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Supplementary data

Mutual Influence of Backbone Proline Substitution and Lipophilic Tail Character on the Biological Activity of Simplified Analogues of Caspofungin

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Additional CD spectra:

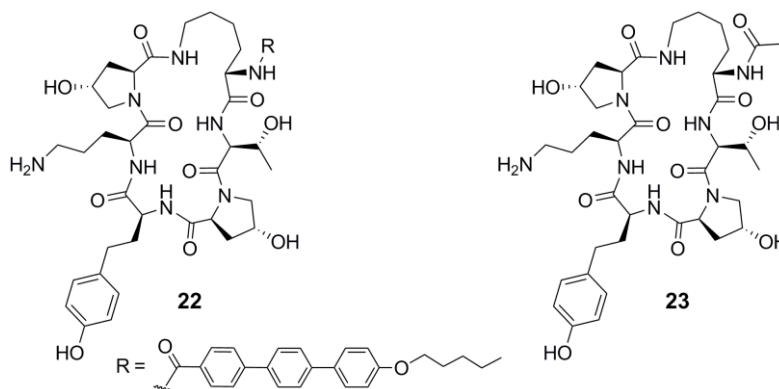


Figure S 1. 22-membered ring size analogues **22** and **23** with a terphenyl and acetyl tail, respectively.

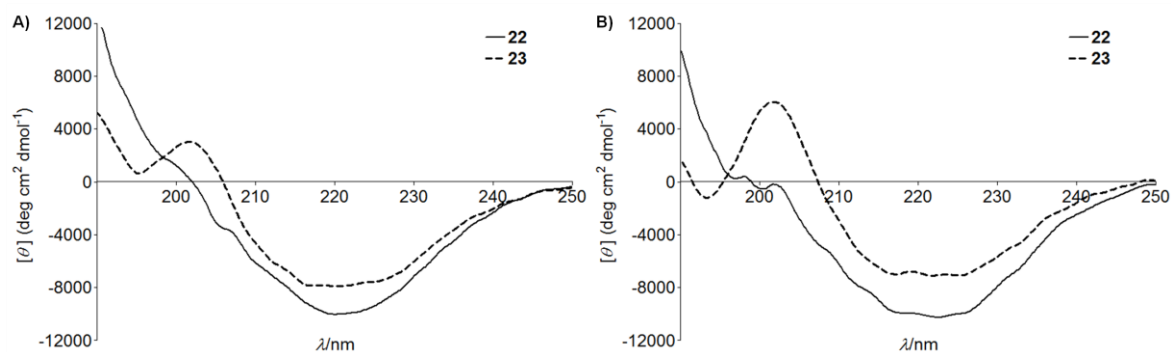


Figure S 2. CD spectra of analogues (**22** and **23**). A) Measured in MeCN/H₂O (1/1, v/v); B) Measured in TFE/H₂O (1/1, v/v). All peptides were measured at 0.1 mM concentration.

A distinct different pattern in CD of analogue **22** with a terphenyl tail was observed, at wavelengths below 210 nm, compared to analogue **23** (Figure S 2). This corroborates the observation regarding the influence of the terphenyl side chain on CD spectra. And may be explained by a large contribution of the aromatic residues present in the terphenyl side chain.

Modelling:

Modeling of the structures **3** and **6** was accomplished using the YASARA Structure 10.5.2.1 software package. Structures were energy minimized using the simulated annealing protocol employing the AMBER99¹ force field. A 2500 ps MD in water was run of each structure. After 250 ps equilibration, the structure with the lowest energy trajectory (between 250-2500 ps) was saved as a job file. Molecules were superimposed, with the reported crystal structure of ECBN, by minimizing the rmsd between the backbone atoms in the ring.

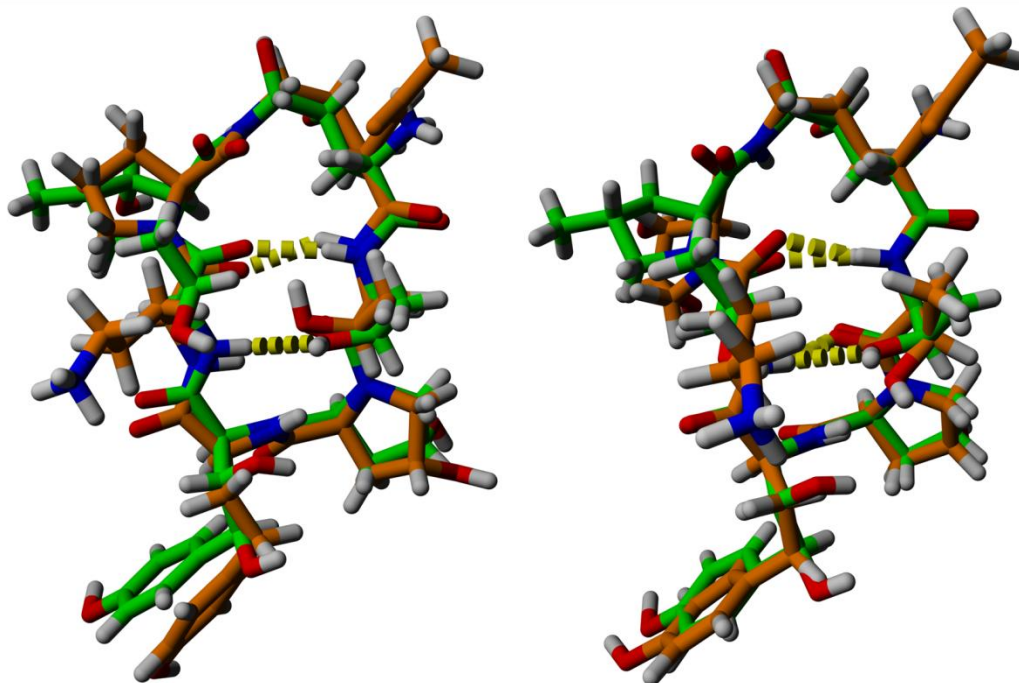
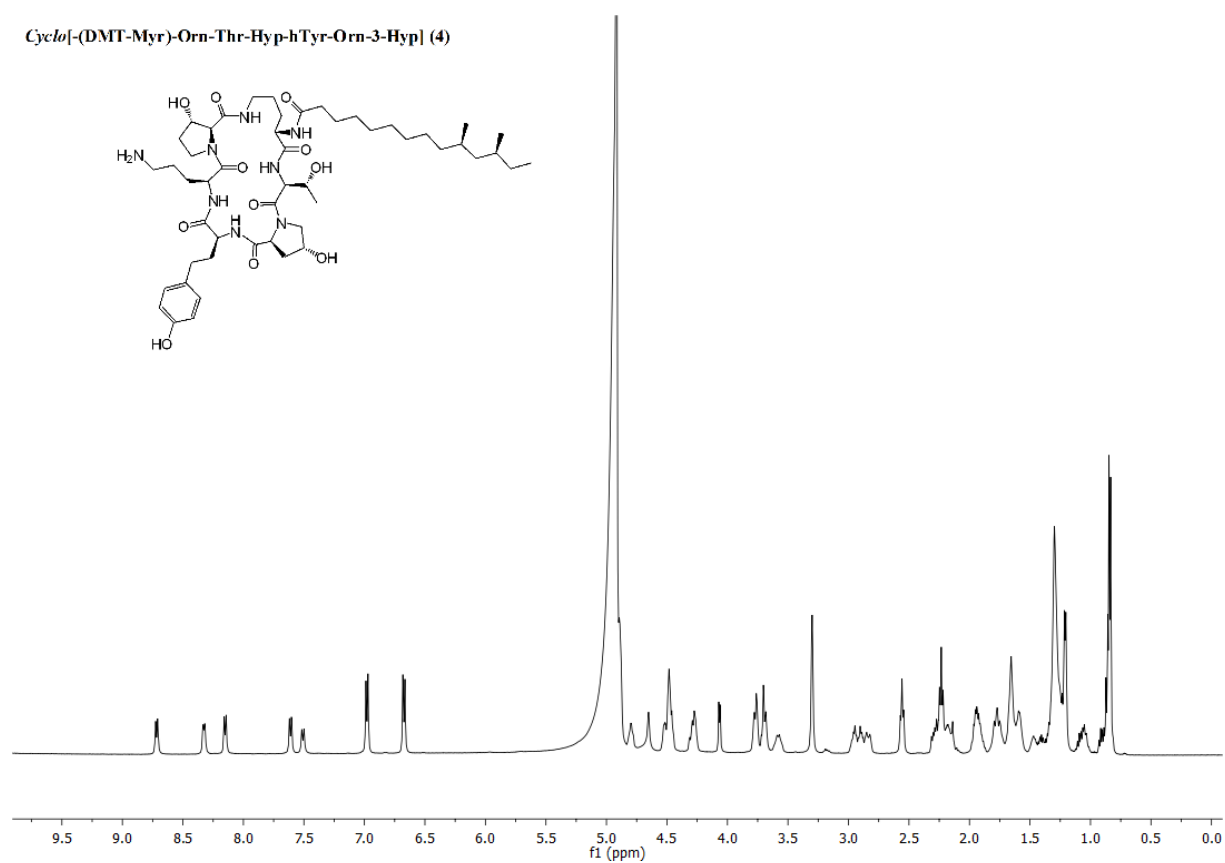


Figure S 3. Superimposition of ECBN (carbons colored green) with analogues **3** (right) and **6** (left) (carbons colored orange). The backbone atoms have been used as fixed coordinates for superimposition.

