CYCLIZATION OF CEMBRANE DITERPENOIDS.
V. SELECTIVITY OF THE FORMATION OF A PRODUCT OF THE CYCLIZATION OF CEMBRENE UNDER THE ACTION OF N-BROMOSUCCINIMIDE, AND THE CRYSTAL STRUCTURE OF THIS PRODUCT


Under the action of N-bromosuccinimide in aqueous acetone, cembrene has given a low yield of a cyclization product, the structure and stereochemistry of the molecule of which have been established by x-ray structural analysis. In contrast to the cyclization of cembrene under the action of formic acid, in the reaction under consideration a 1,5-hydride shift in the last stage dominates substantially over the splitting out of a proton from the methyl group at C-4.

N-Bromosuccinimide in aqueous acetone is an effective cyclizing agent for polyolefins and, in particular, for germacrane sesquiterpenoids [3], and humulene [4]. Its interaction with cembrene (I) leads to the dominant formation of bromohydrins — 5β-bromo derivatives of isocembrol and of 4-epioscembrol [5].

The TLC analysis of the reaction mixture obtained by the procedure described in [5] from cembrene and N-bromosuccinimide showed the presence in it of a substance giving a spot with a blue-violet coloration, which is not characteristic for cembranoids. This substance was isolated by chromatography; it crystallized well and had the empirical formula C₃₀H₃₂OBr₂ (mass spectrometry and elementary analysis). According to its IR spectrum, its molecule contained a hydroxy and an exomethylene group. According to x-ray structural analysis, the structure and accurate configuration of the molecule of the compound obtained is expressed by formula (II), all three carbon rings in the molecule having the chair form.

The conformation of the ring with the bromine atoms was retained in deuterochloroform solution. Thus, the SSCC values J₅,₄ = J₅,₆a = J₅,₆b = 2.3 Hz in the PMR spectrum show the actual position of the C(5)-Br bond, while the SSCC values J₇,₆a = 12.5 Hz and J₇,₆b = 4.0 Hz agree with the equatorial position of the bromine atom at C-7.

In the crystal, the molecules of (II) are linked by hydrogen bonds into tetramers. The lengths of the bonds are averaged for the four independent molecules composing the tetramer. The intermolecular contacts are the usual ones [6].

The positions of the bromine atoms in the (II) molecule and its absolute configuration permit us to describe the process in which the dibromoalcohol (II) is formed from cembrene by the following scheme

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One of the directions for the cyclization of cembrene under the action of HCOOH proceeds analogously, but in this case in the last stage two alternative processes are realized — a 1,5-hydride shift with the participation of the methine proton of the isopropyl group (as the conversion of (IV) into (II)) and the splitting out of a proton from the methyl group at C-4. They lead, respectively, to the formates of alcohols (V) and (VI) (12:47) and to the alcohols (V) and (VI), themselves (18:20) [7].

In our case it was not clear whether both processes took place or only the one with the 1,5-hydride shift. It was possible to answer this question by determining the presence or absence in the complex mixture of the products of the reaction of cembrene with N-bromosuccinimide of the 5,7-dibromo derivative of the alcohol (VI). To detect the latter we made use of the photoinitiation of the debromination of alkyl bromides by tri-n-butylstannane, under which conditions the dibromoalcohol (II) was converted completely into the alcohol (V) [7]. When this reaction was carried out with the initial mixture of the products of the reaction of cembrene with N-bromosuccinimide, we obtained (after chromatography) a fraction containing the chromatographically inseparable alcohols (V) and (VI), the ratio of which, according to GLC, was 49:1.

Thus, in contrast to the acid cyclization of cembrene [7], on its reaction with N-bromosuccinimide in aqueous acetone the 1,5-hydride shift in the intermediate cation (IV) predominates substantially over the splitting out of a proton from the Me-4 group which, is undoubtedly determined by the presence of an axial bromine atom at C-5 in the cation (IV).

EXPERIMENTAL

The instruments and conditions for chromatography have been described previously [7].

The Dibromoalcohol (II). By chromatographing the mixture of products obtained by the method of [5] from 14.00 g of cembrene and 11.0 g of N-bromosuccinimide we obtained 0.97 g of a fraction (the eluent being a 7:3 mixture of petroleum ether and diethyl ether) containing compound (II) (blue-violet spot on TLC, after spraying with conc. H$_2$SO$_4$ followed by keeping for 10-15 min). To eliminate impurities susceptible to acetylation, this fraction was treated with 5 ml of acetic an-