

# **The synthesis and antitumor activity of novel 1-alkyl-3-phenyl- and 3-alkyl-1-phenylimidazothiazolotriazines**

**Alexei N. Izmet'sev<sup>1\*</sup>, Sergey S. Isakov<sup>1,2</sup>, Angelina N. Kravchenko<sup>1</sup>, Galina A. Gazieva<sup>1</sup>**

<sup>1</sup> *N. D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences,  
47 Leninsky Ave., Moscow 119991, Russia; e-mail: nebeli@mail.ru*

<sup>2</sup> *D. Mendeleev University of Chemical Technology of Russia,  
9 Miusskaya Sq., Moscow 125047, Russia*

## **Supplementary Information**

---

## Table of Contents

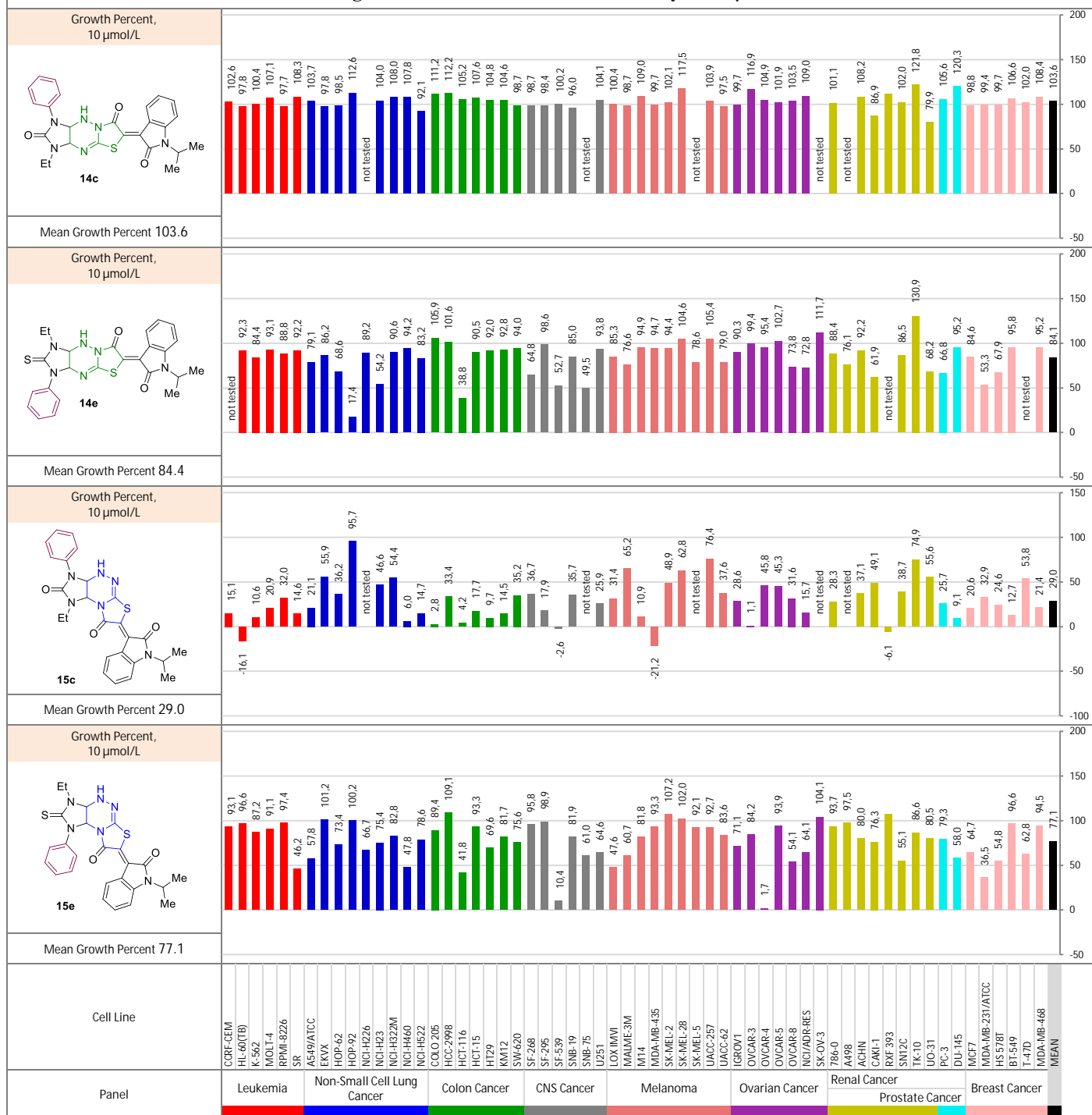
1. NCI-60 Screening Methodology .....	S2
2. Anticancer Screening Data of 60 Cancer Cell Lines of 14c,e and 15c,e.....	S3
3. Anticancer Screening Data of 60 Cancer Cell Lines of Taxol, Doxorubicin, Daunorubicin and Camptothecin .....	S4
4. Five Dose Testing of compound 15c.....	S5
5. Spectra $^1\text{H}$ and $^{13}\text{C}$ NMR of compounds <b>4a,b</b> and $\{^1\text{H}-^1\text{H}\}$ NOESY NMR of <b>4a</b> .....	S8
6. Spectra $^1\text{H}$ and $^{13}\text{C}$ NMR of compounds <b>6a,b</b> .....	S13
7. Spectra $^1\text{H}$ NMR of compounds <b>7a,b</b> and <b>8b</b> .....	S17
8. Spectra $^1\text{H}$ and $^{13}\text{C}$ NMR of compounds <b>9a,b</b> and <b>10b</b> .....	S20
9. Spectra $^1\text{H}$ and $^{13}\text{C}$ NMR of compounds <b>11b</b> and <b>12b</b> .....	S26
10. Spectra $^1\text{H}$ and $^{13}\text{C}$ NMR of compounds <b>14a-e</b> .....	S30
11. Spectra $^1\text{H}$ and $^{13}\text{C}$ NMR of compounds <b>15a-e</b> .....	S40

## **Antiproliferative activity assay against 60 cancer cell lines at the National Cancer Institute**

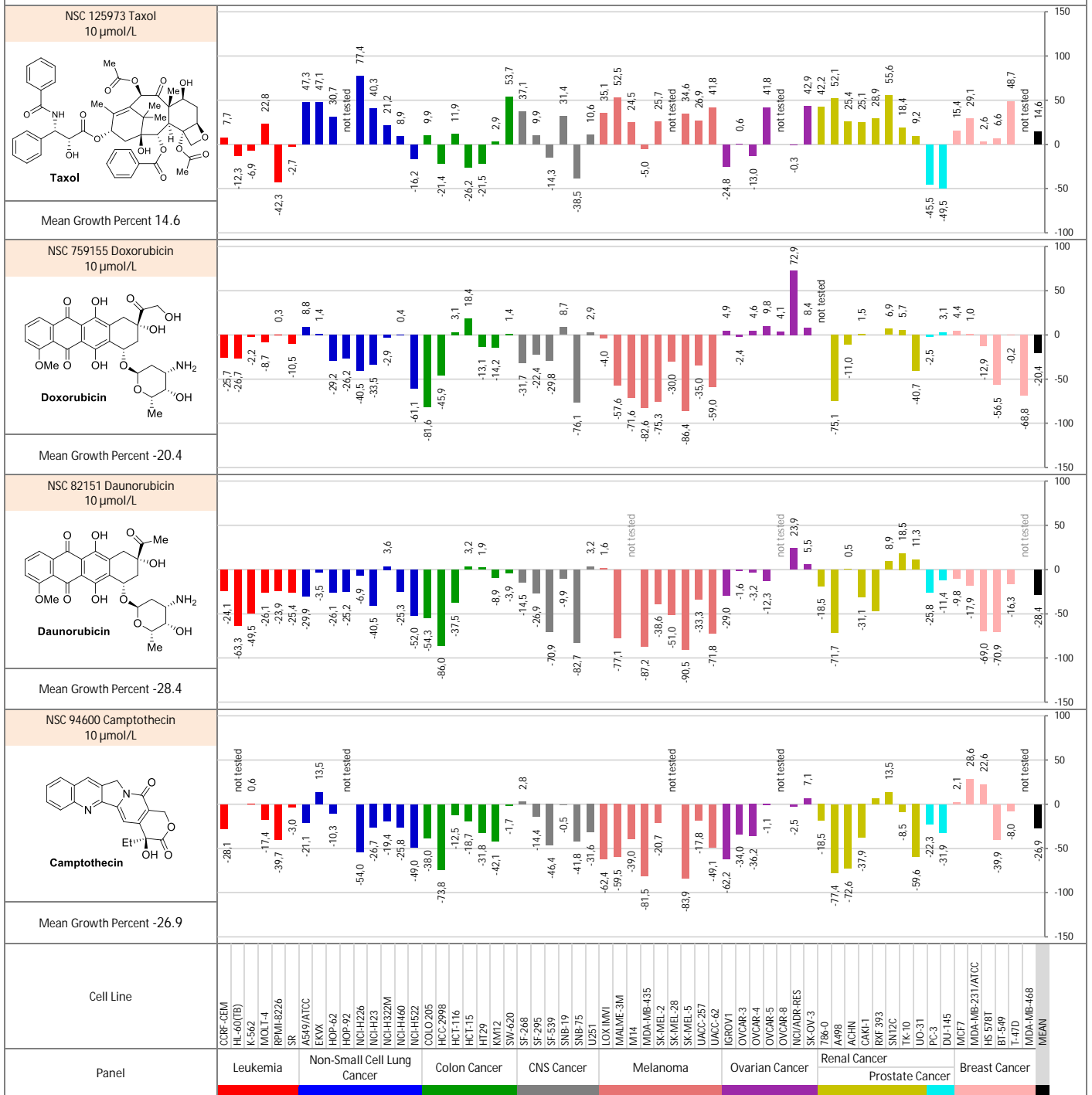
Primary antiproliferative activity assay was performed on a panel of sixty human tumor cell lines derived from nine neoplastic diseases in accordance with the protocol of the Drug Evaluation Branch, National Cancer Institute, USA (<https://portal.gdc.cancer.gov>). The tested compounds were added to the culture at a single concentration ( $10^{-5}$  M) and the cultures were incubated for 48 h. Endpoint determinations were made with a protein binding dye, sulforhodamine B (SRB). Results for each tested compound were reported as the percent growth of the treated cells when compared to the untreated control cells. The percent growth was evaluated spectrophotometrically versus controls not treated with the test agents.

The cytotoxic and/or growth inhibitory effects of the most active selected compounds were tested in vitro against the full panel of about 60 human tumor cell lines at 10-fold dilutions of five concentrations ranging from  $10^{-4}$  to  $10^{-8}$  M. The 48-h continuous drug exposure protocol was followed and an SRB protein assay was used to estimate cell viability or growth.

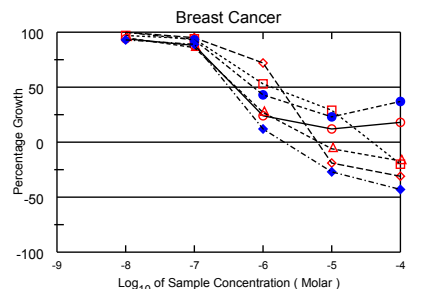
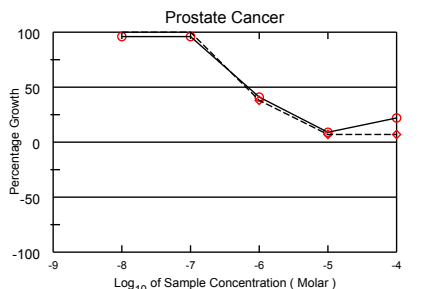
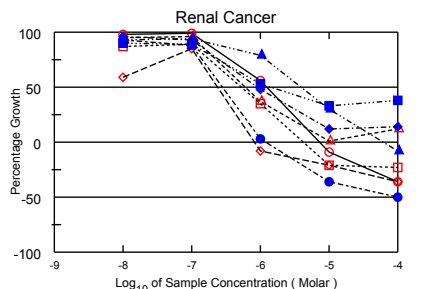
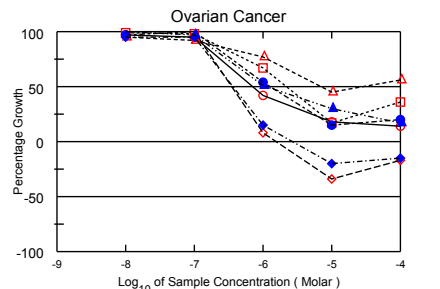
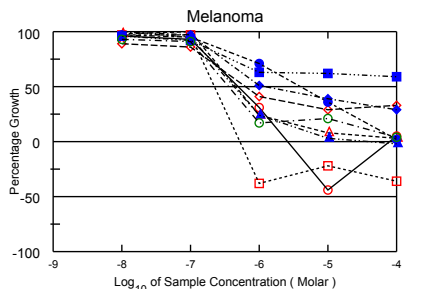
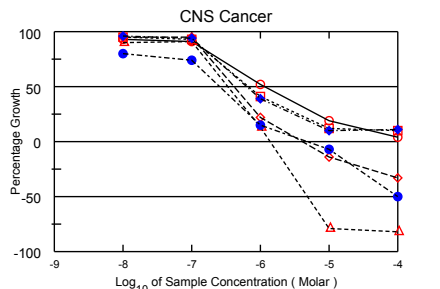
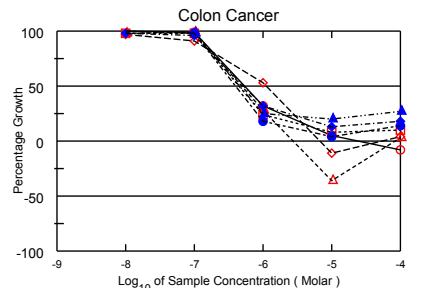
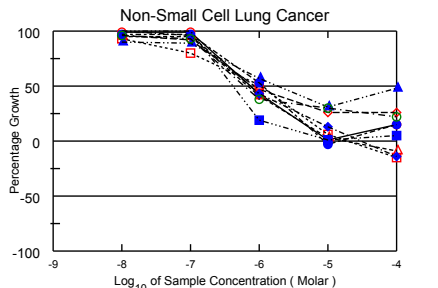
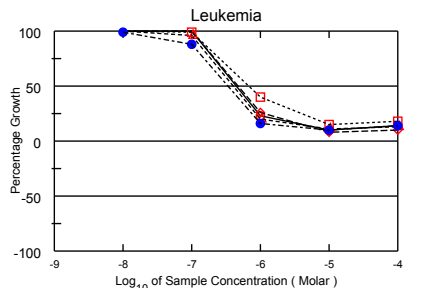
## Anticancer Screening Data of 60 Cancer Cell Lines Assay at 10 μmol/L Concentration



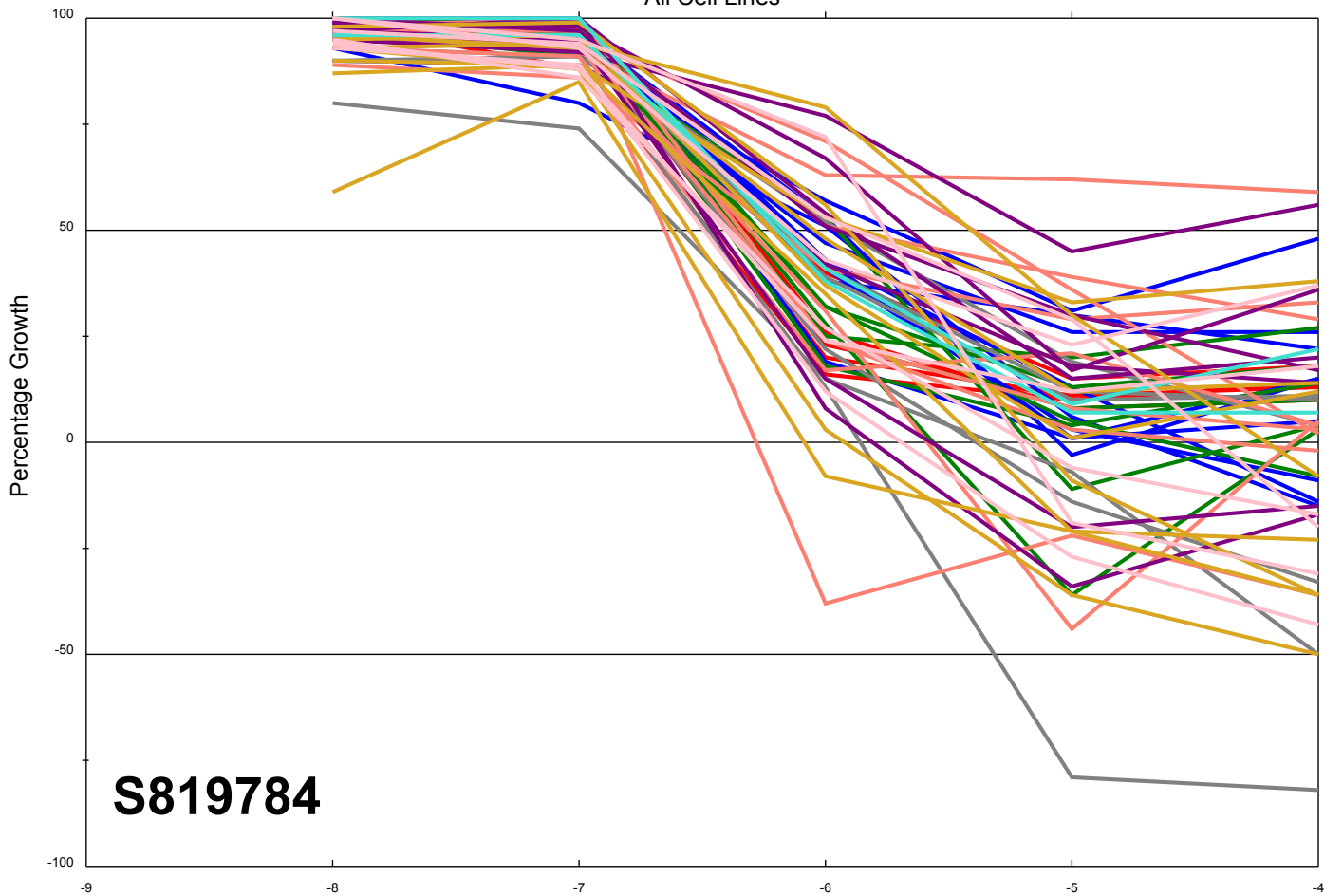
## Anticancer Screening Data of 60 Cancer Cell Lines Assay at 10 µmol/L Concentration







All Cell Lines

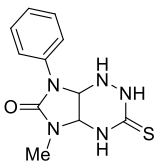


**S819784**

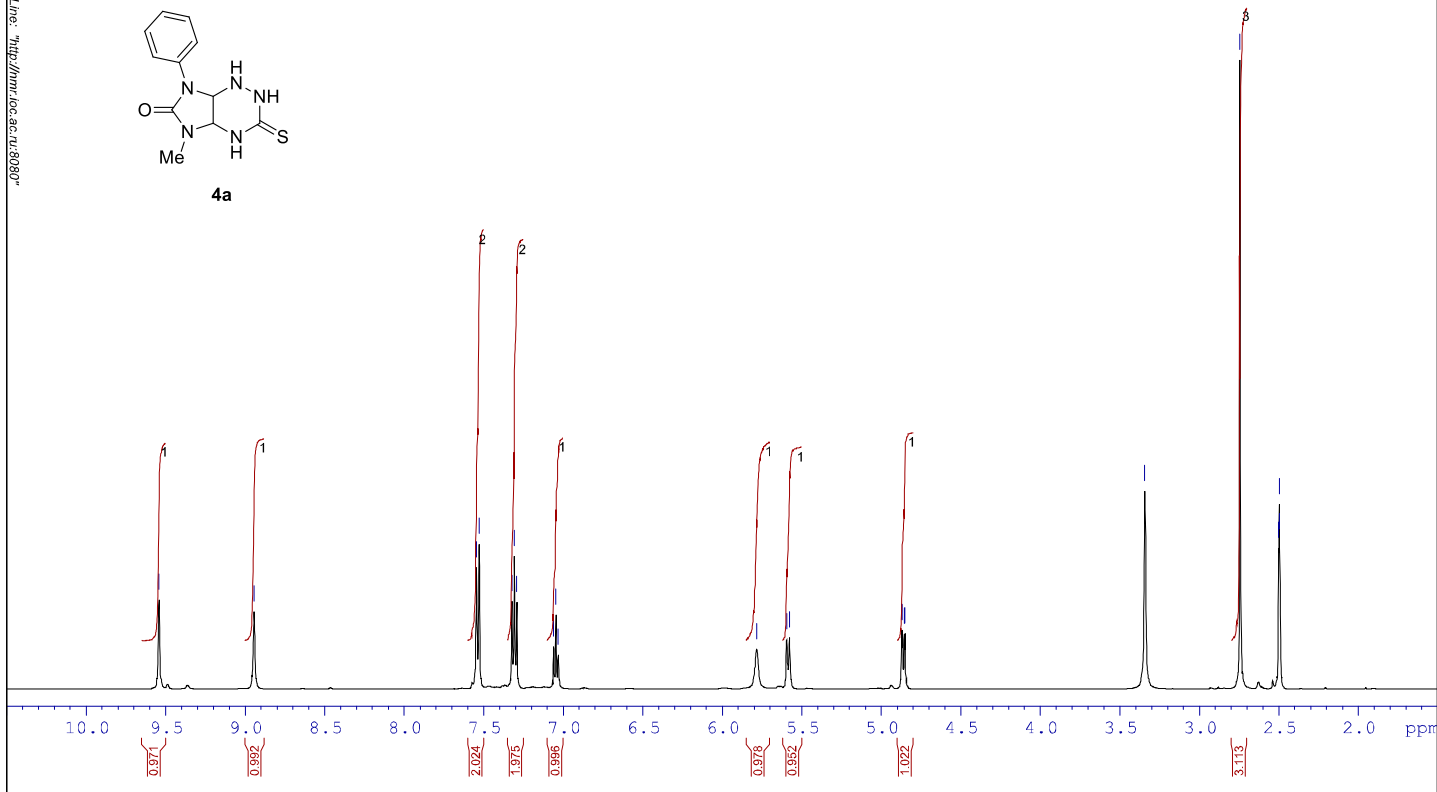
$\log_{10}$  of Sample Concentration (Molar)



