

CYCLIZATION OF SOME LINEAR TERPENOLS INITIATED BY "ACTIVATED" DMSO

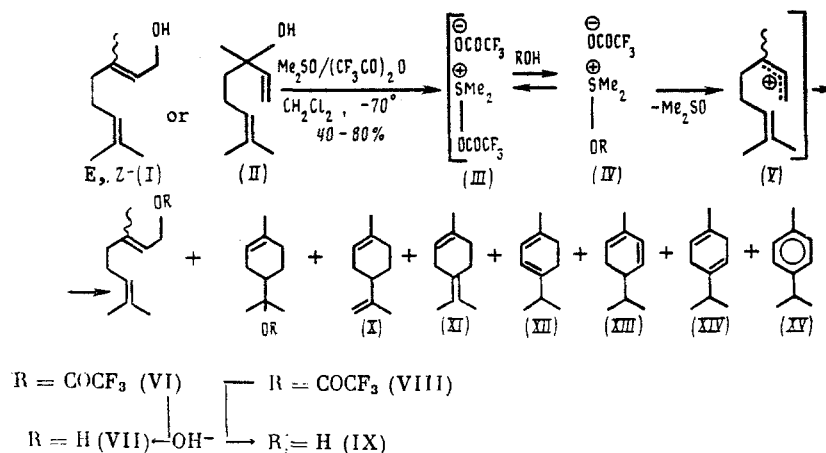
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It was shown that the acylhydroxysulfonium salt generated in situ from DMSO and trifluoroacetic anhydride causes low-temperature cyclization of geraniol, linalool, and nerol in an aprotic medium to a mixture of p-menthane monoterpenoids, and the maximum yield is obtained in the case of the last two terpenols. A similar result was obtained for E-nerolidol.

The biogenetically similar electrophilic cyclization of geraniol E-(I), nerol Z-(I), linalool (II), and a large number of their derivatives has been studied in great detail [1]. The data from a study of the solvolytic variant of conducting this reaction, believed to model processes in the living cell that result in the formation of monoterpenoids of the p-menthane series and some other isoprenoids, are very interesting [1-3]. The previously uninvestigated possibility of using the trifluoroacetoxysulfonium salt (III), easily generated from DMSO [4], and recently proposed for selective ω -functionalization of the acetates of these alcohols [5], is discussed from this point of view in the present study.

We found that low-temperature treatment of DMSO in CH_2Cl_2 medium with trifluoroacetic anhydride in the presence of ~1 mole equiv. of compounds (I) and (II) rapidly yields a mixture



of trifluoroacetates (VI) and (VIII) with a good yield, and they are easily saponified into the corresponding alcohols (VII) and (IX), together with p-menthane hydrocarbons (X)-(XV). The minimum relative concentration (<5%; GLC and PMR data) of linear ethers (VI) (E/Z \approx 3:2) is observed for linalool (II) and the maximum concentration (~30%) is obtained for geraniol E-(I). The total yield of cyclic products (VIII), (X)-(XV) from E-(I), II), and Z-(I) was, respectively, ~10, 60, and 65% with a significant (up to 40 rel. %) concentration of terpineol trifluoroacetate (VIII) in both cases. The relative concentration of individual hydrocarbons (X)-(XV) in the separated mixtures was determined by GLC using known samples of dipentene, terpinolene, α -terpinene, α -phellandrene, γ -terpinene, and p-cymene, respectively (Table 1).

The results can be completely explained based on transformation of the products of ligand exchange of the sulfonium cation (III) with alcohols (I) and (II), including the stage of

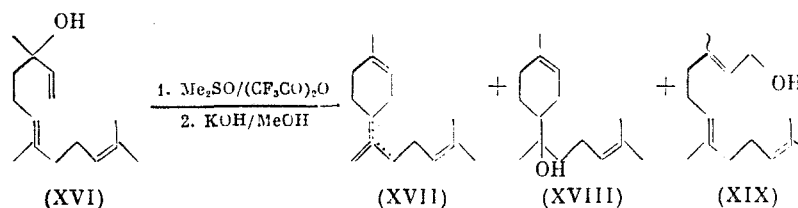
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TABLE 1. Relative Percentage Composition of Mixtures of p-Menthane Hydrocarbons (X)-(XV) in the Products of Electrophilic Cyclization of Monoterpenols (I) and (II)

Monoterpenol	(X)	(XI)	(XII)	(XIII)	(XIV)	(XV)
E-(I)	33	33	7	6	7	14
(II)	53	28	6	4	3	6
Z-(I)	70	23	2	5	Traces	Traces

heterolysis of the allyl C-O bond in intermediates (IV) and generation of carbocations (V). Stabilization of the latter by the external trifluoroacetate ion results in linear ethers (VI), while the intramolecular participation of the trisubstituted C=C bond yields the observed cyclic products (VIII), (X)-(XV).

