

# Symmetrical Bifurcated Halogen Bond: Design and Synthesis

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Supporting Information

**ABSTRACT:** The main purpose of this work is to extend the application of the symmetrical bifurcated halogen bond in crystal engineering. For this purpose, the optimization of this supramolecular synthon was performed first by using quantum mechanical calculations. The results obtained from theoretical calculations showed that 1,4-diiodotetrafluorobenzene, 1,10-phenanthroline-5,6-dione, and 4,4',6,6'-tetramethyl-2,2'-bipyrimidine are good candidates for the formation of the symmetrical bifurcated halogen bond. This was further confirmed by the successful synthesis of two cocrystals that are composed of the three compounds and formed mainly via symmetrical bifurcated halogen bonds. The good agreement between the theoretical design and the experimental



synthesis also indicates that the quantum mechanical calculation can play an important role in increasing the probability of discovering useful supramolecular synthons.

#### INTRODUCTION

The halogen bond, the noncovalent interaction involving a halogen atom (Hal; Cl, Br, or I) as an acceptor of electron density, has been the subject of study by a number of authors.<sup>1–18</sup> Considering, however, that the halogen atom and the halogen bond electron donor are both negatively charged, the very existence of halogen bonds is a little surprising. The problem was recently explained by Politzer et al. who showed the existence of an electropositive crown called  $\sigma$ -hole at the top of the halogen atom directed to the electron donor.<sup>7</sup> In recent years, many studies have focused on the role of halogen bonds in the field of crystal engineering and showed that the halogen bond could be used as an alternative to the hydrogen bond and metal ion coordination in crystal engineering applications.<sup>1</sup> In fact, Desiraju and co-workers found that the noncovalent interactions involving chlorine, bromine, and iodine may be used for constructing three-dimensional (3D) host-guest solids and that these interactions, which were defined as supramolecular synthons at a later time, seem to have much of the directional specificity that is required for such geometry-based design.<sup>14</sup> Among the halogen bond supramolecular synthons<sup>14c</sup> proposed by Desiraju et al., the robustness of the  $NO_2 \cdots Hal$  synthons is noted. Allen et al. classified the  $NO_2 \cdot \cdot \cdot Hal$  synthons into three different motifs [(I) the halogen bond in which the halogen atom forms monocoordinate interaction with one nitro O atom, (II) the asymmetric bifurcated halogen bond, and (III) the symmetric bifurcated halogen bond (Scheme 1)] and analyzed in detail the three different motifs using a combination of Cambridge

Scheme 1.  $NO_2 \cdots Hal$  Synthons



Structure Database searches and high-level ab initio molecular orbital calculations.<sup>14d</sup> After examining the geometrical preferences of  $NO_2 \cdots Hal$  synthons, they concluded that the C-Hal···O angle tends to linearity as the Hal···O distance becomes shorter.<sup>14d</sup> This indicates that the monocoordinate halogen bond (I) should be stronger than the asymmetric bifurcated halogen bond (II) and the symmetric bifurcated halogen bond (III) is the weakest one. The results obtained from the quantum chemical calculations and the topological analysis of the electron density further confirmed this conclusion.<sup>9b,14d</sup>

As the number of crystal structures determined has increased hugely in recent years, we conducted a new statistical analysis of the three different motifs also employing the Cambridge

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 Table 1. Number of Crystal Structures Containing Supramolecular Synthons I–III

synthon	$NO_2 \cdots Cl$	$NO_2 \cdots Br$	$NO_2 \cdots I$
Ι	437	180	79
II	9	13	16
III	0	2	4

Scheme 2. Molecular Components Used in This Work



Structure Database (CSD version 5.22 + 29 updates).<sup>19,20</sup> ConQuest,<sup>21</sup> part of the CSD, was used to construct each interaction search because it offers a user-friendly interface. All searches required that the *R*-factor be less than 0.05 and that there be no disorder or errors in the crystal structures, as defined by ConQuest. For the sake of simplicity, we were concerned about the number of crystal structures containing supramolecular synthons I–III. As shown in Table 1, the percentage occurrence of the symmetric bifurcated halogen bond in the crystal structures is very low and there is even no symmetric bifurcated NO<sub>2</sub>····Cl halogen bond to be found, which is in agreement with experimental and theoretical results mentioned above.