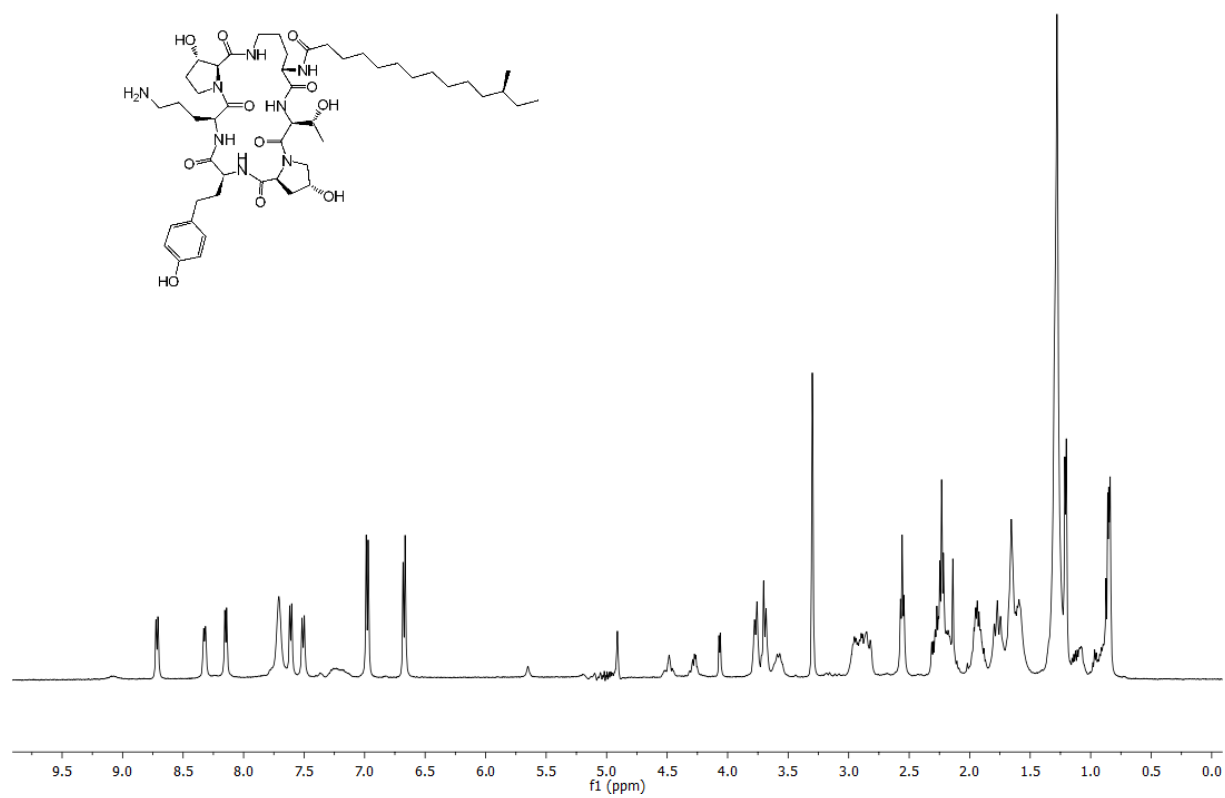
¹ Ponder, J.W.; Case, D.A. *Adv. Protein Chem.*, **2003**, 66, 27-85.

NMR

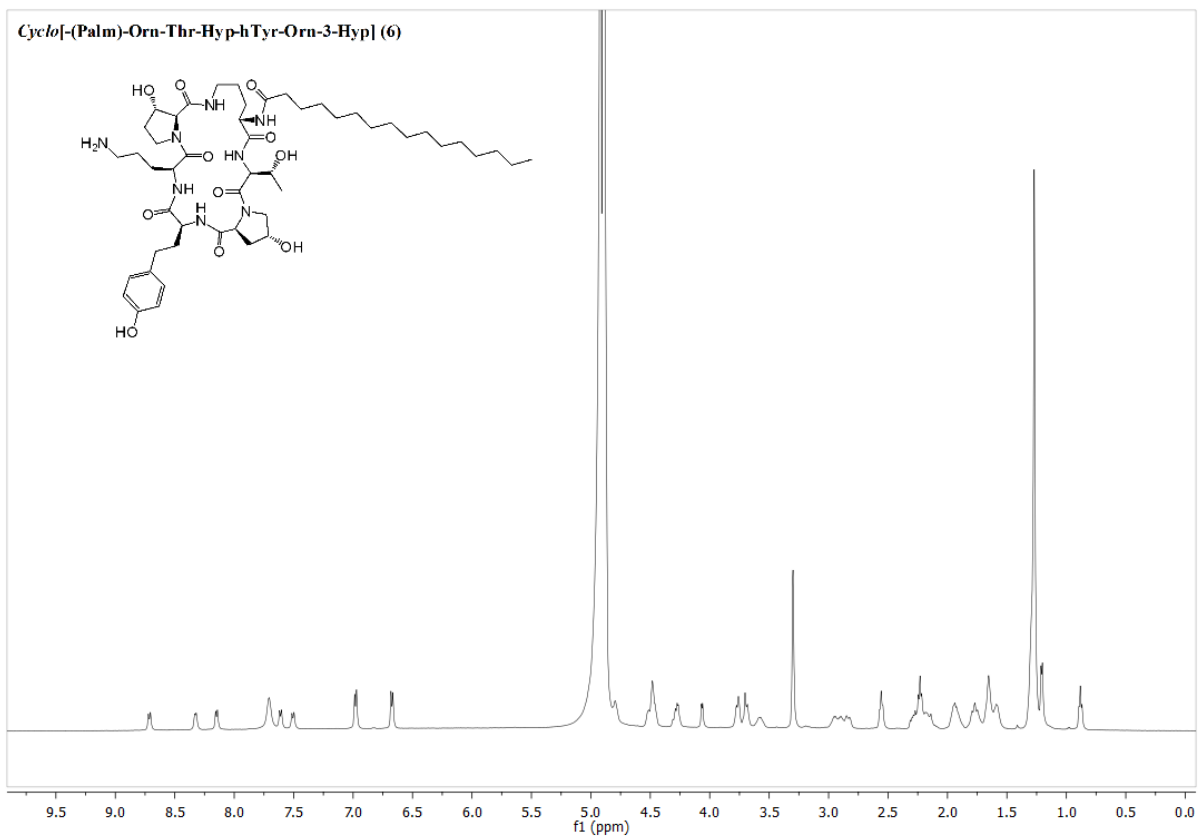
Cyclo[-(DMT-Myr)-Orn-Thr-Hyp-hTyr-Orn-3-Hyp] (4)



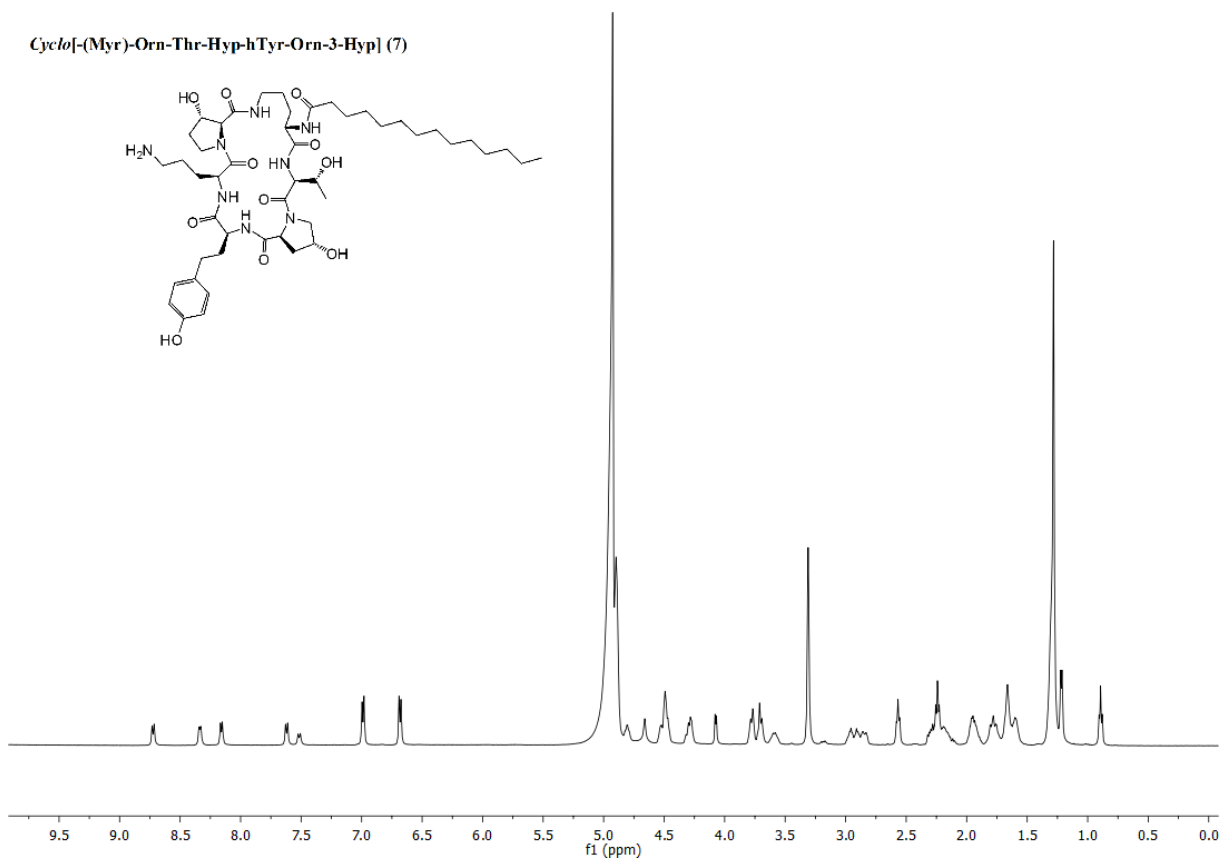
Cyclo[-(Me-Myr)-Orn-Thr-Hyp-hTyr-Orn-3-Hyp] (5)



