

Supplementary materials

Novel Anthraquinone-Based Benzenesulfonamide Derivatives and Their Analogues as Potent Human Carbonic Anhydrase Inhibitors with Antitumor Activity: Synthesis, Biological Evaluation, and In Silico Analysis

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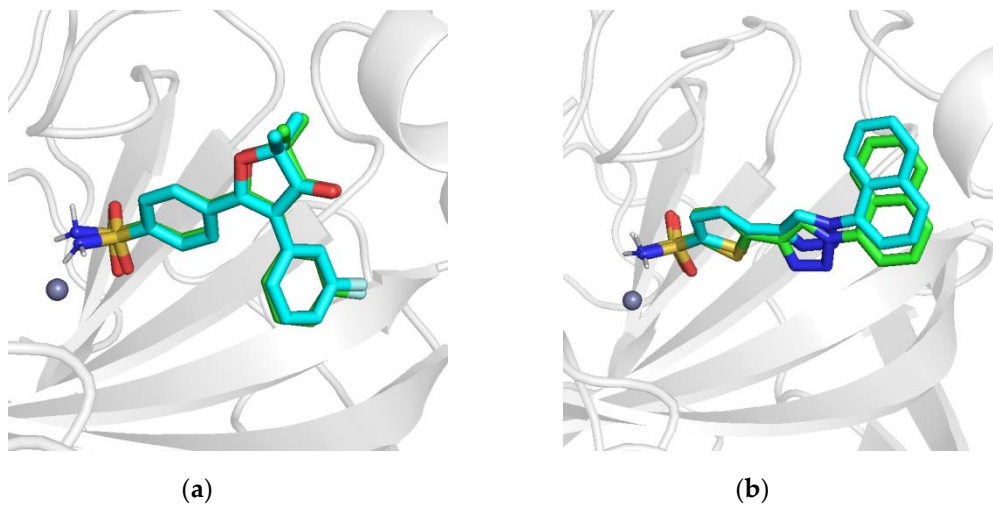


Figure S1. Result of redocking. (a) Crystal conformation of CA II and original ligand (cyan) and docked conformation (green); (b) Crystal conformation of CA IX and original ligand (cyan) and docked conformation (green).

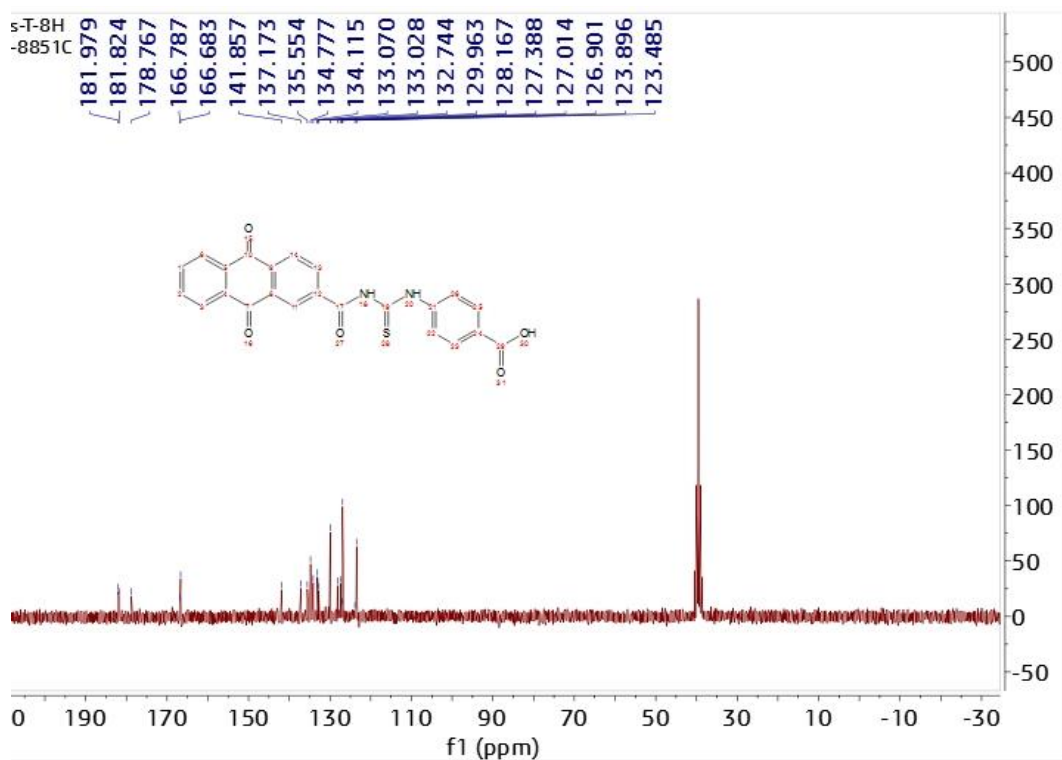
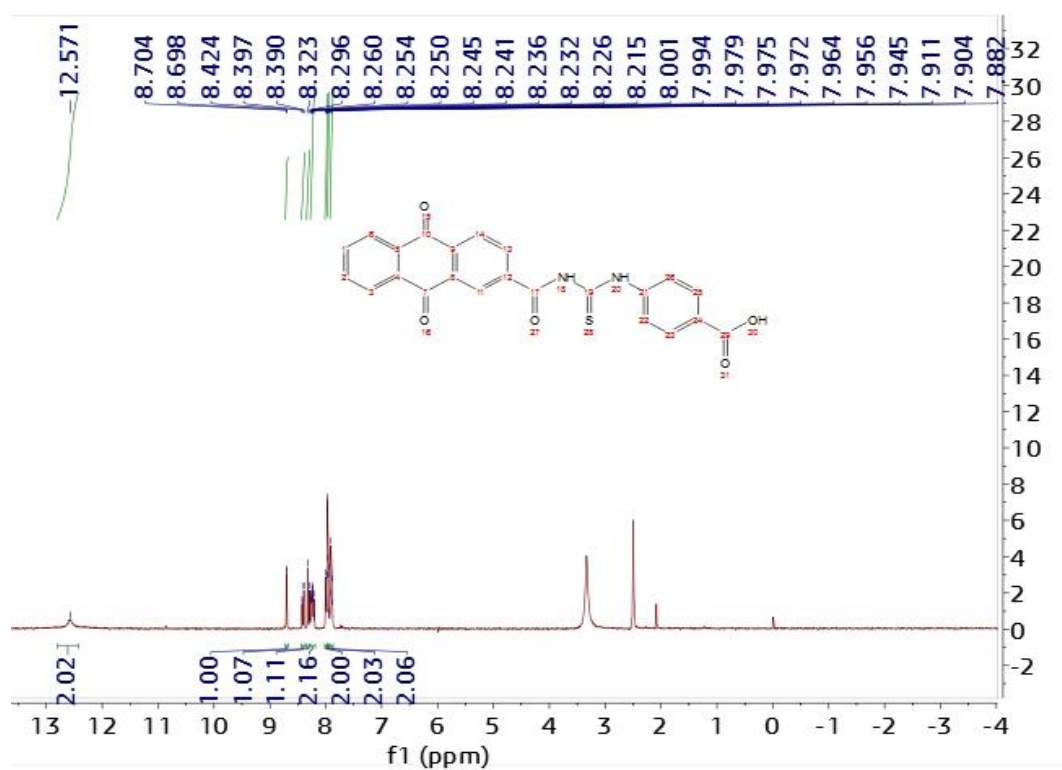
Table S1. The docking score, binding interactions, and IC₅₀ of the active compounds in *hCA II* enzyme

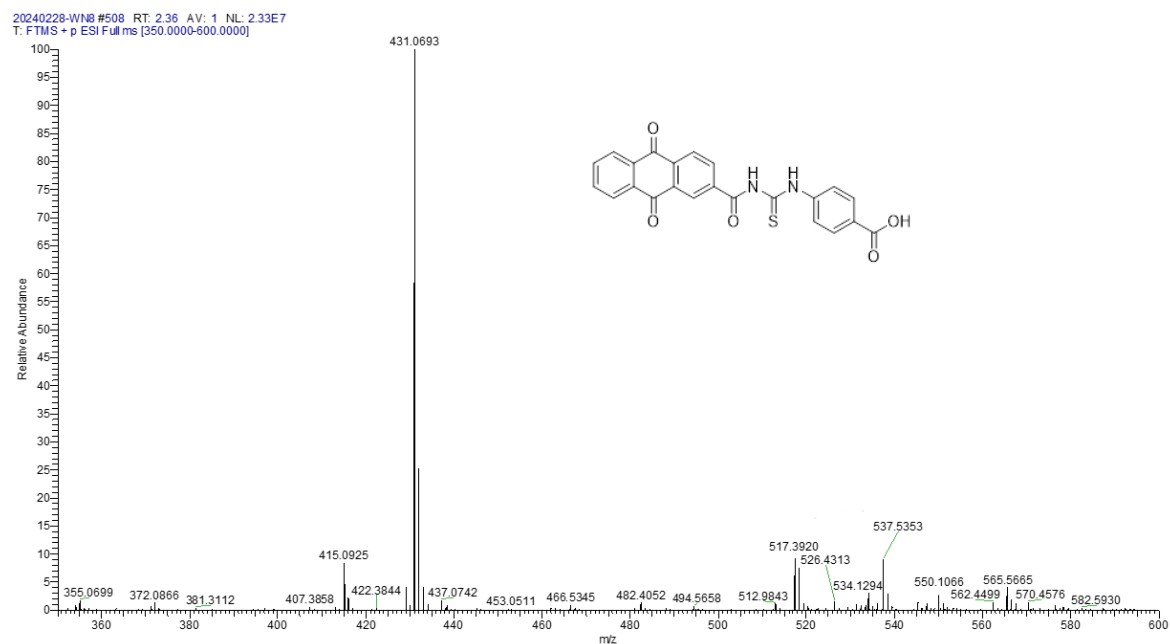
Compound	Docking score (Kcal/mol)	Amino acid interactions	Interacting groups	IC ₅₀ (nM)
5c	-12.98	Zn ²⁺ (metal)	NH of SO ₂ NH ₂	41.58
		T198 (H-bond)	NH and O of SO ₂ NH ₂	
		F130 (pi-stacking)	Anthraquinone ring	
		E69 (hydrophobic)		
		I91 (hydrophobic)		
		Q92 (hydrophobic)		
		V121 (hydrophobic)		
		L197 (hydrophobic)		
5h	-13.17	Zn ²⁺ (metal)	NH of SO ₂ NH ₂	21.19
		N67 (H-bond)	O of anthraquinone ring	
		Q92 (H-bond)	O of anthraquinone ring	
		T198 (H-bond)	NH and O of SO ₂ NH ₂	
		F130 (pi-stacking)	Anthraquinone ring	
		L60 (hydrophobic)		
		L91 (hydrophobic)		
		V121 (hydrophobic)		
		L140 (hydrophobic)		
		V142 (hydrophobic)		
6c	-12.83	Zn ²⁺ (metal)	NH of SO ₂ NH ₂	68.34
		T198 (H-bond)	NH and O of SO ₂ NH ₂	
		T199 (H-bond)	O of SO ₂ NH ₂	
		F130 (pi-stacking)	Anthraquinone ring	
		E69 (hydrophobic)		
		I91 (hydrophobic)		
		Q92 (hydrophobic)		
		L197 (hydrophobic)		
5k	-9.97	N67 (H-bond)	O of SO ₂ NH	155.91
		Q92 (H-bond)	O of SO ₂ NH	
		T199 (H-bond)	O of anthraquinone ring	
		H94 (pi-stacking)	Anthraquinone ring	
		F130 (pi-stacking)	Benzene ring	
		GLU69 (hydrophobic)		
		GLN92 (hydrophobic)		
		VAL121 (hydrophobic)		
		LEU140 (hydrophobic)		
		VAL142 (hydrophobic)		
		LEU197 (hydrophobic)		
		THR198 (hydrophobic)		
		TRP208 (hydrophobic)		

Table S2. The docking score, binding interactions, and IC₅₀ of the active compounds in *hCA IX* enzyme

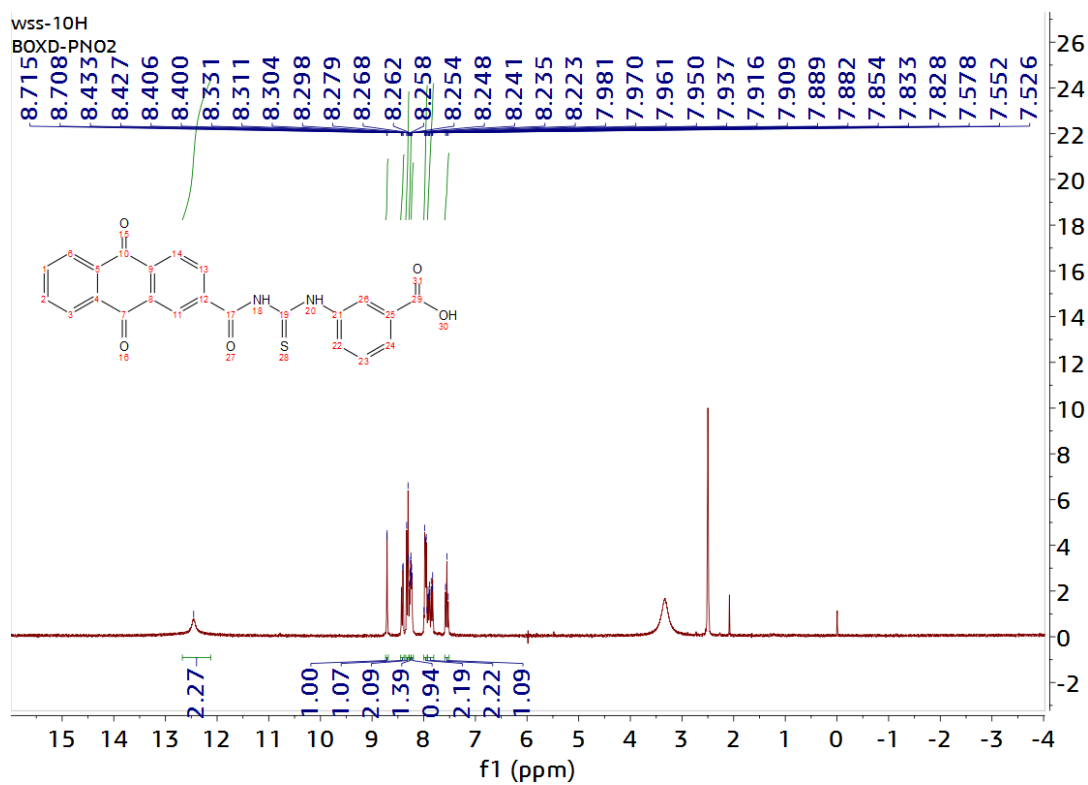
Compound	Docking score (Kcal/mol)	Amino acid interactions	Interacting groups	IC ₅₀ (nM)
5c	-13.08	Zn ²⁺ (metal)	NH of SO ₂ NH ₂	40.58
		W9 (H-bond)	O of amide	
		E106 (H-bond)	NH of SO ₂ NH ₂	
		T200 (H-bond)	O of SO ₂ NH ₂	
		T201 (H-bond)	NH of amide	
		P202 (H-bond)	NH of amide	
		V20 (hydrophobic)		
		L199 (hydrophobic)		
		P202 (hydrophobic)		
		P203 (hydrophobic)		
5h	-13.19	Zn ²⁺ (metal)	NH of SO ₂ NH ₂	46.19
		W9 (H-bond)	O of amide	
		E106 (H-bond)	NH of SO ₂ NH ₂	
		T200 (H-bond)	O of SO ₂ NH ₂	
		P202 (H-bond)	NH of amide	
		V20 (hydrophobic)		
		L199 (hydrophobic)		
		P202 (hydrophobic)		
		P203 (hydrophobic)		
6c	-12.06	Zn ²⁺ (metal)	NH of SO ₂ NH ₂	34.88
		Q92 (H-bond)	NH of amide	
		E106 (H-bond)	NH of SO ₂ NH ₂	
		T200 (H-bond)	O of SO ₂ NH ₂	
		V121 (hydrophobic)		
		V130 (hydrophobic)		
		D131 (hydrophobic)		
		L134 (hydrophobic)		
		L199 (hydrophobic)		
5k	-9.46	W9 (H-bond)	O of amide	226.58
		T200 (H-bond)	O of anthraquinone ring	
		T201 (H-bond)	O of anthraquinone ring	
		P202 (H-bond)	NH of amide	
		H94 (pi-stacking)	Anthraquinone ring	
		W9 (hydrophobic)		
		H119 (hydrophobic)		
		V121 (hydrophobic)		
		V142 (hydrophobic)		
		L199 (hydrophobic)		
		P203 (hydrophobic)		
		W210 (hydrophobic)		

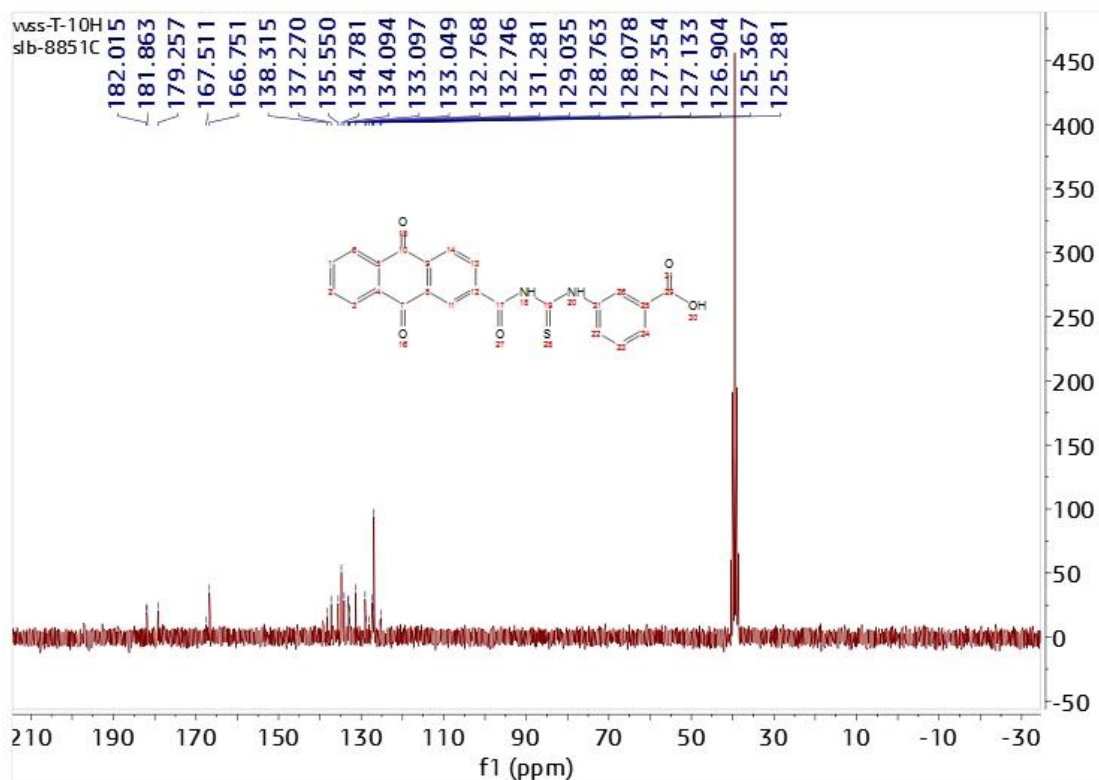
Data S1. ^1H -NMR, ^{13}C -NMR and HRMS data of compound 5a



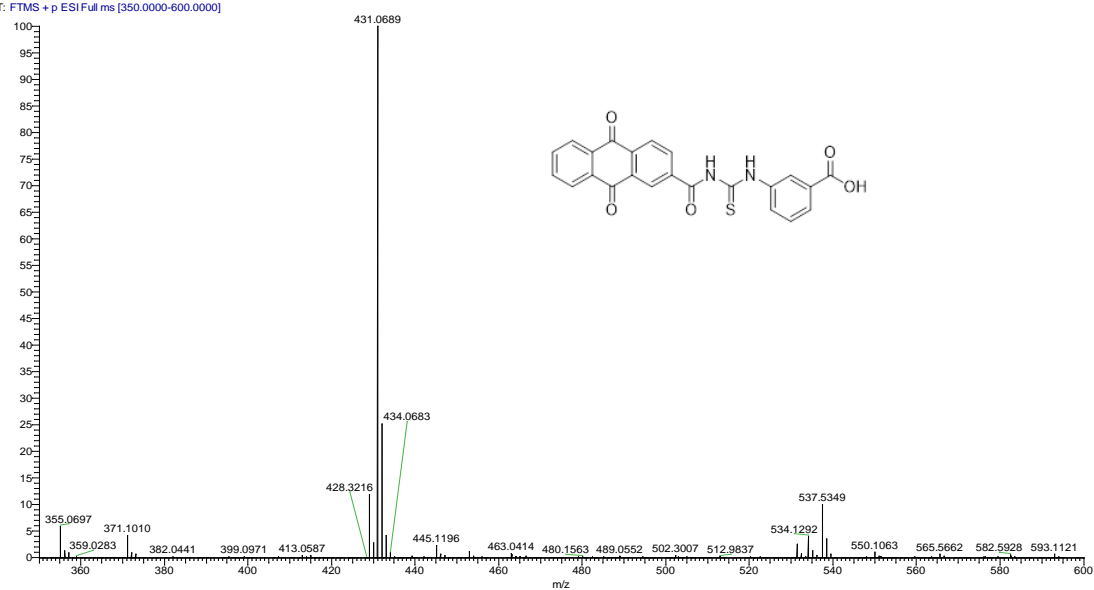


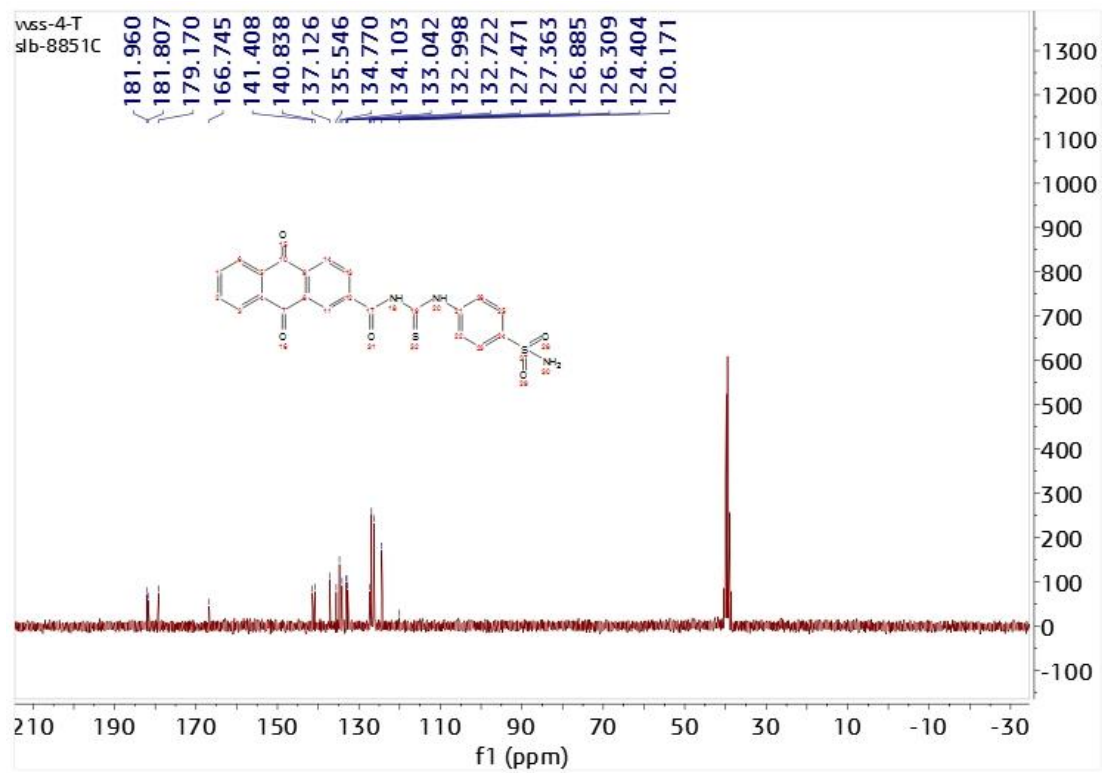
Data S2. ^1H -NMR, ^{13}C -NMR and HRMS data of compound 5b