Applying the same search criteria, except for the symmetric bifurcated halogen bonds shown in Table 1, we found only two other types of symmetric bifurcated halogen bonds in the CSD structures (Refcodes MEZGUT and PEXZEX). Thus, the weaker symmetric bifurcated halogen bonds seem to play a minor role in crystal growth and design. Naturally, a challenging question is whether we can design much stronger symmetric bifurcated halogen bonds for application in crystal engineering. To answer this question, in this study, we first designed several candidates according to the physical nature of the symmetric



**Figure 1.** Molecular electrostatic potential maps of nitromethane, DAFONE, PDONE, and TMBPM on their respective molecular planes. The black lines represent the positive parts of the electrostatic potential, and the blue lines represent the negatives part of the electrostatic potential. The contour interval is 0.005 au. The unit of the axes is angstrom. Numbers in red are the distances between the two local most negative electrostatic potentials.



Figure 2. Structures and selected geometrical parameters of halogenbonded complexes Sym-CINNO, Sym-BrNNO, Sym-INNO, Asym-CINNO, Asym-BrNNO, Asym-INNO, Sym-CINNOO, Sym-BrNNOO, Sym-INNOO, Sym-CIOONN, Sym-BrOONN, Sym-IOONN, Sym-CINNNN, Sym-BrNNNN, and Sym-INNNN.

Table 2. C–Hal Bond Lengths (r, angstroms) and Their Changes upon Complexation ( $\Delta r$ , angstroms), Distances between Hal and N(O) [d (d'), angstroms], Sums of the van der Waals Radii [ $r_w$ (Hal) +  $r_w$ (N(O)), angstroms], Numbers of Imaginary Frequencies ( $N_{img}$ ), and Binding Energies (kilocalories per mole) for the 15 Studied Halogen-Bonded Complexes

				$r_{\rm w}({\rm Hal})$ +		
complex	r	$\Delta r$	d(d')	$\mathit{r}_w(N(O))$	$N_{\mathrm{img}}$	$\Delta E^{\rm CP}$
Sym-ClNNO	1.7334	-0.0046	3.41	3.32	1	2.78
Sym-BrNNO	1.9000	0.0015	3.39	3.47	1	4.64
Sym-INNO	2.1135	0.0104	3.43	3.61	1	6.75
Asym-ClNNO	1.7343	-0.0038	3.22 (3.68)	3.32	0	2.85
Asym-BrNNO	1.9050	0.0065	3.04 (3.81)	3.47	0	4.89
Asym-INNO	2.1253	0.0221	2.98 (3.78)	3.61	0	7.38
Sym-ClNNOO	1.7348	-0.0032	3.29	3.32	1	3.60
Sym-BrNNOO	1.9030	0.0045	3.24	3.47	1	5.89
Sym-INNOO	2.1182	0.0150	3.28	3.61	0	8.35
Sym-ClOONN	1.7334	-0.0046	3.37	3.29	1	1.88
Sym-BrOONN	1.8983	-0.0002	3.34	3.44	1	3.18
Sym-IOONN	2.1095	0.0064	3.37	3.58	0	4.68
Sym-ClNNNN	1.7352	-0.0028	3.30	3.32	1	4.74
Sym-BrNNNN	1.9044	0.0059	3.24	3.47	1	7.44
Sym-INNNN	2.1200	0.0169	3.28	3.61	0	9.96

bifurcated halogen bond and then predicted their stability on the basis of the quantum chemical calculations and, finally, synthesized and characterized successfully three new binary cocrystals driven by the desired symmetric or asymmetric bifurcated halogen bonds.



Figure 3. Molecular graphs of the halogen-bonded Sym-INNO, Asym-INNO, Sym-INNOO, Sym-IOONN, and Sym-INNNN complexes. Small red dots represent the bond critical points.

