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Assessing the formation of weak sodium complexes with negatively charged ligands

S. Berto,*[a] E. Chiavazza,[a] P. Canepa,[b,c] E. Prenesti,[a] and P. G. Daniele,[a]

The stability of sodium complexes with poly-carboxylic and polyamino-carboxylic acids is investigated with ion-selective electrode-Na^+ potentiometry, working at strictly constant ionic strength. It is observed that the formation constants of the Na^+ complexes with monoligand stoichiometry (ML) increase with the number of charges on the ligand. For example, in poly-carboxylic acids this dependency is linear and is well captured by an experimetal equation. A different behaviour is observed for the poly-amino carboxylic acids, which show higher complexation capabilities reaching a plateau of the binding energy past a specific ligand size. The experimental results are discussed qualitatively using *ab initio* calculations based on DFT B3LYP, and identifiy the principal electronic caractheristics of the ligands under investigation. As a result of the flexibility imparted by the long chains of polyamino-carboxylic ligands, both experimental and theorethical models demonstrate that nitrogen atoms in proximity of Na^+ ions can participate to the metal coordination, thus providing further stabilization for the complexes. Moreover, by increasing the ligand size the stabilization gained in terms of ΔG reached a plateau for EDTA, in agreement with experimental observations.

Introduction

Elucidating the formation of sodium ion complexes is of paramount importance in order to identify the correct speciation of natural fluids and providing insights into the chemical behavior of Na^+ ions in vital solutions.[1] Despite the low thermodynamic stability of alkali metal complexes, the existence of large concentrations of such metals in ubiquitous fluids attracts the attention from different scientific disciplines comprising biology, geology and medicine. The formation of weak alkali metal complexes together with low weight ligands (<400 g mol^{-1}), has been primarily investigated using pH-metric techniques (at variable ionic strength) by comparing the protonation constants determined in different alkali metal ionic media with those obtained in tetraalkylammonium salts.[2-6] A review of Daniele *et al*.[7] on the subject discusses most of the results together with data referred to species of multidentate ligands.

As a consequence of the uncertainty connected with the estimation of activity coefficients from different ionic strengths (due to the low values of formation constants) the stability constants and even the existence (in some cases) of the sodium complexes in water is still debated.[8] Recently, the detection of sodium ion complexes and relative stability constants were performed at constant values of ionic strength, by employing a sodium ion-selective electrode (ISE), and it was confirmed unequivocally the formation of sodium complexes, even with bidentate carboxylic ligands.[9] Furthermore, the values of stability constants of the sodium complexes, determined by ISE, fall in agreement with those measured with pH-metric technique.

Daniele *et al.* suggested that the chemical bond in these compounds has a predominately ionic nature, favouring ligand with negatively charged oxygen donor groups,[9] which is also supported by theoretical calculations (see discussion). However, our preliminary observations suggested[9] that the stability of the Na complexes is highly affected by nitrogen donor groups of the ligands.

In order to assess the interaction of ligands of various nature with Na, this work sets to investgate the complexation properties of benzenehexacarboxylic acid (*mlt*), benzenepentacarboxylic acid (BPC), 1,2,4,5-benzenetetracarboxylic acid (*pyr*), 1,2,4-benzenetricarboxylic acid (*tmlt*), diethylenetriaminepentaacetic acid (DTPA) and iminodiacetic acid (IDA) with Na, providing clarity on the effect of oxygen and nitrogen donors groups in the formation of stable Na complexes. The data reported in this study were obtained by working at constant values of ionic strength in order to overcome the uncertainty related to the estimation of activity coefficients. The analysis of the stability of the Na complex with various organic ligands is assessed using first-principles calculations, providing insight on the role of the different donor groups during the complexation process.

Results and discussion

Experimental evidence of weak complexes formation

During titrations the free sodium concentration is lower than the total sodium added, for each Na-ligand system, reviling the capacity of the organic molecules to capture the cation.

In Figure 1, we report a comparison between the measured pNa at different titrant volumes and the pNa obtained from the total Na concentration in solution. Since the value of ionic strength during experiments was kept constant and the values of activity coefficients did not vary significantly, we claim that this effect can only depend on the complexation of sodium ions. This phenomenon becomes more prominent as the number of potential donor groups increases.

