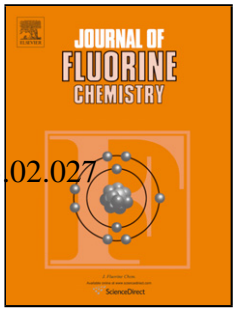

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Highlights:

• Synthesis of polyfluorinated multidentate halogen-bond donors with azo linkage

• Geometry of iodine centers almost identical to pyridinium-based halogen-bond donors

• Much weaker activation of test substrate compared to cationic variants

• Comparison of Lewis acidity by DFT calculations supports experiments

Polyfluorinated versus Cationic Multidentate Halogen-Bond Donors: A Direct Comparison

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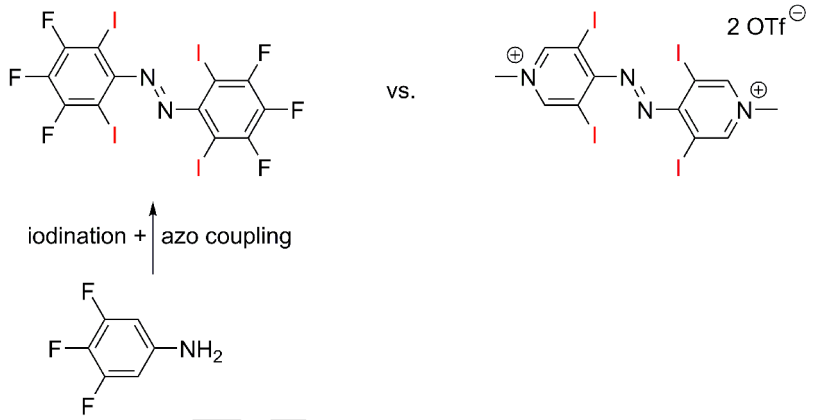
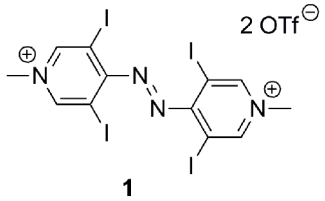
ABSTRACT. Two *polyfluorinated* azo-linked halogen-bond donors were synthesized and their relative Lewis acidities were compared to a known *dicationic* azo-linked halogen-bond donor with almost identical geometrical arrangement of the iodine substituents. This structural similarity was confirmed by the results of x-ray structural analyses. In a benchmark reaction to gauge the activation potential of these halogen-based Lewis acids in halide abstraction reactions, we found that the polyfluorinated compounds were markedly less active than the cationic ones and did, in fact, show very little activation at all. Repeated measurements seem to indicate however, that there is a small effect of the iodinated versus the non-iodinated polyfluorinated compound in their role as potential activators. Quantum-chemical calculations confirmed the experimentally observed trend.

GRAPHICAL ABSTRACT.



1. Introduction

Halogen-bonds, i.e. non-covalent interactions between Lewis bases and compounds with electrophilic terminal halogen substituents, have seen renewed interest in the last two decades.[1,2] Traditionally, most of the applications of halogen-bonds concern the solid phase,[3] although several studies on halogen-bonds in solution have also been published lately.[4] Halogen-bonds share many similarities with hydrogen-bonds, but feature a markedly higher directionality: the R-X -- LB angle (R = backbone; X = Cl, Br, I; LB = Lewis base) is always found to be close to 180° in halogen-bond-based complexes. A second prerequisite for the formation of a reasonably strong halogen-bond adduct is the presence of electronegative substituents R in the halogen-bond donor R-X (i.e., the halogen-based Lewis acid). In crystal engineering, this has mostly been achieved by the use of polyfluorinated backbones, preferentially polyfluoroiodoarenes.[1;5] Based on these building blocks, liquid crystalline and conductive materials have e.g. been designed.[6] Somewhat less prominent are cationic backbones,[4c,7] which have e.g. been used for the construction of catenanes and anion receptors.[4g;5b,c;8] Recently, we could show that bidentate imidazolium-,[9a] pyridinium-,[9b] or triazolium-based[9c] halogen-bond donors may be employed as activators for the cleavage of a carbon-bromine bond (see Figure 1 for the iodopyridinium-based Lewis acid **1**). In these reactions, we found that neutral (polyfluorinated) halogen-bond donors like 1,4-diiodotetrafluorobenzene were *not* active in the same timeframe.[9a] This could be due to a reduced electrophilicity of the C-I bonds of these compounds (compared to cationic ones) or due to the monodentate binding of these Lewis acids (or both).



