

SUPPORTING INFORMATION FOR

Design, synthesis and biological evaluation of arylsulfonamides as ADAMTS7 inhibitors

*Doretta Cuffaro,^{1,¶} Tina Burkhard,^{2,¶} Bianca Laura Bernardoni,¹ Riccardo Di Leo,¹ Xiaohan Zhang,³
Salvatore Galati,¹ Tiziano Tuccinardi,¹ Marco Macchia,¹ Armando Rossello,¹ Salvatore Santamaria,^{2,#,*}
Rens de Groot,^{3,#,*} and Elisa Nuti^{1,#,*}*

¹ Department of Pharmacy, University of Pisa, Via Bonanno 6, 56126 Pisa, Italy

² Department of Biochemical and Physiological Sciences, School of Biosciences, Faculty of Health and Medical Sciences, Edward Jenner Building, University of Surrey, Guildford GU2 7XH, UK

³ Institute of Cardiovascular Science, University College London, 51 Chenies Mews, London WC1E 6HX, UK.

*Correspondence: Salvatore Santamaria, e-mail: s.santamaria@surrey.ac.uk; Rens de Groot, e-mail: R.deGroot@ucl.ac.uk; Elisa Nuti: e-mail: elisa.nuti@unipi.it

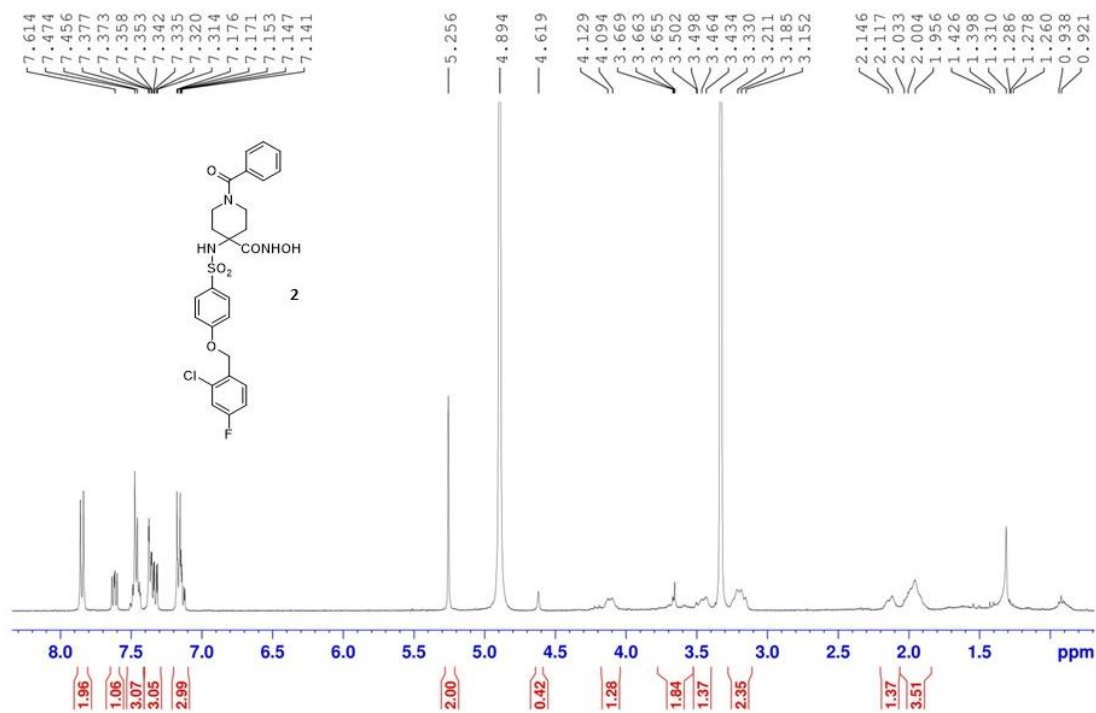
¶ D.C. and T.B. contributed equally to this work.

E.N. and RdG and S.S. contributed equally to this work.

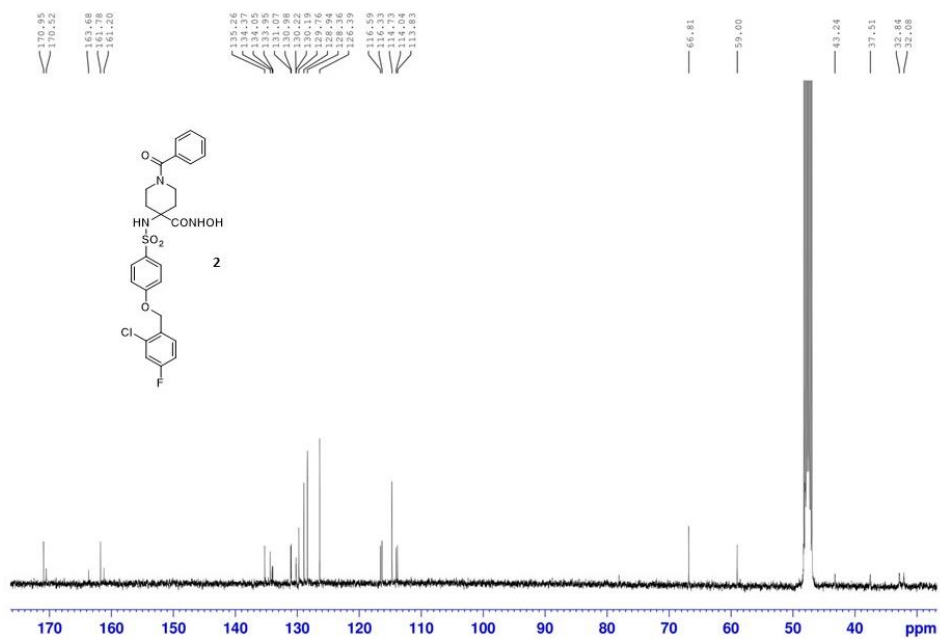
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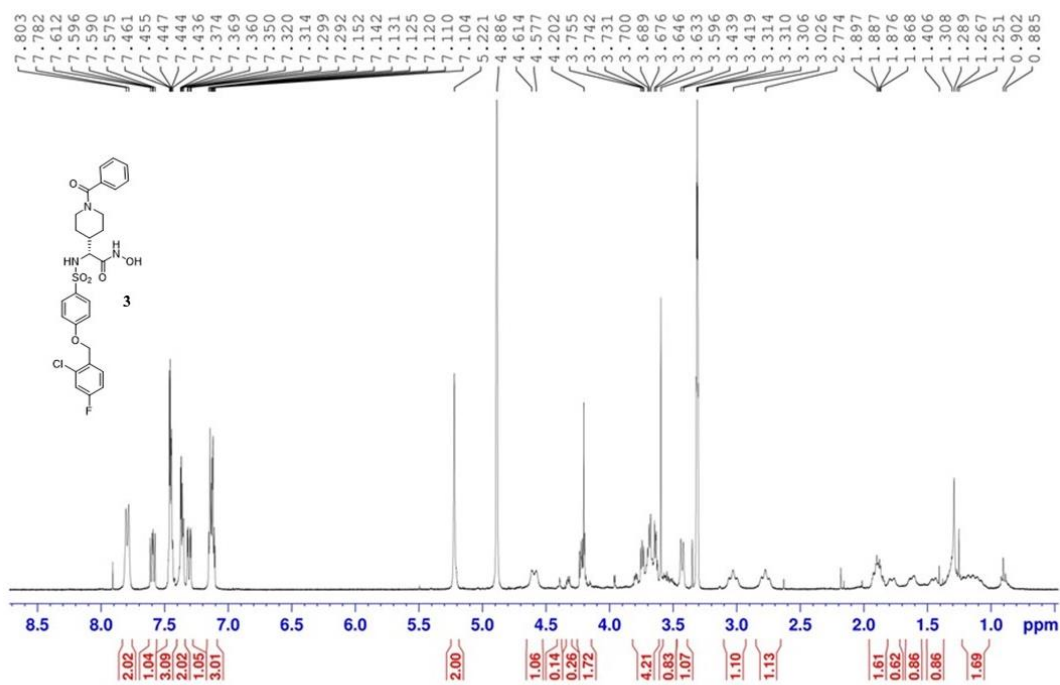
Compound 2: ^1H NMR (400 MHz, CD_3OD)



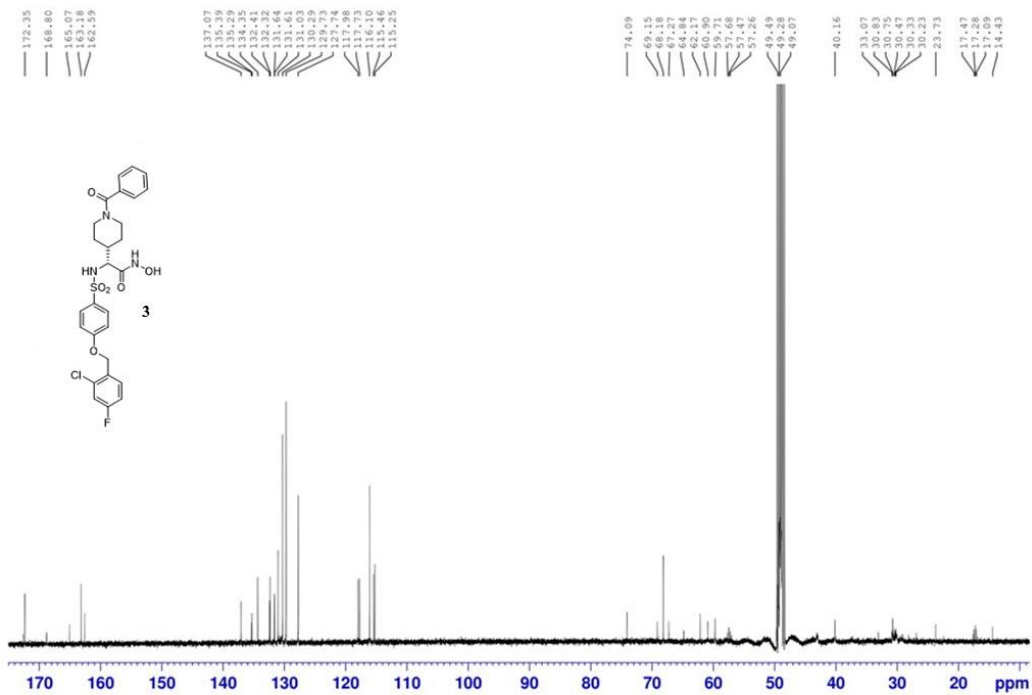
Compound 2: ^{13}C NMR (100 MHz, CD_3OD)



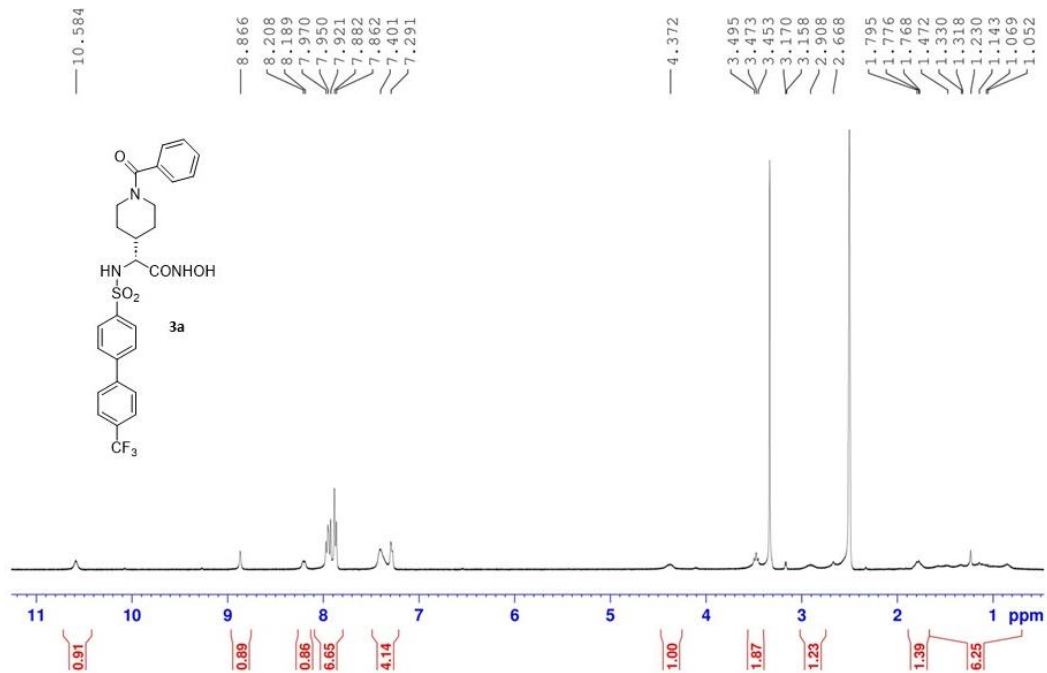
Compound 3: ^1H NMR (400 MHz, CD_3OD).



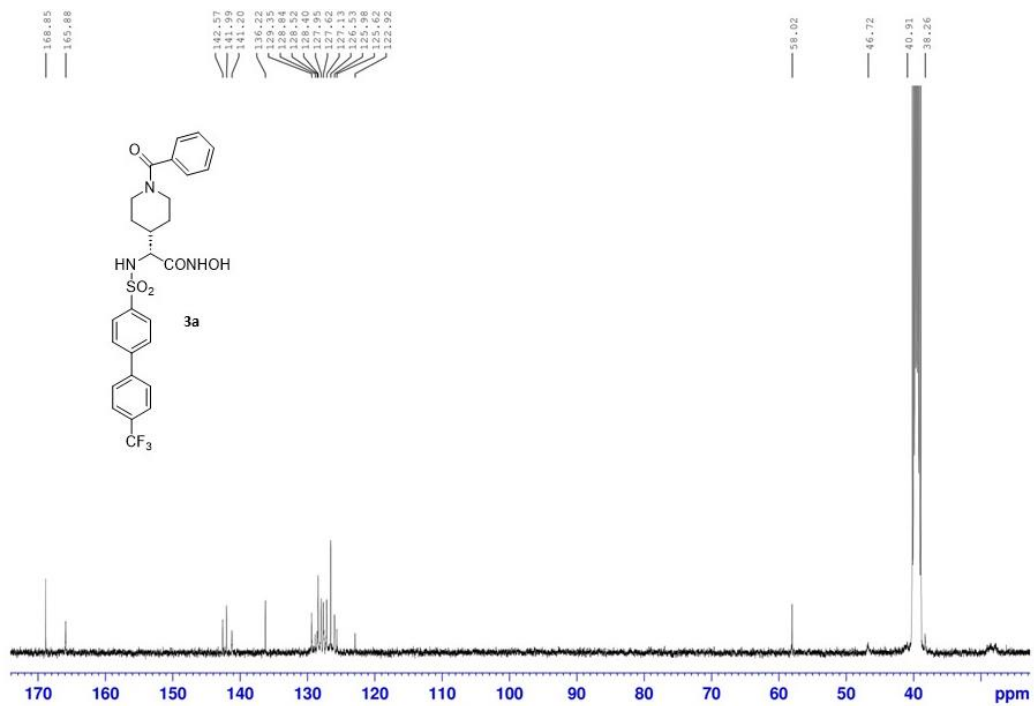
Compound 3: ^{13}C NMR (100 MHz, CD_3OD).



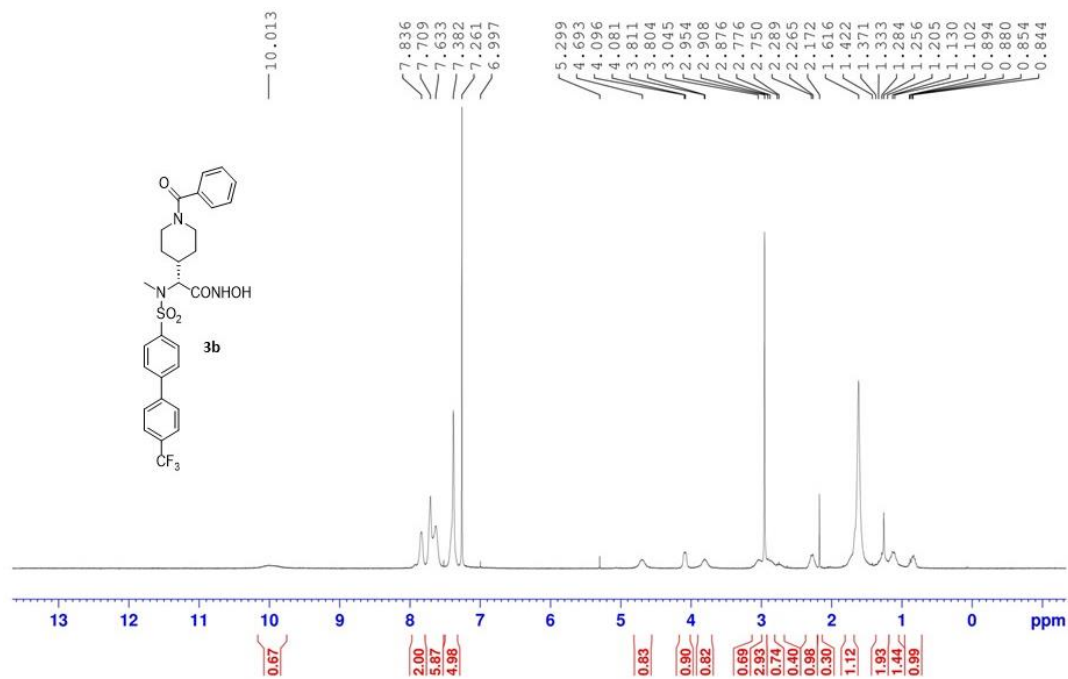
Compound **3a**: ^1H NMR (400 MHz, $\text{DMSO-}d_6$).



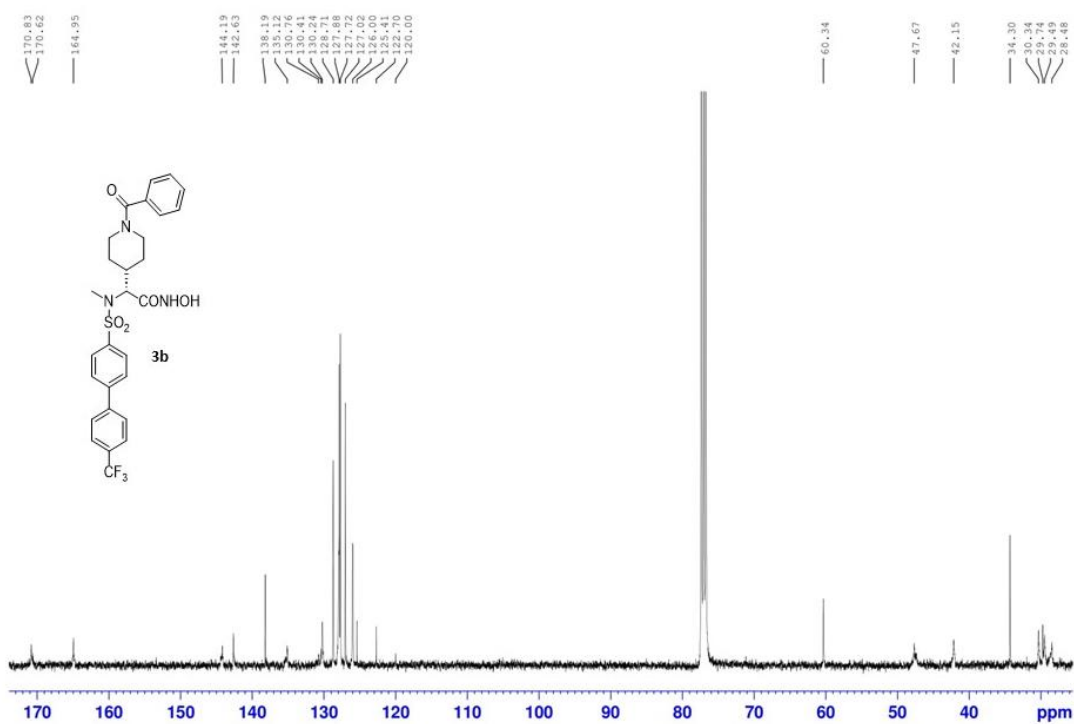
Compound **3a**: ^{13}C NMR (100 MHz, $\text{DMSO-}d_6$).



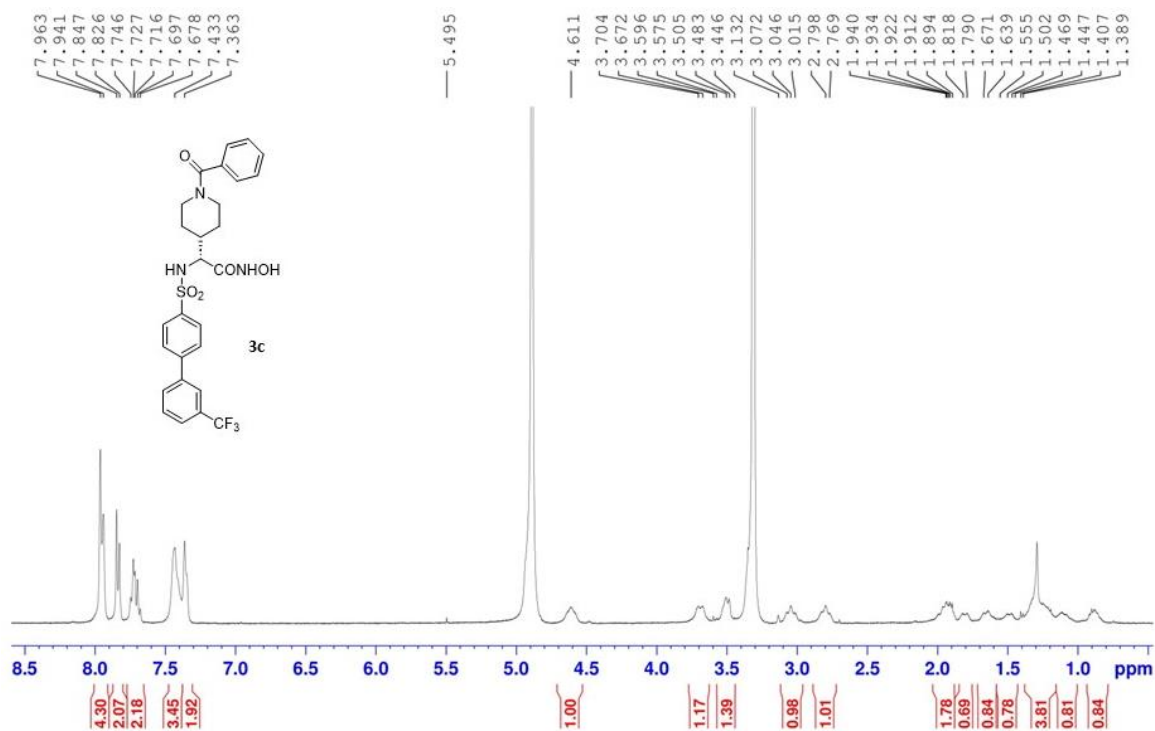
Compound **3b**: ^1H NMR (400 MHz, CDCl_3).



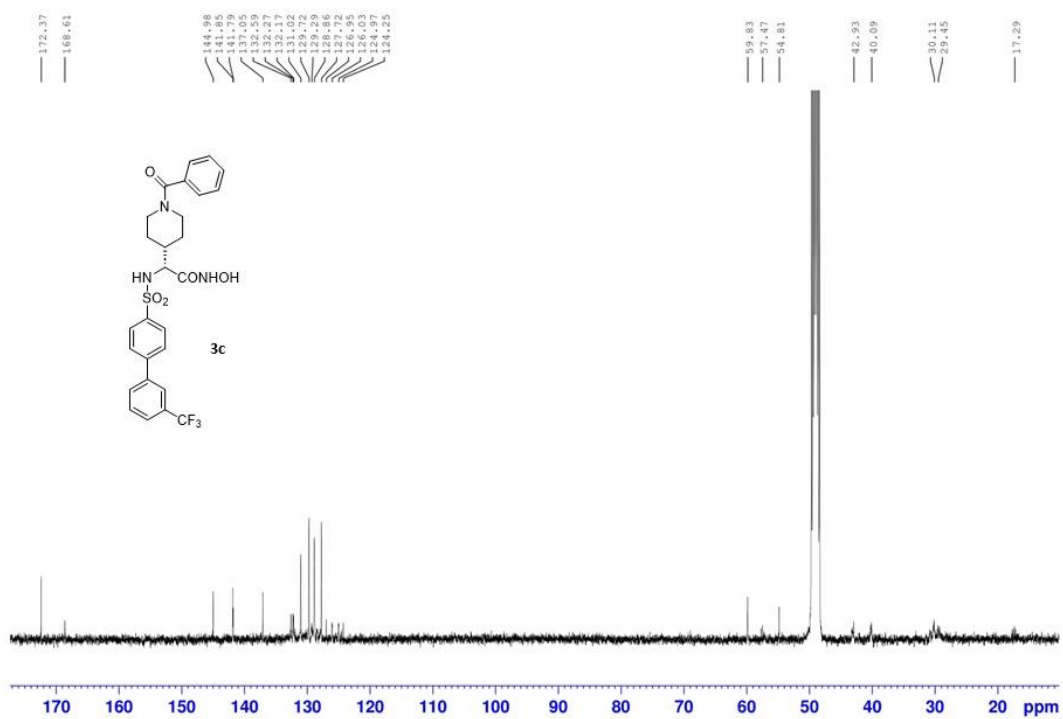
Compound **3b**: ^{13}C NMR (100 MHz, CDCl_3).



