Available online at www.sciencedirect.com
ScienceDirect
Spectrochimica Acta Part A 67 (2007) 1210–1219
SPECTROCHIMICA ACTA PART A
www.elsevier.com/locate/saa

Electronic absorption study on acid–base equilibria for some keto and thioketo pyrimidine derivatives Experimental and theoretical evidence of enolization and solute–solvent interactions

H. Kılıç *

Department of Physical Chemistry, Faculty of Sciences and Letters, Marmara University, Ziverbey 34722, Istanbul, Turkey

Received 4 August 2006; received in revised form 2 October 2006; accepted 5 October 2006

Abstract

The UV–vis spectra of recently synthesized 1-amino-5-benzoyl-4-phenyl-1H-pyrimidine-2-one, (**I**), and 1-amino-5-benzoyl-4-phenyl-1H-pyrimidine-2-thione (**II**), were studied in aqueous methanol (5%, v/v, methanol) and pure methanol. The nature of the electronic transitions and the role of carbonyl oxygen of **I** and thiocarbonyl sulfur of **II** in the behavior of the observed UV–vis spectra were discussed.

The carbonyl group at position 2 of **I** and the thiocarbonyl group of **II** were found to be enolized instead of protonation. Quantum chemical calculations showed agreement with the experimental evidence. However, the carbonyl group of the benzoyl moiety at position 5 of both compounds underwent neither enolization nor protonation.

Acid–base equilibria of the compounds against varying pH have been examined in detail. The pK_a values of all related equilibria were determined at room temperature and an ionic strength of 0.10 M from the pH-dependence of the absorbance values using the Henderson–Haselbalch equation and graphical logarithmic analysis. The mean acidity constants for the protonated forms of the compounds were determined as pK_{a1} = 4.214 and pK_{a2} = 6.678 for **I** and pK_{a1} = 3.739 and pK_{a2} = 6.258 for **II**. The mean acidity constants (pK_{a3}) for the enol form of **I** and the thioenol form of **II** were determined as 11.278 and 11.063, respectively. The preferred dissociation mechanisms were discussed based on the data of UV–vis spectroscopy and a mechanism was proposed for each compound.

The formation of intramolecular and intermolecular hydrogen bonding were found with **I** but not with **II**. The intramolecular bonding stabilizing the enol form was favoured at pH values corresponding to pK_{a1} and above. On the other hand, the intermolecular hydrogen bonding stabilizing the free form of the carbonyl group was favoured at all pH values.

Keywords: Hydrogen bonding interactions; Acidity constant; Enolization; Carbonyl; Thiocarbonyl; UV/vis spectroscopy

1. Introduction

Pyrimidine bases are minor constituents of nucleic acids. The chemistry of these compounds has been the subject of extensive research because of their applications in molecular biology and medicine [1–5]. These compounds display antibacterial, antifungal, antiviral, insecticidal and miticidal activities [6,7].

Considering the importance of the pyrimidine derivatives, recently synthesized 1-amino-5-benzoyl-4-phenyl-1H-pyrimidine-2-one, (**I**), and 1-amino-5-benzoyl-4-phenyl-1H-pyrimidine-2-thione (**II**) may display novel biological and medicinal features, as well. The structures of the compounds studied are given in Fig. 1.

As shown in Fig. 1, the compounds are analog of each other and containing amino and carbonyl functional groups that are important in biochemical compounds [8,9]. These compounds establish one of the most popular model systems for studying hydrogen bonding formation but to date no literature data is available about the properties of these compounds.

We studied the electrochemical behavior of these compounds previously [10]. Later, we investigated the acid–base properties of these compounds by using potentiometric titration method [11]. However, we could not determine any constants related with the carbonyl and thiocarbonyl groups of compounds **I** and **II**, respectively. Thus, they are still unknown, that

* Tel.: +90 216 346 4553; fax: +90 216 347 8783.
E-mail address: hkilic@marmara.edu.tr.

1386-1425/$ – see front matter © 2006 Elsevier B.V. All rights reserved.
doi:10.1016/j.saa.2006.10.010

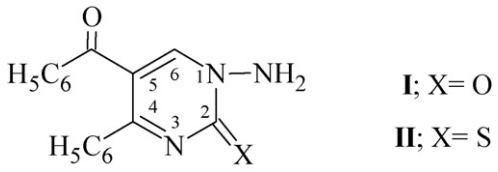

Fig. 1. Molecular structures of the compounds.

necessitates comprehensive study of acid–base properties of these compounds.