1

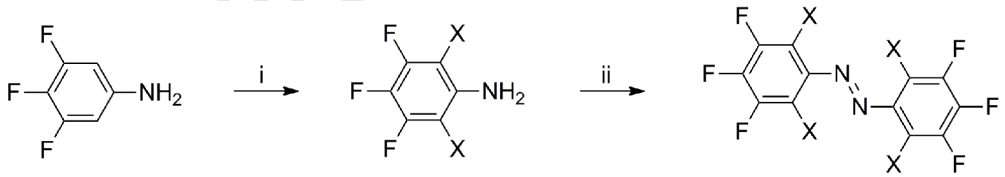
Figure 1: Iodopyridinium-based bidentate halogen-bond donor **1**.[9b]

In general, although both polyfluorinated and cationic multidentate halogen-bond donors have been used in various applications (see above), it is difficult to directly compare the influence of the two types of backbones on the electrophilicity of the corresponding halogen-bond donors. Because of the high directionality of the interaction, a fair comparison would need to be based on topologically identical halogen-bond donors. Herein we present, to the best of our knowledge, the first comparison of a bidentate *polyfluorinated* with a bidentate *dicationic* halogen-bond donor, where both feature the same geometric arrangement of the electrophilic iodine substituents.

2. Results and discussion

2.1 Synthesis of neutral multidentate halogen-bond donors **4a** and **4b**

Previously, we could show that halogen-bond donor **1** is a potent electrophile.[9b] Since compound **1** was obtained by azo coupling of the corresponding aminopyridine precursors (and subsequent methylation), we reasoned that a structurally very similar *neutral* halogen-bond donor should be accessible by azo coupling of two polyfluorinated iodoaniline derivatives **2a** (see Scheme 1). The latter ones could be synthesized by iodination of 3,4,5-trifluoroaniline with potassium iodide and potassium iodate in methanol, in analogy to a literature-known procedure, in 82 % yield.[10] Oxidative coupling of two anilines **2a** with the powerful hypervalent iodine reagent $PhIL_2(OTf)_2$ **3**[11] (L = 4-dimethylaminopyridine) gave the target structure **4a** in 44 % yield after several days. This rather moderate yield, which could not be improved, is likely due to the very electron-poor nature of aniline **2a**. Although it is disappointing that the synthesis of **4a** could not be realized in higher yield, the amount of product obtained was still sufficient for the intended benchmarking studies (see below). For comparison reasons, we also synthesized the analogous tetrabromo-substituted halogen-bond donor **4b**. The required precursor, 2,5-dibromo-3,4,5-trifluoroaniline **2b**, was obtained by bromination of 3,4,5-trifluoroaniline with N-bromosuccinimide in 95 % yield. Azo coupling with oxidant **3** again gave the target compound **4b** in low to moderate yield (38 %), despite a reaction time of several days at room temperature (decomposition was observed at higher temperatures). Finally, the non-iodinated/brominated reference compound **4c** could by synthesized by direct azo coupling of 3,4,5-trifluoroaniline (32 % yield).



2a (X = I)
2b (X = Br)

4a (X = I)
4b (X = Br)
4c (X = H)

Scheme 1: Synthesis of polyfluorinated halogen-bond donors **4a** and **4b**; i) KI, KIO_3, HCl, MeOH (X = I) or N-bromosuccinimide, CH_2Cl_2 (X = Br); ii) $PhIL_2(OTf)_2$ (L = 4-dimethylaminopyridine), CH_2Cl_2.

All azo compounds could be obtained in pure form, as evidenced by elemental analysis and ^{19}F NMR spectra. In the latter, the chemical shift of the triplett (or multiplett) corresponding to the fluorine substituents at the *para*-positions does only change by few ppm from **4a** (-151 ppm) to **4c** (-154 ppm). The doublet (or multiplett) of the fluorine substituents at the *meta*-position, however, shifts markedly high-field from **4a** (-107 ppm) via **4b** (-123 ppm) to **4c** (-132 ppm).

2.2 X-ray structural analysis: Comparison of the orientations of the iodine substituents in compounds **4a** and **1**

Single crystals of compound **4a** that were suitable for an X-ray structural analysis were obtained by slow evaporation of the solvent from a solution of **4a** in chloroform.[12] Since the structural analysis of dicationic halogen-bond donor **1** in the solid state has also been published,[9b] a direct comparison between these two halogen-based Lewis acids is now possible (see Figures 2a and 2b).

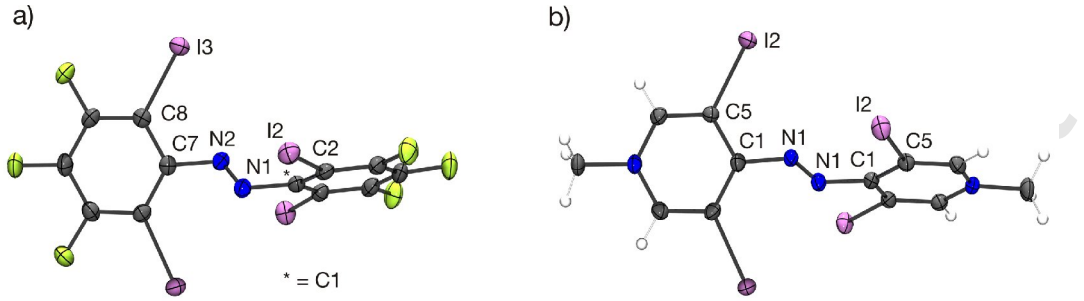


Figure 2: X-ray structural analyses of halogen-bond donors **4a** (a) and **1**[9b] (b) (ellipsoids at 50 % probability). In the case of **1**, the anions have been omitted for clarity. Selected bond lengths [Å] and angles [°]: (a) N1–N2 = 1.250(3), C8–I3 = 2.088(2); C8–C7–N2–N1 = 132.1(2), C2–C1–N1–N2 = 129.6(2), C2–C1–C7–C8 = 61.8(3); (b) N1–N1 = 1.242(3), C5–I2 = 2.090(3); C5–C1–N1–N1 = -58.8(3); C5–C1–C1–C5 =75.4(3); symmetry code for equivalent atoms in **1**: -x, y, 0.5 - z.

