Supporting Information

A Peptide Nucleic Acid-Aminosugar Conjugate Targeting Transactivation Response Element of HIV-1 RNA Genome Shows a High Bioavailability in Human Cells and Strongly Inhibits Tat-mediated Transactivation of HIV-1 Transcription

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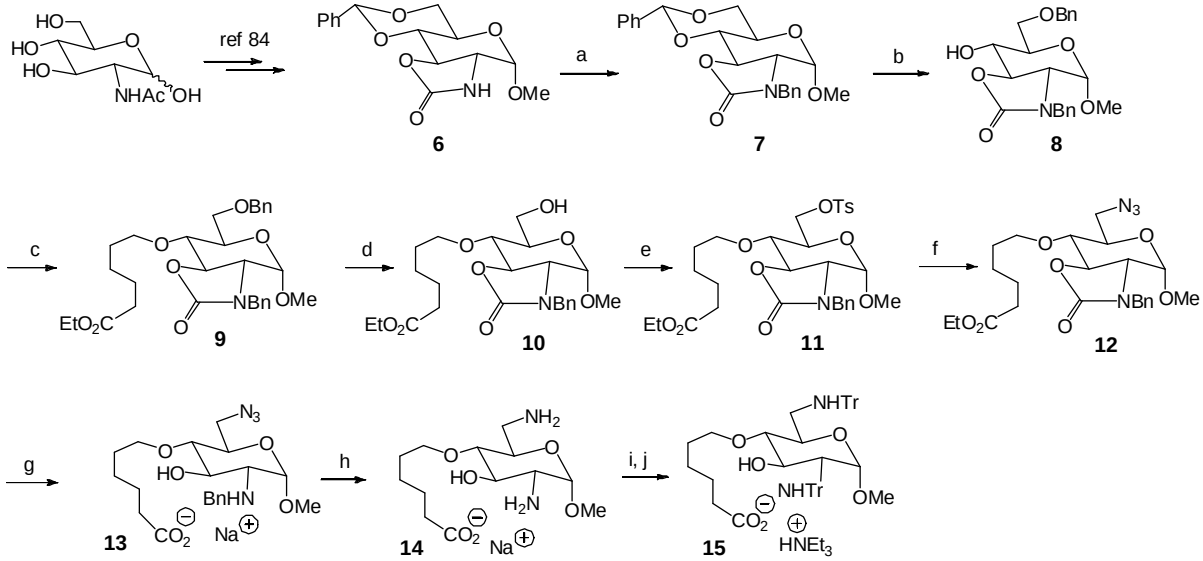
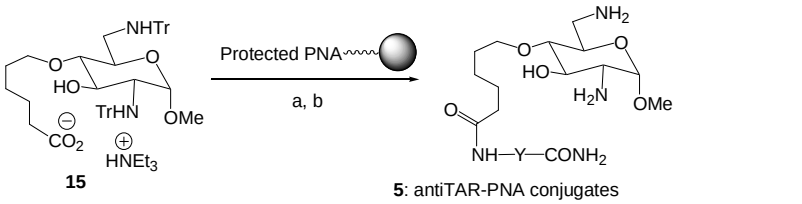
I. Synthesis of glucosamine derivatives

Scheme 1.[a] Synthesis of the glucosamine derivative **15** for further coupling to the anti-TAR PNAs.



[a]Reagents and conditions: (a) BnBr, K_2CO_3, DMF, rt, 10 h, 84%; (b) Et_3SiH, $BF_3.OEt_2$, CH_2Cl_2, 0 °C, 2 h, 81%; (c) 6-bromohexanoic acid ethyl ester, NaH, DMF, rt, 8 h, 92%; (d) H_2, Pd/C (10%), EtOH, rt, 12 h, 98%; (e) TsCl, pyridine; rt, 10 h, 96%; (f) NaN_3, DMF, 80 °C, 3 h, 91%; (g) 1M NaOH, dioxane/H_2O (4/1), 100 °C, 14 h, 74%; (h) HCO_2NH_4, $Pd(OH)_2$/C (20%), MeOH/H_2O (9/1), reflux, 1.5 h, 95%; (i) TrCl, DMF, Et_3N, rt, 8 h, 68%; (j) 1M NaOH/dioxane (1/1), 80 °C, 6 h, 85%.

Scheme 2.[a] Synthesis of the PNA-aminoglucosamine conjugates **5a** and **5b**.

