

# Non-electrostatic components of short and strong hydrogen bonds induced by compression inside fullerenes

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## ARTICLE INFO

### Article history:

Received 18 November 2009

In final form 5 January 2010

Available online 11 January 2010

## ABSTRACT

Hydrogen bond shortening and strengthening induced by confinement within fullerenes for a series of hydrogen bonded bivalides were studied. Significant increase in the electron localizability at the hydrogen bond region occurs as the confinement takes place. This result suggests that in confined systems there are additional effects that are beyond the 'electrostatic only' explanation offered for the existence of short and strong hydrogen bonds. We propose that these additional effects are factors on which the enhanced bonding strength energetic stabilization and basicity also depend.

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## 1. Introduction

Short and strong hydrogen bonds (sshb) are found in several chemical [1,2] and biochemical [3–7] systems. sshb show structural and energetic characteristics that markedly differ from normal or weak hydrogen bonds. While the former present donor-acceptor distance within the range (2.4–2.6) Å and formation enthalpies within the range (12–24) kcal/mol, the latter present average distances within the range (2.7–3.0) Å and formation enthalpies within the range (2.5–12) kcal/mol [5]. In chemical systems, such as proton sponges, a release of the internal static strain induced by sshb formation have been argued to be a major factor to explain the enhanced basicity of Alder's 1,8-bis(dimethyl-amino)-naphthalene [1], and in proton sponges derivatives [2]. Also, in biological systems sshb have been proposed as factor that drives enzymatic catalysis [3–7]. For instance, in bovine protease  $\alpha$ -chymotrypsin, a sshb formation by dynamic steric strain induced by substrate docking have been postulated to explain the noteworthy enhancement in basicity (i.e. a  $pK_a$  variation from 7.4 to 12.0 at Hystidine 57 catalytic residue [3,4]) and also in nucleophilicity (i.e. increases in reaction rates [3,4]) In this system the formation of a sshb may provide a stabilization energy of 12–20 kcal/mol at the transition state [7], thereby explaining in part the high catalytic effect shown by this system. We have recently proposed an electronic mechanism that describes the observed catalysis in bovine protease  $\alpha$ -chymotrypsin including sshb formation. In that model, the catalytic effect in the presence of a confining environment was explained on the basis of a pair site reactivity model framed on the

second order static density response function including fluctuation in regional softness [8]. This result prompted us to examine whether some non-electrostatic contributions to sshb formation and its effect on enzymatic catalysis could be operative. This is mainly due to the fact that normal hydrogen bonding (i.e. in the absence of confinement) has been considered for decades as a specific molecular interaction which is mainly electrostatic in nature [9,10]. In this Letter we show that these non-electrostatic factors can contribute to the enhanced strength and the energy stabilization as well as enhanced basicity observed in systems. The proof is based on the theoretical characterization of structural and electron localization properties of guest hydrogen bonded (H-bonded) systems encapsulated inside fullerenes, as a model for enhanced basicity induced by steric strain involving sshb formation.

## 2. Model and computational details

The guest systems consist in a series of well characterized H-bonded bivalides [11] complexes  $[FHX]^-$ , with X = F, Cl, Br and I, taking hydrogen bonding (HB) in the gas phase as the reference state. The confining matrix are capped tubular armchair [5,5] fullerenes of stoichiometry  $C_n$  with  $n = 70, 80, 90, 100$  including  $C_{60}$ . First of all, the empty fullerenes were optimized at the semiempirical AM1 level and the gas phase geometry of the bivalides was optimized at the B3LYP/dgdzvp [12] level of theory. Secondly, the host-guest interaction was evaluated using a two layer ONIOM methodology [13] using the universal force field, UFF to model the fullerenes as the low level layer, and B3LYP/dgdzvp calculations for the high level layer for the bivalide series. In these latter calculations fullerene coordinates obtained from AM1 calculations were kept fixed and the guests were allowed to relax. The geometries of the bivalides in gas phase and inside fullerenes were used to perform further analysis.

