Nitroalkanes as Electrophiles: Synthesis of Triazole-Fused Heterocycles with Neuroblastoma Differentiation Activity

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Electronic Supplementary Information

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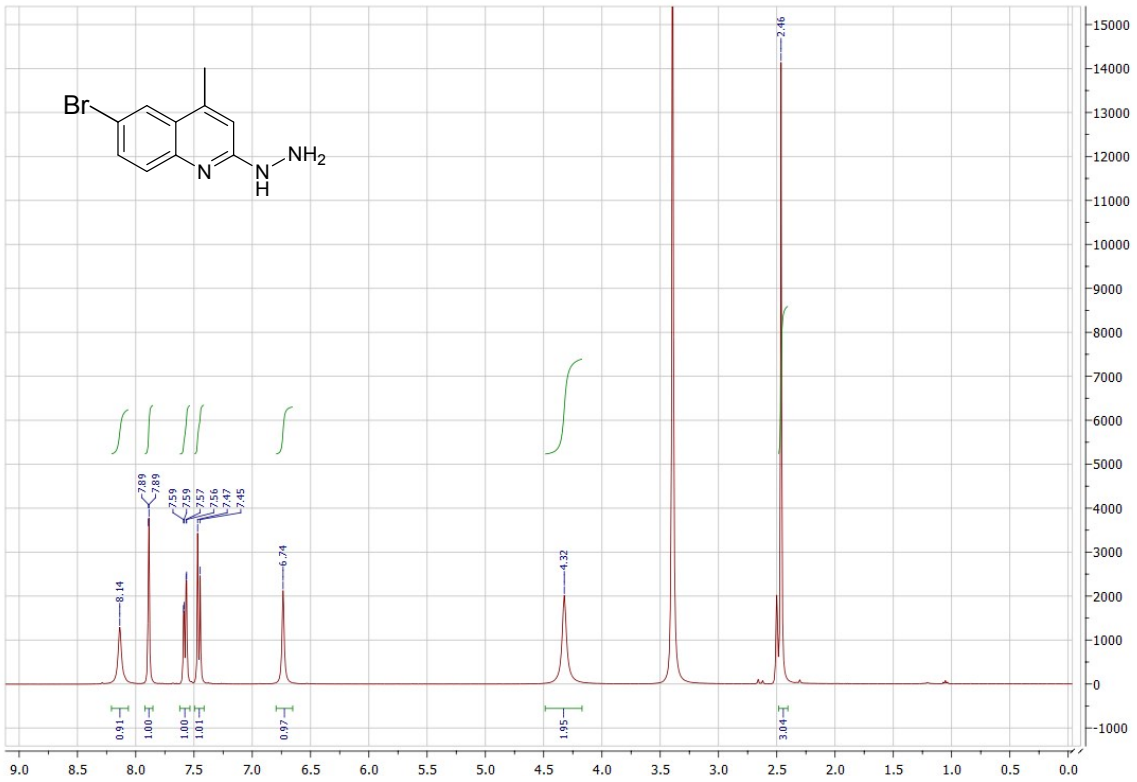
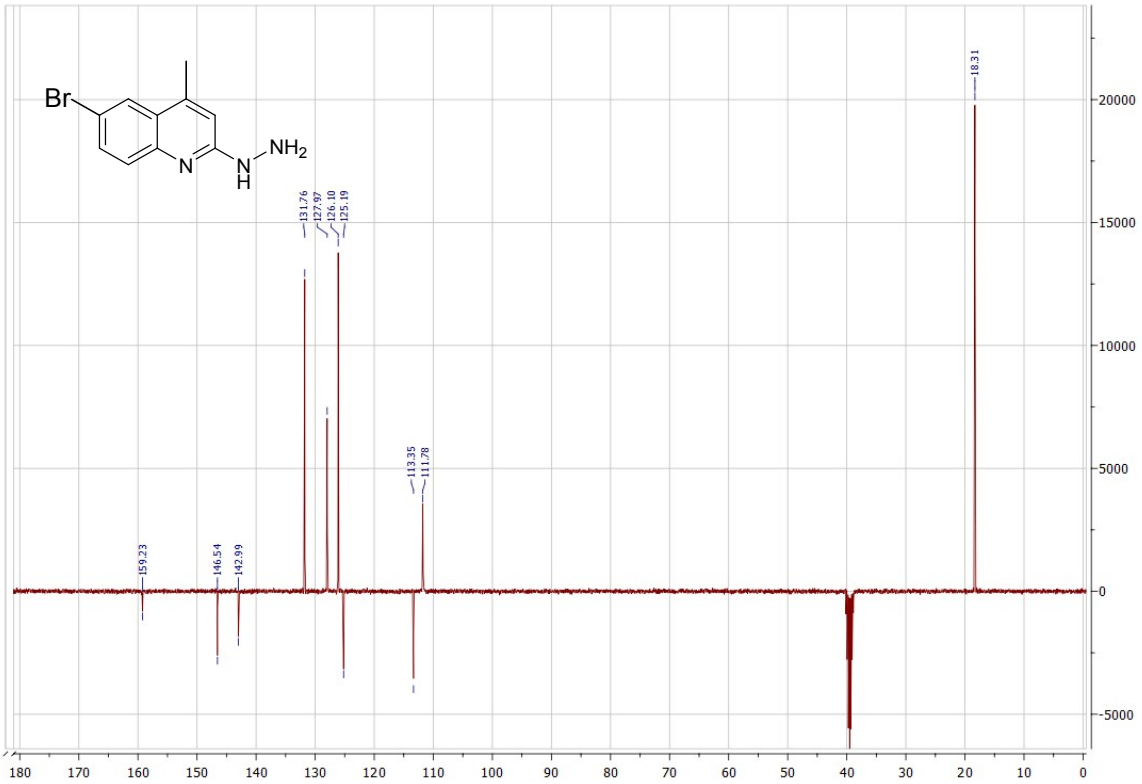
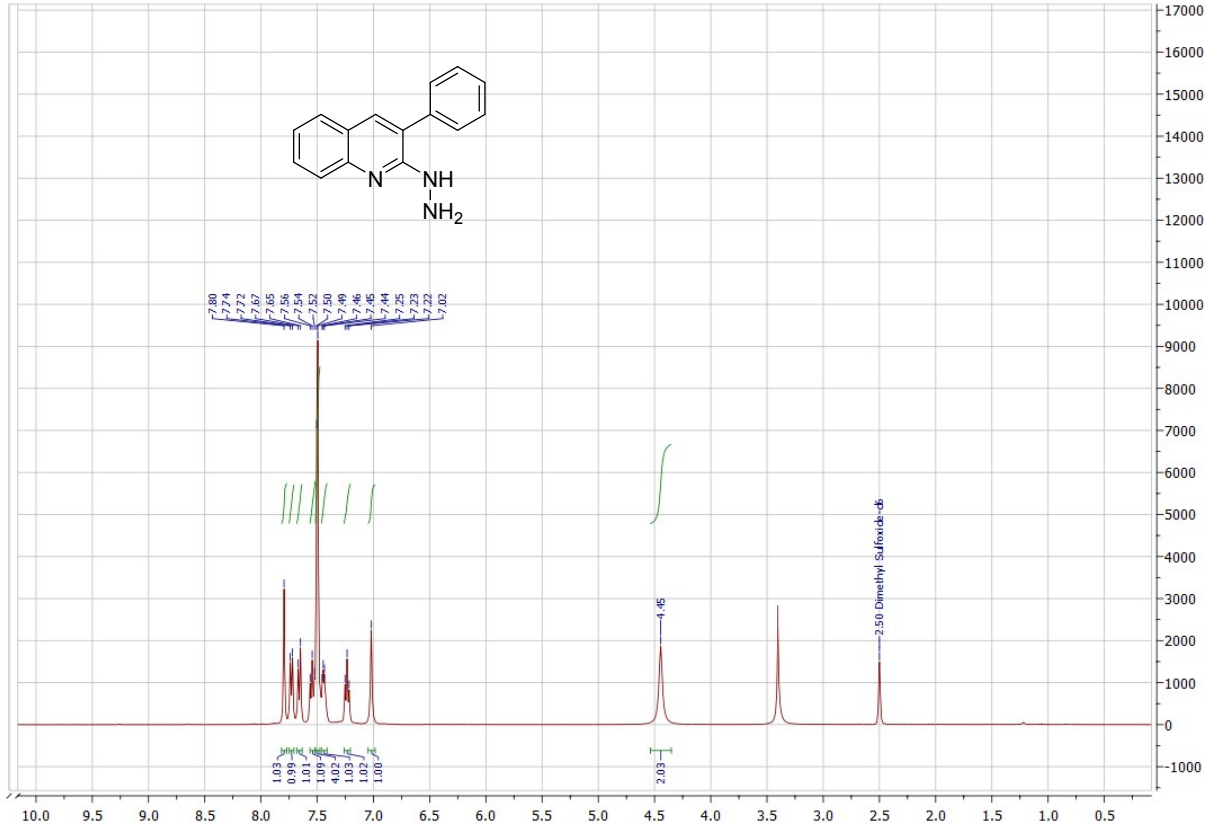
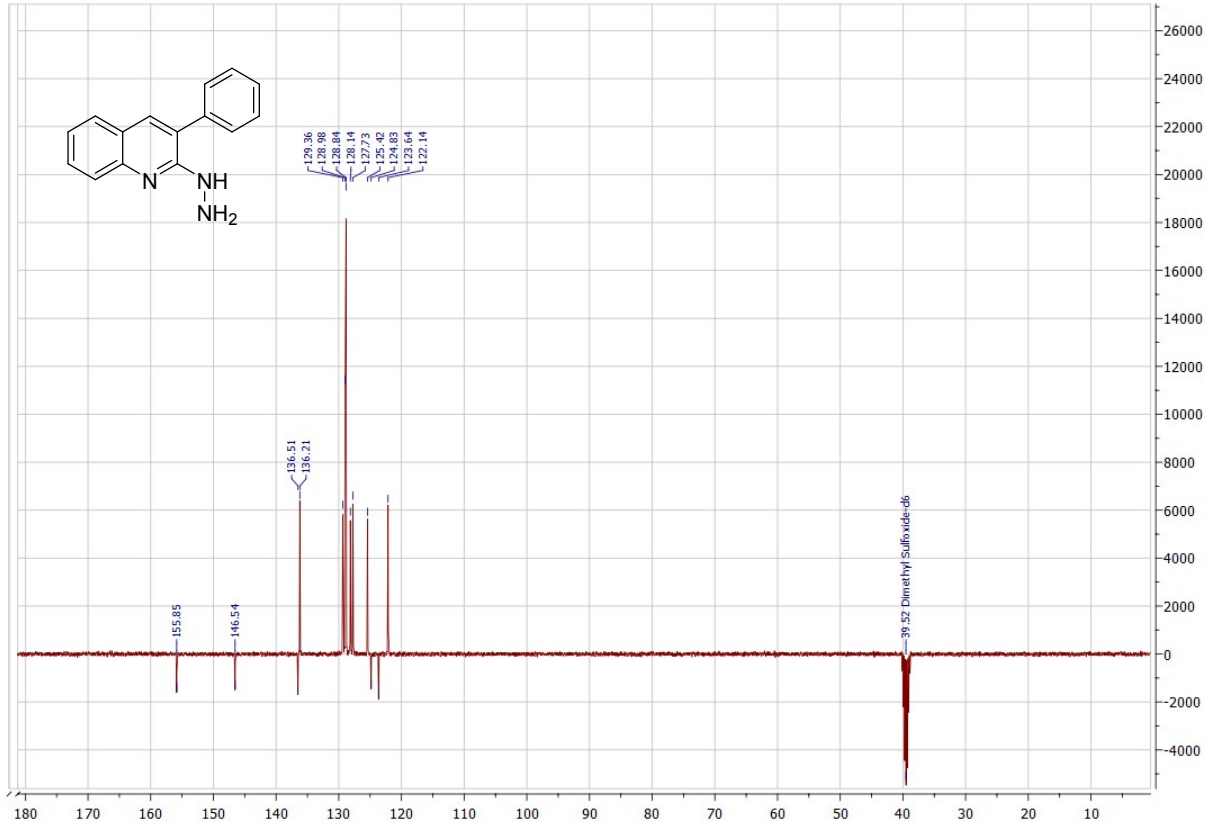
^{1}H and ^{13}C NMR spectra of **1c** in DMSO-d_6.





^{1}H and ^{13}C NMR spectra of **1e** in DMSO-d_6.





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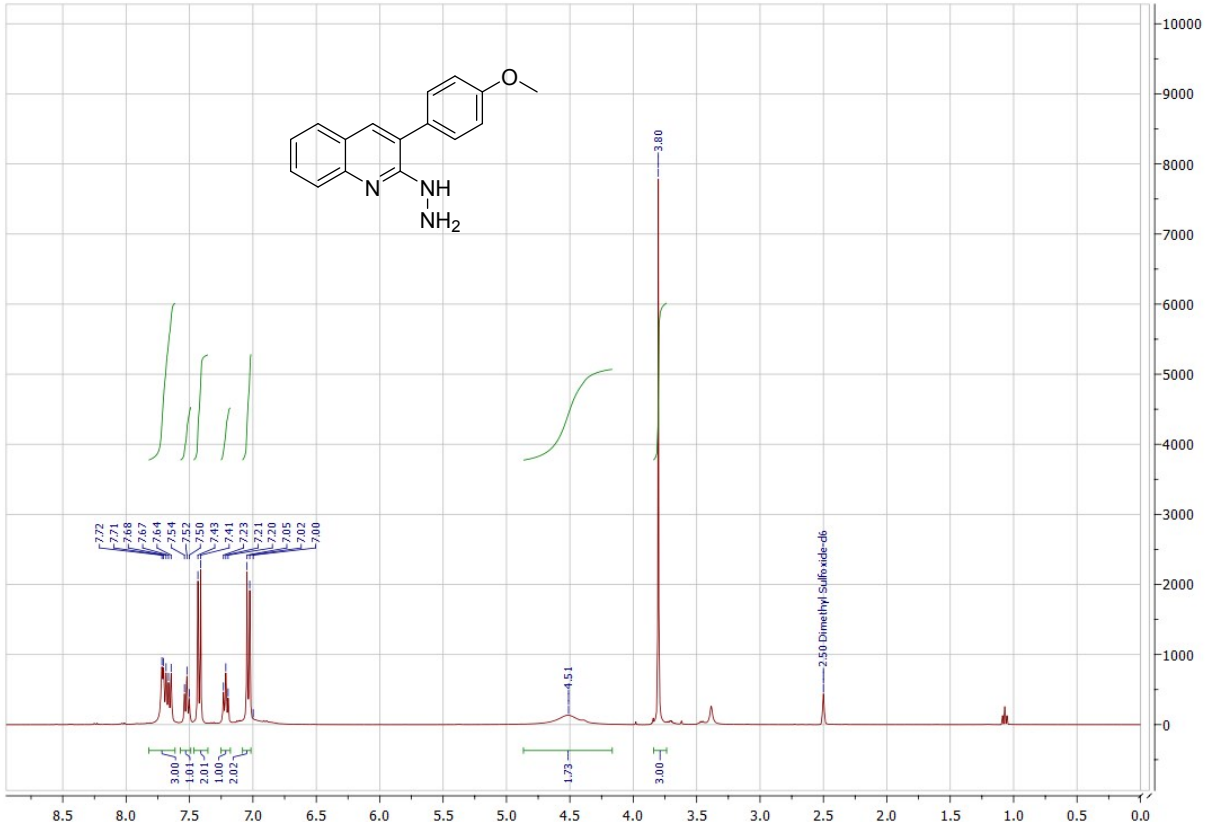

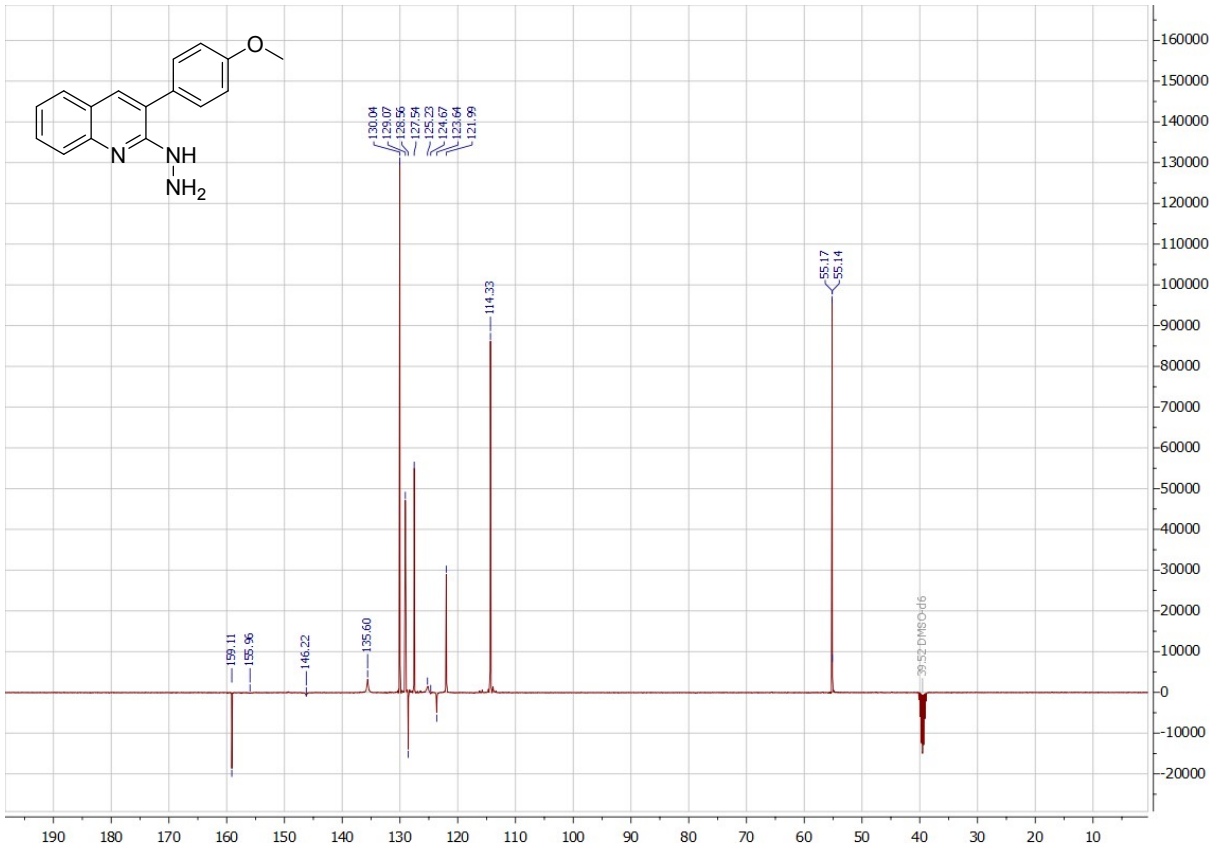

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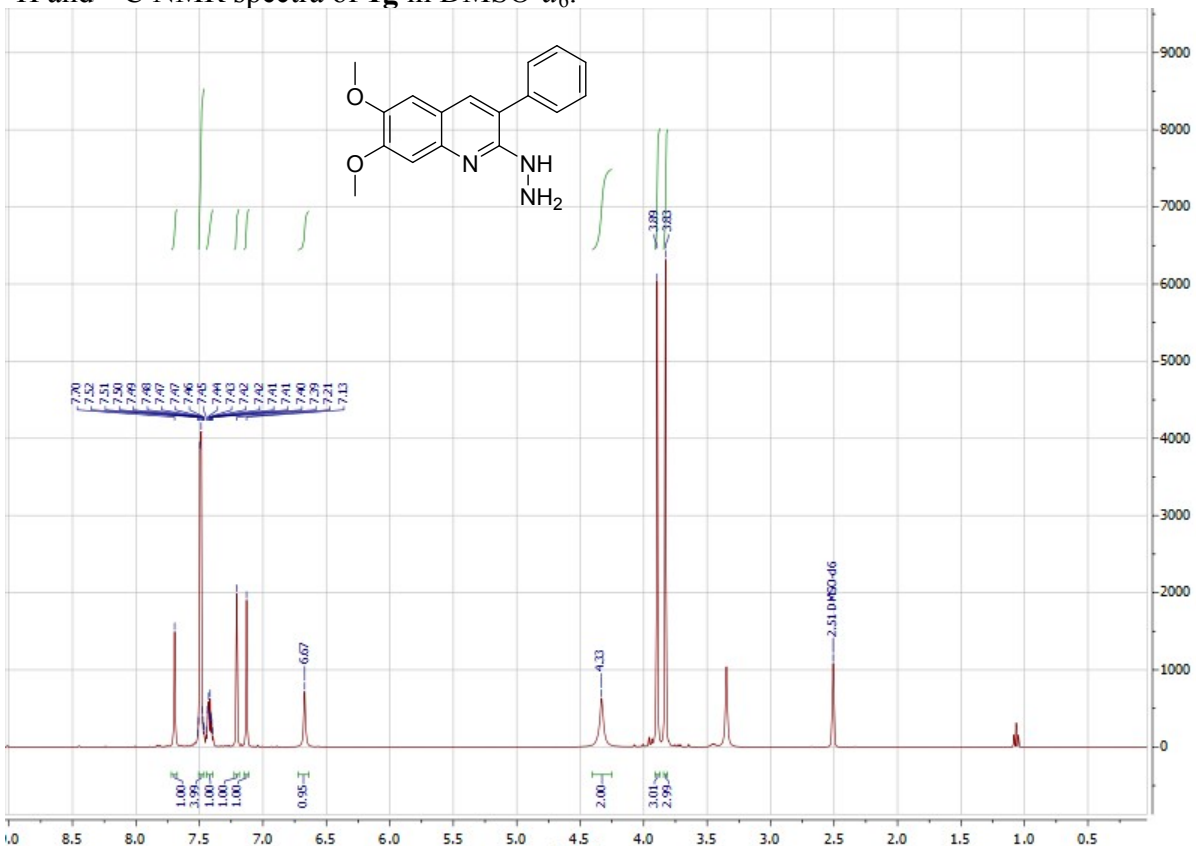

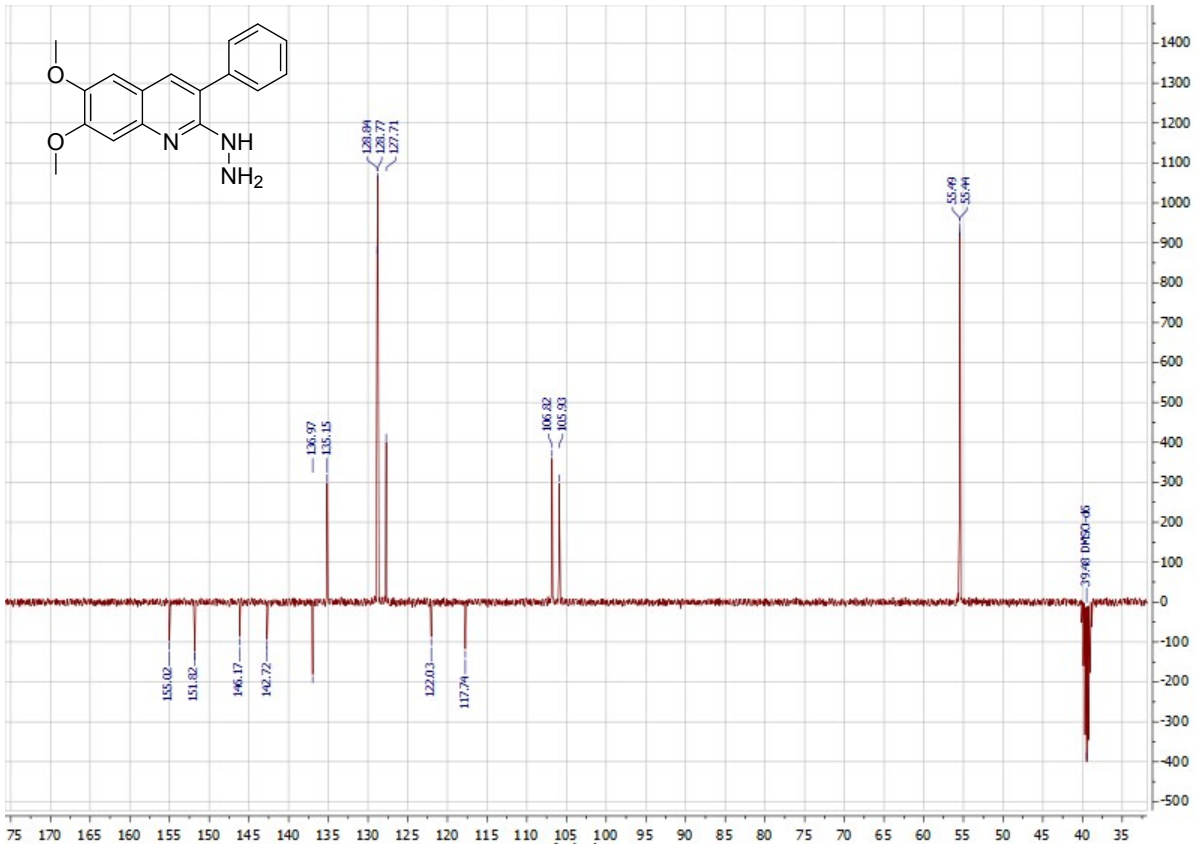

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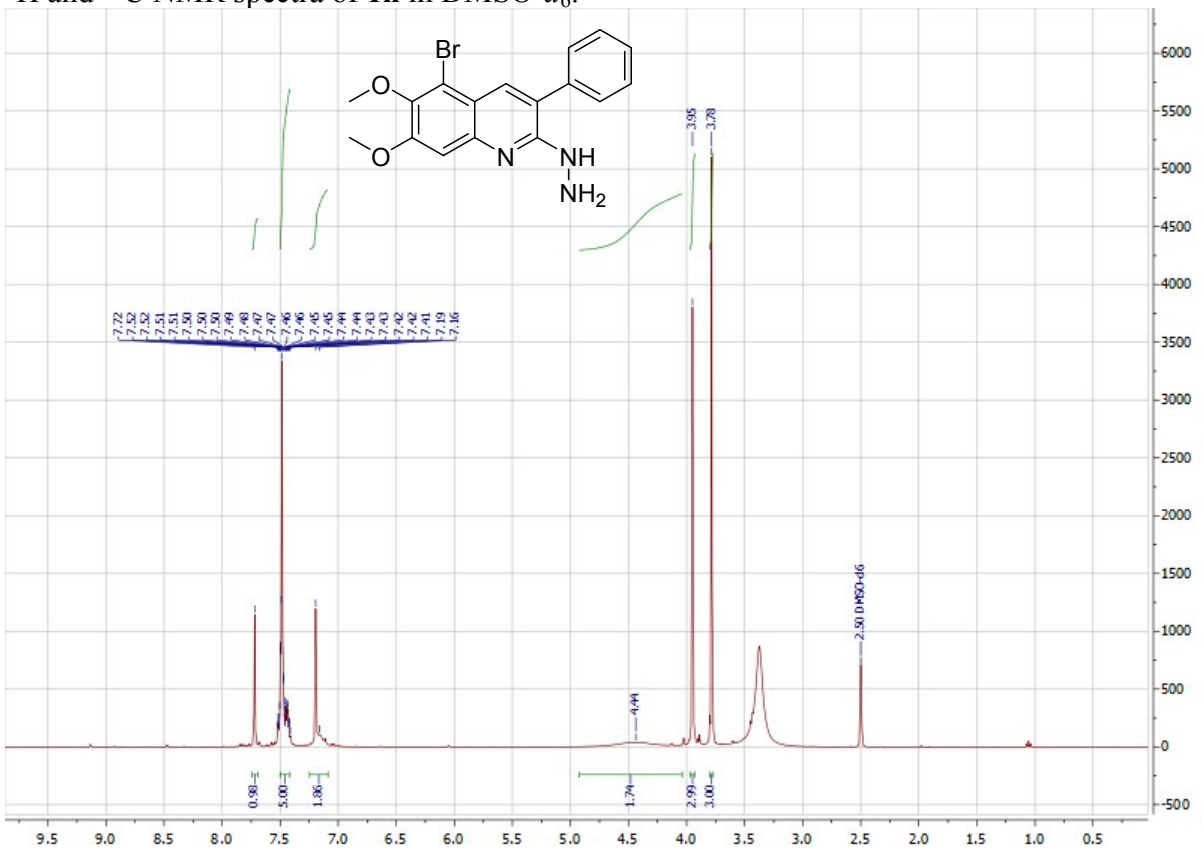

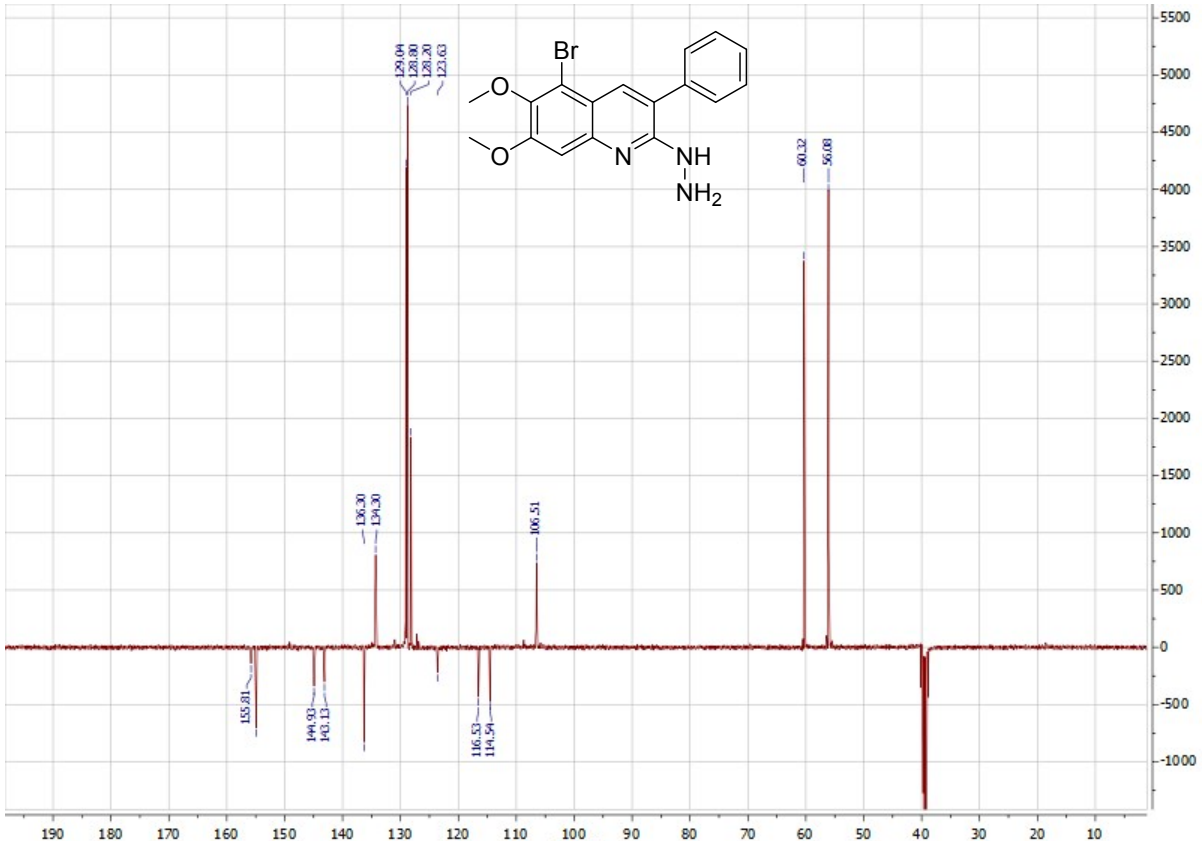

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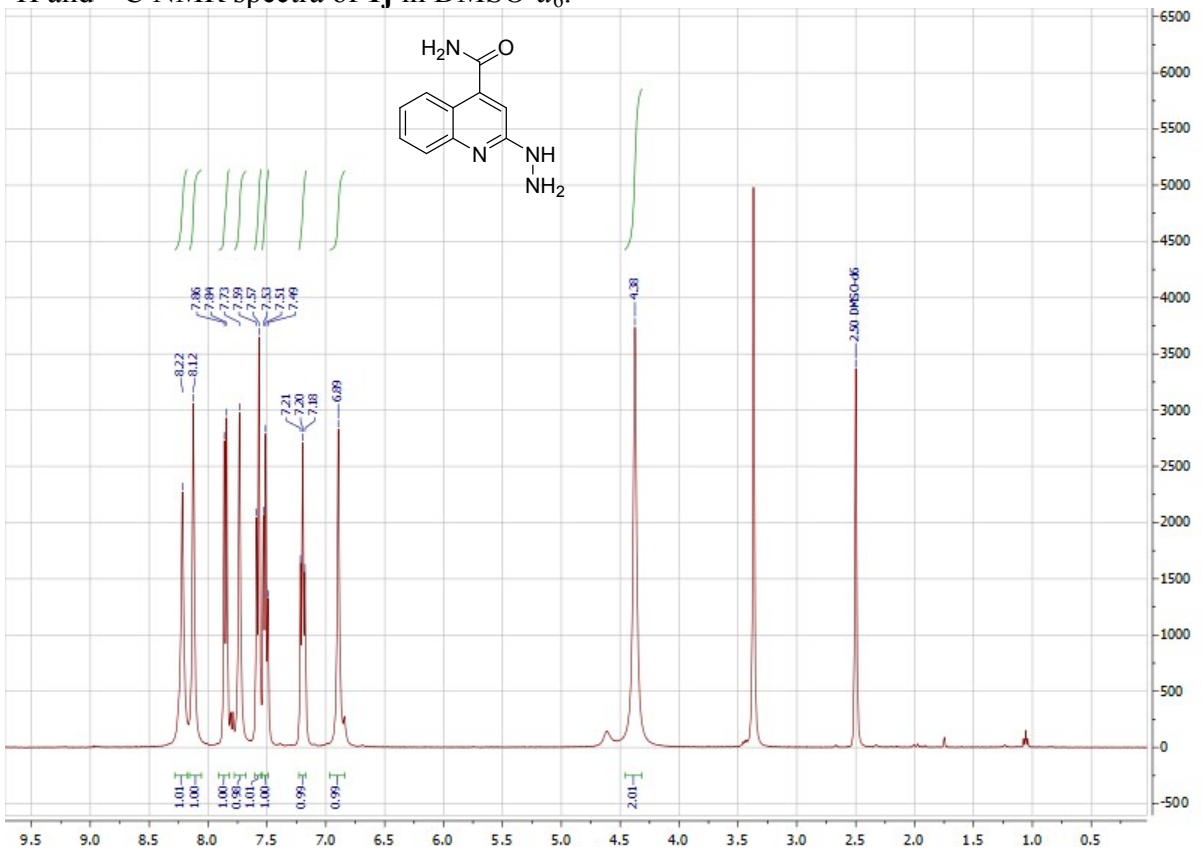

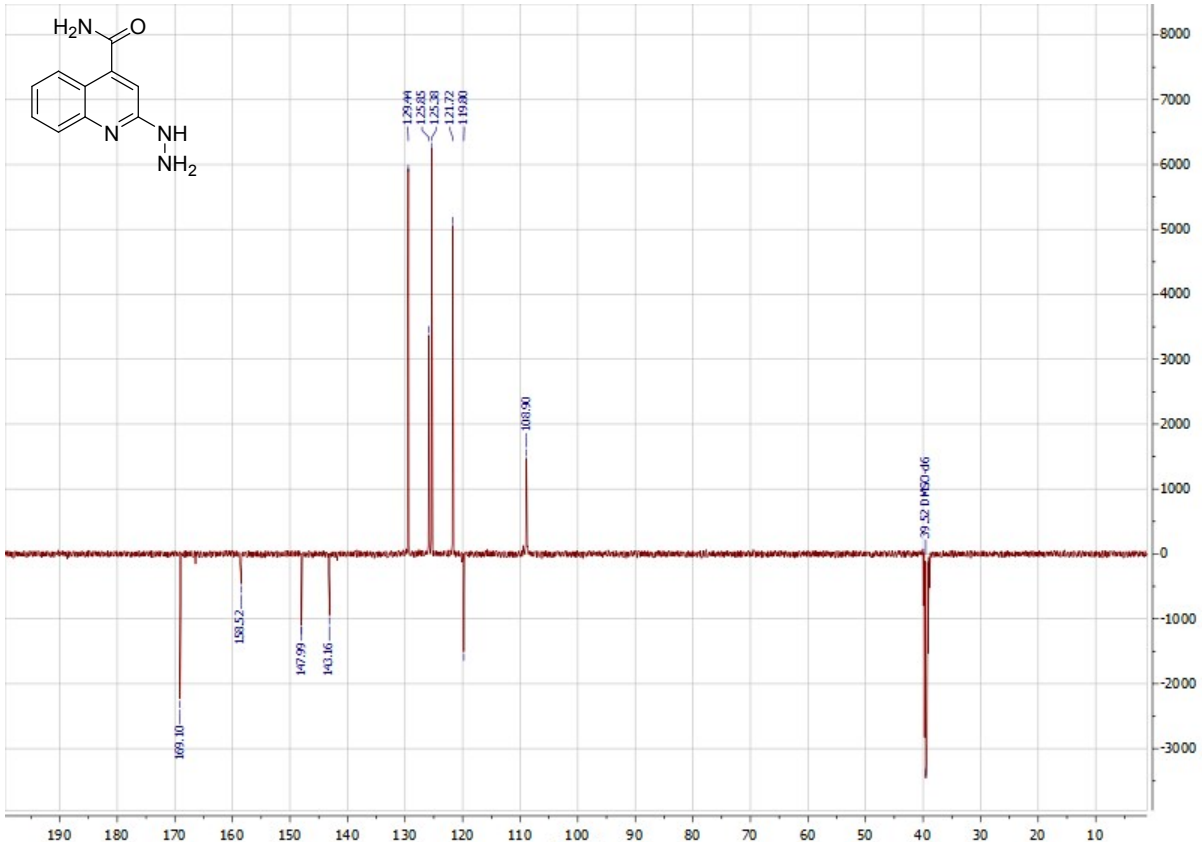

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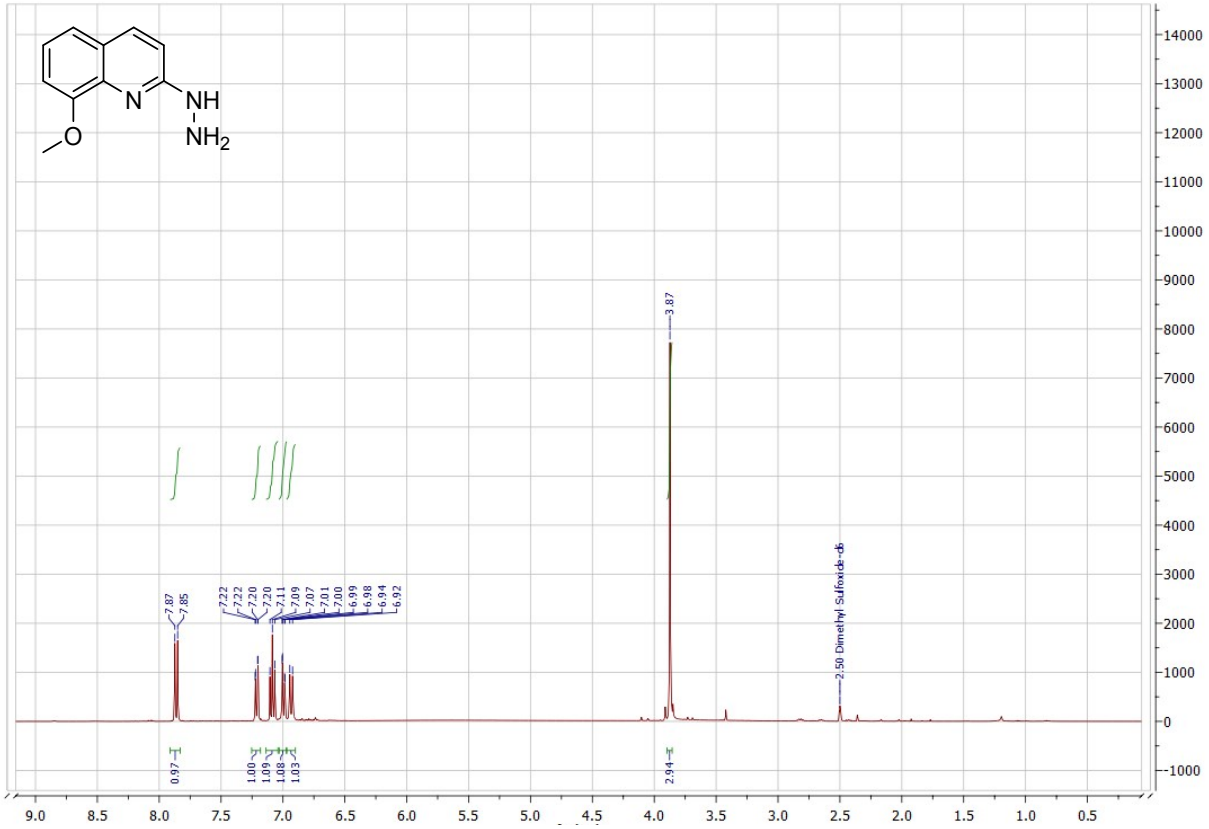

