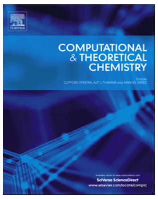
Computational and Theoretical Chemistry 1026 (2013) 1–6

Contents lists available at ScienceDirect

Computational and Theoretical Chemistry

journal homepage: www.elsevier.com/locate/comptc



Weak energetic effects between halogen and hydrogen bonds in crystal structures of halo-perfluorobenzenes (X-PFCs) and pyrazine molecules: A computational study

Yanhua Wang [a], Haiying Li [b], Yingtao Liu [c], Weihong Wu [b], Yunxiang Lu [b,*]

[a] College of Biology and Environment Engineering, Zhejiang Shuren University, Hangzhou 310015, China
[b] Key Laboratory for Advanced Materials and Department of Chemistry, East China University of Science and Technology, Shanghai 200237, China
[c] Drug Discovery and Design Center, Shanghai Institute of Materia Medica, Chinese Academy of Sciences, Shanghai 201203, China

ARTICLE INFO

Article history:
Received 28 August 2013
Received in revised form 7 October 2013
Accepted 7 October 2013
Available online 17 October 2013

Keywords:
Halogen bonds
Hydrogen bonds
X-PFCs
Energetic effects
M05-2x

ABSTRACT

The interplay between halogen and hydrogen bonds in certain crystal structures of halo-perfluorobenzenes (X-PFCs) and pyrazine molecules has been investigated by means of the DFT/M05-2x method. Very weak energetic effects are observed in the studied complexes, which indicates that the two kinds of noncovalent interactions have some additive aspects. These effects have been fully examined by the geometric and energetic features of the complexes.

1. Introduction

Noncovalent interactions, such as hydrogen bonding, ion-π, lone pair-π and π–π stacking interactions, play vital roles in a wide range of chemical and biological fields [1–4]. Hydrogen bonding, the most frequently employed tool for crystal engineering of solid-state materials and molecular recognition of biomolecules, has been thoroughly studied in the past few decades. Recently, a specific noncovalent interaction between halogen atoms that act as electrophilic centers (Lewis acids) and neutral or anionic Lewis bases has also attracted a great deal of interest, due to its importance in supramolecular architecture, molecular recognition, and biological engineering [5–9]. This interaction has been termed as halogen bonding (XB) to emphasize its analogies with hydrogen bonding (HB). As revealed by Politzer and co-workers [10–14], covalently bound halogens display a small region of positive electrostatic potential (ESP), known as the σ-hole, along the extension of the R–X bonds. An electronegative atom or molecule tends to approach the σ-hole, thus giving rise to a linear halogen bond.

In current years, intensive theoretical attempts have been dedicated to explore the mutual influence between halogen and hydrogen bonds that coexist in the same complexes [15–21]. It was found that the interplay between the two kinds of interactions can lead to strong cooperative or diminutive effects. For example, Li et al. studied the mutual influence between halogen and hydrogen bonds in $H_3N–XY–HF$ complexes (X, Y = F, Cl, Br) and found a cooperativity in these complexes [15]. More recently, cooperative and diminutive interplay between the two kinds of interactions was revealed in ternary complexes of HCCX (X = Cl, Br) with HCN and HNC [18]. However, it must be pointed out that in these studies only small model complexes were considered and thus the results obtained should be somewhat limited. In fact, the major breakthrough in the application of XB in solid-state chemistry was attributed to the strong and well-characterized N···X-PFC synthons, where PFC denotes a perfluorocarbon moiety and N is typically sp^2 (pyridine and pyrazine derivatives) nitrogen [5–7]. In view of the prevalent concurrence of halogen and hydrogen bonds in the crystal structures of X-PFCs and pyrazine derivatives [22–25], a deep understanding of the interplay between the two types of interactions in these real systems would be of great value in XB-based supramolecular synthesis and biological design.

