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Isothermal Calorimetric Titrations on Charge-Assisted Halogen Bonds: Role of Entropy, Counterions, Solvent, and Temperature

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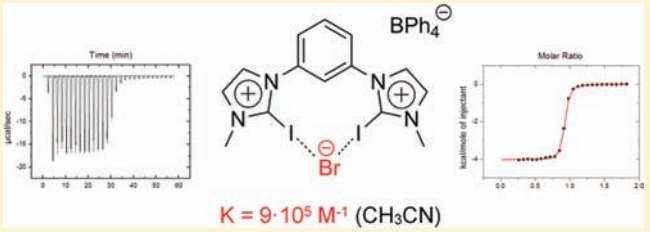
Supporting Information

ABSTRACT: We have conducted isothermal calorimetric titrations to investigate the halogen-bond strength of cationic bidentate halogen-bond donors toward halides, using bis(iodoimidazolium) compounds as probes. These data are intended to aid the rational design of halogen-bond donors as well as the development of halogen-bond-based applications in solution. In all cases examined, the entropic contribution to the overall free energy of binding was found to be very important. The binding affinities showed little dependency on the weakly coordinating counteranions of the halogen-bond donors but became slightly stronger with higher temperatures. We also found a marked influence of different solvents on the interaction strength. The highest binding constant detected in this study was 3.3×10^6 M^{-1}.



INTRODUCTION

Weak non-covalent interactions called "halogen bonds"[1,2] (XBs) occur between Lewis bases and compounds which feature an electrophilic halogen substituent. The latter is usually achieved by using strongly electron-withdrawing perfluorinated backbones.[2] Alternatively, cationic core structures have also been employed occasionally[3] in order to design strong XB donors (i.e. halogen-based Lewis acids). Halogen bonds find their main use in *crystal engineering*, and fittingly investigations regarding XBs have mostly been performed in the solid state.[4] In these cases, the strength of the bond was usually inferred by the amount to which the interaction distance falls below the sum of the van der Waals radii of the involved atoms.[4] Although the occurrence of XBs in solution[5] (and in the gas phase)[6] is also well established, relatively few applications based on XBs in solution have been developed so far.[7]

Determinations of the XB interaction strength in solution have mostly been limited to isolated, scattered cases,[8] with only very few systematic studies.[9] The overwhelming majority of these measurements were performed on neutral XB donors, especially elemental bromine or iodine. To be precise, more than 600 interaction free energies have been determined for XBs with iodine in alkanes at 298 K,[9c] with typical binding constants in the range of $K \approx 0.5-1000$ M^{-1}. The strongest such interaction was found for the complex of iodine with quinuclidine ($K = 1.6 \times 10^5$ M^{-1}).[10a] In contrast, only about a dozen such data are known for XB donors with a carbon backbone (all of them being neutral compounds).[11] Typical binding constants for such interactions are in the range $K \approx 5-100$ M^{-1},[11] and the maximal value of $K = 1.9 \times 10^4$ M^{-1} was obtained for the binding of chloride to a tridentate XB-based receptor introduced by Taylor and co-workers.[7b] For charge-assisted XBs between cationic XB donors and neutral or anionic Lewis bases, to the best of our knowledge only one set of binding constants is presently known:[10b,c] the interaction of halides with a bidentate bromo-imidazoliophane receptor reported by Beer et al. The binding of this receptor to bromide corresponds to a binding constant of $K = 889$ M^{-1} in CD_3OD/D_2O (9:1) at 295 K.[7e]

We have recently introduced bis(haloimidazolium)-based activators for the solvolysis of benzhydryl bromide, which served as a test substrate for C–X bond activation.[7f] These activators presumably act through the formation of an XB complex with the substrate and/or the liberated bromide, providing additional driving force for the overall reaction. Very little is known, however, about the thermodynamics of XB complex formation involving cationic XB donors in solution, as already indicated above. Open questions include the relative contributions of enthalpy and entropy, as well as the dependency of the interaction strength on the counteranions, solvent, and temperature. In general, means to maximize the interaction strength[12] would provide a solid basis for the rational application of cationic XB donors for various applications, including the C–X bond activation of diverse systems (which represents one of our long-term goals). In the following, we aim to address these open questions by isothermal titration calorimetry (ITC),[13,14] using our previous XB donors[7f] as probes (see Scheme 1).

