Supplementary material

In Vitro and *In Silico* Evaluation of Anticancer Activity of New Indole-based 1,3,4-Oxadiazoles as EGFR and COX-2 Inhibitors

Belgin Sever [1,*], Mehlika Dilek Altıntop [1], Ahmet Özdemir [1], Gülşen Akalın Çiftçi [2], Doha E. Ellakwa [3], Hiroshi Tateishi [4], Mohamed O. Radwan [4,5,6], Mahmoud A. A. Ibrahim[7], Masami Otsuka [4,5], Mikako Fujita [4,*], Halil I. Ciftci [4,5,*], Taha F.S. Ali [4,8]

[1] Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Anadolu University, Eskişehir 26470, Turkey; mdaltintop@anadolu.edu.tr (M.D.A.); ahmeto@anadolu.edu.tr (A.Ö.)
[2] Department of Biochemistry, Faculty of Pharmacy, Anadolu University, Eskişehir 26470, Turkey; gakalin@anadolu.edu.tr (G.A.Ç.)
[3] Department of Biochemistry and Molecular Biology, Faculty of Pharmacy, Al-Azhar University, Cairo 11765, Egypt; profdoha@gmail.com (D.E.E.)
[4] Medicinal and Biological Chemistry Science Farm Joint Research Laboratory, School of Pharmacy, Kumamoto University, Kumamoto 862-0973, Japan; htateishi@kumamoto-u.ac.jp (H.T.); mohamedradwan@kumamoto-u.ac.jp (M.O.R.); motsuka@gpo.kumamoto-u.ac.jp (M.O.); tahafaroukali@gmail.com (T.F.S.A.)
[5] Department of Drug Discovery, Science Farm Ltd., Kumamoto 862-0976, Japan
[6] Chemistry of Natural Compounds Department, Pharmaceutical and Drug Industries Research Division, National Research Centre, Dokki, Cairo 12622, Egypt
[7] Computational Chemistry Laboratory, Chemistry Department, Faculty of Science, Minia University, Minia 61519, Egypt; m.ibrahim@compchem.net (M.A.A.I.)
[8] Medicinal Chemistry Department, Faculty of Pharmacy, Minia University, Minia 61519, Egypt
* Correspondence: belginsever@anadolu.edu.tr (B.S.); mfujita@kumamoto-u.ac.jp (M.F.); hiciftci@kumamoto-u.ac.jp (H.I.C.); Tel.: +90-222-335-0580 (ext. 3807)

Table of Contents

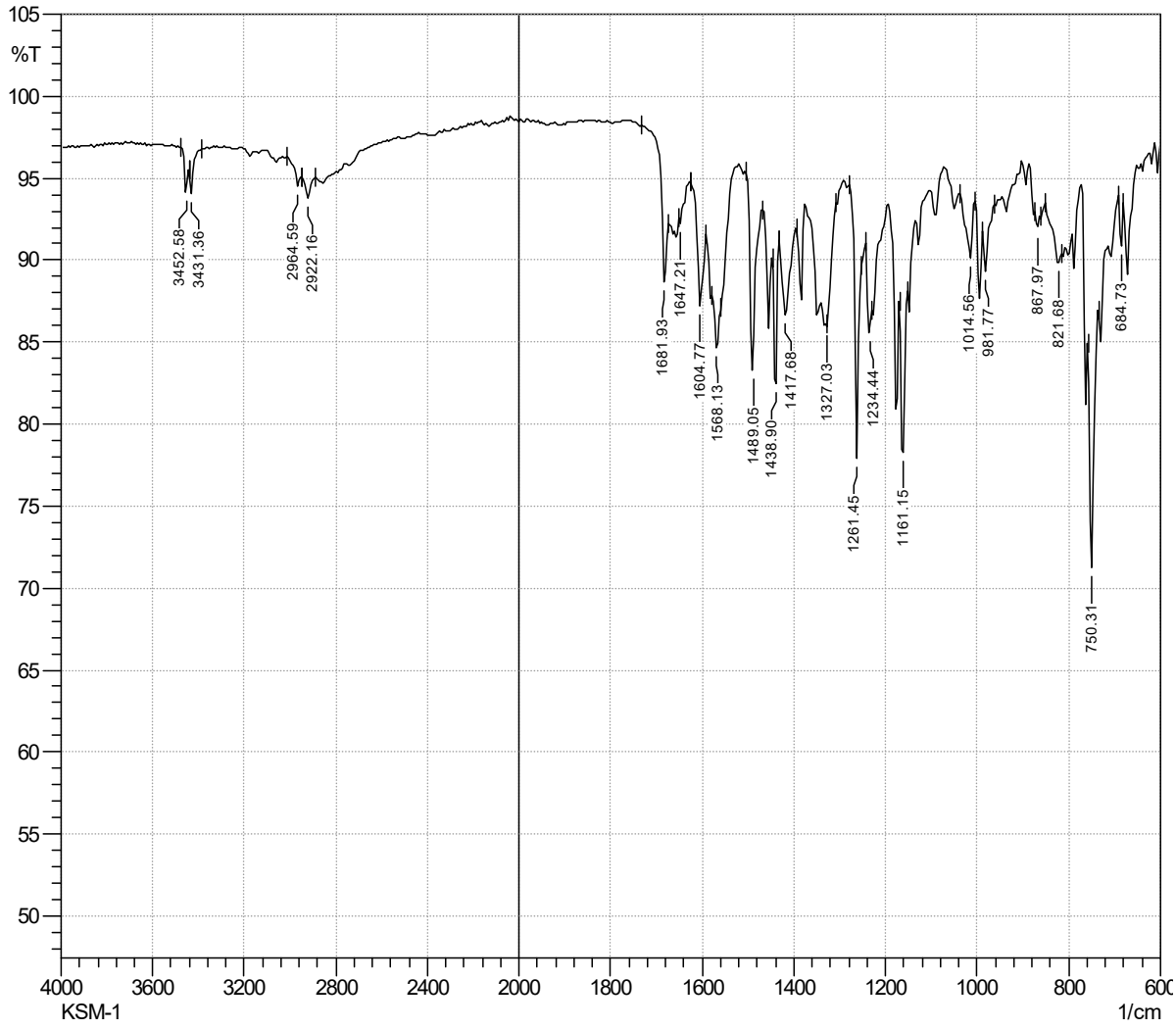


Figure S1. IR spectrum of compound **2a**.

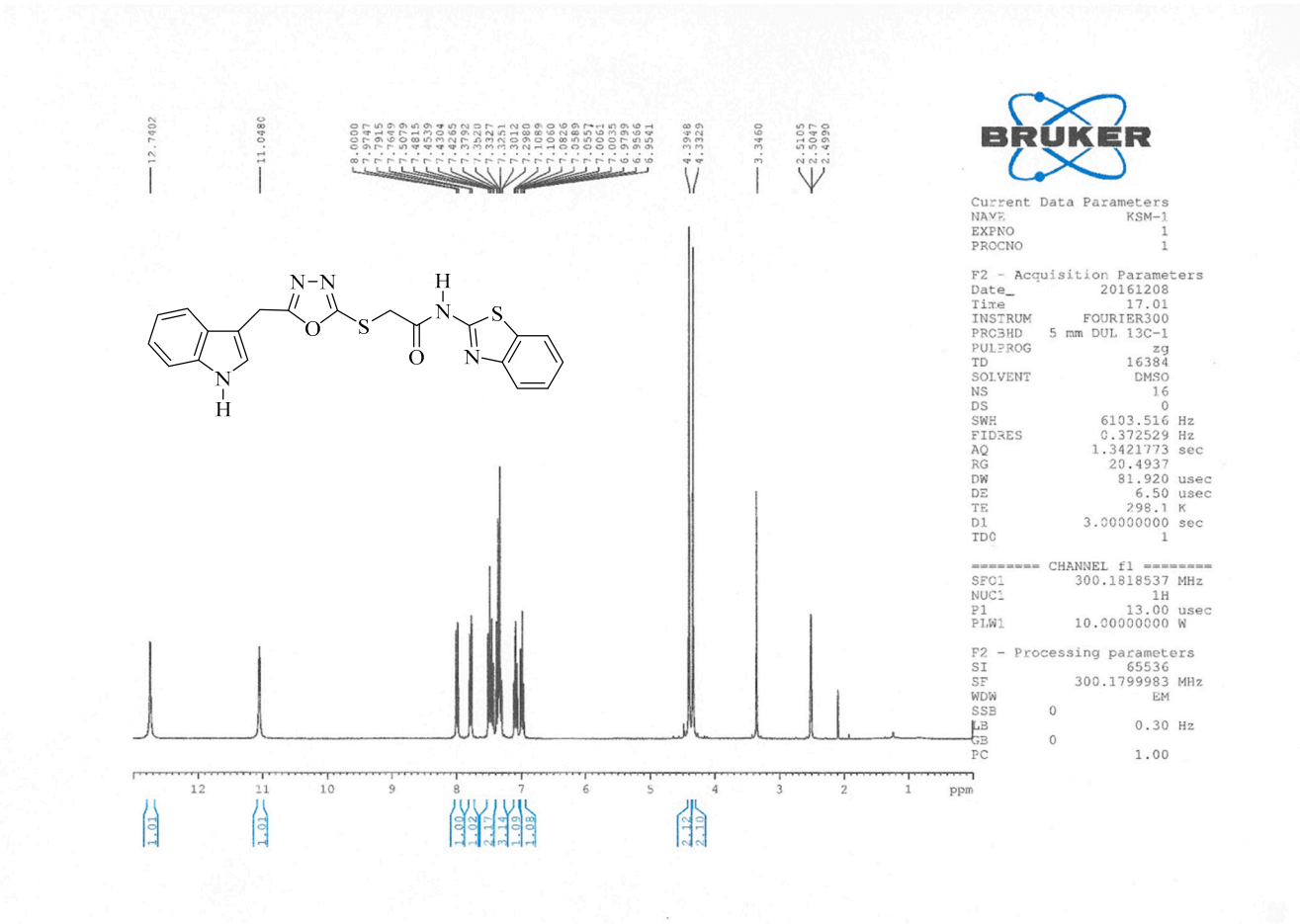


Figure S2. ^{1}H NMR spectrum of compound **2a**.

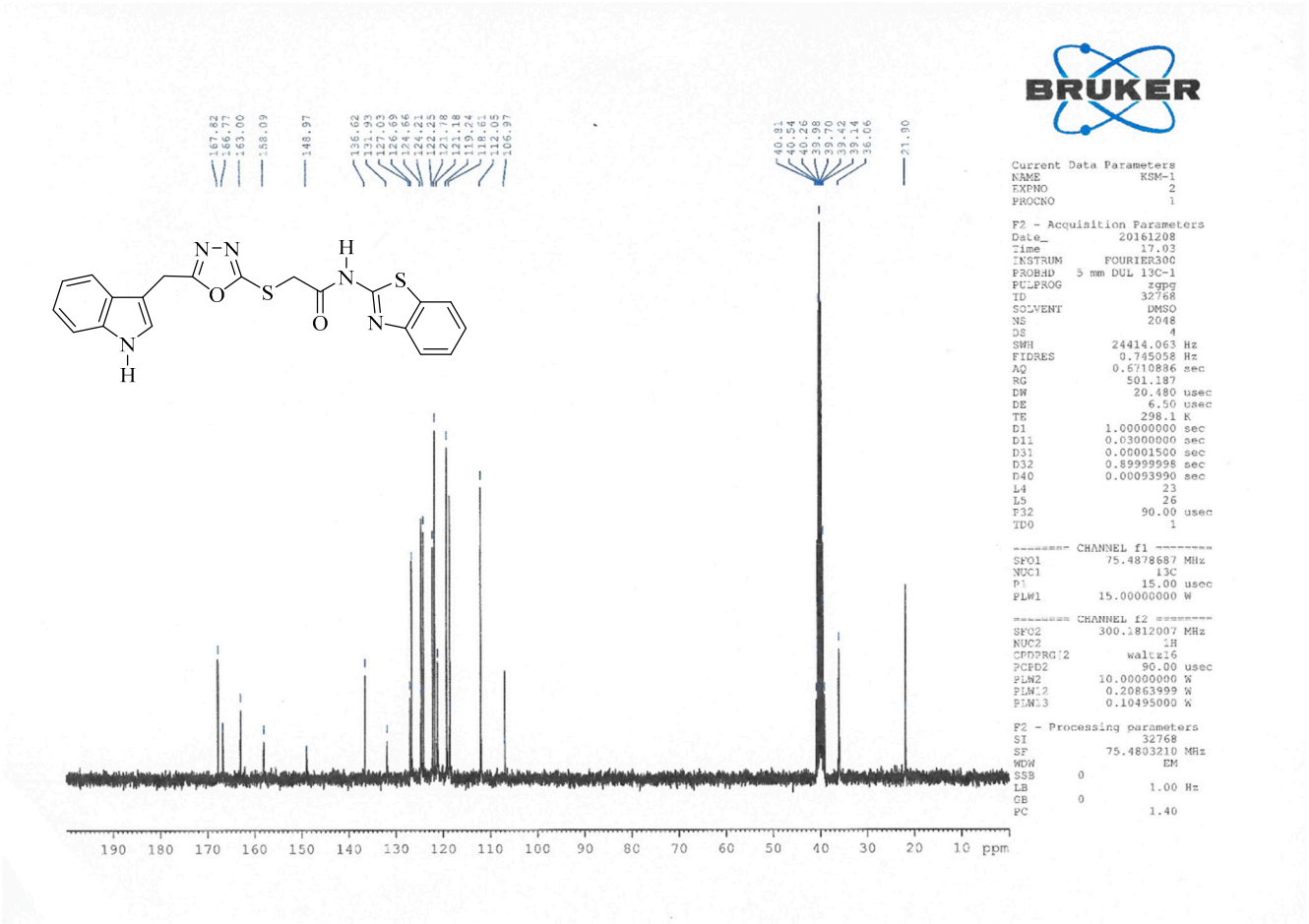


Figure S3. ^{13}C NMR spectrum of compound **2a**.

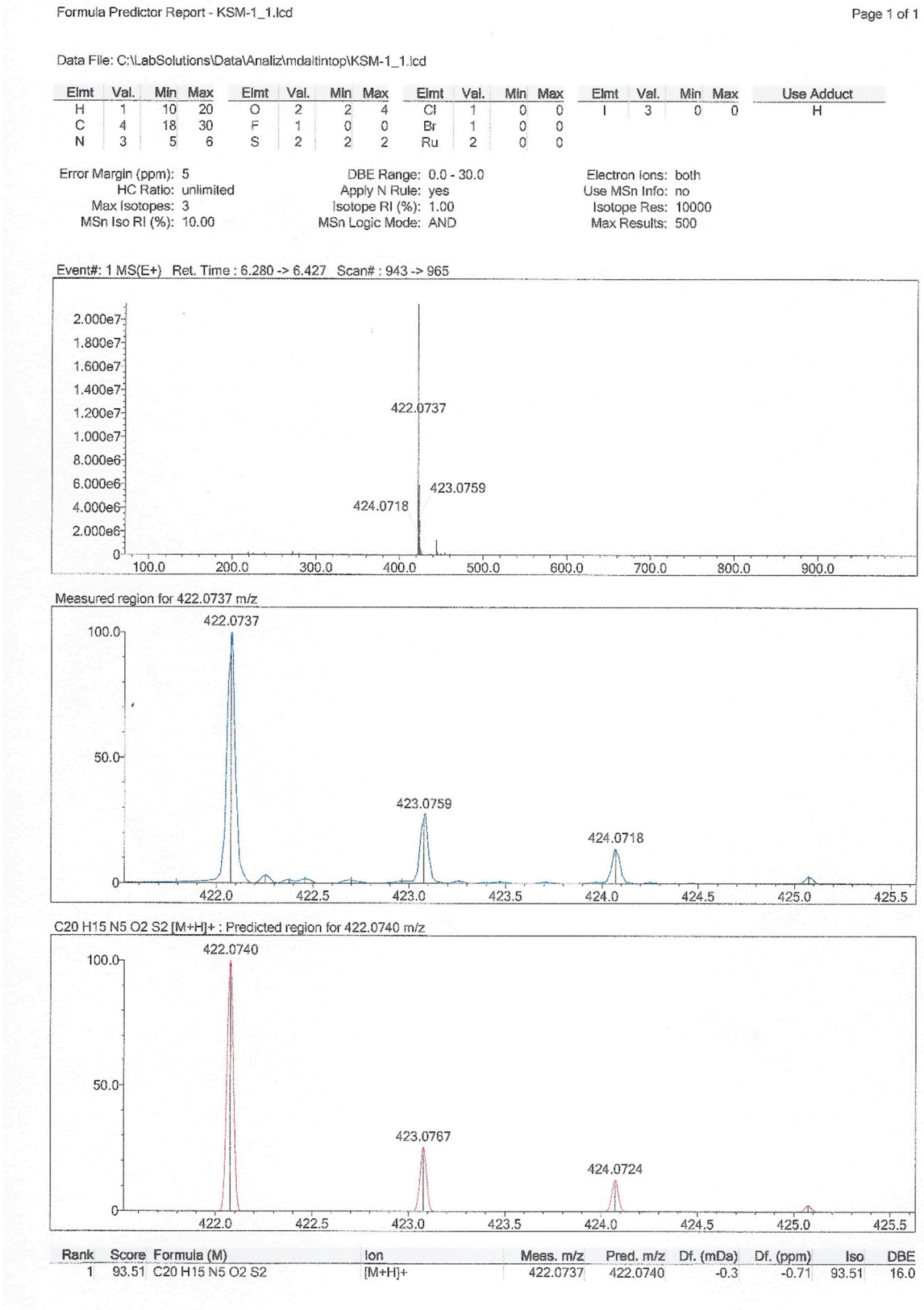


Figure S4. HRMS spectrum of compound **2a**.

