

Molecular Heteroconjugation Equilibria in (*n*-Butylamine + Acetic Acid) Systems in Binary (Dimethyl Sulfoxide + 1,4-Dioxane) Solvent Mixtures

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The acidity constants of molecular acid, $K_a(\text{HA})$, cationic acid, $K_a(\text{BH}^+)$, as well as the equilibrium constants of anionic homoconjugation, K_{AHA^-} , cationic homoconjugation, K_{BHB^+} , and molecular heteroconjugation, K_{AHB} , have been determined in (*n*-butylamine + acetic acid) systems without proton transfer in binary [dimethyl sulfoxide (DMSO) + 1,4-dioxane (D)] solvent mixtures. The constants were determined by using the potentiometric titration method at a fixed ionic strength. It is concluded that the molecular heteroconjugation constants in the mixed solvent systems studied are linearly related to the 1,4-dioxane content. Furthermore, in the (acid + base) systems without proton transfer, the direction of titration (direct $\text{B} + \text{HA}$ or reverse $\text{HA} + \text{B}$) has been found to affect the precision of determination of reliable values of molecular heteroconjugation constants. Moreover, it has been found that the relative dielectric constants of the solvent mixtures studied change linearly as a function of solvent composition, as well as solvent components do not show interactions of solvent–solvent type.

KEY WORDS: acetic acid; acid–base equilibria; binary solvent mixtures; dimethyl sulfoxide; *n*-butylamine; potentiometric titration method; 1,4-dioxane.

1. INTRODUCTION

The acid–base interaction together with ongoing processes of hydrogen-bond formation are crucial for the formation of structures of biomolecules

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and biochemical reactions, as reflected by the rapidly increasing number of reports on the subject [1,4]. In non-aqueous media, relatively, well-explored are equilibria of acid–base dissociation of both molecular (1) and cationic acids (2), as well as those of anionic homoconjugation (3), and more recently, of cationic homoconjugation (4):



However, far less attention has been focused on heteroconjugation equilibria in these media, especially in aprotic binary solvent mixtures. In these media, in (B + HA) systems, where B is a proton acceptor (an organic base) and HA is a molecular acid or a phenol, the following equilibria of molecular heteroconjugation (5) can be present:



The location of a proton within the BHA complex depends on relative strength of the acid and base and on the medium's properties. For the base B, using a weak proton donor affords a complex with a weak asymmetric hydrogen bond, wherein the proton remains at the donor molecule (a complex without proton transfer). Appropriate selection of the strength of the acid (HA) and base (B), as well as of the medium enables freezing of the proton-transfer reaction at a stage of partial proton transfer to produce a hydrogen-bond stabilized molecular complex. These systems are referred to as systems without proton transfer (PT).

On the other hand, in analytical chemistry there is an upsurge of interest in binary solvent systems in which solvent–solvent interactions are mostly responsible for modulating the properties of these mixtures. Also, the solvent–solute interactions in mixed solvents are more intricate than those in simple solvents, resulting from deviations from the Born equation and structural changes in solvents. These features induce such phenomena characteristic of mixed solvent systems as specific geometry of charge distribution in ions [5], variations in auto-dissociation constants of solvents [6], and preferential solvation [7]. One of the outcomes of these phenomena includes non-typical variations of the acid–base equilibrium constants in binary solvent systems.

In view of the above-mentioned lack of literature evidence, there have been experimental efforts to establish relationships between the acid–base equilibrium constants (pK_a 's), in a particular mixed solvent, and its composition. The most frequently studied systems in this respect are (water + alcohol) mixtures [8]. Some authors [9,10] describe the relationships between pK_a of acids and relative dielectric constants (ϵ^{-1}), as being almost linear, while others [11,12] consider these relationships as being non-linear. Far less attention has been given to binary systems consisting of non-aqueous solvents. The results obtained so far for this type of systems are also divergent, some of them demonstrating a linear dependence between pK_a and mole fraction, while others are showing non-linear relationships [13,14]. Similar to acidity constants, some authors describe a non-linear nature of variations of the anionic homoconjugation constants as a function of composition of the binary solvent system [15–18].

