Supporting Information

Anti-Biofilm Agents against *Pseudomonas aeruginosa*: a Structure-Activity Relationship Study of *C*-Glycosidic LecB Inhibitors

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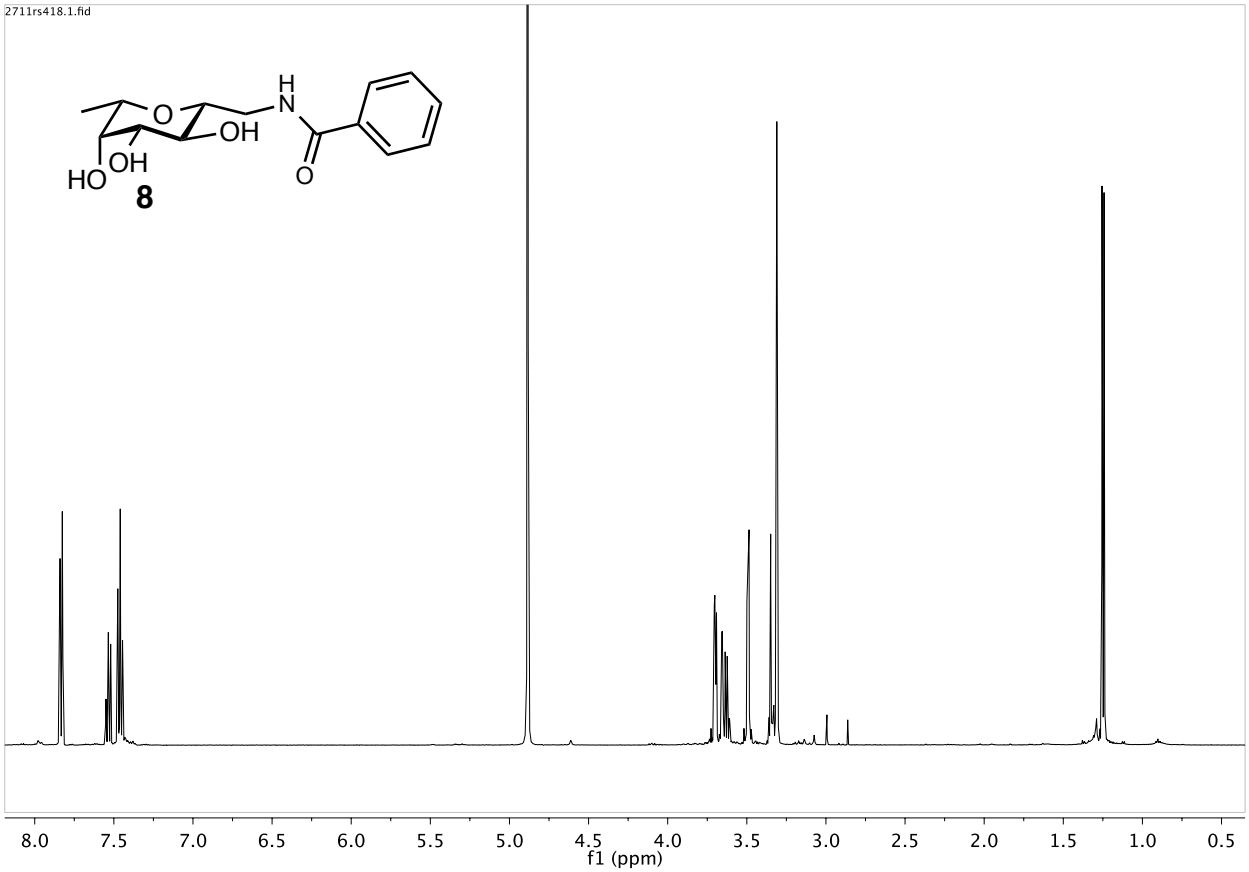

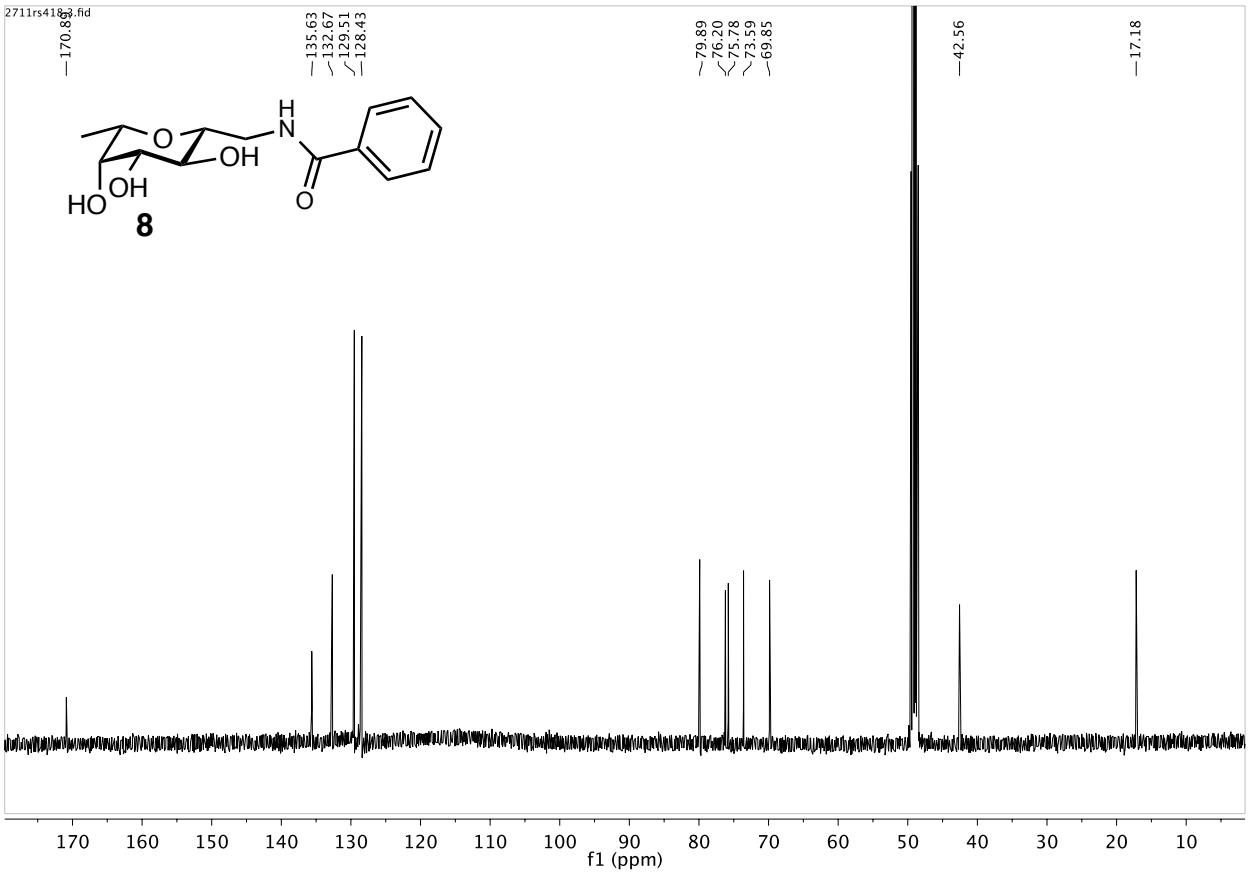

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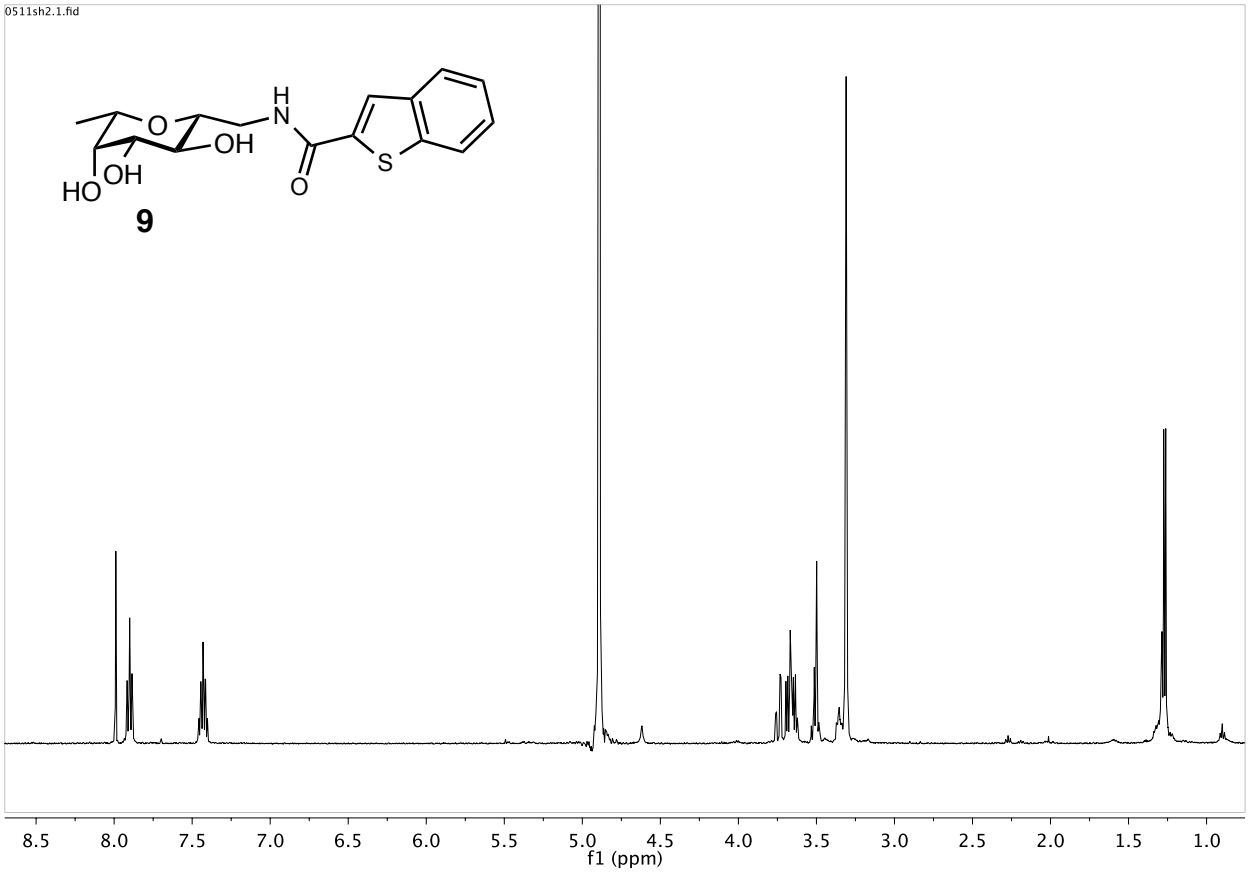

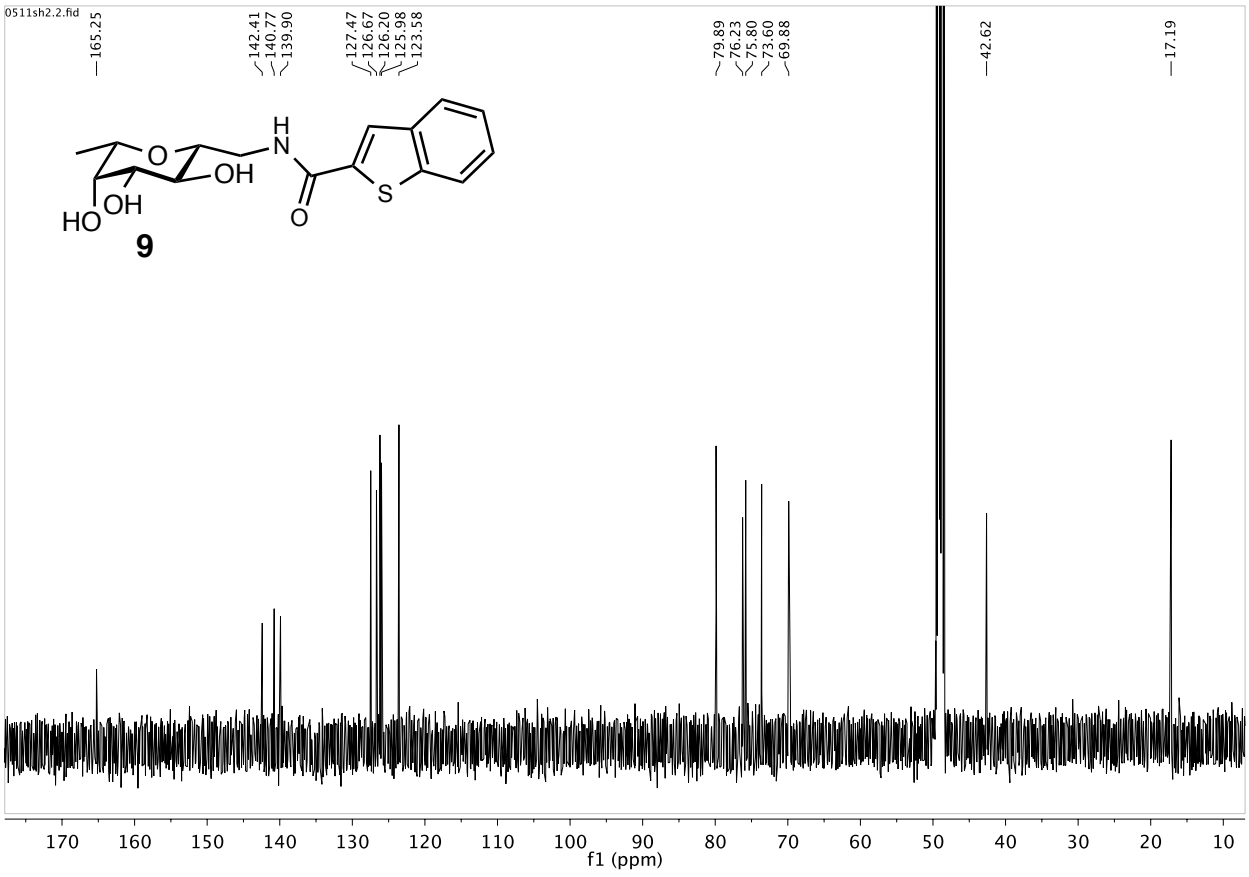

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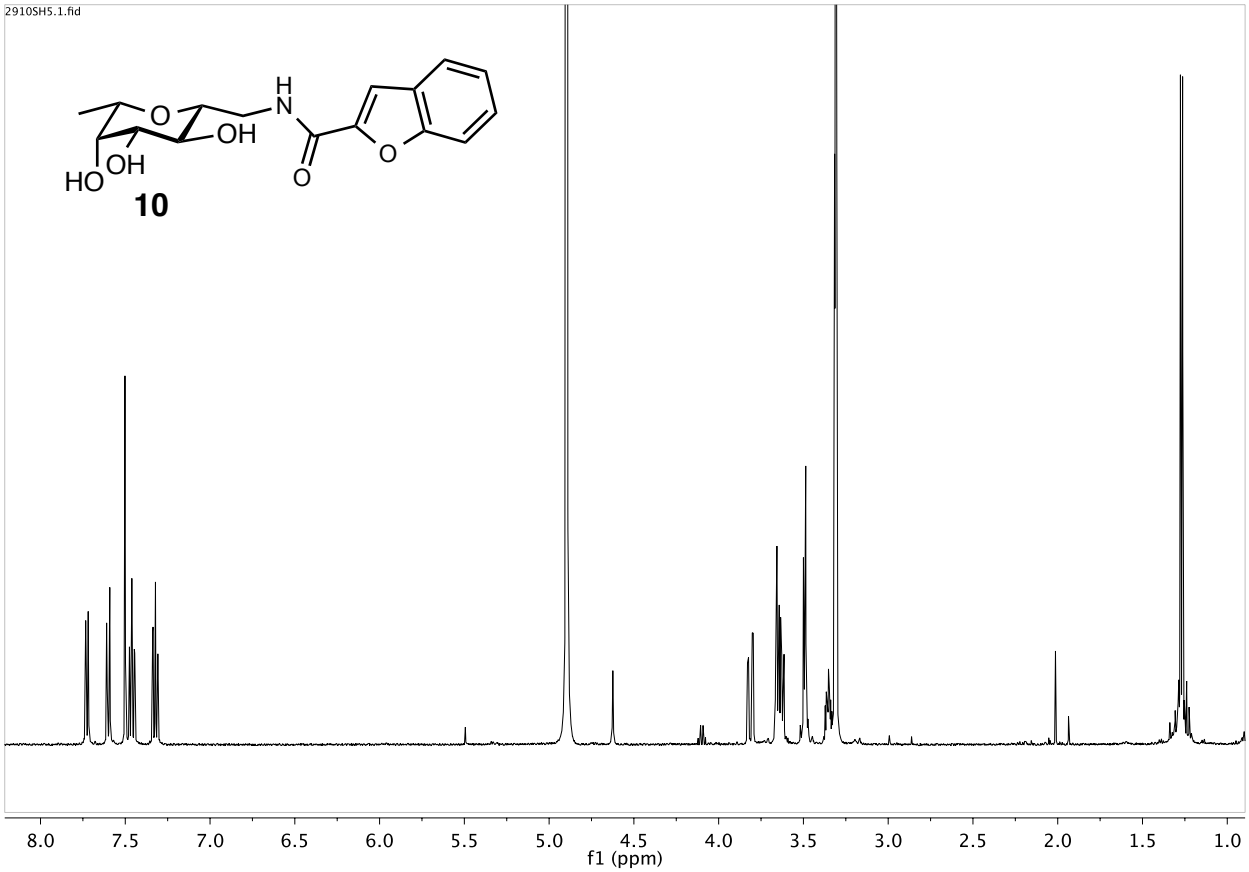

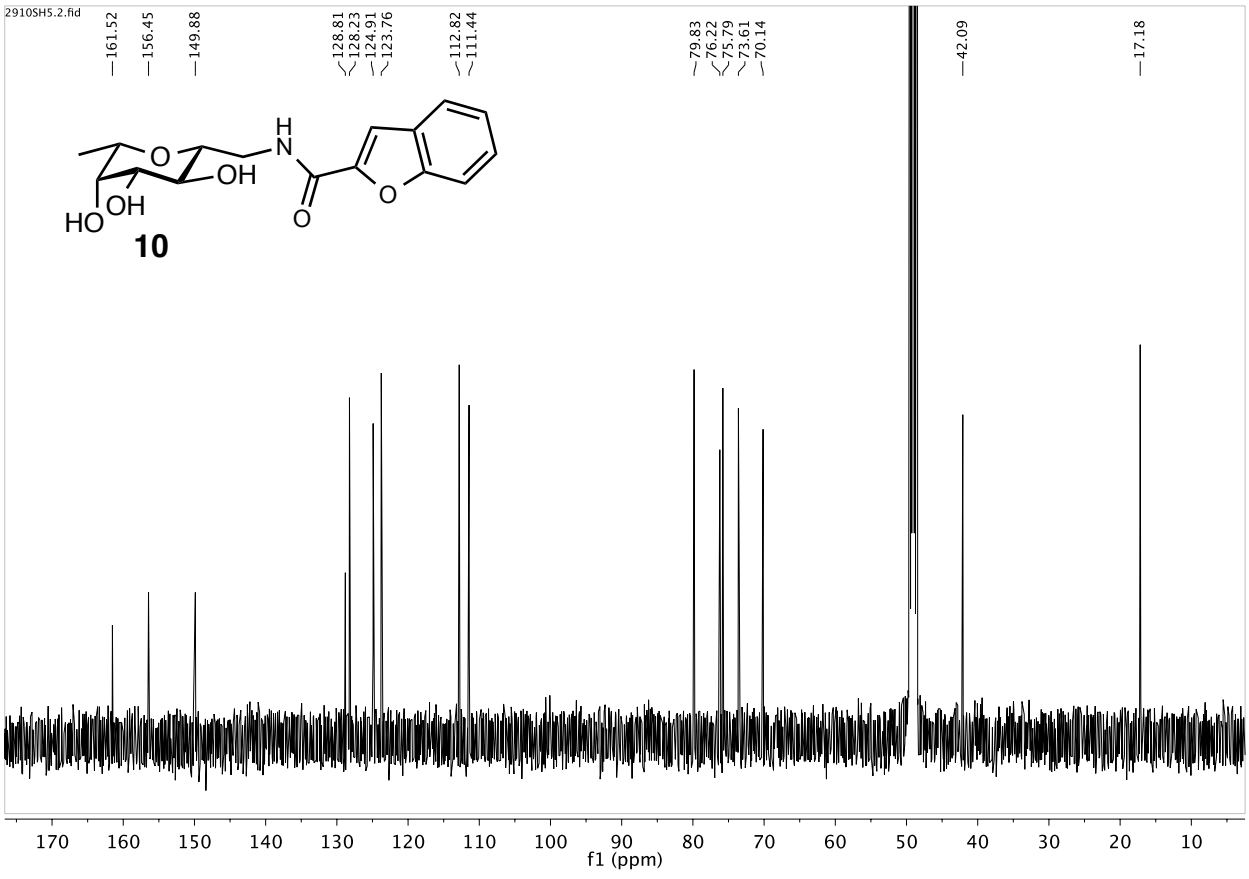

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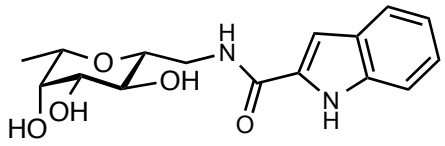

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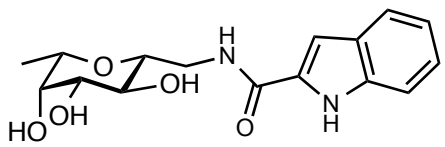

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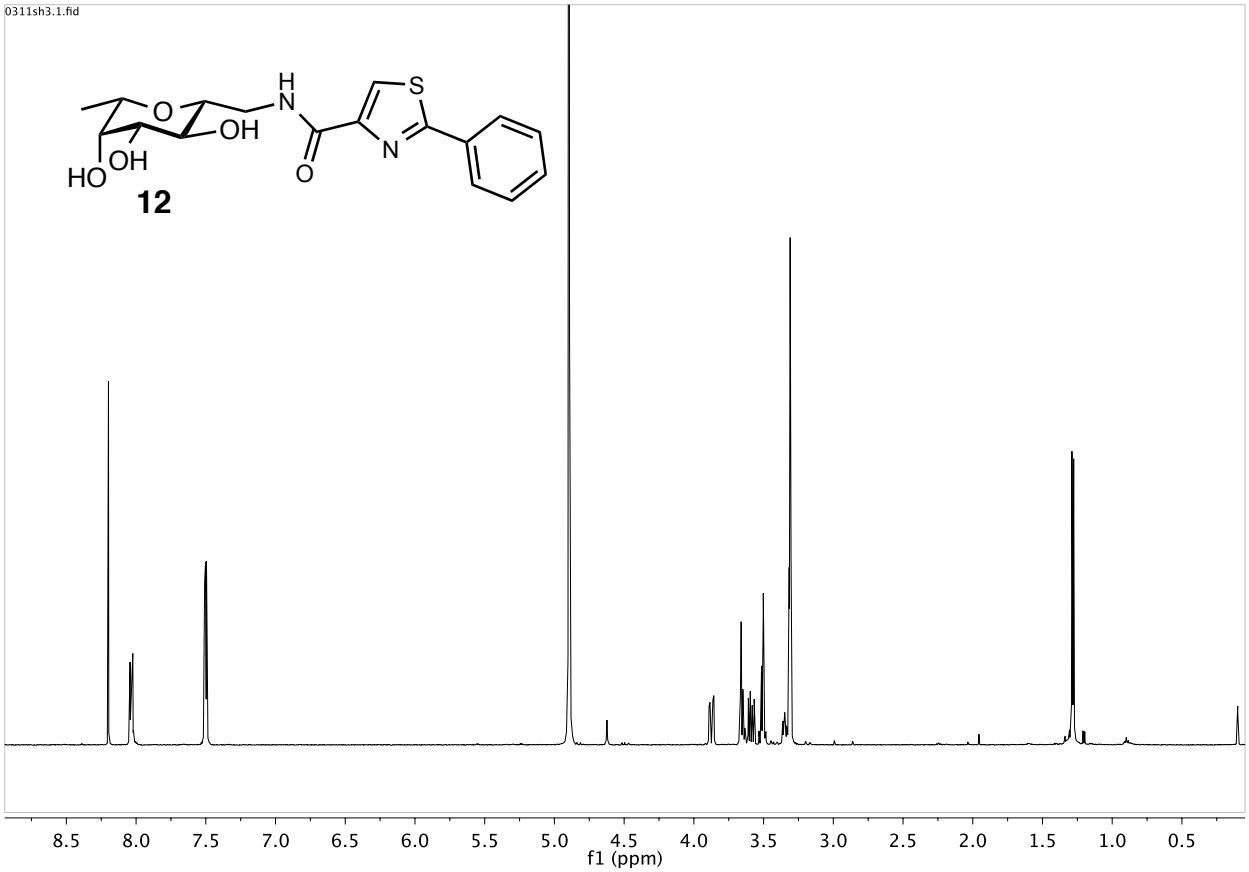

