A reducing-difference IR-spectral study of 4-aminopyridine

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Abstract: The IR-spectra of 4-aminopyridine (4-AP) in solution and in the solid state have been analyzed, using the reducing-difference procedure. Defining a more precise band assignment of a part of the characteristic frequencies of 4-AP, the data obtained proved in particular a Fermi-resonance splitting of the symmetric NH$_2$-stretch.

Keywords: 4-aminopyridine, difference IR spectral analysis

1 Introduction

The renovated interest in 4-aminopyridine (4-AP) and its protonated form is provoked by their biological activity as Ca$^{2+}$ and K$^+$ channel inhibitors [1-2]. The structure of the 4-AP metal complexes is also investigated because of their wide application as chemical reagents in analytical practice and as luminophores in supramolecular photochemistry [3]. The experimental data show that 4-AP is a monodentate ligand as is shown by the formation of Ni(II) complex with a bidentate coordination of 4-AP through both N atoms [5] and this is attributed to the the stronger basicity of the nitrogen of the pyridine [4]. The protonation and coordination ability of 4-AP is connected with the potential possibility of amino-imino tautomerisation. The published data suggest an aromatic character of the neutral 4-AP molecule while protonation leads to imino-form [6, 7].

The premise given above provoke a more detailed IR-spectral study of the characteristic frequencies of 4-AP. Our results obtained by linear-dichroic IR-spectral (IR-LD) analysis of 4-AP in solid state allowed a more precise assignment of 4-AP characteristic

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bands, assuming in particular a Fermi-resonance splitting of the NH$_2$-symmetric stretch [8]. It may be proposed that this phenomenon exists in solution of 4-AP as well, and this problem is studied in the present paper using the possibilities of the difference-reducing procedure.

2 Experimental

2.1 Material and methods

The 4-AP (Fluka, purum) was used after additional recrystallization from benzene. Spectral quality solvents (Uvasol, Merck) were employed and only triethylamine (Carlo Erba, purum) was additionally redistilled and dried over molecular sieves. The solid state 4-AP deuterated derivatives were obtained from the solutions of 4-AP CH$_3$OD and D$_2$O solutions (Merck) by solvent evaporation. A Bomem-Michelson 100 FTIR-spectrometer (4000 – 400 cm$^{-1}$) was used for the IR-spectral measurements. The spectral data of solutions in 1.10$^{-1}$ – 2.10$^{-3}$ M concentration range were recorded using 0.01 cm KBr cell while 5 cm and 1 cm quartz cells were used to obtain spectra in dilute (< 0.001 M) carbon tetrachloride and chloroform solutions, respectively. KBr disk and Nujol mull-techniques were utilized for obtaining solid state IR spectra.

The reducing difference procedure was developed for analysis of IR-LD spectra [9-11]. Its modification for interpretation of non-polarized IR-spectra [12, 13], consists in the subtraction of two spectra, measured under the same experimental conditions of samples, containing non-equal concentration of a given structural unit viz monomeric and associated 4-AP in this case. Using the elimination procedure, the vanishing of a band characteristic for one of both molecule fragments, resulted in the complete disappearance of the bands belonging to the same structural units. The elimination method described above is graphically performed using the subtracting procedure included in the processing program for the IR spectra.

3 Results and discussion

Figure 1 compares both NH$_2$-stretching and scissoring regions of 4-AP diluted solutions (< 0.001M) in carbon tetrachloride (Fig. 1.1) and chloroform (Fig. 1.2) with those in the solid state (Fig. 1.3). The data obtained for the monomeric (free) 4-AP at 3507 cm$^{-1}$, 3413 cm$^{-1}$ and 1623 cm$^{-1}$ correspond to $\nu_{as}(\text{NH}_2)$, $\nu_{s}(\text{NH}_2)$ and $\delta^f(\text{NH}_2)$, respectively and are in accordance with the results of other authors [14 - 18]. The band assignments in the solid state at 3435 cm$^{-1}$ ($\nu_{as}(\text{NH}_2)$) and 1645 cm$^{-1}$ ($\delta^a(\text{NH}_2)$) are also commonly accepted [6, 17, 18]. Some ambiguity with respect to the $\nu_{s}(\text{NH}_2)$ exists. According to the Spiner’s results two bands at 3302 cm$^{-1}$ and/or 3075 cm$^{-1}$ should belong to this mode [6]. The first value (3300 cm$^{-1}$) is tacked in [19] and is supported by the authors [20] by performing a normal coordinate treatment of 4-AP.