This work is a continuation of a series of scheduled investigations into acid–base equilibria, especially those of molecular heteroconjugation in binary mixed solvent systems [19]. The primary objective of this work was to determine the acid–base equilibrium constant values, in particular, to those of molecular heteroconjugation, in (*n*-butylamine + acetic acid) systems in a non-aqueous binary mixed solvent consisting of dimethyl sulfoxide (DMSO) and 1,4-dioxane (D). Other aims were the determination of the influence of the composition of the binary solvent system (i.e., solvent polarity), and of the direction of titration on the molecular heteroconjugation constants in the systems without proton transfer. Potentiometric measurements were carried out in experimental systems, a direct one (B + HA) and the reverse (HA + B), where HA denotes acetic acid and B *n*-butylamine, in binary (dimethyl sulfoxide – DMSO + 1,4-dioxane – D) mixed solvent systems of the following varying mole fractions of diluent (D) in the principal solvent (DMSO): M₁ ($X_{\text{DMSO}}:X_{\text{D}}=0.9:0.1$), M₂ ($X_{\text{DMSO}}:X_{\text{D}}=0.8:0.2$), M₃ ($X_{\text{DMSO}}:X_{\text{D}}=0.7:0.3$), M₄ ($X_{\text{DMSO}}:X_{\text{D}}=0.6:0.4$), M₅ ($X_{\text{DMSO}}:X_{\text{D}}=0.5:0.5$), M₆ ($X_{\text{DMSO}}:X_{\text{D}}=0.4:0.6$), M₇ ($X_{\text{DMSO}}:X_{\text{D}}=0.3:0.7$), M₈ ($X_{\text{DMSO}}:X_{\text{D}}=0.2:0.8$).

2. MEASUREMENTS

Dimethyl sulfoxide (DMSO) and 1,4-dioxane (D) were purified, as reported elsewhere [20,21]. The binary solvent mixtures of predetermined composition were prepared on a volume basis and stored in bottles with ground-in stoppers, additionally tightened with a high-viscosity silicone grease and parafilm. Acetic acid and *n*-butylamine were purified as usual [22], and auxiliary materials were obtained as described previously [23]. The detailed description of our laboratory equipment for potentiometric

titrations, as well as the experimental procedure could be found in one of our previous papers [19,20,23,24].

All the equilibrium constants were calculated by using a STOICHIO computer program based on the general Kostrowicki and Liwo method [25–27].

The relative dielectric constant values of the solvent mixtures studied were determined by an electrochemical impedance method using the Schlumberger 1255 transmittance analyzer equipped with ATLAS 9181 accessory.

ATR FTIR spectra were recorded on a BRUKER IFS 66 Fourier transform infrared spectrometer equipped with a GatewayTMATR 6 Reflection Horizontal ATR Accessory Kit (Specac LTD). The internal reflection element was a zinc selenide ATR plate with an aperture angle of 45°. Spectra were recorded with a resolution of 1 cm⁻¹, and the number of scans was 64.

3. RESULTS

Prior to each series of potentiometric titrations in the *n*-butylamine–acetic acid systems, the glass electrode was calibrated in a standardizing 2,6-dinitrophenol–2,6-dinitrophenolate–tetra-*n*-butylammonium system. For this system, over the concentration range studied, there was a linear relationship among the potential difference, *E*, and the logarithm of the acid/base ratio, $\{E = f(\lg \frac{c_{HA}}{c_{A^-}})\}$; and the slope of the glass electrode response, *s*, matched that of the theoretical Nernst slope being in the range of 57–62 mV. As the *pK*_a value for the reference compound, 2,6-dinitrophenol, in the mixed solvent system was unknown, it was determined by a previously reported procedure [15].

