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A theoretical study of the neutral and the double-charged cation of cyclo[8]pyrrole and its interaction with inorganic anions

Invited Paper

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Abstract: A theoretical study of the complexation of cyclo[8]pyrrole dication, **2**, and the corresponding system in neutral form, **3**, with six anionic molecules has been carried out up to the B3LYP/6-311++G(2d,2p) computational level. The effect of the water solvation has been taken into account by means of the PCM method. The gas phase results correspond to the very large interaction energies expected for the interaction of molecules of opposite charge. In all the complexes, the analysis of the electron density by means of the Atoms In Molecules (AIM) methodology shows the presence of eight intermolecular interactions between the individual molecules. The results, using the water solvent model, indicate that the **2**:SO_4^{2-} complex is more stable than the **2**:NO_3^-, in agreement with experimental results.

Keywords: *cyclo[8]pyrrole • Cations • Anions • DFT calculations*

1. Introduction

In 2007, Sessler, Moyer and coworkers reported the synthesis and complexation properties of octamethyloctaundecylcyclo[8]pyrrole dication **1** as a promising sulfate anion extractant [1] (the importance of this paper was highlighted in Chemical & Engineering News [2]; for preceding Sessler papers on this compound, see [3,4]). The main conclusion was that **1** is able to extract the sulfate anion, SO_4^{2-}, in the presence of a large excess of the nitrate anion, NO_3^-, from a water solution overcoming the Hofmeister bias [5,6].

In 1888, Franz Hofmeister noted a particular ordering of anions in the ability of salts of a common cation to precipitate egg-white globulin [7-9]. The original ordering from this work was: sulfate > phosphate (tabulated by Hofmeister as phosphate but considered by him to be the monohydrogen phosphate dianion) > acetate > citrate > tartrate > hydrogen carbonate > chromate ≈ chloride > nitrate > chlorate. Hofmeister's famous conclusion was that the effectiveness of the salts in precipitating the egg-white globulin increases with "their water attracting capacity." Because ion hydration is so strong and dominates in many chemical phenomena, it is not surprising that the "Hofmeister order" or variations of it have been broadly observed [10-13]. The series of anions have been extended to other anions by Zhao *et al*. [14] who used the terms kosmotropic and chaotropic. Kosmotropes are strongly hydrated species and thus called water 'structure-makers'. Kosmotropic ions include $CH_3CO_2^-$, SO_4^{2-}, HPO_4^{2-}, Mg^{2+}, Ca^{2+}, Li^+, H^+, OH^-, etc. Chaotropes are weakly hydrated species and thus called water 'structure-breakers'. They include SCN^-, I^-, NO_3^-, BF_4^-, Cs^+, K^+, $(NH_2)_3C^+$ (guanidinium), $(CH_3)_4N^+$ (tetramethyl-ammonium), and others. One of the most difficult aspects of explaining salt effects in solution has been the consideration of how the ions, particularly the sulfate dianion, change the nature of water hydrogen bonding [15,16].

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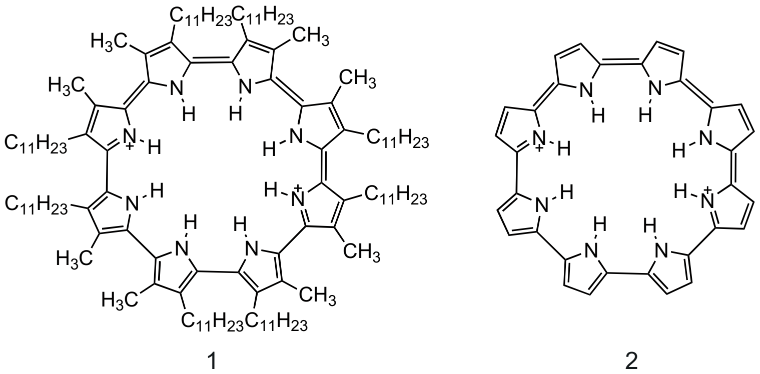


Scheme 1. Octamethyloctaundecylcyclo[8]pyrrole dication (**1**) and model compound (**2**)

We decided to use model compound **2**, where all C-alkyl groups of **1** have been removed, to calculate the stability of its complexes with anions trying to explain its properties.