Scant information about the influence of the NH$_2$ characteristic frequencies is obtained
by the study of solutions with increasing 4-AP concentration. A 1% chloroform solution of 4-AP shows an additional band at 3216 cm\(^{-1}\) however no interpretation [14] was given. Ramiach and Puranik assigned the bands at 3330 cm\(^{-1}\) and 3175 cm\(^{-1}\) to the \(\nu_{as}^a(NH_2)\) and \(\nu_{as}^s(NH_2)\), respectively, for the dimeric form of 4-AP in the same solvent. They established that the concentration change of the solute in the 2.10\(^{-2}\) – 1.10\(^{-2}\)M interval shifts the NH\(_2\)-scissoring band from 1623 cm\(^{-1}\) to 1645 cm\(^{-1}\) [17].

All results stated above discount the possibility of a Fermi-resonance splitting of the NH\(_2\)-stretching bands. The effect is typical of NH...N hydrogen bonding when only one hydrogen atom is connected. This asymmetric association weakly affects the \(\nu_{as}^a(NH_2)\), but leads to the strong disturbance of the \(\nu_{as}^s(NH_2)\). The corresponding band is shifted to low frequency region of 3250 – 3200 cm\(^{-1}\) where the overtone of the NH\(_2\)-scissoring vibration occurs. Since transition moments of overtone and symmetric NH\(_2\)-stretch are co-linear a Fermi-resonance splitting of \(\nu_{as}^s(NH_2)\) band could be provoked [21-26]. This
phenomenon was described in the IR-spectral study of the self-association effects of 2-aminopyridine [27].

According to the X-ray results [28] 4-AP forms (H)NH...N(Py) thereby self-associates with the participation of one amino hydrogen, therefore, a Fermi-resonance splitting of the $\nu'_{as}(NH_2)$ band could also be expected. The data shown in Fig. 2 are in accordance with this presumption. The increase in solute concentration from $1.10^{-1}$ M (Fig. 2.1) to a saturated solution (Fig. 2.2) in chloroform decreases the characteristic absorption maxima of the monomeric form and simultaneously increases the intensity of bands at 3483 cm$^{-1}$, 3321 cm$^{-1}$ and 3165 cm$^{-1}$. The same effects are observed with the $\delta(NH_2)$ scissoring peaks at 1623 cm$^{-1}$ and 1645 cm$^{-1}$, respectively. These bands belonging to the free and perturbed 4-AP species can be divided using the subtraction procedure described in the experimental part. The consequent elimination of the peaks of $\nu'_{as}(NH_2)$ at 3507 cm$^{-1}$ and $\delta'(NH_2)$ at 1645 cm$^{-1}$ reveals the reduced spectral characteristic of associated (Fig. 2.3) and monomeric form (Fig. 2.4). The absorption maximum at 3483 cm$^{-1}$ in Fig. 2.3, not discussed here, should be attributed to the $\nu''_{as}(NH_2)$ frequency which is weakly perturbed by the NH...N(Py) hydrogen bond formation. The mutual origin of the remaining two bands at 3321 cm$^{-1}$ and 3163 cm$^{-1}$ assumed as a Fermi-resonance effect can be additionally substantiated by the IR-spectral study of 4-AP adducts with triethylamine (TEA).

The behaviour of the NH$_2$-stretching bands on adduct formation between primary and ternary amines was thoroughly examined in [21, 24, 29]. It was found that the increase in concentration of the ternary amino components leads to the consequent appearance of RNH$_2$:R$_3$N adducts in the ratio of 1:1 and 1:2. The structure of the 1:1 product is stabilized by asymmetrical (H)N-H...N hydrogen bonding which causes the already mentioned weak disturbance of the $\nu_{as}(NH_2)$ peak and the strong low-frequency shift of the $\nu_4(NH_2)$ band accomplished by its Fermi-resonance splitting. The subsequent formation of the 1:2 adducts slightly affect the Fermi-doublet obtained, but an additional lowering of the antisymmetric NH$_2$ stretch is also present. The theoretical analysis of this Fermi-resonance effect was discussed by H. Wolf and D. Horn [24], where a method for the calculation of the unperturbed symmetrical NH$_2$-stretching frequency was also developed.