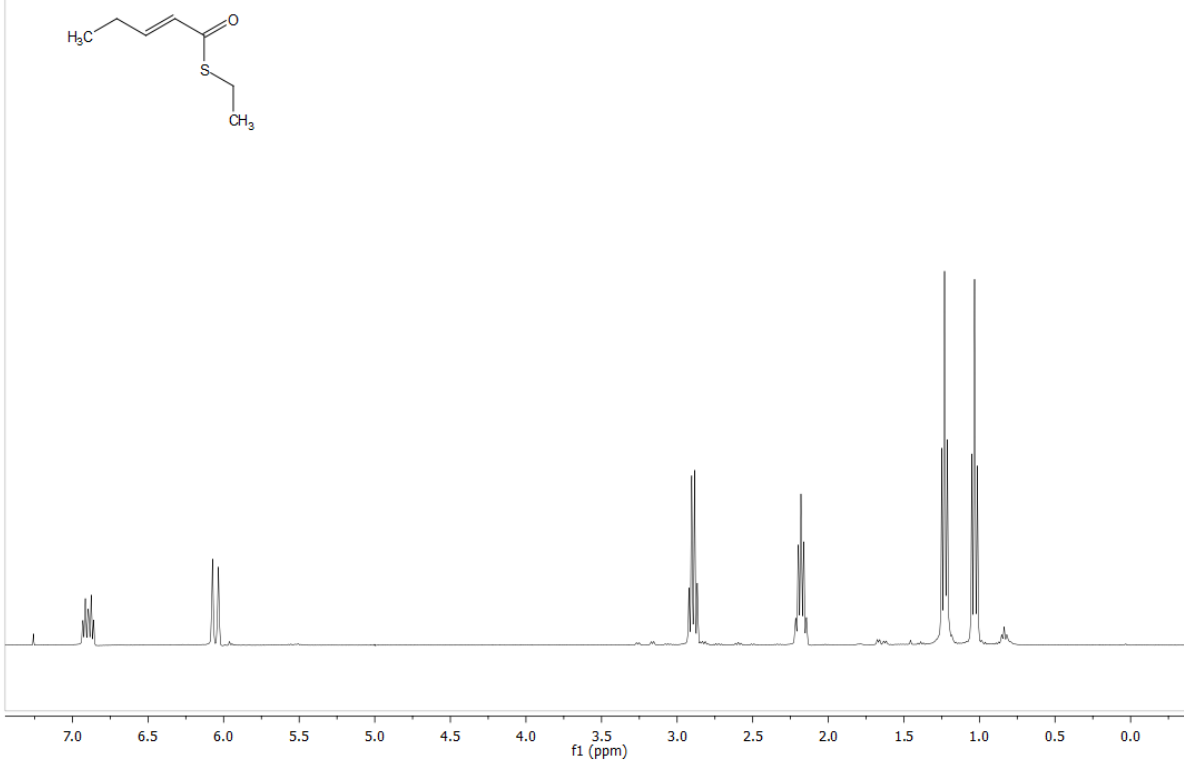
Cyclo[-(Palm)-Orn-Thr-Hyp-hTyr-Orn-3-Hyp] (6)



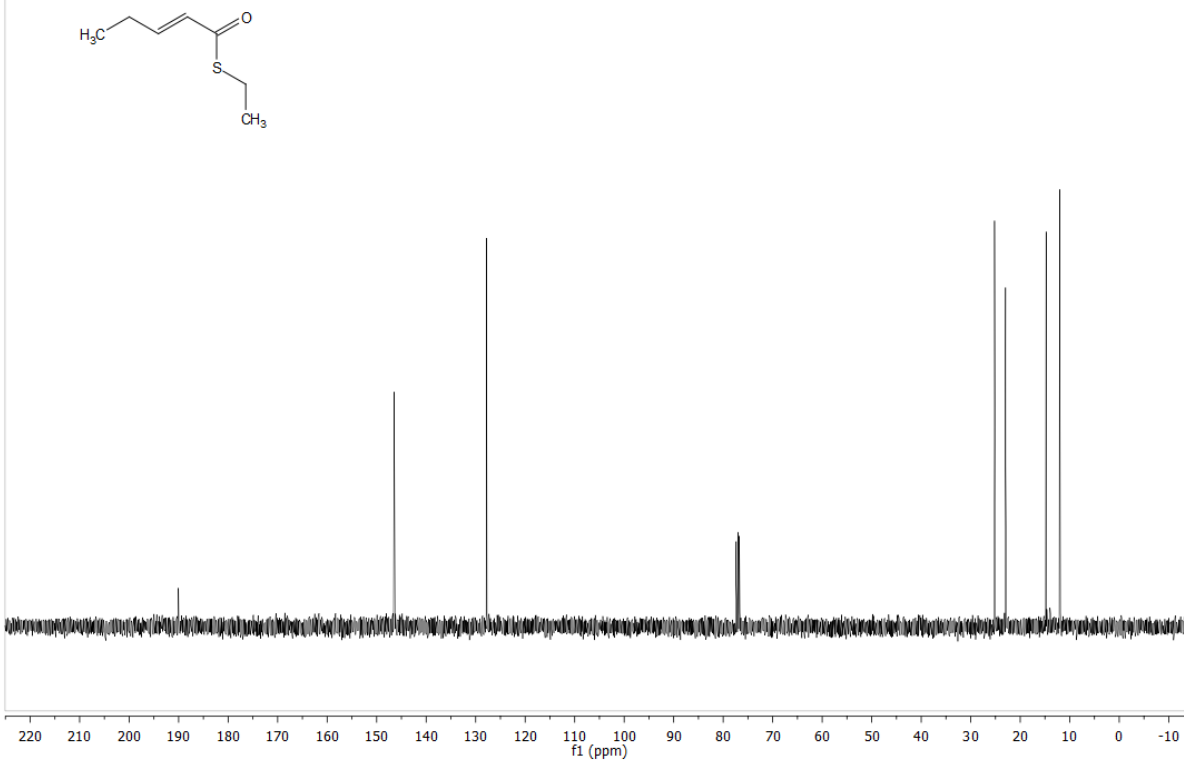
Cyclo[-(Myr)-Orn-Thr-Hyp-hTyr-Orn-3-Hyp] (7)



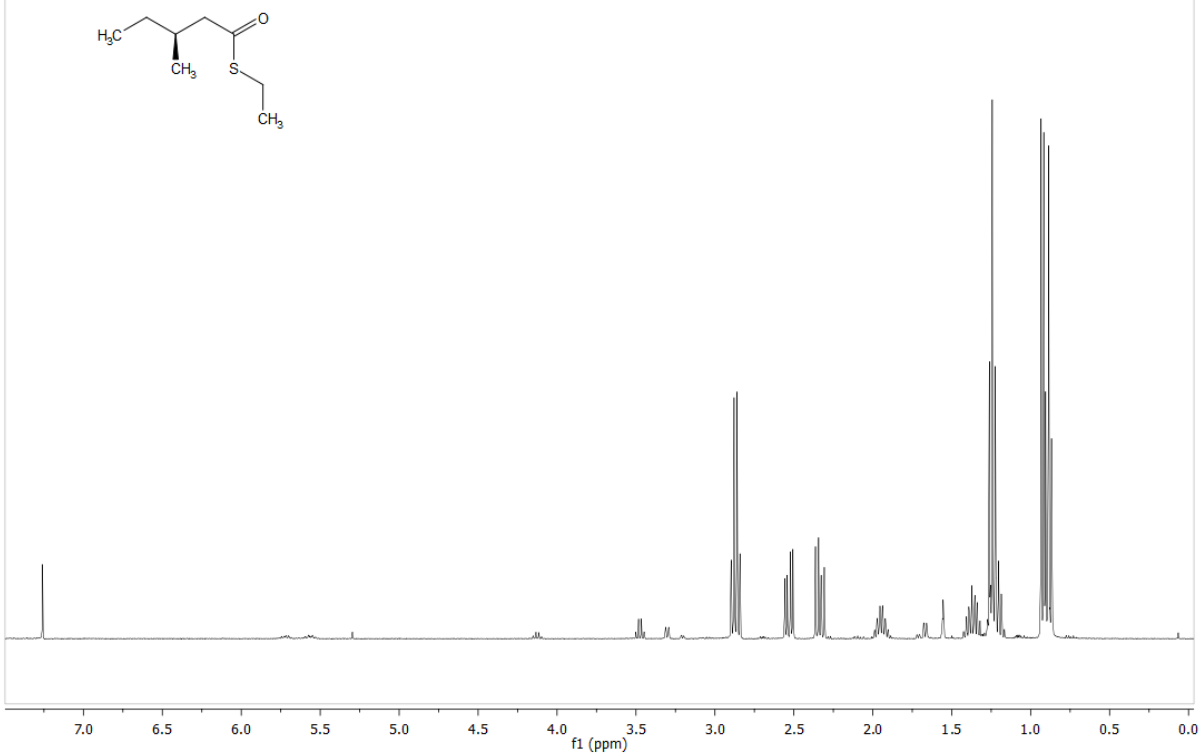
(*E*)-S-ethyl pent-2-enethioate (10)



