Asymmetric synthesis of cyclo-archaeol and beta-glucosyl cyclo-archaeol

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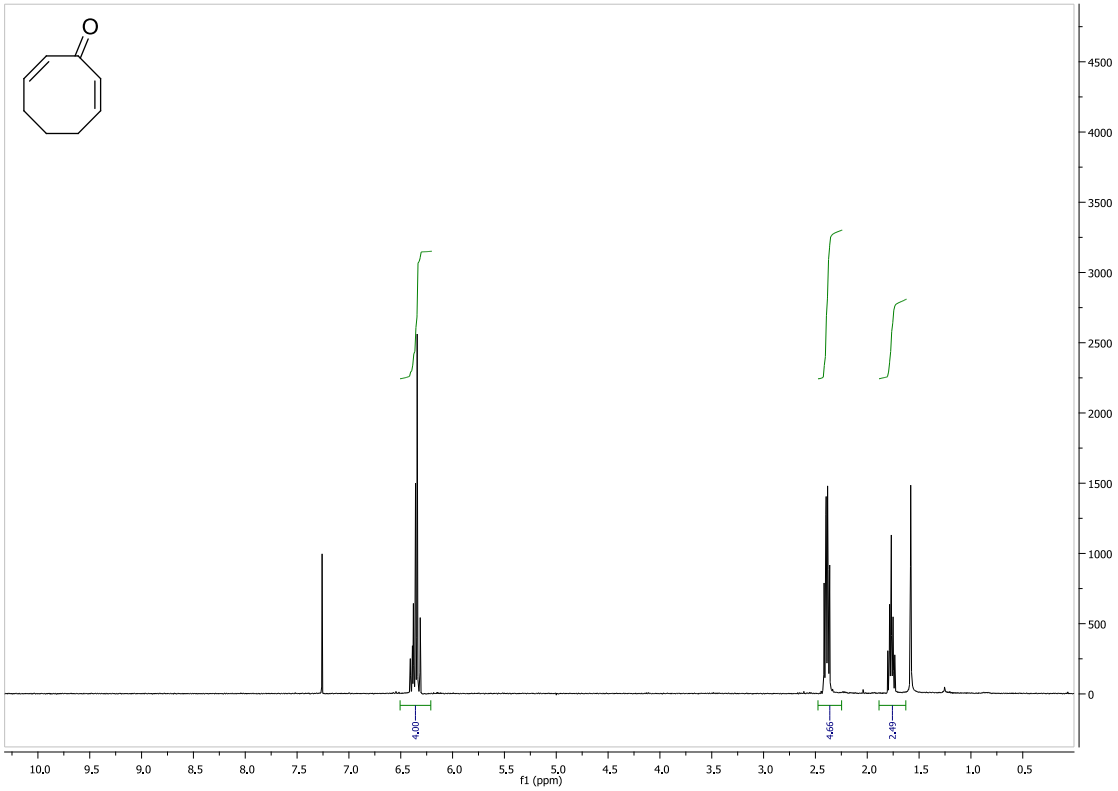
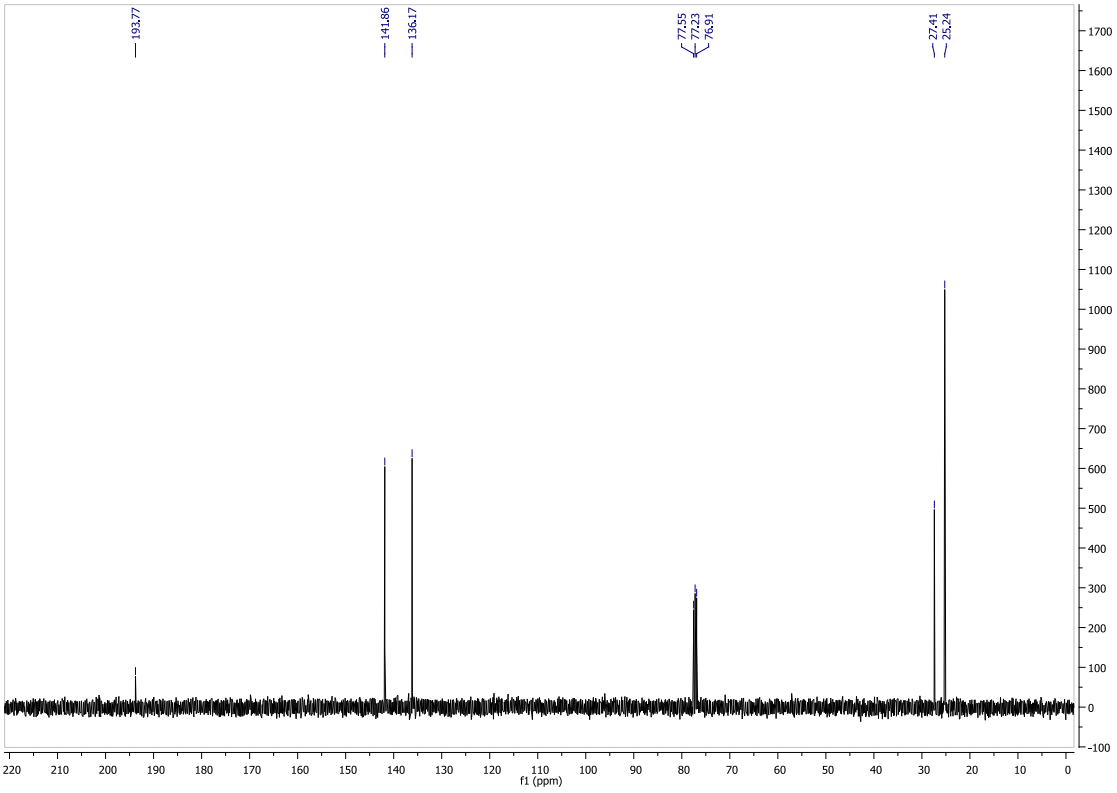
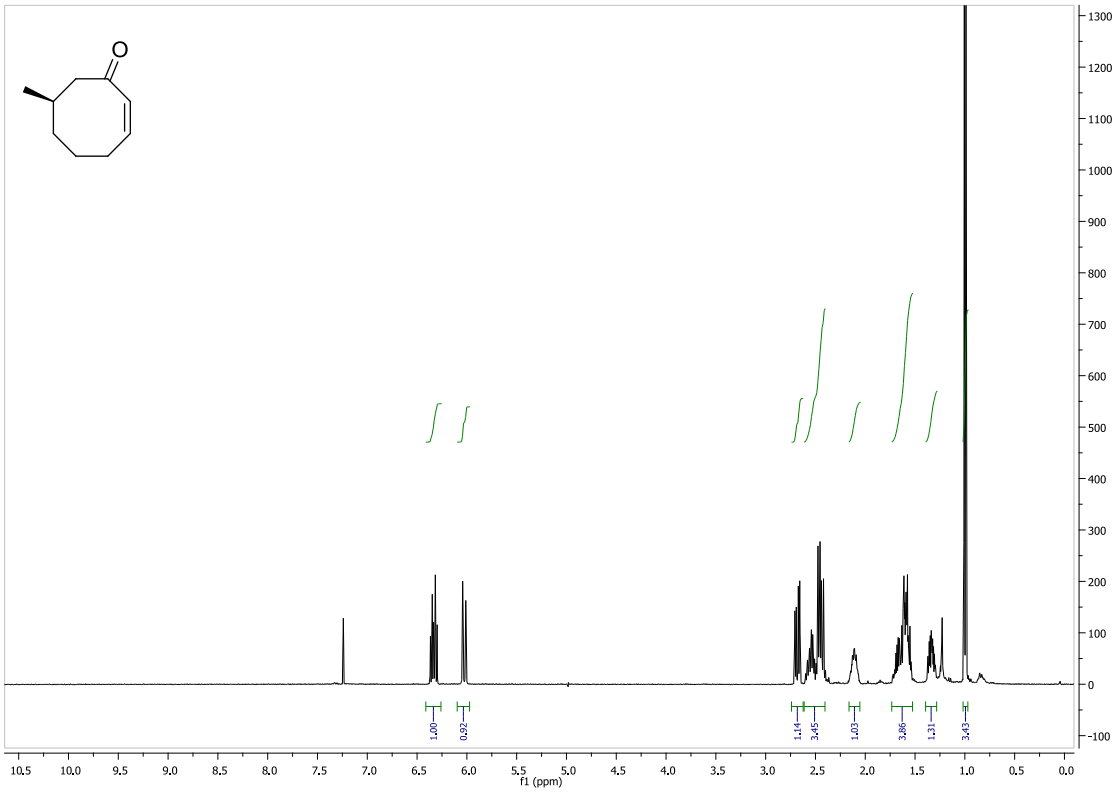
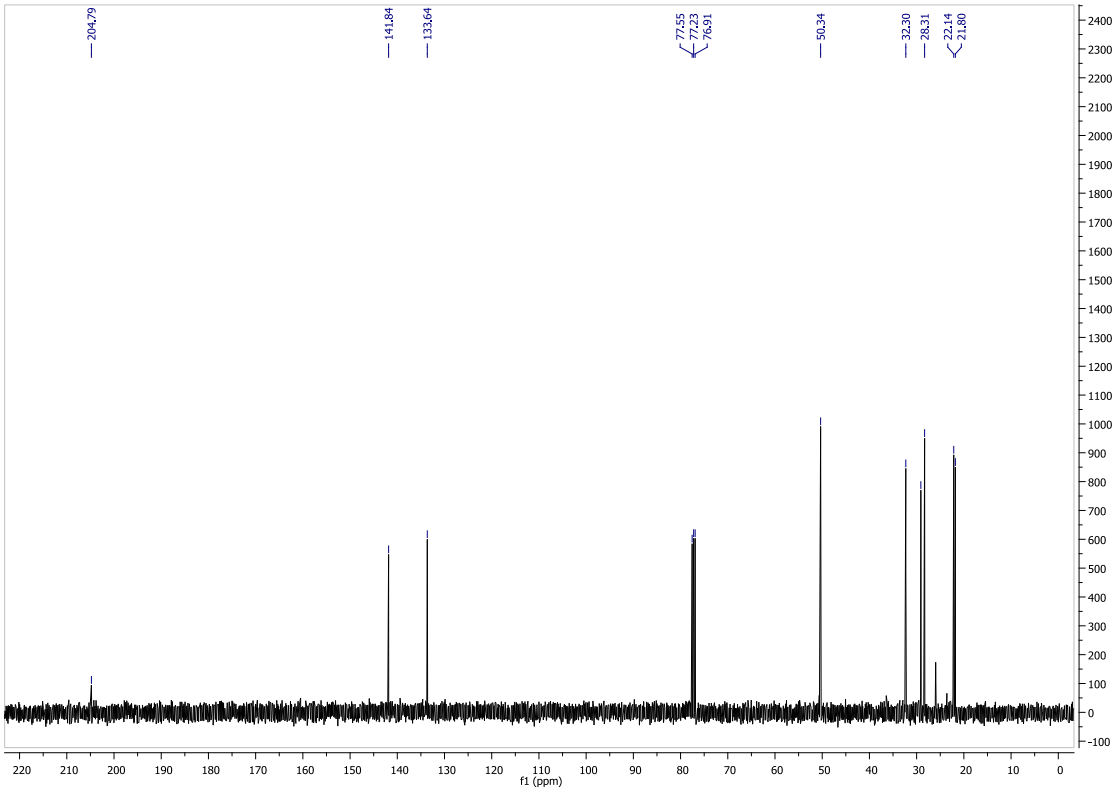
(2*Z*,7*Z*)-Cycloocta-2,7-dienone 4



