Supporting Information

Aromatic heterocycle galectin-1 interactions for selective single-digit nM affinity ligands

Kristoffer Peterson,[a] Patrick M. Collins,[b] Xiaoli Huang,[c] Barbro Kahl-Knutsson,[d] Sofia Essén,[a] Fredrik R. Zetterberg,[e] Stina Oredsson,[c] Hakon Leffler,[d] Helen Blanchard[b*] and Ulf J. Nilsson[a*]

[a] *Centre for Analysis and Synthesis, Department of Chemistry, Lund University, POB 124, 221 00, Lund, Sweden*

[b] *Institute for Glycomics, Griffith UniversityGold Coast Campus, Queensland 4222, Australia*

[c] *Department of Biology, Lund University, POB 118, 221 00, Lund, Sweden*

[d] *Department of Laboratory Medicine, Section MIG, Lund University BMC-C1228b, Klinikgatan 28, 221 84 Lund, Sweden*

[e] *Galecto Biotech AB, Sahlgrenska Science Park, Medicinaregatan 8 A, 413 46 Gothenburg, Sweden*

*Corresponding author. *Email*: ulf.nilsson@chem.lu.se

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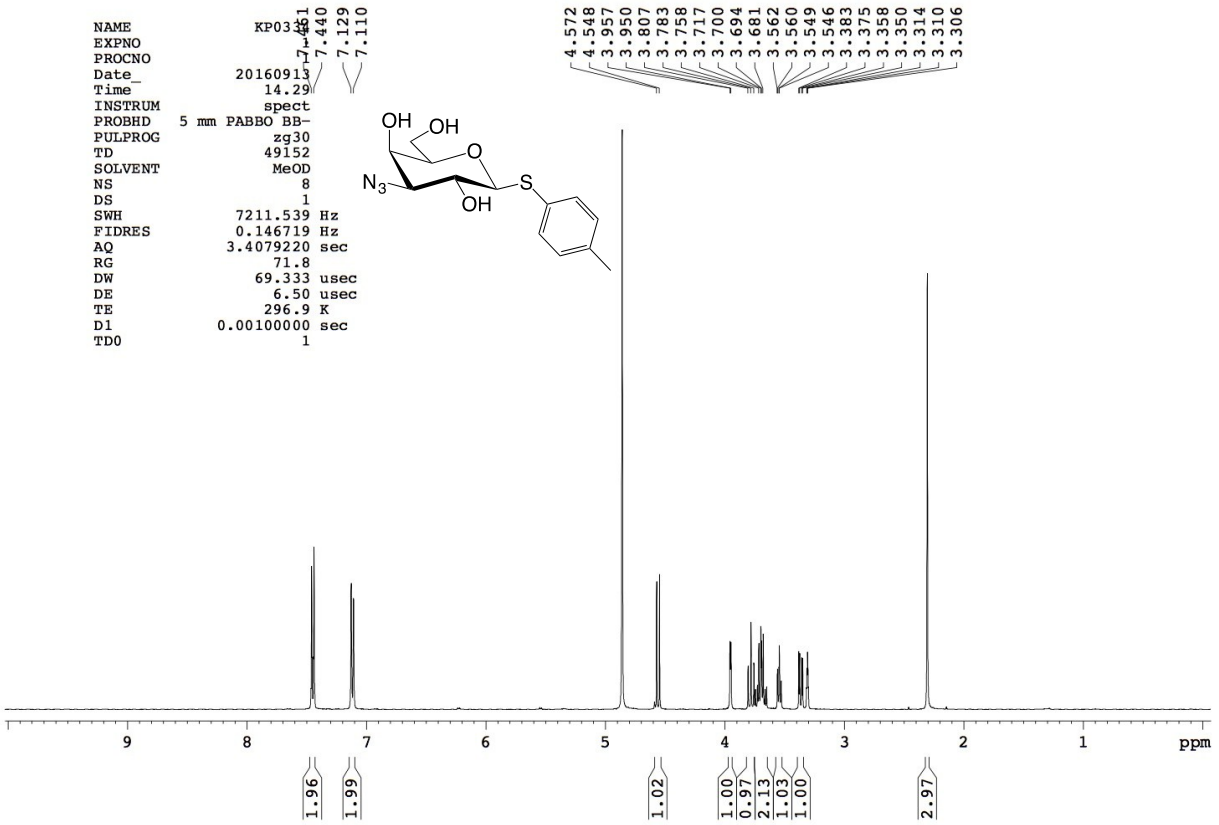
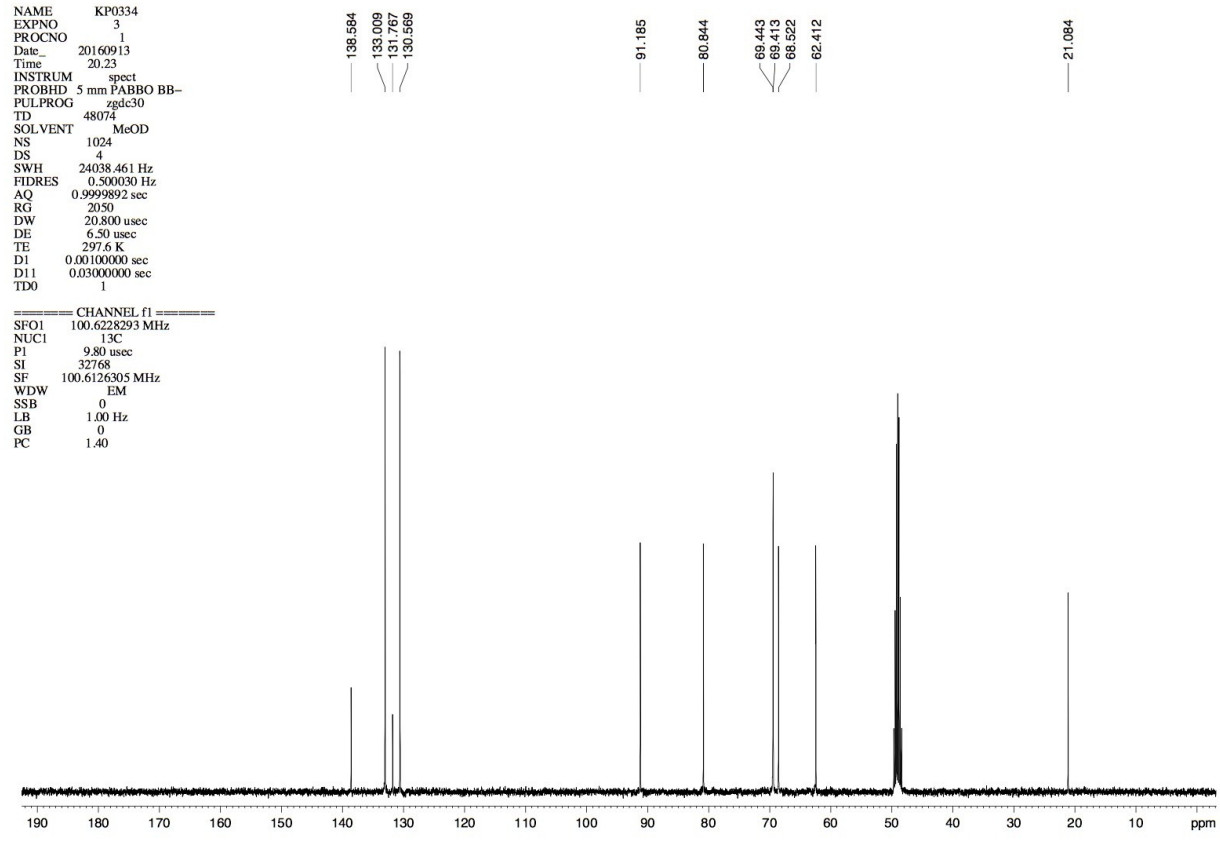
NMR spectra of synthesized compounds

p-Methylphenyl 3-azido-3-deoxy-1-thio-β-D-galactopyranoside 3





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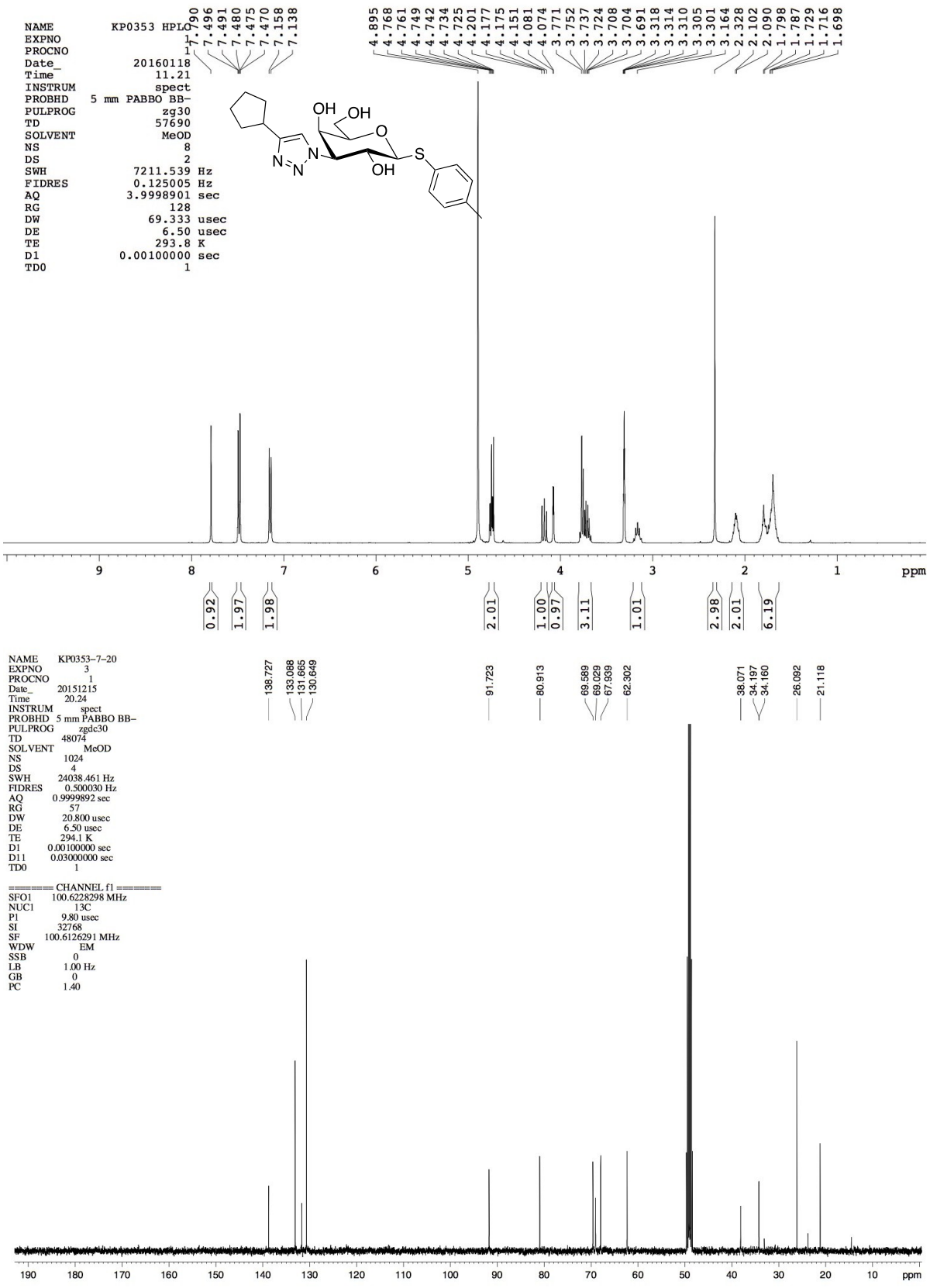

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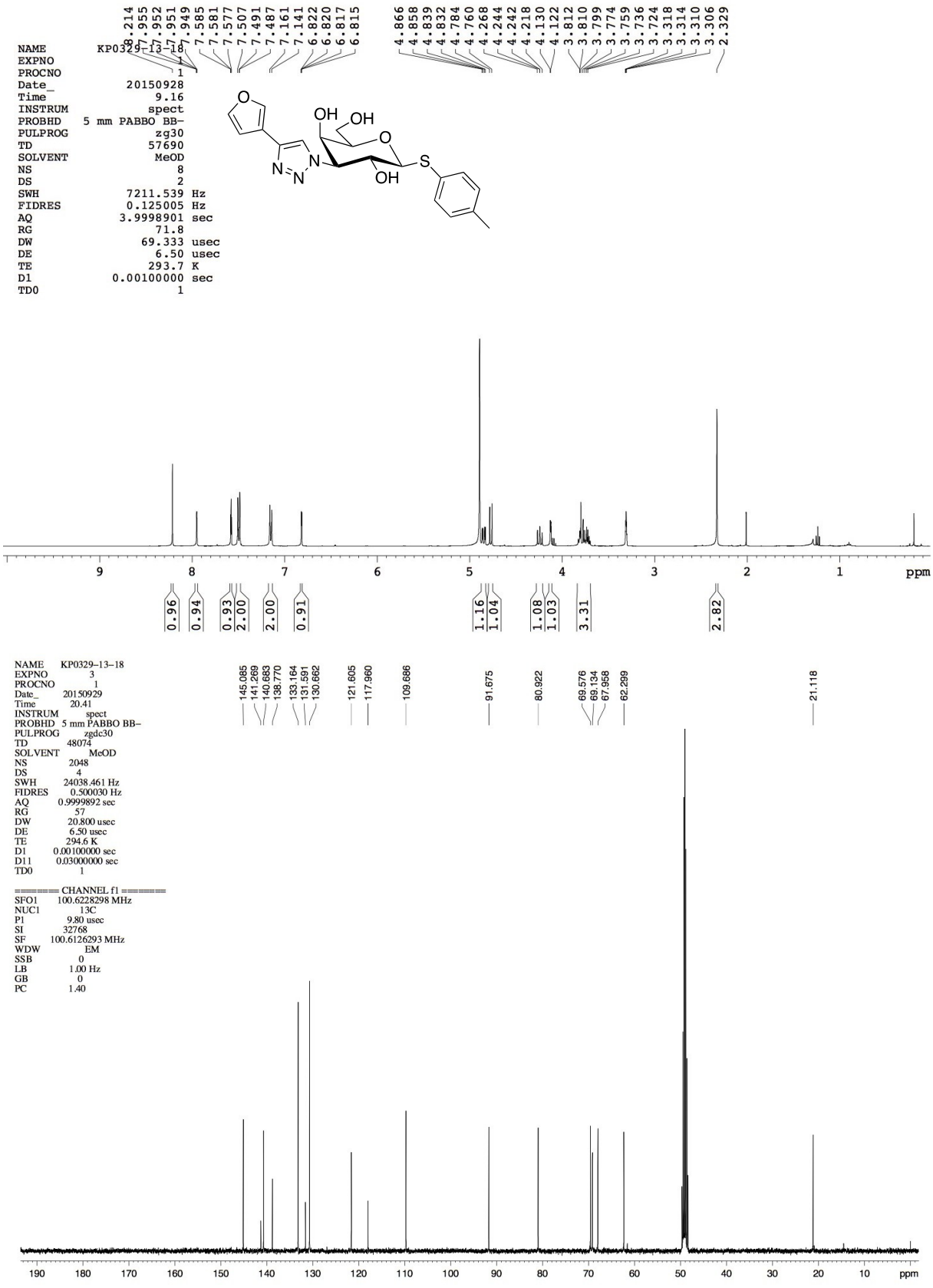

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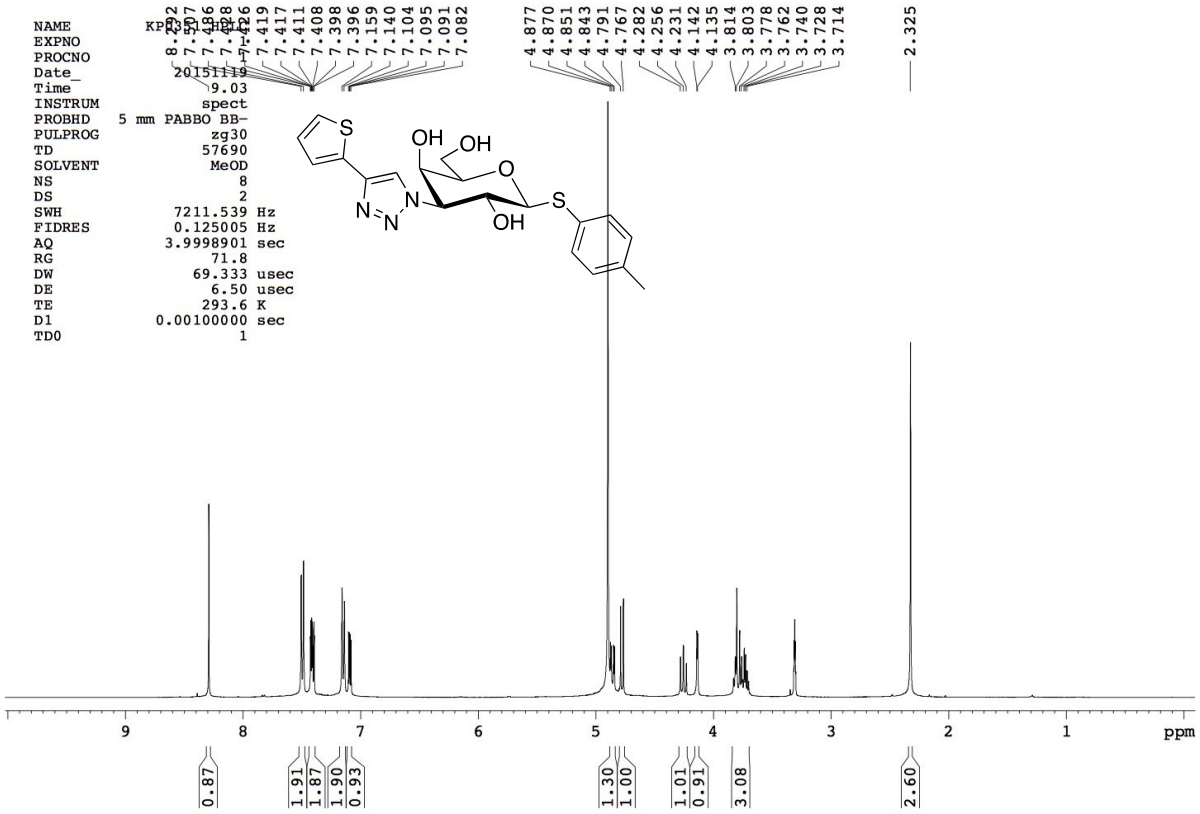