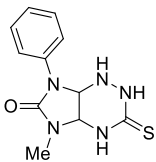
/KANI IA326



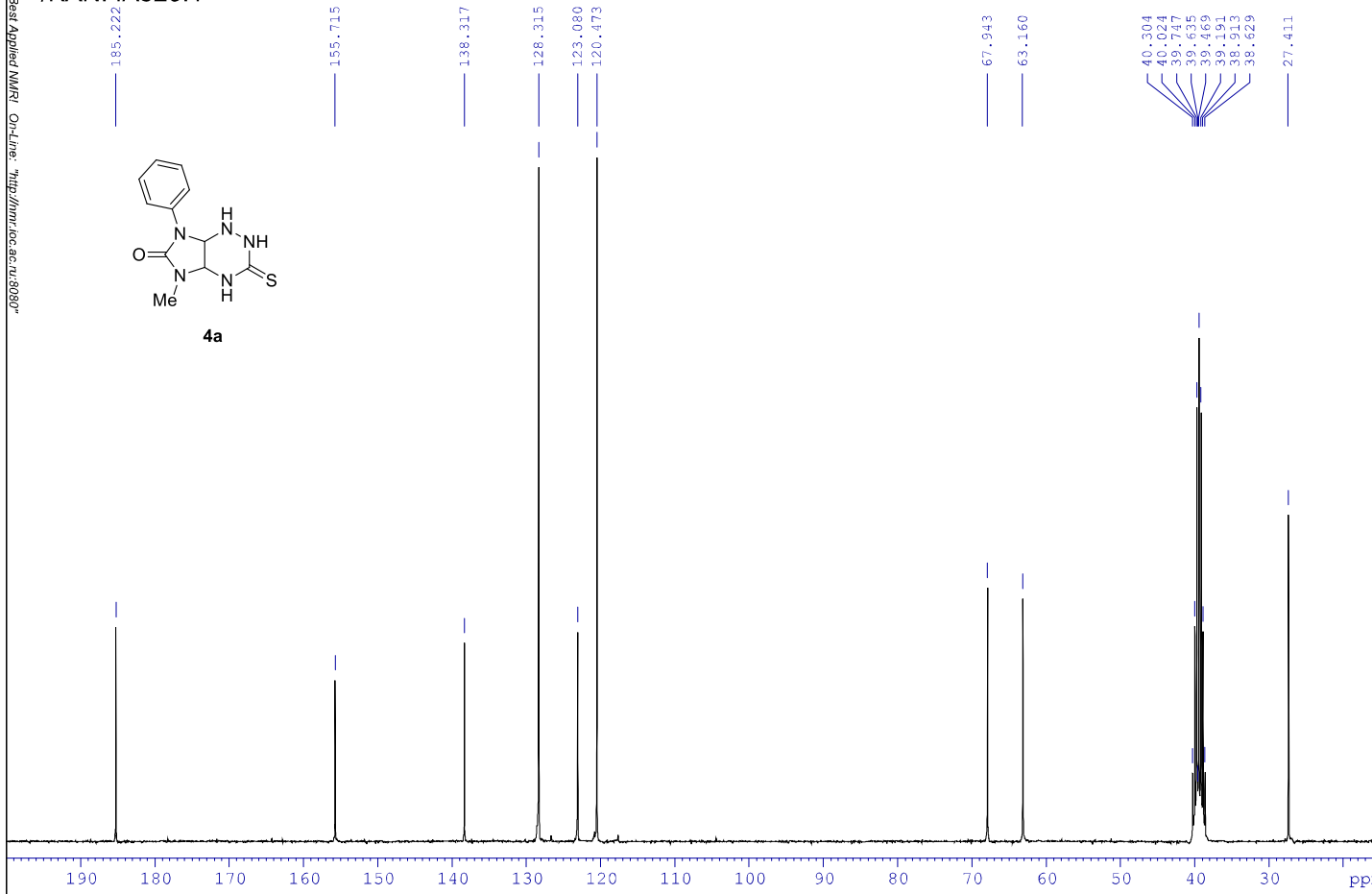
4a



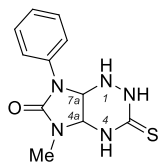
/KANI IA326.1



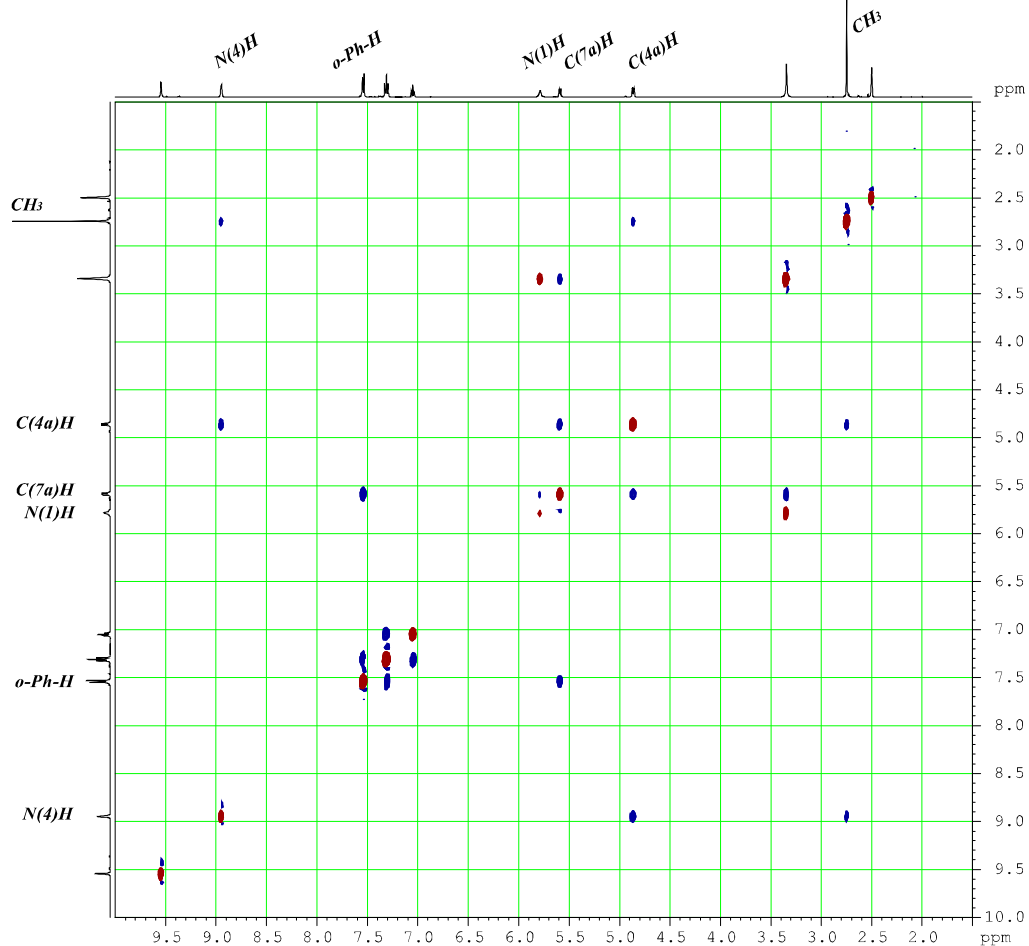
4a



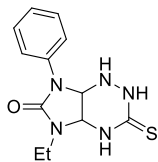
/KANI IA326  
NOESY



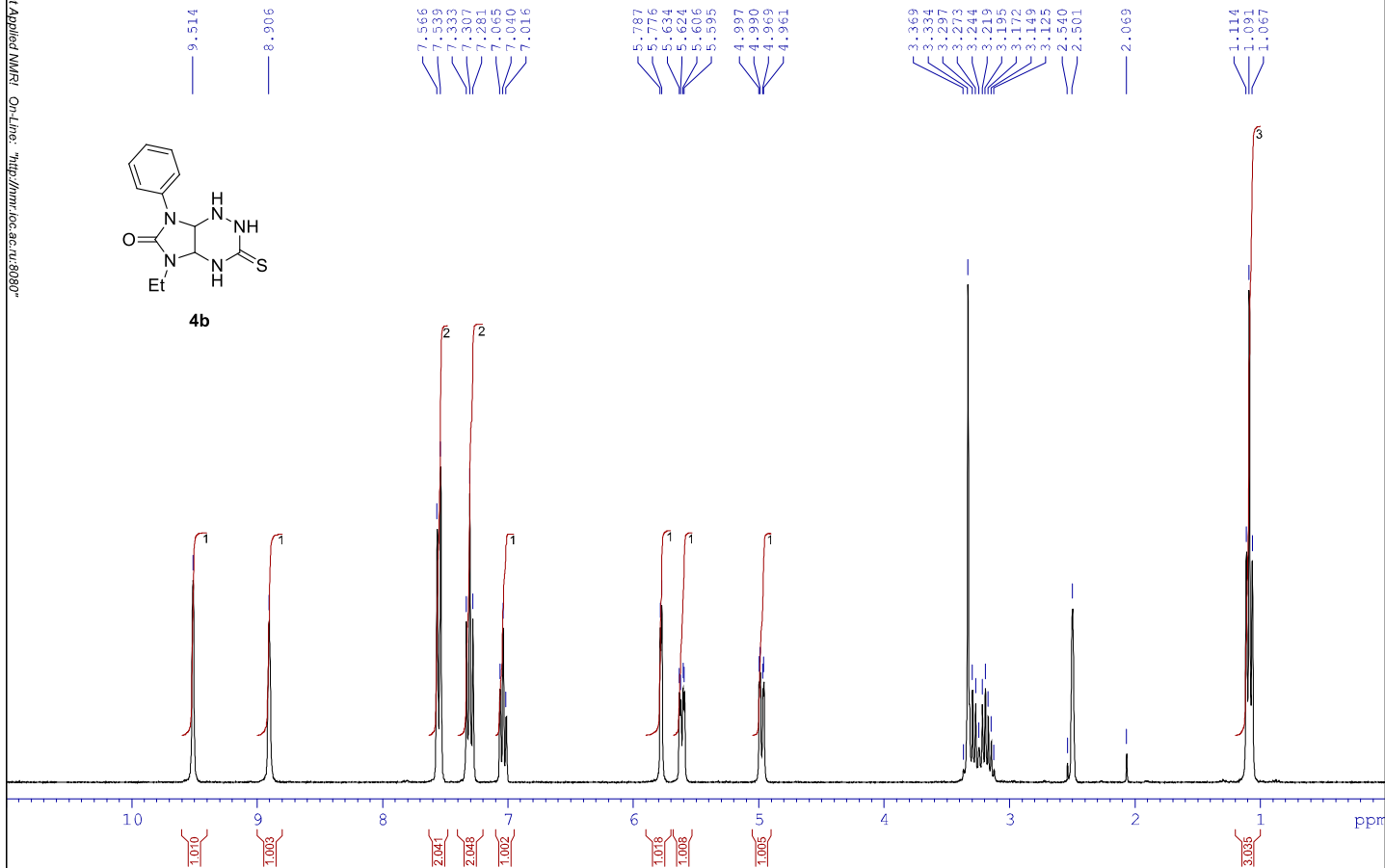
4a



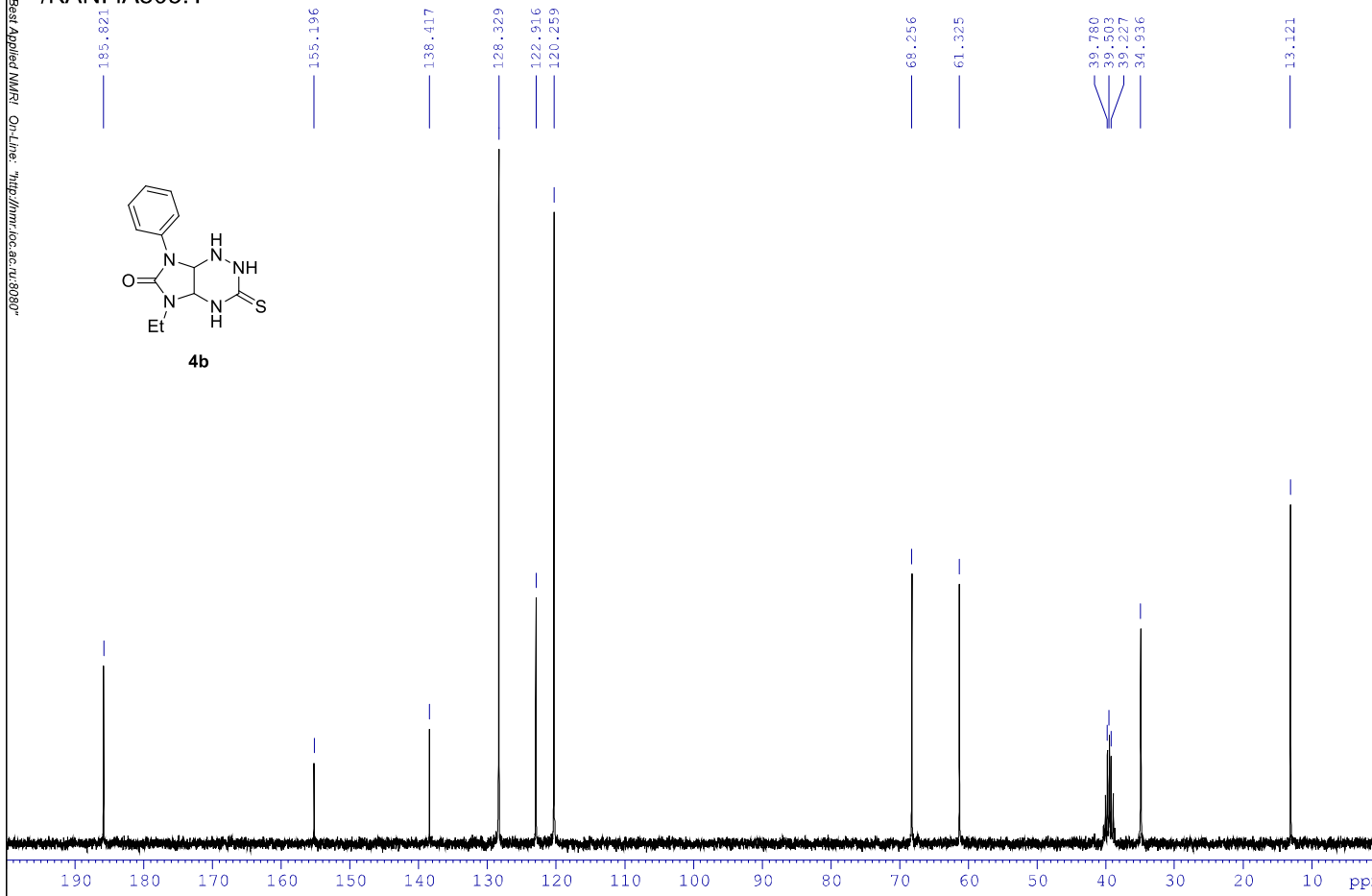
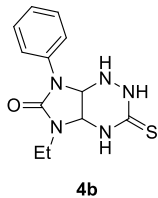
/KANI IA503.1



4b

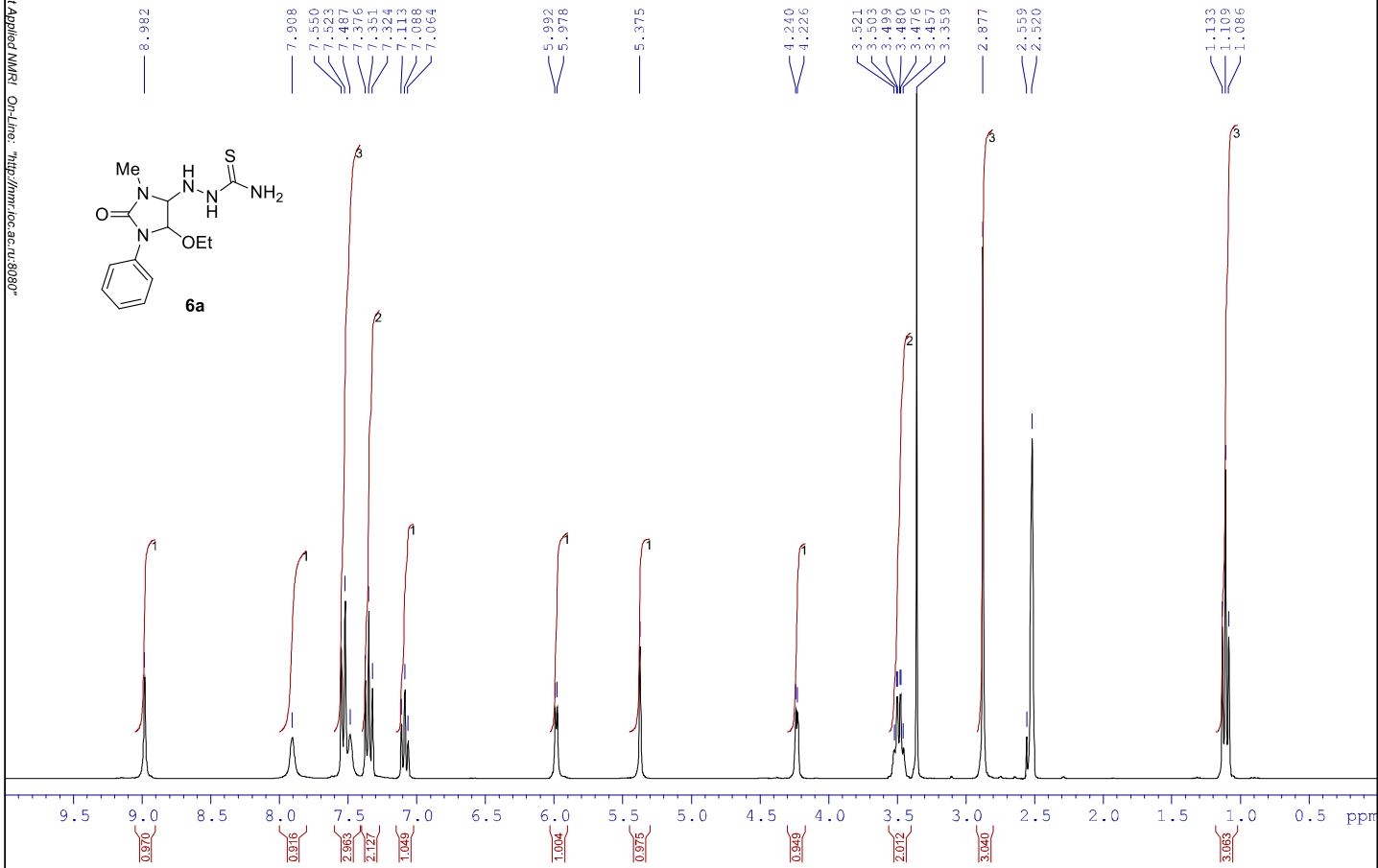
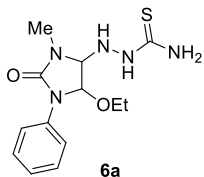


/KANI IA503.1

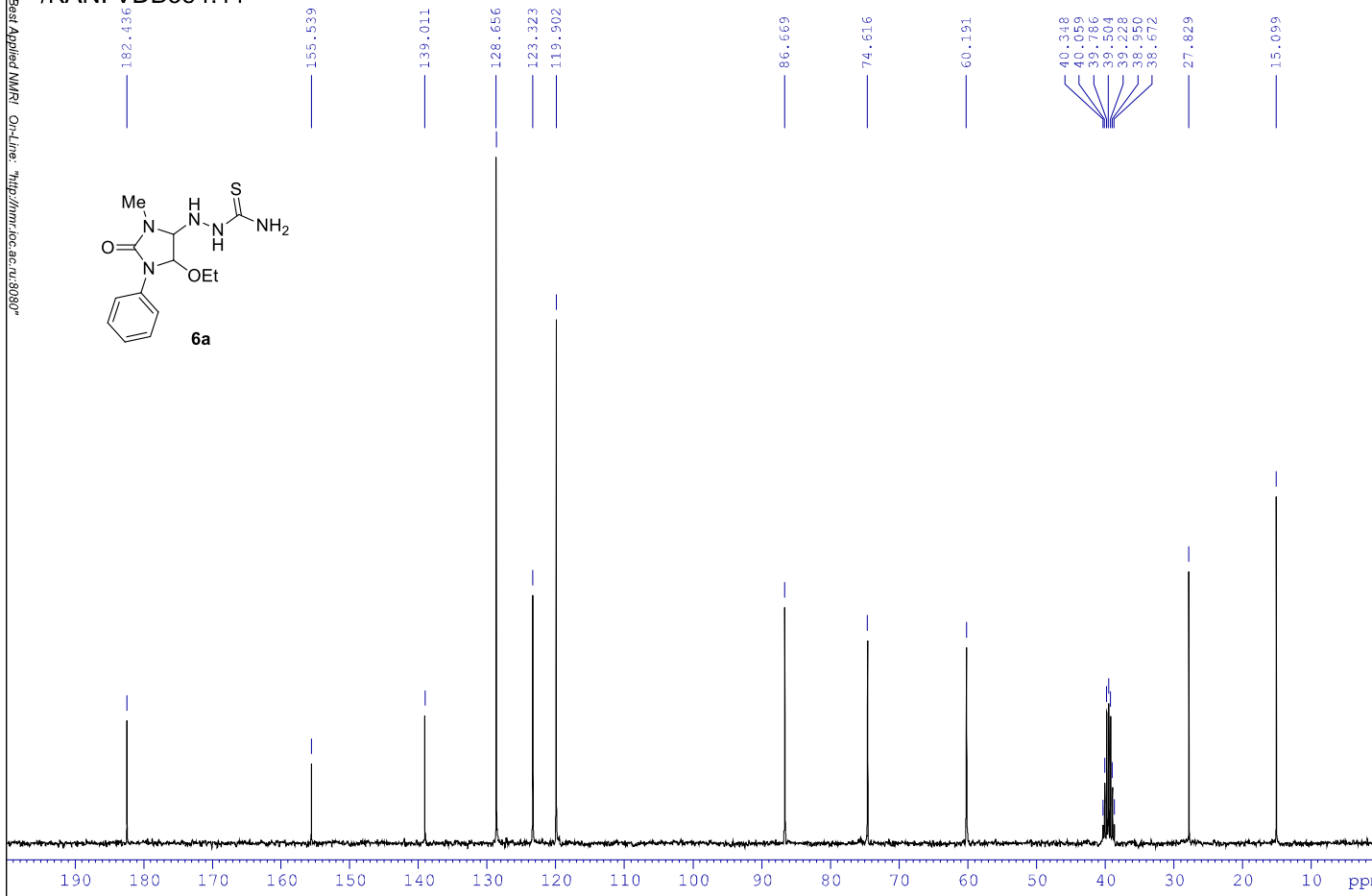
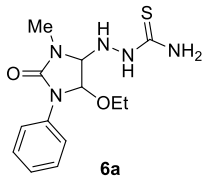


