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Communication

# Solvent effects on halogen bond symmetry

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**The symmetric arrangement of the iodine and bromine centred 3-center-4-electron halogen bond is revealed to remain preferred in polar, aprotic solvent environment. Acetonitrile is unable to compete with pyridine for halogen bonding; however, its polarity weakly modulates the energy of the interaction and influences IPE-NMR experiments.**

## Introduction

Halogen bonding is the noncovalent interaction of halogens in which they act as electron acceptors.[1] The phenomenon was first reported one and a half centuries ago by Guthrie[2] and subsequent studies in the gas-phase,[3] in the solid state,[1] *in silico*,[4] and in solution[5] revealed its immense potential for applicability in supramolecular chemistry[6] and in medicine,[7,8] for example. In the exploration of its proposed utility as a molecular tool complementary to hydrogen bonding,[1,9] the thorough understanding of its properties, especially with regard to its similarities and differences to hydrogen bonding is of critical importance.

The strongest halogen bond so far has been reported for the triiodide ion.[1] The valence shell of the central halogen ($X^+$) of trihalide ions ($X_3^-$) possesses the electron configuration $s^2p^4$ with the p-orbitals being occupied in the spin paired $p_x^2p_y^2p_z^0$ arrangement, induced by the electrostatic field of the two Lewis basic halides ($X^-$).[10] The empty $p_z^0$ orbital is capable of efficient interaction with two Lewis basic electron donors, here two halide ions, in a linear arrangement. It should be noted that the $X^+$ of the $X_3^-$ complex is formally not a halonium ion, but a halogen(I) complexing to two halide ions that each contribute to the triatomic system with an electron pair, yielding a 3-center-4-electron system. A trihalide ion, and in general all systems encompassing a positively charged halogen (here $I^+$) and two identical electron donor functionalities (here $I^-$), can arrange in an asymmetric (*a*) or in a symmetric (*b*) linear geometry (Fig. 1).[11,12] The asymmetric arrangement (*a*) corresponds to a linear system encompassing a stronger and shorter covalent bond (I-I), and a weaker and longer conventional halogen bond (I···I). This geometry is best described by a double-well potential (Fig. 2a) which itself is symmetric, but it originates from an asymmetric atomic arrangement. The symmetric geometry (*b*) is interpretable as a molecular system comprising of two equal halogen bonds giving rise to a 3-center-4-electron system that corresponds to a single well potential (Fig. 2b). In both geometries, the central $I^+$ is shared between the two donor atoms ($I^-$), yet in an energetically different manner; the first is a mixture of two rapidly exchanging tautomers, $[\text{I-I}\cdots\text{I}]^-$ and $[\text{I}\cdots\text{I-I}]^-$, whereas the latter is a static, symmetric structure, $[\text{I}\cdots\text{I}\cdots\text{I}]^-$.[11, 12] These arrangements may have different chemical properties resulting in different reaction dynamics, rates and yields. For the closely related[1] hydrogen bonds, the corresponding symmetric arrangement was proposed to possess unusual strength[13] and was therefore frequently entitled "short-strong", "low-barrier" bond that was anticipated to play a key role in enzyme catalysis and in stabilizing intermediates.[14] In this context, the unusual strength (180 kJ/mol) of the halogen bond of $I_3^-$ may originate from a particularly short and strong symmetric halogen bond (*b*) or may alternatively be explained by resonance stabilization (*a*). In either case, the exceptional strength of the 3-center-4-electron halogen bond makes $I^+$ the strongest known halogen bond donor.

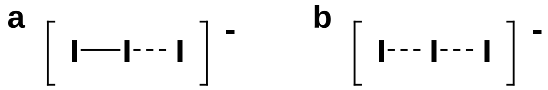


**Figure 1.** The possible symmetric and asymmetric arrangements of halogen bonding, shown on the example of the triiodide ion.