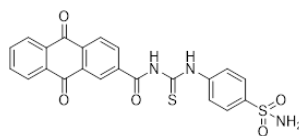
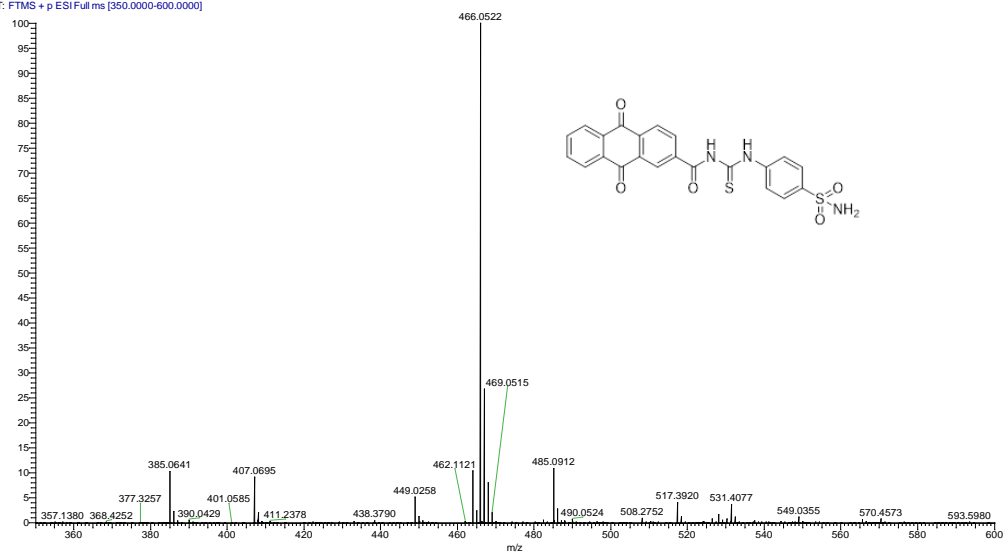


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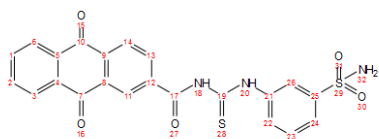
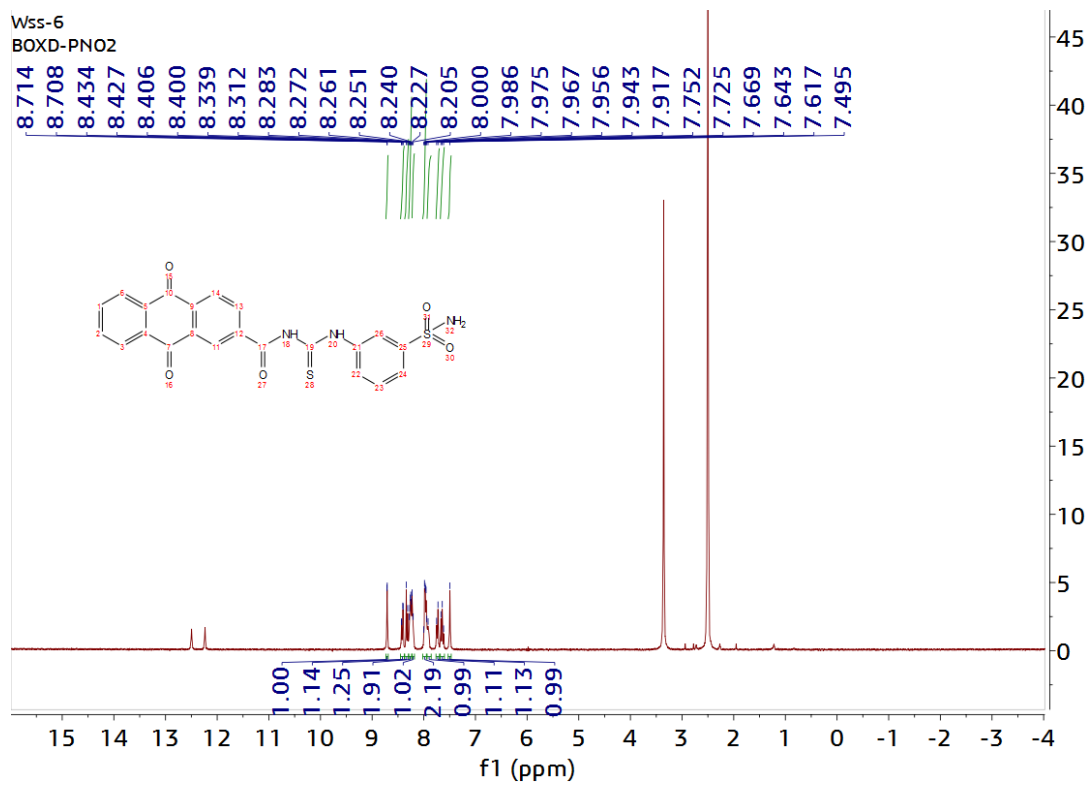


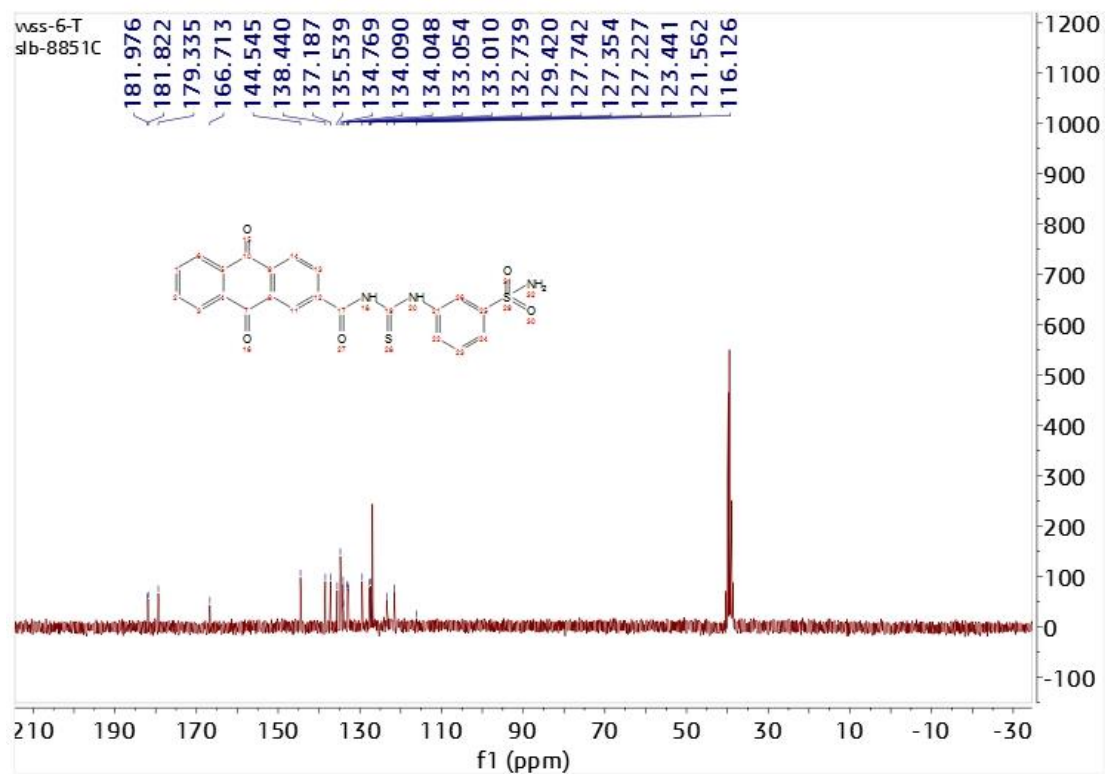


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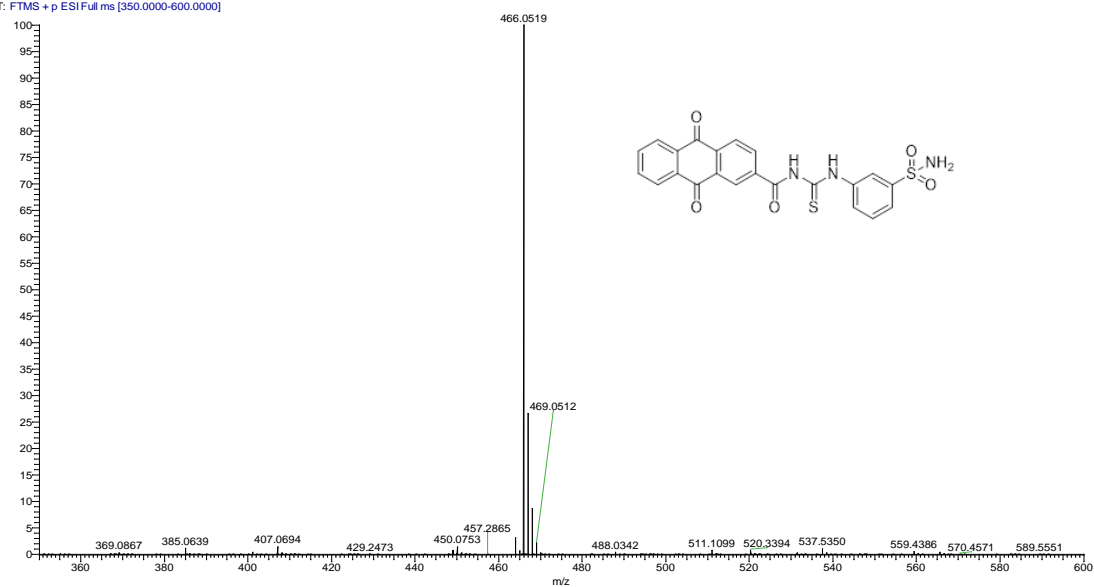


Data S4. ^1H -NMR, ^{13}C -NMR and HRMS data of compound 5d

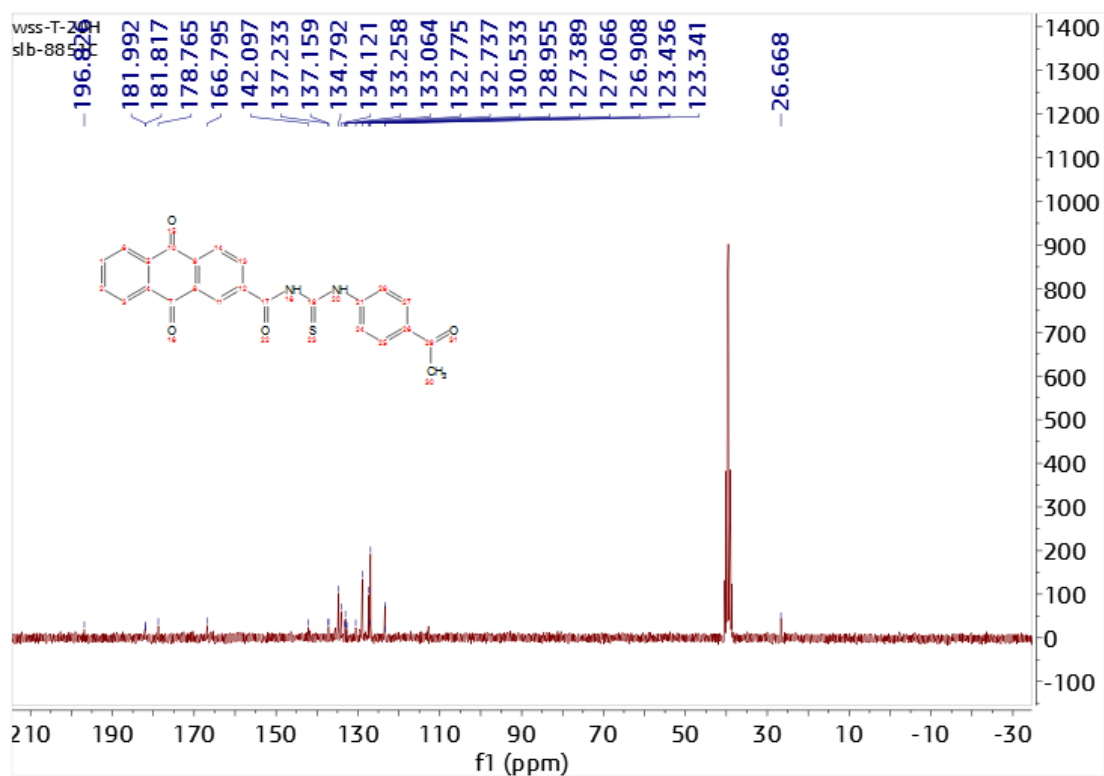
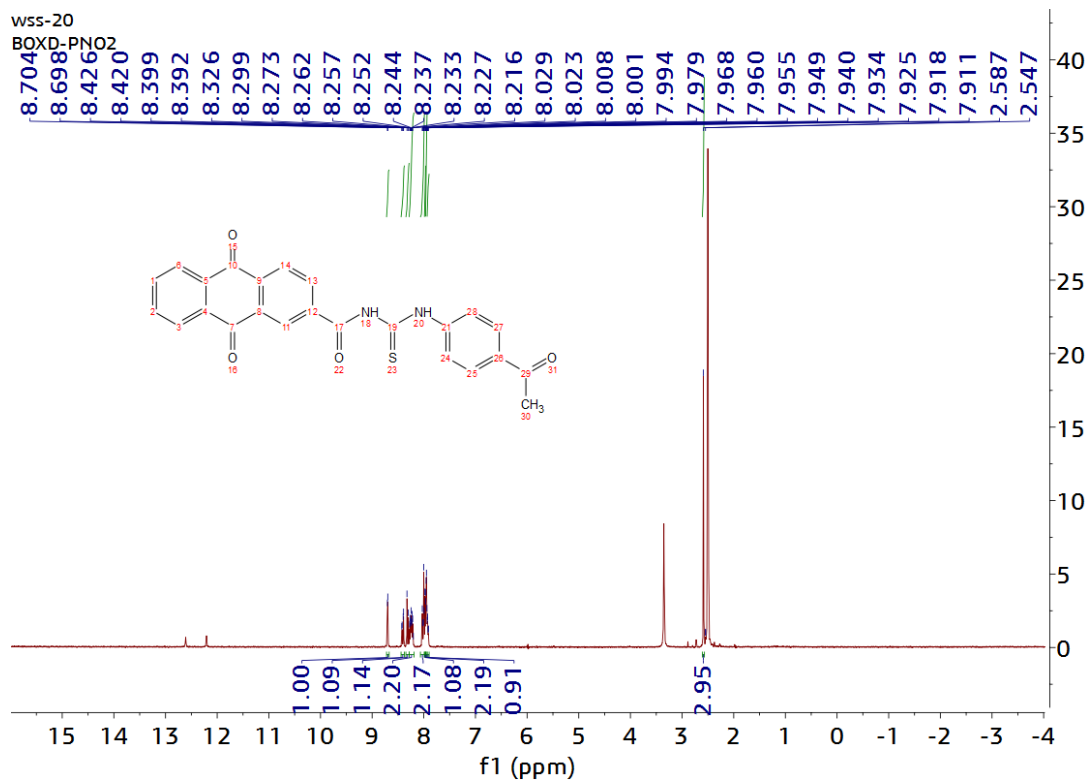




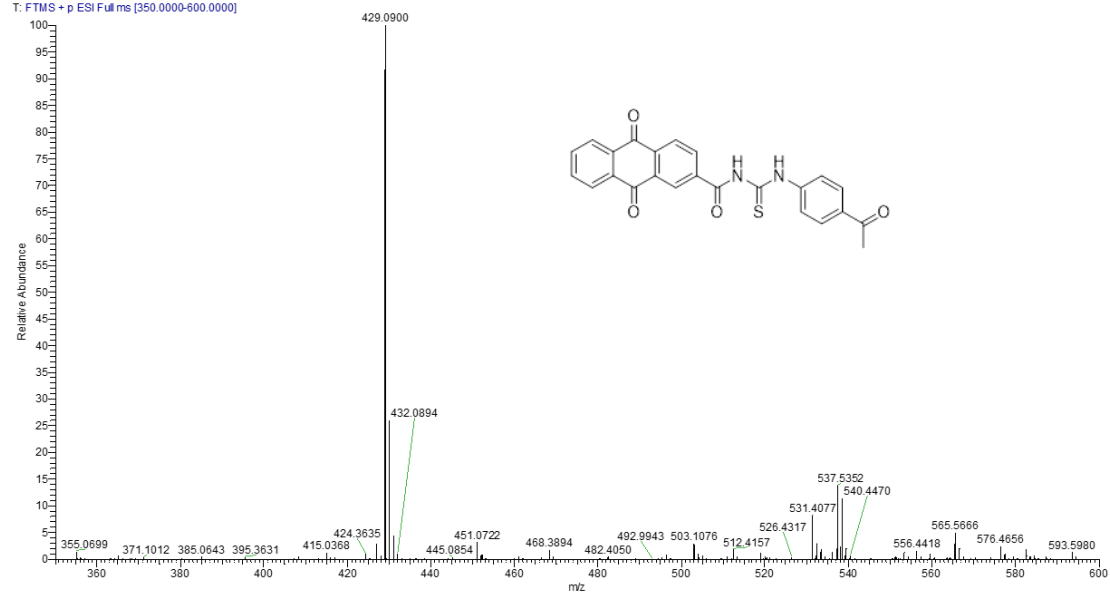
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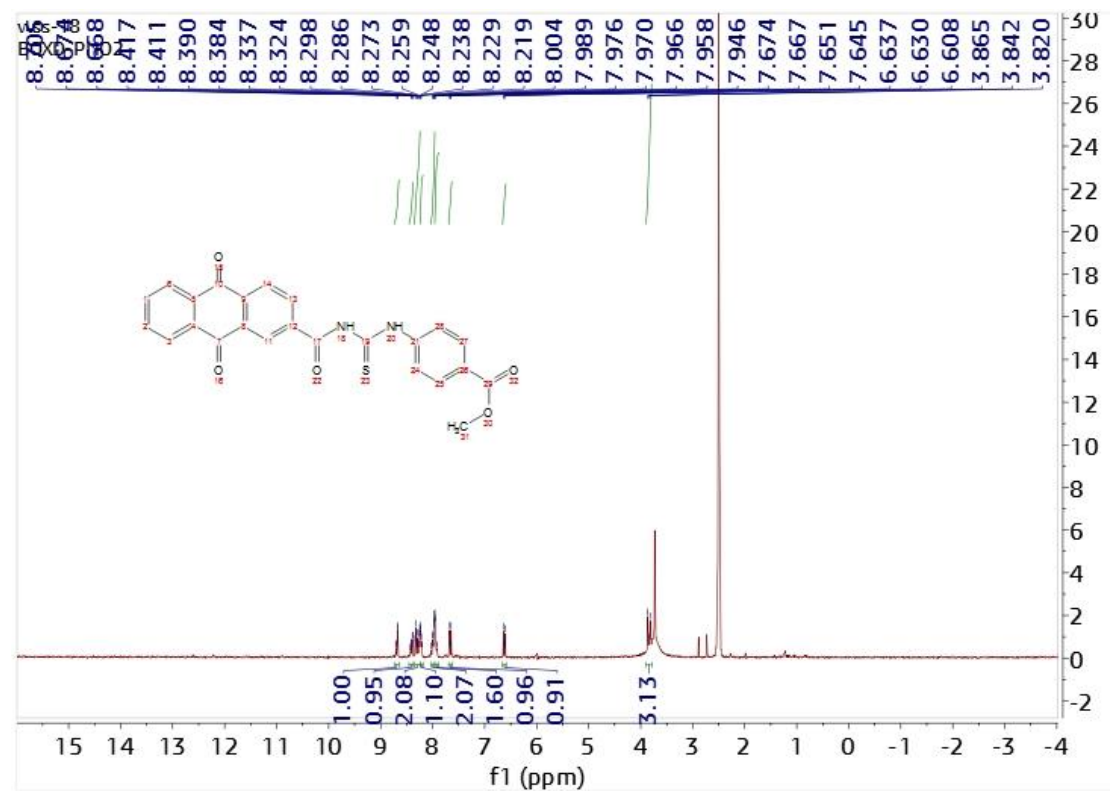
Data S5. ^1H -NMR, ^{13}C -NMR and HRMS data of compound 5e