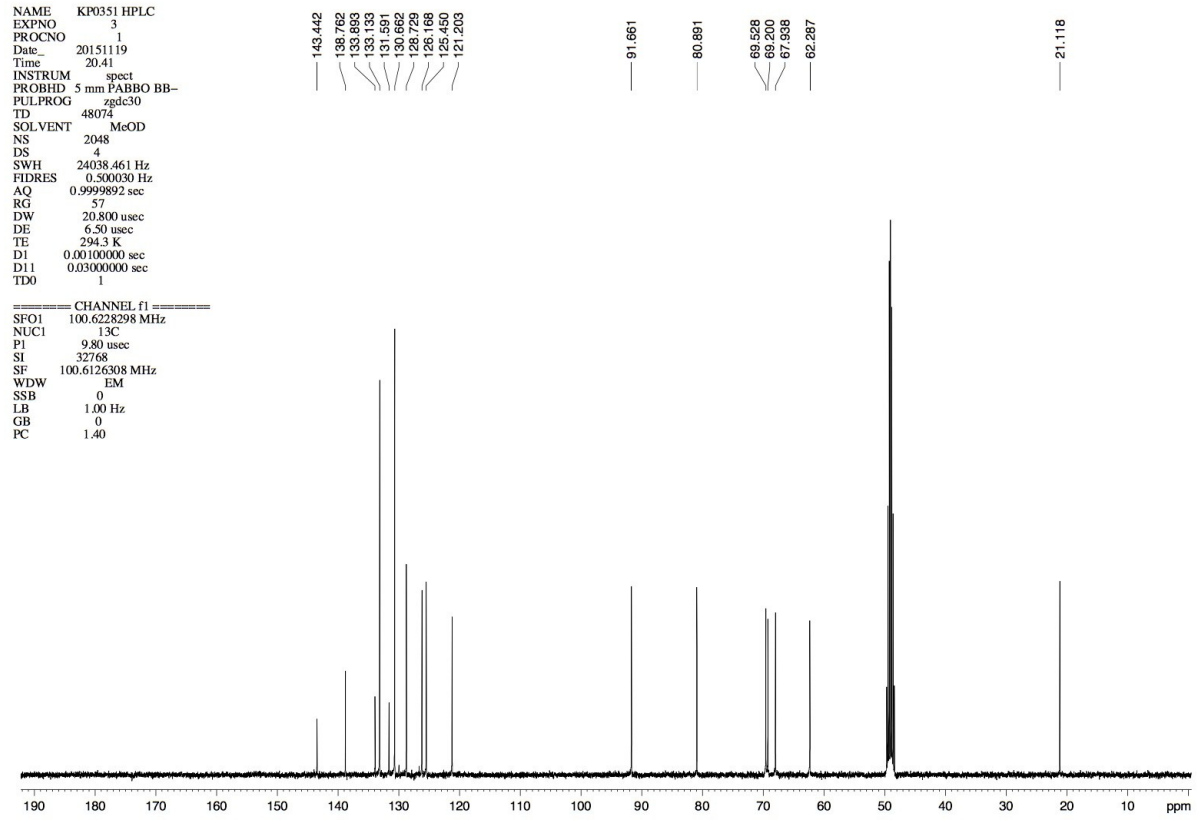

***p*-Methylphenyl 3-deoxy-3-[4-(thien-3-yl)-1*H*-1,2,3-triazol-1-yl]-1-thio-β-D-galactopyranoside**

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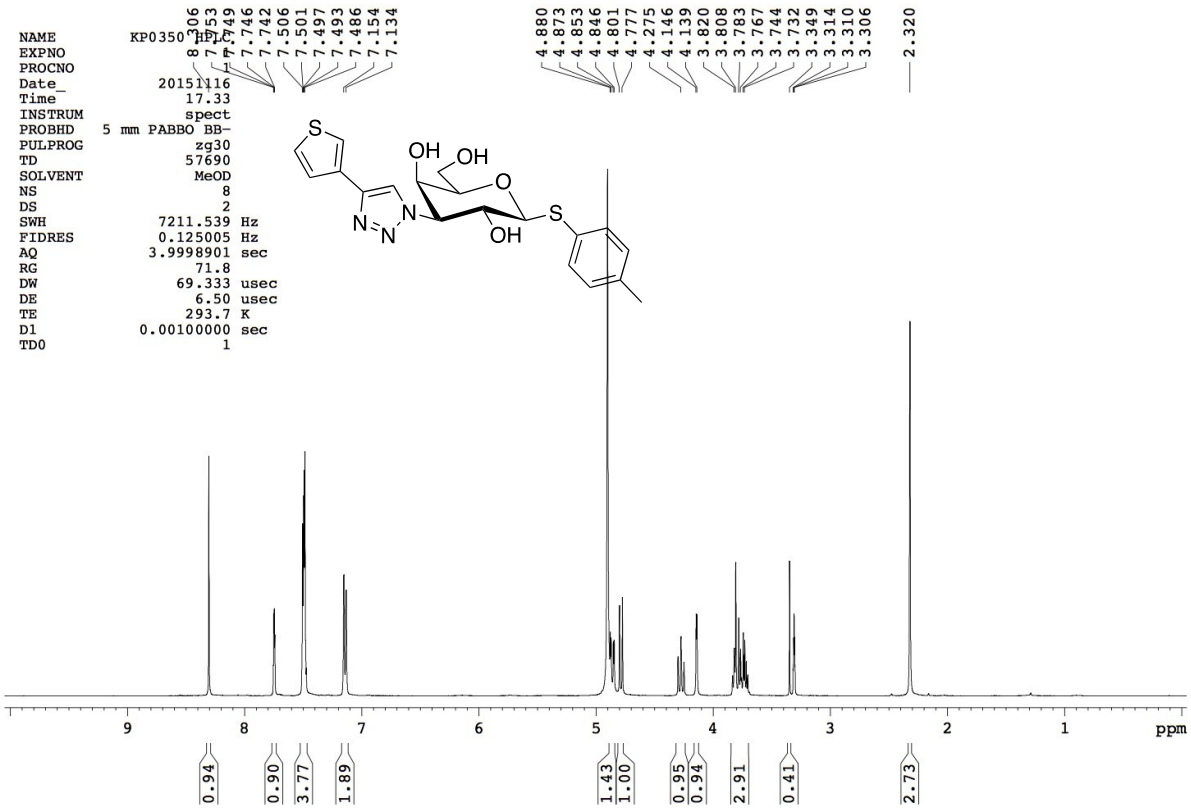
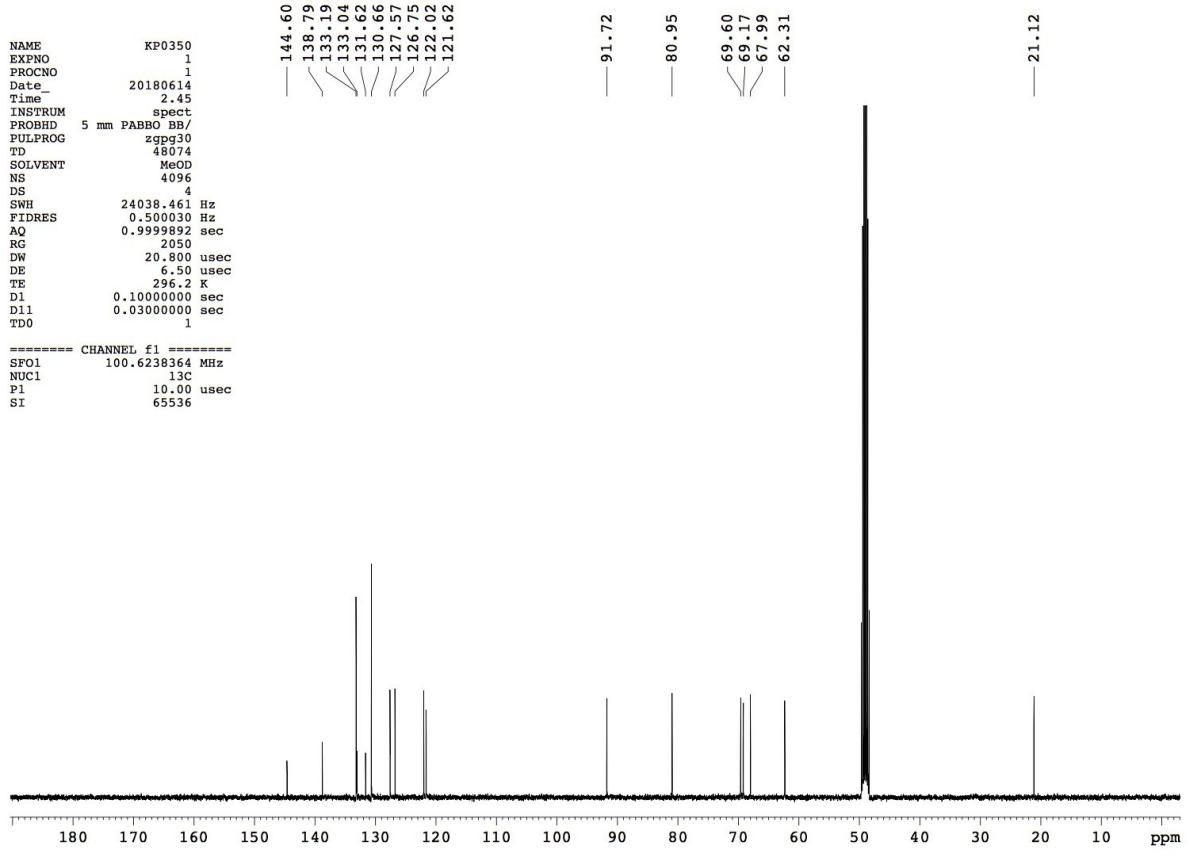
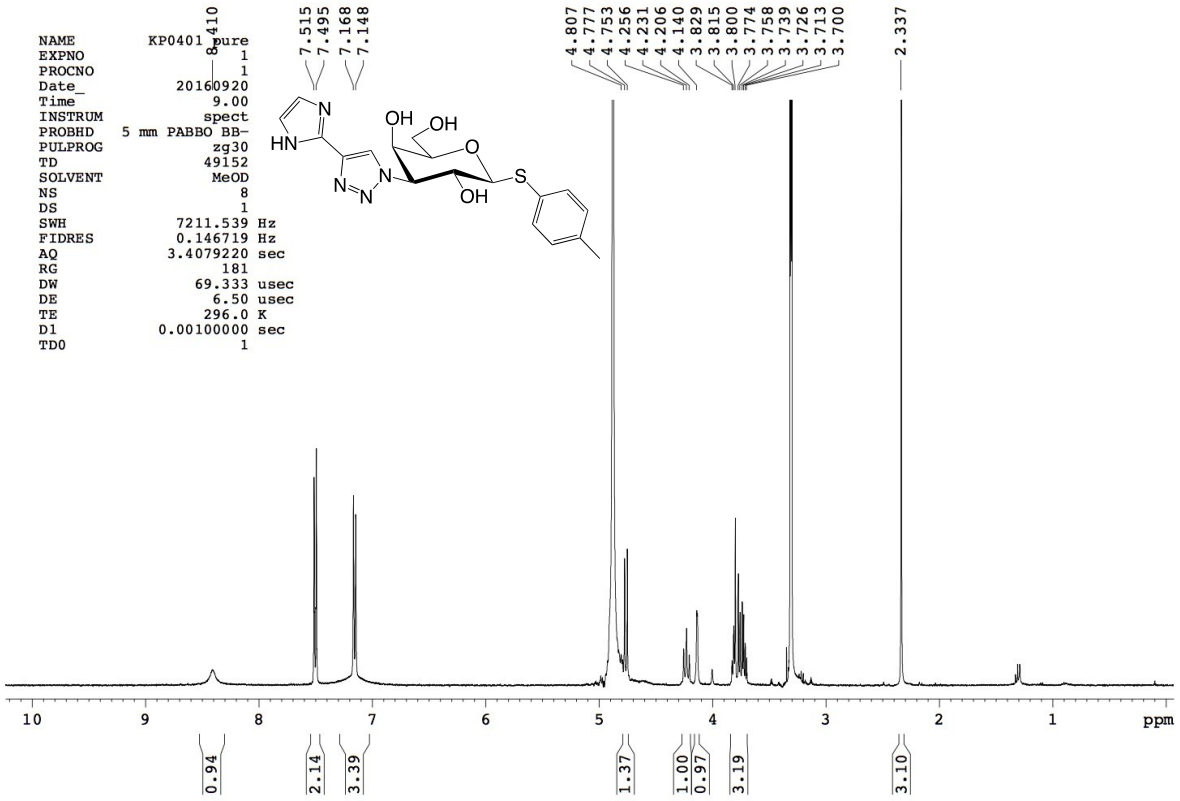
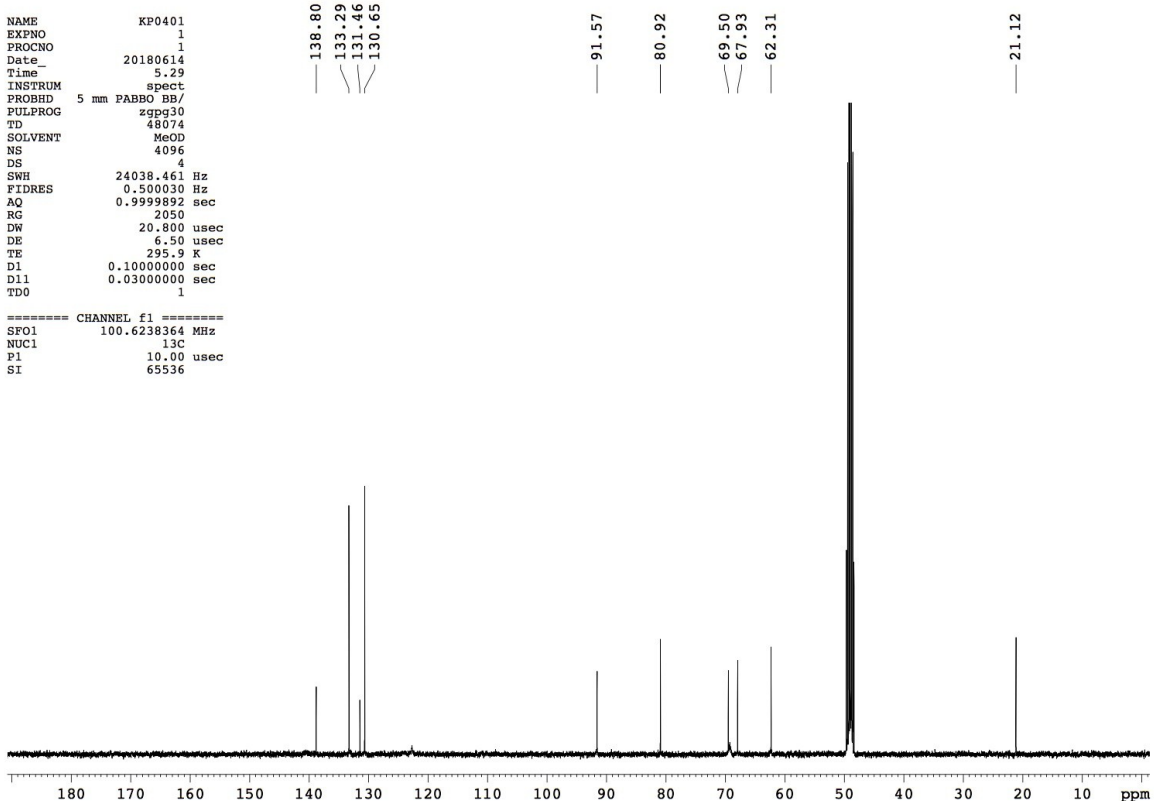




