Search for an Exothermic Halogen Bond between Anions

Journal:	*Physical Chemistry Chemical Physics*
Manuscript ID	CP-ART-12-2021-005628.R1
Article Type:	Paper
Date Submitted by the Author:	17-Feb-2022
Complete List of Authors:	Scheiner, Steve; Utah State University, Department of Chemistry and Biochemistry

Search for an Exothermic Halogen Bond between Anions

Steve Scheiner*
Department of Chemistry and Biochemistry
Utah State University
Logan, Utah 84322-0300

email: steve.scheiner@usu.edu

Abstract

The literature contains numerous instances where pairs of anions engage in a stable complex with one another, held together by hydrogen, halogen, and related noncovalent bonds, within the confines of a polarizable medium such as a crystal or solvent. But within the context of the gas phase, such pairs are only metastable, higher in energy than separated monomers, whose favorable dissociation is hindered by an energy barrier. Quantum calculations search for pairs of anions that might engage in a fully stable halogen-bonded dimer in the gas phase, lower in energy than the separate monomers. Each Lewis acid candidate contains an I atom attached to an alkyne, alkene, or alkane chain of variable length, terminated by a O^- or COO^- group, and decorated with electron-withdrawing CN substituents. Also considered are aromatic systems containing I and COO^-, along with four CN substituents on the phenyl ring. Lewis bases considered were of two varieties. In addition to the simple Cl^- anion, an NH_2 group was separated from a terminal carboxylate by an alkyne chain of variable length. Exothermic association reactions are achieved with Cl^- paired with CN-substituted alkenes and alkanes where the I and COO^- of the Lewis acid are separated by at least four C atoms. The energetics are especially favorable for the longer alkanes where ΔE is roughly -30 kcal/mol.

keywords: gas-phase reaction; halogen transfer; AIM; MEP; NBO

INTRODUCTION

Within the realm of H-bonds, the vast majority of cases studied involve a pair of electrically neutral species [1, 2]. The water dimer is a classic example of a neutral H-bond, as would be the NH···O=C interaction within an α-helix or β-sheet within a protein [3]. But there are also a sizable number of cases, commonly referred to as charge-assisted H-bonds, where one of these partners bears a charge [4, 5]. The interaction between a H_3O^+ hydronium ion and a neutral water molecule represents one such example, or its converse of $HOH{\cdot\cdot}OH^-$ involving a hydroxide anion. Such bonds tend to be considerably stronger than their neutral counterparts, due in part to the added element of a charge-dipole stabilization. For example, while the neutral water dimer H-bond is assessed at roughly 5 kcal/mol [6-9], the interaction energy of either of its two charged sisters lies in the range of 30 kcal/mol [10, 11]. Salt bridges, involving two ions of opposite charge, as in a $Arg^+{\cdot\cdot}Asp^-$ pair as might occur in proteins, or the Na^+ interactions with Cl^- in crystalline NaCl, are even stronger as they involve a sizable Coulombic attraction.

For parallel reasons, one would anticipate that the approach of two ions of like charge ought to be opposed by a strong Coulombic repulsion which would prevent the formation of a H-bond. Nonetheless, this intuitive idea has been countered by a growing number of observations, from both experimental and theoretical quarters, that like-charged ions can engage in H-bonds with one another under certain conditions. Examples of such bonds involve $H_2PO_4^-$ [12-15], (RPO_3H^-) [16], HSO_4^- [17, 18], HCO_3^- [19, 20], carboxylates [21, 22], and aspartate [23], as well as an assortment of others [24-29].

Very similar considerations apply to the noncovalent bonds that are closely related to H-bonds in which the bridging proton is replaced by any of a large set of nominally electronegative atoms, as in halogen, chalcogen, etc bonds [30-35]. Again, the Coulombic repulsions between ions of like charge can be successfully countered by attractive short-range forces and lead to a stable complex. The bulk of these findings pertain to halogen bonds [36-46] but there are recent studies beginning to emerge that indicate similar sorts of attractive anion-anion interactions apply to pnicogen bonds [47] and to those between systems such as $AuCl_4^-$ pairs [48]. Our own group has been actively engaged in studies to test the boundaries of these ideas. Calculations have indicated that anions that can engage in complexes with one another include MCl_3^- where M refers to Group 2 [49] and Group 12 (so-called spodium bonds) [50-52], pnicogen bonds of the ZCl_4^- type [53], triel bonds involving $TrCl_4^-$ [54], and aerogen bonds with AeX_5^- [55].

The overarching conclusion from these numerous studies is that the general Coulombic repulsion between a pair of anions can be balanced to some extent by short-range attractive elements. In the gas phase, a complex can be formed between these two ions, but its energy is somewhat higher than that of the pair of separated anions, so ΔE for the association reaction is endothermic. However, the dissociation of the complex is impeded by an energy barrier so that the dimer can be categorized as metastable. The situation changes within a polarizable environment, whether a simulated solvent or a set of counterions mimicking a crystal. Not only does this medium remove the barrier, but it frequently makes the association process an exothermic one, so that the complex will form spontaneously.

These observations raise a fundamental question. Are there pairs of ions of like charge that might form a complex with one another spontaneously in the gas phase, without the intermediacy of a polarizable environment? It stands to reason that such a scenario would be more likely if the center of charge of each ion can be displaced some distance away from the partner, thereby mitigating the overall Coulombic repulsion, and permitting the short-range attractions to take hold. There is in fact some evidence that this idea might aid the complexation, at least in the case of H-bonds. When a pair of diphthalate anions, each with a carboxylate group separated from the -COOH group by a phenyl ring, were paired, they were able to form a H-bonded complex with only a small positive ΔE [25]. But this endothermicity is increased when these two groups are separated by a shorter alkyl chain [22]. As the separation between the -OH group and the pyridinium is increased along an alkyl chain [56], there is a clear propensity for ΔE to diminish for a pair of $\{Py\text{-}(CH_2)_n\text{-}OH\}^+$ cations, and even turn negative, albeit only slightly so, as the chain length rises above 15.

With some resolution just beginning to emerge for H-bonds, the question turns to halogen bonds. While there are a number of endothermic halogen-bonded complexes that have been found to be metastable in the gas phase due to an energy barrier in their dissociation process, there have as yet been no such ion pairs of like charge identified for which the dimerization process is an exothermic one. In an effort to confront this question in a systematic manner, a series of Lewis acids are constructed, each containing an I atom as this heavy halogen has been shown to form the strongest halogen bonds. The I is situated on a C-chain of varying type and length, and at the terminus of each is placed a center of negative charge, either $-COO^-$ or $-O^-$. The chains are of alkyne, alkene, or alkane type, as well as an aromatic phenyl ring, and each is fully per-substituted with electron-withdrawing cyano groups so as to maximize the depth of the σ-hole on the I. With regard to the electron donor partner, a NH_2 group is placed on an alkyne chain of varying length, and the Lewis base receives its overall negative charge from a carboxylate group on the opposite end of this chain. As alternative anionic base, a simple Cl^- anion has its electron donating site coincident with its center of negative charge, so offers a distinctly different sort of binding.