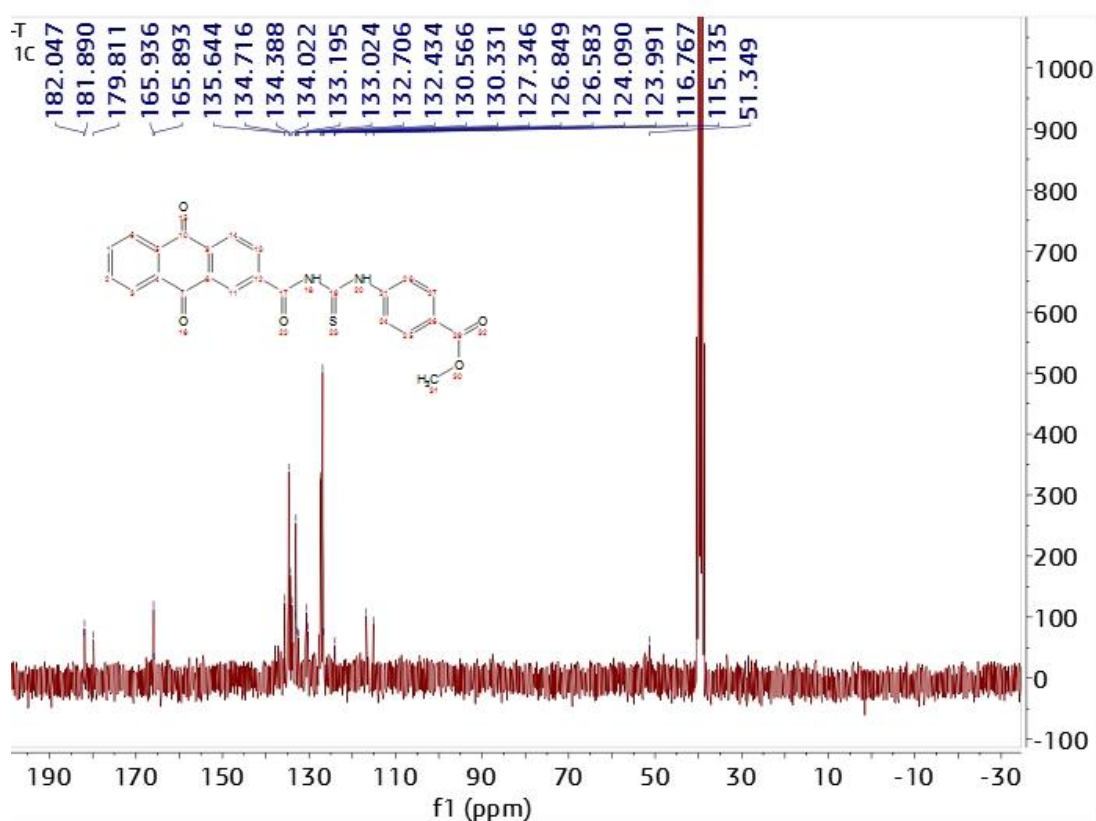


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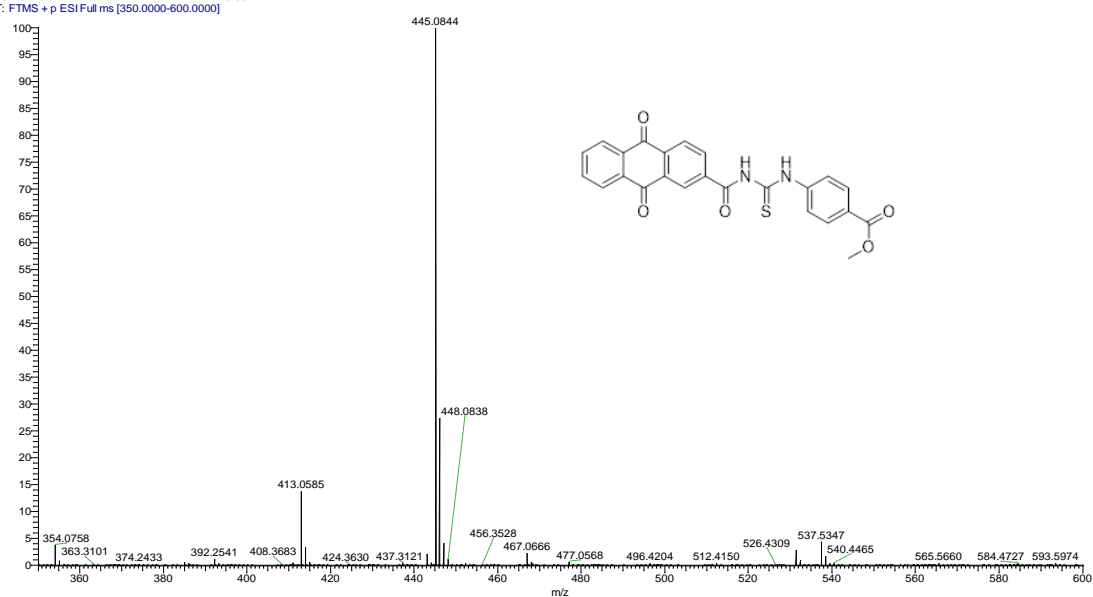


Data S6. ^1H -NMR, ^{13}C -NMR and HRMS data of compound 5f

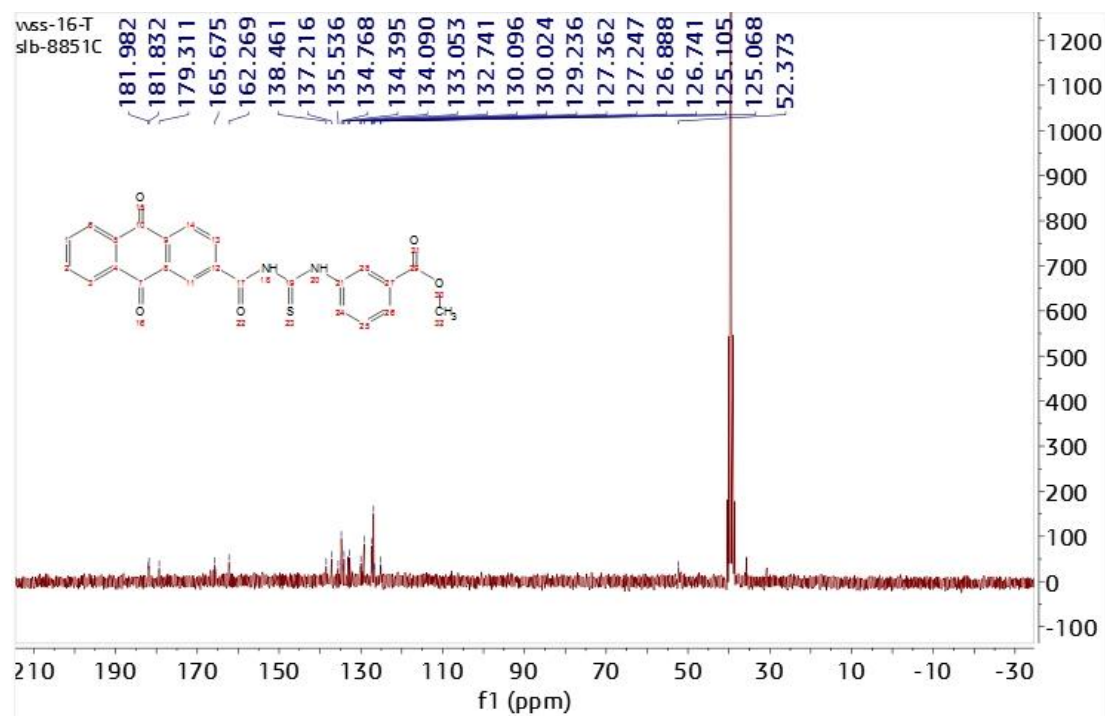
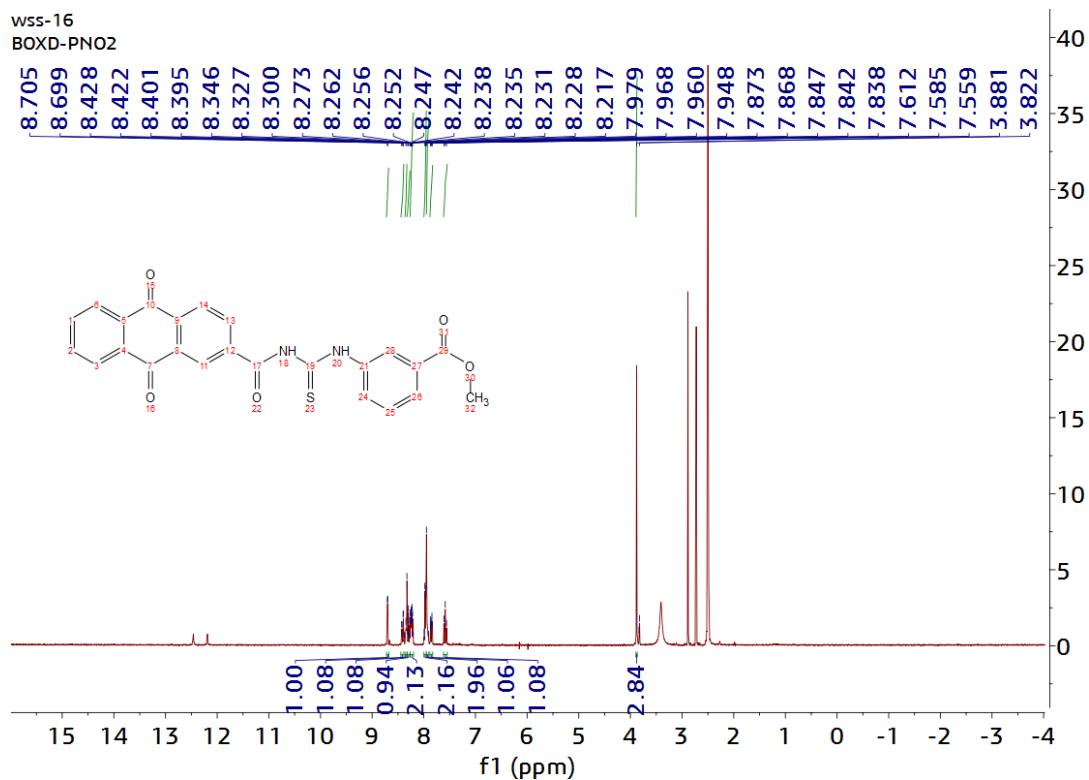




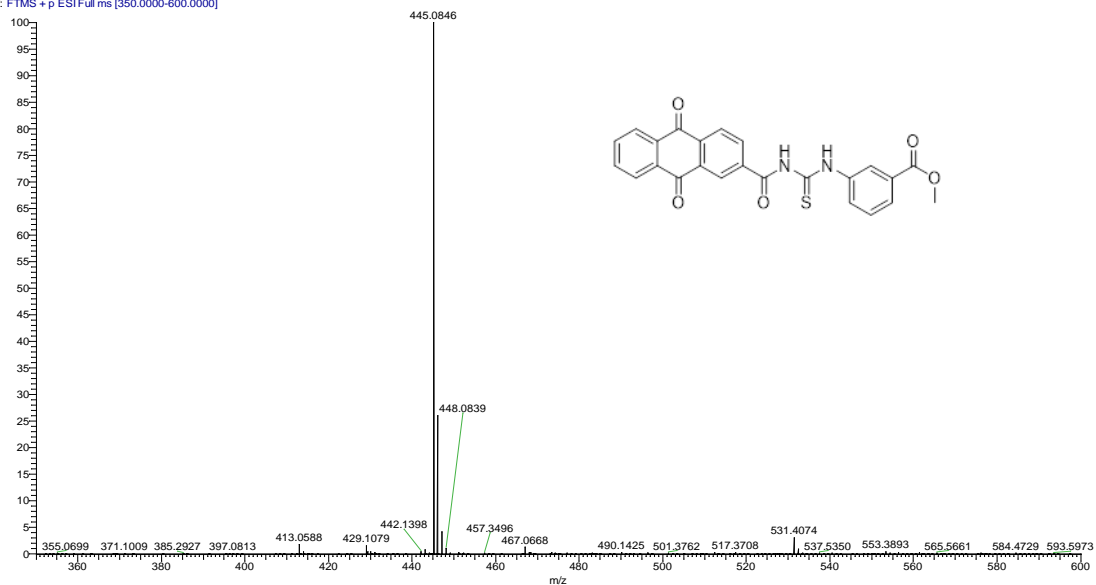
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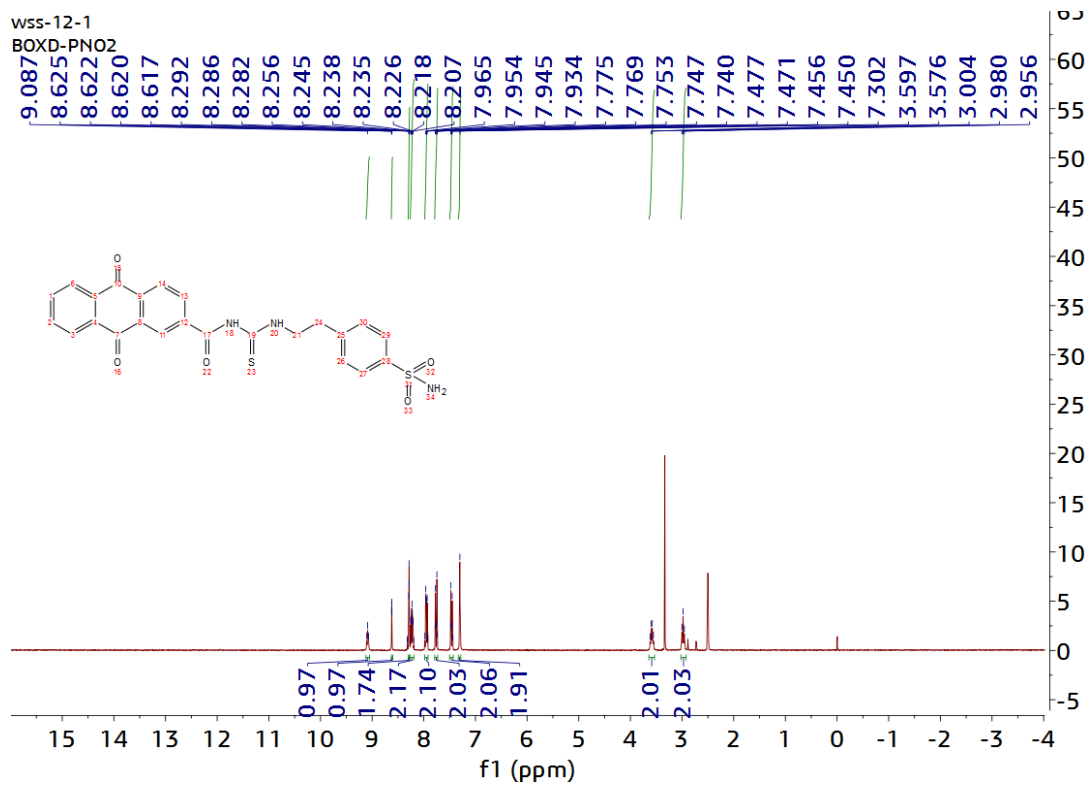
Data S7. ¹H-NMR, ¹³C-NMR and HRMS data of compound 5g

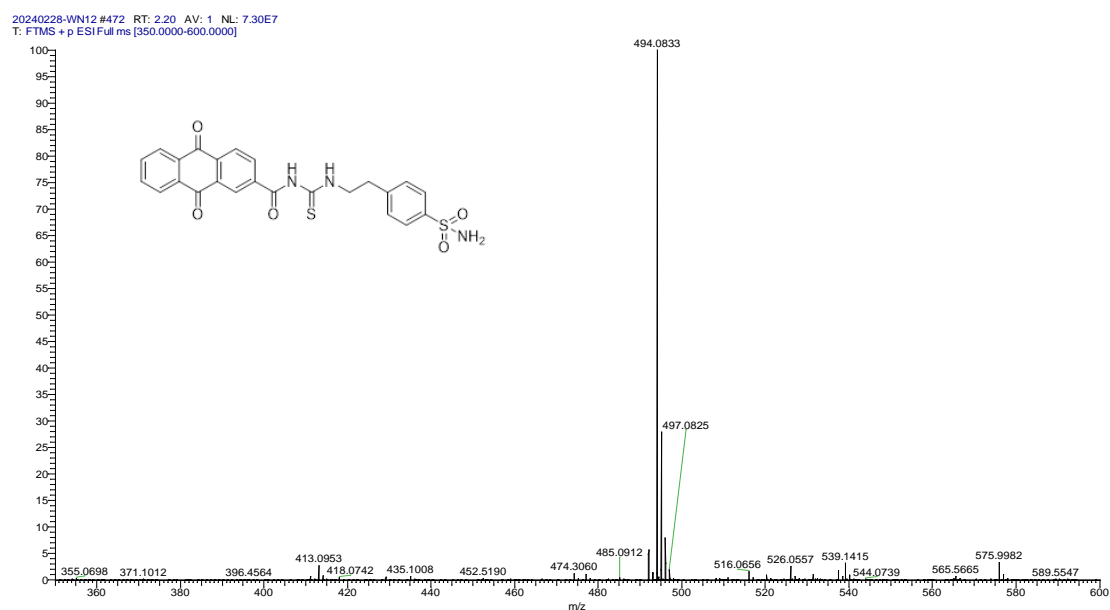
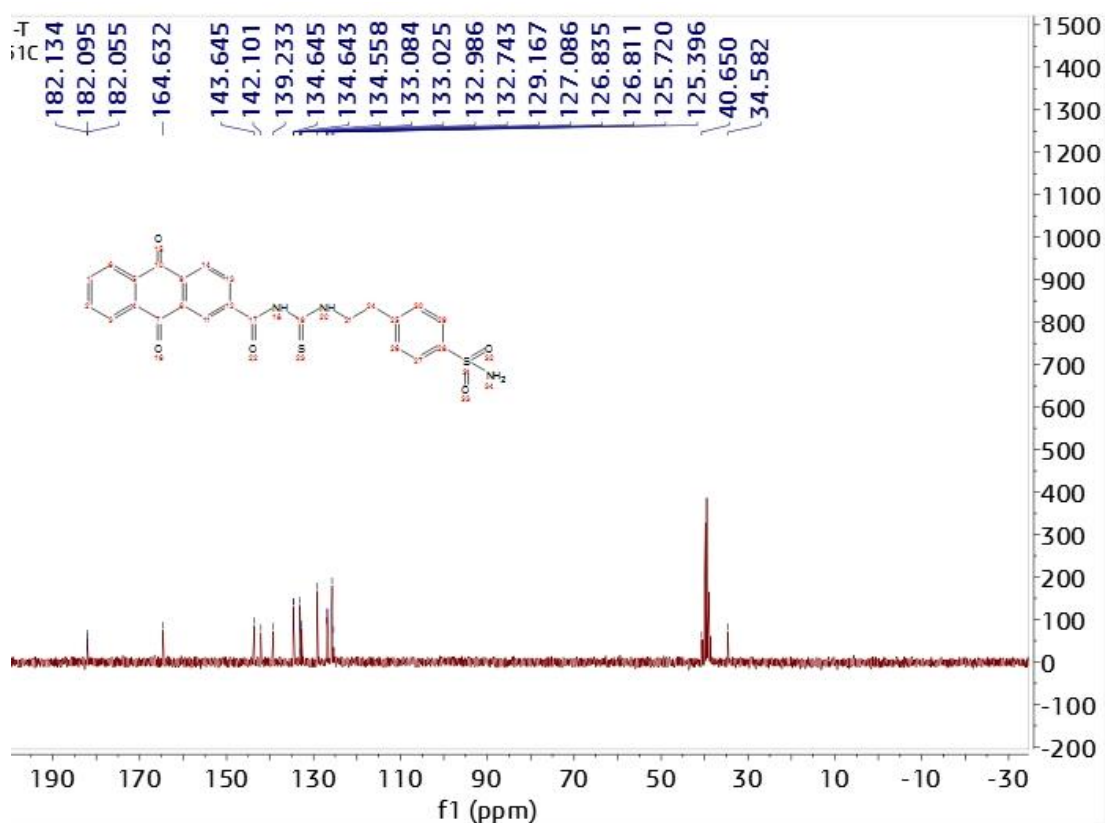


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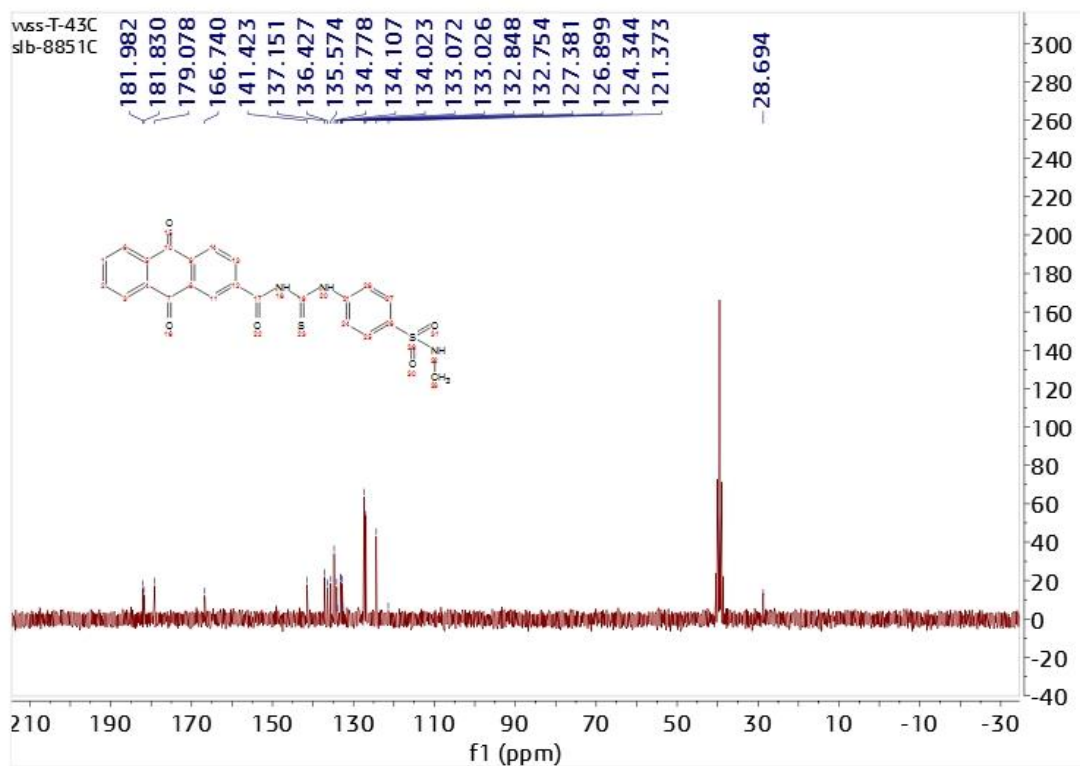
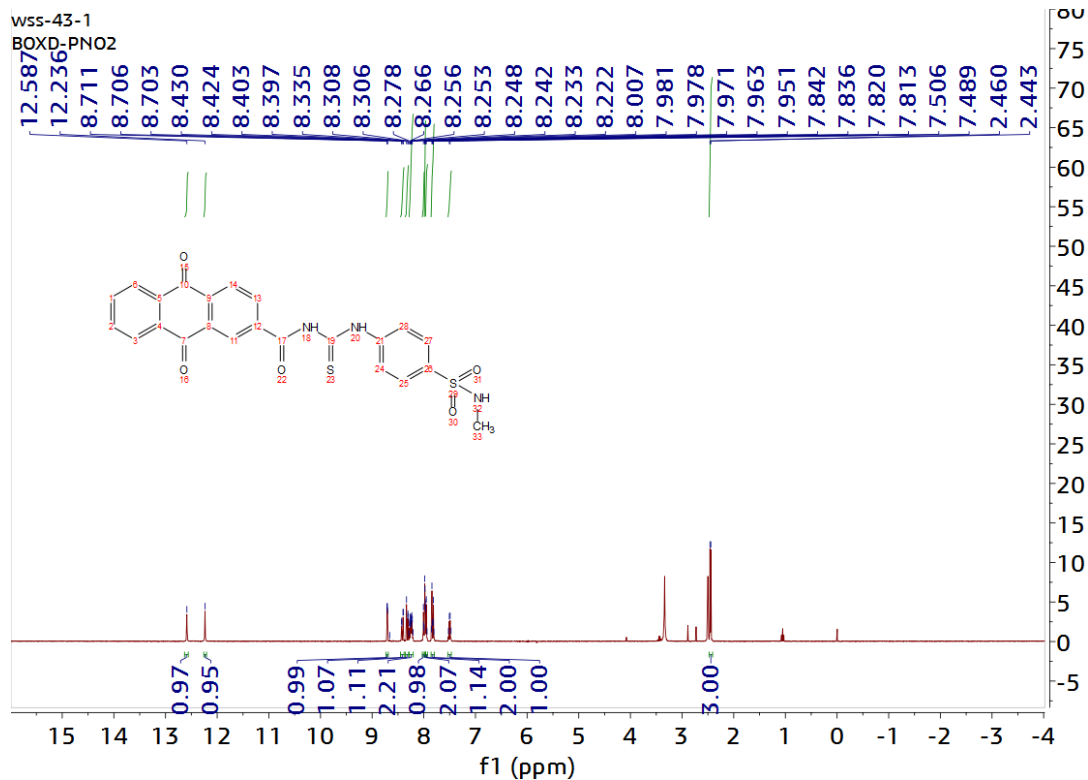


