

Interaction between anions and naphthalendiimides

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Abstract

The process of anion transport through a synthetic ion channel based in anion $\cdots\pi$ interactions is studied by means of computational methods. Employing two models for the units forming the channel, the calculations indicate that stable complexes are formed with any of bromide, chloride, fluoride or hydroxide anions. All these complexes exhibit strong interactions in the gas phase. When studied in water no favourable complexation was obtained for any of the anions studied, so anion $\cdots\pi$ interactions, though strong, are not capable of overcoming the cost of anion dehydration. However, it has been found that a process of hydroxide displacement by another anion is indeed favourable in water.

1. Introduction

Intermolecular interactions involving aromatic rings are important processes in both chemical and biological recognition. Their understanding is essential for the rational design of drugs and other new functional materials. On the basis of these intermolecular interactions, not only theoretical design but also experimental realization of novel functional receptors has become possible.¹⁻⁵ Therefore, the study of the fundamental intermolecular interactions is important for aiding the design of new materials as well as for understanding cluster formation. In particular, novel types of interaction involving aromatic rings have been an important subject in the past decade. In this regard, if the interaction involves the aromatic system, it is usually one of the following three types: cation $\cdots\pi$, $\pi\cdots\pi$ or X-H $\cdots\pi$.²

Cation $\cdots\pi$ interactions have proven of importance on different aspects of molecular recognition and stability in biological systems. Cation $\cdots\pi$ contacts can be found on almost any protein due to the presence of amino-acids containing aromatic residues in their side chain, together with other amino-acids which present cationic groups, usually depending on the pH of the medium. These cation $\cdots\pi$ interactions are usually very strong in the gas phase, but much weaker in the presence of solvent, though there is some controversy about the contribution of the cation $\cdots\pi$ interactions in real systems.^{2,4}

On the other hand $\pi\cdots\pi$ interactions are essentially weak and dispersive in nature, which makes them quite difficult to describe. Different studies have dealt with this type of interactions, mainly centred in the study of benzene dimer, but also dedicated to stacking interactions on larger systems.^{2,3}

X-H $\cdots\pi$ interactions have also been the subject of many previous works, since this type of contact implies a hydrogen bond with the participation of an aromatic cloud. Thus, O-H $\cdots\pi$ and N-H $\cdots\pi$ contacts have been the frequently studied, but there are also other possibilities as the C-H $\cdots\pi$ interaction. These contacts are more dispersive than typical hydrogen bonds and need rigorous methods to be described in detail.^{2,5}

Recently, it has also aroused interest the possibility of stabilizing interactions between anions and electron deficient aromatic systems in the so-called anion $\cdots\pi$ interaction. The extensive work of Fradera et al. has already shown that the interaction is mainly electrostatic in nature, so one must have an electron deficient aromatic system with positive quadrupole moment, such as hexafluorobenzene or triazine.^{6,7} The attractive interaction between this quadrupole and the negative

charge of the anion is mainly responsible of the stabilizing interaction, with strengths similar to those observed for cation $\cdots\pi$ interactions.

Most studies on anion $\cdots\pi$ interactions have been carried out employing benzene as a model for the aromatic system, so these works have mostly considered hexafluorobenzene, trifluorobenzene or triazine complexes with halogen anions. However there is a lack of studies of the interaction with more complex anions or with more extended aromatic systems. Recently, Hermida-Ramón et al. have performed a study of the interaction of iodine anion with a perfluorinated molecular tweezer showing a significant interaction, thus suggesting the possibility of complexation of the anion by the tweezer.^{8,9}

It can be expected that for more extended aromatic systems, the contribution of inductive forces will be larger than in benzene derivatives. Also, as indicated by Kim et al.,¹⁰ the anion $\cdots\pi$ interaction presents a more dispersive character than the cation $\cdots\pi$ contact, so in complexes formed by large aromatic systems and more complex anions the dispersion contribution could be significant.

Very recently, Matile et al. have presented a new ion channel allowing anion transport through lipid bilayers.¹¹ The channel is based in oligomers of naphthalendiimide, and exhibits a quite unusual selectivity for anion transport, which was supposed to be due to the presence of important anion $\cdots\pi$ interactions compensating the cost of anion dehydration. The system synthesised by Matile et al. is shown in Figure 1 together with an schematic representation of the mechanism for ion transport proposed, where the anion moves through the channel formed by naphthalendiimide molecules establishing anion $\cdots\pi$ interactions.¹¹

In the present work, a computational study is carried out for establishing the characteristics of the interaction between anions and systems similar to those proposed by Matile et al.¹¹ Taking into account the large size and complexity of the ion channel synthesised by these authors, the system was simplified to make it affordable for a computational approach. Therefore, considering that the ion channel is formed by repeating naphthalenediimide units, only this species was considered when studying anion $\cdots\pi$ interactions. As a result, in the present work, the systems studied were dimers formed by one naphthalendiimide unit and one anion. Only halide anions were considered except iodine to avoid using core effective potentials. Hydroxide anion was included since a mechanism for anion transport was proposed based on anion exchange. Also, a larger system was considered consisting on naphthalendiimide substituted with phenyl rings in both end as indicated in Figure 2.

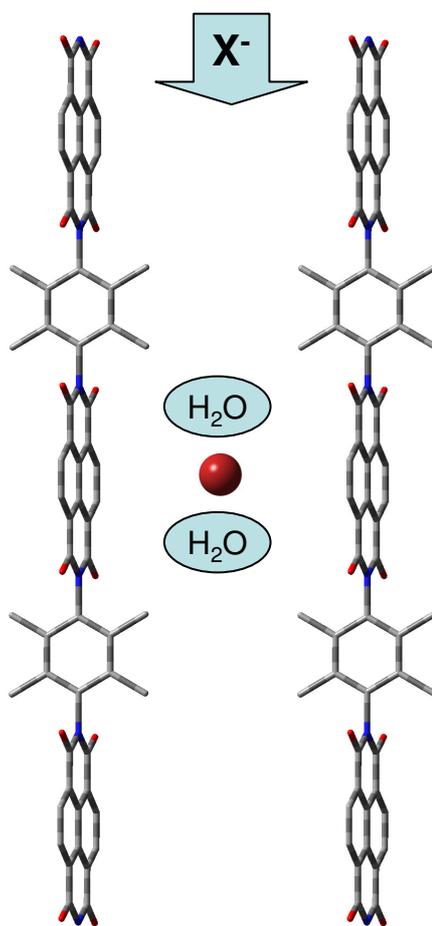


Figure 1. Synthetic anion channel proposed by Matile et al.

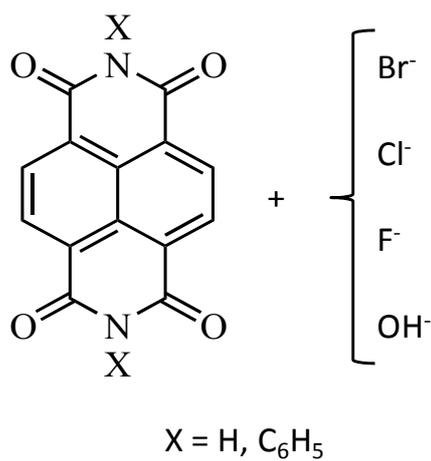


Figure 2. Naphthalendiimide molecules and anions employed in the present study.

2. Computational details

In this study, complexes formed by naphthalendiimide and several anions as indicated in Figure 2 were computationally studied by using density functional theory. The measurement of the interaction between polar systems is usually quite straightforward, but it is much more difficult to measure the magnitude of the interaction when dispersion forces play an important role. The interaction in complexes involving aromatic moieties is only accurately described by employing the most rigorous methods, mainly due to the large correlation/dispersive component of the interaction.