In order to support the experimental evidence of the complex formation, an estimation of pNa-combined uncertainty is proposed. The uncertainty budgets were evaluated following the procedure described elsewere[9,11] for a potentiometric

[a.] *Department of Chemistry, University of Torino, Via P. Giuria, 7, 10125 Turin. E-mail: silvia.berto@unito.it*
[b.] *Massachusetts Institute of Technology, Department of Materials Science & Engineering, 77 Massachusetts Avenue, Cambridge, USA.*
[c.] *Materials Science Division, Lawrence Berkeley National Laboratory, Berkeley, USA. E-mail: pcanepa@lbl.gov*
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apparatus calibrated according to the concentration scale. The procedure follows the metrological literature recommendations.[11-15] The uncertainty of the total Na concentration in solution - $u_c(pNa_{tot})$ - was also calculated as previously reported by Berto *et al.*[9]

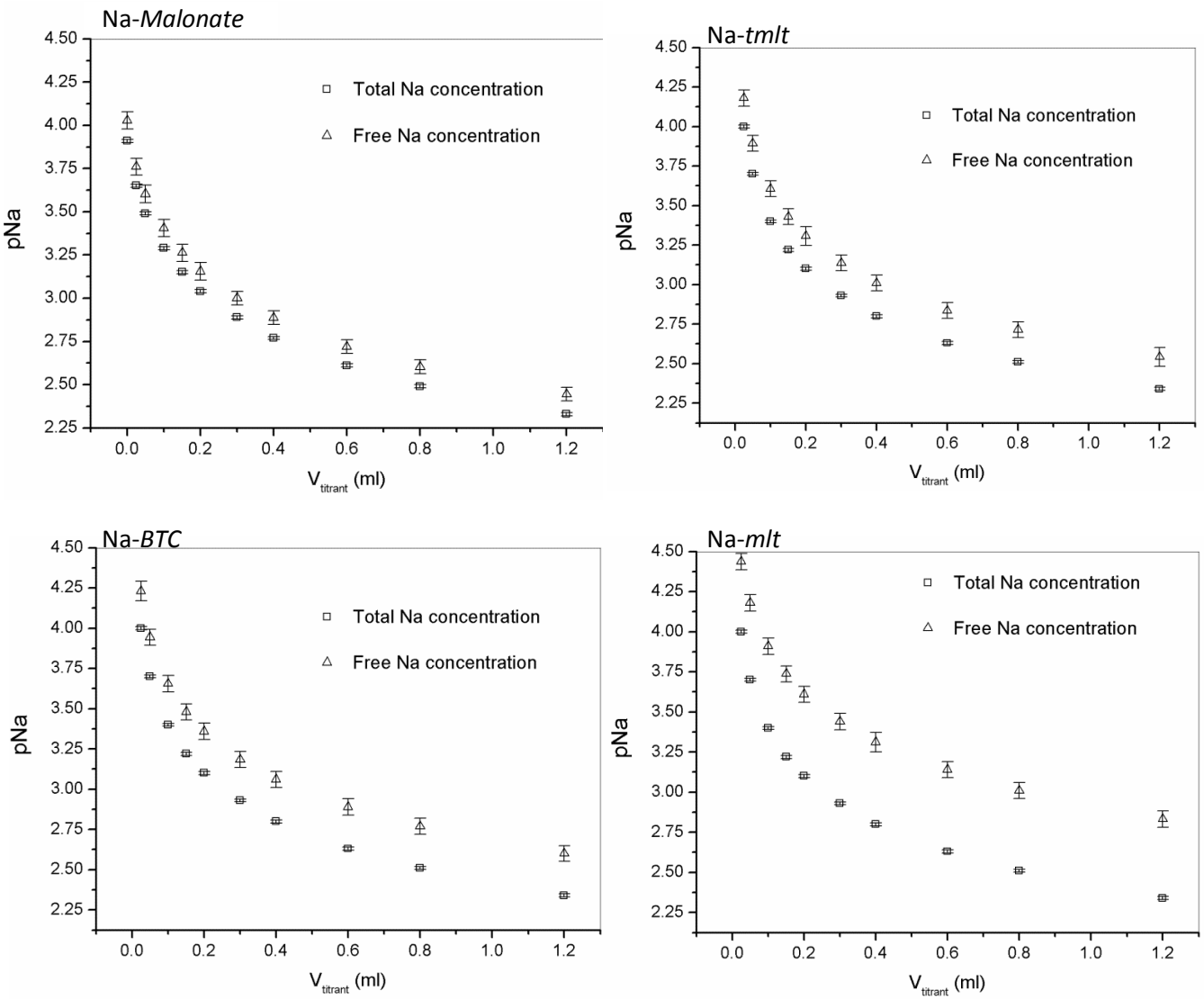

Figure 1 Comparison between the measured pNa at different titrant volumes (titrant NaCl 0.1 mol L^{-1}) and the pNa resultant from the total Na concentration in the solution for different Na-ligand systems. The measured pNa are the means of values obtained with 6 replicates and the error bars represent the extended uncertainty *U*(pNa) (see ref.(9)). Total Na concentration takes into account the concentration of Na^+ at $V_{titrant}$ = 0 mL.

Table 1. Stability constant values of the NaL complexes expressed as $\log\beta_{NaL} \pm u$. The experimental values were determined for various ligands (L) in TBABr at I = 0.1 or 0.3 mol L^{-1} and t = 25°C. In grey are reported the $\log\beta_{NaL}$ of polyamino-carboxylic acids.

