Structural and spectroscopic characterization of 2-amino-3, 5-dibromopyridine

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The correlation between the structure and spectroscopic properties of 2-amino-3, 5-dibrompyridine (**1**) is studied, using the methods as single crystal X-ray diffraction, IR- and UV-spectroscopy. The X-ray diffraction investigation showed that, the unit cell contains 4 molecules, forming dimmers by means of the NH…N hydrogen bonding. In particular, the linear-dichroic IR-spectroscopy coupled with the orientation technique of solid samples as liquid crystal suspension is applied for identification of the IR-bands, characteristic for the structural fragments. The presence of dimmers formation in the unit cell assumed Fermiresonance splitting effect of the ν^s_{NH2} of (1) in the solid-state IR-spectra. Quantum chemical calculations are performed in order to obtain the electronic structure and spectroscopic properties of the compound studied (**1**).

***Keywords*:** 2-amino-3, 5-dibromopyridine, Crystal structure, Linear-Dichroic Infrared Spectroscopy (IR-LD), Quantum chemical calculations.

INTRODUCTION

The substituted aminopyridines are N-heterocyclic amines possessing biological activity. Their action and biological effect as K_+ and Ca_{2+} channel inhibitor and the role of the transition metal complexes and coordination capability has been discussed systematically [1–6]. It is known, that aminopyridines are weak bases and they can exist in neutral or protonated cationic form at physiological pH. This characteristic however complicates the elucidation of the mechanism and the site of action [7, 8]. On the other hand any *in vivo* studies are based on the detail investigations and correlations between the structure and spectroscopic properties *in vitro*. In our previously works [9–13] it was established the influence of the protonation on the charge redistribution in pyridinium ring and the effect on the optical and magnetic properties, as well the self-association of different substituted pyridines in solution and solid state applying various methods for analysis. As a part of our systematic study of pyridine derivatives in this paper is presented structural and spectroscopic investigation of the titled compound, which structure is shown in **S**cheme **1**. For that purpose were used different methods as a single crystal X-ray diffraction, comparatively characterization by means of Irand UV-
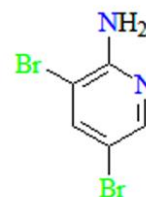
Scheme 1. Chemical diagram of 2-amino-3,5-dibromopyridine (**1**)

spectroscopy in particular, the linear-dichroic infrared (IR–LD) spectroscopy. Quantum chemical calculations at the DFT, MP2 and CIS levels of theory using 6-311++G**basis set are employed for predicting and supporting of the experimentally observed properties.

EXPERIMENTAL
Materials and methods

Starting compound (**1**) is trade product (Sigma-Aldrich). The suitable for the single Xray diffraction measurements crystals were obtained by recrystallization from ethanol.

The *IR-spectra* were measured using a Bomem-Michelson 100 FT-IR-spectrometer (4000 – 400 cm^{-1}, ± 2 cm^{-1} resolution, 150 scans) equipped with a Perkin Elmer wire-grid polarizer. The non-polarized solid state IR spectra were recorded using KBr disk technique.

The oriented samples were obtained as suspension in a nematic 4'-cyano-4'-alkyl-bicyclohexyl mixture (ZLI-1695 in the Merck

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notation), mesomorphic at room temperature. The poor Irspectrum makes possible to record the guest-compound bands in the whole 4000–400 cm^{-1} range. The presence of an isolated nitrile stretching IR-band at 2233 cm^{-1}additionally serves as an orientation indicator. The effective orientation of the solid state sample was achieved through the following procedure: about 5 mg of the compound studied was added to the appropriate liquid crystal substance until a slightly viscous mixture is obtained. The suspension thus prepared was pressed between two KBr-plates rubbed out in advance in one direction by means of fine sandpaper. The grinding of the prepared mull in the rubbing direction promotes an additional orientation of the sample [14–17].