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The strength of H-bonding was determined using an empirical HB strength scale proposed by Alikhani et al. [14] It is based on the electron localization function ELF,  $\eta(r)$ . This scale is derived from the information of electronic localization contained in the profile of  $\eta(r)$ , along the principal axis of a H-bonded complexes, defined by a proton donor AH and a proton acceptor B. The core valence bifurcation index, which is our number of HB strength, is defined as

$$\vartheta(\text{AHB}) = \eta_{cv}(\text{AH}) - \eta_{vv}(\text{AHB}). \quad (1)$$

This index can be used to discriminate between normal, medium and strong HB. Here,  $\eta_{cv}(\text{AH})$  is the value of ELF at saddle connection of core C(A) and monoprotonated V(A, H) basins of the proton donor, and  $\eta_{vv}(\text{AHB})$  is the value at the saddle connection between the valence V(A, H) and V(B) basins [14]. This index is positive in the case of weak H-bonded complexes and increasingly negative for stronger ones. In the present study is difficult to make a direct estimation of the HB strength because the confining matrices are not fully optimized, and therefore polarization effects due to the relaxation of fullerenes are not included in the analysis. Thus, validation of  $\vartheta(\text{AHB})$  as predictor of HB strength for an extended series of [YHX], with X, Y = F<sup>-</sup>, Cl<sup>-</sup>, Br<sup>-</sup> and I<sup>-</sup> including HB complexes with NH<sub>3</sub>, H<sub>2</sub>O and N<sub>2</sub> were performed. They are included in Table 1.

Finally, in order to reinforce the ELF results for confined bivalides, a valence bond like analysis of the structures that contribute to the resonance expansion was performed using a natural resonance theory (NRT) analysis [15]. The resonance structures and their respective resonance weights  $w_x$  were determined at the different conditions of confinement. All the calculations were performed using the GAUSSIAN03 suite of programs [16]. ELF profiles were obtained using the TOPMOD [17,18] suite of programs. The NRT analysis was performed using NBo 5.G stand-alone algorithm [19].

### 3. Results and discussion

The validation of  $\vartheta(\text{AHB})$  as an index of HB strength is shown in Table 1. Good correlation coefficients were found for the series considered in this study and the results are consistent with previ-

**Table 1**  
Linear Correlation analysis of the calculated HB strength versus  $\vartheta(\text{AHB})$  values for the series [YHX], with X = F<sup>-</sup>, Cl<sup>-</sup>, Br<sup>-</sup> and I<sup>-</sup> including HB complexes with NH<sub>3</sub>, H<sub>2</sub>O and N<sub>2</sub>. Calculated HB strength was performed considering basis set superposition error (bsse).

	Energy (bsse) (kcal/mol)	$\vartheta(\text{AHB})$	Regression coefficient	
<i>[FH...X]</i>				
F <sup>-</sup>	53	-0.556	$r = -0.9617$	
Cl <sup>-</sup>	26	-0.155		
Br <sup>-</sup>	22	-0.127		
I <sup>-</sup>	18	-0.078		
NH <sub>3</sub>	14	-0.166		
H <sub>2</sub> O	10	-0.045		
N <sub>2</sub>	2	0.034		
<i>[ClH...X]</i>				
Cl <sup>-</sup>	27	-0.637		$r = -0.9770$
Br <sup>-</sup>	22	-0.388		
I <sup>-</sup>	16	-0.234		
NH <sub>3</sub>	10	-0.192		
H <sub>2</sub> O	6	-0.024		
N <sub>2</sub>	1	0.057		
<i>[BrH...X]</i>				
Br <sup>-</sup>	24	-0.546	$r = -0.9820$	
I <sup>-</sup>	17	-0.311		
NH <sub>3</sub>	9	-0.201		
H <sub>2</sub> O	5	0.055		
N <sub>2</sub>	1	0.141		