Electrophilic cyclization of E- and Z-nerolidols under the conditions indicated above was a structurally unselective reaction. A mixture of substances in the ratio of (XVII)/(XVIII)/(XIX) \approx 2:2:1 was obtained with a yield of \sim 65% from E-isomer (XVI) after alkaline treatment of the reaction mixture and flash chromatography on SiO₂. This was established by comparing the high-resolution PMR spectral data found for the cyclic products with the published data for bisabolenes (XVII) and bisabolols (XVIII) [3, 6, 7] and by direct comparison with known samples of 3E/Z-farnesols (XIX) (E/Z \approx 3:2) by GLC.



In agreement with the available data on solvolysis of the derivatives of terpenols (I), (II), and (XVI) [1-3], the latter undergo soft, although uncontrollable, heterolysis of their C-O allyl bond under the effect of DMSO "activated" by trifluoroacetic anhydride with the formation of monocyclic products, and the maximum yield in the monoterpene series was determined for nerol Z-(I) and linalool (II).

EXPERIMENTAL

The PMR spectra were made on a Bruker WM-250 spectrometer in solutions of CDCl₃. The GLC analyses were conducted on a Biokhrom-1 chromatograph with a glass capillary column, $l = 5$ m, XE-60.

Cyclization of Monoterpenols (I) and (II). Here 6.3 g (30 mmoles) of (CF₃CO)₂O was added to a solution of 3.08 g (20 mmoles) of linalool (II) and 2 g (26 mmoles) of DMSO in 30 ml of CH₂Cl₂, mixed at -70°C (Ar), over 5 min. The reaction mixture was diluted by three times with ether after 20 min, then evaporated in a vacuum, and the residue (3.6 g) was chromatographed on 150 g of SiO₂. Elution with hexane yielded 0.71 g (27%) of hydrocarbons (X)-(XV) (Table 1) in the form of a light-yellow liquid, R_f 0.69 (Silufol, hexane), and 1.95 g (39%) of a mixture of ethers (VIII)/(VI) \approx 95:5 (GLC, PMR data) in the form of a colorless liquid, bp $69-71^{\circ}\text{C}$ (2 mm), n_D^{20} 1.4211.

For (VIII), PMR spectrum (δ , ppm): 1.55 s, 1.57 s, and 1.66 br.s (9H, CH₃), 1.6-2.1 m (7H, CH, CH₂), 5.37 m (1H, HC=C).

A solution of 1.43 g of sample (VIII) indicated above in 30 ml of 5% KOH in MeOH was held for 30 min at $\sim 25^{\circ}\text{C}$ then neutralized with 5% H₂SO₄, the solvent was eliminated in a vacuum, and the residue (1.2 g) was chromatographed on 50 g of SiO₂. Elution with a hexane-ether mixture (4:1) yielded 0.75 g (85%) terpeneol (IX), bp $77-78^{\circ}\text{C}$ (2 mm), n_D^{20} 1.4819 (cf. [6]). PMR spectrum (δ , ppm): 1.13 s, 1.15 s, and 1.62 br.s (9H, CH₃), 1.4-2.1 m (7H, CH, CH₂), 5.35 m (1H, HC=C).

As described for (II), 0.48 g (36%) of a mixture of hydrocarbons (X)-(XV) (Table 1) and 1.08 g (43%) of a mixture of trifluoroacetates (VIII)/(VI) \approx 2:1 (GLC, PMR data), was

obtained from 1.54 g (10 mmoles) of nerol Z-(I), 1 g (13 mmoles) of DMSO, and 3.15 g (15 mmoles) of $(\text{CF}_3\text{CO})_2\text{O}$ in 15 ml of CH_2Cl_2 .

Analogously, 80 mg (2%) of a mixture of hydrocarbons (X)-(XV) (Table 1) and 2.92 g (39%) of a mixture of trifluoroacetates (VIII)/(VI) \approx 1:3 (GLC, PMR data) was obtained from 4.62 g (30 mmoles) of geraniol E-(I), 3 g (39 mmoles) of DMSO, and 9.45 g (45 mmoles) of $(\text{CF}_3\text{CO})_2\text{O}$ in 45 ml of CH_2Cl_2 .

Cyclization of Sesquiterpenol (XVI). As described for (II), 1.15 g of oily product was obtained from 1.55 g (7 mmoles) of (XVI), 0.7 g (9 mmoles) of DMSO, and 2.1 g (10 mmoles) of $(\text{CF}_3\text{CO})_2\text{O}$ in 15 ml of CH_2Cl_2 and a solution of the product in 30 ml of 5% KOH in MeOH was held for 30 min at -25°C . Then 0.95 g of a mixture of substances was separated by the usual treatment of the reaction mixture and chromatographed on 70 g of SiO_2 . Gradient elution from hexane to ether (up to 30% of the latter) yielded, in the order of elution, 0.42 g (29%) of bisabolenes (XVII), bp $60-64^\circ\text{C}$ (0.04 mm), n_D^{20} 1.4962 (cf. [3, 6, 7]), 0.32 g (24%) of bisabolols (XVIII), bp $118-119^\circ\text{C}$ (2 mm), n_D^{20} 1.4977 (cf. [6]), and 0.17 g (11%) of farnesols (XIX).

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