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RING CONTRACTION OF A 3-HYDROXY-1-PYRAZOLINE DERIVATIVE TO A CYCLOPROPANOL DERIVATIVE*

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The recent publication of several communications regarding the preparation and properties of a 3-hydroxy-1-pyrazoline (1) and other cyclic and acyclic α-hydroxyalkyldiazenes (2) prompts us to report the preparation of a new group of compounds (V) containing a 3-hydroxy-1-pyrazoline structure which, unlike the 3-hydroxy-1-pyrazoline previously described, readily lose nitrogen with ring contraction to yield products (VII) incorporating a cyclopropanol structure.

Hydrazine reacted at 0° in ethanol with 4-benzylidene-2,3-dioxopyrrolidines (I) to yield adducts to which the 5-substituted-6a-hydroxy-6-oxo-3-aryloctahydropyrrolo[3,4-c] pyrazole structure (II) has been assigned. These compounds appear to be the first in which a 3-hydroxypyrazolidine structure has been sufficiently stable to permit characterization. Spectroscopic and analytical data were consistent only with structure II among the reasonable possibilities for these hydrazine adducts; their ultraviolet spectra showed only the absorption of an alkyl-substituted phenyl group, the infrared spectra indicated the presence of NH and/or OH groups but the absence of a ketonic carbonyl, and the n.m.r. spectra revealed the presence of the system of four coupled protons represented by Ha, Hb, Hc and Hd in

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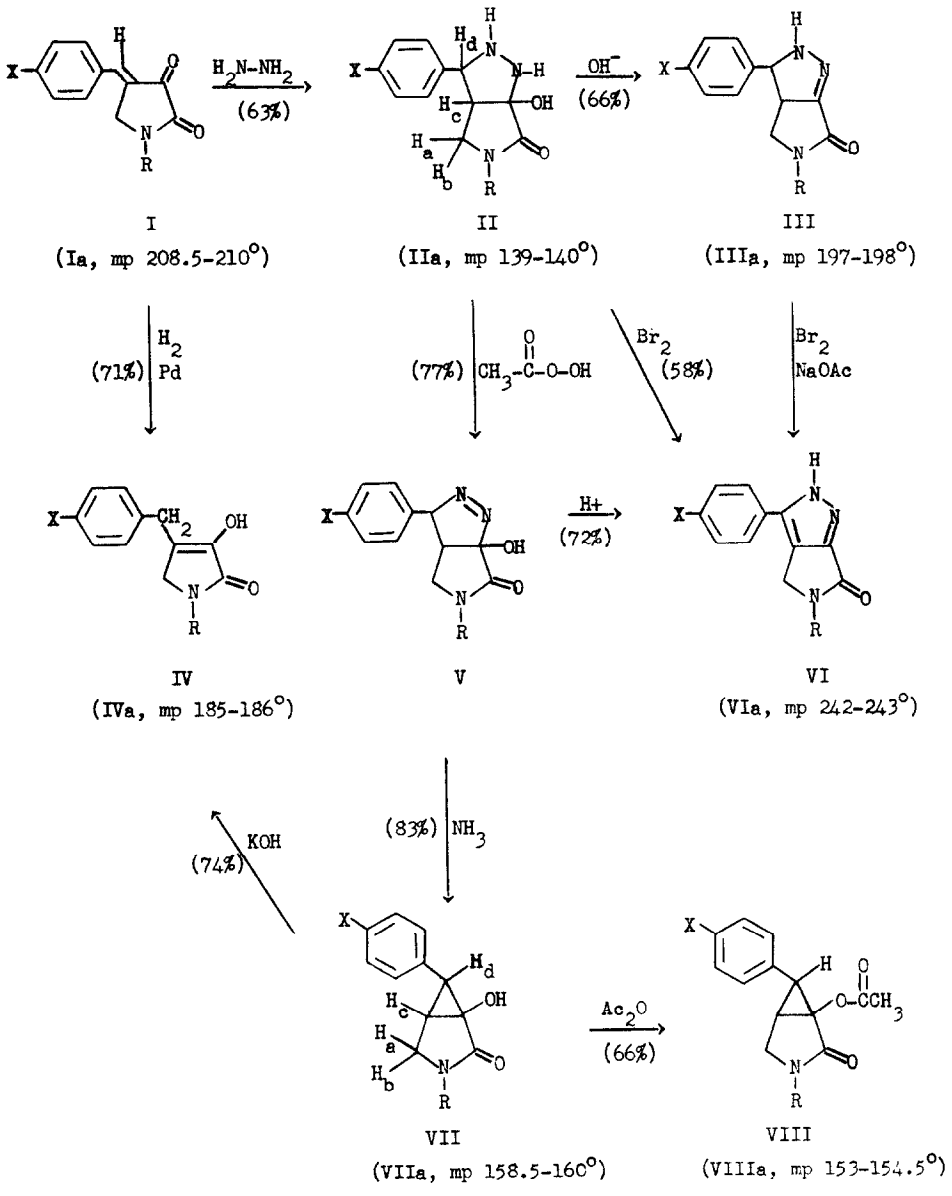
‡Results taken in part from the Ph.D. Thesis of John G. O'Connor, May, 1969 and from the Ph.D. Thesis of James E. Klijanowicz, 1970 (in preparation).

