

On the Emerging Role of Chemistry in the Fashioning of Biologics: Synthesis of a Bidomainal Fucosyl GM1-Based Vaccine, for the Treatment of Small Cell Lung Cancer

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Supporting Information

Contents

General Information	2
Compound 4 (¹ H and ¹³ C NMR)	3-4
Compound 5 (¹ H and ¹³ C NMR)	5-6
Compound 7 (¹ H NMR and LC/MS data)	7-9
Compound 8a (¹ H NMR and LC/MS data)	10-12
Compound 8 (LC/MS data)	13-14
Compound 9 (¹ H NMR and LC/MS data)	15-17
Compound 10b (¹ H NMR and LC/MS data)	18-20
Compound 10 (LC/MS data)	21-22
Compound 11a (¹ H NMR and LC/MS data)	23-25
Compound 11 (¹ H NMR and LC/MS data)	26-28

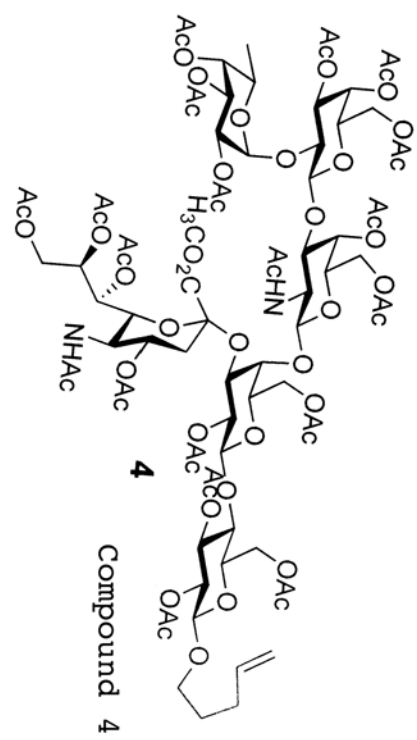
General Information

All reactions were carried out under an atmosphere of dried nitrogen in flame-dried or oven-dried glassware with magnetic stirring, unless otherwise noted. Air-sensitive reagents and solutions were transferred *via* syringe or cannula and were introduced to the apparatus through rubber septa. Reactions were cooled via external cooling baths: ice water (0 °C), dry ice-acetone (−78 °C), ice-acetone (−10 °C), or immersion cooler (−20 → −80 °C). Heating was accomplished by heating mantle or silicon oil bath using a temperature controller. Analytical thin layer chromatography (TLC) was performed on 0.25 mm silica gel 60-F plates. Visualization was accomplished with UV light and exposure to aqueous ceric ammonium molybdate (CAM) solution or anisaldehyde followed by heating. Flash chromatography was performed using silica gel 60 (230-240 mesh). Solvents for extraction and chromatography were HPLC grade.

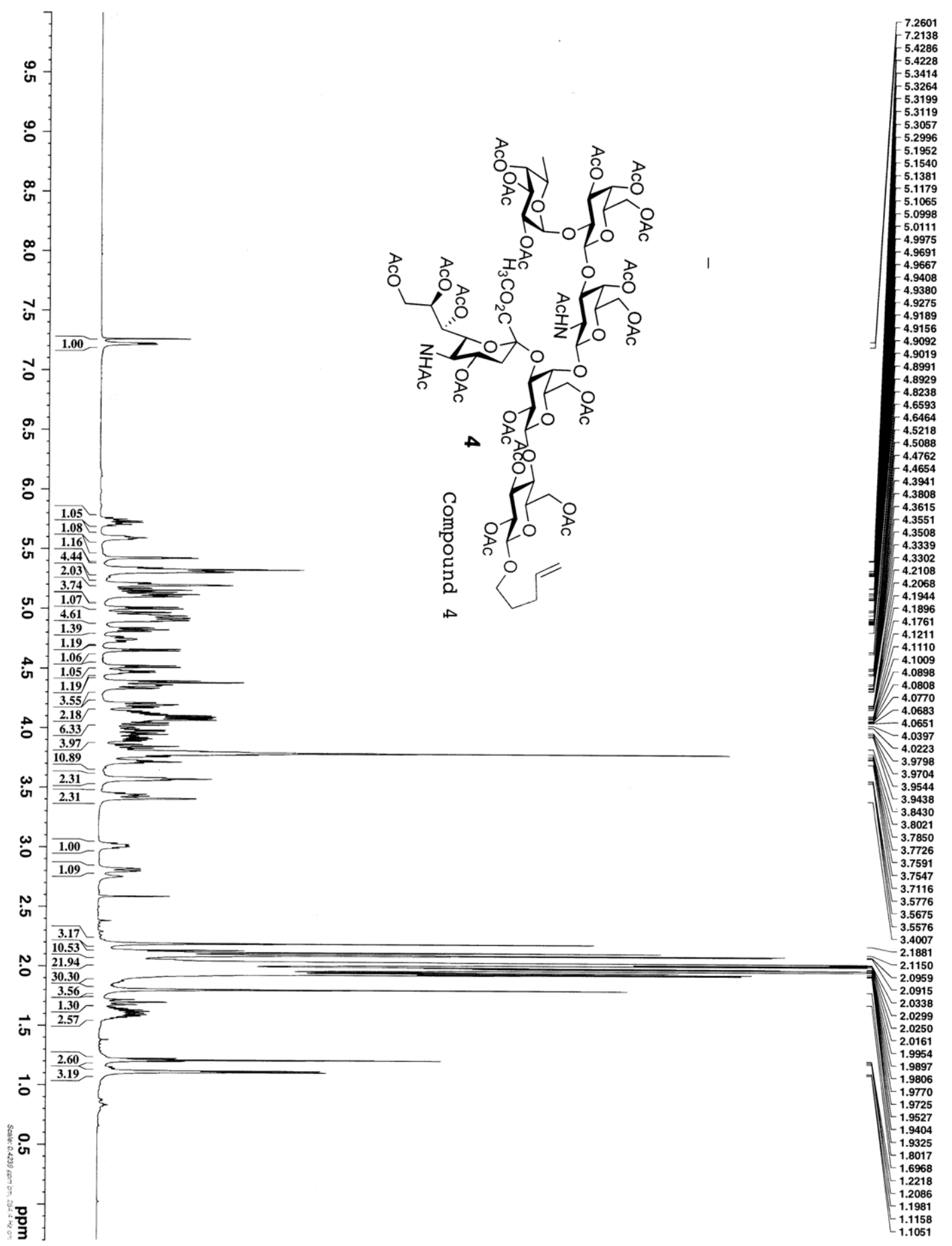
When necessary, solvents and reagents were dried prior to use. Tetrahydrofuran (THF), dichloromethane (CH₂Cl₂), toluene, diethyl ether (Et₂O) and Benzene were filtered through a column of activated alumina under an argon atmosphere. Pyridine, *N,N*-diisopropylethylamine, and triethylamine were distilled from calcium hydride. DBU (Diazabicycloundecene) and piperidine were purchased and used without further purification. HATU (*O*-(7-azabenzotriazol-1-yl)-*N,N,N',N'*-tetramethyluronium hexafluorophosphate) was purchased and used without further purification.

Analytical Equipment: ¹H- and ¹³C NMR spectra were recorded on a 500 MHz, or a 600 MHz spectrometer in CDCl₃, DMF-d₇, CD₃OD or D₂O. Chemical shifts (δ) are reported from tetramethylsilane with the solvent resonance as the internal standard (CDCl₃: δ 7.26; DMF-d₇: δ 8.03; 2.92, 2.75; CD₃OD: δ 4.78, 3.34; D₂O: δ 4.65). Data are reported as follows: chemical shift (δ), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br = broad, m = multiplet), coupling constants (Hz), integration, and assignment. ¹³C NMR spectra were recorded with complete proton decoupling. Chemical shifts are reported in ppm from tetramethylsilane with the solvent as the internal standard (CDCl₃: δ 77.0). HPLC purifications were run with TFA (trifluoroacetic acid)-buffered eluents: A = 0.05 % v/v TFA/Water, B = 0.04 % TFA/Acetonitrile using HPLC grade solvents.