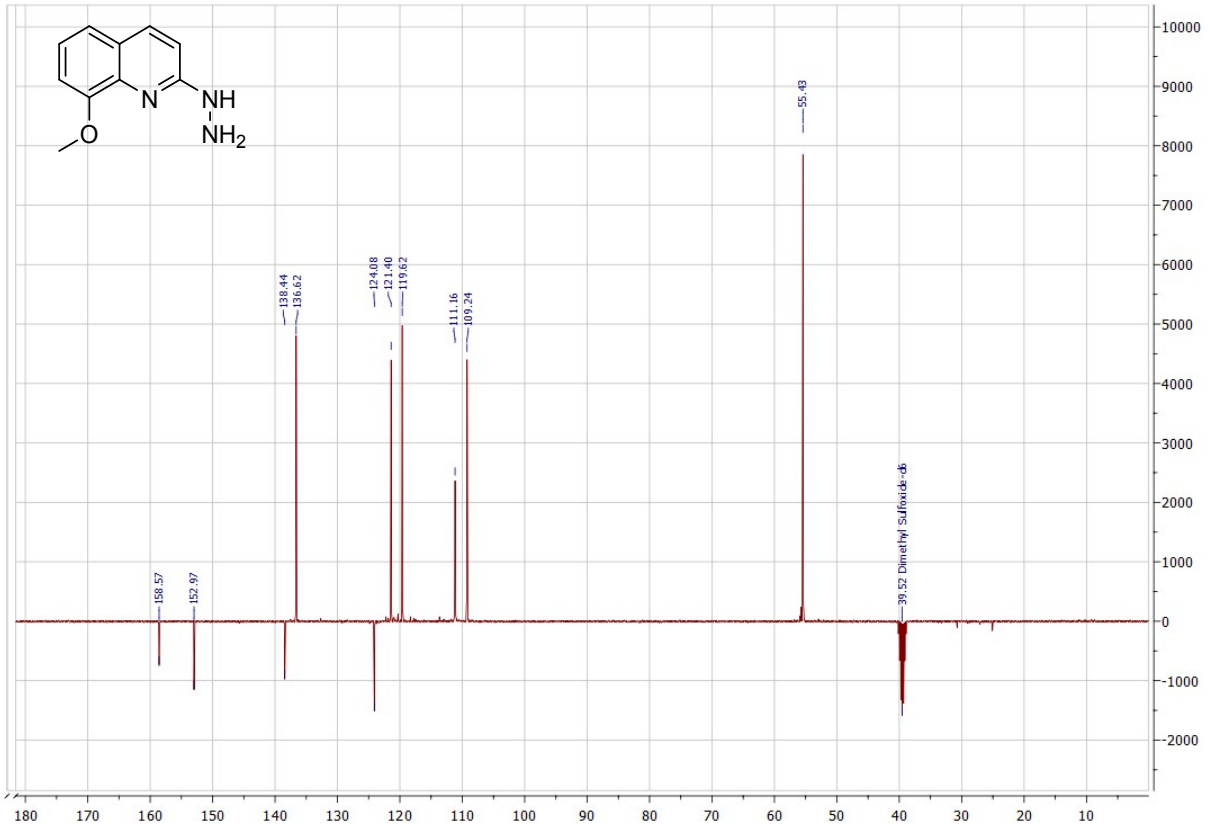

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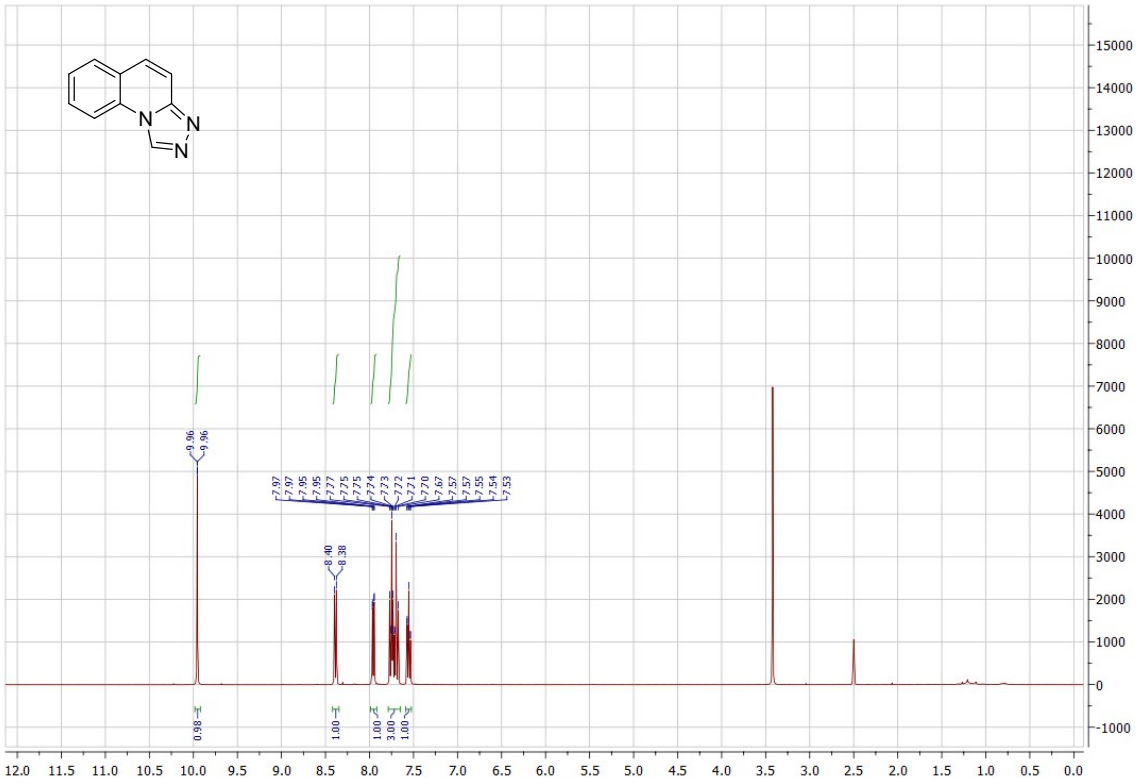
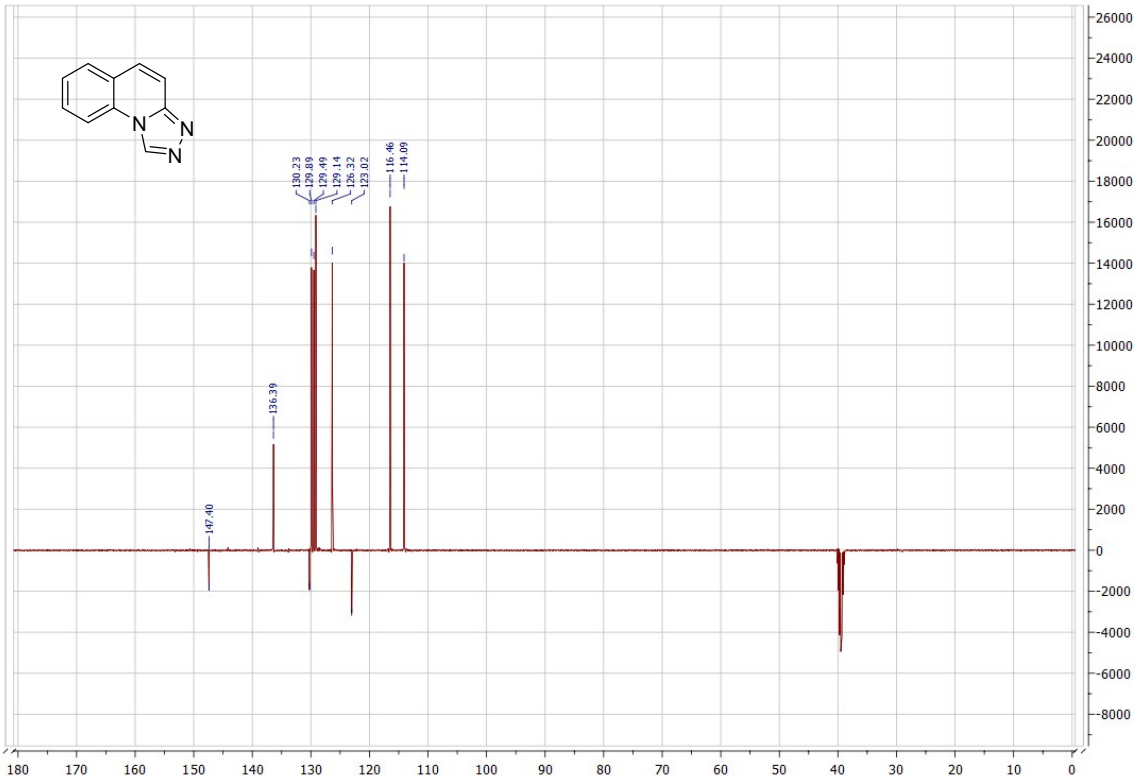
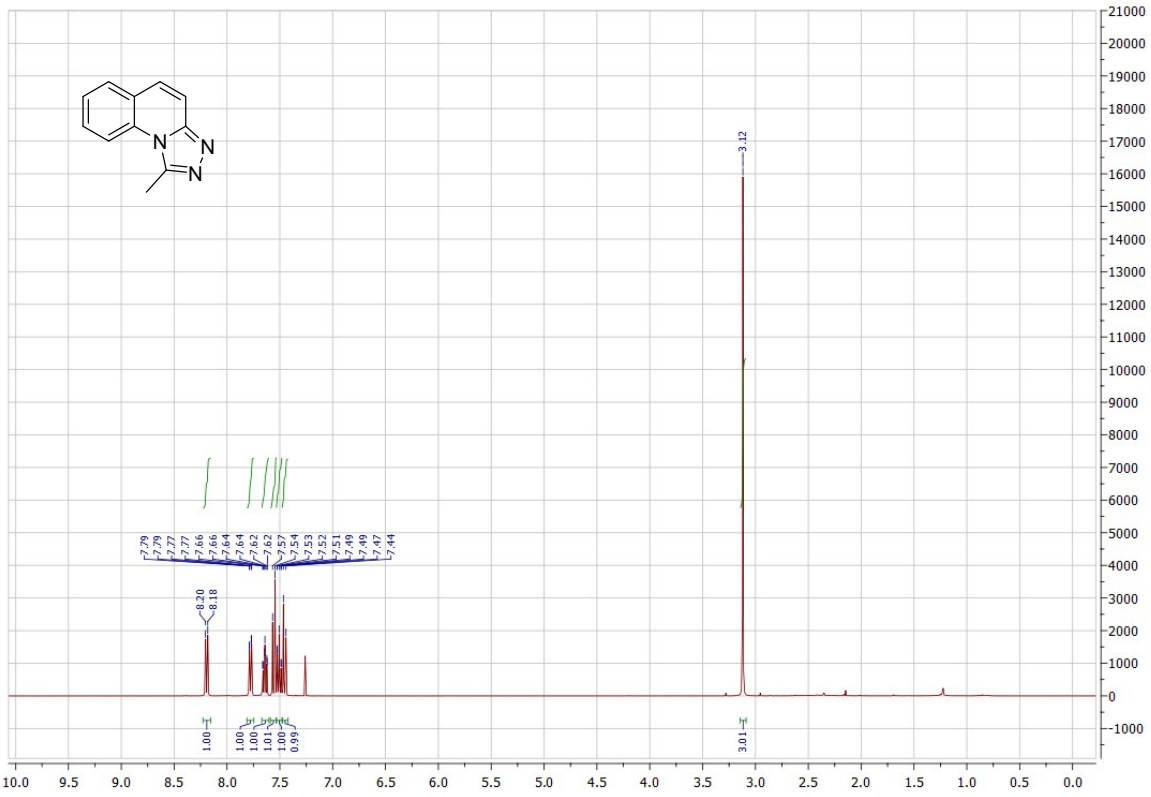
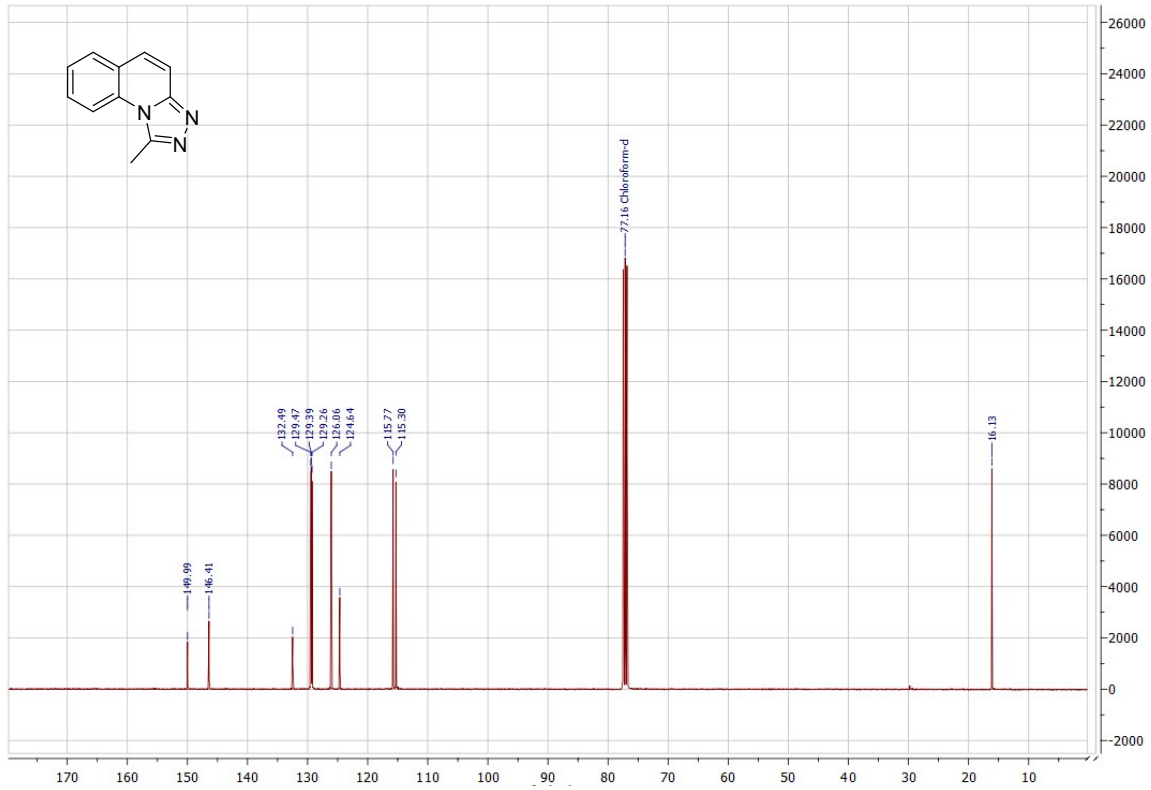




^{1}H and ^{13}C NMR spectra of **3ab** in $CDCl_3$.





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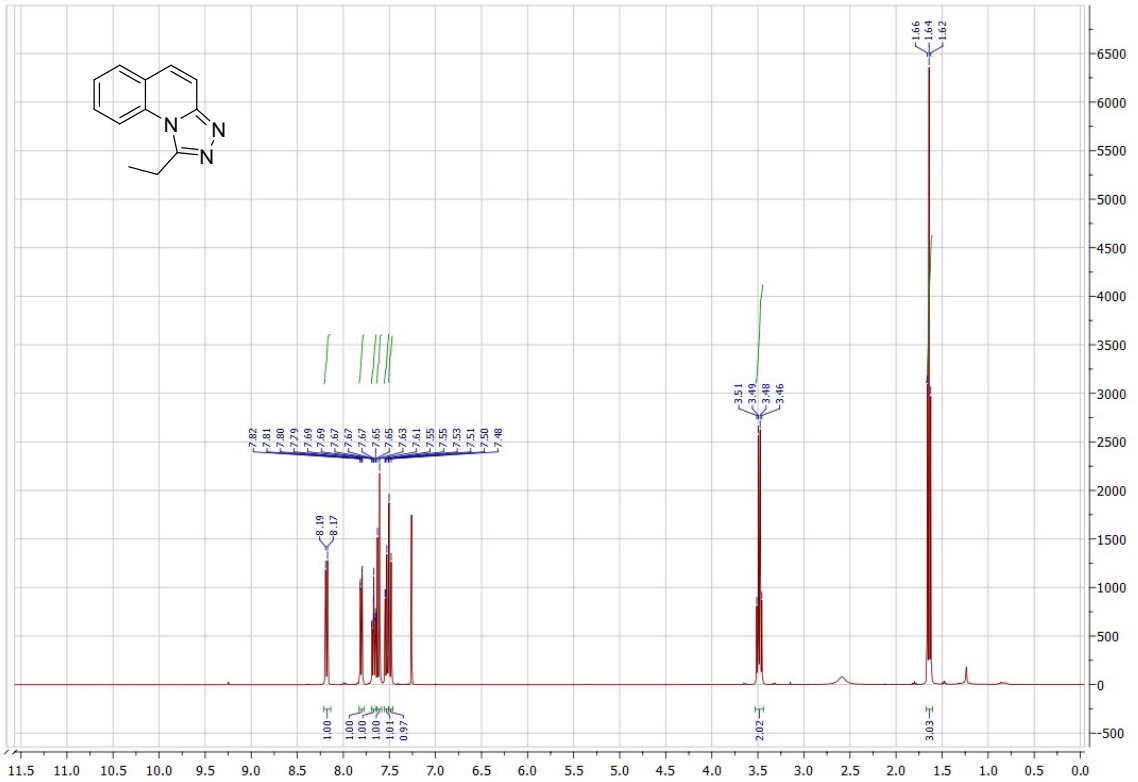

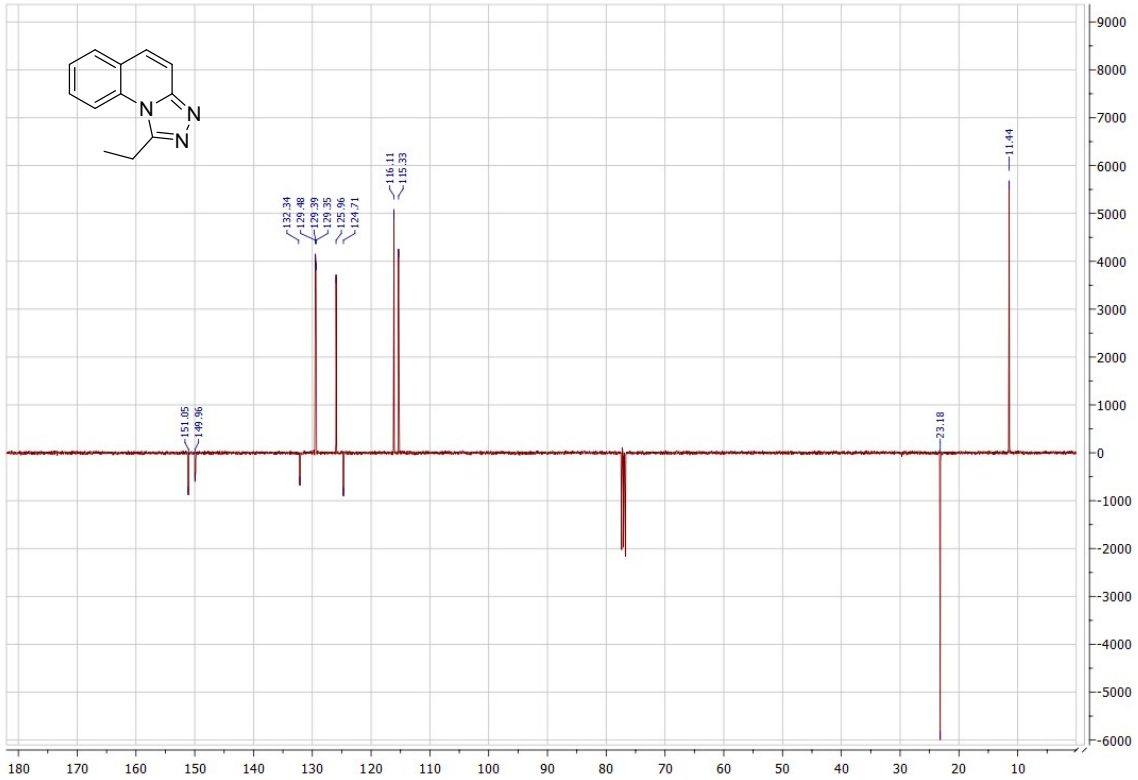

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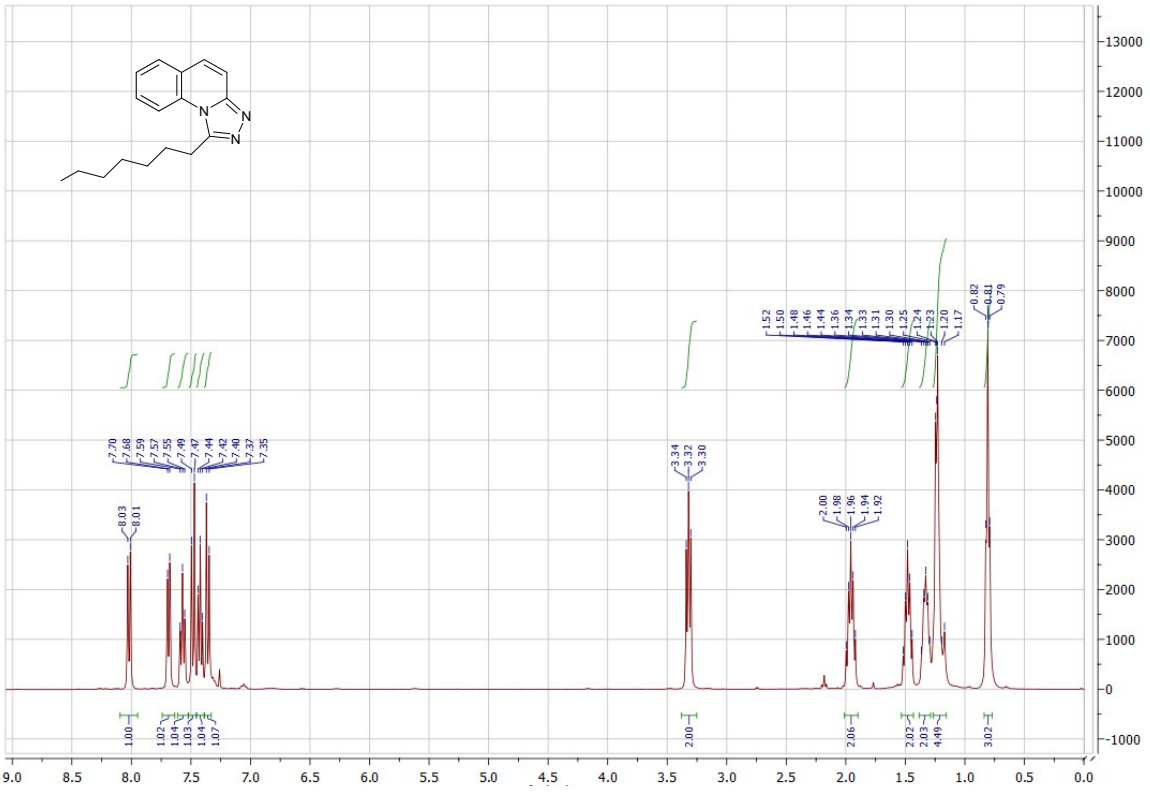

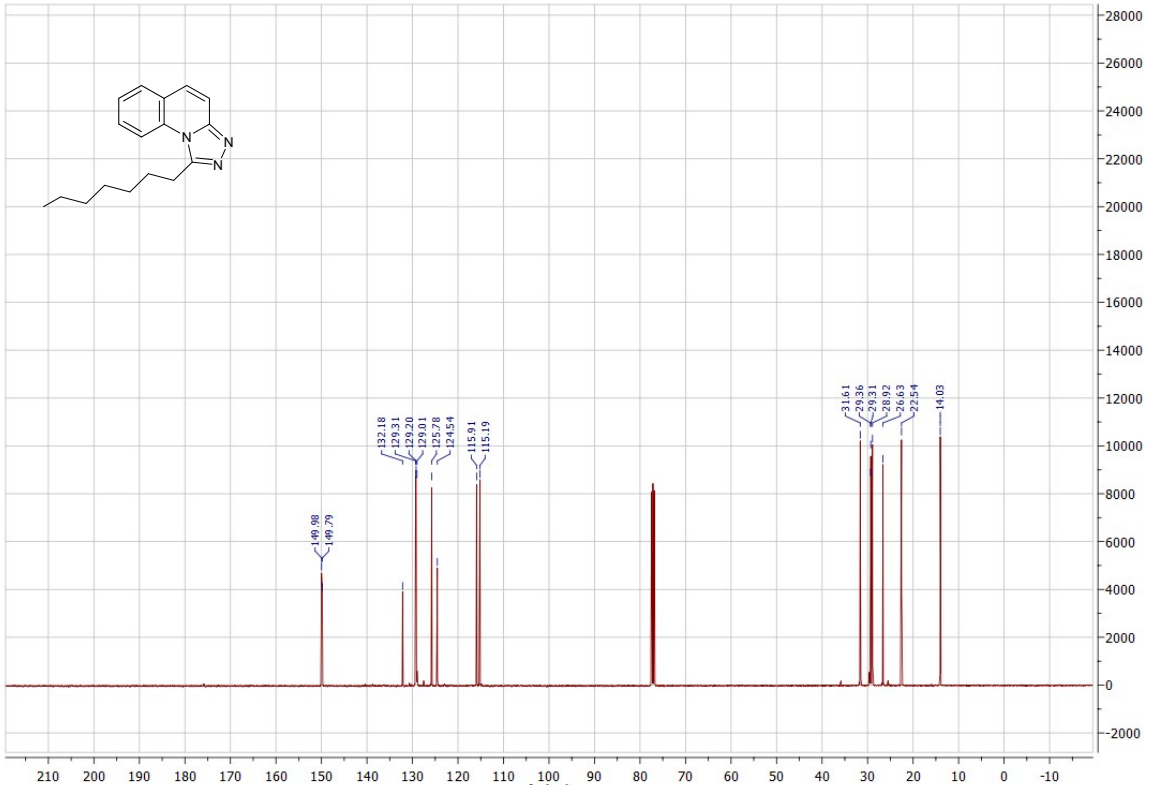

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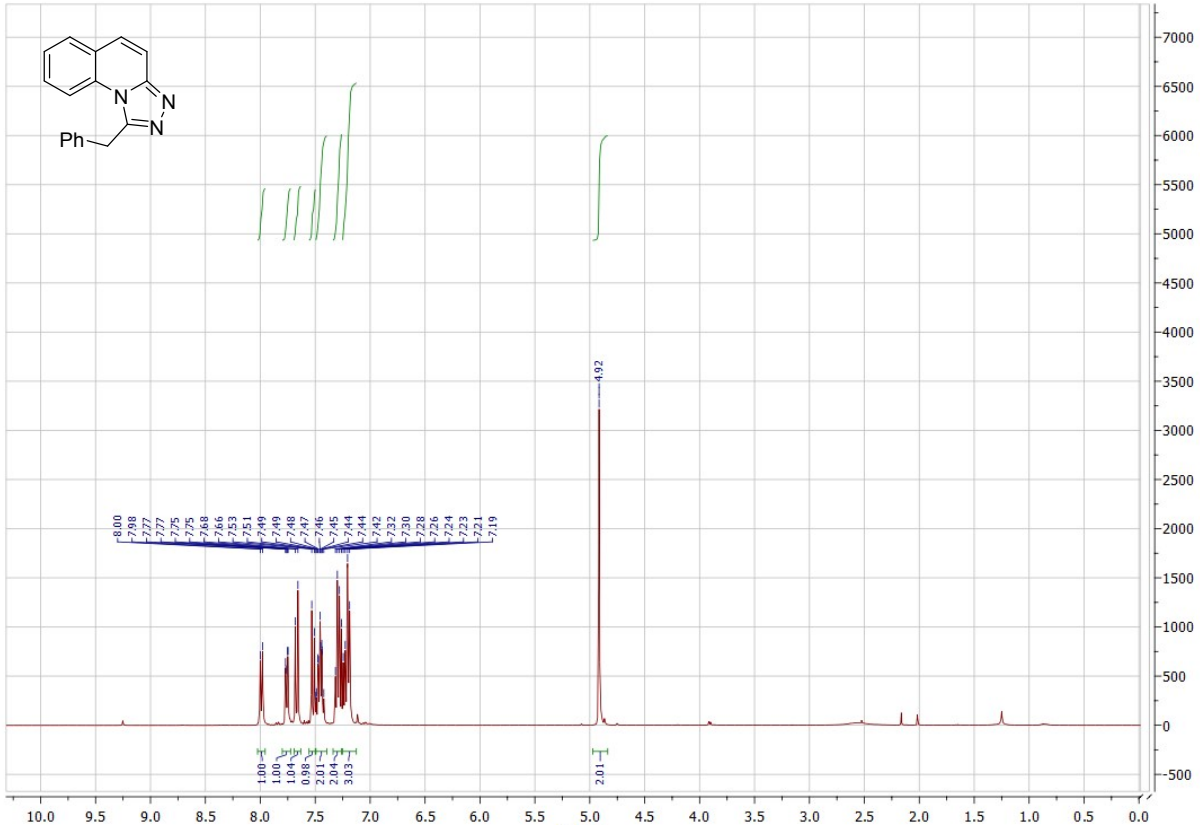

