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Spectroscopic investigation on proton transfer reaction in the complex of 2-aminopyridine with 2, 6-dichloro-4-nitrophenol in different solvents

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ABSTRACT

Proton transfer (PT) reaction between 2-aminopyridine (2AP) with 2,6-dichloro-4-nitrophenol (DCNP) has been investigated spectrophotometrically in methanol (MeOH), acetonitrile (AN) and acetonitrile with 1,2-dichloroethane binary mixtures (1:1, ANDEI) and (3:1, ANDEII). A long wavelength band in the range 395–424 nm due to the proton transfer complex formation has been recorded. The formation constants of the PT-reaction (K_{PT}) have been estimated using Benesi–Hildebrand equation. It has been found that K_{PT} recorded larger value in AN than MeOH and binary mixtures. This result was interpreted in terms of solvatochromic parameters like, solvent polarizability (π^*), hydrogen bond donor (α), and hydrogen bond acceptor (β). The molecular composition of the PT-complex has been identified by Job's and photometric titration methods where 1:1 complex is formed. Based on the rapidity and simplicity of the PT-reaction as well as the stability and simple composition of the formed complex, a rapid, accurate and sensitive spectrophotometric method for determination of 2AP was proposed. In addition, the solid PT-complex (2AP-DCNP) has been isolated and characterized using elemental analyses and FTIR measurements.

1. Introduction

Proton transfer is one of the most investigated chemical reactions in chemistry and biochemistry [1–4]. They play an important role in various chemical and biological processes like stabilizing biomolecular structures [5], controlling the speed of enzymatic reactions [6] as well as constructing supramolecular structures [7].

Complexes of phenols with nitrogen and oxygen bases belong to the most frequently investigated H-bonded and proton transfer systems. These complexes have been investigated by many experimental and theoretical studies. Several physical properties of H-bonded complexes, e.g. excess of dipole moment ($\Delta\mu$), change of ^{1}H, ^{13}C, ^{15}N chemical shifts ($\Delta\delta$) and ^{35}Cl NQR frequency when plotted against ΔpKa (pKa (BH^+) − pKa (AH)), a sigmoidal titration curves are obtained which were usually treated as evidence of the proton transfer equilibrium [8–11]. This equilibrium is strongly affected by the properties of the proton donor, proton acceptor and solvent polarity [12,13].

Aminopyridines are bioactive N-heterocyclic tertiary amines, which increase the strength of the nerve signal by blocking of the voltage-dependent K^+ channel [14,15]. Also, aminopyridines have been proposed as drugs for the treatment of many diseases such as antithrombus drugs and antimicrobial agents [16–18]. In particular, 2-aminopyridine is one of the potential impurities in piroxicam and teroxicam which are non-steroided antiflammatory drugs that used in musculo-skeletal and joint disorders [19]. Moreover, aminopyridines are commonly present in synthetic and natural products [20]. They form repeated moiety in many large molecules with interesting photophysical, electrochemical and catalytic applications [21].

In connectivity with our work on proton transfer reactions [22–24] and due to the industrial, biological and pharmaceutical applications of aminopyridines, we wish to report in the present article our finding on the spectroscopic studies of the proton transfer complex formed

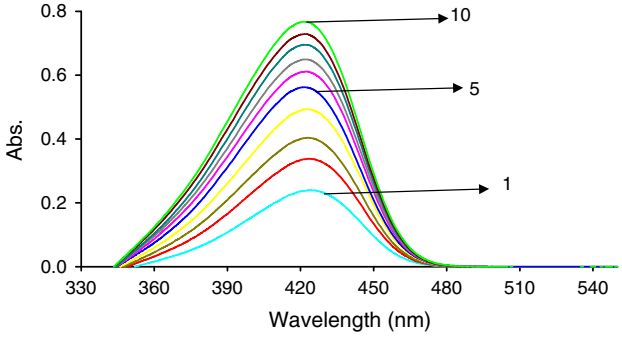

Fig. 1. Electronic spectra of 1:1 complex of 1×10^{-4} M DCNP with various concentrations of 2AP in AN: (1) 2×10^{-5}, (2) 4×10^{-5}, (3) 6×10^{-5}, (4) 8×10^{-5}, (5) 1×10^{-4}, (6) $1.\times210^{-4}$, (7) 1.4×10^{-4}, (8) 1.6×10^{-4}, (9) 1.8×10^{-4} and (10) 2×10^{-4} M.

