

## $^{13}\text{C}$ NMR Study of Halogen Bonding of Haloarenes: Measurements of Solvent Effects and Theoretical Analysis<sup>‡</sup>

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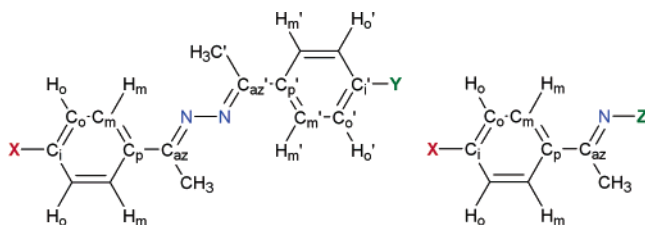
Ⓜ This paper contains enhanced objects available on the Internet at <http://pubs.acs.org/journals/jacsat>.

**Abstract:** Solvent effects on the NMR spectra of symmetrical ( $X = \text{F}$  (**1**),  $X = \text{Cl}$  (**2**),  $X = \text{Br}$  (**3**),  $X = \text{I}$  (**4**),  $X = \text{NO}_2$  (**5**),  $X = \text{CN}$  (**6**)) and unsymmetrical ( $X = \text{I}$ ,  $Y = \text{MeO}$  (**7**),  $Y = \text{PhO}$  (**8**)) para-disubstituted acetophenone azines  $X\text{-C}_6\text{H}_4\text{-CMe=N=N=CMe-C}_6\text{H}_4\text{-Y}$  and of models  $X\text{-C}_6\text{H}_4\text{-CMe=N-Z}$  ( $X = \text{I}$ ,  $Z = \text{H}$  (**9**),  $Z = \text{NH}_2$  (**10**)), 4-iodoacetophenone (**11**), and iodobenzene (**12**) were measured in  $\text{CDCl}_3$ , DMSO, THF, pyridine, and benzene to address one *intramolecular* and one *intermolecular* issue. Solvent effects on the  $^{13}\text{C}$  NMR spectra are generally small, and this finding firmly establishes that the azine bridge indeed functions as a “conjugation stopper,” an important design concept in our polar materials research. Since intermolecular halogen bonding of haloarenes do occur in polar organic crystalline materials, the NMR solution data pose the question as to whether the *absence of solvent shifts* indicates the *absence of strong halogen bonding* in solution. This question was studied by the theoretical analysis of the DMSO complexes of iodoarenes **4**, **9–12**, and of iodoacetylene. DFT and MP2 computations show iodine bonding, and characteristic structural and electronic features are described. The nonrelativistic complexation shifts and the change in the spin–orbit induced heavy atom effect of iodine compensate each other, and iodine bonding thus has no apparent effect on  $\text{C}_i$  in the iodoarenes. For iodides, complexation by DMSO occurs and may or may not manifest itself in the NMR spectra. The absence of complexation shifts in the NMR spectra of halides does not exclude the occurrence of halogen bonding in solution.

### Introduction

It has been known for a long time that the halogen atoms iodine, bromine, chlorine, and even fluorine can function as Lewis acids and engage in electron donor–acceptor interactions with atoms with lone pairs, such as nitrogen, oxygen, phosphorus, and sulfur.<sup>1</sup> This interaction is now referred to as halogen bonding, as suggested by Legon,<sup>2</sup> and the topic has recently been reviewed by Resnati.<sup>3</sup> Halogen bonding may involve dihalogens  $\text{X}_2$  and  $\text{X-Y}$  as well as organic halides. Halogen bonding between organic halides and electron donors has been employed as an effective synthon in crystal engineering, and illustrative examples are provided by the work of Resnati<sup>4,5</sup> and by Pennington and Hanks.<sup>6</sup> Halogen bonding also has played a special role in studies of dipole alignment. Halogen

**Scheme 1.** Atom Numbering of the Azines<sup>a</sup>



<sup>a</sup> The alkoxy groups in the unsymmetrical azines are in the Y-position.

bonding between iodine and nitro groups was claimed to yield parallel-aligned crystals of 4-iodo-4'-nitrobiphenyl,<sup>7</sup> but the crystals structure was later shown to be disordered due to admixtures of 4,4'-dinitrobiphenyl.<sup>8</sup> We accomplished near-perfect polar order in molecular organic crystals of unsymmetrical acetophenone azines (Scheme 1) using a rational design. The crystal structures of the (MeO,I)-azine,<sup>9</sup> the (MeO,Br)-azine,<sup>10,11</sup> and the (MeO,Cl)-azine,<sup>12</sup> respectively, are similar but differ in subtle details because of the occurrence of one,

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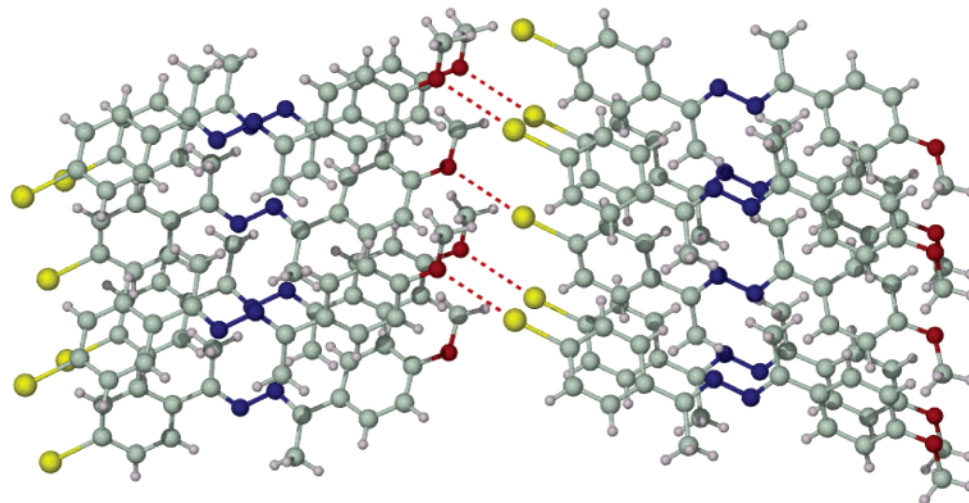
(1) Bent, H. A. *Chem. Rev.* **1968**, *68*, 587.

(2) (a) Legon, A. C. *Angew. Chem., Int. Ed.* **1999**, *38*, 2686. (b) Legon, A. C. *Chem.-Eur. J.* **1998**, *10*, 1890.

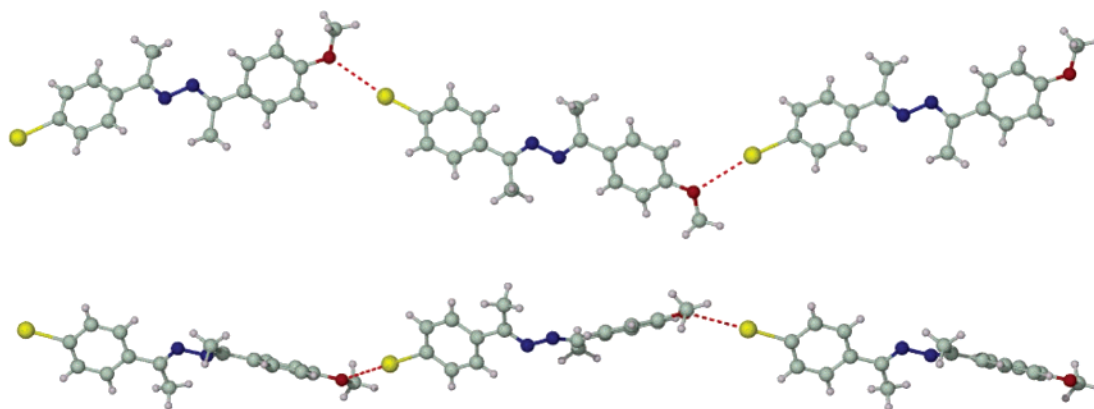
(3) Metrangolo, P.; Resnati, G. *Chem.-Eur. J.* **2001**, *7*, 2511.