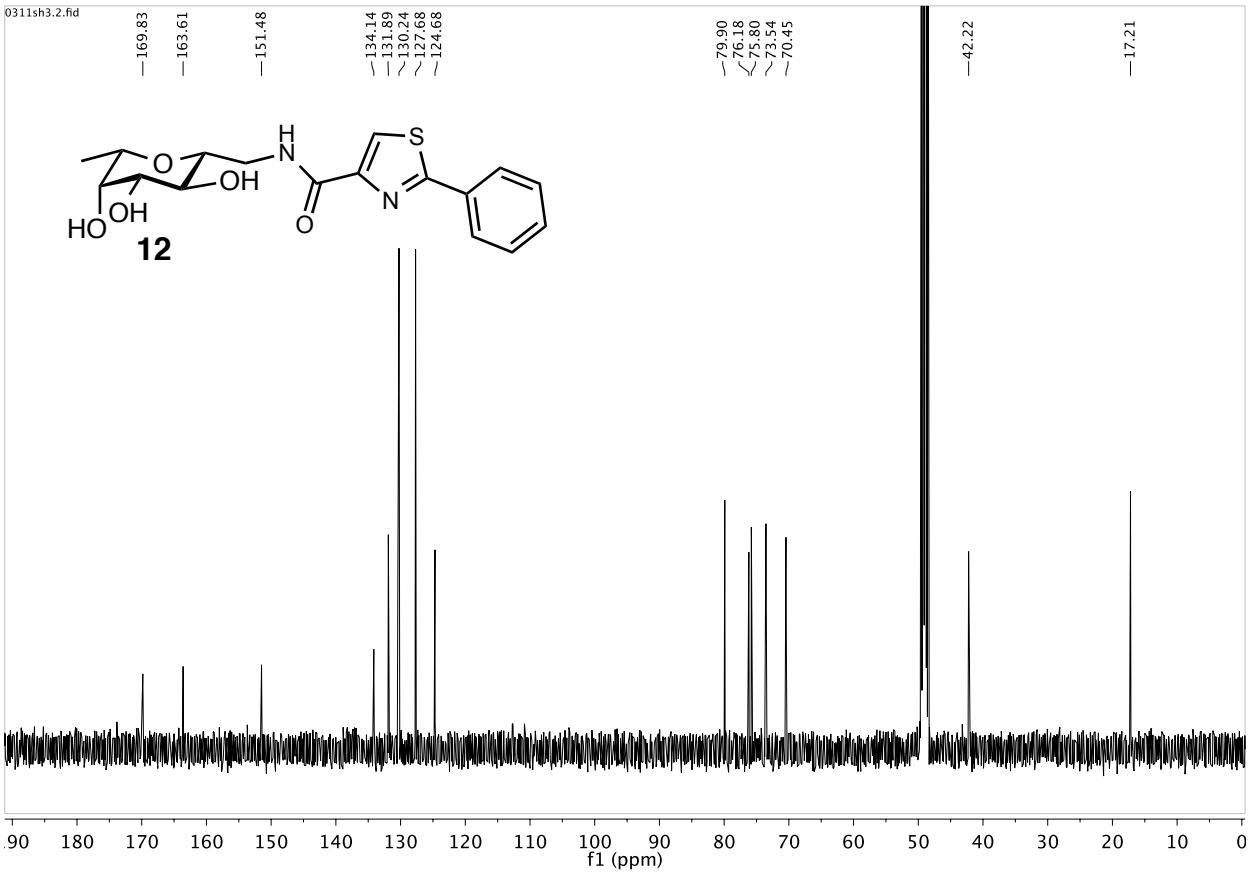

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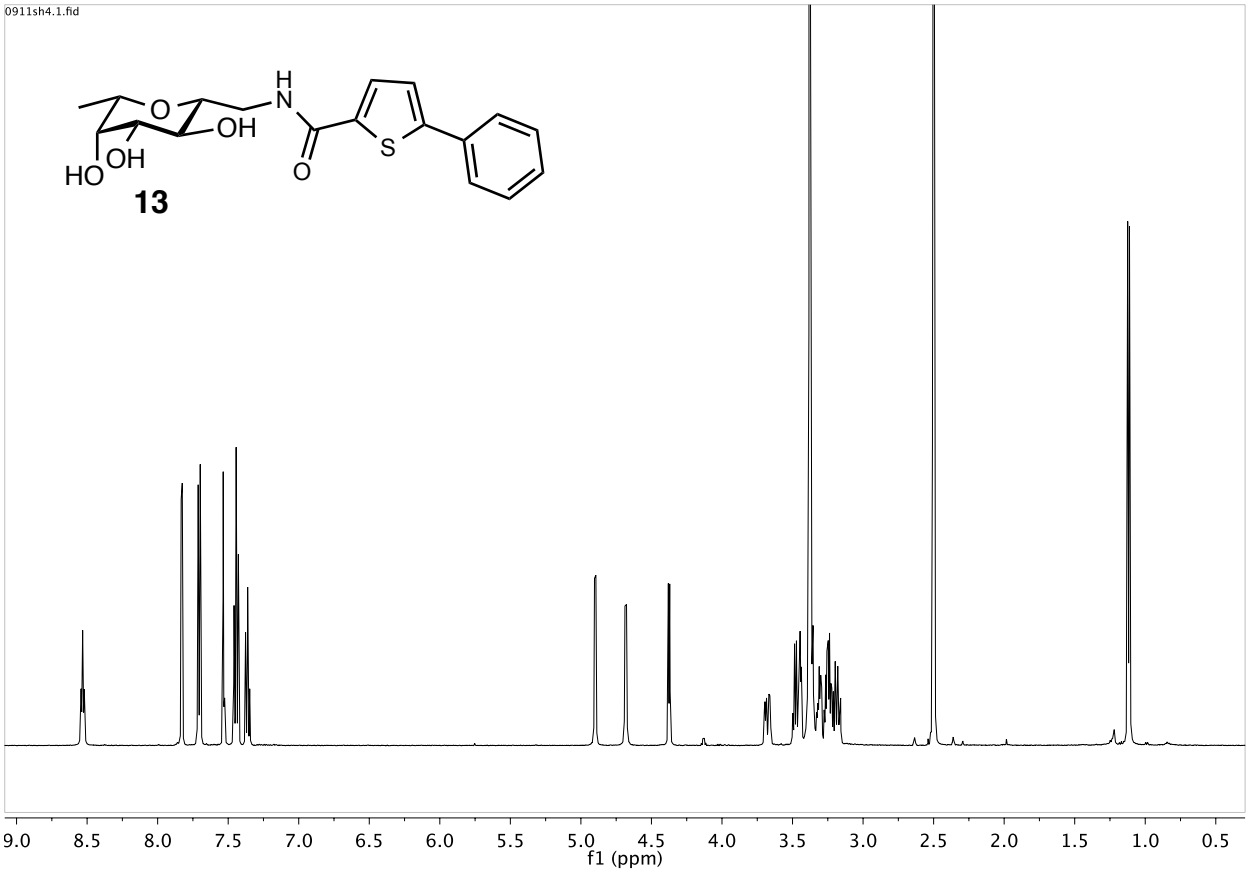

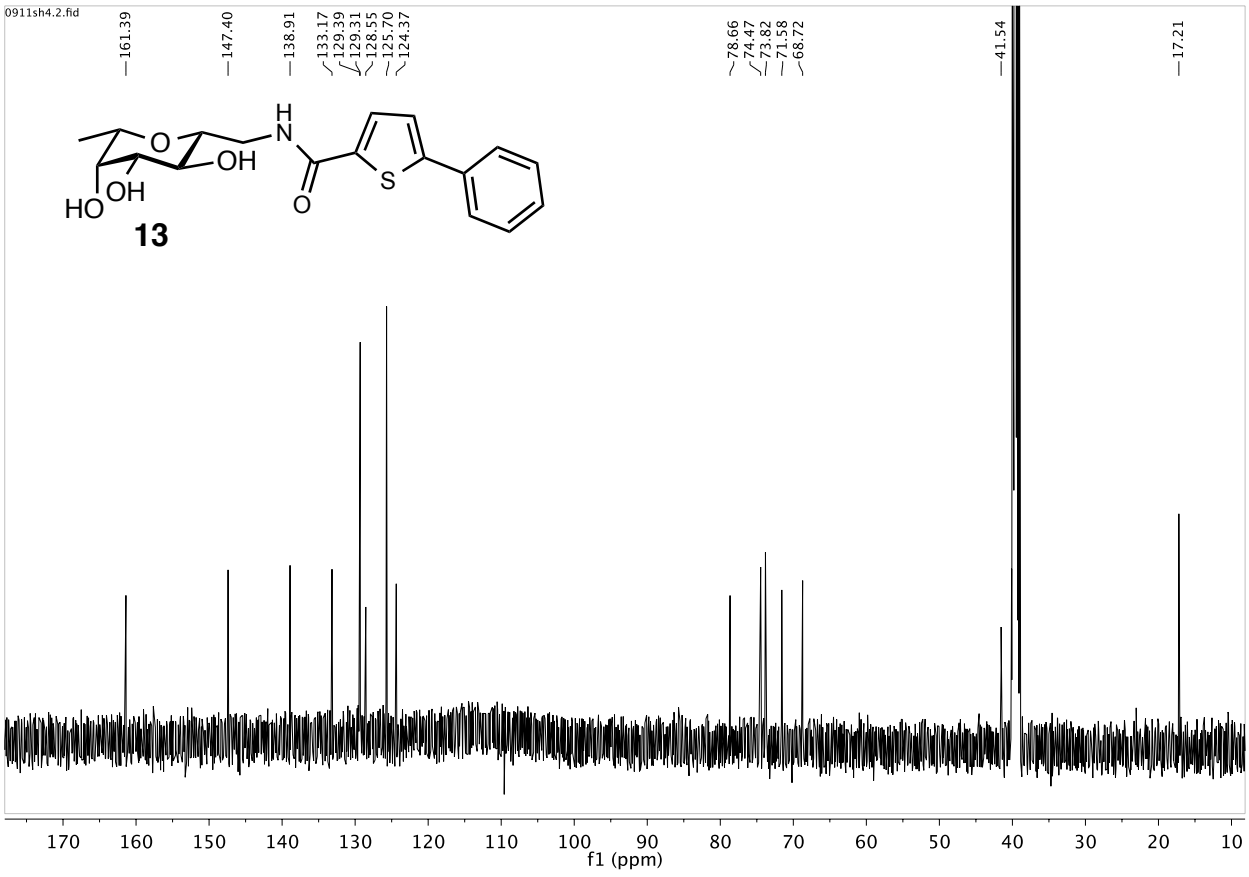

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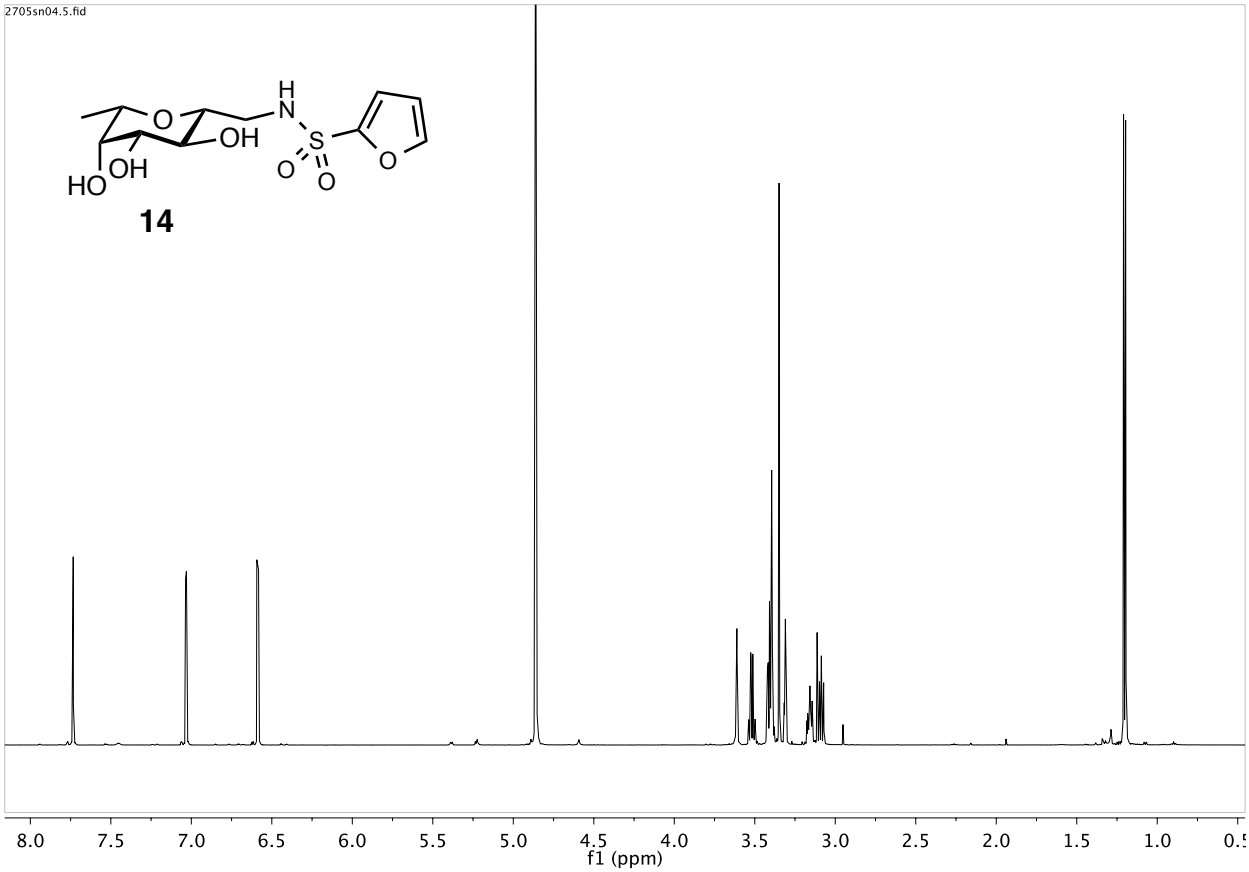

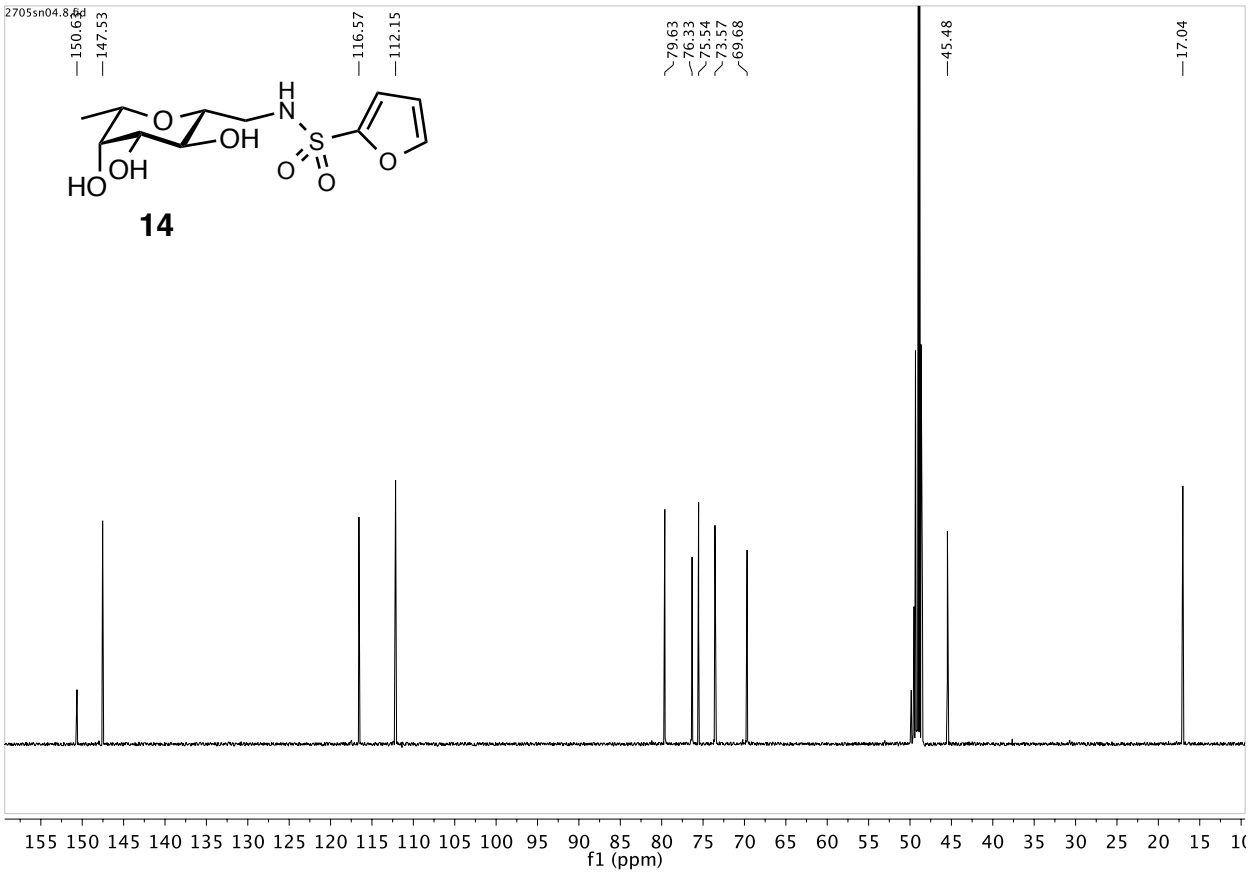

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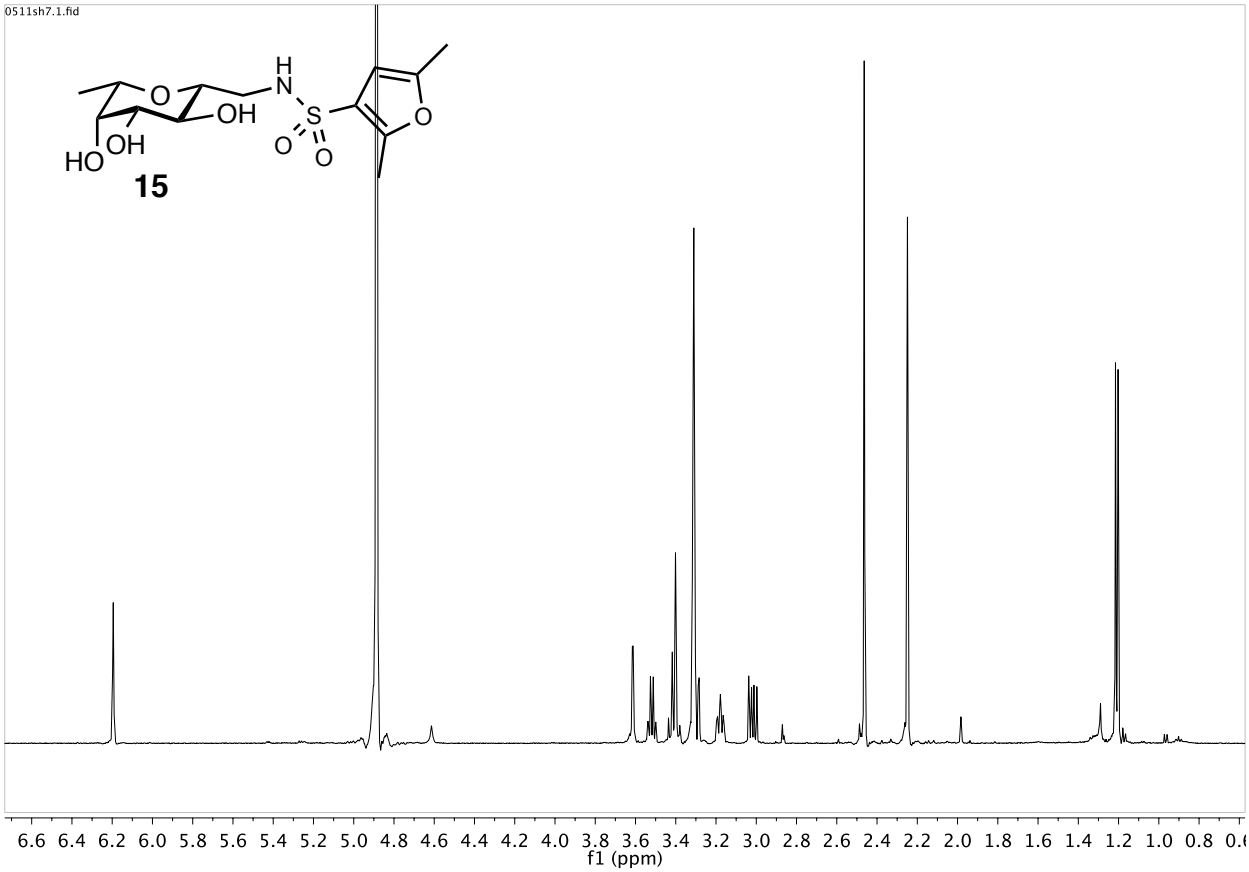

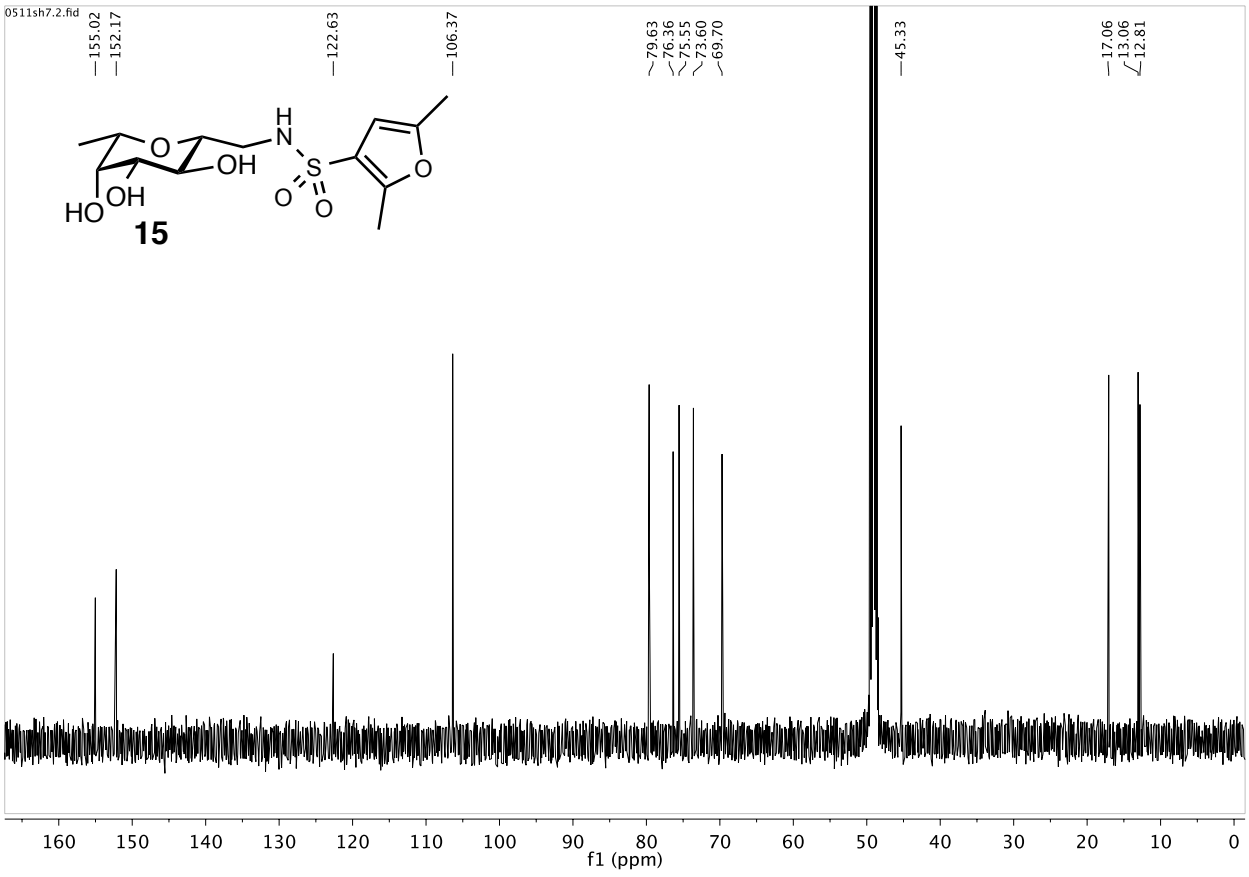

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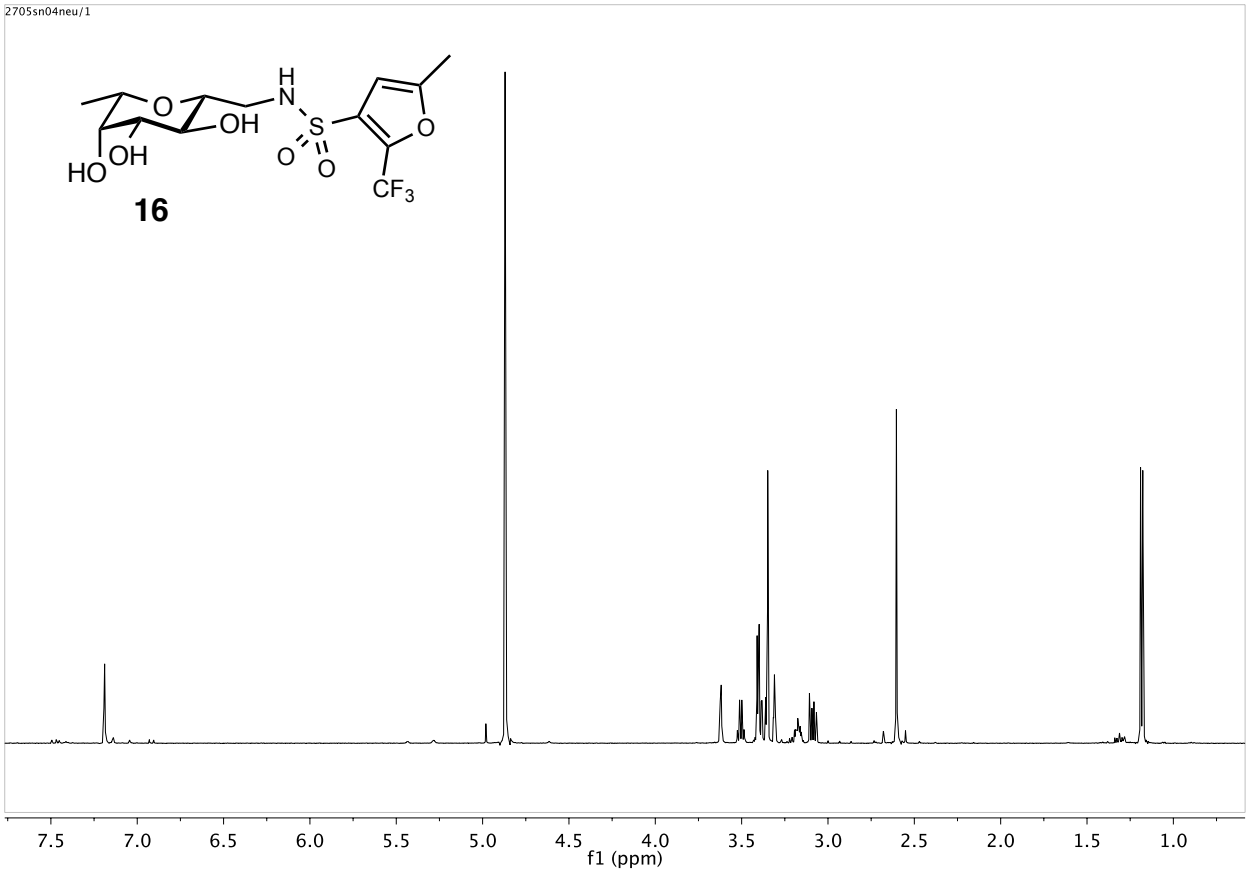