Moreover, the measurements of relative dielectric constants by using the electrochemical impedance method were carried out over almost the complete mole-fraction range of dimethyl sulfoxide in 1,4-dioxane (except 0.1) in DMSO at 0.1 intervals, as well as for DMSO to have an insight into polarity variations in the media considered. The experimental relative dielectric constants were as follows: 46.60 (*X*_{DMSO} = 1.0), 40.64 (*X*_{DMSO} = 0.9), 33.18 (*X*_{DMSO} = 0.8), 30.10 (*X*_{DMSO} = 0.7), 24.81 (*X*_{DMSO} = 0.6), 20.23 (*X*_{DMSO} = 0.5), 17.61 (*X*_{DMSO} = 0.4), 12.02 (*X*_{DMSO} = 0.3), 9.26 (*X*_{DMSO} = 0.2), 6.94 (*X*_{DMSO} = 0.1), and 2.21 (*X*_{DMSO} = 0.0). In Fig. 1 a plot is shown presenting the relative dielectric constants vs. mole fraction of dimethyl sulfoxide in 1,4-dioxane (single points). The solid line represents the relationship corresponding to values expected on the basis of the additivity rule. Examination of this figure leads to the conclusion

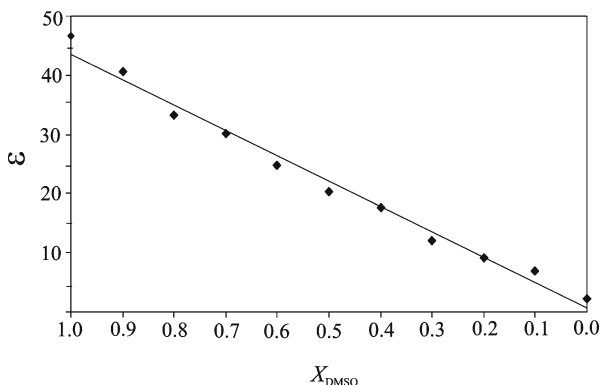


Fig. 1. Experimental relative dielectric constants, ϵ , vs. 1,4-dioxane mole fraction in DMSO.

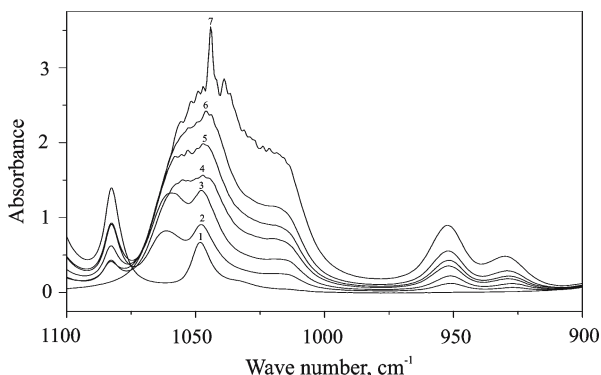


Fig. 2. ATR FTIR spectra of DMSO-1,4-dioxane mixtures in the range of 1070–1030 cm^{-1} . Mole fraction of DMSO increases from 0 to 1 from spectrum 1 to spectrum 7 (D, M₉, M₇, M₅, M₃, M₁, DMSO, respectively).

that the changes in the relative dielectric constant as a function of solvent composition are close to those postulated assuming the additivity principle. The correlation coefficient for the assumed linear relationship is $R = 0.9928$.

Furthermore, to check whether interactions of the solvent-solvent type exist between the solvent components of binary systems studied, ATR FTIR spectra of the solvents studied, as well as all binary solvent mixtures were carried out (Fig. 2). Liquid alkyl sulfoxides are characterized by a strong absorption band in the range of 1070–1030 cm^{-1} . In this case it is the 1044 cm^{-1} band for DMSO (Fig. 2).