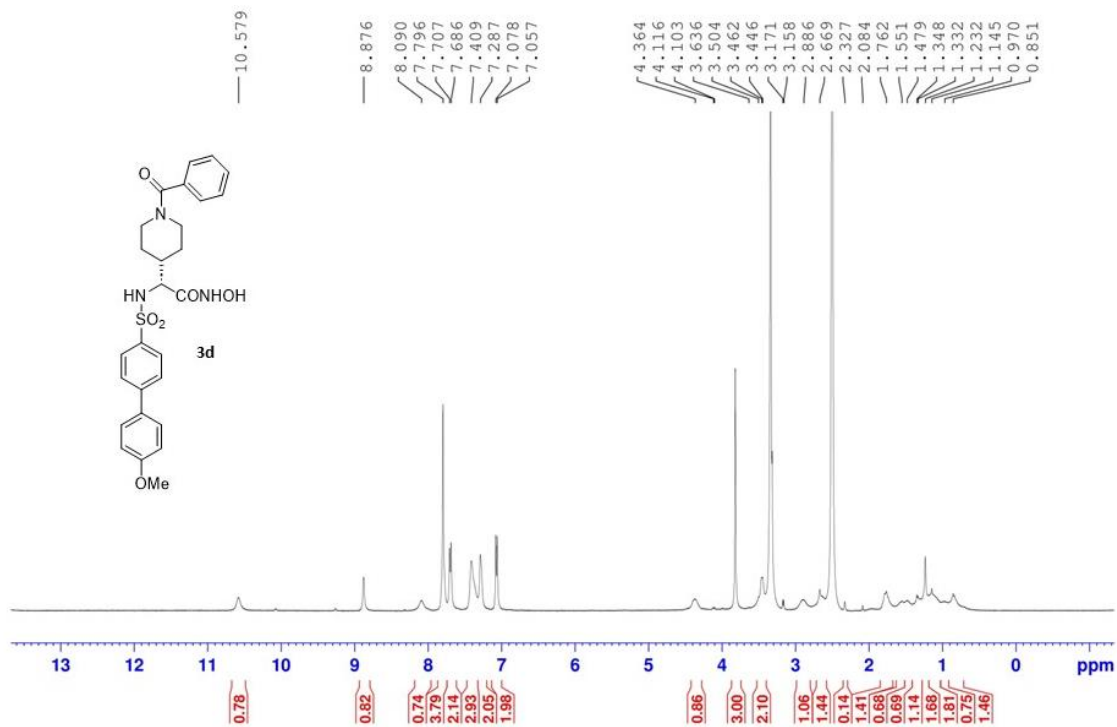
Compound **3c**: ^1H NMR (400 MHz, CD_3OD).



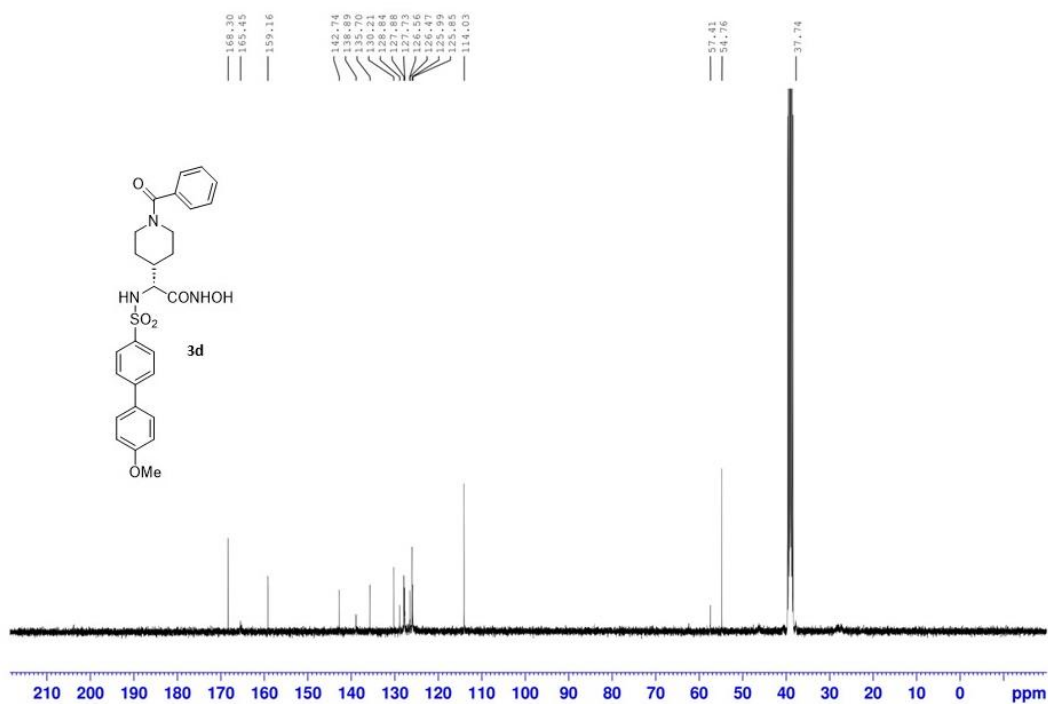
Compound **3c**: ^{13}C NMR (100 MHz, CD_3OD).



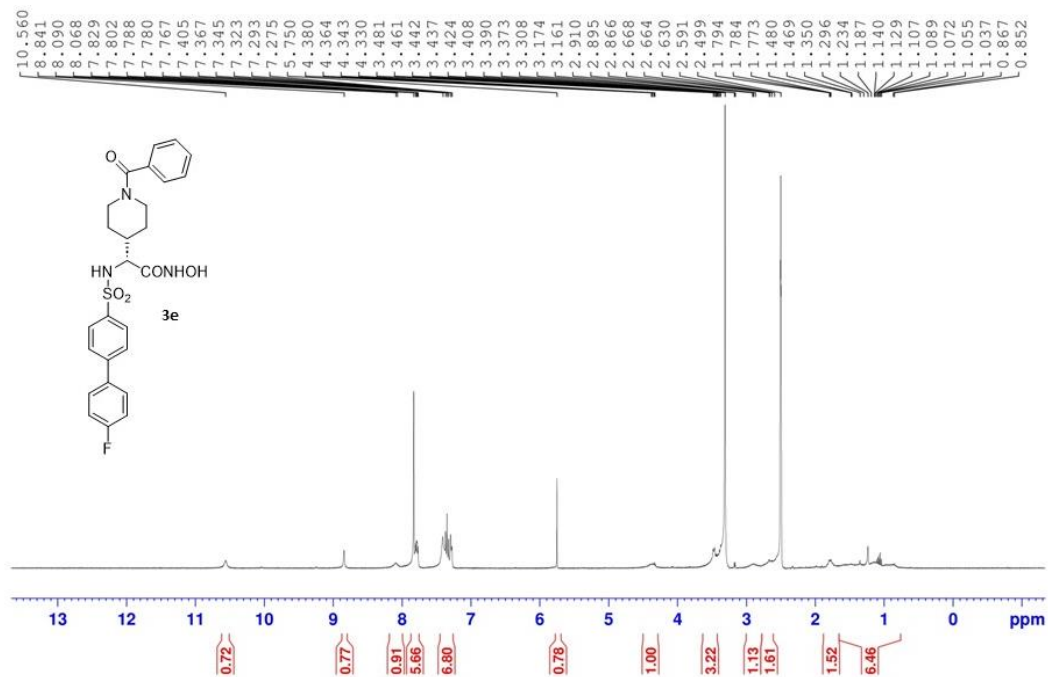
Compound **3d**: ^1H NMR (400 MHz, $\text{DMSO-}d_6$).



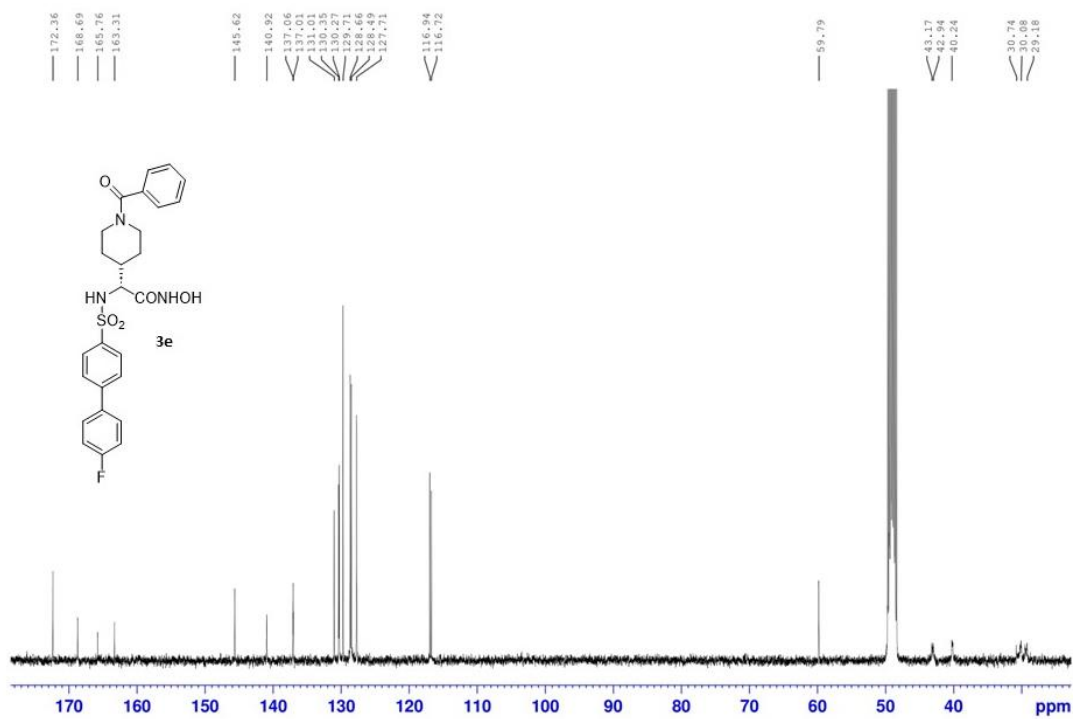
Compound **3d**: ^{13}C NMR (100 MHz, $\text{DMSO-}d_6$).



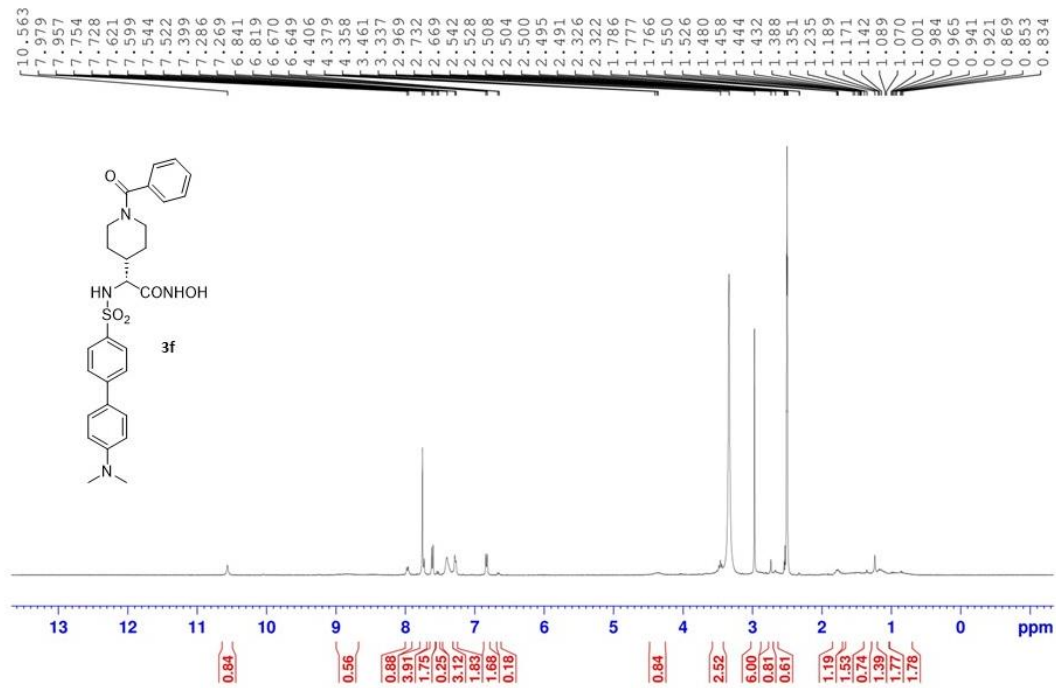
Compound **3e**: ^1H NMR (400 MHz, $\text{DMSO-}d_6$).



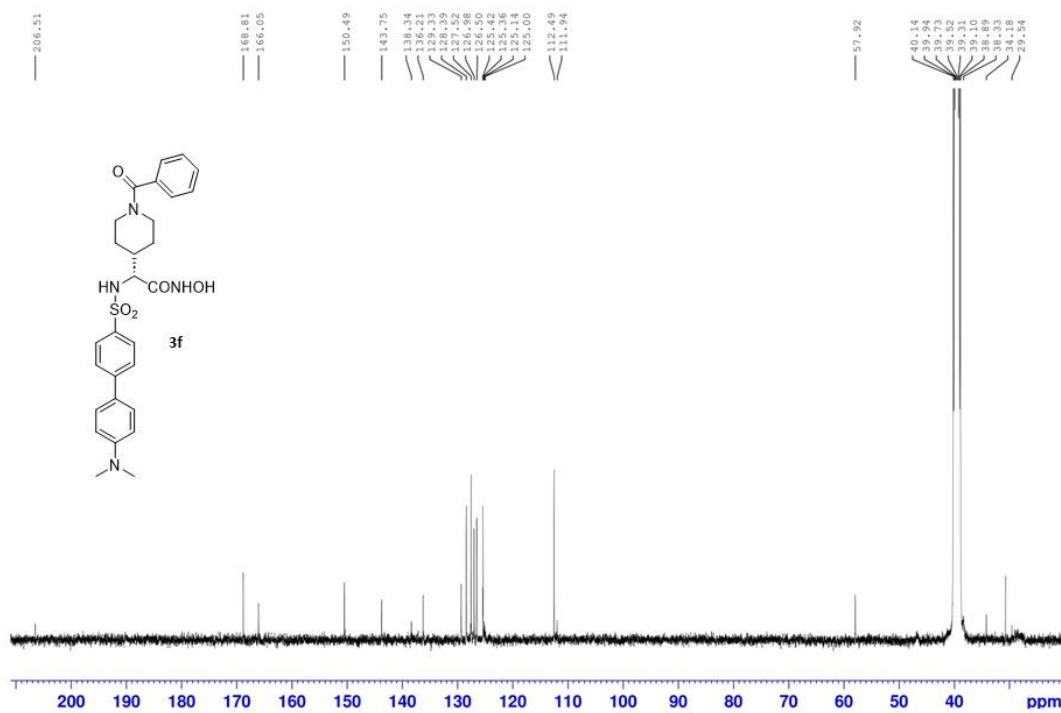
Compound **3e**: ^{13}C NMR (100 MHz, CD_3OD).



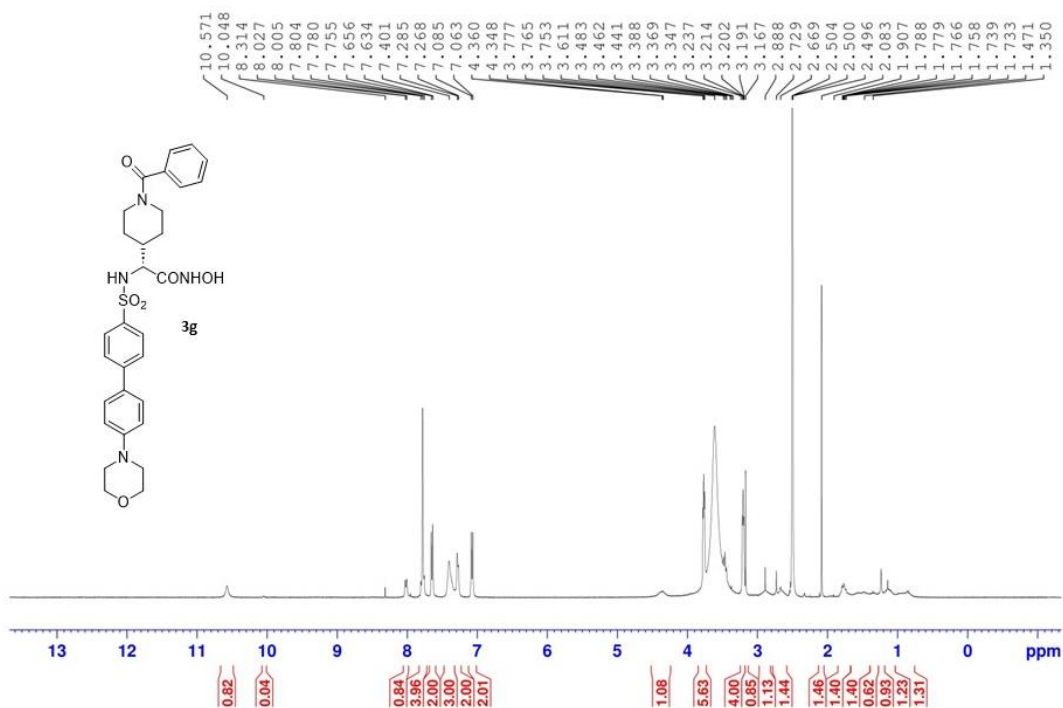
Compound **3f**: ^1H NMR (400 MHz, $\text{DMSO-}d_6$).



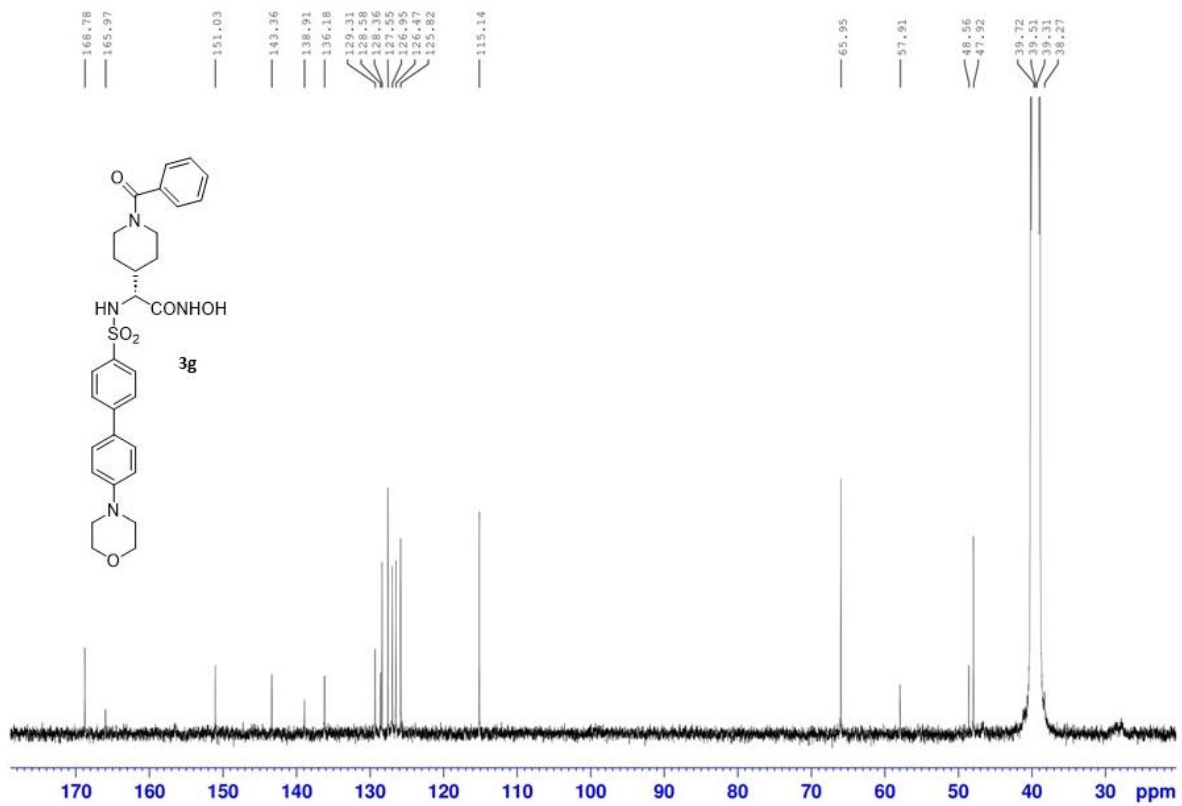
Compound **3f**: ^{13}C NMR (100 MHz, $\text{DMSO-}d_6$).



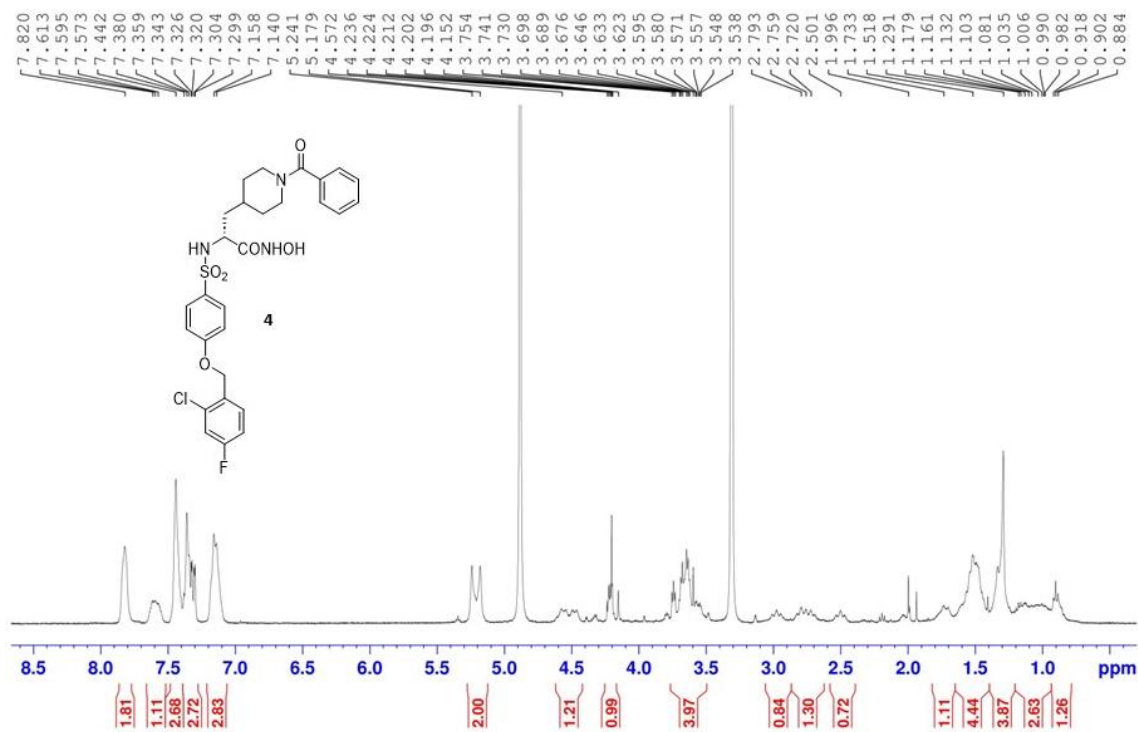
Compound **3g**: ^1H NMR (400 MHz, $\text{DMSO-}d_6$).