In both cases, the orientation of the two aryl moieties towards each other is very roughly perpendicular, with an angle of about 60° between the two planes in the case of **4a** (compared to 75° for compound **1**). The azo bridge forms a torsion angle of approx. 130° with an attached aryl group, also similar in both cases. The bond length of the azo bridge itself is marginally higher for **4a** compared to **1** (1.250 Å vs. 1.242 Å),[13] and the C–I bond lengths are also almost identical in both structures (2.088 Å vs. 2.090 Å). These data illustrate that the structural environment of the Lewis acidic iodine substituents is indeed very similar for both halogen-bond donors.

There is one marked difference in the solid-phase structures, however, namely the crystal packing arrangement: in contrast to the dicationic compound **1**, there are no further Lewis basic counterparts (i.e., anions) to interact with for the neutral halogen-bond donor **4a**. Thus, the solid-phase structure of **4a** is built up by interactions between different molecules of **4a** (Figure 3).

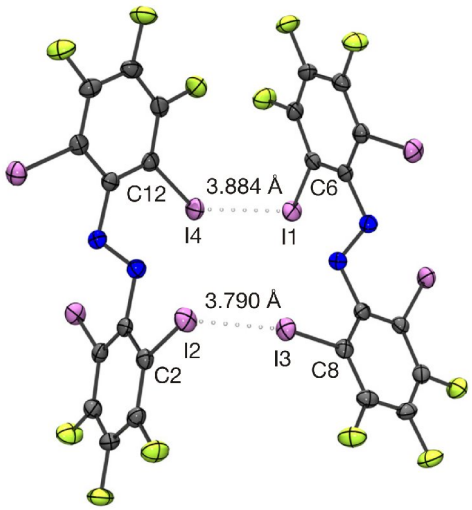


Figure 3: Intermolecular halogen-bonds formed in the crystal packing of **4a**; selected angles [°]: C12–I4···I1 = 68.67(6), C6–I1···I4 = 146.91(7), C8–I3···I2 = 76.13(6), C2–I2···I3 = 166.18(6). In the crystal structure of3

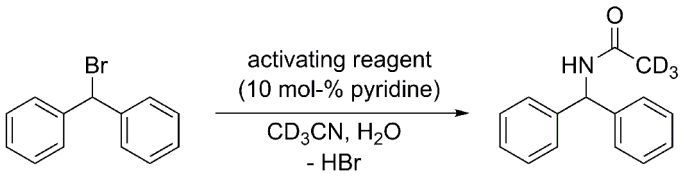
compound **4a**, each of the four iodine substituents is connected to neighbouring molecules by one of the two kinds of halogen-bonds shown in this figure.

In principle, there are two electron-rich kinds of substituents in **4a**: the azo nitrogen atoms and the iodine substituents. The azo group, however, does not engage in any short contact with other molecules of **4a**, most likely for steric reasons (including the shielding by the four surrounding iodine atoms). This leaves the iodine atoms as the only remaining groups which could act as Lewis basic centers. A peculiar feature of such terminal halogen substituents attached to highly electron-withdrawing groups is the anisotropy of their electron density: there is comparably little electron density in the extension of the C–X bond (which is the reason for the electrophilicity of these atoms), but also increased electron density in a belt perpendicular to the C–X bond (which is due to the filled p-orbitals on the halogen atom). Thus, for an ideal intermolecular iodine-iodine contact, one would expect the C–I--I angles to be 180° at the iodine atom acting as the electrophile and to be 90° at the iodine substituent acting as the nucleophile. In the solid-state structure of **4a**, two short I-I contacts are found. The shorter of those, with an I–I distance of 3.790 Å (see Figure 3; sum of van-der-Waals radii: 3.96 Å)[14] indeed features structural parameters close to the ones just discussed (with C-I--I angles of 166° and 76°). In the second intermolecular contact, the I–I distance is 3.884 Å, and thus this interaction is apparently weaker than the other contact. In line with this, the geometric parameters deviate even more strongly from the ideal values (with C–I--I angles of 147° and 69°). In fact, the rather strong deviation of the C–I--I angle from 180° in the second contact is in some contrast to the high directionality of halogen-bonds, and thus this interaction may not constitute a "classical" halogen-bond, but rather a weak van-der-Waals contact. In the crystal packing of compound **4a**, each of the four iodine substituents is connected to neighbouring molecules of **4a** by one of the two types of halogen bonds described above. This situation is thus somewhat similar to the crystal packing of the cationic halogen-bond donor **1**, in which also all four halogen substituents of **1** form halogen bonds (to the triflate anions, in this case).

