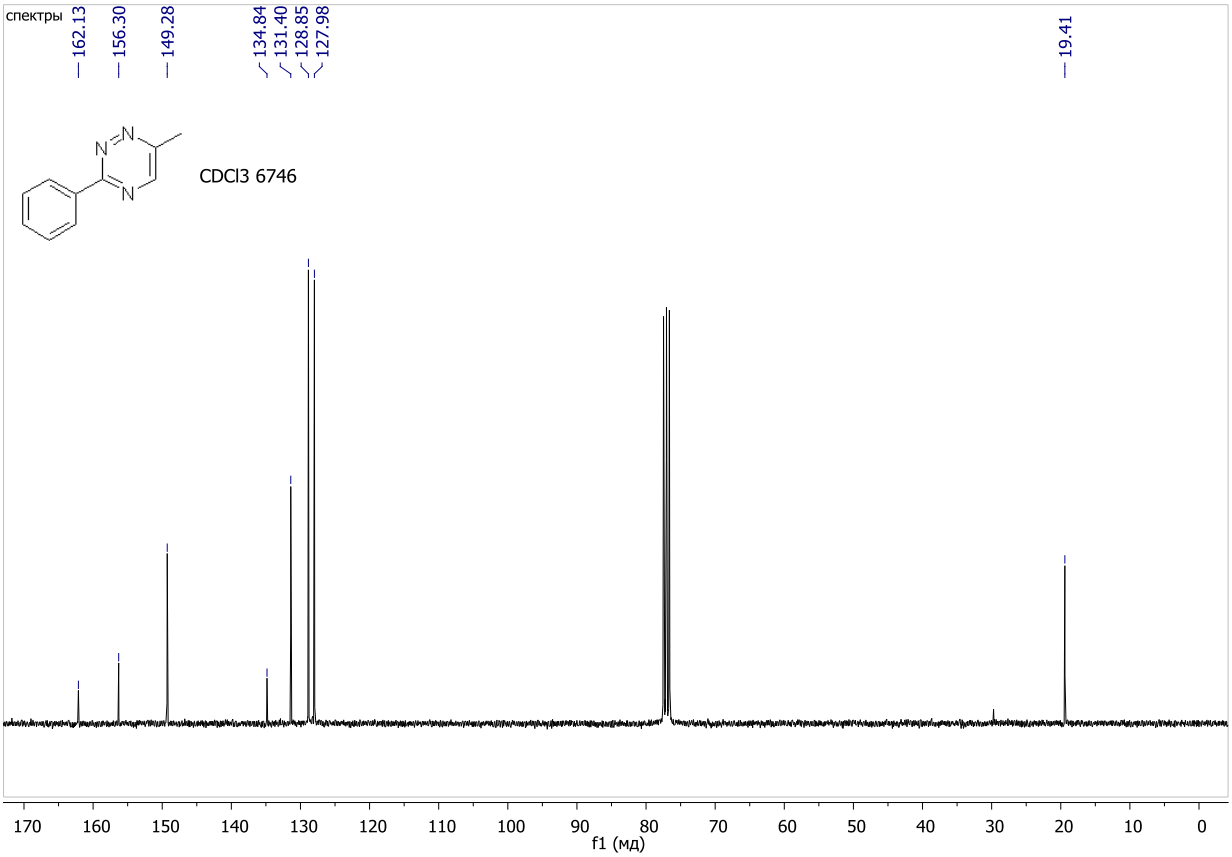
Compound **9a**:


nmr_imidazoles_2013
2.04
3.16
2.00
3.04
f1 (мд)

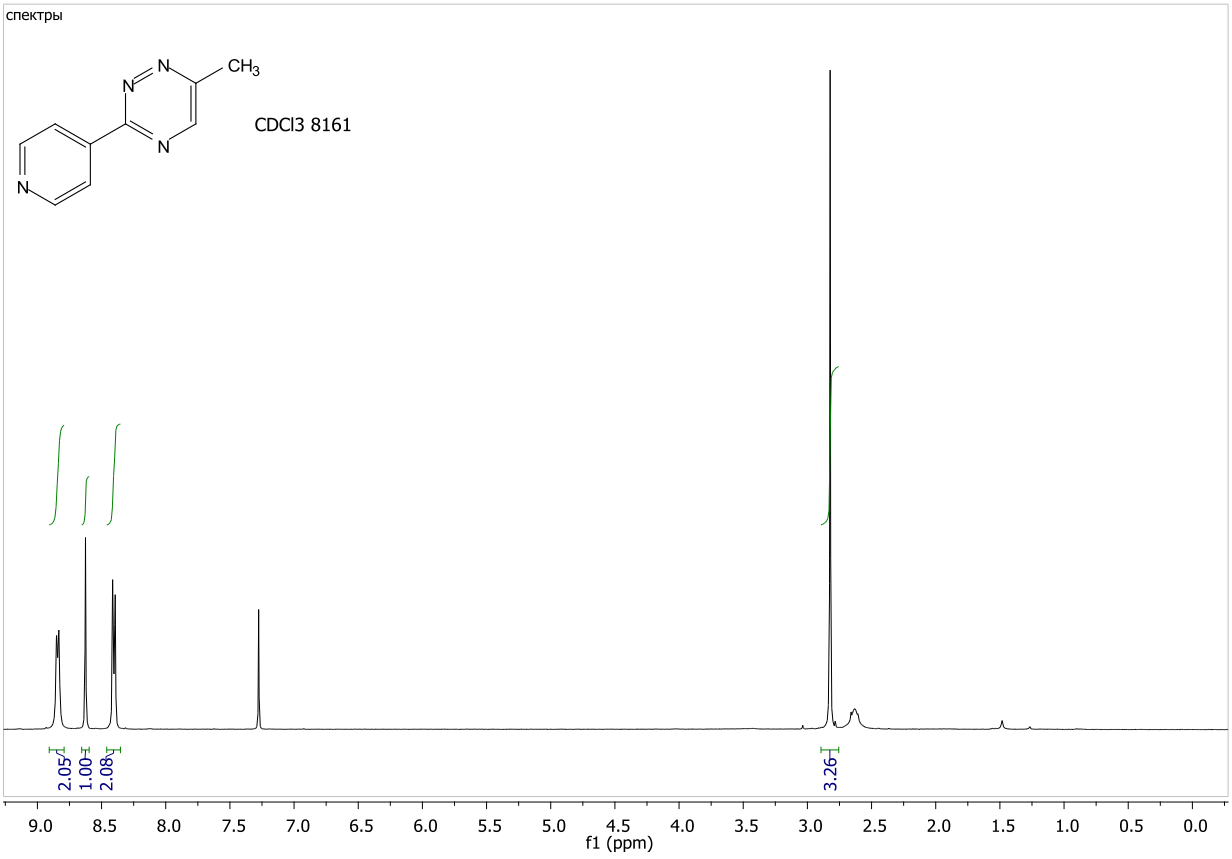

nmr_imidazoles_2013
154.88
145.61
132.72
130.86
128.76
126.38
47.58
20.39
f1 (мд)

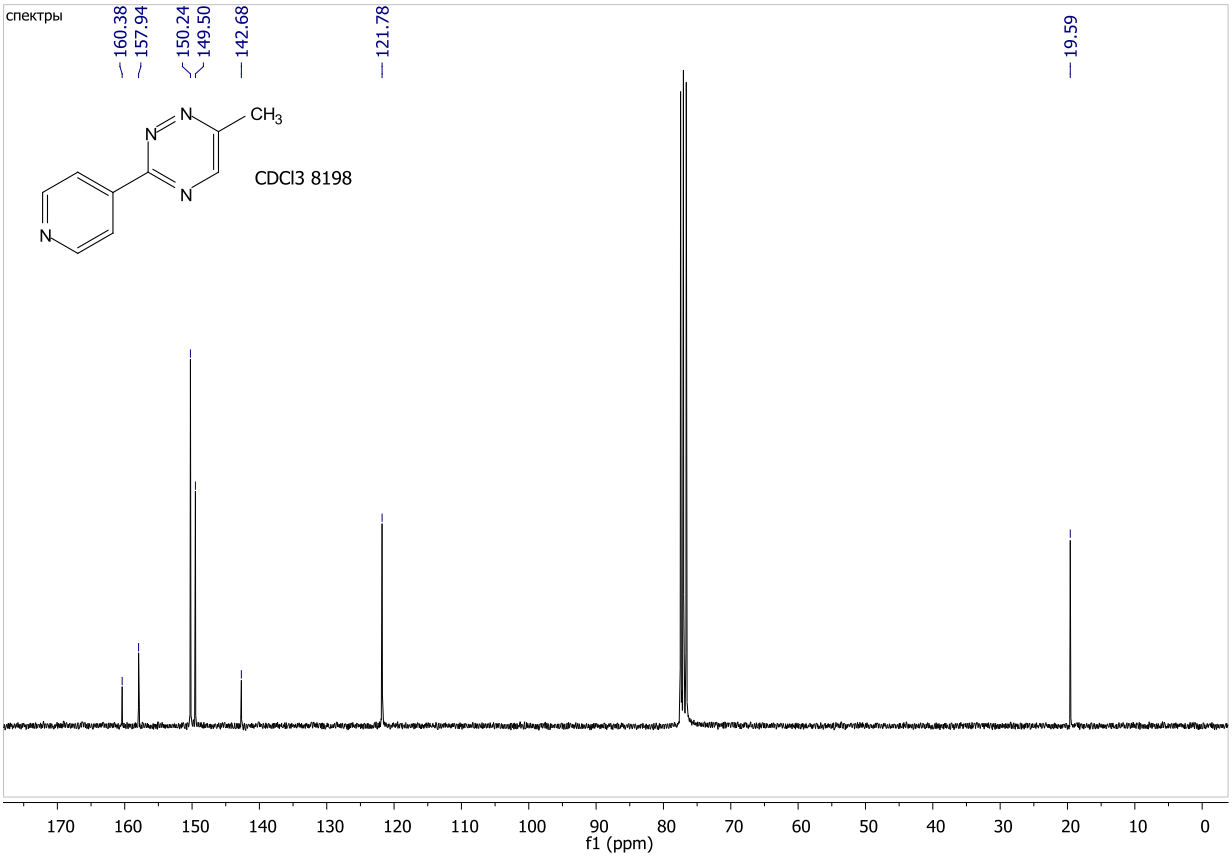
Compound **10a**:



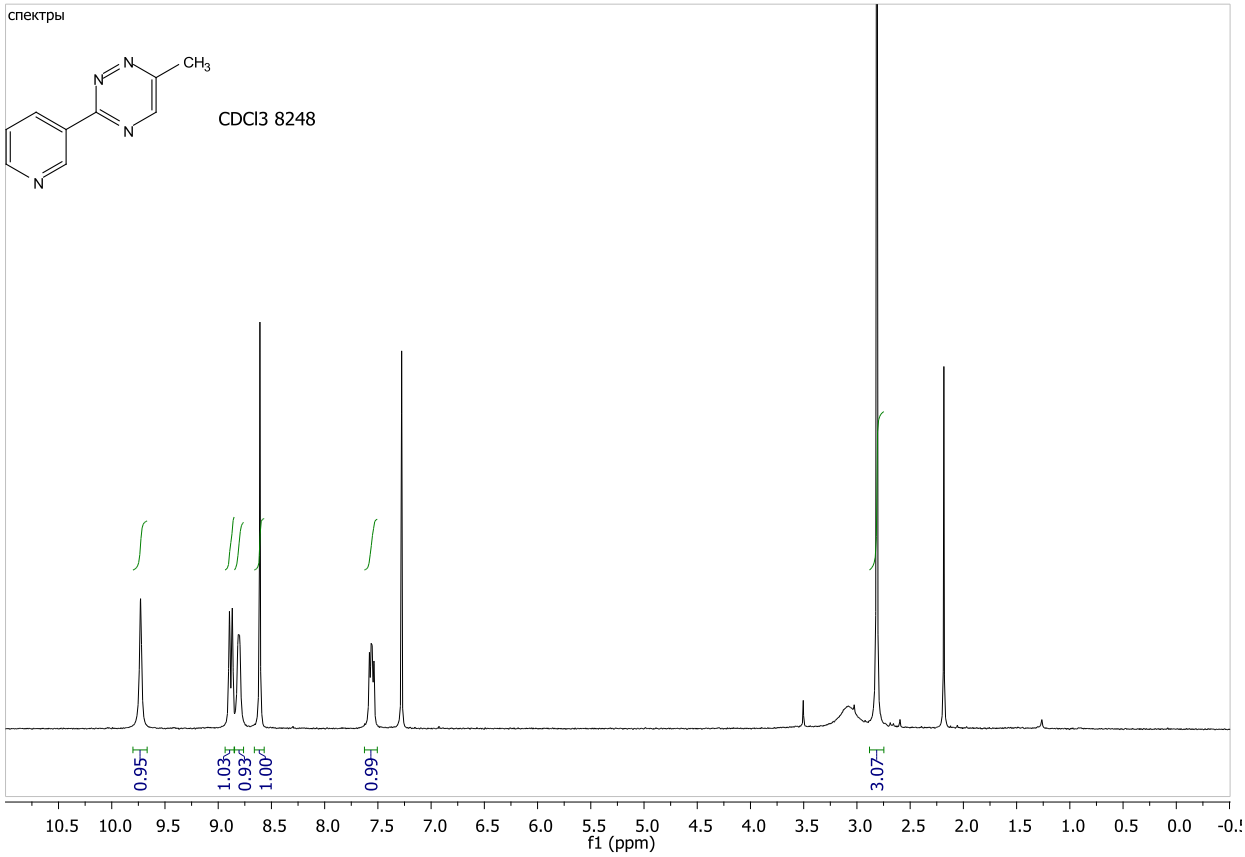


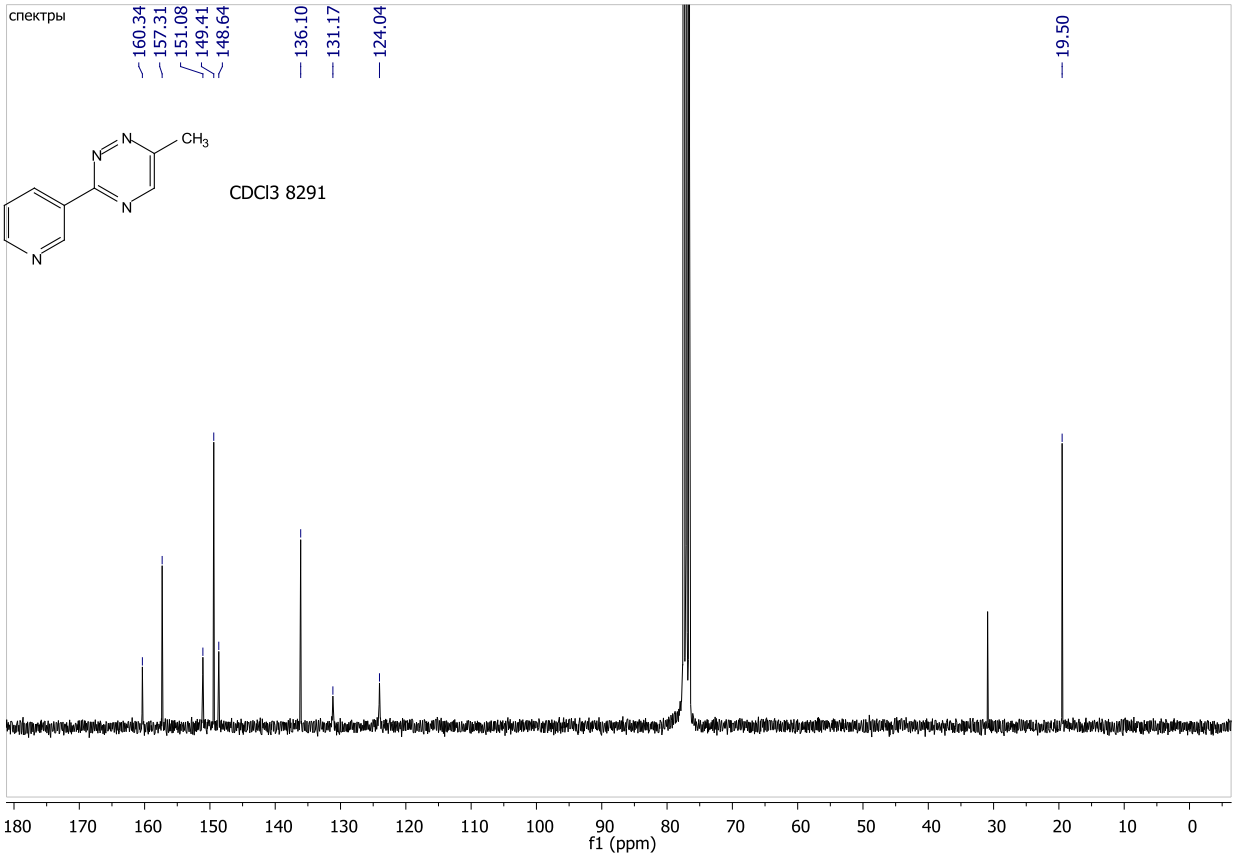
Compound **10b**:



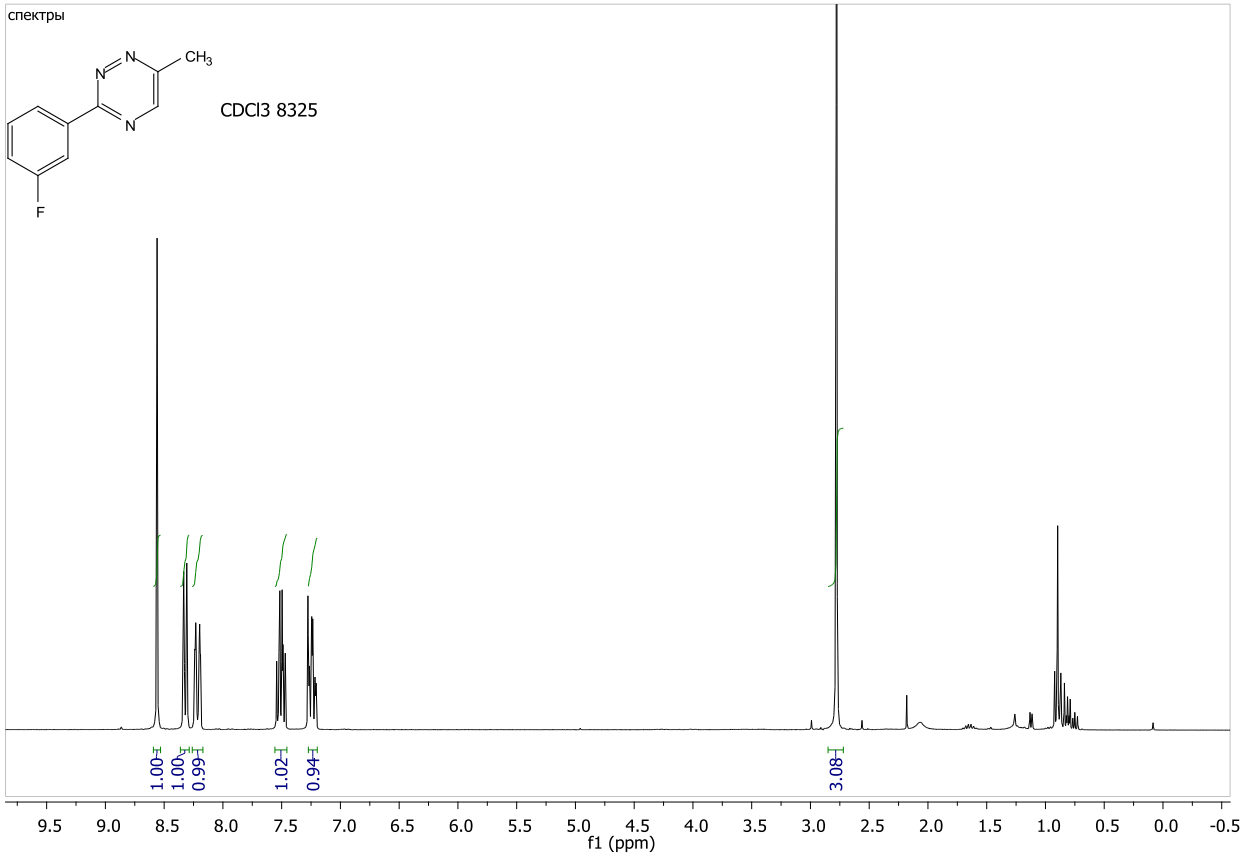


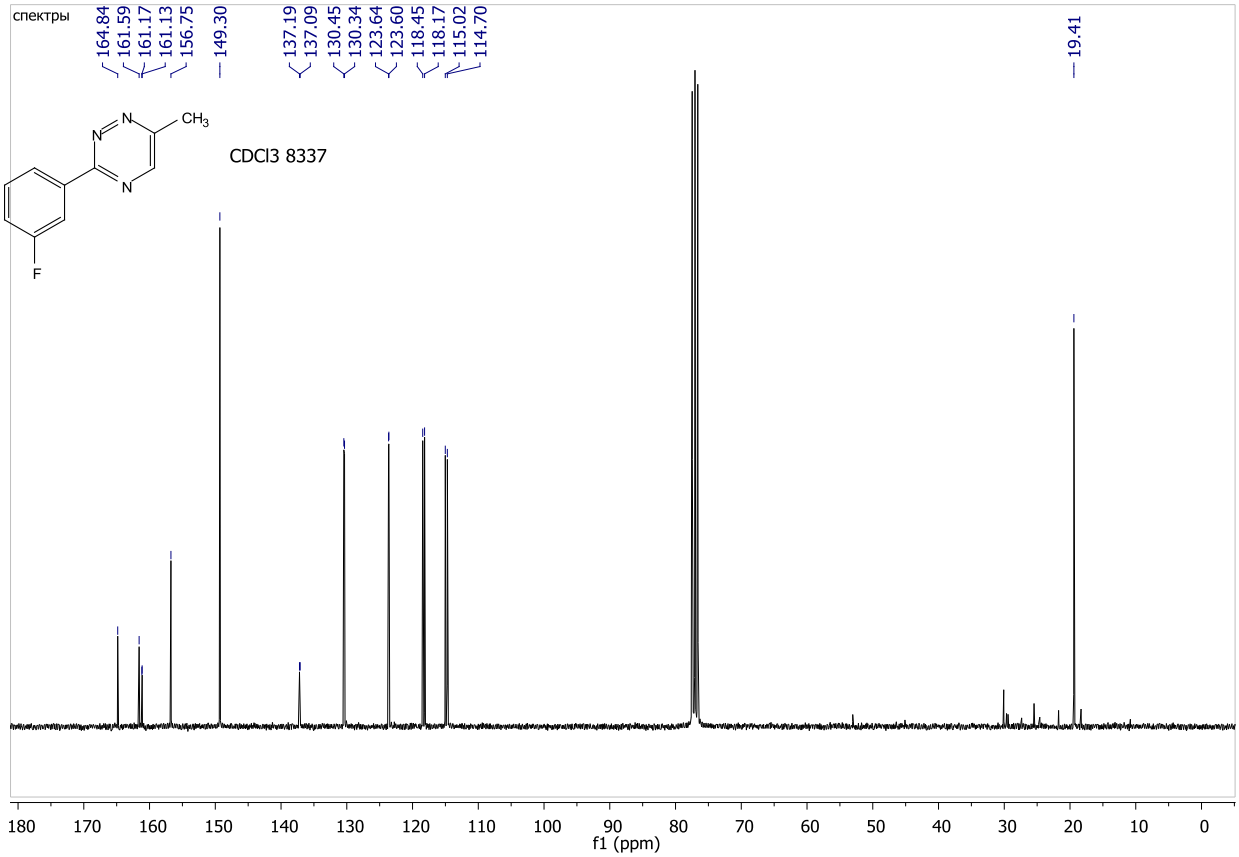
Compound **10c**:



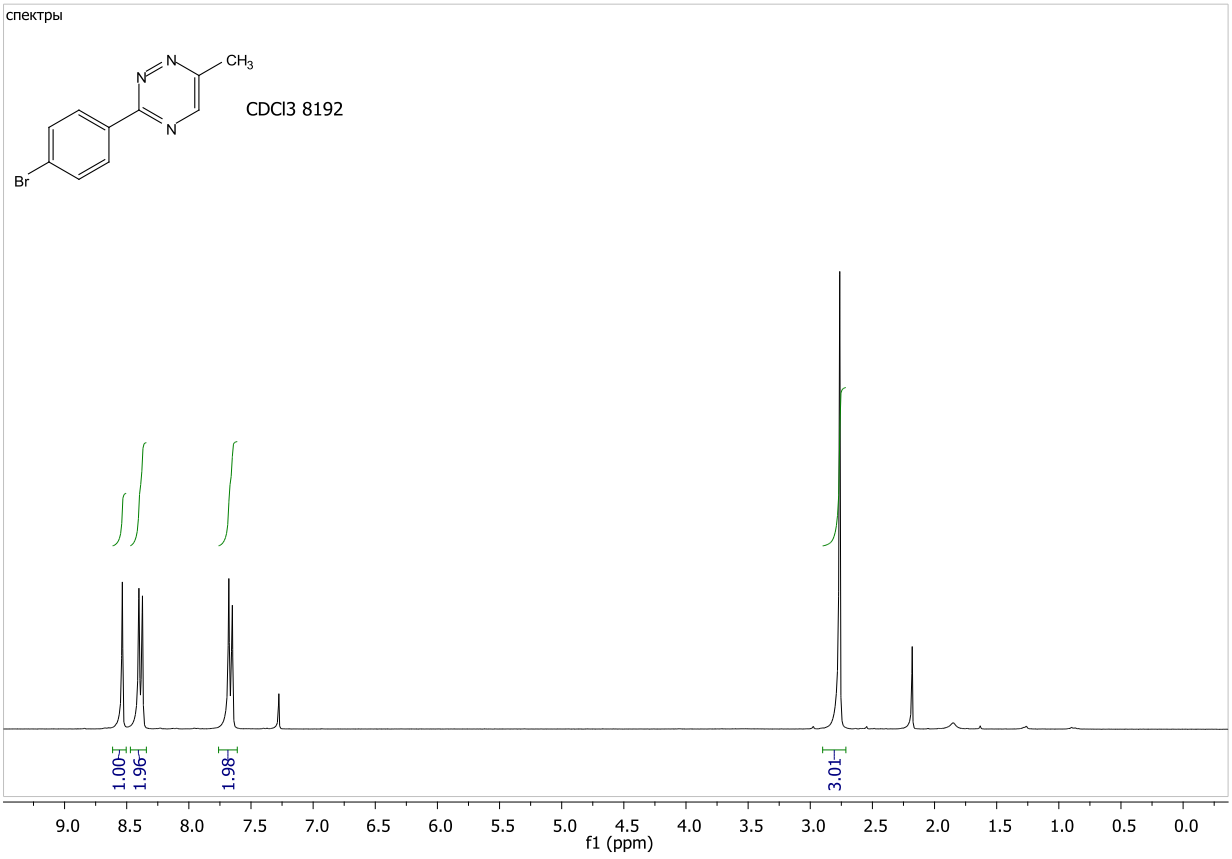


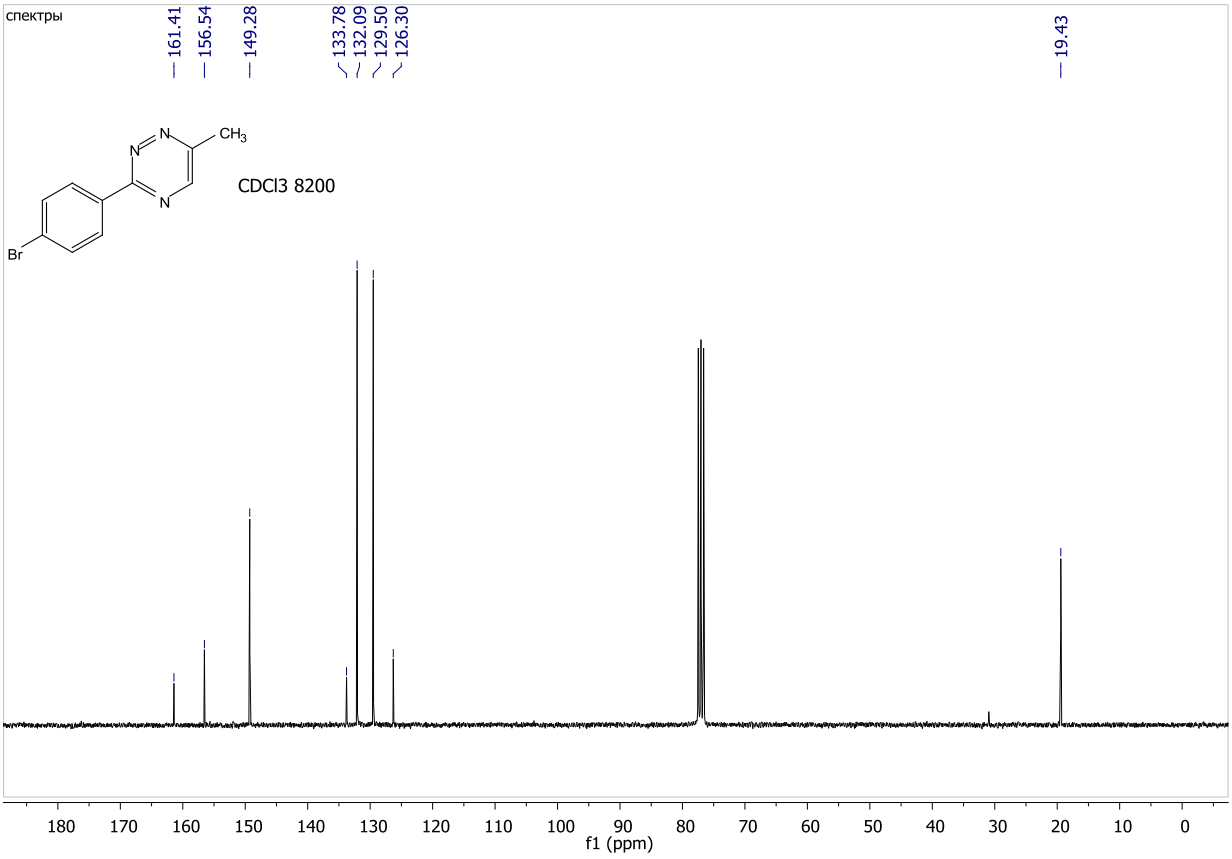
Compound**10d**:



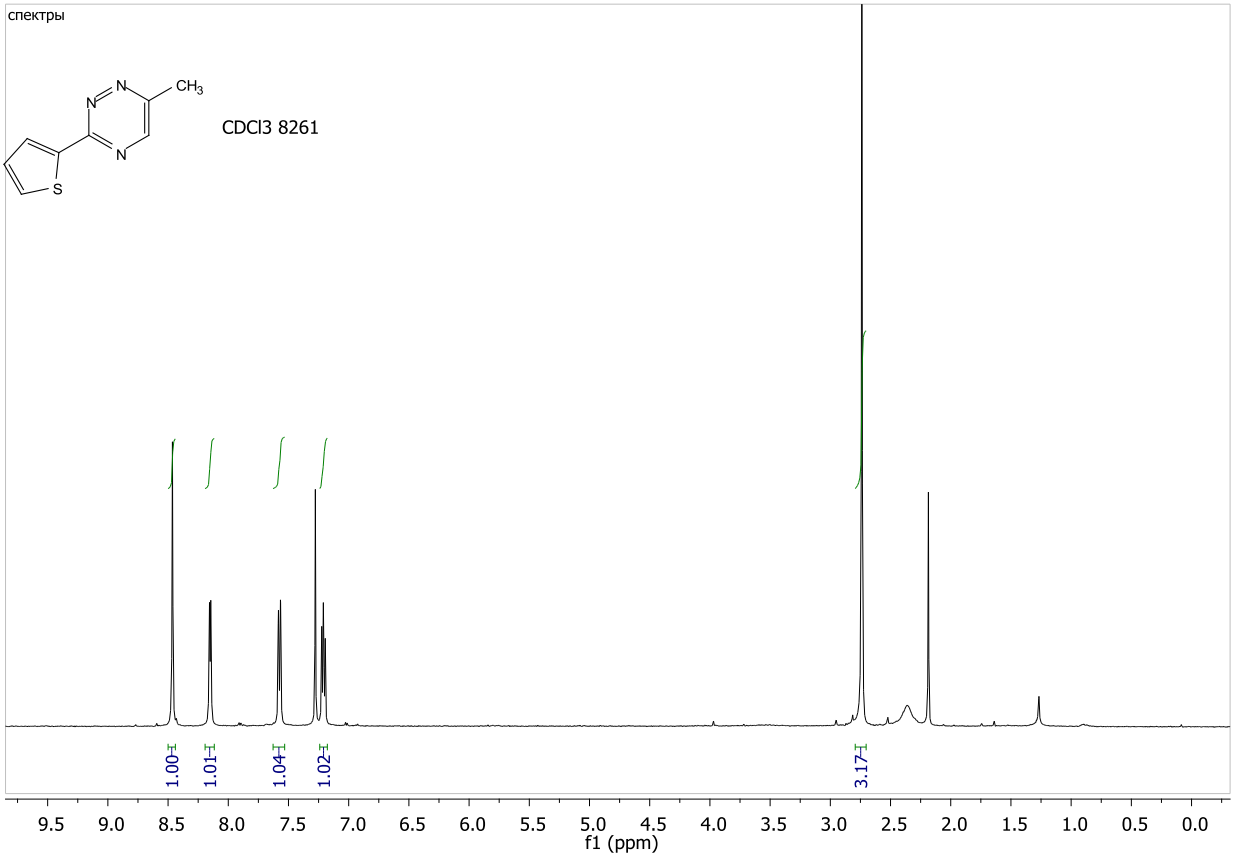


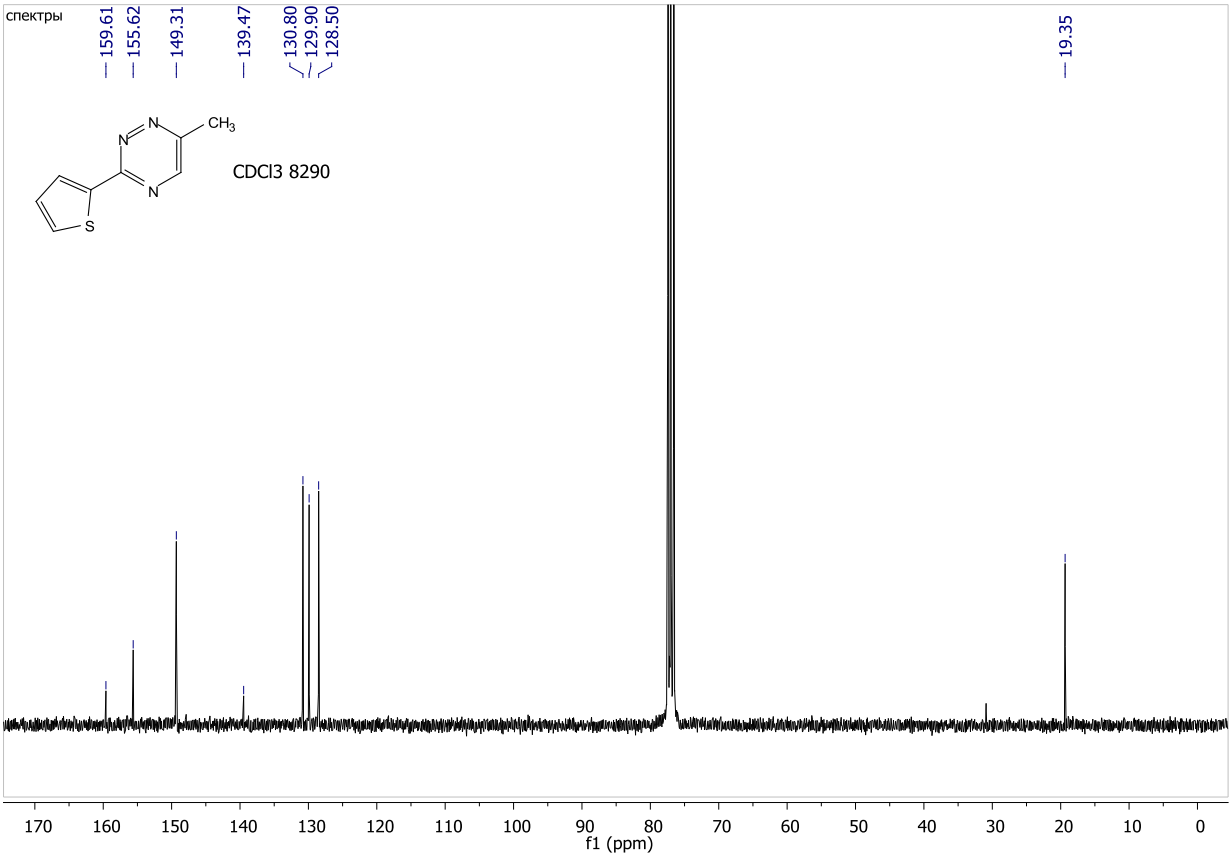
Compound**10e**:



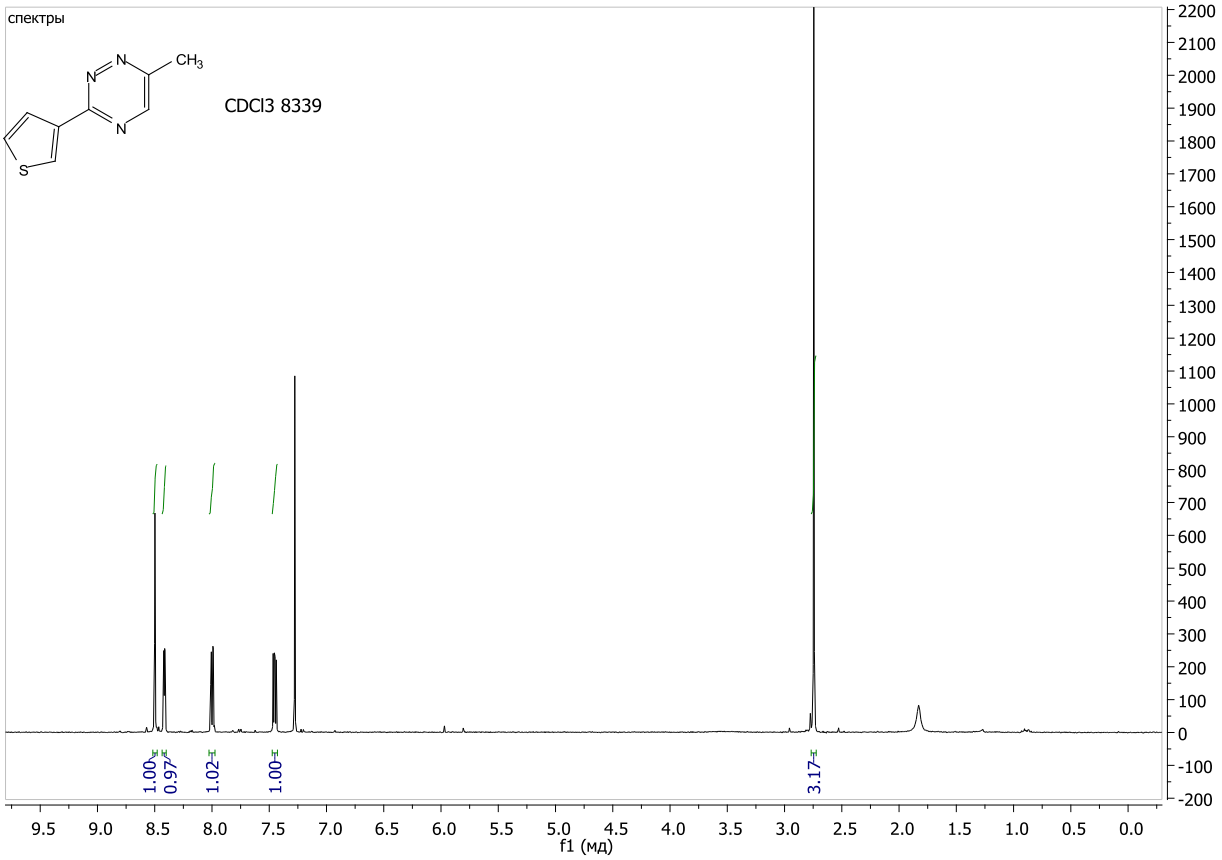


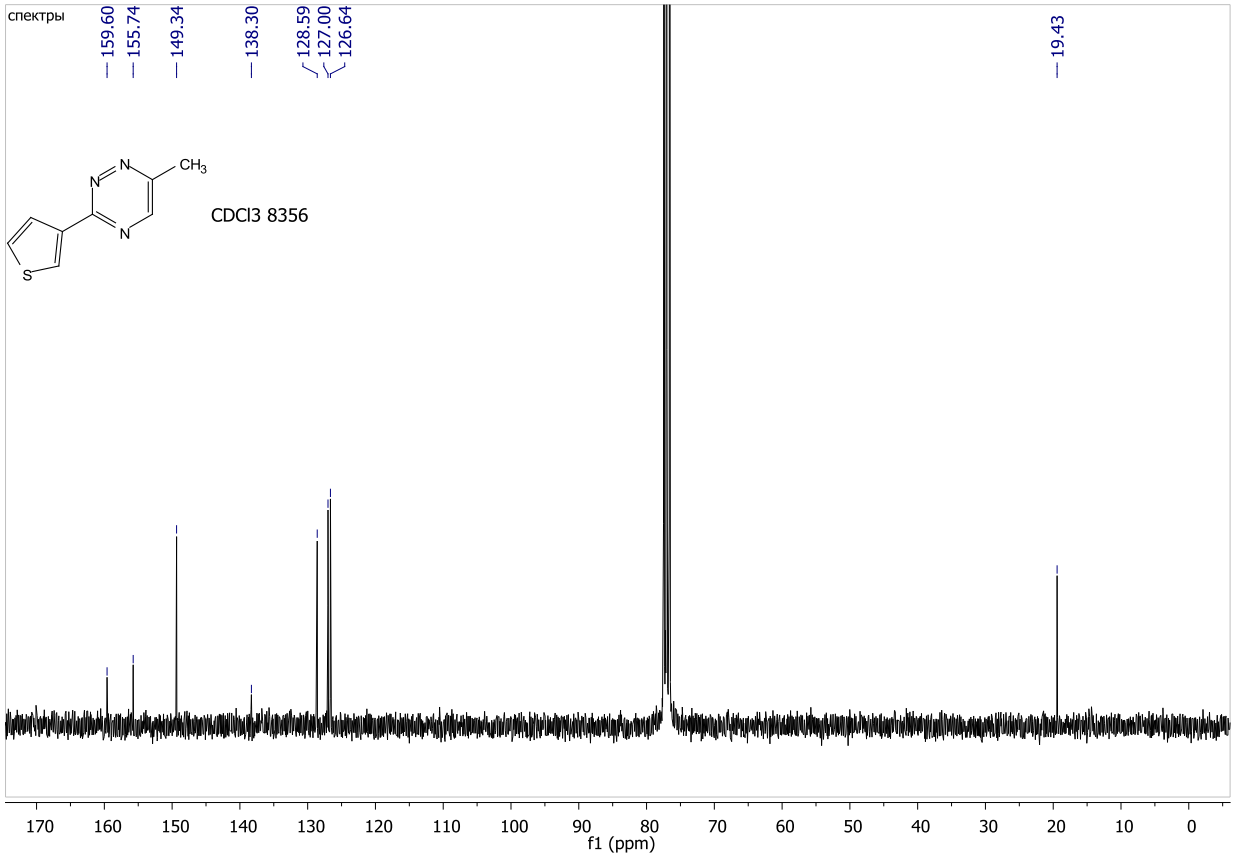
Compound**10f**:



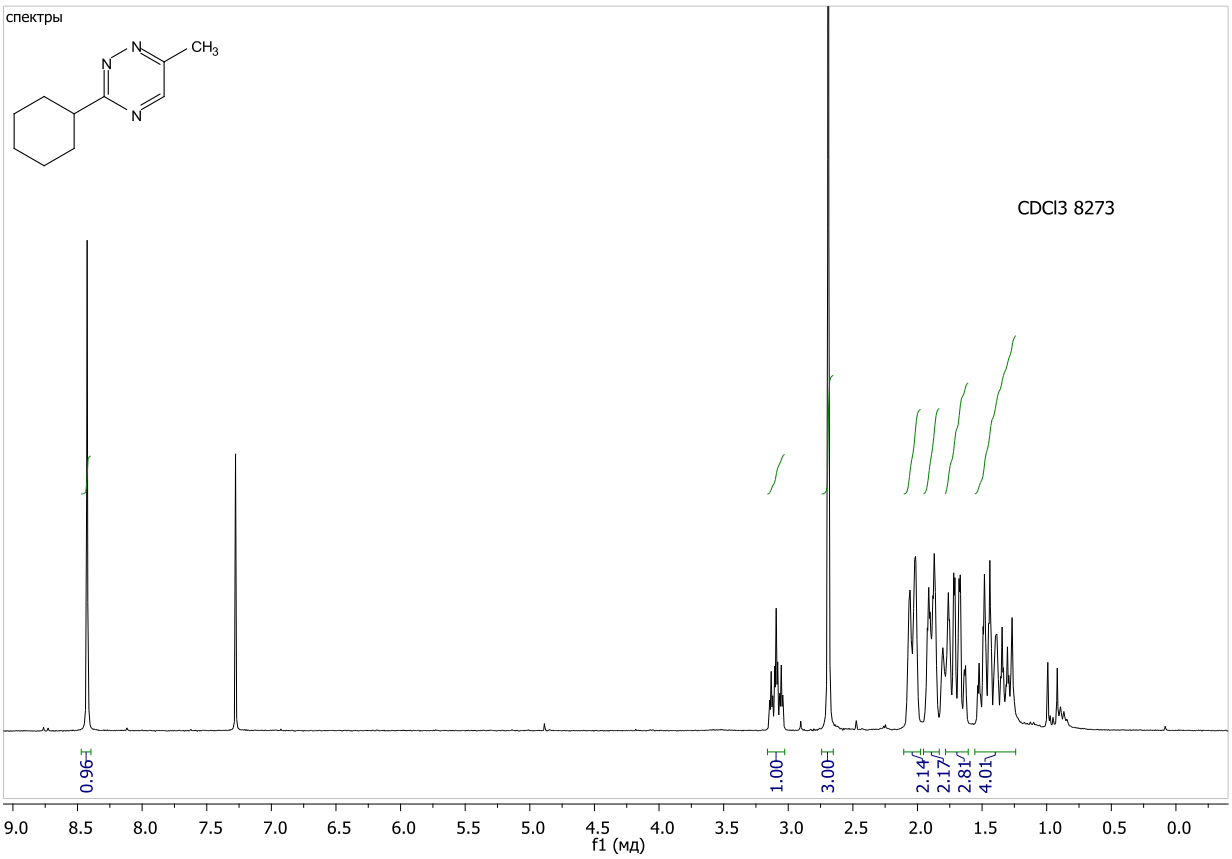


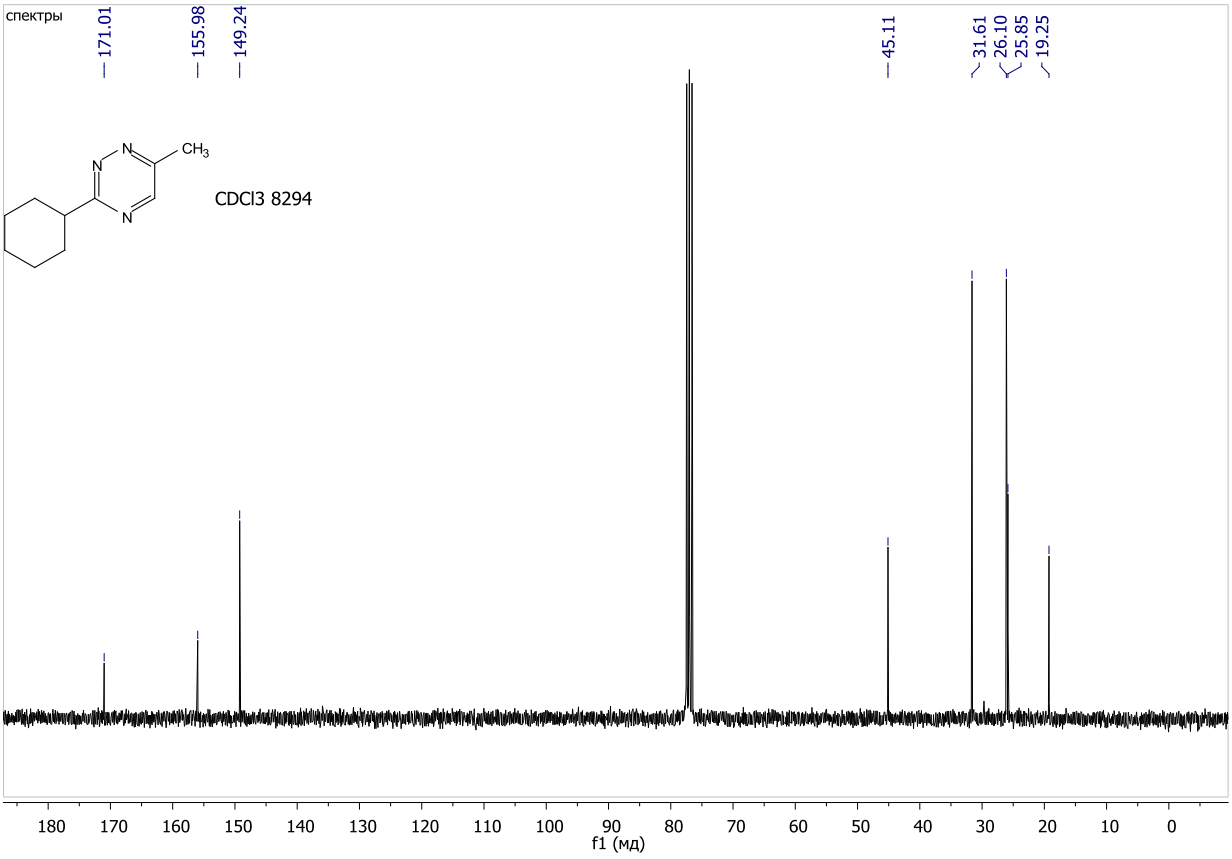
Compound **10g**:



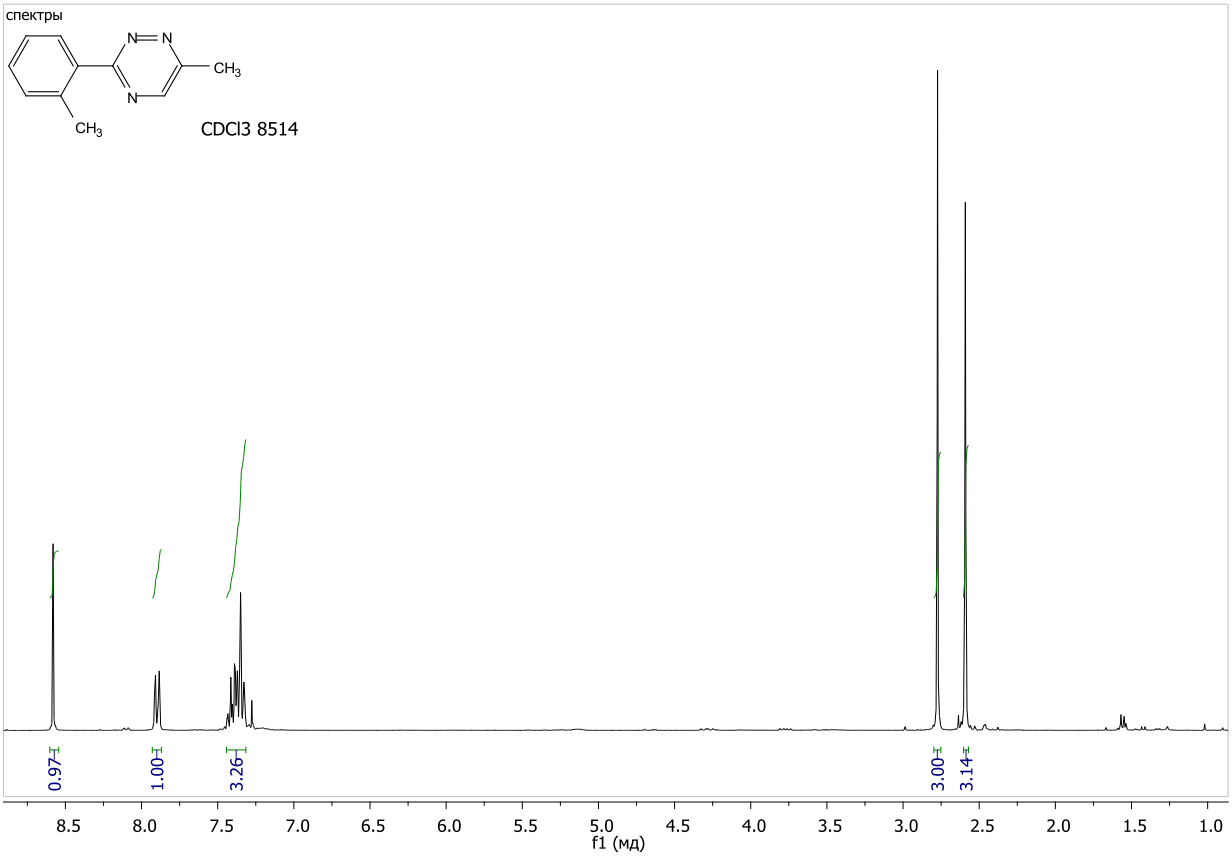


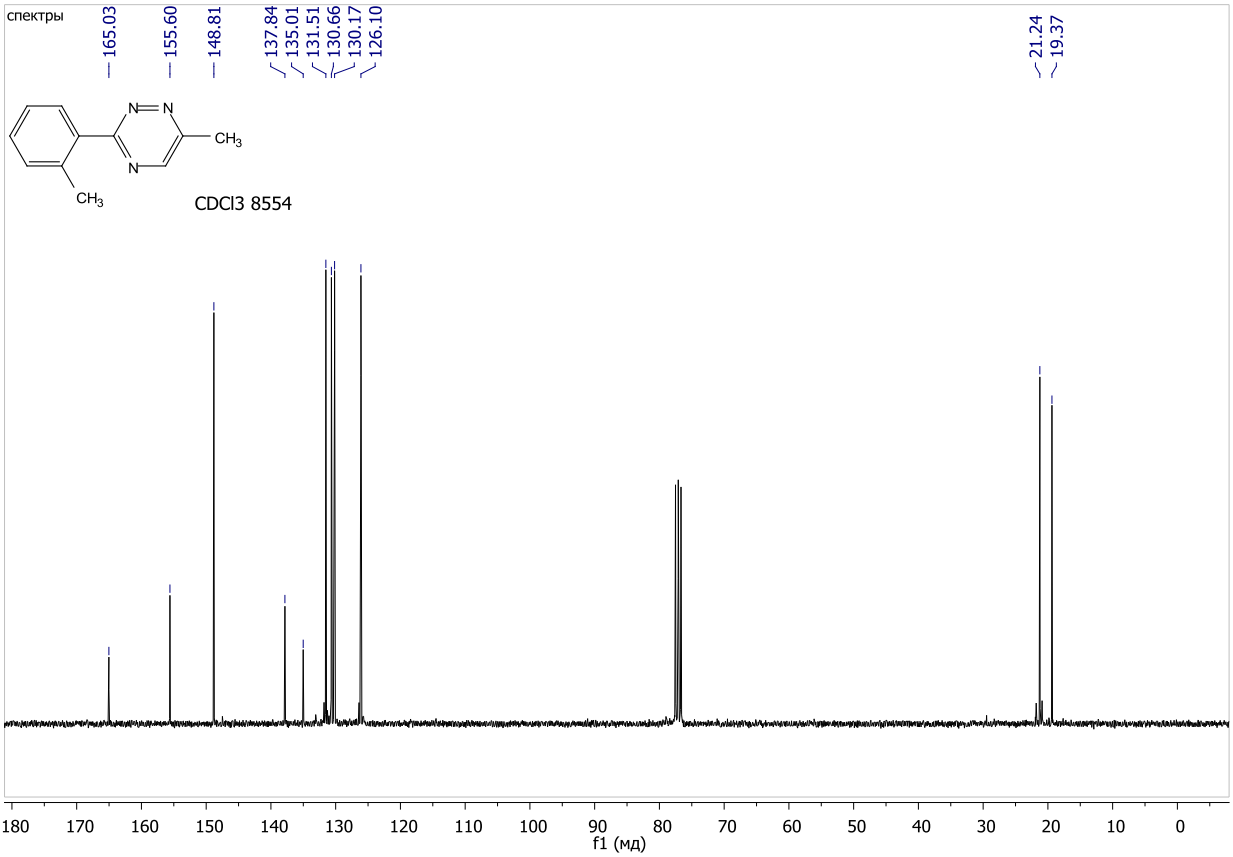
Compound **10h**:



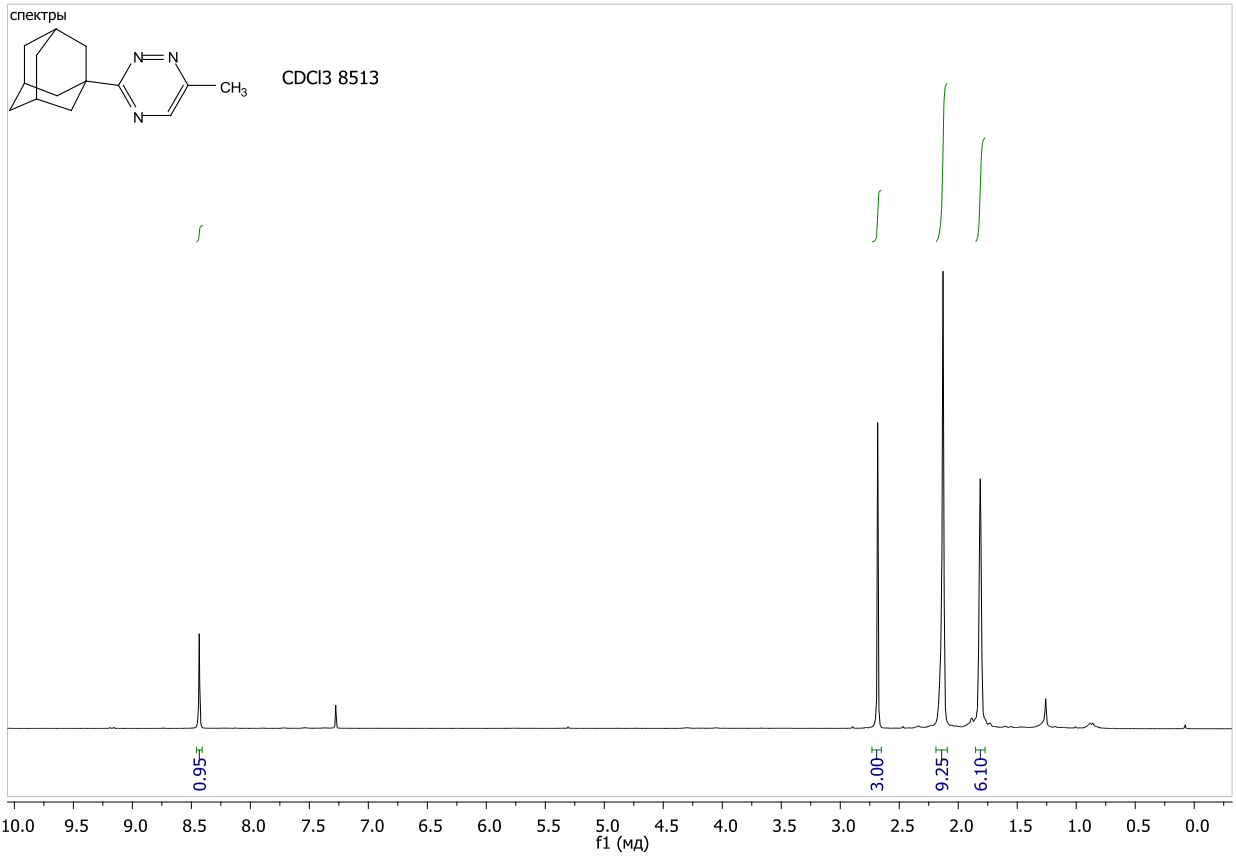


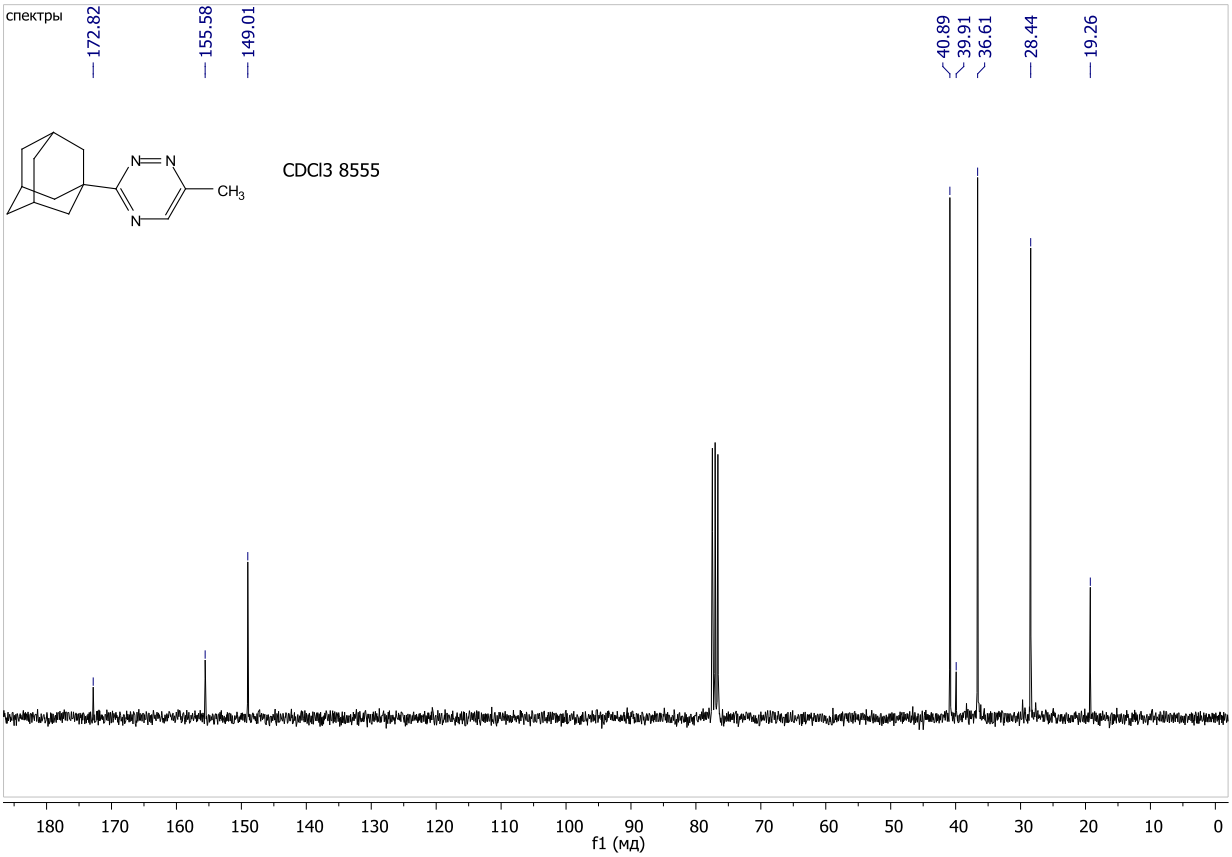
Compound**10i**:



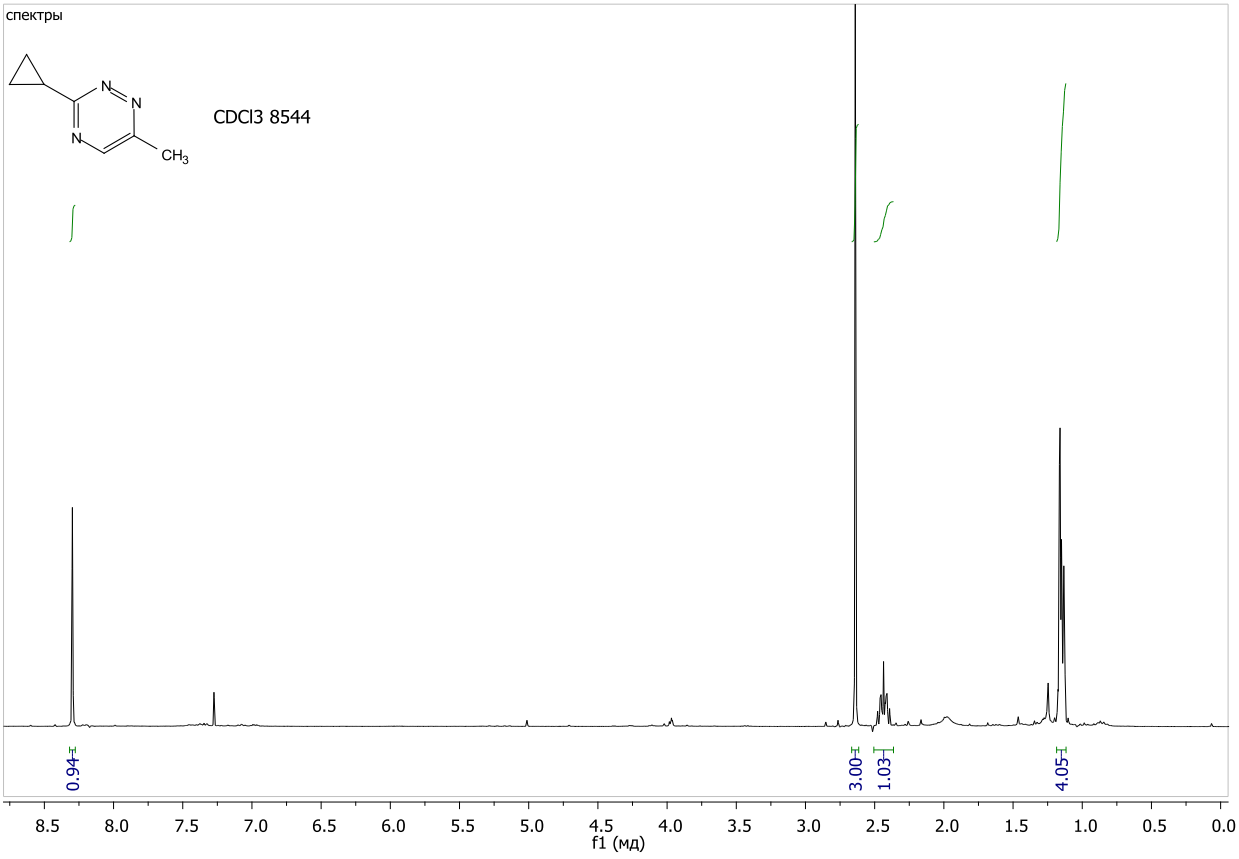


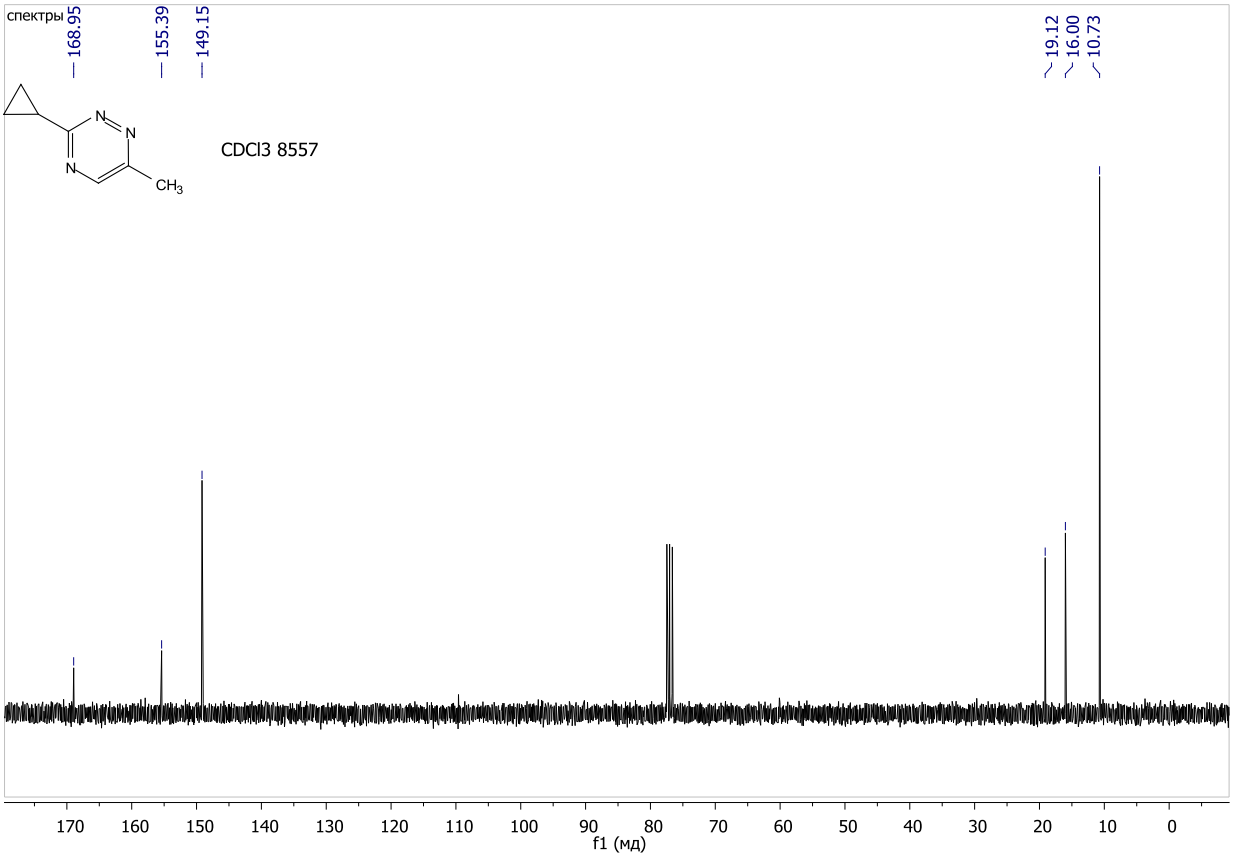
Compound**10j**:



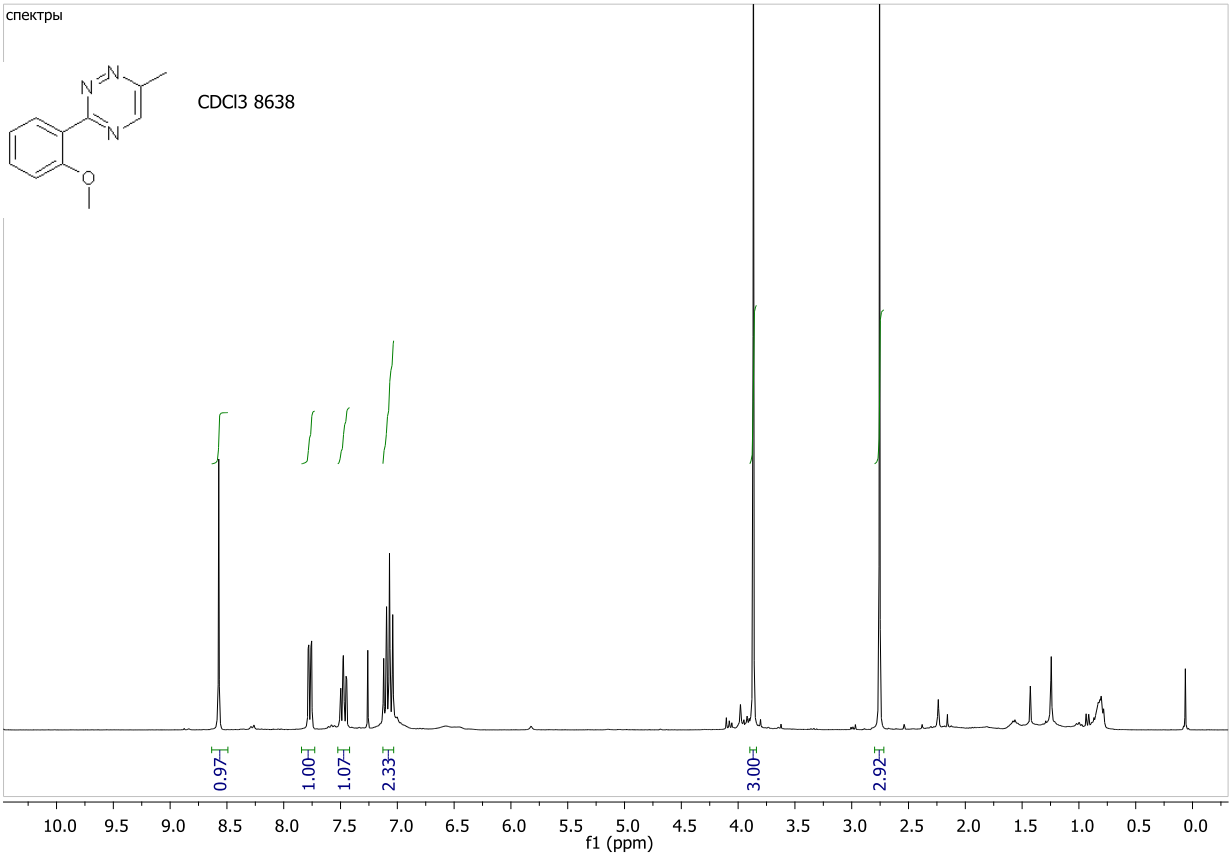


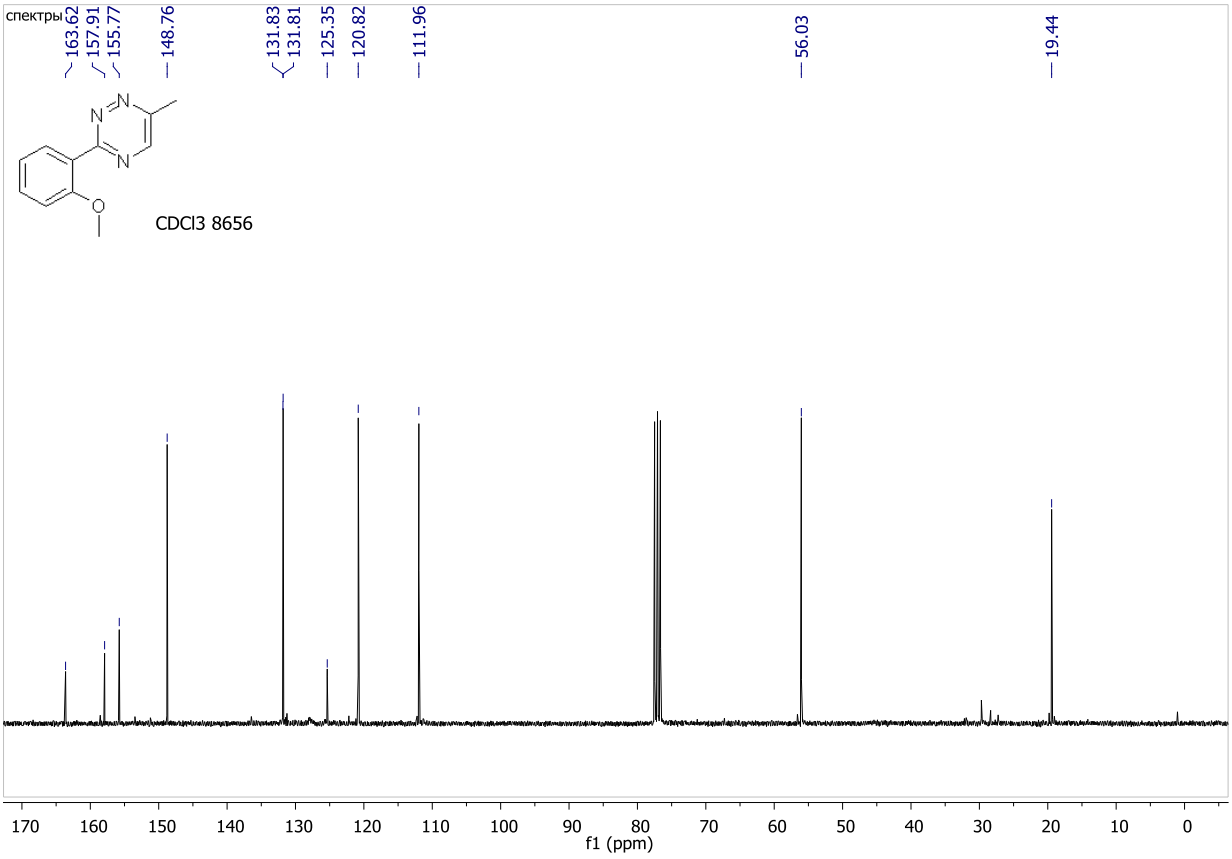
Compound **10k**:



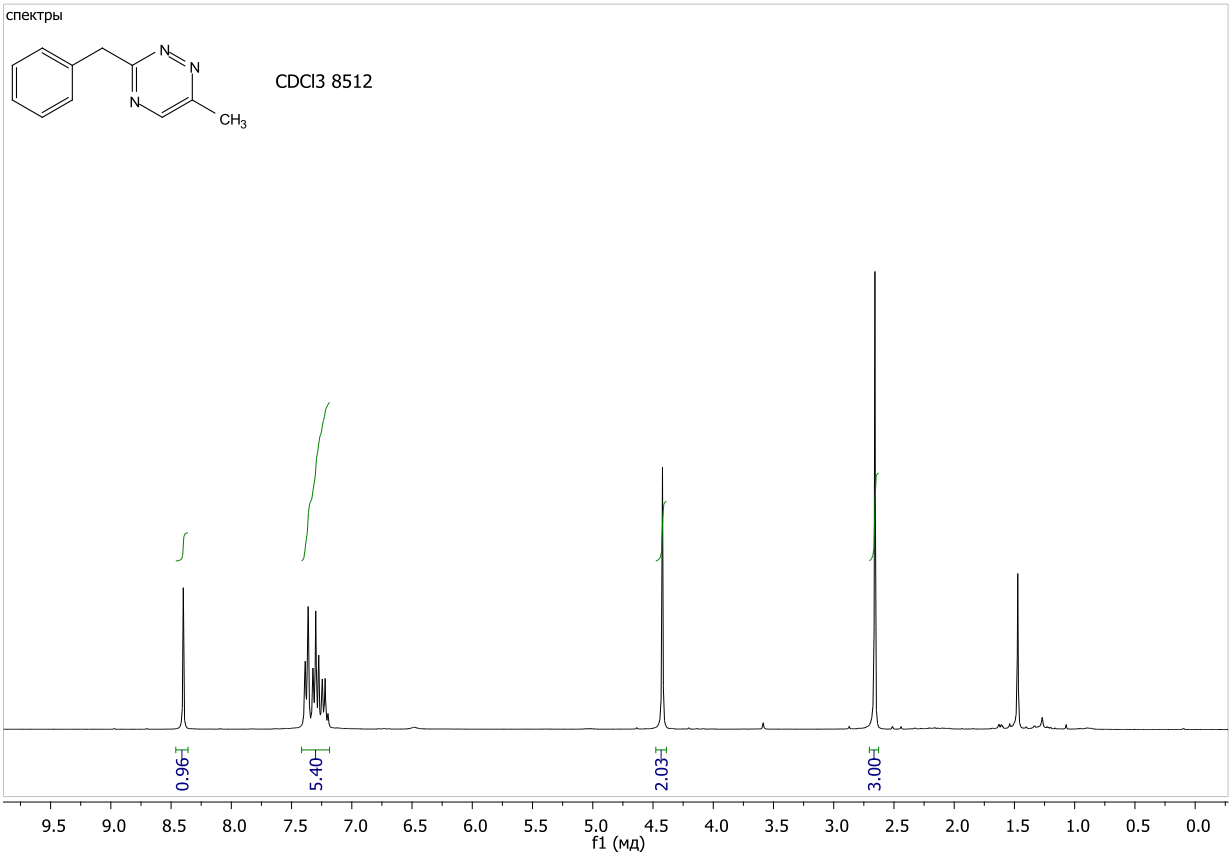


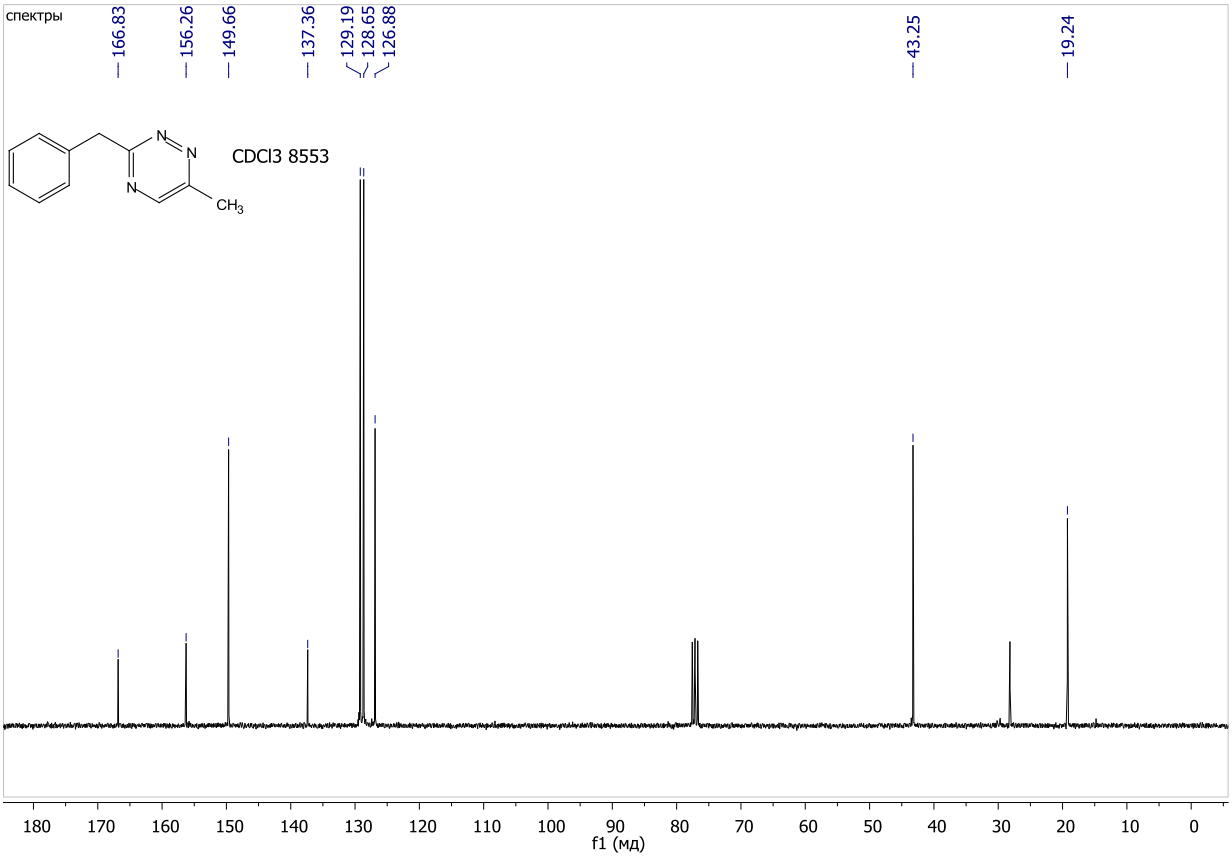
Compound **10l**:



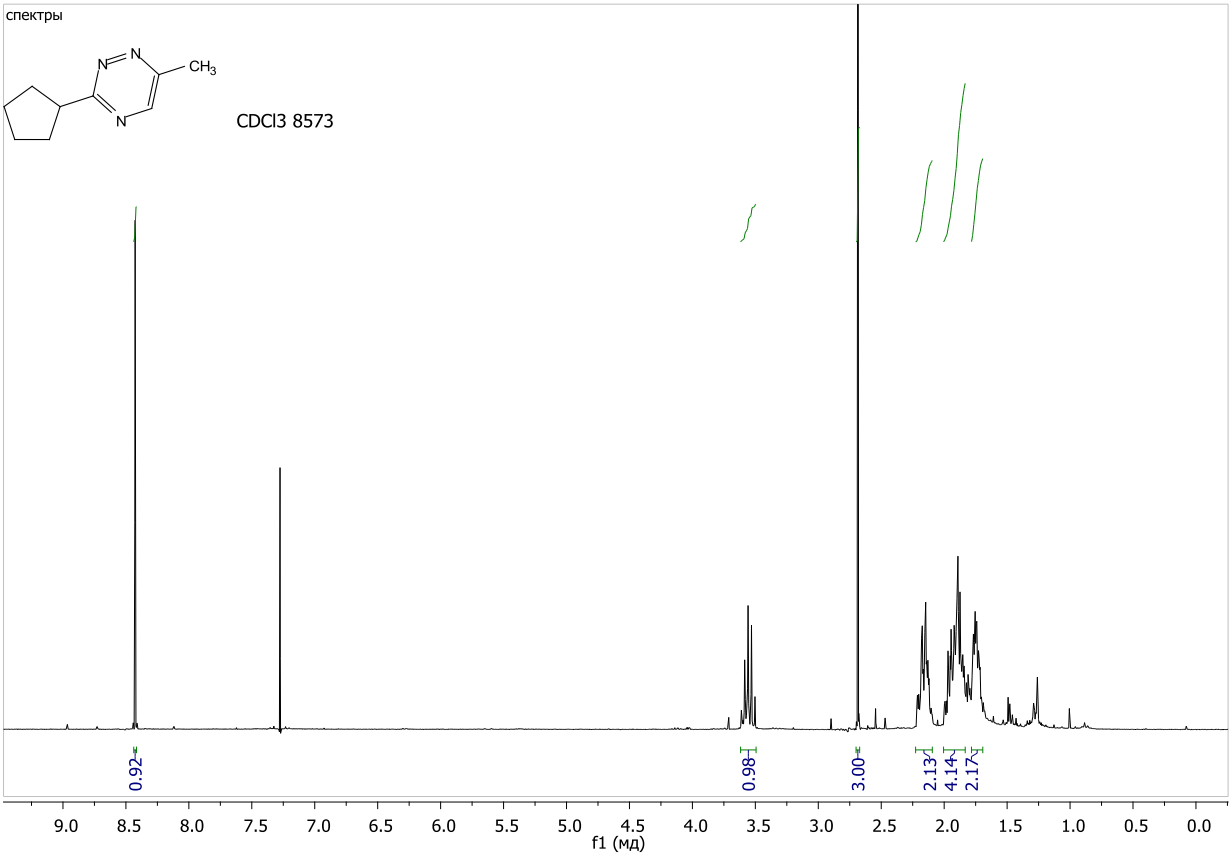


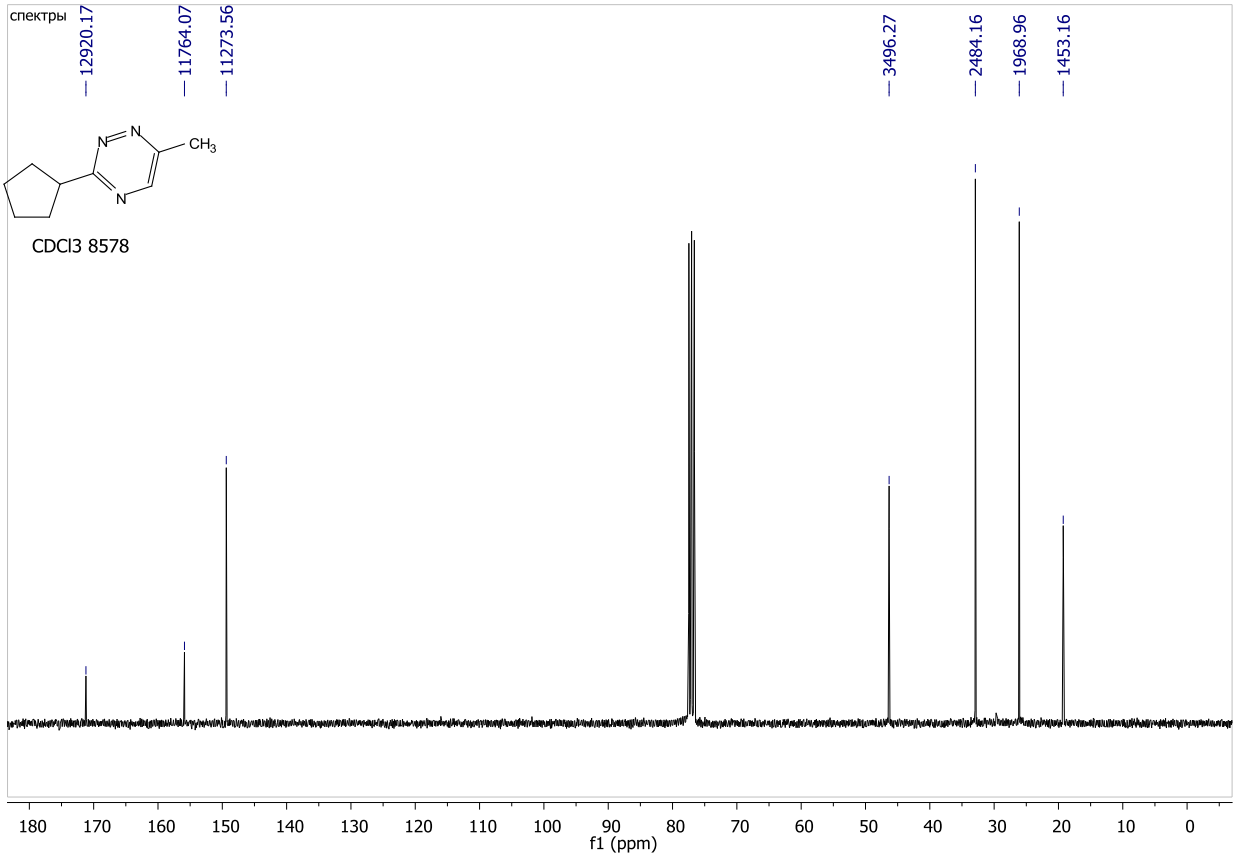
Compound **10m**:



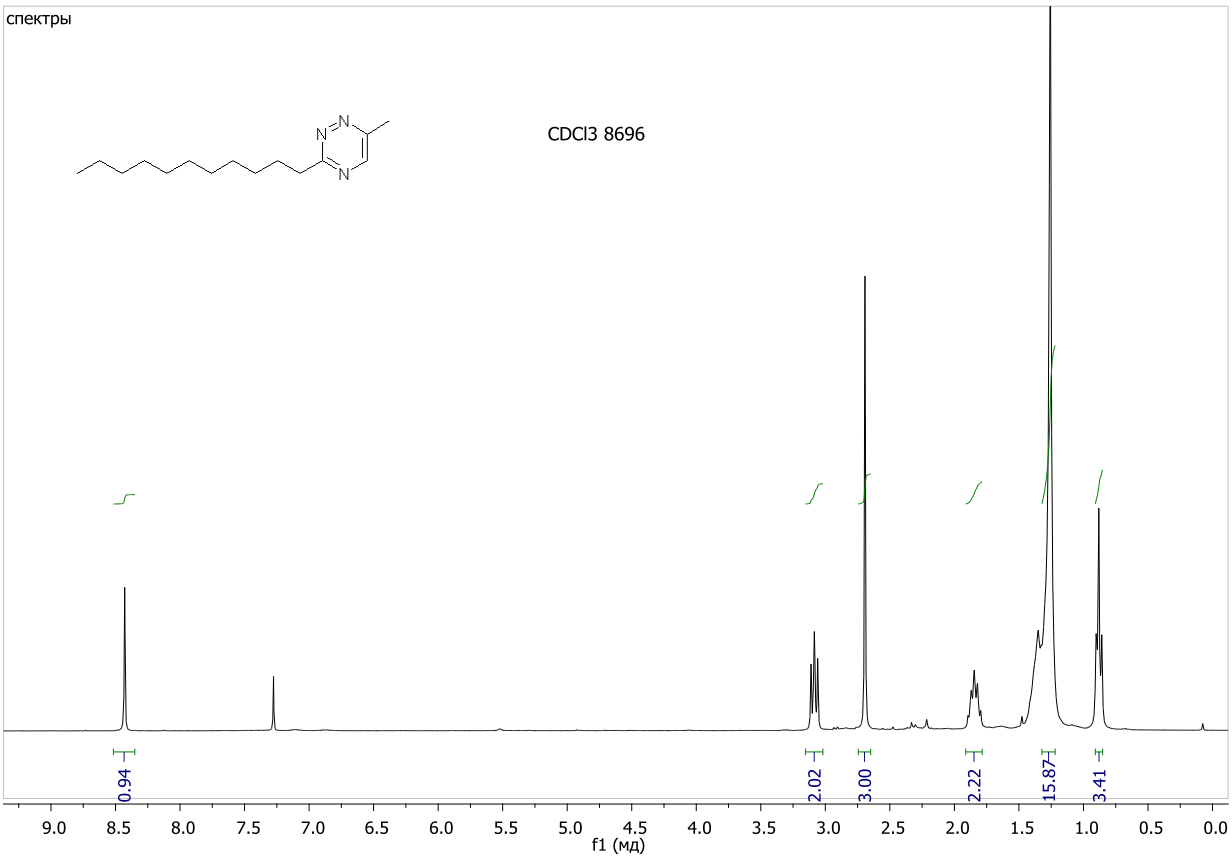


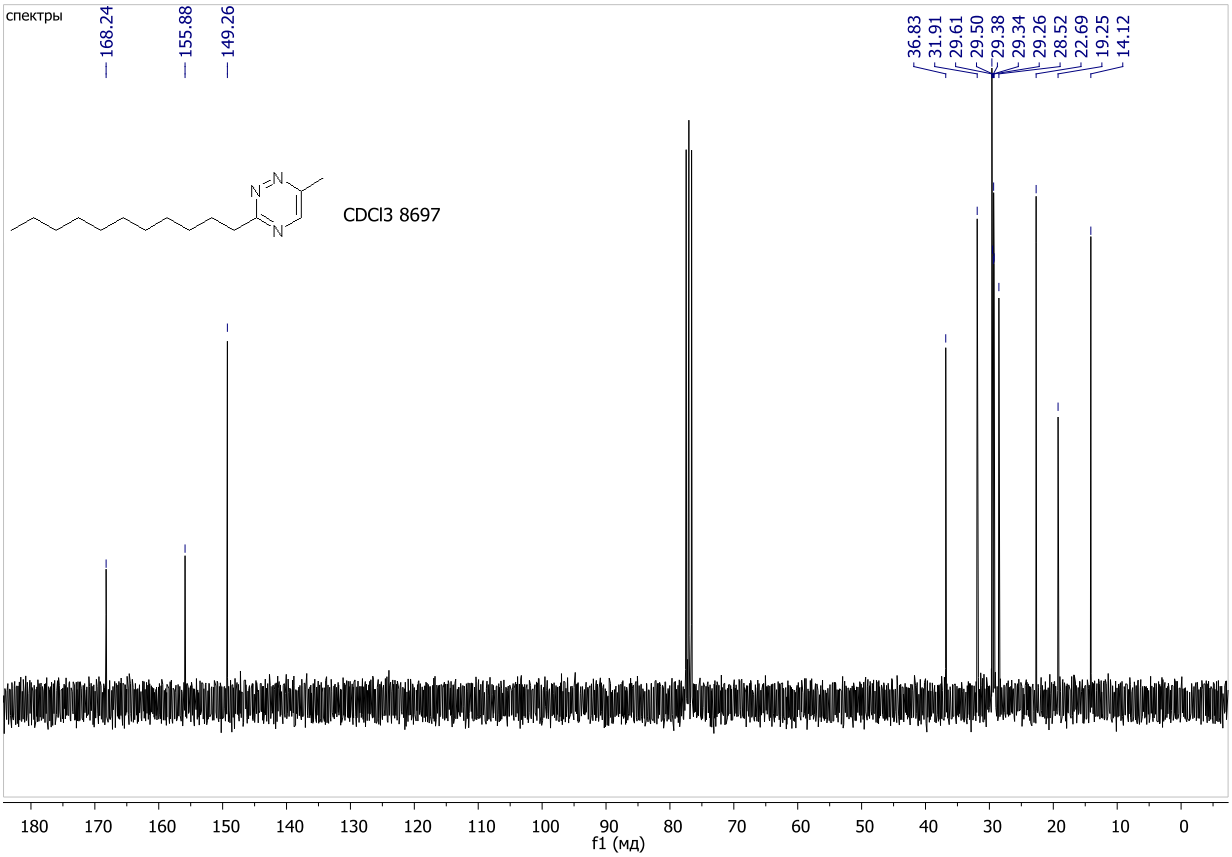
Compound **10n**:



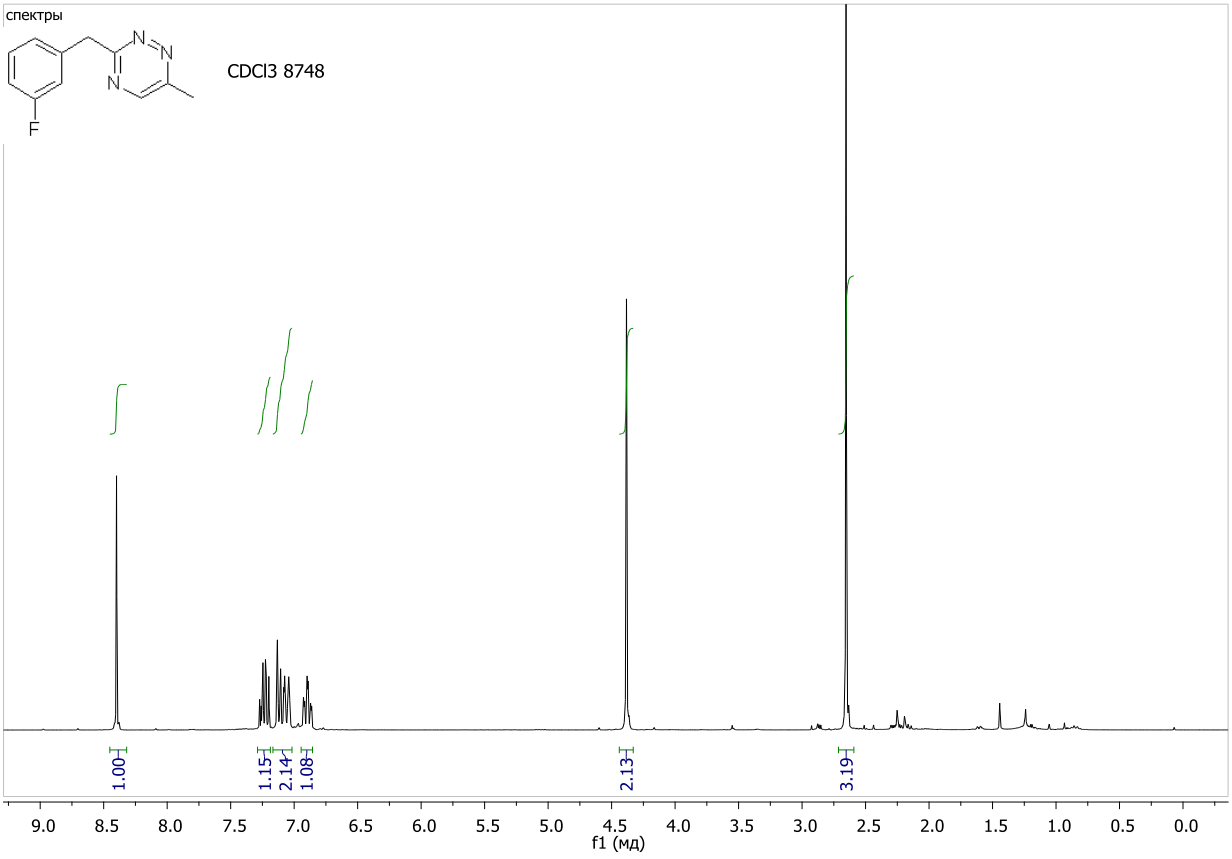


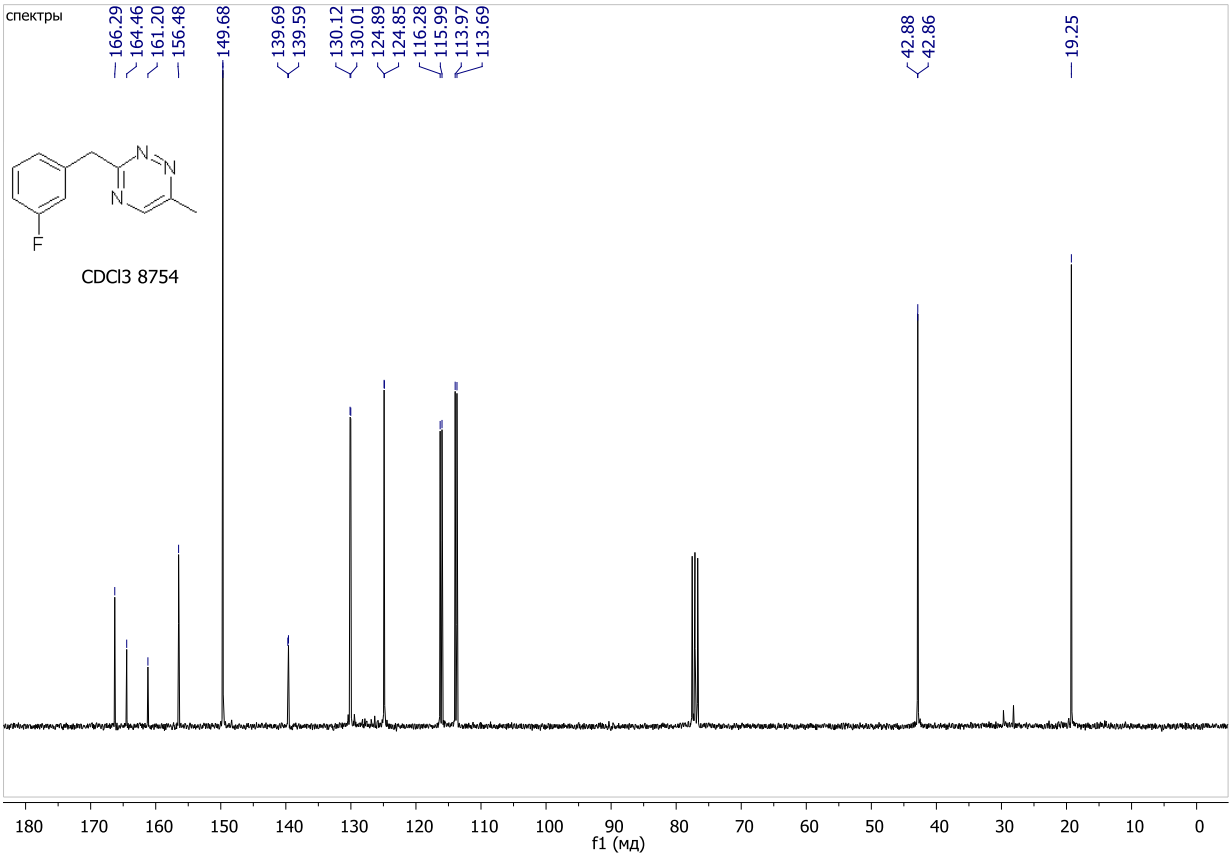
Compound **10o**:





Compouns **10p**:





Compound **10q**: