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Spectroscopic studies on the proton transfer reactions of 4-hydroxy-2-oxo-1,2-dihydroquinolin-3-carbonitrile with different amines in acetonitrile

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ABSTRACT

Proton transfer reactions between 4-hydroxy-2-oxo-1,2-dihydroquinolin-3-carbonitrile (HQC) and propylamine (PA), triethylamine (TEA) and piperidine (Pip) have been studied spectro-photometrically in acetonitrile as a polar solvent. The molecular compositions of the formed complexes (I, II, and III) were determined using Job's and photometric titration methods. Minimum–maximum absorbances' method has been applied to estimate the formation constants of the formed complexes (K_{PT}). It has been found that K_{PT} reached higher value for HQC–TEA complex than PA and Pip ones. On the basis of the rapidity of the PT-reactions, a simple and accurate spectro-photometric method for determination of HQC was proposed. Beer's law was obeyed in the concentration range 0.19 to18.60 μg mL^{-1} with excellent correlation coefficients. The recovery percentages ranged from 99.63 to 99.99%. The solid complexes were synthesized and characterized using i.r., NMR spectroscopy and elemental analyses.

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 bio-molecular structures [5], controlling the speed of enzymatic reactions [6] as well as constructing supra-molecular structures [7]. Several physical properties of H-bonded complexes, e.g. excess of dipole moment (Δμ), change of ^{1}H, ^{13}C, ^{15}N chemical shifts (Δδ) and ^{35}Cl NQR frequency when plotted against Δp*K*a (p*K*a (B^{+}H) − p*K*a (AH)), 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].

Functionalized quinolines are important constituents of pharmacologically active compounds, as these systems have displayed a broad spectrum of biological activities such as antiasthmatic [14], antibacterial [15], antifungal [16], antimalarial [17], antiviral [18], and anti-inflammatory [19] activities. In addition, quinolines are valuable precursors used for the synthesis of nano- and meso structures with enhanced electronic and photonic properties [20–22]. Of special interest, a series of new quinolin-3-carbonitrile derivatives have recently been synthesized reported to show significant activity as excellent selective cytotoxicity towards SMMC-772 cell line [23], antitumor [24], a novel type of EGFR inhibitor [25] and potent inhibitors of TP12 kinase [26]. Keeping in view the biological and pharmaceutical importance of the above mentioned quinolines and in continuation to our work on proton and electron transfer [10–12,27,28], herein we are gratified to report our results on the spectroscopic studies of the proton transfer reactions between 4-hydroxy-2-oxo-1,2-dihydroquinolin-3-carbonitrile (HQC) and different amines including propylamine (PA), piperidine (Pip) and triethylamine (TEA) in acetonitrile. In addition, we will study the molecular compositions of the formed complexes using Job's and photometric titration methods. Also, the formation constants of the complexes will be investigated and evaluated using the minimum–maximum absorbances' method. Furthermore, a sensitive spectroscopic method for estimating HQC has been chosen based on the fast production of the formed proton transfer complexes. The synthesis and characterization of the solid proton transfer complexes are important aims of this work.

2. Experimental

2.1. Materials, instrumentation and physical measurements

All chemical used were of analytical grade. Propylamine (PA), triethylamine (TEA) and pipridine (Pip) were supplied by Acros organic. Acetonitrile was supplied by Panreac.

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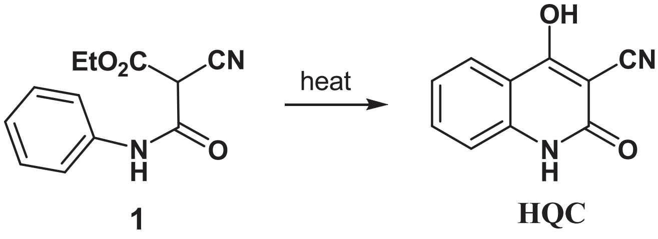


Scheme 1. Synthesis of HQC.

The electronic absorption spectra were recorded in the region (700 to 250) nm using UV–vis model Shimadzu UV-1601 with personal spectroscopy software version 3.7, connected to Shimadzu TCC-ZUOA temperature controller.

The infrared spectra of the prepared solid complexes were measured as KBr disks on Shimadzu FTIR-8400 S Fourier transform infrared spectrophotometer (Japan).

^{1}H NMR (600 MHz) and ^{13}C NMR (150 MHz) spectra were measured on a Bruker DPX spectrometer using 10 mg of the sample in DMSO-d_6 (0.5 mL) as solvent and TMS as an internal standard; chemical shifts are expressed as δ ppm.

