3-[*N,N*-Bis(sulfonyl)amino]isoxazolines with spiro-annulated or 1,2-annulated cyclooctane rings inhibit reproduction of tick-borne encephalitis, yellow fever, and West Nile viruses

Kseniya N. Sedenkova [1], Artem S. Sazonov [1], Dmitry A. Vasilenko [1], Kristian S. Andriasov [1], Marina G. Eremenko [1], Yuri K. Grishin [1], Evgeny V. Khvatov [2], Alexander S. Goryashchenko [2], Victoria I. Uvarova [2], Aydar A. Ishmukhametov [2,3], Dmitry I. Osolodkin [2,3] and Elena B. Averina [1,*]

[1] Department of Chemistry, Lomonosov Moscow State University, Moscow, Russia
[2] FSASI "Chumakov FSC R&D IBP RAS" (Institute of Poliomyelitis), Moscow, Russia
[3] Institute of Translational Medicine and Biotechnology, Sechenov Moscow State Medical University, Moscow, Russia

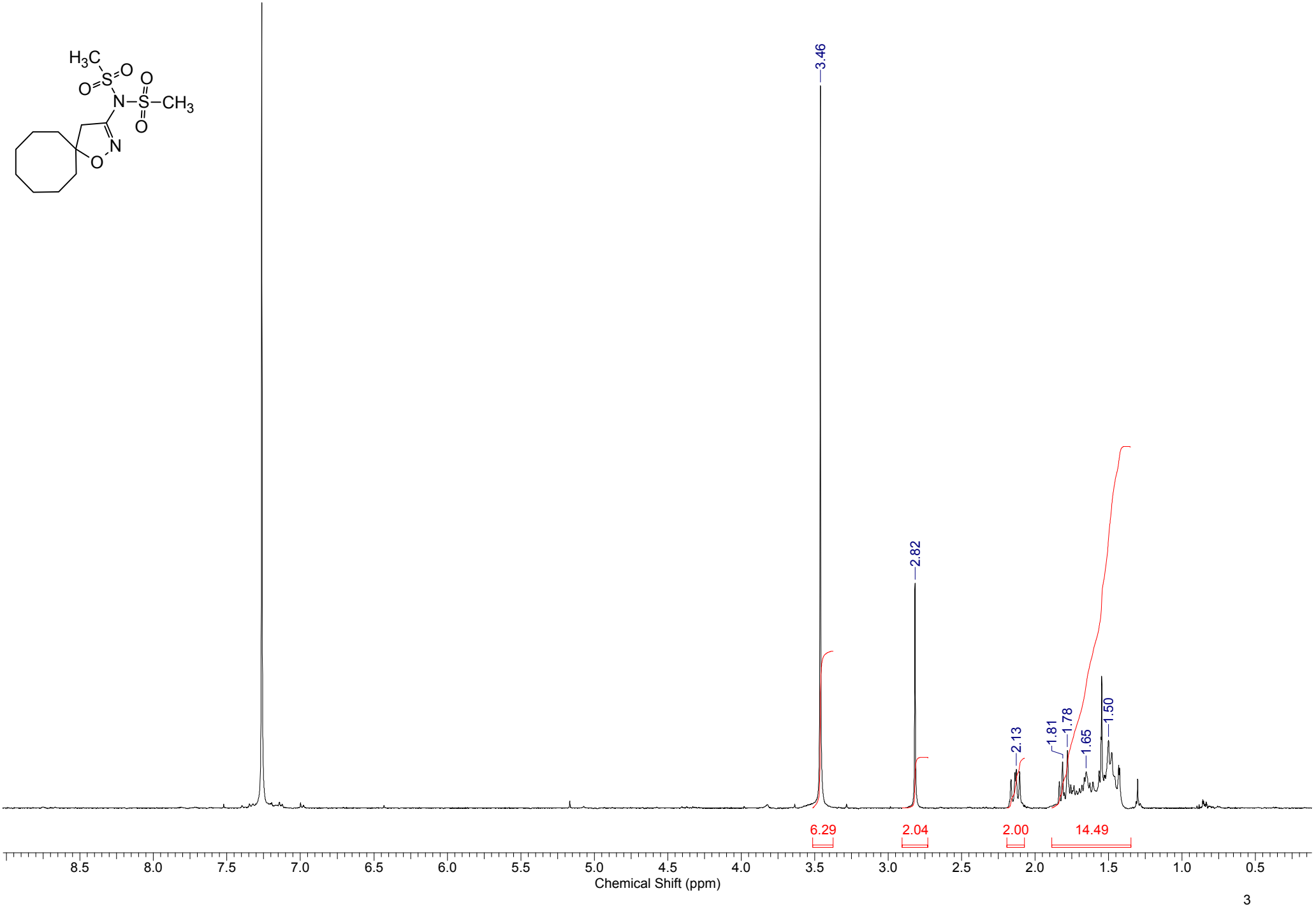
* Correspondence: elaver@med.chem.msu.ru

Supplementary materials

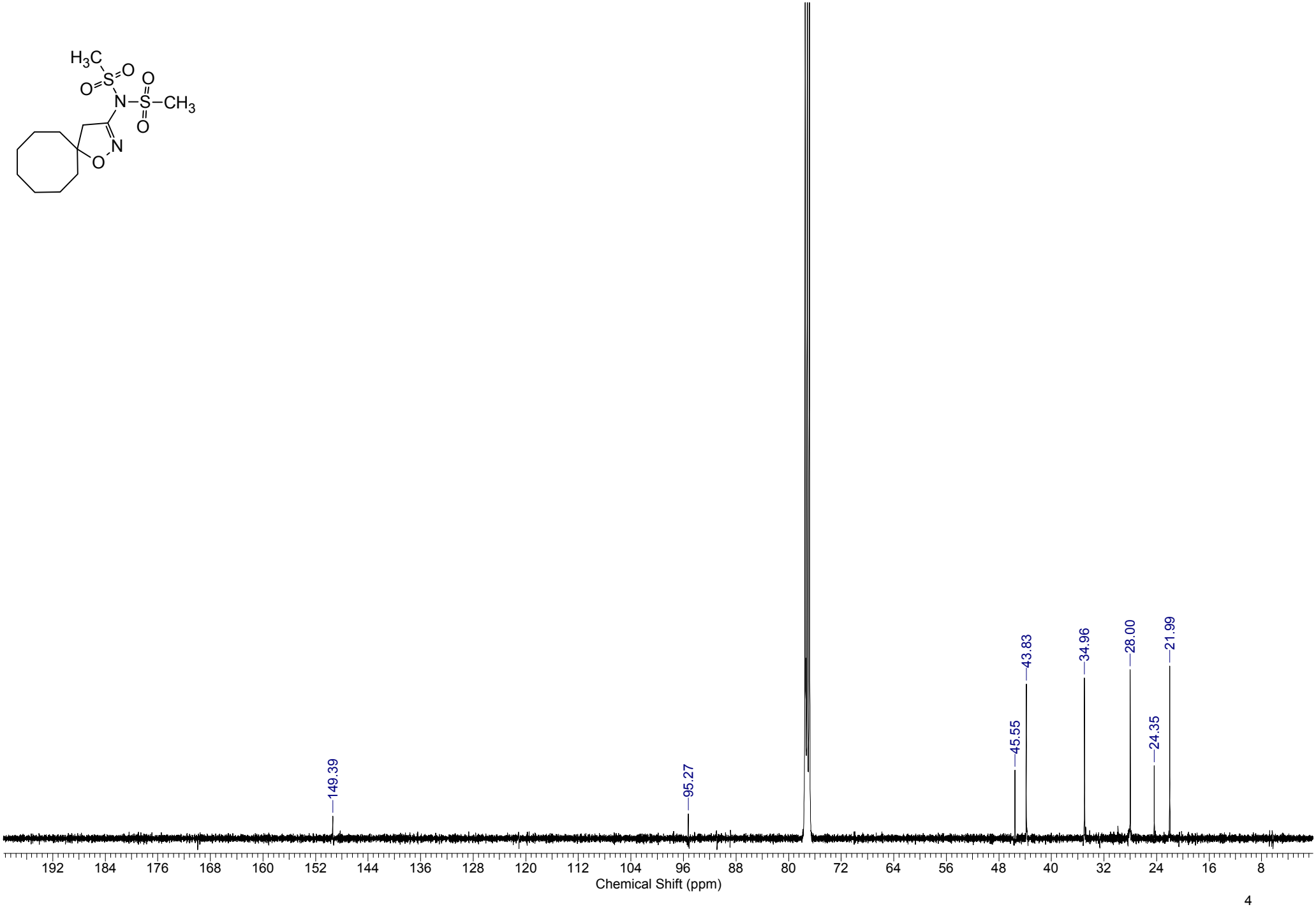
Table S1. Acute toxicity of compounds **3-5**.

Compound	CC_{50} Vero 24h, μM	CC_{50} PEK 24h, μM
6	>100	>100
Favipiravir	>1000	>1000
3a	>50	>50
3b	>50	>50
3c	>50	>50
3d	>50	>50
3e	>50	>50
3f	>50	>50
3g	>50	>50
3h	>50	>50
3j	40 ± 3	>50
3k	>50	>50
3l	>50	>50
4a	>50	>50
4b	>50	>50
4c	>50	>50
4d	>50	>50
4e	>50	>50
4f	>50	>50
4g	>50	>50
4h	>50	>50
4i	35 ± 4	>50
4j	>50	>50
4k	>50	>50
4l	>50	>50
5b	>50	>50
5c	>50	>50
5d	>50	>50
5e	>50	>50
5f	>50	>50
5g	>50	>50
5h	39 ± 8	>50
5i	>50	>50
5j	>50	>50
5k	14.9 ± 1.5	>50
5l	>50	>50

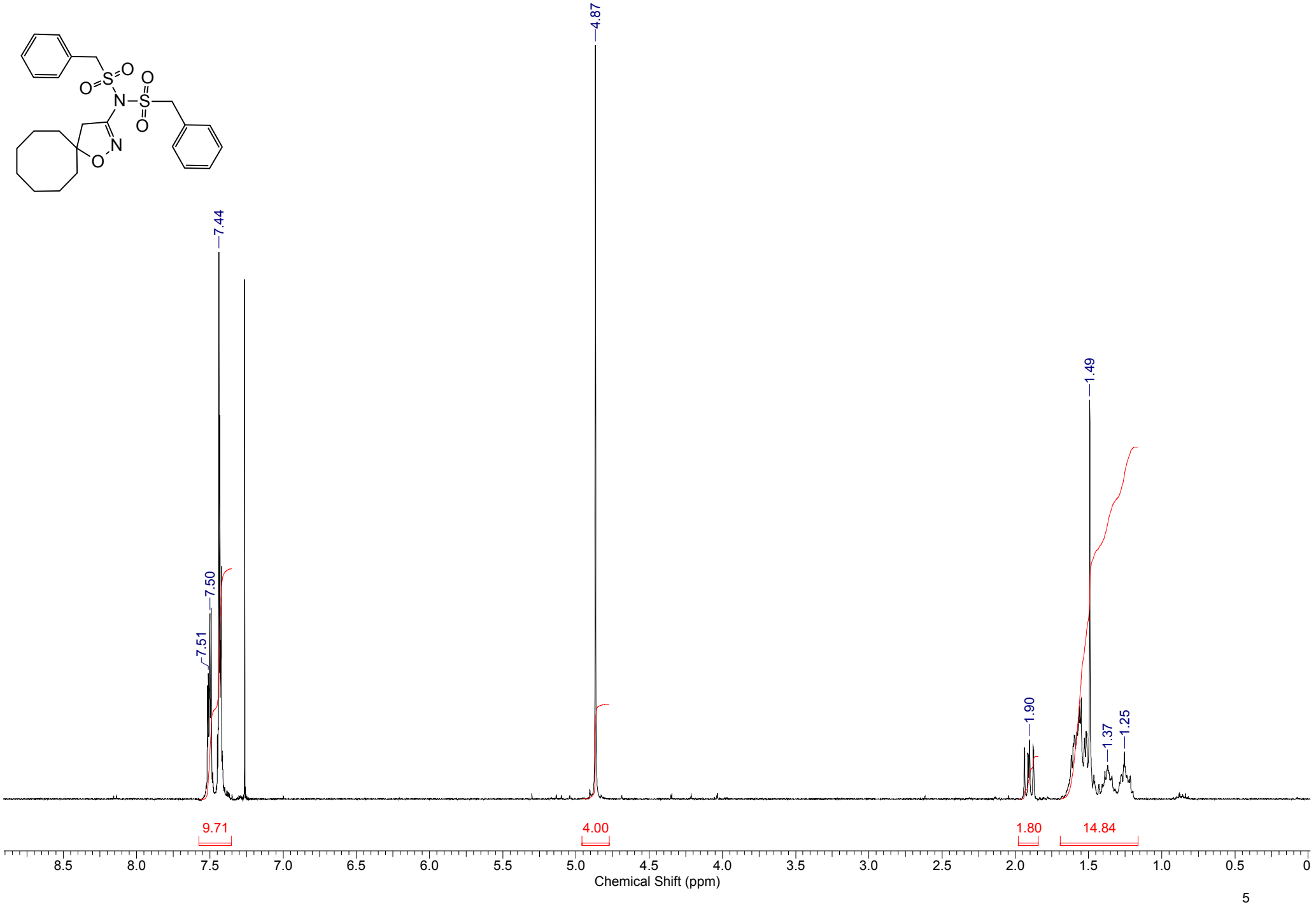
^{1}H NMR spectrum of compound **4a** ($CDCl_3$)



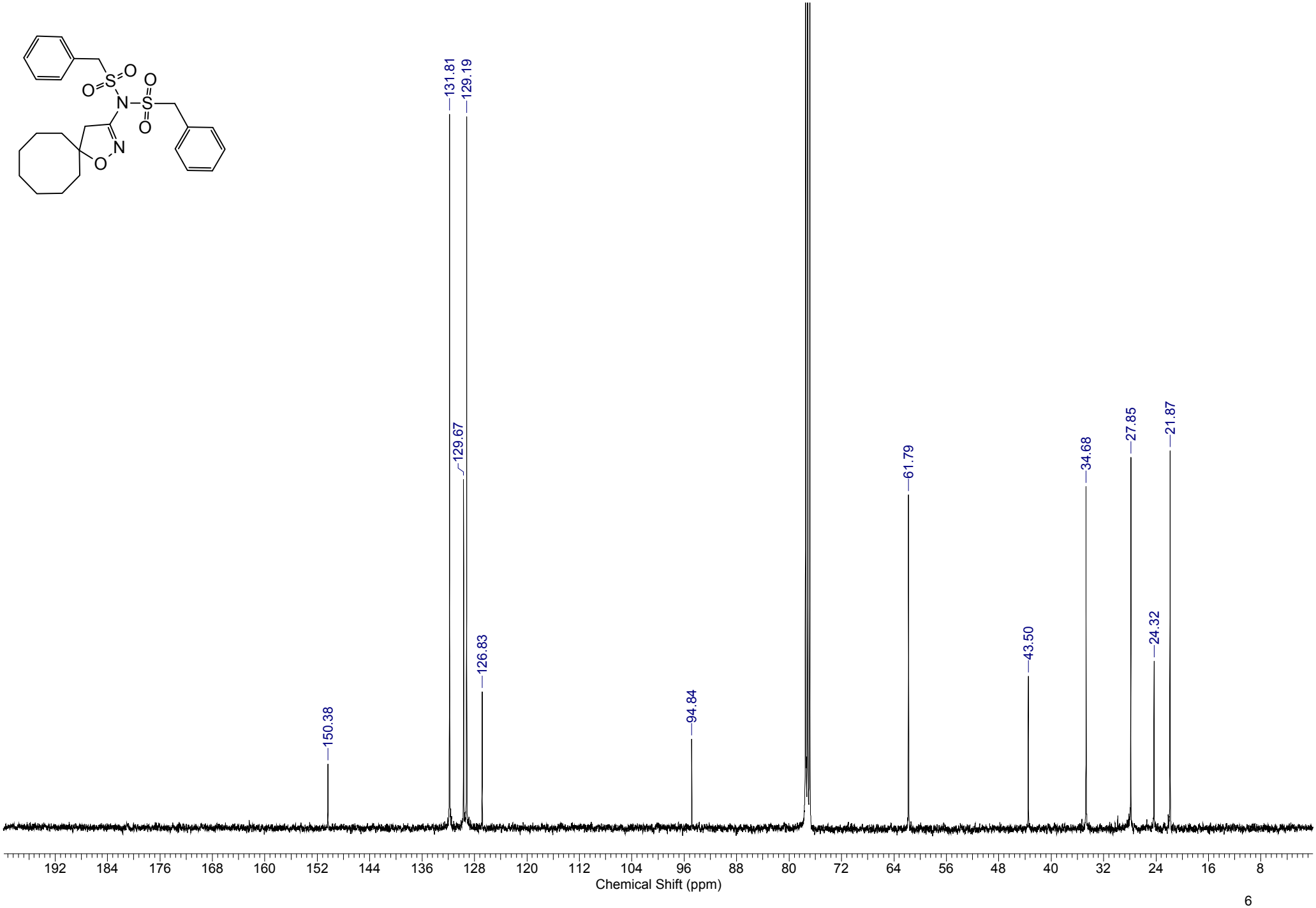
^{13}C NMR spectrum of compound **4a** ($CDCl_3$)



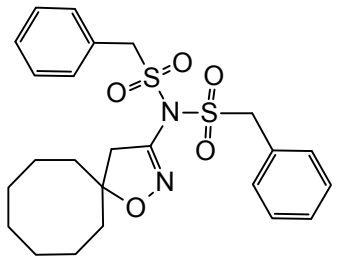
^{1}H NMR spectrum of compound **4b** ($CDCl_3$)

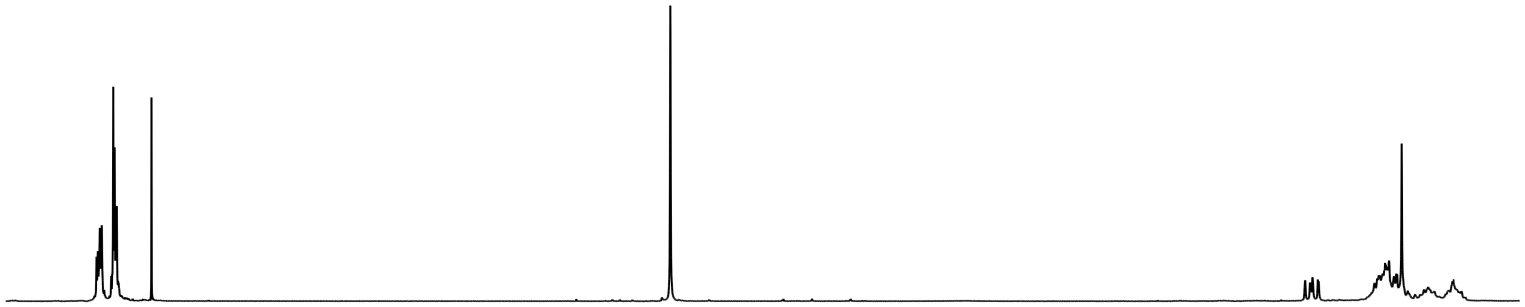


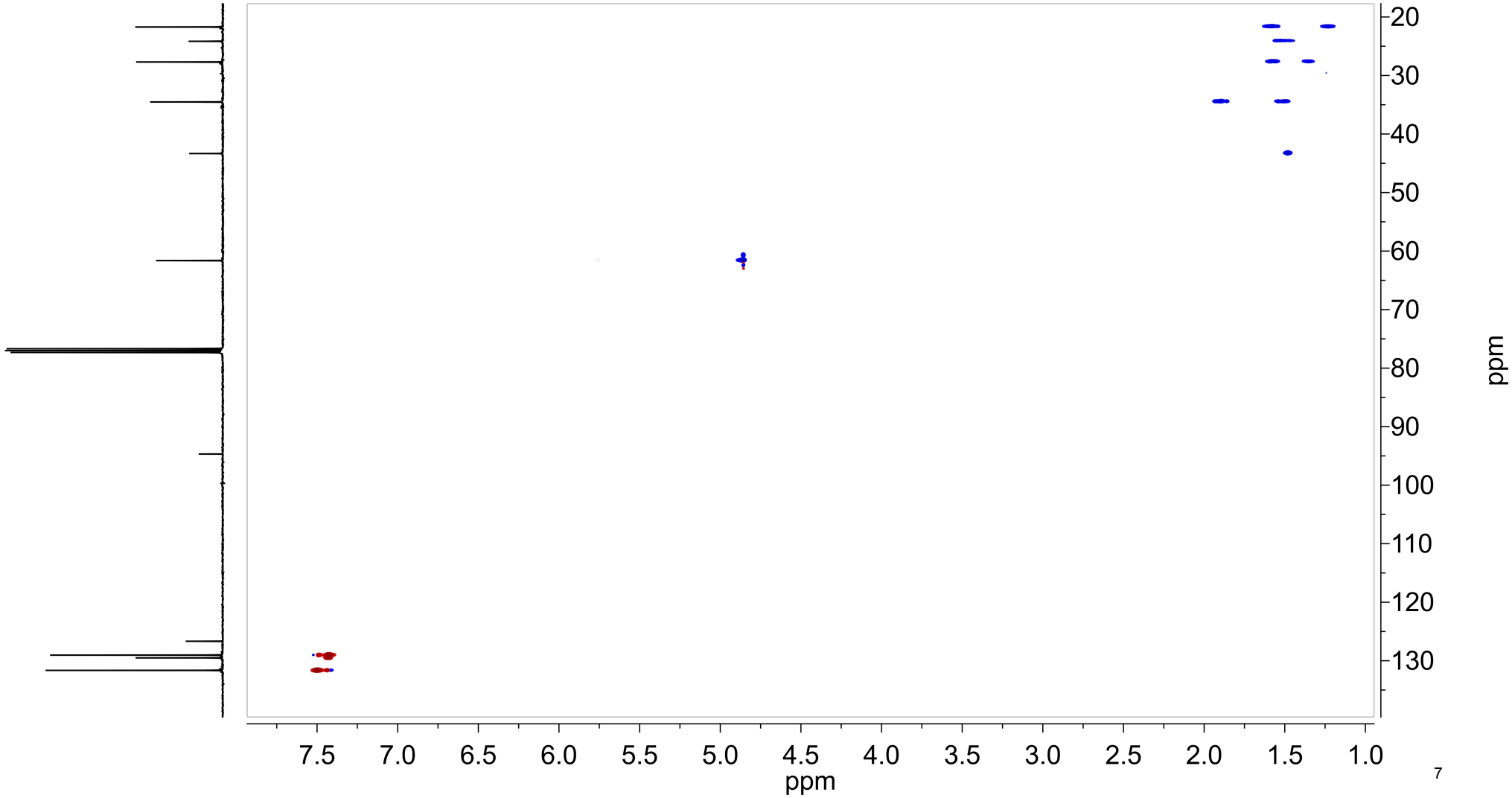
^{13}C NMR spectrum of compound **4b** ($CDCl_3$)



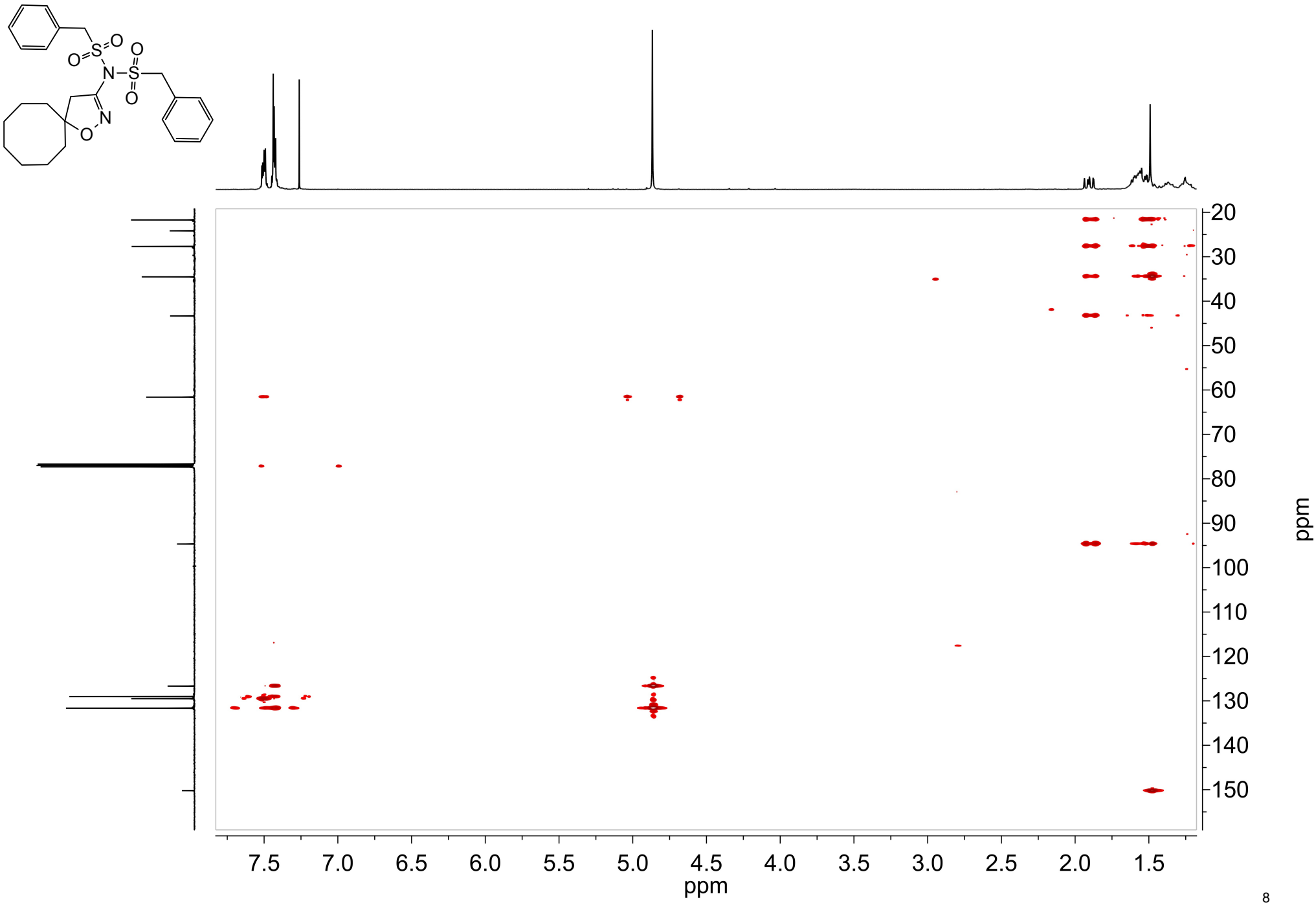
HSQC NMR spectrum of compound **4b** ($CDCl_3$)



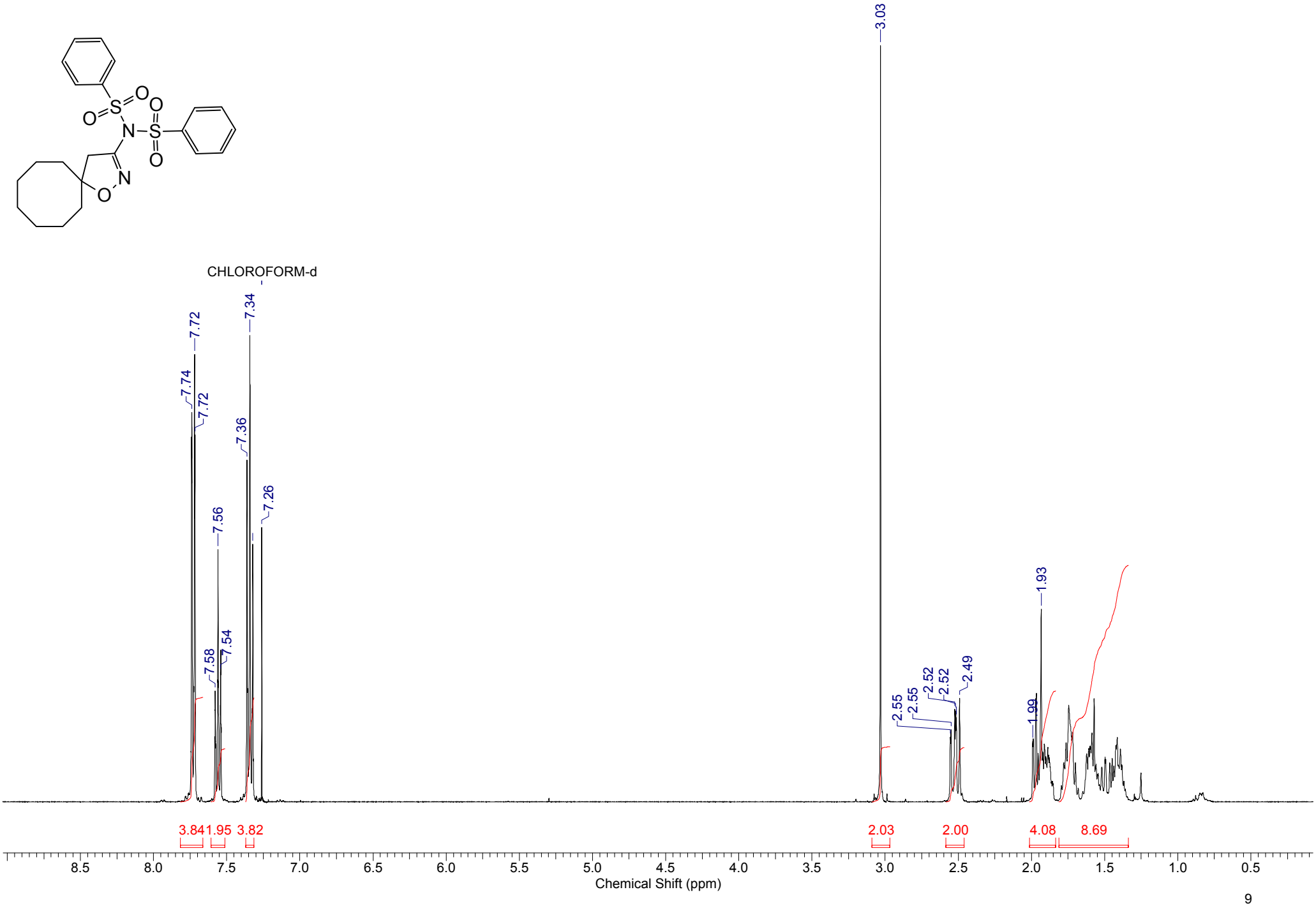




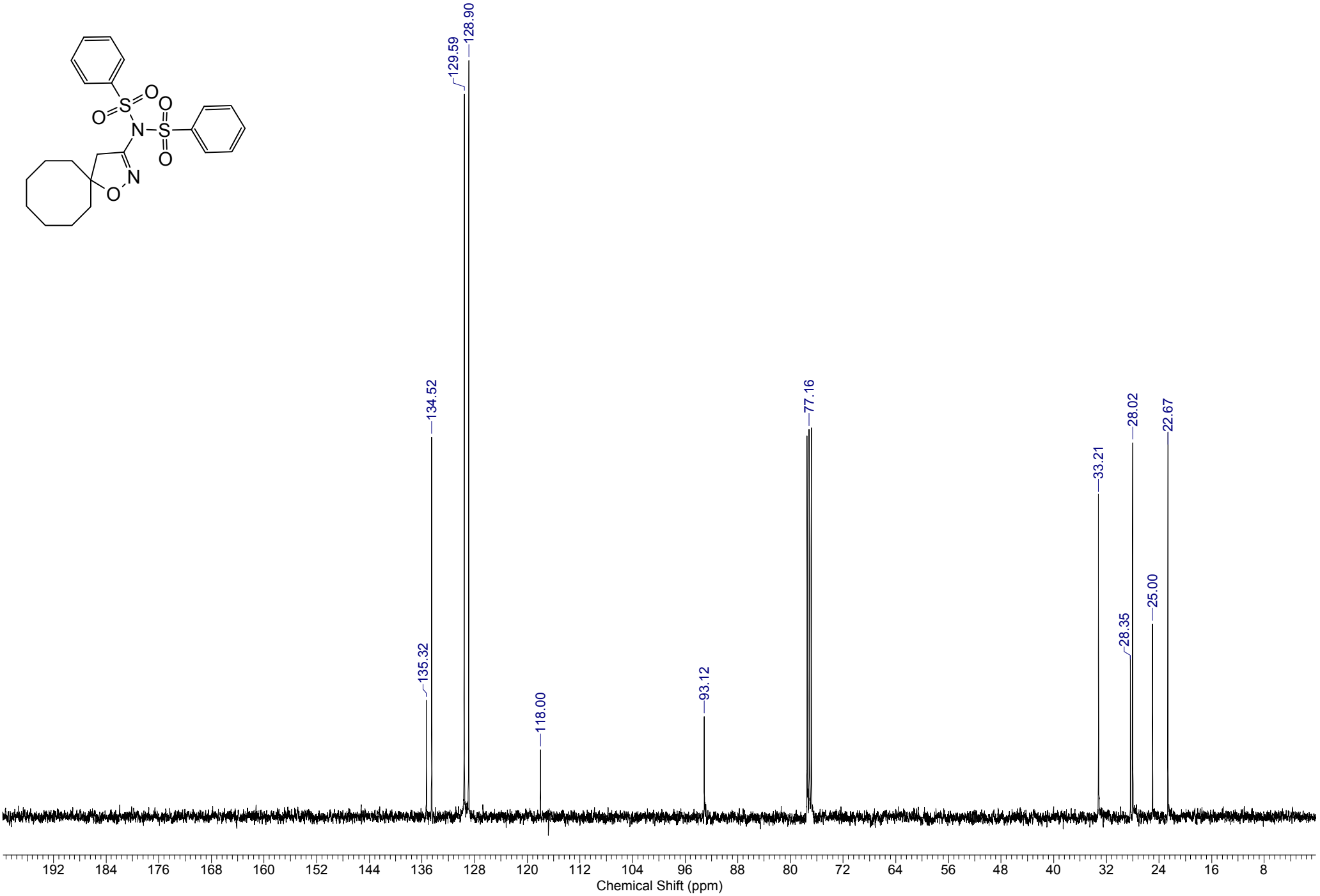
HMBC NMR spectrum of compound **4b** ($CDCl_3$)