Chart I



I
(Ia, mp 208.5-210°)

II
(IIa, mp 139-140°)

III
(IIIa, mp 197-198°)

IV
(IVa, mp 185-186°)

V

VI
(VIa, mp 242-243°)

VII
(VIIa, mp 158.5-160°)

VIII
(VIIIa, mp 153-154.5°)

formula II. (Figure 1b gives this portion of a spectrum taken in $CDCl_3$.) The transformations shown in Chart I also supported structure II for the hydrazine adducts. Melting points and yields quoted in Chart I, and n.m.r. spectra shown in Figure 1 are for the compound IIa and products derived from it (IIIa, etc.), in which R = tert-butyl and X = H, but a number of other compounds of each type were made and characterized by similar spectral data as well as correct elemental analyses.

Oxidation of the adducts II with 40% peracetic acid in carbon tetrachloride produced the 5-substituted-6a-hydroxy-6-oxo-3-phenyl-3,3a,4,5,6,6a-hexahydropyrrolo[3,4-c]pyrazoles (V) (R = methyl, tert-butyl, cyclo-C_6H_{11}, or β-phenylethyl, X = H). These products were crystalline compounds which could be purified by rapid recrystallization from ethanol containing a trace of acetic acid. The presence of the cis-azo linkage in these compounds was shown by infrared absorption at 6.45 μ (3) and ultraviolet absorption at 342 mμ (ε = 274 for Va). The conclusion that the substances were 3-hydroxy-1-pyrazoline derivatives was supported by their ready conversion upon treatment with hydrogen chloride to the pyrazole derivatives VI.

The 3-hydroxy-3,5,5-trimethylpyrazoline described by Freeman and Rothjen (1) was remarkably stable under alkaline conditions, and the open chain tert-butyl-α-hydroxyalkyldiazenes of Hünig and Büttner (2a) merely dissociated in alkaline media to a small extent reversibly to tert-butyldiazene and a carbonyl compound. However, the compounds of type V, when treated with weak bases such as ammonia in ether at room temperature or below, or even when dissolved in the aprotic dipolar solvent dimethylsulfoxide, underwent rapid decomposition with evolution of nitrogen and the formation of 3-substituted-6-phenyl-1-hydroxy-2-oxo-3-azabicyclo[3.1.0]hexanes (VII). Heating in neutral solvents (benzene, carbon tetrachloride) or in the dry state (as in melting-point tubes) induced the same reaction. The cyclopropanol derivatives VII showed the ultraviolet absorption of an alkyl-substituted phenyl group, hydroxyl absorption in the infrared at ca. 3.10 μ, and the n.m.r. patterns expected of the system of four coupled protons Ha, Hb, Hc and Hd of structure VII (Figure 1a). The high-precision mass spectrum of compound VIIa showed the parent ion at m/e 245.1414 (calculated for VIIa, $C_{15}H_{19}NO_2$, 245.1416). When treated with potassium hydroxide the compounds of type VII underwent the ring opening characteristic of cyclopropanols, which normally leads to ketones (4). In these instances the ketones produced were 4-benzyl-2,3-dioxopyrrolidines, which are fully enolized, as shown in structure IV. The same enols of type IV were obtained by direct reduction of the 4-benzylidene derivatives (I) (5).

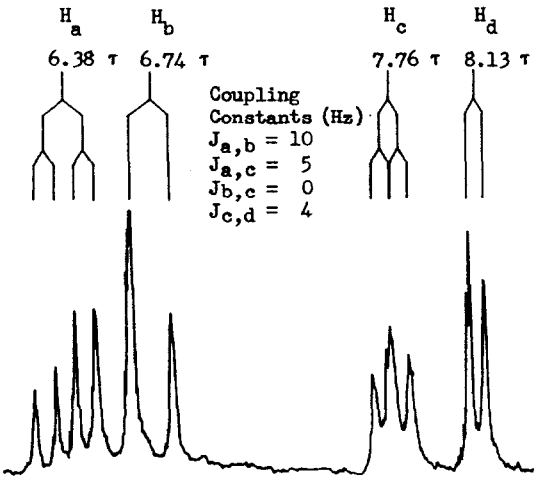


Figure 1a - 60 MHz Spectrum of VIIa

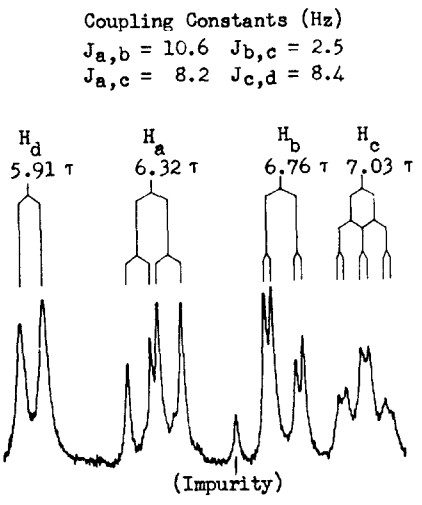


Figure 1b - 100 MHz Spectrum of IIa*

*The authors are indebted to Dr. Richard F. Sprecher for the 100 MHz spectrum obtained at the NMR Facility for Biomedical Studies supported by National Institutes of Health Grant FR-00292. Chemical shifts and coupling constants were computed as described by S. Castellano and A. A. Bothner-By, J. Chem. Phys., 41, 3863 (1964).

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