

Dehydration of a polyether type extraction agent and of the corresponding K^+ complex: insights into liquid-liquid extraction mechanisms by quantum chemical methods

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Abstract In this paper we report a quantum chemical study performed at the B3LYP/6-311G++(d,p) level of theory on structural and energetic aspects of the sequential dehydration of a tetra-hydrated polyethylene-glycol type podand (1,2-bis-{2-[2-(2-methoxy-ethoxy)-ethoxy]-ethoxy}-benzene, hereafter *b33*) and its complex with the K^+ cation. Thermodynamical parameters were determined by hessian quantum calculations performed using a self-consistent reaction field (SCRf) method, taking into account solvent (dichloromethane) effects. The results allowed the estimation of dehydration enthalpies, entropies and free energies for the hydrated free *b33* podand and its corresponding K^+ cation complex in dichloromethane. The low absolute values found for the dehydration free energies as well as the structural features found for the optimized structures and the corresponding basis superposition calculated interaction energies, support the hypothesis of an interfacial complexation type mechanism governing the assisted extraction of K^+ from an aqueous toward an organic phase, in liquid/liquid extraction.

Keywords Alkali cation extraction · Assisted liquid/liquid extraction · Extraction mechanisms · Polyethylene-glycol type podands

Introduction

It is a common experience that alkali metal cations dissolved in water do not extract significantly by themselves into an organic solvent such as dichloromethane (DCM) [1, 2], nonetheless, since the early works of Pedersen [3], polyether type molecules such as crown ethers are renowned for their ability to extract these ions in what is usually known as assisted extraction. The ability that these molecules show to complex alkali metal cations mimics the capacity of some biological molecules such as valinomycin (a K^+ specific cyclic ionophore) [4] and monensin (a Na^+ specific linear ionophore) [5] to selectively transport alkali cations through cell membranes. This capacity has been widely used in separation processes (*e.g.*, liquid-liquid extraction [6]), as well as in synthesis (*e.g.*, phase transfer catalysis [7]).

Although alkali metal cation extraction has been known for a long time, the mechanisms by which assisted extraction occurs are not unequivocally established. Three possible mechanisms have been proposed [8, 9]: (1) transfer of both the cation, M^+ , and the extraction agent, *E*, from the starting phase to the interface, where complexation occurs, followed by migration to the bulk organic solvent in what we here denominate *cation and extraction agent transfer to interface (CETI)* mechanism; (2) transfer of the cation from the aqueous phase to the bulk organic phase, where complexation occurs, in what we here denominate the *cation transfer to the organic phase (CTOP)* mechanism; and (3) transfer of the extraction agent from the organic phase to the bulk aqueous phase, where complexation occurs, followed by complex extraction to the bulk organic phase in what we here denominate the *extraction agent transfer to the aqueous phase (ETAP)* mechanism. These three mechanisms are schematically presented in Fig. 1. In them we considered the

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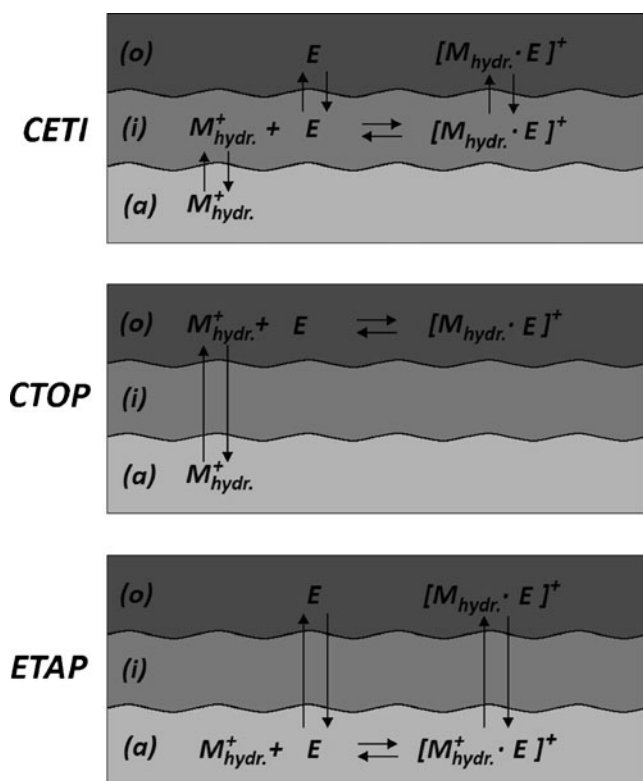


Fig. 1 Schematic representation of the three ion transfer mechanisms (CETI, CTOP and ETAP) from an aqueous phase (a) across the interface (i) to an organic phase (o)

free and/or complexed cation to transfer to the organic phase as a hydrated ion as there is good evidence to support this assumption [10–14].

Elucidation of the extraction mechanism by theoretical means has been a major goal in our investigation and, as such, recourse to molecular dynamics (MD) studies allowed us to determine the highly unstable character of the complexes involving alkali metal cations and the *b33* podand (Fig. 2), in bulk water [15]. This observation putatively rules out the ETAP mechanism. Further quantum chemical [16], MD [17] and steered MD studies [18, 19] suggest that the extracted K^+ cation is at least partially accompanied by its hydration sphere to the organic layer. The results from one of the steered MD studies in particular [18] suggest that the hydrated cation may be complexed by the *b33* podand,

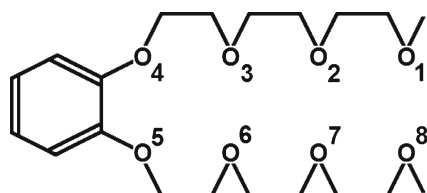


Fig. 2 Schematic representation of the *b33* podand and the oxygen atom numbering scheme used in the text

while forming protrusions (water fingers). These observations support the CETI type mechanism, as already hinted by electrochemical studies on other systems involving crown ethers [20].

It is well known that even organic solutes drag water molecules while transferring from an aqueous phase to an organic phase [21, 22]. A recent calorimetric study showed the significance of the interactions between water molecules and crown-ethers in halogenated solvents [23]. Another study on the hydration of benzo-crown-ethers (*benzo-15-crown-5* and *benzo-18-crown-6*) and the *benzo-18-crown-6* complex with the K^+ cation showed that the hydration of the free crown ethers is not negligible and that upon complexation (with the K^+ cation) the corresponding hydration is reduced [24].

To investigate this subject further, we present here a quantum chemical study on the energetics involved in the dehydration of the *b33* podand and of its complex with the K^+ cation. We aim to provide some meaningful insight into the above described mechanism of transference, in particular in its last step (in the organic phase) where the gradual loss of hydration water molecules by the hydrated complex takes place.

Methods

All quantum calculations were performed at the B3LYP/6-311++G(d,p) level of theory, using the GAUSSIAN09 package [25]. DFT was chosen as the fundamental method in our work as it has been widely used to study similar systems [16] and is considered to be an adequate method to predict structural and thermodynamical properties [26]. Among the various DFT functionals, we chose the hybrid B3LYP [26, 27] as it is widely tested and used [28].

The optimization calculations for the various systems studied were performed on starting structures that were built from previous MD results [17, 18] using Accelrys DS Visualizer (vers. 2.0.1.7347, Accelrys Software Inc., 2005). The resulting optimized structures were used for hessian calculations in order to analyze their stationary nature, by looking at the number of imaginary vibrational frequencies and to estimate the zero point corrected enthalpies and free energies of formation. In order to account for solvent effects (here dichloromethane, see ref. [18]), these calculations were performed considering the polarizable continuum model, by use of the integral equation formalism (IEFPCM) variant [29] that constitutes the self-consistent reaction field (SCRF) method used as default in the GAUSSIAN09 package.

The full Boys and Bernardi [30] counterpoise correction method was also applied, in order to get an estimation of the basis set superposition error (BSSE) associated to the

predicted interaction energies between the various system sub-groups considered (see below).

A note is in order here to acknowledge that for fluxional systems such as those considered here, the search for a global minimum energy structure is unfeasible but, as in previously published work [16], the assumption that the structures considered may be taken as representative of the corresponding system is justifiable as hinted by an unpublished study performed at the group, at the HF/6-31 G(d) level of theory, on 22 different conformations of the isolated *b33* molecule, where it was found that the mean free energy of formation was 2.4 ± 2.1 kcal·mol⁻¹ relative to the most stable conformation found.

Results and discussion

We proceed with a brief description of pertinent structural features found for the optimized structures considered, followed by a discussion on the energetic aspects (at the thermodynamic and at the counterpoise corrected interaction energy levels) calculated for the dehydration processes for the $[b33 \cdot (H_2O)_n]$ and for the $[K \cdot b33 \cdot (H_2O)_n]^+$ systems (with $n=4$ to 0).

Structural features of the hydrated podand

In the following descriptions the parameters reported for the hydrogen bonds correspond to a widely used geometric definition: the oxygen-oxygen distance, $R_{OO} < 3.5$ Å, and the angle between the OH bond and the OO vector, $\theta_{HOO} < 30^\circ$ [31].

In the optimized structure for the $[b33 \cdot (H_2O)]$ system (Fig. 3a) one hydrogen atom of the water molecule interacts

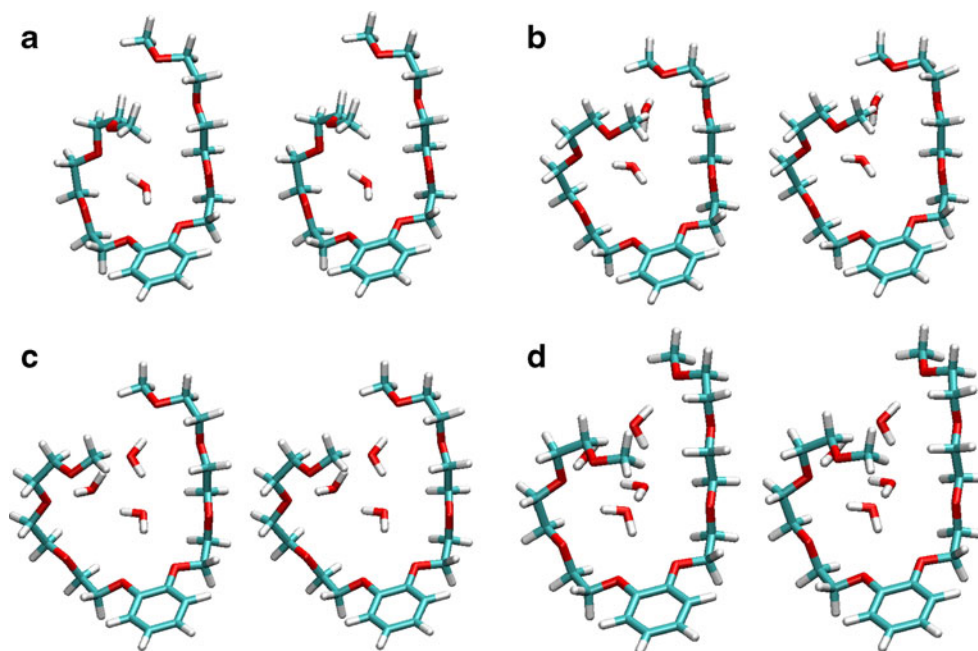
simultaneously with two podand oxygen atoms, O_4 ($R_{OO} = 3.237$ Å; $\theta_{HOO} = 21.5^\circ$) and O_5 ($R_{OO} = 3.150$ Å; $\theta_{HOO} = 28.4^\circ$) in what could be seen as a three centered hydrogen bond, while simultaneously the other hydrogen atom interacts with another podand oxygen atom, O_2 ($R_{OO} = 2.938$ Å; $\theta_{HOO} = 7.3^\circ$).

The optimized structure for the $[b33 \cdot (H_2O)_2]$ system (Fig. 3b) shows that the two water molecules engage in hydrogen bonding with one another ($R_{OO} = 2.858$ Å; $\theta_{HOO} = 9.8^\circ$) and, separately, with two podand oxygen atoms, O_7 ($R_{OO} = 2.885$ Å; $\theta_{HOO} = 13.7^\circ$) and, O_1 ($R_{OO} = 2.961$ Å; $\theta_{HOO} = 12.6^\circ$).

As for the $[b33 \cdot (H_2O)_3]$ system, its optimized structure (Fig. 3c) shows that a first water molecule hydrogen bonds with a podand oxygen atom, O_2 ($R_{OO} = 2.865$ Å; $\theta_{HOO} = 5.2^\circ$), with a second water molecule ($R_{OO} = 2.808$ Å; $\theta_{HOO} = 17.6^\circ$) and with a third water molecule ($R_{OO} = 2.811$ Å; $\theta_{HOO} = 18.3^\circ$). The second water molecule also forms hydrogen bonds with another podand oxygen atom, O_8 ($R_{OO} = 2.918$ Å; $\theta_{HOO} = 12.6^\circ$) and with the third water molecule ($R_{OO} = 2.896$ Å; $\theta_{HOO} = 21.3^\circ$). The third water molecule engages in a distant hydrogen bond simultaneously with two podand oxygen atoms O_4 ($R_{OO} = 3.707$ Å; $\theta_{HOO} = 23.0^\circ$) and O_5 ($R_{OO} = 3.320$ Å; $\theta_{HOO} = 27.0^\circ$).

Finally, in the optimized structure for the $[b33 \cdot (H_2O)_4]$ system (Fig. 3d) a first water molecule forms hydrogen bonds with a podand oxygen atom, O_8 ($R_{OO} = 2.897$ Å; $\theta_{HOO} = 3.1^\circ$) with a second water molecule ($R_{OO} = 2.829$ Å; $\theta_{HOO} = 20.1^\circ$) and with a third water molecule ($R_{OO} = 2.825$ Å; $\theta_{HOO} = 18.0^\circ$). The second water molecule also hydrogen bonds to a podand oxygen atom, O_2 ($R_{OO} = 2.937$ Å; $\theta_{HOO} = 2.1^\circ$). The third water molecule also establishes a hydrogen bond with a fourth water molecule ($R_{OO} =$

Fig. 3 Stereo-view of the optimized structures found for the hydrated podands: (a) $[b33 \cdot (H_2O)]$; (b) $[b33 \cdot (H_2O)_2]$; (c) $[b33 \cdot (H_2O)_3]$; (d) $[b33 \cdot (H_2O)_4]$



2.776 Å; $\theta_{\text{HOO}}=3.4^\circ$). The fourth water molecule engages in two distant three centered hydrogen bonds with podand oxygen atoms: O₄ ($R_{\text{OO}}=3.239$ Å; $\theta_{\text{HOO}}=27.3^\circ$), O₅ ($R_{\text{OO}}=3.093$ Å; $\theta_{\text{HOO}}=21.5^\circ$), O₆ ($R_{\text{OO}}=3.188$ Å; $\theta_{\text{HOO}}=36.1^\circ$), and O₇ ($R_{\text{OO}}=3.136$ Å; $\theta_{\text{HOO}}=26.6^\circ$).

Structural features of the hydrated complex

In the optimized structure for the $[\text{K}\cdot b33]^+$ complex (Fig. 4a) the *b33* podand surrounds the K⁺ cation in an almost spherical way with a mean K⁺ to podand oxygen atom distance of 2.92 ± 0.06 Å.

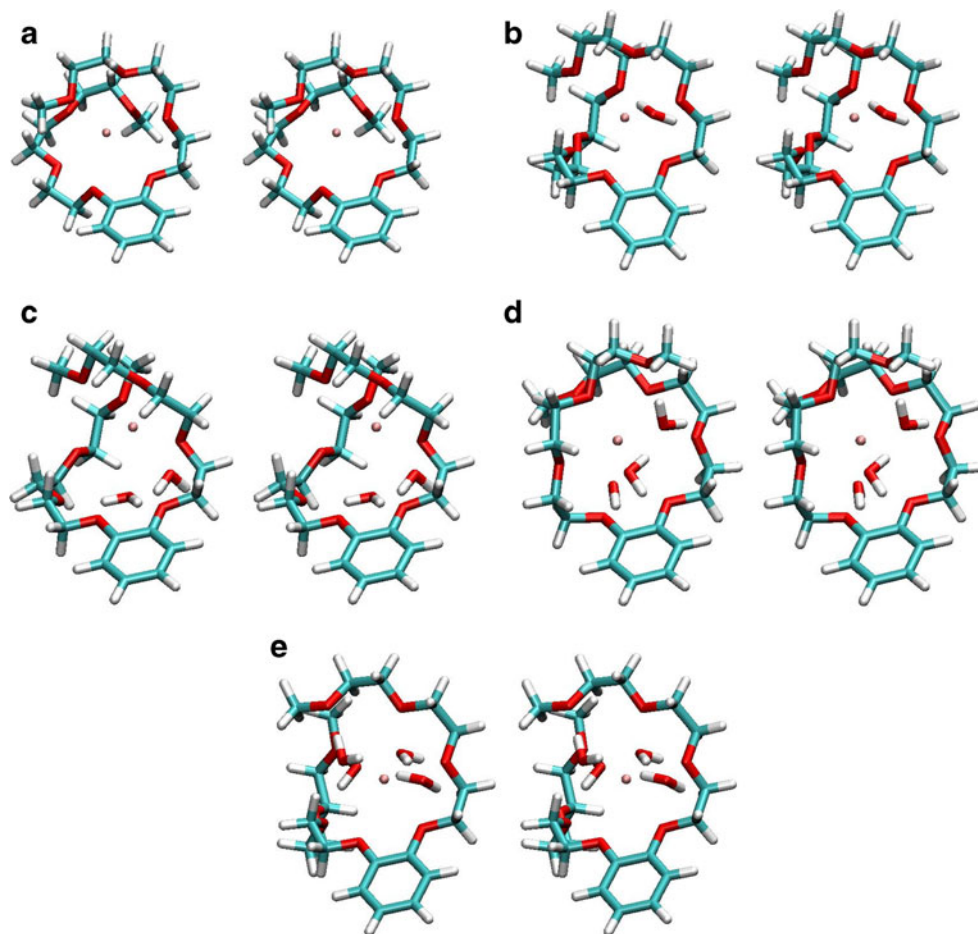
As expected, the presence of water molecules disturbs the spherical environment provided by the *b33* podand. In the optimized structure of the $[\text{K}\cdot b33\cdot(\text{H}_2\text{O})]^+$ system (Fig. 4b) the water molecule interacts directly with the K⁺ cation (at a distance of 2.699 Å; 13.5° Note 1) and with a podand oxygen atom, O₁, through a hydrogen bond ($R_{\text{OO}}=2.792$ Å; $\theta_{\text{HOO}}=2.1^\circ$), and as a consequence another podand oxygen atom, O₂, is kept away from the cation with a mean K⁺ to podand oxygen atom distance of 2.90 ± 0.04 Å (considering only the remaining six podand oxygen atoms).

Note 1- The presented angles are measured between two lines; the first one uniting the K⁺ cation and the water oxygen atom and the second line corresponding to the water C₂ axis of rotation.

In the optimized $[\text{K}\cdot b33\cdot(\text{H}_2\text{O})_2]^+$ system structure (Fig. 4c), the presence of two water molecules highly disturb the environment surrounding the cation: one water molecule is interposed between the cation and the two podand oxygen atoms linked to the benzene ring establishing two hydrogen bonds with two podand oxygen atoms, O₃ ($R_{\text{OO}}=2.808$ Å; $\theta_{\text{HOO}}=8.0^\circ$) and O₅ ($R_{\text{OO}}=2.873$ Å; $\theta_{\text{HOO}}=9.0^\circ$). This water molecule also establishes a hydrogen bond with the second water molecule ($R_{\text{OO}}=2.686$ Å; $\theta_{\text{HOO}}=21.5^\circ$). Both water molecules interact slightly with the K⁺ cation (at 2.793 Å; 60.2° and at 2.859 Å; 45.2°). The remaining five podand oxygen atoms are at a mean distance of 2.89 ± 0.11 Å from the K⁺ cation.

In the optimized $[\text{K}\cdot b33\cdot(\text{H}_2\text{O})_3]^+$ system structure (Fig. 4d), two of the three water molecules don't interact directly with the cation (at 2.825 Å; 69.7° and at 3.976 Å; 89.2°) as they prefer to hydrogen-bond to themselves ($R_{\text{OO}}=2.846$ Å; $\theta_{\text{HOO}}=10.3^\circ$) and to the podand through O₁ ($R_{\text{OO}}=2.924$ Å; $\theta_{\text{HOO}}=27.2^\circ$) and O₆ ($R_{\text{OO}}=2.924$ Å;

Fig. 4 Stereo-view of the optimized structures found for the complexes: (a) $[\text{K}\cdot b33]^+$; (b) $[\text{K}\cdot b33\cdot(\text{H}_2\text{O})]^+$; (c) $[\text{K}\cdot b33\cdot(\text{H}_2\text{O})_2]^+$; (d) $[\text{K}\cdot b33\cdot(\text{H}_2\text{O})_3]^+$; (e) $[\text{K}\cdot b33\cdot(\text{H}_2\text{O})_4]^+$

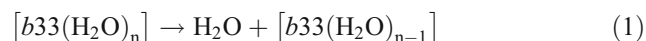


$\theta_{\text{HOO}}=27.2^\circ$), thus preventing one podand oxygen atom, O_1 , from interacting with the K^+ cation. The third water molecule interacts directly with the cation (at 2.78 Å; 38.3°) while hydrogen-bonding to O_4 ($R_{\text{OO}}=2.806$ Å; $\theta_{\text{HOO}}=27.6^\circ$). The remaining seven podand oxygen atoms are at a mean distance of 2.98 ± 0.13 Å from the K^+ cation.

The optimized structure for the $[\text{K}\cdot b33\cdot(\text{H}_2\text{O})_4]^+$ system (Fig. 4e) shows two water molecules that do not interact strongly with the K^+ cation (at 3.767 Å; 74.7° and at 2.702 Å; 73.7°) while hydrogen bonding with two podand oxygen atoms, O_6 ($R_{\text{OO}}=2.931$ Å; $\theta_{\text{HOO}}=14.3^\circ$) and O_8 ($R_{\text{OO}}=2.816$ Å; $\theta_{\text{HOO}}=15.9^\circ$) while hydrogen bonding with themselves ($R_{\text{OO}}=2.859$ Å; $\theta_{\text{HOO}}=15.4^\circ$), and other two molecules that interact slightly with the K^+ cation (at 2.898 Å; 41.7° and at 2.748 Å; 51.4°), while still hydrogen bonding with themselves ($R_{\text{OO}}=2.755$ Å; $\theta_{\text{HOO}}=15.4^\circ$) and with two podand oxygen atoms, O_1 ($R_{\text{OO}}=2.821$ Å; $\theta_{\text{HOO}}=5.0^\circ$) and O_3 ($R_{\text{OO}}=2.871$ Å; $\theta_{\text{HOO}}=14.6^\circ$). The number of strong interactions between the podand oxygen atoms and the K^+ cation is in this complex reduced to five, with a mean distance of 3.00 ± 0.22 Å.

Energetics of podand dehydration

Similarly to what is well known in general [10–14], and for crown ethers [32] in particular, the *b33* podand is certainly able to bind to water molecules by hydrogen bonds. This is especially true in solution in wet DCM, where the *b33* podand is sure to be somewhat hydrated and, in particular, in liquid-liquid extraction experiments involving water as one of the phases, a situation where the organic solvent is naturally saturated with water. Thus, the knowledge of pertinent energetic (thermodynamic) aspects of *b33* dehydration may provide meaningful insight on its function as an extracting agent. In Table 1 (and in Fig. 5) we present the estimated free energy (ΔG), enthalpy (ΔH) and entropy (as $T\cdot\Delta S$) variations found upon the sequential loss of water molecules by the $[b33\cdot(\text{H}_2\text{O})_n]^+$ systems, as defined by Eq. 1 (with $n=4$ to 1).



The estimated thermodynamical data suggests that the gradual loss of water molecules in dichloromethane is

Table 1 Calculated thermodynamical parameters (in kcal·mol⁻¹) estimated for the sequential dehydration of the *b33* podand, as defined by Eq. 1

n	ΔG	ΔH	$T\cdot\Delta S$
4	-0.2	7.0	7.2
3	-7.9	4.5	12.4
2	-6.7	4.6	11.3
1	-1.6	5.4	7.0

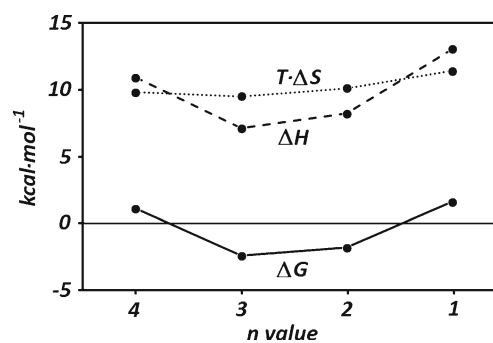
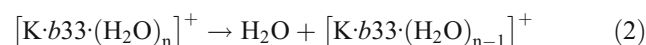


Fig. 5 Calculated thermodynamical parameters (in kcal·mol⁻¹) estimated for the sequential dehydration of the *b33* podand, as defined by Eq. 1

mostly dominated by its uniformly favorable entropy, against the unfavorable enthalpy. The enthalpy/entropy compensation results in small free energy absolute values, pointing to an easy loss of water molecules by the podand. Nonetheless, strictly in accord with the results here presented, the loss of a water molecule in dichloromethane is only slightly favorable for the $[b33\cdot(\text{H}_2\text{O})_4]^+$ and $[b33\cdot(\text{H}_2\text{O})]^+$ systems and quite favorable for the $[b33\cdot(\text{H}_2\text{O})_3]^+$ and $[b33\cdot(\text{H}_2\text{O})_2]^+$ systems.

Energetics of complex dehydration

As already stated above, the step following complexation of the hydrated K^+ cation by the hydrated *b33* podand corresponds to the loss of hydration water molecules. We present in Table 2 (and in Fig. 6) the estimated thermodynamical parameters for the sequential loss of water molecules by the $[\text{K}\cdot b33\cdot(\text{H}_2\text{O})_n]^+$ systems, as defined by Eq. 2 (with $n=4$ to 1).



As reported for the podand dehydration processes in dichloromethane, all complex dehydration processes are enthalpically unfavorable but entropically favorable, resulting in low absolute values for the dehydration free energies, which correspond to a relative ease of water loss until up to four water molecules. Strictly, the loss of a water molecule by the tetrahydrated complex ($[\text{K}\cdot b33\cdot(\text{H}_2\text{O})_4]^+$) is only slightly favorable as seen from the free energy point of view,

Table 2 Calculated thermodynamical parameters (in kcal·mol⁻¹) estimated for the sequential dehydration of the $[\text{K}\cdot b33\cdot(\text{H}_2\text{O})_n]^+$ complex, as defined by Eq. 2

n	ΔG	ΔH	$T\cdot\Delta S$
4	-5.8	9.3	15.1
3	-8.5	3.0	11.5
2	-5.9	2.2	8.1
1	-3.2	4.6	7.8

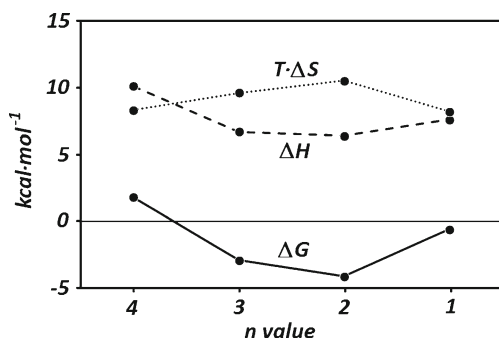


Fig. 6 Calculated thermodynamical parameters (in $\text{kcal}\cdot\text{mol}^{-1}$) estimated for the sequential dehydration of the $[\text{K}\cdot b33\cdot(\text{H}_2\text{O})_n]^+$ complex, as defined by Eq. 2

but loss of the subsequent water molecules is quite favorable up to the completely dehydrated complex.

As expected, the strongest K^+ cation-to-*b33* podand (BSSE corrected) interaction energy (see Table 3, column *a*) was found for the dehydrated complex, whereas the lowest one was found for the tetrahydrated complex.

The unfavorable loss of a water molecule reported for the tetrahydrated complex is justified by the strong stabilizing interaction energies found for the $(b33+(\text{H}_2\text{O})_4)$ and $(\text{K}^+ + (\text{H}_2\text{O})_4)$ systems pertaining to this complex.

The K^+ cation-to- $(\text{H}_2\text{O})_n$ stabilizing interaction energies (see Table 3, column *b*) increase ($-4.8 \text{ kcal}\cdot\text{mol}^{-1}$ per water molecule, as determined by linear regression) with the increase in the number of water molecules, as do the $(\text{H}_2\text{O})_n$ -to-*b33* podand interaction energies (see Table 3, column *c*) ($-4.1 \text{ kcal}\cdot\text{mol}^{-1}$ per water molecule, as determined by linear regression).

Conclusions

The structural features found for the optimized structures, in particular the extensive hydrogen bonding found in the hydrated free podand and in the hydrated complex, suggest that water molecules may play a key role in the K^+ cation extraction process.

Table 3 BSSE corrected interaction energies (in kcal mol^{-1}) calculated between: (a) the K^+ cation and the *b33* podand systems; (b) the K^+ cation and the $(\text{H}_2\text{O})_n$ systems and (c) the *b33* podand and the $(\text{H}_2\text{O})_n$ systems, for the $[\text{K}\cdot b33\cdot(\text{H}_2\text{O})_n]^+$ complexes ($n=4$ to 0)

n	(a)	(b)	(c)
4	-61.2	-33.7	-12.2
3	-78.7	-22.8	-7.3
2	-71.9	-23.2	-3.5
1	-73.6	-17.5	0.3
0	-85.7		

The relatively strong interaction energies found between the water molecules and the cation, as well as between the water molecules and the podand, hint to a stabilizing synergic effect that may induce cation capture by the podand. In dichloromethane, the (hydration) water molecules may first establish a (hydrogen bonding) bridge between the cation and the podand before effective complexation, thus effectively forcing an approach between the cation and the podand. This is then followed by the gradual loss of water molecules and the concomitant increase in the interaction energy between the podand and the K^+ cation.

Also supporting this hypothesis, the low dehydration free energies found for the hydrated podand and for the hydrated complex in dichloromethane allow for the inference that upon complexation of the hydrated K^+ cation by a hydrated *b33* podand the loss of water molecules is very likely to occur.

These observations support the hypothesis of a *CETI* type mechanism for the (*b33* podand) assisted extraction of K^+ from an aqueous toward an organic phase as already hinted by other studies.

Further theoretical work is under way to clarify the influence of the counterion in the extraction process.

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