## EXPERIMENTAL SECTION

Quantum Mechanical Calculations. All the structures were fully optimized with tight convergence criteria and characterized by frequency computations and wave function stability checks at the B97D/ TZVP level of theory,<sup>22</sup> except for the molecular complexes with iodine atoms, for which the B97D calculations using the TZVPP basis set for I and the TZVP basis set for the other atoms were performed. An "ultrafine" integration grid (99 radial, 590 angular points) was used for all the DFT calculations to prevent possible integration grid errors. The binding energies of the halogen-bonded dimers were calculated using the supermolecule method, and all of them are corrected for the basis set superposition error using the counterpoise method of Boys and Bernardi.<sup>23</sup> The bonding characteristics of the different complexes were analyzed by using the "atoms in molecules" (AIM) theory of Bader,<sup>24</sup> which is based on a topological analysis of the electron charge density and its Laplacian. The AIM theory has proved itself to be a valuable tool for conceptually defining what an atom is and above all what a bond is in a quantum calculation of a molecular structure. Electronic structure calculations were conducted using the Gaussian 09 suite of electronic structure programs.<sup>25</sup> AIM analysis was performed with the AIM2000 software package.<sup>26</sup> Here we will note that the value of the bond length change is given as the difference in the bond length between the complex and the monomer, so that a negative value of the bond length change refers to a bond contraction and a positive value of the bond length change indicates a bond elongation.

**Cocrystallization.** The structural formulas of the molecular components considered in this work are shown in Scheme 2. 1,4-Dichlorote-trafluorobenzene ( $F_4DCIB$ ), 1,4-dibromotetrafluorobenzene ( $F_4DBrB$ ), 1,4-diiodotetrafluorobenzene ( $F_4DIB$ ), 4,5-diazafluoren-9-one (DAFONE), 1,10-phenanthroline-5,6-dione (PDONE), and the solvents for crystallization were purchased from Aldrich Chemical Co. and used as received. 4,4',6,6'-Tetramethyl-2,2'-bipyrimidine (TMBPM) was prepared by the method reported previously (see the Supporting Information). The donor and acceptor in a molar ratio of 1:1 were dissolved in approximately 50 mL

	INNO	INNOO	INNNN
formula	$C_{17}H_6F_4I_2N_2O$	C <sub>9</sub> H <sub>3</sub> F <sub>2</sub> INO	$C_9H_7F_2IN_2$
formula weight	584.04	306.02	308.07
crystal size (mm <sup>3</sup> )	0.50 imes 0.18 imes 0.14	0.50 imes 0.19 imes 0.16	0.40 imes 0.18 imes 0.14
crystal system	triclinic	monoclinic	monoclinic
space group	$P\overline{1}$	$P2_1/m$	C2/m
a (Å)	4.9382(7)	5.3613(13)	13.985(2)
b (Å)	12.6849(18)	15.321(4)	15.550(3)
c (Å)	14.696(2)	11.904(3)	4.6026(7)
$\alpha$ (deg)	108.0410(10)	90	90
$\beta$ (deg)	92.996(2)	101.207(2)	101.769(2)
$\gamma$ (deg)	97.953(2)	90	90
volume (Å <sup>3</sup> )	862.5(2)	959.1(4)	979.8(3)
Z	2	4	4
$\rho_{\rm calc}  ({\rm g/cm}^3)$	2.249	2.119	2.088
T (K)	296(2)	296(2)	296(2)
heta range for data collection (deg)	2.59-25.50	2.66-25.50	2.62-25.49
no. of reflections collected	6402	7063	3661
no. of unique data [R(int)]	3171 (0.0165)	1865 (0.0262)	951 (0.0158)
final $R[I > 2\sigma(I)]$	0.0250	0.0267	0.0183
final $wR_2$ (all data)	0.0626	0.0732	0.0460
goodness of fit	1.035	1.008	1.049

Table 3. Crystallographic Data and Structure Refinement Parameters for INNO, INNOO, and INNNN

of chloroform with gentle stirring at room temperature. The undissolved materials were removed by filtration. The filtrate was set aside for crystallization at 6-10 °C. After a few days, single crystals suitable for X-ray analysis were obtained.