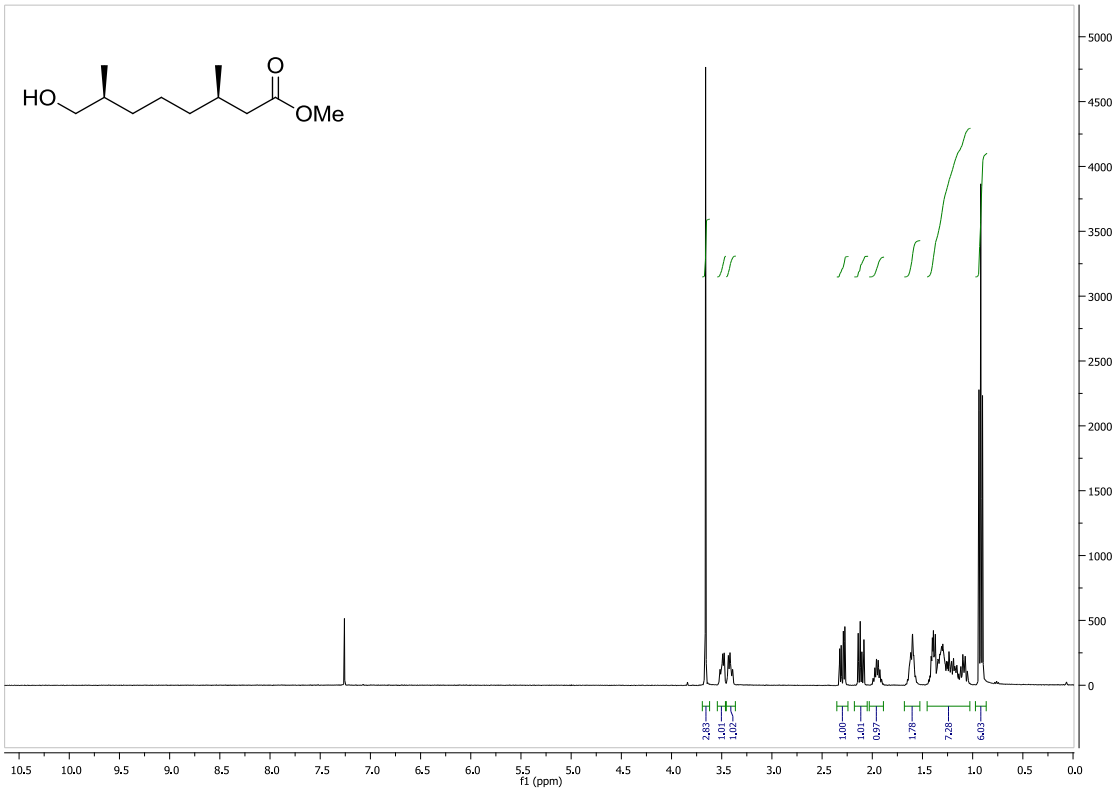


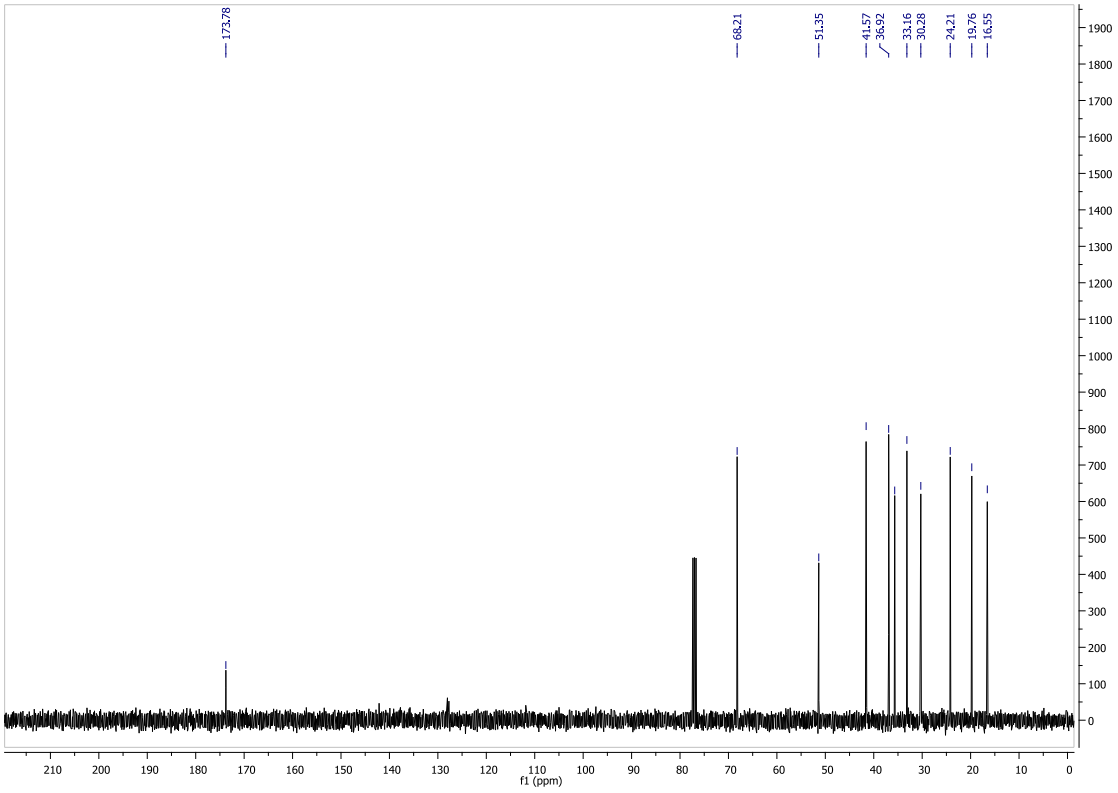
(*R,Z*)-7-Methylcyclooct-2-enone 5



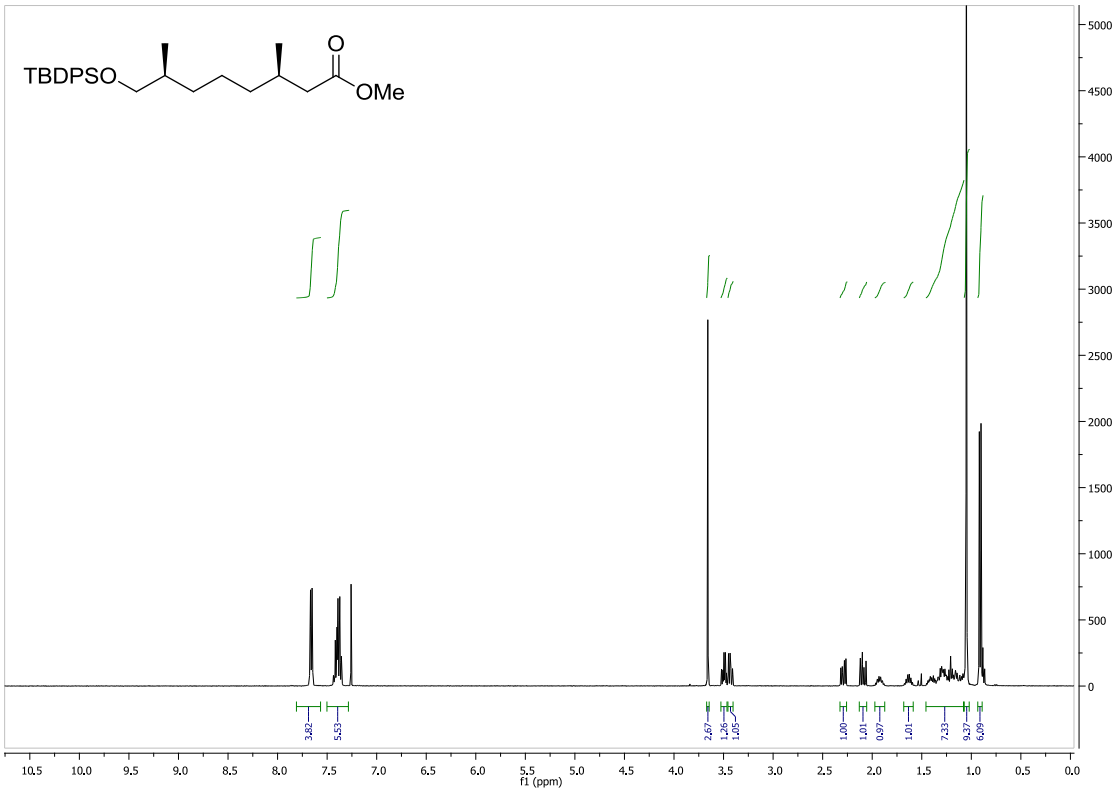


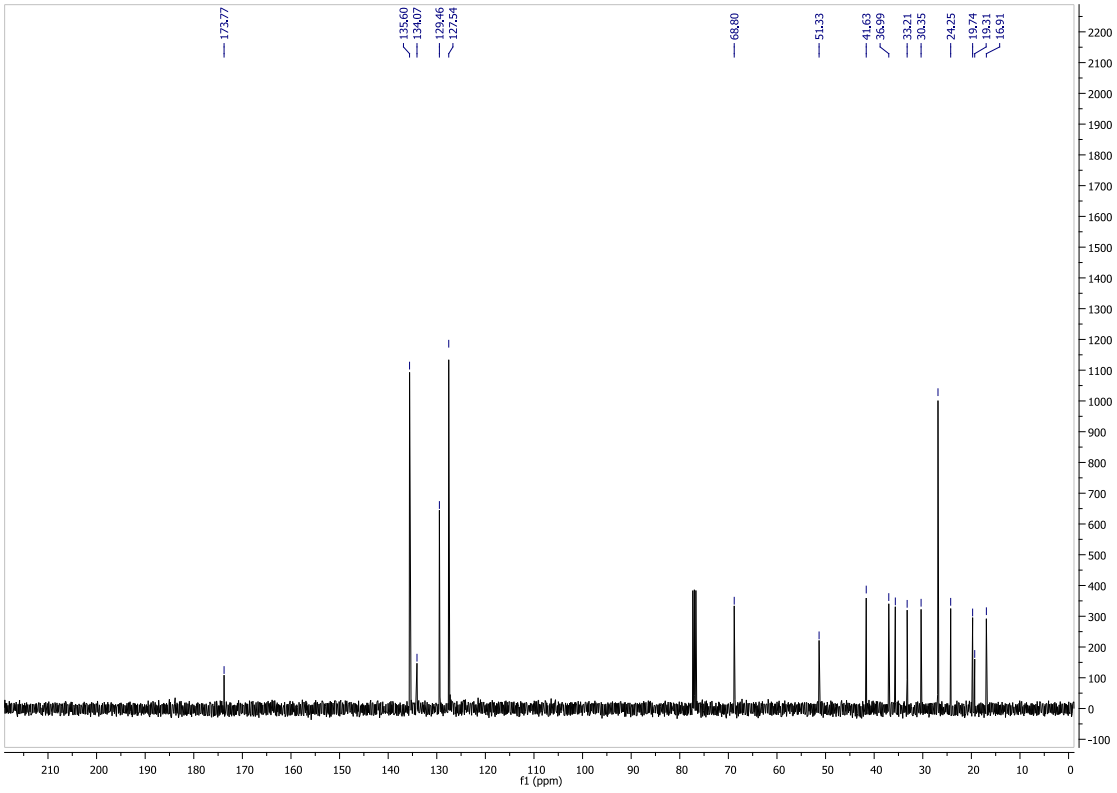
(3*R*,7*S*)-Methyl 8-hydroxy-3,7-dimethyloctanoate 3





(3*R*,7*S*)-Methyl 8-((*tert*-butyldiphenylsilyl)oxy)-3,7-dimethyloctanoate 7





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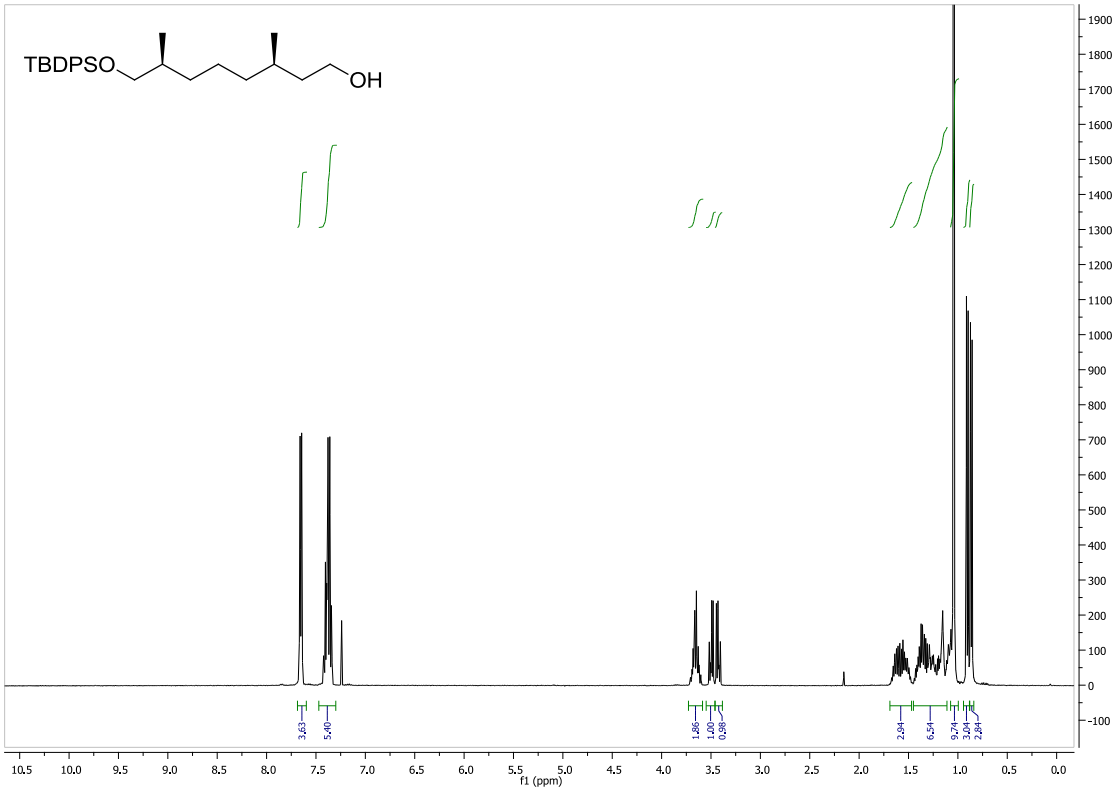

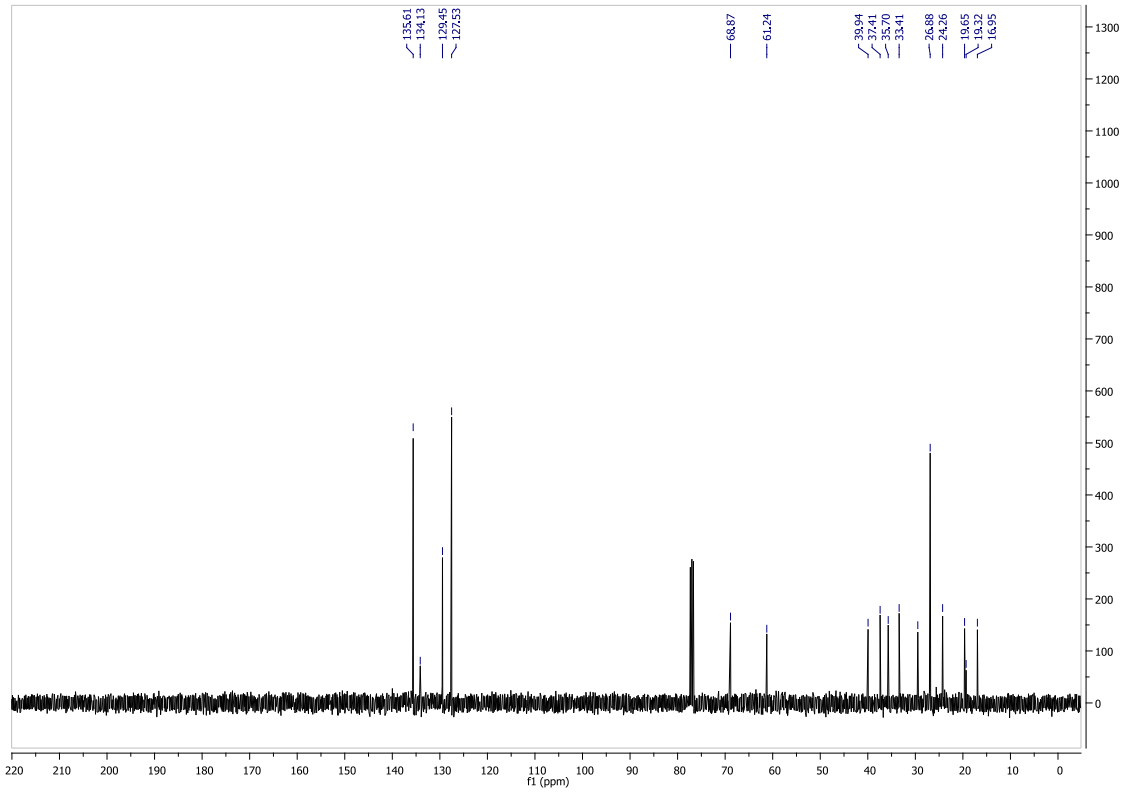

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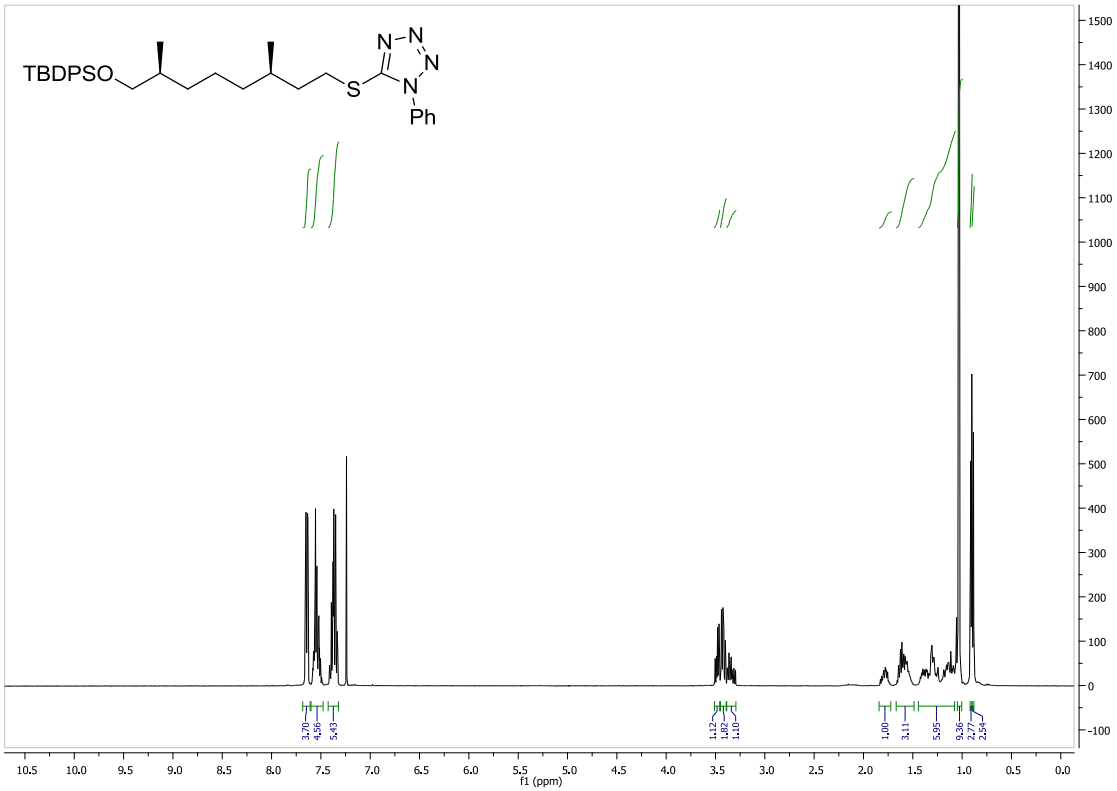

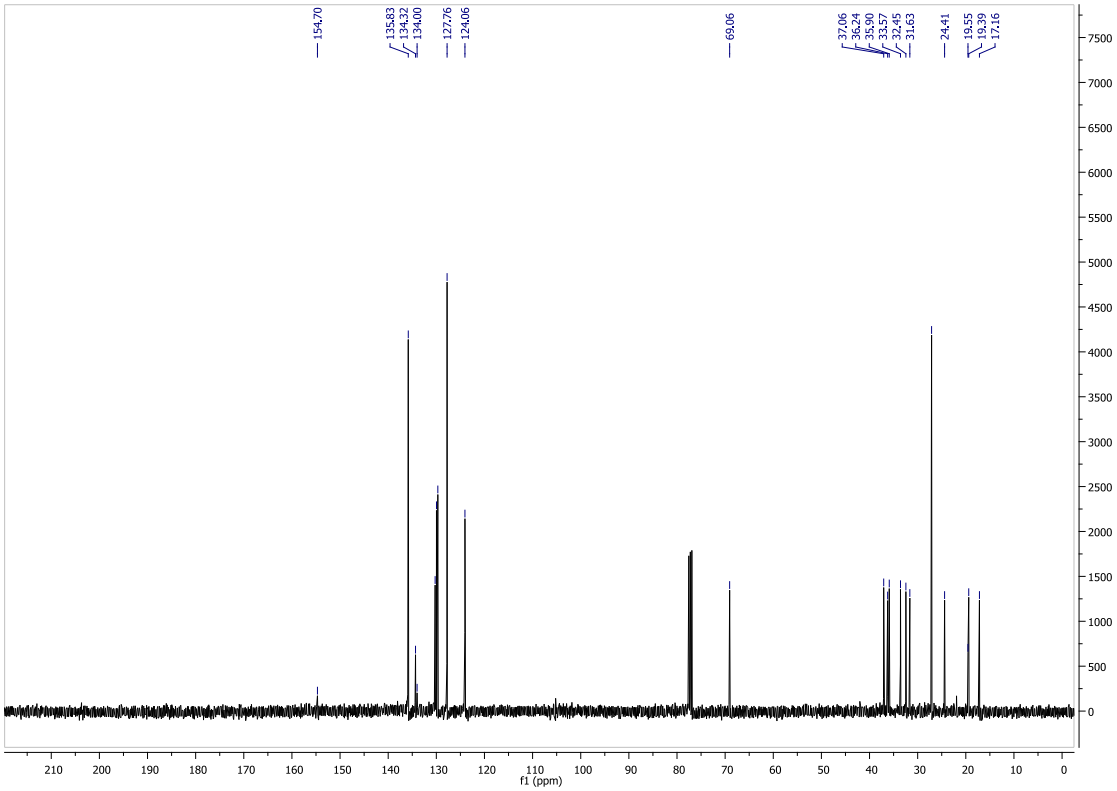

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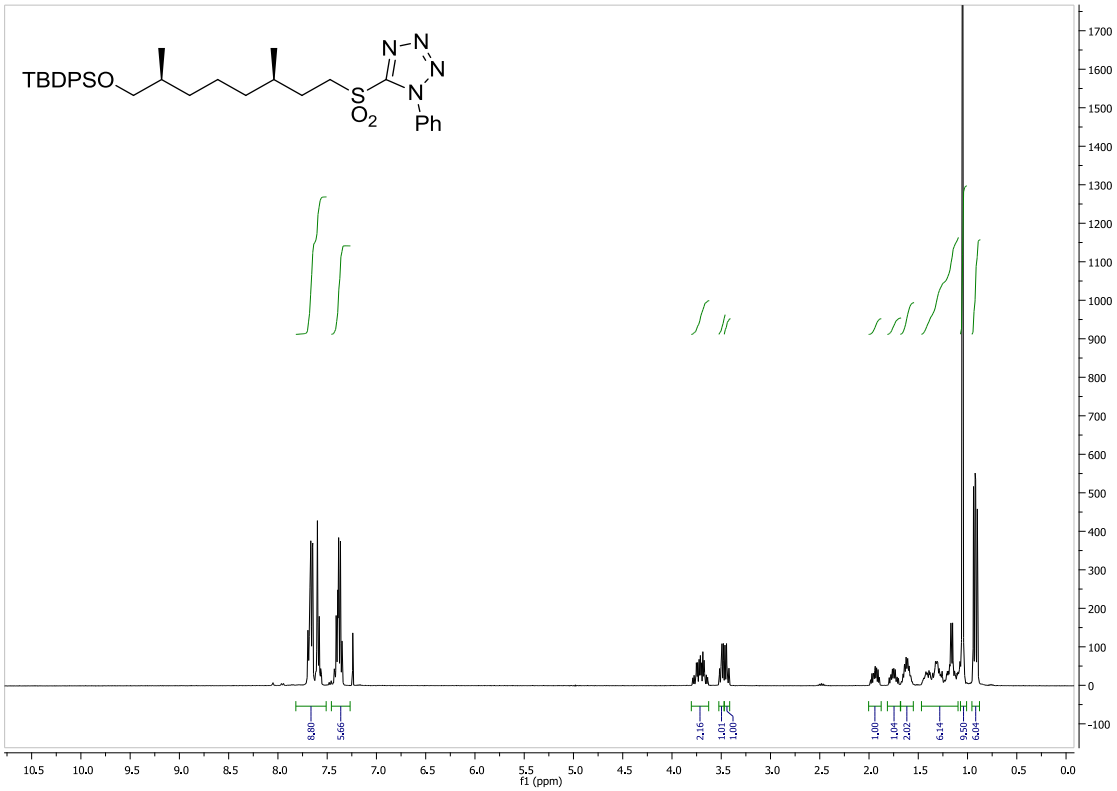

