Inorganica Chimica Acta, 56 (1981) L45–L47
© Elsevier Sequoia S.A., Lausanne – Printed in Switzerland

The Formation of Proton and Alkali-Metal Complexes with Ligands of Biological Interest in Aqueous Solution. Potentiometric and PMR Investigation of Li^+, Na^+, K^+, Rb^+, Cs^+ and NH_4^+ Complexes with Citrate

VINCENZO CUCINOTTA

Instituto Dipartimentale di Chimica e Chimica Industriale, Università di Catania, V. 1e A. Doria 8, Catania, Italy

PIER GIUSEPPE DANIELE

Istituto di Analisi Chimica Strumentale, Università di Torino, via Bidone 36, Turin, Italy

CARMELO RIGANO

Seminario Matematico, Università di Catania, v. 1e A. Doria 8, Catania, Italy

and SILVIO SAMMARTANO

Istituto di Chimica Analitica, Università di Messina, via dei Verdi, Messina, Italy

Received February 24, 1981

Recently we studied the complex formation of citrate (Cit^{3-}) with Na^+ and K^+ using potentiometric and calorimetric techniques [1, 2]. To have a better picture of the complexing capacities of citrate toward alkali-metal ions, we have extended this study to Li^+, Cs^+ and Rb^+ using the potentiometric technique, at 37 °C and at different ionic strengths. Furthermore, in order to have a more direct evidence of the interactions occuring in our systems, we have used PMR technique, observing the shift of the peaks of the quadruplet due to the four methylenic protons of citrate. As known [3, 4], the quadruplet is due to the non-equivalence of the conformations arising from the rotation around the methylene bonds, which cause the non-equivalence of the two protons of each methylene. Though in literature the influence of alkaline cations on PMR spectra of citrate had already been investigated [5], we thought it interesting to carry out a systematic investigation, including ammonium ion and all the alkaline cations. To make a quantitative comparison among the different cations studied, the analytical concentrations and pH were held constant for all the systems in the PMR experiments.

H_3Cit, Na_3Cit, K_3Cit, LiOH, $LiNO_3$, CsCl, RbI and THAM were all pure reagents for analysis and were used without further purification. KOH and HNO_3 stock solutions were prepared by diluting concentrated ampoules (Merck). For all solutions twice distilled water was employed. Grade A glassware was used. Potentiometric measurements were carried out using a model E600 Metrohm potentiometer equipped with a glass electrode and a calomel reference one supplied by the same firm. The glass electrode was calibrated, in pH units, by titrating HNO_3 (5–8 mmol dm^{-3}) with standard CO_2-free 1 mol dm^{-3} KOH.

The potentiometric data were first analyzed without allowing for M^+-citrate complexes ($M^+ = Li^+$, Rb^+, Cs^+) by ACBA program [6]. In Table I the experimental conditions and log K_J^H values are reported. The protonation constants, calculated taking into account only H^+–Cit^{3-} interactions,

TABLE I. Experimental Details of Potentiometric Measurements, at 37 °C. The Protonation Constants Given in this Table and the Analytical Concentrations of Citric Acid were Refined simultaneously by the ACBA Program, without allowing for Alkali-metal Complex Formation.

M	C_M[a]	log K_1^H	log K_2^H	log K_3^H	10^3C_{cit}[b]	$10^3\sigma_v$[c]	10^3R[d]
Li^+	0.04	5.83(2)[e]	4.47(2)	2.98(2)	3.02(2)	0.74	2.21
	0.09	5.62(1)	4.310(6)	2.867(6)	3.175(6)	0.43	1.04
	0.49	5.21(2)	4.11(2)	2.90(2)	4.14(2)	1.23	3.33
	0.98	4.96(1)	3.96(1)	2.77(1)	4.24(1)	0.52	1.14
Rb^+	0.03	5.87(2)	4.46(2)	2.97(3)	6.23(2)	1.88	5.84
	0.1	5.69(1)	4.32(1)	2.87(1)	6.34(1)	0.76	2.35
	0.3	5.49(1)	4.22(1)	2.84(1)	6.303(6)	0.58	1.79
Cs^+	0.03	5.89(1)	4.454(6)	2.948(6)	6.368(6)	0.45	1.38
	0.1	5.70(1)	4.33(1)	2.90(1)	6.341(3)	0.64	1.90
	0.3	5.50(1)	4.19(1)	2.80(1)	6.341(3)	0.64	1.93

[a] Concentrations in mol dm^{-3}. [b] Initial volume 25 cm^3, titrant KOH 1 mol dm^{-3} dispensed by a microsyringe with 2500 div/0.5 cm^3. [c] Standard deviation in titre. [d] Hamilton's factor, see ref. 1. (and references therein). [e] 3σ in parenthesis.

