Synthesis, Characterization, Mechanism of Decomposition, and Antiproliferative Activity of a Class of PEGylated Benzopolysulfanes Structurally Similar to the Natural Product Varacin

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Supporting Information

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S50 Figure 46: (A) Extracted ion chromatogram of norbornenetrithiolane **17** formed in the reaction of **6A**-**F** and norbornene in the presence of ethanethiol, Rt 16.75 min. (B) MS spectrum of norbornenetrithiolane **17**, Rt 16.75 min.

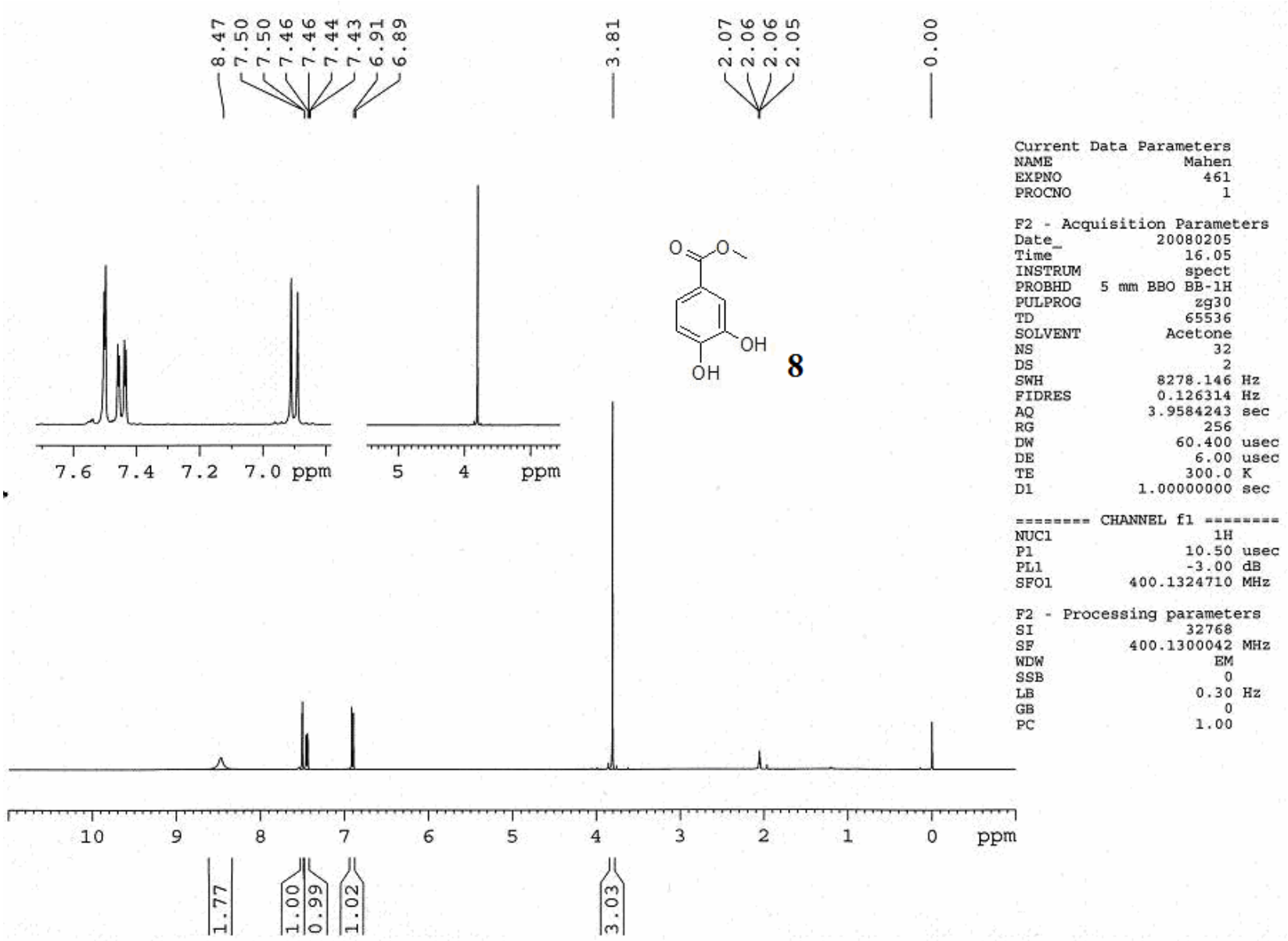


Figure 1. ^{1}H NMR of 3,4-dihydroxybenzoic acid methyl ester– acetone-d_6.

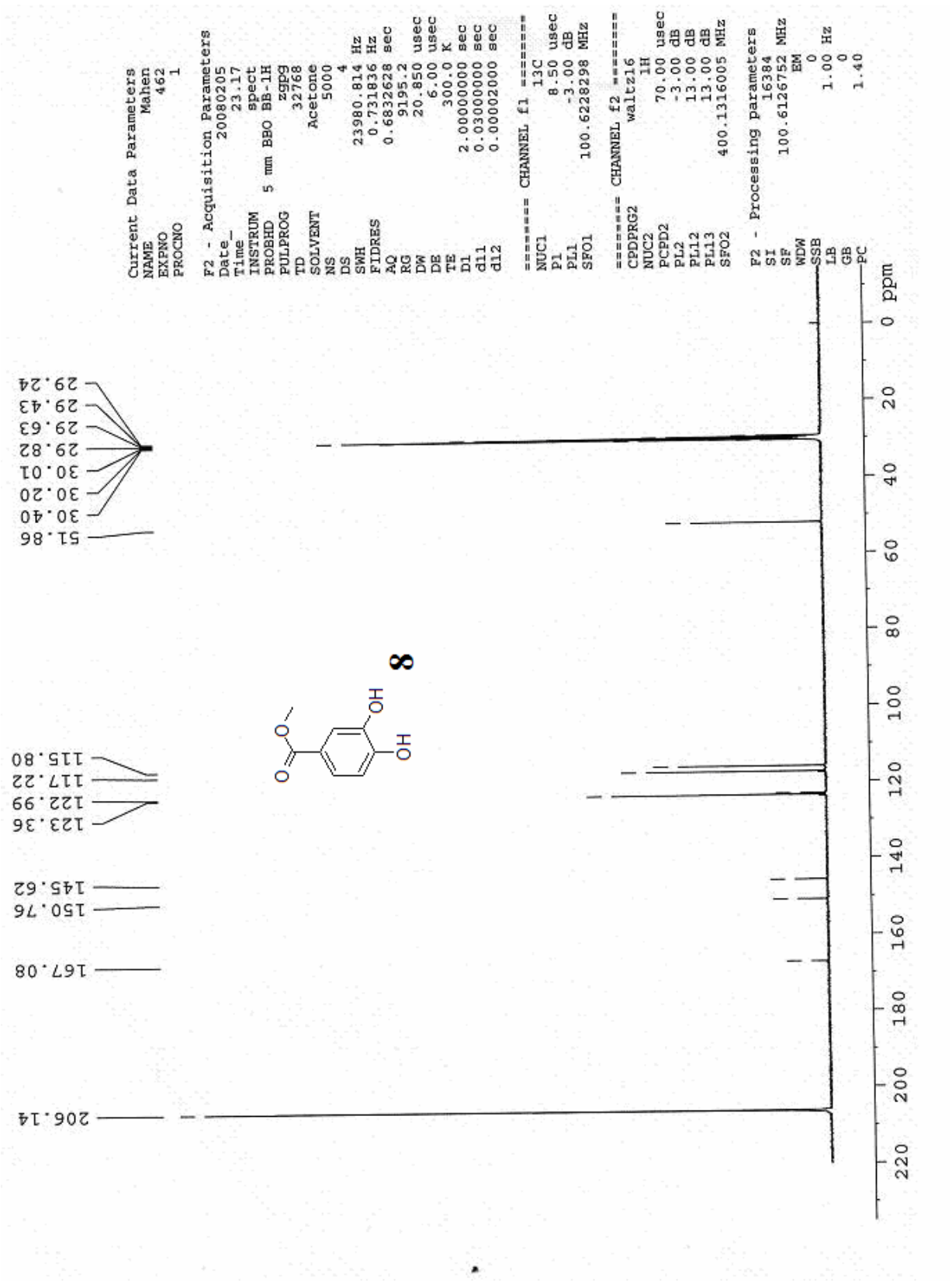


Figure 2. ^{13}C NMR of 3,4-dihydroxybenzoic acid methyl ester– acetone-d_6.

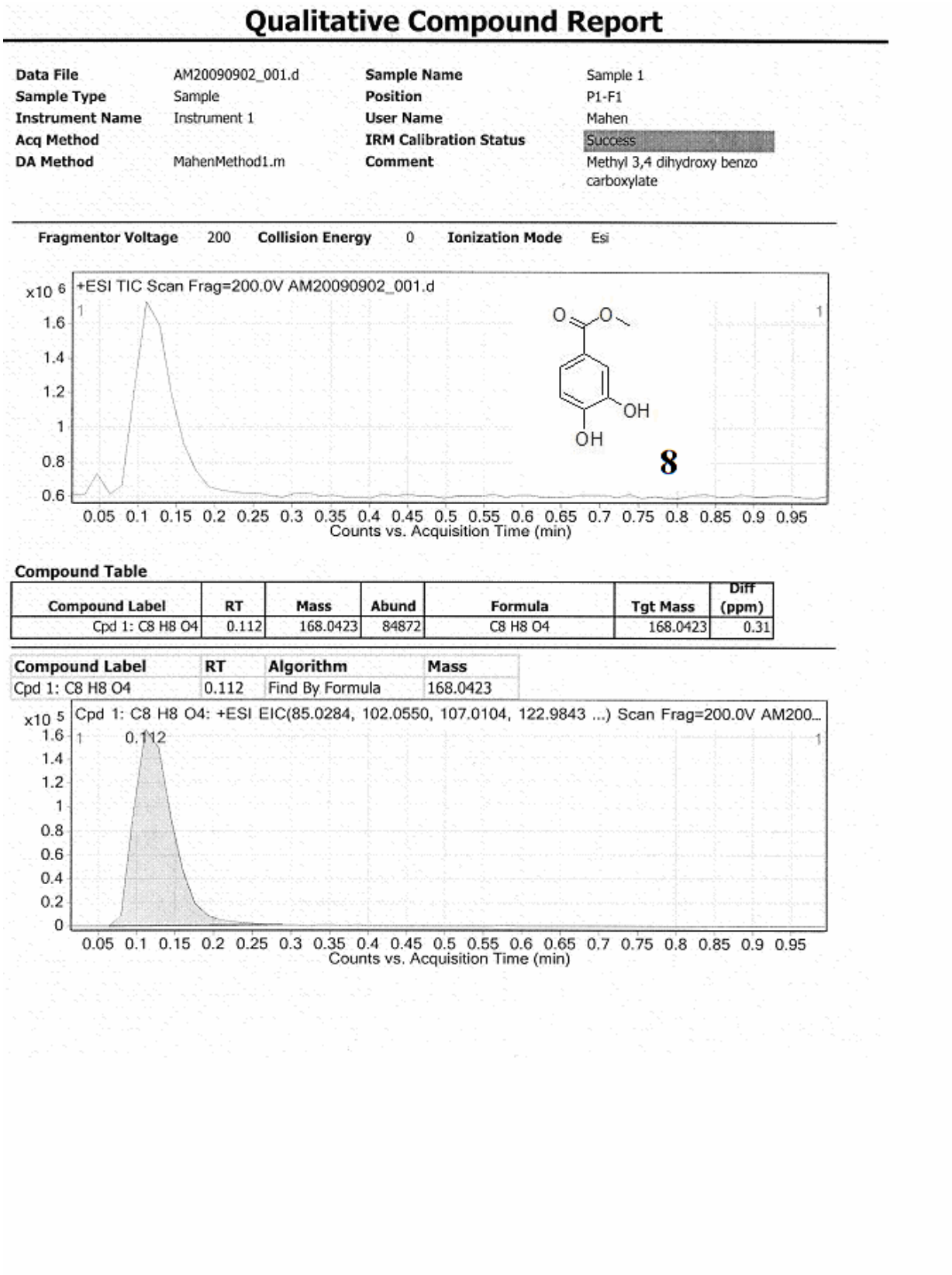
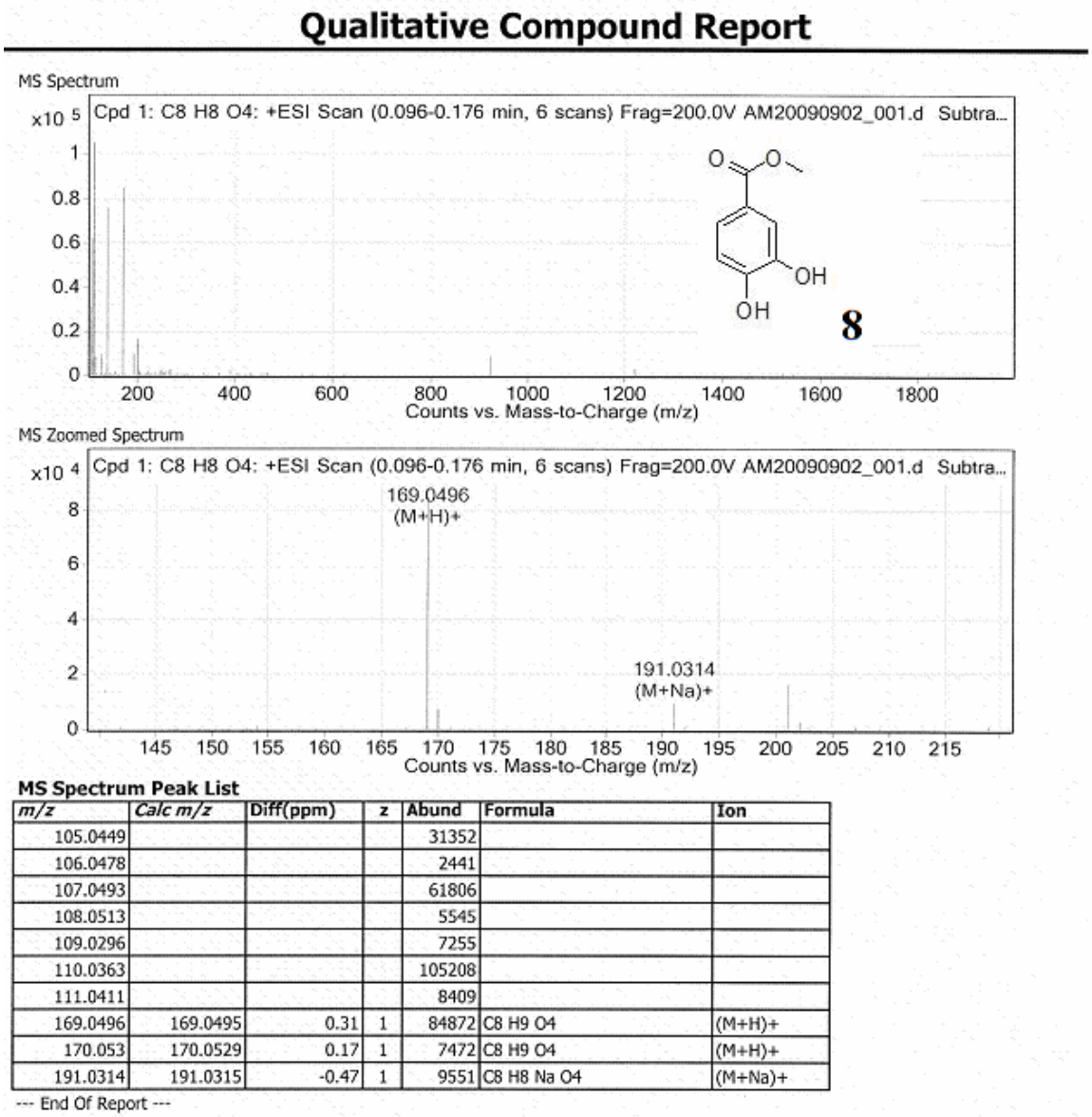


Figure 3. HRMS of 3,4-dihydroxybenzoic acid methyl ester.



m/z	Calc m/z	Diff(ppm)	z	Abund	Formula	Ion
105.0449				31352		
106.0478				2441		
107.0493				61806		
108.0513				5545		
109.0296				7255		
110.0363				105208		
111.0411				8409		
169.0496	169.0495	0.31	1	84872	C8 H9 O4	(M+H)+
170.053	170.0529	0.17	1	7472	C8 H9 O4	(M+H)+
191.0314	191.0315	-0.47	1	9551	C8 H8 Na O4	(M+Na)+

Figure 4. HRMS of 3,4-dihydroxybenzoic acid methyl ester.

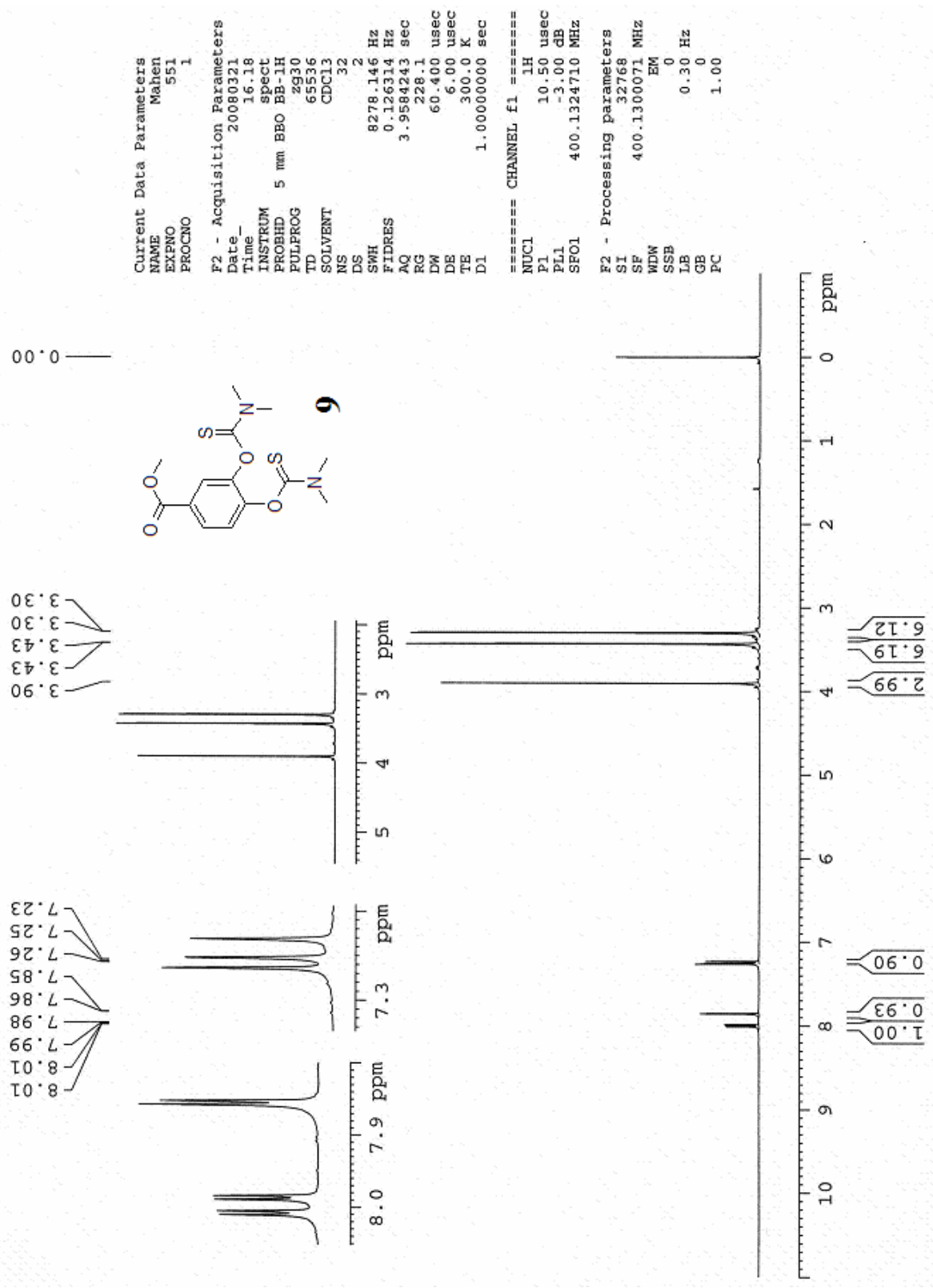


Figure 5. ^{1}H NMR of methyl-3,4-bis{[dimethylamino)carbothioyl]oxy}benzoate – $CDCl_3$.

