Reduction of 2-benzylideneindane-1,3-dione (II) by Tetrahydropyridine (V). A 0.04 ml portion of concentrated HCl is added to a solution of 0.12 g (500 mmoles) of compound II and 0.17 g (500 mmoles) of compound V in 10 ml of 80% ethanol, and the mixture is boiled for 20 h. The reaction mixture is diluted with water and extracted by chloroform (2 x 30 ml). The chloroform extract is dried and evaporated. According to the data of liquid chromatography (Zorbah SIL; ethyl acetate–hexane, 35:15), the residue contains 49% of 2-benzylindane-1,3-dione III.

**LITERATURE CITED**


**1,2,5-TRIMETHYL-4-(p-HYDROXYARYL)-Δ³-TETRAHYDROPYRIDINES AND THEIR SPATIAL STRUCTURE**

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The condensation of 1,2,5-trimethylpiperidine-4-one with phenol and isomeric cresols yields 1,2,5-trimethyl-4-(p-hydroxyphenyl)- and (p-hydroxytolyl)-Δ³-tetrahydropyridines, the structure and conformation of which have been studied by proton NMR spectroscopy.

The condensation of γ-piperidones with phenol (cresols) is of interest for the preparation of piperidine derivatives containing hydroxyphenyl groups in the γ-position. Compounds of this type are examined for their physiological activity [1].

We have studied the compounds formed by condensation of 1,2,5-trimethylpiperidine-4-one (I) with phenol and isomeric cresols in the presence of boron trifluoride etherate. In all cases, the compounds obtained were dehydration products of 1,2,5-trimethyl-4-(p-hydroxyaryl)piperidine-4-ones.
The structure and stereochemistry of the substituted tetrahydropyridines obtained were established by examination of the proton NMR spectra (Tables 1 and 2).

It follows from these results that in all cases Δ³-tetrahydropyridines are formed, not the Δ⁴-isomers as would be expected. This can be unambiguously deduced, for example, from the fact that the methylene protons at the α-carbon atom of the tetrahydropyridine ring have as a neighbor the 5-H methylene proton with which vicinal spin-spin coupling is observed (Table 2). Taking into account the fact that the initial piperidone (I) is a mixture of trans- and cis-isomers, according to the position of the methyl groups, with a considerable predominance of the first [2], the formation of isomers of the tetrahydropyridines would be expected. However, only in the case of the condensation of the piperidone (I) with phenol was the separation accomplished, with the aid of column chromatography, into the individual isomers, precominantly the trans-2,5-isomer IIa with very small amounts of the cis-2,5-isomer IIb. Examination of the spin-spin coupling constants JHH (Table 2) enables one also to determine the preferred conformation of these configurational isomers. In the case of the trans-isomers of IIa, III, and IV this is semi-chair, with equatorial orientation of the 2- and 5-methyl substituents, and in the case of the cis-isomer of IIb, semi-chair with 2e,5a-orientation of these substituents:

\[ \text{IIa, III, IV} \]

\[ \text{IIb} \]

Change in the orientation of the 5-methyl substituent on transition from the trans-isomers IIa, III, and IV to the cis-isomer IIb can be traced in terms of the values of the two vicinal spin-spin coupling constants of the protons on C(5) and C(6) (Table 2). Thus, in the trans-isomers the large value of one of these constants (9-10 Hz) points to trans-biaxial orientation, and the value of the second constant (5.5 Hz) could be ascribed to gauche interaction which in the aggregate supports the equatorial orientation of the 5-methyl group. The small value of one of these constants in the cis-isomer (2.5 Hz) can be explained only by gauche-biequatorial orientation of the corresponding protons, which have between them a dihedral angle close to 90° and this also leads to a minimal value of the vicinal spin-spin coupling constant according to the Karplus relationship [3]. The value of the second of these constants in the cis-isomer (4.2 Hz, Table 2) is such that one can assign it to the gauche-interaction \(^3\)J_{ae} whence the axial orientation of the 5-methyl substituent in the cis-isomer IIb can be unequivocally deduced.

It is interesting to note that change in the orientation of the methyl substituent from equatorial to axial on transition from isomer IIa to IIb leads to deshielding of its protons, in contrast to a saturated six-membered ring, which can be explained by the vicinity of the \(\pi\)-electron system of the double bond. The exceptionally large values of the long-range spin-spin coupling constants — homoallylic \(^5\)J_{1,3} = 2.5–3, and \(^4\)J_{5,3} = 1.5–1.7 Hz (Table 2) — are characteristic for the spatial structure of the trans-isomers and result from the effect of \(\pi\) overlap [4] with axial orientation of the interacting protons in the vicinity of the