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

2.2. Synthesis of HQC and the solid complexes

A suspension of ethyl 2-cyano-3-oxo-3-(phenylamino)-propanoat (**1**) [29] (2.60 g, 11.2 mmol) in 1,2-dichlorobenzene (40 mL) was refluxed for 1 h. After cooling to room temperature, the resulting solid product was collected by filtration, washed well with dioxane, dried and recrystallized from methanol to HQC (**2**) (Schemes 1) [29,30] as colorless crystals, yield (1.68 g, 81%); mp. 290–293 °C.

The solid 1:1 complexes of HQC with PA, TEA and Pip were synthesized by mixing equimolar amounts of both HQC and amine in acetonitrile and the resulting complex solutions were left standing overnight at room temperature. The solid complexes were separated as colorless crystals and dried over anhydrous calcium chloride for 24 h. The analytical data of the complexes (C, H, and N content) along with some of the physical properties are listed in Table 1.

2.3. Preparation of standard solutions of the proton donor and proton acceptor

Stock solutions of the proton donor (HQC, $1.0\cdot10^{-3}$ mol L^{-1}) and the proton acceptors (PA, TEA and Pip, $1.0\cdot10^{-3}$ mol L^{-1}) were freshly prepared before each series of measurements by dissolving precisely weighed amounts in the appropriate volume of acetonitrile. Solutions for spectroscopic measurements were made by mixing appropriate volumes of stock donor and acceptors solutions and pure solvent.

2.4. Determination of the formation constants of the complexes (K_{PT})

For the purpose of UV–vis spectral determination of the formation constants (K_{PT}), the minimum–maximum absorbances' method was applied according to the following procedure. An amount of 1 mL of freshly prepared standard stock solutions of HQC in acetonitrile ($1.0\cdot10^{-3}$ mol L^{-1}) was transferred into a series of 10 mL calibrated flasks. To each of these were added different concentrations of freshly prepared stock amines solutions ($1.0\cdot10^{-3}$ mol L^{-1}) and diluted to the mark with acetonitrile. The absorbance of the mixture solutions was recorded against a solvent blank. The lowest amine concentration led to the minimum absorbance of the complex ($A_{min.}$). The concentration of the amine was increased gradually and the absorbance was recorded at the maximum absorption band of the complex ($A_{mix.}$) until the highest and constant absorbance of the formed complex was obtained ($A_{max.}$). The complex formation constants (K_{PT}) were estimated as given by the following equation [12,27,28,31].

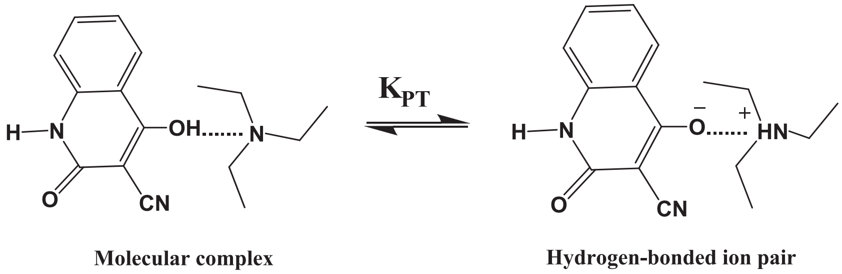
$$A_{\mathrm{max.}} = A_{mix.} + \frac{A_{mix.} - A_{\mathrm{min.}}}{K_{PT}\cdot C_{a\,\mathrm{mine}}} \tag{2}$$

where $A_{max.}$ and $A_{min.}$ are the maximum and minimum absorbances of the proton transfer complex. $A_{mix.}$ is the complex absorbance between $A_{max.}$ and A_{min}. C_{amine} is the concentration of the added amine in moles per liter. The set of equilibrium constants was averaged to extract the central K_{PT} value with minimum error.

3. Results and discussion

3.1. Electronic spectra

The electronic spectra of $1.0\cdot10^{-4}$ mol L^{-1} HQC and the proton transfer complexes resulting from mixing $1.0\cdot10^{-4}$ mol L^{-1} HQC



Scheme 2. Proton transfer equilibrium.

Table 1
Elemental analyses, stoichiometry, melting point and color of complexes: (I) HQC–PA, (II) HQC–TEA and (III) HQC–Pip.

Complex	Expected			Found			Stoichiometry	mp (°C)	Color
	%C	%H	%N	%C	%H	%N			
I	63.15	6.88	17.00	62.98	6.91	16.88	1:1	227–229	Colorless
II	66.44	7.96	14.53	66.11	8.03	14.43	1:1	141–143	Colorless
III	66.35	6.27	15.48	66.29	7.71	15.14	1:1	235–236	Colorless