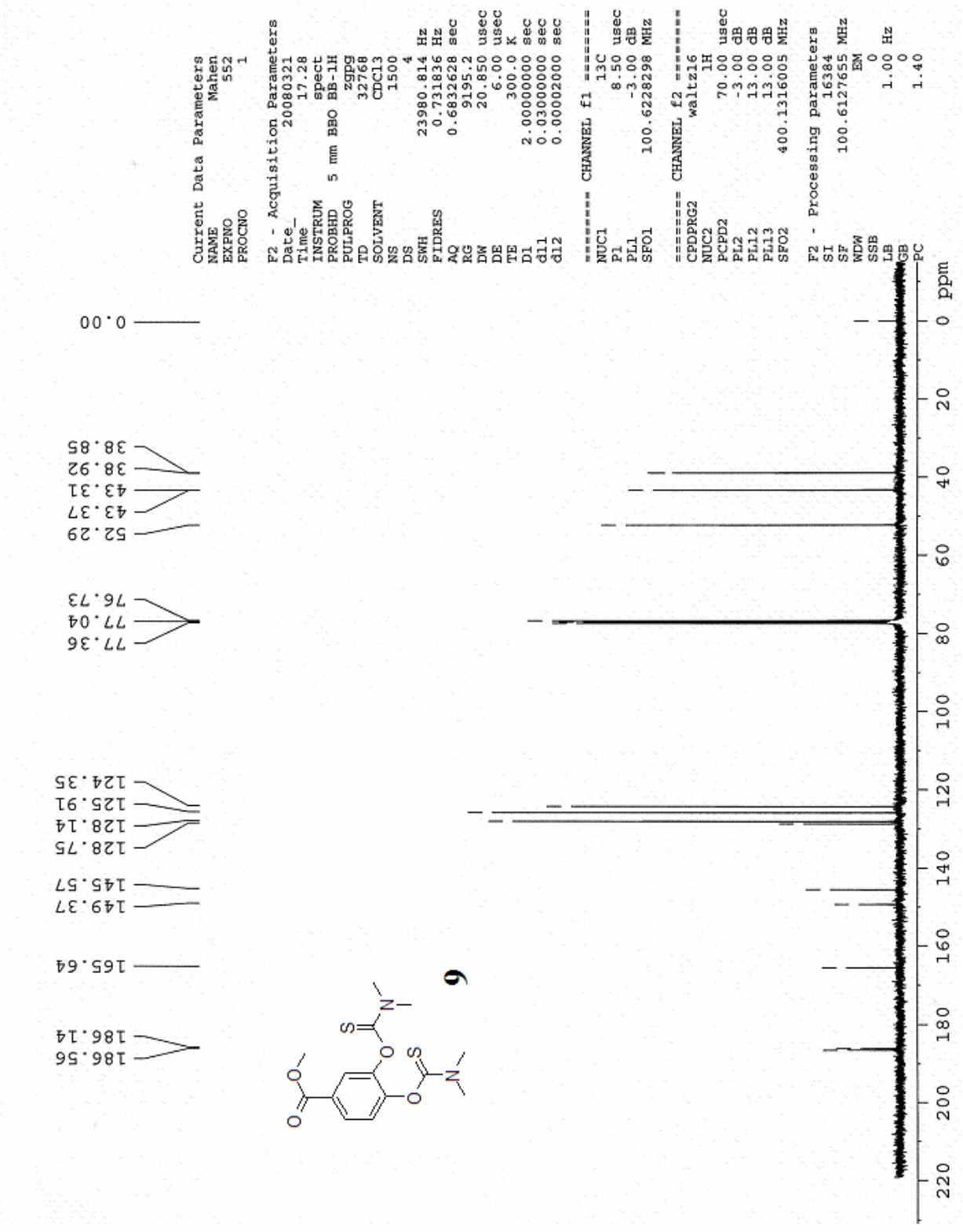


Figure 6. ^{13}C NMR of methyl-3,4-bis{[dimethylamino)carbothioyl]oxy}benzoate - $CDCl_3$.

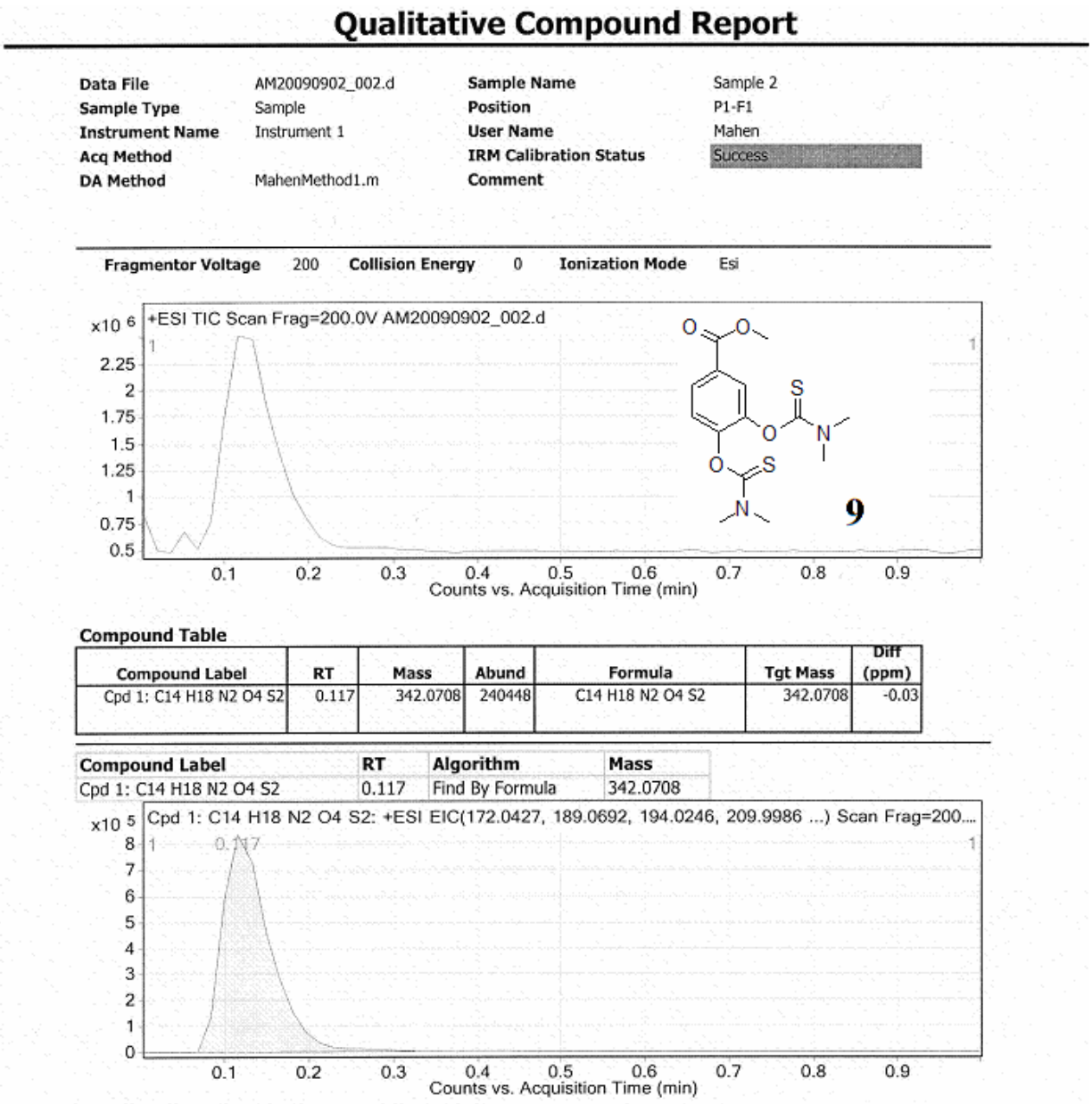
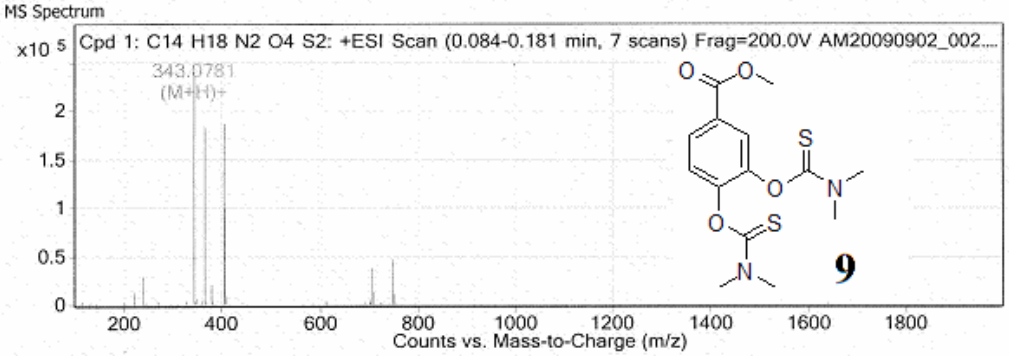


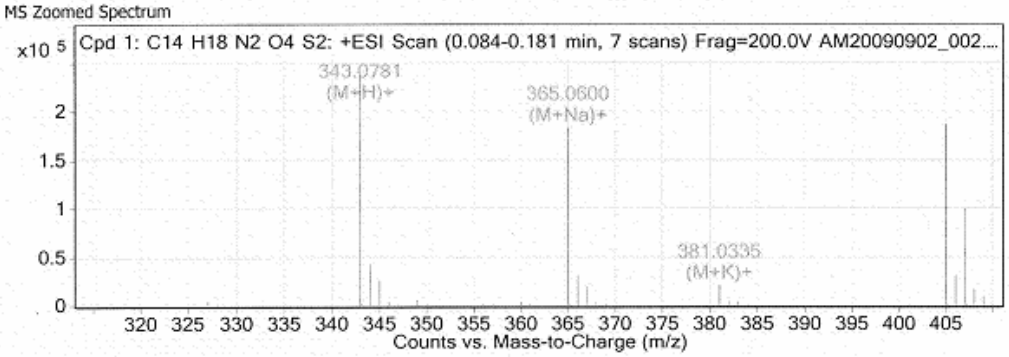
Figure 7. HRMS of methyl-3,4-bis{[dimethylamino)carbothioyl]oxy}benzoate.

Qualitative Compound Report

MS Spectrum



MS Zoomed Spectrum



MS Spectrum Peak List

m/z	*Calc m/z*	Diff(ppm)	z	Abund	Formula	Ion
343.0781	343.0781	0.03		240448	C14 H19 N2 O4 S2	(M+H)+
344.0809	344.0809	0.17		42901	C14 H19 N2 O4 S2	(M+H)+
345.0758	345.0758	0.04		25743	C14 H19 N2 O4 S2	(M+H)+
346.0777	346.0779	-0.8		4196	C14 H19 N2 O4 S2	(M+H)+
360.1042	360.1046	-1.04	1	4505	C14 H22 N3 O4 S2	(M+NH4)+
365.06	365.06	-0.14	1	183559	C14 H18 N2 Na O4 S2	(M+Na)+
366.0624	366.0628	-1.03	1	31429	C14 H18 N2 Na O4 S2	(M+Na)+
367.0574	367.0577	-0.91	1	19764	C14 H18 N2 Na O4 S2	(M+Na)+
381.0335	381.034	-1.12	1	21248	C14 H18 K N2 O4 S2	(M+K)+
383.0314	383.0318	-1.19	1	4132	C14 H18 K N2 O4 S2	(M+K)+

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Figure 8. HRMS of methyl-3,4-bis{[dimethylamino)carbothioyl]oxy}benzoate.

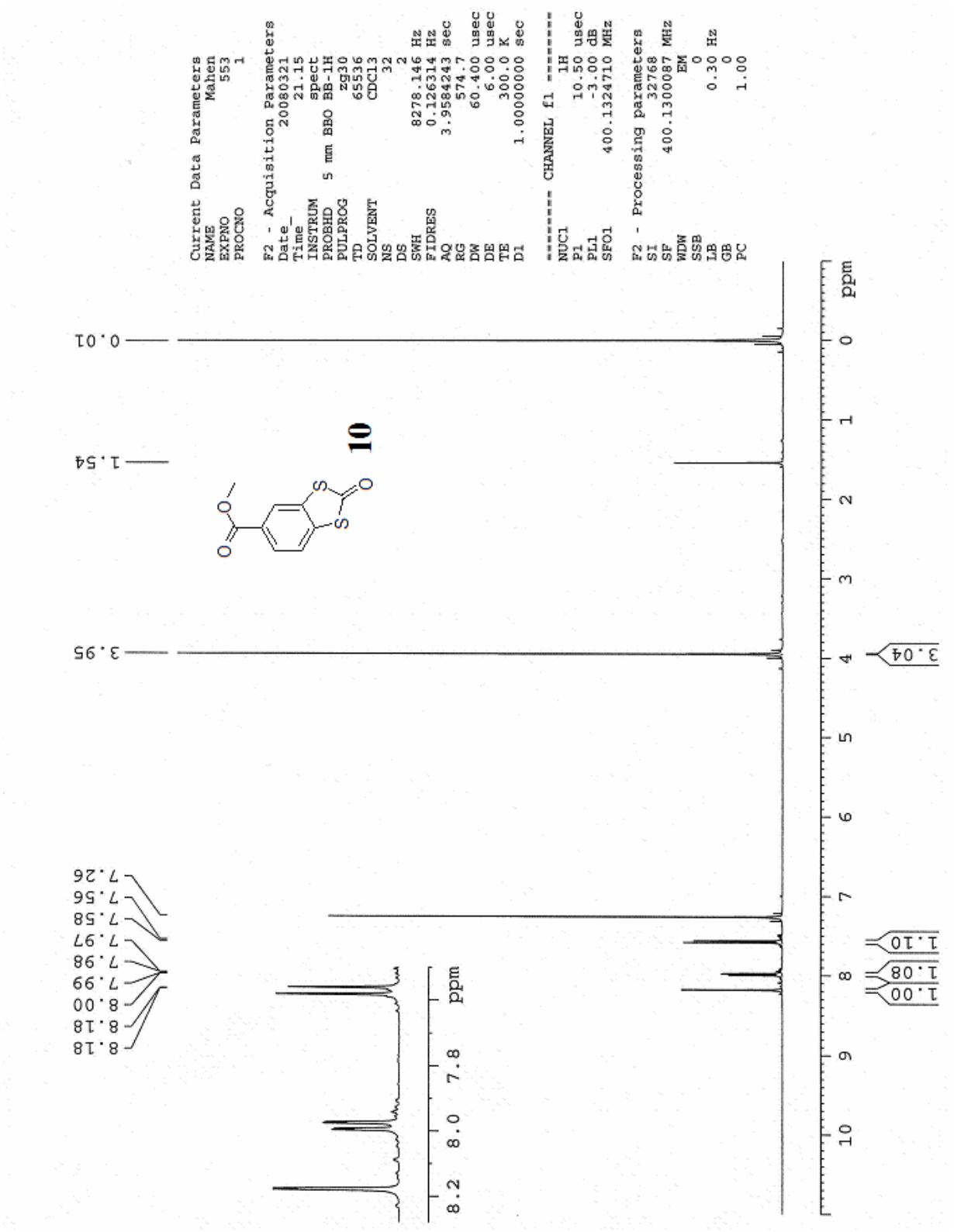


Figure 9. ^{1}H NMR of methyl-2-oxo-1,3-benzodithiole-5-carboxylate - $CDCl_3$.

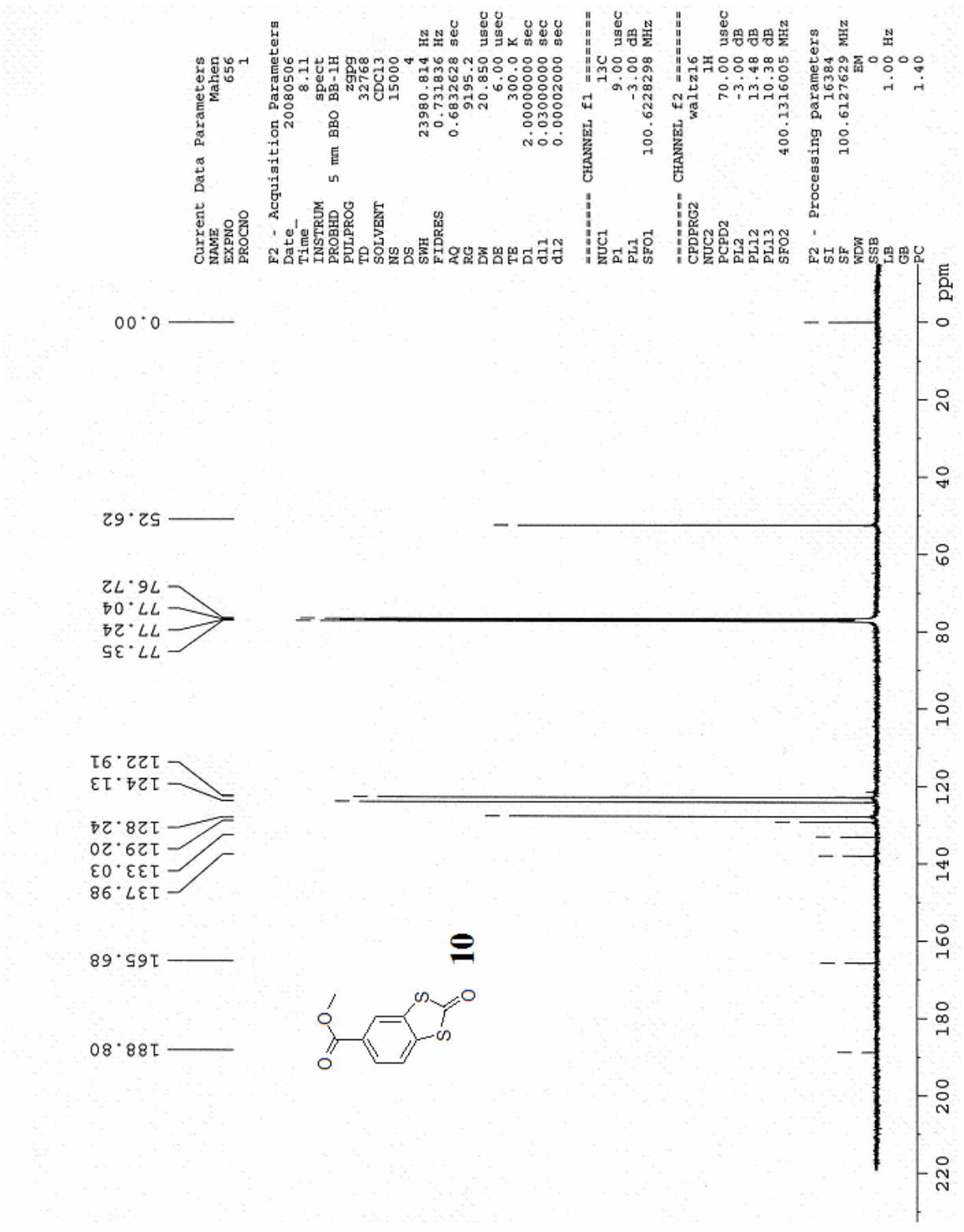


Figure 10. ^{13}C NMR of methyl-2-oxo-1,3-benzodithiole-5-carboxylate - $CDCl_3$.

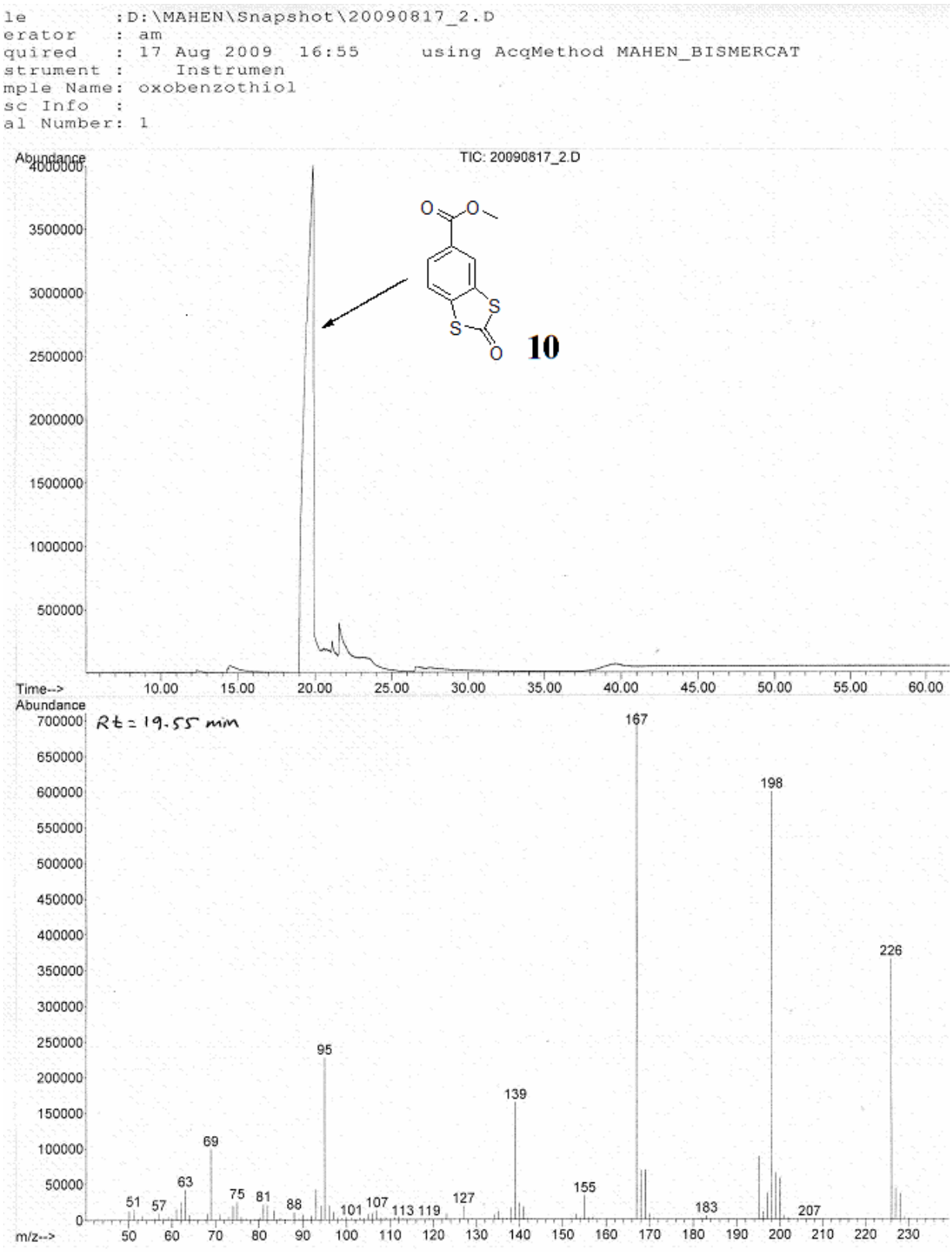


Figure 11. GC/MS of methyl-2-oxo-1,3-benzodithiole-5-carboxylate (Rt = 19.55 min).