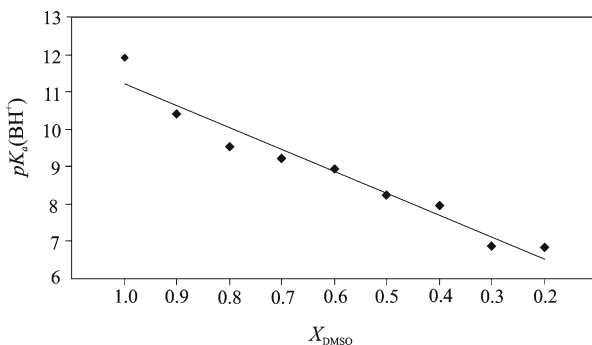


Fig. 3. Dependence between $pK_a(\text{BH}^+)$ and composition of the binary (DMSO + D) solvent mixture.

The acidity constants of the cationic and molecular acids, the cationic and anionic homoconjugation, and molecular heteroconjugation equilibrium constants in the mixed solvent systems studied are reported in Table I. The data presented in Table I show that the $pK_a(\text{BH}^+)$ values of the protonated *n*-butylamine decrease linearly (Fig. 3) with increasing 1,4-dioxane content in the mixtures. Consequently, the acidity constants of the protonated *n*-butylamine (i.e., the strength of the cationic acid) increase beginning from DMSO through mixtures of increasing 1,4-dioxane content up to M₈). Similar variations in the acid strength can be seen for the molecular acid. The acidity constants of acetic acid increase (i.e., $pK_a(\text{HA})$ values decrease) with increasing content of 1,4-dioxane. After accounting for standard deviations, the $pK_a(\text{HA})$ values can be regarded as linearly decreasing (Fig. 4).

For comparison, it was also found [22] that the pK_a values of BH^+ and HA studied in this work change in different solvents according to the donor numbers of solvents. The pK_a values of the protonated *n*-butylamine (cationic acid) are 18.26, 16.95, 11.92, 9.70, and 11.22 in acetonitrile (AN), propylene carbonate (PC), acetone (AC), dimethyl sulfoxide (DMSO), and methanol (MeOH), respectively. The order of the pK_a values of molecular acid (acetic acid) is the same as observed for cationic acid except for the fact that $pK_a(\text{HA})$ in methanol is lower by about two orders of magnitude than in DMSO. The pK_a values for the molecular acid are 21.56, 19.04, 18.17, 11.75, and 9.67 in AN, PC, AC, DMSO, and MeOH, respectively.

A closer inspection of the variations of the strength of the cationic and molecular acids show them to be opposite to those expected (strength increases with decreasing solvent polarity; relative dielectric constants for

Table I. Logarithms of Acidity Constants of Molecular (HA) and Cationic (BH⁺) Acids, and Cationic (lg K_{BHB^+}) and Anionic (lg K_{AHA^-}) Homoconjugation and Molecular Heteroconjugation (lg K_{AHB}) Equilibrium Constants in the Binary (DMSO + D) Solvent Mixtures.

X_{DMSO}	$pK_a(\text{BH}^+)$	$pK_a(\text{HA})$	lg K_{BHB^+}	lg K_{AHA^-}	lg K_{AHB}^a
1.0	11.91 ± 0.11	11.82 ± 0.21	2.19 ± 0.15	2.25 ± 0.48	2.66 ± 0.10
0.9	10.41 ± 0.06	11.96 ± 0.29	1.74 ± 0.06	2.25 ± 0.44	2.67 ± 0.11
0.8	9.52 ± 0.08	11.17 ± 0.17	2.35 ± 0.03	2.68 ± 0.37	2.57 ± 0.33
0.7	9.26 ± 0.07	10.83 ± 0.20	2.35 ± 0.03	2.42 ± 0.45	3.25 ± 0.15
0.6	8.95 ± 0.13	10.24 ± 0.33	2.07 ± 0.07	3.01 ± 0.64	3.89 ± 0.13
0.5	8.23 ± 0.21	10.33 ± 0.25	2.67 ± 0.07	— ^b	3.71 ± 0.27
0.4	7.95 ± 0.24	10.48 ± 0.39	2.45 ± 0.07	— ^b	— ^b
0.3	6.86 ± 0.28	9.81 ± 0.22	2.84 ± 0.09	— ^b	— ^b
0.2	6.84 ± 0.40	9.78 ± 0.24	2.73 ± 0.14	— ^b	— ^b

^a In direct B + HA experimental system.