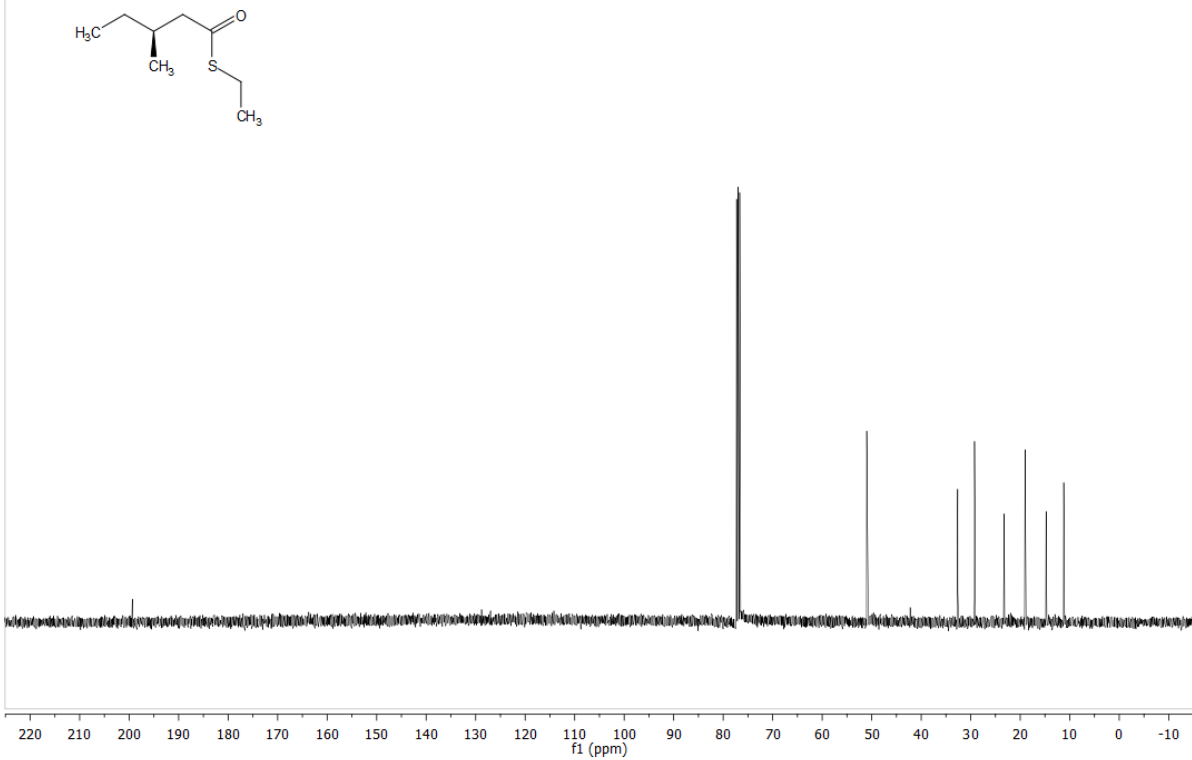
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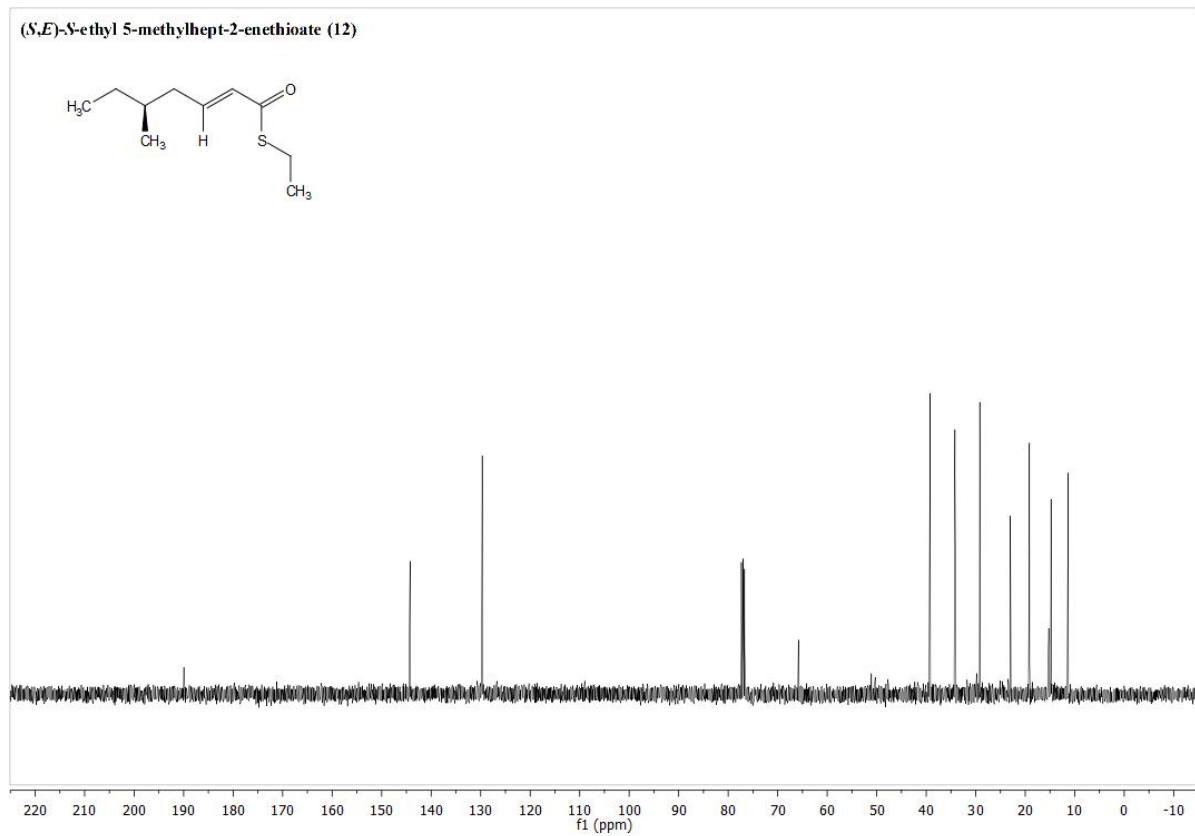
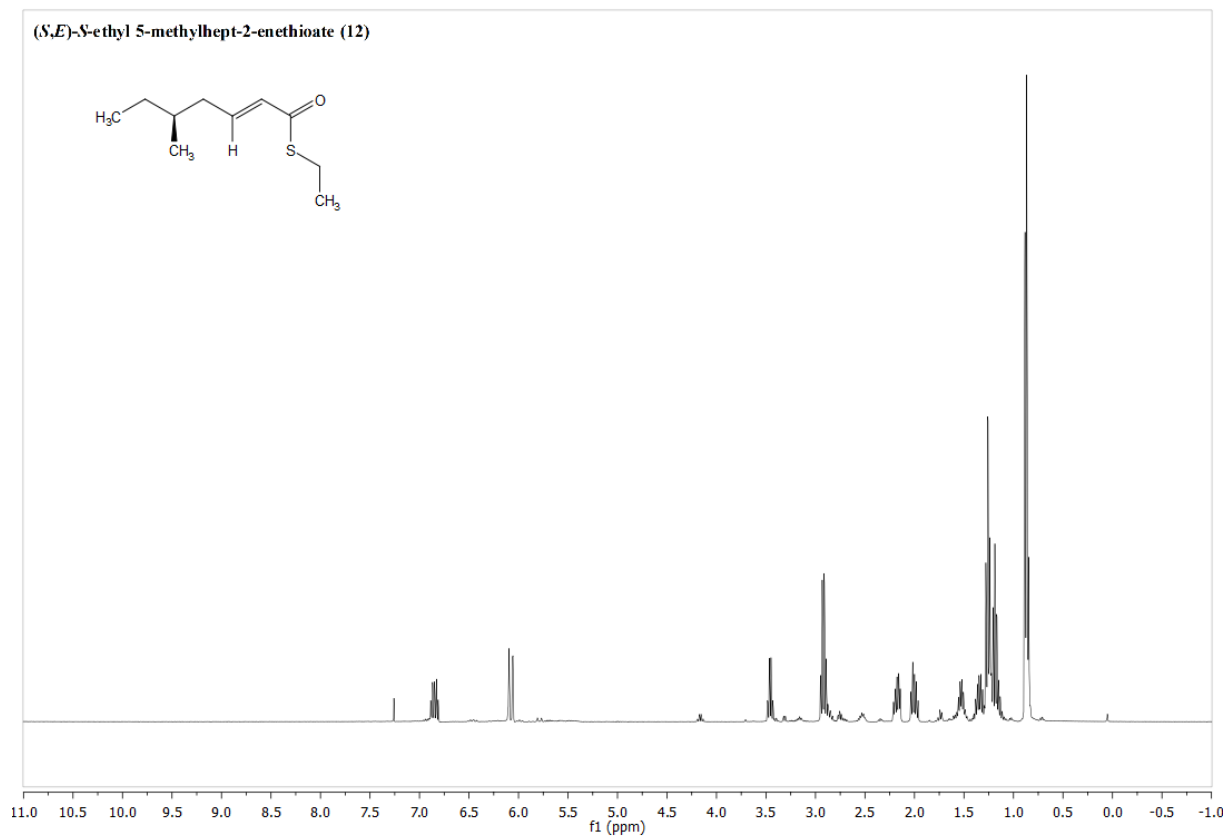


(S)-S-ethyl 3-methylpentanethioate (11)