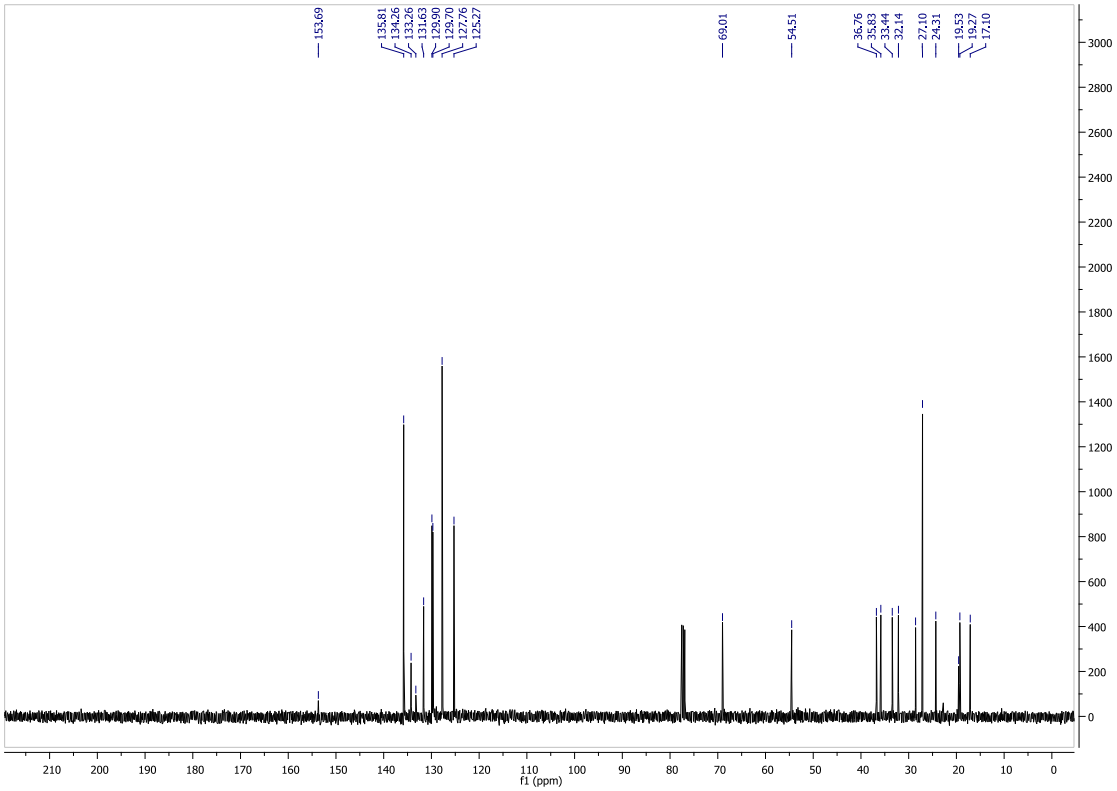

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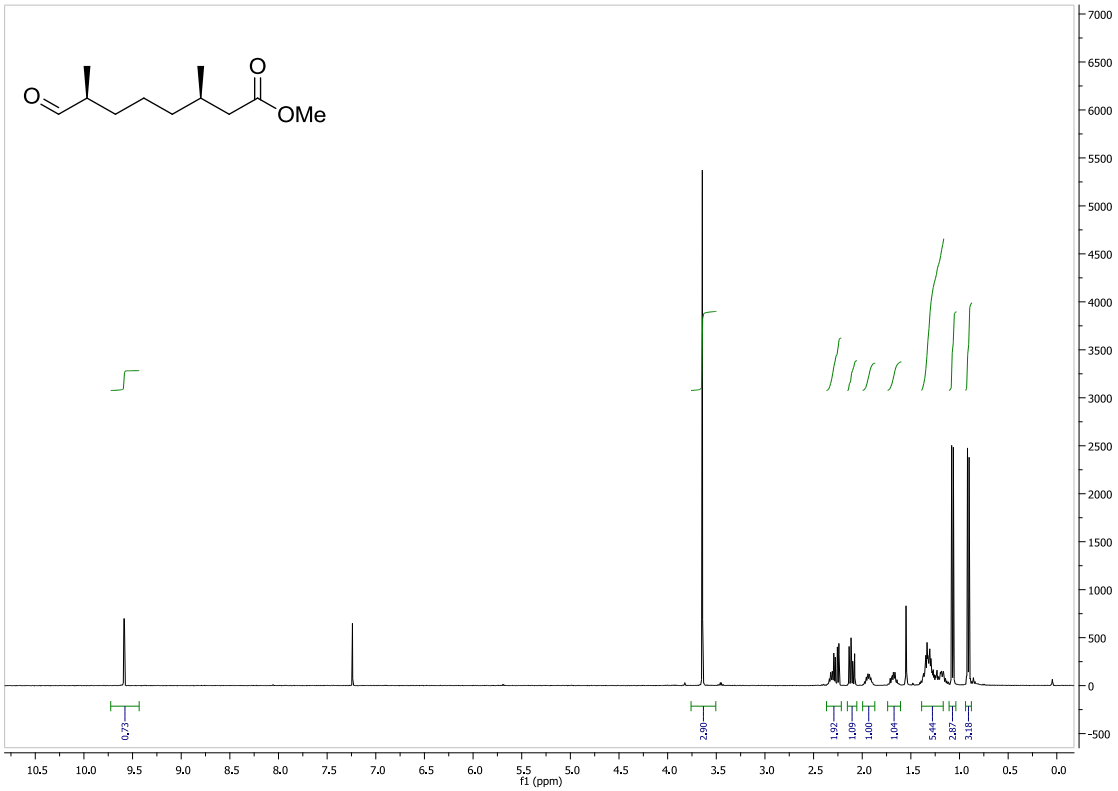
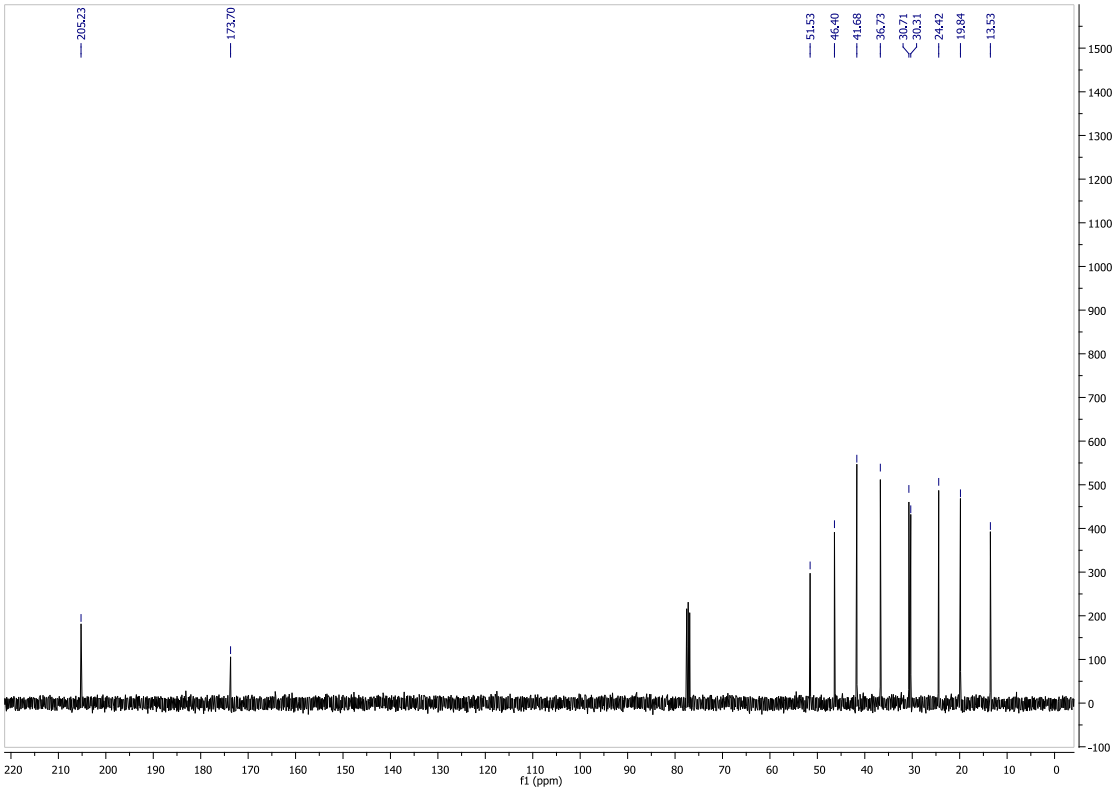
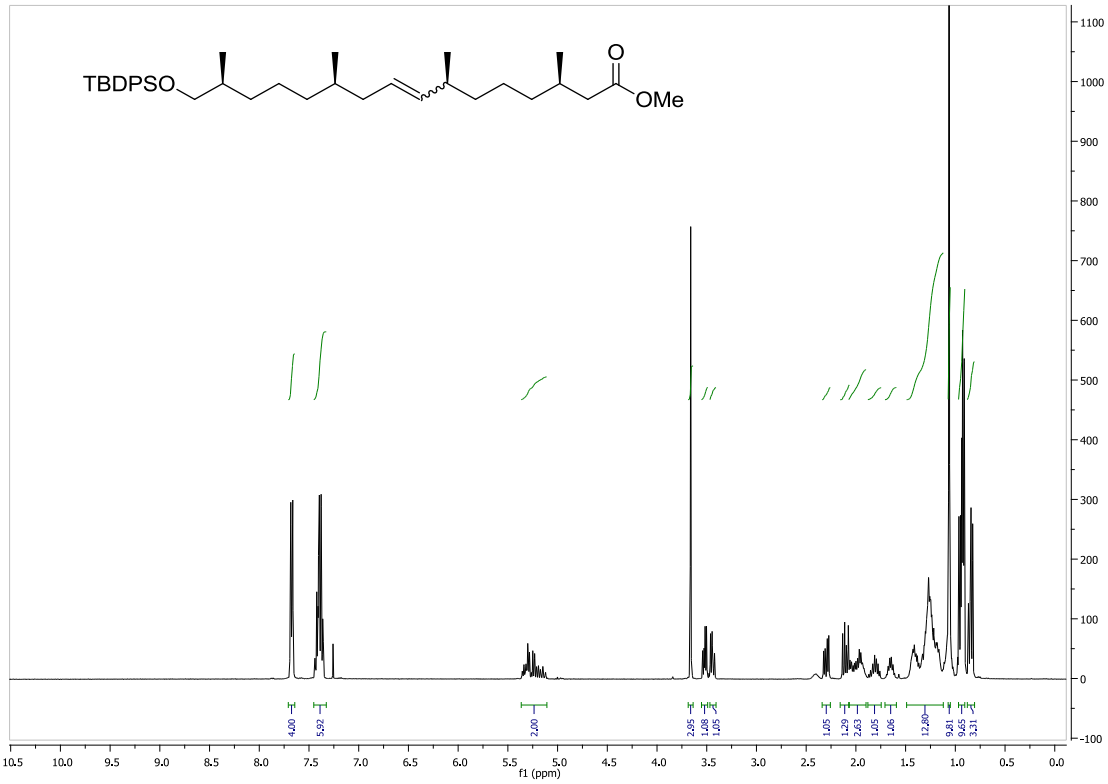
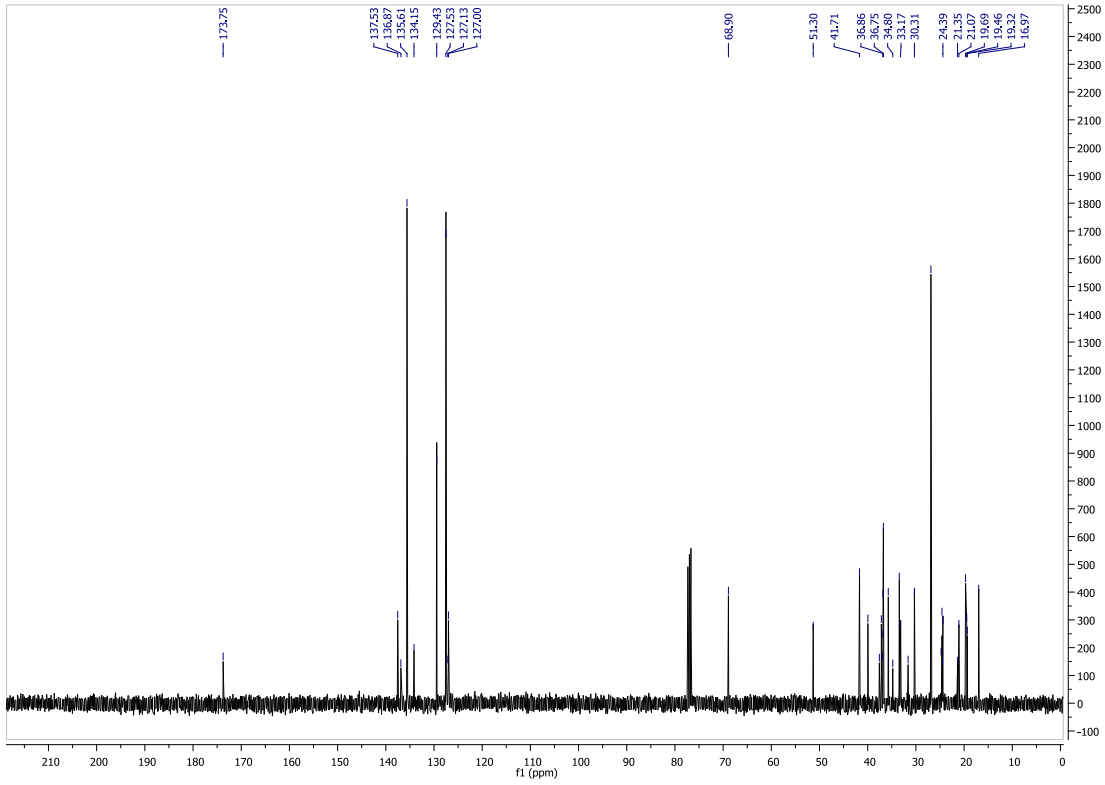




(3*R*,7*S*,11*R*,15*S*)-Methyl 16-((*tert*-butyldiphenylsilyl)oxy)-3,7,11,15-tetramethylhexadec-8-enoate 11





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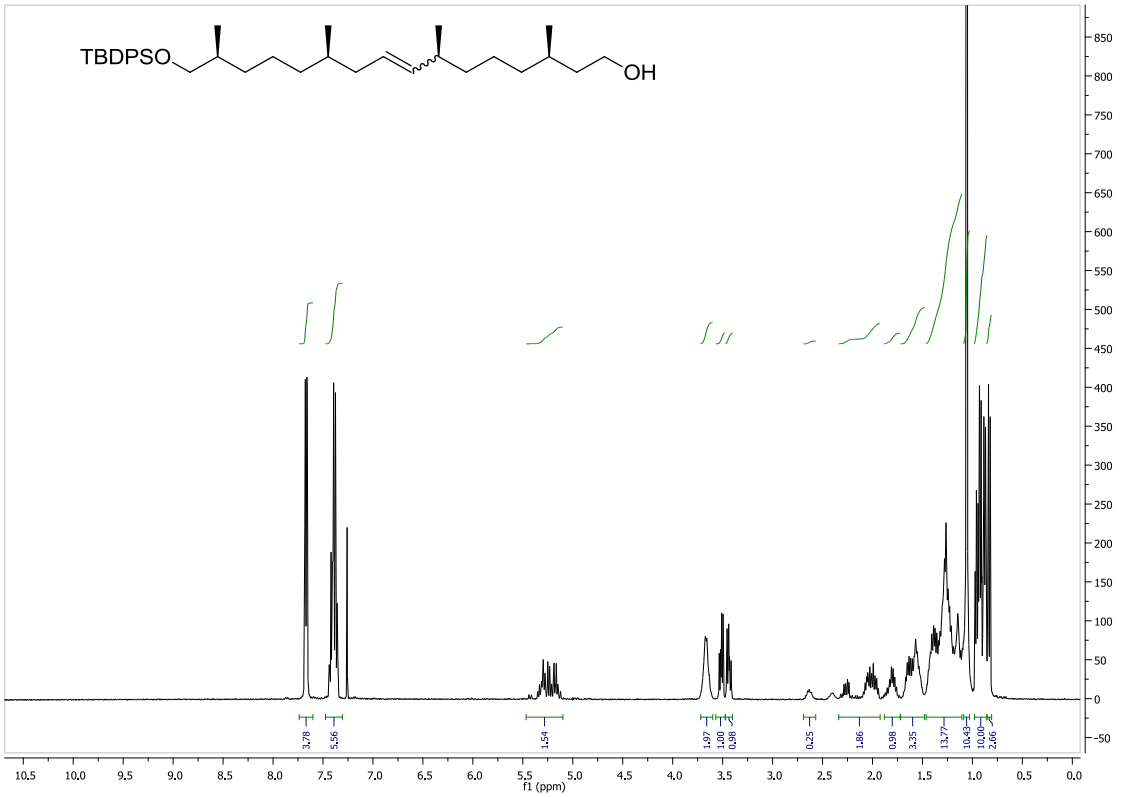