***p*-Methylphenyl 3-deoxy-3-[4-(1*H*-imidazol-2-yl)-1*H*-1,2,3-triazol-1-yl]-1-thio-β-D-galactopyranoside 8**





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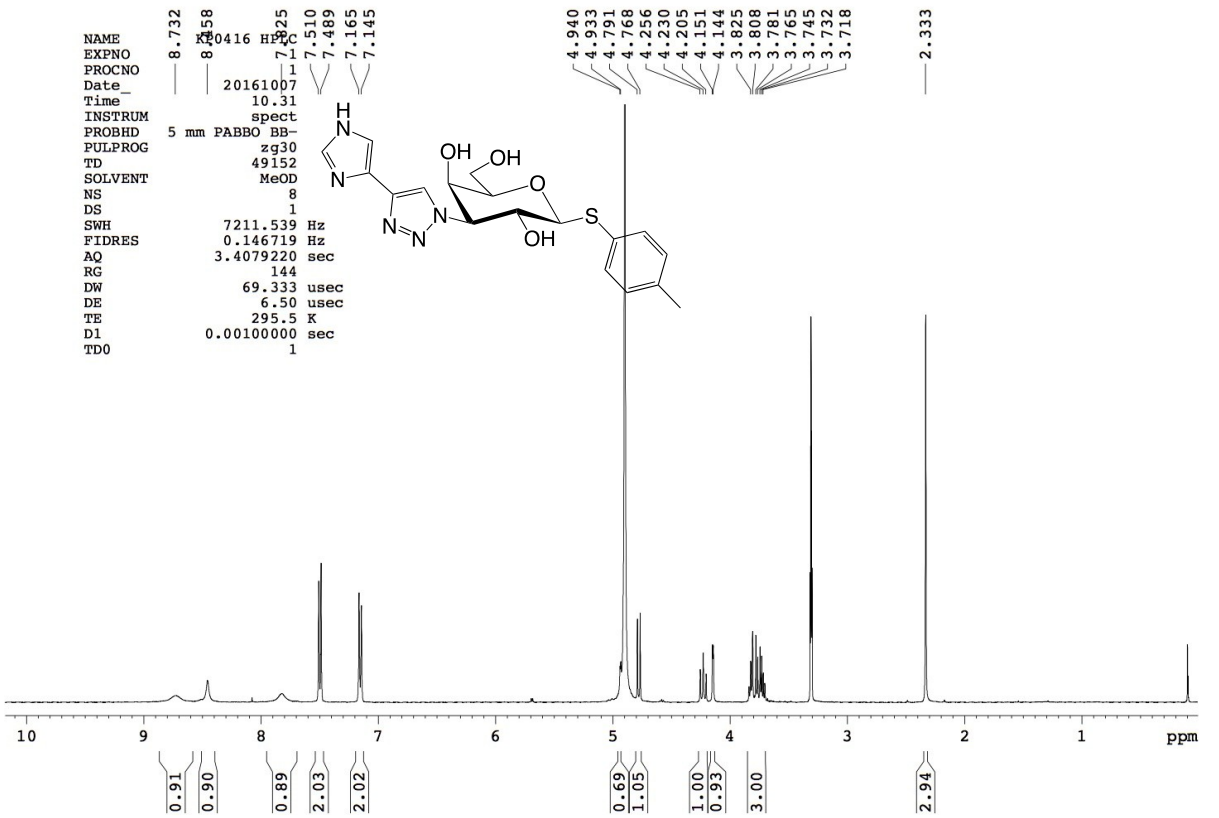
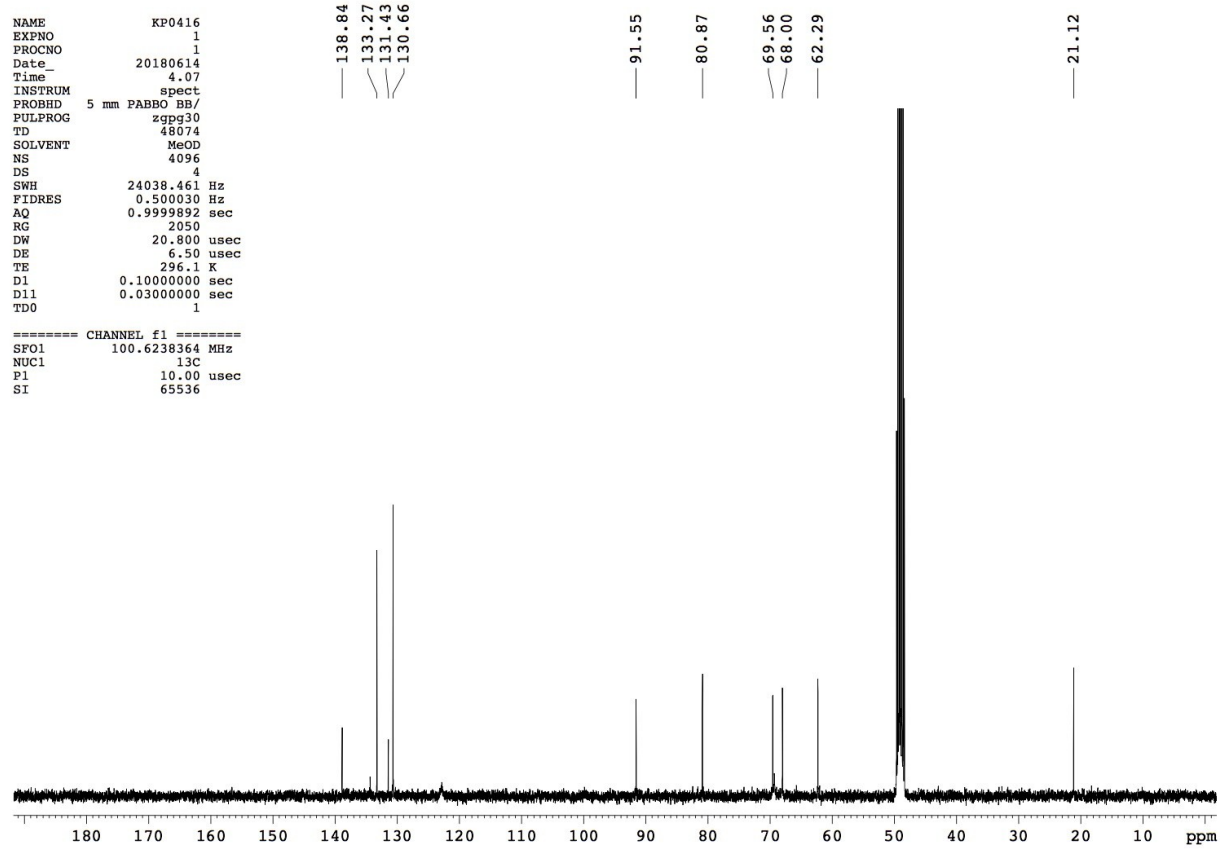
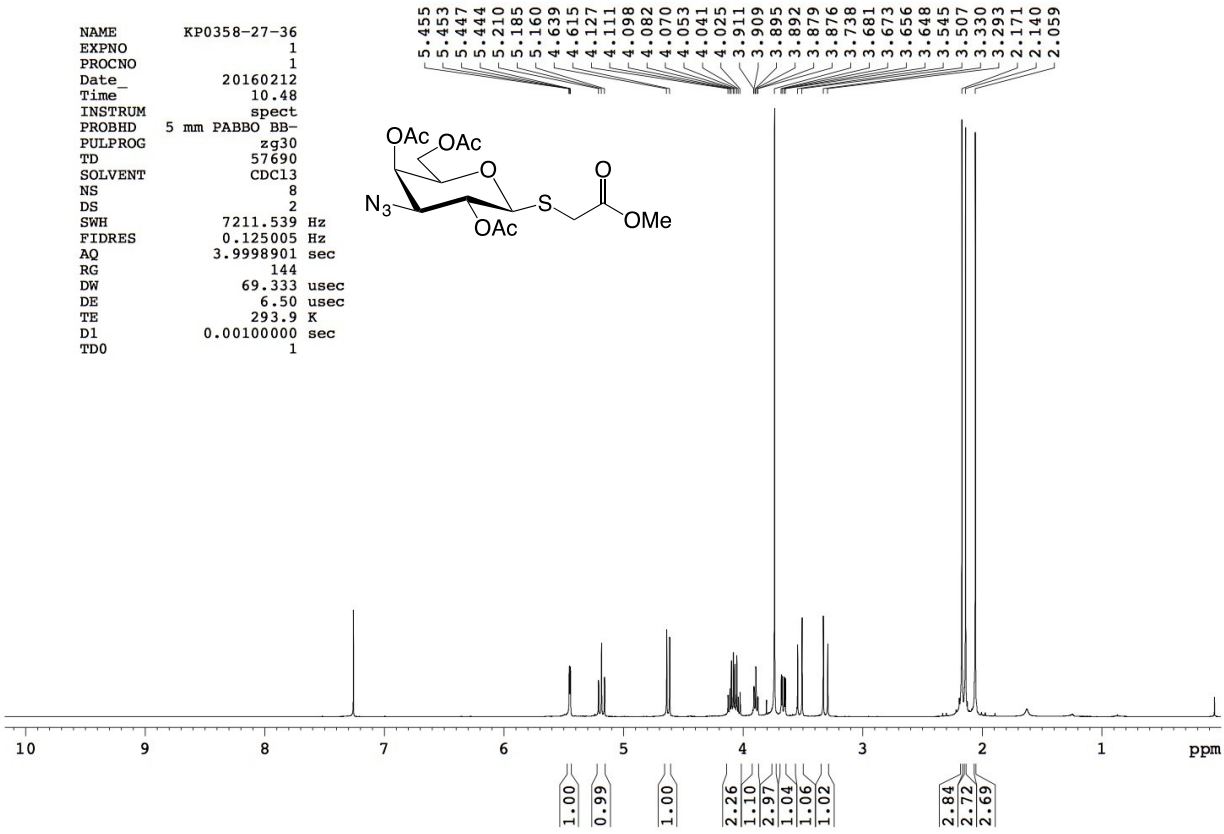
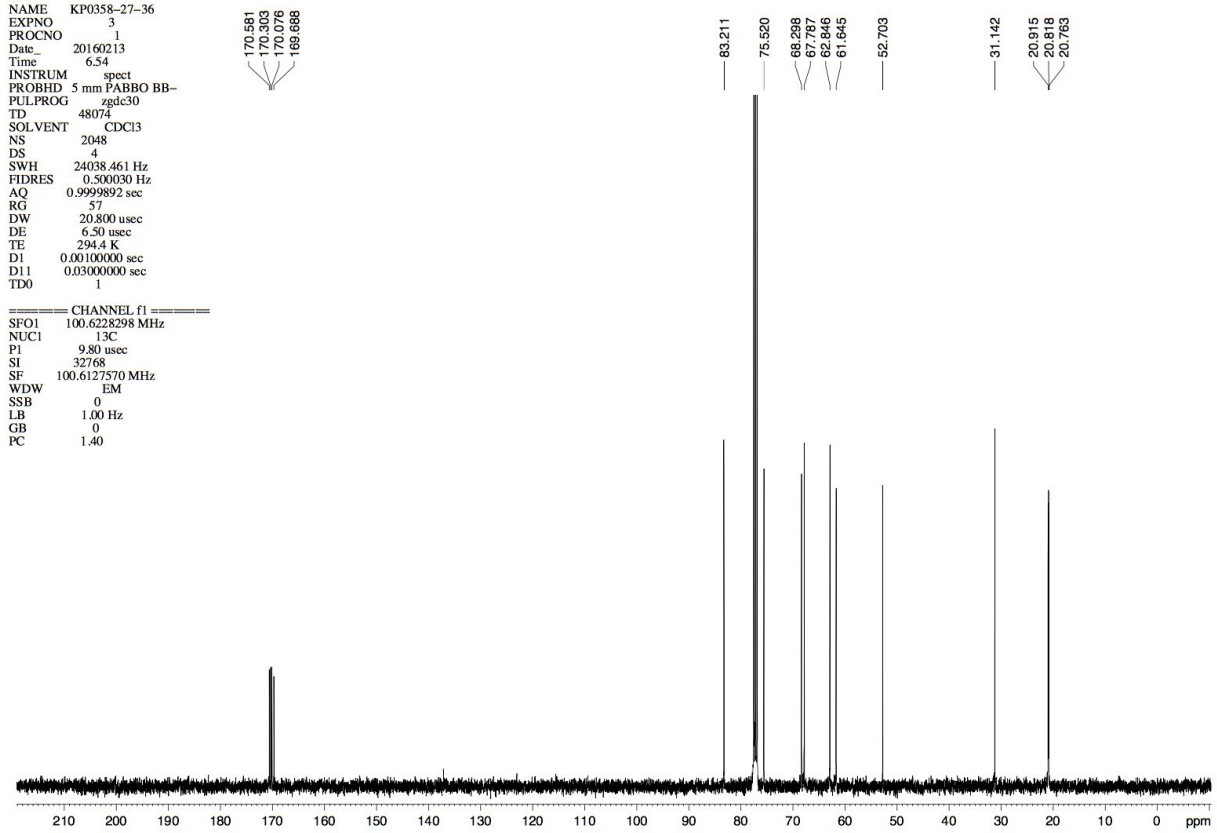




Methyl glycolate-2,4,6-tri-*O*-acetyl-3-azido-3-deoxy-1-thio-β-D-galactopyranoside 11





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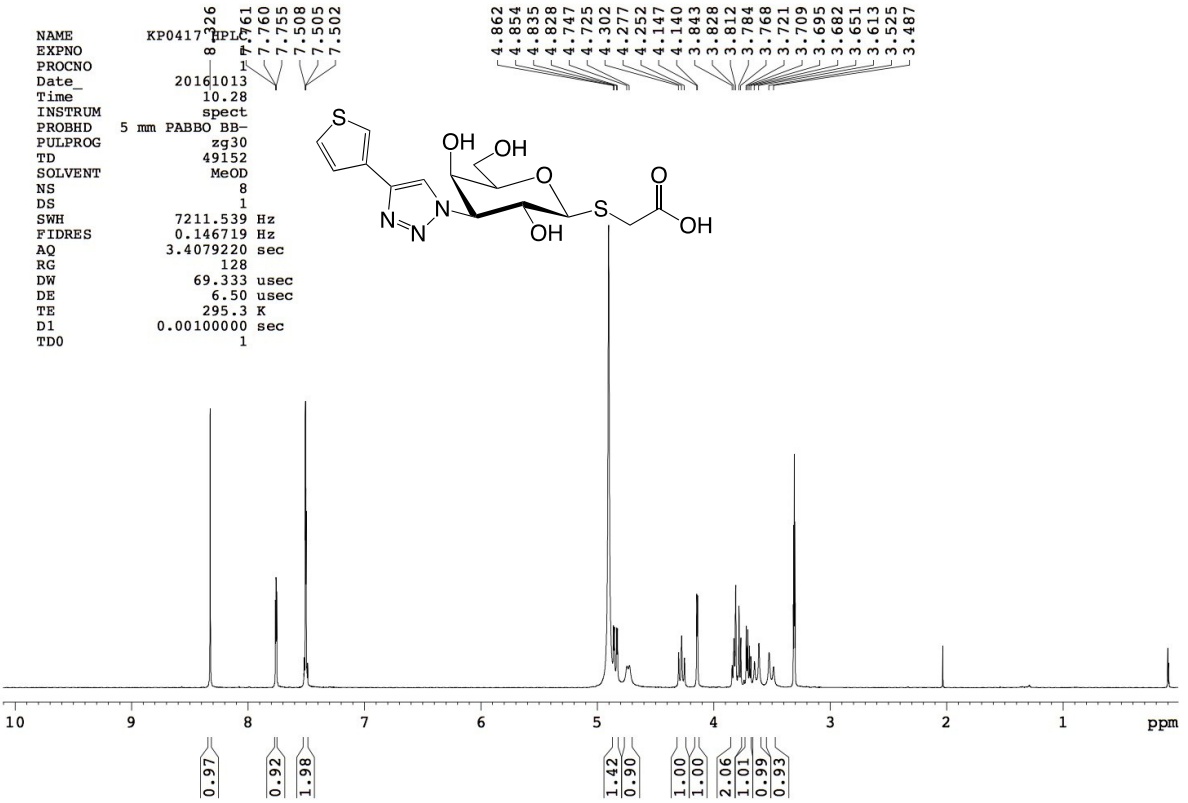

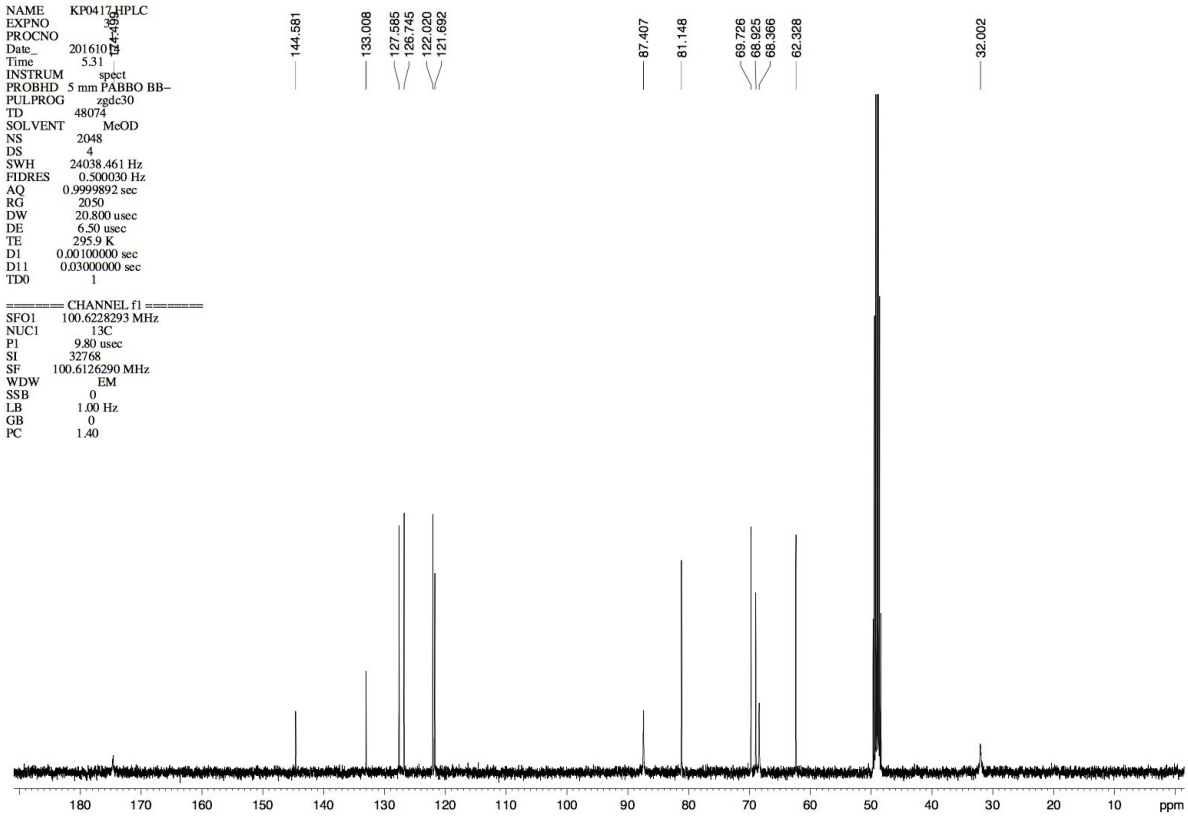

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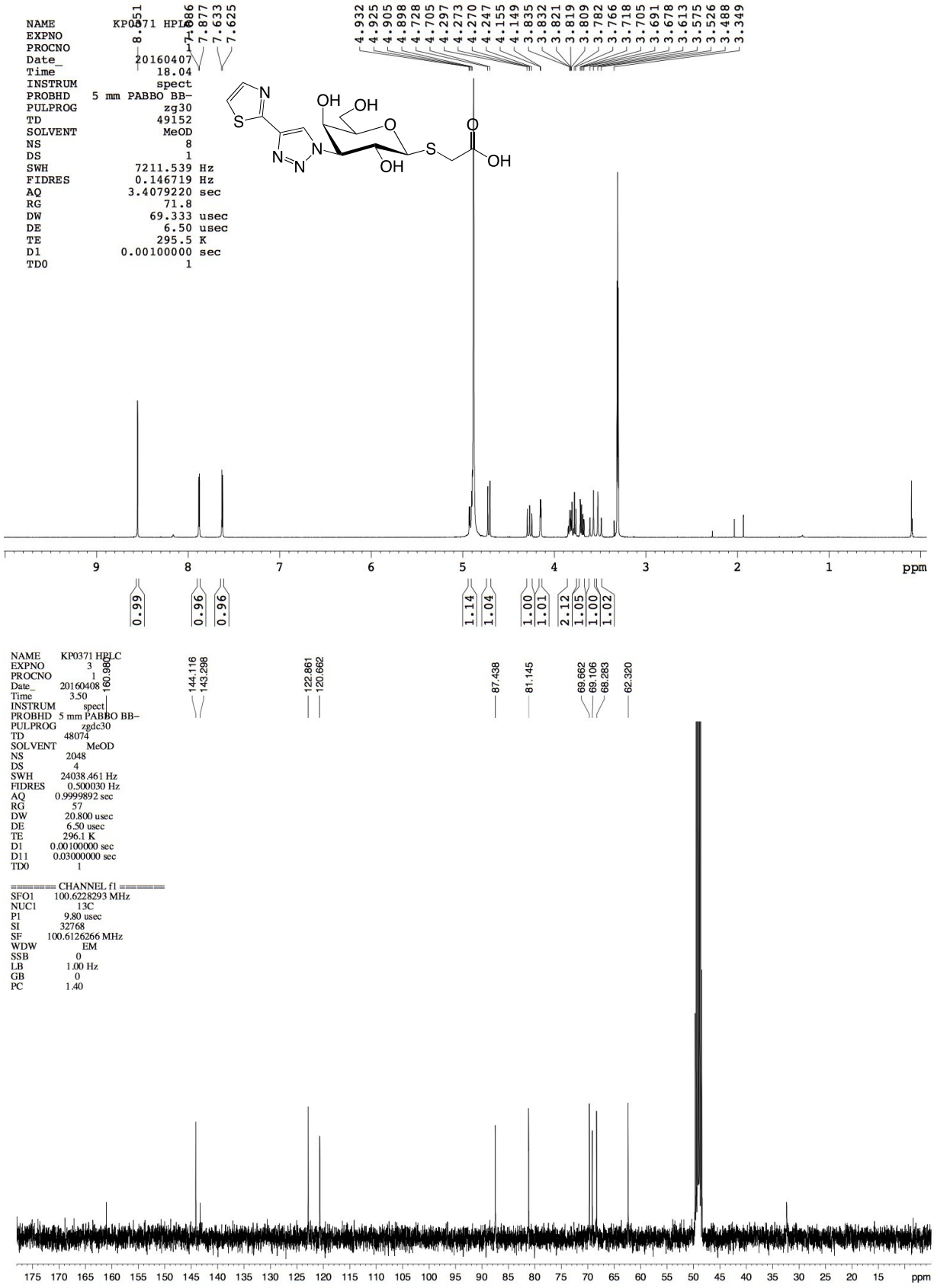