(4) (a) Corradi, E.; Meille, S. V.; Messina, M. T.; Metrangolo, P.; Resnati, G. *Angew. Chem., Int. Ed.* **2000**, *39*, 1782. (b) Amico, V.; Meille, S. V.; Corradi, E.; Messina, M. T.; Resnati, G. *J. Am. Chem. Soc.* **1998**, *120*, 8261. (c) Valerio, G.; Raos, G.; Meille, S. V.; Metrangolo, P.; Resnati, G. *J. Phys. Chem. A* **2000**, *104*, 1617.

(5) (a) Cardillo, P.; Corradi, E.; Lunghim A.; Meille, S. V.; Messina, M. T.; Metrangolo, P.; Resnati, G. *Tetrahedron* **2000**, *56*, 5535. (b) Liantonio, R.; Metrangolo, P.; Pilati, T.; Resnati, G.; Stevenazzi, A. *Cryst. Growth Des.* **2003**, *3*, 799. (c) Navarrini, W.; Metrangolo, P.; Pilati, T.; Resnati, G. *New J. Chem.* **2000**, *24*, 777. (d) Burton, D. D.; Fontana, F.; Metrangolo, P.; Pilati, T.; Resnati, G. *Tetrahedron Lett.* **2003**, *44*, 645. (e) Liantonio, R.; Metrangolo, P.; Pilati, T.; Resnati, G. *Cryst. Growth Des.* **2003**, *3*, 355.



**Figure 1.** Crystal structure of (MeO,I)-azine **7** features perfect dipole-parallel alignment within 2-D layers and near-perfect dipole-parallel alignment in the direction in which the layers are stacked. The directionality of the halogen bonding might control the stacking of the layers.



**Figure 2.** Crystals of 4-iodoacetophenone azine **7** contain halogen-bonded strings. The halogen bonding is characterized by  $d(\text{O}\cdots\text{I}) = 3.138 \text{ \AA}$ ,  $\angle(\text{C}-\text{O}\cdots\text{I}) = 126.28^\circ$ , and  $\angle(\text{O}\cdots\text{I}-\text{C}) = 171.34^\circ$ . The I-Ph bond approximately coincides with the direction of an O- $\text{sp}^3$  lone pair.

two, and four independent molecules, respectively. The crystal structure of the (MeO,I)-azine (**7**) is shown in Figure 1. The perspectives of the halogen-bonded string shown in Figure 2 illustrate the  $\text{O}\cdots\text{I}-\text{C}$  geometry. A similar interaction of type  $(\text{R}_2\text{N})_3\text{P}=\text{O}\cdots\text{I}-\text{C}$  was described by Zhu et al.,<sup>13</sup> and the same group<sup>14</sup> also recently described  $\text{O}\cdots\text{Br}-\text{C}$  and  $\text{N}\cdots\text{Br}-\text{C}$  interactions of the type observed in the (MeO,Br)-azine.<sup>11</sup> This directionality of the halogen bonding (Figure 2) might control the stacking of the layers.<sup>15a</sup>

We are studying halogen bonding for two reasons, and these address one *intramolecular* and one *intermolecular* issue. First,

we are examining one of our important design assumptions, namely, that the azine bridge functions as a “conjugation stopper”. We have previously studied acetophenone azines with theoretical methods<sup>16</sup> and by <sup>1</sup>H and <sup>13</sup>C NMR spectroscopy in chloroform,<sup>17,18</sup> and the results provide evidence that the azine bridge is indeed a conjugation stopper. Realizing that weak intermolecular interactions (e.g., halogen bonding) between solvent and solute may occur, corroboration by extension of the NMR measurements to a range of solvents is desirable. Second, we want to learn about the geometries and binding energies of halogen-bonded complexes of haloarenes because such interactions do occur in the polar organic crystalline materials we designed and prepared (Figures 1 and 2), and they may occur in solution.

Solvent effects were measured on the NMR spectra of the symmetrical azines with X = Y = F (**1**), Cl (**2**), Br (**3**), I (**4**), NO<sub>2</sub> (**5**), and CN (**6**), the unsymmetrical azines with X = I and

- (6) (a) Crihfield, A.; Hartwell, J.; Phelps, D.; Walsh, R. B.; Harris, J. L.; Payne, J. F.; Pennington, W. T.; Hanks, T. W. *Cryst. Growth Des.* **2003**, *3*, 313. (b) Jay, J. I.; Padgett, C. W.; Walsh, R. D. B.; Hanks, T. W.; Pennington, W. T. *Cryst. Growth Des.* **2001**, *1*, 501. (c) Walsh, R. B.; Padgett, C. W.; Metrangolo, P.; Resnati, G.; Hanks, T. W.; Pennington, W. T. *Cryst. Growth Des.* **2001**, *1*, 165.
- (7) Jagarlapudi, A. R. P. S.; Allen, F. H.; Allen, F. H.; Hoy, V. J.; Howard, J. A. K.; Thaimattam, R.; Biradha, K.; Desiraju, G. R. *Chem. Commun.* **1997**, 101.
- (8) (a) Masciocchi, N.; Bergamo, M.; Sironi, A. *Chem. Commun.* **1998**, 1347. (b) Hulliger, J.; Langley, P. J. *Chem. Commun.* **1998**, 2557.
- (9) Lewis, M.; Barnes, C.; Glaser, R. *J. Chem. Crystallogr.* **2000**, *30*, 489.
- (10) Glaser, R. E.; Chen, G. S. Dipole Aligned Molecular Materials with Nonlinear Optical Properties. U.S. Patent 6,229,047, May 8, 2001.
- (11) Chen, G. S.; Wilbur, J. K.; Barnes, C. L.; Glaser, R. *J. Chem. Soc., Perkin Trans. 2* **1995**, 2311.
- (12) Lewis, M.; Barnes, C.; Glaser, R. *Acta Crystallogr., Sect. C* **2000**, *56*, 393.
- (13) Chu, Q.; Wang, Z.; Huang, Q.; Yan, C.; Zhu, S. *J. Am. Chem. Soc.* **2001**, *123*, 11069.
- (14) Zhu, S.; Xing, C.; Xu, W.; Jin, G.; Li, Z. *Cryst. Growth Des.* **2004**, *4*, 53.

- (15) Reviews: (a) Glaser, R.; Knotts, N.; Wu, H. *Chemtracts: Org. Chem.* **2003**, *16*, 443. (b) Lewis, M.; Wu, Z.; Glaser, R. Arene-Arene Double T-Contacts. Lateral Synthons in the Engineering of Highly Anisotropic Organic Crystals. In *Anisotropic Organic Materials—Approaches to Polar Order*; Glaser, R., Kaszynski, P., Eds.; ACS Symposium Series, Volume 798; American Chemical Society: Washington, DC, 2001; Chapter 7.
- (16) Glaser, R.; Chen, G. S. *J. Comput. Chem.* **1998**, *19*, 1130.
- (17) (a) Lewis, M.; Glaser, R. *J. Org. Chem.* **2002**, *67*, 1441. (b) Lewis, M.; Glaser, R. *J. Org. Chem.* **2002**, *67*, 7168.
- (18) See also: Neuvonen, K.; Fülöp, F.; Neuvonen, H.; Koch, A.; Kleinpeter, E.; Pihlaja, K. *J. Org. Chem.* **2003**, *68*, 2151.