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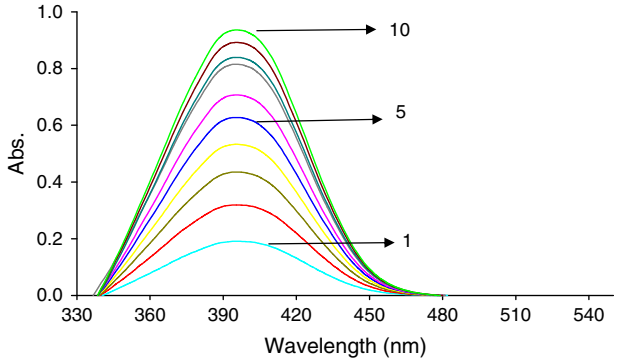


Fig. 2. Electronic spectra of 1:1 complex of 1×10^{-4} M DCNP with various concentrations of 2AP in MeOH: (1) 1×10^{-5}, (2) 2×10^{-5}, (3) 3×10^{-5}, (4) 4×10^{-5}, (5) 5×10^{-5}, (6) 6×10^{-5}, (7) 7×10^{-5}, (8) 8×10^{-5}, (9) 9×10^{-5} and (10) 1×10^{-4} M.

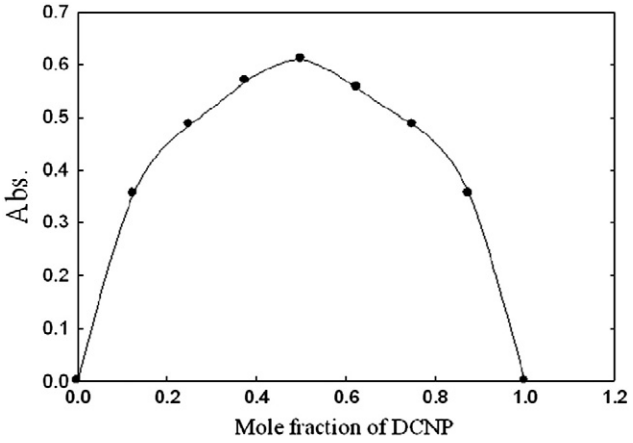


Fig. 3. Job's plot of 1:1 complex of 2AP with DCNP in AN.

between 2AP as proton acceptor and DCNP as proton donor in different solvents. The formation constant of the formed complex K_{PT} has been calculated. The solvation effect on K_{PT} was discussed and evaluated. Based on the rapidity and simplicity of the studied proton transfer reaction, we proposed in this work a sensitive and accurate spectrophotometric method for determination of 2AP in different solvents. In addition, the solid PT-complex (2AP-DCNP) has been isolated and characterized using elemental analyses and FTIR measurements.

2. Experimental

2.1. Physical measurements

2.1.1. Electronic spectra

The electronic spectra were recorded in the region 700–250 nm using UV–Vis Shimadzu UV-1601 spectrophotometer connected to Shimadzu TCC-ZUOA temperature controller unit (Japan).

2.1.2. Infrared spectra

The infrared spectra were measured as KBr discs on Bruker-Tensor 37 Fourier transform infrared spectrophotometer (USA), evacuated to avoid water and CO_2 absorption.

2.1.3. Elemental analyses

C, H and N contents were determined with the Micro analyzer Perkin Elmer 2400 (USA).

2.2. Chemicals

All chemicals used were of analytical grade. 2-aminopyridine was supplied by Acros organic, 2,6-dichloro-4-nitrophenol was supplied by Fluka. Acetonitrile and methanol were supplied by PAI-ACS. KBr was spectroscopic grade supplied by Aldrich.