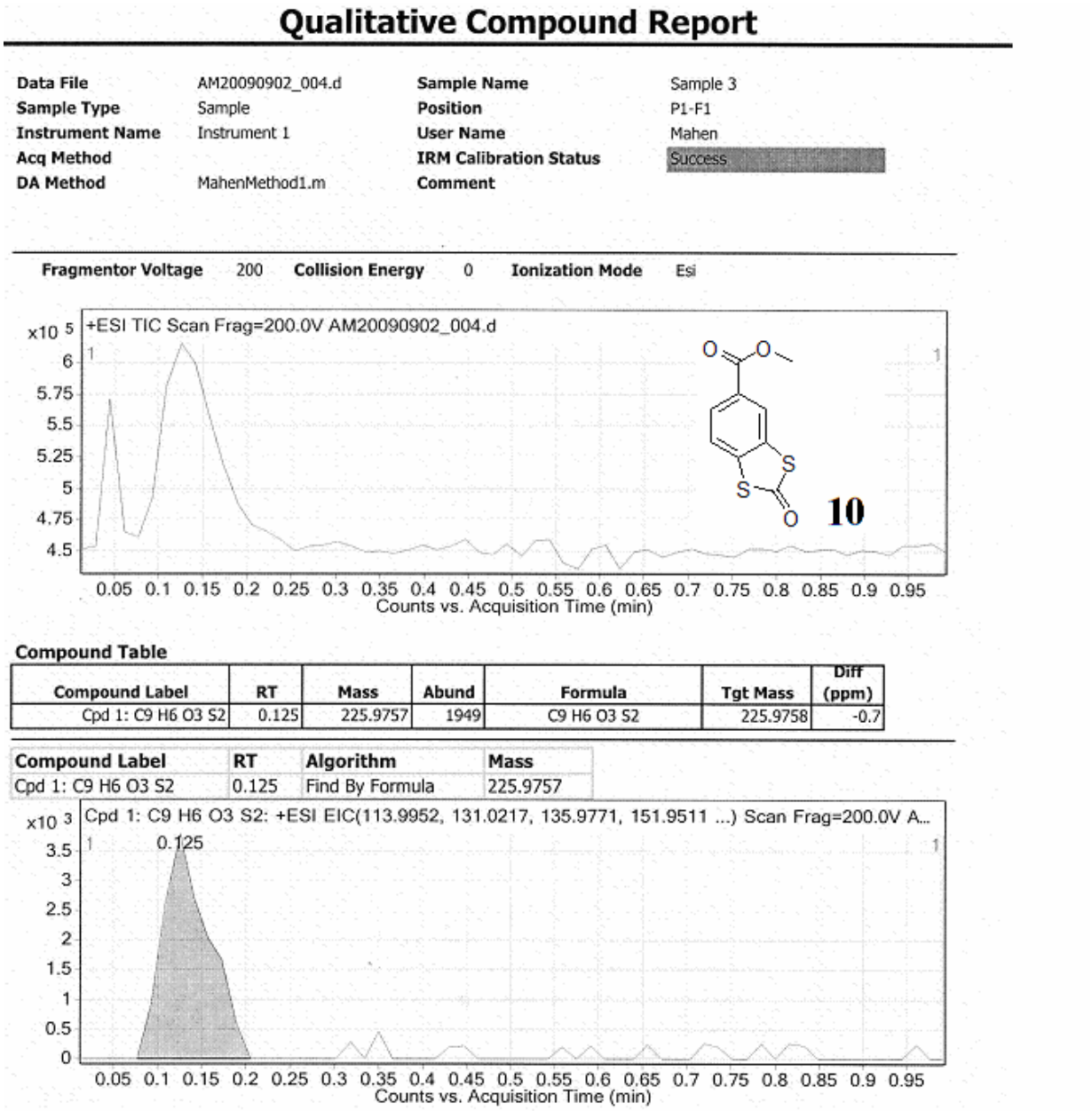


Figure 12. HRMS of methyl-2-oxo-1,3-benzodithiole-5-carboxylate.

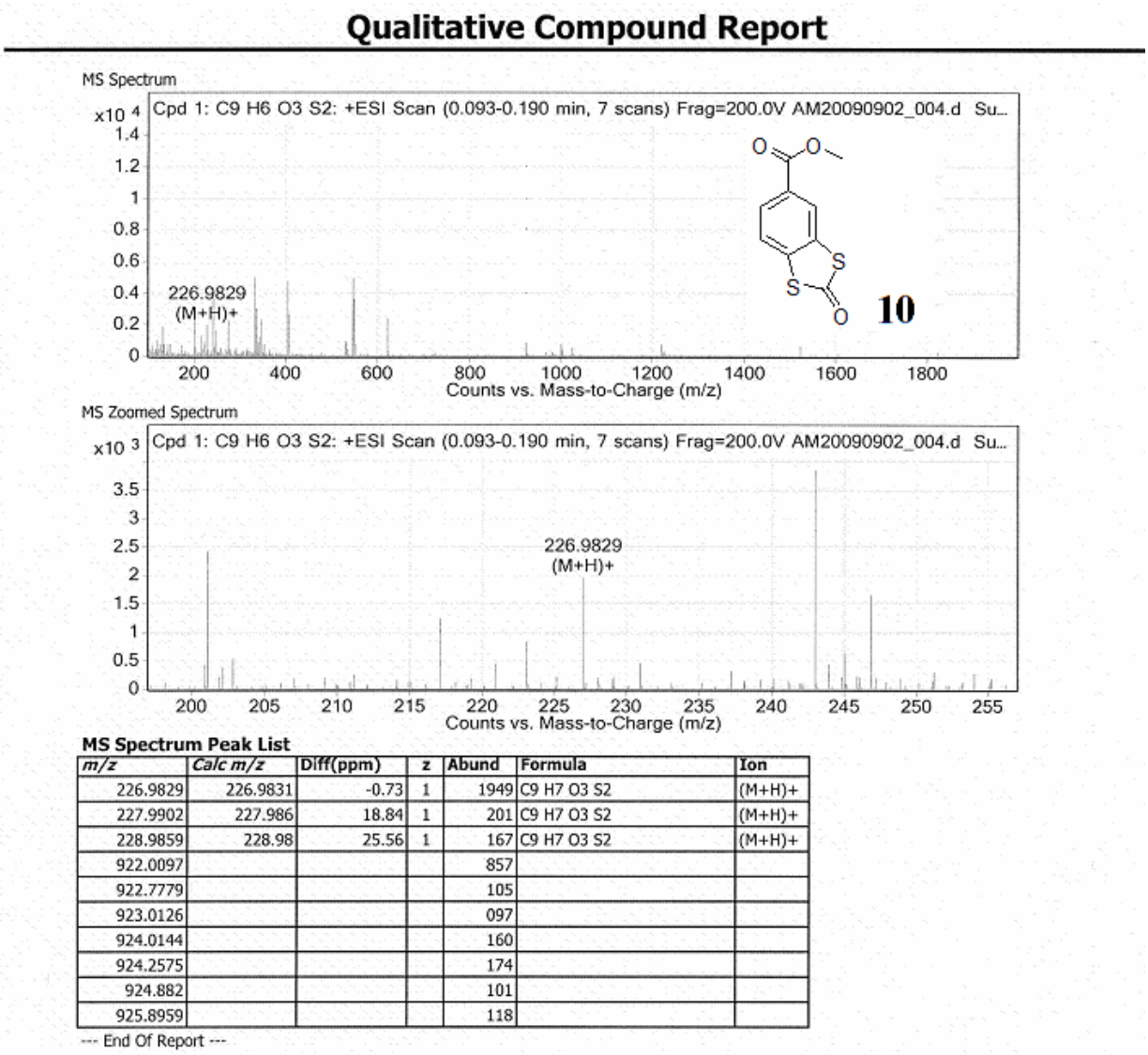


Figure 13. HRMS of methyl-2-oxo-1,3-benzodithiole-5-carboxylate.

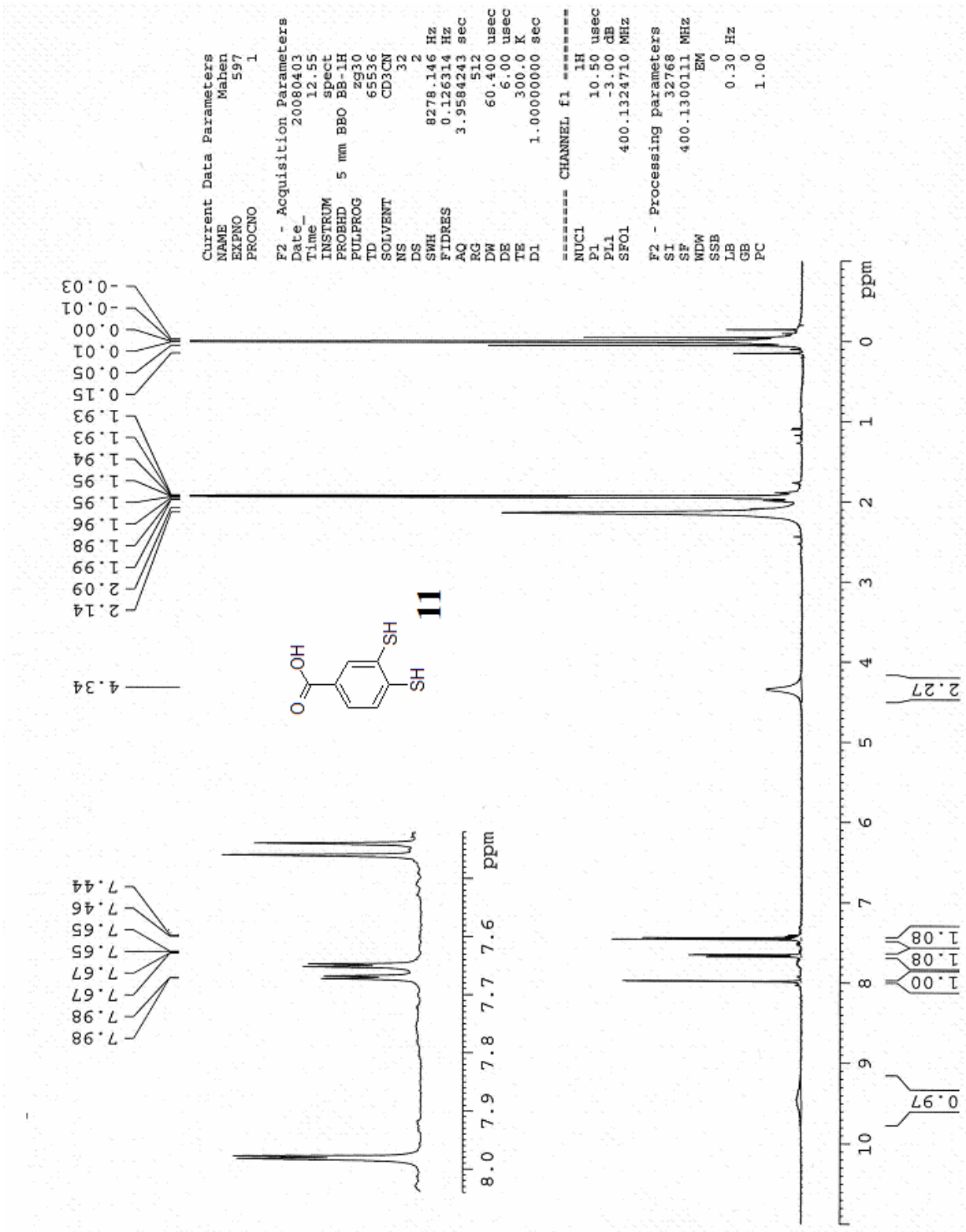


Figure 14. ^{1}H NMR of 3.4- disulfanylbenzoic acid - CD_3CN.

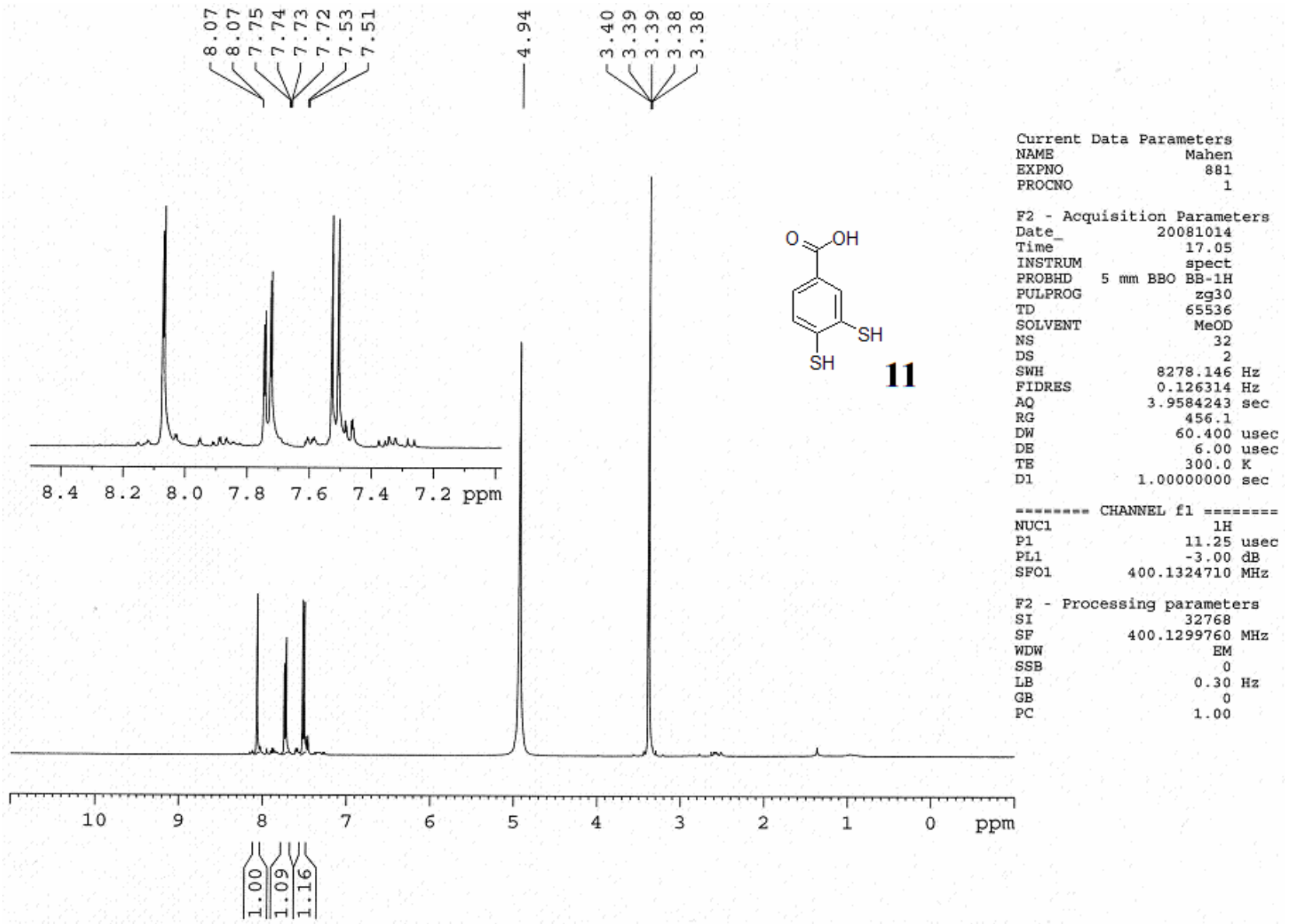


Figure 15. ^{1}H NMR of 3.4- disulfanylbenzoic acid - CD_3OD.

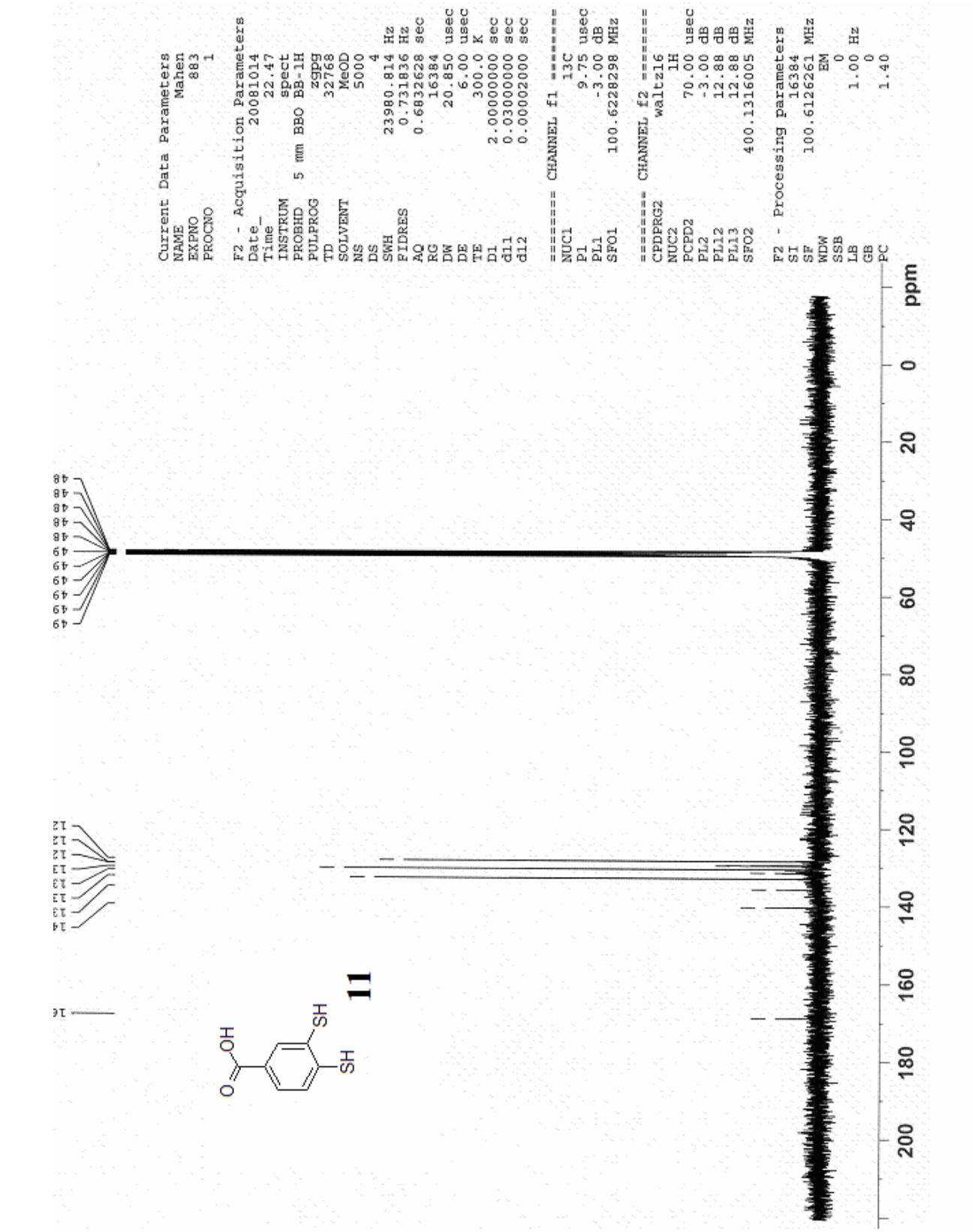


Figure 16. ^{13}C NMR of 3,4- disulfanylbenzoic acid - CD_3OD.

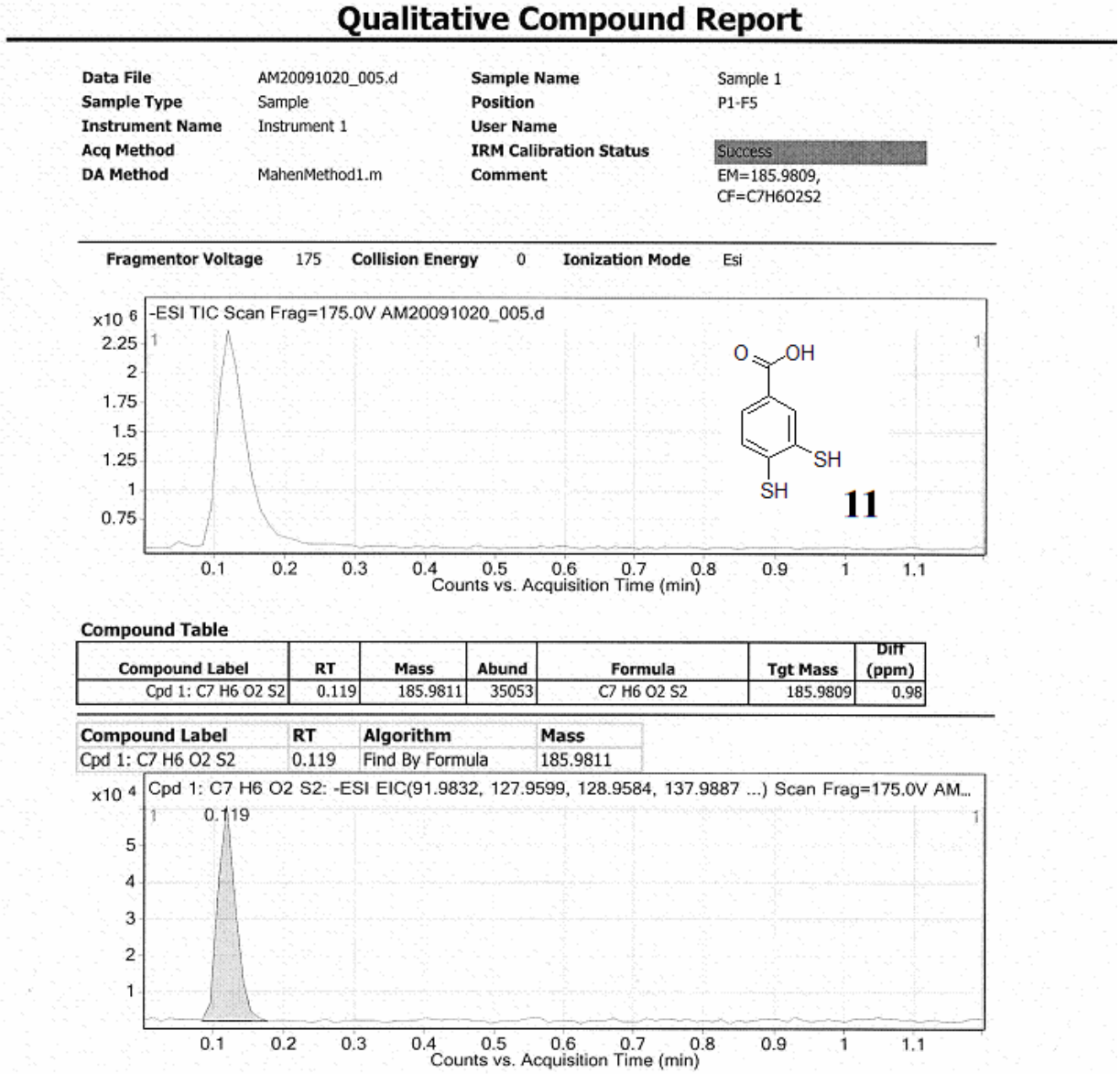
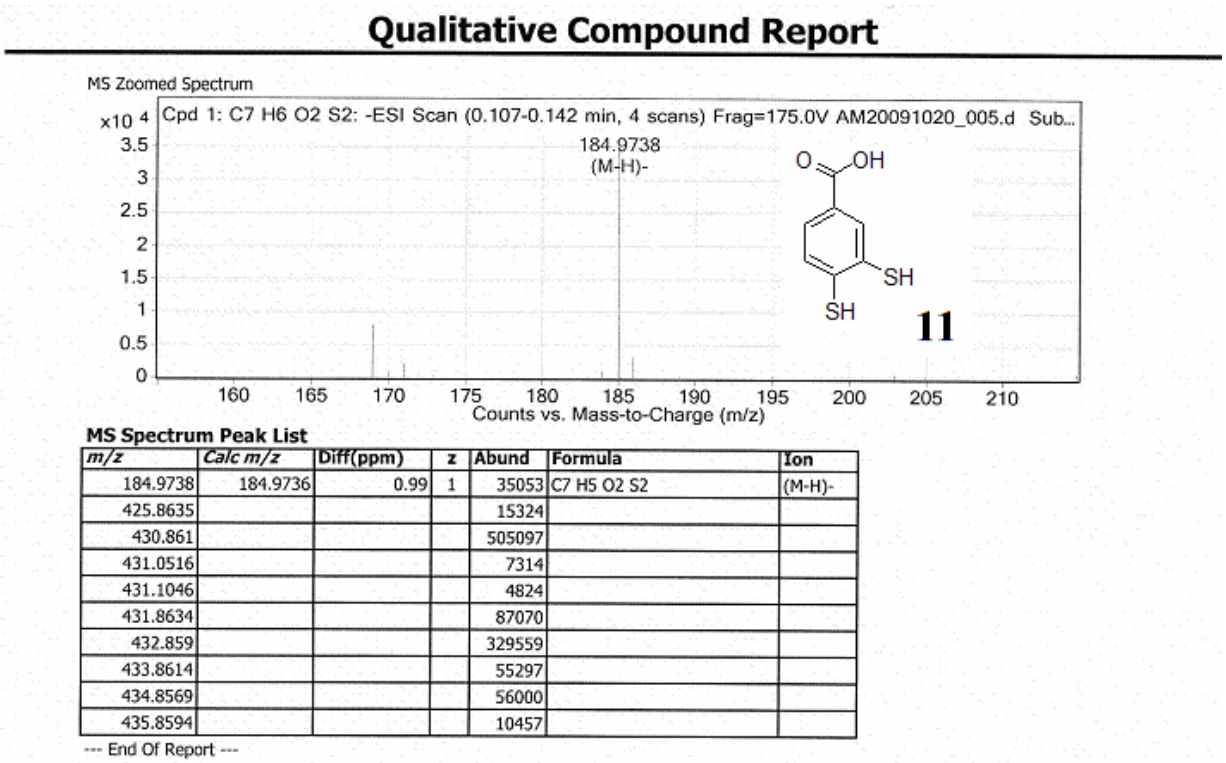


Figure 17. HRMS of 3,4- disulfanylbenzoic acid.



m/z	Calc m/z	Diff(ppm)	z	Abund	Formula	Ion
184.9738	184.9736	0.99	1	35053	C7 H5 O2 S2	(M-H)-
425.8635				15324		
430.861				505097		
431.0516				7314		
431.1046				4824		
431.8634				87070		
432.859				329559		
433.8614				55297		
434.8569				56000		
435.8594				10457		

Figure 18. HRMS of 3,4- disulfanylbenzoic acid.