# /KANI VDB354.11

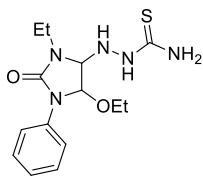
The Best Applied MMR - On-Line: "http://mr.ice.ac.ru:8080"



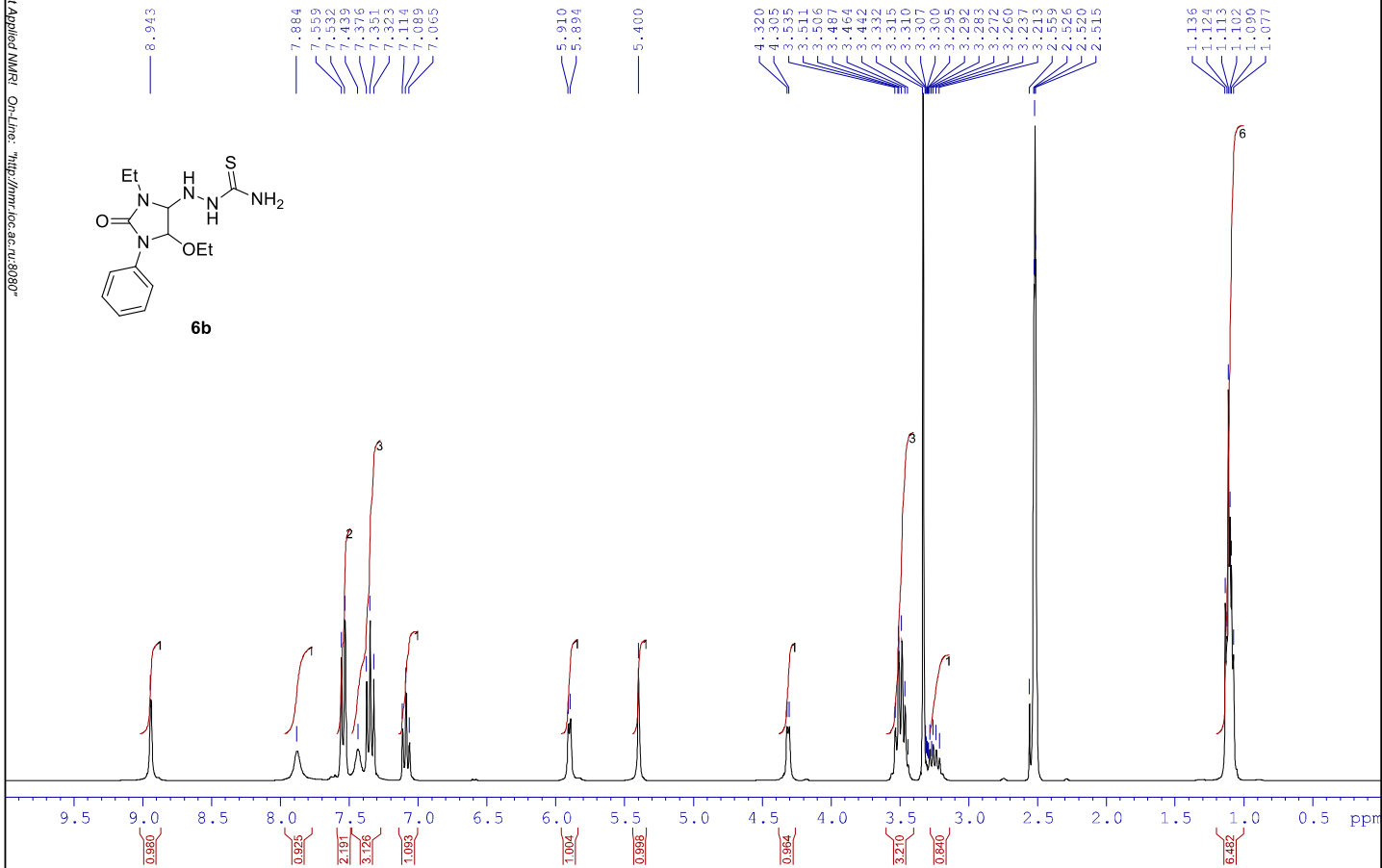
/KANI VDB354.11



/KANI RES175.22

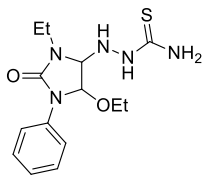


6b

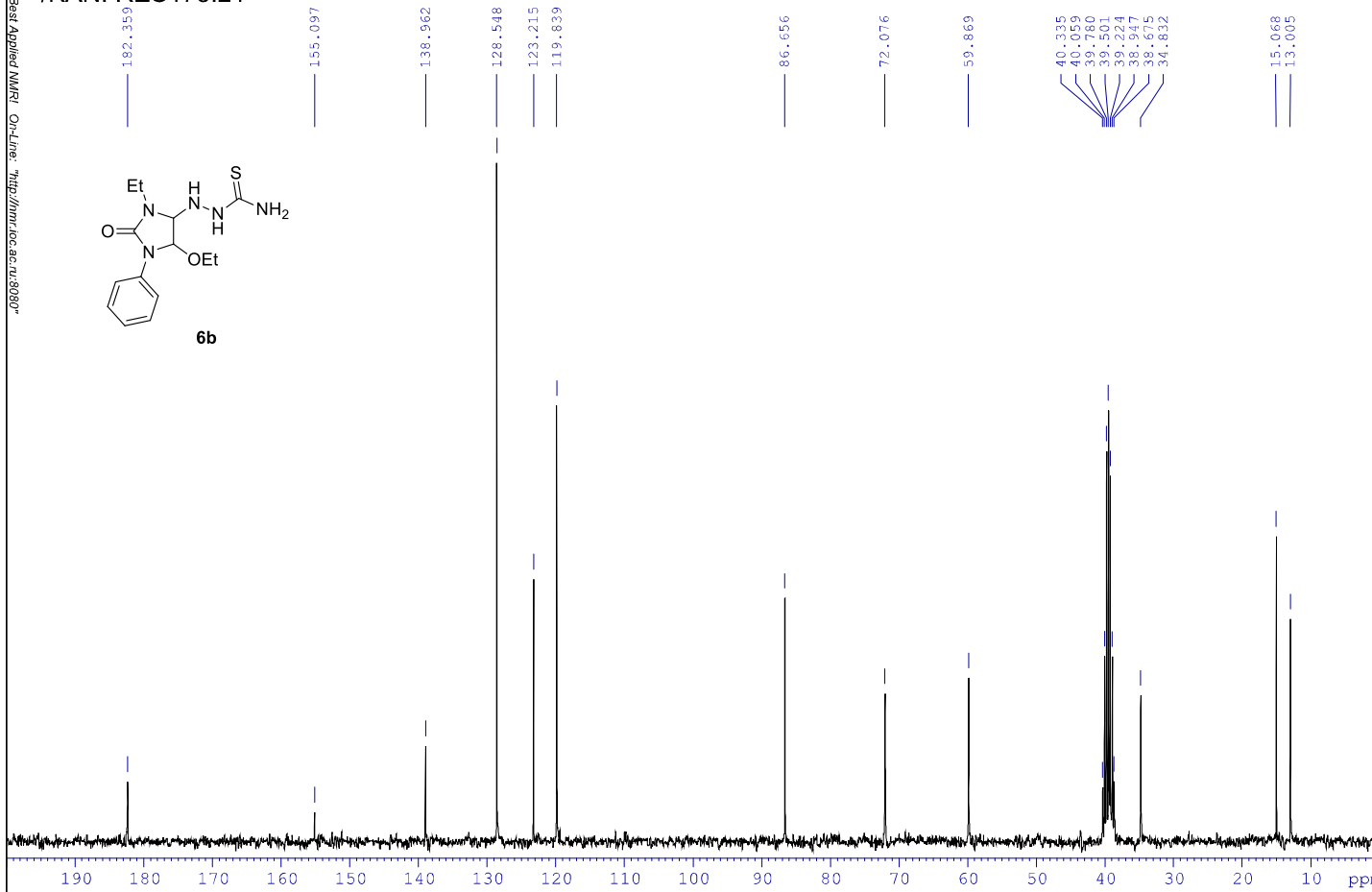




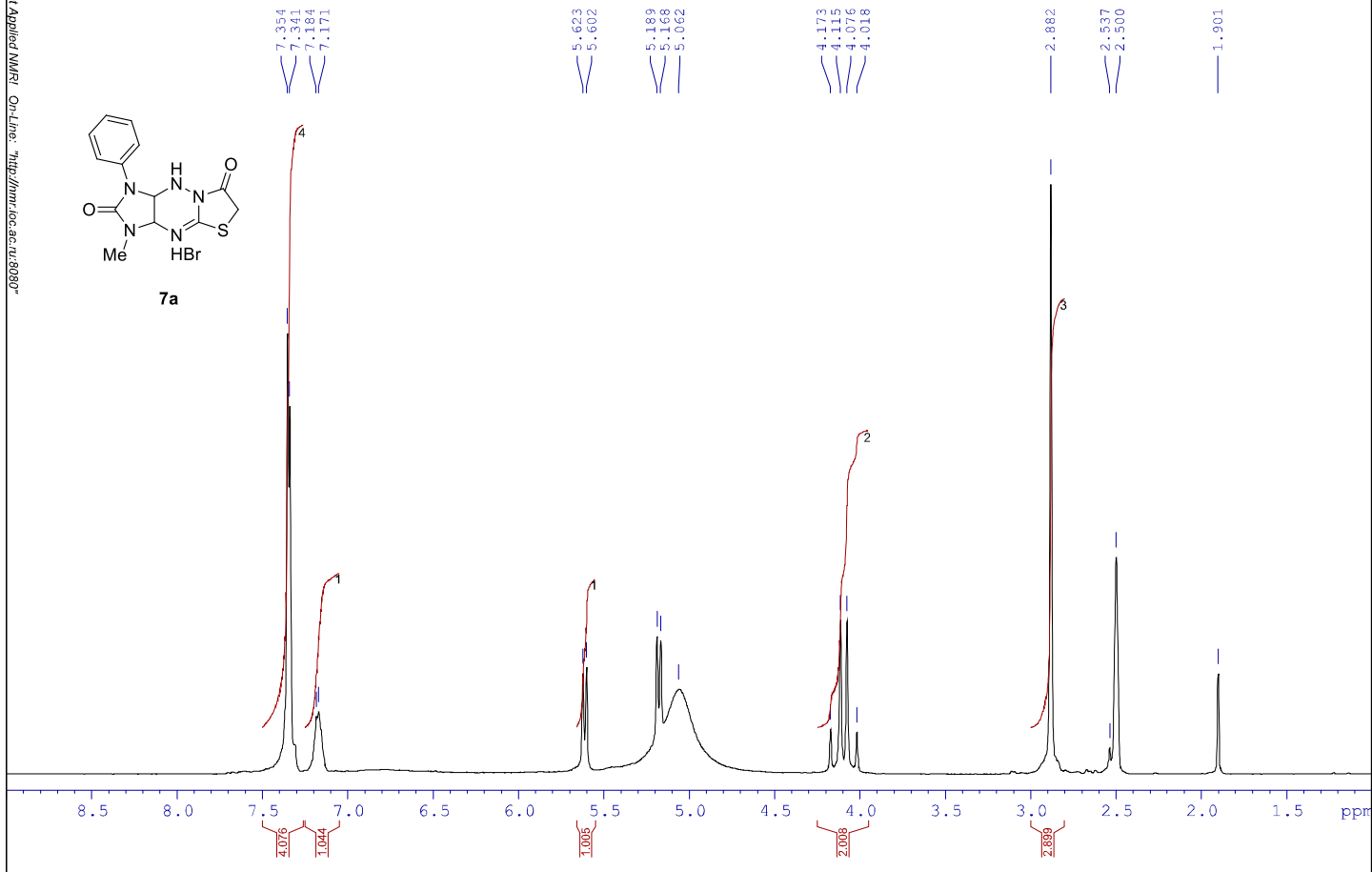
/KANI RES175.21



6b

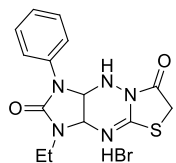


/KANI MM47.1

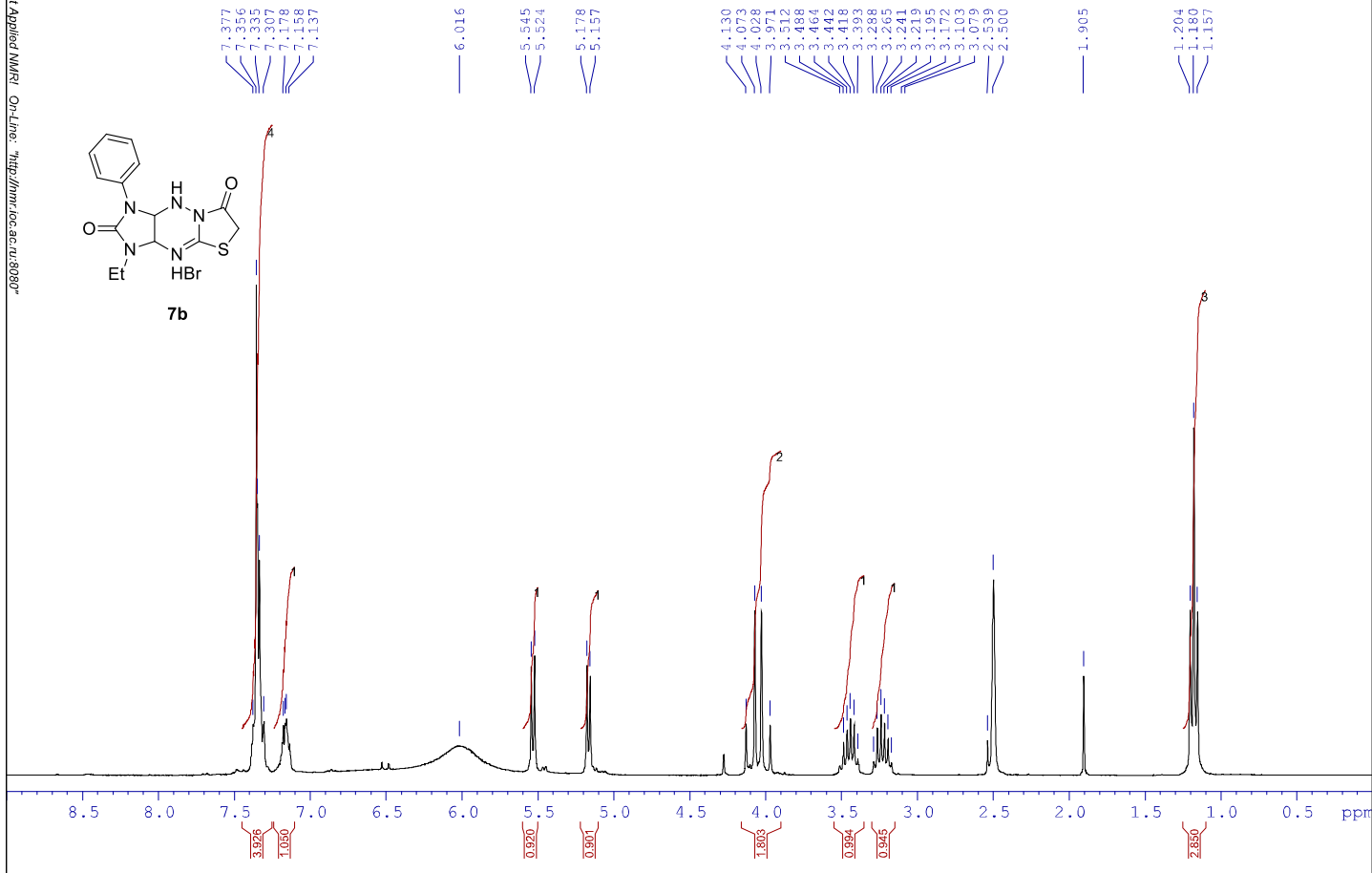


# /KANI IA912.1

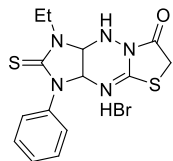
The Best Applied MMR1 On-Line: <http://mr1.ico.ac.ru:3080/>



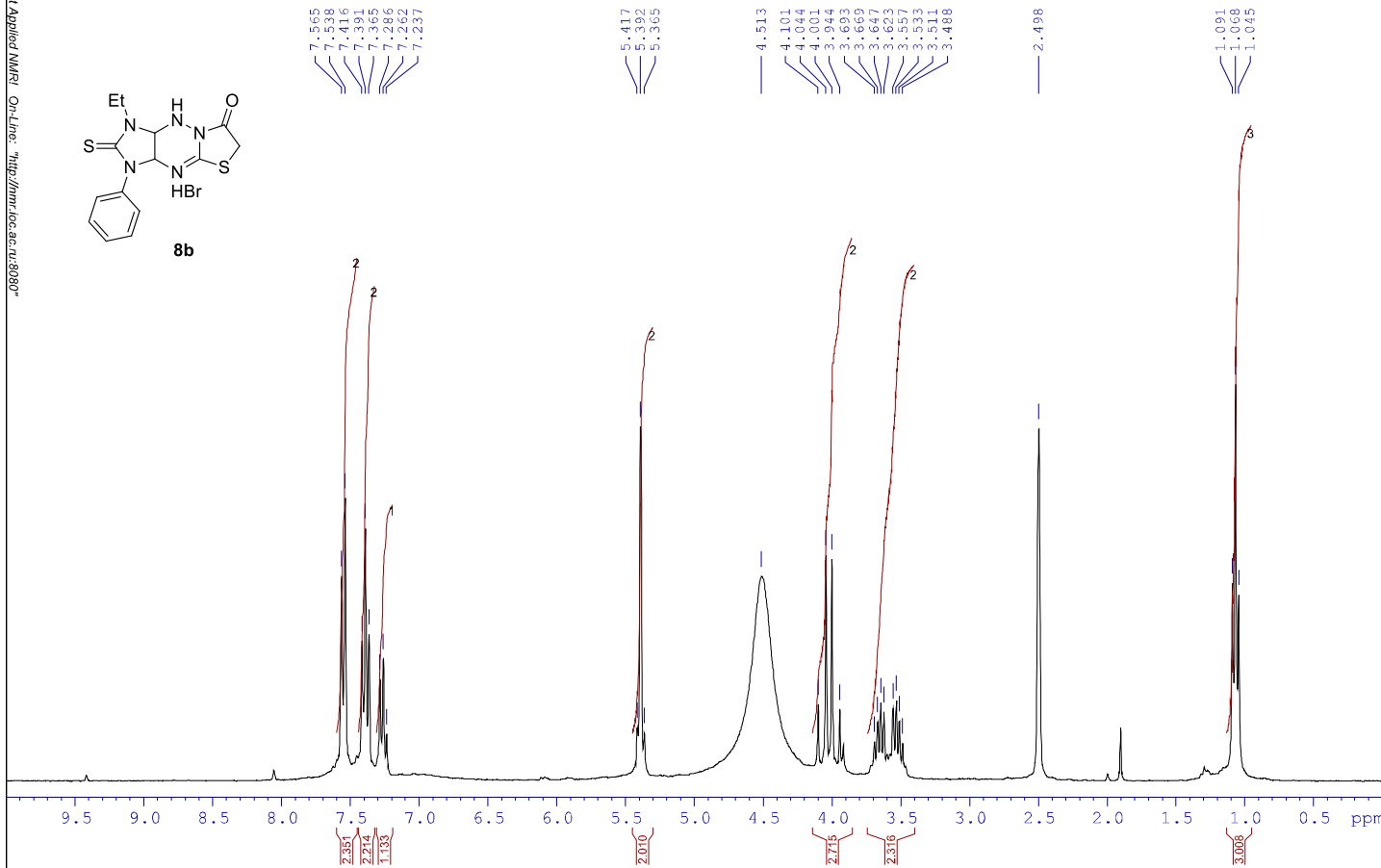
7b



/KANI MM90.2/

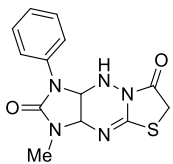


8b

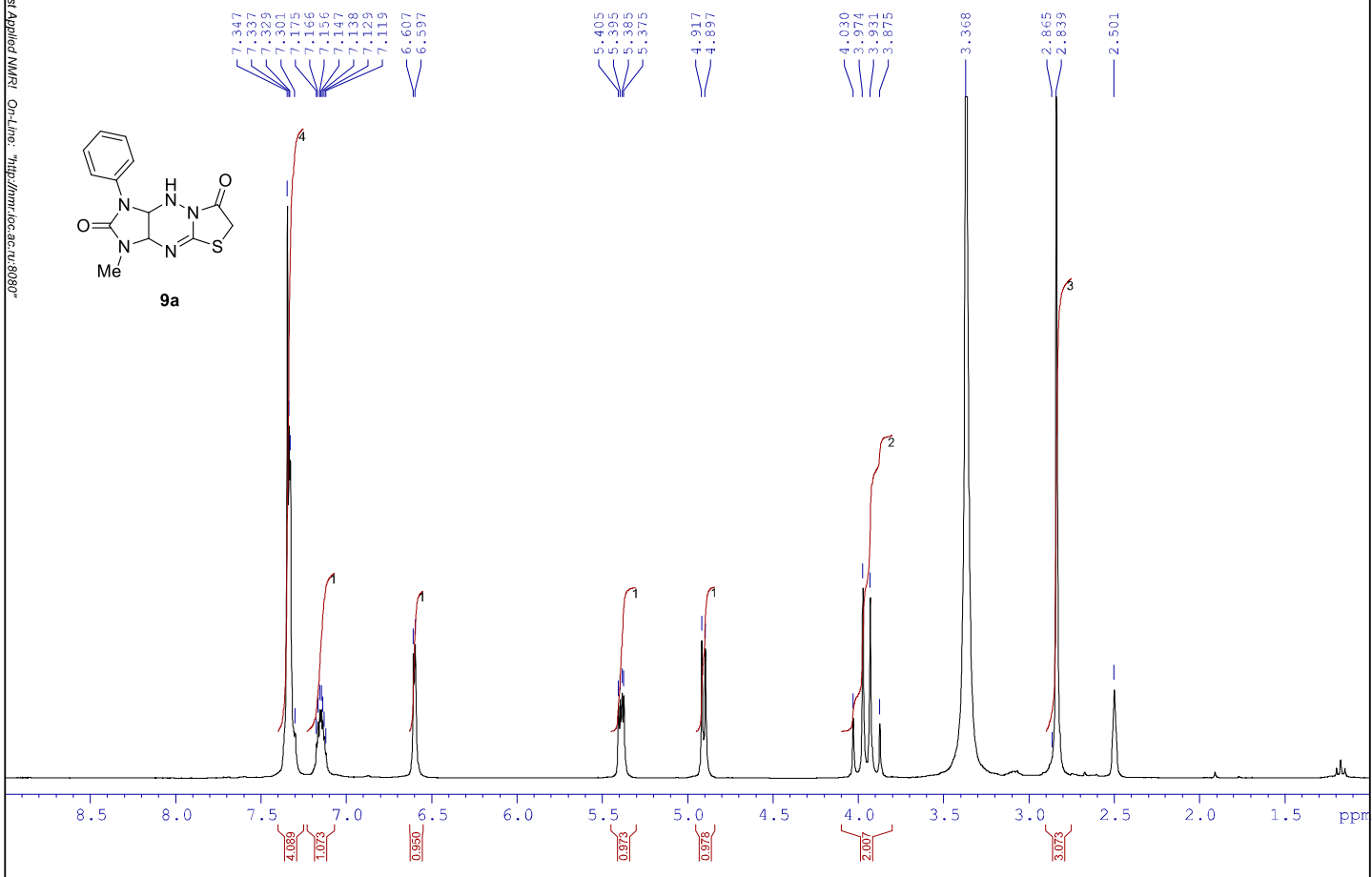


# /KANI MM131.1

The Best Applied MMR - On-Line: "http://mr.loc.ac.ru/8080"