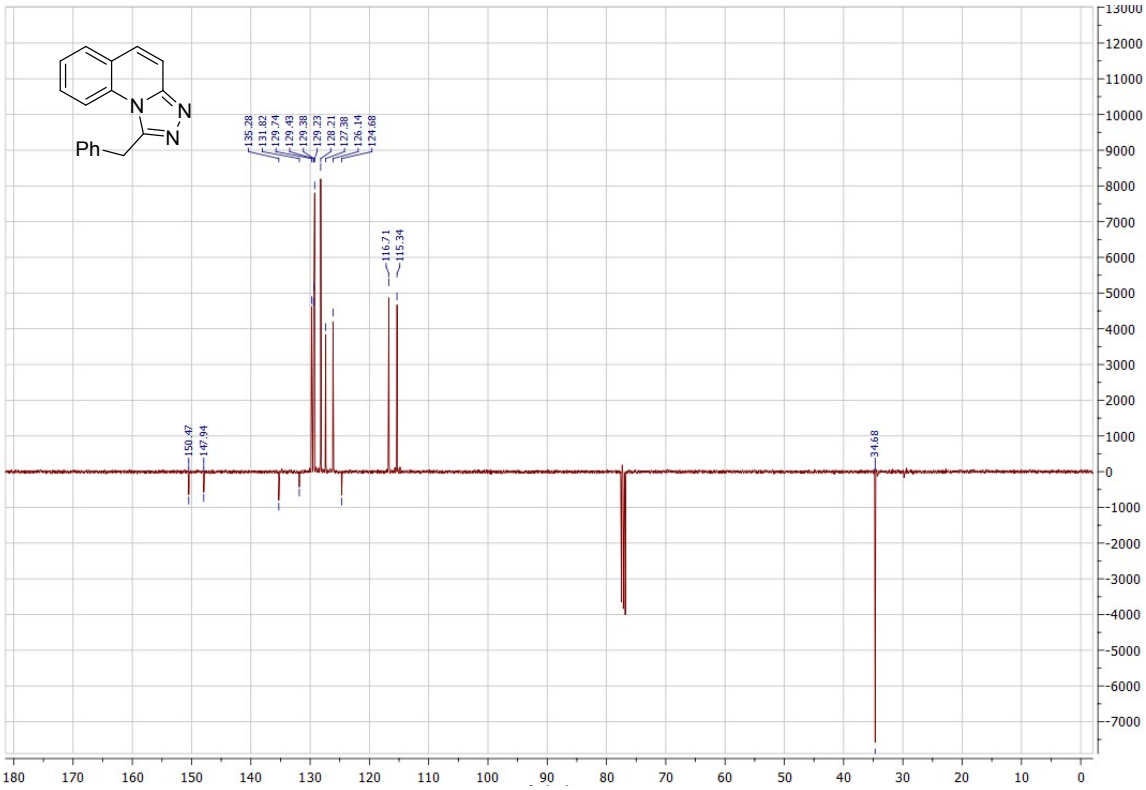

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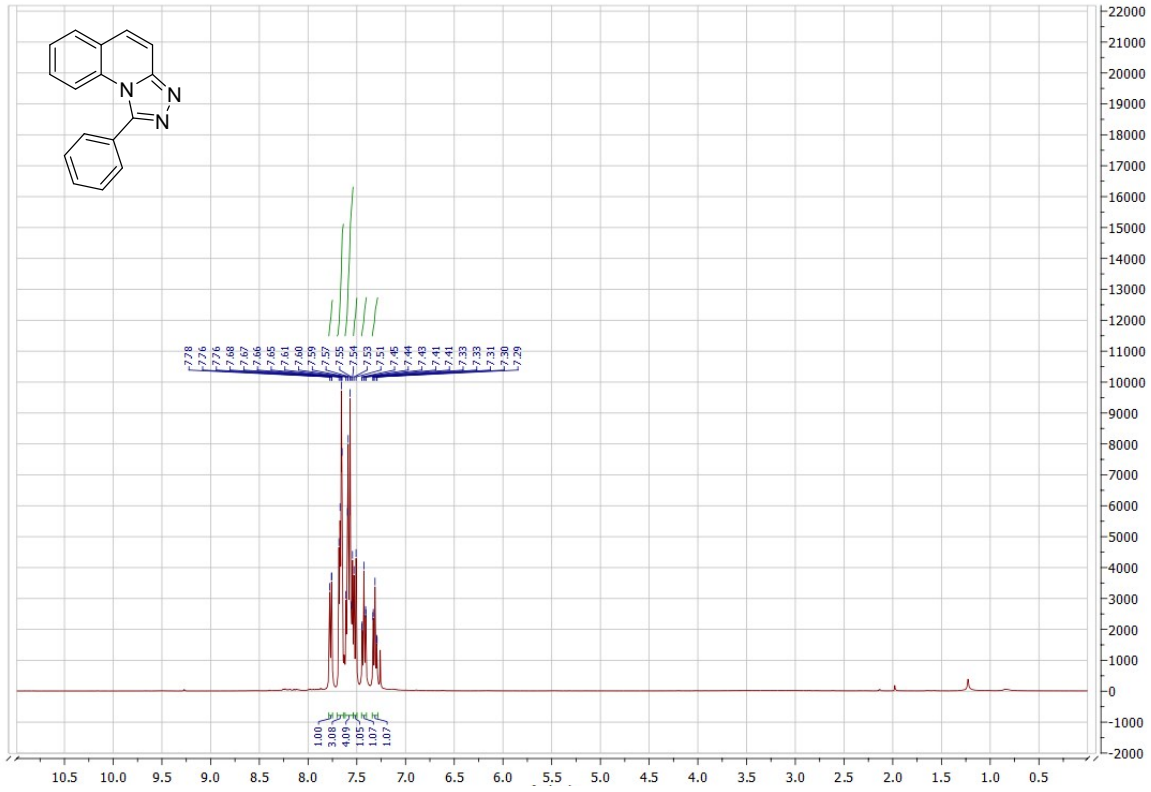
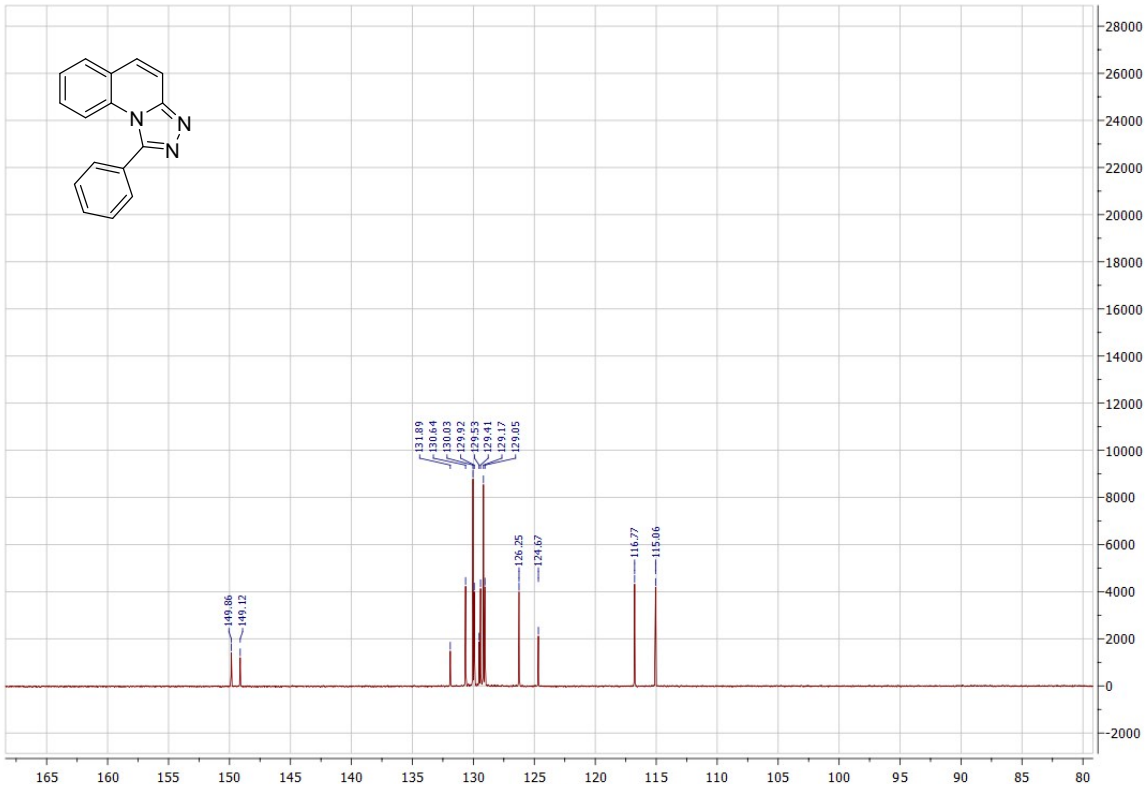
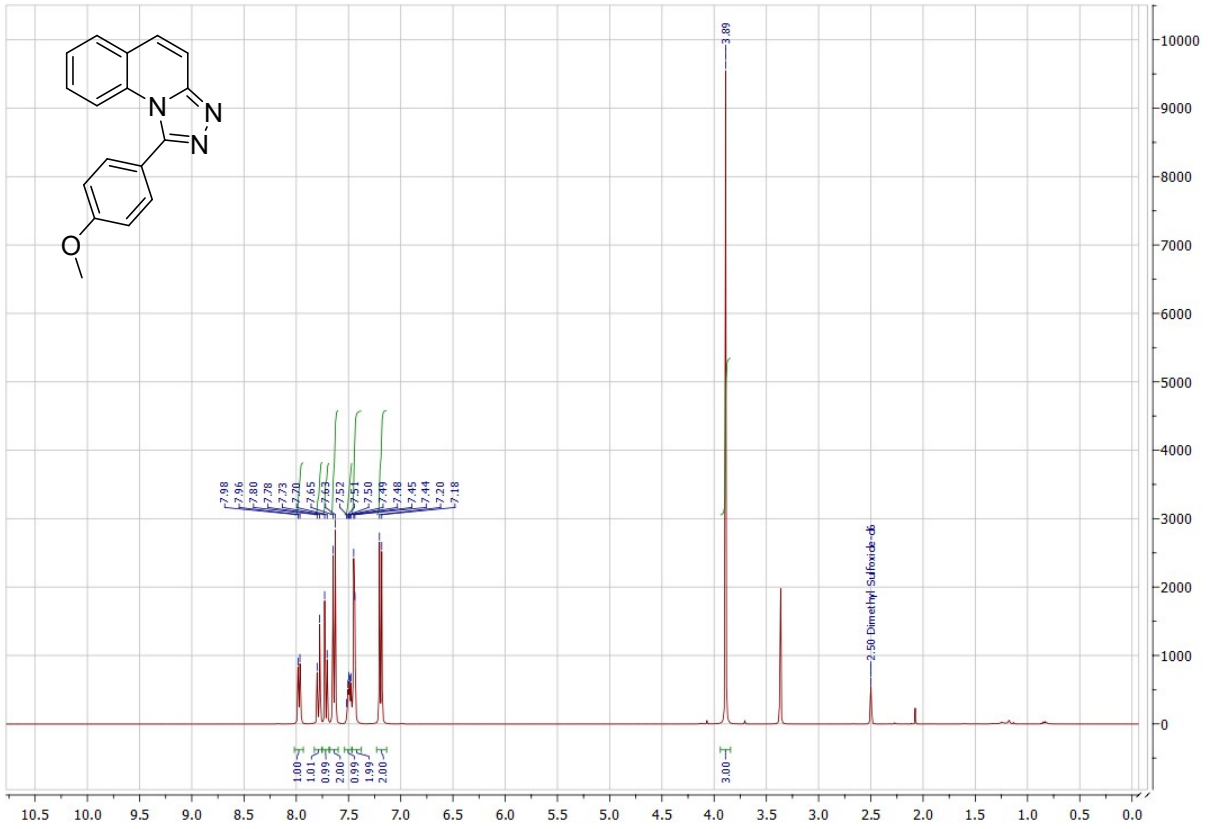
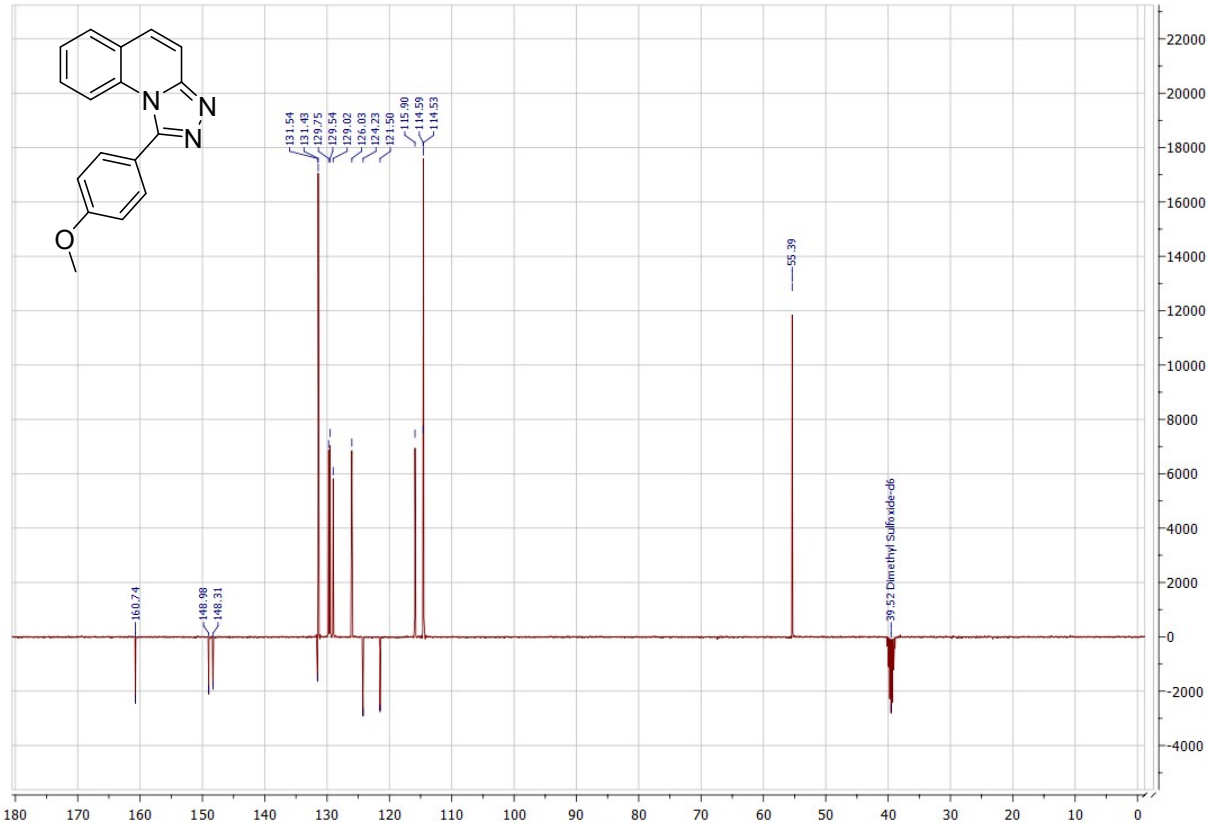


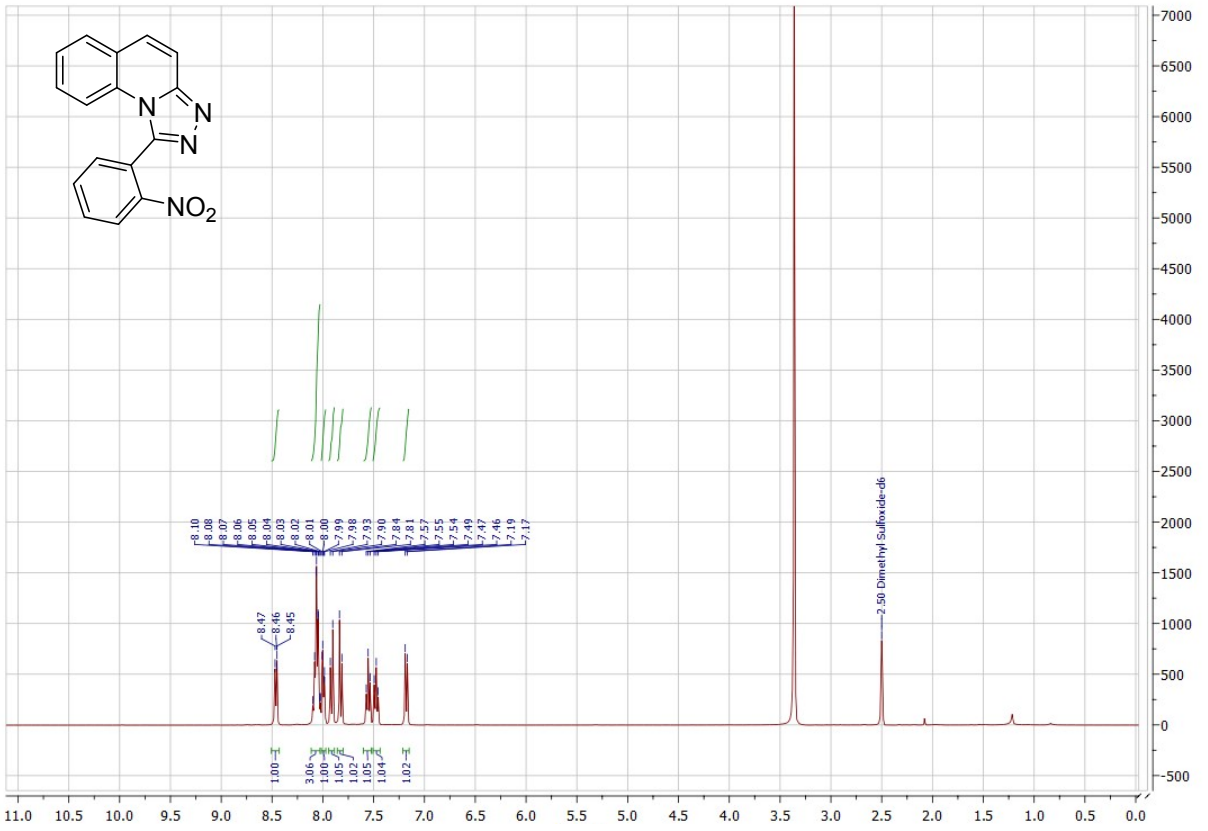


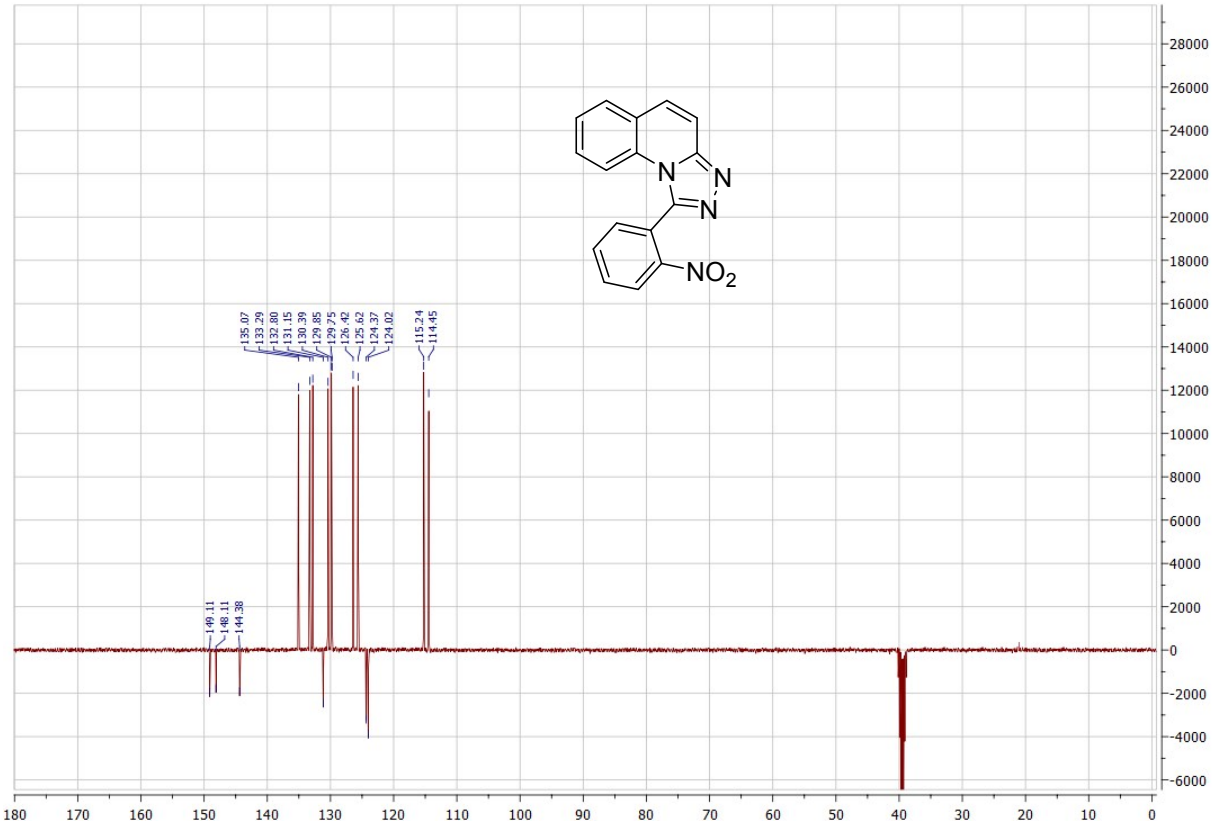
^{1}H and ^{13}C NMR spectra of **3ah** in DMSO-d_6.





^{1}H and ^{13}C NMR spectra of **3ai** in DMSO-d_6.





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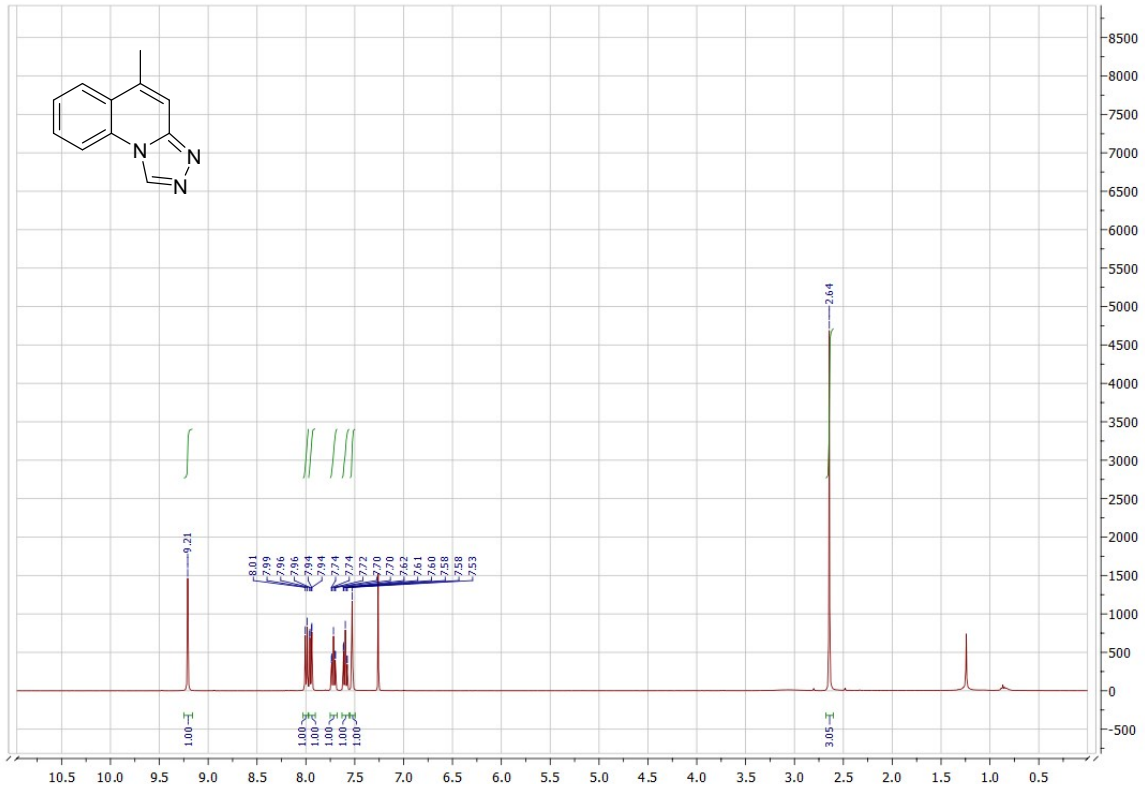

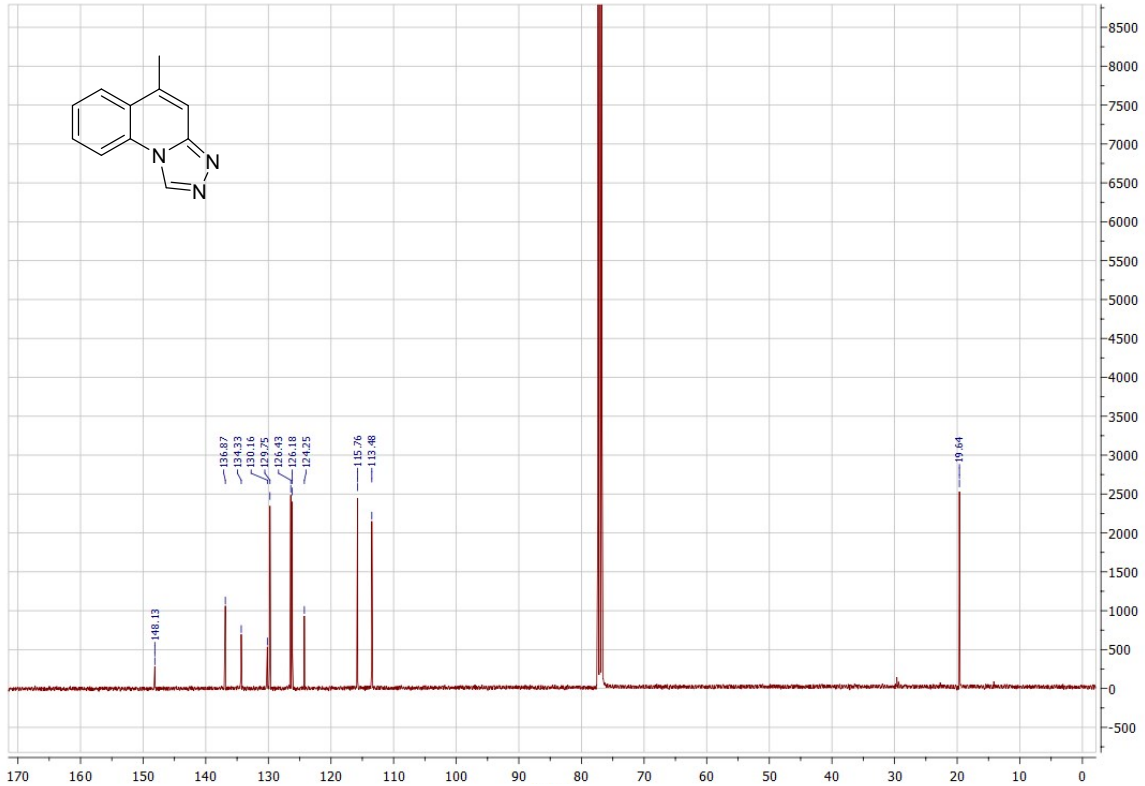

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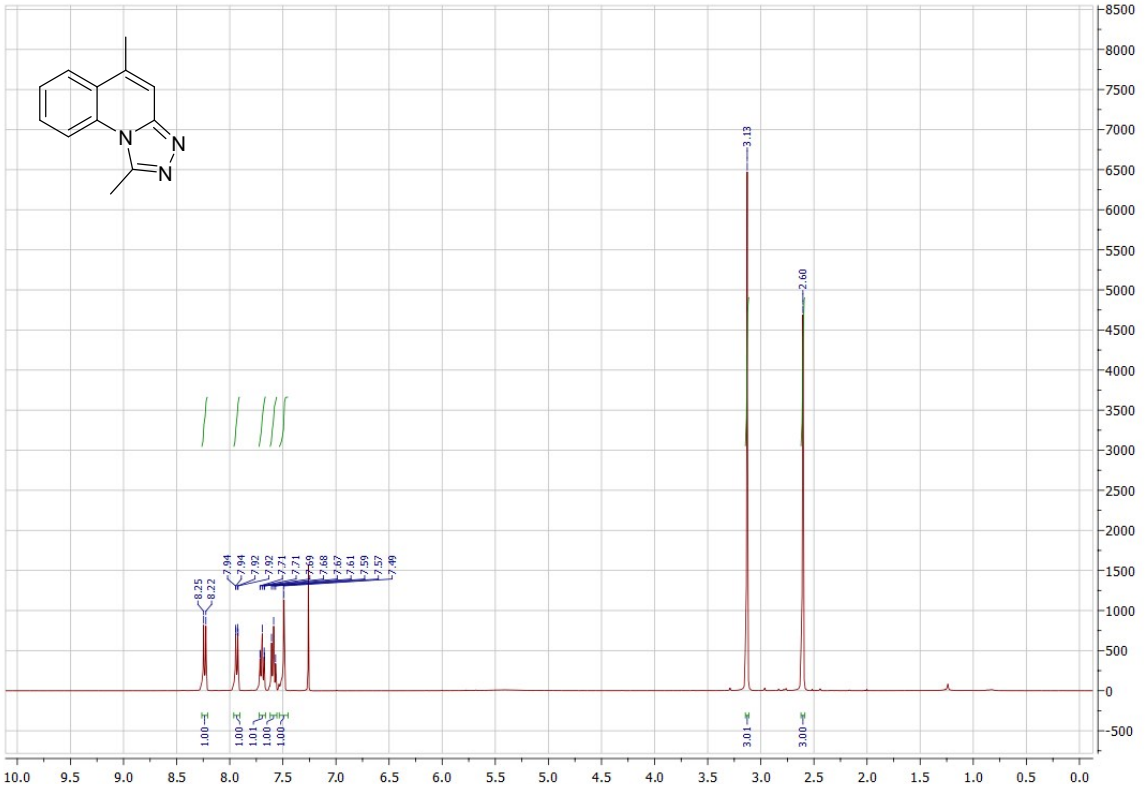

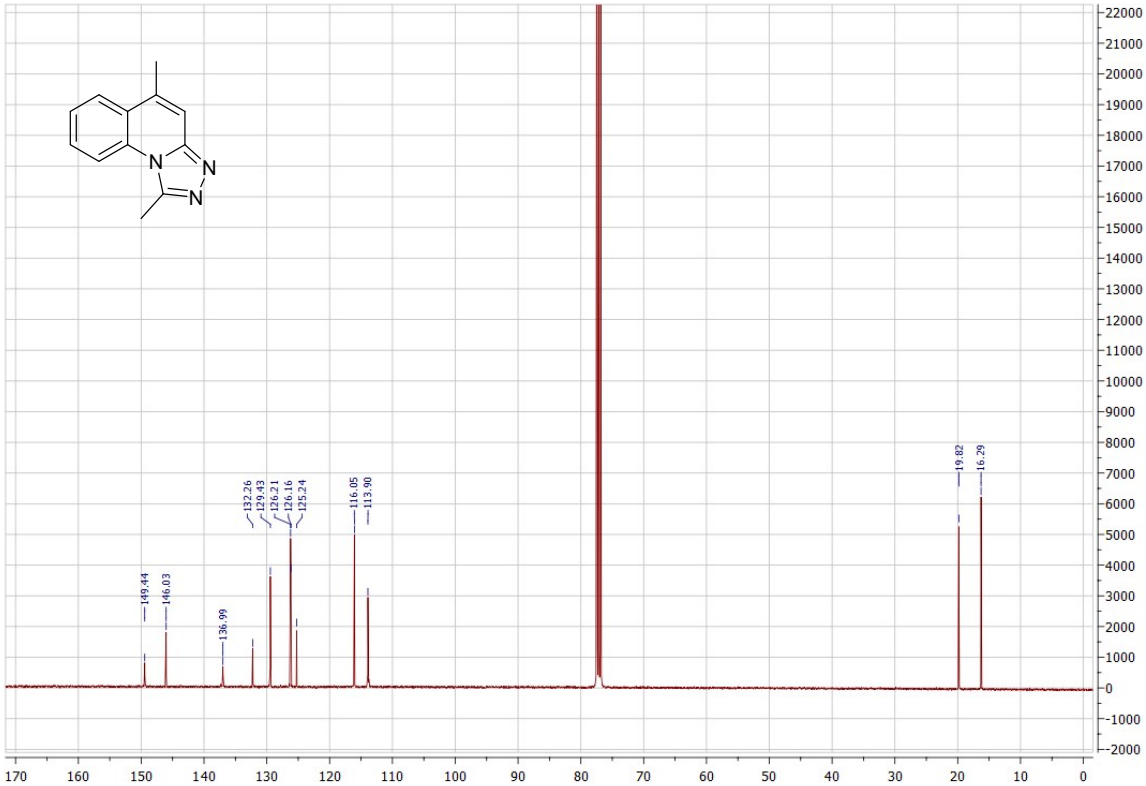

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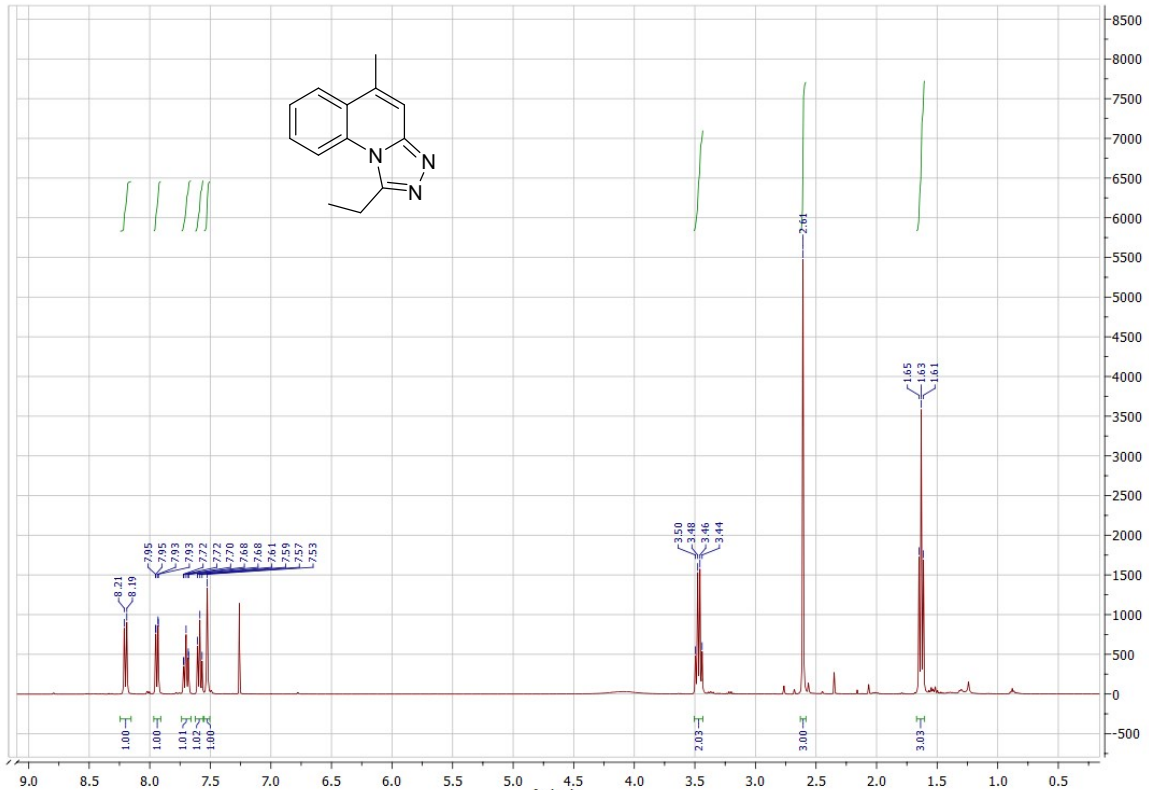

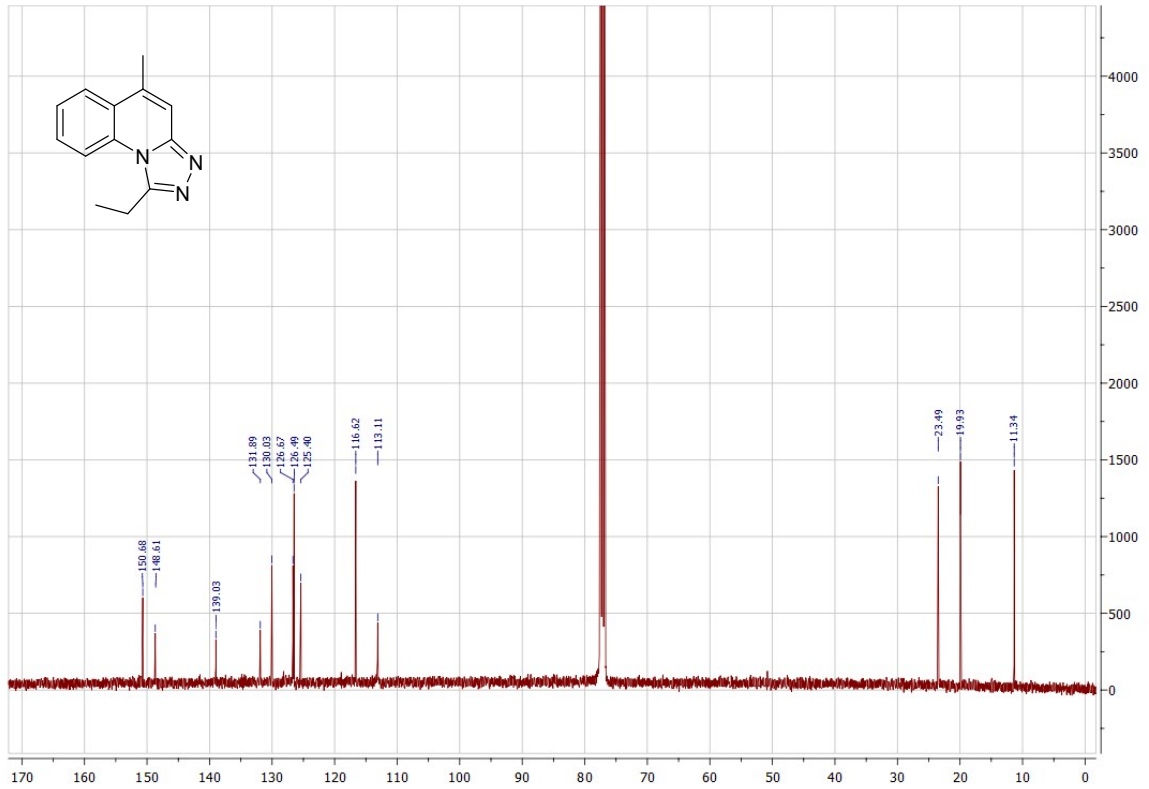

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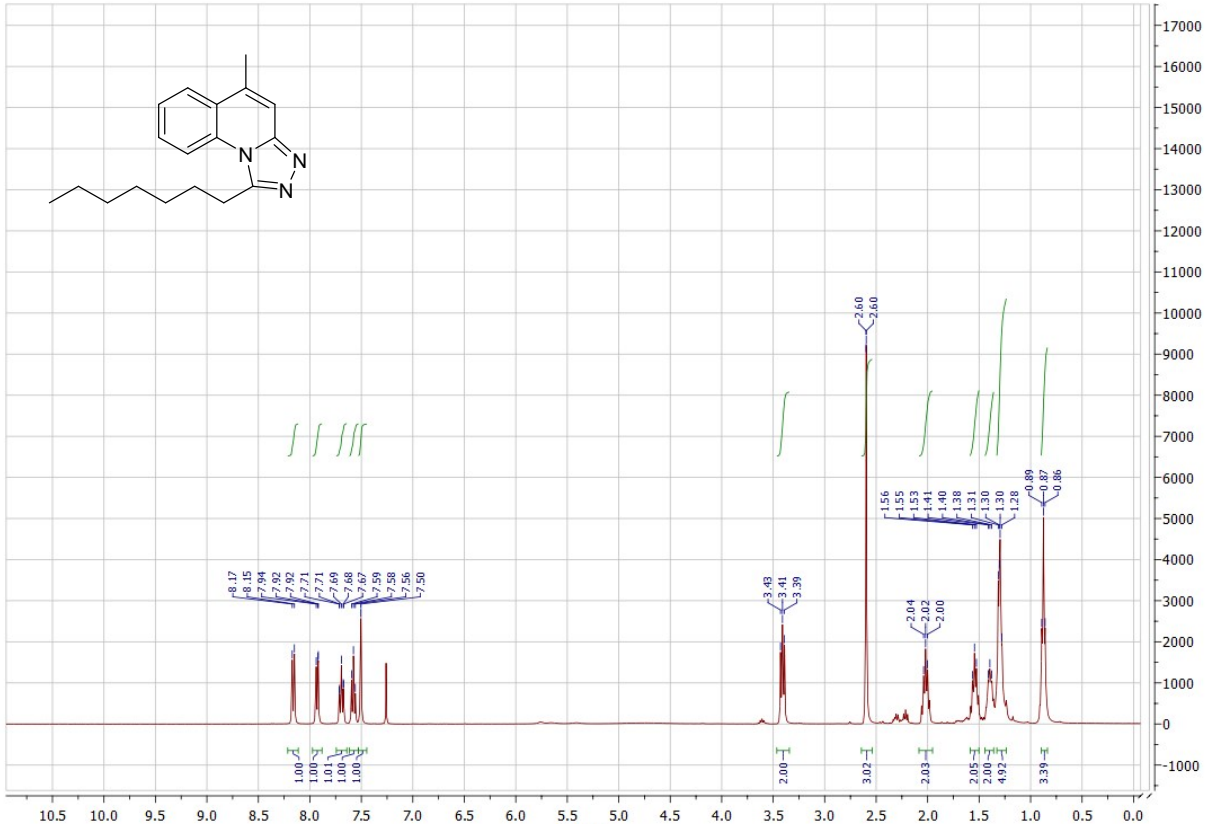

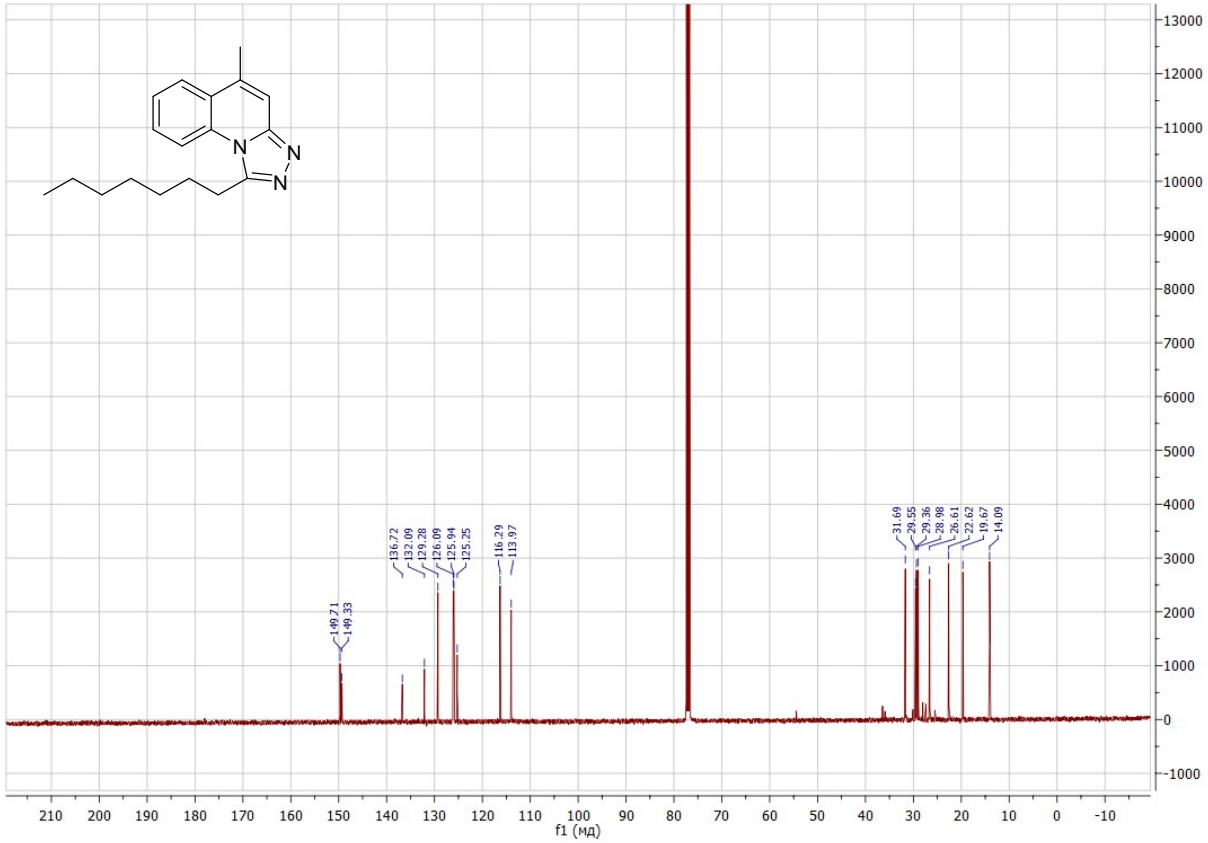

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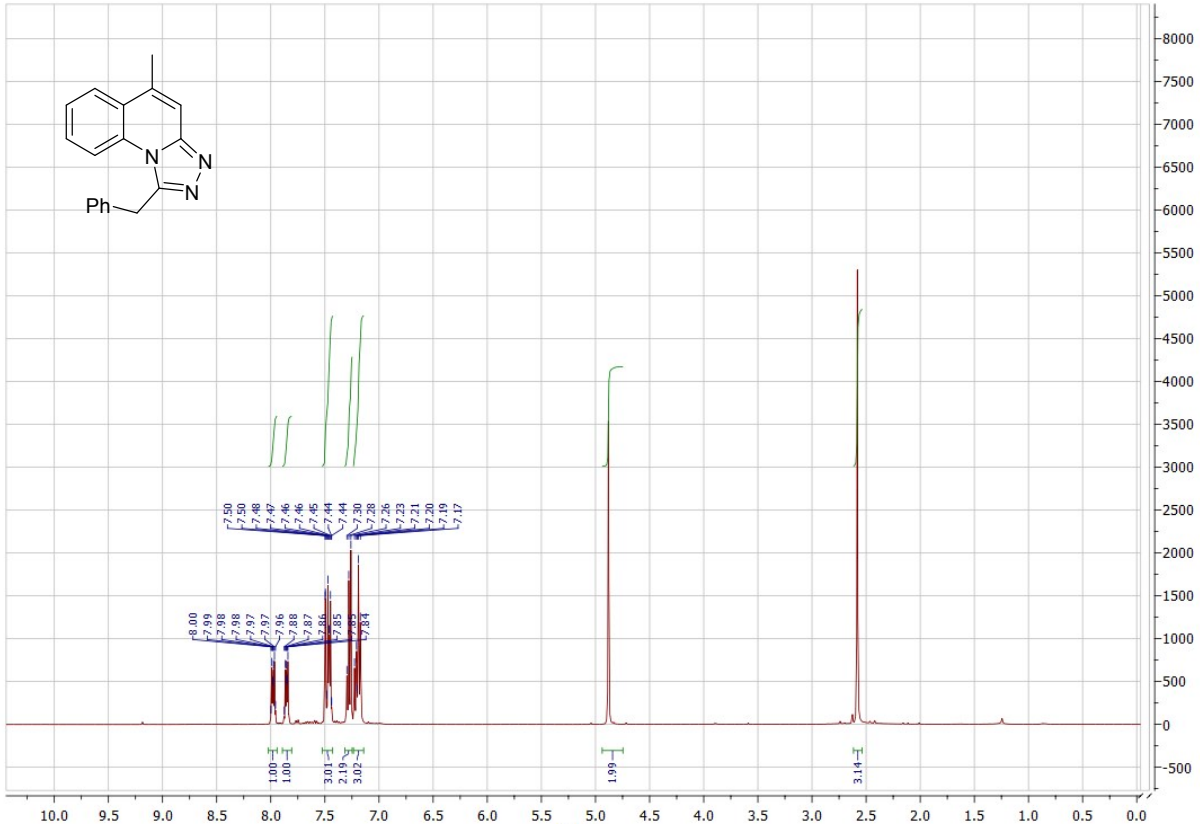