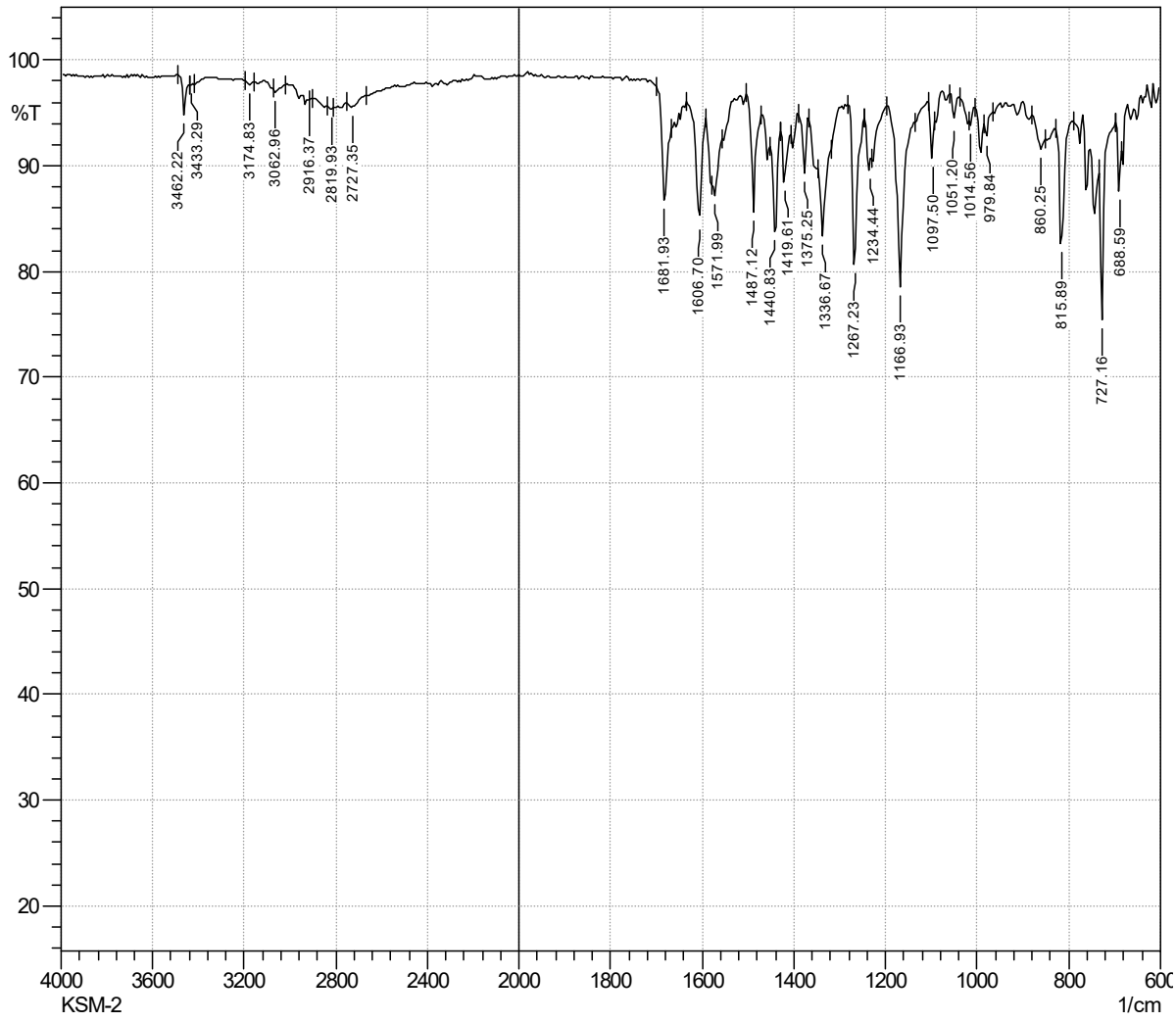


Figure S5. IR spectrum of compound **2b**.

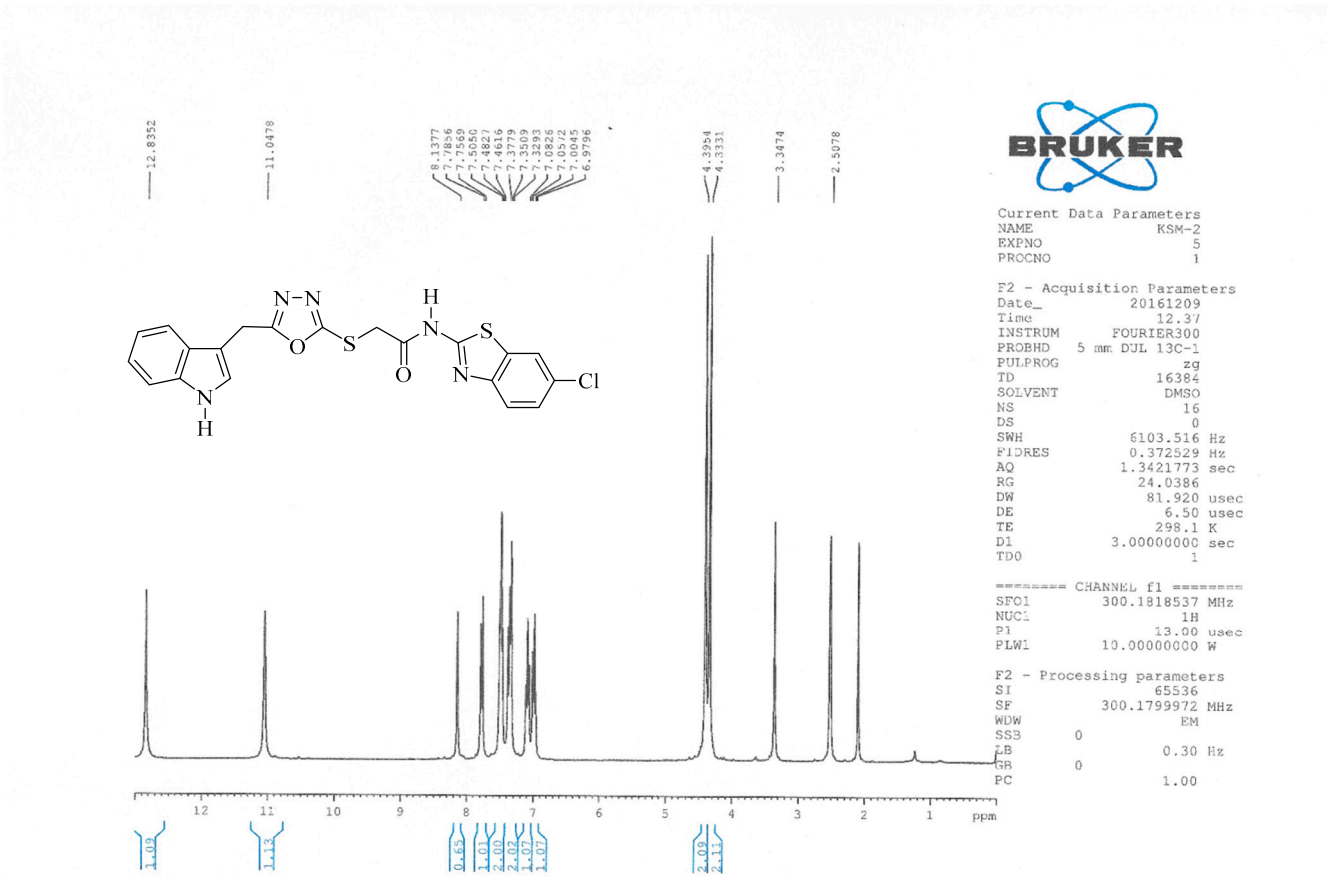


Figure S6. ^{1}H NMR spectrum of compound **2b**.

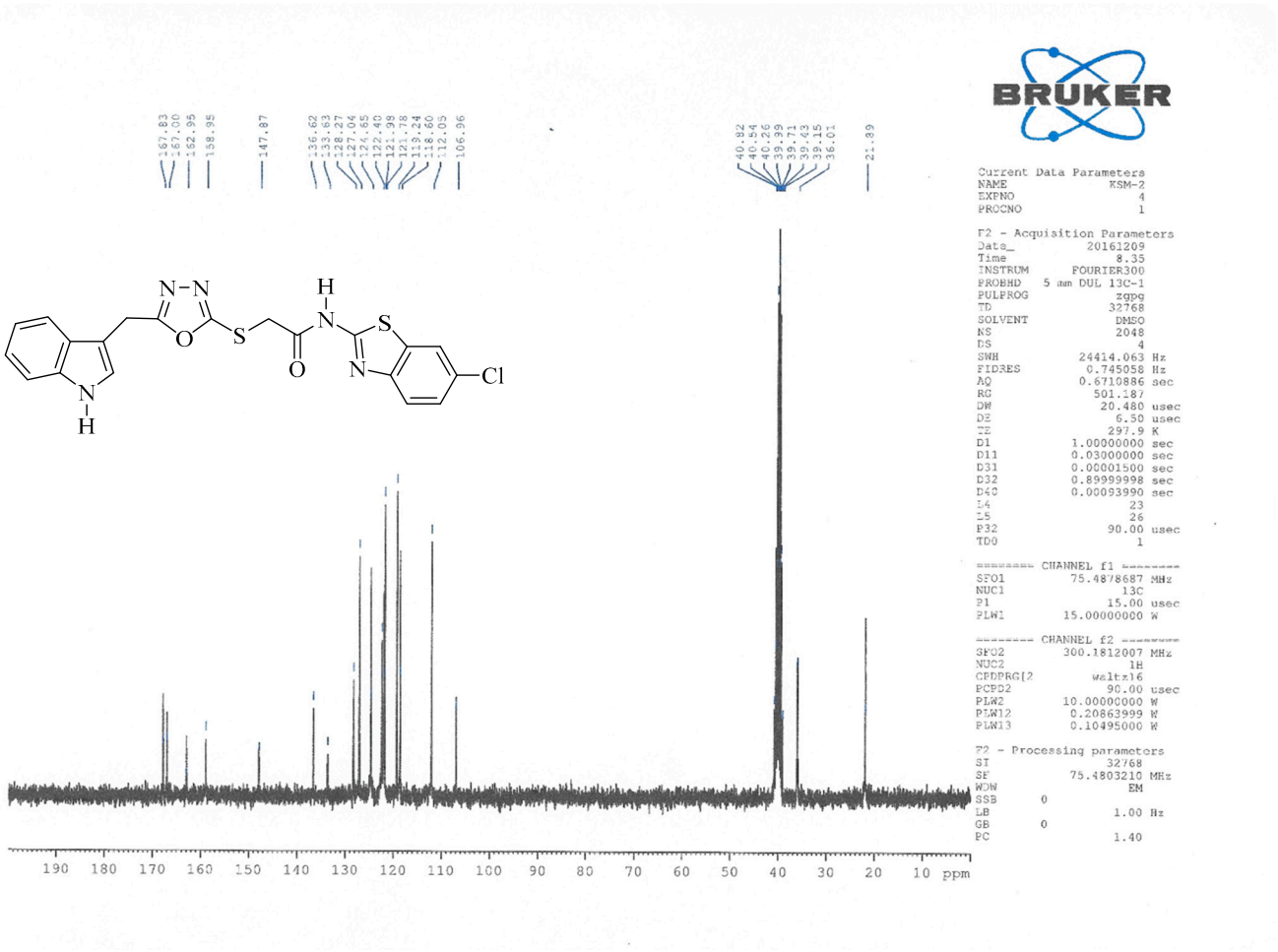


Figure S7. ^{13}C NMR spectrum of compound **2b**.

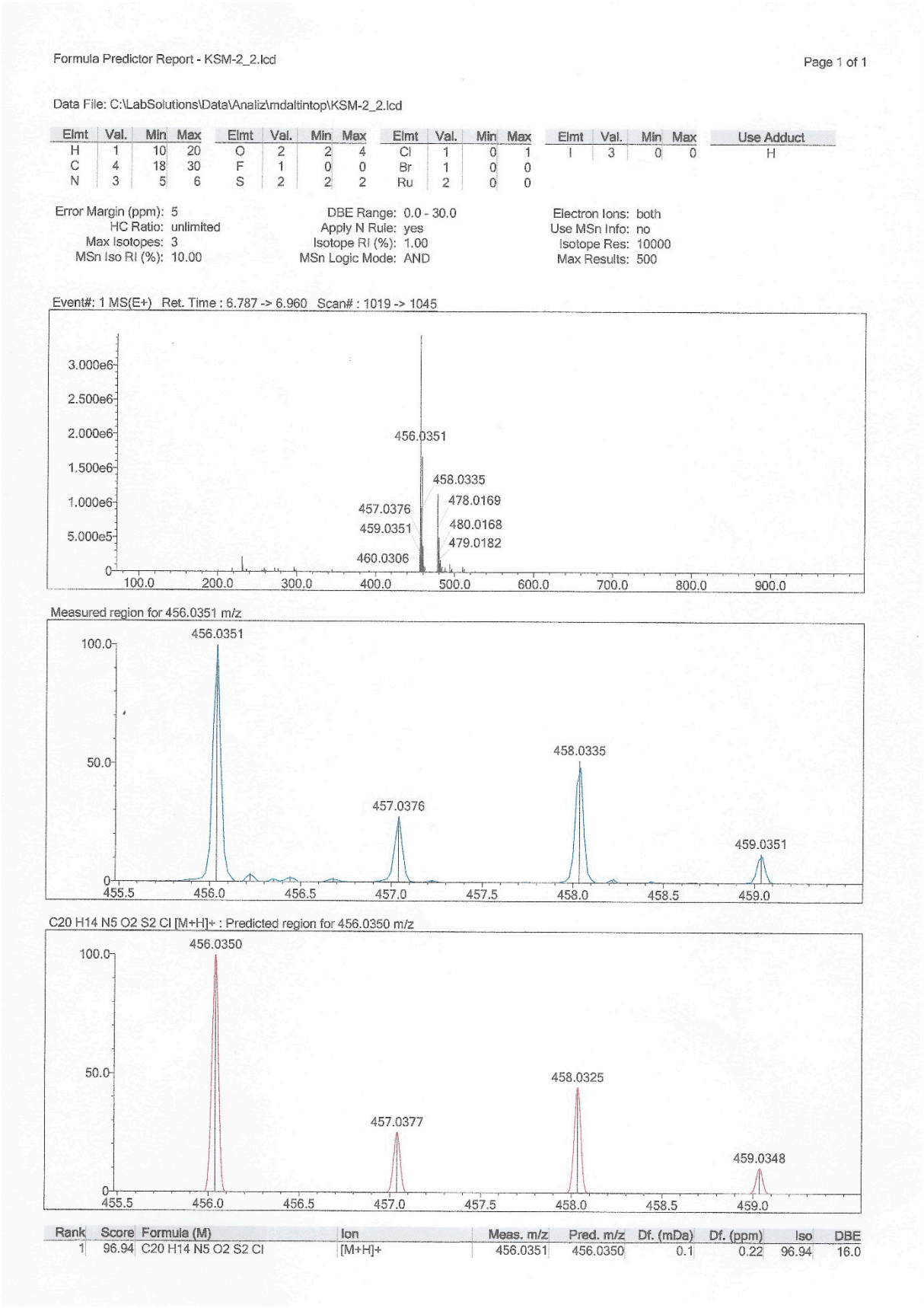


Figure S8. HRMS spectrum of compound **2b**.