The *UV-VIS* spectra of the compound studied as 1.10^{-4} mol/l solutions (1-cm quartz cell) in acetonitrile were recorded on Evolution 300 spectrometer (Thermo Scientific, USA) with ± 2 nm resolution.

The *X-ray diffraction* intensities were measured on a Bruker Smart X2S diffractometer, using microsource Mo-K · radiation and employing the ω-scan mode. The data were corrected for Lorentz and Polarization effects. An absorption correction based on multiple scanned reflections [18]. The crystal structures were solved by direct methods using SHELXS-97 [19]. The crystal structures were refined by full-matrix least-squares refinement against F_2 [18–21]. Anisotropic displacement parameters were introduced for all nonhydrogen atoms. The hydrogen atoms attached to carbon were placed at calculated positions and refined allowing them to ride on the parent carbon atom.

Quantum chemical calculations were performed with GAUSSIAN 98 and Dalton 2.0 program packages [22, 23]. The output files were visualized using the GausView03 program [24]. The geometry of (**1**) was optimized at two levels of theory: second-order Moller-Pleset perturbation theory (MP2) and density functional theory (DFT) using the 6-311++G** basis set. The DFT method employed is B3LYP, which combines Backe's three-parameter nonlocal exchange function with the correlation function of Lee, Yang and Parr. The molecular geometries of the studied species were fully optimized by the force gradient method using Bernys' algorithm. For every structure the stationary points found on the molecule potential energy hypersurfaces were characterized using standard analytical harmonic vibrational analysis. The absence of the imaginary frequencies, as well as of negative eigenvalues of the second-derivative

matrix, confirmed that the stationary points correspond to minima of the potential energy hypersurfaces. The calculation of the vibrational frequencies and infrared intensities were checked to establish which kind of performed calculations agree the best with the experimental data. The empirical scaling factors 0.9614 and 0.8929 are made to achieve better correspondence between the experimental and theoretical values. The *UV spectra* in the gas phase and in acetonitrile solution are obtained by CIS/6-311++G** and TDDFT calculations at the same basis set. We use the methods of Hartree-Fock theory and density functional theory, systematically explained in [25–29].

RESULTS AND DISCUSSION
Crystal and molecular structure of (1)

The *X-ray diffraction* investigation of the 2-amino-3, 5-dibromopyridine (1) was carried out. The obtained crystallographic data show, that compound (**1**) crystallizes in the monoclinic space group *P*2$_1$/*n*. The presented in Fig. 1 an ORTEP plot illustrates the structure at the 50% thermal ellipsoids. The unit cell of the compound (**1**) contains 4-molecules, which form dimmers by means of the NH…N hydrogen bonding (3.041 A) as is shown in Fig. 2.
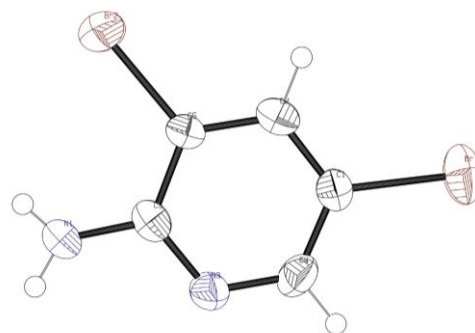

Fig. 1. ORTEP plot of (**1**) at the 50% thermal ellipsoids; Hydrogen atoms are shown as spheres of arbitrary radii.
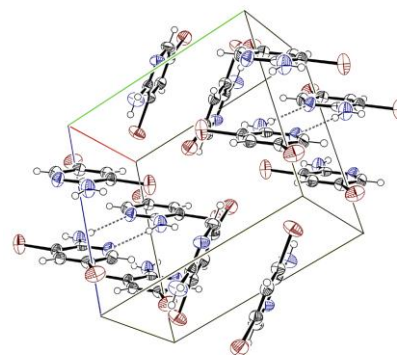

Fig. 2. Unit cell contents and hydrogen bonding scheme in (**1**).