Herein, four reported X-ray crystal structures of X-PFCs and pyrazine derivatives were selected to examine the interplay between halogen and hydrogen bonds. In these structures, 1,4-diiodo-tetrafluorobenzen (compound **1**) and 4-carboxyl–bromo/iodo-perfluorobenzene (compounds **2** and **3**) act as XB donors, while two pyrazine molecules **4** and **5** behave as Lewis bases [22,23] The graphic illustration of the ESP surfaces of the five

---

[*] Corresponding author. Tel./fax: +86 21 64252767.
E-mail address: yxlu@ecust.edu.cn (Y. Lu).

2210-271X/$ - see front matter
http://dx.doi.org/10.1016/j.comptc.2013.10.012

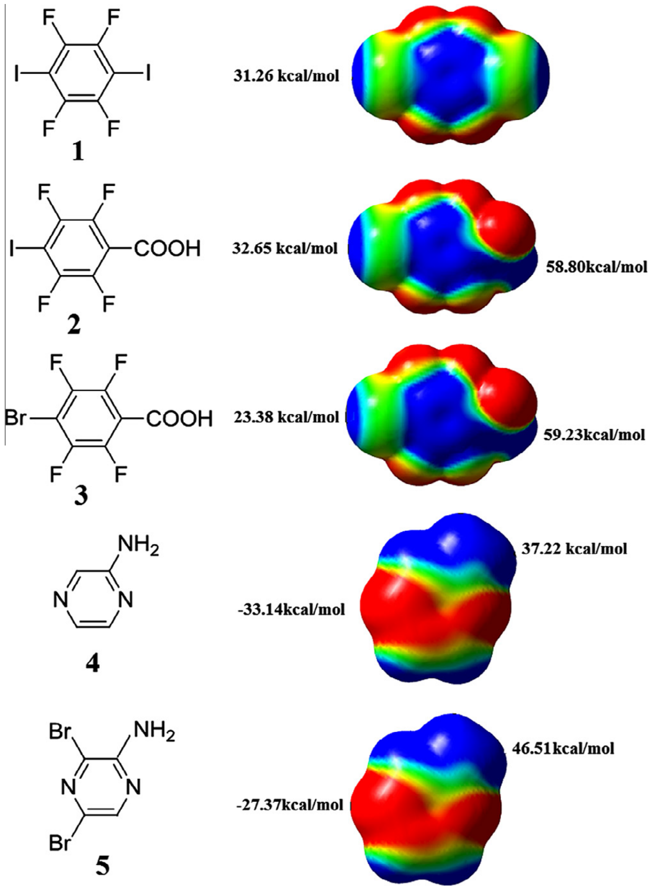


Fig. 1. Electrostatic potential surfaces of the five molecules.

molecules is depicted in Fig. 1. The most positive surface ESPs ($V_{S,\text{max}}$) for X and H atoms that are involved in halogen bonds or hydrogen bonds in the structures are also given in Fig. 1. It is clear that as compared to Br, the I atom displays a larger σ-hole, in accordance with the greater values of $V_{S,\text{max}}$ for I. Moreover, the H atom in the carboxyl moiety in **2** and **3** exhibits a large $V_{S,\text{max}}$ with respect to the amino group in **4** and **5**, which indicates stronger hydrogen bonds in the complexes of **2** and **3** (vide infra).

First, calculations were performed on isolated XB dimers **6–9** and HB dimers **10–13** (Fig. 2). Then, the geometric and energetic features of XB–HB complexes **14–19** (Fig. 3) were computed, to explore the mutual influence between XB and HB interactions. This paper was organized as follows: computational methods used in this work are described in the next section; Section 3 contains results and discussion; in Section 4 we show concluding remarks.

2. Computational methods

The geometries of all the studied complexes were fully optimized at DFT/M05-2x [26] level using the Gaussian 09 suite of programs [27]. This hybrid functional has proved to be reliable in the description of various noncovalent interactions [28]. The aug-cc-pVDZ-PP basis set, which uses pseudopotentials to describe the inner core orbitals, was employed for iodine, while for the rest atoms aug-cc-pVDZ was applied. This Dunning's basis set has been commonly utilized for studying the interplay between halogen and aromatic interactions, such as ion-π, lone pair-π and π–π stacking interactions [29–32]. During geometry optimizations no symmetry or geometry constraint was imposed. Frequency calculations performed at the same theoretical level validated that the structures found correspond to real minima on the potential energy surface.