Ligand		n.° of charges	$\log\beta_{NaL}$ calc.[a]	$\log\beta_{NaL} \pm u$		
				I = 0 mol L^{-1} [b]	I = 0.1 mol L^{-1}	I = 0.3 mol L^{-1}
Benzenehexacarboxylic acid	*mlt*	6	2.95	3.40 ± 0.04	2.36 ± 0.03[b]	2.26 ± 0.03[c]
Benzenepentacarboxylic acid	BPC	5	2.44	2.86 ± 0.07	1.20 ± 0.05[b]	1.91 ± 0.05[c]
Diethylenetriaminepentaacetic acid	DTPA	5		3.0 ± 0.1	2.10 ± 0.07[c]	2.02 ± 0.07[b]
1,2,4,5-benzenetetracarboxylic acid	*pyr*	4	1.93	2.22 ± 0.08	1.53 ± 0.05[b]	1.47 ± 0.05[c]
1,2,3,4-butanetetracarboxylic acid	BTC	4		2.20 ± 0.08	1.51 ± 0.05[b]	1.45 ± 0.05[d]
Ethylenediaminetetraacetic acid	EDTA	4		2.73 ± 0.05	2.04 ± 0.04[d]	1.98 ± 0.04[b]
1,2,4-benzenetricarboxylic acid	*tmlt*	3	1.40	1.68 ± 0.09	1.16 ± 0.06[b]	1.12 ± 0.06[c]
Citric acid	*cit*	3		1.7 ± 0.1	1.16 ± 0.08[b]	1.12 ± 0.08[d]
Nitrilotriacetic acid	NTA	3		1.97 ± 0.08	1.46 ± 0.05[d]	1.42[b]
Phthalic acid	*phthal*	2	0.85	1.0 ± 0.1	0.62 ± 0.08[b]	0.60 ± 0.08[d]
Malonic acid	*mal*	2		0.8 ± 0.2	0.5 ± 0.1[b]	0.5 ± 0.1[d]
Iminodiacetic acid	IDA	2		1.1 ± 0.2	0.8 ± 0.1[c]	0.7 ± 0.1[b]

(a) $\log\beta_{NaL}$ calculated, at I = 0, by the application of the Eq. 4 of ref. (10) (b) Calculated from the experimental values by the application of the Eq.(1). (c) Measured in this work. (d) From ref. (9), except for the BTC because the previous value has been wrongly reported.

Na-ligand formation constants

The formation constants of 1:1 sodium:ligand complexes obtained in this work are shown in Table 1, together with the stability constants of NaL complexes obtained previously using the same methodology.[9] The expanded Debye-Hückel formalism of Eq. (1) is applied to compute the formation constants for various ionic strengths:

$$\log K_{eq}(I) = \log K_{eq}(I') - z^{*}A\left(\frac{\sqrt{I}}{1+B\sqrt{I}} - \frac{\sqrt{I'}}{1+B\sqrt{I'}}\right) + C(I - I') + D(I^{3/2} - I'^{3/2}) \quad (1)$$

where $K_{eq}(I')$ is the experimental formation constant at ionic strength I', $K_{eq}(I)$ is the formation constant obtained at ionic strength I, C and D are calculated from Eq. (2) and (3):

$$C = c_0 p^* + c_1 z^* \quad (2)$$

$$D = d_0 p^* + d_1 z^* \quad (3)$$

where p^* = Σ (stoichiometric coef.)$_{react}$ – Σ (stoichiometric coef.)$_{prod}$ and z^* = Σ (charge)$^2_{react}$ – Σ (charge)$^2_{prod}$. A = 0.5, B = 1.5, c_0 = 0.1, c_1 = 0.23, d_0 = 0 and d_1 = -0.1 are empirical parameters suitable for solutions with tetralkyl ammonium salt as ionic medium.[16]

The main contribution to the uncertainty of the formation constants ($u(\log\beta_{NaL})$) is the uncertainty of E^0 ($u(E^0)$), therefore, in order to estimate $u(\log\beta_{NaL})$ the $u(E^0)$[9] was applied in the elaboration of titration data with the BSTAC software. The difference between the $\log\beta_{NaL}$ obtained using $E^{0'} = E^0 - u(E^0)$ and $E^{0''} = E^0 + u(E^0)$ was expressed as absolute uncertainty of $\log\beta_{NaL}$ and are reported in Table 1. The uncertainty of the e.m.f. values and of the total volume of the solution were accounted in the elaboration process. The uncertainty values obtained are in accordance with values proposed by Koort *et al.*[17]

With regards to the speciation models, only in the case of BTC and *mtl* was possible to evaluate the stability of the M_2L complexes: $\log\beta_{Na(BTC)2}$ = 2.73 ± 0.04; $\log\beta_{Na(mlt)2}$ = 4.0 ± 0.1. This is due to the experimental procedure adopted, in particular we performed measurements at high pH values, therefore we could not determine the formation of protonated species, such as NaHL or successive NaH_qL species, which are reported for many systems. Furthermore, owing to the relative low M:L concentration ratio, the formation percentages of polynuclear Na_pL species was low, thus hindering their determination.