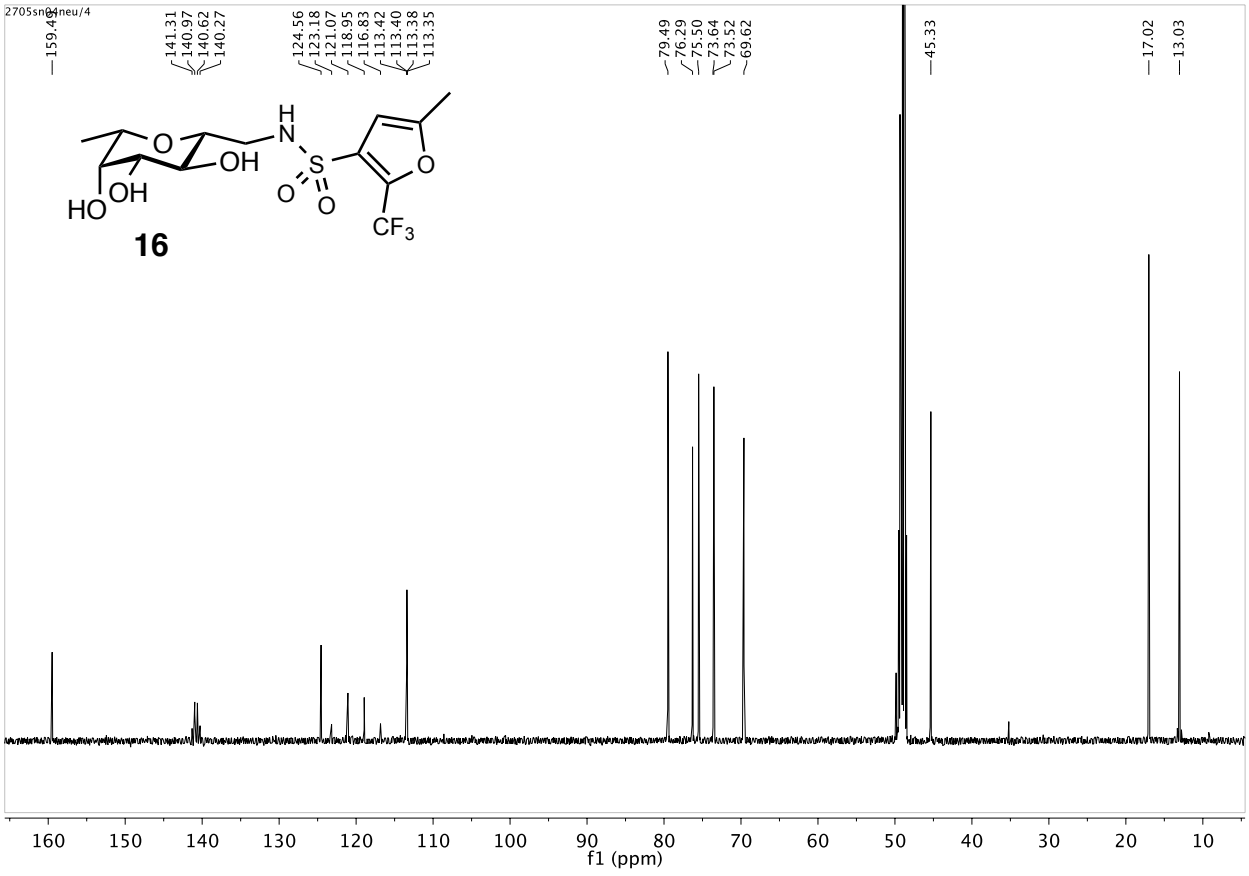

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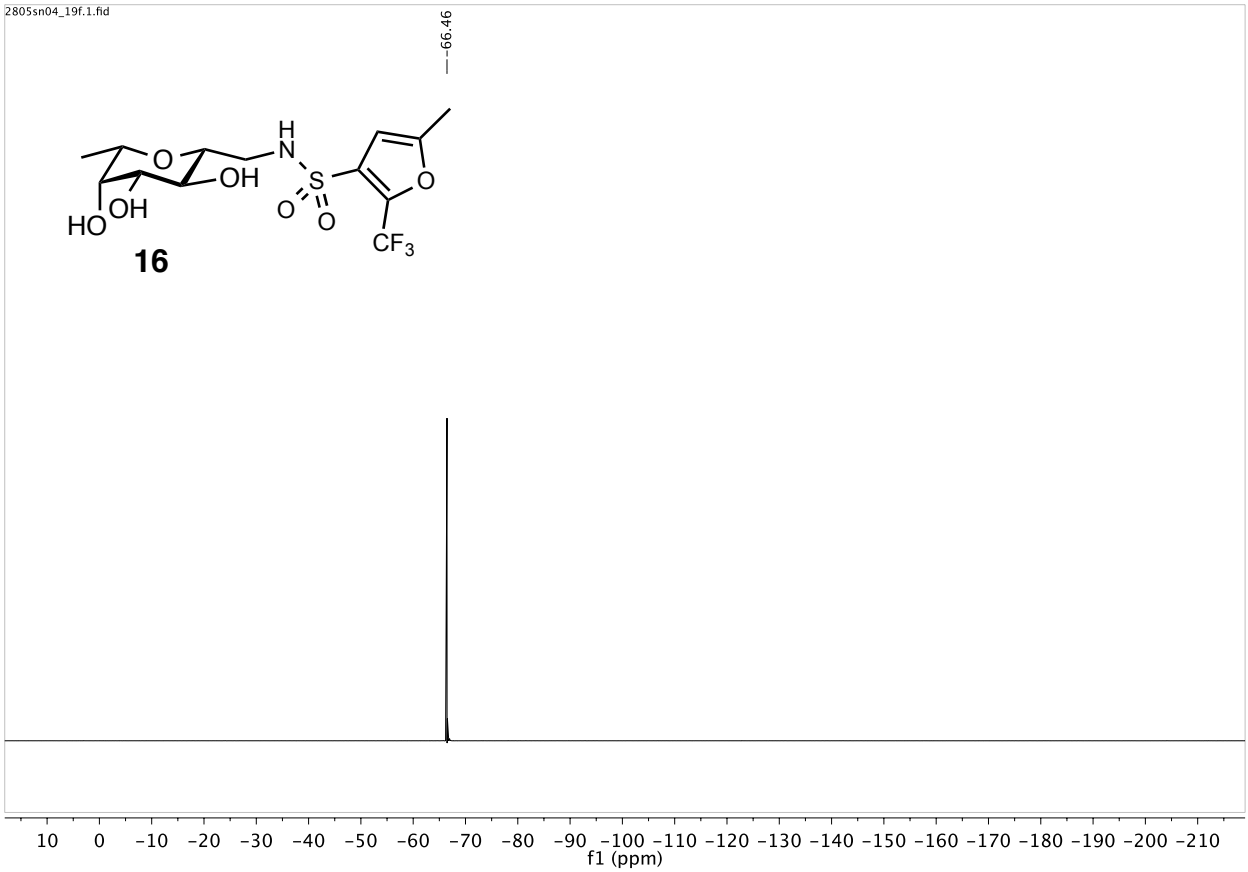

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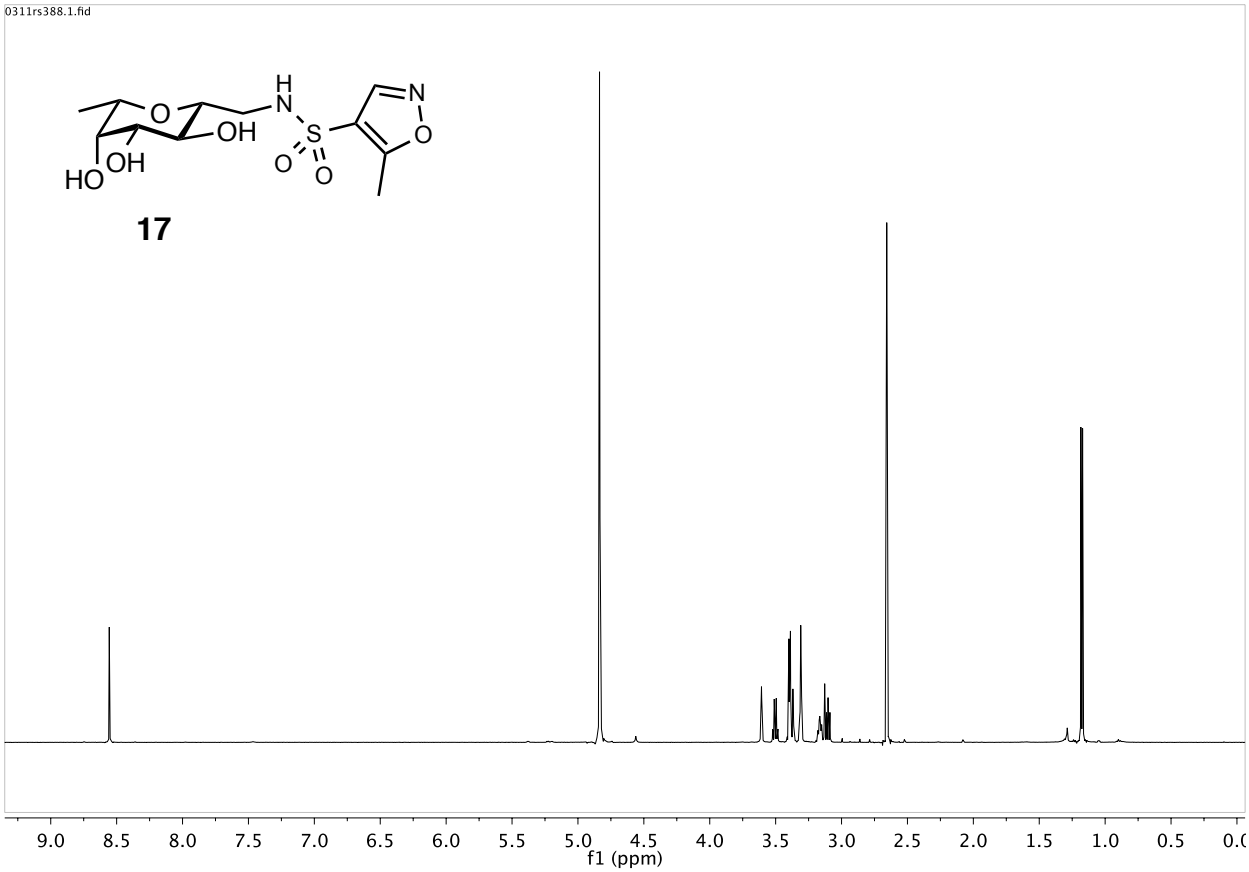

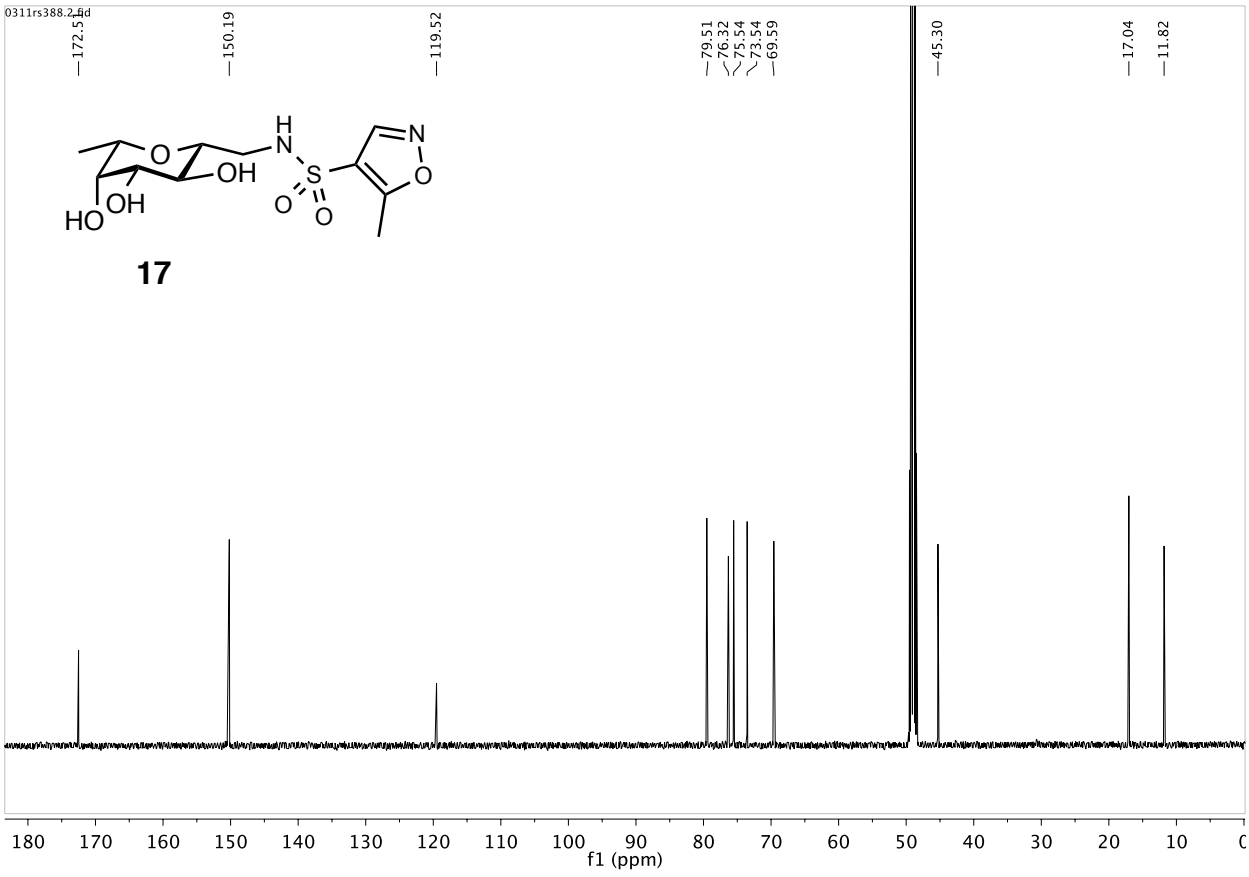

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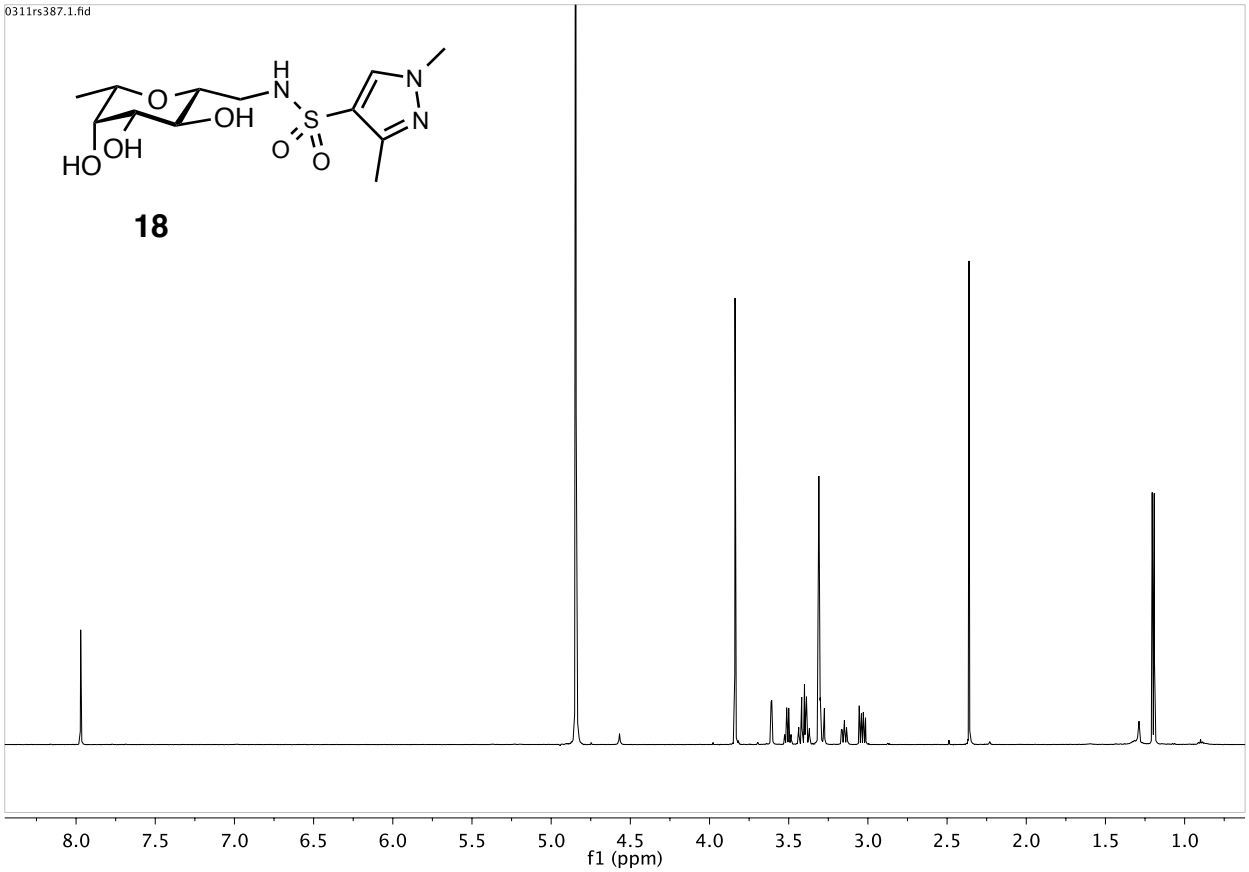

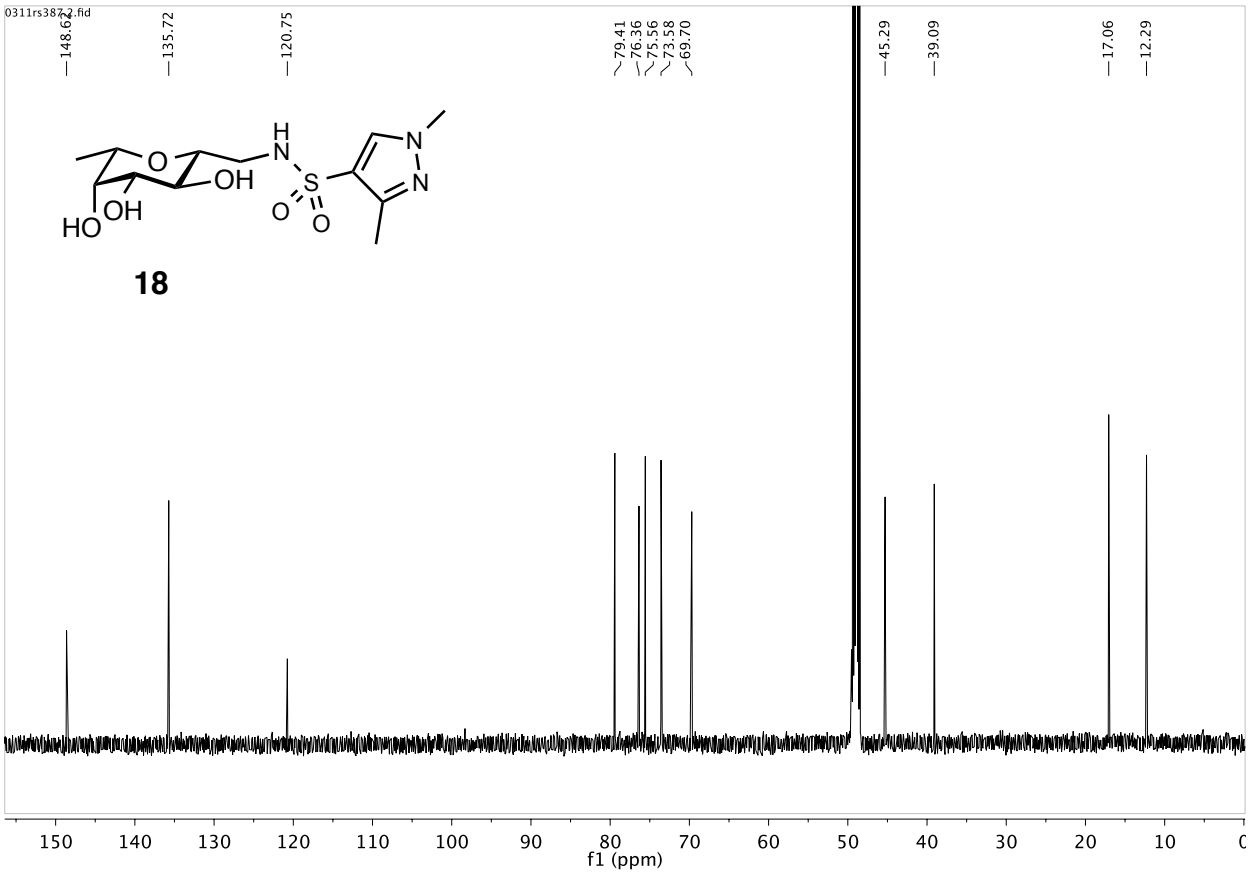

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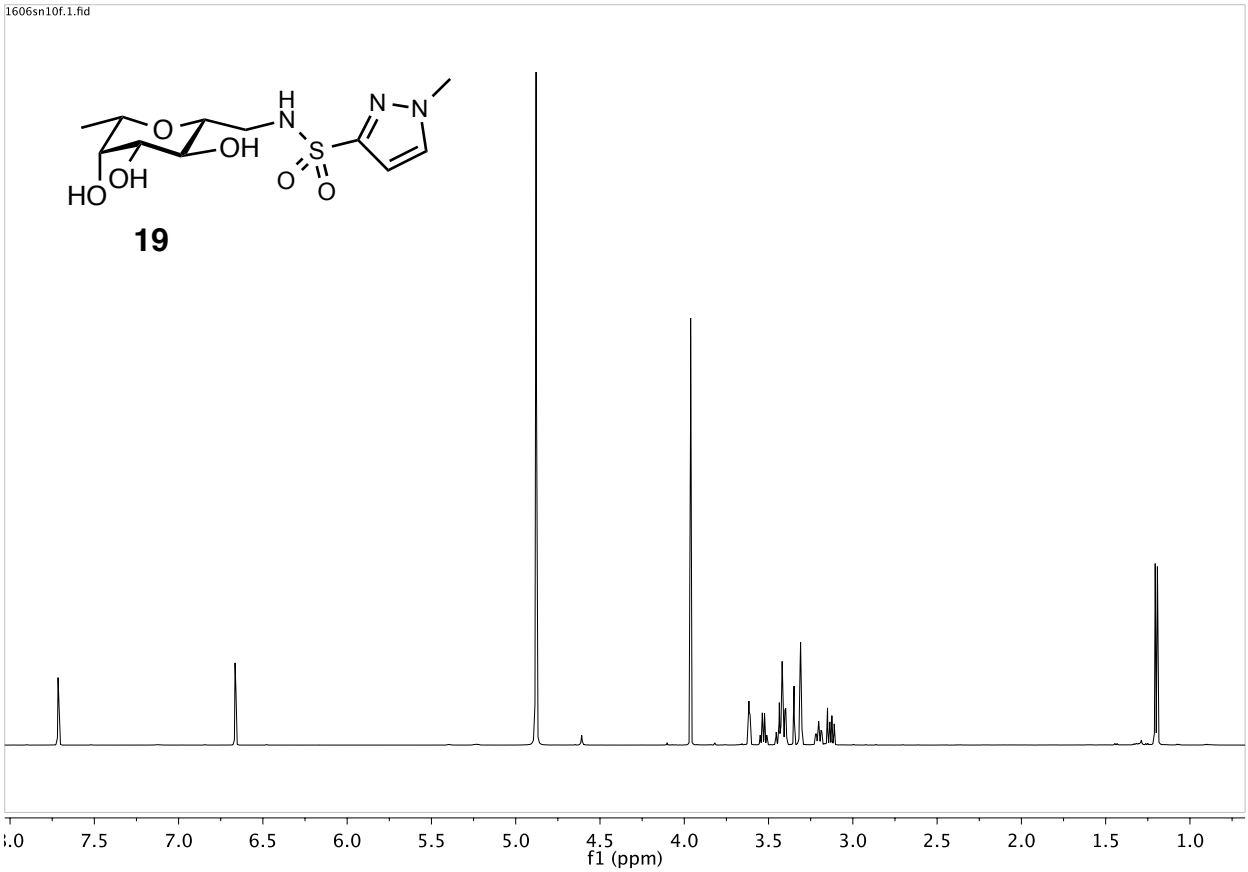

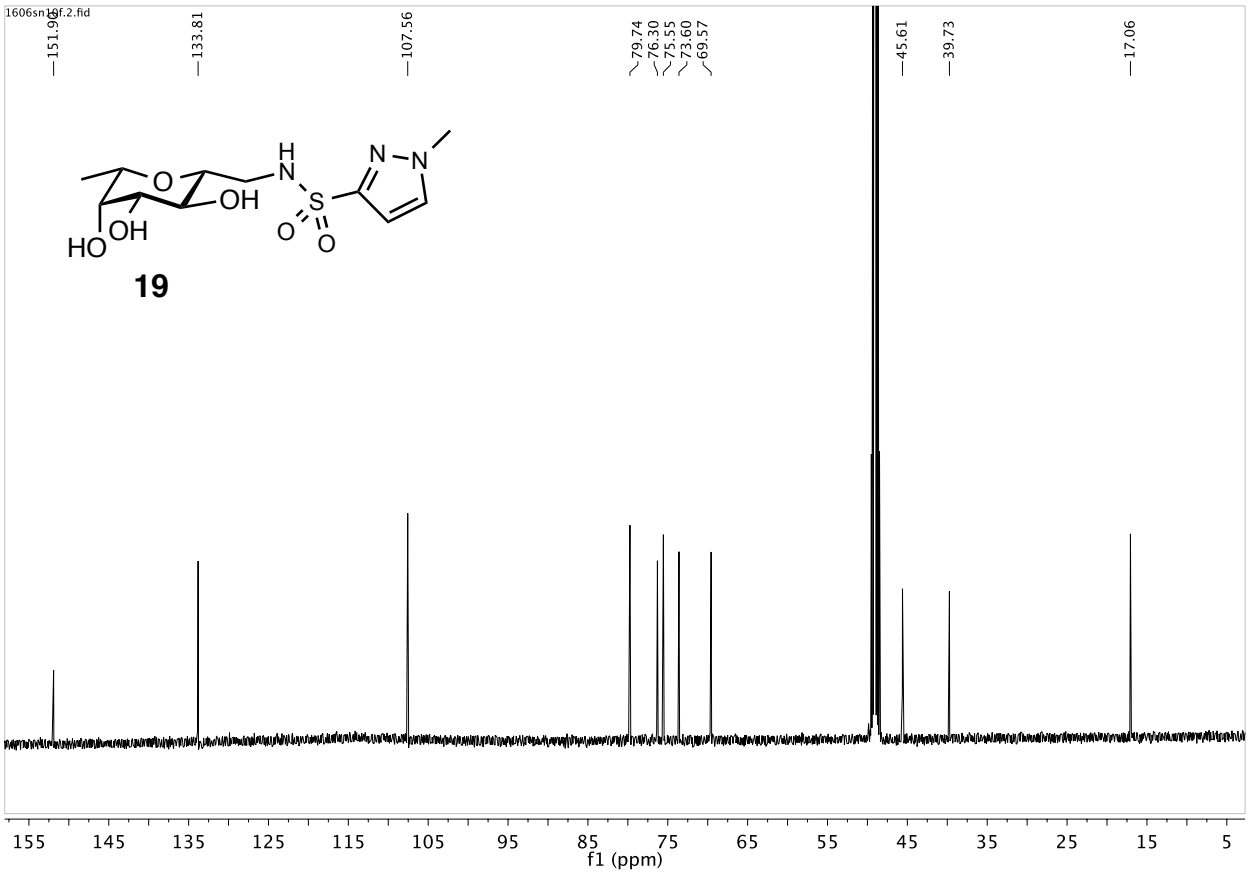

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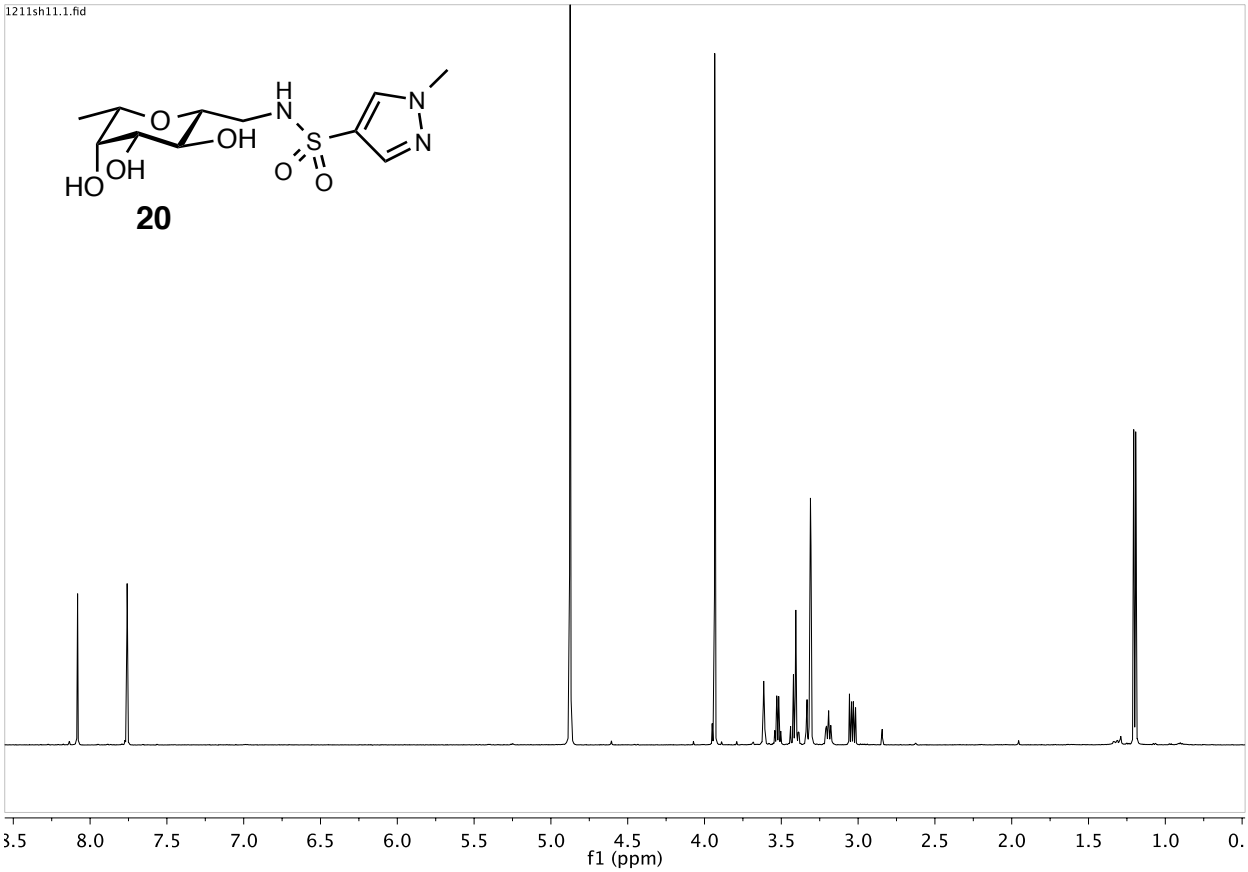