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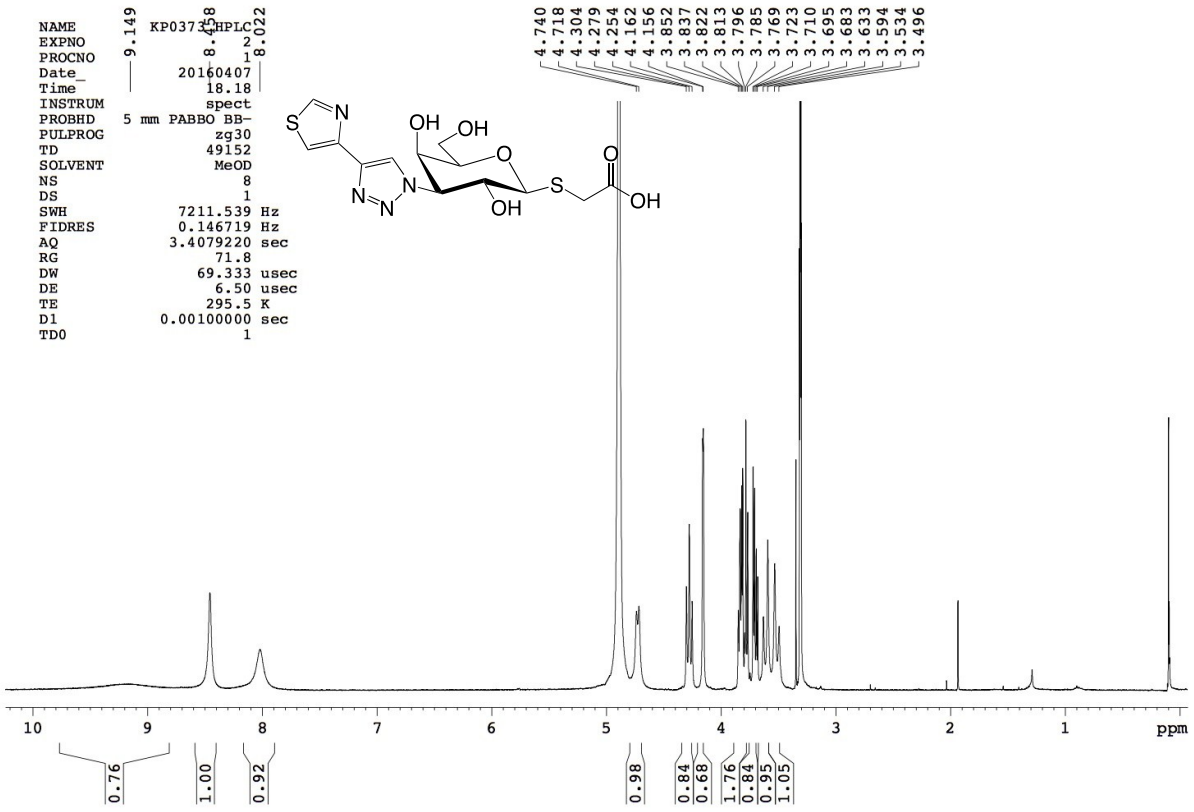
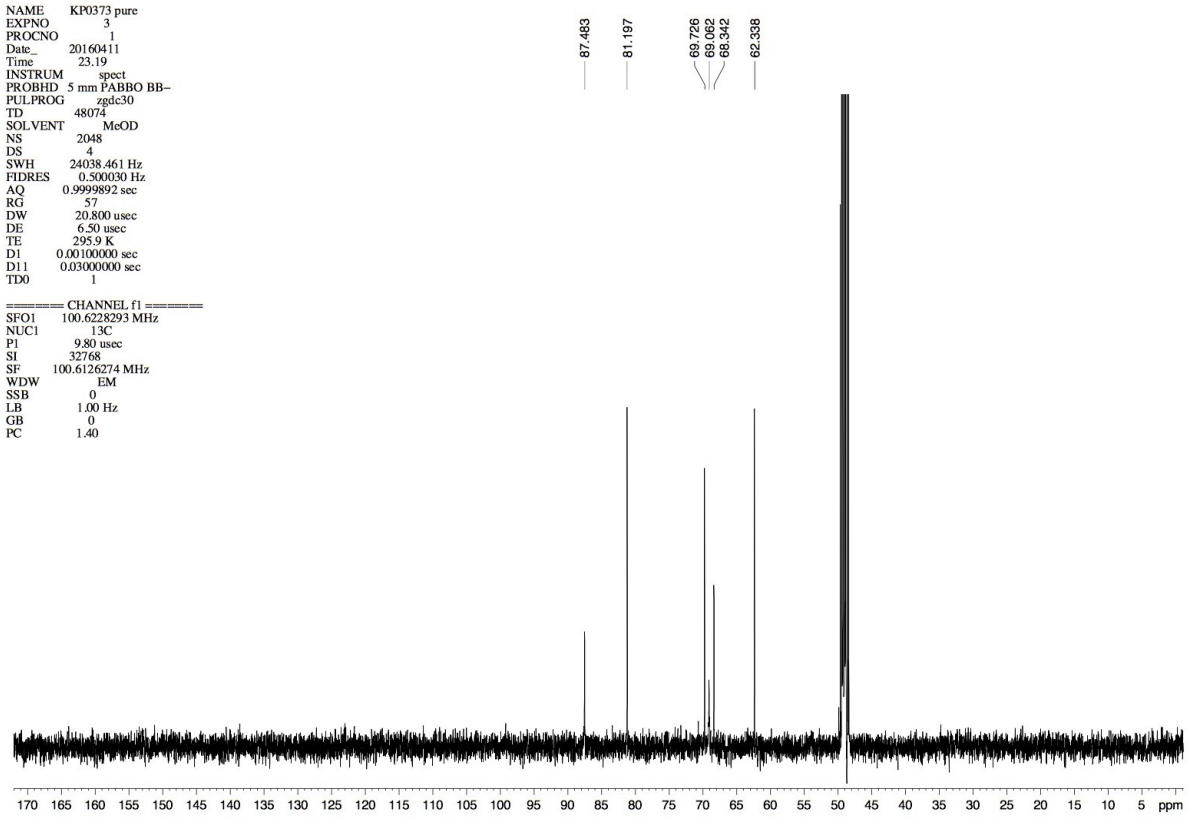
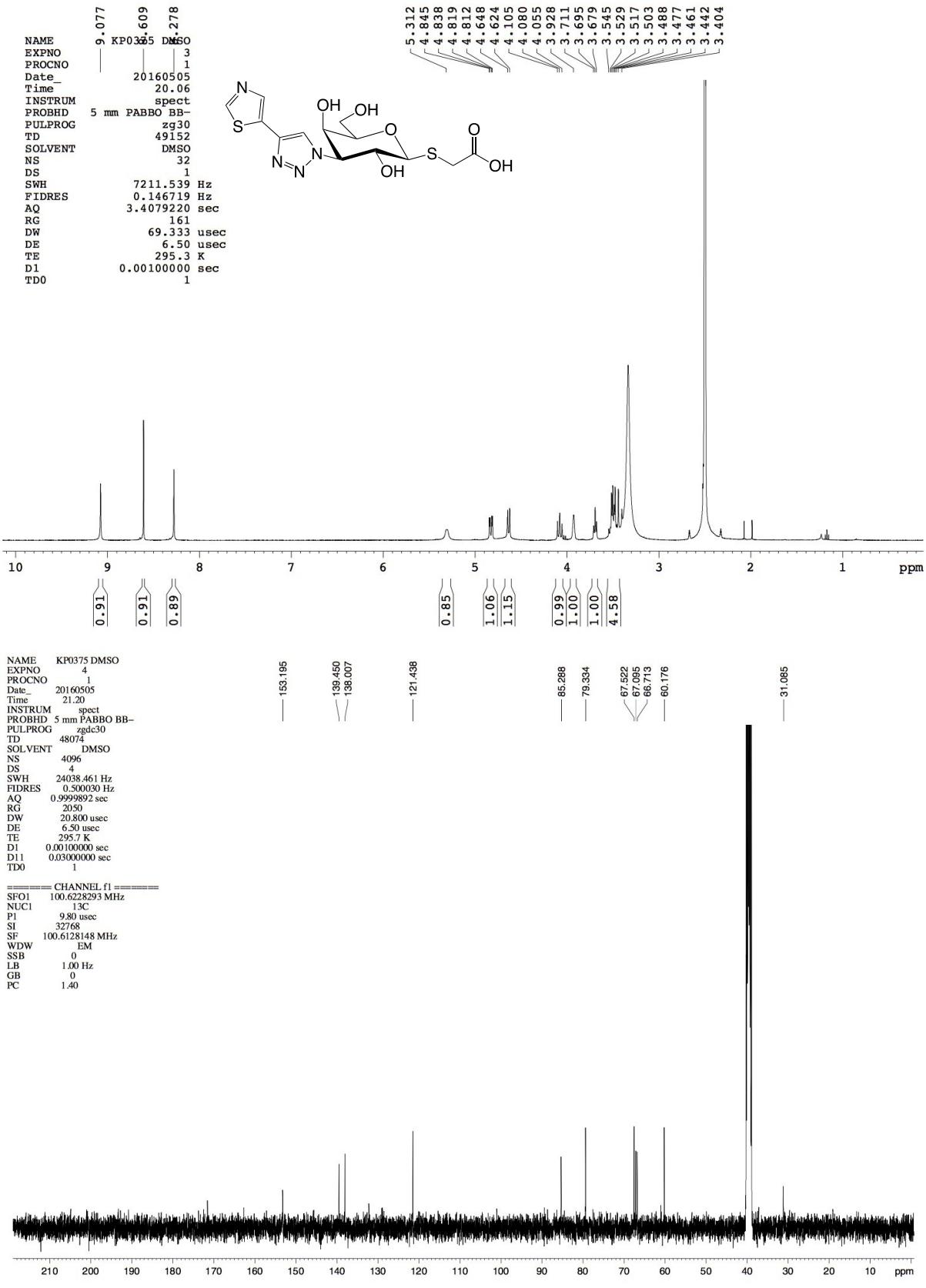
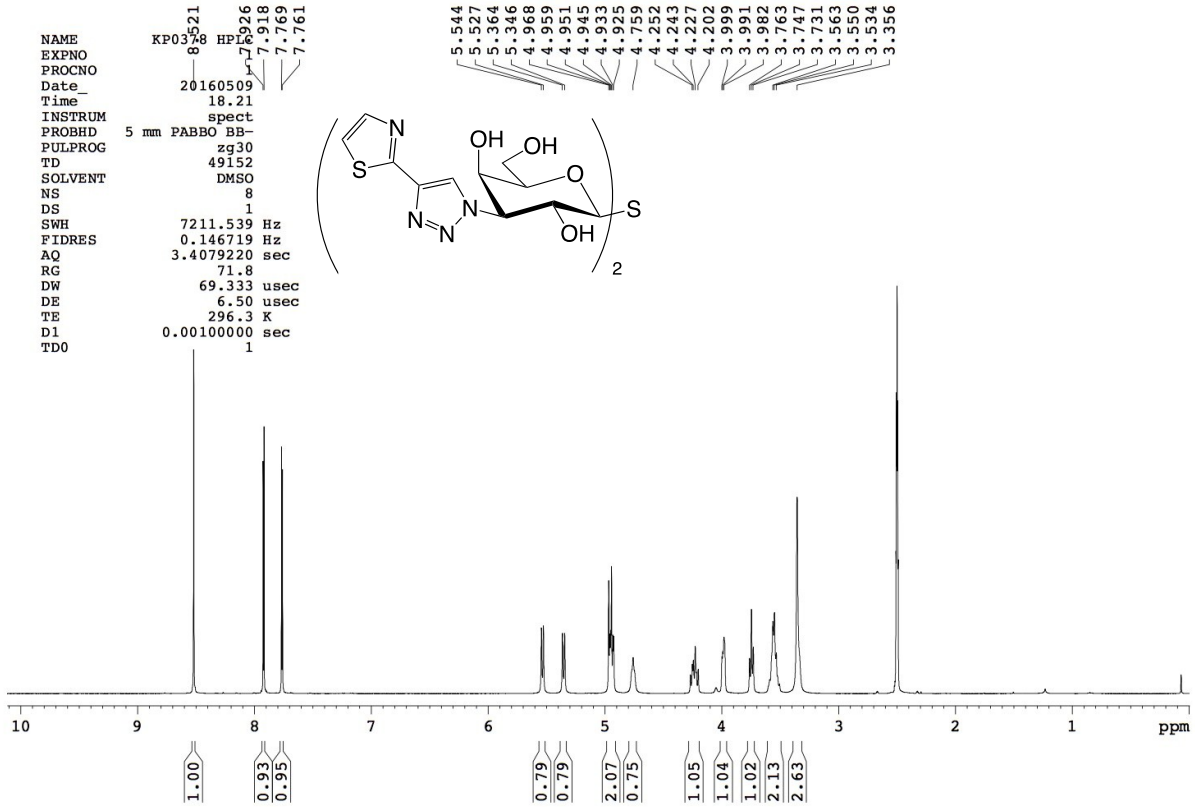


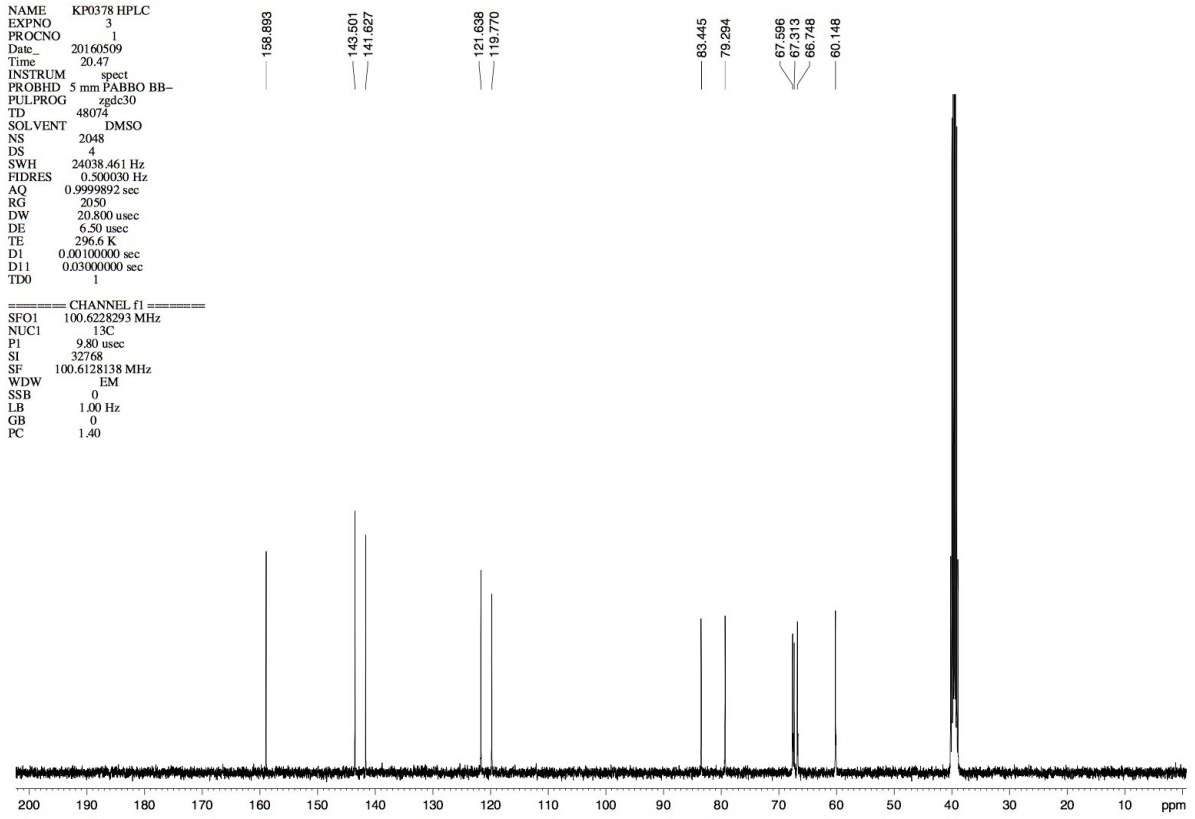


1,3-Dideoxy-3-[4-(thiazol-5-yl)-1*H*-1,2,3-triazol-1-yl]-1-thiocarboxymethyl-β-D-galactopyranoside 15