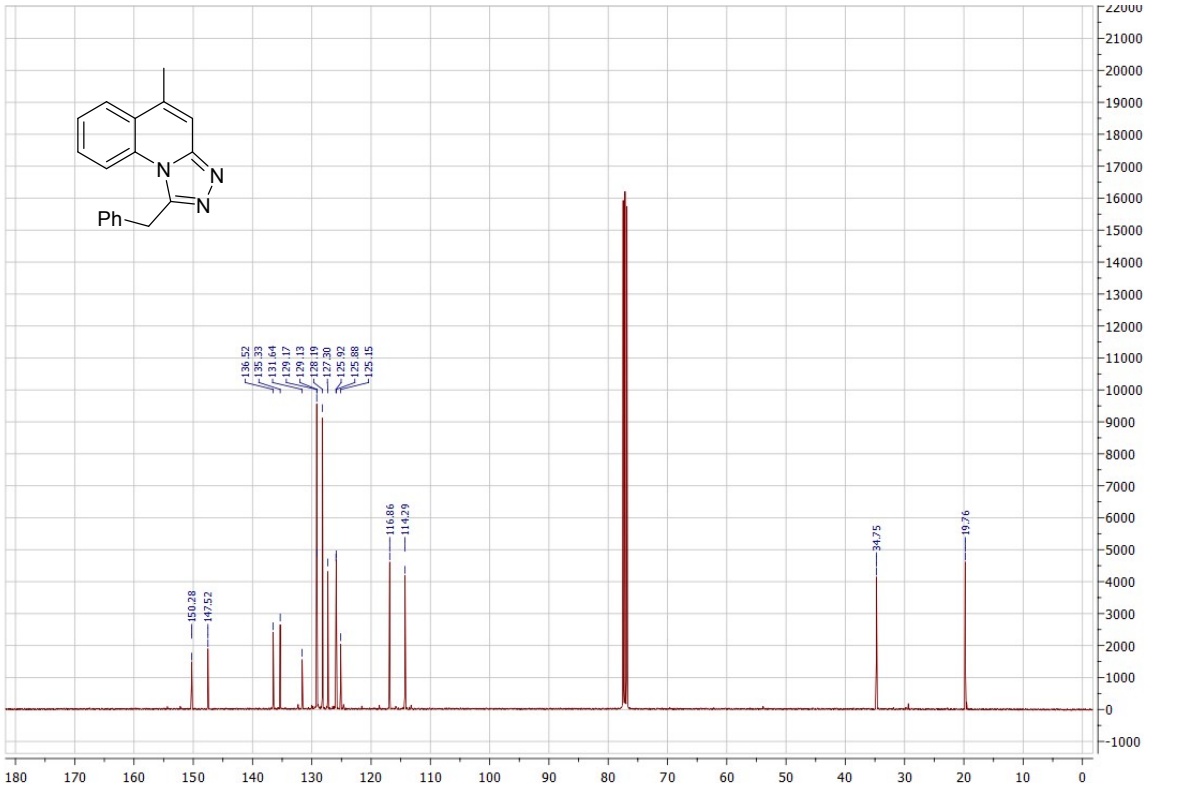

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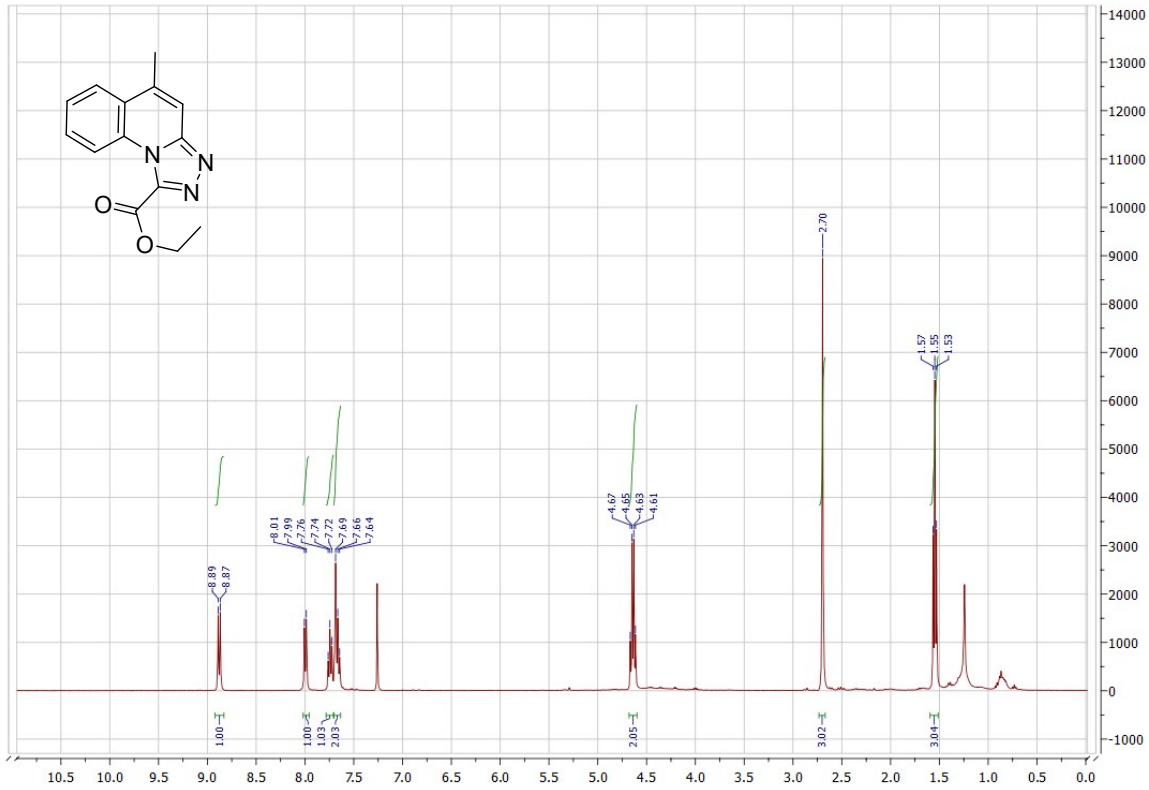

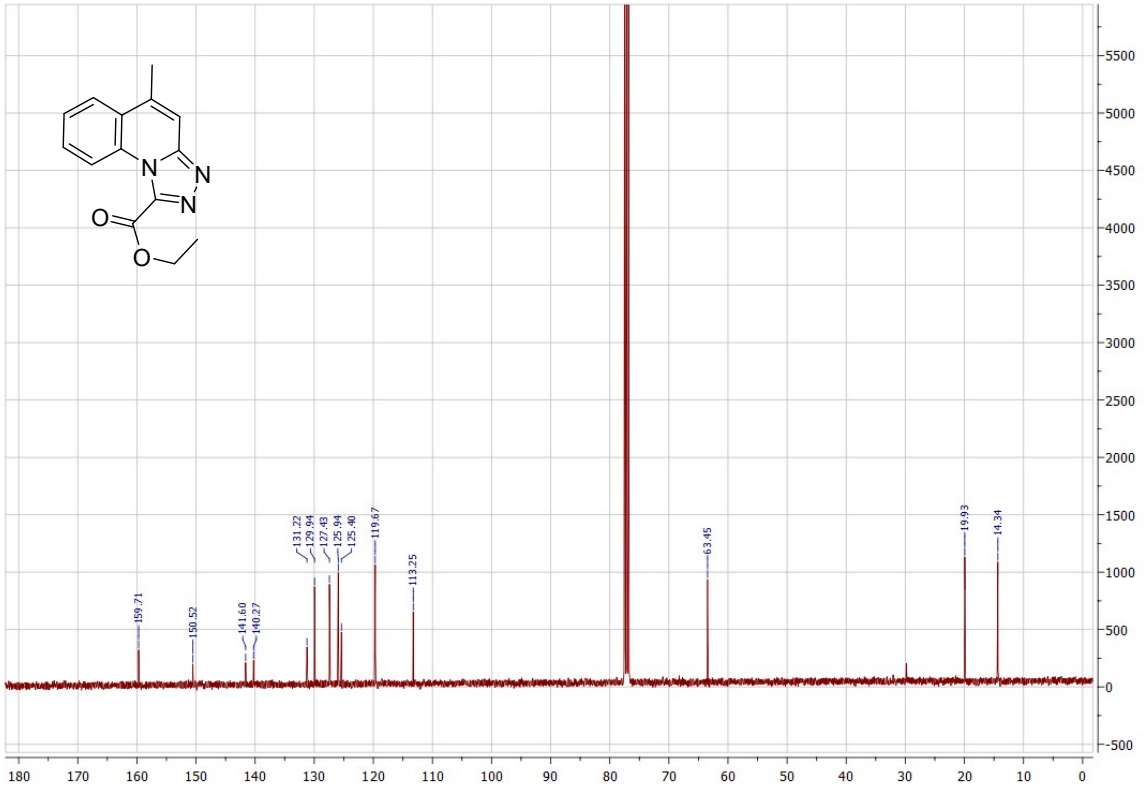

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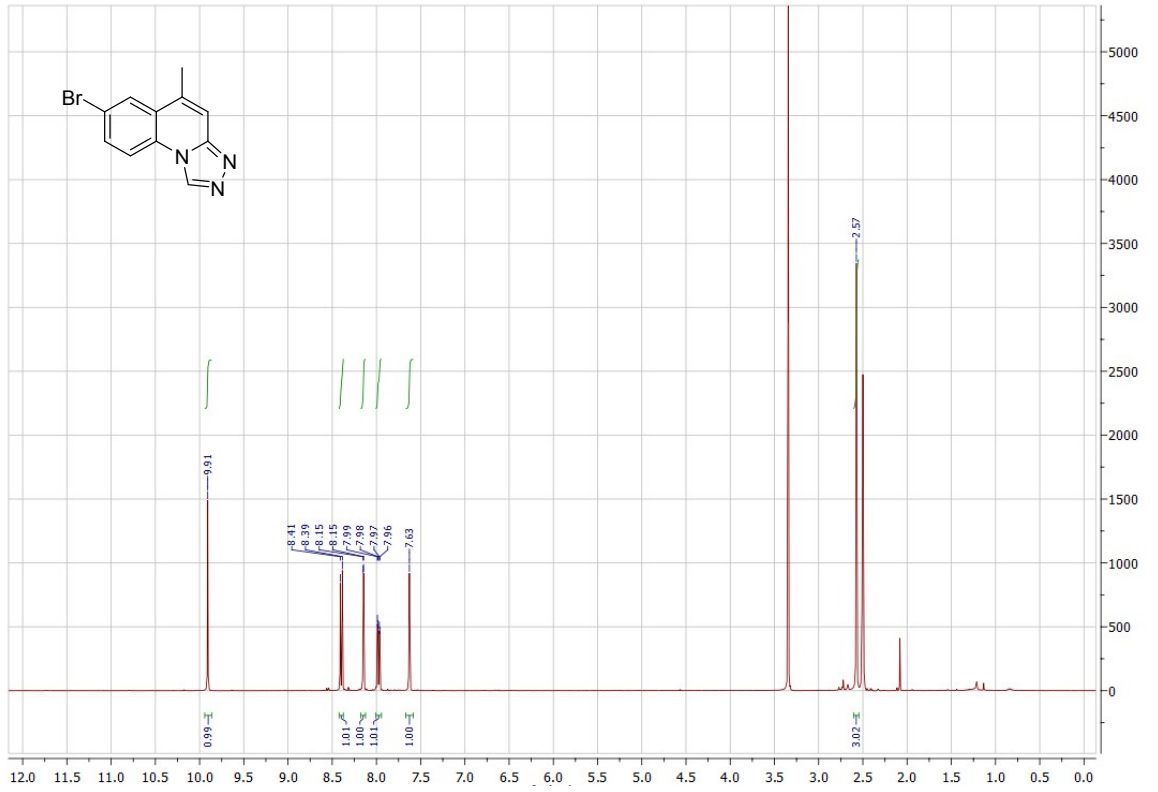

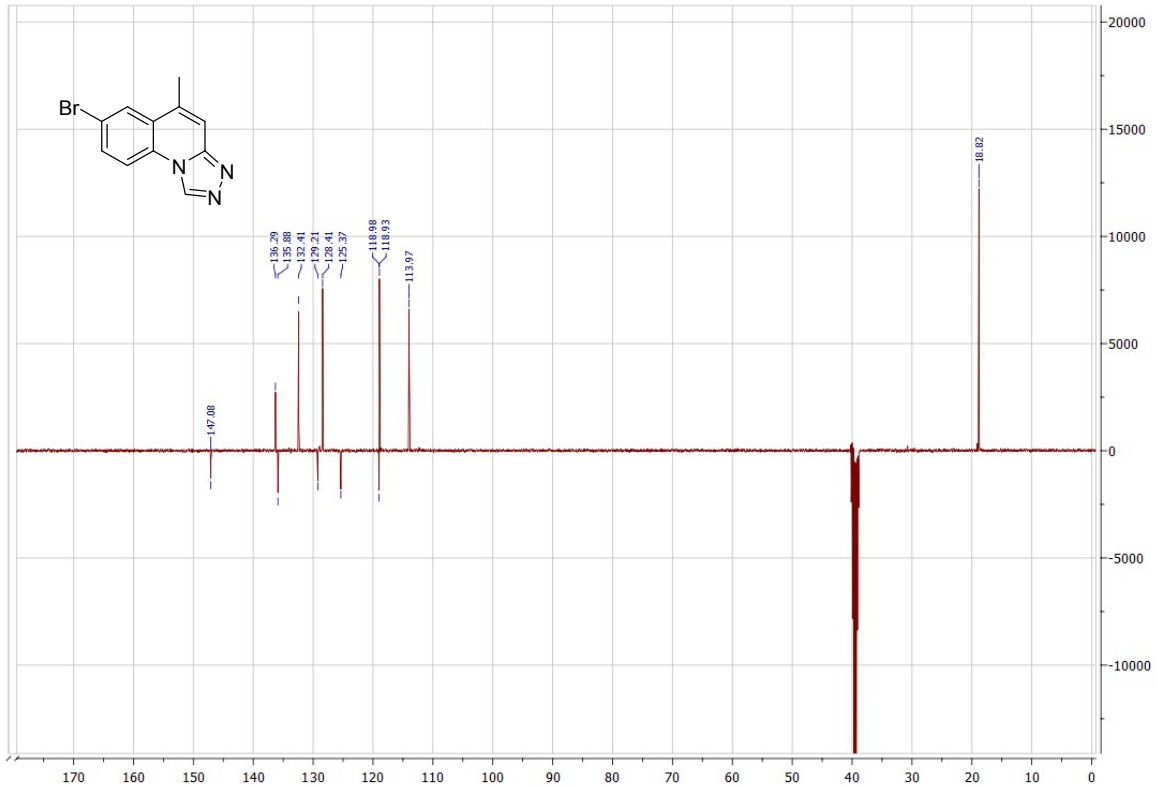

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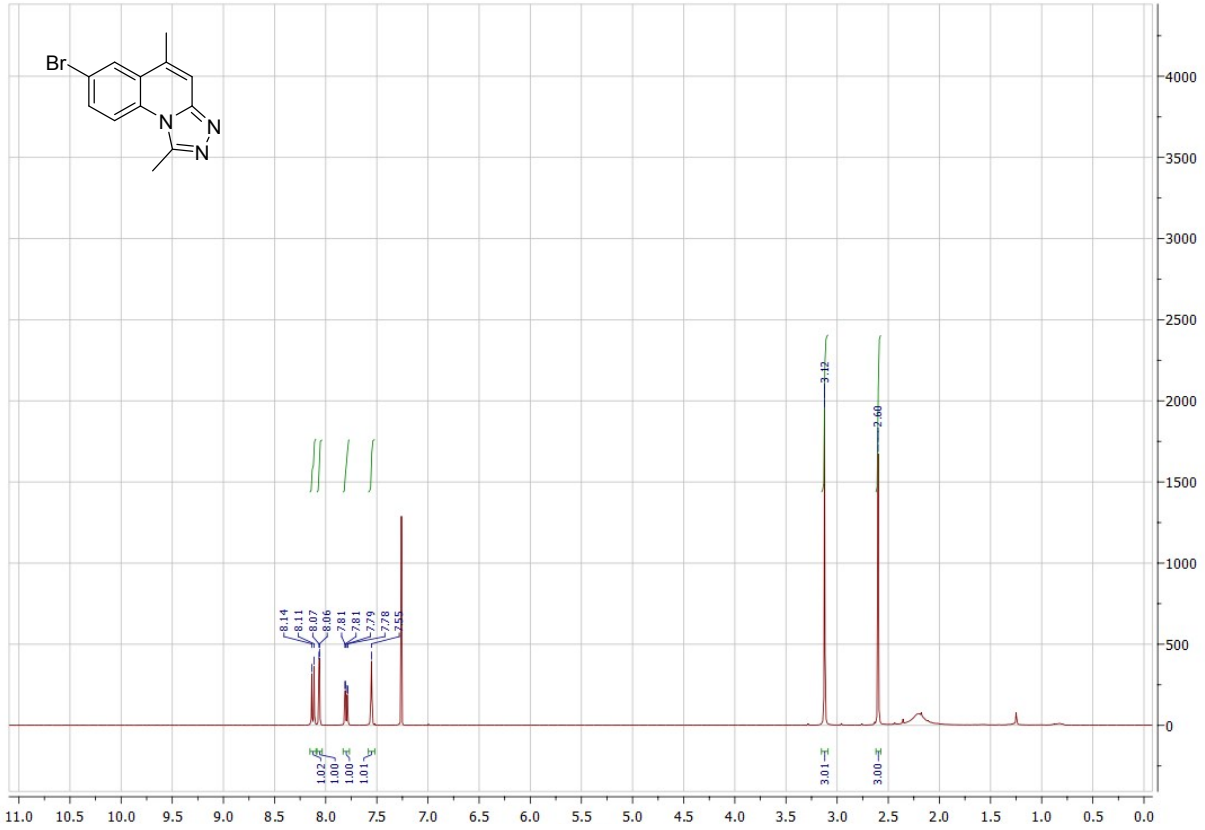

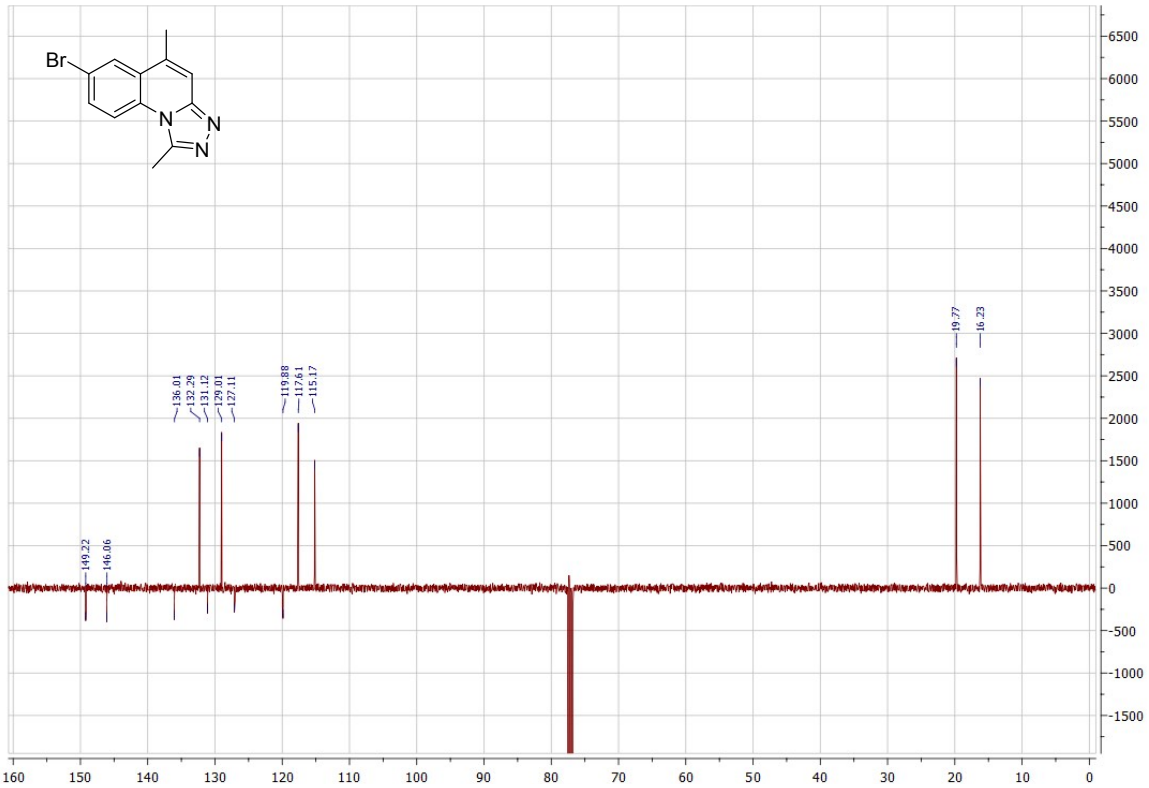

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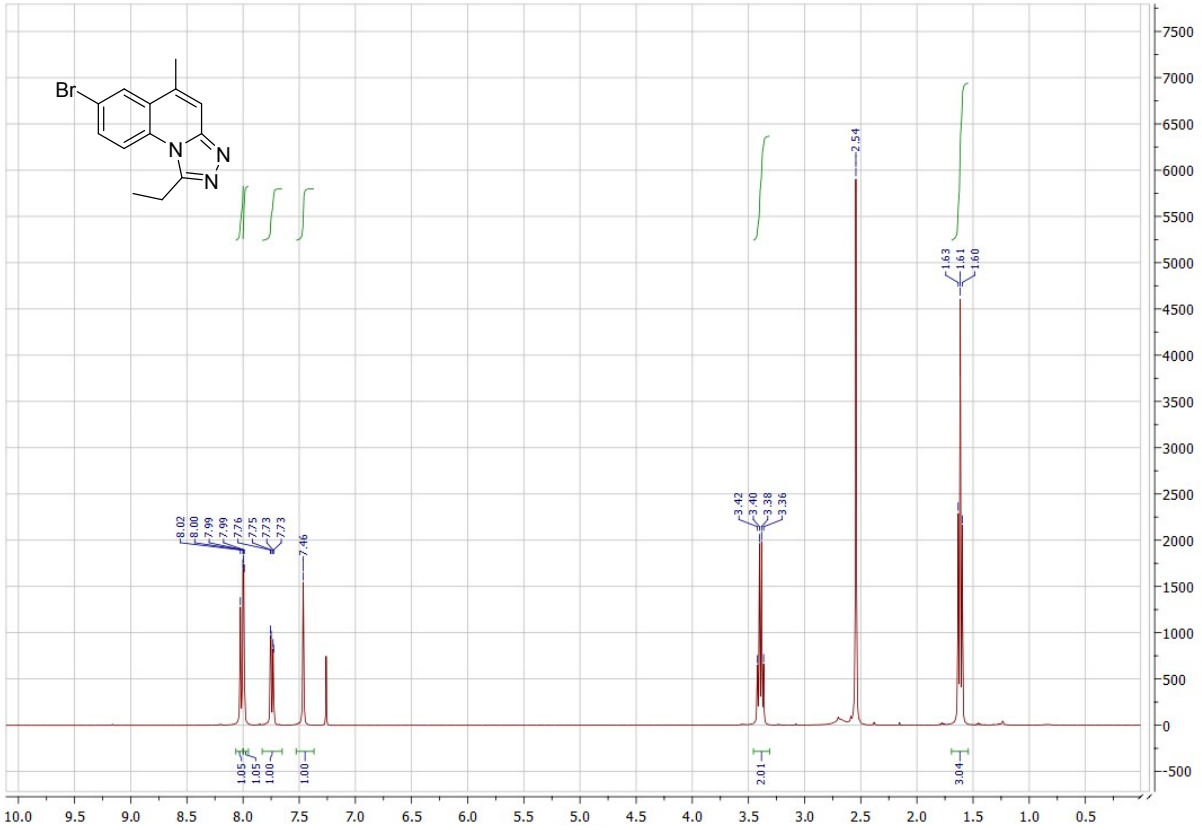

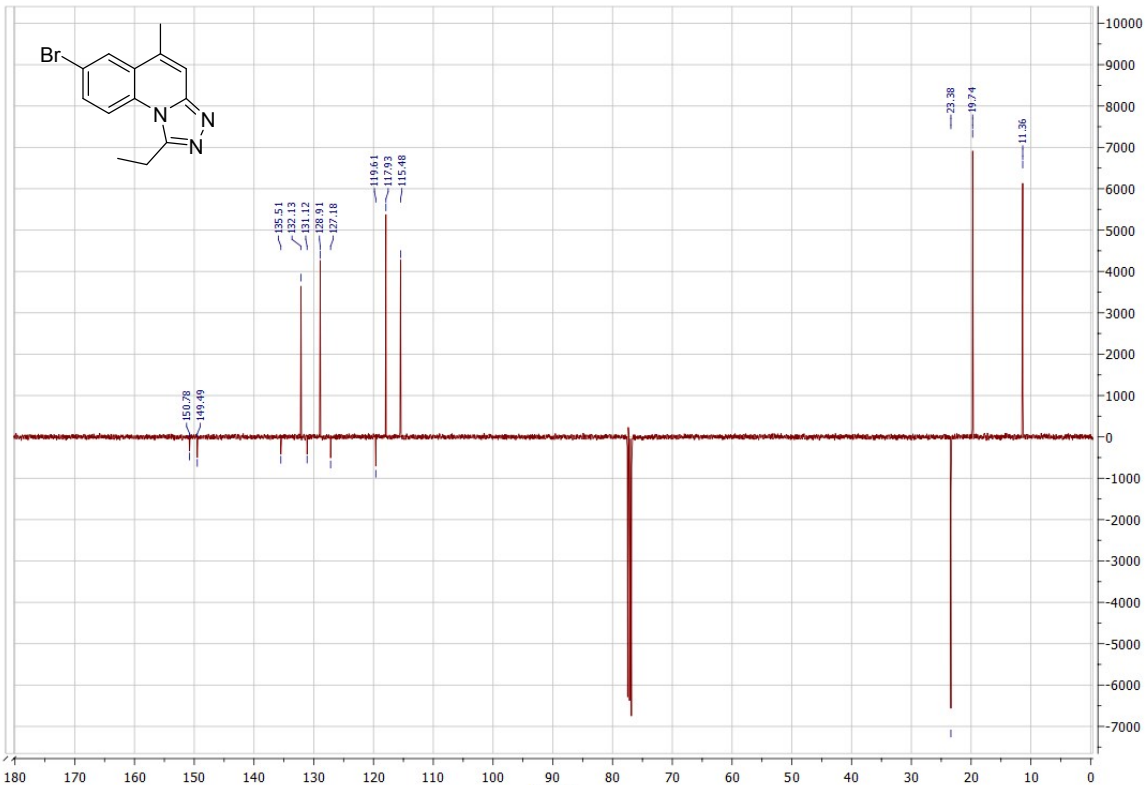

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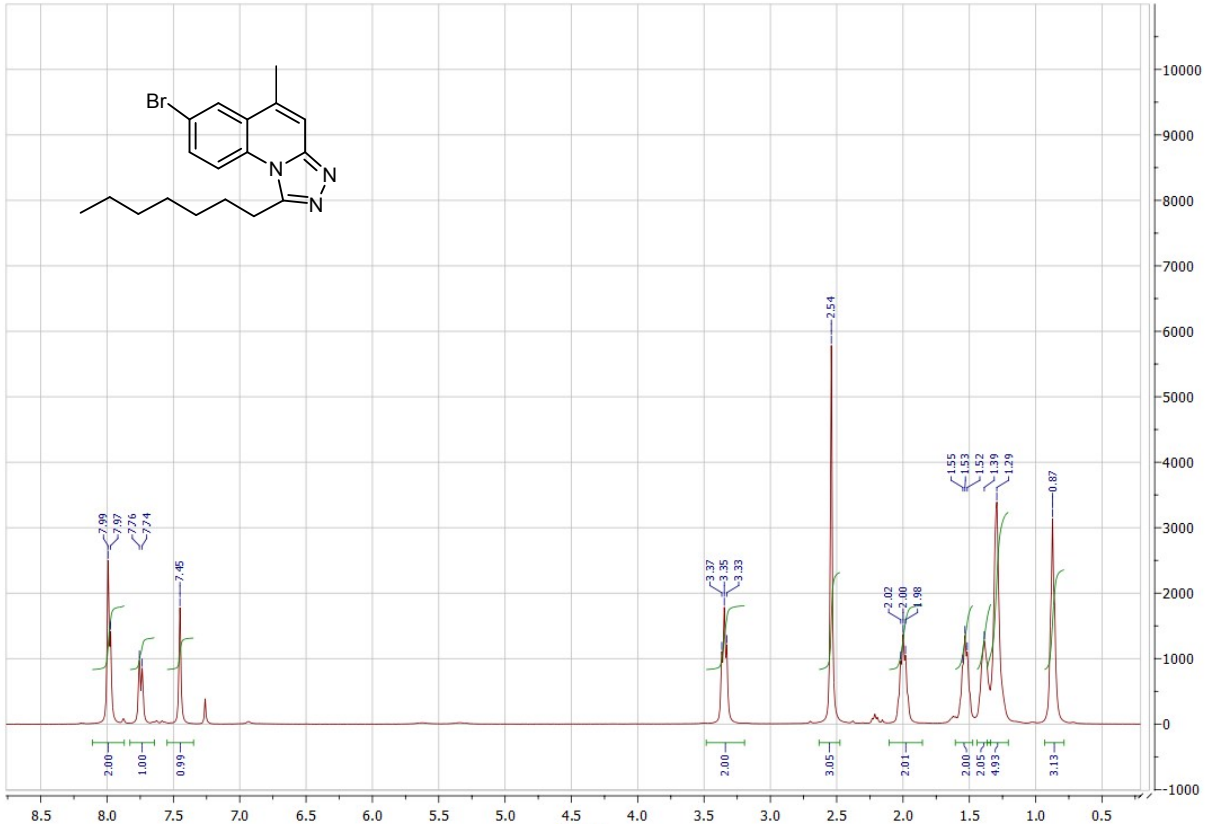

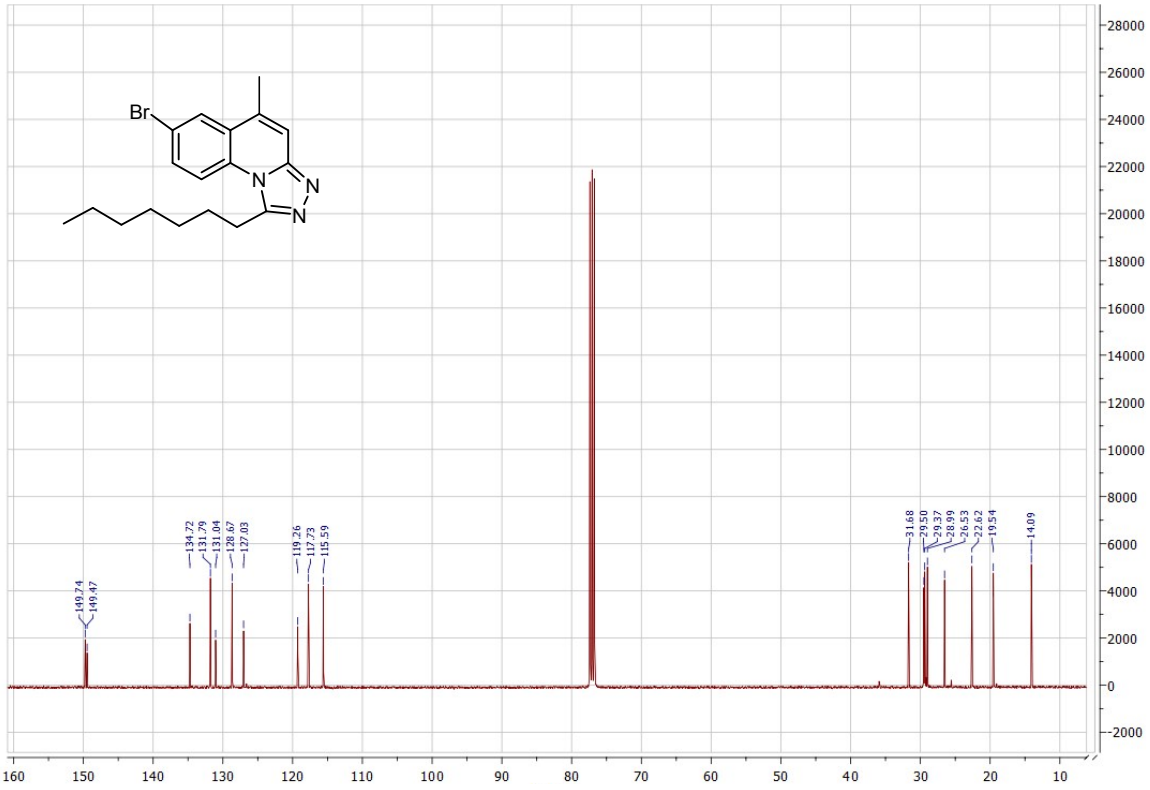

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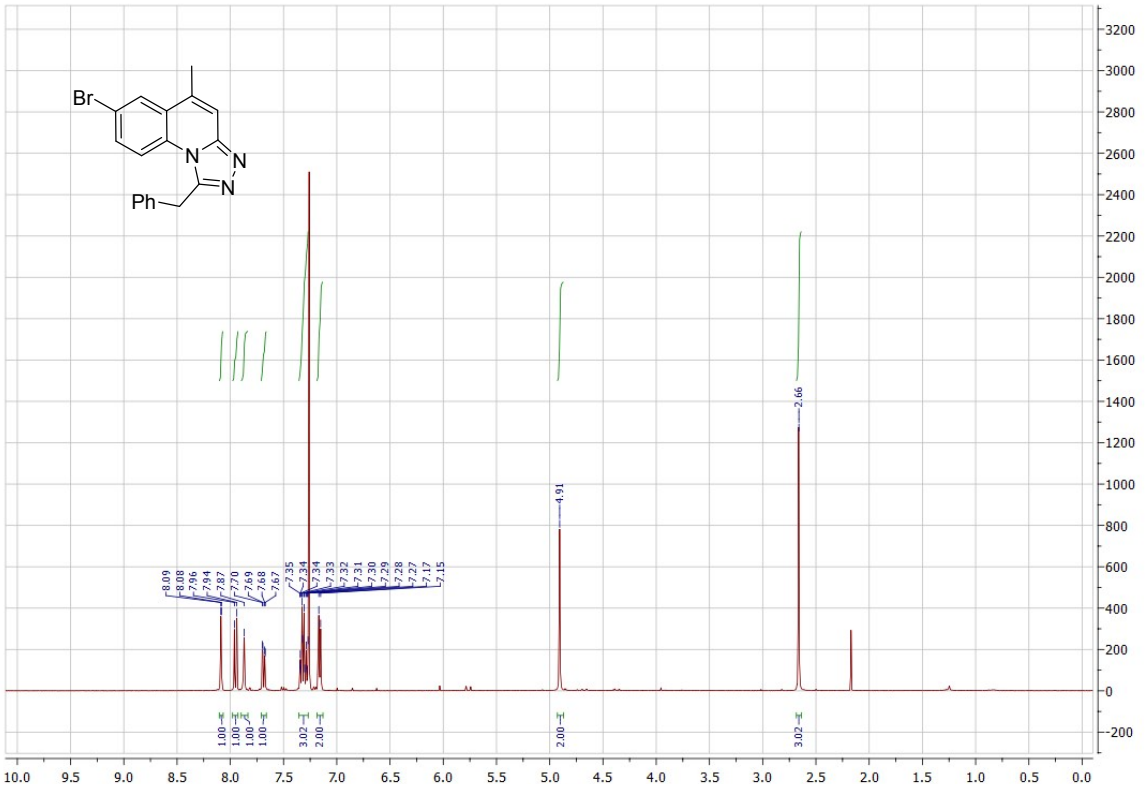