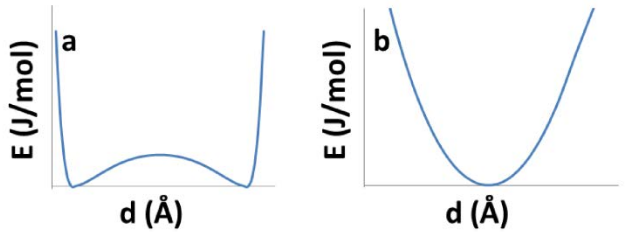


**Figure 2.** Possible energy potentials for the halogen motion in a 3-centered-4-electron system: (a) double-well, and (b) single-well.

The triiodide ion was reported to be symmetric in the gas phase, but both symmetric ($d_{\text{I-I}}$=2.90 Å)[15, 16] and asymmetric ($d_{\text{I-I}}$=2.83 and 3.03 Å)[17-20] in the solid state, suggesting that its geometry depends on its environment. Whereas the symmetry of $I_3^-$ was straightforwardly assessed in the solid state by x-ray crystallography, the investigation of its behaviour in solutions is more challenging. It has so far been attempted *in silico*[21-29] and by Raman[30-33] and femtosecond[34-37] spectroscopic techniques. Computation predicts solvent dependent symmetry.[21,23,25,29] Hence, the symmetric geometry in nonpolar solutions is predicted to be desymmetrized by hydrogen bond donors and possibly by polar nonprotic solvents.[27,28] Stabilization of the more polar geometry by a polar environment may explain the latter. This argument is in line with the disputed[38] suggestion that the symmetry of the related 3-center hydrogen bond might be affected by solvent polarity.[39] For $I_3^-$ the asymmetric geometry in polar, hydrogen bond donor solvents was confirmed by detection of moderate intensity antisymmetric Raman stretches indicative of symmetry breakage[30] and thus a double-well potential.[27,28] Raman and infrared spectra reflect a symmetric arrangement in nonpolar solvents;[28] however, contradictory opinion has also been expressed.[40] The geometry of $I_3^-$ in the non-hydrogen-bonding, polar acetonitrile remains, however, ambiguous; although no direct sign of asymmetry was observed, Johnson and Myers concluded that the Raman spectroscopic data is consistent with both a low barrier flipping of two identical states (*a*) and a static, symmetric geometry (*b*).[31] In similarity to other conventional spectroscopic techniques, the time scale of Raman spectroscopy makes it incapable of differentiating tautomers (*a*) interconverting with a rate constant of at least 0.5 ps from a static structure (*b*). The interpretation of Johnson and Myers was supported by the theoretical work of Margulis *et al.*, who proposed that the system is best described by a double-well potential with a high energy barrier for flipping in hydrogen bonding solvents, but by a double-well with a low barrier allowing dynamic averaging (*b*) or possibly with no barrier (*a*) for the acetonitrile solution.[27] Originating from the limitations of standard spectroscopic techniques, the symmetry of $I_3^-$ and in general of three-center halogen bonding in polar, nonprotic solvents remains to be determined unambiguously.

The NMR technique isotopic perturbation of equilibrium (IPE) has been demonstrated to be capable of distinguishing a static symmetric structure from rapidly interconverting asymmetric tautomers[41] and has successfully been utilized for solution studies of hydrogen[41-43] and halogen[11,12] bond symmetry. It requires selective isotopic labelling, which is not feasible for trihalide ions. Bis(pyridine)halonium ions provide a versatile model for exploration of the properties of 3-center-4-electron halogen bonds in solution, with available synthetic routes to their $^2$H-labeled analogues suitable for IPE experiments.[11,12] In this study, the effect of solvent polarity on halogen bond symmetry has been assessed making use of this model system.