Y = MeO (**7**, 4-iodoacetophenone-(4-methoxy-phenylethylidene)-hydrazone) or Y = PhO (**8**, 4-iodoacetophenone-(4-phenoxy-phenylethylidene)hydrazone), two models (imine **9**, Z = H; hydrazone **10**, Z = NH<sub>2</sub>), as well as 4-iodoacetophenone **11** and iodobenzene **12**. The theoretical analysis focuses on DMSO complexes of iodoarenes **4** and **9–12** for reasons given below.

## Experimental Section

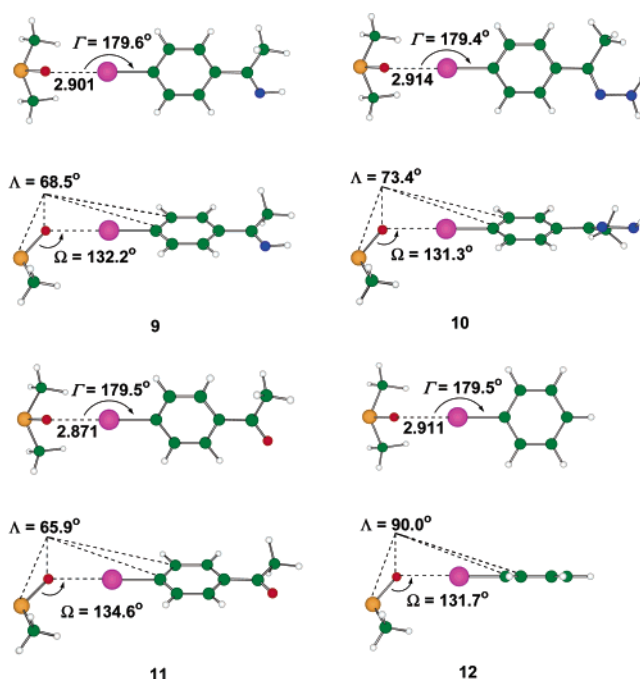
Iodobenzene, 4-iodoacetophenone, and hydrazine hydrate were purchased from the Aldrich Chemical Co. 4-Iodoacetophenone was recrystallized from ethanol. The preparation of **4** was described previously. 4-Iodoacetophenone hydrazone was prepared (yield >95%) by refluxing 4-iodoacetophenone and hydrazine hydrate (ratio 1:3) in ethanol (4 h).

The deuterated NMR solvents CDCl<sub>3</sub>, DMSO, THF, pyridine, and benzene were employed. CDCl<sub>3</sub> and deuterated DMSO were purchased from Cambridge Isotopes Laboratories, and deuterated THF, pyridine, and benzene were purchased from the Aldrich Chemical. The <sup>13</sup>C NMR sample preparation of the (I, MeO)-azine **7** in DMSO required heating and sonication. The heteronuclear multiple quantum correlation (HMQC) method was used to help identify the peaks by establishing the C–H connectivities. The HMQC spectrum of the symmetrical (I,I)-azine **4** in DMSO shows cross-peaks at 128.4, 137.0, and 14.5 ppm, which correspond to C<sub>o</sub>, C<sub>m</sub>, and methyl-C, respectively. The <sup>13</sup>C NMR spectrum of **4** shows only five peaks. The APT NMR was recorded for **4** in DMSO, and it showed the expected three positive signals for the quaternary carbons C<sub>az</sub>, C<sub>p</sub>, C<sub>i</sub>, and two negative signals for C<sub>o</sub> and C<sub>m</sub>. Importantly, the two signals for C<sub>p</sub> and C<sub>o</sub>, a positive signal for C<sub>p</sub> and a negative signal for C<sub>o</sub>, are nearly isochronous with δ(C<sub>p</sub>) = 137.267 and δ(C<sub>o</sub>) = 137.239 ppm. A DEPT spectrum provided further confirmation. The spectra are provided as Supporting Information.

The <sup>1</sup>H- and <sup>13</sup>C NMR spectra were measured with a 300 MHz instrument (operating frequencies for <sup>1</sup>H and <sup>13</sup>C of 300.1317008 and 75.4769164 MHz, respectively) and a 250 MHz NMR spectrometer (operating frequencies for <sup>1</sup>H and <sup>13</sup>C of 250.1315321 and 62.9023694 MHz, respectively). The chemical shifts were assigned by comparison to empirical data.<sup>17</sup>

## Theoretical and Computational Section

**Structures and Vibrations of Halogen-Bonded Complexes.**<sup>19,20</sup> Structure optimizations were performed at the MP2 level<sup>21</sup> and with the B3LYP implementation of hybrid density functional theory. The effective-core-potential valence basis set LANL2DZ<sup>22</sup> was employed for all optimizations (basis set A). Symmetric molecules were optimized with the appropriate symmetry constraints. Vibrational frequency analyses were carried out at the level of optimization to confirm that a stationary structure indeed had been located, to confirm the character of the stationary structure (minimum: all eigenvalues are real), and to



**Figure 3.** Computed MP2 structures of the iodine bonding complexes between DMSO and 4-iodoacetophenone imine **9**, 4-iodoacetophenone hydrazone **10**, 4-iodoacetophenone **11**, and 4-iodobenzene **12**.

⊙ For the DMSO complexes of **12**, animated GIFs are available of the six lowest vibrations with frequencies ⊙ 7 cm<sup>-1</sup> (torsion mode of the ∠(S–O···C<sub>ipso</sub>–C<sub>ortho</sub>) dihedral angle Λ), ⊙ 20 cm<sup>-1</sup> (rotational motion about the S–O bond), ⊙ 22 cm<sup>-1</sup> (∠(S–O···I) angle bending Ω), ⊙ 48 cm<sup>-1</sup> (∠(O···I–C<sub>ipso</sub>) angle bending Γ), ⊙ 52 cm<sup>-1</sup> (∠(S–O···I) angle bending in combination with ∠(O···C<sub>ipso</sub>–Ph) bending), ⊙ 106 cm<sup>-1</sup> (d(O···I) stretching mode).

obtain thermochemical data. The potential energy surfaces of the complexes are rather flat with regard to the precise relative position of the iodoarene and the DMSO molecule, and most optimization of the complexes required optimizations with computed gradients and curvatures at all steps. Molekel 4.2<sup>23</sup> was employed to examine molecular vibrations and to generate the animations provided as web-enhanced objects. The vibrational analysis of **4**·(DMSO)<sub>2</sub> could not be carried out at the MP2 level even with the modern equipment. Total energies and thermochemical data (Table S3) and the complexation energies (Table S4) are provided as Supporting Information. Molecular models of all optimized structures are shown in Figures S1–S4 in the Supporting Information, and the MP2 structures of the DMSO complexes are shown in Figures 3 and 4.

**Halogen Bonding Strength.** Binding energies, enthalpies, and free Gibbs enthalpies were determined at the level of optimization. Total energies also were recomputed with those structures but employing an all-electron basis set. The 6-31+G\* basis set was used for H, C, N, O, and S. For I, the 3-21G\* basis set was used with augmentation by single diffuse s- and p-functions with the exponents 0.0468 and 0.0286 recommended by Radom et al.<sup>24</sup> (basis set B). We also employed a basis set C which is like basis set B except that it replaces the 3-21G\* basis set with the 6-311G\* basis set for iodine.<sup>24</sup> For iodobenzene, we applied coupled-cluster theory which considers all single and double excitations variationally and also includes triple excitations via a perturbational scheme, CCSD(T).<sup>25,26</sup> CCSD(T) calculations employed basis sets B and C and were based on the MP2/A structures.

(19) *Essentials of Computational Chemistry*, Cramer, C. J., Ed.; John Wiley & Sons: Chichester, U.K., 2002.