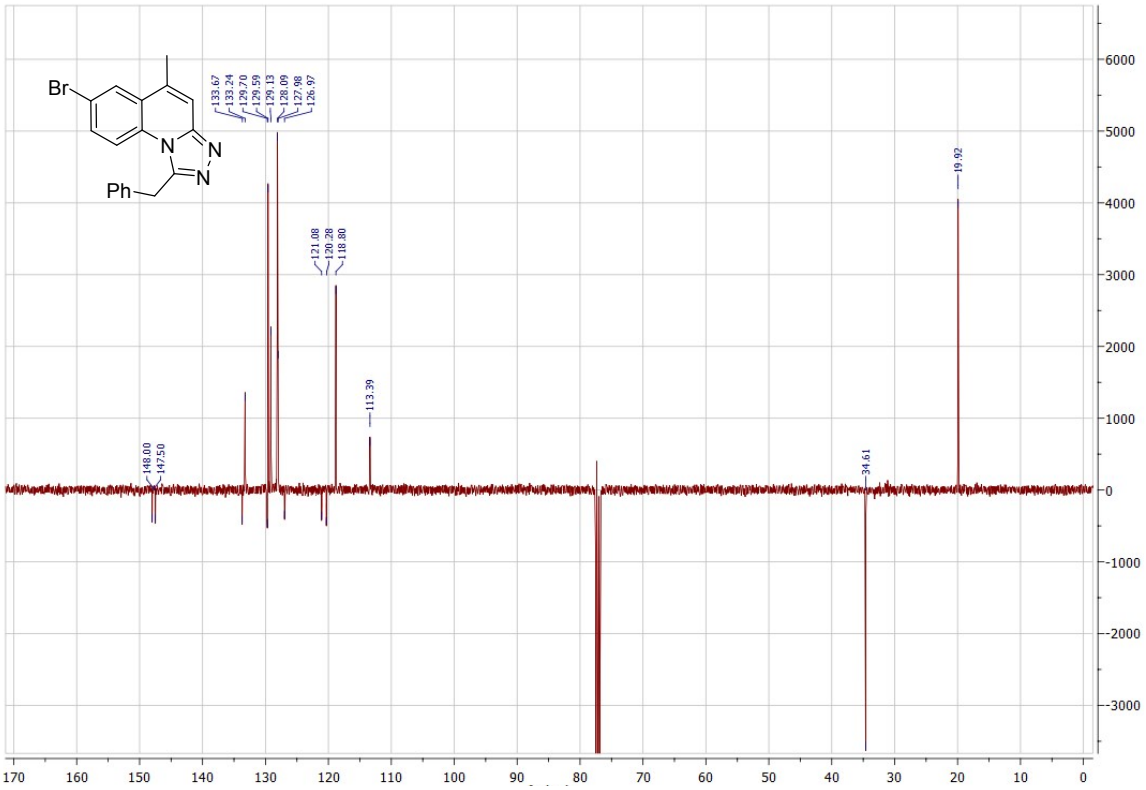

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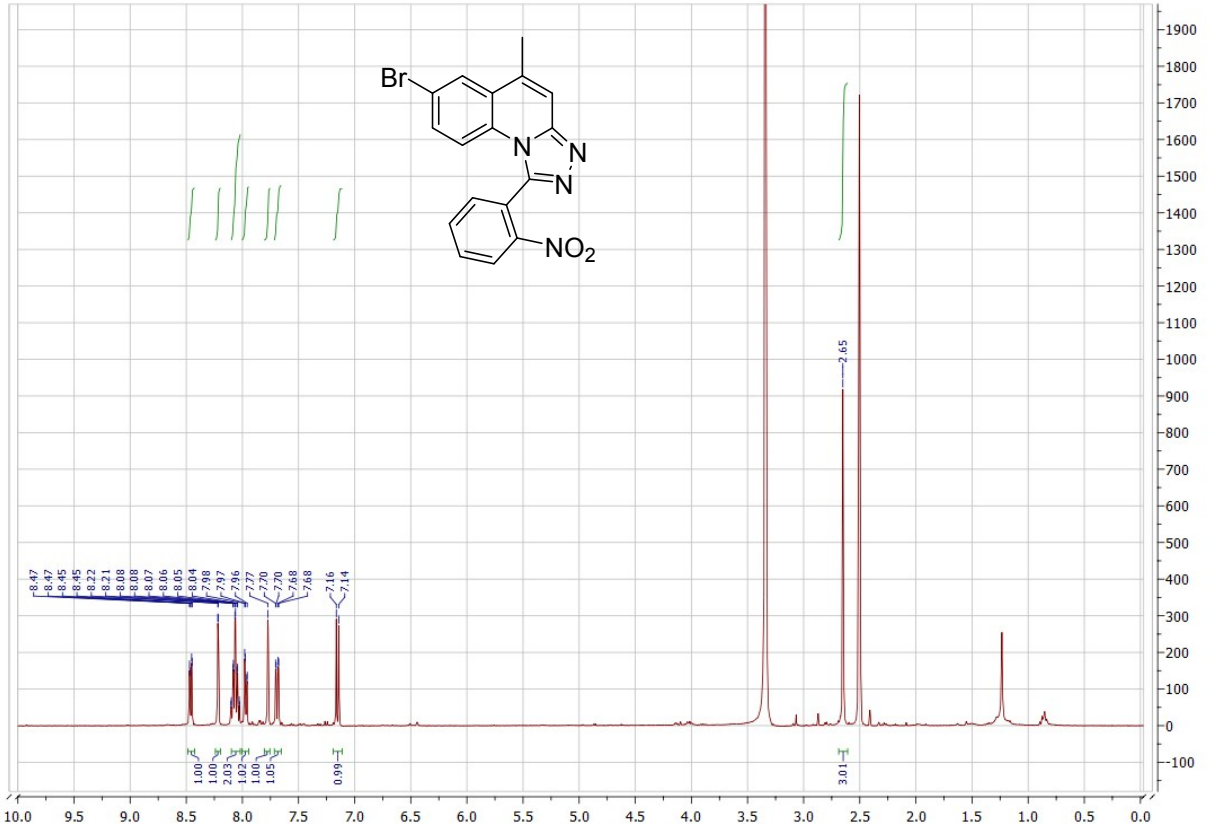
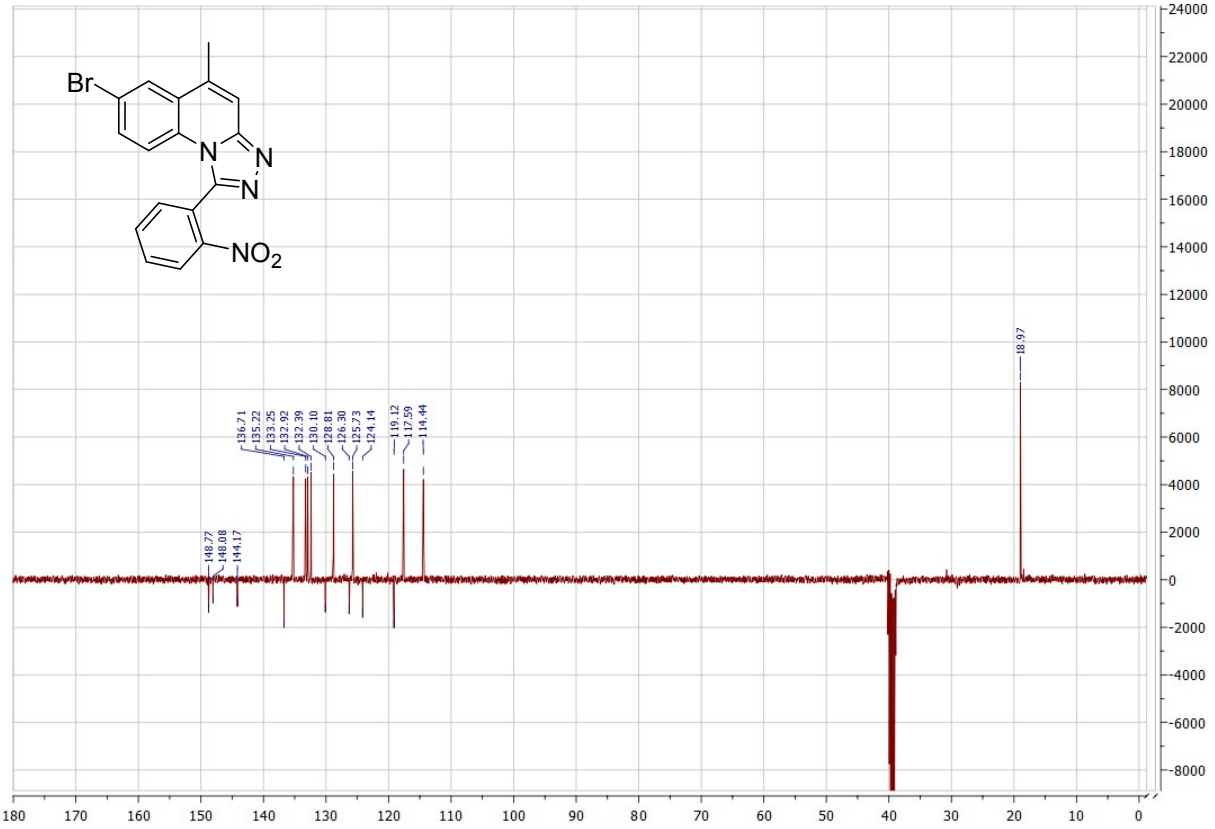
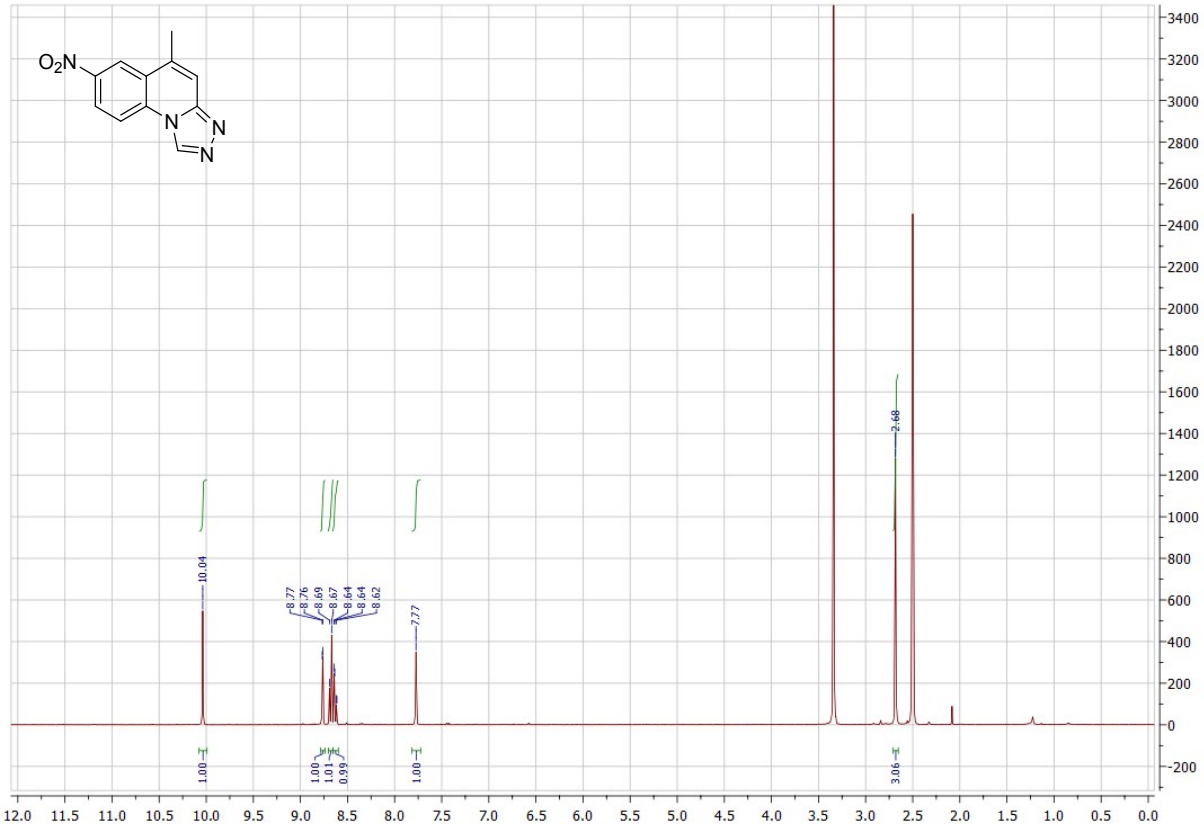
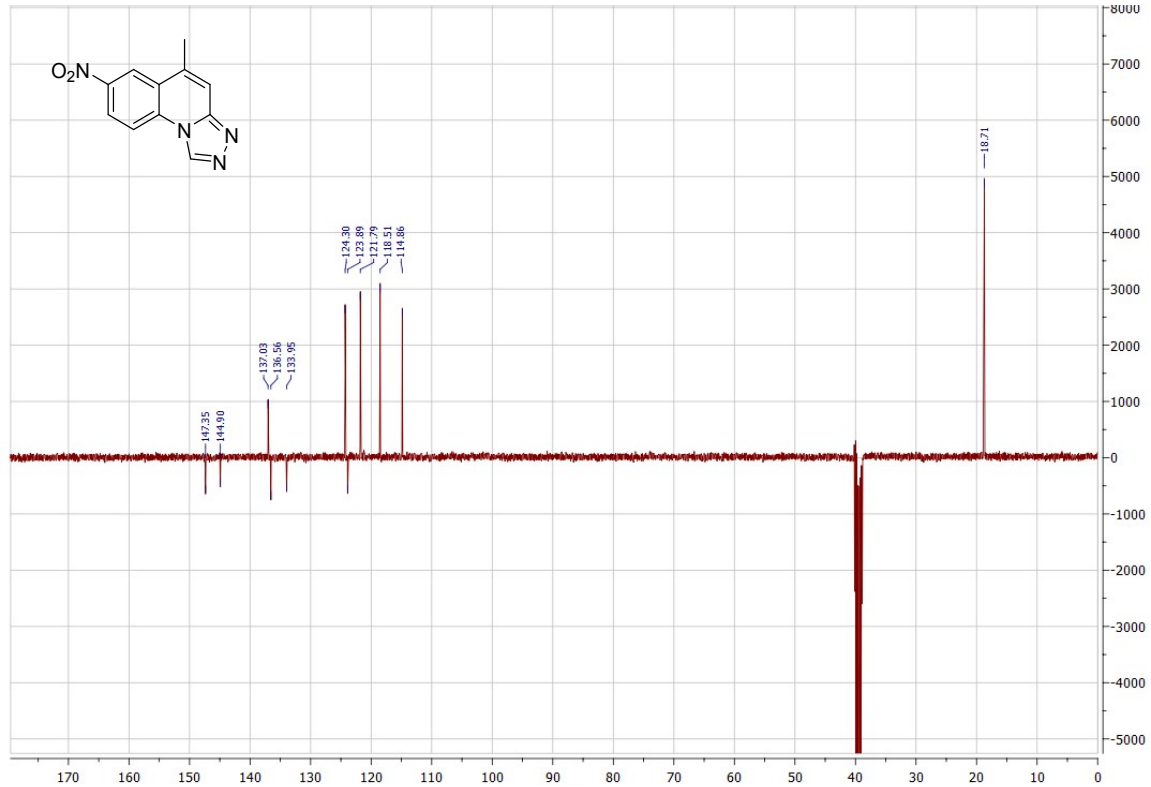


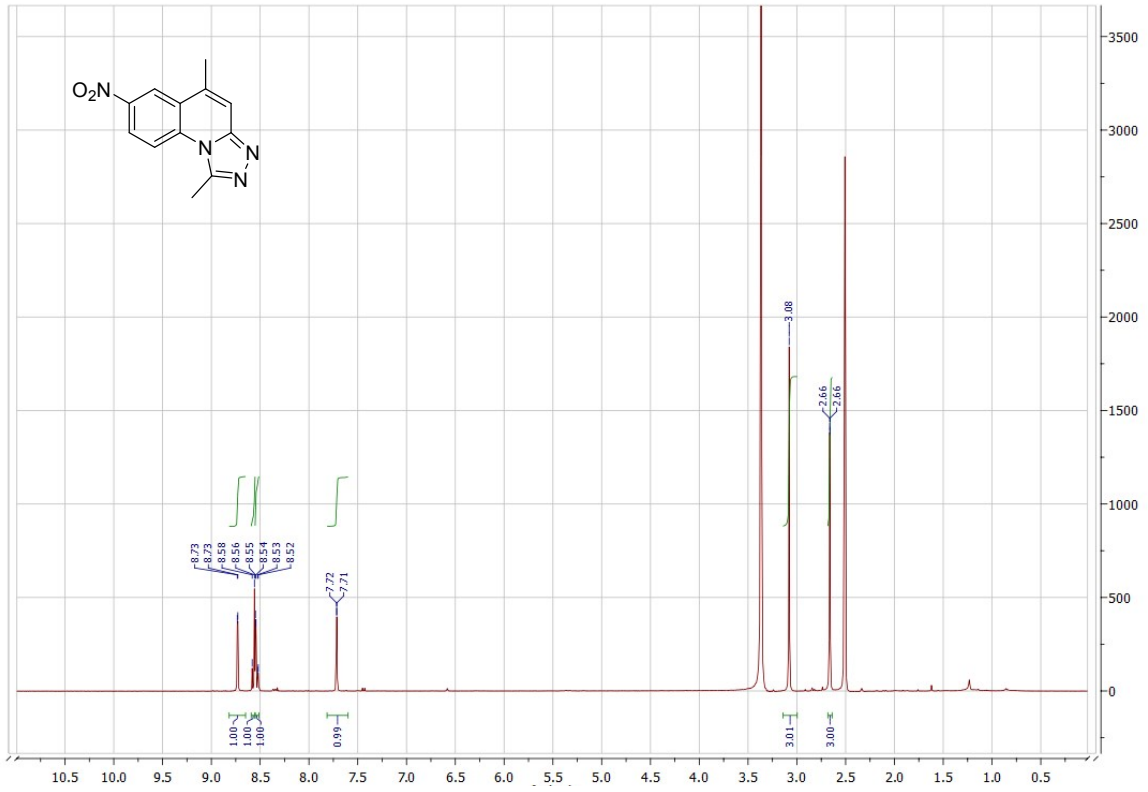


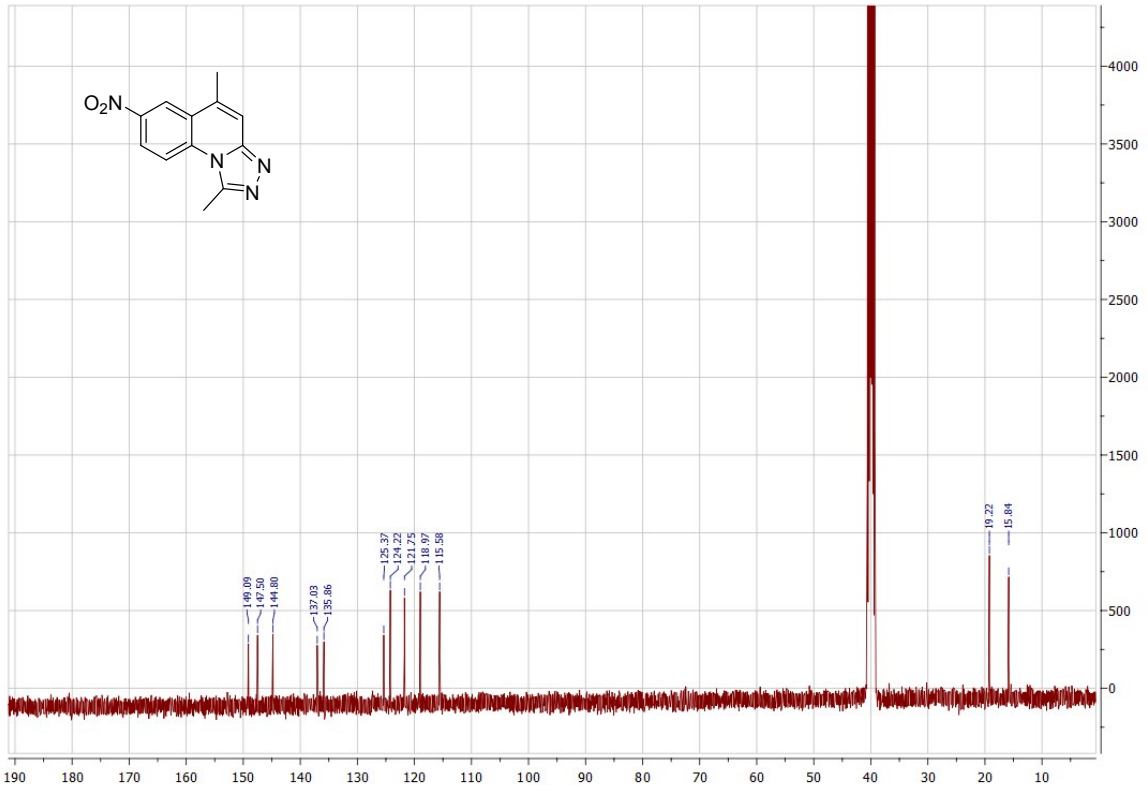
^{1}H and ^{13}C NMR spectra of **3da** in DMSO-d_6.



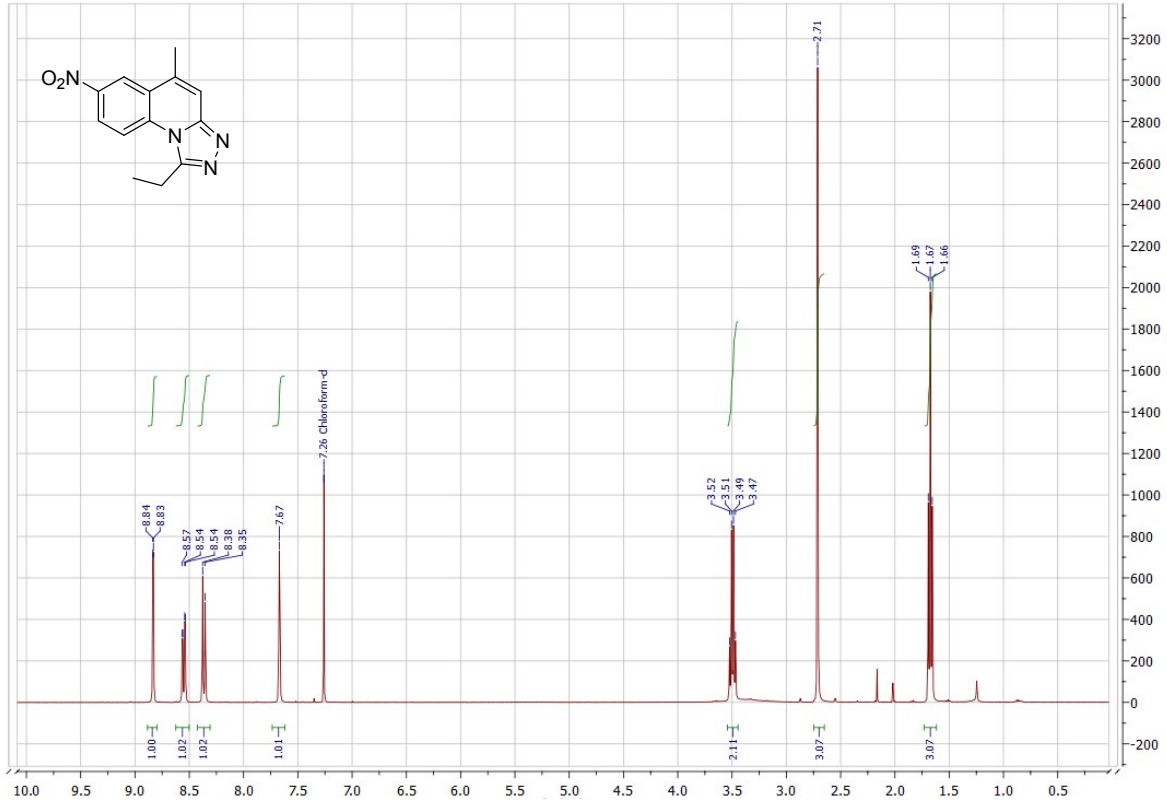


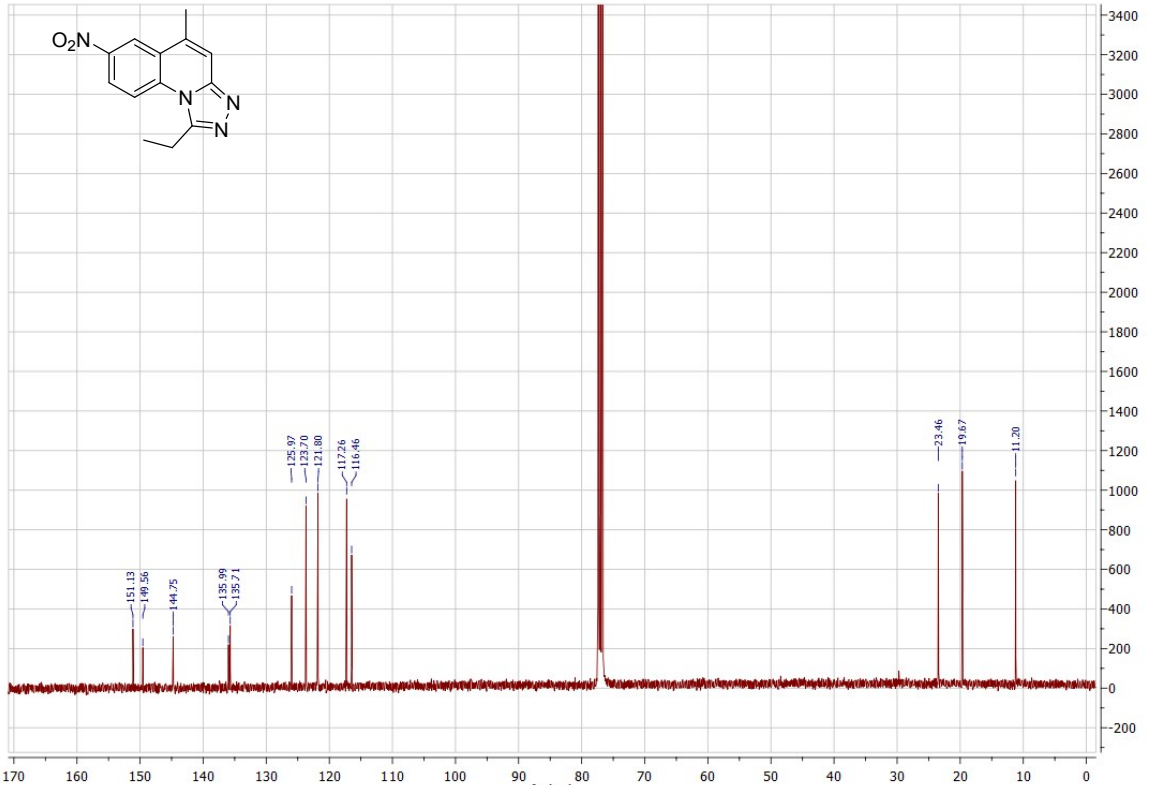
^{1}H and ^{13}C NMR spectra of **3db** in DMSO-d_6.



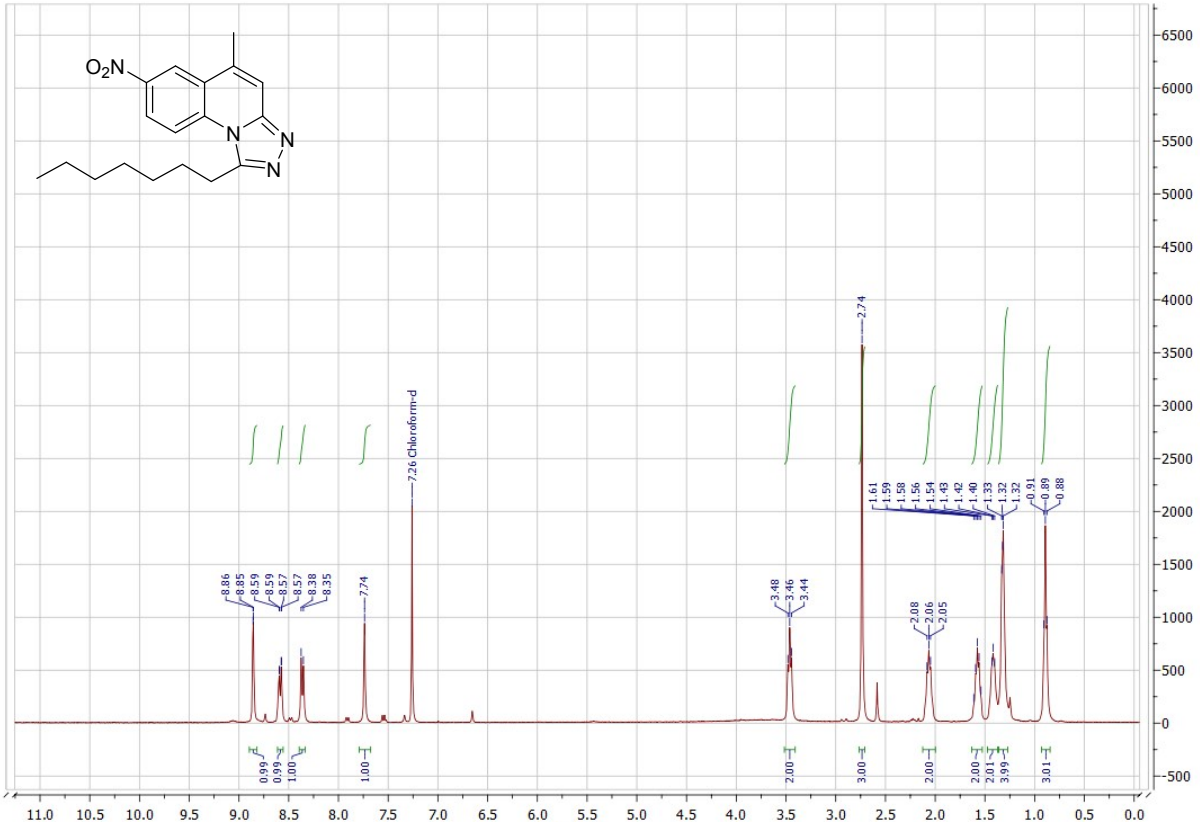


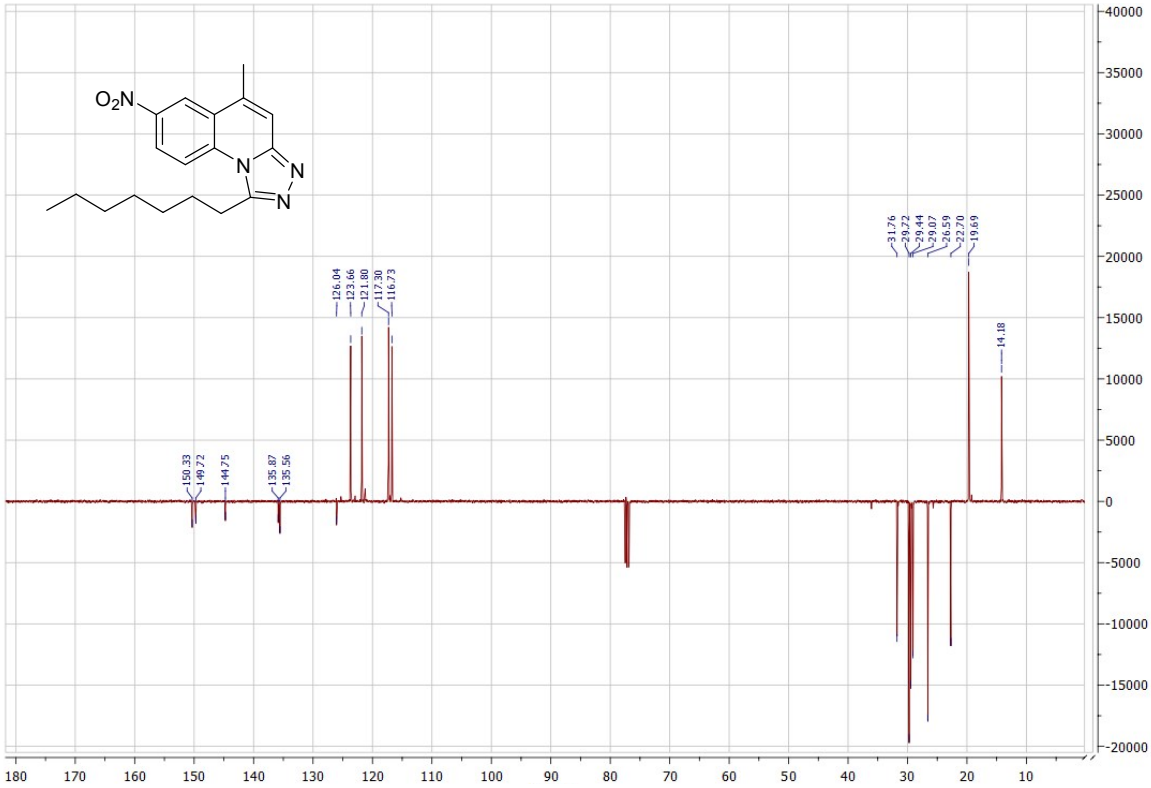
^{1}H and ^{13}C NMR spectra of **3dc** in $CDCl_3$.



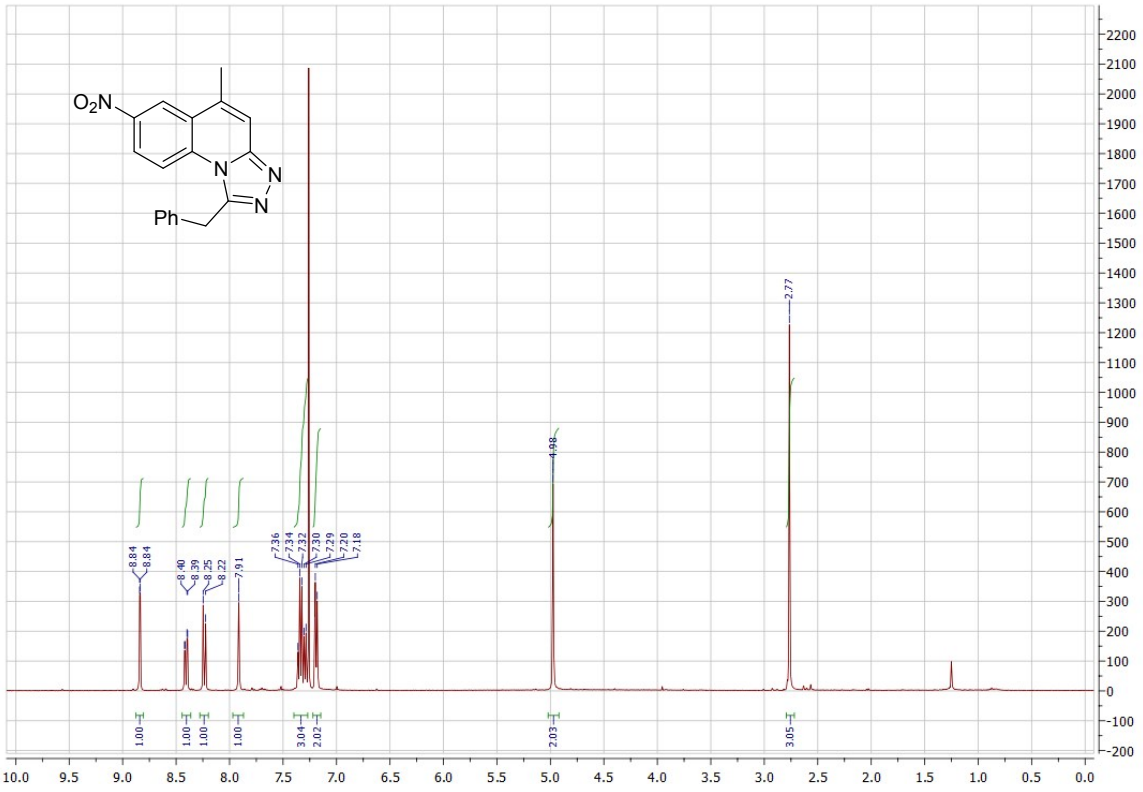


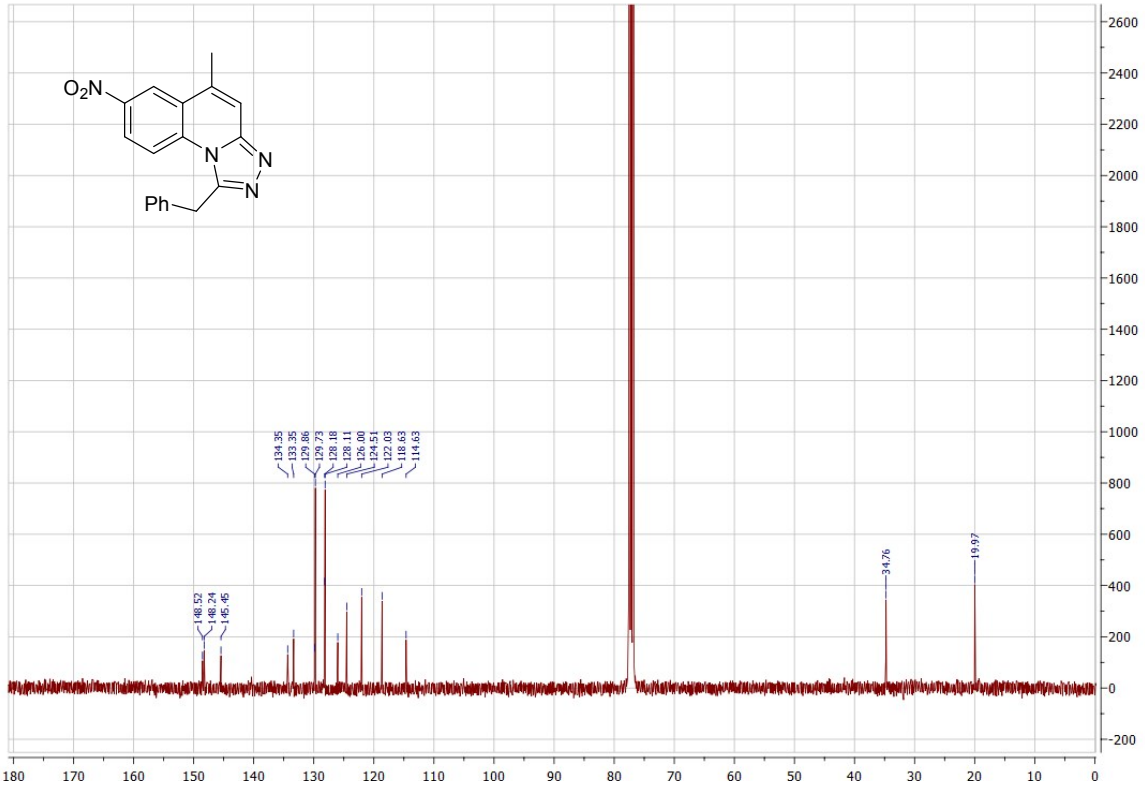
^{1}H and ^{13}C NMR spectra of **3dd** in $CDCl_3$.