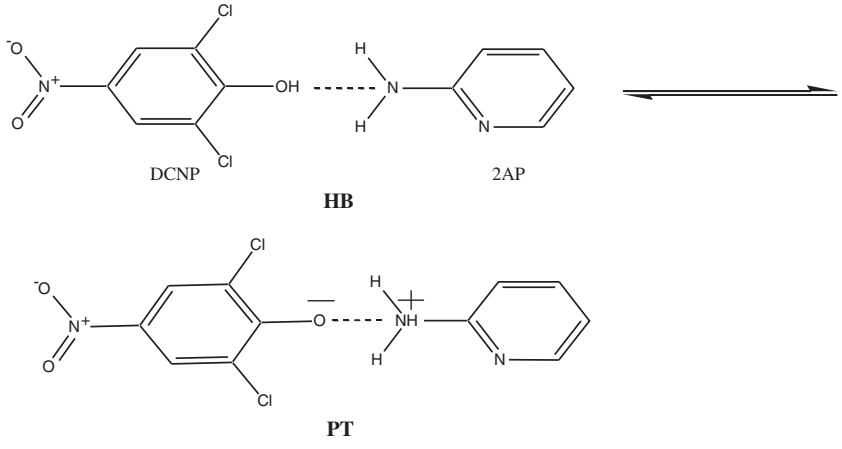
2.3. Preparation of the solid 1:1complex between 2AP with DCNP

The solid PT-complex (1:1) between 2AP and DCNP was prepared by mixing equimolar amounts of 2AP with DCNP in acetonitrile. The resulting complex solution was allowed to evaporate slowly at room temperature where the complex was isolated as yellow crystals. The separated complex was filtered off, washed well with acetonitrile and dried over calcium chloride for 24 h. Anal. Calc. for (DCNP-2AP) $C_{11}H_9Cl_2N_3O_3$ complex: C, 43.73%; H, 3.00%; N, 13.19%. Found: C, 43.64%; H, 3.20%; N, 13.19%. MP. 174–176 °C.

3. Results and discussion

3.1. Electronic spectra

The conversion of phenol in to the corresponding phenolate results in the bathochromic shifts of ^1L_a and ^1L_b bands and an increase in ε_{max} [25]. When a phenol forms proton transfer complex, the electronic spectrum resembles that of the phenolate ion. The electronic spectra of the proton transfer complexes of DCNP with various nitrogen bases were reported by Szafran et al. in different solvents where the phenolate ion of DCNP exhibited absorption band near 425 nm [9].



Scheme 1. Proton transfer equilibrium of 2AP-DCNP complex.

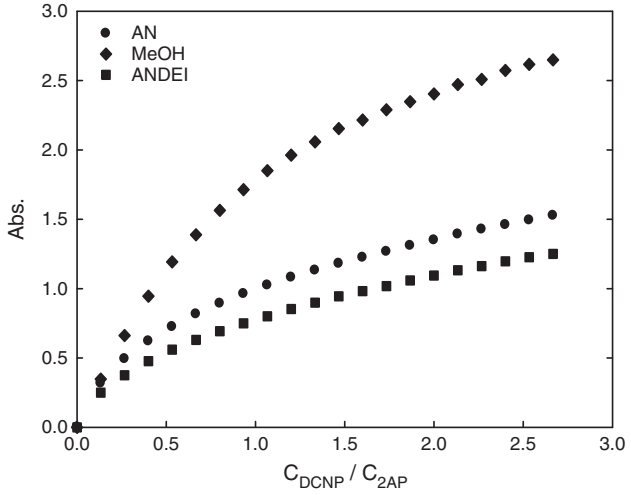


Fig. 4. Photometric titration curves of 1:1 complex of 2AP with DCNP in different solvents.

Figs. 1 and 2 represent the electronic absorption spectra of the proton transfer reaction between different concentrations of 2AP with 1×10^{-4} mol.L^{-1} DCNP in different solvents. A new band in the range 395–424 nm due to the π–π* transition of the formed PT-complex was observed. The increase in the intensity of absorbance with increasing 2AP concentration suggests that the prototropic equilibrium (Scheme 1) is shifted toward the hydrogen-bonded ion-pair $O^-\ldots HN^+$. It seems that the high basicity of 2AP (pK = 6.86) [26] as well as the high acidity of DCNP (pKa = 3.55) [27] are responsible for this situation. It is worth to mention that the blank used has the same concentration of DCNP to eliminate the possible overlap that may arise between the complex band and that of DCNP.