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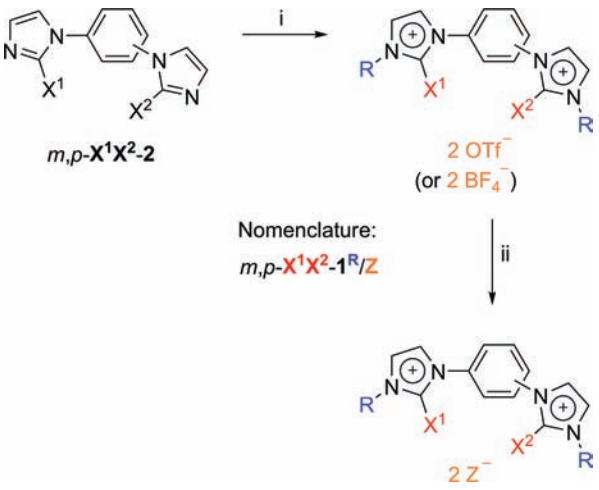
Scheme 1. Synthesis and Derivatization of Bis(haloimidazolium)-Based Halogen-Bond Donors[a]



[a]Reagents and conditions: (i) 2 equiv of ROTf, CH_2Cl_2, or 2 equiv of Me_3OBF_4, CH_2Cl_2; (ii) 2 equiv of NaZ, MeOH. For yields of previously unkown compounds, see Supporting Information. X^1, X^2 = Br, I, H; R = methyl, octyl; Z = PF_6^-, BPh_4^-.

RESULTS AND DISCUSSION

Derivatization of XB Donors. An important prerequisite for these investigations was the further derivatization of our imidazolium-based XB donors **1** so that the solubility of the compounds could be increased and the available range of counteranions could be broadened (Scheme 1). Thus, while our previous *N*-bis(methylated) XB donors were reasonably soluble only in acetonitrile, acetone, DMSO, and water, introducing octyl substituents at the external imidazolium nitrogens dramatically increased the solubility in DCM and THF (while, expectedly, reducing the solubility in water). As we had seen a counterion effect in the activation of benzhydryl bromide (with the tetrafluoroborate salt being more active than the triflate one),[7f] we also exchanged the triflate counterions with PF_6^- and BPh_4^- by anion metathesis in methanol. With these variably modified XB donors in hand, the basis for our calorimetric measurements was set.

Role of Entropy and First Assessment of Binding. Table 1 shows binding constants (translating in free energies ΔG^0) and stoichiometry coefficients (n) as well as ΔH^0 and ΔS^0 values for various complexes of XB donors **1** with tetrabutylammonium halides in solution. Quite remarkably, in almost all complexes investigated the entropic term accounts for more than 50% of the overall free energy of binding (ΔG^0). Hence, inclusion of the entropy term in these kinds of investigations is crucial, as data based solely on ΔH^0 values will neglect a substantial proportion of the overall interaction energy.

The titration of ***m*-II-1^{Me}/OTf** and ***p*-II-1^{Me}/OTf** with tetrabutylammonium chloride, bromide, and iodide in acetonitrile at room temperature (Table 1, nos. 1–6) allowed a first assessment of the nature and strength of the charge-assisted halogen bonds considered in this publication (see Figure 1 for a typical titration curve).

The association constants for ***m*-II-1^{Me}/OTf** with all three halides are rather similar and in the range of 2.5×10^5–5.2×10^5 M^{-1}, with the iodide complex being slightly weaker than the chloride and bromide ones. Interestingly, while the enthalpic contribution becomes more favorable from chloride to iodide, this effect is counterbalanced by the opposite trend within the entropy part. The stoichiometry coefficients are close to unity for all halides, pointing toward a bidentate binding mode of the XB donor (see Scheme 2).

