

See discussions, stats, and author profiles for this publication at: <https://www.researchgate.net/publication/244404133>

# On the Cooperativity of Cation- $\pi$ and Hydrogen Bonding Interactions

ARTICLE in THE JOURNAL OF PHYSICAL CHEMISTRY B · JULY 2008

Impact Factor: 3.3 · DOI: 10.1021/jp804219e · Source: PubMed

CITATIONS

79

READS

54

## 3 AUTHORS:



**Dolly Vijay**

University of Delhi

24 PUBLICATIONS 557 CITATIONS

SEE PROFILE



**Hendrik Zipse**

Ludwig-Maximilians-University of Munich

137 PUBLICATIONS 2,558 CITATIONS

SEE PROFILE



**G Narahari Sastry**

Indian Institute of Chemical Technology

262 PUBLICATIONS 5,292 CITATIONS

SEE PROFILE

On the Cooperativity of Cation– $\pi$  and Hydrogen Bonding InteractionsDolly Vijay,<sup>†</sup> Hendrik Zipse,<sup>‡</sup> and G. Narahari Sastry<sup>\*,†</sup>*Molecular Modeling Group, Organic Chemical Sciences, Indian Institute of Chemical Technology, Tarnaka, Hyderabad 500 007, AP, India, and Department Chemie and Biochemie, LMU München, Butenandstrasse 5-13, D-81377 München, Germany**Received: May 13, 2008; Revised Manuscript Received: June 18, 2008*

Quantum chemical calculations are performed to gauge the effect of cation– $\pi$  and hydrogen bonding interactions on each other. M–phenol–acceptor (M = Li<sup>+</sup> and Mg<sup>2+</sup>; acceptor = H<sub>2</sub>O, HCOOH, HCN, CH<sub>3</sub>OH, HCONH<sub>2</sub> and NH<sub>3</sub>) is taken as a model ternary system that exhibits the cation– $\pi$  and hydrogen bonding interactions. Cooperativity is quantified and the computed positive cooperativity between cation– $\pi$  and hydrogen bonding interactions is rationalized through reduced variational space (RVS) and charge analyses.

## Introduction

Noncovalent interactions such as hydrogen bonding,  $\pi$ – $\pi$  interaction, cation– $\pi$  interaction, hydrophobic, ionic, and van der Waals interactions govern the organization of multicomponent supramolecular assemblies.<sup>1</sup> A molecular level understanding of these interactions is of outstanding importance for the rationalization of effects observed in fields as different as materials science and molecular biology. Quantum chemical studies on small model systems have, in combination with appropriate experiments, been rather helpful in developing a quantitative picture of these interactions.<sup>2</sup> An important feature of noncovalent interactions in condensed matter is a multitude of interactions operate simultaneously at any given point of time. It is, for example, well-known that hydrogen bonding works in a highly cooperative fashion; i.e., the cumulative strength of networks of hydrogen bonds is larger than the sum of the individual bond strengths when they work in concert.<sup>3</sup> Similar observations have been made for the interplay of stacking and hydrogen bonding interactions, a combination of outstanding importance for the structural control in oligonucleotides.<sup>4</sup> More recently, the cation– $\pi$  and  $\pi$ – $\pi$  interactions were also shown to work in a cooperative fashion.<sup>5</sup> A recent study also estimates the interplay between cation– $\pi$  and hydrogen bonding interactions.<sup>6</sup>

Cation– $\pi$  and hydrogen bonding interactions are among the strongest noncovalent interactions in absolute terms. The present communication therefore examines how these two interactions influence each other.

## Computational Details

The calculations were performed using the Gaussian 03 program package.<sup>7</sup> All complexes considered in the study were initially optimized at the density functional level of theory using the B3LYP functional with the 6-31G(d) basis set, followed by

