Supplementary Information (SI) for RSC Advances.
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Design, Synthesis, Antimicrobial and Antioxidant Evaluation, Cytotoxicity Assessment, and Molecular Dynamics-Based Computational Studies of Novel PABA Analogues as Dual DHPS/DHFR Inhibitors

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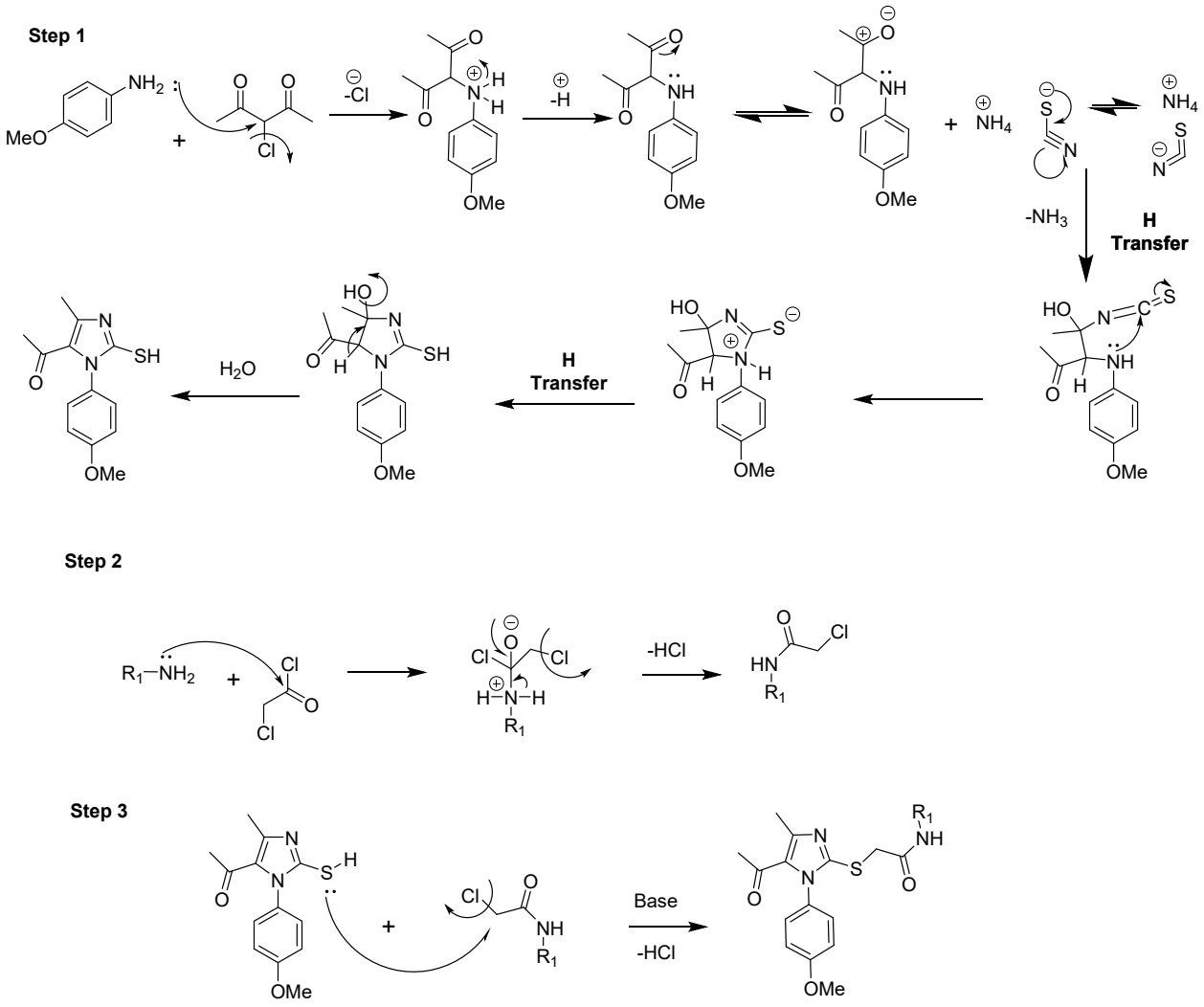
Table S1. MIC Determination against MRSA and XDR *E.coli*

Figure S1: Reaction mechansim of synthesied compounds SB1-SB7



Complete Characterization Data

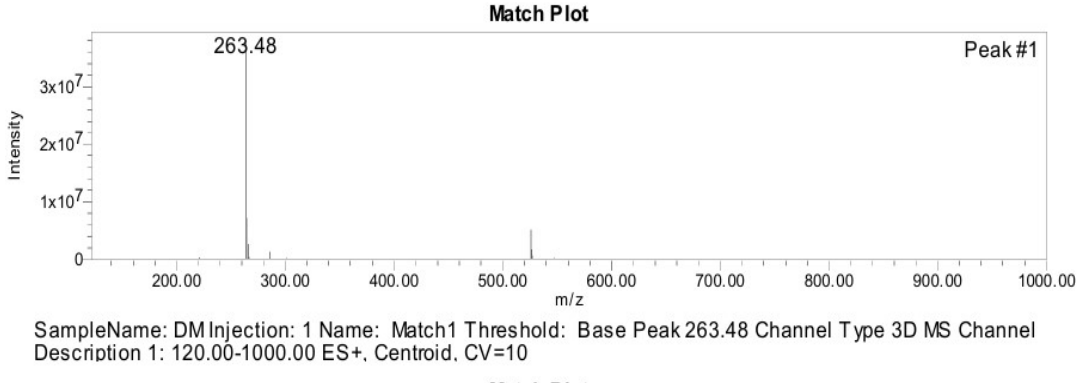


Figure S2. ESI-MS spectrum of the lead molecule

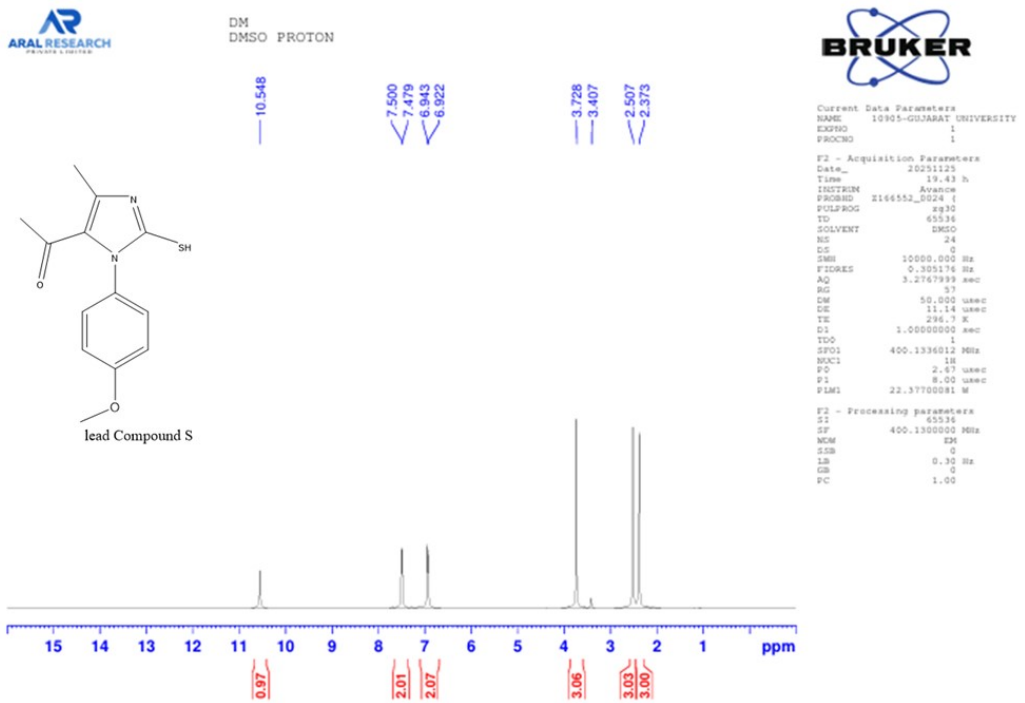


Figure S3. ^{1}H NMR spectrum of the lead molecule.

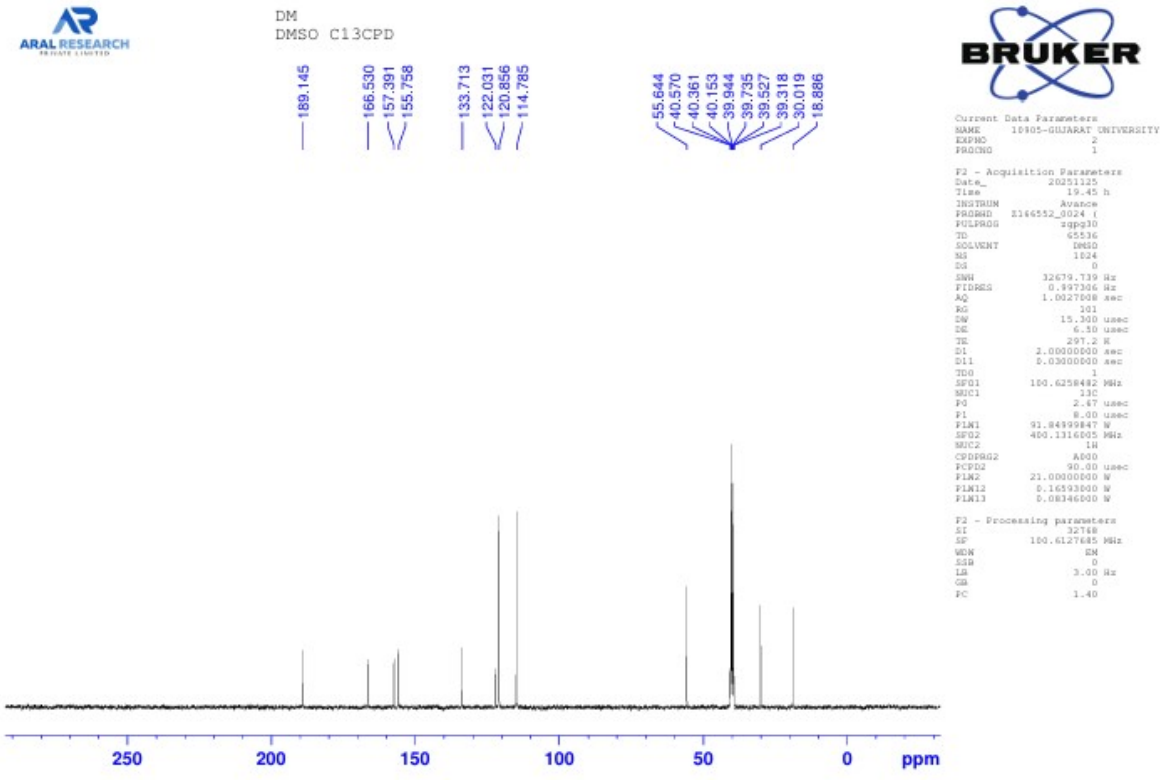


Figure S4. ^{13}C NMR spectrum of the lead molecule.

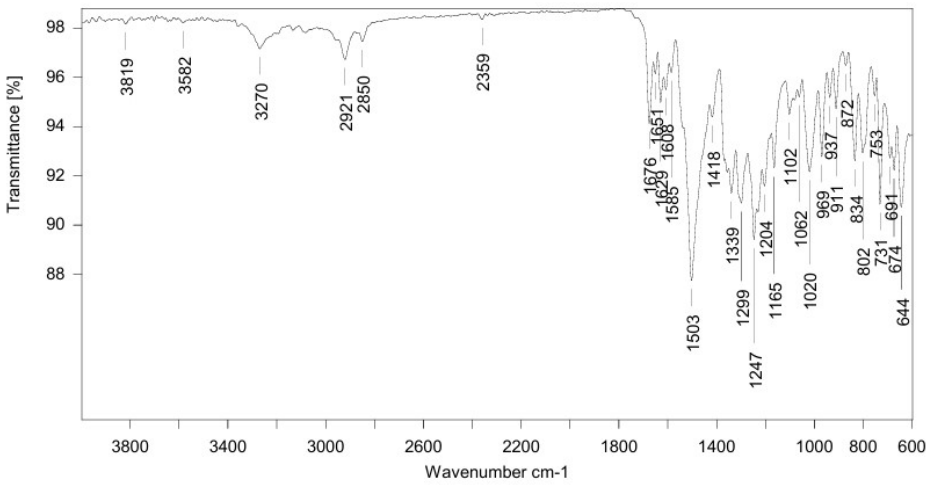


Figure S5. FTIR spectrum of SB1.

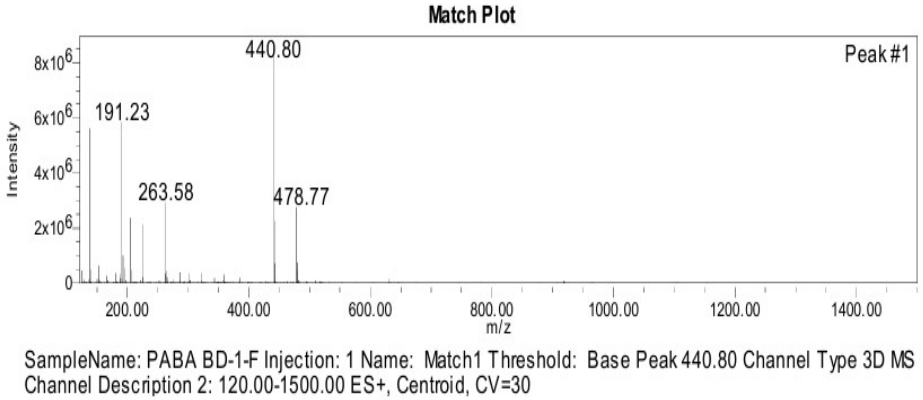


Figure S6. ESI-MS spectrum of SB1.

