

Potentiometric Studies on the Protonation Constants and Solvation of Some α -Amino Acid Benzyl- and t-Butyl- Esters in Ethanol-Water Mixtures

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To gain more information about the effect of solvent on α -amino acid benzyl- and t-butyl- esters, the stoichiometric protonation constants of 10 esters (glycine benzyl ester, *L*-alanine benzyl ester, *L*-valine benzyl ester, *L*-serine benzyl ester, glycine t-butyl ester, *L*-alanine t-butyl ester, *L*-valine t-butyl ester, *L*-leucine t-butyl ester, *L*-phenylalanine t-butyl ester and *L*-isoleucine t-butyl ester) in 20%-80% (v/v) ethanol-water mixtures were determined at an ionic strength of 0.10 M NaCl and at 25.0 ± 0.1 °C under nitrogen atmosphere. A potentiometric method was used and the calculation of constants was carried out using the PKAS computer program. The logarithm of the protonation constants of the above-mentioned α -amino acid esters linearly decreased with increases in ethanol contents but the values that determined 80% ethanol did not follow this linear trend. The variation of these constants is discussed on the basis of specific solute-solvent interactions.

Key Words: Potentiometry; protonation constants, solvent effect, amino acid esters.

Introduction

Acidity measurements of organic compounds have a long history dating back to the end of the 19th century, when the first pK_a was measured. Since then a vast body of data on acidities in various solvents has been collected¹⁻⁴. The measurements have mostly been limited to polar solvents, however, with water being by far the most exploited medium, followed by alcohols and dipolar aprotic solvents.

The acidity or basicity of a compound in a given medium is influenced by both the electronic effects of the substituents and the solvent effects of the medium. Moreover, it is sometimes extremely difficult to assess how much each effect contributes to the acidity or basicity. Small differences in acidity or basicity between similar molecules are also extremely difficult to interpret and one must be very careful in deciding which structural effect is the main influence on acidity or basicity.

A number of studies have been reported on the protonation constants of α -amino acids in different media^{5,8}, however, very little information on the protonation constants of α -amino acid ethyl and methyl

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esters in water and organic solvent-water mixtures has been published so far⁹⁻¹¹. There have been no reports dealing with these esters investigated either in water or in organic solvent-water mixtures.

This paper, therefore, deals with the determination of the stoichiometric protonation constants of glycine benzyl ester, *L*-alanine benzyl ester, *L*-valine benzyl ester, *L*-serine benzyl ester, glycine *t*-butyl ester, *L*-alanine *t*-butyl ester, *L*-valine *t*-butyl ester, *L*-leucine *t*-butyl ester, *L*-phenylalanine *t*-butyl ester and *L*-isoleucine *t*-butyl ester. Moreover this work reports an investigation aimed at gaining information about the effect of solvent composition on the protonation constants of α -amino acid esters.

Experimental

Chemicals and standard solutions

Glycine benzyl ester, *L*-alanine benzyl ester, *L*-valine benzyl ester, *L*-serine benzyl ester, glycine *t*-butyl ester, *L*-alanine *t*-butyl ester, *L*-valine *t*-butyl ester, *L*-leucine *t*-butyl ester, *L*-phenylalanine *t*-butyl ester and *L*-isoleucine *t*-butyl ester were purchased from Sigma and the purity of the substances was determined by potentiometric titration. The ethanol utilized was purified as described elsewhere¹². Doubly distilled conductivity water was used as aqueous medium as well as for the preparation of ethanol-water mixtures. All other chemicals used in this investigation were reagent grade purity.

Hydrochloric acid solution 0.10 *M* was prepared in water and standardized against sodium carbonate. Sodium hydroxide solutions 0.10 *M* were prepared as 10%, 20%, 30%, 40%, 50%, 60%, 70% and 80% (v/v) aqueous ethanol solutions and stored in a glass bottle protected against the atmosphere. The base solutions were standardized via a linear least-squares fit of Gran plots for end-point determination obtained from hydrochloric acid¹³⁻¹⁴.

Procedure

All potentiometric measurements were performed in an 80-mL jacketed titration cell thermostated at 25.0 \pm 0.1 °C and under nitrogen atmosphere. An Orion 720A Model pH-ionmeter, fitted with a combined pH electrode (Ingold) containing a filling solution of 0.10 *M* NaCl, was used for measuring the cell e.m.f. values. The potentiometric cell was calibrated before each experiment so that the hydrogen ion concentration rather than the activity was measured¹⁵⁻¹⁶. For all the solvent mixtures examined, reproducible values of autoprotolysis constants, K_{ap} , were calculated from several series of [H] and [OH] measurements at 0.10 *M* NaCl^{15,17}.