Similar intermolecular C–I--I–C halogen-bonds as just described for the crystal structure of 4a have already been reported in the literature, e.g. in the solid state structures of 1,3,5-trifluoro-2,4,6-triiodibenzene[15] and 1,1,2,2-tetrafluoro-1,2-diiodoethane.[16] In these cases, short I-I distances of 3.74 Å and 3.89 Å have been observed, respectively.

2.3 Performance in a benchmark carbon-halogen bond activation reaction

As the structural similarity of the core part of compounds **4a** and **1** was also confirmed by the x-ray analyses presented above, we next turned our attention towards the activation potential of the neutral halogen-bond donors **4a** and **4b** in an actual chemical reaction. Previously, we had established the solvolysis of benzhydryl bromide (**5**) in acetonitrile as a suitable benchmark reaction to test the activation of a carbon-bromine bond by halogen-bond donors (Scheme 2).[9a] After heterolytic cleavage of the C-Br bond, the resulting cationic intermediate is transformed into the amide **6** by attack of acetonitrile and subsequent hydrolysis in a Ritter-type reaction. Importantly, it is possible to rule out traces of acid as the actual activating reagent by addition of a substoichiometric amount of pyridine.[9a] For all previously examined halogen-bond donors, the corresponding non-iodinated reference compounds were not similarly active in this reaction. The dicationic halogen-bond donor **1** had converted more than 90% of benzhydryl bromide to the amide after 36 hours at room temperature.[9b,17]



5 **6**

Scheme 2: Benchmark carbon-halogen bond activation reaction.

Most likely, the cationic backbone in compound **1** is more electronegative than the polyfluorinated one in **4a** (see also chapter 2.4) and thus the electrophilicity of the iodine substituents in halogen-bond donor **1** might be expected to be higher than in **4a**. The dicationic Lewis acid **1**, however, invariably is accompanied by two

triflate anions, which will compete with the substrate (**5**) and the liberated bromide for the electrophilic iodine centers, an effect that will reduce the activation potential of the dicationic halogen-bond donor.

Figure 4 shows the formation of amide **6** in a solution of benzhydryl bromide in deuterated acetonitrile, in which equimolar amounts of the neutral azo compounds **4a**, **4b** or **4c** were present with otherwise identical conditions. We have also added 10 mol-% of pyridine to each solution to quench any acid impurities. The yield of amide **6** over time could be conveniently determined by ^{1}H-NMR spectroscopy. For comparison, we have also added the analogous graph for the formation of **6** in the presence of one equivalent of activator **1** from our previous measurement.[9b]

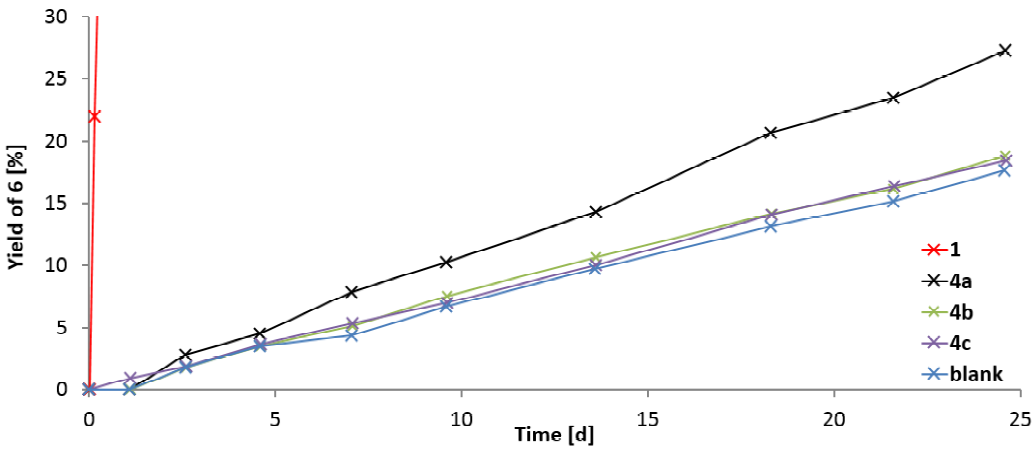


Figure 4: Yield-versus-time profile of the solvolysis of benzhydryl bromide (see Figure 2) in the presence of one equivalent of various potential activating reagents.

It is immediately obvious that the neutral halogen-bond donors are markedly less active in this benchmark reaction than the cationic variant **1**: while the solvolysis of benzhydryl bromide is almost quantitative in the presence of **1** after 36 hours, only ca. 2% of amide were formed in the presence of halogen-bond donor **4a** in the same time. In fact, even after 25 days of reaction time, only ca. 18% of benzhydryl bromide were converted to amide **6** in the presence of one equivalent of **4a**. As this slow solvolysis reaction is only marginally more pronounced than in the background reaction (see Figure 4), we repeated the measurement several times and found the same trend in all measurements. While this does not completely rule out the possibility that the observed difference is due to the margin of error of the measurements, it provides at least a weak indication that compound **4a** is indeed capable of activating the solvolysis of **5**, even if marginally. With the same caution in the interpretation of the results, it seems that the brominated compound **4b** and the reference compound **4c** are both not capable of activating the substrate. This provides an, albeit weak, indication, that the electrophilicity of the iodine centers is indeed responsible for the activation by **4a**.[18] The most important finding, however, remains the fact that the polyfluorinated halogen-bond donors presented in this study are much less potent than analogous cationic ones, where all structural parameters are virtually identical. This fact constitutes an important orientation for the future design of potent halogen-bond based activators and catalysts.