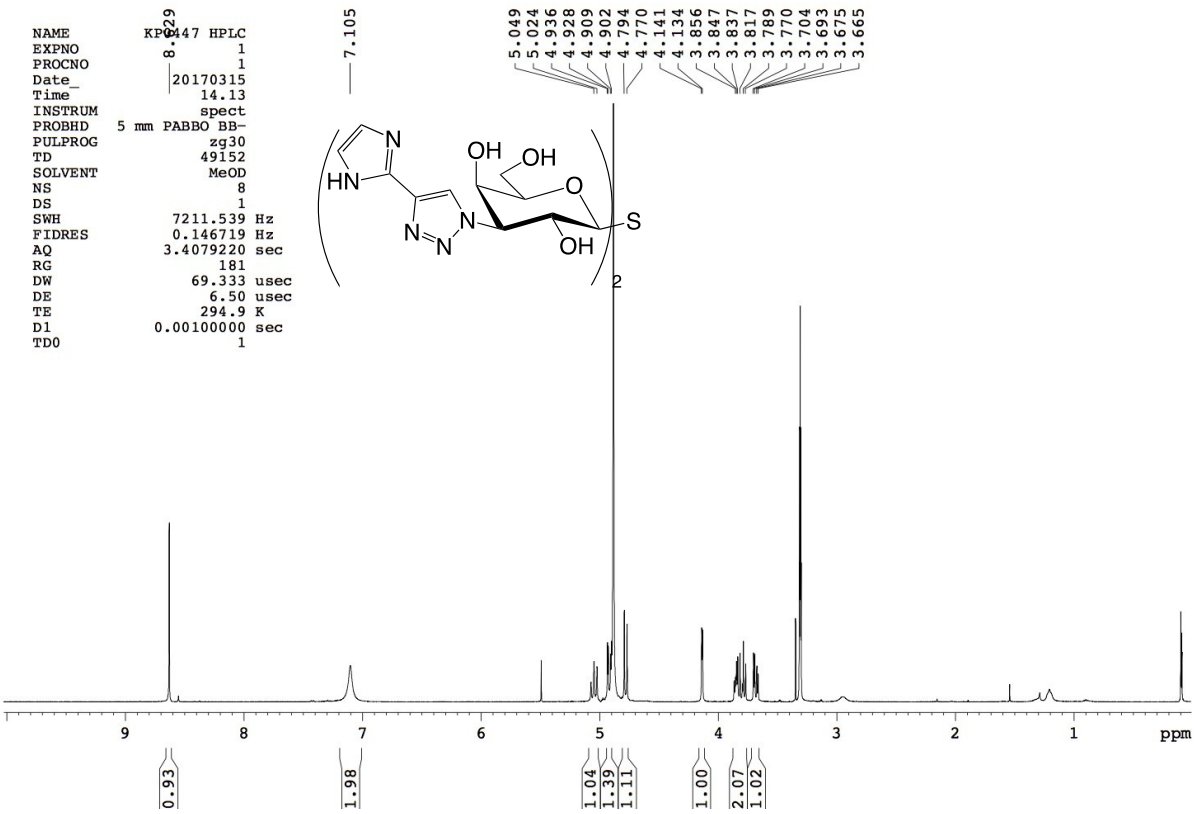


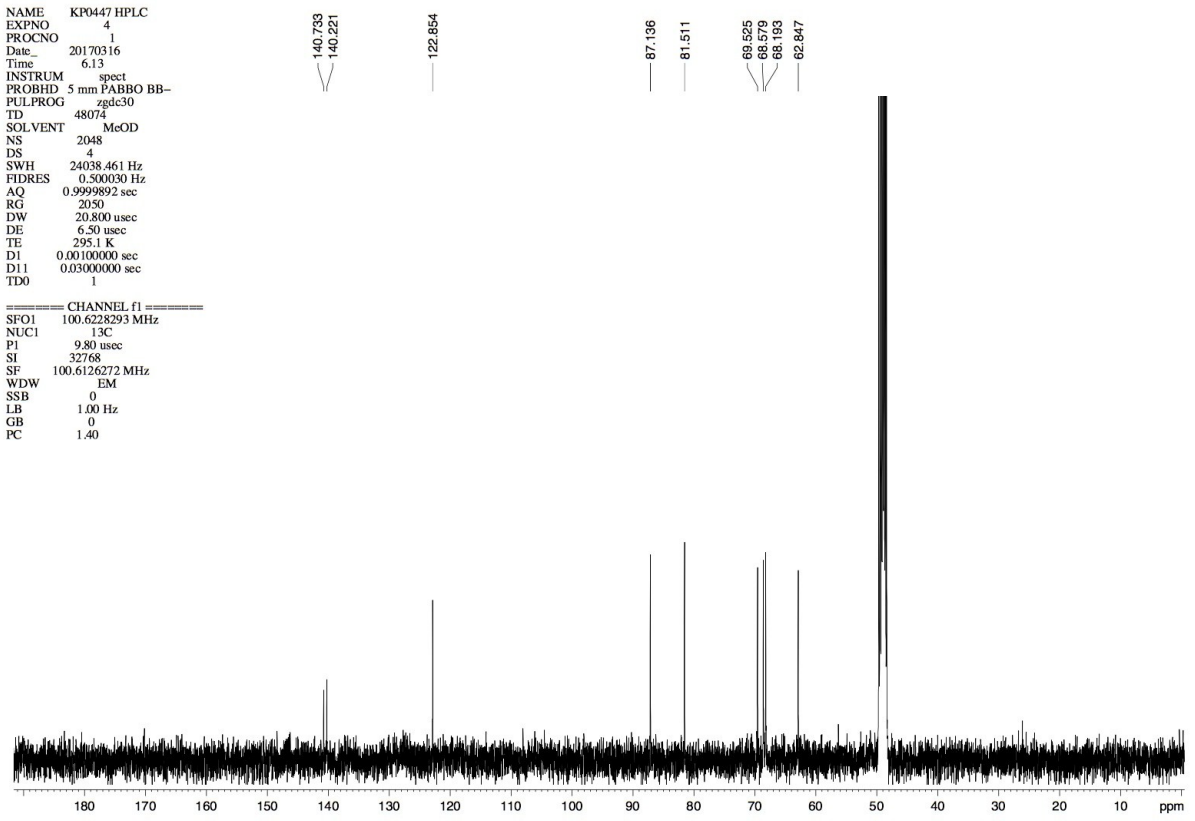
1-1’-sulfanediyl-bis-{3-deoxy-3-[4-(thiazol-2-yl)-1*H*-1,2,3-triazol-1-yl]-β-D-galactopyranoside} 19



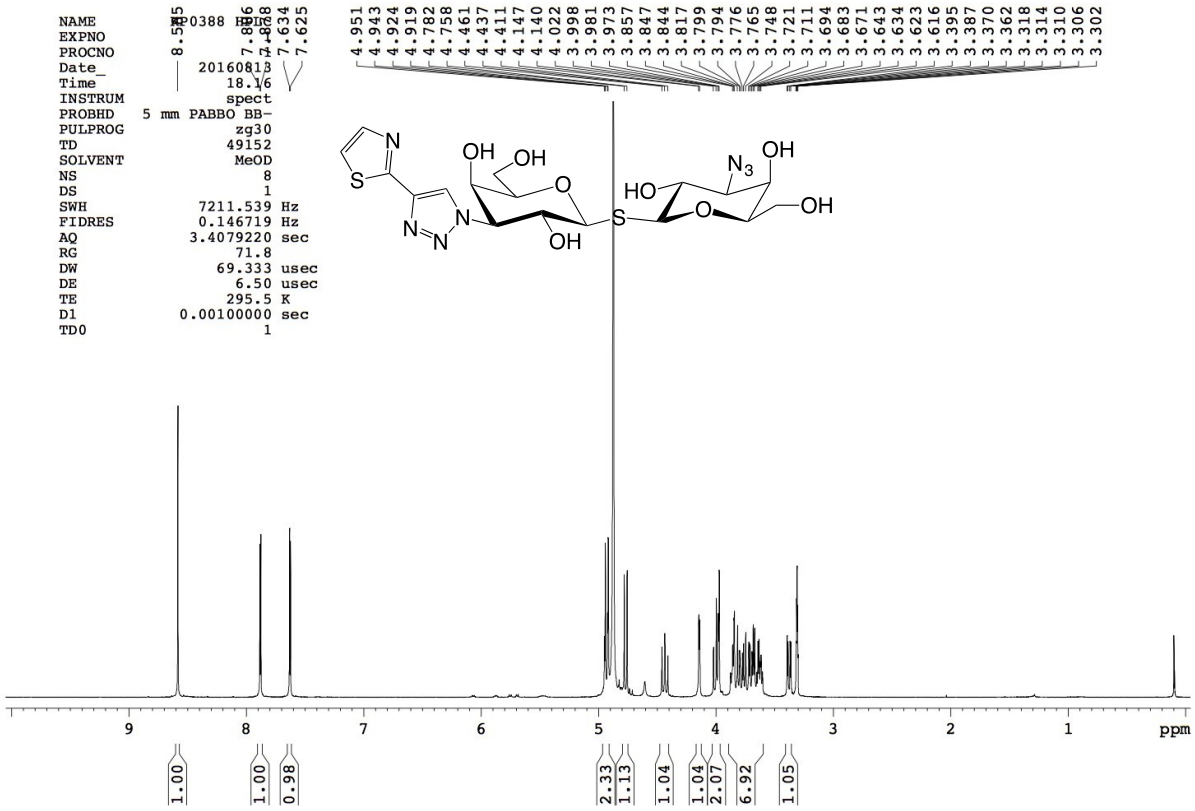


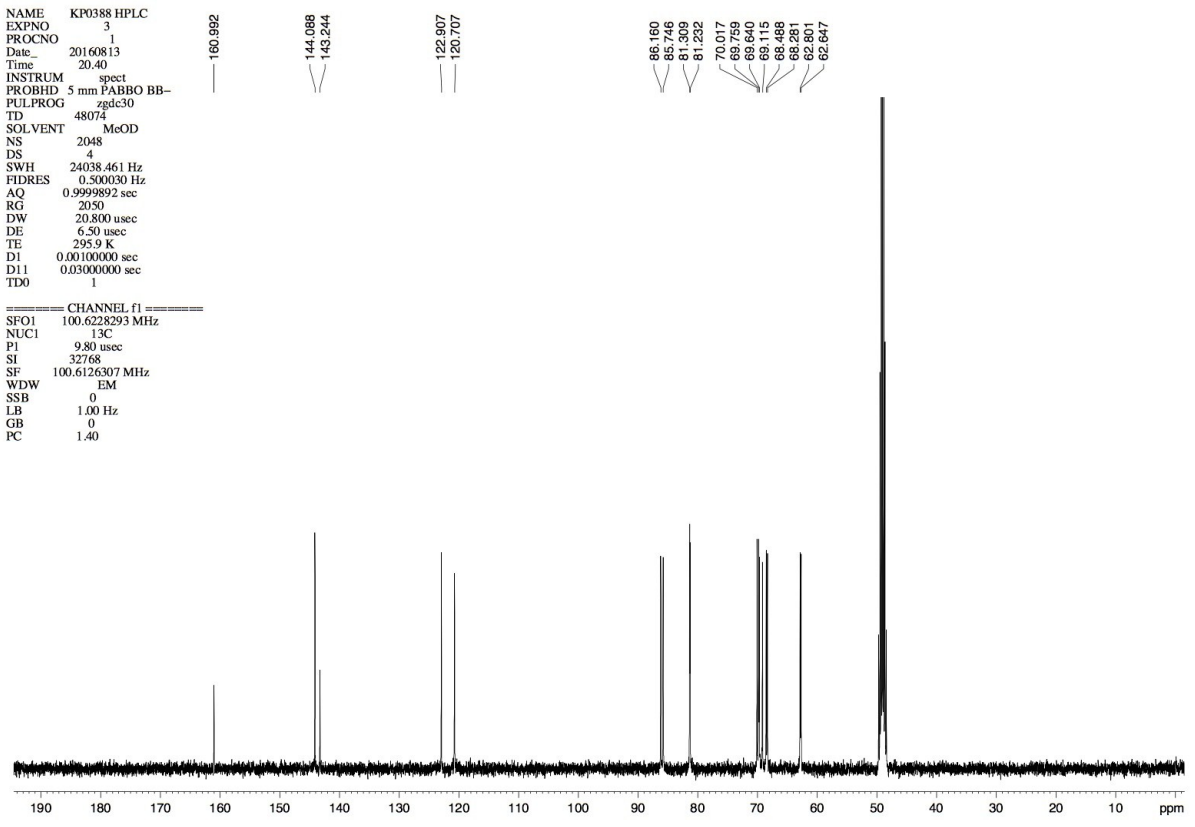
1-1'-sulfanediyl-bis-{3-deoxy-3-[4-(1*H*-imidazol-2-yl)-1*H*-1,2,3-triazol-1-yl]-β-D-galactopyranoside} 20



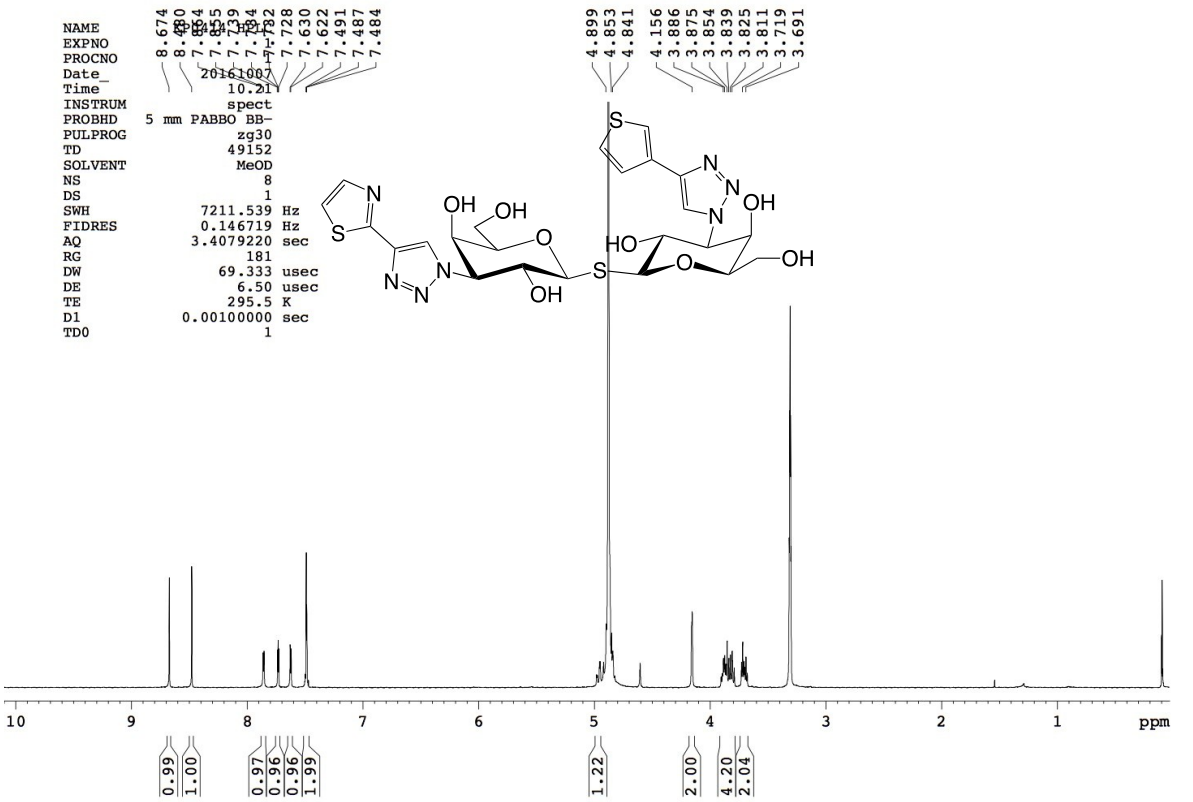


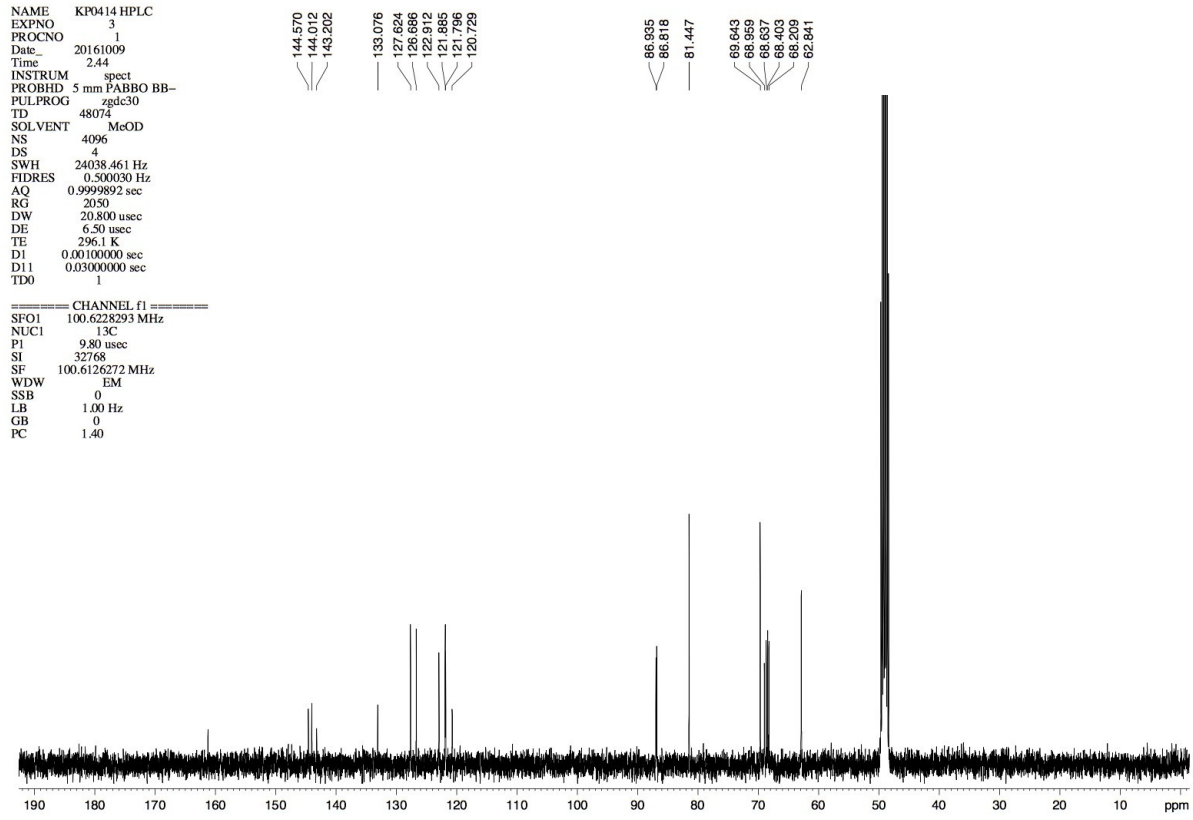
3'-Azido-3-3'-dideoxy-3-[4-(thiazol-2-yl)-1*H*-1,2,3-triazol-1-yl]-1,1'-sulfanediyl-di-β-D-galactopyranoside 21