(20) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Zakrzewski, V. G.; Montgomery, J. A., Jr.; Stratmann, R. E.; Burant, J. C.; Dapprich, S.; Millam, J. M.; Daniels, A. D.; Kudin, K. N.; Strain, M. C.; Farkas, O.; Tomasi, J.; Barone, V.; Cossi, M.; Cammi, R.; Mennucci, B.; Pomelli, C.; Adamo, C.; Clifford, S.; Ochterski, J.; Petersson, G. A.; Ayala, P. Y.; Cui, Q.; Morokuma, K.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Cioslowski, J.; Ortiz, J. V.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Gonzalez, C.; Challacombe, M.; Gill, P. M. W.; Johnson, B. G.; Chen, W.; Wong, M. W.; Andres, J. L.; Head-Gordon, M.; Replogle, E. S.; Pople, J. A. *Gaussian 98*, revision A.9; Gaussian, Inc.: Pittsburgh, PA, 1998.

(21) Head-Gordon, M.; Pople, J. A.; Frisch, M. J. *Chem. Phys. Lett.* **1988**, *153*, 503.

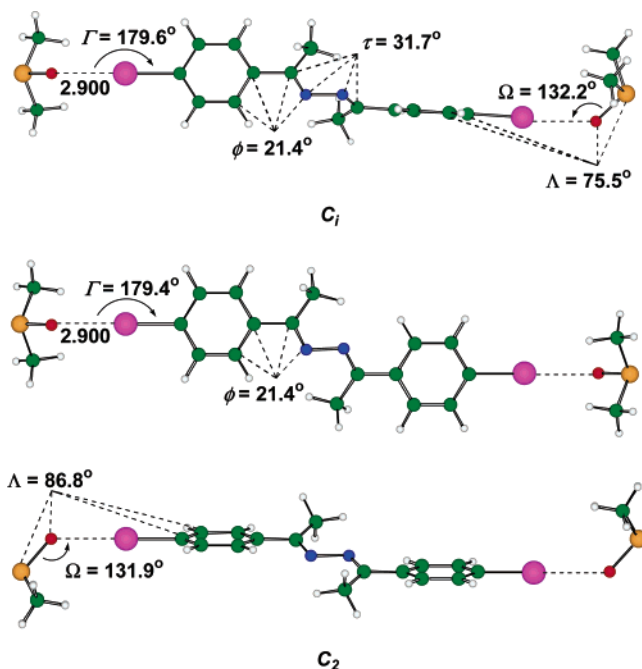
(22) (a) Dunning, T. H.; Hay, P. J. In *Methods of Electronic Structure Theory*; Schaefer, H. F., III, Ed.; Plenum Press: New York, 1977; Vol. 2. (b) Hay, P. J.; Wadt, W. R. *J. Chem. Phys.* **1985**, *82*, 270. (c) Hay, P. J.; Wadt, W. R. *J. Chem. Phys.* **1985**, *82*, 284. (d) Hay, P. J.; Wadt, W. R. *J. Chem. Phys.* **1985**, *82*, 299.

(23) (a) *Molekel*, version 4.2; Flükiger, P.; Lüthi, H. P.; Portmann, S.; Weber, J. Swiss Center for Scientific Computing: Manno, Switzerland, 2000–2002. (b) Portmann, S.; Lüthi, H. P. *Chimia* **2000**, *54*, 766.

(24) Glukhovtsev, M. N.; Pross, A.; McGrath, M. P.; Radom, L. *J. Chem. Phys.* **1995**, *103*, 1878.

(25) (a) Purvis, G. D.; Bartlett, R. J. *J. Chem. Phys.* **1982**, *76*, 1910. (b) Scuseria, G. E.; Schaefer, H. F. *J. Chem. Phys.* **1989**, *90*, 3700.





**Figure 4.** Computed MP2 structures of the doubly iodine bonded complexes between two molecules of DMSO and azine **4**. The  $C_1$  and the  $C_2$  symmetric complexes are minima.

**Nonrelativistic NMR Chemical Shift Calculations.** The gauge-including atomic orbital (GIAO) method is a proven, efficient, and accurate method for the calculation of NMR shielding tensors,<sup>27</sup> and GIAO NMR calculations were carried out at the B3LYP and MP2 levels with basis set B.

**Spin–Orbit Corrections to Shielding Constants.** Spin–orbit (SO) effects are well-known to be particularly important for carbon atoms directly bonded to iodine.<sup>28</sup> We therefore used the combined finite-perturbation/sum-over-states approach of ref 29 to compute SO corrections to the <sup>13</sup>C shifts of carbon atoms directly bonded to iodine ( $C_i$ ). The calculations were performed for the B3LYP/A- or MP2/A-optimized structures, respectively, using the gradient-corrected P86 functional,<sup>30</sup> IGLO-II basis sets,<sup>31</sup> and a finite-perturbation parameter  $\lambda = 10^{-3}$ . The common gauge origin for the magnetic vector potential was chosen to be on the nearest iodine nucleus. One- and two-electron SO matrix elements were computed within the atomic meanfield approximation,<sup>32</sup> using the AMFI code.<sup>33</sup> The finite-perturbation Kohn–Sham SCF calculations employed the deMon program,<sup>34</sup> and the subsequent perturbation treatment employed the corresponding property module.<sup>29</sup>

## Results and Discussion

**Solvent Effects on <sup>13</sup>C NMR Spectra.** The solvent contributes in several ways<sup>35,36</sup> to the solvent screening constant  $\sigma_{\text{solvent}}$  (eq 1). The term  $\sigma_a$  arises from the solvent magnetic anisotropy,

$$\sigma_{\text{solvent}} = \sigma_a + \sigma_b + \sigma_w + \sigma_e + \sigma_s \quad (1.1)$$

$$\sigma_{\text{solvent}} = \sigma_{\text{ns}} + \sigma_s \quad (1.2)$$

and this term is positive for disk-shaped solvents (e.g., benzene) and negative for rod-shaped solvents.<sup>35</sup> The term  $\sigma_b$  relates to the bulk diamagnetic susceptibility of the solvents. The terms  $\sigma_w$  and  $\sigma_e$  account for van der Waals interactions and electrostatic interactions (“polar effects”), respectively, of the solvent. Finally,  $\sigma_s$  considers the effects of specific complexation. To assess the importance of specific halogen bonding, one needs to measure the spectrum in two solvents that either do not (e.g., CDCl<sub>3</sub>) or do (e.g., DMSO) allow for complexation. Since the combined effects of the first four terms ( $\sigma_{\text{ns}} = \sigma_a + \sigma_b + \sigma_w + \sigma_e$ ) might serendipitously offset any effect of halogen bonding, it is good practice to examine several solvents of each kind. Hence, we employed pyridine and THF in addition to DMSO as halogen bond donor solvents, and we also employed benzene as a second non-Lewis base solvent. Furthermore, our study of symmetrical azines includes some azines with nonhalogen substituents. If the effects of the nonspecific solvent shielding would serendipitously offset any effect of halogen bonding in the halogen-substituted azines (e.g., **1–4**), then one should expect a significant observable nonspecific effect in the absence of halogen bonding opportunities (e.g., **5** and **6**).

The chemical shifts of **1–6** were measured in CDCl<sub>3</sub> and DMSO, and the data show no abnormal changes (Table S1 in Supporting Information). Azine **4**, most likely to engage in halogen bonding, was measured in other solvents as well, and no significant chemical shift changes were found (Table 1). The chemical shifts of  $C_i$  vary by no more than 1.2 ppm, and changes of this magnitude are “normal.” Similarly, no major solvent effects are observed in the NMR spectra of the unsymmetrical azines **7** and **8** (Table 1). Thus, our NMR experiments do not show any unusual effects.

