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THE NATURE OF METAL–LIGAND BONDING IN THE PRIMARY HYDRATION SHELL AND IN IONOPHORES WITH ALKALI METAL IONS

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SUMMARY

1. Transport of alkali ions in model membranes mediated by ionophores is associated with at least two basic problems: (a) a conceivable physical model for the metal–ligand bonding in the primary hydration shell and (b) migration of ions from the primary hydration shell to ionophores to form ion complexes.

2. The nature of metal–ligand bonding both in the primary hydration shell and in the ionophores has been found to be around 80 % ionic and 20 % covalent in both cases by independent investigation. Clearly the energetics being equivalent in both systems, ions will not migrate from the former to the latter.

3. A novel model is proposed in terms of hydrogen bonding in the primary hydration shell for Li^+ and Na^+ so that the migration of these ions to ionophores is easily envisaged. Hydrogen bonding contributes 18 % and 5 % of the energy to the total hydration shell energy of Li^+ and Na^+, respectively.

INTRODUCTION

The metal–ligand bonds in the primary hydration shell of Li^+ and Na^+ have been proposed to be around 80 % ionic and 20 % covalent [1–7]. Alkali ions are also known to ligand with organic compounds e.g., *N*,*N*-dimethylformamide, methylacetate, *N*,*N*-dimethylacetamide etc., and with macrocyclic ionophores e.g., valinomycin, enniatin-B, nonactin and the polypeptide antamanide. The nature of metal–ligand bonds in the above mentioned compounds have also been proposed to be 80 % ionic and 20 % covalent for Li^+ and Na^+ [8, 9]. Experimentally, alkali ions are known to migrate from their primary hydration shell to such organic compounds and form ion complexes [10, 11]. Migration of alkali ions from the hydration shell to the ionophores is difficult to envisage since the energetics of both systems are equivalent in nature.

Therefore, in this paper, a novel physical model is discussed for the geometry of the hydration number of six for the primary hydration shell of alkali ions, so that

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the migration of ions from the hydration shell to ionophores or polypeptides can easily be envisaged.

The extent of delocalisation of electrons from the ligand oxygen to the vacant orbitals of the alkali ions causes the 20 % covalent character of the metal–ligand bonds in the model compound complexes [8, 9]. Such an interaction is found to be true and consistent on examination of alkali ion–ionophore/polypeptide complexes, in a geometrical arrangement where the alkali ion faces one of the lone pairs of the ligand oxygen.

In the hexa-coordinated primary hydration shell model proposed here, it is observed that none of the lone pairs of the water ligand face the alkali ions, but form twelve, non-linear hydrogen bonds around the Li^+ and Na^+ and none around the larger ions. The only other study in literature which suggests hydrogen bonding in the primary hydration shell of alkali ions is that of Tredgold [12], based on the Born approximation later modified by including the effect of dielectric saturation [13].

The model

Metal–ligand bonding in Li^+/Na^+–OH_2 complexes. In Table I data is compiled from the experimental and calculated values obtained from different sources for the mono-hydration energy of Li^+ and Na^+ [1, 2, 6, 7, 14]. The important point to note is the angle Ψ which is the orientation angle of the alkali ion with respect to the plane of the ligand water molecule. This is shown in Fig. 1. Positions marked 1 and 3 of the alkali ion (Ψ = 120° and 240°) are energetically equivalent. In these positions the alkali ion is facing one or the other lone pair of the ligand oxygen. In such a geometrical arrangement it can be seen from reference [1] that the CNDO (Complete Neglect of Differential Overlap) method shows delocalisation of electrons from the oxygen ligand to the alkali ion. This delocalisation amounts to the suggested 20 % covalent character of the Li^+/Na^+–OH_2 bonds, however the equilibrium distances and interaction energies calculated are much higher than the experimental values [6, 7].

The most accurate calculated mono-hydration energy, in agreement with the experimental values, is given by source reference [14]. The calculated Li^+/Na^+–OH_2 equilibrium distances are 1.89 Å/2.24 Å as compared to the experimental values of

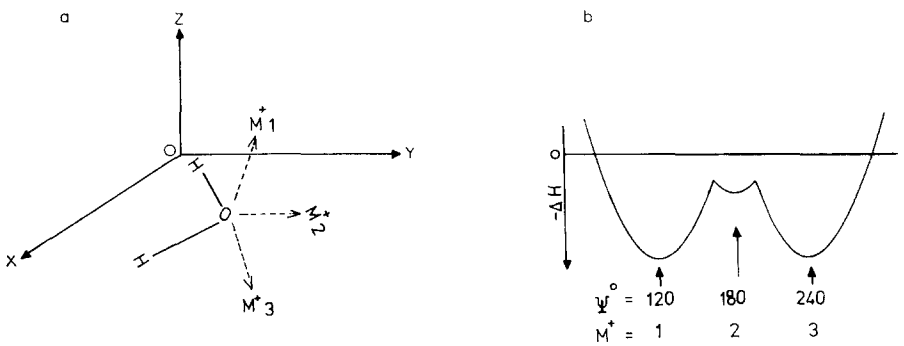

Fig. 1. Positioning of the alkali ion with respect to the plane of the ligand water molecule. (a) The water molecule lies in the XOY plane, the two lone pairs point into the + Z and − Z quadrants. Correspondingly the metal ion takes +Z(1), in the XOY plane (2) or the − Z (3) positions. (b) A hypothetical energy curve is drawn for the three positions with the corresponding out of plane angles.

TABLE I

COMPARISON OF THEORETICAL AND EXPERIMENTAL MONO-HYDRATION ENERGIES AND EQUILIBRIUM GEOMETRIES OF THE Li^+ AND Na^+ IONS

The out-of-ligand plane angle $\psi = 0°$ or 180° is equivalent and corresponds to the position marked 2 of Fig. 1a.

References & methods	Geometry of water molecule		M^+–OH_2 distance (Å)		ψ (°)		$-\Delta H^{M^+}_{n=1}$ kcals/mole	
	$O–H_1/H_2$ (Å)	$H_1–O–H_2$ (°)	Li^+	Na^+	Li^+	Na^+	Li^+	Na^+
CNDO [1]	1.030	107.10	2.42	2.98	64	84	51.60	34.90
SCF-MO-LCGO [2]	0.958	104.50	1.81	—	180	—	47.40	—
	0.958	104.50	1.82	—	180	—	46.60	—
	0.958	104.50	1.83	—	180	—	43.60	—
SCF-MO-LCGO [14]	0.960	104.52	1.89	2.24	0	0	36.02	25.16
Gas phase Mass spectra [6, 7]	—	—	1.92	2.26	—	—	34.00	24.00

1.92 Å/2.26 Å and the energies are nearly equal. Energy minima by SCF-MO-LCGO (Self Consistent Field-Molecular Orbital-Linear Combination of Gaussian Orbital) calculations [14], are obtained for $\Psi = 0°$ equivalent to 180°, the position marked 2 in Fig. 1a. In this position, the alkali ion lies on the common bisector of lone-pair–oxygen–lone-pair and hydrogen–oxygen–hydrogen angles. Comparison of theoretical and experimental values of $-\Delta H$, Ψ and r clearly show that the alkali ions do not face either of the lone pairs of the ligand oxygen, hence partial covalency of these bonds should not be expected.

Metal–ligand bonding in Li^+/Na^+–$(OH_2)_6$ complexes. Gas-phase mass spectra results [6, 7] and relaxation time constants measured by relaxation technique [15] strongly suggest an optimum coordination number of six water molecules in the primary hydration shell of alkali ions. Three major arguments have been proposed in favour of the partial covalent nature of the metal–ligand bonds in the Li^+/Na^+–$(OH_2)_6$ complexes. These are summarised below.

1. Rapid fall in energy estimated by gas phase mass spectra [6, 7] as a function of increasing hydration number, $n(-\Delta H^{Li^+}_{n=1\to6} = 34.0 \to 25.8 \to 20.7 \to 16.4 \to 13.9 \to 12.1$ and $-\Delta H^{Na^+}_{n=1\to6} = 24.0 \to 19.8 \to 15.8 \to 13.8 \to 12.3 \to 10.7$ kcals/mole) has been attributed to the partial covalent nature of the metal–ligand bonds in the primary hydration shell. This rapid fall in energy is doubtful for the K^+ hydrate and almost absent for the Rb^+ and Cs^+ hydrates. 2. Lone pairs of the ligand oxygen are believed to be in the near vicinity of the vacant orbitals of the Li^+ and Na^+, resulting in covalency of the metal–ligand bonds as well as shielding the charge on the metal ion from other water molecules [6, 7, 16]. 3. Formal charge transfer from the ligand oxygen to the vacant orbitals of Li^+ and Na^+ has been shown using the CNDO/2 method. The magnitude of charge transfer accounts for the 20 % covalent nature of the metal–ligand bonds in the primary hydration shell of the Li^+ and Na^+ [1–5].

It is pointed out here, for the first time in the literature, that the delocalisation of electrons from the ligand water molecules to the alkali ions, resulting in the sug-

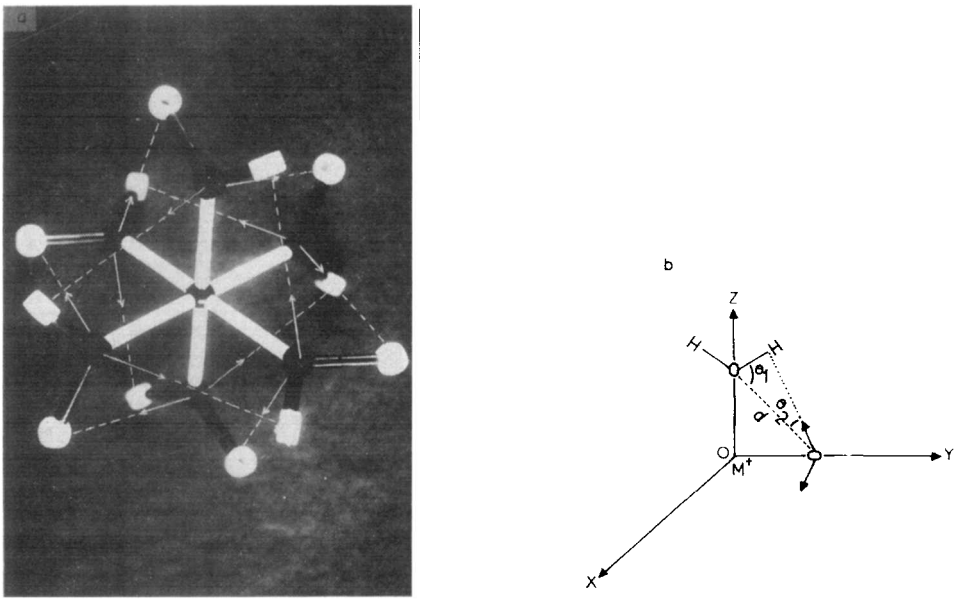

Fig. 2. Geometry of the proposed primary hydration shell of alkali ions. (a) Model of the proposed six coordinates of the alkali ions. The lone-pairs are represented by dashed arrows. (b) Showing the direction of one such lone pair pointing towards the hydrogen of another water molecule in the other plane. For description see text.

gested covalency of the metal–ligand bonds, is not consistent with the value of the geometric parameter Ψ. Lone pairs of ligand oxygen do not face the alkali ion when $\Psi = 0°$ or $180°$.

Geometry of the proposed model. Based on the arguments in the preceding sections, a hexa-coordinated model of the primary hydration shell is proposed for the alkali ions having the following geometrical structure.

The alkali ion lies at the origin of axes, two water molecules are placed on each axis, so that each water molecule lies on the positive and negative x, y and z-axis with the oxygens facing the alkali ion. The alkali ion will then lie on the common bisector of lone-pair–oxygen–lone-pair and hydrogen–oxygen–hydrogen angles of all the six water molecules i.e., $\Psi = 0°$ or $180°$. The planes of the three pairs of water molecules are mutually perpendicular. This is shown in Fig. 2a. In this arrangement, it is observed that the lone pairs of oxygens point in the direction of hydrogens of the other planes. The distances between the lone pairs and hydrogens and the corresponding angles involved are listed in Table II below.

The geometry for the individual water molecule is the same as that entered in Table I, reference [14]. Lone pair distance is taken to be 1.0 Å from the centre of the oxygen and the lone-pair–oxygen–lone-pair angle as 120°. The lone pairs lie in a plane perpendicular to the plane of the water molecule.

The alkali-ion–oxygen distances (r) are taken to be the same as those given by gas phase mass spectra results for six coordination [6, 7] and also those given by the Volta potential method [17] corresponding to the distances used by Halliwell and Nyburg for the calculation of hydration energy by class II methods [18].

TABLE II

DATA USED FOR THE CALCULATION OF HYDROGEN BONDING ENERGY IN THE PRIMARY HYDRATION SHELL OF ALKALI IONS

θ_1, θ_2 and d-values are calculated from the model shown in Fig. 2b. Two sets of metal-oxygen distances (r) have been used, r-values yielded by Volta potential method §[17] and later used by Halliwell and Nyburg for the calculation of hydration energy by class II methods §[18], and those yielded by gas phase mass spectra §§[6, 7]. Both sets of distances refer to six coordination of the alkali ions.

Ion type	$M^+-OH_2^{\S}$ r (Å)	$O_1-O_2^{\S}$ d (Å)	$M^+-OH_2^{\S\S}$ r (Å)	$O_1-O_2^{\S\S}$ d (Å)	θ_1 (°)	θ_2 (°)	$-12V_{hb}^{\S}$ (kcals/mole)	$-12V_{hb}^{\S\S}$
Li^+	1.98	2.800	2.16	3.055	82.75	15	65.5	22.56
Na^+	2.33	3.295	2.44	3.455	82.75	15	7.6	4.68
K^+	2.71	3.833	2.74	3.876	82.75	15	1.3	1.80
Rb^+	2.86	4.044	2.84	4.016	82.75	15	—	—
Cs^+	3.07	4.342	3.06	4.326	82.75	15	—	—

The distances between any two oxygen centres, d (shown in Fig. 2b) for Li^+/Na^+, listed in Table II, are well within the range of distances found in a variety of water-molecule hydrogen-bonded crystal structures and that in water and ice [19, 20]. The angles for the formation of hydrogen bonds in this model deviate quite a bit from strict linearity. Hydrogen bonds may deviate from strict linearity by as much as 30°, as has been found in fourteen different hydrates compiled in source reference [19]. The large d-values do not allow the formation of hydrogen bonds in the primary hydration shell of K^+, Rb^+ and Cs^+.

Calculation of hydrogen bonding energy. A simple potential function for the calculation of linear hydrogen bond energy was put forward by Lippincott and Schroeder [20, 21], and later modified for angular dependence by Moulton and Kromhout [22].

$$V_{hb} = D[1-\cos^2\theta_1 \cdot \exp[-n(r-r_0)^2/2r]] \\ -D^{\S}[1-\cos^2\theta_2 \cdot \exp[-n^{\S}(d-r-r^{\S}{}_0)^2/2(d-r)]] \\ +B \cdot e^{-\mu \cdot d}-A/d^m. \qquad (1)$$

All the parameters were as in the original work, given in the source reference [20, 21]. The values for θ_1 and θ_2 as shown in Fig. 2b are constant for varying d-values for different ion sizes, these are calculated from the model shown in Fig. 2b and are presented in Table II. The resulting sum of $-12V_{hb}$ is also presented in the same table.