single point calculations with the 6-311++G(d,p) basis set. Electron correlation was included via the second-order Møller–Plesset (MP2) treatment in conjugation with 6-31G(d) basis set. The MP2/6-31G(d) optimized geometries were then taken to perform single point calculations at the MP2(FULL)/6-311++G(d,p) level. The optimization and frequency analysis of all complexes was further carried out at the MP2(FC)/AUG-cc-pVDZ. The frequency calculations performed at the MP2(FC)/AUG-cc-pVDZ and MP2/6-31(d) level characterize the complexes as minima on the potential energy surface. In the case of some Mg<sup>2+</sup> complexes the acidity of phenolic proton is so high that it dissociates into phenoxide ion and proton. In such cases, the O–H bond of phenol was frozen during the optimization (see SI). The interaction energies obtained at each level were corrected for the basis set superposition error (BSSE) using the counterpoise method (CP) described by Boys and Bernardi.<sup>8</sup> The “Counterpoise=N” keyword is used to calculate the BSSE corrected total energy of a complex, where N holds for the total number of fragments composing the complex.<sup>9</sup> The geometry optimization with counterpoise correction reveals that the effect of BSSE correction on the geometry is negligible for the model system (Figure S2). The maximum difference in the hydrogen bonding distance when the optimization is carried out in the presence and absence of the counterpoise correction is about 0.06 Å and that of the cation  $\pi/\sigma$  distance is about 0.08 Å and hence all the geometries are reported without BSSE correction. Due to the necessity to impose constraints on selective Mg complexes, we did not include ZPE correction to the energy. However, inclusion of ZPE does not affect the trends, as can be seen in Table 22SI. Unless otherwise specified the BSSE corrected interaction energies of the various complexes at the MP2(FC)/AUG-cc-pVDZ level is taken for the discussion in the paper.

## Results and Discussion

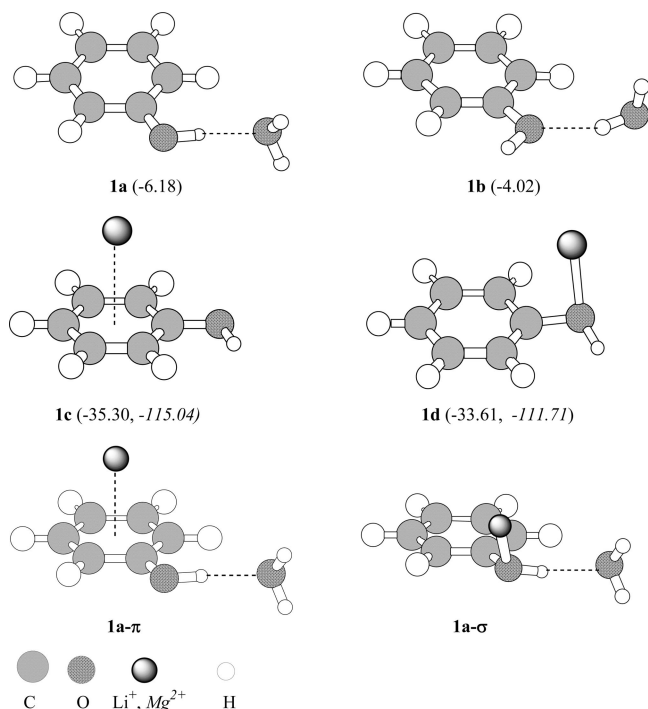
Phenol has been chosen here as the model system as it possesses both aromatic and hydroxyl groups, which can participate in cation– $\pi$  interaction with cations and in hydrogen

\* Corresponding author. E-mail: gnsastry@gmail.com. Fax: ++91-40-27160512. Phone: ++91-40-27160123, Ext.: 1619.

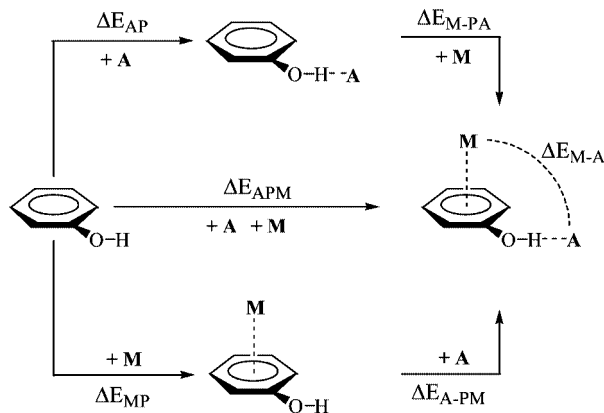
<sup>†</sup> Institute of Chemical Technology.

<sup>‡</sup> LMU München.