COMPUTATIONAL METHODS

Calculations were carried out within the framework of the Gaussian 16 [57] set of programs. Systems were examined via density functional theory (DFT), with the M06-2X functional. The aug-cc-pVDZ basis set was adopted as it includes both polarization and diffuse functions, and its reliability has been documented in the past, particularly when used in conjunction with M06-2X [58-66]. I was represented by the aug-cc-pVDZ-PP pseudopotential so as to account for relativistic effects.

Geometries were fully optimized with no symmetry restrictions. The complexation energy ΔE is defined as the difference between the energy of the entire complex and the sum of the isolated energies of the two monomers in their optimized structures. The electron density and molecular electrostatic potential (MEP) were analyzed via the Multiwfn program [67]. The σ-hole was defined as the locus of points that constitute the MEP maximum on an isodensity surface of ρ=0.001 au, and the MEP there defined as V_{max}. AIMAll [68] was used to implement the AIM formalism that identifies bond paths and computes the properties of their critical points. Charge transfers between individual orbitals and their associated second-order energies, were derived by Natural Bond Orbital (NBO) theory [69, 70] by way of the NBO3 program incorporated into Gaussian.

RESULTS

The Lewis base anion is of two types. First are the NH_2-C_n-COO^- chains where *n* C atoms separate the carboxylate from the amine which acts as electron donor, by virtue of a conjugated set of triple C≡C bonds. Adjustment of *n* allows the distance between the carboxylate center of negative charge and the amine group to be tuned. The second base considered is the simple Cl^- anion where the atom acting as electron donor is also the center of negative charge. Lewis acids were of the alkyne, alkene, and alkane variety. The ^-OOC-C_n-I alkynes place a carboxylate group at one end of the chain and an I on the opposite end, with an intervening number *n* of C atoms separating them. Again the separation of the locus of negative charge from the halogen I atom, acting as electron acceptor can be adjusted via *n*. Alkenes of the ^-OOC-$C_n(CN)_n$-I sort place an electron-withdrawing cyano substituent on each of the intervening C atoms. Alkane chains permit a doubling of the number of CN substituents in ^-OOC-$C_n(CN)_{2n}$-I, which ought to further amplify any possible σ-hole on the I. (For some of the shorter chains, the carboxylate group was replaced by -O so as to further concentrate the charge, as indicated below.) The last sort of Lewis acid considered was aromatic, with a carboxylate *para* to the I, and with the other four positions occupied by CN.

When paired together, each Lewis acid and base formed a complex, a minimum on their potential energy surface. However, most of these dimers were only metastable in the sense that the energy is higher than that of the two fully separated optimized monomers from which they arise. The dissociation process is exothermic, but must surmount an energy barrier. This metastable character is indicated by the numerous positive quantities for ΔE in Table 1, where ΔE represents the energy change in transitioning from separate monomers to dimer (also commonly referred to as binding energy E_b in the literature).

Alkynes

The trends in these energetics are of paramount importance. First considering the alkyne Lewis acids with no CN substituents, all values of ΔE are positive. One can see however that as the chains are lengthened, i.e. as the center of negative charge is moved further from the interacting atoms (I or N), ΔE becomes less positive. More specifically, if both chains are of length 4, ΔE is +16.2 kcal/mol. Lengthening the base chain to n=8 reduces this quantity to +12.4, and then also lengthening the acid to n=8 further reduces ΔE to +9.6. The value of V_{max} in the next column of Table 1 offers an insight into the reason for this lowering. V_{max} refers to the value of the maximum of the molecular electrostatic potential (MEP) on the 0.001 a.u. isodensity surface surrounding the acid, located along the extension of the C-I bond axis, the so-called σ-hole. Whereas this quantity is negative for a chain of length 4, it reverses its sign and becomes positive when n=8. This trend is consistent with the further removal of the $-COO^-$ group from the I. Replacement of the alkyne base by the chloride anion further stabilizes the system, lowering ΔE down to only +2.3 kcal/mol.

Sample geometries of some of these dimers are displayed in Fig 1. It may be noted first that the Cl approaches more closely to the I than does the amine N atom, despite the larger atomic size of the former. This shorter R(I··Cl) distance is consistent with the smaller ΔE. Whereas the Cl lies directly along the C-I extension, coincident with the σ-hole, the amine is somewhat removed from this axis. More will be said below about these angular features.

There are additional aspects of these intermolecular interactions that can be gleaned by analysis of the wave functions. The next column of Table 1 lists the value of the electron density at the bond critical point along the bond path between I and N or Cl. Of the three complexes involving an alkynic Lewis base, it is the 8-8 dimer that has the highest ρ_{BCP} at 0.0124. But this quantity is much higher, 0.0307 when the Cl^- anion is applied as base. The same patterns appear in the NBO analysis of these interactions. The second-order perturbation energy E(2) involving the charge transfer from the N/Cl lone pair to the σ*(IC) antibonding orbital of the acid is by far the largest for Cl^-, and the 8-8 complex is highest among the alkyne base subset. The last two columns of Table 1 indicate that there may be some minor secondary interactions supplementing the binding energies for the alkynes. There appears to be a weak pnicogen bond, in which there is a charge transfer from the I lone pair to the σ*(NC) orbital, and even perhaps a very weak H-bond from I lone pairs to NH groups of the amine. On the other hand, these auxiliary bonds are not supported by AIM analysis which shows only the primary I··N/Cl bond path.

Alkenes

Changing the C≡C triple bonds in the alkynes to double bonds allows the placement of highly electron-withdrawing substituents on all of the intervening C atoms, as is evident in Fig 2. The values of ΔE in the corresponding section of Table 1 suggests only a minimal effect upon the strength of the intermolecular halogen bonds. For example, ΔE for the 4-4 complex involving the alkene is slightly more positive than for the alkyne. Lengthening the Lewis acid slowly reduces ΔE but it remains positive even for the 8-4 dimer. On the other hand, the alkyne→alkene transition induces a substantial change in the I··Cl halogen bonds. Although the 4-Cl ΔE remains positive, the lengthening to 6 and then to 8 of the Lewis acid reverses the sign, dropping ΔE down to -10.0 kcal/mol for 8-Cl.

