Probing the Influence of Linker Length and Flexibility in the Design and Synthesis of New Trehalase Inhibitors

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5) Associated with Consorzio Interuniversitario Nazionale di ricerca in Metodologie e Processi Innovativi di Sintesi (CINMPIS)

Supplementary Materials

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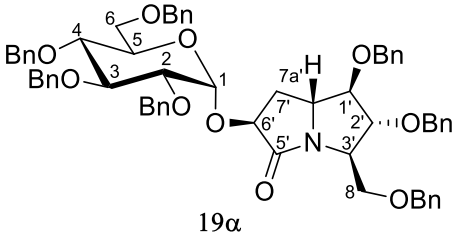
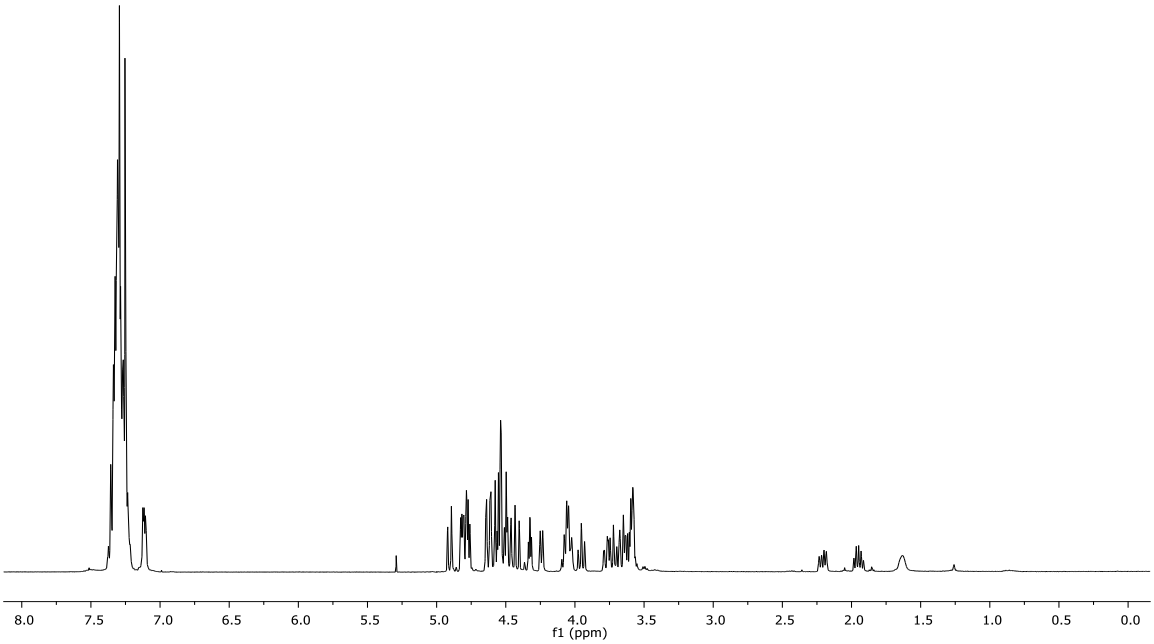


19α



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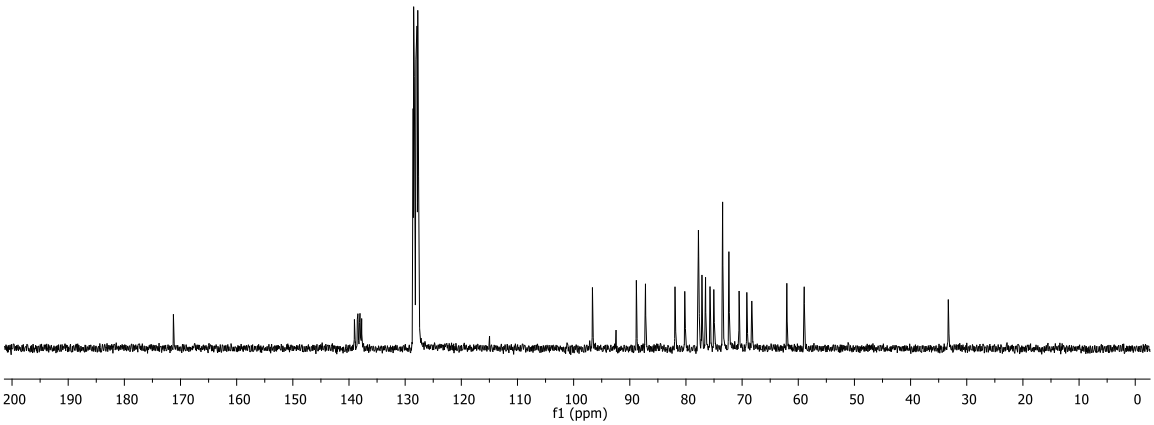

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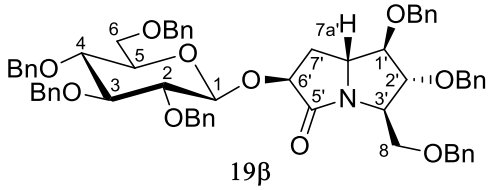
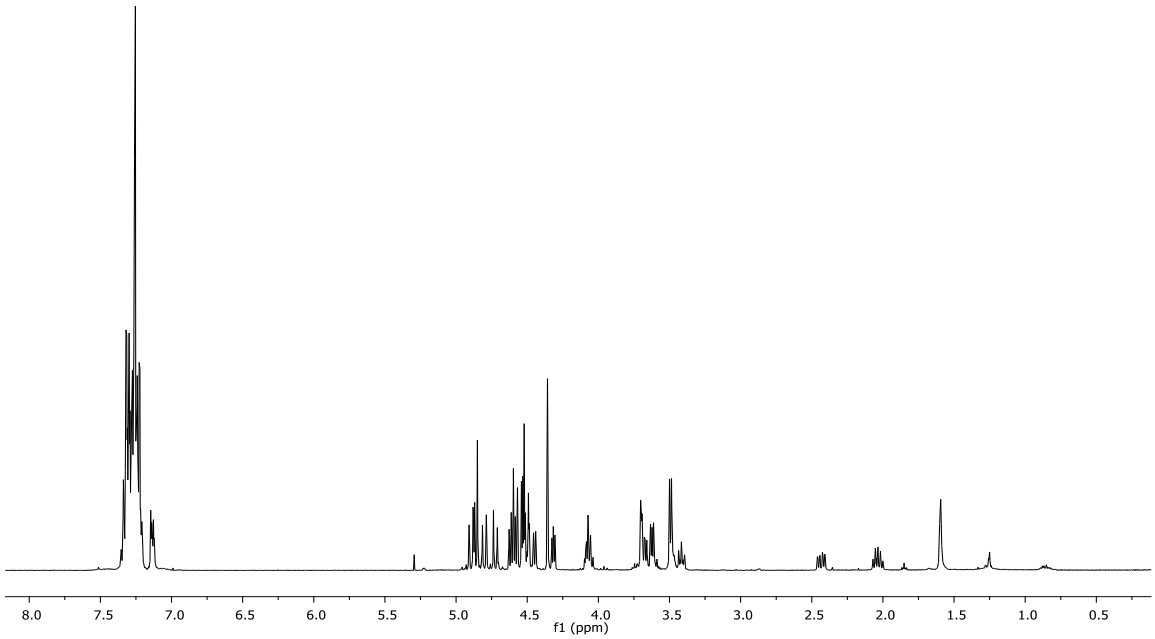


19β



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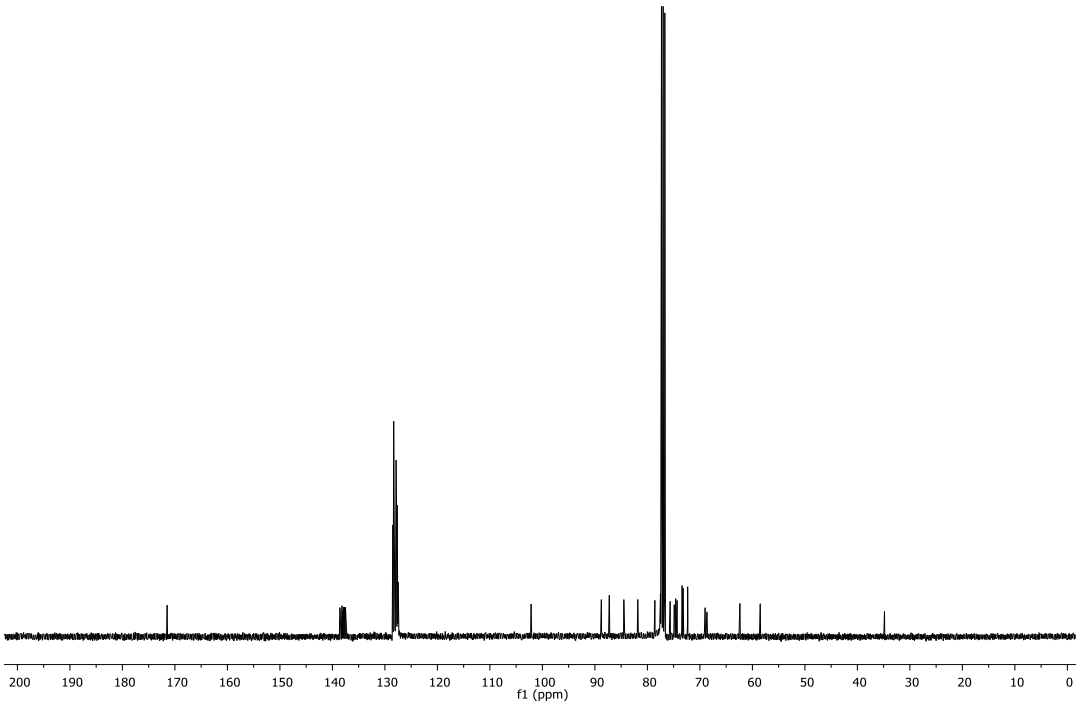

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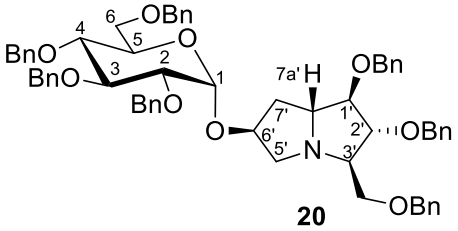

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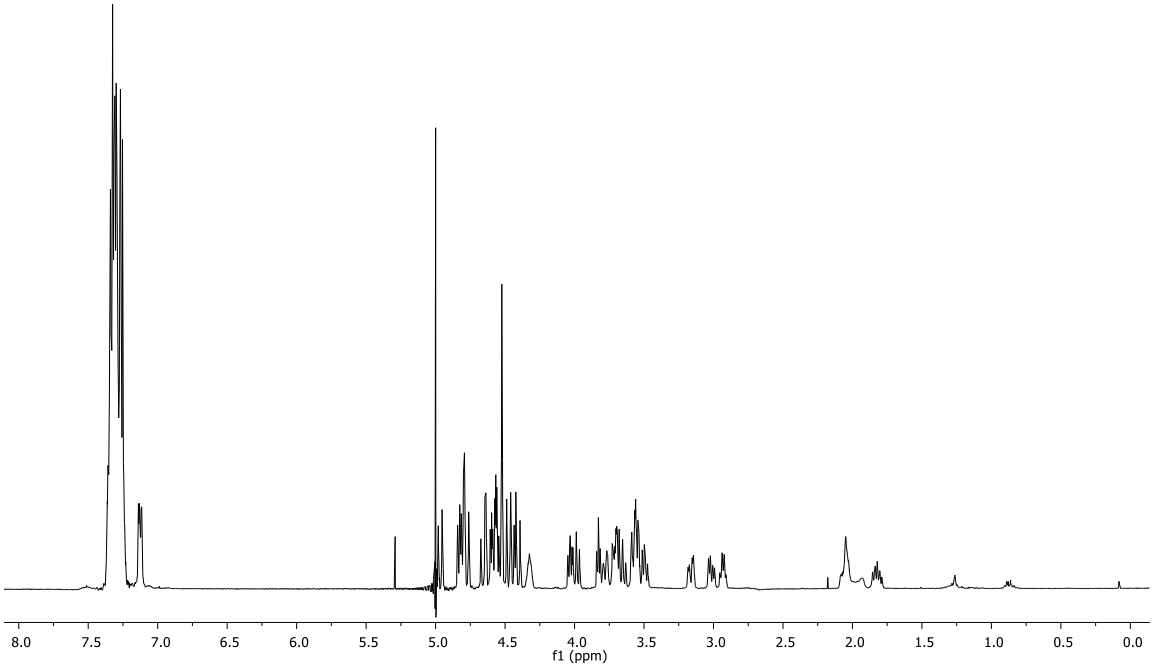

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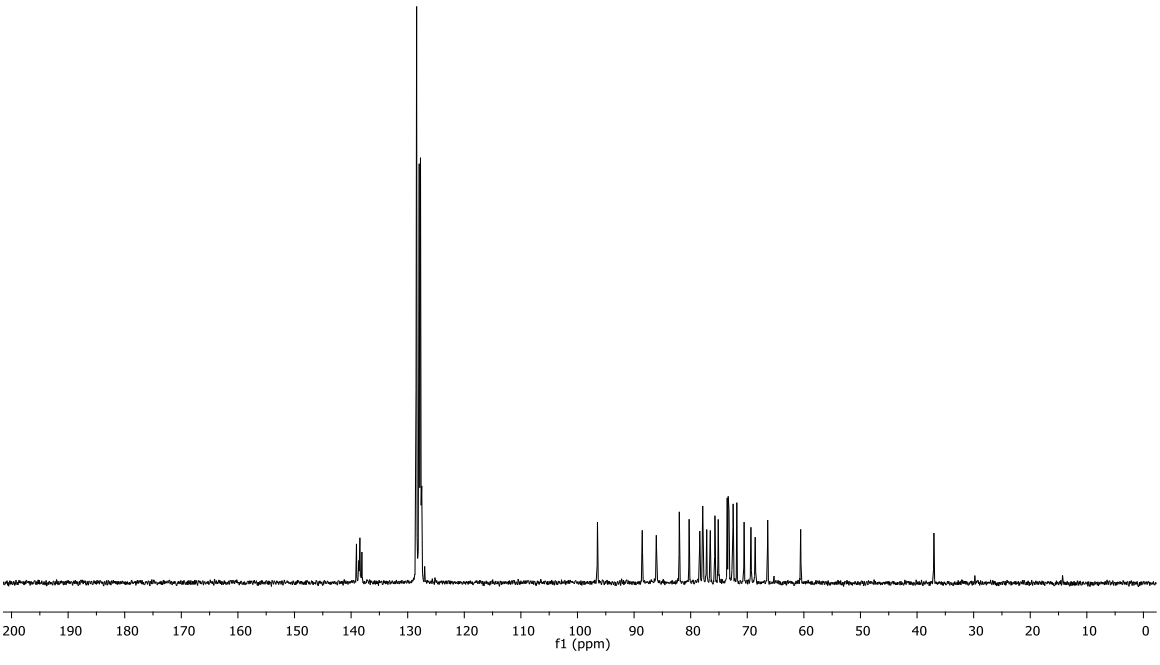

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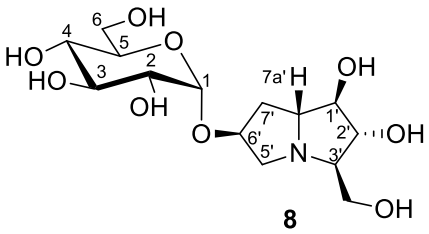