From data collected in Table 1 it is possible to observe that the formation constants of NaL increase with the number of the charges of the ligand, confirming that the stability of the complexes is mainly due to the electrostatic interaction. The Figure 2 reports the trend of the $\log\beta_{NaL}$ *vs*. the number of charges, where the ligand is considered completely deprotonated, as in the measurement conditions. There are two different trends of experimental points, one for the polycarboxylic and a second for the polyamino-carboxylic acids.

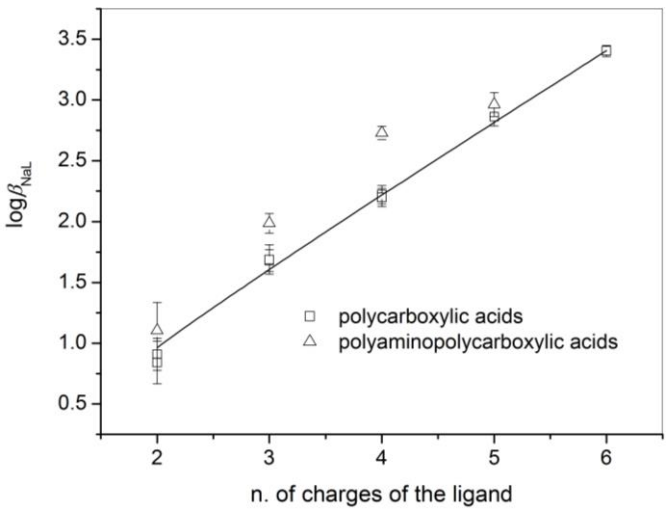

Figure 2 Values of $\log\beta_{NaL} \pm u$ *vs*. the number of charges of the ligand (I = 0 mol L^{-1}). The line is the graphical representation of the Eq. 4 reported in the text.

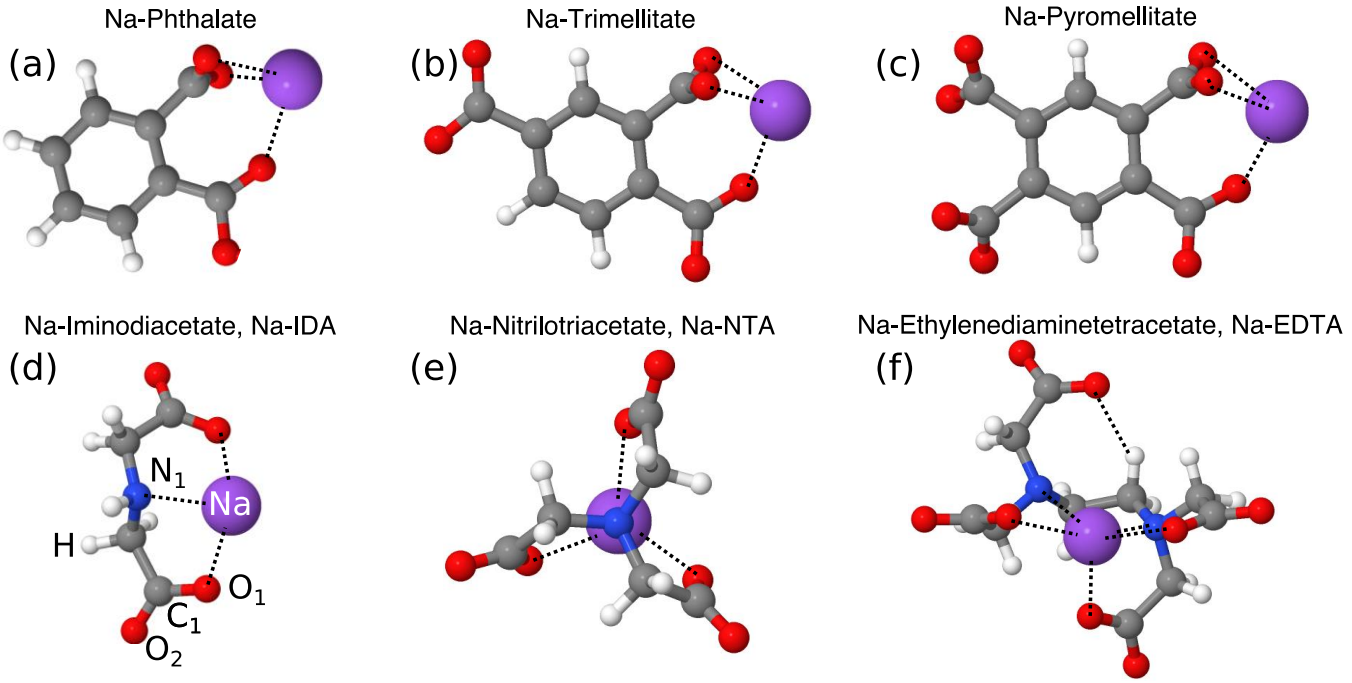

Figure 3 Sodium complexes investigated with *ab initio* calculations. Poly-carboxylic complexes in panels (a) Na-*Phthal*, (b) Na-*tmlt* and (c) Na-*Pyr*, whereas polyamino-carboxylic (d) Na-IDA, (e) Na-NTA and (f) Na-EDTA, respectively. Atomic species are indicated in panel (d), while bonds, holding together the Na-complex and possible H-bonds, are indicated by dashed black lines. Subscripts on specific atoms serve to assign bond distances and Mulliken charges, see text.