2.4 Quantum-chemical calculations

In order to complement the experimental comparison between compounds **1** and **4a**, we also performed quantum chemical calculations on the complexes of **1** and **4a** with bromide (which is liberated during the benchmark reaction presented above). Due to the size of the complexes, we used density functional theory with the M06-2X functional[19] that has been recommended for non-covalent interactions and a triple-zeta basis set with polarization functions (including the corresponding pseudopotential for iodine).[20] All calculations were performed with Gaussian09.[21] The counteranions were not included in the case of compound **1**. Since the complex formation involves charges species, we added an intrinsic solvation model, namely the PCM method[22] that is available in Gaussian09, using parameters for acetonitrile.

First we were interested to see whether bidentate coordination of the halogen-bond donors to the halide is geometrically possible.[23] In both cases, optimization of the bidentate adducts resulted in true energetic minima, as was evident from the absence of imaginary frequencies. In the case of Lewis acid **4a**, the planes of the two phenyl moieties form an angle of approx. 30°, to enable best-possible overlap of the electrophilic part of the iodine atoms with the bromide. A very similar angle of the corresponding planes is observed in compound **1**.[9b] The anion is bound more closely in the dicationic halogen-bond donor than in the polyfluorinated one (see distances in Figure 5), indicating stronger halogen-bonds for the former. In both adducts, the C–I–Br angles deviate somewhat from the ideal of 180° (156° and 162° for the complex with **4a**, 159° for both bonds in the adduct with **1**). This indicates that although the backbones feature some flexibility, it is not possible to align both iodine substituents for perfectly linear halogen-bonds, and thus a compromise is realized.

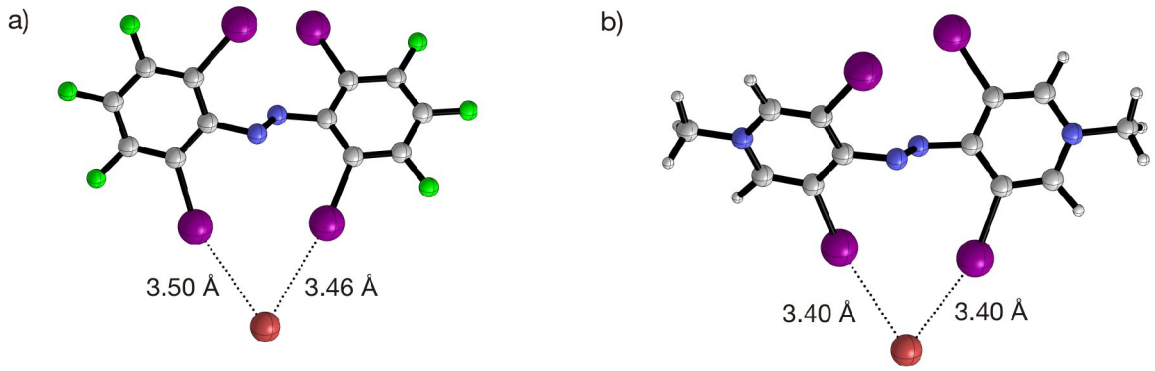


Figure 5: Adducts of the halogen-bond donors with bromide, as calculated with M06-2X/TZVPP/PCM(CH_3CN); a) complex of **4a** with bromide; b) complex of **1** with bromide. The graphic representations have been prepared with CYLview.[24] C-I--Br halogen-bond angles: a) 156° (halogen-bond shown left) and 162° (halogen-bond shown right); b) 159° (both halogen-bonds).

Additionally, we sought to obtain a rough estimate of the relative complexation energies of both complexes.[25] We note that the calculation of absolute complexation energies (and Gibbs free energies) poses several challenges due to the presence of counterions and solvation, and we are aware that these computations will have only orientating character. Consequently, we were primarily interested in the energies of both adducts relative to each other, as this should give a coarse indication of the relative Lewis acidities of the two halogen-bond donors. We computed the complexation energy as the difference between the adduct and the isolated Lewis acid and bromide in the intrinsic solvation environment. Adduct formation is predicted to be favourable in both cases, namely by approx. 3 kcal/mol for the complex with **4a** and by approx. 8 kcal/mol for the complex with **1**.[26] The markedly higher complexation energy for the adduct with **1** indicates a higher Lewis acidity for this compound and is in agreement with the experimental findings presented above.