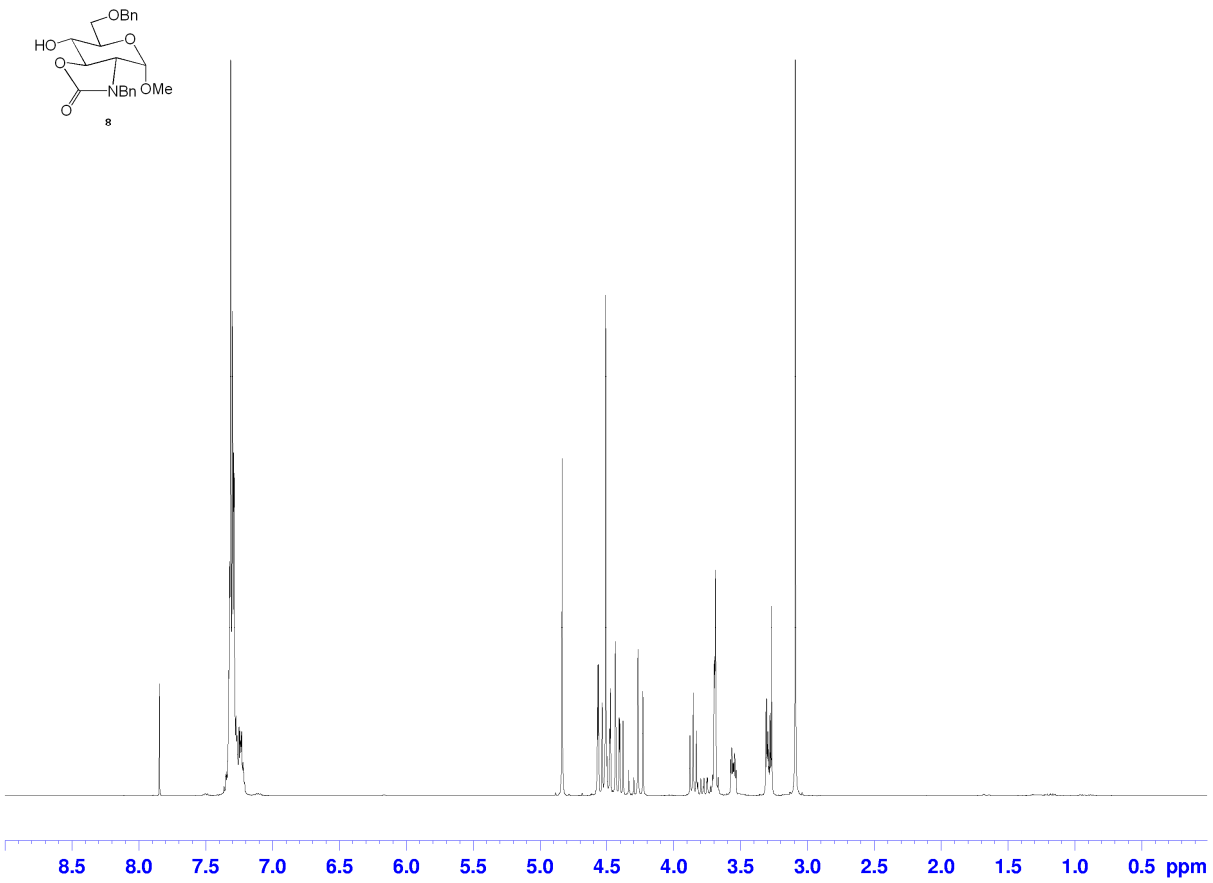


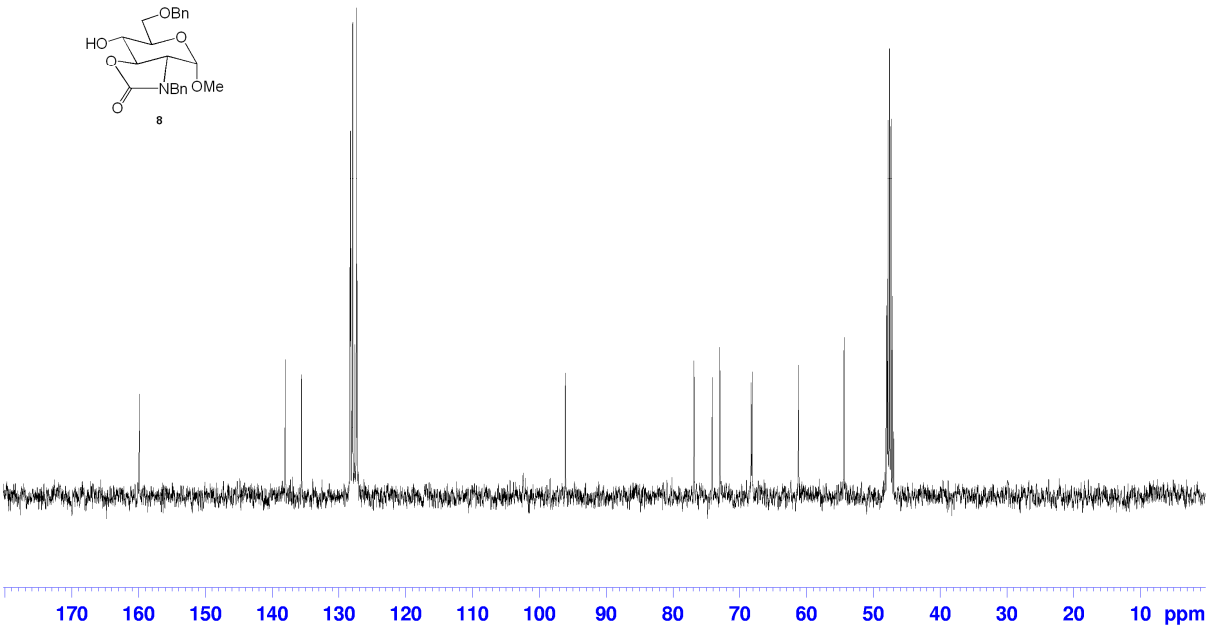
[a]Reagents and conditions: (a) EDC, HOBt, DMF, protected PNA **3a** or **3b**; (b) TFA/Anisole (1/1), rt, 2h.