Since azines are conjugation stoppers and any halogen bonding would be local, the solvent effects on iodo-substituted azines should be very similar to the solvent effects of 4-iodoacetophenone hydrazone **10**. We prepared this hydrazone, and its NMR spectra data are given in Table S2 in the Supporting Information along with the respective data for the related 4-iodoacetophenone **11** and iodobenzene **12**. The chemical shift of  $C_i$  varies by less than 1.1 ppm as with the azines. However, a significant solvent effect of  $\Delta\delta = -5.7$  ppm does occur for  $C_{\text{az}}$  in that this atom’s chemical shift decreases from 146.0 ppm in CDCl<sub>3</sub> to 140.7 ppm in DMSO. There is some specific interaction affecting  $C_{\text{az}}$ . The data in Table S2 show that the chemical shift of the amino-H changes from 5.4 ppm in CDCl<sub>3</sub> to 6.5 ppm in DMSO due to hydrogen bonding between the amino group and solvent oxygen, which deshields the H-atom.

The data resolve the *intramolecular* issue stated in the Introduction. Solvent effects on <sup>13</sup>C NMR spectra are generally

- (26) (a) Urban, M.; Noga, J.; Cole, S. J.; Bartlett, R. J. *J. Chem. Phys.* **1985**, *83*, 4041. (b) Noga, J.; Bartlett, R. J. *J. Chem. Phys.* **1987**, *86*, 7041. (c) Pople, J. A.; Head-Gordon, M.; Raghavachari, K. *J. Chem. Phys.* **1987**, *87*, 5968.
- (27) Wolinski, K.; Hinton, J. F.; Pulay, P. *J. Am. Chem. Soc.*, **1990**, *112*, 8251.
- (28) Kaupp, M.; Malkina, O. L.; Malkin, V. G.; Pyykkö, P. *Chem.–Eur. J.* **1998**, *4*, 118.
- (29) (a) Malkin, V. G.; Malkina, O. L.; Salahub, D. R. *Chem. Phys. Lett.* **1996**, *261*, 335. (b) Malkina, O. L.; Schimmelpfennig, B.; Kaupp, M.; Hess, B. A.; Chandra, P.; Wahlgren, U.; Malkin, V. G. *Chem. Phys. Lett.* **1998**, *296*, 93. (c) Vaara, J.; Malkina, O. L.; Stoll, H.; Malkin, V. G.; Kaupp, M. *J. Chem. Phys.* **2001**, *114*, 61.
- (30) (a) Perdew, J. P. *Phys. Rev. B* **1986**, *33*, 8822. (b) Perdew, J. P.; Wang, Y. *Phys. Rev. B* **1986**, *33*, 8800.
- (31) Kutzelnigg, W.; Fleischer, U.; Schindler, M. *NMR—Basic Principles and Progress*; Springer: Heidelberg, Germany, 1990; Vol. 23, 165 ff.
- (32) Hess, B. A.; Marian, C. M.; Wahlgren, U.; Gropen, O. *Chem. Phys. Lett.* **1996**, *251*, 365.
- (33) AMFI code: Schimmelpfennig, B. *Atomic Spin–Orbit Mean-Field Integral Program*; University of Stockholm: Stockholm, Sweden 1996.
- (34) (a) deMon program: Salahub, D. R.; Fournier, R.; Mlynarski, P.; Papai, I.; St-Amant, A.; Ushio, J. In *Density Functional Methods in Chemistry*; Labanowski, J., Andzelm, J., Eds.; Springer: New York 1991. (b) St-Amant, A.; Salahub, D. R. *Chem. Phys. Lett.* **1990**, *169*, 387.

- (35) Buckingham, A. D.; Schaefer, T.; Schneider, W. G. *J. Chem. Phys.* **1960**, *32*, 1227.
- (36) Foster, R. *Organic Charge-Transfer Complexes*; Academic Press: London, 1969; Chapter 5.

**Table 1.** Experimental  $^{13}\text{C}$  Chemical Shifts (ppm) of 4-Iodoacetophenone Azine **4**, 4-Iodoacetophenone-(4-methoxyphenyl-ethylidene)hydrazone **7**, and 4-Iodoacetophenone-(4-phenoxyphenyl-ethylidene)hydrazone **8** as a Function of Solvent

solvent	(I, I)-azine <b>4</b>					
	$C_i$	$C_o$	$C_m$	$C_p$	$C_{az}$	$\text{CH}_3$
$\text{CDCl}_3$	96.2	137.5	128.3	137.7	157.3	14.8
DMSO	96.9	137.2	128.5	137.3	157.1	14.6
THF	96.7	138.3	129.2	139.0	158.4	14.5
benzene	96.4	137.7	128.6	138.2	157.9	14.4
pyridine	97.2	137.9	128.9	138.2	157.9	14.7
solvent	(MeO, I)-azine <b>7</b>					
	$C_i$	$C_o$	$C_m$	$C_p$	$C_{az}$	$\text{CH}_3$
$\text{CHCl}_3$	95.9	137.5	128.3	138.1	157.3	14.9
DMSO	97.0	137.3	128.2	137.7	157.2	14.5
THF	96.3	138.2	128.9	139.3	158.2	14.6
benzene	96.0	137.6	128.8	138.6	157.8	14.7
pyridine	97.0	137.8	128.9	138.6	157.9	14.8
solvent	(PhO, I)-azine <b>8</b>					
	$C_i$	$C_o$	$C_m$	$C_p$	$C_{az}$	$\text{CH}_3$
$\text{CDCl}_3$	96.0	137.5	128.3	138.0	157.4	15.0
DMSO	96.9	137.3	128.5	137.5	157.2	14.7
solvent	(PhO, I)-azine <b>8</b>					
	$C'_i$	$C'_o$	$C'_m$	$C'_p$	$C'_{az}$	$\text{C}'\text{H}_3$
$\text{CHCl}_3$	161.0	113.7	128.1	131.0	158.0	14.7
DMSO	160.8	113.9	128.6	130.5	157.2	14.7
THF	162.2	114.3	129.2	131.5	159.1	14.3
benzene	161.5	114.0	131.6	130.7	158.8	14.3
pyridine	161.6	114.2	131.5	130.9	158.7	14.6
solvent	(PhO, I)-azine <b>8</b>					
	$C'_i$	$C'_o$	$C'_m$	$C'_p$	$C'_{az}$	$\text{C}'\text{H}_3$
$\text{CDCl}_3$	159.0	119.4	129.9	133.2	157.7	14.7
$\text{DMSO-}d_6$	158.5	119.4	128.5	132.9	157.3	14.5

small. Independent of the choice of the NMR solvent, hardly any electronic communication is found between the two halves of the unsymmetrical azines, and the spectroscopic properties of the symmetrical azines carry over to the unsymmetrical azines. But the NMR data pose a dilemma as far as the *intermolecular* issue is concerned, that is, the occurrence of halogen bonding. Gao and Goroff<sup>37</sup> reported an unusual solvent effect in the  $^{13}\text{C}$  NMR spectra of diiodohexatriyne,  $\text{I}-\text{C}\equiv\text{C}-\text{C}\equiv\text{C}-\text{C}\equiv\text{C}-\text{I}$ , and of diiodooctatetrayne,  $\text{I}-\text{C}\equiv\text{C}-\text{C}\equiv\text{C}-\text{C}\equiv\text{C}-\text{C}\equiv\text{C}-\text{I}$ , in  $\text{CDCl}_3$  and DMSO. The chemical shift of  $\text{C}_\alpha$  in  $\text{C}_6\text{I}_2$  shifted from 0.9 ppm in  $\text{CDCl}_3$  to 14.6 ppm in DMSO. For  $\text{C}_8\text{I}_2$ , the chemical shift changed from 1.9 ppm in  $\text{CDCl}_3$  to 17.9 ppm in DMSO. These  $^{13}\text{C}$  downfield shifts were attributed to halogen bonding between iodine and DMSO. Hence, we must ask whether the *absence of solvent shifts* for haloarenes indicates the *absence of strong halogen bonding* in solution. Our theoretical analysis of DMSO complexes of iodoarenes will provide an interesting answer to this question. This system was selected for theoretical analysis because this halogen bonding is one of the stronger intermolecular interactions and because of its relevance to our materials (Figures 1 and 2).