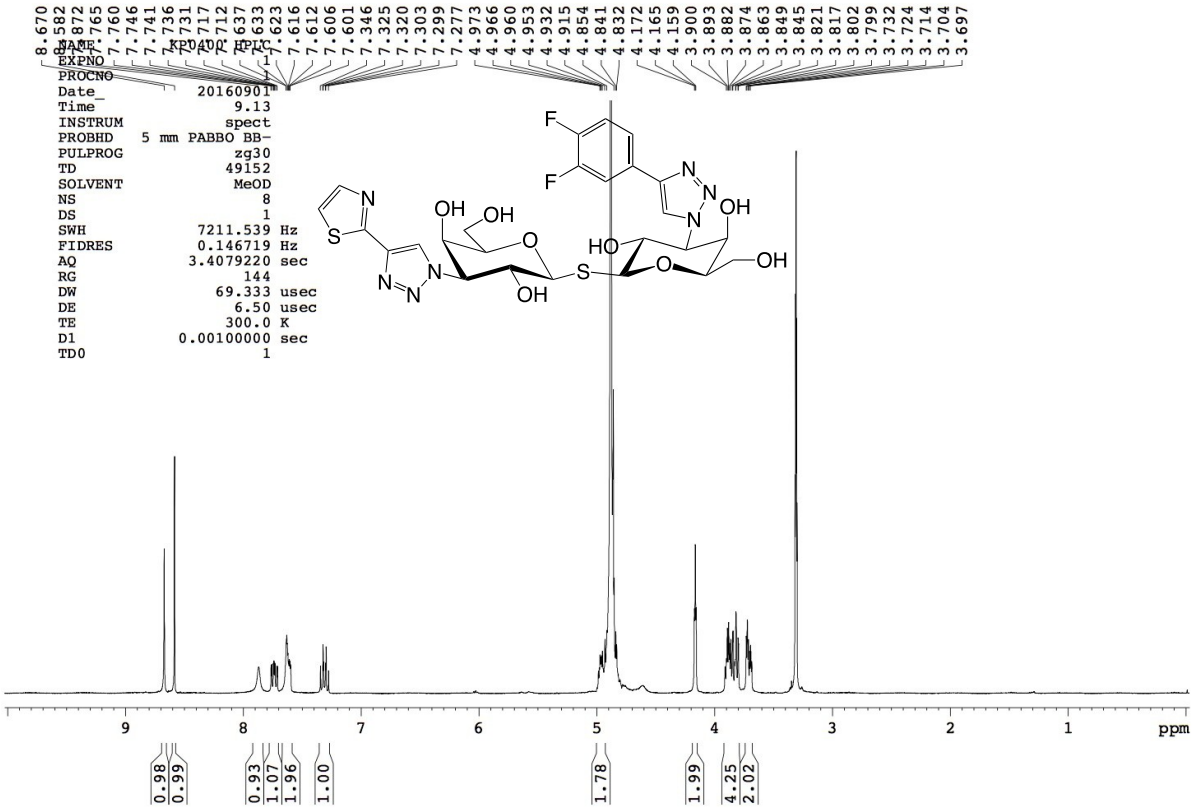


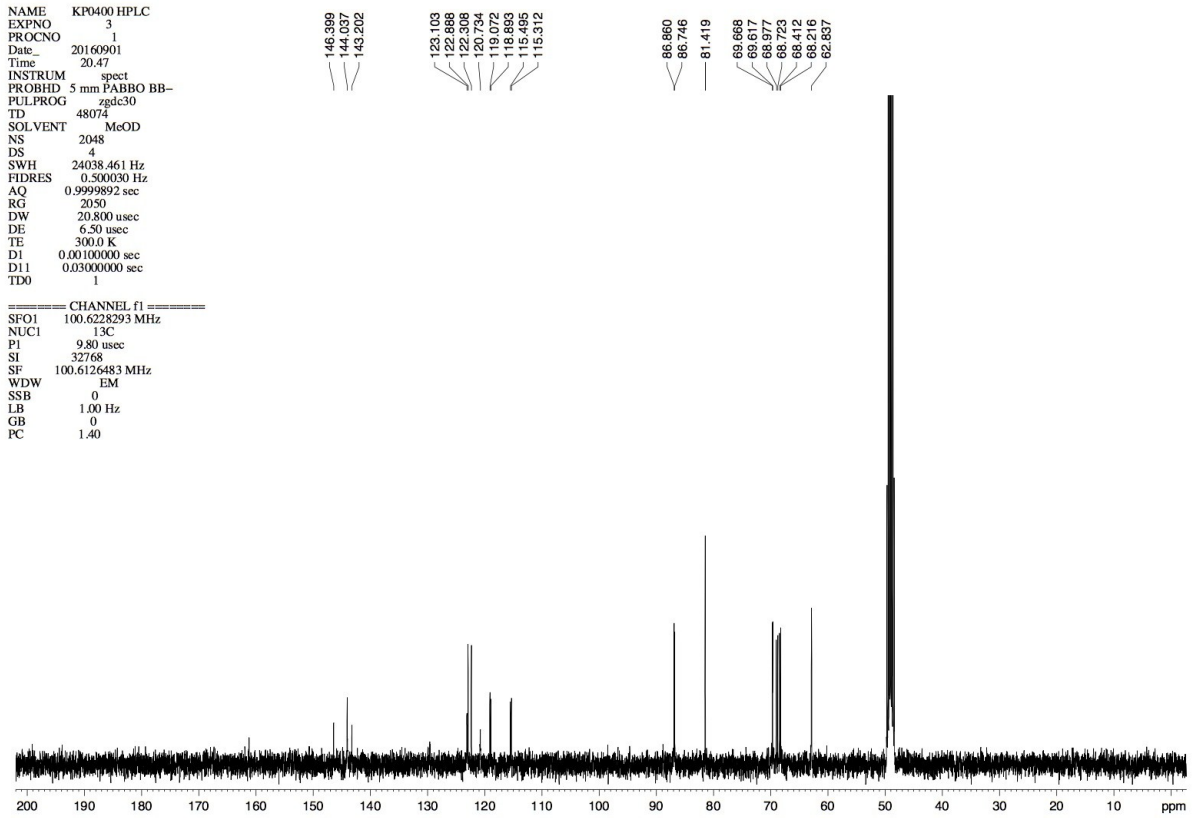
3,3'-Dideoxy-3-[4-(thiazol-2-yl)-1*H*-1,2,3-triazol-1-yl]-3'-[4-(thien-3-yl)-1*H*-1,2,3-triazol-1-yl]-1,1'-sulfanediyl-di-β-D-galactopyranoside 22



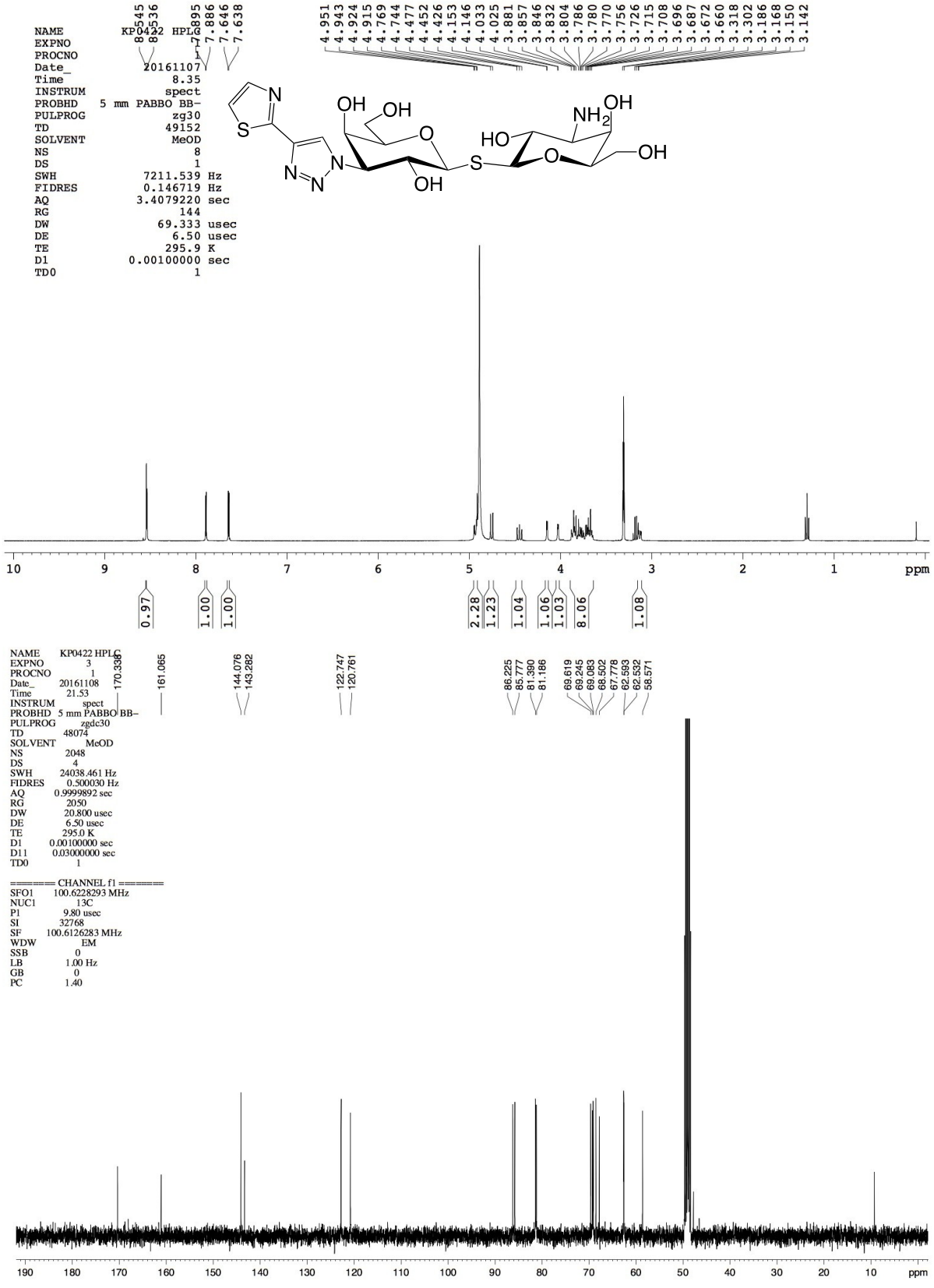


3,3'-Dideoxy-3-[4-(thiazol-2-yl)-1*H*-1,2,3-triazol-1-yl]-3'-[4-(3,4-difluorophenyl)-1*H*-1,2,3-triazol-1-yl]-1,1'-sulfanediyl-di-β-D-galactopyranoside 23

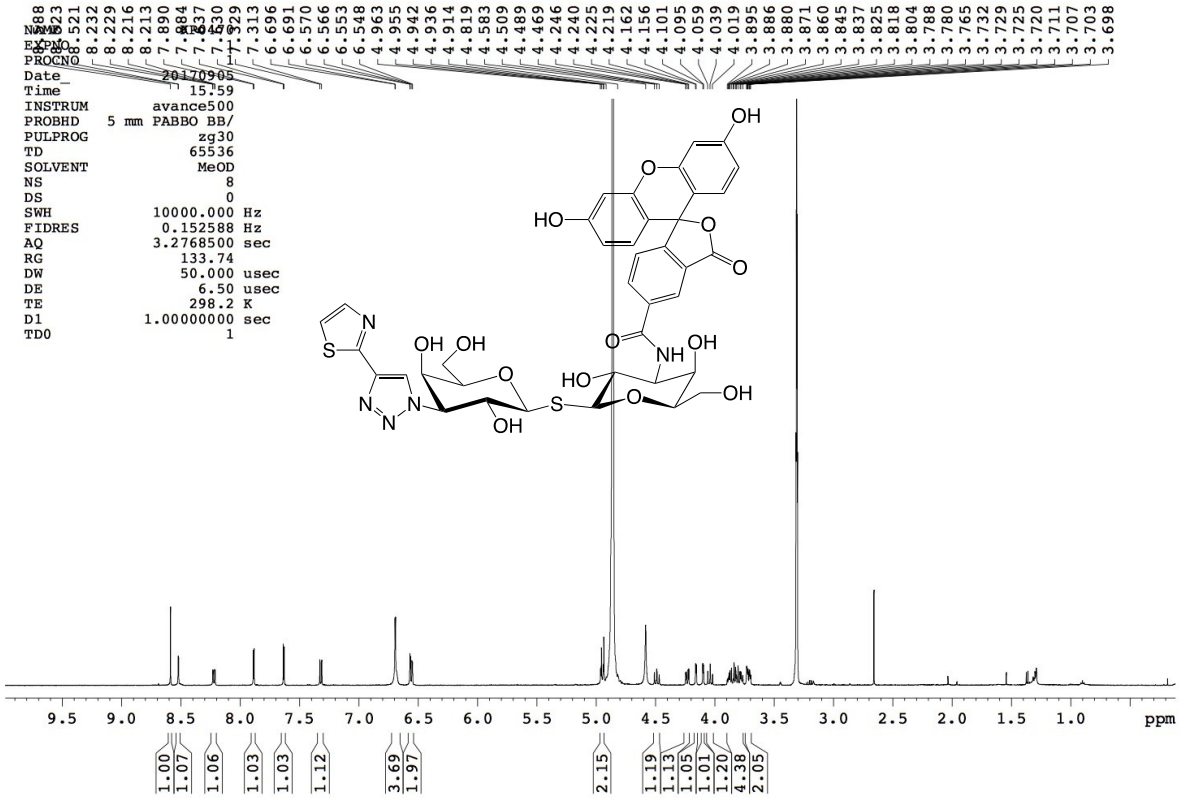


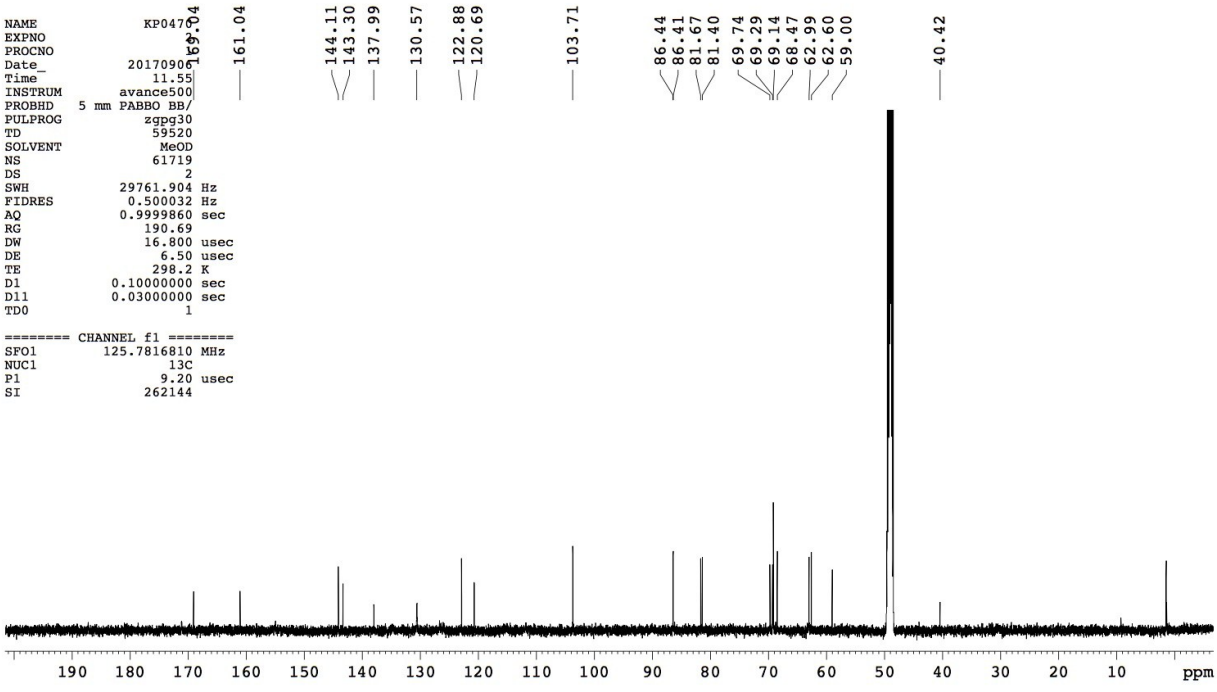


3'-Amino-3-3'-dideoxy-3-[4-(thiazol-2-yl)-1*H*-1,2,3-triazol-1-yl]-1,1'-sulfanediyl-di-β-D-galactopyranoside 24



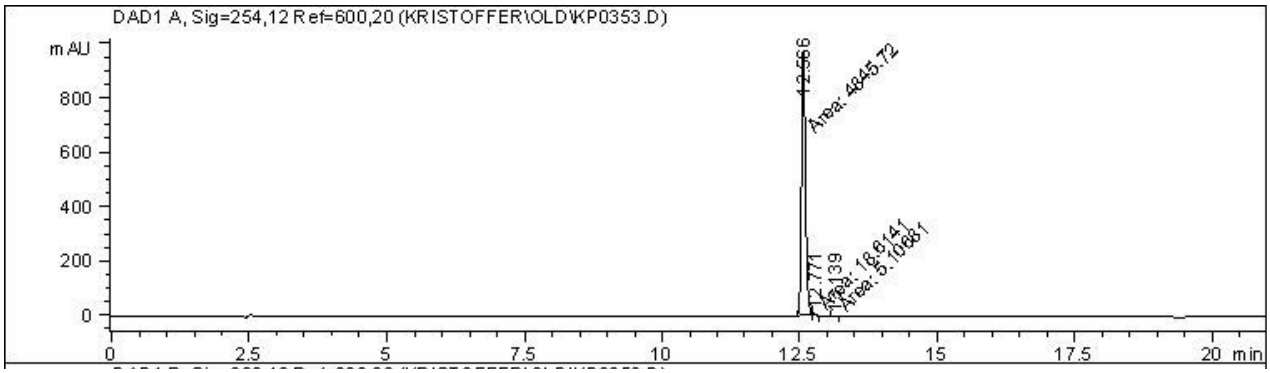
3,3'-Dideoxy-3-(fluorescein-5-yl-carbonylamino)-3'-[4-(thiazol-2-yl)-1*H*-1,2,3-triazol-1-yl]-1,1'-sulfanediyl-di-β-D-galactopyranoside 25



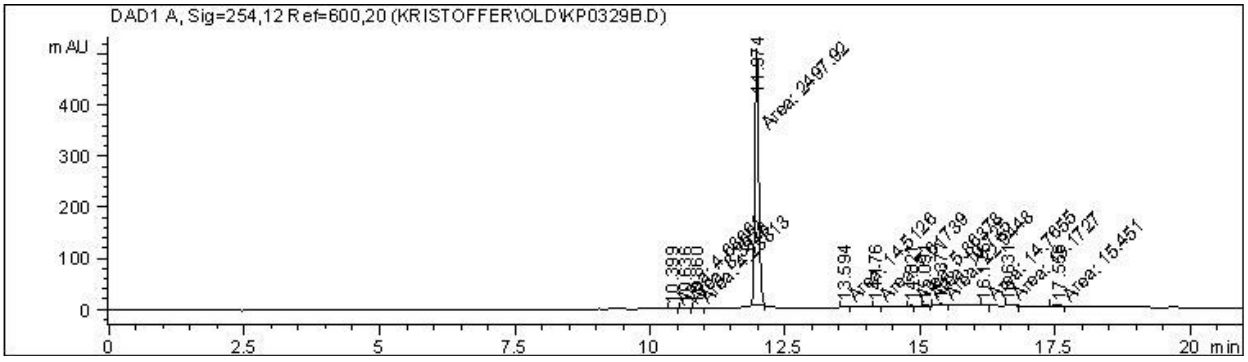


Purity chromatograms

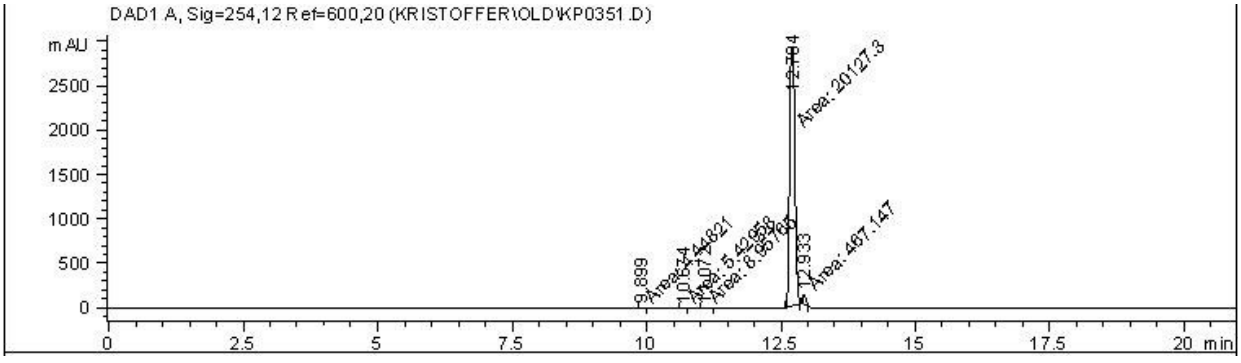
***p*-Methylphenyl 3-deoxy-3-[4-(cyclopentyl)-1*H*-1,2,3-triazol-1-yl]-1-thio-β-D-galactopyranoside 4**