## Results and discussion

Bis(pyridine)halonium triflates and their selectively deuterated analogues (Fig. 3) were synthesized following published procedures.[11, 12] Deuterium isotope effects were measured by acquisition of $^{13}C\{^1H,^2H\}$ NMR spectra of a *ca* ~1:1 mixture of isotopologues dissolved in $CD_2Cl_2$[12] or $CD_3CN$ (20 mg in 0.6 mL) and were calculated as the difference of the chemical shift of the signals of the deuterated and the nondeuterated analogues (Fig. 4). The observed isotope shift, $^{n}\Delta_{obs}$, is the sum of the intrinsic isotope shift, $^{n}\Delta_0$, and the equilibrium isotope shift, $^{n}\Delta_{eq}$, where *n* denotes the number of intervening bonds between the site of the $^1$H-to-$^2$H substitution and the investigated carbon; i.e. for C3 it is $^{2}\Delta_{obs}$. Whereas $^{n}\Delta_{obs} = {}^{n}\Delta_0$ for static structures, it is the sum of $^{n}\Delta_0$ and $^{n}\Delta_{eq}$ for systems in rapid tautomeric equilibrium.[11,12] Originating from the temperature dependence of solvent polarity[42] that modulates the electron density of the nitrogen lone pair of pyridine, the magnitude of $^{n}\Delta_0$ is slightly temperature dependent. However, the temperature dependence of $^{n}\Delta_{eq}$ is greater as it reflects the temperature induced alteration of the equilibrium constant, K, of the tautomerisation process according to $^{n}\Delta_{eq} = D(K-1)/[2(K+1)]$, where *D* is the chemical shift difference of the signals of the tautomeric forms. This different extent of temperature dependence of $^{n}\Delta_{obs}$ of a static geometry and a closely related rapidly equilibrating tautomeric system is generally applicable for their distinction.

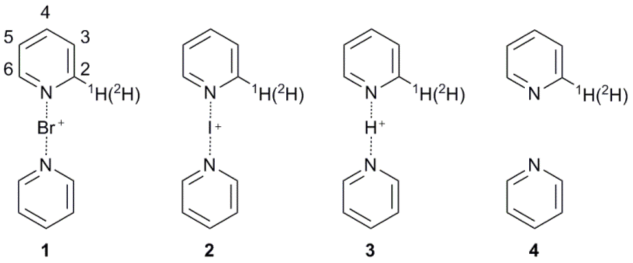


**Figure 3.** The model systems assessed for elucidation of the effect of solvent on the symmetry of the bromine (**1**) and iodine (**2**) centred halogen bond. The hydrogen bonded analogue (**3**) and pyridine (**4**) were utilized as references for an equilibrating mixture and a static analogue.

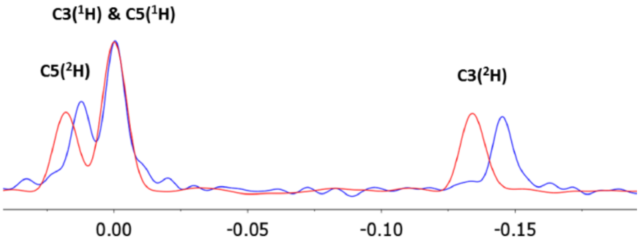


**Figure 4.** Overlaid $^{13}C\{^1H,^2H\}$NMR spectra of the C3/C5-region of pyridine/2-deuteropyridine (1:1, blue) and pyridine/2-deutero-pyridine/triflic acid (1:1:1, red) in acetonitrile acquired at 125.71 MHz. The isotope shifts were measured as the chemical shift difference of the corresponding signals of the deuterated and nondeuterated signals, thus for the C3 position $^{2}\Delta = \delta C_{(2H)} - \delta C_{(1H)}$. Atom numbering is shown in Fig. 3. Following literature convention,[43] the chemical shift of C3($^1$H) and C5($^1$H) are set to zero for both samples to ease visual comparison.

As part of our on-going studies for gaining an improved understanding of halogen bonding, the temperature dependence of the isotope shifts of bis(pyridine)bromonium (**1**) and iodonium