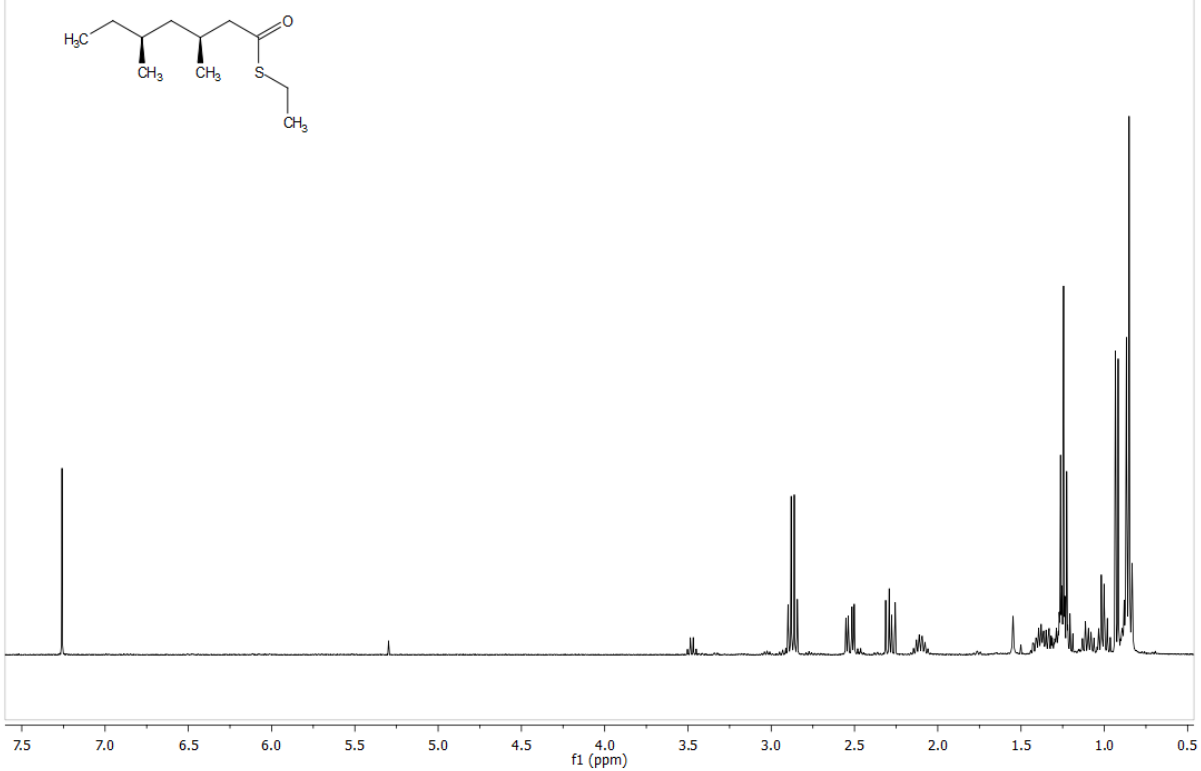


(S)-S-ethyl 3-methylpentanethioate (11)

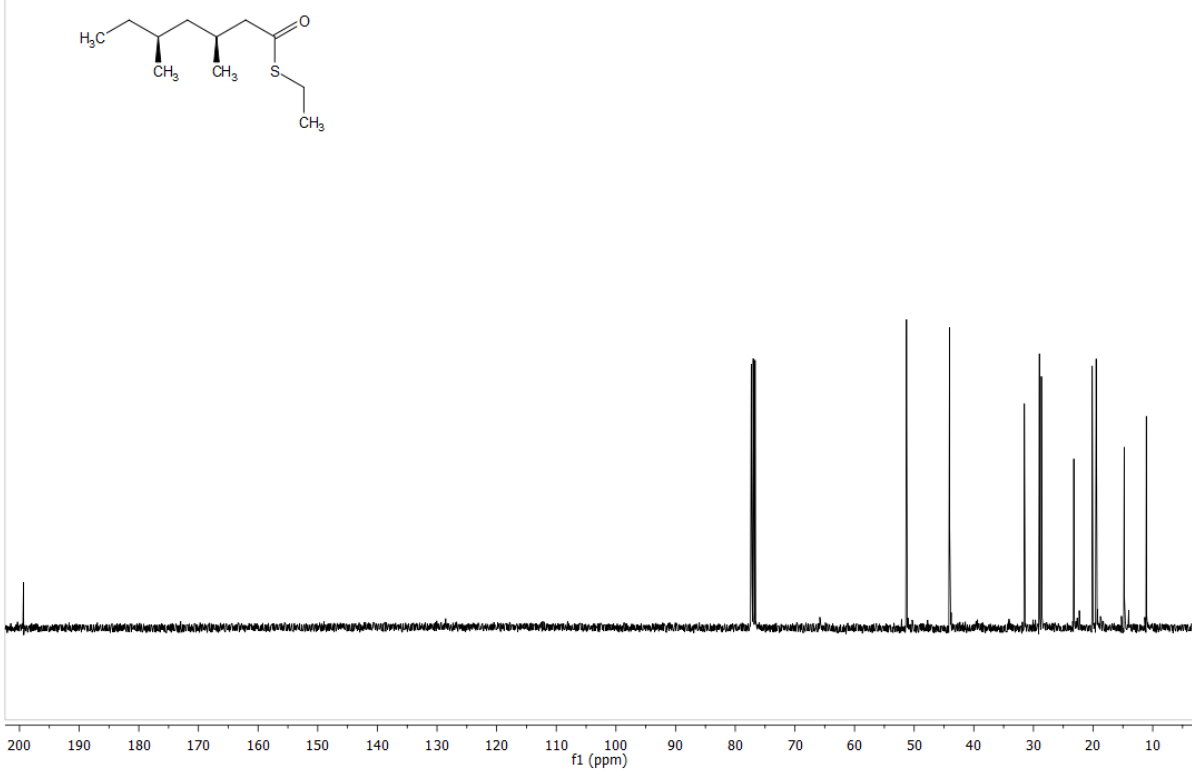




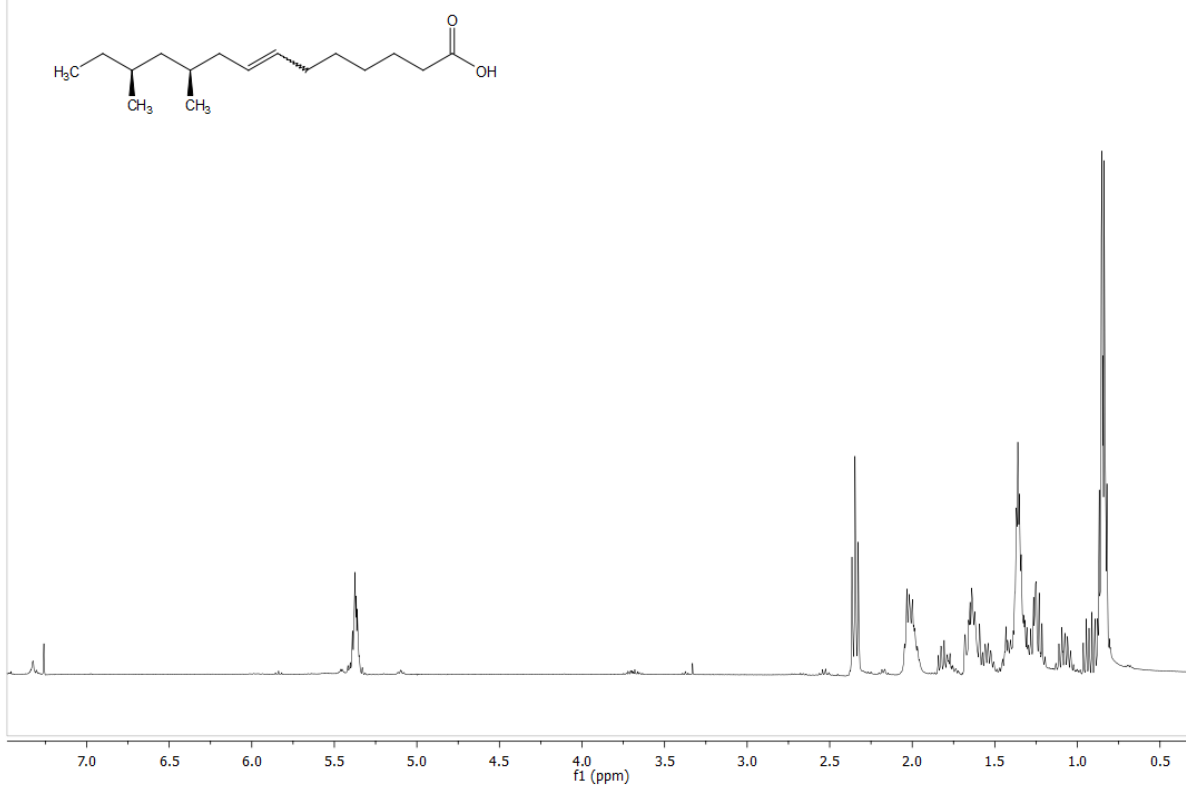
(3*S*,5*S*)-*S*-ethyl 3,5-dimethylheptanethioate (13)



