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Research Article

Protonation Constants of Valin in Different Aqueous Solutions of Dimethylsulfoxide

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ABSTRACT

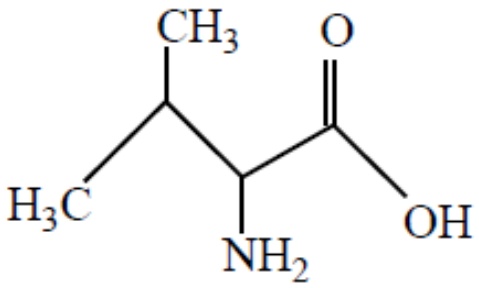
The protonation constants of valin (K1 and K2) was determined in binary mixtures of water with dimethylsulfoxide containing (0, 10, 20, 30, 40, and 50) % (v/v) using a combination of potentiometric method at 25 ˚C and constant ionic strength (0.1mol ·dm-3 sodium perchlorate). The protonation constants were analyzed using the normalized polarityparameter (ETN) and Kamlet, Abboud, and Taft (KAT) parameters. A very good linear correlation of log K versus the normalized polarity parameter was obtained. Dual-parameter correlation of log K versus π*(dipolarity/polarizability) and R (hydrogen-bond donor acidity) as well as π* and (hydrogen-bond acceptor basicity) also gives good results in various aqueous organic solvent mixtures. Finally, the results are discussed in terms of the effect of the solvent on the protonation constants.

Keywords: Solvent Effect; Valine; Tautomeric; Dissociation Constant; Dimethylsulfoxide.

1. Introduction

Amino acids are formally named by the IUPAC-IUBMB Joint Commission on Biochemical Nomenclature [1]. The systematic names and formulas given refer to hypothetical forms in which amino groups are protonated and carboxyl groups are

dissociated. This convention is useful to avoid various nomenclatural problems but should not be taken to imply that these structures represent an appreciable fraction of the amino-acid molecules. They can be classified according to the locations of the core structural functional groups, as alpha- (α-), beta- (β-), gamma- (γ-) or delta- (δ-) amino acids; other categories relate to polarity, ionization, and side chain group type (aliphatic, acyclic, aromatic, containing hydroxyl or sulfur, etc.). In the form of proteins, amino acid residues form the second-largest component (water being the largest) of human muscles and other tissues Beyond their role as residues in proteins, amino acids participate in a number of processes such as neurotransmitter transport and biosynthesis. The acid-base behavior of nucleotides, nucleosides, bases, and polynucleotides is essential to deduce the speciation and the possible conformational changes with pH or the amount of organic solvent in solution [2]. Acid dissociation constants are among the most useful physicochemical measurements describing the extent of ionization of functional groups with respect to pH. This parameter is important in research areas such as pharmaceutical drug discovery and development, where it often has a vital role in understanding the pharmaco dynamic properties of new drug substances.5-9 processes occur in solution. In a variety of chemical fields such as chemical synthesis, solvent extraction, liquid chromatography, etc., binary solutions of water and organic solvents are used [3].



Scheme 1: Chemical Structures of Valin

Aqueous organic solvent, mainly methanol and ethanol, mixtures have been widely used due to the sparingly or insolubility of many compounds in pure water as solvent [3]. Further, any physicochemical property of solutions can be easily varied by changing the compositions of water or the organic solvent in the mixtures. However, chemists have usually attempted to understand solvent effects in terms of polarity, defined as the overall solution capabilities that depend on all possible (specific and nonspecific) intermolecular interactions between solute and solvent molecules. Many reports on solvent polarity scales have been published in the last few decades.10 Previously, the solvent effect on the protonation equilibrium was believed to be guided chiefly by electrostatic interactions (Born model).11 However, recent studies have revealed that the change in macroscopic properties such as the dielectric constant of the solvent cannot be the sole factor.[4]10 It is desirable to develop other empirical functions to take into account the complete picture of all intermolecular forces acting between solute and solvent molecules [5].

In continuation of our previous work, in this study the protonation constants of adenine and adenosine have been determined in different aqueous methanol and ethanol mixtures to examine the dependence of acid-base equilibria on solvent composition [6].

2. Experimental

2.1. Chemicals Valin ($C_5H_{11}NO_2$)

(Scheme 1) was obtained from protein as analytical reagent grade materials and used without further purification [7]. dimethylsulfoxidel was from Merck (reagent grade) and was used as received. Sodium perchlorate was from Merck and was dried under vacuum at room temperature for at least 72 h before use [8].