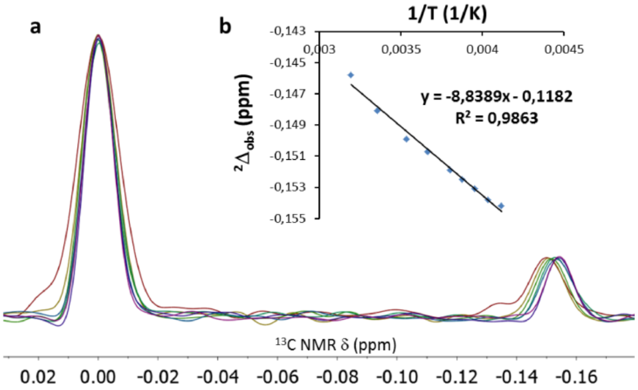


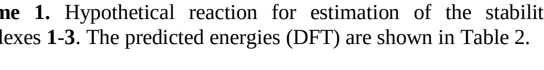
**Figure 5.** (a) Temperature dependence of the isotope shift of C3 of **2**. The $^{13}C\{^1H,^2H\}$ NMR spectra at nine temperatures between 243 and 313 K are shown expanded about the frequencies of C3($^1$H) to the left, and C3($^2$H) to the right. Following literature conventions,[43] the signal of C3($^1$H)/C5($^1$H) is set to zero for visualization of the alteration. (b) The corresponding 2-bond isotope effect ($^{2}\Delta_{obs}$) *vs.* reciprocal temperature plot is shown along with the regression parameters.

**Table 1.** Temperature coefficients $\Delta^2\Delta_{obs}/(1/\Delta T)$ observed for C3, given in $10^{-3}$ ppb/K, over the temperature range of -80 – +25 C° for $CD_2Cl_2$, and of -30 – +70 C° for $CD_3CN$ solutions.[a]

| Structure | $CD_2Cl_2$ | $CD_3CN$ |
|---|---|---|
| **1** | -6.4 ± 0.015 | -11.2 ± 0.005 |
| **2** | -6.4 ± 0.018 | -8.8 ± 0.005 |
| **3** | -9.8 ± 0.001 | -9.1 ± 0.006 |
| **4** (pyridine) | -4.8 ± 0.022 | -9.6 ± 0.005 |

[a]The standard error of the slopes was estimated with two-variable regression using the LINEST function of MS Excel.

(**2**) triflates were acquired in acetonitrile and were compared with those observed for dichloromethane solutions. Similar to previous studies, a mixture of pyridine and 2-*d*-pyridine (**4**) was used as a reference for a static structure, and the structurally closely related N-H···N complex **3** was applied as reference for a structurally closely related system in equilibrium, based on the previous knowledge that N-H-N hydrogen bonded systems exist as tautomeric mixtures in solutions.[38,44] Temperature coefficients $\Delta^n\Delta_{obs}/(1/\Delta T)$ were determined from the slopes of $^n\Delta_{obs}$ *vs.* reciprocal temperature plots (Fig. 5, ESI). In agreement with the reported observation that the isotope effect measured at the C3 position of pyridines reflect the electron density variation of the pyridine nitrogen best,[45] the largest temperature dependence of the isotope shift was observed for this position. For example, over a temperature range of 100 K, the temperature dependence of the secondary isotope effect of **1** in $CD_3CN$ was determined to $^1\Delta_{obs}$ -5.9 ppb/K, $^2\Delta_{obs}$ -11.2 ppb/K, $^3\Delta_{obs}$ 1.1 ppb/K whereas $^4\Delta_{obs}$ was undetectably small. Moreover, the temperature coefficients $\Delta^n\Delta_{obs}/(1/\Delta T)$ of the C3 position provided the most reliable data as reflected by the ≥0.98 correlation coefficients of the corresponding $^n\Delta_{obs}$ *vs.* $1/T$ plots of **1**-**4** (ESI). Consequently, for assessment of the symmetry of **1** and **2**, the temperature dependence of $^2\Delta_{obs}$ measured on C3 was acquired for **1**-**4** for their nonpolar, aprotic $CD_2Cl_2$[12] and for their polar, nonprotic $CD_3CN$ solutions (Table 1). The $\Delta^2\Delta_{obs}/(1/\Delta T)$ of **1** and **2** in $CD_2Cl_2$ solutions are significantly lower than of **3** indicating a static symmetric structure in solution. On the contrary, the temperature coefficients obtained for $CD_3CN$ solutions are similar and high for **1**-**4**. Unexpectedly, the temperature coefficient observed for pyridine (**4**) C3 is comparable to that of **3.** This observation suggests that the temperature dependence of the isotope effects here is influenced by additional factors. A plausible explanation may be provided by the several times larger temperature dependence of the dielectric constant of polar liquids as compared to those of nonpolar ones.[46] The dielectric constant of acetonitrile is highly temperature dependent.[47] The electron density of the nitrogen lone pair is affected by the alteration of the polarity of the environment, which in turn may influence the magnitude of the isotope effect in a temperature dependent manner for **1**-**4**.[11] Moreover, the temperature coefficients observed for **1**-**3** may additionally be modulated by competition of the Lewis basic solvent for coordination to the positively charged halogen or proton, as it has been reported for closely related complexes.[48]