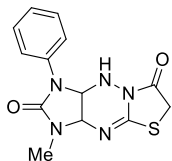


9a

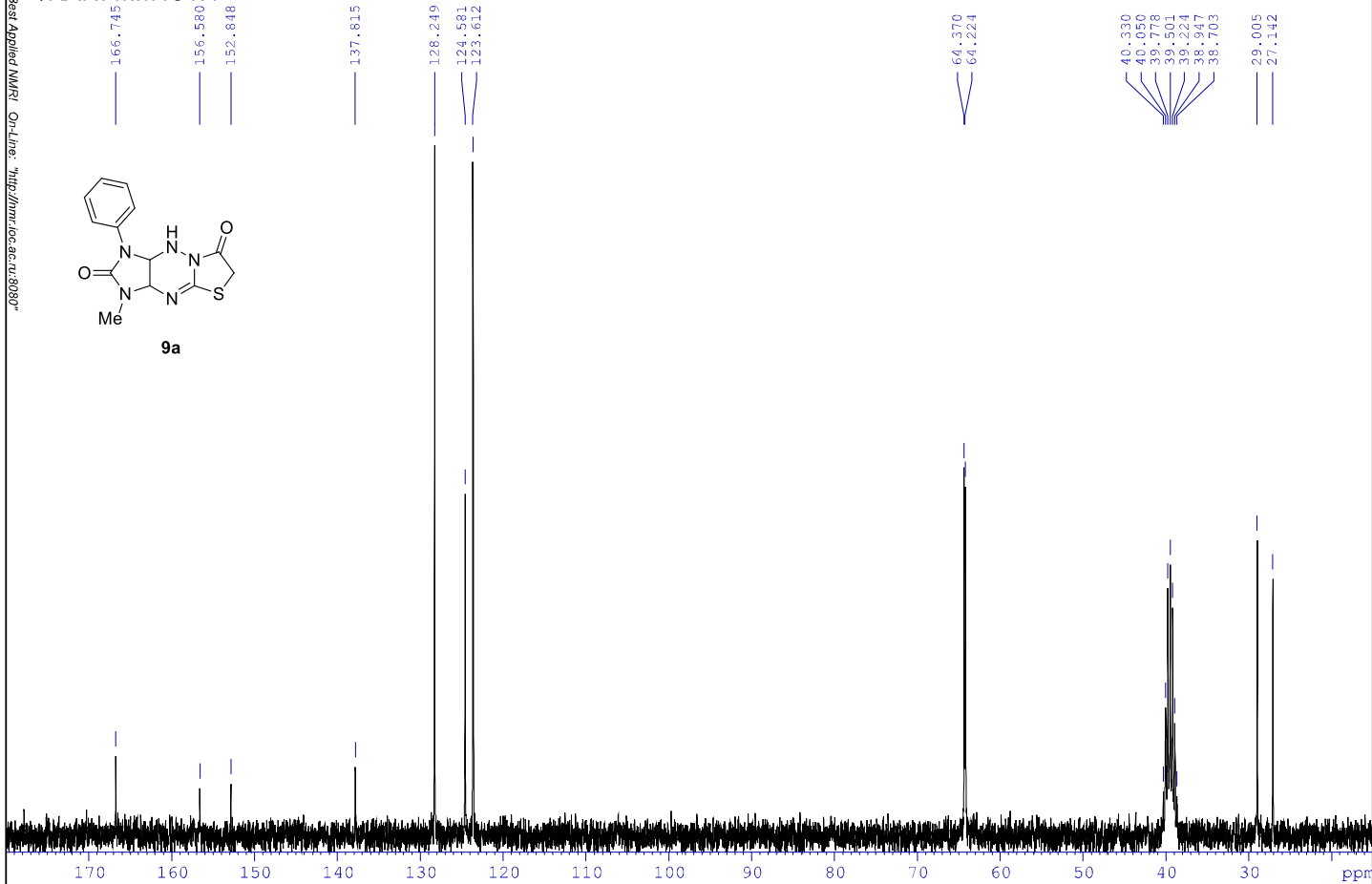


/KANI MM131.1

The Best Applied MMR - On-Line: "http://mr.loc.ac.ru/8080"

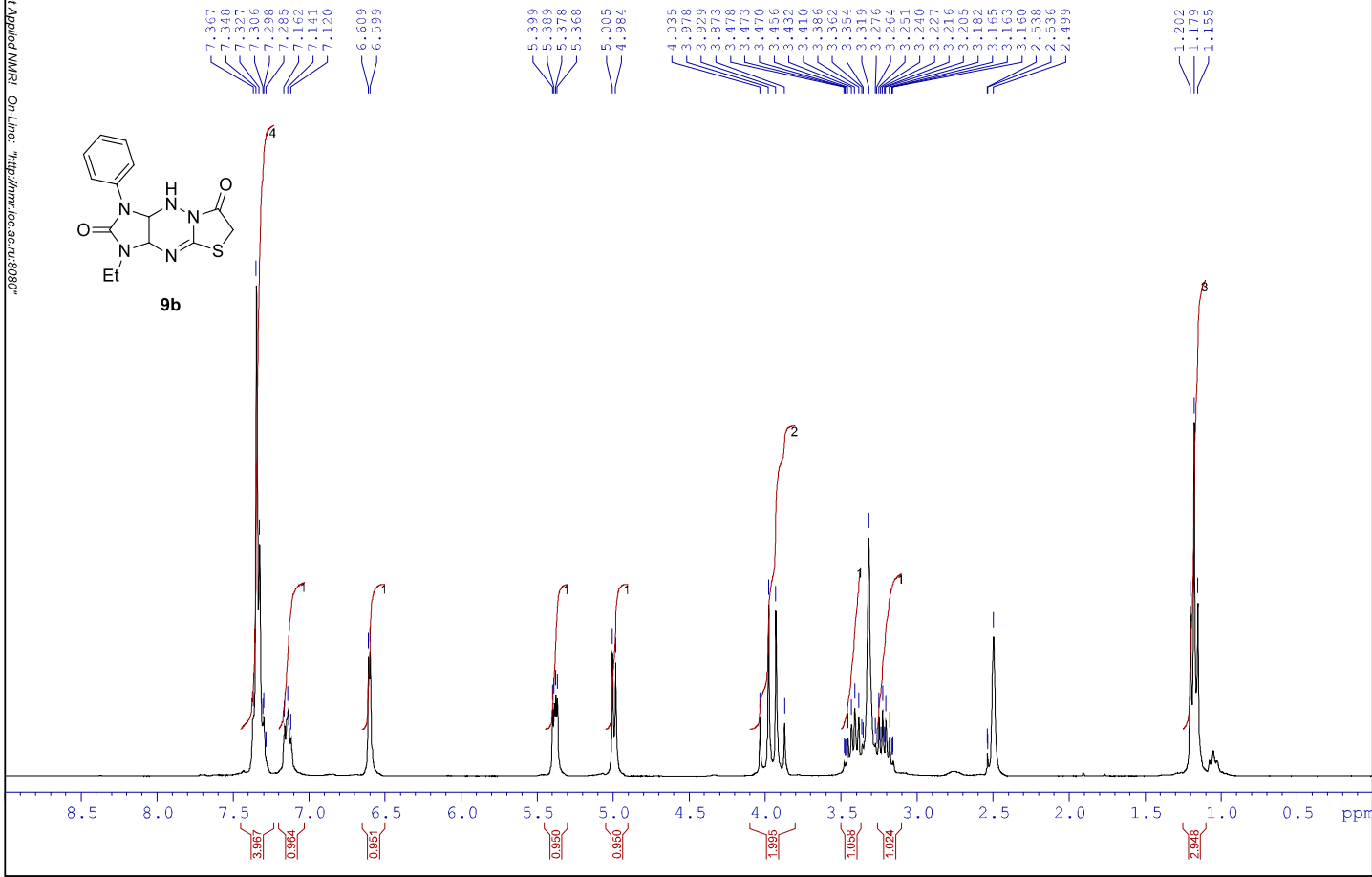
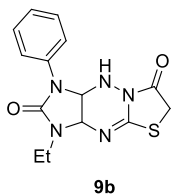


9a



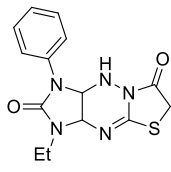
/KANI IA916.1

The Best Applied MMR - On-Line: <http://mr.ia.oi.ac.ru:8080/>

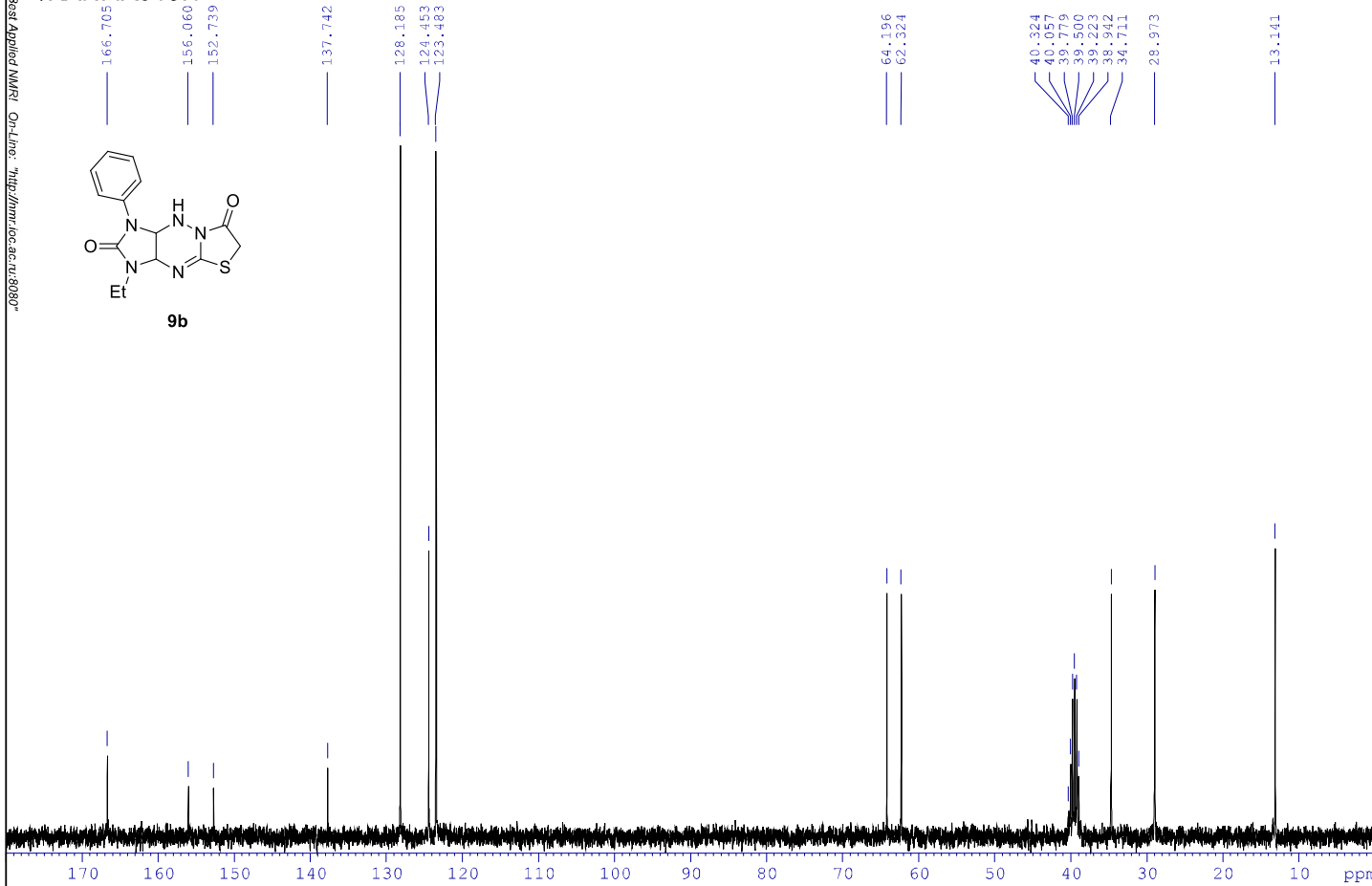


/KANI IA916.1

The Best Applied MMR - On-Line: "http://mri.zo.ac.ru/8080"



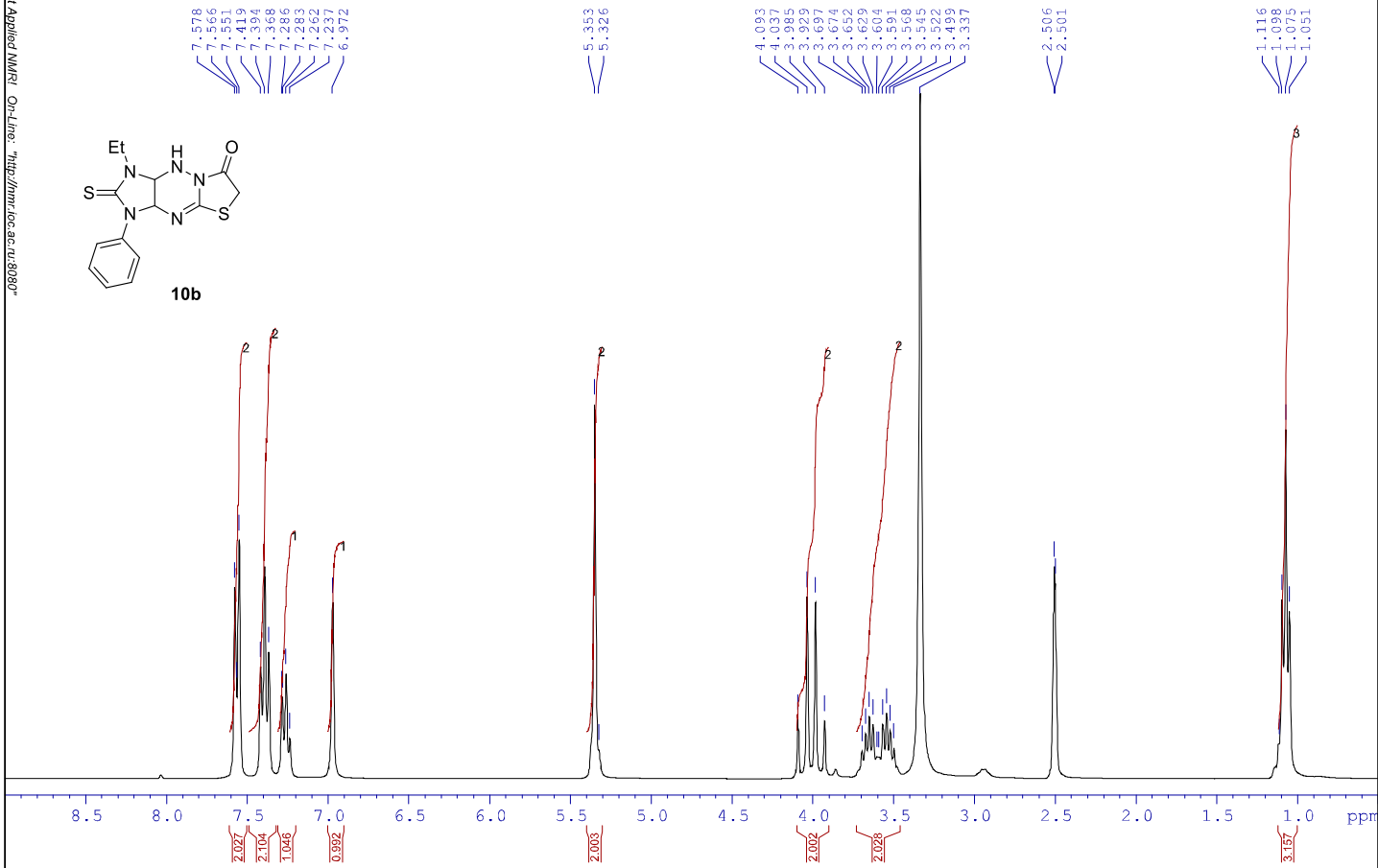
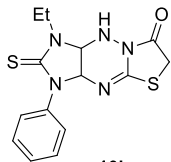
9b



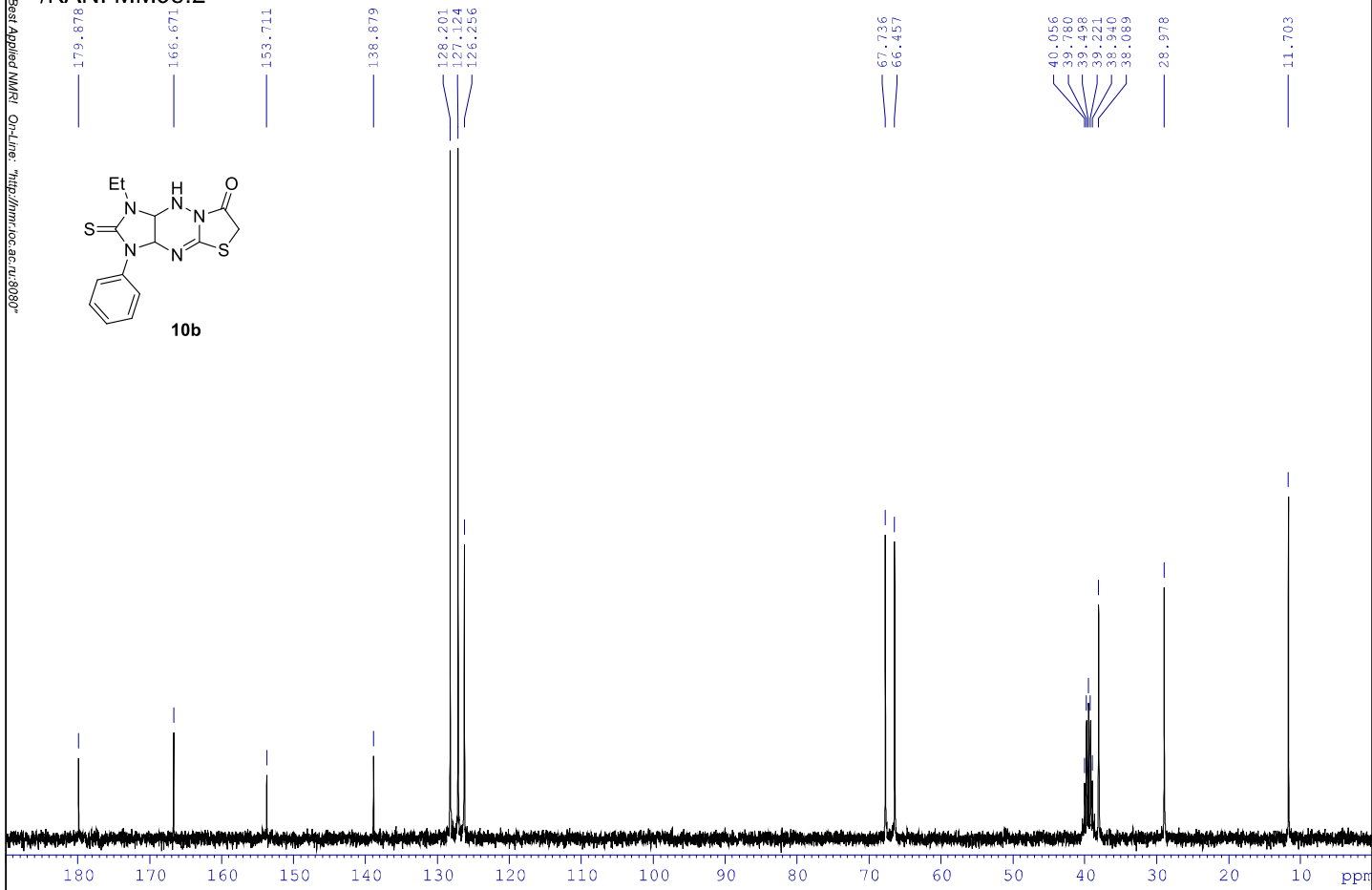


# /KANI MM95.2

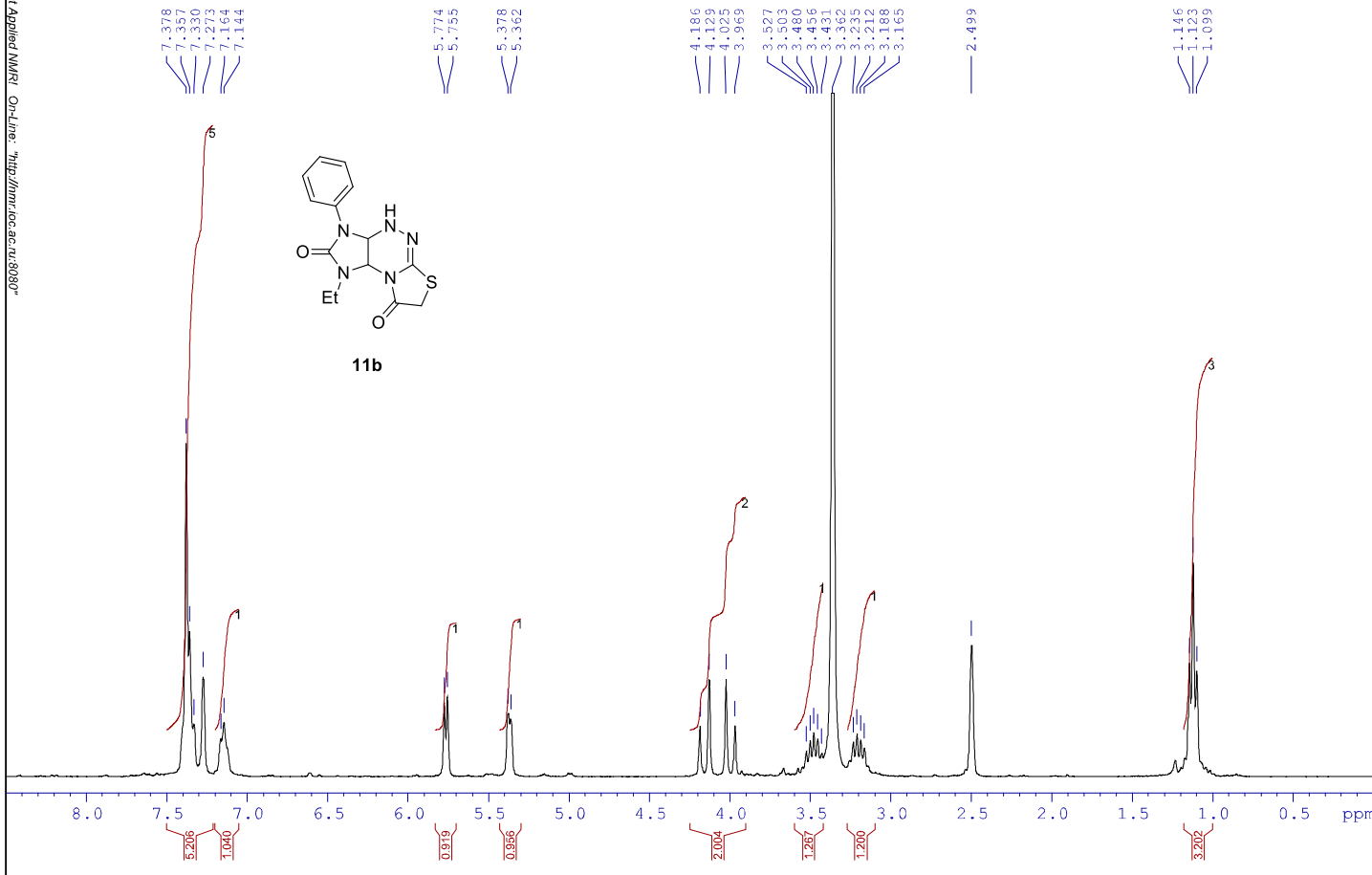
The Best Applied MMR - On-Line: "http://mr.ia.ac.ru:8080"



