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LETTERS TO THE EDITOR

HYDROXYLATION OF THE DOUBLE BOND IN 1-BENZYL-3-METHYL-Δ^3-PIPERIDINE BY MYCELIUM FUNGI

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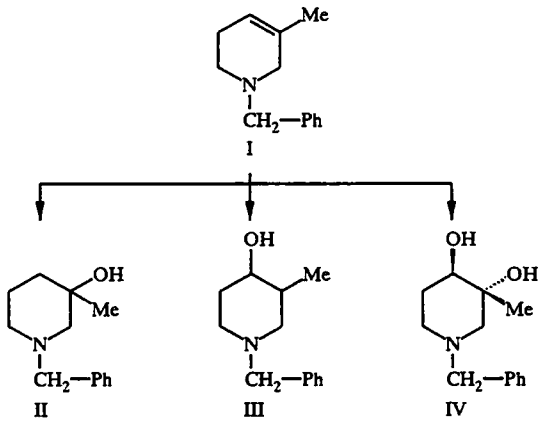
Chiral polyhydroxypiperidine derivatives have recently attracted attention due to the anticancer and antiviral properties displayed by some of these compounds [1-3]. However, the enantioselective synthesis of such compounds is difficult and laborious [4]. On the other hand, the microbiological oxidation of organic compounds, in particular, nitrogen heterocycles, proceeds, as a rule, with regio- and enantioselectivity [5-8].

We have studied the microbiological oxidation of 1-benzyl-3-methyl-Δ^3-piperidine (I) by mycelium fungi.

Of the five strains of *Aspergillus niger*, two strains of *Beauveria bassiana*, *Rizopus oryzae* VKPM F-431, *Penicillium simplicissimum* KM-16, and *Cunninghamella verticillata* VKPM F-430, the latter fungus proved the most active [9]. The transformation was carried out in a growing cell culture of these fungus strains at pH 5.0 according to our previous procedure [10]. The concentration of substrate for the transformation was 100 mg/liter. The transformation products were extracted thrice with chloroform from the culture liquid at pH 10.0. The chloroform extracts were evaporated to dryness and the residue was dissolved in a small amount of methanol and analyzed on an HP-5890 Series II GC/MS with HP 5972 mass-selective detector equipped with a 30 m × 0.2 mm quartz capillary column packed with HP-5MS as the stationary phase. Temperature programming was carried out at from 70 to 250°C at 30°C/min.



II : III : IV = 1 : 2 : 16

The GC/MS analysis of the culture liquid showed the presence of the following transformation products (see scheme). The retention time and mass spectrum are given for each product. The *m/z* values are given for the major ions along with the relative intensities and formation pathway or ion composition in parentheses. Starting piperidine I: 7.05 min; 187 (67) (M), 186 (20) (M-H), 172 (43) (M-CH_3), 110 (5) (M-C_6H_5), 96 (9) (M-C_7H_7), 91 (100) (C_7H_7). 1-Benzyl-3-hydroxy-3-methylpiperidine (II): 7.71 min, 205 (5) (M), 204 (9) (M-H), 148 (7) (M-C_3H_4OH), 134 (16) (M-C_4H_6OH), 128 (71) (M-C_6H_5), 114 (9) (M-C_7H_7), 91 (100) (C_7H_7). 1-Benzyl-4-hydroxy-3-methylpiperidine (III): 7.78 min, 205 (26) (M),

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204 (19) (M-H), 188 (5) (M-OH), 160 (5) (M-C_2H_4OH), 146 (12) (M-C_3H_6OH), 134 (5) (M-C_4H_6OH), 128 (15) (M-C_6H_5), 114 (28) (M-C_7H_7), 91 (100) (C_7H_7). 1-Benzyl-*trans*-3,4-dihydroxy-3-methylpiperidine (IV): 8.22 min, 221 (16) (M), 204 (9) (M-OH), 203 (3) (M-H_2O), 188 (5) (M-H_2O-CH_3), 186 (4) (M-OH−H_2O), 146 (7) (M-$C_3H_7O_2$), 144 (4) (M-C_6H_5), 134 (34) (M-$C_4H_7O_2$), 130 (14) (M-C_7H_7), 112 (9) (M-H_2O−C_7H_7), 91 (100) (C_7H_7). The ratio of areas of the chromatographic peaks I:II:III:IV was 2:1:2:16, which indicates high regioselectivity of the transformation, i.e., predominant dihydroxylation of the double bond. The 3-epoxide may be an intermediate in this reaction. Comparison of the chromatographic and mass spectral parameters of diol II with the corresponding data of an authentic sample with *trans* configuration indicated that they were identical. These results indicate the feasibility of a preparative synthesis of products of the microbiological hydroxylation of piperidines.

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