**Scheme 1.** Hypothetical reaction for estimation of the stability of complexes **1**-**3**. The predicted energies (DFT) are shown in Table 2.

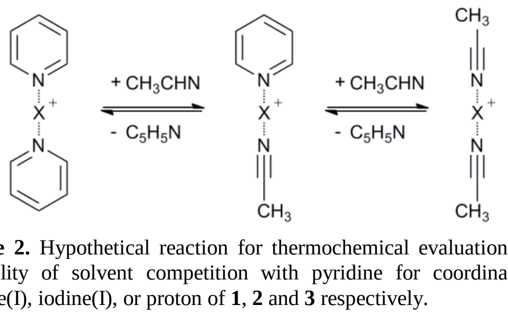
**Table 2.** Computationally predicted N-X and N-N distances (Å) and stabilities (kJ mol$^{-1}$) for the equilibrium geometries of **1-4** in $CH_2Cl_2$ and $CH_3CN$, computed for the process shown in Scheme 1.[a]

| Structure | Solvent | $d_{N(1)-X}$ | $d_{N(2)-X}$ | $\Delta E$ | $\Delta G$ |
|---|---|---|---|---|---|
| **1** | $CD_2Cl_2$ | 2.139 | 2.139 | -180.5 | -126.6 |
|  | $CD_3CN$ | 2.139 | 2.139 | -207.7 | -149.5 |
| **2** | $CD_2Cl_2$ | 2.301 | 2.301 | -167.8 | -105.1 |
|  | $CD_3CN$ | 2.301 | 2.301 | -197.5 | -134.3 |
| **3** | $CD_2Cl_2$ | 1.078 | 1.678 | -94.8 | -39.1 |
|  | $CD_3CN$ | 1.076 | 1.689 | -122.3 | -77.4 |

[a]Calculations were done at the B3LYP level along with PCM. Details are given in the ESI. $\Delta E$ denotes the pure electronic energy and $\Delta G$ the Gibbs free energy at 298 K.

To gain further insights, the equilibrium geometries and energies of **1**-**3** (Scheme 1)were calculated with DFT applying the B3LYP exchange and correlation functional following a previously described protocol[12] using the Gaussian09 program package (for details, see the ESI). The validity of DFT for N-X-N complexes was confirmed by reference calculations on the MP2 level.[12] Solvent effects were accounted for by the Polarizable Continuum Model (PCM)[49,50] with $CH_2Cl_2$[12] or $CH_3CN$ as solvent. For assessing specific solvent coordination, explicit $CH_3CN$ molecules were utilized. The symmetric equilibrium geometry of **1** and **2** reported for dichloromethane solution[11, 12] is predicted to remain unaffected upon changing the solvent to acetonitrile. The N-X bond lengths (Table 2) are inviolate. This result is in good agreement with the largely intact IR spectrum of **1** and **2** upon changing the solvent from $CH_2Cl_2$ to $CH_3CN$,[51] with the Raman spectroscopic data of Johnson and Myers[31] and the Monte Carlo simulations of Lynden-Bell *et al.*[27]

