SUPERACID CYCLIZATION OF 13E,17E- AND 13E,17Z-BICYCLOGERANYLFARNESOLS AND THEIR ACETATES – AN EFFECTIVE STRUCTURALLY SELECTIVE STEREOSPECIFIC ROUTE TO SCALARANE SESTERTERPENOIDS

P. F. Vlad, N. D. Ungur, and Nguyen Van Hung

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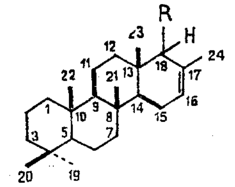
Scalaranes are sesterterpenoids with the carbon skeleton (I). The synthesis of two compounds of this series (II and III) have been described [1]. They were obtained by the cyclization of the bicyclic precursors (IV) and (V) with tin tetrachloride in benzene. However, the yields of substance (II) and (III) were low (25 and 18%), and their isolation was associated with certain experimental difficulties.

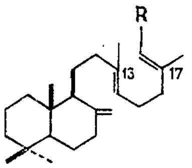
We have investigated the cyclization of 13E,17E- and 13E,17Z-dicyclogeranylfarnesols (VI and VII) and their acetates (VIII and IX) by fluorosulfonic acid, which has proved to be an effective cyclizing agent for sesqui- and diterpenoids [2, 3]. The alcohols (VI) and (VII) were synthesized from the ketone (X) [1]. Its interaction with triethyl phosphonoacetate gave a mixture (3:1) of the esters (XI) and (XII) (~78%). They were separated by chromatography on a column of silica gel and were reduced with $LiAlH_3(OC_2H_5)$ to the alcohols (VI) (91%) and (VII) (88%), which were acetylated with acetic anhydride in pyridine to the esters (VIII) (92%) and (IX) (93%).

When the alcohol (VI) was treated with fluorosulfonic acid in 2-nitropropane (substrate: FSO_3H ratio ~1:25; concentration of substrate 0.15 M and of cyclizing agent 2.14 M; –(80-85)°C, 1.5 h; NEt_3 was added to the reaction mixture and it was then worked up in the usual way), and the reaction product was chromatographed on a column of silica gel, a hydrocarbon fraction (6%) and the tetracyclic alcohol (XIII) (57.6%) were isolated [1]. Under the same conditions, the cis-alcohol (VII) gave the tetracyclic alcohol (XIV) (55%) [1] and 11.5% of hydrocarbons.

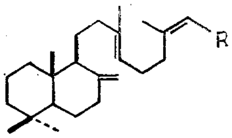
The cyclization of the trans-acetate (VIII) under the conditions described above led to the hydroxy acetate (XV) [mp 203-205°C (from petroleum ether); $[\alpha]_D^{20}$ –1.6° (c 2.9; $CHCl_3$); yield 60.5%], and that of the cis-acetate (IX) to the diastereomeric hydroxy acetate (XVI) [viscous colorless liquid, $[\alpha]_D^{20}$ –32.4° (c 4.7; $CHCl_3$); yield 56%]. In addition to these compounds, as in the cyclization of the alcohols, small amounts of hydrocabrons were formed, in yields of 7.3 and 10%, respectively. The residue of cyclization products after the isolation of the substances mentioned above consisted of polymeric material in all cases.



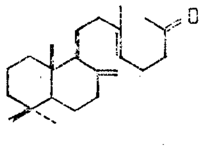
I. R=CH_3; dihydro
II. R=CO_2CH_3; 18αH
III. R=CO_2CH_3; 18βH
XIII. R=CH_2OH; 18αH
XIV. R=CH_2OH; 18βH



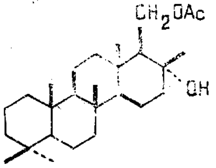
IV. R=CO_2CH_3
VI. R=CH_2OH
VIII. R=CH_2OAc
XI. R=CO_2Et



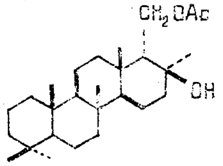
V. R=CO_2CH_3
VII. R=CH_2OH
IX. R=CH_2OAc
XII. R=CO_2Et



X



XV



XVI

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The structures and stereochemistries of the compounds synthesized were shown on the basis of spectral features and by a comparison of their physicochemical and spectral characteristics with those given in the literature [1].

Thus, fluorosulfonic acid in 2-nitropropane is an effective reagent for the structurally selective stereospecific cyclization of 13E,17E- and 13E,17Z-bicyclogeranylfarnesols and their acetates into tetracyclic compounds of the scalarane series.

LITERATURE CITED

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2. P. F. Vlad, N. D. Ungur, and V. B. Perutskii, Khim. Prir. Soedin., 793 (1986).
3. P. F. Vlad, N. D. Ungur, and V. B. Perutskii, Khim. Prir. Soedin., 514 (1986).

STRUCTURALLY SELECTIVE STEREOSPECIFIC CYCLIZATION OF E,E,E,E-GERANYLFARNESOL AND ITS ACETATE BY FLUOROSULFONIC ACID

P. F. Vlad, N. D. Ungur, and
Nguyen Van Hung

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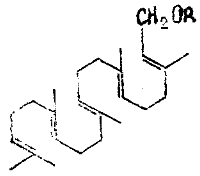
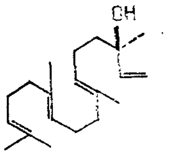
We have shown previously for the case of sesqui- and diterpenes that fluorosulfonic acid is an effective cyclizing agent, ensuring the structurally selective stereospecific occurrence of the reaction [1, 2]. It appeared of interest to investigate the interaction of fluorosulfonic acid with E,E,E,E-geranylfarnesol (I) and its acetate (II), since, in the first place, the cyclization of acyclic sesterterpenoids has not yet been studied at all and, in the second place, the result of the reaction should be the formation of tetracyclic hydrocarbon systems which it has not yet been possible to obtain in satisfactory yields by the cyclization of aliphatic compounds without the introduction into the molecules of the latter of additional structural fragments arranged in a definite way which stabilize the carbocations arising during the reaction [3].

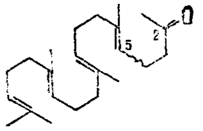
Compounds (I) and (II) were synthesized from E,E-geranyllinalool (III). The latter on interaction with acetoacetic ester by the Carrol reaction gave a mixture (~3:1) of the ketones (IV) and (V) (85%), which was separated by column chromatography on silica gel. The E,E,E-geranylgeranylacetyl (IV) was converted by the Wittig–Horner reaction with triethyl phosphonoacetate into a mixture (9:1) of the esters (VI) and (VII) (~70%). Reduction of the first of them with lithium ethoxytrihydroaluminate led to the alcohol (I) (93%), which was acetylated with acetic anhydride in pyridine to the acetate (II) (~92%).



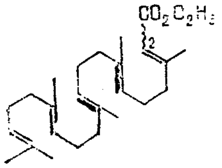
I. R = H
II. R = Ac



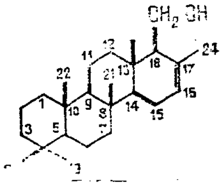
III



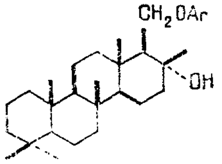
IV. 5E
V. 5Z



VI. 2E
VII. 2Z



VIII



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