With regard to the σ-hole depth, the alkenes are more sensitive to chain length than are the alkynes. Whereas the alkyne lengthening from 4 to 8 raises V_{max} by 17 kcal/mol from -13.6 to +3.7 kcal/mol, the same addition of 4 more C atoms adds 38 kcal/mol to the alkenes, rising from -25.9 to +11.6 kcal/mol. One can attribute much of this effect to the presence of the electron-withdrawing CN units in the alkenes. This enhanced sensitivity is clearly more effective in stabilizing the complex with chloride than with the alkyne base. The AIM critical point densities are consistent with the energetics. There is only a slow rise in ρ_{BCP} for elongation of the Lewis acid for the alkyne base, whereas this quantity is much larger for Cl^-, and rises quickly along with acid chain length. Parallel observations apply to the NBO charge transfer energies.

Alkanes

Using singly bonded C atoms in the Lewis acid chain permits a doubling of the number of CN substituents on each C, as can be seen in Fig 3. Although this switch to alkanes does deepen some of the σ-holes, making most of them positive, the values of ΔE remain stubbornly positive with the alkyne base. Such is clearly not the case for the Cl^- base. Again, ΔE is quite sensitive to Lewis acid chain length and V_{max}, to the point that ΔE is negative for acids with more than two C atoms. In fact, ΔE can be quite exothermic, surpassing -30 kcal/mol.

There is a new issue that arises in connection with the interactions between these substituted alkanes and the Cl^- anion. A glance at the complex in Fig 3b indicates that the I nucleus lies in a nearly central position, almost equally distant from the C of the alkane and the Cl. This near equality is particularly notable in light of the larger atomic radius of Cl as compared to C. In fact, this central location is characteristic of not only the 8-C alkane, but is true to some degree of the shorter ones as well. The R(C-I) and R(I-Cl) distances are equal to 2.49 and 2.55 Å for C6, and a little more different from each other for C4, at 2.44 and 2.60 Å, respectively. So the sharing of the I is closely associated with the high exothermicity of these complexes between anions, even in the gas phase. This near central location of the I, with two roughly equal bond lengths, can be considered a sign of a hypervalent atom.

The alkyne acids also present some contradictions between AIM and NBO analysis of the wave functions. Whereas AIM supports the presence of halogen bonds as the only connection between the acid and base, NBO suggests substantial secondary interactions with the alkyne base, albeit with some inconsistency. On one hand the C6-C4 dimer contains a sizable NH··I H-bond E(2), but this bond disappears for the slightly longer C8 acid, being replaced by a weaker CN··I pnicogen bond. This switch occurs although there is little difference between the intermolecular orientations (see below), so one might question the validity of the NBO interpretation.

Phenyl Groups

Another sort of internally bonded Lewis acid that was considered was the phenyl group. The I and carboxylate group were placed *para* to one another, and the other four positions were occupied by cyano groups. Such a species developed a σ-hole on the I of depth -13.0 kcal/mol, a negative value intermediate between the n=4 and n=6 linear alkenes, also with sp^2 hybridized C atoms. Like both of the latter, the aromatic system also combines with amine anions with a positive ΔE, regardless of the chain length of this partner. Note that this indifference to chain length even applies to the n=0 NH_2COO^- anion pictured in Fig 4a, where the carboxylate directly abuts the electron donor N atom, and the R(I··N) distance is much shorter than for n=4 in Fig 4b. The shorter amine anion also leads to a surprisingly large NBO E(2) signaling a H-bond, but ΔE remains positive nonetheless. Unlike the linear Lewis acids, the value of ΔE is not lowered by very much as a result of replacement of the amine base by chloride.

Geometric Aspects

The salient geometrical properties of the various complexes are compiled in Table 2. The intermolecular R(I··N) distances for the amine bases exceed 3 Å for the alkyne acids, and are somewhat shorter for alkenes, and shorter still for the alkanes. The shortest such distance is 2.60 Å for the complex between $^-OOC\text{-}C_6(CN)_6\text{-}I$ and $NH_2\text{-}C_4\text{-}COO^-$. Replacing the amine by Cl^- results in a contraction of varying degree. This R(I··Cl) reduction is particularly notable for the partial I-transferred structures involving the longer alkanes, where it is accompanied by a lengthening of R(C-I).

The reader may have noticed in the figures that the Cl^- anion lies directly along the C-I bond extension, coincident with the location of the σ-hole on I. This position is amplified by the θ(CI··Cl) entries in the penultimate column of Table 2. The disposition of the amine is quite different. In most cases, the amine N is removed from the C-I bond axis, with θ(CI··N) angles that vary between 134° and 172°. As a secondary consideration, the θ(I··NC) angles in the last column of Table 2 are quite a bit larger than the 109° one might expect from a tetrahedral sp^3 N atom with a lone pair occupying one of the tetrahedron legs.

These relative orientations can be understood on the basis of a synergy between electrostatics and orbital interactions. The MEP of the C_6 alkene dimer and the C_4 amine are exhibited in Fig 5a, disposed as they are in the optimized complex. The MEPs of these anions are of course negative throughout so the blue regions indicate the least negative and red most negative. In addition to the blue σ-hole on the I atom of the acid, there is a more negative red region along the equator of the C-I bond. Thus, by moving down and away from the C-I bond extension, and rotating as it does in Fig 5a, the base can achieve two stabilizing interactions, both indicated by the green double-headed arrows. The red N lone pair region can align with the I σ-hole, while the less negative NH atoms can approach the lateral negative belt of I to some degree.

The orbital aspects are illustrated in Fig 5b where the grey regions represent filled orbitals, the N and I lone pairs. The white shapes indicate vacant antibonding orbitals, σ*(CI) and σ*(NC). By adopting the bent geometry, the N lone pair can donate charge to the σ*(CI) orbital as is typical of a halogen bond, represented by the curved blue arrows. But one can achieve also a $I_{lp}\rightarrow\sigma^*(NC)$ transfer as well, even if to a lesser extent. Since these two transfers move in opposite directions, they can reinforce one another. This auxiliary pnicogen bond manifests itself within the NBO analysis of some of the complexes, even if E(2) is less than 1 kcal/mol.

Another lens through which to view these two interactions is derived from electron density shifts. Fig 5c illustrates these shifts in the alkyne 8-8 dimer, computed as the difference in density between the complex and the sum of densities of the individual non-interacting monomers. Purple regions designate gains of density arising from the interaction and losses are shown in green. It might first be noted that these shifts are localized in the region where the two molecules interface. In addition to the loss/gain pattern along the I··N axis characteristic of a halogen bond, there are also smaller colored regions below the I··N axis which may be taken as indications of the secondary interaction.