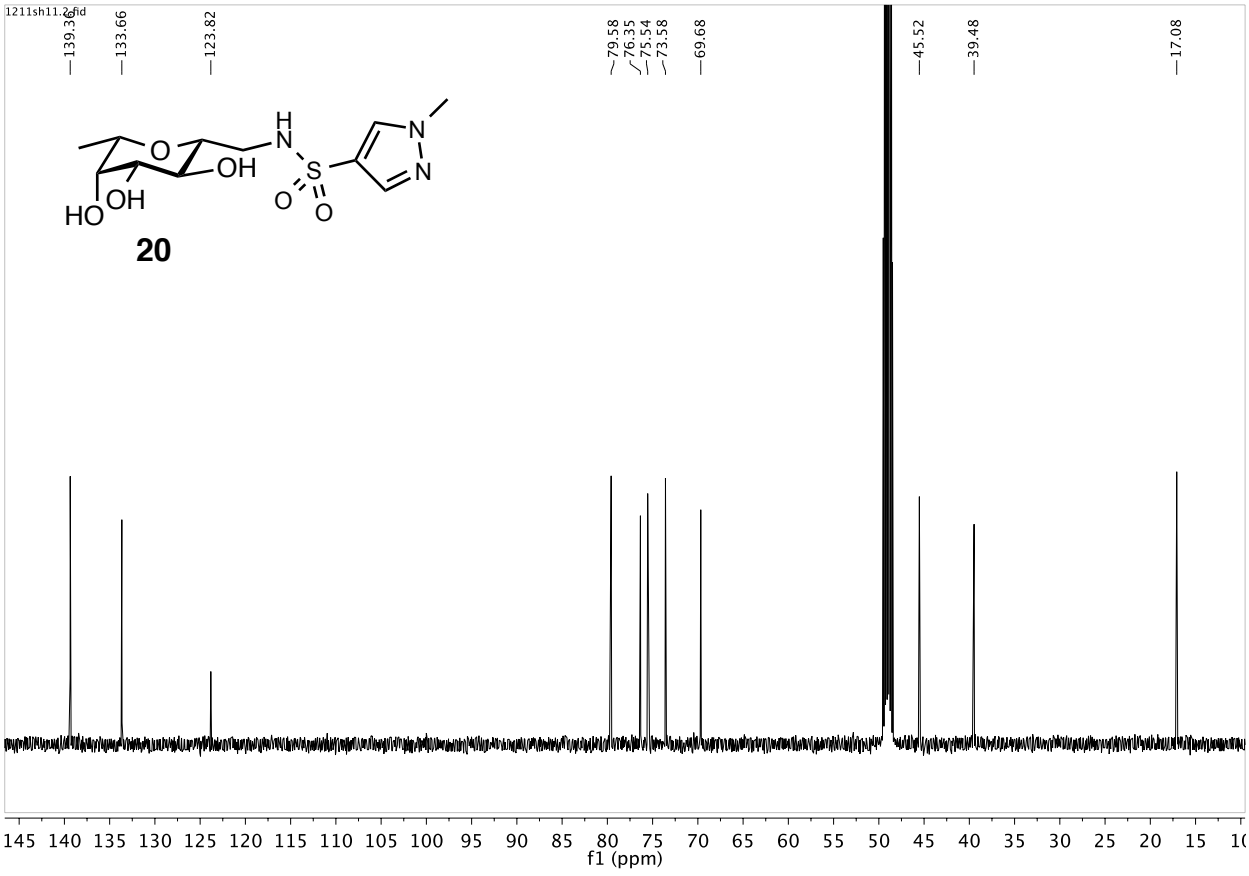

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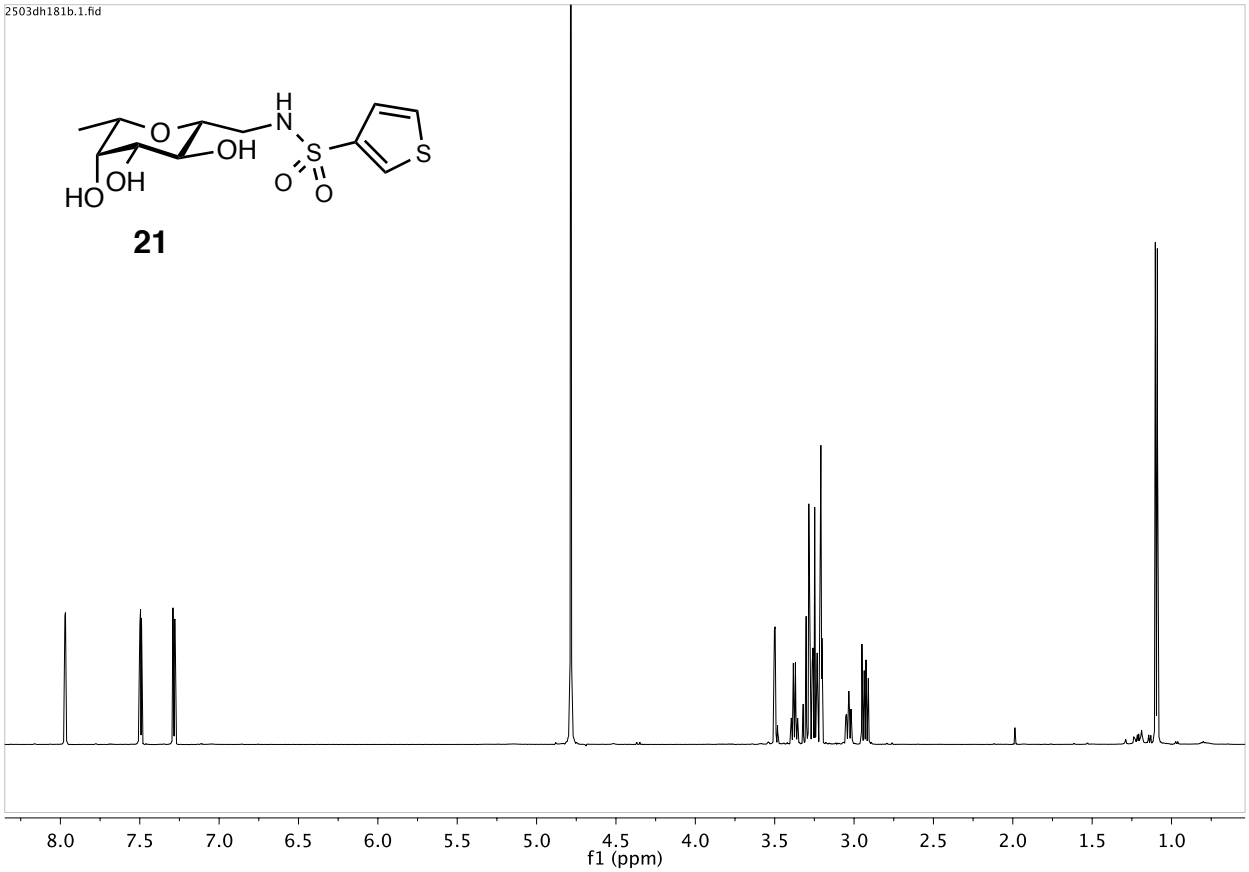

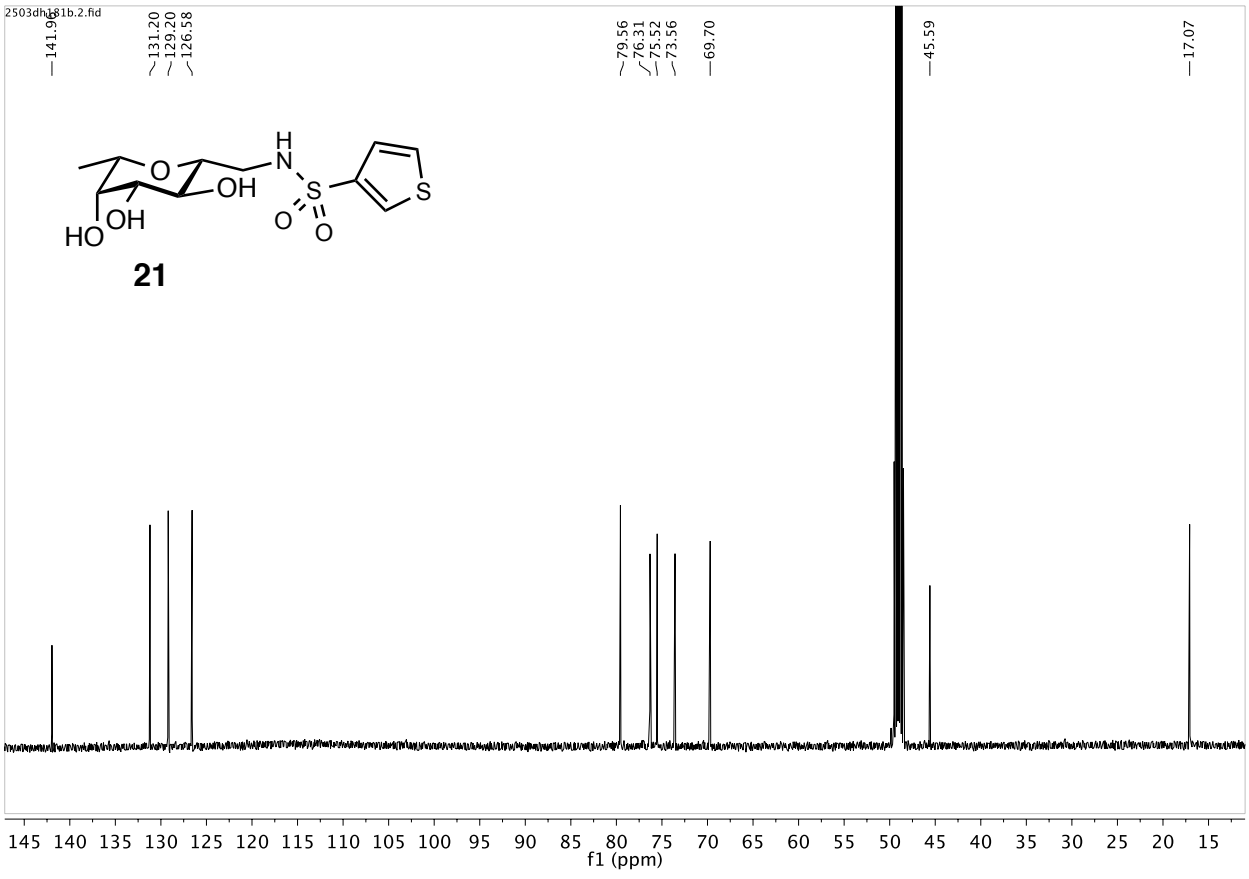

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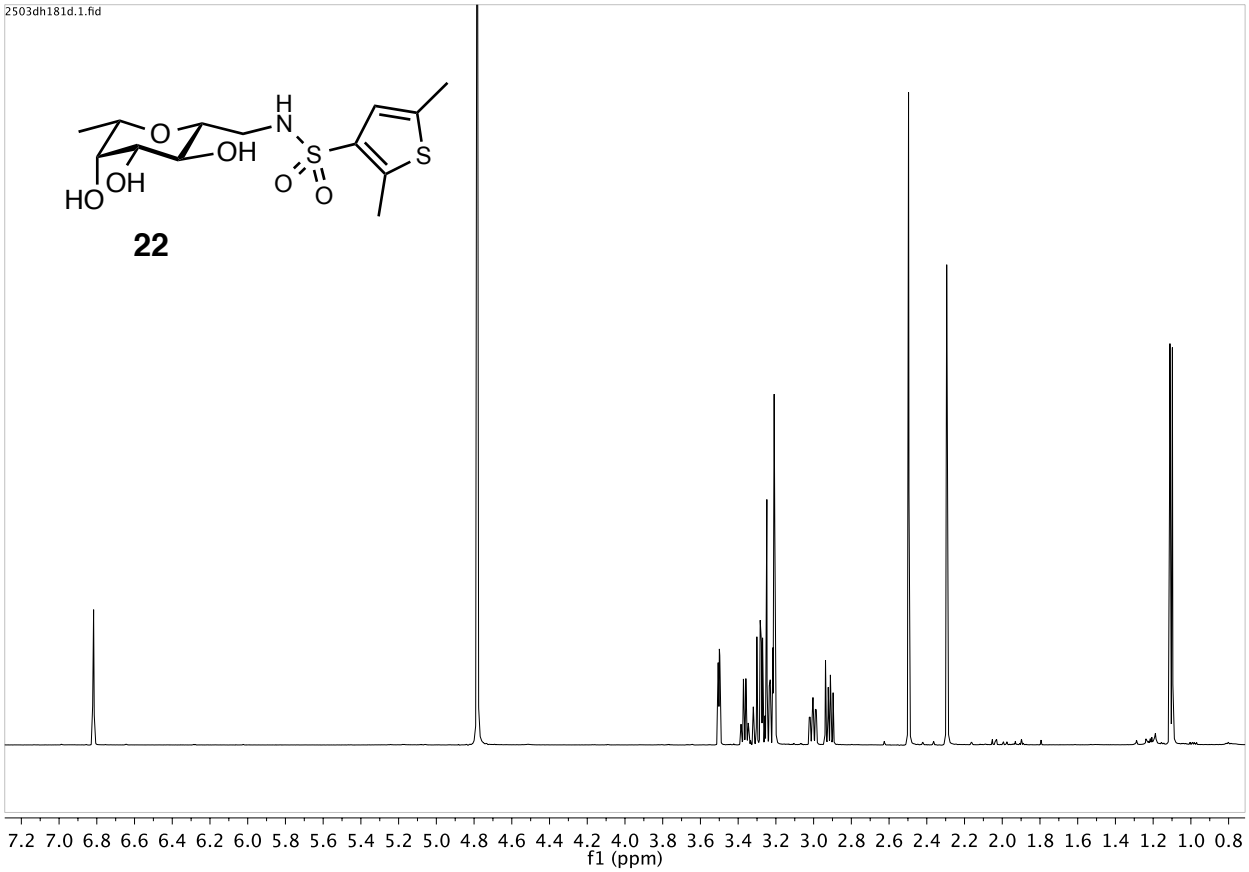

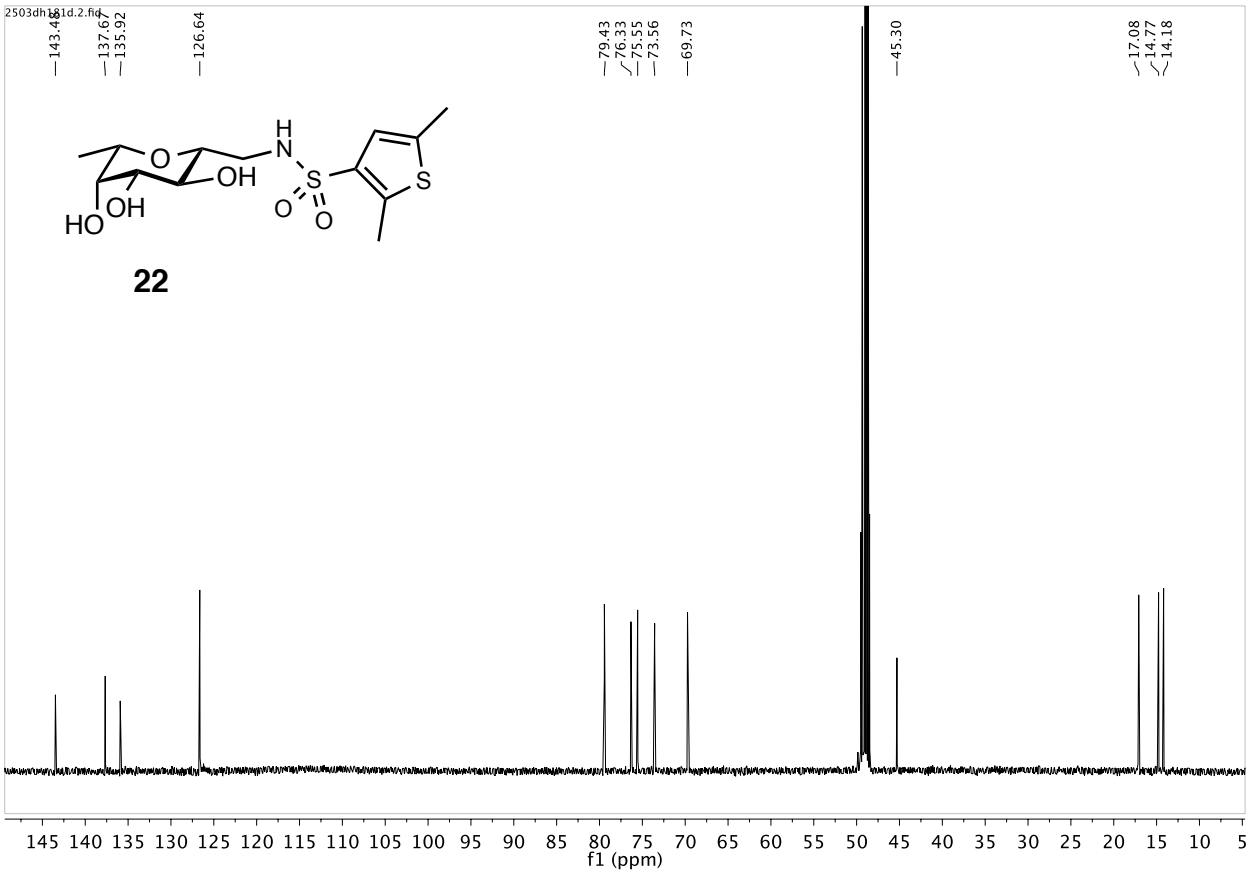

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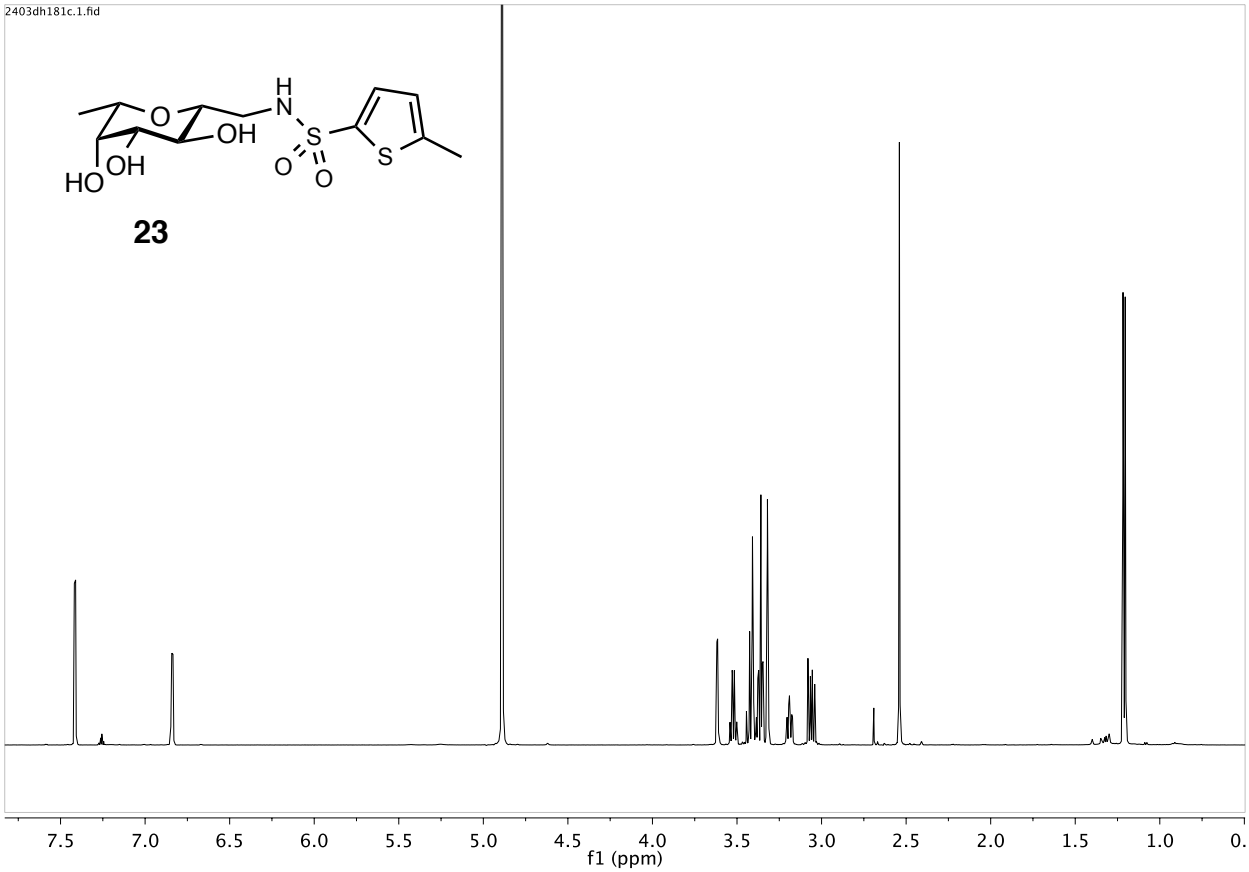

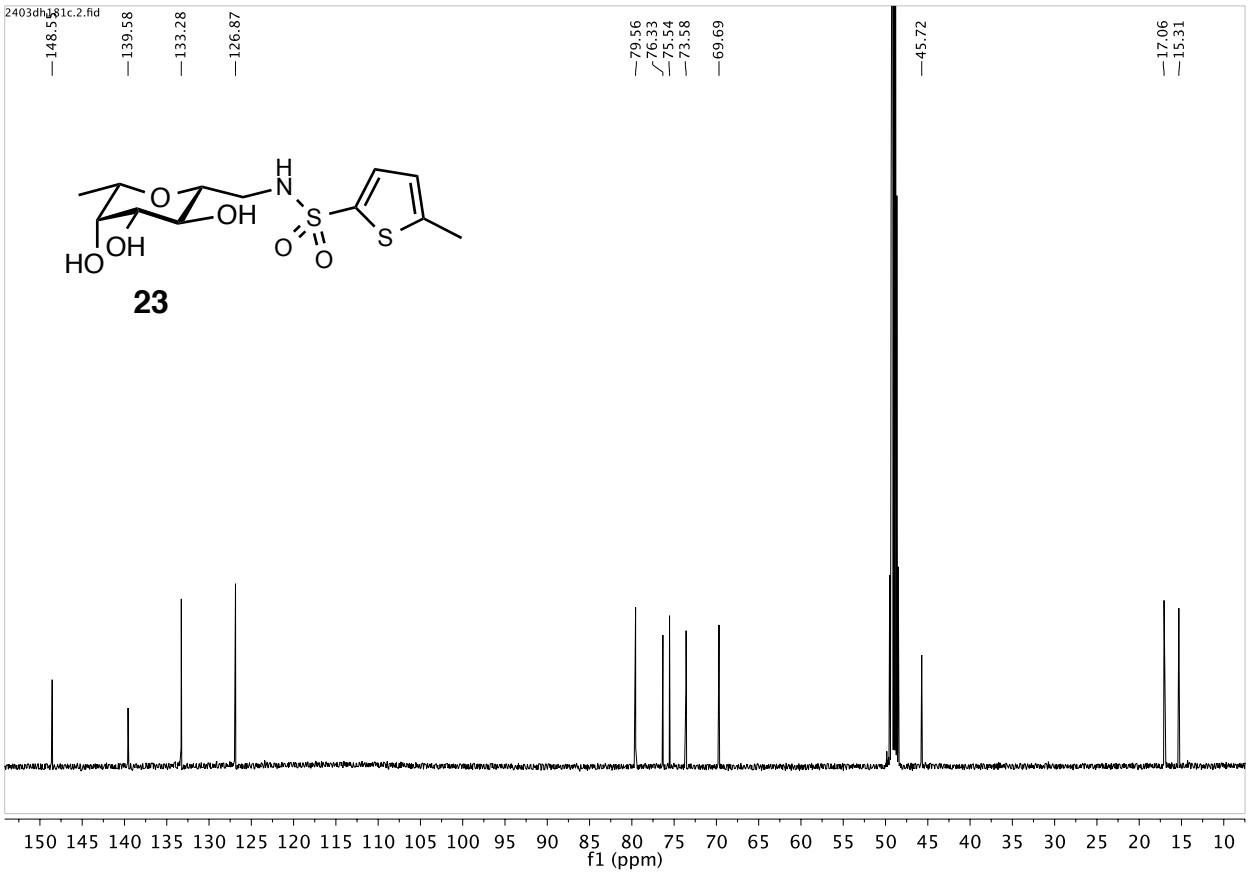

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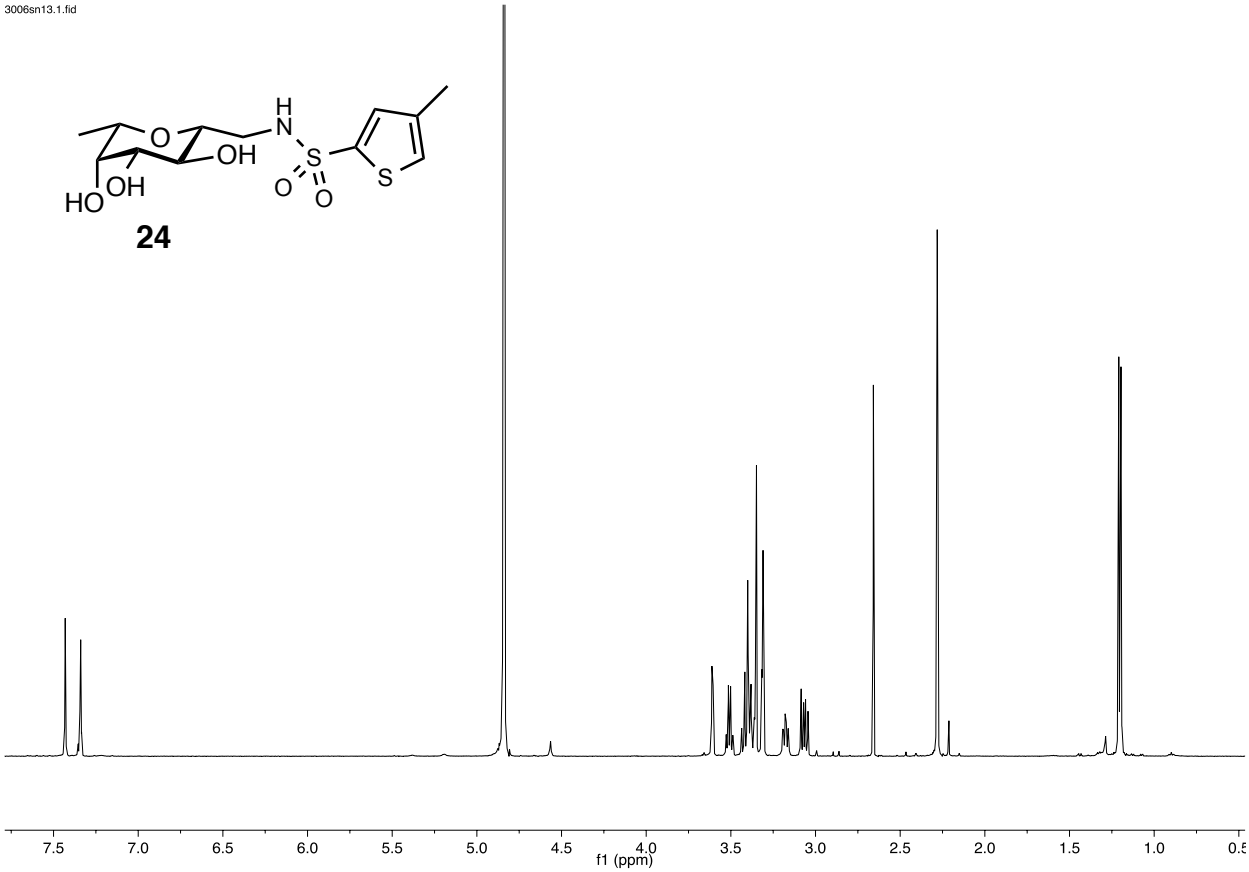