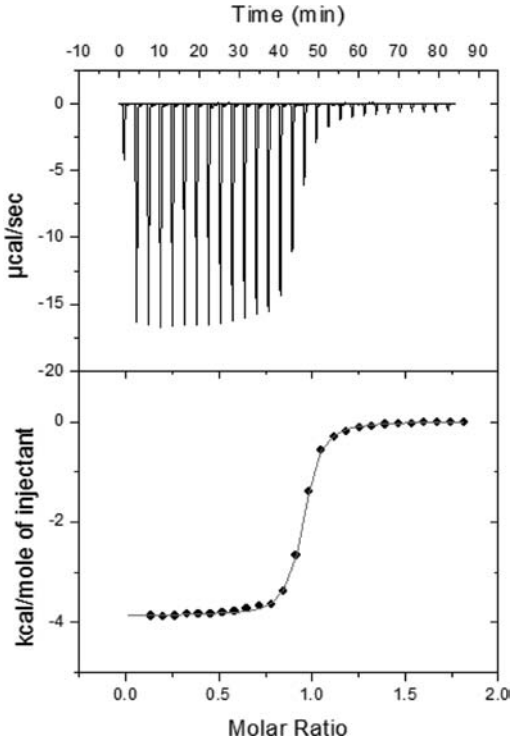


Figure 1. Exemplary isothermal titration calorimetry data for the titration of ***m*-II-1^{Me}/OTf** with NBu_4Br in CH_3CN at 30 °C.

This binding motive was also confirmed for the solid state, as an X-ray structural analysis of the complex of ***m*-II-1^{Me}/BPh$_4$** with bromide (generated *in situ* from CBr_4) also showed a bidentate coordination of the halide (Figure 2).[15]

In contrast, ***p*-II-1^{Me}/OTf** shows a 2:1 stoichiometry in its complex with chloride (Table 1, no. 4), indicating an independent monodentate binding mode. The binding constant is about 1 order of magnitude lower than that of ***m*-II-1^{Me}/OTf** with chloride, and this difference in interaction free energy is entirely due to a reduced enthalpy contribution. The binding constants of ***p*-II-1^{Me}/OTf** with bromide and iodide are similar to that of the chloride complex.[16] For all following investigations, we chose ***m*-II-1^{Me}/OTf** as our reference system, focusing mainly on its complex with NBu_4Br.

Nature of the Interaction. Next we addressed the obvious question of whether the binding is actually based on halogen-bond formation or due to another type of interaction (e.g., hydrogen bonds with the protons at C4 and C5 of the imidazolium moieties). To this end, we tested several structurally related compounds for their affinity toward bromide. While the binding of ***m*-BrBr-1^{Me}/OTf** with bromide (Table 1, no. 8) was substantially lower than that of ***m*-II-1^{Me}/OTf** (as is expected from halogen-bond theory), there was no detectable halide binding for ***m*-HH-1^{Me}/OTf** or ***p*-HH-1^{Me}/OTf** under our experimental conditions (Table 1, nos. 10, 11),[17,18] ruling out all other types of interactions not involving the iodine atoms of ***m*-II-1^{Me}/OTf**. To make sure the binding was not simply dependent on a voluminous substituent at position C2 of the imidazolium moieties, we also tested the bis-

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Table 1. Results of the Isothermal Calorimetric Titrations of Various Halogen-Bond Donors with Halides NBu_4X

