Supplementary Information

Hydrazonylthiazole Derivatives as Dual EGFR and ALR2 Inhibitors: Design, Synthesis, and Comprehensive In Vitro and In Silico Evaluation for Potential Anticancer Activity

Belgin Sever [1,2], Cüneyt Türkeş [3,*], Yeliz Demir [4], Khaled M. Elamin [5], Wadah Osman [6], Kübra Oral [1], Selenay Akıncı Genç [1], Zerrin Cantürk [7], Takuya Masunaga [2], Naoki Kishimoto [5,8], Shogo Misumi [5,8], Masami Otsuka [2,9], Mikako Fujita [2] and Halilibrahim Ciftci [2,9,10,*]

[1] Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Anadolu University, Eskisehir 26470, Türkiye; belginsever@anadolu.edu.tr (B.S.); kbrorl78@gmail.com (K.O.); selenayakinci@gmail.com (S.A.G.)

[2] Medicinal and Biological Chemistry Science Farm Joint Research Laboratory, Faculty of Life Sciences, Kumamoto University, Kumamoto 862-0973, Japan; tmasunaga@kumamoto-u.ac.jp (T.M.); motsuka@gpo.kumamoto-u.ac.jp (M.O.); mfujita@kumamoto-u.ac.jp (M.F.)

[3] Department of Biochemistry, Faculty of Pharmacy, Erzincan Binali Yıldırım University, Erzincan 24100, Türkiye; cuneyt.turkes@erzincan.edu.tr (C.T.)

[4] Department of Pharmacy Services, Nihat Delibalta Göle Vocational High School, Ardahan University, Ardahan 75700, Türkiye; yelizdemir@ardahan.edu.tr (Y.D.)

[5] Global Center for Natural Products Research, Faculty of Life Sciences, Kumamoto University, 5-1 Oe-honmachi, Chuo-ku, Kumamoto 862-0973, Japan; khaled@kumamoto-u.ac.jp (K.M.E.); naokishi@kumamoto-u.ac.jp (N.K.); misumi@gpo.kumamoto-u.ac.jp (S.M.)

[6] Department of Pharmacognosy, Faculty of Pharmacy, Prince Sattam Bin Abdulaziz University, Al-kharj 11942, Saudi Arabia, w.osman@psau.edu.sa (W.O.)

[7] Department of Pharmaceutical Microbiology, Faculty of Pharmacy, Anadolu University, Eskişehir 26470, Türkiye; zkcanturk@anadolu.edu.tr (Z.C.)

[8] Department of Environmental and Molecular Health Sciences, Faculty of Medical and Pharmaceutical Sciences, Kumamoto University, Kumamoto 862-0973, Japan

[9] Department of Drug Discovery, Science Farm Ltd., Kumamoto 862-0976, Japan

[10] Department of Molecular Biology and Genetics, Burdur Mehmet Akif Ersoy University, Istiklal Campus, Burdur 15200, Türkiye; hciftci@mehmetakif.edu.tr (H.C.)

* Correspondence: hciftci@mehmetakif.edu.tr (H.C.); cuneyt.turkes@erzincan.edu.tr (C.T.)

Supplementary Figures

Figure S1. ^{1}H NMR Spectrum of **A**

Figure S2. ^{13}C NMR Spectrum of **A**

Figure S3. ^{1}H NMR Spectrum of compound **1** (0-15 ppm)

Figure S4. ^{1}H NMR Spectrum of compound **1** (7-9 ppm)

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Figure S6. Mass Spectrum of compound **1**

Figure S7. ^{1}H NMR Spectrum of compound **2** (0-15 ppm)

Figure S8. ^{1}H NMR Spectrum of compound **2** (7-9 ppm)

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Figure S12. ^{1}H NMR Spectrum of compound **3** (7-9 ppm)

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Figure S21. ^{13}C NMR Spectrum of compound **5**

Figure S22. Mass Spectrum of compound **5**

Figure S23. ^{1}H NMR Spectrum of compound **6** (0-15 ppm)

Figure S24. ^{1}H NMR Spectrum of compound **6** (7-9 ppm)

Figure S25. ^{13}C NMR Spectrum of compound **6**

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Figure S27. ^{1}H NMR Spectrum of compound **7** (0-15 ppm)

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Figure S42. Mass Spectrum of compound **10**

Figure S43. ^{1}H NMR Spectrum of compound **11** (0-15 ppm)

Figure S44. ^{1}H NMR Spectrum of compound **11** (7-9 ppm)

Figure S45. ^{13}C NMR Spectrum of compound **11**

Figure S46. Mass Spectrum of compound **11**

Figure S47. ^{1}H NMR Spectrum of compound **12** (0-15 ppm)

Figure S48. ^{1}H NMR Spectrum of compound **12** (7-9 ppm)

Figure S49. ^{13}C NMR Spectrum of compound **12**

Figure S50. Mass Spectrum of compound **12**

Figure S51. ^{1}H NMR Spectrum of compound **13** (0-15 ppm)

Figure S52. ^{1}H NMR Spectrum of compound **13** (7-9 ppm)

Figure S53. ^{13}C NMR Spectrum of compound **13**

Figure S54. Mass Spectrum of compound **13**

Supplementary Table

Table S1. Prime MM-GBSA binding free energy (ΔG_{bind}) and energetic decomposition (kcal/mol) at the EGFR and AR binding sites

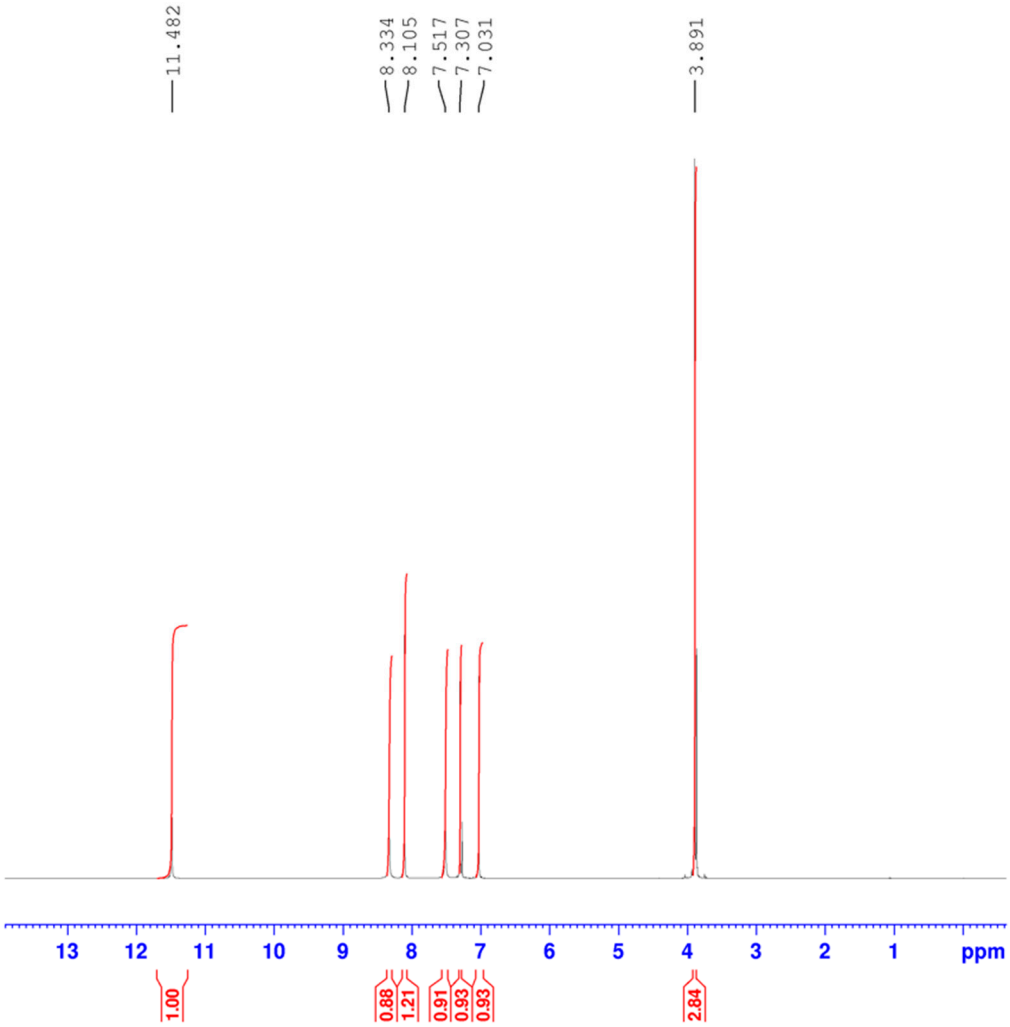


Figure S1. ^{1}H NMR Spectrum of **A**

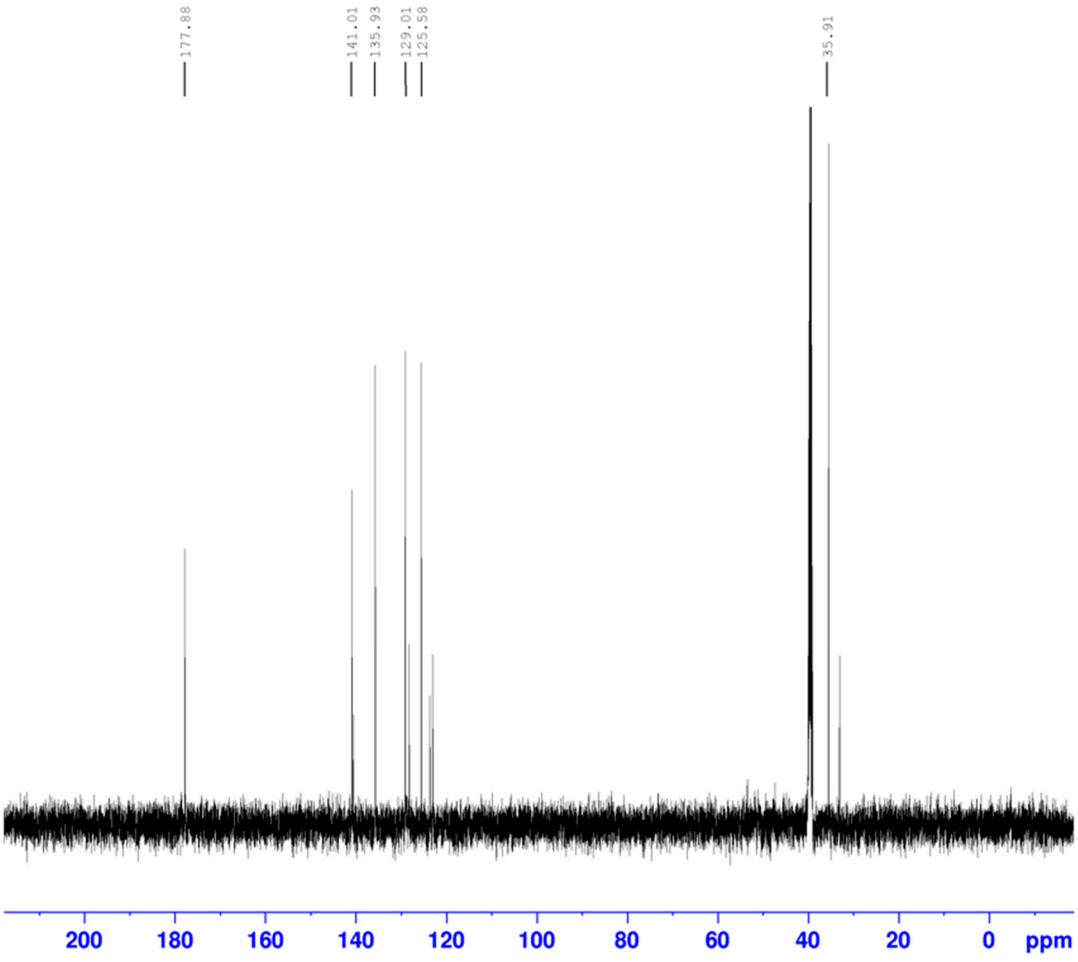


Figure S2. ^{13}C NMR Spectrum of **A**

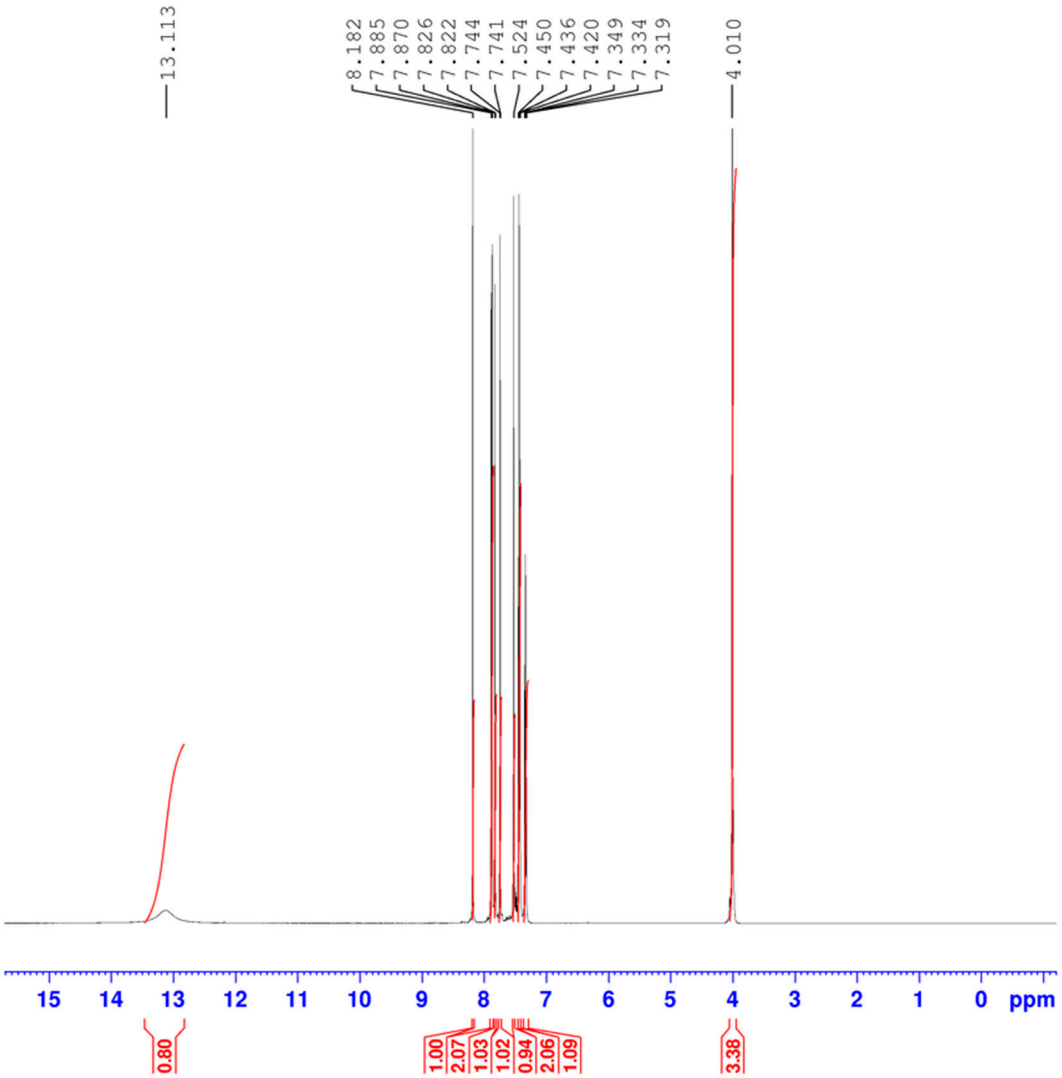


Figure S3. ^{1}H NMR Spectrum of compound **1** (0-15 ppm)

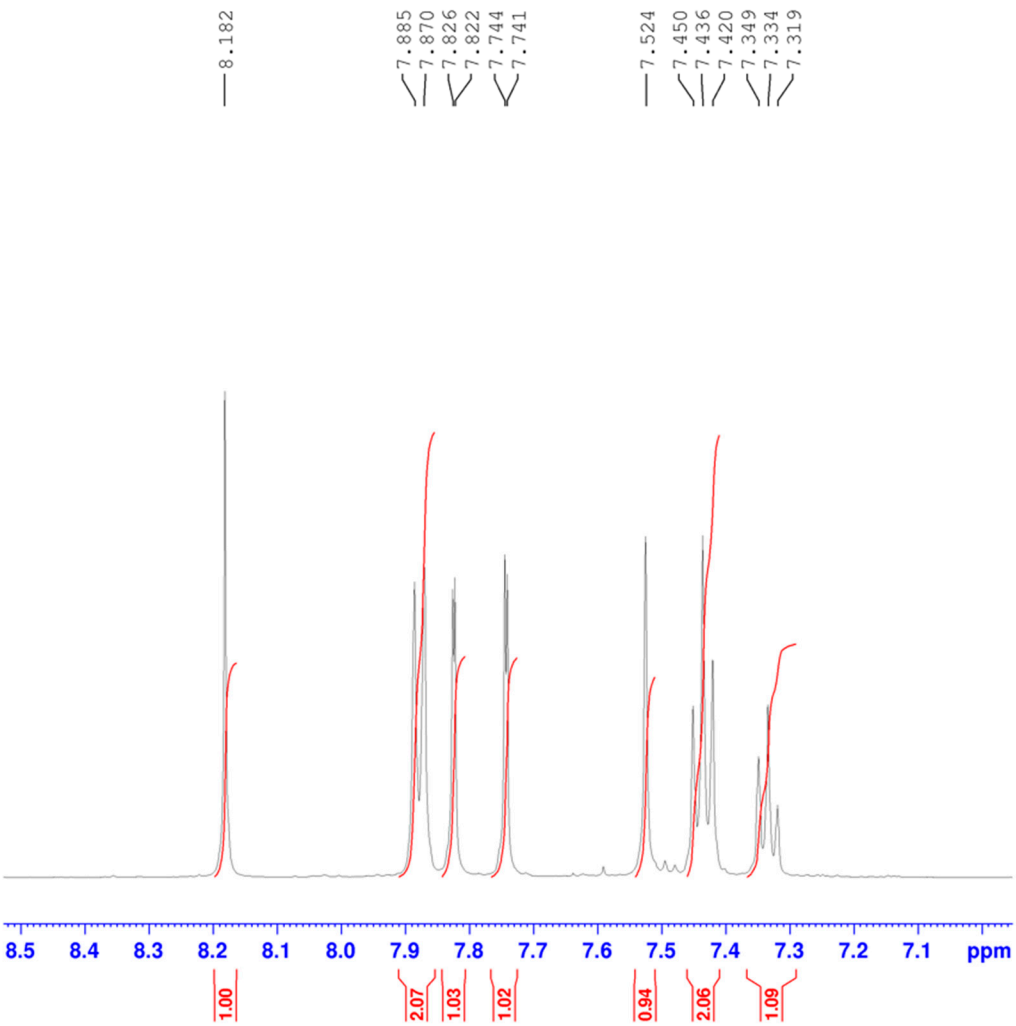


Figure S4. ^{1}H NMR Spectrum of compound **1** (7-9 ppm)