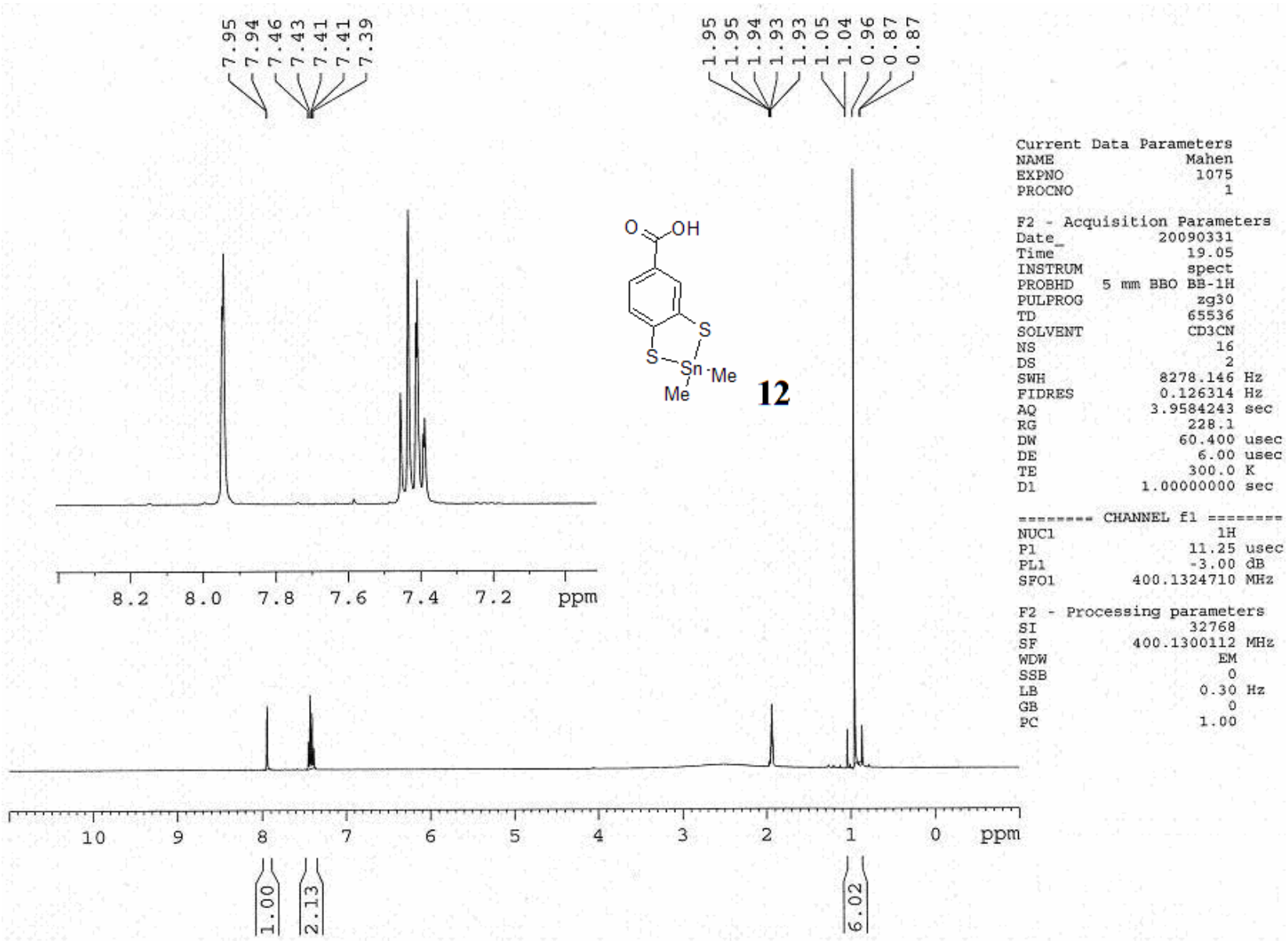


Figure 19. ^{1}H NMR of 2,2-dimethylbenzo[d][1,3,2]dithiastannole-5-carboxylic acid - CD_3CN.

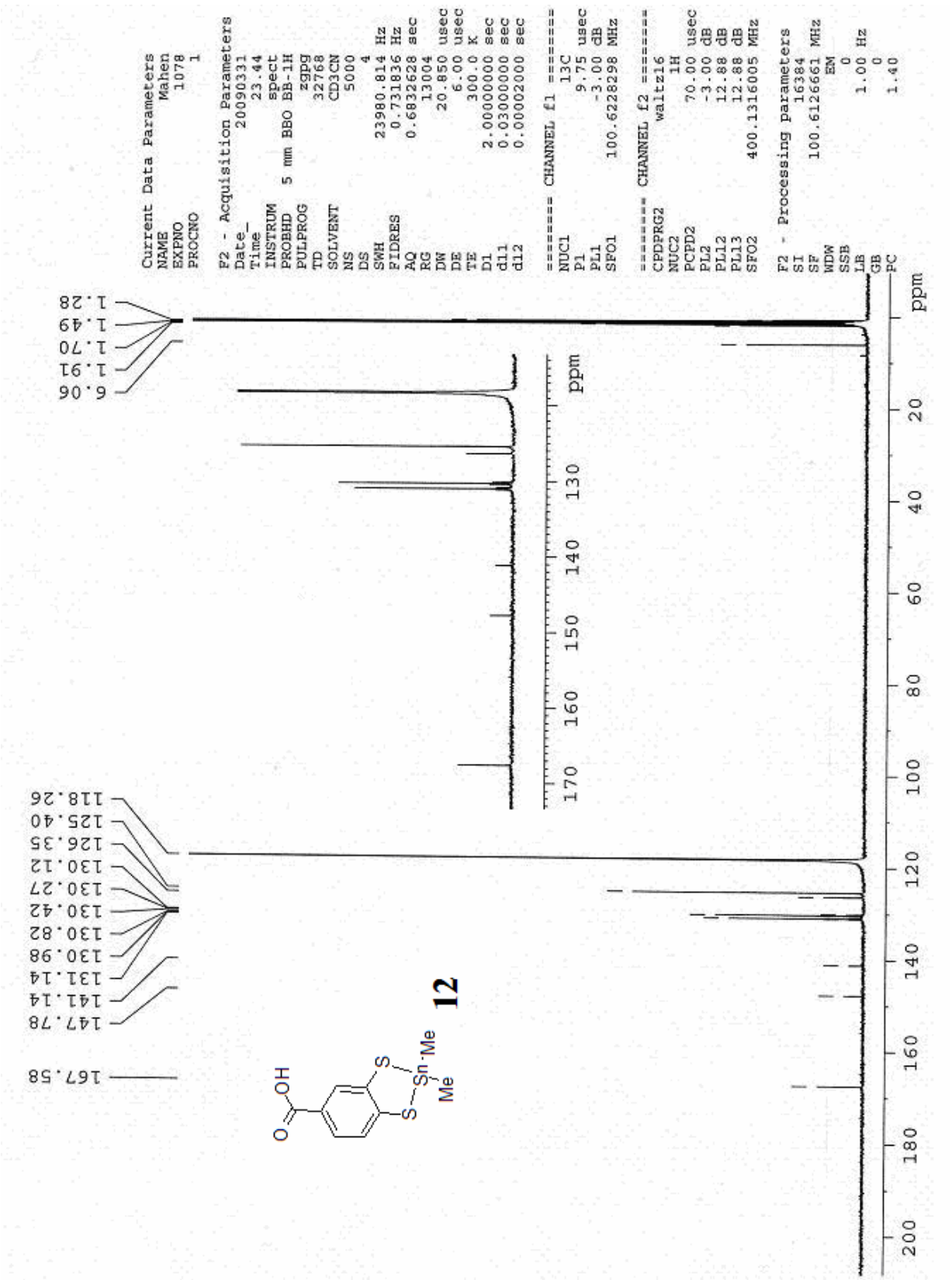


Figure 20. ^{13}C NMR of 2,2-dimethylbenzo[d][1,3,2]dithiastannole-5-carboxylic acid - CD_3CN.

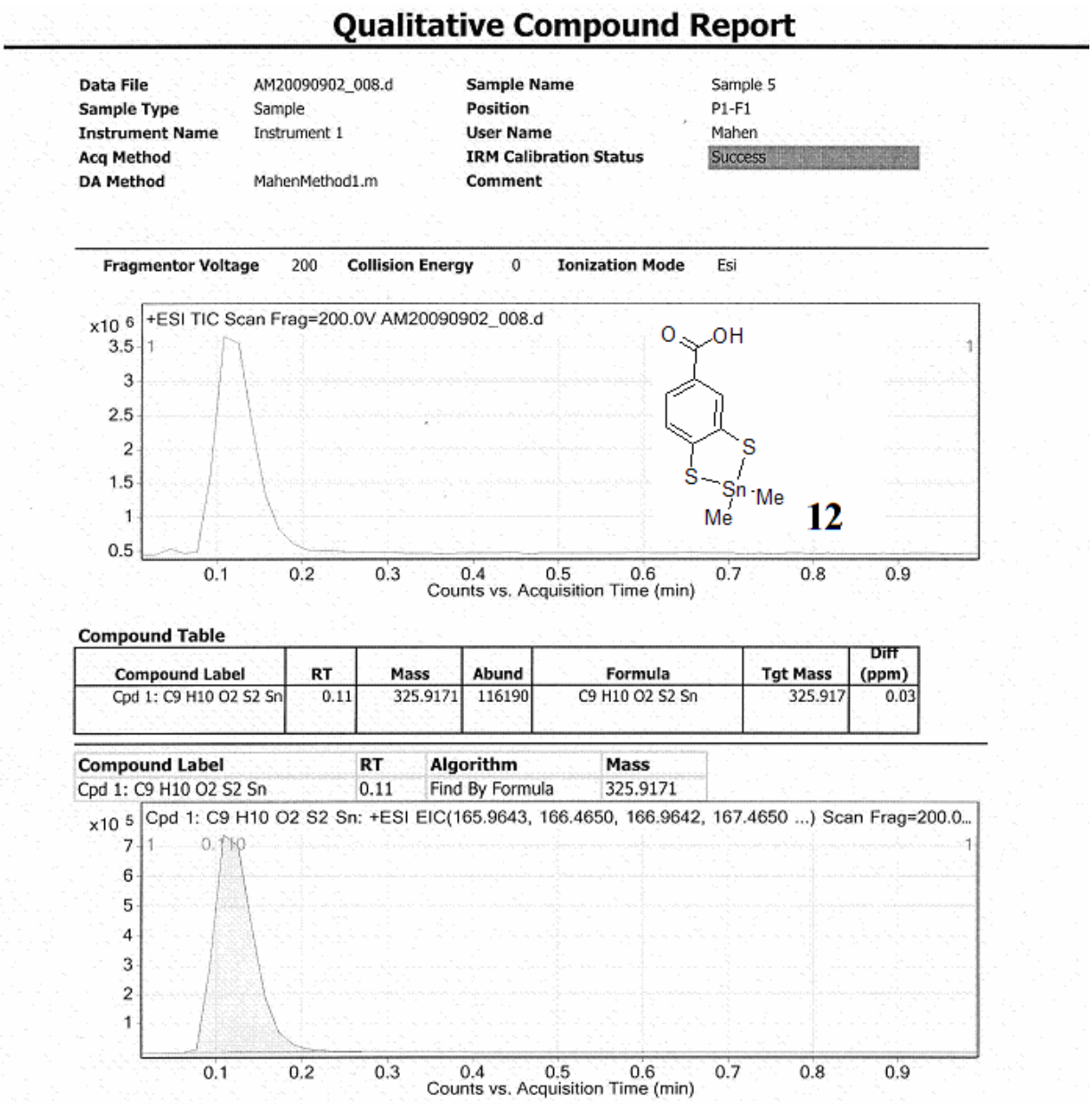
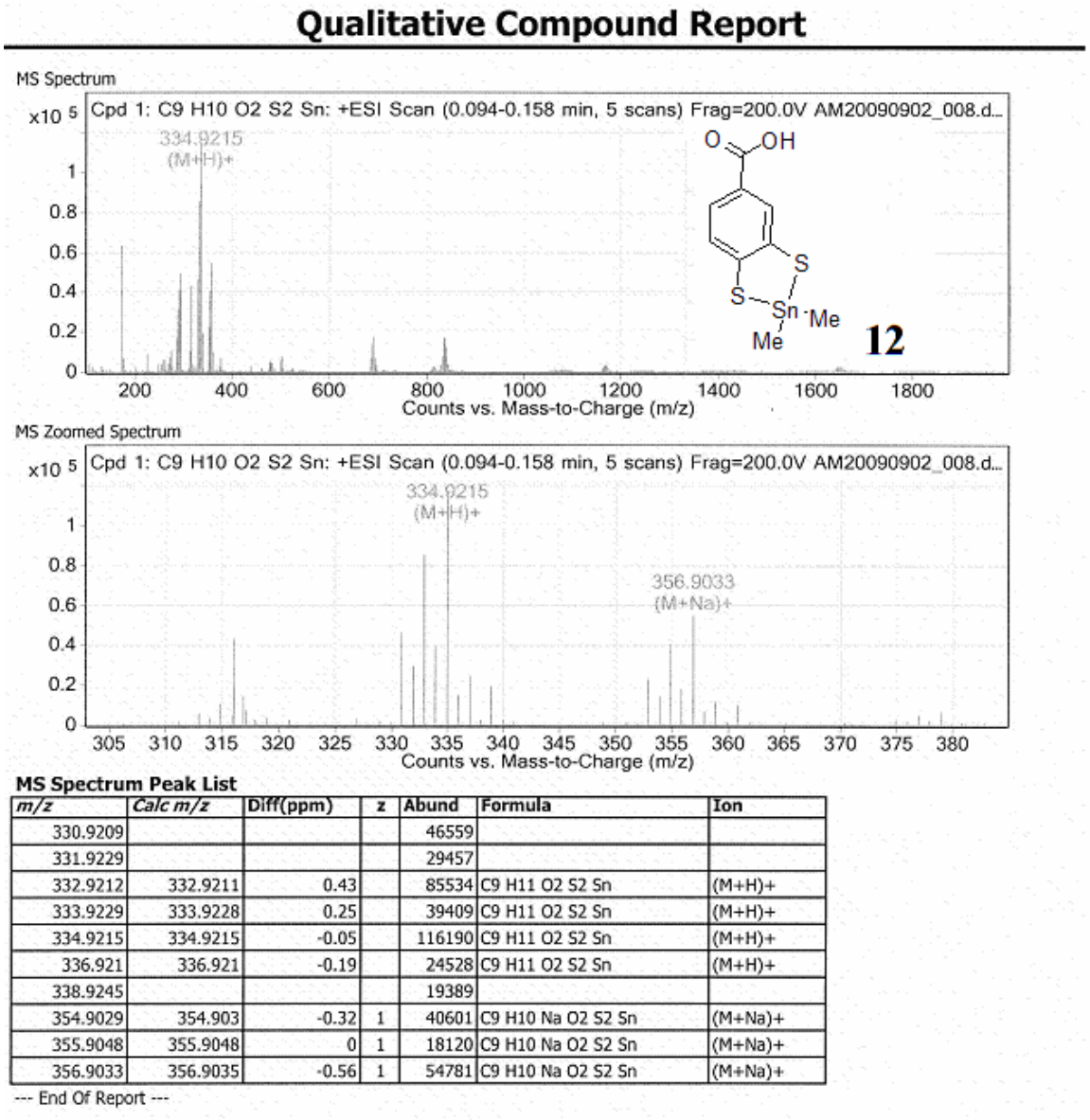


Figure 21. HRMS of 2,2-dimethylbenzo[d][1,3,2]dithiastannole-5-carboxylic acid.



MS Spectrum Peak List

m/z	*Calc m/z*	Diff(ppm)	z	Abund	Formula	Ion
330.9209				46559		
331.9229				29457		
332.9212	332.9211	0.43		85534	C9 H11 O2 S2 Sn	(M+H)+
333.9229	333.9228	0.25		39409	C9 H11 O2 S2 Sn	(M+H)+
334.9215	334.9215	-0.05		116190	C9 H11 O2 S2 Sn	(M+H)+
336.921	336.921	-0.19		24528	C9 H11 O2 S2 Sn	(M+H)+
338.9245				19389		
354.9029	354.903	-0.32	1	40601	C9 H10 Na O2 S2 Sn	(M+Na)+
355.9048	355.9048	0	1	18120	C9 H10 Na O2 S2 Sn	(M+Na)+
356.9033	356.9035	-0.56	1	54781	C9 H10 Na O2 S2 Sn	(M+Na)+

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Figure 22. HRMS of 2,2-dimethylbenzo[d][1,3,2]dithiastannole-5-carboxylic acid.

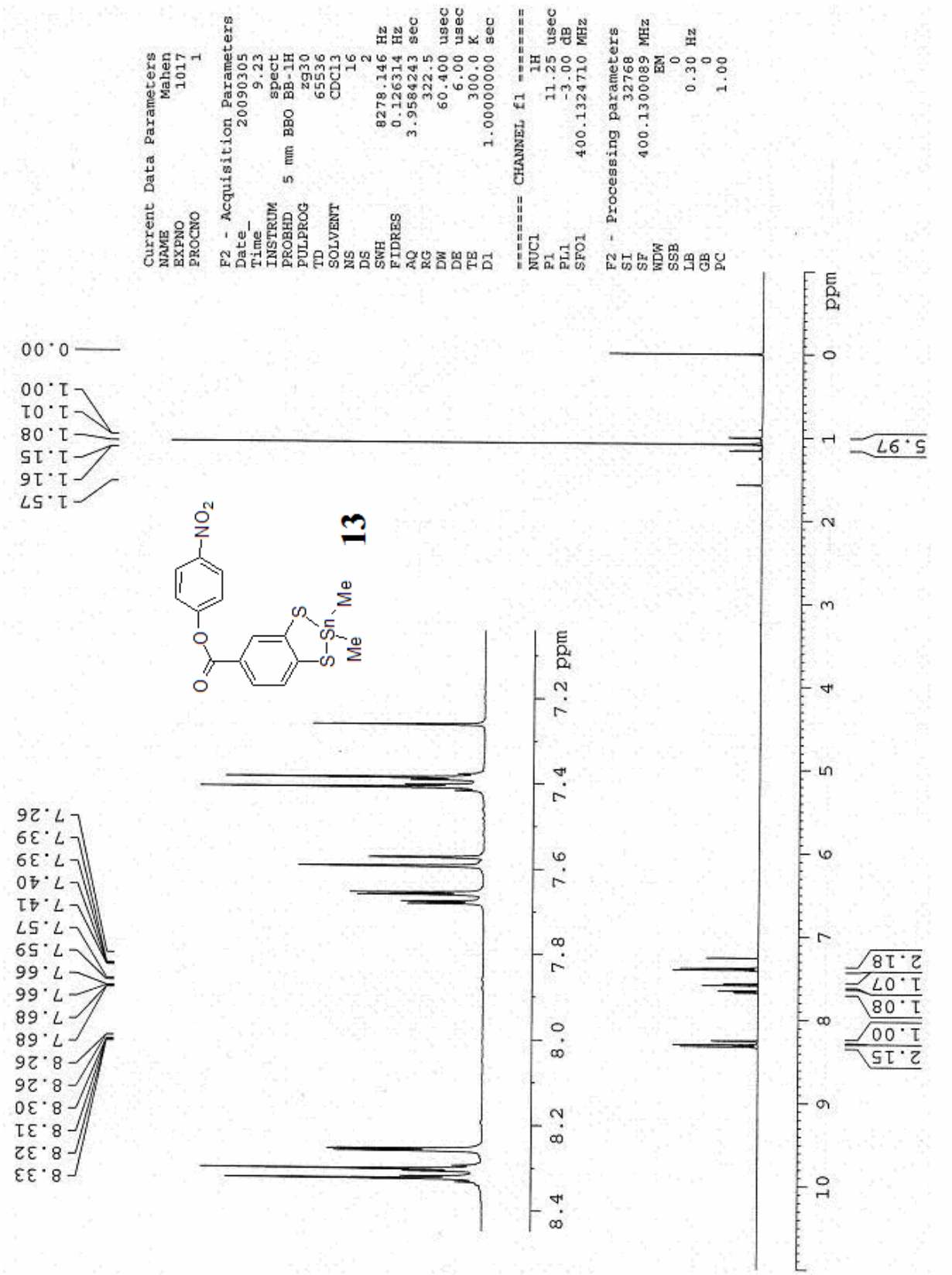


Figure 23. ^{1}H NMR of 4-nitrophenyl-2,2-dimethylbenzo[d][1,3,2]dithiastannole-5-carboxylate – $CDCl_3$.