3. Conclusions

In summary, we have synthesized azo-linked polyfluorinated halogen-bond donors **4a** and **4b** in order to compare their relative Lewis acidities to the known halopyridinium-based azo compound **1**, which features a virtually identical geometric arrangement of the iodine substituents. Thus, for the first time it was possible to directly study the influence of a cationic vs. a polyfluorinated backbone on the Lewis acidity of the corresponding halogen-bond donor. A comparison of the results of x-ray structural analyses of halogen-bond donors **4a** and **1** illustrated the high geometrical similarity of the core part of these Lewis acids. Using a previously established test reaction to gauge the activation potential of halogen-bond-based Lewis acids in a solvolysis reaction, we found that the polyfluorinated compound **4a** was markedly less active than **1** and did indeed show very little activation of the substrate at all. Repeated measurements seem to indicate however, that there is a small effect of the iodinated (**4a**) versus the non-iodinated (**4c**) compound in their role as potential activators. Quantum-chemical calculations confirmed that **4a** might act as a bidentate halogen-bond donor, but also showed that its Lewis acidity is much lower than that of compound **1** (in agreement with experiment).[6]

These findings should be interesting for the future design of strong multidentate halogen-bond donors. In cases were both a cationic and a polyfluorinated backbone are available for the synthesis of such a halogen-based Lewis acid, it seems that the cationic core structure will lead to the stronger halogen-bond donor, in spite of the fact that its counteranions will compete with the respective substrate for the Lewis-acidic halogen substituent. Still, further comparisons with other multidentate binding motives will be necessary to gain a better understanding towards the rational design of highly potent halogen-bond donors.

4. Experimental

General

Commercially available reagents and starting materials were used without further purification. Solvents were used after single distillation. Nuclear magnetic resonance spectra (NMR-spectra) were obtained on instruments of the type *AV-500c* from *Bruker*. Chemical shifts (δ) are given as parts per million (ppm) and refer to the shift of the hydrogen, carbon or fluorine atoms in $CDCl_3$. Reference (^{1}H-NMR): residual $CHCl_3$ (δ = 7.26 ppm); reference (^{13}C-NMR): residual $CDCl_3$ (δ = 77.0 ppm); reference (^{19}F-NMR): external standard hexafluorobenzene (δ = -162.0 ppm). The following abbreviations were used for the assignment of the signals and their multiplicities: s (singulet), bs (broad singulet), ddd (doublet of doublets of doublets), dt (doublet of triplets), q (quartet), m (multiplet). The given coupling constants *J* (in Hertz) are listed as the average of the experimental findings. Mass spectrometry spectra (MS-spectra) were obtained by using electrospray ionization (ESI) or gas chromatography (GC-MS). Assigned m/z-relations are listed in ascending order. Infrared-spectra (IR-spectra) were measured directly from the substance via attenuated total reflectance (ATR-IR). The signals are labelled with the following abbreviations: vs (very strong), s (strong), m (medium), w (weak), vw (very weak).

Halide abstraction benchmark reactions

From stock solutions (in CD_3CN), the respective substrate (10.0 µmol, 1.0 eq.) and, if applicable, the activating reagent (10.0 µmol, 1.0 eq.) as well as, if applicable, pyridine (1.0 µmol, 0.1 eq.) were mixed in an NMR tube, and the solution was filled up to an overall volume of 0.60 mL. All experiments were started simultaneously and the yield was determined by NMR spectroscopy after approx. 1, 2, 4, 7, 10, 14, 18, 21 and 24 days of reaction time.

*4.1.1 3,4,5-Trifluoro-2,6-dibromoaniline (**2b**)*

1.00 g (6.80 mmol) of 3,4,5-trifluoroaniline and 2.42 g (13.6 mmol, 2 eq.) of *N*-bromosuccinimide were dissolved in 45 mL of CH_2Cl_2. The yellow solution was stirred at room temperature for 24 h, resulting in a deeply violet solution and an off-white precipitate. The mixture was filtered over a silica pad, collecting a light-brown and a violet fraction. The solvent was removed from the light-brown fraction to yield **2b** as 1.95 g (6.44 mmol, 95%) of an off-white solid.

Analytical data for **2b**: ^{1}H-NMR (500 MHz, $CDCl_3$): δ (ppm) = 4.64 (bs); ^{13}C-NMR (126 MHz, $CDCl_3$): δ (ppm) = 148.36 (ddd, $^1J_{CF}$ = 246.2, $^2J_{CF}$ = 12.1, $^3J_{CF}$ = 5.5 Hz), 139.17 – 138.56 (m), 133.03 (dt, $^1J_{CF}$ = 246.7, $^2J_{CF}$ = 17.3 Hz), 91.33 – 91.00 (m); ^{19}F-NMR (471 MHz, $CDCl_3$): δ (ppm) = -125.5 (d, $^3J_{FF}$ = 22.5 Hz), -169.1 (t, $^3J_{FF}$ = 22.6 Hz); *Elemental Analysis*: calculated C: 23.6, H: 0.66, N: 4.59, found C: 24.2, H:0.58, N: 4.46; *MS (GC)*: calculated for $C_6H_2Br_2F_3N$: 305, found: 305 [M], 226 [M - Br], 144 [M - 2·Br]; *IR*: 3485 (m), 3386 (m), 1625 (m), 1585 (s), 1480 (s), 1445 (vs), 1287 (m), 1115 (m).