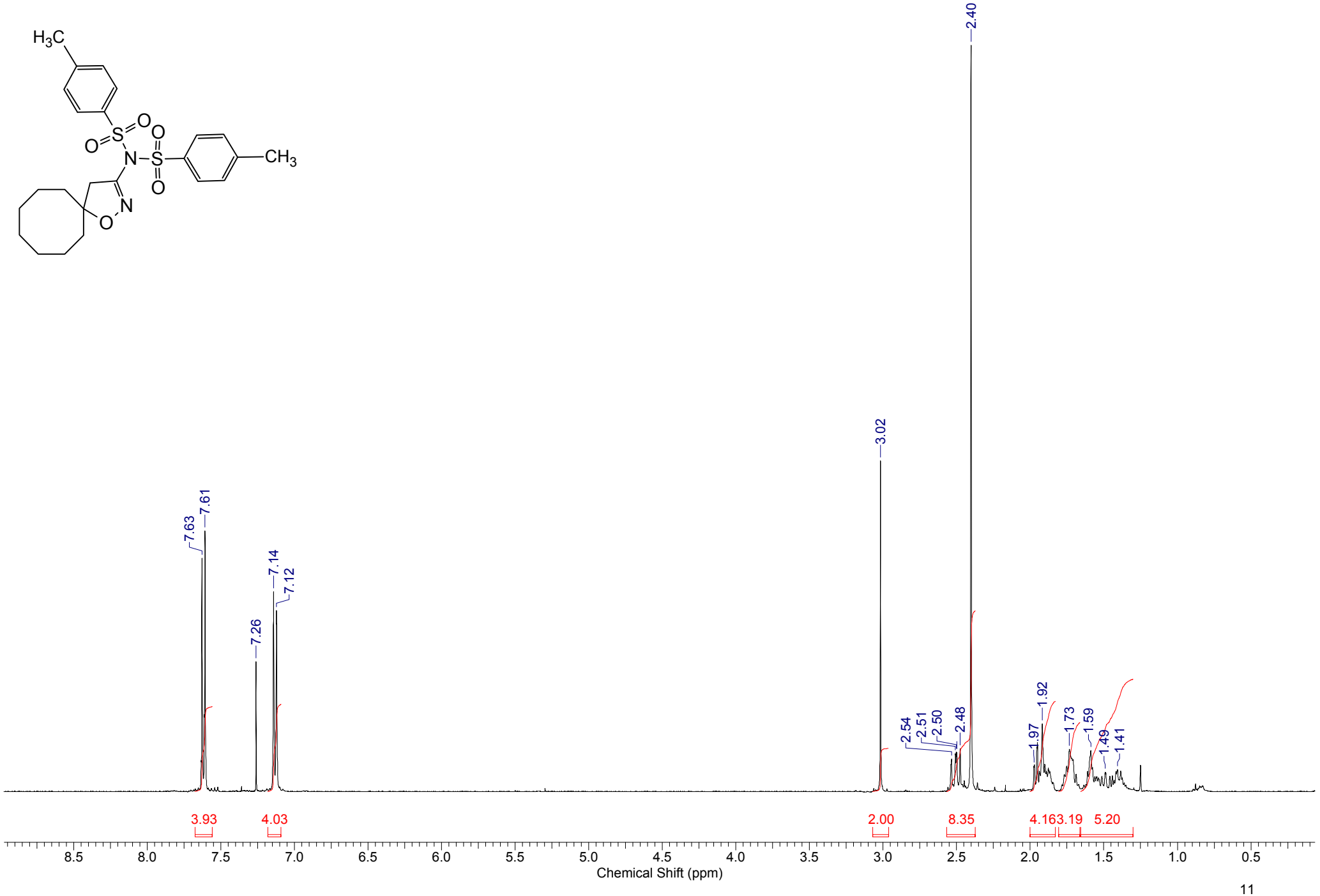
^{1}H NMR spectrum of compound **4c** ($CDCl_3$)



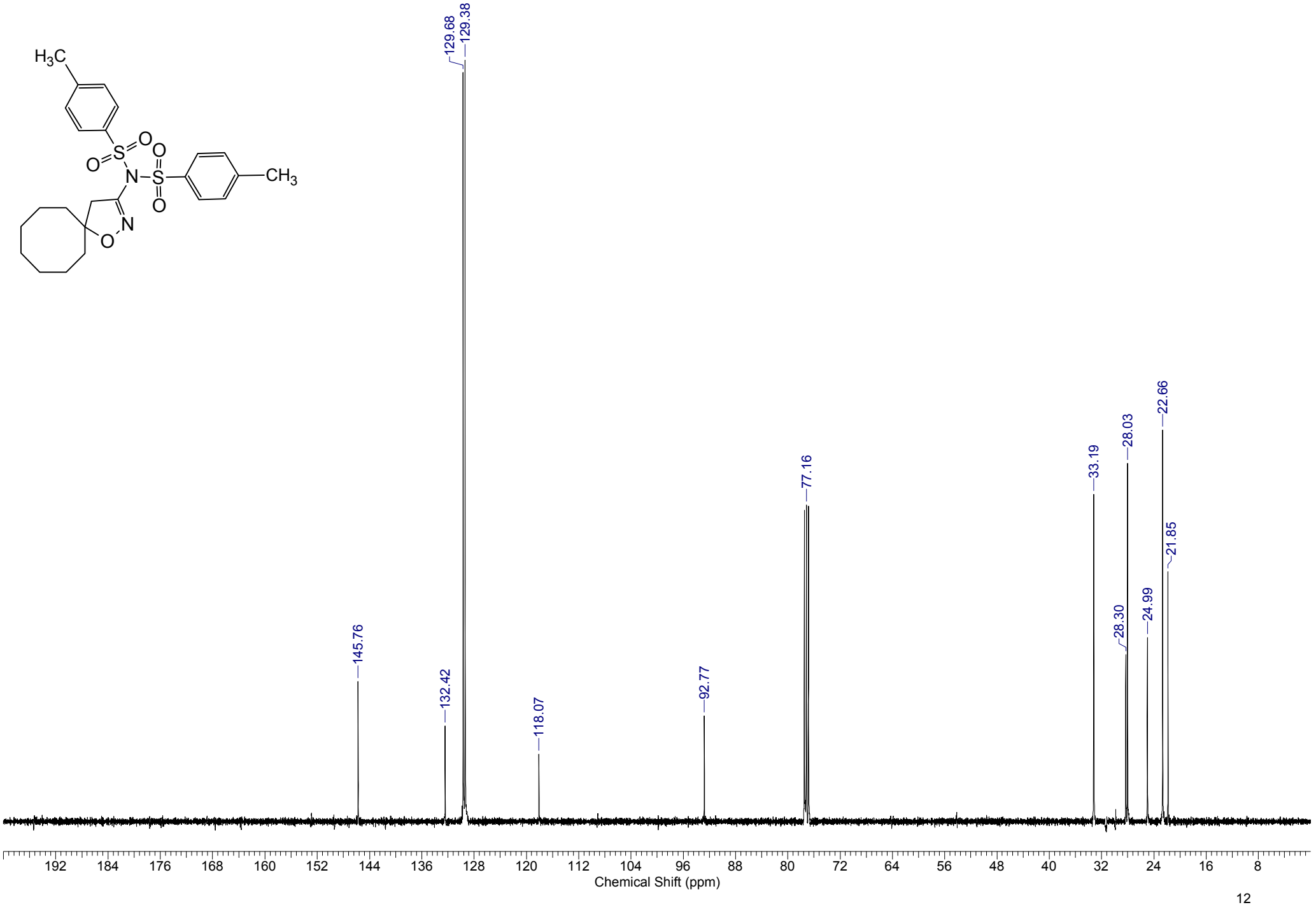
^{13}C NMR spectrum of compound **4c** ($CDCl_3$)



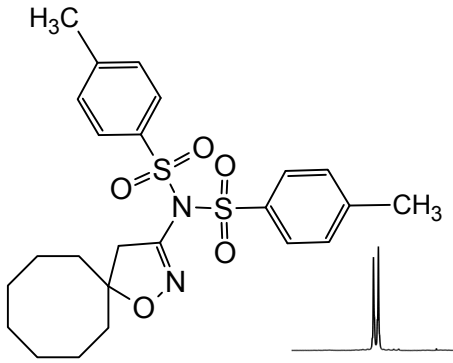
^{1}H NMR spectrum of compound **4d** ($CDCl_3$)

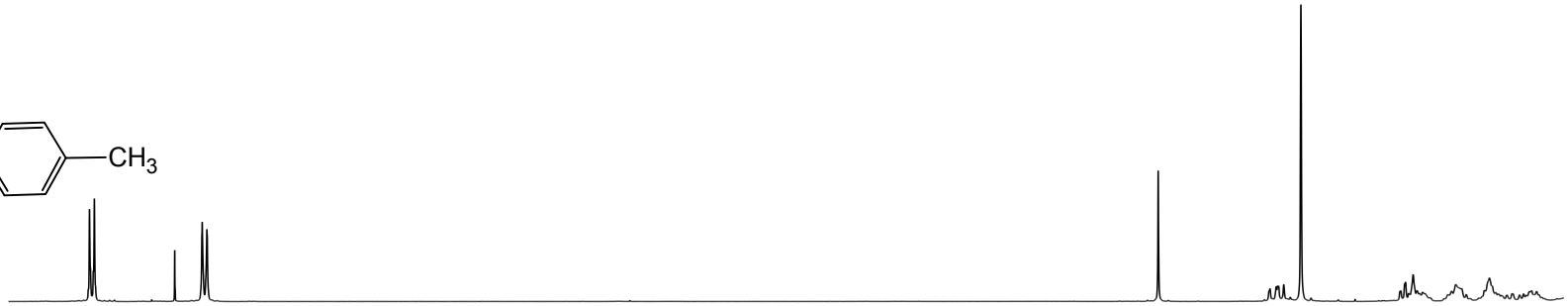


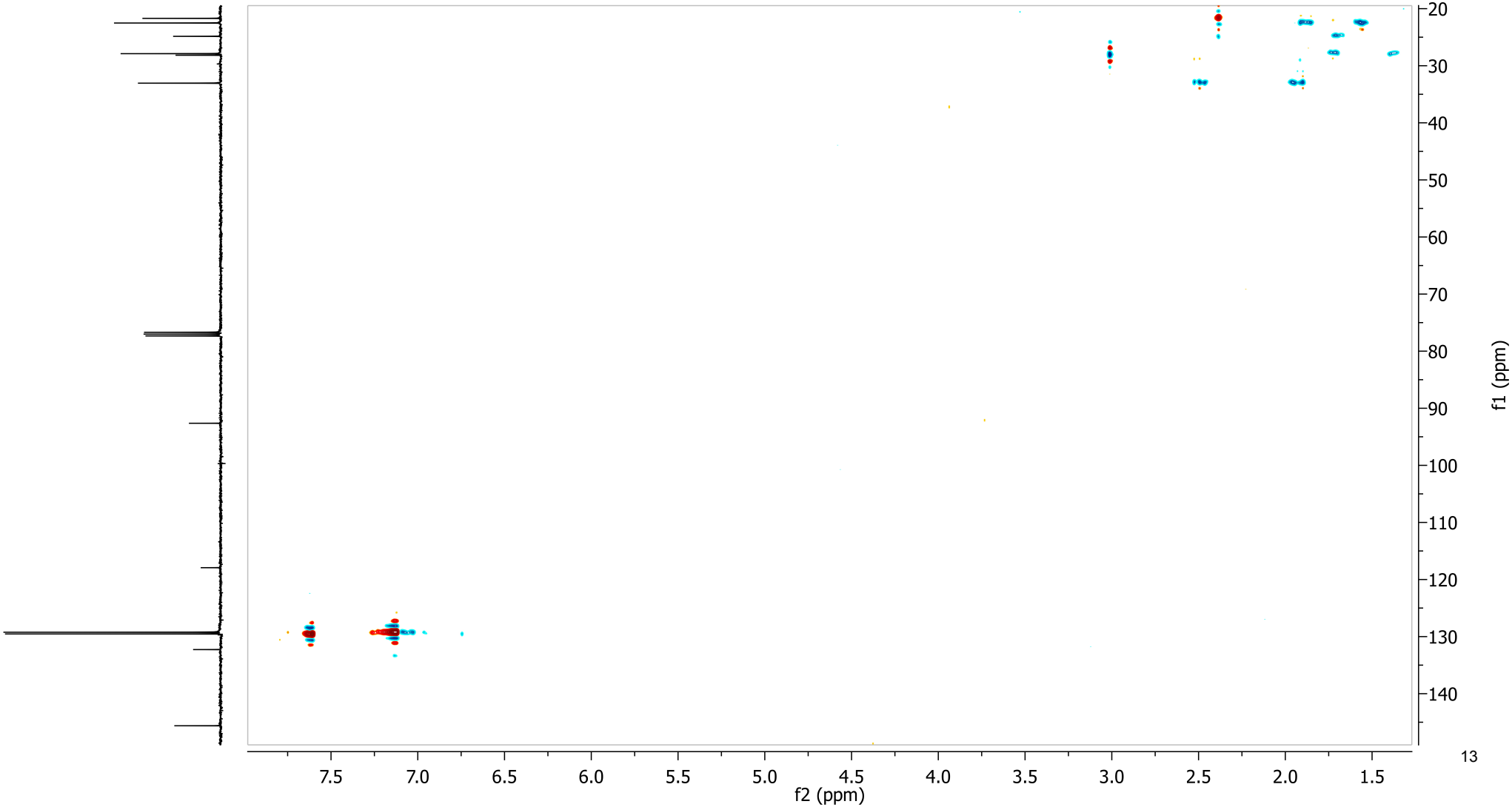
^{13}C NMR spectrum of compound **4d** ($CDCl_3$)



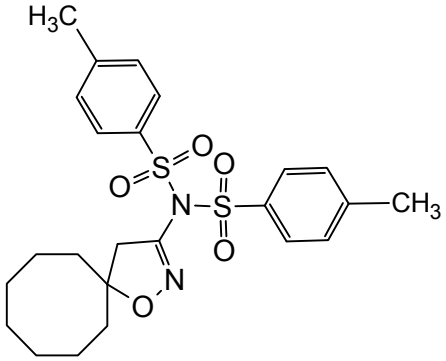
HSQC NMR spectrum of compound **4d** ($CDCl_3$)

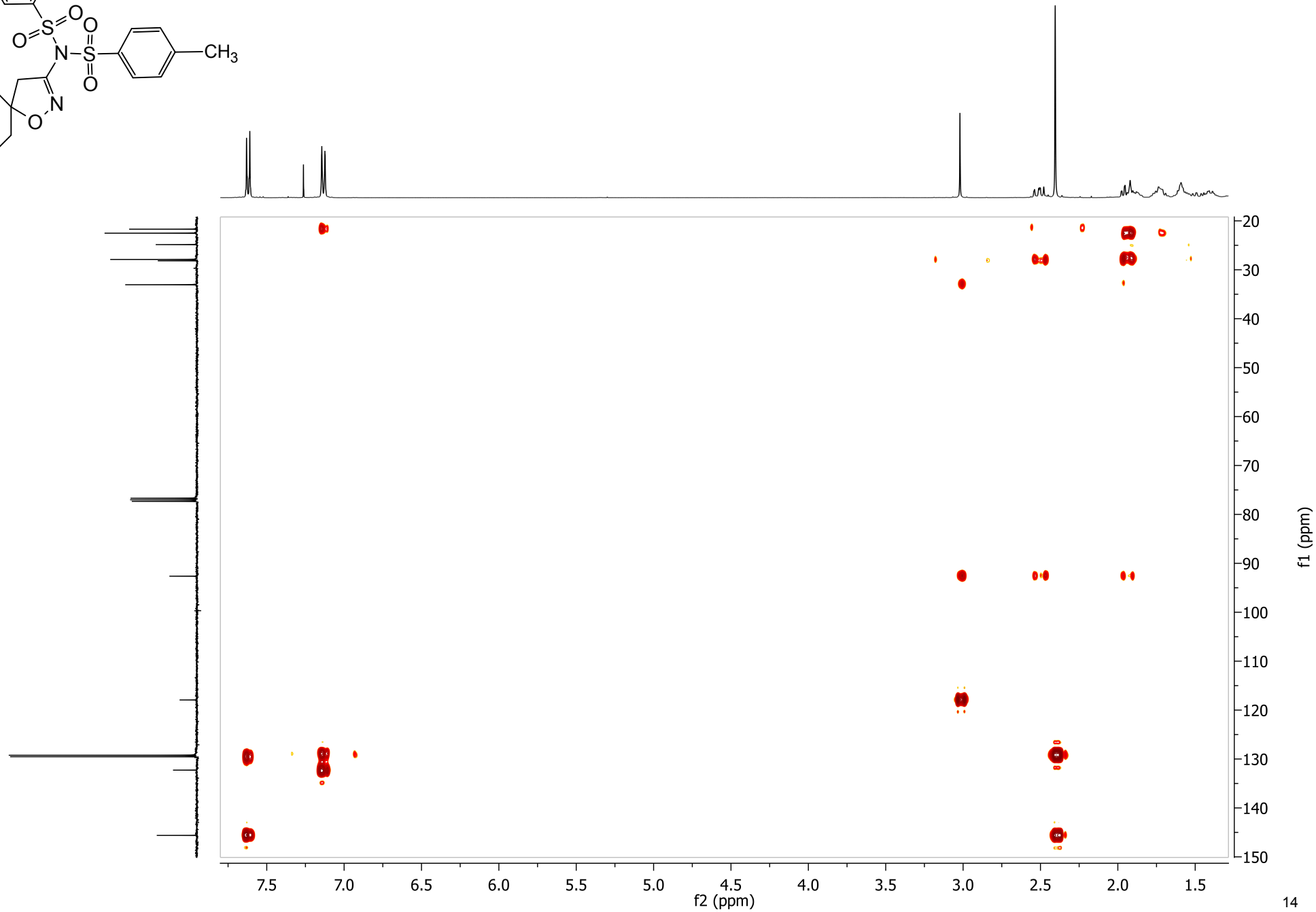




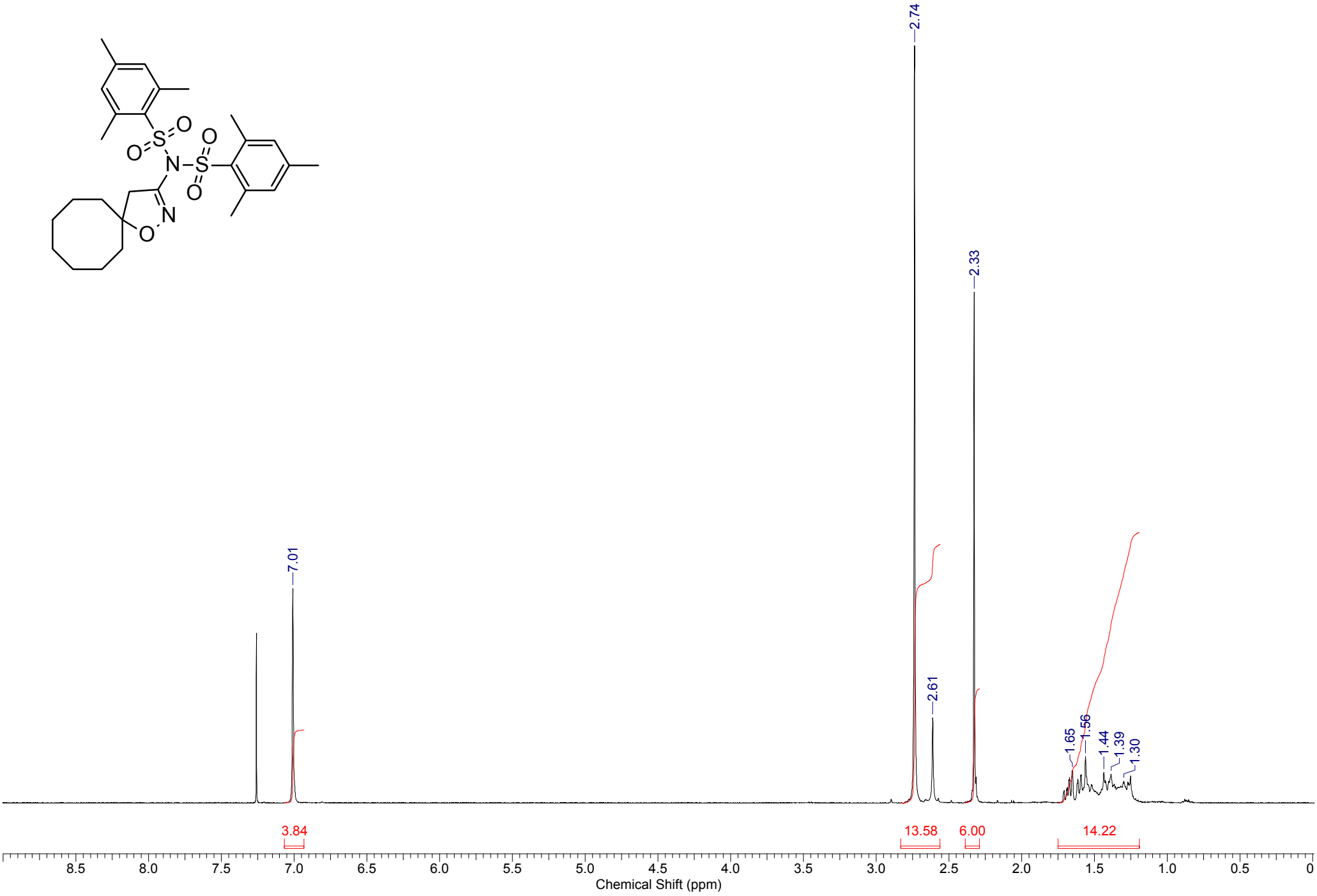


HMBC NMR spectrum of compound **4d** ($CDCl_3$)

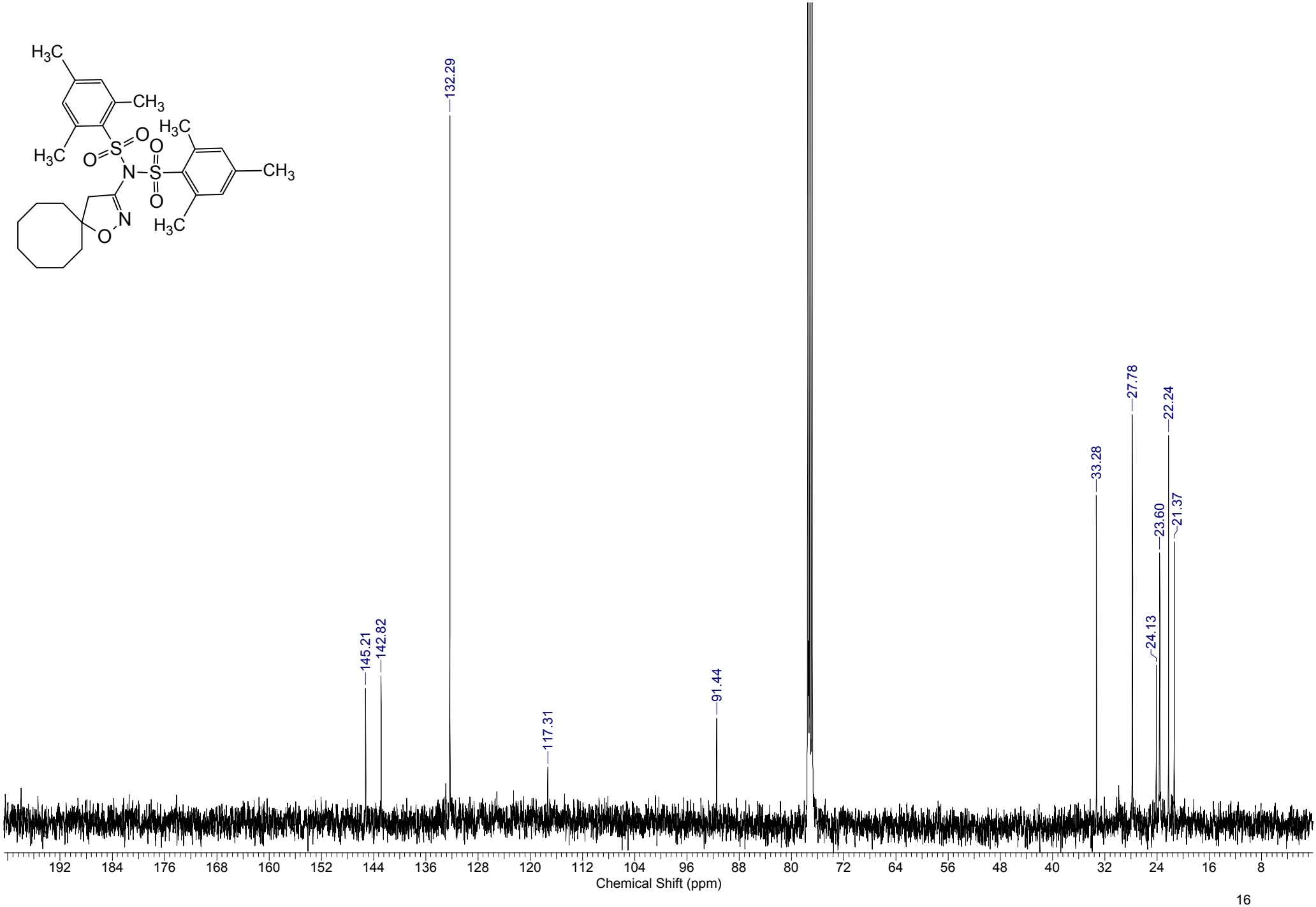




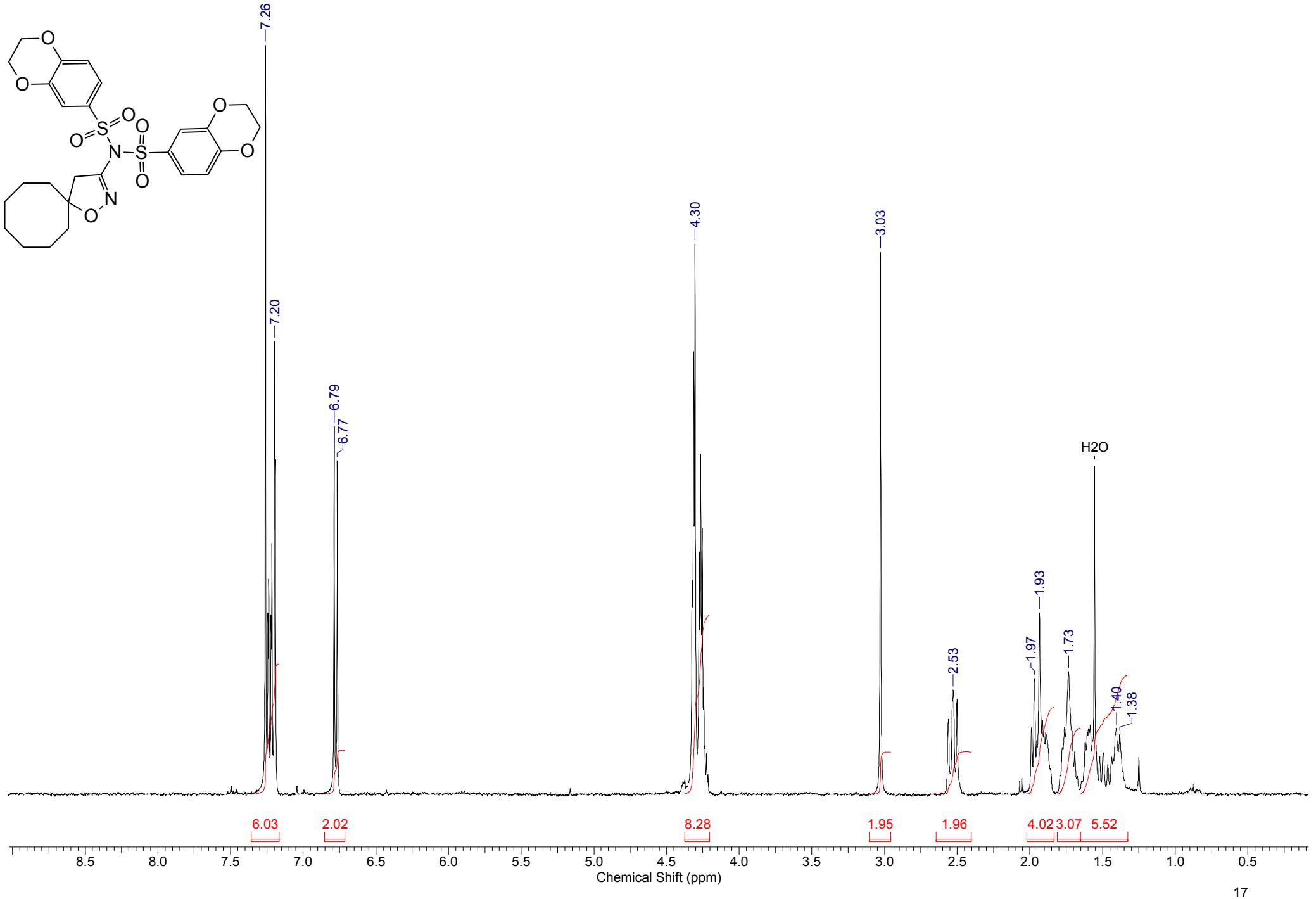
^{1}H NMR spectrum of compound **4e** ($CDCl_3$)



^{13}C NMR spectrum of compound **4e** ($CDCl_3$)

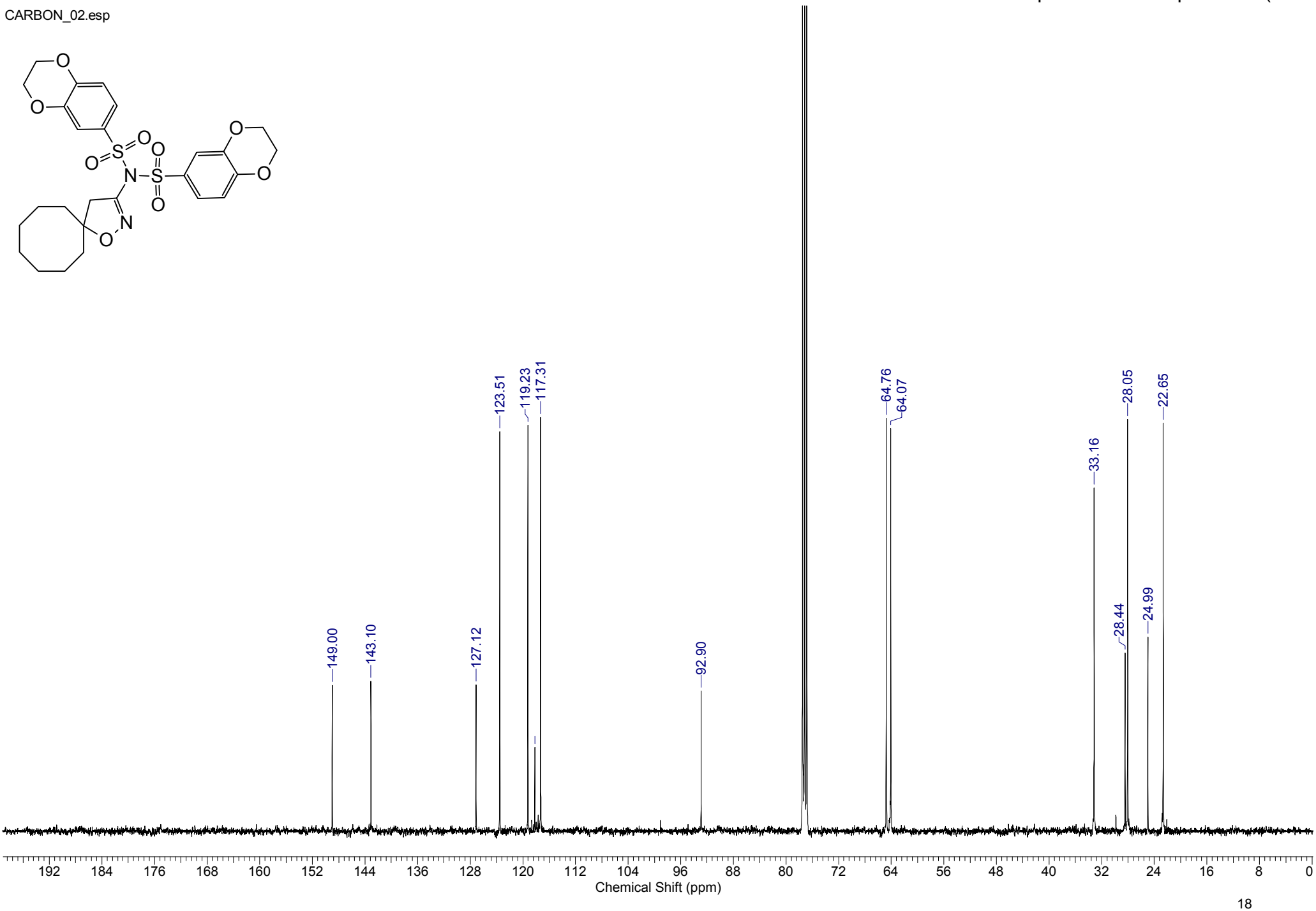


^{1}H NMR spectrum of compound **4f** ($CDCl_3$)