**X-ray Diffraction.** Crystallographic data were collected on a Bruker Smart Apex-II CCD area detector equipped with graphite-monochromatic Mo K $\alpha$  radiation ( $\lambda = 0.71073$  Å) at room temperature. An empirical absorption correction was applied. All structures were determined and refined by a combination of direct methods and difference Fourier syntheses, using SHELXTL.<sup>27,28</sup> Anisotropic thermal parameters were assigned to all non-hydrogen atoms. The hydrogen atoms were set in calculated positions and refined as riding atoms with a common isotropic thermal parameter.

## RESULTS AND DISCUSSION

Design of the Symmetrical Bifurcated Halogen Bond. A large number of experimental as well as computational studies indicate that the X-Hal····Y halogen bond is typically nearlinear (the X–Hal–Y angles are close to 180°). The directionality of the halogen bond can be explained by its electrostatic nature.7 Let us add here that, although the electrostatic effect is proven to be the dominant factor, the polarization, charge transfer, and dispersion contributions also play a significant role in describing the geometry and stabilization of the halogen bond. Evidently, the electrostatic nature of the halogen bond leads to most of the bifurcated halogen bonds, especially the symmetrical bifurcated halogen bonds, being weaker than the corresponding monocoordinate halogen bonds. On the other hand, the electrostatic nature of the halogen bond also indicates that the symmetrical bifurcated halogen bond will become stronger and stronger if the distance between the two electron-rich atoms (YY commonly) in the bifurcated halogen bond becomes shorter and shorter. Hence, to design the symmetrical bifurcated halogen bond, we must select the molecules containing the shorter YY

distance as the halogen atom acceptors. Figure 1 shows the molecular electrostatic potential maps of nitromethane, DAFONE, PDONE, and TMBPM on their respective molecular planes. It can be clearly seen from Figure 1 that, in molecules PDONE and TMBPM, the distances between the two local most negative electrostatic potentials are all shorter than 1.5 Å whereas the distances are larger than 2.0 Å in nitromethane and DAFONE. Evidently, PDONE and TMBPM should be better halogen atom acceptors for the formation of the symmetrical bifurcated halogen bond.

Further, we studied theoretically the geometry and stabilization of the complexes formed by F<sub>4</sub>DClB, F<sub>4</sub>DBrB, and F<sub>4</sub>DIB with DAFONE, PDONE, and TMBPM, respectively. During the geometry optimizations, the asymmetrical bifurcated halogenbonded structures are all transformed into the symmetrical bifurcated halogen-bonded structures for the complexes formed by F<sub>4</sub>DClB, F<sub>4</sub>DBrB, and F<sub>4</sub>DIB with PDONE and TMBPM. The symmetrical bifurcated halogen-bonded structures and the asymmetrical bifurcated halogen-bonded structures coexist only in the complexes formed by F<sub>4</sub>DClB, F<sub>4</sub>DBrB, and F<sub>4</sub>DIB with DAFONE. These results are in accord with the prediction given above, which suggests that PDONE and TMBPM are better halogen atom acceptors for the formation of the symmetrical bifurcated halogen bonds. Finally, we obtained only 15 dimer structures. The structures of the 15 complexes can be seen in Figure 2. Some selected geometrical parameters, the number of imaginary frequency and binding energies of the 15 studied halogen-bonded complexes, are listed in Table 2. For comparison, the sums of the van der Waals radii<sup>29</sup> of the Hal atom and the Y atom are also listed in Table 2.

Table 2 shows that, upon formation of the complexes, all the C–Cl bonds are contracted whereas the C–Br and C–I bonds are all elongated except the C–Br bond in the **Sym-BrOONN** complex. This is consistent with our previous results for the monocoordinate halogen bond.<sup>13d</sup> The rigorous AIM theory has



**Figure 4.** Packing diagrams for cocrystals **INNO** (a), **INNOO** (b), and **INNNN** (c). The red dotted lines represent the halogen bonds.