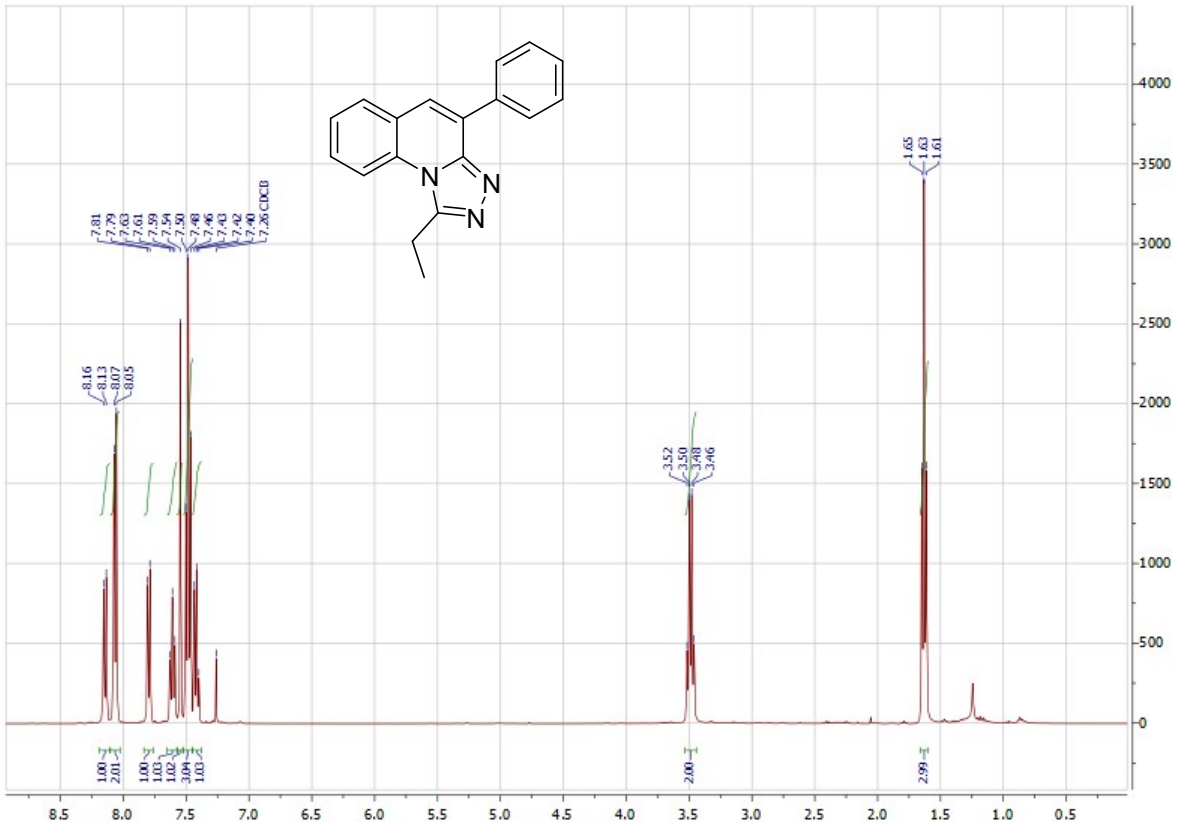


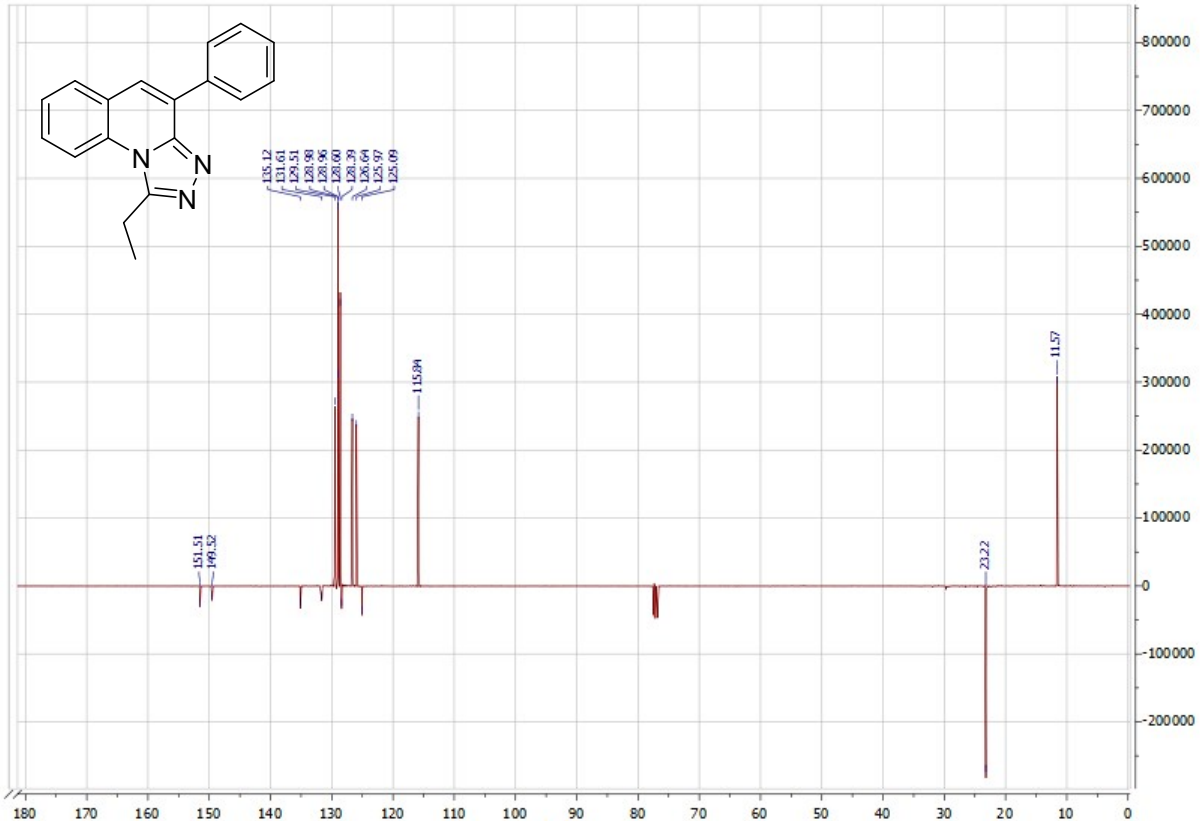
^{1}H and ^{13}C NMR spectra of **3de** in $CDCl_3$.



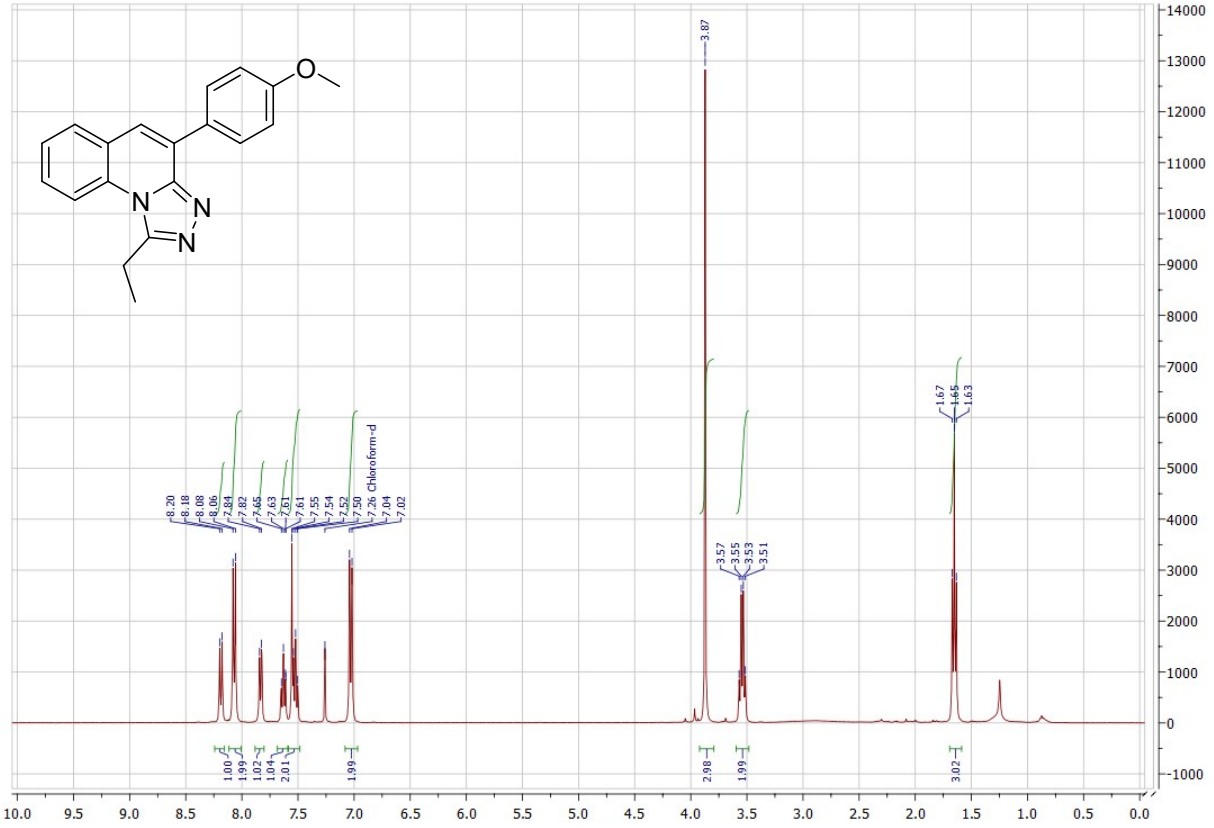


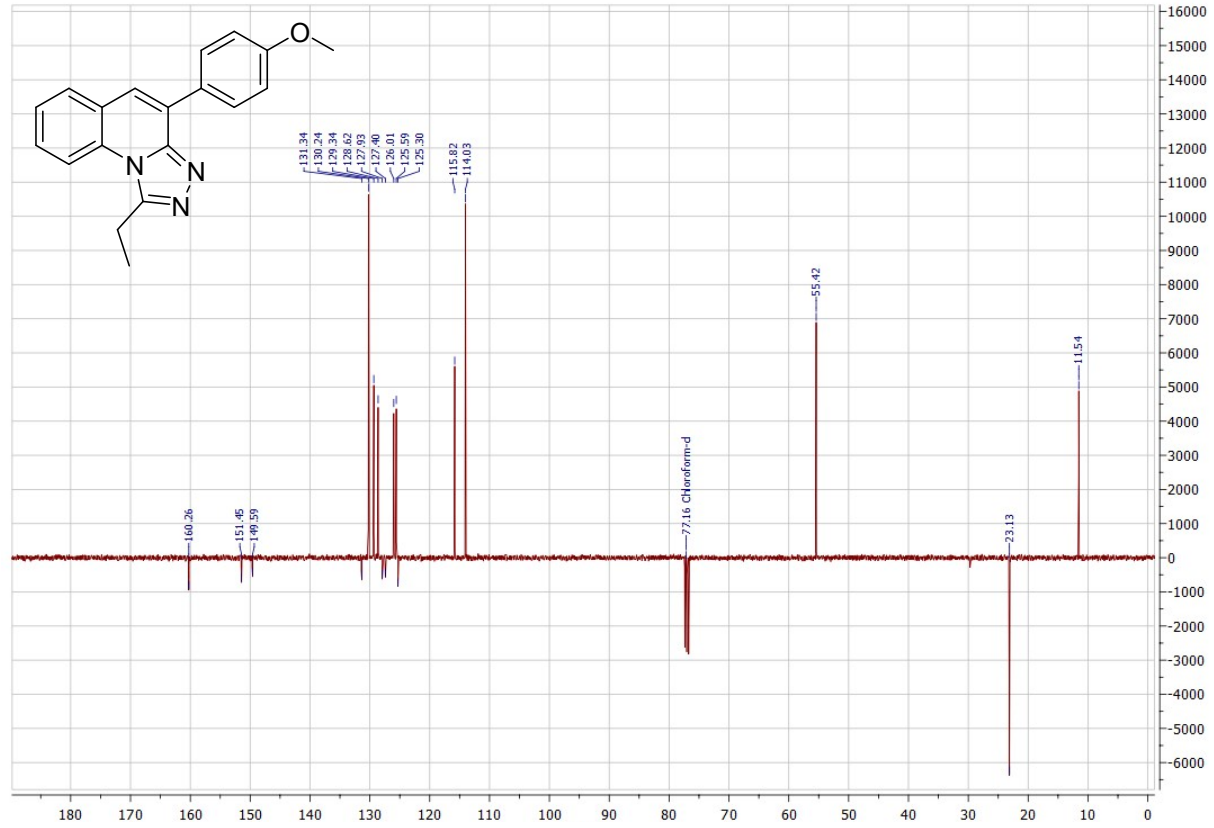
^{1}H and ^{13}C NMR spectra of **3ec** in $CDCl_3$.



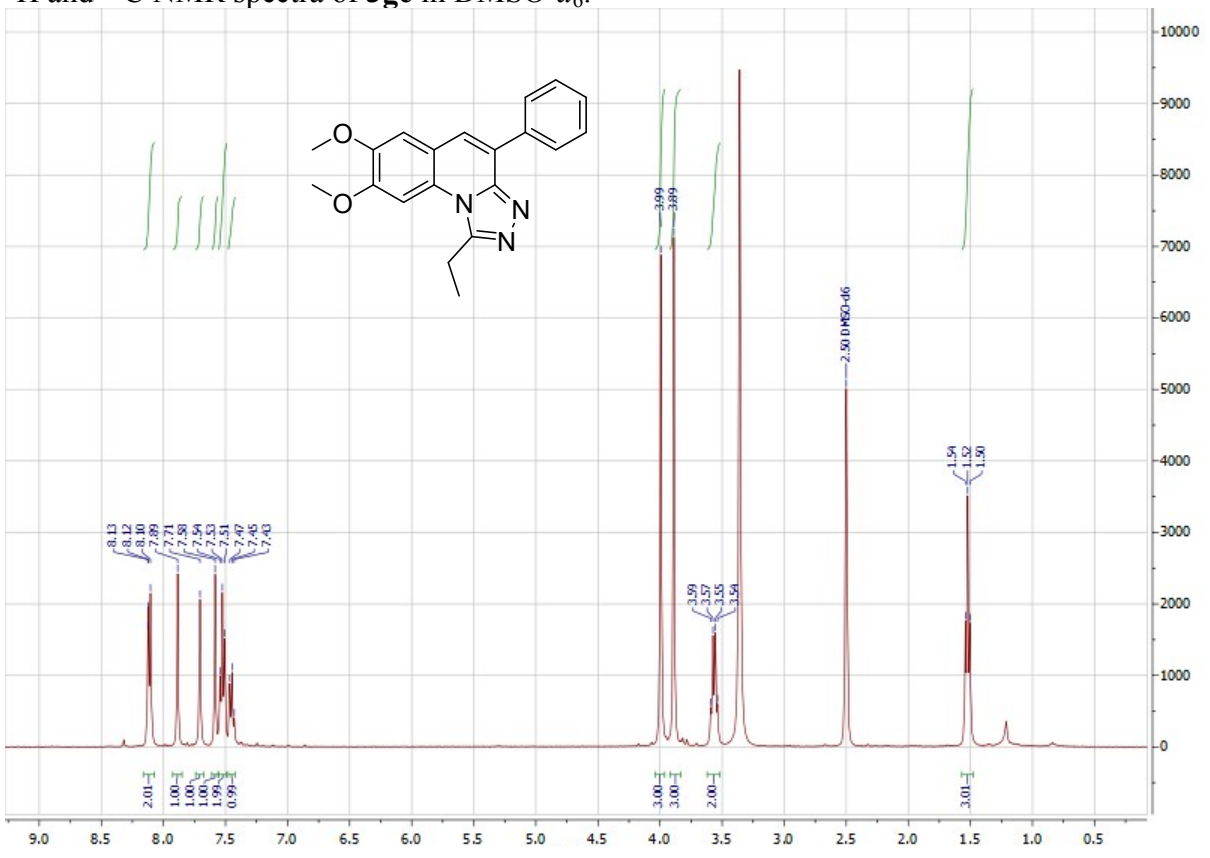


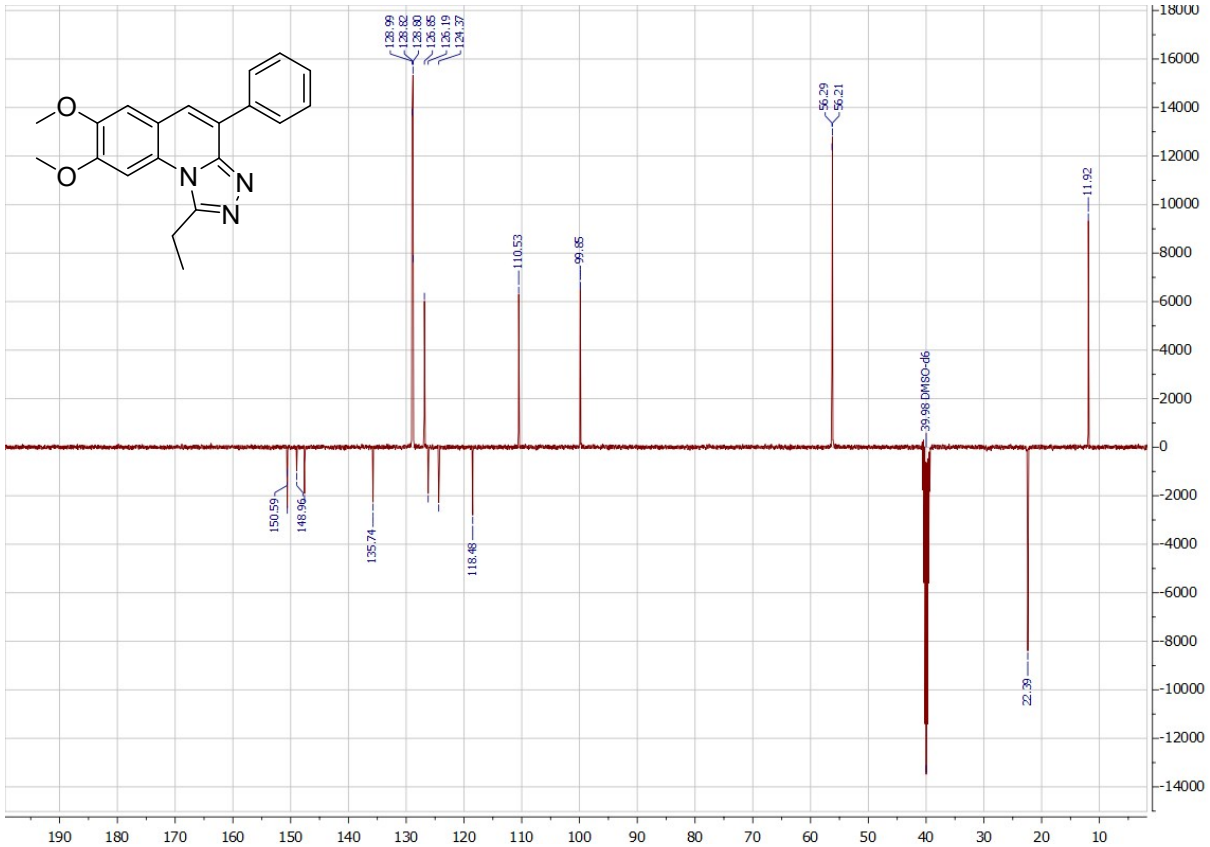
^{1}H and ^{13}C NMR spectra of **3fc** in $CDCl_3$.



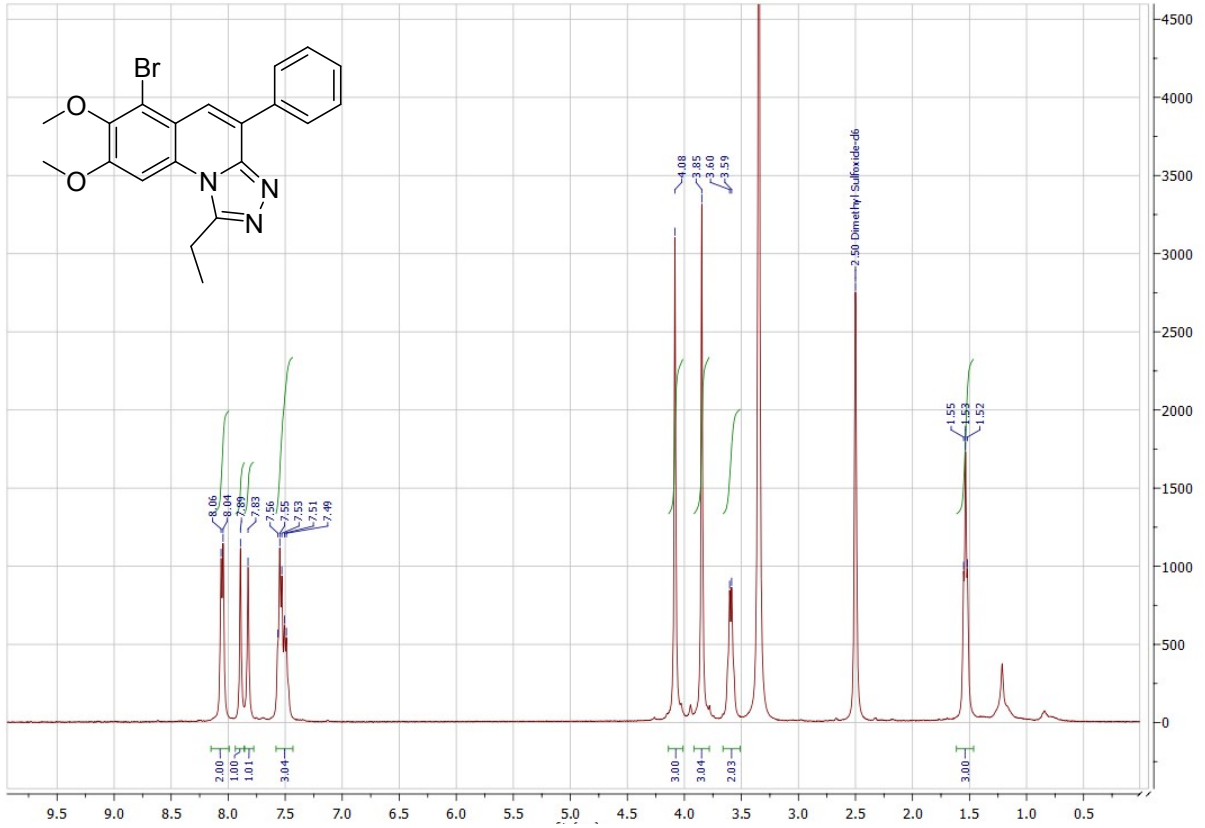


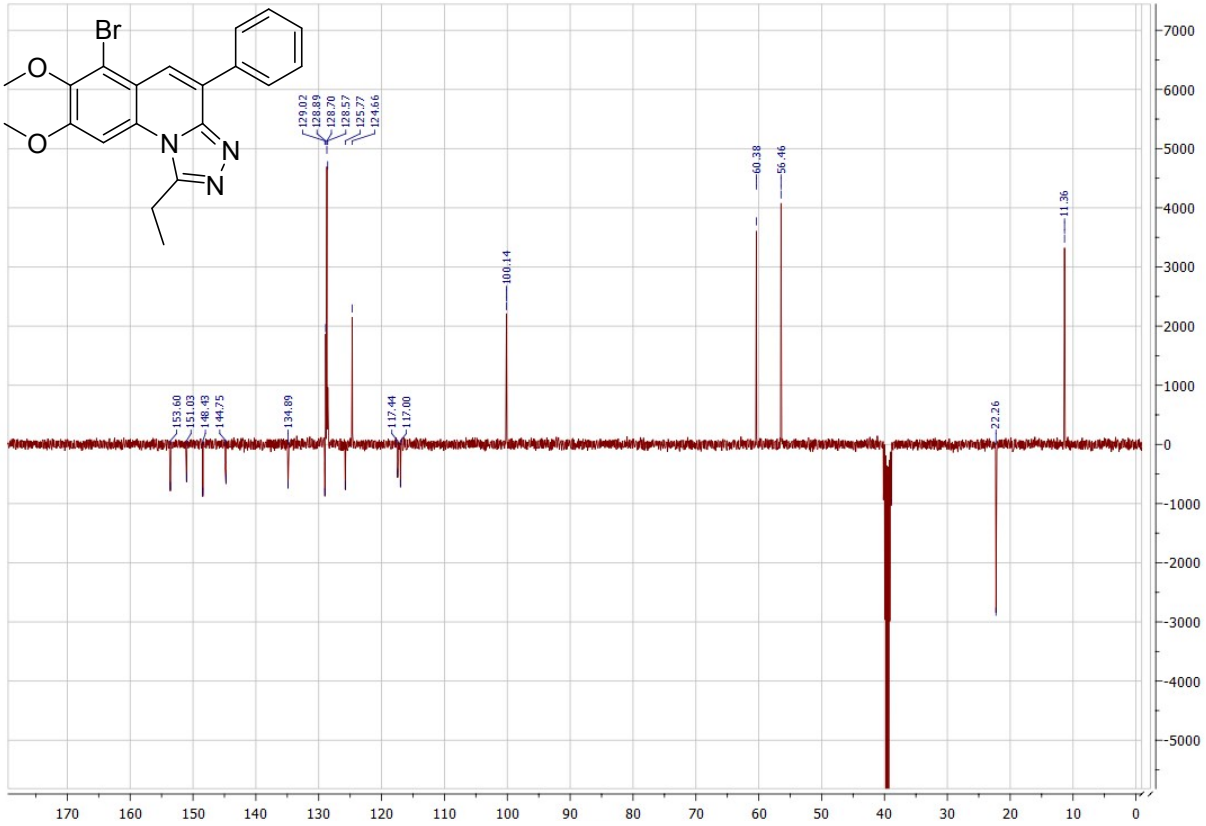
^{1}H and ^{13}C NMR spectra of **3gc** in DMSO-d_6.



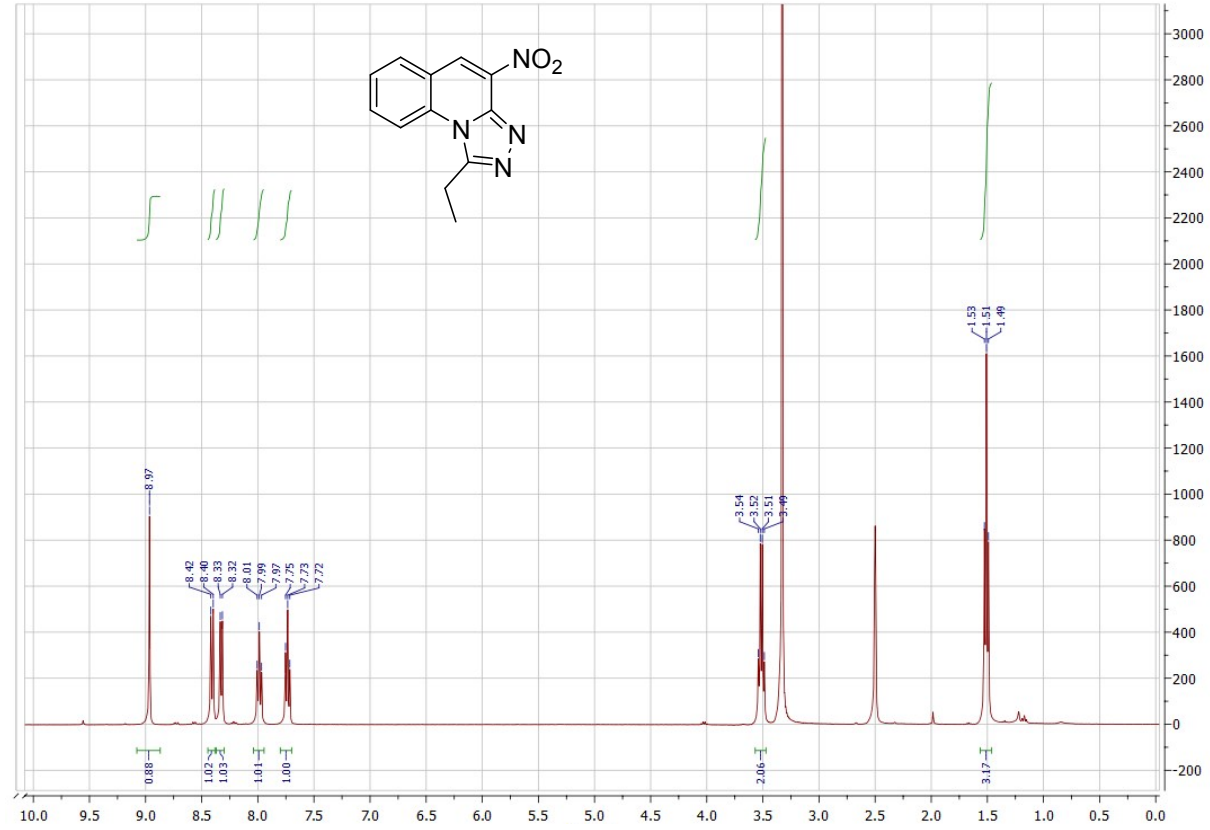


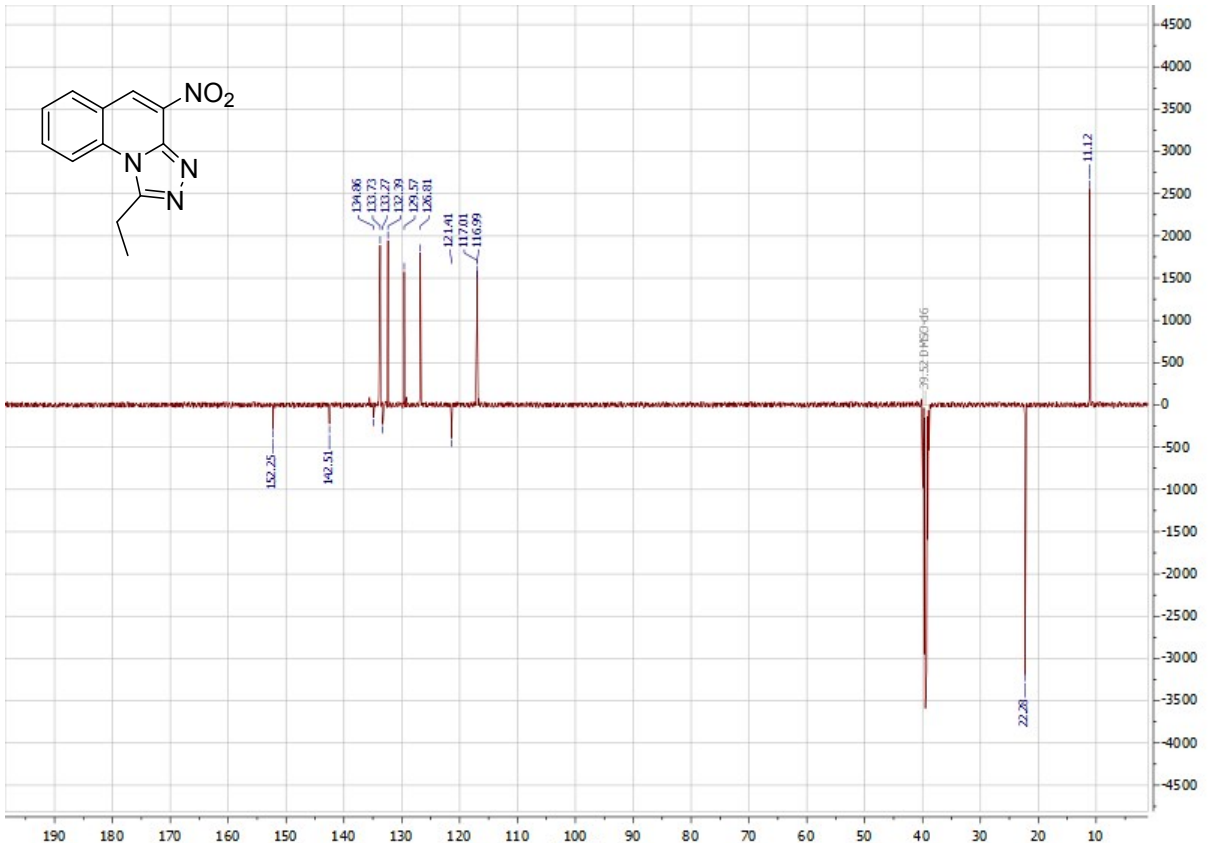
^{1}H and ^{13}C NMR spectra of **3hc** in DMSO-d_6.



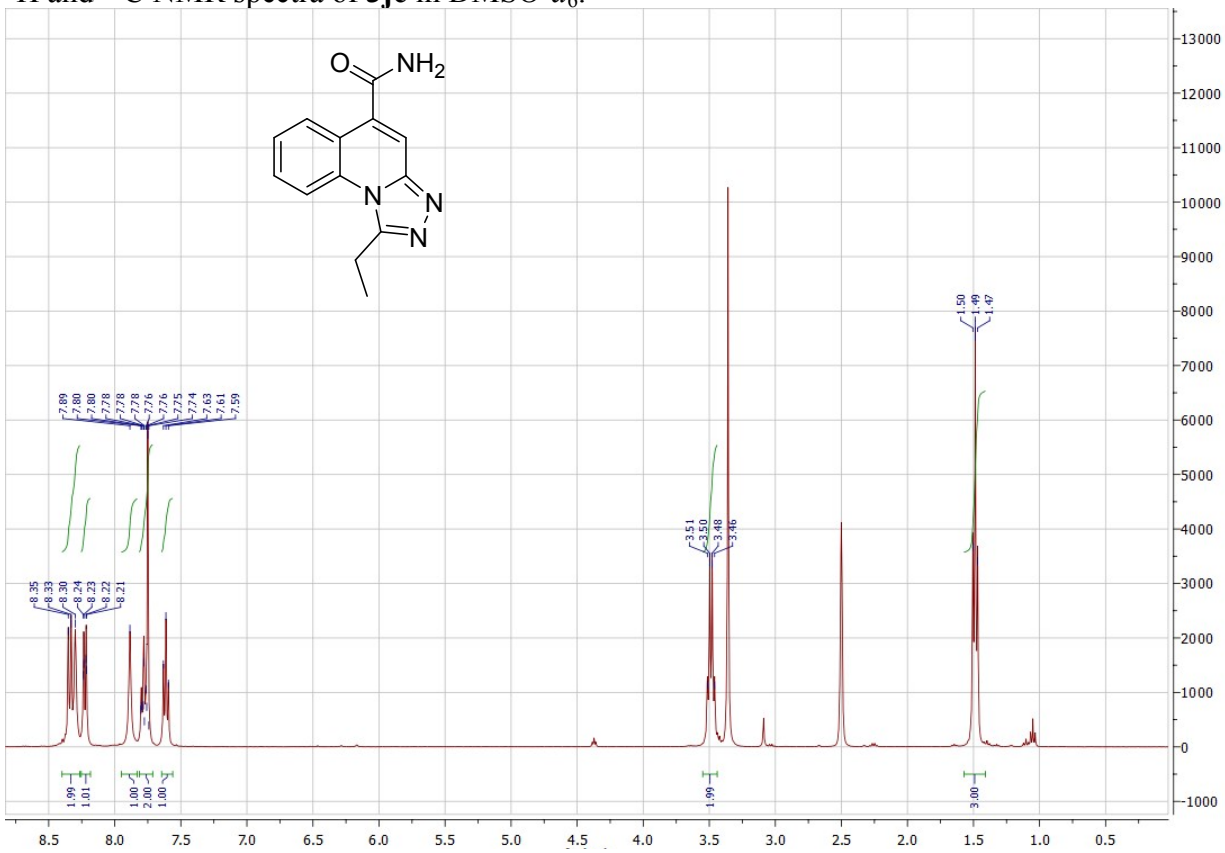


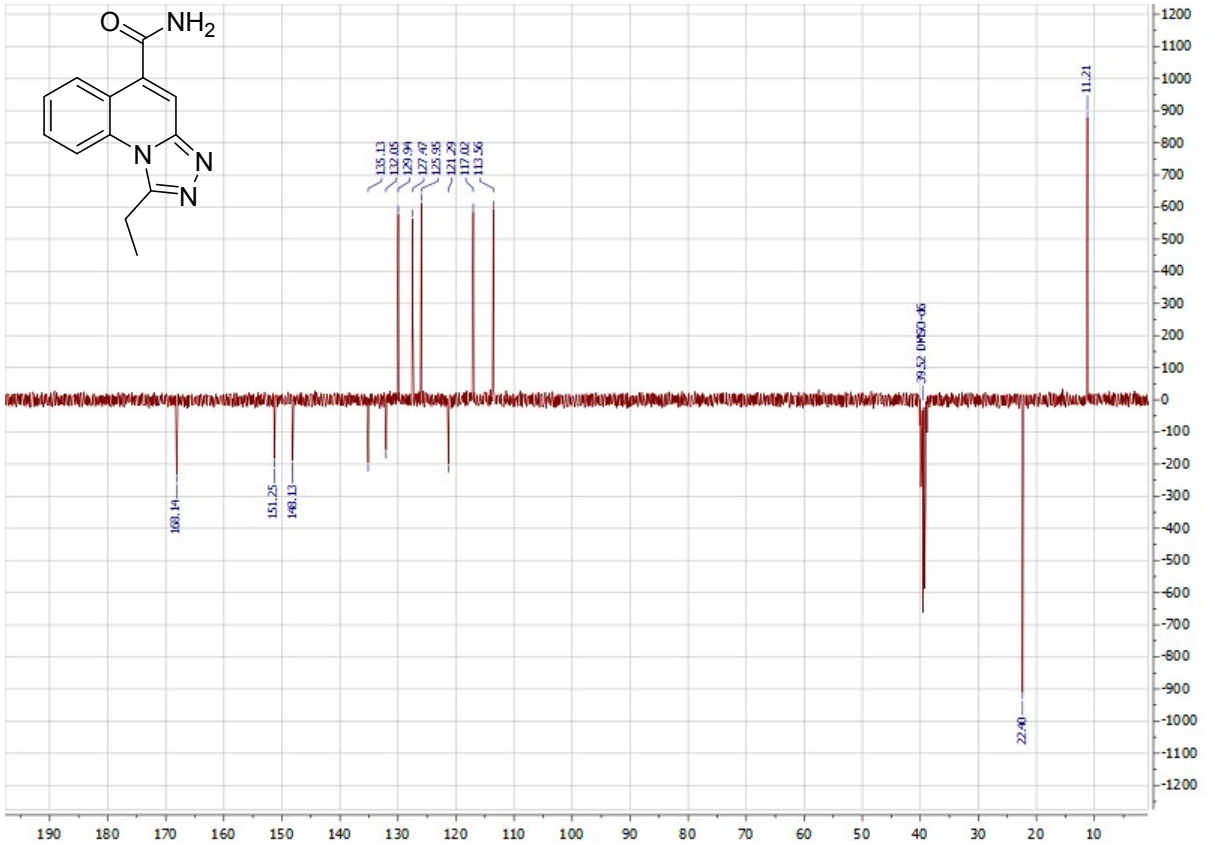
^{1}H and ^{13}C NMR spectra of **3ic** in DMSO-d_6.