The asymmetric hydrogen bonding type with participation of the NH2-group proposes an observation of the Fermi-resonance splitting effect [30–33] of the ν_s NH2 in the corresponding solid-state IR-spectra of (**1**). The performed quantum chemical calculations of the molecular geometry of (**1**) show a good correlation of the obtained bond lengths and angles, in comparing with the experimental crystallographic data. The obtained difference of 0.012 A and 1.0(2) ° is a good background for the next vibrational spectral analysis.

Vibrational and IR-LD spectral analysis

The calculated IR-spectrum of (**1**) is shown in Fig. 3. From the spectrum can be see that, the most typical in this respect are the characteristic bands of the pyridine skeleton vibrations at 1619 cm^{-1}, 1587 cm^{-1}, 1496 cm-1 and out-of-plane peak at 966 cm-1 assigned according to Wilson notation [34] as **8a**, **8b**, **19a** and **11**-γCH, respectively. Comparing with the data of other pyridine derivatives [14-18], the presence of the Br-substituents leads to the higher-frequency shifting of the in-plane skeleton vibrations. The band at 1360 cm-1 belongs to ν_{C-N} vibration. Comparing the theoretical and experimental IR-bands a difference of 2 cm^{-1} is obtained for the above stated frequencies. Significantly different are the IR-bands for the NH2-vibrations, as a result of the participation of the group in the intermolecular interactions.

The theoretical IR-bands of ν^{as}_{NH2}, ν^{s}_{NH2}, δ_{NH2} and ω_{NH2} are at 3505 cm^{-1}, 3385 cm^{-1}, 1619 cm-1 and 377 cm-1 (Fig. 3).
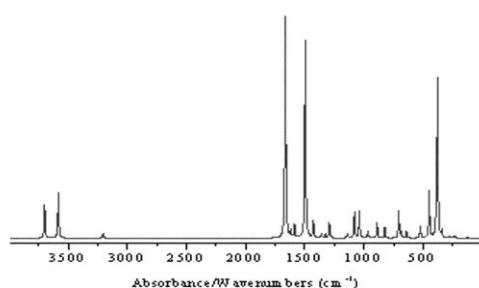

Fig. 3. Calculated IR-spectrum of (**1**).

The corresponding bands at the experimental solid-state spectrum are at 3464 cm-1, 3280/3210 cm^{-1}, 1627 cm^{-1}and 700 cm^{-1}, respectively (Fig. 4.1). The band of ν^{s}_{NH2} is Fermi resonance splitted [25-29]. However, both bands are with the same sign in the corresponding difference IR-LD spectrum in Fig. 4.2. Direct proof of this statement follows by the obtained elimination of these

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maxima at the same dichroic ratio (Fig. 4.3). The last elimination leads to strong reduction of the band at 1627 cm-1 of δ_{NH2} as a result of the difference of the transition moments of the ν^{s}_{NH2} and δ_{NH2} an angle of 12.3(1)° according to the crystallographic data. The elimination of the ν^{as}_{NH2} leads to the reduction of the i.p. maxima at 888 and 706 cm^{-1}, which is also in accordance with the calculated resulting transition moments (Fig. 4.4). The elimination of the o.p. band at 960 cm-1 leads to disappearance of the bands at 824 cm^{-1} and 687 cm-1, which directly shows their belonging to the same symmetry class (Fig. 4.5).
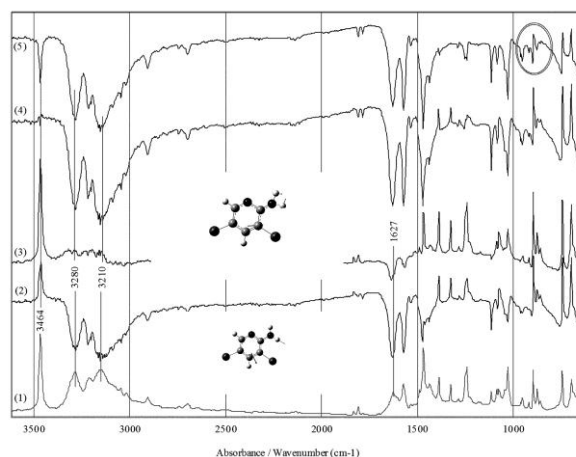

Fig. 4. Non-polarized IR-(**1**), difference (**2**) and reduced IR-LD spectra of (**1**) after the elimination of the bands at 3280 cm^{-1} (**3**), 3464 cm^{-1} (**4**) and 687 cm^{-1} (**5**).