TABLE II. Formation Constants for H^+, alkali-metal and NH_4^+–Citrate Complexes at 37 °C, Calculated by Modified MINIQUAD 76A Program. $I' = 0.15$ mol dm^{-3}.

M	log K_1		C_1	log K_2	C_2	I range
Li^{+a}	0.88(6)*	[0.83] [e]	0.99(15)	0.25(15)	0.5(2)	0.05–0.9
Na^{+b}	0.68(5)	[0.70]	0.77(13)	0.10(15)	0.45(20)	0.05–0.9
K^{+c}	0.56	[0.59]	1.09	−0.3	0.5	0.05–0.8
Rb^{+a}	0.52(6)	[0.49]	0.84(18)	−0.4(2)	0.5(2)	0.05–0.3
Cs^{+a}	0.47(5)	[0.32]	1.3(3)	−0.4(2)	0.3(3)	0.05–0.3
NH_4^{+d}	0.95	–	0.83	0.4	0.3	0.05–0.5
H^{+c}	5.80	–	0.80	4.31	0.42	0.05–0.8

*3σ in parenthesis. [a] This work. [b] Ref. 1 and this work. [c] Ref. 2. [d] Ref. 11. [e] In brackets are reported the values of Rechnitz *et al.* [12], I = 0.1 mol dm^{-3}, t = 25 °C.

TABLE III. Correlation between the Chemical Shifts δ of the Investigated Complexes and the Reciprocals of Ionic Radii (1/r) of the Corresponding Cations. The Chemical Shifts are Downfield with Respect to DSS.

		Li^+	Na^+	K^+	NH_4^+	Rb^+	Cs^+	(Cit^{3-})
δ	(ppm)	2.641	2.624	2.612	2.610	2.609	2.603	2.585
1/r	($Å^{-1}$)	1.47	1.03	0.752	0.699	0.680	0.592	(0)
		$\delta = 2.585 + 0.0337(1/r) + 0.00328\,(1/r)^2$			$R^a = 0.99984$			
		$\delta = 2.584 + 0.0385(1/r)$			$R^a = 0.99866$			

[a] R is the correlation coefficient.

follow the order $Cs^+ > Rb^+ > (K^+) > (Na^+) > Li^+ > (NH_4^+)$ (the cations previously studied are in parentheses) and, in their turn, they are all lower than the values obtained in Et_4N^+ [2]. By assuming that the difference in log K_J^H is due only to Cit^{3-}–M^+ complex formation, it is possible to calculate the constants K_i for the reaction

$$M^+ + [H_{i-1}(Cit)]^{(4-i)-} \rightleftarrows [MH_{i-1}(Cit)]^{(3-i)} \qquad (1)$$

from the equation

$$K_i = (10^{\delta \log k_i} - 1)C_M^{-1} \qquad (2)$$

where $\delta \log k_i = [\log K_j^H(\text{corr}) - \log K_i^H]_{j=i}$, and c_M is the free concentration of cation. If C_M (analytical concentration of cation) $\gg c_{Cit}$, we can assume $c_M \sim C_M$. Therefore, approximate values of K_i for reaction (1) can be obtained from (2). These values were used as input for MINIQUAD 76A [7] modified in such a way to calculate simultaneously the parameters of equation (3):

$$\log K = \log K^{I'} - Az^*\left(\frac{\sqrt{I}}{1 + 1.5\sqrt{I}} - \frac{\sqrt{I'}}{1 + 1.5\sqrt{I'}}\right) + C(I - I') \qquad (3)$$

where I is the ionic strength, I′ is the reference ionic strength, A is the Debye–Hückel constant (A = 0.523 at 37 °C) $z^* = 8 - 2i$, log $K^{I'}$ and C are the parameters to be calculated [2]. In Table II the values of log $K^{I'}$ and C are given both for the systems studied here and for the systems already reported.

The formation constants follow the inverse order of protonation constants $NH_4^+ > Li^+ > Na^+ > K^+ > Rb^+ > Cs^+$ and this is the order followed by all alkali metal–carboxylate ligands studied till now [8, 9].