The following solutions prepared in water and each of the solvent mixtures studied (total volume 50.0 mL) were titrated potentiometrically with CO₂-free standard 0.1 *M* sodium hydroxide dissolved in the corresponding solvents: (i) 2.5×10^{-3} *M* HCl (for cell calibration); (ii) 2.0×10^{-3} *M* HCl + 2.5×10^{-3} *M* α -amino acid esters. During each titration the ionic strength was maintained at 0.1 *M* NaCl and a potential reading was taken after a suitable time (normally 2-3 min) for equilibration.

The protonation constants of the α -amino acid esters were calculated by analyzing the titration data using the computer programme developed by Motekaitis and Martell^{15,18}.

Results and discussion

The stoichiometric protonation constants (β) for t-butyl esters and benzyl esters of α -amino acids determined in ethanol-water mixtures (20-80 volume % ethanol) 25.0 ± 0.1 °C are given in Tables 1 and 2, respectively. All the values presented are the average of at least 5 measurements. These values are the equilibrium constants of the $A + H^+ \rightleftharpoons AH^+$, where A and AH^+ show α -amino acid esters and their protonated species respectively. The protonation constants given in Tables 1 and 2 are considered in more detail in order to gain more information about the effect of solvent composition and specific effects of substituents on the basicities of the esters in solvent mixtures.

The numerical $\log \beta$ values for t-butyl esters of α -amino acids determined in ethanol-water mixtures decrease with increasing ethanol content in the solvent mixture, an example of which is given in the Figure. It is observed that a nearly linear relationship exists between the aforementioned protonation constants and the mole fraction of ethanol from 0.0331 to 0.4183 for all α -amino acid esters investigated. However, $\log \beta$ values at a mole fraction of ethanol of 0.4183 are slightly higher than those expected from the linear trend. The linear equations and the related correlation coefficients for all α -amino acid esters are given in Tables 3 and 4. This linear variation is very similar to that found for ammonia aliphatic alkyl amines, pyridine and salicylideneanilines^{19–20}.

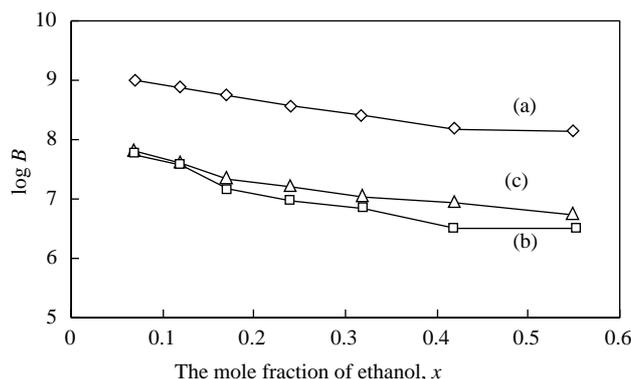


Figure. Variation in the protonation constants of t-butyl esters against the mole fraction of ethanol: (a) *L*-alanine t-butyl ester; (b) *L*-valine t-butyl ester; (c) *L*-leucine t-butyl ester.

Many studies have shown that the equilibrium constant is linearly related to the fraction of organic solvent^{21–25}. Our results obtained for α -amino acid esters are in good agreement with these. The dissociation constants of charged acids in ethanol-water mixtures vary with solvent composition in a manner that is not completely understood. Bates and co-workers^{26–27} and Chattopadhyay and Lahiri²⁸ have examined the effect of a change in solvent composition on the dissociation of BH^+ and the related Gibbs energies of transfer in mixed solvents. In this paper it is suggested that electrostatic charging effects resulting from the change in dielectric constant with solvent effects and the solute-solvent interactions have greater significance in the interpretation of solvent effects. Thus, we can explain our results obtained for α -amino acid esters by specific solvation effects. Since ethanol would solvate A better than AH^+ , the $\log \beta$ values, which are related to the formation of AH^+ , would decrease upon addition of ethanol. The derivations of linearity in 80% ethanol may result from the preferential solvation of solute by one of the components of the solvent mixture that could change the effective dielectric constant value in the cibotactic region²⁹.

Table 1. Stoichiometric protonation constants of some α -amino acid t-butyl esters at 25.0 ± 0.1 °C for different ethanol-water mixtures ($\mu = 0.1$ M NaCl).