been successfully applied in characterizing halogen bonds of different strengths in a wide variety of molecular complexes.<sup>13a</sup> Figure 3 shows the molecular graphs of the halogen-bonded complexes Sym-INNO, Asym-INNO, Sym-INNOO, Sym-IOONN, and Sym-INNNN. The molecular graphs for 10 other complexes were omitted because they are very similar to the corresponding ones shown in Figure 3. Figure 3 clearly demonstrates the existence of a bond critical point (BCP) for each noncovalent bond. The expected bond paths associated with the noncovalent bond BCPs can also be visualized in Figure 3. At the same time, it is also found that the values of the Laplacian of the electron density at the noncovalent bond BCPs are all positive. According to the "atoms in molecules" (AIM) theory of Bader, the contacts between Hal and Y are all true halogen bonds, which rationalizes the terms monocoordinate halogen bond, asymmetric bifurcated halogen bond, and symmetric bifurcated halogen bond. Table 2 lists both the calculated distances between Hal and Y and the values of the sums of the van der Waals radii of Hal and Y. We notice that in the Asym-INNO complex the calculated distance between I and N<sub>2</sub> (3.78 Å) is larger than the sum of the van der Waals radii of I and  $N_2$  (3.61 Å). This means that the contact between I and  $N_2$  is not a halogen bond, which is obviously different from the AIM result. The case shown here is a warning about the conventional

method of judging the existence of the halogen bond with the empirical van der Waals radii.

The last column in Table 2 gives the values of the BSSEcorrected binding energies for the 15 complexes. We know that the combined effect of polarizability and electronegativity is to make the halogen potential more positive in the following order: Cl < Br < I. Table 2 shows that, for a given halogen atom acceptor, the binding energy increases in the following order:  $F_4DClB < F_4DBrB < F_4DIB$ . This reflects the fact that the strength of the halogen bond correlates well with the magnitude of the halogen positive potential. Again, the electrostatic nature of the halogen bond makes  $F_4DIB$  a better halogen atom donor for the formation of the symmetrical bifurcated halogen bond. In a recent paper, Riley and co-workers investigated the halogen bonding interactions involving halobenzene, *m*-difluorohalobenzene, *o*-difluorohalobenzene, and pentafluorohalobenzene. The results are very similar for both.

The numbers of imaginary frequencies in Table 2 further prove that  $F_4DIB$ , PDONE, and TMBPM are better candidates for the formation of the symmetrical bifurcated halogen bond. We notice because of Table 2 that the symmetrical bifurcated halogenbonded structures are all transition states (only one imaginary frequency) on their respective potential energy surfaces except the three formed by  $F_4DIB$  with PDONE and TMBPM (all real frequencies). Although the interactions in the crystal may be a little different from those calculated here in the gas phase, at least it indicates that the symmetrical bifurcated halogen-bonded structures studied here will be not stable in the crystal except the three formed by  $F_4DIB$  with PDONE and TMBPM.

In summary, we have designed two new supramolecular synthons in this section. Further, we predicted that two binary cocrystals should be easily synthesized: one cocrystal composed of  $F_4DIB$  and PDONE and the other composed of  $F_4DIB$  and TMBPM. Both of them are formed mainly via symmetrical bifurcated halogen bonds.

**Crystal Structures.** To verify our theoretical predictions, we selected  $F_4DClB$ ,  $F_4DBrB$ , and  $F_4DIB$  as halogen atom donors and DAFONE, PDONE, and TMBPM as halogen atom acceptors to synthesize the adducts. It was found that  $F_4DIB$  crystallizes readily with DAFONE, PDONE, and TMBPM in a chloroform solvent, yielding cocrystals **INNO**, **INNOO**, and **INNNN**, respectively (see the Supporting Information). The crystallographic data and structure refinement parameters are listed in Table 3. However, many attempts to cocrystallize  $F_4DClB$  and  $F_4DBrB$  with DAFONE, PDONE, and TMBPM were all unsuccessful. These experimental results are consistent with our theoretical predictions.