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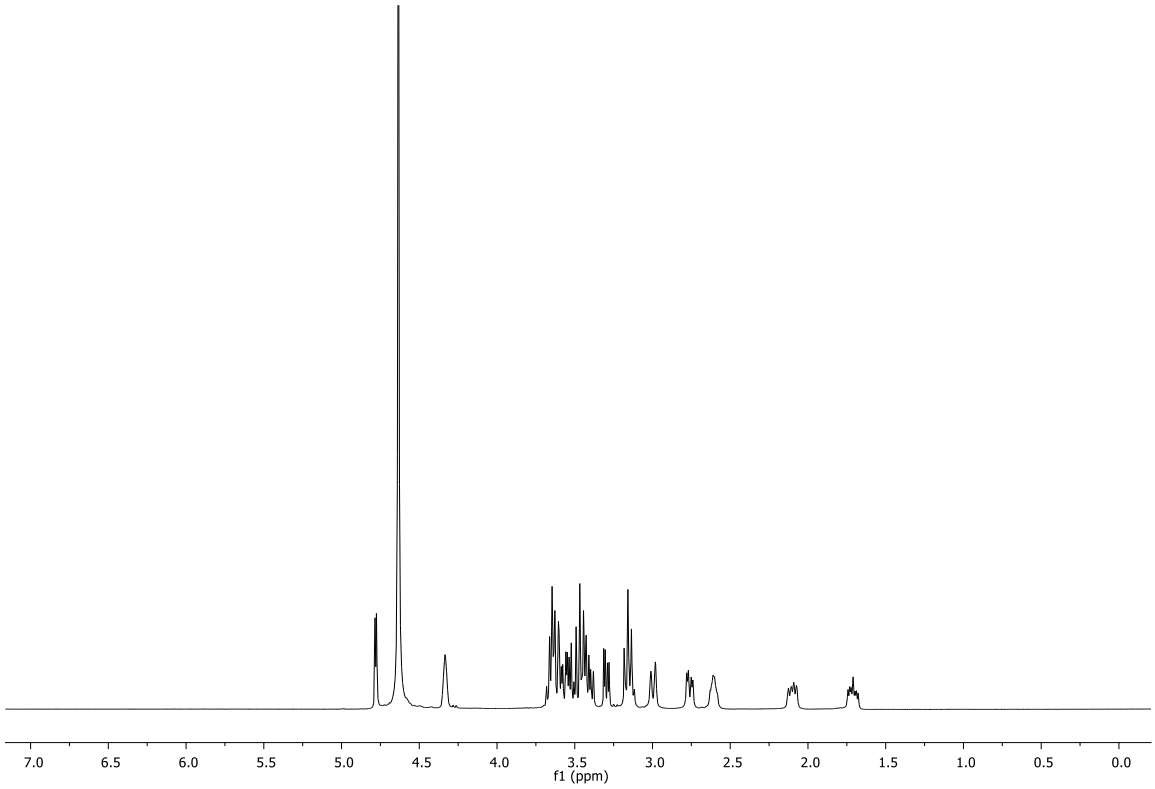

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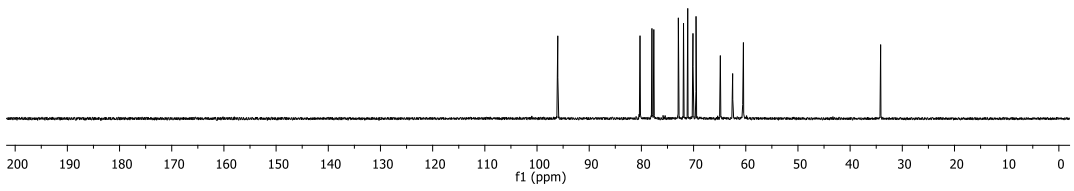

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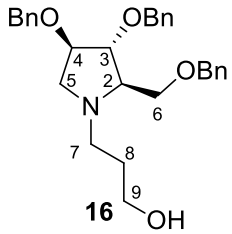

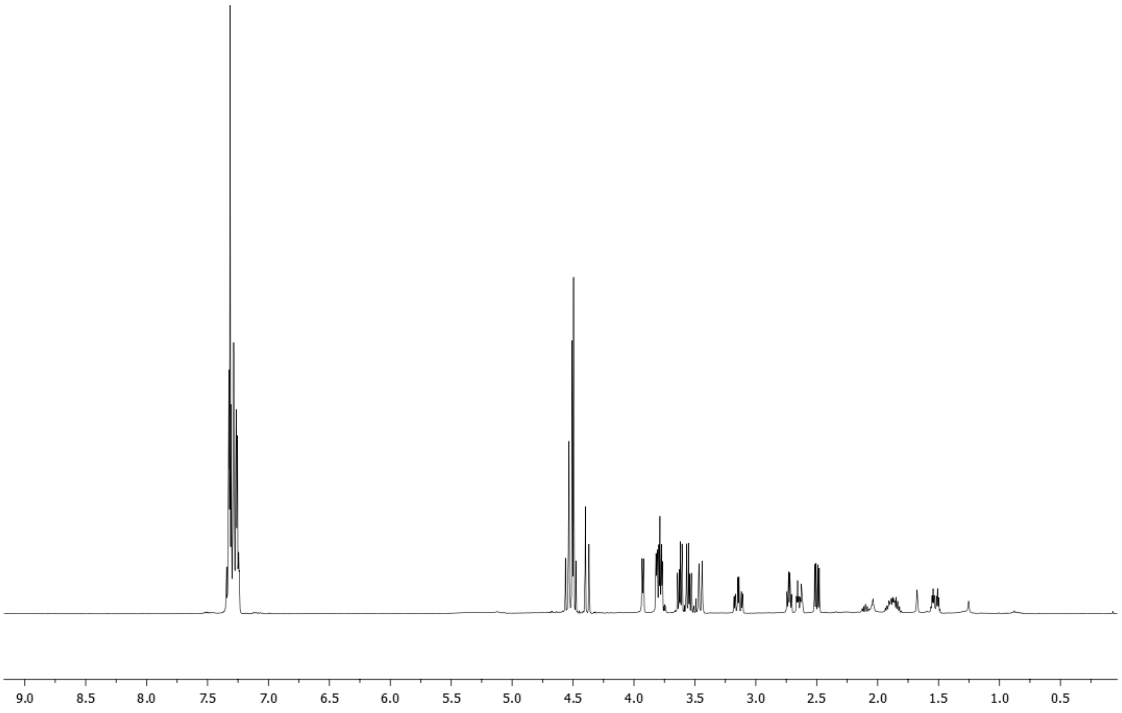

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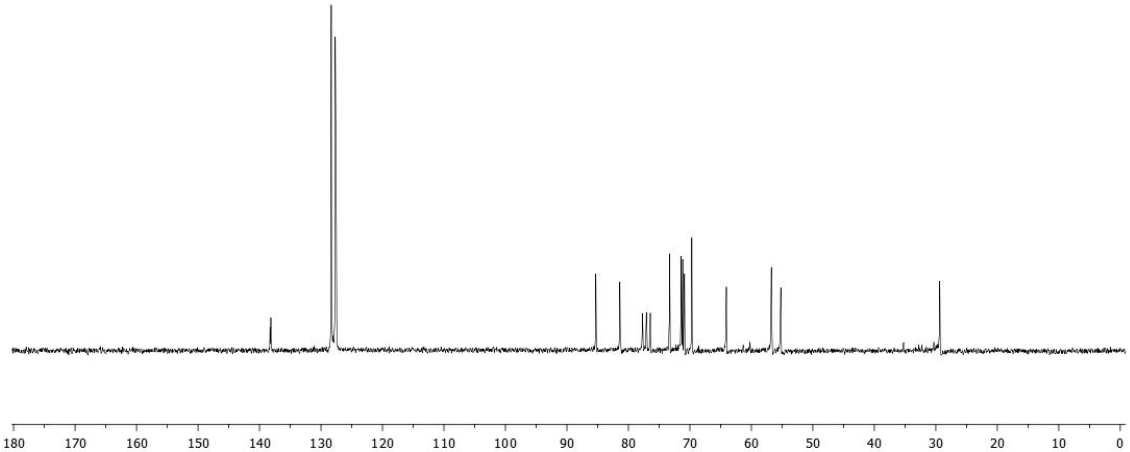

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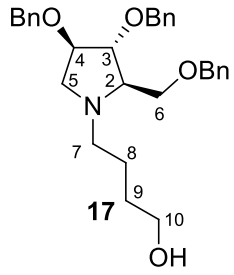

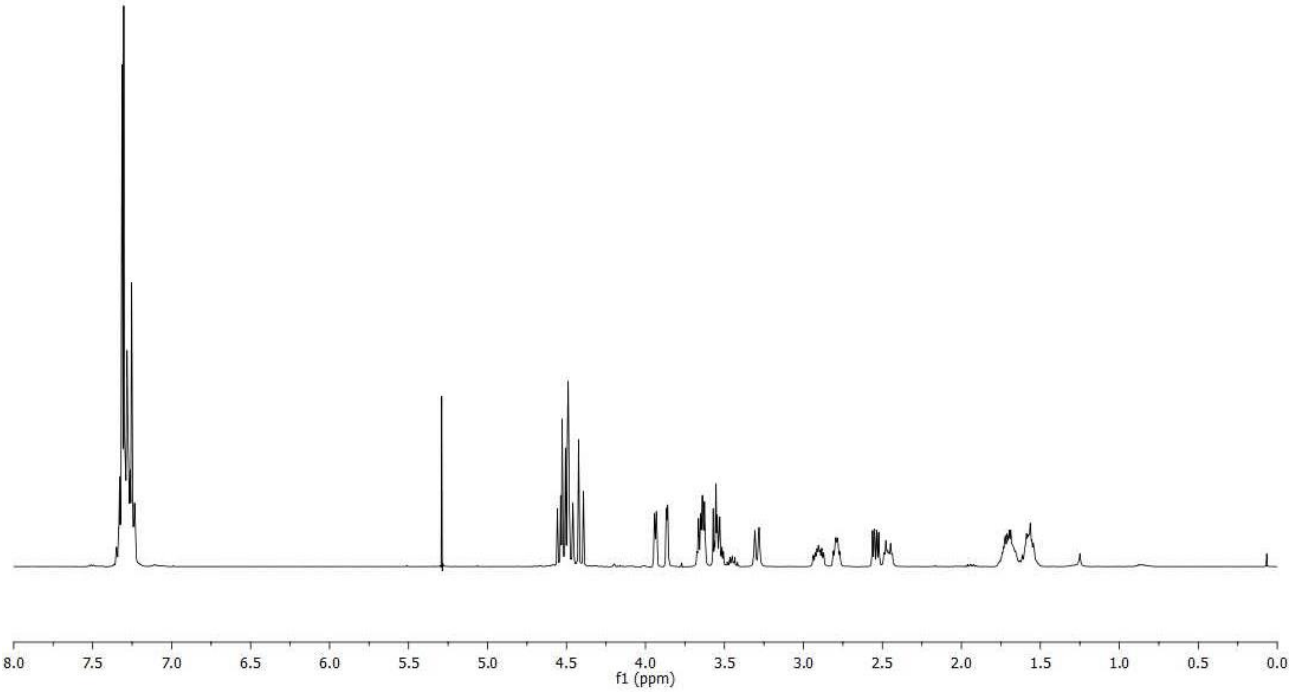

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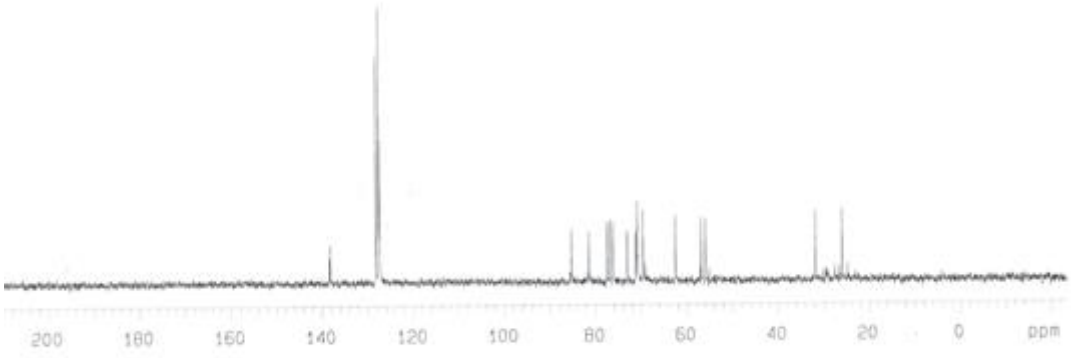

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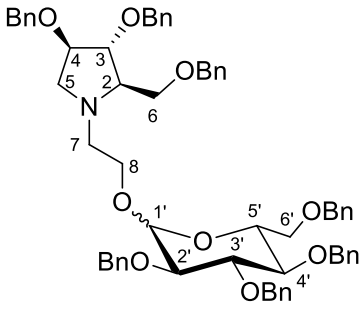
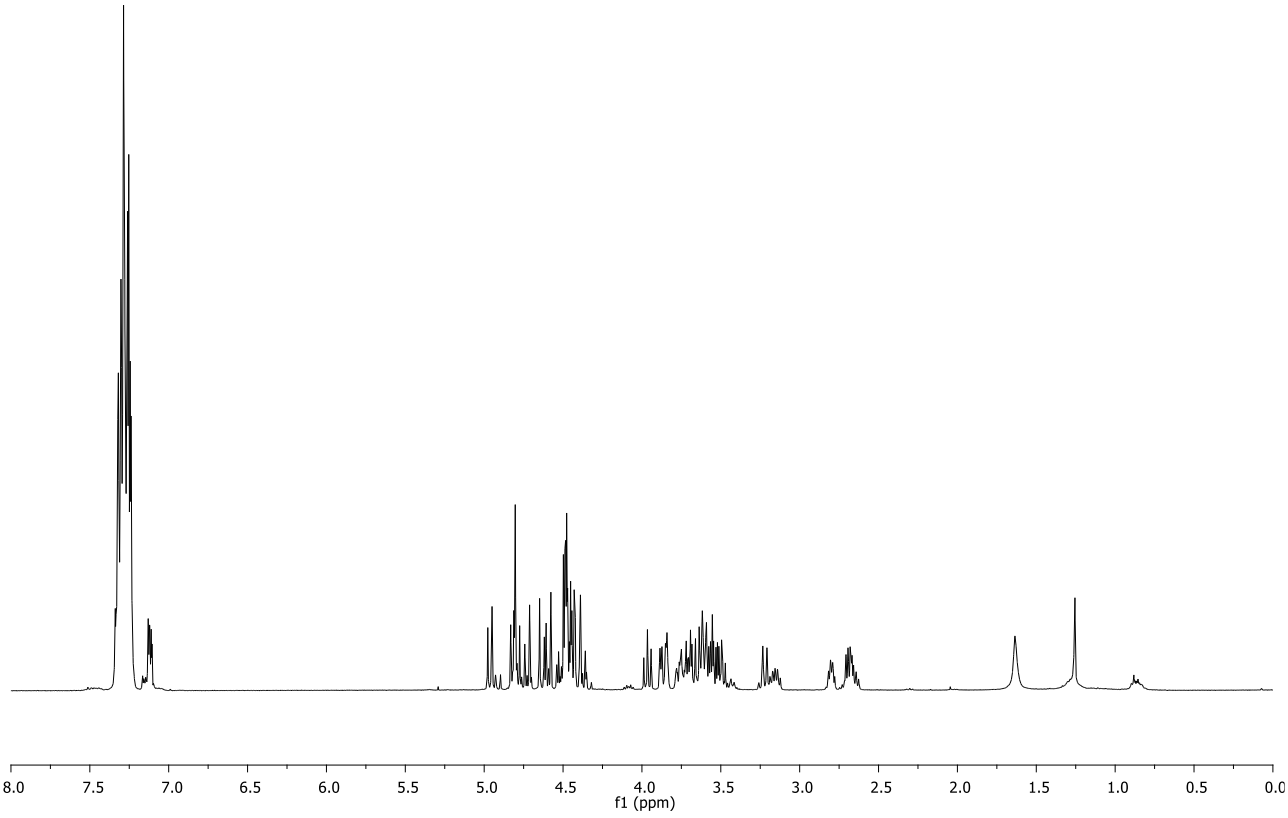
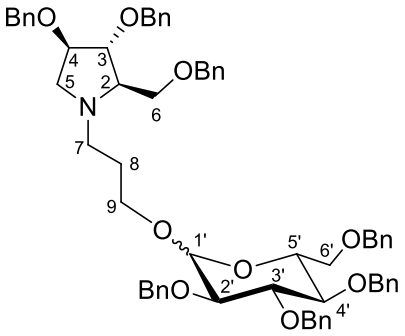