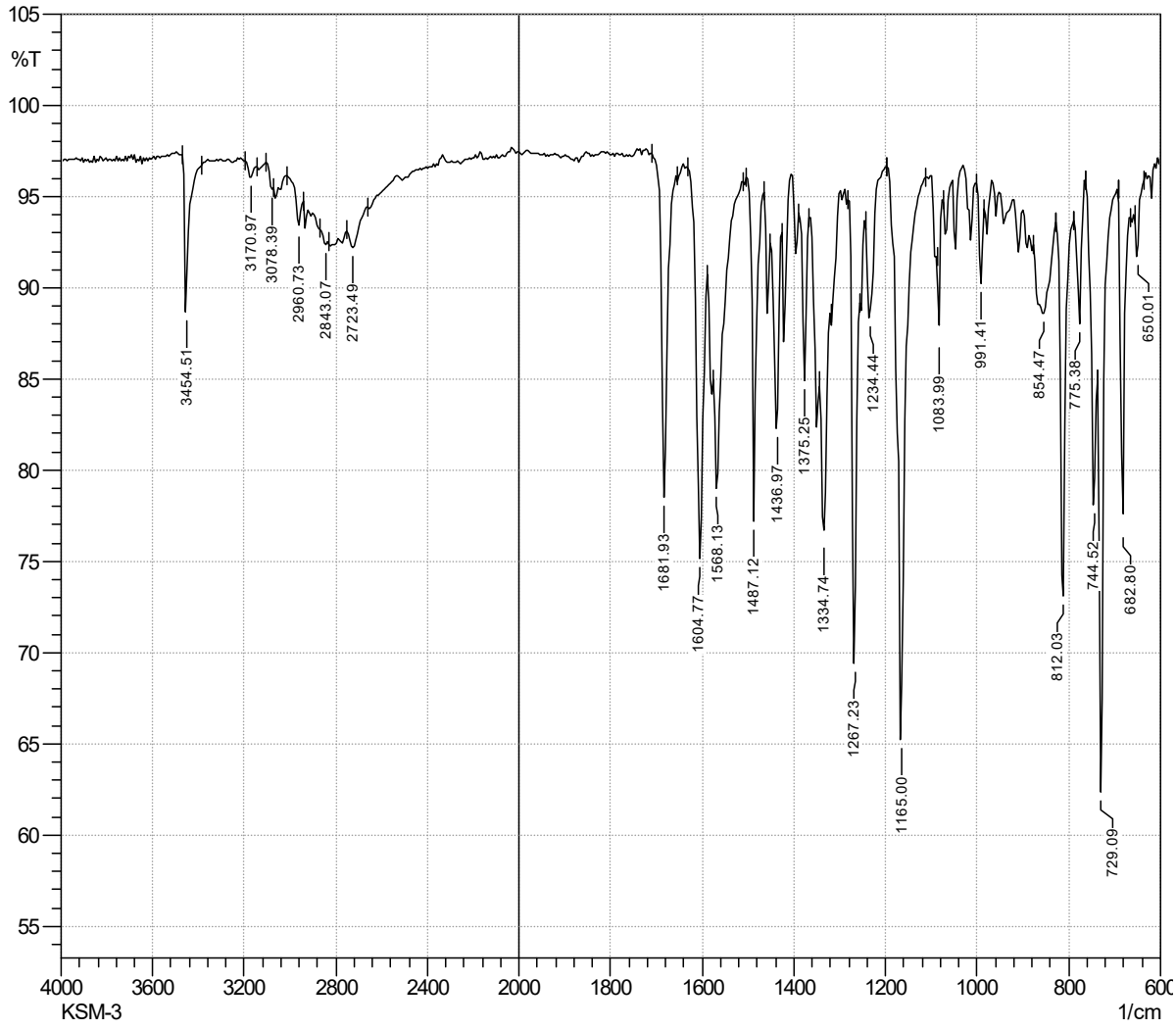


Figure S9. IR spectrum of compound **2c.**

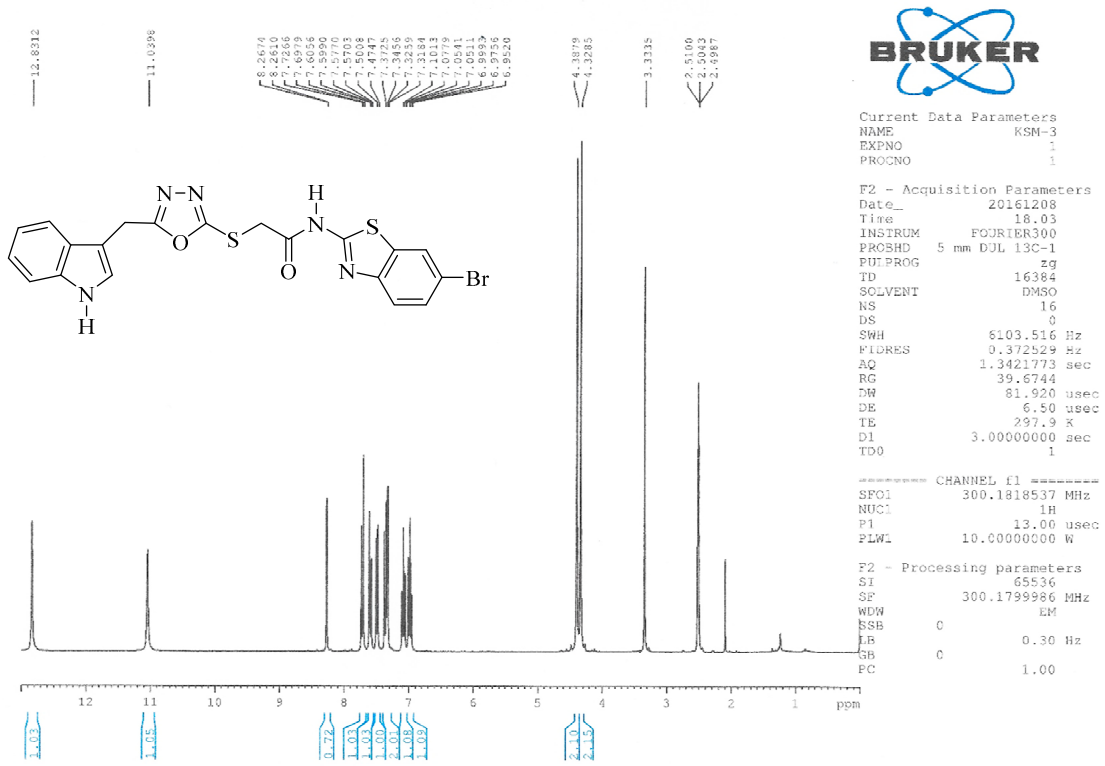


Figure S10. ^{1}H NMR spectrum of compound **2c**.

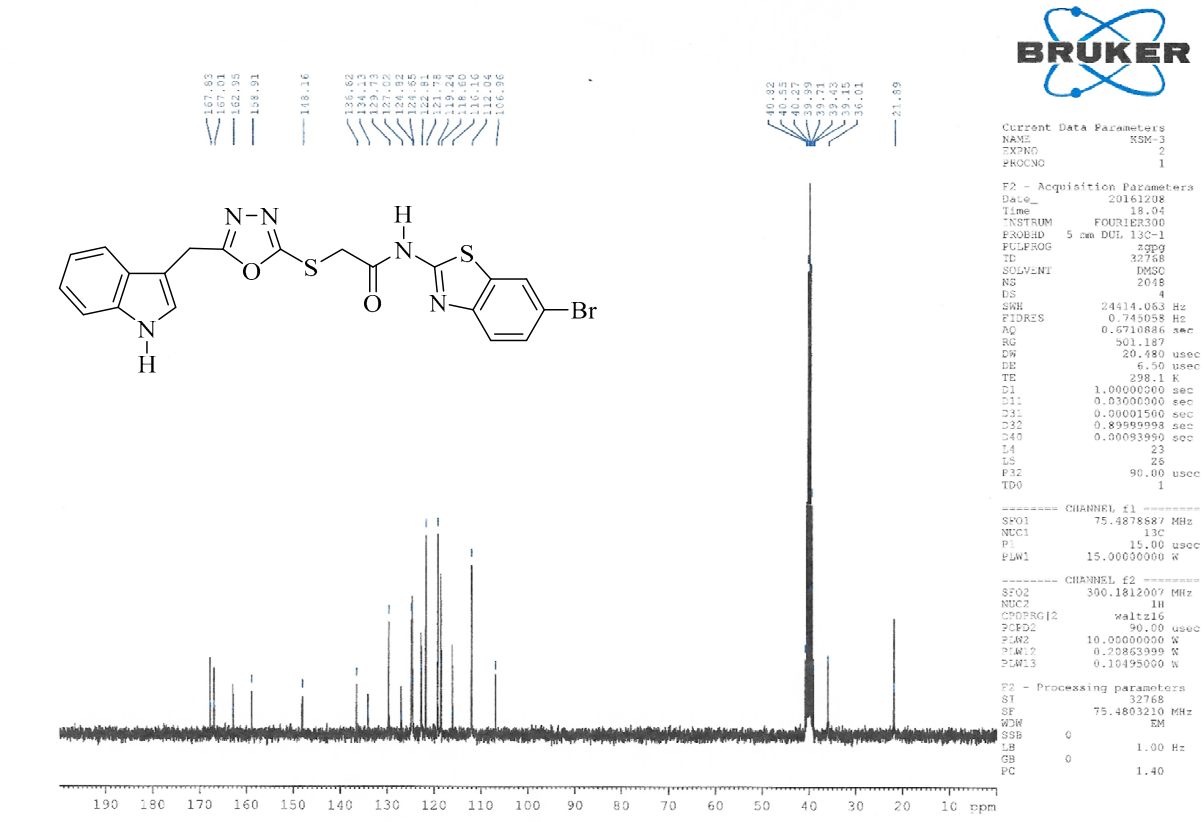


Figure S11. ^{13}C NMR spectrum of compound **2c**.

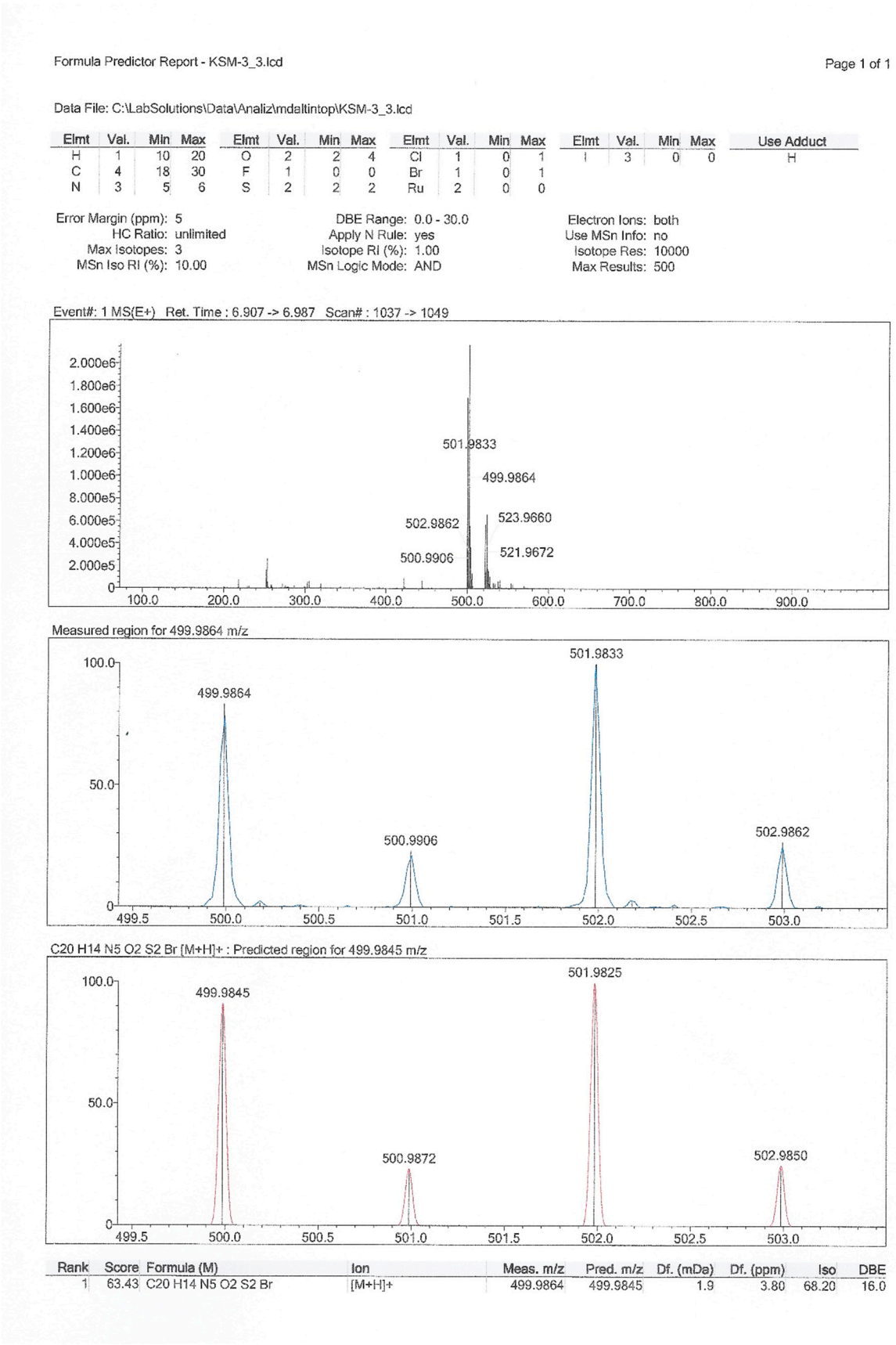


Figure S12. HRMS spectrum of compound **2c**.