**SCHEME 1: MP2/AUG-cc-pVDZ (BSSE Corrected) Interaction Energies of the Phenol–Water and Phenol–Metal ( $\text{Li}^+$  in Plain and  $\text{Mg}^{2+}$  in Italics) Dimers**



**SCHEME 2: The Three Possible Pathways for the Formation of an Acceptor (A)–Phenol (P)–Metal (M) Ternary Complex from the Individual Monomers**



**M** :  $\text{Li}^+$  or  $\text{Mg}^{2+}$  ; **P** :  $\text{C}_6\text{H}_5\text{OH}$  ; **A** :  $\text{H}_2\text{O}$ ,  $\text{HCO}_2\text{H}$ ,  $\text{HCN}$ ,  $\text{CH}_3\text{OH}$ ,  $\text{HCONH}_2$ ,  $\text{NH}_3$

bonding with hydrogen bond acceptors and donors. The hydrogen bonded complex of phenol with water has been studied thoroughly in the past using experimental and theoretical methods.<sup>10</sup> Scheme 1 illustrates the two possibilities in which water and phenol can interact to form a hydrogen bonded complex. In agreement with earlier observations, dimer 1a (phenol acting as the donor) is found to be more stable by about 2 kcal/mol compared to 1b (where phenol acts as hydrogen bond acceptor).  $\text{Li}^+$  and  $\text{Mg}^{2+}$  have been selected as prototypical mono and divalent cations respectively. The calculations indicate that the metal ion interaction with the phenol group is slightly more stabilizing in a  $\pi$ -fashion (1c) rather than in a  $\sigma$ -fashion (1d). With the individual hydrogen bonding and cation– $\pi$  interaction energies in hand, we can now characterize the combined presence of both motives in quantitative terms.

The conformational space available to the ternary complex has been searched extensively to identify structures, in which hydrogen bonding and cation– $\pi$  interactions are present simultaneously (See Figure S1 of the Supporting Information, SI). The only two structures emerging from these searches are 1a– $\pi$  and 1a– $\sigma$  (Scheme 1), involving phenol as the hydrogen-bond donor and binding the metal cation either in a  $\pi$ - or a  $\sigma$ -fashion. Attempts to locate stationary points involving phenol as the hydrogen bond acceptor have not been successful.

The strengths of hydrogen bonding and cation– $\pi$  interactions in ternary complexes such as 1a can be discussed with respect to the three formation pathways shown in Scheme 2.

Direct assembly of the ternary complex from its constituents phenol (P), metal cation (M), and hydrogen bond acceptor (A) proceeds with reaction energy  $\Delta E_{\text{APM}}$ , which can be calculated according to (1) as the energy difference between the ternary complex and the energies of components P, M, and A (see Computational Details section for technical aspects of this type of calculation).

$$\Delta E_{\text{APM}} = E_{\text{APM}} - E_{\text{P}} - E_{\text{A}} - E_{\text{M}} \quad (1)$$

$$\Delta E_{\text{AP}} = E_{\text{AP}} - E_{\text{P}} - E_{\text{A}} \quad (2)$$

$$\Delta E_{\text{M-PA}} = E_{\text{APM}} - E_{\text{AP}} - E_{\text{M}} \quad (3)$$

$$\Delta E_{\text{M-A}} = E_{\text{M-A}} - E_{\text{A}} - E_{\text{M}} \quad (4)$$

$$\Delta E_{\text{c,M-PA}} = \Delta E_{\text{M-PA}} - \Delta E_{\text{M-A}} \quad (5)$$