	no.	XB donor	X^-	T [°C]	solvent	K [mol^{-1}]	ΔG^0 [$kJ \cdot mol^{-1}$]	ΔH^0 [$kJ \cdot mol^{-1}$]	$T\Delta S^0$ [$kJ \cdot mol^{-1}$]	n
m vs. *P*	1	*m*-II-1^{Me}/OTf	Cl^-	30	CH_3CN	$5.20 \cdot 10^5$	-33.2	-13.5	19.7	1.09
	2[d]	*m*-II-1^{Me}/OTf	Br^-	30	CH_3CN	$4.54 \cdot 10^5$	-32.8	-16.2	16.6	0.92
	3	*m*-II-1^{Me}/OTf	I^-	30	CH_3CN	$2.54 \cdot 10^5$	-31.4	-16.8	14.6	0.94
	4	*p*-II-1^{Me}/OTf	Cl^-	30	CH_3CN	$3.34 \cdot 10^4$	-26.3	-7.1	19.2	2.11
	5[a]	*p*-II-1^{Me}/OTf	Br^-	30	CH_3CN	$3.74 \cdot 10^4$	-26.5	-8.4	18.1	1.62
	6[a]	*p*-II-1^{Me}/OTf	I^-	30	CH_3CN	$2.23 \cdot 10^4$	-25.2	-7.7	17.5	1.45
References	7	*m*-BrBr-1^{Me}/OTf	Cl^-	30	CH_3CN	$1.26 \cdot 10^3$	-18.0	-10.2	7.8	0.90
	8	*m*-BrBr-1^{Me}/OTf	Br^-	30	CH_3CN	$1.01 \cdot 10^3$	-17.5	-14.5	3.0	1.06
	9	*m*-BrBr-1^{Me}/OTf	I^-	30	CH_3CN	$4.89 \cdot 10^2$	-15.6	-12.4	3.2	1.03
	10	*m*-HH-1^{Me}/OTf	Br^-	30	CH_3CN	-[c]	-	-	-	-
	11	*p*-HH-1^{Me}/OTf	Br^-	30	CH_3CN	-[c]	-	-	-	-
	12	*m*-MeMe-1^{Me}/OTf	Br^-	30	CH_3CN	-[c]	-	-	-	-
	13	*m*-HI-1^{Me}/OTf	Br^-	30	CH_3CN	$2.70 \cdot 10^4$	-25.7	-8.8	16.9	0.88
	14	3	Br^-	30	CH_3CN	$3.48 \cdot 10^3$	-20.5	-8.8	11.7	0.91
	15	*m*-II-2	Br^-	30	CH_3CN	-[c]	-	-	-	-
	16	4	Br^-	30	CH_3CN	$1.49 \cdot 10^3$	-18.4	-6.8	11.6	0.72
Temperature	17	*m*-II-1^{Me}/OTf	Br^-	10	CH_3CN	$6.74 \cdot 10^5$	-31.7	-16.3	15.4	0.93
	18	*m*-II-1^{Me}/OTf	Br^-	20	CH_3CN	$4.39 \cdot 10^5$	-31.4	-16.2	15.2	0.94
	[b]	*m*-II-1^{Me}/OTf	Br^-	30	CH_3CN	$4.54 \cdot 10^5$	-32.8	-16.2	16.6	0.92
	19	*m*-II-1^{Me}/OTf	Br^-	40	CH_3CN	$4.28 \cdot 10^5$	-33.7	-16.5	17.2	0.88
	20	*m*-II-1^{Me}/OTf	Br^-	50	CH_3CN	$3.46 \cdot 10^5$	-34.2	-16.5	17.7	0.81
	21	*m*-II-1^{Me}/BPh_4	Br^-	10	CH_3CN	$9.08 \cdot 10^5$	-32.3	-16.0	16.3	0.97