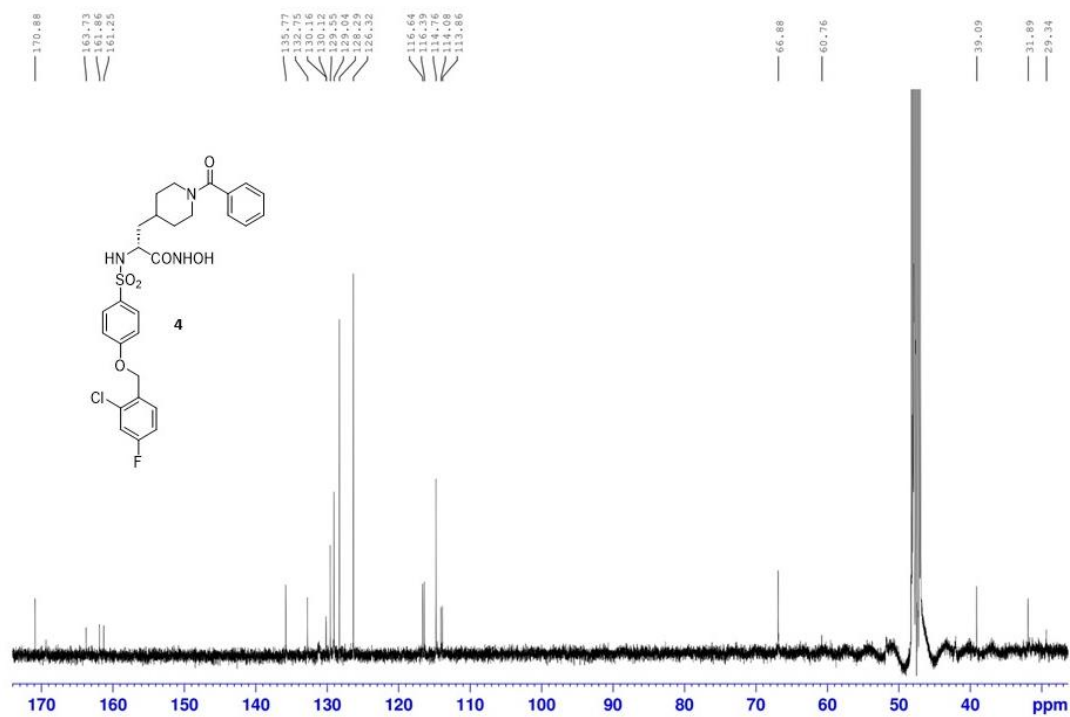
Compound **3g**: ^{13}C NMR (100 MHz, $\text{DMSO-}d_6$).



Compound 4: ^1H NMR (400 MHz, CD_3OD).

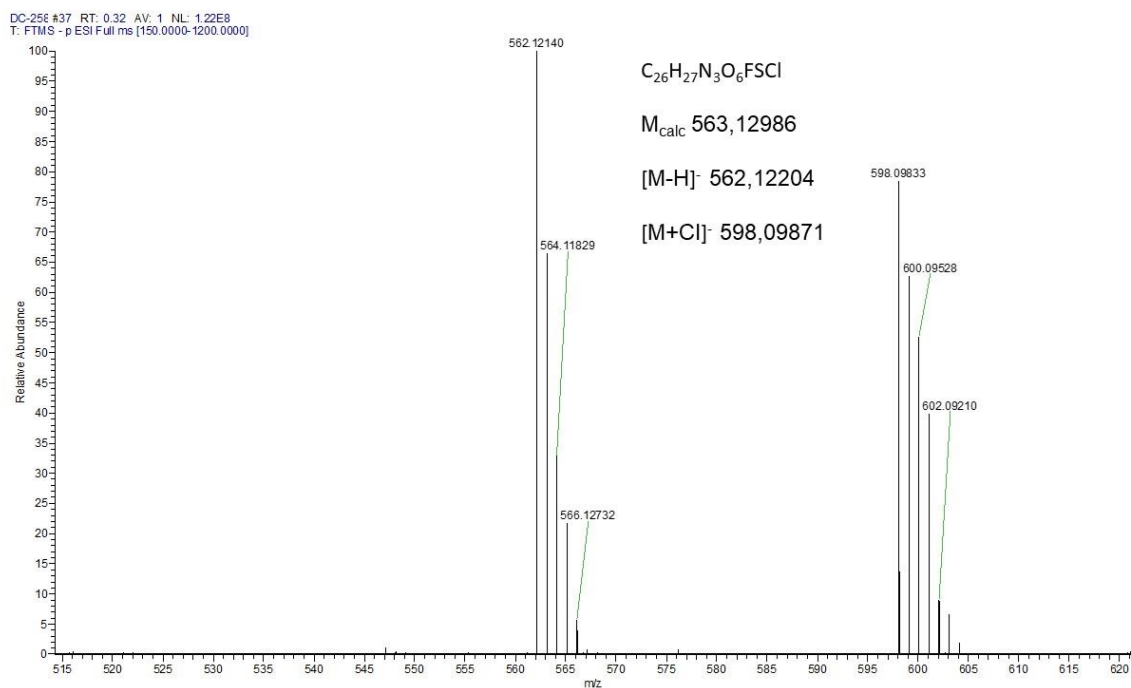


Compound 4: ^{13}C NMR (100 MHz, CD_3OD).