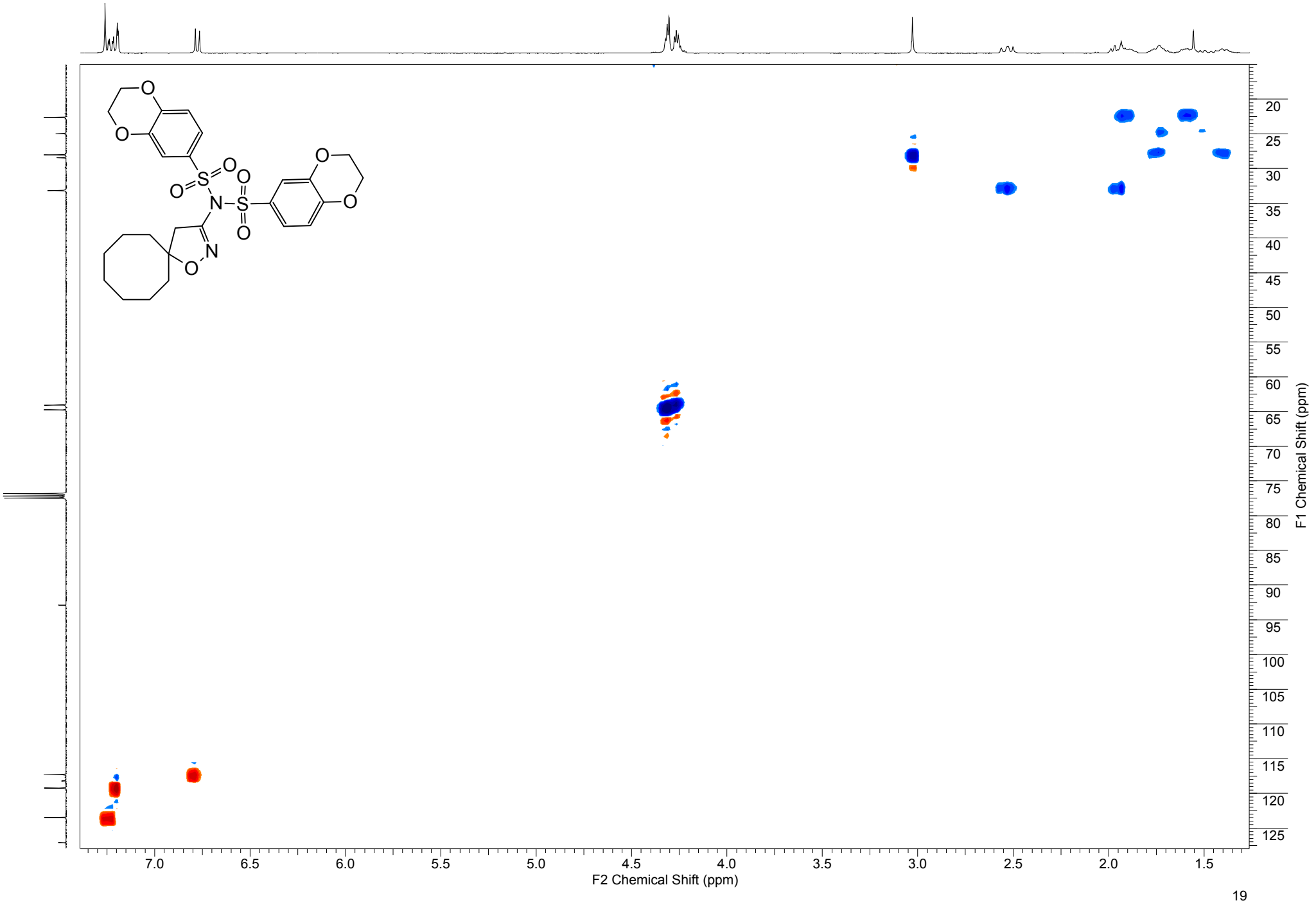


^{13}C NMR spectrum of compound **4f** ($CDCl_3$)

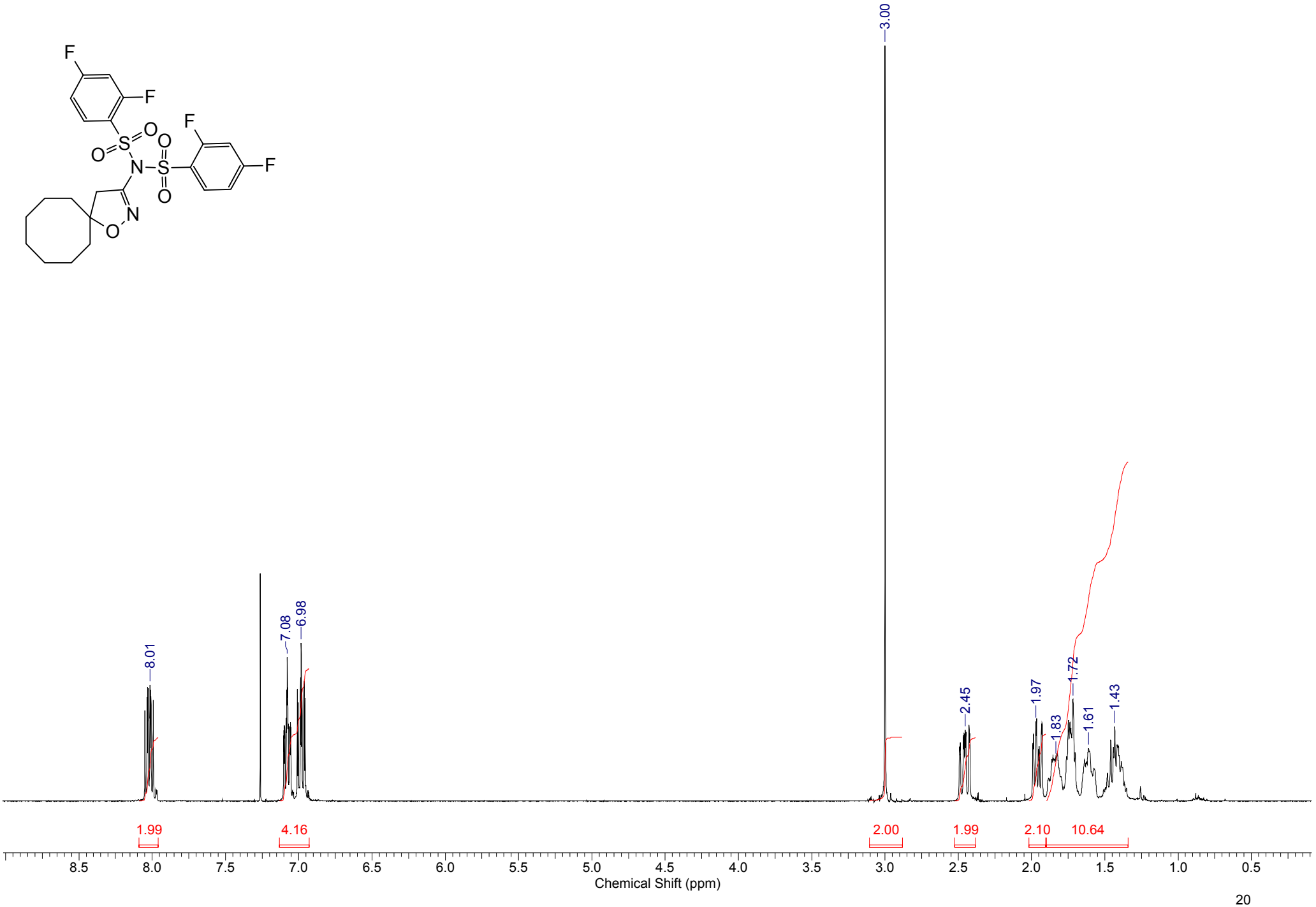
CARBON_02.esp



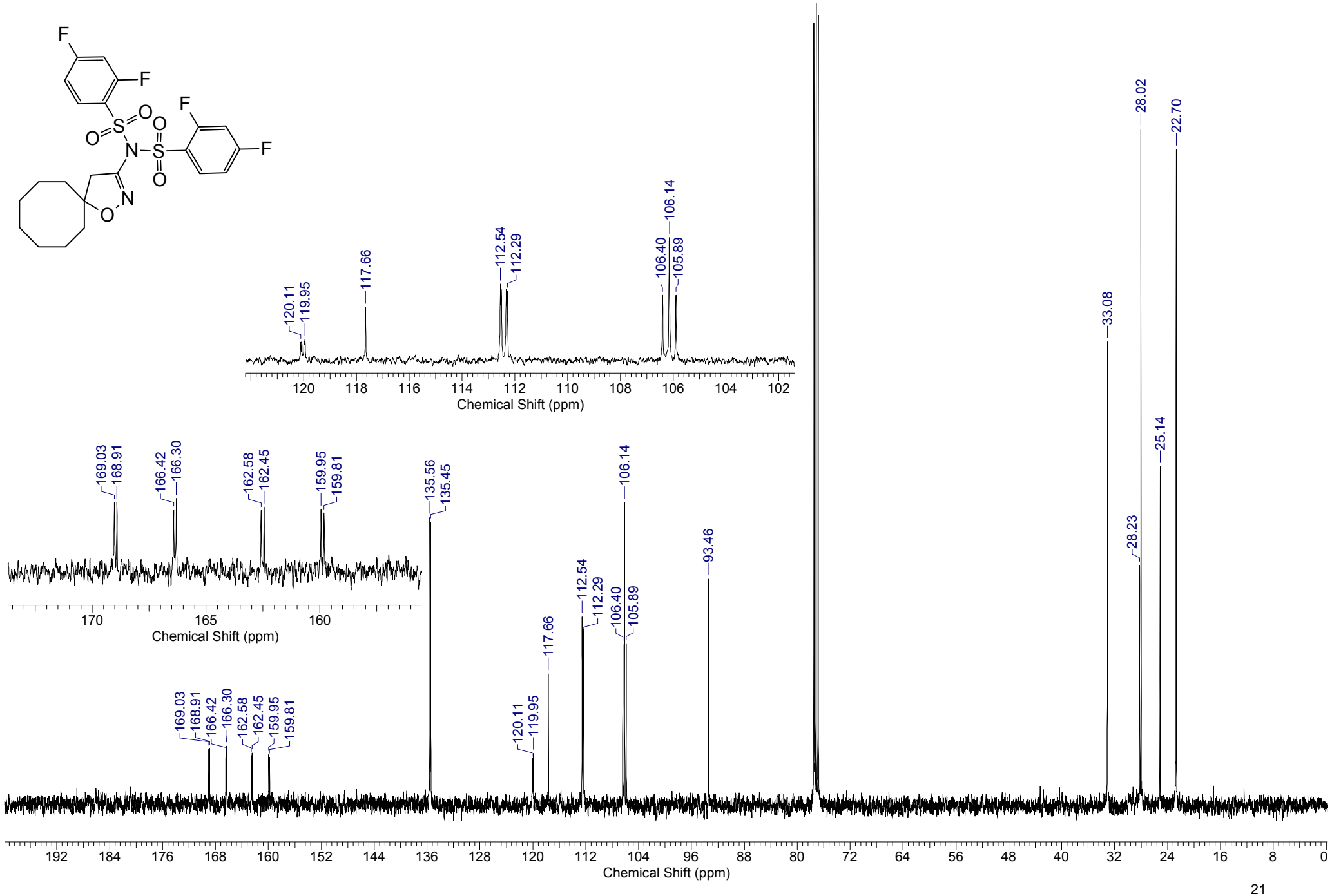
HSQC NMR spectrum of compound **4f** ($CDCl_3$)



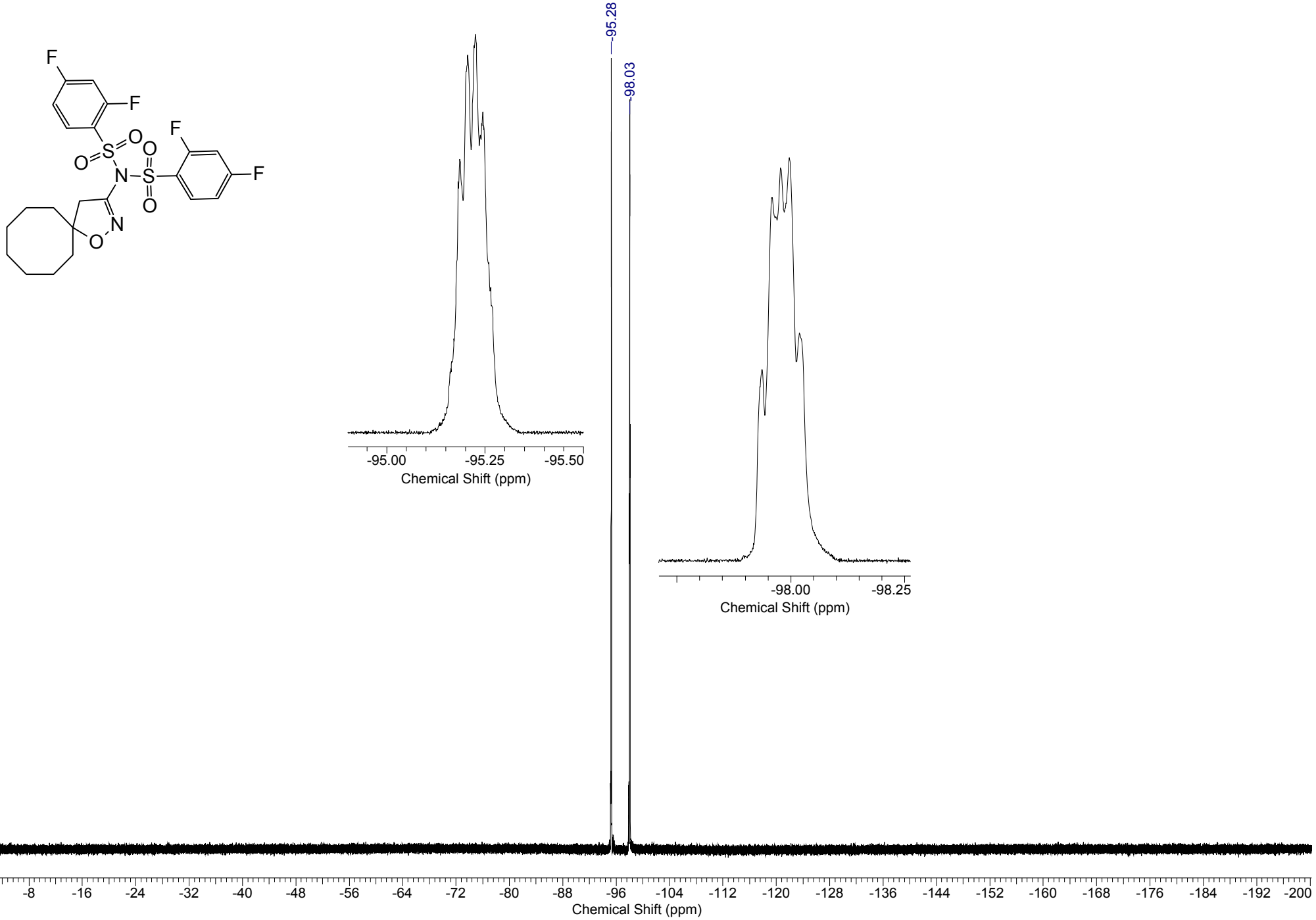
^{1}H NMR spectrum of compound **4g** ($CDCl_3$)



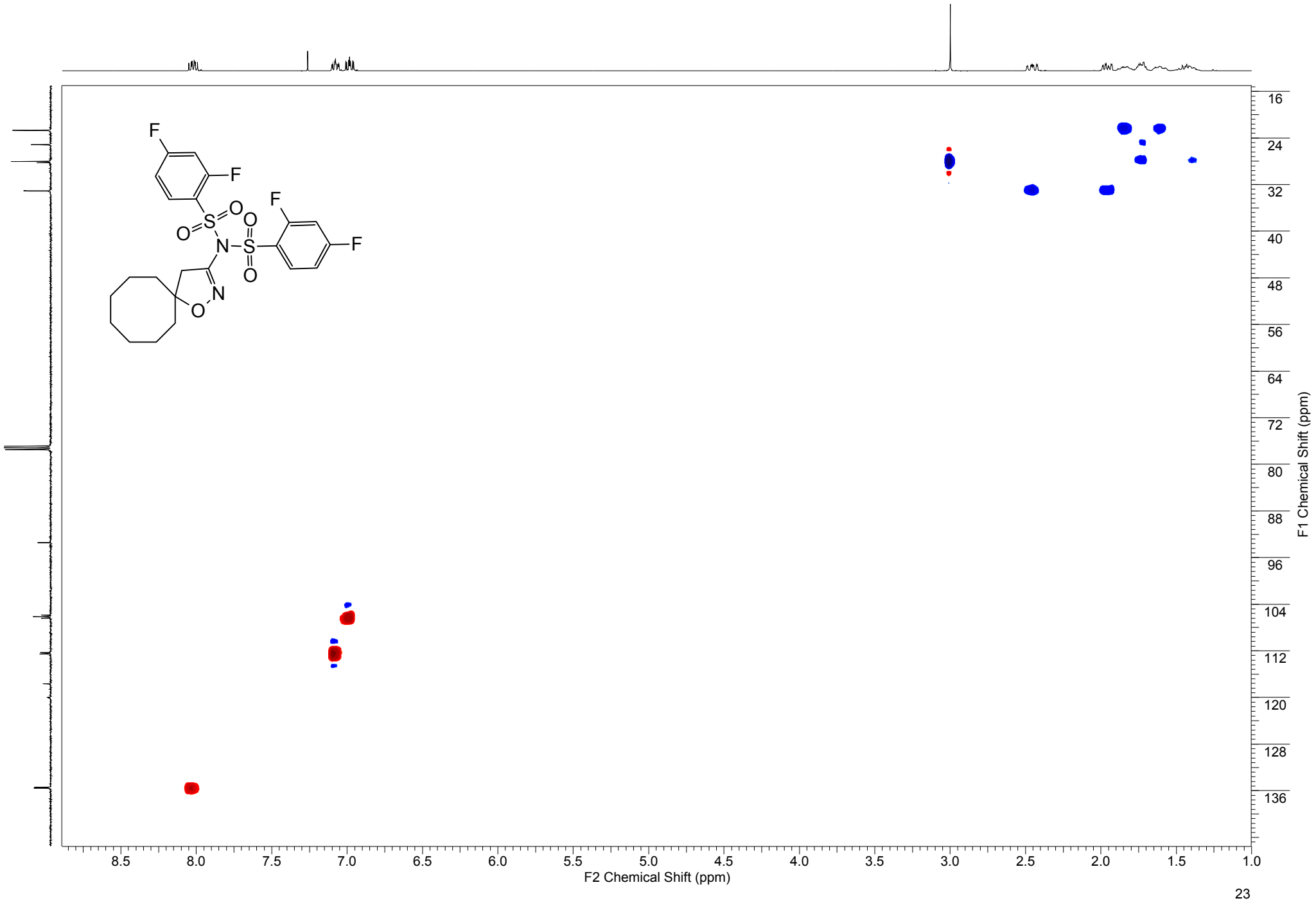
^{13}C NMR spectrum of compound **4g** ($CDCl_3$)



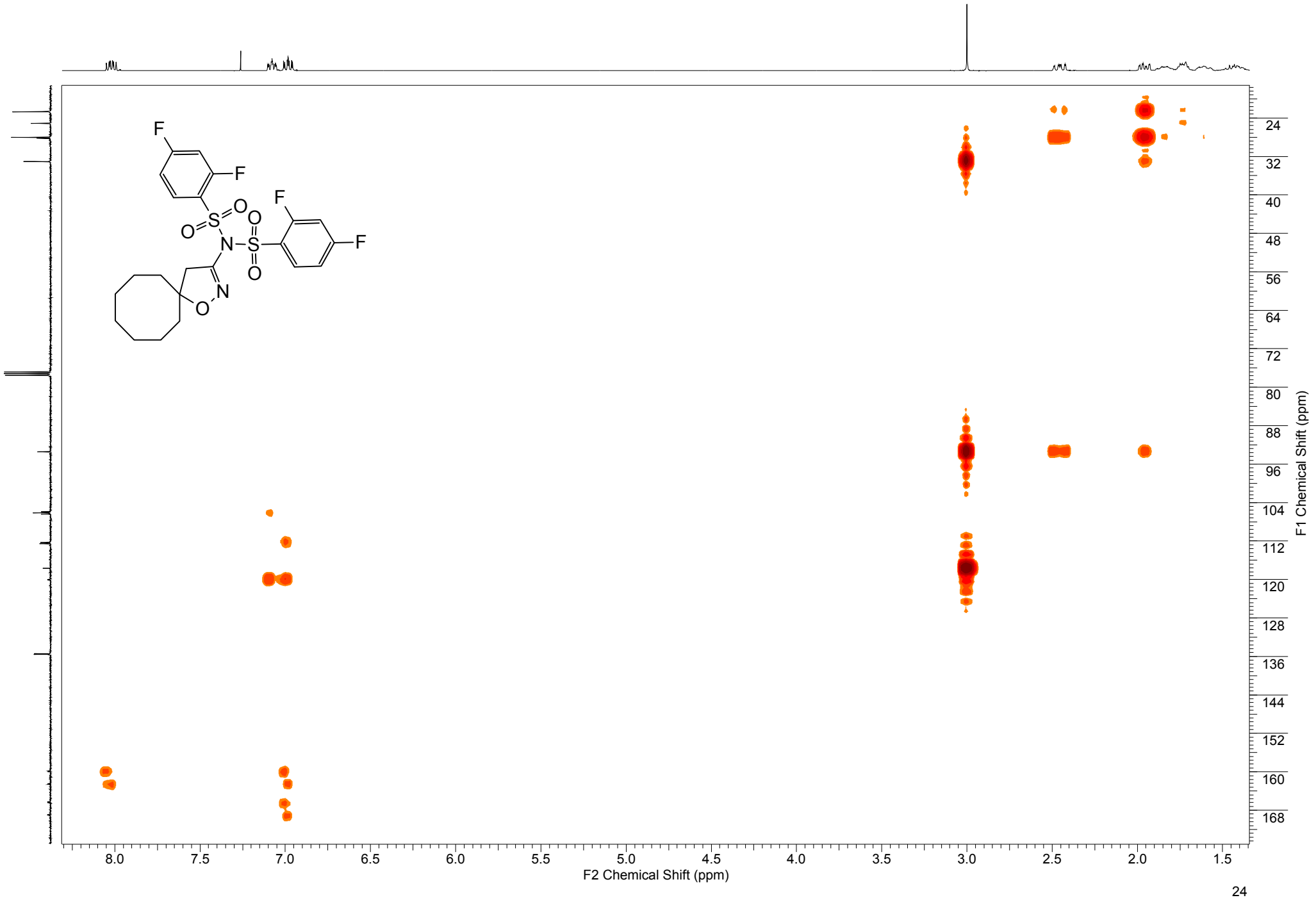
^{19}F NMR spectrum of compound **4g** ($CDCl_3$)



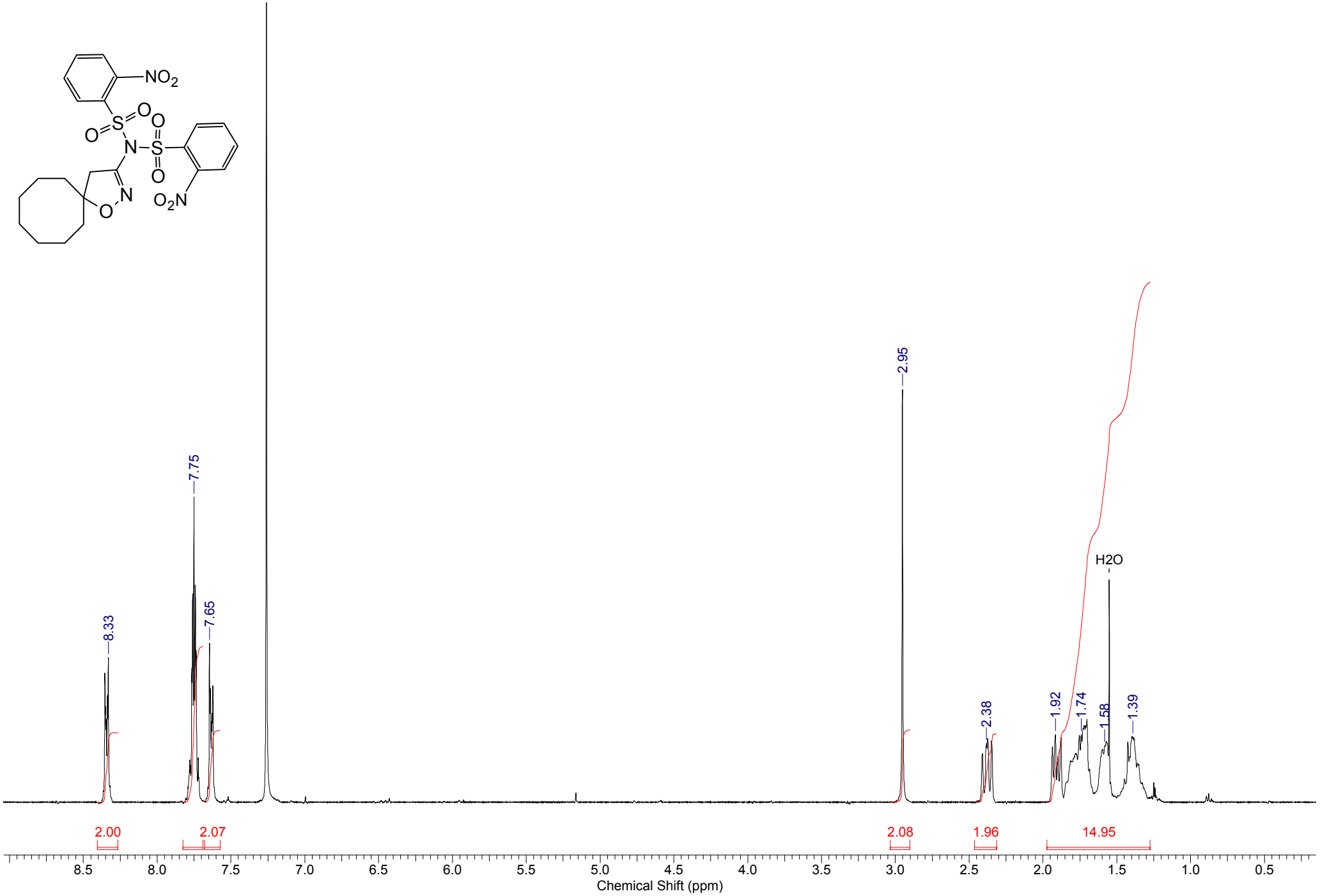
HSQC NMR spectrum of compound **4g** ($CDCl_3$)



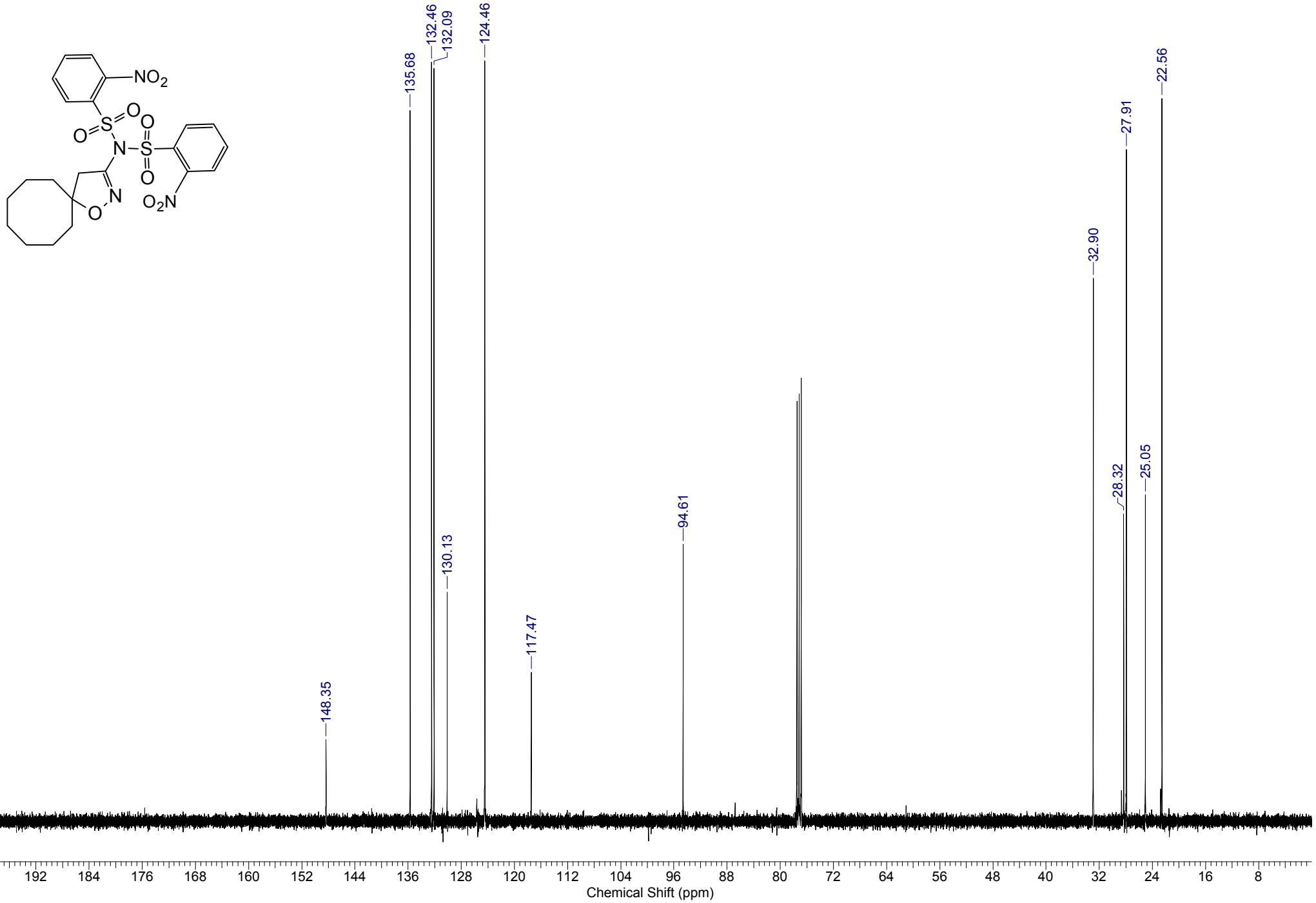
HMBC NMR spectrum of compound **4g** ($CDCl_3$)



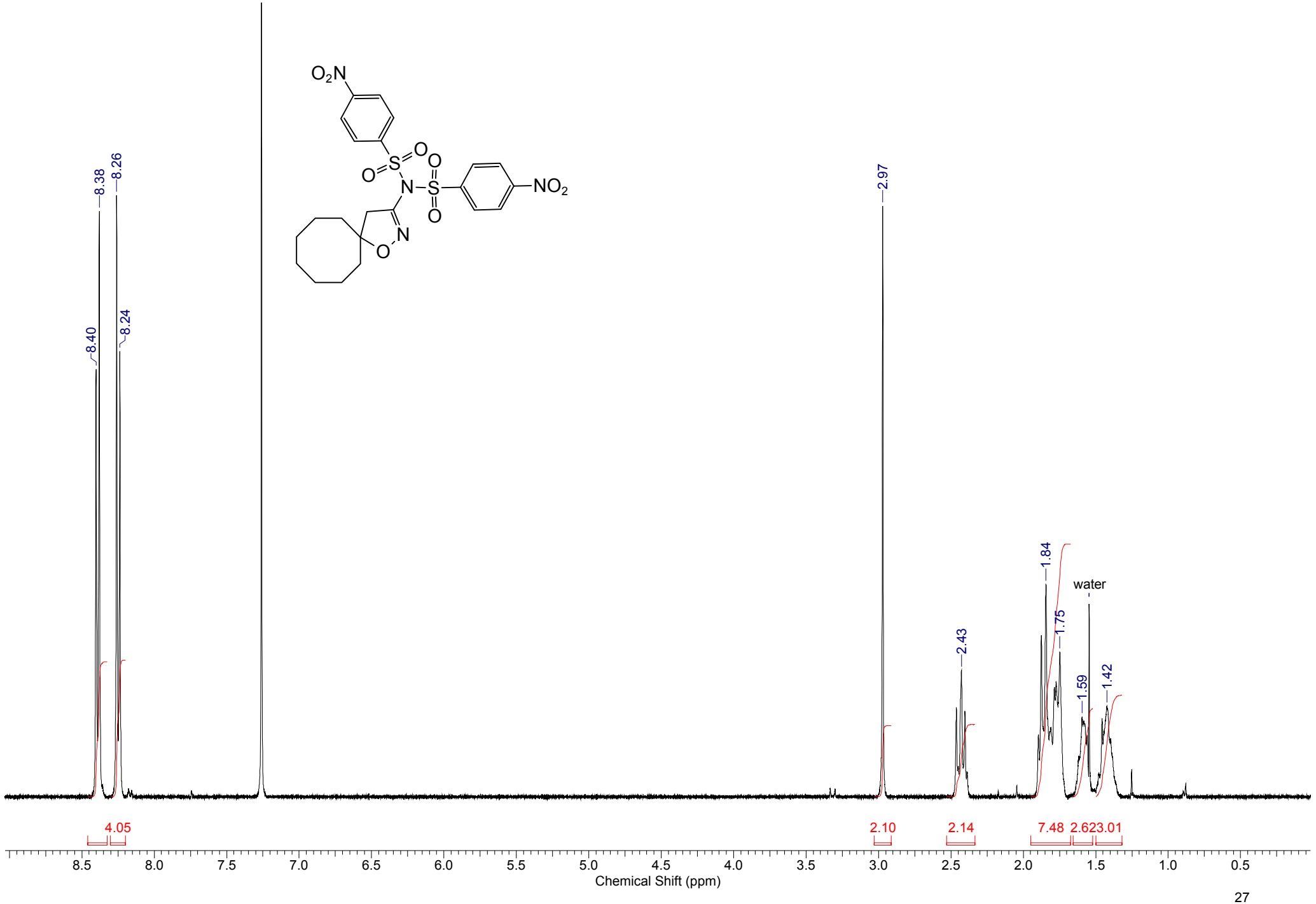
^{1}H NMR spectrum of compound **4h** ($CDCl_3$)



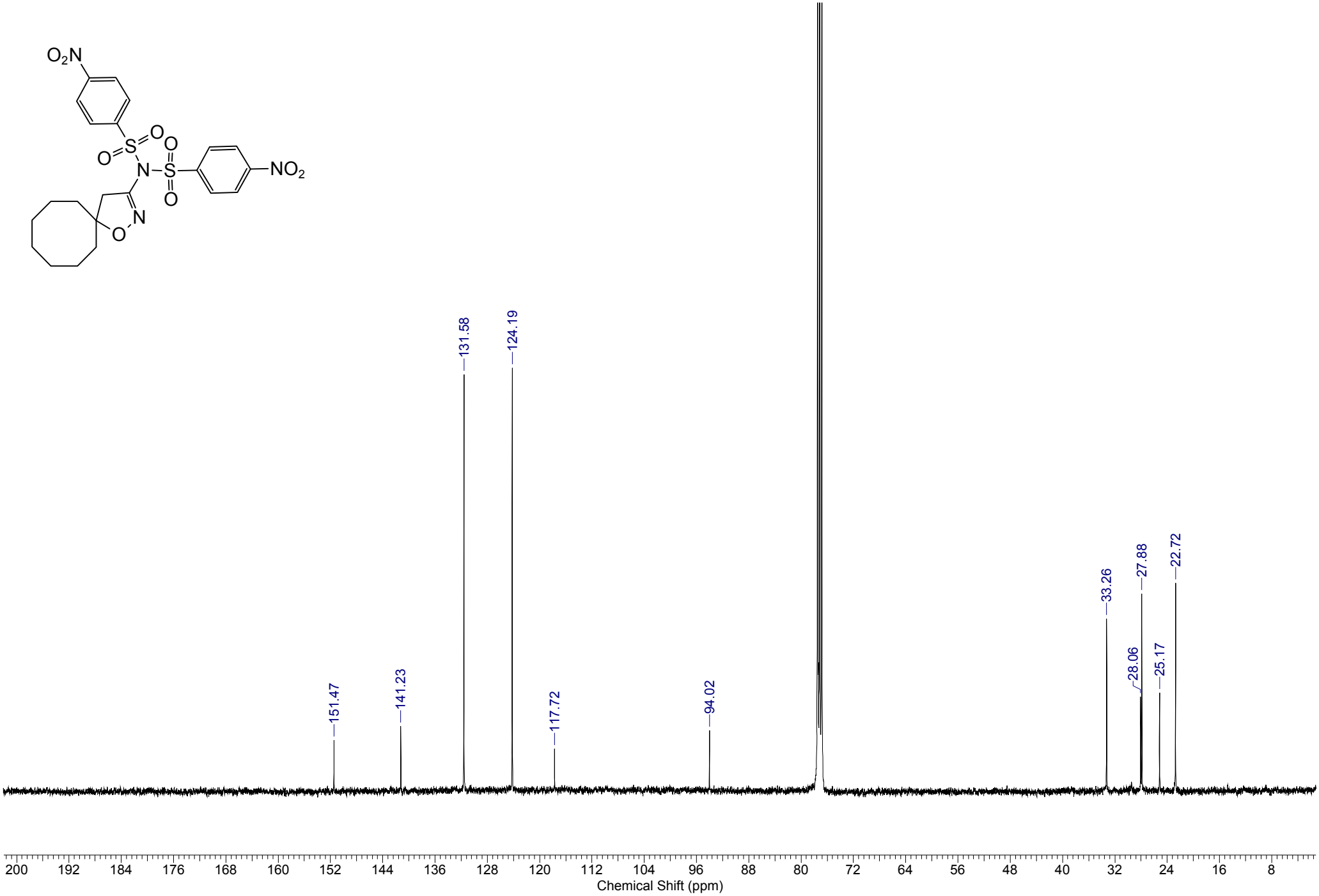
^{13}C NMR spectrum of compound **4h** ($CDCl_3$)



