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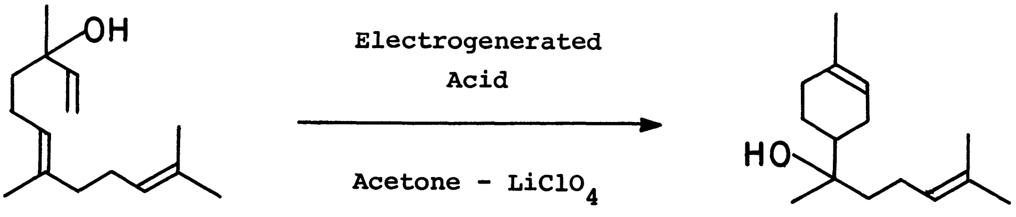
AN ELECTROCHEMICAL METHOD SPECIFICALLY DIRECTED TO THE PREPARATION OF DL-BISABOLOL FROM DL-NEROLIDOL

Kenji UNEYAMA, Yosinori MASATSUGU, Takesi UEDA, and Sigeru TORII*
Department of Industrial Chemistry, School of Engineering,
Okayama University, Okayama 700

A product-selective electrosynthesis of dl-bisabolol from dl-nerolidol was accomplished by a constant current electrolysis in commercial acetone containing a small amount of $LiClO_4$

In spite of many efforts to realize an effective transformation of dl-nerolidol 2 into dl-bisabolol 1, an important fragrant constituent, no successful procedure for the preparation of 1 from 2 has appeared. Most of the acid-catalyzed cyclization so far studied by the use of HCO_2H in pentane,1) $AlCl_3$ in ether,1) 2-fluorobenzothiazolium salt in CH_2Cl_2,2) $KHSO_4$,3) and BF_3 etherate in $CH_2Cl_2$4) resulted in the predominant formation of bisabolenes 3 and cedrenes rather than bisabolol 1. The best result so far known in literatures was achieved by the action of 100% HCO_2H, where 1 was obtained in 32% yield after 100% conversion and alkaline hydrolysis along with polyenes (19%) and diols (25%).5) Apparently these results suggest that deprotonation from bisabolyl cation 4 rather than internal return of hydroxy group to 4 would proceed preferentially and/or bisabolol 1 would be unstable in the reaction conditions employed. Therefore, an adequate solvent-acid-catalyst system should be chosen so as to realize a selective transformation of 2 into 1. Here, we describe an electrochemical procedure specifically directed to the preferential preparation of 1 from 2 which is characterized by generation of an electrogenerated acid in situ in a neutral solvent-electrolyte system at room temperature.



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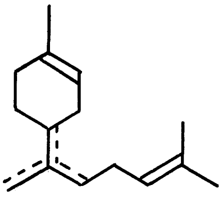
A typical electrolysis is as follows; A mixture of 2 (222 mg, 1 mmol), $LiClO_4$ (10 mg, 0.1 mmol) in commercial acetone6) (8 ml) was electrolyzed under a constant current (10 mA for 1 h, 0.36 Faradays/mol) using platinum foil electrodes (2 x 1.5 cm^2) in an undivided cell and the mixture was stirred at ca. 25-30 °C for 2 h, affording 1 (52%) as a diastereomeric mixture (1:1) and 3 (25%) as a mixture of α-, β-, and γ-isomers. While, the reaction of 2 with perchloric acid in acetone at 30°C gave **1** (23%) and **3** (54%), demonstrating the efficiency of the electrolysis method.

The effect of solvents is remarkable. Acetone is an excellent solvent for the selective preparation of **1** presumably because it traps bisabolyl cation **4** leading to **5** [R; $CH_2CH_2CH=C(CH_3)_2$] which would be hydrolyzed to give **1**.[7] On the other hand, the use of THF (60 °C) and $ClCH_2CH_2Cl$-THF (9:1 at 50 °C)[8] promoted dehydration exclusively leading to the formation of **3** (72% and 66%), respectively. The use of MeOH and MeCN gave complex mixtures from which neither **1** nor **3** was detected after 1.5 Faradays/mol of electricity was passed. The yield of bisabolenes **3** in the present electrolysis is satisfactory as compared with those obtained by BF_3 etherate in CH_2Cl_2(trace),[4] HCO_2H in pentane (59%),[1] 2-fluorobenzothiazolium salt in CH_2Cl_2 (72%),[2] and $KHSO_4$ by thermolysis (18%).[3]

Metal perchlorates are essential to induce the transformation (**2** → **1**). Sodium, lithium, and magnesium perchlorates provided **1** in satisfactory yields (49% for Na, 52% for Li, and 39% for Mg). However, other conventional electrolytes such as Et_4NOTs, Et_4NBr, and Et_4NClO_4 were found to be useless. The increase of the reaction temperature enhanced the rate and affected the preferential formation of bisabolenes:[**1**(%), **3**(%), °C; 52%, 25% at 30 °C; 32%, 52% at 40 °C; 20%, 63% at 50 °C]. Electrolysis of an aprotic solution containing metal perchlorates generates a strong acid.[7,9] The electrogenerated acid-catalysis in commercial acetone is so effective for carbon-hydroxy bond breaking and reforming sequence as shown in the cyclization (**2** → **1**) that it seems applicable for the biogenetic type cyclization of various polyisoprenols which is under active investigation.



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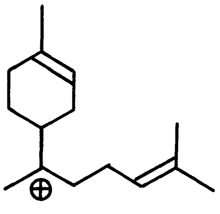

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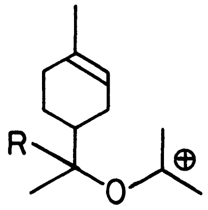

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6) The use of the distilled acetone resulted in lower yield of **1** (35%).

7) To our knowledge this work is the first case which demonstrates acetone to be a useful solvent for the acid-catalyzed cyclization of terpenoids. Tertiary carbenium ion can be trapped with acetone in the acid-catalyzed acetonidation. K. Uneyama, A. Isimura, K. Fujii, and S. Torii, Tetrahedron Lett., 1983, 2857.

8) Because of the low solubility of $LiClO_4$ in $ClCH_2CH_2Cl$ 10% of THF was mixed.

9) S. Torii and T. Inokuchi, Chem. Lett., 1983, 1349.

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