Acidity constants (pK_a values) of a reactant in a chemical treatment are useful physico-chemical measurements describing the extent of dissociation of functional groups with respect to pH. These parameters are important to choose appropriate acidic or basic reagents in drug discovery and development in that knowledge of the dissociation state of a particular functional group is critical to understand the pharmacokinetic and pharmacodynamic properties of new drug substances [12].

The analog of the compounds **I** and **II**, e.g. barbituric and thiobarbituric acid, have also received considerable attention in analytical chemistry because of their high sensitivity toward many metals and organometals, especially in spectroscopic studies [13–17]. It is therefore important to understand molecular properties and certain chemical phenomena, such as the binding of these molecules to environmental matrices for designing new methods of synthesis and characterization of metal complexes.

In view of the above discussion, the present paper reports UV–vis spectrophotometric investigation of acid–base equilibria of the compounds **I** and **II** in detail against varying pH, in 5% (v/v) methanol–water and in pure methanol, in order to (i) gain some insight about the species that might be present in solution at different pHs, (ii) explain the mechanism of protonation–deprotonation of such compounds and determine their acidity constants, (iii) investigate the characteristics of hydrogen bonding interactions.

In order to establish the dissociation constants of organic compounds, the UV/vis spectrophotometric method affords high precision and accuracy. To better understand some parts of the above experimental results a computer-assisted quantum chemical calculations are also conducted on the compounds interested in this study.

2. Experimental

2.1. Reagents and materials

The synthesis of the compounds were described elsewhere [6,7]. Purity was tested as described elsewhere [11]. All chemicals were obtained from Fluka, as reagent grade materials. Triple-distilled water that was used in the preparation of the aqueous methanol solutions were prepared as described previously [11]. Methanol was used after distilling.

2.2. Instrumentation

Studies were carried out by a Shimadzu 1601 PC UV/VIS spectrophotometer with quartz cells (1 cm path length). Measurements were repetaed in some cases by a double beam Shimadzu 240 ultraviolet visible spectrophotometer. The slit width is 0.2 nm for both instrumensts. The pH of the solutions were measured by a Schott CG 841 digital pH meter with an accuracy of ±0.001 units. The meter was equipped with a combined pH electrode filled with a solution of 3 M KCl and standardized using standard aqueous buffers (pH 4.00, 7.00 and 9.0) as described in the literatures [18–20]. An Eppendorf micropipette was used for the addition of solutions. A Sartorius A120 S analytical balance (sensitivity of ±0.0001 g) was used for measuring the masses of the compounds (**I** and **II**) and chemicals.

2.3. Measurements

The compounds are poorly soluble in water, therefore, the experiments were performed in a mixture of methanol–water (5 %, v/v, methanol). The experiments were also repeated in pure methanol medium to see qualitatively, how the spectral characteristics change. Thus, the stock solutions of the compounds were prepared in an appropriate volume of pure methanol.

A Britton–Robinson (B.R.) buffer solution [21] composed of a mixture of acetic acid, orthophosphoric acid and boric acid (each 0.04 M) was prepared to buffer the experimental solutions. Buffer solutions with pHs from 3.0 to 11.0 were prepared by adding different volumes of 0.10 NaOH solution to the stock B.R. buffer solution. For experiments performed in pure methanol, the B.R. buffer did not contain orthophosphoric acid due to the precipitation upon addition of sodium hydroxide. The pH values measured in aqueous methanol and pure methanol media were not corrected and we used the symbol pH (defined as $-\log[H^+]$) in all cases.

Experimental solutions were prepared by diluting the appropriate amount of stock solution of the compounds with the Britton–Robinson buffer to give a compound concentration in the range from 2.060×10^{-5} to 5.630×10^{-5} M for **I** and from 3.611×10^{-5} to 7.962×10^{-5} M for **II**. The final alcohol content was adjusted to 5% (v/v).

The absorption spectra of the working solutions were recorded at constant ionic strength of 0.10 M with LiCl at room temperature. In both aqueous methanol and pure methanol, the UV/vis spectra were taken from 500 to 230 nm for each compound. The reference beam contained a blank of buffer containing the same amount of pure methanol as the solvent.

2.4. Computational details

Quantum chemical calculations were performed at the B3LYP/6-31 + G(d,p) level using Gaussian 03 software on personal computer [22].

2.5. Determination of acidity constants

The acidity constants for the protonated form of the compounds were determined from their spectral behavior in buffer solutions of varying pHs, at selected wavelengths, by using the Henderson–Haselbalch equation as described by Albert and Serjeant [23]. For this purpose, the pH range from 3.0 to 11.0 was