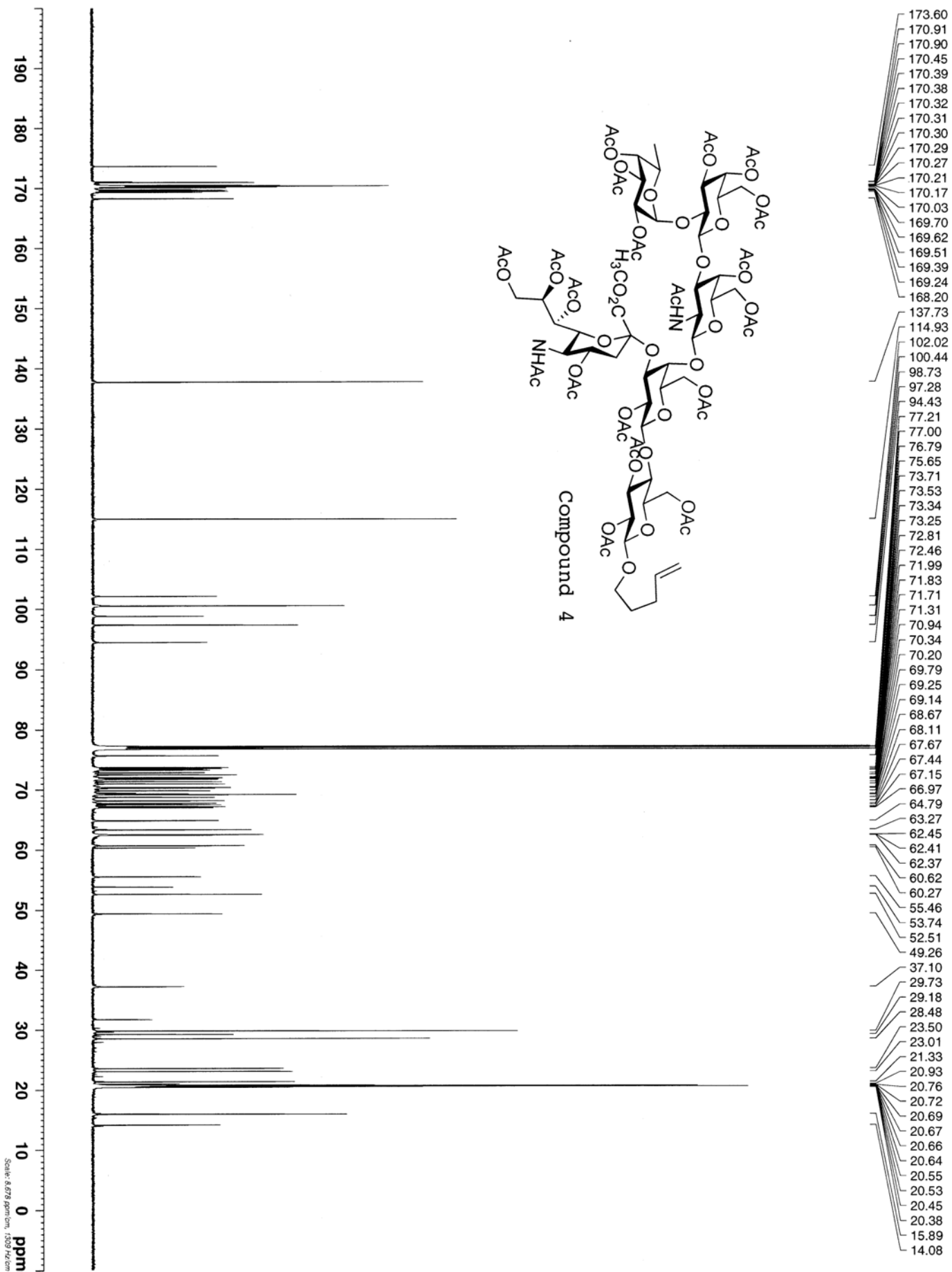
* Kimw12_FUC_GM1_OPn (20 1) CDCI3 24.0C December_14,2008_22:17 Bruker AVII+ 600MHz RRL1326: zg30 : 1H 7.500 ppm *



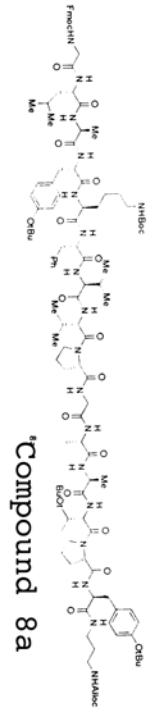
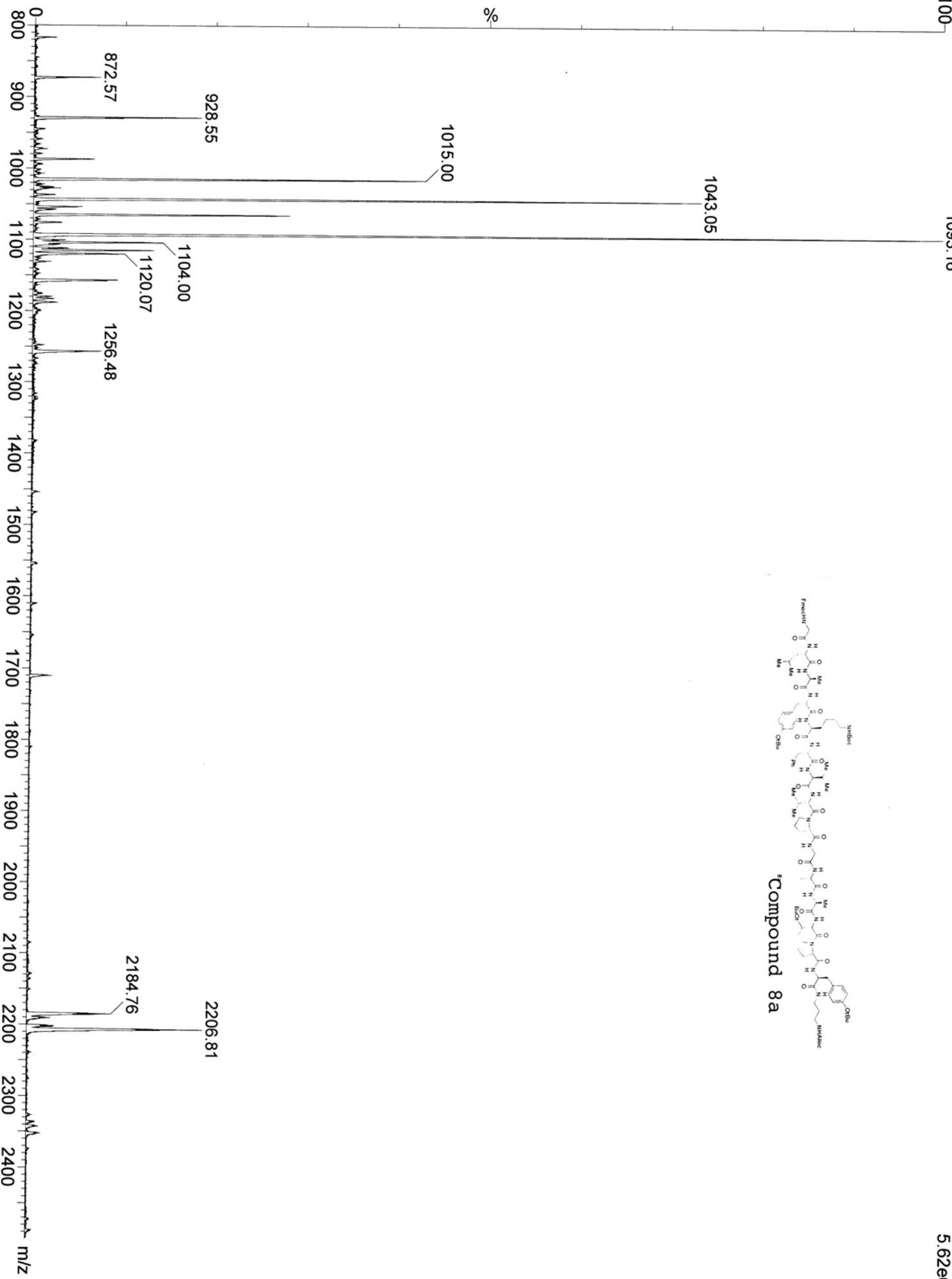
Compound 4

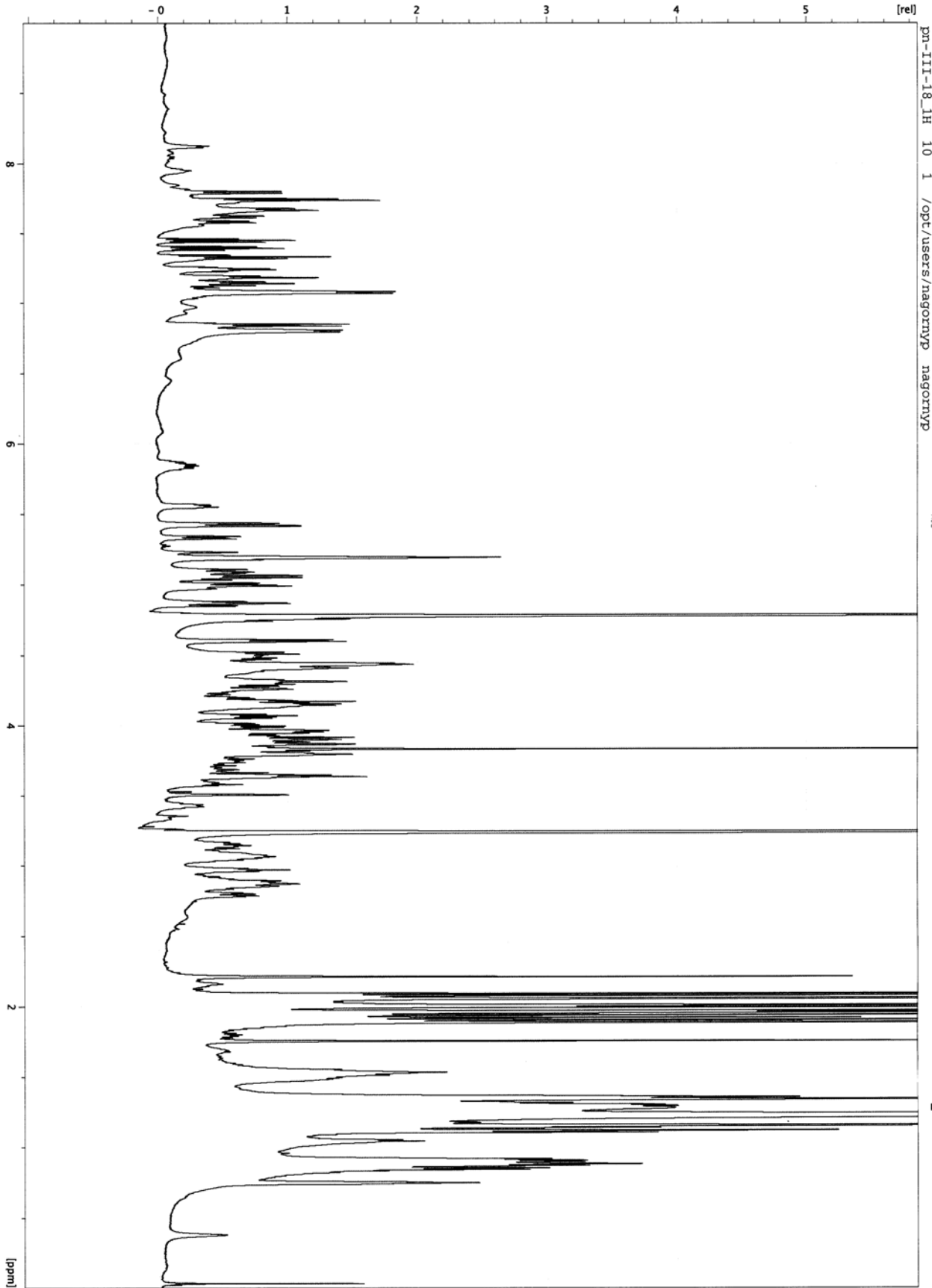


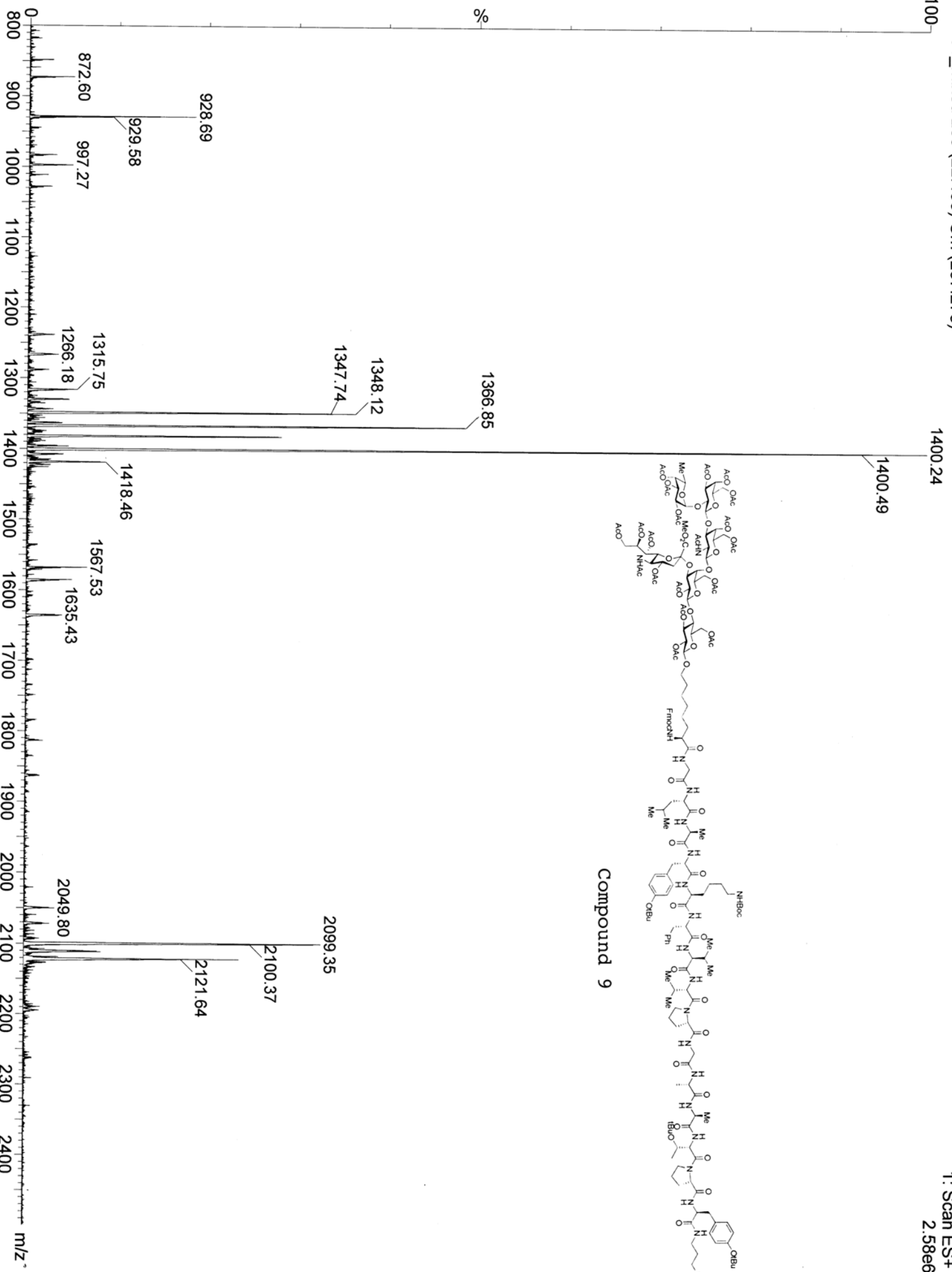
Scale: 0.4239 ppm/cm, 254.4 Hz/cm



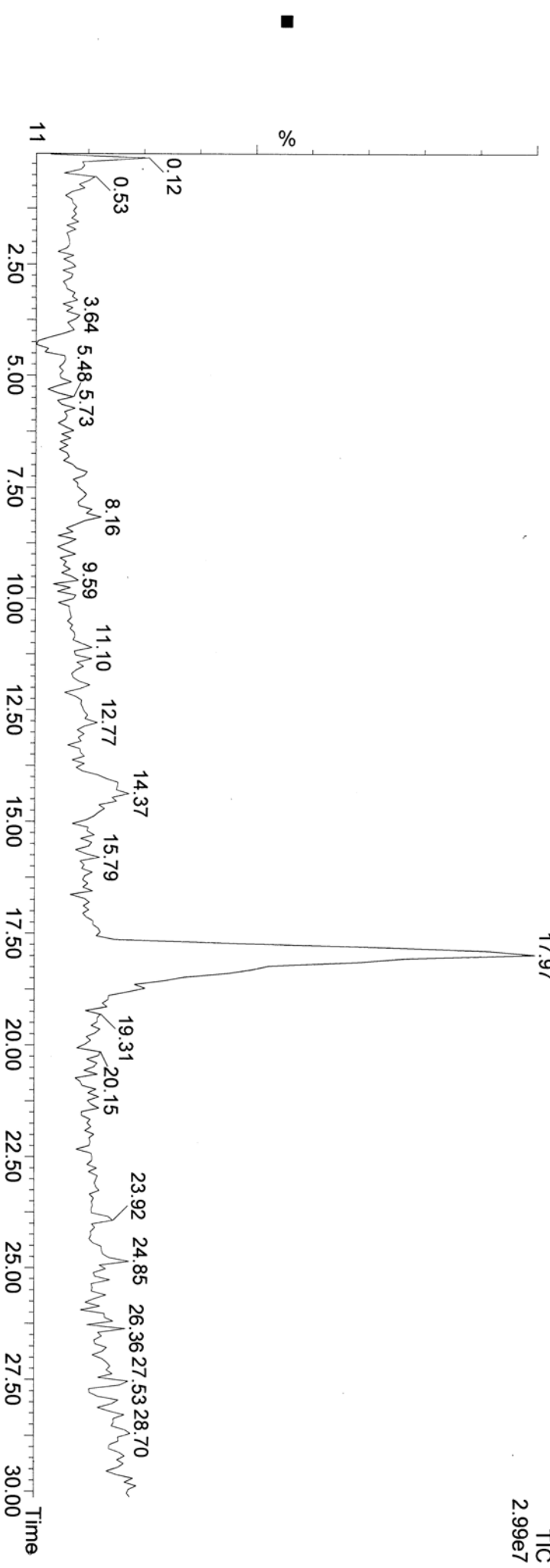
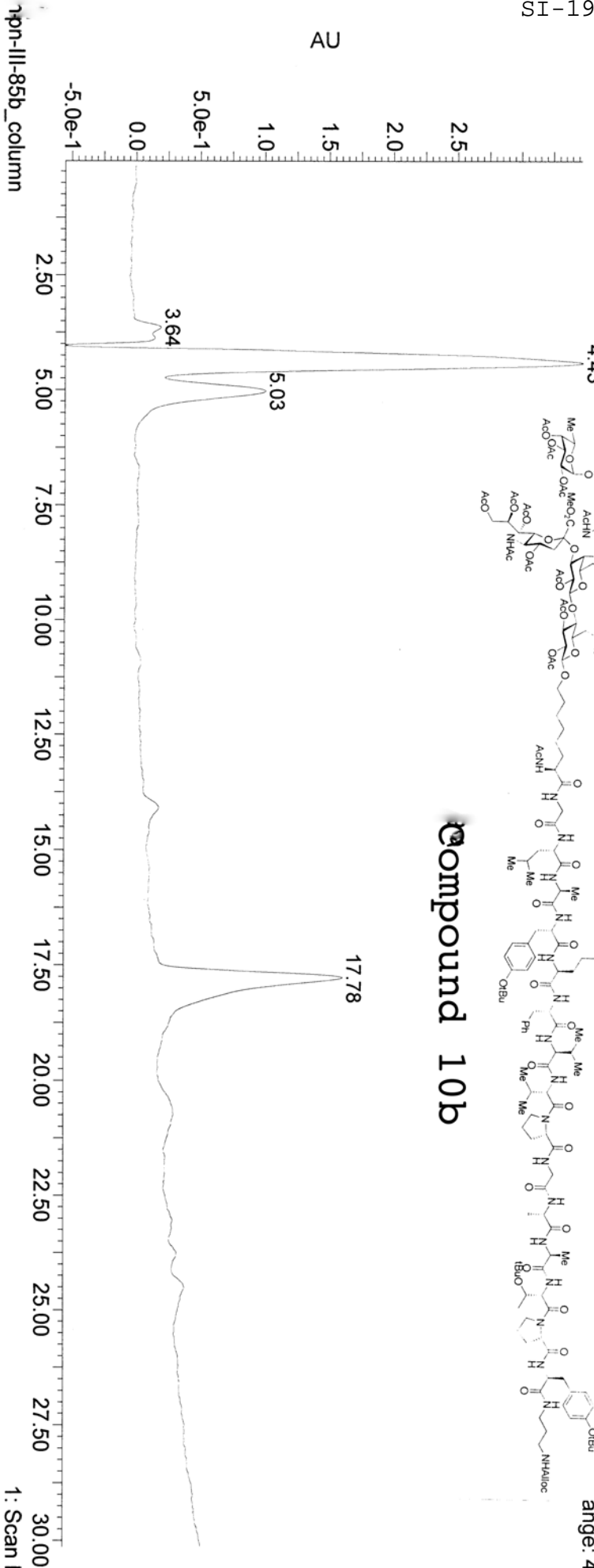
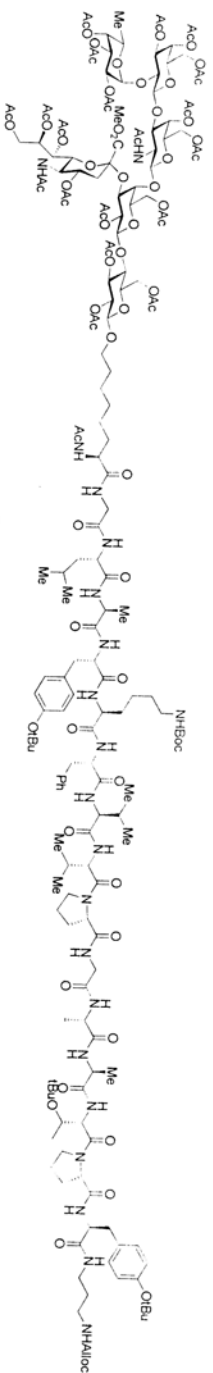
SI-12



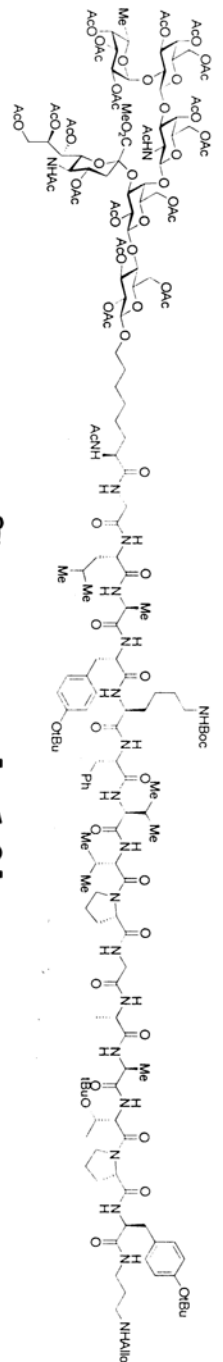




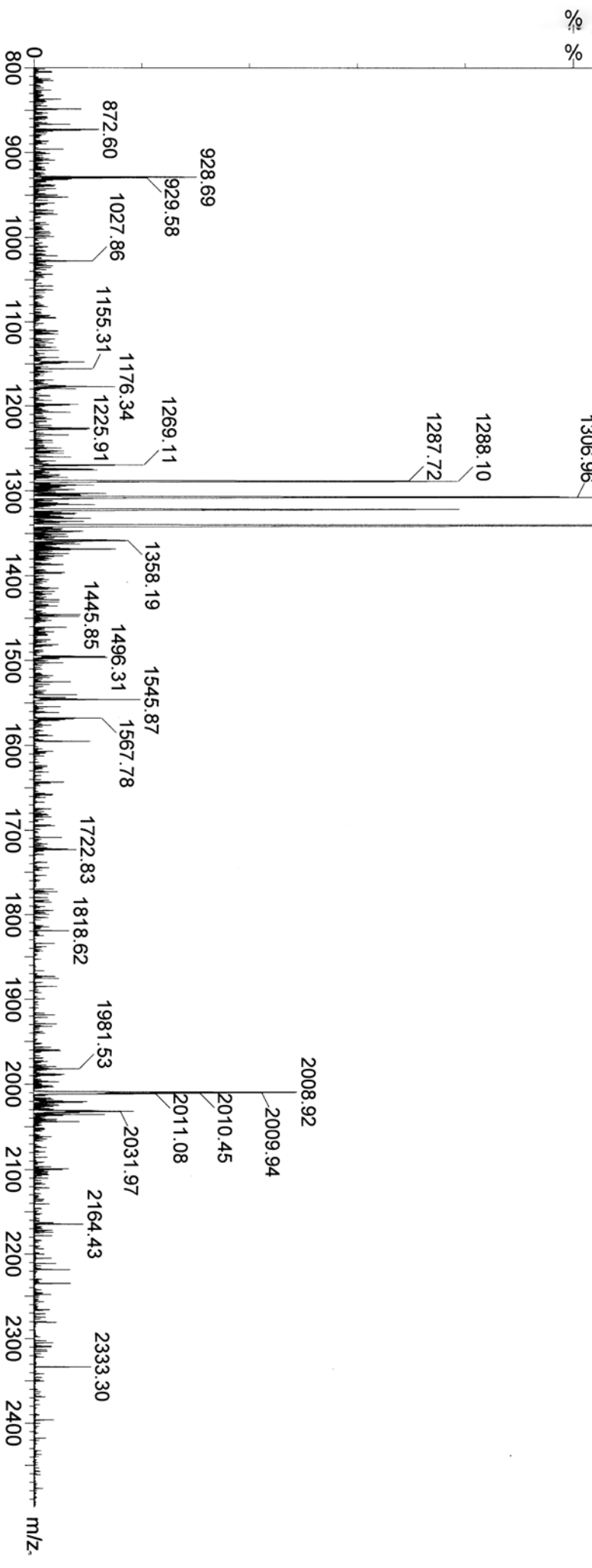
Compound 10b



SI-20



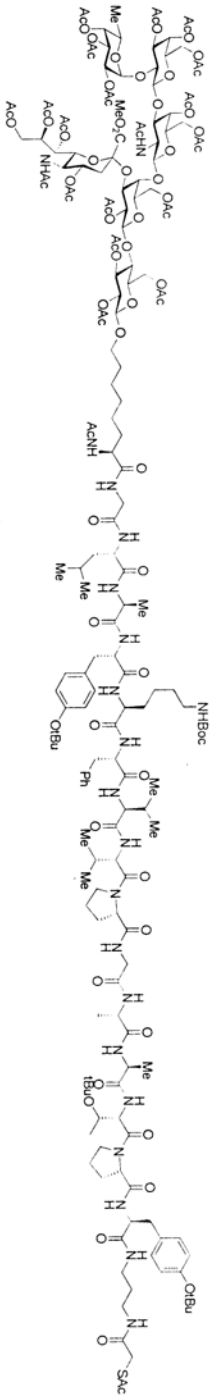
Compound 10b



SI-21

AU

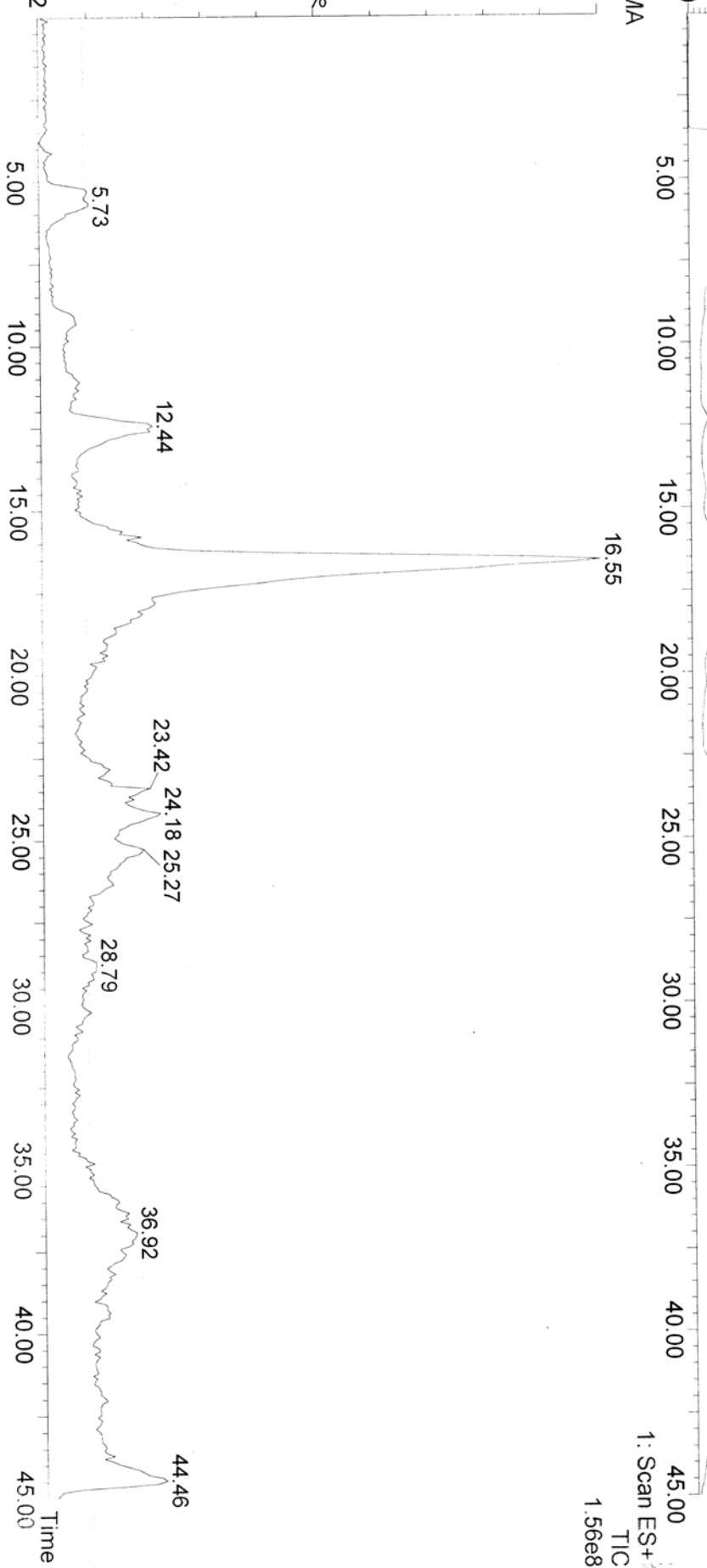
2.0e+2
1.75e+2
1.5e+2
1.25e+2
1.0e+2
7.5e+1
5.0e+1
2.5e+1

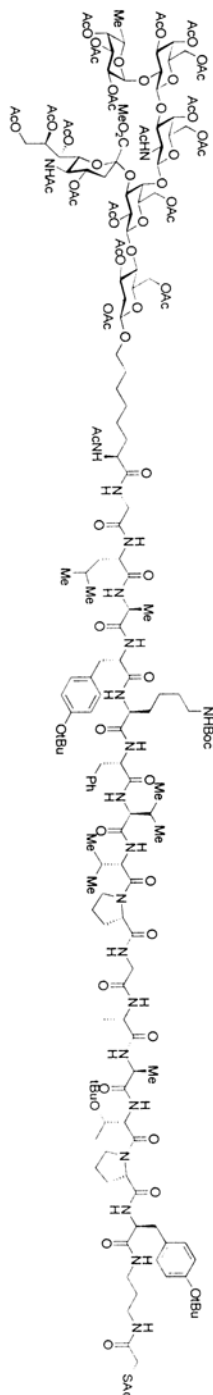


Compound 10

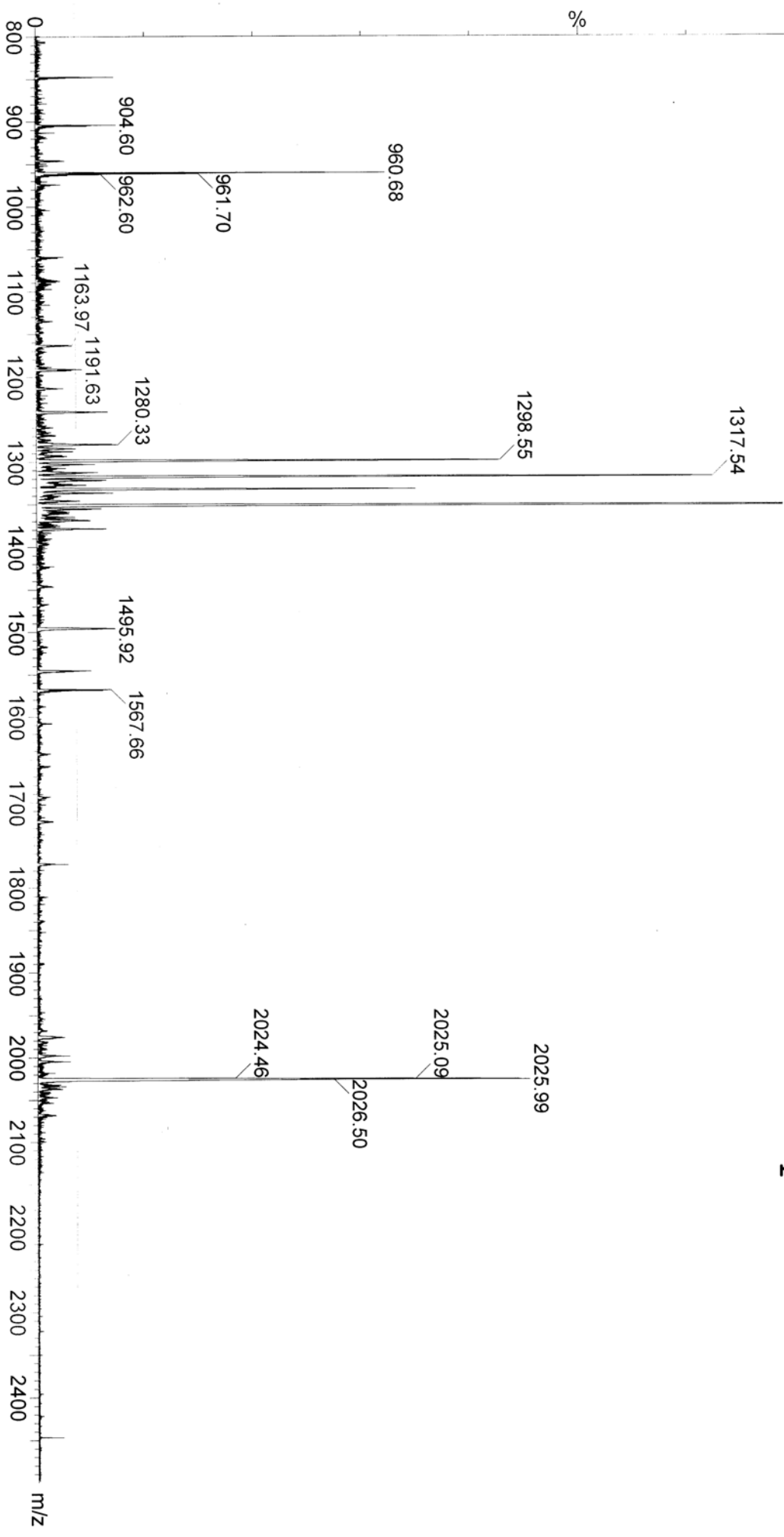
pn-III-87b_SAMMA

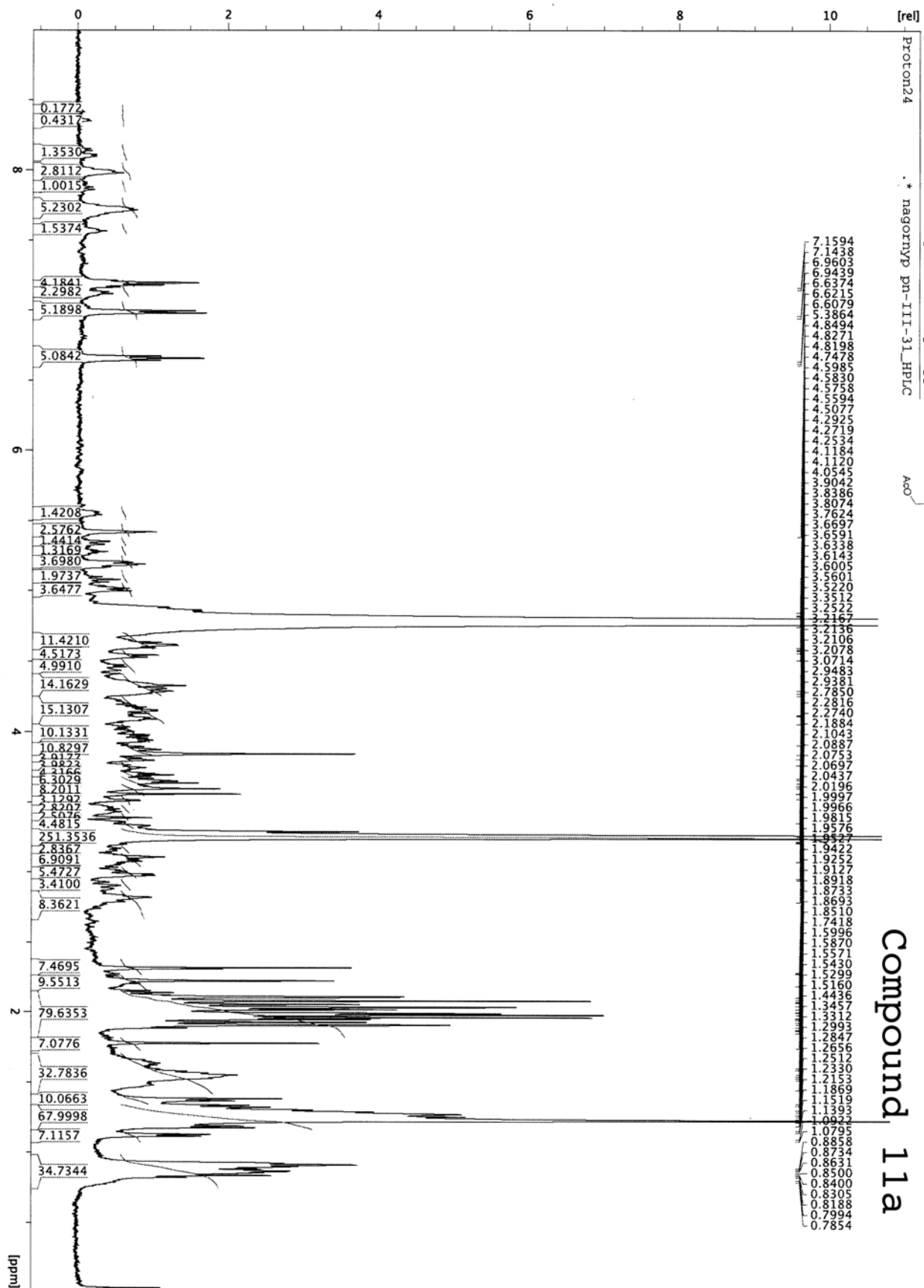
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TIC
1.56e8



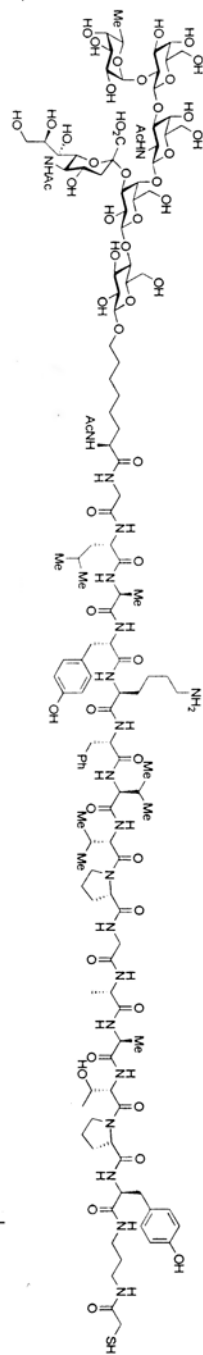


Compound 10

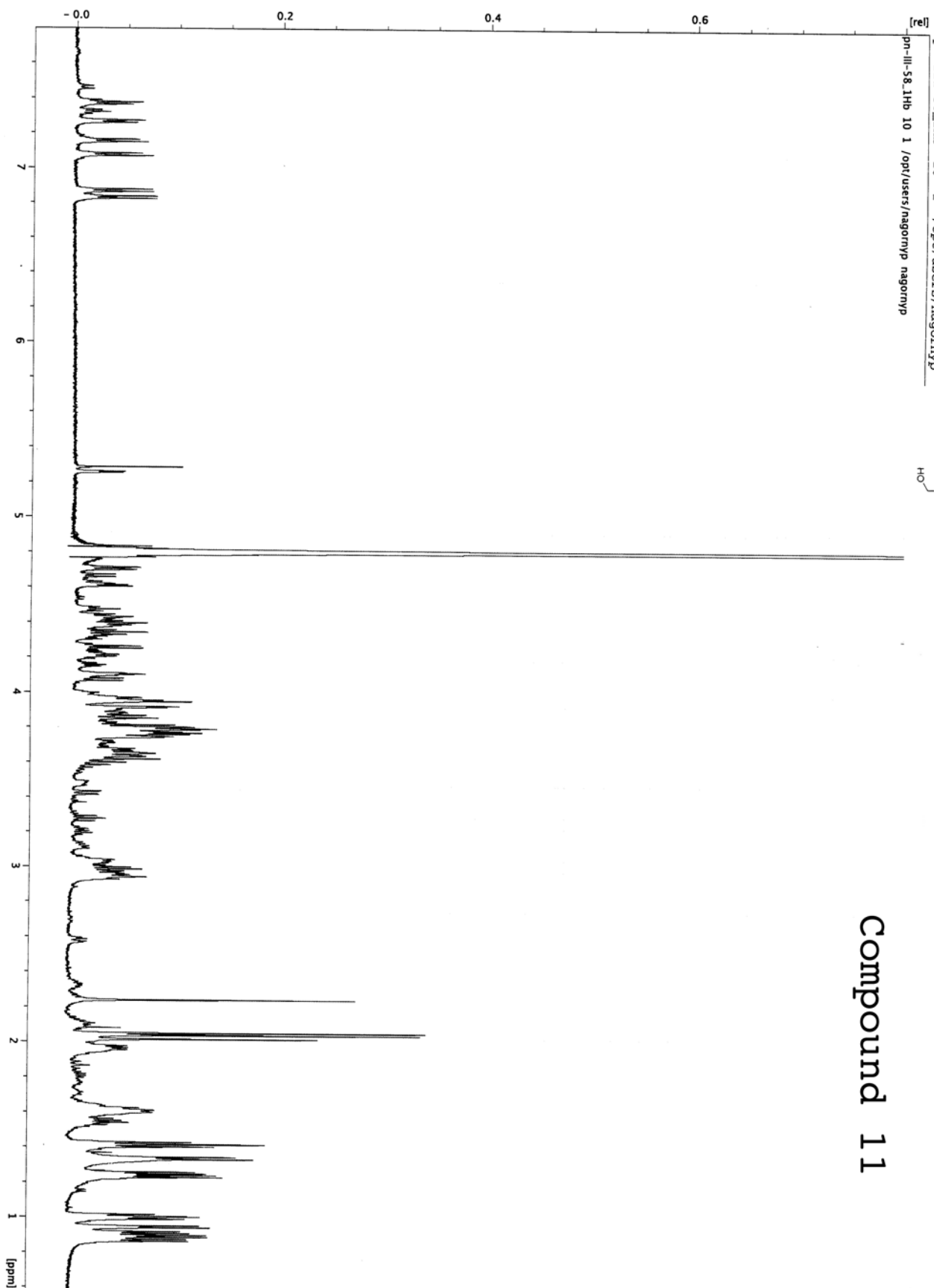




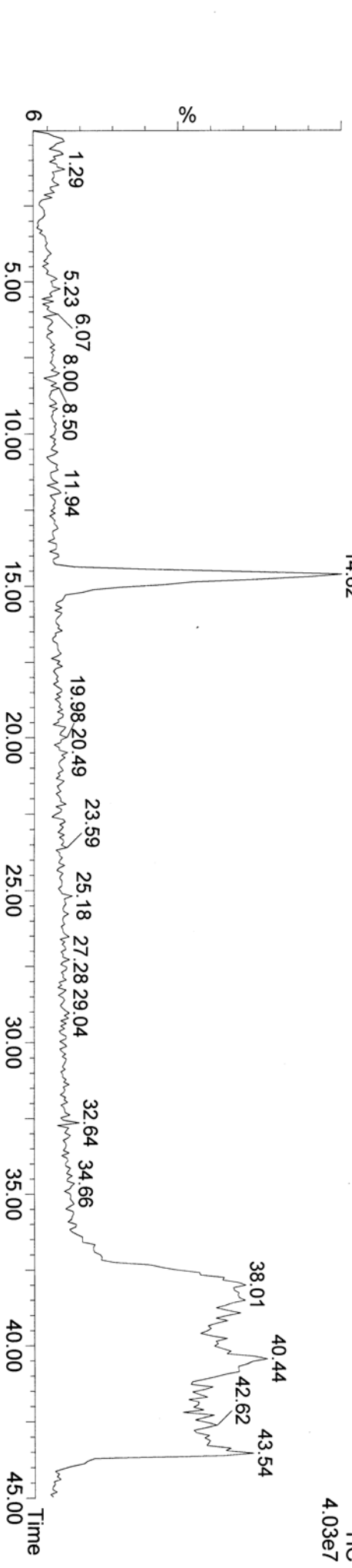
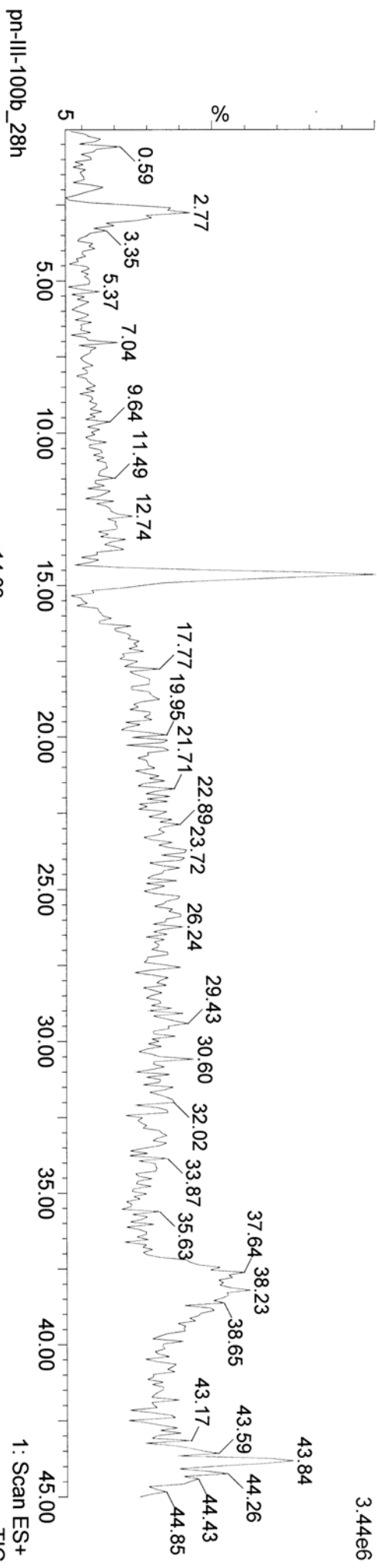
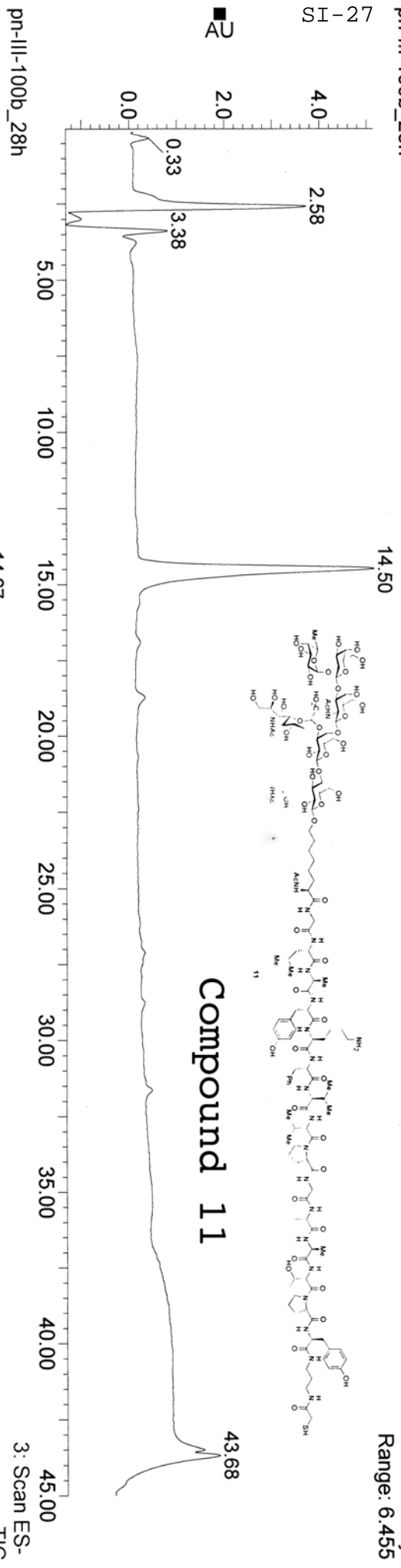
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 pn-III-58_1hb 10 1 /opt/users/nagornyp



Compound 11



SI-27



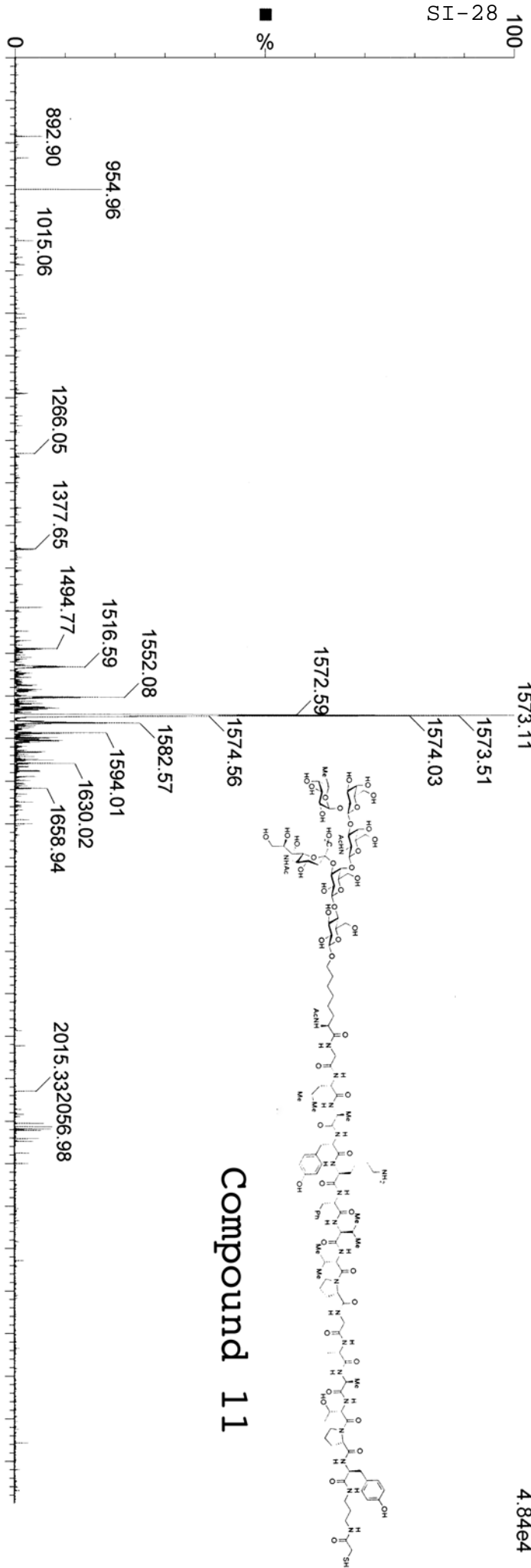
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TIC
4.03e7

3: Scan ES-
TIC
3.44e6

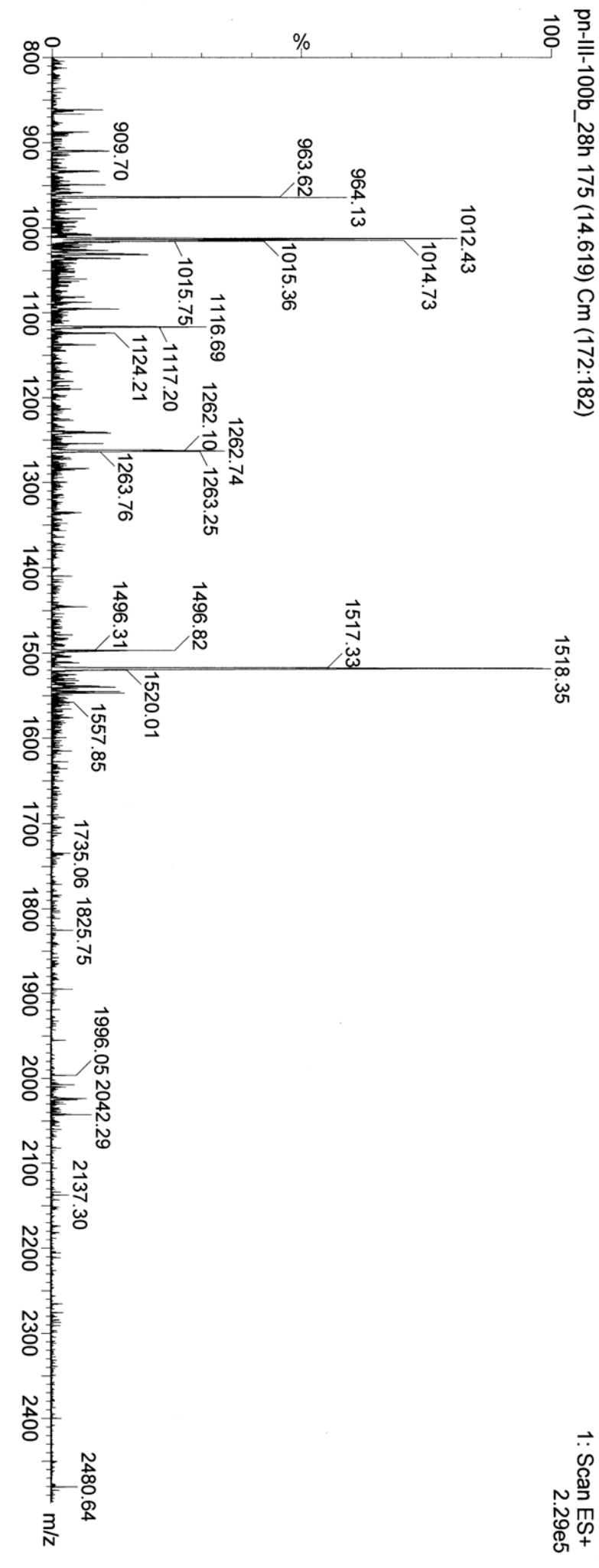
C18_10-85

pn-III-100b_28h 175 (14.671) Cm (171:183)

3: Scan ES-
4.84e4



Compound 11



1: Scan ES+
2.29e5