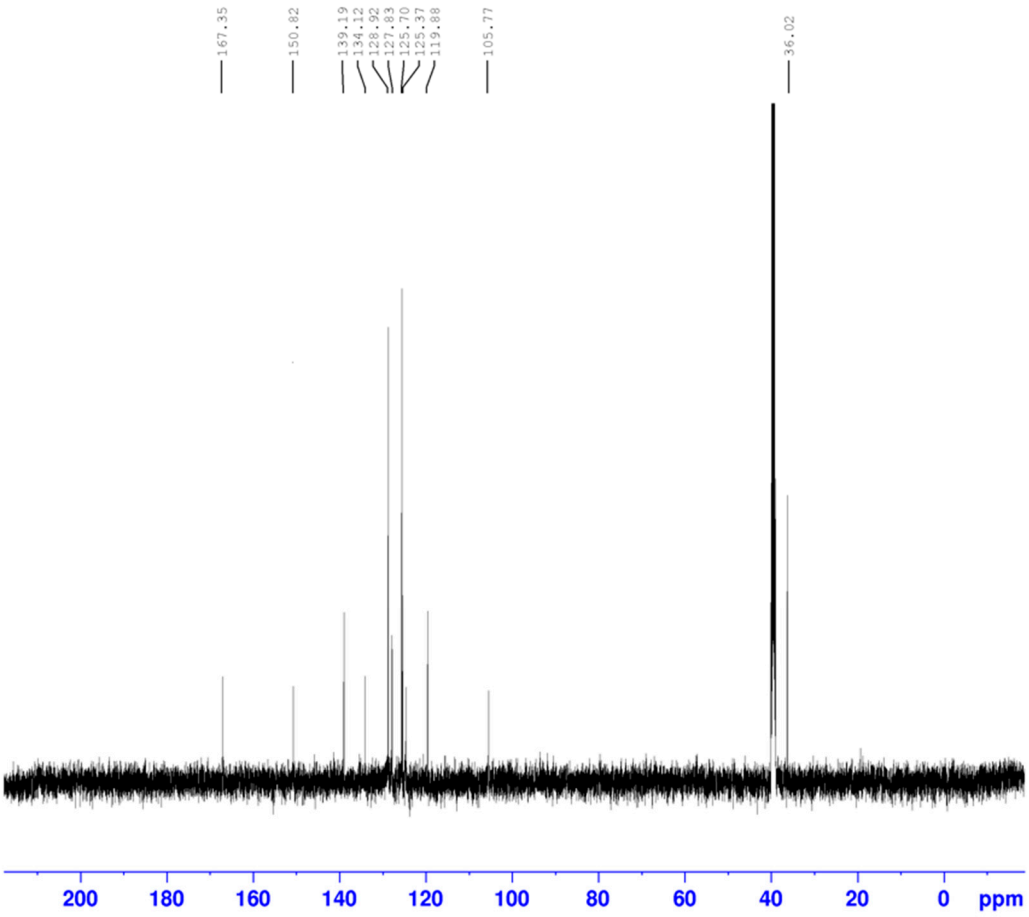


Figure S5. ^{13}C NMR Spectrum of compound **1**

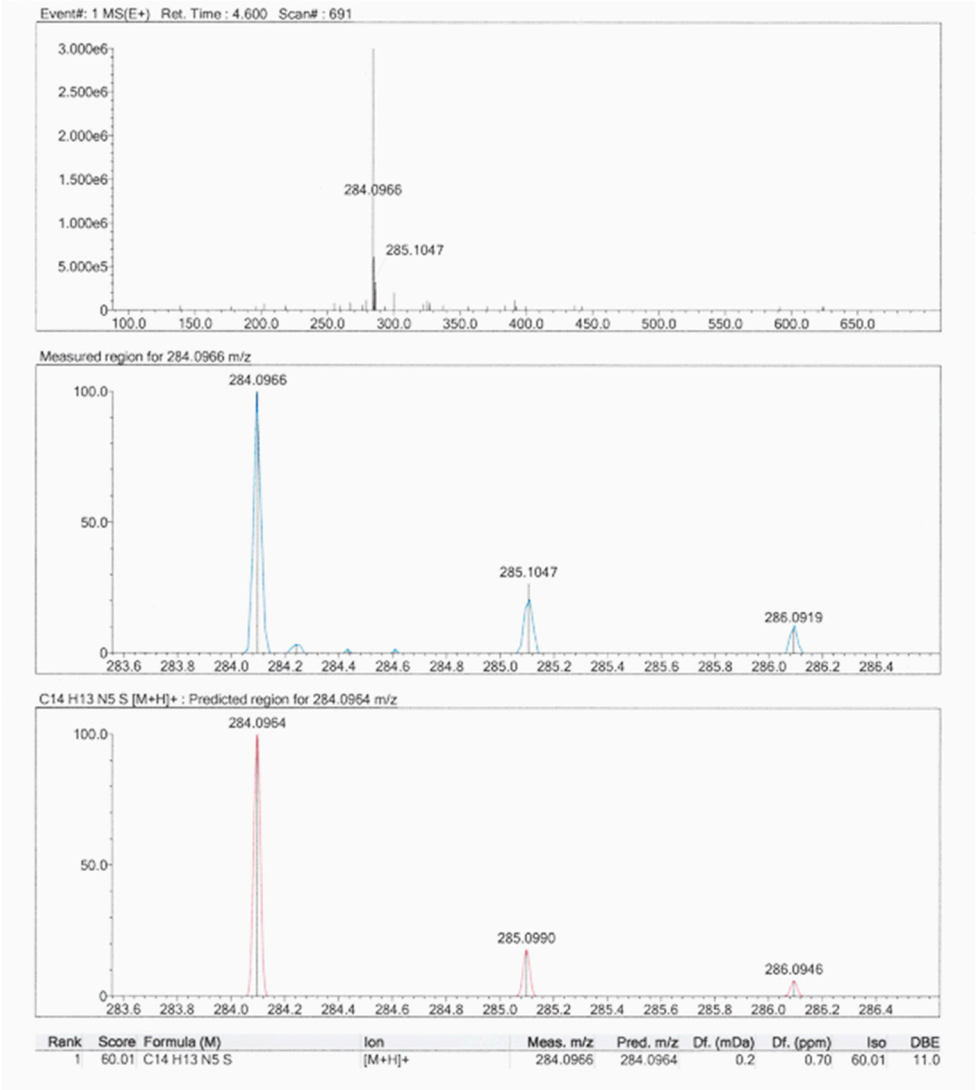


Figure S6. Mass Spectrum of compound **1**

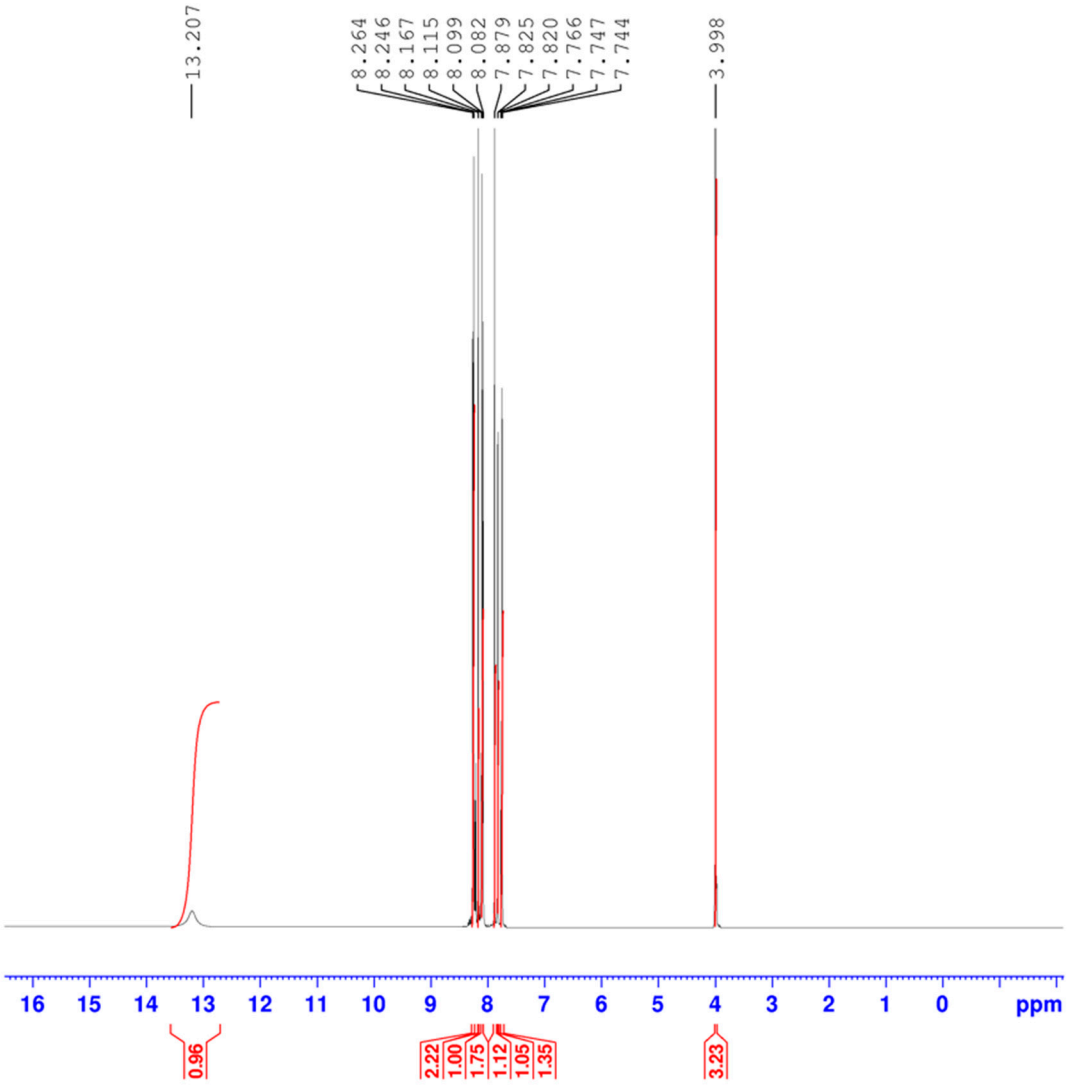


Figure S7. ^{1}H NMR Spectrum of compound **2** (0-15 ppm)

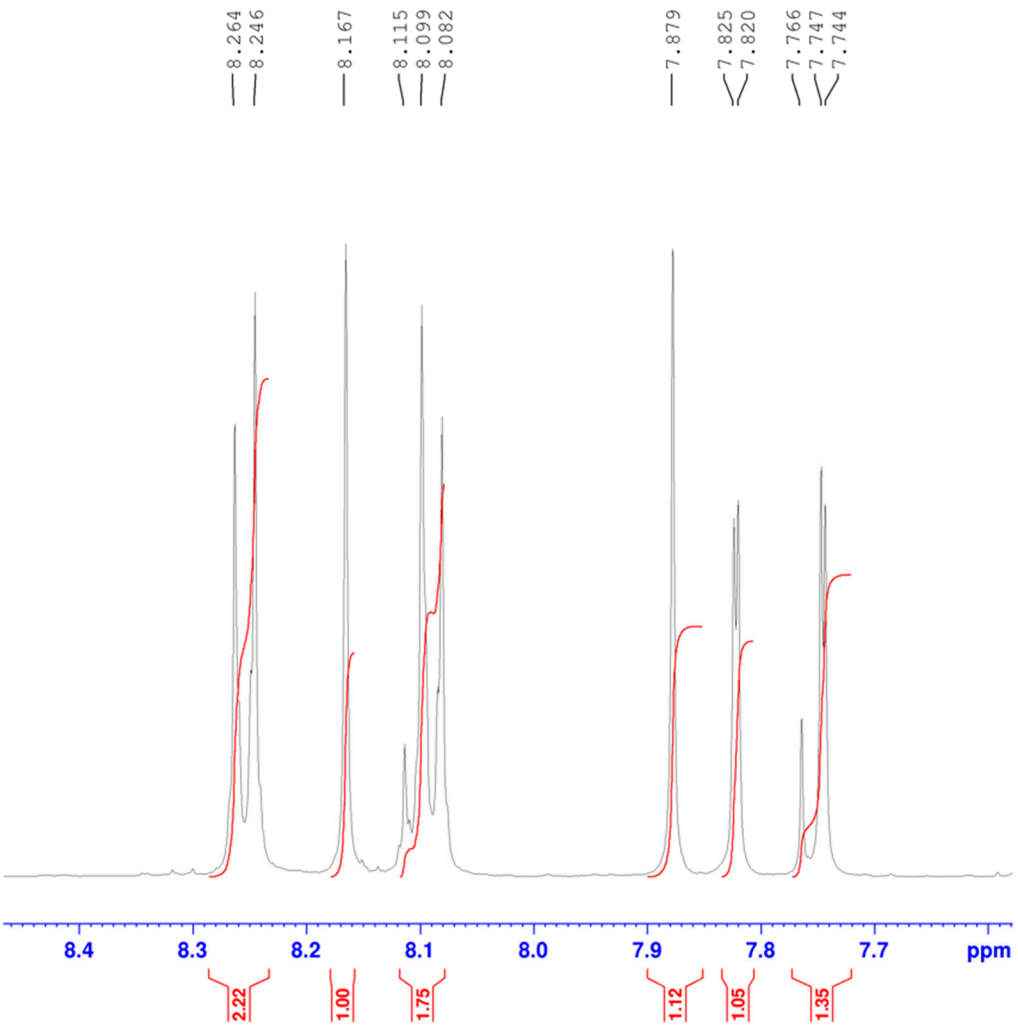


Figure S8. ^{1}H NMR Spectrum of compound **2** (7-9 ppm)

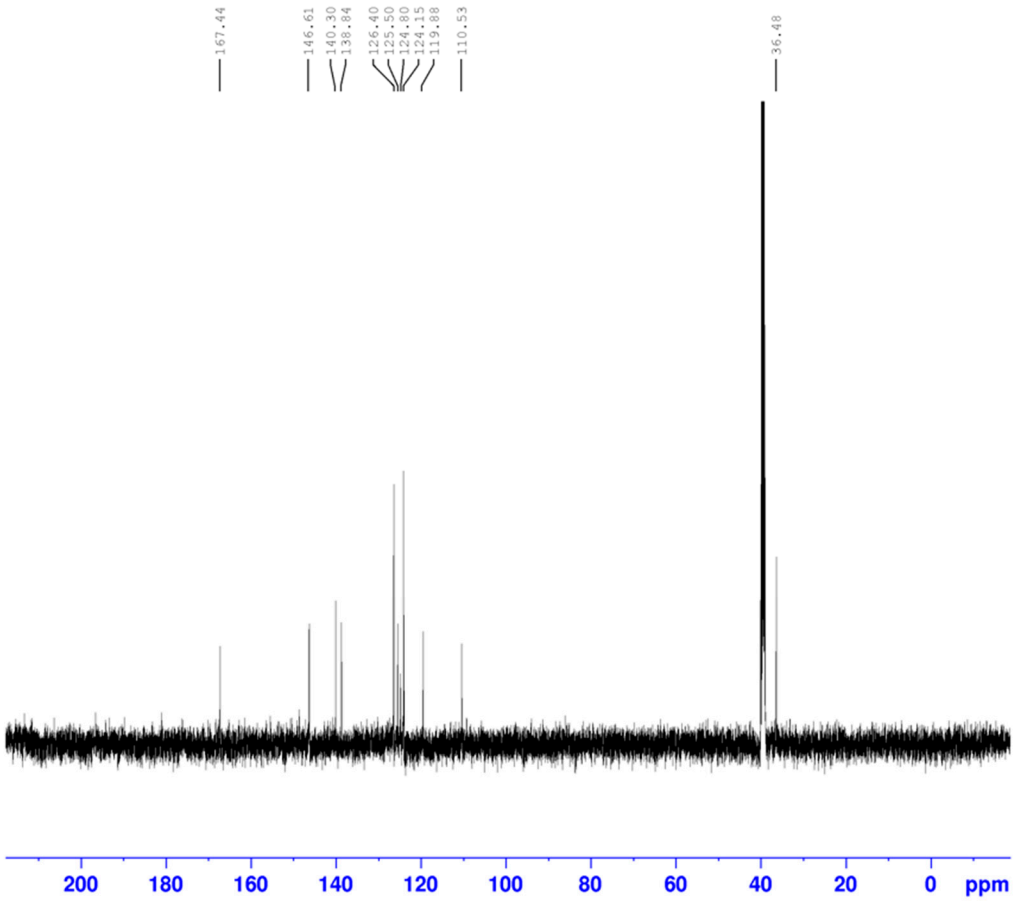


Figure S9. ^{13}C NMR Spectrum of compound **2**

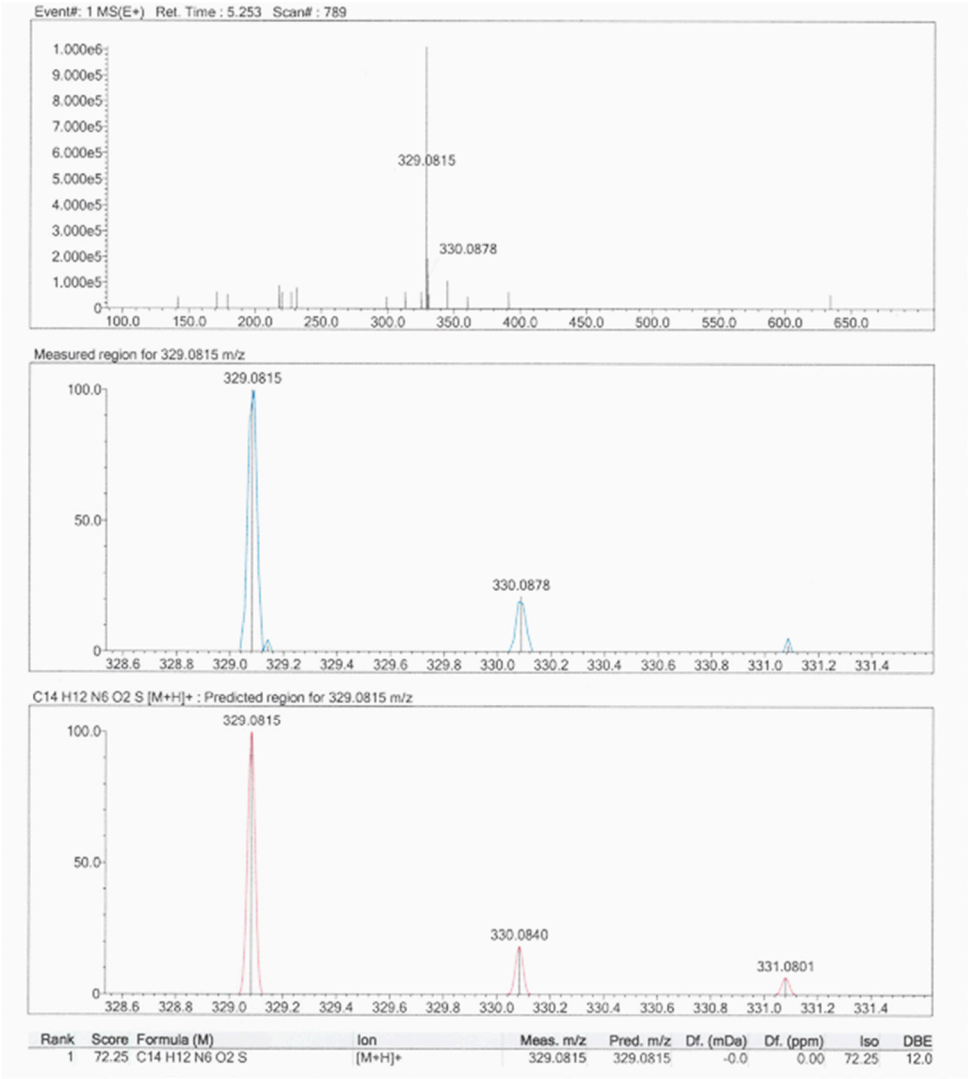


Figure S10. Mass Spectrum of compound **2**

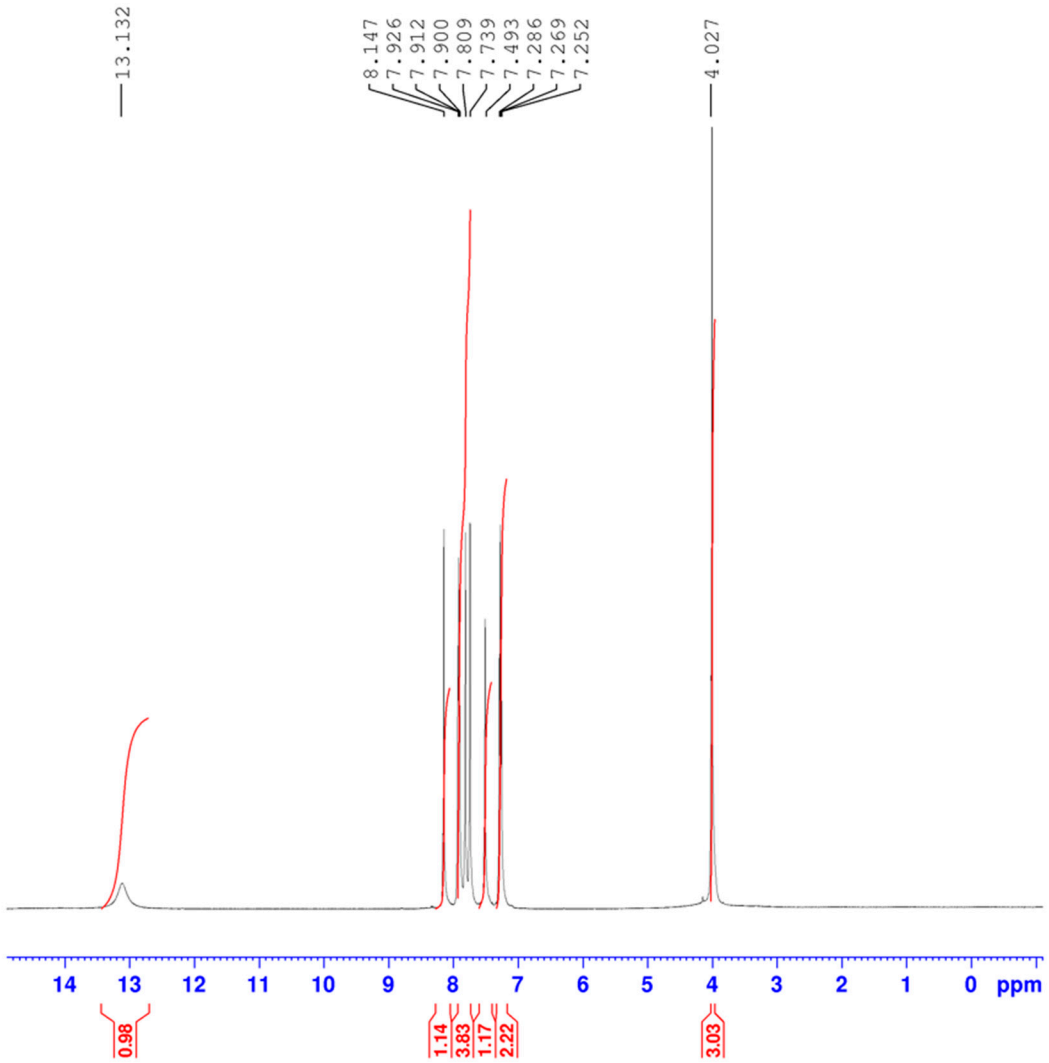


Figure S11. ^{1}H NMR Spectrum of compound **3** (0-15 ppm)

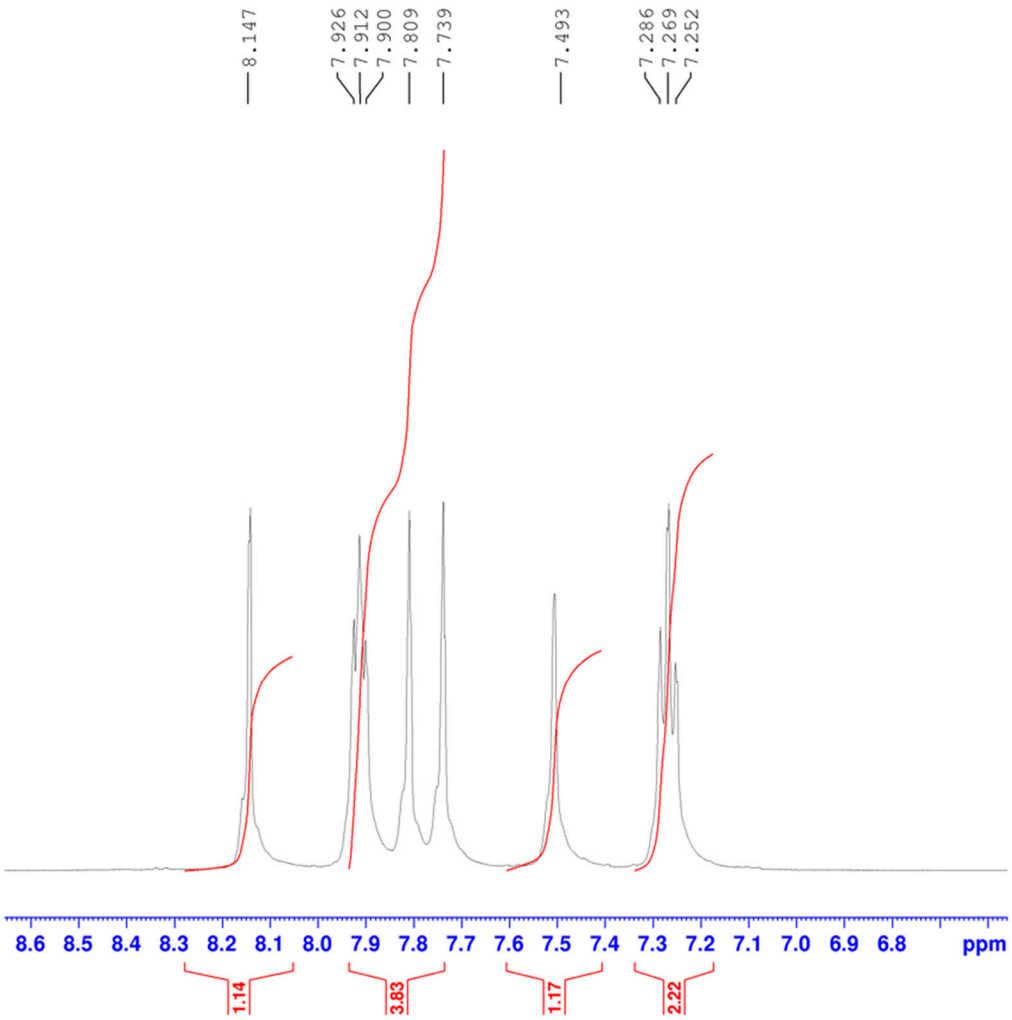


Figure S12. ^{1}H NMR Spectrum of compound **3** (7-9 ppm)