Data S8. ^1H -NMR, ^{13}C -NMR and HRMS data of compound 5h

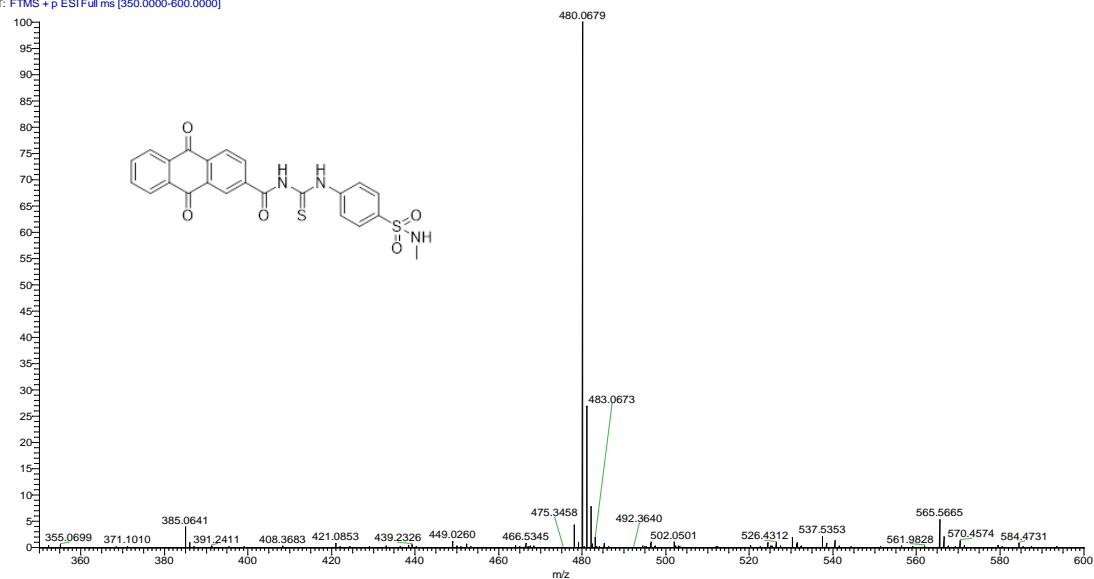




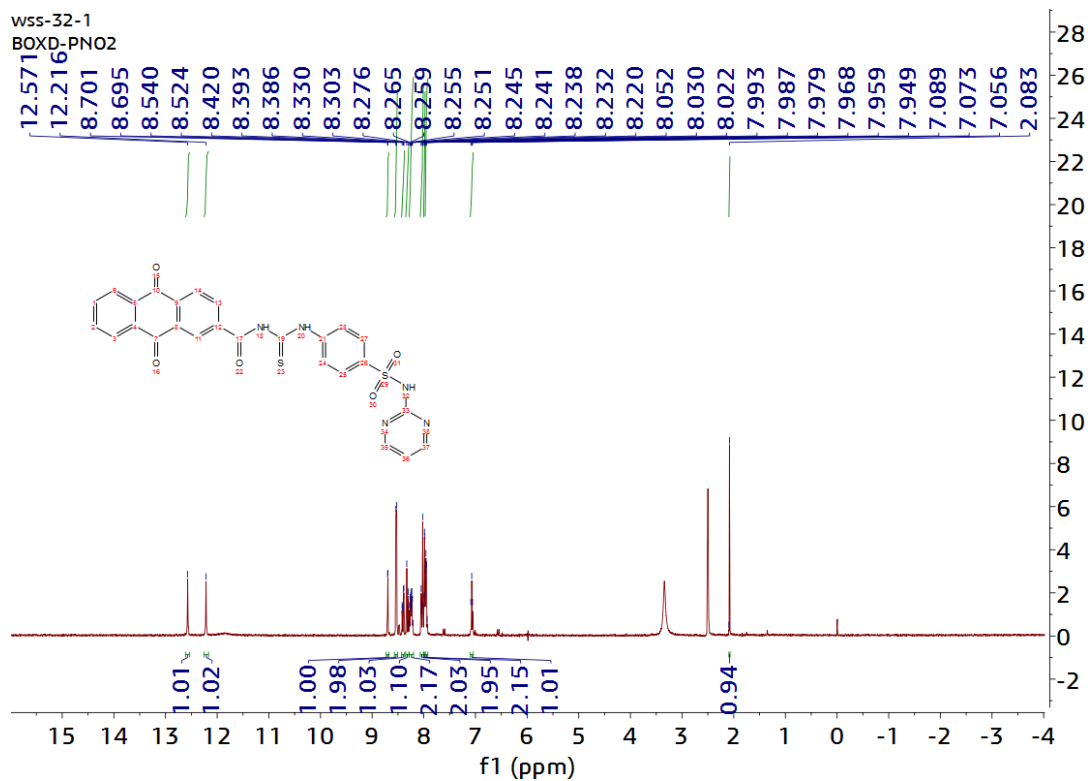
Data S9. ¹H-NMR, ¹³C-NMR and HRMS data of compound 5i

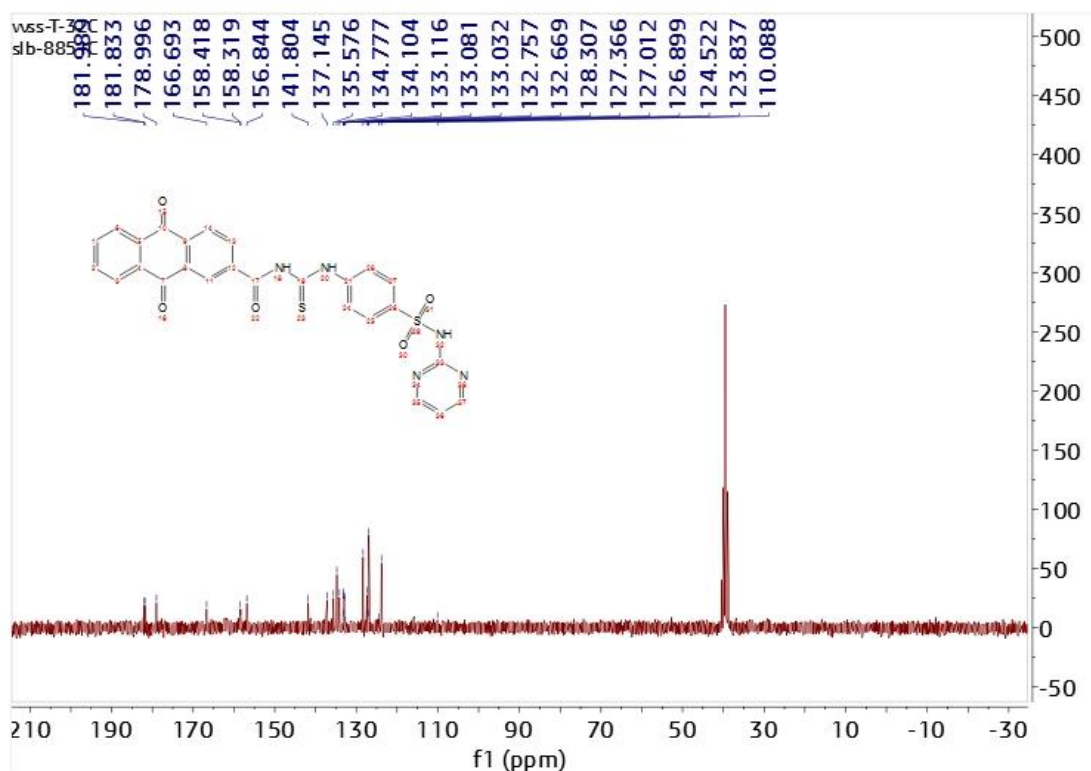


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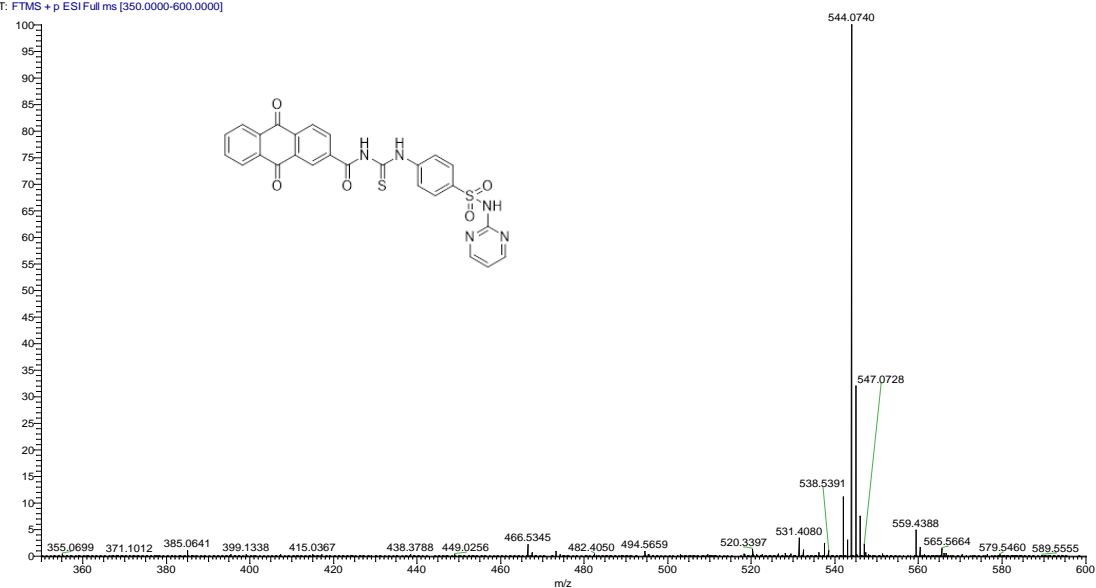


Data S10. ^1H -NMR, ^{13}C -NMR and HRMS data of compound 5j

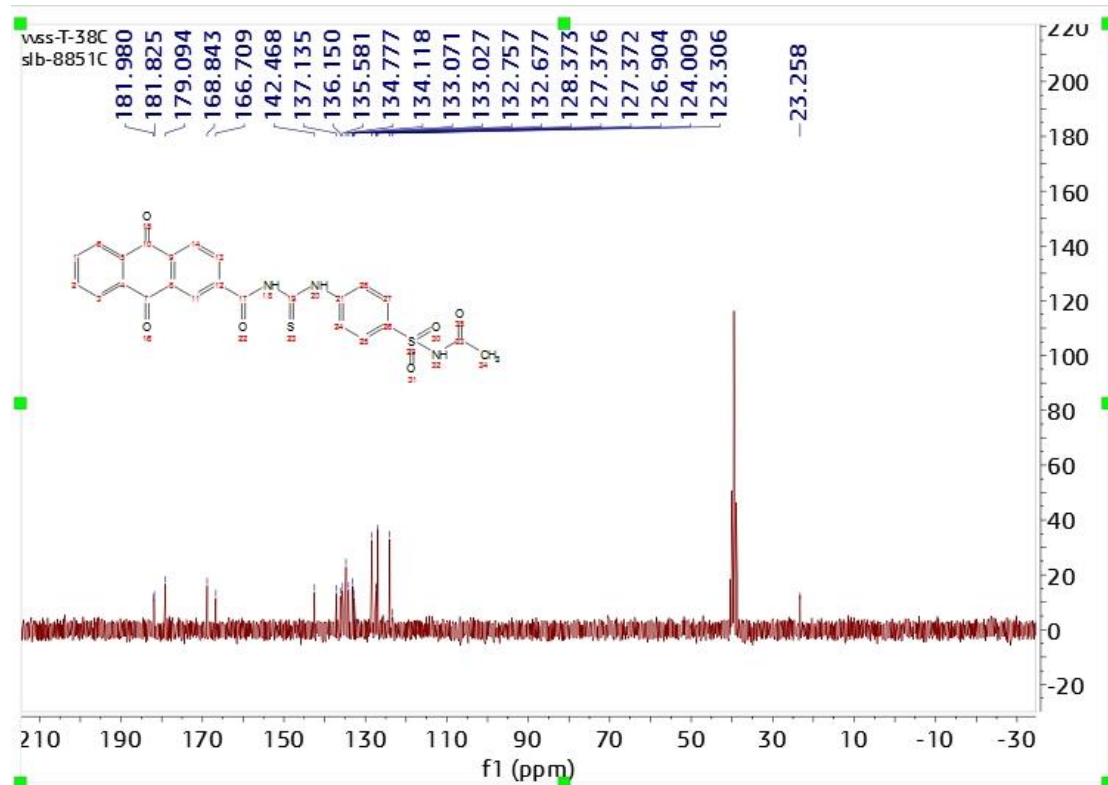
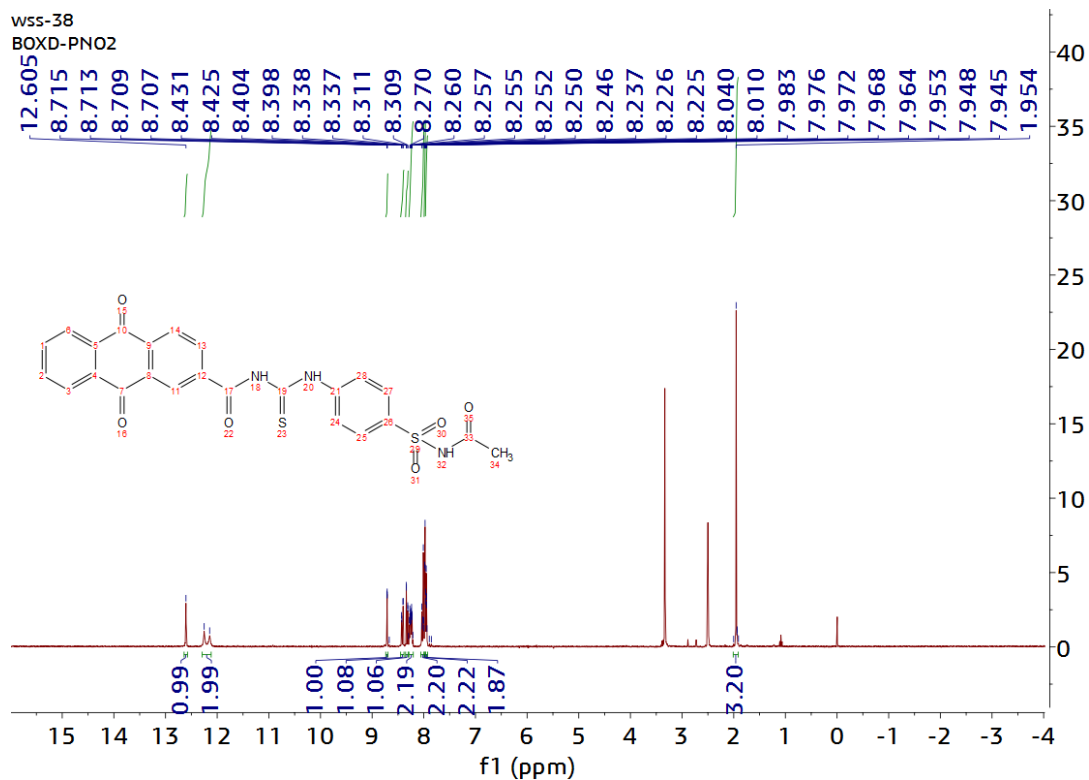




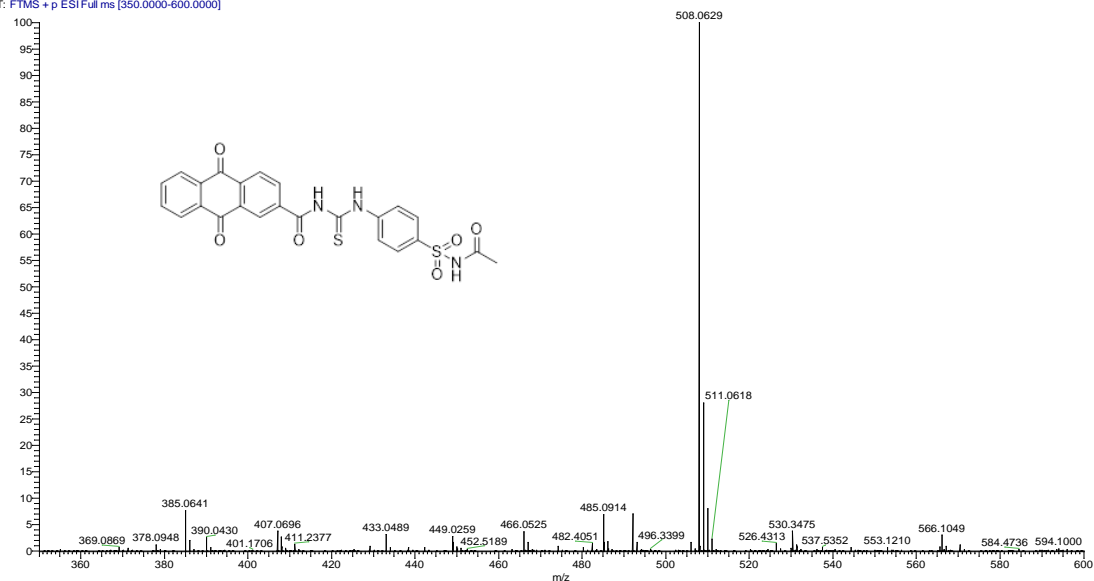
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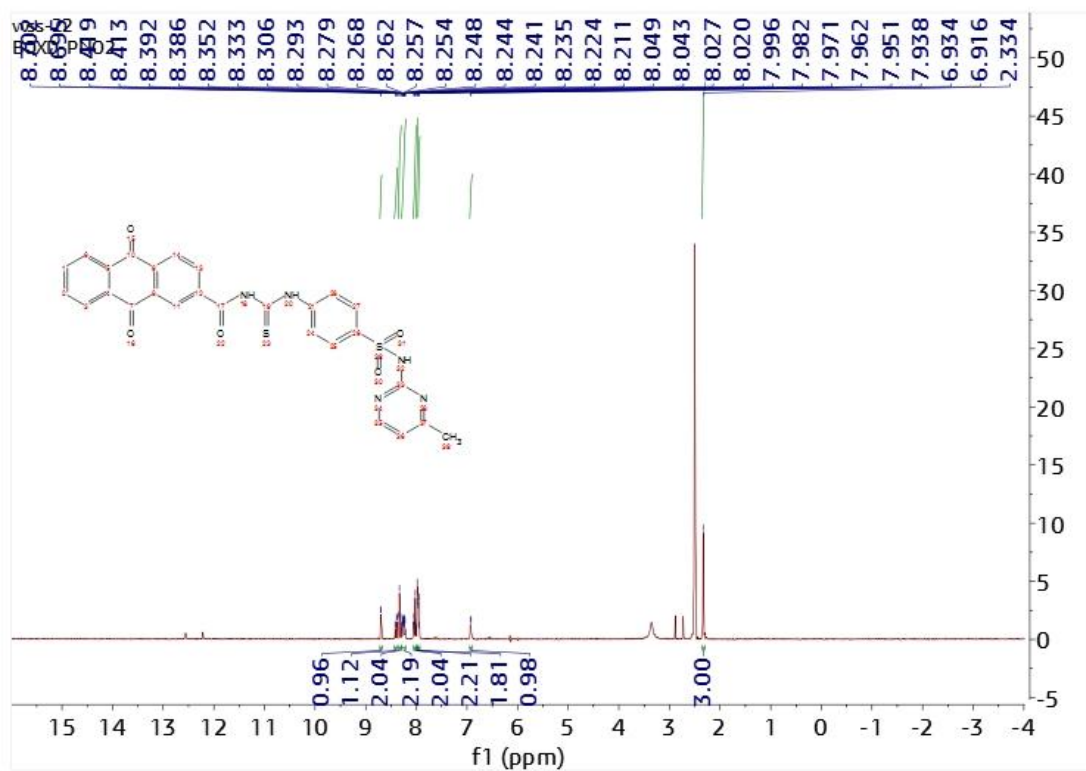
Data S11. ¹H-NMR, ¹³C-NMR and HRMS data of compound 5k

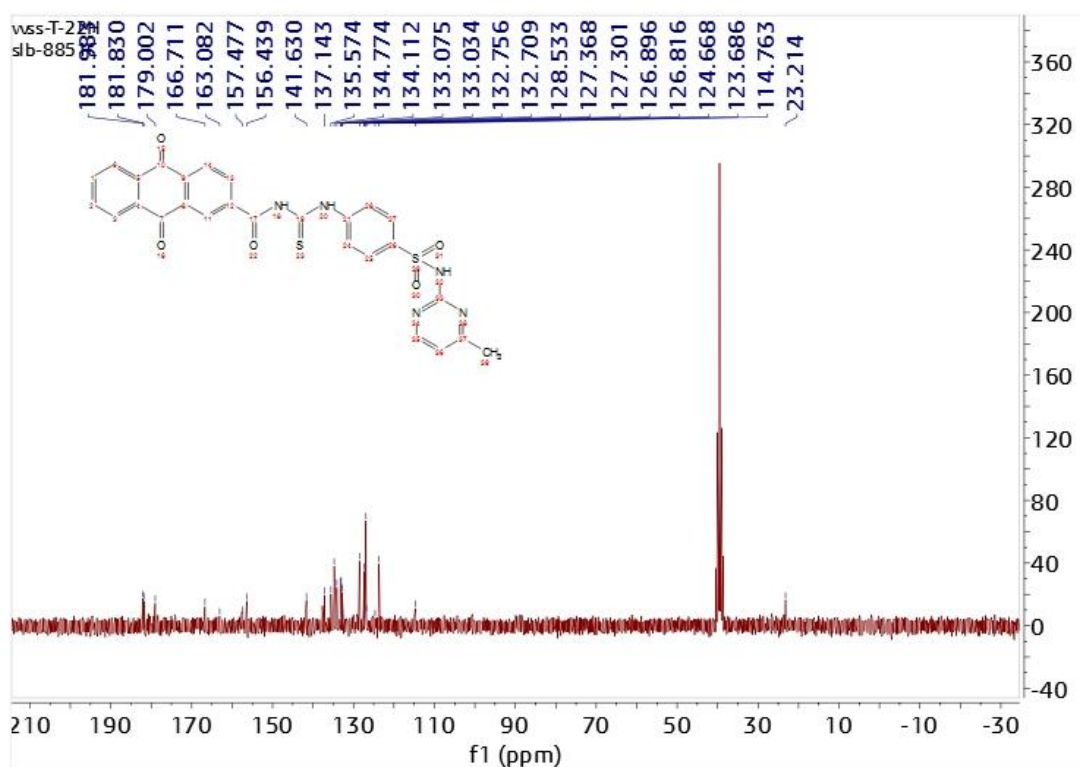


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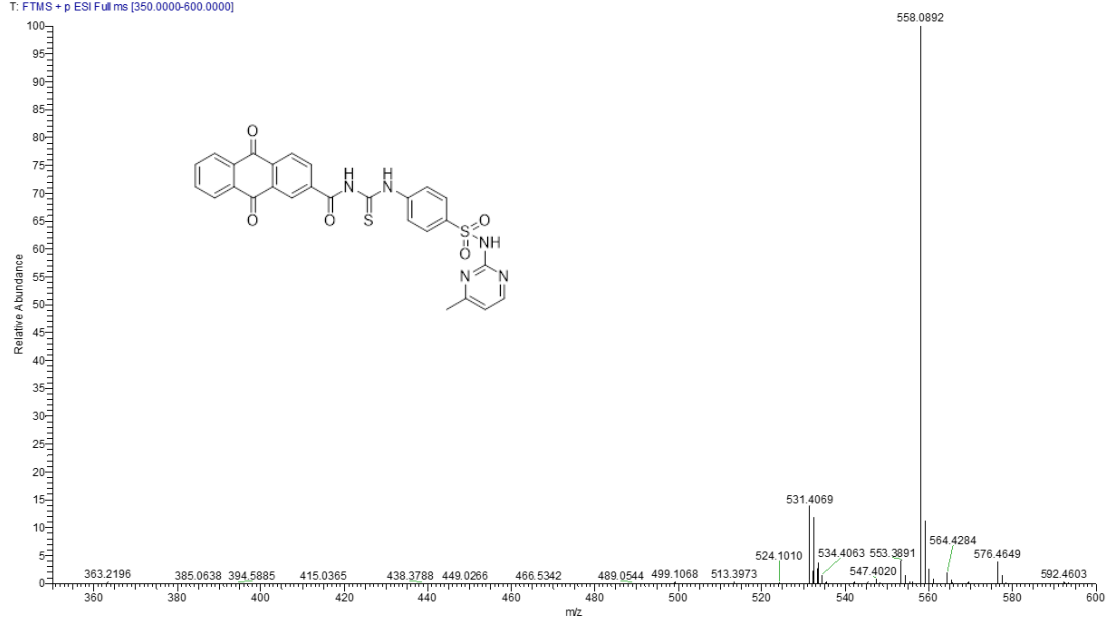