F<sub>4</sub>DIB with DAFONE formed 1:1 cocrystal **INNO** in triclinic space group  $P\overline{1}$ . The propagation of the monocoordinate halogen bond constructs a one-dimensional (1D) chain, as depicted in Figure 4a. The 1D chains pack on each other via  $\pi \cdot \cdot \cdot \pi$  stacking interactions between the two DAFONE molecules, generating a two-dimensional (2D) layer structure. According to our theoretical calculation, the CP-corrected binding energy of the paralleldisplaced DAFONE dimer in the crystal structure of **INNO** is ~4.16 kcal/mol, larger than that of the parallel-displaced benzene dimer.<sup>30</sup> The C–H···I and F···F interactions are also observed in the crystal structure of **INNO**, and these interactions further extend the 2D layer structures to 3D networks. As expected, there is no symmetric bifurcated halogen bond in the crystal structure of **INNO**. However, we noticed that the distance between I and N<sub>1</sub> is only 2.924 Å whereas the distance between I and N<sub>2</sub> is increased to 4.137 Å (Figure 4a). Evidently, in cocrystal INNO, the monocoordinate  $C-I \cdots N$  halogen bond is preferred over the asymmetric bifurcated  $C-I \cdots NN$  halogen bond. This is slightly different from our theoretical prediction that indicates that the asymmetric bifurcated  $C-I \cdots NN$  halogen bond should be formed. Inspection of the crystal structure of INNO reveals it is the greater steric hindrance at the N<sub>2</sub> atom that prevents the formation of the other weaker  $C-I \cdots N_2$  halogen bond.

Crystallization of F<sub>4</sub>DIB with PDONE and TMBPM in a chloroform solvent yielded cocrystals INNOO and INNNN, respectively. Cocrystal INNOO has the symmetry of monoclinic space group  $P2_1/m_1$  and cocrystal INNNN has the symmetry of monoclinic space group C2/m. It can be clearly seen in panels b and c of Figure 4 that the symmetric bifurcated C-I···NN and C-I···OO halogen bonds are formed in the crystal structures of INNOO and INNNN, in good agreement with our theoretical predictions. The crystal structures of IN-NOO and INNNN are very similar to that of INNO. First, the 1D chains are formed by the symmetric bifurcated C-I···NN and  $C-I \cdots OO$  halogen bonds. Then, the 1D chains pack on each other via  $\pi \cdots \pi$  stacking interactions, generating a 2D layer structure. The calculated  $\pi \cdots \pi$  binding energy of the paralleldisplaced PDONE dimer in the crystal structure of INNOO is ~5.35 kcal/mol, and the calculated  $\pi \cdots \pi$  binding energy of the parallel-displaced TMBPM dimer in the crystal structure of INNNN is ~7.70 kcal/mol. Finally, the 2D layer structures further assemble into 3D networks via the  $C-H \cdots F$  interactions.

## CONCLUSION

The CSD searches show that the number of crystal structures that contain the symmetrical bifurcated halogen bond is very small. To extend the application of the symmetrical bifurcated halogen bond in crystal engineering, we successfully designed and synthesized two cocrystals formed mainly by the symmetrical bifurcated halogen bonds in this study. One cocrystal is composed of  $F_4$ DIB and PDONE and the other of  $F_4$ DIB and TMBPM. Both the experimental results and the theoretical analyses showed that the symmetrical bifurcated halogen bond may be stronger than the asymmetrical bifurcated halogen bond and even the monocoordinate halogen bond. This means that the symmetrical bifurcated halogen bond and even the monocoordinate halogen bond. This means that the symmetrical bifurcated halogen bond will be revealed in the near future.

## ASSOCIATED CONTENT

**Supporting Information.** Cartesian coordinates of all the halogen-bonded complexes in Table 1, synthesis of 4,4',6,6'-tetramethyl-2,2'-bipyrimidine, and CIF files for INNO, INNOO, and INNNN. This material is available free of charge via the Internet at http://pubs.acs.org.

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## REFERENCES

 (a) Metrangolo, P.; Neukirch, H.; Pilati, T.; Resnati, G. Acc. Chem. Res. 2005, 38, 386–395. (b) Metrangolo, P.; Meyer, F.; Pilati, T.; Resnati, G.; Terraneo, G. Angew. Chem., Int. Ed. 2008, 47, 6114–6127.
 (c) Cavallo, G.; Metrangolo, P.; Pilati, T.; Resnati, G.; Sansotera, M.; Terraneo, G. Chem. Soc. Rev. 2010, 39, 3772–3783. (d) Bertani, R.; Sgarbossa, P.; Venzo, A.; Lelj, F.; Amati, M.; Resnati, G.; Pilati, T.; Metrangolo, P.; Terraneo, G. Coord. Chem. Rev. 2010, 254, 677–695.