Whereas $CH_2Cl_2$ presumably does not interact with **1** and **2**, $CH_3CN$ is a Lewis base present in large excess as compared to pyridine in the solutions that were experimentally examined. The interaction of $CH_3CN$ with closely related [N-Ag-N]$^+$ complexes was shown to be non-negligible and to influence significantly the NMR chemical shifts.[48] Therefore, the ability of $CH_3CN$ to compete with pyridine for coordination to the $p_z$ orbital of $X^+$ of **1** and **2** was evaluated by computational thermochemical analysis. Calculations were performed at the B3LYP level using the $CH_3CN$ continuum solvent model with the computational details given in the ESI. The hypothetical reaction of exchanging a pyridine with acetonitrile (Scheme 2) is predicted to be endothermic with Gibbs free energies, $\Delta G$, +42.8 and +50.4 kJ/mol at 298 K, for complexes **1** and **2**, respectively, revealing that that the solvent is unlikely to directly interact with the halogen(I). On the contrary, the corresponding $\Delta G$ of +8.6 kJ/mol for **3** suggests a likely ligand exchange in $CH_3CN$ at room temperature.



**Scheme 2.** Hypothetical reaction for thermochemical evaluation of the probability of solvent competition with pyridine for coordination to bromine(I), iodine(I), or proton of **1**, **2** and **3** respectively.

**Table 3.** $^{15}N$ NMR chemical shifts, and $^{1}H$ and $^{19}F$ NMR translational diffusion coefficients. Experimental details are given in the ESI.

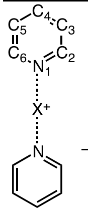
| Structure | Solvent | $\delta_{15N}$ (ppm) | $\Delta^{15}N^{coord}$ (ppm) | $D_{1H} \times 10^{-10}$ ($m^2/s$) | $D_{19F} \times 10^{-10}$ ($m^2/s$) |
|---|---|---|---|---|---|
| **1** | $CD_2Cl_2$ | -143 | -76 | 13.9 | 14.2 |
| | $CD_3CN$ | -145 | -81 | 12.3 | 6.5 |
| **2** | $CD_2Cl_2$ | -175 | -108 | 14.0 | 15.0 |
| | $CD_3CN$ | -174 | -110 | 8.2 | 6.3 |

This in turn is expected to influence the IPE experiments. The existence of the bis(acetonitrile) complex in solution is less probable, with predicted Δ*G*'s for the second step in Scheme 2 being +106.7 (**1**), +75.9 (**2**) and +92.9 kJ/mol (**3**). The absence of solvent competition for the halogen bonded systems is supported by the experimental observation of virtually identical $^{15}N$ NMR chemical shifts of **1** and **2** in $CD_2Cl_2$ and $CD_3CN$ (Table 3), and in addition by the computationally predicted solvent independent electron densities of the complexes (Table 4). A significant extent of solvent competition for coordination is expected to yield larger chemical shift changes, as it was shown for closely related metal complexes.[48] In agreement with our expectations, attempts at computational generation of tri-and tetracoordinated mixed pyridine-acetonitrile halonium complexes analogous to those reported for silver(I)[48] were fruitless. Thus, acetonitrile is unable to destabilize bis(pyridine)halonium complexes and has no direct influence on their geometry.

Previous investigation of closely related silver complexes demonstrated that $CH_3CN$ considerably better solubilizes the counter ion triflate than $CH_2Cl_2$.[48] The translational diffusion coefficients of the $[N\text{-}X\text{-}N]^+$ and $OTf^-$ sites of **1** and **2** (Table 3), observed by $^{1}H$ and $^{19}F$ NMR, respectively,[11] indicate weak coordination of triflate to the positively charged site in the polar $CD_3CN$, whereas tight complexation in the apolar $CD_2Cl_2$. The comparable diffusion coefficients of $OTf^-$ of **1** and **2** in $CD_3CN$ suggests independent diffusion of the counter ion from the bis(pyridine)halonium ion in this solvent. Correspondingly, the halogen(I) of bis(pyridine) halonium complexes is expected to be easier accessible for reactants in more polar solutions.