Data S12. ¹H-NMR, ¹³C-NMR and HRMS data of compound 5l

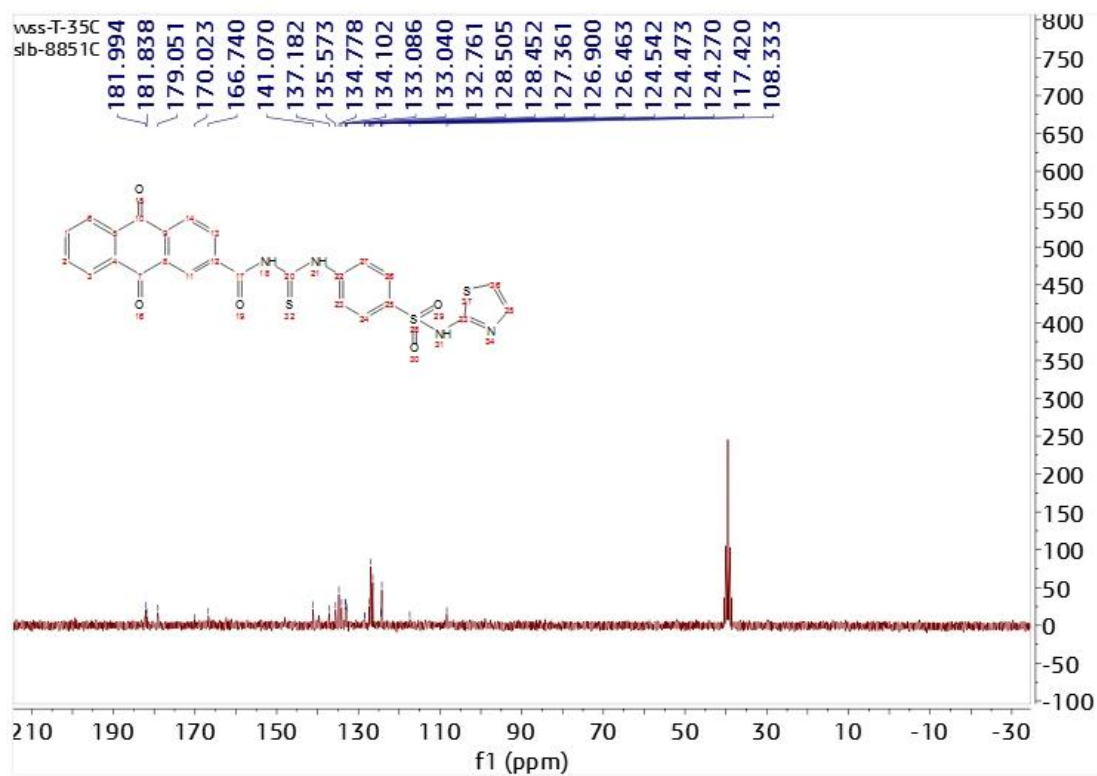
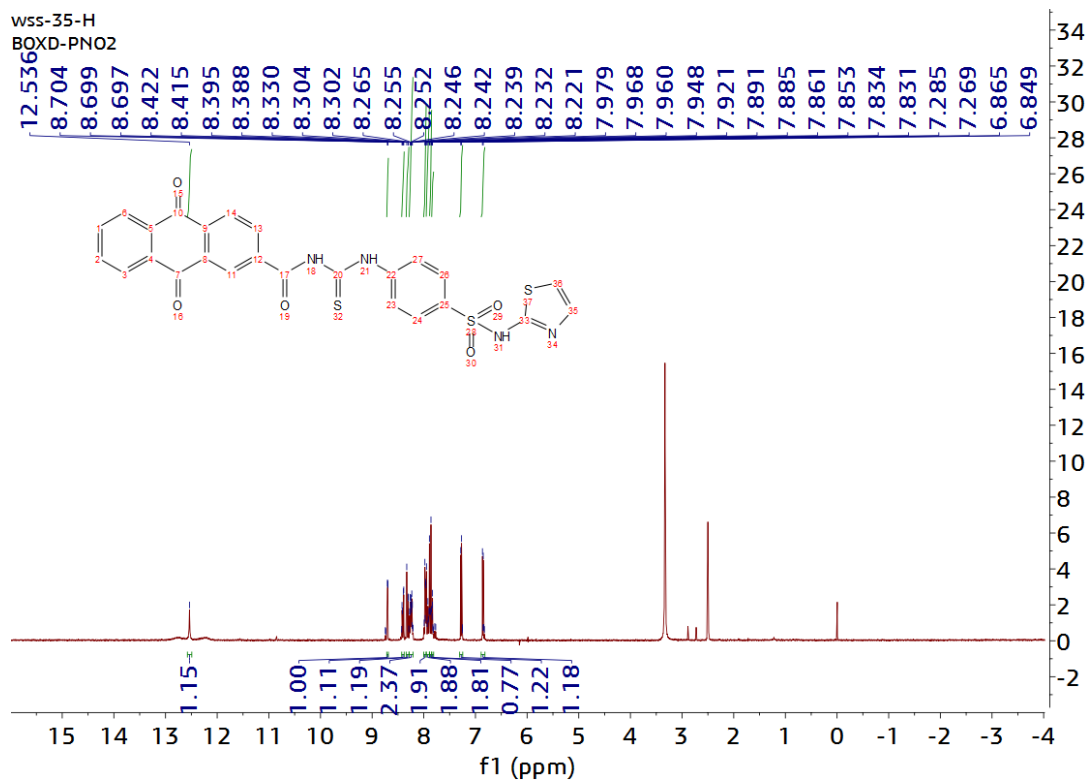




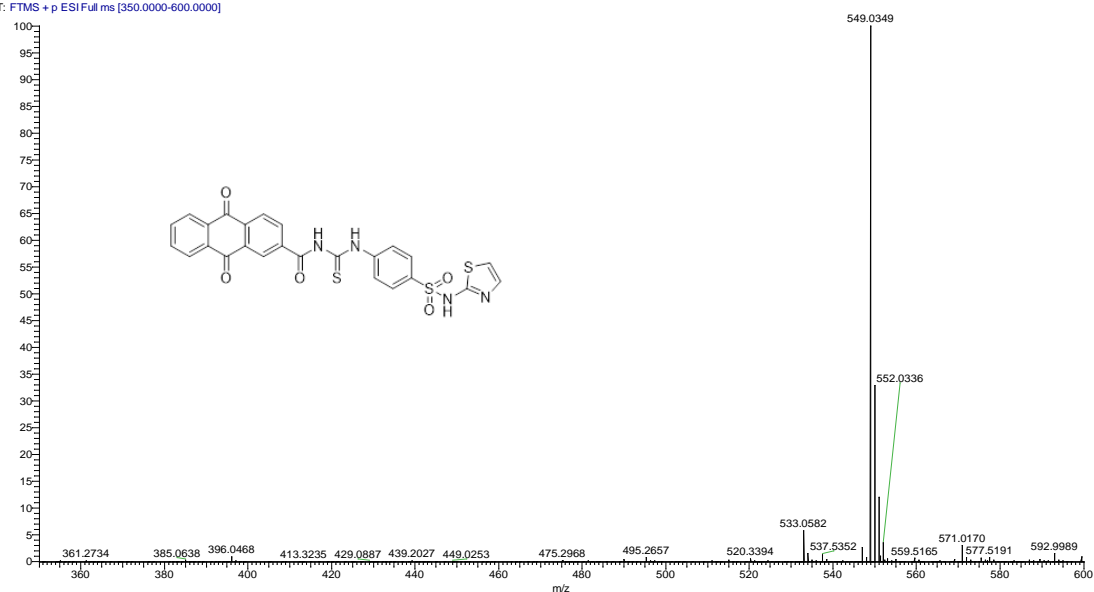
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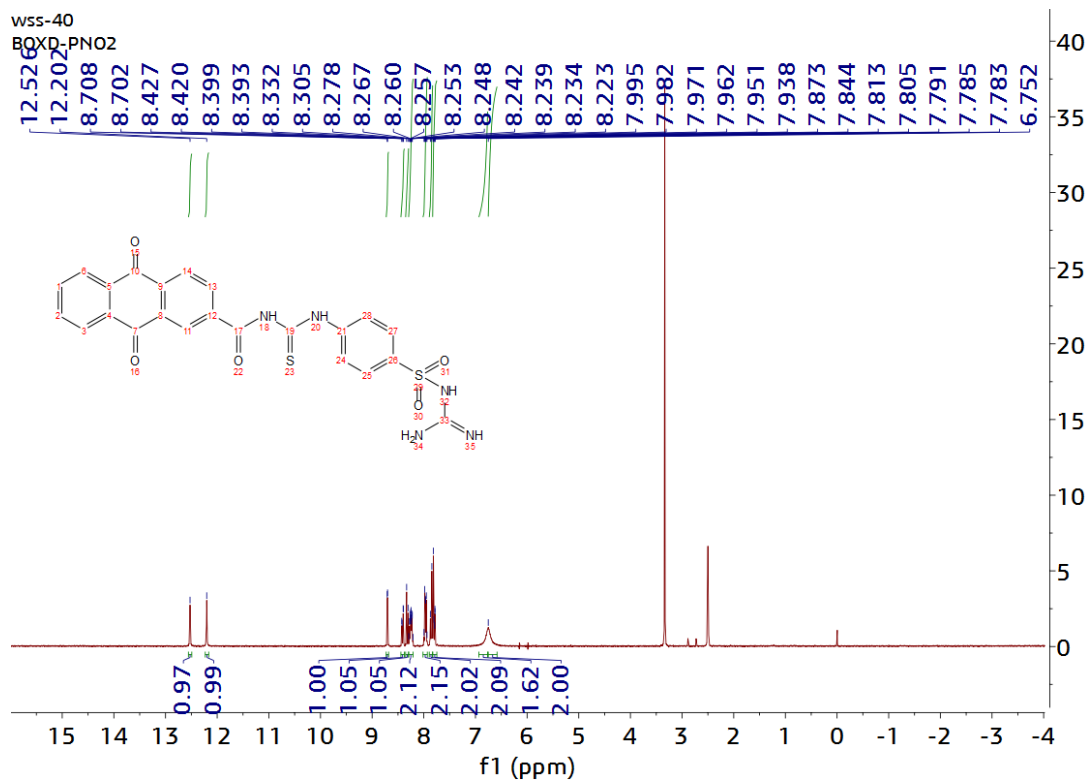
Data S13. ^1H -NMR, ^{13}C -NMR and HRMS data of compound 5m

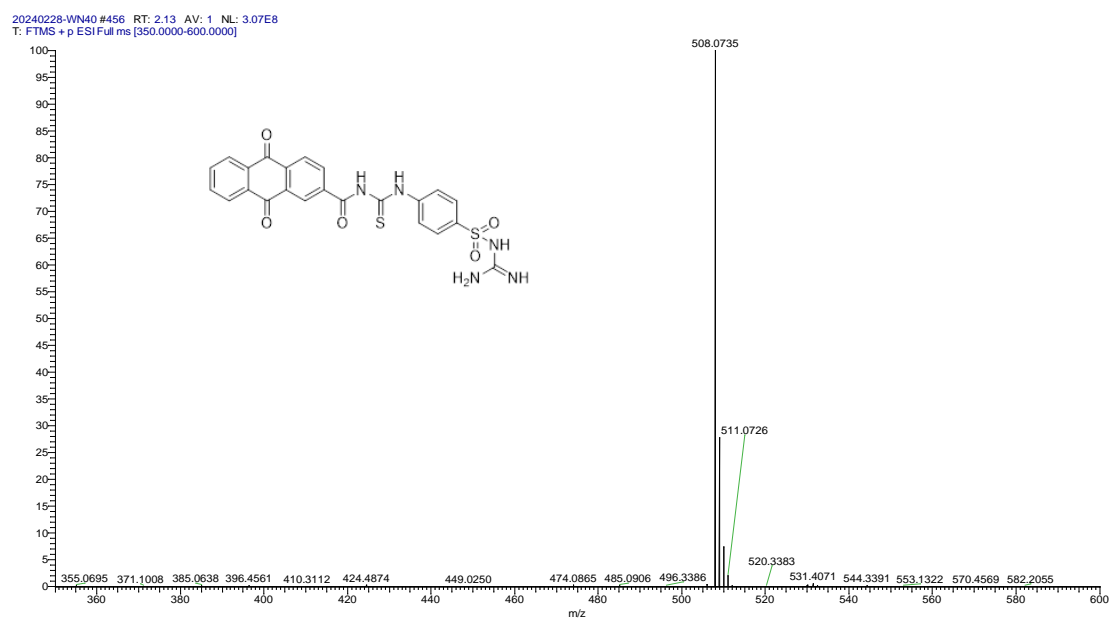
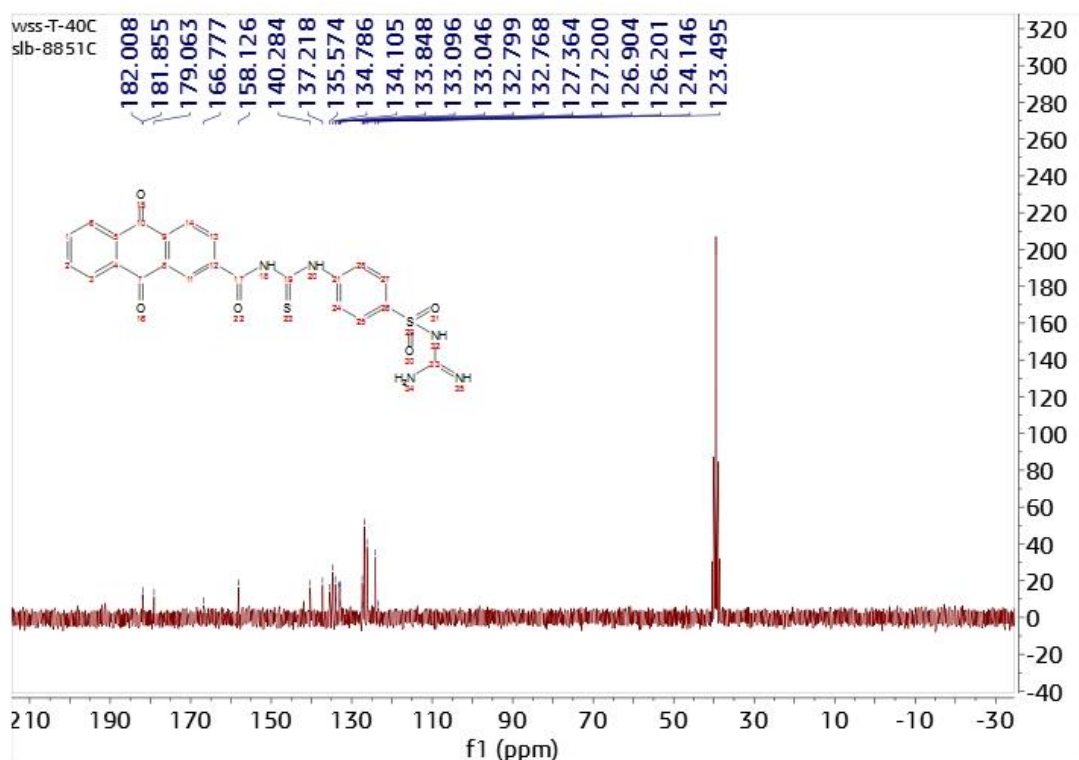


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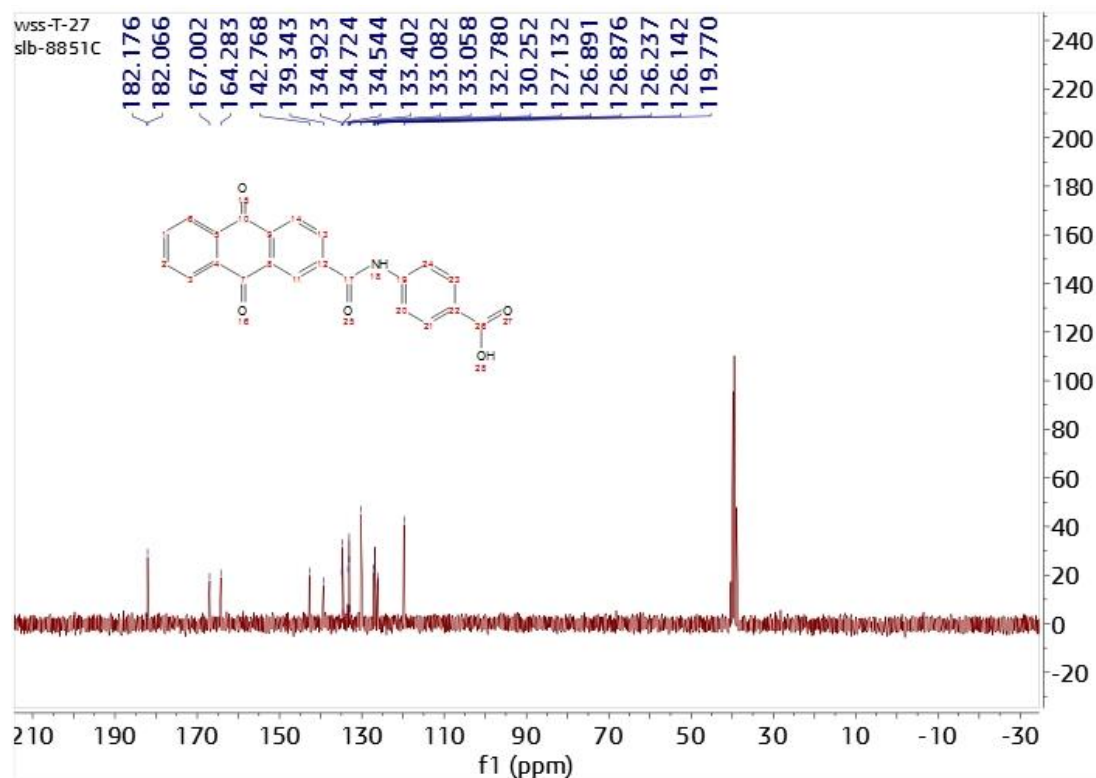
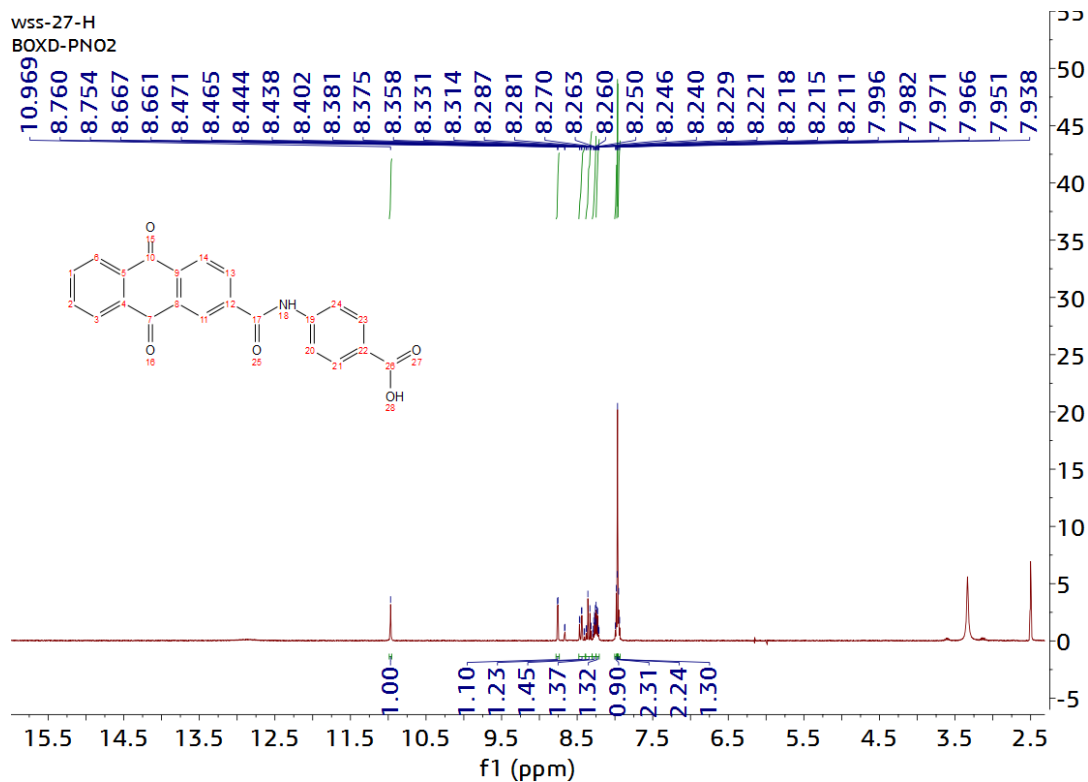


Data S14. ^1H -NMR, ^{13}C -NMR and HRMS data of compound 5n

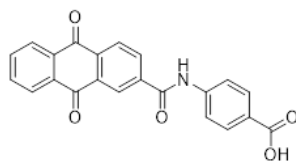
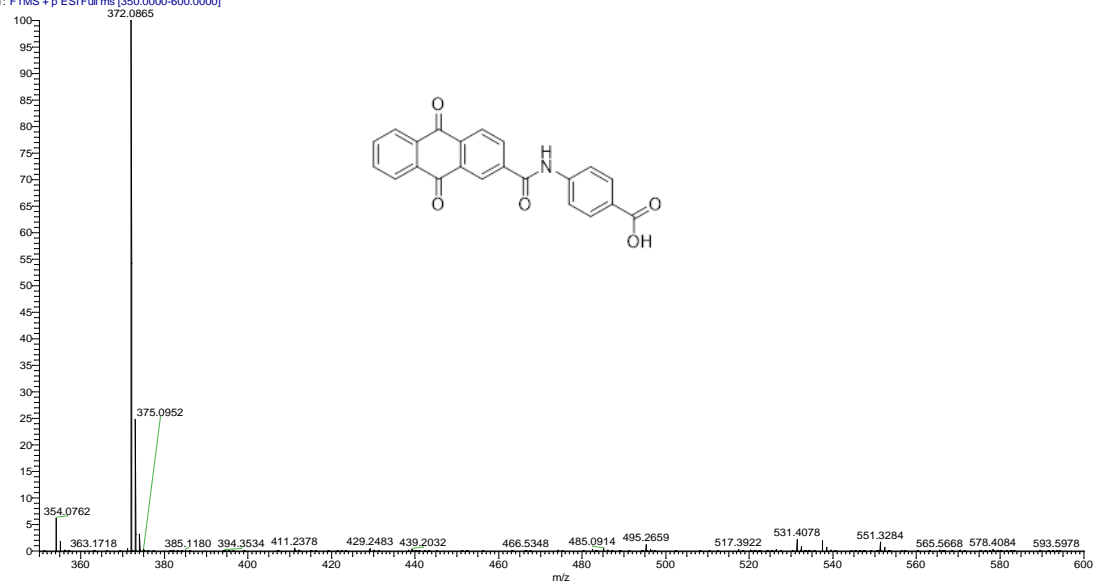