ous reports [20]. In order to evaluate the changes in the strength of HB's inside confining fullerenes, we performed an exploration of the electron localization properties along the main axis of symmetry of the bivalides using the HB strength scale proposed by Alikhani et al. [14]. We are of course interested in looking at a possible electron localizability changes around the HB region which would contribute a covalent component responsible for the unexpected strength observed in sshb systems. Table 2 summarizes the results obtained for the  $\vartheta(\text{FHX}^-)$  values along the halogen series within all fullerenes used. Fig. 1a–d shows the ELF profiles for the gas phase and the corresponding profiles within C80 for the whole series of bivalides considered in the present work. In the gas phase the numerical values of the  $\vartheta(\text{FHX}^-)$  index for the complexes [FH...F]<sup>-</sup>, [FH...Cl]<sup>-</sup>, [FH...Br]<sup>-</sup> and [FH...I]<sup>-</sup> are -0.556; -0.155; -0.127 and -0.078, respectively. The corresponding HB strength experimentally determined are 39, 22, 17, 15 kcal/mol [5], respectively. Linear correlation coefficient for this two set of data shows a value  $r = -0.98878$ , thereby showing a quantitative concordance between the topological scale of Alikhani et al. [14], and the experimentally based hydrogen bond strength data [5]. For the C100 and to C90 matrices only marginal changes in electron localizability with respect to gas phase results were observed for the bivalides involving X = Cl<sup>-</sup>, Br<sup>-</sup> and I<sup>-</sup>. As the condition of confinement is enhanced, an increase in the electron localizability is observed at the saddle connection between the valence V(F, H) and V(X<sup>-</sup>) basins with no significant changes in other saddle point connectors as can be observed in Fig. 1b–d. This trends fall down in the case C60, probably due a loss of linearity in the HB structures (see Table 3). It is well known that bifurcated hydrogen bonds are weaker than the corresponding linear ones [21]. As suggested by a reviewer, the bifurcation inside C60 and C70 of other [XHY]<sup>-</sup> systems with X, Y = Cl, Br and I, could have a direct relationship with the atomic/ionic radii of the halogen atoms. Table 4 shows the results for the bond angle  $\alpha$  (°) in C60 and C70. It may be seen that for C70 there is an increase of the bifurcation angle as the atomic and ionic radii is increased, thereby verifying this argument. For the case of FHF<sup>-</sup> bivalide a slight change in the  $\vartheta(\text{FHX}^-)$  index is observed only for C60. This result is probably due to the fact that this bivalide has already been described as sshb complex and therefore it does not require an extreme condition to further shortening and strengthening. Note further that according to Alikhani et al.'s model [14], the  $\vartheta(\text{AHB})$  index consistently becomes increasingly negative. Therefore the changes of the  $\vartheta(\text{AHB})$  ELF index suggest that an increase in the electron localizability at the HB region may be responsible for the enhanced strength, energy stabilization and basicity observed in systems that forms sshb structures. Therefore our results strongly suggest that some non-electrostatic effects may contribute to the formation of these anomalous HB's under steric strain or confinement.

In order to quantitatively determine the weights of the contributing resonant structures as compression is enhanced, further NRT analysis was performed. The analysis in gas phase revealed the appearance of three resonant structures for the complete bivalide series. The schematic structures are depicted in Scheme 1. Table 5 shows the resonance weights  $w_x$  obtained after performing the

**Table 2**  
 $\vartheta(\text{FHX}^-)$  values for the bivalide series in gas phase and confined into C100 to C60 fullerenes.

Environment	[FH...F] <sup>-</sup>	[FH...Cl] <sup>-</sup>	[FH...Br] <sup>-</sup>	[FH...I] <sup>-</sup>
Gas phase	-0.556	-0.155	-0.127	-0.078
C100	-0.558	-0.152	-0.138	-0.074
C90	-0.558	-0.157	-0.137	-0.077
C80	-0.556	-0.206	-0.213	-0.227
C70	-0.558	-0.371	-0.390	-0.253
C60	-0.564	-0.367	-0.268	-0.237