3.2. Composition of the PT-complex

Job's method [28] of continuous variation was used to identify the composition of the formed PT-complex between 2AP with DCNP in different solvents. The plots of the absorbance against the mole fraction of DCNP were presented in Fig. 3 where the maximum absorbance was recorded at mole fraction 0.5 indicating the formation of 1:1 PT-complex. Fig. 4 represents the spectrophotometric titration

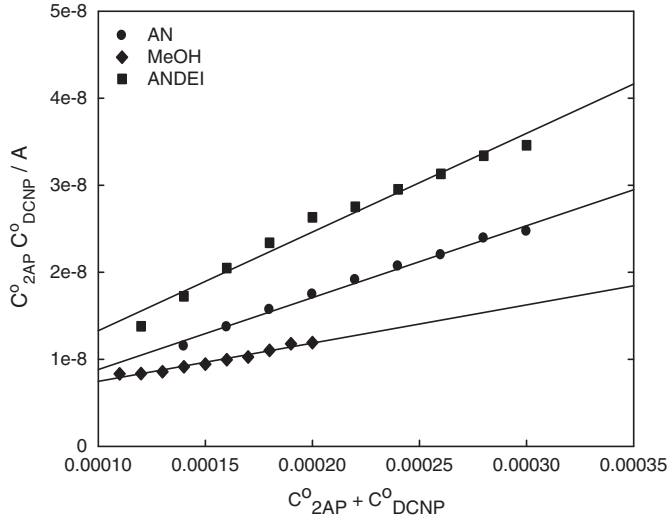


Fig. 5. Spectral determination of formation constants and molar extinction coefficients of 1:1 complex of 2AP with DCNP in different solvents.

Table 1
Formation constant, molar extinction coefficient and wavelength of 1:1 complex of 2AP with DCNP in different solvents.

Solvent	$K_{PT}\times10^{-4}$	$\varepsilon_{PT}\times10^{-4}$	λ_{max}
	L molL^{-1}	L mol^{-1}cm^{-1}	nm
AN	14.93 ± 2.08	1.21 ± 0.11	424
MeOH	1.43 ± 0.34	2.28 ± 0.21	396
ANDEI	2.02 ± 0.32	1.06 ± 0.03	423
ANDEII	5.82 ± 0.54	0.88 ± 0.09	423

[29] plots where two straight lines are produced intercepting at 1:1 ratio (proton donor: proton acceptor). Accordingly we can conclude from Figs. 3 and 4 that the PT-complex is formed based on a 1:1 stoichiometric ratio.

3.3. Formation constant of 1:1 complex of 2AP with DCNP (K_{PT})

Based on the formation of 1:1 proton transfer complex, Benesi–Hildebrand equation has been applied to estimate the proton transfer formation constant K_{PT} between 2AP and DCNP in different solvents [30].

$$\frac{C^\circ d C^\circ a}{A}=\frac{1}{K_{PT}\ \varepsilon_{PT}}+\frac{C^\circ d + C^\circ a}{\varepsilon_{PT}}$$

where C°d and C°a are the initial concentrations of the proton donor and proton acceptor respectively, and A is the absorbance of the PT-band. Plotting $\frac{C^\circ d C^\circ a}{A}$ versus (C°d+C°a) for the formed PT-complex, straight lines were obtained supporting our conclusion of the formation of the 1:1 complex (Fig. 5). From the slopes and intercepts of the plots, one can calculate K_{PT} and the molecular extinction coefficients ϵ_{PT}. The results are compiled in Table 1. As one observes in Table 1 both K_{PT} and ϵ_{PT} recorded high values confirming the formation of stable complex. An important finding from Table 1 is the highest value of K_{PT} in acetonitrile compared with those in methanol and binary mixtures. It seems that methanol exhibited dual roles in the studied PT-reaction through solvation of both 2AP as hydrogen bond donor (α = 0.98) and DCNP as hydrogen bond acceptor (β = 0.66) [31]. Under this condition, the competition among different molecular species resulting from a hydrogen-bonding interaction between the solute and solvent molecules becomes inevitable which hinders the PT-interaction between 2AP with DCNP and consequently decreases K_{PT}.

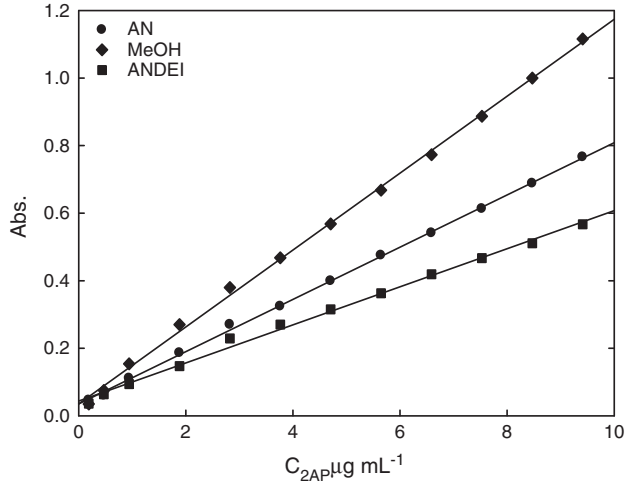


Fig. 6. Beer's law curves of 1:1 complex of 2AP with DCNP in different solvents.