These two attractive forces work against one another in a sense. That is, as the amine moves up closer to the I σ-hole, and as θ(CI··N) approaches 180°, it will be less possible for the second connection to be made between the I lone pair and σ*(NC) orbital, so θ(CN··I) can lean closer to its tetrahedral angle near 110°. This concept is in fact observed. Fig 6 plots these two angles against one another and evidences a clear trend that θ(CN··I) drops down toward 110° as θ(CI··N) approaches 180°.

DISCUSSION

One can expect that immersion of these systems in solvent or any other sort of dielectric material ought to stabilize the complex. Indeed, there are now numerous instances in the literature wherein a metastable complex was formed between two ions of like charge, separated from the more stable dissociated pair of ions by a small energy barrier [14, 21, 22, 26, 38, 71-75]. The imposition of a polarizable dielectric continuum as a model of solvation converts this dimer into a stable complex, lower in energy than the pair of separated ions [12, 23, 24, 28, 36, 37, 40-45, 76-78].

This idea was tested out here for two systems. The alkene 4-4 complex has a complexation energy of +19.0 kcal/mol. When surrounded by a model aqueous solvation medium via the PCM method, this complexation reaction became slightly exothermic, with ΔE= -1.9 kcal/mol. Part of the reason for this 21 kcal/mol stabilization is the deepening of the σ-hole, with V_{max} rising from -25.9 kcal/mol in vacuo to -10.2 kcal/mol in water. A stabilization of similar magnitude occurred with the alkane 4-4 dimer, with ΔE dropping from +15.4 kcal/mol in vacuo to -6.4 kcal/mol in aqueous medium. This solvation process again causes a dramatic deepening of V_{max} from +2.2 to +24.1 kcal/mol. It is worth noting that this large reduction in ΔE is not the direct result of a stronger interaction within the confines of the polarizable medium, as the bond critical point density is barely changed by this solvation.

Despite the fact that both acid and base participants carry a full negative charge, the interactions are clearly halogen bonds, even when ΔE is positive. This character is revealed by AIM analysis which contains bond paths between the I and N or Cl atom of the base, with no other intermolecular paths. NBO shows the characteristic charge transfers from the lone pair of the base atom to the σ*(IC) antibonding orbital within the acid. Electron density maps, e.g. Fig 5c, also buttress this conclusion, showing patterns of charge shifts that are characteristic of a halogen bond.

Regarding the goal of identifying systems for which a pair of anions might engage in a stable complex, with negative ΔE in vacuo, there are only a few such systems which fit this criterion. Considering an amine anion as the electron acceptor, there was no anionic acid which fulfilled this criterion. Both the acid and base were of variable lengths, with the center of negative charge, both O^- and COO^-, lying at different distances from the I and N sites of halogen bond formation. ΔE was positive whether the acid consisted of an alkyne, alkene, or alkane chain, or comprised an aromatic system. Adding electron-withdrawing cyano substituents to the acid did not deepen the σ-holes to the point that they could sustain an exothermic dimer. It might be noted that some of these systems did provide a positive σ-hole on the I, particularly the CN-substituted alkanes, for which V_{max} rose to as high as +23 kcal/mol despite the overall negative charge on the acid. In terms of the magnitude of ΔE, this quantity tends to become less positive as either the acid or base are elongated, further removing the center of negative charge from the I or N atoms that interact with one another. This concept is consistent with prior calculations [79] albeit in a different context pairing an anionic Lewis acid with a neutral base.

The situation changes when the amine base is replaced by the simple chloride anion. The values of ΔE are consistently smaller than is observed for the amines, even though there is no separation between the nucleophilic atom and the center of charge, which are one and the same. When combined with the fully CN-substituted alkane acids, ΔE reaches down to -36 kcal/mol. This quantity also becomes negative when combined with alkene acids of chain length greater than 4. Even in the case of the alkynes where there are no CN substituents, ΔE is quite small, even if still positive. Note, however, that Cl^- fails to engage in an exothermic dimer with the aromatic $^-OOC\text{-}C_6(CN)_4\text{-}I$ anion, with ΔE=+14 kcal/mol. There does appear to be a relationship between ΔE for the chloride and the depth of the σ-hole on the I of the acid: In most cases, ΔE becomes negative if V_{max} is positive.

Basis set superposition error [80-85] is much too small to influence any of the above conclusions. When evaluated by the standard Boys-Bernardi counterpoise procedure [86], this artifact amounts to less than 0.3 kcal/mol for the interactions of Cl^- with either the 4 or 6 alkanes, leaving both of these complexations as clearly exothermic. If one were to shift attention away from the electronic energy of reaction ΔE to the Gibbs free energy of reaction ΔG at 25 C, the latter are more positive than the former by roughly 8 kcal/mol. This rise changes the slightly exothermic combinations of Cl^- with the 6-alkene and 4-alkane to slightly positive ΔG of +4.7 and +1.9 kcal/mol. The more exothermic reaction of the chloride with 8-alkene, and particularly the 6- and 8-alkanes, remains exothermic with respect to ΔG, at -2.2, -29.8, and -22.1, respectively.

There is the interesting finding that the I atom moves further away from the C atom to which it is covalently bonded as ΔE becomes more negative. Indeed, for the complexes with ΔE particularly large in magnitude, the I lies roughly halfway between the C and the Cl of the base, which can be thought of as a half transfer. The partial transfer of a halogen between two entities has been noted earlier in certain types of systems, particularly Cl [38, 87-91]. Some examples of I transfer occur in the F--I--NH_3 and the FO--I--NH_3 complexes [92] where transfer to the N base atom is roughly 25% to 37%; a more complete transfer occurs in F_2NO--I--NH_3. In the case of an overall cationic system [93], the I will be situated midway between a pair of O, N, or C atoms, but only if the intermolecular distance is rather short; longer separations lead to a double-well potential.

There are several other interesting questions that might be pursued with respect to these systems. How important are the electron-withdrawing CN groups in enabling the Lewis acid to draw in an anion? As a test, these substituent were replaced by H for the interaction of Cl^- with both the C8-alkene and the C8-alkane. This replacement causes the negative ΔE in both cases to become positive. Specifically, the alkene value rises from -10.0 to +15.6 kcal/mol, while that of the alkane increases from -29.2 to 16.8 kcal/mol. Not unexpectedly, the removal of the CN groups causes the σ-hole on the I atom to weaken and even reverse sign. V_{max} drops from +11.6 kcal/mol on the C8-alkene to -18.8 kcal/mol. Likewise for the C8 alkane where V_{max} diminishes from +23.4 to -19.7 kcal/mol. These dramatic changes are clear evidence of the necessity of these CN groups.