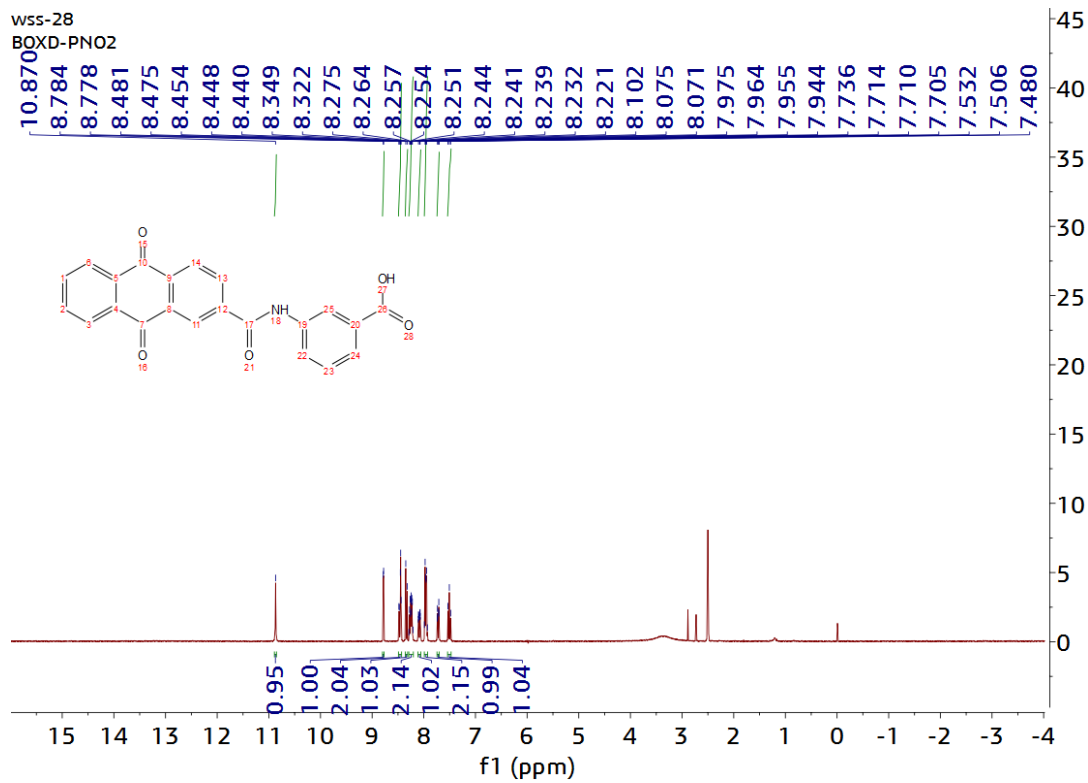
Data S15. ^1H -NMR, ^{13}C -NMR and HRMS data of compound 6a

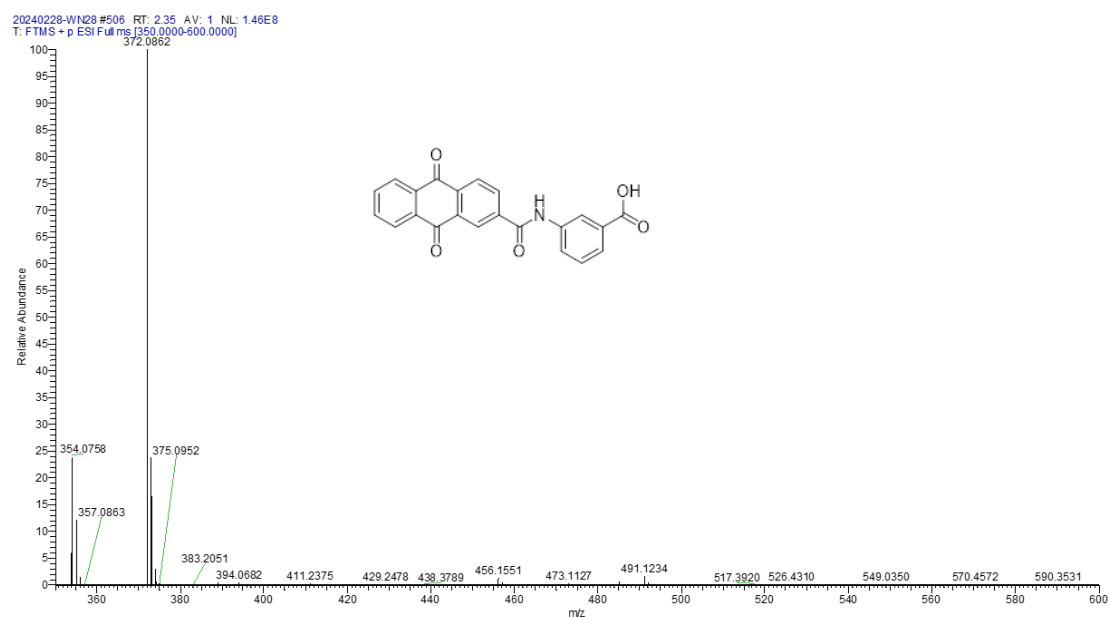
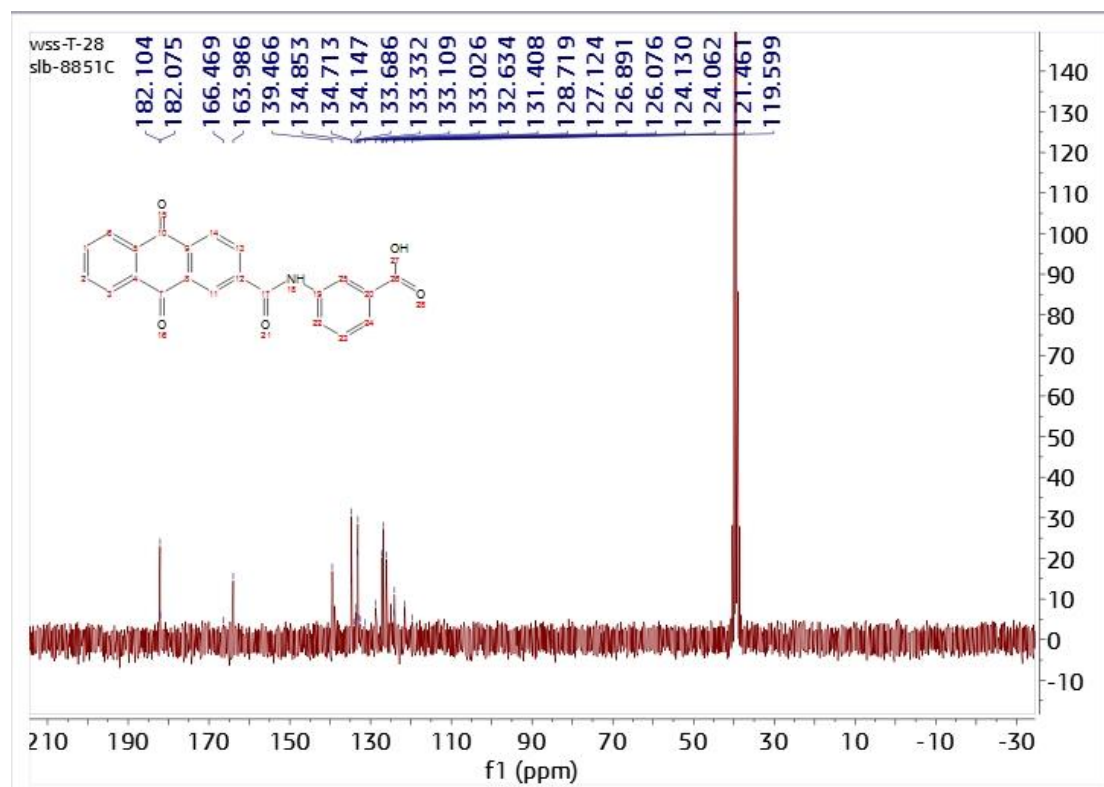


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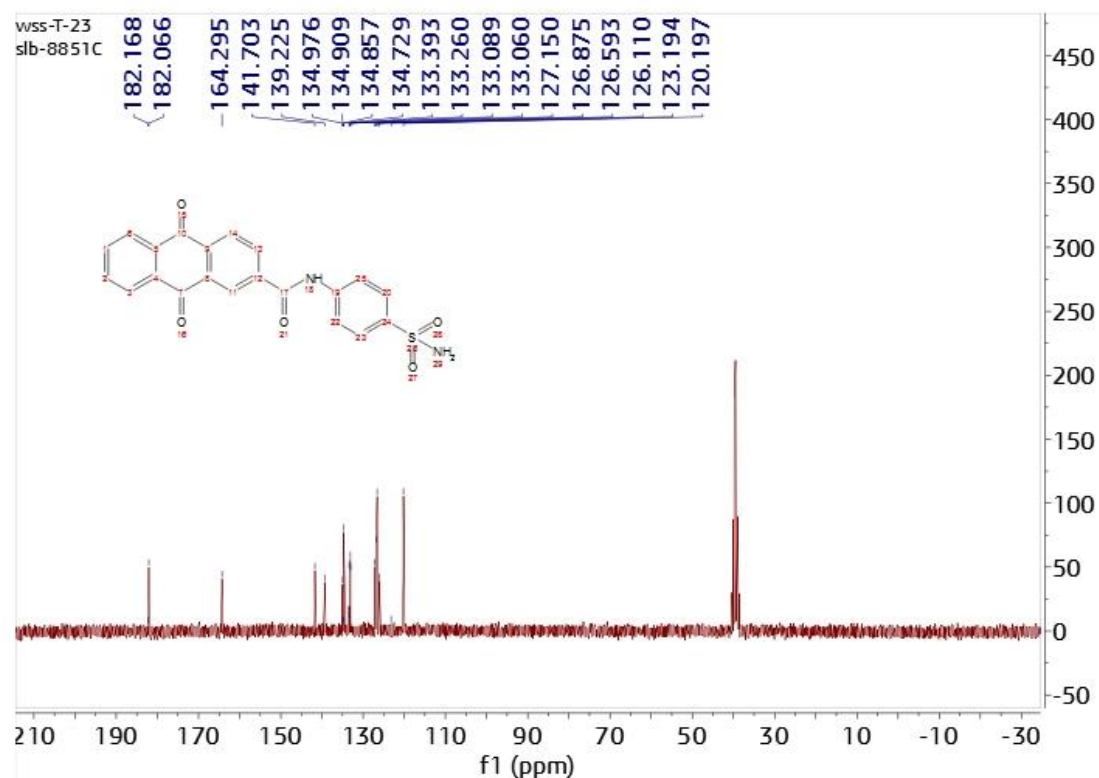
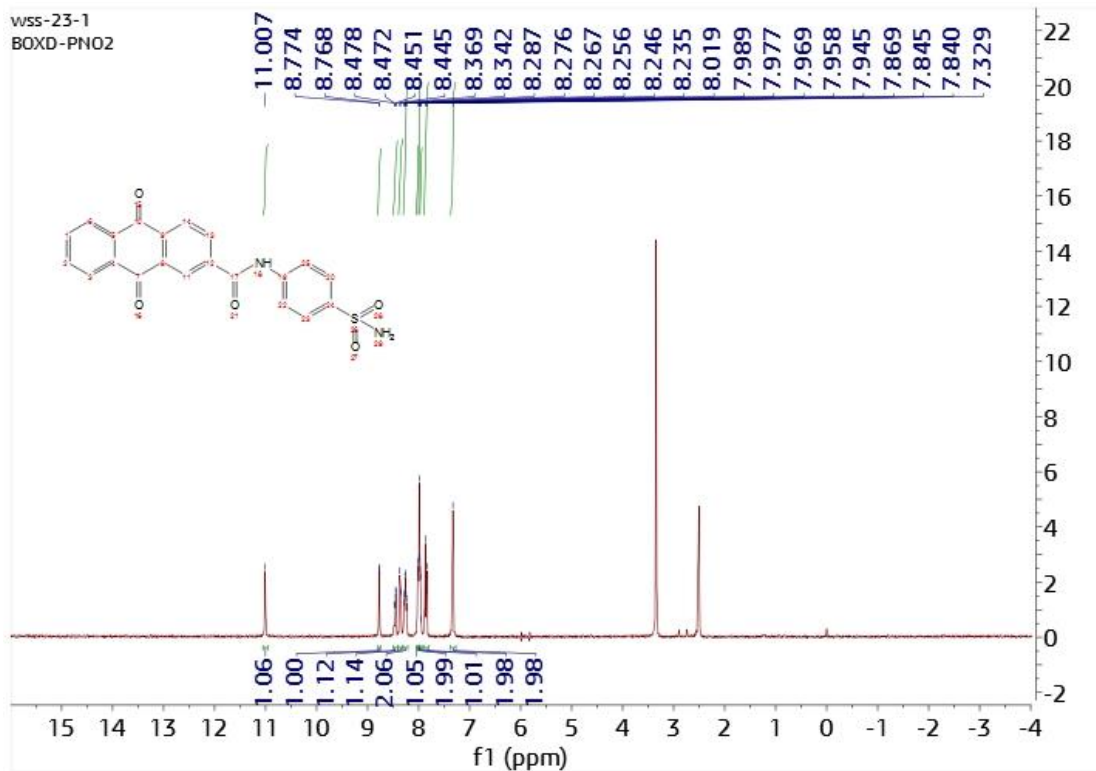


Data S16. ^1H -NMR, ^{13}C -NMR and HRMS data of compound 6b

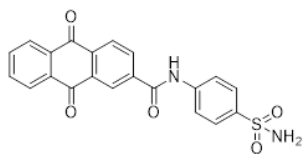
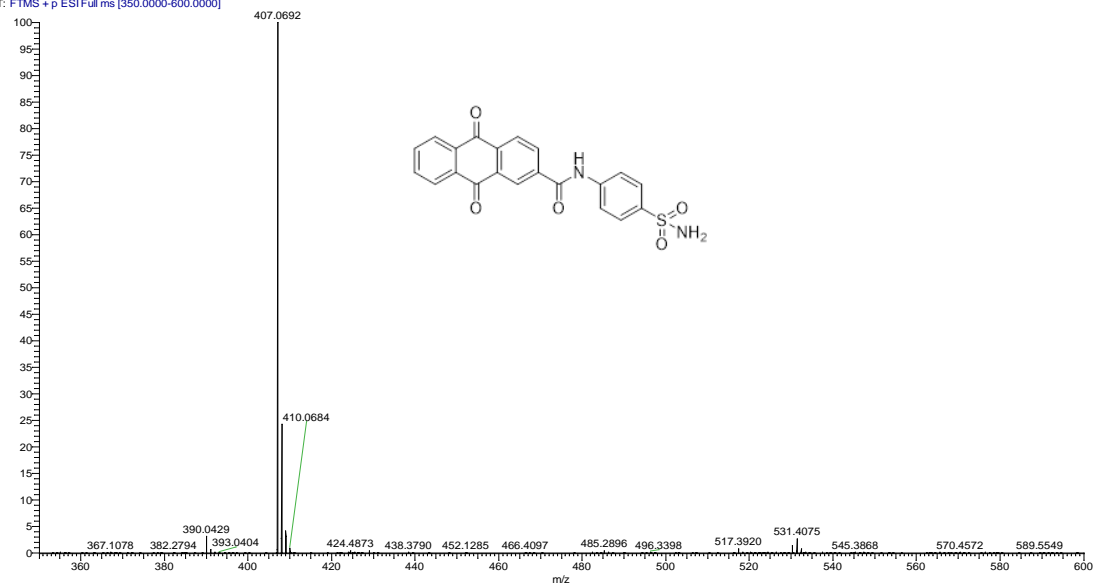




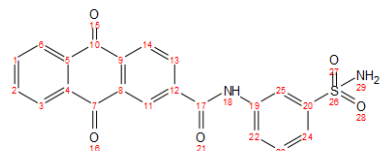
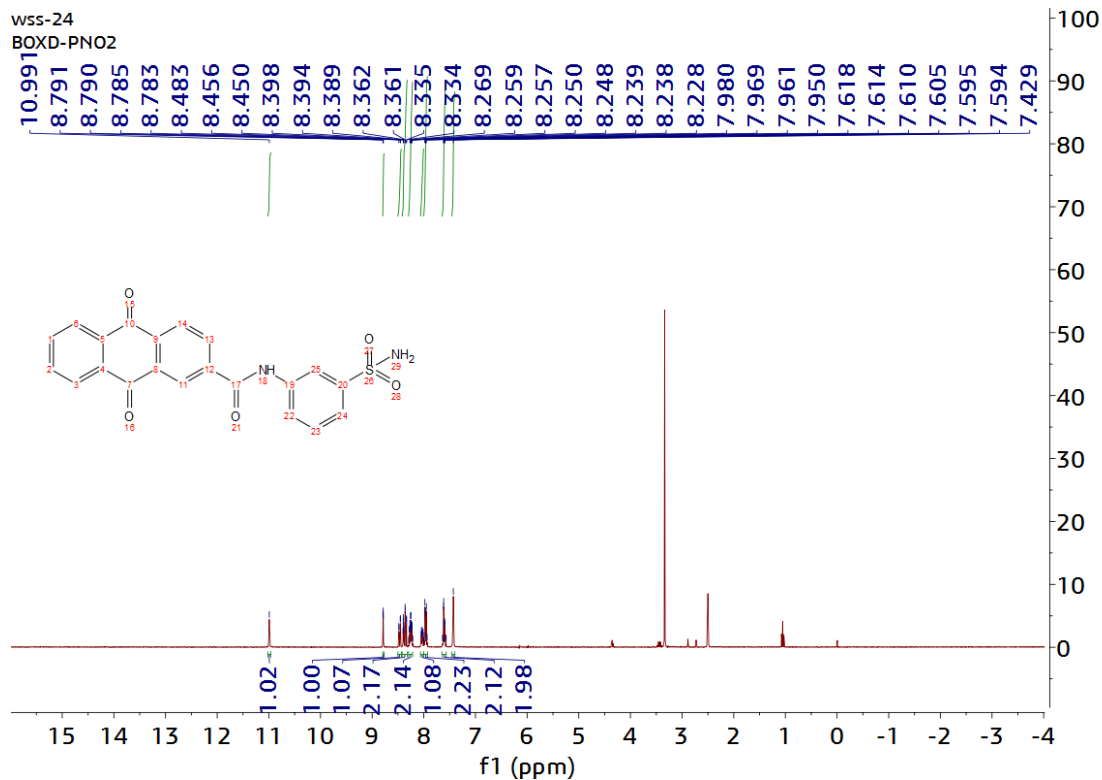
Data S17. ^1H -NMR, ^{13}C -NMR and HRMS data of compound 6c

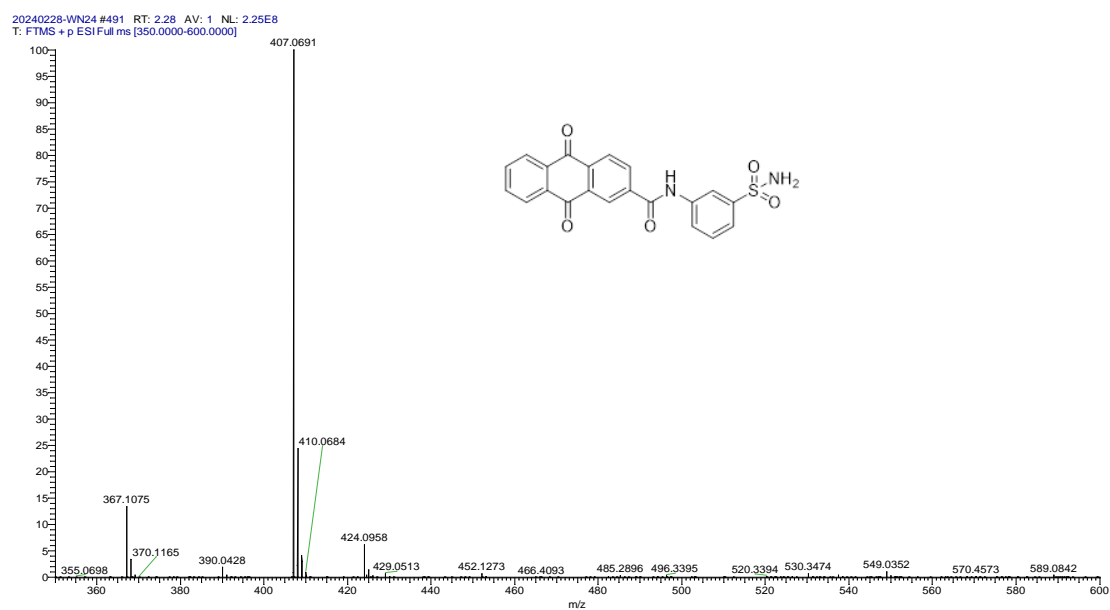
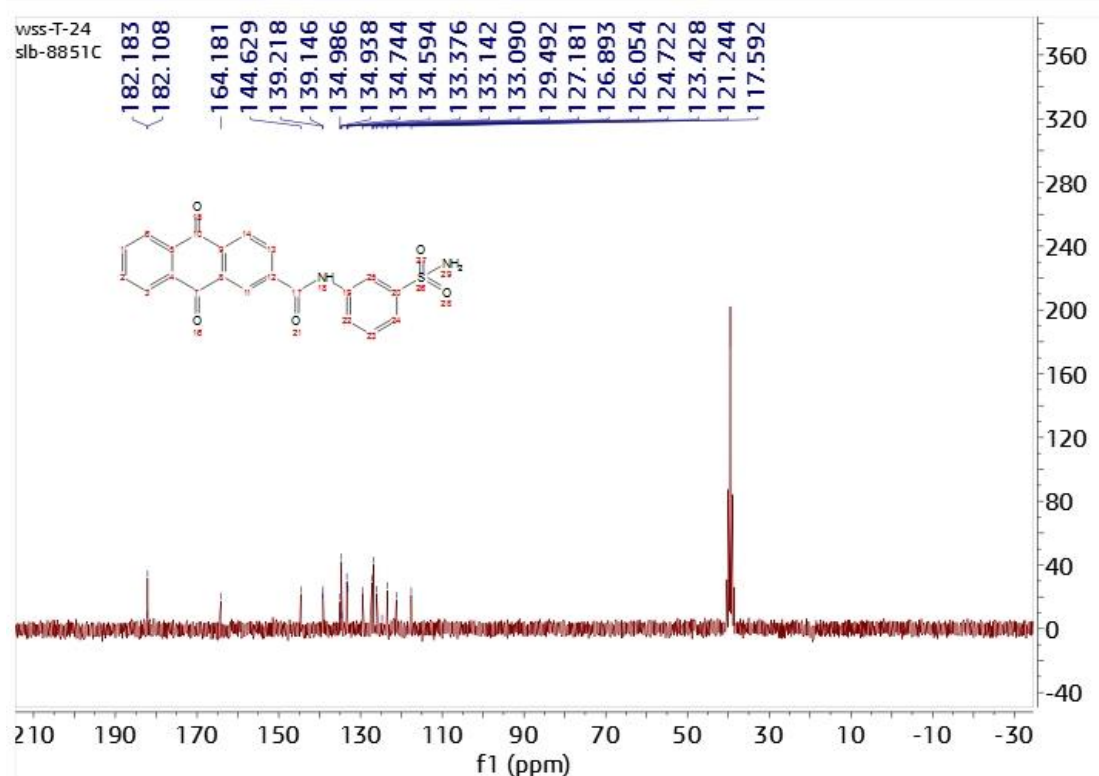