Esters	20%E-80%W $x = 0.0331$	30%E-70%W $x = 0.1167$	40%E-60%W $x = 0.1740$	50%E-50%W $x = 0.2356$	60%E-40%W $x = 0.3161$	70%E-20%W $x = 0.4183$	80%E-20%W $x = 0.5521$
	$\log\beta$						
Glycine t-butyl ester	7.66 ± 0.01	7.51 ± 0.01	7.40 ± 0.01	7.30 ± 0.01	7.20 ± 0.01	7.05 ± 0.01	6.64 ± 0.01
L-Alanine t-butyl ester	9.01 ± 0.01	8.86 ± 0.01	8.75 ± 0.01	8.55 ± 0.01	8.39 ± 0.01	8.16 ± 0.01	8.14 ± 0.01
L-Valine t-butyl ester	7.74 ± 0.01	7.56 ± 0.01	7.15 ± 0.01	6.95 ± 0.01	6.85 ± 0.01	6.51 ± 0.01	6.50 ± 0.01
L-Leucine t-butyl ester	7.79 ± 0.01	7.63 ± 0.01	7.38 ± 0.01	7.21 ± 0.02	7.02 ± 0.01	6.92 ± 0.01	6.75 ± 0.01
L-Phenylalanine t-butyl ester	7.15 ± 0.01	7.00 ± 0.01	6.67 ± 0.01	6.56 ± 0.01	6.50 ± 0.01	6.40 ± 0.01	6.33 ± 0.01
L-Isoleucine t-butyl ester	7.75 ± 0.01	7.65 ± 0.01	7.35 ± 0.01	7.18 ± 0.01	7.12 ± 0.01	6.89 ± 0.01	6.64 ± 0.01

 E: ethanol, W: water; x = the mole fraction of ethanol

Table 2. Stoichiometric protonation constants of some α -amino acid benzyl esters at 25.0 ± 0.1 °C for different ethanol-water mixtures ($\mu = 0.1M$ NaCl).

Esters	20%E-80%W	40%E-60%W	60%E-40%W	80%E-20%W
	$x = 0.0331$	$x = 0.1740$	$x = 0.3161$	$x = 0.5521$
	$\log\beta$	$\log\beta$	$\log\beta$	$\log\beta$
Glycine benzyl ester	7.27 ± 0.01	7.07 ± 0.01	6.94 ± 0.01	6.85 ± 0.01
L-Alanine benzyl ester	7.35 ± 0.01	7.17 ± 0.01	7.01 ± 0.01	7.00 ± 0.01
L-Valine benzyl ester	7.16 ± 0.01	6.88 ± 0.01	6.77 ± 0.01	6.68 ± 0.01
L-Serine benzyl ester	6.75 ± 0.01	6.60 ± 0.01	6.51 ± 0.01	6.54 ± 0.01

E: ethanol, W: water; x = the mole fraction of ethanol

Table 3. Linear relationship between the protonation constants of some α -amino acid esters and the the mole fraction of ethanol (x) (from 0.0331 to 0.4183).

Amino acid esters	Equation	Correlation coefficients, r
Glycine t-butyl ester	$\log \beta = -1.570(x) + 7.691$	-0.997
L-Alanine t-butyl ester	$\log \beta = -2.262(x) + 9.108$	-0.997
L-Valine t-butyl ester	$\log \beta = -3.237(x) + 7.824$	-0.980
L-Leucine t-butyl ester	$\log \beta = -2.410(x) + 7.844$	-0.980
L-Phenylalanine t-butyl ester	$\log \beta = -2.015(x) + 7.147$	-0.941
L-Isoleucine t-butyl ester	$\log \beta = -2.307(x) + 7.820$	-0.975

Table 4. Linear relationship between the protonation constants of some α -amino acid esters and the the mole fraction of ethanol (x) (from 0.0331 to 0.3161).

Amino acid esters	Equation	Correlation coefficients, r
Glycine benzyl ester	$\log \beta = -1.166(x) + 7.296$	-0.992
L-Alanine benzyl ester	$\log \beta = -1.201(x) + 7.386$	-0.999
L-Valine benzyl ester	$\log \beta = -1.377(x) + 7.176$	-0.970
L-Serine benzyl ester	$\log \beta = -0.848(x) + 6.767$	-0.989

Furthermore, another factor why an increase in the $\log \beta$ values of all α -amino acid esters is produced in ethanol-rich regions can be satisfactorily explained by differences in the solvent stabilization of the ionic species (H^+ and AH^+), brought about by changing the percentage of ethanol ^{27,30}.

Using the protonation constants obtained in this work, the effects of the type of ester groups on the basicity of the amine groups of α -amino acid esters studied have been discussed. The most important factor that affects the basicity and therefore the protonation constant of a compound is the structural effect.

