REARRANGEMENT OF 1-ACETYLINDOXYL OXIME INTO 1-ACETYL-2-ACETOXY-3-IMINOINDOLINE HYDROSULFATE

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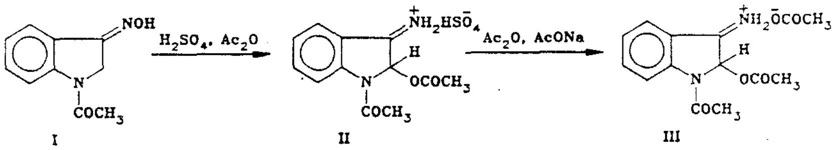
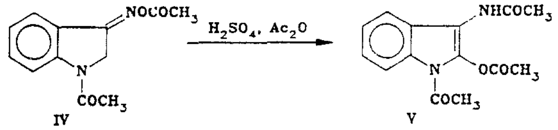
1-Acetyl-2-acetoxy-3-iminoindoline hydrosulfate was obtained by rearrangement of 1-acetylindoxyl oxime by the action of concentrated H_2SO_4. The hydrolysis and oxidative dimerization reactions of the above iminoindoline hydrosulfate were investigated.

It was previously shown that the rearrangement of 1-acetylindoxyl oxime (I) by the action of acetic acid in the presence of acetic anhydride results in 1-acetyl-2-acetoxy-3-acetylaminoindole (V) [1]. Methods of synthesis of 2-acetoxy derivatives of indole with the amino group at the 3-position have until now not been described.

In the present work, a preparative method is described for the synthesis of 1-acetyl-2-acetoxy-3-iminoindoline hydrosulfate (II), which is of interest for the preparation of 3-aminoindole and indolin-3-one derivatives. According to the method proposed by us, iminoindoline hydrosulfate II is formed by treatment of oxime I with concentrated H_2SO_4 in acetic anhydride.



It should be noted that oxime I undergoes rearrangement into 3-iminoindoline hydrosulfate II in an acylating medium without acylation of the amino group. On the contrary, from O-acetyl derivative of oxime IV, 3-acetylaminoindole V is formed under these conditions



Hydrosulfate II decomposes in air, but in vacuo over P_4O_{10} it is preserved for 5 to 7 days. The more stable acetate III was obtained from hydrosulfate II by the action of sodium acetate in acetic anhydride, and did not change in air for one to two days. In the PMR spectrum of acetate III, a singlet signal of the 2-H proton is observed at 7.07 ppm, which is characteristic for the indoline form.

In the IR spectra of salts II and III, the absorption bands of the $COCH_3$ and $OCOCH_3$ appear at 1710 and 1665 cm^{-1}. The system of bands at 2700-2500 cm^{-1} indicates the presence of the $=\overset{+}{N}H_2$ group.

Salts II and III are readily soluble in water, but in aqueous solutions they rapidly hydrolyze to 1-acetyl-2-acetoxyindolin-3-one (VI). On heating in acetic anhydride, salts II and III undergo an oxidative dimerization with the formation of dihydroxyindole VII.

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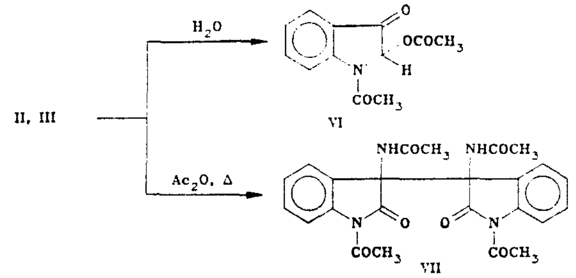
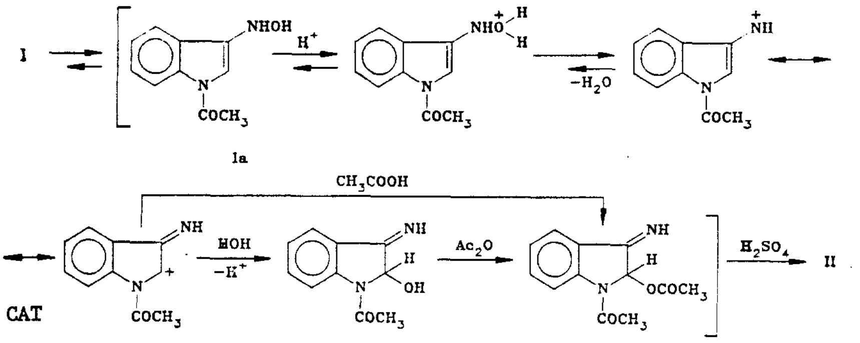


In the mass spectrum of dihydroxyindole VII, a peak of molecular ion is observed, the m/z of which corresponds to the molecular weight of this compound. Three absorption bands are observed at 1745, 1720, 1675 cm^{-1} in the IR spectrum, corresponding to six symmetric in pairs C=O groups, as well as the absorption bands of the NH groups at 3360 and 3380 cm^{-1}.

In the proton-coupled ^{13}C NMR spectrum (in DMSO), the following are observed: a quartet of methyl group carbon atoms at 26.4 and 21.9 ppm; a singlet of quaternary sp^3-hybridized carbon atoms at 62.9 ppm; signals of twelve phenyl ring carbon atoms (eight of these tertiary at 129.6; 124.7; 122.2; 114.9 and four quaternary at 123.4 and 139.6 ppm); a quartet, a multiplet and a doublet at 169.4 (J = 7 Hz); 169.7, 173.3 ppm (J = 3 Hz) of the C atoms of the C=O groups in the $1\text{-}COCH_3$, $3\text{-}NHCOCH_3$ substituents, and the 2-position, respectively. The multiplicity of the two last signals is explained by the interaction with the $3\text{-}NHCOCH_3$ group protons.