Another question concerns how much the presence of the charge of terminal carboxylate group influences the interaction. That is, is this group placed far enough away from the site of interaction that its effect has been moderated. In order to answer this question, the $-COO^-$ was replaced by a methyl group on the C6 and C8 alkanes. The metamorphosis of the anion-anion interaction to a neutral-anion one permits a much more exothermic association with Cl^-. The ΔE values for the C6 and C8 alkanes of -35.6 and -29.2 kcal/mol, respectively, were dropped down to -60.1 and -62.2 kcal/mol. These much stronger bonds are due in part to much deeper σ-holes on the neutral iodoalkanes. The values of V_{max} rise from 14.7 and 23.4 kcal/mol in the C6 and C8 anions, respectively, up to 54.6 and 55.9 kcal/mol in the neutral methyl-substituted systems. So even when removed from the I site of interaction by a fairly long alkyl chain, the anionic terminus maintains a strong destabilizing influence upon the halogen bond strength.

The idea of trying to combine a pair of ions of like charge into a stable complex was also tested for smaller systems, both pairs of anions and pairs of cations. With regard to the former, CN^- was brought up toward the central atom of GeF_3^-, SeF_3^-, AsF_4^-, and BrF_2^-, which might in principle have engaged in a tetrel, chalcogen, pnicogen, or halogen bond, respectively. However, none of these anion pairs were stable, immediately dissociating with no intervening energy barrier. The same inability to form a stable dimer was true of pairs of cations, with CN^+ approaching GeF_3^+ in an attempt toward a dicationic tetrel bond. Similar failures to form a stable H-bonded complex between anions occurred when CN^- interacted with OH^-, HSO_3^-, and HCO_3^-.

CONCLUSIONS

Elongation of the Lewis acid, which further separates the I site of halogen bonding from the center of negative charge along the C-chain, tends to lower the energy of the dimer relative to the two monomer anions. This effect is muted when combined with an amine base situated on a negatively charged alkyne chain, and is unable to yield a negative value of ΔE, even when the alkane Lewis acid is fully substituted with numerous electron-withdrawing CN groups. The same is true for an aromatic acid where the four sites of the ring intermediate between the I and COO^- contain CN. The binding energetics are much more sensitive to Lewis acid chain length when paired with the simple Cl^- anion. Elongation of the chain to 6 in the case of alkene, and 4 for alkane, results in a negatie ΔE. The halogen bond complexation reaction is particularly exothermic for n=6 or n=8 alkanes, with ΔE exceeding -30 kcal/mol.

Acknowledgements

This material is based upon work supported by the National Science Foundation under Grant No. 1954310.

Conflict of Interest

The author declares no competing financial interest.

REFERENCES

1. G. R. Desiraju and T. Steiner, *The Weak Hydrogen Bond in Structural Chemistry and Biology*, Oxford, New York, 1999.
2. S. Scheiner, *Hydrogen Bonding: A Theoretical Perspective*, Oxford University Press, New York, 1997.
3. G. A. Jeffrey and W. Saenger, *Hydrogen Bonding in Biological Structures*, Springer-Verlag, Berlin, 1991.
4. E. Bosch and N. P. Bowling, *Cryst. Growth Des.*, 2020, **20**, 1565-1571.
5. G. Gilli and P. Gilli, *The Nature of the Hydrogen Bond*, Oxford University Press, Oxford, UK, 2009.
6. B. E. Rocher-Casterline, L. C. Ch'ng, A. K. Mollnera and H. Reisler, *J. Chem. Phys.*, 2011, **134**, 214501.
7. M. W. Feyereisen, D. Feller and D. A. Dixon, *J. Phys. Chem.*, 1996, **100**, 2993-2997.
8. Y.-B. Wang, F.-M. Tao and Y.-K. Pan, *J. Mol. Struct. (Theochem)*, 1994, **309**, 235-239.
9. S. Scheiner, *Annu. Rev. Phys. Chem.*, 1994, **45**, 23-56.

10. Y. Xie, R. B. Remington and H. F. Schaefer, *J. Chem. Phys.*, 1994, **101**, 4878-4884.
11. S. S. Xantheas, *J. Am. Chem. Soc.*, 1995, **117**, 10373-10380.
12. I. Mata, I. Alkorta, E. Molins and E. Espinosa, *Chem. Phys. Lett.*, 2013, **555**, 106-109.
13. A. Rajbanshi, S. Wan and R. Custelcean, *Cryst. Growth Des.*, 2013, **13**, 2233-2237.
14. F. Weinhold, *Inorg. Chem.*, 2018, **57**, 2035-2044.
15. T. S. C. MacDonald, B. L. Feringa, W. S. Price, S. J. Wezenberg and J. E. Beves, *J. Am. Chem. Soc.*, 2020, **142**, 20014-20020.
16. W. Zhao, B. Qiao, J. Tropp, M. Pink, J. D. Azoulay and A. H. Flood, *J. Am. Chem. Soc.*, 2019, **141**, 4980-4989.
17. E. M. Fatila, E. B. Twum, A. Sengupta, M. Pink, J. A. Karty, K. Raghavachari and A. H. Flood, *Angew. Chem. Int. Ed.*, 2016, **55**, 14057-14062.
18. E. M. Fatila, E. B. Twum, J. A. Karty and A. H. Flood, *Chem. Eur. J.*, 2017, **23**, 10652-10662.
19. J. S. McNally, X. P. Wang, C. Hoffmann and A. D. Wilson, *Chem. Commun.*, 2017, **53**, 10934-10937.
20. D. A. Cullen, M. G. Gardiner and N. G. White, *Chem. Commun.*, 2019, **55**, 12020-12023.
21. I. Alkorta, I. Mata, E. Molins and E. Espinosa, *Chem. Eur. J.*, 2016, **22**, 9226-9234.
22. R. Barbas, R. Prohens, A. Bauzá, A. Franconetti and A. Frontera, *Chem. Commun.*, 2019, **55**, 115-118.
23. M. O. Miranda, D. J. R. Duarte and I. Alkorta, *ChemPhysChem.*, 2020, **21**, 1052-1059.
24. I. Mata, E. Molins, I. Alkorta and E. Espinosa, *J. Phys. Chem. A*, 2015, **119**, 183-194.
25. P. R. Horn, Y. Mao and M. Head-Gordon, *Phys. Chem. Chem. Phys.*, 2016, **18**, 23067-23079.
26. F. Weinhold, *Angew. Chem. Int. Ed.*, 2017, **56**, 14577-14581.
27. N. G. White, *CrystEngComm*, 2019, **21**, 4855-4858.
28. L. M. Azofra, J. Elguero and I. Alkorta, *J. Phys. Chem. A*, 2020, **124**, 2207-2214.
29. L. M. Azofra, J. Elguero and I. Alkorta, *Phys. Chem. Chem. Phys.*, 2020, **22**, 11348-11353.
30. S. Scheiner, *Chem. Eur. J.*, 2016, **22**, 18850-18858.
31. V. d. P. N. Nziko and S. Scheiner, *Phys. Chem. Chem. Phys.*, 2016, **18**, 3581-3590.
32. S. Scheiner, *J. Phys. Chem. A*, 2015, **119**, 9189-9199.
33. T. Kar, H. F. Bettinger, S. Scheiner and A. K. Roy, *J. Phys. Chem. C*, 2008, **112**, 20070-20075.
34. K. Luth and S. Scheiner, *J. Phys. Chem.*, 1994, **98**, 3582-3587.
35. Z. Latajka and S. Scheiner, *J. Chem. Phys.*, 1984, **81**, 4014-4017.
36. D. Quinonero, I. Alkorta and J. Elguero, *Phys. Chem. Chem. Phys.*, 2016, **18**, 27939-27950.
37. G. Wang, Z. Chen, Z. Xu, J. Wang, Y. Yang, T. Cai, J. Shi and W. Zhu, *J. Phys. Chem. B*, 2016, **120**, 610-620.
38. S. M. Chalanchi, I. Alkorta, J. Elguero and D. Quiñonero, *ChemPhysChem.*, 2017, **18**, 3462-3468.
39. C. Wang, Y. Fu, L. Zhang, D. Danovich, S. Shaik and Y. Mo, *J. Comput. Chem.*, 2018, **39**, 481-487.
40. Z. Zhu, G. Wang, Z. Xu, Z. Chen, J. Wang, J. Shi and W. Zhu, *Phys. Chem. Chem. Phys.*, 2019, **21**, 15106-15119.