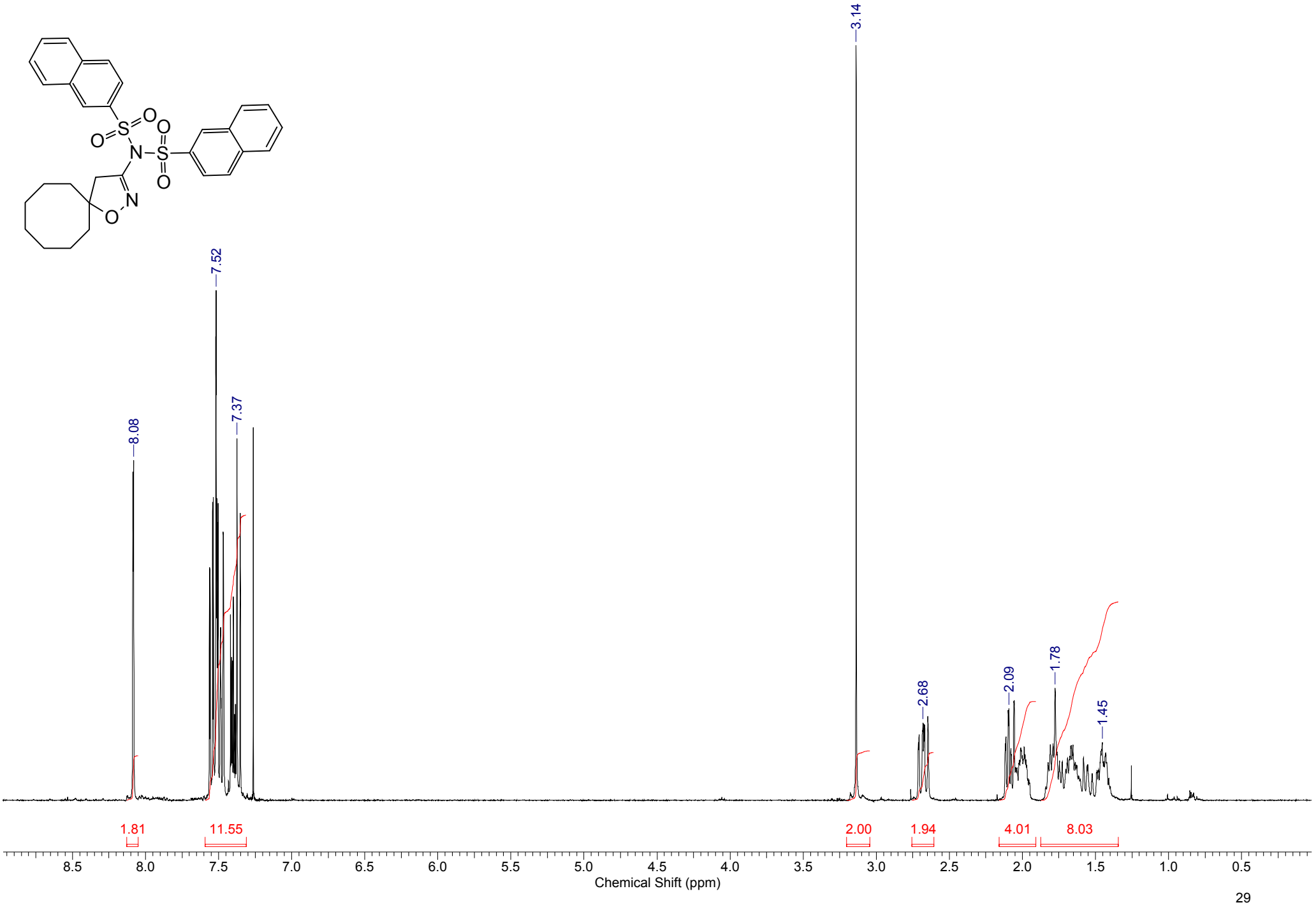
^{1}H NMR spectrum of compound **4i** ($CDCl_3$)



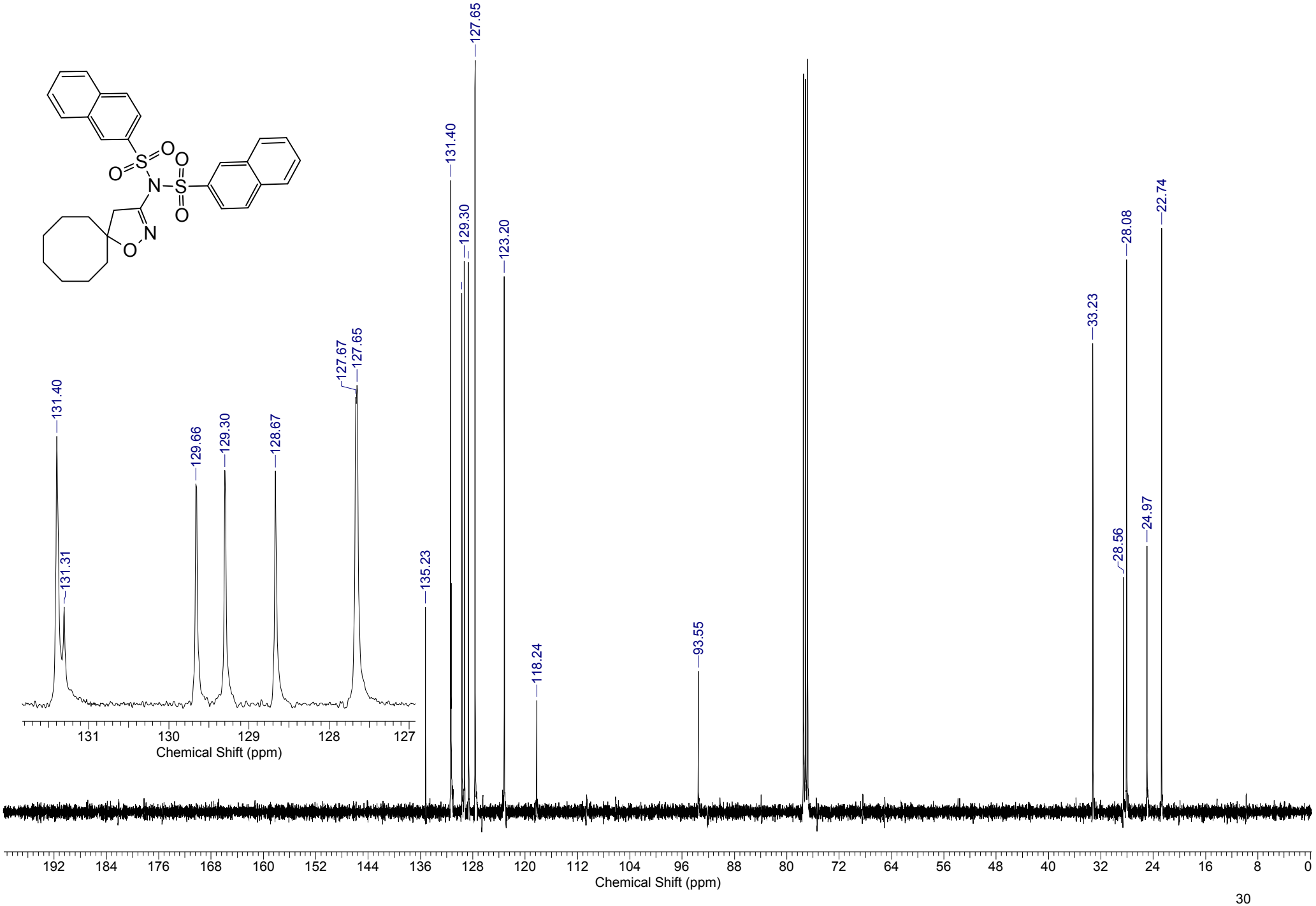
^{13}C NMR spectrum of compound **4i** ($CDCl_3$)



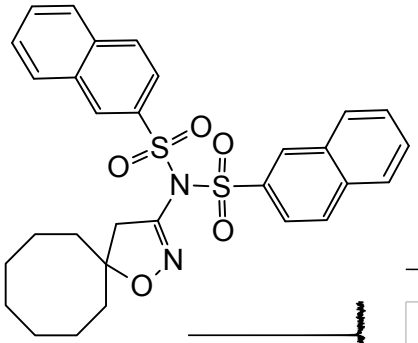
^{1}H NMR spectrum of compound **4j** ($CDCl_3$)

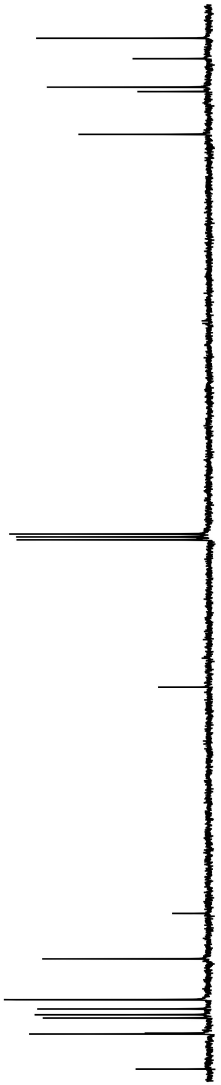


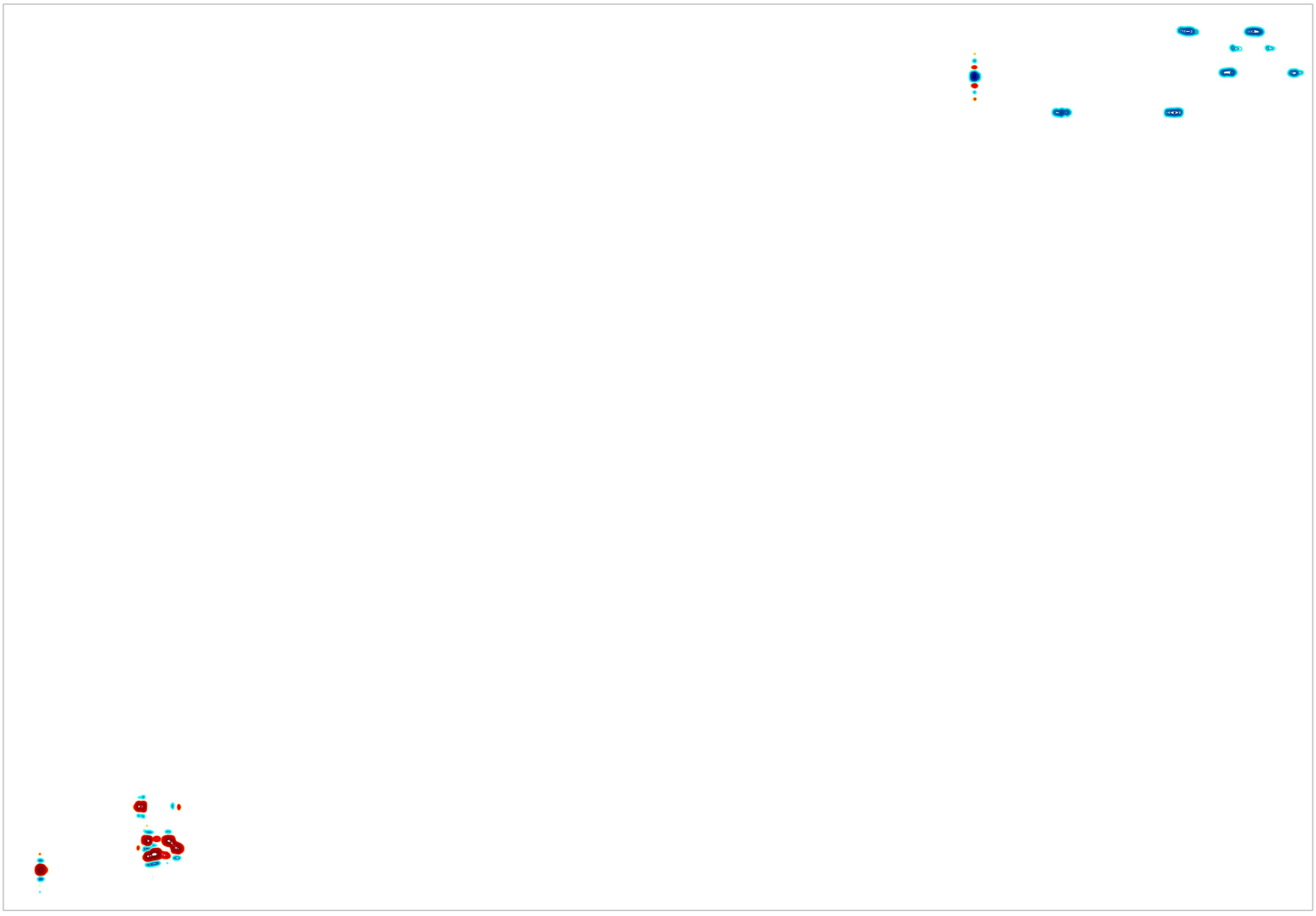
^{13}C NMR spectrum of compound **4j** ($CDCl_3$)



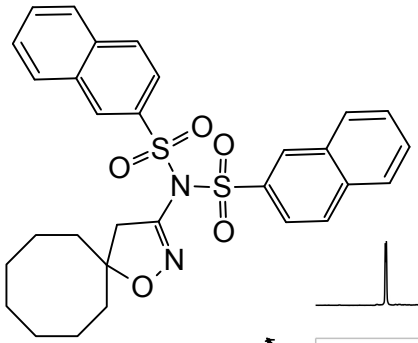
HSQC NMR spectrum of compound **4j** ($CDCl_3$)

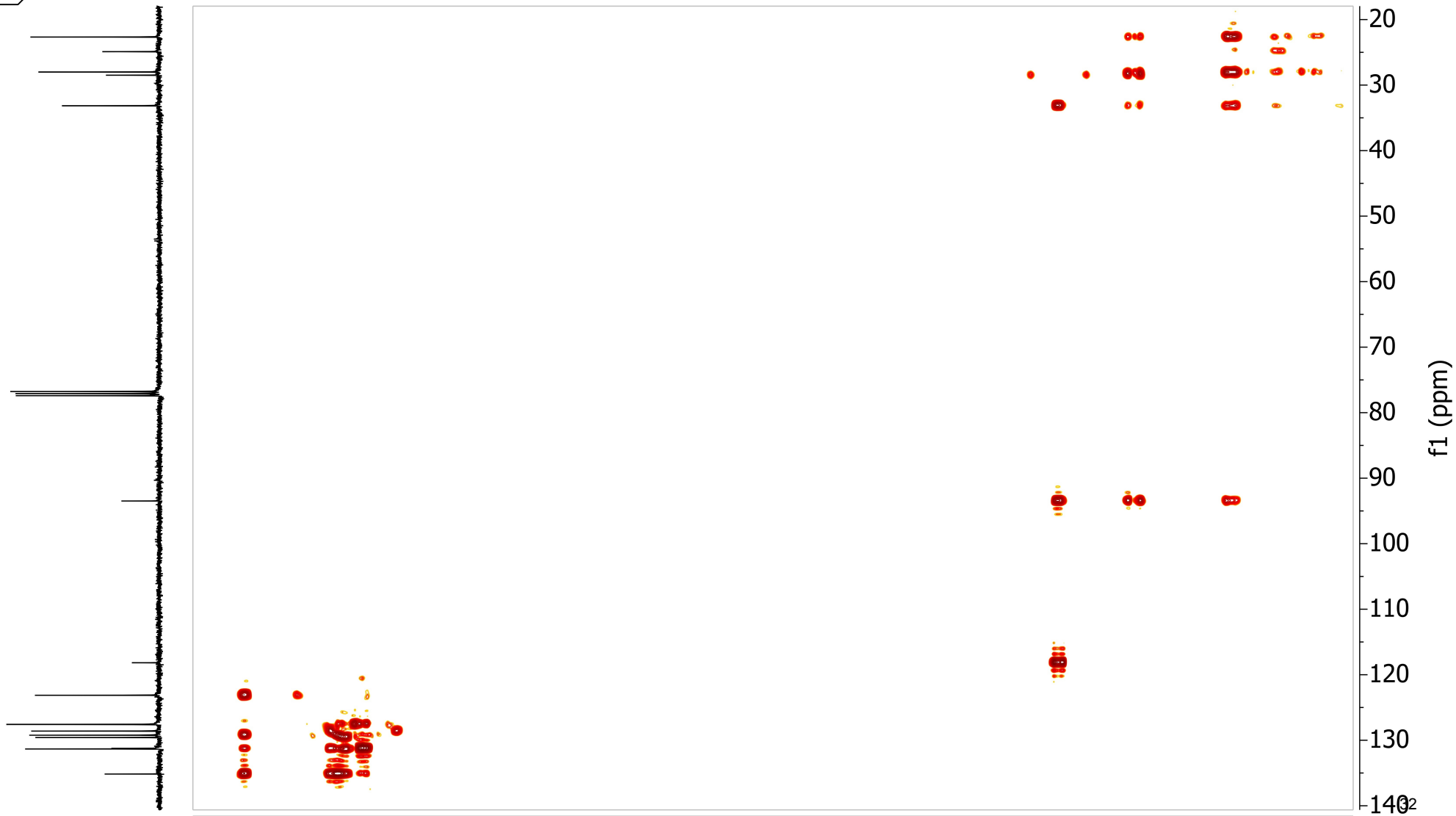




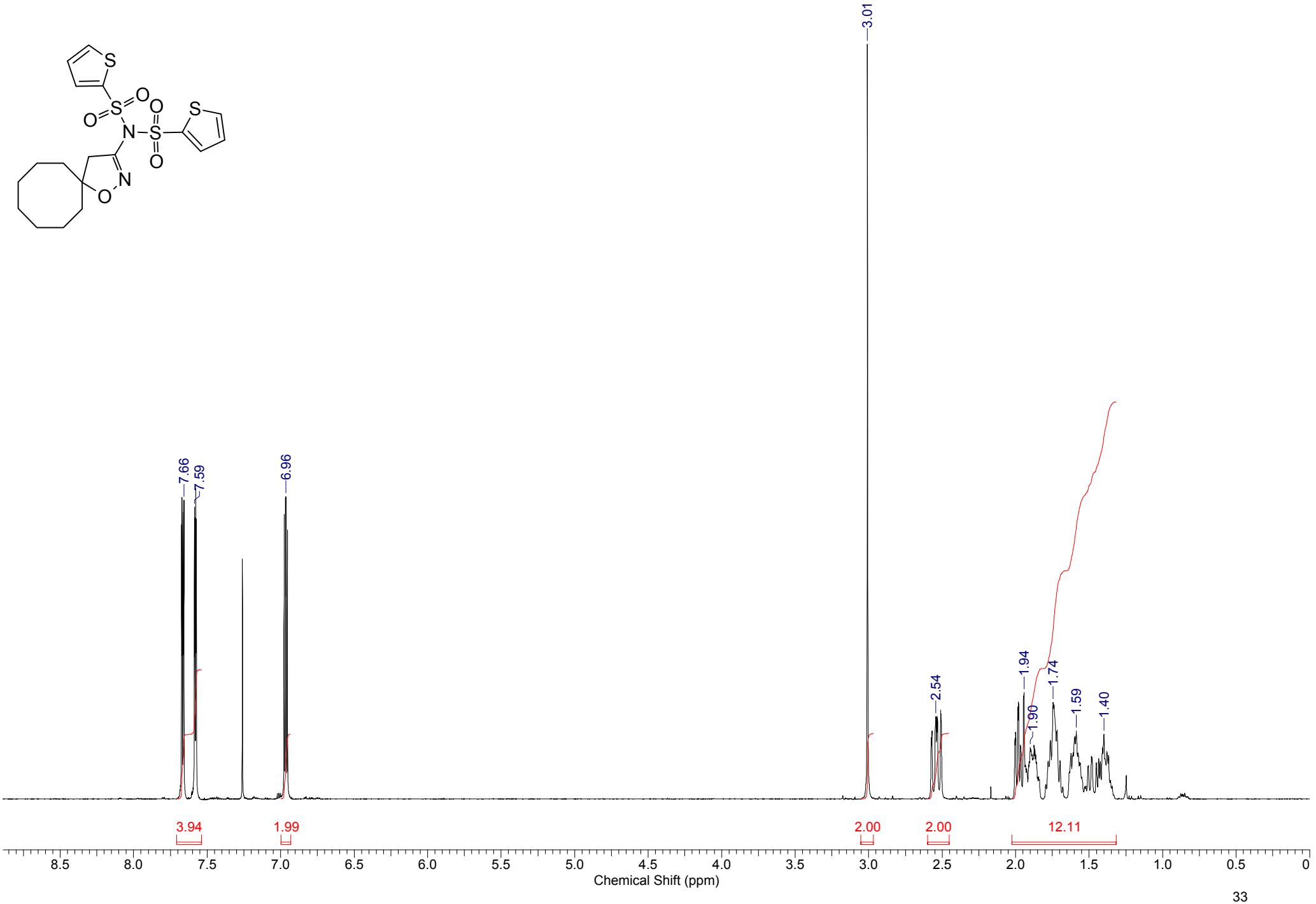


HMBC NMR spectrum of compound **4j** ($CDCl_3$)

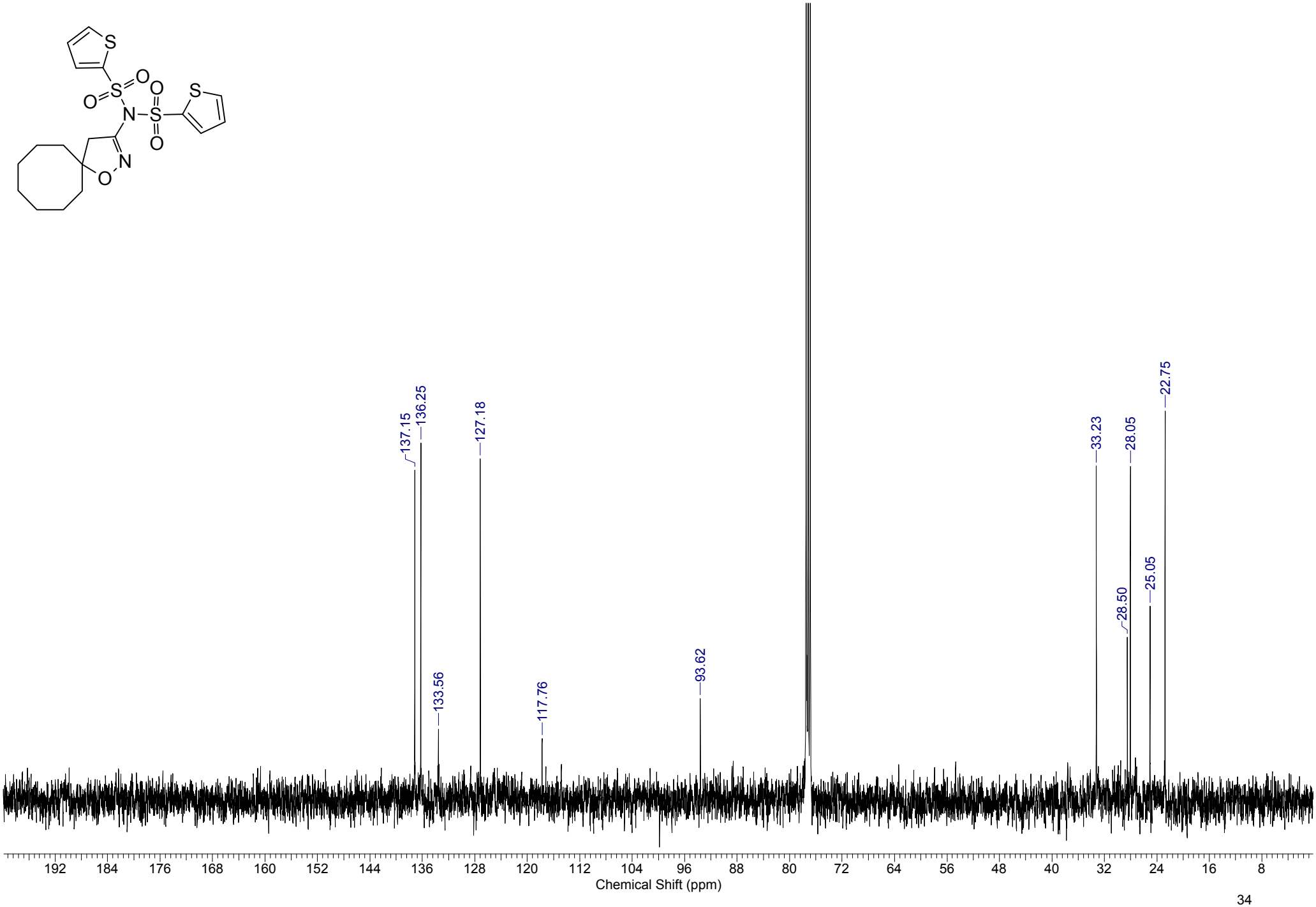




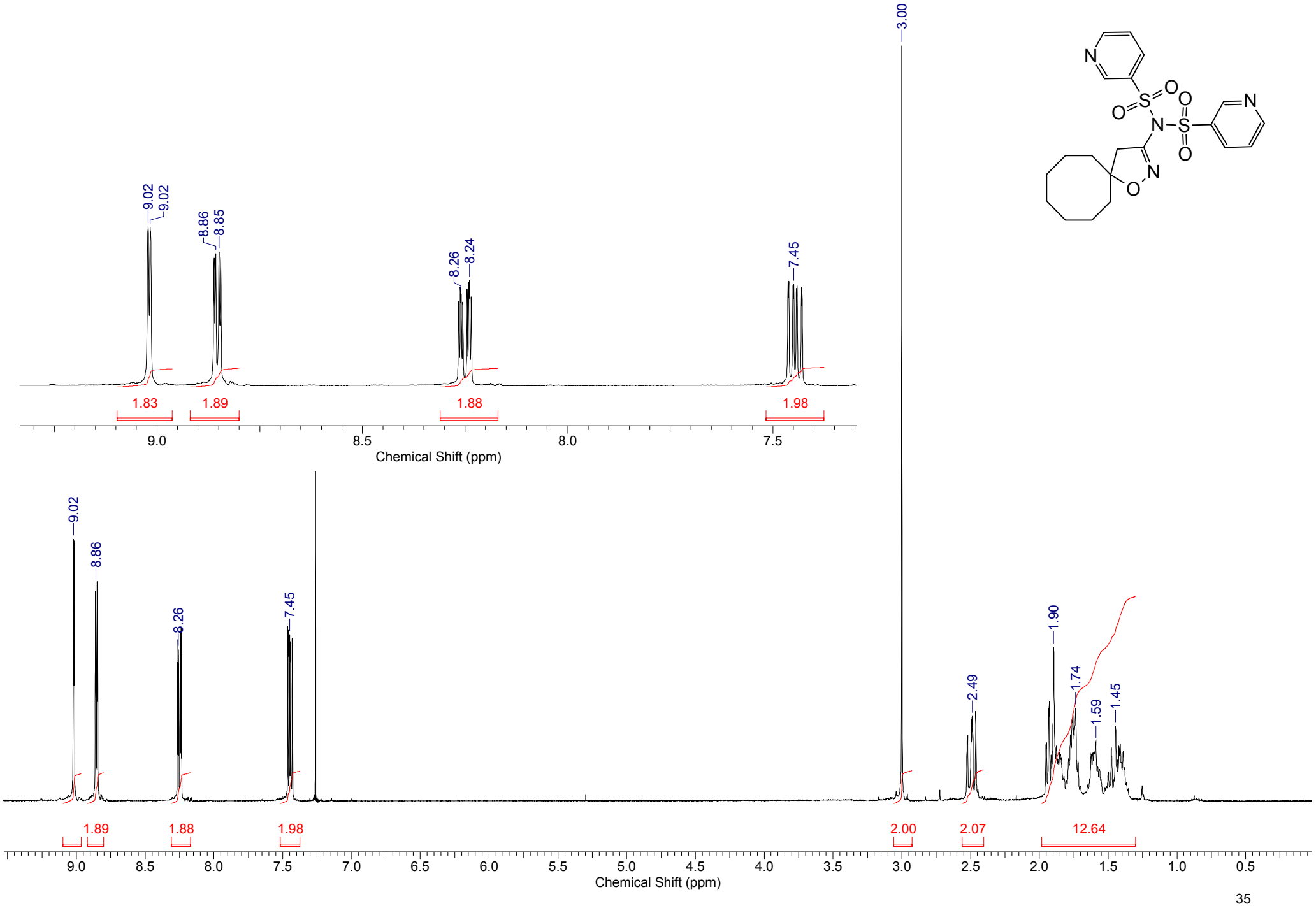
^{1}H NMR spectrum of compound **4k** ($CDCl_3$)



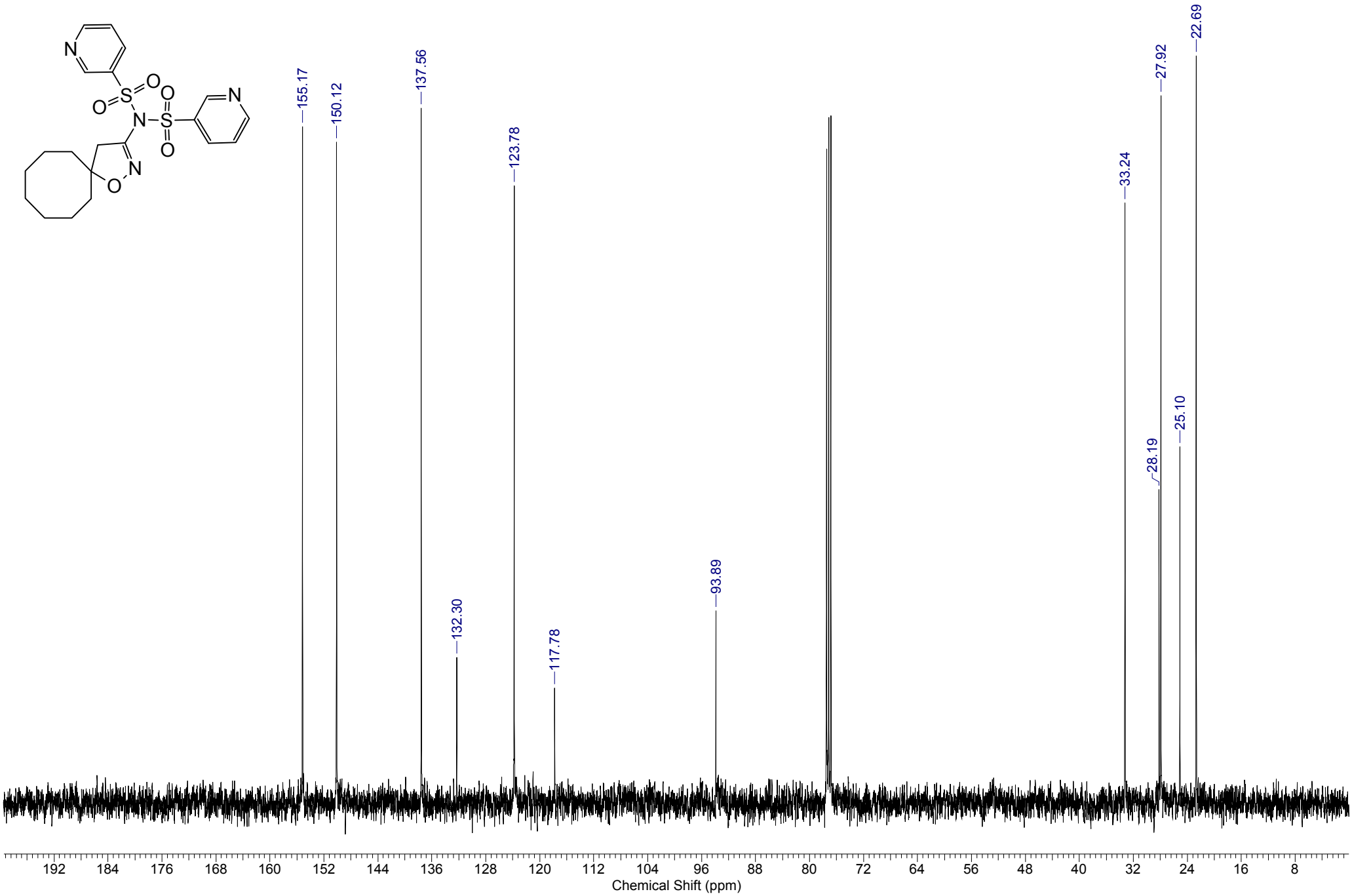
^{13}C NMR spectrum of compound **4k** ($CDCl_3$)