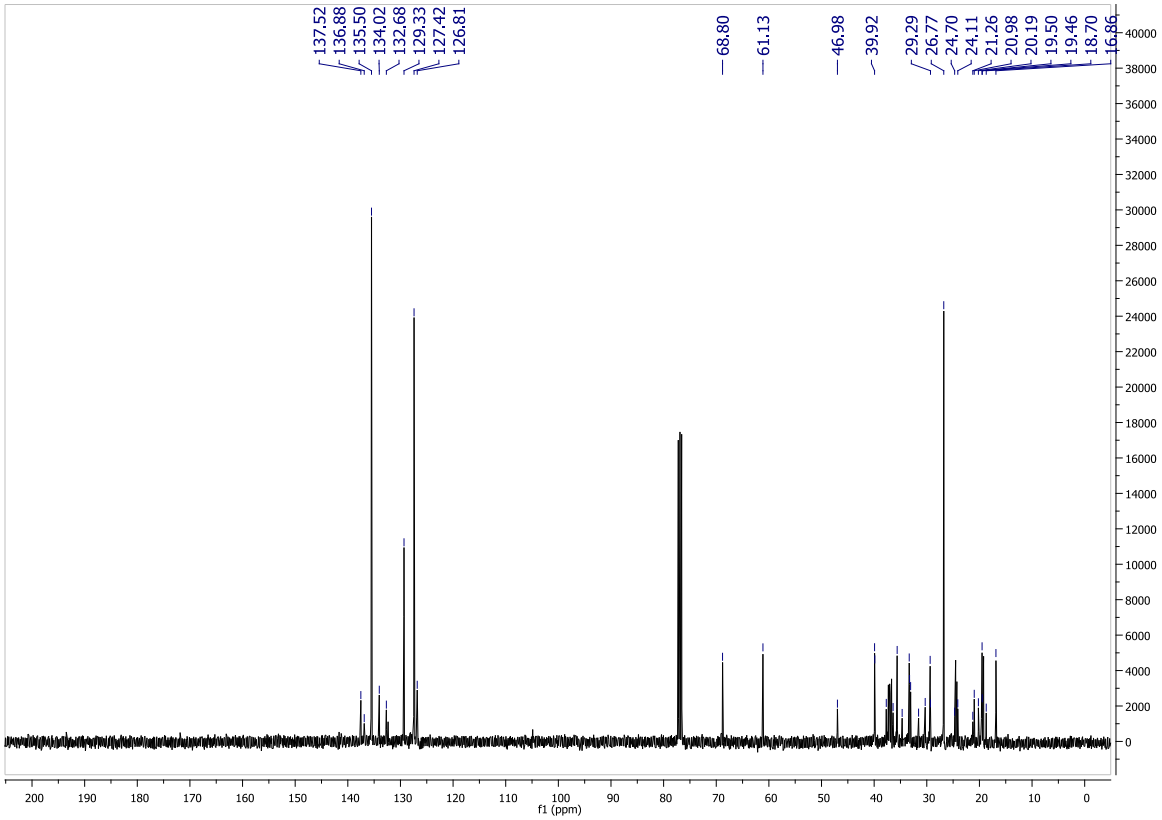

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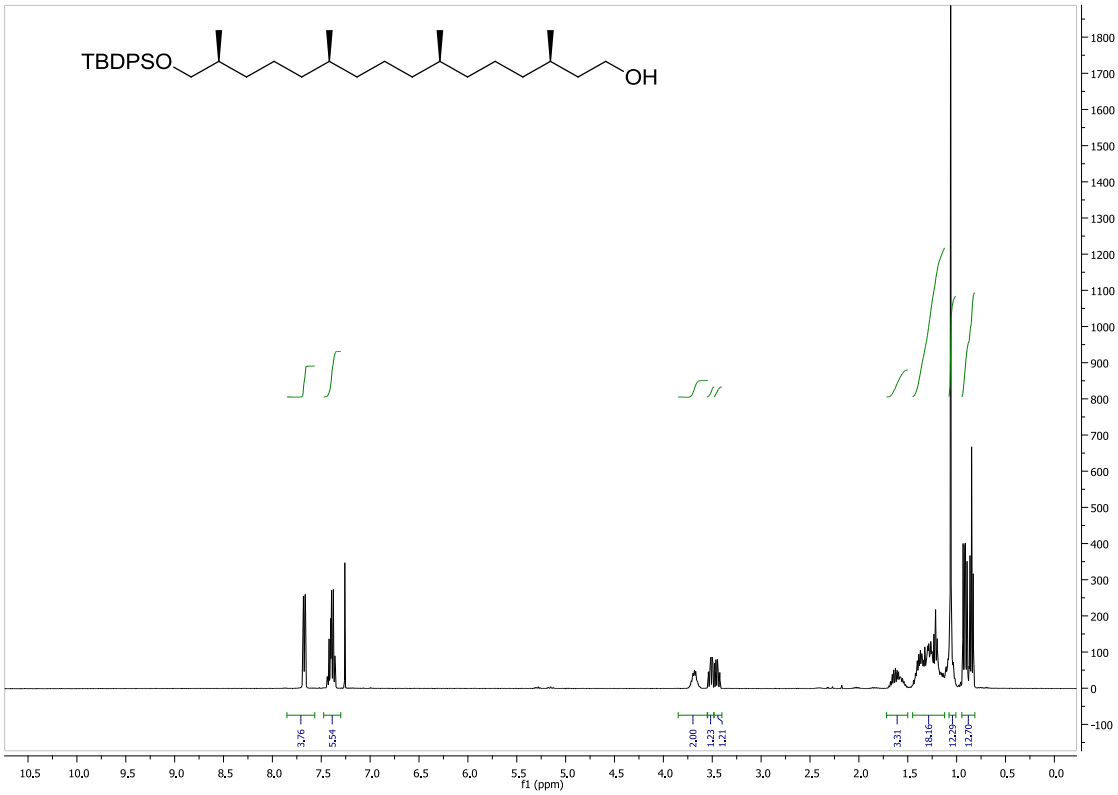
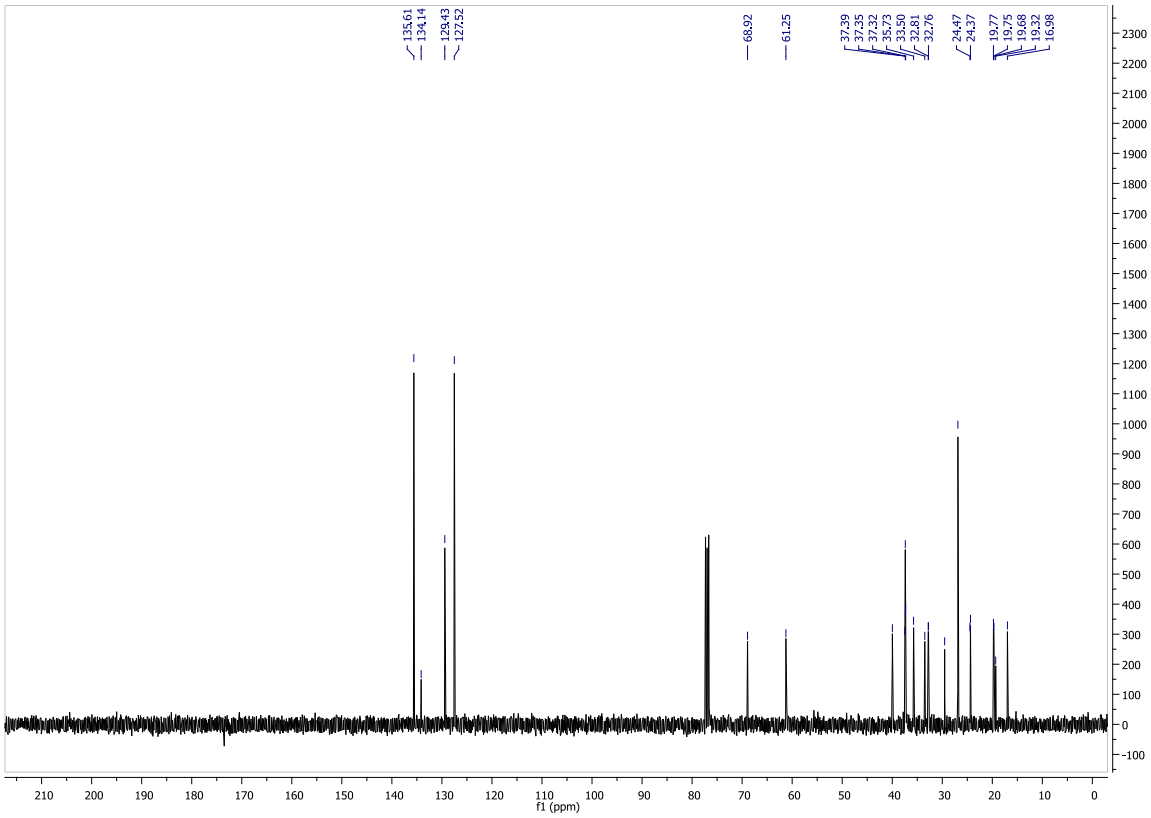
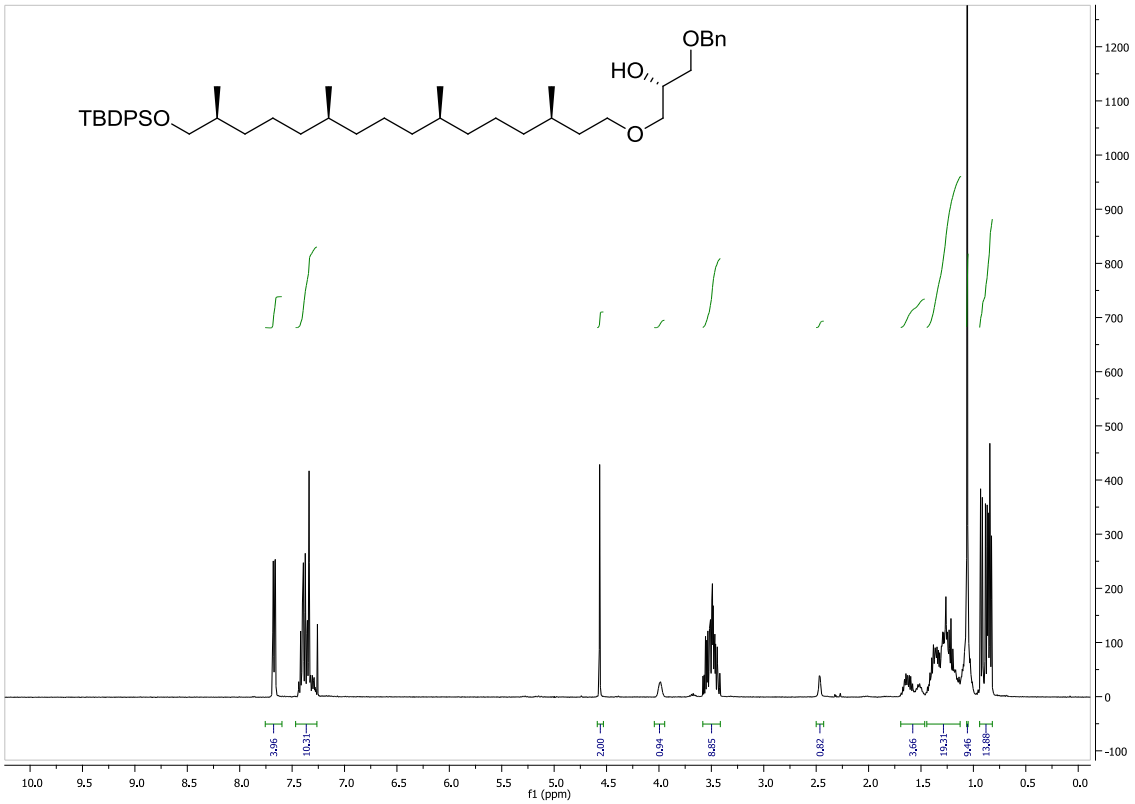
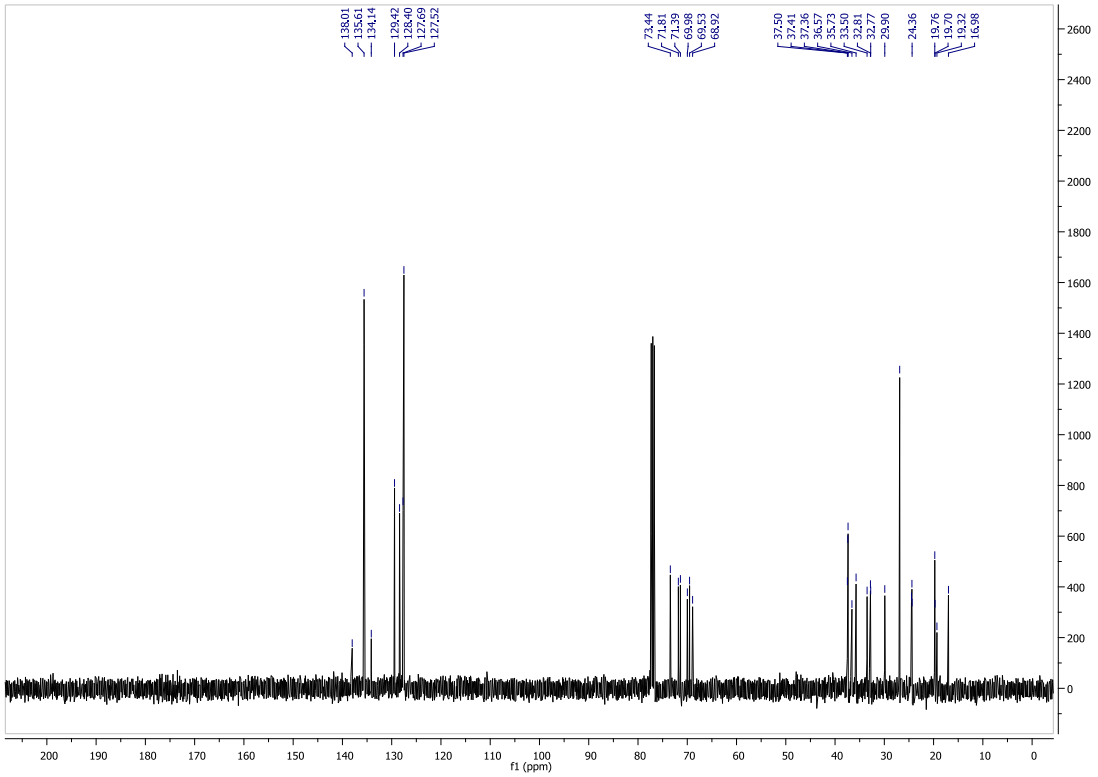


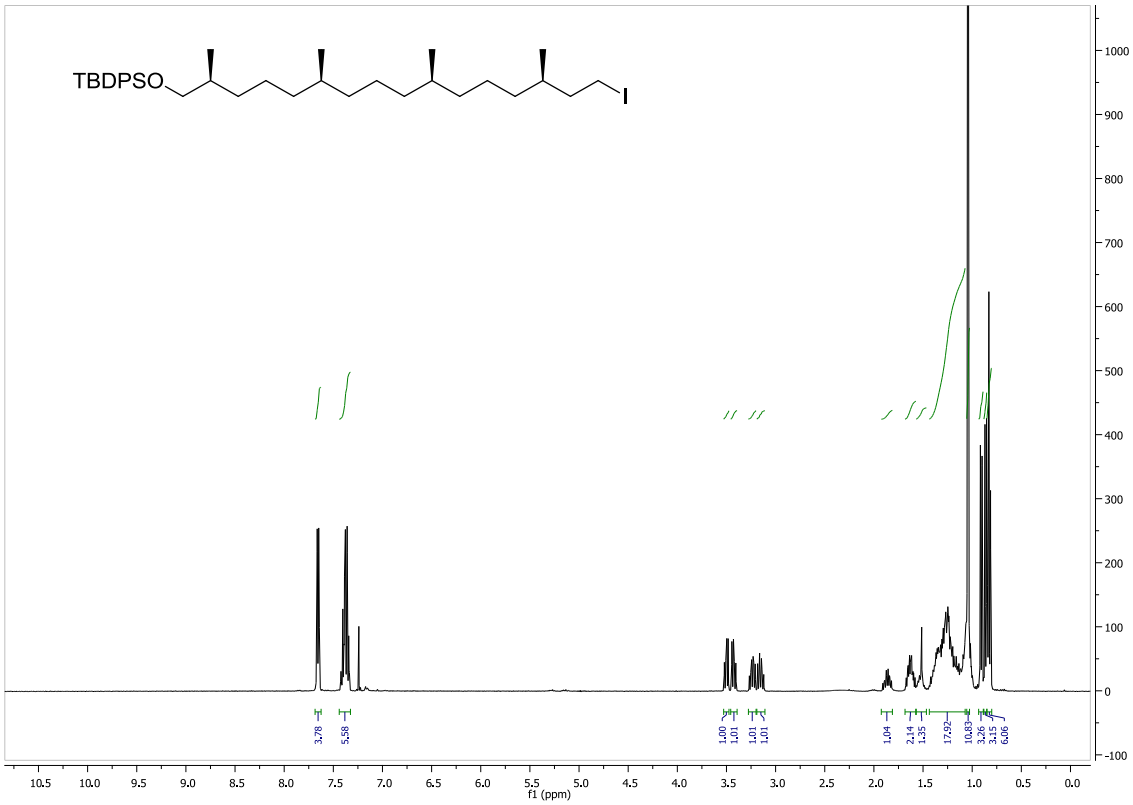


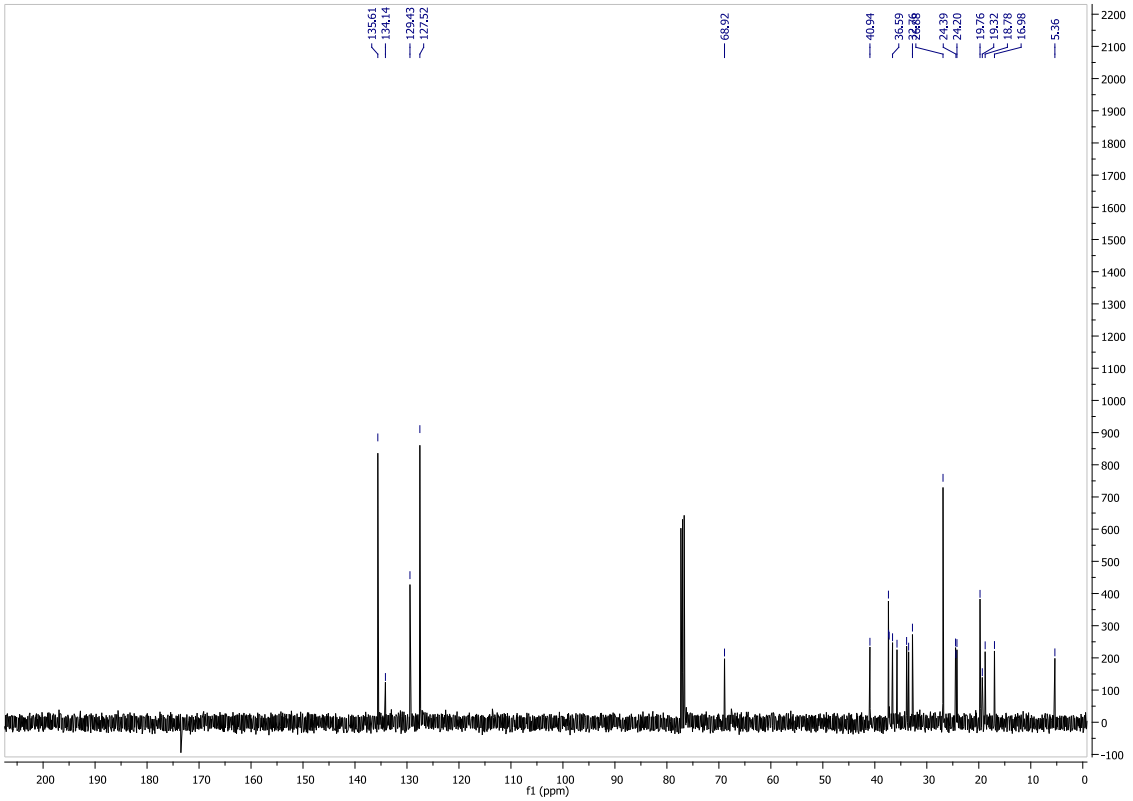
(4*S*,9*R*,13*R*,17*S*,21*S*)-9,13,17,21,25,25-Hexamethyl-1,24,24-triphenyl-2,6,23-trioxa-24-silahexacosan-4-ol 14





tert-Butyl(((2_S_,6_S_,10_R_,14_R_)-16-iodo-2,6,10,14-tetramethylhexadecyl)oxy)diphenylsilane 15