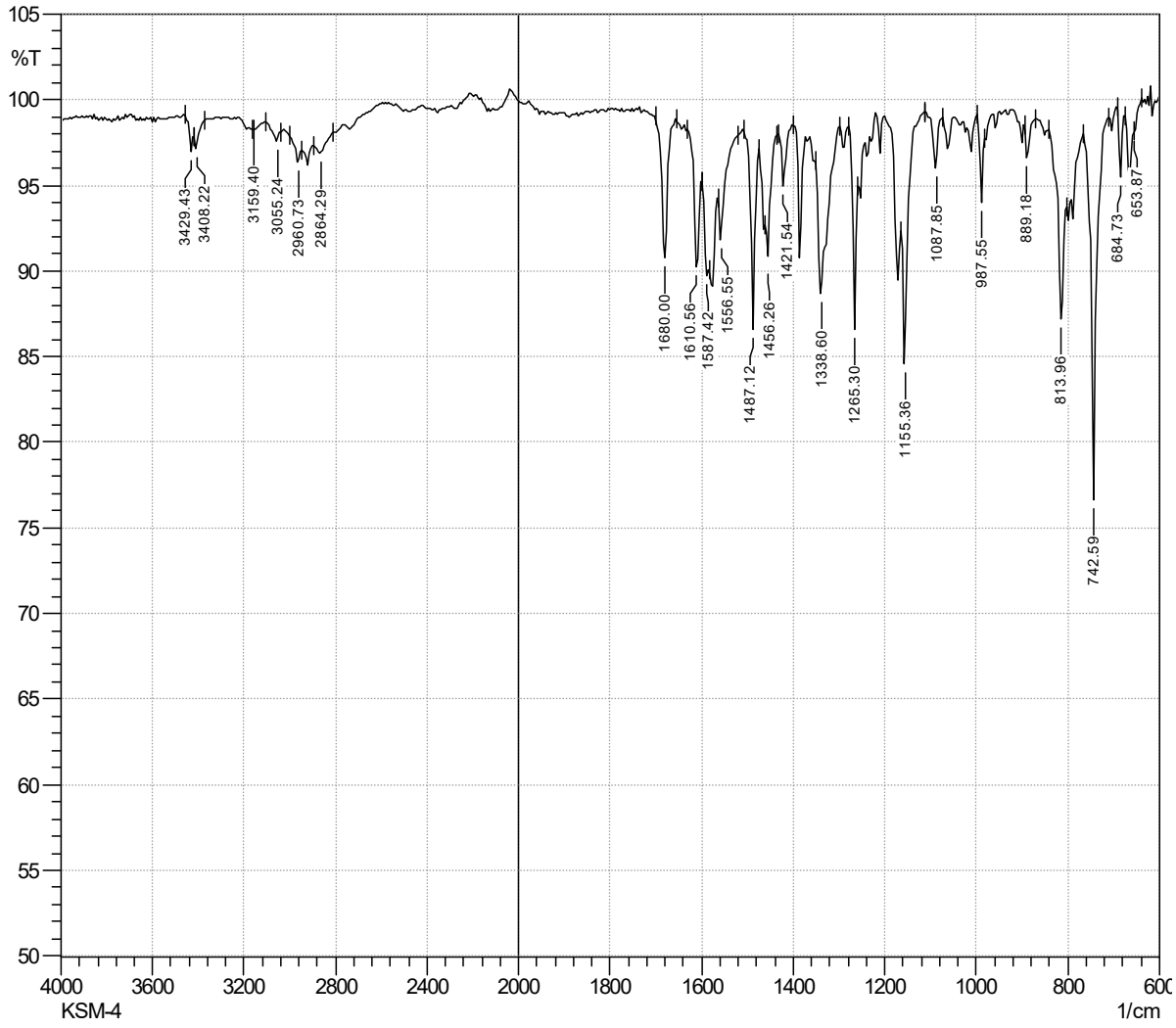


Figure S13. IR spectrum of compound **2d.**

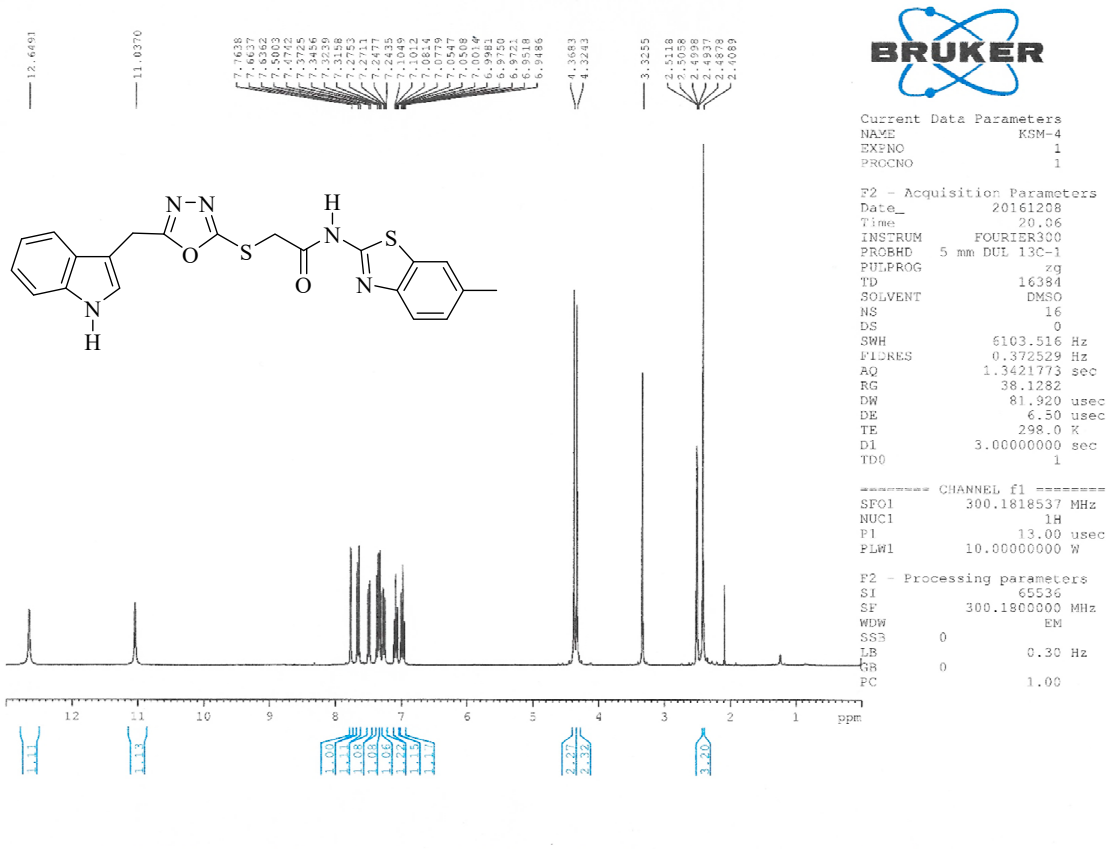


Figure S14. ^{1}H NMR spectrum of compound **2d**.

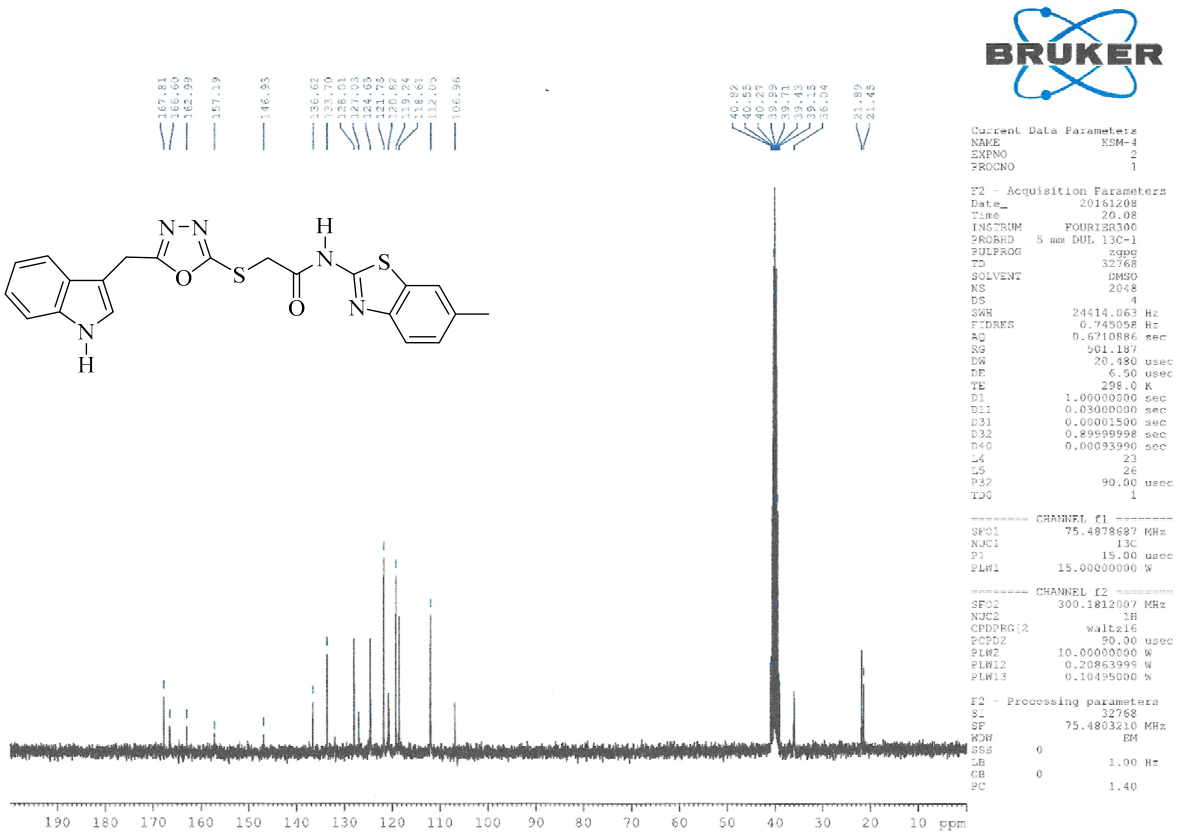


Figure S15. ^{13}C NMR spectrum of compound **2d.**

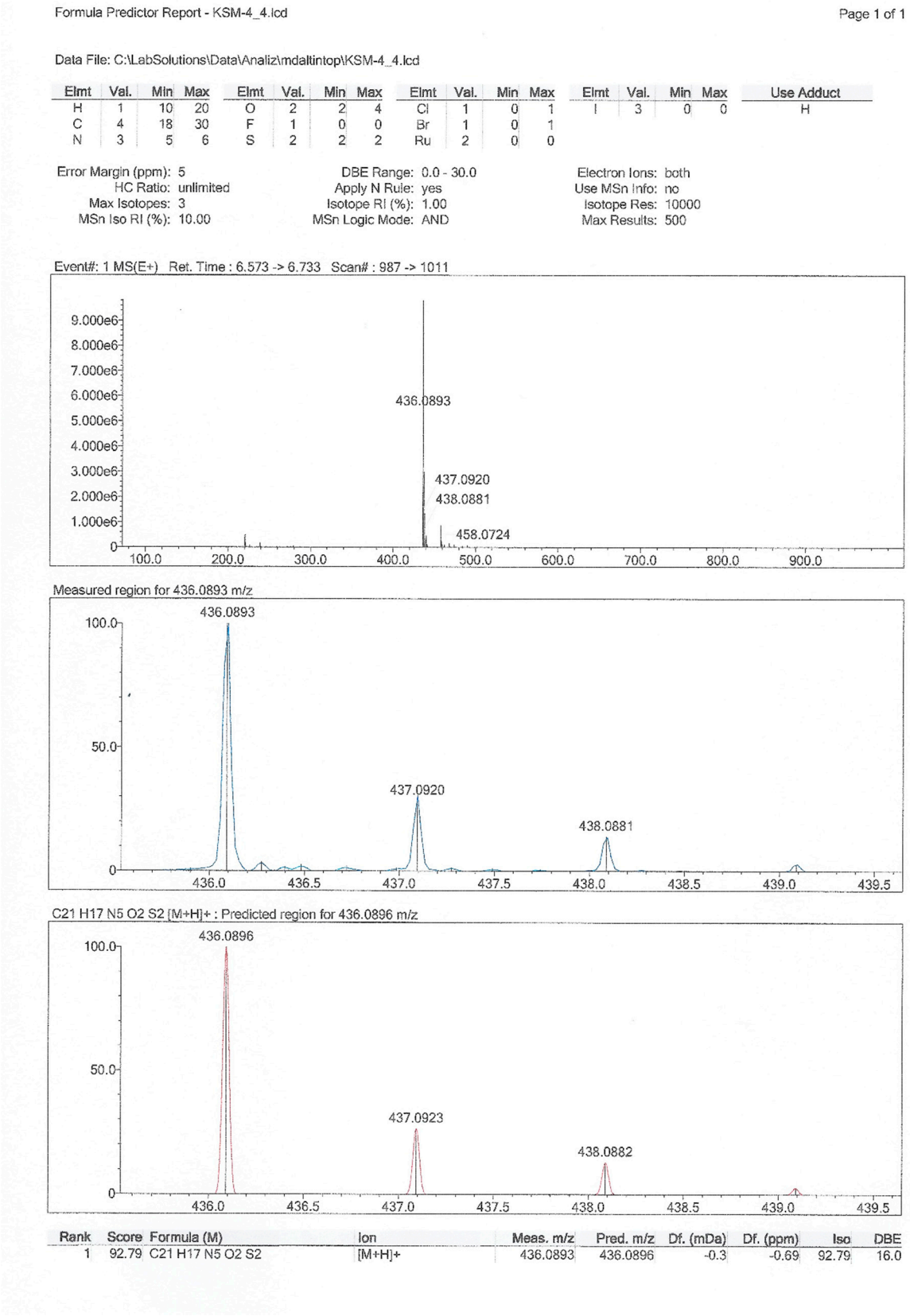


Figure S16. HRMS spectrum of compound **2d.**

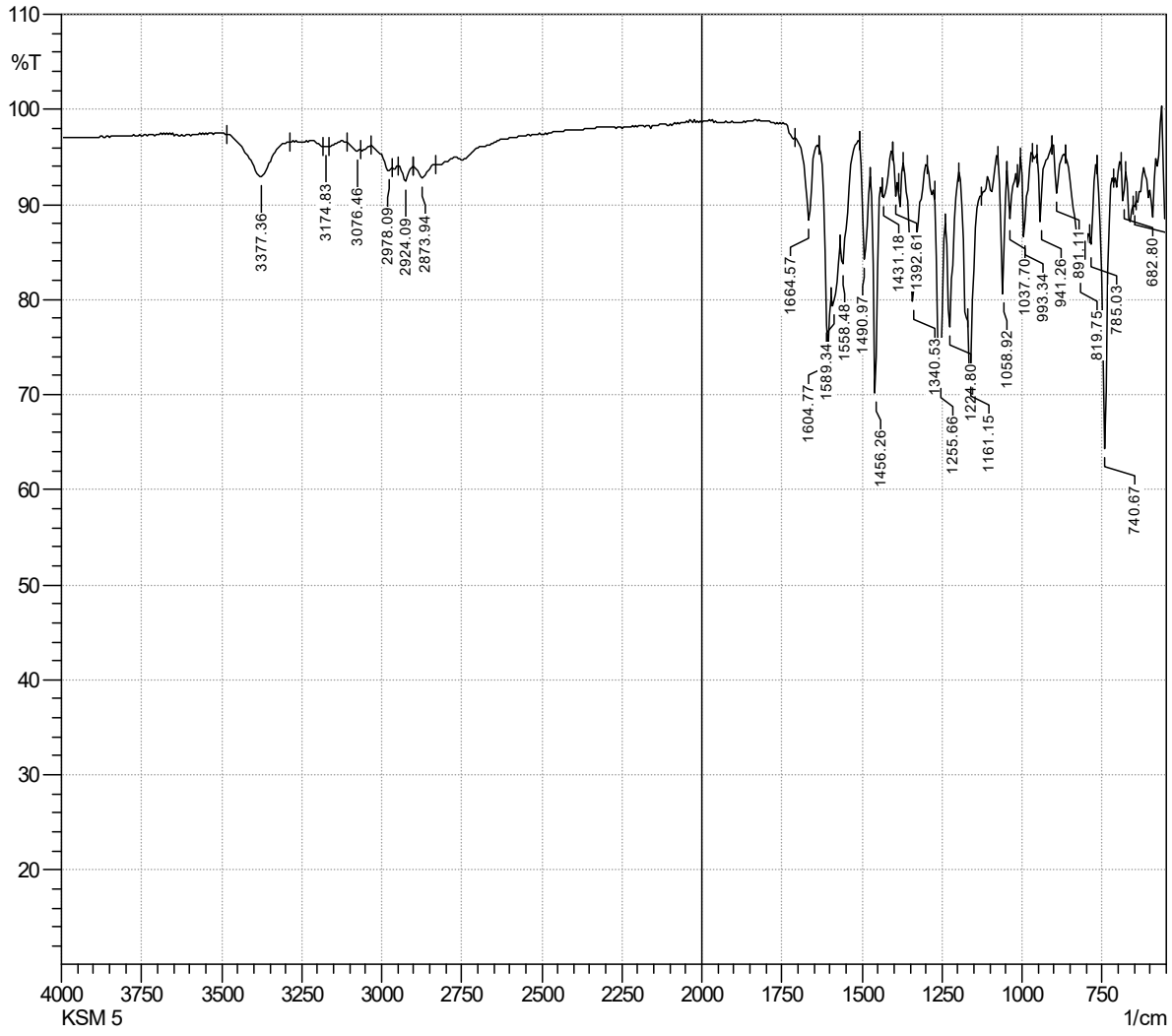


Figure S17. IR spectrum of compound **2e**.

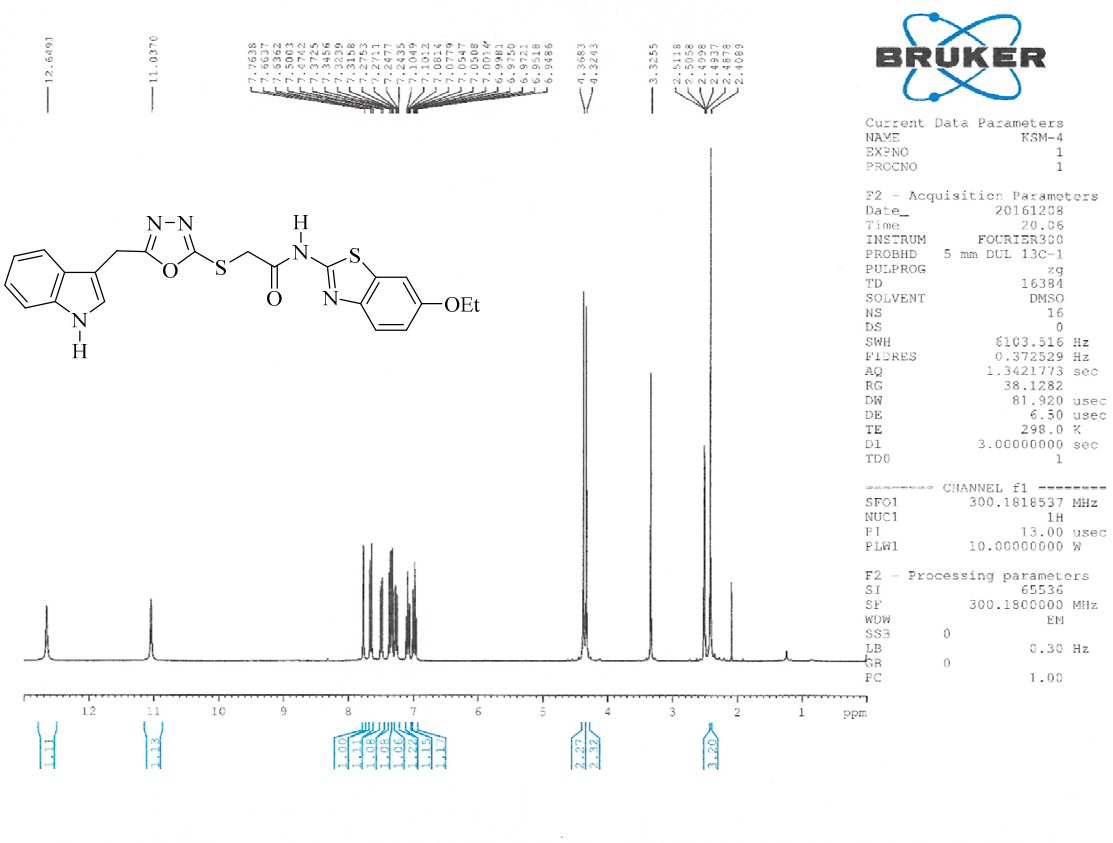


Figure S18. ^{1}H NMR spectrum of compound **2e**.