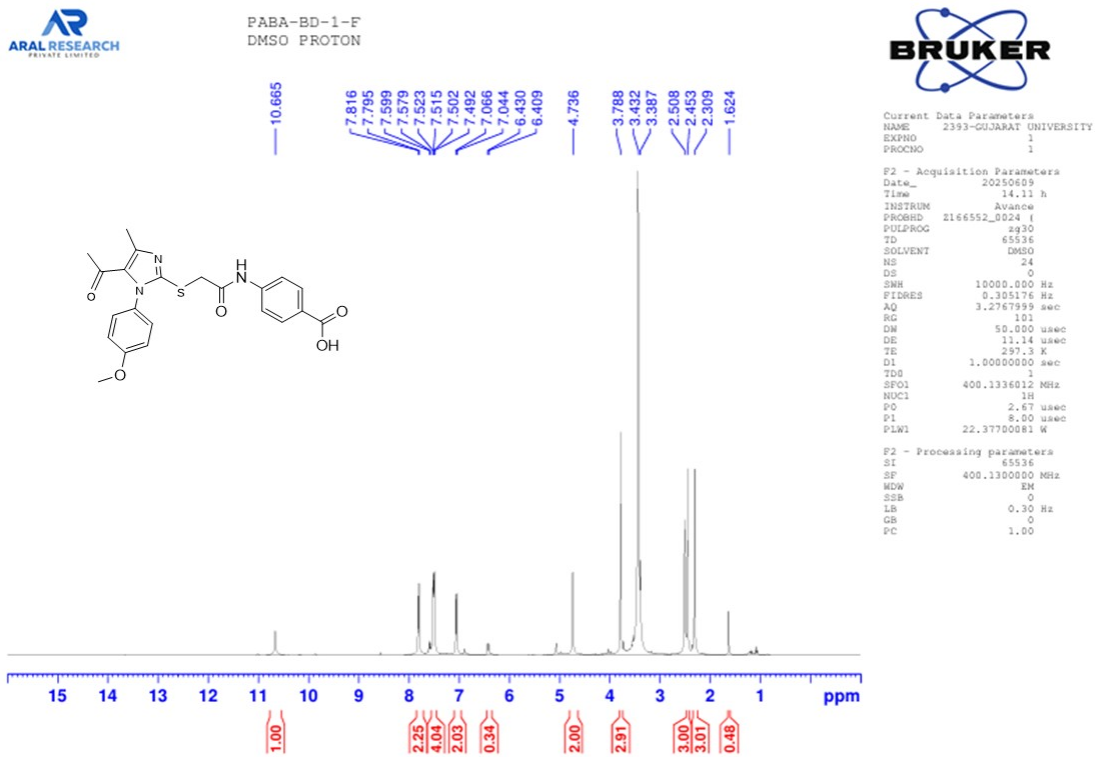


Figure S7. ^{1}H NMR spectrum of SB1.

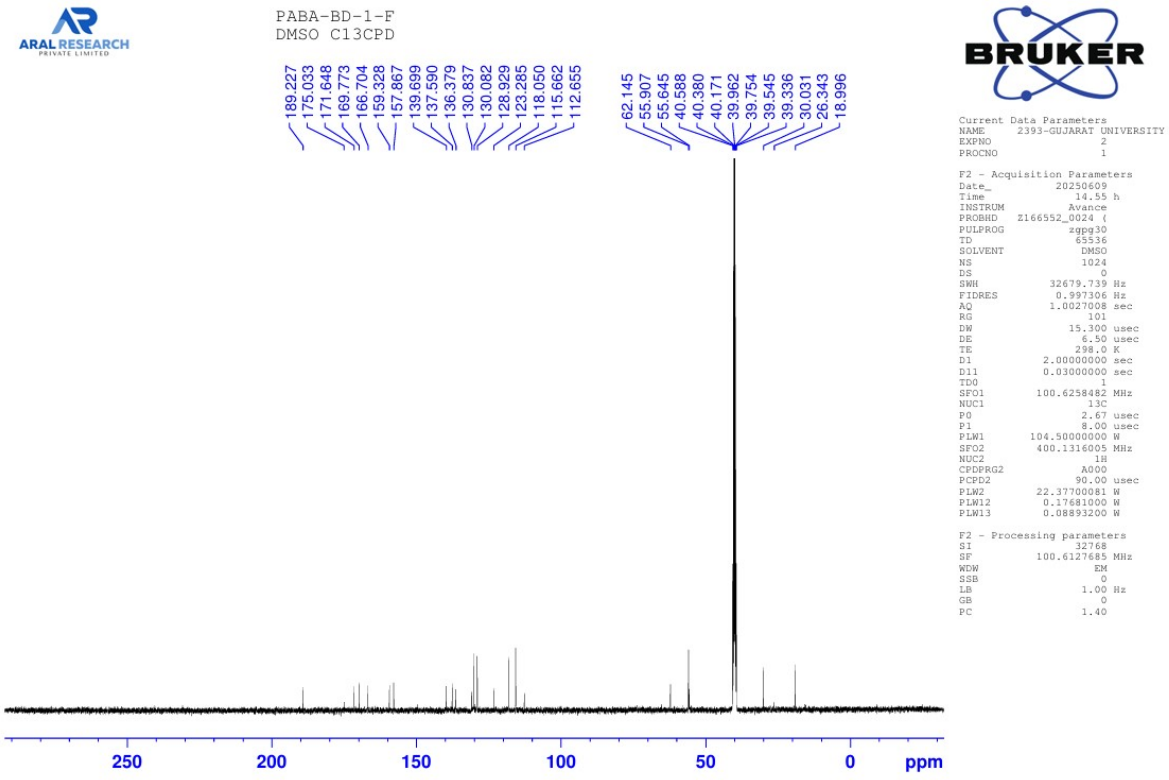
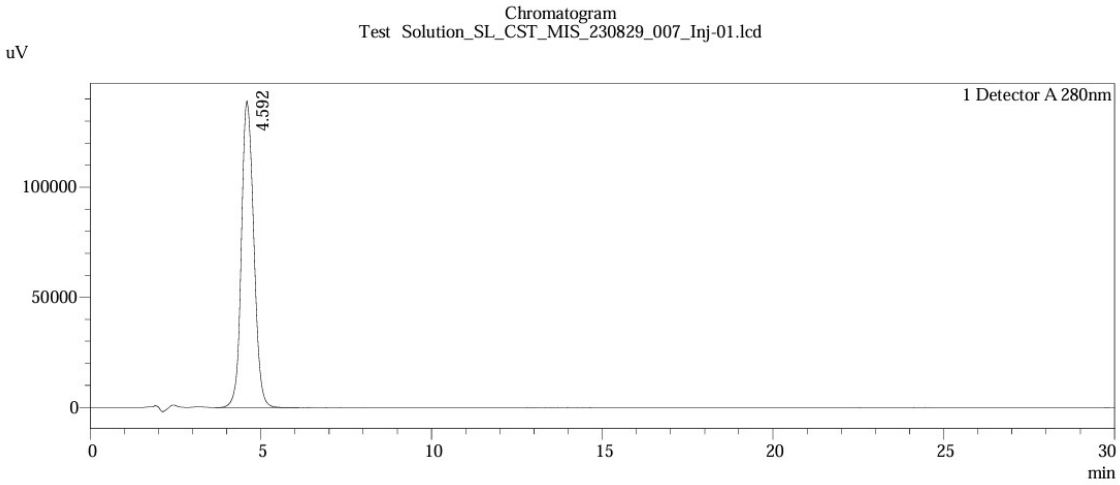


Figure S8. ^{13}C NMR spectrum of SB1.



Peak Table Test Solution_SL_CST_MIS_230829_007_Inj-01.lcd

Detector A 280nm

Peak#	Ret. Time	Name	Area	Area%	Tailing Factor	Theoretical Plates/meter(USP)
1	4.592	SB-1	3531599	100.000	1.126	5218
Total			3531599	100.000		

Figure S9: HPLC purity analysis of SB1

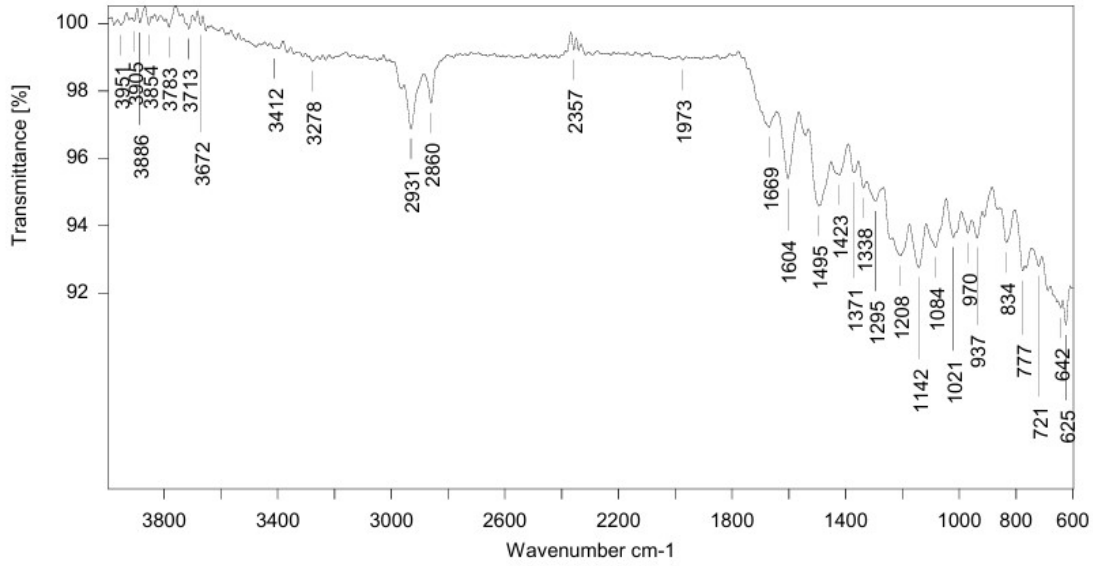


Figure S10. FTIR spectrum of SB2.

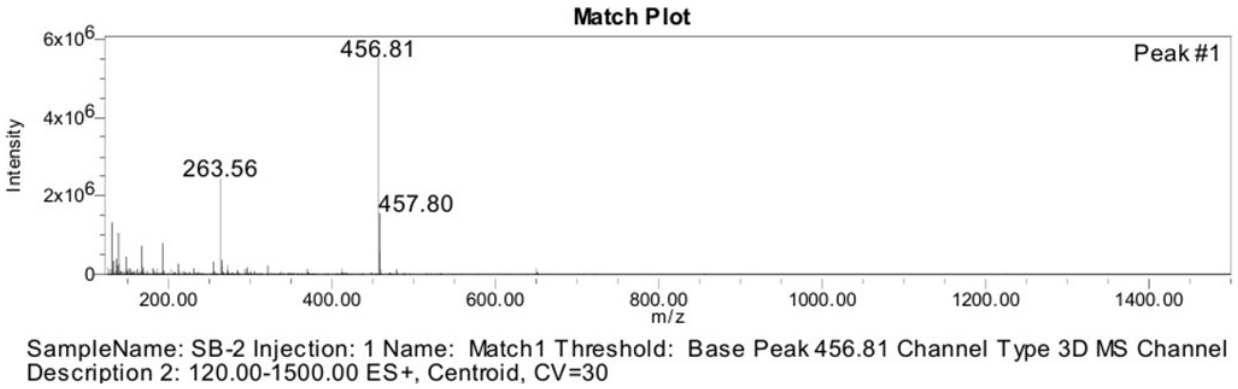


Figure S11. ESI-MS spectrum of SB2.

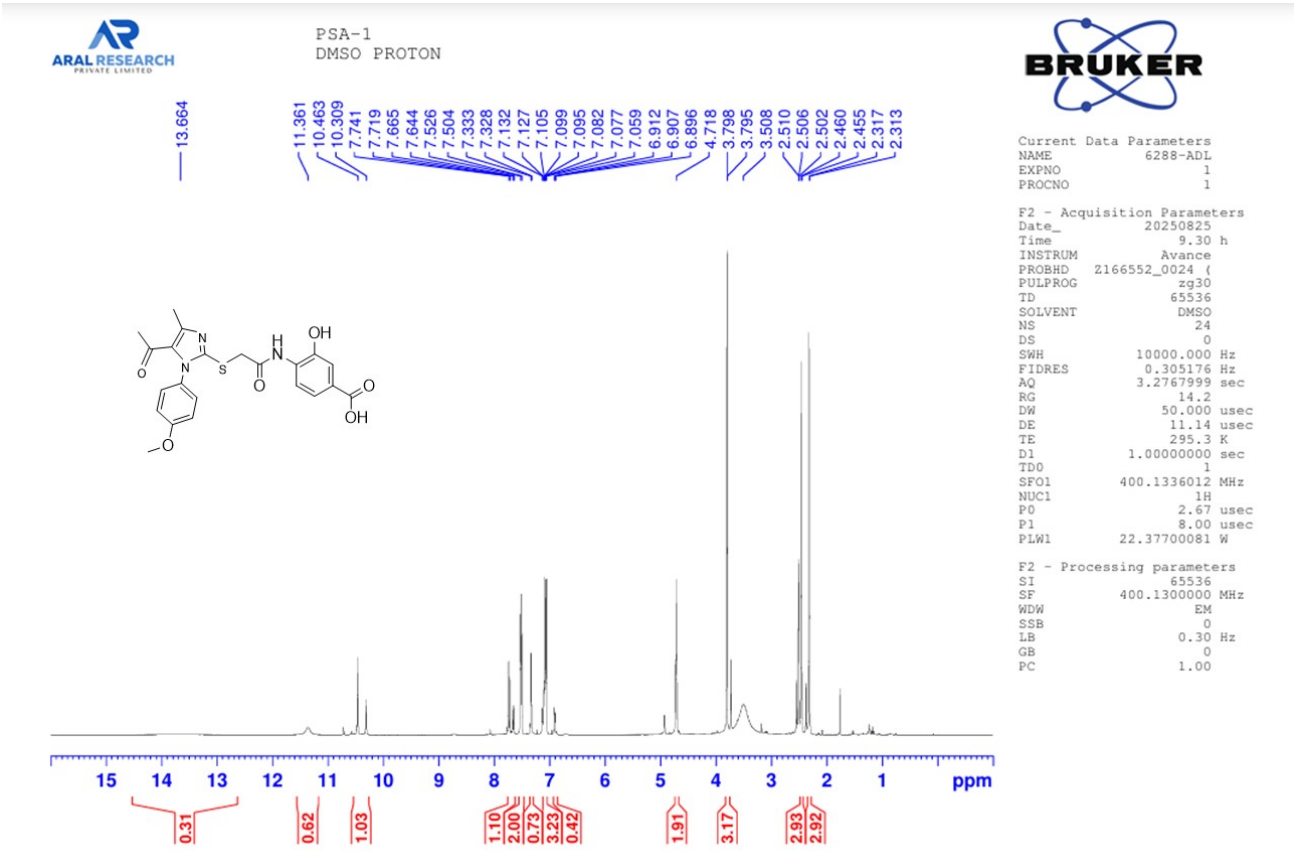


Figure S12. ^{1}H NMR spectrum of SB2.