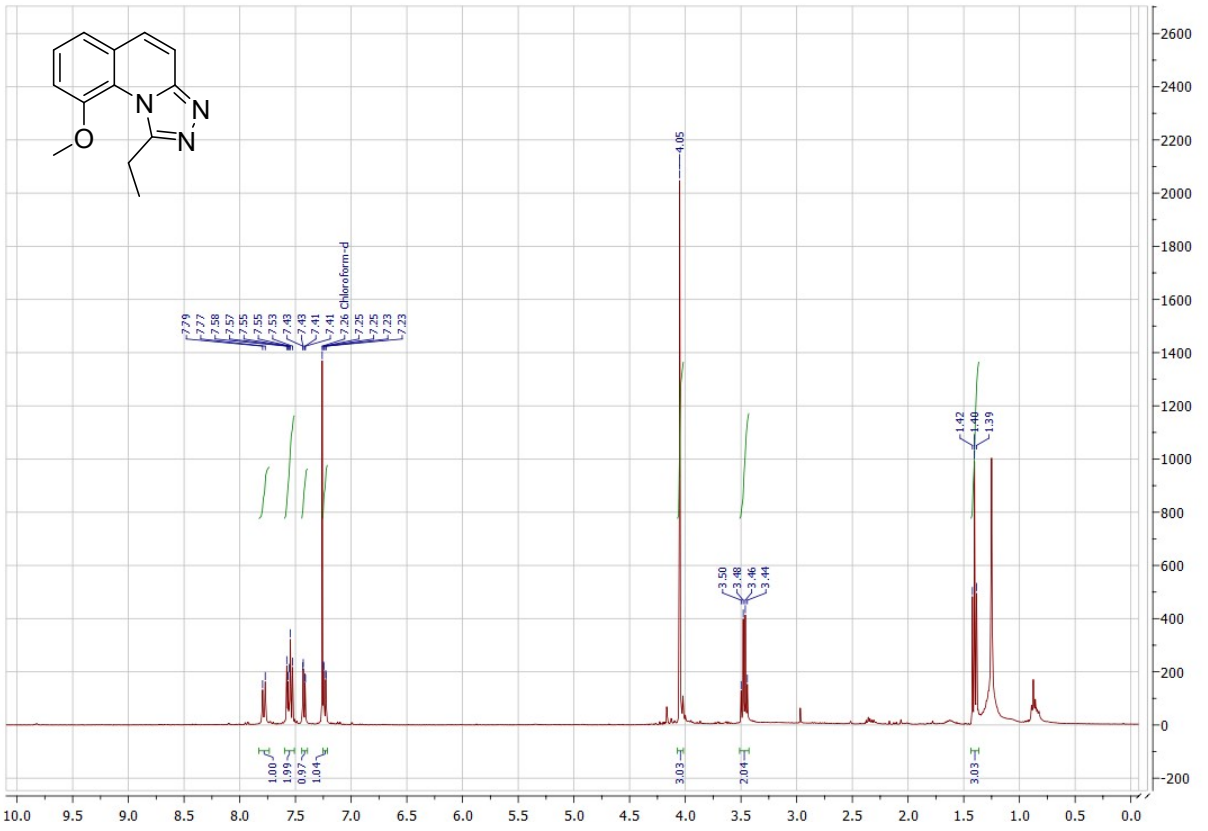


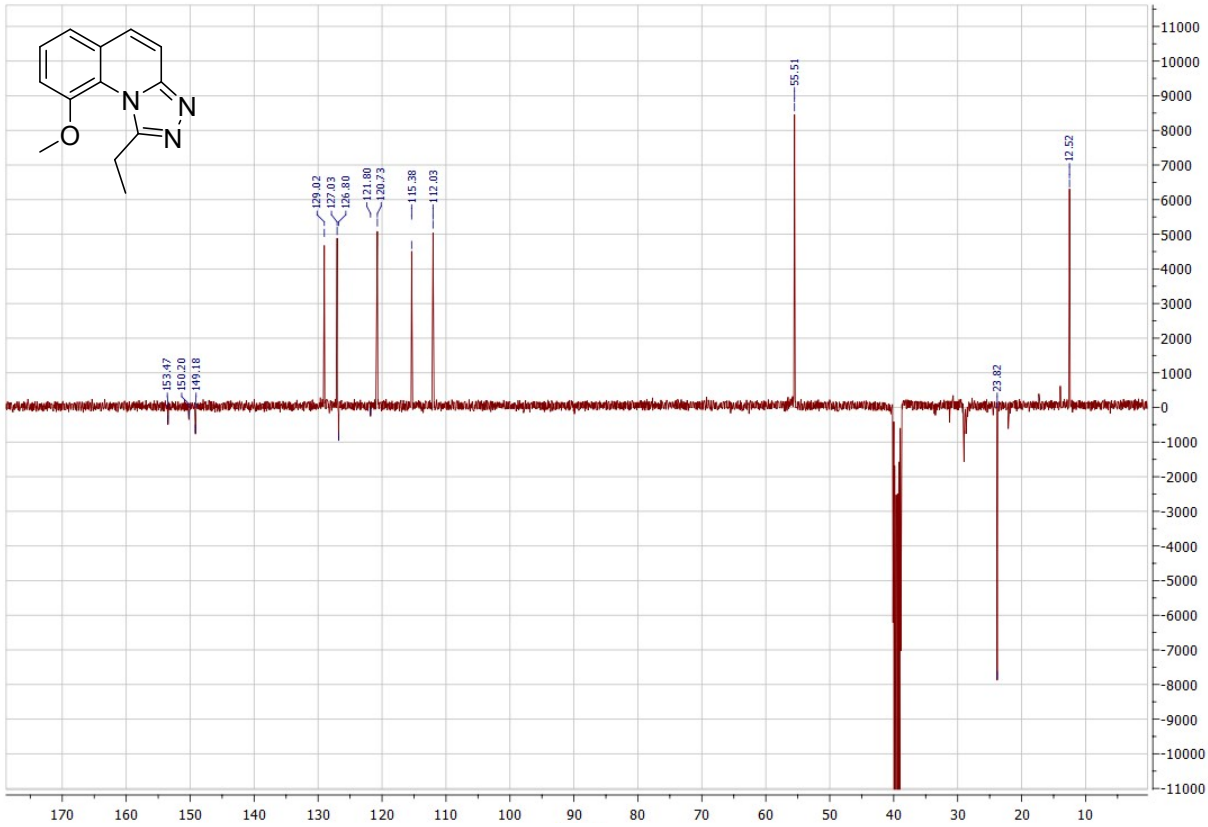
^{1}H and ^{13}C NMR spectra of **3jc** in DMSO-d_6.



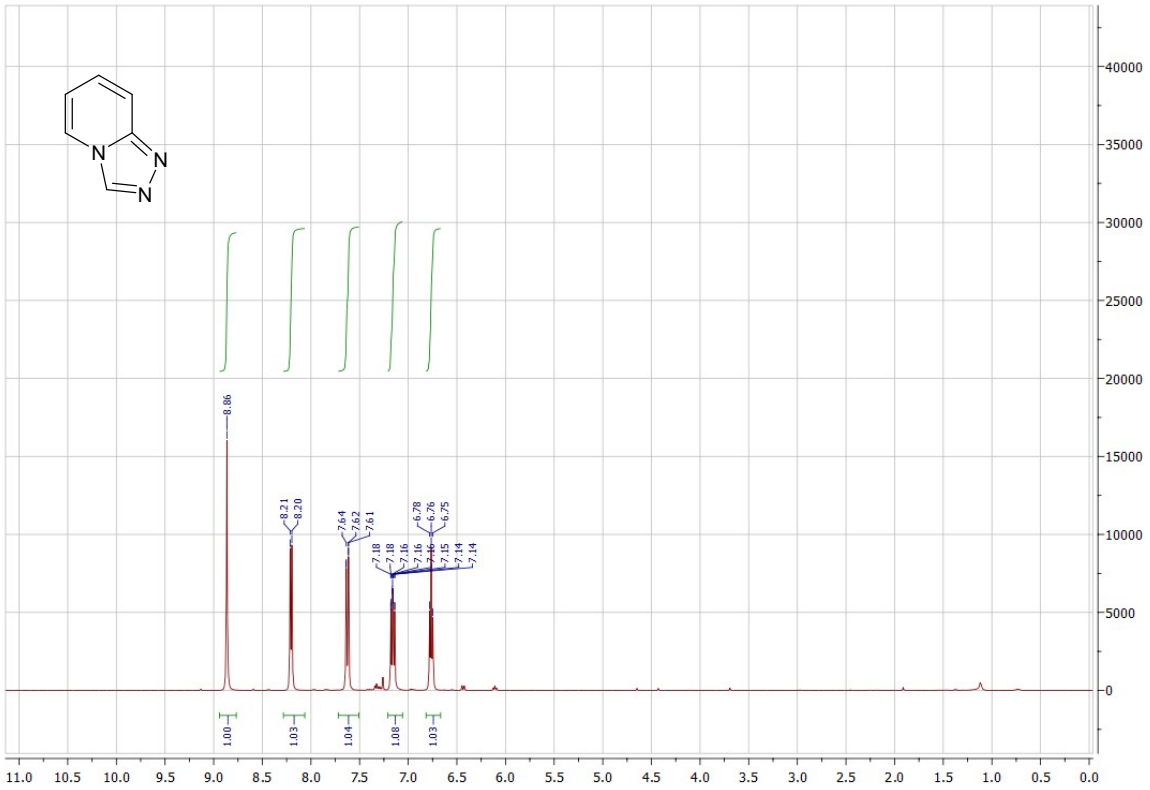


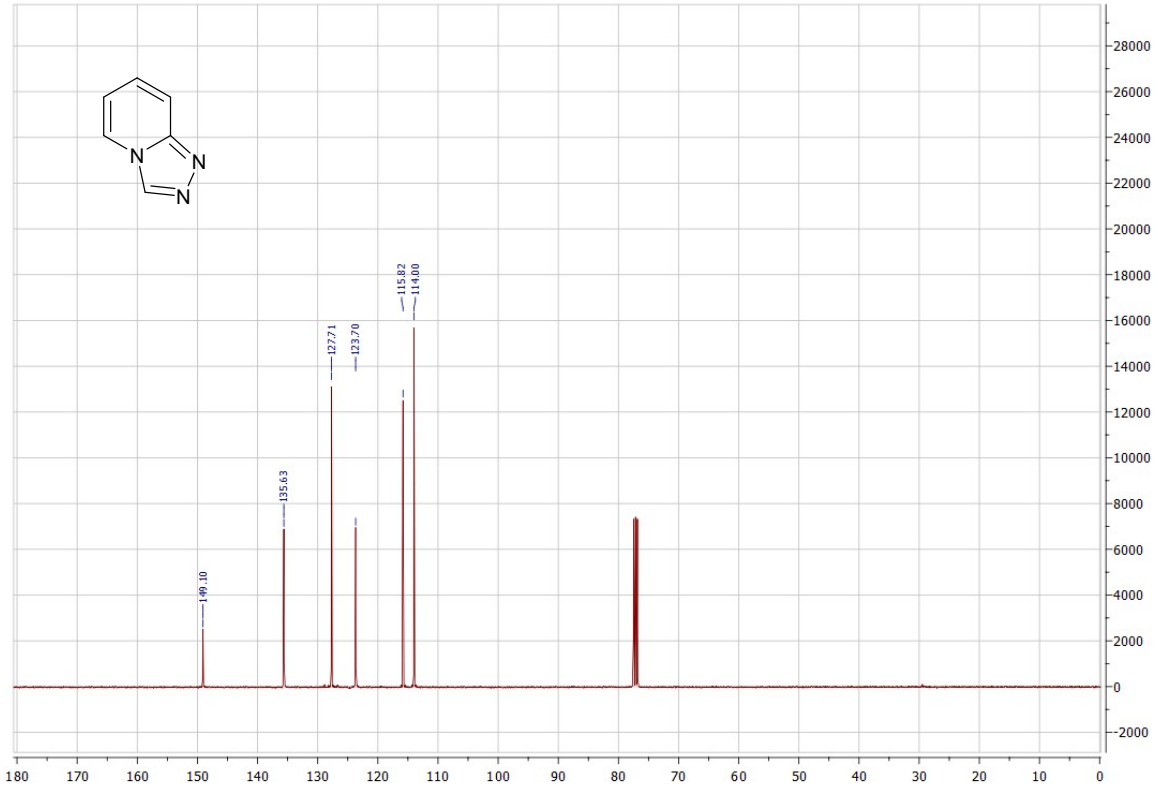
^{1}H spectrum of **3kc** in $CDCl_3$ and ^{13}C NMR spectrum of **3kc** in DMSO-d_6



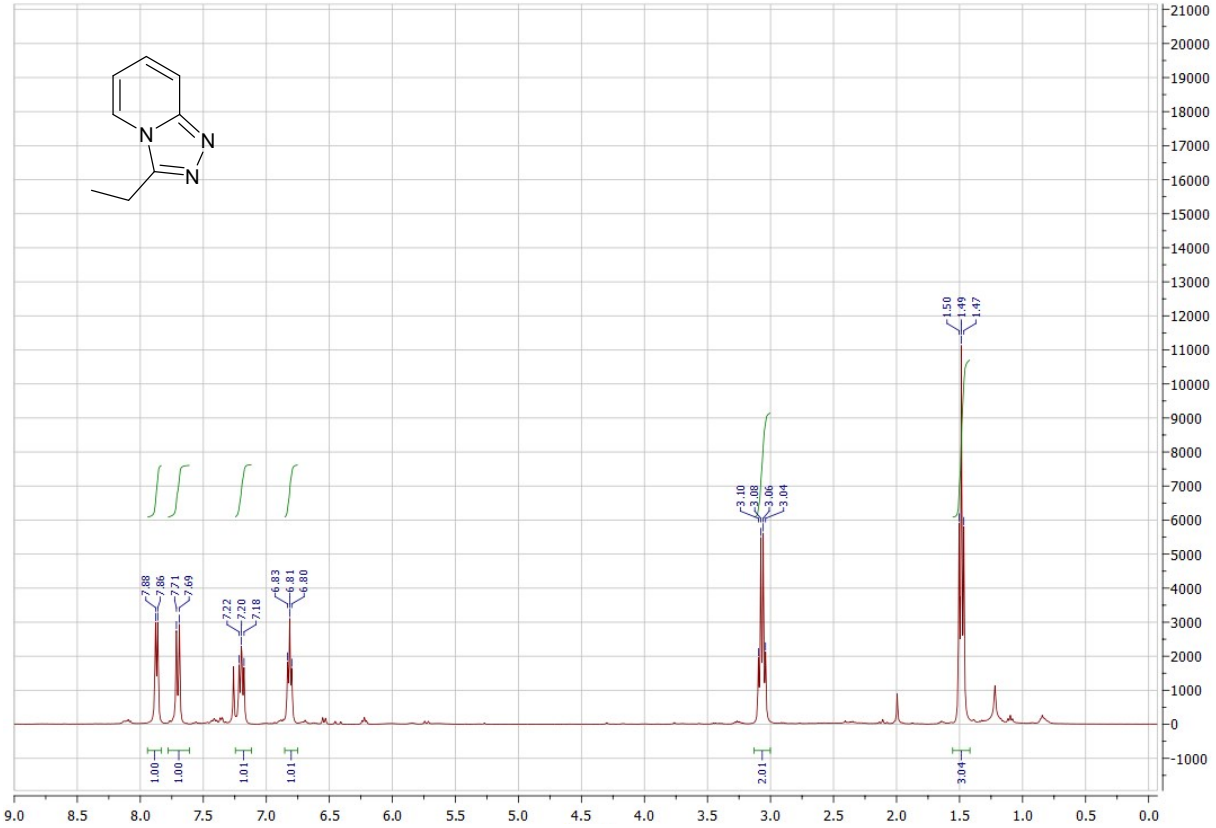


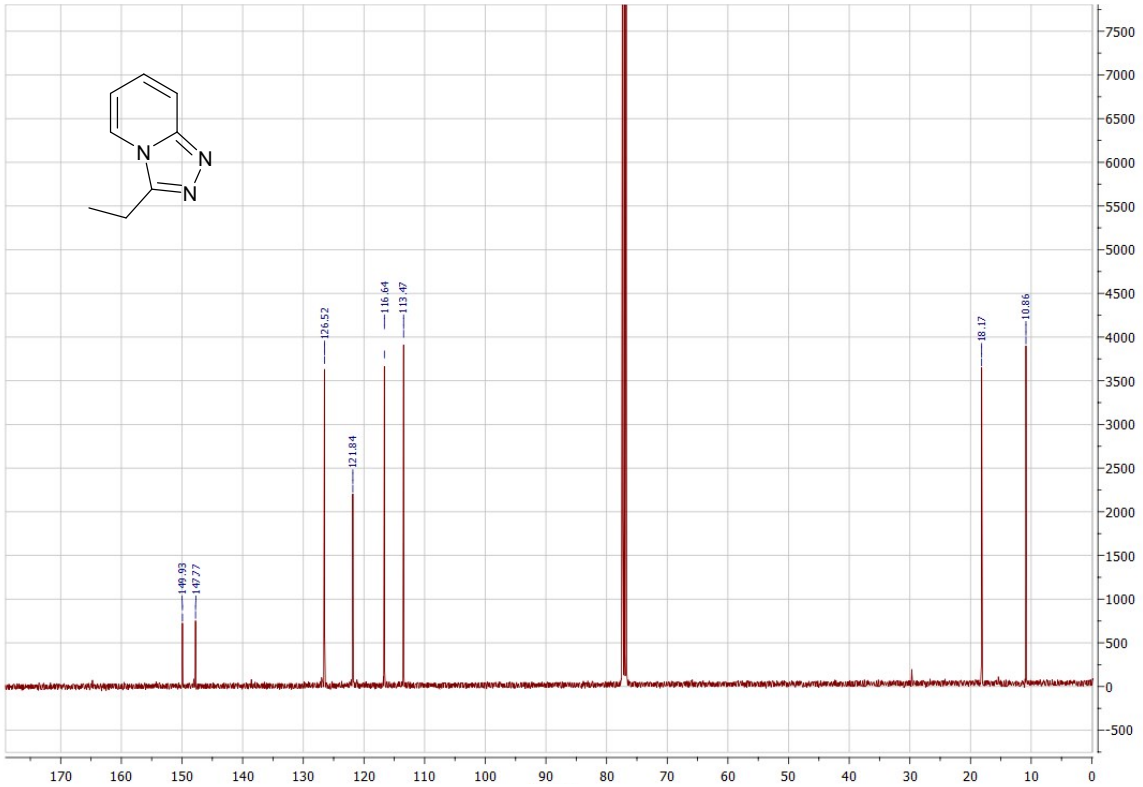
^{1}H and ^{13}C NMR spectra of **5a** in $CDCl_3$.



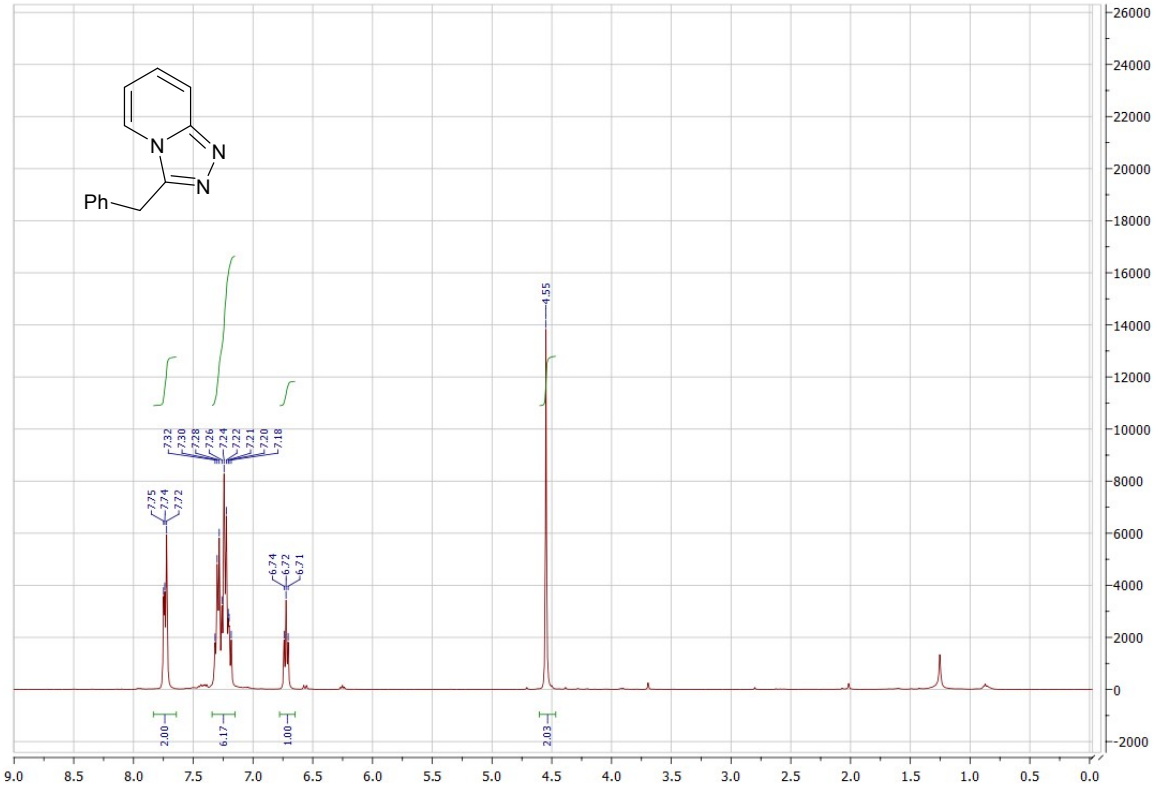


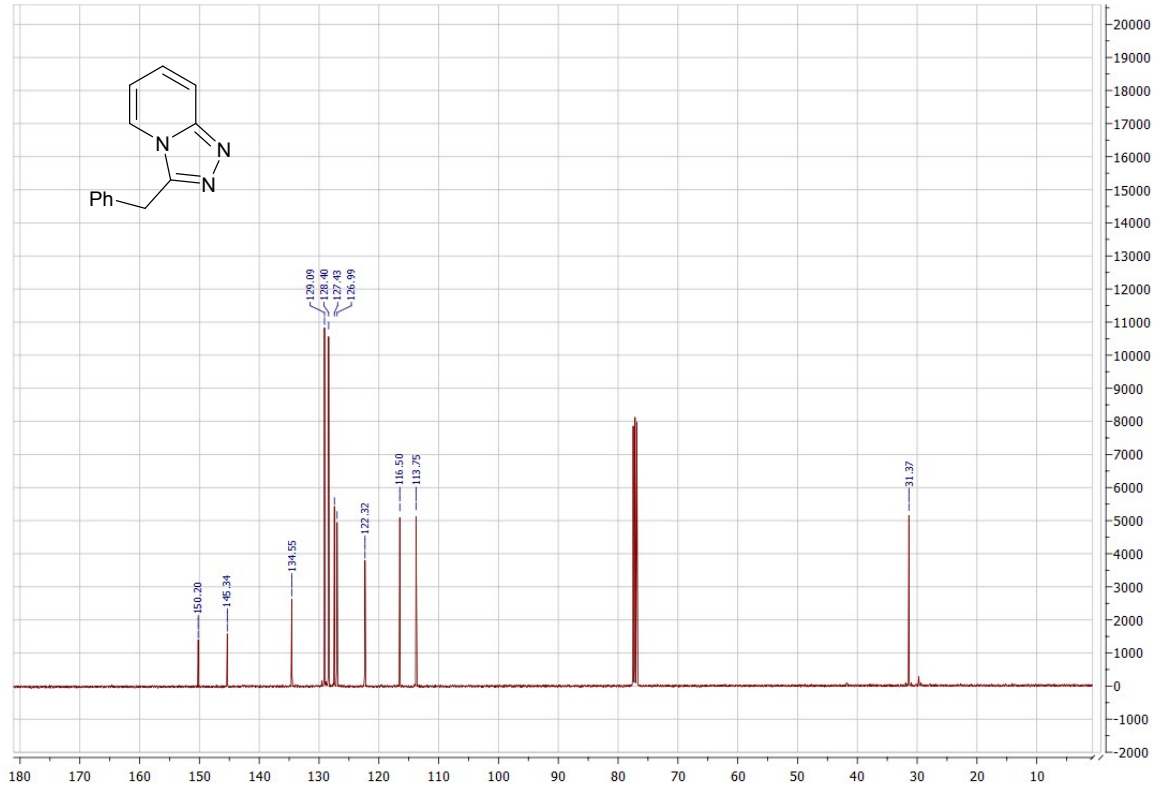
^{1}H and ^{13}C NMR spectra of **5c** in $CDCl_3$.



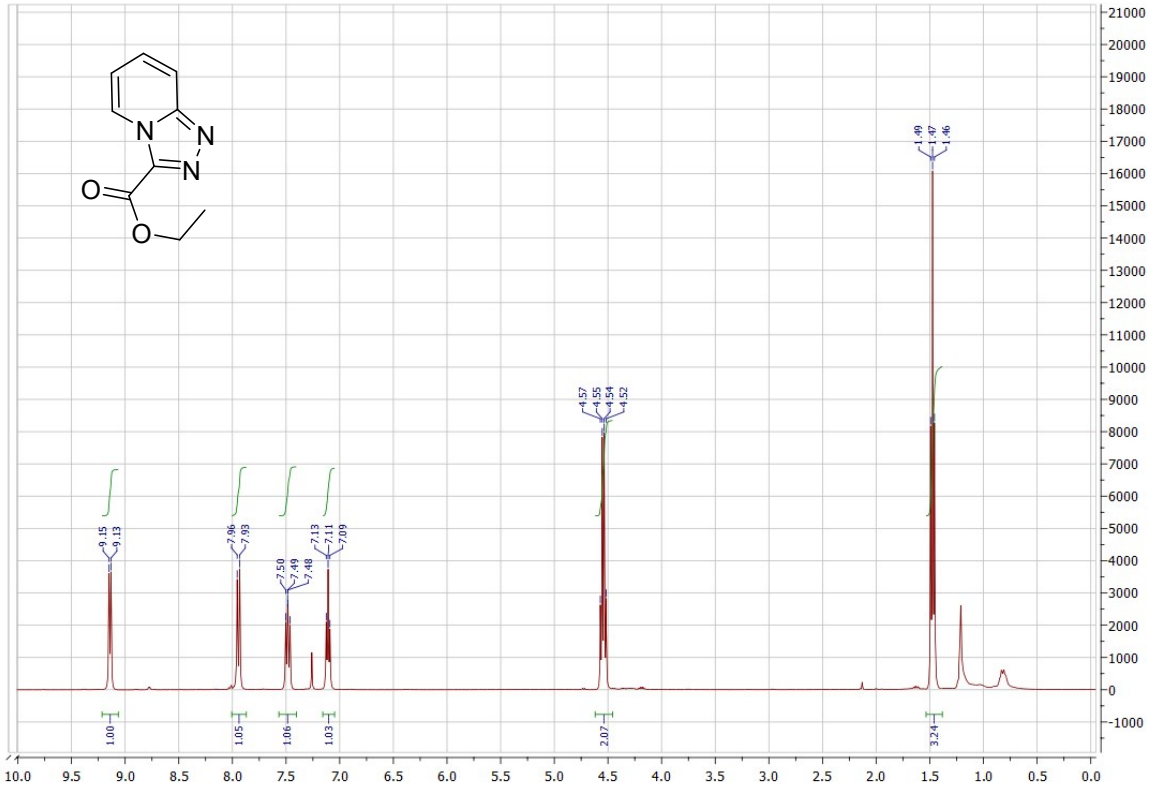


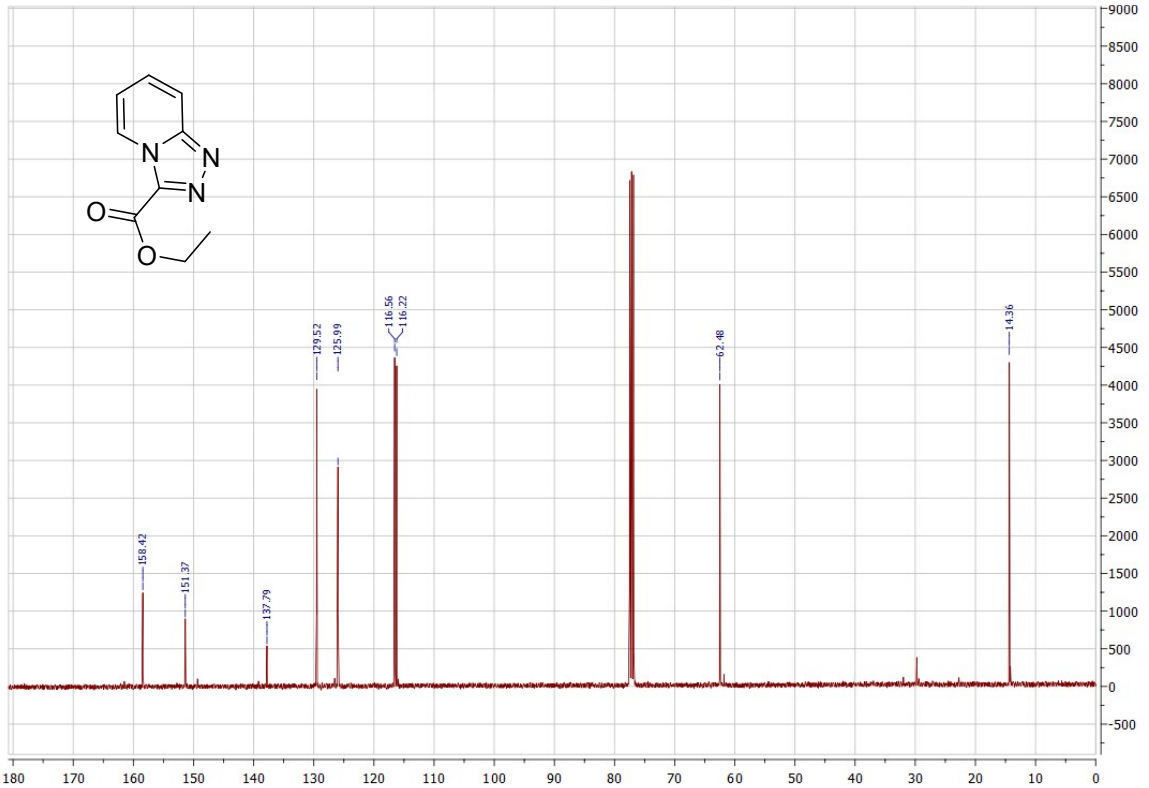
^{1}H and ^{13}C NMR spectra of **5e** in $CDCl_3$.



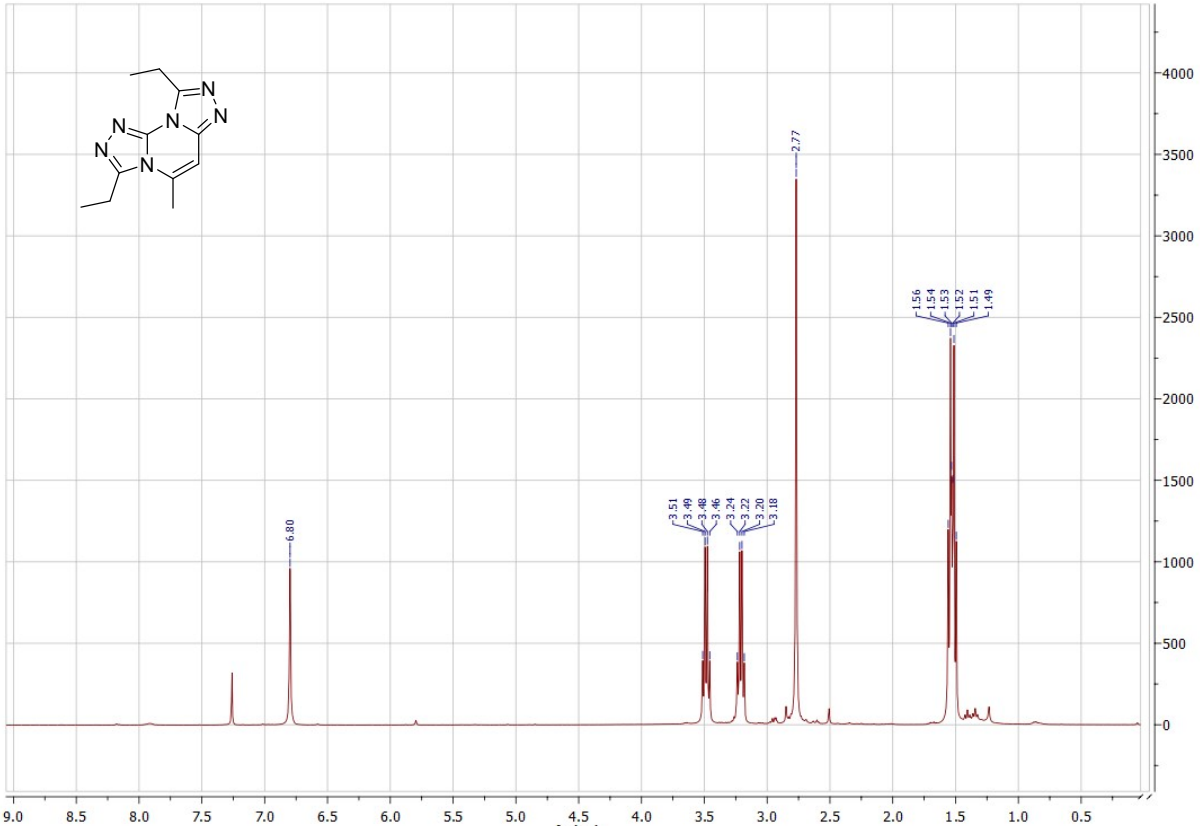


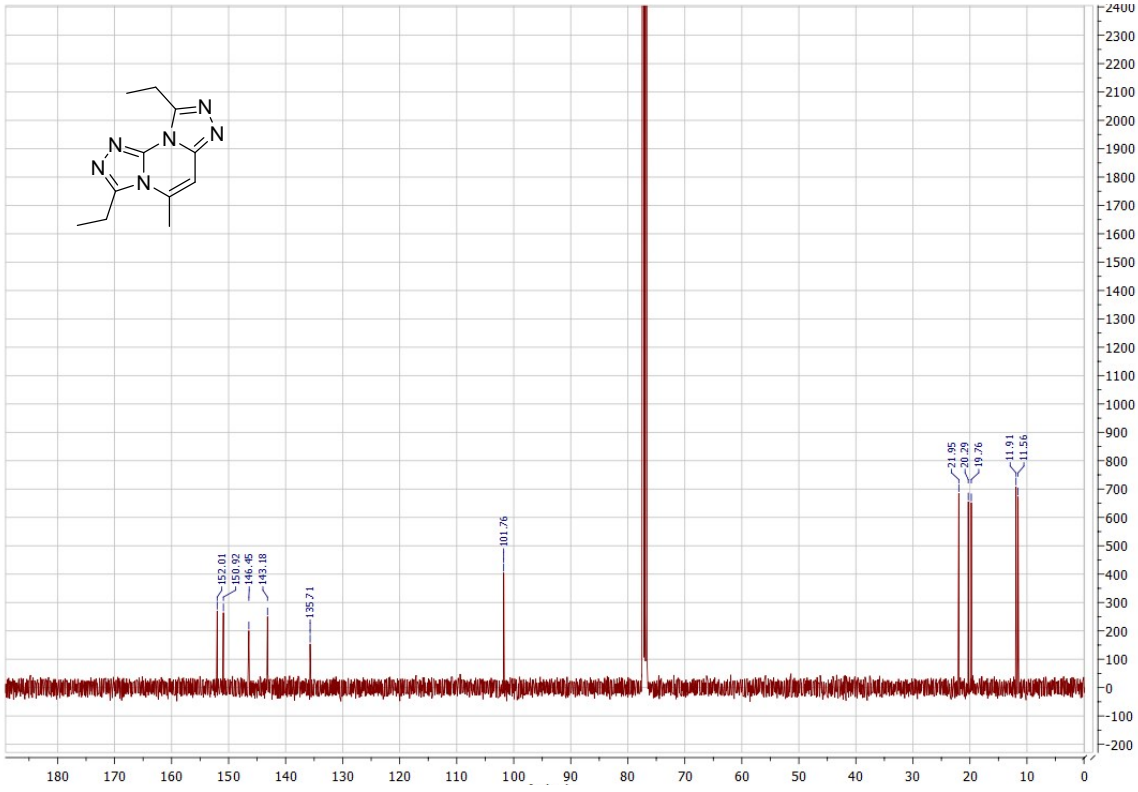
^{1}H and ^{13}C NMR spectra of **5g** in $CDCl_3$.



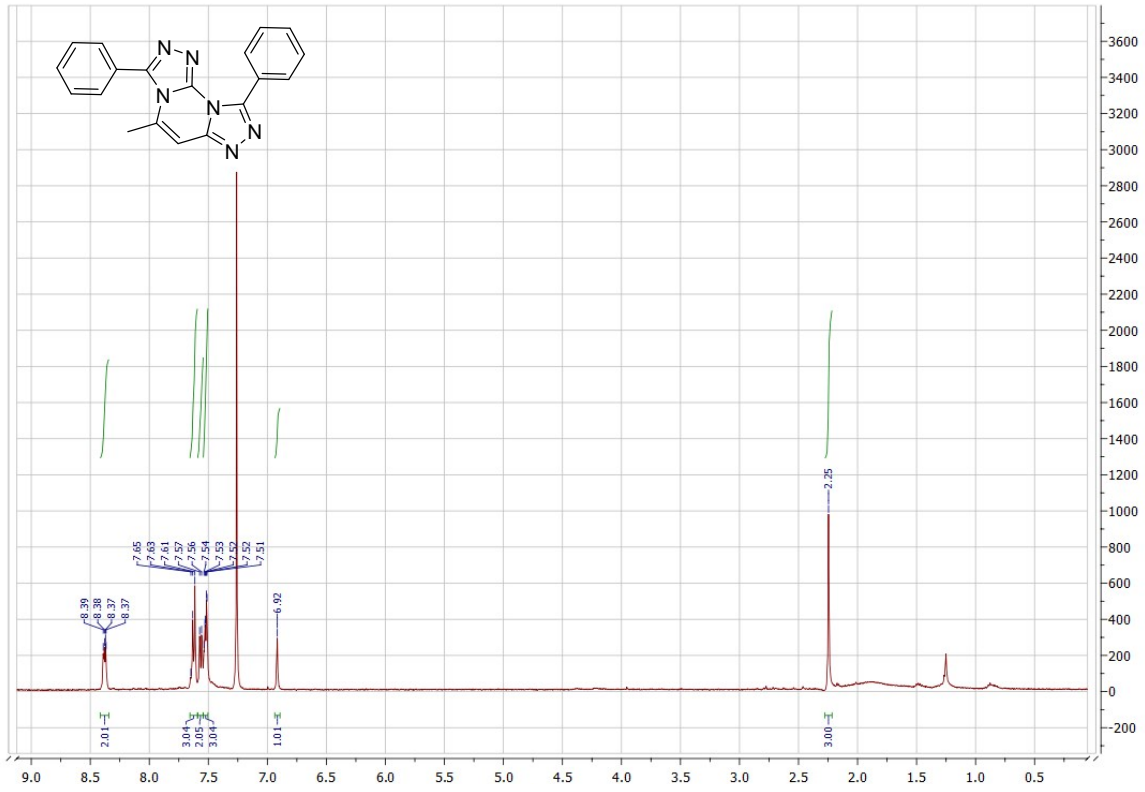


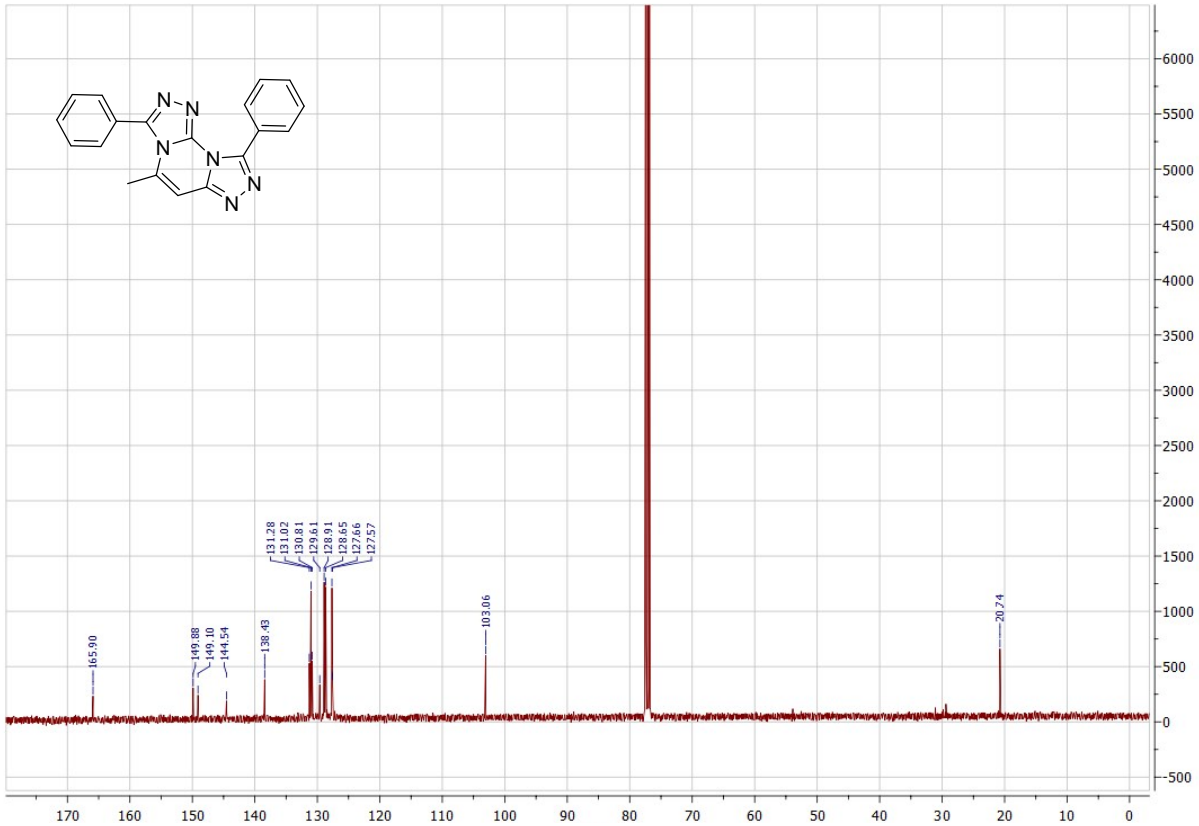
^{1}H and ^{13}C NMR spectra of **7c** in $CDCl_3$.