The magnitude of coordination shifts, defined as the difference between the chemical shift of a ligand in its complex and its free state ($\Delta^{15}N_{coord} = \delta^{15}N_{complex} - \delta^{15}N_{ligand}$), is a commonly used experimental indicator of interaction strength.[48, 52] Observation of an approximately 30% larger $^{15}N$ chemical shift change upon complexation of iodine(I) as compared to bromine(I) (Table 3) reveals that the I > Br trend for halogen bond donor strength previously described for 2-center halogen bonds[1] are valid for the 3-center bonds as well. It should be emphasized that the *ΔG*s given in Table 2 describe the energy gain associated with the formation of bis(pyridine)halonium triflate complexes according to the process shown in Scheme 1. Being influenced by additional factors than the formation of the $[N\text{-}X\text{-}N]^+$ bond itself they should not directly be interpreted in terms of halogen bond strength. A more negative *ΔG* upon formation of **1** than of **2** simultaneously reflects the overall energy gain upon formation of the $[N\text{-}X\text{-}N]^+$ bonds, the energetic consequences of the dissociation of the Br-OTf and I-OTf bonds, of charge delocalization and of the changes in solvation. In the attempts of generation of multicoordinated halogen(I) complexes, similar to those observed for silver(I),[48] a higher preference of $OTf^-$ for coordination to the partially positively charged aromatic system of the pyridines of **1** and **2** (Table 4) over coordination to their halogens was seen. Hence, the more negative *ΔG* of formation of **1** as compared to **2**, shown in Table 2, may as well reflect an indirect energetic consequence of a larger degree of charge delocalization of **1** as compared to **2** (Table 4). Keeping these arguments in mind, the thermodynamic data of **1** and **2** given in Table 2 still points towards the higher strength of 3-center-4-electron halogen bonds as compared to the corresponding neutral, 2-center-2-electron halogen bond interactions. Accordingly the predicted N-Br (2.1 Å) and N-I (2.3 Å) bond lengths are significantly closer to the sum of the covalent (**1**, 1.9 Å; **2**, 2.1 Å) than the sum of the van der Waals radii (**1**, 3.4 Å; **2**, 3.5 Å) of the involved atoms. Strong, charge transfer driven halogen bonding was previously reported by Lu *et al.* for negatively charged complexes.[53]

**Table 4.** Computationally predicted charges for the equilibrium geometries of **1** and **2**.

| Structure | | **1** | | **2** | |
|---|---|---|---|---|---|
| Solvent | | $CH_2Cl_2$ | $CH_3CN$ | $CH_2Cl_2$ | $CH_3CN$ |
|  | N1 | -0.47053 | -0.47094 | -0.52306 | -0.52306 |
| | C2 | +0.10174 | +0.10116 | +0.09959 | +0.09959 |
| | C3 | -0.21216 | -0.21336 | -0.21378 | -0.21378 |
| | C4 | -0.11950 | -0.12076 | -0.11881 | -0.11881 |
| | C5 | -0.21216 | -0.21336 | -0.21378 | -0.21378 |
| | C6 | +0.10174 | +0.10116 | +0.09959 | +0.09959 |
| | Sum: | -0.81087 | -0.81610 | -0.87025 | -0.87729 |
| | X | +0.27893 | +0.27859 | +0.41110 | +0.41116 |