*4.1.2 3,4,5-Trifluoro-2,6-diiodoaniline (2**a**)*

3.97 g (27.0 mmol) of 3,4,5-trifluoroaniline and 6.13 g (36.9 mmol) of potassium iodide were dissolved in a mixture of 65 mL of methanol and 350 mL of water. 4.12 g (19.3 mmol) of potassium iodate were added to the clear solution, resulting in a slowly clearing suspension. 36 mL of hydrochloric acid (1.5 M) were slowly added over a period of 45 min. The mixture was stirred at room temperature under exclusion of light for 21 h. The off-7 white precipitate was filtered off and washed twice with water. Upon dissolving the solid, an orange solution

resulted. It was filtered over a silica pad, dried over $MgSO_4$ and the solvent removed under reduced pressure to yield a reddish-brown oil. From this oil, 8.80 g (22.1 mmol, 82%) of **2a** were isolated by sublimation under high vacuum as a white solid.

Analytical data for **2a**: ^{1}H-NMR (500 MHz, $CDCl_3$): δ (ppm) = 4.78 (bs); ^{13}C-NMR (126 MHz, $CDCl_3$): δ (ppm) = 151.37 (ddd, $^{1}J_{CF}$ = 243.3, $^{2}J_{CF}$ = 11.2, $^{3}J_{CF}$ = 6.0 Hz), 143.34 – 142.93 (m), 131.05 (dt, $^{1}J_{CF}$ = 248.6, $^{2}J_{CF}$ = 18.7 Hz), 63.57 – 62.57 (m); ^{19}F-NMR (471 MHz, $CDCl_3$): δ (ppm) = -109.4 (d, $^{1}J_{FF}$ = 23.4 Hz), -167.2 (t, $^{2}J_{FF}$ = 23.2 Hz); *Elemental Analysis*: calculated C: 18.1, H: 0.51, N: 3.51, found C: 18.4, H: 0.44, N: 3.49; *MS (GC)*: calculated for $C_6H_2I_2F_3N$: 399, found: 399 [M], 272 [M - I], 145 [M - 2·I]; *IR*: 3459 (m), 3367 (m), 1617 (m), 1592 (s), 1467 (vs), 1428 (s), 1280 (m), 1117 (s).

*4.1.3 (E)-1,2-bis(3,4,5-trifluorophenyl)diazene (**4c**)*

0.80 g (1.10 mmol) of $PhIL_2(OTf)_2$ (L = 4-dimethylaminopyridine)[11] were suspended in 10 mL of absolute CH_2Cl_2 under argon in a flame-dried Schlenk flask. 0.10 g (0.68 mmol) of 3,4,5-trifluoroaniline were added in 10 mL of CH_2Cl_2. The mixture was stirred at reflux for 3 h, and subsequently at room temperature for 24 h. Afterwards, it was filtered over a silica pad with pentane. Solvent was removed under reduced pressure from the first yellow fraction to yield 32 mg (0.11 mmol, 32%) of **4c** as an orange solid.

Analytical data for **4c**: ^{1}H-NMR (500 MHz, $CDCl_3$): δ (ppm) = 7.69 – 7.55 (m); ^{13}C-NMR (126 MHz, $CDCl_3$): δ (ppm) = 151.75 (ddd, $^{1}J_{CF}$ = 252.5, $^{2}J_{CF}$ = 10.9, $^{3}J_{CF}$ = 4.2 Hz), 147.30 – 146.41 (m), 142.27 (dt, $^{1}J_{CF}$ = 259.1, $^{2}J_{CF}$ = 15.8 Hz), 108.19 – 107.70 (m); ^{19}F-NMR (471 MHz, $CDCl_3$): δ (ppm) = -132.32 – -132.12 (m), -153.9 – -154.1 (m); *Elemental Analysis*: calculated C: 49.7, H: 1.39, N: 9.65, found C: 49.4, H: 1.34, N: 9.59; *MS (ESI)*: calculated for $C_{12}H_4F_6N_2$: 290, found: 290 [M], 159 [M - $C_6H_3F_3$], 131 [M - $C_6H_3N_2F_3$]; *IR*: 3091 (w), 1624 (m), 1598 (m), 1509 (vs), 1444 (s), 1355 (vs), 1299 (m), 1230 (s), 1188 (m), 1111 (w), 1041 (vs), 990 (m), 875 (vs), 791 (vs), 706 (m), 663 (s).

*4.1.4 (E)-1,2-bis(3,4,5-trifluoro-2,6-dibromophenyl)diazene (**4b**)*

0.80 g (1.10 mmol) of $PhIL_2(OTf)_2$ (L = 4-dimethylaminopyridine)[11] were suspended in 10 mL of absolute CH_2Cl_2 under argon in a flame-dried Schlenk flask. 0.32 g (1.06 mmol) of ***2b*** were added in 10 mL of CH_2Cl_2. The mixture was stirred at room temperature for 3 d. Afterwards, it was filtered over a silica pad with CH_2Cl_2, yielding a dark and a yellow fraction. The dark fraction was filtered over a silica pad with pentane. Solvent was removed under reduced pressure to yield 126 mg (0.21 mmol, 38%) of ***4b*** as a dark red solid.