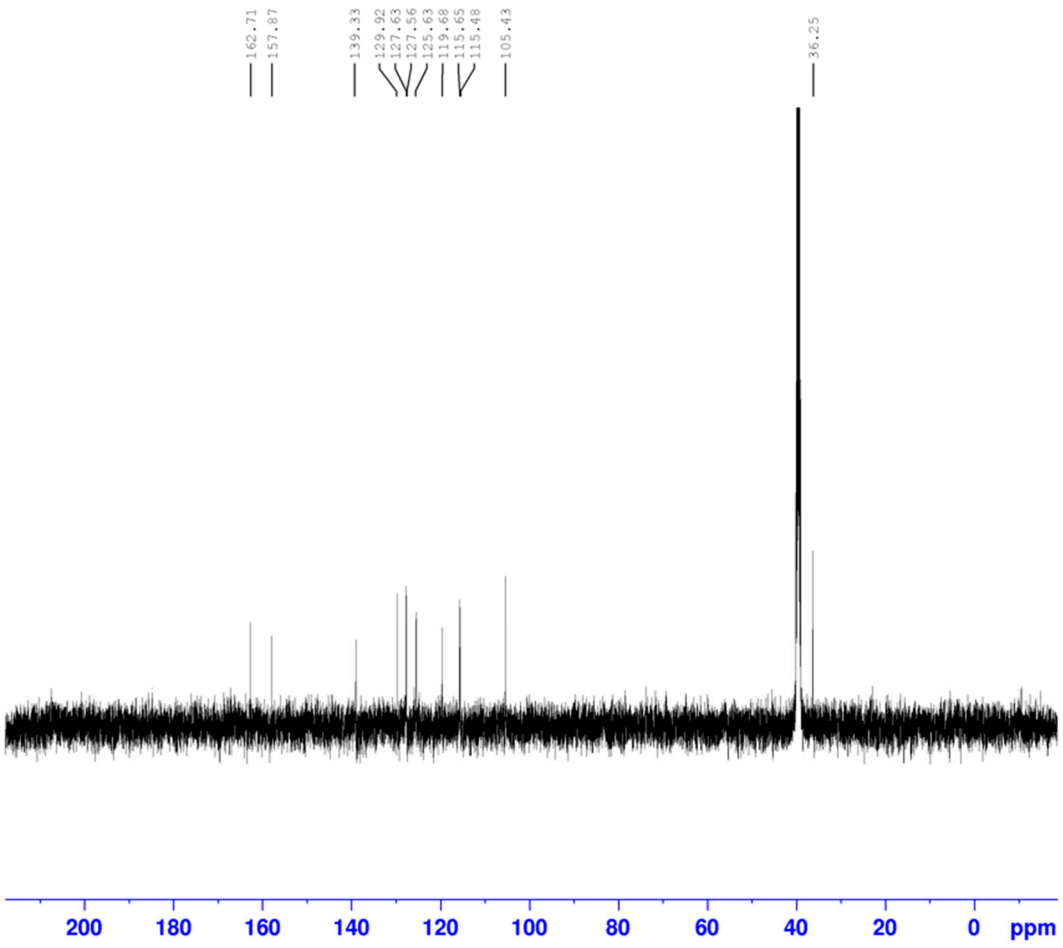


Figure S13. ^{13}C NMR Spectrum of compound **3**

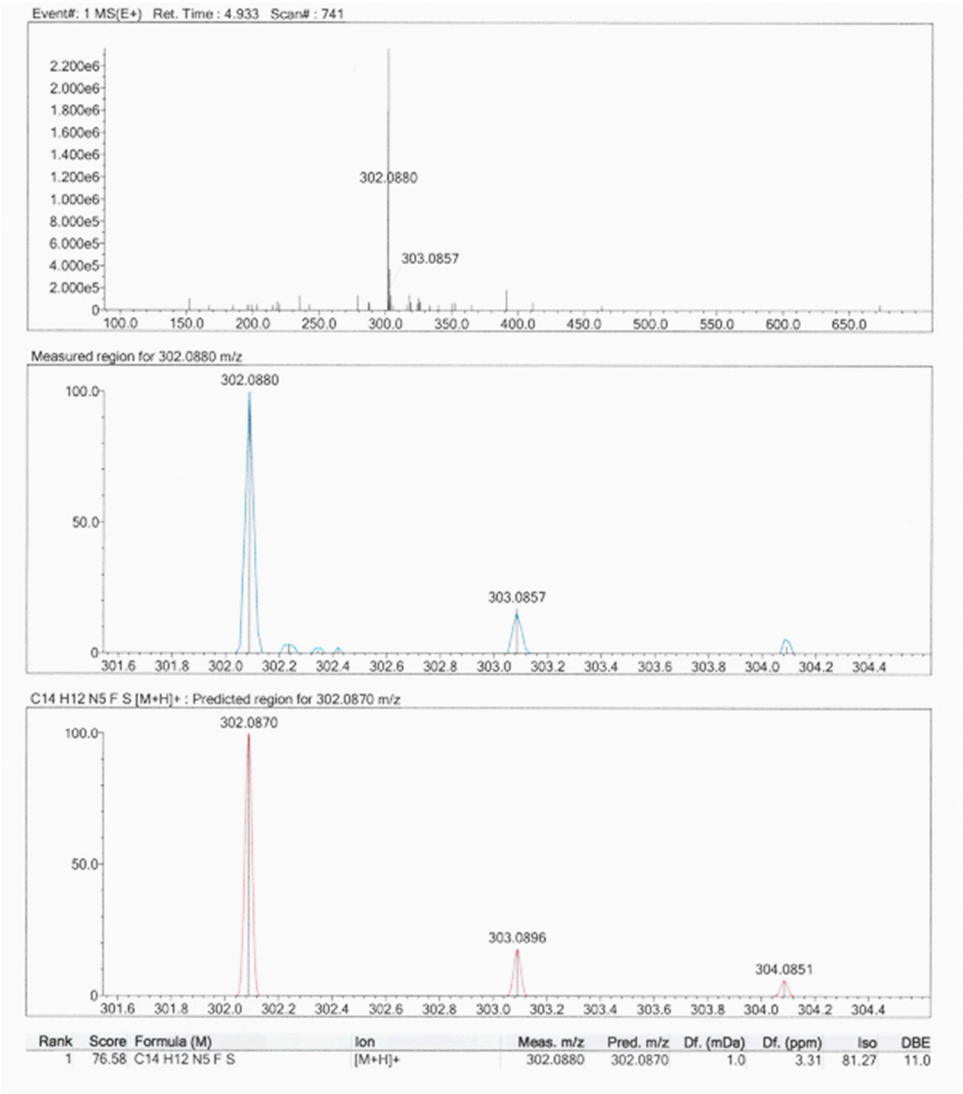


Figure S14. Mass Spectrum of compound **3**

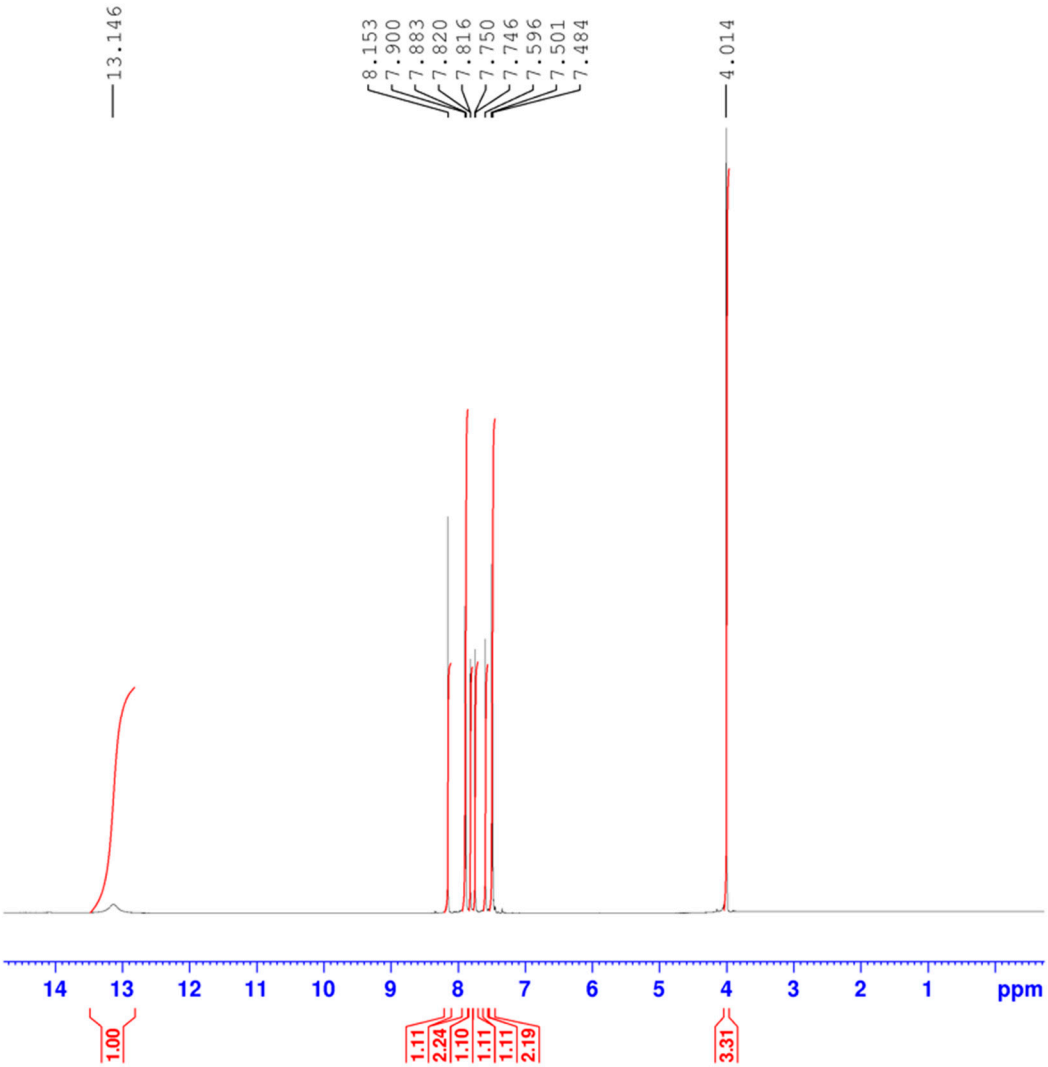


Figure S15. ^{1}H NMR Spectrum of compound **4** (0-15 ppm)

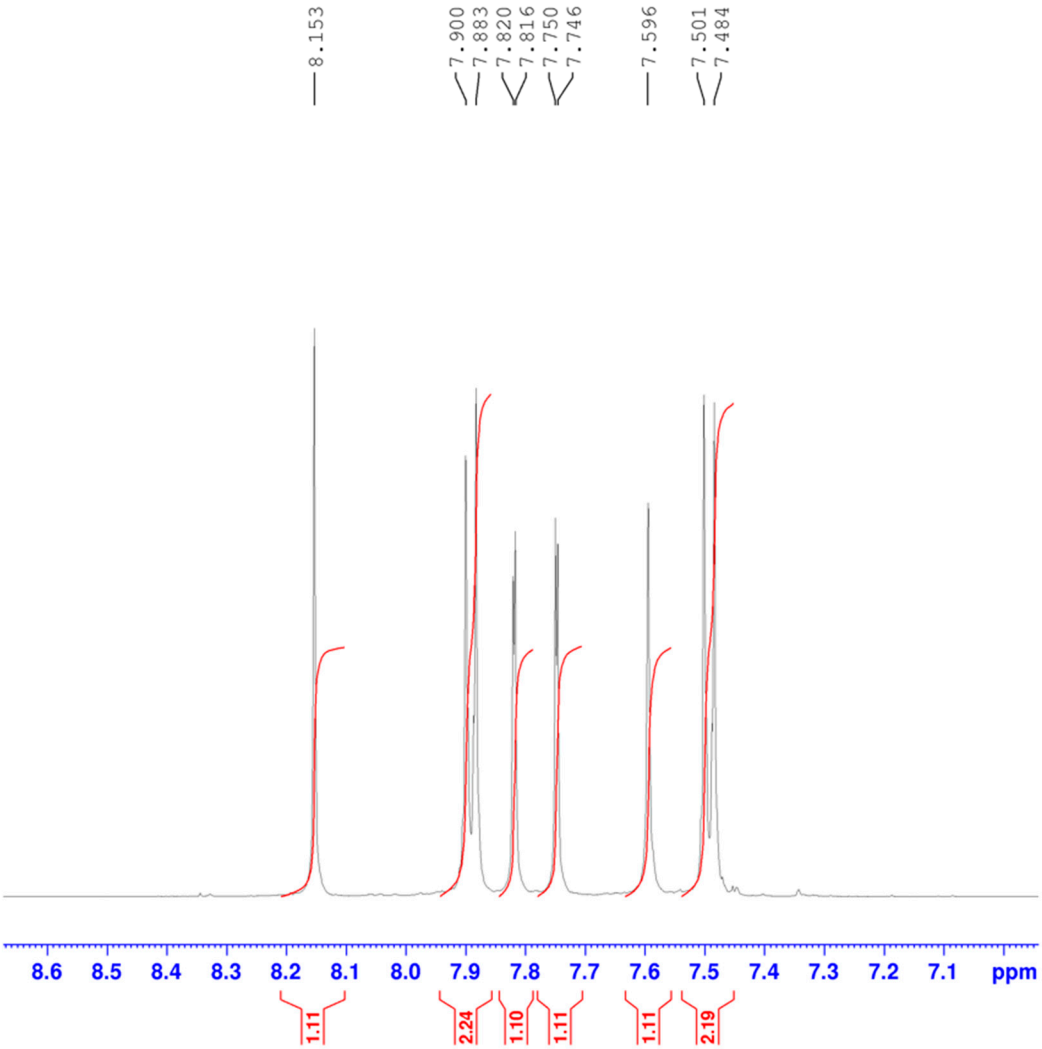


Figure S16. ^{1}H NMR Spectrum of compound **4** (7-9 ppm)

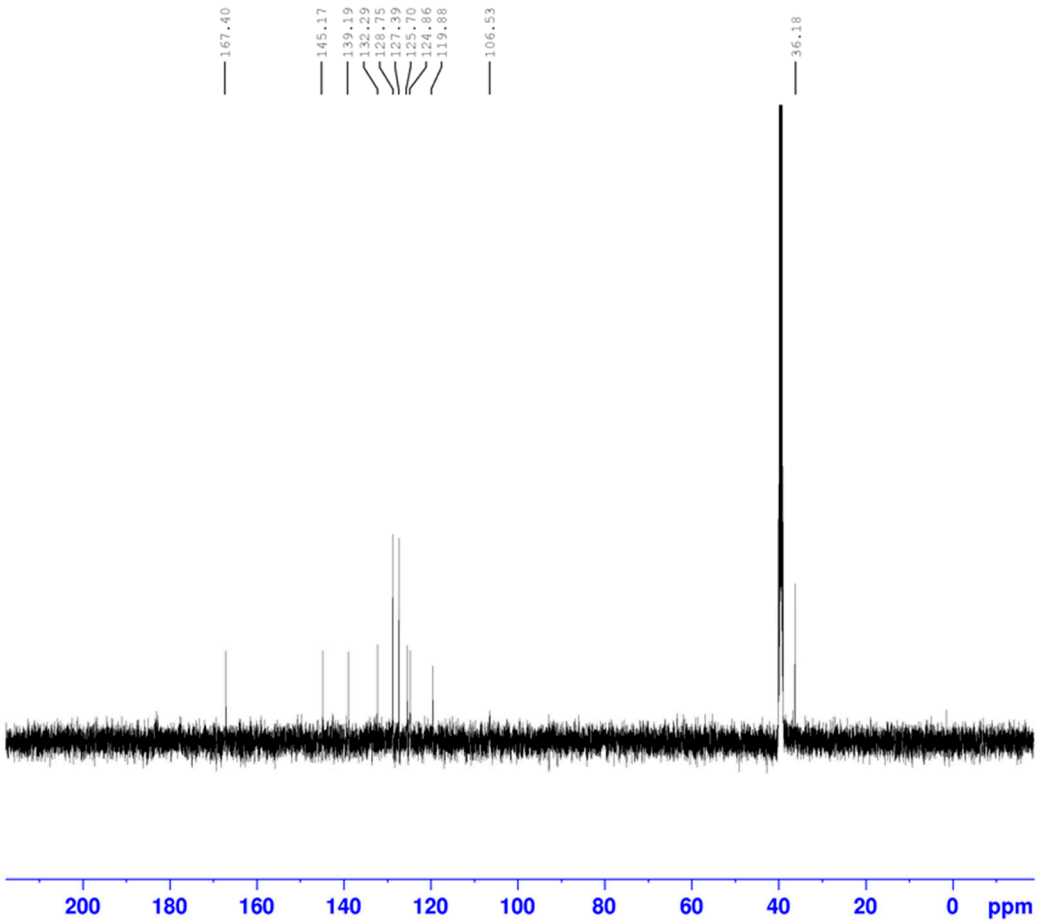
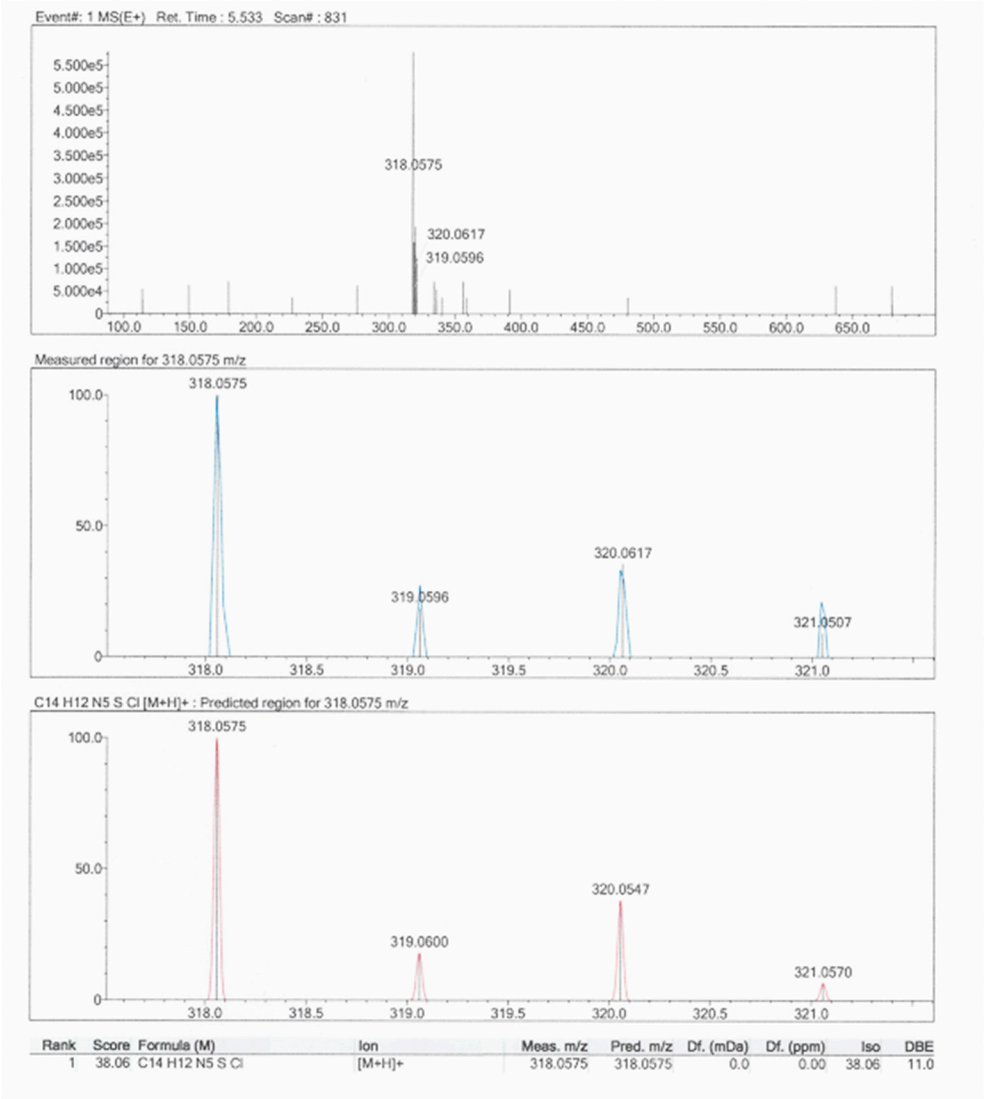


Figure S17. ^{13}C NMR Spectrum of compound **4**



Rank	Score	Formula (M)	Ion	Meas. m/z	Pred. m/z	Df. (mDa)	Df. (ppm)	Iso	DBE
1	38.06	C14 H12 N5 S Cl	[M+H]+	318.0575	318.0575	0.0	0.00	38.06	11.0

Figure S18. Mass Spectrum of compound **4**

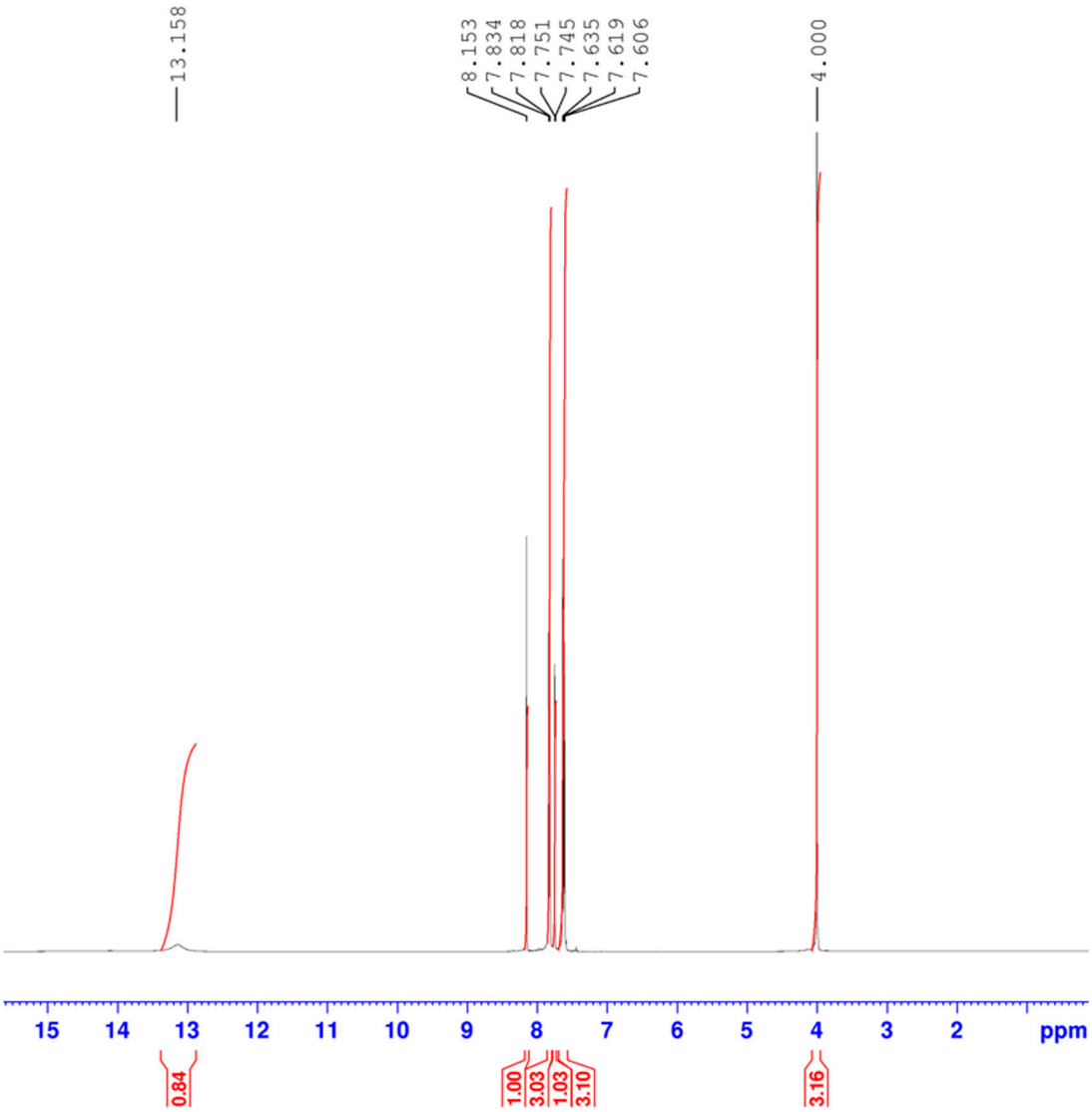


Figure S19. ^{1}H NMR Spectrum of compound **5** (0-15 ppm)