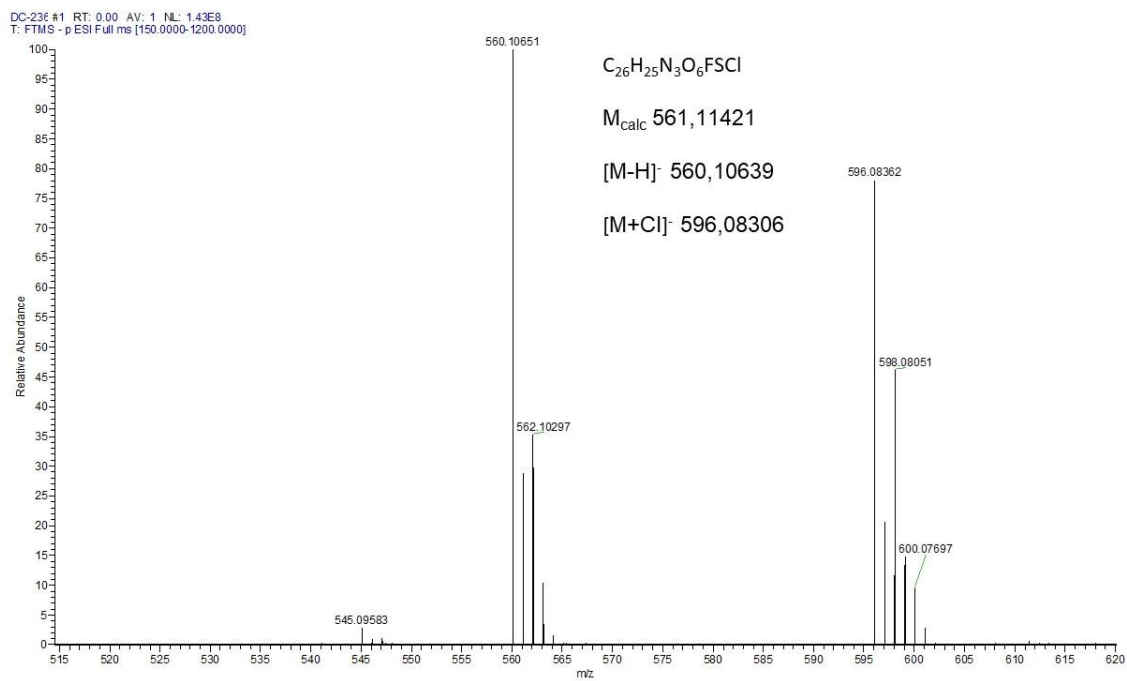


II. Representative HRMS spectra of final compounds (1, 2, 3, 3a-g, and 4)

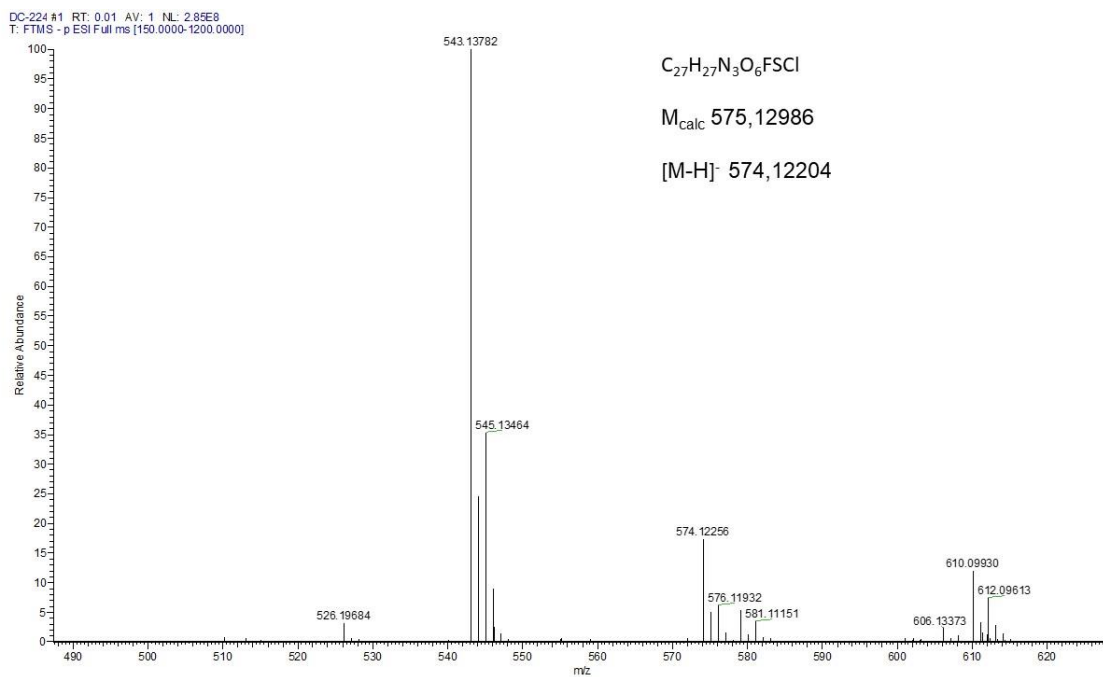
HRMS spectrum of compound 1



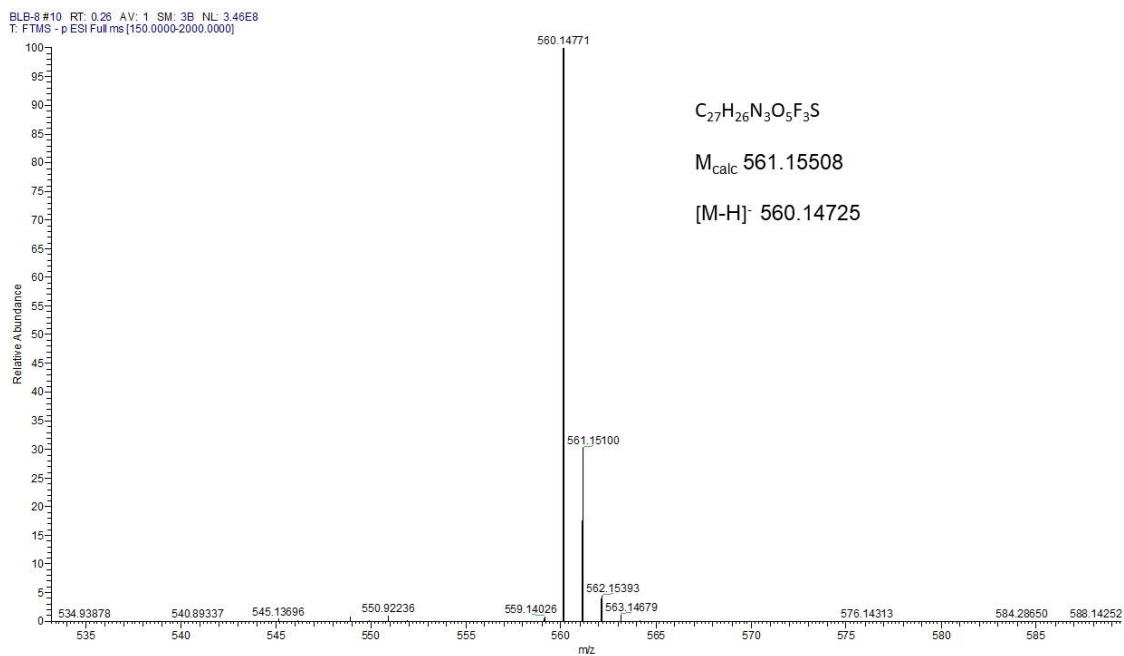
HRMS spectrum of compound 2

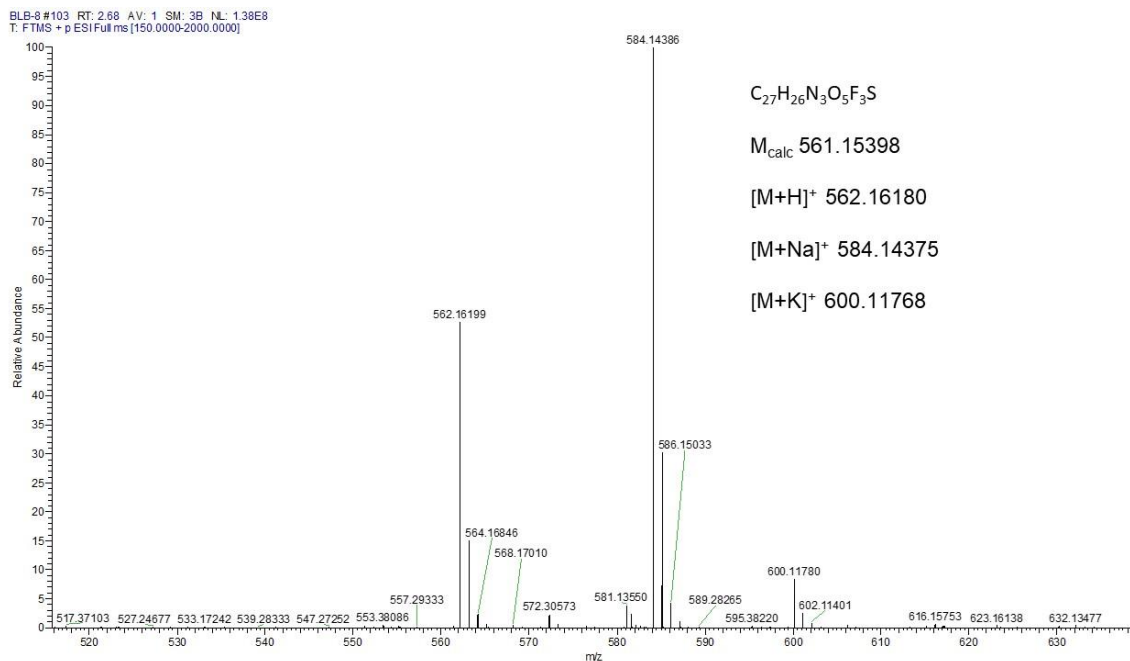


HRMS spectrum of compound **3**

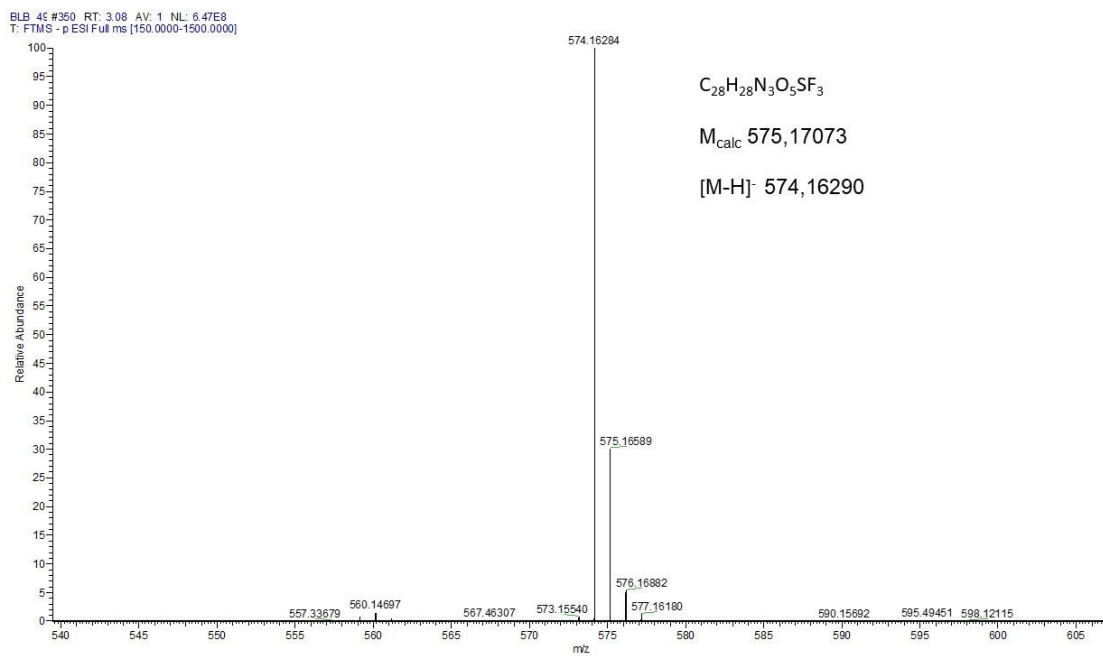


HRMS spectrum of compound **3a**

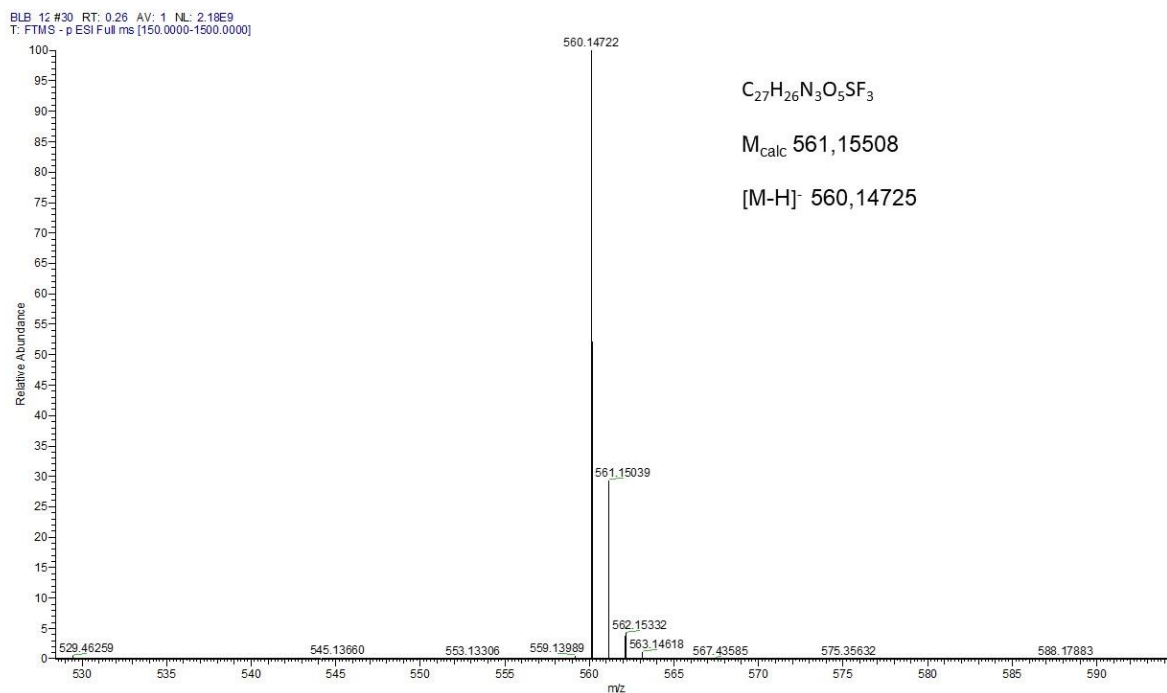




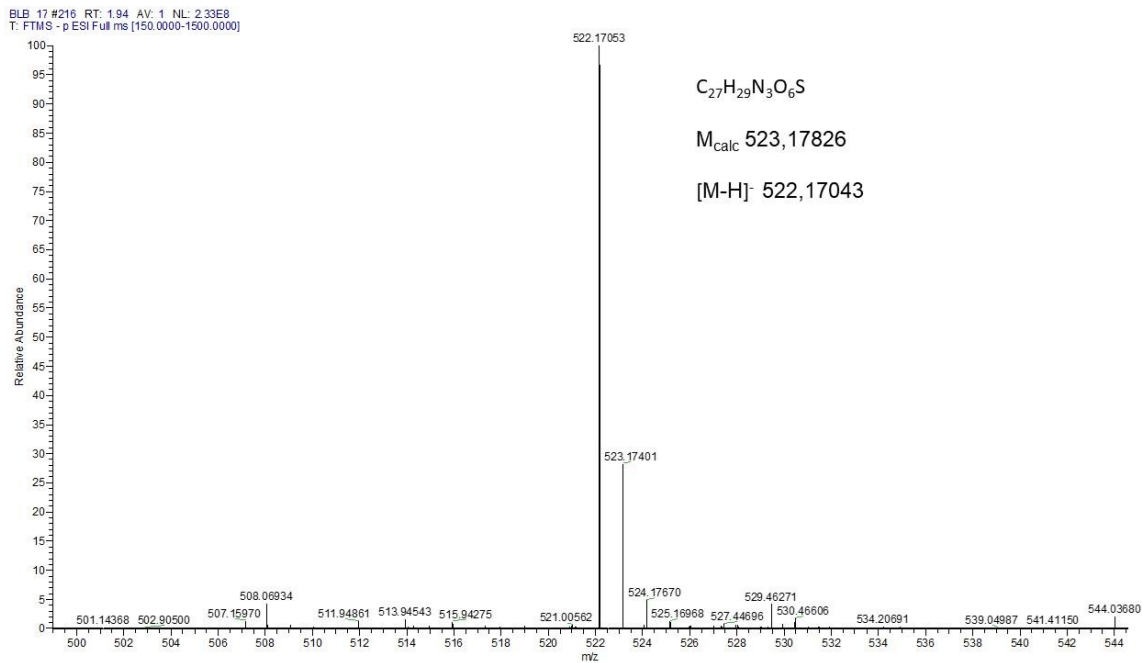
HRMS spectrum of compound **3b**



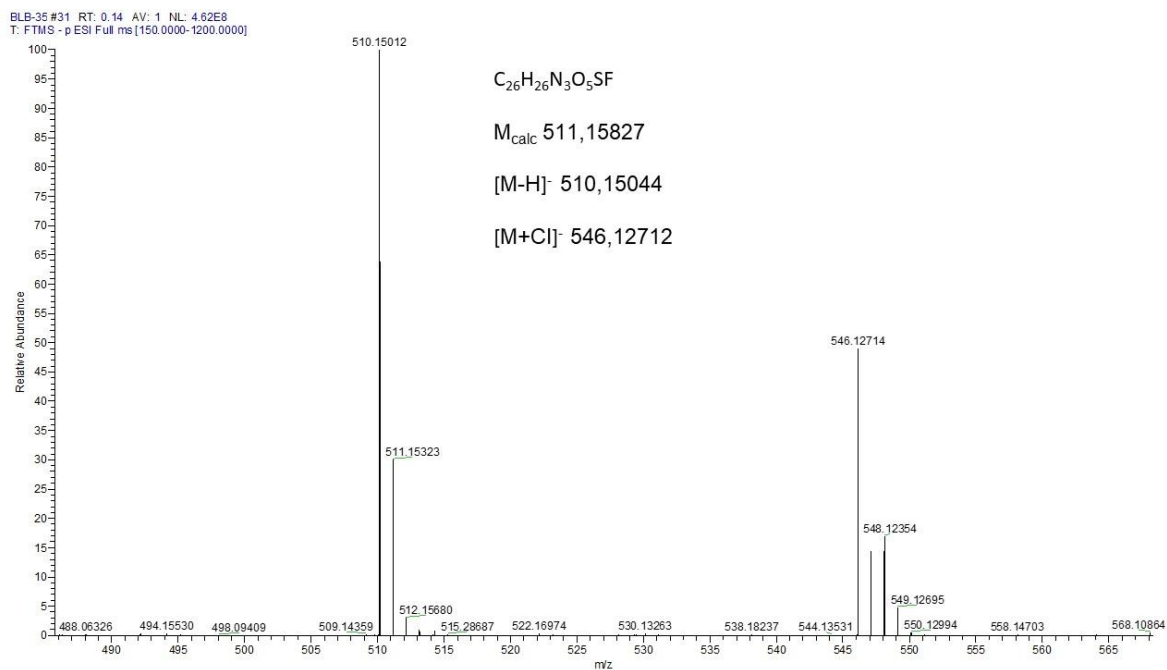
HRMS spectrum of compound **3c**



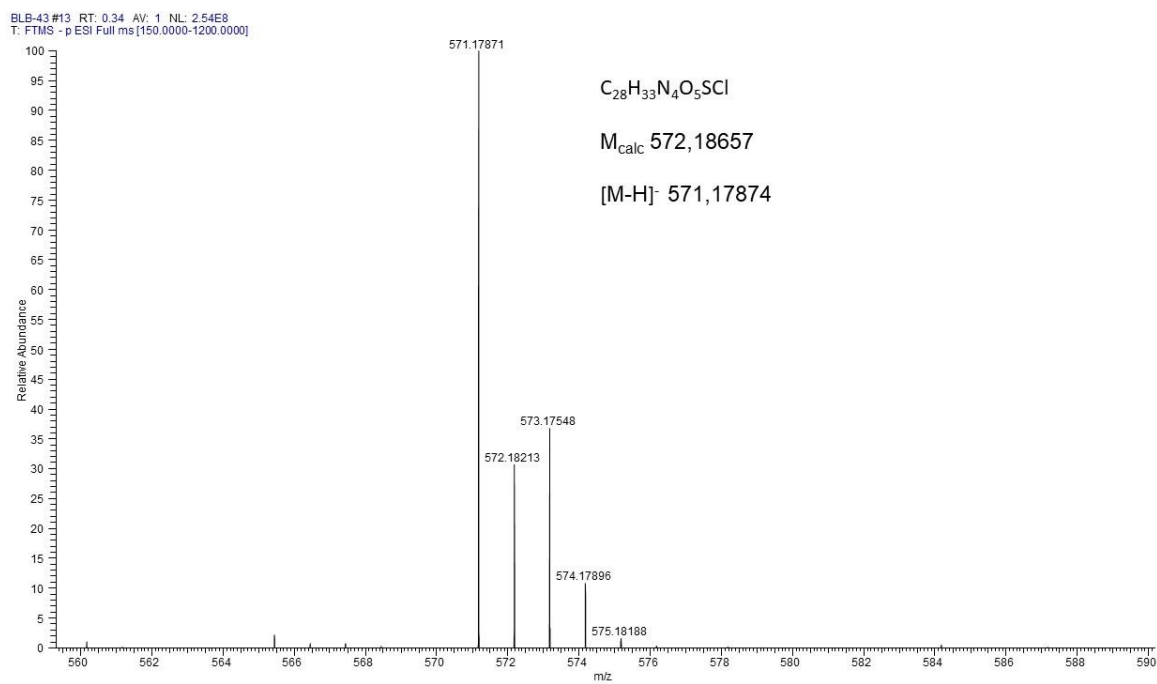
HRMS spectrum of compound **3d**

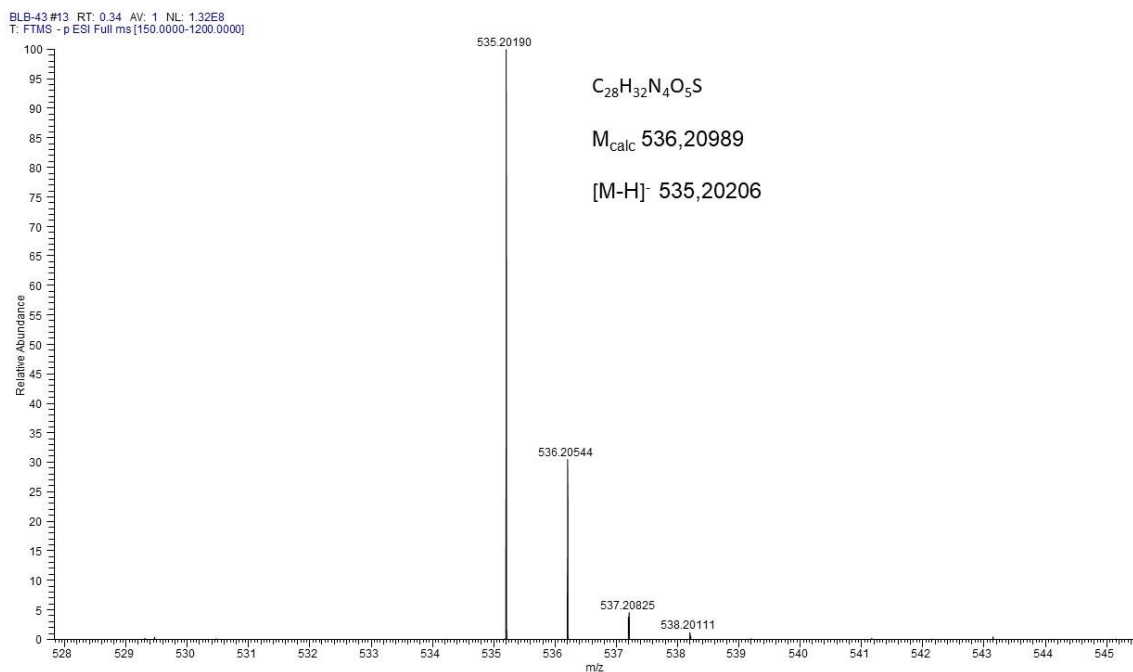


HRMS spectrum of compound 3e

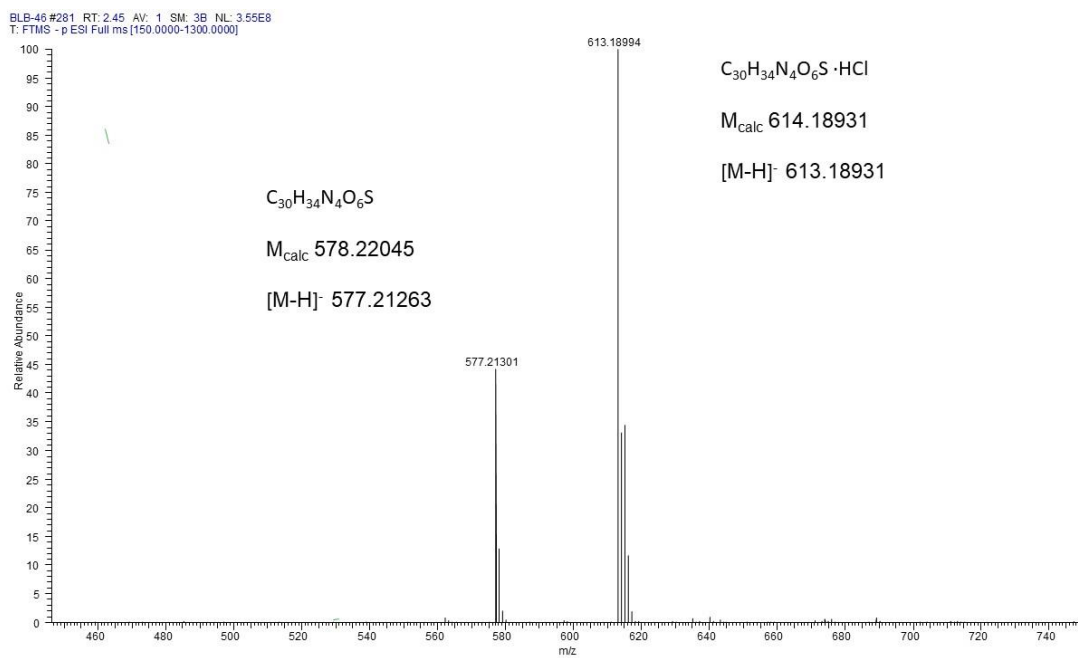


HRMS spectrum of compound 3f



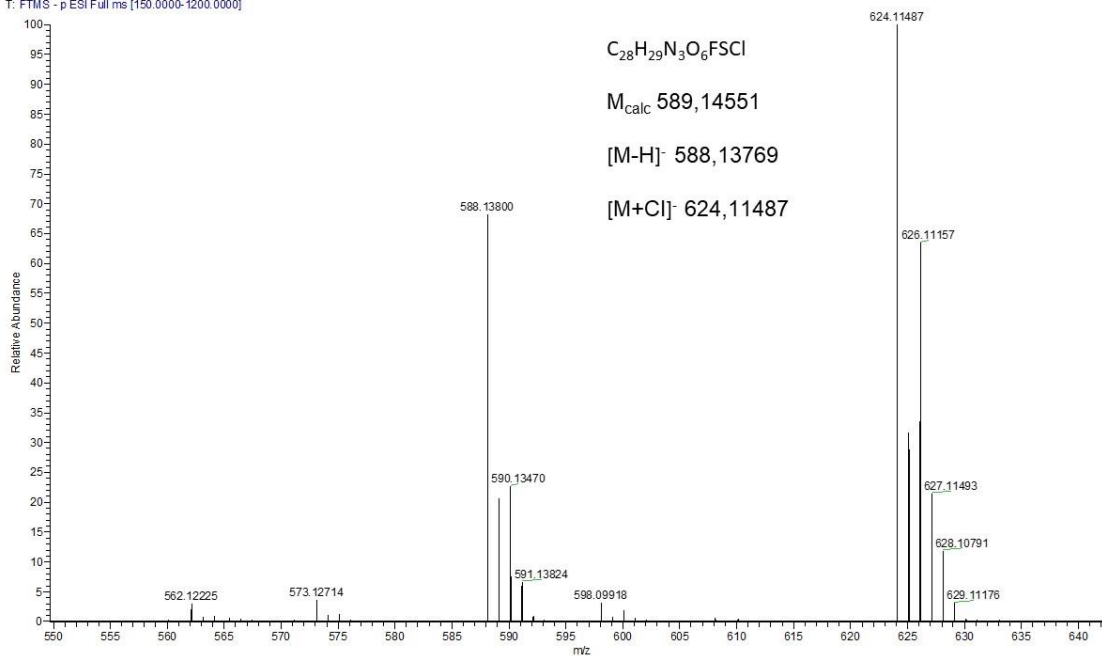


HRMS spectrum of compound **3g**



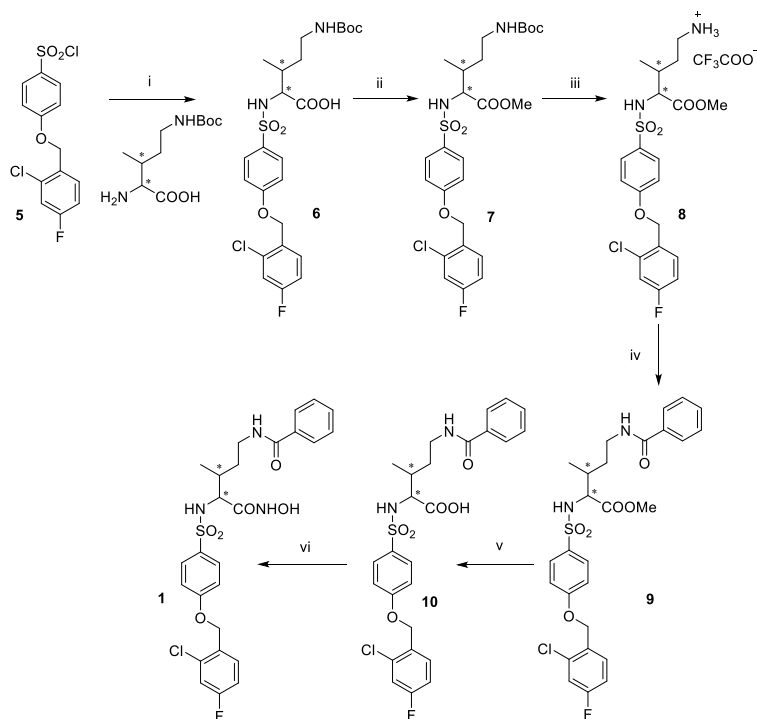
HRMS spectrum of compound 4

DC-263 #1 RT: 0.01 AV: 1 NL: 5.92E8
T: FTMS - p ESI Full ms [150.0000-1200.0000]

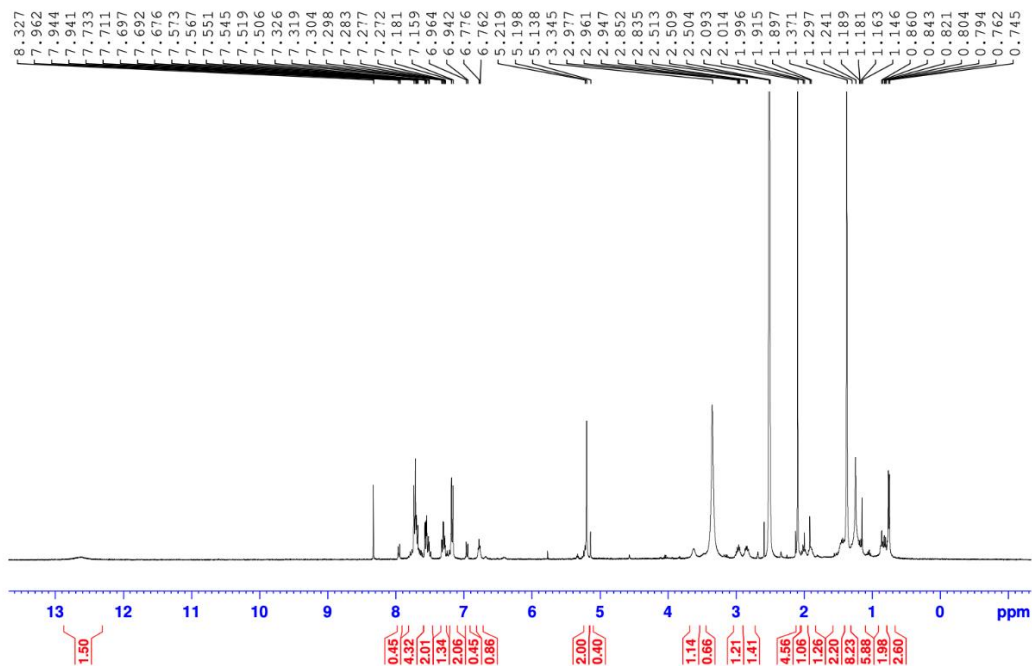


III. Representative NMR spectra of intermediate compounds

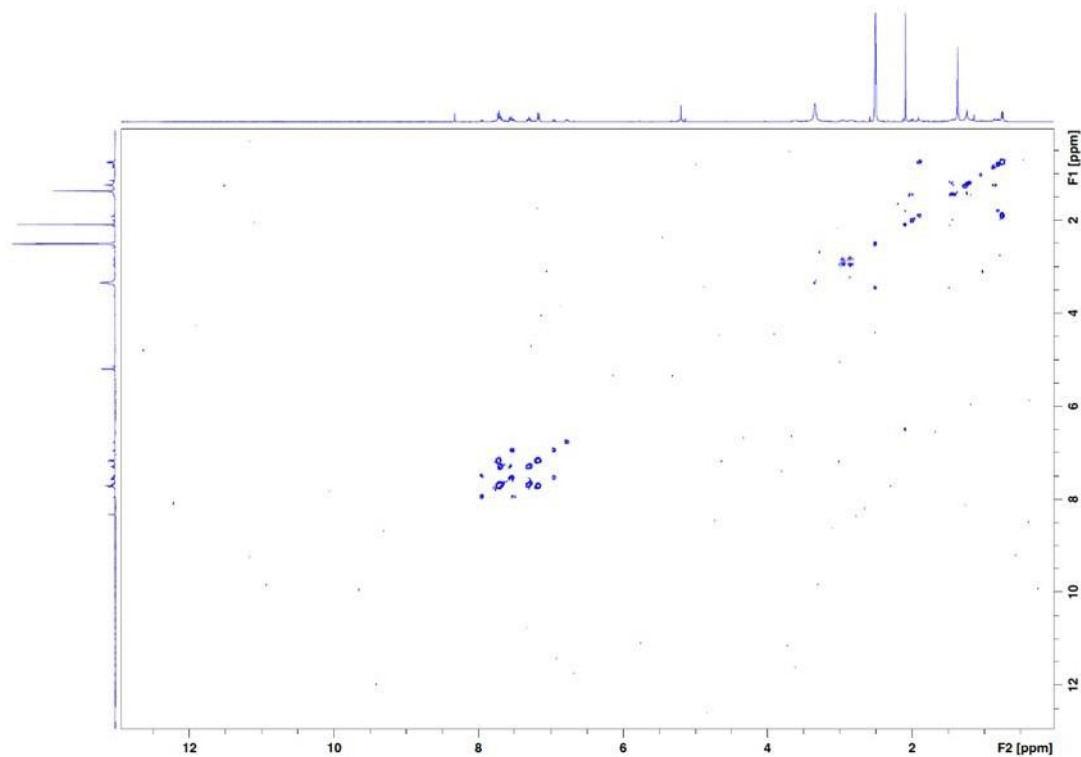
Scheme 1: Synthesis of final compound 1



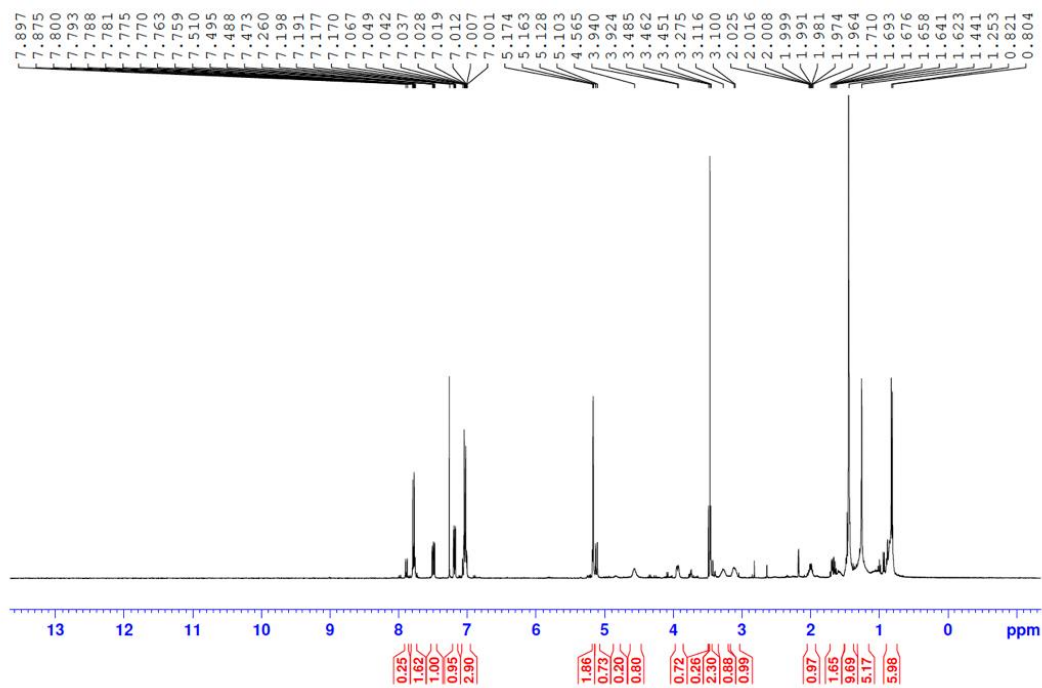
Compound 6: ¹H NMR (400 MHz, DMSO).



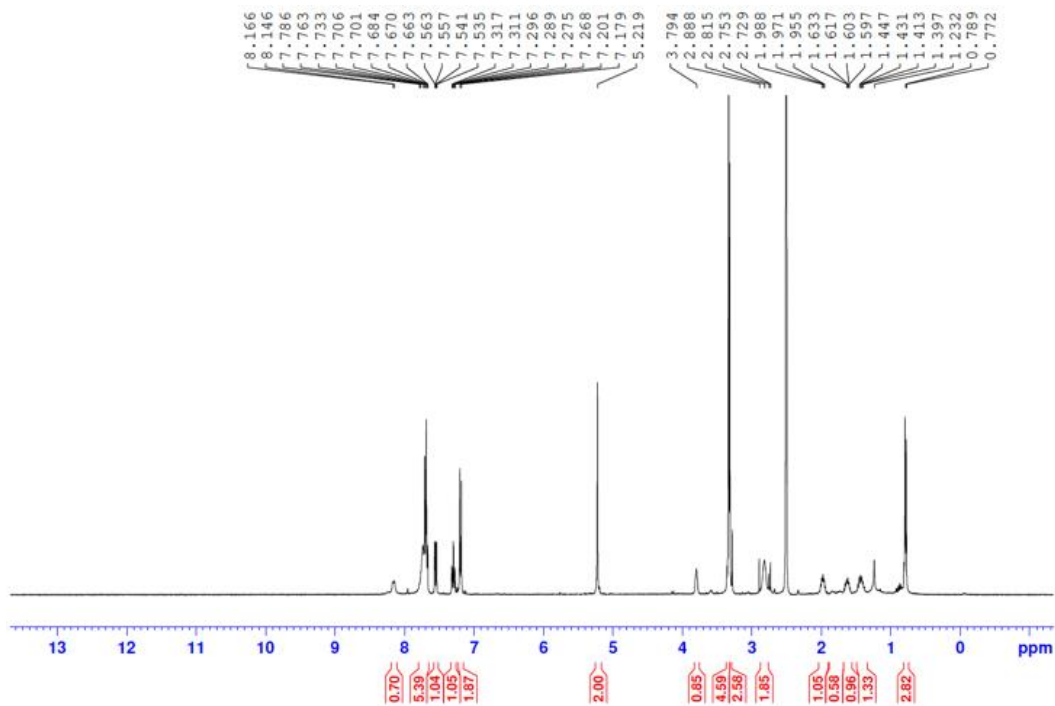
Compound 6: ^1H - ^1H COSY NMR (400 MHz, DMSO).



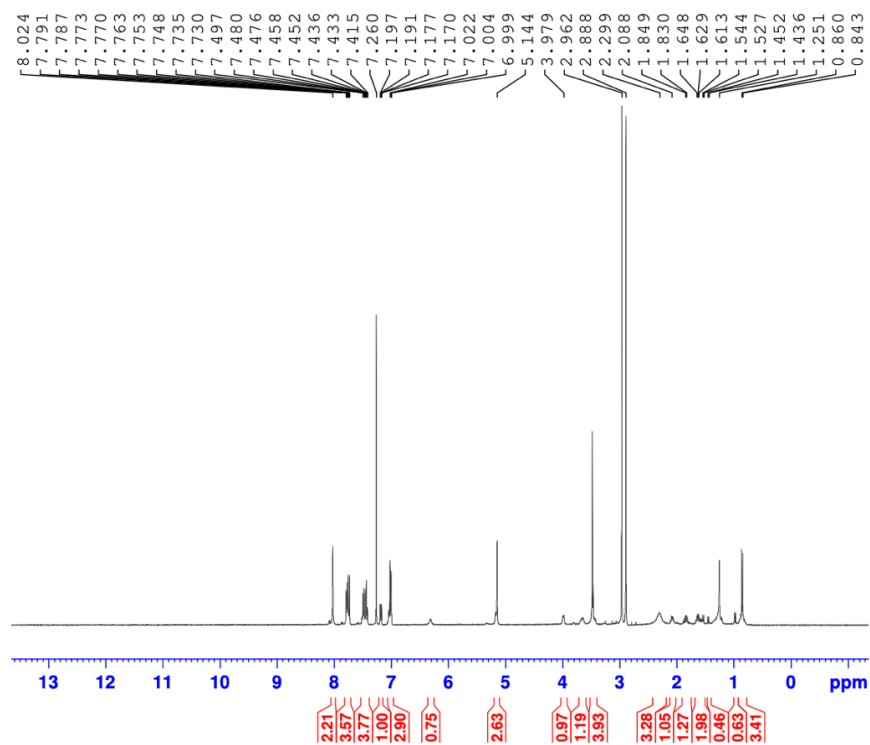
Compound 7: ^1H NMR (400 MHz, CDCl_3).