	22	*m*-II-1^{Me}/BPh_4	Br^-	30	CH_3CN	$6.76 \cdot 10^5$	-33.8	-15.7	18.1	0.93
	23	*m*-II-1^{Me}/BPh_4	Br^-	50	CH_3CN	$4.91 \cdot 10^5$	-35.2	-15.5	19.7	0.89
H-Analogues	24	*m*-HH-1^{Me}/BF_4	Br^-	30	CH_3CN	-[c]	-	-	-	-
	25	*m*-HH-1^{Me}/PF_6	Br^-	30	CH_3CN	-[c]	-	-	-	-
	26	*m*-HH-1^{Me}/BPh_4	Br^-	30	CH_3CN	-[c]	-	-	-	-
	27	*m*-HH-1^{Oct}/OTf	Br^-	23	CH_2Cl_2	-[c]	-	-	-	-
	28	*m*-HH-1^{Oct}/OTf	Br^-	30	THF	-[c]	-	-	-	-
Anions	[b]	*m*-II-1^{Me}/OTf	Br^-	30	CH_3CN	$4.54 \cdot 10^5$	-32.8	-16.2	16.6	0.92
	29	*m*-II-1^{Me}/BF_4	Br^-	30	CH_3CN	$4.56 \cdot 10^5$	-32.9	-16.3	16.6	0.93
	30	*m*-II-1^{Me}/PF_6	Br^-	30	CH_3CN	$5.70 \cdot 10^5$	-33.5	-16.1	17.4	0.92
	[b]	*m*-II-1^{Me}/BPh_4	Br^-	30	CH_3CN	$6.76 \cdot 10^5$	-33.8	-15.7	18.1	0.93
	31	*m*-II-1^{Oct}/OTf	Br^-	30	CH_3CN	$7.54 \cdot 10^5$	-34.1	-16.2	17.9	0.96
	32	*m*-II-1^{Oct}/BPh_4	Br^-	30	CH_3CN	$9.42 \cdot 10^5$	-34.7	-16.9	17.8	0.90
Solvents	33	*m*-II-1^{Me}/OTf	Br^-	30	acetone	$6.02 \cdot 10^5$	-33.6	-15.8	17.8	0.90
	34	*m*-II-1^{Me}/OTf	Br^-	30	H_2O/MeOH (1/9)	-[c]	-	-	-	-
	35	*m*-II-1^{Me}/OTf	Br^-	30	ethanol	-[c]	-	-	-	-
	36	*m*-II-1^{Me}/OTf	Br^-	30	DMSO	-[c]	-	-	-	-
	37	*m*-II-1^{Oct}/OTf	Br^-	30	THF	$3.25 \cdot 10^6$	-37.8	-20.1	17.7	0.94
	38	*m*-II-1^{Oct}/OTf	Cl^-	23	CH_2Cl_2	$1.75 \cdot 10^6$	-36.0	-12.7	23.3	1.17
	39	*m*-II-1^{Oct}/OTf	Br^-	23	CH_2Cl_2	$2.61 \cdot 10^6$	-36.6	-16.2	20.6	0.99
	40	*m*-II-1^{Oct}/OTf	I^-	23	CH_2Cl_2	$2.07 \cdot 10^6$	-36.2	-17.0	19.2	1.03
	41	*m*-II-1^{Oct}/OTf	Cl^-	30	acetone	$2.46 \cdot 10^6$	-37.1	-14.3	22.8	1.14
	42	*m*-II-1^{Oct}/OTf	Br^-	30	acetone	$2.04 \cdot 10^6$	-36.7	-17.6	19.1	0.95
	43	*m*-II-1^{Oct}/OTf	I^-	30	acetone	$2.58 \cdot 10^6$	-37.2	-15.9	21.3	0.95