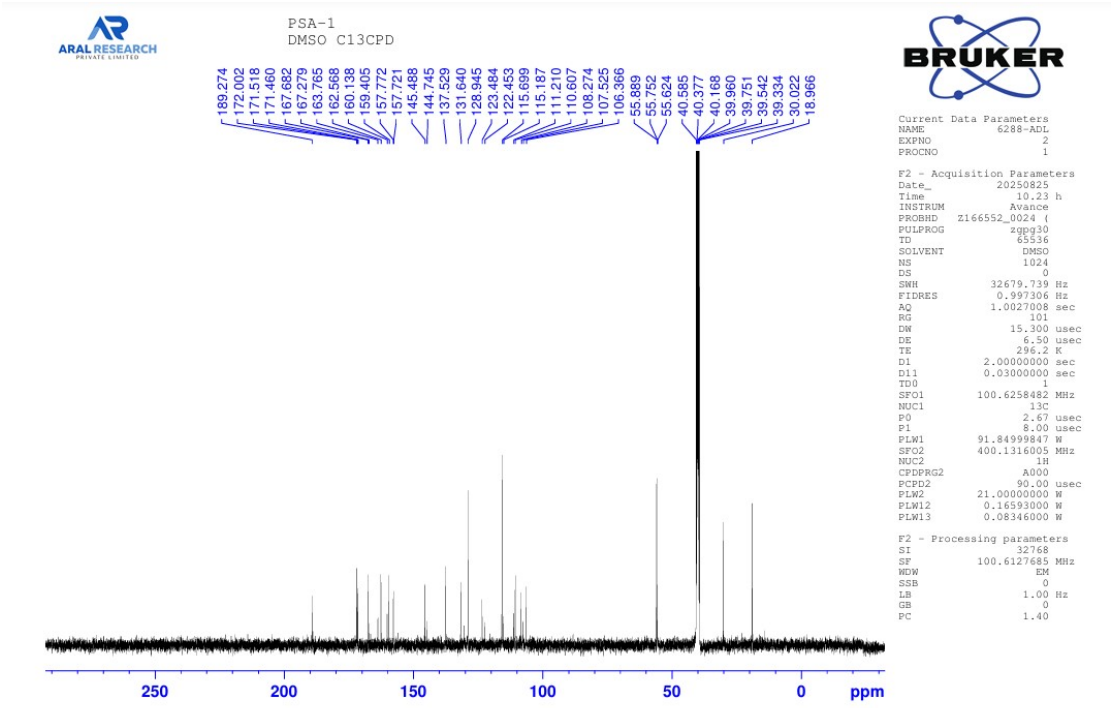
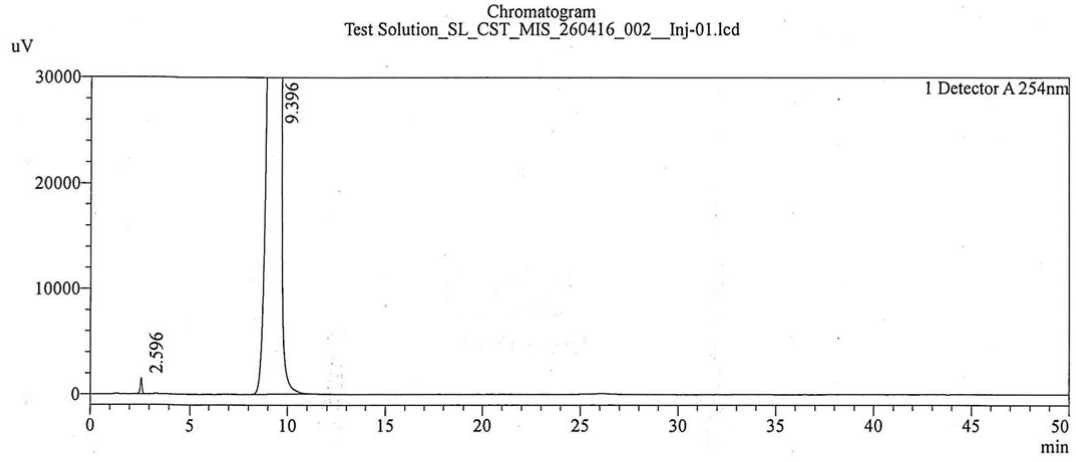


Figure S13. ^{13}C NMR spectrum of SB2.



Peak Table Test Solution_SL_CST_MIS_260416_002__Inj-01.lcd

Detector A 254nm

Peak#	Ret. Time	Name	Area	Area%	Tailing Factor	Theoretical Plates/meter(USP)
1	2.596	Impurity	9961	0.069	0.873	22404
2	9.396	SB-2	14484762	99.931	0.743	30704
Total			14494723	100.000		

Figure S14: HPLC purity assay of SB2

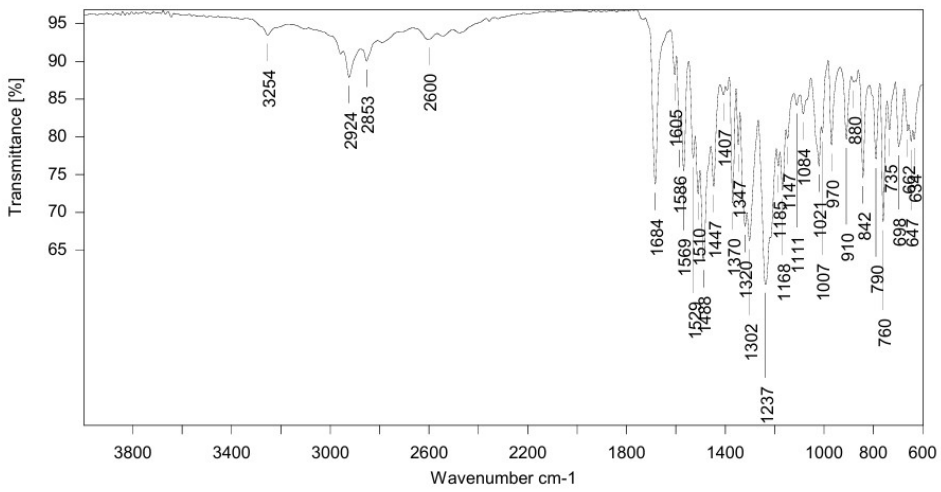


Figure S15. FTIR spectrum of SB3.

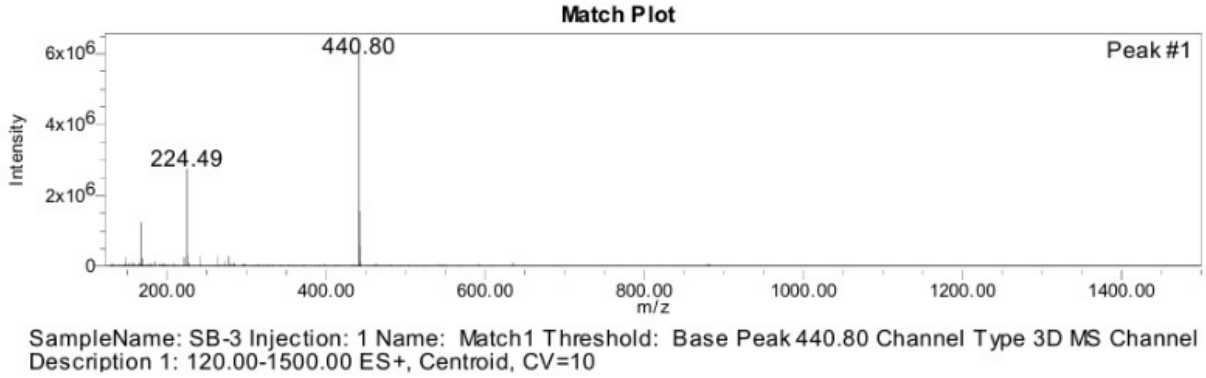


Figure S16. ESI-MS spectrum of SB3.

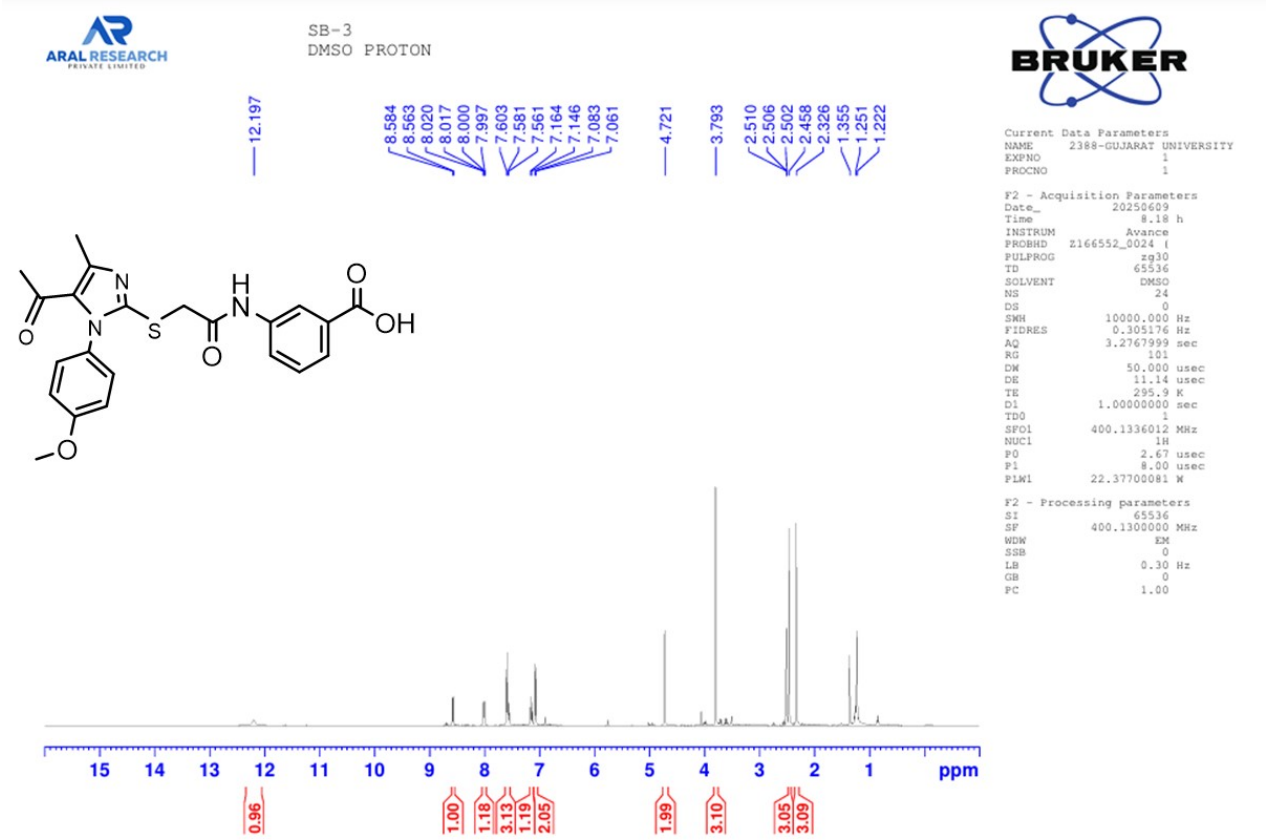


Figure S17. ^{1}H NMR spectrum of SB3.