Common DFT functionals are unable to describe the interaction between aromatic systems properly, usually predicting non-bonded situations.³ Though the interaction with anions should be more easily described due to its electrostatic character (at least its main features), it can be expected that the dispersive component will be lost by using common functionals. Very recently, following an old idea applied to the HF method, Grimme proposed adding an empirical term to several common functionals as an easy and unexpensive way of including dispersion, in the so called DFT-D approach.^{12,13} Doing so, the performance of commonly used functionals is greatly improved without extra computational costs. Thus, all calculations in this work were performed by employing the BLYP-D method together with the cc-pVTZ basis set. Taking into account that the description of anions could need more diffuse basis functions, the aug-cc-pVTZ basis set was employed for F, Cl, Br and O atom in hydroxide. Being BLYP a non-hybrid functional, computational effort can be saved by applying the resolution of the identity (RI) approach using the def2-TZVPP fitting basis set.¹⁴ All calculations were performed with the program Orca.¹⁵

After locating the stationary points of the potential energy surface of each cluster, the interaction energies were calculated by means of the counterpoise method to avoid basis set superposition error.^{16,17} Thus, the interaction energy results from subtracting the energies of the fragments that constitute the clusters employing the geometry and the whole basis set of the cluster. Thus,

$$\Delta E_{\text{int}} = E_{ij}(ij\dots) - \sum_i E_i^{\text{clus.}}(ij\dots)$$

where terms in parentheses indicate the basis set employed and superscripts the geometry used in the calculation.

As the geometry of the molecules changes when the cluster is formed, an additional contribution describing this effect must be included, obtained as the energy difference between the molecules in the cluster geometry and in isolation.

$$E_{def} = \sum_i (E_i^{clus.}(i) - E_i^{isol.}(i))$$

The total complexation energy results from adding these two contributions, though deformation effects are usually small and negligible for many clusters.

$$\Delta E_{compl.} = \Delta E_{int} + E_{def}$$

Finally, taking into account that BLYP-D method is just BLYP plus an empirical dispersion term, the complexation energy will be further divided as:

$$\Delta E_{compl.} = \Delta E_{BLYP} + \Delta E_{disp} + E_{def}$$

Figure 3 shows the molecular electrostatic potential (MEP) of naphthalendiimide (NDI). It can be observed that the electrostatic potential is mostly positive in the whole molecule with the exception of the carbonyl groups. Therefore, naphthalendiimide molecule is suitable for establishing favourable electrostatic interaction with anions. In any case, the most favourable regions for these interactions are located over the carbon atom of the carbonyl groups, over the C-C external bonds of phenyl rings and also in the regions near the N-H and C-H groups. In consequence, starting structures for the complexes studies were constructed trying to locate anions near the electrostatically favourable regions.

The same conclusions could be extracted from the analysis of Figure 4, which shows the relative energies for complexes formed by NDI and a chloride anion located 2.5 Å above the molecular plane. There are two attractive regions located above the rings of NDI molecule, which roughly correspond to the more positive regions observed in the MEP in Figure 3. It must be indicated, however, that the anion prefers to be located not over the phenyl ring center, but displaced to the edge of the molecule, where it can interact with the positive regions around the C-H groups. Therefore, from the analysis of Figures 3 and 4, four starting structures were selected for optimization. Two of these structures correspond to the regions located over the rings in NDI, whereas in the other two the anion is located in the molecular plane near the C-H and N-H groups.

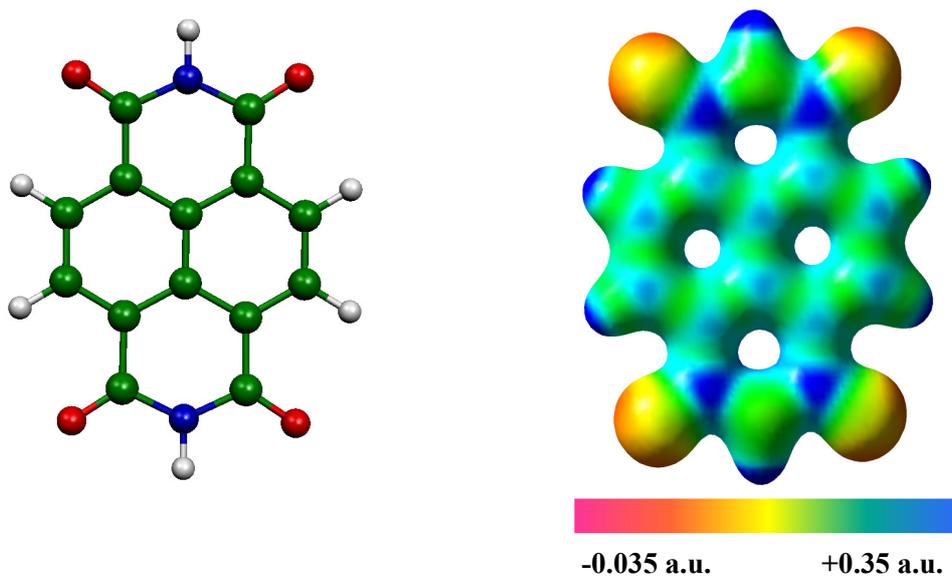


Figure 3. Molecular electrostatic potential of naphthalendiimide as obtained at the BLYP-D/cc-pVTZ level of calculation, mapped onto an isosurface of electron density of 0.05 a.u.

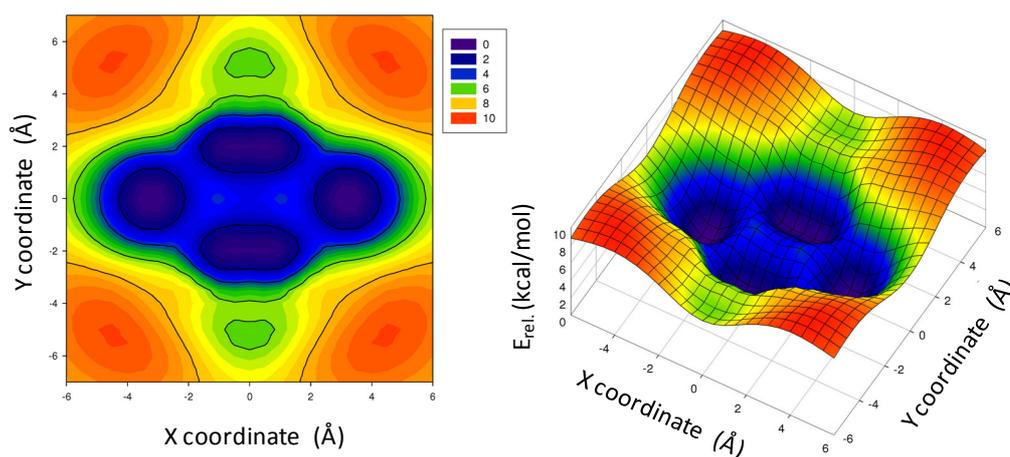


Figure 4. Energy for complexes formed by placing a chlorine anion on a plane 2.5 Å above the molecular plane of NDI. Energies relative to the most stable geometry. NDI molecule is in the XY plane, with the nitrogen atoms along the Y axis.

