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Thematic course: Synthesis, structure and properties of biologically active derivatives. Part 1.

Synthesis of some organosilicon derivatives of squalene

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Abstract

Acyclic triterpenoid squalene $C_{30}H_{50}$ is a biologically active natural compound that participates as a key precursor in the synthesis of very important regulatory compounds – steroids in humans and animals. Proceeding from this, synthetic squalene derivatives can exhibit antimetabolite activity against enzymes of the late stage of cholesterol biosynthesis: squalene synthase, squalene oxidase, and oxydosqualene cyclase, and can prove to be important drugs in the treatment of a number of pathologies that do not have deficiencies of acting preparations such as bisphosphonates. This work is devoted to the search for selective sterol synthesis inhibitors at later stages of their formation, which is a significant advantage compared to the widespread inhibitors of farnesyl pyrophosphate synthase (such as bisphosphonates). Hydrosilylation of squalene by a number of organochlorohydrosilanes R_3SiH (R_3 = Cl_3, $MeCl_2$, Me_2Ph) and a mixture of α- and β-isomers of adducts of vinyltrimethoxysilane to tetramethyl disiloxane: $HSi(Me_2)O(Me_2)Si$-$C(Me)$-$Si(OMe)_3$ and $HSi(Me_2)O(Me_2)Si$-$(CH_2)_2$-$Si(OMe)_3$ using a Carstedt catalyst. A detailed spectral study of a mixture of their α- and β-isomers, including with the use of NMR on ^{29}Si nuclei, is carried out. Various attempts to vary the conditions to react with squalene trichlorosilane was unsuccessful. The reaction with squalene and methyldichlorosilane, and triethylsilane did not observed. In other cases, accession is characterized by a lack of regioselectivity. It was found that hydrosilanes with chlorine atoms in silicon are not active in this reaction, and Me_2PhSiH is attached to squalene in a small yield. In contrast, the α- and β-addition adducts of vinyltrimethoxysilane to tetramethyldisiloxane (a mixture of these) are well attached to squalene.

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