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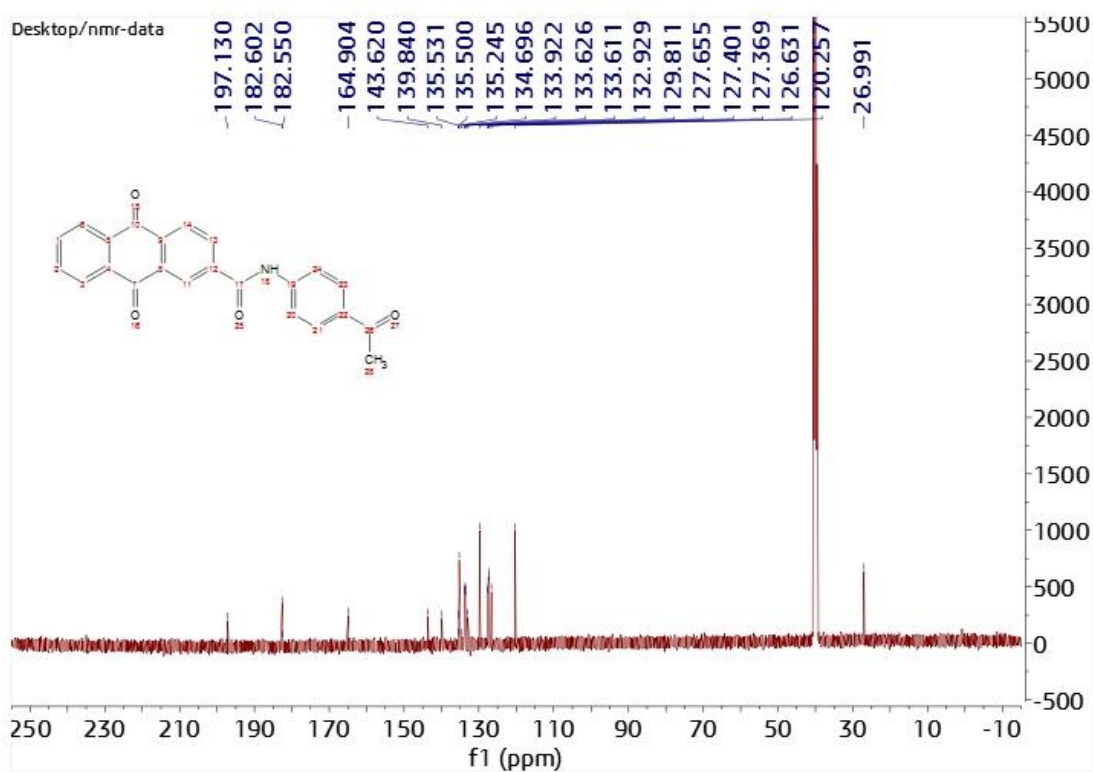
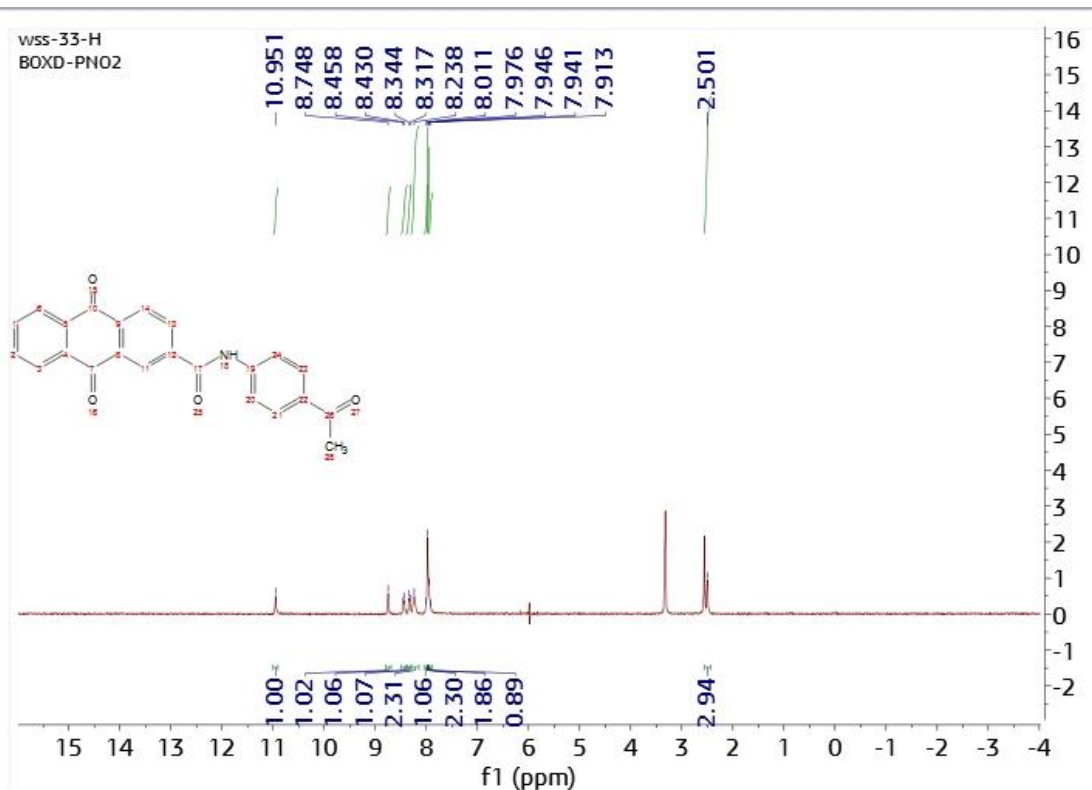


Data S18. ¹H-NMR, ¹³C-NMR and HRMS data of compound 6d

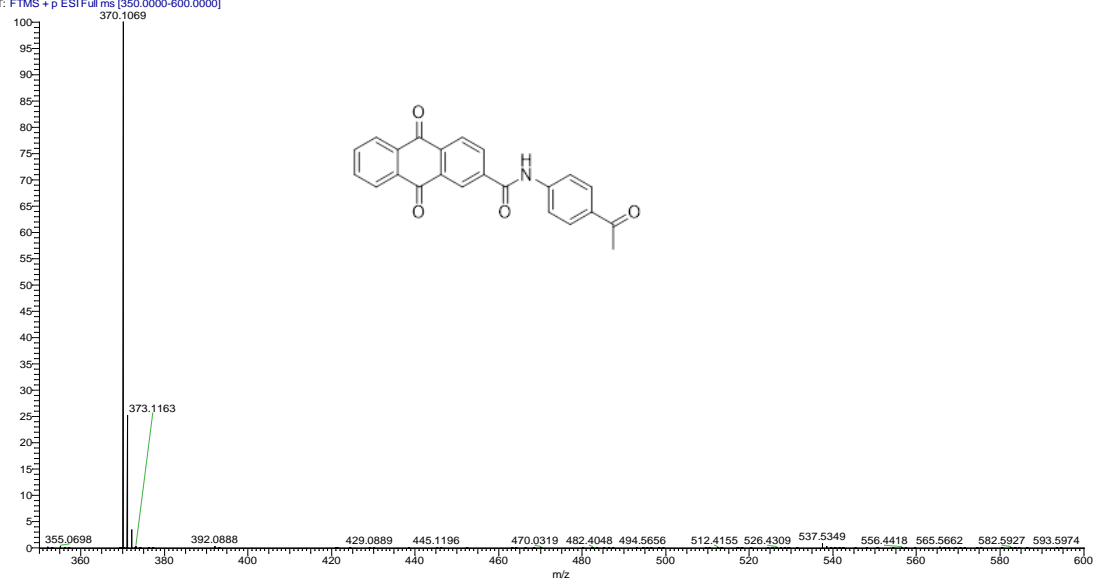




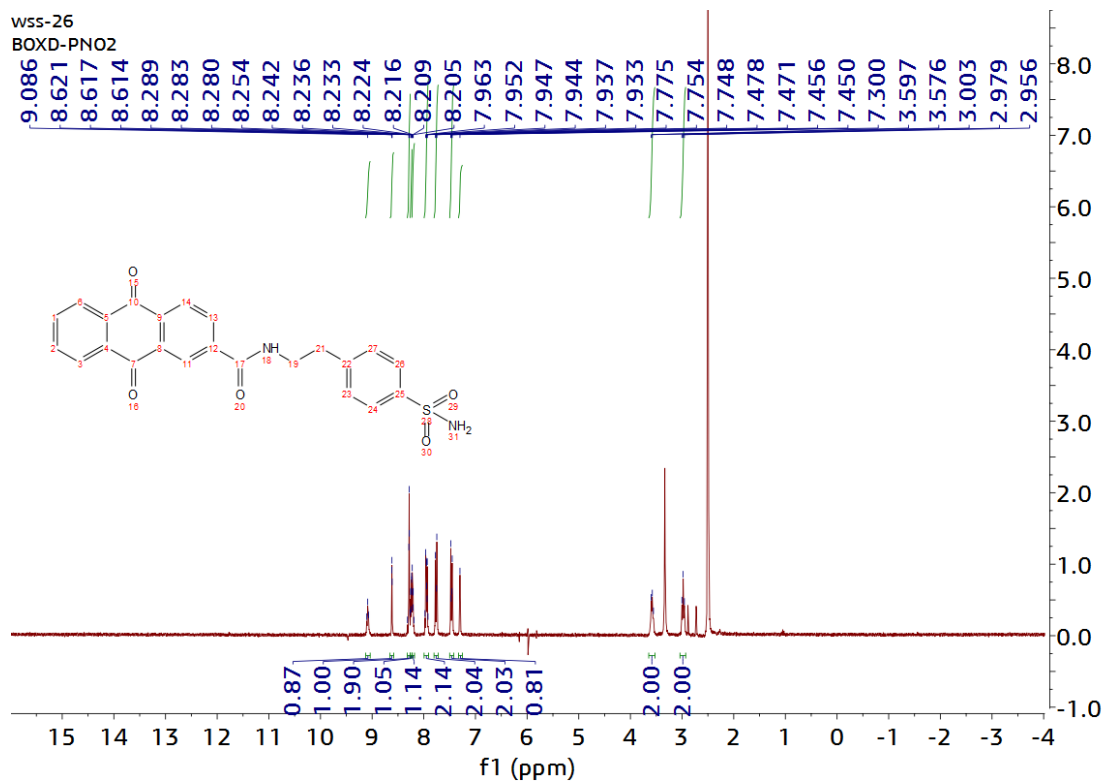
Data S19. ¹H-NMR, ¹³C-NMR and HRMS data of compound 6e

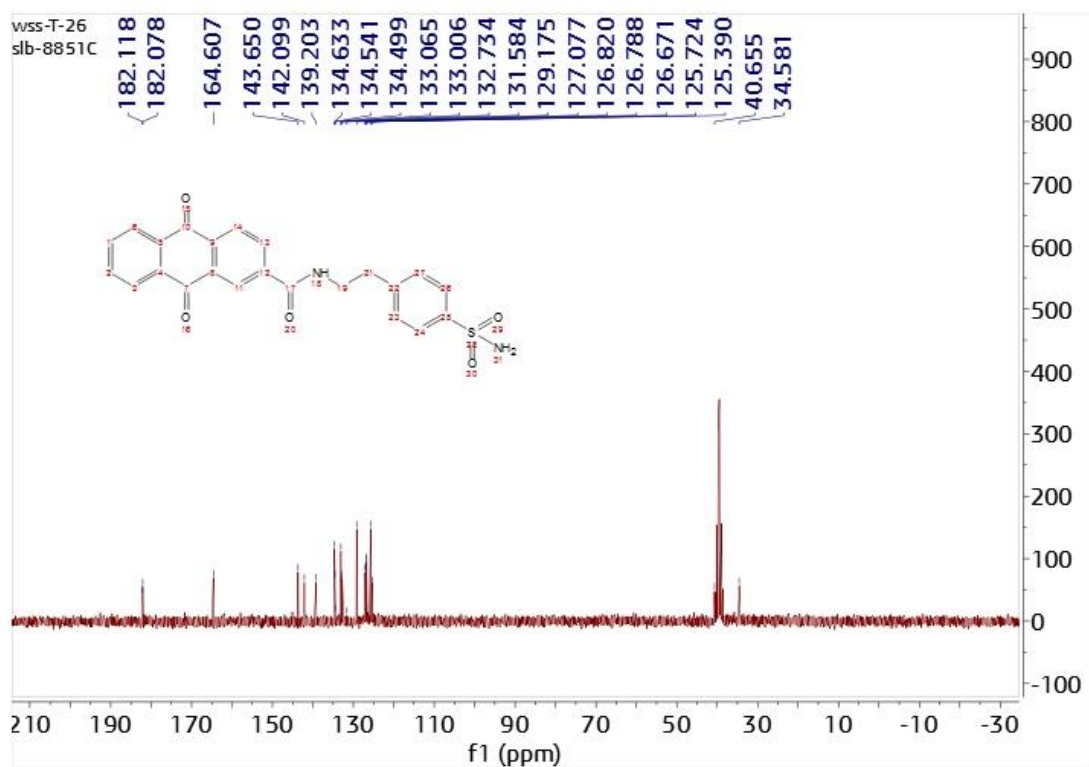


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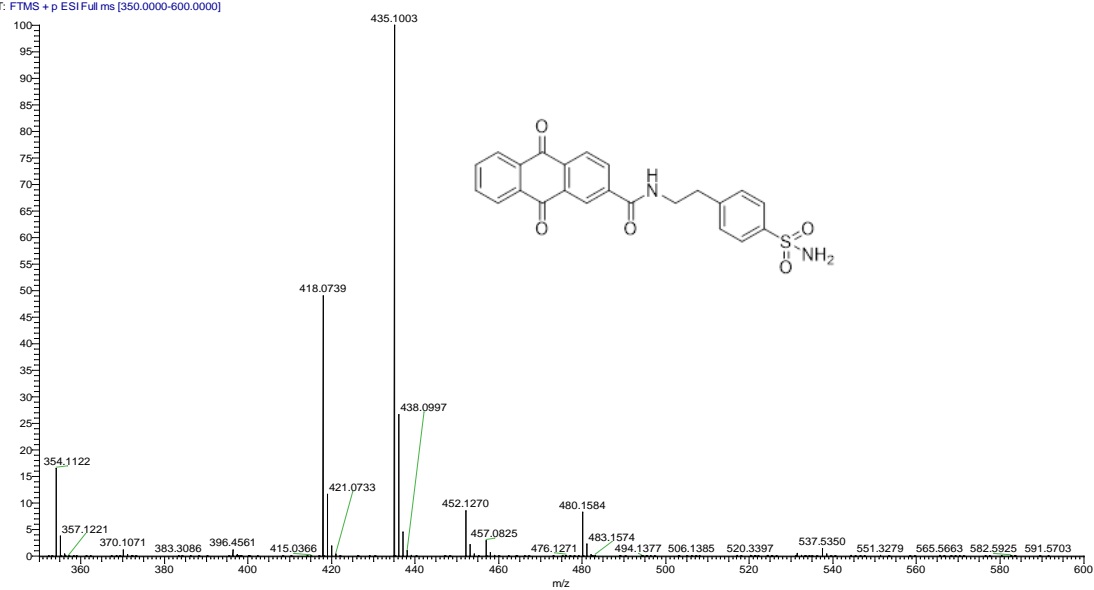


Data S20. ¹H-NMR, ¹³C-NMR and HRMS data of compound 6h

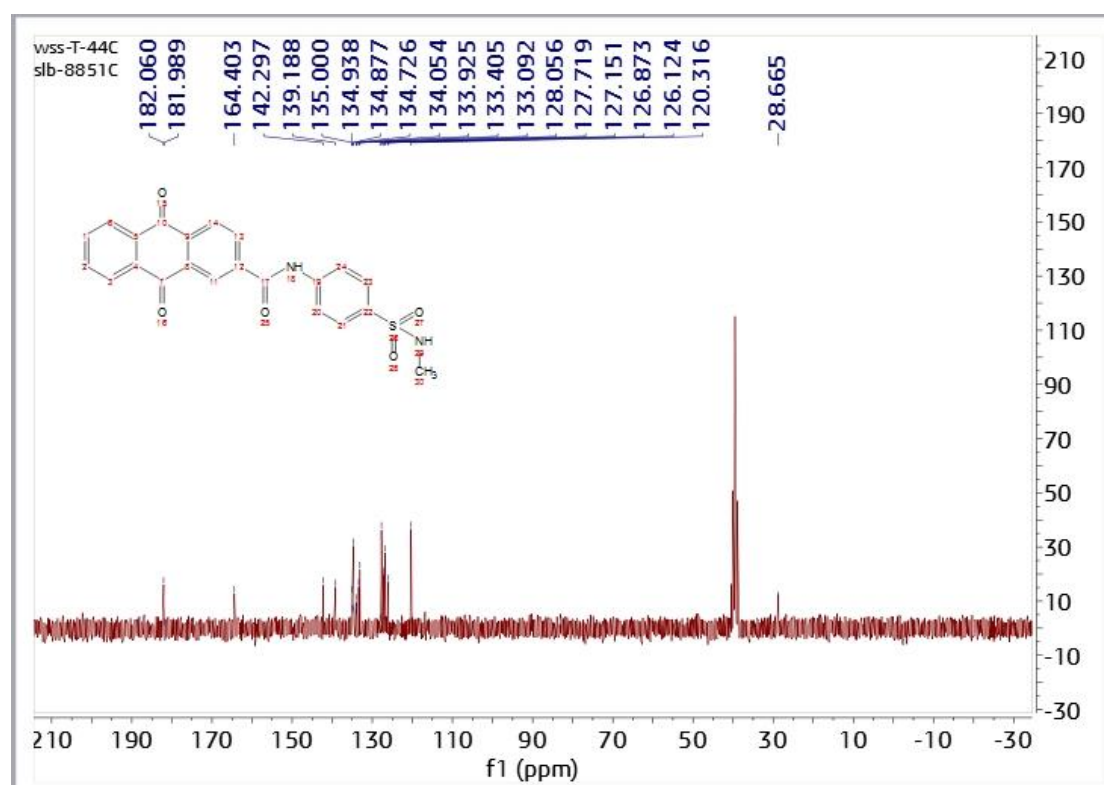
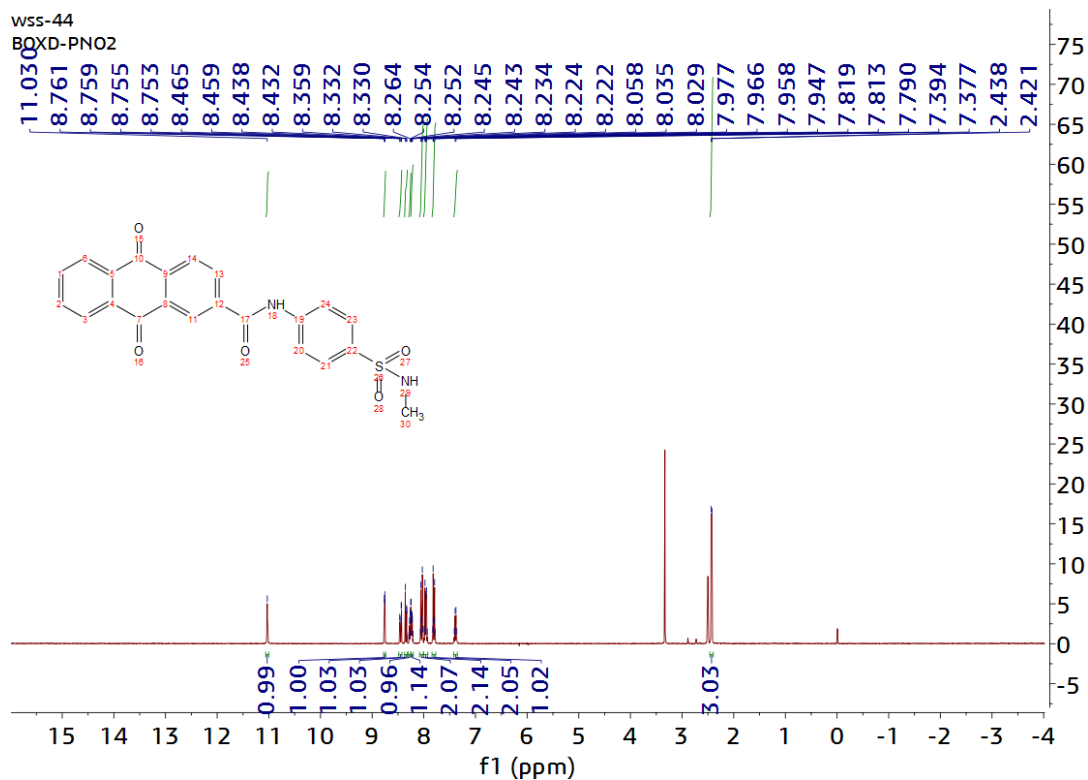




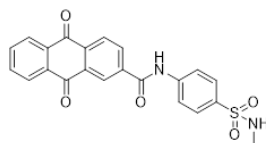
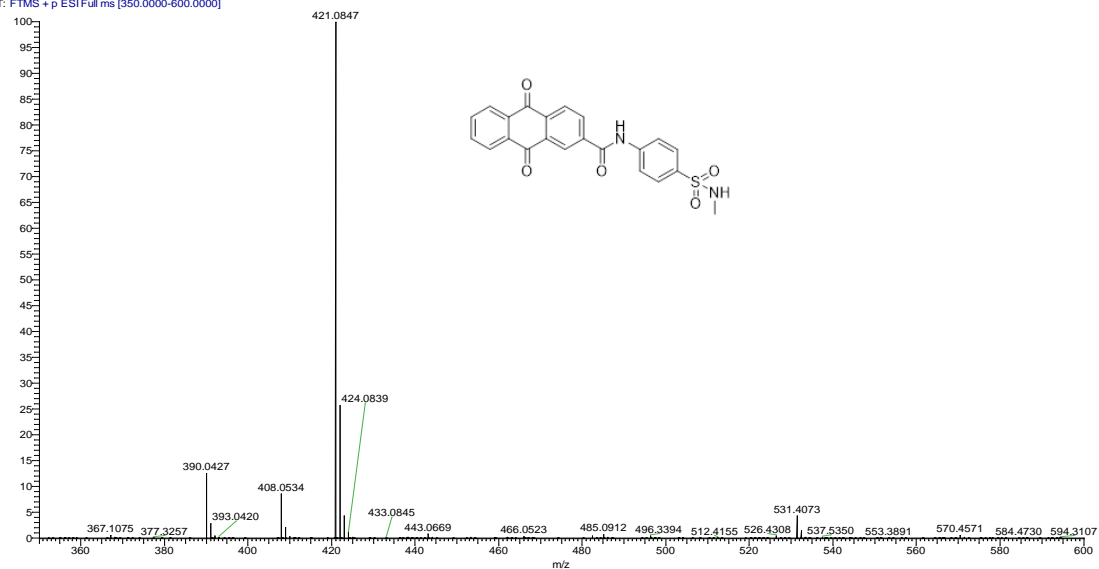
20240226-WN26 #456 RT: 2.13 AV: 1 NL: 1.20E8
T: FTMS + p ESI Full ms [350.0000-600.0000]