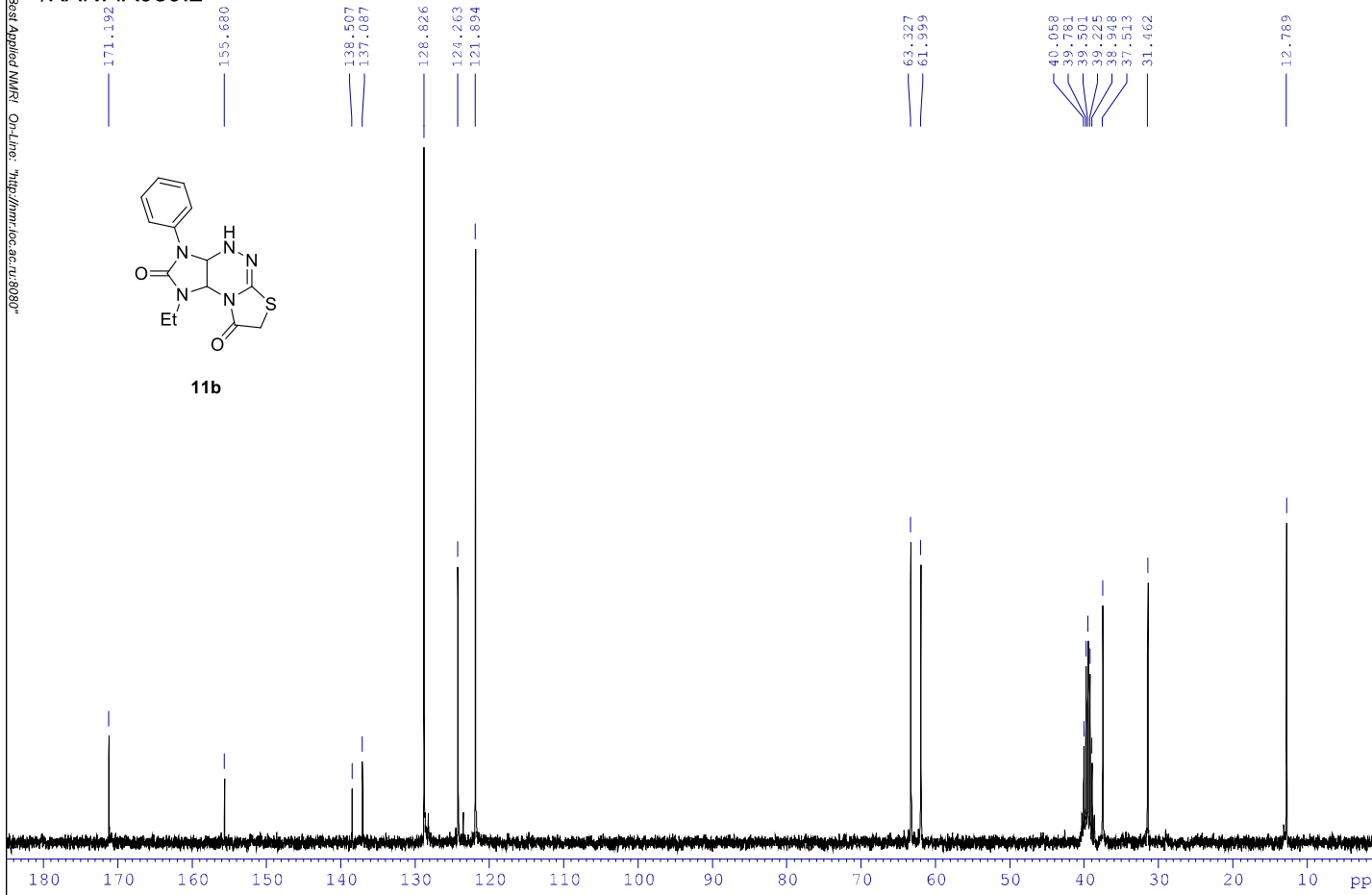
# /KANI MM95.2



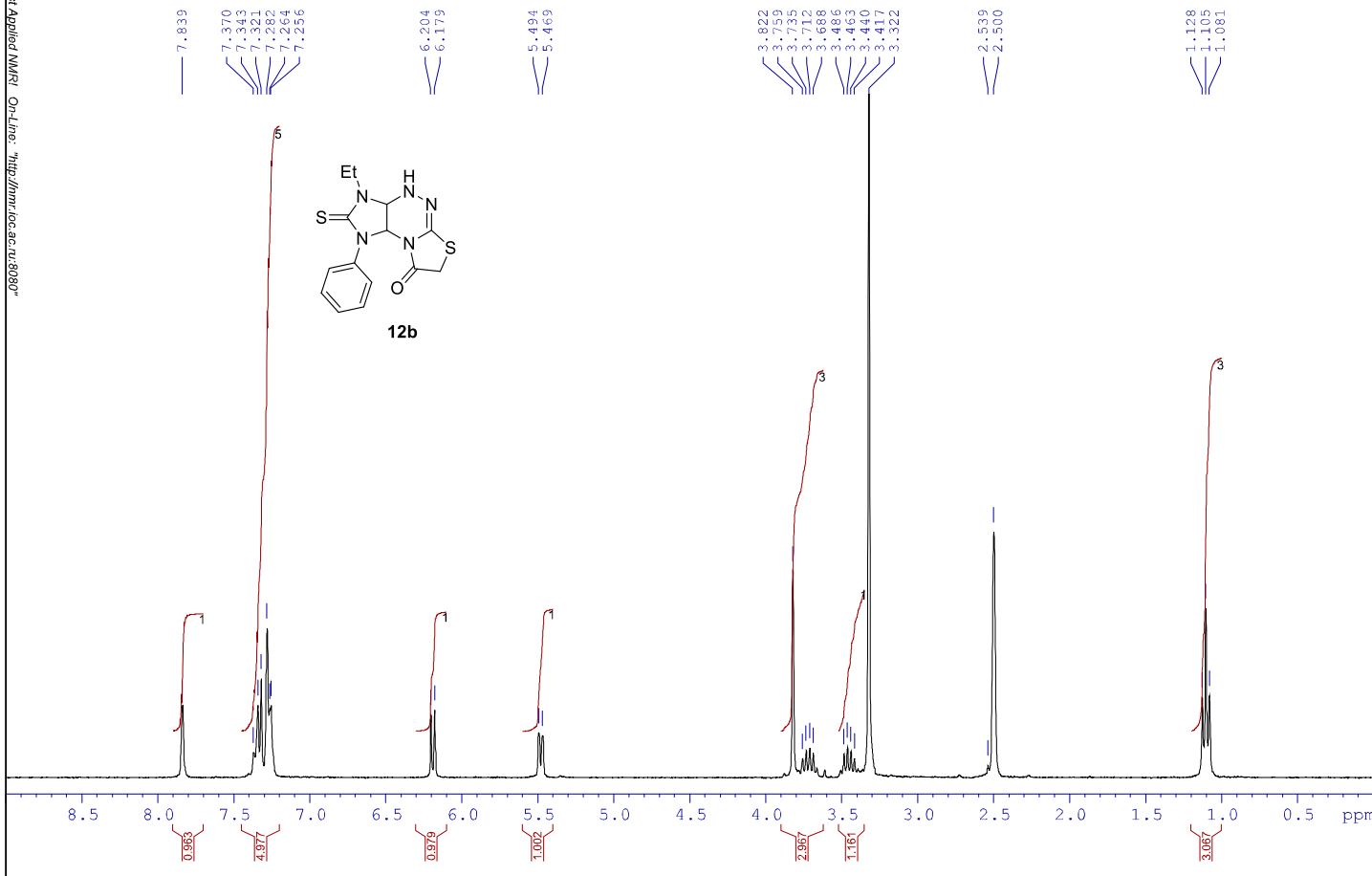
/KANI IA959.2



/KANI IA959.2

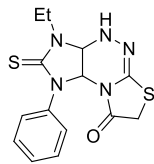


/KANI IA984.1

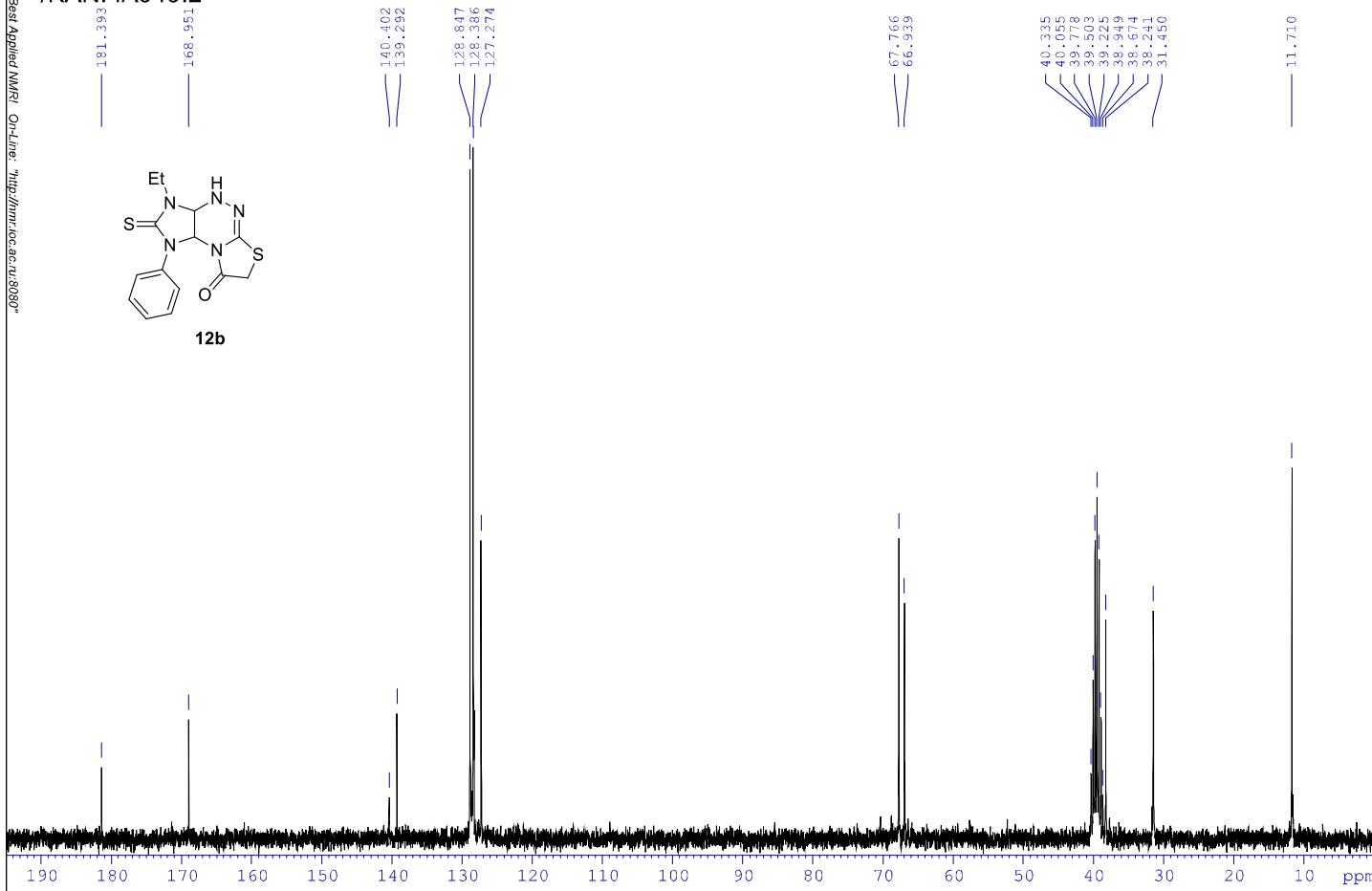


/KANI IA949.2

The Best Applied NMR CH-Line: "13p2/1m1oc.ac.ru:8080"

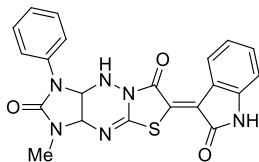


12b

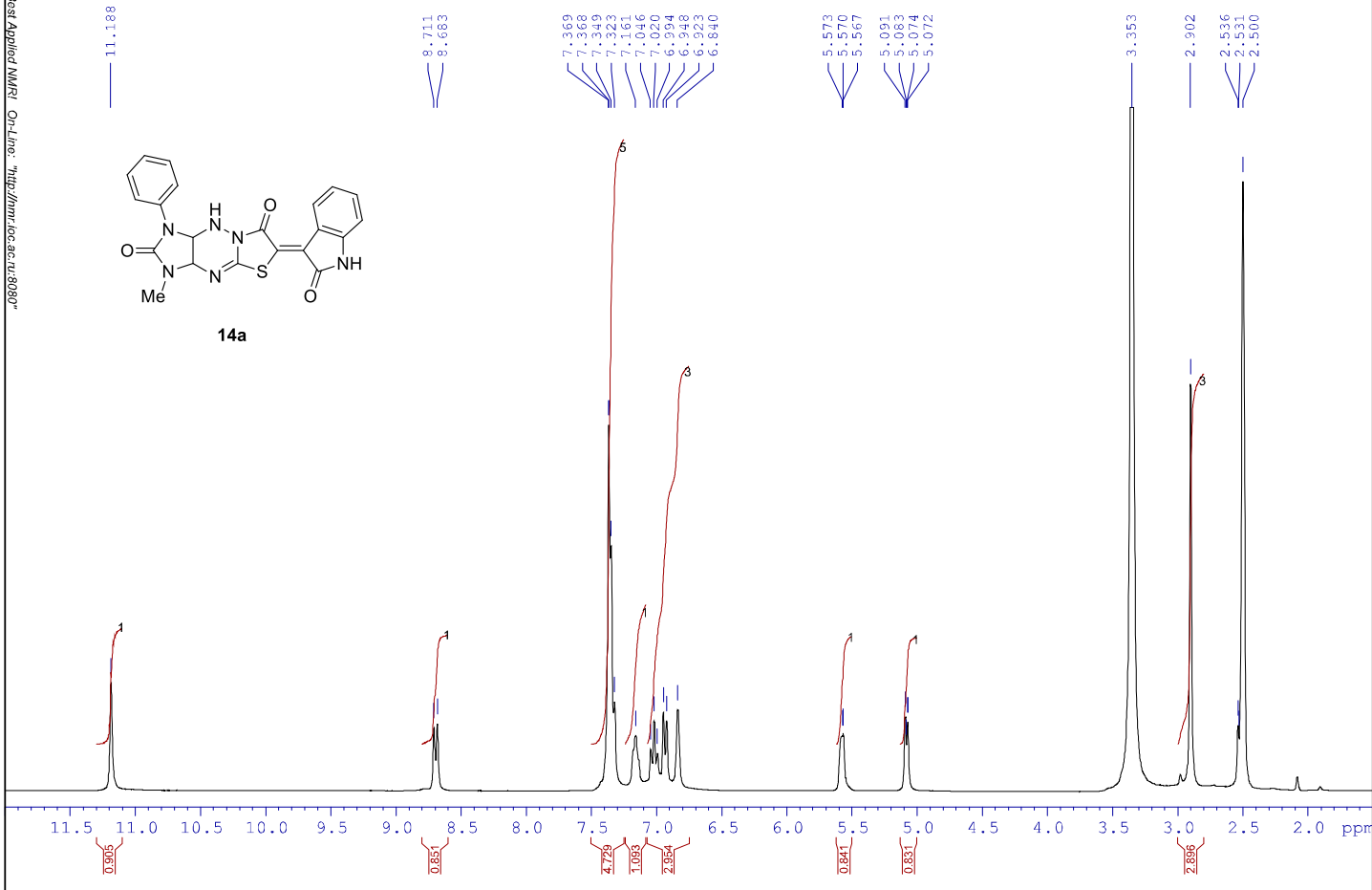


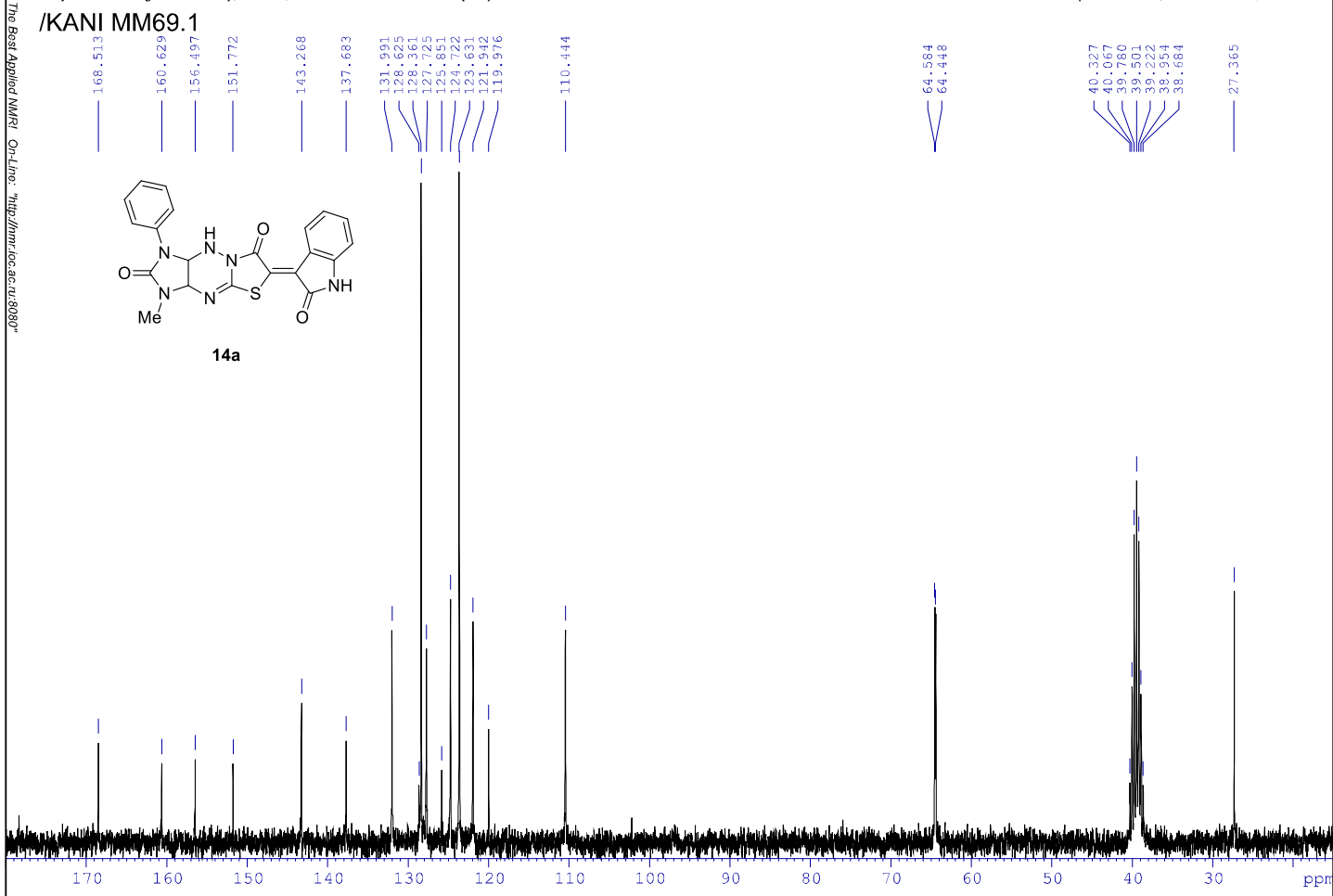
/KANI MM69.2

The Best Applied MMR. On-Line: "http://mri.zo.ac.ru/8080"