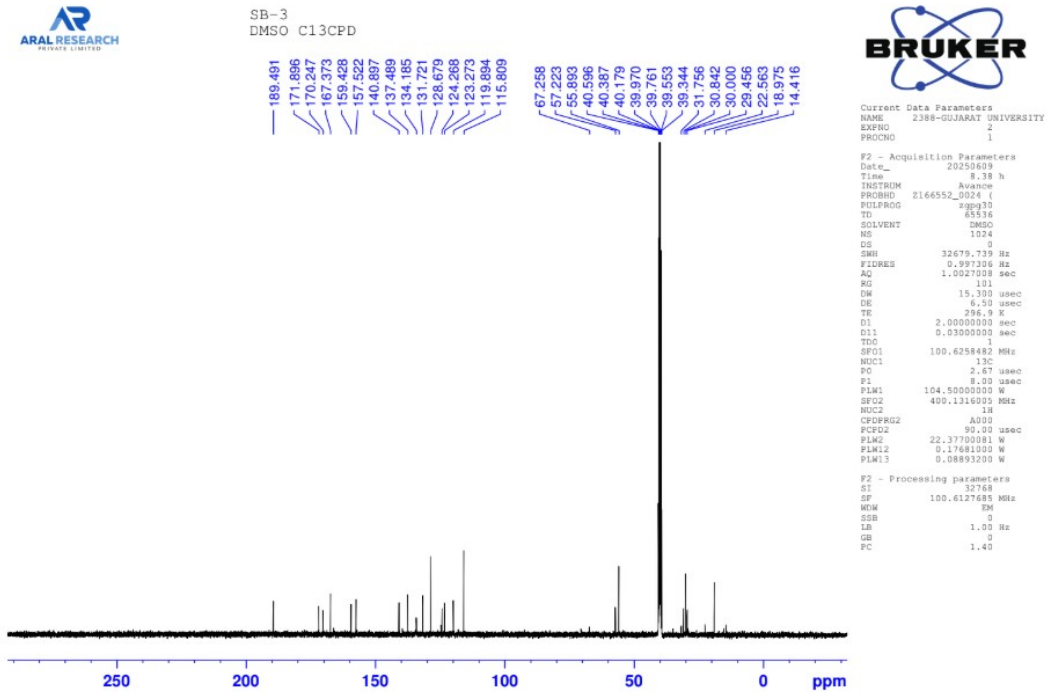
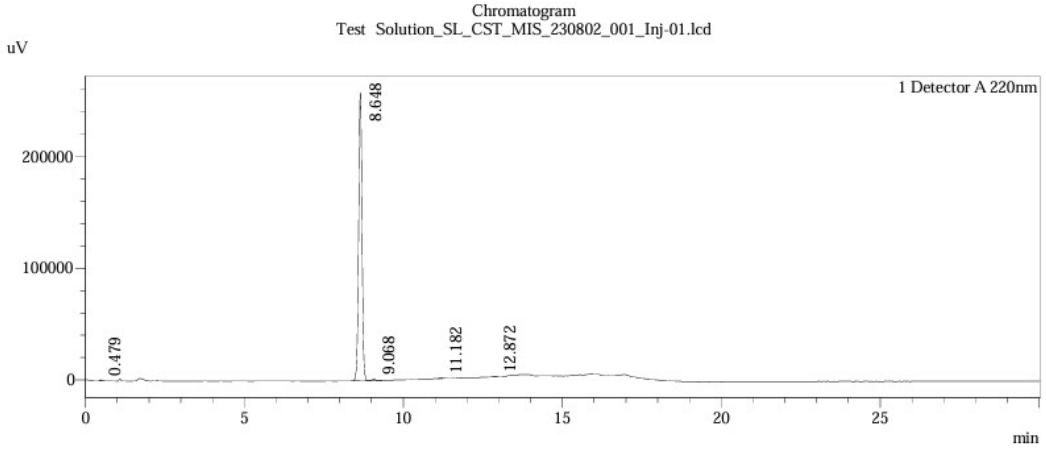


Figure S18. ^{13}C NMR spectrum of SB3.



Peak Table Test Solution_SL_CST_MIS_230802_001_Inj-01.lcd

Detector A 220nm

Peak#	Ret. Time	Name	Area	Area%	Tailing Factor	Theoretical Plates/meter(USP)
1	0.479	Unknown	3302	0.172	1.399	2014
2	8.648	SB-3	1903109	99.109	0.994	189378
3	9.068	Unknown	9104	0.474	1.192	272445
4	11.182	Unknown	2880	0.150	1.144	700962
5	12.872	Unknown	1826	0.095	1.014	821089
Total			1920221	100.000		

Figure S19. HPLC purity assay of SB3

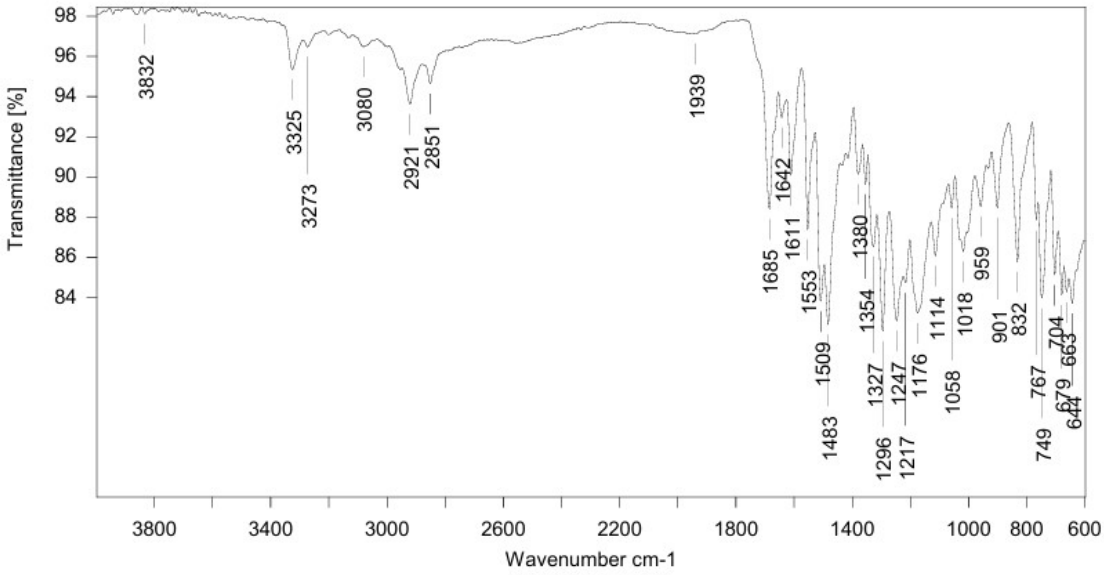


Figure S20. FTIR spectrum of SB4.

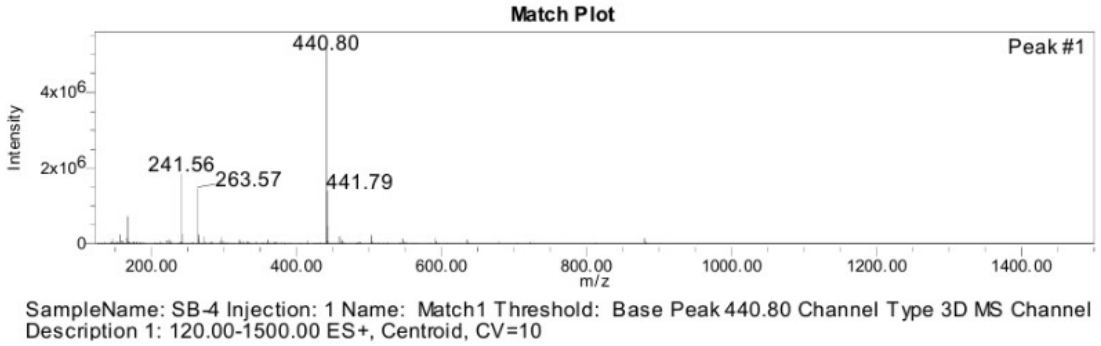


Figure S21. ESI-MS spectrum of SB4.

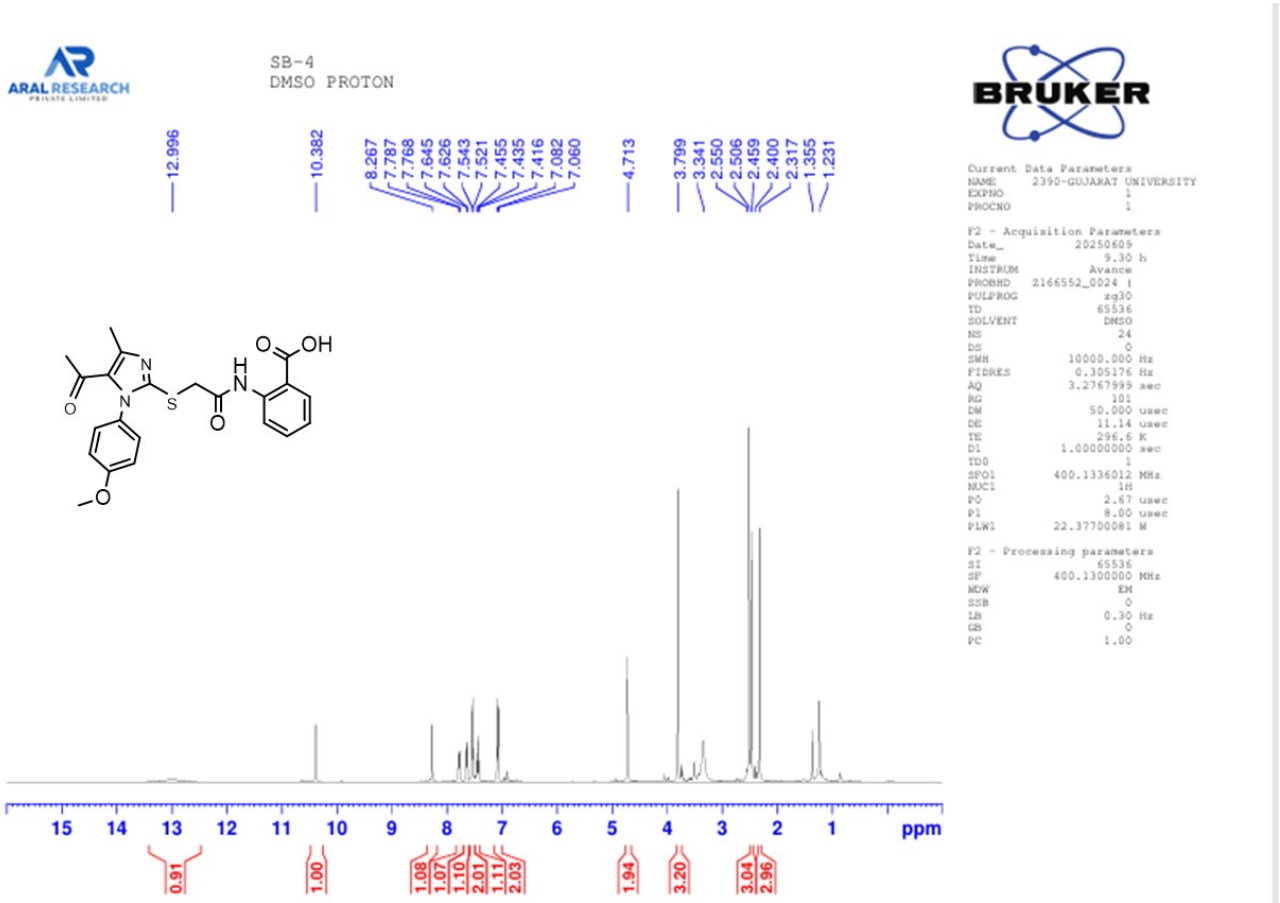


Figure S22. ^{1}H NMR spectrum of SB4.

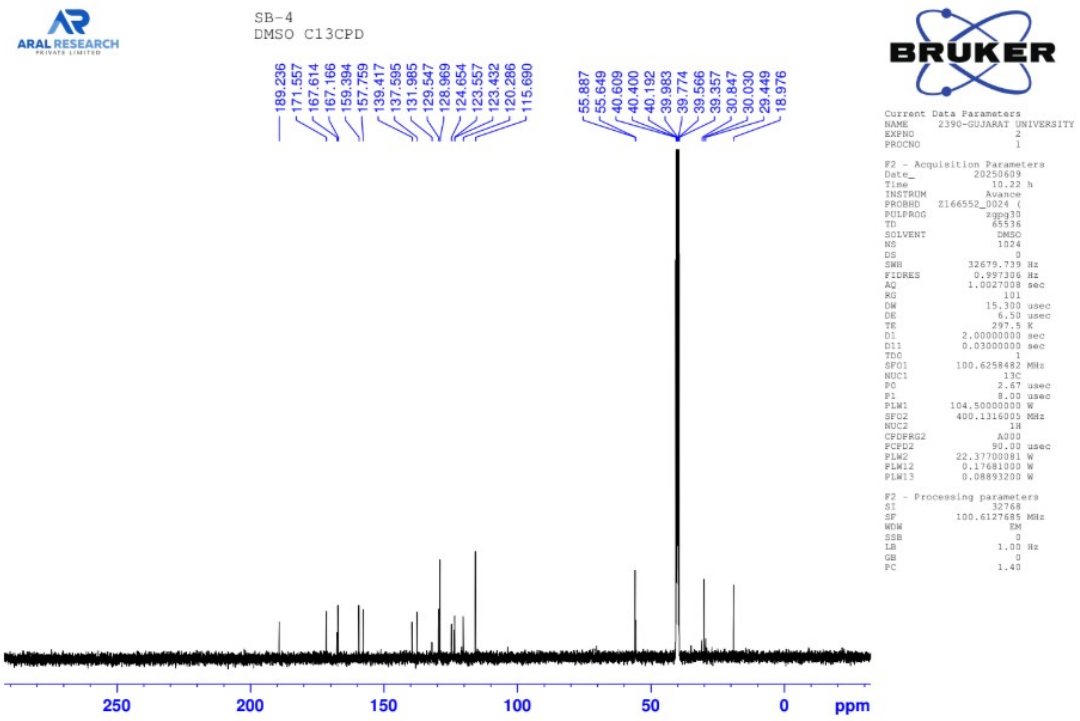
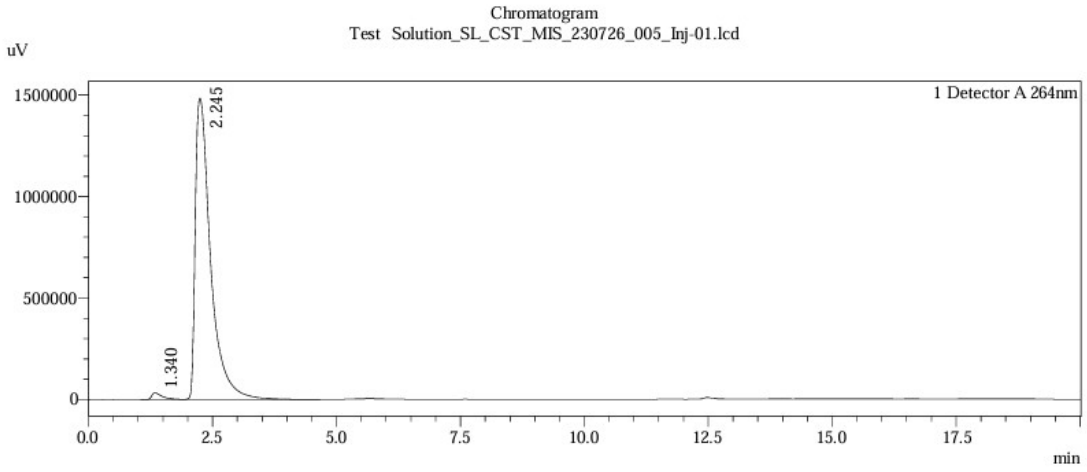


Figure S23. ^{13}C NMR spectrum of SB4.