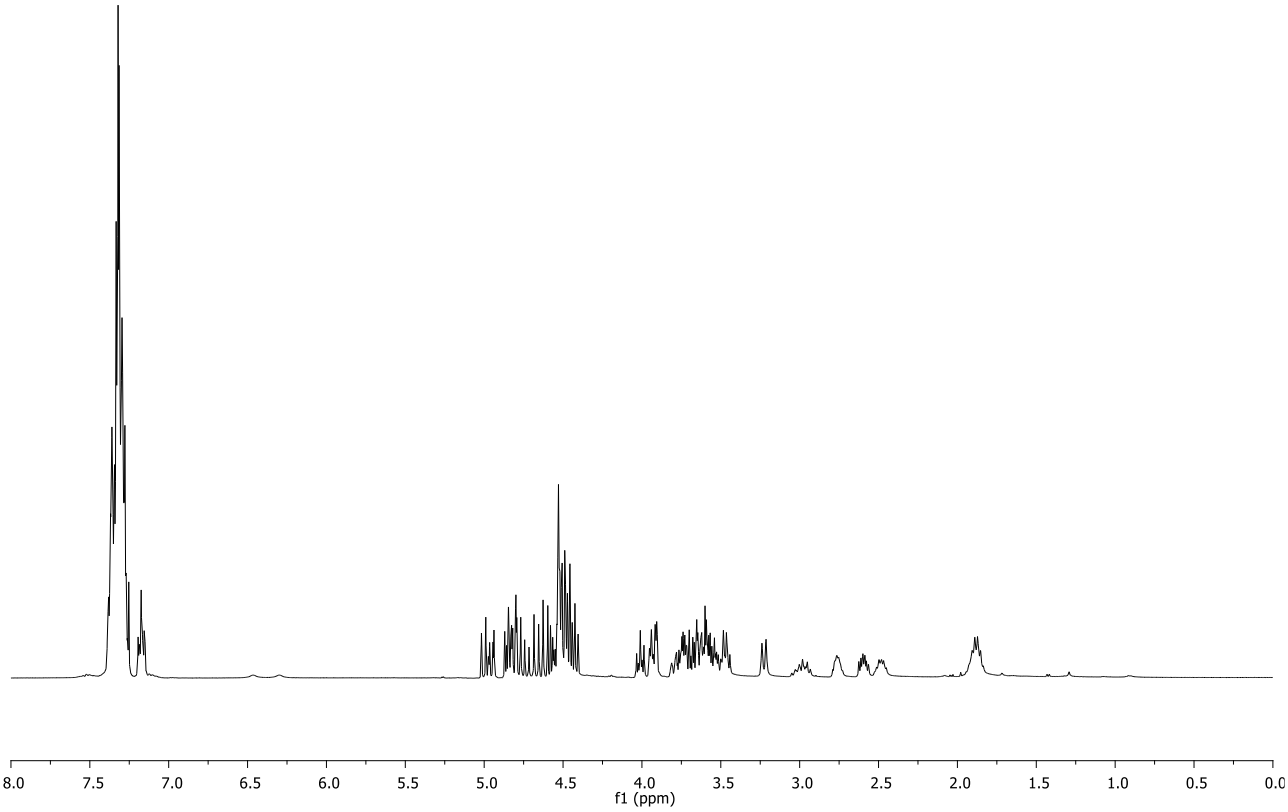
21α,β



^{1}H-NMR spectrum of the purified mixture of anomers 21α and 21β (400 MHz, $CDCl_3$)



22α,β



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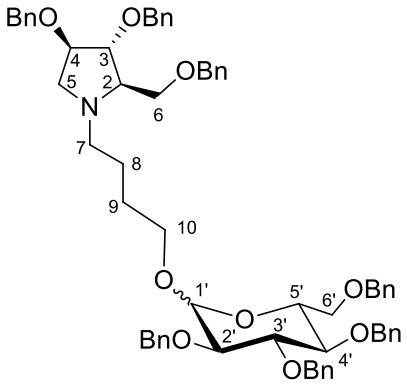
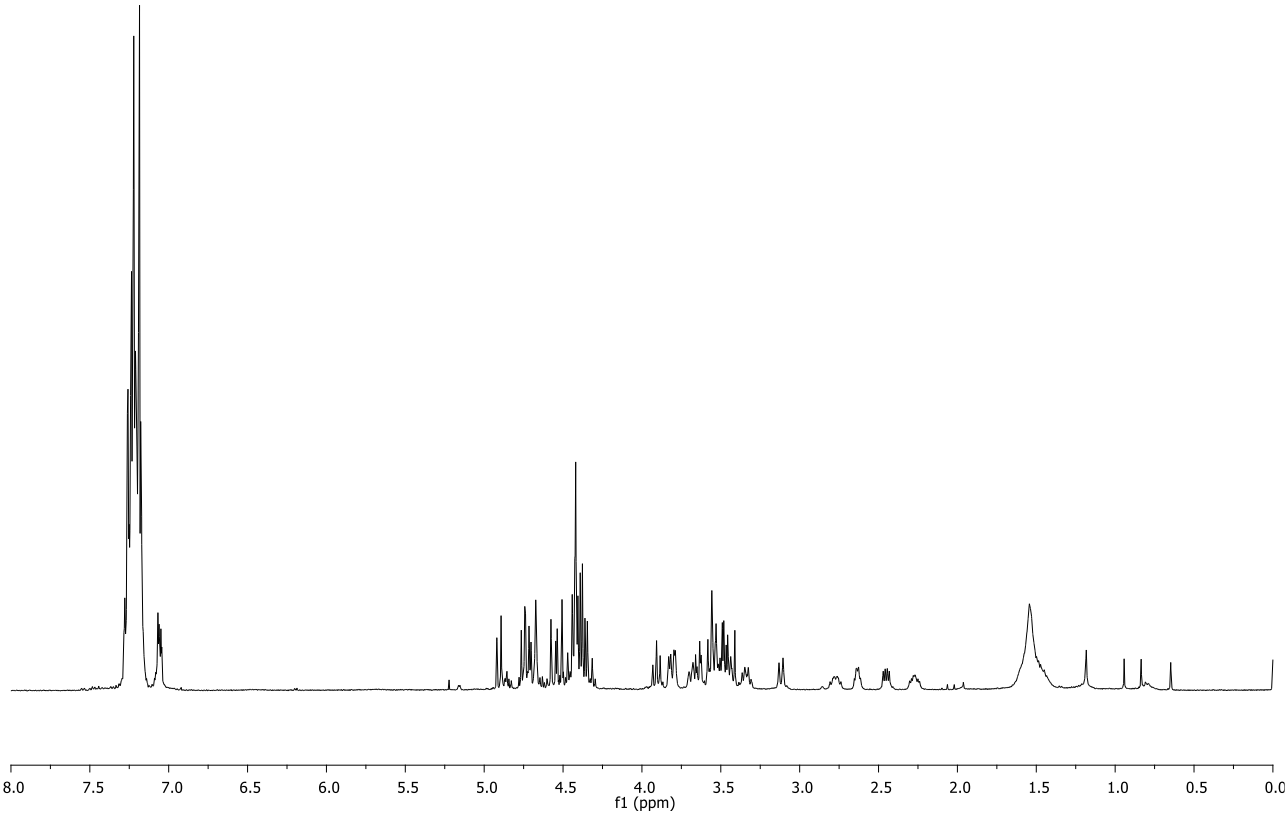
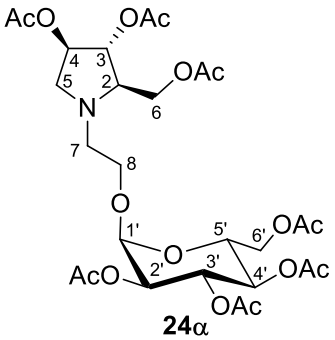


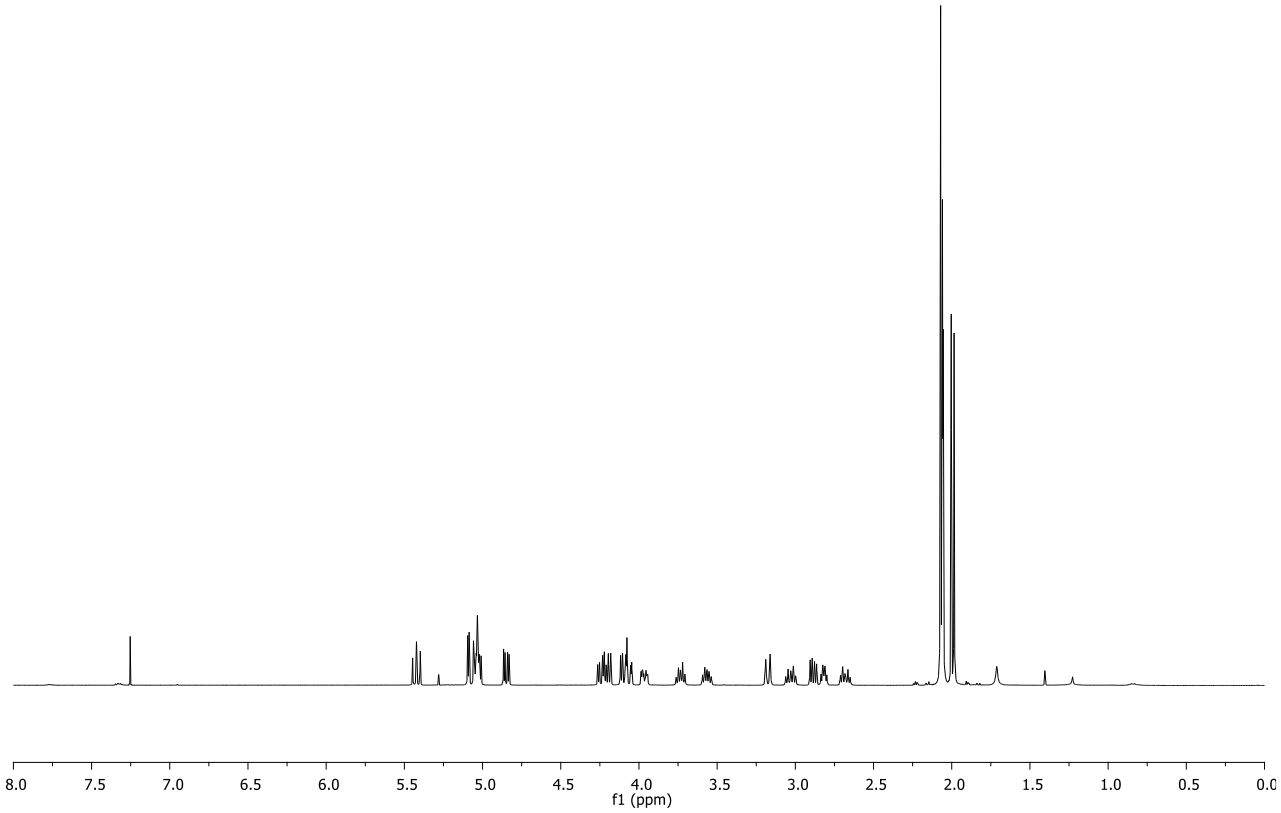
23α,β



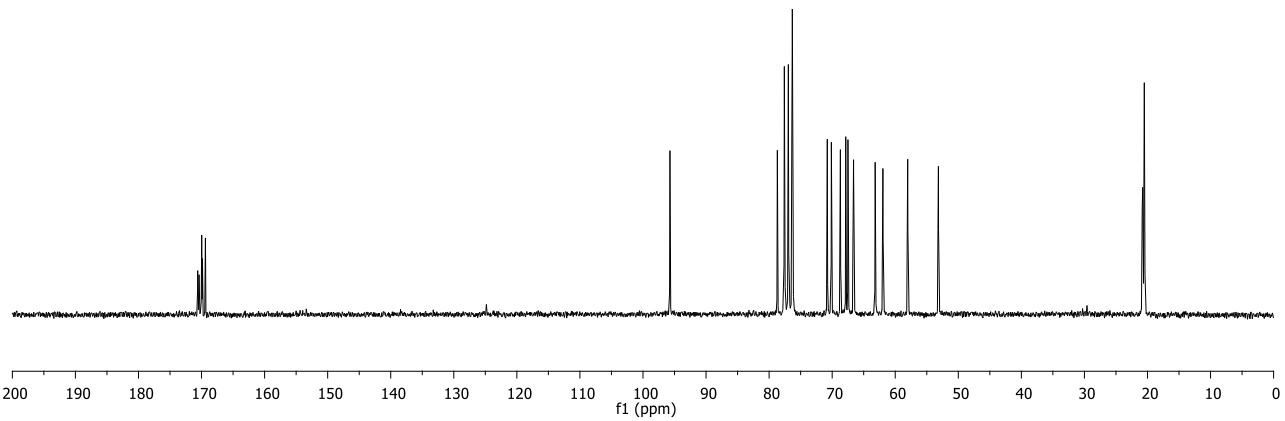
^{1}H-NMR spectrum of the purified mixture of anomers 23α and 23β (400 MHz, $CDCl_3$).



24α



^{1}H-NMR spectrum of compound 24α (400 MHz, $CDCl_3$)



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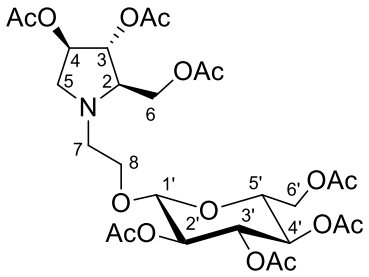
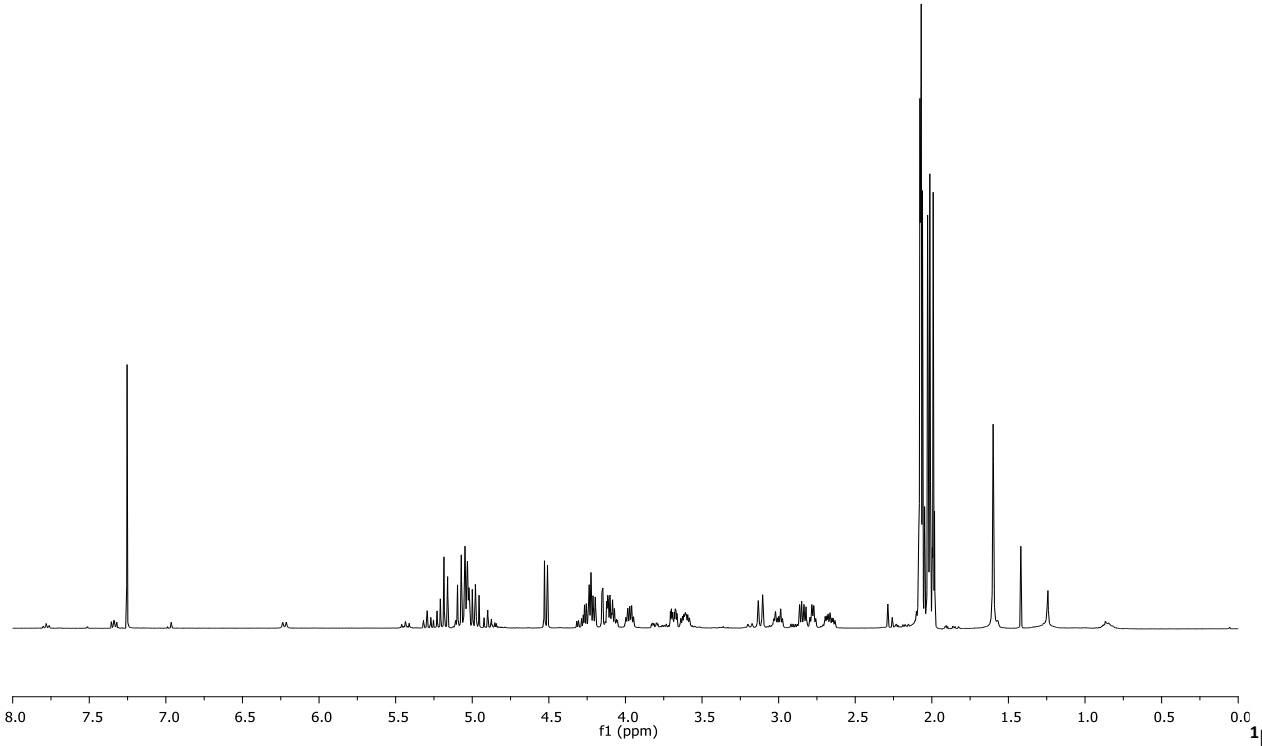