Data S21. ¹H-NMR, ¹³C-NMR and HRMS data of compound 6i



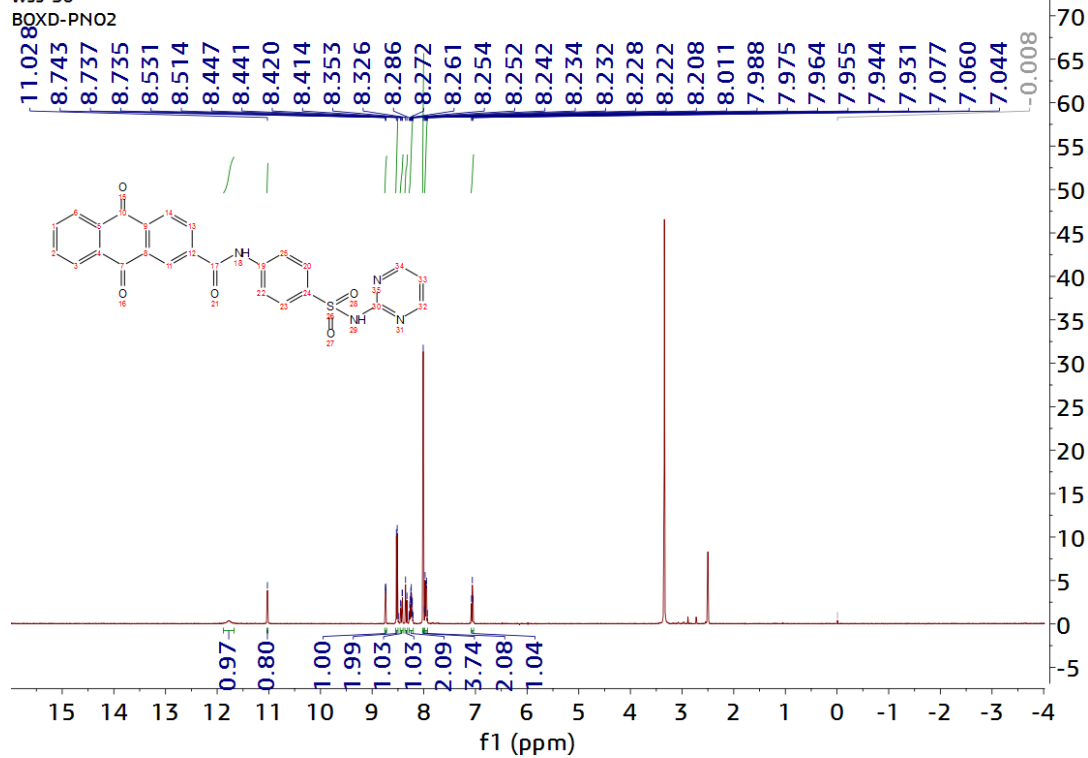
20240228-WN44 #531 RT: 2.47 AV: 1 NL: 1.24E8
T: FTMS + p ESI Full ms [350.0000-600.0000]

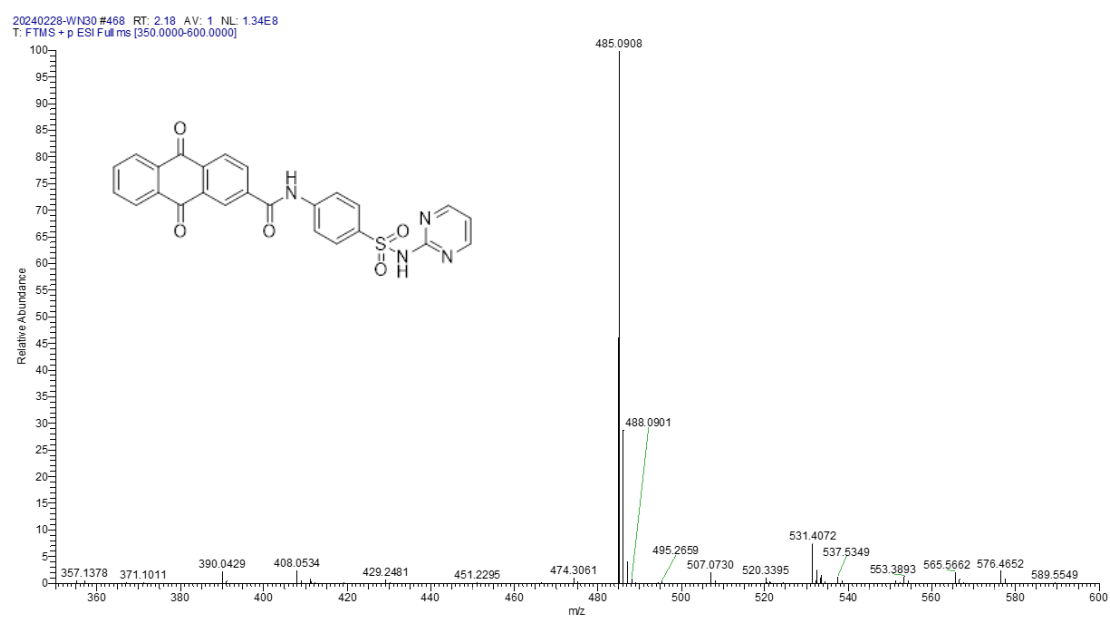
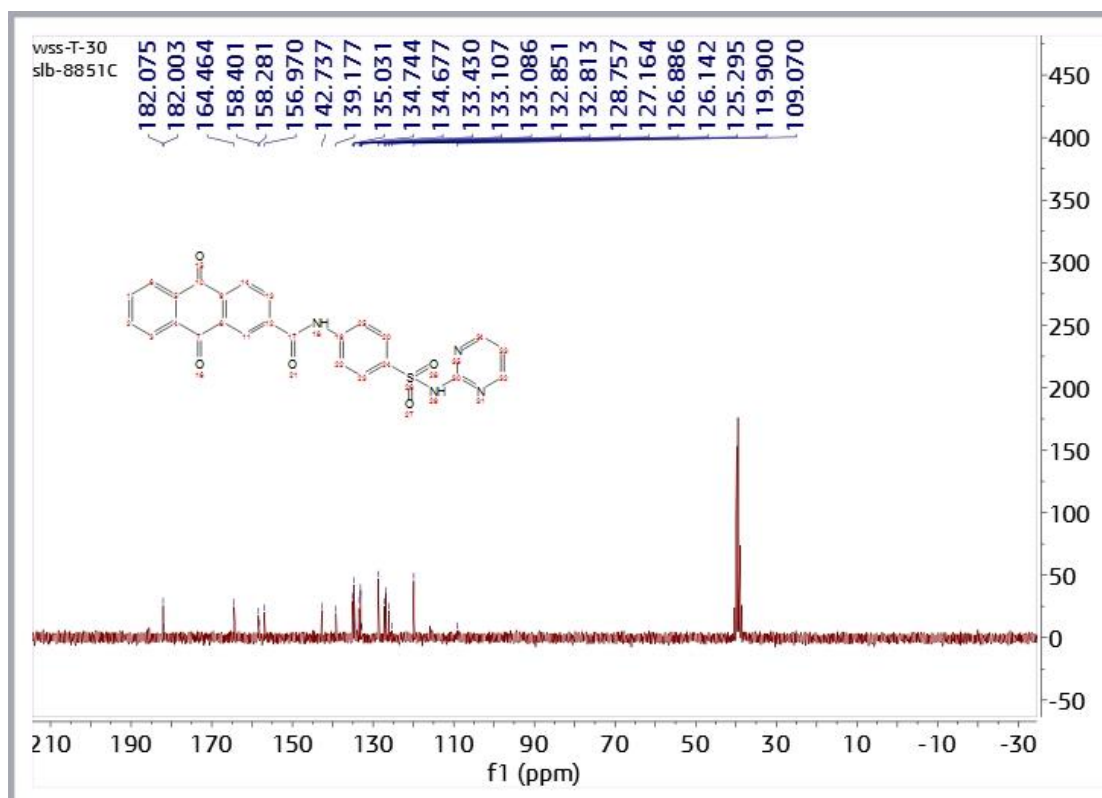


Data S22. ¹H-NMR, ¹³C-NMR and HRMS data of compound 6j

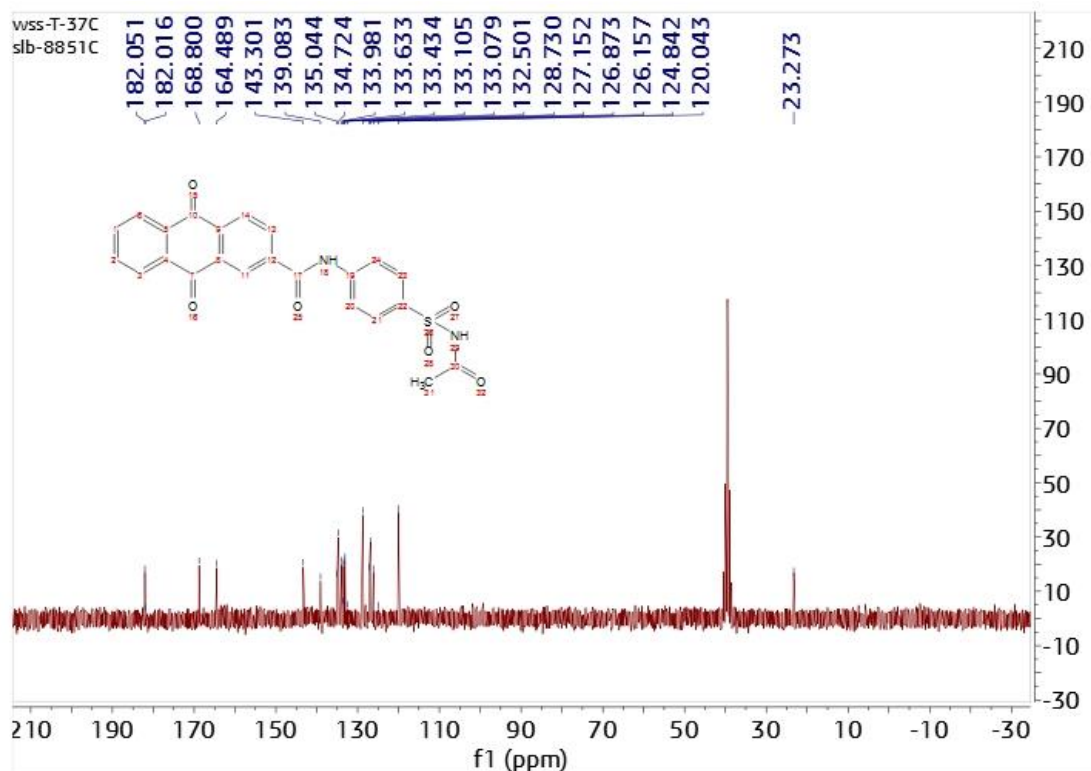
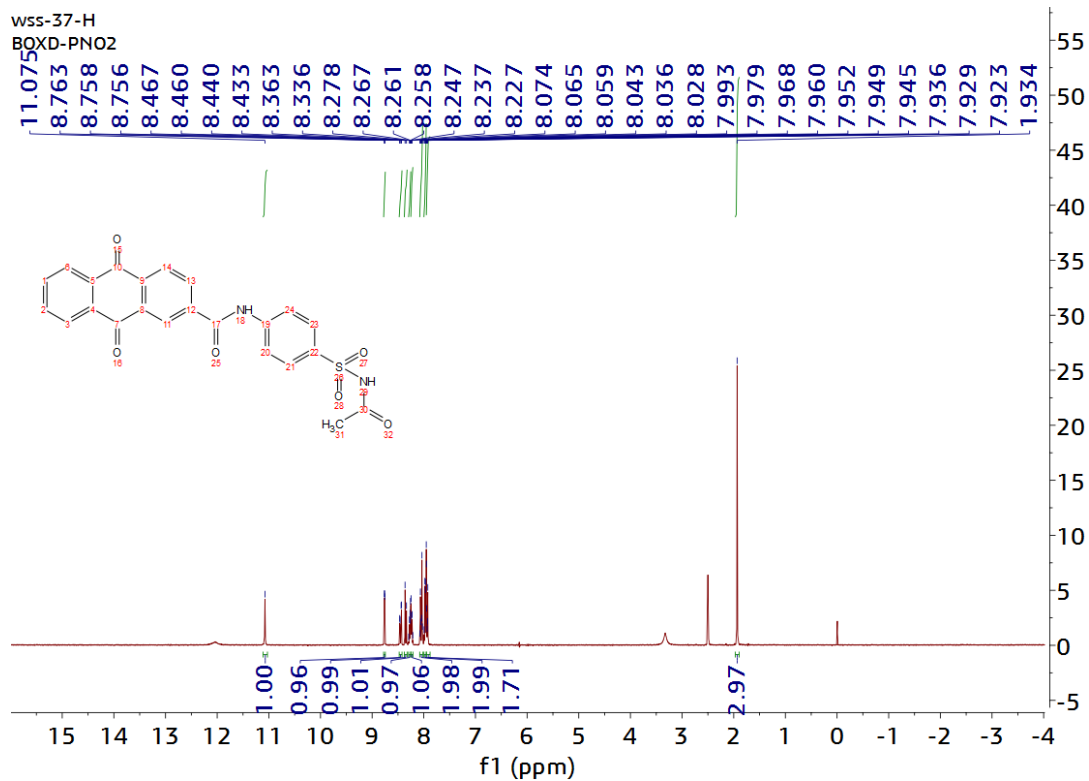
wss-30

BOXD-PNO2

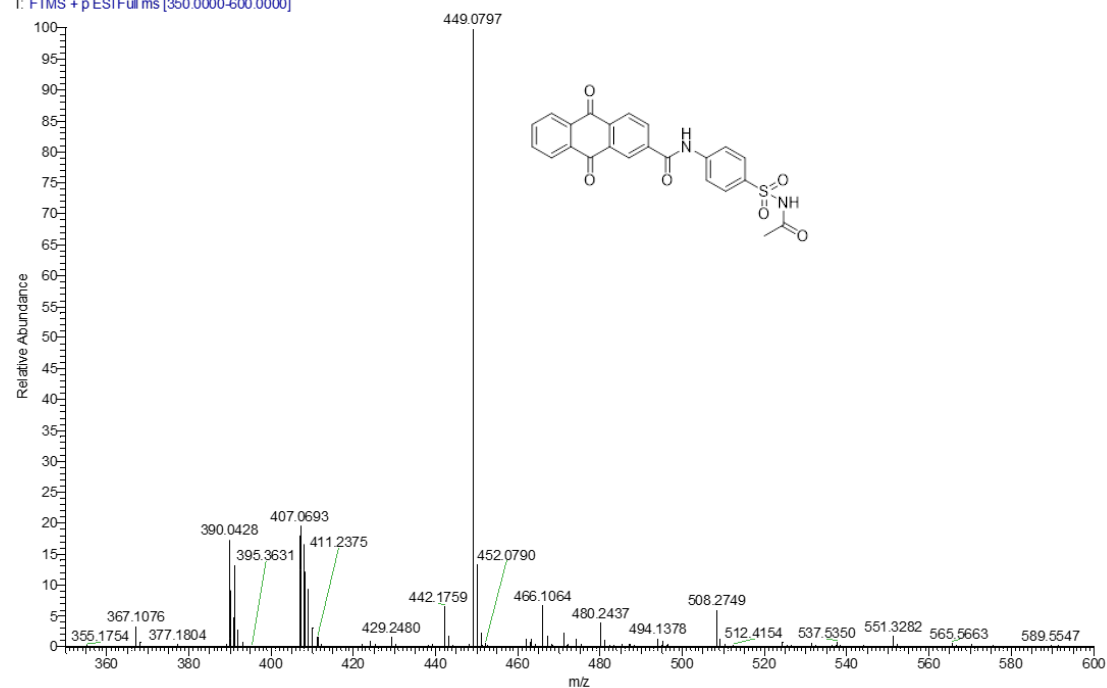




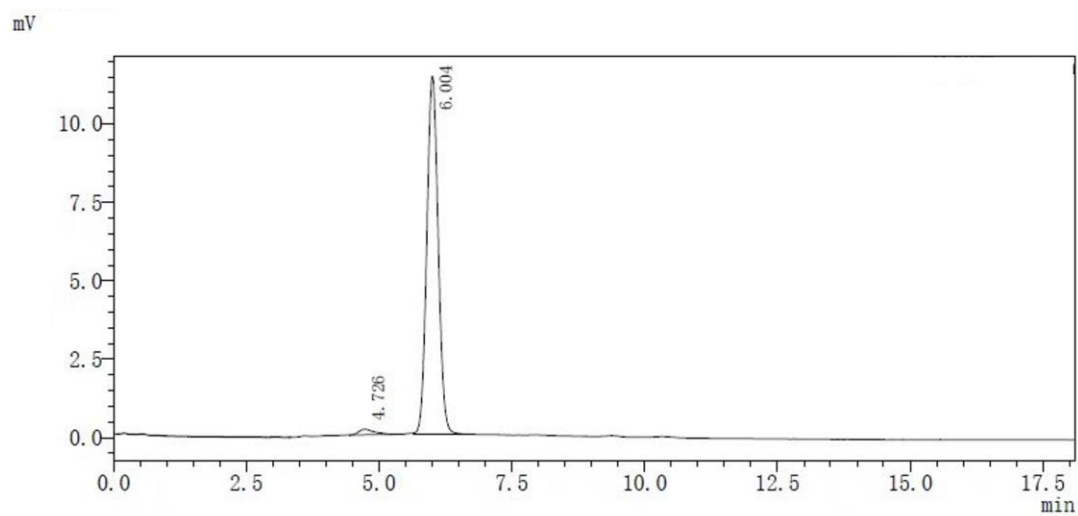
Data S23. ^1H -NMR, ^{13}C -NMR and HRMS data of compound 6k



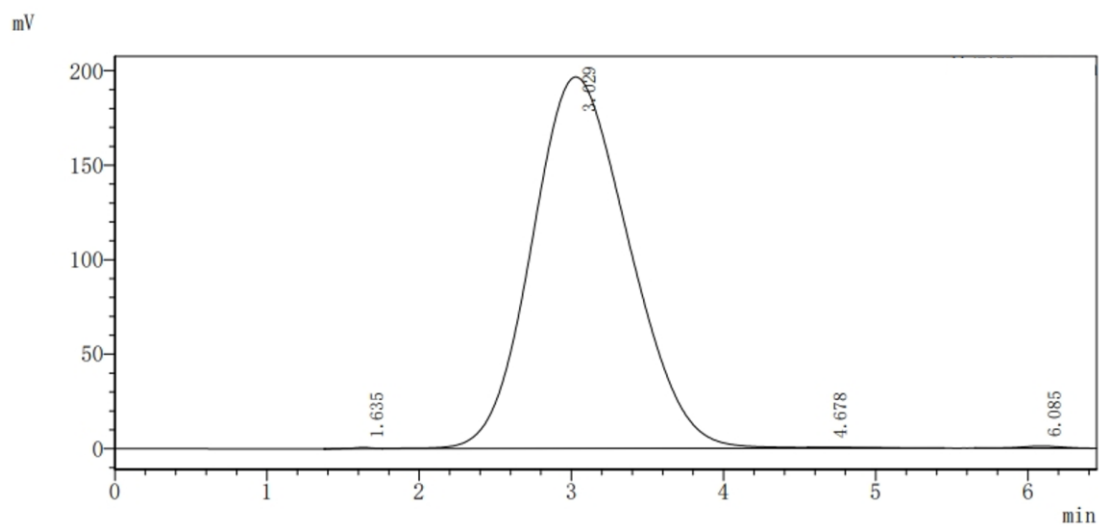
20240228-WN37-pos #497 RT: 2.31 AV: 1 NL: 2.87E7
T: FTMS + p ESI Full ms [350.0000-600.0000]



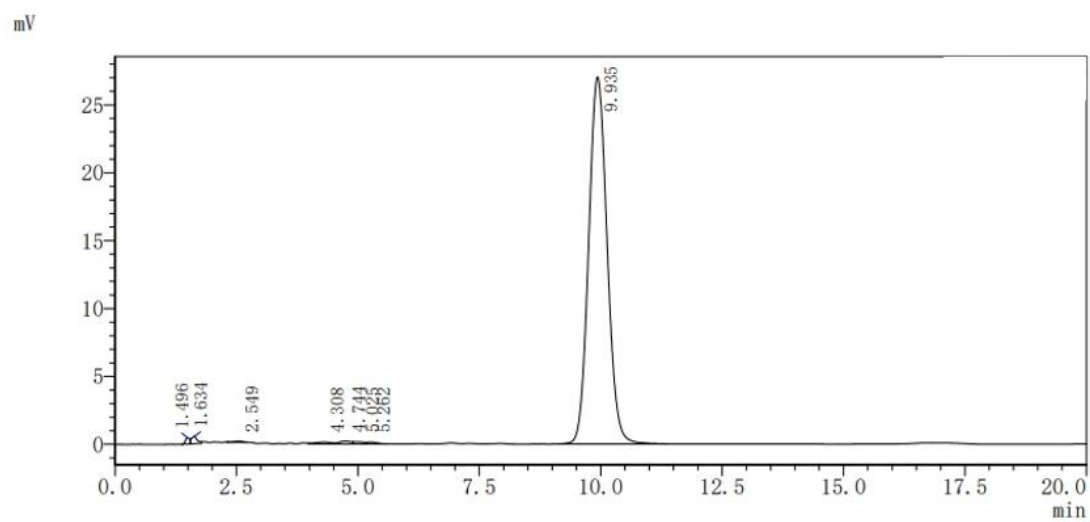
Data S24.HPLC data of compound 5c, 5h, 6c and 6h.



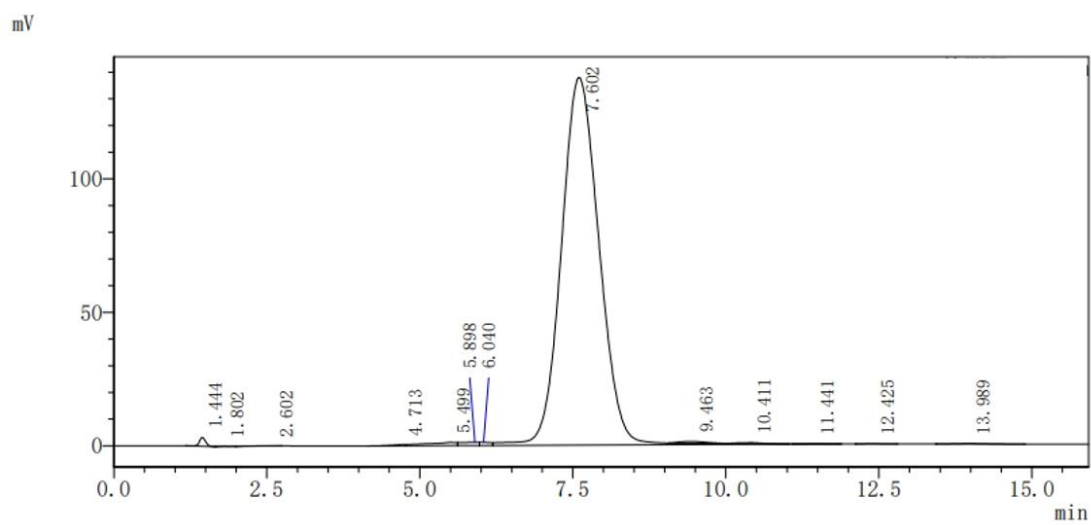
compound 5c



compound 5h



compound 6c



compound 6h