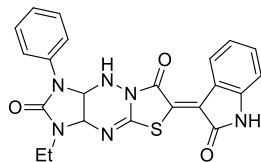
14a



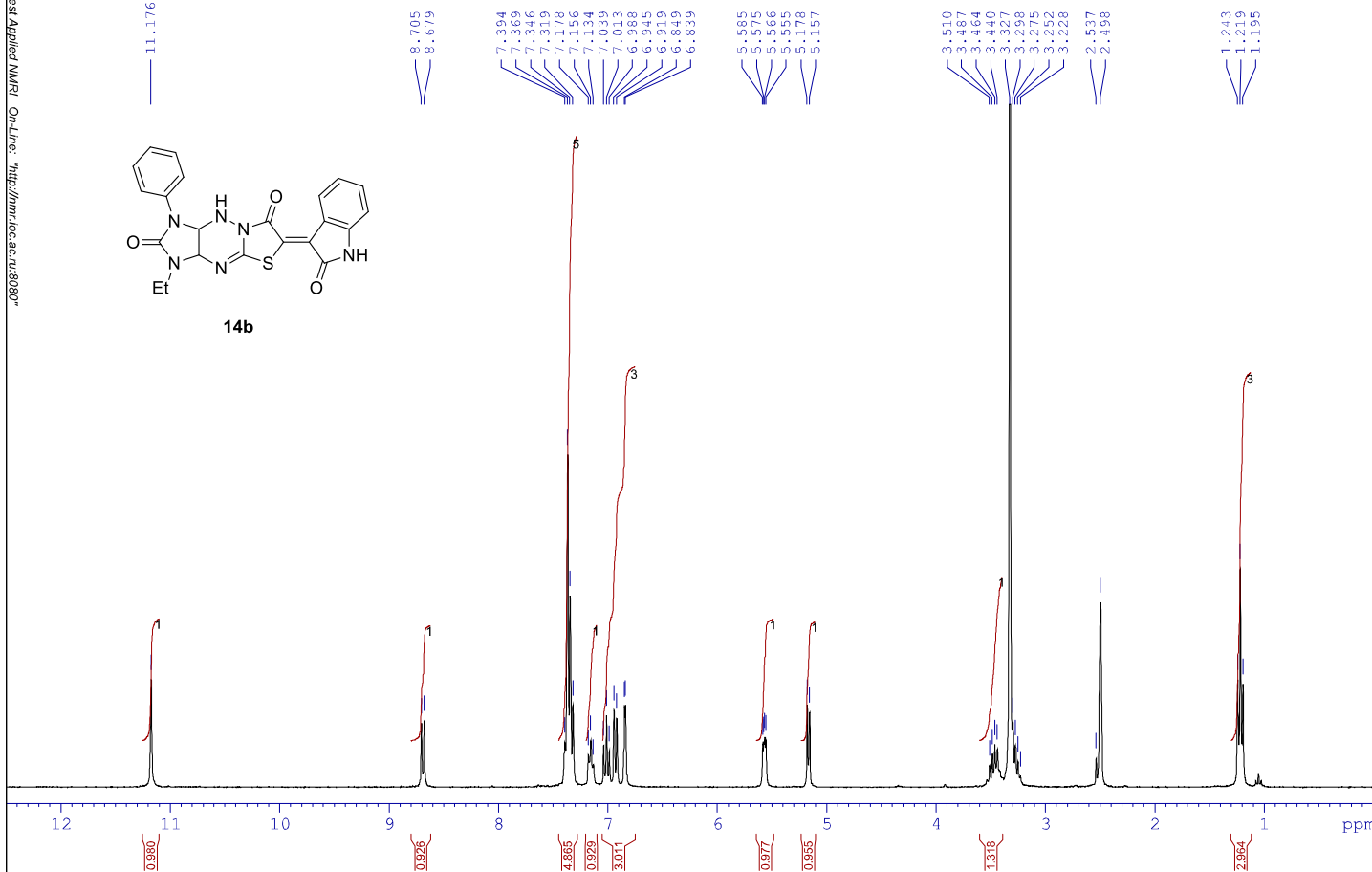




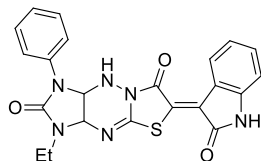
/KANI IA918.1



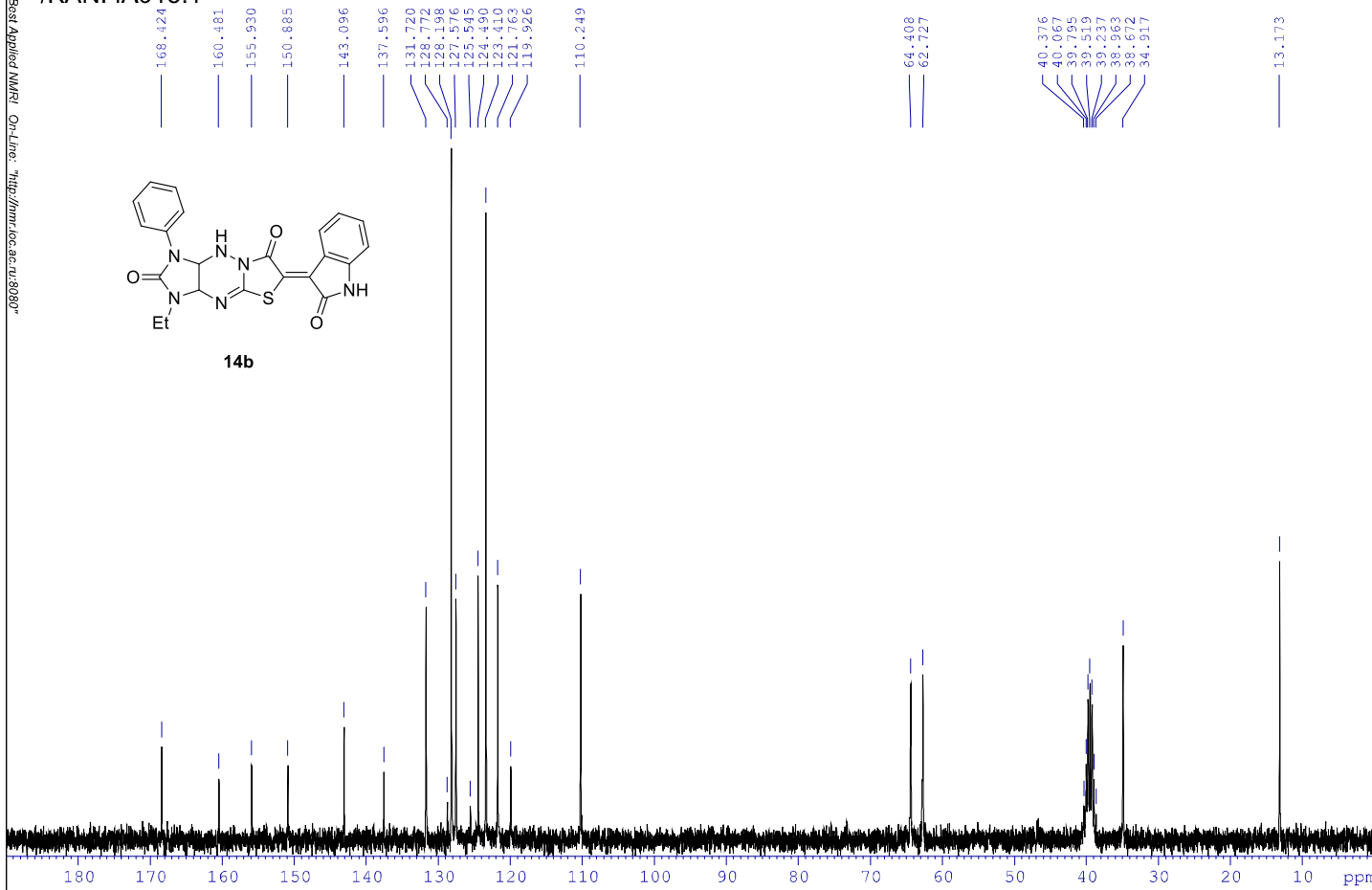
14b



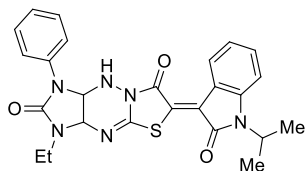
/KANI IA918.1



14b



# /KANI IA923.1



8.776  
8.751

7.420  
7.392  
7.367  
7.344  
7.319  
7.290  
7.185  
7.179  
7.158  
7.135  
7.082  
7.057  
7.031

5.575  
5.554

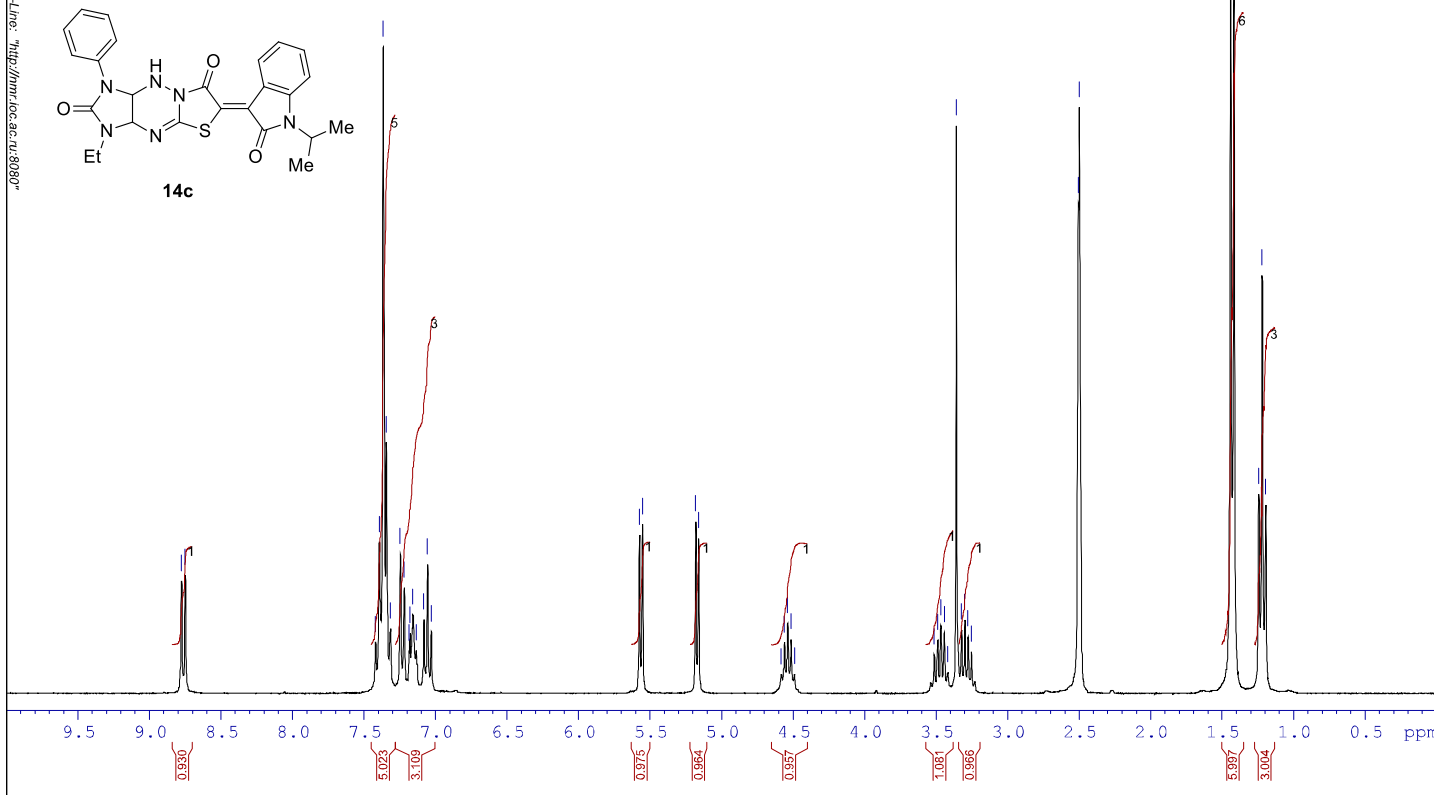
5.182  
5.161

4.584  
4.561  
4.538  
4.515  
4.491

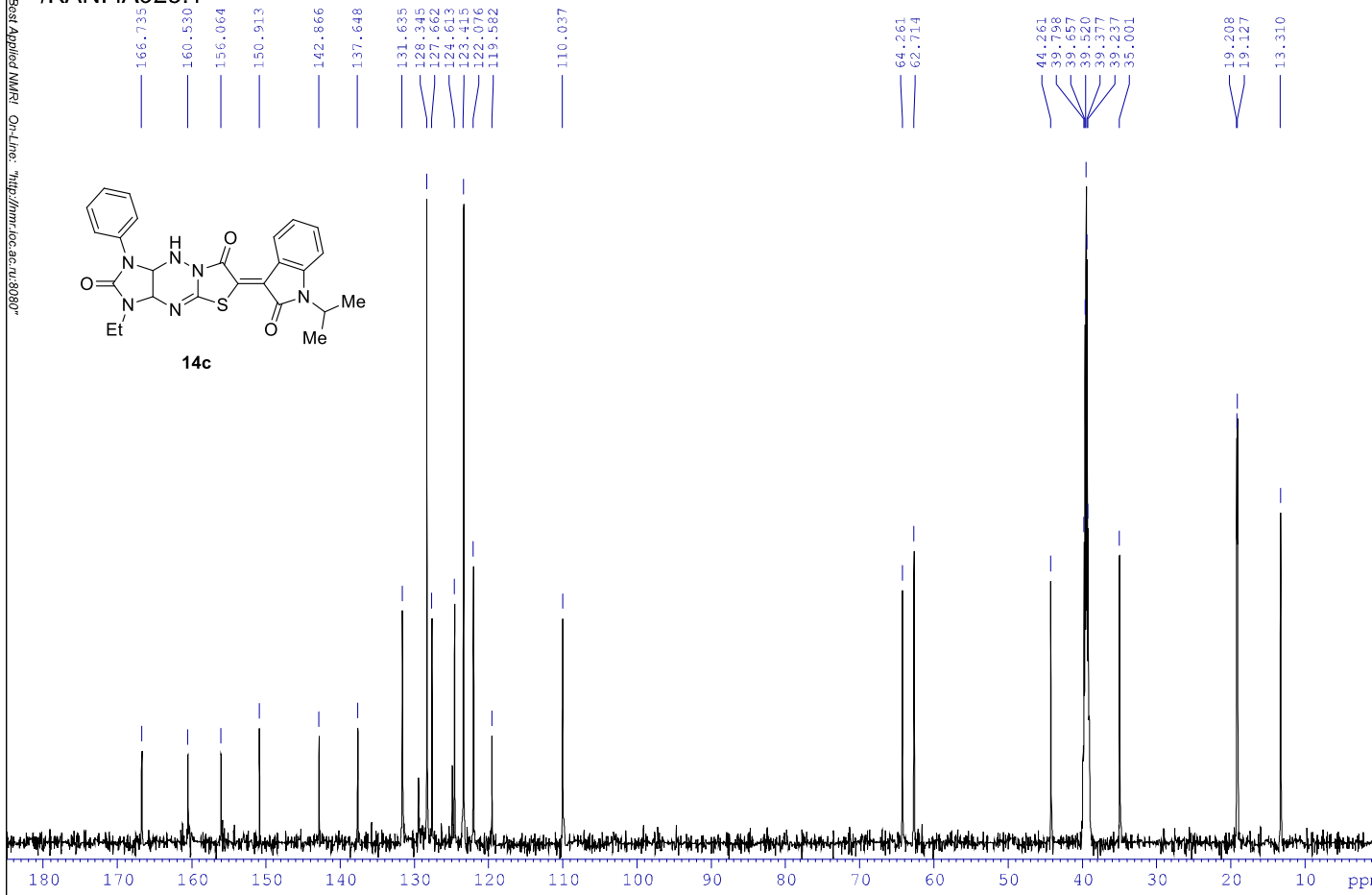
3.513  
3.489  
3.467  
3.443  
3.419  
3.359  
3.323  
3.299  
3.277  
3.254

2.505  
2.500

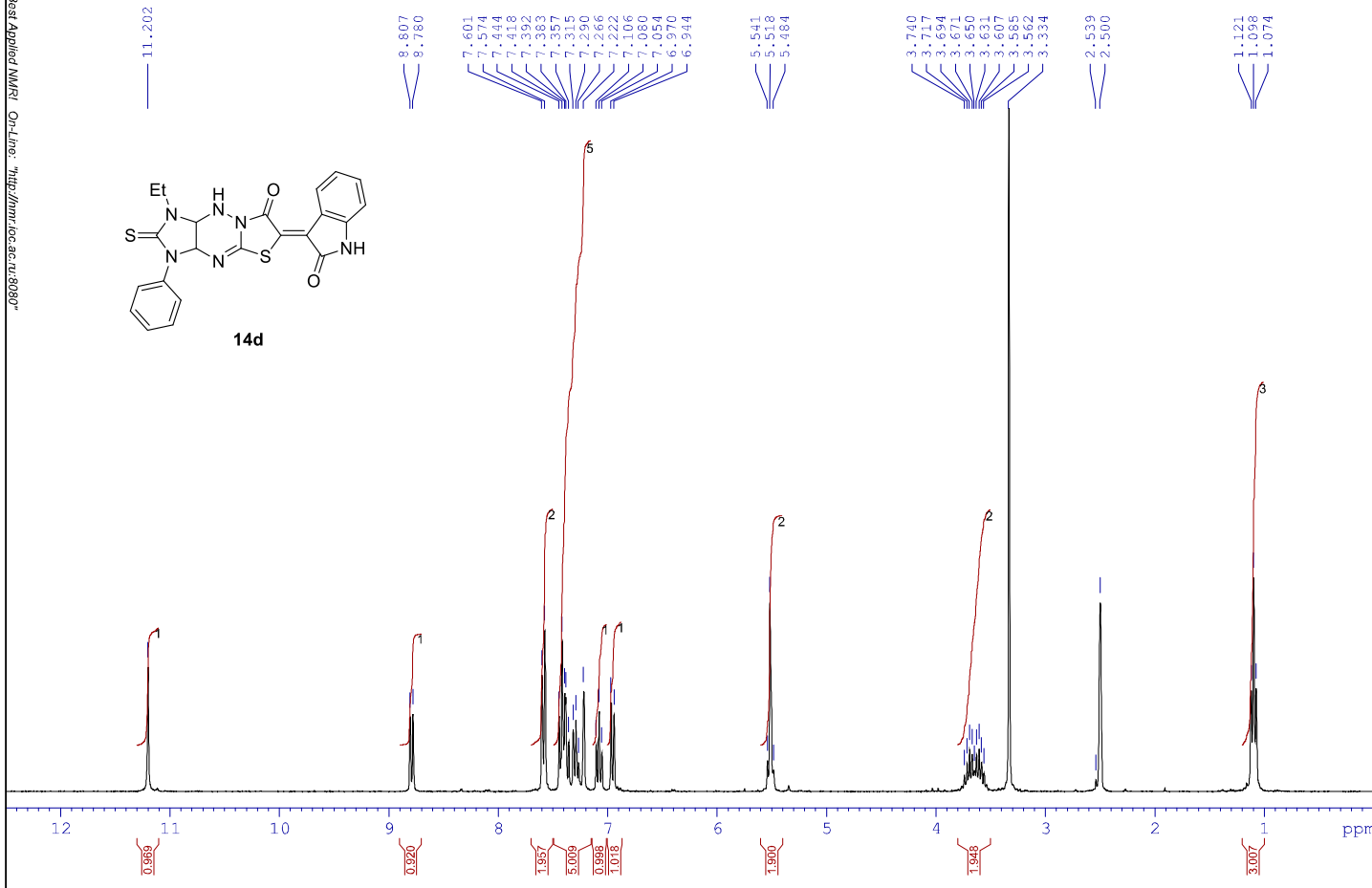
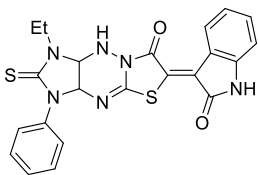
1.441  
1.418  
1.244  
1.220  
1.196