All interaction energies were calculated with corrections for the basis set superposition error (BSSE) by the standard counterpoise method [33]. The quantum theory of atoms in molecules (QTAIM) analysis was performed by the AIM 2000 software [34] and the ESP analysis was undertaken via the Multiwfn 2.4 program [35], using the wave functions generated with M05-2x/aug-cc-pVDZ(-PP).

For the complexes in which halogen and hydrogen bonds coexist, the cooperativity energy was estimated using the following equation:

$$E_{\text{coop}} = \Delta E(\text{XB} + \text{HB}) - \Delta E(\text{XB}) - \Delta E(\text{HB}) - \Delta E(\text{PI}) \qquad (1)$$

where $\Delta E(\text{XB})$, $\Delta E(\text{HB})$, and $\Delta E(\text{XB} + \text{HB})$ are the interaction energies of the corresponding optimized XB, HB, and XB + HB complexes, respectively. The last term is the interaction between two molecules that are not in contact in the trimer, that is, the geometry of this pair is frozen and taken from the trimer [20]. This expression of cooperativity energy was previously used to study cooperativity in multiple weak noncovalent bonds [20,21].

The synergetic energy was also calculated using the first three terms of Eq. (1), as shown in Eq. (2):

$$E_{\text{syn}} = \Delta E(\text{XB} + \text{HB}) - \Delta E(\text{XB}) - \Delta E(\text{HB}) \qquad (2)$$

The cooperativity and synergetic energies (E_{coop} and E_{syn}) has been widely used in the study of the interplay between halogen and aromatic interactions [29–32].

3. Results and discussion

3.1. Selected fragments in four reported crystal structures

The structures of the complexes **14–19**, in which halogen and hydrogen bonds coexist, were extracted from four reported X-ray crystal structures of X-PFCs and pyrazine derivatives, as shown in Fig. 3. In the complex **14**, a I atom in 1,4-diiodo-tetrafluorobenzen (compound **1**) establishes a strong halogen bond (d(I···N) = 2.82 Å, ∠(C–I···N) = 176.8°) with a ring N atom in one pyrazine molecule **4**, and this pyrazine molecule also forms two symmetrical hydrogen bonds (d(H···N) = 2.13 Å, ∠ (N–H···N) = 176.9°) with the other pyrazine molecule [23]. The structure of the complex **15** is very similar to **14**, with the exception of brominated pyrazine molecular **5** acting as Lewis base in **15** [22]. The structures of the complexes **16** and **17** were taken from the same crystal structure determined by the group of Aakeröy: in the complex **16** the I atom in one 4-carboxyl-iodo-perfluorobenzen (compound **2**) establishes a I···N interaction with the brominated pyrazine **5** that is also involved in two hydrogen bonds with the carboxyl moiety in the other iodo-perfluorobenzen molecule, while in the complex **17** the I atom and the carboxyl moiety in **2** forms a I···N interaction and two hydrogen bonds with two brominated pyrazine molecules, respectively [24]. The structures of the complexes **18** and **19** are quite similar to **16** and **17**, except that in the former two complexes 4-carboxyl–bromo–perfluorobenzen (compound **3**) behaves as XB donor [24].

It is worth mentioning that the X···N interactions in these structures are essentially linear (∠ (C–X···N) > 170°) and the intermolecular X···N distances correspond to 10–20% reduction of the sums of van der Waals (vdW) radii of X and N atoms [36]. These suggest very strong halogen bonds in the structures, which can be ascribed to the powerful electron-withdrawing ability of PFC moieties bound to halogens. In fact, X-PFCs have been widely used in XB-based crystal engineering and molecular recognition, as noted above.