STEREOCHEMICAL ENZYMATIC SYNTHESIS OF MENTHYL ESTERS

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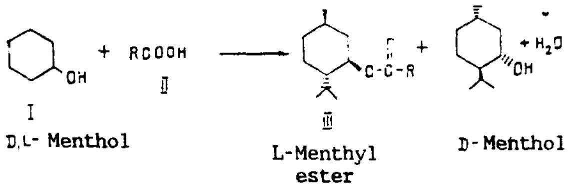
The synthesis of menthyl esters by hydrolytic enzymes such as lipase is very important from the industrial point of view. Thus, one of the most important intermediates in the synthesis of Validol is menthyl isovalerate. Moreover, the stereospecific synthesis of menthyl esters from D,L-menthol and fatty acids followed by the hydrolysis of these esters to L-menthol will enable the L- isomer to be obtained from the industrially produced synthetic D,L-menthol in place of plant raw material.

It is known [1, 2] that lipase are capable of catalyzing synthetic reactions under certain conditions. However, relatively few investigations of the stereospecific synthesis of menthyl esters have been performed at the present time [3, 4].

We have investigated the possibility of synthesizing the L-menthyl ester (III) from D,L-menthol (I) and a fatty acid (II, R = alkyl) using industrial lipase preparations — lipolaktin G10x and lipoorizin G3x, obtained from the fungi Oospora lactis and Aspergillus oryzae (lipase 1 and lipase 2, respectively).

The synthesis was carried out by the following scheme:



It was established that a definite difference exists in the synthetic activities of the two enzyme preparations. The highest synthetic capacity was observed for lipase 1, having a temperature optimum for its action of 37-40°C, the percentage conversion amounting to 47-54% as compared with 21-30% in the case of lipase 2 (with a temperature optimum for its action of 30-35°C).

In addition, lipase 1 possessed a higher stereospecificity (Table 1). The rate of synthesis of the L-menthyl esters for lipase 1 was approximately 12 times that for lipase 2. A doubling of the concentration of the enzyme increased the yield of menthyl ester by a factor of 1.5.

TABLE 1. Influence of the Stereospecificity of the Lipases on the Synthesis of Menthyl Esters

Enzyme	Experimental conditions	Menthol	Conversion, %
Lipase 1 (150 units/mg), 120 mg	Temperature 38°C, (±)-menthol, 0.6 M; caproic acid, 0.6 M; isooctane	30 ml L D,L	65 45
Lipase 2 (380 units/ml), 120 mg	Temperature 35°C, (±)-menthol, 0.6 M; caproic acid, 0.6 M; isooctane	30 ml L D,L	5.0 3,6

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Both for lipase 1 and for lipase 2 the greatest affinity was shown for fatty acids of medium chain length. An increase in the length of the acyl donor led to a rise in the percentage conversion from 26% for butyric acid to 54% for caprolic acid. The physicochemical characteristics of the menthyl esters synthesized agreed with those given in the literature.

Thus, the investigations performed have shown that D,L-menthol can be esterified by lipase 1 under the optimum conditions if a suitable acyl donor is selected.

LITERATURE CITED

1. S. Okumura, M. Iwai, and Y. Tsujisaka, Biochim. Biophys. Acta, 575, 156-165 (1979).
2. C. Marlot, G. Langrand, C. Triantaphylides, and I. Baratti, Biotechnol. Lett., 9, 647-650 (1985).
3. G. Langrand, I. Baratti, G. Buono, and C. Triantaphylides, Tetrahedron Lett., 27, 29-32 (1986).
4. S. Koshiro, K. Sonomoto, A. Tanaka, and S. Fukui, J. Biotechnology, 2, 47-57 (1985).

CHEMICAL COMPOSITION OF THE RHIZOMES WITH ROOTS OF VALERIANA WOLGENSIS FROM THE VALERIANA OFFICINALIS GROUP

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The quantitative level and qualitative composition of the essential oil and valepotriates [the main pharmacologically active substances in ecotypes (species) of *V. officinalis* L. *s. l.*] vary considerably. In view of this, we have studied the component composition of the essential oil and the valepotriates of the rhizomes with roots of the Volga valerian *V. wolgensis* Kazak. (= *V. nitida* Kreyer) cultivated in the sovkhozes [collective farms] of Lekrasprom [All-Union Combine for the Production, Collection, and Processing of Medicinal PLants, USSR Ministry of the Medical Industry].

ℓ,α-Pinene, ℓ-camphene, cadinene, and esters of borneol with isovaleric acid and with other acids have been isolated from this essential oil previously [1]. The component composition of the valepotriates had not been studied.

By the steam-distillation method, 97 ml of essential oil was obtained from the rhizomes with roots of Volga valerian grown in 1988 in the Voronezhskii sovkhoz (yield 0.61%). The following were isolated by column chromatography and also by preparative TLC on neutral alumina (activity grade III) and type L silica gel and were identified (from their IR, mass, and PMR spectra): ,α-pinene, terpinolene, fenchene, camphene, alloaromadendrene, β-bisabolene, ar-curcumene, valerenal, valeranone, valerenic acid, (−)-pacifigorgiol, fauronyl acetate, kessanyl acetate, and a previously undescribed sesquiterpene alcohol in the form of a viscous liquid, $C_{15}H_{24}O_4$, which we have called valerol. IR spectrum, ν_{max} (cm^{-1}): 3400-3370 (OH); 3070 and 1640 (C=C); 890 (CH_2=C). The UV spectrum gave no indication of the presence of a conjugated system of double bonds.

On the addition of bromine to a chloroform solution of valerol a deep blue coloration arose, which indicated the presence of an azulene skeleton, while the number of carbon atoms (C_{15}) in the valerol molecule showed that it contained a guaiane skeleton.

It followed from the ^{1}H NMR spectrum that the valerol molecule includes an isopropyl group (d, 6 H; 1.02 ppm); a methyl and a hydroxy group on the same carbon atom (s, 3 H; 1.28 ppm); an exocyclic double bond (two br.s, 2 H; 4.7-4.9 ppm) and a double bond in a ring (br.s, 1 H, 5.6 ppm).

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