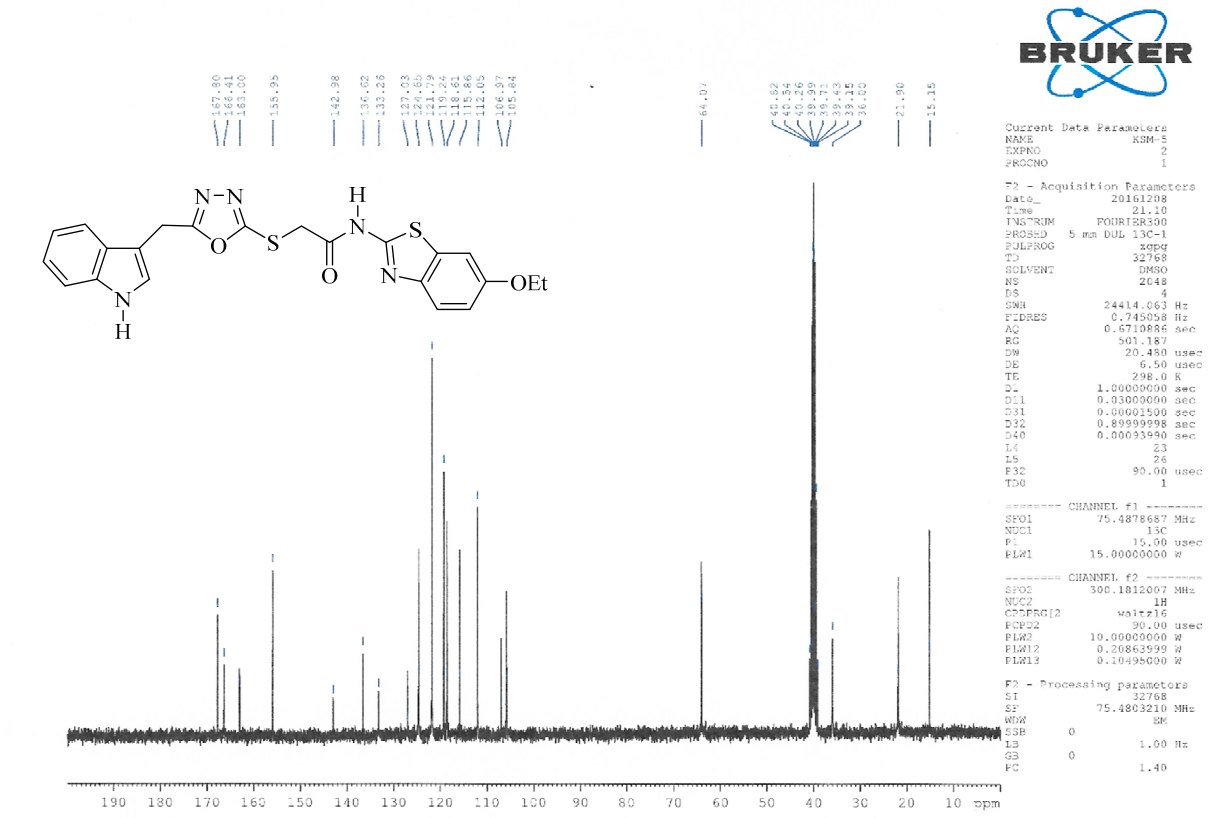


Figure S19. ^{13}C NMR spectrum of compound **2e**.

Formula Predictor Report - KSM-5_5.lcd

Data File: C:\LabSolutions\Data\Analiz\mdaltintop\KSM-5_5.lcd

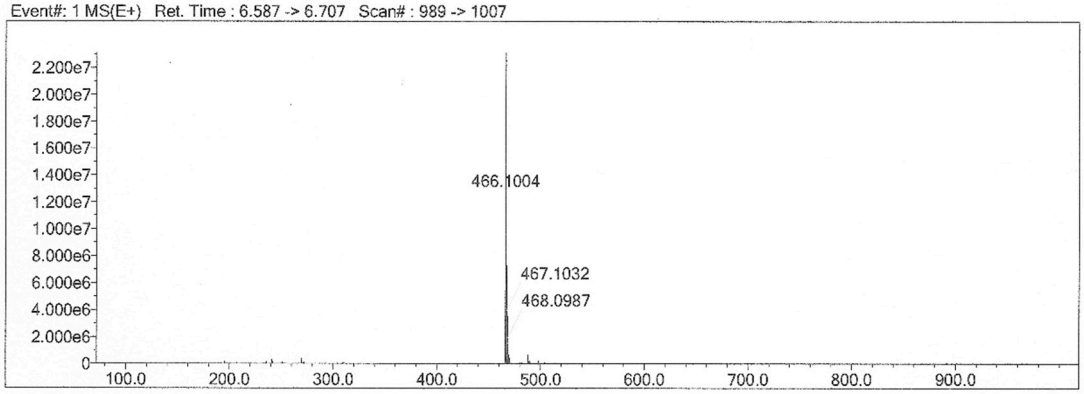
Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Use Adduct
H	1	10	20	O	2	2	4	Cl	1	0	1	I	3	0	0	H
C	4	18	30	F	1	0	0	Br	1	0	1					
N	3	5	6	S	2	2	2	Ru	2	0	0					

Error Margin (ppm): 5
HC Ratio: unlimited
Max Isotopes: 3
MSn Iso RI (%): 10.00

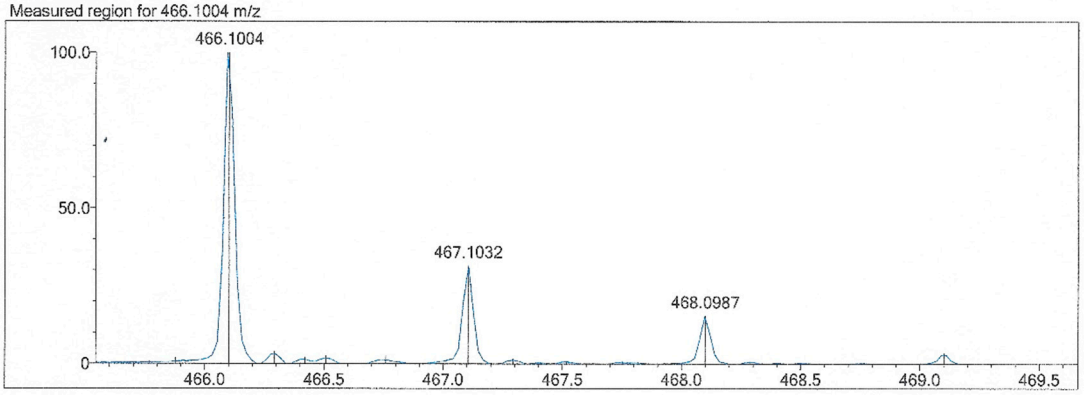
DBE Range: 0.0 - 30.0
Apply N Rule: yes
Isotope RI (%): 1.00
MSn Logic Mode: AND

Electron Ions: both
Use MSn Info: no
Isotope Res: 10000
Max Results: 500

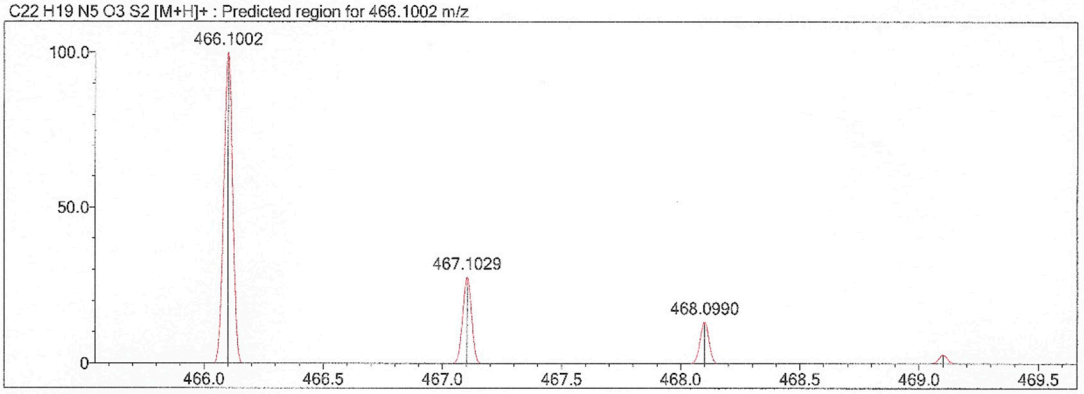
Event#: 1 MS(E+) Ret. Time : 6.587 -> 6.707 Scan# : 989 -> 1007



Measured region for 466.1004 m/z



C22 H19 N5 O3 S2 [M+H]+ : Predicted region for 466.1002 m/z



Rank	Score	Formula (M)	Ion	Meas. m/z	Pred. m/z	Df. (mDa)	Df. (ppm)	Iso	DBE
1	86.85	C22 H19 N5 O3 S2	[M+H]+	466.1004	466.1002	0.2	0.43	86.85	16.0

Figure S20. HRMS spectrum of compound **2e**.

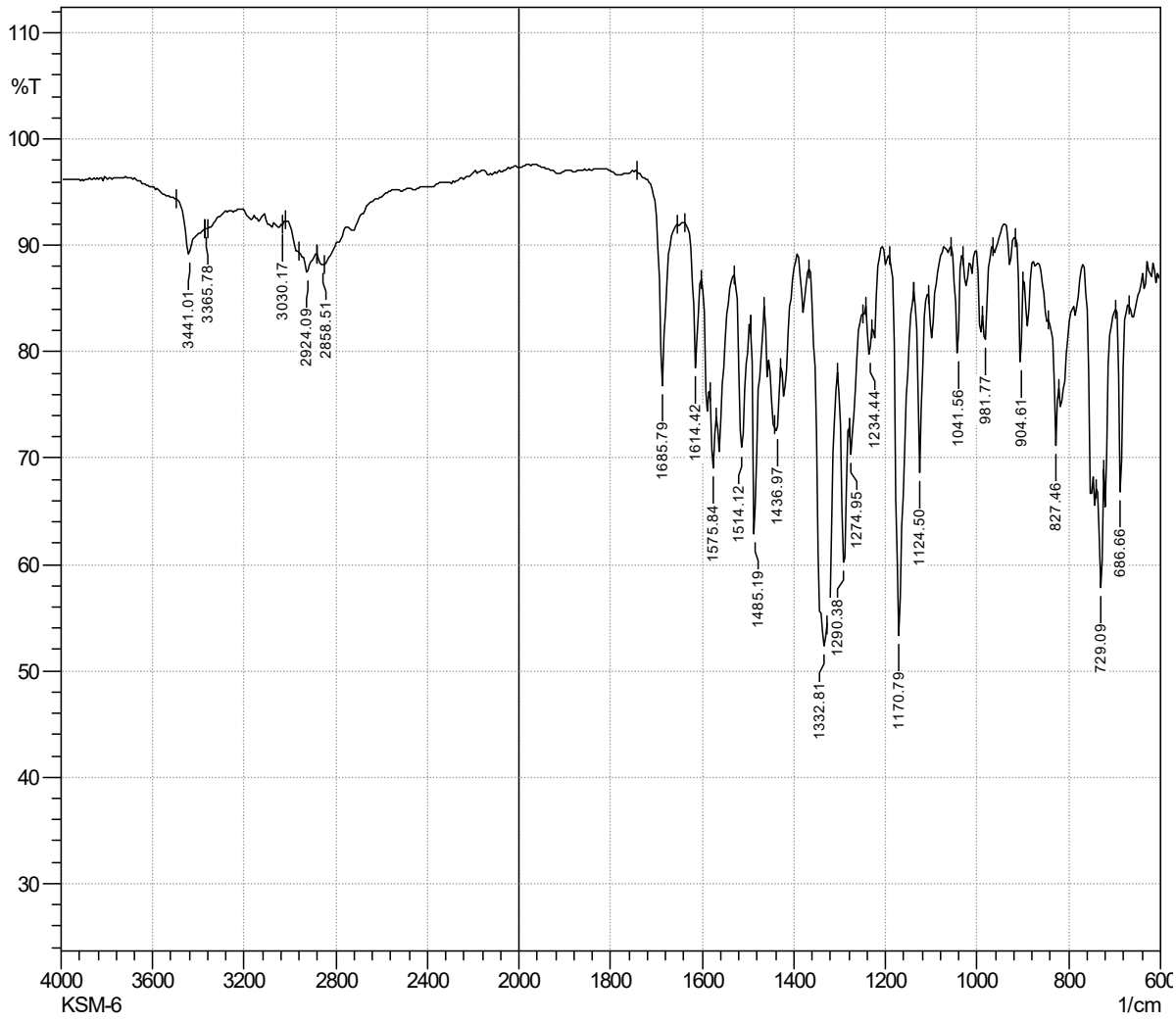


Figure S21. IR spectrum of compound **2f**.

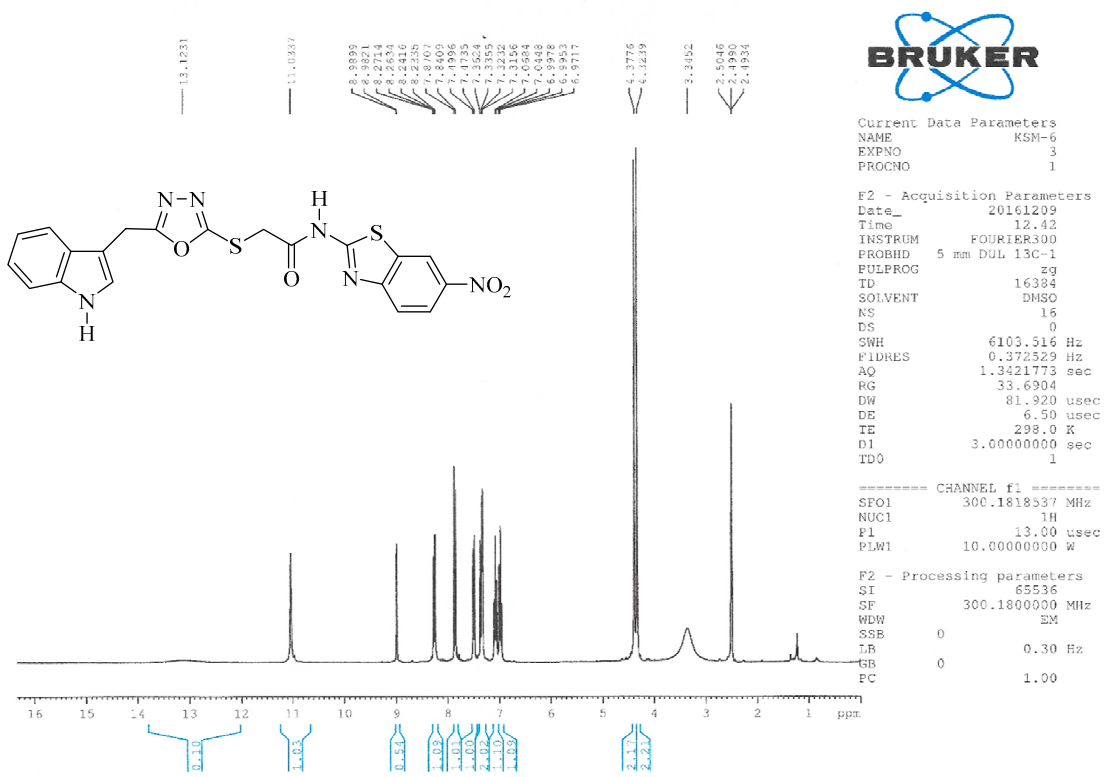


Figure S22. ^{1}H NMR spectrum of compound **2f**.