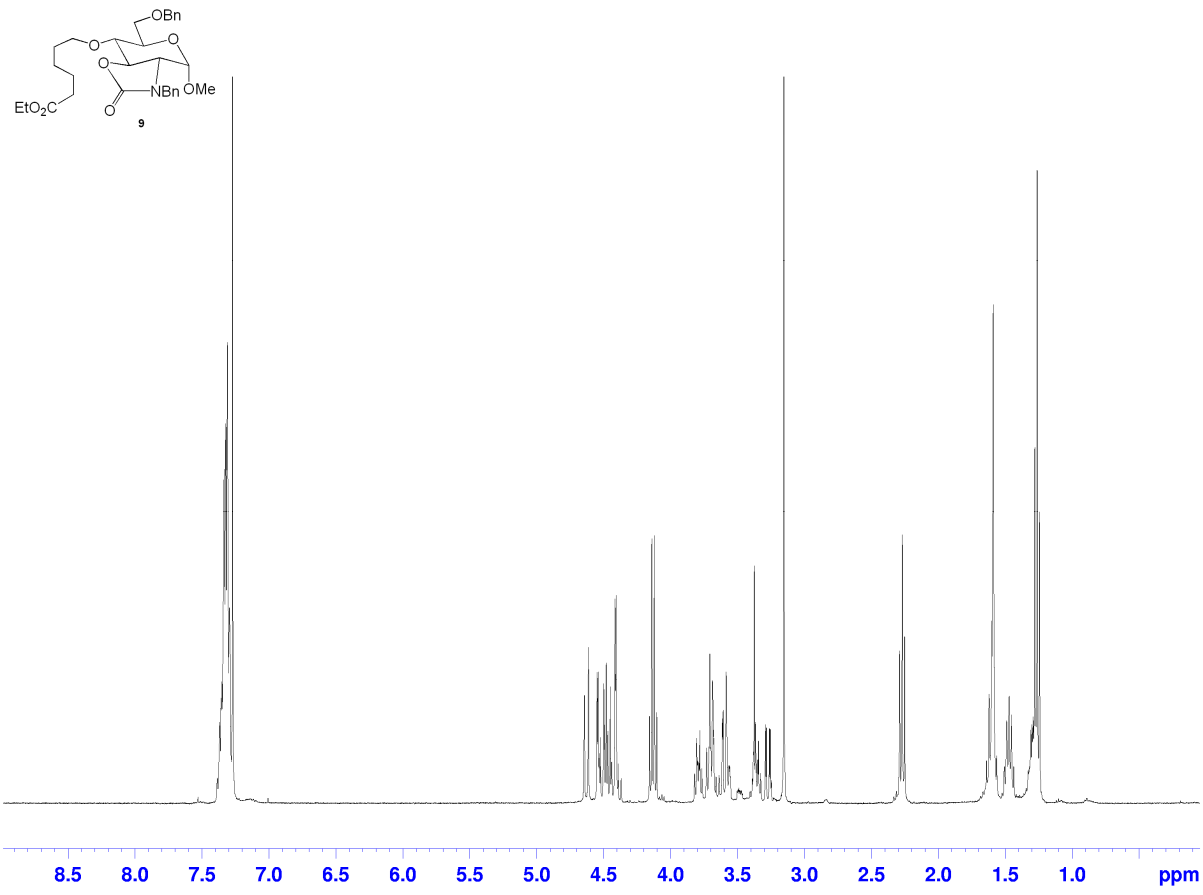
General experimental data

All reagents were used as purchased from suppliers without further purification. The protected 16-mer PNA oligomers were purchased from Eurogentec. DMF was distilled in the presence of CaH_2, and stored under argon atmosphere prior to use. Thin layer chromatographies were performed on silica gel (Alugram Sil G/UV_{254}) or Alumina gel (Alugram Alox N/UV_{254}) from Macherey-Nagel and spots were detected either by UV absorption or by charring with ninhydrin. HPLC purifications were carried out on a C_{18} reversed-phase column (Macherey-Nagel, 10.0 x 25.0 mm) with a Dionex Ultimate 3000. Melting points were determined with a BUCHI 510 apparatus and are reported uncorrected. ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded with a BRUKER ADVANCE 400 spectrometer using the residual solvent signal as internal standard. HRMS were obtained from the Mass Spectrometry Service, CRMPO, at the University of Rennes I, France, using a MICROMASS ZABSPEC-TOF spectrometer and a VARIAN MAT311 spectrometer or with a 4700 reflector spectrometer.