Peak Table Test Solution_SL_CST_MIS_230726_005_Inj-01.lcd

Detector A 264nm

Peak#	Ret. Time	Name	Area	Area%	Tailing Factor	Theoretical Plates/meter(USP)
1	1.340	Impurity	463051	1.431	2.088	1507
2	2.245	SB-4	31889161	98.569	2.374	2112
Total			32352212	100.000		

Figure S24. HPLC purity assay of SB4

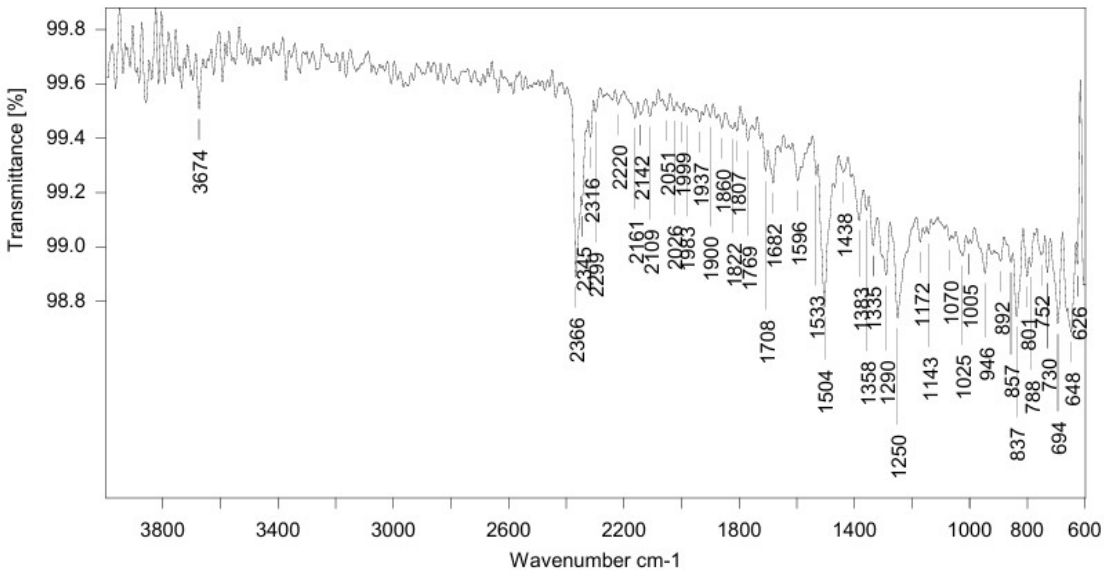


Figure S25. FTIR spectrum of SB5.

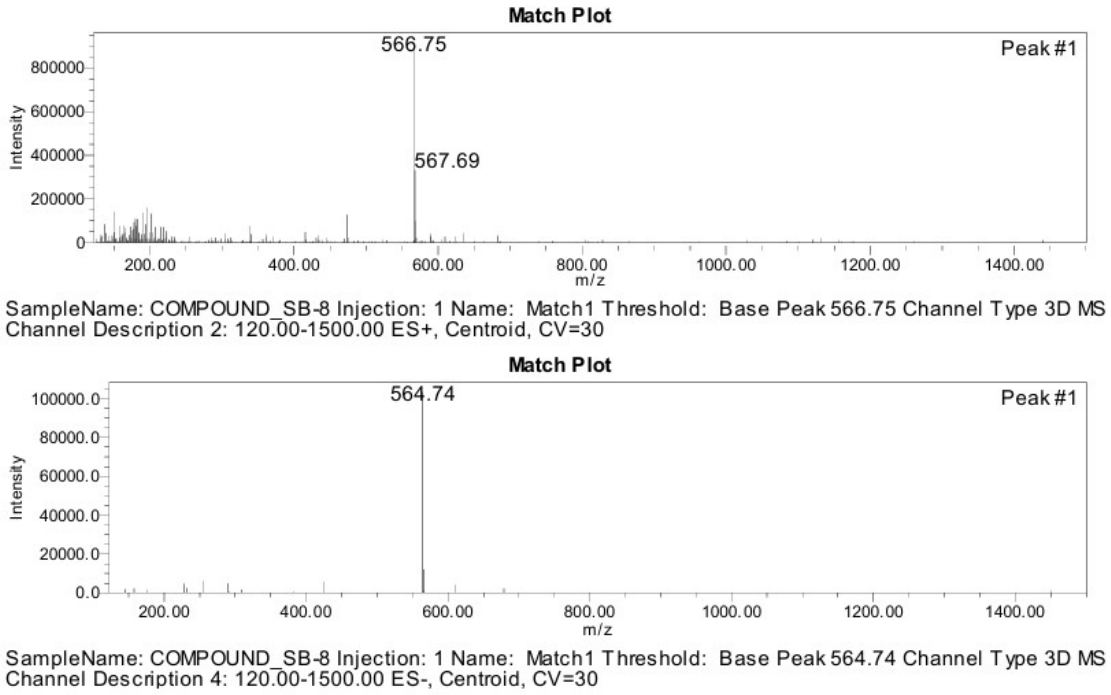


Figure S26. ESI-MS spectrum of SB5.

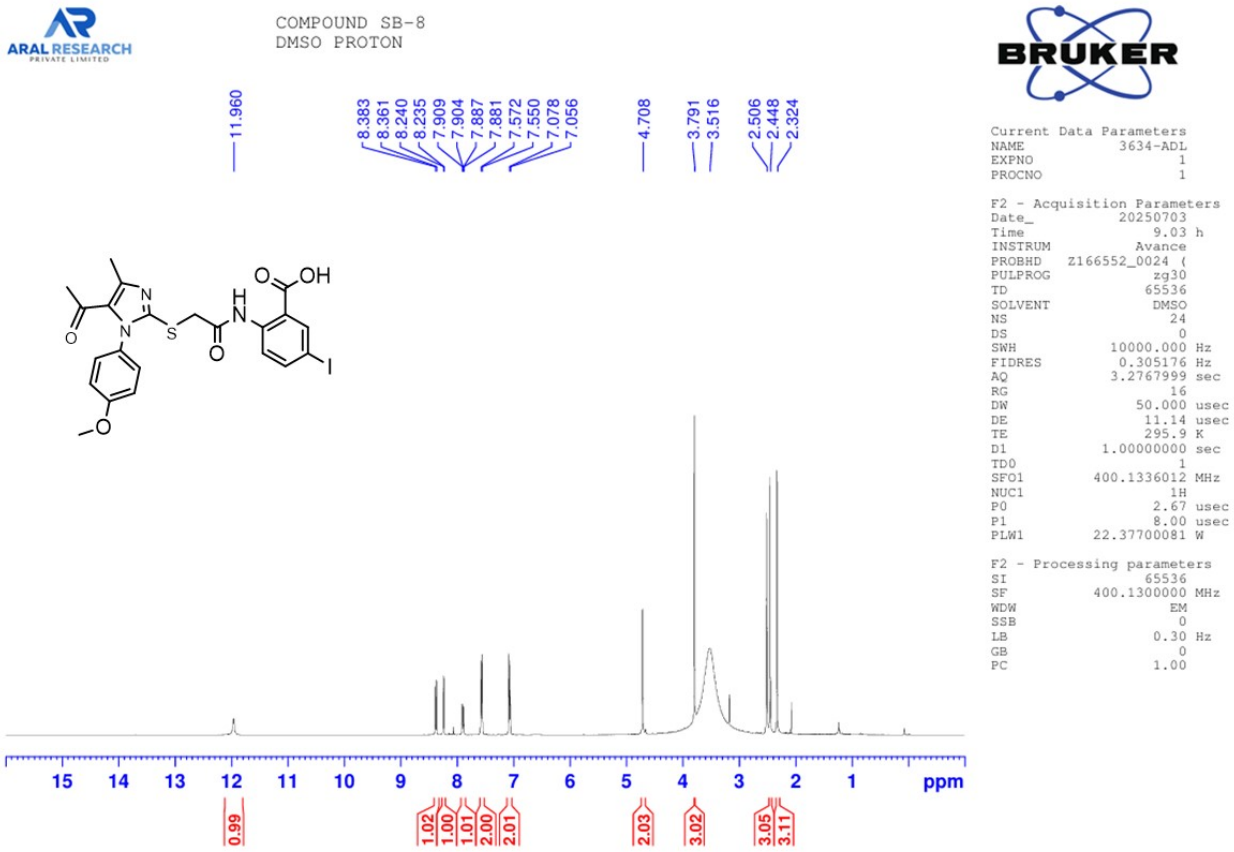


Figure S27. ^{1}H NMR spectrum of SB5.

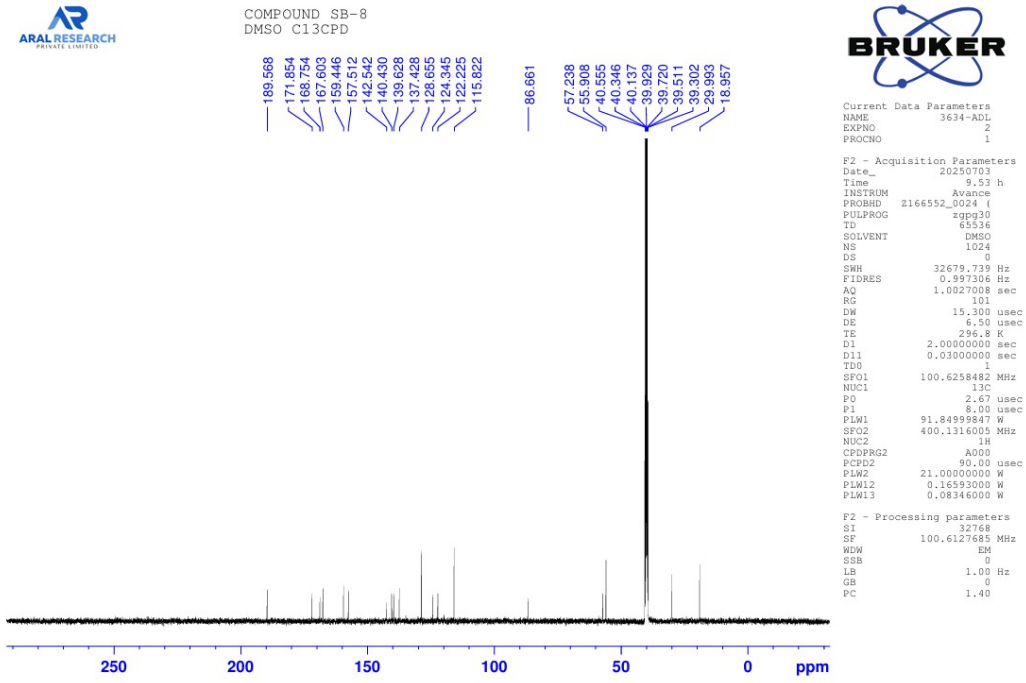
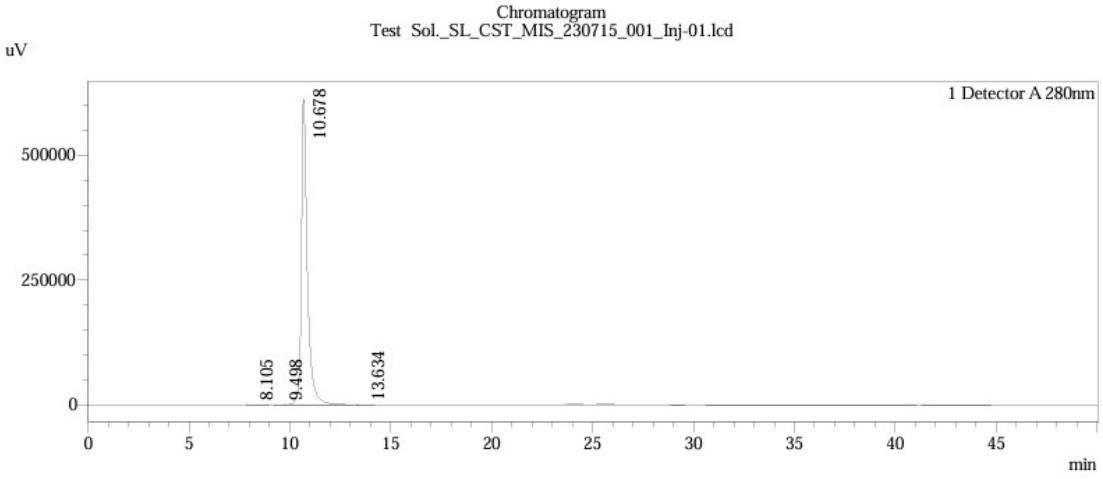


Figure S28. ^{13}C NMR spectrum of SB5.