In the case of polycarboxylic acids, the dependency of the stability constant $\log\beta_{NaL}$ from the charge *z* of the ligand can be expressed by the Eq. 4:

$$\log b_{NaL} = A|z| + \frac{B}{|z|} \qquad (4)$$

where A = 0.579 ± 0.005 and B = 0.4 ± 0.1, coefficient of determination $R^2 = 0.997$.

This equation is quite similar to that proposed in ref. (10). This confirms the quite good predictive power of the previous equation, nevertheless the parameters A and B were calculated from $\log\beta_{NaL}$ not always evaluated at constant ionic strength. The $\log\beta_{NaL}$ calculated by the application of the equation of Ref. 10 were reported in Table 1 for a direct comparison with the experimental values.

The stability constants of the polyamino-carboxylate complexes are quite high, overcoming the polycarboxylic acids, while the stability increases with the number of donor groups. This is true until the total number of donor groups is six, as in the case of EDTA (four carboxylic and two amino groups). When the donor groups are more than six, such as for DTPA, the increase of stability becomes negligible because no more than six donors can be inserted in the coordination sphere of the cation. This behaviour, and the gap between the $\log\beta_{NaL}$ of polyamino-carboxylate and polycarboxylic complexes suggest the contribution of the N-donors in the coordination of the sodium cation.

Theoretical calculations

The experimental results are discussed qualitatively using *ab initio* calculations based on DFT B3LYP as exposed in the methodology section.

Few approximations were undertaken: *i*) only one Na atom per ligand molecule is considered, observing the experimental conditions of either low sodium concentration or large excess of the organic ligand, *ii*) the series of poly-carboxylic and polyamino-carboxylic compared posses an equal number of carboxylic groups allowing us to provide a consistent comparison throughout the chemical series – for example Na-phthalate (Na-*phthal*) has 2 carboxylic groups and is directly comparable with Na-iminodiacetate. *iii*) Large size molecules investigated experimentally, e.g. BTC, are computationally prohibitive and therefore not considered here. Our preliminary investigation suggest that the interaction between Na ions and benzene rings, carbonyl groups, and hydrogen atoms are energetically less favorable, hence they are not discussed further.

Figure 3 displays the structural models of the poly-carboxylic complexes, i.e. (a) Na-*phthal*, (b) Na-*tmlt* and (c) Na-*Pyr*, and the polyamino-carboxylic complexes, i.e. (d) Na-IDA, (e) Na-NTA and (f) Na-EDTA, respectively. In Figure 3 (a), (b) and (c) the poly-carboxylic ligands with increasing number of carboxylic species from 2 to 4 for Na- *phthal*, Na-*tmlt* and Na-*Pyr*, respectively, set "sturdy" Na-ligand bonds as indicated by the black dashed lines. In particular, each carboxylic group can establish up to three Na-ligand bonds (see Figure 3 (b) and(c)) ranging from 2.30 – 2.36 Å (see Table 2). Similarly, the interactions of the polyamino-carboxylic ligands can set up to 3 carboxylic-Na bonds, which are aided by the presence of additional amino groups that can coordinate further the metal ion.

Table 2 Bond distances (in Å) of relevant atoms (O_1 and N_1) to the Na center and relative Mulliken charges (in unit of the electronic charge). The ΔG (in kJ/mol) for the complex of Fig. 3 are also reported. ΔG in brackets are corrected with the BSSE.

Complex	ΔG	C_1	O_1	O_2	N_1	Na
Na-*phthal*	-18.5 (-5.3)	0.763	2.30, -0.365	2.30, -0.365	–	+0.788
Na-*tmlt*	-23.0 (-9.8)	0.386	2.31, -0.450	2.31, -0.423	–	+0.896
Na-*pyr*	-30.5 (-12.9)	0.184	2.34, -0.450	2.34, -0.416	–	+0.903
Na-IDA	-34.2 (-29.2)	0.353	2.16, -0.640	-0.554	2.35, -0.465	+0.902
Na-NTA	-63.5 (-54.0)	0.479	2.36, -0.594	-0.556	2.60, 0.217	+0.738
Na-EDTA	-76.9 (-63.7)	0.227	2.36, -0.552	-0.553	2.65, 0.394	+0.631

As a result of the flexibility imparted by the long chains of the polyamino-carboxylic ligands, the nitrogen atoms in proximity of the Na^+ ions can also participate to the metal coordination (e.g., in Na-EDTA see Figure 3 (f)), with variable effects as will be demonstrated later.