NaOH solution was prepared from a titrisol solution (Merck). Perchloric acid was from Merck and was used as supplied. All dilute solutions were prepared from double-distilled

water with a specific conductance equal to (1.3 (0.1) S Cm^{-1} Apparatus. The electromotive force was measured using a Metrohm mod el 781 pH ion-meter Procedure. All measurements were performed at 25°C and a constant ionic strength of 0.1 mol. Dm^{-3} sodium perchlorate [9]. The protonation constants were evaluated from the measurements of absorbance versus emf by titration of 25 mL of valin with 0.1 mol dm^{-3} sodium hydroxide solution with both the same ionic strength and mole fraction of organic solvent [(0 to 50) % dimetylsulfoxide v/v]. In the first step, the electrode system calibration was performed by Gran's method. For this purpose, a measured amount of an acidic solution, at the same condition of temperature,ionic strength, and solvent composition to be used in later experiments, was placed in the doublewall thermostatted vessel [10].

The electrode was immersed in the solution in the vessel, and the acidic solution was titrated with a strong base (0.1 mol ·dm^{-3}NaOH). The potential was allowed to stabilize after each addition of the titrant, and the recorded emf values were then used to obtain *E*° [11]. The procedure was continued to pH = 2.5(lower than the p*K* of each base).[12] In the second step, 25 mL of an acidic solution (0.01 mol dm^{-3} $HClO_4$) of valin at the same conditions of temperature, ionic strength, and solvent composition was titrated with a sodium hydroxide solution (0.1 mol ·dm^{-3}). The emf and the absorbance [in the interval of (250 to 310) nm] values were then determined. The procedures were repeated in different compositions of the organic solvents [13].

The recorded emf values were then converted to pcH (-log[H^+]) using a method described in the literature. In acidicsolution, the measured potential of the cell, *E*cell, glass elec./HClO4-$NaClO_4$ in water-organic solvent // NaCl-$NaClO_4$ can be written as

$$E\text{cell (mV)))} = E\text{cello} + k \cdot \log [H_+] + k \cdot \log \gamma H_+ + E\text{LJ} \quad (1)$$

where E°cell is the standard potential of the cell; ELJ is the liquid junction potential; k 2.303RT/F in which R, T, and F have the usual meaning; and γH^+ is the activity coefficient of

the hydrogen ion [14]. Difficulties in computing the activity coefficients of the hydrogen ion in various aqueous mixtures of organic solvents lead to measurement of emf (electromotive force) versus H+ concentration in solution. Because the ionic strength of the solution is kept constant, the activity coefficient of the hydrogen ion is constant too [15]. The non-ideality of solutions is then included in Ea′ (the specific constant of the potentiometric cell in the acidic region), so:

$$Ecell = Ea' + k \cdot \log [H+]. \quad (2)$$

Where E'a is $E°$cell + $k \cdot \log \gamma$H+ + ELJ. The use of a glass electrode (with an aqueous inner solution) in non-aqueous media introduces a deviation from ideality, but it has been shown that the deviation is negligible and that the glass electrode is always usable in such media to measure H+ concentrations with a linear relation of Ecell versus log [H+].[16,19,20] In the acidic region, the hydrogen ion concentration can be expressed as:

$$[H+]) (M\text{HClO}_4\ V0 - M\text{NaOH}V1)/(V0 + V1) \quad (3)$$

where MHClO$_4$ and MNaOH are the molarities of perchloric acid and sodium hydroxide, and V0 and V1 are the initial volume of perchloric acid and the added volume of sodium hydroxide solution, respectively [17]. Finally:

$$pcH) (Ea' - Ecell)/k \quad (4)$$

3. Result and discussion

The protonation constants of valin has been determined titration was conducted using the computer program Squad [22,23]. The data in the computer program were fitted to eq 5 by minimizing the error square sum of the difference in the experimental absorbances and the calculated ones. The program allows calculation of the protonation constants with different stoichiometries.

The number of experimental points (absorbance versus pcH) was more than 35 (maximum 50) for each titration run. During the experiments, the solutions were stable, and the absorbance values did not change with time. The results obtained using and potentiometric pH titrations for the various acidity constants of the proton donors of valin in different aqueous solutions of dimethylsulfoxide, eq 5, are listed in 1together with the values reported in the literature for comparison. [24,25]

$$H_nL_{n-1} + H^+ \rightleftharpoons H_{1+n}L_n K_{1+n} = [H_{1+n}L_n]/[H_nL_{n-1}][H^+] \quad (5)$$

Where L represents adenine or adenosine and *n* may be 0, 1, or 2 for the different protonation equilibria of the bases. In Figure1, the species mole fractions of both systems in different pH are shown in pure water. With little differences, the protonation constant values obtained in this work are in agreement with those reported before. The differences are possibly due to the different experimental method and the different background electrolyte used. It was proposed that adenine shown in Scheme 1 may combine with its first and second protons from N9 and N1 sites, respectively. Also, a third proton is combined in a very acidic pH range from the N7 site. However, adenosine may release one proton at the ribose group (in a very alkaline pH range) and N1 site in the purine moiety, respectively. It should be noted that the release of the third proton from the N7 site in valin (pK =12).