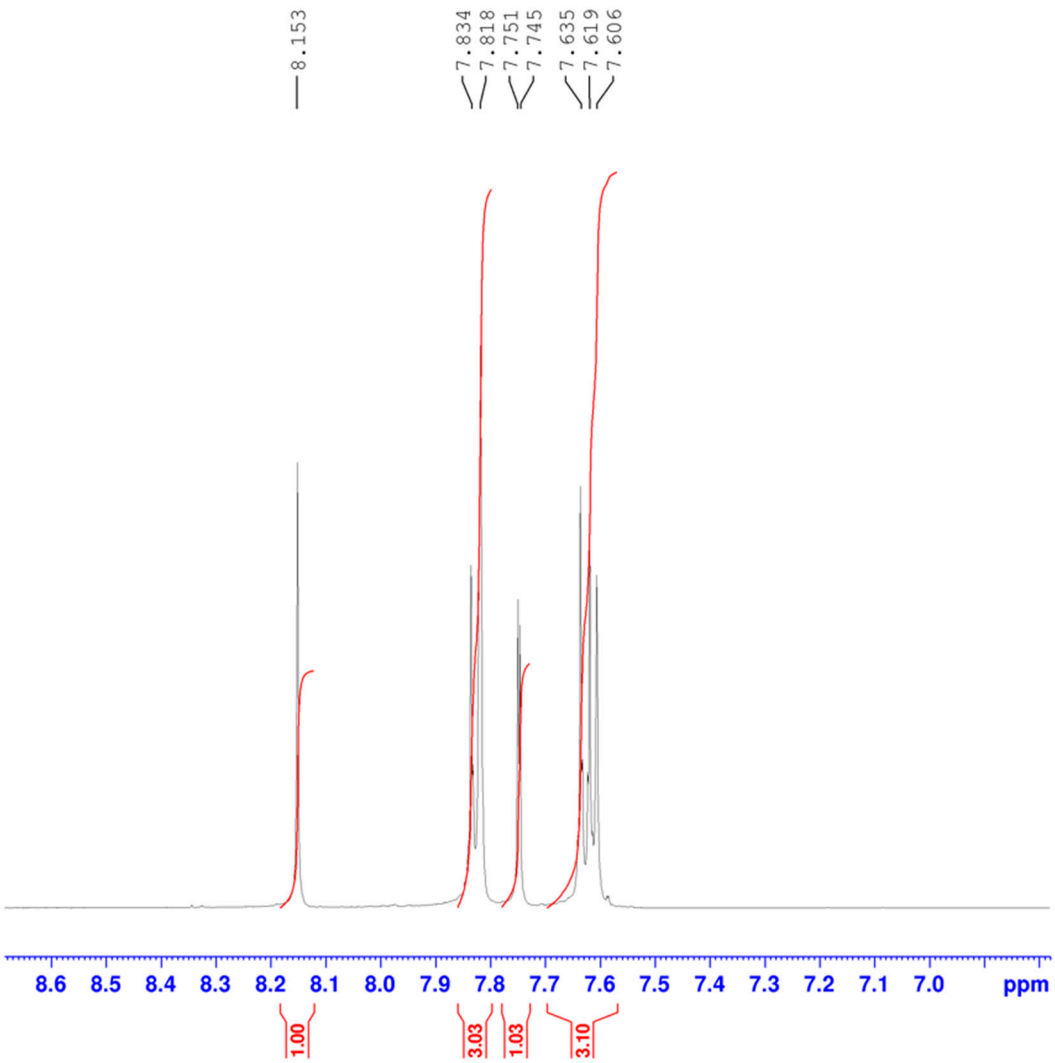


Figure S20. ^{1}H NMR Spectrum of compound **5** (7-9 ppm)

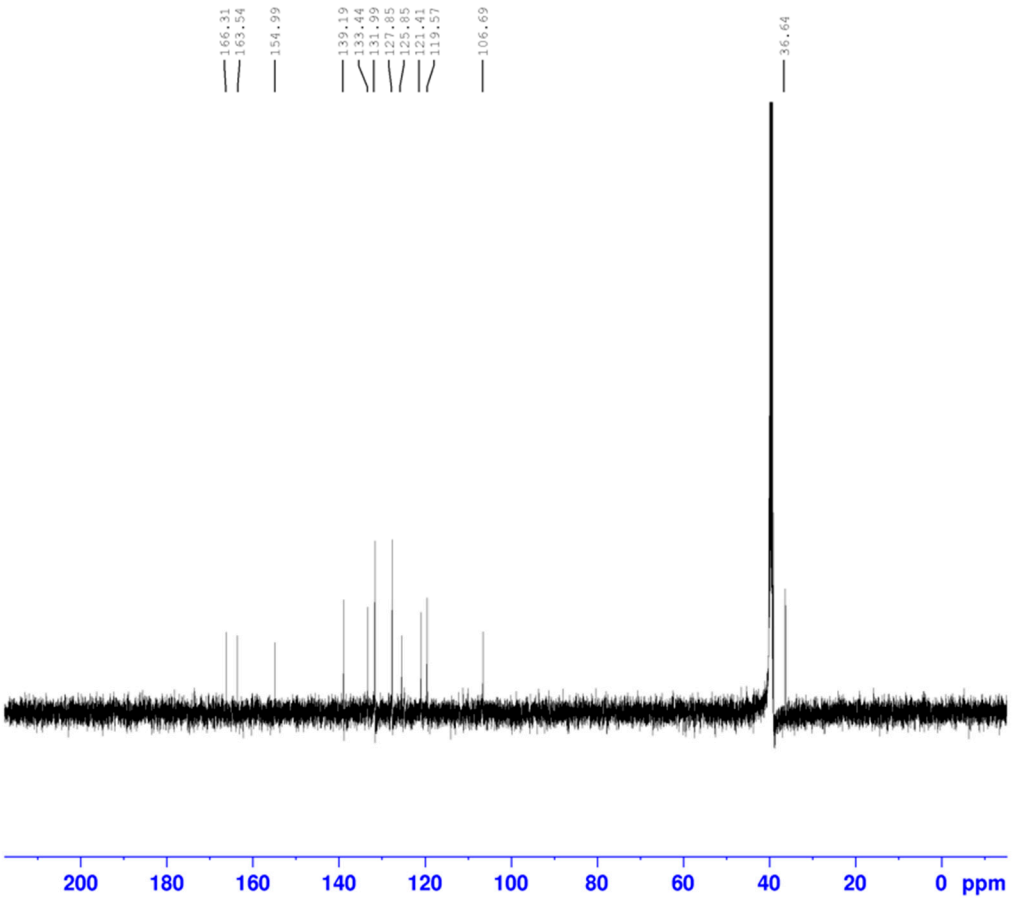


Figure S21. ^{13}C NMR Spectrum of compound **5**

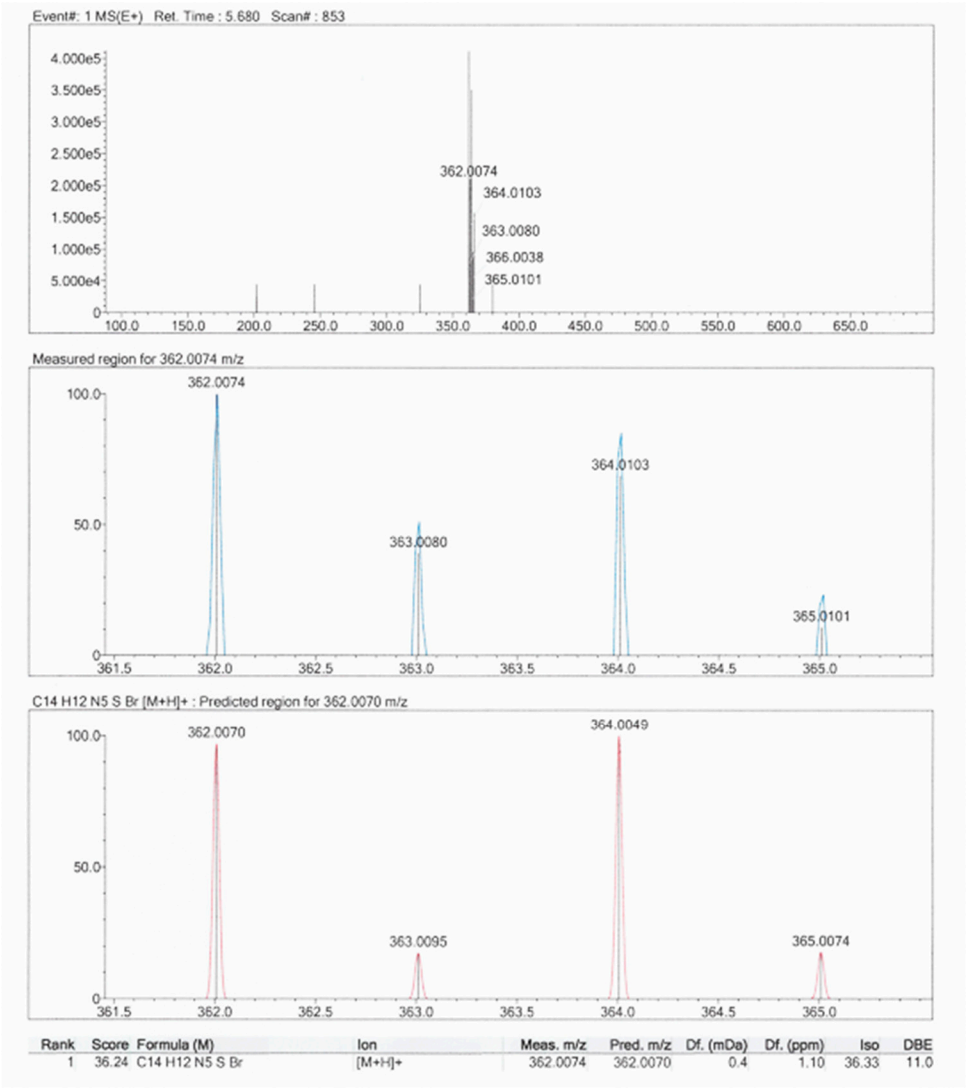


Figure S22. Mass Spectrum of compound **5**

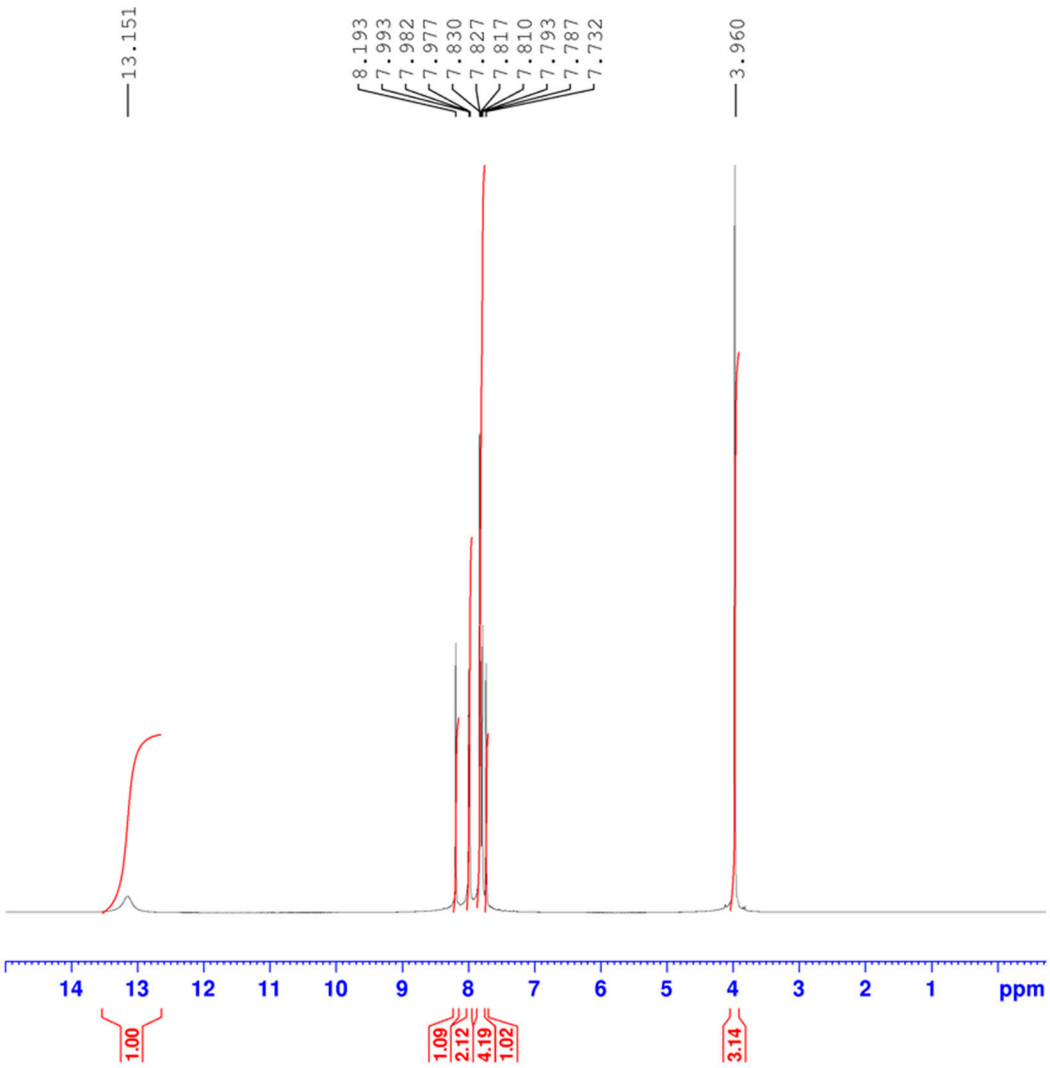


Figure S23. ^{1}H NMR Spectrum of compound **6** (0-15 ppm)

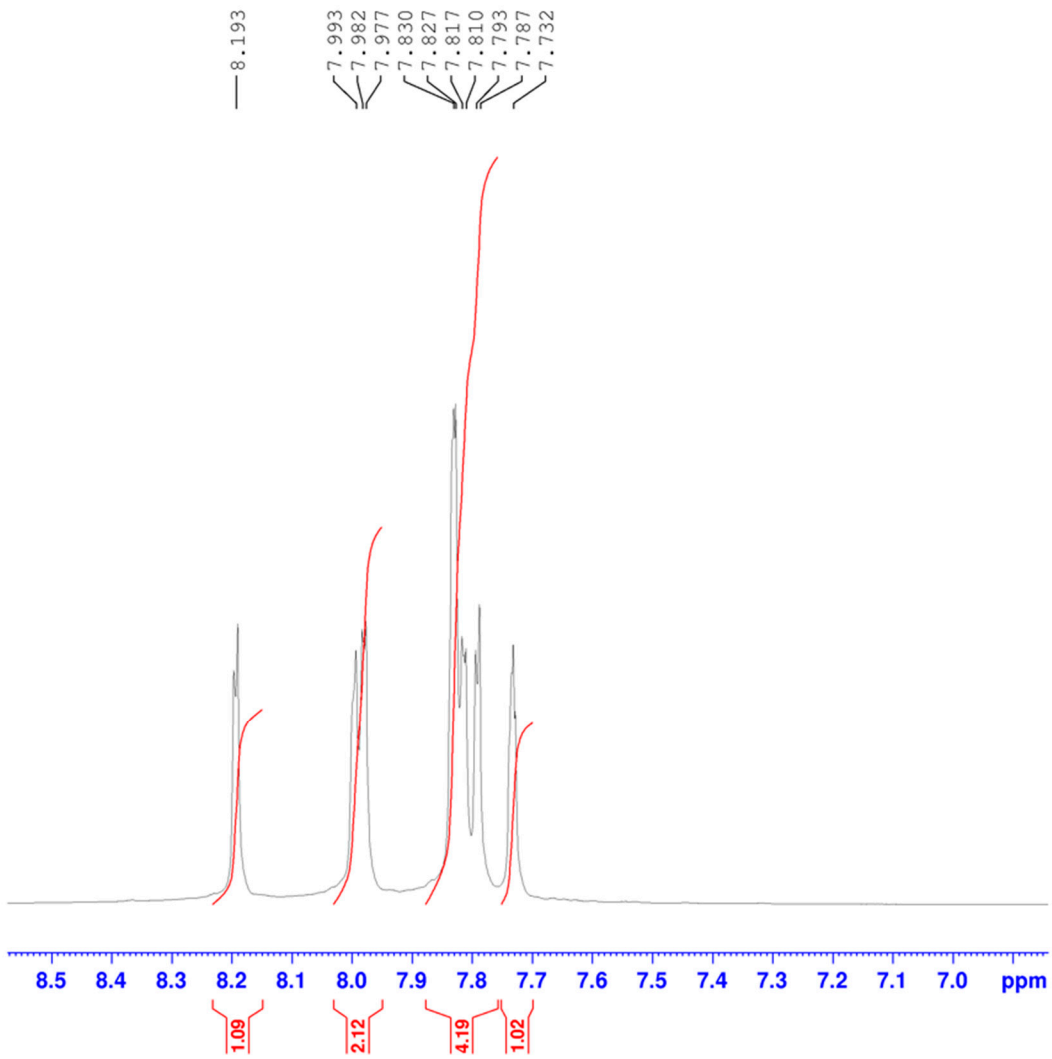


Figure S24. ^{1}H NMR Spectrum of compound **6** (7-9 ppm)

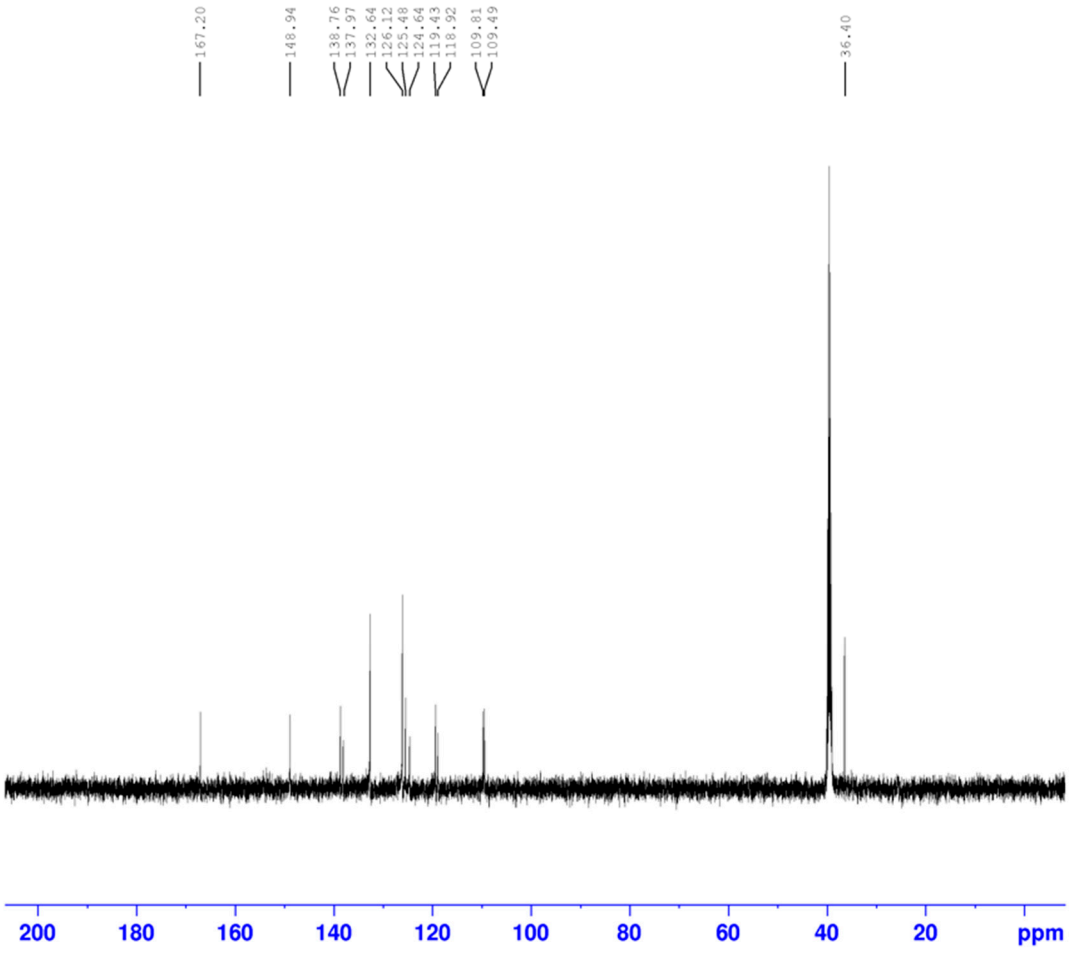
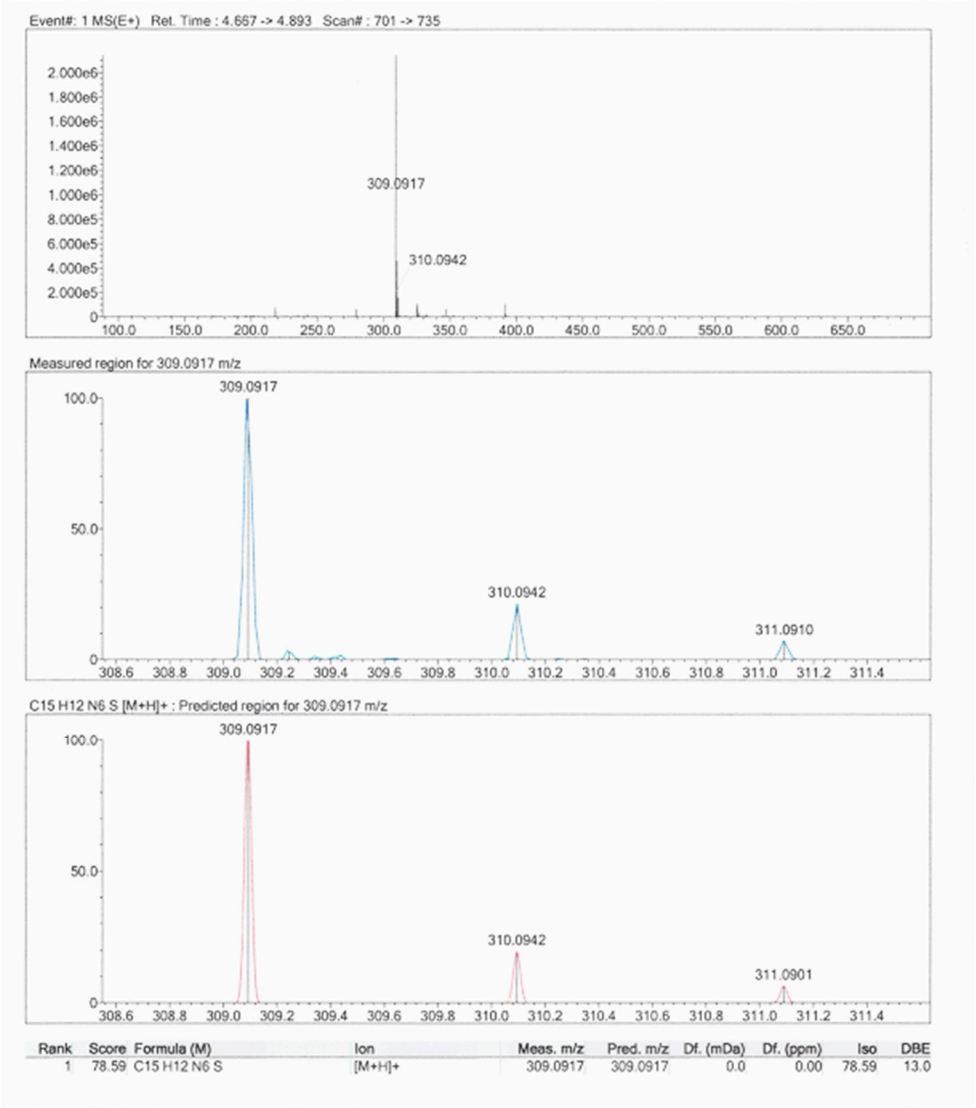


Figure S25. ^{13}C NMR Spectrum of compound **6**



Rank	Score	Formula (M)	Ion	Meas. m/z	Pred. m/z	Df. (mDa)	Df. (ppm)	Iso	DBE
1	78.59	C15 H12 N6 S	[M+H]+	309.0917	309.0917	0.0	0.00	78.59	13.0