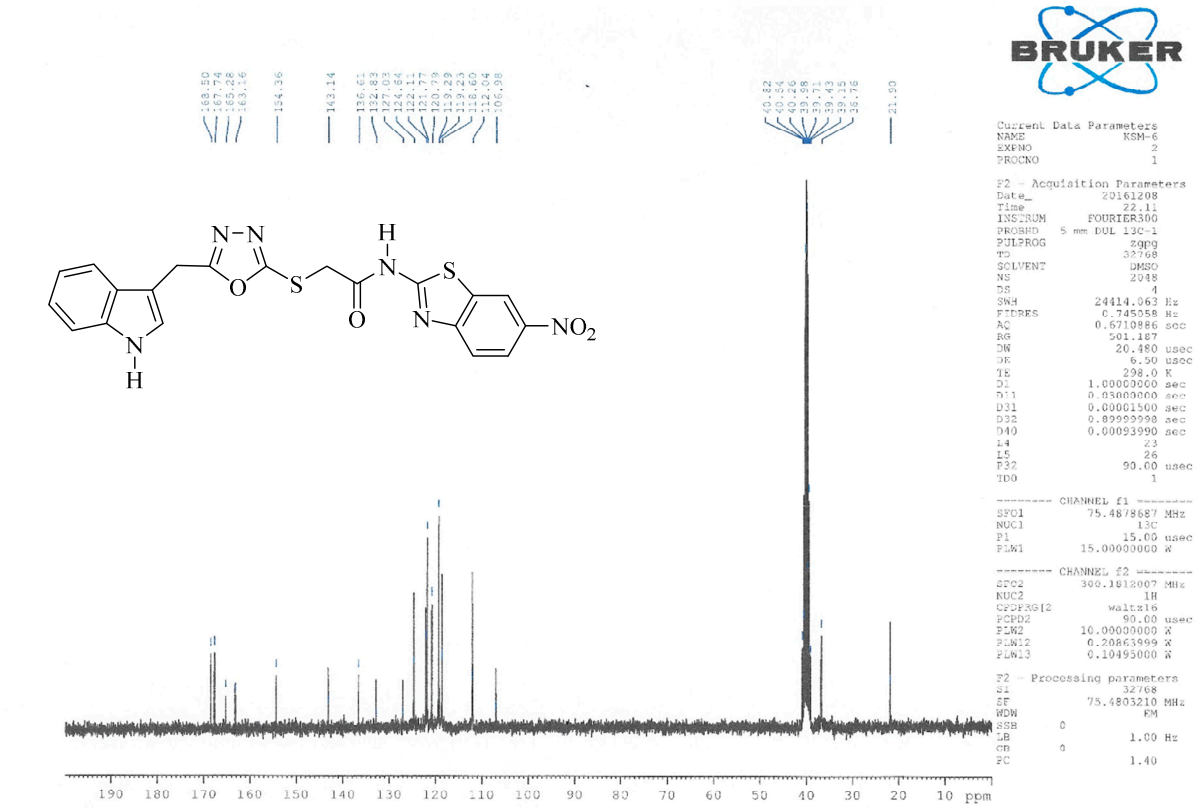


Figure S23. ^{13}C NMR spectrum of compound **2f**.

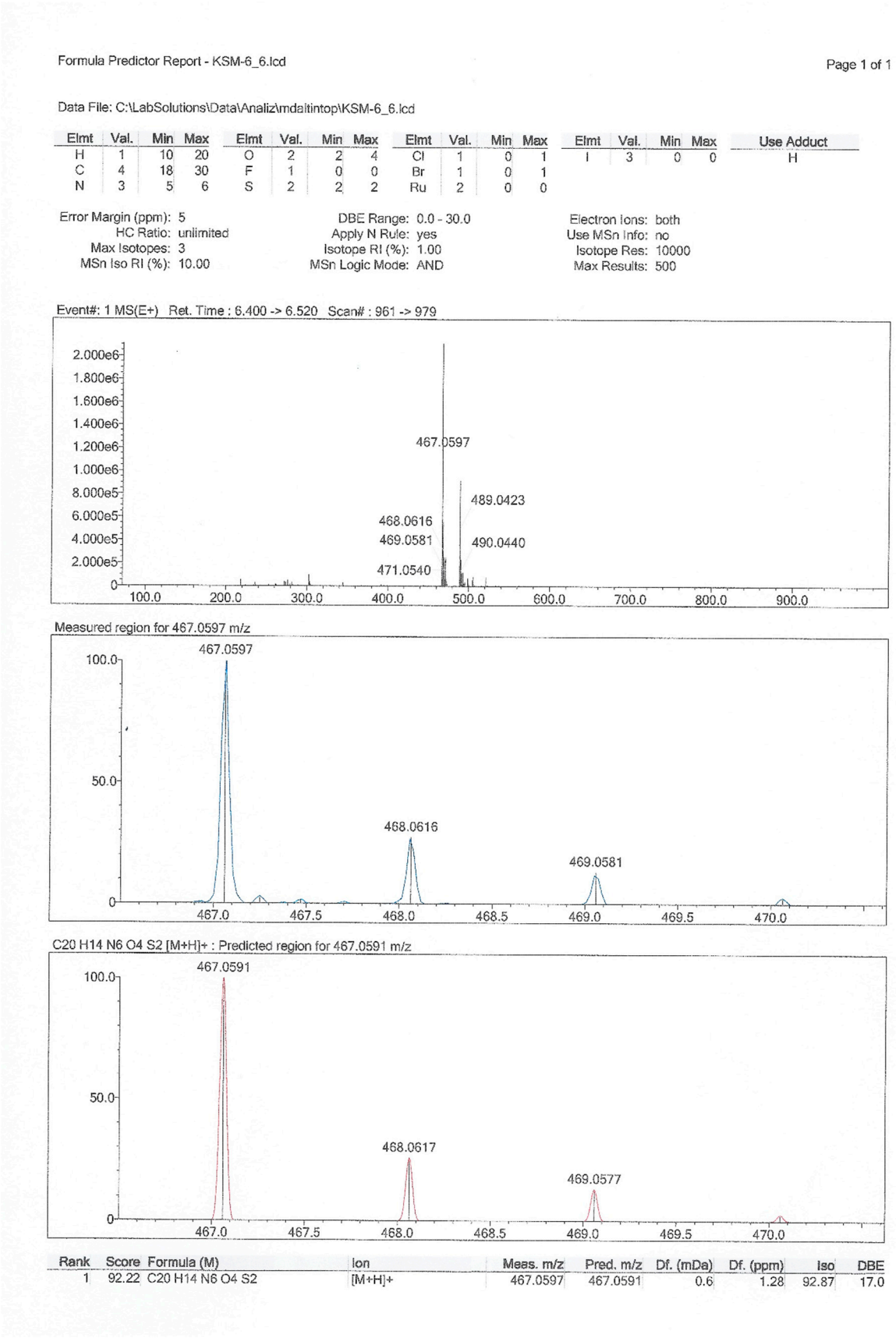


Figure S24. HRMS spectrum of compound **2f**.

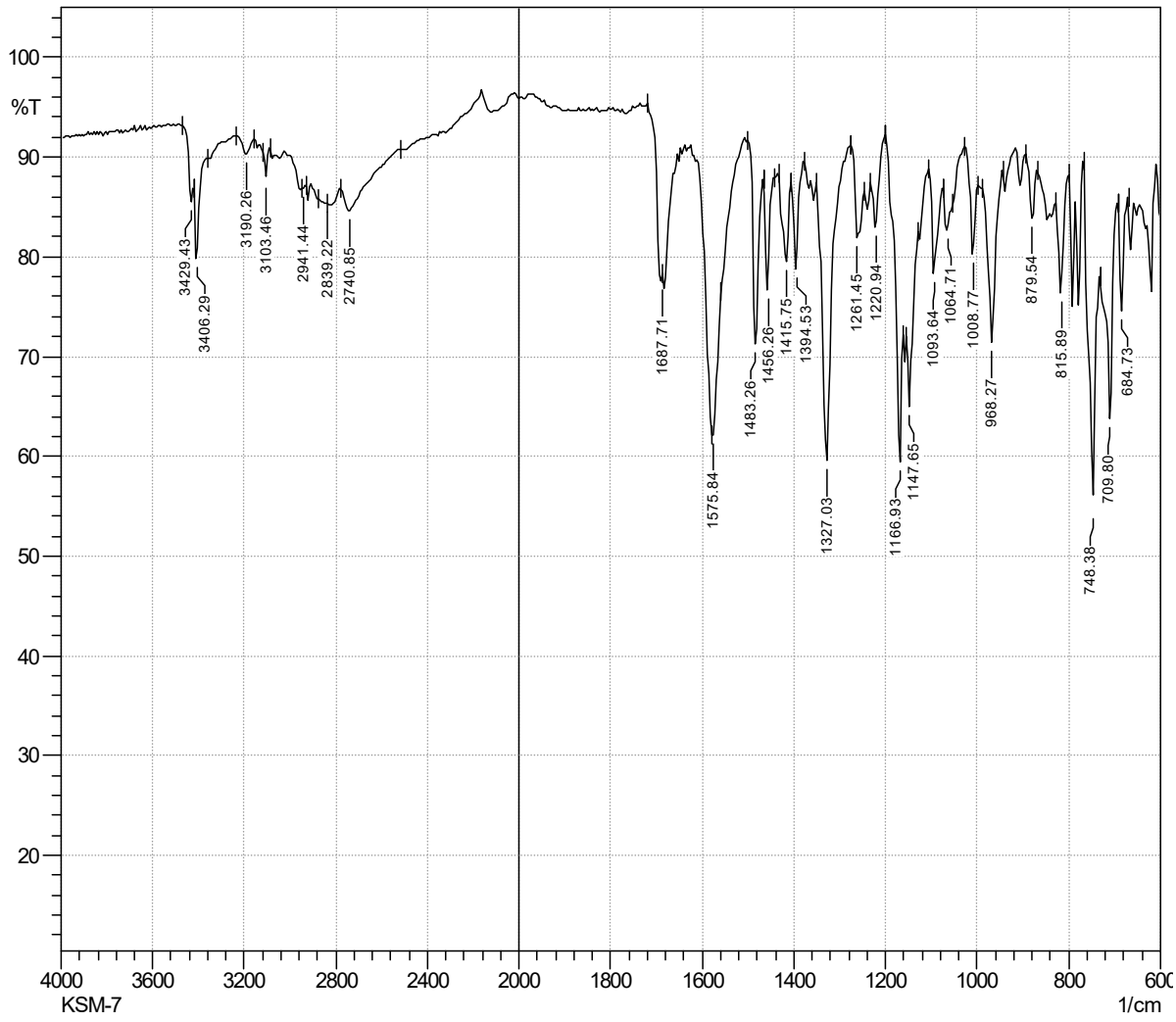


Figure S25. IR spectrum of compound **2g**.

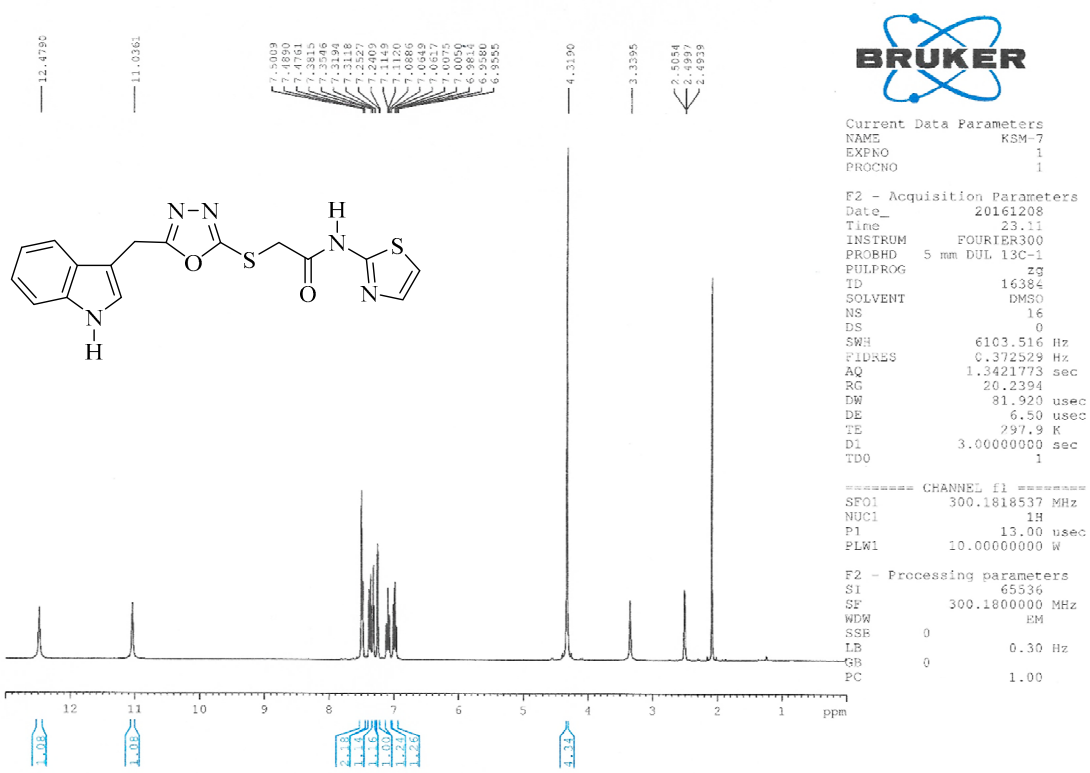


Figure S26. ^{1}H NMR spectrum of compound **2g**.

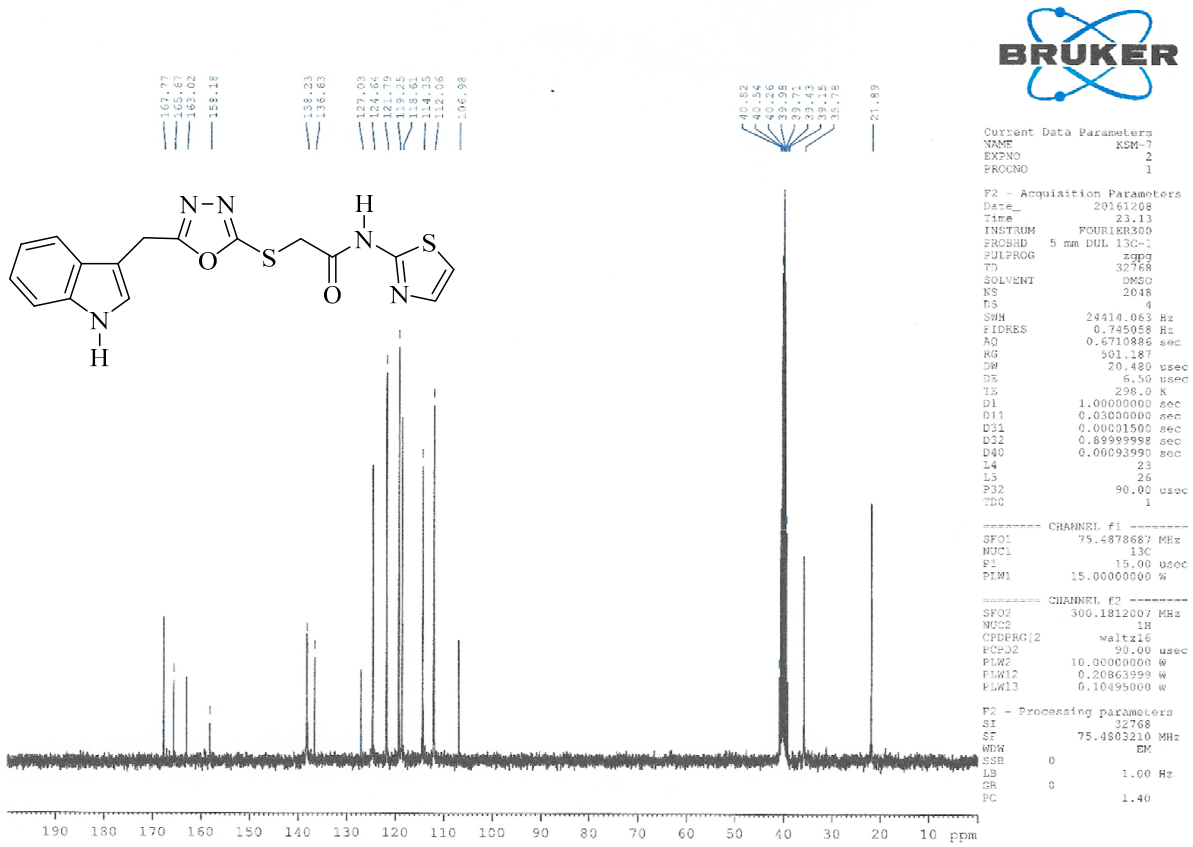


Figure S27. ^{13}C NMR spectrum of compound **2g**.