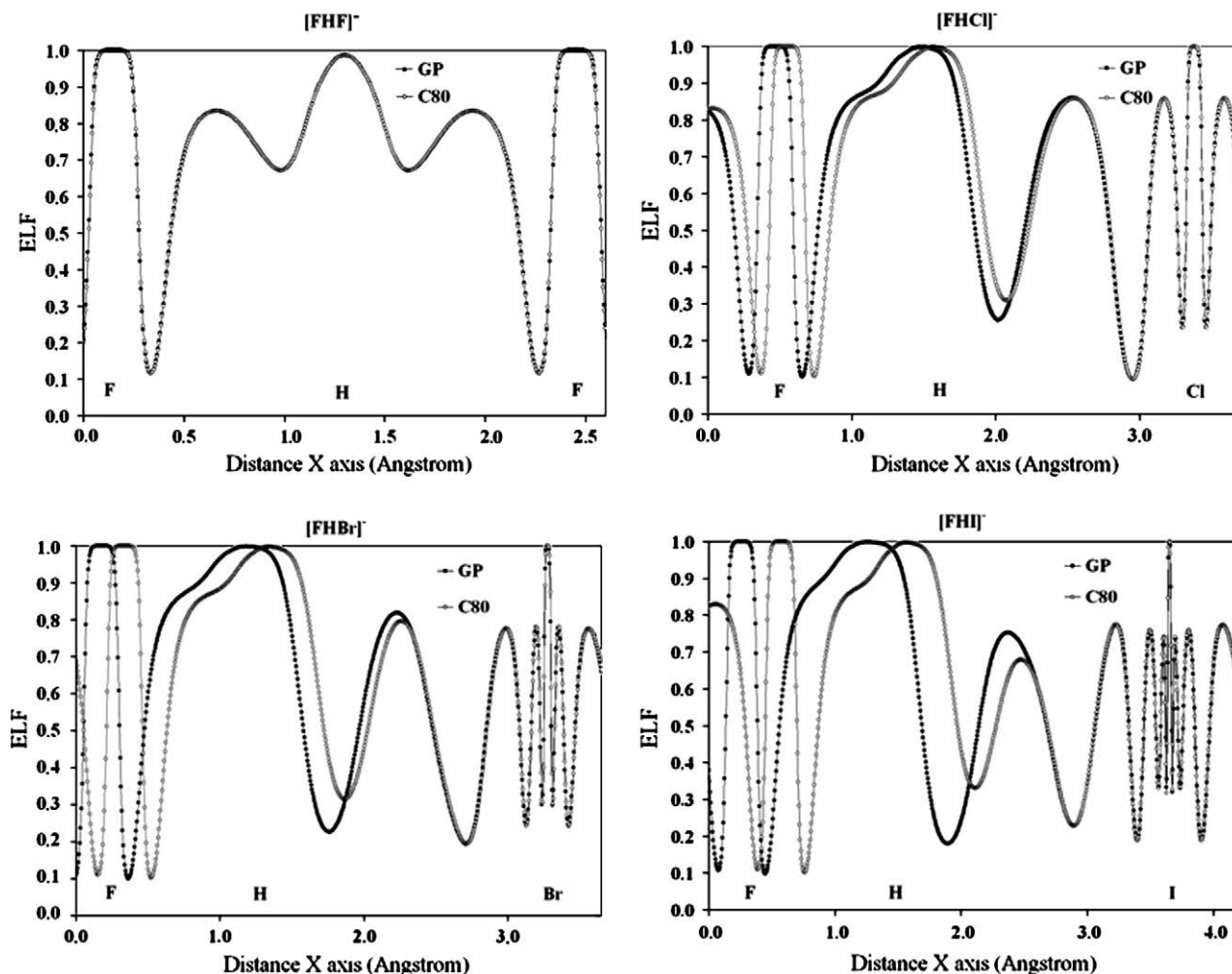


Fig. 1. ELF profiles for  $\text{FHX}^-$  complexes in the gas phase (GP, filled circles) and inside  $\text{C}_{80}$  ( $\text{C}_{80}$ , open circles) for  $\text{FHF}^-$ ,  $\text{FHCl}^-$ ,  $\text{FHBr}^-$  and  $\text{FHI}^-$  bihalides.

Table 3

Structural parameters the bihalides series in the gas phase and embedded in different environments.

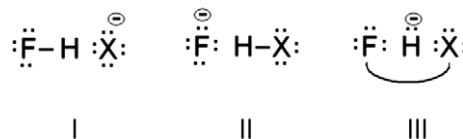
Environment	$[\text{FH}\cdots\text{F}]^-$	$[\text{FH}\cdots\text{Cl}]^-$	$[\text{FH}\cdots\text{Br}]^-$	$[\text{FH}\cdots\text{I}]^-$
<i>Gas phase</i>				
$R_{\text{F-X}}$ (Å)	2.30	2.91	3.10	3.39
$R_{\text{F-H}}$ (Å)	1.15	0.99	0.98	0.97
$\alpha$ (°)	180.0	180.0	180.0	180.0
<i>C100</i>				
$R_{\text{F-X}}$ (Å)	2.30	2.92	3.10	3.40
$R_{\text{F-H}}$ (Å)	1.15	0.99	0.98	0.97
$\alpha$ (°)	180.0	180.0	180.0	180.0
<i>C90</i>				
$R_{\text{F-X}}$ (Å)	2.31	2.91	3.08	3.38
$R_{\text{F-H}}$ (Å)	1.15	0.99	0.98	0.97
$\alpha$ (°)	180.0	180.0	180.00	180.0
<i>C80</i>				
$R_{\text{F-X}}$ (Å)	2.30	2.83	2.94	3.08
$R_{\text{F-H}}$ (Å)	1.15	0.99	0.98	0.97
$\alpha$ (°)	180.0	180.0	180.0	180.0
<i>C70</i>				
$R_{\text{F-X}}$ (Å)	2.28	2.61	2.67	2.63
$R_{\text{F-H}}$ (Å)	1.14	0.99	0.97	0.96
$\alpha$ (°)	180.0	179.1	179.6	128.6
<i>C60</i>				
$R_{\text{F-X}}$ (Å)	2.13	2.11	2.08	2.62
$R_{\text{F-H}}$ (Å)	1.06	0.97	0.97	0.96
$\alpha$ (°)	179.6	115.0	101.9	126.8