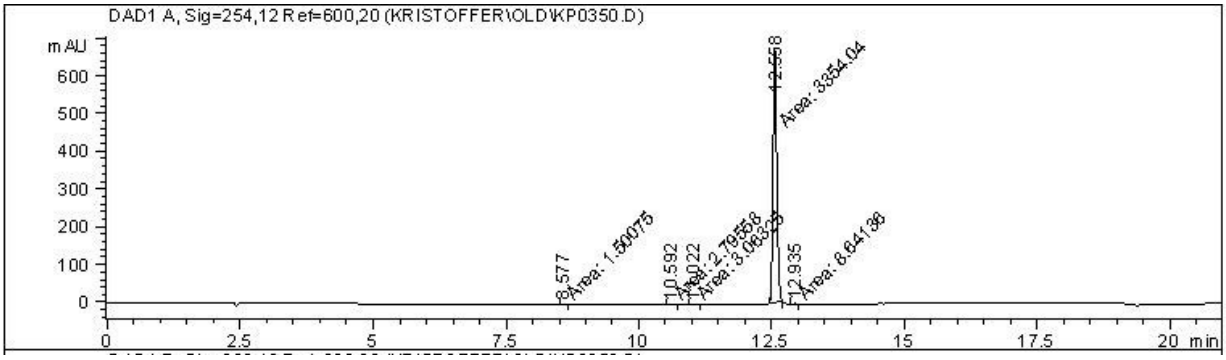
***p*-Methylphenyl 3-deoxy-3-[4-(furan-3-yl)-1*H*-1,2,3-triazol-1-yl]-1-thio-β-D-galactopyranoside 5**



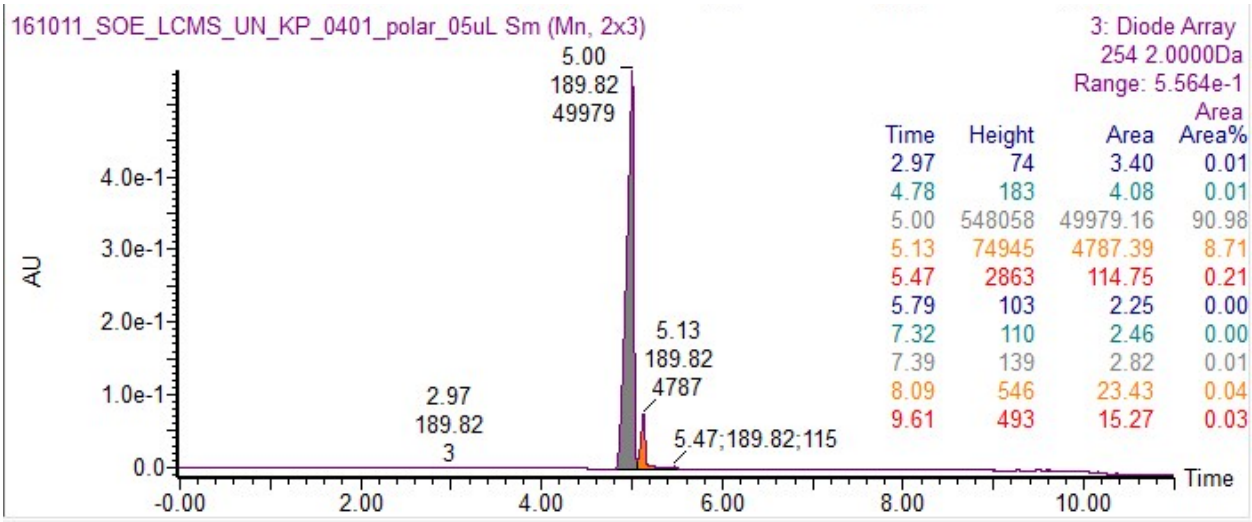
***p*-Methylphenyl 3-deoxy-3-[4-(thien-2-yl)-1*H*-1,2,3-triazol-1-yl]-1-thio-β-D-galactopyranoside 6**



***p*-Methylphenyl 3-deoxy-3-[4-(thien-3-yl)-1*H*-1,2,3-triazol-1-yl]-1-thio-β-D-galactopyranoside 7**

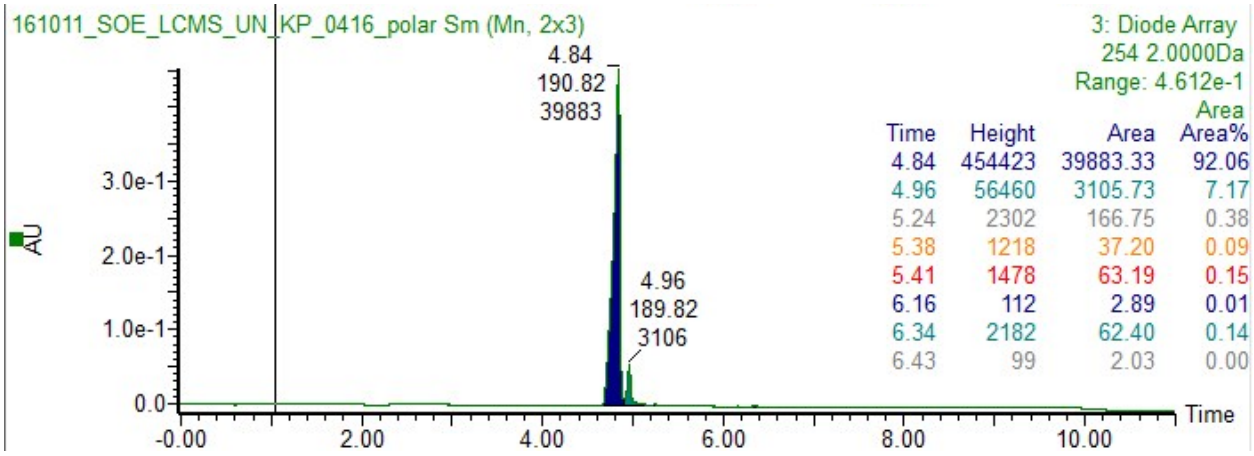


***p*-Methylphenyl 3-deoxy-3-[4-(1*H*-imidazol-2-yl)-1*H*-1,2,3-triazol-1-yl]-1-thio-β-D-galactopyranoside 8**



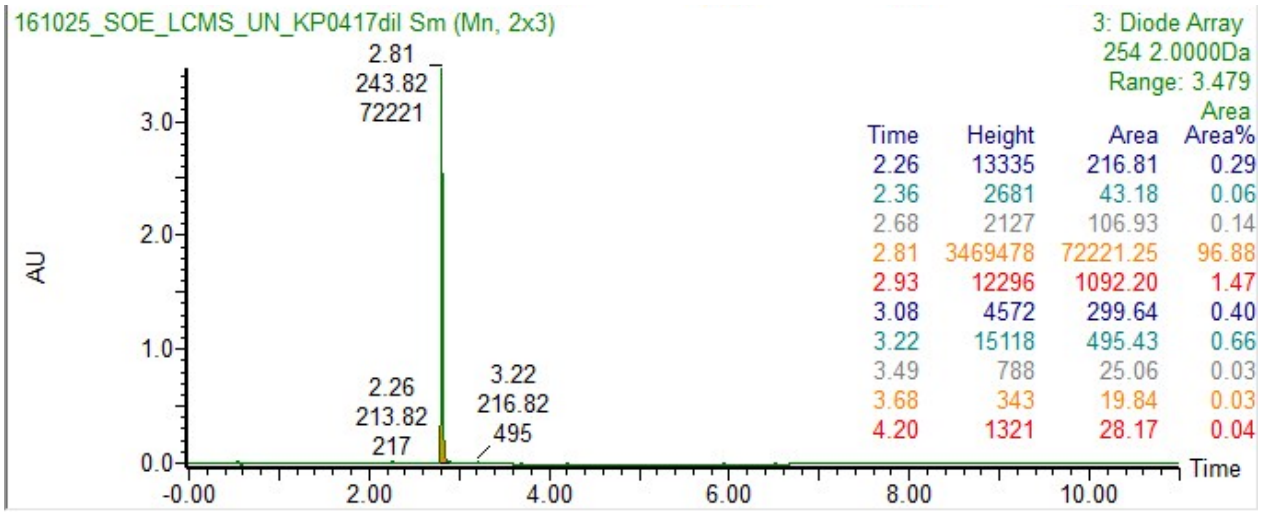
Comment: The two main peaks are isomers with exact mass corresponding to compound **8** and when the analyzed at higher temperature the two peaks merge into one, indicating an equilibrium of isomers.

***p*-Methylphenyl 3-deoxy-3-[4-(1*H*-imidazol-4-yl)-1*H*-1,2,3-triazol-1-yl]-1-thio-β-D-galactopyranoside 9**

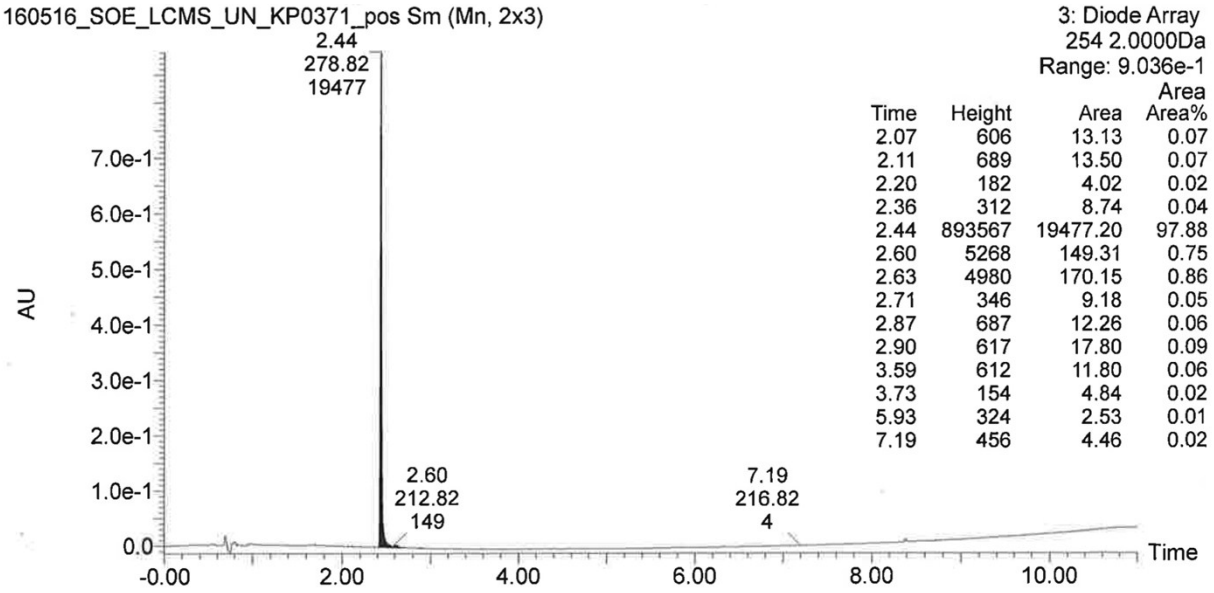


Comment: The two main peaks are isomers with exact mass corresponding to compound **8** and when the analyzed at higher temperature the two peaks merge into one, indicating an equilibrium of isomers.

1,3-Dideoxy-3-[4-(thien-3-yl)-1*H*-1,2,3-triazol-1-yl]-1-thiocarboxymethyl-β-D-galactopyranoside 12



1,3-Dideoxy-3-[4-(thiazol-2-yl)-1*H*-1,2,3-triazol-1-yl]-1-thiocarboxymethyl-β-D-galactopyranoside 13



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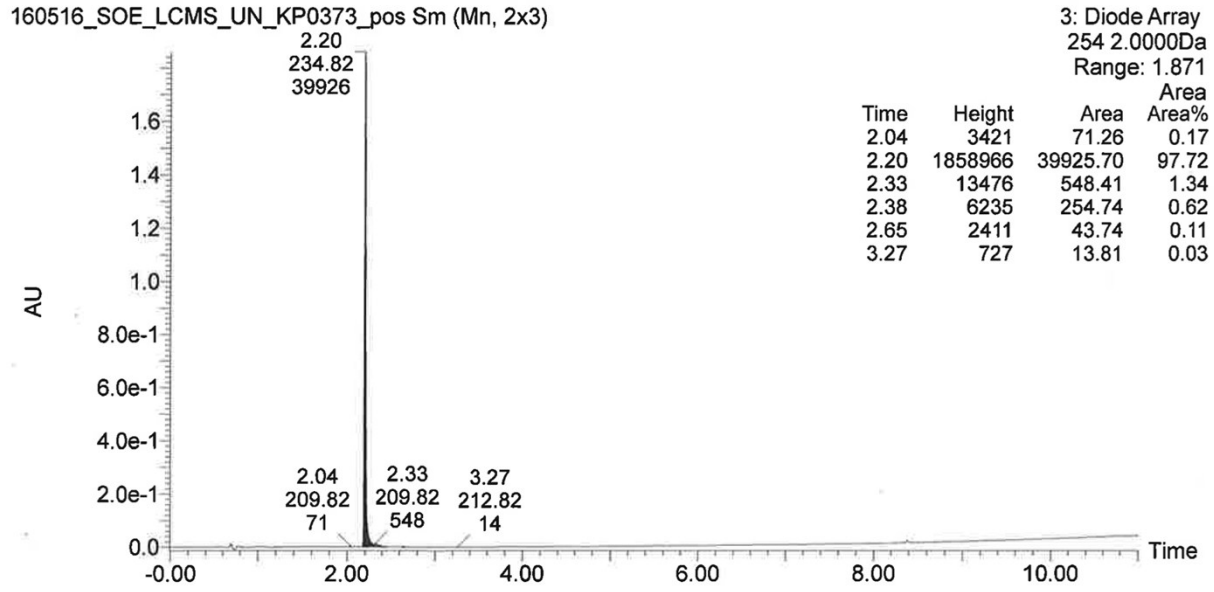
2.11	689	13.50	0.07
2.20	182	4.02	0.02
2.36	312	8.74	0.04
2.44	893567	19477.20	97.88
2.60	5268	149.31	0.75
2.63	4980	170.15	0.86
2.71	346	9.18	0.05
2.87	687	12.26	0.06
2.90	617	17.80	0.09
3.59	612	11.80	0.06
3.73	154	4.84	0.02
5.93	324	2.53	0.01
7.19	456	4.46	0.02

1,3-Dideoxy-3-[4-(thiazol-4-yl)-1*H*-1,2,3-triazol-1-yl]-1-thiocarboxymethyl-β-D-galactopyranoside 14



Time	Height	Area	Area%
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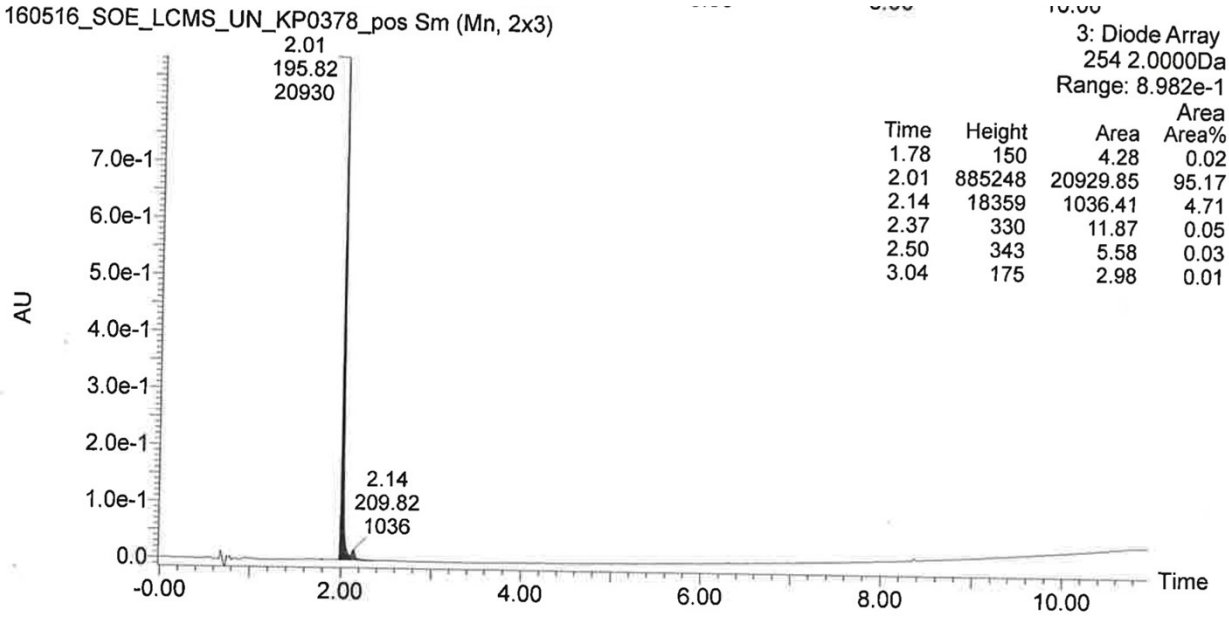
2.33	13476	548.41	1.34
2.38	6235	254.74	0.62
2.65	2411	43.74	0.11
3.27	727	13.81	0.03

1,3-Dideoxy-3-[4-(thiazol-5-yl)-1*H*-1,2,3-triazol-1-yl]-1-thiocarboxymethyl-β-D-galactopyranoside 15