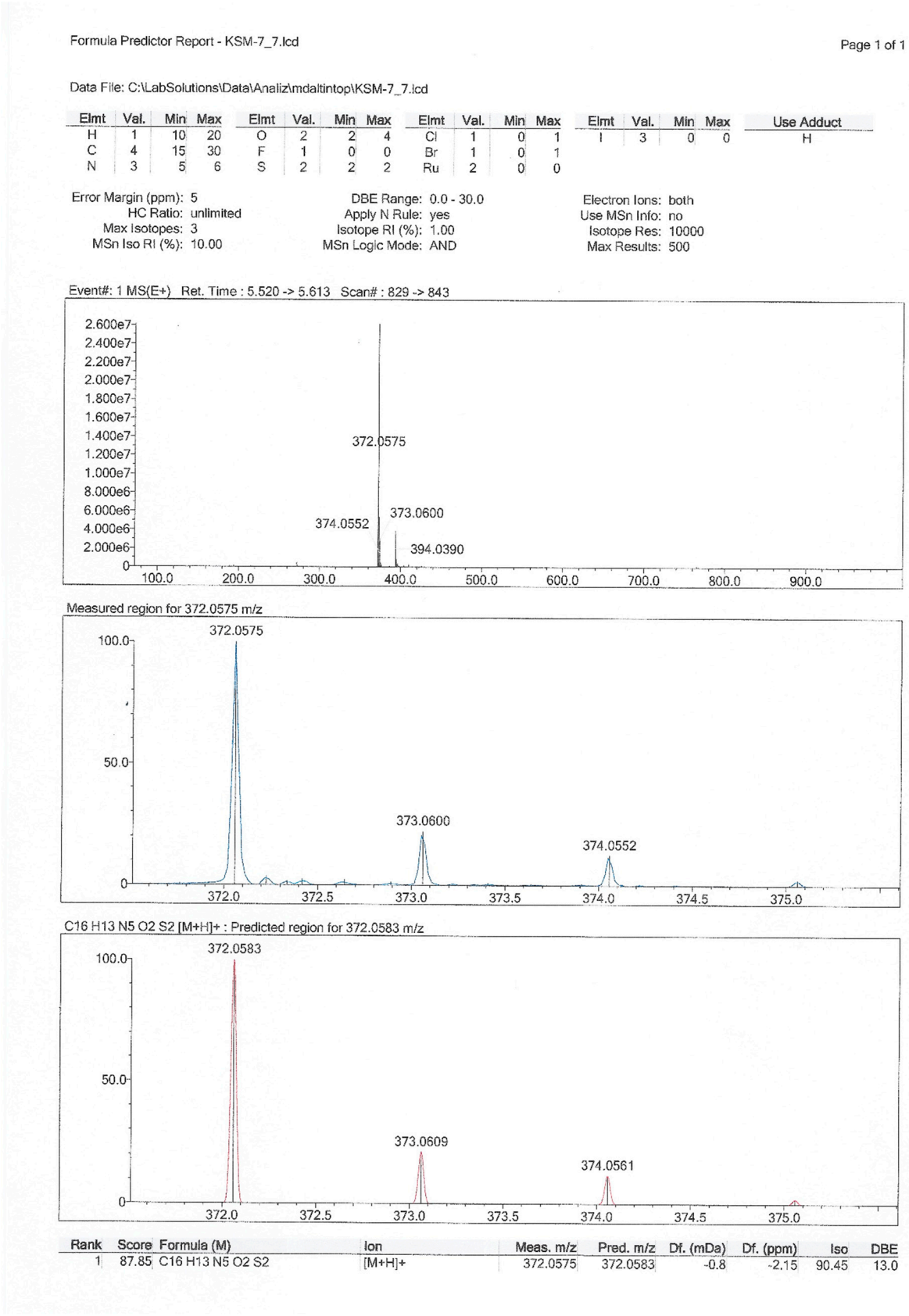


Figure S28. HRMS spectrum of compound **2g.**

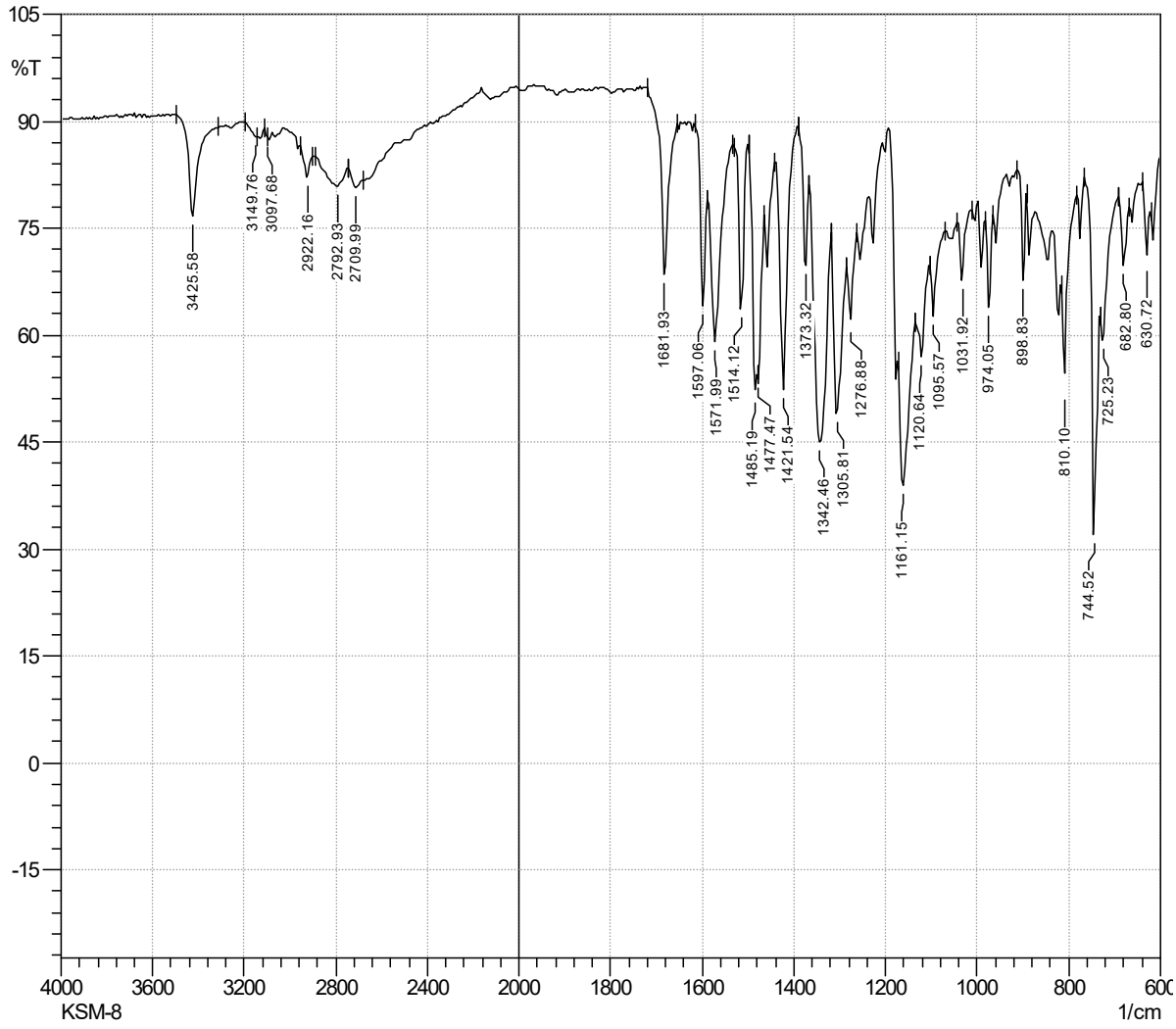


Figure S29. IR spectrum of compound **2h**.

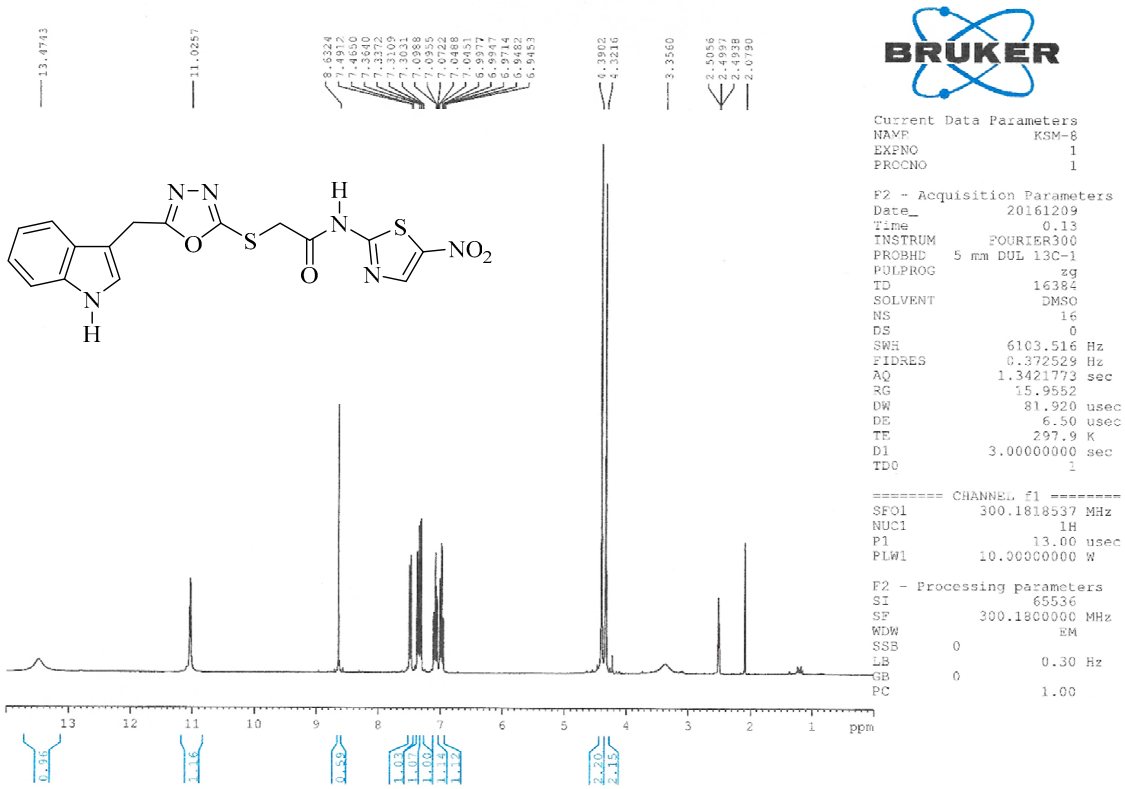


Figure S30. ^{1}H NMR spectrum of compound **2h.**

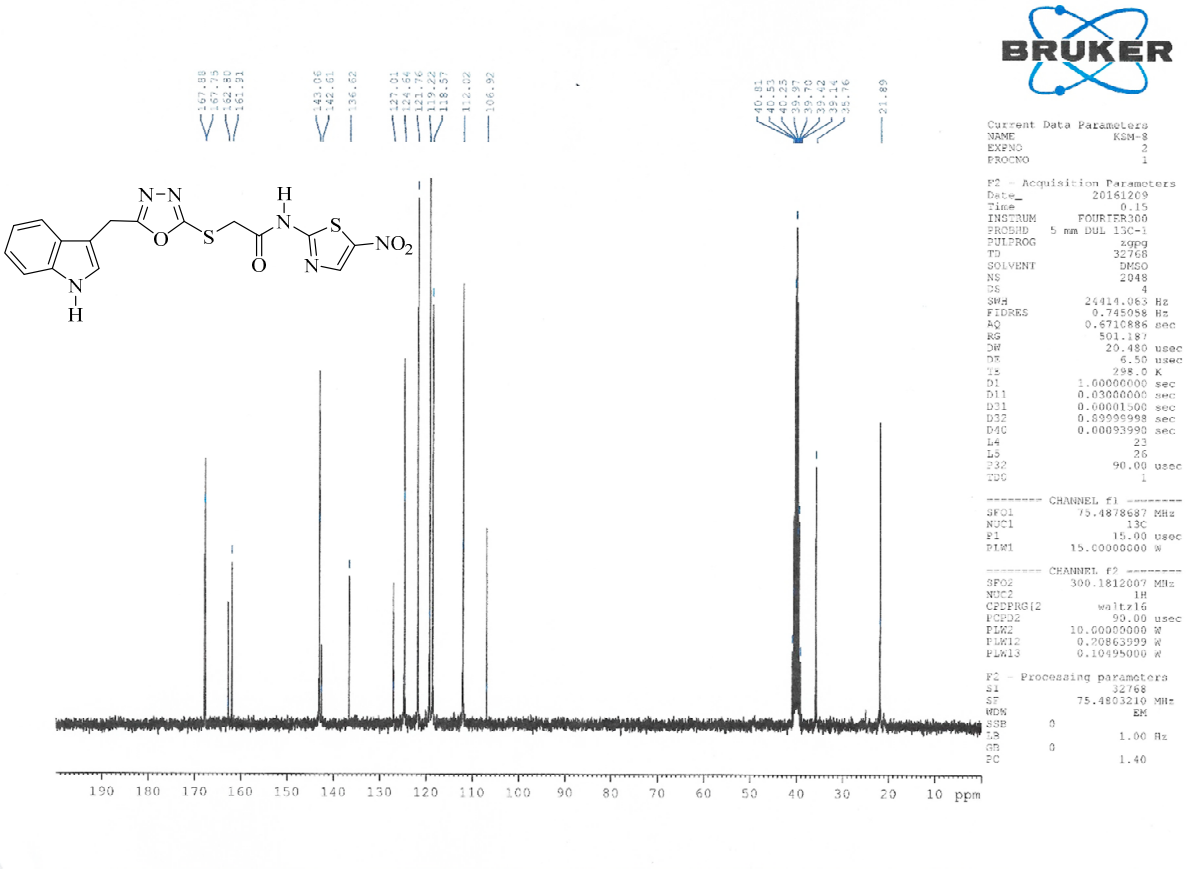


Figure S31. ^{13}C NMR spectrum of compound **2h**.

Formula Predictor Report - KSM-8_8.lcd

Data File: C:\LabSolutions\Data\Analiz\mdaltintop\KSM-8_8.lcd

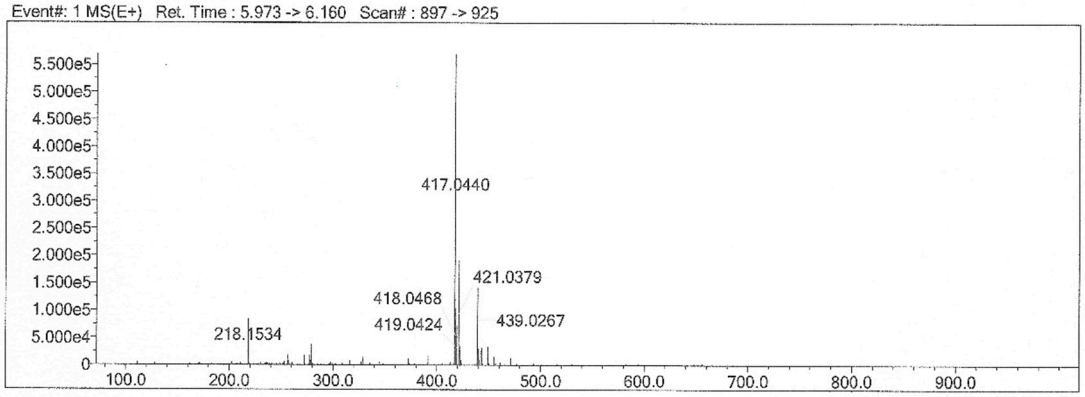
Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Use Adduct
H	1	10	20	O	2	2	4	Cl	1	0	1	I	3	0	0	H
C	4	15	30	F	1	0	0	Br	1	0	1					
N	3	5	6	S	2	2	2	Ru	2	0	0					

Error Margin (ppm): 5
HC Ratio: unlimited
Max Isotopes: 3
MSn Iso RI (%): 10.00

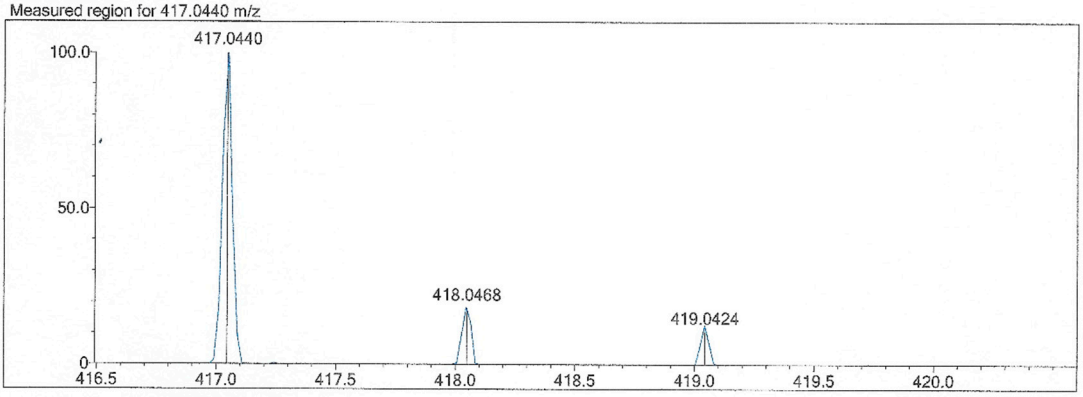
DBE Range: 0.0 - 30.0
Apply N Rule: yes
Isotope RI (%): 1.00
MSn Logic Mode: AND