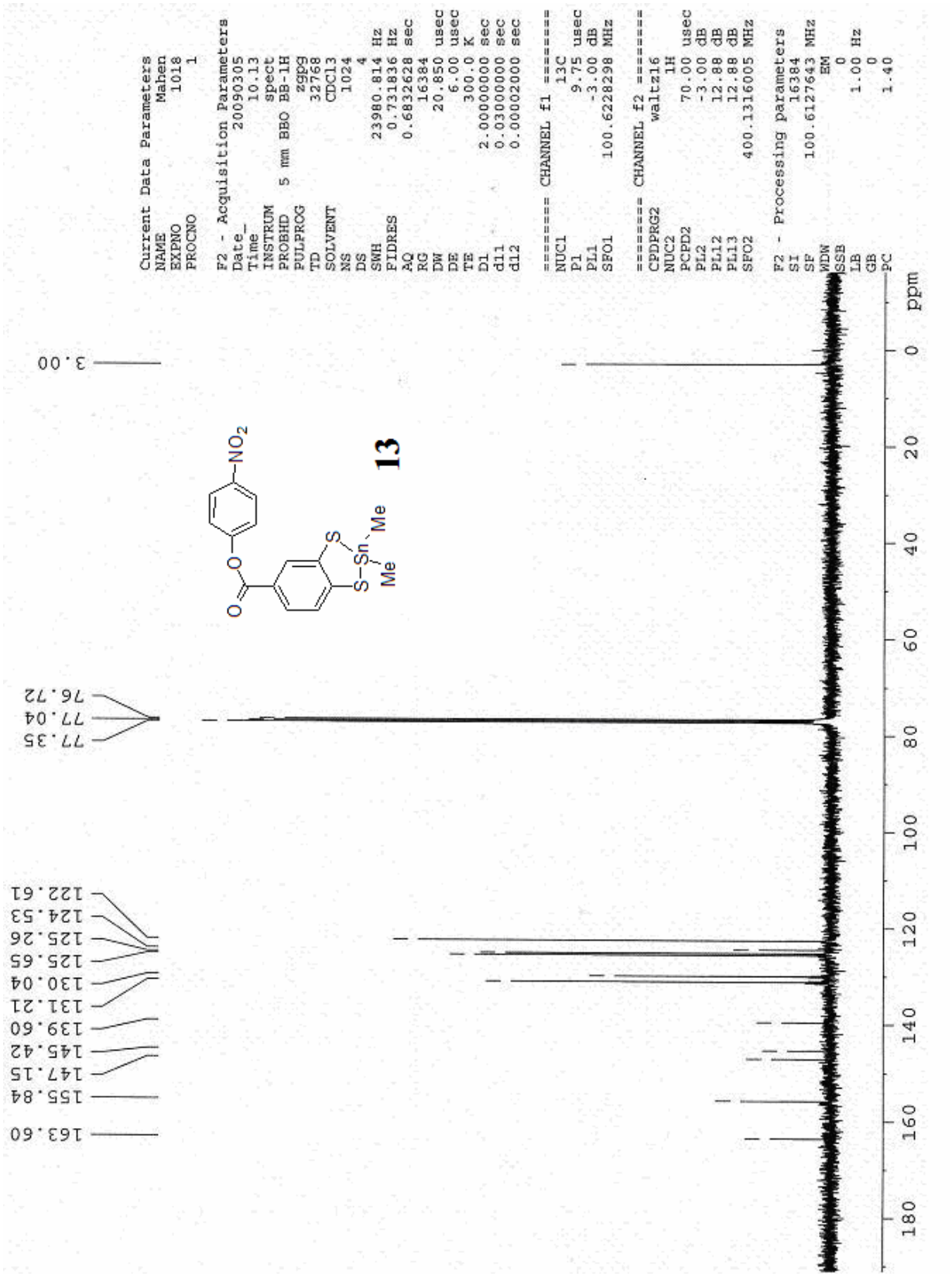


Figure 24. ^{13}C NMR of 4-nitrophenyl-2,2-dimethylbenzo[d][1,3,2]dithiastannole-5-carboxylate – $CDCl_3$.

Qualitative Compound Report

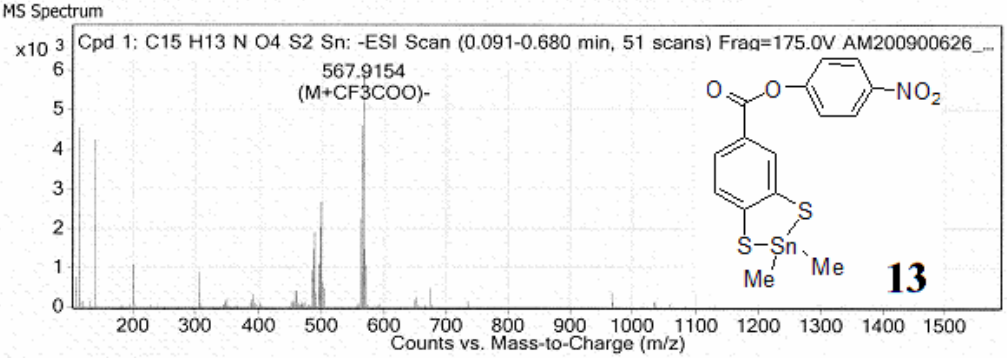
Data File	AM200900626_002 low and high mass.d	**Sample Name**	Sn-PNP
Sample Type	Sample	**Position**	P1-F3
Instrument Name	Instrument 1	**User Name**	Mahen
Acq Method		**IRM Calibration Status**	Success
DA Method	HCEmpirical1.m	**Comment**	FI

Compound Table

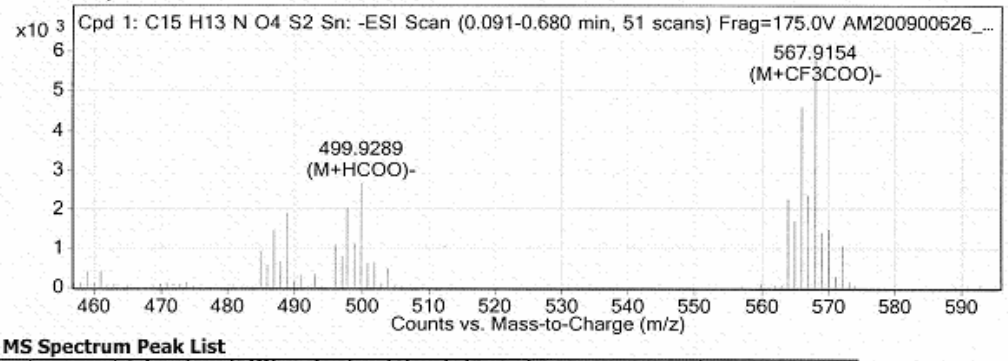
Compound Label	RT	Mass	Abund	Formula	Tgt Mass	Diff (ppm)
Cpd 1: C15 H13 N O4 S2 Sn	0.115	446.9324	5940	C15 H13 N O4 S2 Sn	446.9334	-2.34

Compound Label	RT	Algorithm	Mass
Cpd 1: C15 H13 N O4 S2 Sn	0.115	Find By Formula	446.9324

MS Spectrum



MS Zoomed Spectrum



MS Spectrum Peak List

m/z	*Calc m/z*	Diff(ppm)	z	Abund	Formula	Ion
486.9047	486.9014	6.94	1	1491	C15 H13 Cl N O4 S2 Sn	(M+Cl)-
487.907	487.8993	15.79	1	688	C15 H13 Cl N O4 S2 Sn	(M+Cl)-
488.905	488.9009	8.38	1	1882	C15 H13 Cl N O4 S2 Sn	(M+Cl)-
489.9082	489.8995	17.65	1	174	C15 H13 Cl N O4 S2 Sn	(M+Cl)-

Figure 25. HRMS of 4-nitrophenyl-2,2-dimethylbenzo[d][1,3,2]dithiastannole-5-carboxylate.

Qualitative Compound Report

m/z	Calc m/z	Diff(ppm)	z	Abund	Formula	Ion
490.907	490.9009	12.29	1	309	C15 H13 Cl N O4 S2 Sn	(M+Cl)-
491.9263	491.8983	56.82	1	37	C15 H13 Cl N O4 S2 Sn	(M+Cl)-
497.9285	497.9285	0	1	2017	C16 H14 N O6 S2 Sn	(M+HCOO)-
498.9304	498.9304	0.18	1	1134	C16 H14 N O6 S2 Sn	(M+HCOO)-
499.9289	499.929	-0.27	1	2675	C16 H14 N O6 S2 Sn	(M+HCOO)-
500.9315	500.9313	0.4	1	603	C16 H14 N O6 S2 Sn	(M+HCOO)-
501.9287	501.9288	-0.34	1	637	C16 H14 N O6 S2 Sn	(M+HCOO)-
502.9311	502.9315	-0.66	1	106	C16 H14 N O6 S2 Sn	(M+HCOO)-
562.9158				59		
563.9157				2238		
564.9176				1698		
565.914	565.9159	-3.48		4588	C17 H13 F3 N O6 S2 Sn	(M+CF3COO)-
566.1206				10		
566.917	566.9178	-1.32		2344	C17 H13 F3 N O6 S2 Sn	(M+CF3COO)-
567.0853				5		
567.9154	567.9164	-1.81		5940	C17 H13 F3 N O6 S2 Sn	(M+CF3COO)-
568.0776				10		
568.2491				5		
568.2786				5		
568.9174	568.9187	-2.2		1429	C17 H13 F3 N O6 S2 Sn	(M+CF3COO)-
569.1225				10		
569.9155	569.9163	-1.38		1484	C17 H13 F3 N O6 S2 Sn	(M+CF3COO)-
570.9175	570.9189	-2.44		293	C17 H13 F3 N O6 S2 Sn	(M+CF3COO)-
571.9193	571.919	0.54		1048	C17 H13 F3 N O6 S2 Sn	(M+CF3COO)-
572.9221	572.922	0.14	1	160	C17 H13 F3 N O6 S2 Sn	(M+CF3COO)-
573.9193	573.9177	2.75	1	68	C17 H13 F3 N O6 S2 Sn	(M+CF3COO)-

--- End Of Report ---

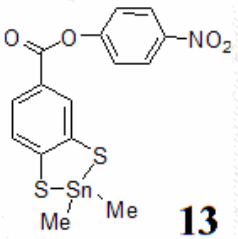


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Figure 26. HRMS of 4-nitrophenyl-2,2-dimethylbenzo[d][1,3,2]dithiastannole-5-carboxylate.

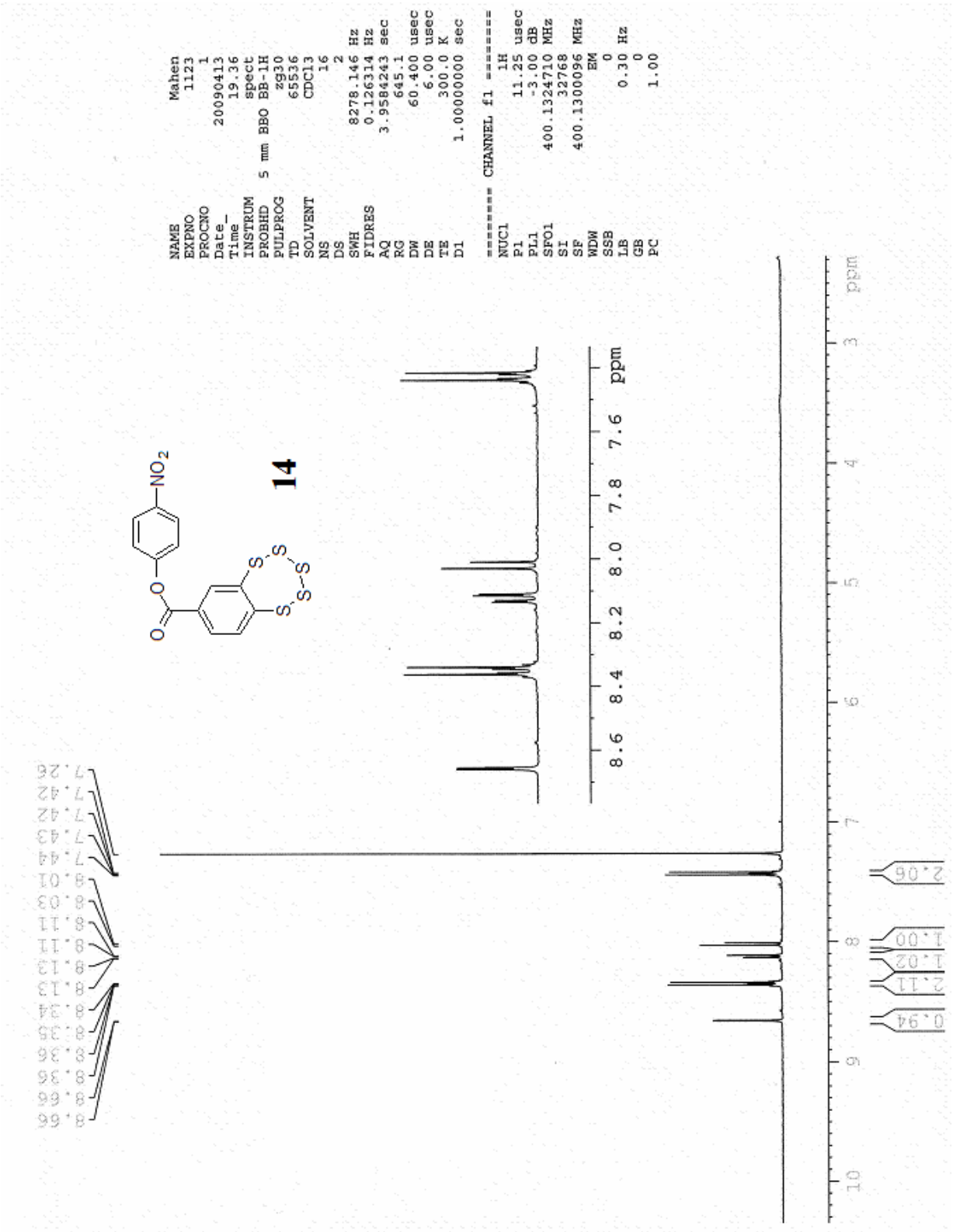


Figure 27. ^{1}H of NMR 4-nitrophenylbenzo[f][1,2,3,4,5]pentathiepine-7-carboxylate - $CDCl_3$.

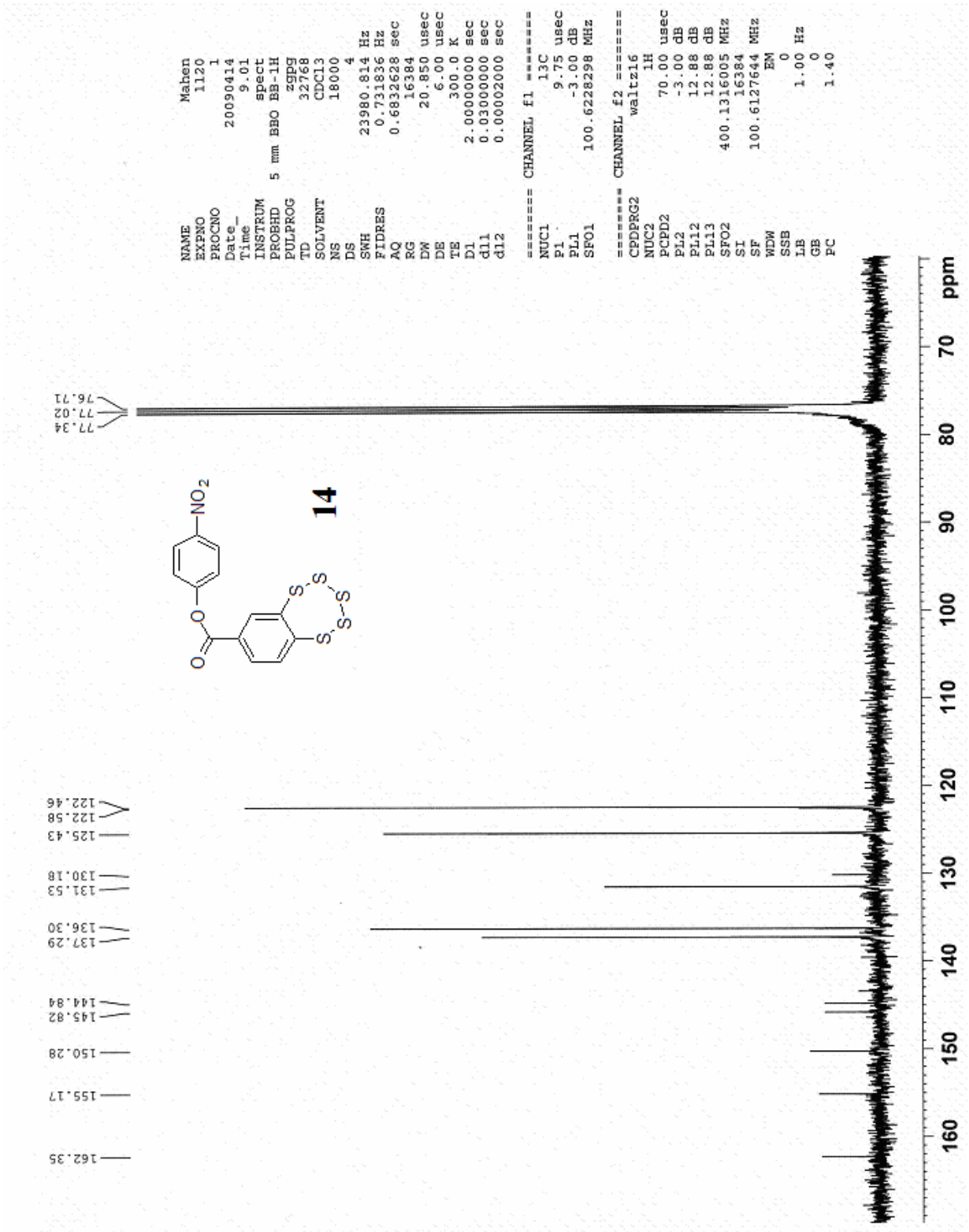


Figure 28. ^{13}C NMR of 4-nitrophenylbenzo[f][1,2,3,4,5]pentathiepine-7-carboxylate - $CDCl_3$.

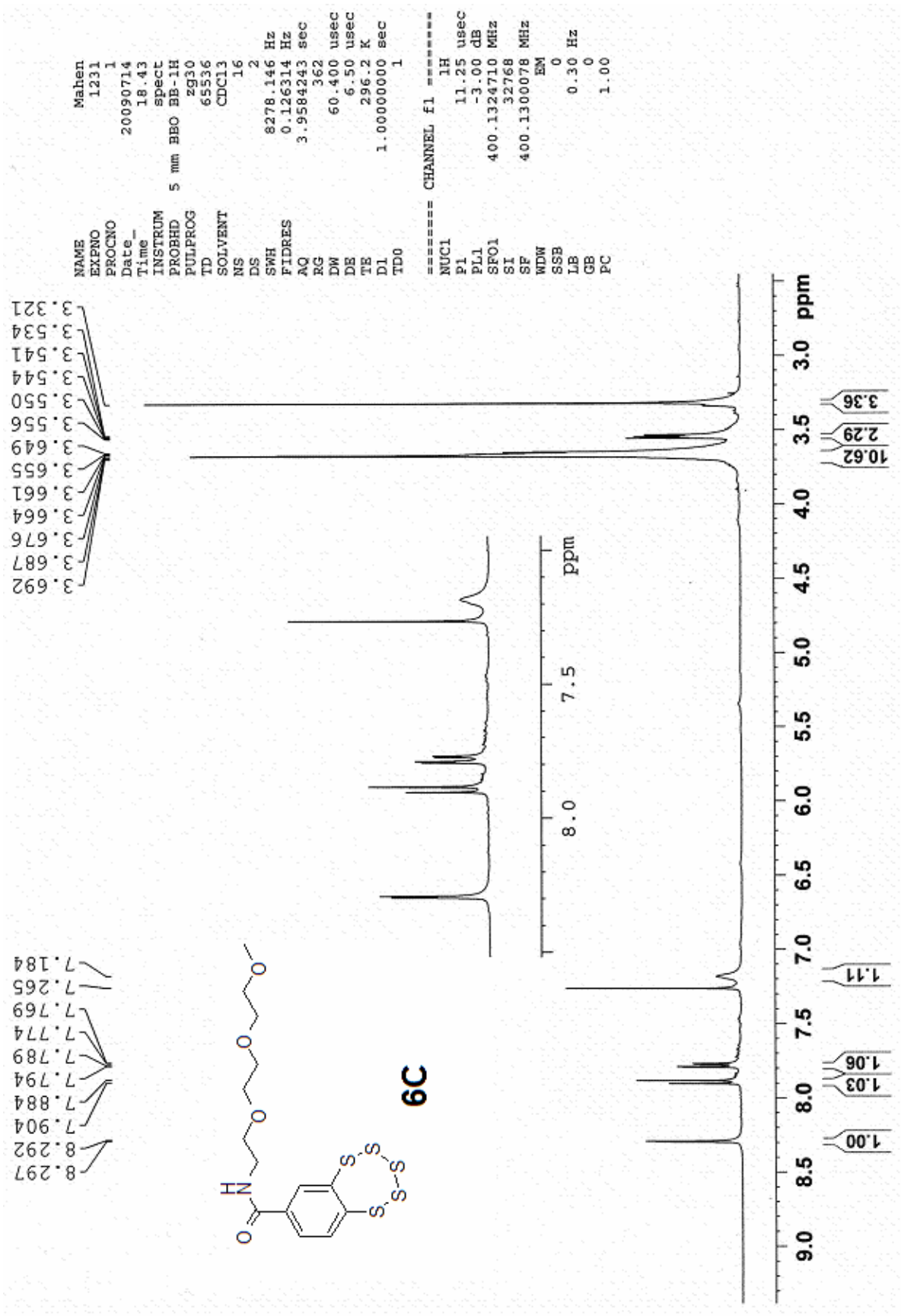


Figure 29. ^{1}H NMR of N-(2-(2-(2-methoxyethoxy)ethoxy)ethyl)benzo[f][1,2,3,4,5]pentathiepine-7-carboxamide - $CDCl_3$.