As regards the ionic strength dependence, it is interesting to note that for both log K_1 and log K_2 the values of C are quite constant for all the cations (C_1 = 0.9 and C_2 = 0.4). This would suggest that, taking into account all the interactions, at least for $I < 1$, the ionic strength dependence is the same in all ionic media.

PMR spectra were carried out at 80 MHz on a Bruker WP-80 spectrometer in the fourier transform mode at 37 °C. The analytical concentrations of the used solutions, in D_2O, were 20 mmol dm^{-3} in citrate and 60 mmol dm^{-3} in the cation. As regards the experiments concerning free citrate, Rb^+ and Cs^+ (in order to adjust the pH to 9.2, a value corresponding to the complete deprotonation of citrate), the solutions were 0.60 mol dm^{-3} in THAM (trishydroxymethylaminomethane). The experimental uncertainty in the evaluation of chemical shifts is about 0.002 ppm. The chemical shifts refer to the middle of the strong doublet and are downfield respect to DSS (sodium 2,2-dimethyl-2-silapentane-5-sulfonate) peak, though experiments have been carried out using either TMA (tetramethylammonium bromide) or DSS, or both of them together. The concentration of reference was 1–2 mmol dm^{-3}. Generally, the chemical shifts agree for the two references. However, unreliable results are obtained in the case of free citrate when using TMA, probably because also this cation interacts with citrate.

As regards the coupling constants, the observed differences among the different systems are of the same magnitude as the experimental uncertainty and, therefore, the influence of the cation on the coupling constant cannot be rationalized.

The experimental value of chemical shift for each system is the weighted mean between the shift due to the complex and that due to the free citrate present. Using the formation constants to account for this fact, we have calculated the chemical shift due to each complex, that we report in Table III together with the reciprocal of ionic radius (according to Pauling) of the corresponding cation.

De Palma and Arnett [10], using more techniques to investigate their systems, have verified the usefulness of PMR in the study of ion pairs. In particular, they considered the linear correlation between chemical shifts and reciprocals of ionic radii as evidence of the presence of contact ion pairs in their systems. This is likely, considering that the polarizability of the cation (inversely proportional to the ionic radius) should influence the electronic density in the anion, if the cation and the anion are not solvent-separated. However, in the mentioned paper, no chemical shift could be measured for the free anion.

In our investigation, whilst one could easily expect the occurrence of contact ion pairs in the case of citrate, considering its strong complexing ability, it seemed interesting to verify the type of correlation found between the chemical shifts and the reciprocals of ionic radii, when taking into account the free anion too. Both a linear and a second-order correlation have been tested for our experimental data and the corresponding equations are reported in Table III, together with their correlation coefficients.

Though an improvement is observed introducing a second degree term, the statistical analysis shows that a second-order correlation is not required. It is our aim to make this aspect clearer in subsequent investigations on the basis of further experimental data.

References

1 G. Arena, R. Calì, M. Grasso, S. Musumeci, S. Sammartano and C. Rigano, *Thermochim. Acta, 36,* 329 (1980).
2 P. G. Daniele, C. Rigano and S. Sammartano, *Ann. Chim. (Italy), 70,* 119 (1980).
3 P. M. Nair and J. D. Roberts, *J. Am. Chem. Soc., 79,* 4565 (1957).
4 A. Loewenstein and J. D. Roberts, *ibid., 82,* 2705 (1960).
5 A. Loewenstein and H. Gilboa, *Spectrochim. Acta, 22,* 1939 (1966).
6 G. Arena, E. Rizzarelli, S. Sammartano and C. Rigano, *Talanta, 26,* 1 (1979).
7 A. Sabatini, A. Vacca and P. Gans, *Talanta, 21,* 53 (1974); P. Gans, A. Sabatini and A. Vacca, *Inorg. Chim. Acta, 18,* 237 (1976); A. Vacca, personal communication.
8 D. Midgeley, *Chem. Soc. Rev., 4,* 549 (1975).
9 L. G. Sillèn and A. E. Martell, 'Stability Constants', *Chem. Soc. Spec. Publ, London,* No. 17 (1964); No. 25 (1971).
10 V. M. De Palma and E. M. Arnett, *J. Am. Chem. Soc., 100,* 3514 (1978).
11 P. Amico, P. G. Daniele, C. Rigano and S. Sammartano, work in progress.
12 G. A. Rechnitz and S. B. Zamochnick, *Talanta, 11,* 1061 (1964).