41. J. M. Holthoff, E. Engelage, R. Weiss and S. M. Huber, *Angew. Chem. Int. Ed.*, 2020, **59**, 11150-11157.
42. T. Maxson, A. S. Jalilov, M. Zeller and S. V. Rosokha, *Angew. Chem. Int. Ed.*, 2020, **59**, 17197-17201.
43. K. Ghosh, A. Frontera and S. Chattopadhyay, *CrystEngComm*, 2021, **23**, 1429-1438.
44. Y. Li, L. Meng and Y. Zeng, *ChemPlusChem*, 2021, **86**, 232-240.
45. C. Loy, J. M. Holthoff, R. Weiss, S. M. Huber and S. V. Rosokha, *Chem. Sci.*, 2021, **12**, 8246-8251.
46. J. M. Holthoff, R. Weiss, S. V. Rosokha and S. M. Huber, *Chem. Eur. J.*, 2021, **27**, 16530-16542.
47. A. Bauzá, A. Frontera and T. J. Mooibroek, *Nat. Comm.*, 2017, **8**, 14522.
48. A. Daolio, A. Pizzi, G. Terraneo, M. Ursini, A. Frontera and G. Resnati, *Angew. Chem. Int. Ed.*, 2021, **60**, 14385-14389.
49. W. Zierkiewicz, R. Wysokiński, M. Michalczyk and S. Scheiner, *ChemPhysChem.*, 2020, **21**, 870-877.
50. R. Wysokiński, W. Zierkiewicz, M. Michalczyk and S. Scheiner, *ChemPhysChem.*, 2020, **21**, 1119-1125.
51. R. Wysokiński, W. Zierkiewicz, M. Michalczyk and S. Scheiner, *ChemPhysChem.*, 2021, **22**, 818-821.
52. R. Wysokiński, W. Zierkiewicz, M. Michalczyk and S. Scheiner, *Phys. Chem. Chem. Phys.*, 2021, **23**, 13853-13861.
53. S. Scheiner, R. Wysokiński, M. Michalczyk and W. Zierkiewicz, *J. Phys. Chem. A*, 2020, **124**, 4998-5006.
54. R. Wysokiński, M. Michalczyk, W. Zierkiewicz and S. Scheiner, *Phys. Chem. Chem. Phys.*, 2021, **23**, 4818-4828.
55. A. Grabarz, M. Michalczyk, W. Zierkiewicz and S. Scheiner, *Molecules*, 2021, **26**, 2116.
56. T. Niemann, P. Stange, A. Strate and R. Ludwig, *Phys. Chem. Chem. Phys.*, 2019, **21**, 8215-8220.
57. M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, G. A. Petersson, H. Nakatsuji, X. Li, M. Caricato, A. V. Marenich, J. Bloino, B. G. Janesko, R. Gomperts, B. Mennucci, H. P. Hratchian, J. V. Ortiz, A. F. Izmaylov, J. L. Sonnenberg, Williams, F. Ding, F. Lipparini, F. Egidi, J. Goings, B. Peng, A. Petrone, T. Henderson, D. Ranasinghe, V. G. Zakrzewski, J. Gao, N. Rega, G. Zheng, W. Liang, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, K. Throssell, J. A. Montgomery Jr., J. E. Peralta, F. Ogliaro, M. J. Bearpark, J. J. Heyd, E. N. Brothers, K. N. Kudin, V. N. Staroverov, T. A. Keith, R. Kobayashi, J. Normand, K. Raghavachari, A. P. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, J. M. Millam, M. Klene, C. Adamo, R. Cammi, J. W. Ochterski, R. L. Martin, K. Morokuma, O. Farkas, J. B. Foresman and D. J. Fox, Wallingford, CT2016.
58. A. P. Orlova and P. G. Jasien, *Comput. Theor. Chem.*, 2018, **1139**, 63-69.
59. A. Forni, S. Pieraccini, D. Franchini and M. Sironi, *J. Phys. Chem. A*, 2016, **120**, 9071-9080.
60. A. Bauzá, X. García-Llinás and A. Frontera, *Chem. Phys. Lett.*, 2016, **666**, 73-78.
61. M. D. Esrafili and E. Vessally, *Chem. Phys. Lett.*, 2016, **662**, 80-85.
62. N. Mardirossian and M. Head-Gordon, *J. Chem. Theory Comput.*, 2016, **12**, 4303-4325.