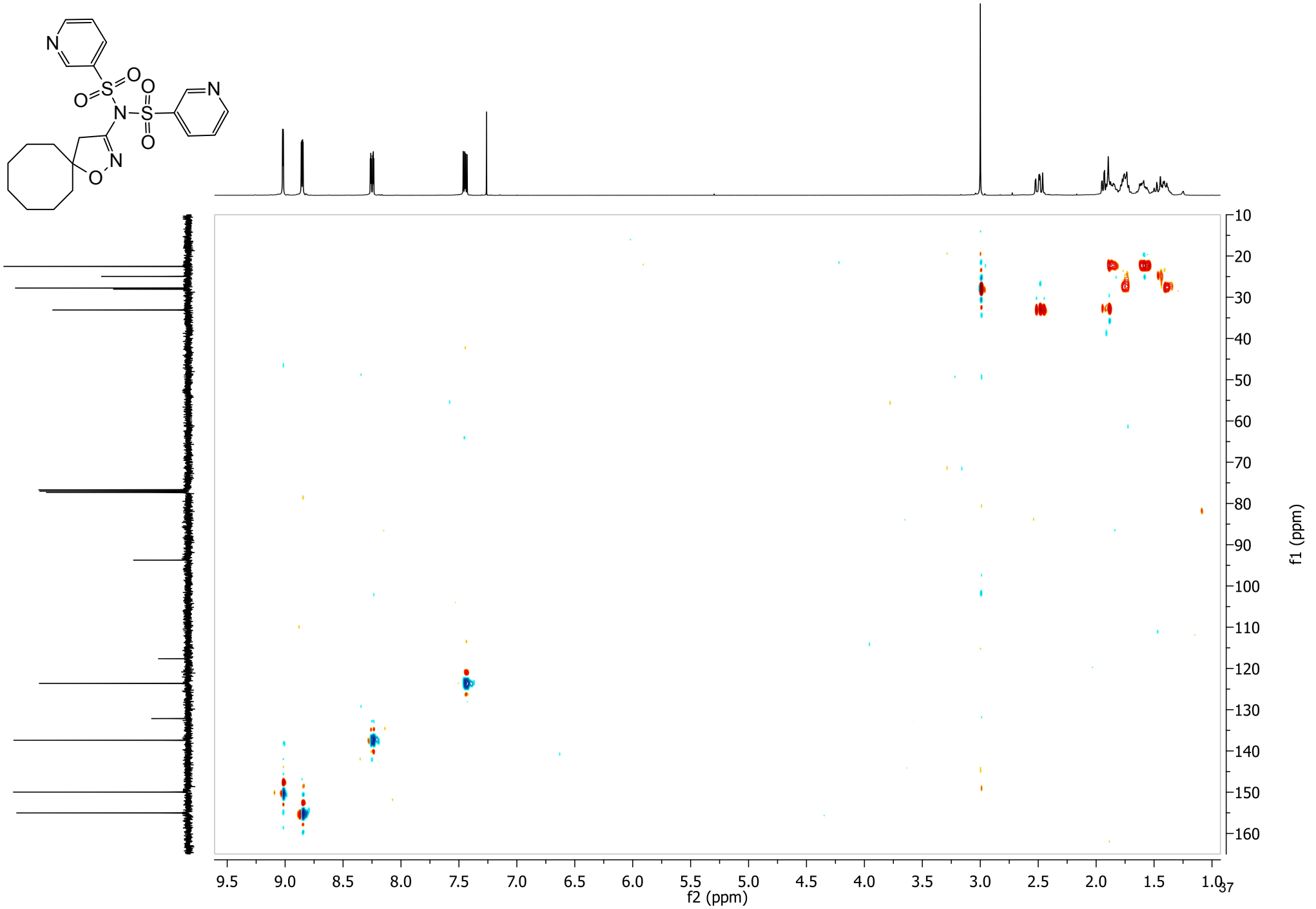
^{1}H NMR spectrum of compound **4l** ($CDCl_3$)



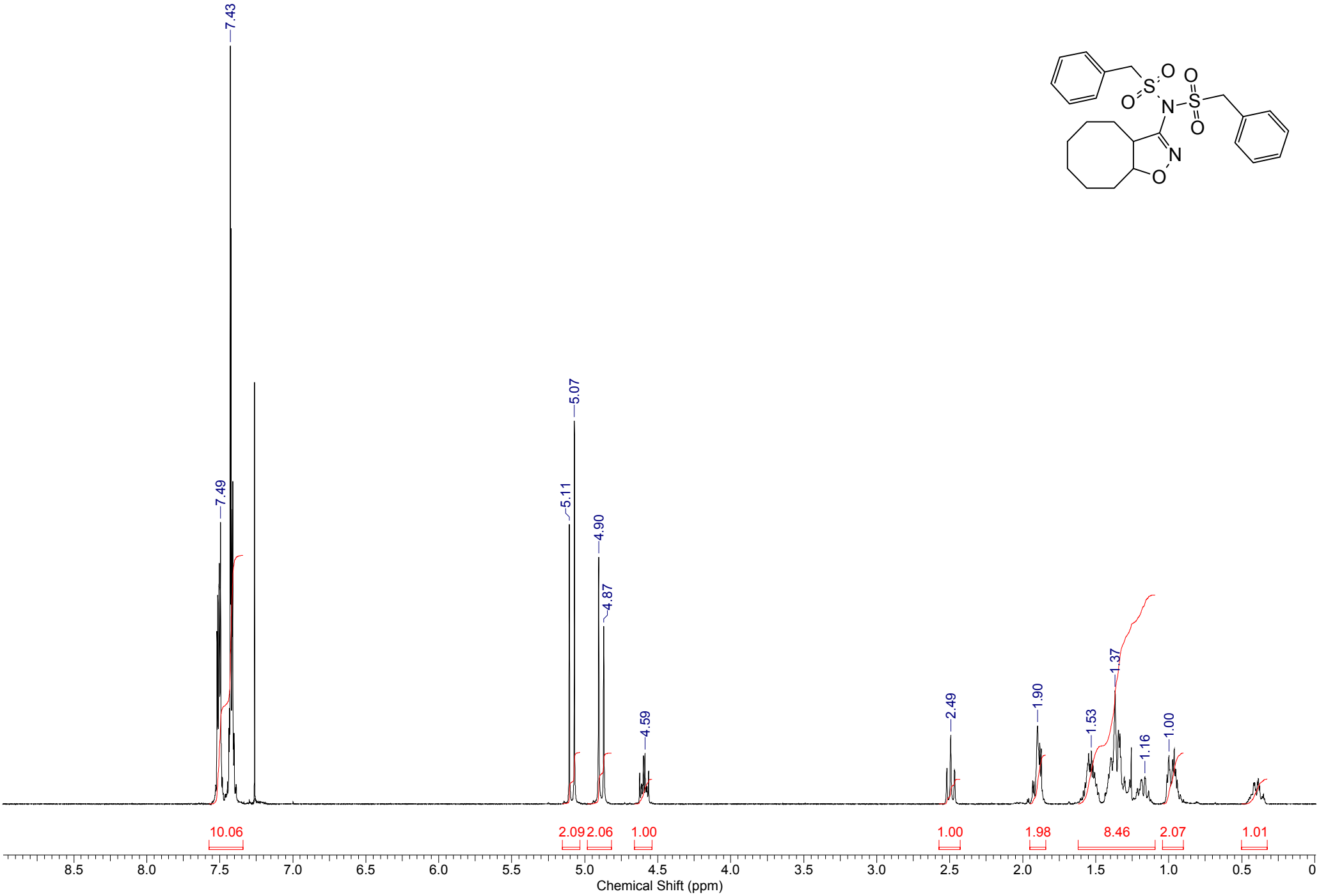
^{13}C NMR spectrum of compound **4l** ($CDCl_3$)



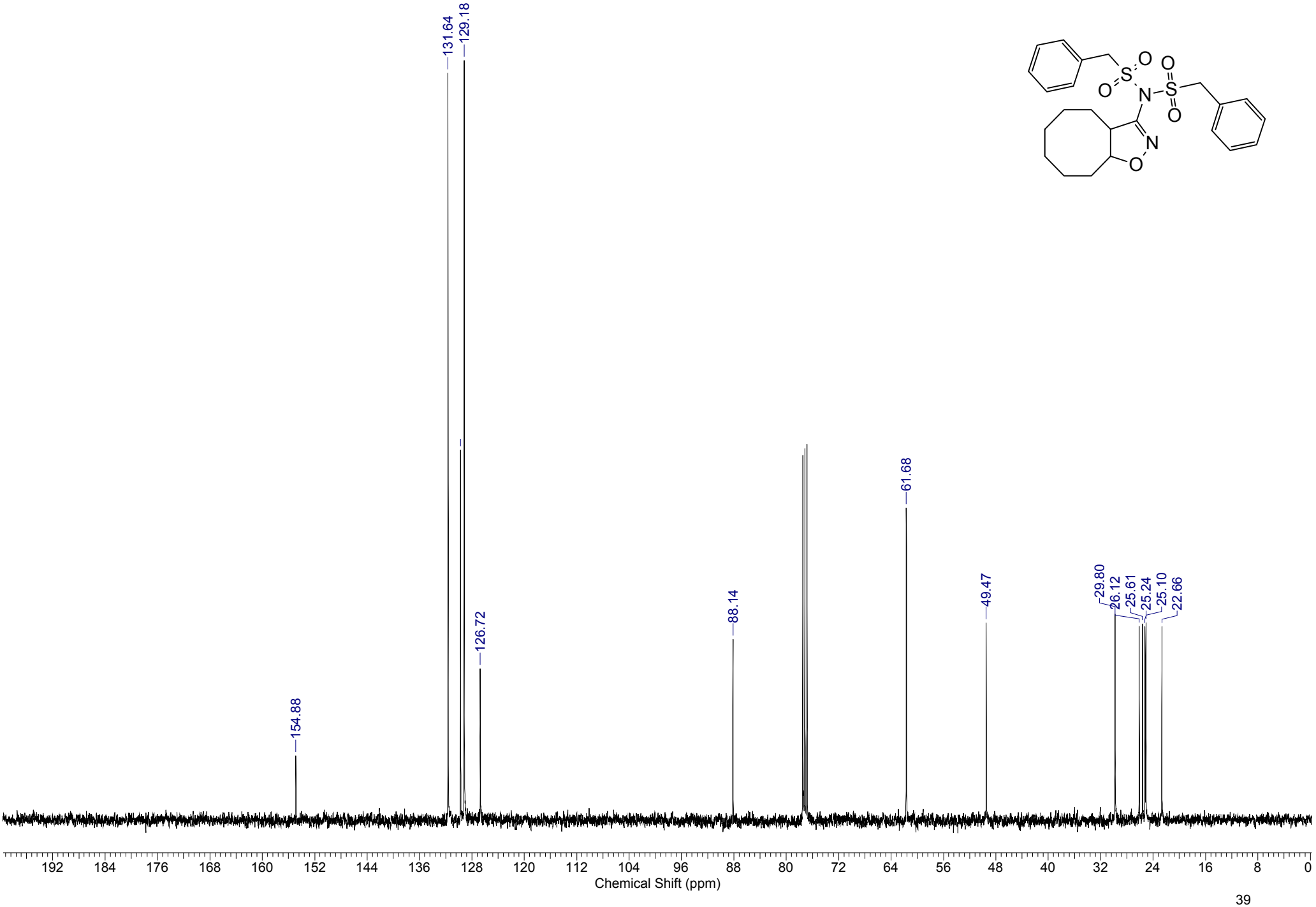
HSQC NMR spectrum of compound **4l** ($CDCl_3$)



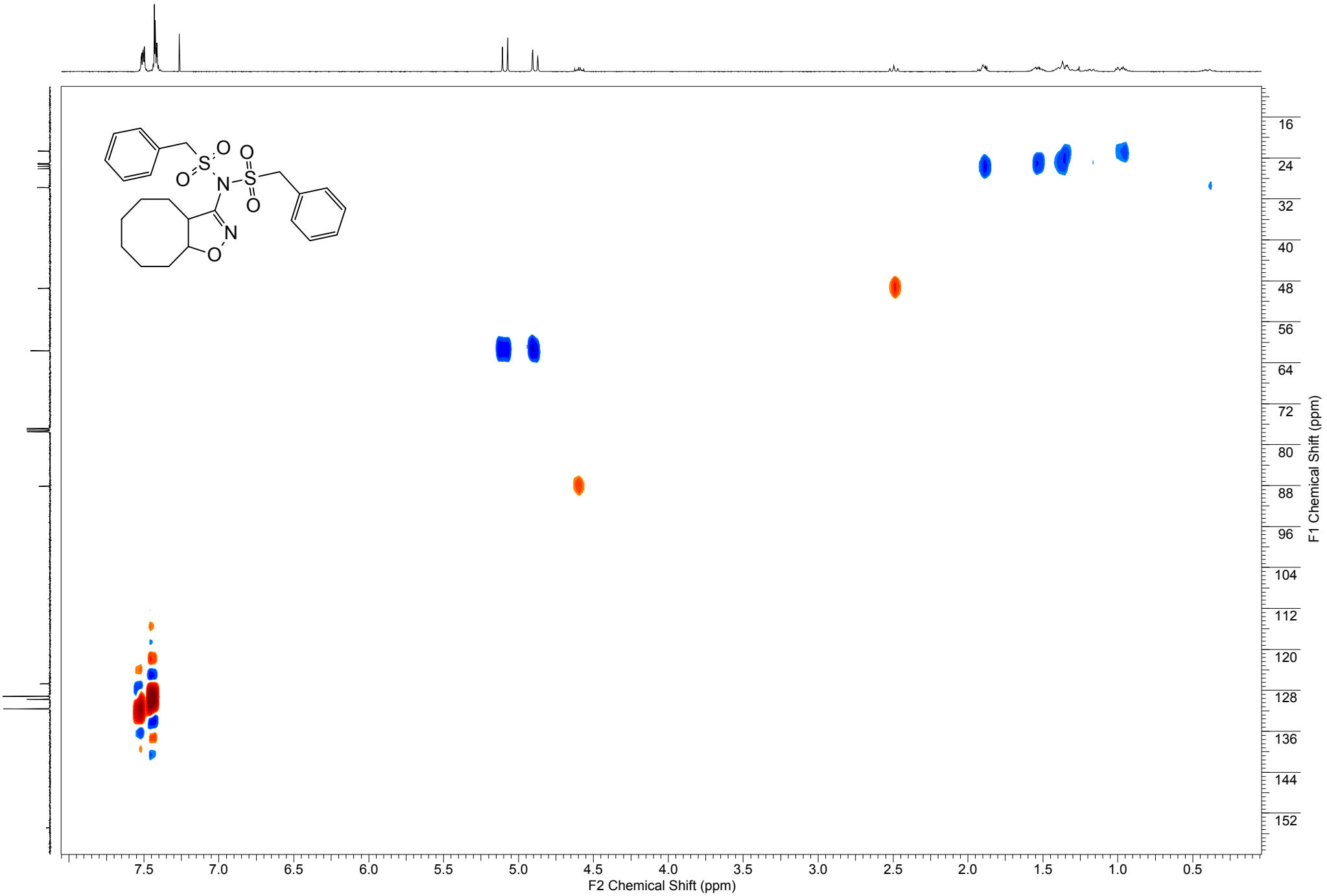
^{1}H NMR spectrum of compound **5b** ($CDCl_3$)



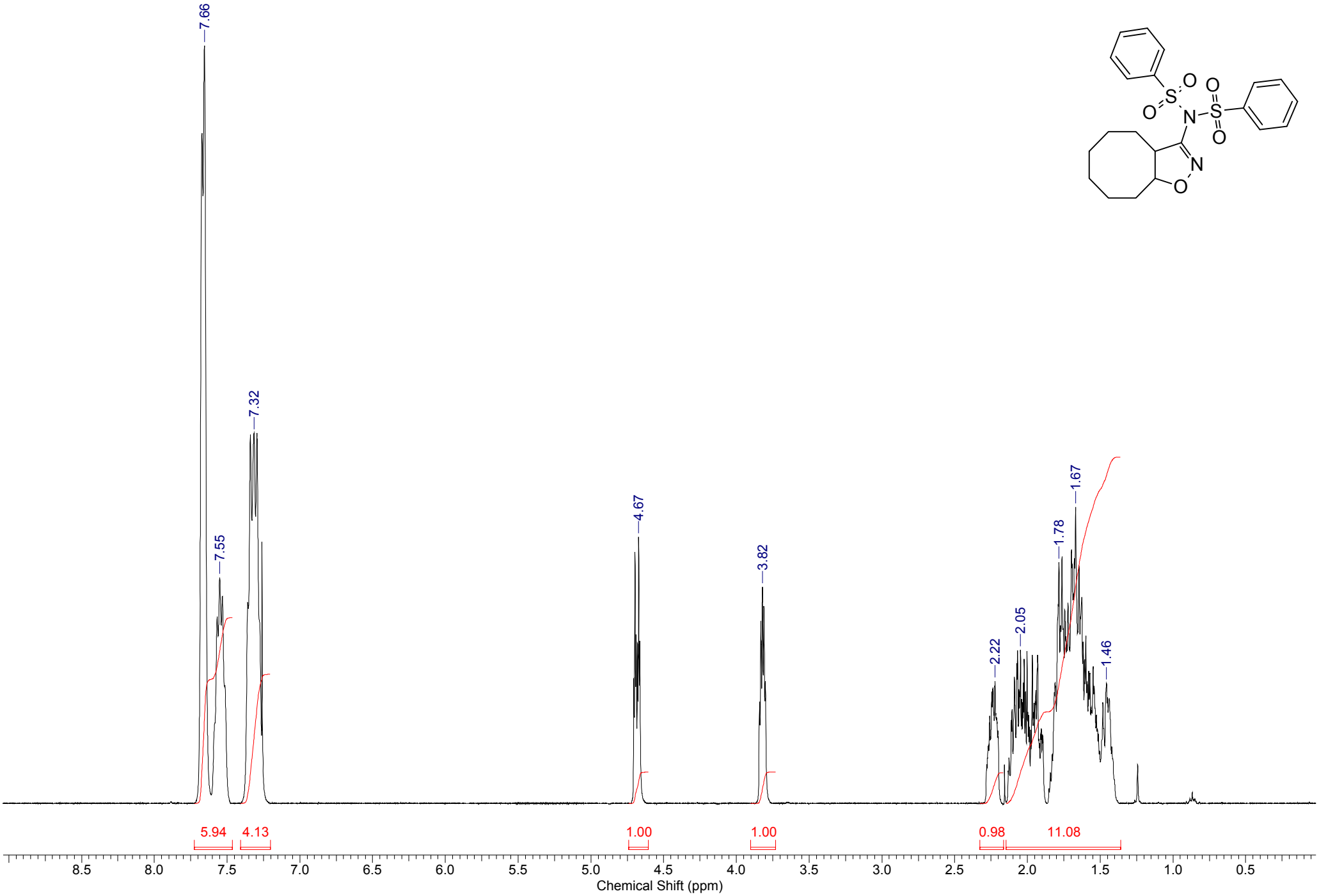
^{13}C NMR spectrum of compound **5b** ($CDCl_3$)



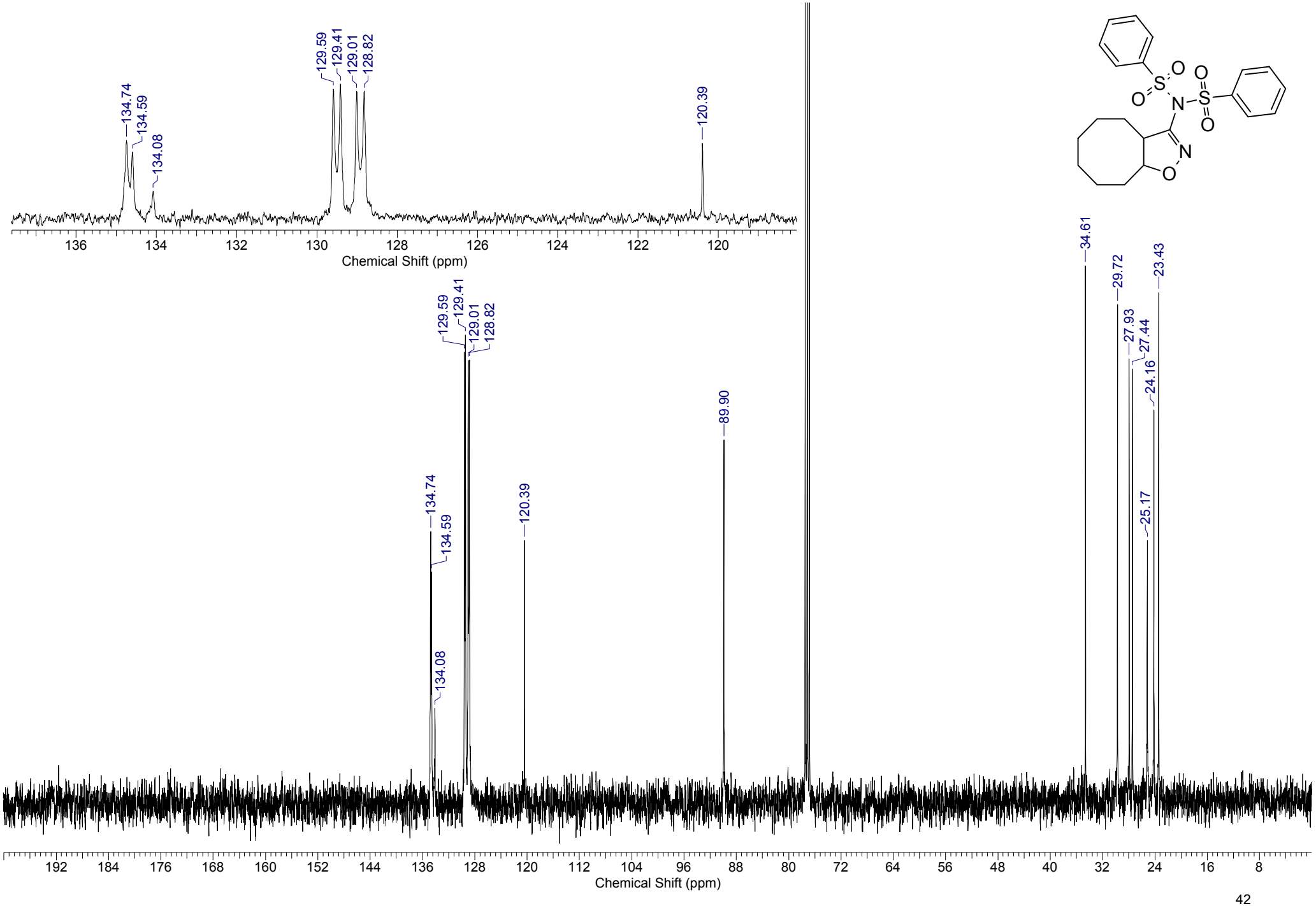
HSQC NMR spectrum of compound **5b** ($CDCl_3$)



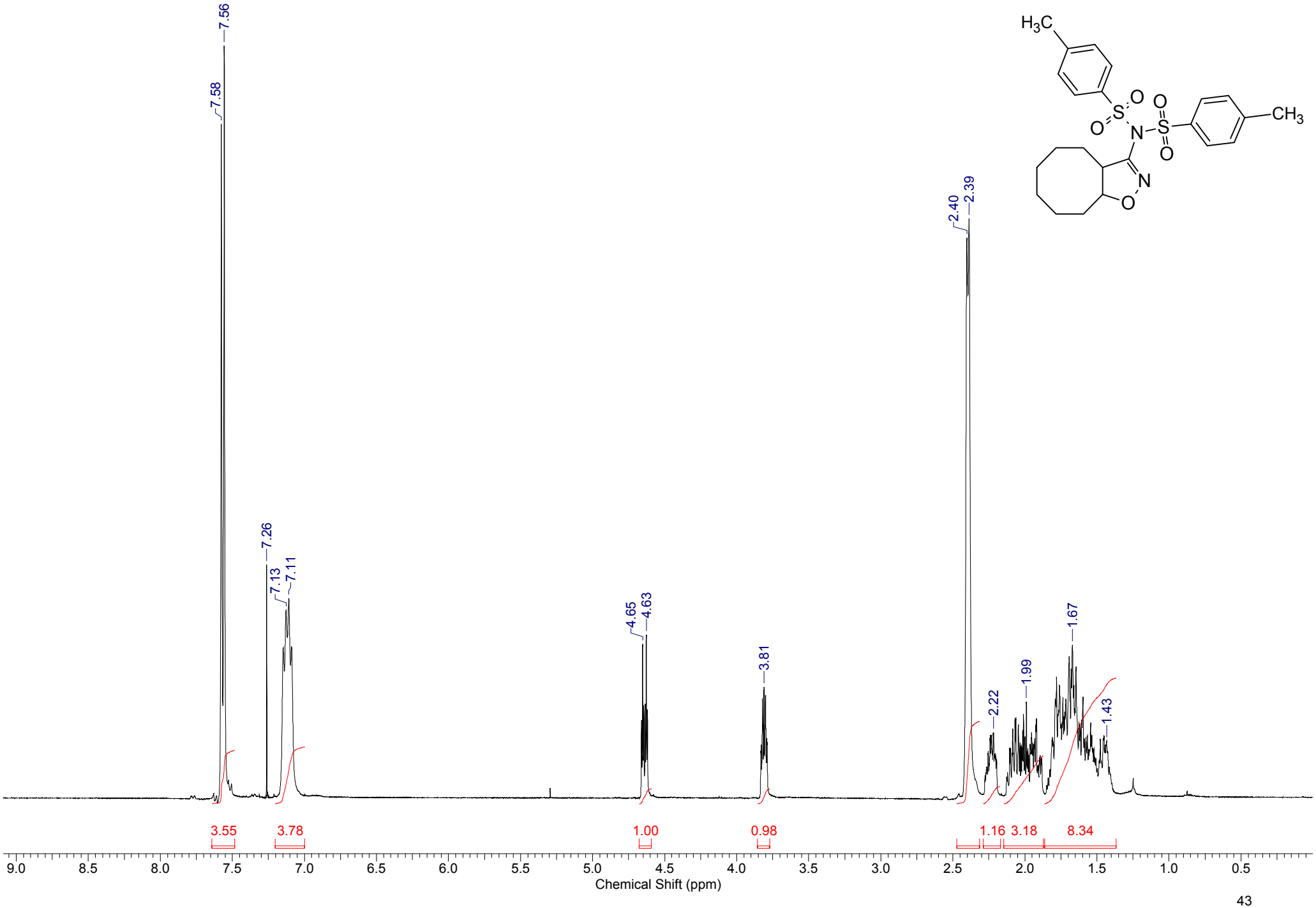
^{1}H NMR spectrum of compound **5c** ($CDCl_3$)



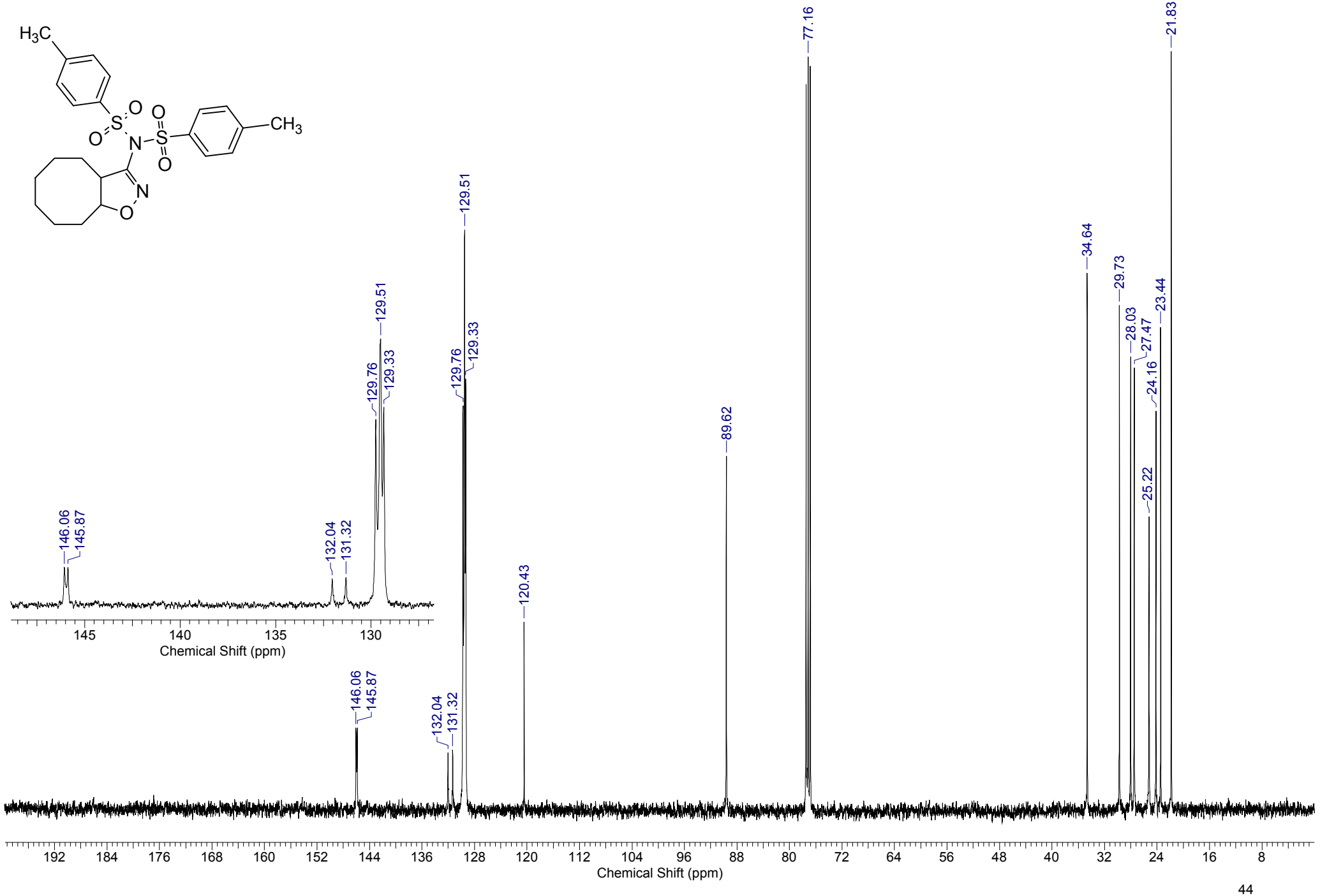
^{13}C NMR spectrum of compound **5c** ($CDCl_3$)



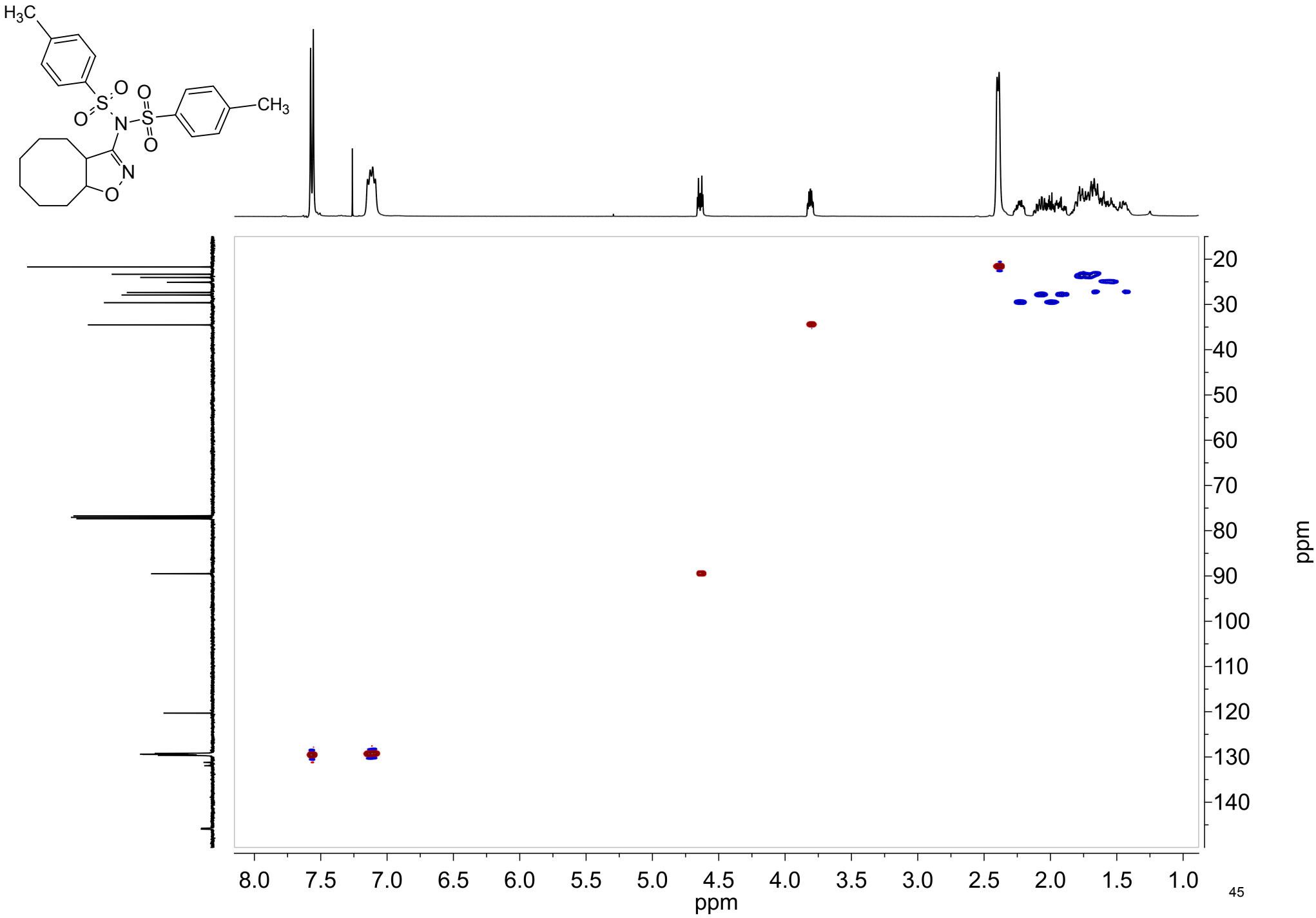
^{1}H NMR spectrum of compound **5d** ($CDCl_3$)



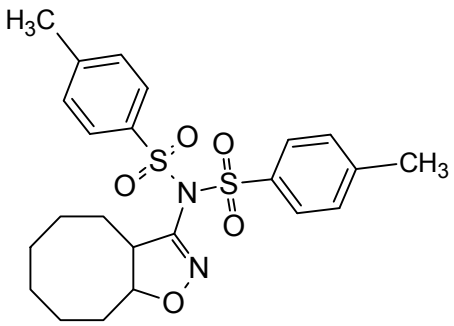
^{13}C NMR spectrum of compound **5d** ($CDCl_3$)