Table 2
Quantitative parameters of 1:1 complex of 2AP with DCNP in different solvents.

Parameter	AN	MeOH	ANDEI	ANDEII
Beer's law limits, μg ml^{-1}	0.19–9.41	0.19–9.41	0.19–9.41	0.47–9.41
Limit of detection, μg ml^{-1}	0.08	0.11	0.20	0.27
Limit of quantification, μg ml^{-1}	0.27	0.37	0.62	0.90
Regression equation	$Y^*=0.077\,X+0.035$	$Y^*=0.144\,X+0.035$	$Y^*=0.056\,X+0.044$	$Y^*=0.042\,X+0.046$
Intercept, a	0.035	0.035	0.044	0.046
Slope, b	0.077	0.144	0.056	0.042
Confidence interval of intercept, α	±0.001	±0.002	±0.002	±0.002
Confidence interval of slope, β	±0.0007	±0.0014	±0.0018	±0.0013
Correlation coefficient, R^2	0.99	0.99	0.99	0.99

*Y is the absorbance for concentration, X in μg mL^{-1}.

Concerning acetonitrile, it seems that its high polarity is the predominating factor ($\pi^*=0.75$) [31] which increases K_{PT}. To confirm this assumption, the PT-reaction was carried out in the binary mixtures ANDEI and ACDEII, respectively. It has been found that in ANDEI K_{PT} is reduced up to 87% while in ANDEII is reduced up to 61% confirming that the polarizability of AN is the leading parameter in this case.

3.4. Application of the studied PT-reaction

3.4.1. Optimization of reaction time and temperature

The effect of temperature on the PT-reaction was studied by following the absorbance of the PT-complexes resulting from mixing 1.0×10^{-4} mol L^{-1} DCNP with various concentrations of 2AP. It has been found that 20 °C is the optimum temperature where the absorbance of the PT-complex recorded the highest and constant value. In addition, the complex was stable for more than 2 h.

3.4.2. Analytical data

Based on the formation of 1:1 PT-complex between DCNP and 2AP, we proposed in this section a simple, rapid and accurate spectrophotometric method for determination of 2AP. Hence, under the optimum reaction conditions Beer's plot at various 1:1 molar ratios between 2AP and DCNP was constructed (Fig. 6). The regression equations in different solvents were calculated by the least square method. In all cases Beer's law plots were linear with very small intercepts, slopes and good correlation coefficients in the general concentration range (0.18 to 9.41) μg mL^{-1}, Table 2. The limits of detection and quantification were calculated according to the IUPAC definition [32]. The calculated values were listed in Table 2. They recorded small values confirming high accuracy of the method. It has been found also that the confidence intervals of intercept and slope recorded small values confirming excellent linearity between the absorbance and concentration, Table 2.

The accuracy of the method was established by performing analysis of solutions containing four different amounts (within Beer's law limits) of 2AP and measuring the absorbance of their PT-complexes with DCNP in all solvents. The concentration of 2AP was determined from the regression equation and then calculated the recovery percentages, the standard deviation S, and relative standard deviation RSD. The recovery percentages recorder values near 100% with RSD ranging from 0.91 to 2.90 confirming high accuracy and precision of the proposed method, Table 3.

Comparison of the difference between the mean and true value ($X^- - \mu$) [33] with the largest difference that could be executed as a result of indeterminate error $\frac{\pm tS}{\sqrt{n}}$ has been carried out and the results were collected in Table 3. It has been found that ($X^- - \mu$)were less than $\frac{\pm tS}{\sqrt{n}}$ indicating that no significant difference exists between the mean and true values.