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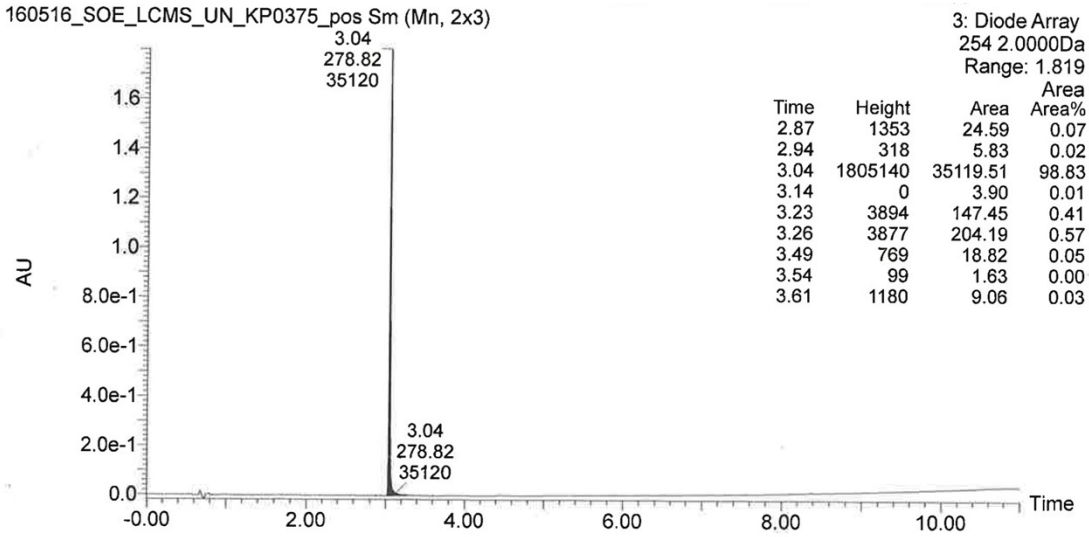
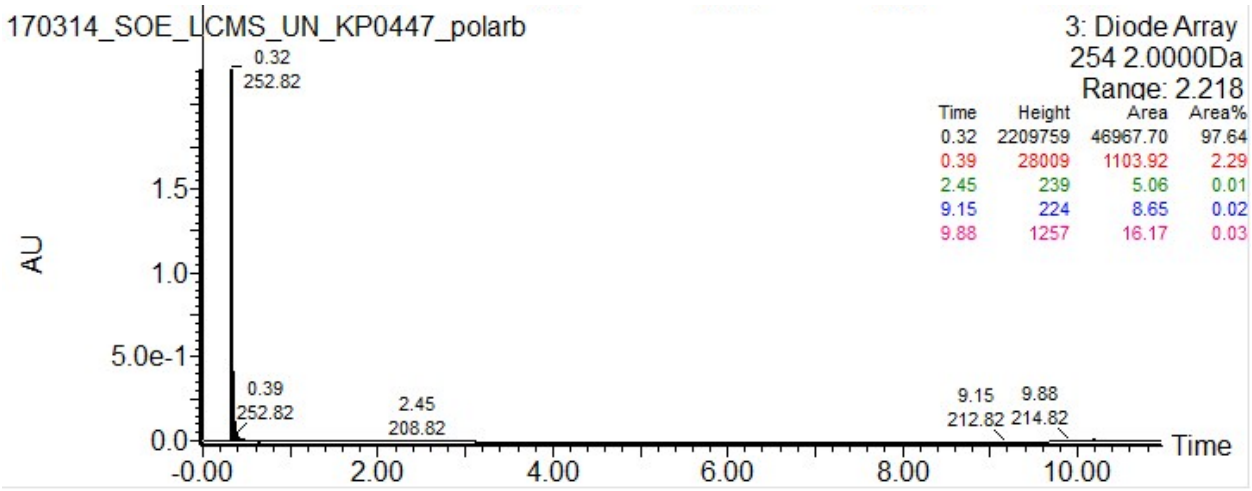
2.14	18359	1036.41	4.71
2.37	330	11.87	0.05
2.50	343	5.58	0.03
3.04	175	2.98	0.01

1-1'-sulfanediyl-bis-{3-deoxy-3-[4-(thiazol-2-yl)-1*H*-1,2,3-triazol-1-yl]-β-D-galactopyranoside} 19

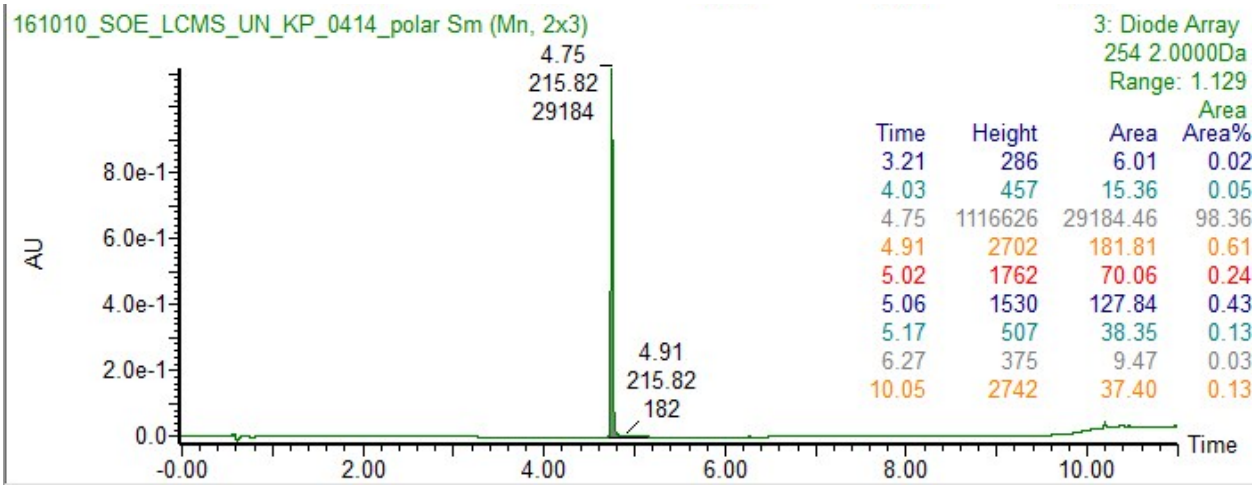


Time	Height	Area	Area%
2.87	1353	24.59	0.07
2.94	318	5.83	0.02
3.04	1805140	35119.51	98.83
3.14	0	3.90	0.01
3.23	3894	147.45	0.41
3.26	3877	204.19	0.57
3.49	769	18.82	0.05
3.54	99	1.63	0.00
3.61	1180	9.06	0.03

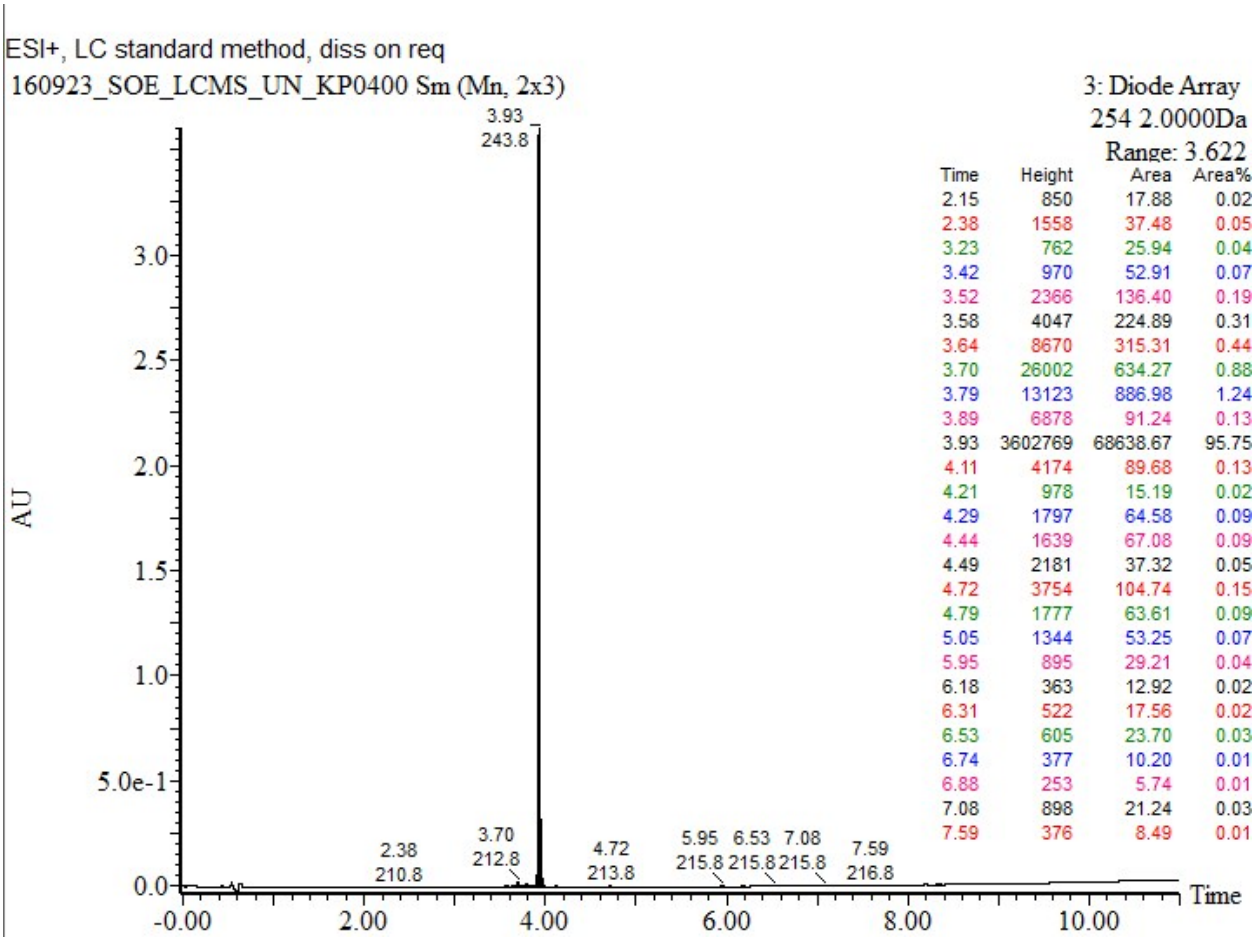
1-1'-sulfanediyl-bis-{3-deoxy-3-[4-(1*H*-imidazol-2-yl)-1*H*-1,2,3-triazol-1-yl]-β-D-galactopyranoside} 20



3,3'-Dideoxy-3-[4-(thiazol-2-yl)-1*H*-1,2,3-triazol-1-yl]-3'-[4-(thien-3-yl)-1*H*-1,2,3-triazol-1-yl]-1,1'-sulfanediyl-di-β-D-galactopyranoside 22



3,3'-Dideoxy-3-[4-(thiazol-2-yl)-1*H*-1,2,3-triazol-1-yl]-3'-[4-(3,4-difluorophenyl)-1*H*-1,2,3-triazol-1-yl]-1,1'-sulfanediyl-di-β-D-galactopyranoside 23



3,3'-Dideoxy-3-(fluorescein-5-yl-carbonylamino)-3'-[4-(thiazol-2-yl)-1*H*-1,2,3-triazol-1-yl]-1,1'-sulfanediyl-di-β-D-galactopyranoside 25

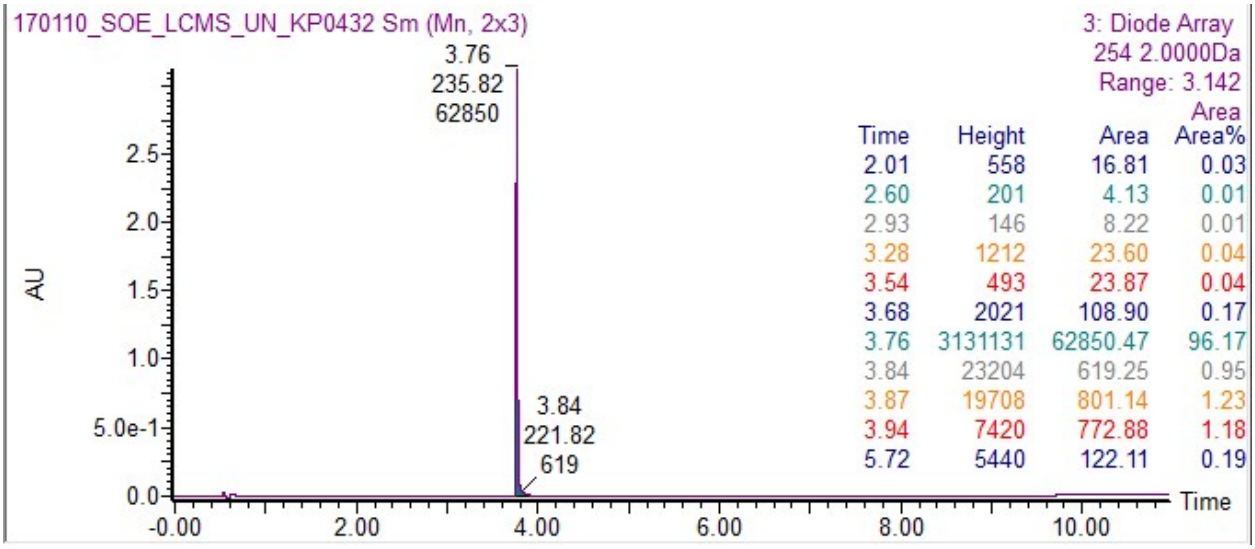


Figure S1. Fluorescence polarization titration of galectin-1 with fluorescent probe molecule **25**.

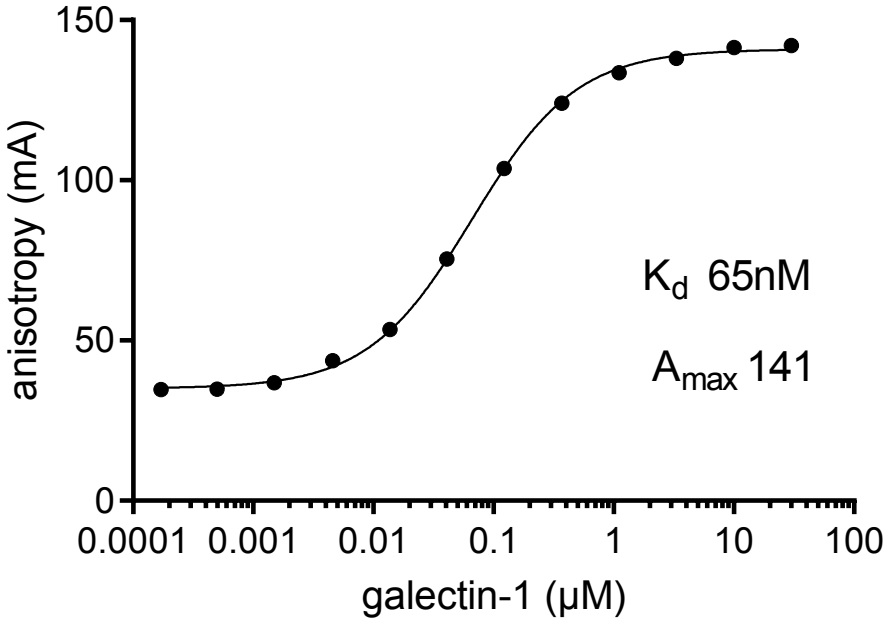


Figure S2. Dose response curves compounds **1**, **6-7**, **12-14** and **19** in a MTT assay.

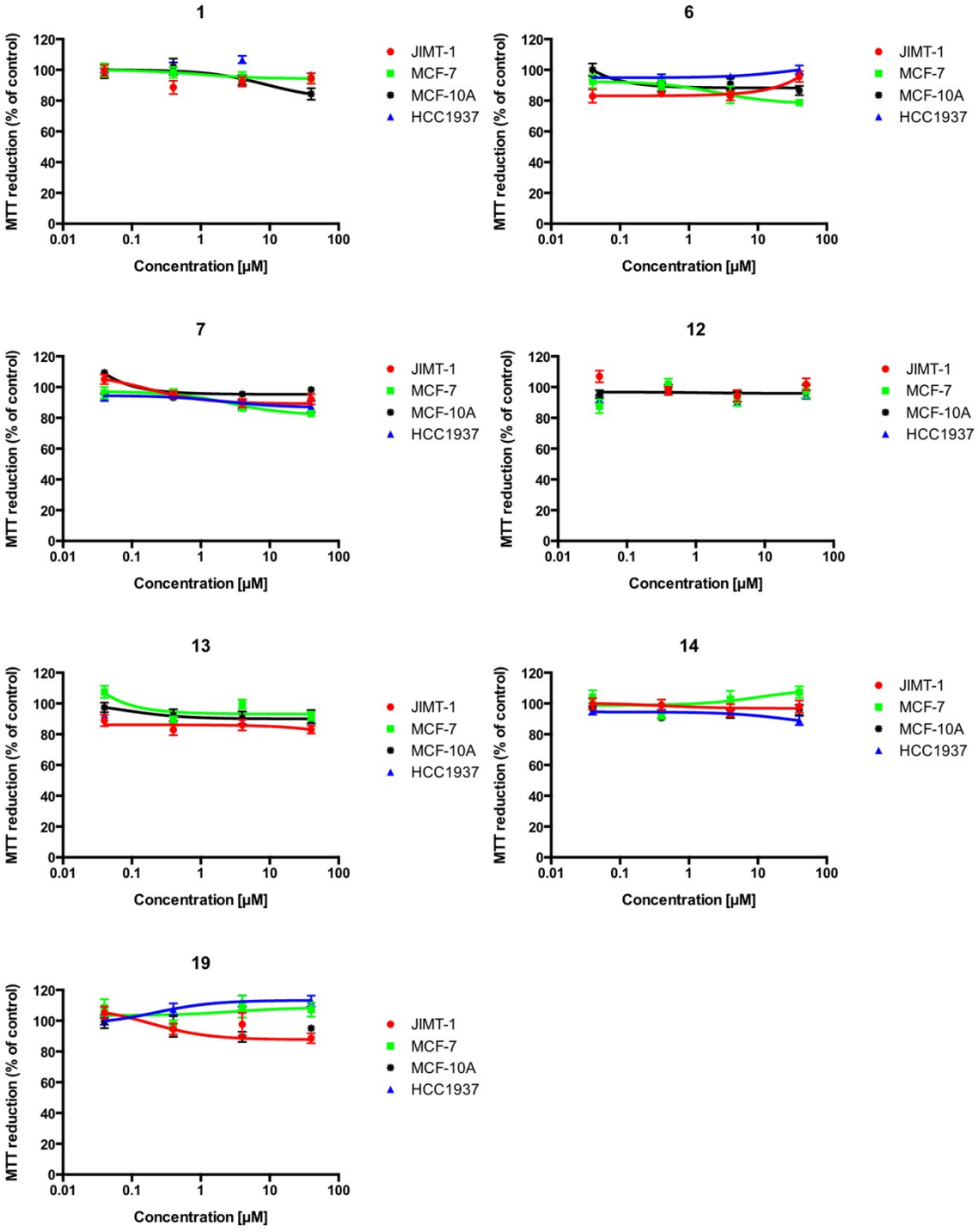


Table S1. Crystallographic data and refinement statistics for galectin-1 in complex with **1**.

Ligand	**1**
PDB code	6F83
Wavelength	1.5418
Resolution range (Å)	40.58–2.20 (2.279–2.20)
Space group	$P2_12_12_1$
Cell dimensions *a*, *b*, *c* (Å)	44.4, 58.7, 112.4
Total reflections	25 972 (1 310)
Unique reflections	14 260 (872)
Completeness (%)	91.71 (57.00)
Multiplicity	1.8 (1.5)
Wilson B-factor	27.85
R_{merge}	0.047 (0.407)
R_{meas}	0.066 (0.575)
R_{pim}	0.047 (0.407)
$I / \sigma I$	12.08 (1.80)
$CC_{1/2}$	0.998 (0.68)
CC*	0.999 (0.9)
Reflections used in refinement	14 253 (871)
Reflections used for *R*free	712 (38)
R_{work}	0.216 (0.289)
R_{free}	0.252 (0.324)
CC_{work}	0.964 (0.791)
CC_{free}	0.942 (0.650)
No. of non-hydrogen atoms	2 315
macromolecules	2 156
ligands	82
solvent	77
Protein residues	268
RMS bond length (Å)	0.012

RMS bond angle (°)	1.59
Ramachandran favored (%)	97.01
Ramachandran allowed (%)	2.56
Ramachandran outliers (%)	0.43
Rotamer outliers (%)	5.09
Clashscore	5.32
Average *B*-factors (Å^2)	16.0
macromolecules	13.8
ligands	55.0
solvent	35.3
Number of TLS groups	2

Statistics for the highest-resolution shell are shown in parentheses