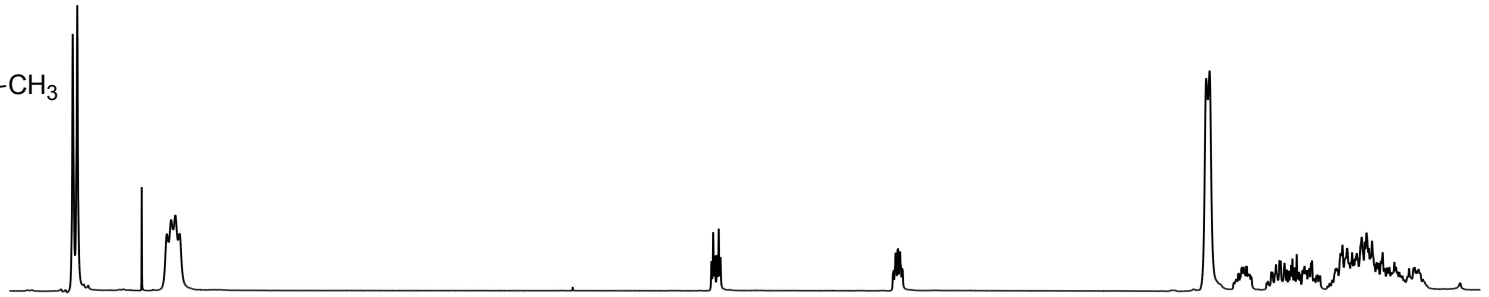


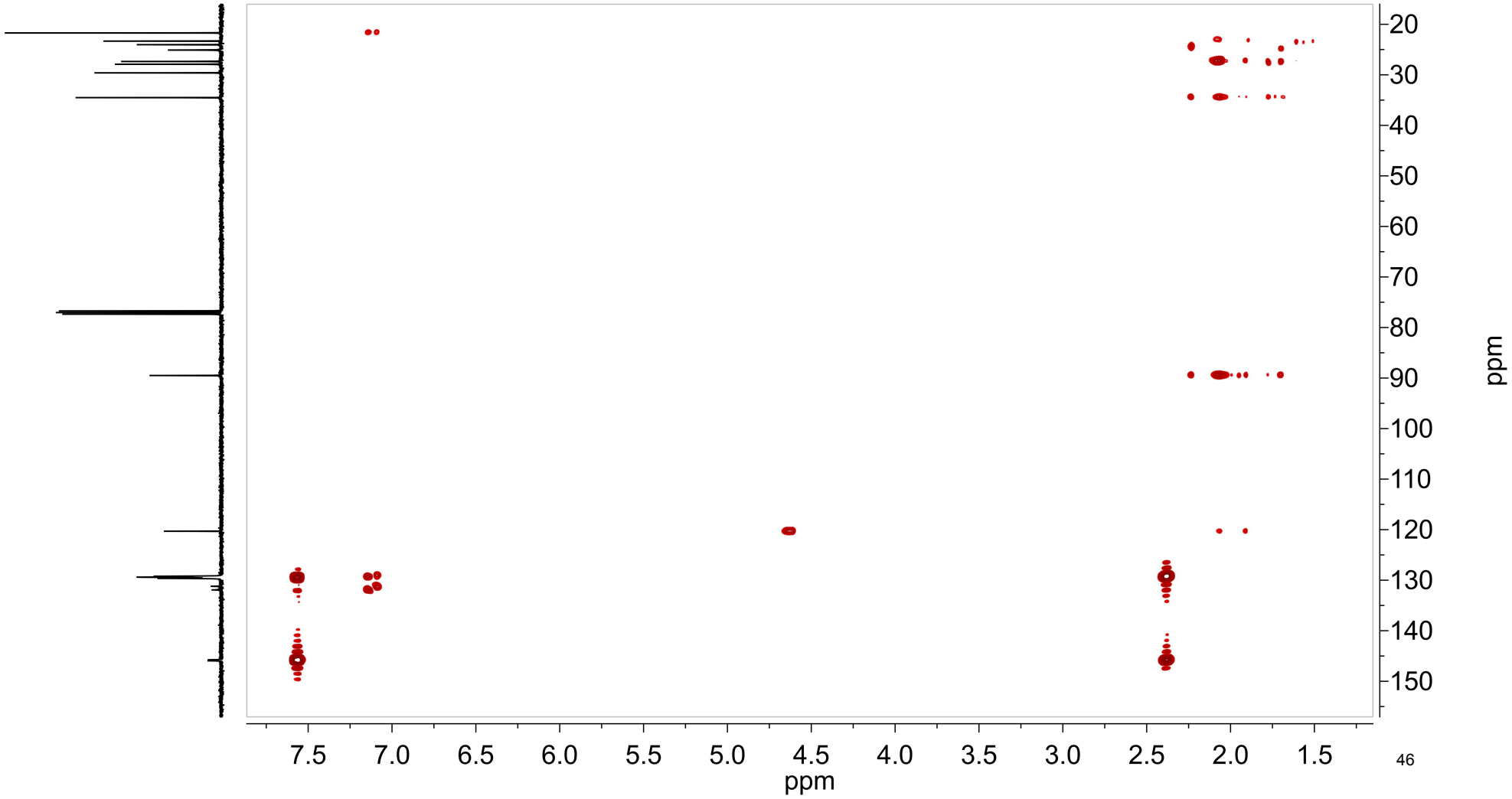
HSQC NMR spectrum of compound **5d** ($CDCl_3$)



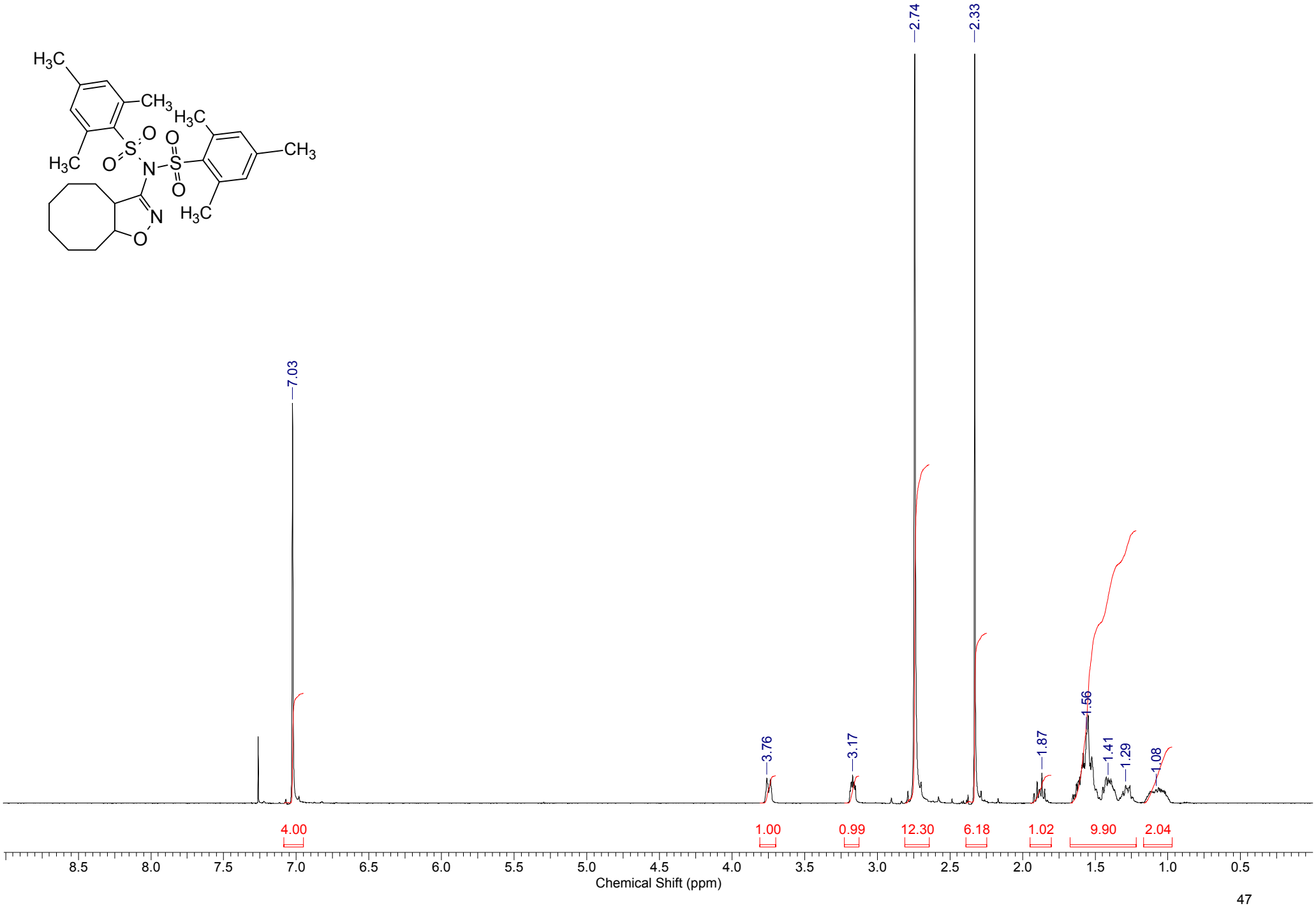
HMBC NMR spectrum of compound **5d** ($CDCl_3$)



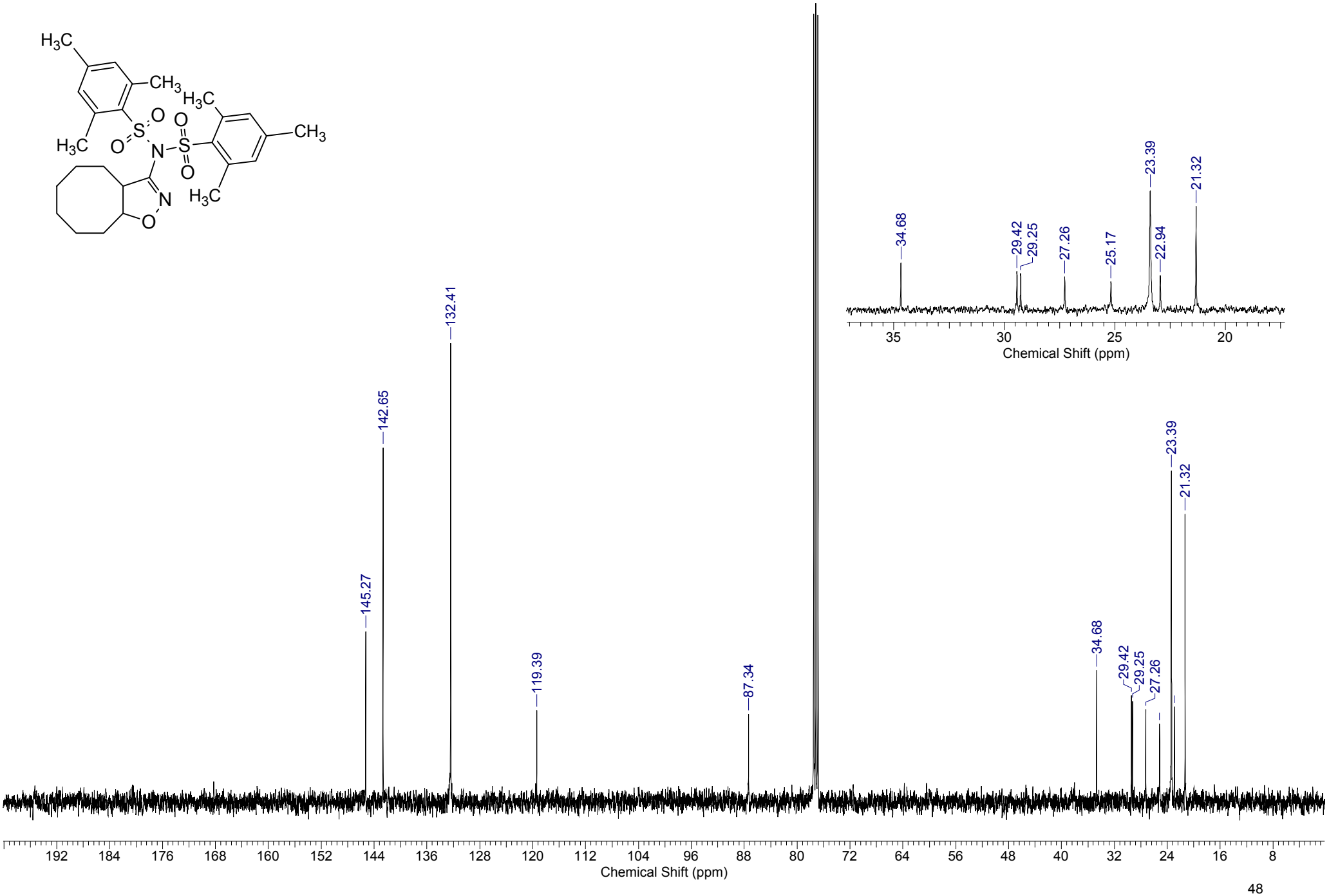




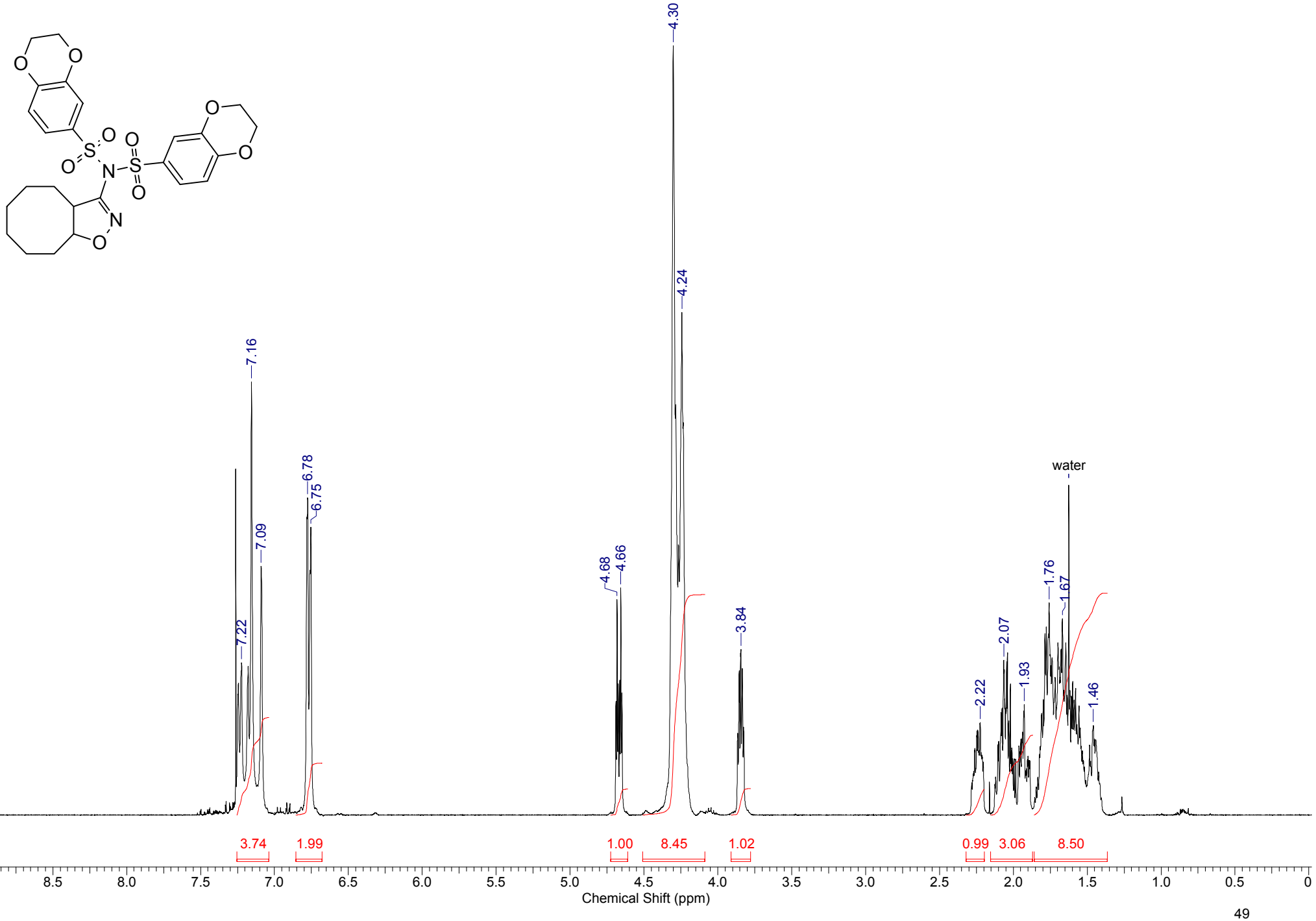
^{1}H NMR spectrum of compound **5e** ($CDCl_3$)



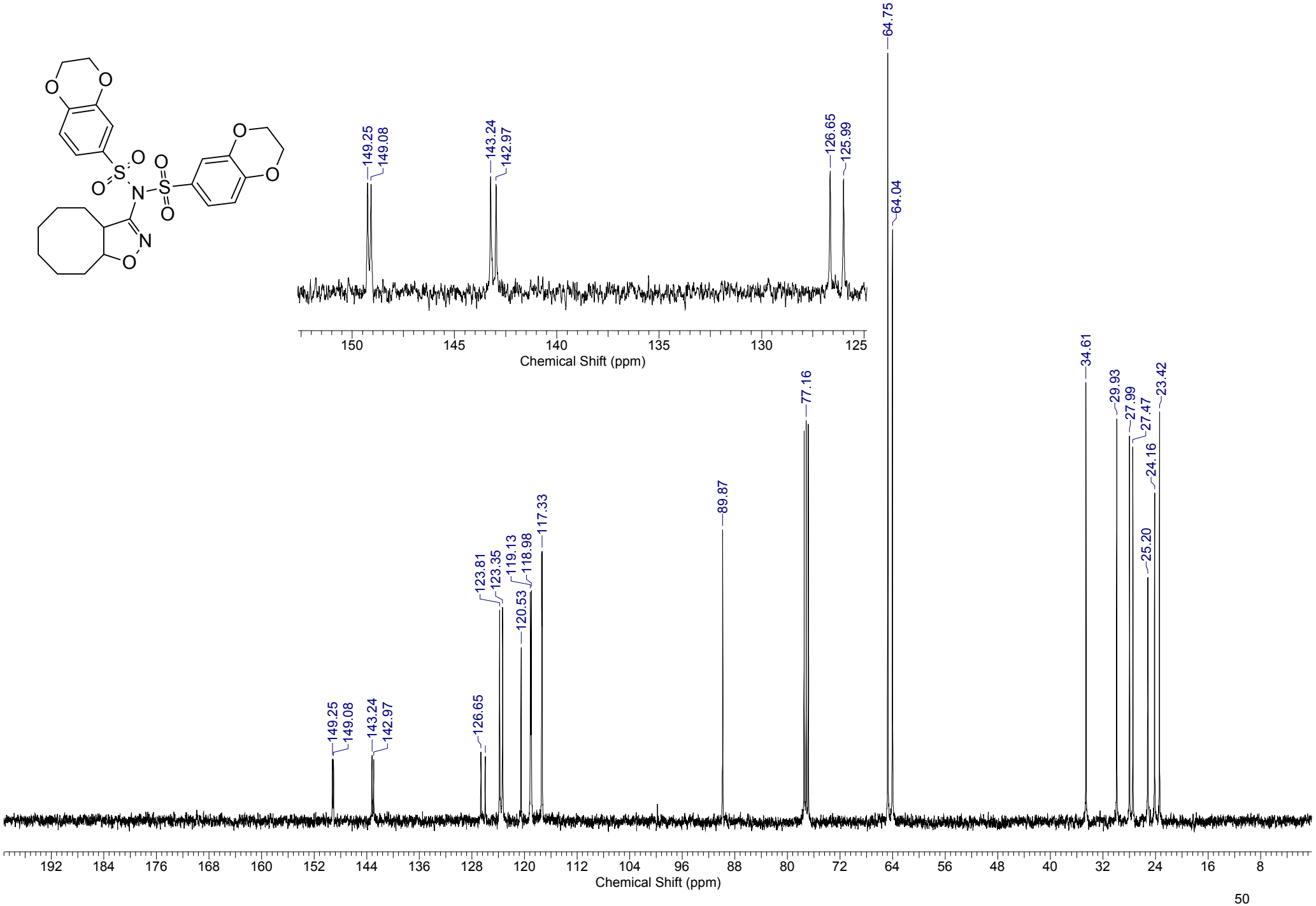
^{13}C NMR spectrum of compound **5e** ($CDCl_3$)



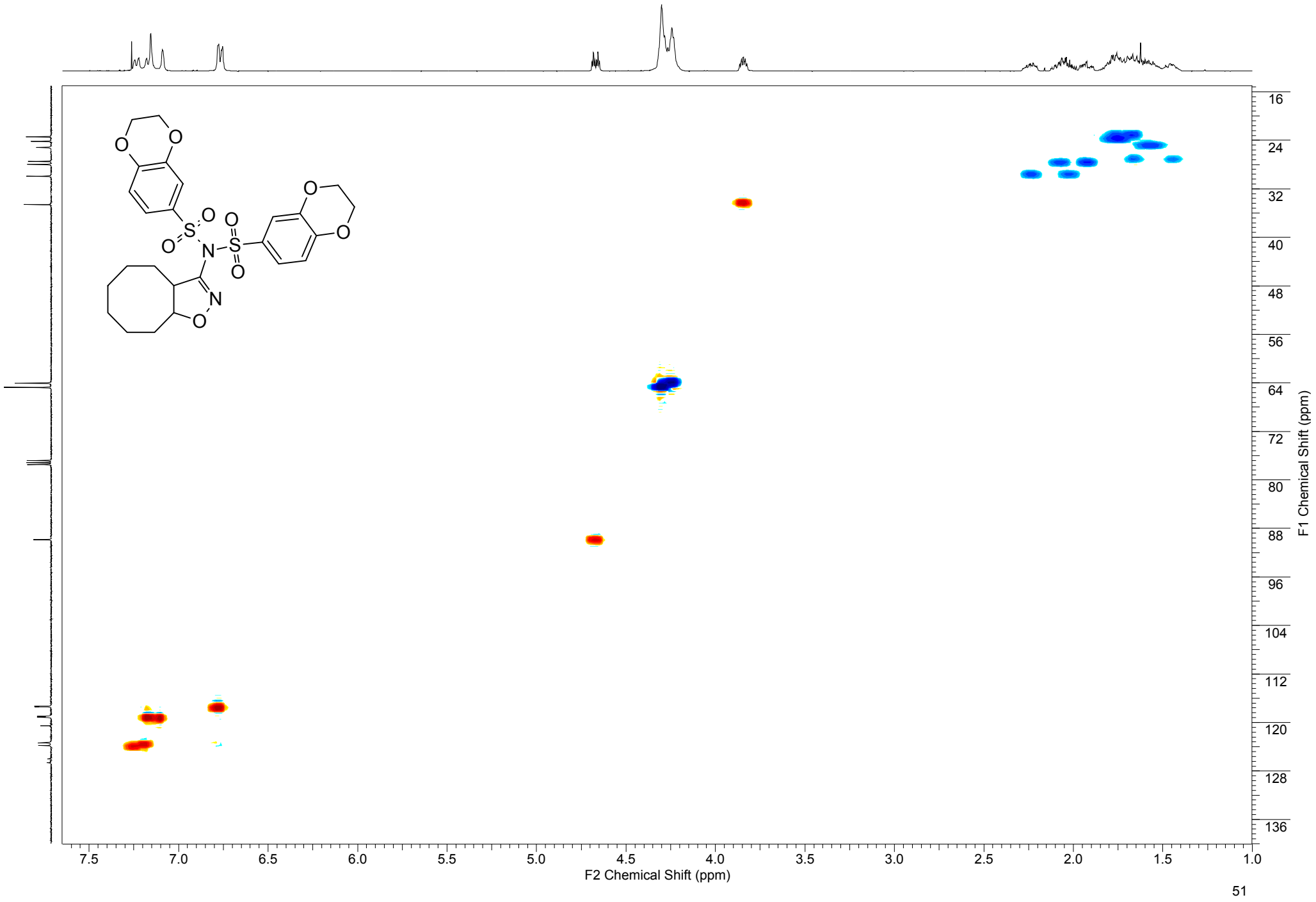
^{1}H NMR spectrum of compound **5f** ($CDCl_3$)



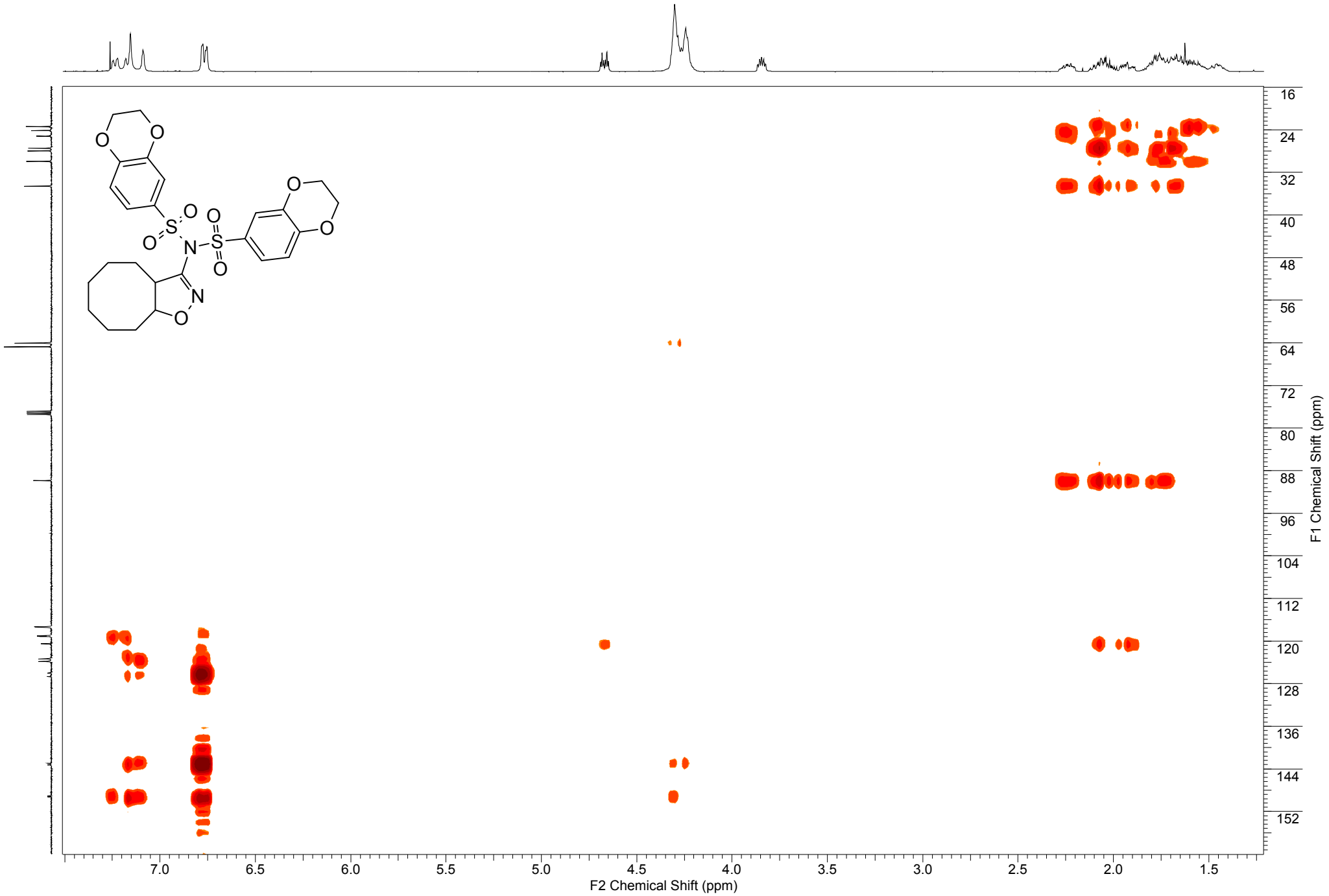
^{13}C NMR spectrum of compound **5f** ($CDCl_3$)



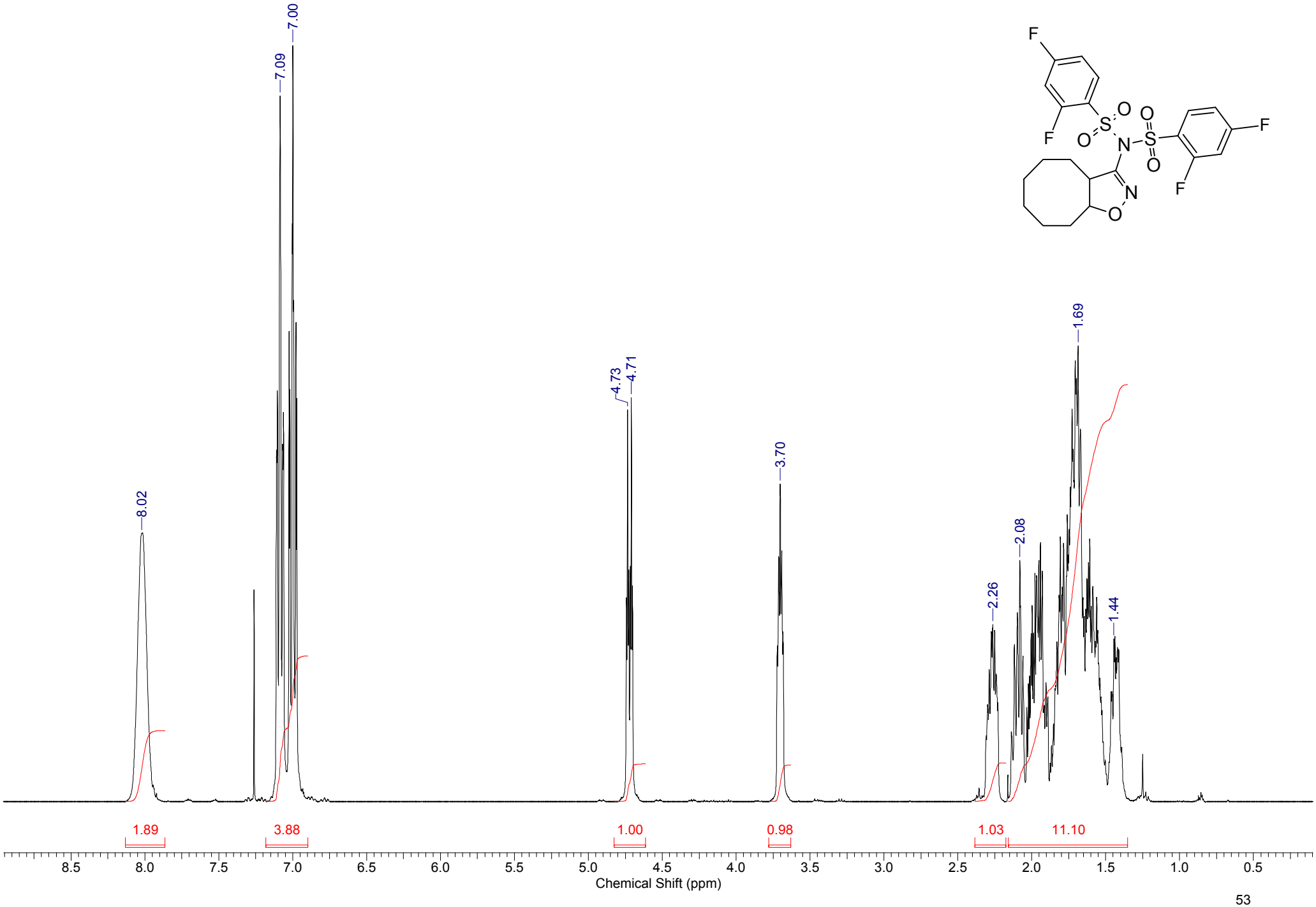
HSQC NMR spectrum of compound **5f** ($CDCl_3$)



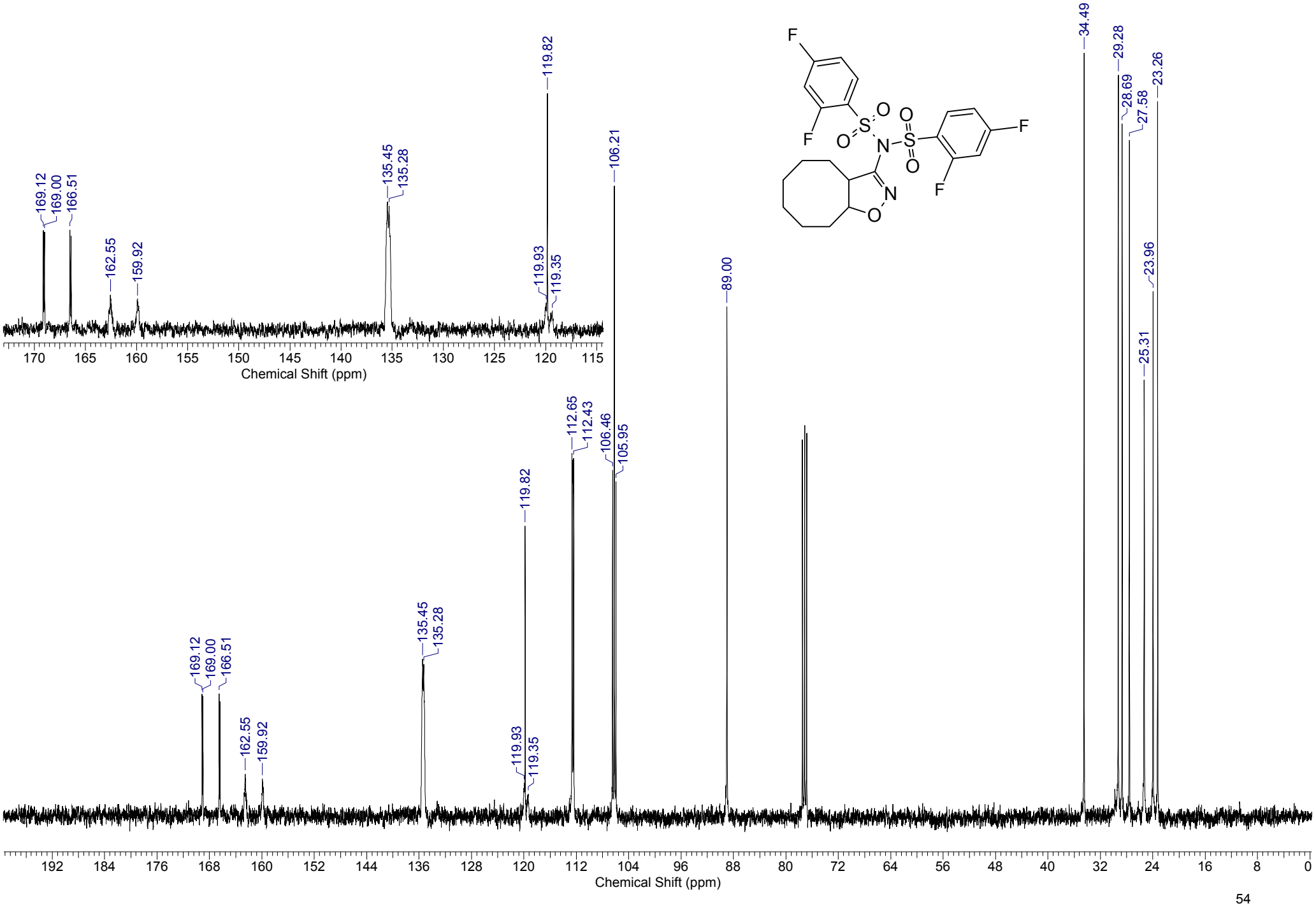
HMBC NMR spectrum of compound **5f** ($CDCl_3$)



