Thematic Section: Preparative Research. **Full Paper**
Subsection: Organic Chemistry. *The Reference Object Identifier* – ROI: jbc-01/20-63-7-11
The Digital Object Identifier – DOI: 10.37952/ROI-jbc-01/20-63-7-11
Submitted on July 22, 2020.

Synthetic meroterpenoids based on terpene alcohols: synthesis, self-assembly, and membranotropic properties

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Keywords: terpenoids, meroterpenoids, archaeal lipids, aggregation, model membranes, dipalmitoylphosphatidylcholine.

Abstract

Currently, targeted drug delivery is of great interest in the field of medicine. The study of compounds capable of permeating cell membranes is a major problem in this area. The synthesis of pharmacologically active compounds includes the formation of structures with various combinations of pharmacophore fragments and properties. Amphiphilic compounds tend to exhibit membranotropic activity. From this point of view, the modification of natural products, especially terpenoids, is of particular interest. Terpenoid structures are used as membrane anchors in the development of modulators for membrane-integrated proteins or structures for creating nanocontainers. In this paper we synthesized a number of water-soluble amphiphilic meroterpenoids containing a charged pyridinium fragment on the basis of acyclic terpene alcohols. Residue of terpene alcohols – geraniol (monoterpenol), farnesol (sesquiterpenol), and phytol (diterpenol) – were used as the hydrophobic part of the amphiphilic structure. Linear acyclic alcohols are commercially available reagents and have a structure similar to that of polyprenols in archaeal lipids, which made it possible to obtain synthetic lipid-like meroterpenoids capable of self-assembly in aqueous solutions. The charged pyridinium fragment, which is included in numerous natural compounds, was of interest as a polar component. This meroterpenoids are synthetic analogs of archaeal lipids. It was shown that the studied meroterpenoids form nanosized aggregates in aqueous solutions by the method of dynamic light scattering and the Doppler microelectrophoresis method. Turbidimetric titration on model dipalmitoylphosphatidylcholine vesicles revealed that the synthesized compounds are embedded into the bilayer membrane without destroying it. Self-assembled aggregates of synthesized compounds in water can find application for drug delivery – in the creation of nanocontainers containing membrane anchors capable of interacting with the outer surface of the cell (lipid membrane).

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