Figure S26. Mass Spectrum of compound **6**

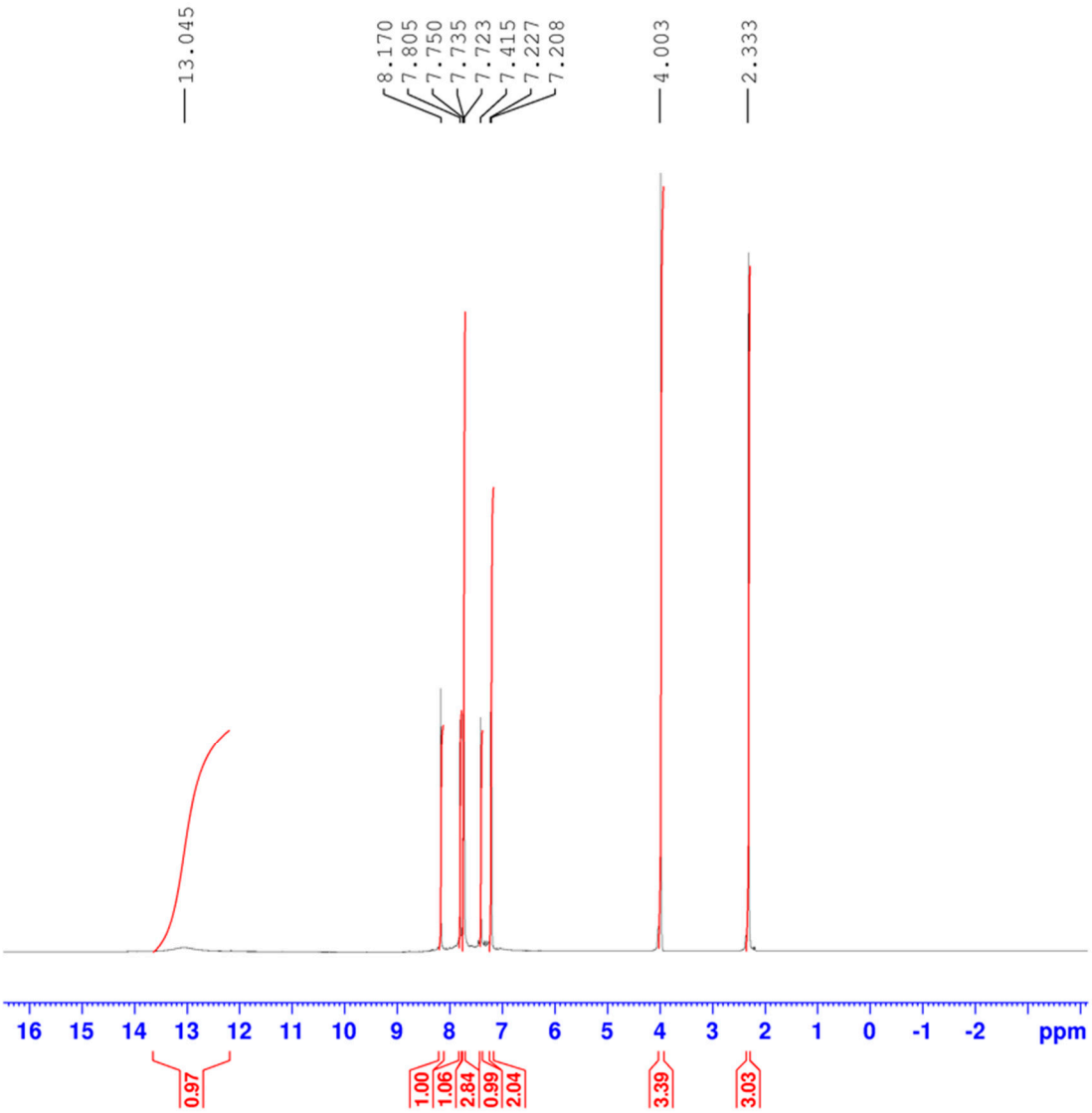


Figure S27. ^{1}H NMR Spectrum of compound **7** (0-15 ppm)

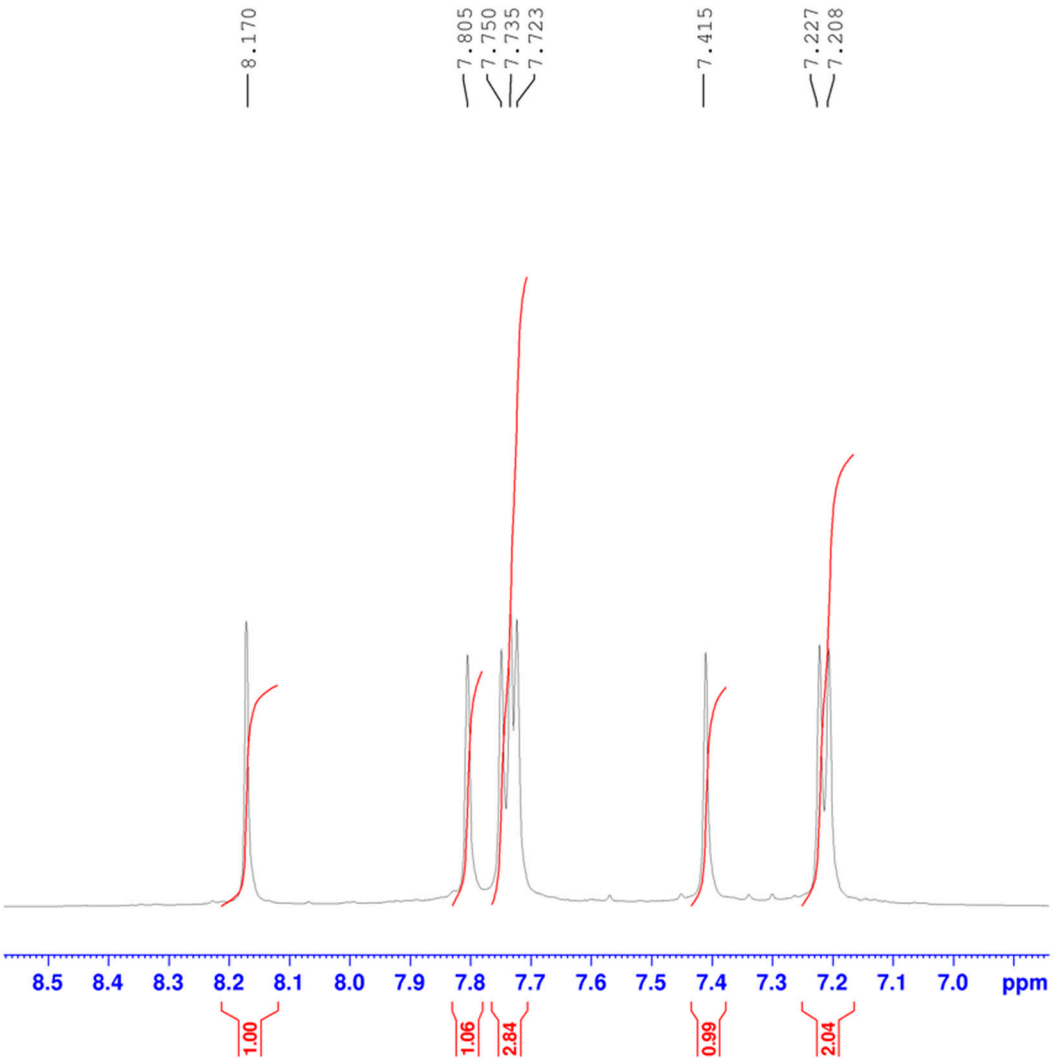


Figure S28. ^{1}H NMR Spectrum of compound **7** (7-9 ppm)

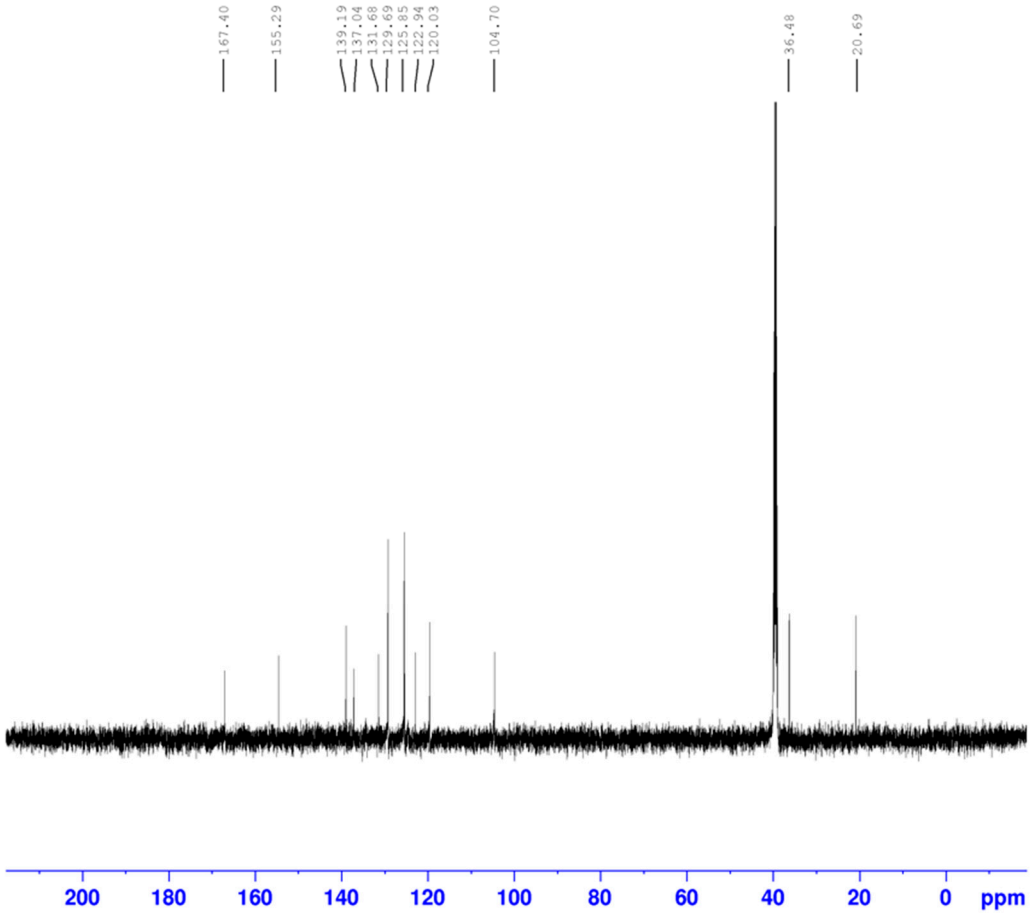


Figure S29. ^{13}C NMR Spectrum of compound **7**

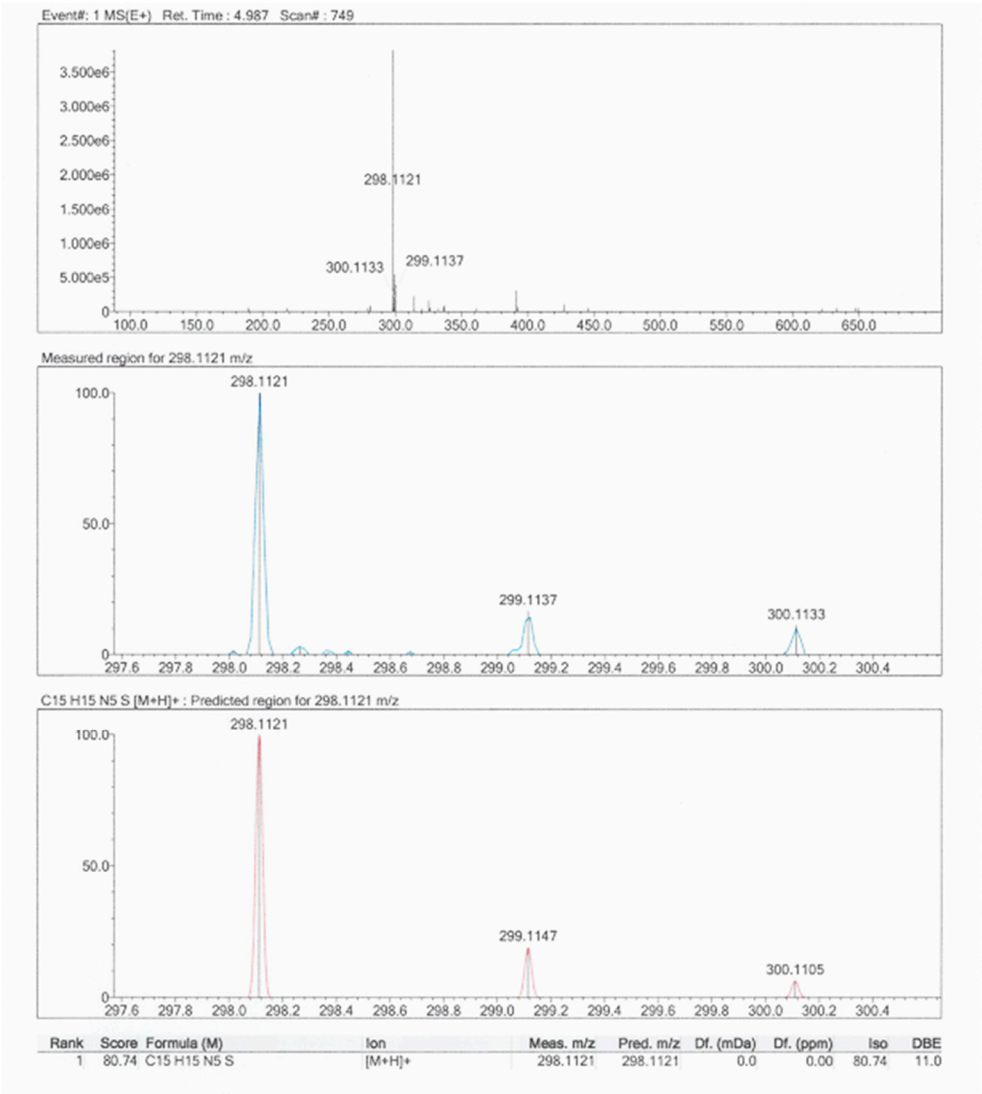


Figure S30. Mass Spectrum of compound **7**

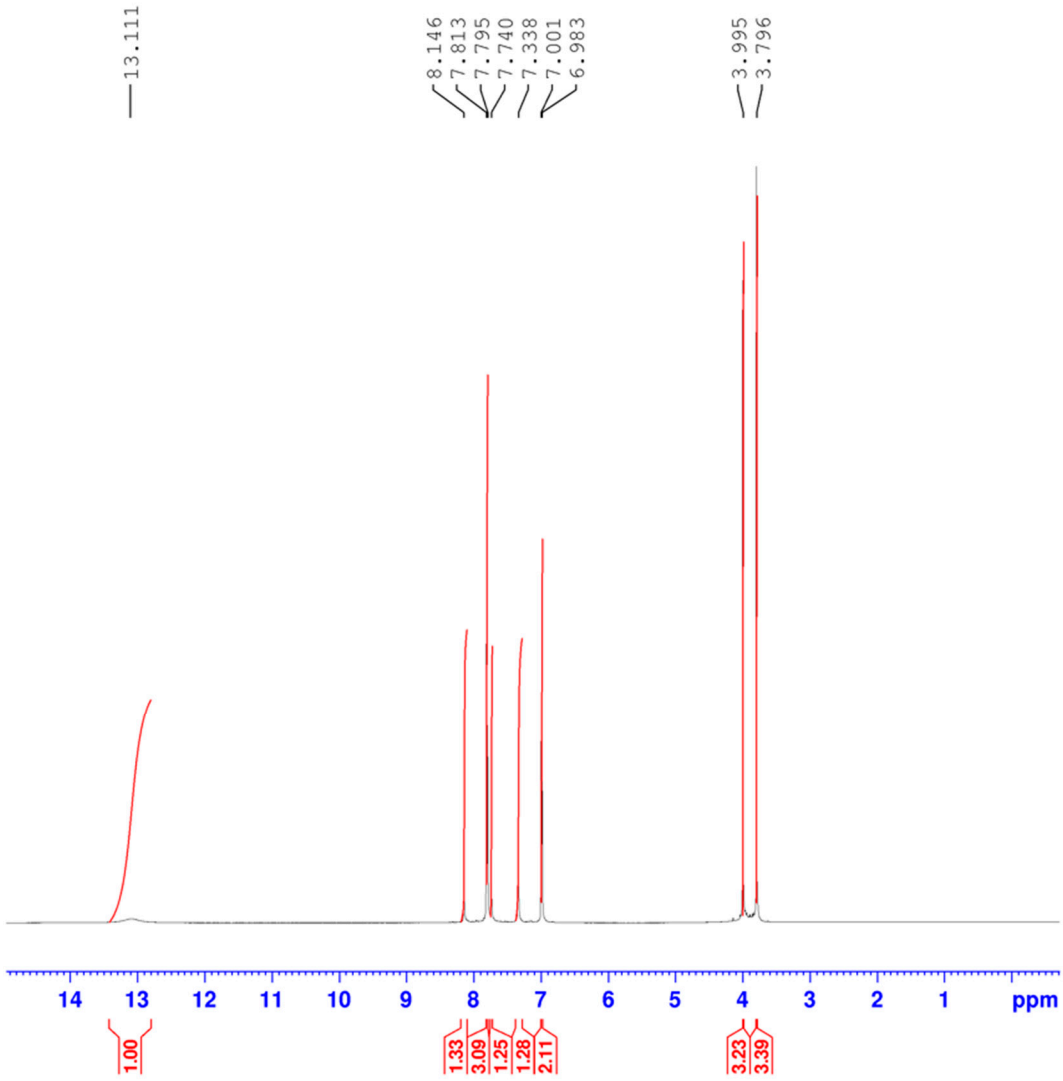


Figure S31. ^{1}H NMR Spectrum of compound **8** (0-15 ppm)

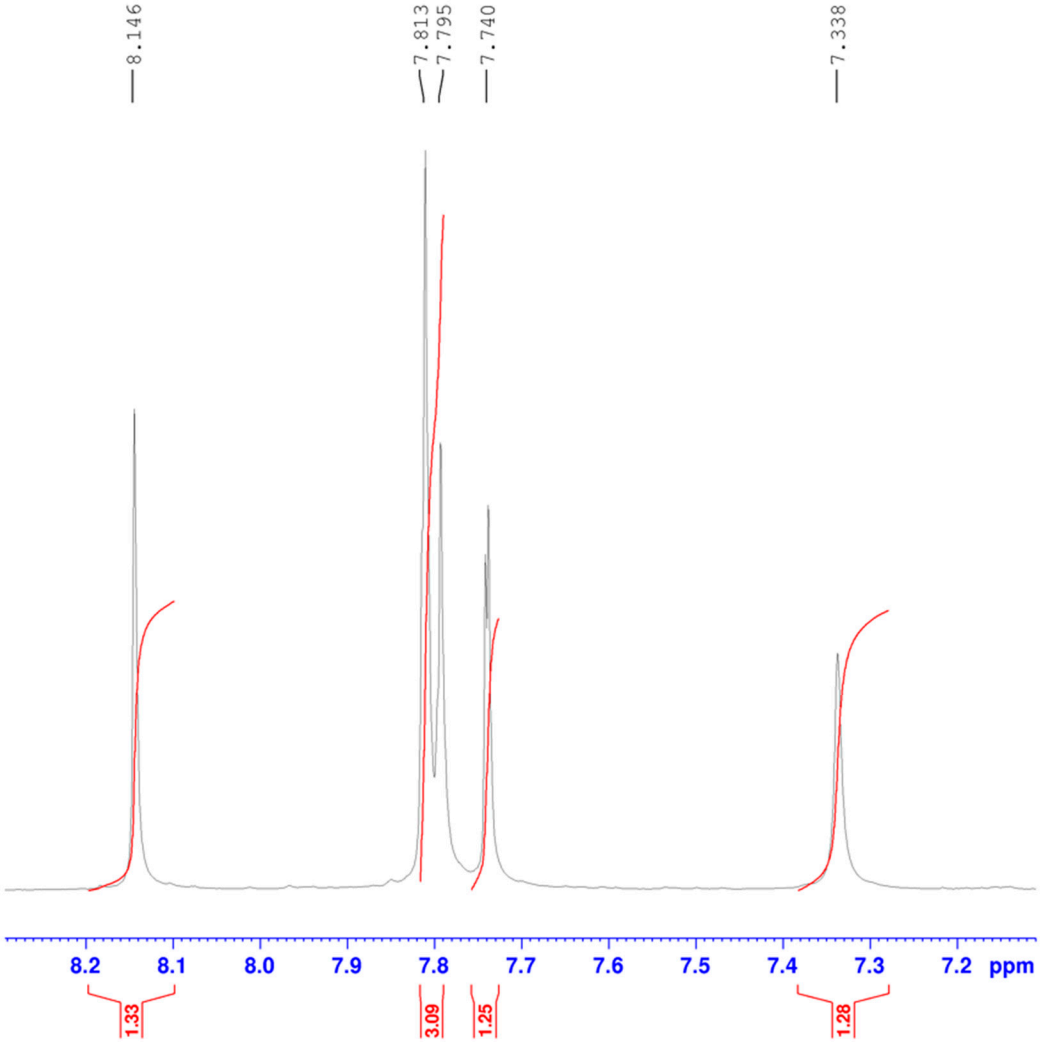


Figure S32. ^{1}H NMR Spectrum of compound **8** (7-9 ppm)