Predicted bond distances and the Mulliken charges are discussed to assess the interactions of Na^+ ions with the carboxylic and amino groups of the complexes under investigation. Table 2 reports the relevant bond distances and Mulliken charges for some of the atoms (as indicated in Figure 3) forming the complexes. The Mulliken analysis is an intuitive, but not unique way, of repartitioning the wave-function on each atom and orbital by projecting it onto individual orthonormalized atomic orbitals.[18]

Table 2 shows that as the size of the molecule increases the distance between the coordinating atoms, i.e., O_1 and O_2 for the poly-carboxylic ligands, and O_1 and N_1 for the polyamino-carboxylic ligands, and the Na^+ increases proportionally. This is especially true for polyamino-carboxylic ligands; for example, the distance between atom N_1 and Na changes from ~2.35 Å to ~2.65 Å in Na-IDA and Na-EDTA, respectively. The variation in distance between ligand and Na as function of size is associated with two chief factors: *i*) larger molecules, despite highly flexible, need to buckle more around Na, which tends to increase the distance between ion and ligand, and *ii*) the repulsive Columbic interactions between ligands tend to keep them apart. In the case polyamino-carboxylic, the trend of the Mulliken charges reinforces this observation –for example the positive charge on Na^+ ions decreases as function of the ligand denature (from IDA to EDTA)– explaining that more electrons are pushed on Na (refer to Table 2). Nevertheless, this effect is not shown for the poly-carboxylic ligands, and perhaps because they can only bind the metal ion with two carboxyl groups at the time.

The formation free energies of the complexes comprising both poly-carboxylic and amino-poly-carboxylic ligands provide another way to inspect the formation of the Na^+ complexes.

Figure 4 shows the variation of Gibbs free energy stemming from the complexation of Na^+ ions as function of various ligands, i.e. poly-carboxylic and polyamino-carboxylic, as well as No. of ligand groups. According to the experimental observations, the computed trend for poly-carboxylic acids follows a *quasi*-linear behavior. As shown in Table 2, the BSSE correction to the ΔG can substantial (~50% in certain cases) decreases the formation energies by more than half. While the PCM method brings the computed data closer to the experimental data,[19] this method still overestimates the value measured by more than 50% (the computed data without PCM are not reported for the sake of clarity). On the other hand, when adding an explicit water hydration sphere in the PCM the computed binding energies assume very large positive values (> 100 kJ/mol for Na-*pyr*), which are unphysical and limit our predictive capabilities. The BSSE correction also brings the ΔGs "closer" to the experimental values; hence, the uncorrected free energies of Figure 4 and Table 2 represent a lower-bound of the computational data. Given the substantial discrepancy between the experimental and computed data, the discussion will be only focused to the behavior of each trends, which is maintained through various sets of computations.

In general, the stabilization of the Na^+ complexes by polyamino-carboxylic ligands is more pronounced, and this is due to the chelation capabilities of these molecules. By increasing the ligand size the stabilization gained in terms of ΔG reaches a plateau for EDTA (No = 4 in Figure 4) and in agreement with the experimental observations (see Figure 2).

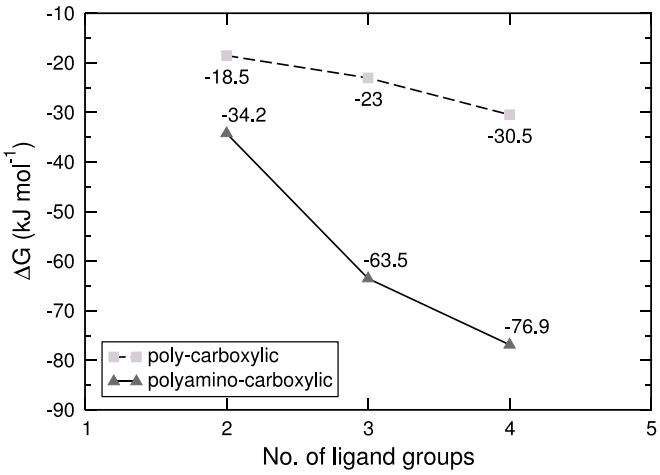

Figure 4 Formation Gibbs free energy (ΔG in kJ mol^{-1}) for Na^+ ions and ligand with different size and chemical functionalities, poly-carboxylic (square), polyamino-carboxylic (triangle). Structure with two ligand carboxylic groups are Na-Phthalate and Na-iminodiacetate (IDA), with three ligand groups, NA-Trimelitate and Na-Nitrilotriacetate (NTA), and with four carboxylic Na-Pyromellitate and Na-Ethylenediamintetracetate (EDTA), respectively. As indicated in Figure 2 the number of amino groups for IDA, NTA and EDTA is 1, 1 and 2. The Gibbs free energies reported are not corrected with the BSSE.