Peak Table Test Sol._SL_CST_MIS_230715_001_Inj-01.lcd

Detector A 280nm

Peak#	Ret. Time	Name	Area	Area%	Tailing Factor	Theoretical Plates/meter(USP)
1	8.105	Unknown	7435	0.059	2.360	25357
2	9.498	Unknown	2799	0.022	0.957	70927
3	10.678	SB-5	12593152	99.896	1.550	52140
4	13.634	Unknown	2824	0.022	1.618	110539
Total			12606211	100.000		

Figure S29. HPLC purity assay of SB5

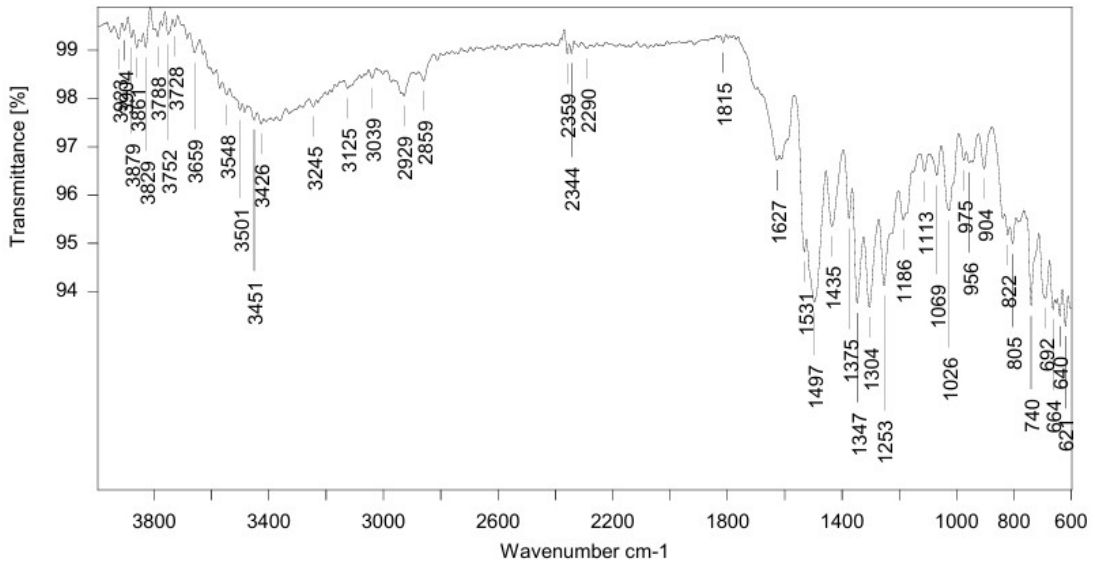


Figure S30. FTIR spectrum of SB6.

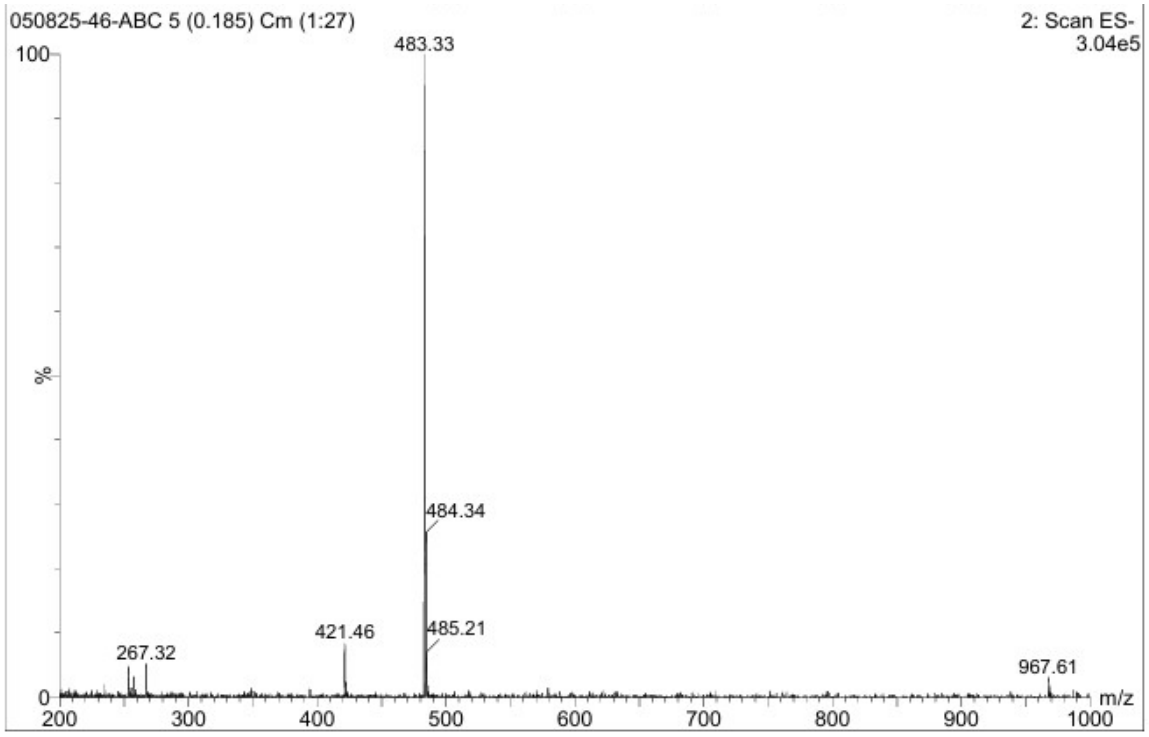


Figure S31. ESI-MS spectrum of SB6.

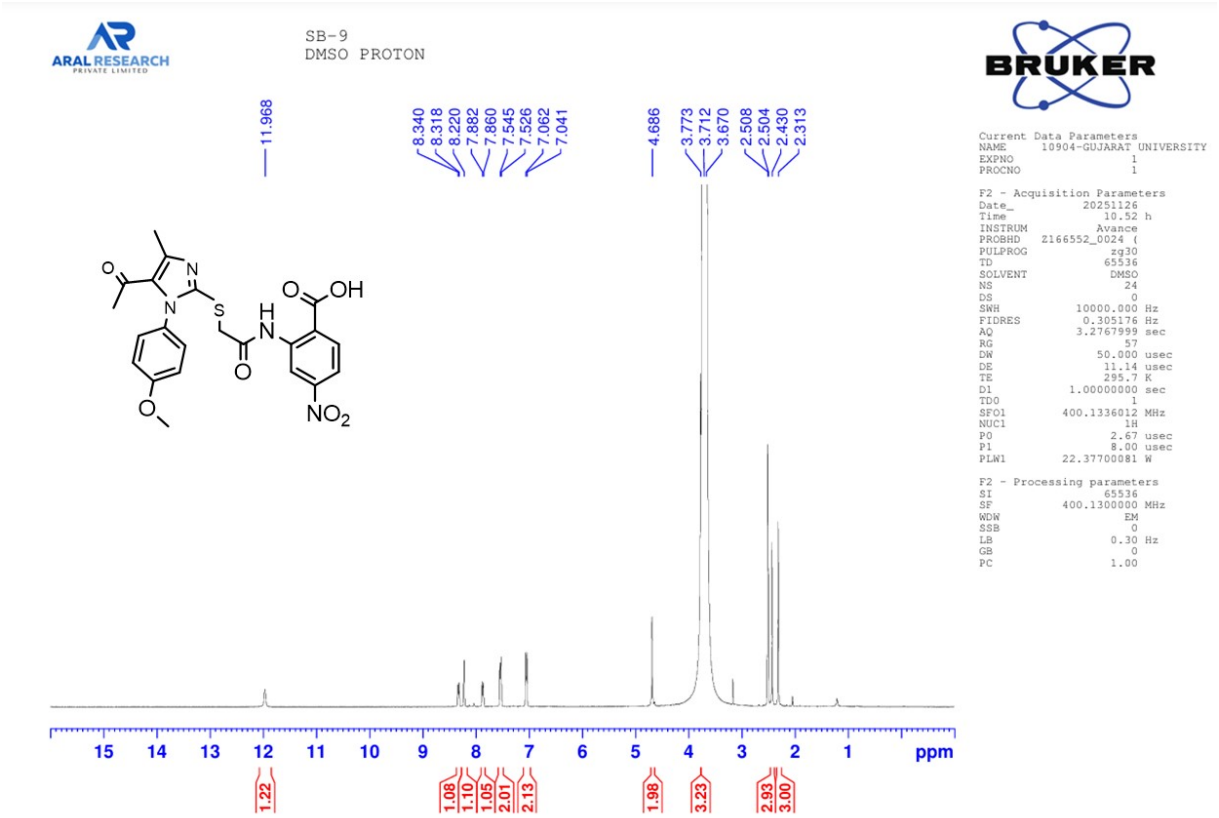


Figure S32. ^{1}H NMR spectrum of SB6.

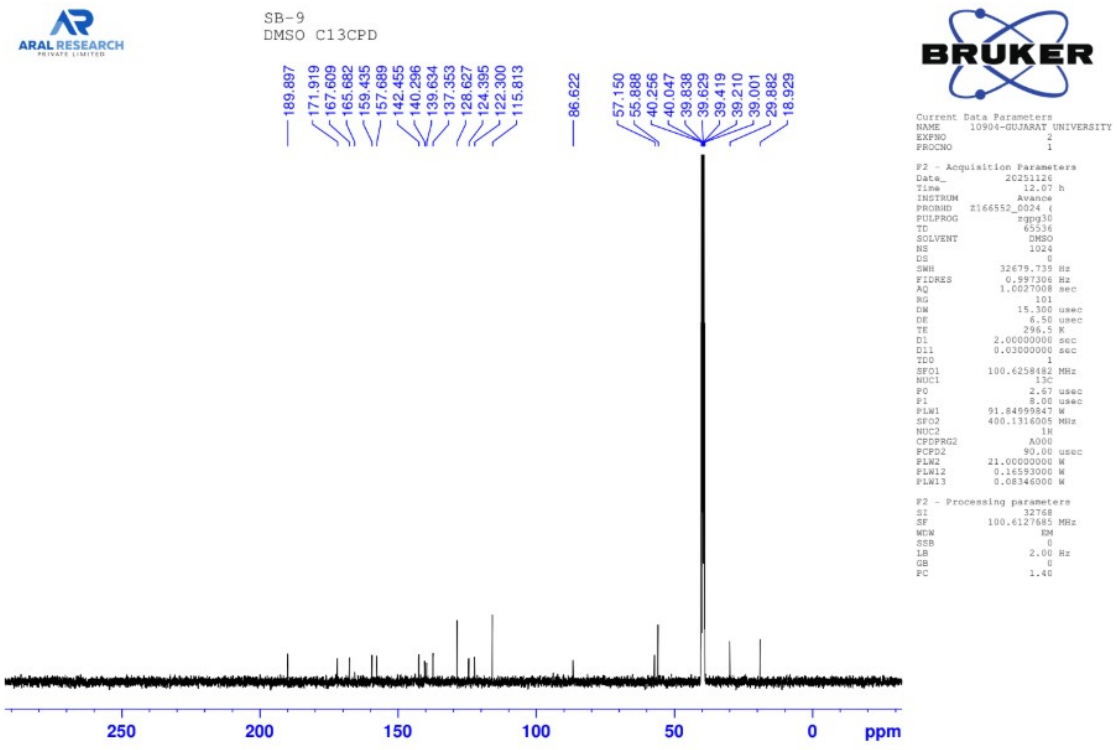
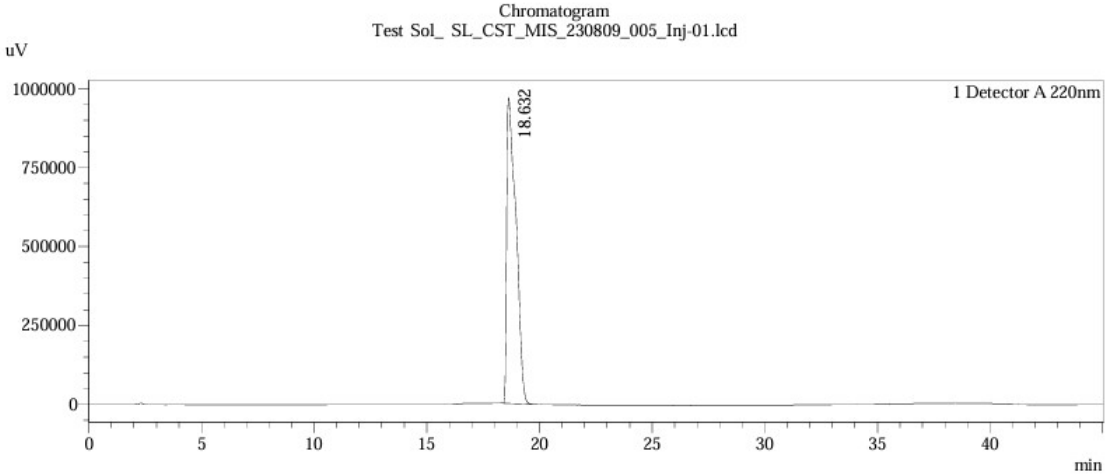


Figure S33. ^{13}C NMR spectrum of SB6.