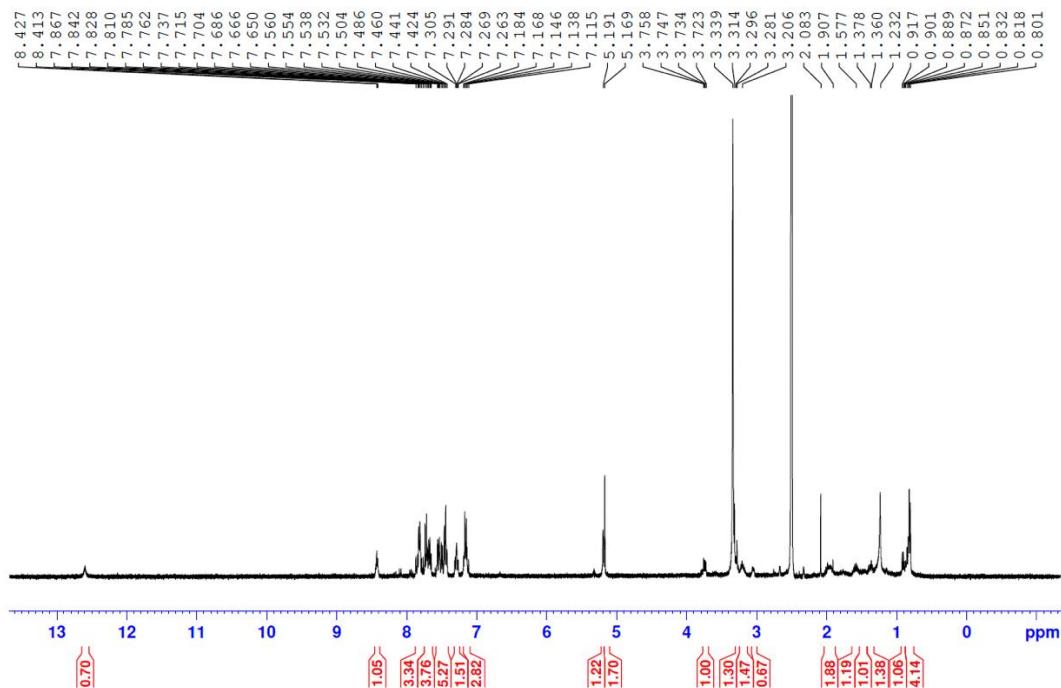
Compound **8**: ^1H NMR (400 MHz, DMSO).



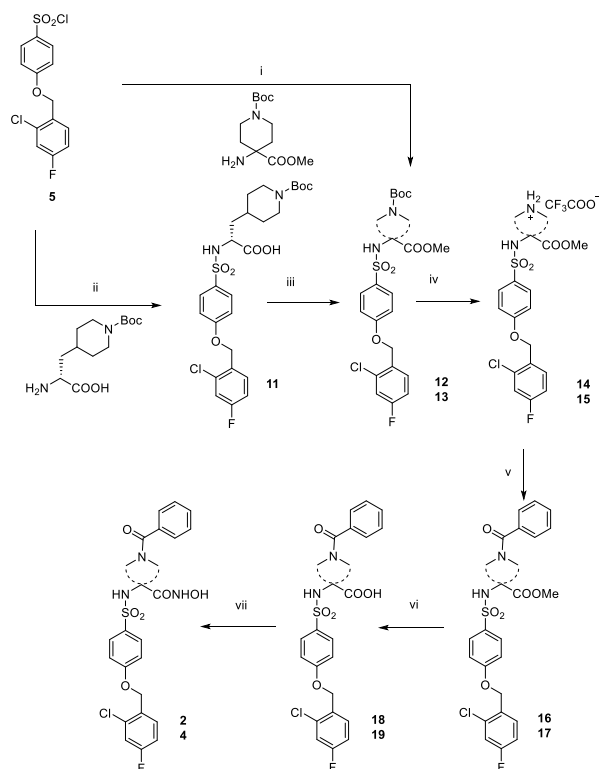
Compound **9**: ^1H NMR (400 MHz, CDCl_3).



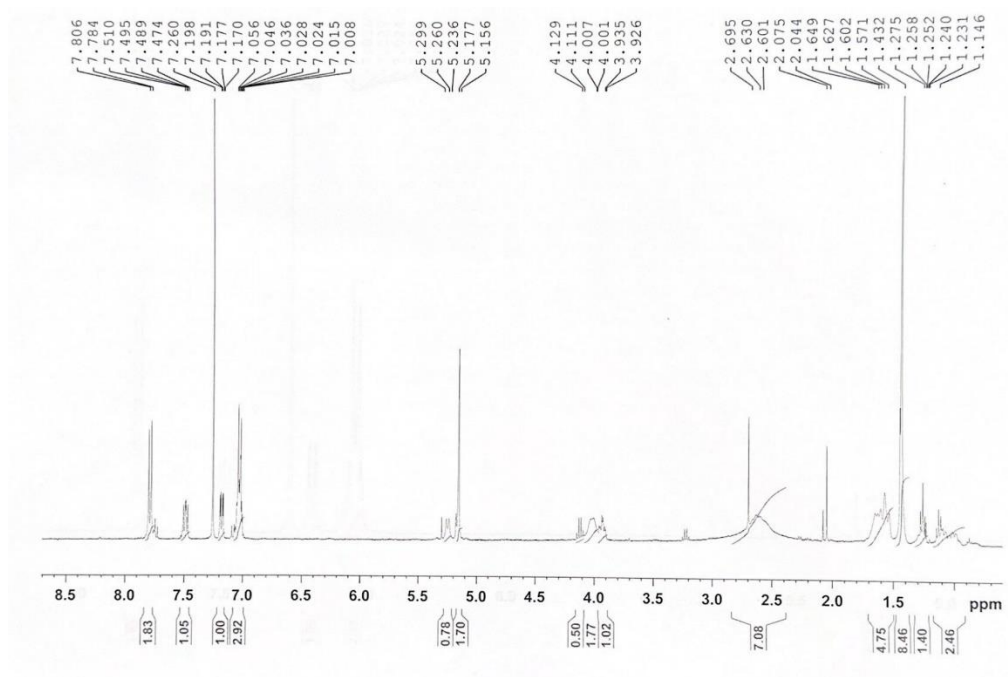
Compound **10**: ^1H NMR (400 MHz, DMSO).



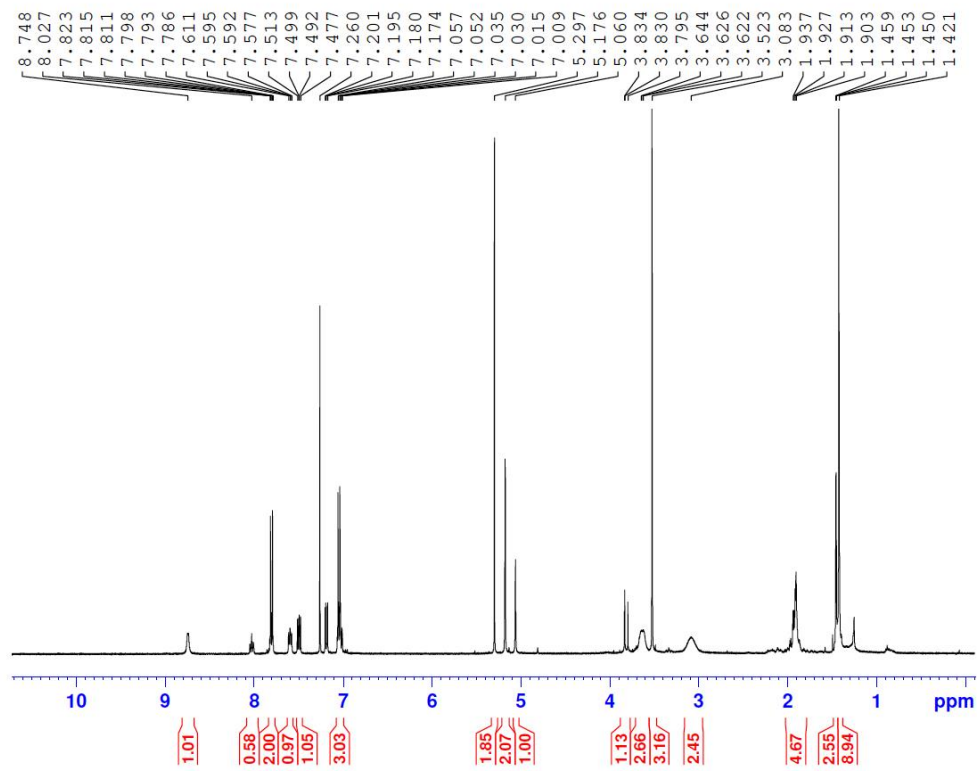
Scheme 2: Synthesis of final compounds **2,4**



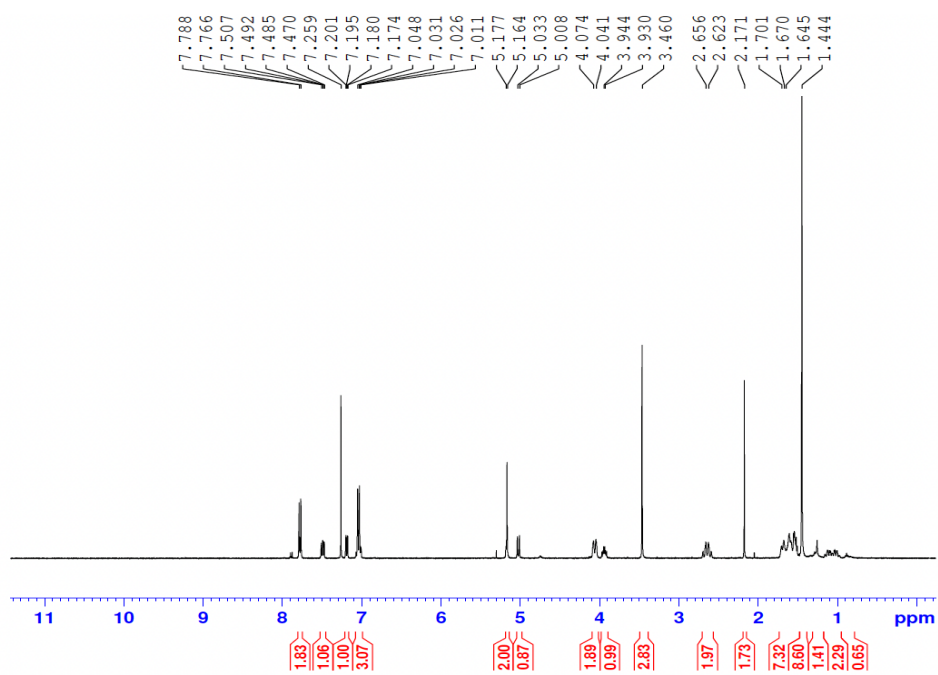
Compound 11: ^1H NMR (400 MHz, CDCl_3).



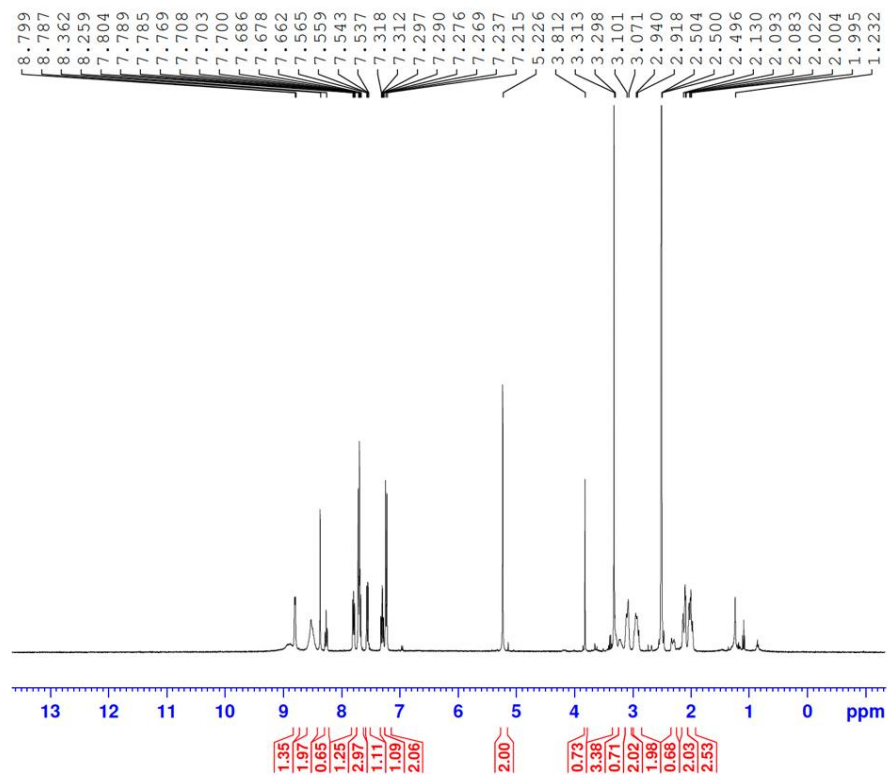
Compound 12: ^1H NMR (400 MHz, CDCl_3).



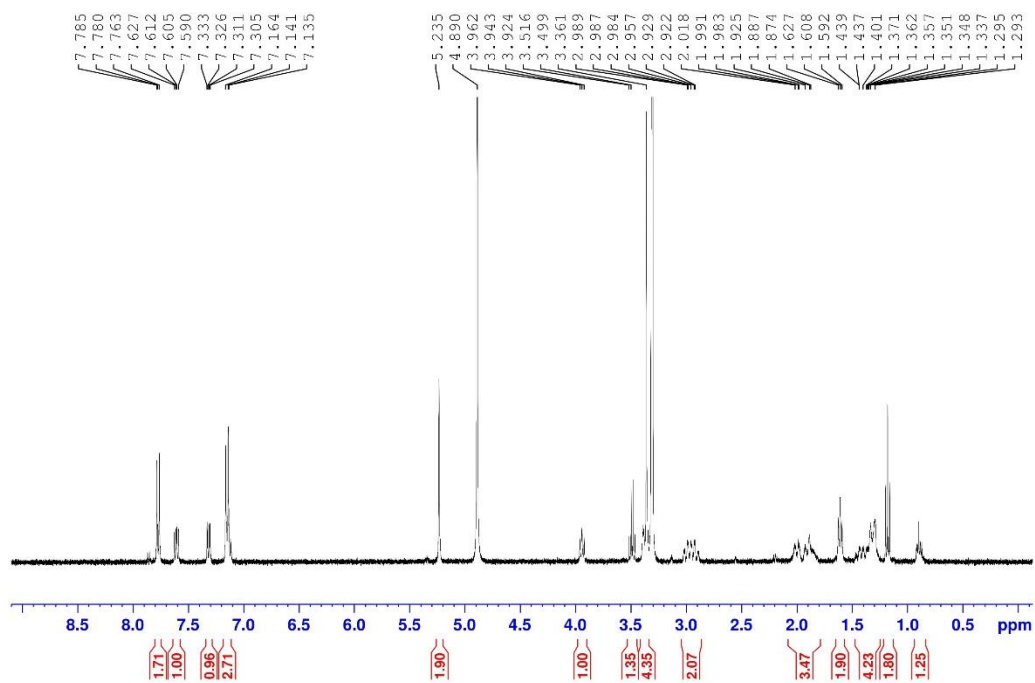
Compound 13: ^1H NMR (400 MHz, CDCl_3).



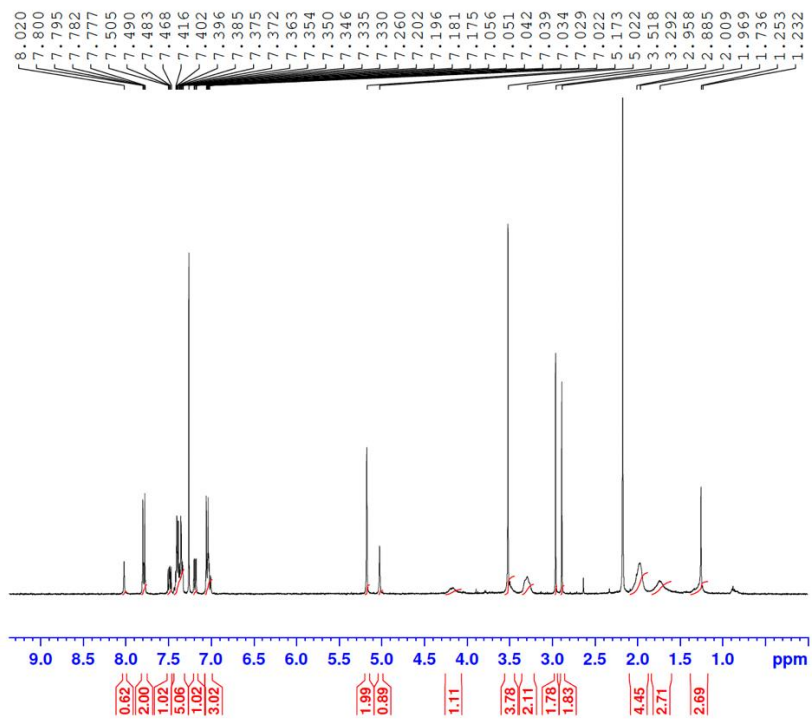
Compound 14: ^1H NMR (400 MHz, DMSO).



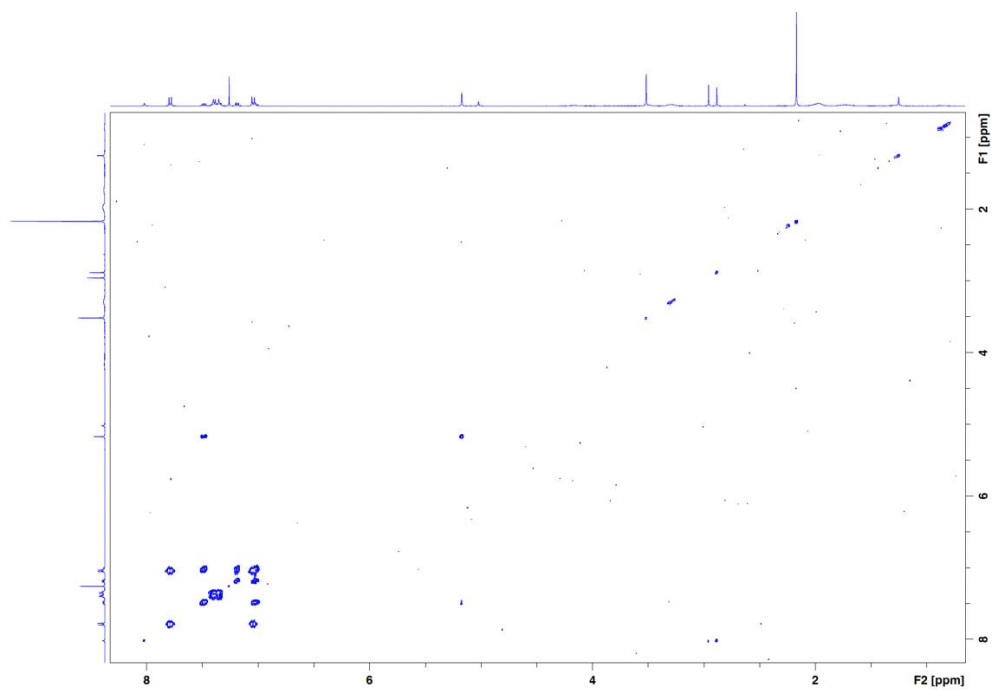
Compound 15: ^1H NMR (400 MHz, MeOD).



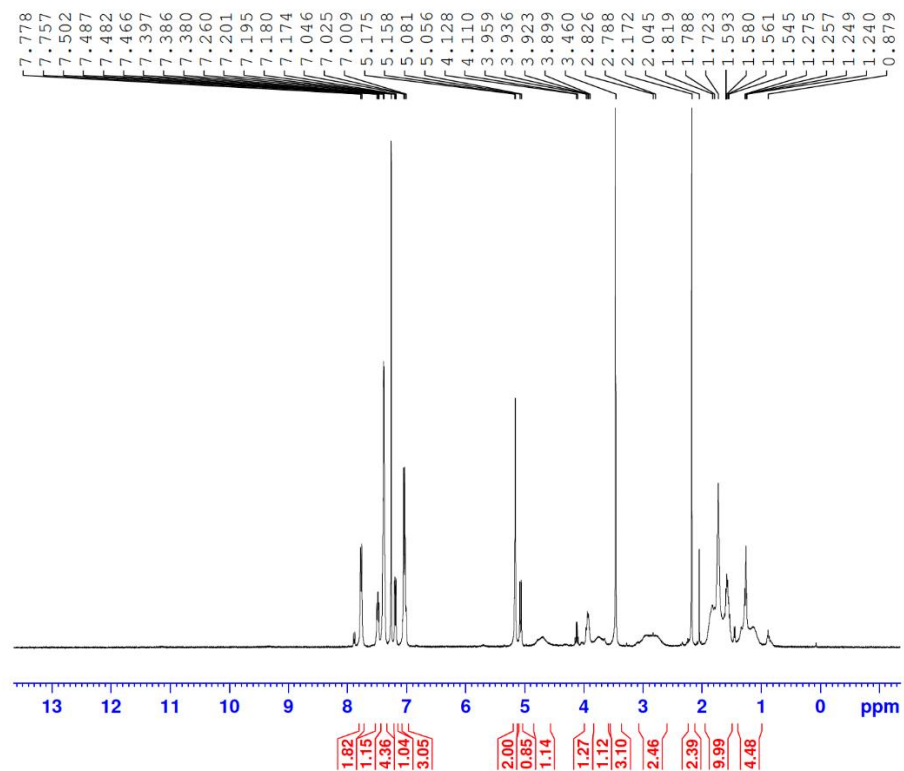
Compound 16: ^1H NMR (400 MHz, CDCl_3).



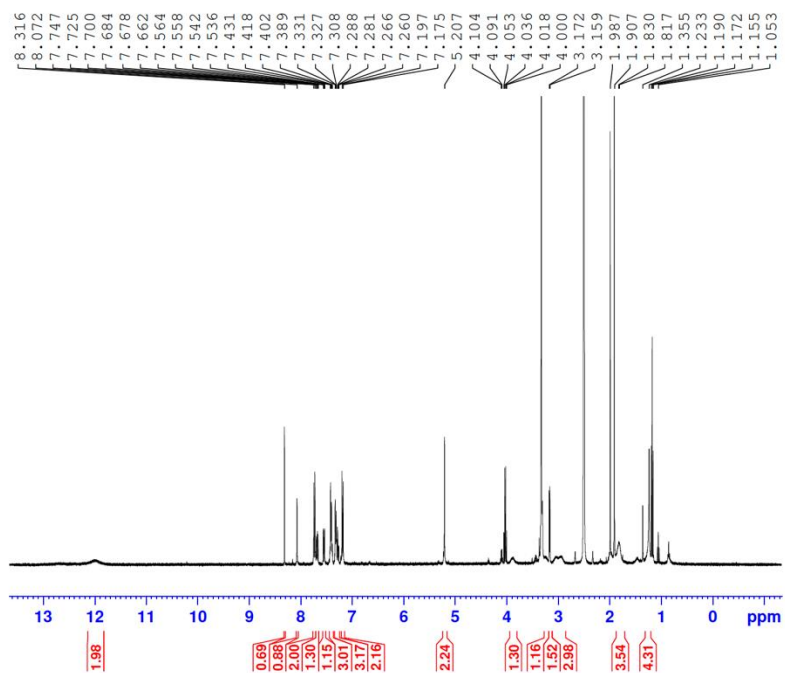
Compound 16: ^1H - ^1H COSY NMR (400 MHz, CDCl_3).