24β



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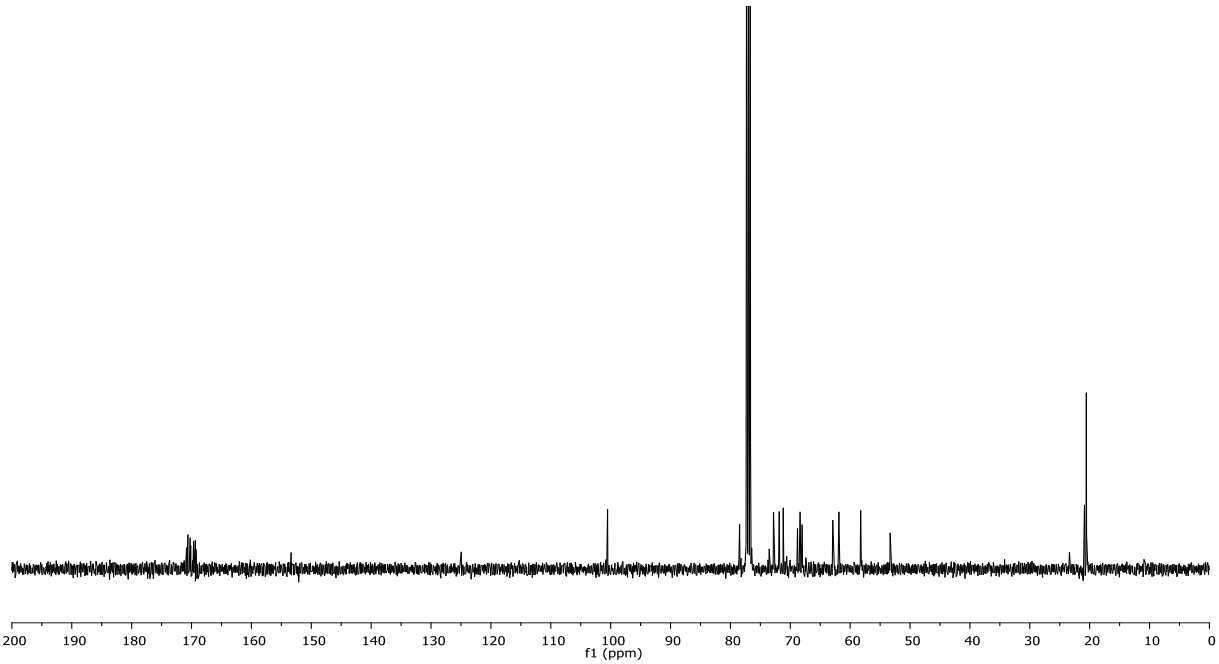

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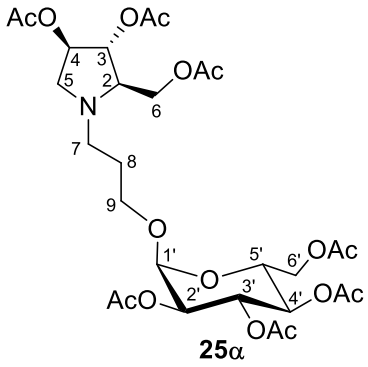
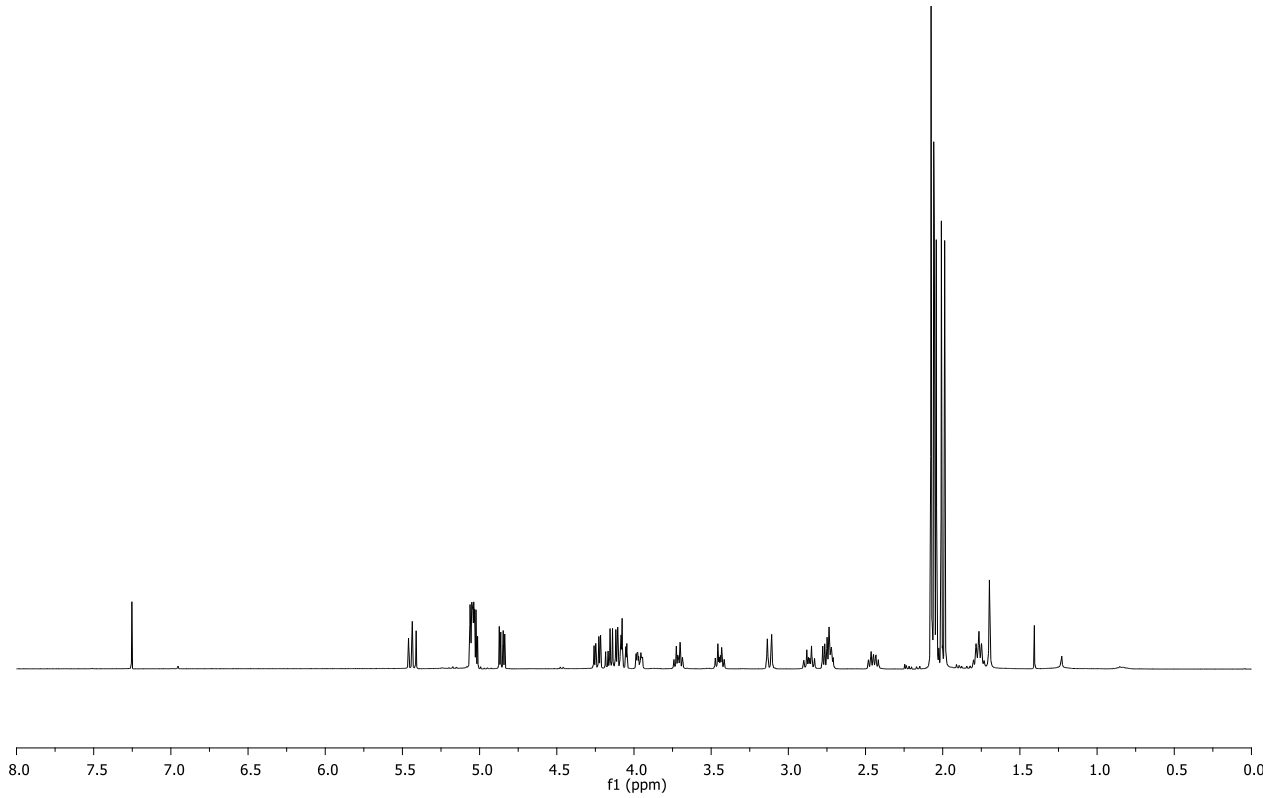
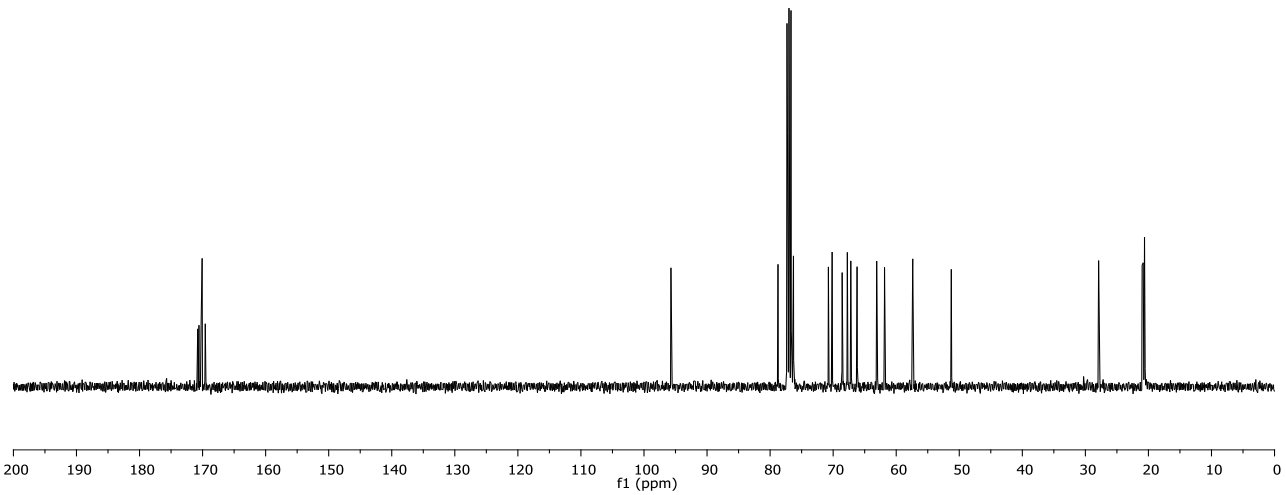


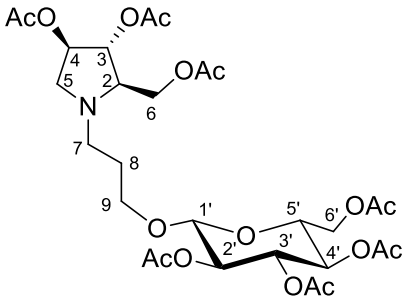
25α



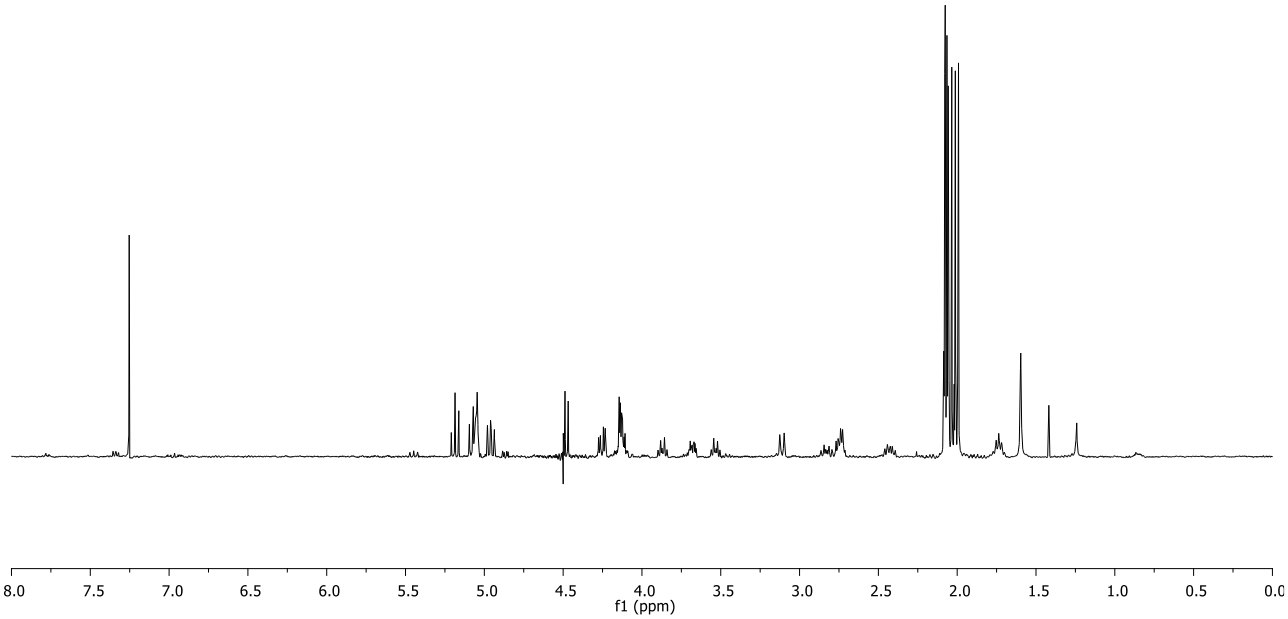
^{1}H-NMR spectrum of compound 25α (400 MHz, $CDCl_3$)



^{13}C-NMR spectrum of compound 25α (100 MHz, $CDCl_3$)



25β



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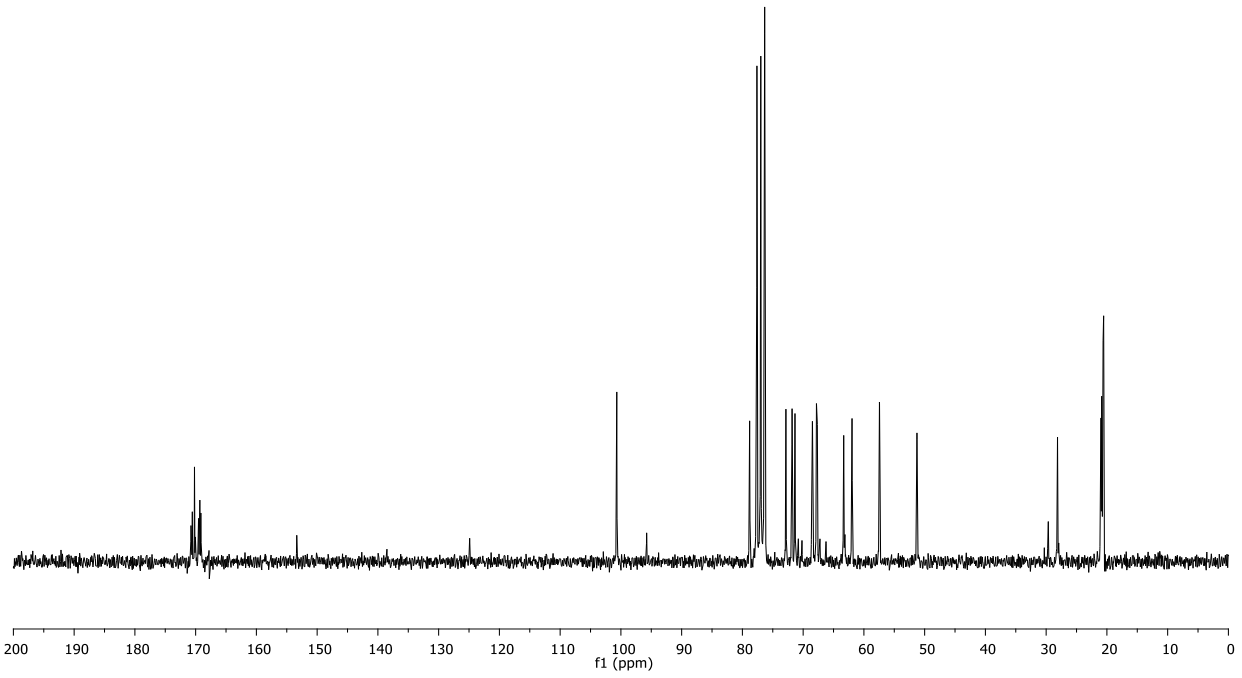