^b Constant associated with very high standard deviation (much higher than constant value).

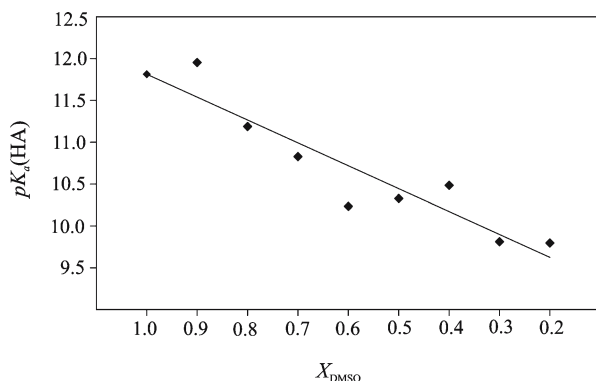


Fig. 4. Dependence between $pK_a(\text{HA})$ and composition of the binary (DMSO + D) solvent mixture.

1,4-dioxane and DMSO are 2.2 and 46.6, respectively [28]), because the strength should increase with increasing solvent polarity resulting from an increase in the solvation energy of the dissociation products. Moreover, the variations cannot be explained on the basis of basicity variations of the medium, because DMSO has a higher donicity number (DN = 29.8 [29]) than 1,4-dioxane (DN = 14.8), as well as solvent–solvent interactions [30]. This non-typical trend can only be explained in terms of the complexity of factors affecting the acid strength such as variations of auto-ionization

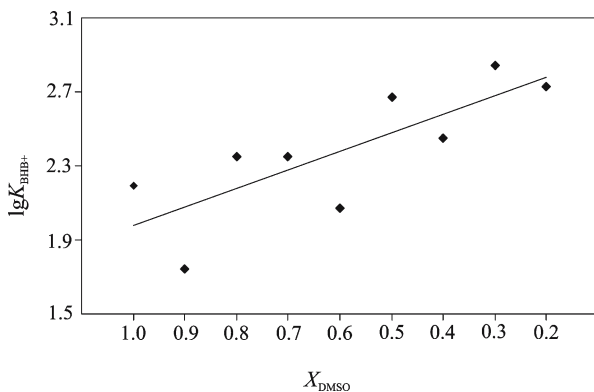


Fig. 5. Dependence between $\lg K_{\text{BHB}^+}$ and composition of the binary (DMSO + D) solvent mixture.

constants of solvents [6] and specific solvation [6]. In particular, the last factor may be crucial when considering the electron configuration of both solvents. Namely, the 1,4-dioxane molecule has two oxygen atoms with lone electron pairs, while that of DMSO has one electron pair only. Consequently, in the mixed solvent (DMSO + D), 1,4-dioxane is likely to be a stronger solvating component in spite of being formally a weaker base than DMSO.

Logarithms of the cationic homoconjugation equilibrium constants increase linearly within the solvent series beginning from DMSO up to M_8 (Fig. 5), i.e., with increasing 1,4-dioxane content, which depresses solvent polarity. Similar variations are noticed in the anionic homoconjugation equilibrium constants which increase linearly over the DMSO– M_8 range (Fig. 6). Beginning from the M_5 mixture, the constants are becoming associated with relatively large-standard deviations. In mixture M_7 the anionic homoconjugation equilibrium constant can be regarded as indeterminable from potentiometric measurements, while in mixture M_8 it is virtually indeterminable. It can thus be concluded that the magnitude of the homoconjugation equilibrium constants in the mixed solvents depends on solvent polarity (they increase with decreasing polarity), because in this case the medium's solvation capacity, and in particular, the energy of non-specific solvation, decreases, this is favorable for establishing both anionic and cationic homoconjugation equilibria.