Providing important insights for the fundamental understanding and the broad utility of halogen bonding, the solvent dependence of its stability became the subject of intense debates. Conventional 2-center halogen bonds are commonly assumed to be weakened by polar media, based on the electrostatic interpretation of halogen bonding that has certain theoretical[54] and experimental[55] support. However, the solvent dependence of the strength of halogen bonding is more complex. Blackstock and co-workers reported the Br···N halogen bond of the $CBr_4$···DABCO complex to show the solvent dependent strength order of $CH_3CN > CHCl_3 > CH_3OH$, with association constants 4.2, 1.7 and 0.06 $M^{-1}$ in the three solvents, respectively.[56] This data may be interpreted by the neutral complex being more stable in polar, nonprotic acetonitrile than in apolar chloroform and being destabilized by a hydrogen bond donor solvent, such as methanol. In Taylor's work,[57] the $Et_3N \cdots IC_8F_{17}$ halogen bond was disclosed to be critically weakened in competitive hydrogen bond donor solvents and show only minor solvent polarity dependence; no significant difference in halogen bond strength was seen for the $CH_2Cl_2$ and $CH_3CN$ solutions, for example. The interaction strength of the iodoalkyne model system of Goroff and co-workers showed only small dependence on solvent polarity and correlated better to bulk solvent basicity.[58] The computational work of Lu and co-workers[53] suggest an increased interaction strength for neutral ($R\text{-}I \cdots OH_2/NH_3$) whereas decreased for negatively charged ($R\text{-}I \cdots X^-$) halogen bonding complexes upon an increase in solvent polarity. Destabilization of the charged systems of Lu *et al.* is to a large degree accountable to the improved solubilisation of the negatively charged halide ion in more polar media. The diffusion NMR data (Table 2) of the $[N\text{-}X\text{-}N]^+$ $OTf^-$ complexes discussed herein indicates analogous trend, i.e. a larger degree of dissociation in the more polar $CD_3CN$ is interpretable as the consequence of an improved solvation of charged species in the polar solvent as compared to $CD_2Cl_2$. Importantly, owing to ultimate structural differences, the halogen bond of the $R\text{-}I^{\cdots}X^-$ complex studied by Lu *et al*. becomes destabilized upon the increased solvation of the charged interaction partner ($X^-$), whereas the 3-center halogen bond of $[N\text{-}X\text{-}N]^+$ $OTf^-$ is not directly affected by solvation of the counter ion, $OTf^-$. However, better solvation of $OTf^-$ is expected to provide a more accessible halogen(I) for **1** and **2** in more polar environment. Accordingly, **1** and **2** were observed to be significantly more stable in $CD_2Cl_2$ as compared to $CD_3CN$ solution, with half times of decomposition being weeks as compared to days, respectively. Decomposition is catalysed by humidity making the higher hygroscopicity of $CD_3CN$ as compared to $CD_2Cl_2$ presumably play an additional role in this process. It should be emphasized a second time that the $\Delta G$s given in Table 2 are not directly interpretable in term of halogen bond strength as they reflect formation energies of bis(pyridine)halonium triflate complexes according to Scheme 1 and not purely the dissociation of an $N^{\cdots}Br/I$ bond. The $\Delta^{15}N_{coord}$s observed for the $[N\text{-}X\text{-}N]^+$ complexes in $CD_2Cl_2$ and $CD_3CN$ solutions (Table 3) indicates comparable halogen bond strengths in the two solvents, with a slight, barely significant strengthening of the N-X interaction in $CD_3CN$. This data is in good agreement with the above discussed observations of Blackstock,[56] Taylor,[57] and Goroff[58] and the suggestion that increased solvent polarity is prone to stabilize polar molecular arrangements[59] such as charge transfer complexes.[60, 61] Importantly, the above conclusion should not be generalized to structurally unrelated halogen bonding systems, but rather reflect the need for thorough, well-thought through assessment of the interplay of electrostatic, charge transfer and dispersion forces along with solvation and solvent competition for evaluation of solvent effects on a specific type of halogen bonding.

## Conclusions

A strong preference for a linear, symmetric arrangement of the 3-center-4-electron halogen bond in the polar, aprotic solvent $CH_3CN$ is shown. The predicted single-well energy potential of the studied N-X-N system is in agreement with the conclusions drawn for the isoelectronic $I_3^-$ by Raman spectroscopy. [27,29,31] Acetonitrile is unable to destabilize the 3-center halogen bond; however, due to its polarity slightly modulates the energy of the interaction as well as the solubilisation of the counter ion. This observation is significant as it may explain the reported need for careful solvent optimization for successful utilization of Barluenga's reagent; for particular examples changing the solvent from $CH_2Cl_2$ to $CH_3CN$ was reported necessary for the reaction to proceed.[62] As neither the N-X-N bond lengths nor the charge distribution of the bis(pyridine)halonium complexes are affected by a more polar solvent, the different reactivity in the two media may be best explained by an altered degree of solvation and a consequent charge separation providing easier access to the halogen(I) in $CH_3CN$.

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## References and Notes

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