Of course, the dilemma exists only if complexation does occur and if complexation causes a chemical shift change. The complexation of iodoarenes by chloroform<sup>38</sup> is very weak, and the weak complexation does not cause any complexation shift in the NMR spectra. We consider solute–solvent interactions

(37) (a) Gao, K.; Goroff, N. S. *J. Am. Chem. Soc.* **2000**, *122*, 9320. (b) Rege, P. D.; Malkina, O. L.; Goroff, N. S. *J. Am. Chem. Soc.* **2002**, *124*, 370.

only because this interaction is conceptually rather different from any solute–solute aggregation because of the entirely different entropy situations. The solute–solute aggregation may involve solutes that are different (e.g., ion pairing) or the same (self-association, ion pair aggregation). Any such aggregation requires significant solute–solute bonding to overcome the entropy term. Charge–charge interaction allows for ion pairing in solvents of low polarity.<sup>39</sup> Ion pair aggregation is rare and requires less polar solvents.<sup>40</sup> Association between solutes that interact only by dipole–dipole interactions is still less likely, and the self-association of water in chloroform is one of the very few examples.<sup>41</sup> While all the solute–solute aggregates considered in that study allow for rather strong solute–solute intermolecular binding, only the water dimer was observed in chloroform. In particular, these considerations suggest that halogen bonding between two solute molecules does not occur. In crystals, iodine bonding to  $\text{sp}^2\text{N}$  is of course possible, and there are examples in the literature.<sup>14,42,43</sup> For the azines, however, the structural record contains no examples of halogen bonding involving an azine N. We determined the crystal structures of the (F, F)-, (Cl, Cl)-, (Br, Br)-, and (I, I)-azines **1–4**, and none features halogen bonding to an azine N,<sup>44</sup> even in the absence of competition for halogen bond acceptors.

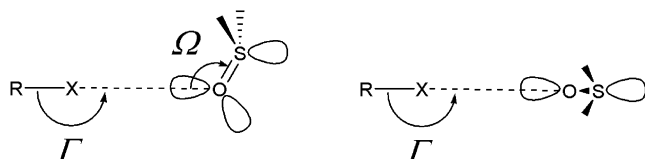
**Halogen Bonding between Iodoarenes and DMSO. Iodo-Donor Molecules.** The optimized structures of **4** and **9–12** are shown in the Supporting Information. The structures of **9–12** are unremarkable, while **4** warrants a brief discussion. At the MP2 level,  $\text{C}_{2h}$ -**4** is a second-order saddle point structure ( $i31.8$  and  $i21.7\text{ cm}^{-1}$ ),  $\text{C}_2$  and  $\text{C}_i$  minima were located, and they are almost isoenergetic ( $\Delta E_{\text{rel}} = 0.23\text{ kcal/mol}$  preference for the  $\text{C}_2$  structure,  $\Delta G_{\text{rel}} = 0.4\text{ kcal/mol}$  preference for the  $\text{C}_i$  structure). At the B3LYP level, the  $\text{C}_2$  structure again is preferred but the  $\text{C}_{2h}$ -**4** now is a minimum, and an essentially isoenergetic  $\text{C}_i$  structure is a transition state structure ( $i1.9\text{ cm}^{-1}$ ,  $\text{C}_2$  distortion). While the details of the potential energy surface are subtle and therefore also sensitive to the theoretical model, it is clear that the azine can access a large conformational space at regular temperature.

**Halogen-Bonded DMSO Complexes of **9–12** and **4**.** The structures of the complexes between **9–12** and DMSO are shown in Figure 3, and all complexes are chiral. The structures of the doubly halogen-bonded DMSO complexes of **4** are shown in Figure 4, and the phenyl twist angles  $\phi$  and the  $\tau$  values remain unaffected by complexation. The van der Waals radii of O and I are 1.52 and 1.98 Å,<sup>45</sup> and their sum is 3.5 Å. The  $\text{O}\cdots\text{I}$  distances in all complexes are close to 2.9 Å and significantly shorter ( $\sim 0.6\text{ Å}$ ) than the sum of the vdW radii.

Parthasarthy et al.<sup>46</sup> mined the crystallographic record for evidence of directional preferences of intermolecular forces

- (38) Two complexes of iodobenzene and chloroform (both  $\text{C}_1$ ) were considered; one complex involves two hydrogen bonds and the other features one  $\text{IH}_2\text{C}_6-\text{H}/\text{Cl}$  contact (but no chlorine–iodine contact).
- (39) Dedonder-Lardeux, C.; Gregoire, G.; Jouviet, C.; Martrenchard, S.; Solgadi, D. *Chem. Rev.* **2000**, *100*, 4023.
- (40) (a) Gareyev, R.; Clula, J. C.; Streitwieser, A. *J. Org. Chem.* **1996**, *61*, 4589. (b) Facchetti, A.; Streitwieser, A. *J. Org. Chem.* **1999**, *64*, 2281.
- (41) Eblinger, F.; Schneider, H.-J. *J. Phys. Chem.* **1996**, *100*, 5533.
- (42) Nguyen, H. L.; Horton, P. N.; Hursthouse, M. B.; Legon, A. C.; Bruce, D. W. *J. Am. Chem. Soc.* **2004**, *126*, 16.
- (43) (a) Forni, A.; Metrangolo, P.; Pilati, T.; Resnati, G. *Cryst. Growth Des.* **2004**, *4*, 291–295. (b) De Santis, A.; Forni, A.; Liantonio, R.; Metrangolo, P.; Pilati, T.; Resnati, G. *Chem.–Eur. J.* **2003**, *9*, 3974.
- (44) (a) X = Y = F, Cl, Br: Chen, G. S.; Anthamatten, M.; Barnes, C. L.; Glaser, R. *J. Org. Chem.* **1994**, *59*, 4336. (b) X = Y = I: Lewis, M.; Barnes, C.; Glaser, R. *J. Chem. Crystallogr.* **1999**, *29*, 1043.
- (45) Bondi, A. *J. Phys. Chem.* **1964**, *68*, 441.

**Scheme 2.** Iodoarene–DMSO Halogen Bonding Geometry



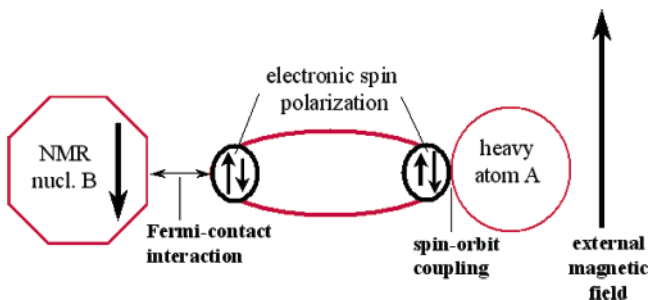
around halogen atoms. It was found that nucleophiles in general tend to approach the C–X bond in a “head-on” fashion with  $\Gamma \approx 158(13)^\circ$  (Cl),  $\Gamma \approx 162(12)^\circ$  (Br), and  $\Gamma \approx 165(8)^\circ$  (I). Similar results were obtained by Allen et al.<sup>47</sup> The DMSO complexes with the iodoarenes are “head-on” with  $\angle(\text{O}\cdots\text{I}-\text{C})$  angles  $\Gamma$  close to  $180^\circ$  as in the case of the iodoalkyne–DMSO complexes (Scheme 2).<sup>37</sup> This near-linear head-on coordination contrasts with the  $\Gamma$  angles of  $110\text{--}140^\circ$  between DMSO and  $\text{F}_3\text{C-I}$  reported by Romaniello and Lej<sup>48</sup> based on DFT studies. Iodine–DMSO bonding thus shows significant intrinsic iodo-donor specificity, and the variations documented by Parthasarthy et al.<sup>46</sup> are not all due to crystal packing.