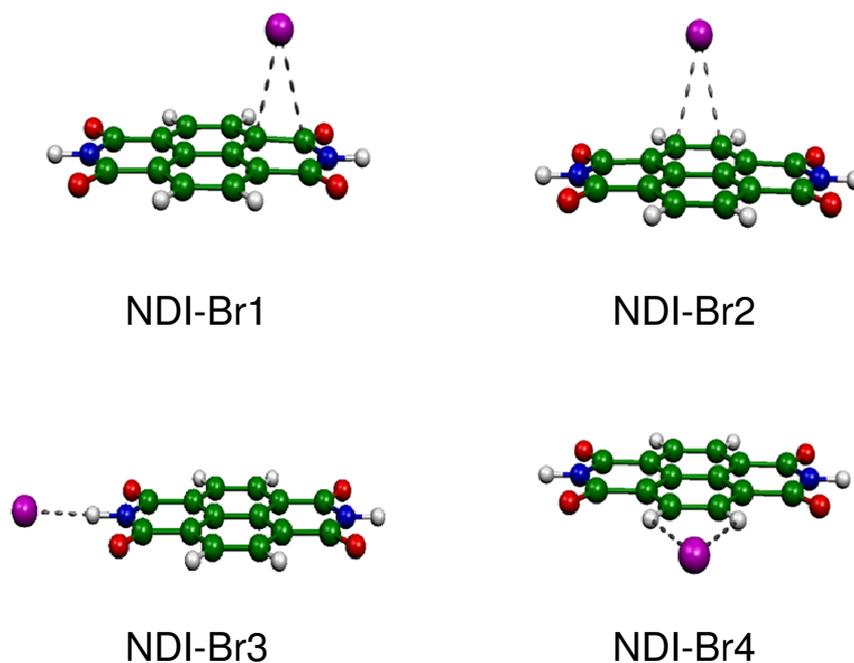


Figure 5. Optimized structures of the complexes formed by NDI and bromide anion as obtained at the BLYP-D/pVTZ level of calculations.

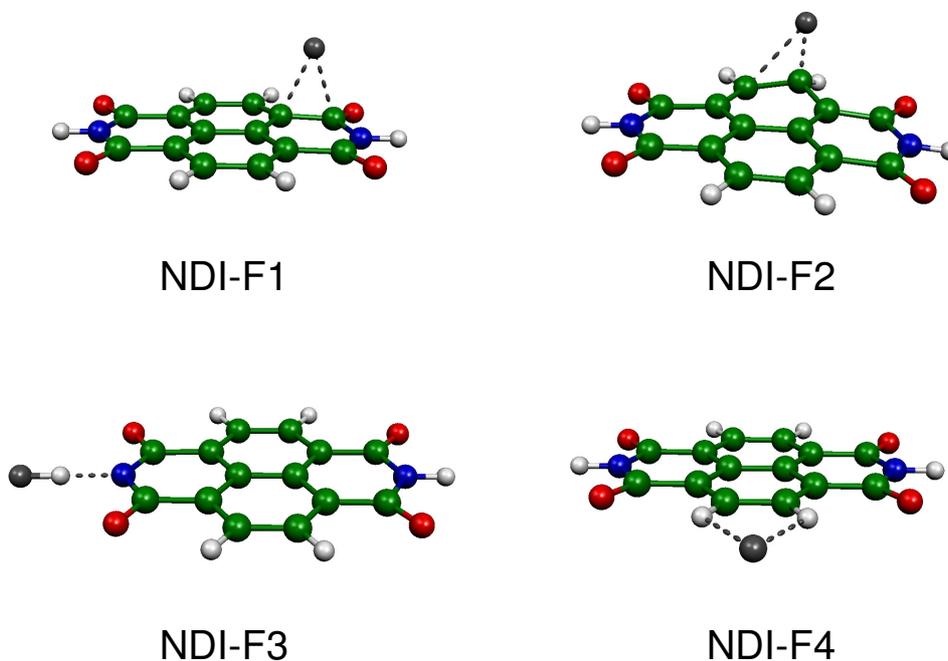


Figure 6. Optimized structures of the complexes formed by NDI and fluoride anion as obtained at the BLYP-D/pVTZ level of calculations.

3. Results

3.1. NDI...anion complexes

3.1.1. Geometries

Figure 5 shows the optimized structures for the complexes formed by NDI and bromide anion as obtained with the BLYP-D method together with the cc-pVTZ basis set in all atoms and aug-cc-pVTZ basis set for bromine (hereafter pVTZ). As indicated above, different starting points were employed for the optimizations, leading to four different structures, in accordance with the favourable regions observed in the MEP of NDI shown in Figure 3. Thus, two structures of minimum energy are located corresponding to anion... π interactions (**NDI-Br1** and **NDI-Br2**) whereas in the other two (**NDI-Br3** and **ndi-Br4**) hydrogen bonds are established between the anion and N-H or C-H groups of the NDI molecule. Complexes formed with chloride are similar to those presented in Figure 5. On the other hand, Figure 6 shows the minimum energy structures found for NDI complexes with fluoride, which are also similar to those found for hydroxide complexes. The structures found in complexes with fluoride and hydroxide anions are quite similar to those obtained for the larger anions. However, due to the larger polarizing power of fluoride and hydroxide anions, several differences arise. First, in structure **NDI-F2** an ordinary bond is formed between fluoride and a carbon atom of NDI, leading to an important deformation of NDI structure due to the pyramidalization of the carbon atom participating in the bond. This behaviour is similar to that reported in complexes formed by anions and substituted benzenes.¹⁸ Also, in structure **NDI-F3**, NDI is deprotonated leading to the formation of HF molecule. It is worth noting the structures **X3** are included for consistency but they are not possible in the real system. The behaviour in complexes with hydroxide is similar (O-C bond formed in **NDI-OH2** and formation of H₂O in **NDI-OH3**) but a O-C bond is also formed in structure **NDI-OH1**.

Table 1 lists selected geometric parameters of the complexes located with the anions studied in this work. It is clear from the data in Table 1 that intermolecular distances correlate with anion size though, as commented above, in structures **NDI-F2**, **NDI-OH1** and **NDI-OH2** the anion is located very close to one carbon atom of the phenyl ring (around 1.5-1.6 Å), establishing a proper bond instead of an intermolecular interaction.

Table 1. Selected geometric parameters of the complexes formed with NDI. *next* indicates the nearest heavy atom; *ringcent* the nearest ring center and *molcent* the middle C-C bond in the center of the molecule.

	NDI-Br1	NDI-Br2	NDI-Br3	NDI-Br4	NDI-Cl1	NDI-Cl2	NDI-Cl3	NDI-Cl4
$R_{X\cdots next}$	3.067	3.041	3.267	3.590	3.006	2.967	3.093	3.427
$R_{X\cdots ringcent}$	3.140	3.603	4.657	4.739	3.043	3.570	4.487	4.572
$R_{X\cdots molcent}$	3.738	4.487	6.818	5.974	3.703	4.486	6.650	5.807
	NDI-F1	NDI-F2	NDI-F3	NDI-F4	NDI-OH1	NDI-OH2	NDI-OH3	NDI-OH4
$R_{X\cdots next}$	2.195	1.602	2.595	2.841	1.560	1.487	2.849	2.918
$R_{X\cdots ringcent}$	3.361	2.521	4.018	3.969	2.503	2.685	4.249	4.054
$R_{X\cdots molcent}$	3.252	3.463	6.201	5.205	2.812	3.759	6.417	5.291

3.1.1. Energies

Figure 7 shows the complexation energies obtained for the complexes with bromide and chloride anions, and the values calculated by decomposing the complexation energy as indicated in Computational Details. The most stable structure for bromide complexes corresponds to **NDI-Br2**, with the anion located above the carbon atoms of the edge of the phenyl ring. **NDI-Br1**, the other complex showing an anion $\cdots\pi$ interaction is slightly less stable by about 1.5 kcal/mol. On the other hand, structures with the anion located in the molecular plane are less stable. **NDI-Br3** presents a complexation energy about 2.5 kcal/mol less negative than the most stable complex, despite the formation of a Br \cdots H-N hydrogen bond. Finally, **NDI-Br4** is the least stable structure, though with complexation energy similar to **NDI-Br3**, reflecting the less favourable interaction of the anion with the C-H groups of the phenyl rings. In the case of chloride complexes, also shown in Figure 7, the behaviour is pretty similar. These complexes are slightly more stable than bromide ones due to the larger polarizing power of chloride anion. In this case **NDI-Cl3** is almost as stable as structures showing anion $\cdots\pi$ contacts, as a consequence of the greater strength of the Cl \cdots HN hydrogen bond.