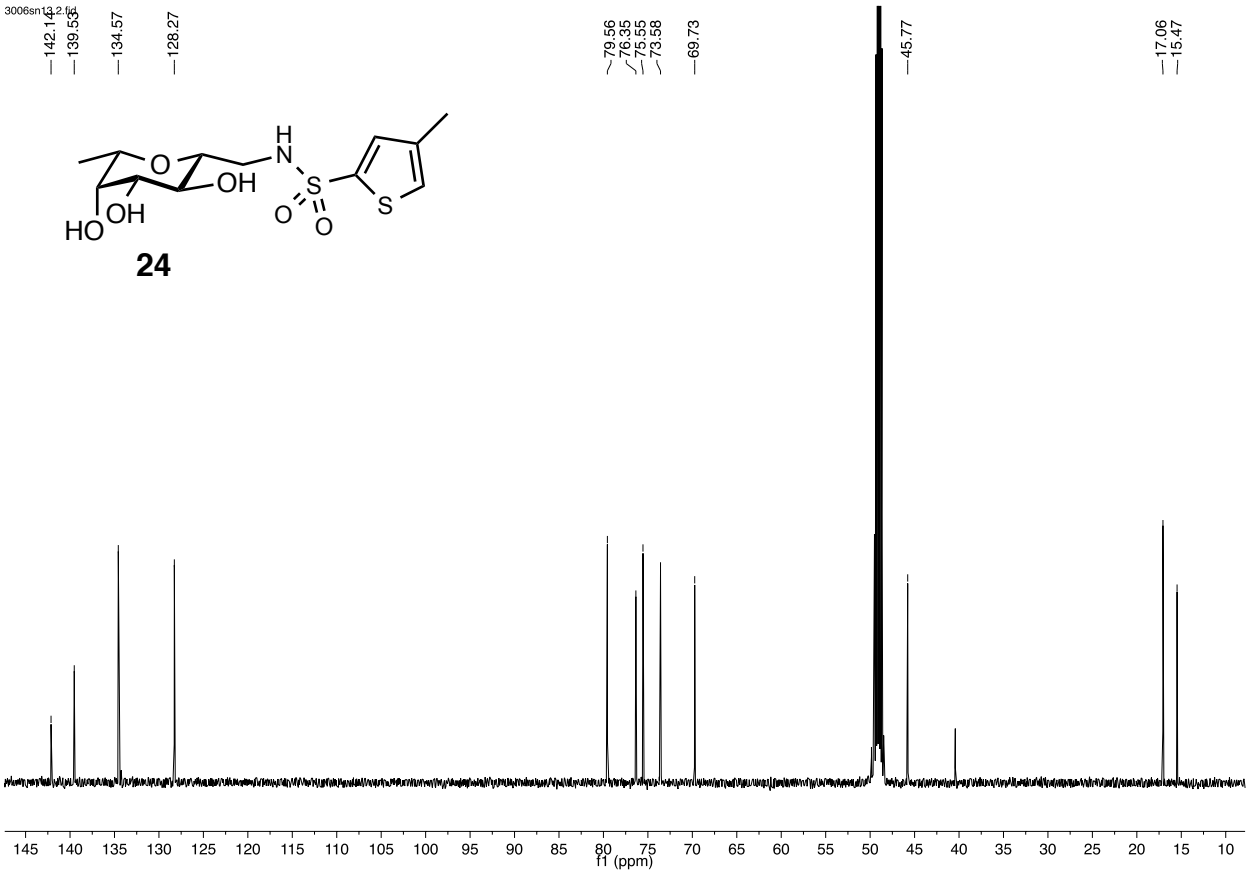

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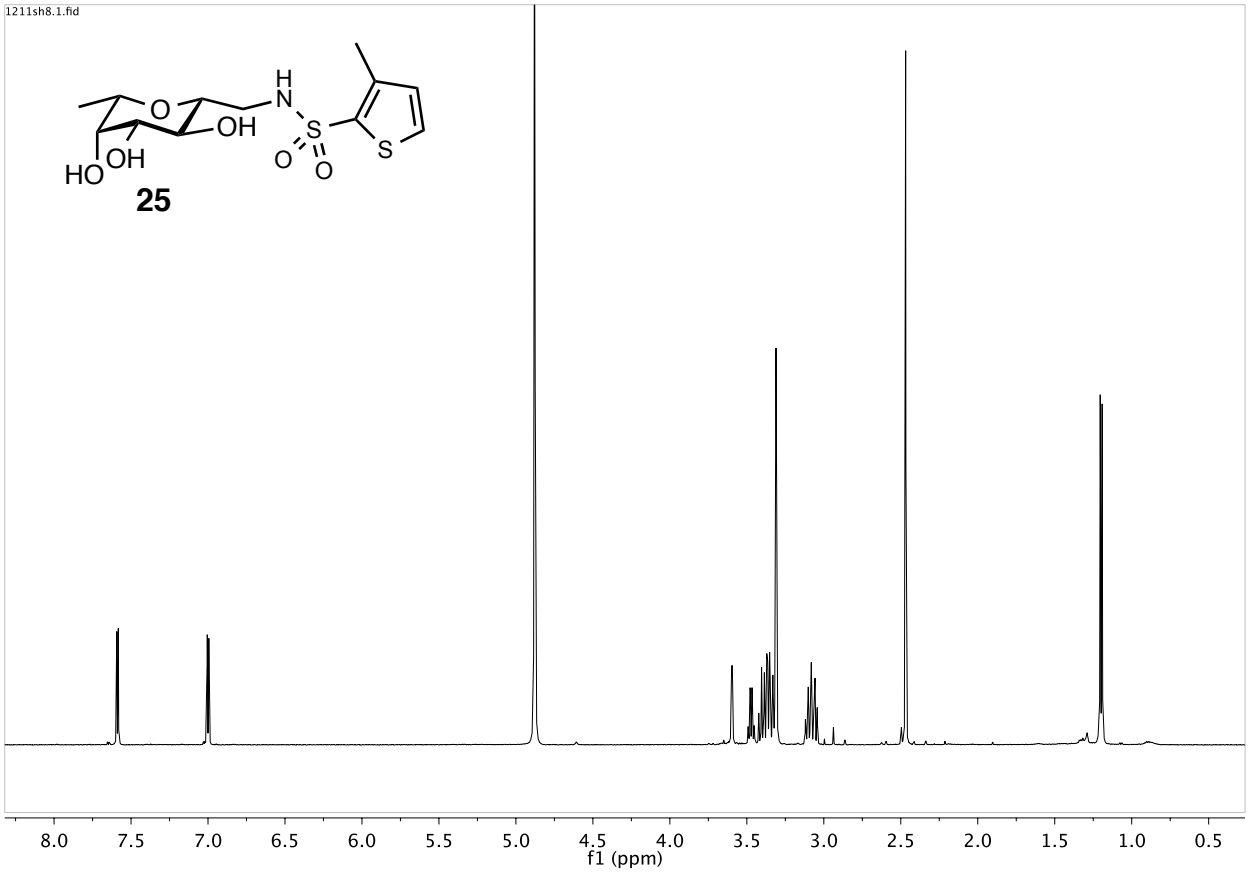

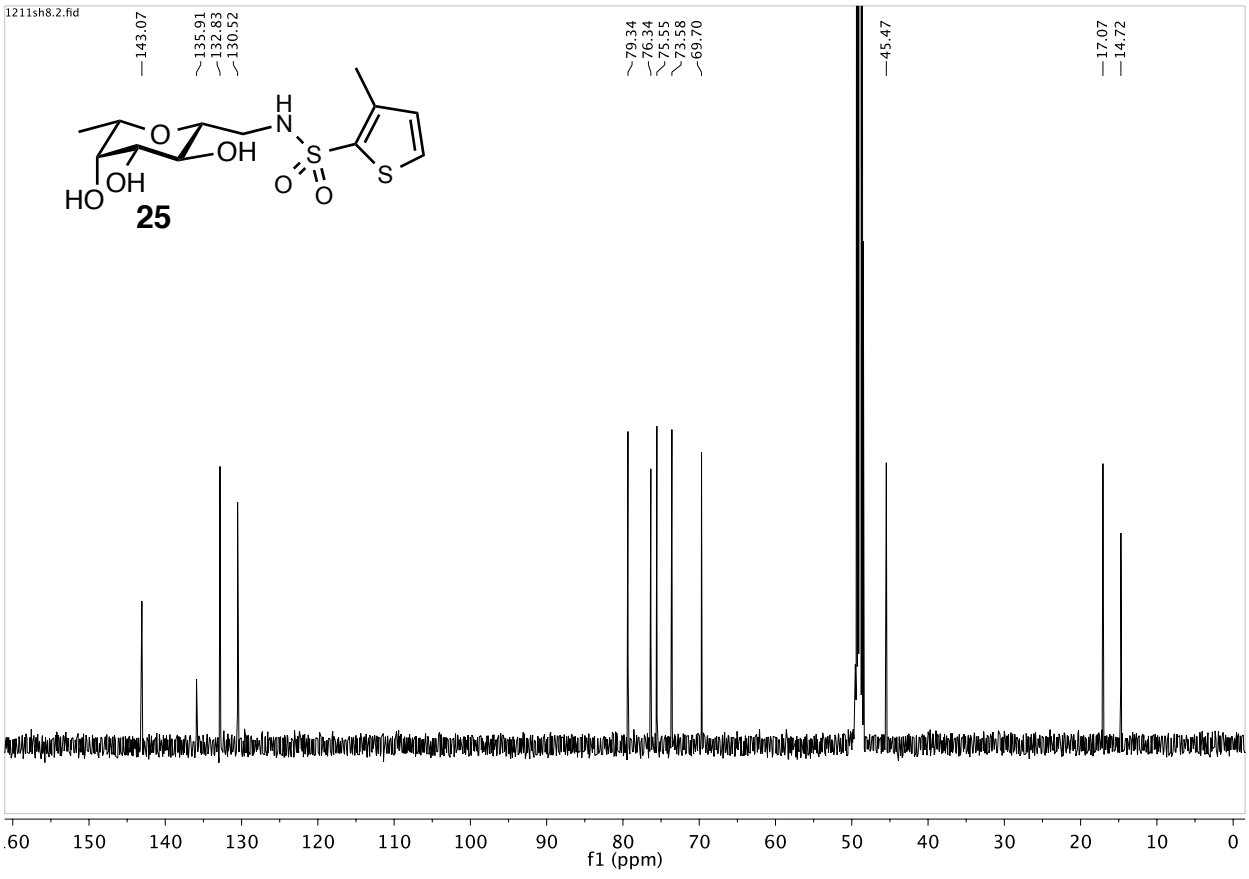

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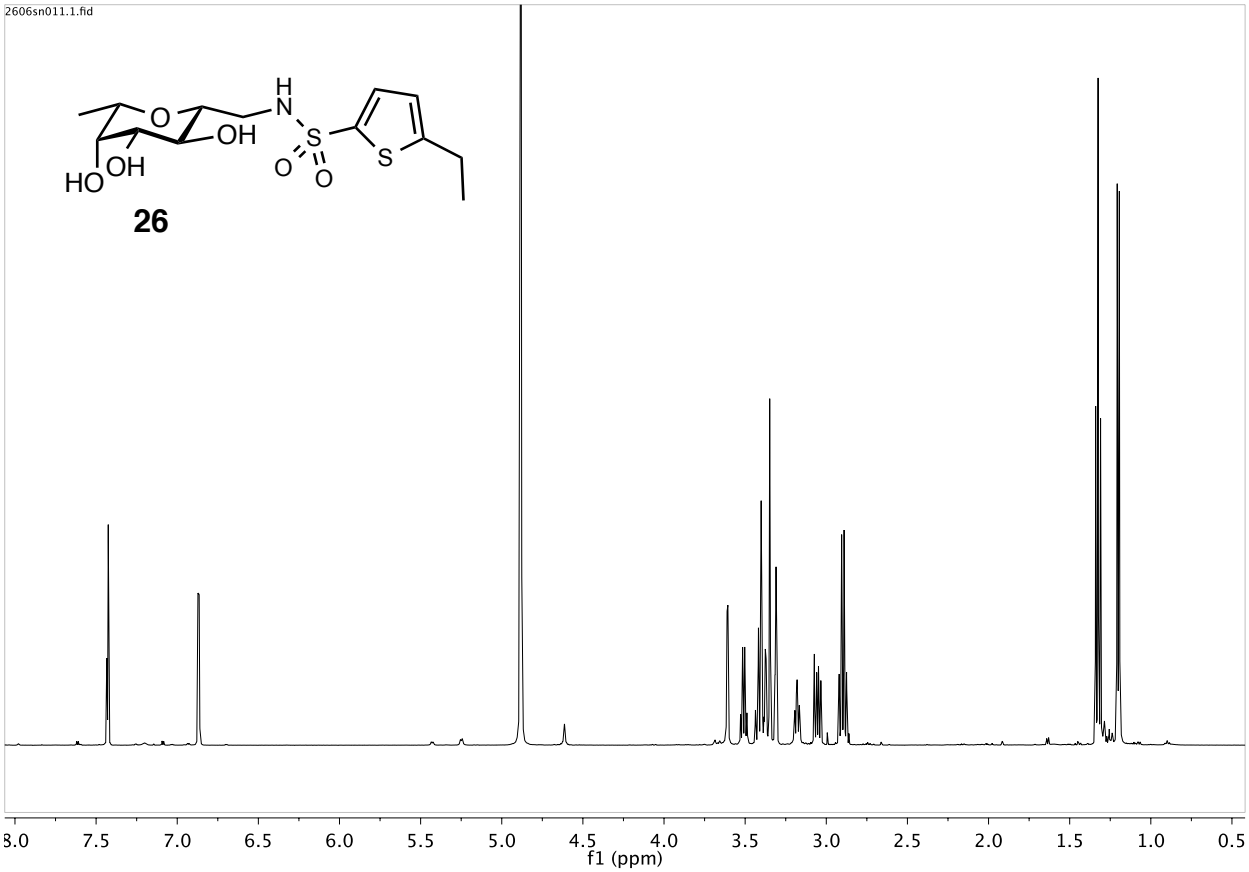

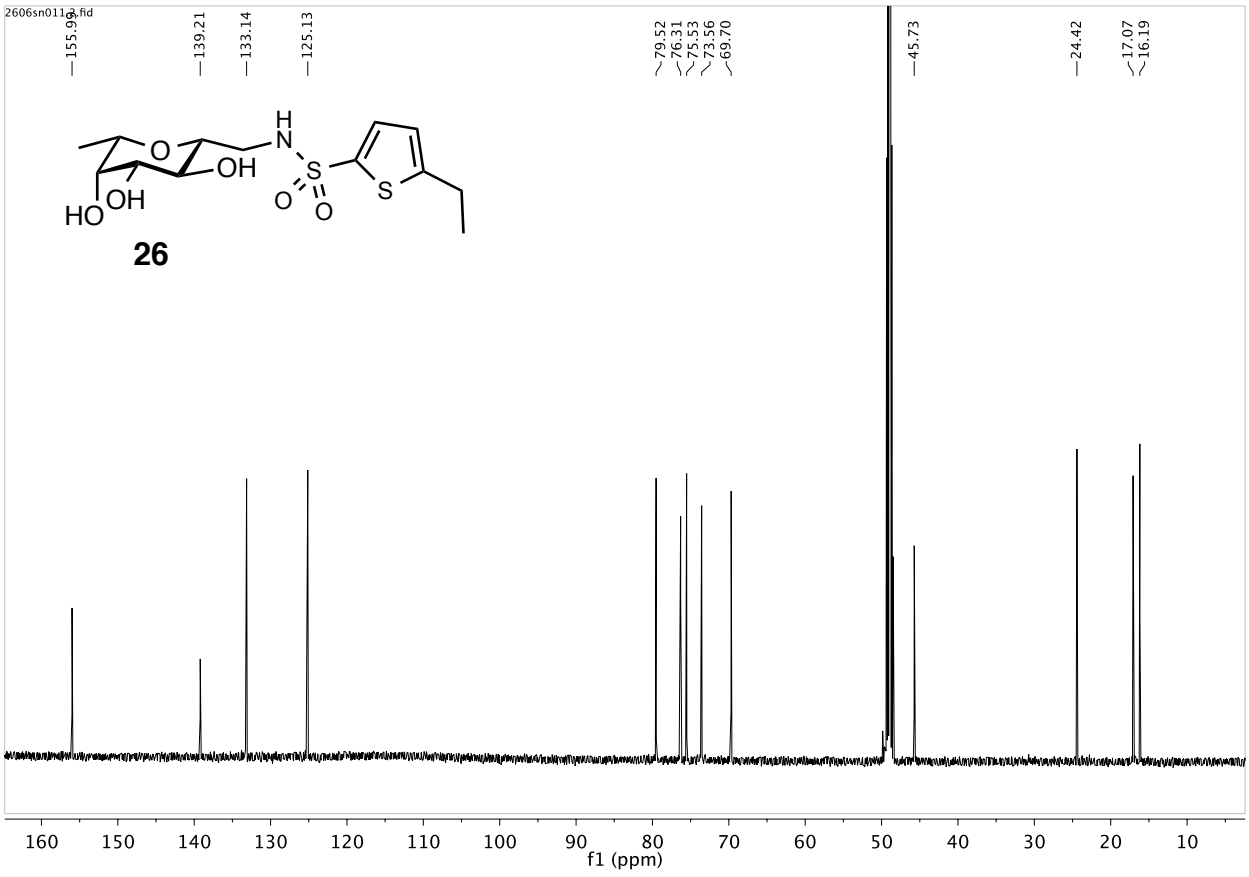

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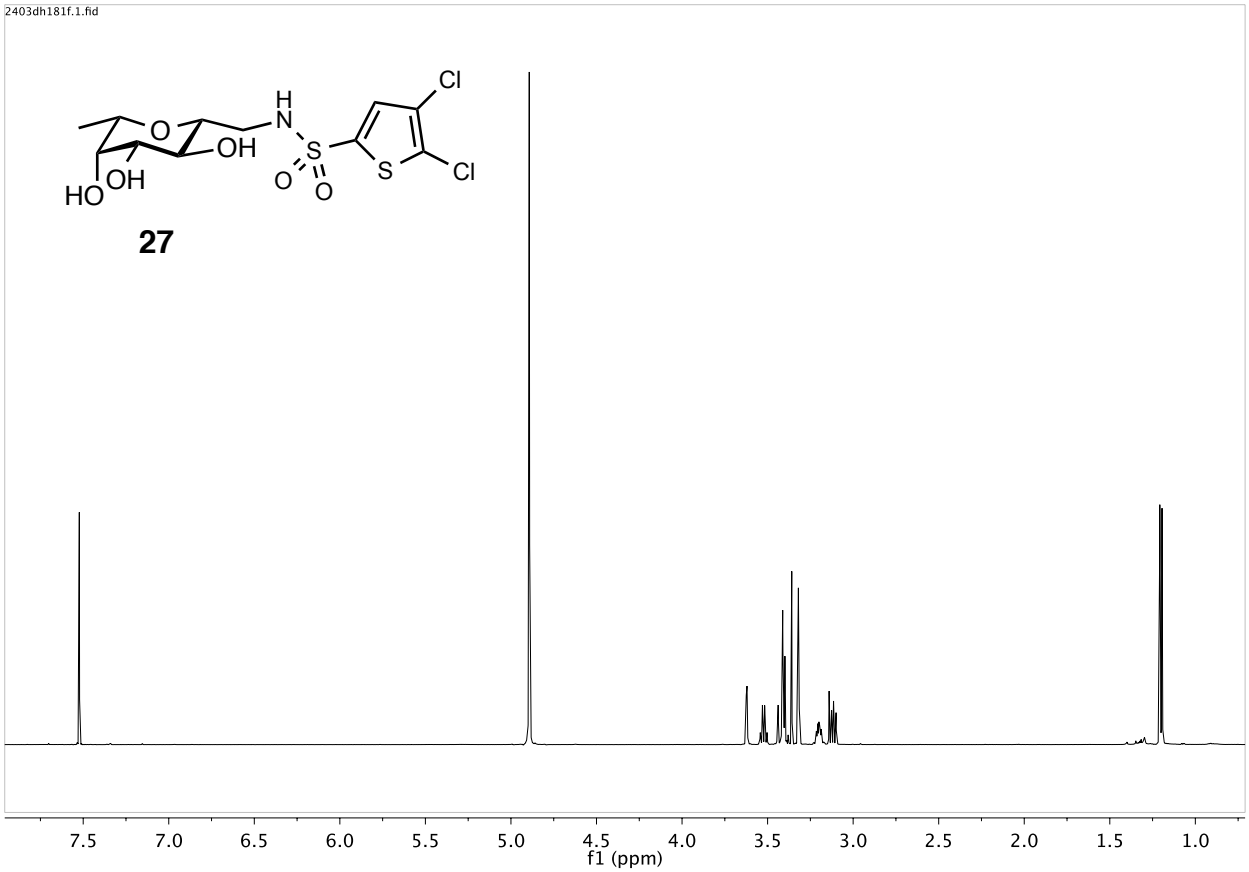

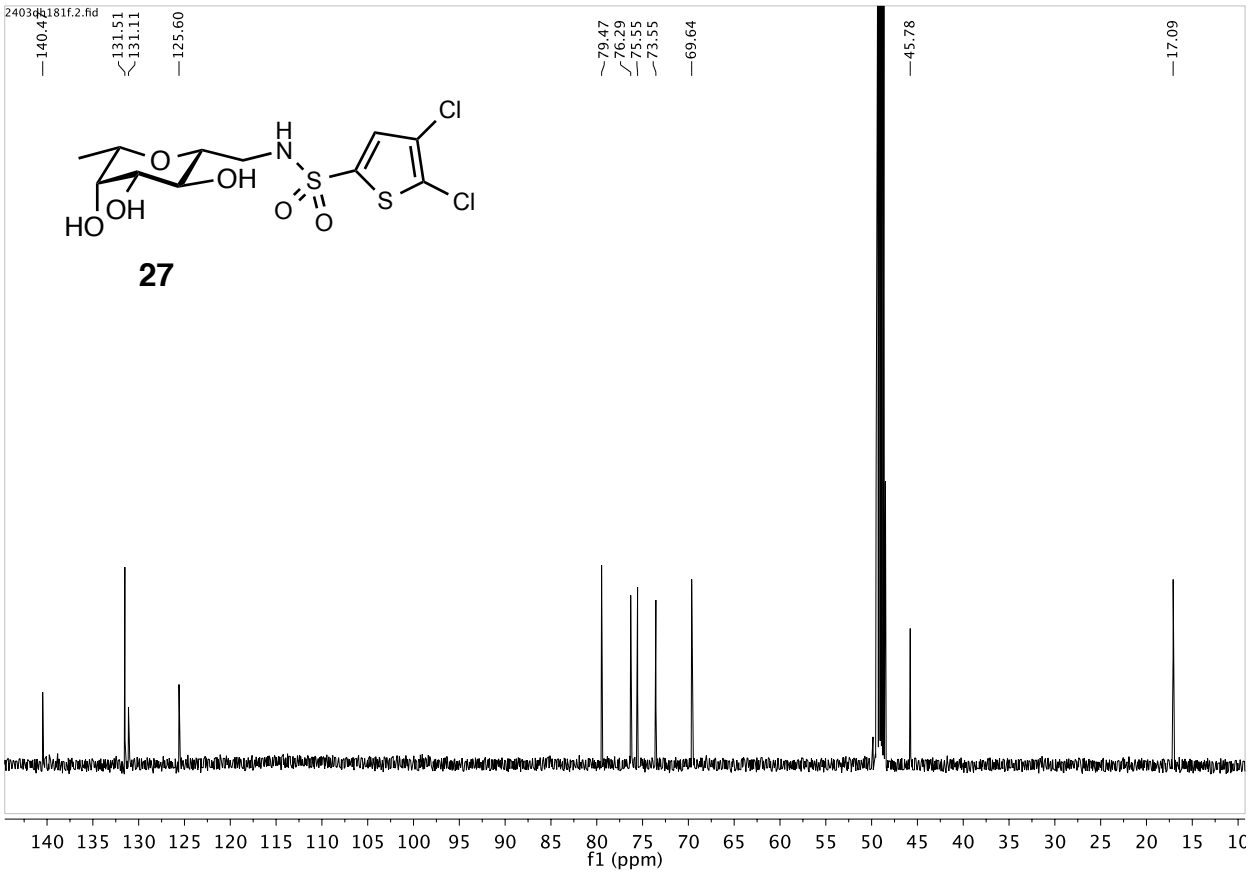

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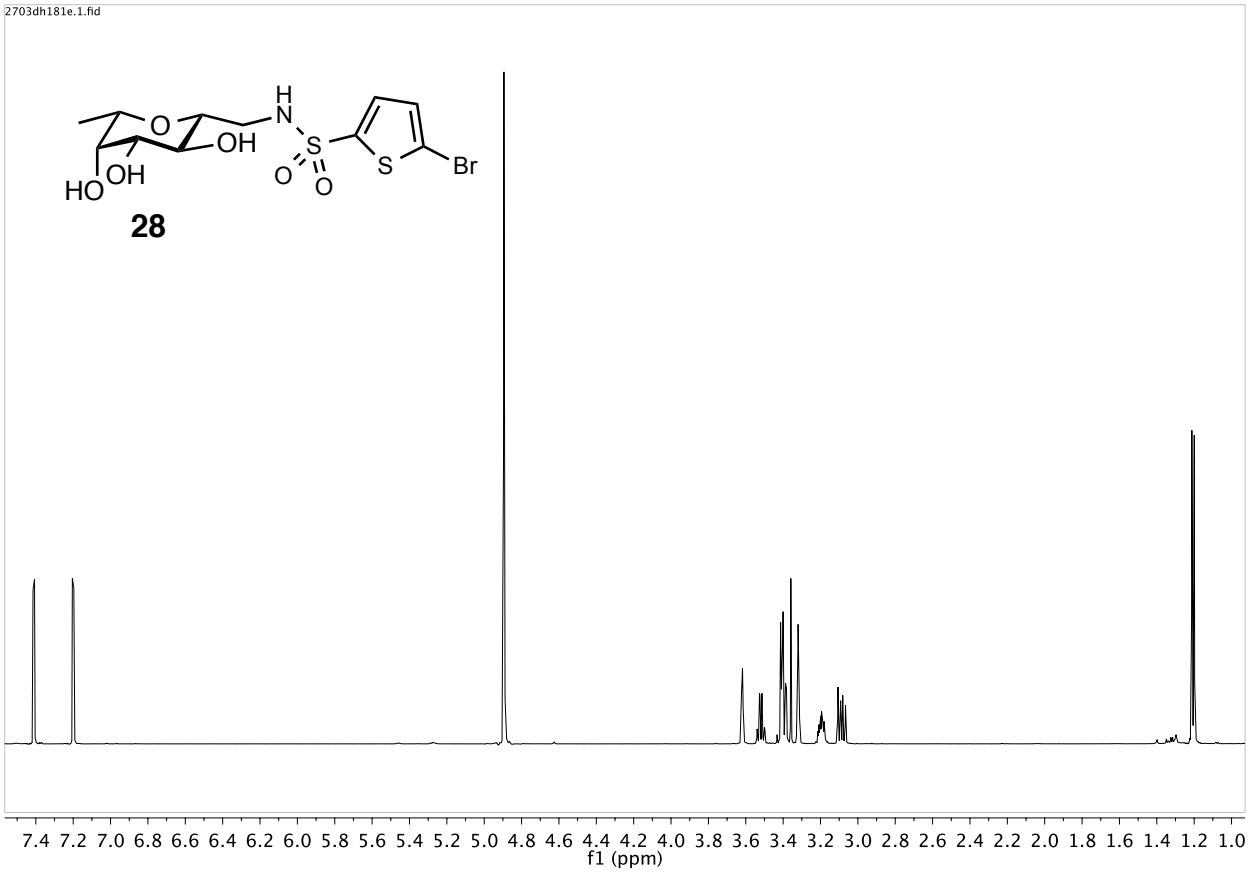