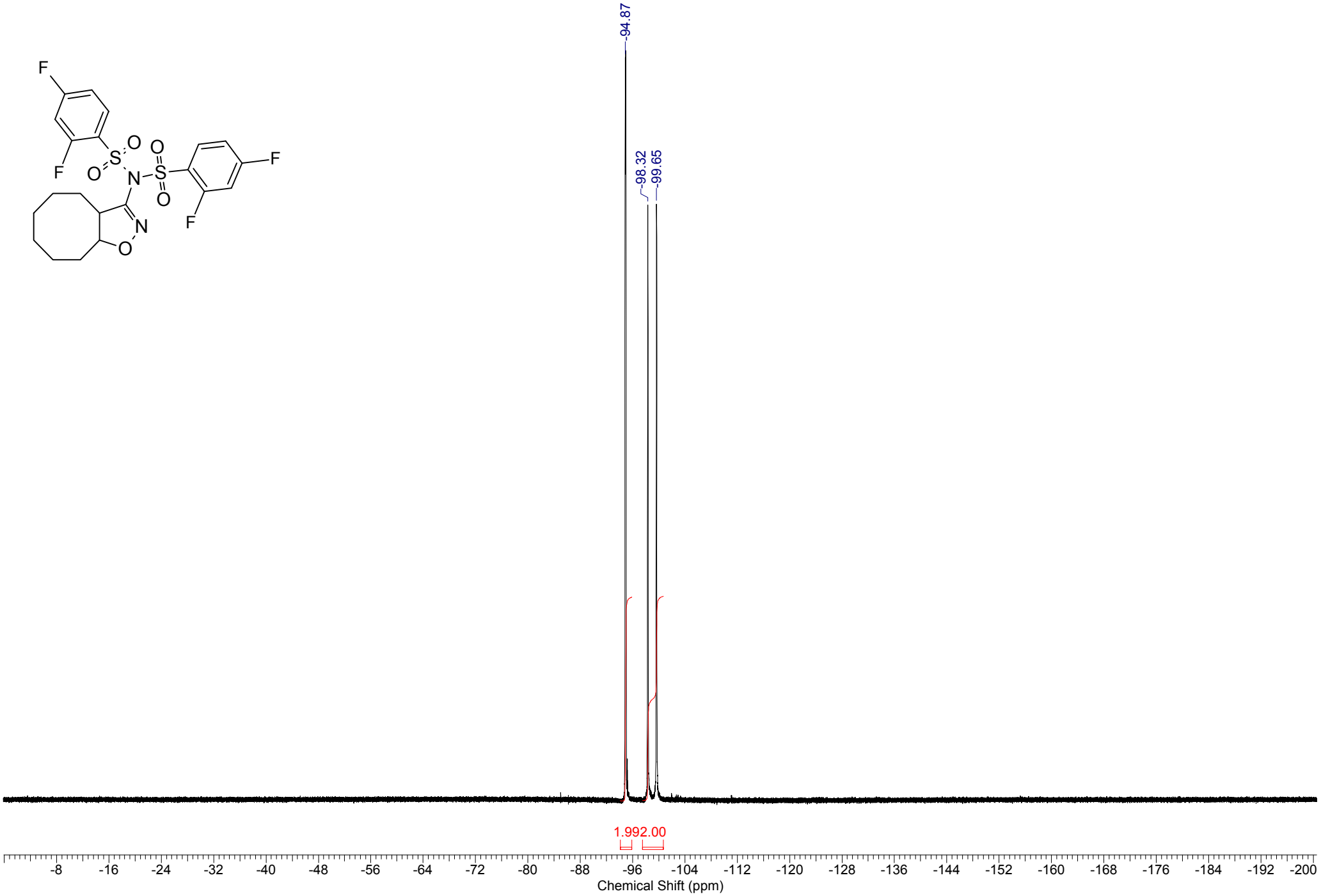
^{1}H NMR spectrum of compound **5g** ($CDCl_3$)



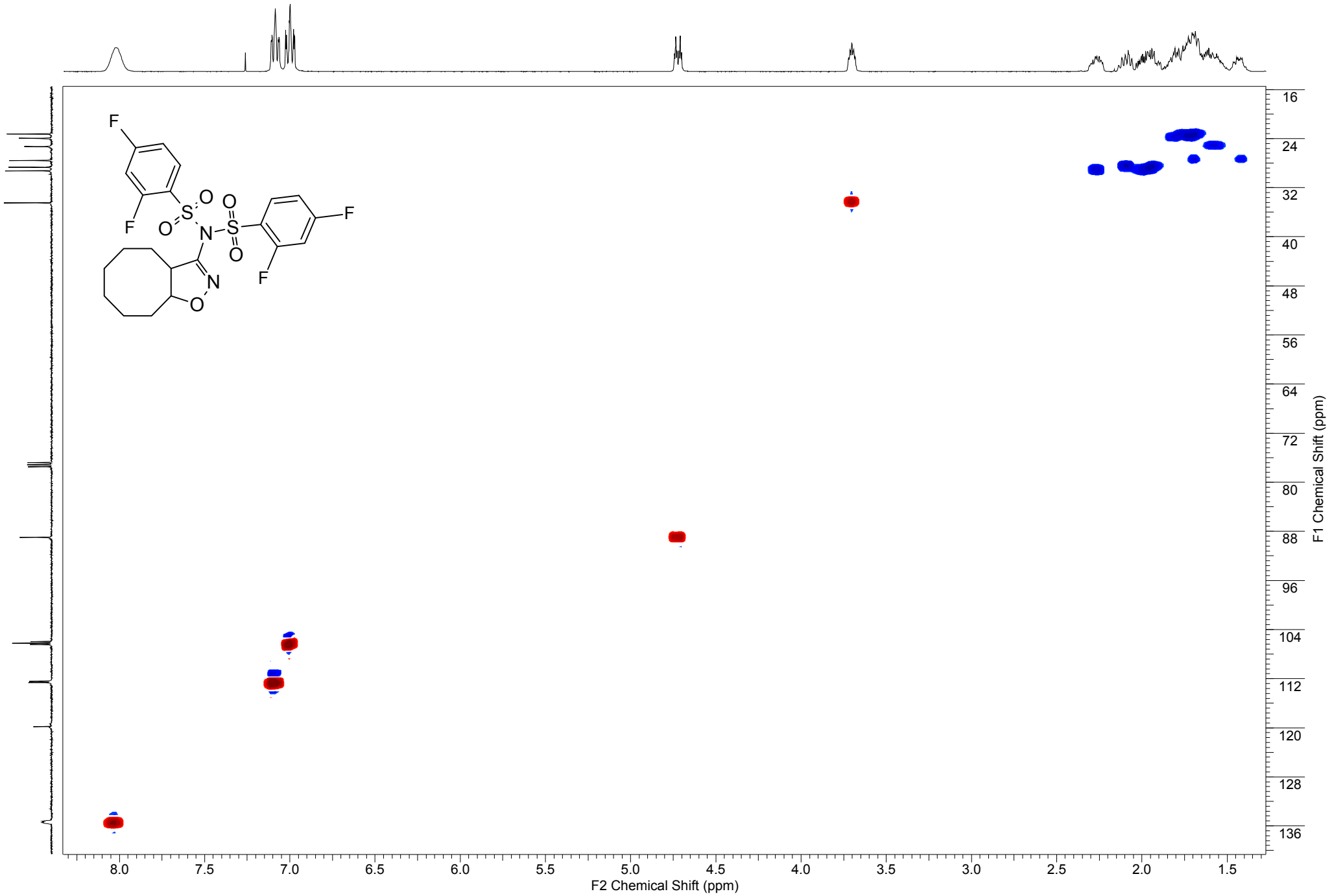
^{13}C NMR spectrum of compound **5g** ($CDCl_3$)



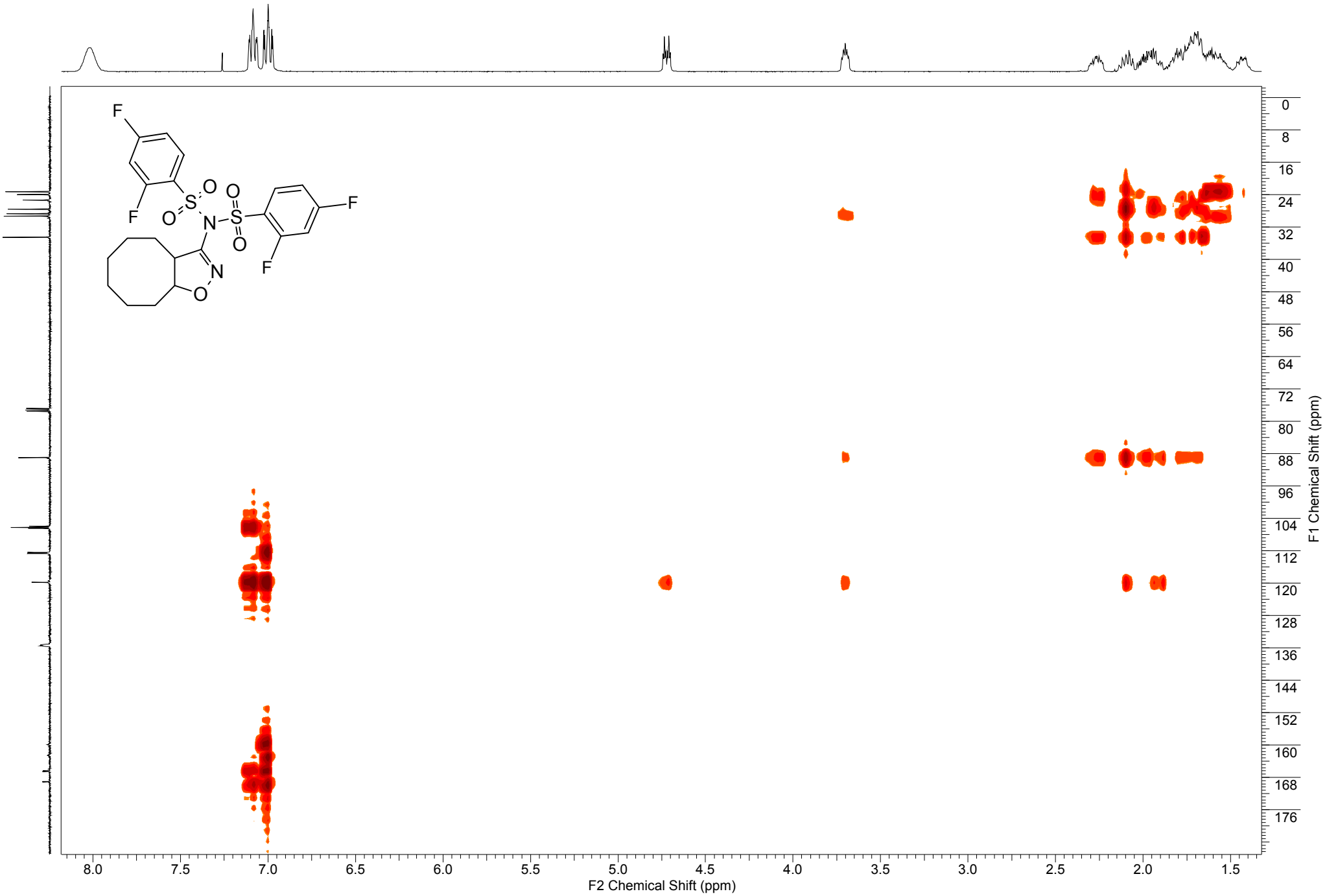
^{19}F NMR spectrum of compound **5g** ($CDCl_3$)



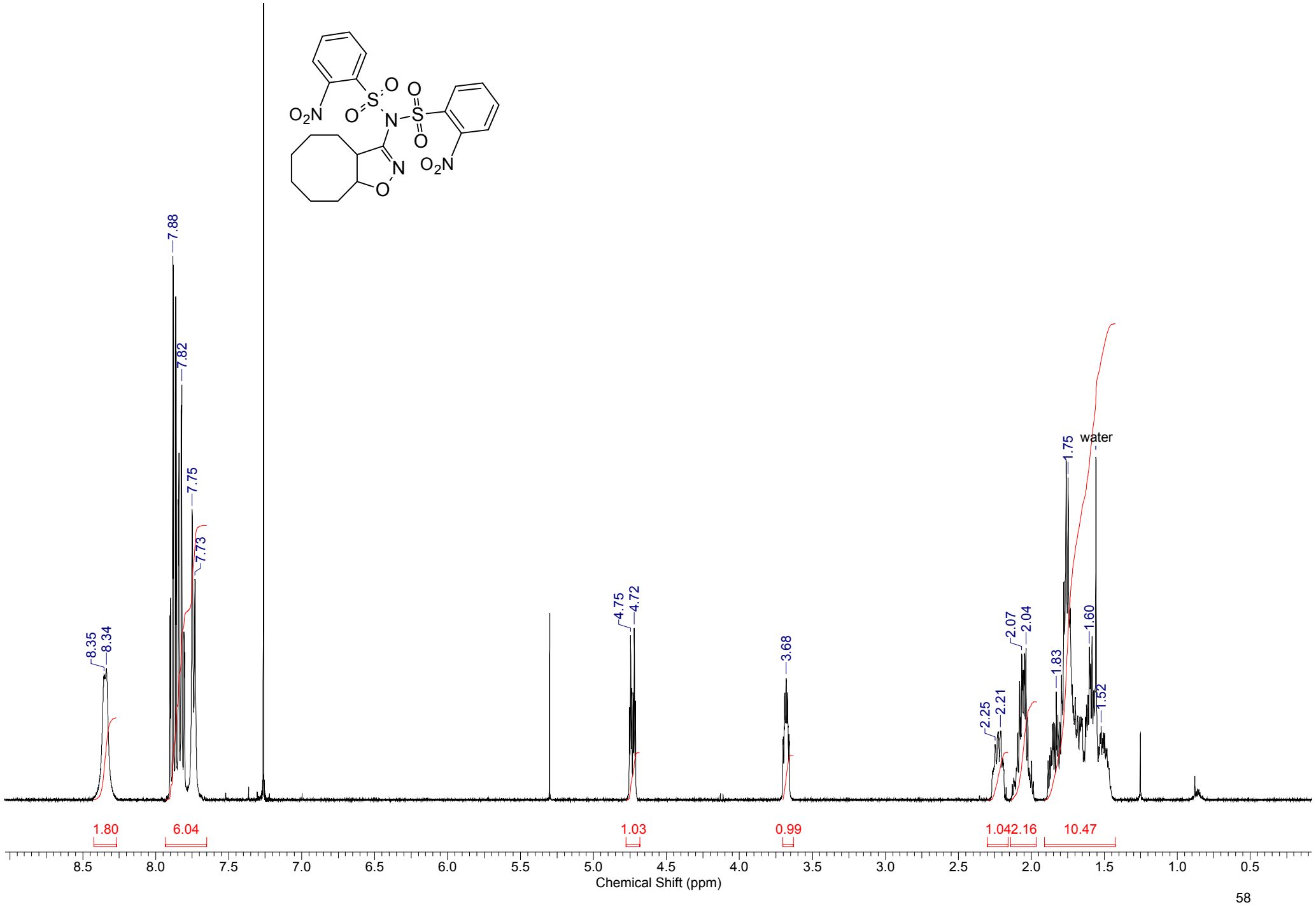
HSQC NMR spectrum of compound **5g**($CDCl_3$)



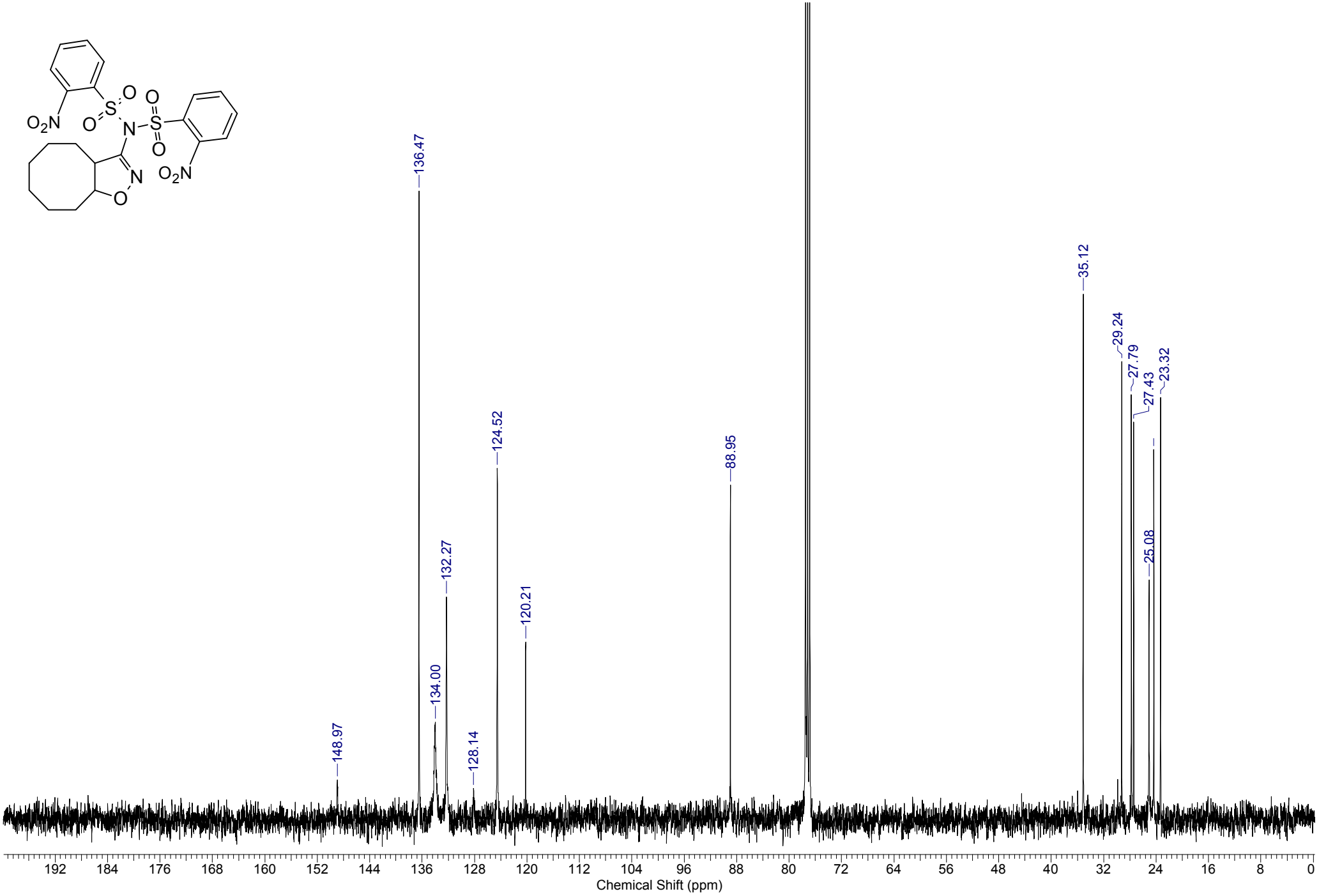
HMBC NMR spectrum of compound **5g** ($CDCl_3$)



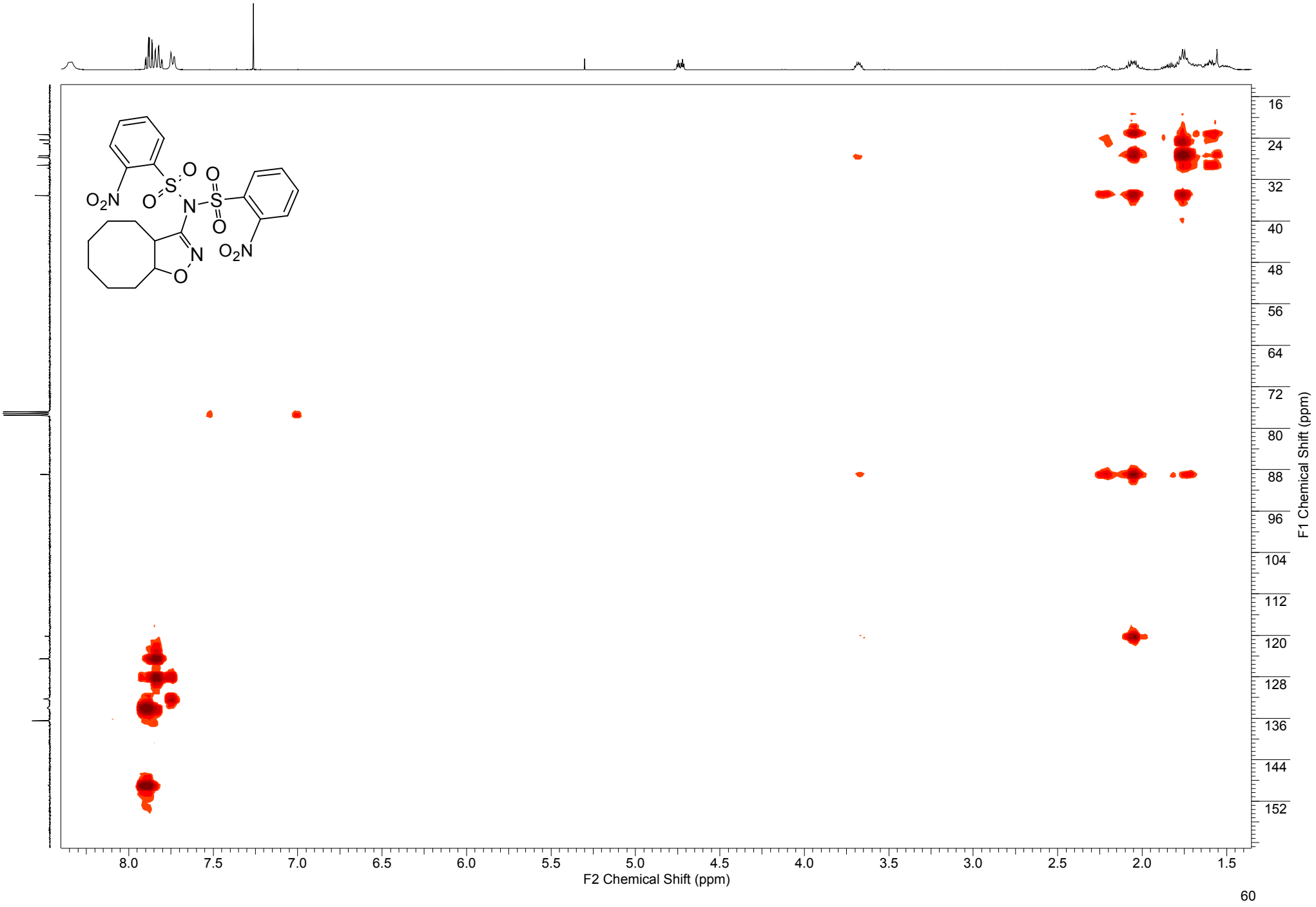
^{1}H NMR spectrum of compound **5h** ($CDCl_3$)



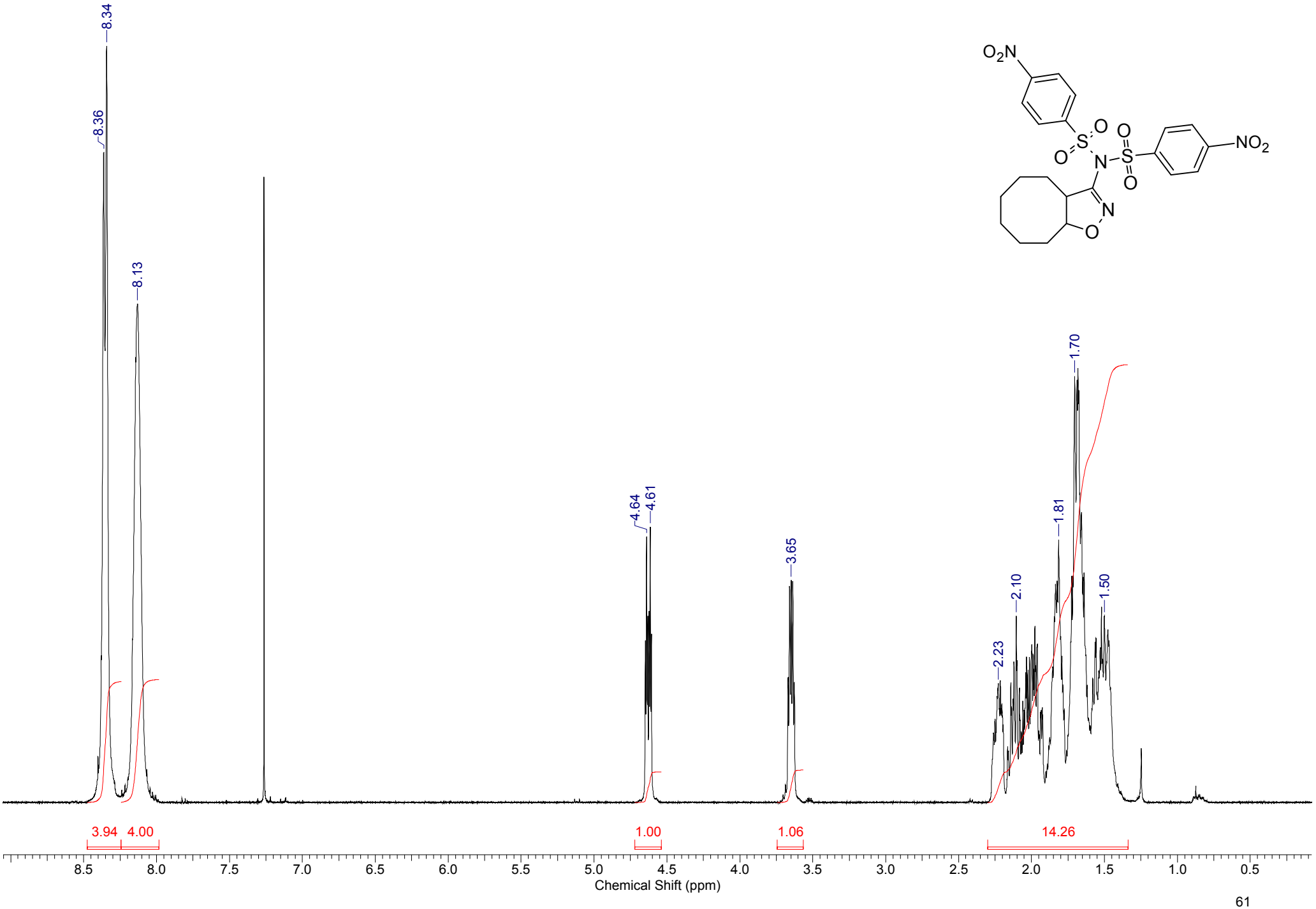
^{13}C NMR spectrum of compound **5h** ($CDCl_3$)



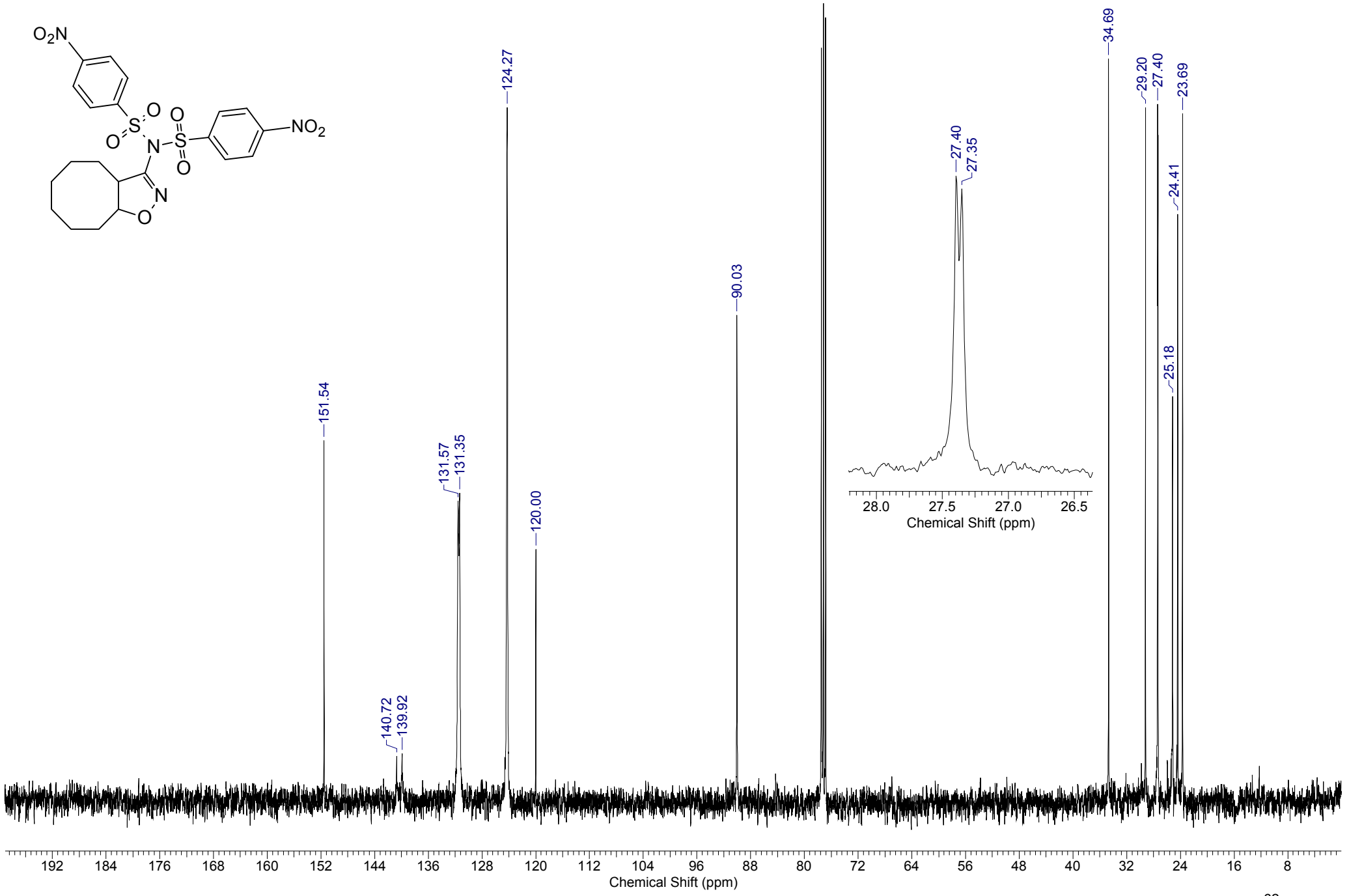
HMBC NMR spectrum of compound **5h** ($CDCl_3$)



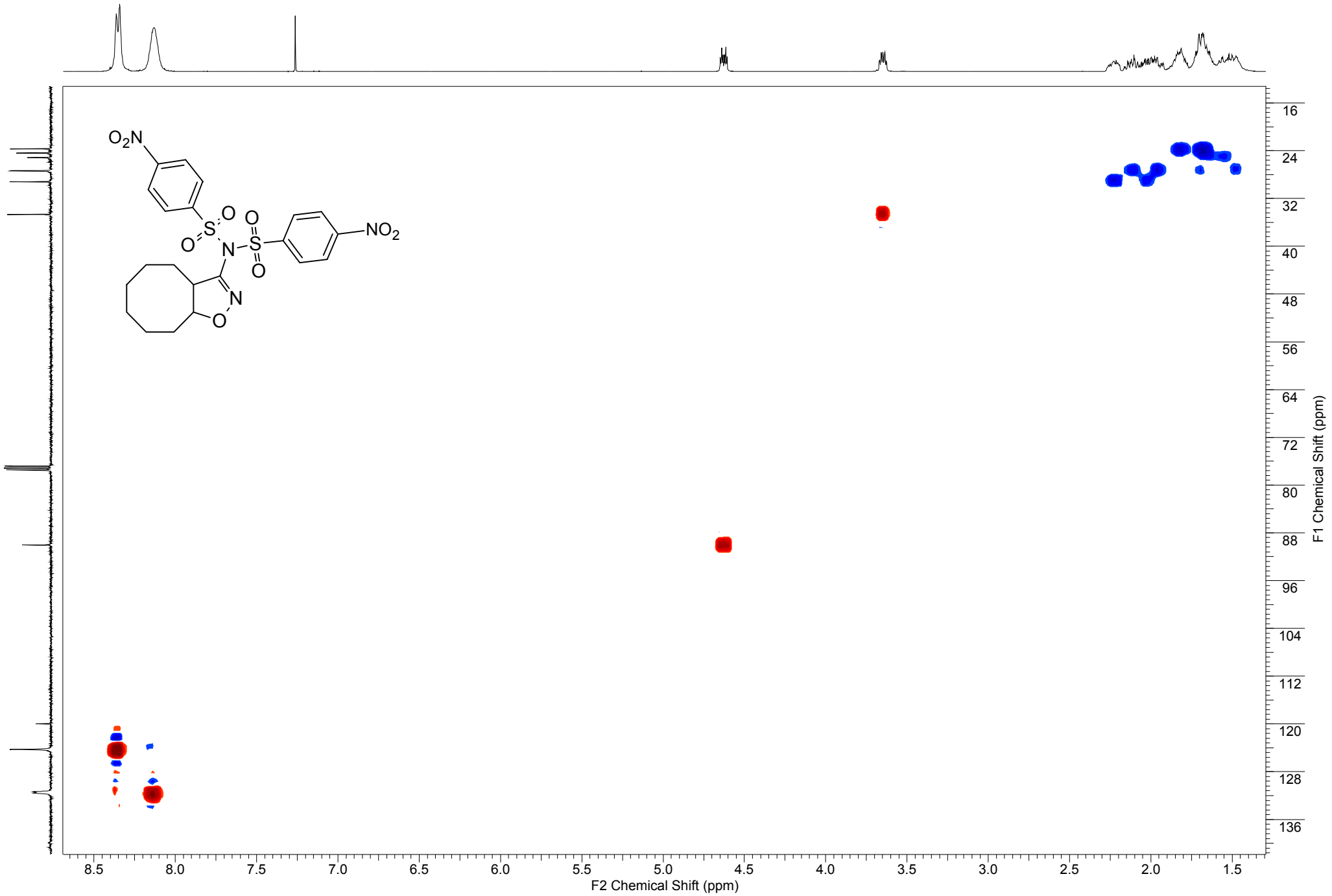
^{1}H NMR spectrum of compound **5i** ($CDCl_3$)