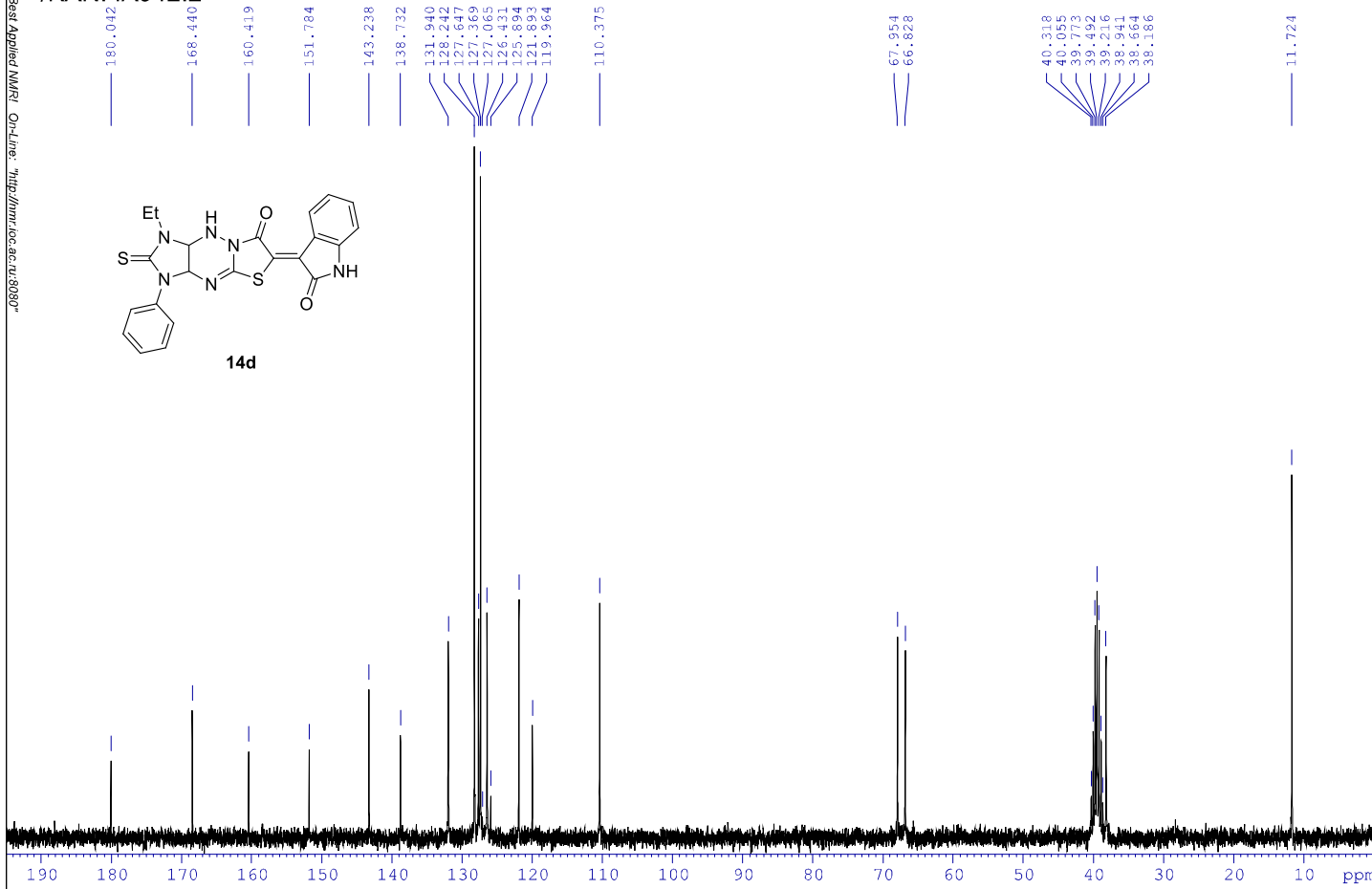
/KANI IA923.1



/KANI IA942.2

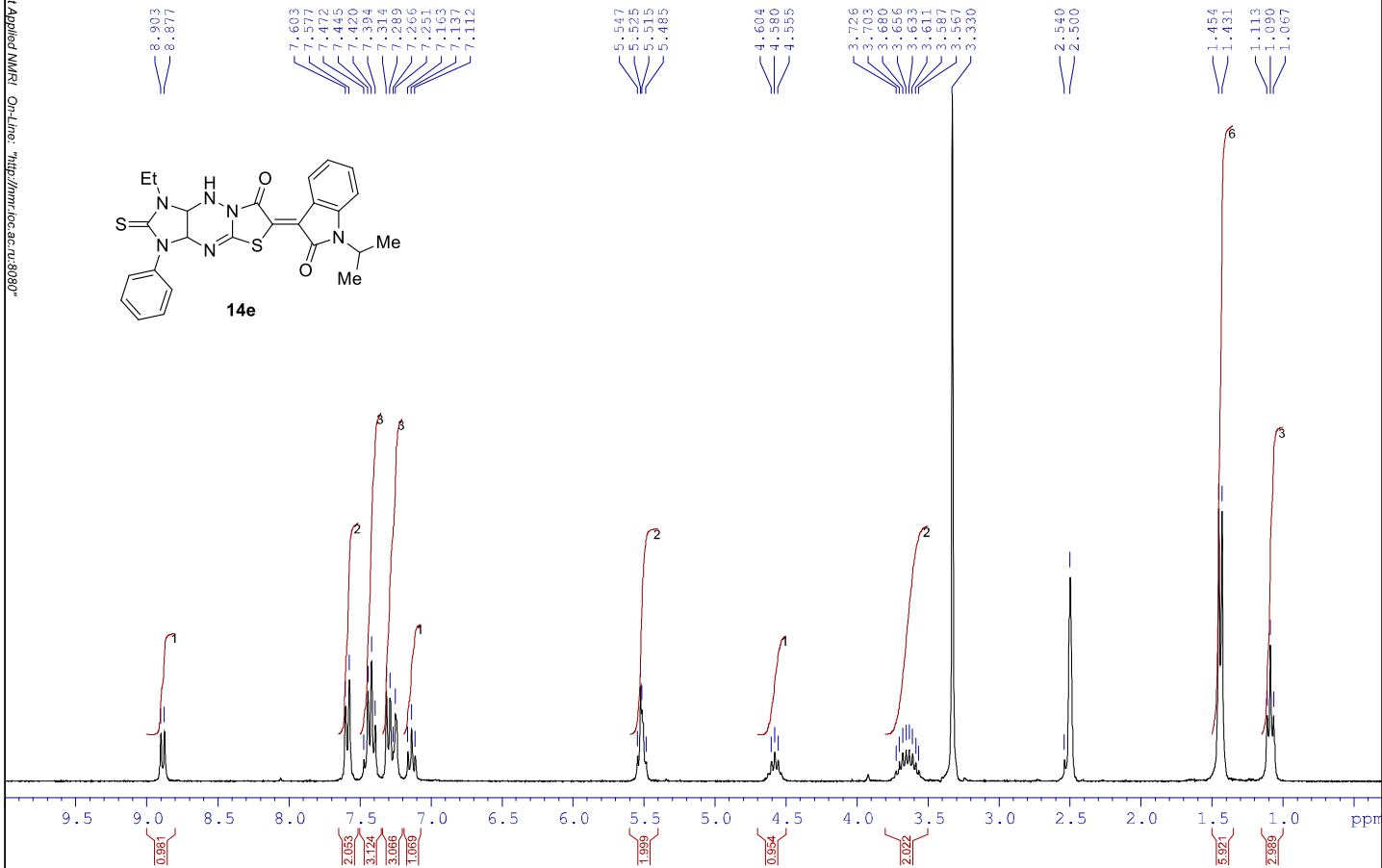
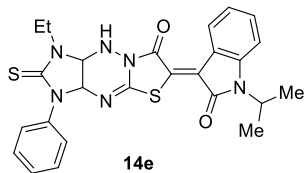


/KANI IA942.2

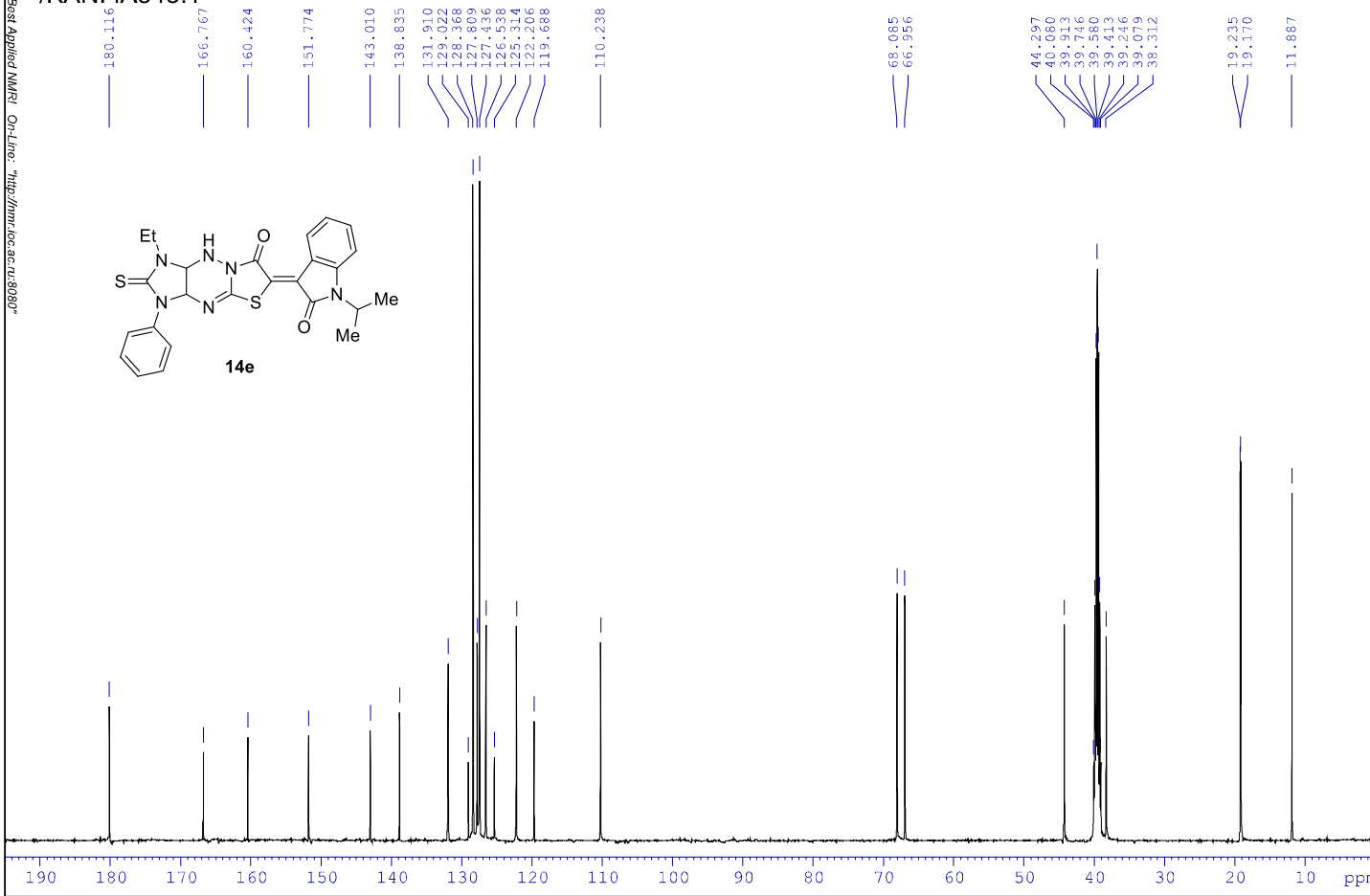


/KANI IA543.1

The Best Applied NMR On-Line: <http://mr.ice.ac.ru/8080/>



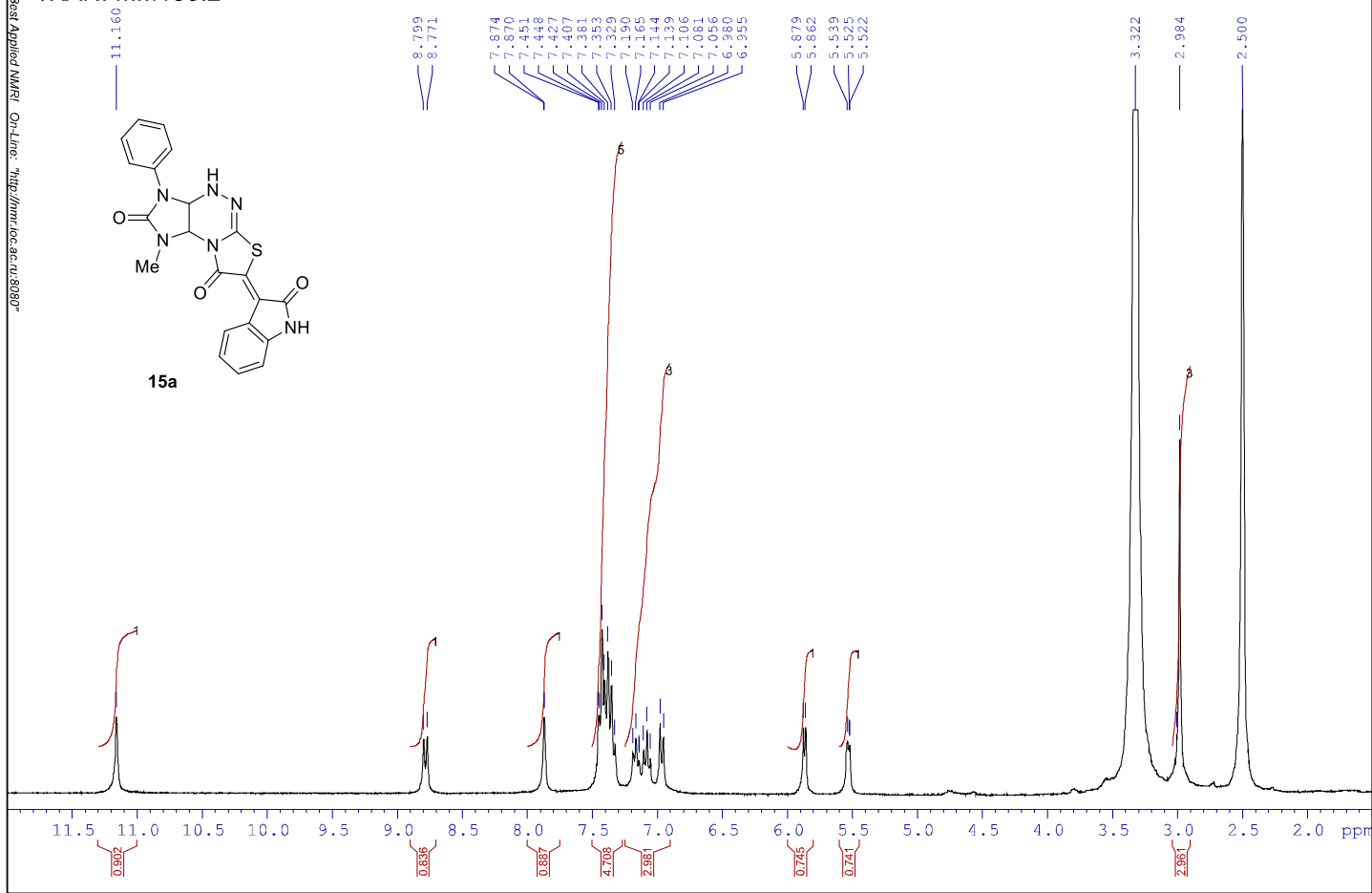
/KANI IA543.1



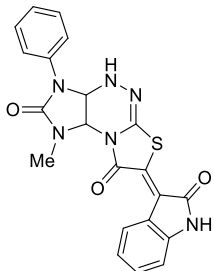
The Best Applied MMR - On-Line: <http://mr.ice.ac.ru/8080/>



