

Total Synthesis of Enantiopure all-*cis*-(2'*R*)-1-*O*-(2'-methoxy-4,7,10,13,16,19-docosahexaenyl)-*sn* -glycerol

Gudmundur G. Haraldsson, Carlos D. Magnusson, Einar Luthersson, Haraldur G. Gudmundsson and Gudmundur G. Haraldsson, Science Institute, University of Iceland, Dunhagi 3, 107 Reykjavík.

Ether lipids of the 1-*O*-alkyl-*sn*-glycerol type occur widely in Nature. They are particularly abundant in the liver oil of sharks and other elasmobranch fish. Such ether lipids have shown various beneficial effects on human health. Methoxylated alkylglycerols possess a methoxyl group located at the 2-position of the 1-*O*-alkyl chain and they constitute 0.3 – 4% of the total amount of the alkylglycerols in the liver oil of shark and related species. Methoxylated alkylglycerols have been reported to offer immune stimulating effects and anticarcinogenic properties. The chief objective of the work described was the first total synthesis of enantiopure all-*cis*-(2'*R*)-1-*O*-(2'-methoxy-4,7,10,13,16,19-docosahexaenyl)-*sn*-glycerol found in shark liver oil. This fascinating compound belongs to the methoxylated 1-*O*-alkyl-*sn*-glycerol type ether lipids. The alkyl chain is unusual in the sense that it is not only methoxylated at the 2-position, but highly polyunsaturated and possessing the omega-3 framework of double bonds identical to DHA, one of two of the most important omega-3 polyunsaturated fatty acids that are characteristic of marine fat. The multi-step total synthesis was executed by a highly convergent approach involving (*R*)-epichlorohydrin and (*R*)-solketal as chiral C₃-synthons and using repeated condensations of terminal acetylenes with propargyl halides in the presence of copper(I) iodide, sodium iodide and a carbonate base at room temperature to sort out the polyunsaturated methylene-interrupted all-*cis*-skipped polyene hydrocarbon chain.