(2) (a) Auffinger, P.; Hays, F. A.; Westhof, E.; Ho, P. S. Proc. Natl. Acad. Sci. U.S.A. 2004, 101, 16789–16794. (b) Voth, A. R.; Hays, F. A.; Ho, P. S. Proc. Natl. Acad. Sci. U.S.A. 2007, 104, 6188–6193. (c) Voth, A. R.; Khuu, P.; Oishi, K.; Ho, P. S. Nat. Chem. 2009, 1, 74–79.

(3) (a) Legon, A. C. Chem.—Eur. J. 1998, 4, 1890–1897. (b) Legon, A. C. Phys. Chem. Chem. Phys. 2010, 12, 7736–7747.

(4) Lommerse, J. P. M.; Stone, A. J.; Taylor, R.; Allen, F. H. J. Am. Chem. Soc. 1996, 118, 3108–3116.

(5) Saha, B. K.; Nangia, A.; Jaskólski, M. *CrystEngComm* **2005**, 7, 355–358.

(6) (a) Karpfen, A. J. Phys. Chem. A 2000, 104, 6871-6879. (b) Karpfen, A. Struct. Bonding (Berlin, Ger.) 2008, 126, 1-15.

(7) (a) Clark, T.; Hennemann, M.; Murray, J. S.; Politzer, P. J. Mol. Model. 2007, 13, 291–296. (b) Politzer, P.; Lane, P.; Concha, M. C.; Ma, Y.; Murray, J. S. J. Mol. Model. 2007, 13, 305–311. (c) Göbel1, M.; Tchitchanov, B. H.; Murray, J. S.; Politzer, P.; Klapötke1, T. M. Nat. Chem. 2009, 1, 229–235. (d) Politzer, P.; Murray, J. S.; Clark, T. Phys. Chem. Chem. Phys. 2010, 12, 7748–7757.

(8) (a) Rissanen, K. *CrystEngComm* **2008**, *10*, 1107–1113. (b) Raatikainen, K.; Rissanen, K. *Cryst. Growth Des.* **2010**, *10*, 3638–3646.

(9) (a) Zou, J. W.; Jiang, Y. J.; Guo, M.; Hu, G. X.; Zhang, B.; Liu, H. C.; Yu, Q. S. *Chem.—Eur. J.* **2005**, *11*, 740–751. (b) Lu, Y. X.; Zou,

J. W.; Wang, Y. H.; Yu, Q. S. *THEOCHEM* **2006**, *767*, 139–142.

(10) (a) Lu, Y. X.; Shi, T.; Wang, Y.; Yang, H. Y.; Yan, X. H.; Luo, X. M.; Jiang, H. L.; Zhu, W. L. J. Med. Chem. 2009, 52, 2854–2862. (b) Lu, Y. X.; Wang, Y.; Zhu, W. L. Phys. Chem. Chem. Phys. 2010, 12, 4543–4551.

(11) Li, Q. Z.; Lin, Q. Q.; Li, W. Z.; Cheng, J. B.; Gong, B. A.; Sun,
 J. Z. ChemPhysChem 2008, 9, 2265–2269.

(12) (a) Riley, K. E.; Merz, K. M. J. Phys. Chem. A 2007, 111, 1688–1694. (b) Riley, K. E.; Murray, J. S.; Politzer, P.; Concha, M. C.; Hobza, P. J. Chem. Theory Comput. 2009, 5, 155–163. (c) Riley, K. E.; Murray, J. S.; Fanfrlík, J.; Řezáč, J.; Solá, R. J.; Concha, M. C.; Ramos, F. M.; Politzer, P. J. Mol. Model 2011DOI 10.1007/s00894-011-1015-6.