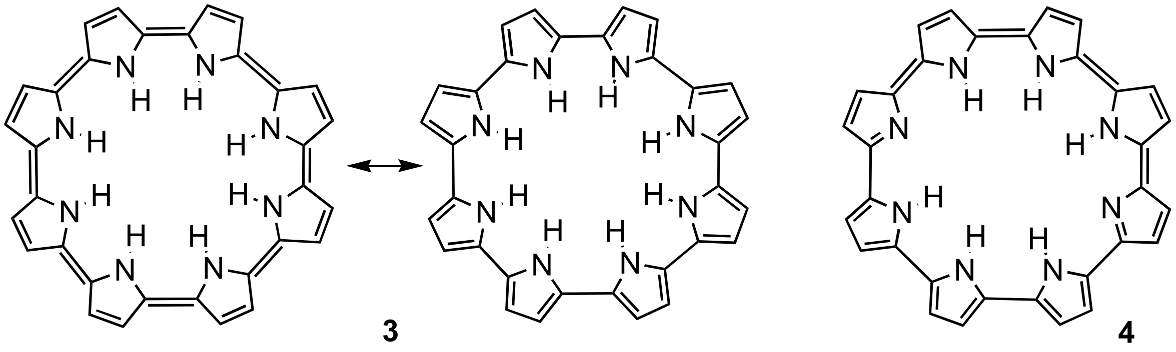
2. Computational Details

The geometry of the systems, isolated monomers and complexes, has been optimized at the B3LYP/6-31G* computational level [17,18] using the Gaussian03 facilities [19]. Symmetry restrictions have been used whenever possible. In all the cases, frequency calculations were carried out to establish that all the structures obtained correspond to energetic minima. A further geometry optimization has been performed at the B3LYP/6-311+G(d,p) level. In order to obtain accurate interaction energies, single point calculation has been performed at the B3LYP/6-311++G(2d,2p) level on the B3LYP/6-311+G(d,p) optimized geometries. No Basis Set Superposition Error (BSSE) correction has been considered since the basis set used for the evaluation calculations is large enough to minimize the effect of this error. The solvation effect of the different sytems has been evaluated with the PCM (Polarizable Continuum Model) method [20] using the water parameters. Atoms-in-Molecules methodology [21] has been used to analyze the electron density with the MORPHY98 and AIM200 programs [22,23]. The value of the integrated Laplacian has been used as a measure of the quality of the integration within the atomic basins. It has been shown that values of this parameter smaller than 0.001 provides small error in the obtained charges [24].

3. Results and Discussion

Cation **2** ($C_{32}H_{24}N_8^{2+}$) is related to neutral molecule **3** ($C_{32}H_{24}N_8$) by removing two electrons, but while the neutral molecule is aromatic having 32-π electrons, the dication is a 30-π electron antiaromatic ring, both of D_{4d} symmetry and not described up to date. Cation **2** is the conjugated acid of **4**. We have calculated the complexes formed by **2** and **3** with the following anions: PO_4^{3-}, SO_4^{2-}, CO_3^{2-}, NO_3^-, Cl^- and BF_4^-.

First we have calculated the standard absolute molar enthalpies of hydration of these anions using the PCM method (Table 1).



Scheme 2. Neutral cyclo[8]pyrrole derivatives (**3**) and (**4**)

Table 1. Solvation of anions and of **2** and **3** calculated at the B3LYP/6-311+G(d,p) computational level.

Molecule	**Energy (Gas phase) (hartree)**	**Energy (Water solution) (hartree)**	**Solvation Calc. (kJ mol⁻¹)**	**Solvation exp. [25] (kJ mol⁻¹)**
PO_4^{3-}	–642.087380	–642.883171	–2089.3	–2880
SO_4^{2-}	–699.115907	–699.476979	–948.0	–1080
CO_3^{2-}	–263.771028	–264.164058	–1031.9	–1315
NO_3^-	–280.457551	–280.554546	–254.7	–300
Cl^-	–460.303727	–460.416827	–296.9	–340
BF_4^-	–424.679691	–424.768559	–233.3	–190
2	–1671.797616	–1672.024845	–596.6	-----
3	–1672.283227	–1672.321113	–99.5	-----

The calculated values for the singly charged anions follow the same trend to those of the experimentally reported data, which is remarkable taking into account the difficulties to obtain the experimental values [25]. These results are worse in the case of the dianions and still more in the case of the PO_4^{3-} that is the only calculated trianion. However, a linear correlation can be derived from Table 1 values: Exp.=(123.8±53.8)+(1.41±0.05) ×Calcd.,n=6, R^2=0.995. The 1.41 slope explain why the large solvation values of Table 1 (trianion and dianions) correspond to the large errors, in other words, the calculations underestimate the solvation energies by a 1.4 factor.

Then, we calculated the twelve complexes (Table 2) formed between **2** and **3** and the mentioned six anions. The strength of the interaction in gas phase is clearly dominated by the electrostatic term and thus the stronger interaction corresponds to the complex of the dication **2** with the trianion PO_4^{3-}. Thus, the representation of the interaction energy *vs.* the sum of absolute value of the charges in the isolated monomers that constitutes the complex (Fig. 1) shows a linear relationship for the complexes formed by **2** and **3**.

