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To be cited as: *Chem. Eur. J.* 10.1002/chem.201604313

Link to VoR: http://dx.doi.org/10.1002/chem.201604313

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Solution and Solid State Studies on Anion-π Interaction Enhanced Halide Binding with a Perfluorophenyl armed Uranyl Salophen Receptor

Luca Leoni,[a] Rakesh Puttreddy,[b] Ondřej Jurček,[b] Andrea Mele,[a] Ilaria Giannicchi,[a] Francesco Yafteh Mihan,[a] Kari Rissanen*[b] and Antonella Dalla Cort*[a]

Abstract: The enhancement of the binding between halide anions and a Lewis acidic uranyl salophen receptor has been achieved by the introduction of pendant electron-deficient arene units into the receptor skeleton. The association and the occurrence of the elusive anion-π interaction with halide anions (as tetrabutylammonium salts) has been demonstrated in solution and in the solid state, providing an unambiguous evidence about the interplay of the concerted interactions responsible for the anion binding.

Anion recognition is an active area of research in supramolecular chemistry since anions are important and ubiquitous in biological processes. Thus, the development of novel artificial anion receptors represents an important research field, and the study of the non-covalent interactions on which host-anion recognition relies is crucial for the understanding of the biological processes and designing systems for environmental monitoring.[1]

Among these receptors that are recently used to this purpose, are the strongly Lewis acidic uranyl salophen [(N,N-phenylene-bis(salicylimine)] complexes. They are easily available through the condensation of two equivalents of salicylaldehyde and one equivalent of phenylenediamine in the presence of uranyl acetate.[2] The large number of synthetic routes to ortho-substituted phenols and to the corresponding ortho-salicylaldehydes gives access to a variety of structures with subtle sterical and electronical variations on the receptor structure, thus making them perfect candidates for systematic studies. Clearly the main driving force for anion complexation in these systems is the hard Lewis acidic uranyl center, where the fifth equatorial coordination site of the uranium atom acts as the binding site. Nevertheless, these complexes do have an additional feature as they can act as multitopic receptors.[3] For example, the presence of appended benzyloxy groups in the ortho-positions of the salicylimine shown in Figure 1 results in the cooperative ion pair binding. The Lewis acidic uranyl center binds the anions, while the appropriately spatially situated electron-rich π system binds cations (typically tetra-alkylammonium) via multiple cation-π and C-H···π interactions. This has been demonstrated by extensive studies in solid state and in solution.[4]

As the distance and electronic features of the pendant aromatic arms of the salophen skeleton is easy to tune, this gives rise to a possibility to enhance the interactions with the anion bound to the metal through weaker, secondary interactions, namely anion-π interactions.[5]

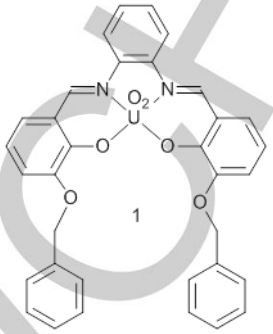

Figure 1. The chemical structure of the ortho-disubstituted benzyloxy uranyl salophen complex **1** for cooperative ion pair binding.

Such interactions, which take place between anions and electron-deficient arenes, are attracting considerable attention within the supramolecular community, and appear as an appealing non-covalent tool with interesting applications in the design of highly selective anion receptors[6], channels[7] and more recently in catalysis.[8]

Although this interaction has been underscored in many crystal structures,[9] the unambiguous proof of its occurrence in solution is still a challenging task.[10] Furthermore the majority of artificial, neutral anion receptors reported in the literature so far, combine hydrogen bonding and anion-π interactions, while the uranyl salophen complexes herein described, to the best of our knowledge, are the first example of receptors that manifest Lewis acid-base and anion-π interactions simultaneously to reach the goal.

Here, we report the study of the binding of tetrabutylammonium halide salts TBAX (X= Cl^-, Br^-, I^-) with three uranyl-salophen receptors decorated with appended aromatic arms, differently substituted, **2a-c**. The data obtained in chloroform solution and the analysis of the solid-state structures of [TBA][**2a**Cl] and [TBA][**2a**Br] provide a comprehensive view about the contribution of the anion-π interactions to the overall binding event in both media.

For this investigation, we prepared the uranyl salophen complexes as depicted in Scheme 1. The fact that only one appended aromatic substituent is present is due to our previous observations on similar derivatives for which we found, specifically in the solid state, that only one side arm is involved in the interaction with the bound substrate.[11] We synthesised the properly functionalized salicylaldehyde derivatives by palladium-catalyzed cross-coupling reaction (Suzuki coupling) of either pentafluorophenyl boronic acid and 2-bromoanisole or 3,5-dimethoxyphenylboronic acid and 1-benzyloxy-2-iodobenzene, followed by the deprotection of the phenolic groups and ortho formylation.