II. ^{1}H and ^{13}C NMR spectra of compounds **8-15**



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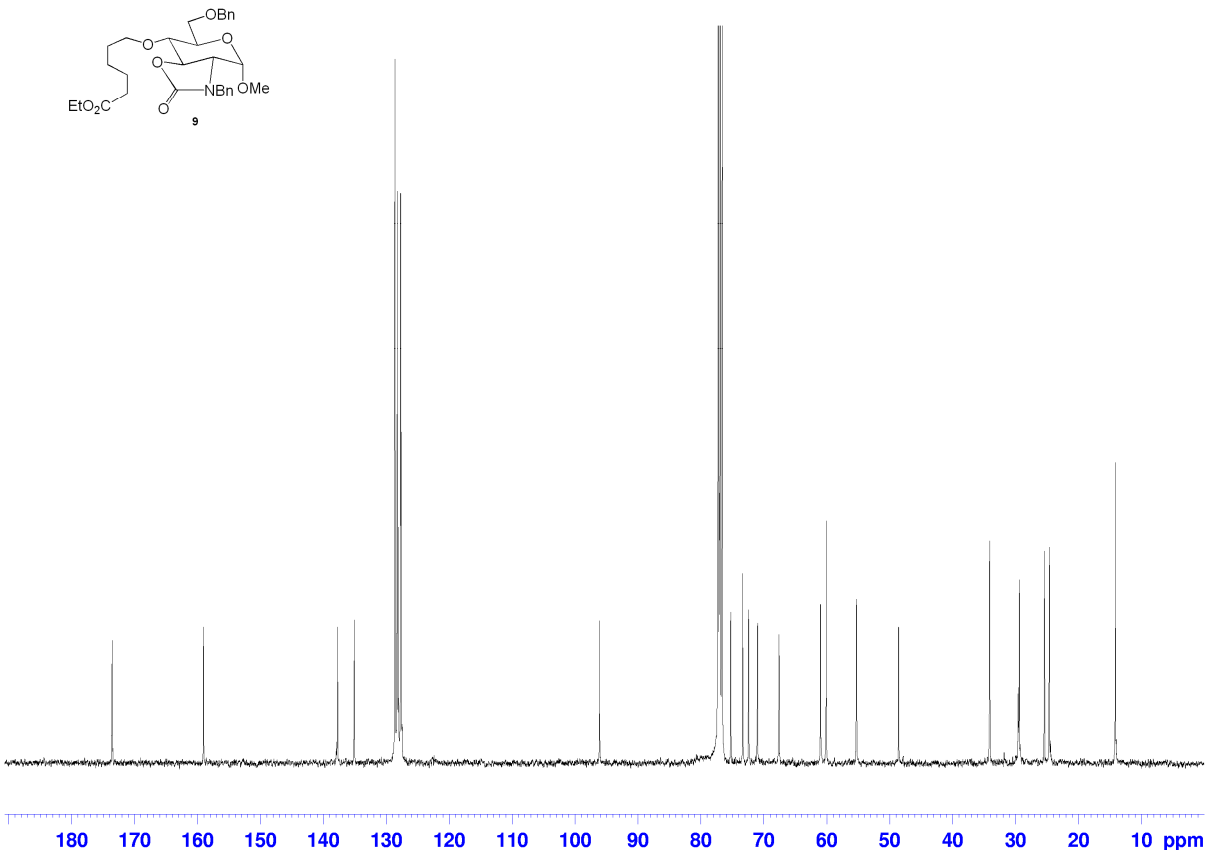
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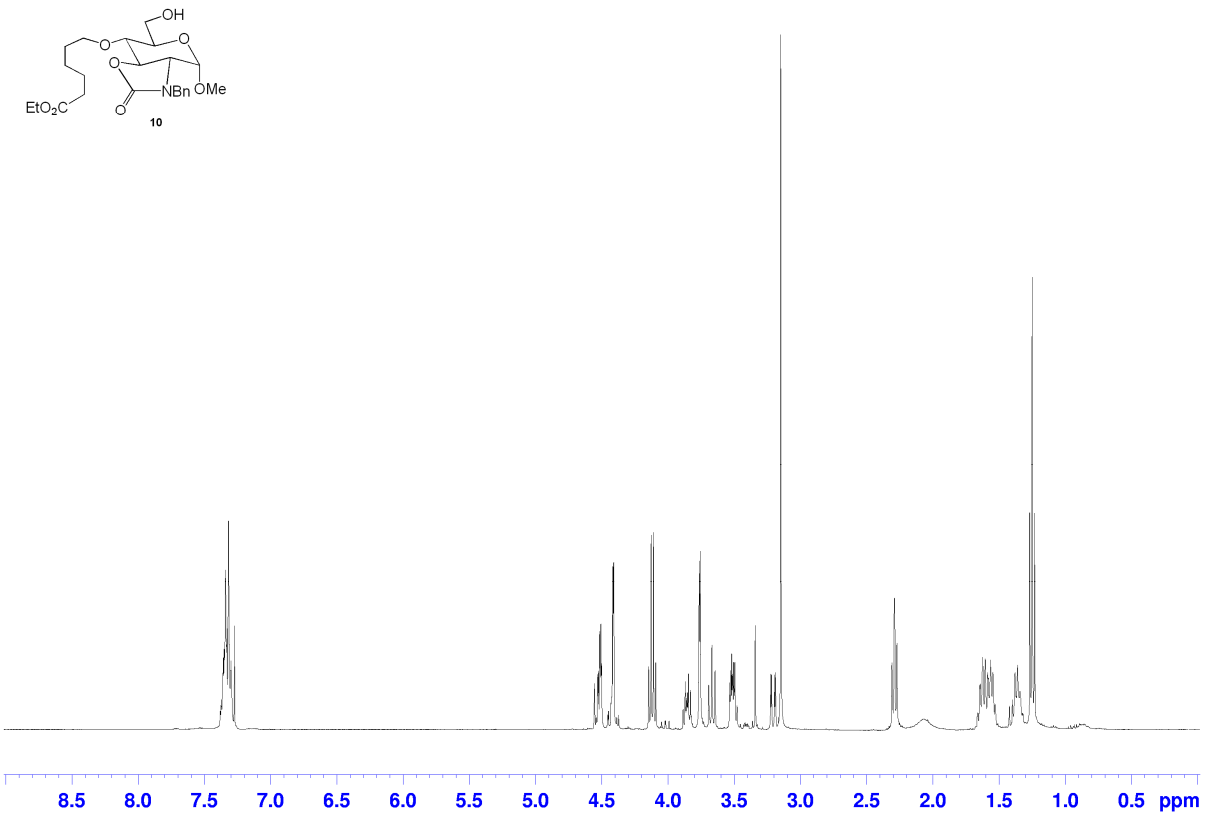
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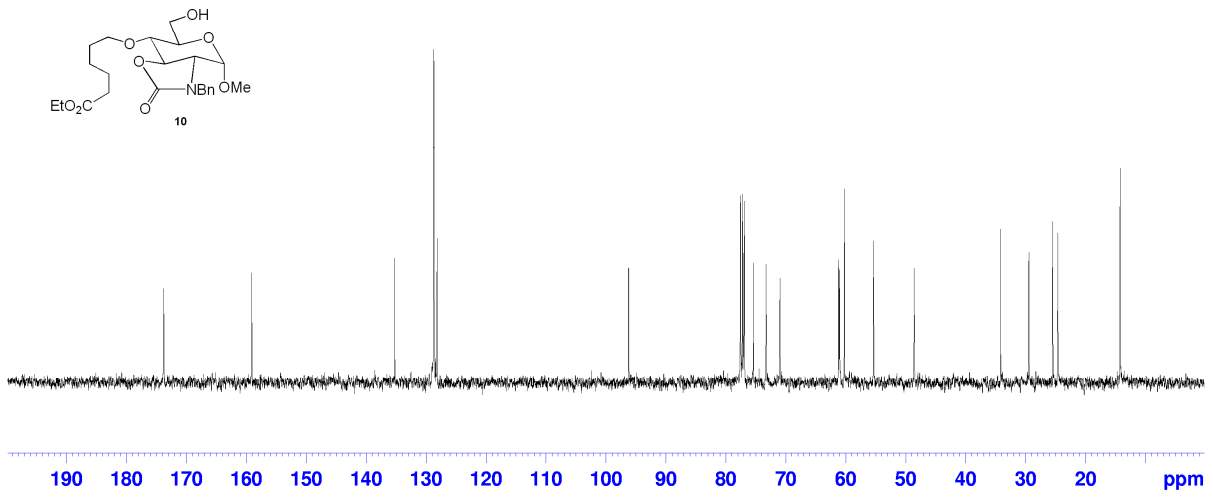
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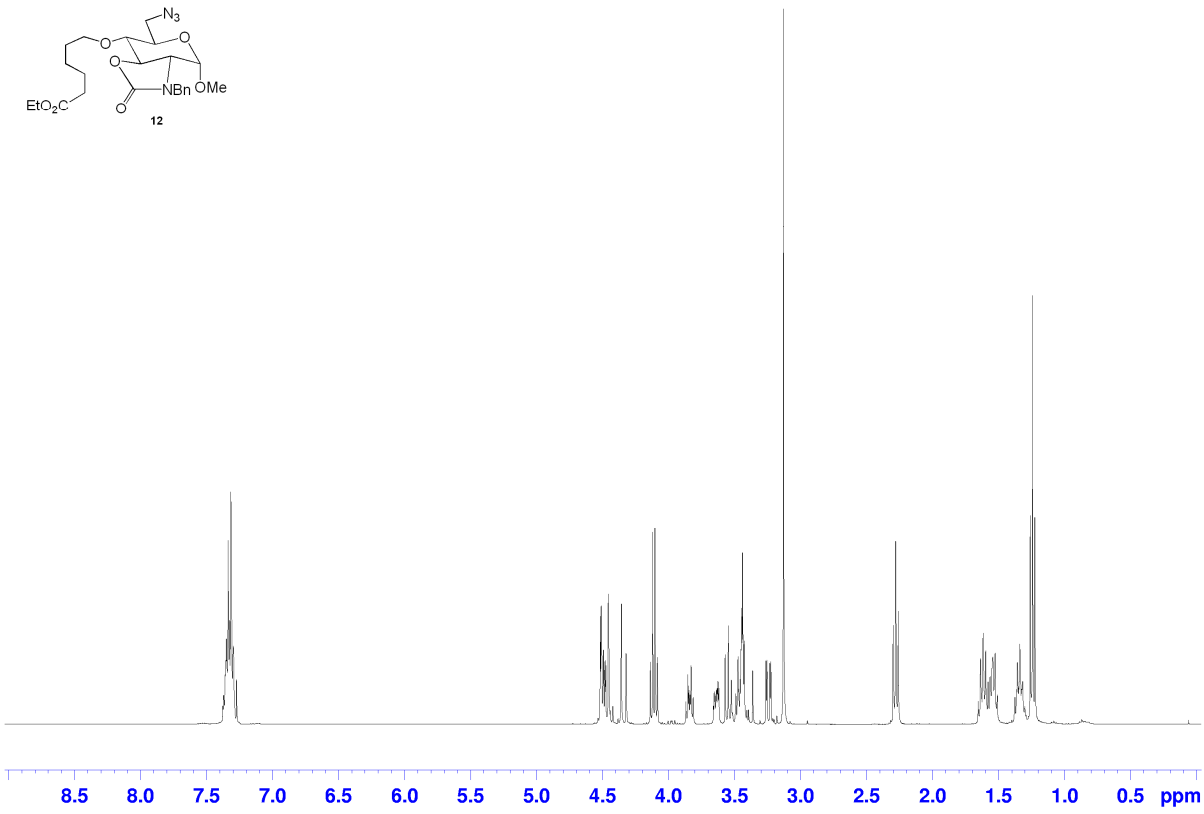
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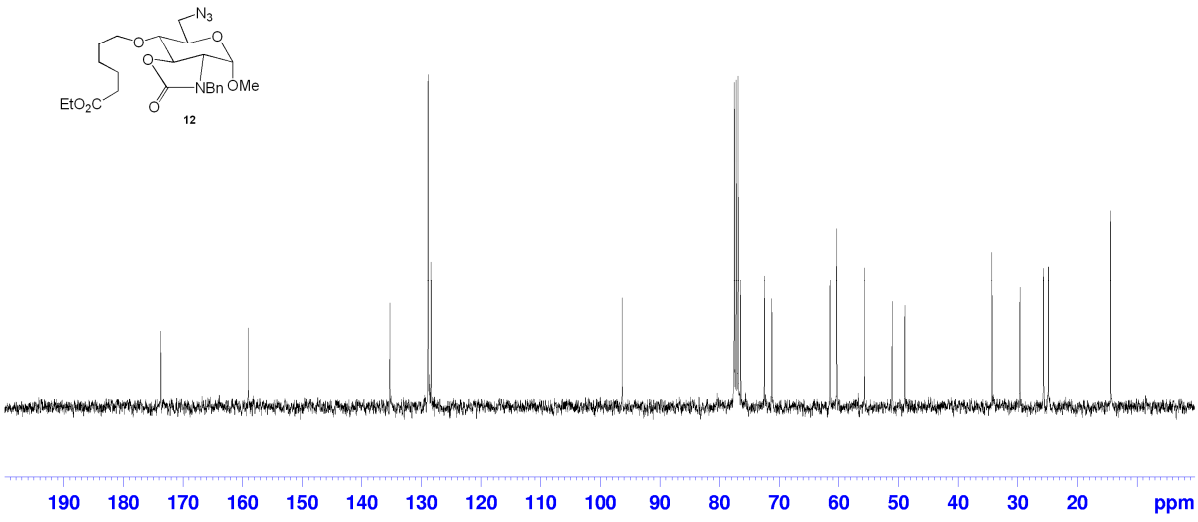
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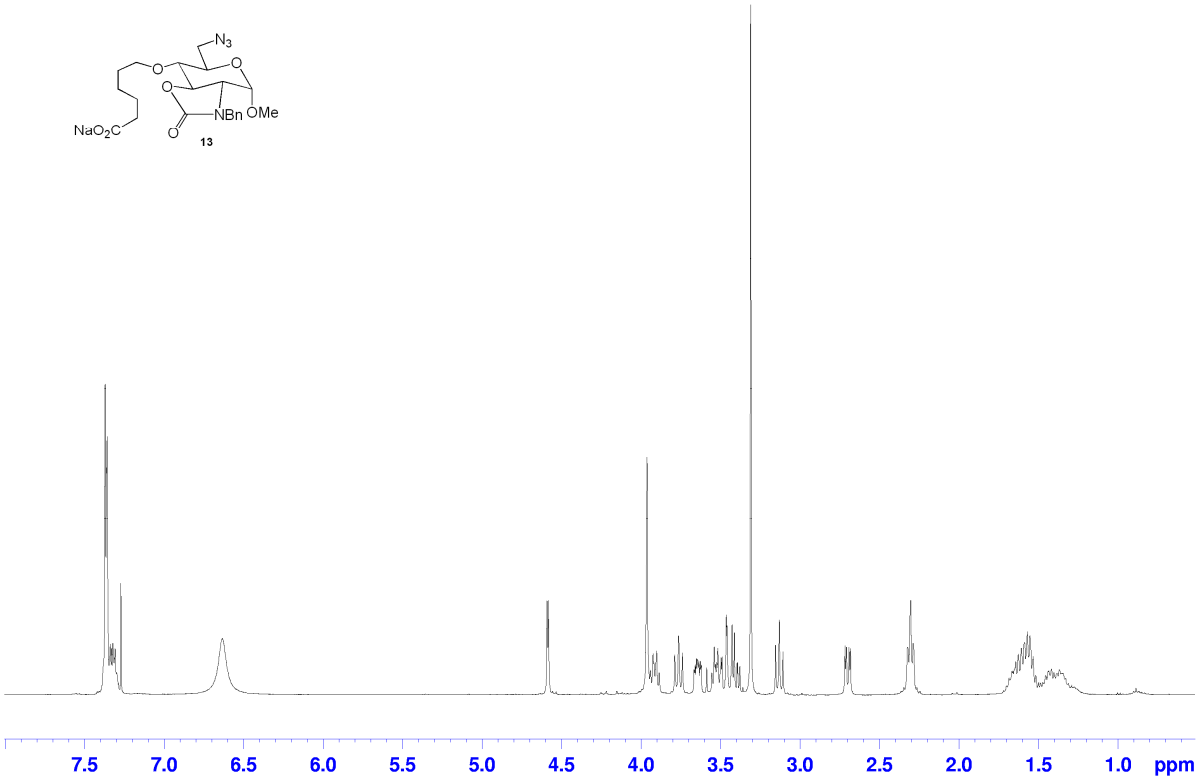
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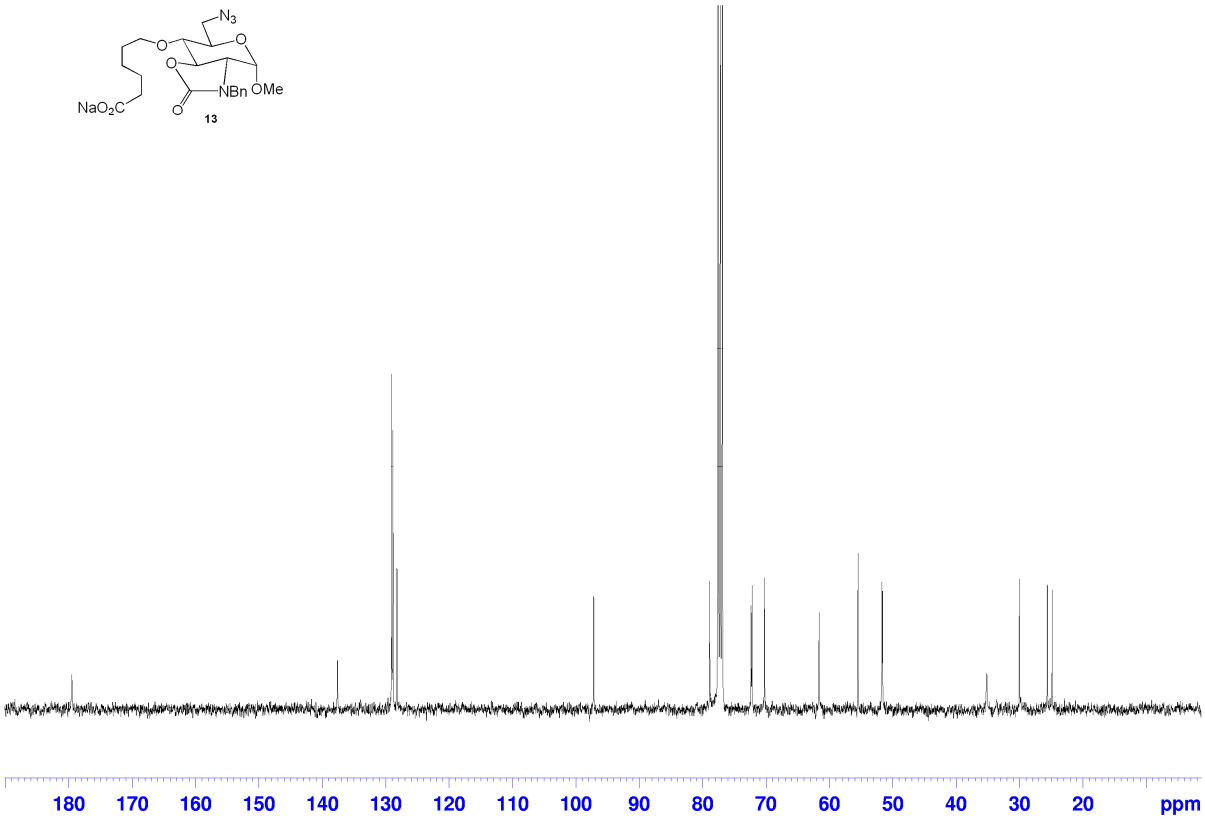
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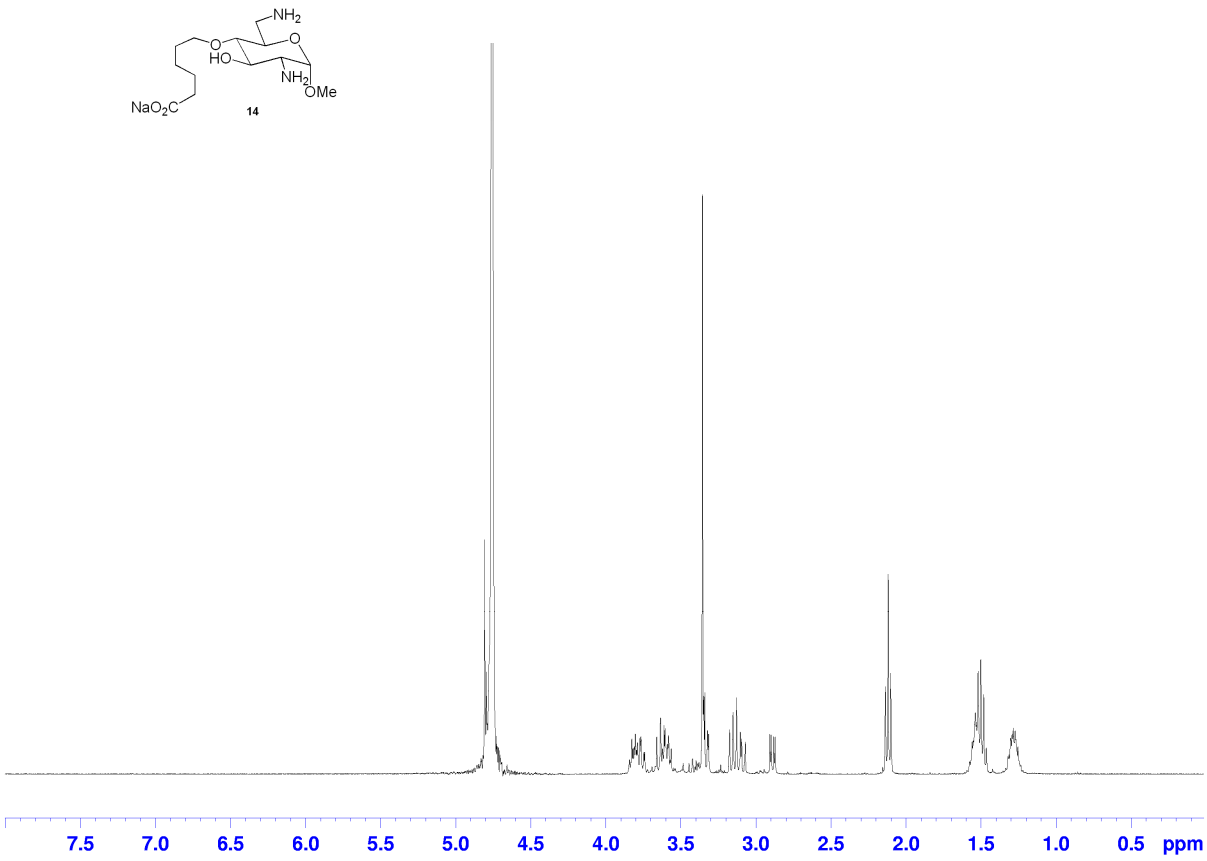