Electron Ions: both
Use MSn Info: no
Isotope Res: 10000
Max Results: 500

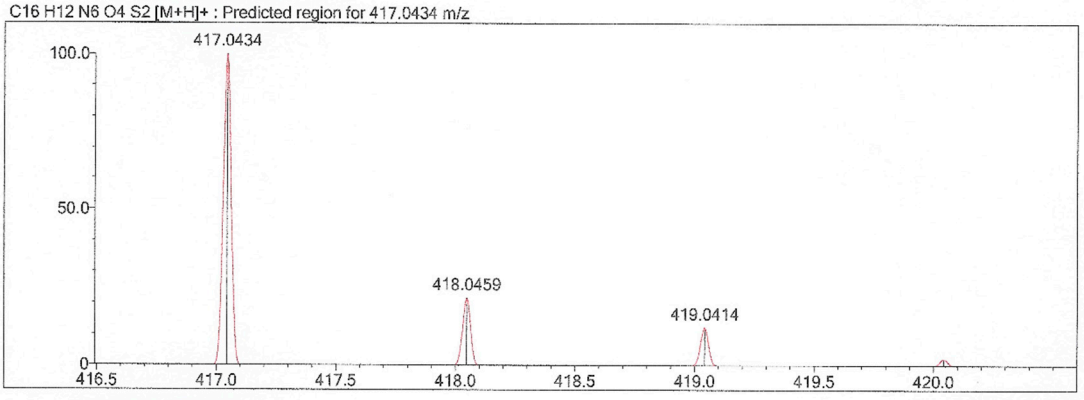
Event#: 1 MS(E+) Ret. Time : 5.973 -> 6.160 Scan# : 897 -> 925



Measured region for 417.0440 m/z



C16 H12 N6 O4 S2 [M+H]+ : Predicted region for 417.0434 m/z



Rank	Score	Formula (M)	Ion	Meas. m/z	Pred. m/z	Df. (mDa)	Df. (ppm)	Iso	DBE
1	77.58	C16 H12 N6 O4 S2	[M+H]+	417.0440	417.0434	0.6	1.44	78.45	14.0

Figure S32. HRMS spectrum of compound **2h.**

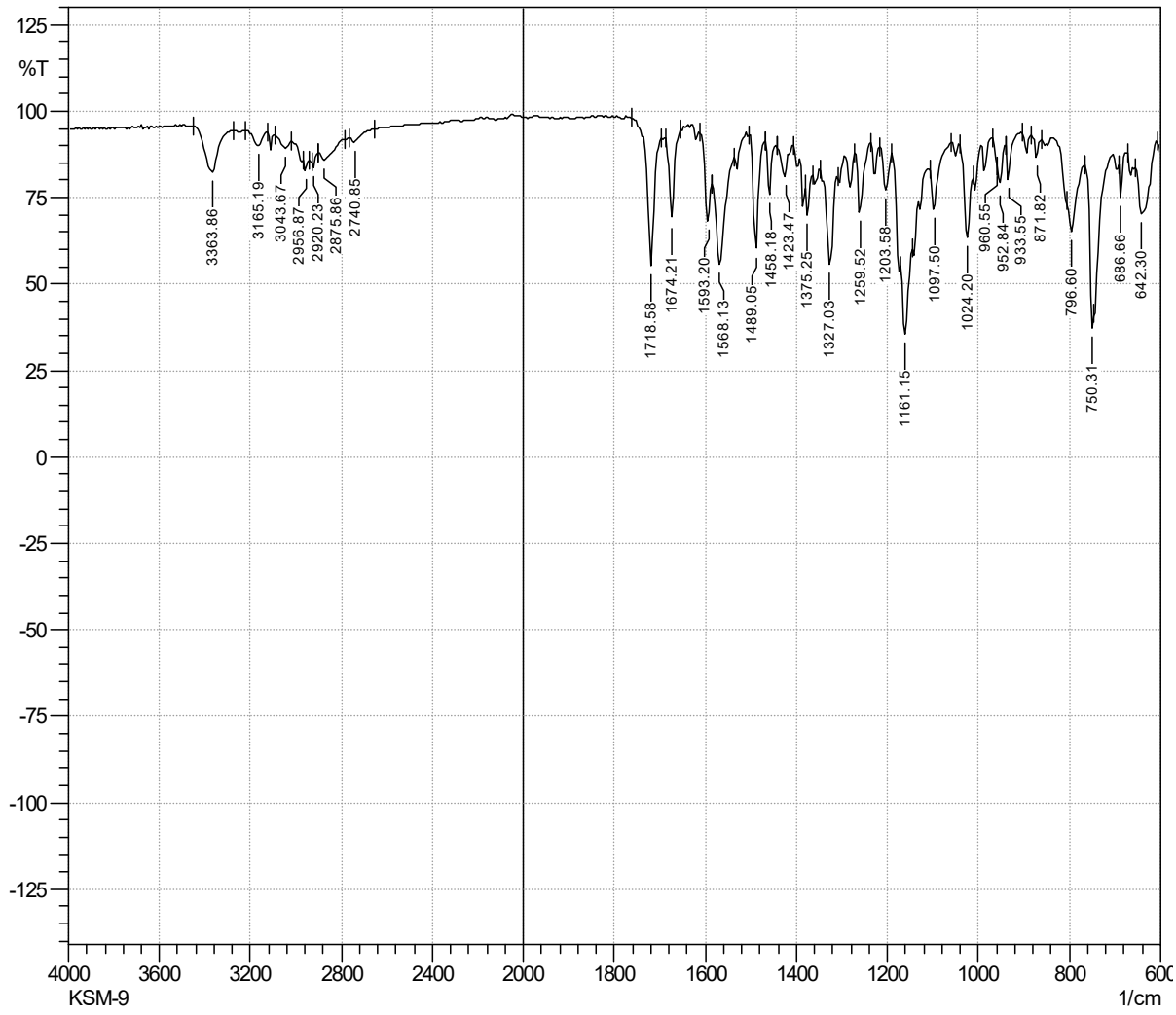


Figure S33. IR spectrum of compound **2i**.

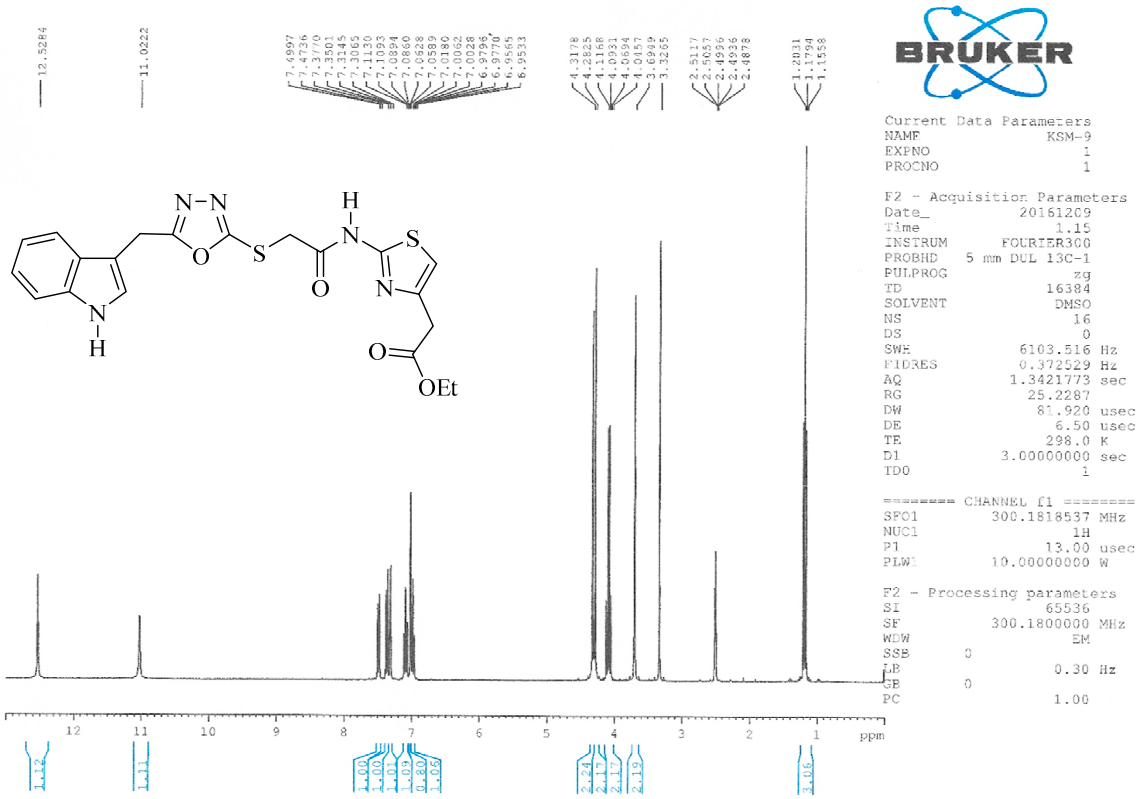


Figure S34. ^{1}H NMR spectrum of compound **2i**.

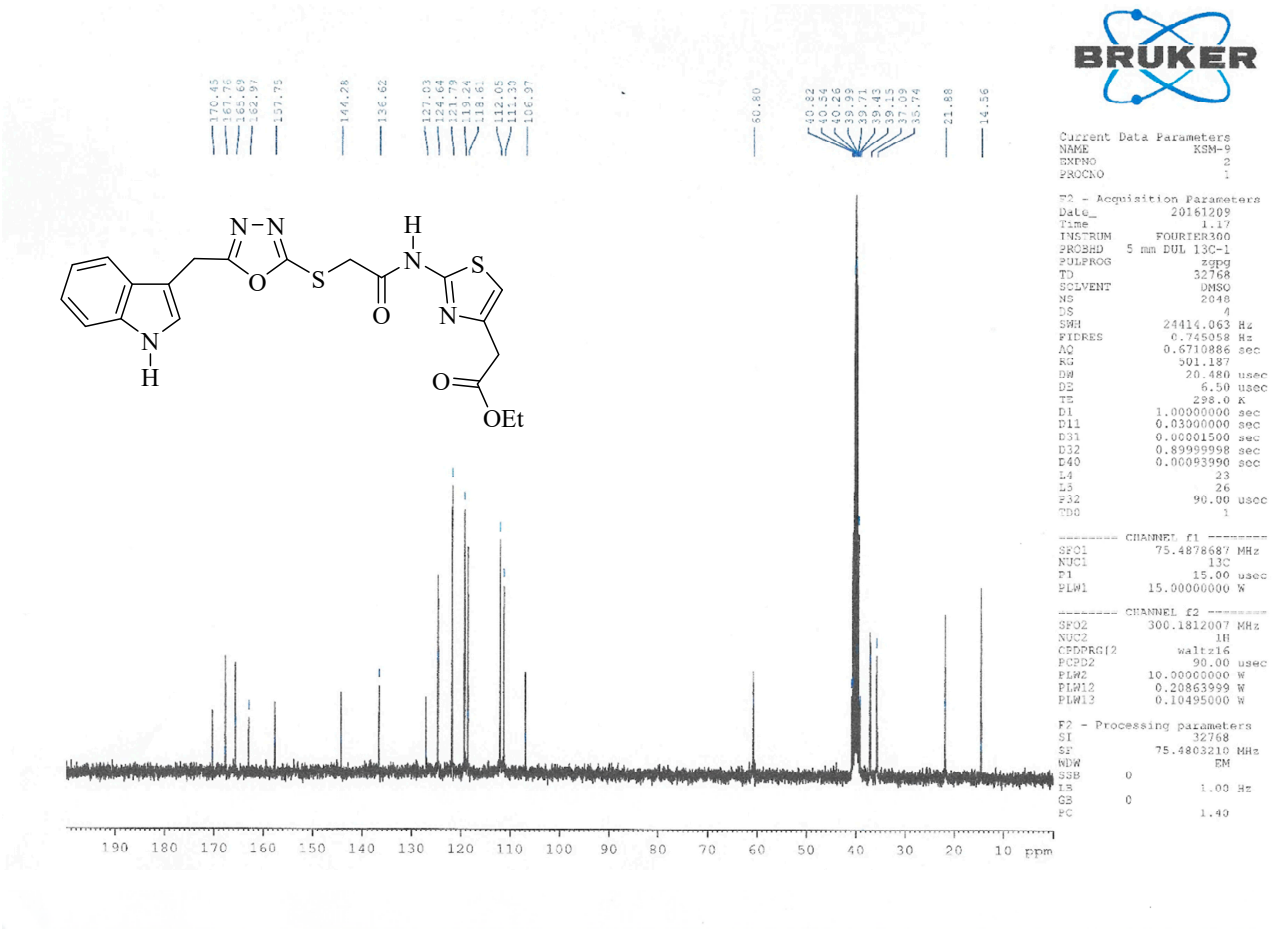


Figure S35. ^{13}C NMR spectrum of compound **2i**.

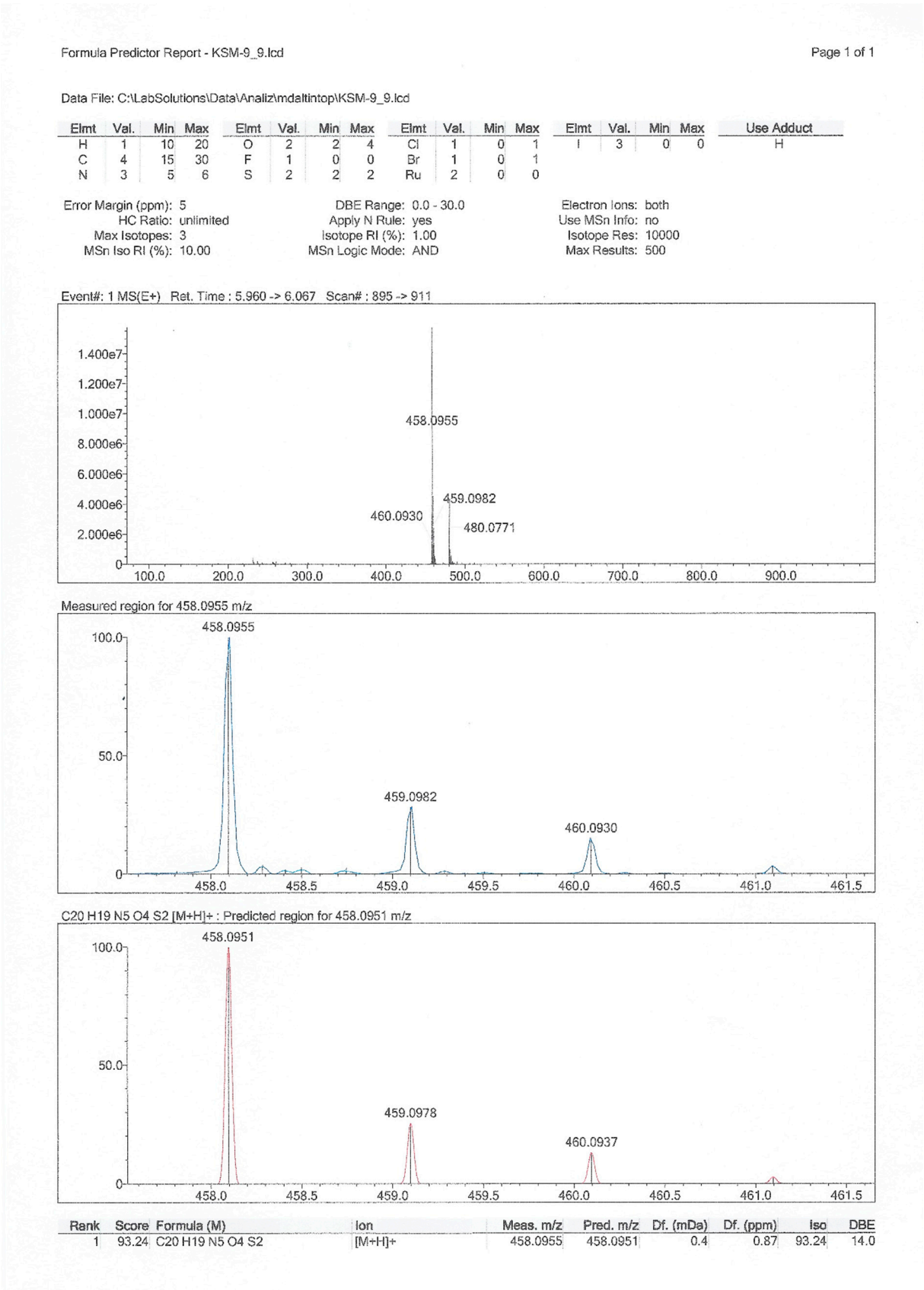


Figure S36. HRMS spectrum of compound **2i**.