Analytical data for **4b**: ^{13}C-NMR (126 MHz, $CDCl_3$): δ (ppm) = 148.63 (ddd, $^{1}J_{CF}$ = 251.5, $^{2}J_{CF}$ = 12.0, $^{3}J_{CF}$ = 4.0 Hz), 144.98 – 144.07 (m), 140.54 (dt, $^{1}J_{CF}$ = 262.4, $^{2}J_{CF}$ = 17.3 Hz), 101.00 – 100.45 (m); ^{19}F-NMR (471 MHz, $CDCl_3$): δ (ppm) = -122.6 (d, $^{3}J_{FF}$ = 21.3 Hz), -151.3 (t, $^{3}J_{FF}$ = 21.4 Hz); *Elemental Analysis*: calculated C: 23.8, H: 0.00, N: 4.62, found C: 24.0, H: < 0.1, N: 4.56; *MS (ESI)*: calculated for $C_{12}Br_4F_6N_2$: 606, found: 606 [M], 319 [M - $C_6HBr_2F_3$], 289 [M - $C_6HN_2Br_3F_3$]; *IR*: 1602 (m), 1581 (m), 1483 (s), 1414 (s), 1324 (m), 1224 (m), 1072 (s), 883 (s), 723 (s), 696 (m).

*4.1.5 (E)-1,2-bis(3,4,5-trifluoro-2,6-diiodophenyl)diazene (**4a**)*

1.61 g (2.16 mmol) of $PhIL_2(OTf)_2$ (L = 4-dimethylaminopyridine)[11] were suspended in 22 mL of absolute CH_2Cl_2 under argon in a flame-dried Schlenk flask. 0.57 g (1.43 mmol) of **2a** were added in 15 mL of CH_2Cl_2. The mixture was stirred at reflux for 2 h, and subsequently at room temperature for 10 d. Afterwards, it was filtered over a silica pad with CH_2Cl_2 and again with pentane. Solvent was removed under reduced pressure to yield 256 mg (0.32 mmol, 44%) of **4a** as a violet solid.

Analytical data for **4a**: ^{13}C-NMR (126 MHz, $CDCl_3$): δ (ppm) = 151.98 (ddd, $^{1}J_{CF}$ = 248.4, $^{2}J_{CF}$ = 11.4, $^{3}J_{CF}$ = 4.6 Hz), 146.33 – 145.24 (m), 138.80 (dt, $^{1}J_{CF}$ = 264.6, $^{2}J_{CF}$ = 18.7 Hz), 74.60 – 74.25 (m); ^{19}F-NMR (471 MHz, $CDCl_3$): δ (ppm) = -107.4 (d, $^{3}J_{FF}$ = 21.9 Hz), -150.8 (t, $^{3}J_{FF}$ = 2.1 Hz); *Elemental Analysis*: calculated C: 18.2,

H: 0.00, N: 3.53, found C: 18.8, H: < 0.1, N: 3.5; *MS (ESI)*: calculated for $C_{12}I_4F_6N_2$: 794, found: 793 [M], 667 [M - I]; *IR*: 2924 (w), 2853 (vw), 1591 (m), 1465 (vs), 1401 (s), 1317 (m), 1208 (m), 1066 (vs), 858 (vs), 728 (w), 704 (m), 672 (s).

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In addition, we have also obtained single crystals of compound **4b** that were suitable for X-ray structural analysis. Similar to the case of **4a**, the crystal packing of **4b** is based on a complex network of Br-Br halogen-bonds, in which bromine substituents act both as halogen-bond donor and acceptor.

Crystal data for **4b**: formula: $C_{12}Br_4F_6N_2$; M_r=605.74; crystal color and shape: orange fragment, crystal dimensions: 0.13×0.23×0.30 mm; crystal system: orthorhombic; space group: $Pna2_1$ (no. 33); *a*=23.0474(9), *b*=11.6967(4), *c*=5.4749(2) Å, V=1475.92(9) Å^3 ; *Z*=4; $\mu(Mo_{K\alpha})$=10.972 mm^{-1}; ρ_{calcd}=2.726 g cm^{-3}; θ–range=1.77–25.36°; data collected: 44989; independent data [$I_o>2\sigma(I_o)$/all data/R_{int}]: 2669/2705/0.057; data/restraints/parameter: 2705/1/219; R1 [$I_o>2\sigma(I_o)$/all data]: 0.0174/0.0179; wR2 [$I_o>2\sigma(I_o)$/all data]: 0.0445/0.0452; GOF=1.110; $\Delta\rho_{max/min}$: 0.50/-0.36 eÅ^{-3}. For detailed information see Supporting information. CCDC XXX *{will be inserted prior to publication}* (**4b**) contains the supplementary crystallographic data for this compound.

The data of **4a** and **4b** can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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[26] We note that the complexation Gibbs free energies are estimated to be +4 kcal/mol for the adduct with **4a** and -1 kcal/mol for the complex with **1**, and thus feature the same trend. However, the calculation of exact Gibbs free energies is likely to be even more challenging than for the energies itself.