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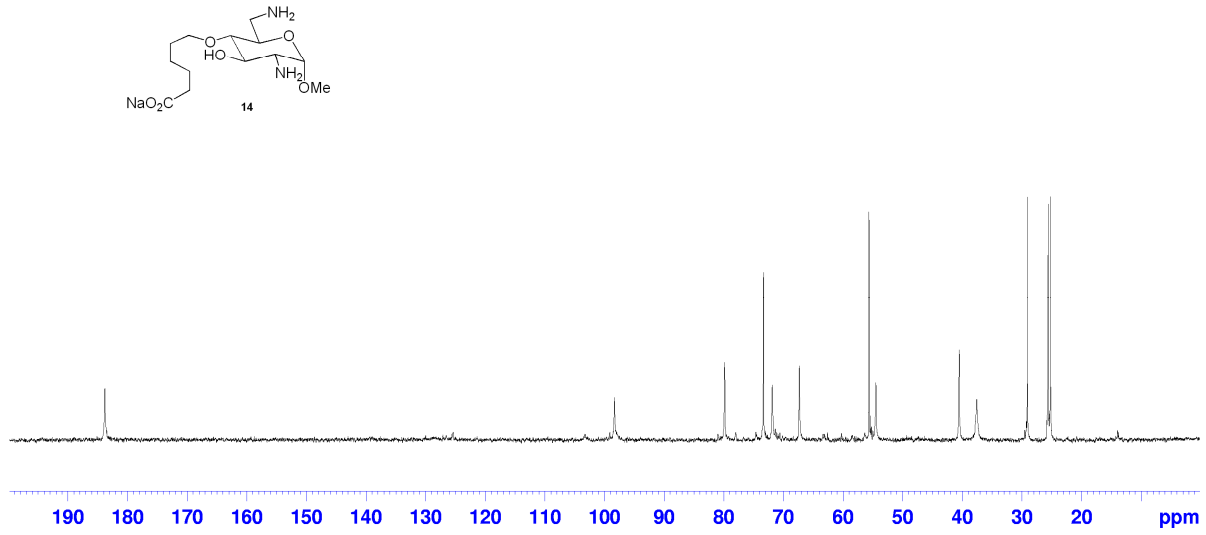
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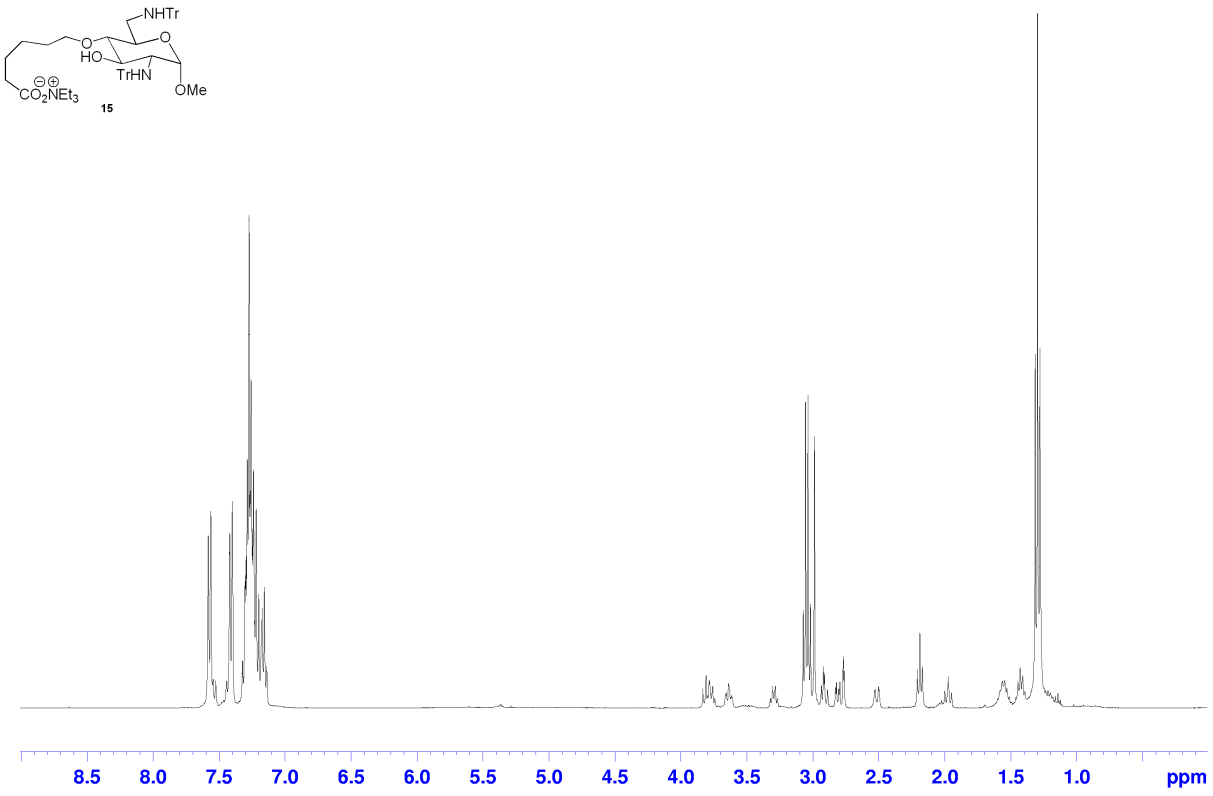
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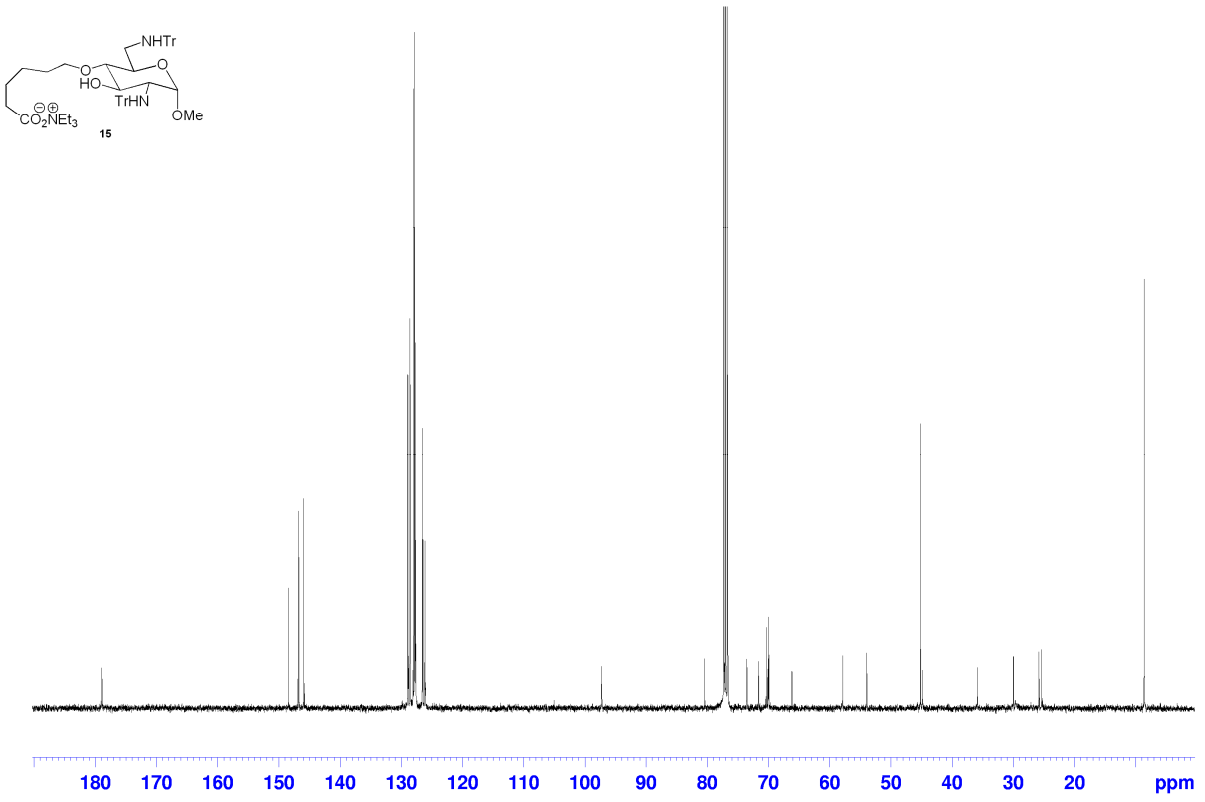
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40
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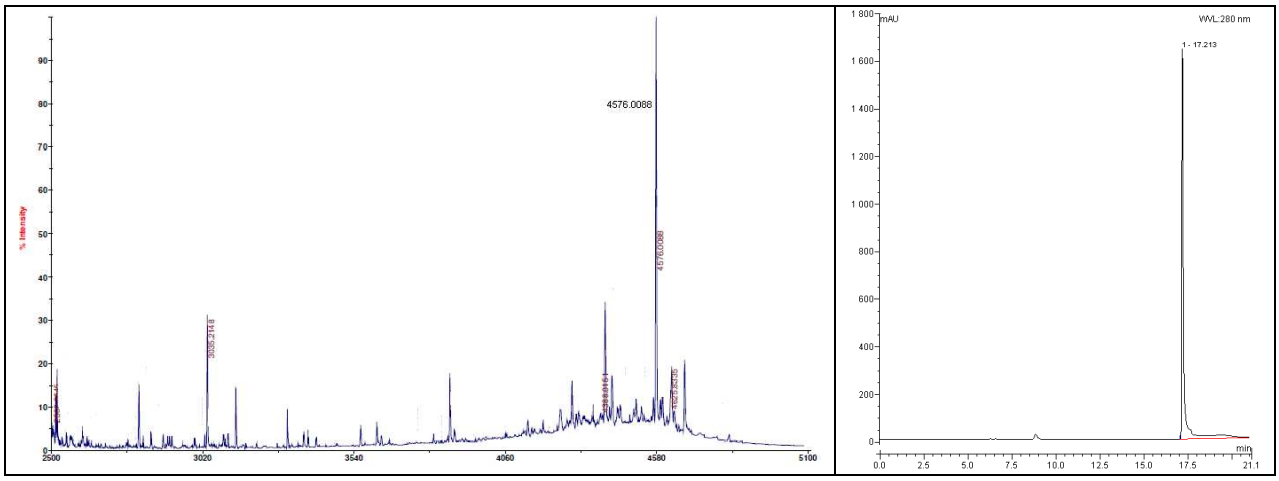
20
ppm

III. MALDI mass spectra and HPLC profiles for conjugates **5a** and **5b**

HPLC purification and analysis was carried out on a C_{18} reversed-phase column (Macherey-Nagel, 10.0 x 250 mm) with a Dionex Ultimate 3000 (detection at 260 and 280 nm). Elution was performed at 60 °C at a flow rate of 2 mL/min by building up the following gradients: 0.1% TFA in acetonitrile/0.1% TFA in water (10/90 v/v) for 10 min, then 0.1% TFA in acetonitrile/0.1% TFA in water/methanol (10/85/5 v/v/v) for **5a** or 0.1% TFA in acetonitrile/0.1% TFA in water (10/90 to 40/60 v/v for 30 min) for **5b**.
The purities of the conjugates **5a** and **5b** determined by C_{18} reversed phase HPLC were found to be higher than 95% (96.2 and 98.5%, respectively).

Conjugate **5a**



Conjugate **5b**