RESULTS AND DISCUSSION

Using Li^+ and Na^+–$(OH_2)_6$ equilibrium distances of 1.98 Å and 2.33 Å determined by the Volta potential method [17], calculated hydrogen bonding energy is 65.5 and 7.6 (kcals/mole), equivalent to 52 % and 8 % of the total hydration shell energy of 122.1 and 98.2 (kcals/mole), respectively. Similarly, using the Li^+ and Na^+–$(OH_2)_6$ equilibrium distance of 2.16 Å and 2.44 Å determined by gas phase mass spectra [6, 7], calculated hydrogen bonding energy is 22.56 and 4.68 (kcals/mole), equivalent to 18 % and 5 % of the total hydration shell energy of 122.9 and 92.4

(kcals/mole), respectively. The hydrogen bonding energy values based on the gas phase mass spectra metal–ligand equilibrium distances [6, 7], may be taken to be of a more correct order of magnitude. However, these percentage values of hydrogen bond energies probably will have to be revised in view of (a) a better potential function for the calculation of hydrogen bond energy and (b) the fact that mere addition of a single hydrogen bond energy term to twelve must be abandoned in favour of cooperate behaviour of hydrogen bonds.

The proposed hydration model derives further support from the following observations:

1. The ion–water ligand plane orientation angle $\Psi = 0°$ or $180°$ (position marked 2 in Fig. 1a) demands that no delocalisation of electrons should occur from the latter to the former.

2. Shielding of the charge on the alkali ion is better achieved by twelve non-linear hydrogen bonds rather than by the lone-pairs shielding the ionic charge [6, 7, 16].

3. 18 % and 5 % hydrogen bonding effect in the primary hydration shell for the Li^+ and Na^+ are figures of reasonable magnitude when compared to the 20 % suggested covalent character of these bonds [1–7].

4. From the gas phase mass spectra data [6, 7], the maximum fall in energy occurs when the hydration number, $n = 1 \rightarrow 2$, for the Li^+ this fall in energy is 8.2 kcals/mole and for the Na^+, 4.2 kcals/mole. These values are far more indicative of non-linear hydrogen bonds than of partial covalent effects.

5. Hydrogen bonding in the primary hydration shell of Li^+ and Na^+ is consistent with the suggestions of Tredgold based on the effects of dielectric saturation [13]. No unfilled space remains in the near vicinity of the ions.

Implications of the proposed hydration model on the migration of ions to ionophores or polypeptides

Metal–ligand bonding in Li^+/Na^+–OX complexes. In this section the geometry of the oxygen-containing organic ligand (OX) is examined with respect to the position-

TABLE III

GEOMETRY AND ENERGY OF STABILISATION OF Li^+/Na^+–OX COMPLEXES

Calculations have been performed varying ψ from 0° to 180° and not beyond, so the values at ψ = 240° have not been reported§. Calculations were made in several orientations but values are only reported for $\psi = 60°$§§. This is equivalent to $\psi = 120°$ given in terms of the internal angle.

References & methods	Ligand type (OX)	Ion type	M^+–OX r (Å)	ψ (°)	$\lvert E_{M^+-OX} \rvert$ (kcals/mole)
§CNDO/2 [8]	*N,N*-Dimethylacetamide	Li^+	2.1	120	83
	Methylacetate	Li^+	2.1	120	80
	N,N-Dimethylacetamide	Na^+	3.0	120	65
	Methylacetate	Na^+	3.0	120	60
§§CNDO/2 [9]	Formamide	Li^+	2.2	60	72
	N-Methylacetamide	Li^+	2.2	60	88
	N,N-Dimethylformamide	Li^+	2.2	60	83

ing of the alkali ions. Calculations on Li^+/Na^+–OX complexes have been reported using the CNDO/2 method [8, 9]. The energy of stabilisation and the geometry of these complexes is presented in Table III.

In all complexes reported above, it is observed that the alkali ions prefer to come out of the plane of the ligand molecule. This out of plane angle $\Psi = 120°$ corresponds to the position marked 1 of Fig. 1a, in which the alkali ion faces one of the lone pairs of the ligand oxygen. In this geometrical arrangement the extent of charge transfer from the ligand oxygen to the alkali ion accounts for the 20 % covalent character of metal–ligand bonds in these complexes [8]. A recent SCF-ab initio study by Perricaudet and Pullman [23] does not confirm the angular dependance of metal–ligand bonds in the model complexes. The reason for this finding may well lie in the use of minimal basis set for calculation, as evidenced by the large values obtained for the interaction energy and short distances of metal–ligand bonds.

Metal–ligand bonding in $Li^+/Na^+/K^+$–$(OX)_n$ *complexes.* Based on the NMR and binding constant studies, it is now quite well established that alkali ions migrate from the aqueous phase and bind to oxygen-containing ionophores e.g., valinomycin, enniatin-B, and nonactin [10, 11].

No theoretical study has been reported on the nature of metal–ligand bonds in the ion–ionophore complexes, except our earlier attempt using the point charge approximation [24]. The point charge approximation is limited and did not reveal the partial covalent nature of the metal–ligand bonds in these complexes.

The nature of metal–ligand bonds in ion–ionophore complexes can be taken to be some function of Ψ i.e., the metal–ligand bonds are maximally bonding with a partial covalent character when $\Psi = 120°$ or 240°, a local minima at 0° or 180° and comparatively antibonding for all other values of Ψ. This argument is found to be true and consistent on examination of the geometry of the Na^+ and K^+ complex of valinomycin [10, 25], the Na^+ and K^+ complex of enniatin-B [10, 26], K^+ complex of nonactin [27] and the Li^+ and Na^+ complex of the polypeptide antamanide [28]. The ion–ionophore complex conformations in the above mentioned studies are reported on the basis of NMR and X-ray diffraction data. In all cases the alkali ion orientation to the ligand groups is $\Psi = 120°$ and/or 240°. Delocalisation must therefore be expected, leading to a partial covalent nature of the metal–ligand bonds in these complexes [8].

CONCLUSIONS

Ion selectivity and migration of ions from the aqueous phase to ionophores have been discussed in the literature in terms of steric size fit and structural parameters [10], free energy of solvation and binding constants [29], polarisation of ligands [30], quadrupole repulsion and dispersion interactions [31], electron transfer from ligand groups to ions [8, 32] and in terms of an electrostatic model [33]. None of the above studies touched upon the possibility of differences in the nature of metal–ligand bonds in the primary hydration shell and in ionophores.

The primary hydration shell energy of the alkali ions can be expressed as:

$$-\Delta H_{M^+-(OH_2)_6} = f(\Psi, r) \qquad (2)$$

where $\Psi = 0°$ or 180°, leading to the formation of twelve non-linear hydrogen bonds

(weaker in character) around the smaller alkali ions. Similarly the ion–ionophore interaction energy can be expressed as:

$$-\Delta E_{M^+-(OX)_n} = f(\Psi, r) \tag{3}$$

where $\Psi = 120^\circ$ and/or 240°, leading to the formation of partial covalent bonds (stronger in character). Thus a single incoming OX ligand is capable of completely disrupting the proposed hydration shell structure. Further, it is expected that the disruption of hydrogen bonds would be a cooperative phenomena.

The occurrence of hydrogen bonding in the primary hydration shell of smaller alkali ions agrees well with the discussed theoretical and experimental data, particularly with the suggestion of Tredgold [13].

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