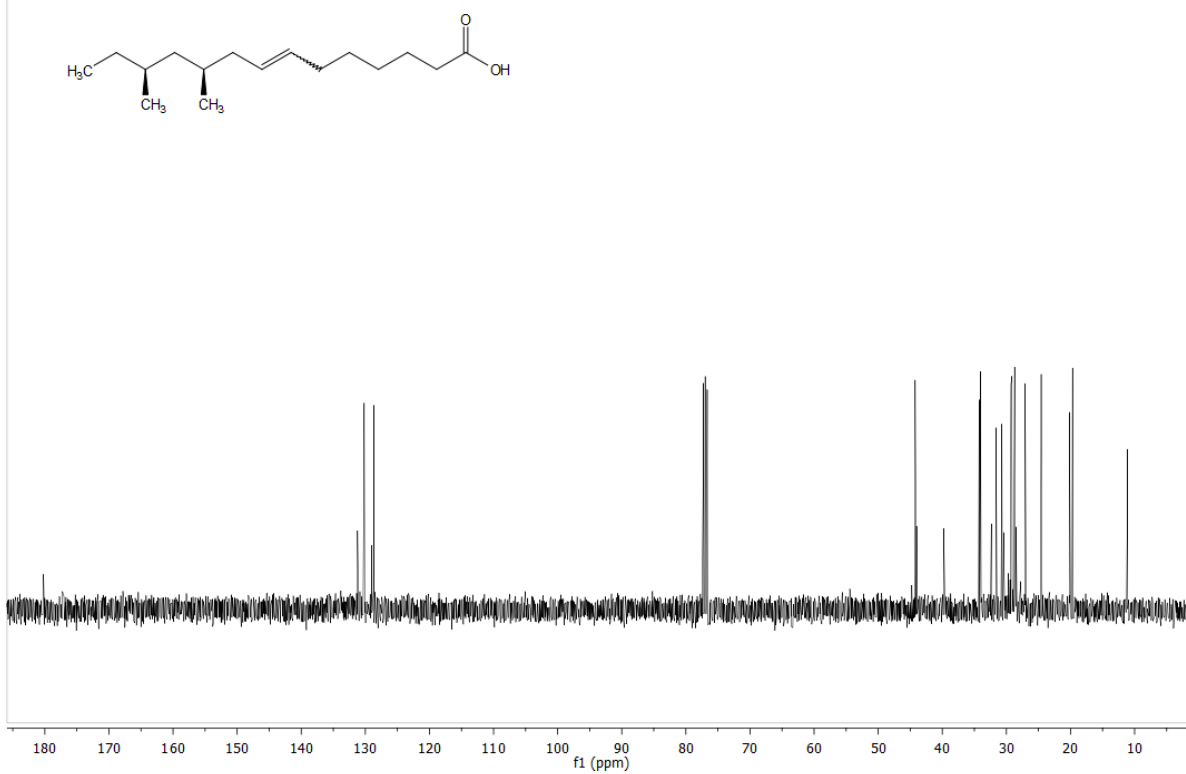
(3*S*,5*S*)-*S*-ethyl 3,5-dimethylheptanethioate (13)



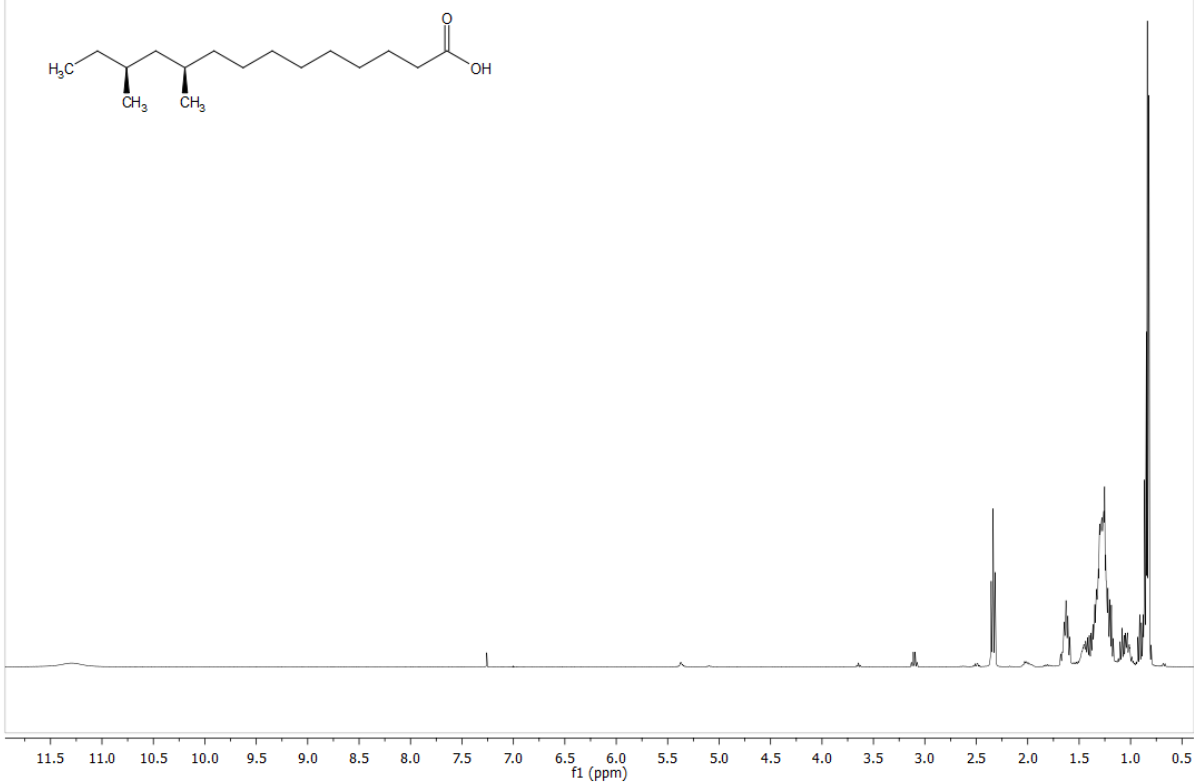
(10*S*,12*S*)-10,12-dimethyltetradec-7-enoic acid (14)



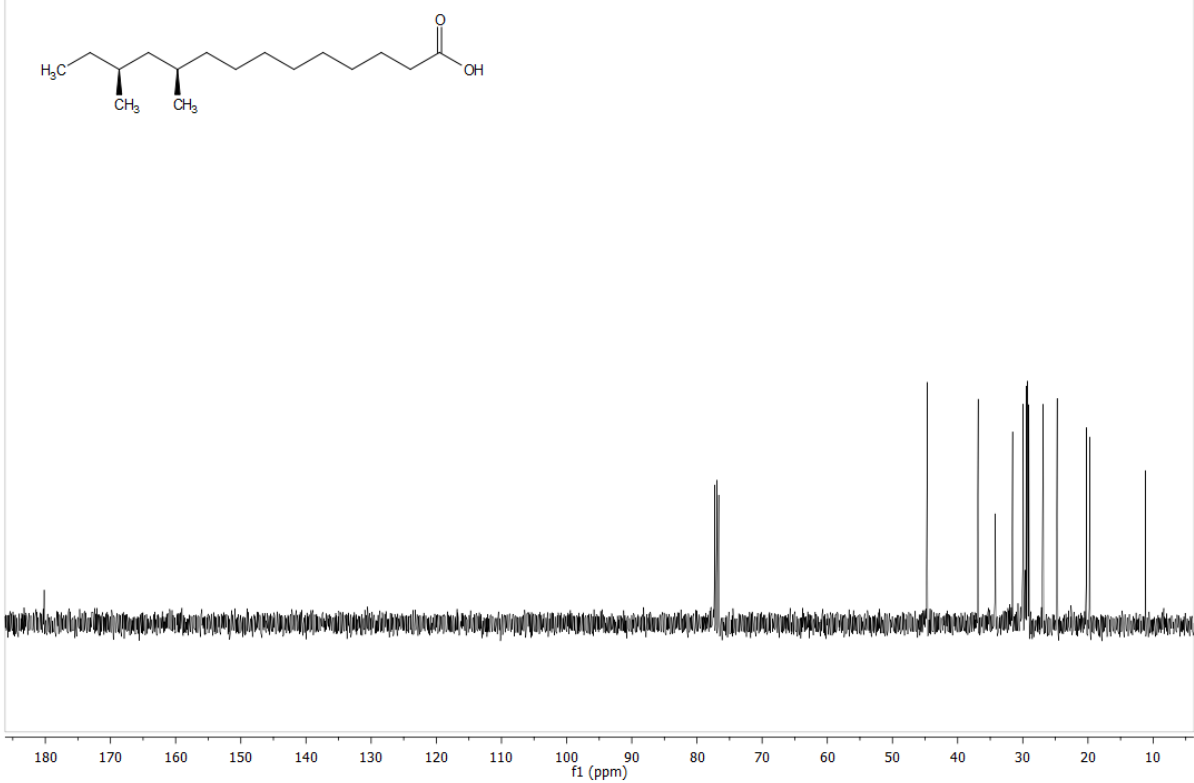
(10*S*,12*S*)-10,12-dimethyltetradec-7-enoic acid (14)