The  $\angle(\text{S}-\text{O}\cdots\text{I})$  angles  $\Omega$  are in the range  $125\text{--}135^\circ$ , and there is general agreement that the O=S bond is coordinated in a side-on fashion so that the DMSO oxygen can orient an  $n$ -electron density to iodine. The orientation of the S–O bond relative to the benzene plane also is of interest, and we use the  $\angle(\text{S}-\text{O}\cdots\text{C}_{\text{ipso}}-\text{C}_{\text{ortho}})$  dihedral angle  $\Lambda$  for its description. The  $\Lambda$  angle falls in the range  $55\text{--}75^\circ$  for the complexes of **9–11** and the  $C_2$  complexes of **4**. A theoretical level dependency occurs for the structure of **12**·DMSO in that it is chiral with  $\Lambda \approx 50^\circ$  at B3LYP while it has  $C_s$  symmetry at MP2 ( $\Lambda = 90^\circ$ ). The same kind of level dependency is seen in the  $C_i$  complexes **4**·(DMSO)<sub>2</sub>. The halogen bond is easily distorted; Figure 3 of the online version of the paper provides links to animations of the six lowest frequency vibrations of the DMSO complex of iodobenzene **12** as Web-enhanced objects.

**Halogen Binding Energies.** We computed binding energies  $\Delta E$ , enthalpies  $\Delta H$ , and Gibbs free enthalpies  $\Delta G$  at several levels, and they are summarized in Table S4 of the Supporting Information. The negative  $\Delta G$  values indicate that complex formation in the gas phase will not occur because of entropy. In condensed phase, the entropy term is much smaller, and our discussion focuses on binding energies and enthalpies. The binding energies show some theoretical level effects in that MP2 theory shows larger binding than B3LYP theory, and basis set effects are significantly higher at the MP2 level. The halogen bonding is about the same for each halogen bond in the complexes of **4** and **9–12**, but the numbers computed at the DFT and MP2 levels still differ by a factor of 2. For iodobenzene **12** we also computed binding energies at levels CCSD(T)/B//MP2/A and CCSD(T)/C//MP2/A (last row of Table S4). The CCSD(T)/B//MP2/A data are slightly lower than the MP2/B data, and the CCSD(T)/C//MP2/A data give a still lower binding energy that is similar to the DFT data. Our best levels suggest a binding energy of about 3 kcal/mol per iodide–DMSO contact.

**<sup>13</sup>C NMR Chemical Shift Calculations.** The results of nonrelativistic GIAO NMR calculations for **4** and **9–12** and for their DMSO complexes are given in the Supporting

**Scheme 3.** Iodine Spin–Orbit Coupling Causes Electron Spin Polarization and Affects the Attached C-Atom by a Fermi Contact Mechanism



Information, and the most pertinent results are summarized in Table 2. Computations were carried out for all systems at the level B3LYP/B//B3LYP/A. For **9–12** and their complexes, calculations also were performed at the MP2(full)/B//MP2/A level, while this proved too demanding for the DMSO complexes of **4**.

Generally, good agreement is achieved between the measurements and the chemical shift computations with both the MP2 and B3LYP methods. However, neither method reproduces the experimental chemical shift of  $C_i$  attached to iodine; these were measured to be  $\delta(C_i) = 92\text{--}102$  ppm in DMSO, while the calculations suggested much higher values of  $120\text{--}143$  ppm (Table 2). Moreover, the comparison of the nonrelativistically calculated chemical shifts in the free molecules and their complexes shows noticeable chemical shift changes for  $C_i$  (column 5 in Table 2), while the measurements show hardly any change (last column in Table 2).

These systematic deviations may be attributed to the neglect of the spin–orbit-induced heavy atom effect of iodine<sup>28</sup> in the nonrelativistic GIAO calculations. The so-called “normal halogen dependence” (NHD), that is, the successively larger chemical-shift decrease of light atoms bonded to a heavy element (e.g., halogen) with increasing atomic number of the substituent was described in the 1950s, and spin–orbit coupling was first suggested as its cause in 1969.<sup>49</sup> It is now known<sup>28,50</sup> that the spin polarization induced by SO coupling at the heavy atom center contributes to NMR shielding tensors predominantly by a Fermi contact mechanism (Scheme 3). Using the same FPT/SOS approach as in the present work<sup>29</sup> to compute SO corrections to chemical shifts, Kaupp et al. found an SO-induced heavy atom shielding by  $-33.3$  ppm for  $C_i$  in iodobenzene. SO shifts of comparable magnitude are expected for the  $C_i$  atoms in the iodo-substituted systems studied here, and it was of interest to investigate how the SO shifts are affected by complexation.

The SO corrections calculated here for the  $C_i$  atoms (Table 2) are indeed of similar magnitude as for iodobenzene (the effect is known to increase with the s-character of the  $C_i\text{--I}$  bond).<sup>28</sup> They reduce the computed  $C_i$  shifts from ca.  $130\text{--}140$  ppm to ca.  $90\text{--}100$  ppm and thus bring them into much better agreement with experiment.

Moreover, the SO effects are notably smaller for the free molecules than for the DMSO complexes, and they thus affect the coordination shifts. The nonrelativistic shifts increase by

(46) Ramasubbu, N.; Parthasarathy, R.; Murray-Rust, P. *J. Am. Chem. Soc.* **1986**, *108*, 4308.

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

(48) Romaniello, P.; Lej, F. *J. Phys. Chem. A* **2002**, *106*, 9114.

(49) Nomura, Y.; Takeuchi, Y.; Nakagawa, N. *Tetrahedron Lett.* **1969**, *8*, 639.

(50) For a recent review, see: Kaupp, M. Relativistic Effects on NMR Chemical Shifts. In *Relativistic Quantum Chemistry*; Schwerdtfeger, P., Ed.; Elsevier: Amsterdam, 2003; Vol. 23, in press.



**Table 2.** Computed and Measured  $C_i$  Chemical Shifts and Chemical Shift Changes (in ppm) upon Complexation (Coordination Shifts), with and without SO Corrections

system	$\delta(\text{NR})^a$	SO corrections <sup>b</sup>	$\delta(\text{NR}+\text{SO})$	coordination shift (NR) <sup>a</sup>	coordination shift (NR+SO)	coordination shift (exptl)
<b>9</b>	135.6 (124.2)	-34.3 (-36.5)	101.3 (88.0)			
<b>9</b> ·DMSO	143.7 (130.9)	-42.4 (-43.2)	101.3 (87.7)	+8.1 (+6.7)	0.0 (-0.3)	
<b>10</b>	127.5 (121.4)	-35.2 (-38.8)	92.3 (82.6)			
<b>10</b> ·DMSO	135.6 (128.2)	-43.6 (-44.8)	92.0 (83.4)	+8.1 (+6.8)	-0.3 (+0.8)	-1.1
<b>11</b>	140.0 (126.3)	-34.6 (-36.6)	105.4 (89.7)			
<b>11</b> ·DMSO	148.8 (133.5)	-37.7 (-39.0)	111.1 (94.5)	+8.8 (+6.8)	+5.7 (+4.8)	0.6
<b>12</b>	131.6 (123.2)	-31.1 (-36.5)	100.5 (86.7)			
<b>12</b> ·DMSO	139.2 (129.5)	-42.1 (-42.6)	97.1 (86.9)	+7.6 (+6.3)	-3.4 (+0.2)	0.4
<b>4</b>	134.5	-27.8	106.7			
<b>4</b> ·(DMSO) <sub>2</sub> <sup>c</sup>	142.5	-33.4	109.1	+8.0	+2.4	0.7

<sup>a</sup> Nonrelativistic (NR) shifts and coordination shifts at B3LYP/B//B3LYP/A (MP2(full)/B//MP2/A) level from Table S5. <sup>b</sup> SO corrections added at P86 level, using B3LYP/A (MP2/A) structure data, respectively. <sup>c</sup> Based on the  $C_i$  symmetric structure of **4**·(DMSO)<sub>2</sub>.