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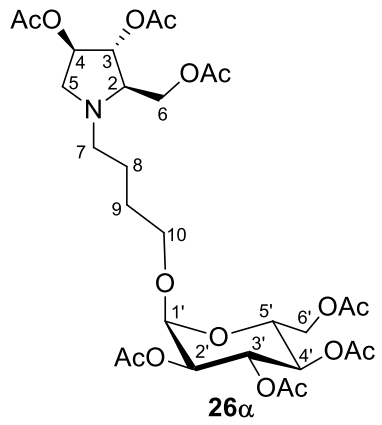
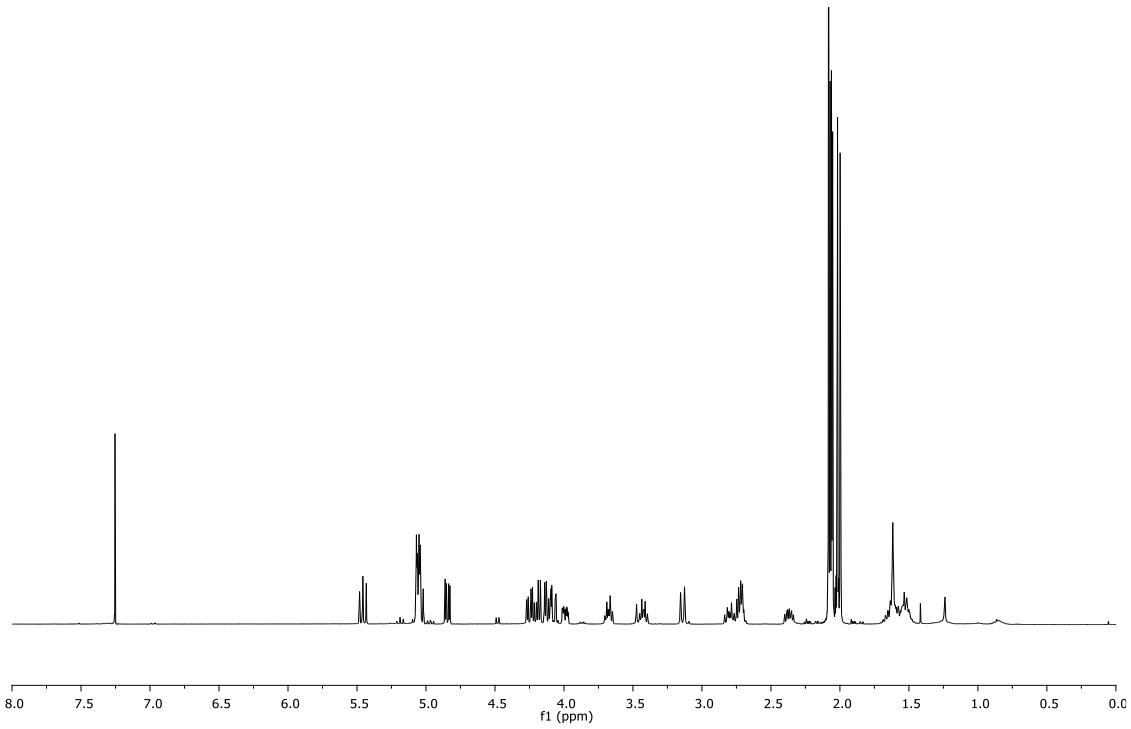
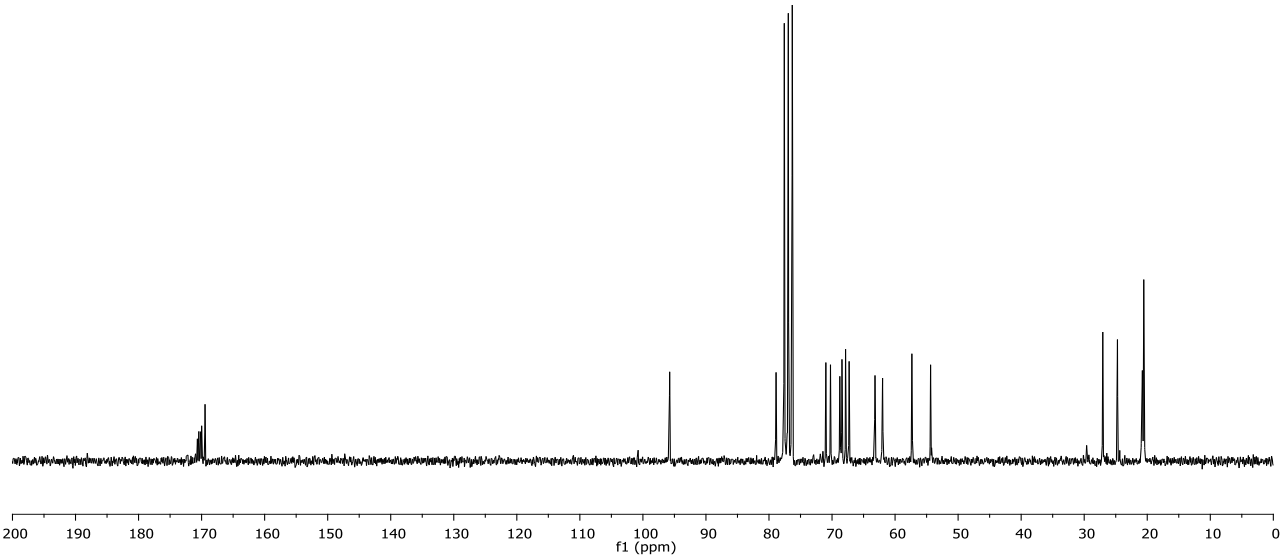


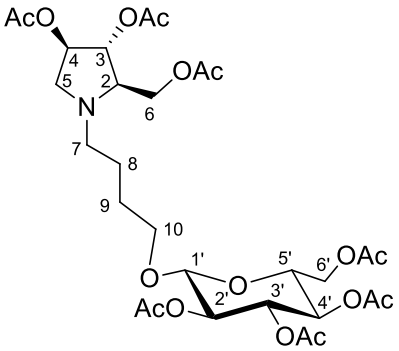
26α



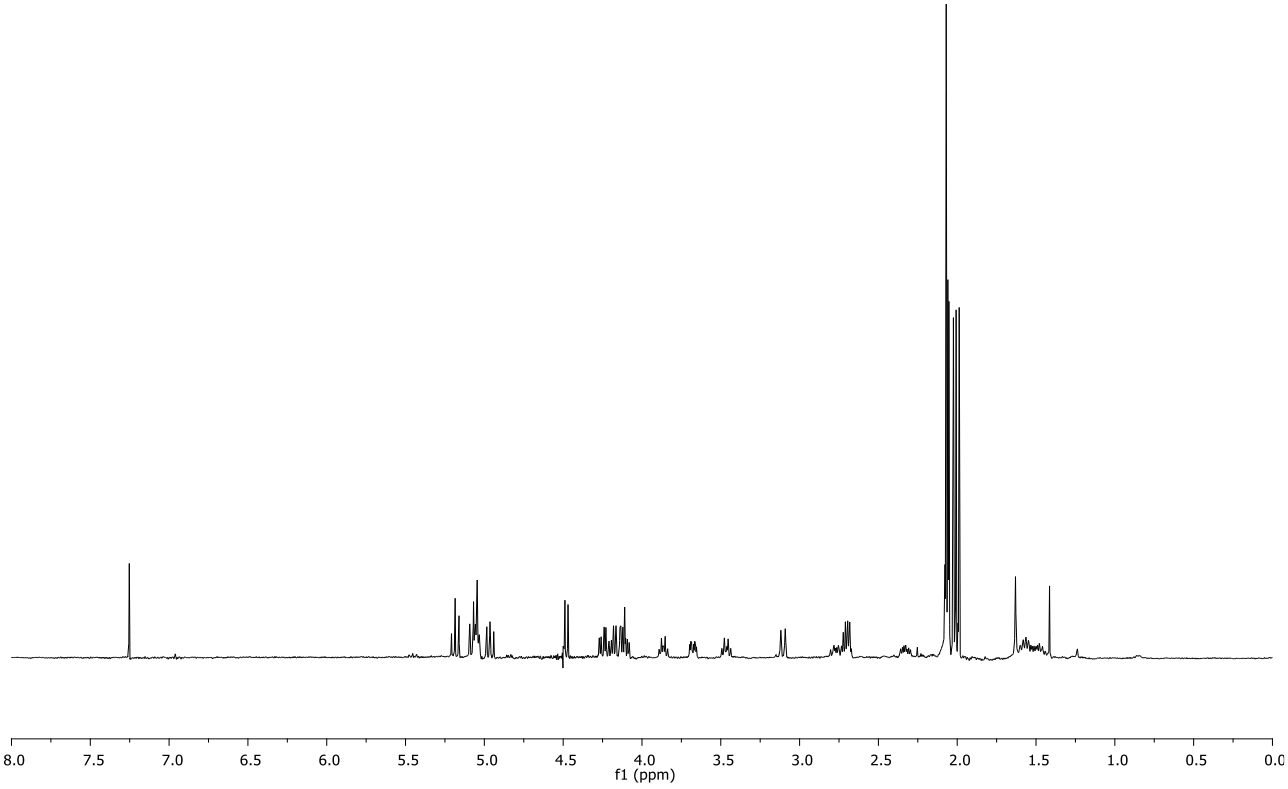
^{1}H-NMR spectrum of compound 26α (400 MHz, $CDCl_3$)



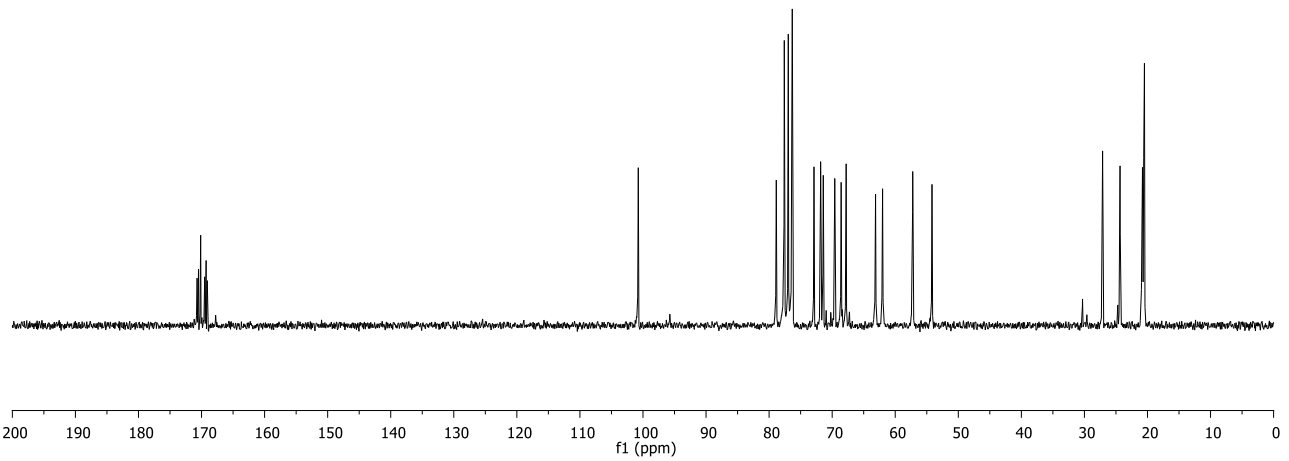
^{13}C-NMR spectrum of compound 26α (50 MHz, $CDCl_3$)



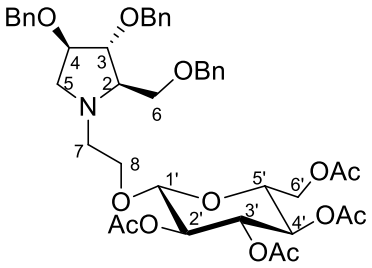
26β



^{1}H-NMR spectrum of compound 26β (400 MHz, $CDCl_3$)



^{13}C-NMR spectrum of compound 26β (400 MHz, $CDCl_3$)



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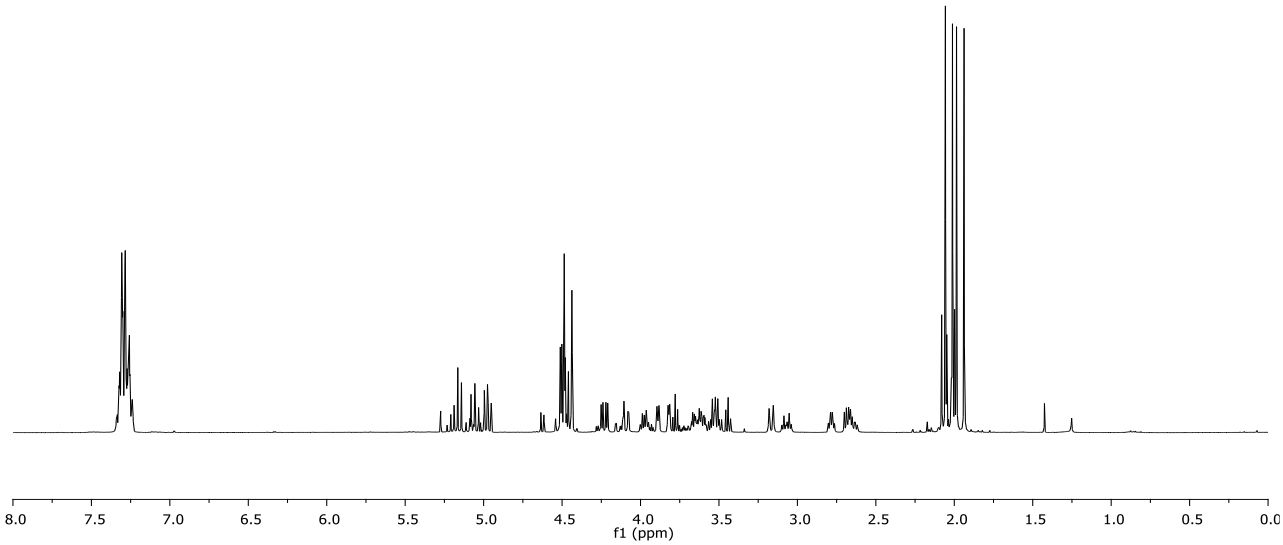
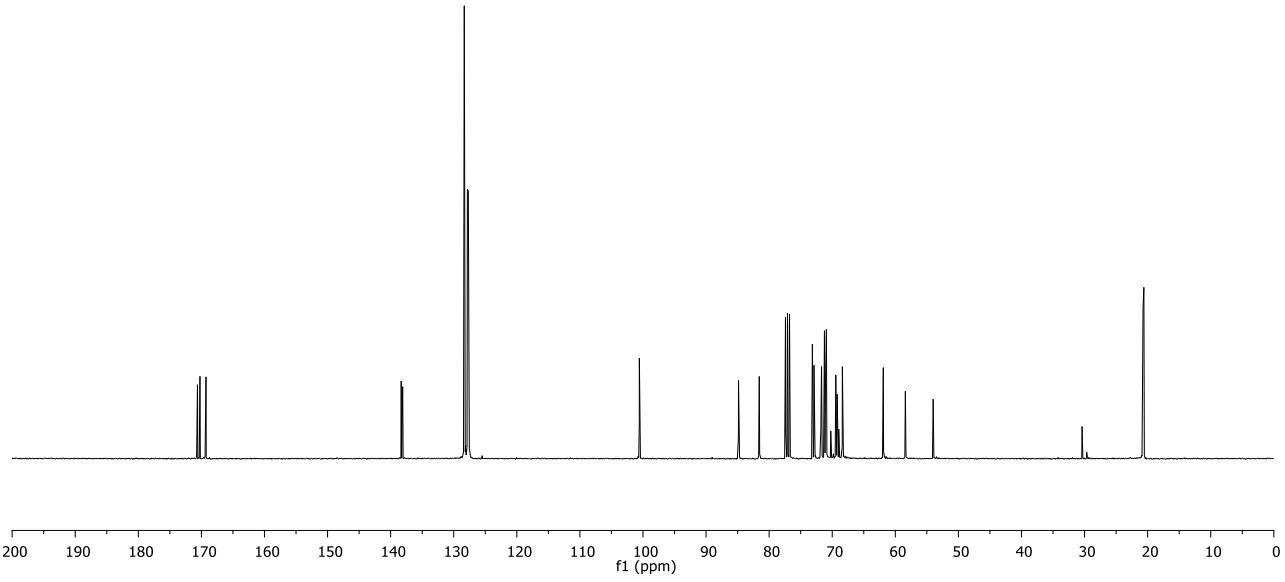
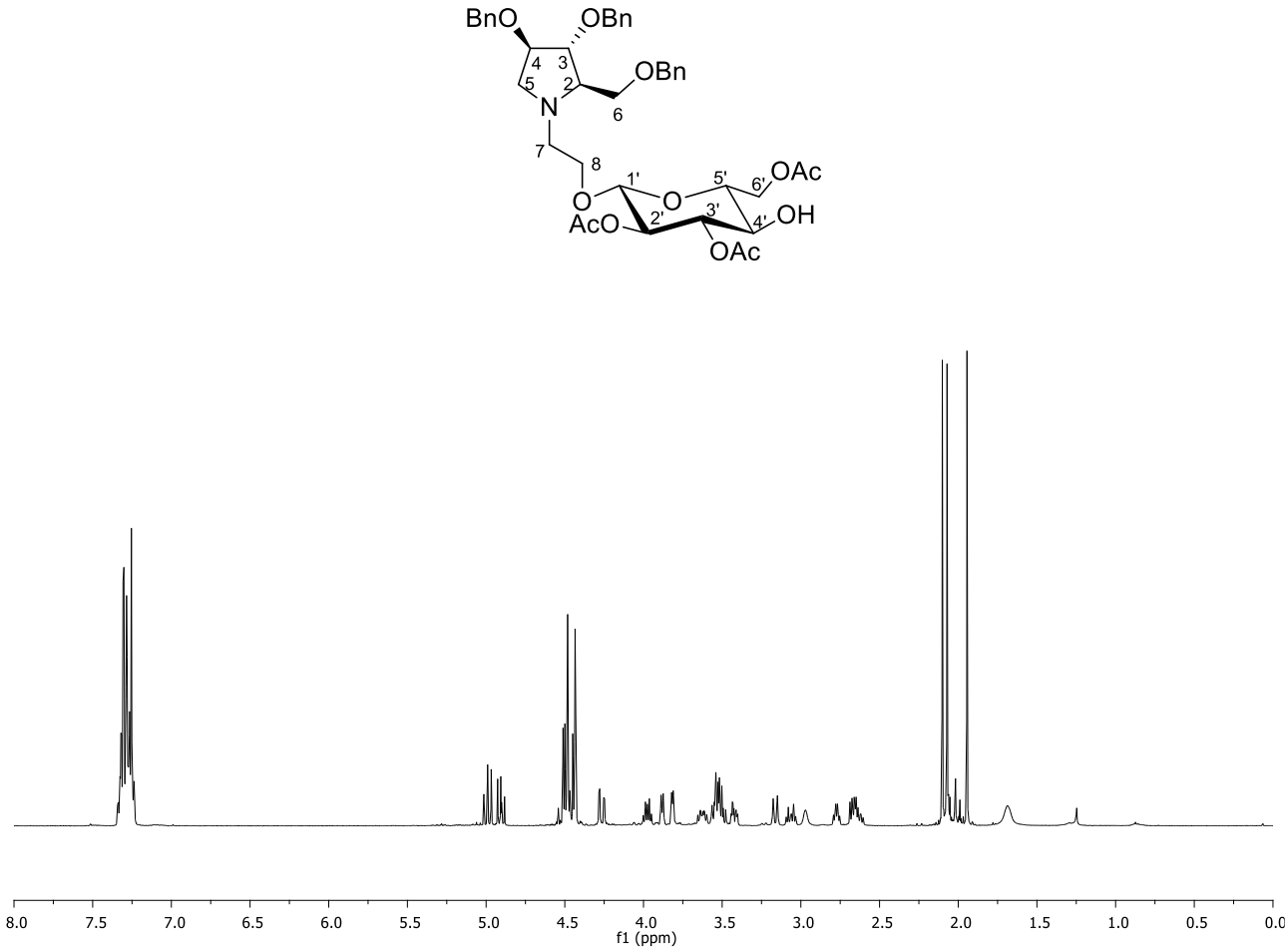