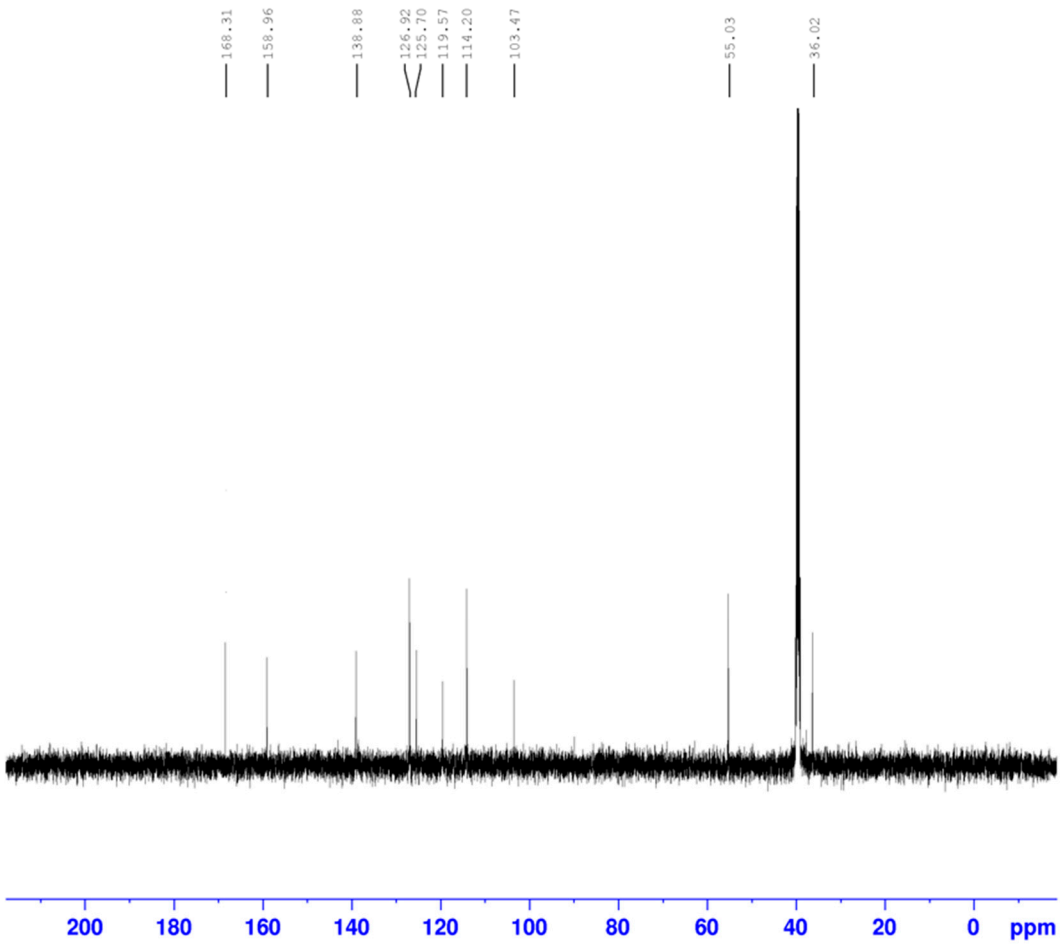


Figure S33. ^{13}C NMR Spectrum of compound **8**

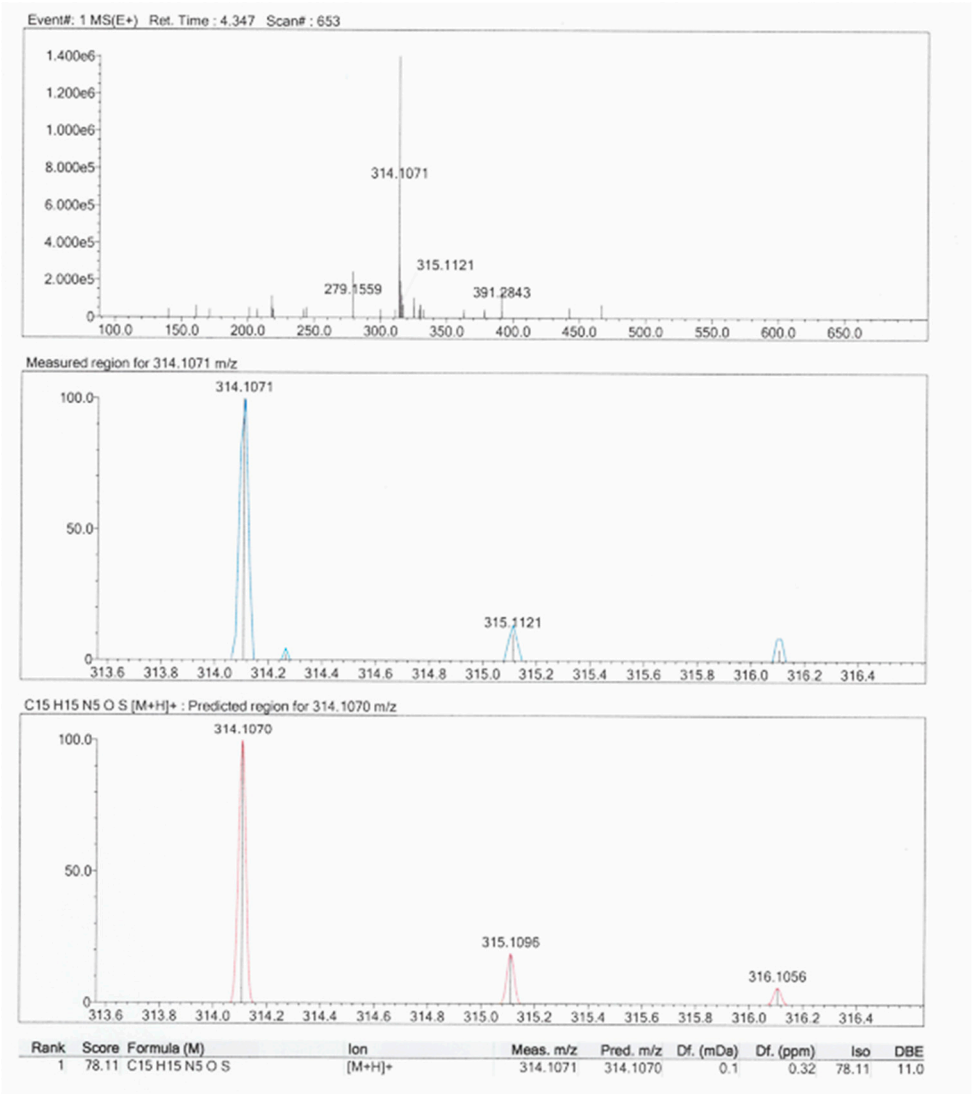


Figure S34. Mass Spectrum of compound **8**

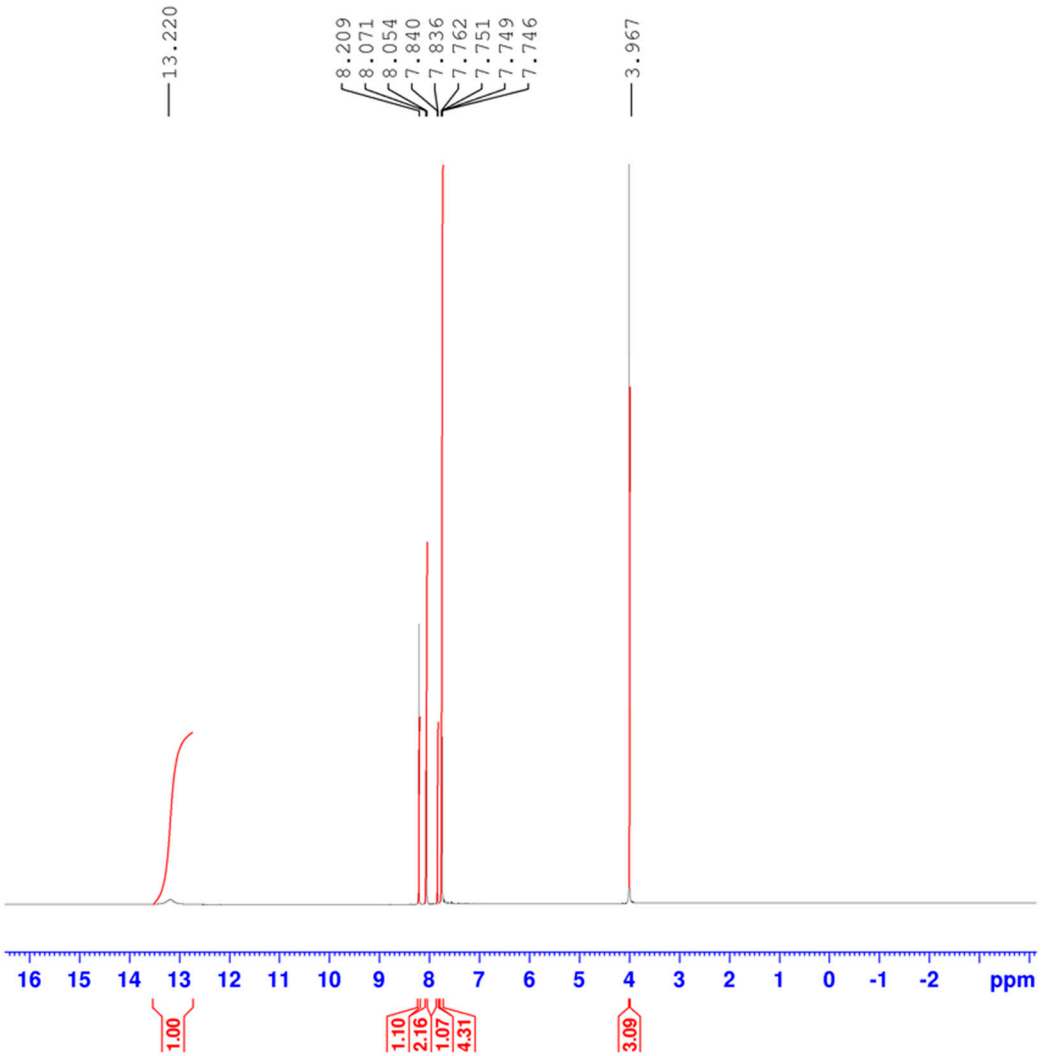


Figure S35. ^{1}H NMR Spectrum of compound **9** (0-15 ppm)

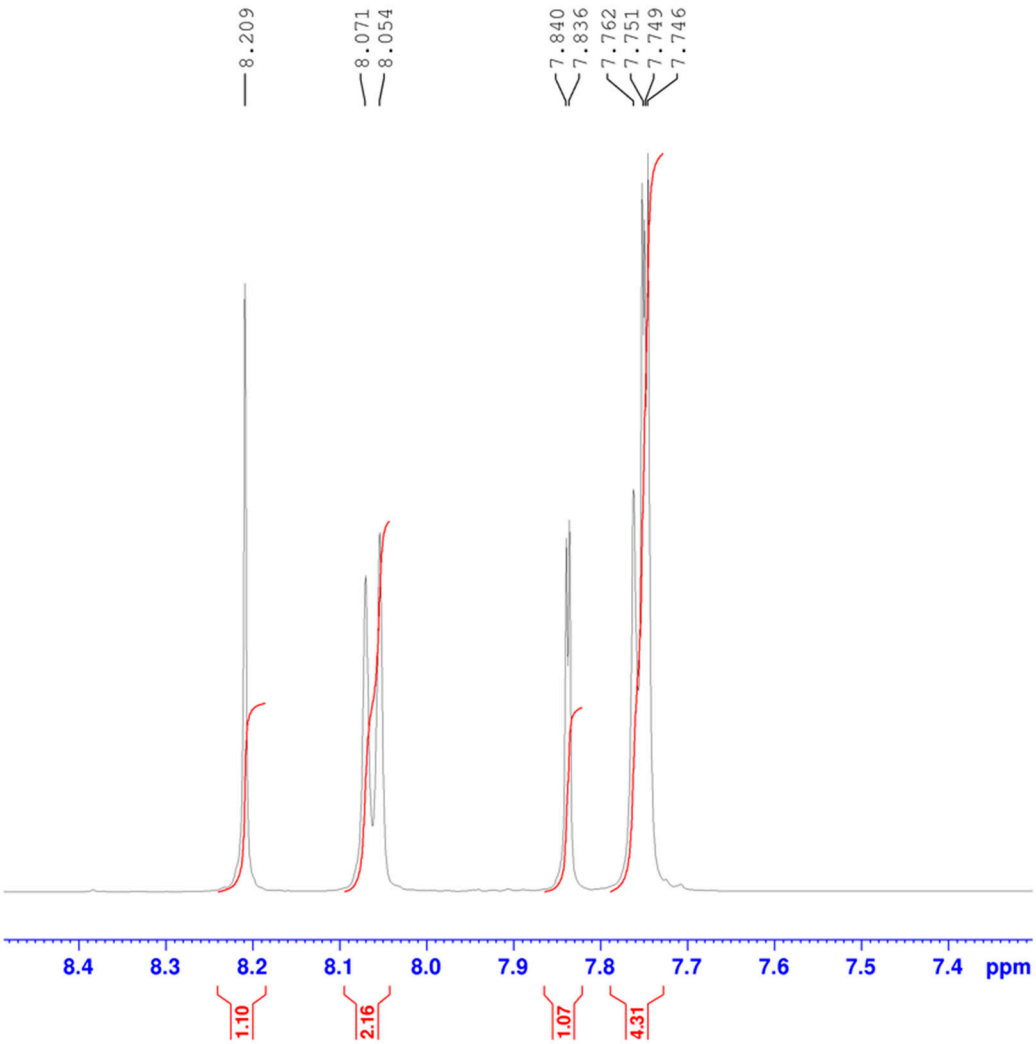


Figure S36. ^{1}H NMR Spectrum of compound **9** (7-9 ppm)

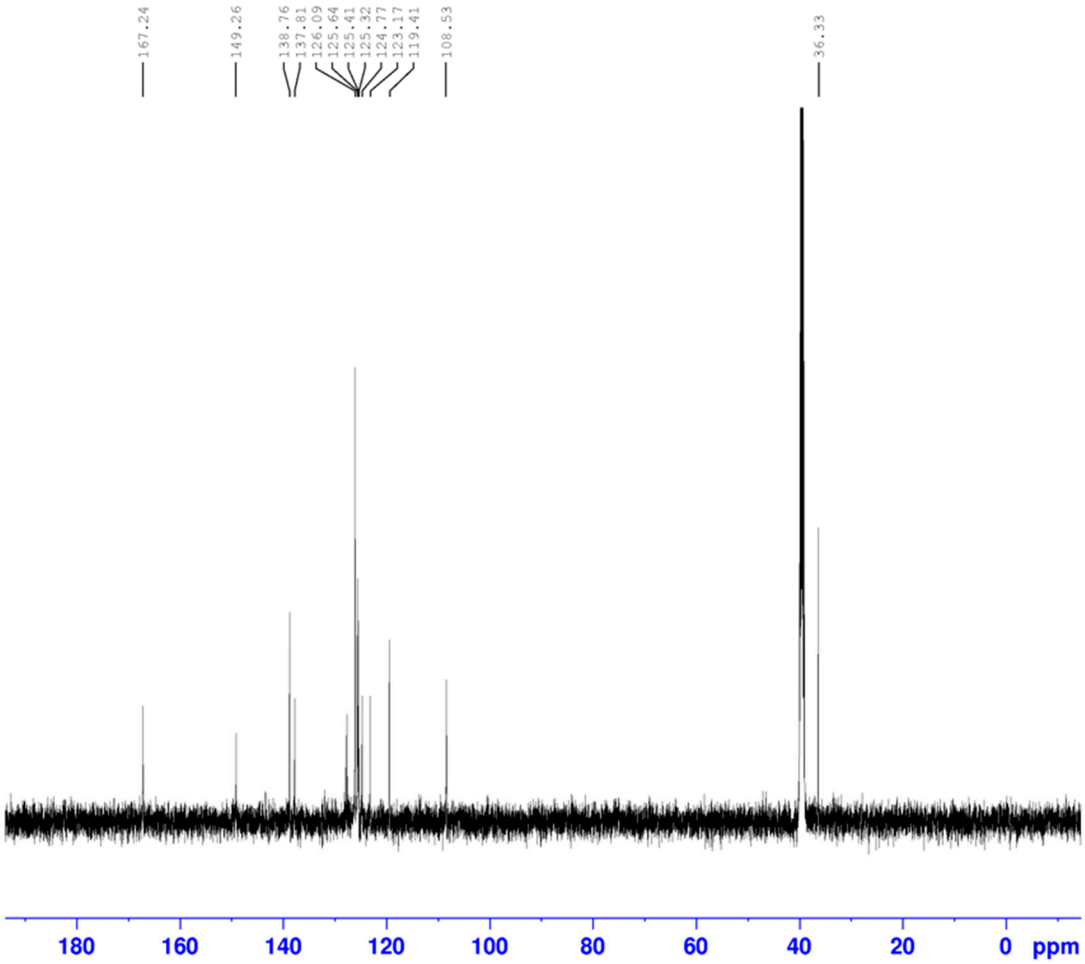


Figure S37. ^{13}C NMR Spectrum of compound **9**

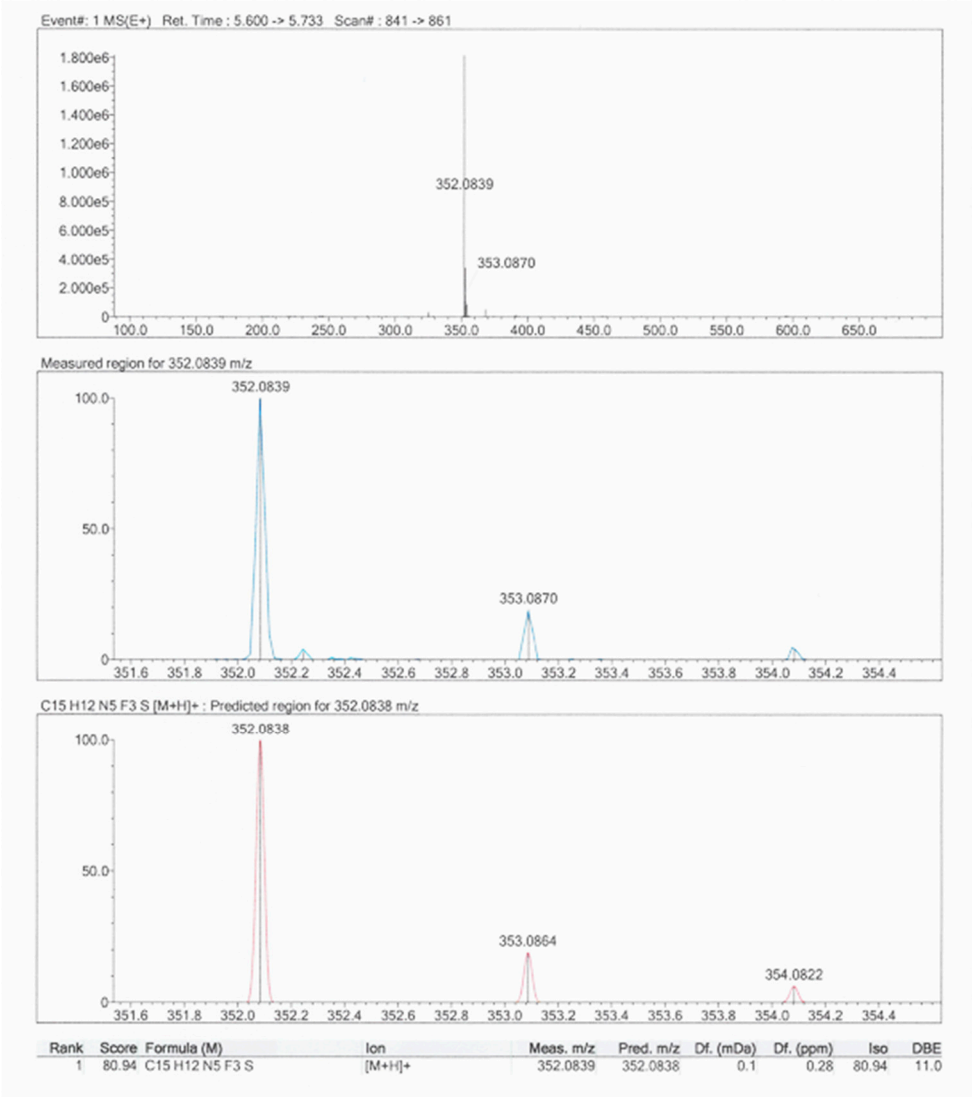


Figure S38. Mass Spectrum of compound **9**

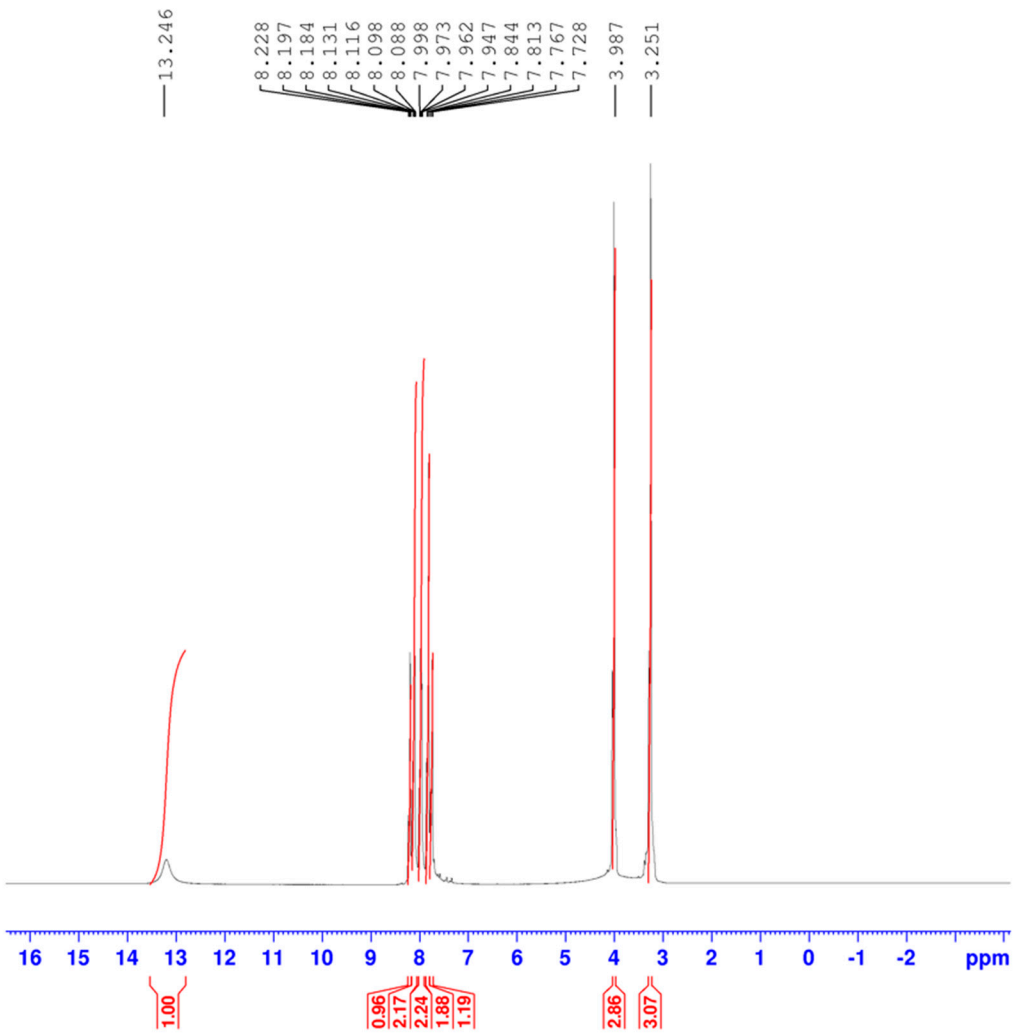


Figure S39: ^{1}H NMR Spectrum of compound **10** (0-15 ppm)

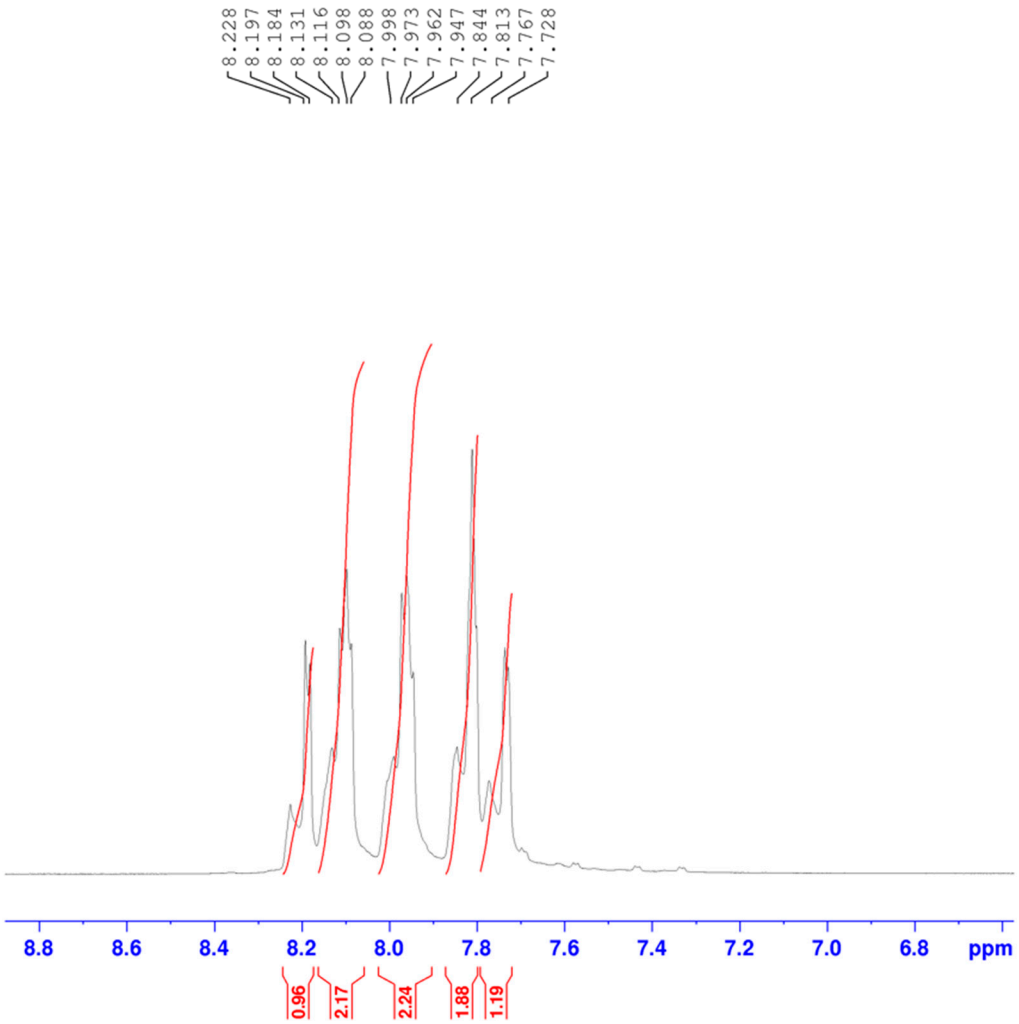


Figure S40: ^{1}H NMR Spectrum of compound **10** (7-9 ppm)