(13) (a) Wang, W.; Wong, N.-B.; Zheng, W.; Tian, A. J. Phys. Chem. A 2004, 108, 1799–1805. (b) Wang, W.; Tian, A.; Wong, N.-B. J. Phys. Chem. A 2005, 109, 8035–8040. (c) Wang, W.; Hobza, P. J. Phys. Chem. A 2008, 112, 4114–4119. (d) Wang, W.; Zhang, Y.; Ji, B. J. Phys. Chem. A 2010, 114, 7257–7260. (e) Wang, W.; Wang, D.; Zhang, Y.; Ji, B.; Tian, A. J. Chem. Phys. 2011, 134, 054317. (f) Wang, W.; Zhang, Y.; Ji, B.; Tian, A. J. Chem. Phys. 2011, 134, 224303.

(14) (a) Pedireddi, V. R.; Sarma, J. A. R. P.; Desiraju, G. R. J. Chem. Soc., Perkin Trans. 2 1992, 311–320. (b) Allen, F. H.; Goud, B. S.; Hoy, V. J.; Howard, J. A. K.; Desiraju, G. R. Chem. Commun. 1994, 23, 2729–2730. (c) Desiraju, G. R. Angew. Chem., Int. Ed. 1995, 34, 2311–2327. (d) Thalladi, V. R.; Goud, B. S.; Hoy, V. J.; Allen, F. H.; Howard, J. A. K.; Desiraju, G. R. Chem. Commun. 1996, 3, 401–402. (e) Allen, F. H.; Lommerse, J. P. M.; Hoy, V. J.; Howard, J. A. K.; Desiraju, G. R. Acta Crystallogr. 1997, B53, 1006–1016.

(15) George, S.; Nangia, A.; Lam, C.-K.; Mak, T. C. W.; Nicoud, J.-F. Chem. Commun. 2004, 10, 1202–1203.

(16) Ramana, C. V.; Chatterjee, S.; Durugkar, K. A.; Gonnade, R. G. *CrystEngComm* **2009**, *11*, 143–150.

(17) Roper, L. C.; Präsang, C.; Kozhevnikov, V. N.; Whitwood, A. C.; Karadakov, P. B.; Bruce, D. W. *Cryst. Growth Des.* **2010**, 10, 3710–3720.

(18) (a) Serpell, C. J.; Kilah, N. L.; Costa, P. J.; Félix, V.; Beer, P. D. Angew. Chem., Int. Ed. **2010**, 49, 5322–5326. (b) Caballero, A.; White, N. G.; Beer, P. D. Angew. Chem., Int. Ed. **2011**, 50, 1845–1848.

(19) Allen, F. H. Acta Crystallogr. **2002**, B58, 380–388.

(20) Allen, F. H.; Motherwell, W. D. S. Acta Crystallogr. 2002, B58, 407-422.

(21) Bruno, I. J.; Cole, J. C.; Edgington, P. R.; Kessler, M.; Macrae, C. F.; McCabe, P.; Pearson, J.; Taylor, R. *Acta Crystallogr.* 2002, *B58*, 389–397.

(22) Grimme, S. J. Comput. Chem. 2006, 27, 1787-1799.

(23) Boys, S. F.; Bernardi, F. Mol. Phys. 1970, 19, 553-566.

(24) Bader, R. F. W. Atoms in Molecules: A Quantum Theory; Clarendon; Oxford, U.K., 1990.

(25) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery, J. A., Jr.; Peralta, J. E.; Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, J. M.; Klene, M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Dapprich, S.; Daniels, A. D.; Farkas, O.; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; Fox, D. J. Gaussian 09, revision B.01; Gaussian, Inc.: Wallingford, CT, 2009.

(26) Biegler-König, F.; Schönbohm, J.; Bayles, D. J. Comput. Chem. 2001, 22, 545–559.

(27) SHELXTL, version 5.1; Bruker AXS: Madison, WI, 1998.

(28) Sheldrick, G. M. SHELXL-97: Program for the refinement of crystal structure; University of Göttingen: Göttingen, Germany, 1997.

(29) Bondi, A. J. Phys. Chem. 1964, 68, 441-451.
(30) Wang, W.; Pitoňák, M.; Hobza, P. ChemPhysChem 2007,

8, 2107–2111.