[a]See ref 16. [b]Entry repeated for better comprehensibility. [c]No heat effect was observed in the ITC measurements. [d]In order to get a rough estimate of the experimental error associated with these measurements, the titration corresponding to entry no. 2 was performed four times (with different batches of activator and on two different ITC instruments). Binding constants of 1.59×10^5, 2.53×10^5, 4.54×10^5, and 4.76×10^5 mol^{-1} were obtained, indicating that only differences in the K value exceeding a factor of 2−3 are to be considered significant.[25] The value given here corresponds to the exact same conditions also employed for entries 1−6 and should therefore offer the best comparability.

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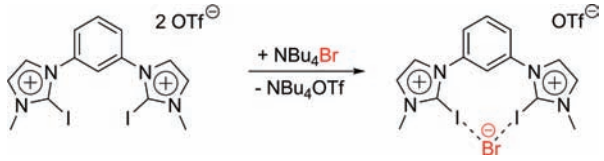
Scheme 2. Formation of a Bidentate Halogen-Bond Complex[a]



[a]Chemical equation for the titration of *m*-**II-1**^{Me}/**OTf** with NBu_4Br in CH_3CN.

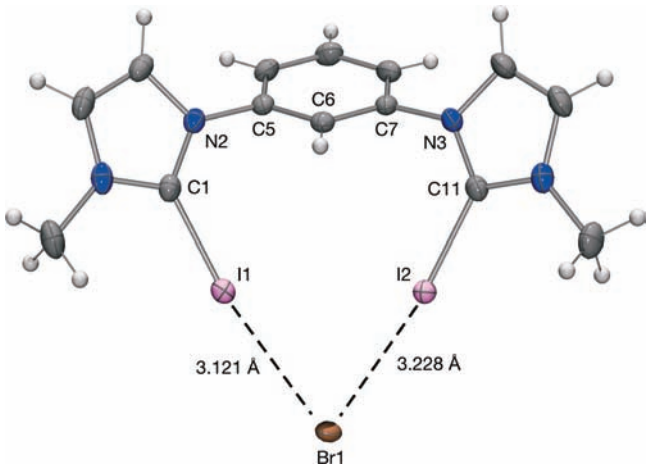
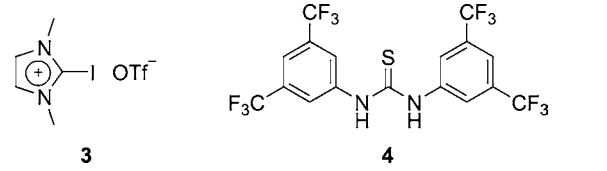


Figure 2. X-ray structural analysis of the complex of bromide with *m*-**II-1**^{Me}/BPh_4 (anion omitted for clarity; ellipsoids at 50% probability). Selected bond lengths [Å] and angles [°]: C1–I1 2.090, C11–I2 2.083, C11–I2–Br1 170.5, C1–I1–Br1 172.1, C11–N3–C7–C6 54.4, C6–C5–N2–C1 −60.0.

methylated compound *m*-**MeMe-1**^{Me}/**OTf**, which again gave no detectable binding (Table 1, no. 12). These combined observations provide a very strong indication that with the present complexes, halogen bonding is indeed the main interaction responsible for halide binding.

Interestingly, the difference between *m*-**II-1**^{Me}/**OTf** and *m*-**BrBr-1**^{Me}/**OTf** is mostly based on a significantly less favorable entropic contribution to ΔG^0 for *m*-**BrBr-1**^{Me}/**OTf**. As the bromo substituents of *m*-**BrBr-1**^{Me}/**OTf** feature a smaller surface area than the iodo substituents of *m*-**II-1**^{Me}/**OTf**, one might speculate that the former compound binds less solvent molecules in solution and consequently releases less solvent molecules during the binding event – resulting in a less favorable entropic contribution. To obtain more insight into the nature of the binding of *m*-**BrBr-1**^{Me}/**OTf** with halides, we also determined the binding parameters for the chloride and iodide complexes (Table 1, nos. 7 and 9). The chloride complex features a similar overall binding strength as the bromide complex, but the relative enthalpic contribution is lower, and the relative entropic contribution is higher than in the bromide case. This trend is similar to the one observed for the chloride and bromide complexes of *m*-**II-1**^{Me}/**OTf**. The iodide complex of *m*-**BrBr-1**^{Me}/**OTf** is markedly less favorable than the chloride and bromide adducts, though, and the decrease in the free energy of binding, compared to the bromide complex, is entirely due to a reduced enthalpic contribution.

As expected, the binding constant of the mono-iodinated XB donor *m*-**HI-1**^{Me}/**OTf** lies in the range of that of *p*-**II-1**^{Me}/**OTf** (Table 1, no. 13), while the binding of a simple imidazolium salt **3** (Figure 3) to bromide is still a bit weaker (Table 1, nos. 14)—so either there is an additional hydrogen-bond interaction in *m*-**HI-2**^{Me}/**OTf** or the second cationic charge of the non-iodinated imidazolium moiety increases the overall halide affinity.