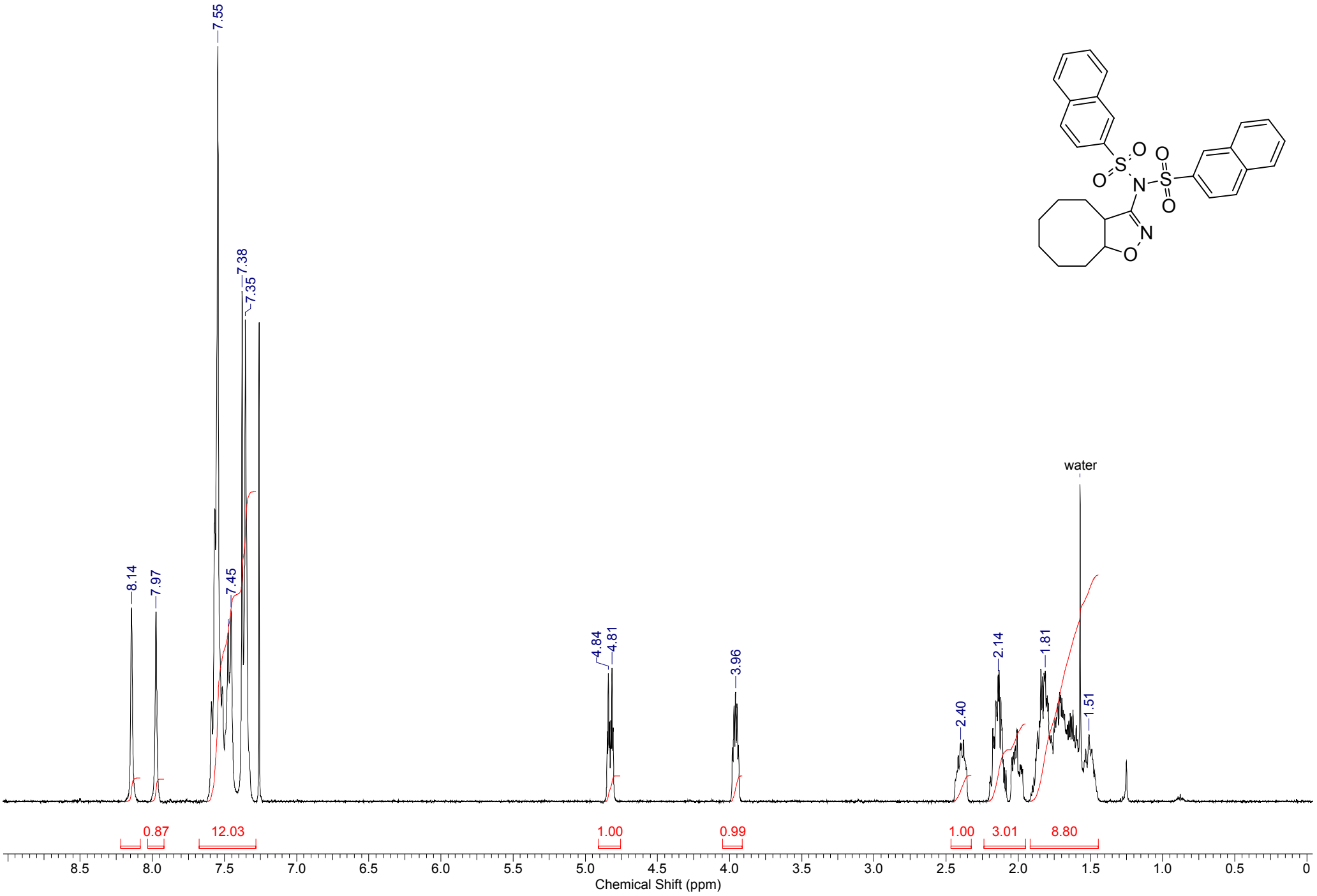
^{13}C NMR spectrum of compound **5i** ($CDCl_3$)



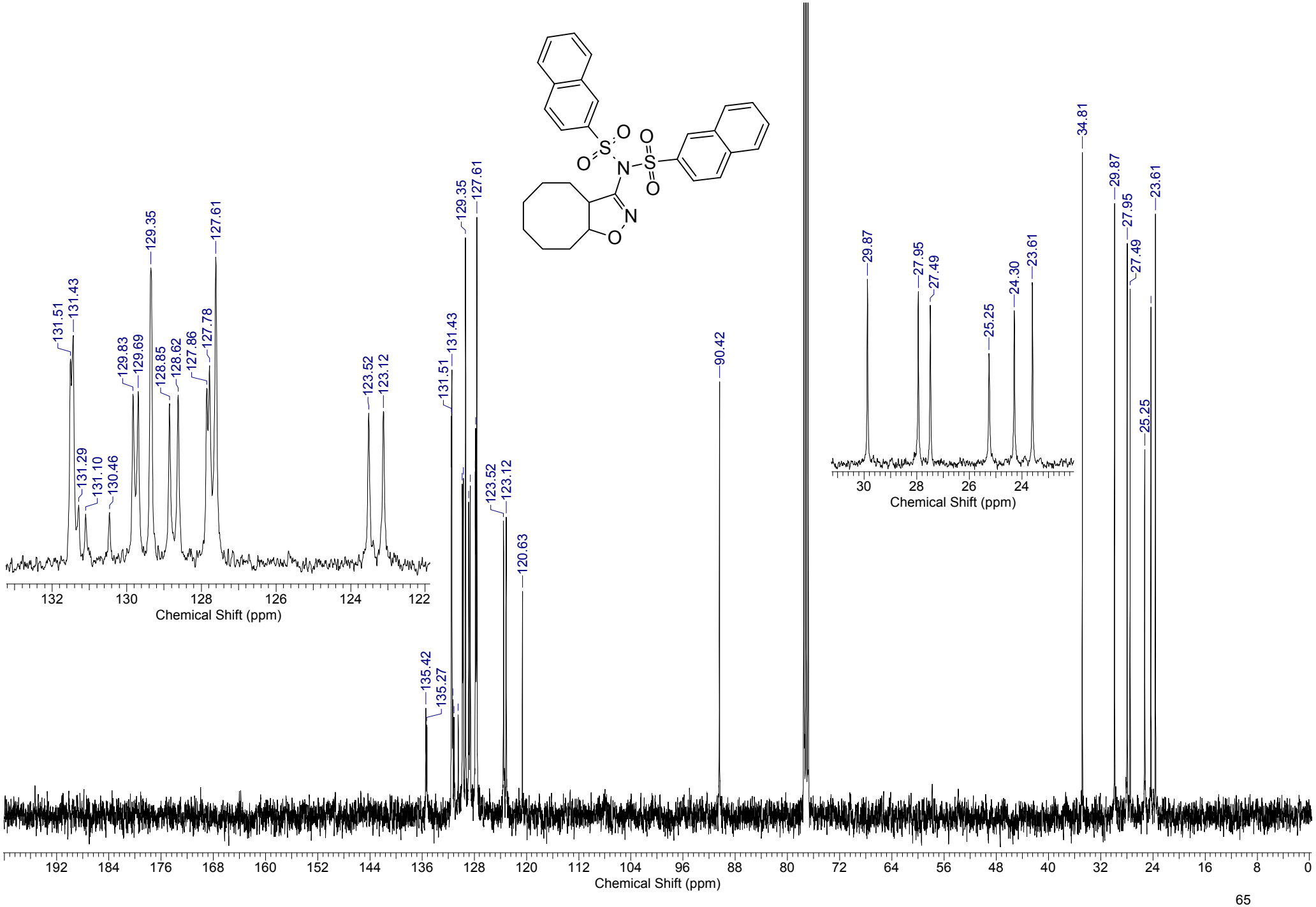
HSQC NMR spectrum of compound **5i** ($CDCl_3$)



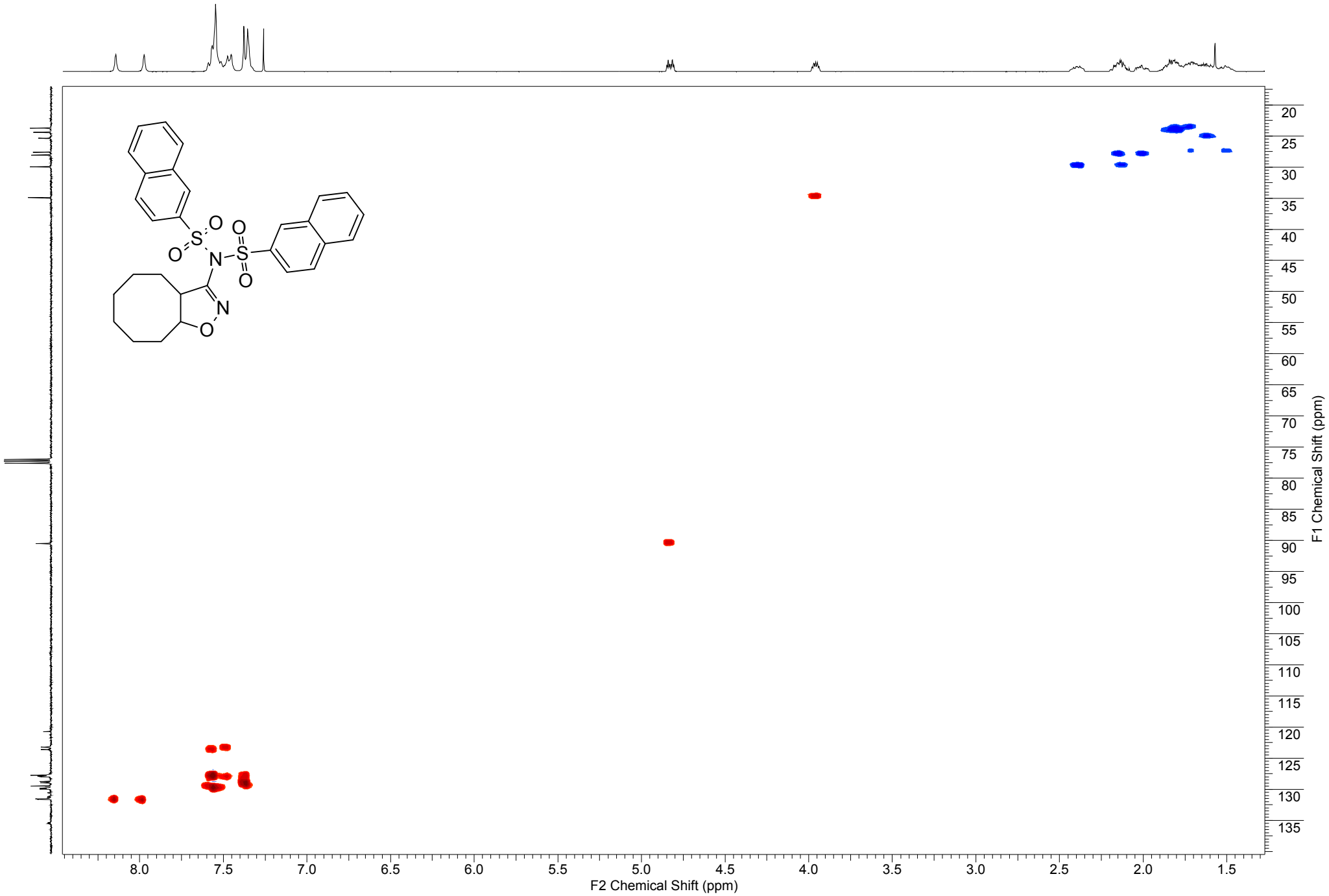
^{1}H NMR spectrum of compound **5j** ($CDCl_3$)



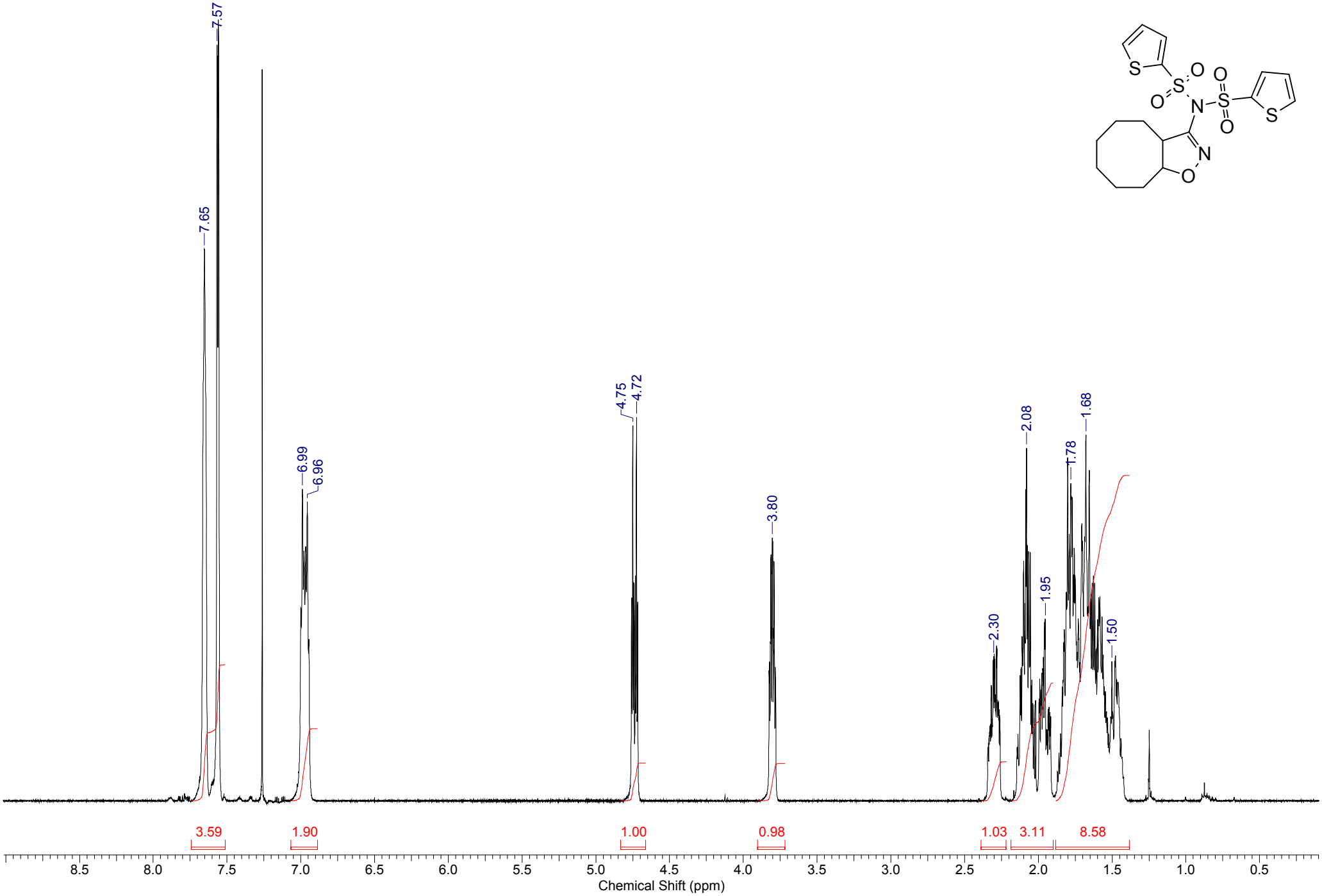
^{13}C NMR spectrum of compound **5j** ($CDCl_3$)



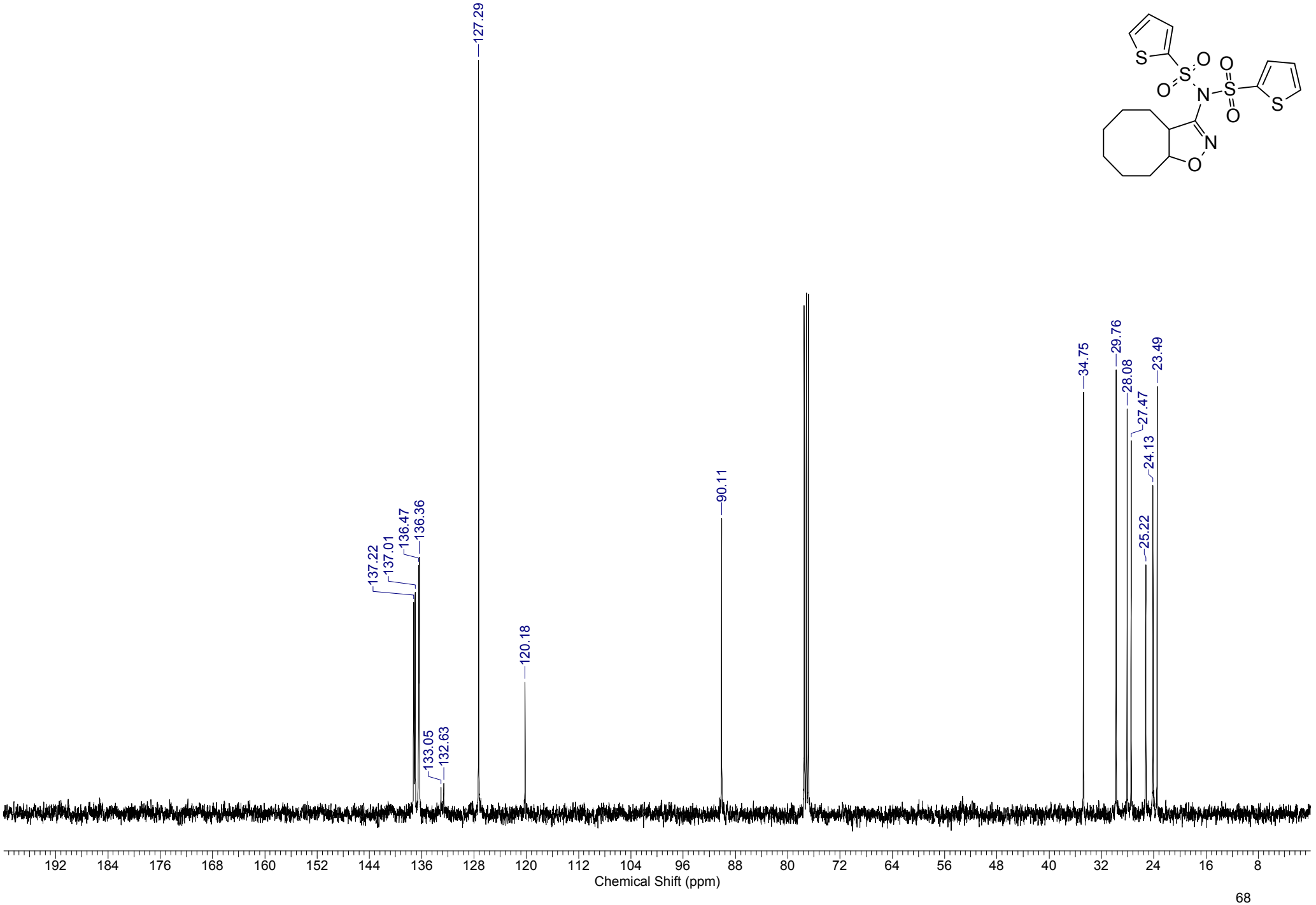
HSQC NMR spectrum of compound **5j** ($CDCl_3$)



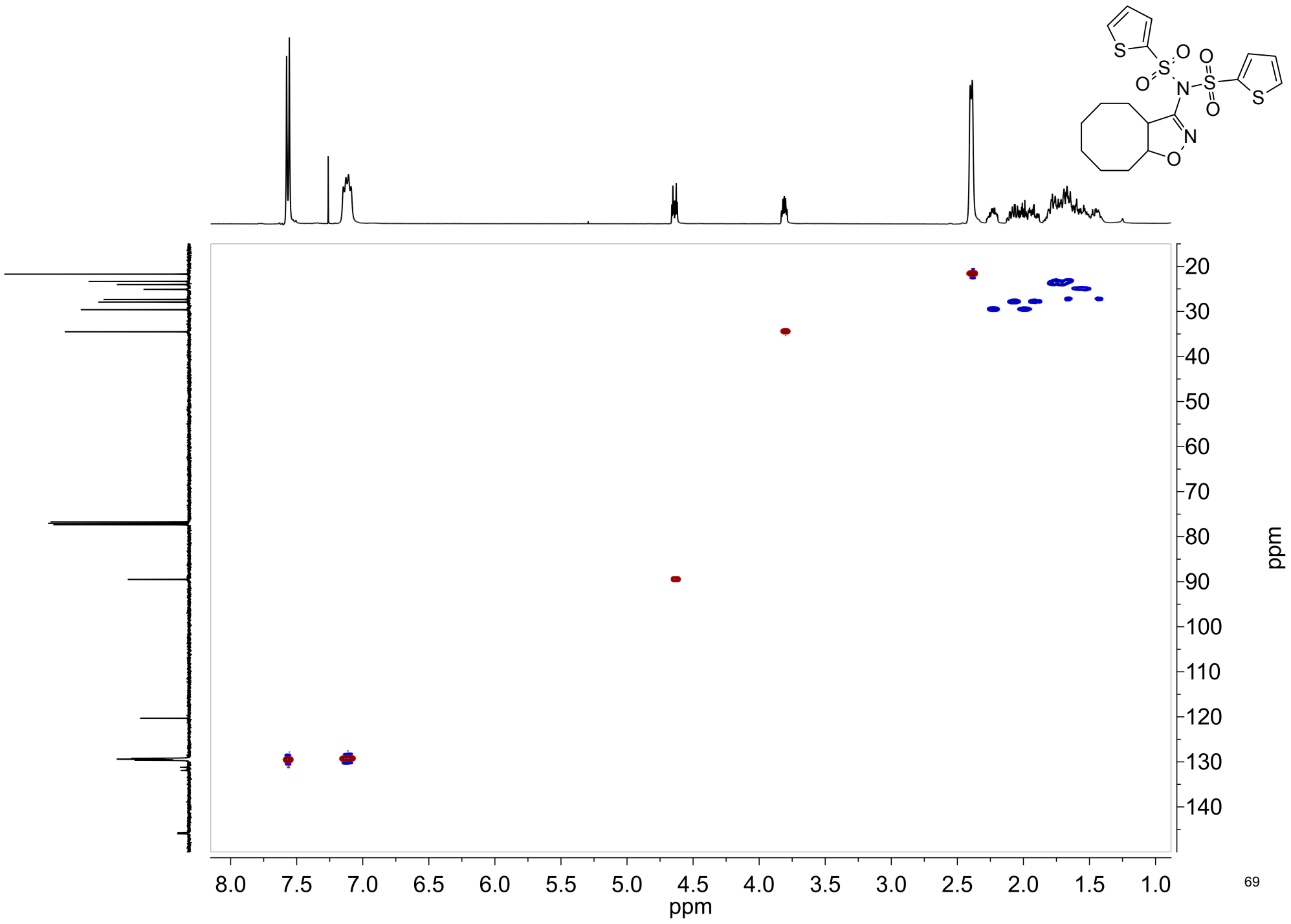
^{1}H NMR spectrum of compound **5k** ($CDCl_3$)



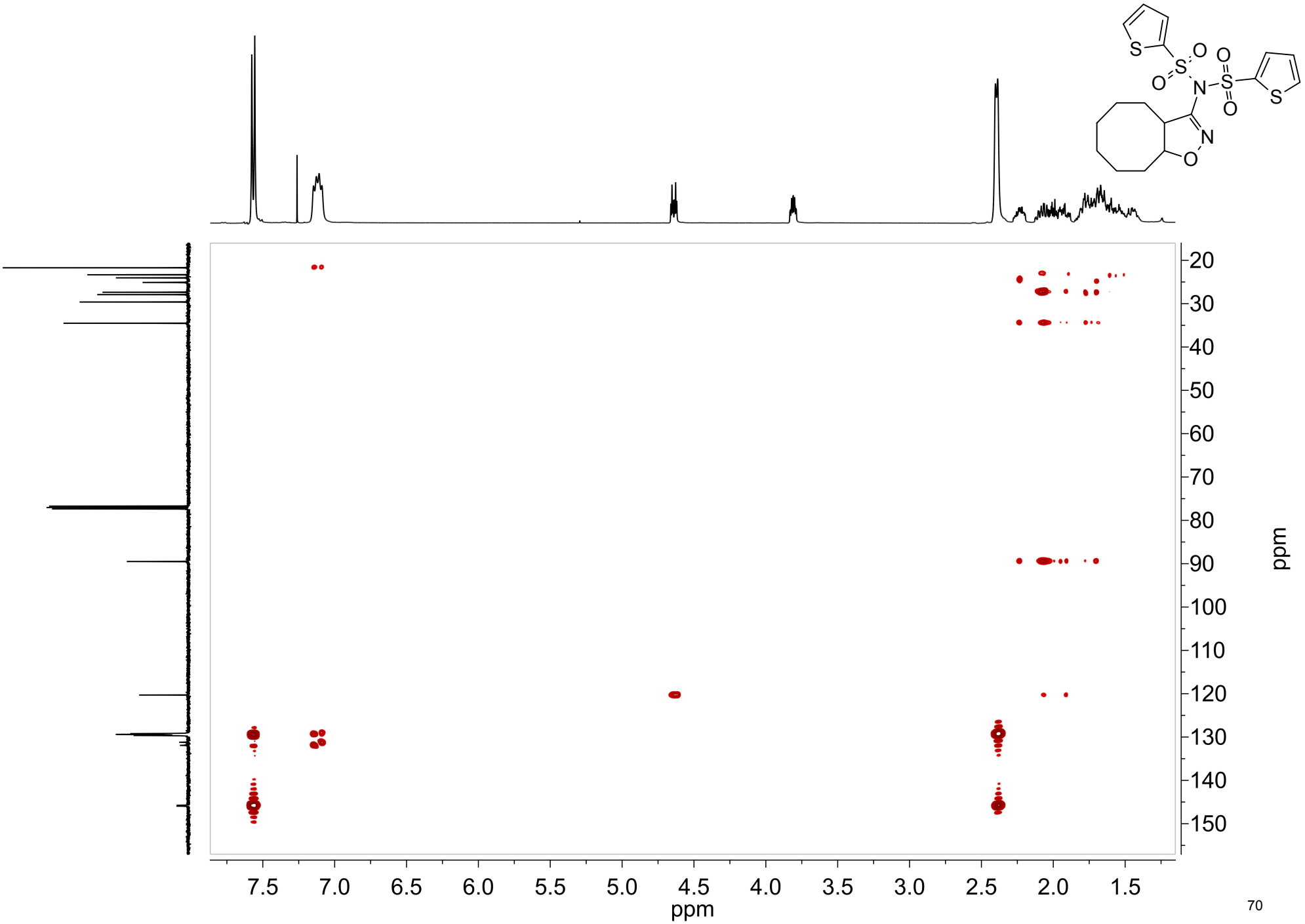
^{13}C NMR spectrum of compound **5k** ($CDCl_3$)



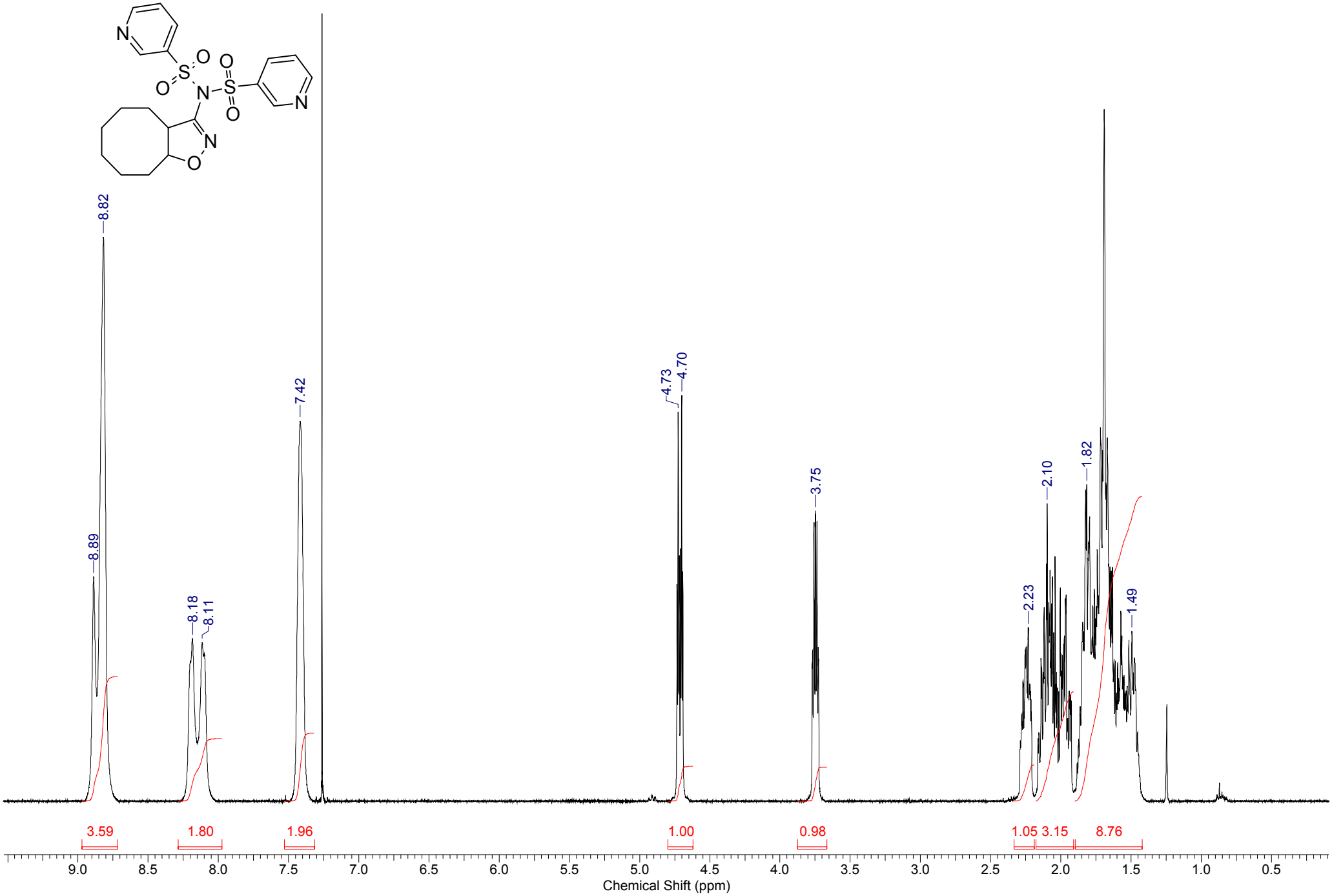
HSQC NMR spectrum of compound **5k** ($CDCl_3$)



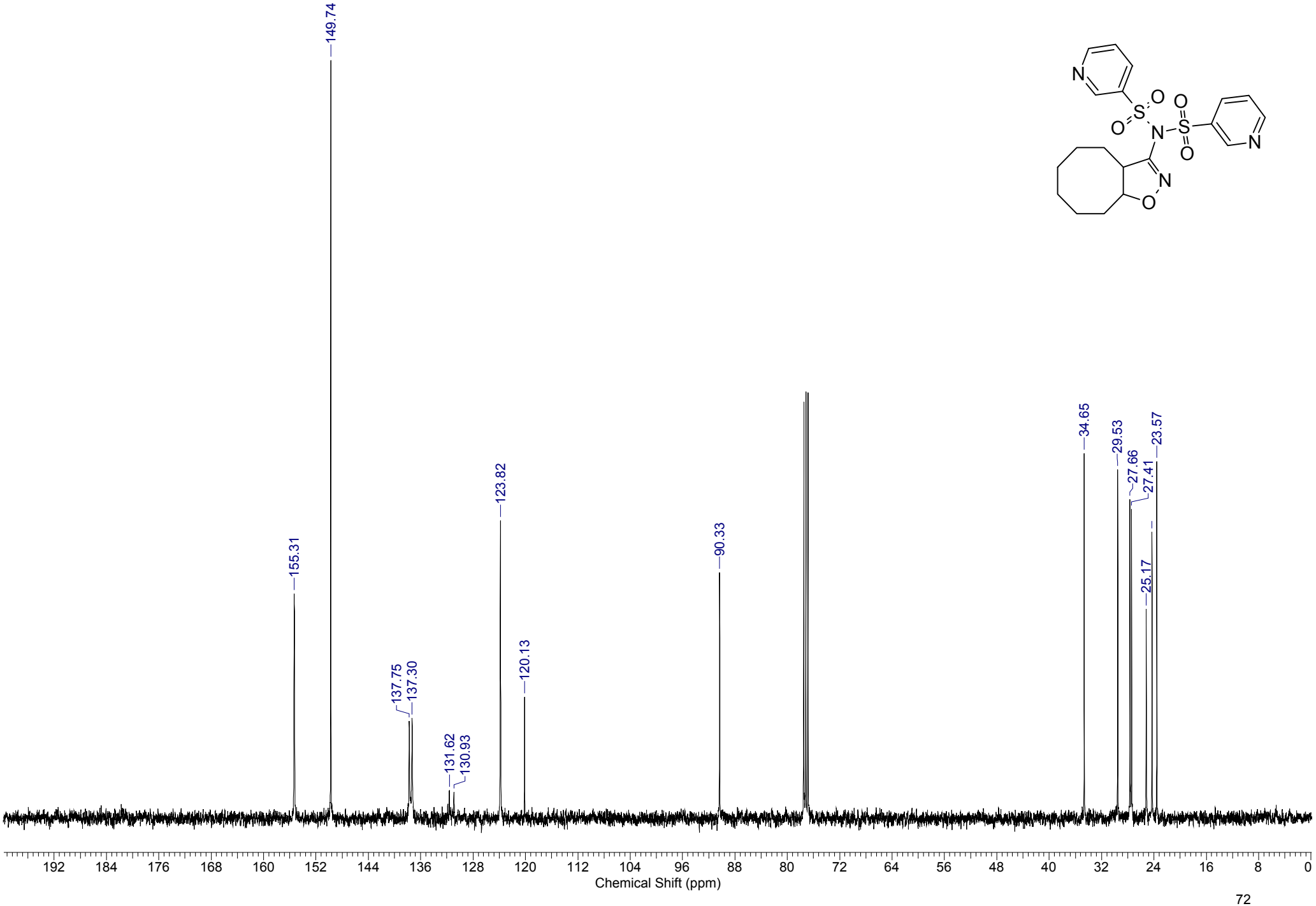
HMBC NMR spectrum of compound **5k** ($CDCl_3$)



^{1}H NMR spectrum of compound **5l** ($CDCl_3$)



^{13}C NMR spectrum of compound **5l** ($CDCl_3$)



HSQC NMR spectrum of compound **5k** ($CDCl_3$)