**Table 3.** Natural Population Analysis for Hydrazone **10**, Acetophenone **11**, Iodobenzene **12**, and Iodoacetylene at MP2(full)/B//MP2/A<sup>a</sup>

compd	$q(\text{R-I})$	$q(\text{C}_i)$	$q(\text{I})$	$q(\text{O})$	$q(\text{S})$
DMSO				-0.947	1.077
<b>10</b>		-0.217	0.168		
<b>10</b> ·DMSO	-0.022	-0.246	0.219	-0.968	1.098
<b>11</b>		-0.214	0.183		
<b>11</b> ·DMSO	-0.025	-0.243	0.235	-0.962	1.092
<b>12</b>		-0.215	0.166		
<b>12</b> ·DMSO	-0.022	-0.244	0.216	-0.958	1.089
H-C≡C-I		-0.345	0.314		
H-C≡C-I·DMSO	-0.036	-0.354	0.334	-0.966	1.097

<sup>a</sup> Basis set A is LANL2DZ. Basis set B is the all-electron basis described in the text.

about 6–8 ppm upon complexation by DMSO (Table 2). In most cases, these positive coordination shifts are offset by the change in the SO contributions, which are more negative for the DMSO complexes than for the free molecules. The two effects compensate each other, and halogen bonding thus has no apparent effect on  $C_i$  in the iodoarenes (for **11**, the calculations provide somewhat smaller SO effects, and the cancellation is thus incomplete in these data). In the halogen bonding of the iodoalkynes, the two factors are not balanced, and halogen bonding becomes manifest in the NMR chemical shifts.<sup>37b</sup>

**Electronic Mechanism of Halogen Bonding of Iodoarenes.** Iodoalkynes should be better halogen bond acceptors than iodoarenes because of the higher electronegativity of  $sp^3$ -C compared to  $sp^2$ -C. Stabilization energies and interaction distances show that 1-iodo-phenylacetylene is more strongly halogen bonded than **10**, and this is true for the parent iodoacetylene as well (Table S4). Further corroboration and insight into the halogen bonding mechanism are provided by the results of population analysis (Table 3).

The overall charge transfer from the O-donor to the iodide acceptor is very small, less than 0.04, and the charge transfer is almost twice as large for iodoacetylene than for any of the iodoarenes. Aside from a dispersion contribution, the halogen bonding between iodoarenes and DMSO largely is a dipole–dipole interaction and synergistically reinforced by the  $C^{\delta-}-I^{\delta+}$  and  $O^{\delta-}-S^{\delta+}$  bond polarity increases upon halogen bonding (Scheme 4).

For the iodobenzenes, we find that the overall charge on R–I is just about equal to the sum of the charge changes on the  $C_i$  and I atoms, and halogen bonding with iodoarenes thus is mostly a local event of the  $C^{\delta-}-I^{\delta+}$  bond, with only a slightly higher

**Scheme 4.** Halogen Bonding Mechanism for Iodoarenes

change in  $|q(\text{C}_i)|$  than in  $|q(\text{I})|$ . On the other hand, halogen bonding is a nonlocal event in the iodoacetylene. In this case, the  $C^{\delta-}-I^{\delta+}$  polarization is stronger to begin with but the synergistic effect is less pronounced. In particular, there is *much less* buildup of negative charge at  $C_i$  upon halogen bonding.

The nonrelativistic GIAO calculations showed an increase in the chemical shift of  $C_i$  upon complexation. The charge analysis reveals that this chemical shift increase occurs *despite* the increased negative charge on carbon. Only the SO contributions decrease the chemical shift of  $C_i$ .

## Conclusion

Solvent effects on the  $^{13}\text{C}$  NMR spectra of para-disubstituted acetophenone azines  $X-C_6H_4-CMe=N-N=CMe-C_6H_4-Y$  are generally small. Independent of the choice of the solvent, hardly any electronic communication is found between the two halves of the unsymmetrical azines, and the spectroscopic properties of the symmetrical azines carry over to the unsymmetrical azines. Our previous  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectroscopic study of azines in chloroform suggested that the azine bridge functions as a “conjugation stopper”, and the results presented here provide important corroboration. Hence, one of our important assumptions for the design of polar materials, the assumption that the azine bridge functions as a “conjugation stopper”, is now firmly established by both theory and experimentation.

In the absence of evidence for solute–solvent interactions in the NMR spectra of the haloarenes, the question occurs as to whether there are no specific interactions or, if specific solvation occurs, why there is no manifestation of the specific solvation in the chemical shifts. The complexation of iodoarenes by DMSO was studied as iodine bonding should be one of the stronger intermolecular interactions and because of the prior evidence that DMSO complexation does cause NMR shifts for some iodides.

DFT and MP2 theory show the same characteristics of the iodine bonding between iodoarenes and DMSO, and similar structures are obtained with the following features: (1) The  $O\cdots I$

distances in all complexes are close to 2.9 Å and about 0.6 Å shorter than the sum of the van der Waals radii. (2) The DMSO–oxygen approaches the C–I bond in a “head-on” fashion with  $\angle(\text{O}\cdots\text{I}-\text{C})$  angles  $\Gamma$  close to 180°. (3) The  $\angle(\text{S}-\text{O}\cdots\text{I})$  angles  $\Omega$  are in the range 125–135°, and there is general agreement that the O=S bond is coordinated in a side-on fashion so that the DMSO oxygen can orient  $n$ -electron density toward iodine. The binding energies show some dependencies on the method and the basis set, and there clearly is a need for measurements of binding energies. Our best levels suggest a binding energy of about 3 kcal/mol per iodide–DMSO contact. The population analysis shows the halogen bonding between iodobenzene and DMSO to be a local event. Iodine–DMSO bonding largely is a dipole–dipole interaction which is synergistically reinforced by  $\text{C}^{\delta-}-\text{I}^{\delta+}$  and  $\text{O}^{\delta-}-\text{S}^{\delta+}$  bond polarity increases upon halogen bonding.

Good agreement is generally achieved between the measurements and the nonrelativistic GIAO NMR chemical shift computations with both the MP2 and B3LYP methods. However, neither method reproduces the experimental chemical shift of  $\text{C}_i$  attached to iodine because of the neglect of the spin–orbit-induced heavy atom effect of iodine in the nonrelativistic GIAO calculations. We computed the SO corrections for the  $\text{C}_i$  atoms, and these corrections bring the computed  $\text{C}_i$  shifts in much better agreement with experiment. The nonrelativistic shifts increase by about 6–8 ppm upon complexation by DMSO. In most cases, these positive coordination shifts are offset by the change in the SO contributions, which are more negative for the DMSO complexes than for the free molecules. The two

effects compensate each other, and halogen bonding thus has no apparent effect on  $\text{C}_i$  in the iodoarenes.

For the iodides, complexation by DMSO occurs and may or may not manifest itself in the NMR spectra. Halogen bonding by other halides is weaker and less likely in solution; there are no reports of complexation effects on their NMR spectra, and we have not observed any such effects in the present study. In any case, the absence of complexation shifts in the NMR spectra does not exclude the occurrence of halogen bonding.

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**Supporting Information Available:** Four figures showing the HMQC, <sup>13</sup>C NMR, APT, and the DEPT spectra of **4** in DMSO, two tables with measured NMR data of the symmetrical azines and the model compounds, four figures showing models of optimized structures (B3LYP and MP2, isolated and complexed), two tables providing the total energies and thermochemical data and binding energies, respectively, and one table of computed NMR shifts (PDF). This material is available free of charge via the Internet at <http://pubs.acs.org>.

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