3 **4**

Figure 3. Imidazolium derivative **3** and thiourea **4**, tested for comparison with the bidentate XB donors.

We also did not detect any binding with the neutral (non-N-alkylated) precursor compound of *m*-**1** (i.e., *m*-**II-2**), proving the importance of the cationic charge on the electrophilicity of the iodine centers (Table 1, no. 15). When testing thiourea **4**[19] for a comparison with a neutral hydrogen-bond donor, we found a binding constant of approximately 1.5×10^3 M^{-1} (Table 1, no. 16), about 2 orders of magnitude lower than that of *m*-**II-1**^{Me}/**OTf**, although related thiourea derivatives have already been successfully employed in catalyses based on an "anion binding mechanism".[20]

Temperature Dependence and Structural Variations. In order to investigate the temperature dependence of the halide binding, we determined the binding parameters of *m*-**II-1**^{Me}/**OTf** with NBu_4Br in acetonitrile in the (experimentally accessible) temperature range of 10–50 °C (Table 1, nos. 17–20). From lowest to highest temperature, the binding constant decreases only by a factor of 2, which means that the free energy of binding actually becomes slightly *more negative* (cf. Figure 4). This is due to both a slightly more favorable

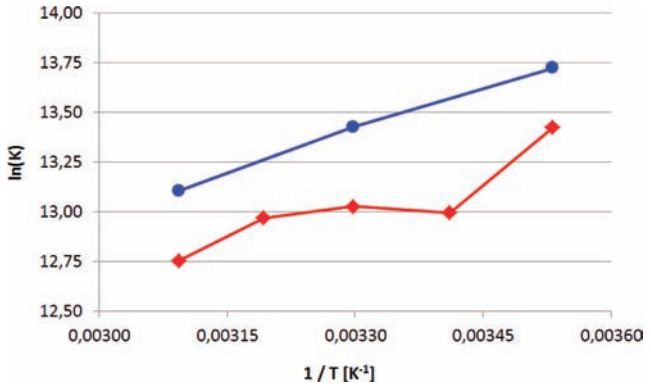


Figure 4. Temperature-dependence of the binding of tetrabutylammonium bromide to *m*-**II-1**^{Me}/**OTf** (red graph) and *m*-**II-1**^{Me}/BPh_4 (blue graph) in CH_3CN.

enthalpic part and the positive sign of the entropy. The same trend is seen for *m*-**II-1**^{Me}/BPh_4 (Table 1, nos. 21–23). The temperature dependence of halogen bonds had previously been studied for complexes of C_6F_5I with metal fluorides in toluene (or heptane),[9d,21a] and in all cases the free energy of binding became *less negative* for higher temperatures.[21b] In addition, the temperature dependence had also been studied in the solid phase,[21c] with shorter interaction distances being found at lower temperatures.

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The composition of the XB donors should also influence the strength of the halide binding. First, we replaced the triflate counteranions in *m*-**II-1^{Me}/OTf** with other weakly coordinating ones, either via the methylating reagent (for BF_4^-) or by anion exchange (for PF_6^- and BPh_4^-). We note that for all counteranions, the respective non-iodinated compounds *m*-**HH-1^{Me}/(BF_4, PF_6 or BPh_4)** again showed no detectable binding to bromide (Table 1, nos. 24–26). As for the XB donors themselves, only a very small effect, if at all, is seen for the different counteranions. The compounds *m*-**II-1^{Me}/PF_6** (Table 1, no. 30) and *m*-**II-1^{Me}/BPh_4** seem to bind a tad stronger than *m*-**II-1^{Me}/OTf** and *m*-**II-1^{Me}/BF_4** (Table 1, no. 29), but this might also still be within the experimental error. Thus, either the ion pairing in solution is either very weak to nonexistent or very similar for the different counteranions.[22]

As a further structural variation, we compared the binding strengths of the *N*-methylated and *N*-octylated compounds *m*-**II-1^{Me}/OTf** and *m*-**II-1^{Oct}/OTf** (Table 1, no. 31) as well as *m*-**II-1^{Me}/BPh_4** and *m*-**II-1^{Oct}/BPh_4** (Table 1, no. 32). In both cases, the *N*-octylated XB donor exhibited a slightly stronger halide affinity. However, the difference is mainly due to the entropic part for the triflate salts, and mainly based on the enthalpic part for the tetraphenylborate salts. Thus, while there seems to be a notable effect of the N-substituent, it is difficult to rationalize (and generalize) its influence.