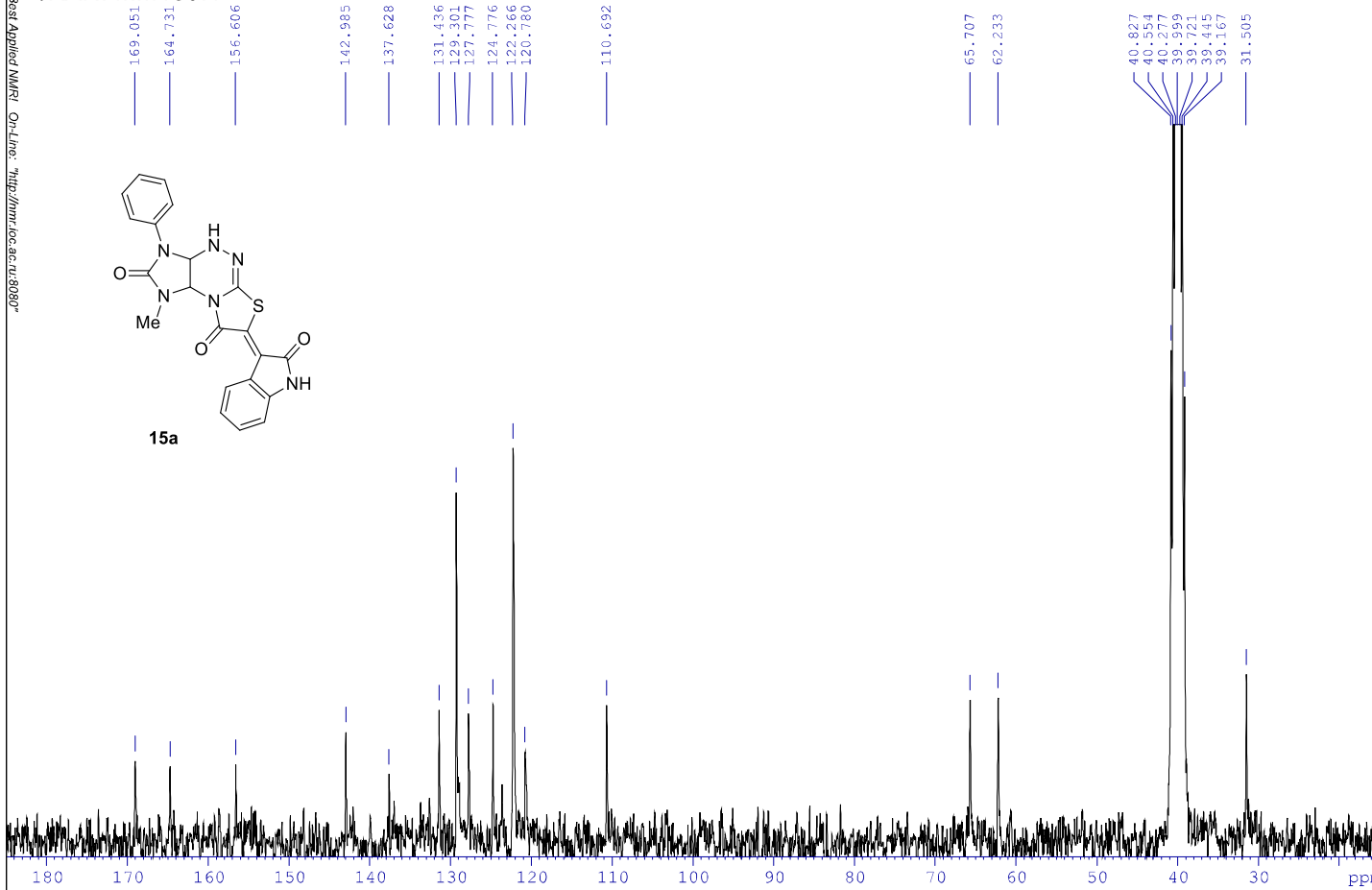
/KANI MM136.2



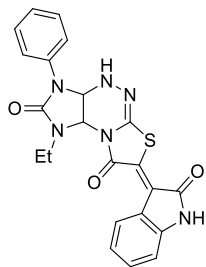
# /KANI MM136.1



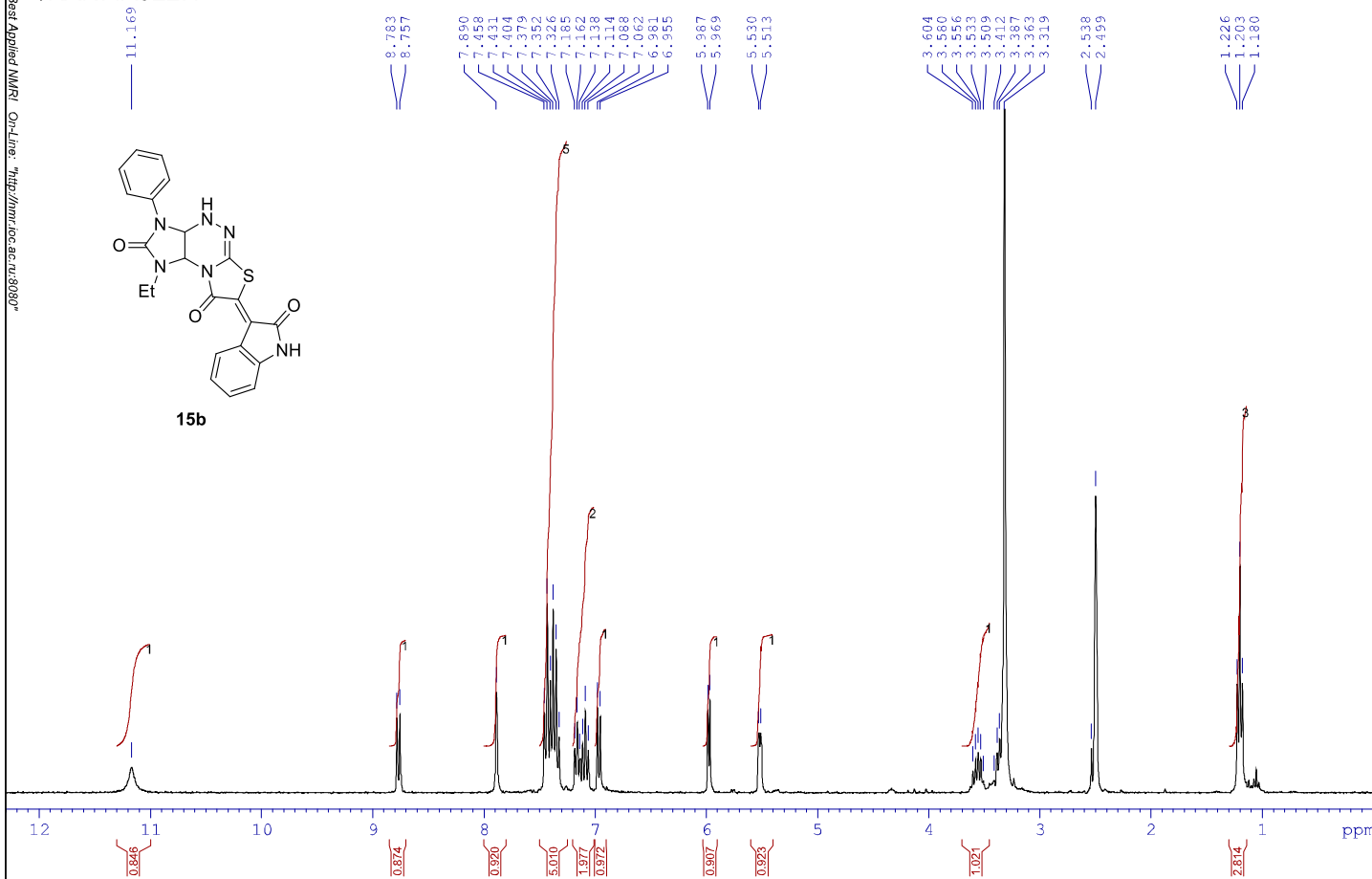
15a



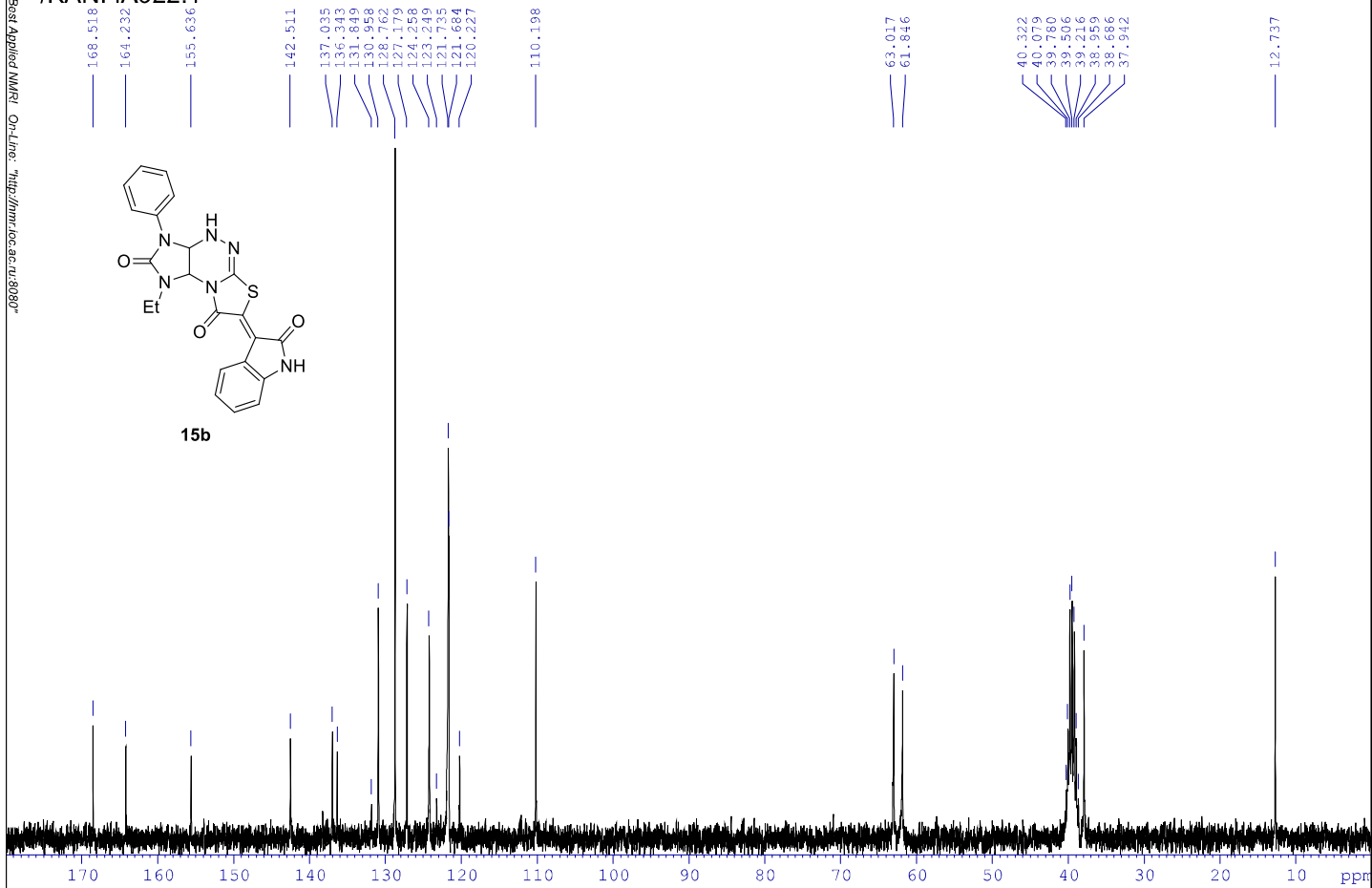
/KANI IA922.1



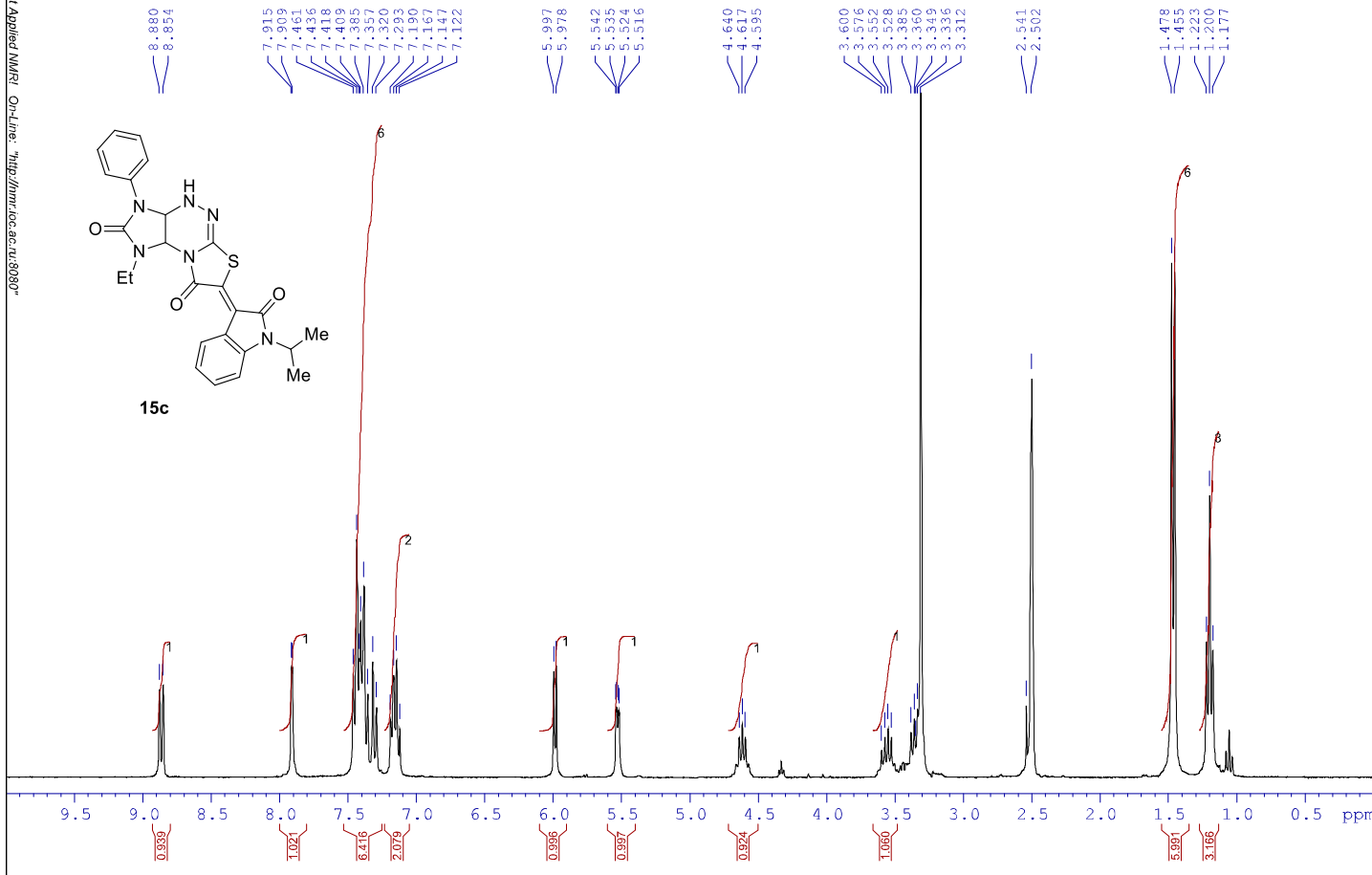
15b



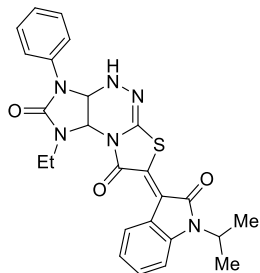
/KANI IA922.1



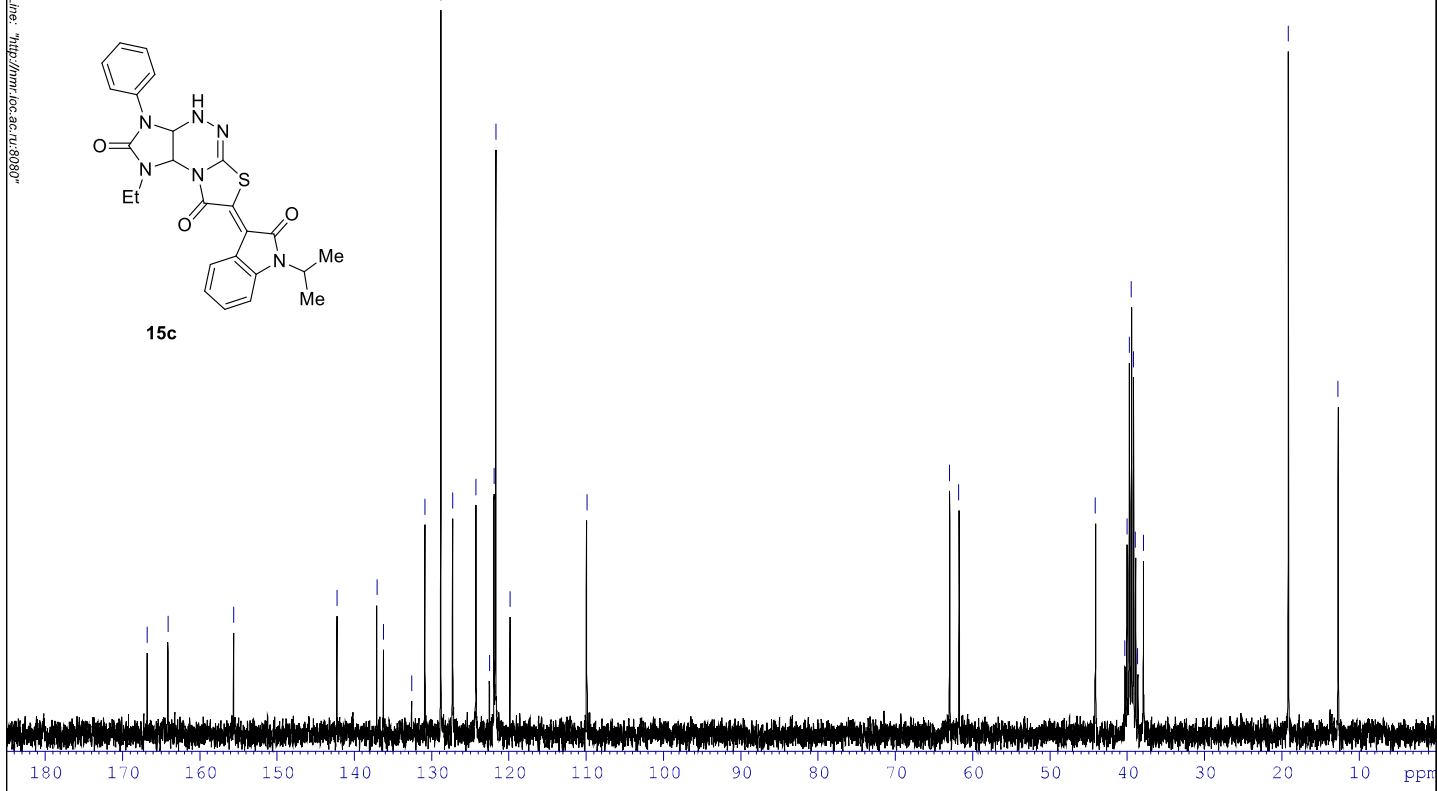
# /KANI IA924.1



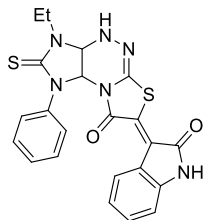
/KANI IA924.1



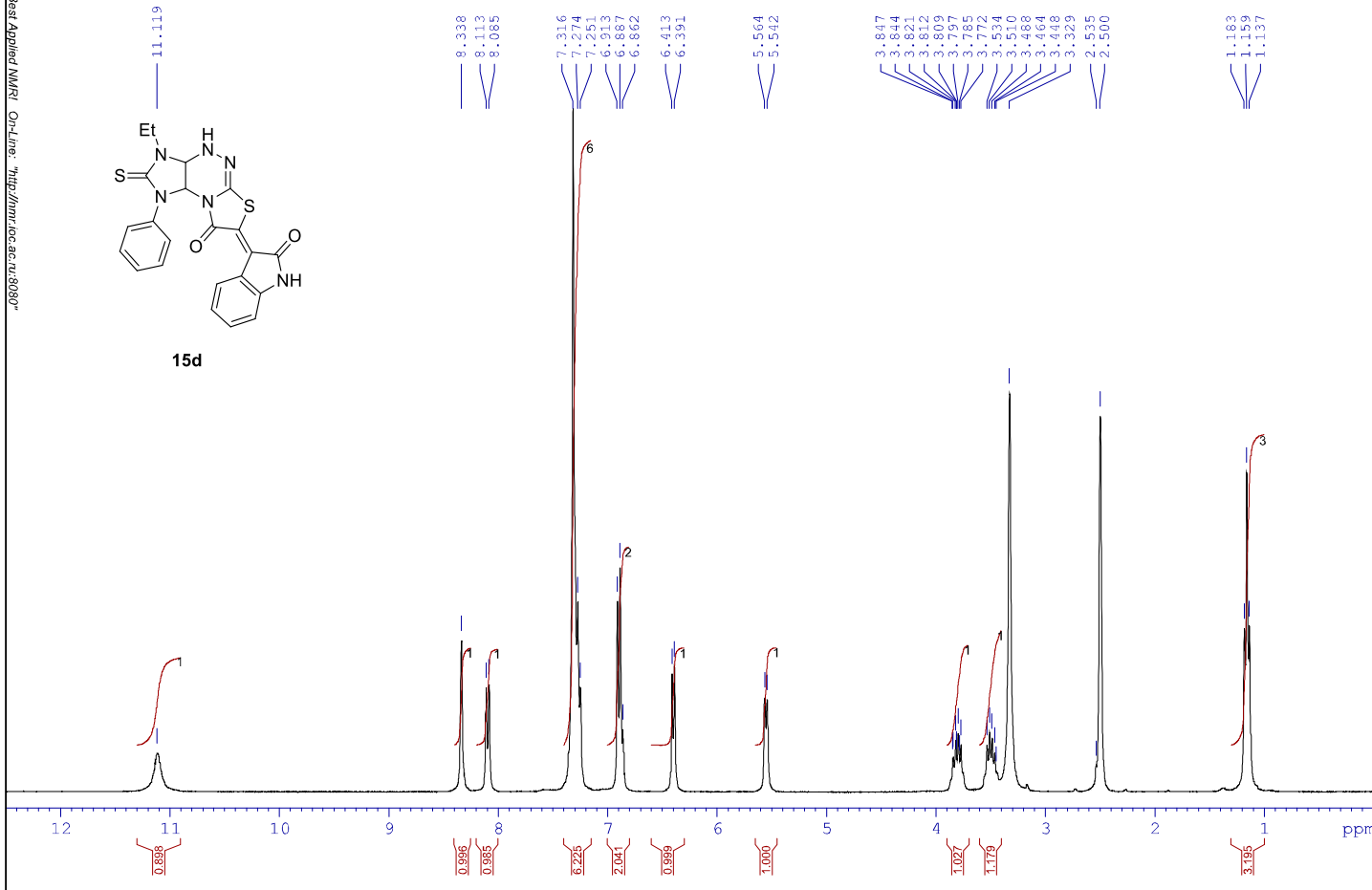
15c



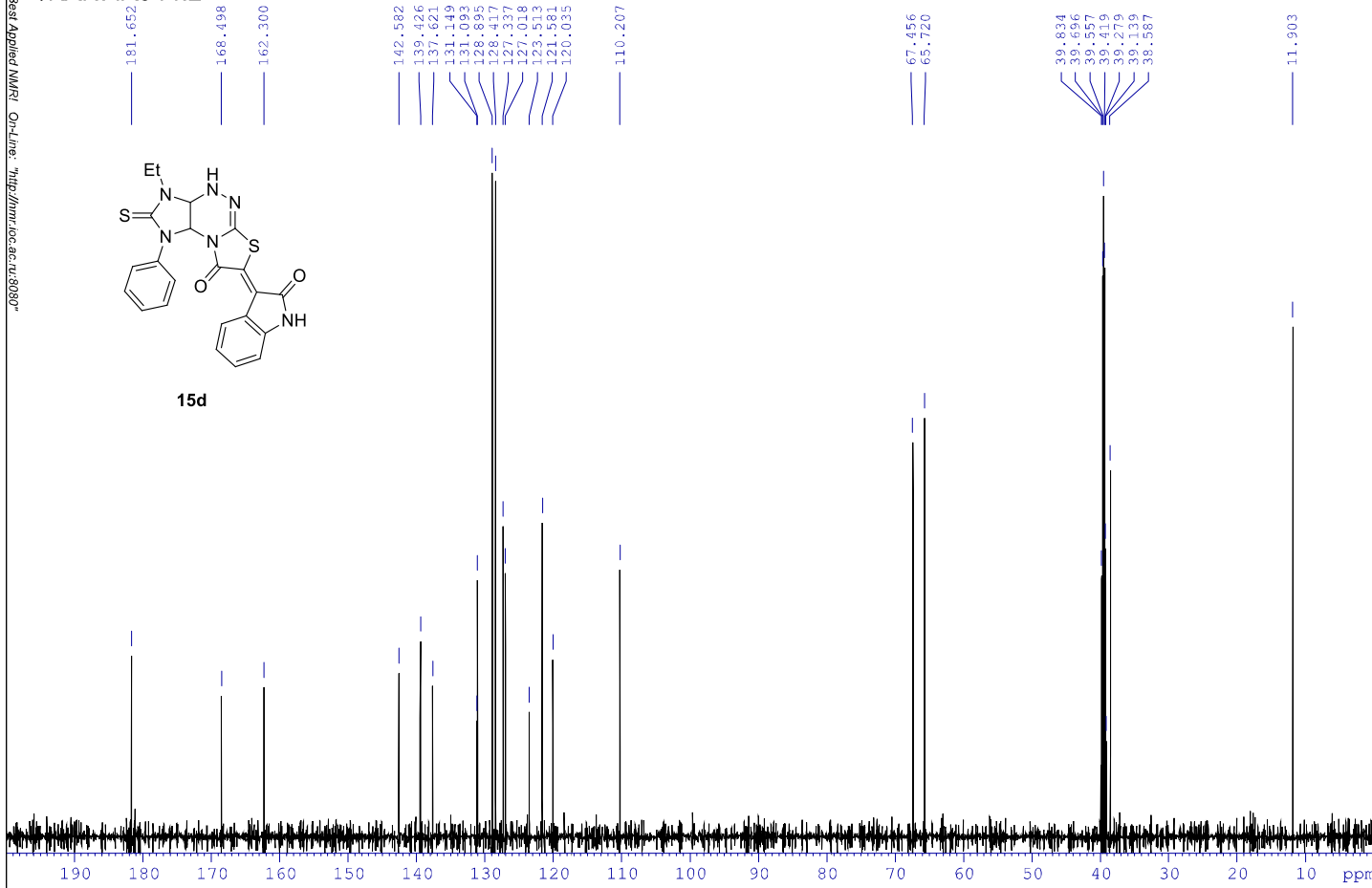
/KANI IA944.2



15d

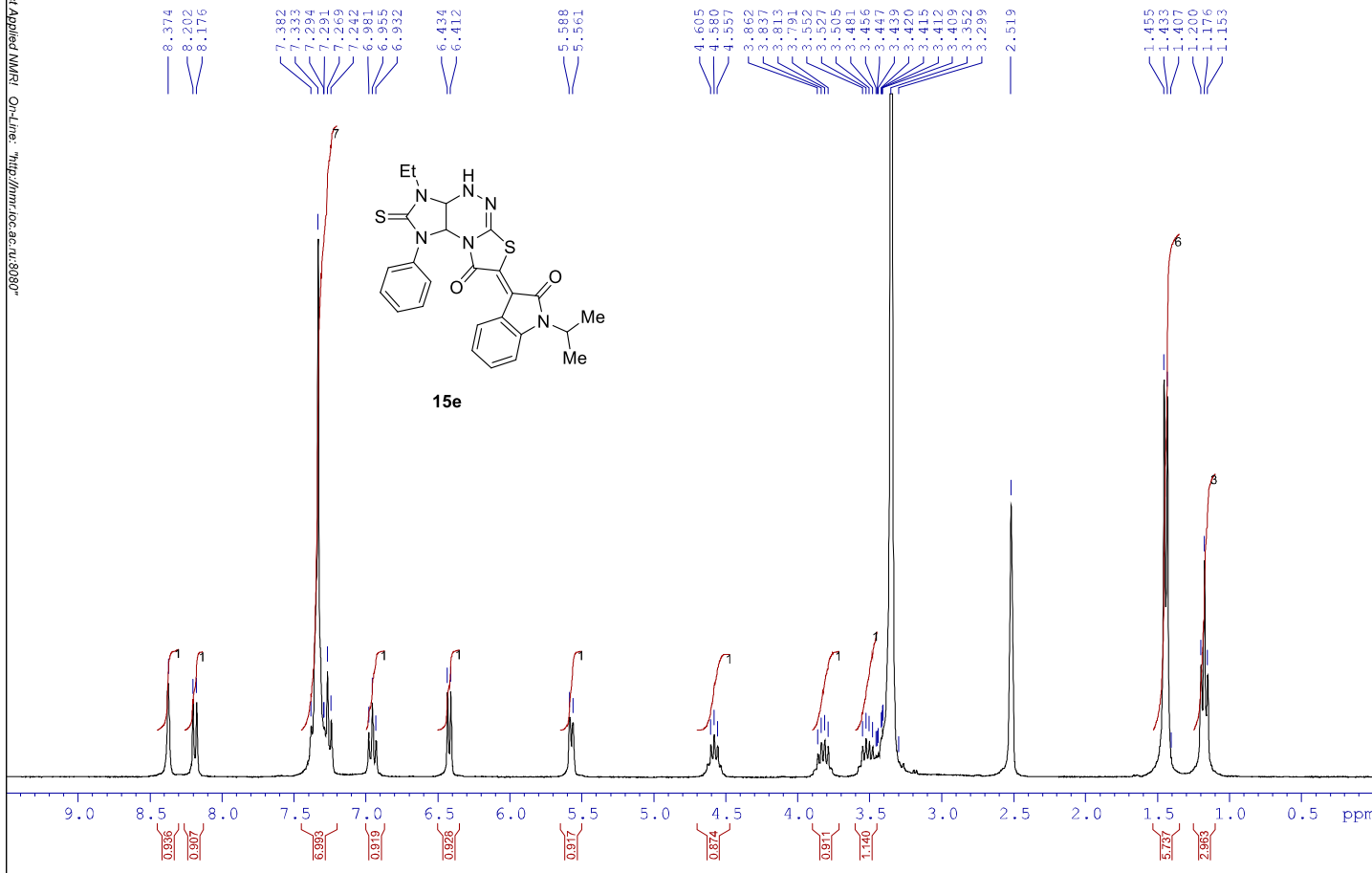


/KANI IA944.2





# /KANI MM99.1



The Best Applied NMR Online - <http://nmr.ioc.ac.ru/3000/>

/KANI MM99.1