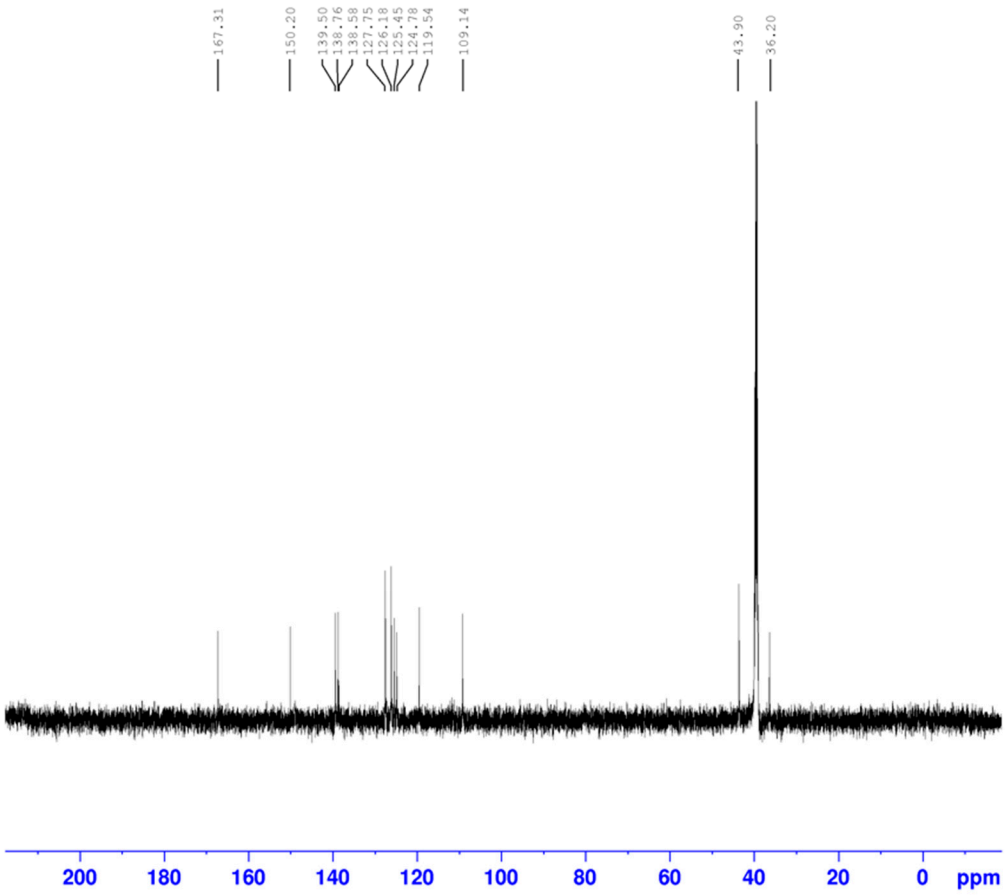


Figure S41. ^{13}C NMR Spectrum of compound **10**

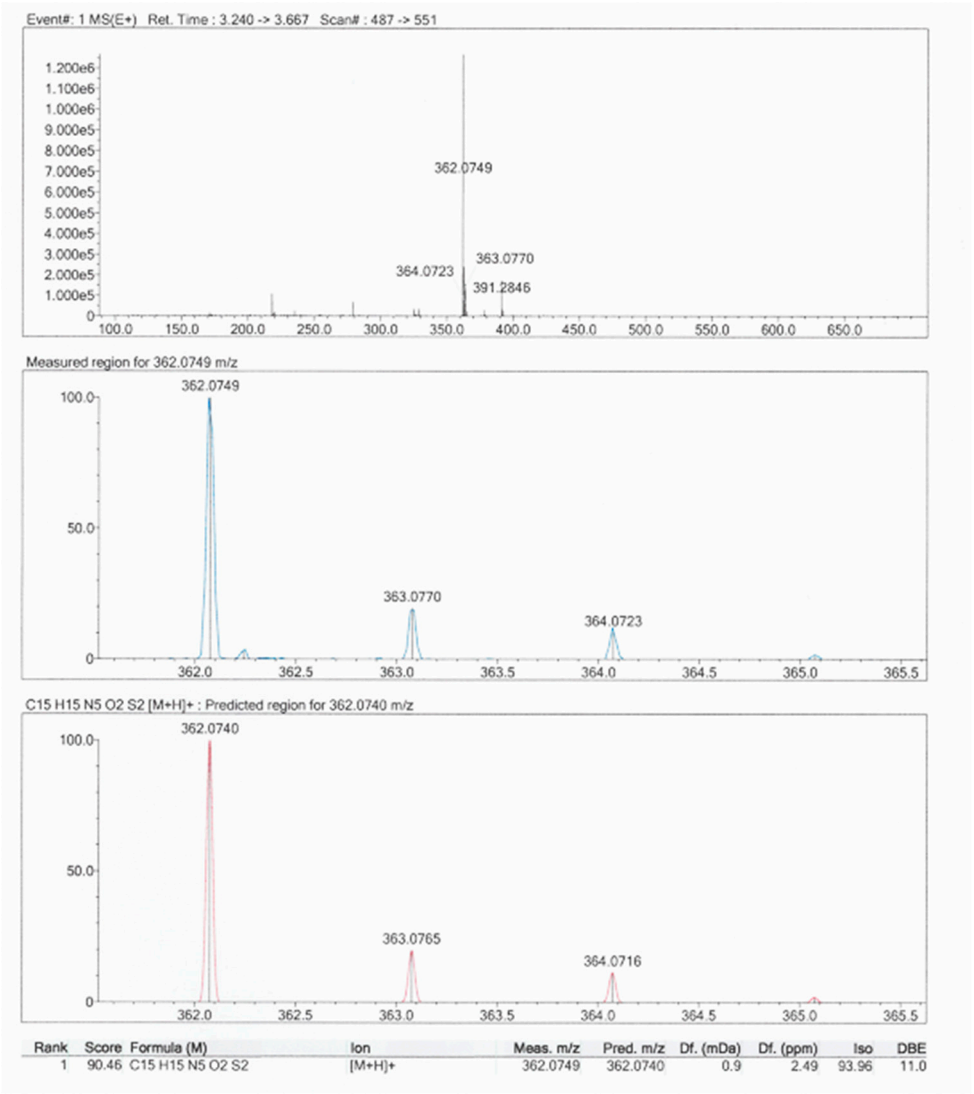


Figure S42. Mass Spectrum of compound **10**

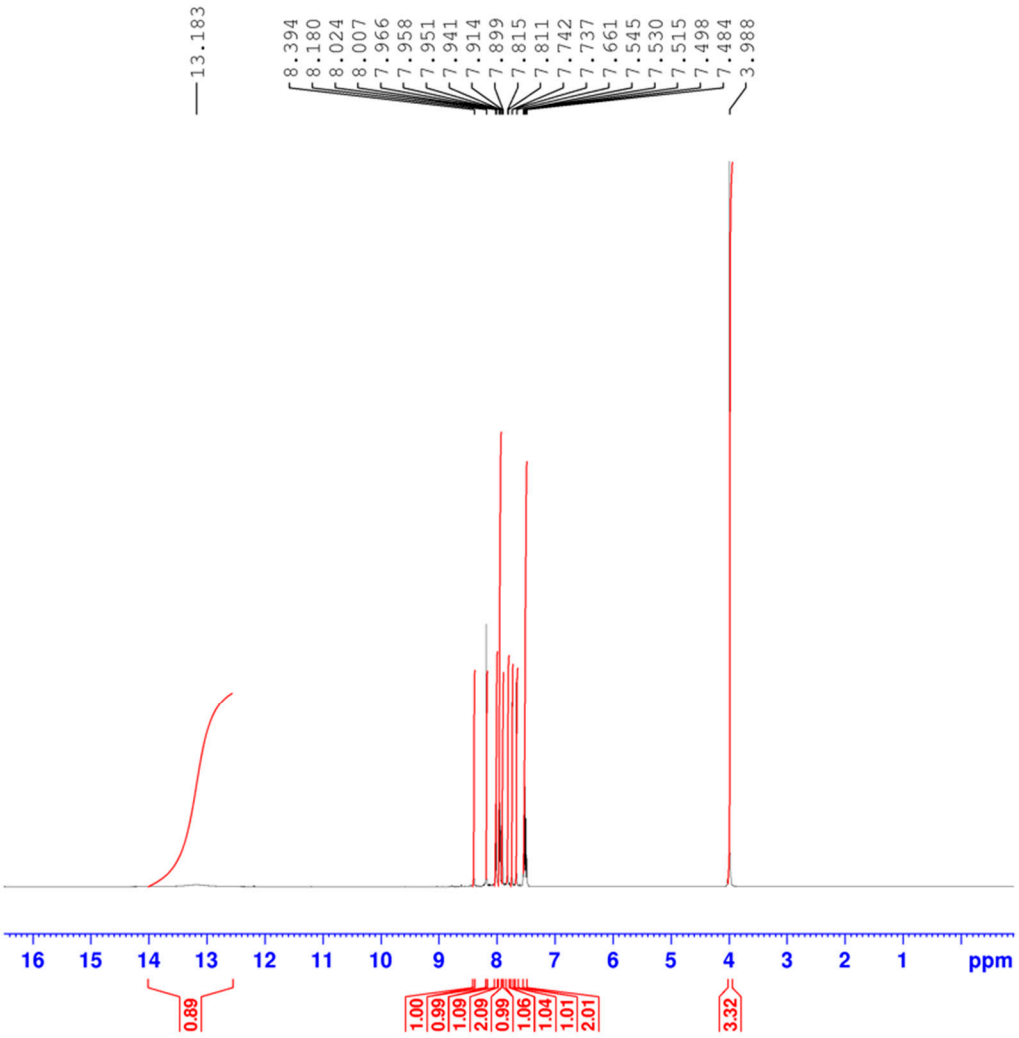


Figure S43. ^{1}H NMR Spectrum of compound **11** (0-15 ppm)

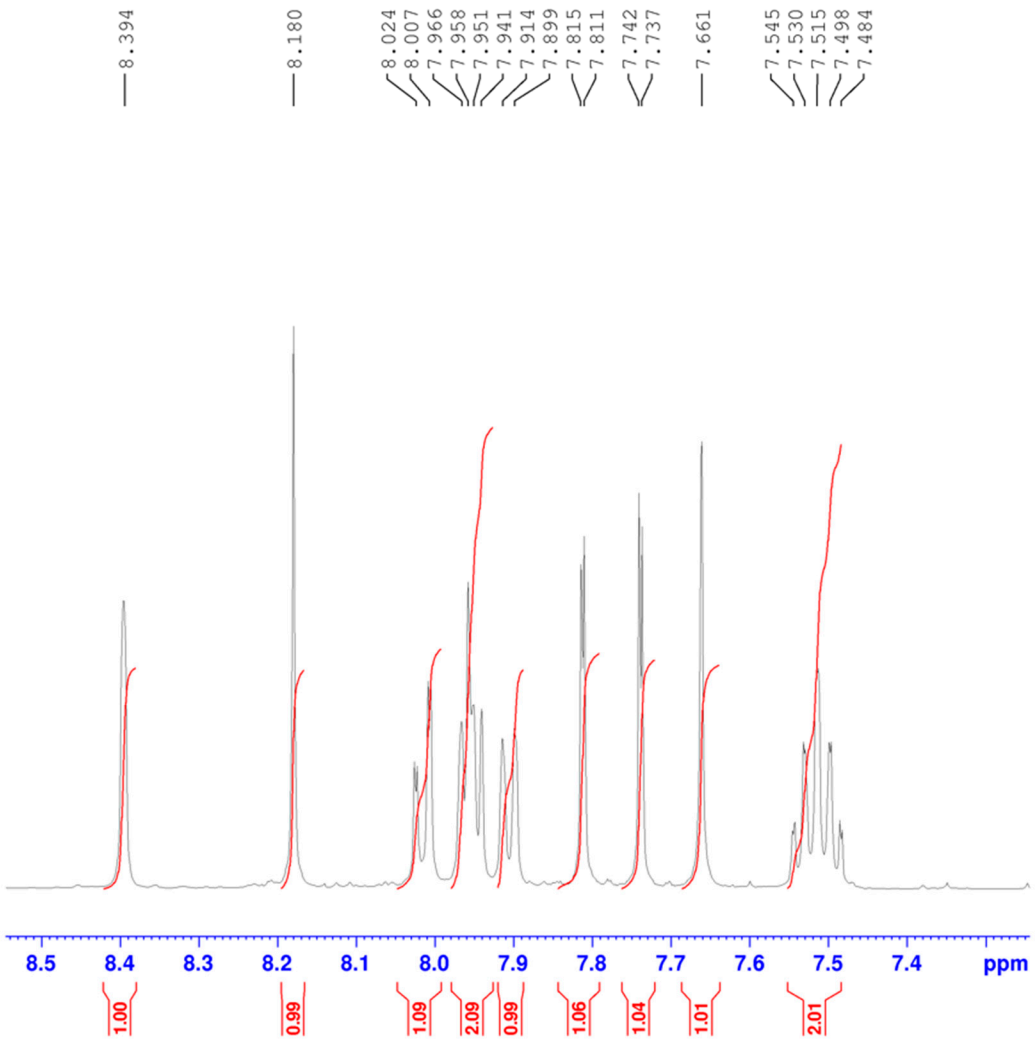


Figure S44. ^{1}H NMR Spectrum of compound **11** (7-9 ppm)

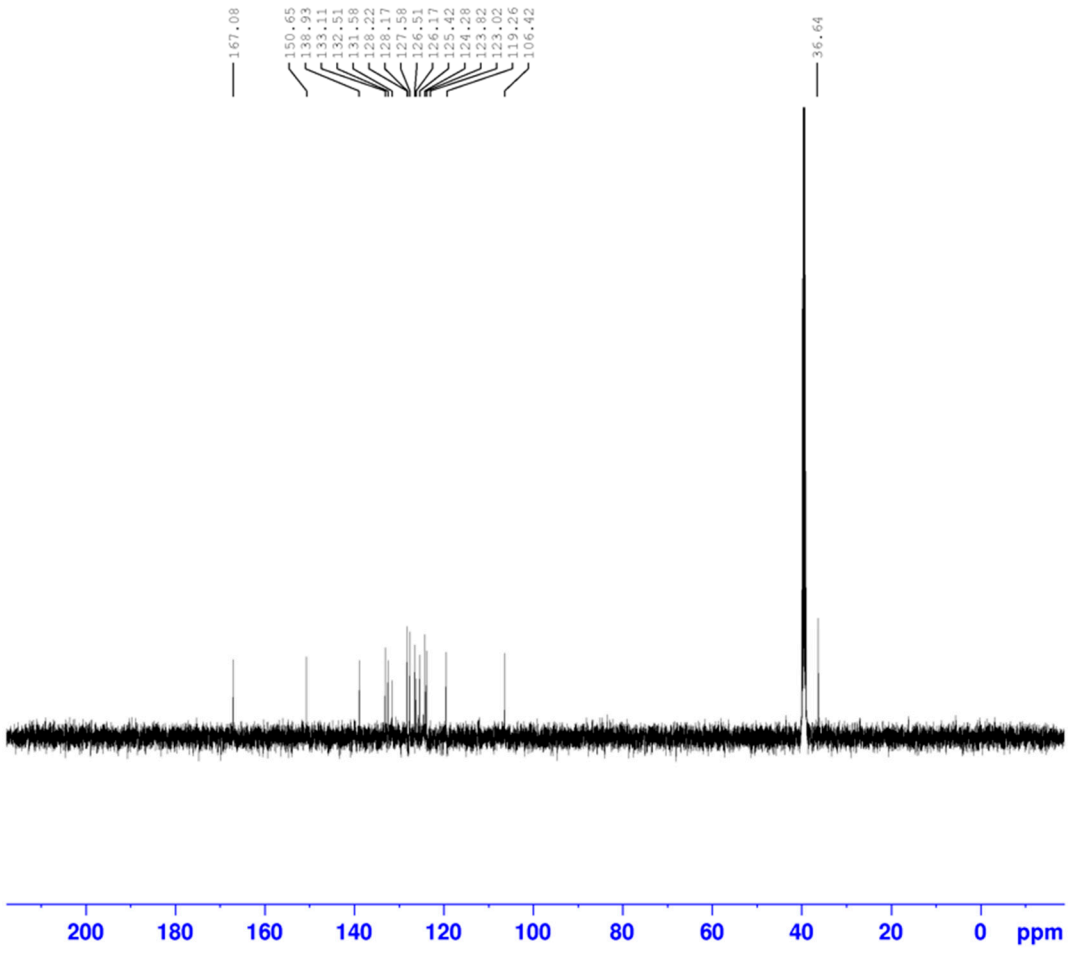


Figure S45. ^{13}C NMR Spectrum of compound **11**

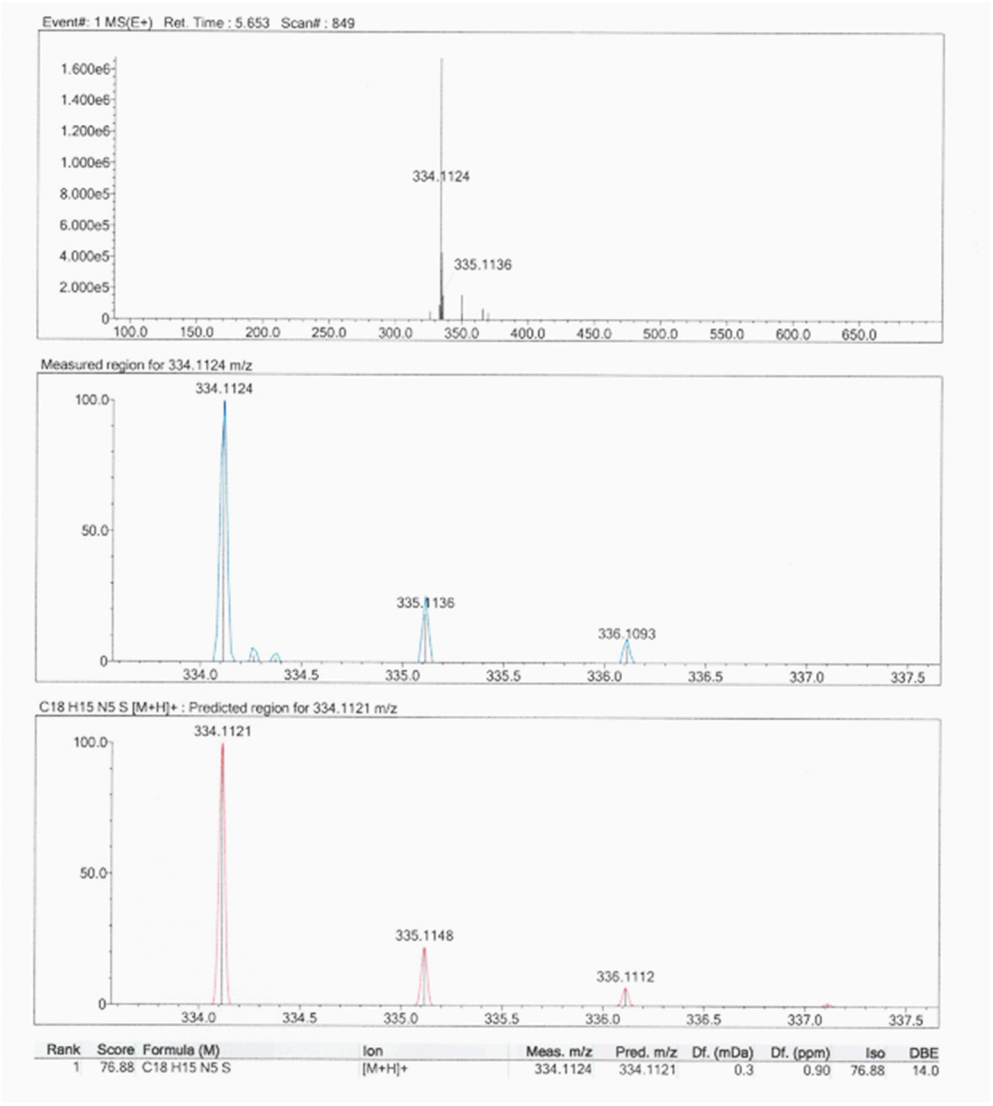


Figure S46. Mass Spectrum of compound **11**

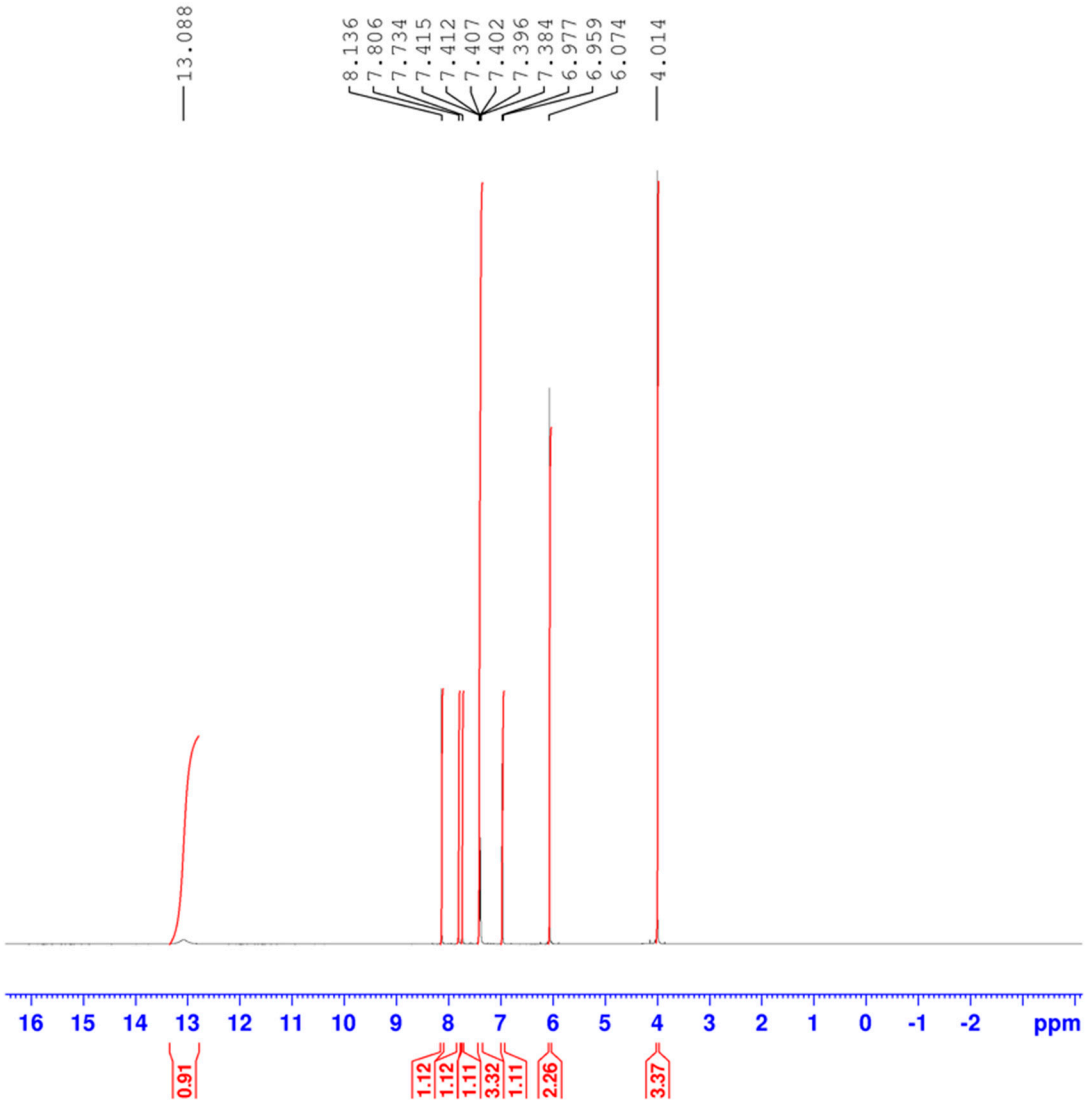


Figure S47. ^{1}H NMR Spectrum of compound **12** (0-15 ppm)

