SYNTHESIS OF 6-AZAOXINDOLE AND ITS DERIVATIVES

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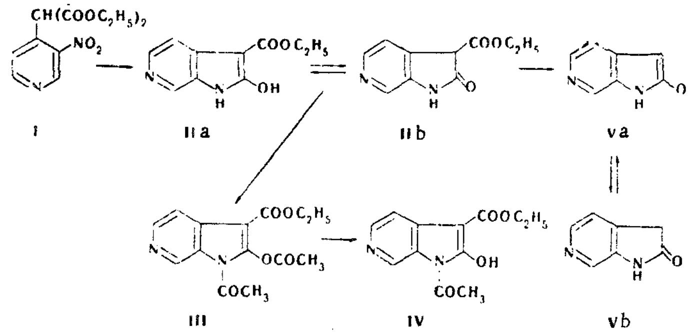
We have developed a method for the synthesis of the previously unknown 6-azaoxindole and its derivatives via the scheme



The basis of the synthesis is the reductive cyclization of 3-nitro-4-pyridylmalonic ester (I) [1], which we isolated from the products of the reaction of 3-nitro-4-chloropyridine with disodiomalonic ester in the form of the crystalline hydrochloride with mp 125-126° (from alcohol). The hydrochloride is readily hydrolyzed, and base I can be extracted with ether from its aqueous solution without alkalization in practically quantitative yield. 3-Ethoxycarbonyl-6-azaoxindole (II) [mp 299-300° (dec.)] was obtained in quantitative yield (9.8 g) in the hydrogenation of 13.4 g of base I in 400 ml of alcohol with 10 g of 5% Pd/C at room temperature. Compound II (according to its IR and PMR spectra) apparently exists in two tautomeric forms (IIa and IIb), and the equilibrium is shifted markedly to favor the 2-hydroxy form (IIa). When 0.2 g of II was refluxed with 1 ml of acetic anhydride for 6 h and the mixture was cooled, 0.24 g (85%) of the O,N-diacetyl derivative (III), with mp 300-301° (dec.), crystallized out. IR spectrum: 1740 and 1640 cm^{-1}. PMR spectrum (d_6-dimethyl sulfoxide): 1.28 (t), 4.2 (q), 2.61 (s), and 2.76 (s) ppm, and the signals of three aromatic protons at 7.50-8.45 ppm. Mono-N-acetyl derivative IV, with mp 315-317° (dec.), was formed in high yield when diacetate III was heated with water or phenylhydrazine. IR spectrum: 1695 and 1625 cm^{-1}. PMR spectrum: 1.28 (t), 4.16 (q), and 2.64 (s) ppm and aromatic protons at 7.47-8.64 ppm. Both acyl groups in diacetate III were saponified when it was heated with dilute acids and alkalis for 30 min; the product was II. Under more severe conditions, (refluxing for 5 h, 1.6 g of II with 15 ml of 18% hydrochloric acid), III underwent saponification and decarboxylation. The reaction products were evaporated to dryness, treated with 0.57 g of $NaHCO_3$ in 5 ml of water, and extracted with butanol to give 0.9 g (83%) of 6-azaoxindole (V) with mp 231-232° (dec., from alcohol) as colorless slightly yellowish crystals. IR spectrum: 1660 cm^{-1}. PMR spectrum: doublets (4-H and 5-H) at 6.67, 7.30, 7.35, and 8.15 ppm; singlets (7-H) at 7.37 and 8.10 ppm and 10.15 and 10.59 (NH) ppm; and singlet at 5.02 ppm. On the basis of the spectral data, V exists in the form of a mixture of commensurable amounts of the hydroxy (Va) and oxo (Vb) forms. A more detailed examination of the tautomerism of II, IV, and V will be the subject of future studies.

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COMPLEXES OF AZOLES WITH ACETYLACETONATES

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A number of the most important inorganic biological systems are coordination adducts formed as a result of the axial addition of azoles to chelates of the transition metals [1].

We have synthesized adducts by heating solutions of azoles (L), acetylacetone (A), and metal (nickel, cobalt, and vanadyl) chlorides in methanol or an aqueous methanol mixture with the addition of NH_4OH up to pH ~ 7-8. According to the results of elementary analysis, the adducts of the nickel and cobalt acetylacetonates have the $MA_2 \cdot 2L$ composition, as compared with the $MA_2 \cdot L$ composition in the case of vanadyl chloride, regardless of the basicity of the azoles and steric factors. The following imidazoles were used: imidazole, N-ethylbenzimidazole, benzimidazole, 3,5-dimethylpyrazole, and benzotriazole (the pK values range from 7.02 to 1.60).

A systematic increase in most of the frequencies of the deformation vibrations of the coordinated donors as compared with the free azoles is observed in the IR spectra of mineral oil suspensions of the adducts, and this constitutes evidence [2] for localization of the coordinate bond on a nitrogen atom of the pyridine type. The frequencies increase regularly in the order $Co < Ni < VO$, and this is associated with an increase in the stability of the adducts in the same order. The decreases in the $\nu_{C=O}$ bands of the acetylacetonates (~20 cm^{-1}) upon adduct formation are independent of the nature of the metal and the azole ring. The basicity and the volume of the heterocyclic fragment have little effect on the decrease in the frequency of the vibrations of the vanadyl group ($\Delta \nu = 50\text{-}70$ cm^{-1}) during complexing.

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