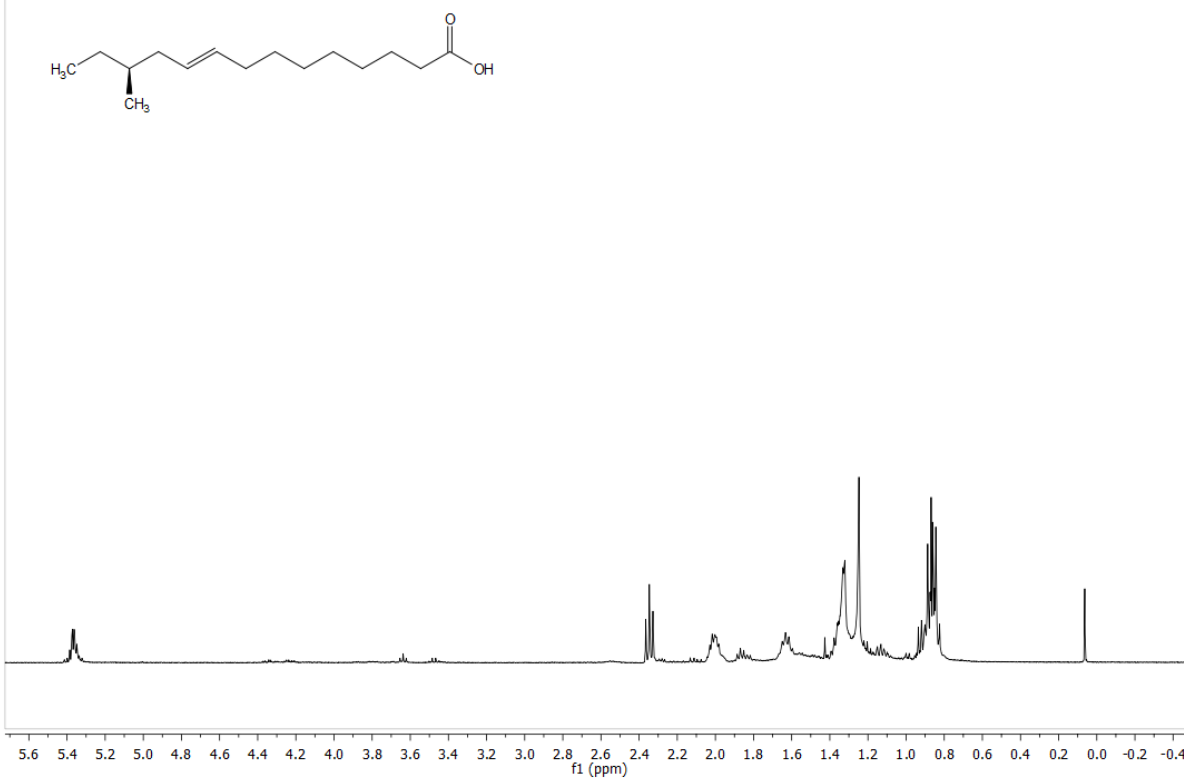
(10*R*,12*S*)-10,12-dimethyltridecanoic acid (**8**)



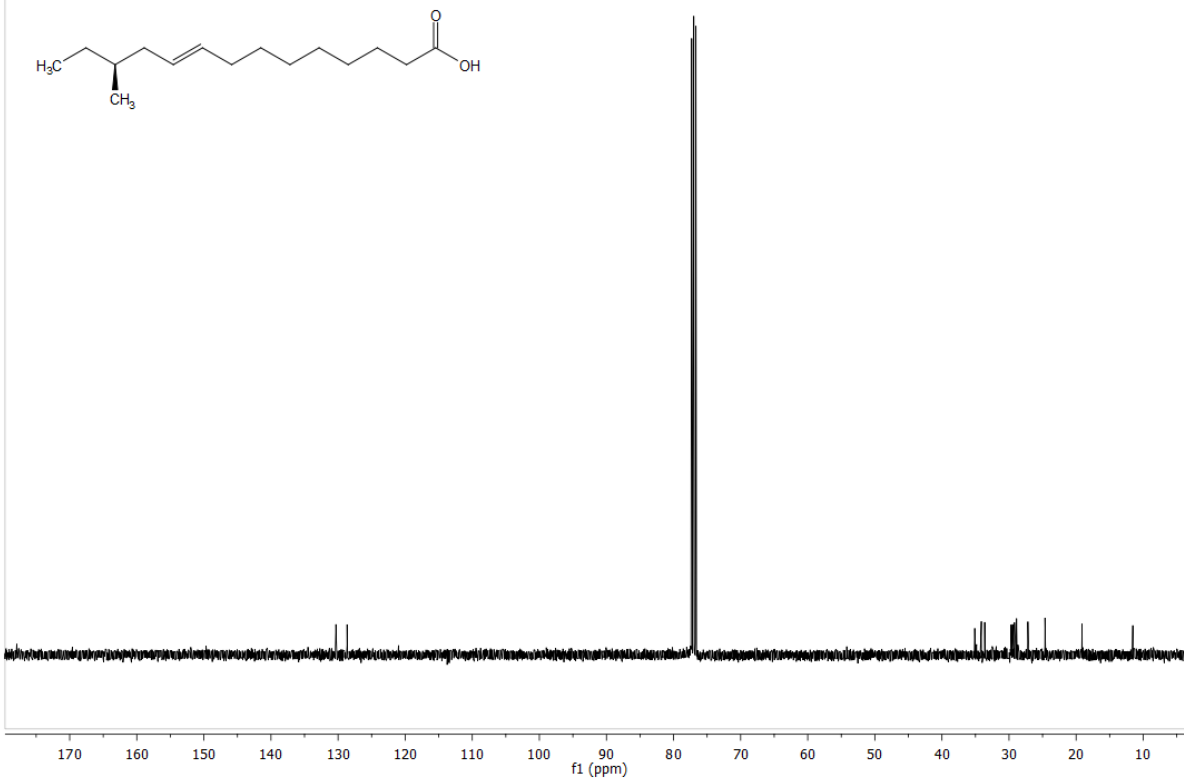
(10*R*,12*S*)-10,12-dimethyltridecanoic acid (**8**)

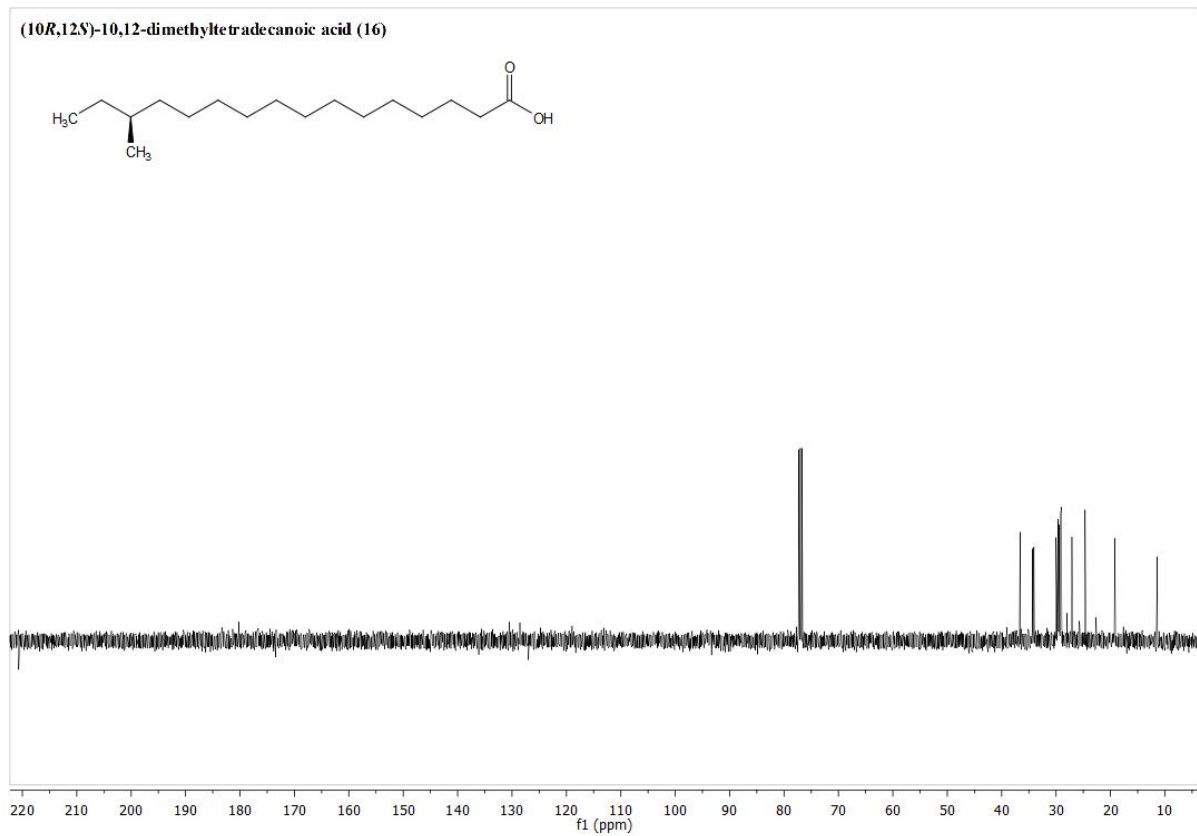
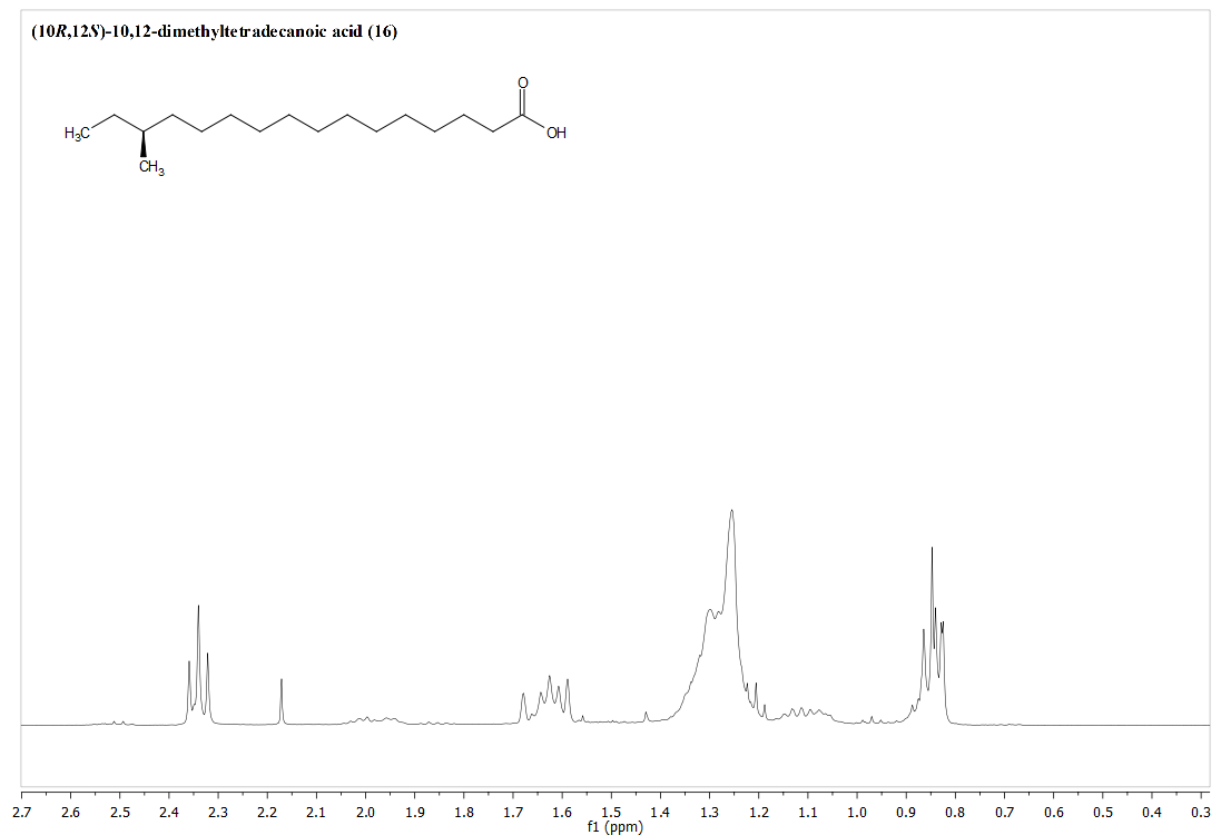