63. A. Forni, S. Pieraccini, S. Rendine and M. Sironi, *J. Comput. Chem.*, 2014, **35**, 386-394.
64. A. Bauzá, I. Alkorta, A. Frontera and J. Elguero, *J. Chem. Theory Comput.*, 2013, **9**, 5201-5210.
65. H. C. Georg, E. E. Fileti and T. Malaspina, *J. Mol. Model.*, 2013, **19**, 329-336.
66. J. Lu and S. Scheiner, *Molecules*, 2019, **24**, 2822.
67. T. Lu and F. Chen, *J. Comput. Chem.*, 2012, **33**, 580-592.
68. T. A. Keith, TK Gristmill Software, Overland Park KS2013.
69. A. E. Reed, L. A. Curtiss and F. Weinhold, *J. Chem. Phys.*, 1985, **83**, 735-746.
70. A. E. Reed, L. A. Curtiss and F. Weinhold, *Chem. Rev.*, 1988, **88**, 899-926.
71. Y. Chen, L. Yao and F. Wang, *J. Mol. Model.*, 2021, **27**, 110.
72. F. Yang, K. A. Behrend, H. Knorke, M. Rohdenburg, A. Charvat, C. Jenne, B. Abel and J. Warneke, *Angew. Chem. Int. Ed.*, 2021, **60**, 24910-24914.
73. D. Quiñonero, I. Alkorta and J. Elguero, *ChemPhysChem.*, 2020, **21**, 1597-1607.
74. I. Mata, E. Molins, I. Alkorta and E. Espinosa, *J. Phys. Chem. A*, 2014, **119**, 183-194.
75. I. Mata, I. Alkorta, E. Molins and E. Espinosa, *ChemPhysChem.*, 2012, **13**, 1421-1424.
76. G. Bélanger-Chabot and H. Braunschweig, *Angew. Chem. Int. Ed.*, 2019, **58**, 14270-14274.
77. Í. Iribarren, M. M. Montero-Campillo, I. Alkorta, J. Elguero and D. Quiñonero, *Phys. Chem. Chem. Phys.*, 2019, **21**, 5796-5802.
78. A. Shokri, M. Ramezani, A. Fattahi and S. R. Kass, *J. Phys. Chem. A*, 2013, **117**, 9252-9258.
79. Z. Chen, G. Wang, Z. Xu, J. Wang, Y. Yu, T. Cai, Q. Shao, J. Shi and W. Zhu, *J. Phys. Chem. B*, 2016, **120**, 8784-8793.
80. S. Simon, M. Duran and J. J. Dannenberg, *J. Chem. Phys.*, 1996, **105**, 11024-11031.
81. Z. Latajka and S. Scheiner, *J. Mol. Struct. (Theochem)*, 1989, **199**, 9-22.
82. E. R. Davidson and S. J. Chakravorty, *Chem. Phys. Lett.*, 1994, **217**, 48-54.
83. Z. Latajka and S. Scheiner, *Chem. Phys. Lett.*, 1987, **140**, 338-343.
84. M. Gutowski and G. Chalasinski, *J. Chem. Phys.*, 1993, **98**, 5540-5554.
85. M. M. Szczesniak and S. Scheiner, *J. Chem. Phys.*, 1982, **77**, 4586-4593.
86. S. F. Boys and F. Bernardi, *Mol. Phys.*, 1970, **19**, 553-566.
87. I. Alkorta, J. Elguero and J. E. Del Bene, *ChemPhysChem.*, 2016, **17**, 3112-3119.
88. J. Crugeiras and A. Rios, *Phys. Chem. Chem. Phys.*, 2016, **18**, 30961-30971.
89. J. E. Del Bene, I. Alkorta, M. M. Montero-Campillo and J. Elguero, *Chem. Phys. Lett.*, 2018, **710**, 123-128.
90. O. Mó, M. M. Montero-Campillo, I. Alkorta, J. Elguero and M. Yáñez, *Chem. Eur. J.*, 2019, **25**, 11688-11695.
91. S. Yu, J. S. Ward, K.-N. Truong and K. Rissanen, *Angew. Chem. Int. Ed.*, 2021, **60**, 20739-20743.
92. J. Lu and S. Scheiner, *Comput. Theor. Chem.*, 2021, **1204**, 113398.
93. J. Lu and S. Scheiner, *Chem. Phys. Lett.*, 2019, **731**, 136593.

Table 1. Binding energy, BCP density, and NBO perturbation energy of dimers, and maximum of MEP of Lewis acid monomer. LA$^-$ and LB$^-$ refer respectively to Lewis acid and base anion. All in kcal/mol except ρ_{BCP} in a.u.

n(LA$^-$)	n(LB$^-$)	ΔE	V_{max}	ρ_{BCP}	E(2)		
alkynes [a]					$N/Cl_{lp}\rightarrow\sigma^*(IC)$	$I_{lp}\rightarrow\sigma^*(NC)$	HB
4	4[b]	16.2	-13.6	0.0108	2.51	0.42	
4	8[b]	12.4	-13.6	0.0092	1.48	0.40	0.19
8	8	9.6	+3.7	0.0124	3.30	0.37	
8	Cl	2.3	+3.7	0.0307	29.30		
alkenes [c]							
4	4	19.0	-25.9	0.0103	2.35		
6	4	9.4	+4.7	0.0189	7.47	0.41	
8	4	8.0	+11.6	0.0218	9.52		
4	Cl	22.8	-25.9	0.0259	22.29		
6	Cl	-3.5	+4.7	0.0415	46.93		
8	Cl	-10.0	+11.6	0.0451	48.58		
alkanes[d]							
2	8	14.7	-31.3	0.0065	0.45	0.38	0.47
4	4	15.4	+2.2	0.0331	21.19	0.73	
6	4	0.7	+14.7	0.0338	31.57		23.43
8	4	3.3	+23.4	0.0411	13.51	8.15	
2	Cl	25.9	-31.3	0.0319	34.24		
4	Cl	-6.8	+2.2	0.0576	130.91[f]		
6	Cl	-35.6	+14.7	0.0636	g		
8	Cl	-29.2	+23.4	0.0659	g		
phenyl[e]							
Phe	0	18.0	-13.0	0.0290	38.45		
Phe	4	17.0	-13.0	0.0118	6.97		23.05
Phe	Cl	14.3	-13.0	0.0308	25.92		

[a] $^-OOC\text{-}C_n\text{-}I$

[b] $NH_2\text{-}C_n\text{-}COO^-$

[c] $^-O\text{-}C_n(CN)_n\text{-}I$ and $^-OOC\text{-}C_n(CN)_n\text{-}I$ for n>4

[d] $^-O\text{-}C(CN)_2\text{-}C(CN)_2\text{-}I$ and $^-OOC\text{-}C_n(CN)_{2n}\text{-}I$ for n>2 where r(C-COO) held fixed at 1.54 Å when combined with amine base