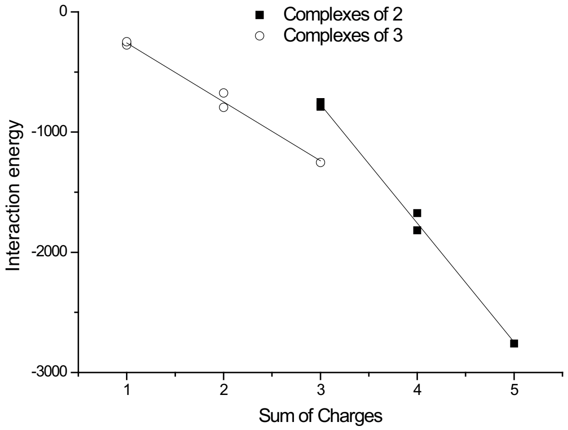


Figure 1. The interaction energy (kJ mol⁻¹) *vs*. sum of the absolute value of the charges of the isolated monomers (e) *vs*. the interaction energy (kJ mol⁻¹). The fitted linear relationships present correlation coefficients of 0.987 and 0.995 for the complexes of 2 and 3, respectively (six points).

There is a linear relationship between the interaction energies of Table 2:

Ei(**3**:anion)=(123.9±17.1)+(0.50±0.01)×Ei(**2**:anion)
n = 6, R^2 = 0.998

Table 2. Total energy and interaction energies in gas phase for the complexes calculated at the B3LYP/6-311++G(2d,2p)//B3LYP/6-311+G(d,p) computational level.

Complex	**Total Energy (hartree)**	**E_I (kJ mol⁻¹)**	**Complex**	**Total Energy (hartree)**	**E_I (kJ mol⁻¹)**
2:PO_4^{3-}	–2315.01651	–2759.0	**3**:PO_4^{3-}	–2314.92464	–1252.0
2:SO_4^{2-}	–2371.64708	–1674.1	**3**:SO_4^{2-}	–2371.74828	–674.0
2:CO_3^{2-}	–1936.32165	–1817.0	**3**:CO_3^{2-}	–1936.41433	–794.5
2:NO_3^-	–1952.61638	–778.1	**3**:NO_3^-	–1952.90363	–266.5
2:Cl^-	–2132.46019	–789.6	**3**:Cl^-	–2132.74653	–275.5
2:BF_4^-	–2096.83508	–750.4	**3**:BF_4^-	–2097.12565	–247.4

The previous linear relationships pointed to the possibility that a Free-Wilson model (presence/absence matrix) [26] could be used to analyze the interaction results. The coefficients of Table 3 (n = 12, R^2 = 0.998) indicate that the interactions with the dication **2** are, in average, 843 kJ mol^{-1} stronger than those with the neutral molecule **3**. The anions that form the stronger interactions are the trianion phosphate, the dianion carbonate and the monoanion chloride.

Table 3. Coefficients of the Free-Wilson model.

Variable	Coefficient (kJ mol^{-1})
2 *vs.* **3**	–843.1
PO_4^{3-}	–1584.0
SO_4^{2-}	–742.5
CO_3^{2-}	–884.2
NO_3^-	–100.8
Cl^-	–111.0
BF_4^-	–77.4

The analysis of the electron density shows, in all the complexes studied, the presence of eight intermolecular bond critical points (bcp) between the anions and each one of the NH groups of **2** and **3** (Fig. 2). The values of the electron density and its Laplacian and total energy density at the bond critical points have been previously used to characterize the strength of the hydrogen bonds (HBs) [27]. In several cases (Table 4), the total energy density at the bond critical points is negative while for all the cases the Laplacian is positive. Thus, it can be concluded that the HBs are between medium and weak based on the previously mentioned classification. The electron density of the intermolecular bcp's are larger for the complexes of **2** with a given anion when compared to the corresponding of **3** due to the shorter distances observed in the former cases.

The values of the electron density and its Laplacian have been correlated exponentially *vs*. the interatomic distance in the O···H interactions as shown in Fig. 3. Similar results have been described for other hydrogen bonds [28-30].

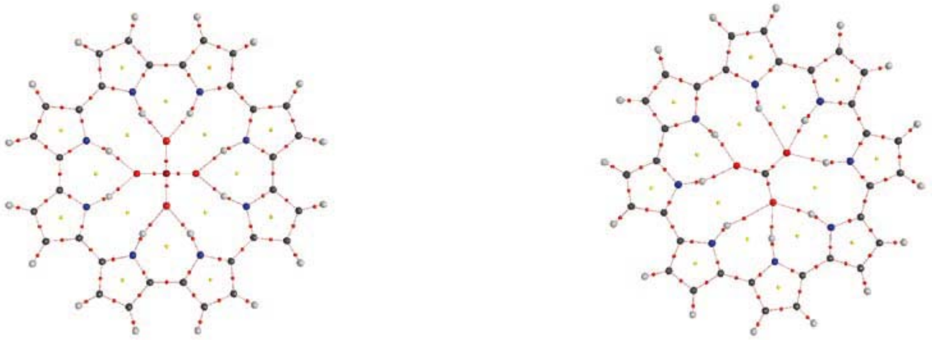
An important charge transfer is observed between the interacting molecules. As expected, the charge transfer is larger in the complexes with dication **2** than in the corresponding ones with neutral molecule **3**. A clear relationship is observed between this parameter and the interaction energy. Thus, as the charge transfer increases, the absolute value of the interaction energy also increases.

In order to consider the solvation effect on the isolated monomers (Table 1) and complexes (Table 5), the thermodynamic cycles shown in Fig. 4 could be built up for the twelve cases studied here. For instance, including water solvation, the dication **2** presents an interaction with the sulfate dianion and the nitrate monoanion of –134.9 and –22.1 kJ mol^{-1}, respectively.

The first interesting result is the small value observed in the solvation of the complexes formed by **2** with the dianions (SO_4^{2-} and CO_3^{2-}) which results in a neutral complex. The solvation energy of the complexes of **3** is somehow related to those of the isolated anions but with smaller values since the polar moieties of them are not accessible to the solvent.

The most stable complex in water solution corresponds to the **3**:SO_4^{2-} followed by the **2**:PO_4^{3-}. The two complexes studied with BF_4^- are the ones with the smaller stability in the two series studied, and the **3**:BF_4^- complex is unstable in water solution based on the computational results.

With respect to the two cases studied by Sessler, the complex **2**:SO_4^{2-} is more favorable than the **2**:NO_3^-. Since the solvation of dication **2** is common to both thermodynamic cycles, the difference between these anions comes from three contributions: the solvation of



2: $PO_4^{\equiv}$

2:$CO_3^{=}$

Figure 2. Molecular graph of the **2**:PO_4^{3-} and **2**:CO_3^{2-}. The bond and ring critical points are represented by red and yellow dots, respectively. The lines that connect the atoms represent the bond paths. The molecular graphs of the rest of the complexes are similar to the ones shown here.

Table 4. Properties of the intermolecular hydrogen bonds, distance, electron density ρ, Laplacian $\nabla^2\rho$ and total energy H. In addition, the charge transfer obtained within the AIM methodology is listed.

Complex	Interatomic distance (Å)	ρ (a.u.)	$\nabla^2\rho$ (a.u.)	H (a.u.)	Charge transfer (e)
2:PO_4^{3-}	1.617	0.058	0.139	–0.0113	0.694
2:SO_4^{2-}	1.784	0.037	0.123	–0.0010	0.349
2:CO_3^{2-}	1.583	0.056	0.181	–0.0086	0.410
	1.623	0.055	0.157	–0.0083	
	1.753	0.042	0.122	–0.0031	
	2.234	0.015	0.046	0.0012	
2:NO_3^-	1.815	0.031	0.129	0.0022	0.144
	1.861	0.030	0.112	0.0019	
	2.060	0.019	0.070	0.0022	
	2.191	0.015	0.052	0.0017	
2:Cl^-	2.772	0.008	0.022	0.0011	0.172
2:BF_4^-	1.903	0.024	0.096	0.0020	0.089
3:PO_4^{3-}	1.683	0.049	0.128	–0.0068	0.621
3:SO_4^{2-}	1.840	0.033	0.111	0.0003	0.302
3:CO_3^{2-}	1.625	0.050	0.170	–0.0055	0.375
	1.671	0.048	0.147	–0.0052	
	1.811	0.037	0.111	–0.0012	
	2.276	0.014	0.042	0.0011	
3:NO_3^-	1.910	0.026	0.106	0.0030	0.118
	1.917	0.026	0.099	0.0023	
	2.102	0.018	0.064	0.0021	
	2.222	0.014	0.048	0.0016	
3:Cl^-	2.867	0.007	0.018	0.0009	0.147
3:BF_4^-	1.955	0.021	0.085	0.0020	0.068

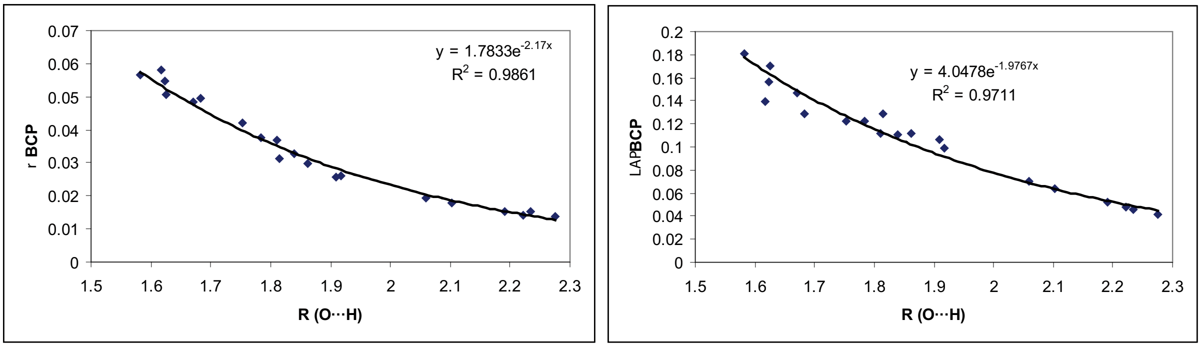


Figure 3. Rho (ρ) and Lap (au) *vs*. the O···H distance (Å). The exponential relationships are shown.

Table 5. Solvation energy and interaction energy (kJ mol^{-1}) calculated by the PCM solvation model.

Complex	Solvation (kJ mol^{-1})	E_I (PCM model) (kJ mol^{-1})	Complex	Solvation (kJ mol^{-1})	E_I (PCM model) (kJ mol^{-1})
2:PO_4^{3-}	–184.5	–257.5	**3**:PO_4^{3-}	–1103.1	–166.3
2:SO_4^{2-}	–5.3	–134.9	**3**:SO_4^{2-}	–680.7	–307.2
2:CO_3^{2-}	10.8	–177.7	**3**:CO_3^{2-}	–444.8	–107.9
2:NO_3^-	–95.2	–22.1	**3**:NO_3^-	–89.6	–1.9
2:Cl^-	–241.7	–137.7	**3**:Cl^-	–231.1	–110.2
2:BF_4^-	–81.2	–1.7	**3**:BF_4^-	–75.4	10.0

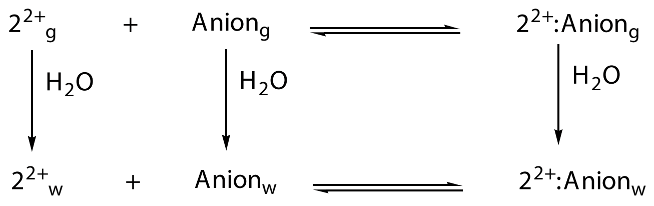


Figure 4. Thermodynamic cycle (a similar one has been used for the complexes with 3).

the anion, that is highly unfavorable for the sulfate (948.0- – 254.7 = 693.3 kJ mol^{-1}), the complexation energy, that is highly favorable for the sulfate (–1674.1 + 778.1 = =–896.0 kJ mol^{-1}), and the solvation of the complex that favors the nitrate (–5.3 + 95.2 = 89.9 kJ mol^{-1}). The combination of these three effects (693.3 – 896.0 + 89.9= = –112.8 kJ mol^{-1}) is the difference between –134.9 and –22.1 kJ mol^{-1}. Therefore, the Sessler designed ligand (–896.0 kJ mol^{-1}) overcomes Hofmeister effect (693.4 kJ mol^{-1}) and the solvation of the complex (92.6 kJ mol^{-1}). The extraction abilities of **1** mainly result from a compromise of its structure and the solvation of the free anions in water.

4. Conclusion

A DFT study of the interaction of a model of Sessler molecule **1** and its corresponding neutral form with six inorganic anions has been carried out. Very large interaction energies were obtained in the gas phase, as expected for interactions between oppositely charged molecules.

The experimental observation that **1** extracts small quantities of the sulfate dianion in the presence of huge quantities of the nitrate monoanion in water solution [1] has been explained using model **2**. The E_I+solvation energy is –122.2 kJ mol^{-1} for SO_4^{2-} (T_d) and –29.3 kJ mol^{-1} for NO_3^- (D_{3h}). According to our calculations **1** should even better extract CO_3^{2-} (a planar D_{3h} anion). The calculations provide „intrinsic effects", *i.e.*, those corresponding to the gas phase that can be measured by mass spectrometry including ICR.

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