

Note

ASPARTAME COMPLEXES OF CALCIUM AND PRASEODYMIUM CATIONS

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ABSTRACT

Aspartame, α -L-Asp-L-PheOMe dipeptide, is known through its artificial sweetener property [1,2]. The presence of the free α -amino and β -carboxyl groups on the aspartyl residue and a blocked carboxyl group on the phenyl alanine residue means that metal ions are most likely to be complexed by the aspartyl amine and β -carboxyl groups [3]. Very little data are available on the aspartame derivatives' affinity for metal ions [4]. An attempt has been made to study the stability of two metallic cation–aspartame systems pH-metrically in solution and by ^1H NMR data.

EXPERIMENTAL

All the reagents were of analytical grade. Aspartame was from Sigma Chemical Company, CaCl_2 and Pr_6O_{11} from Fluka. PrCl_3 was prepared from the oxide [5]. Potentiometric titrations on thermostated and degassed samples were made using a Metrohm E 603 potentiometer with a Metrohm EA 120 microelectrode. All measurements on a standardized solution of aspartame (10^{-2} M) were made at constant ionic strength (0.5 M KCl). The PrCl_3 and CaCl_2 salt concentrations were varied between 0 and 5×10^{-2} M. ^1H NMR spectra were recorded on a Bruker WH 200 spectrometer equipped with an Aspect 2000 computer in D_2O ($\text{pD} = \text{pH} + 0.39$) once all exchangeable protons had been deuterated, in identical concentration and temperature conditions as potentiometric experiments.

RESULTS AND DISCUSSION

Potentiometry

The plot of the measured pH vs. \bar{q} permits us to estimate the p , q and r parameters of $\text{M}_p\text{H}_q\text{A}_r$ species



The treatment of the curves allows \bar{r} to be computed, the mean number of ligand molecules fixed per metallic cation [6]. In the present case \bar{r} is always less than unity. Therefore, the equilibria should be interpreted on an MH_qA type model complex. The values of the stability constant β_{1q1} for complexes bearing q protons have been computed by a parameter-fitting method [7]. Plots of β_{111} and β_{101} vs. m (metallic concentration) with a good convergence, gave a set of provisional values which have been further improved by a reverse fitting to the experimental pH vs. \bar{q} plots. This is a criterion to the postulated model for the species in equilibrium at each pH and relative concentration values. The results are given in Table 1. From the computed constants one can predict the relative concentration of the species present at each pH value. Thus, the determined range in which one is strongly dominant was used for the NMR measurements. The complex bearing one exchangeable MHA proton was investigated at pH 2.70.

NMR data

^1H NMR chemical shifts of aspartame have been followed during titration of 10^{-2} M solution adjusted to pH 2.70 either in the absence or in the presence of praseodymium salt. The principal induced shift concerns the H_β and H_α nuclei of the aspartyl residue. The stability constant β_{111} for the MHA complex has been determined using an equation deduced from the observed chemical shifts [8].

$$\delta_{\text{obs}} = f_{\text{MHA}}\delta_{\text{MHA}} + \sum f_{\text{HqA}}\delta_{\text{HqA}} \quad (2)$$

Further analysis of Table 1 shows that calcium and praseodymium complexes of aspartame are monitored by a pH dependence. For both cations,

TABLE 1

Stability constants and thermodynamic parameters of calcium- and praseodymium-aspartame systems

System	Temp. (°C)	log β_{101}	log β_{111}	ΔG^0 (kcal mol $^{-1}$)	ΔH^0 (kcal mol $^{-1}$)	ΔS^0 (cal mol $^{-1}$ deg $^{-1}$)
Ca(II)	25	0.92		-1.25		
			2.17	-2.96		
	35	0.84		-1.18	-3.36	-7.08
Pr(III)	25	0.85, 0.78 ^a	2.10	-2.86	-2.94	-0.26
			2.40	-1.16		
	35	0.80, 0.72 ^a		-3.27		
			2.32	-1.13	-2.10	-3.15
			-3.27	-3.36	-0.29	

^a From eqn. (2), NMR data.

acidic conditions involve only one site-carboxylate group for a rather labile complexation denoted by the low value of β_{111} . At higher pH the difference in stability ($\sim 10^2$) is a result of the partial loss of protons of the α -amino-group. Log β_q of the two metallic aspartame systems decreases with a decrease in temperature showing that a low temperature is favourable for interaction because of the decreased number of collisions with a decreased kinetic energy of the molecules and, hence, a stable system is obtained. ΔG^0 assumed negative values for both systems at both temperatures indicating the feasibility of the reactions. The entropy change (ΔS^0) is, in all probability, due to the solvent effect.

During titration with KOH the mixture turned turbid in all cases (pH < 6.2). Calculations under these conditions were restricted to a pH below that of precipitation. Further conformation analysis, by paramagnetic shift probes, should be made over the pH range investigated.

REFERENCES

- 1 R.H. Mazur, J.M. Schlatter and A.H. Goldkamp, *J. Am. Chem. Soc.*, 91 (1969) 2684.
- 2 R.H. Mazur, A.H. Goldkamp, P.A. James and J.M. Schlatter, *J. Med. Chem.*, 13 (1970) 1217.
- 3 M.L.D. Touche and D.R. Williams, *J. Chem. Soc., Dalton Trans.*, (1976) 2001.
- 4 C. Gilen, R. Leshem, Y. Tapuhi and E. Grushka, *J. Am. Chem. Soc.*, 101 (1979) 7612.
- 5 M. Asso, J. Mossoyan, D. Benlian and A. François, *J. Chim. Phys.*, 73 (1976) 315.
- 6 J. Bjerrum (Ed.), *Metal Ammine Formation in Aqueous Solutions*, Hasse, Copenhagen, 1941.
- 7 L. Asso, M. Asso, J. Mossoyan and D. Benlian, *J. Chim. Phys.*, 75 (1978) 56.
- 8 M. Asso, J. Mossoyan, L. Asso and D. Benlian, *J. Chim. Phys.*, 80 (1983) 251.