The molecular heteroconjugation equilibria have been studied in two types of experimental systems, the direct titration system ($B + HA$) and the reverse one ($HA + B$; back titration). Logarithms of the molecular heteroconjugation equilibrium constants determined in direct systems are

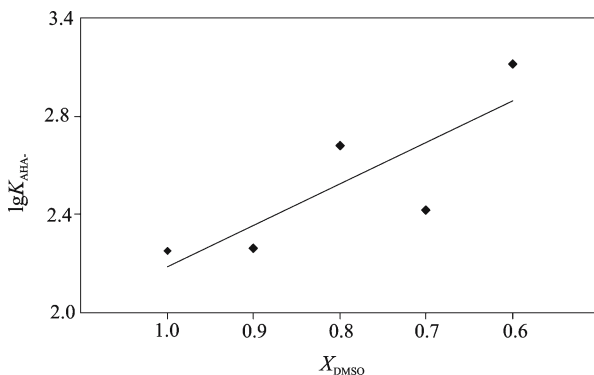


Fig. 6. Dependence between $\lg K_{\text{AHA}^-}$ and composition of the binary (DMSO + D) solvent mixture.

presented in Table I together with standard deviations. It should be also noted that heteroconjugation process, similar to homoconjugation, belong to simultaneous reactions [28,31]. A comparison of the constants in both systems show them to be, by far more precisely determined for the direct (B + HA) systems. Logarithms of the molecular heteroconjugation constants (K_{AHB}) increase linearly up to M_5 (Fig. 7), whereas in M_6 , M_7 , and M_8 , they become either associated with large-standard deviations or indeterminable. For the case of the reverse (HA + B) systems, all the molecular heteroconjugation equilibrium constants are associated with large-standard deviations and can be regarded as being virtually indeterminable. For comparison K_{AHB} obtained in AC is 2.30 [24]. Similarly, in our previous paper [32] molecular heteroconjugation equilibrium constants were also determined by potentiometric titration for substituted phenol + *n*-butylamine systems in DMSO, which range from 2.77 to 5.32 on a logarithmic scale. An increasing tendency toward molecular heteroconjugation was observed in these systems with increasing pK_a values of a molecular acid, i.e., with decreasing phenol acidity.

It can thus be concluded that in the (DMSO + D) mixed solvents the precision of the determination of molecular heteroconjugation equilibrium constants depend on the direction of titration. The binary solvent systems studied enable differentiation of the determinability of the molecular heteroconjugation equilibrium constants, unlike the previously studied (acetone + cyclohexane) [24] and (acetonitrile + 1,4-dioxane) [19] systems. In these systems only a qualitative indication for a determinability of the molecular heteroconjugation equilibrium constants in the direct (B + HA) systems could be obtained.

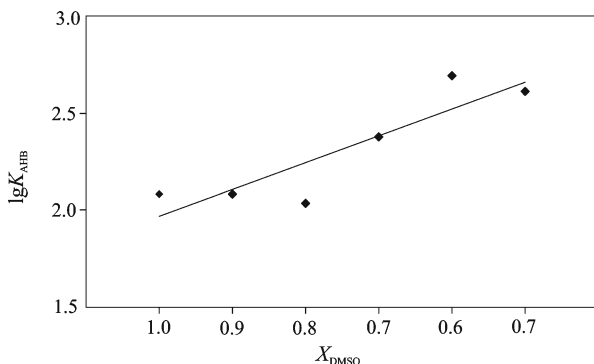


Fig. 7. Dependence between $\lg K_{\text{HB}}$ and composition of the binary (DMSO + D) solvent mixture.

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