The IR-spectra of carbon tetrachloride solutions of two 4-AP adducts with triethylamine in molar ratio 4-AP:TEA = 1:1 and 1:3 are given in Figs 3.1 and 3.2, respectively. They contain the bands attributed to both the monomeric and associated 4-AP species thus indicating the presence of equilibrium between these forms. The corresponding Figs. 3.3 and 3.4 illustrate the reduced spectra appearing after the elimination of the $\nu'_{as}(NH_2)$ band at 3504 cm$^{-1}$ and $\delta''(NH_2)$ absorption maximum at 1645 cm$^{-1}$ (see above). The reduction procedure does not reveal an additional peak at about 3350 cm$^{-1}$ characteristic of the $\nu''_{as}(NH_2)$ of the 1:2 adducts with triethylamine, indicating the formation of only asymmetric (H)NH...N hydrogen bonding in the mixed systems investigated. The situation should be analogous to the self-association observed in chloroform solution of 4-AP presented in Fig. 2, further the same band profile in the IR-spectra in both cases proves
Fig. 2 NH$_2$ – stretching and scissoring region of 4-AP in chloroform: 1.10$^{-1}$ M (1) and saturated solution (2); Corresponding reduced spectra after elimination of the bands at 3507 cm$^{-1}$ (3) and 1645 cm$^{-1}$ (4).

this suggestion (Compare the Figs. 3.3 and 3.4 with Figs. 2.3 and 2.4). The juxtaposing of the results discussed above is in accordance with the statement of the Fermi-resonance splitting of the symmetric NH$_2$-stretching band due to the NH...N(Py) self-association formation between 4-AP molecules.

The Fermi-resonance components of $\nu_s^a$(NH$_2$) stretching band in the solid state are proved by the application of the reduction procedure to the 4-AP derivative mono deuterated at the amino group. Two samples containing different amounts of deuterated and non-deuterated compound were processed and one of them is illustrated in Fig. 4.1. The appearance of two new bands at the 2532 cm$^{-1}$ and 3425 cm$^{-1}$ is notable (see also [30]). The first one belongs to the ND- stretching frequency of the (H)ND group and its elimination provides the vanishing of the peak at 3425 cm$^{-1}$ assigned to the NH-vibration of
Fig. 3 NH$_2$ – stretching and scissoring region of 4-AP aducts with triethylamine (TEA): molar ratio: 4-AP:TEA = 1:1 (1) and 4-AP:TEA = 1:3 (2); corresponding reduced spectra after elimination of the bands at 3503 cm$^{-1}$ (3) and 1645 cm$^{-1}$ (4).

The same structural fragment (Fig. 4.2). The reverse elimination of the $\nu_{as}$ (NH$_2$) at 3437 cm$^{-1}$ leads to the disappearance of the remaining bands characteristic of the amino group of non-deuterated 4-AP. In particular, both the maxima at 3305 cm$^{-1}$ and 3085 cm$^{-1}$ which we assign as Fermi-components of $\nu_{as}$ (NH$_2$) frequency are also eliminated revealing the absorption maxima of the pyridine CH-stretch between 3100 – 3000 cm$^{-1}$ (Fig. 4.3). However, the band at 3205 cm$^{-1}$ probably due to the overtone of 8a-ring vibration about at 1600 cm$^{-1}$ is not perturbed (Fig. 4.3).

The reducing procedure discussed here also eliminates two absorption maxima at 660 and 440 cm$^{-1}$, exhibiting a broad outline typical of formation of a strong hydrogen bonds. This result suggests vibrations correspond to associated NH$_2$-group. According to an earlier IR-spectral study of the solid state 4-AP [20], a value at 661 cm$^{-1}$ is calculated (experimental one is not given) for the wagging ($\omega$-NH$_2$) mode and we assign it to ‘itself’ band at 660 cm$^{-1}$. The corresponding twisting ($\tau$-NH$_2$) vibration is predicted to be in 260-300 cm$^{-1}$ interval [20, 31] and overlaps with 90 cm$^{-1}$ high-frequency shift on
Fig. 4 Solid state spectra of a mixture of 4-AP and 4-AP deutero derivative (1); the corresponding reduced spectra after elimination of the bands at 2565 cm$^{-1}$ (2) and 3437 cm$^{-1}$ (3).

(H)NH$_2$...OH$_2$-hydrogen bond formation [31]. The IR-LD-spectral band study of phenol as 5% (m/m) liquid crystal solution demonstrates a 7-OH band at 620 cm$^{-1}$ [32] which corresponds to an increase of 310 cm$^{-1}$ with respect to this frequency in dilute non-polar solvent. As a result of these assumptions the 440 cm$^{-1}$ peak in the IR-spectra of the solid state 4-AP should be treated as torsional NH$_2$-vibration.

Using an original modification of the reducing-difference method, a Fermi-resonance splitting of the NH$_2$-stretching band is proved both in solution and in the solid state, thus confirming the results obtained by the IR-LD spectral analysis.

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