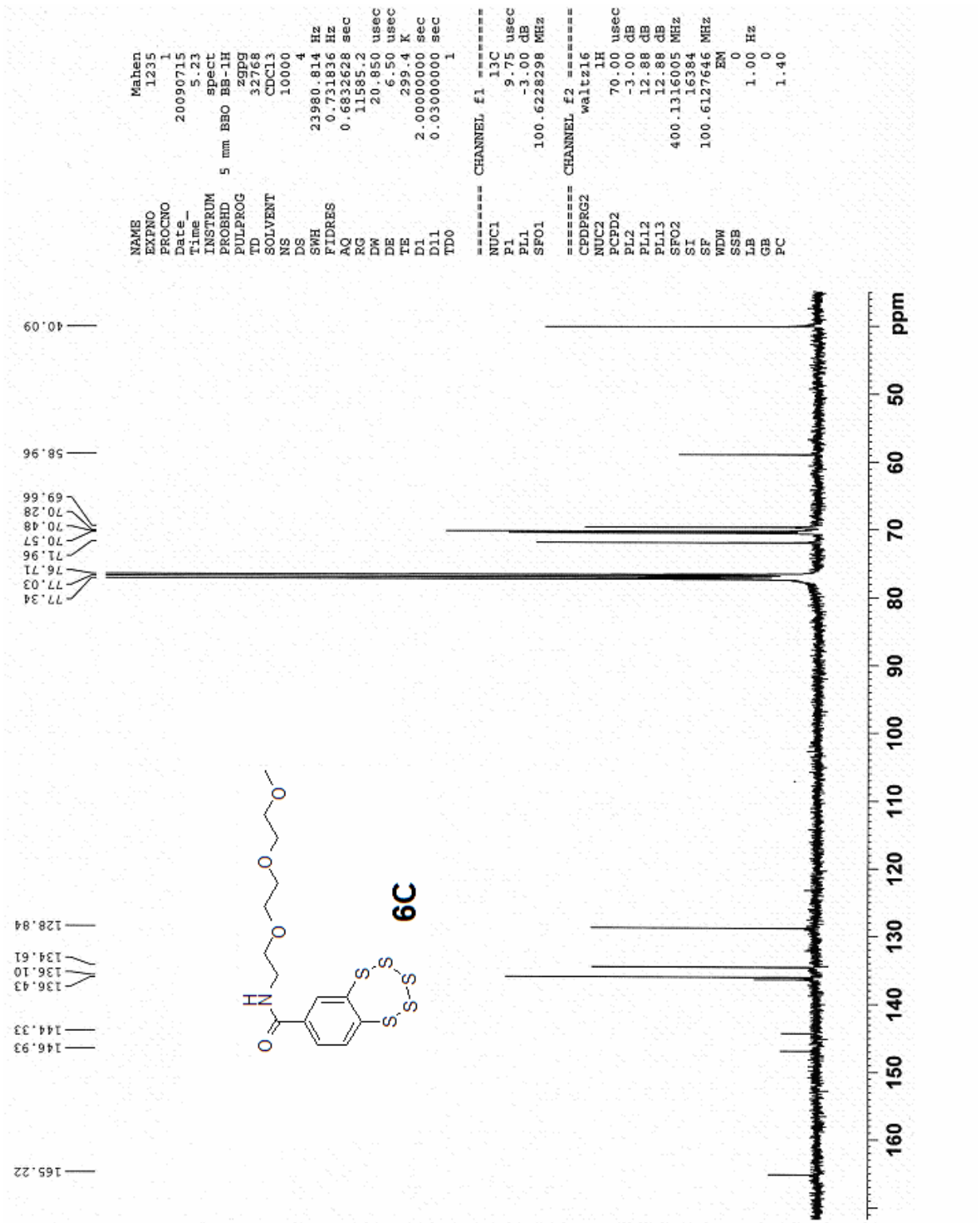


Figure 30. ^{13}C NMR of N-(2-(2-(2-methoxyethoxy)ethoxy)ethyl)benzo[f][1,2,3,4,5]pentathiepine-7-carboxamide - $CDCl_3$.

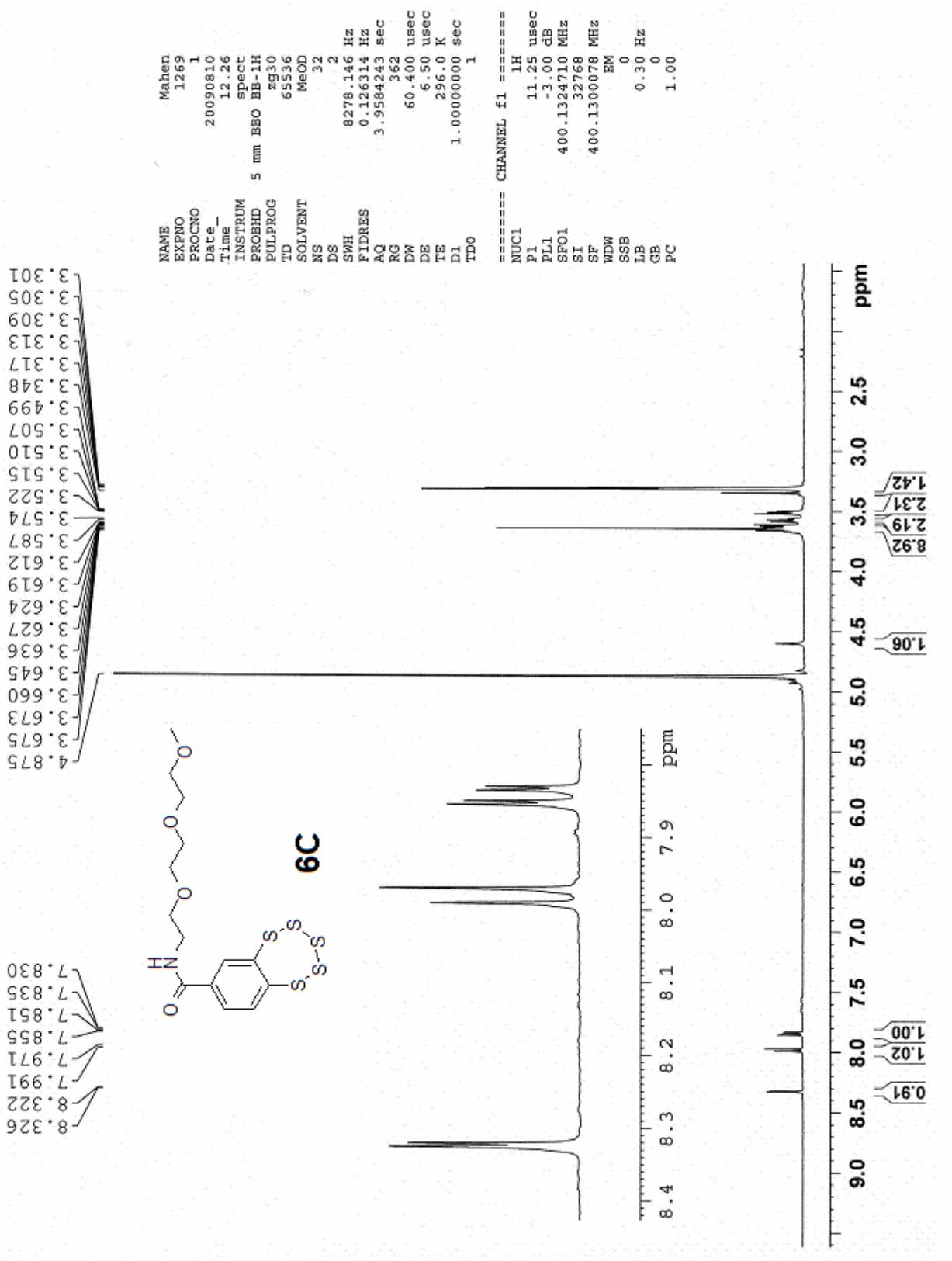


Figure 31. ^{1}H NMR of N-(2-(2-(2-methoxyethoxy)ethoxy)ethyl)benzo[f][1,2,3,4,5]pentathiepine-7-carboxamide – CD_3OD.

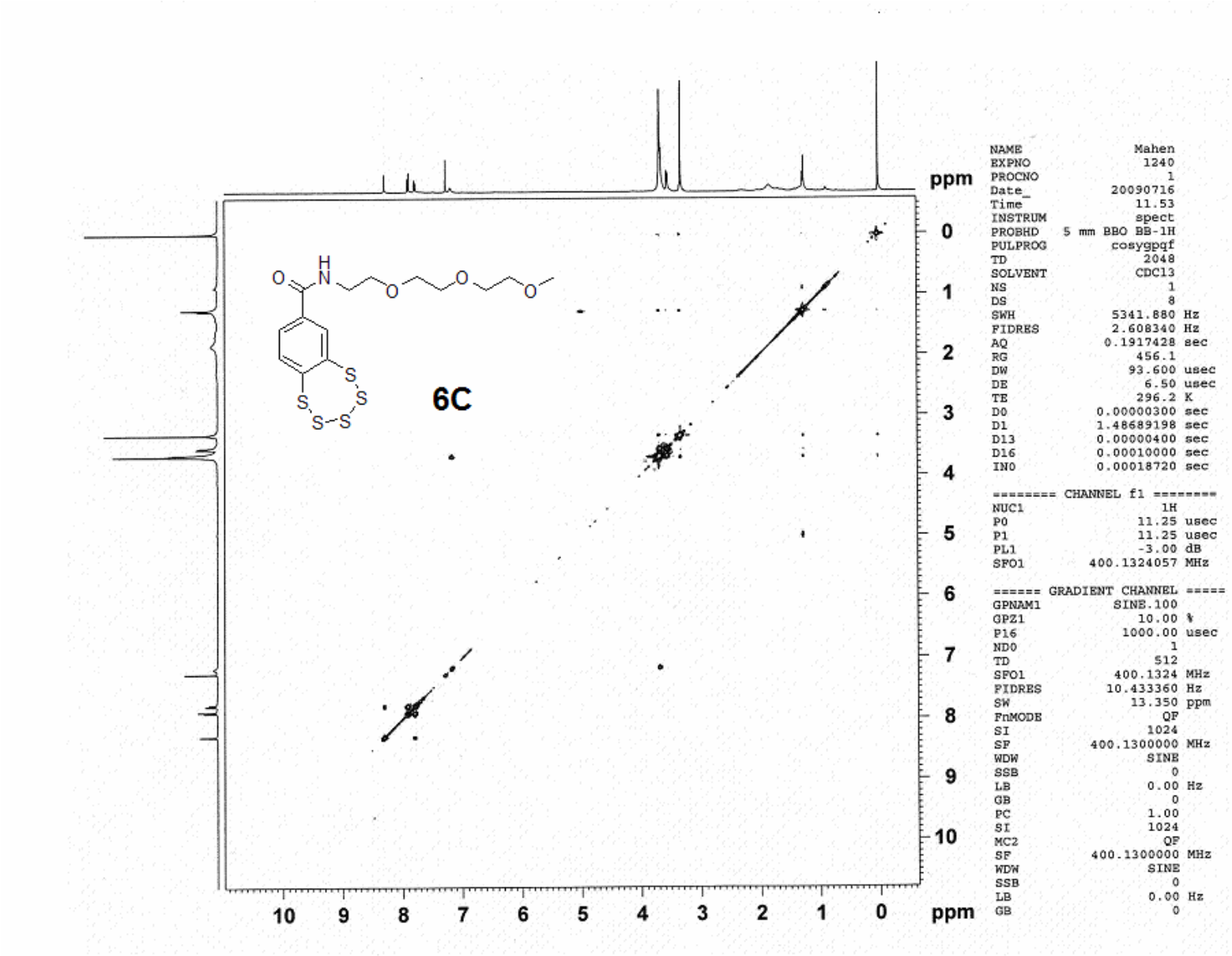


Figure 32. COSY NMR of N-(2-(2-(2-methoxyethoxy)ethoxy)ethyl)benzo[f][1,2,3,4,5]pentathiepine-7-carboxamide - $CDCl_3$

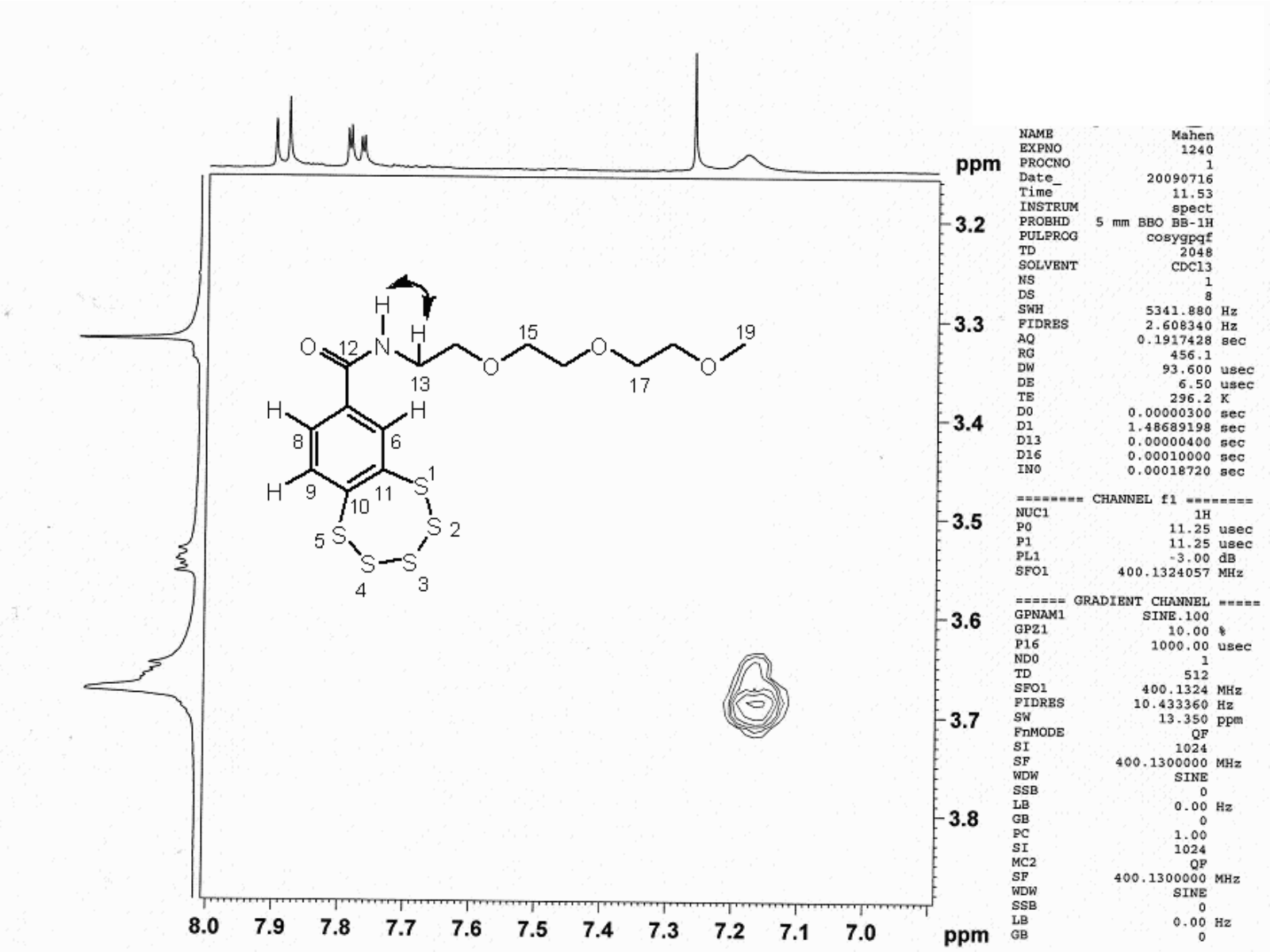


Figure 33. COSY NMR of N-(2-(2-(2-methoxyethoxy)ethoxy)ethyl)benzo[f][1,2,3,4,5]pentathiepine-7-carboxamide - $CDCl_3$.

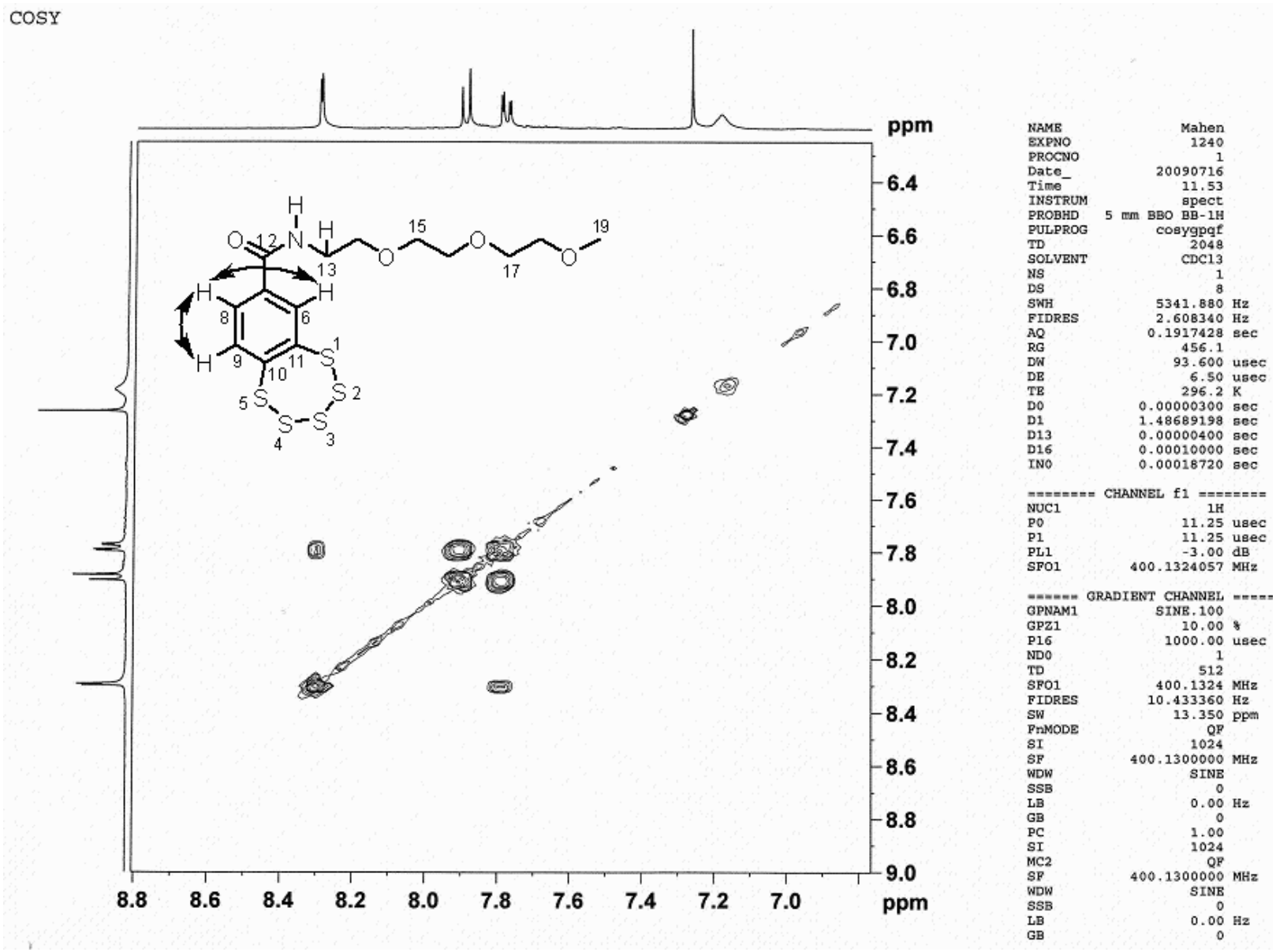


Figure 34. COSY NMR of N-(2-(2-(2-methoxyethoxy)ethoxy)ethyl)benzo[f][1,2,3,4,5]pentathiepine-7-carboxamide - $CDCl_3$.