Experimentally we observe an increase of the complexation β of Na^+ ions with poly-carboxylic ligands as function of ligand size (i.e. increasing the number of carboxylic groups, Figure 2), whereas in polyamino-carboxylic follow a linear trend. The discrepancies between the measured and computed absolute values of ΔG are ascribed to delicate balances of enthalpic and entropic contributions on the final Gibbs free energies. The entropic term encloses the vibrational entropy, properly

accounted in these simulations, but perhaps the most important contribution –the configurational entropy– is not taken into account in our models. The configurational entropy depends on the number of degrees of freedom in which the ligand can accommodate one Na^+ atom. In the case of poly-carboxylic acid each ligand provides several complexation possibilities – for example, Na-*pyr* can chelate one Na on four different carboxylic sites, as shown in Figure 3. Therefore, for poly-carboxylic increasing the configurational entropy contributes to the monotonic behavior of the βs as observed experimentally (Figure 2) and not captured by the DFT calculations. In contrast, the configurational entropy for polyamino-carboxylic acids decreases for increasing molecule size (e.g., from IDA to EDTA) due to the chelating effects imparted by the ligand, and reduces the total number of degrees of freedom. On the other hand, the chelating effect observed experimentally and theoretically in polyamino-carboxylic ligands improves the binding properties (ligand-Na), therefore reducing the enthalpies of interaction to more negative values. The balance of entropic and entalphic effects on the Gibss free energies of the polyamino-carboxylic ligands explain the plateau observed both experimentally (Figure 2) and through theory (Figure 4).

Experimental

Chemicals

Sodium chloride (purity of 99.5 %) from Sigma-Aldrich (St. Louis, MO, USA) was kept at 120°C for almost 2 hours before usage. Tetrabutylammonium bromide (TBABr, purity of 99.0 %) and tetrabutylammonium hydroxide (TBAOH), stock solution 1.0 mol L^{-1}, were from Sigma-Aldrich. Benzenehexacarboxylic acid (or mellitic acid, *mlt*), purity 99%, benzenepentacarboxylic acid (BPC), purity not defined by the supplier, 1,2,4,5-benzenetetracarboxylic acid (or pyromellitic acid, *pyr*), purity 98.9%, 1,2,4-benzenetricarboxylic acid (or trimellitic, *tmlt*), purity >99%, diethylenetriaminepentaacetic acid (DTPA), purity ≥99%, iminodiacetic acid (IDA), purity ≥98% were Sigma Aldrich products. The benzenepentacarboxylic acid (BPC) was titrated by pHmetric titration and its titre was 84.5%, in accordance with the loss of weight obtained when the product Q5 was maintained at 120 1C for a night. Therefore, we assumed that the product contains about 15% (w/w) of water.
Grade A glassware and deionised and twice distilled water were used to prepare all the solutions. To assess the purity of tetrabutylammonium hydroxide, and its solution was standardized against potassium hydrogen phthalate (Sigma-Aldrich), while the purity of the acids evaluated by pH-metric titrations.

Potentiometric apparatuses

The potentiometric titration were performed by the Metrohm 713 potentiometer (resolution of ±0.1 mV) equipped with a combined sodium-selective electrode – ISE-Na^+ (Orion, model 86-11), whereas for the pH measurements a combined H^+ glass electrode (Metrohm, model 6.0224.100) was used. Temperature control was achieved by means of water circulation, in the outer chamber of the titration cell from a thermocryostat (model D1-G Haake). The titrant (NaCl solution 0.1 mol L^{-1}) was delivered with a 665 Dosimat burette by Metrohm (minimum deliverable volume of ±0.001 mL).

Procedure for potentiometric titrations

A series of potentiometric titrations were executed adding successive aliquots of titrant (NaCl 0.1 mol L^{-1}) to the ligand solution. The ligand to metal ratios and the quantities of sodium titrant added were chosen in order to keep constant the value of the ionic strength during the experiment and obtain the maximum of percentage complex formation with respect to sodium. The procedure adopted was as follows: the concentration of the ligands were between $6.7\cdot10^{-3}$ – $5.0\cdot10^{-2}$ mol L^{-1} and the solutions were basified at pH ~ 10-11 with TBAOH to maintain the acids in their dissociated form as well as to avoid the interference of H^+ ions. When necessary, the ionic strength was adjusted with TBABr, at I = 0.3 mol L^{-1} (or at I = 0.1 mol L^{-1}). During each titration the variation of the ionic strength was maintained below 5% ensuring negligible variations of the activity coefficients. The titrations were carried out in a stream of purified nitrogen gently bubbled in the titration cell to avoid CO_2 contamination, which can acidify the solution interfering with the e.m.f. measurements.
The ISE-Na^+ was calibrated in $-\log[Na^+]$ units (pNa) recording the e.m.f. values obtained by adding known volumes of NaCl solution 0.1 mol L^{-1}. The Na^+ concentration of the calibrating solutions ranges between $2\cdot10^{-4}$ and $5\cdot10^{-3}$ mol L^{-1}. The ionic strength was controlled by TBABr and was the same as the ligand solutions successively examined. The calibration solutions were basified at pH ~ 10-11 with TBAOH, for avoid the interference of H^+ ions and, in order to check the stability of the electrode response, the calibration procedure was repeated before each titration.