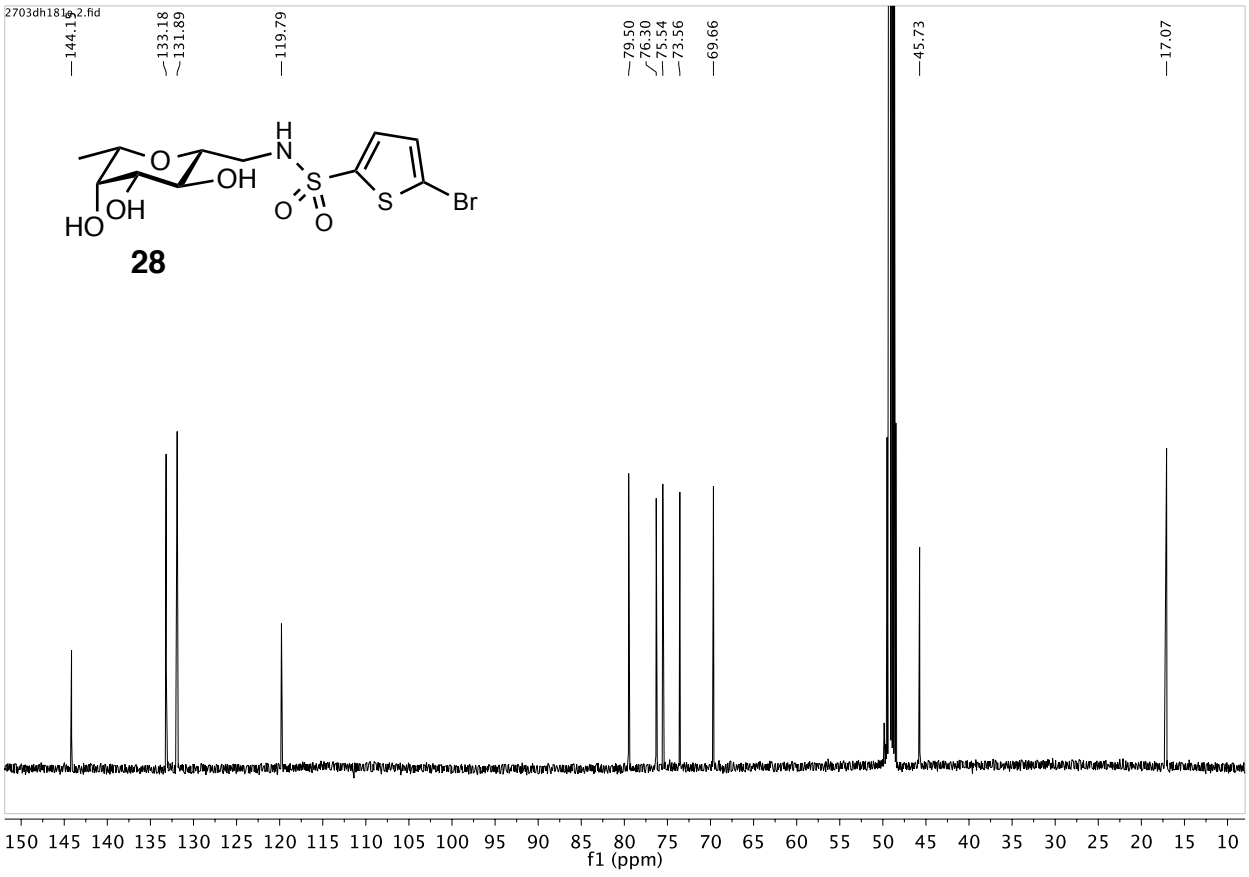

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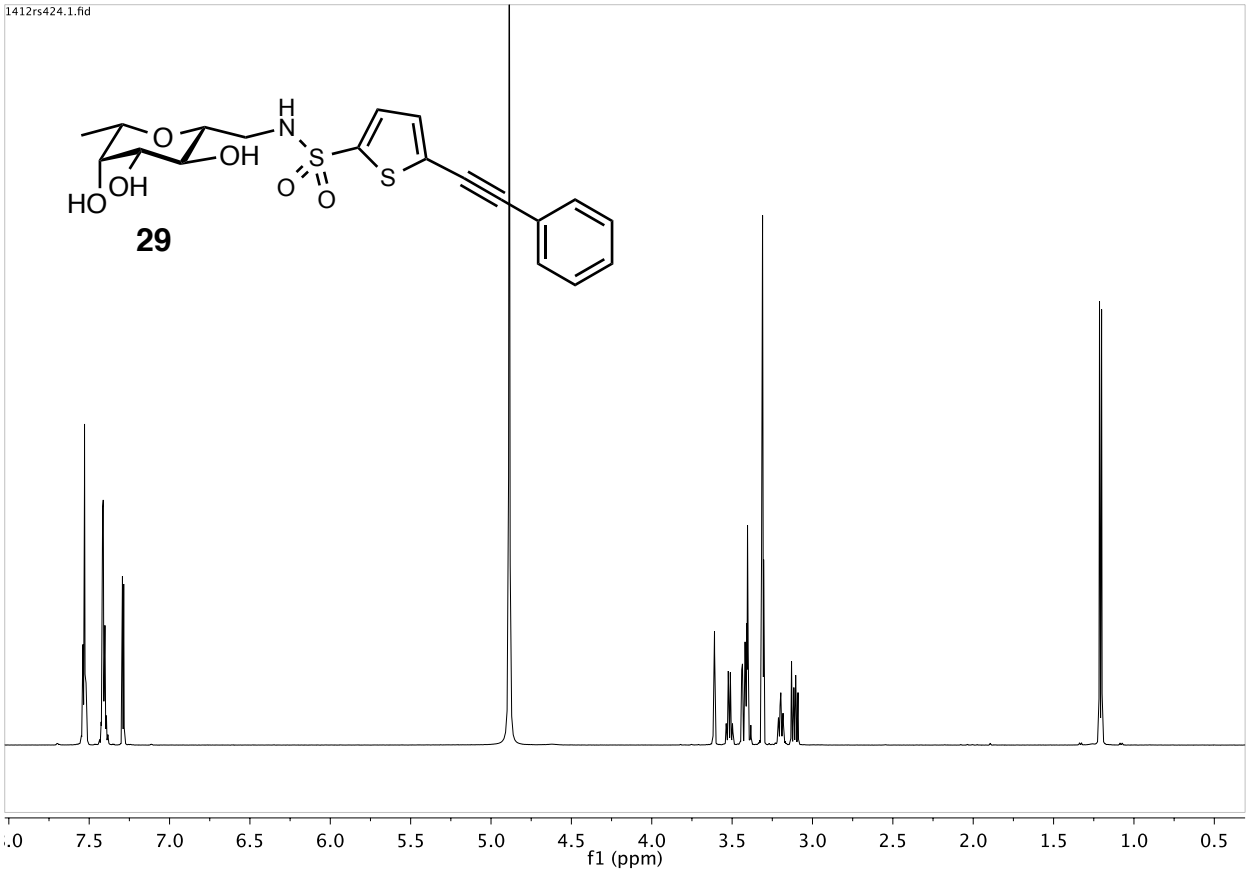

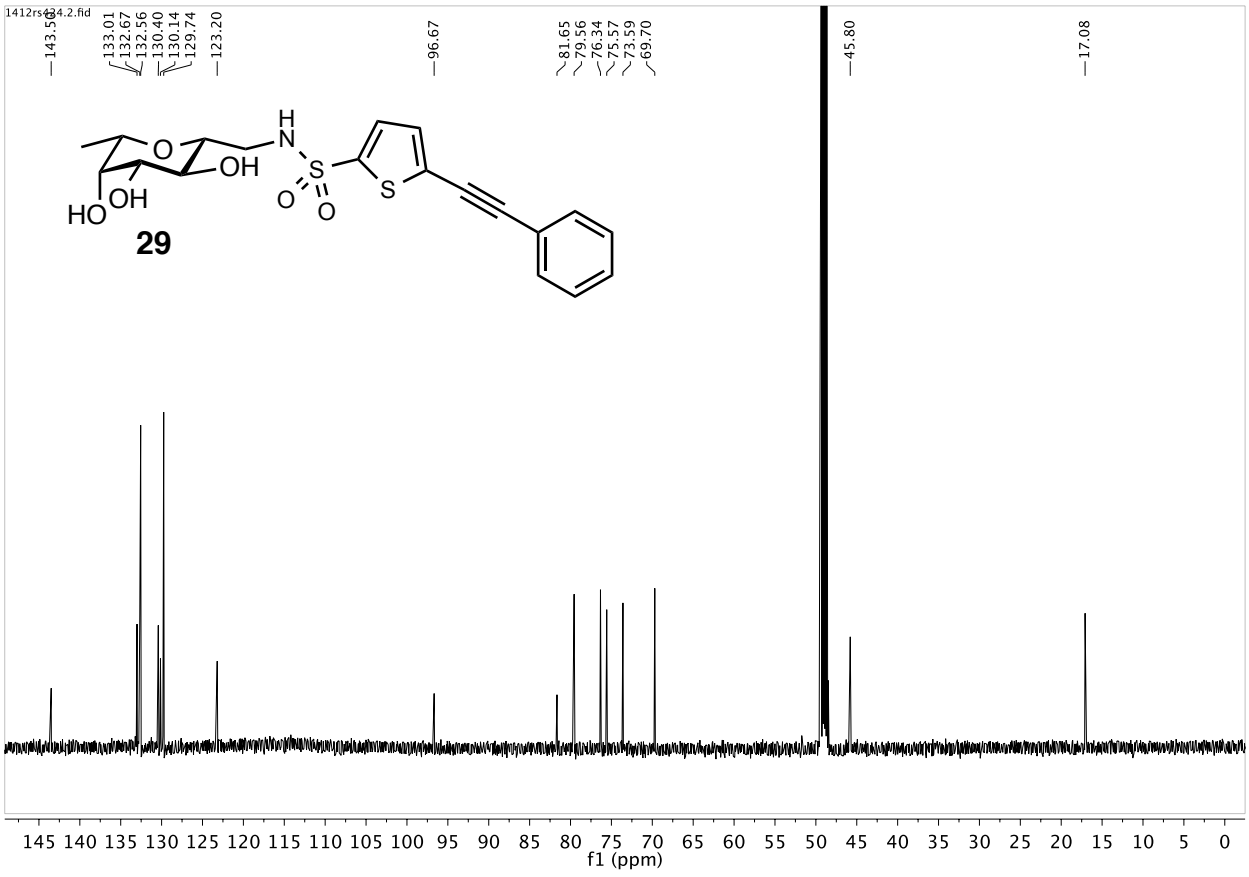

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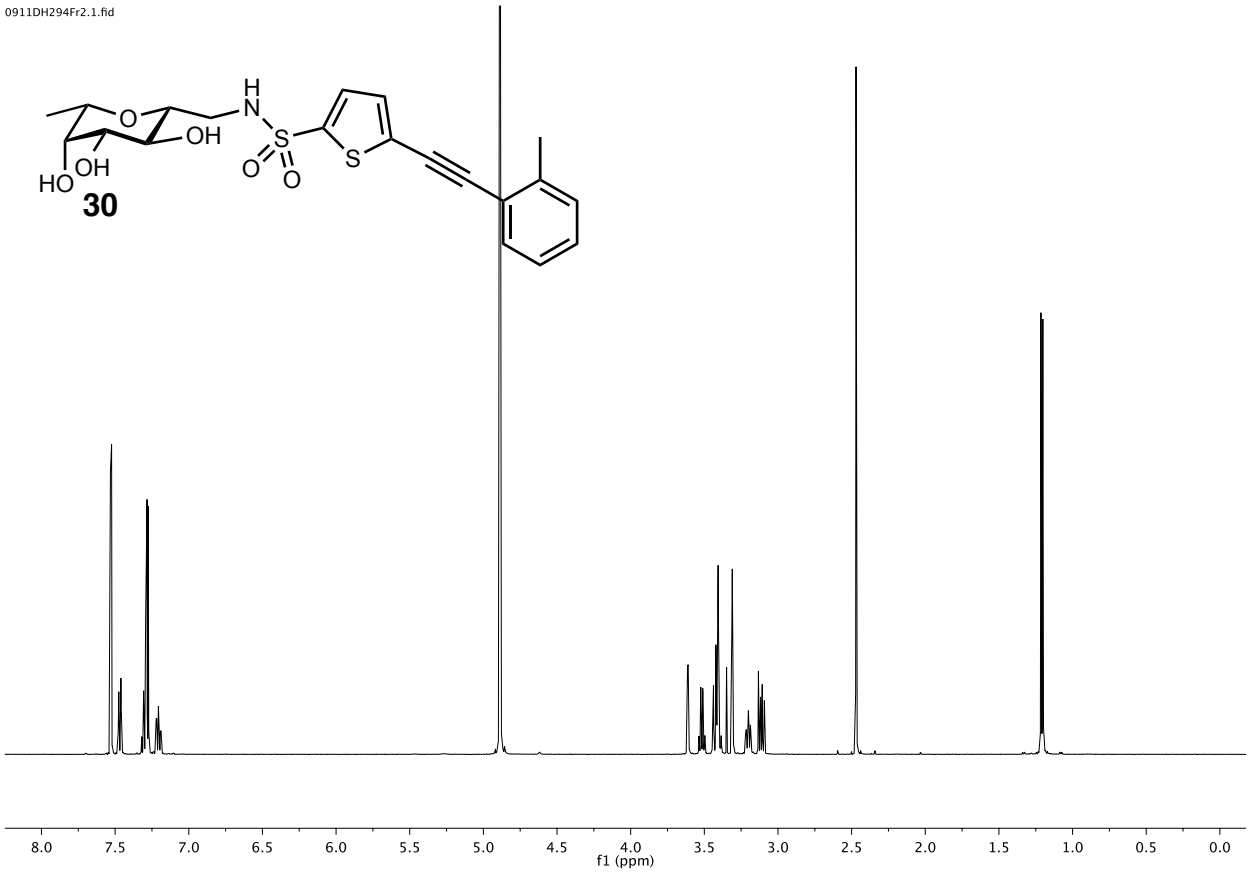

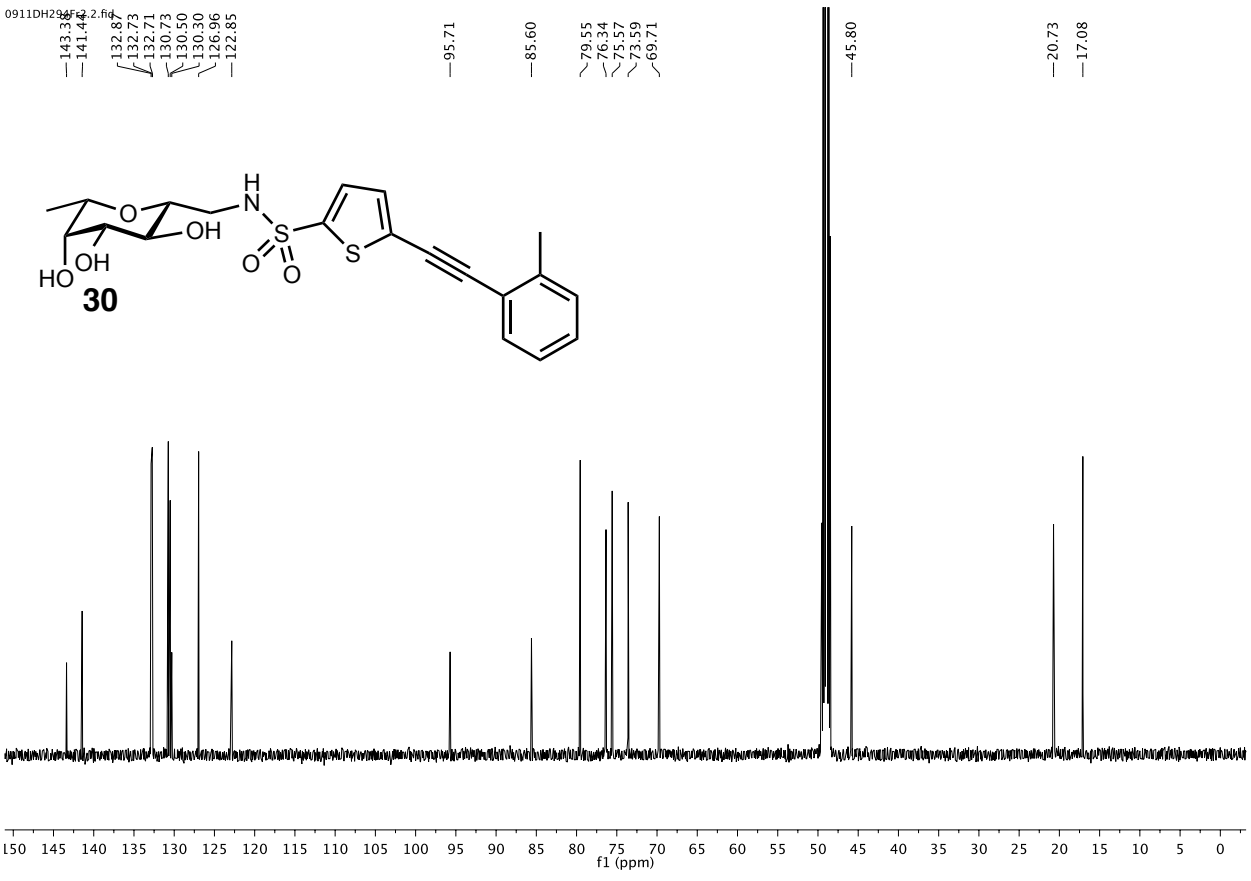

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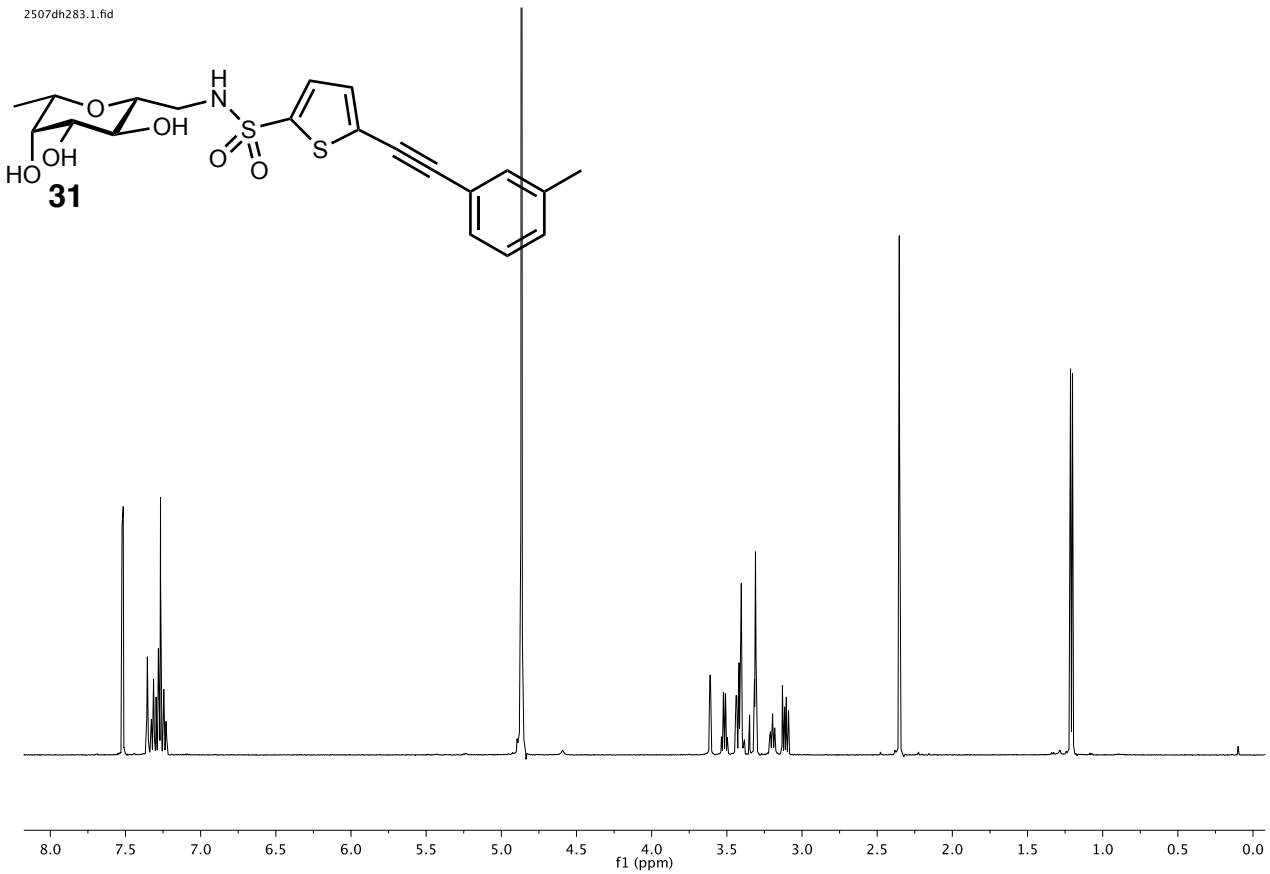