Tables 1 and 2 show that the basicity of t-butyl esters of glycine, L-alanine and L-valine is higher than that of the corresponding benzyl esters of the same amino acids in 20%-60% ethanol-water mixtures. This effect can be explained by taking the electronic effect of the t-butyl and benzyl groups investigated into account.

Conclusion

The basicity of a compound is a result of various factors such as (i) the solvent effect: solvation power, the tendency of forming hydrogen bonds, selective solvation, dielectric constant and the composition of the

solution in the first solvation layer in the case of mixed solvents and (ii) structural effect, electronic effect, steric effect and the formation of hydrogen bonding.

The protonation constants of the t-butyl and benzyl esters of some α -amino acids studied are very important for calculating the microscopic constants of the corresponding α -amino acids.

References

1. G. Kortüm, W. Vogel, K. Andrussov, **Dissociation Constants of Organic Acids in Aqueous Solution**, Plenum, New York, 1961.
2. V. Palm, **Tables of Rate and Equilibrium Constants of Heterolytic Organic Reactions**, Ed.; Moscow-Tartu, 1975-1985.
3. K. Izutsu, **Acid-base Dissociation Constants in Dipolar Aprotic Solvents**; IUPAC Chemical Data Series No: 35; Blackwell Scientific: Oxford, 1990.
4. F.G. Bordwell, **Acc. Chem. Res.**, **21**, 456 (1988).
5. S.H. Herbert, C.M. Birdsall, **J. Am. Chem. Soc.** **65**, 54 (1943).
6. B. Nowak, Z. Pawlak, **J. Chem. Soc. Faraday Trans. I**, **78**, 2693 (1982)
7. G. Wada, E. Tamura, M. Okina and M. Nakamura, **Bull. Chem. Soc. Jpn.** **55**, 3064 (1982).
8. F. Köseoğlu, E. Kılıç and A. Doğan, **Anal. Biochem.** **277**, 243 (2000).
9. D.L. Hughes, J.J. Bergan and E.J.J. Grabowski, **J. Org. Chem.** **55**, 2579 (1986).
10. E.R. Benesch and R. Benesch, **J. Am. Chem. Soc.** **77**, 5877 (1955).
11. J.T. Edsall, M.H. Blanchard, **J. Am. Chem. Soc.** **55**, 2337 (1933).
12. D.D. Perrin, W.L.F. Armerega, **Purification of Laboratory Chemicals**, 1st edn, Pergamon, Oxford, 1966.
13. G. Gran, **Acta. Chem. Scand.** **4**, 559 (1950)
14. G. Gran, **Analyst**, **77**, 661 (1952).
15. A.E. Martell and R.J. Motekaitis, **The Determination and Use of Stability Constants**, VCH, Weinheim, 1988
16. M. Meloun, J. Havel and H. Högfelt, **Computation of Solution Equilibria**, Wiley, New York, 1988.
17. E.M. Woolley, D.G. Hurkot and L.G. Hepler, **J. Phys. Chem.** **74**, 3908 (1970).
18. R. J Motekaitis, A.E Martell, **Can. J. Chem.**, **60**, 168 (1982).
19. E. Kılıç, G. Gökçe and E. Canel, **Turk. J. Chem.** **26**, 843 (2002).
20. E. Kılıç, F. Köseoğlu and Ö. Başgut, **Anal. Chim. Acta.** **294**, 215 (1994).
21. M.S.K. Niazi and J. Mollin, **Bull. Chem. Soc. Jpn.** **60**, 2605 (1987).
22. C.C Panichajakul and E.M. Woolley, **Anal. Chem.** **47**, 1880 (1975).
23. H. Irving and H. Rossotti, **Acta. Chem. Scand.** **10**, 72 (1986).
24. H. Irving and H. Rossotti, **Analyst**, **80**, 245 (1955).
25. P.S. Gentile, M. Cefole and A.V. Celiano, **J. Phys. Chem.** **67**, 1447 (1963).

26. M. Paabo, R.G. Bates and R.A. Robinson, **J. Phys. Chem.** **70**, 247 (1965).
27. R.G. Bates, **J. Electroanal. Chem.** **29**, 1 (1971).
28. A.K. Chattopadhyay and S.C. Lahiri, **Electrochim. Acta.** **27**, 269 (1982).
29. N.S. Isaacs, **Physical Org. Chem.** Longman, New York, 1986.
30. R.G. Bates, **Determination of pH, Theory and Practice**, 2nd edn., Wiley, New York, 1973.