UV-spectral data

In accordance with the data literature [35, 36] the electronic spectrum of 2-amino pyridine posses two characteristic bands at 242 nm (ε = 11000 L mol^{-1}cm^{-1}) and 262^{sh} nm (ε = 788 L mol^{-1}cm^{-1}) belonging to pyridine aromatic system. Other result is observed looking on the UV–VIS spectrum of 2-amino-3, 5-dibromopyridine. The spectrum of (**1**) contains one broad band at 255 nm (ε = 10160 L mol^{-1}cm^{-1}) as a result of the presence and influence of the bromine atoms as a substituents in the 2-amino pyridine structure. These data are in a good agreement with the theoretically predicted electronic spectrum. The HOMO-LUMO Mos gaps of (**1**) are given in the Scheme 2 and correlated well with the obtained experimental data.
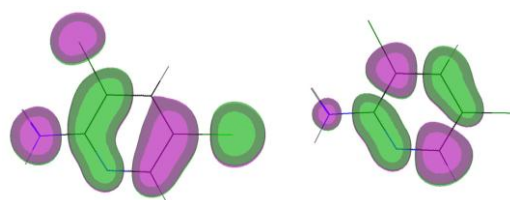
Scheme 2. HOMO and LUMO MOs gaps of (**1**)

CONCLUSION

In this work is has performed structural and spectroscopic analysis of 2-amino-3,5-dibromopyridine by means of X-ray diffraction, IR- and linear-polarized IR-spectroscopy of oriented colloid suspensions in nematic host, UV–VIS spectroscopy and theoretical calculations. It was established the presence of dimers formation by NH…N hydrogen bonding in the unit cell, which proposes Fermi-resonance splitting effect of the v_s NH2 of (**1**) in the solid-state IR-spectra. The quantum chemical calculations of (**1**) show a good agreement of the obtained data (bond lengths and angles) with the experimental crystallographic data.

SUPPLEMENTARY MATERIAL

Crystallographic data for the structural analysis have been deposited with the Cambridge Crystallographic Data Centre, CCDC 761691. Copies of this information may be obtained from the Director, CCDC, 12 Union Road, Cambridge, CB2 1EZ, UK (Fax: +44 1223 336 033; e-mail: deposit@ccdc.cam.ac.uk or http://www.ccdc.cam.ac.uk)

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СТРУКТУРНО И СПЕКТРОСКОПСКО ОХАРАКТЕРИЗИРАНЕ НА 2-АМИНО-3,5-ДИБРОМОПИРИДИН

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(Резюме)

Изследвана е взаимната зависимост между структура и спектроскопските свойства на 2-амино-3,5-дибромопиридин използвайки методите на рентгено-структурния анализ, ИЧ- и УВ-спектроскопията. Данните от рентгено-структурния анализ показват, че елементарната клетка съдържа 4 молекули, образувайки димери чрез NH…N водородно свързване. Отделно е приложена линейно-дихроичната ИЧ-спектроскопия в съчетание с техниката на ориентирани твърди проби като суспензия в течен кристал за идентифициране на на ИЧ-ивиците, характерни за съответните структурни фрагменти. Наличието и образуването на димери в елементарната клетка предполага ефекта на Ферми резонансното разцепване на ν^s NH$_2$ на (**1**) в ИЧ-спектъра в твърдо състояние. Извършените квантово-химични изчисления са с цел да бъдат получени електронната структура и спектроскопските свойства на изучаваното съединение (**1**).