Considering the contributions in which the complexation energy was decomposed it can be observed that, as expected, the dispersion contribution is small in all cases, though slightly larger for bromide complexes and anion $\cdots\pi$ structures. Deformation energies are also small, the largest corresponding to structure **NDI-Cl3** due to the formation of the hydrogen bond. In summary, in complexes formed by NDI and chloride or bromide anion, the complexation energies amount to about 20-21 kcal/mol, with small contributions from dispersion or deformation.

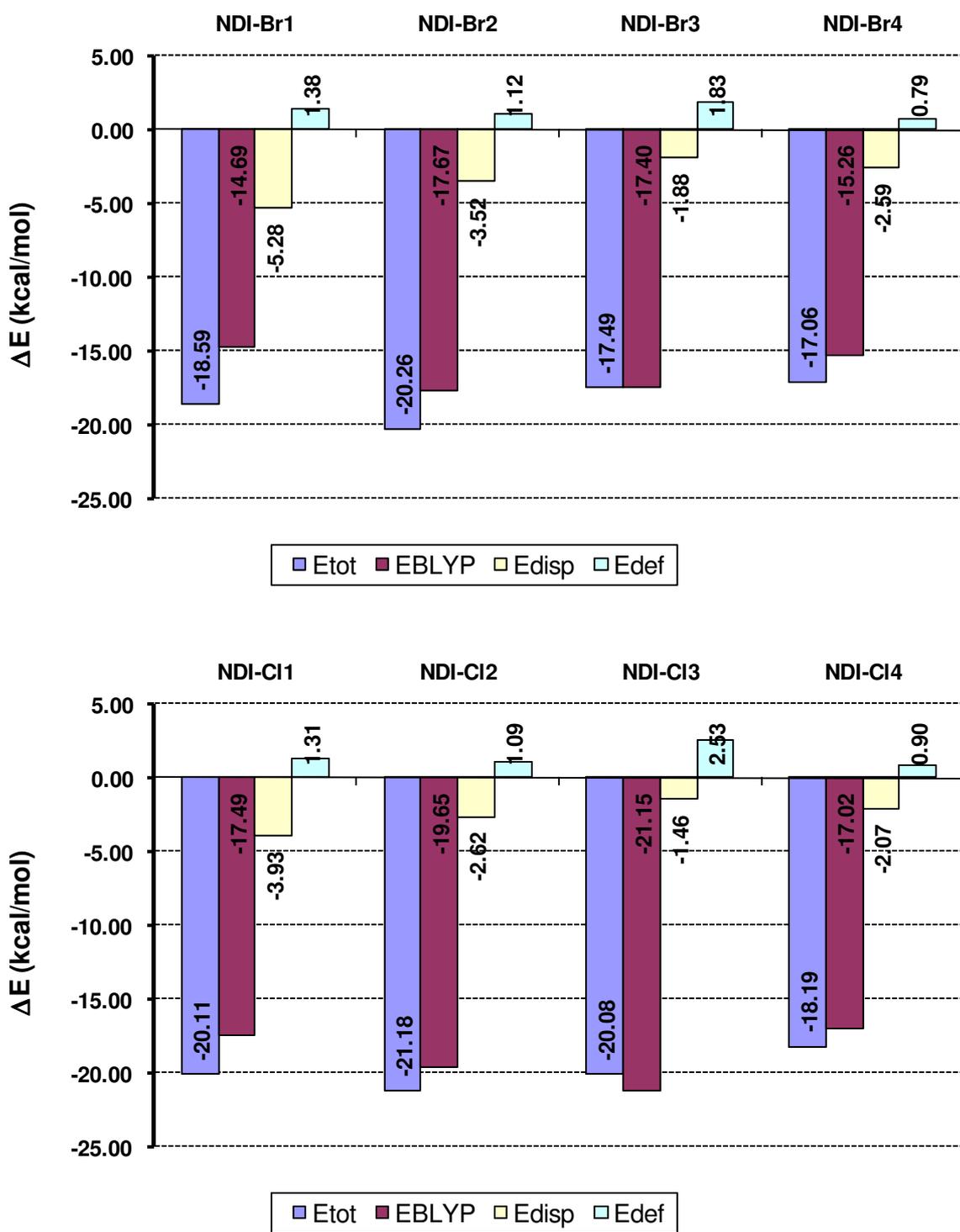


Figure 7. Decomposition of the complexation energy of the dimers formed by NDI and bromide and chloride anions obtained at the DFT-D/pVTZ level.

The behaviour is totally different when complexes of NDI with fluoride or hydroxide are considered, as shown in Figure 8. In fluoride complexes exhibiting anion $\cdots\pi$ contacts, the complexation energies amount to -35.4 for **NDI-F1** and -36.50 for **NDI-F2**. Therefore, a similar behaviour as obtained for bromide or chloride complexes is found, with **NDI-F2** slightly more stable than **NDI-F1**, though the complexation energies are much larger. However, the decomposition of the complexation energies shows larger differences. **NDI-F1** exhibits a similar pattern to that observed for the larger anions, with small contributions from dispersion and deformation (this is larger due to the more intense interaction). On the other hand, **NDI-F2** shows an interaction energy amounting to -51.2 kcal/mol, which is partially compensated with a large deformation energy contribution. This happens because in **NDI-F2**, the fluoride anion is located at almost bond distance, producing an important deformation of the NDI molecule, which loses the planarity of one carbon atom in the phenyl ring as shown in Figure 6. Thus, the formation of the complex is favourable, but overcoming a large deformation of NDI molecule. This effect is even more evident in **NDI-F3**. In this case, the NDI molecule is deprotonated, and a HF molecule is formed. In consequence, the interaction energy is huge, partially balanced by a large deformation term, leading to the most stable complex (-50.2 kcal/mol). However, as indicated before, it should be taken into account that **NDI-X3** structures are not possible in the real system.

In hydroxide complexes, all structures except **NDI-OH4** exhibit large deformation energies, suggesting the formation of a bond between OH and a carbon atom of NDI. As in fluoride systems, this bond is more evolved in structure **NDI-OH2** than in **NDI-OH1**, though in the latter the deformation energy is already large. Complexes formed with OH are the most stable among the ones studied in this work. Structure **NDI-OH3** presents a similar behaviour as **NDI-F3**, whereas **NDI-F4** presents a pattern typical of intermolecular interactions as those found in bromide or chloride complexes.

Figure 9 compares the complexation energies of the complexes studied. It is clear that bromide and chloride anion behave in a very similar way, with the four structures presenting similar complexation energies, being **X2** the most stable one. Also, both hydroxide and fluoride complexes present similar behaviour, though differences are larger especially in structures where the anions are placed at bond distance.

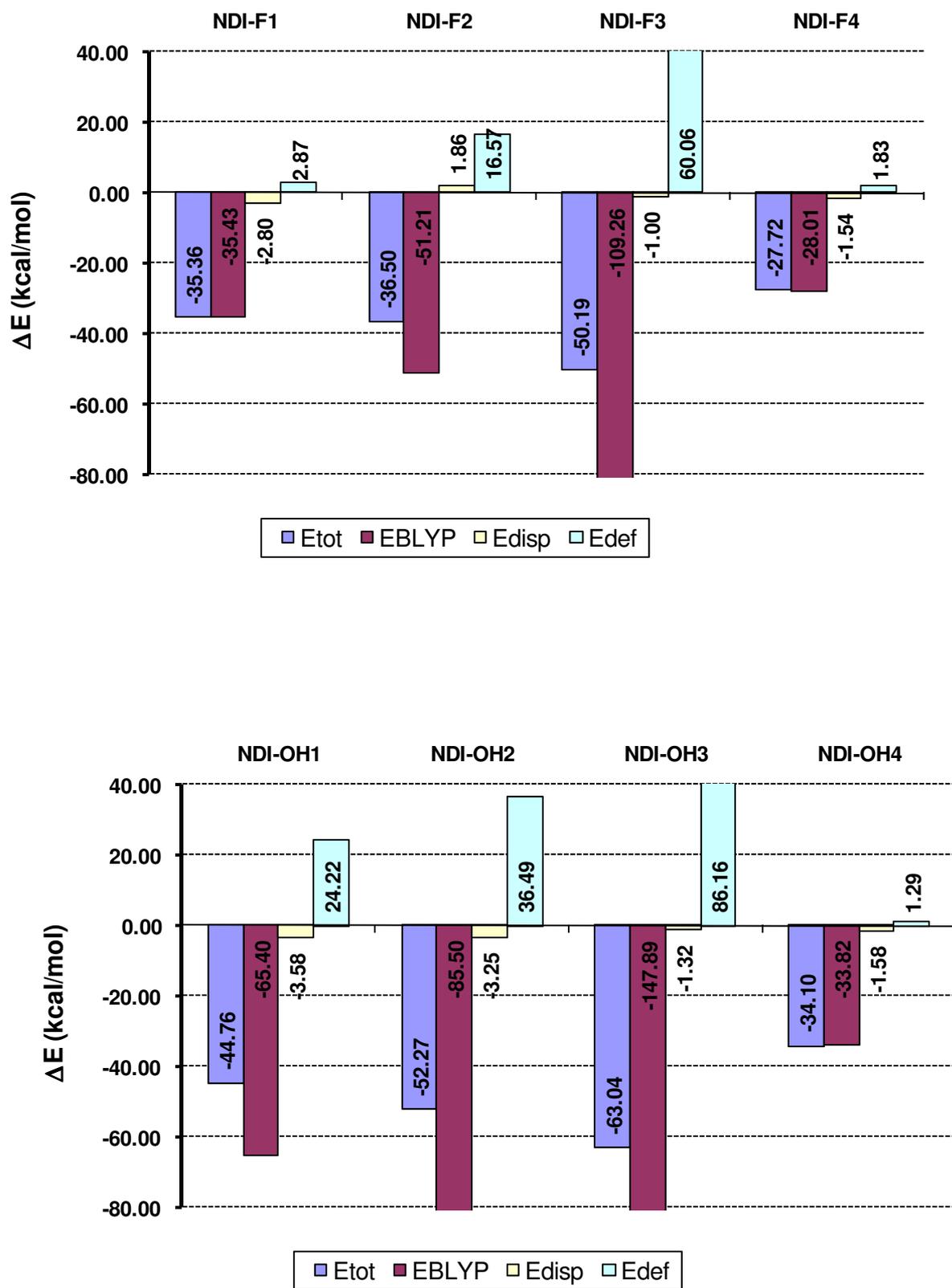


Figure 8. Decomposition of the complexation energy of the dimers formed by NDI and fluoride and hydroxide anions obtained at the DFT-D/pVTZ level.

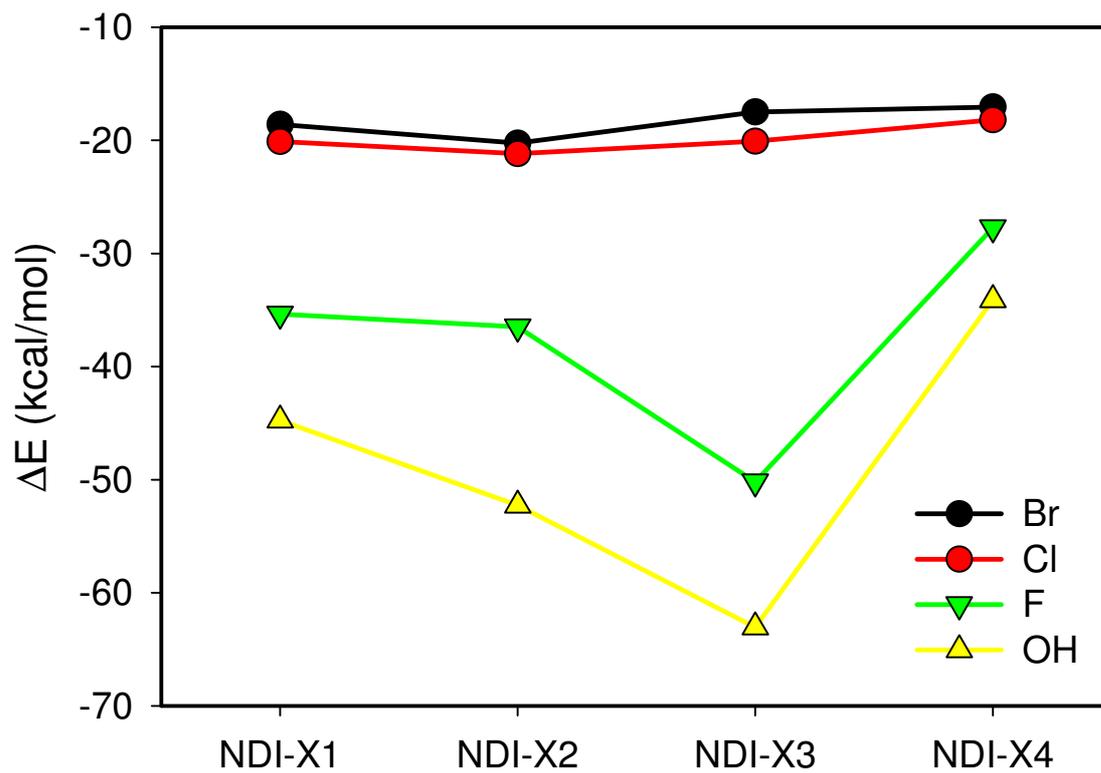


Figure 9. Complexation energy for the dimers formed by NDI and the anions studied.

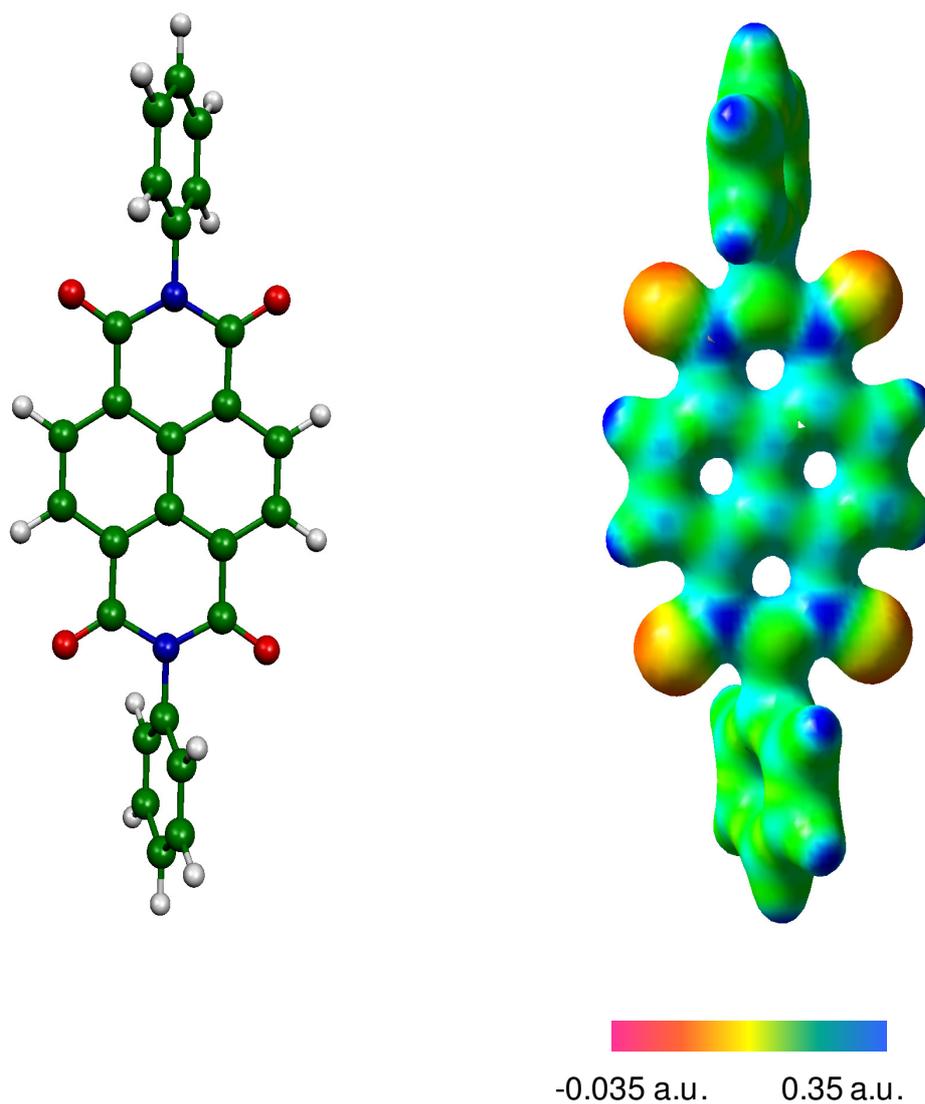


Figure 10. Molecular electrostatic potential of 2Φ-naphthalendiimide as obtained at the BLYP-D/cc-pVTZ level of calculation, mapped onto an isosurface of electron density of 0.05 a.u.

3.2. Complexes with para-diphenylnaphthalendiimide

As indicated in the Computational Details section, naphthalendiimide molecule is a simple model trying to represent the trimeric units which constitute the walls of the ion channel. In an attempt to assess if this model is an oversimplification, calculations were carried out employing the para-diphenylnaphthalendiimide (2Φ -NDI) shown in Figure 10. This molecule is the same as NDI but including phenyl substituents in both ends, thus representing in a more realistic way the system studied. Figure 10 also shows the MEP as obtained at the BLYP-D/cc-pVTZ level of calculation. It can be observed that there are no significant differences with the MEP shown in Figure 3 for NDI. The most relevant aspect is that in 2Φ -NDI there are no N-H groups, so the anions must interact with the aromatic systems or with the hydrogen atoms of the phenyl groups.

Table 2. Selected geometric parameters of the complexes formed with 2Φ -NDI. Next indicates the nearest heavy atom. *next* indicates the nearest heavy atom; *ringcent* the nearest ring center and *molcent* the middle C-C bond in the center of the molecule.

	2Φ -Br1	2Φ -Br2	2Φ -Br3	2Φ -Br4	2Φ -Cl1	2Φ -Cl2	2Φ -Cl3	2Φ -Cl4
$R_{X\cdots next}$	3.190	3.070	3.717	3.591	3.061	2.945	3.574	3.428
$R_{X\cdots ringcent}$	3.209	3.652	4.871	4.738	3.090	3.544	4.733	4.571
$R_{X\cdots molcent}$	3.878	4.531	8.047	5.968	3.818	4.442	7.972	5.801
	2Φ -F1	2Φ -F2	2Φ -F3	2Φ -F4	2Φ -OH1	2Φ -OH2	2Φ -OH3	2Φ -OH4
$R_{X\cdots next}$	2.137	1.596	3.025	2.817	2.149	1.476	3.115	2.919
$R_{X\cdots ringcent}$	3.424	2.518	4.162	3.969	2.439	2.678	4.273	4.051
$R_{X\cdots molcent}$	3.443	3.457	7.592	5.200	3.461	3.751	7.740	5.283

Figure 11 shows the optimized structures of the complexes formed with bromide and fluoride anions with 2Φ -NDI. It can be observed that the structures are similar to those found in complexes with NDI. Of course, structure **NDI-X3** is not possible, but there is a new possibility of the anion interacting with the hydrogen atoms in the phenyl substituents as in **2Φ -NDI-X3**. For structures **X2** and **X4** there are no significant differences independently of considering complexes with NDI or 2Φ -NDI, as indicated by the geometrical parameters in Table 2. The only significant difference is observed in structures **X1**, where the presence of a near phenyl group allows a secondary interaction with the anion. As a consequence, for the hydroxide complex the distance to the molecular plane is much longer than in complexes with NDI, corresponding to a typical intermolecular distance.

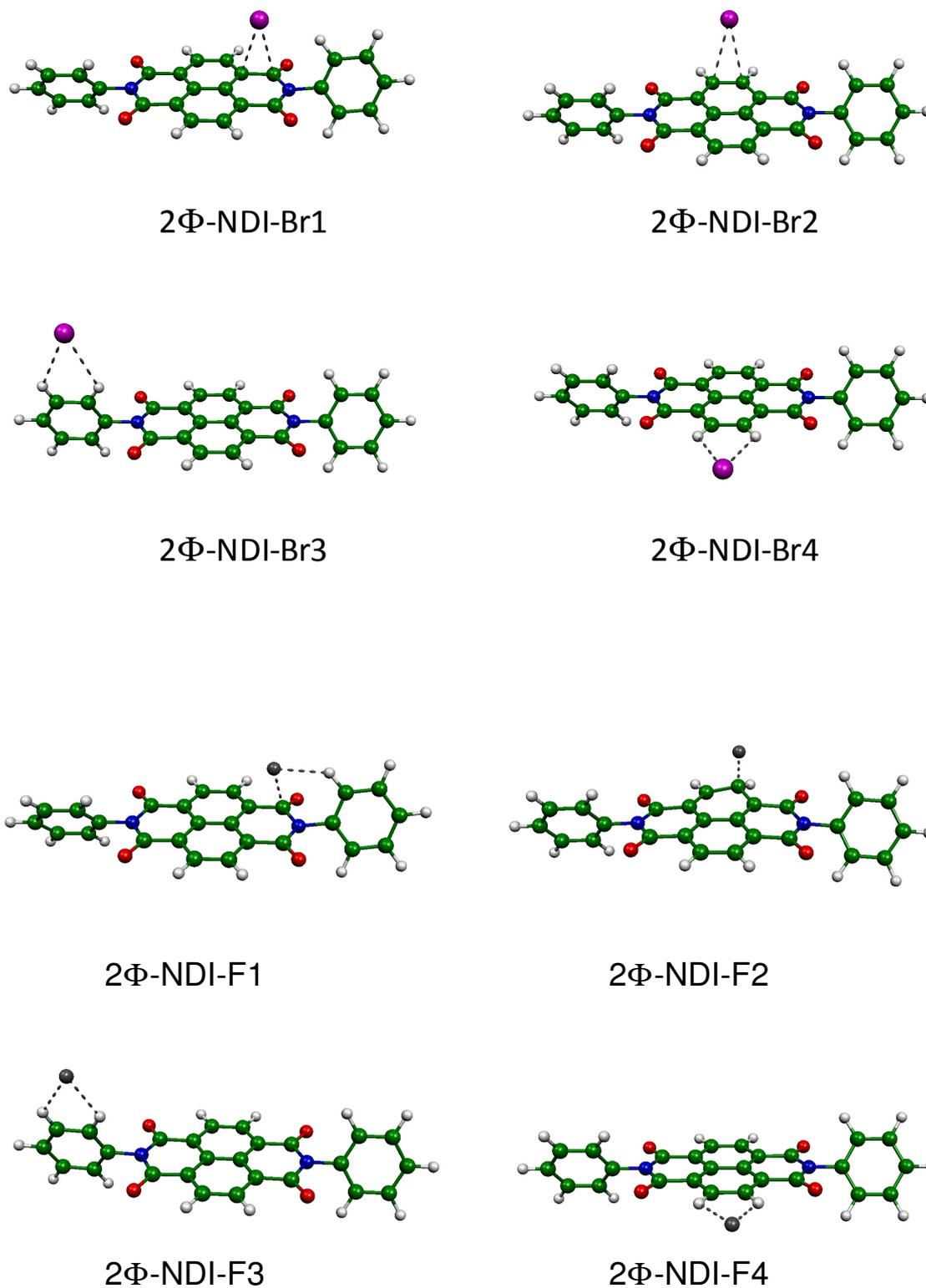


Figure 11. Optimized structures of the complexes formed by 2Φ-NDI with bromide and fluoride anion as obtained at the BLYP-D/pVTZ level of calculations.

Table 3 lists the calculated complexation energies and related quantities for the complexes formed with 2Φ-NDI, whereas Figure 12 compares the complexation energies with our two models for structures **X1** and **X2**; that is, those showing anion⋯π interactions. It can be appreciated in Figure 12 that the extension of our model to include phenyl groups only affects marginally the complexation energies. In any case, a general trend can be observed so structures **X1** are always more stable for 2Φ-NDI, whereas structures **X2** are more stable for **NDI**. In the case of **X1** structures this is related to the new anion⋯HC contacts established with the terminal phenyl rings.

In summary, it can be concluded that employing the simplified **NDI** molecule as model of the real system does not introduce significant errors compared to larger models, which resemble more closely the real unit forming the walls of the ion channel.

Table 3. Complexation energies (kcal/mol) of the complexes formed with 2Φ-NDI.

	ΔE_{BLYP}	ΔE_{disp}	E_{def}	$\Delta E_{\text{complex}}$
2Φ-NDI-Br1	-15.85	-6.35	1.46	-20.73
2Φ-NDI-Br2	-16.94	-3.60	1.32	-19.23
2Φ-NDI-Br3	-12.96	-2.27	0.57	-14.66
2Φ-NDI-Br4	-13.99	-2.64	0.96	-15.67
2Φ-NDI-CI1	-18.96	-4.80	1.62	-22.14
2Φ-NDI-CI2	-18.81	-2.71	1.33	-20.18
2Φ-NDI-CI3	-14.24	-1.81	0.63	-15.42
2Φ-NDI-CI4	-15.75	-2.60	1.08	-16.77
2Φ-NDI-F1	-38.42	-3.50	4.36	-37.56
2Φ-NDI-F2	-51.27	-1.92	17.30	-35.89
2Φ-NDI-F3	-22.81	-1.63	1.06	-23.38
2Φ-NDI-F4	-26.84	-1.54	2.06	-26.32
2Φ-NDI-OH1	-53.70	-4.73	5.60	-52.83
2Φ-NDI-OH2	-86.94	-3.33	38.54	-51.73
2Φ-NDI-OH3	-30.37	-1.51	1.02	-30.86
2Φ-NDI-OH4	-32.71	-1.60	1.75	-32.56

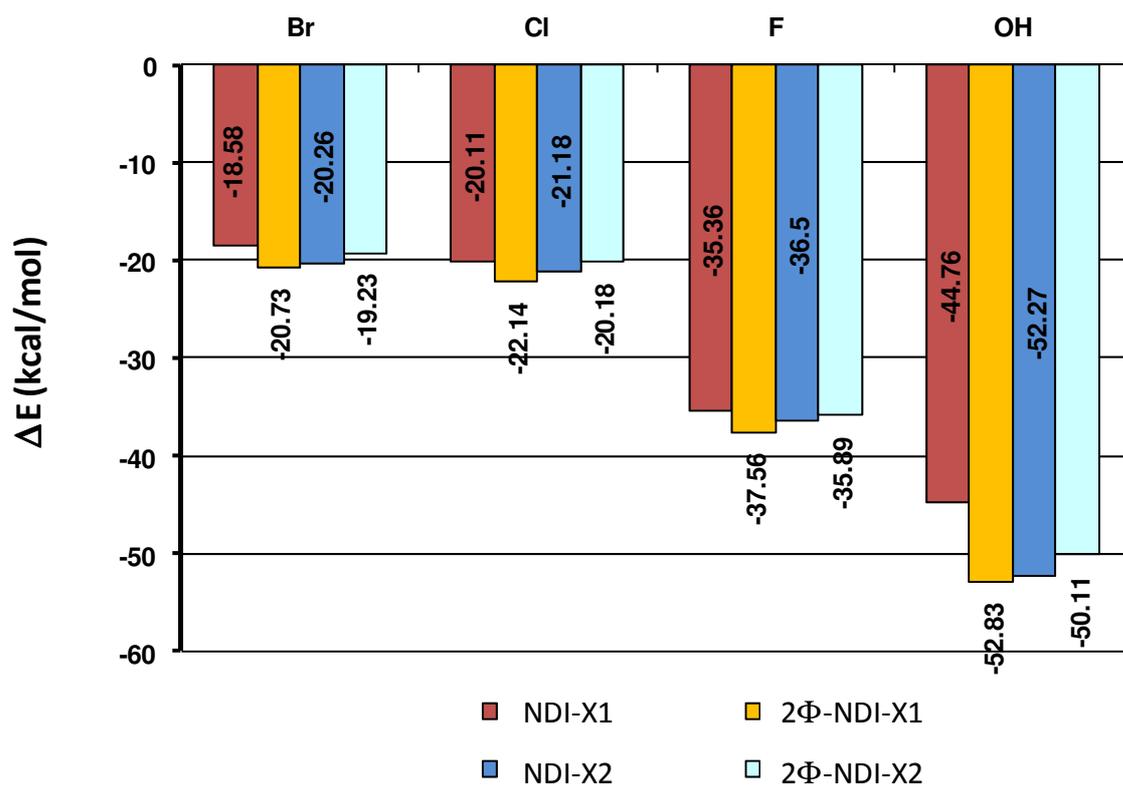


Figure 12. Comparison of the complexation energies for the complexes formed with **NDI** and **2Φ-NDI** presenting anion $\cdots\pi$ interaction.

3.3. Solvent effect

Taking into account the results thus presented, it is evident that all anions are capable of forming complexes with NDI and 2 Φ -NDI molecules, exhibiting large complexation energies associated to anion $\cdots\pi$ interactions. As indicated by Matile,¹¹ this large anion $\cdots\pi$ interactions must be responsible of the transport through the channel, overcoming the dehydration cost of the anions.

Thus, one crucial aspect to be included in the calculations is the effect of the solvent in the interaction. Therefore, the complexes formed with NDI and the anions studied were optimized in water employing the COSMO model to represent bulk water. The results are shown in Figure 13 and are quite disappointing, since no complex between any of the anions and NDI is stable in water, except complexes **NDI-X3** which are not possible in the real complex. Therefore, despite the strong interaction of the anions with NDI molecule, it is not possible to overcome the cost of anion dehydration.

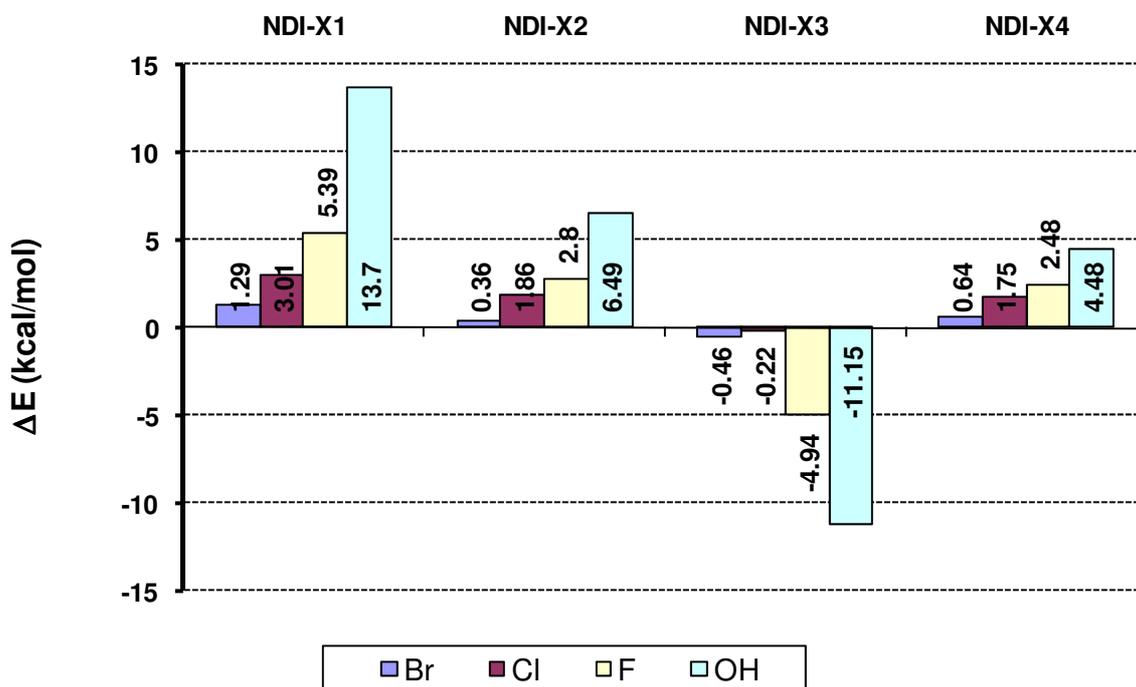


Figure 13. Complexation energies for the complexes studied obtained in water modelled with the COSMO method.

Figure 14 shows the values obtained in a less polar solvent as THF. In this case complexation is favourable in many cases. Thus, as expected, an increase in polarity of the medium hinders the establishment of anion $\cdots\pi$ interactions.

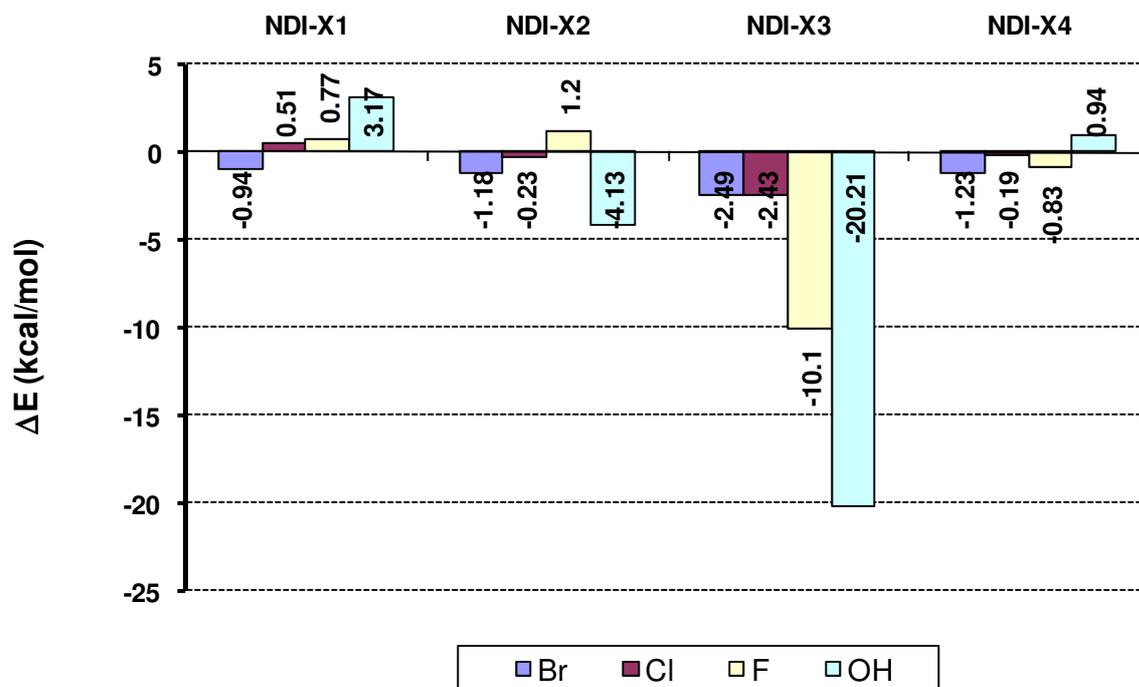
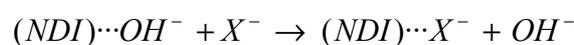


Figure 13. Complexation energies for the complexes studied obtained in THF modelled with the COSMO method.

However, it has been established that the mechanism of anion transport through the channel corresponds to an anion/hydroxide exchange. Therefore, a displacement process where the hydroxide is expelled from the channel by another anion could be expected. That is, the process could be:



The results obtained for this process are shown in Table 4 for the most stable structures showing anion $\cdots\pi$ interactions. Thus, whereas in gas phase the displacement of hydroxide is a highly unfavourable process, it is not the case in bulk solvent. So, in THF the process is still unfavourable despite the stable complexes formed in this solvent, but when bulk water is present the exchange process becomes favourable for all anions studied. The most favourable anion transport would correspond to fluoride, followed by bromide and chloride. Therefore, the process of ion passing through the channel comes from a very delicate balance between complexation energy and solvation energy of the anions involved in the transport.

Table 4. Energy differences for the process of hydroxide displacement by another anion as indicated in the text.

	Br	Cl	F
0-H₂O	31.66	31.68	16.05
bulk-THF	2.95	3.90	4.90
bulk-H₂O	-6.13	-4.63	-3.69

Of course, when passing through the channel the environment of the anion does not correspond to bulk water, so it is possible that a continuum model will not represent properly the interaction into the channel. Therefore, it can be expected that specific effects arising from the few water molecules accompanying the anion through the channel will change the results. Calculations are being performed in order to assess this point.

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