Solvent Effects. Finally, we considered the influence of different solvents on the halide binding.[23] In addition to acetonitrile (which features hydrogen-bond acidity $\alpha^H_2 = 0.09$ and hydrogen-bond basicity $\beta^H_2 = 0.44$),[24] *m*-**II-1^{Me}/OTf** is also sufficiently soluble in acetone ($\alpha^H_2 = 0.04$, $\beta^H_2 = 0.50$), water/methanol (1/9) (H_2O: $\alpha^H_2 = 0.35$, $\beta^H_2 = 0.38$; MeOH: $\alpha^H_2 = 0.37$, $\beta^H_2 = 0.41$), ethanol ($\alpha^H_2 = 0.33$, $\beta^H_2 = 0.44$), and DMSO ($\alpha^H_2 = 0.00$, $\beta^H_2 = 0.77$). Of those solvents, only acetone enabled a detectable binding of bromide to the XB donor (with binding parameters that are very similar to those in acetonitrile: Table 1, nos. 33–36). In line with these findings, it had previously been shown[9b] that *hydrogen*-bonding solvents (i.e., water and ethanol) are detrimental to the formation of halogen bonds. For the N-octylated derivative *m*-**II-1^{Oct}/OTf**, a wider range of solvents is available, most notably THF ($\alpha^H_2 = 0.00$, $\beta^H_2 = 0.51$) and CH_2Cl_2 ($\alpha^H_2 = 0.13$, $\beta^H_2 = 0.05$). In the former solvent, a markedly increased binding constant to bromide was found ($K = 3.3 \times 10^6$ M^{-1}, see Table 1, no. 37), one of the highest binding constants detected so far for halogen-bond-based complexes.[10] An almost identical binding constant was found in CH_2Cl_2 (Table 1, no. 39), but in this case the relative contribution of the entropy is distinctly higher (and consequently the contribution of the enthalpy is lower) compared to THF. Additionally, we determined the binding data for *m*-**II-1^{Oct}/OTf** with tetrabutylammonium chloride and iodide in CH_2Cl_2 (Table 1, nos. 38 and 40). As was the case for *m*-**II-1^{Me}/OTf** in acetonitrile, we found very similar association constants for all three halides (with the chloride complex being perhaps marginally less favorable than the ones of bromide and iodide). Interestingly, there is again a compensation of two opposite trends: from the chloride to the iodide complex, the absolute value of the enthalpy increases while the entropy decreases. The same trend, albeit not as linear as with the other two examples, is found for the complexes of *m*-**II-1^{Oct}/OTf** with chloride, bromide, and iodide in acetone (Table 1, nos. 41–43).

Overall, the dependency of the halogen-bond interaction on the solvent, though clearly existent, is hard to interpret at this point.

CONCLUSIONS

In summary, we have conducted isothermal calorimetric titrations to investigate the halogen-bond strength of cationic bidentate halogen-bond donors toward halides, using bis(iodoimidazolium) compounds **1** as probes. This data is intended to aid the rational design of halogen-bond donors as well as the development of halogen-bond-based applications in solution (e.g., in anion recognition, anion transport, and catalysis). In all cases examined, the entropic contribution to the overall free energy of binding was found to be very important. The binding affinities showed little dependency on the weakly coordinating counteranions of the halogen-bond donors, but became slightly stronger with higher temperatures. We also found a marked influence of different solvents on the interaction strength. The data presented here should constitute a valuable benchmark for the development of theoretical methods concerning the accurate prediction of halogen-bond interactions in solution.

ASSOCIATED CONTENT

Supporting Information

Full experimental details and characterization data, ITC spectra, and X-ray structural analysis. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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