ICP-OES measurements

The sodium impurities in the solution (under titration) were quantified by ICP measurements, performed by a model Liberty – Series II ICP-OES Varian spectrometer. The contribution of sodium impurities was not negligible ($2.5 \cdot 10^{-5}$ mol L^{-1} as mean value), in particular with low concentrations of sodium titrant added.

Data analysis

In order to refine the electrode parameters – formal potential E^0, Nernstian slope and analytical concentration of reagents – the non-linear least squares BSTAC[20] program was used for the elaboration of the calibration data, the same software was also used for elaborating the titration points of each metal-ligand system, which serves to calculate the stability constant of ion pair Na-ligand.
The slope of the Nernst equation for the ISE-Na^+ was checked and always found equal to 59.2 ± 0.1 mV at 25 °C, therefore the tabulated slope of 59.16 mV was used. The electrode formal potential (E^0) used for elaborating the data was the averaged daily value. In the calculation of both $E^{0\prime}$s and the formation constants, we took into account the presence of

unavoidable impurities of sodium in the reactants, and the concentration of sodium impurities was well identified by ICP measurements.

The uncertainty budgets were evaluated in accordance with recommended procedures[11-15] using commercial spreadsheets.

All species reported in this paper can be expressed according to the following equilibria:

$$p\,M^{+} + q\,H^{+} + L^{n-} \leftrightarrows M_pH_qL^{(p+q-n)} \qquad \beta_{pq} \qquad (5)$$

$$p\,M^{+} + H_qL^{(q-n)} \leftrightarrows M_pH_qL^{(p+q-n)} \qquad K_{pq} \qquad (6)$$

where p and q are the stoichiometric coefficients and n the charge of the fully deprotonated ligand (e.g., for EDTA n = 4).

First-principles Formation free energies of Na-ligand complexes

First-principles calculations based on the Density Functional Theory (DFT) approximation are used to elucidate the formation free energies of sodium complexes in the presence of several ligands (see Data Analysis Sec.). While computing complex's formation constants is a challenging task,[19] DFT is used to chart useful trends from the complex formation energies. Due to the importance of strong interactions between solvent molecules (water) and the Na-complexes, we model each structure with an implicit solvation approximation, the polarizable continuous model (PCM), to describe long-range solvent-solvent interactions. The Gibbs free energy (G) of the fully solvated Na-complexes clusters are dictated by Eq. 7.

$$G = E_{PCM} + ZPE + q - T\,S + pV \qquad (7)$$

where E_{PCM} represents the DFT total energy of the water solvated complex. ZPE, q, T and pV are the zero point energy correction, the thermal contribution, the entropic term and the pressure and volume of the system, respectively, approximated by the Na-complexes comprising only by the Na^{+} and the coordinating ligand molecules. E_{PCM} is computed, when available, by Na^{+} complexes taken from existing X-ray structures of homologous geometries and successively relaxed using the B3LYP[21-23] hybrid functional in conjunction with a well-converged 6-311+G(3df,3pd) basis-set, as implemented in Gaussian09.[24] The effect of the solvent is incorporated in E_{PCM} of Eq. 7 by fully relaxing the geometries using the PCM formalism developed by Tomasi *et al*.[25]

The analysis of the normal modes is performed to ensure that the relaxed geometries are real minima as well as to compute the free energy corrections, i.e. ZPE, q and S of Eq. 7. The Gibbs free energies (E_{PCM}) affected by the spurious Basis Set Superposition Error (BSSE) are corrected with the counter-poise method proposed by Boys and Bernardi.[26]

Convergence of the computational setup was tested using a correlation consistent basis-set aug-cc-pVTZ, and for the case of IDA the relative mean error (compared to a 6-311+G(3df,3pd)) is as low as ~0.06 % and below chemical accuracy.

Conclusions

The formation of the Na^{+} complexes with poly-carboxylic and polyamino-carboxylic ligands was assessed. The formation constants of the complexes were evaluated at constant ionic strength. The data show an increase of the formation constants (more stable complexes) with the charge of the ligand. The trend is linear in the case of poly-carboxylic acids, whereas it reaches a plateau past a specific ligand size for the polyamino-carboxylic. Furthermore, the polyamino-carboxylic acids show higher formation constants when compared with poly-carboxylic, but possessing the same number of carboxylic functions. The experimental results are discussed on the basis of a qualitative model that predicts the logβ as function of the ligand charge. First-principles calculations are used to inspect the electronic structure of the complexes. Theoretical models reveled that nitrogen atoms participate synergically to the metal coordination imparted by the flexibility of the long chains of the polyamino-carboxylic ligands, hence providing structures with higher stability. Specifically, by increasing the ligand size the stabilization gained in terms of calculated ΔG reaches a plateau for EDTA. Although the computed values do not provide accurate ΔGs (thus βs), these findings follow the experimental observations, establishing coherence between the experimental theoretical trends observed for the two types of ligands.

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