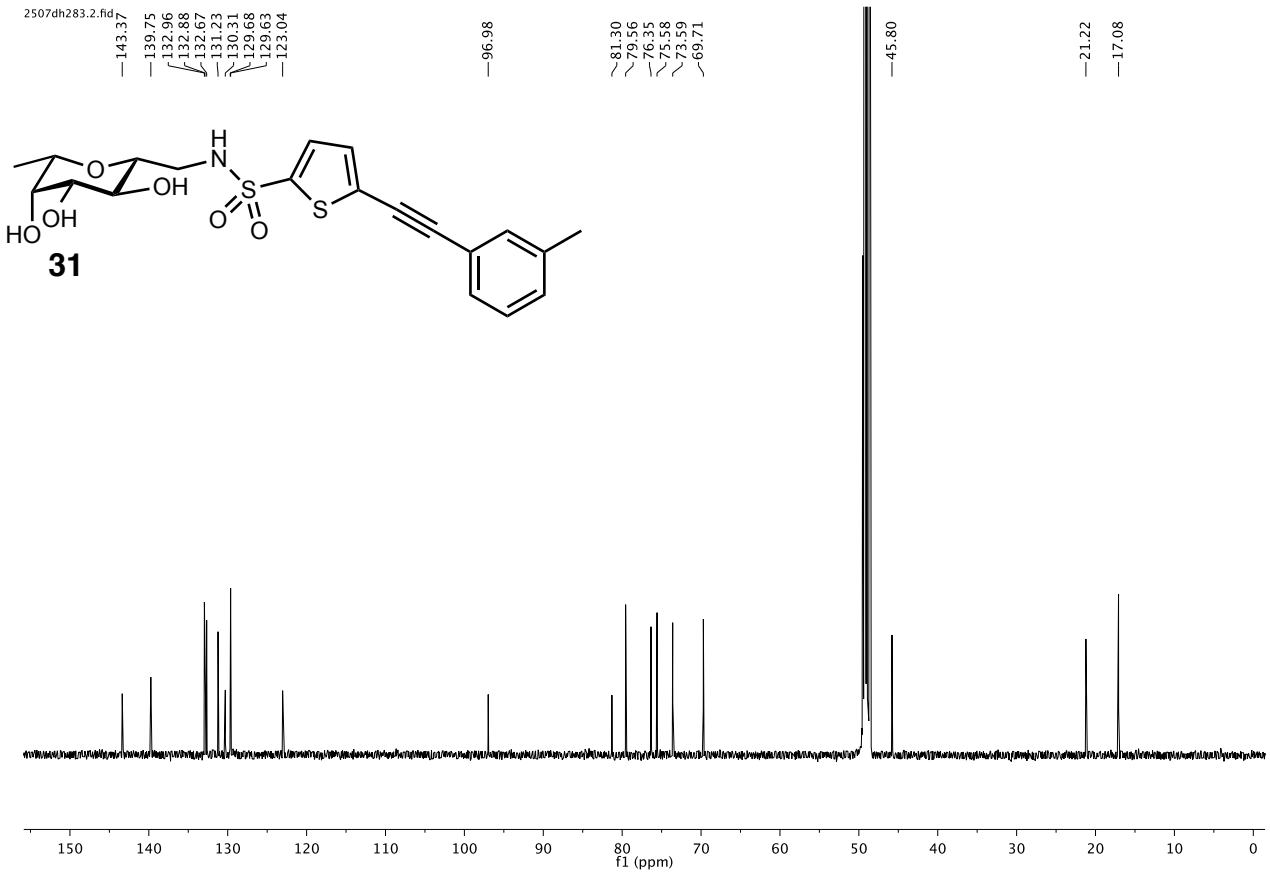

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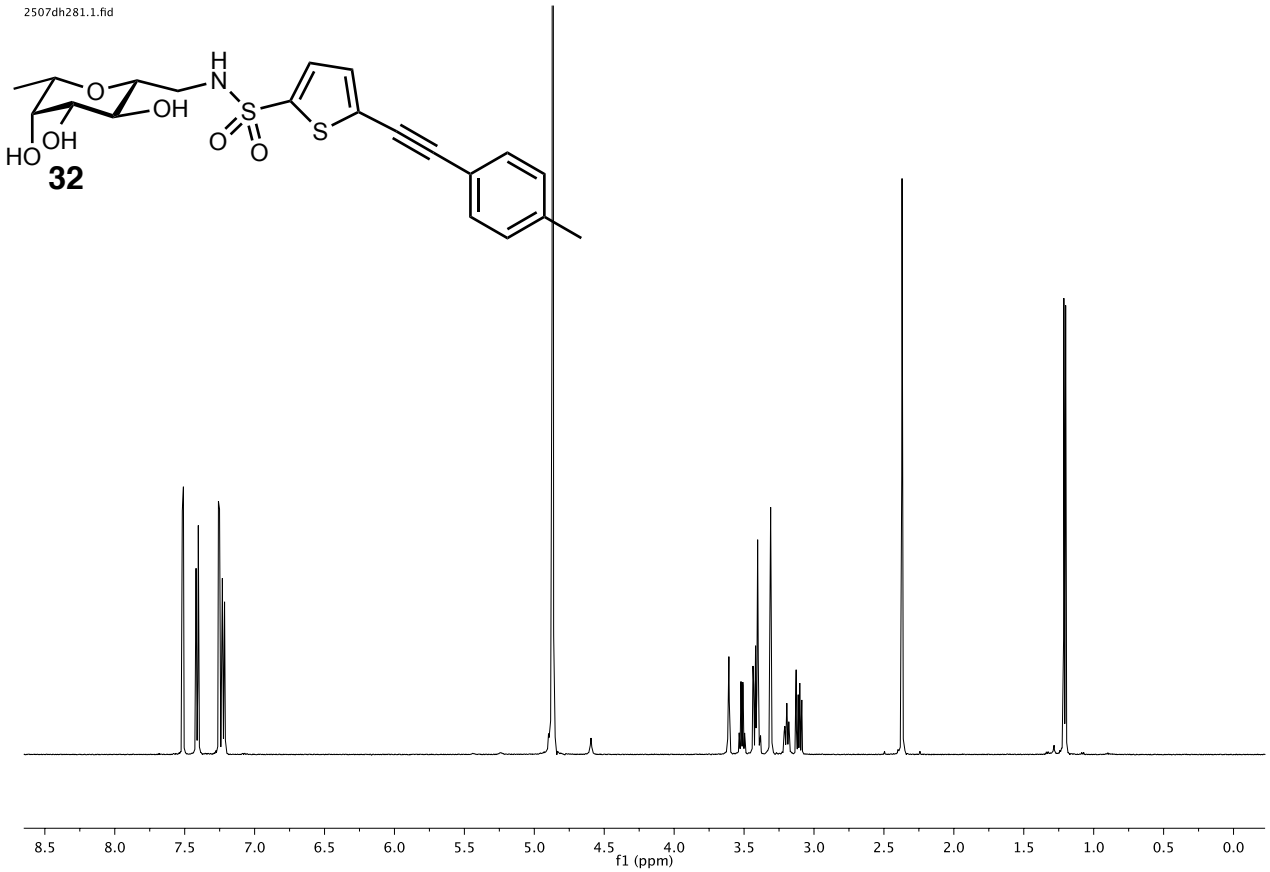

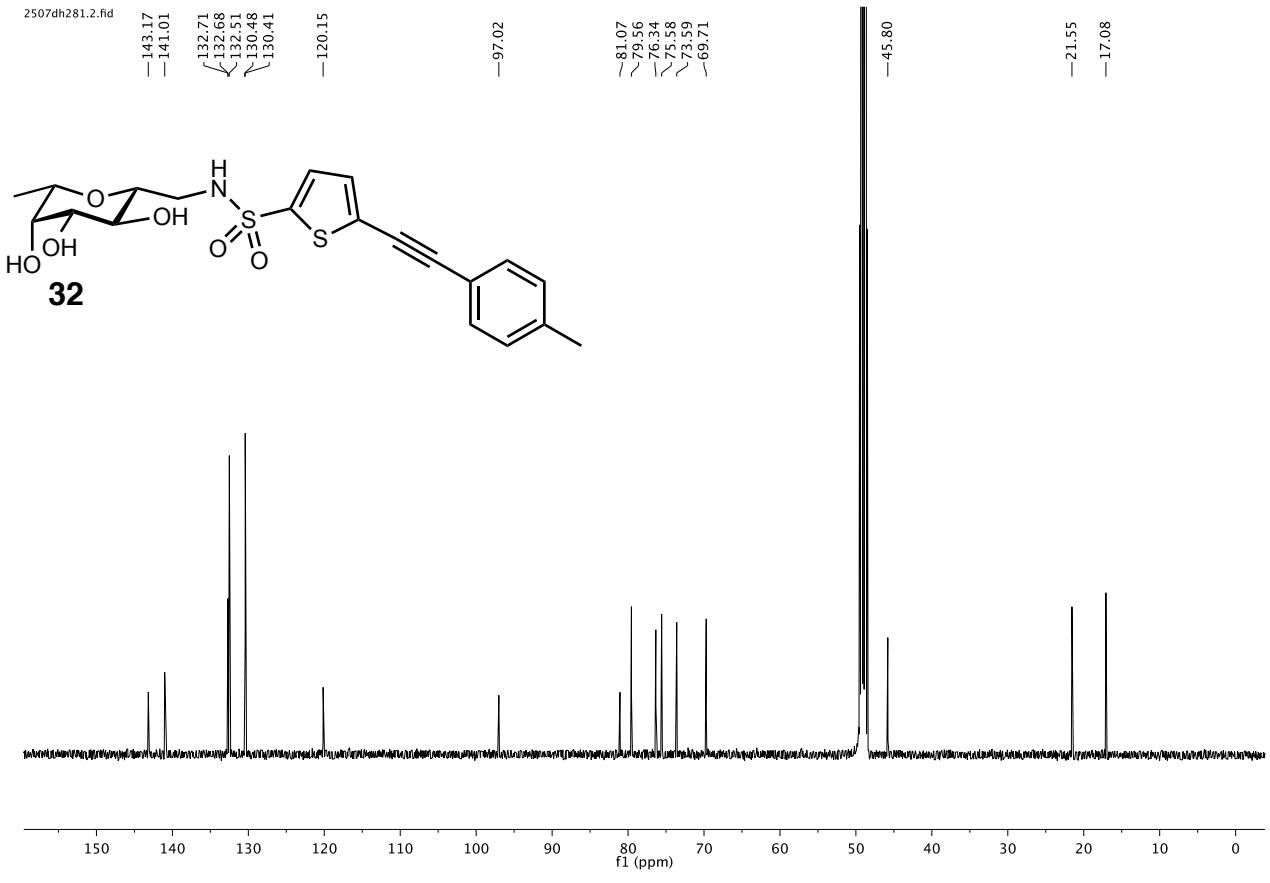

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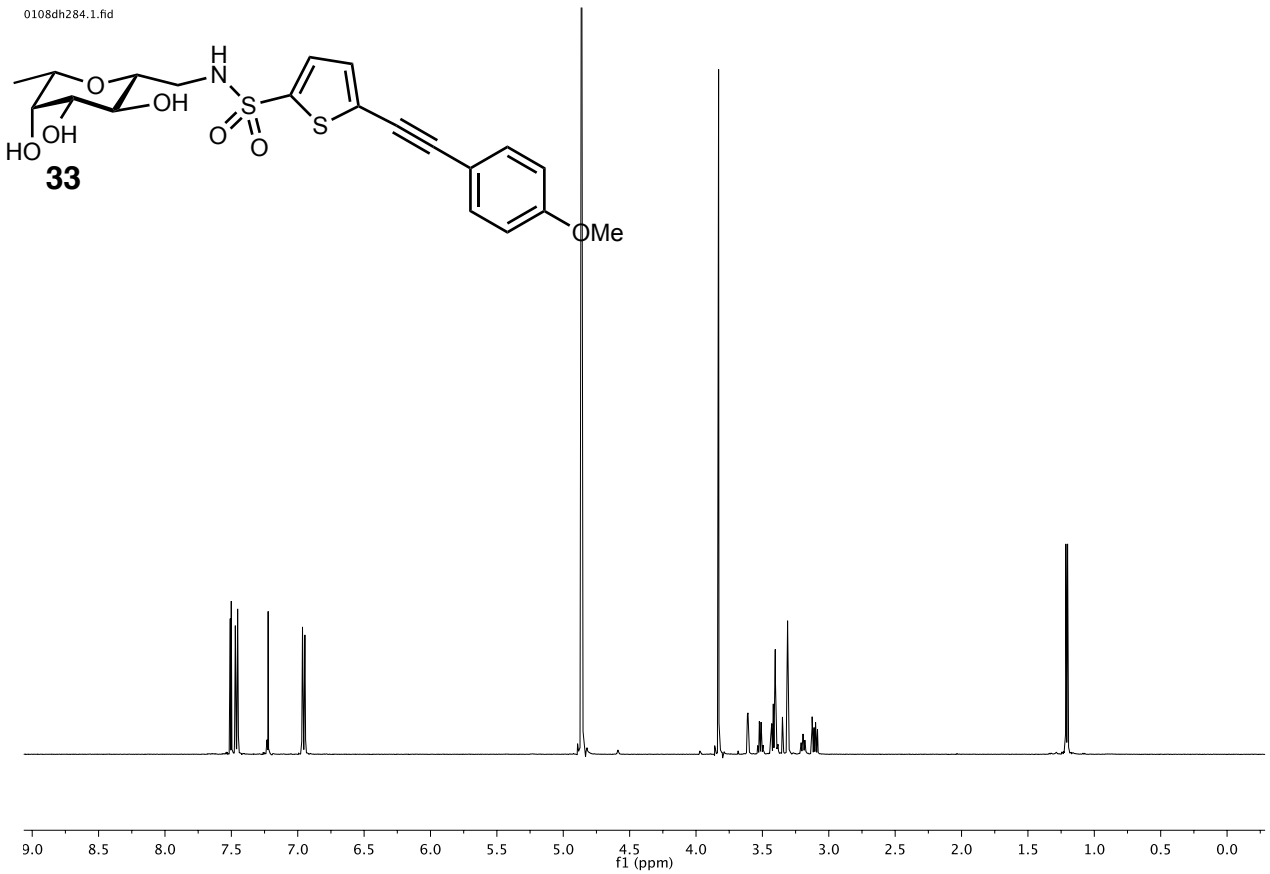
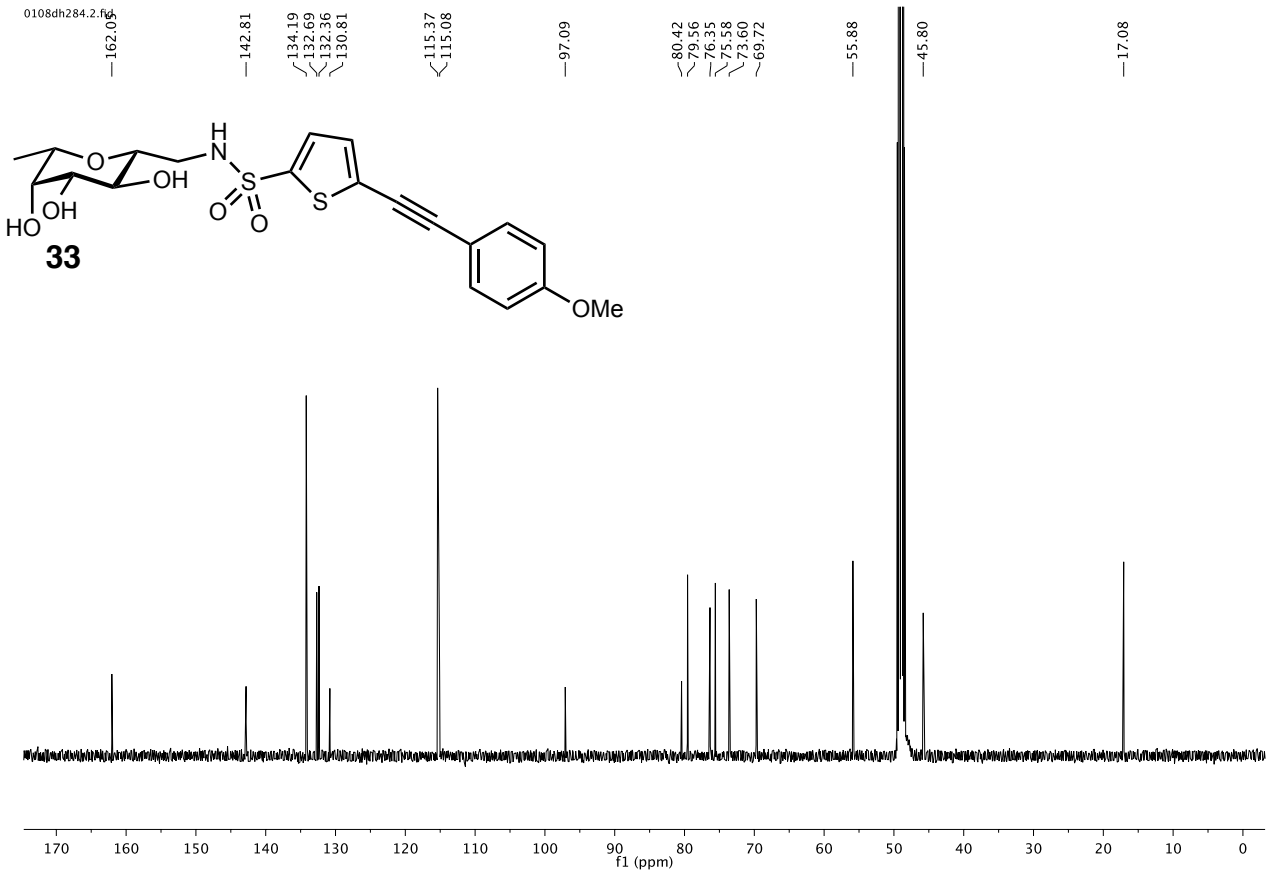
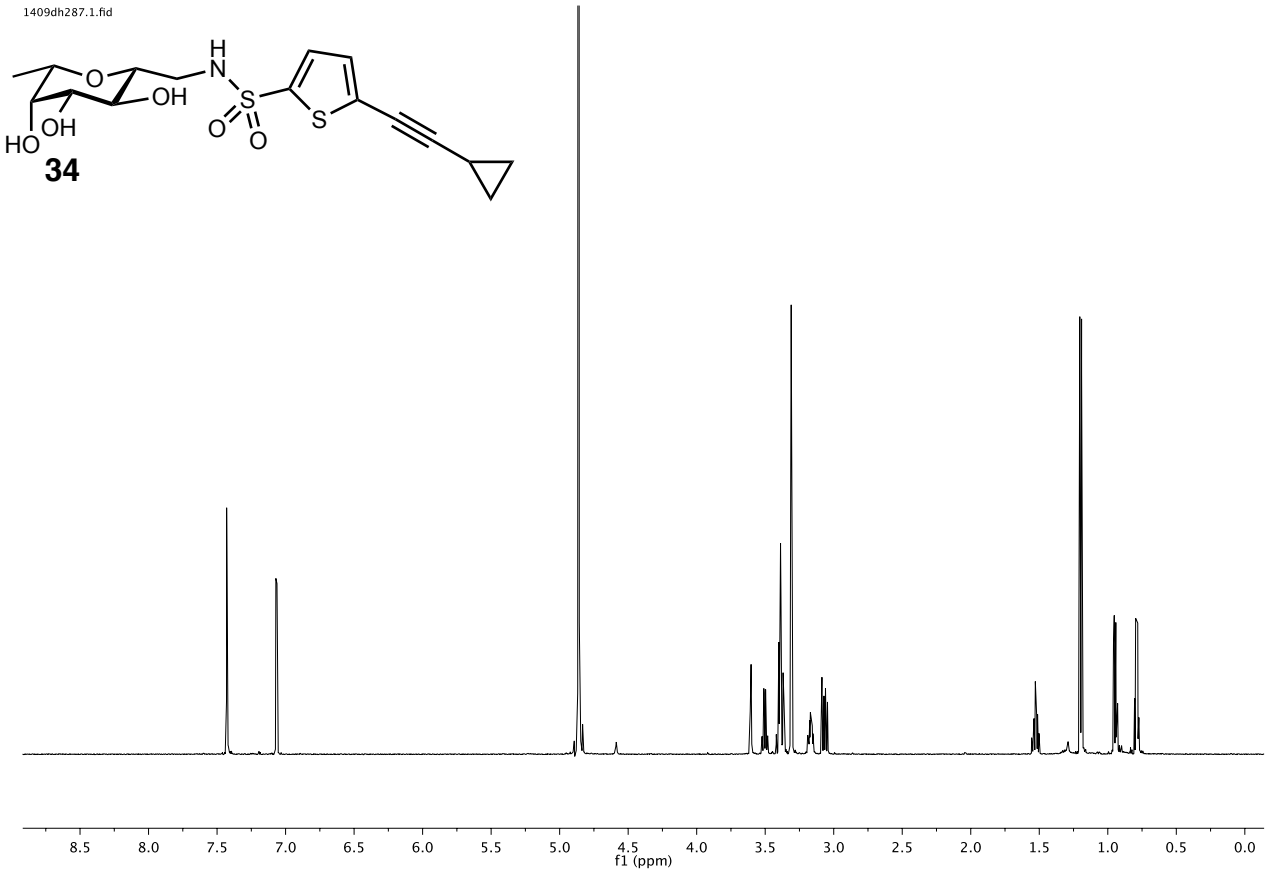
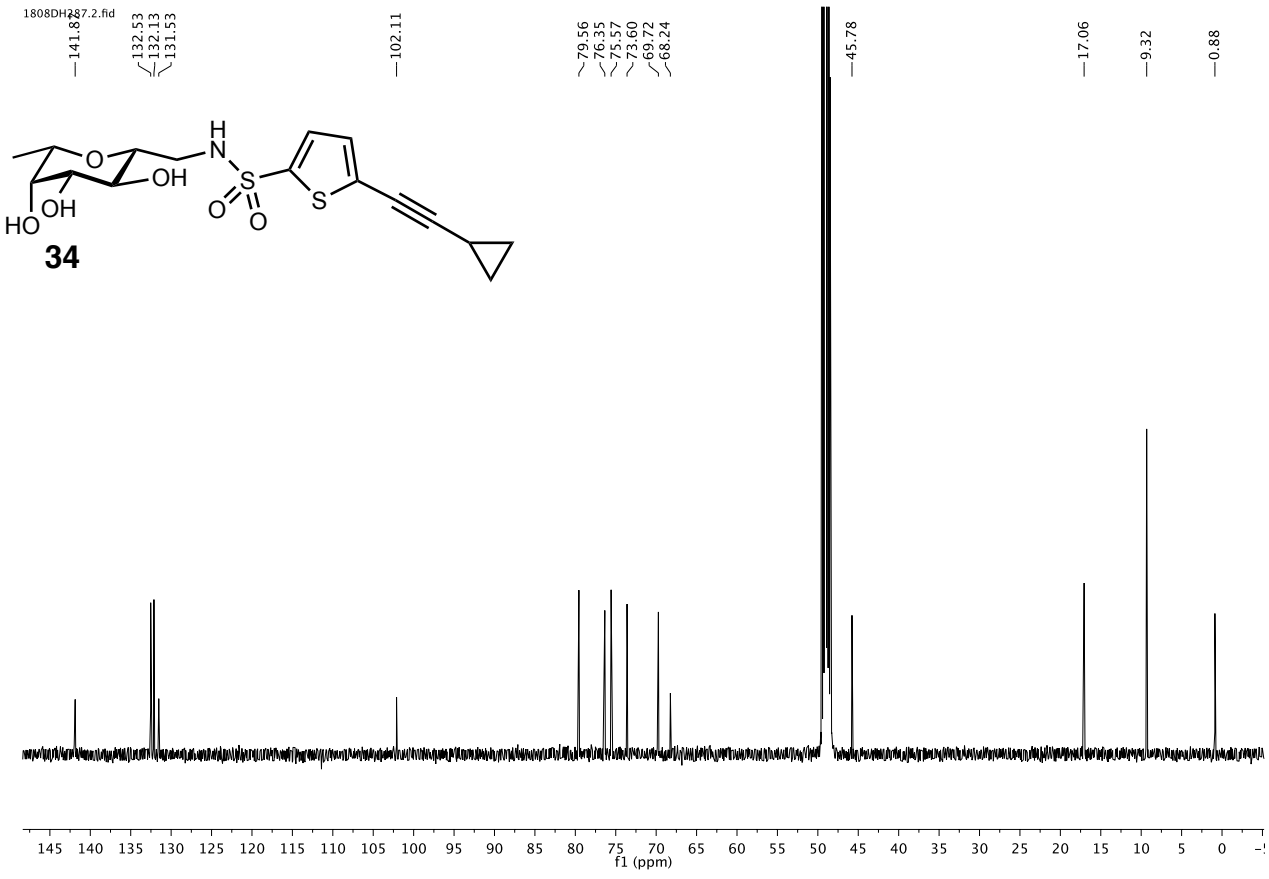


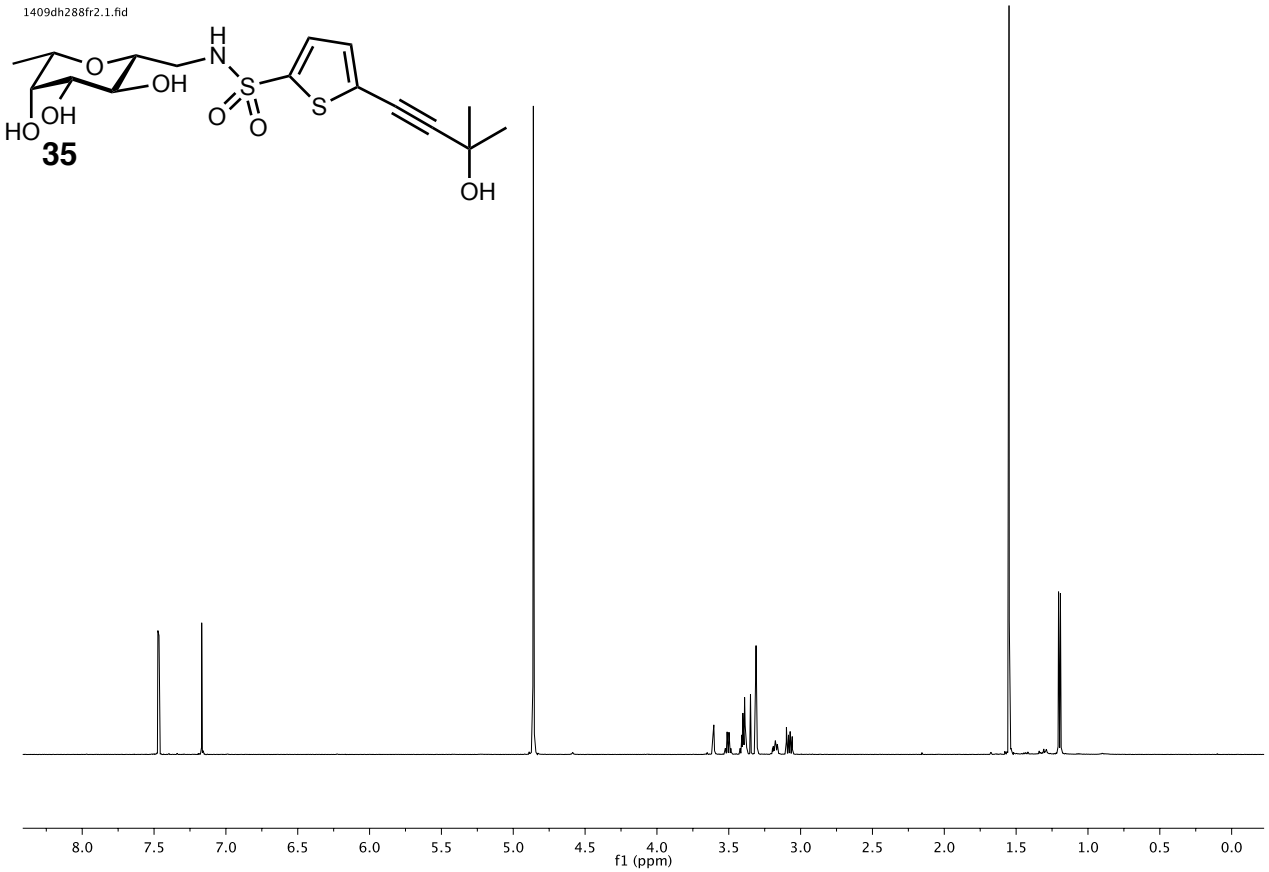


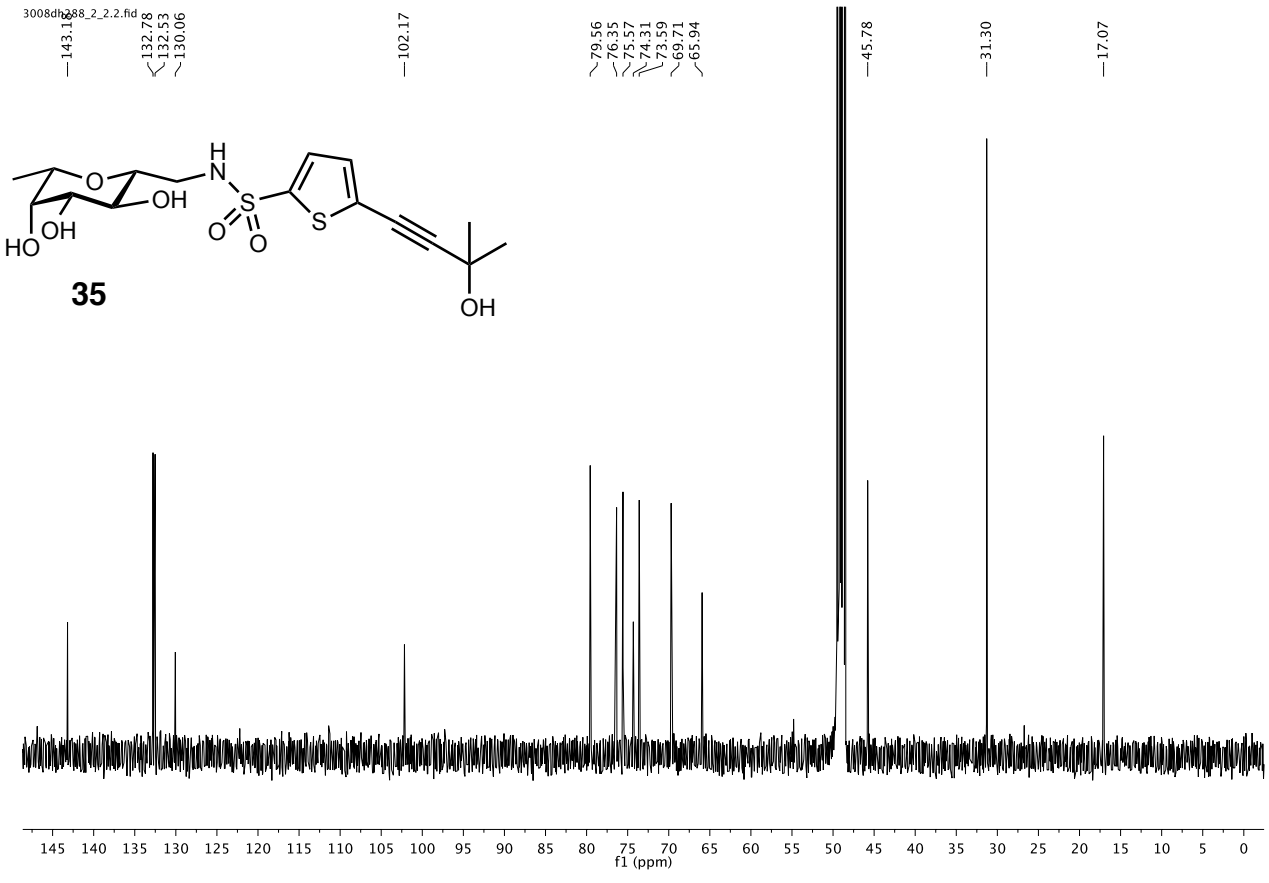
^{1}H, ^{13}C and ^{19}F spectra of new compounds