We are of the opinion that oxime I converts into hydrosulfate II according to the Bamberger type of rearrangement of aryl-hydroxylamines into aminophenols. The transformation here under consideration also includes the stage of isomerization of oxime I into hydroxylamine Ia. The $OCOCH_3$ group is introduced into the 2-position of the molecule of 3-iminoindoline or by a direct interaction of the cation "CAT" with the CH_3COO^- ion, or by the O-acylation of the intermediate 1-acetyl-2-hydroxy-3-iminoindoline.



EXPERIMENTAL

The IR spectra of the compounds were run on a Perkin-Elmer spectrophotometer (in mineral oil), the UV spectra on a Perkin-Elmer 575 spectrophotometer (in ethanol), and the mass spectra on a Varian MAT-112 mass spectrometer (GFR) (70 eV) by the method of a direct introduction of the sample into the ionic source. The temperature of the ionization chamber was 180°C. The PMR spectra of the compounds were recorded on a Varian XL-200 spectrometer, using TMS as internal standard. The course of the reaction and the purity of the compounds were monitored by TLC on a Silufol UV-253 plate in ethyl acetate. The development was carried out in UV light.

The elemental analysis data for C, H, and N corresponded to the calculated values.

1-Acetyl-2-acetoxy-3-iminoindoline hydrosulfate (II). A 0.6 ml portion (12 mmoles) of concentrated H_2SO_4 was added dropwise, with stirring and cooling to 10-15°C to a suspension of 1.9 g (10 mmoles) of oxime I in 50 ml of acetic anhydride. The precipitate formed was filtered off, washed with acetic anhydride and ether. Yield, 3.2 g (97%), mp 170°C (dec.). IR spectrum: 1700, 1660 (2 CO), 2700-2500 cm^{-1} ($=\overset{+}{N}H_2$).

1-Acetyl-2-acetoxy-3-iminoindoline Acetate (III). A 2 ml portion of acetic anhydride was added to a mixture of 0.65 g (2 mmoles) of hydrosulfate II and 0.3 g (3 mmoles) of sodium acetate, and the mixture was stirred for 2 h at 20°C. The precipitate that separated out was filtered off, washed with acetic anhydride and ether. Yield, 0.76 g (92%), mp 210°C (dec.). IR spectrum: 1710, 1660 (2 CO), 2700-2500 cm^{-1} ($=\overset{+}{N}H_2$). PMR spectrum (DMSO-D_6): 1.96 (3H, s, $COCH_3$), 2.32 (3H, s, $OCOCH_3$); 7.07 (1H, s, 2-H); 7.12-8.06 ppm (4H, m, arom. protons).

1-Acetyl-2-acetoxy-3-acetylaminoindole (V). A 0.45 ml portion (8.6 mmoles) of concentrated H_2SO_4 was added at 20°C with stirring to a suspension of 3 g (13 mmoles) of acetyloxime IV in 40 ml of acetic anhydride. The precipitate that separated out after 2 h was filtered off and washed with acetic anhydride and ether. Yield, 1.9 g (55%), mp 160-161°C (from methanol). A mixed melting point with a sample obtained by the method described in [1] showed no depression. The IR, UV, and PMR spectra of these compounds are identical.

1-Acetyl-2-acetoxyindolin-3-one (VI, $C_{12}H_{11}NO_4$). A 21 mmole portion of hydrosulfate II or acetate III was introduced at 18-20°C with stirring to 200 ml of water (in the case of compound III, the solution formed was acidified by concentrated HCl). The mixture was stirred for 1.5 h, the precipitate was filtered off, washed with water and ethanol. Yield 48% (in the case of compound III 0.06%), mp 113-114°C (from 2-propanol). IR spectrum: 1760, 1730, 1685 cm^{-1} (CO). UV spectrum, λ_{max} (log ε): 205 (3.97), 238 (4.42), 263 (3.96), 340 nm (3.48). PMR spectrum ($CDCl_3$): 2.21 (3H, s, $OCOCH_3$); 2.31 (3H, s, $NCOCH_3$); 6.37 (1H, s, 2-H); 8.44 (1H, d, 7-H); 7.25, 7.69 (2H, t, 5,6-H), 7.74 ppm (1H, d, 4-H). M^+ 233.

1,1'-Diacetyl-3,3'-diacetylaminodihydroxyindole (VII, $C_{24}H_{22}N_4O_6$). A mixture of 10 mmoles of hydrosulfate II or acetate III in 10 ml of acetic anhydride was heated with stirring to the boiling point. The solution was then cooled and poured into water. After 1-2 h, the precipitate was filtered off and washed with alcohol and ether. The yield of compound VII was 10-12%, mp 245-246°C (dec., from alcohol). IR spectrum: 3360, 3380 (NH), 1745, 1720, 1675 cm^{-1} (CO). UV spectrum, λ_{max} (log ε): 210 (4.17), 230 nm (3.93) sh. PMR spectrum (DMSO-D_6): 2.79 (6H, s, 1,1'-$COCH_3$); 2.09 (6H, s, 3,3'-$NCOCH_3$); 8.02 (2H, s, 3,3'-NH); 7.85 (2H, d, 7,7'-H); 6.80-7.20 ppm (6H, m, arom. protons). M^+ 462.

LITERATURE CITED

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