$$\Delta E_{\text{MP}} = E_{\text{MP}} - E_{\text{P}} - E_{\text{M}} \quad (6)$$

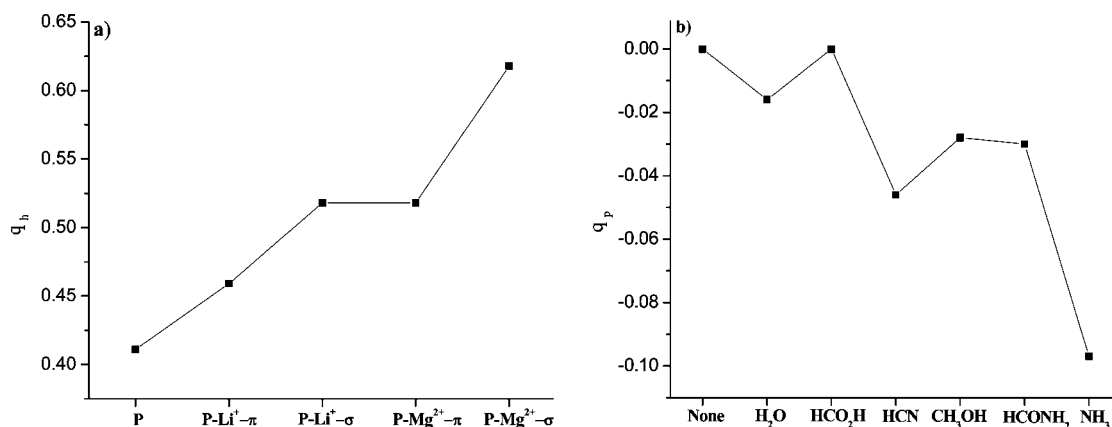
$$\Delta E_{\text{A-PM}} = E_{\text{APM}} - E_{\text{MP}} - E_{\text{A}} \quad (7)$$

$$\Delta E_{\text{c,A-PM}} = \Delta E_{\text{A-PM}} - \Delta E_{\text{M-A}} \quad (8)$$

Stepwise formation of the ternary complex is possible along two different routes. The first of these involves initial formation of the hydrogen bonded complex with reaction energy  $\Delta E_{\text{AP}}$  and subsequent addition of the metal cation to form the ternary complex. However, the reaction energy for this latter step  $\Delta E_{\text{M-PA}}$  reflects not only the interaction of metal cation M with the phenol  $\pi$ -system but also the ion–dipole interaction between cation M and hydrogen-bond acceptor A. Following the analysis by Geerlings et al.<sup>4b</sup> this interaction can be calculated separately and subtracted from  $\Delta E_{\text{M-PA}}$  to yield the interaction energy  $\Delta E_{\text{c,M-PA}}$  between cation M and the phenol  $\pi$ -system ((3)–(5)). A second stepwise pathway can be constructed in a completely analogous way by initial addition of the metal cation to the phenol  $\pi$ -system and subsequent formation of the hydrogen bond, yielding the corresponding interaction energies described in (6)–(8). To what extent the hydrogen bonding and cation– $\pi$  interaction act in concert in these ternary systems can be deduced quantitatively by comparing the overall reaction energy  $\Delta E_{\text{APM}}$  with the three individual interaction energy terms as in (9):

$$E_{\text{coop}} = \Delta E_{\text{APM}} - \Delta E_{\text{AP}} - \Delta E_{\text{MP}} - \Delta E_{\text{M-A}} \quad (9)$$

The “cooperativity energy”  $E_{\text{coop}}$  amounts to  $-2.77$  kcal/mol for the example of  $\text{M} = \text{Li}^+$  and  $\text{A} = \text{H}_2\text{O}$ . The degree of cooperativity may alternatively be quantified by comparing hydrogen bonding energies in the absence of  $\text{Li}^+$  ( $\Delta E_{\text{AP}} = -6.18$  kcal/mol) and in the presence of this cation ( $\Delta E_{\text{c,A-PM}} = -8.95$  kcal/mol). The complexation of phenol with  $\text{Li}^+$  or  $\text{Mg}^{2+}$  in either  $\pi$ - or  $\sigma$ -fashion strengthens the phenol– $\text{H}_2\text{O}$  hydrogen bonding interaction energy by about 2 and 7 kcal/mol in the  $\text{Li}^+$  and  $\text{Mg}^{2+}$  complexes respectively. Essentially the same trends are found when a range of additional acceptors ( $\text{HCO}_2\text{H}$ ,  $\text{HCN}$ ,  $\text{CH}_3\text{OH}$ ,  $\text{HCONH}_2$  and  $\text{NH}_3$ ) are also considered (Table 1). In all these cases an increase in the hydrogen bonding



**Figure 1.** Variation in the charge (CHELPG) of (a) the phenolic hydrogen ( $q_h$ ) when complexed with the metal ions and (b) phenol ( $q_p$ ) when complexed with the acceptors.

**TABLE 1: Various Interaction Energies ( $\Delta E$ , in kcal/mol) That Contribute to the Cooperativity ( $E_{\text{coop}}$ ) in the Ternary Complex of Phenol (P), Acceptor (A) and Metal (M) at the MP2/AUG-cc-pVDZ Level**

		H <sub>2</sub> O	HCOOH	HCN	CH <sub>3</sub> OH	HCONH <sub>2</sub>	NH <sub>3</sub>
M-absent	$\Delta E_{\text{AP}}$	-6.18	-5.91	-5.35	-7.33	-8.29	-8.21
Li <sup>+</sup> - $\pi$ ( $\Delta E_{\text{MP}}$ -35.30)	$\Delta E_{\text{APM}}$	-49.16	-49.39	-49.28	-51.14	-56.38	-52.49
	$\Delta E_{\text{M-A}}$	-4.91	-5.48	-5.95	-5.31	-9.20	-4.79
	$\Delta E_{\text{c,A-PM}}$	-8.95	-8.61	-8.03	-10.54	-11.88	-12.41
	$\Delta E_{\text{c,M-PA}}$	-38.07	-38.00	-37.98	-38.50	-38.89	-39.49
	$E_{\text{coop}}$	-2.77	-2.70	-2.68	-3.20	-3.59	-4.19
Mg <sup>2+</sup> - $\pi$ ( $\Delta E_{\text{MP}}$ -115.04)	$\Delta E_{\text{APM}}$	-138.96	-141.59	-140.57	-143.18	-153.88	-144.84
	$\Delta E_{\text{M-A}}$	-10.22	-12.83	-12.66	-11.45	-26.68	-14.28
	$\Delta E_{\text{c,A-PM}}$	-13.70	-13.72	-12.87	-16.69	-12.17	-15.53
	$\Delta E_{\text{c,M-PA}}$	-122.56	-122.85	-122.56	-124.39	-118.91	-122.35
	$E_{\text{coop}}$	-7.52	-7.81	-7.52	-9.36	-3.87	-7.31
Li <sup>+</sup> - $\sigma$ ( $\Delta E_{\text{MP}}$ -33.61)	$\Delta E_{\text{APM}}$	-48.76	-47.84	-49.67	-51.18	-56.75	-54.38
	$\Delta E_{\text{M-A}}$	-6.81	-7.39	-8.80	-7.37	-12.78	-8.91
	$\Delta E_{\text{c,A-PM}}$	-8.34	-6.85	-7.26	-10.20	-10.36	-11.87
	$\Delta E_{\text{c,M-PA}}$	-35.77	-34.55	-35.52	-36.48	-35.67	-37.26
	$E_{\text{coop}}$	-2.16	-0.93	-1.91	-2.87	-2.07	-3.65
Mg <sup>2+</sup> - $\sigma$ ( $\Delta E_{\text{MP}}$ -111.71)	$\Delta E_{\text{APM}}$	-139.56	-139.35	-142.54	-144.93	-155.66	-149.41
	$\Delta E_{\text{M-A}}$	-14.83	-17.66	-19.81	-18.06	-33.14	-24.32
	$\Delta E_{\text{c,A-PM}}$	-13.02	-9.98	-11.02	-15.16	-10.81	-13.38
	$\Delta E_{\text{c,M-PA}}$	-118.55	-115.78	-117.38	-119.53	-114.23	-116.88
	$E_{\text{coop}}$	-6.84	-4.07	-5.67	-7.83	-2.52	-5.17

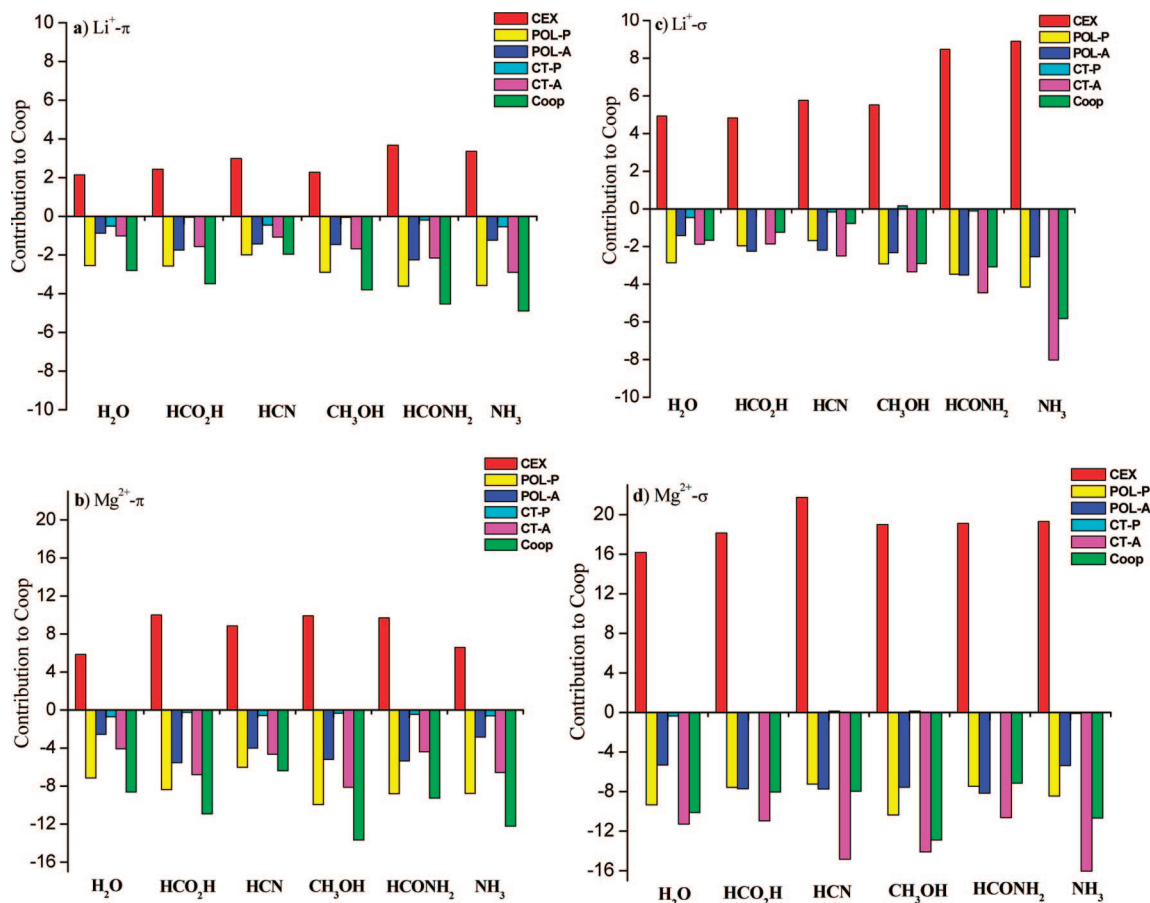
interactions with phenol can be observed upon complexation with a metal ion. Although the hydrogen bond interaction energy increase is almost 3 kcal/mol with Li<sup>+</sup>, it is about 4–9 kcal/mol for Mg<sup>2+</sup>.

The effect of hydrogen bonding interaction on the cation- $\pi$  and cation- $\sigma$  interaction energies  $\Delta E_{\text{MP}}$ , can be assessed by calculating the difference between  $\Delta E_{\text{MP}}$  and  $\Delta E_{\text{c,M-PA}}$ . The interaction energy of Li<sup>+</sup> with phenol is slightly larger in a  $\pi$ -fashion (-35.30 kcal/mol) than in  $\sigma$ -fashion (-33.61 kcal/mol). Similarly, for the Mg<sup>2+</sup> ion the  $\pi$  and  $\sigma$  complexation energies are -115.04 and -111.71 kcal/mol, respectively. The cation- $\pi$  interaction energy with water as the acceptor and Li<sup>+</sup> as the metal, amounts to -35.30 vs -38.07 kcal/mol, in the absence and presence of the hydrogen bonding, respectively. The enhancement in the cation- $\pi$  interaction energy amounts to -2.77 kcal/mol. Thus, coordination of the phenol hydroxy group to H<sub>2</sub>O leads to an increase in the metal cation binding energy. The above analysis has been performed for a series of  $\sigma$ - and  $\pi$ -complexes of Li<sup>+</sup> and Mg<sup>2+</sup> with phenol complexed to a variety of hydrogen bond acceptors. The results for these systems have been summarized in Table 1. Thus, the cation-aromatic

and hydrogen bonding interactions occur cooperatively in all these systems.

A simple explanation to account for the increase in the hydrogen bonding strength may be the variation of the charge of the phenolic hydrogen ( $q_h$ ) (Figure 1a), which is related to the acidity, and therefore the hydrogen bond donating ability of phenol upon complexation with the metal ion. On the other hand, in the hydrogen bonded complexes, charge transfer from the acceptor to the phenol makes the phenol more negatively charged. Figure 1b quantifies the increase of the negative charge on the phenol moiety ( $q_p$ ) in the hydrogen bonded complex. Thus, the charge analysis reveals that the metal ion complexation is expected to be stronger when phenol is involved as a hydrogen bond donor which essentially delineates the origin of cooperativity.<sup>11</sup>

The above discussion reveals that a positive cooperativity is established in ternary phenol-metal-acceptor complexes. To analyze the factors that contribute to the cooperativity, a reduced variational space (RVS) analysis<sup>12</sup> as implemented in the GAMESS program package<sup>13</sup> was carried out at the HF/6-31G(d) level on MP2/AUG-cc-pVDZ geometries. Thereby the



**Figure 2.** Contribution of CEX, POL, CT to the cooperativity as obtained by the RVS analysis of (a)  $\text{Li}^+-\pi$ , (b)  $\text{Mg}^{2+}-\pi$ , (c)  $\text{Li}^+-\sigma$ , and (d)  $\text{Mg}^{2+}-\sigma$  phenol (P)–metal (M)–acceptor (A) complexes. CEX corresponds to the (Coulomb and exchange energy); POL-P and POL-A correspond to polarization energy of phenol and acceptor; CT-P and CT-A correspond to charge transfer energy of phenol and acceptor;  $E_{\text{coop}}$  corresponds to the cooperativity. All values are in kcal/mol.

total interaction energy can be divided into the individual contributions from the Coulomb and exchange energy, denoted as CEX, the polarization energy (POL) of the phenol (P) and the acceptor (A) and the charge transfer energy (CT). (See SI for more details.)

Figure 2 depicts the net increase or decrease of the individual components and that of the interaction energy, when the three pairwise contributions are summed up in the ternary complex. The net difference is equivalent to the cooperativity ( $E_{\text{coop}}$ ). It is quite interesting to note that the cooperativity numbers obtained here are similar to those obtained at MP2(FC)/AUG-cc-pVDZ level. The figure indicates a repulsive contribution of electrostatic interaction (which is expressed by CEX), and therefore the electrostatic component works in an anticooperative fashion during the formation of the ternary complex. However, the anticooperativity is smaller in magnitude compared to the polarization component of phenol which is essentially responsible for the net positive cooperativity. The other component which contributes significantly to the  $E_{\text{coop}}$  is the charge transfer term of the acceptor.

## Conclusions

In summary, the present communication provides solid computational evidence that cation- $\pi$  and hydrogen bonding interactions work in concert in the model systems studied. Although the direct interaction between the metal ion and acceptor contributes also to the cooperative interaction, the enhancement of both the cation- $\pi$  and the hydrogen bonding

energy, even in the absence of such stabilization, is significant. These observations are expected to provide a basis for understanding the intricacy of the complex ways through which nonbonded interactions influence each other.

**Acknowledgment.** D.V. thanks U.G.C., New Delhi, for financial assistance. Financial support from Department of Science and technology, New Delhi, in the form of a Swarnajayanti fellowship to G.N.S. is acknowledged. DAE-BRNS is also thanked for financial assistance. The authors wish to dedicate this paper to Professor Thomas Bally on the occasion of his 60th birthday.

**Supporting Information Available:** MP2(FC)/AUG-cc-pVDZ optimized coordinates of the various complexes considered in the study. The interaction energy values at various levels of theory. The results of RVS analysis are provided. Atomic charges. This material is available free of charge via the Internet at <http://pubs.acs.org>.

## References and Notes

- (1) (a) Meyer, E. A.; Castellano, R. K.; Diederich, F. *Angew. Chem., Int. Ed.* **2003**, *42*, 1210. (b) Dougherty, D. A. *Science* **1996**, *271*, 163. (c) Kim, K. S.; Tarakeshwar, P.; Lee, J. Y. *Chem. Rev.* **2000**, *100*, 4145. (d) Lee, E. C.; Kim, D.; Jurečka, P.; Tarakeshwar, P.; Hobza, P.; Kim, K. S. *J. Phys. Chem. A* **2007**, *111*, 3446. (e) Reddy, A. S.; Sastry, G. N. *J. Phys. Chem. A* **2005**, *109*, 8893. (f) Ěerný, J.; Hobza, P. *Phys. Chem. Chem. Phys.* **2007**, *9*, 5291.



- (2) (a) Rappé, A. K.; Bernstein, E. R. *J. Phys. Chem. A* **2000**, *104*, 6117. (b) Hesselmann, A.; Jansen, G.; Schütz, M. *J. Am. Chem. Soc.* **2006**, *128*, 11730. (c) Piacenza, M.; Grimme, S. *Chem. Phys. Chem.* **2005**, *6*, 1554.
- (3) (a) Ludwig, R. *Angew. Chem., Int. Ed.* **2001**, *40*, 1808. (b) Parthasarathi, R.; Subramanian, V.; Sathyamurthy, N. *J. Phys. Chem. A* **2005**, *109*, 843.
- (4) (a) Mignon, P.; Loverix, S.; Steyaert, J.; Geerlings, P. *Nucleic Acids Res.* **2005**, *33*, 1779. (b) Vanommeslaeghe, K.; Mignon, P.; Loverix, S.; Tourwé, D.; Geerlings, P. *J. Chem. Theory Comp.* **2006**, *2*, 1444. (c) Leist, R.; Frey, J. A.; Ottiger, P.; Frey, H.-M.; Leutwyler, S.; Bachorz, R. A.; Kloppe, W. *Angew. Chem., Int. Ed.* **2007**, *46*, 7449.
- (5) (a) Reddy, A. S.; Vijay, D.; Sastry, G. M.; Sastry, G. N. *J. Phys. Chem. B* **2006**, *110*, 2479. (b) Reddy, A. S.; Vijay, D.; Sastry, G. M.; Sastry, G. N. *J. Phys. Chem. B* **2006**, *110*, 10206.
- (6) Escudero, D.; Frontera, A.; Quiñero, D.; Deyà, P. M. *Chem. Phys. Lett.* **2008**, *456*, 257.
- (7) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Montgomery, Jr., J. A.; Vreven, T.; Kudin, K. N.; Burant, J. C.; Millam, J. M.; Iyengar, S. S.; Tomasi, J.; Barone, V.; Mennucci, B.; Cossi, M.; Scalmani, G.; Rega, N.; Petersson, G. A.; Nakatsuji, H.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Klene, M.; Li, X.; Knox, J. E.; Hratchian, H. P.; Cross, J. B.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Ayala, P. Y.; Morokuma, K.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Zakrzewski, V. G.; Dapprich, S.; Daniels, A. D.; Strain, M. C.; Farkas, O.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Ortiz, J. V.; Cui, Q.; Baboul, A. G.; Clifford, S.; Cioslowski, J.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Gonzalez, C.; Pople, J. A. *Gaussian 03*, revision A.1; Gaussian, Inc.: Pittsburgh, PA, 2003.
- (8) Boys, S. F.; Bernardi, F. *Mol. Phys.* **1970**, *19*, 553.
- (9) Salvador, P.; Duran, M. *J. Phys. Chem. A* **2002**, *106*, 6889.
- (10) (a) Feller, D.; Feyereisen, M. W. *J. Comput. Chem.* **1993**, *14*, 1027. (b) Tsui, H. H. Y.; Mourik, T. v. *Chem. Phys. Lett.* **2001**, *350*, 565. (c) Dimitrova, Y. *J. Mol. Struct. (THEOCHEM)* **1998**, *455*, 9. (d) Benoit, D. M.; Clary, D. C. *J. Phys. Chem. A* **2000**, *104*, 5590.
- (11) Although the CHELPG charges do not show any change in phenol after hydrogen bonding with HCOOH, the natural population analysis (NPA) shows that the phenol moiety is slightly negatively charged even here (See SI).
- (12) Stevens, W. J.; Fink, W. H. *Chem. Phys. Lett.* **1987**, *139*, 15.
- (13) Schmidt, M. W.; Baldridge, K. K.; Boatz, J. A.; Elbert, S. T.; Gordon, M. S.; Jensen, J. J.; Koseki, S.; Matsunaga, N.; Nguyen, K. A.; Su, S.; Windus, T. L.; Dupuis, M.; Montgomery, J. A. *J. Comput. Chem.* **1993**, *14*, 1347.

JP804219E