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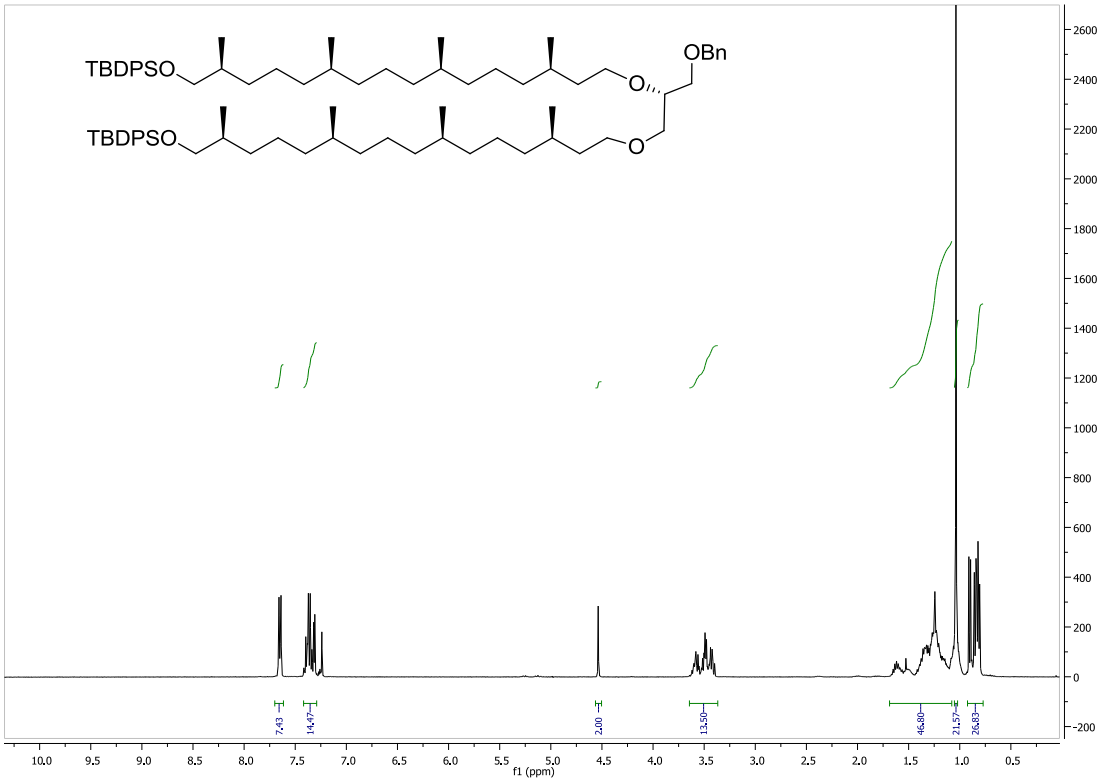

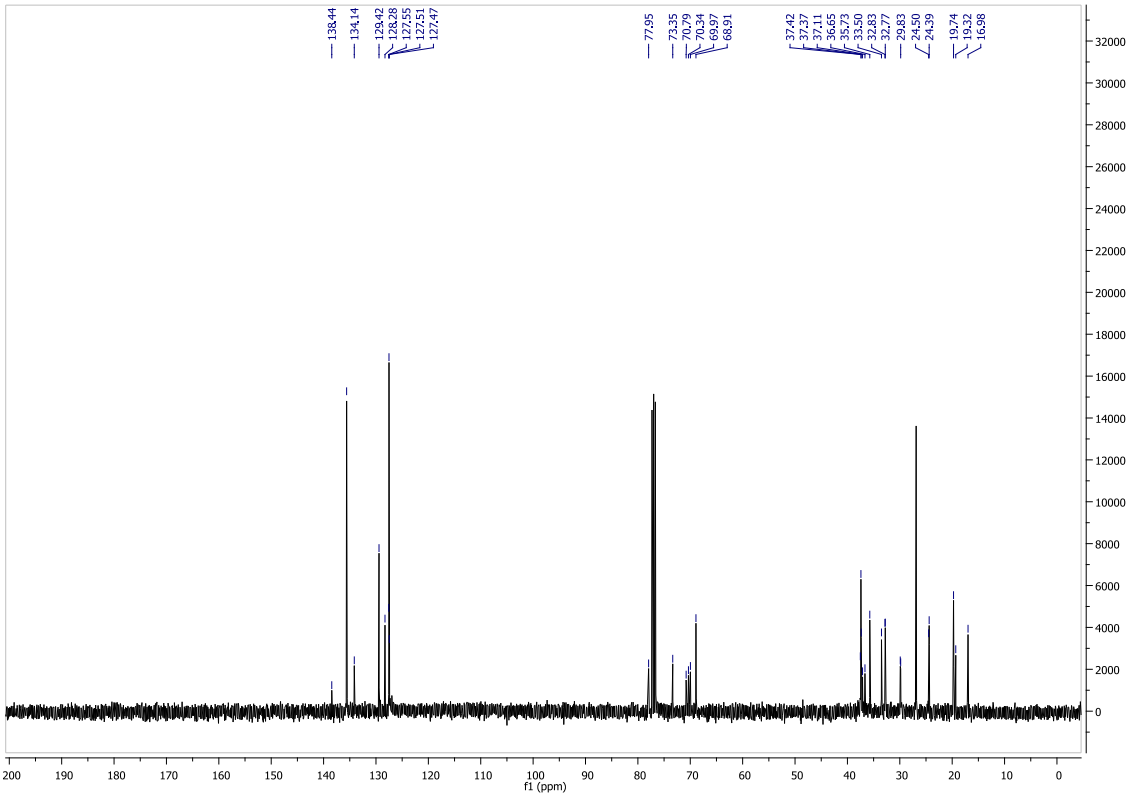

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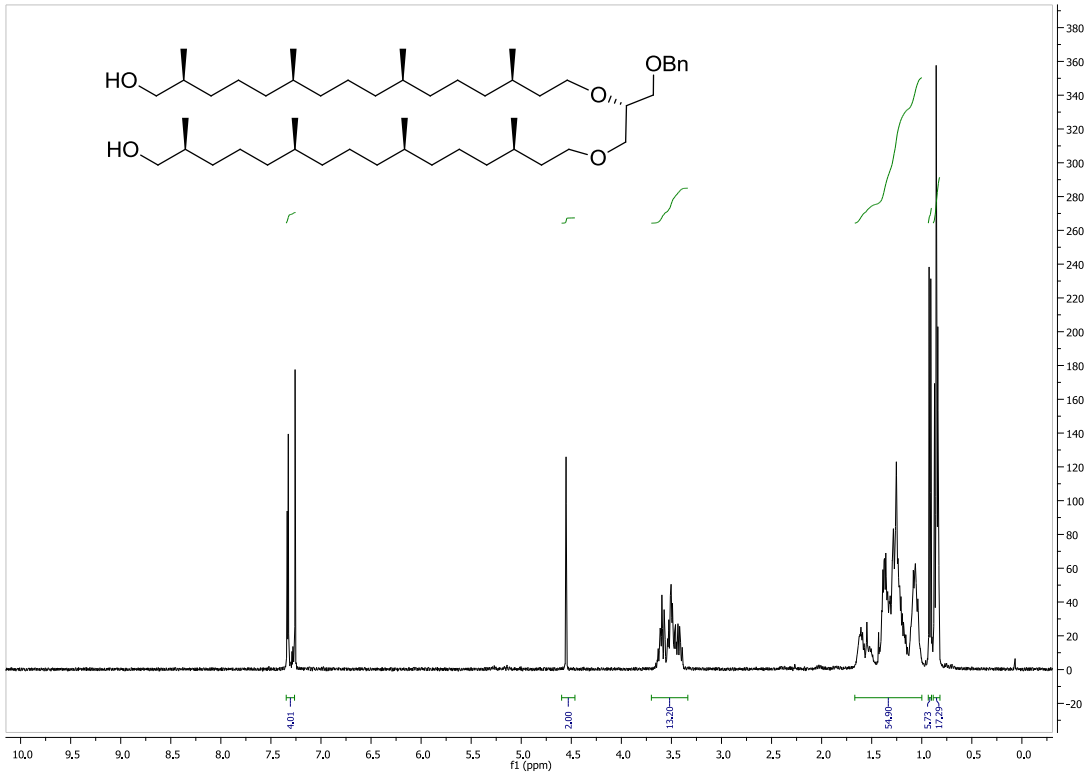

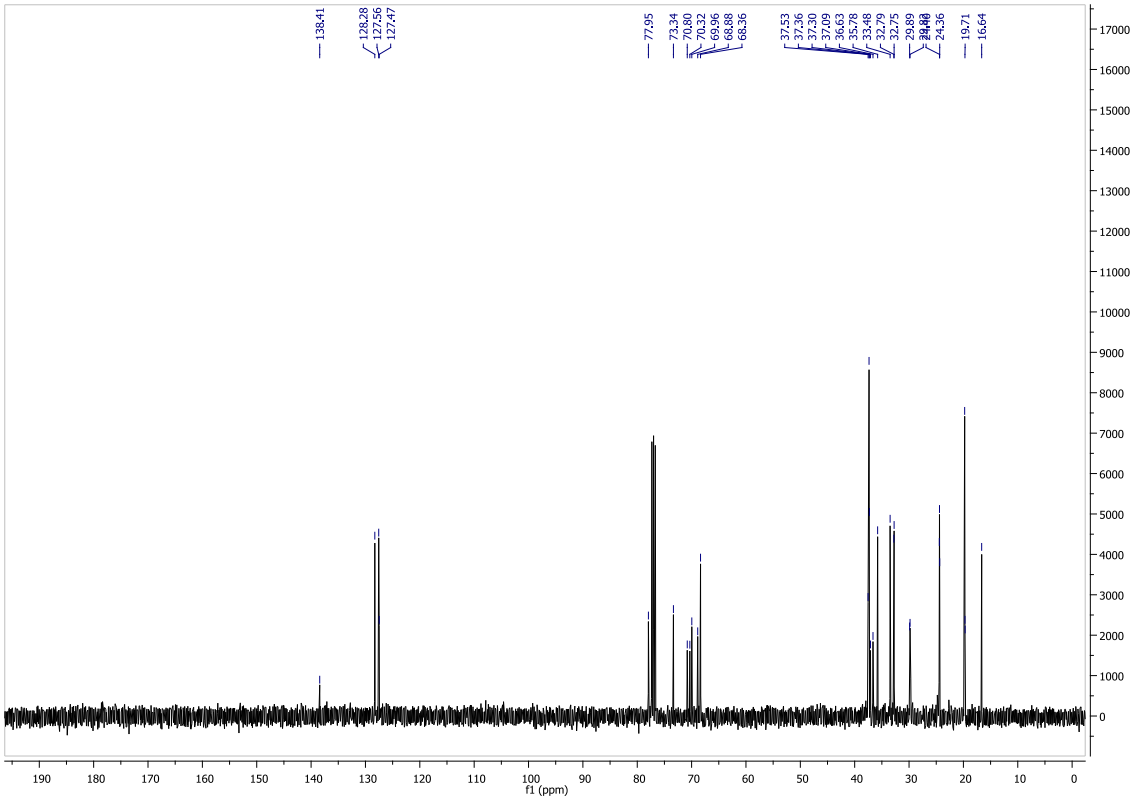

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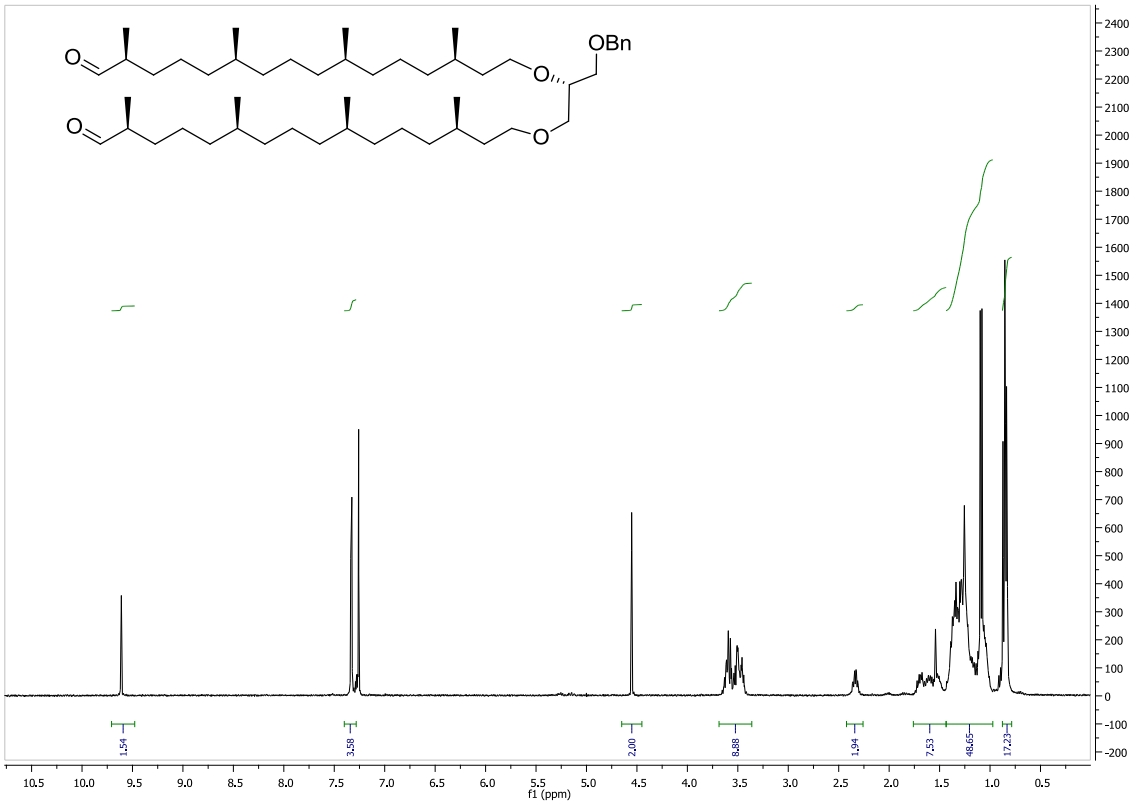

