NITROGEN-CONTAINING BISHETEROCYCLIC SYSTEMS

IV. SYNTHESIS AND STRUCTURE OF 5-HYDROXY-(AMINO)-1-BENZAZOLYLPIRAZOLESS*


A method has been developed for the synthesis of the previously undescribed hydroxy- and amino-1-benzazolyl-2'-pyrazoles. Examination of the IR spectra and determination of the dipole moments has shown that these derivatives exist in the crystalline form and in solution as the hydroxy and amino forms, which are stabilized by intramolecular hydrogen bonding.

Continuing our investigations into nonplanar bisheterocyclic nitrogen-containing systems [1], we have synthesized the previously undescribed 5-hydroxy- and 5-amino-1-(2'-benzazolyl)pyrazoles (I–V), and investigated their physicochemical properties and structure.

The 5-hydroxy- and 5-aminobenzazolylpyrazoles I, II, IV, and V were synthesized from benzazolylhydrazines [2] and β-ketoesters [3] (1), and the 5-amino derivative III, from 2-hydrazinobenzothiazole and benzylphenyliminonitrile (2).

Compounds I–V were identified by their analyses, mp's, Rf values (thin layer chromatography on alumina, and on paper [fast, Volodarsk manufacture]), electrophoretic mobilities, UV and IR spectra, and the values of the dipole moments.

In examining the structures of the 5-hydroxy- and 5-aminobenzazolylpyrazoles, we were interested in the following questions:

* For part III, see [12]

1) The tautomeric forms in which I-V exist in the solid state and in solution.

2) The possible formation of intra- and intermolecular hydrogen bonds.

3) The preferred conformations of molecules I-V.

In the IR spectra of I, II, IV, and V in the solid state, no absorption bands are found above 1640 cm\(^{-1}\), possibly indicating that only the hydroxy forms are present in the crystalline state [4]. No significant changes are observed in the benzazolylpyrazoles when the IR spectra are recorded in chloroform. Only in tetrahydrofuran does a weak absorption band appear at 1720 cm\(^{-1}\), perhaps indicating a slight shift of the tautomeric equilibrium toward the keto form [4].

Among the four bands in the 1500-1600-cm\(^{-1}\) region attributed to the stretching vibrations of the C = C and C=N bonds, all the compounds I-V show a particularly intense band at 1570-1580 cm\(^{-1}\) which, by analogy with [4,5], may be due to the sum of the stretching vibrations of the pyrazole and benzazole rings.

In the LiF-frequency region, I, II, and V show frequencies due to the bound OH group, a wide band with a maximum at 3440 cm\(^{-1}\) in the crystalline state, and a narrow band at 3270 cm\(^{-1}\) in chloroform. The IR spectrum of the benzimidazole IV in this region deserves special consideration. Unlike the benzthiazoles I and II and the 1-benzylbenzimidazoles V, in the solid state a wide, intense band is found at 2500-3100 cm\(^{-1}\), and a narrow one at 3270 cm\(^{-1}\). The first of these absorptions is characteristic of the stretching vibration of the imino group in the imidazole ring, involved in strong intermolecular hydrogen bonding of the type NH\(_2 \ldots \cdot \overline{\text{N}}\) [6], and the second, as mentioned above, may be due to the bound OH group. In chloroform solution, in addition to the vibrations of the bound OH group, low-intensity bands appear at 3430 and 3610-3640 cm\(^{-1}\). We may conclude that, in solution at low concentrations, IV can exist partially in the hydroxy form, with free NH and OH group.

Thus, the 5-hydroxy derivatives of 1-benzthiazolyl(2'-imidazolyl)pyrazoles, both in the solid state and in solution, exist predominantly in the hydroxy form. Stabilization of the latter in these compounds is apparently determined by the formation of intra- or intermolecular hydrogen bonds.

The changes observed in the LiF-prism region on passing from the crystalline state to solution indicate clearly [7] the presence of intramolecular hydrogen bonds in I, II, and V. Instead of the wide, diffuse bands at 3300-3500 cm\(^{-1}\), a narrow band appears at 3270 cm\(^{-1}\).

A regularity similar to that described above is seen in the IR spectra of the 5-amino derivatives III. The narrow, clear peaks which appear at 3300 (crystalline state), 3330 (CCl\(_4\)), 3400, and 3480 cm\(^{-1}\) correspond to the stretching vibrations of the NH\(_2\) group involved in intramolecular interactions of the type \(\text{N}^\ldots\cdot\text{H}^\ldots\cdot\text{N}\) [7]. Actually, the symmetrical stretching vibrations of the NH\(_2\) group (\(\nu_{\text{calc}}\)), according to calculation, should occur at 3394 cm\(^{-1}\) [8], the deviation from this figure does not usually amount to more than 5 cm\(^{-1}\). In this case, it reaches 64 cm\(^{-1}\) (\(\nu_{\text{calc}} - \nu_{\text{exp}} = 3394 - 3330\) cm\(^{-1}\)), which is characteristic for intramolecular hydrogen bonds between one of the H-atoms of the NH\(_2\) group (participation of both the H-atoms in bonding does not destroy the symmetry, and the frequency \(\nu_{\text{NH}}\) agrees with that calculated, 3394 ± 5 cm\(^{-1}\)).

Molecules I-V, therefore, show intramolecular hydrogen bonding of the OH...N or H−N−H...N type. This conclusion is confirmed by both spectral and dipole moment determinations.

The straight-line relationship between the dielectric permeability and concentration (10\(^{-3}\) to 10\(^{-4}\) M) shows the absence of association in the solutions of these compounds [9], and, consequently, the absence of intermolecular hydrogen bonds.

5-Hydroxy- and 5-amino-1-(2'-benzthiazolyl)pyrazoles (I-III) can exist in solution in the form of two planar conformers, either with intramolecular hydrogen bonds (A), or without (B) (the sulfur atom of the benzthiazole ring does not usually participate in coordination and the formation of hydrogen bonds), and also with the angular structure involving bending of the azole ring at the N\(_1\)-C\(_7\) bond connecting the pyrazole and benzazole fragments of the molecule [1,9]. The similar 1-benzimidazolylpyrazole derivative...