^{1}H-NMR spectrum of compound 30 (400 MHz, $CDCl_3$)

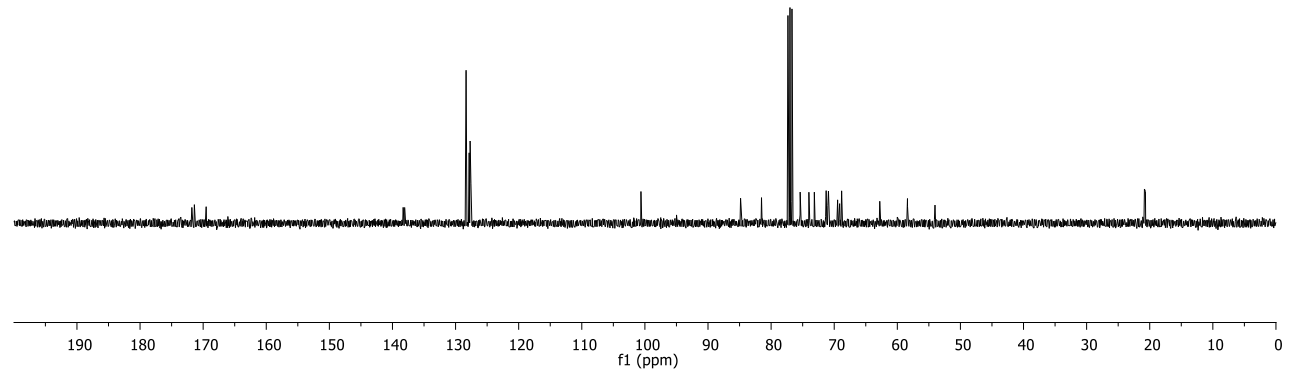


^{13}C-NMR spectrum of compound 30 (100 MHz, $CDCl_3$)

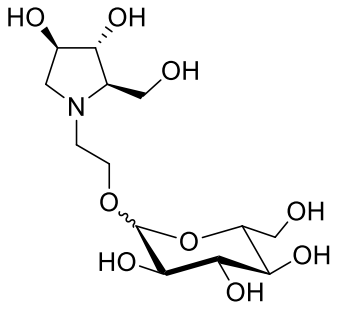
During an attempt of glucosylation of **29** (1 equiv) with **15** (1.5 equiv) performed in the presence of a high quantity of TMSOTf (2 equiv), we were able to isolate a fraction containing a glucosyl derivative deacetylated at C4'-OH (11% yield), identified by the ESI-MS signal at 736.55 $[M+H]^+$ and confirmed by ^{1}H and ^{13}C spectra. The signals of this deacetylated compound are present as impurities in the glycosylation compound **30** reported above.



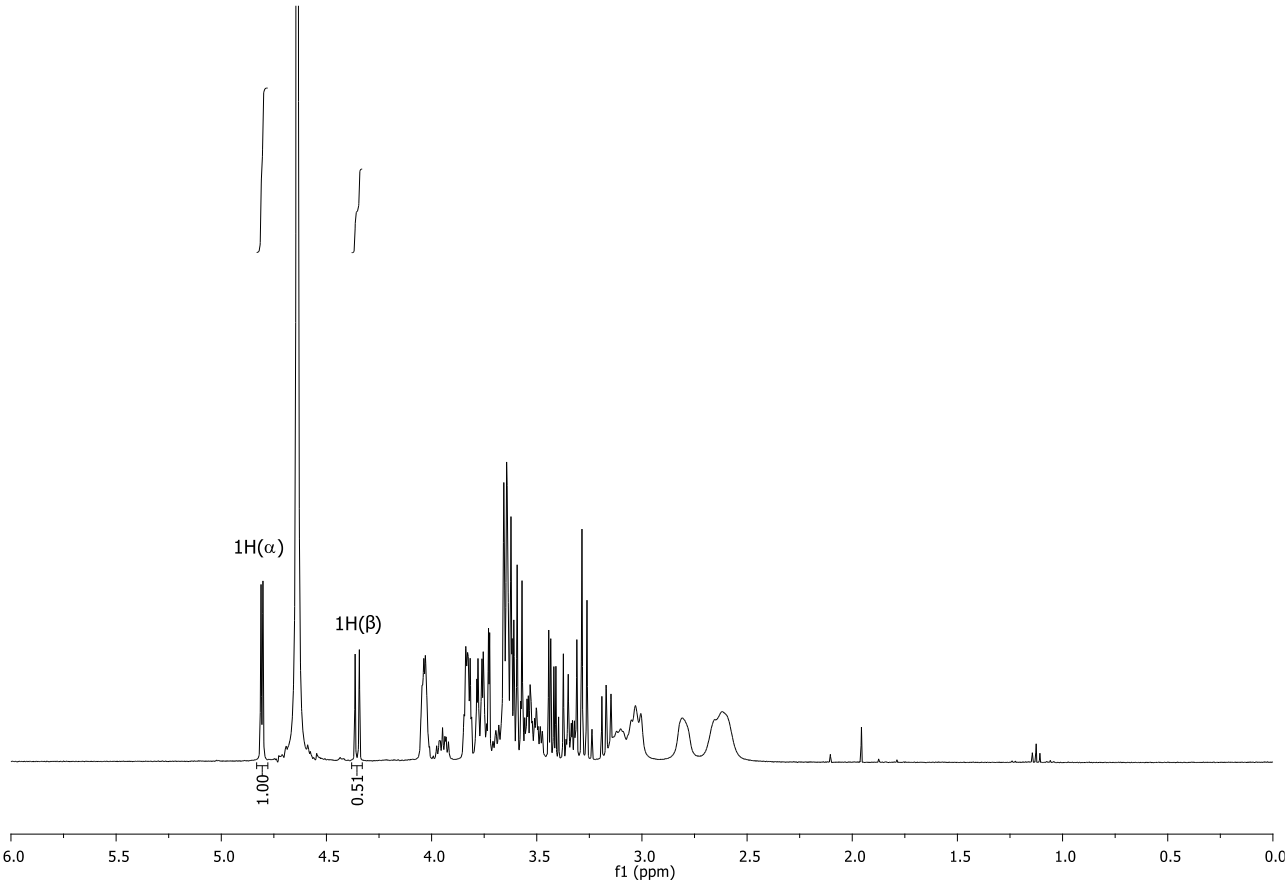
^{1}H-NMR spectrum (400 MHz, $CDCl_3$)



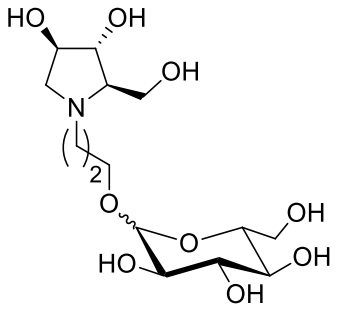
^{13}C-NMR spectrum (100 MHz, $CDCl_3$)



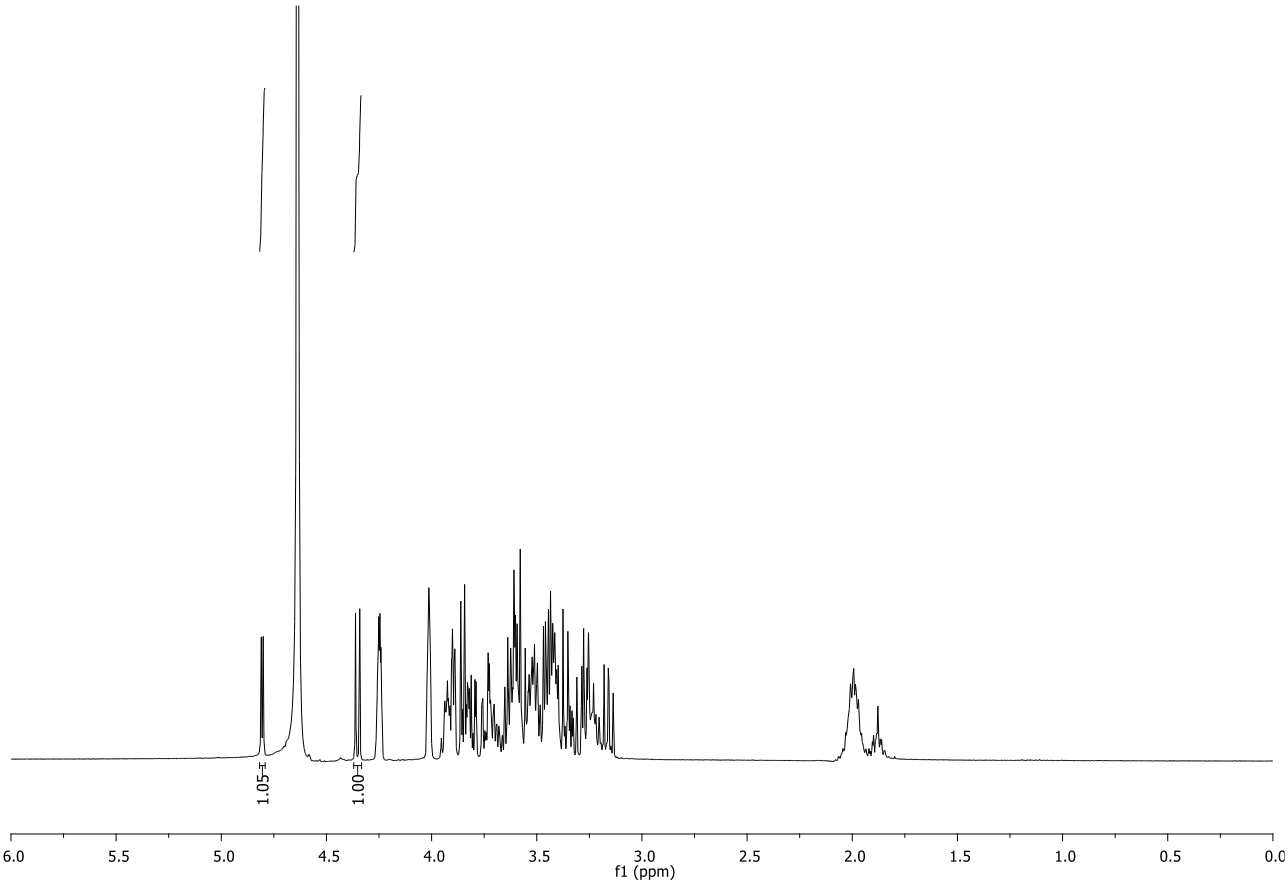
9α,β



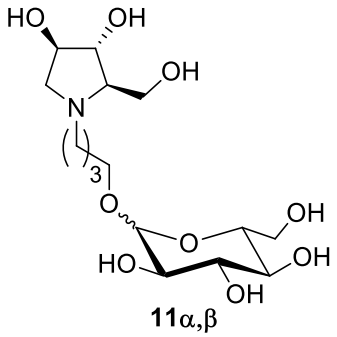
^{1}H-NMR spectrum of the mixture 9α,β (400 MHz, D_2O)



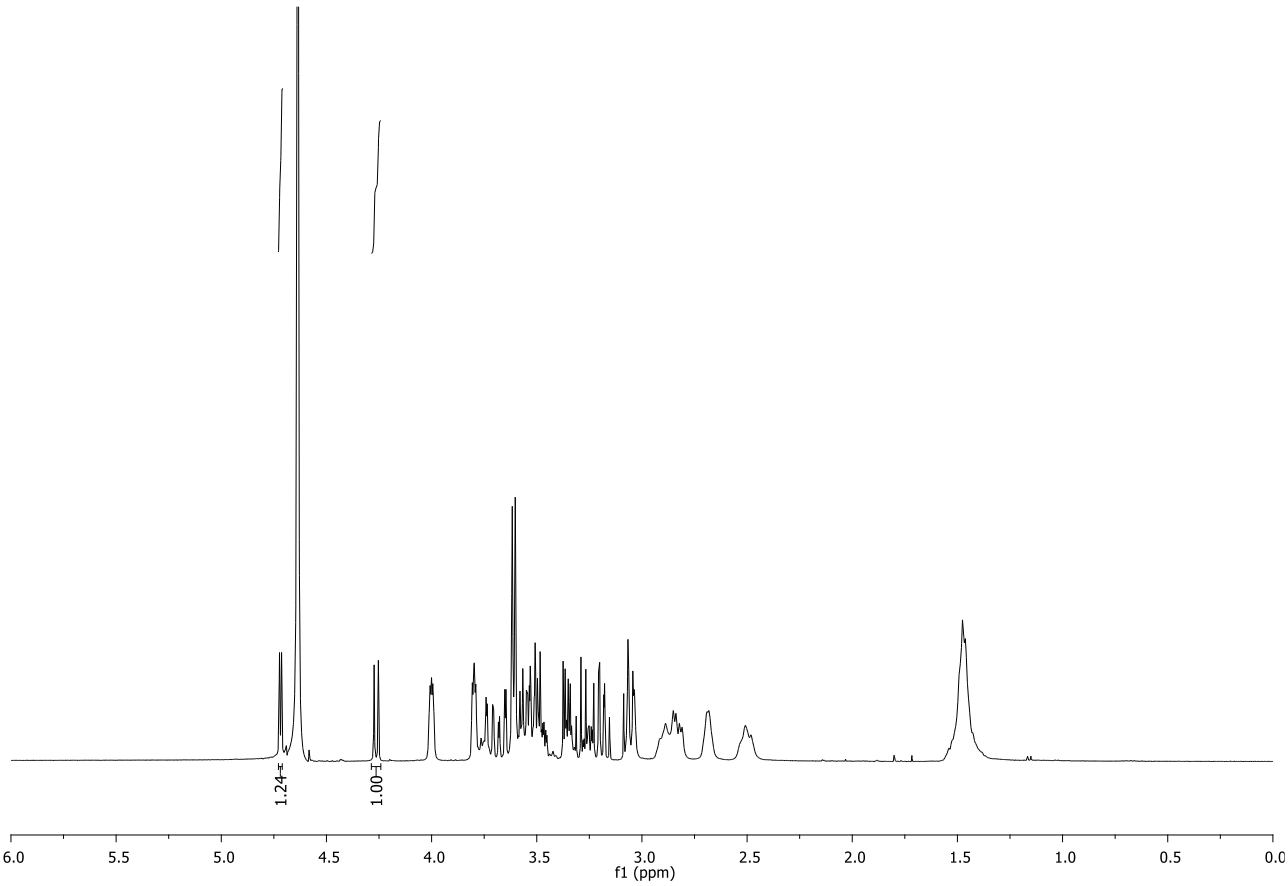
10α,β



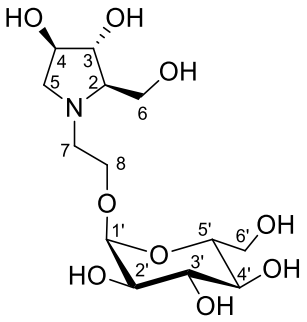
^{1}H-NMR spectrum of the mixture 10α,β (400 MHz, D_2O)