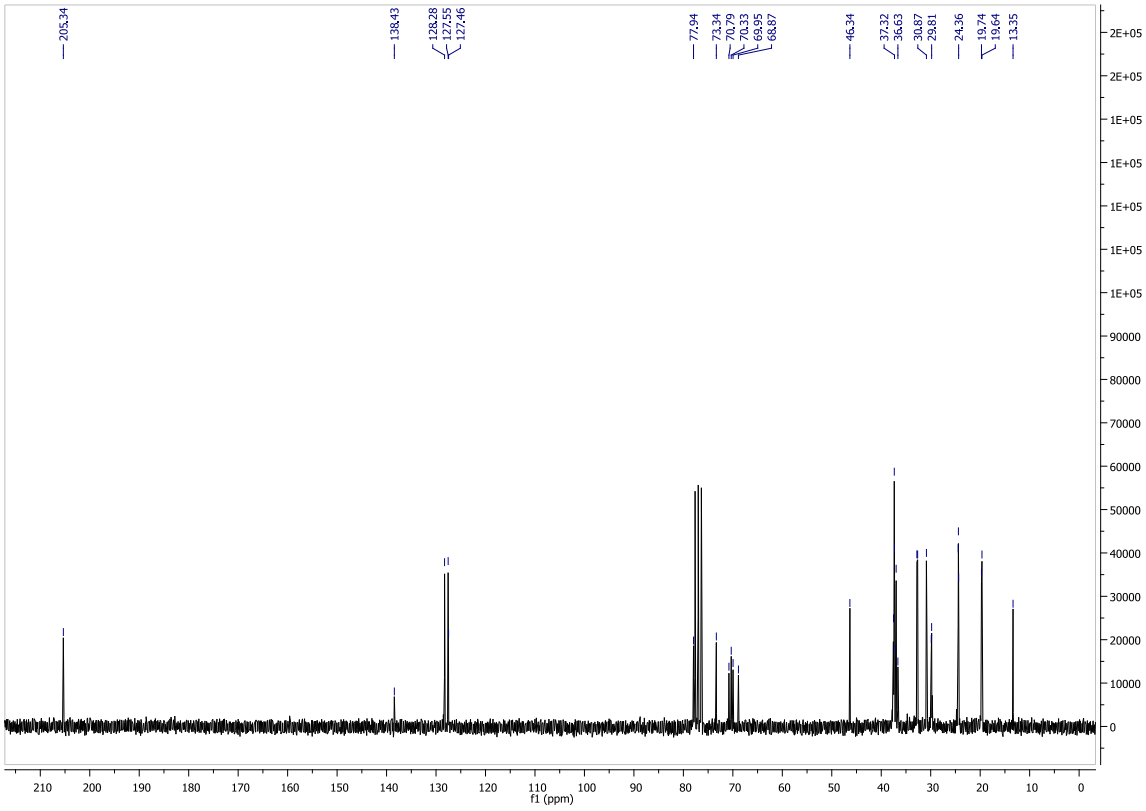

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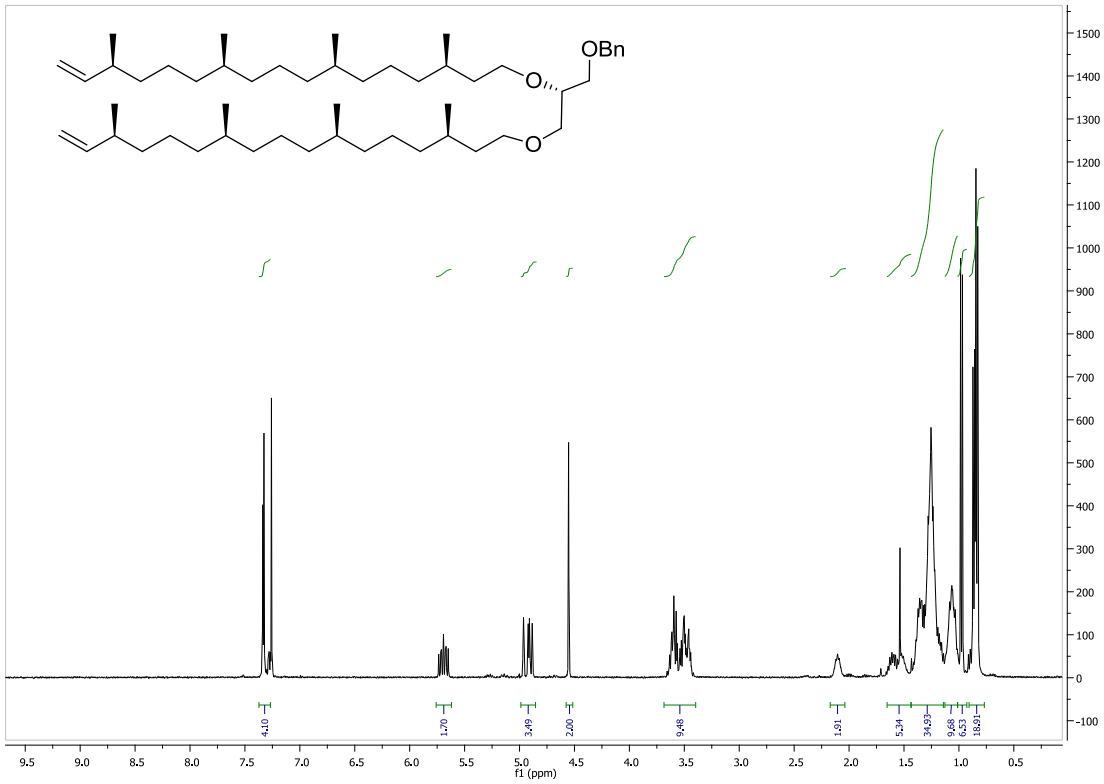
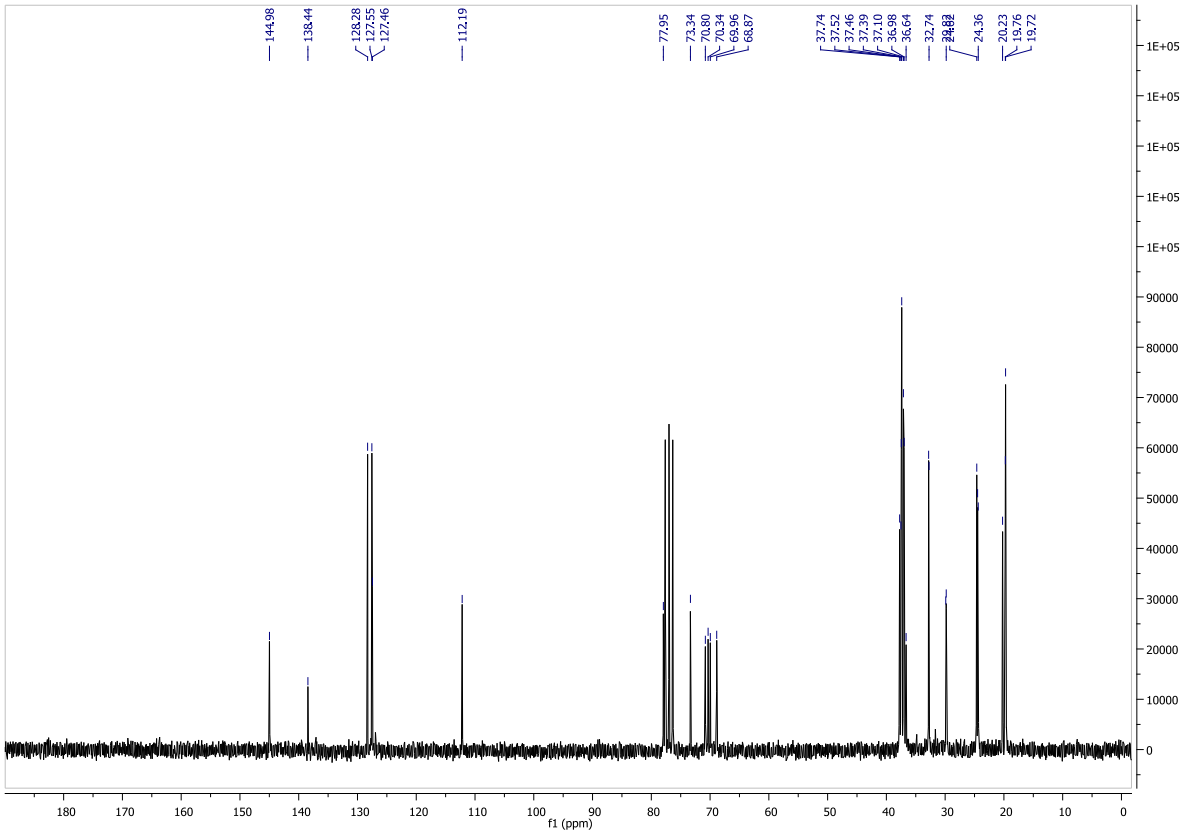
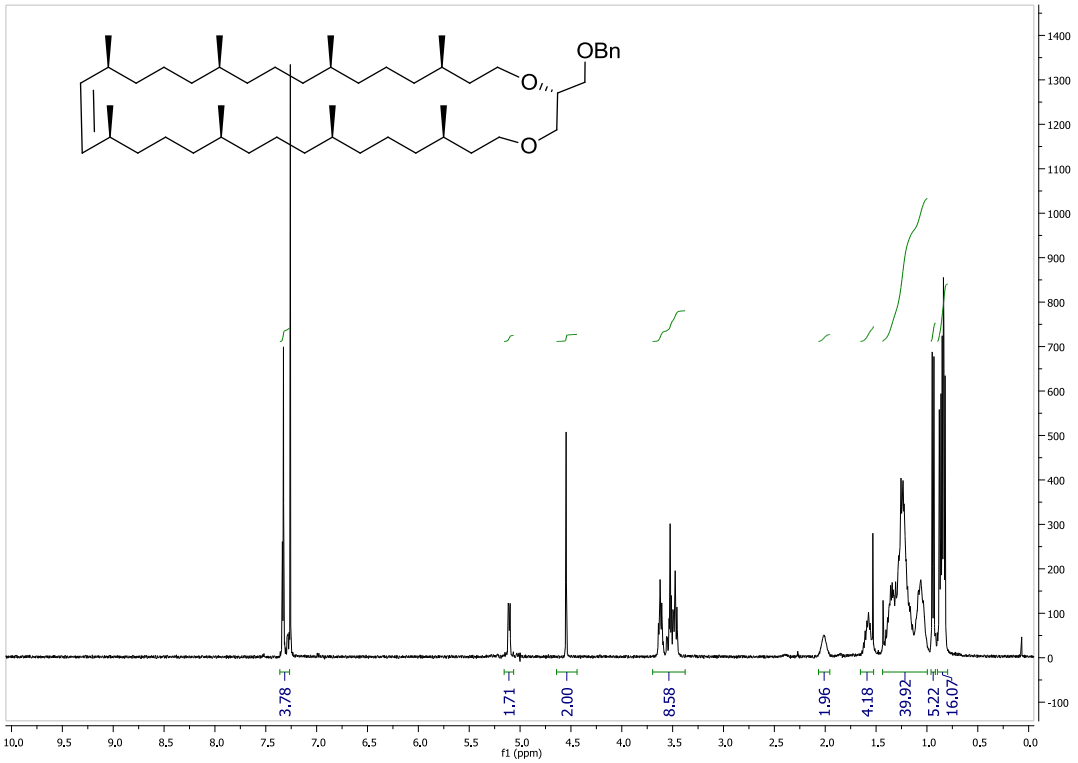
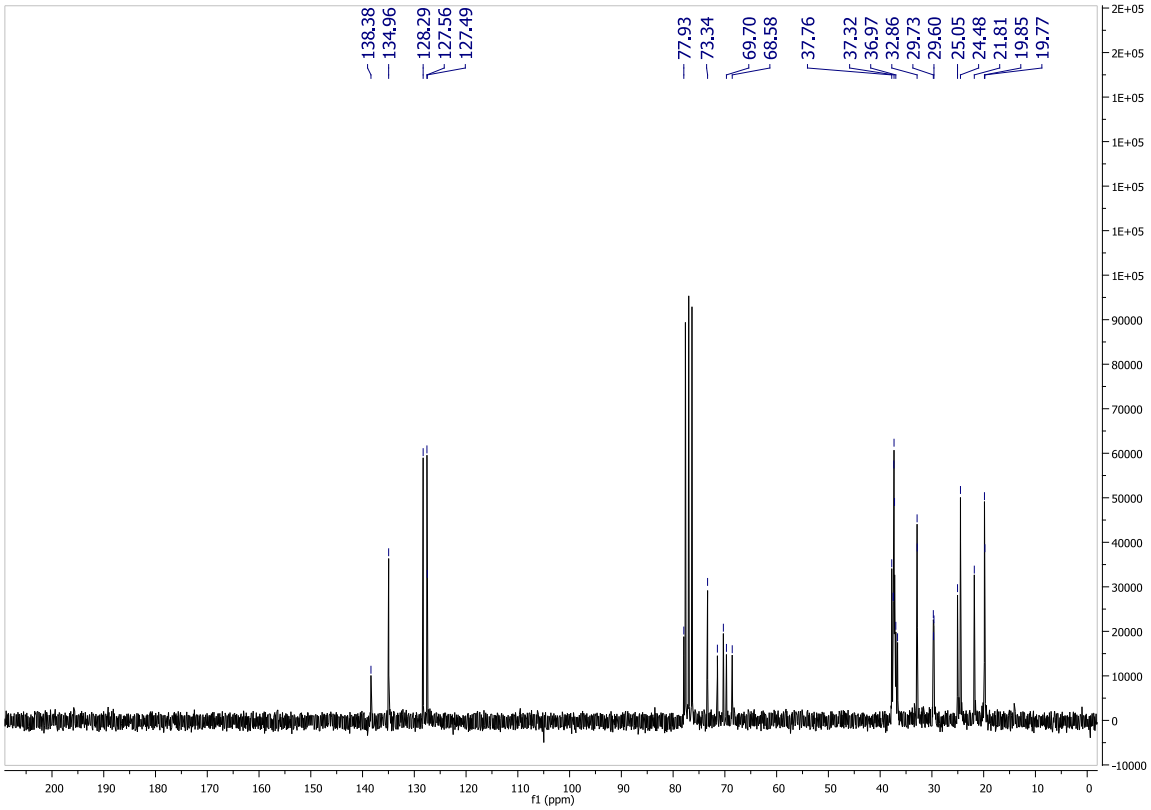




(2*S*,7*R*,11*R*,15*S*,19*S*,22*S*,26*S*,30*R*,34*R*,*E*)-2-((Benzyloxy)methyl)-7,11,15,19,22,26,30,34-octamethyl-1,4-dioxacyclohexatriacont-20-ene 20





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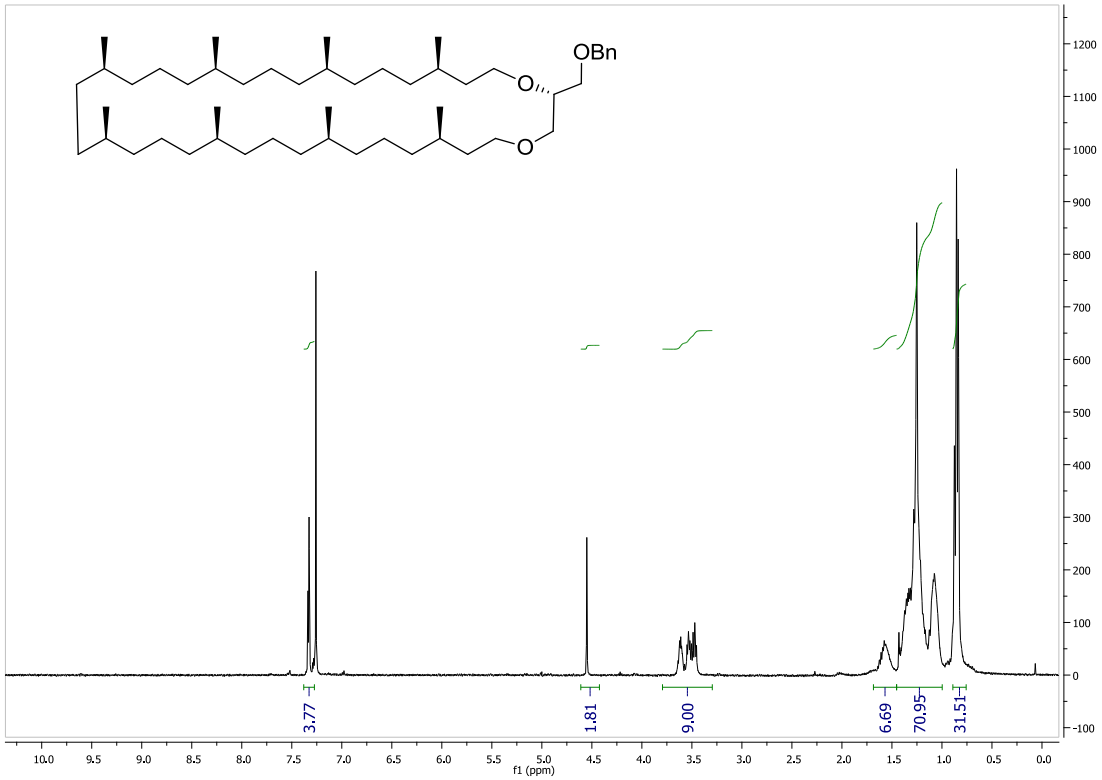
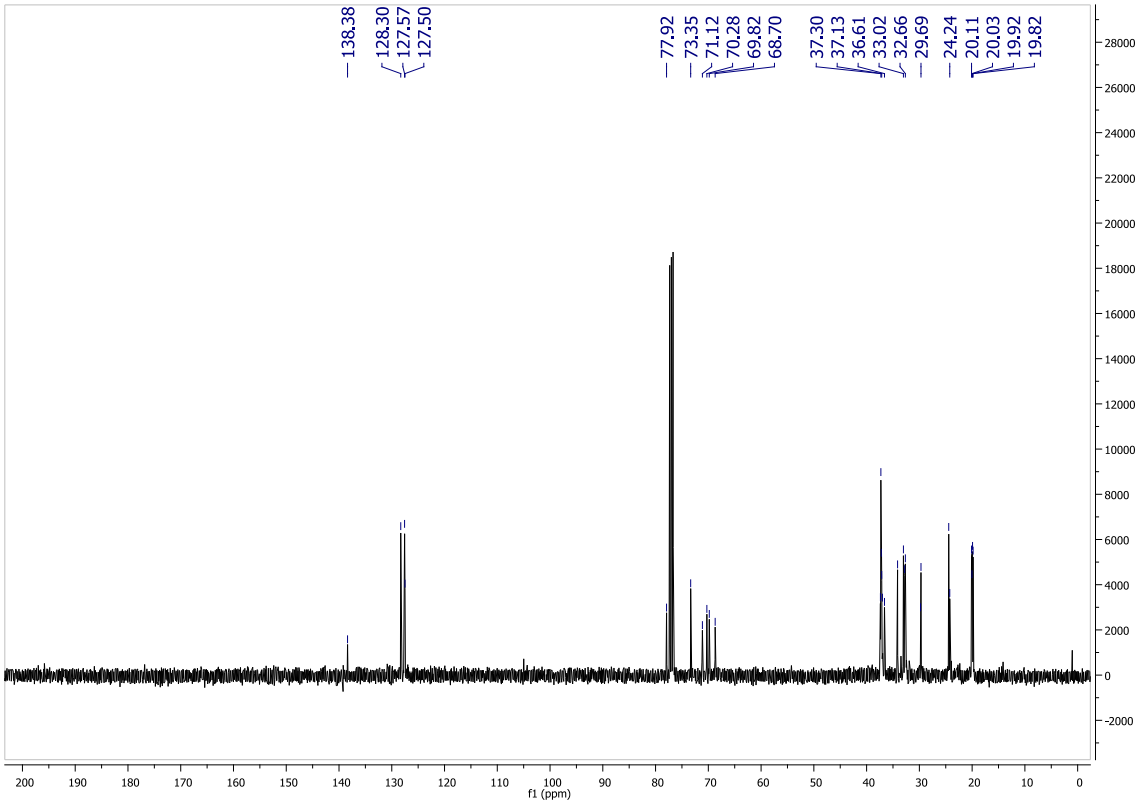
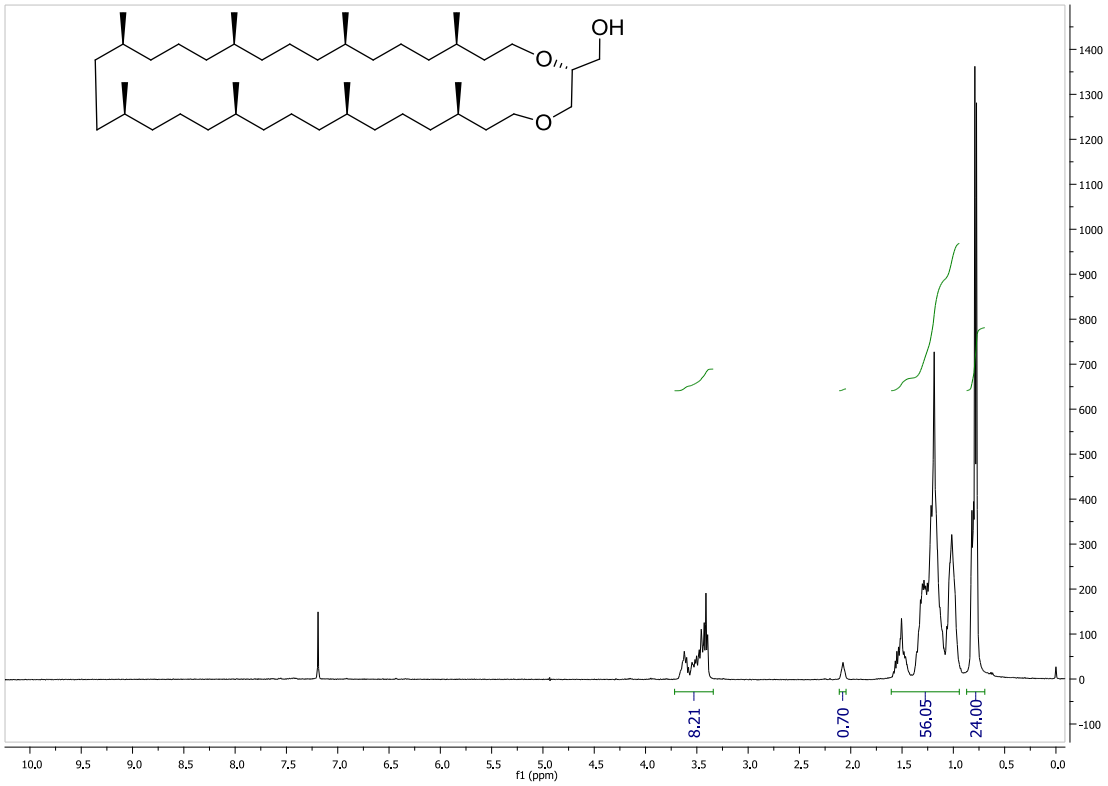
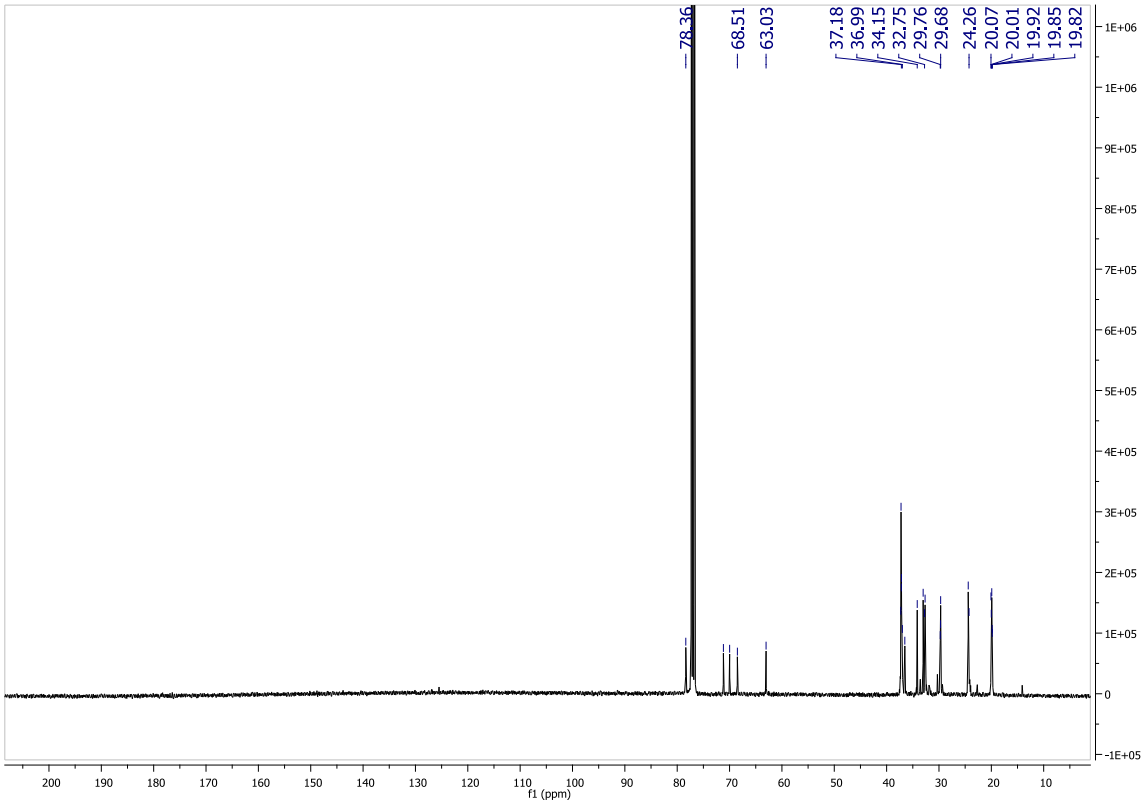
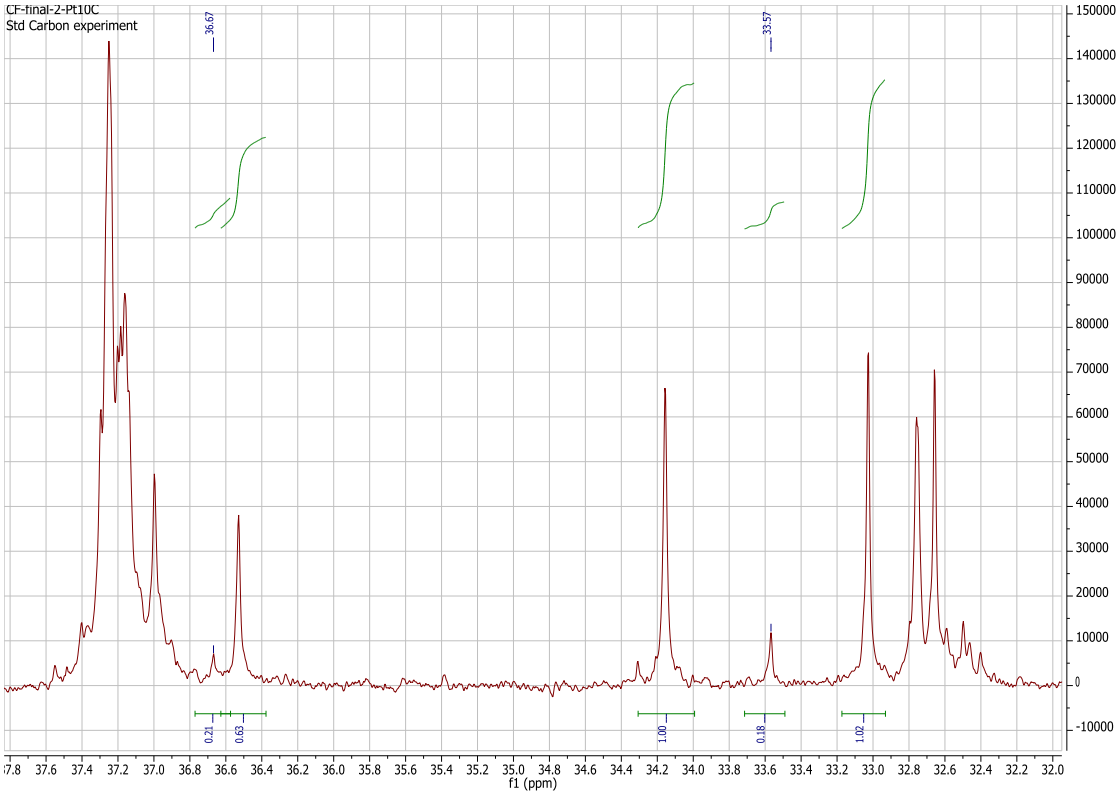