^{1}H and ^{13}C NMR spectra of **7f** in $CDCl_3$.





2. Crystal data

Crystallographic data for compound **3ab** (CCDC-1994548) have been deposited with the Cambridge Crystallographic Data Centre, copies of the data can be obtained, free of charge, on application to CCDC (Email:deposit@ccdc.cam.ac.uk)

Single crystals of $C_{11}H_9N_3$ **3ab** were obtained by evaporation of a saturated ethyl acetate solution. A suitable crystal was selected, mounted by acrylic glue on the glass stick, and X-ray intensity data of the compound was collected using SuperNova, Dual, Cu at zero, AtlasS2 diffractometer. The crystal was kept at 293(2) K during data collection. Using Olex2,[1] the structure was solved with the ShelXT[2] structure solution program using Intrinsic Phasing and refined with the ShelXL[3] refinement package using Least Squares minimisation.

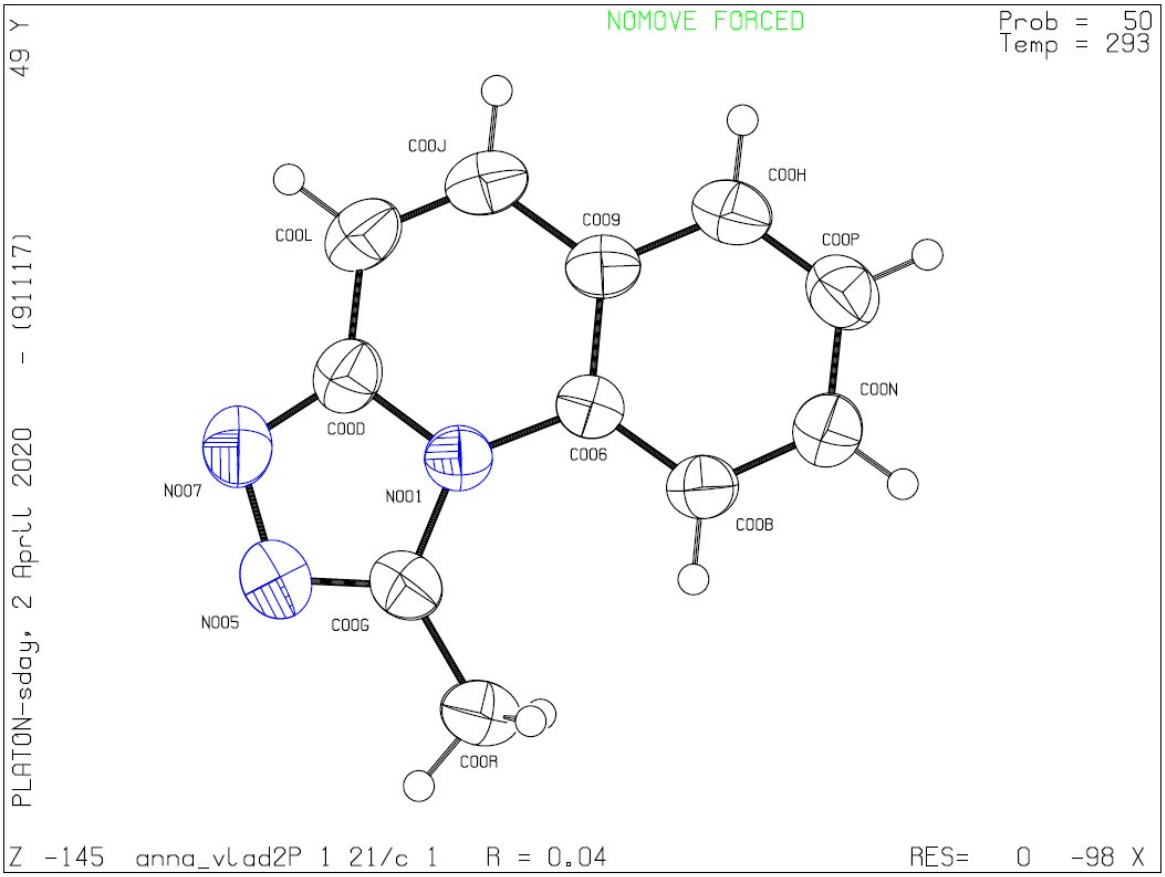


Table 1. Crystal data and structure refinement for **3ab**.

Identification code	ANNA_VLAD279_2
Empirical formula	$C_{11}H_9N_3$
Formula weight	183.21
Temperature/K	293(2)
Crystal system	monoclinic
Space group	$P2_1/c$

a/Å	9.1934(5)
b/Å	10.6902(5)
c/Å	18.2767(8)
α/°	90
β/°	100.449(5)
γ/°	90
Volume/Å^3	1766.43(15)
Z	8
ρ_{calc}g/cm^3	1.378
μ/mm^{-1}	0.686
F(000)	768.0
Crystal size/mm^3	0.512 × 0.361 × 0.289
Radiation	CuKα (λ = 1.54184)
2Θ range for data collection/°	9.626 to 152.3
Index ranges	$-11 \leq h \leq 11$, $-12 \leq k \leq 13$, $-22 \leq l \leq 22$
Reflections collected	18678
Independent reflections	3685 [R_{int} = 0.0247, R_{sigma} = 0.0156]
Data/restraints/parameters	3685/0/256
Goodness-of-fit on F^2	1.031
Final R indexes [I>=2σ (I)]	R_1 = 0.0401, wR_2 = 0.1074
Final R indexes [all data]	R_1 = 0.0462, wR_2 = 0.1147
Largest diff. peak/hole / e Å^{-3}	0.25/-0.12

Table 2 Fractional Atomic Coordinates (×10^4) and Equivalent Isotropic Displacement Parameters (Å^2×10^3) for **3ab**. U_{eq} is defined as 1/3 of of the trace of the orthogonalised U_{IJ} tensor.

Atom	***x***	***y***	***z***	**U(eq)**
N001	1083.6(11)	6811.2(9)	5673.3(5)	46.1(2)
N002	5595.9(11)	1703.3(9)	4628.8(6)	47.7(2)
N003	7246.4(14)	301.0(12)	5139.2(7)	66.5(3)
N004	6867.2(13)	1050.7(13)	5693.7(7)	65.8(3)
N005	1266.7(15)	5983.9(13)	4593.6(7)	67.6(3)
C006	747.2(12)	7517.4(10)	6276.0(6)	43.6(3)
N007	2233.6(15)	5347.1(12)	5135.0(7)	67.6(3)
C008	4631.7(13)	2303.1(11)	4043.4(7)	45.0(3)
C009	1459.9(13)	7154.3(12)	6993.8(7)	47.6(3)
C00A	4609.6(14)	1841.2(11)	3322.0(7)	49.3(3)
C00B	-207.8(14)	8530.7(12)	6183.6(7)	51.4(3)
C00C	6474.7(14)	706.5(12)	4508.1(8)	53.9(3)
C00D	2105.7(14)	5850.1(12)	5775.5(8)	53.6(3)
C00E	3747.6(15)	3308.0(12)	4159.3(7)	53.7(3)
C00F	5895.6(14)	1876.1(13)	5387.8(7)	54.2(3)
C00G	592.9(15)	6844.3(13)	4914.1(7)	54.2(3)
C00H	1150.3(14)	7831.3(13)	7604.4(7)	56.1(3)

C00I	3657.3(16)	2422.9(13)	2732.0(7)	58.1(3)
C00J	2509.3(14)	6144.5(13)	7088.8(8)	56.6(3)
C00K	2777.6(16)	3403.3(13)	2852.2(8)	60.3(3)
C00L	2840.0(16)	5525.0(13)	6503.1(8)	60.0(3)
C00M	6457.6(16)	264.4(13)	3775.9(8)	61.2(3)
C00N	-471.4(16)	9183.6(13)	6795.8(8)	58.6(3)
C00O	2829.7(15)	3848.7(13)	3564.6(8)	58.4(3)
C00P	201.6(16)	8829.0(14)	7508.3(8)	60.4(3)
C00Q	5558.9(16)	817.5(13)	3208.4(8)	59.6(3)
C00R	-525.4(18)	7698.9(16)	4494.9(8)	69.0(4)
C00S	5263.5(17)	2840.6(17)	5821.8(8)	69.7(4)

Table 3 Anisotropic Displacement Parameters (Å2×103) for **3ab**. The Anisotropic displacement factor exponent takes the form: -2π2[h2a*2U11+2hka*b*U12+…].

Atom	**U_{11}**	**U_{22}**	**U_{33}**	**U_{23}**	**U_{13}**	**U_{12}**
N001	46.2(5)	45.9(5)	46.1(5)	1.6(4)	7.7(4)	-1.3(4)
N002	45.1(5)	48.0(5)	48.6(6)	2.8(4)	4.3(4)	-2.5(4)
N003	62.5(7)	63.6(7)	69.1(8)	8.2(6)	0.2(6)	10.7(6)
N004	61.5(7)	73.5(8)	57.7(7)	8.0(6)	-1.7(5)	6.0(6)
N005	75.2(8)	73.1(8)	56.3(7)	-6.3(6)	16.4(6)	8.3(6)
C006	43.1(6)	44.7(6)	42.7(6)	0.9(4)	6.6(5)	-4.7(4)
N007	76.2(8)	64.3(7)	65.0(7)	-3.5(6)	20.0(6)	12.6(6)
C008	43.7(6)	44.1(6)	45.6(6)	3.1(5)	4.2(5)	-5.1(4)
C009	43.3(6)	51.0(6)	47.0(6)	5.7(5)	4.0(5)	-5.2(5)
C00A	51.2(7)	47.1(6)	49.5(7)	-1.9(5)	8.5(5)	-6.3(5)
C00B	52.2(7)	52.9(7)	46.8(6)	2.6(5)	2.6(5)	3.1(5)
C00C	50.2(7)	48.8(7)	61.2(8)	3.7(5)	5.8(6)	-0.7(5)
C00D	54.0(7)	47.4(6)	61.2(8)	3.4(5)	14.8(6)	3.3(5)
C00E	59.2(7)	54.7(7)	46.5(6)	-2.9(5)	8.0(5)	3.0(6)
C00F	49.9(7)	63.9(8)	46.0(6)	4.7(5)	1.4(5)	-2.1(6)
C00G	56.8(7)	60.6(7)	45.5(6)	-1.0(5)	10.0(5)	-2.0(6)
C00H	53.1(7)	68.6(8)	44.1(6)	2.0(6)	2.4(5)	-5.2(6)
C00I	66.9(8)	61.7(8)	43.7(6)	-2.8(5)	4.8(6)	-5.9(6)
C00J	52.2(7)	59.0(7)	56.0(7)	15.5(6)	3.2(6)	0.6(6)
C00K	63.5(8)	61.7(8)	51.3(7)	9.0(6)	-1.2(6)	1.2(6)
C00L	57.7(8)	53.1(7)	69.1(9)	13.6(6)	11.5(6)	9.7(6)
C00M	59.5(8)	53.6(7)	69.9(9)	-7.0(6)	10.1(7)	4.4(6)
C00N	59.6(8)	56.2(7)	59.4(8)	-3.4(6)	8.6(6)	7.1(6)
C00O	60.3(8)	53.6(7)	59.6(8)	3.3(6)	6.3(6)	8.9(6)
C00P	61.1(8)	68.1(8)	51.3(7)	-10.4(6)	8.1(6)	-2.3(6)
C00Q	64.4(8)	57.7(7)	57.4(8)	-11.6(6)	13.1(6)	-3.1(6)
C00R	70.3(9)	86.5(10)	46.3(7)	0.0(7)	0.2(6)	12.7(8)
C00S	66.1(9)	91.2(11)	49.2(7)	-5.8(7)	3.9(6)	9.7(8)

Table 4 Anisotropic Displacement Parameters ($Å^2×10^3$) for **3ab**. The Anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U_{11}+2hka^*b^*U_{12}+\ldots]$.

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
N001	46.2(5)	45.9(5)	46.1(5)	1.6(4)	7.7(4)	-1.3(4)
N002	45.1(5)	48.0(5)	48.6(6)	2.8(4)	4.3(4)	-2.5(4)
N003	62.5(7)	63.6(7)	69.1(8)	8.2(6)	0.2(6)	10.7(6)
N004	61.5(7)	73.5(8)	57.7(7)	8.0(6)	-1.7(5)	6.0(6)
N005	75.2(8)	73.1(8)	56.3(7)	-6.3(6)	16.4(6)	8.3(6)
C006	43.1(6)	44.7(6)	42.7(6)	0.9(4)	6.6(5)	-4.7(4)
N007	76.2(8)	64.3(7)	65.0(7)	-3.5(6)	20.0(6)	12.6(6)
C008	43.7(6)	44.1(6)	45.6(6)	3.1(5)	4.2(5)	-5.1(4)
C009	43.3(6)	51.0(6)	47.0(6)	5.7(5)	4.0(5)	-5.2(5)
C00A	51.2(7)	47.1(6)	49.5(7)	-1.9(5)	8.5(5)	-6.3(5)
C00B	52.2(7)	52.9(7)	46.8(6)	2.6(5)	2.6(5)	3.1(5)
C00C	50.2(7)	48.8(7)	61.2(8)	3.7(5)	5.8(6)	-0.7(5)
C00D	54.0(7)	47.4(6)	61.2(8)	3.4(5)	14.8(6)	3.3(5)
C00E	59.2(7)	54.7(7)	46.5(6)	-2.9(5)	8.0(5)	3.0(6)
C00F	49.9(7)	63.9(8)	46.0(6)	4.7(5)	1.4(5)	-2.1(6)
C00G	56.8(7)	60.6(7)	45.5(6)	-1.0(5)	10.0(5)	-2.0(6)
C00H	53.1(7)	68.6(8)	44.1(6)	2.0(6)	2.4(5)	-5.2(6)
C00I	66.9(8)	61.7(8)	43.7(6)	-2.8(5)	4.8(6)	-5.9(6)
C00J	52.2(7)	59.0(7)	56.0(7)	15.5(6)	3.2(6)	0.6(6)
C00K	63.5(8)	61.7(8)	51.3(7)	9.0(6)	-1.2(6)	1.2(6)
C00L	57.7(8)	53.1(7)	69.1(9)	13.6(6)	11.5(6)	9.7(6)
C00M	59.5(8)	53.6(7)	69.9(9)	-7.0(6)	10.1(7)	4.4(6)
C00N	59.6(8)	56.2(7)	59.4(8)	-3.4(6)	8.6(6)	7.1(6)
C00O	60.3(8)	53.6(7)	59.6(8)	3.3(6)	6.3(6)	8.9(6)
C00P	61.1(8)	68.1(8)	51.3(7)	-10.4(6)	8.1(6)	-2.3(6)
C00Q	64.4(8)	57.7(7)	57.4(8)	-11.6(6)	13.1(6)	-3.1(6)
C00R	70.3(9)	86.5(10)	46.3(7)	0.0(7)	0.2(6)	12.7(8)
C00S	66.1(9)	91.2(11)	49.2(7)	-5.8(7)	3.9(6)	9.7(8)

Table 4 Bond Lengths for **3ab**.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
N001	C006	1.4151(15)	C009	C00H	1.4018(18)
N001	C00D	1.3820(16)	C009	C00J	1.4372(18)
N001	C00G	1.3795(16)	C00A	C00I	1.4048(18)
N002	C008	1.4134(15)	C00A	C00Q	1.4380(19)
N002	C00C	1.3790(16)	C00B	C00N	1.3770(18)
N002	C00F	1.3769(16)	C00C	C00M	1.417(2)

N003	N004	1.3852(18)	C00D	C00L	1.4210(19)
N003	C00C	1.3133(17)	C00E	C00O	1.3766(18)
N004	C00F	1.3069(17)	C00F	C00S	1.482(2)
N005	N007	1.3834(17)	C00G	C00R	1.4809(19)
N005	C00G	1.3056(18)	C00H	C00P	1.369(2)
C006	C009	1.4104(16)	C00I	C00K	1.366(2)
C006	C00B	1.3853(17)	C00J	C00L	1.340(2)
N007	C00D	1.3127(17)	C00K	C00O	1.379(2)
C008	C00A	1.4046(17)	C00M	C00Q	1.341(2)
C008	C00E	1.3863(18)	C00N	C00P	1.3892(19)

Table 5 Bond Angles for **3ab**.

Atom	**Atom**	**Atom**	**Angle/°**	**Atom**	**Atom**	**Atom**	**Angle/°**
C00D	N001	C006	122.05(10)	N002	C00C	C00M	120.16(12)
C00G	N001	C006	133.75(10)	N003	C00C	N002	110.70(12)
C00G	N001	C00D	104.20(10)	N003	C00C	C00M	129.14(13)
C00C	N002	C008	122.33(10)	N001	C00D	C00L	120.28(12)
C00F	N002	C008	133.26(11)	N007	C00D	N001	110.65(12)
C00F	N002	C00C	104.40(10)	N007	C00D	C00L	129.06(13)
C00C	N003	N004	106.50(11)	C00O	C00E	C008	119.81(12)
C00F	N004	N003	108.71(11)	N002	C00F	C00S	127.32(12)
C00G	N005	N007	108.75(11)	N004	C00F	N002	109.69(12)
C009	C006	N001	116.55(11)	N004	C00F	C00S	122.99(12)
C00B	C006	N001	123.05(11)	N001	C00G	C00R	127.29(12)
C00B	C006	C009	120.39(11)	N005	C00G	N001	109.76(12)
C00D	N007	N005	106.64(11)	N005	C00G	C00R	122.95(12)
C00A	C008	N002	116.83(11)	C00P	C00H	C009	121.12(12)
C00E	C008	N002	122.71(11)	C00K	C00I	C00A	121.41(12)
C00E	C008	C00A	120.45(11)	C00L	C00J	C009	121.29(12)
C006	C009	C00J	120.49(12)	C00I	C00K	C00O	119.77(13)
C00H	C009	C006	118.11(11)	C00J	C00L	C00D	119.26(12)
C00H	C009	C00J	121.36(12)	C00Q	C00M	C00C	118.91(13)
C008	C00A	C00I	117.76(12)	C00B	C00N	C00P	120.62(13)
C008	C00A	C00Q	119.82(12)	C00E	C00O	C00K	120.79(13)
C00I	C00A	C00Q	122.42(12)	C00H	C00P	C00N	119.86(13)
C00N	C00B	C006	119.89(12)	C00M	C00Q	C00A	121.94(13)

Table 6 Hydrogen Atom Coordinates ($Å \times 10^4$) and Isotropic Displacement Parameters ($Å^2 \times 10^3$) for **3ab**.

Atom	***x***	***y***	***z***	**U(eq)**

H00B	-670.09	8769.7	5708.91	62
H00E	3774.57	3615.89	4637.5	64
H00H	1597	7598.53	8082.81	67
H00I	3625.16	2134.24	2249.36	70
H00J	2967.84	5916.61	7566.2	68
H00K	2145.55	3769.36	2454.88	72
H00L	3542.18	4889.37	6571.96	72
H00M	7059.87	-398.67	3690.3	73
H00N	-1105.88	9868.24	6731.74	70
H00O	2237.57	4522.41	3644.18	70
H00P	7.92	9268.69	7919.15	73
H00Q	5549.11	530.84	2727.13	71
H00A	-1428.11	7636.7	4686.79	104
H00C	-707.79	7471.08	3978.31	104
H00D	-165.35	8543.03	4548	104
H00F	5540.2	3656.41	5675.42	104
H00G	5636.04	2720.13	6342.62	104
H00R	4205.02	2769.86	5728.56	104

Crystal Data for $C_{11}H_9N_3$ (M =183.21 g/mol): monoclinic, space group $P2_1/c$ (no. 14), a = 9.1934(5) Å, b = 10.6902(5) Å, c = 18.2767(8) Å, β = 100.449(5)°, V = 1766.43(15) Å^3, Z = 8, T = 293(2) K, μ(CuKα) = 0.686 mm^{-1}, *Dcalc* = 1.378 g/cm^3, 18678 reflections measured (9.626° ≤ 2Θ ≤ 152.3°), 3685 unique (R_{int} = 0.0247, R_{sigma} = 0.0156) which were used in all calculations. The final R_1 was 0.0401 (I > 2σ(I)) and wR_2 was 0.1147 (all data).

Refinement model description

Number of restraints - 0, number of constraints - unknown.
Details:
1. Fixed Uiso
 At 1.2 times of:
  All C(H) groups
 At 1.5 times of:
  All C(H,H,H) groups
2.a Aromatic/amide H refined with riding coordinates:
 C00B(H00B), C00E(H00E), C00H(H00H), C00I(H00I), C00J(H00J), C00K(H00K),
 C00L(H00L), C00M(H00M), C00N(H00N), C00O(H00O), C00P(H00P), C00Q(H00Q)
2.b Idealised Me refined as rotating group:
 C00R(H00A,H00C,H00D), C00S(H00F,H00G,H00R)

Crystallographic data for compound **3ad** (CCDC-1994533) have been deposited with the Cambridge Crystallographic Data Centre, Copies of the data can be obtained, free of charge, on application to CCDC (Email:deposit@ccdc.cam.ac.uk)

Single crystals of $C_{17}H_{21}N_3$ **3ad** were obtained by evaporation of a saturated ethyl acetate solution. A suitable crystal was selected, mounted by acrylic glue on the glass stick, and X-ray intensity data of the compound was collected using SuperNova, Dual, Cu at zero, AtlasS2 diffractometer. The crystal was kept at 293(2) K during data collection. Using Olex2,[1] the structure was solved with the ShelXT[2] structure solution program using Intrinsic Phasing and refined with the ShelXL[3] refinement package using Least Squares minimisation.

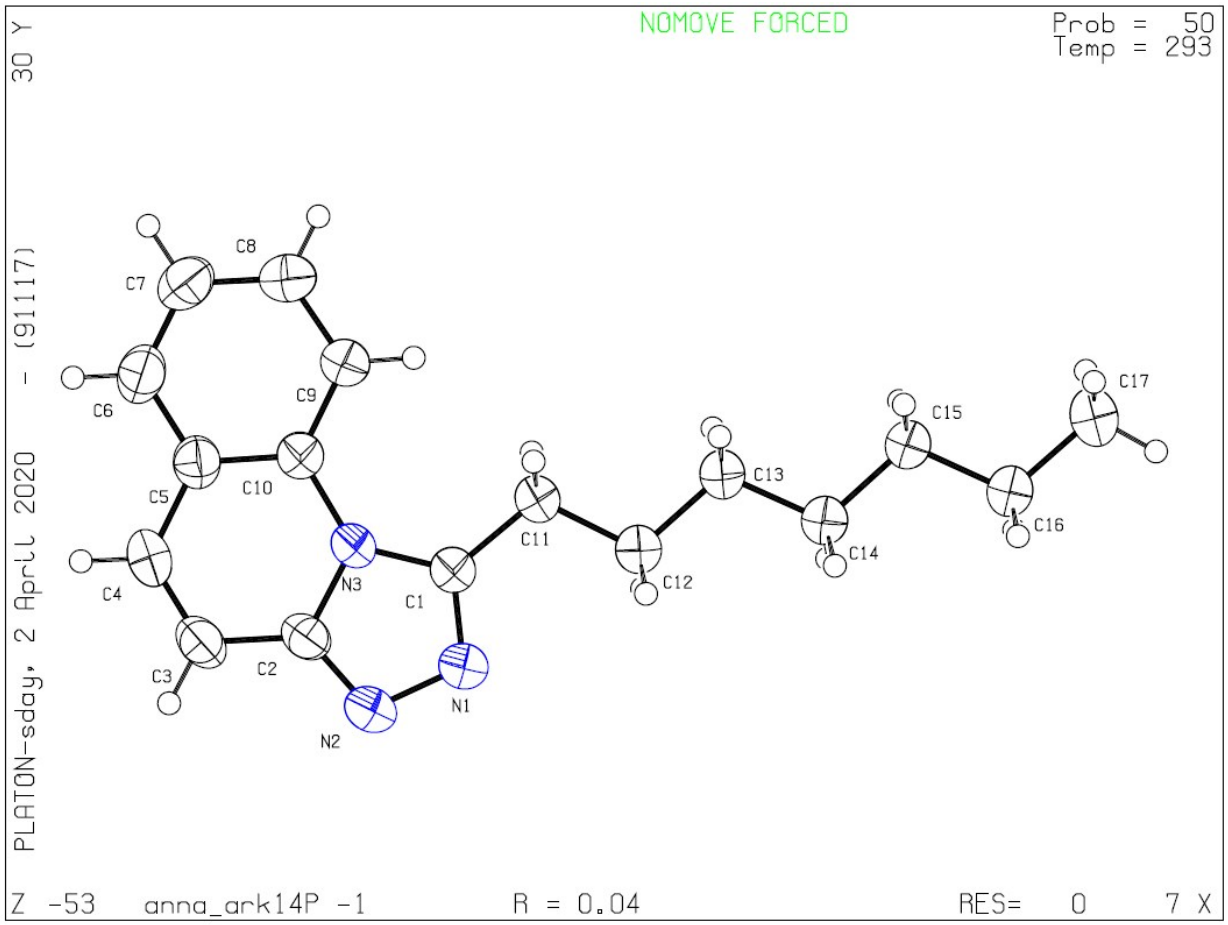


Table 1 Crystal data and structure refinement for **3ad**.

Identification code	ANNA_ARK148_1
Empirical formula	$C_{17}H_{21}N_3$
Formula weight	267.37
Temperature/K	293(2)
Crystal system	triclinic
Space group	P-1
a/Å	6.7441(2)
b/Å	9.9379(3)
c/Å	12.0364(5)

α/°	69.995(3)
β/°	75.972(3)
γ/°	81.277(2)
Volume/Å^3	733.33(5)
Z	2
ρ_{calc}g/cm^3	1.211
μ/mm^{-1}	0.562
F(000)	288.0
Crystal size/mm^3	0.565 × 0.399 × 0.269
Radiation	CuKα (λ = 1.54184)
2Θ range for data collection/°	7.986 to 152.28
Index ranges	-8 ≤ h ≤ 6, -12 ≤ k ≤ 12, -15 ≤ l ≤ 15
Reflections collected	8900
Independent reflections	3031 [R_{int} = 0.0202, R_{sigma} = 0.0164]
Data/restraints/parameters	3031/0/183
Goodness-of-fit on F^2	1.063
Final R indexes [I>=2σ (I)]	R_1 = 0.0402, wR_2 = 0.1132
Final R indexes [all data]	R_1 = 0.0454, wR_2 = 0.1192
Largest diff. peak/hole / e Å^{-3}	0.21/-0.15

Table 2 Fractional Atomic Coordinates (×10^4) and Equivalent Isotropic Displacement Parameters (Å^2×10^3) for **3ad**. U_{eq} is defined as 1/3 of of the trace of the orthogonalised U_{IJ} tensor.

Atom	***x***	***y***	***z***	**U(eq)**
N3	-53.3(12)	6648.2(9)	8475.4(8)	41.8(2)
N1	-5.2(14)	4439.8(10)	8444.7(9)	52.7(3)
N2	-1956.7(14)	4800.9(11)	9013.9(9)	54.8(3)
C10	341.1(15)	8047.8(11)	8368.4(9)	43.3(2)
C1	1108.3(15)	5530.6(11)	8131.9(10)	44.0(2)
C2	-1959.1(15)	6117.0(12)	9021.2(10)	46.5(3)
C5	-1314.4(17)	8899.6(12)	8805.2(10)	49.5(3)
C12	4070.0(16)	4182.5(12)	7135.5(10)	48.5(3)
C11	3296.8(15)	5529.8(12)	7492.9(10)	47.4(3)
C9	2253.6(17)	8599.8(13)	7860.0(11)	54.0(3)
C14	7099.6(16)	2962.2(12)	6022.9(11)	49.1(3)
C4	-3288.3(18)	8325.0(14)	9358.1(12)	58.4(3)
C13	6277.5(16)	4252.9(12)	6444.1(11)	50.2(3)
C15	9299.4(16)	3050.6(11)	5316.8(11)	50.3(3)
C3	-3610.4(17)	6988.2(14)	9473.9(11)	55.3(3)
C16	10137.2(18)	1736.1(13)	4938.7(12)	56.1(3)
C6	-986(2)	10303.2(13)	8704.0(12)	59.2(3)
C7	888(2)	10842.2(13)	8196.0(12)	61.2(3)
C8	2502(2)	9985.4(14)	7777.9(13)	61.6(3)
C17	12342(2)	1790.8(16)	4256.2(15)	74.1(4)

Table 3 Anisotropic Displacement Parameters ($Å^2×10^3$) for **3ad**. The Anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U_{11}+2hka^*b^*U_{12}+\ldots]$.

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
N3	33.8(4)	45.3(5)	45.7(5)	-16.2(4)	-3.1(3)	-5.3(3)
N1	44.0(5)	50.1(5)	64.6(6)	-23.1(4)	-1.4(4)	-10.1(4)
N2	43.1(5)	57.2(6)	63.0(6)	-21.8(5)	0.9(4)	-13.6(4)
C10	41.2(5)	43.8(5)	45.7(5)	-15.7(4)	-7.8(4)	-3.5(4)
C1	38.9(5)	44.5(5)	49.9(5)	-18.8(4)	-5.0(4)	-4.7(4)
C2	36.6(5)	54.1(6)	47.2(5)	-16.0(4)	-2.4(4)	-9.0(4)
C5	48.2(6)	50.4(6)	48.8(6)	-18.6(5)	-6.1(4)	0.1(5)
C12	44.2(6)	46.7(6)	55.0(6)	-21.2(5)	-3.4(4)	-4.2(4)
C11	38.7(5)	47.6(6)	56.0(6)	-21.5(5)	-2.0(4)	-4.3(4)
C9	43.0(6)	50.0(6)	69.5(7)	-23.5(5)	-4.1(5)	-7.1(4)
C14	43.8(6)	45.3(6)	58.9(6)	-21.0(5)	-5.7(5)	-2.7(4)
C4	43.7(6)	64.0(7)	63.9(7)	-28.3(6)	2.9(5)	2.3(5)
C13	42.5(6)	49.0(6)	61.1(7)	-25.3(5)	-3.5(5)	-2.6(4)
C15	45.2(6)	43.5(6)	62.4(7)	-22.3(5)	-4.2(5)	-2.6(4)
C3	38.1(5)	66.9(7)	57.1(6)	-21.7(5)	1.9(4)	-7.1(5)
C16	49.0(6)	48.9(6)	71.6(8)	-28.5(5)	-1.3(5)	-3.1(5)
C6	65.0(7)	50.4(6)	62.4(7)	-25.0(5)	-8.3(6)	4.1(5)
C7	73.6(8)	45.6(6)	66.6(7)	-20.0(5)	-13.6(6)	-7.0(5)
C8	56.2(7)	52.9(7)	76.6(8)	-21.3(6)	-8.3(6)	-13.9(5)
C17	54.0(7)	71.2(9)	96.2(11)	-41.8(8)	7.3(7)	-2.6(6)

Table 4 Bond Lengths for **3ad**.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
N3	C10	1.4124(13)	C5	C6	1.4050(17)
N3	C1	1.3826(13)	C12	C11	1.5242(14)
N3	C2	1.3862(12)	C12	C13	1.5182(14)
N1	N2	1.3850(13)	C9	C8	1.3794(17)
N1	C1	1.3082(14)	C14	C13	1.5174(14)
N2	C2	1.3107(15)	C14	C15	1.5193(14)
C10	C5	1.4046(15)	C4	C3	1.3333(18)
C10	C9	1.3933(15)	C15	C16	1.5137(15)
C1	C11	1.4899(14)	C16	C17	1.5133(16)
C2	C3	1.4223(16)	C6	C7	1.3655(19)
C5	C4	1.4429(16)	C7	C8	1.3819(19)

Table 5 Bond Angles for **3ad**.

Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°

C1	N3	C10	134.21(9)	C10	C5	C6	118.40(11)
C1	N3	C2	103.88(9)	C6	C5	C4	121.41(11)
C2	N3	C10	121.91(9)	C13	C12	C11	111.67(9)
C1	N1	N2	108.67(9)	C1	C11	C12	113.43(9)
C2	N2	N1	106.68(9)	C8	C9	C10	119.72(11)
C5	C10	N3	116.75(9)	C13	C14	C15	113.54(9)
C9	C10	N3	123.43(10)	C3	C4	C5	121.94(11)
C9	C10	C5	119.82(10)	C14	C13	C12	113.87(9)
N3	C1	C11	126.49(9)	C16	C15	C14	113.31(9)
N1	C1	N3	109.87(9)	C4	C3	C2	118.65(10)
N1	C1	C11	123.64(10)	C17	C16	C15	114.09(10)
N3	C2	C3	120.54(10)	C7	C6	C5	121.51(12)
N2	C2	N3	110.90(9)	C6	C7	C8	119.28(11)
N2	C2	C3	128.55(10)	C9	C8	C7	121.27(12)
C10	C5	C4	120.18(11)				

Table 6 Hydrogen Atom Coordinates ($Å \times 10^4$) and Isotropic Displacement Parameters ($Å^2 \times 10^3$) for **3ad**.

Atom	***x***	***y***	***z***	**U(eq)**
H12A	3968.69	3349.53	7857.19	58
H12B	3209.58	4070.53	6638.25	58
H11A	4134.45	5618.05	8012.05	57
H11B	3461.67	6362.34	6771.18	57
H9	3357.88	8036.6	7577.11	65
H14A	6234.04	2872.82	5518.87	59
H14B	7018.99	2102.88	6722.23	59
H4	-4367.63	8904.27	9642.03	70
H13A	6378.5	5112.98	5745.11	60
H13B	7133.68	4333.81	6956.5	60
H15A	9371.3	3889.77	4600.77	60
H15B	10158.16	3175.6	5809.35	60
H3	-4888.87	6632.73	9843.15	66
H16A	10033.1	896.04	5654.78	67
H16B	9290.43	1623.83	4434.27	67
H6	-2069.83	10878.44	8989.4	71
H7	1075.95	11775.76	8132.19	73
H8	3780.37	10350.01	7434.62	74
H17A	12471.63	2634.74	3558.08	111
H17B	12742.55	952.42	4006.25	111
H17C	13209.85	1820.03	4771.48	111

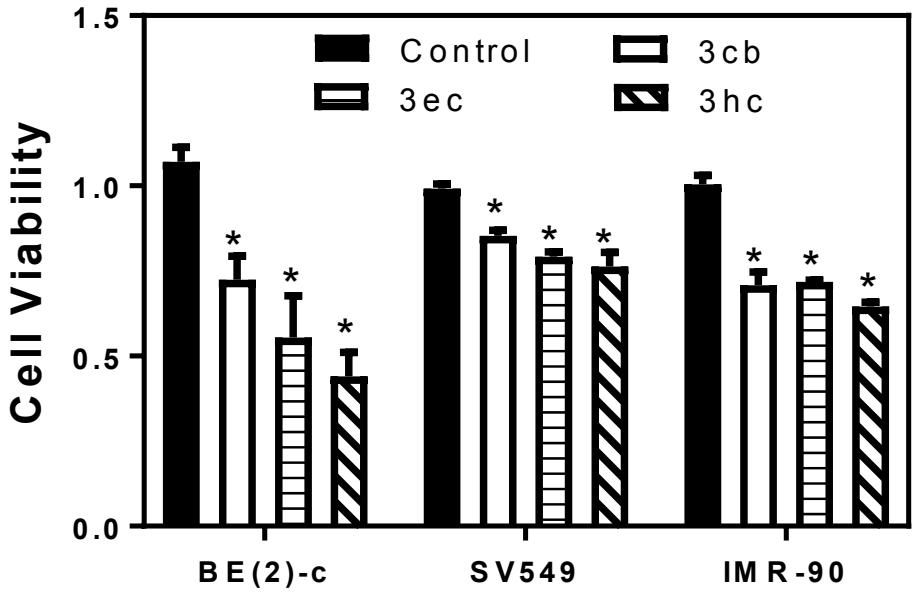
Crystal Data for $C_{17}H_{21}N_3$ (M =267.37 g/mol): triclinic, space group P-1 (no. 2), a = 6.7441(2) Å, b = 9.9379(3) Å, c = 12.0364(5) Å, α = 69.995(3)°, β = 75.972(3)°, γ = 81.277(2)°, V = 733.33(5) Å^3, Z = 2, T = 293(2) K, μ(CuKα) = 0.562 mm^{-1}, $Dcalc$ = 1.211 g/cm^3, 8900 reflections measured (7.986° ≤ 2Θ ≤ 152.28°), 3031 unique (R_{int} = 0.0202, R_{sigma} = 0.0164) which were used in all calculations. The final R_1 was 0.0402 (I > 2σ(I)) and wR_2 was 0.1192 (all data).

Refinement model description

Number of restraints - 0, number of constraints - unknown.
Details:
1. Fixed Uiso
At 1.2 times of:
All C(H) groups, All C(H,H) groups
At 1.5 times of:
All C(H,H,H) groups
2.a Secondary CH2 refined with riding coordinates:
C12(H12A,H12B), C11(H11A,H11B), C14(H14A,H14B), C13(H13A,H13B), C15(H15A, H15B), C16(H16A,H16B)
2.b Aromatic/amide H refined with riding coordinates:
C9(H9), C4(H4), C3(H3), C6(H6), C7(H7), C8(H8)
2.c Idealised Me refined as rotating group:
C17(H17A,H17B,H17C)

3. Cytotoxicity against normal cells

Cell viability was measured by MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide) assay. Briefly, neuroblastoma cell line BE(2)-C were maintained in DMEM/F12 media supplemented with 10% FBS under standard cell culture conditions. 2,500 cells per well were plated into 96-wells plate, and cells were treated with compounds **3ec**, **3cb** and **3hc** at 25 μM in triplicates for four days. By the end of four-day treatment MTT reagent (15 μL at 2.5 mg/mL in 1X PBS) was added into each well and incubated with cells for 1 hour at 37 °C. DMSO was then used to dissolve the crystal formed in each 96 well. Optical density values at wavelength 570 nm and 630 nm were measured using SpectraMax 190 (Molecular Devices, San Jose, CA), and the difference in the two optical density values was used to analyze the relative cell survival in each 96 well. To evaluate the cytotoxicity these compounds in normal cell lines, one normal human skin fibroblast (SV549) and one normal human fetal lung fibroblast (IMR-90) were used. 1,500 fibroblast cells were treated with 25 μM compounds in triplicates for four days. MTT assay was then used to measure the cell viability.



BE(2)-C, SV549 and IMR-90 cells were treated with **3cb**, **3ec** and **3hc** at the concentration of 25 μM in triplicates for four days. Then MTT assay was used to measure the cell viability. *, $p < 0.05$, compared to its corresponding control.

References

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2 G. M. Sheldrick, *Acta Crystallogr. Sect. A*, 2015, **71**, 3–8.
3 G. M. Sheldrick, *Acta Crystallogr. Sect. C*, 2015, **71**, 3–8.