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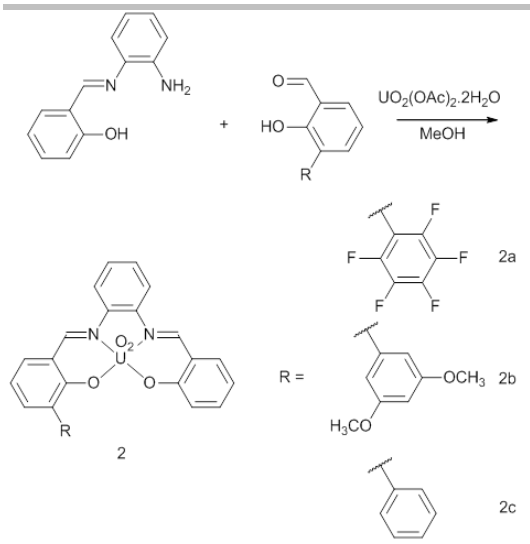

Scheme 1. Synthesis of the ortho- mono-substituted aromatic uranyl salophen complexes.

The obtained aldehyde derivatives were then reacted with the monoimine prepared from *o*-phenylenediamine and salicylaldehyde in the presence of uranyl acetate.[12] For compound **2c**, the ortho formylation of 1,1'-biphenyl-2-ol leads to the corresponding salicylaldehyde, that was reacted with the monoimine as previously described (See ESI for details).

Binding constants for the 1:1 complexes of TBAX, X= F^-, Cl^-, Br^-, with the uranyl-salophen complexes were obtained in $CDCl_3$ at 25°C, from UV-vis titrations. UV-vis spectra and titration curves are reported in ESI. Binding constants K_a (M^{-1}) are listed in Table 1. To evaluate the binding constant with iodine we had to undertake ^1H NMR titrations.

Table 1. Association constant values, K_a (M^{-1}), for the complexation of TBAX with receptors **2a**-**c** obtained by UV-vis titrations in $CHCl_3$ at 298 K.

X	2a	2b	2c
F^-	$>10^6$	$>10^6$	$>10^6$
Cl^-	140000 ± 10000	11000 ± 1200	24000 ± 200
Br^-	2090 ± 15	100 ± 5	650 ± 65
I-	<20[a]	<20[a]	<20[a]

[a] Obtained by ^1H NMR titrations in $CDCl_3$.

Inspection of the results shows that the binding order of the complexes with the TBA salts, namely, $F^- >> Cl^- > Br^- > I^-$, is in good agreement with the hard Lewis acidic character of the uranyl center. The strong affinity of the TBA fluoride salt is dominated by the interaction of the hard fluoride anion with the metal center. Such binding is so high for all the receptors (K_a $>10^6$) that it prevents the observation of any difference, if present, caused by the nature of the substituents on the aromatic appended arm. Instead lower binding affinities in the case of chloride allow interesting considerations. The highest stabilization of the host@chloride complex was found with receptor **2a**, decorated with a perfluorophenyl unit. Indeed fluorine is the most electronegative element, and it is known that when present as a substituent in hexafluorobenzene it induces a large positive quadrupole moment (Q_{zz} (C_6F_6) = +9.50 B).[13] For this reason electron-deficient fluorinated arenes are known to act as π-acceptors.[14] The measured binding affinity towards chloride shown by the other two receptors either displaying two methoxy groups, **2b**, or no substituents, **2c**, are definitely lower. They behave quite similarly although **2c** is slightly more efficient for chloride binding than **2b** confirming the strong electron-donating ability of the methoxy groups. Thus the further stabilization via anion π-interactions takes place only with the receptor **2c** that displays a π-acceptor character that enhances halide binding in solution.[15] The same behavior is observed with bromide, while the association with iodine is so weak that no remark can be done. The directionality of the complexation, the halide is hosted in the fifth equatorial site of the uranyl, provides a suitable geometrical orientation to establish intramolecular contacts with the π-cloud of the pendant arm. The potential electronic effect of the substituents on the Lewis acidity of the uranyl center can be easily ruled out since a direct interaction between the sidearm and the uranyl center is prevented by the marked curvature imposed to the coordinated salophen ligand by the large atomic radius of uranium. This is clearly highlighted by a number of X-ray structures[4,11,16] and also easily reproduced by molecular mechanics calculations.[17] Slight variations in the resonances of the TBA salt during titrations seem to indicate that the uranyl complexes do not behave as ditopic receptors, Fig S28.

In order to quantify the contribution in solution of the anion-π interaction for these systems, we calculated ΔΔG values, being $\Delta\Delta G = \Delta G_{X^-@Host} - \Delta G_{X^-@\mathbf{2c}}$,[18] with respect to the control receptor **2c**, in which the appended phenyl ring does not have any substituent. The free energies relative to anion binding are obviously the sum of two different types of intermolecular interactions: Lewis acid-base interaction with the metal center and anion-π interaction with the pendant aromatic wall. We estimated for receptor **2a** an attractive free energy of -1.0 kcal/mol for chloride binding and -0.7 kcal/mole for bromide; while for receptor **2b** a repulsive free energy of 0.5 kcal/mol for chloride and 1.1 kcal/mol for bromide was calculated. The observed trend is in agreement with the existence of a weak non-covalent stabilizing interaction for the perfluorinated derivative, whose magnitude is in accordance with the values reported by Ballester and coworkers[19] for a series of "two-wall" calix[4]pyrrole receptors bearing two six-membered electronically different aromatic rings.

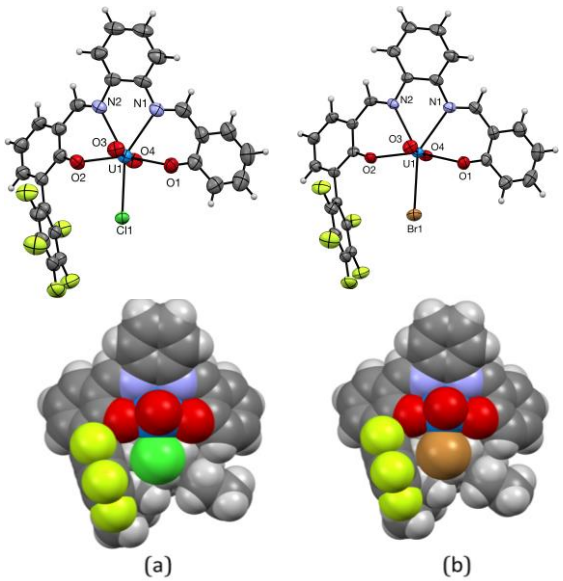

Figure 2. X-Ray crystal structures of [TBA][**2a**Cl] (a) and (b) [TBA][**2a**Br] with the thermal displacement parameters at 50 % propability level (top) and in CPK (bottom) presentations.

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Crystals of the complexes [TBA][**2a**Cl] and [TBA][**2a**Br] were obtained by slow evaporation of $CHCl_3$ and $CHCl_3$:CCl_4, 50:50 solutions, respectively. The crystal structures are isomorphous and crystallize in the monoclinic space group P21/c, Fig. 2.

The biphenyl unit formed by the salicylaldehyde and the pendant perfluoro arene ring displays a very similar twist angle, 63.3(8)° and 64.8(8)°, in the chloride complex and the bromide one, respectively. For comparison, in the 2,3,4,5,6-pentafluoro-2',4'-dimethoxy-1.1'-biphenyl compound[20] the twist angle is 53.6°. The wider twist angle we found can be ascribed to the presence in the equatorial coordination plane of the bound anion, close to the pentafluoro phenyl ring, with which it establishes stabilizing anion π-interactions. The $C_{ring}\cdots X$ (X = Cl^- and Br^-) distances range between 3.82 – 3.94 Å in [TBA][**2a**Cl] and 3.77 – 3.94 Å in [TBA][**2a**Br]. However, remarkably, the π(centroid)···X, [X = Cl^- and Br^-] has the shortest distances of 3.63 and 3.60 Å, respectively, indicating clear η^6 anion-π interactions.[14] The normal U-Cl bond distances in similar uranyl salophen complexes vary between 2.713 – 2.760 Å, the same distance in [TBA][**2a**Cl] 2.843(2) Å is markedly longer (0.083 - 0.130 Å) and statistically significantly different. On the contrary the U-Br distance 2.930(1) Å is only slightly longer that the only reported U-Br distance (HEYXEP, 2.902 Å) in salophen complexes found on CCDC.[4a,11a,11d] The more electron-rich chlorine atom tends to have stronger (yet weak) attractive interactions to the perfluoro group than the corresponding bromide thus supporting the anion-π interactions in solution state in a form of higher association constants. On the other hand there are no observed short contacts between the aromatic ring and TBA cations, like cation-π interactions. The packing of [TBA][**2a**Cl] and [TBA][**2a**Br] starts through numerous intermolecular π-π, C-H···π, C-H···O and C-H···F interactions (See Fig S1-2). The X-ray structures provide additional proof that the perfluoro group, though having five highly electron-withdrawing fluorine substituents, does not influence the Lewis acidity of the uranyl center. The C-O and O-U bond distances are equal in [TBA][**2a**Cl] and [TBA][**2a**Br] (See ESI for bond parameters comparison), and are close to the unsubstituted uranyl salophen@tetraethylammonium chloride (TEACl) complex,[16] Fig.3:

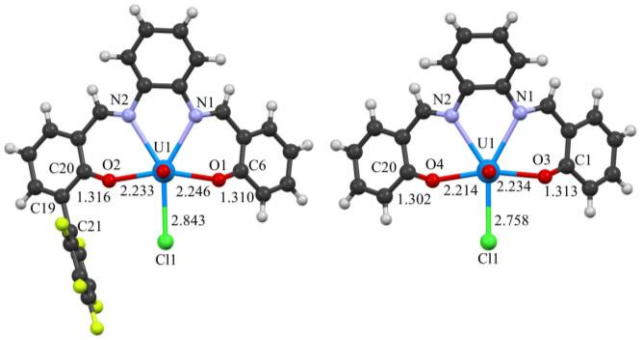

Figure 3. Comparison of C-O and O-U bond distances in [TBA][**2a**Cl] (left), and in UO2-Salophen@TEACl (CCDC code LADCUO).[15b] The TBA cations are omitted for clarity.

In addition although the O2-U1-X1 (X = Cl and Br) angle is around 80 deg in both [TBA][**2a**Cl] and [TBA][**2a**Br] is typical, and similar to reported salophen complexes,[4a] due to the η^6 anion-π interactions, the perfluorobenzene group is "leaning" towards the uranyl bound halide, manifesting reduced biphenylic C20-C19-C21 bond angle. In [TBA][**2a**Cl] and [TBA][**2a**Br] the angle is 117.1° and 115.1°, markedly smaller than in the *tert*-butylpyridine complex of 3,3'-bis(*o*-methoxy)UO_2-salophen, where the same bond angle is 124.2°.[21]

Hence, despite of unsuccessful attempts to isolate single crystals of **2b** and **2c**, the experimental evidence obtained from solution state, together with the X-ray analysis of **2a** complexes with TBACl and TBABr, provide an unbiased view for the existence of interactions between anions and charge-neutral arenes. Strongly electron-deficient systems attract the anions, while in the presence of more electron-rich units the interaction becomes repulsive. The values of the free energies estimated in solution for the interaction of chloride and bromide with the π-aromatic systems are in the range of those already reported, and underscore the role played by them in the recognition event. Moreover, this is the first comprehensive set of data, in solution and in the solid state, for anion recognition relying on the combination of Lewis acid-base and anion-π interactions.

Acknowledgements

The authors acknowledge the European Cooperation in Science and Technology (COST Actions "Supramolecular Chemistry in Water", CM1005 and Crystallize CM1402). A.D.C. acknowledges the financial support of Università La Sapienza, project "Ricerca scientifica di Ateneo 2014" and MIUR "PRIN 2010CX2TLM". K.R. gratefully acknowledges the financial support from the Academy of Finland (prof. no.'s 263256, 265328 and 292746) and University of Jyväskylä.

Keywords: anion-π interactions• Lewis acid-base interactions • uranyl-salophen • halide binding • host-guest complexes

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[12] Caution! While isotopically depleted U was used in these experiments, precautions for handling radioactive materials should be followed.

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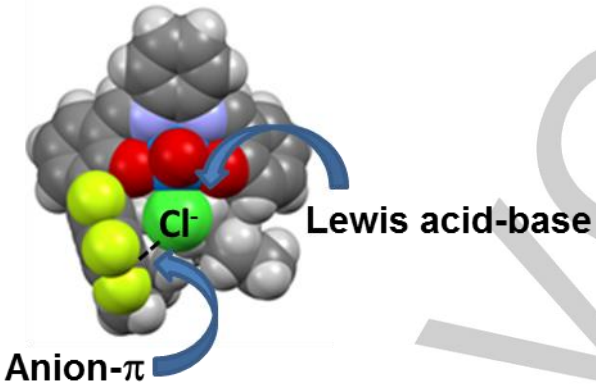

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