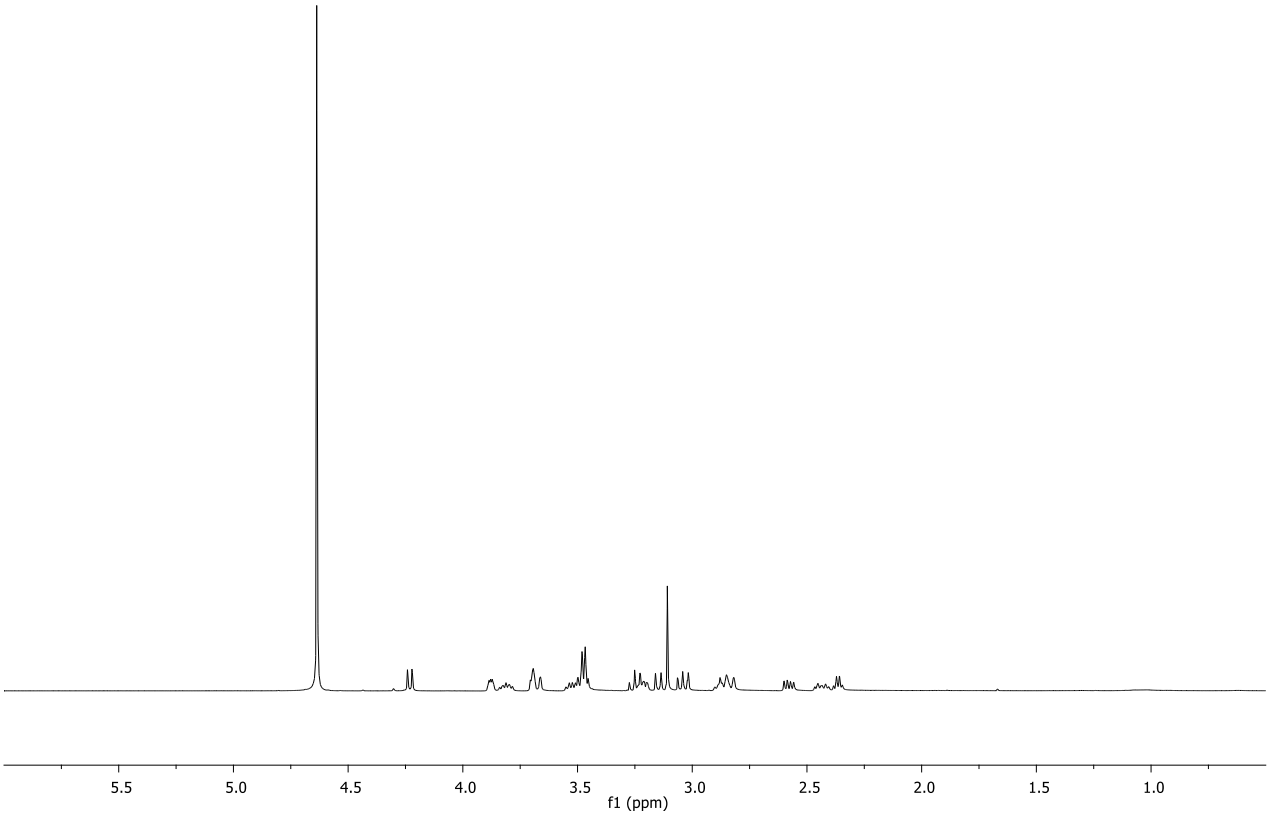
11α,β



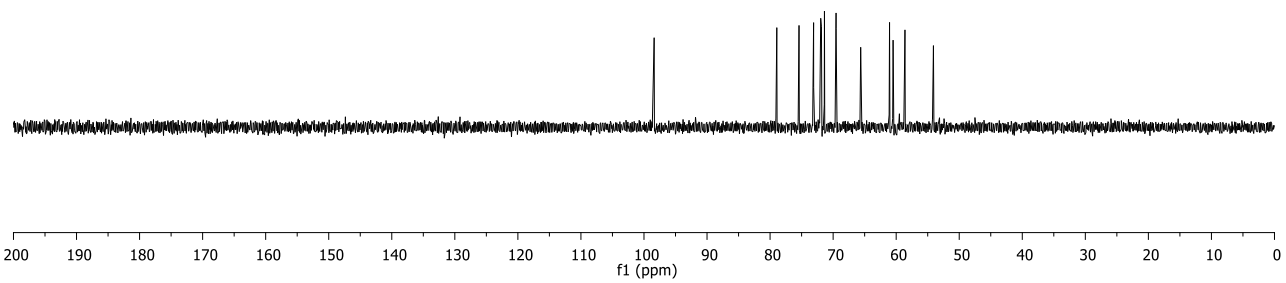
^{1}H-NMR spectrum of the mixture 11α,β (400 MHz, D_2O)



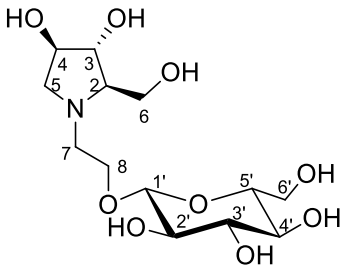
9α



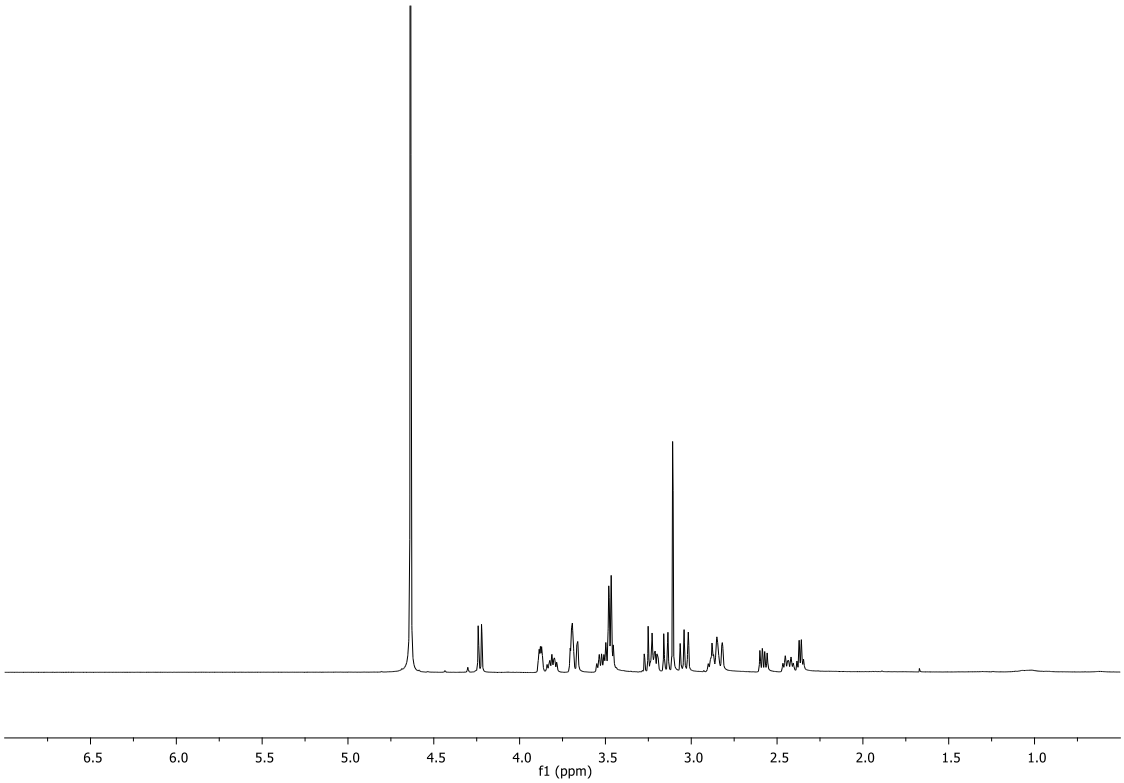
^{1}H-NMR spectrum of compounds 9α (400 MHz, D_2O)



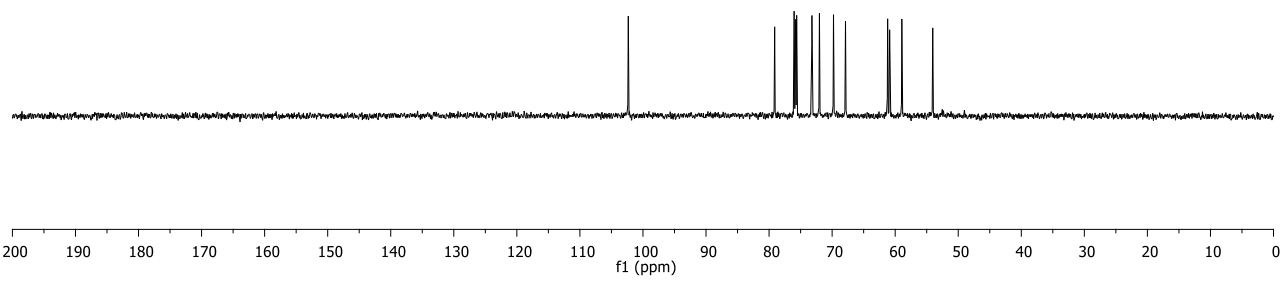
^{13}C-NMR spectrum of compounds 9α (100 MHz, D_2O)



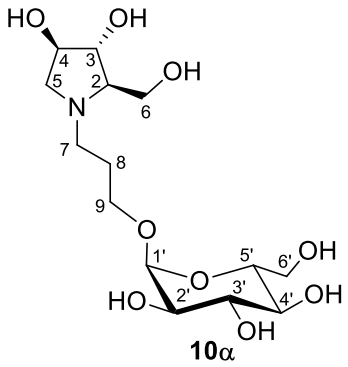
9β



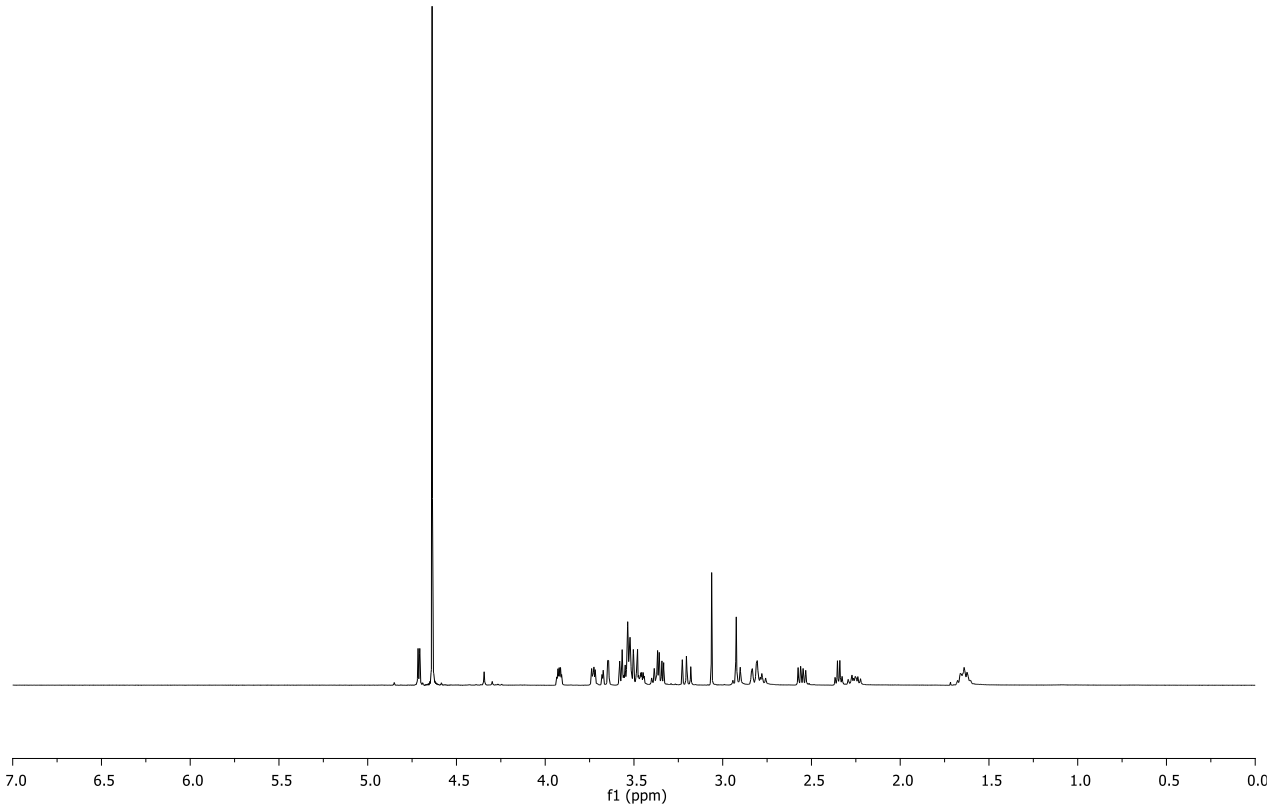
^{1}H-NMR spectrum of compounds 9β (400 MHz, D_2O)



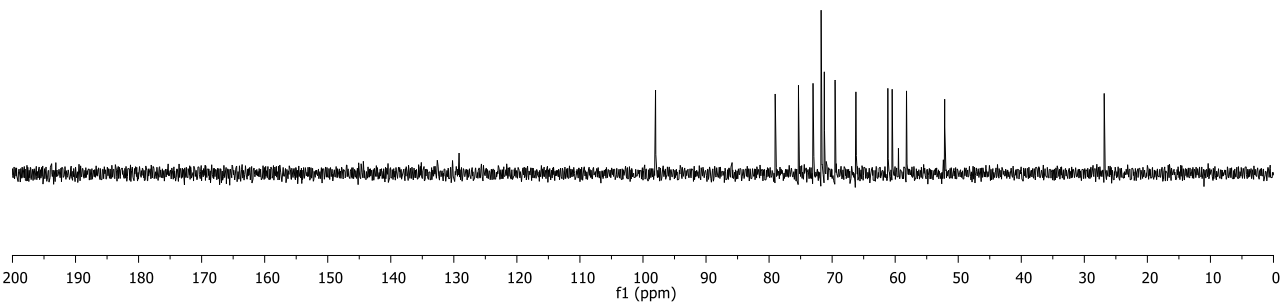
^{13}C-NMR spectrum of compounds 9β (100 MHz, D_2O)



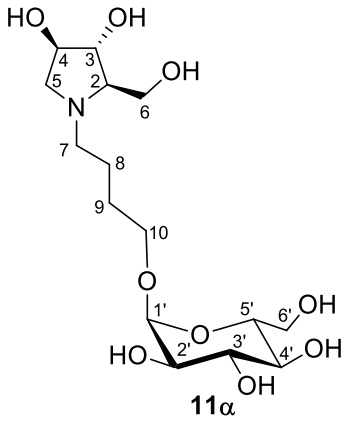
10α



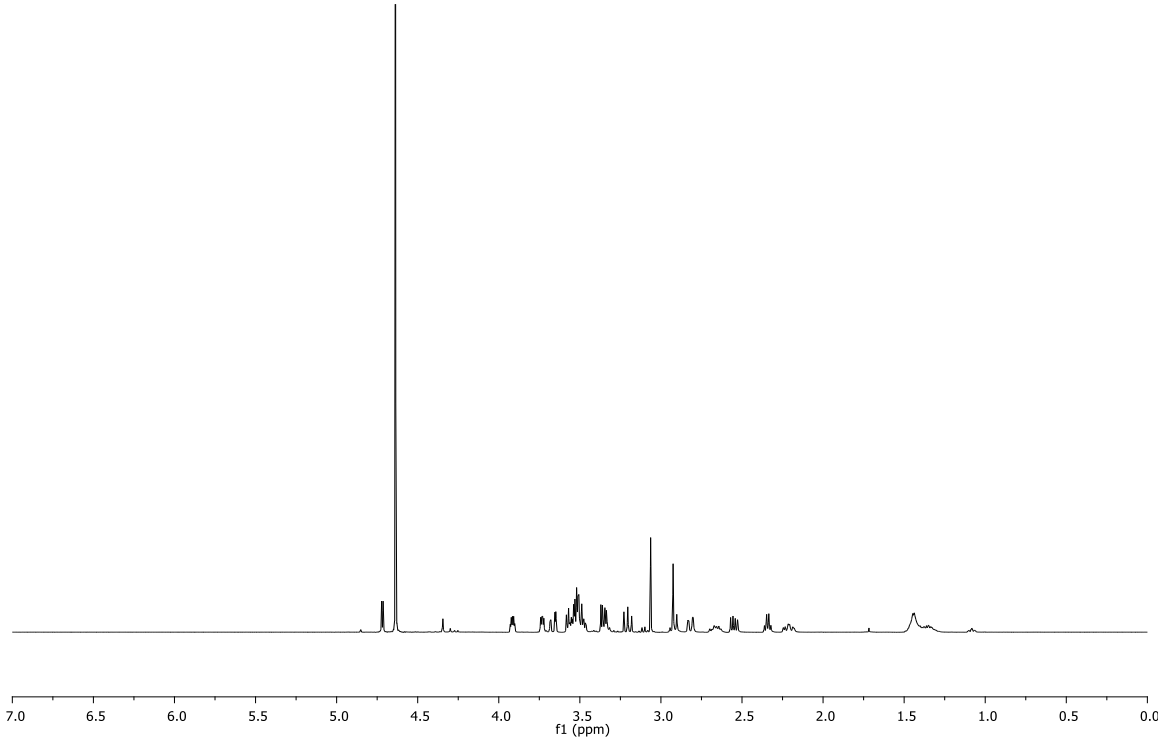
^{1}H-NMR spectrum of compounds 10α (400 MHz, D_2O)