Peak Table Test Sol_ SL_CST_MIS_230809_005_Inj-01.lcd

Detector A 220nm

Peak#	Ret. Time	Name	Area	Area%	Tailing Factor	Theoretical Plates/meter(USP)
1	18.632	SB-6	27547040	100.000	2.582	59916
Total			27547040	100.000		

Figure S34. HPLC purity assay of SB6

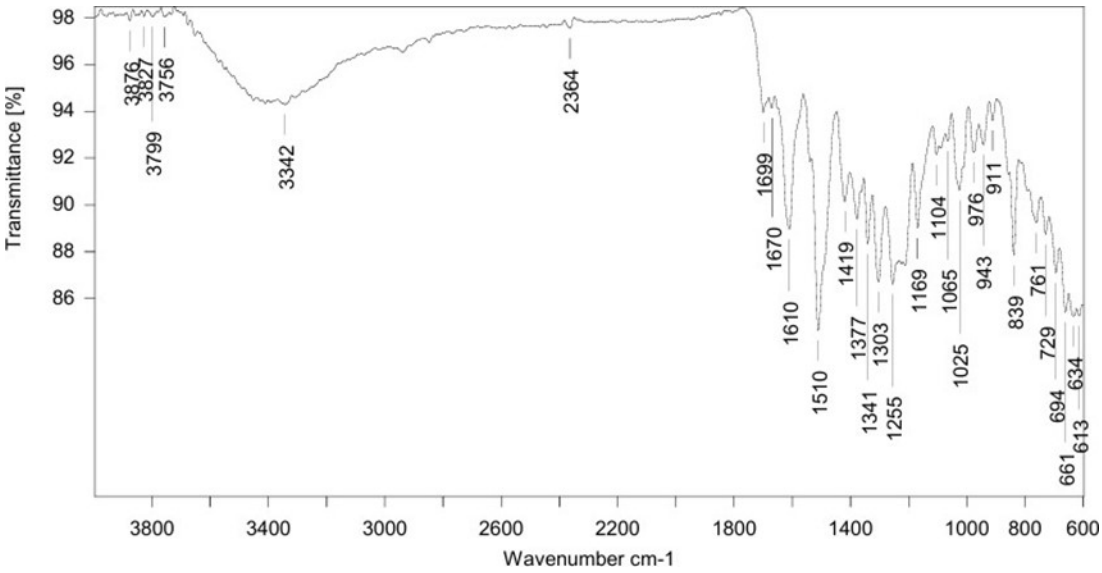


Figure S35. FTIR spectrum of SB7.

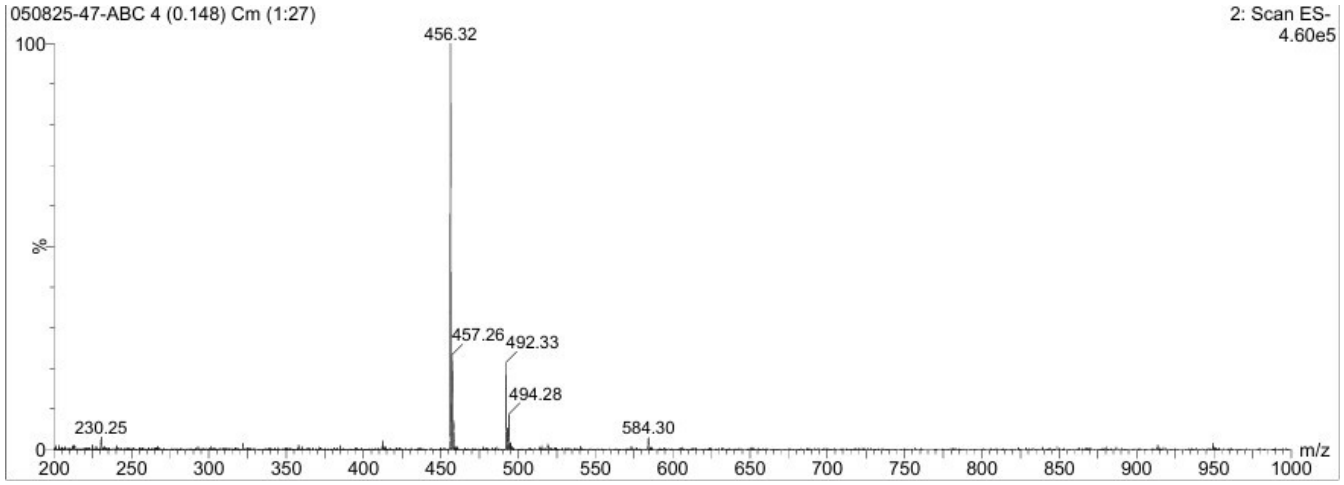


Figure S36. ESI-MS spectrum of SB7.

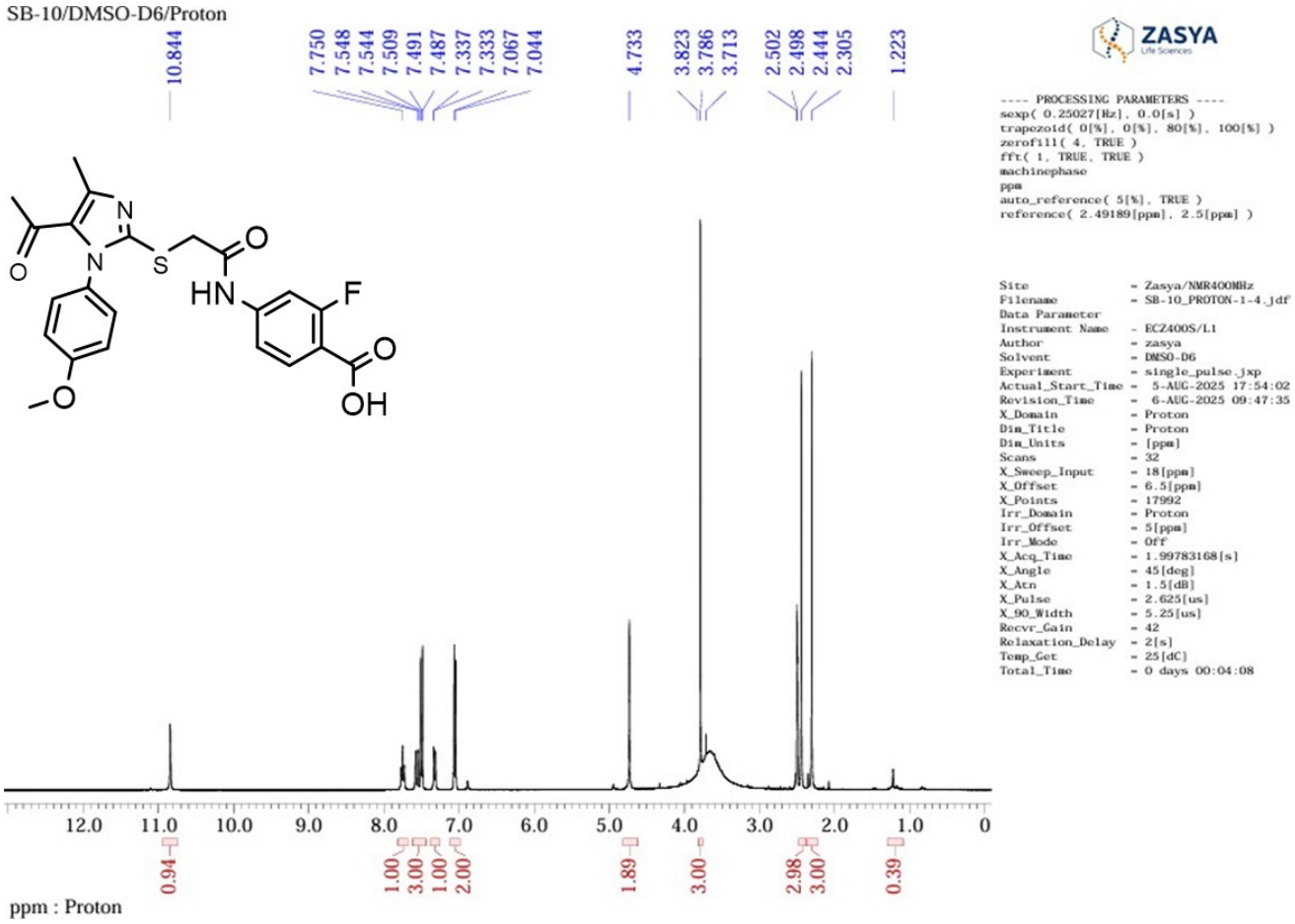


Figure S37. ^{1}H NMR spectrum of SB7.

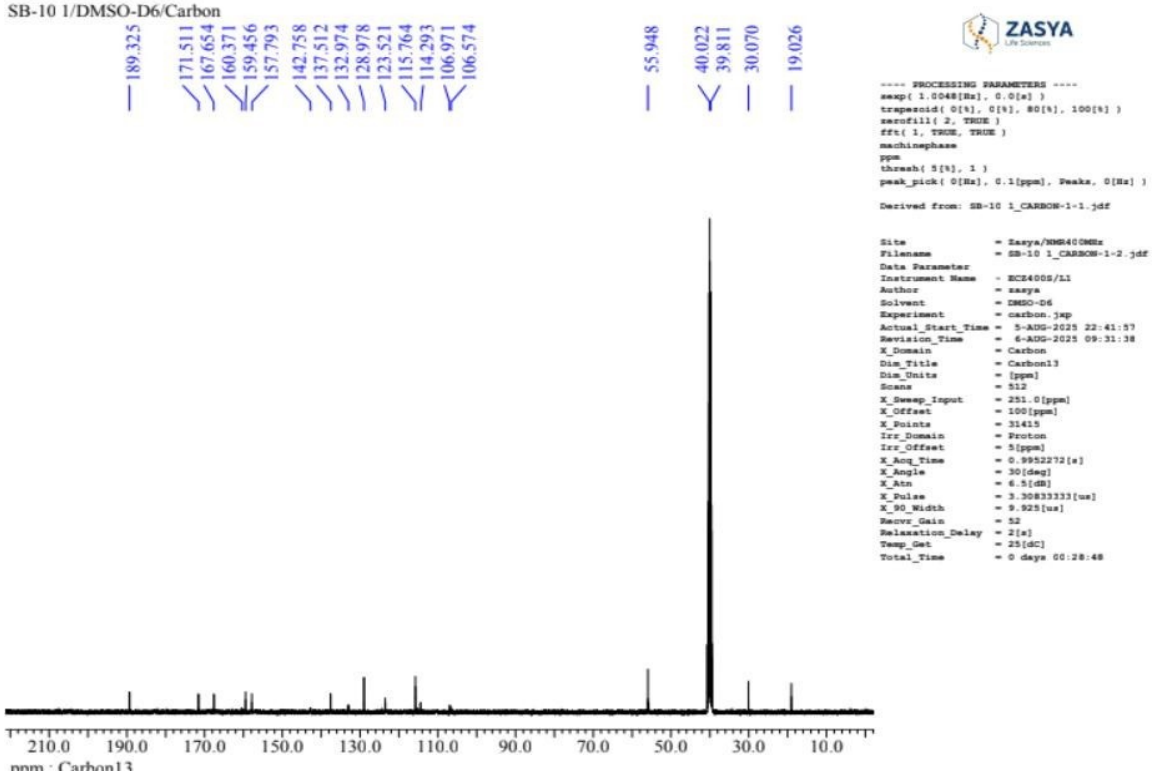


Figure S38. ^{13}C NMR spectrum of SB7.

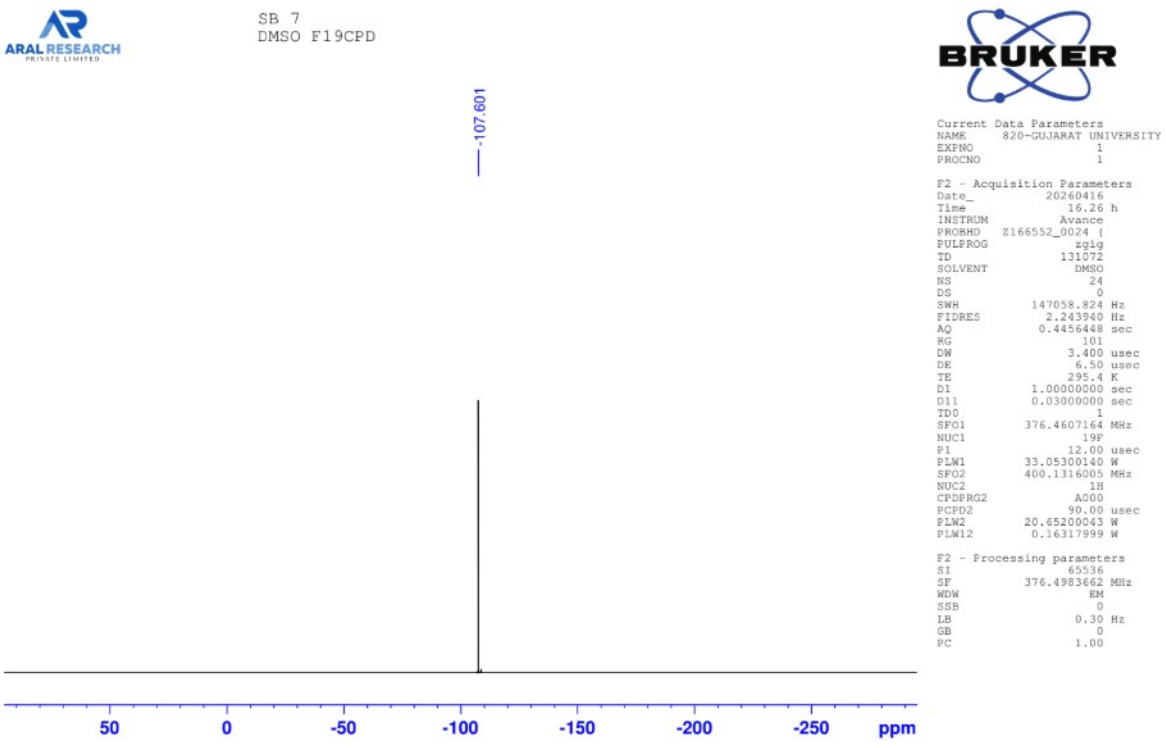
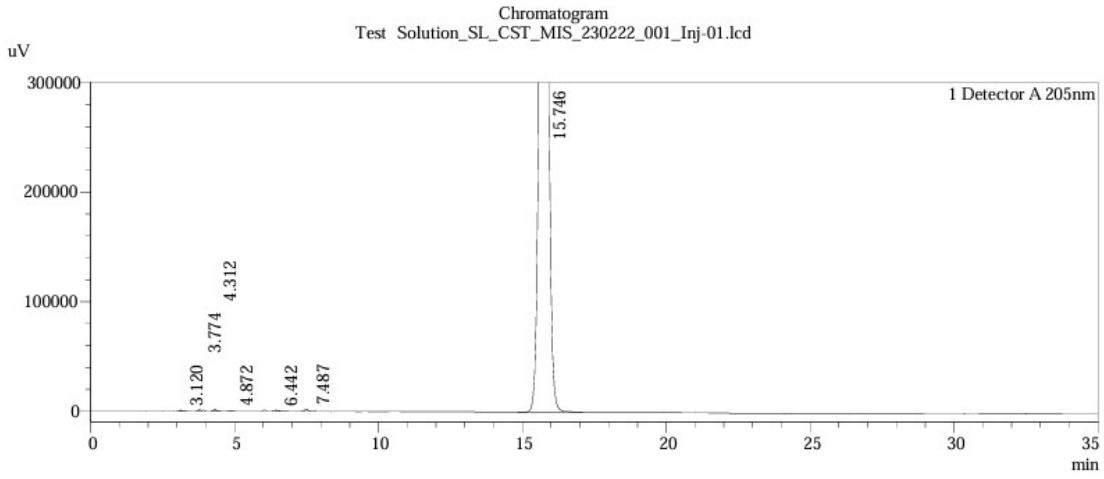