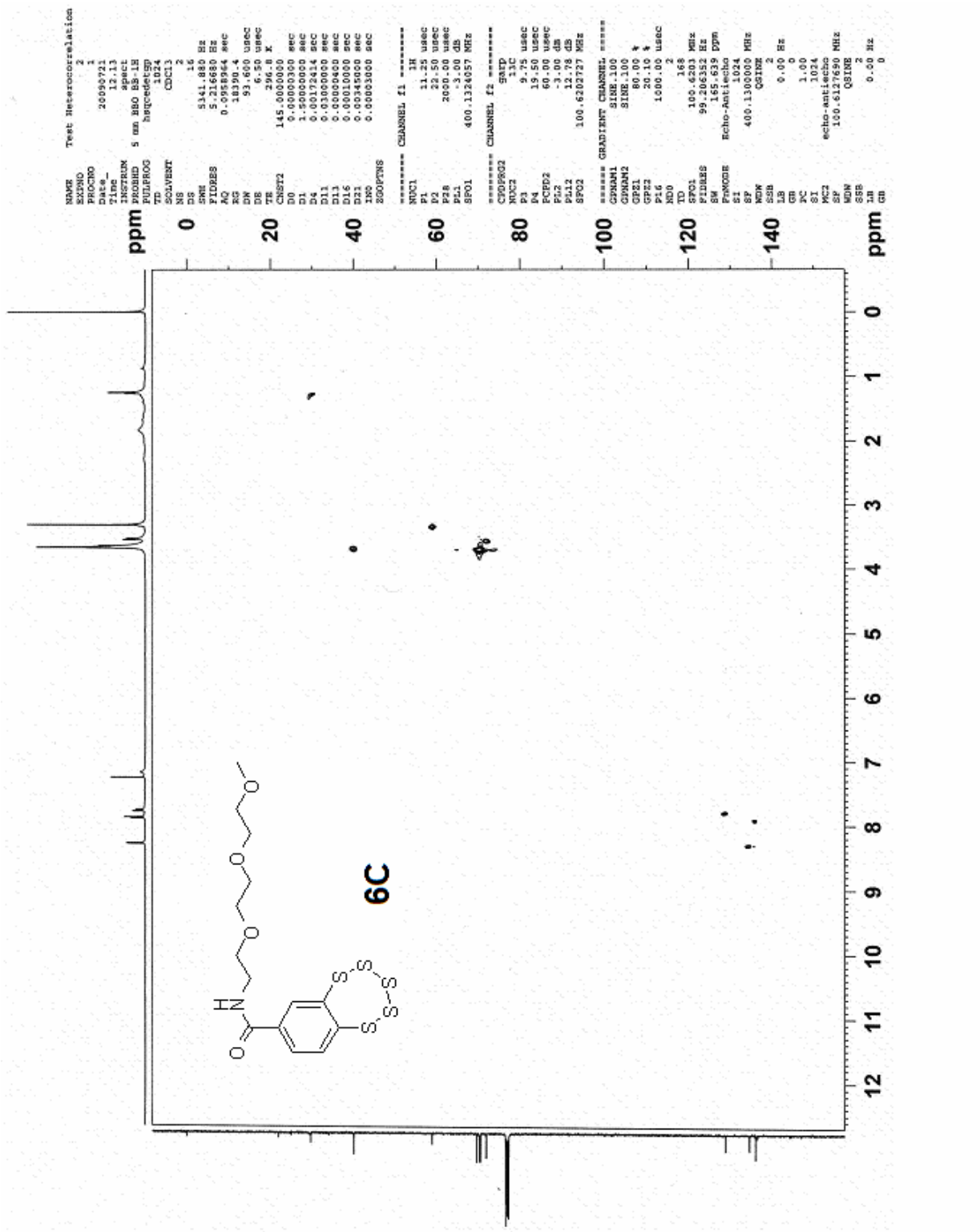


Figure 35. HSQC NMR of N-(2-(2-(2-methoxyethoxy)ethoxy)ethyl)benzo[f][1,2,3,4,5]pentathiepine-7-carboxamide - $CDCl_3$.

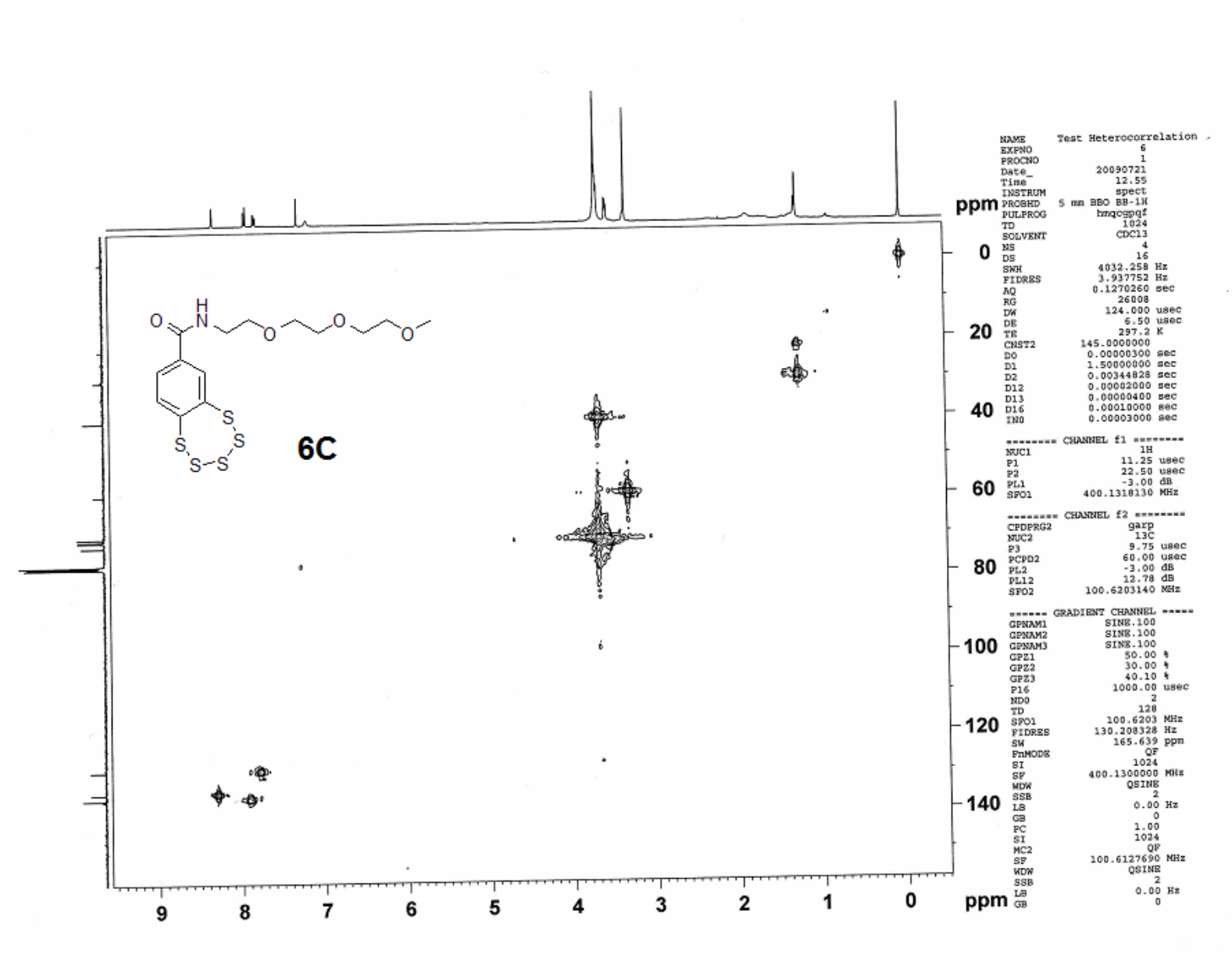


Figure 36. HMBC NMR of N-(2-(2-(2-methoxyethoxy)ethoxy)ethyl)benzo[f][1,2,3,4,5]pentathiepine-7-carboxamide- $CDCl_3$.

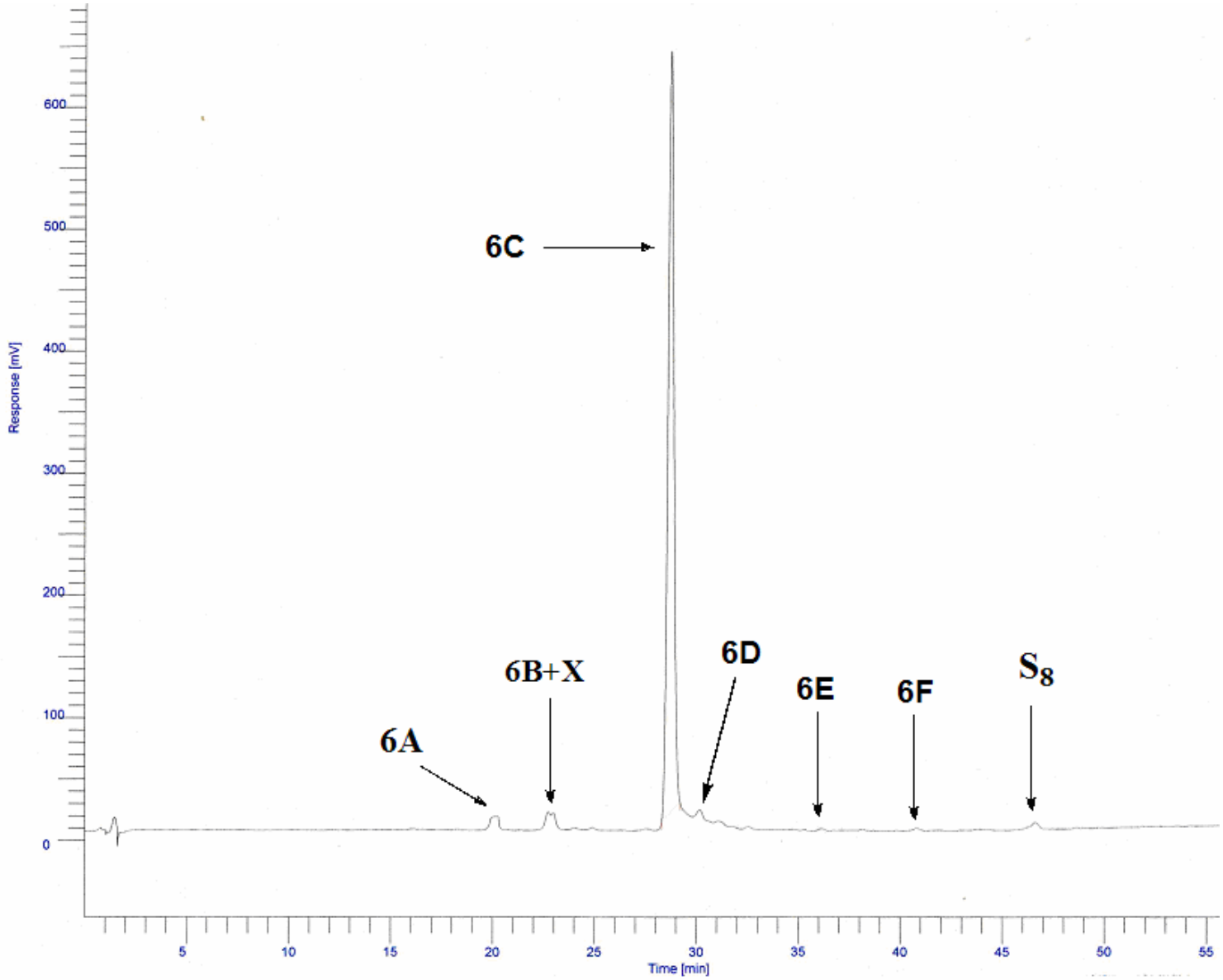


Figure 37. HPLC of N-(2-(2-(2-methoxyethoxy)ethoxy)ethyl)benzo[f][1,2,3,4,5]pentathiepine-7-carboxamide.

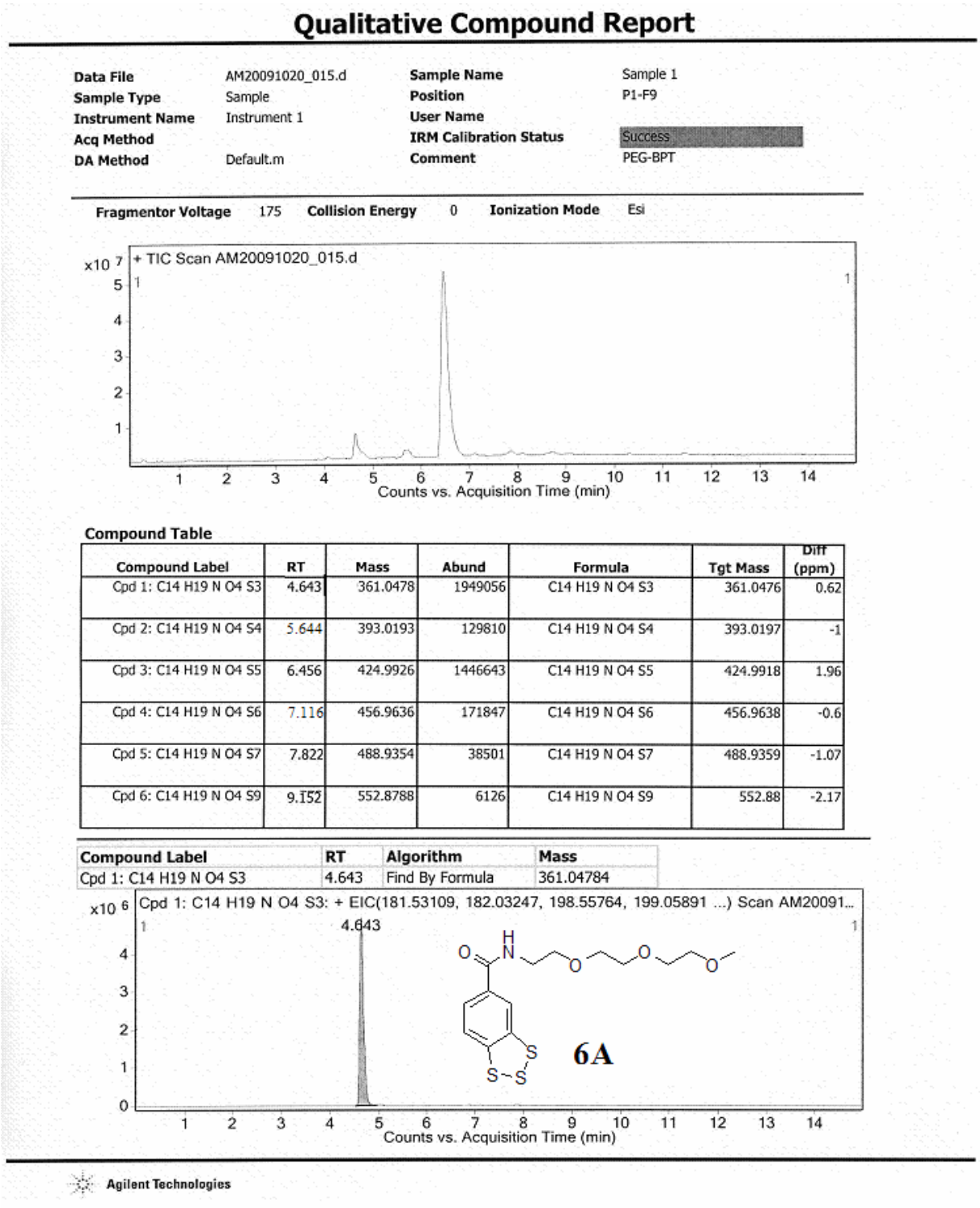
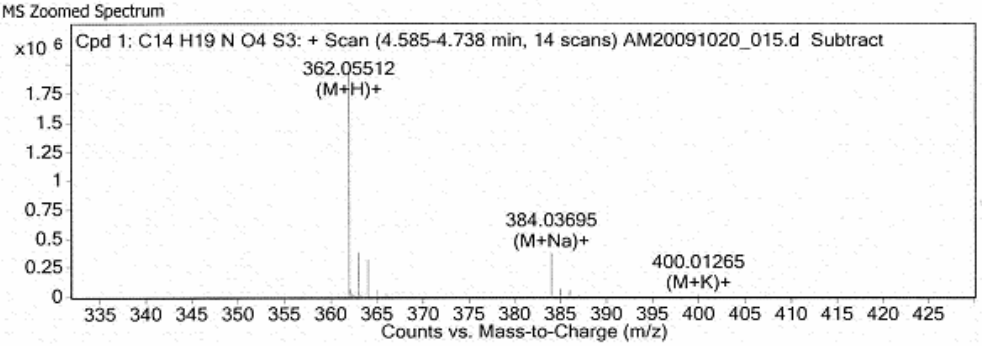


Figure 38. HRMS of N-(2-(2-(2-methoxyethoxy)ethoxy)ethyl)benzo[d] [1,2,3]trithiole-5-carboxamide.

Qualitative Compound Report

MS Zoomed Spectrum



MS Spectrum Peak List

m/z	*Calc m/z*	Diff(ppm)	z	Abund	Formula	Ion
362.05512	362.0549	0.62		1949056	C14 H20 N O4 S3	(M+H)+
362.22313				59205		
362.30833				21866		
363.05794	363.05765	0.79		380735	C14 H20 N O4 S3	(M+H)+
364.05233	364.0521	0.63		317984	C14 H20 N O4 S3	(M+H)+
365.05446	365.0544	0.17		50422	C14 H20 N O4 S3	(M+H)+
384.03695	384.03684	0.29	1	374101	C14 H19 N Na O4 S3	(M+Na)+
385.03935	385.0396	-0.64	1	65545	C14 H19 N Na O4 S3	(M+Na)+
386.03369	386.03404	-0.9	1	54866	C14 H19 N Na O4 S3	(M+Na)+
400.01265	400.01078	4.68	1	6284	C14 H19 K N O4 S3	(M+K)+

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Figure 39. HRMS of N-(2-(2-(2-methoxyethoxy)ethoxy)ethyl)benzo[d] [1,2,3]trithiole-5-carboxamide.

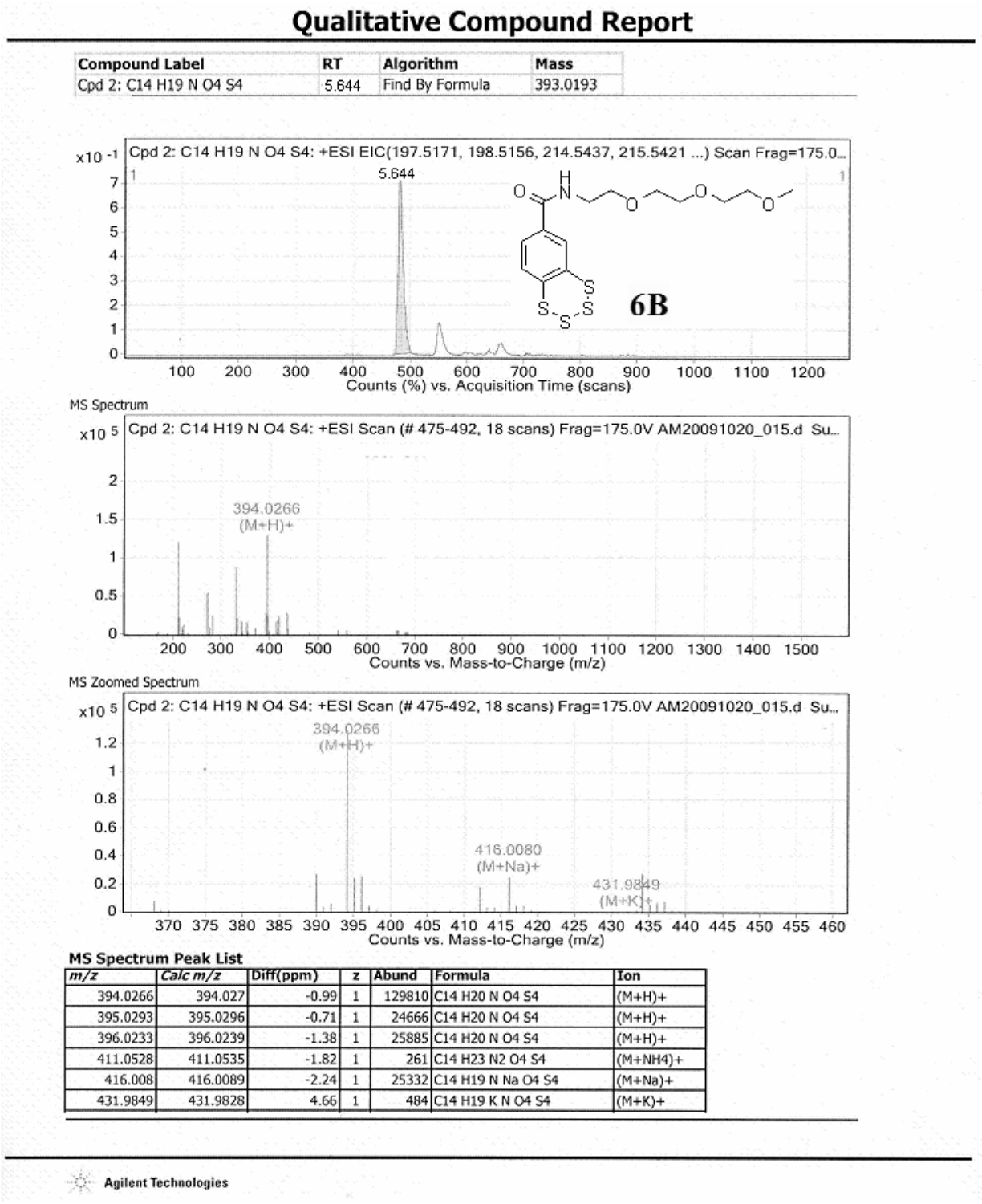
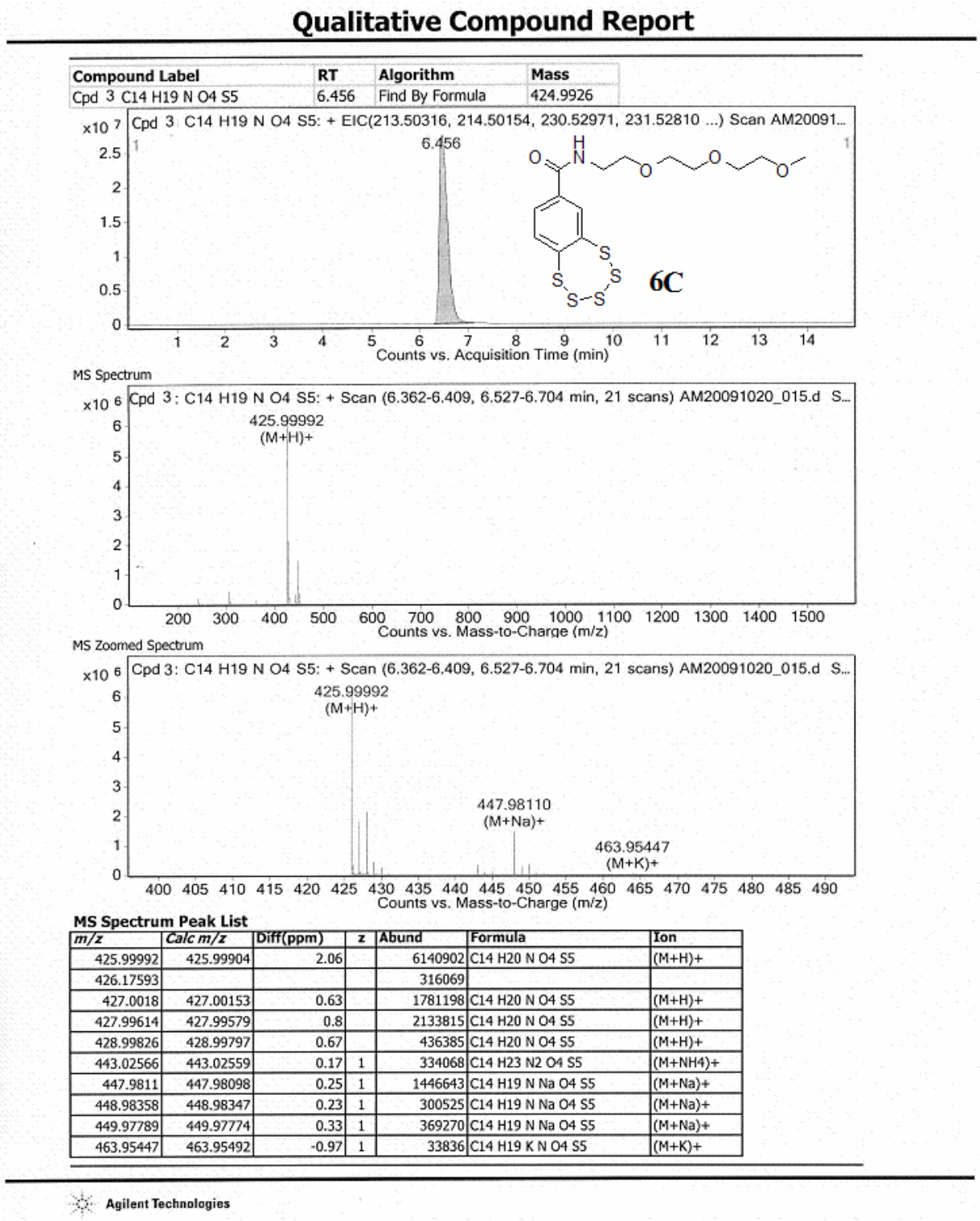