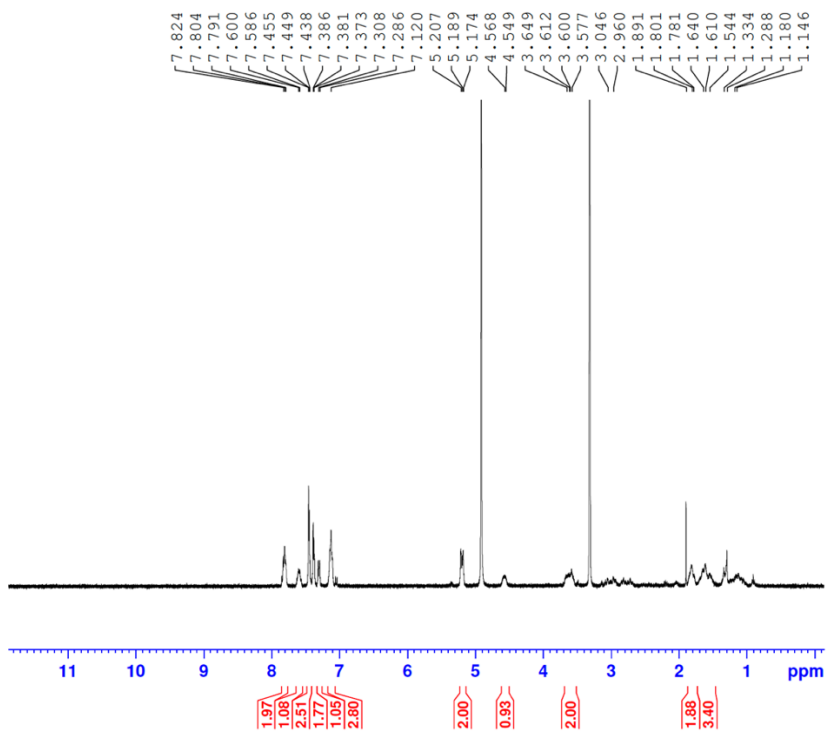
Compound 17: ^1H NMR (400 MHz, CDCl_3).



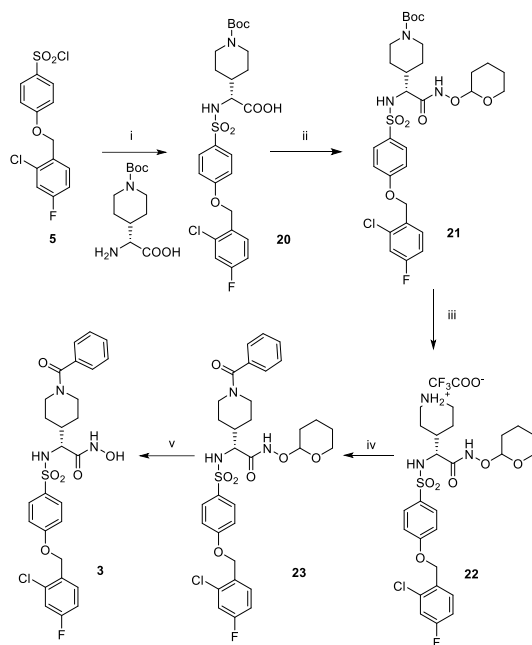
Compound 18: ^1H NMR (400 MHz, DMSO).



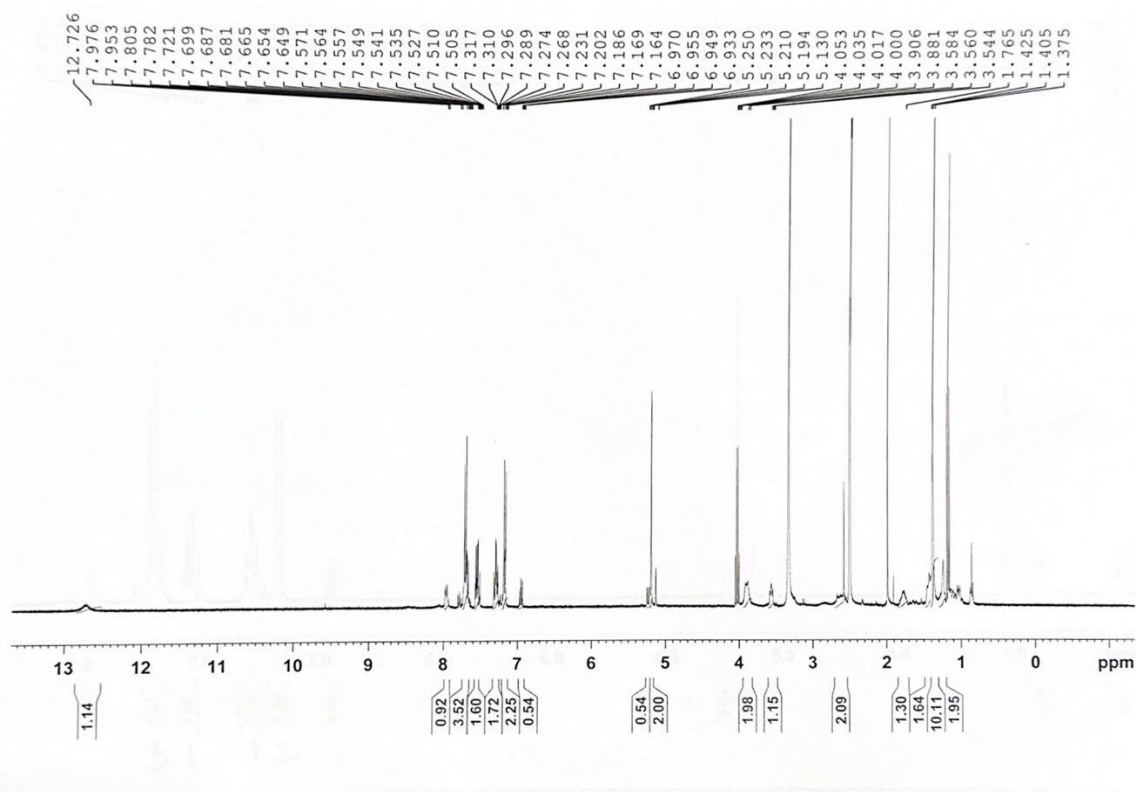
Compound 19: ^1H NMR (400 MHz, MeOD).



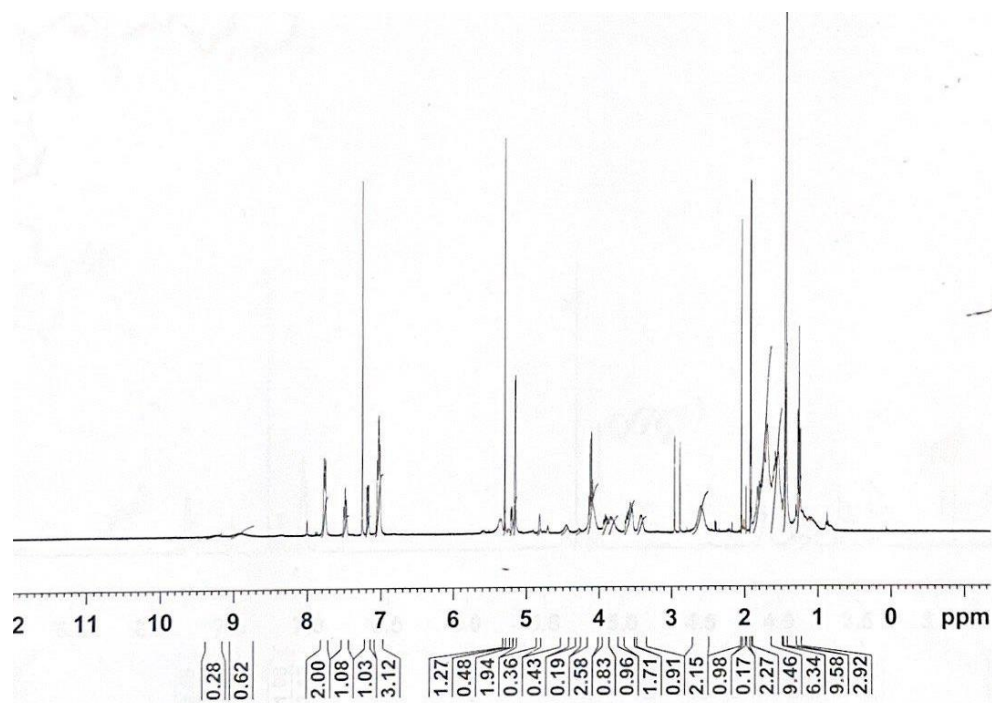
Scheme 3: Synthesis of final compound 3



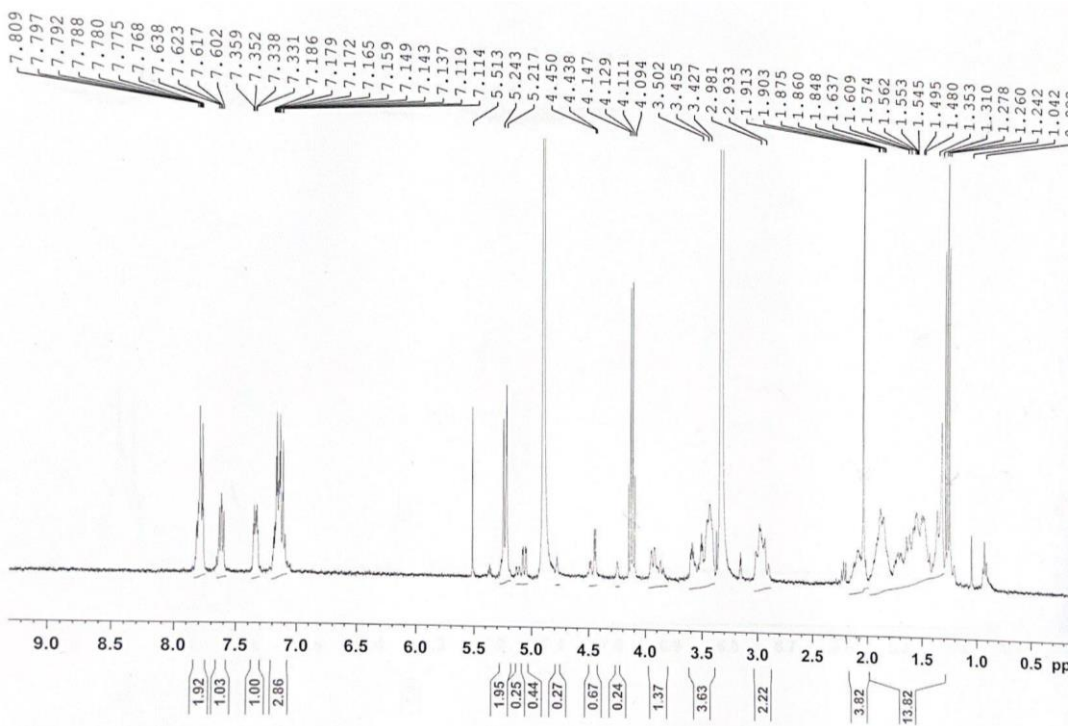
Compound 20: ¹H NMR (400 MHz, DMSO).



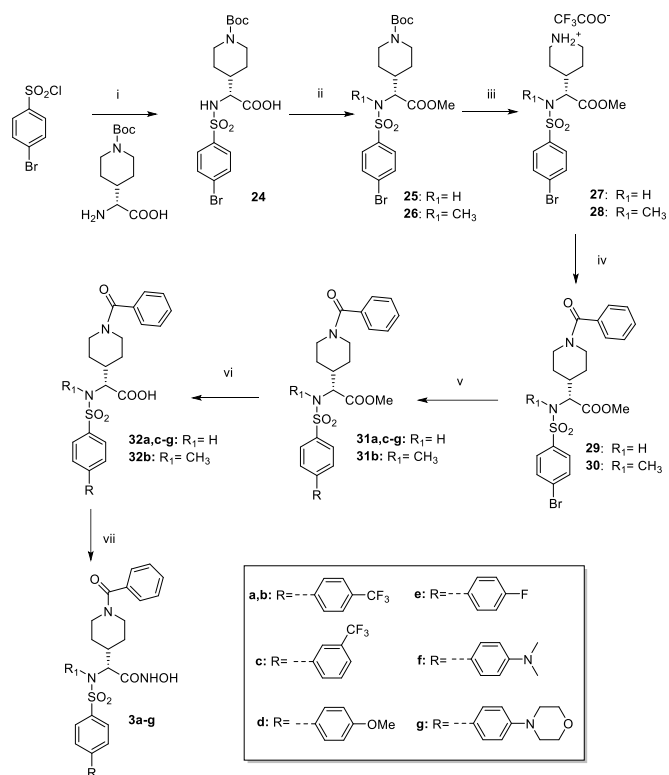
Compound 21: ^1H NMR (400 MHz, CDCl_3).



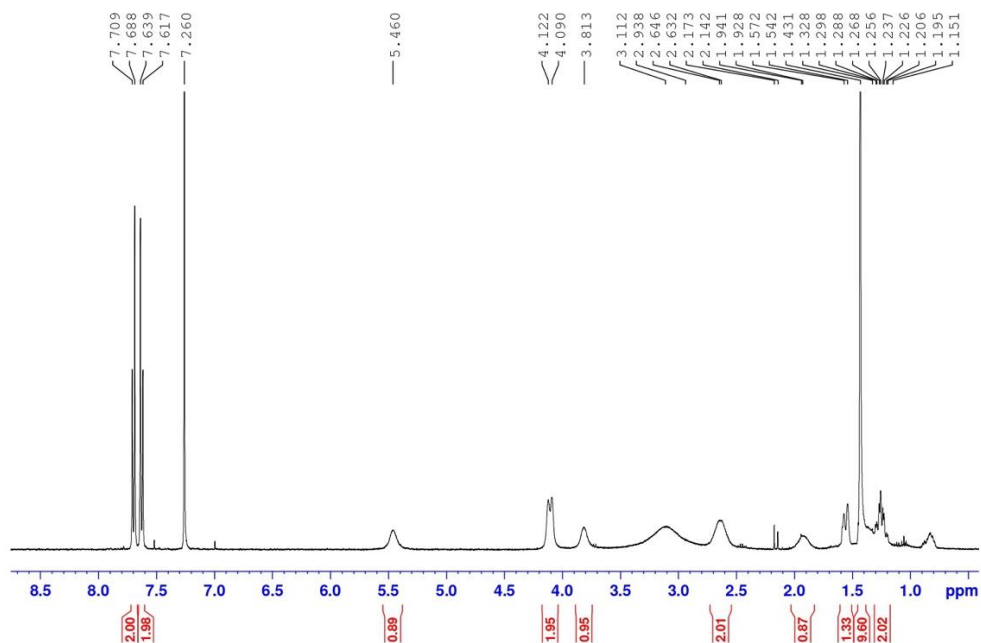
Compound 22: ^1H NMR (400 MHz, MeOD).



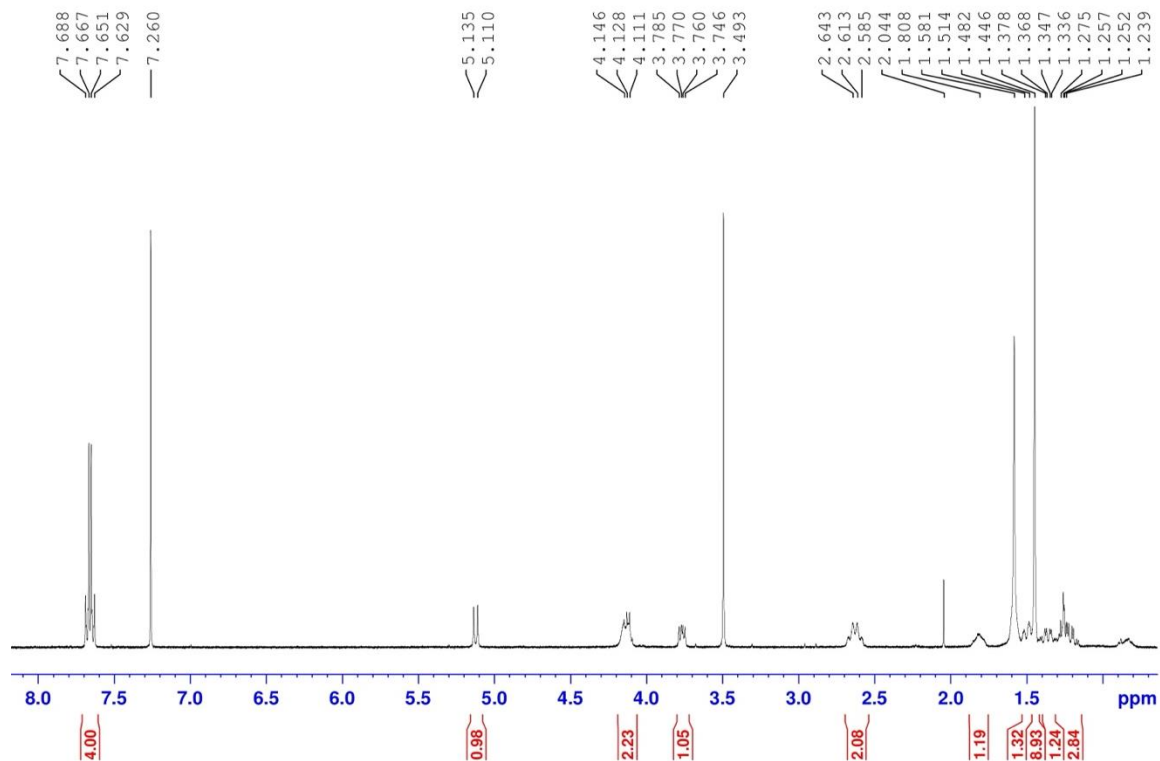
Scheme 4: Synthesis of final compounds 3a-g



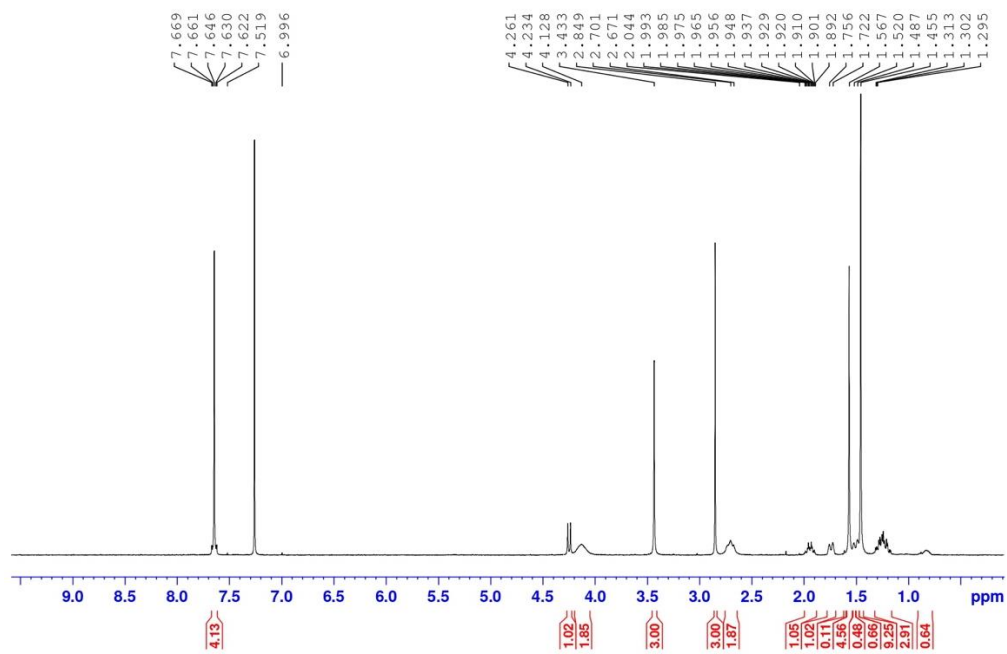
Compound **24**: ¹H NMR (400 MHz, CDCl₃).



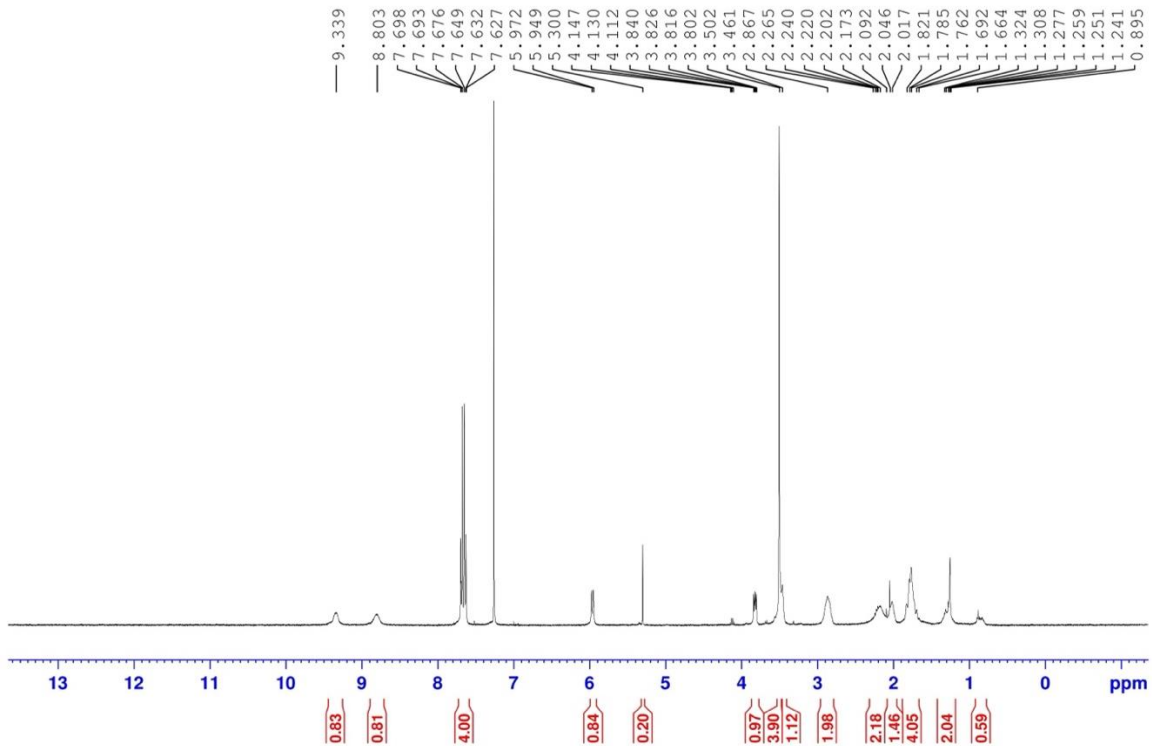
Compound 25: ^1H NMR (400 MHz, CDCl_3).



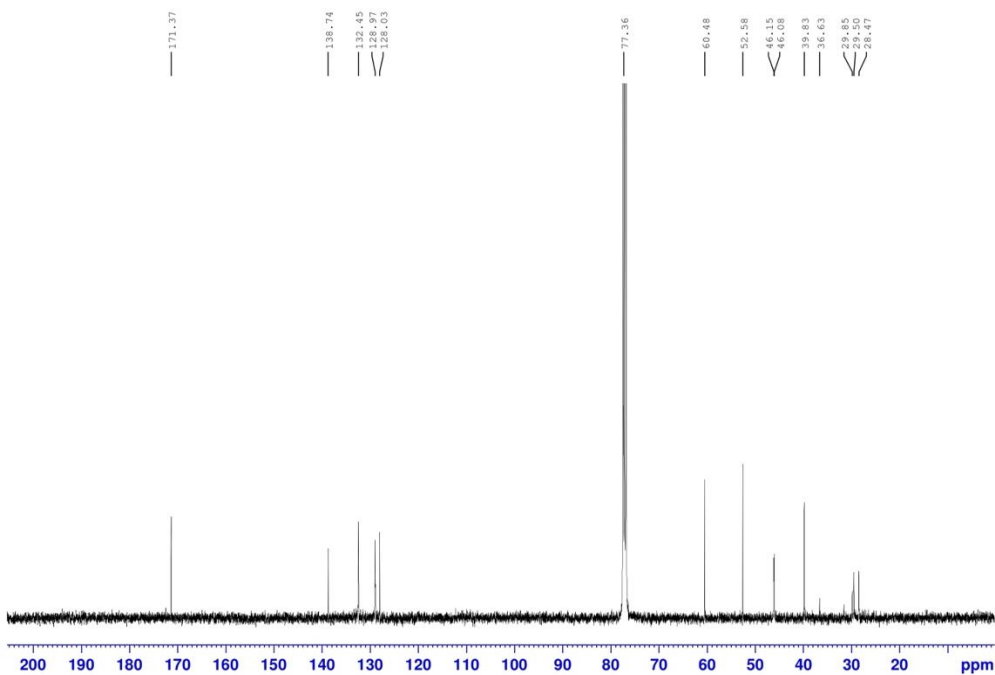
Compound 26: ^1H NMR (400 MHz, CDCl_3).