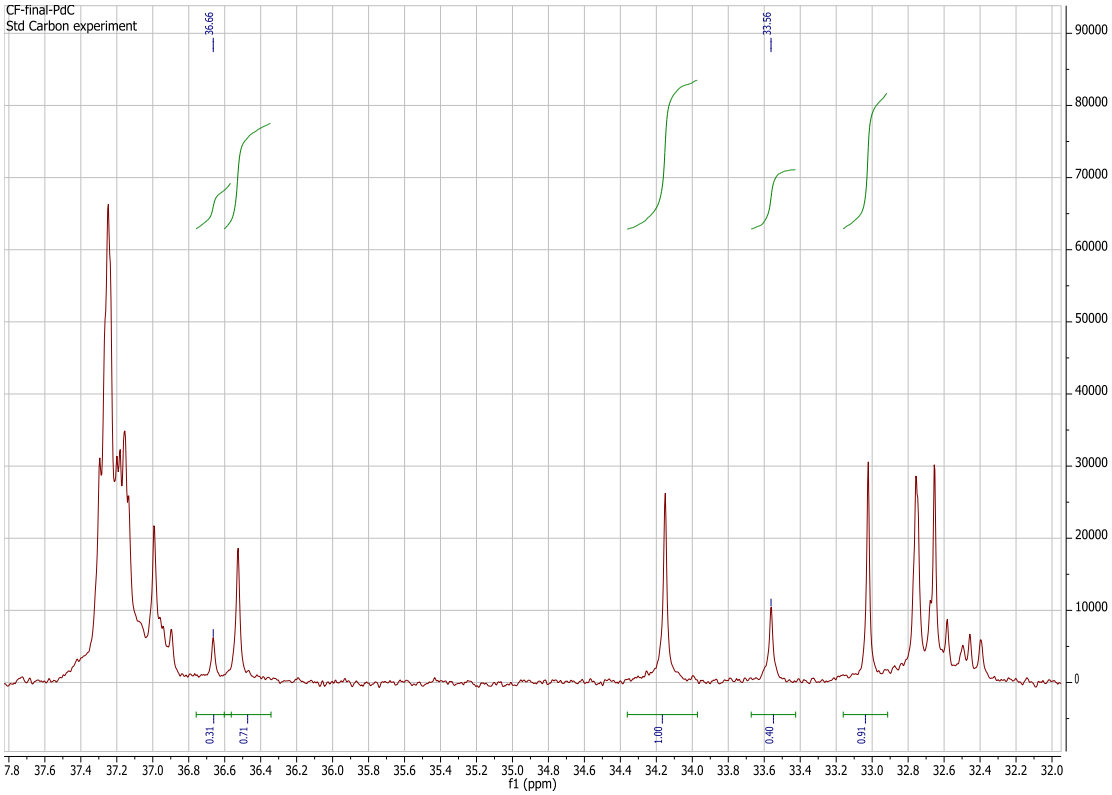


((2*R*,7*R*,11*R*,15*S*,19*S*,22*S*,26*S*,30*R*,34*R*)-7,11,15,19,22,26,30,34-Octamethyl-1,4-dioxacyclohexatriacontan-2-yl)methanol 2

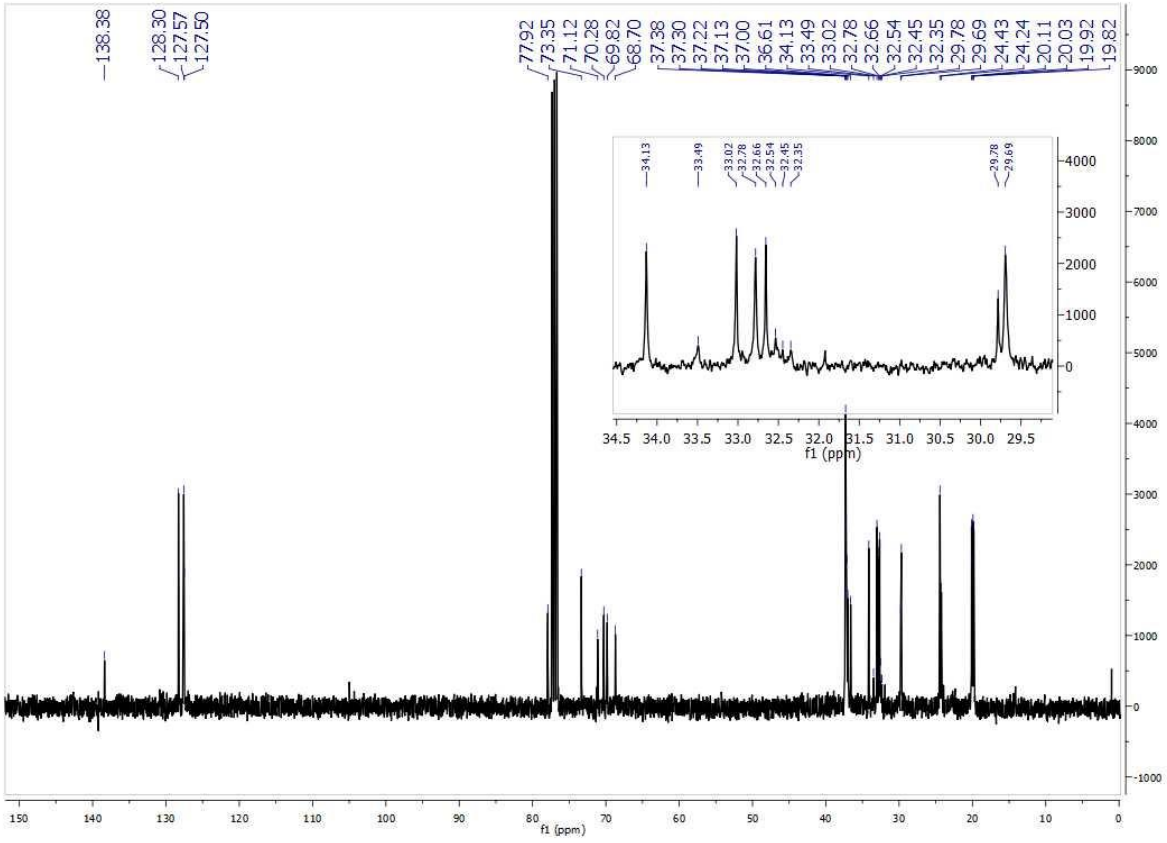




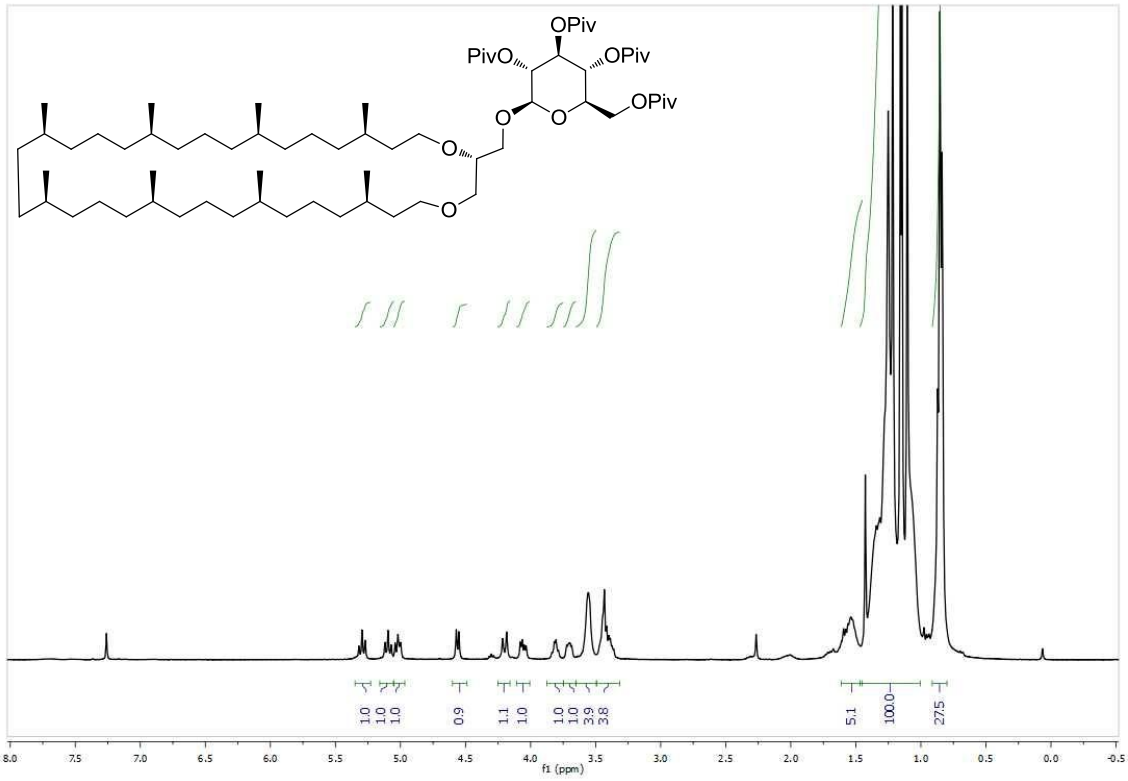


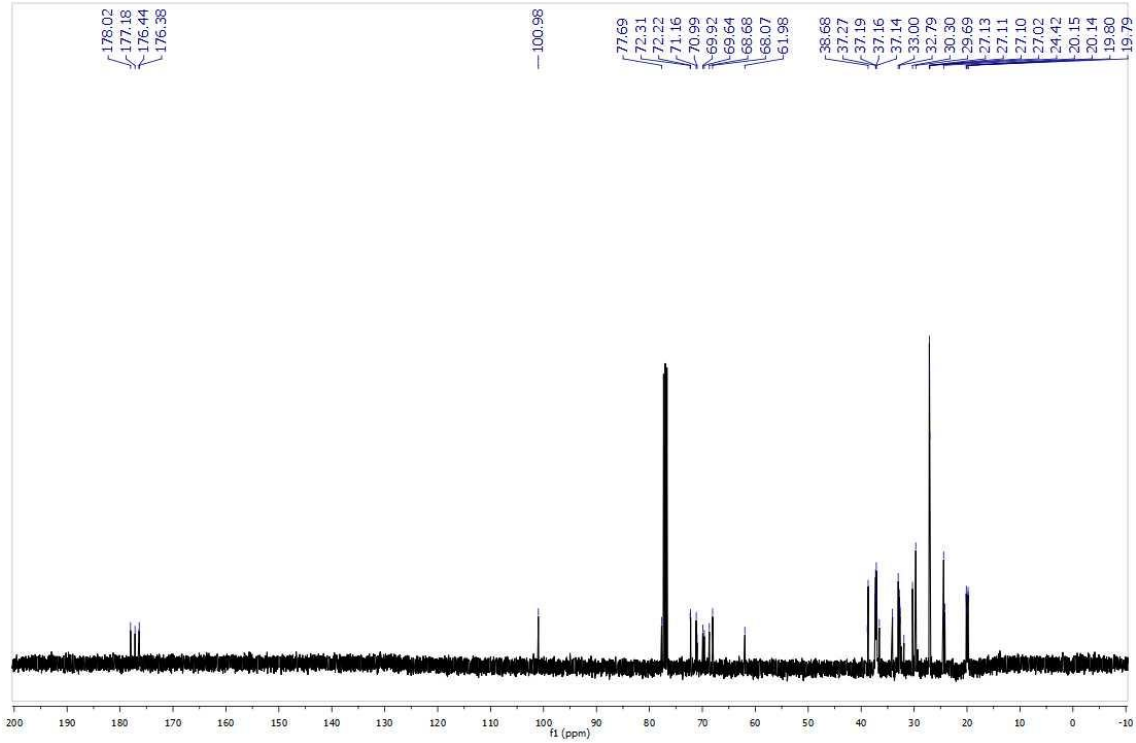


Carbon NMR after Pt reduction of the double bond but still with the benzyl group on:

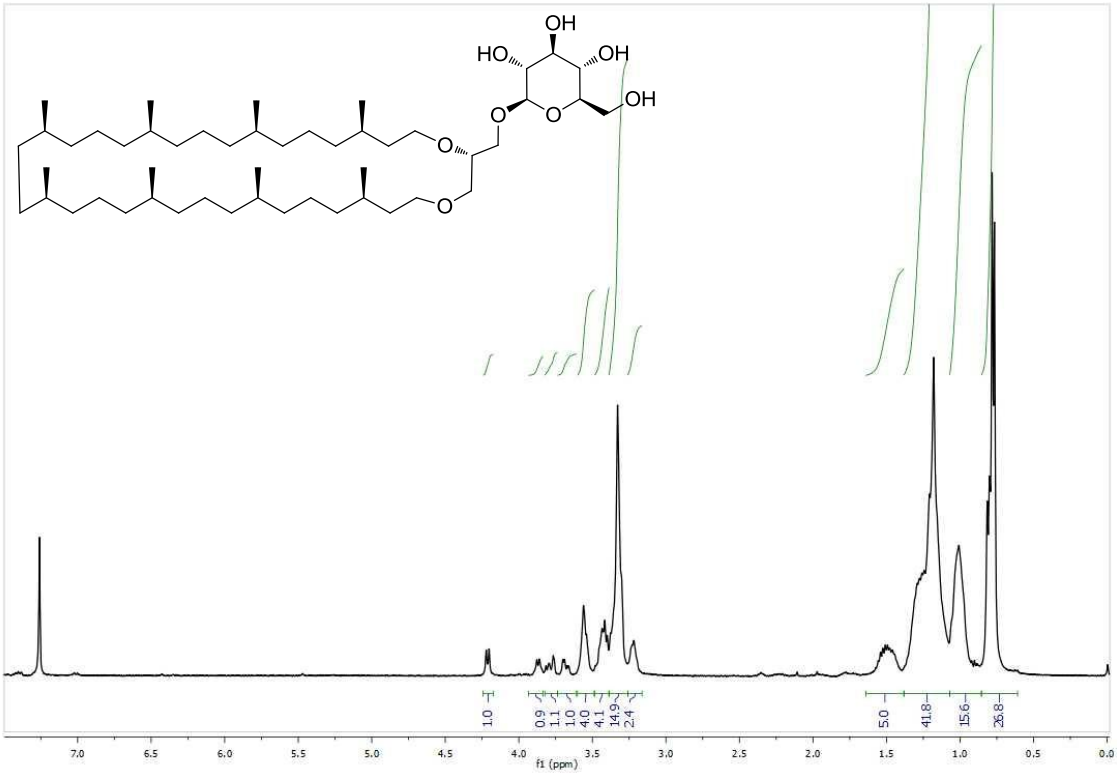


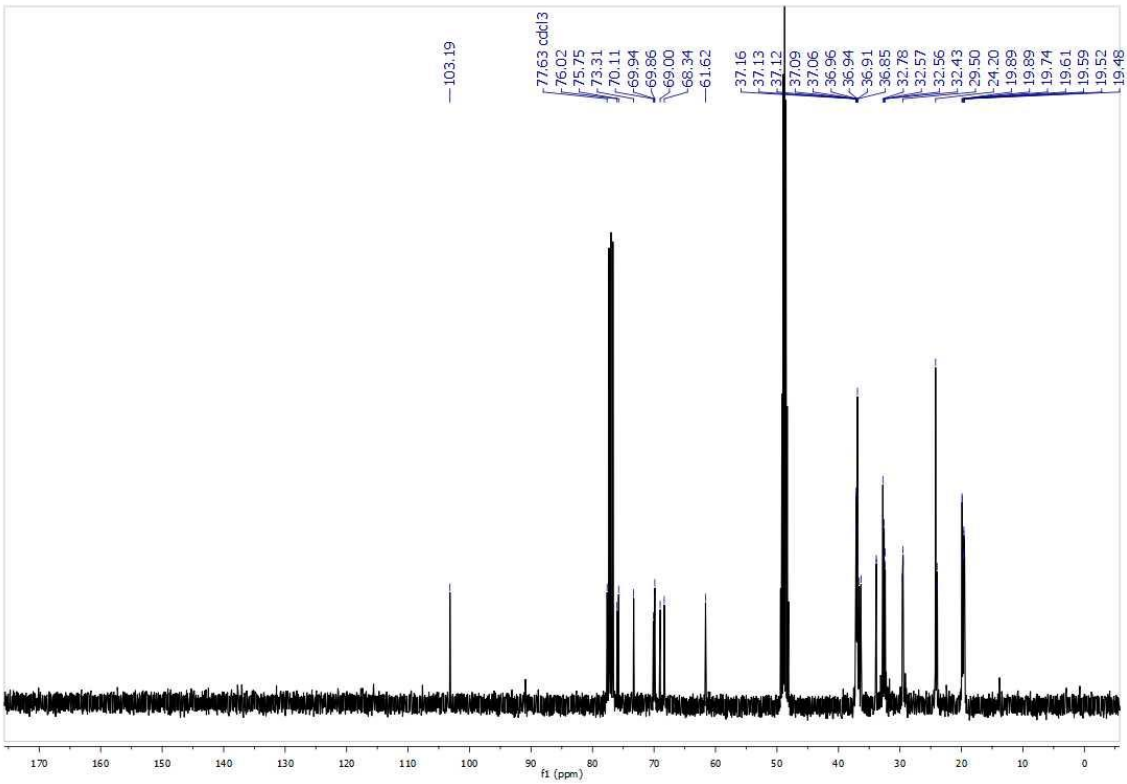
(2*R*,3*R*,4*S*,5*R*,6*R*)-2-(((7*R*,11*R*,15*S*,19*S*,22*S*,26*S*,30*R*,34*R*)-7,11,15,19,22,26,30,34-Octamethyl-1,4-dioxacyclohexatriacontan-2-yl)methoxy)-6-((pivaloyloxy)methyl)tetrahydro-2H-pyran-3,4,5-triyl tris(2,2-dimethylpropanoate) 22





(2*R*,3*S*,4*S*,5*R*,6*R*)-2-(Hydroxymethyl)-6-(((2*S*,7*R*,11*R*,15*S*,19*S*,22*S*,26*S*,30*R*,34*R*)-7,11,15,19,22,26,30,34-octamethyl-1,4-dioxacyclohexatriacontan-2-yl)methoxy)tetrahydro-2H-pyran-3,4,5-triol 23



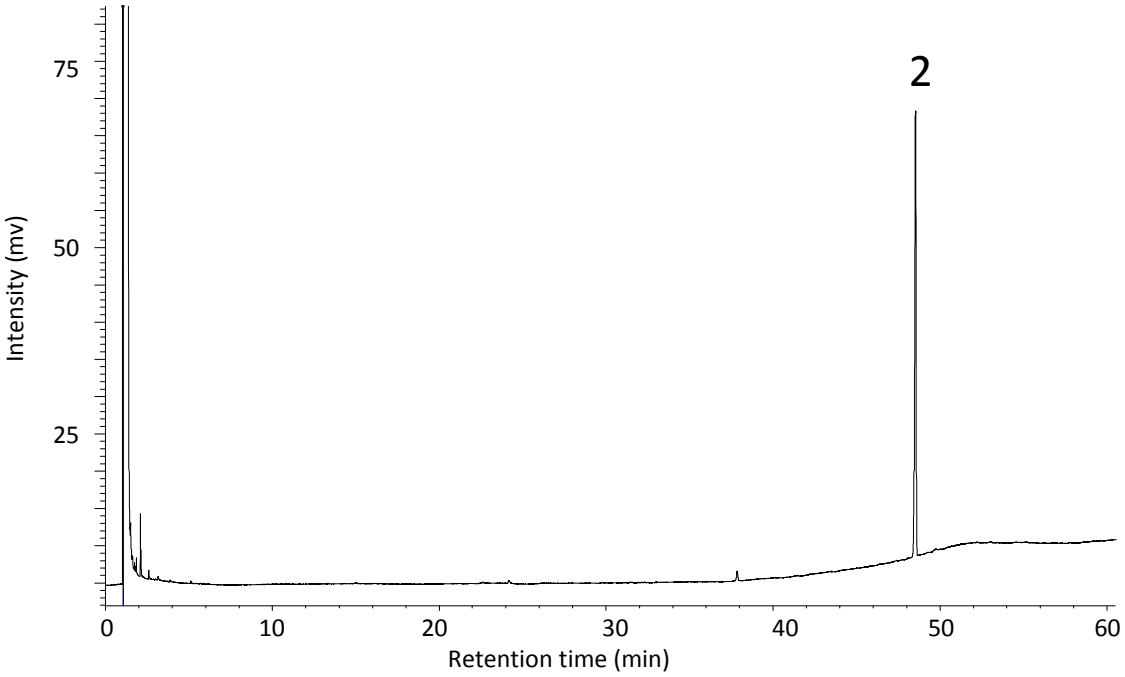


Sample description and analysis for the comparison with natural **2** and **23**

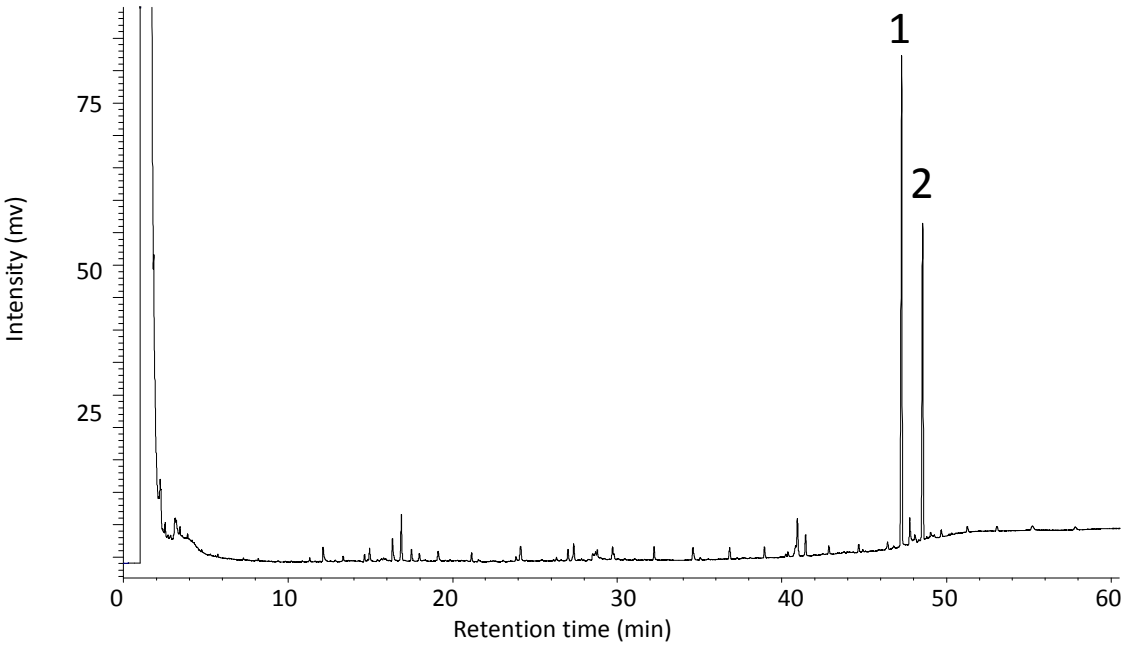
The sample was collected from the Rainbow hydrothermal vent field (RHF) located on the Mid-Atlantic Ridge. RHF has been characterized as an ultra-mafic hydrothermal system with fluids that are known to reach up to 360°C and contain abundant H_2, CH_4 and CO_2.[1] Samples were collected during a sampling campaign in 2008 using the ROV Jason.

The sample analysed is composed of material from the interior of a vent chimney collected at a depth of 2293 m below sea level. The location of the vent is 57°39'N, 32°65'W.

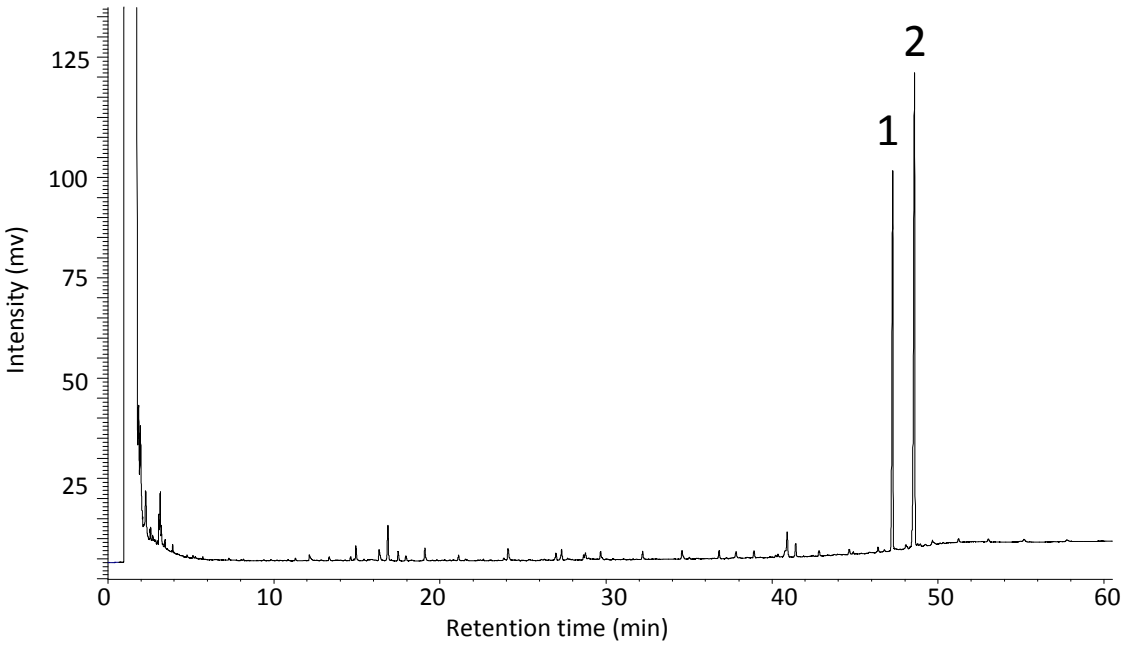
Intact Polar Lipids were extracted from freeze-dried, powdered (approximately 5 g) vent deposit using a modified Bligh and Dyer method described by Pitcher *et al.*.[2] The extract was analysed by high performance liquid chromatography electrospray ionisation mass spectrometry (HPLC-ESI-MS^n) using modified literature methods.[3] The analysis was conducted on an Agilent 1200 series LC equipped with a Lichrosphere diol column (250 x 2.1 μm, 5 μm particles; Alltech Associates Inc.) coupled to a Thermo LTQ XL linear ion trap with Ion Max source with electrospray ionization (ESI) probe (Thermo Scientific, Waltham, MA).
The extract was acid hydrolysed to release **2**.[4] The hydrolyzed extract was reacted with diazomethane to convert free acids to methyl esters then separated over a short Al_2O_3 column using hexane/DCM (9:1; v/v) and DCM/methanol (1:1; v/v). Part of the latter fraction was subsequently silylated using bis(trimethylsilyl)trifluoroacetamide (BSTFA) in pyridine at 60˚C for 15 min. The fatty acid methyl ester and silylated alcohol fraction were analyzed by gas chromatography (GC) and GC-mass spectrometry (MS). GC was performed on a Hewlett-Packard 6890 series GC system with an on-column injector and flame ionization detector. A fused silica capillary column (length 25 m, internal diameter 0.32 μm) coated with CP Sil-5 (film thickness, df = 0.12 μm) was used with helium as the carrier gas. Samples were injected at 70 ˚C and oven temperature was increased to 130 ˚C at 20˚C/min and then increased to 320˚C at a rate of 4˚C/min, where it remained stable for 10 min. GC-MS was performed on a Thermo Trace DSQ mass spectrometer fitted with a Thermo Trace GC Ultra. The mass spectrometer was operated at 70 eV with a mass range of m/z 50 – 800 and a cycle time of 0.33 s. The GC was equipped with a fused silica capillary column as described for GC analysis above and the same temperature program was used.



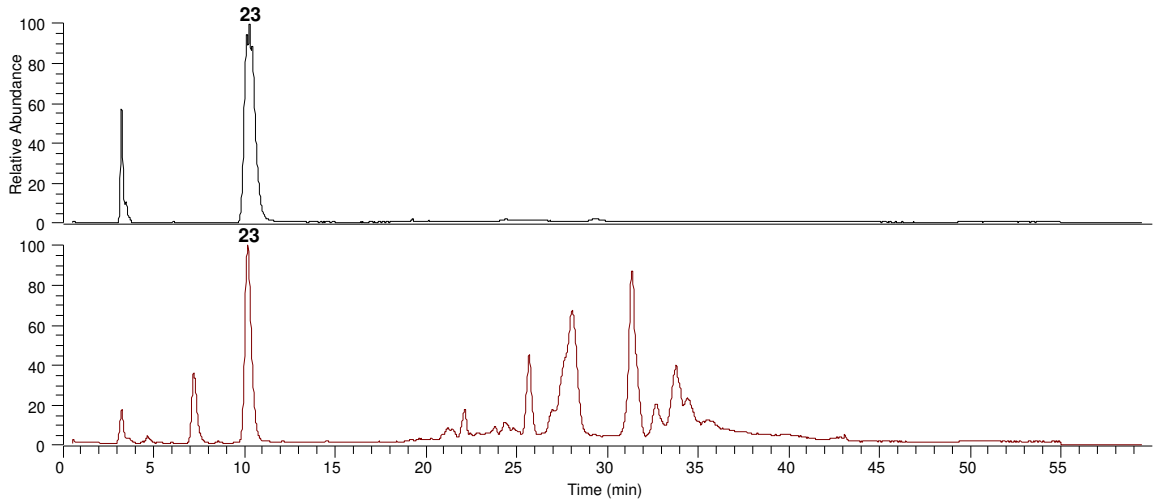
Gas chromatogram of synthetic **2**, R_t = 48.54 min



Gas chromatogram of TMSi-derivatized acid hydrolysed extract of the hydrothermal vent sample,. First peak corresponds to archaeol (**1**), second peak corresponds to **2** with R_t = 48.56 min.



Co-injection of the vent sample with synthetic **2**, showing the same R_t = 48.56 min



HPLC/MS selected ion chromatograms of mass m/z 830.5, the NH_4^+ ion of the molecular mass of **23.** *Top* chromatogram shows synthetic **23** the *lower* chromatogram shows the hydrothermal vent sample at Rainbow hydrothermal field with natural **23**, both eluting at 10.2 min.

[1] C. Konn, J. L. Charlou, J. P. Donval, N. G. Holm, F. Dehairs, and S. Bouillon, *Chemical Geology*, 2009, **258**, 299 – 314.
[2] A. Pitcher, E.C. Hopmans, S. Schouten, and J.S. Sinninghe Damsté, *Organic Geochemistry* 2009, **40**, 12-19.
[3] H. F. Sturt, R. E. Summons, K. Smith, M. Elvert, and K.-H. Hinrichs, *Rapid Comm in Mass Spectr*., 2004, **18**, 617 – 628.
[4] J. S. Sinninghe Damsté, W. I. C. Rijpstra, E. C. Hopmans, J. W. H. Weijers, B. U. Foesel, J. Overmann, and S. N. Dedysh, *Appl. Environm. Microbiol*., 2011, **77**, 4147 - 4154.