Table 1. Average Values of the Protonation Constants of valin at 25 °C (0.1 mol ·dm-3 NaClO4) and Different Aqueous water Mixturesa

water % (v/v)	log K_1	log K_2
0	9.27	2.29
10	9.41	2.34
20	9.58	2.35
30	9.63	2.50
40	9.87	2.75
50	9.96	2.79

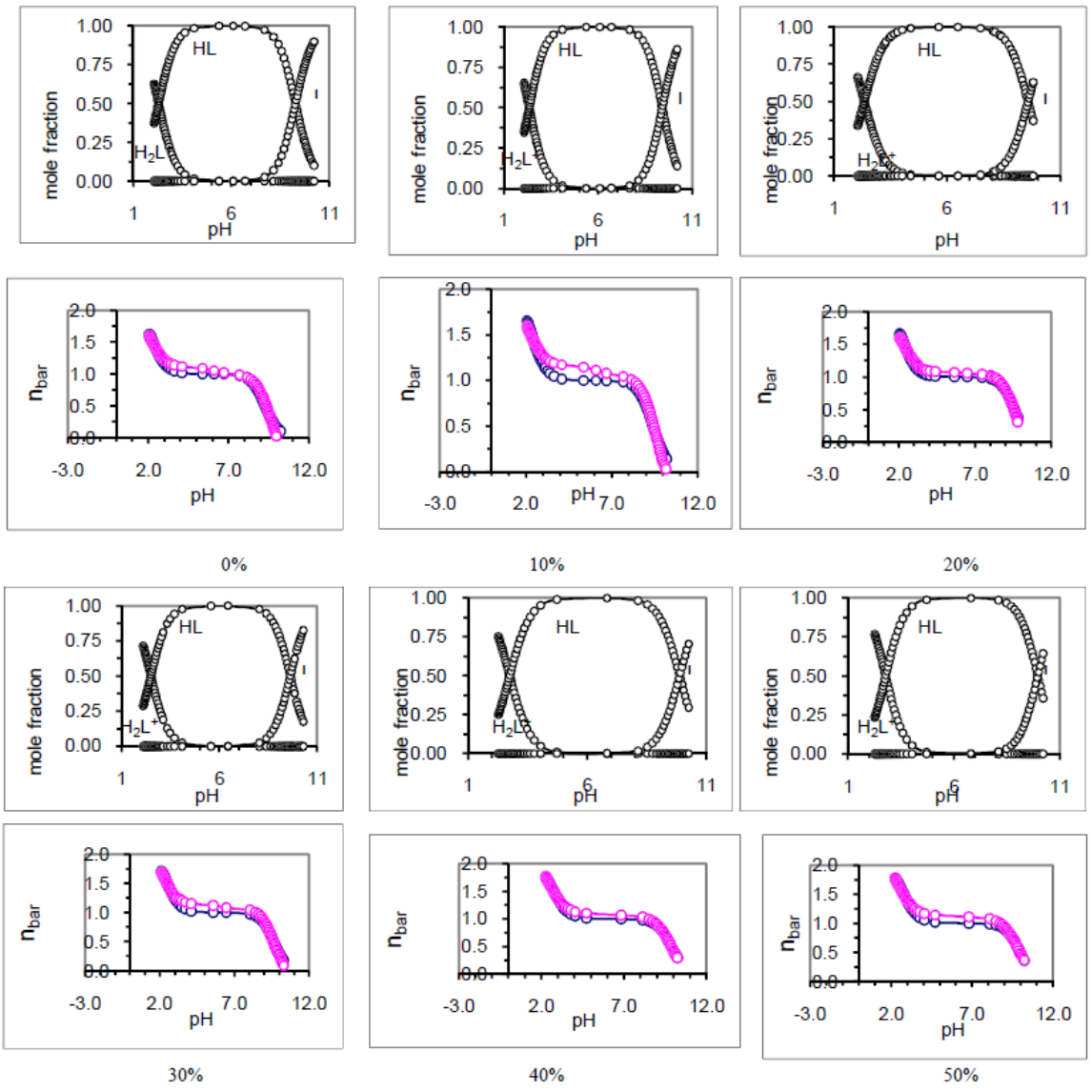


Fig. 1. Distribution diagrams of the different species of valin in dimetylsulfoxide at 25 ˚C and ionic strength of 0.1 mol ·dm-3 $NaClO_4$.

Table 2. Solvatochromic Parameters and the Dielectric Constants of Different Aqueous Dimethylsulfoxide Mixtures at 25 ˚C

DMSO%	α	β	π^*
0	1.17	0.47	1.09
5	1.11	0.46	1.1
10	1.07	0.47	1.1
15	0.99	0.48	1.11
20	0.94	0.51	1.11
25	0.88	0.53	1.12
30	0.82	0.56	1.12
35	0.76	0.58	1.12
40	0.7	0.6	1.12
45	0.64	0.61	1.12
50	0.59	0.62	1.12

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