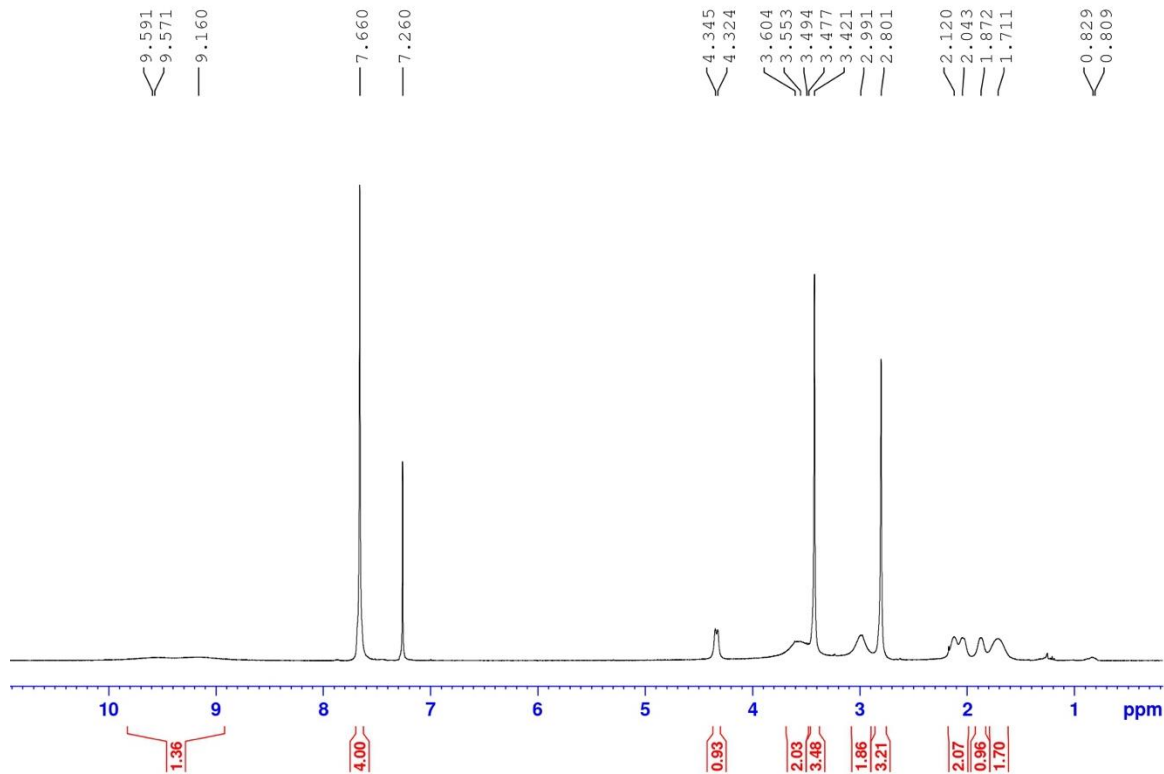
Compound 27: ^1H NMR (400 MHz, CDCl_3).



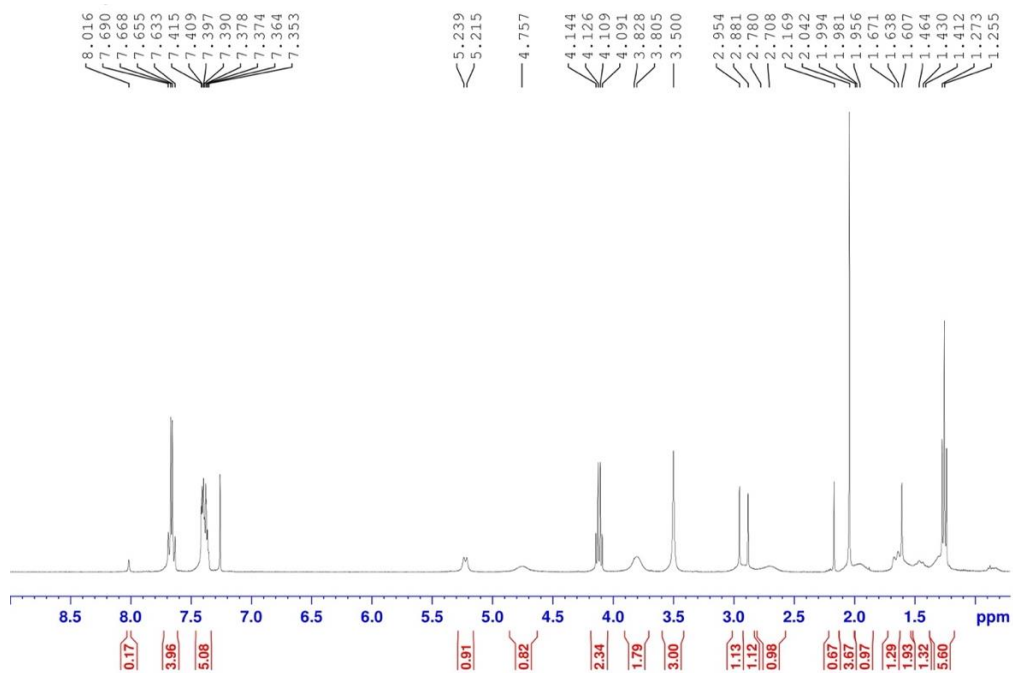
Compound 27: ^{13}C NMR (400 MHz, CDCl_3).



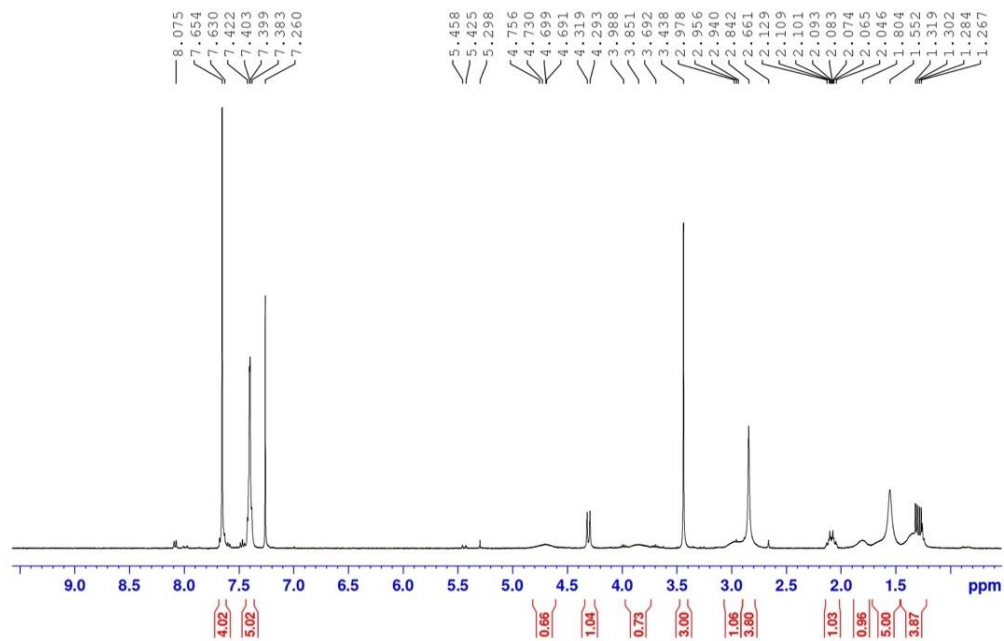
Compound **28**: ^1H NMR (400 MHz, CDCl_3).



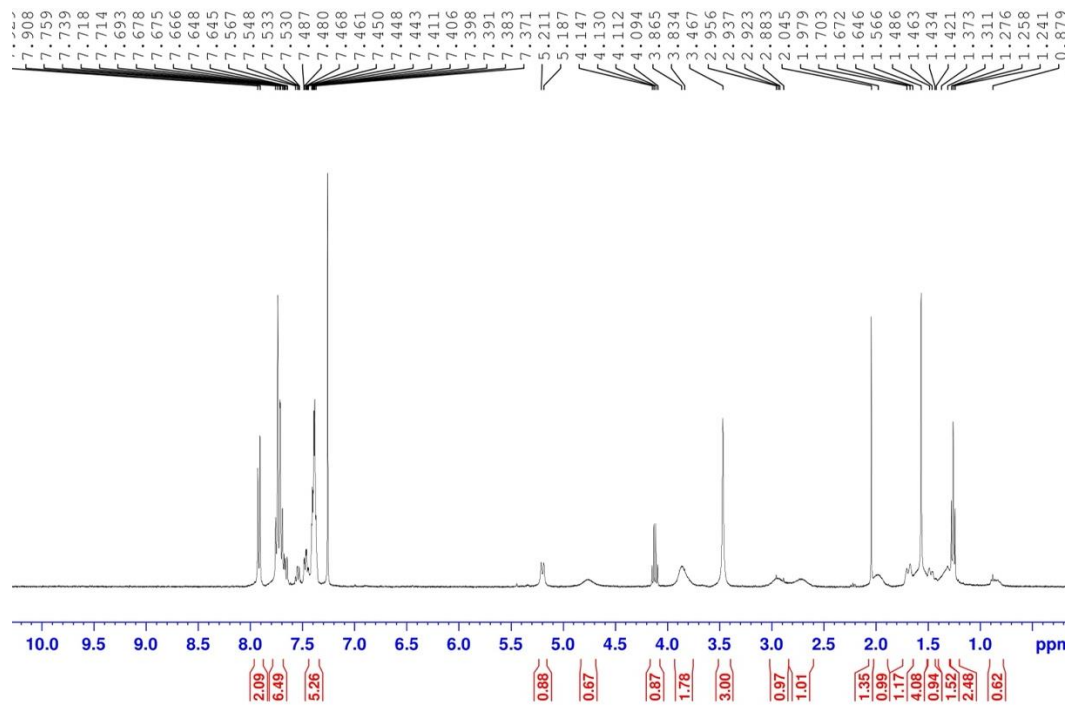
Compound **29**: ^1H NMR (400 MHz, CDCl_3).



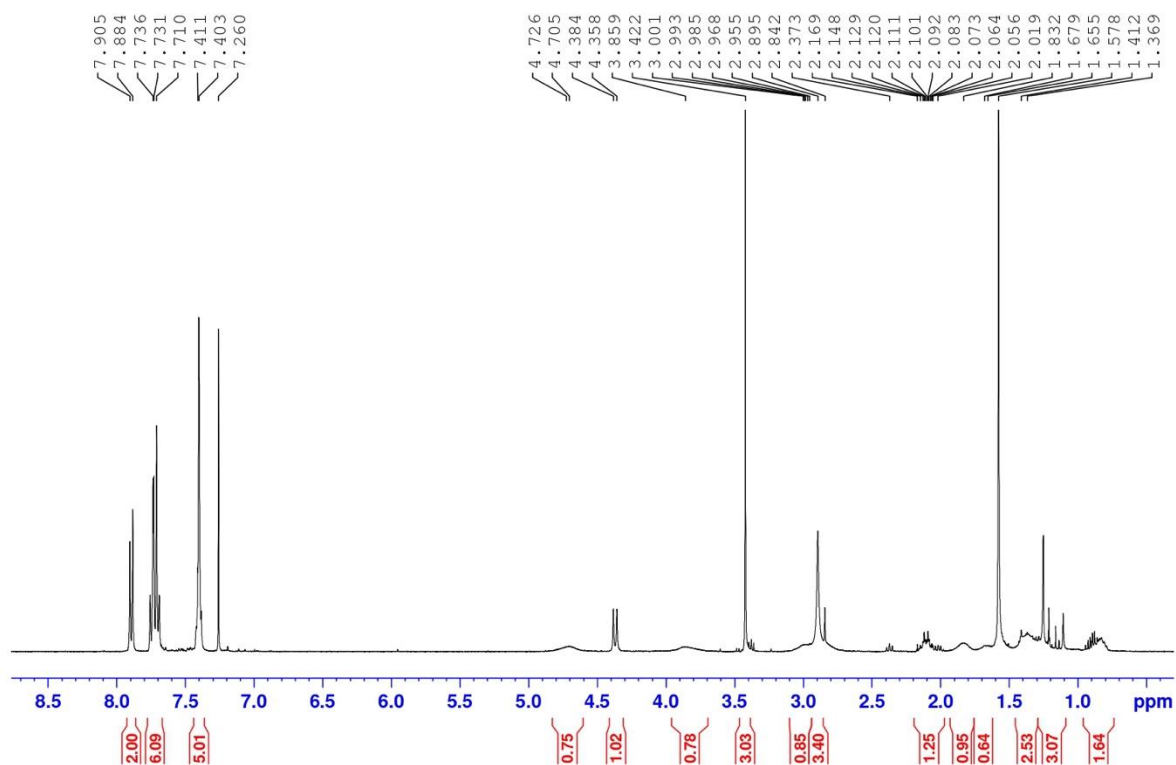
Compound **30**: ^1H NMR (400 MHz, CDCl_3).



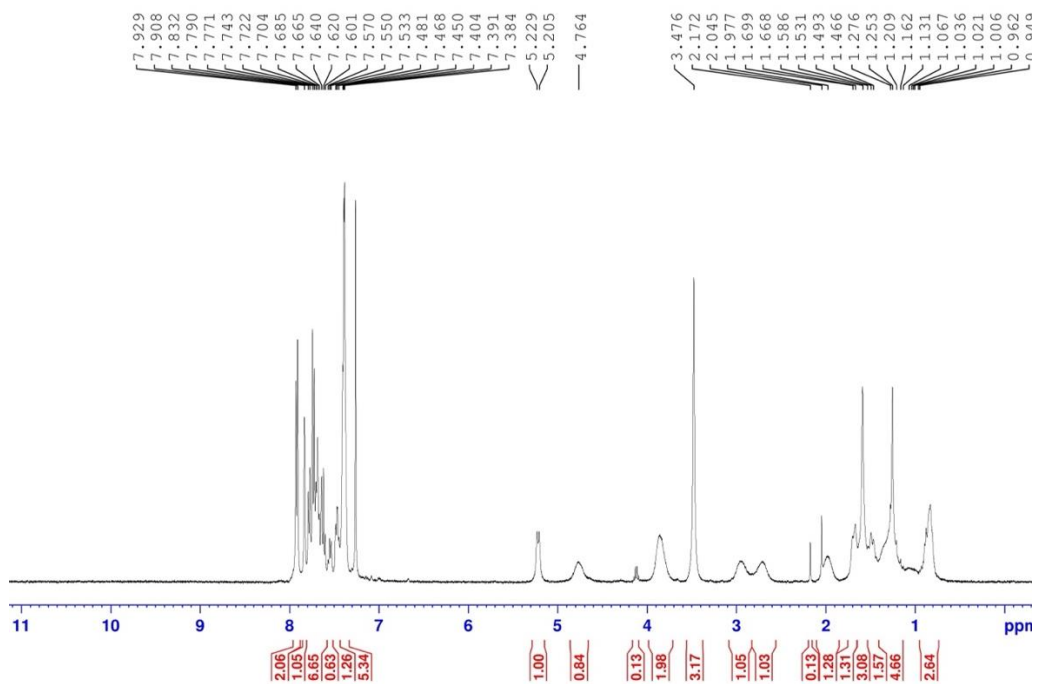
Compound **31a**: ^1H NMR (400 MHz, CDCl_3).



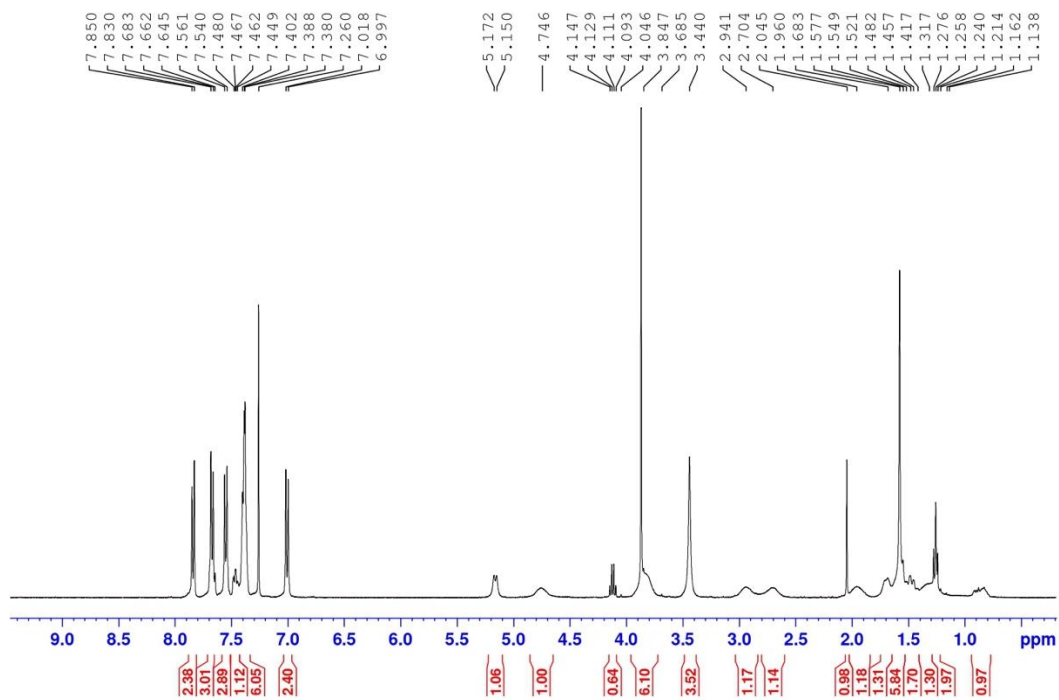
Compound **31b**: ^1H NMR (400 MHz, CDCl_3).



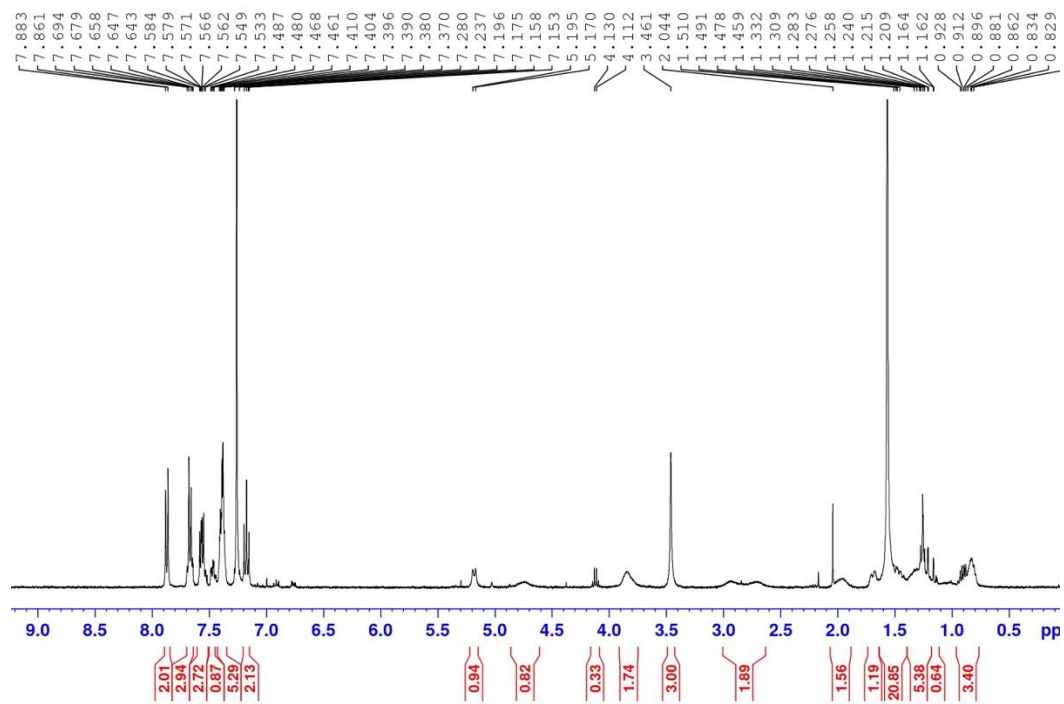
Compound **31c**: ^1H NMR (400 MHz, CDCl_3).



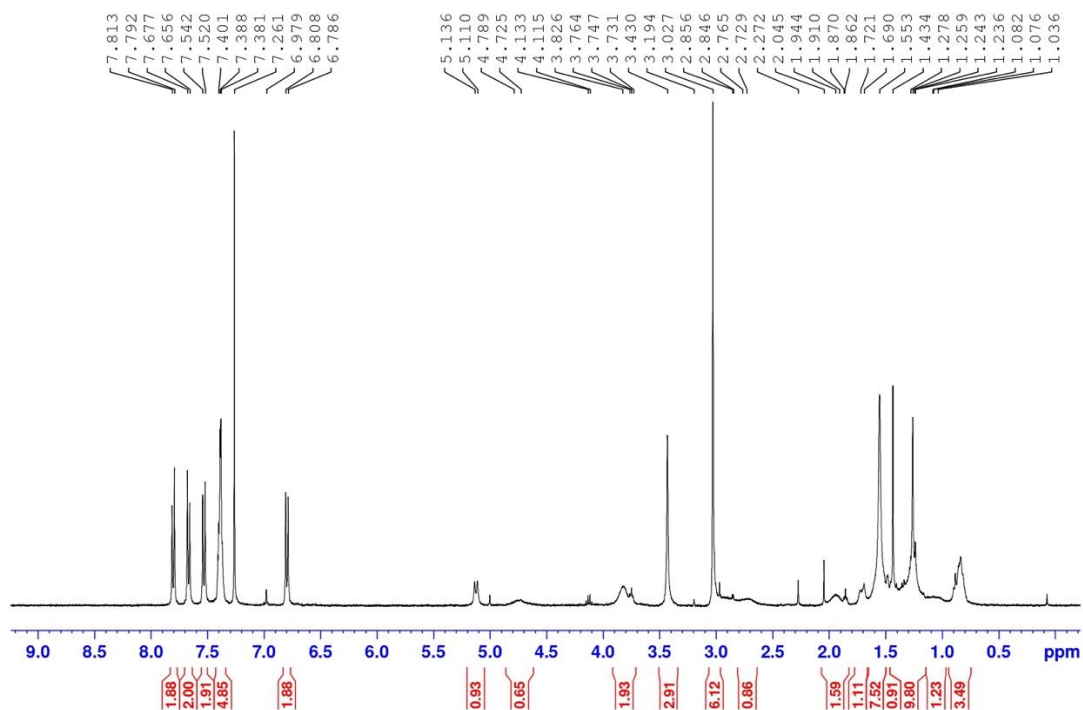
Compound **31d**: ^1H NMR (400 MHz, CDCl_3).



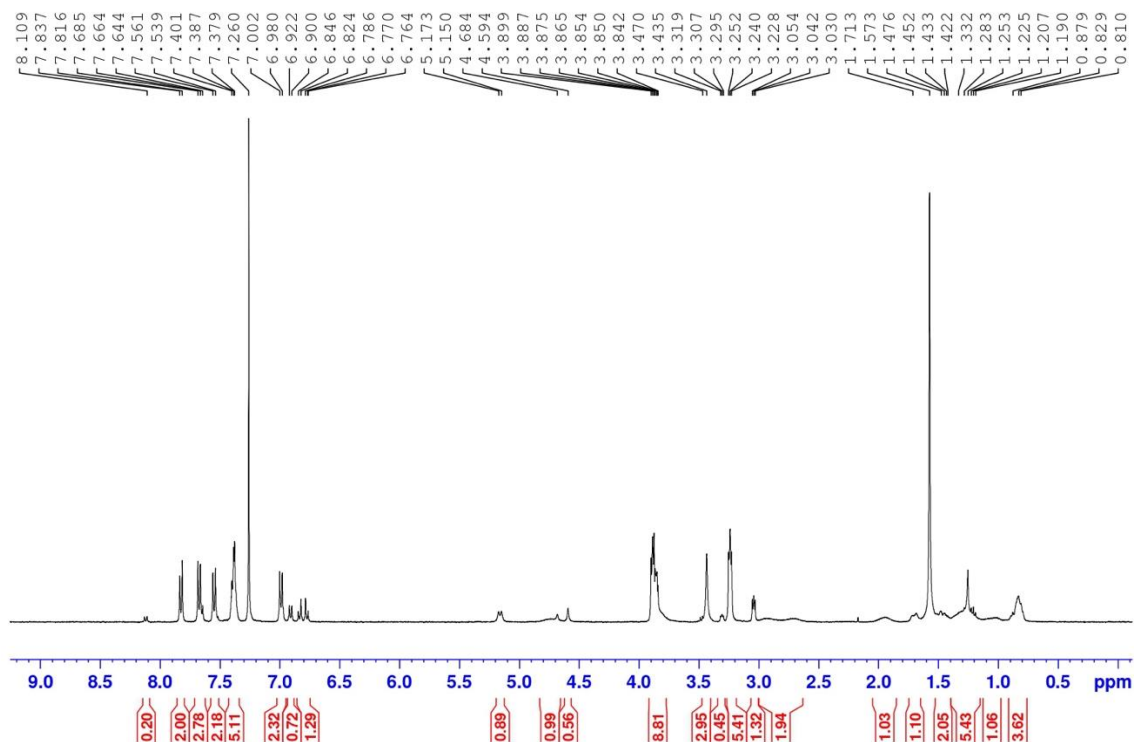
Compound **31e**: ^1H NMR (400 MHz, CDCl_3).