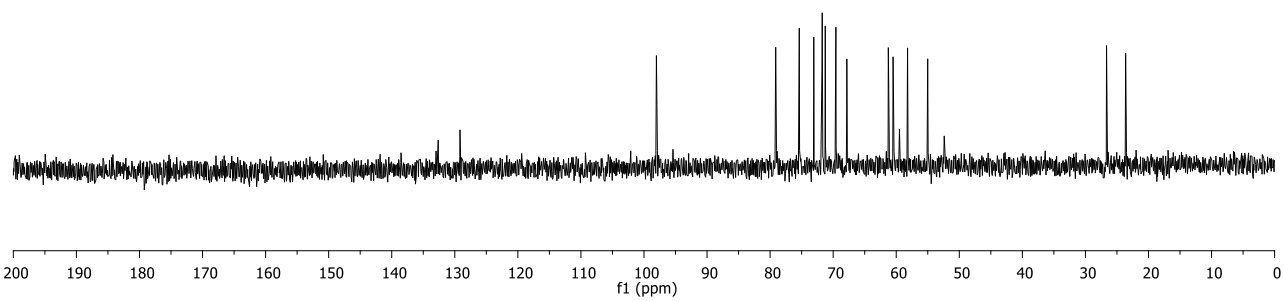
^{13}C-NMR spectrum of compounds 10α (100 MHz, D_2O)



11α



^{1}H-NMR spectrum of compounds 11α (400 MHz, D_2O)



^{13}C-NMR spectrum of compounds 11α (100 MHz, D_2O)

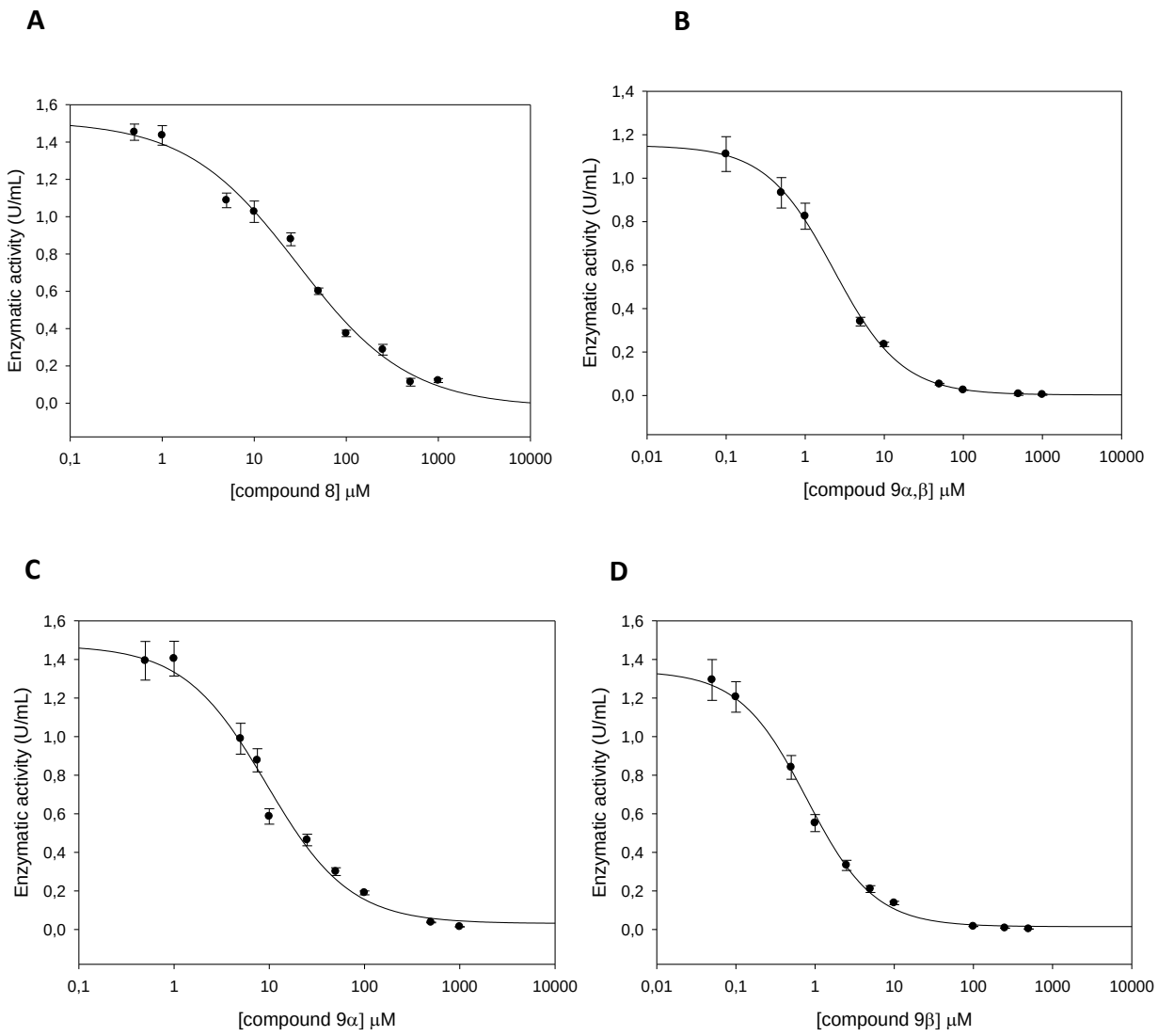


Figure S1. Dose-response curves of compounds **8** (A), **9α,β** (B)**, 9α** (C), **9β** (D) for insect trehalase

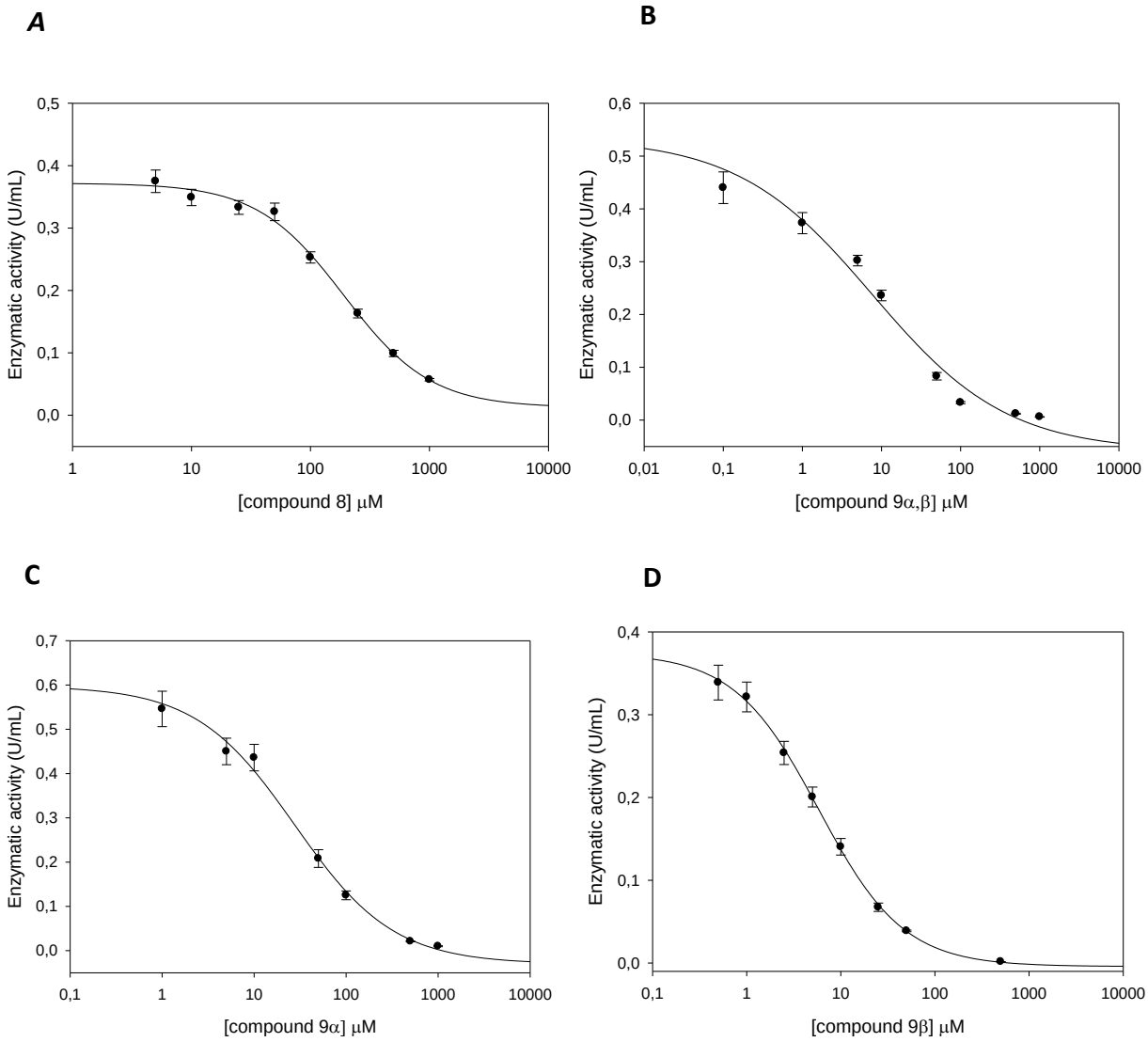
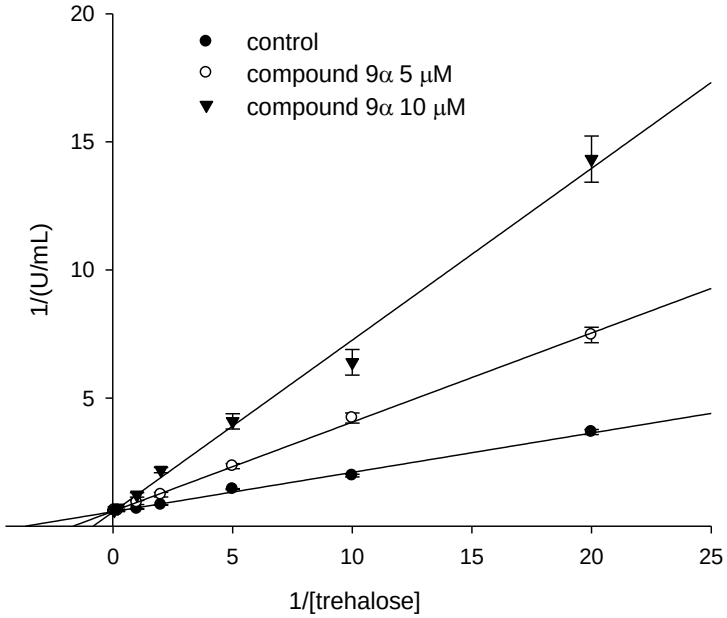


Figure S2. Dose-response curves of compounds **8** (A), **9α,β** (B)**, 9α** (C), **9β** (D) for porcine trehalase

A



B

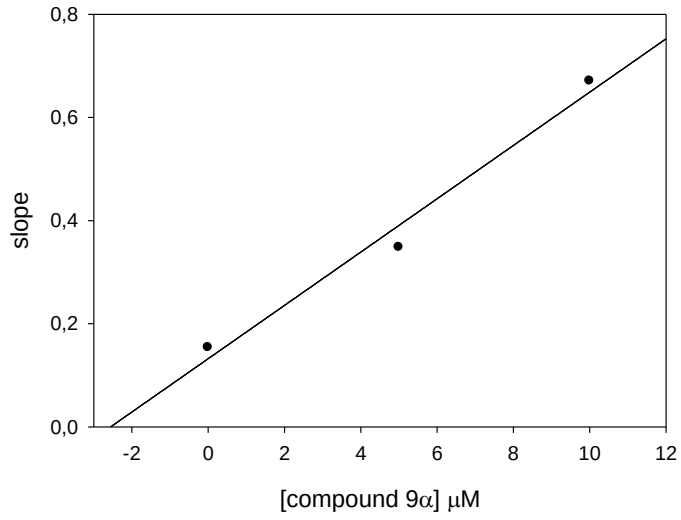
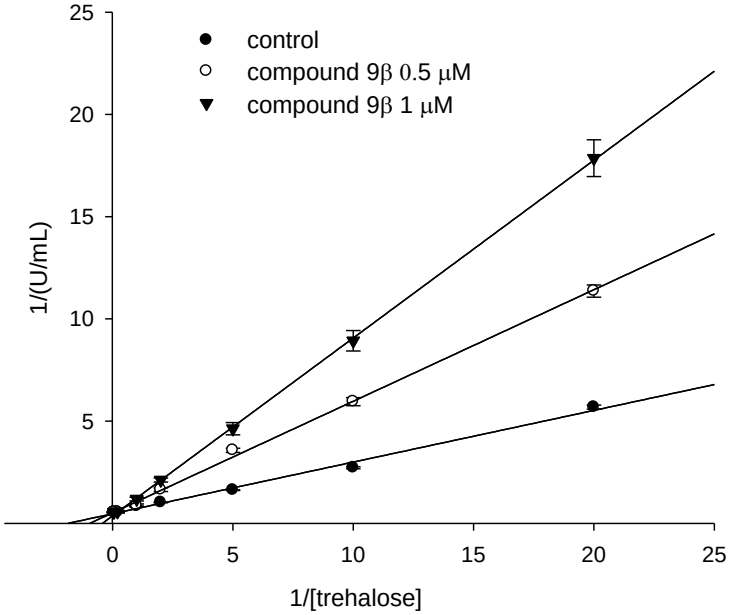


Figure S3. Inhibition kinetics of insect trehalase in the presence of compound **9α**. A) double reciprocal plot in the presence of two fixed inhibitor concentrations (5 and 10 μM); B) replot of the slopes of each reciprocal plot versus the corresponding inhibitor concentration.

A



B

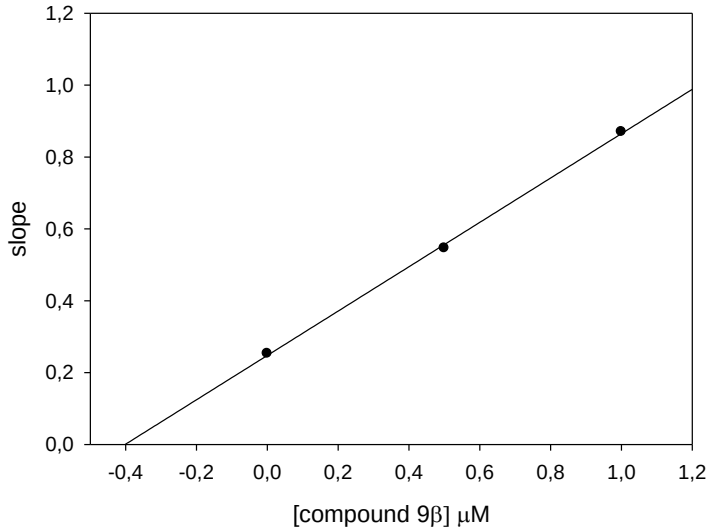


Figure S4. Inhibition kinetics of insect trehalase in the presence of compound **9β**. A) double reciprocal plot in the presence of two fixed inhibitor concentrations (0.5 and 1 μM); B) replot of the slopes of each reciprocal plot versus the corresponding inhibitor concentration.