NRT analysis as function of confinement. In the gas phase and in the moderate confinement regimes, from  $\text{C}_{100}$  to  $\text{C}_{80}$ , there is a predominant population for structure I (see Scheme 1), with  $w_I$  values around 92% for the series involving Cl, Br, and I. When the conditions of confinement are enhanced from  $\text{C}_{70}$  to  $\text{C}_{60}$  there is an increase in the contribution of the resonant form II that reach  $w_{II}$

Table 4

Bond angle  $\alpha$  (°) showing the lost of linearity inside of  $\text{C}_{60}$  and  $\text{C}_{70}$  for the bihalide serie  $[\text{XHY}]^-$  for X, Y = Br, I, Cl.

$[\text{XHY}]^-$	$\text{C}_{60}$	$\text{C}_{70}$
$[\text{ClHCl}]^-$	63.5	137.3
$[\text{ClHBr}]^-$	77.9	120.8
$[\text{ClHI}]^-$	64.9	104.1
$[\text{BrHBr}]^-$	67.2	111.9
$[\text{BrHI}]^-$	64.9	101.1
$[\text{IHI}]^-$	65.1	83.6



Scheme 1. Contributing valence bond structures for  $\text{FHX}^-$  complexes.

**Table 5**  
Resonance weights,  $w_x$ , as function of the environment.

Weight (%)	GP	C <sub>100</sub>	C <sub>90</sub>	C <sub>80</sub>	C <sub>70</sub>	C <sub>60</sub>
<b>[FH...I]<sup>-</sup></b>						
$w_I$	95.5	95.6	95.6	91.9	63.9	63.9
$w_{II}$	3.4	3.2	3.3	8.1	35.8	35.5
$w_{III}$	1.1	1.2	1.2	0.0	0.3	0.6
<b>[FH...Cl]<sup>-</sup></b>						
$w_I$	94.4	94.4	94.2	92.5	59.6	54.6
$w_{II}$	5.4	5.4	5.5	7.4	40.1	39.7
$w_{III}$	0.2	0.1	0.4	0.0	0.2	5.7
<b>[FH...Br]<sup>-</sup></b>						
$w_I$	93.5	93.5	93.4	92.5	60.4	57.3
$w_{II}$	6.4	6.0	6.4	7.4	39.1	40.7
$w_{III}$	0.1	0.5	0.2	0.1	0.5	2.0
<b>[FH...F]<sup>-</sup></b>						
$w_I$	49.3	49.4	49.3	49.3	49.3	49.3
$w_{II}$	49.2	49.1	49.2	49.2	49.3	49.2
$w_{III}$	1.5	1.5	1.5	1.5	1.5	1.5

values between 35% and 40%. For the case of [FHF]<sup>-</sup> complex the NRT analysis shows an expected average of 50% for forms **I** and **II** for all the confinement regimes. Structure **III** oscillates around 1% representing a negligible contribution in the NRT expansion. Structure **III** includes a hydride-like structure. The quantum chemical calculations with one determinant wave functions fail in describing such a highly space correlated state. Therefore it is not surprising to find a low weight for it. The results obtained are consistent with an enhanced covalency at the HB side of the bihalides, represented by the predominance of structure **II**. These results are also consistent with the previous ELF analysis in the sense that during the formation of sshb structures under extreme confinement conditions some non-electrostatic components may be present.

#### 4. Concluding remarks

Short and strong H-bonds have been characterized using a theoretical methodology that emulates the effect of steric compression by encapsulation of them inside fullerenes of axial

symmetry. The electronic properties of these bonds have been analyzed using an empirical strength scale based on electron localizability and complemented with a NRT analysis. This result adds novel information about the controversial origin of sshb complexes: it may be that hydrogen bonding in extremely confined systems encompasses physical effects that are beyond the 'electrostatic only' explanation offered in the literature [9,10] and that some covalent components may arise as a result of the additional electron localization at the HB region induced by steric strain or confinement.

#### Acknowledgement

Fondecyt Grant's 1070715. G. Miño thanks to Universidad Andres Bello and to Comisión Nacional de Investigación Científica y Tecnológica (CONICYT) for doctoral fellowships awarded to him.

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