3.5. Infrared Spectra of 1:1 complex of 2AP with DCNP

The formation of 1:1 complex between 2AP with DCNP was ascertained from a comparison of the i.r. spectra of complex with that of 2AP and DCNP. The FTIR spectrum of the complex is shown in Fig. 7 where the asymmetric stretching vibration of the amino group is broadened and appeared at 3445 cm^{-1}. On the other hand, the symmetrical stretching vibration is also broadened and shifted to lower frequency at 3171 cm^{-1} compared with 3290 cm^{-1} in the i.r. Spectrum of 2-aminopyridin [34]. The disturbance of the amino group vibrations strongly confirms the formation of the PT-complex between the phenolic and amino groups of the proton donor and

Table 3
Precision and accuracy of the analytical method.

Solvent	Amount taken μg mL^{-1}	Amount found μg mL^{-1}	Rec.%	$\overline{X}$	SD	RSD	$\lvert\overline{X}-\mu\rvert$	$\pm\frac{tS}{\sqrt{n}}$	Confidence limits
AN	3.29	3.45	104.65	100.34	2.91	2.90	0.34	±4.63	100.34±4.63
	5.18	5.15	99.57						
	6.12	6.03	98.62						
	8.00	7.88	98.53						
MeOH	5.18	5.22	100.87	100.45	0.90	0.89	0.45	±1.43	100.45±1.43
	6.12	6.12	99.99						
	7.06	7.02	99.47						
	8.00	8.12	101.48						
ANDEI	3.29	3.37	102.37	100.62	1.70	1.70	0.62	±2.71	100.62±3.77
	5.18	5.24	101.14						
	6.12	6.16	100.66						
	7.06	6.94	98.30						
ANDEII	3.29	3.29	99.99	100.74	0.92	0.91	0.74	±1.46	100.74±1.46
	6.12	6.23	101.85						
	7.06	7.14	101.13						
	8.00	8.00	99.97						

$t=3.182$ for $n=4$ at 95% confidence level.
SD = standard deviation, RSD = relative standard deviation.

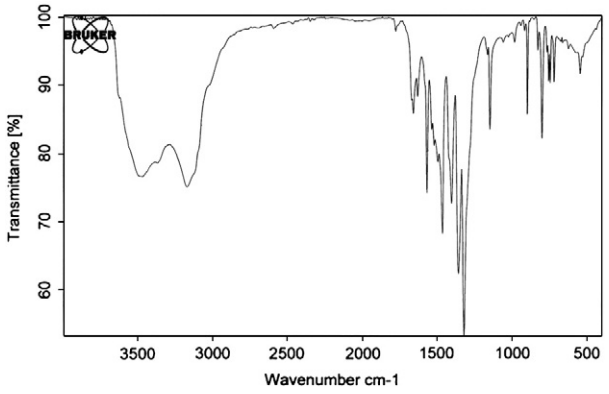


Fig. 7. FTIR spectrum of solid 1:1 complex of 2AP with DCNP in the range 4000–400 cm^{-1}.

proton acceptor. In addition, a weak band was recorded at 1612 cm^{-1} which can be ascribed to the asymmetric deformation of $N^{+}H_3$ vibration. One can also observe (Fig. 7) the presence of abroad and intense absorption in the 1600–800 cm^{-1} region. Its center of gravity ν_H lies at 1220 cm^{-1} which is characteristic of the hydrogen-bonded ion pair ($O^{-}....H_3N^{+}$) [35]. Moreover, the vibrational bands of the complex were shifted compared with those of the reactants. The stretching vibrations $\upsilon C=C$and $\upsilon C=N$are shifted to 1614 and 1562 cm^{-1} compared with 1595 and 1559 cm^{-1} for 2AP. Furthermore, the stretching vibrations of υCl are shifted to 848 and 898 cm^{-1} compared with 808 and 896 cm^{-1} for DCNP. These shifts also confirm the formation of the PT-complex (2AP-DCNP).

4. Conclusion

The present article introduced a spectral study on the PT-complex formation between 2AP with DCNP in different solvents where 1:1 PT-complex (proton donor: proton acceptor) was formed. Based on the simplicity and rapidity of the PT-reaction, a simple, rapid and accurate spectrophotometric method for determination of 2AP was proposed. Beer's law was obeyed in the concentration range 0.19–9.41 μg mL^{-1} with small values of both the limit of detection and limit of quantification. Moreover, the solid PT-complex was isolated and characterized by means of elemental analyses and FTIR measurements. These measurements confirmed that the interaction site with the OH of DCNP is the amino group of 2AP rather than the ring nitrogen.

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