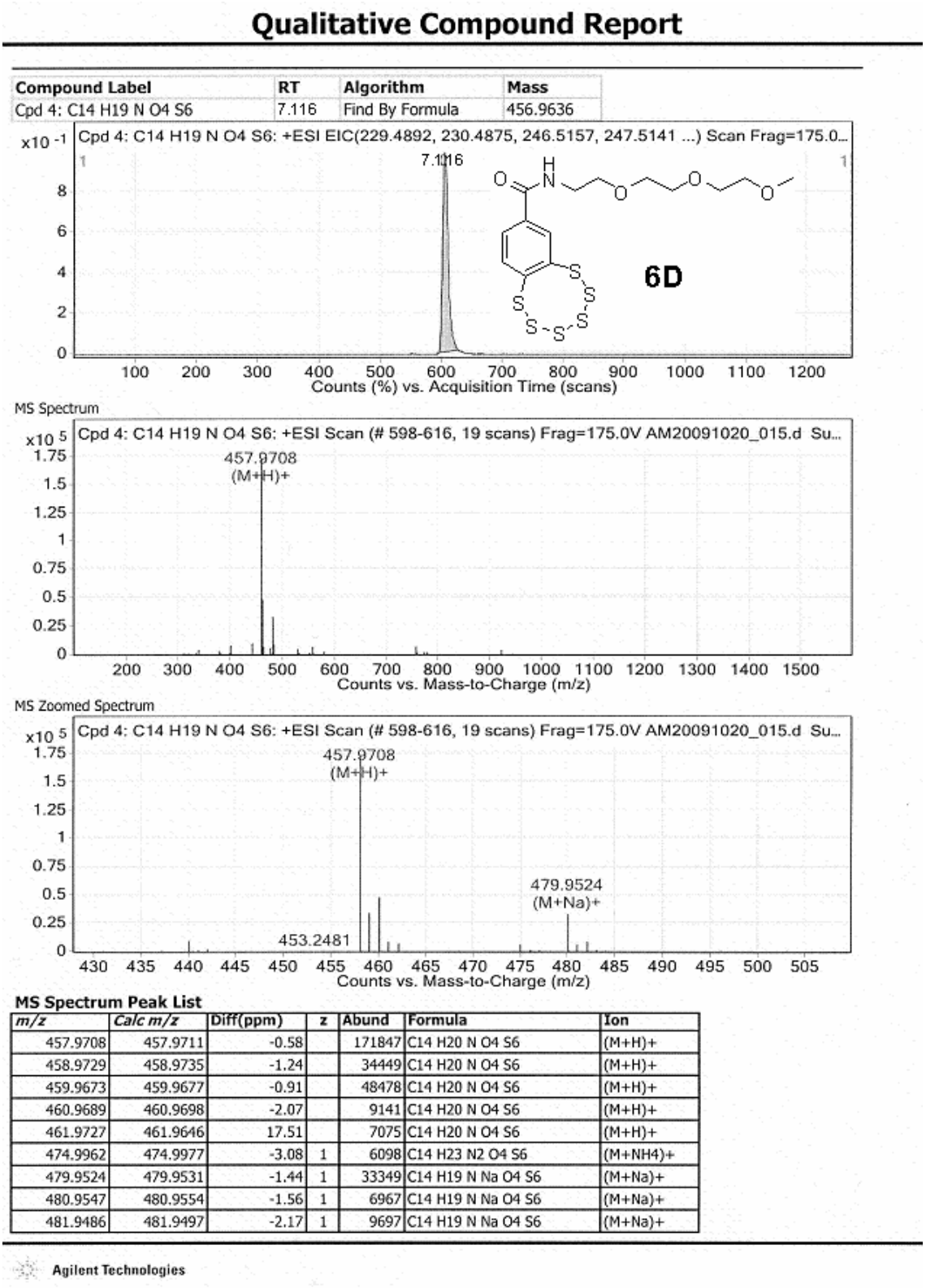
Figure 40. HRMS of N-(2-(2-(2-methoxyethoxy)ethoxy)ethyl)benzo[e][1,2,3,4]tetrathiine-6-carboxamide



MS Spectrum Peak List

m/z	Calc m/z	Diff(ppm)	z	Abund	Formula	Ion
425.99992	425.99904	2.06		6140902	C14 H20 N O4 S5	(M+H)+
426.17593				316069		
427.0018	427.00153	0.63		1781198	C14 H20 N O4 S5	(M+H)+
427.99614	427.99579	0.8		2133815	C14 H20 N O4 S5	(M+H)+
428.99826	428.99797	0.67		436385	C14 H20 N O4 S5	(M+H)+
443.02566	443.02559	0.17	1	334068	C14 H23 N2 O4 S5	(M+NH4)+
447.9811	447.98098	0.25	1	1446643	C14 H19 N Na O4 S5	(M+Na)+
448.98358	448.98347	0.23	1	300525	C14 H19 N Na O4 S5	(M+Na)+
449.97789	449.97774	0.33	1	369270	C14 H19 N Na O4 S5	(M+Na)+
463.95447	463.95492	-0.97	1	33836	C14 H19 K N O4 S5	(M+K)+

Figure 41. HRMS of N-(2-(2-(2-methoxyethoxy)ethoxy)ethyl)benzo[f][1,2,3,4,5] pentathiepine-7-carboxamide



m/z	Calc m/z	Diff(ppm)	z	Abund	Formula	Ion
457.9708	457.9711	-0.58		171847	C14 H20 N O4 S6	(M+H)+
458.9729	458.9735	-1.24		34449	C14 H20 N O4 S6	(M+H)+
459.9673	459.9677	-0.91		48478	C14 H20 N O4 S6	(M+H)+
460.9689	460.9698	-2.07		9141	C14 H20 N O4 S6	(M+H)+
461.9727	461.9646	17.51		7075	C14 H20 N O4 S6	(M+H)+
474.9962	474.9977	-3.08	1	6098	C14 H23 N2 O4 S6	(M+NH4)+
479.9524	479.9531	-1.44	1	33349	C14 H19 N Na O4 S6	(M+Na)+
480.9547	480.9554	-1.56	1	6967	C14 H19 N Na O4 S6	(M+Na)+
481.9486	481.9497	-2.17	1	9697	C14 H19 N Na O4 S6	(M+Na)+

Figure 42. HRMS of N-(2-(2-(2-methoxyethoxy)ethoxy)ethyl)benzo[g][1,2,3,4,5,6] hexathiocine-8-carboxamide

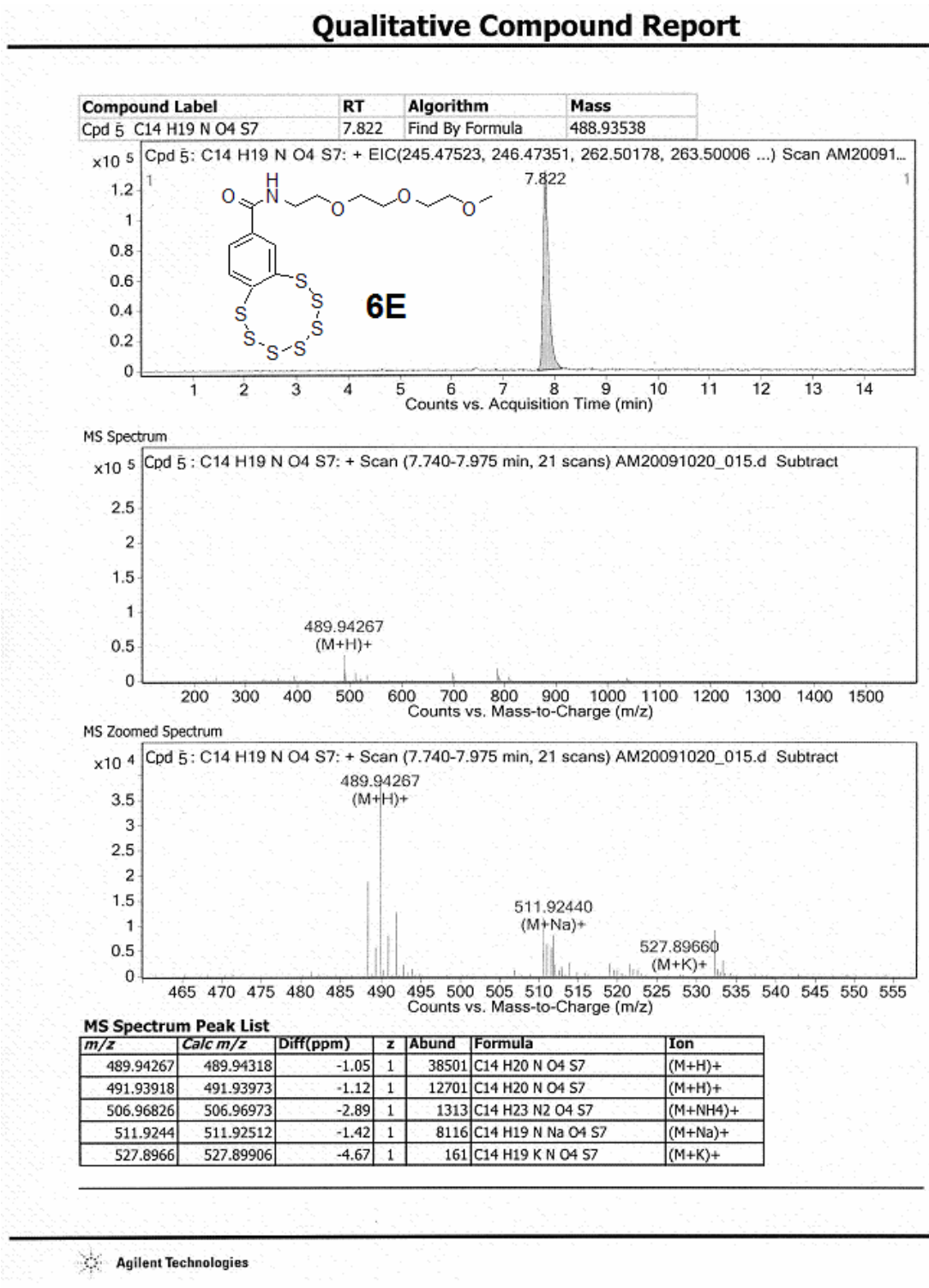
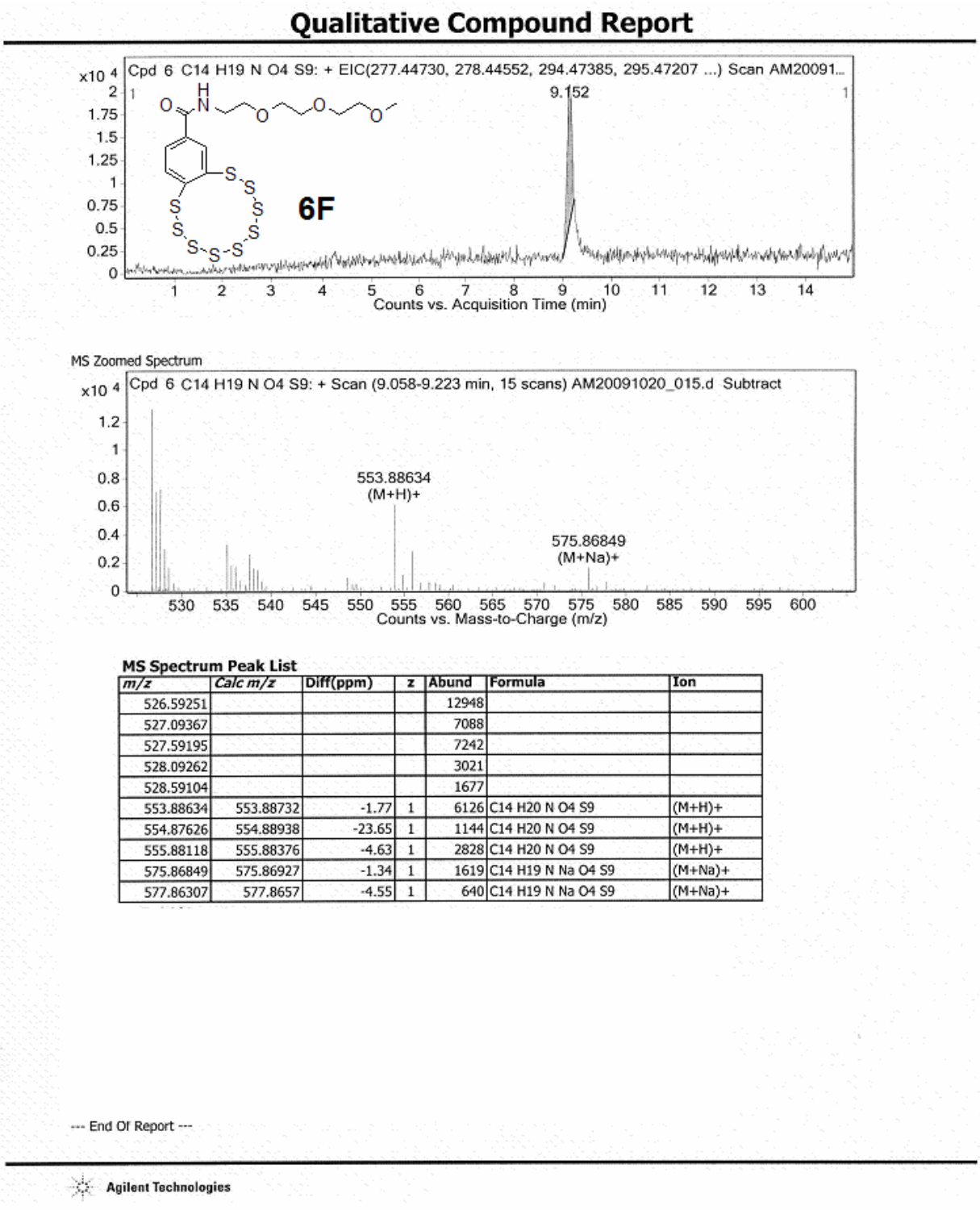


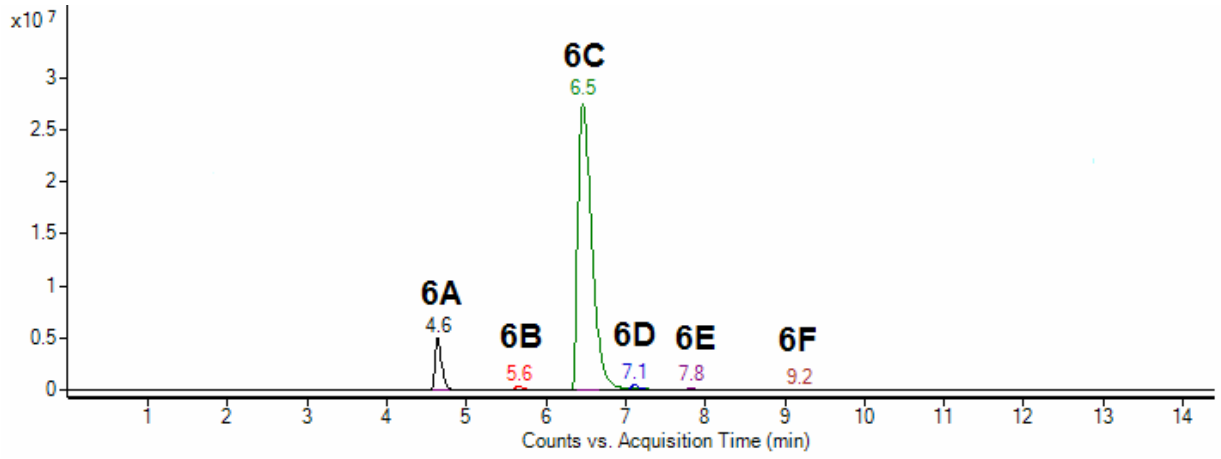
Figure 43. HRMS of N-(2-(2-(2-methoxyethoxy)ethoxy)ethyl)benzo[h][1,2,3,4,5,6,7] heptathionine-9-carboxamide.



m/z	Calc m/z	Diff(ppm)	z	Abund	Formula	Ion
526.59251				12948		
527.09367				7088		
527.59195				7242		
528.09262				3021		
528.59104				1677		
553.88634	553.88732	-1.77	1	6126	C14 H20 N O4 S9	(M+H)+
554.87626	554.88938	-23.65	1	1144	C14 H20 N O4 S9	(M+H)+
555.88118	555.88376	-4.63	1	2828	C14 H20 N O4 S9	(M+H)+
575.86849	575.86927	-1.34	1	1619	C14 H19 N Na O4 S9	(M+Na)+
577.86307	577.8657	-4.55	1	640	C14 H19 N Na O4 S9	(M+Na)+

Figure 44. HRMS of N-(2-(2-(2-methoxyethoxy)ethoxy)ethyl)benzo[j][1,2,3,4,5,6,7,8,9] nonathiacycloundecine-11-carboxamide.

A



B

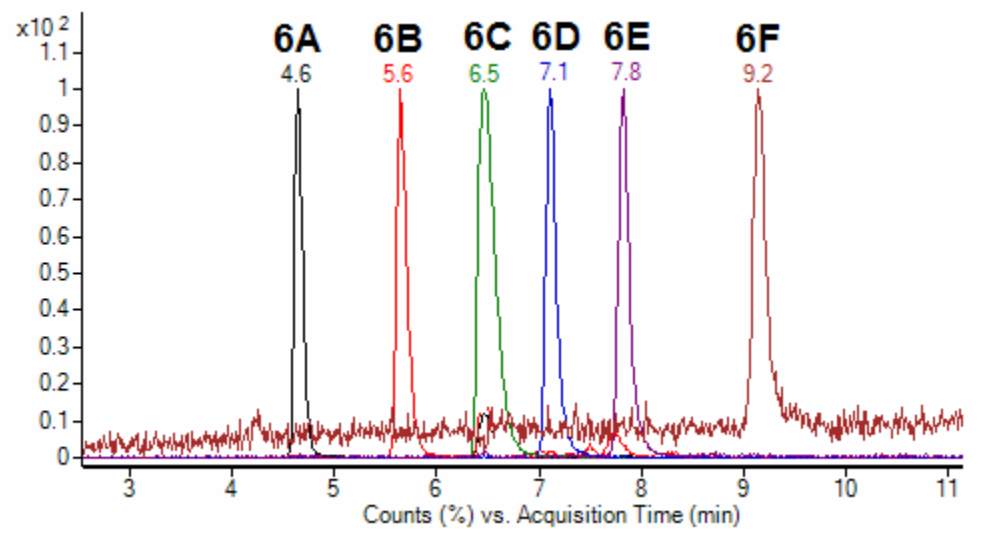
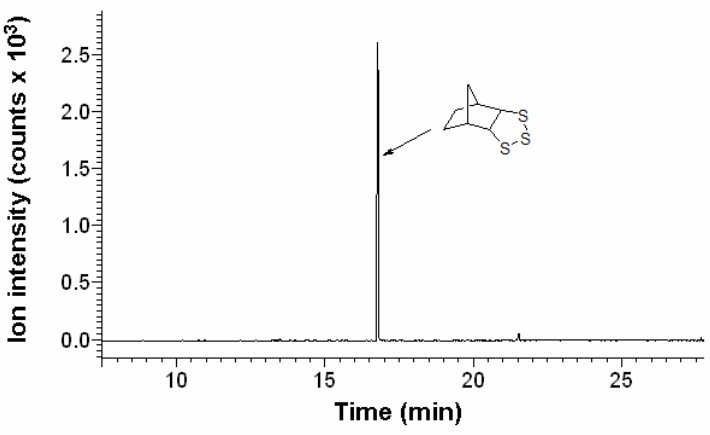


Figure 45. (A) LCMS extracted ion chromatograms of **6A-F**. (B) LCMS extracted ion normalized chromatograms (overlaid) of **6A**-**F**.

A



B

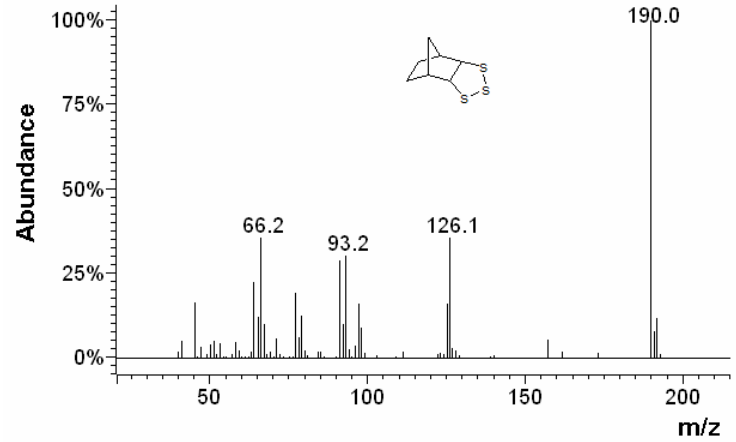


Figure 46. (A) Extracted ion chromatogram of norbornenetrithiolane **17** formed in the reaction of **6A**-**F** and norbornene in the presence of ethanethiol, Rt 16.75 min. (B) MS spectrum of norbornenetrithiolane **17**, Rt 16.75 min.