

Derivatives of benzimidazole. IX. Hydrates of 5-aminobenzimidazoles

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Various substituted 1-(4-X-phenyl)-5-aminobenzimidazoles, where X = H, CH₃, Cl, Br, I, OCH₃, OC₂H₅, SC₂H₅, N(C₂H₅)₂, were found to form stable hydrates. The mode of binding water and also obtaining water-free amines is discussed.

In our previous papers the synthesis and physicochemical properties of 1-aryl-5-aminobenzimidazoles (*I*) [1], 1-aryl-2-methyl-5-aminobenzimidazoles (*II*) [2], 1-methyl-2-aryl-5-aminobenzimidazoles (*III*) [3], 2-furyl-5(6)-aminobenzimidazoles (*IV*) [4], and 2-phenylfuryl-5-aminobenzimidazoles (*V*) [5] were described. All the above-mentioned aminobenzimidazoles were obtained from the corresponding nitro derivatives by reduction with tin(II) chloride and hydrogen chloride in glacial acetic acid and only those of formula *I* were found to crystallize as hydrates.

As known, the ability to bind water was reported with 5(6)-aminobenzimidazole [6] and some further aminobenzimidazoles [7]. It has been shown that 5(6)-aminobenzimidazole prepared according to [8, 9] is not a free base, but a complex salt with hydrogen chloride and water [6]. The base liberated with sodium hydroxide binds one mole of water. The ability to bind water by a so-called reversible "covalent hydration" is indicative of many derivatives of pteridine and other polyanaphthalenes [10].

This paper deals with a more detailed study of hydrates *I* by differential thermal analysis (DTA), differential thermogravimetric analysis (DTGA) and differential enthalpic analysis (DEA), which enable to investigate the process of melting, decomposition of organic compounds, *etc.* [11].

Experimental

Hydrates of 1-(4-X-phenyl)-5-aminobenzimidazoles and also water-free amines were prepared by reduction of the corresponding 5-nitro derivatives with tin(II) chloride and hydrogen chloride in glacial acetic acid [1].

Thermograms DTA and DTGA were measured within 40–200°C range on an MOM derivatograph with an Fe-constantan thermocouple at 1/10 sensitivity and 2°C/min heating rate; samples 100–210 mg, reference substance Al₂O₃. Thermograms DEA were recorded with a DSC-1B Perkin-Elmer differential calorimeter in a dry nitrogen atmosphere at a 12 ml/min flow rate and 1°C/min heating rate in regular sample tubes; sensi-

tivity 2 mcal/min. The apparatus was calibrated in a usual way, indium and lead, or alternatively azobenzene and benzil being the standards.

Infrared absorption spectra were taken with a UR-2P (Zeiss, Jena) spectrophotometer in acetonitrile or chloroform. The ultraviolet absorption spectra were recorded with a Specord UV-VIS (Zeiss, Jena) apparatus in dioxan.

Results and discussion

Of all 5-aminobenzimidazoles under study only 1-(4-X-phenyl)-5-aminobenzimidazoles (I) were found to form stable hydrates of m.p. 60–98°C.

In this temperature range also 1-phenyl- and 1-(4-tolyl)-5-aminobenzimidazoles melted, although their melting points were reported to be 130–131°C [12] and 128°C [13], respectively. The elemental composition was not in agreement with that required for pure compounds, even though they were thoroughly purified. In their infrared spectra bands due to symmetric and asymmetric unassociated N–H vibrations were observed. It has been shown that hydrates of 1-aryl-5-aminobenzimidazoles, from which water could be removed under diminished pressure (20 torr) at elevated temperature (100°C), were involved. The 5-aminobenzimidazoles unsubstituted in position 2 of the benzimidazole ring are capable to form hydrates.

The mode of binding water was studied in detail with 1-(4-bromophenyl)-5-aminobenzimidazole; the course of its thermal curves is seen in Fig. 1 (hydrate) and in Fig. 2 (water-free amine). As seen in Fig. 1, the decrease of weight occurs at 60°C: the thermogram exhibits a broad endothermic wave with three peaks of very good reproducibility. The TGA and DTGA curves evidence that the removal of water proceeds in two stages:

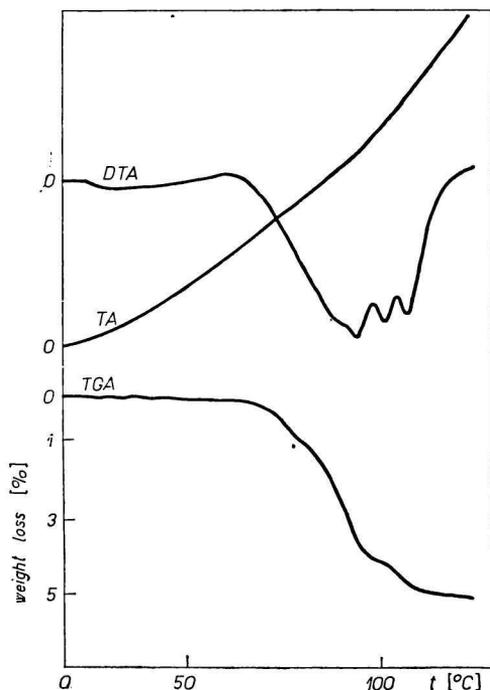
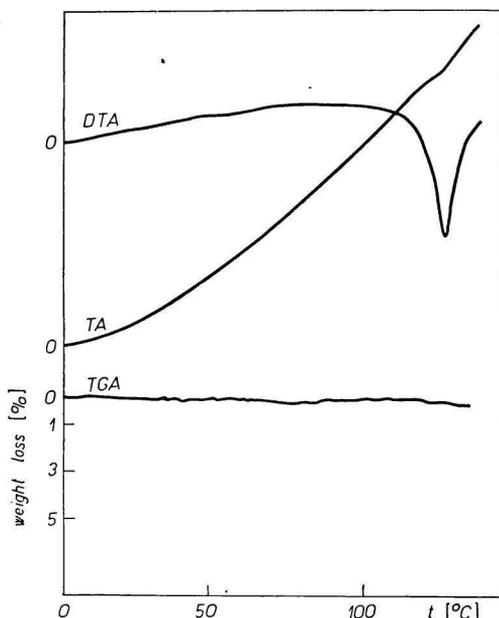


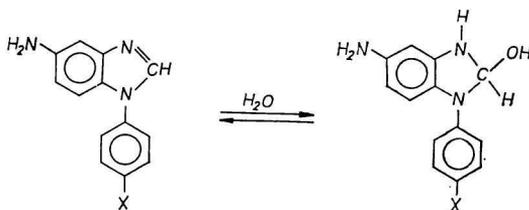
Fig. 1. Thermogram of 1-(4-bromophenyl)-5-aminobenzimidazole hydrate.

Fig. 2. Thermogram of 1-(4-bromophenyl)-
-5-aminobenzimidazole.



the first two peaks of the DTA curve correspond to the removal of water whilst the third one to the melting of the anhydrous substance. The molar ratio of benzimidazole to water was estimated to be 1 : 1. The thermal effect of the first (5 kcal) and second (14 kcal) stage per one mole of water has been calculated by the DEA method from the percent decrease of water (in the first stage 4.6%, in the second one 0.9% of the weight of the original sample).

From the results presented it could be concluded that water is bound to two centres of the aminobenzimidazole molecule, both bonds being markedly different, what could be associated with the basicity of the single centres. It could formally be presumed that centres in question were the nitrogens of the imidazole ring and the amino group. The amino group as a centre of basicity can be excluded since 2-methyl-5-aminobenzimidazoles having the amino group even more basic [14] do not form hydrates, what means that the imidazole ring has to be considered a bifunctional basic centre, the nitrogens of which could interact with hydrogens of water. The energies of hydrogen bonds are different due to their distinct basicity. Since the water to benzimidazole ratio 1 : 1 and the energy of water release is different in single stages, it could be assumed that two molecules of water are bound between two molecules of benzimidazole (Fig. 3).



Scheme 1

The water is presumably of crystalline nature, as anhydrous 1-aryl-5-aminobenzimidazoles are only slightly hygroscopic. If water is added to a benzene solution of benzimidazole, a crystalline hydrate is separated.

Aminobenzimidazoles II–I' substituted in position 2 do not form hydrates what could well be rationalized according to Fig. 3: a more bulky substituent than hydrogen in position 2 of the imidazole ring hinders, due to the steric effect, the formation of both the hydrogen bonds and, consequently, also the hydrates.

An alternative binding of water by "covalent hydration" of the C=H bond [10] of the imidazole ring (Scheme 1) is not likely in this case.

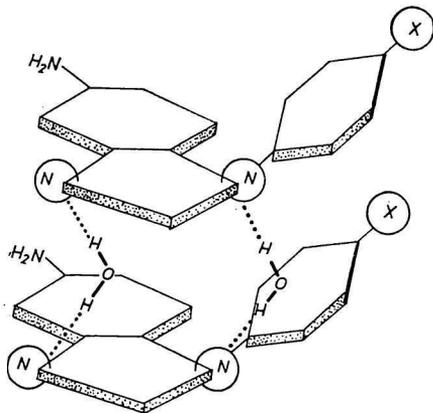


Fig. 3. Bicentric bound water in 1-aryl-5-aminobenzimidazole.

Benzimidazole has a high degree of aromaticity and the imidazole ring resists all oxidation [15] and reduction [16] attempts; the reaction takes place in the benzene moiety. It is therefore unlikely that such a mild reagent as water would affect the imidazole ring in benzimidazole. In this case a modification of the electronic spectrum of the hydrate would occur. Nevertheless, the spectra of the hydrate and anhydrous base were superimposable. Moreover, in both spectra a band indicative of stretching vibrations of the N=C bond appeared at $\sim 1630\text{ cm}^{-1}$. "Covalent hydrations" do not bind water equimolarly and the amount of water varies depending on the structure of the molecule.

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