(S)-12-methyltetradec-9-enoic acid (15)

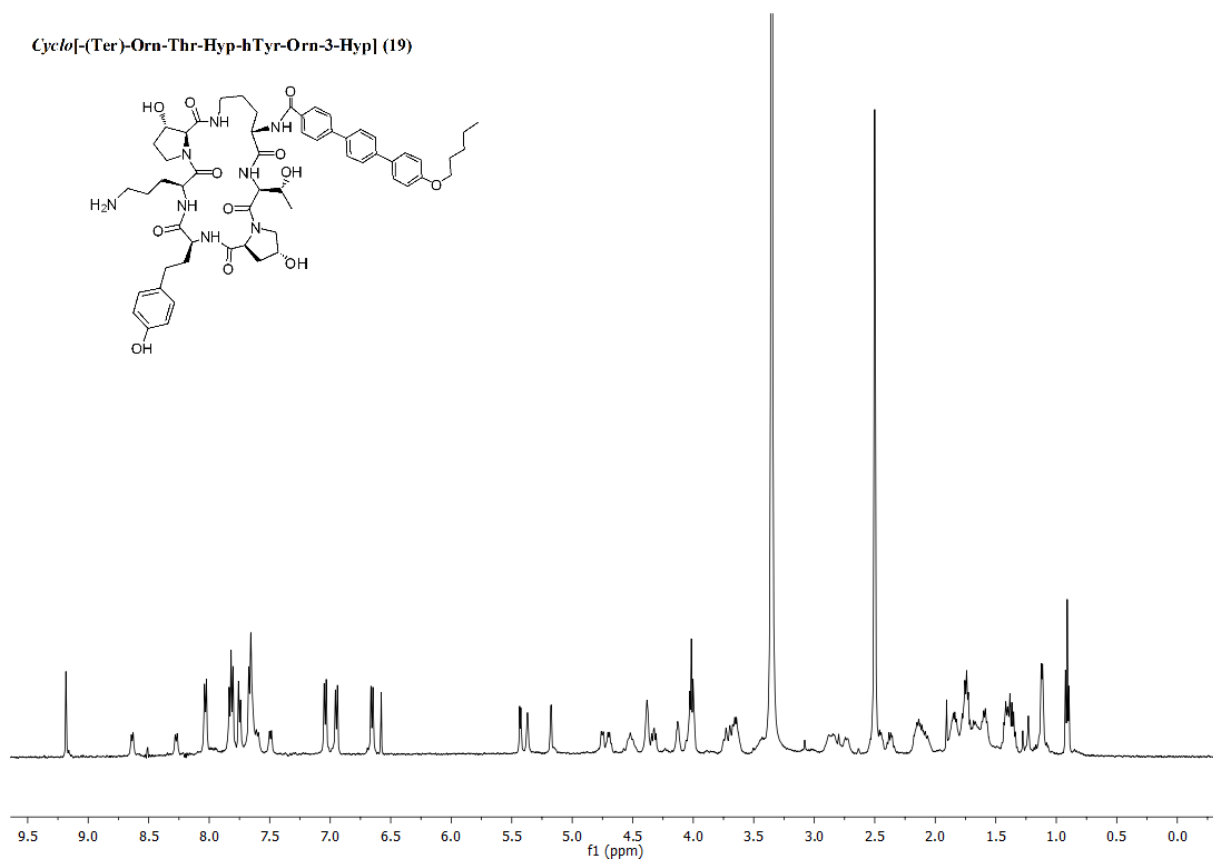


(S)-12-methyltetradec-9-enoic acid (15)

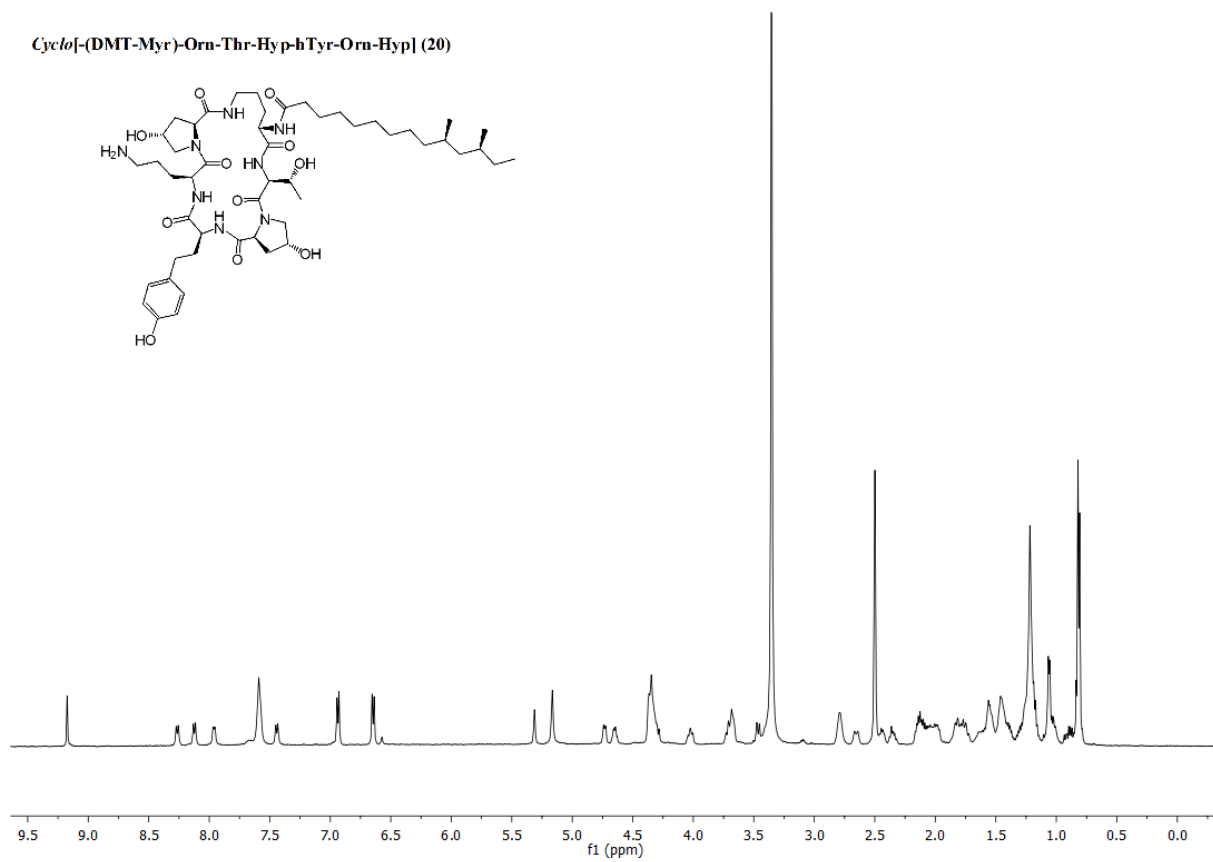




Cyclo[-(Ter)-Orn-Thr-Hyp-hTyr-Orn-3-Hyp] (19)



Cyclo[-(DMT-Myr)-Orn-Thr-Hyp-hTyr-Orn-Hyp] (20)



Cyclo-(Myr)-Orn-Thr-Hyp-hTyr-Orn-Hyp] (21)

