

Computational study of the interaction between sumanene and cations in function of the cation- π separation.

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Abstract

With the aim of enhancing the comprehension of the cation- π interaction, a computational study of the interaction established between sumanene molecule and various cations was performed. Sumanene is a polycyclic aromatic hydrocarbon with a bowl-shaped structure. The curvature of the molecule causes an asymmetry in the distribution of its molecular electrostatic potential that is more negative in its outer (convex) side. This feature allows testing the role of the electrostatic contribution to cation- π interaction by using both sides of the same molecule. Five cations with different sizes and shapes were selected for the study: sodium, potassium, ammonium, tetramethylammonium, guanidinium and imidazolium. These are monoatomic cations and models of cationic amino acid side-chains, all of which are known to participate in the formation of cation- π complexes in biological systems. The polyatomic cations were placed in different orientations with respect to the sumanene molecule including the "T-shaped" and "stacked" configurations of the flat cations. The study was accomplished at the RI-MP2/aug-cc-pVTZ level of calculation, to ensure the correct retrieving of the correlation energy and also that the basis set size is appropriate for the modeling of effects more complicated than the electrostatic contribution. The interaction energy (E_{int}) was computed at different sumanene-cation distances following the C_{3v} symmetry axis of sumanene and exploring its both sides: concave and convex. The rigid scans of the potential energy surface indicate that at sumanene-cation distances around the E_{int} minima, the complexes are more stable with the cation placed by the inner (concave) side of sumanene, with the only exception of the complexes with Na^+ , the smallest of the cations studied. This result is the opposite of that expected from the pure electrostatic interpretation of the cation- π interaction. As the cation moves away from the sumanene molecule the situation is reversed, and at long distances the outer complexes are more stable than its inner partners. These findings suggest that at long cation-molecule separations the electrostatic contribution dominates because its influence propagates to longer distances but at short distances the cation- π interaction is controlled by other stabilizing contributions (induction and dispersion) defining the minimum of the E_{int} profile. The results obtained contribute to a better understanding the cation- π interaction and emphasize the importance of using the correct level of calculations in its theoretical modeling.

Keywords

cation- π interaction, non-bonding interaction, molecular bowls.

Introduction

Cation- π interaction is one of the most important non-bonding interaction because its ubiquitous presence in many fields of chemistry¹⁻³, biology⁴ and technology⁵. Since its discovery, cation- π interaction has been intuitively rationalized in terms of the electrostatic attraction between the cation positive charge and the negative charge distribution of the unsaturated molecule with an isolated or conjugated π cloud.⁶⁻⁸ This approach, confirmed by the first theoretical studies,^{9, 10} was adopted generally. Considering that the cation- π is always an “electrostatically controlled” interaction has led to the use of levels of calculation and basis set sizes that are enough for the modeling of electrostatic interactions but not for revealing high order effects. In this way, dispersive forces, which central importance has been recognized in other non-bonding interactions,¹¹ has been systematically ignored or underestimated in the theoretical study of the cation- π interaction. As the level of calculation was increased and the model systems studied grow,¹²⁻¹⁵ other contributions (for example, inductive and repulsive effects) were revealed as important components in the big picture of the cation- π interaction.¹⁶ Similar strategy is needed for revealing if the dispersion forces are (or not) an important contribution to the cation- π interaction, especially when the size of the studied systems becomes closer to that of structures with practical interest.

For gaining understanding on the nature of the cation- π interaction, the present work develops a systematic theoretical study of the interaction established between sumanene and various cations. Sumanene is a polycyclic aromatic hydrocarbon with a bowl-shaped structure. The curvature of the molecule causes an asymmetry in the distribution of its molecular electrostatic potential that is more negative in its outer (convex) side. This feature allows testing the role of the electrostatic contribution to cation- π interaction by using both sides of just one molecule and has been used before in computational and experimental studies of the cation- π interaction.¹⁶ Five cations with different sizes and shapes were selected for the present study: sodium, potassium, ammonium, tetramethylammonium, guanidinium and imidazolium. These are monoatomic cations and models of cationic amino acid side-chains, all of which are known to participate in the formation of cation- π complexes in biological systems.