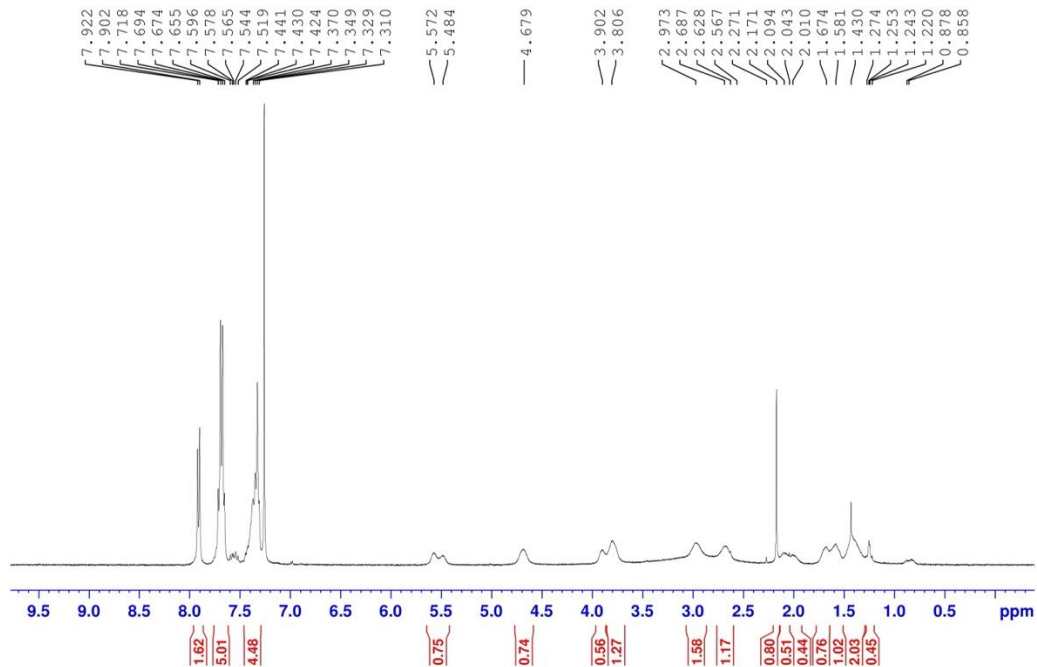
Compound **31f**: ^1H NMR (400 MHz, CDCl_3).



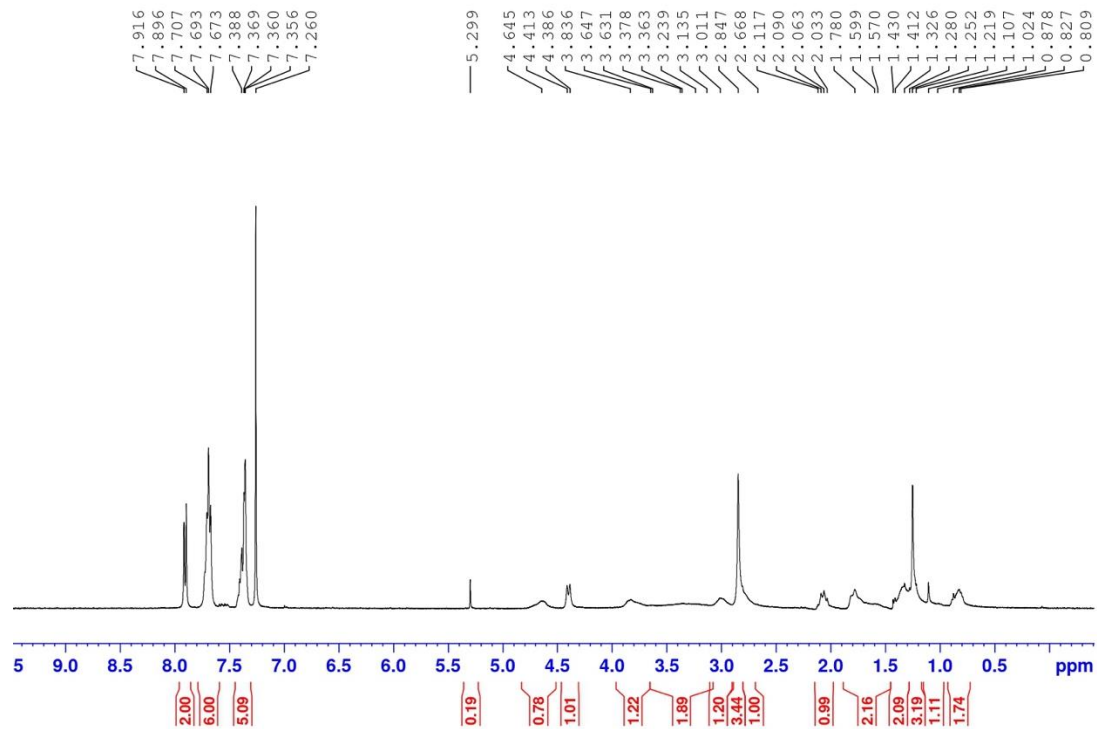
Compound **31g**: ^1H NMR (400 MHz, CDCl_3).



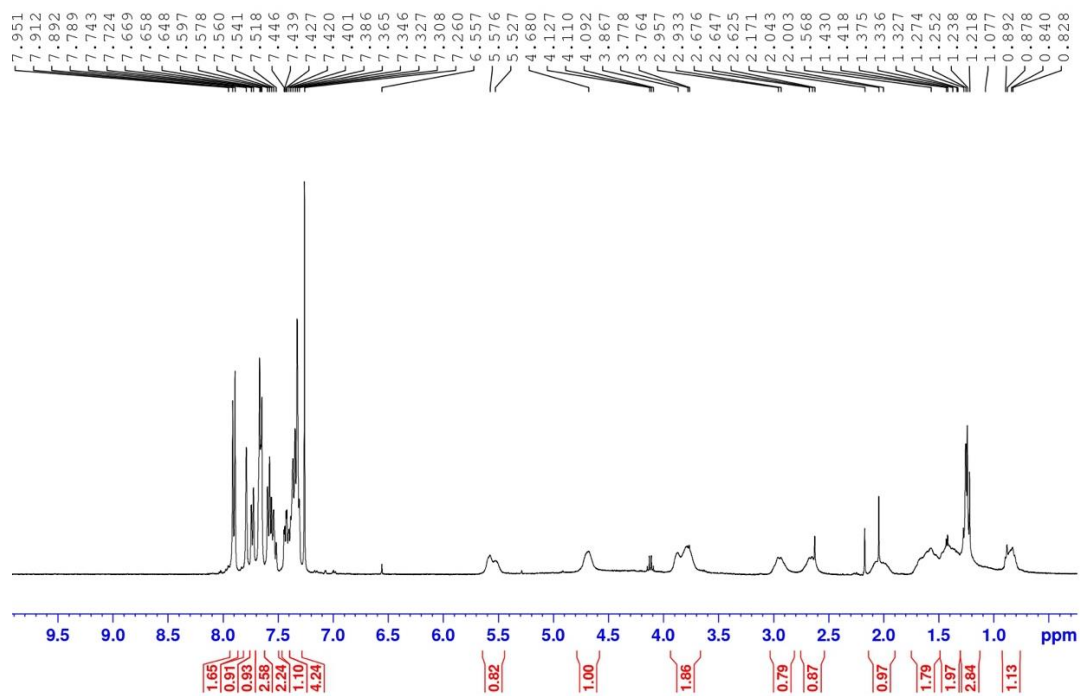
Compound **32a**: ^1H NMR (400 MHz, CDCl_3).



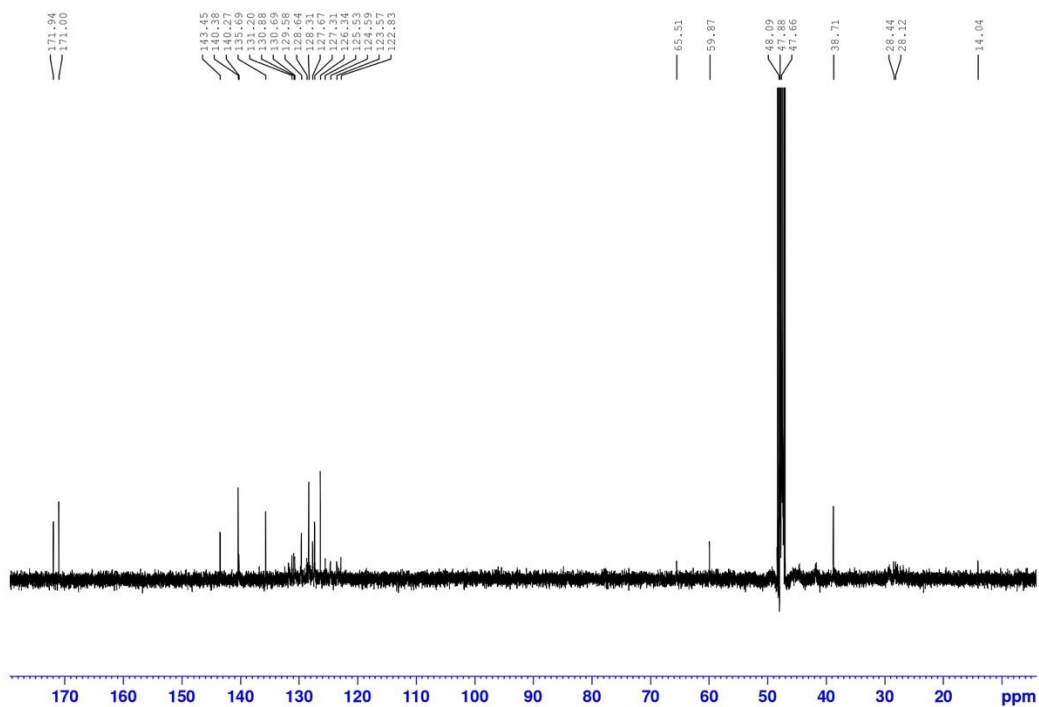
Compound **32b**: ^1H NMR (400 MHz, CDCl_3).



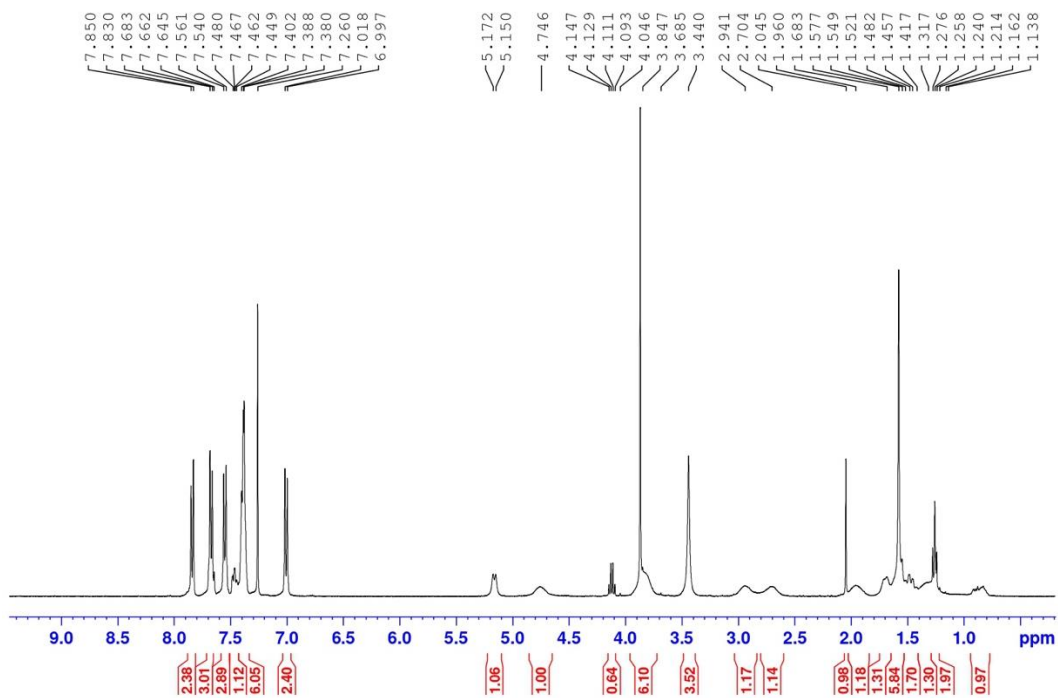
Compound **32c**: ^1H NMR (400 MHz, CDCl_3).



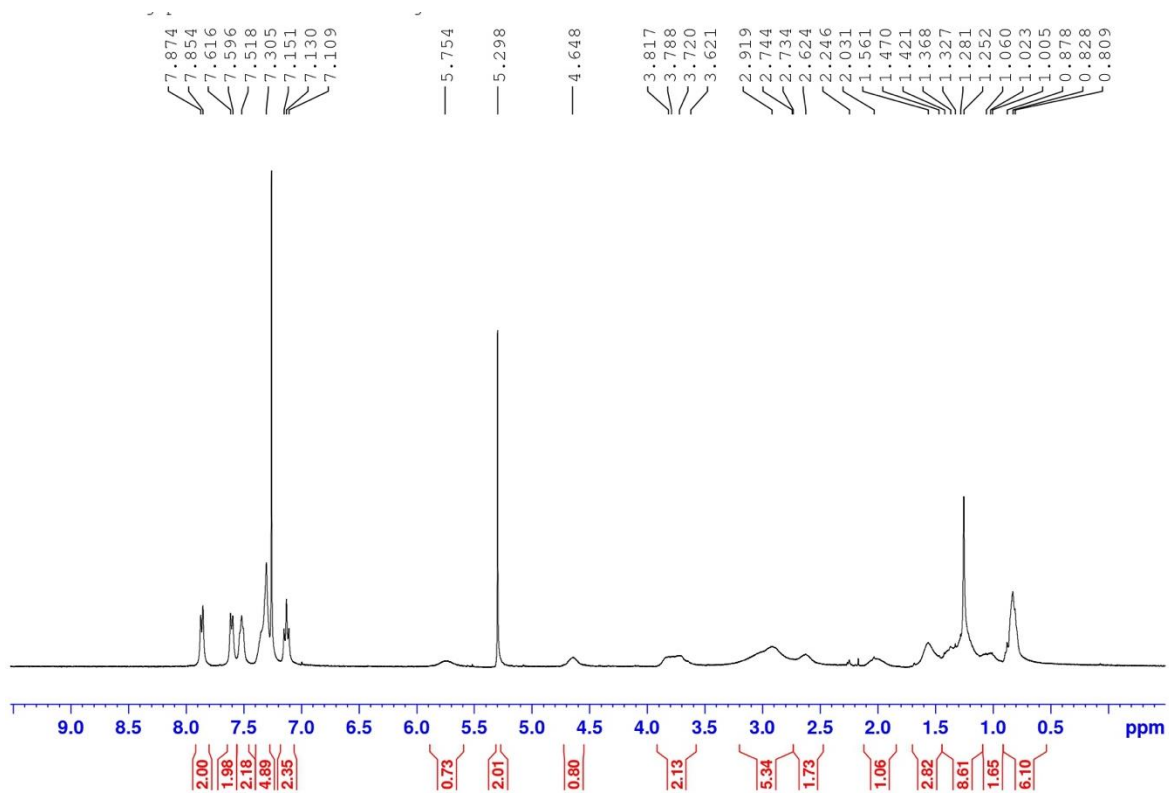
Compound **32c**: ^{13}C NMR (400 MHz, CDCl_3).



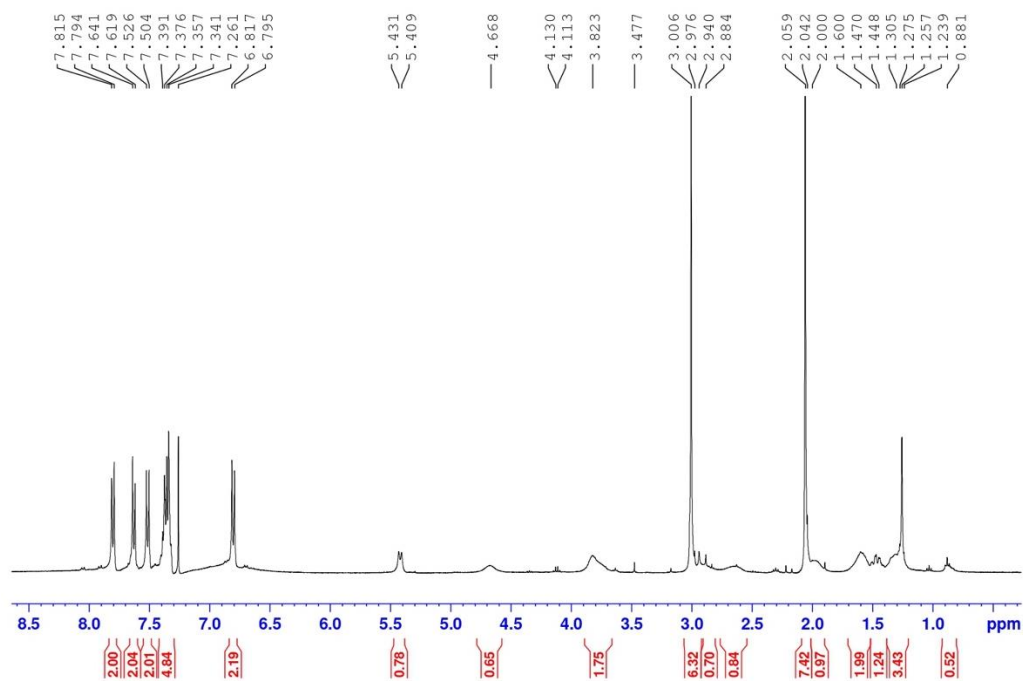
Compound **32d**: ^1H NMR (400 MHz, CDCl_3).



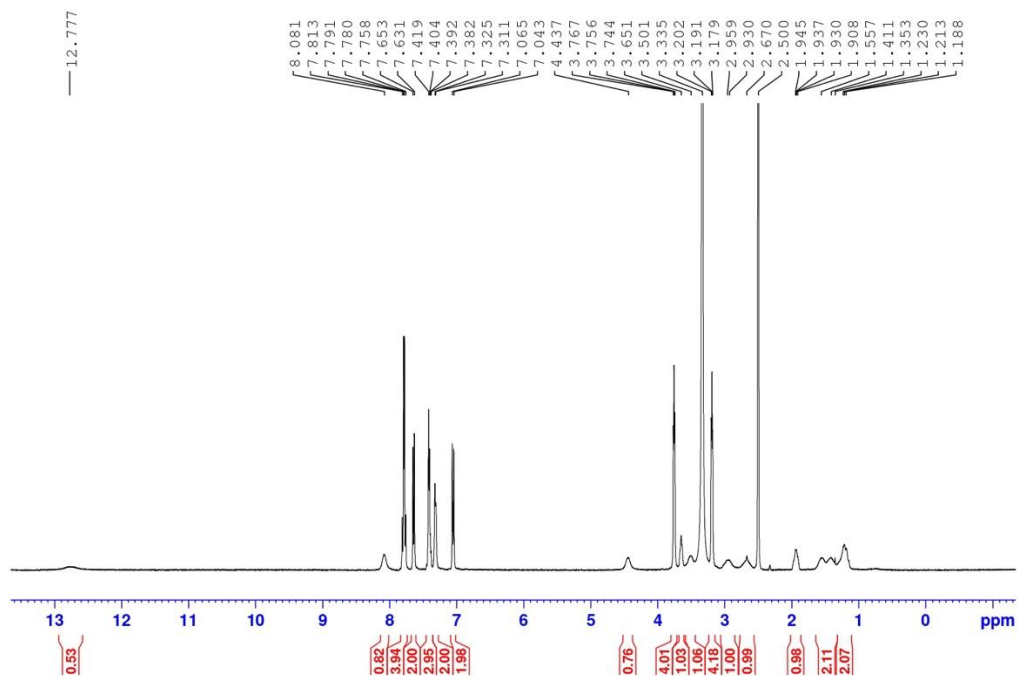
Compound **32e**: ^1H NMR (400 MHz, CDCl_3).



Compound **32f**: ^1H NMR (400 MHz, DMSO).



Compound **32g**: ^1H NMR (400 MHz, DMSO).



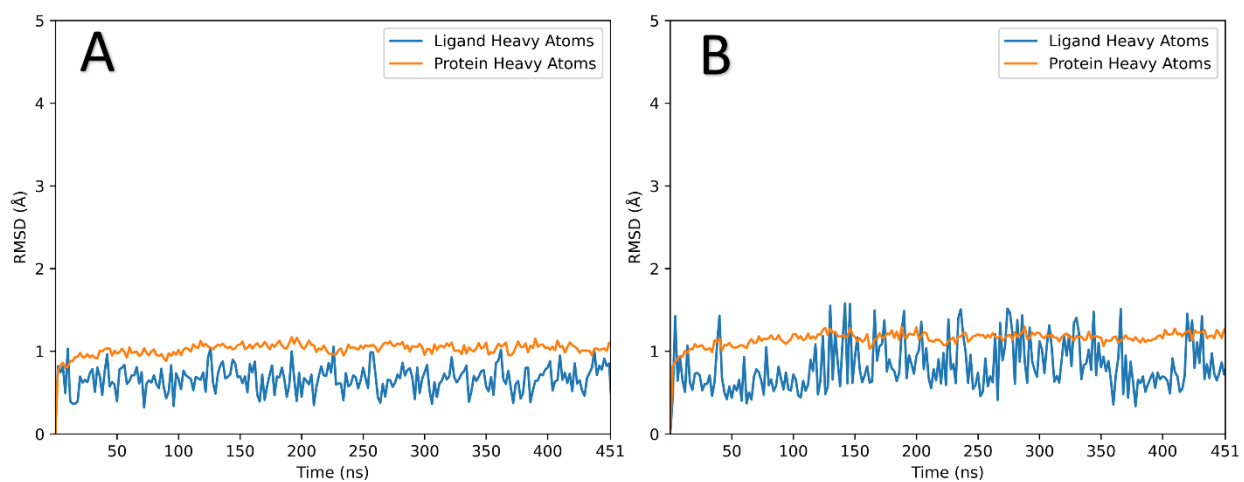


Figure S1. The plot shows the RMSD of **3a** and protein heavy atoms for the ADAMTS5-**3a** (A) and ADAMTS7-**3a** (B) complexes during the MD simulations.

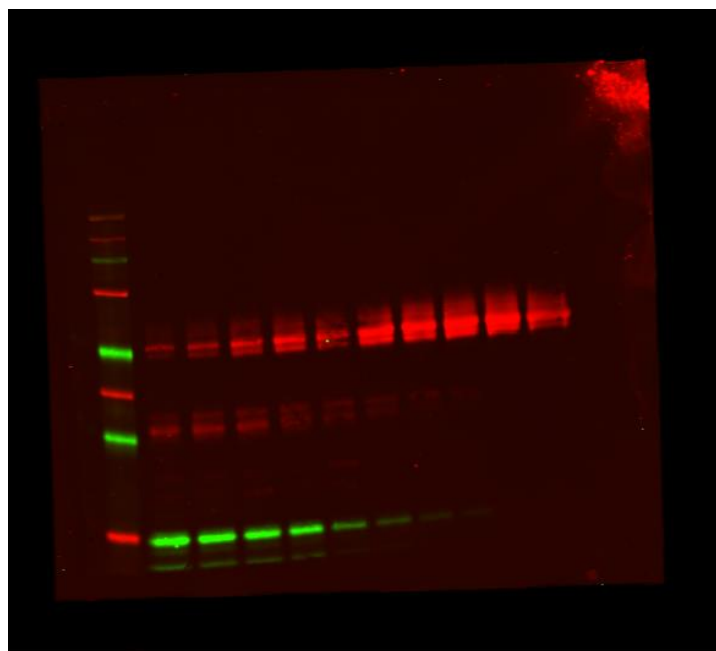


Figure S2. Original Western Blot for the image shown in Figure 2 in the main text. In the latter, the last lane of the original image as shown here was cropped out as it related to a different experiment.