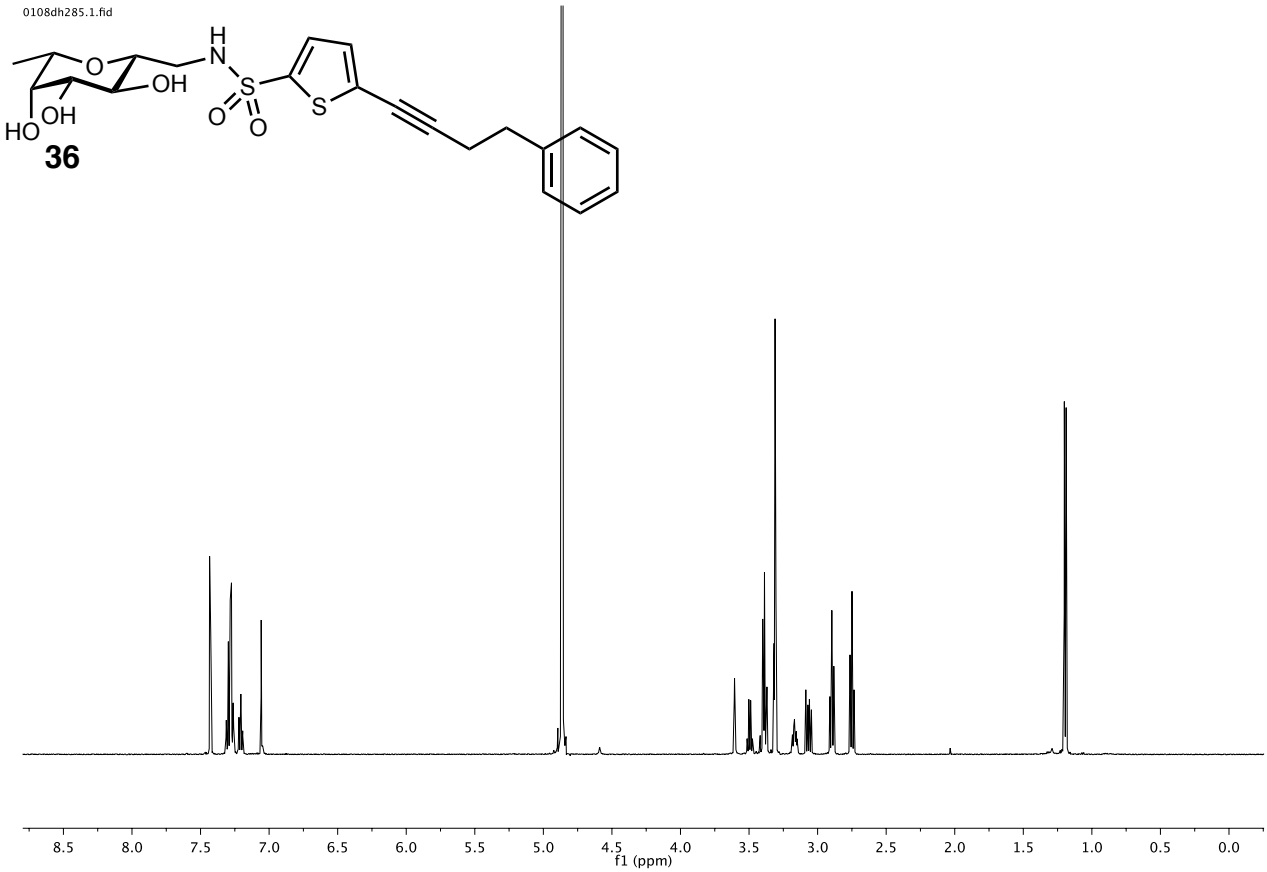


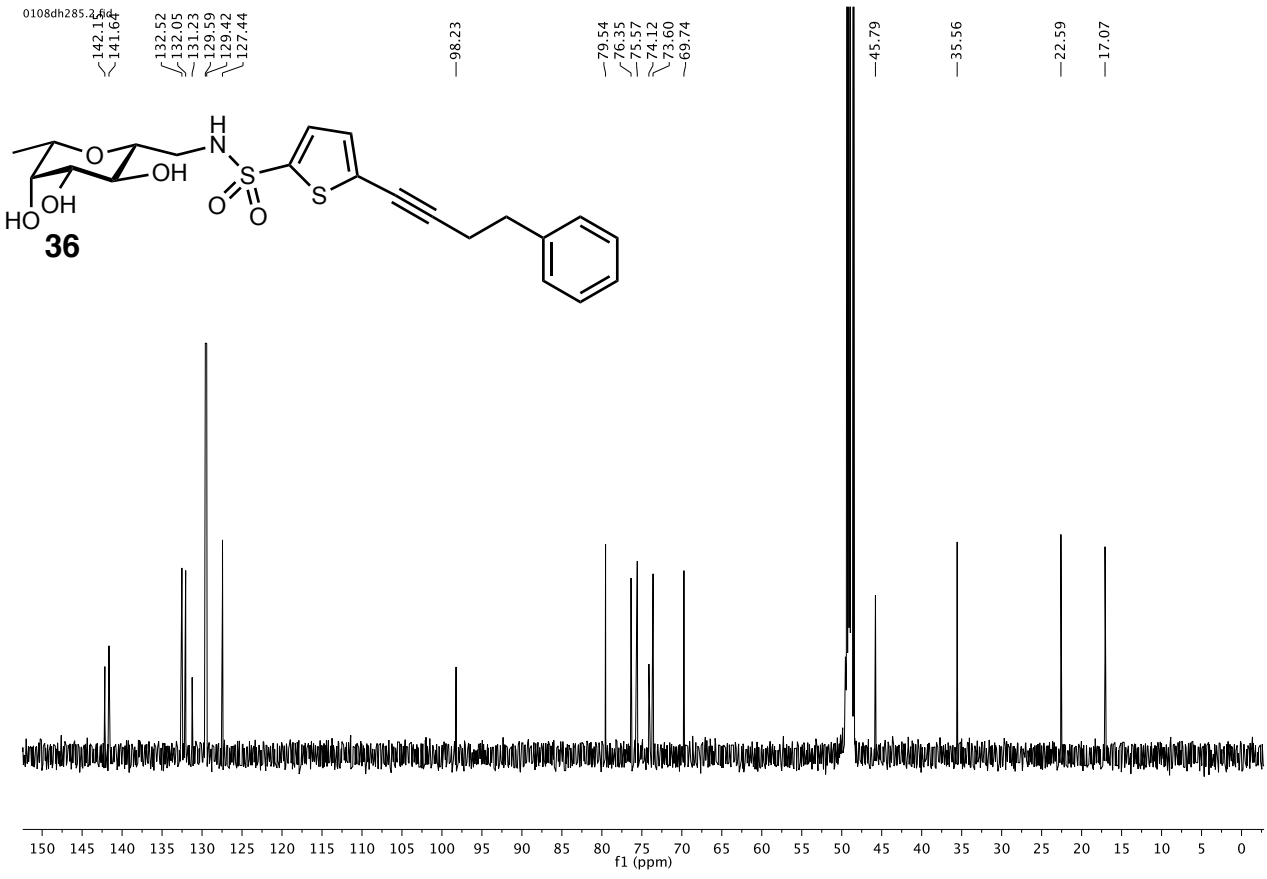
^{1}H, ^{13}C and ^{19}F spectra of new compounds



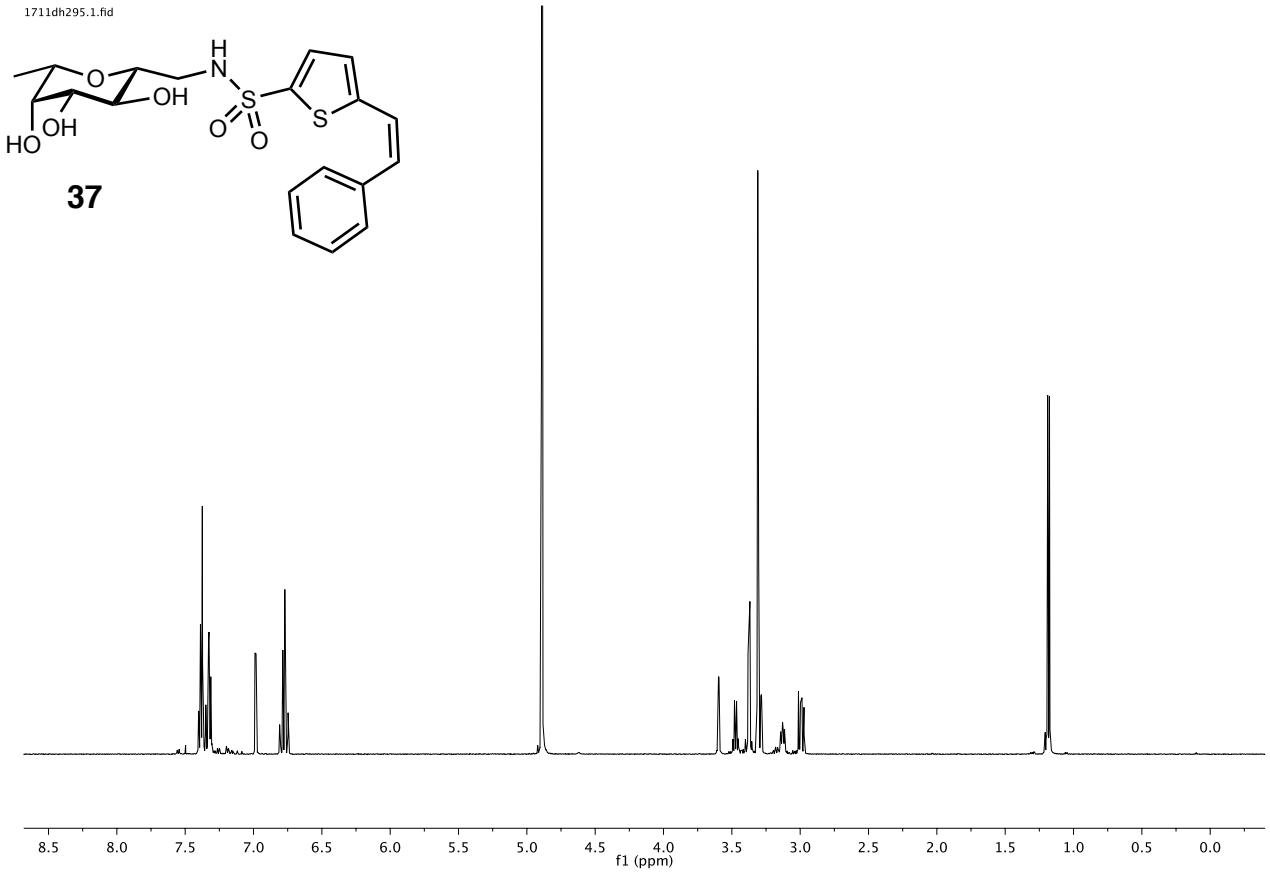


^{1}H, ^{13}C and ^{19}F spectra of new compounds





^{1}H, ^{13}C and ^{19}F spectra of new compounds



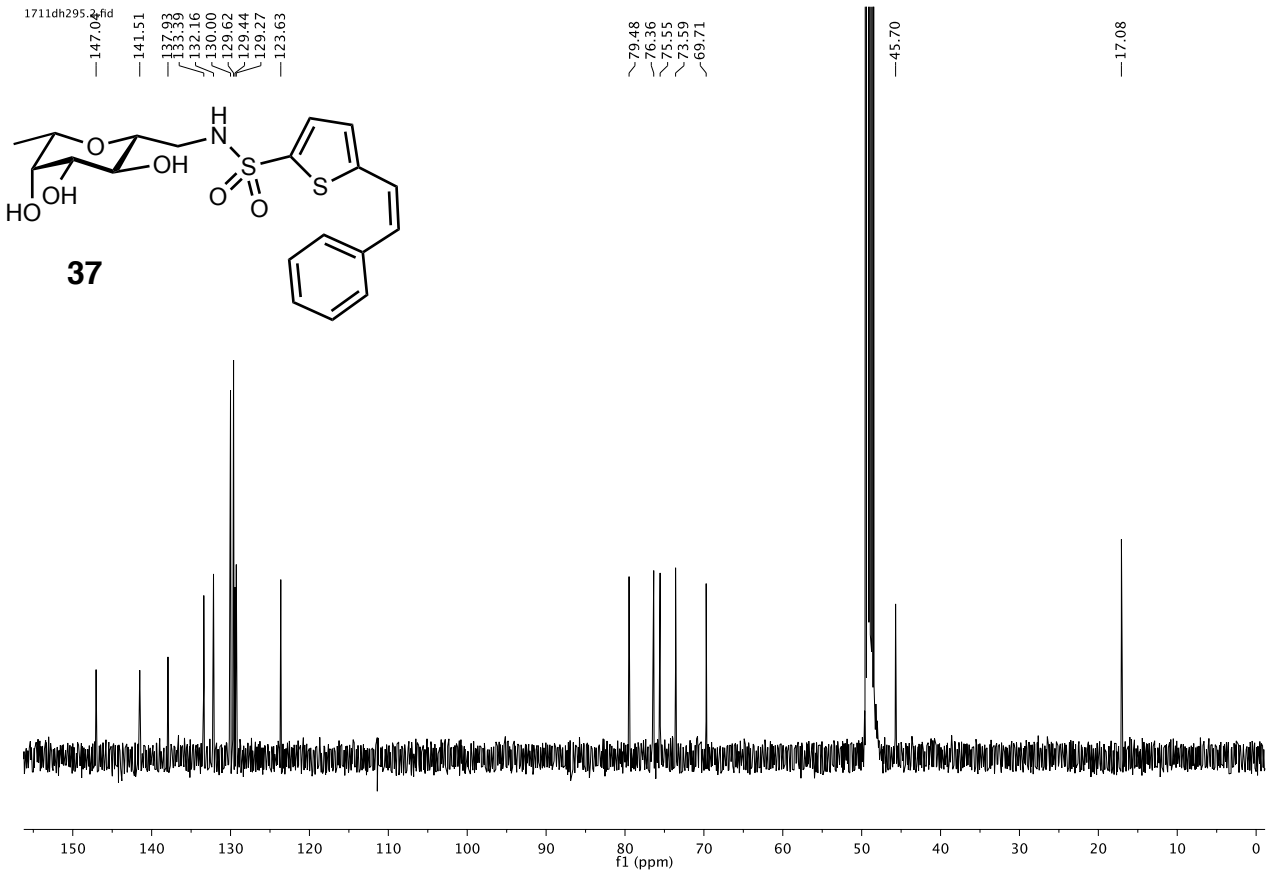
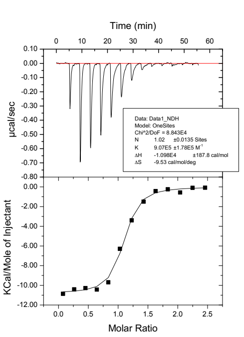
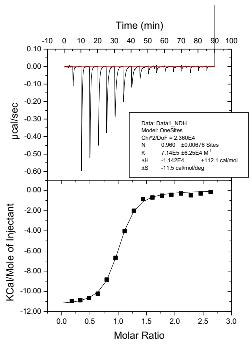
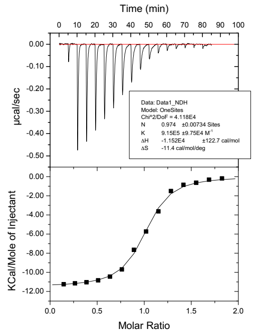


Table S1: ITC measurements with **22**

	LecB$_{PAO1}$ 64.3 µM	**LecB$_{PAO1}$** 60 µM	**LecB$_{PAO1}$** 60 µM
	22 1.0 mM	**22** 750 µM	**22** 600 µM
	TBS supplemented with 1 mM $CaCl_2$	TBS supplemented with 1 mM $CaCl_2$	TBS supplemented with 1 mM $CaCl_2$
			
Ka [1/M]	9.07E+05	7.14E+05	9.15E+05
△H [cal/mol]	-10980	-11420	-11520
△s [cal/molK]	-9.53	-11.5	-11.4
Kd [M]	1.1E-06	1.4E-06	1.09E-06
N	1.02	0.96	0.974
△G [cal/mol]	-8140	-7990	-8120

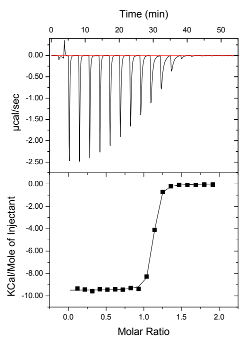
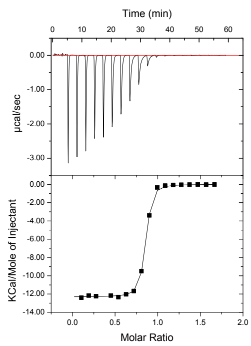
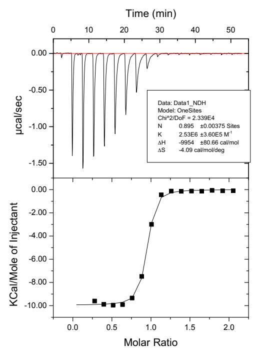
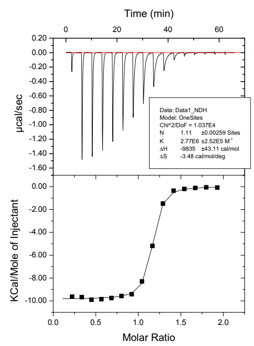
	LecB$_{PA14}$ 236 µM	**LecB$_{PA14}$** 236 µM	**LecB$_{PA14}$** 151 µM	**LecB$_{PA14}$** 140 µM
	22 2.3 mM	**22** 2.0 mM	**22** 1.5 mM	**22** 1.3 mM
	TBS supplemented with 1 mM $CaCl_2$	TBS supplemented with 1 mM $CaCl_2$	TBS supplemented with 1 mM $CaCl_2$	TBS supplemented with 1 mM $CaCl_2$
				
Ka [1/M]	4.11E+06	3.69E+06	2.53E+06	2.77E+06
△H [cal/mol]	-9492	-9402	-9954	-9835
△s [cal/molK]	-1.52	-1.45	-4.09	-3.48
Kd [M]	2.43E-07	2.71E-07	3.95E-07	3.61E-07
N	0.964	1.07	0.895	1.11
△G [cal/mol]	-9040	-8970	-8730	-8800

Table S2: Data collection and refinement statistics for $LecB_{PA14}$ in complex with **22**

	$LecB_{PA14}$ in complex with 22			
Data collection				
Beamline	ID23-2			
Wavelength	0.87260			
Space group	$P6_1$			
Unit cell dimensions	49.88 49.88 288.75 90.00 90.00 90.00			
Resolution (Å)	37.07-1.45 (1.47-1.45)			
Nb reflections	808656			
Nb uniques reflections	71656			
R_{merge}	0.057 (0.308)			
R_{pim}	0.026 (0.141)			
Mean I / σI	27.1 (7.6)			
Completeness (%)	100.00 (100.00)			
Redundancy	11.3 (11.0)			
CC1/2	100.0 (98.0)			
Refinement				
Resolution (Å)	37.07-1.45			
No. reflections/No. free reflections	67895/3598			
R_{work} / R_{free}	12.4 / 14.3			
R.m.s Bond lengths (Å)	0.016			
Rmsd Bond angles (°)	2.043			
Rmsd Chiral (°)	0.103			
No. atoms (Chain)	A	B	C	D
Protein	862	883	853	868
Sugar	22	22	22	22
Calcium	2	2	2	2
Waters	150	175	166	169
B-factors (Å^2)				
Protein	10.5	10.0	10.4	9.6
Sugar	15.3	10.3	12.2	10.8
Calcium	8.6	7.4	8.3	7.0
Waters	24.0	25.8	24.7	24.6
Ramachandran				
Allowed	99.8			
Favored	97.1			
Outliers	1			
PDB Code	5MAZ			

Table S3: m/z search window for plasma stability assay

name	**start-stop [m/z]**
naproxen	230-232
glipizide	444.5-447
procaine	236-237.5
procainamide	235.5-236.6
propoxycaine	294.4-295.8
17	320-321.8
22	349.8-351
23	335.8-337
27	389-390.4
29	421-423.1

Table S4: Mass transitions of compounds

compound	Q1 mass	Q3 mass	Time [msec]	DP [volts]	CE [volts]	CXP [volts]
6	357.966	183.0	30	-140	-34	-19
	357.966	197.9	30	-140	-36	-23
7	321.888	146.8	30	-140	-30	-15
	321.888	230.0	30	-140	-28	-21
17	320.91	238.2	30	-30	-18	-13
	320.91	82.0	30	-30	-20	-9
	320.91	40.0	30	-30	-66	-17
22	349.98	174.6	30	-90	-30	-7
	349.98	110.9	30	-90	-38	-11
23	335.899	175.9	30	-115	-32	-17
	335.899	160.9	30	-115	-30	-15
29	421.93	182.9	30	-135	-40	-19
	421.93	198.8	30	-135	-34	-17
3	374.003	198.0	30	-135	-34	-19
	374.003	182.9	30	-135	-32	-17
45	337.881	161.8	30	-130	-34	-17
	337.881	146.8	30	-130	-30	-15
Naproxene	231.106	185.1	50	80	19	10
	231.106	170.2	50	80	33	12
Caffeine	195.024	138.0	30	80	25	14
	195.024	110.0	30	80	31	18

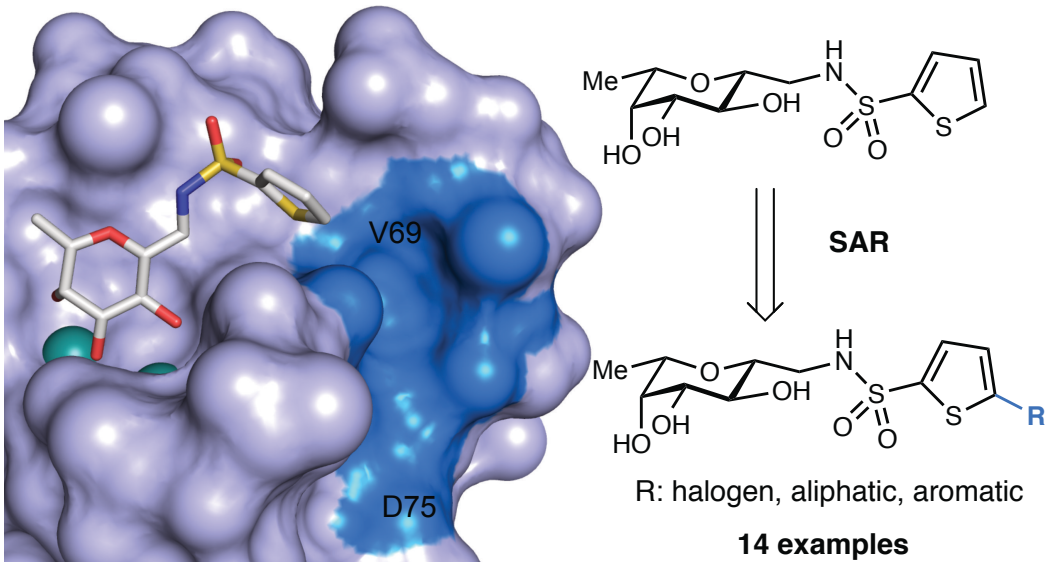


Figure S1: Rationale for the extension of the thiophene moiety in **7** to target an additional patch or a subpocket on the surface of LecB

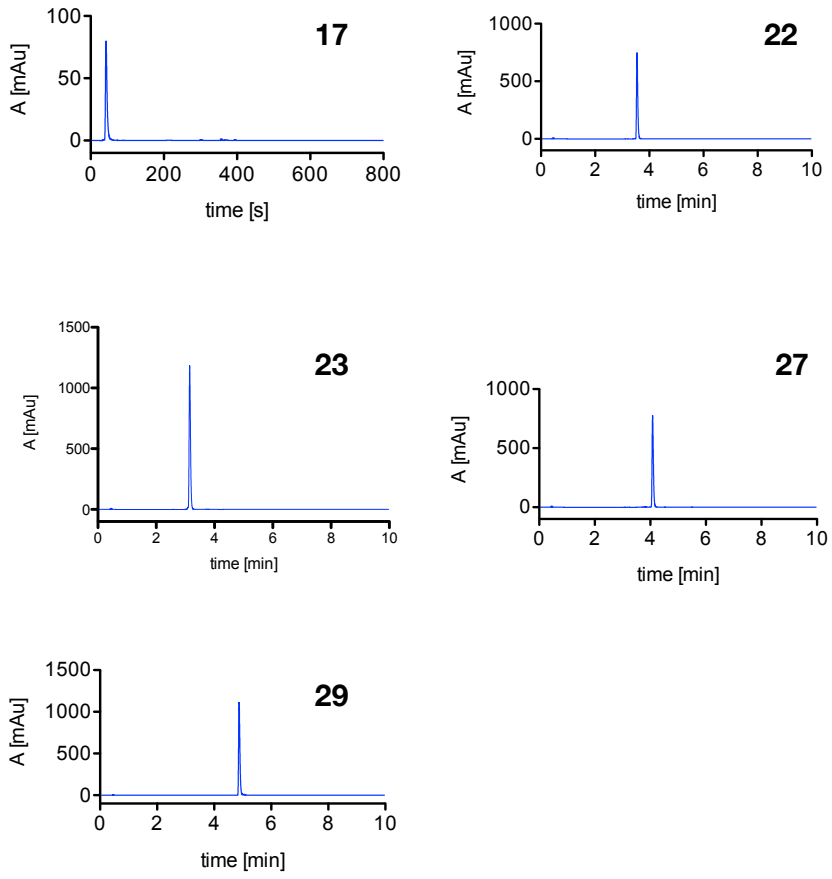


Figure S2: Purity of key compounds **17**, **22**, **23**, **27**, **29** by HPLC-UV