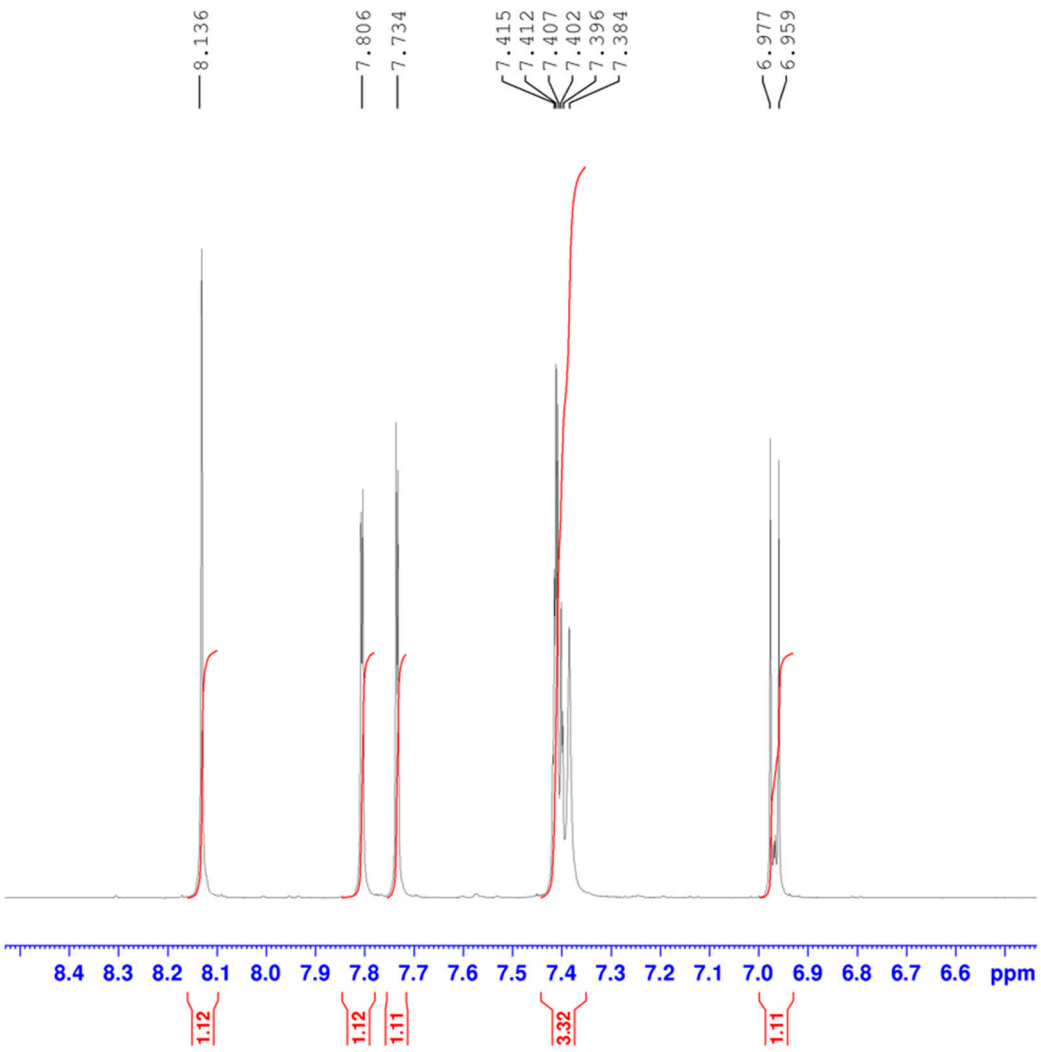


Figure S48. ^{1}H NMR Spectrum of compound **12** (7-9 ppm)

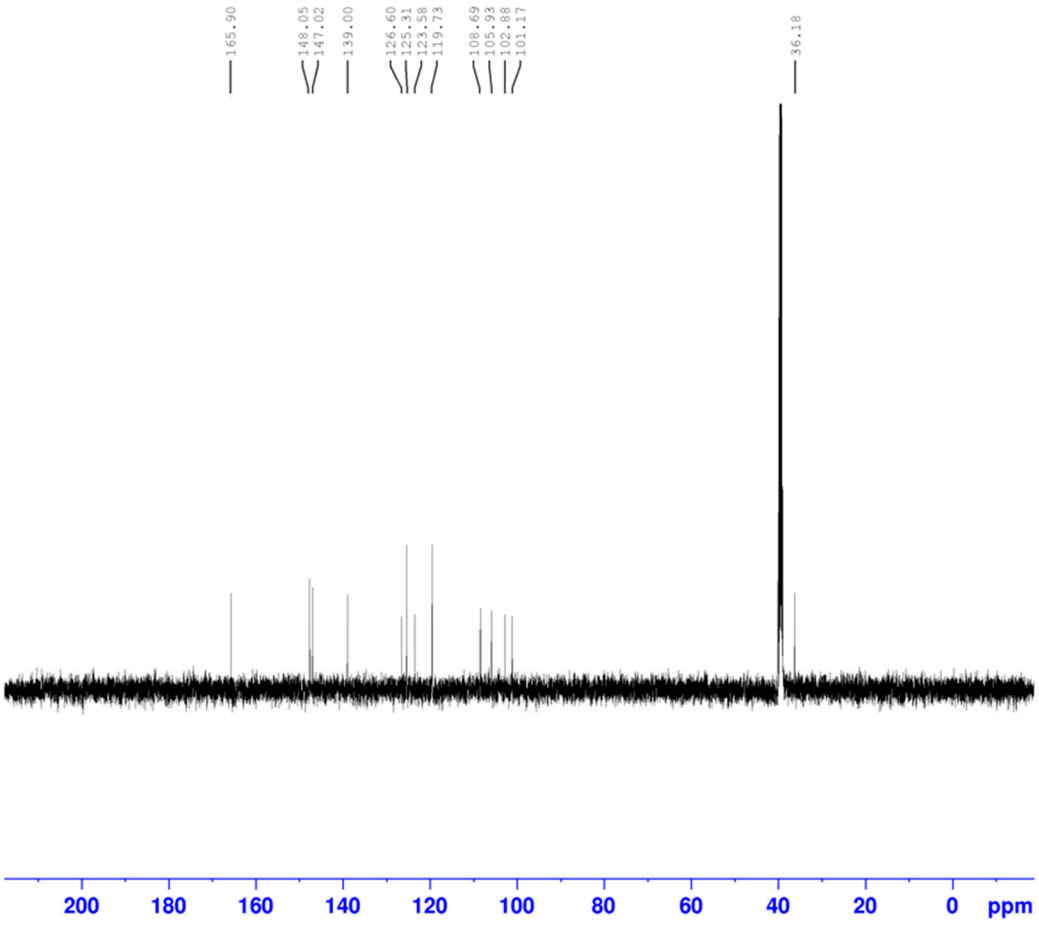


Figure S49. ^{13}C NMR Spectrum of compound **12**

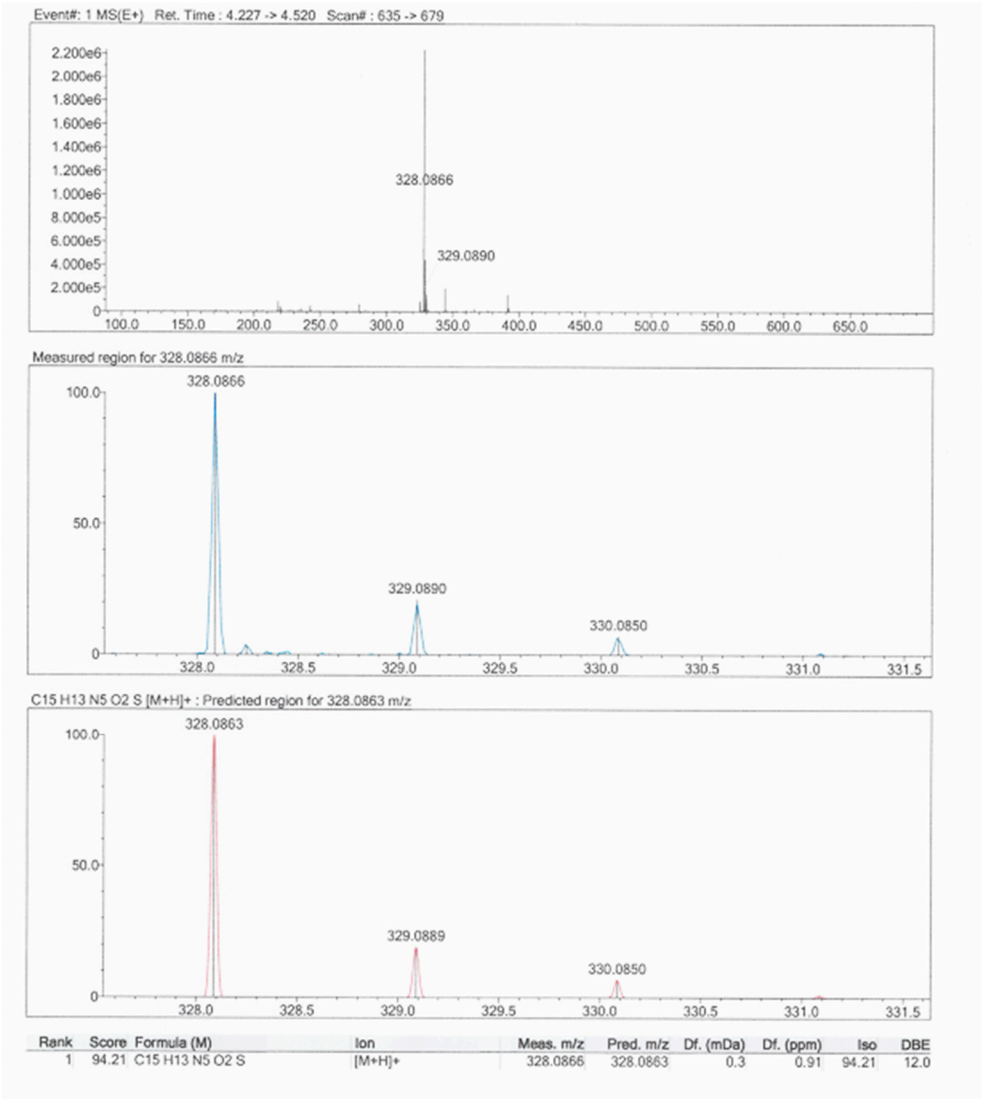


Figure S50. Mass Spectrum of compound **12**

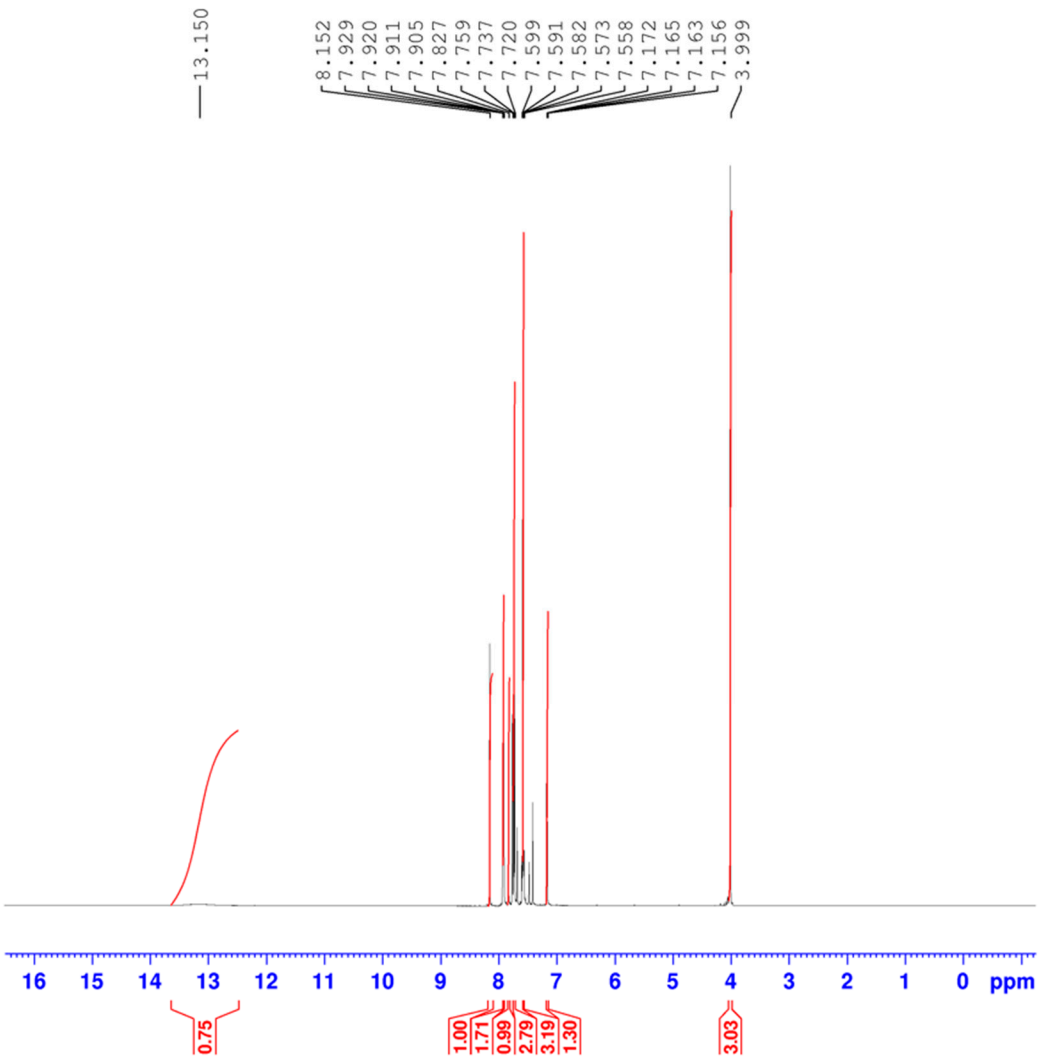


Figure S51. ^{1}H NMR Spectrum of compound **13** (0-15 ppm)

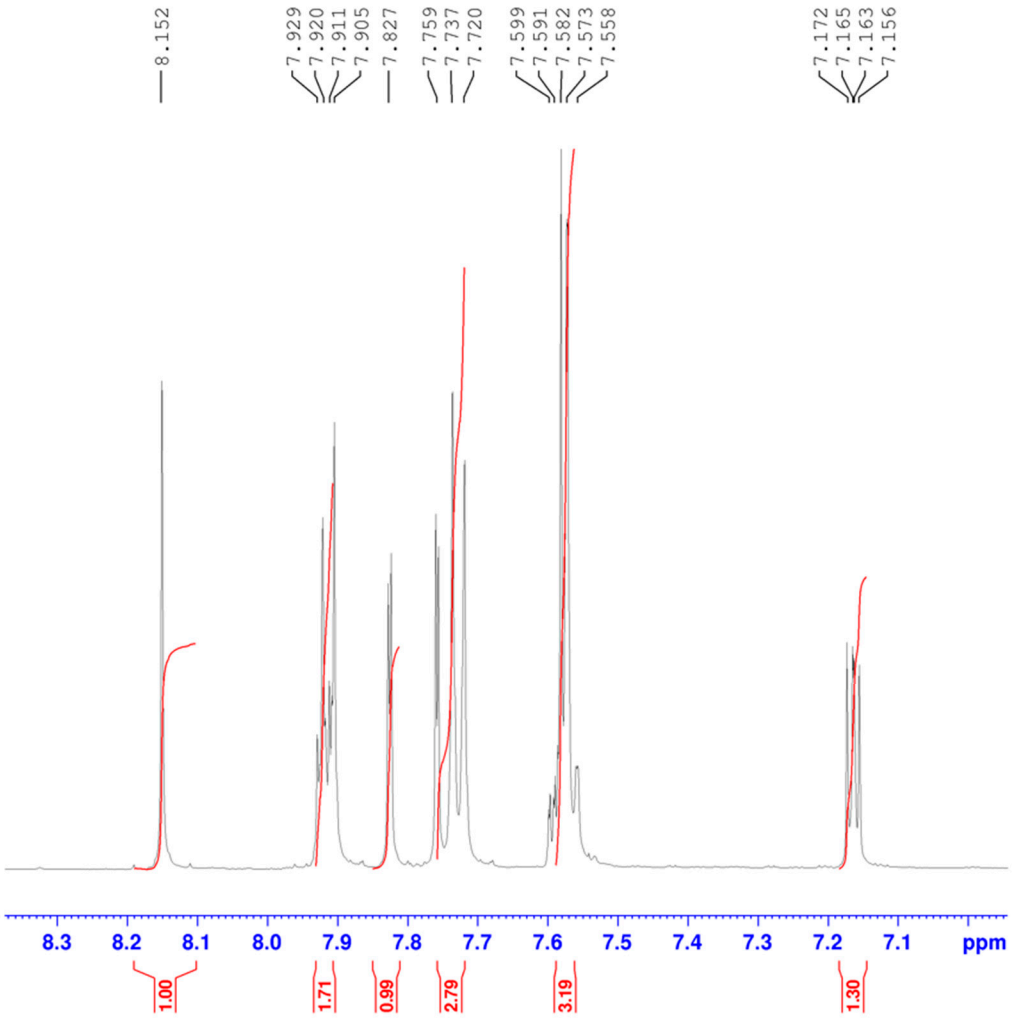


Figure S52. ^{1}H NMR Spectrum of compound **13** (7-9 ppm)

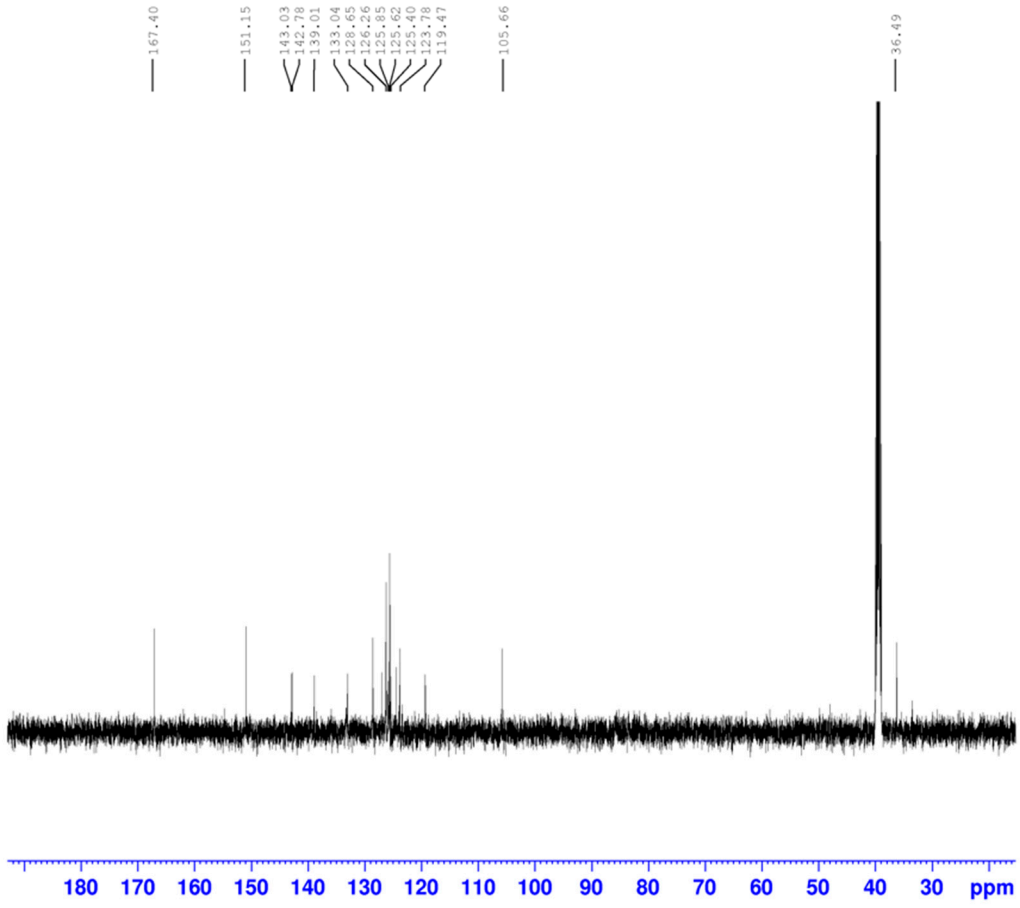


Figure S53. ^{13}C NMR Spectrum of compound **13**

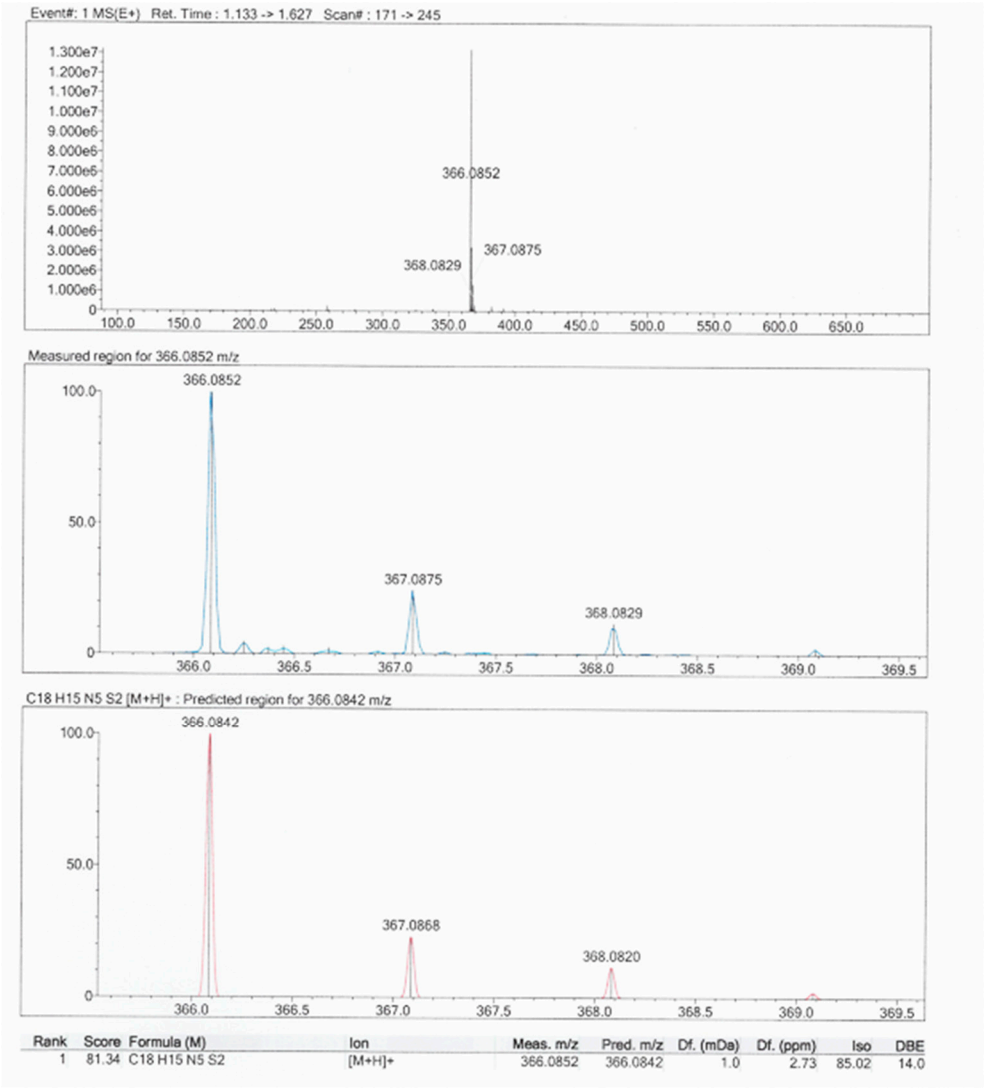


Figure S54. Mass Spectrum of compound **13**

Table S1. Prime MM-GBSA binding free energy (ΔG_{bind}) and energetic decomposition (kcal/mol) at the EGFR and AR binding sites

EGFR								
Compound	**Coulomb**	**Covalent**	**Hbond**	**Lipo**	**Packing**	**$Solv_{GB}$**	**vdW**	**ΔG_{bind}**
5	-9.13	2.78	-1.13	-17.79	-0.88	31.25	-49.20	-44.10
13	-11.26	11.48	-0.15	-24.00	-0.65	34.89	-52.05	-41.75
Tak-285	-27.56	2.54	-2.32	-25.66	-0.26	39.36	-76.46	-90.38
AR								
Compound	**Coulomb**	**Covalent**	**Hbond**	**Lipo**	**Packing**	**$Solv_{GB}$**	**vdW**	**ΔG_{bind}**
5	-11.52	10.30	-1.25	-28.61	-8.50	53.02	-49.57	-35.76