Computational Details

The geometries of the isolated fragments (sumanene and cations M = ammonium, tetramethylammonium, guanidinium and imidazolium) were optimized at the M06-2X/6-31+G* level of calculation and the stationary points found were characterized as minima by means of frequency calculations at the same level. Rigid scans of the potential energy surface of the sumanene-cation (Suma-M) complexes were performed moving the cations following the C_{3v} symmetry axis, perpendicular to the central (bottom) ring, of sumanene and exploring its both sides: concave and convex. For the polyatomic cations, two orientations with respect to sumanene were considered, providing information about different kinds of cation- π contacts, including the “T-shaped” and “stacked” configurations of the flat cations. The images inserted in Figs. 2 and 3 show the structure and mutual arrangement of the fragments in the cation- π complexes studied.

The supermolecule approach was used for the calculation of the BSSE-free interaction energies.^{17, 18} Accordingly, the interaction energy results from subtracting the energies of the fragments that constitute the complex from its energy, all of them calculated using the geometry and the whole basis set of the cluster. Geometry optimizations and frequency calculations have been done with Gaussian09,¹⁹ whereas MP2 calculations have been performed with Turbomole 6.3.²⁰ To save up computational time in MP2 calculations, the resolution of the identity approach has been used. RI-JK-MP2 calculations were made using the aug-cc-pVTZ auxiliary basis set for correlation and the def2-TZVPP auxiliary basis set for both

coulomb and exchange in the calculation of HF energies. The size of the basis sets used ensures the correct modeling of effects more complicated than the electrostatic contribution.

Results and Discussion

The study of the molecular electrostatic potential (MEP) along the line perpendicular to the sumanene central ring corroborates the charge accumulation at both sides of the conjugate molecule. It is observed as well that the MEP minimum by the outer face is more separated from the bowl's bottom and also is more than 2 kcal/mol deeper than the inner minimum, as shown in Fig. 1. This indicates that the electrostatic interaction with the positive charge of a cation is more favored by the outer face of sumanene.

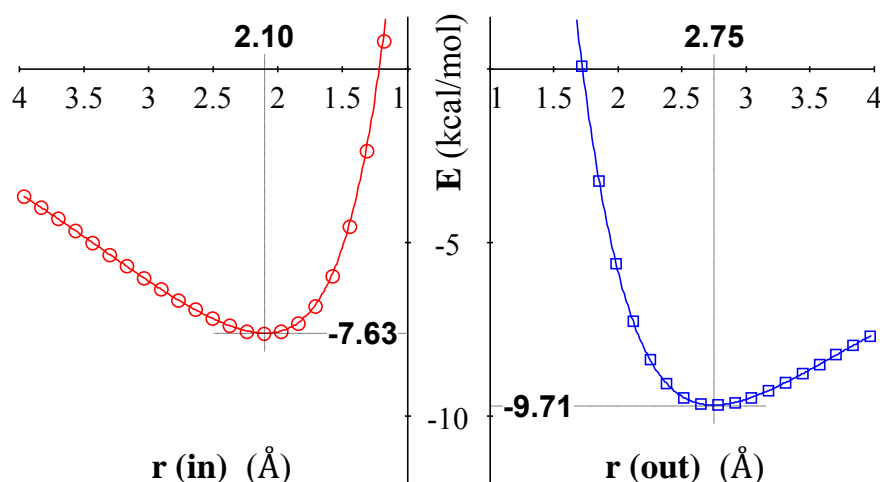


Fig. 1. Molecular electrostatic potential along the line normal to the central ring of sumanene as a function of the distance to the plane defined by such ring. This line defines the trajectories of the sumanene-cation scans shown in Fig. 2 and in Fig. 3. The position and the energy of the inner and outer minima are highlighted in the plot.

When a cation is moved along the same path used in the MEP calculations, the interaction energy describes the behavior shown in Figs. 2 and 3. These plots also show the differences between the E_{int} of the outer and inner complexes at every sumanene-cation distance, simplifying the visualization of where the stability of each kind of complex is favored. In addition, the points in which the preferential stability between inner and outer complexes changes are highlighted. The position and the E_{int} values for the minima observed in these scans are presented in Table 1.

Table 1. Interaction energies (upper values of each cell, in kcal/mol) and sumanene-cation distances (lower values, in Å) in the minima of the scans shown in Figs. 2 and 3. Acronyms used to identify the cations are: **N** = sodium; **K** = potassium; **A-1,3** = ammonium, with 1 or 3 N-H groups oriented toward the sumanene molecule; **T-1,3** = tetramethylammonium, with 1 or 3 $-\text{CH}_3$ groups oriented toward the sumanene molecule; **I-T, S** = imidazolium, in the “T-shaped” or “stacked” configuration; **G-T, S** = guanidinium, in the “T-shaped” or “stacked” configuration, respectively. The complexes are separated in three groups taking into account the kind of cation: monoatomic, tetrahedral or flat.

Cation:	N	K	A-1	A-3	T-1	T-3	I-T	I-S	G-T	G-S
in	-28.27	-27.66	-28.45	-32.22	-18.92	-17.76	-24.06	-24.03	-20.97	-17.49
	2.37	2.67	2.78	2.70	4.43	4.37	4.09	3.38	4.10	3.53
out	-28.31	-24.29	-23.33	-25.19	-13.41	-16.74	-19.75	-18.44	-16.56	-16.24
	2.39	2.77	2.95	2.80	4.62	4.08	4.11	3.24	4.24	3.26

In all the cases studied the interaction is stronger than the pure electrostatic (estimated by the MEPs in Fig. 1) confirming the importance of other stabilizing contributions. In the complexes with monoatomic and tetrahedral cations (those with the more symmetric structure) an inverse relationship between the E_{int} value and the cation size (N Vs. K; A1 Vs. T1; A3 Vs. T3) is clearly observed, confirming the importance of the polarizing power of the cation and, therefore, the fundamental role of the inductive contribution, already identified in these kind of complexes.¹⁶

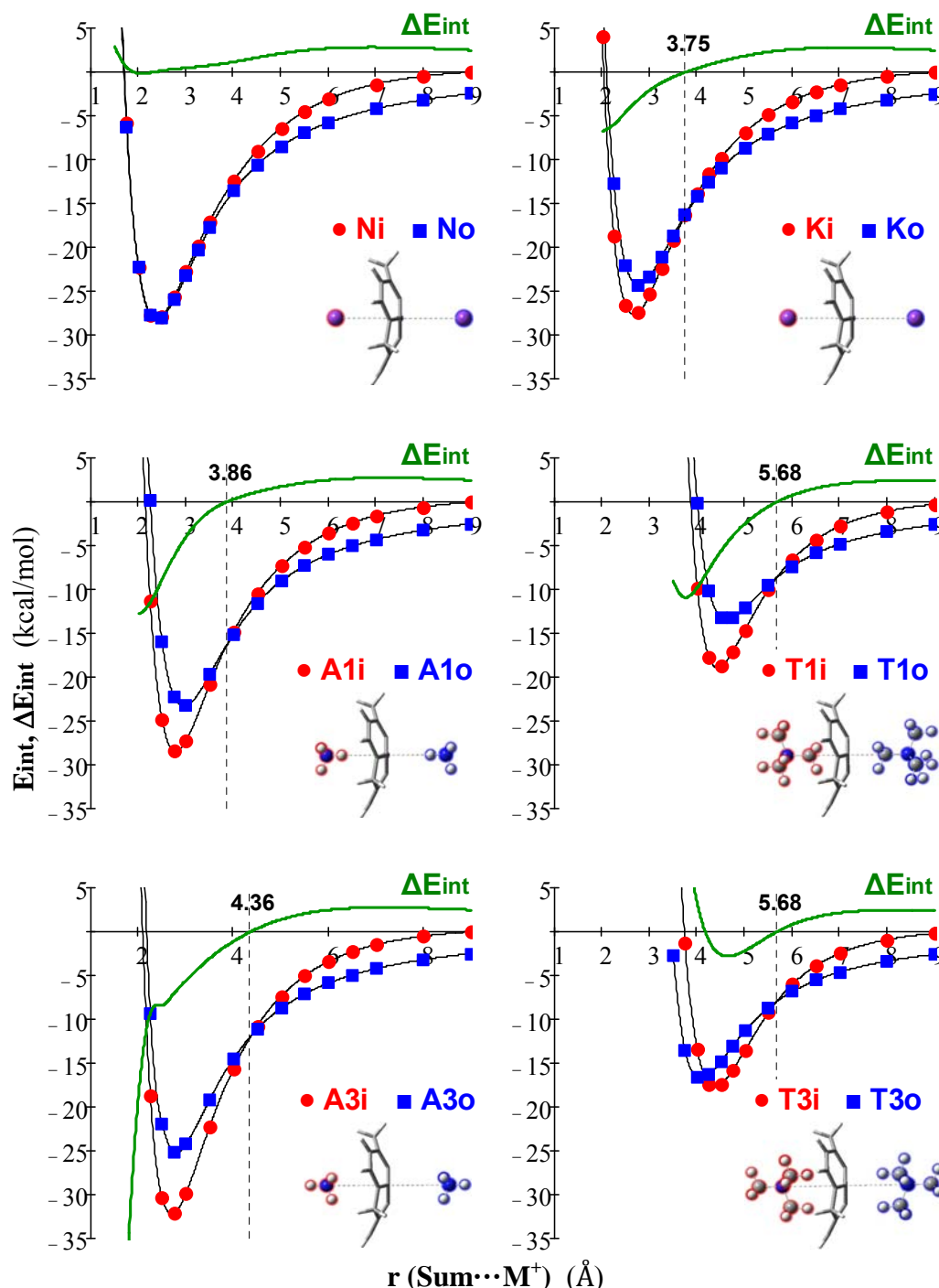


Fig. 2. Interaction energy as a function of the sumanene-cation distance for the complexes formed by the monoatomic cations (sodium and potassium) and the tetrahedral cations (ammonium and tetramethylammonium). The difference between the stabilities of the complexes formed by both sides: $\Delta E_{\text{int}} = E_{\text{int}}(\text{in}) - E_{\text{int}}(\text{out})$ is represented with the green trace, without symbols. Acronyms used to identify the cations are explained in the title of Table 1. The images inserted in the plots show the structure and mutual arrangement of the fragments in the cation- π complexes studied in each scan.

The curvature of sumanene molecule and the presence of three saturated carbon atoms, each one with a C-H group pointing to the concave side of the structure, suggest that repulsion should destabilize more the inner than the outer complexes, mainly with the larger cations. This, joined to the more negative MEP values by the convex side of this molecule should conduce to more stable cation- π complexes by the outer side of sumanene, in comparison with their inner partners. Nevertheless, the results point in the opposite direction. The complexes of potassium and larger cations present more negative values of E_{int} in the minima of the scans when the cation is by the inner side of sumanene (Table 1). This is true even in the cases of large cations like tetramethylammonium (mainly in its T3 orientation) and the flat cations, not only in their “T-shaped” complexes but in the “stacked” configuration too. These are low polarizing cations and the stacked interaction is known that have a very important dispersive contribution. This suggests that dispersion is also playing an important role in the stabilization of the cation- π complexes studied in the present work.

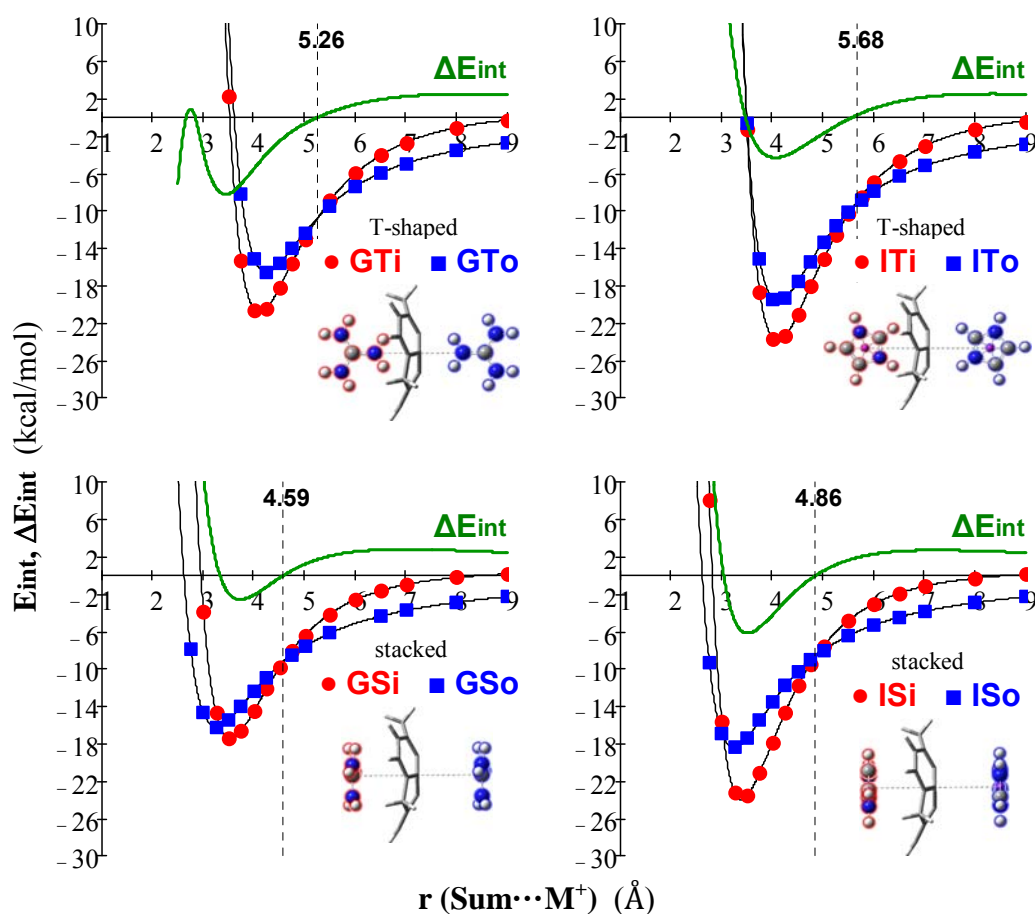


Fig. 3. Interaction energy as a function of the sumanene-cation distance for the complexes formed by the flat cations (imidazolium and guanidinium). The difference between the stabilities of the complexes formed by both sides: $\Delta E_{\text{int}} = E_{\text{int}}(\text{in}) - E_{\text{int}}(\text{out})$ is represented with the green trace, without symbols. Acronyms used to identify the cations are explained in the title of Table 1. The images inserted in the plots show the structure and mutual arrangement of the fragments in the cation- π complexes studied in each scan

The changes in the relative stability of the complexes formed by both sides of sumanene when a particular cation is moved away from the molecule are expressed in the plots of Fig. 2 and Fig. 3 by the trace ΔE_{int} . All the sumanene-cation couples with potassium and larger cations have a common feature: it is observed a “crossing point” point at around 0.9-1.6 Å from the minimum of E_{int} that is closest to the bowl’s bottom, beyond which the outer complex is always the most stable. Before this point, in the distances around the minimum of E_{int} , the interaction of a cation- π complex is the result of the combined action of repulsive, electrostatic, inductive and dispersive contributions. In situations similar to these a

high-level method and a basis set with enough flexibility are required for capture correctly the impact of polarization and, mainly, of the dispersive contributions. A rigorous energy analysis is advised in these cases, for gaining insight in the nature and weight of each contribution to E_{int} . But induction and dispersion are short-range interactions and at long cation- π distances only the electrostatic forces can stabilize the cation- π complexes, causing that beyond the farthest crossing points of ΔE_{int} all the systems fulfill the prediction made by the MEP profile. In consequence, the theoretical modeling of these complexes is less restrictive in terms of the level of calculation. The study of cation- π complexes at distances larger than the one corresponding to the E_{int} minimum is interesting when the fragments of the complex cannot interact at the most favorable distance, for example, in crystals or if they are bound to a protein backbone.

Conclusions

The interaction between sumanene and various cations has been theoretically studied as a function of the cation- π separation using the RI-MP2/aug-cc-pVTZ level of calculation. The results obtained contradict the electrostatic control generally attributed to the cation- π interaction. At sumanene-cation distances around the minima of the interaction energy, the complexes with all of the cations bigger than Na^+ are more stable with the cation placed by the inner (concave) side of sumanene. As the cation is separated from the sumanene molecule the situation is reversed, and at long distances the outer complexes are more stable than its inner partners. These findings suggest that at long cation-molecule separations the electrostatic contribution dominates because its influence propagates to long distances but at short distances the cation- π interaction is controlled by other stabilizing contributions (induction and dispersion) defining the minimum of the E_{int} profile. The results obtained contribute to a better understanding of the cation- π interaction and emphasize the importance of using an appropriate level of calculation in its theoretical modeling, especially when the complexes under study are formed by large fragments that interact at short-to-medium distances.

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