Figure S39. ^{19}F NMR spectrum of SB7

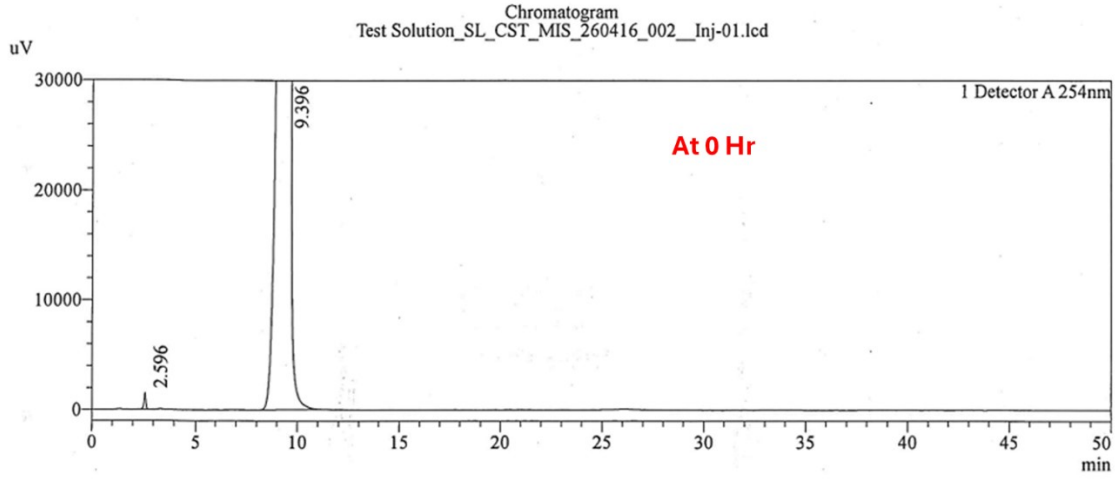


Peak Table Test Solution_SL_CST_MIS_230222_001_Inj-01.lcd

Detector A 205nm

Peak#	Ret. Time	Name	Area	Area%	Tailing Factor	Theoretical Plates/meter(USP)
1	3.120	Unknown Impurity	5847	0.035	1.367	43893
2	3.774	Unknown Impurity	5497	0.033	1.013	79346
3	4.312	Unknown Impurity	11209	0.068	1.401	65100
4	4.872	Unknown Impurity	4534	0.027	1.050	72315
5	6.442	Unknown Impurity	5691	0.034	1.093	114580
6	7.487	Unknown Impurity	16140	0.097	1.102	117552
7	15.746	SB-7	16527980	99.705	1.021	109606
Total			16576898	100.000		

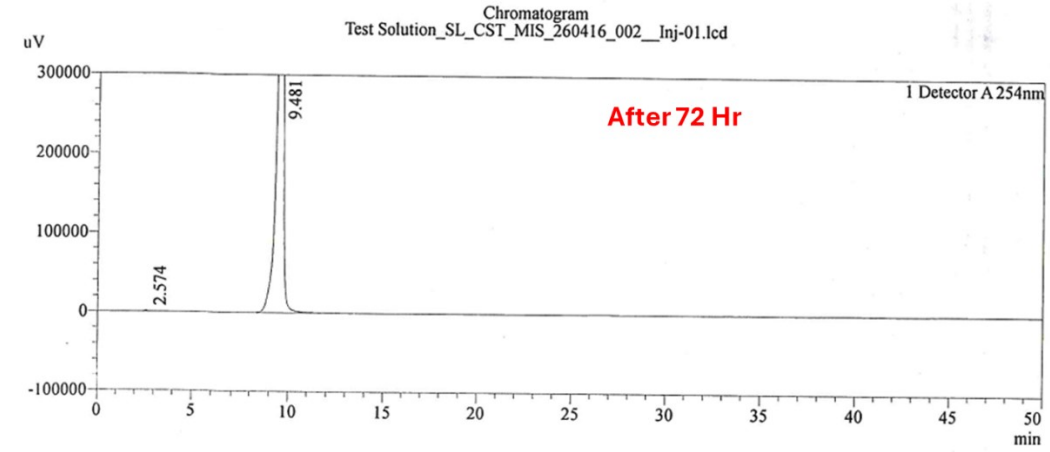
Figure S40. HPLC purity assay of SB7



Peak Table Test Solution_SL_CST_MIS_260416_002__Inj-01.lcd

Detector A 254nm

Peak#	Ret. Time	Name	Area	Area%	Tailing Factor	Theoretical Plates/meter(USP)
1	2.596	Impurity	9961	0.069	0.873	22404
2	9.396	SB-2	14484762	99.931	0.743	30704
Total			14494723	100.000		



Peak Table Test Solution_SL_CST_MIS_260416_002__Inj-01.lcd

Detector A 254nm

Peak#	Ret. Time	Name	Area	Area%	Tailing Factor	Theoretical Plates/meter(USP)
1	2.574	Impurity	9578	0.067	0.956	22506
2	9.481	SB-2	14372988	99.933	0.837	34338
Total			14382566	100.000		

Figure S41: HPLC stability assay for SB2

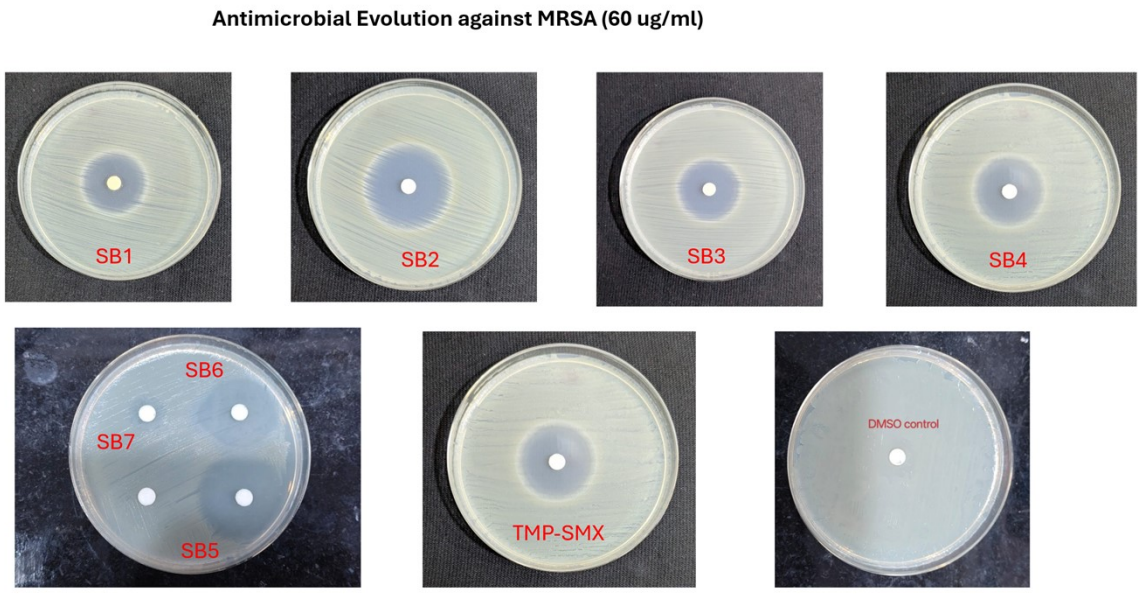


Figure S42. Images of inhibition zone of compound SB1-SB7 in comparison with SUL-TMP against MRSA

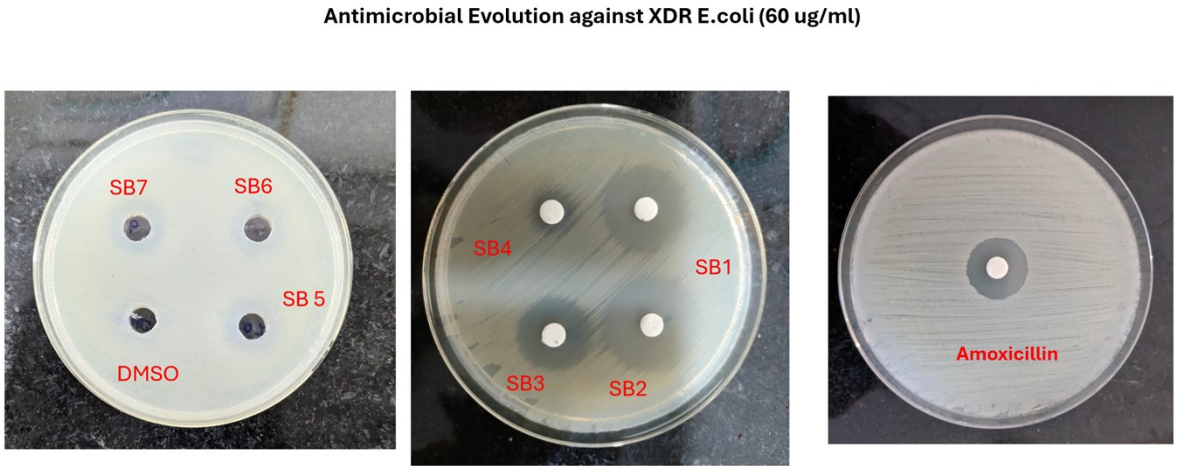


Figure S43. Images of inhibition zone of compound SB1-SB7 in comparison with Amoxicillin against *XDR E.coli*

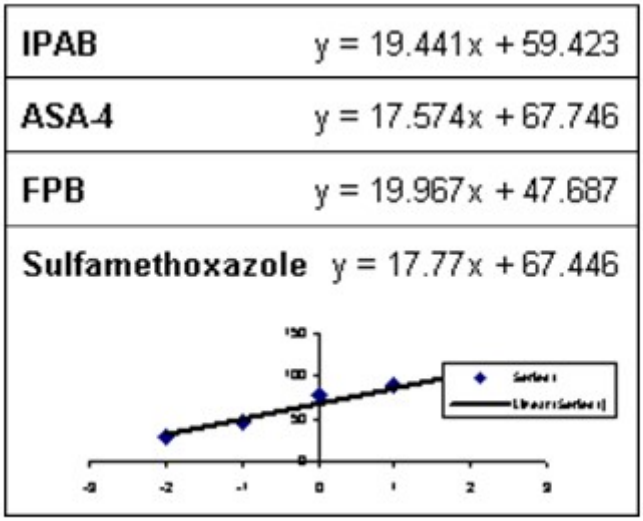


Figure S44. Dose–response curve of compounds against DHPS

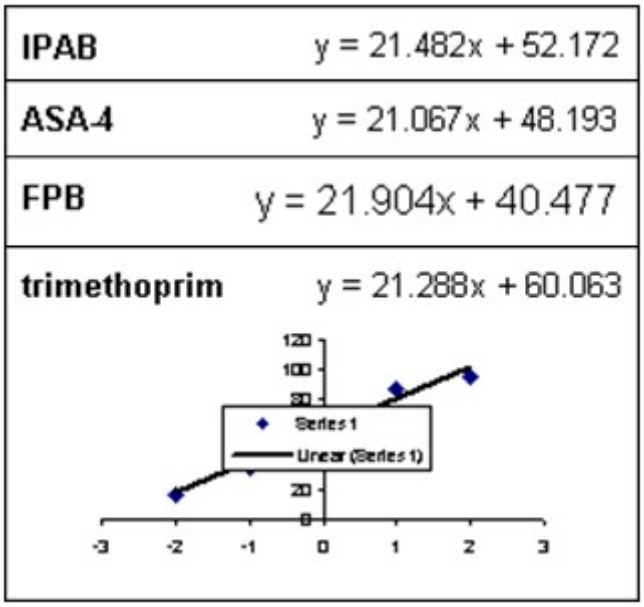


Figure S45. Dose–response curve of compounds against DHFR

Table S1. MIC Determination against MRSA and XDR *E.coli*

Compound SB2	**MRSA (µg/mL)**	**XDR *E.coli* (µg/mL)**	**Compound SB5(µg/mL)**	**MRSA (µg/mL)**	**XDR *E.coli* (µg/mL)**
Replicate 1	2	8	Replicate 1	2	16
Replicate 2	2	8	Replicate 2	2	16
Replicate 3	2	8	Replicate 3	2	16
Reported MIC	**2**	**8**	**Reported MIC**	**2**	**16**