[e] $^-OOC\text{-}C_6(CN)_4\text{-}I$

[f] $C_{lp}\rightarrow\sigma^*(ICl)$

[g] NBO views ICl as single unit

Table 2. Geometric aspects of complexes. Distances in Å, angles in degs.

n(LA^-)	n(LB^-)	r(C-I)	R(I···N/Cl)	θ(CI··N/Cl)	θ(I··NC)
alkynes					
4	4	2.006	3.245	161.3	154.1
4	8	2.002	3.335	155.8	159.2
8	8	2.003	3.182	162.6	143.7
8	Cl	2.071	2.902	180.0	
alkenes					
4	4	2.110	3.289	161.7	152.4
6	4	2.106	2.985	169.0	131.1
8	4	2.108	2.914	171.9	124.6
4	Cl	2.153	2.992	177.6	
6	Cl	2.186	2.767	178.4	
8	Cl	2.194	2.726	178.2	
alkanes					
2	8	2.199	3.596	133.8	172.4
4	4	2.247	2.704	170.8	124.5
6	4	2.262	2.600	171.7	121.8
8	4	2.277	2.635	171.5	124.1
2	Cl	2.269	2.894	178.1	
4	Cl	2.436	2.602	178.6	
6	Cl	2.487	2.552	178.9	
8	Cl	2.498	2.534	179.0	
phenyl					
Phe	0	2.138	2.781	171.8	128.7
Phe	4	2.103	3.224	158.1	150.5
Phe	Cl	2.158	2.910	179.9	

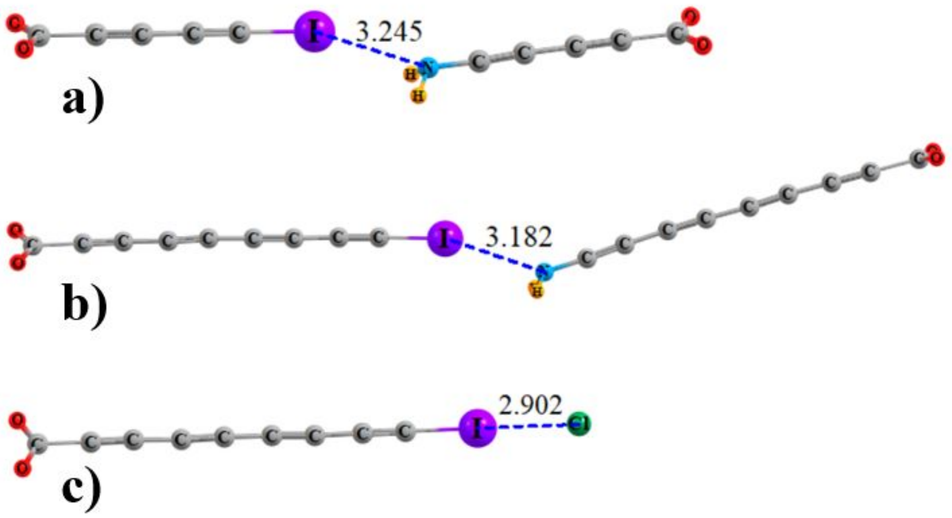

Fig 1. Optimized geometries of complexes involving selected alkyne Lewis acids a) 4-4, b) 8-8, and c) 8-Cl. Distances in Å.

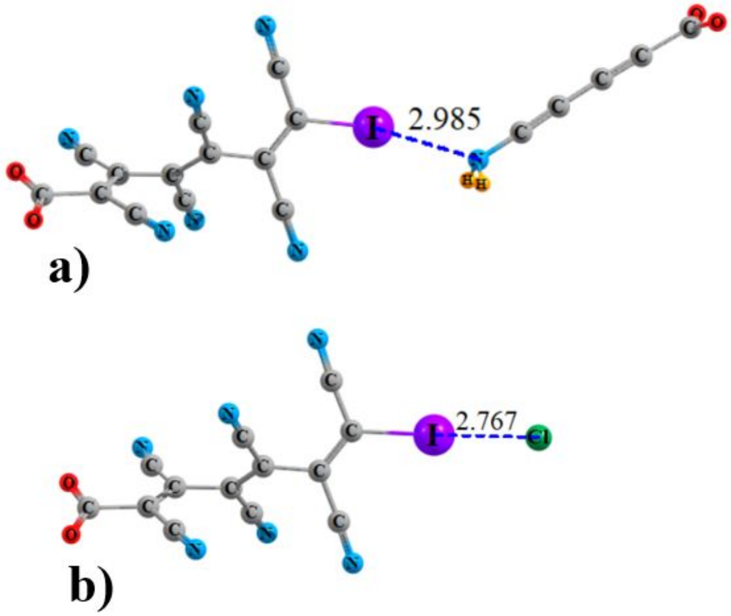

Fig 2. Optimized geometries of complexes involving selected alkenes a) 6-4, b) 6-Cl. Distances in Å.

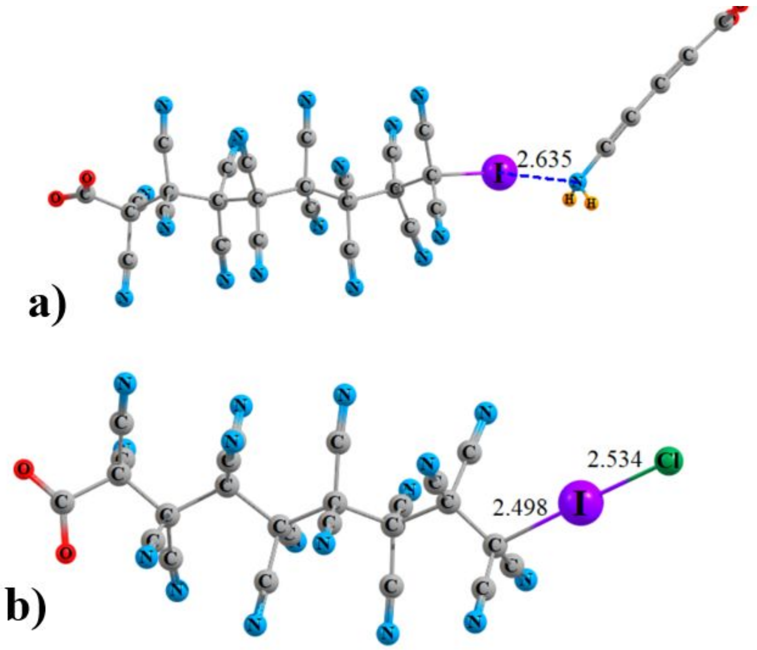

Fig 3. Optimized geometries of complexes involving selected alkanes a) 8-4, b) 8-Cl. Distances in Å.

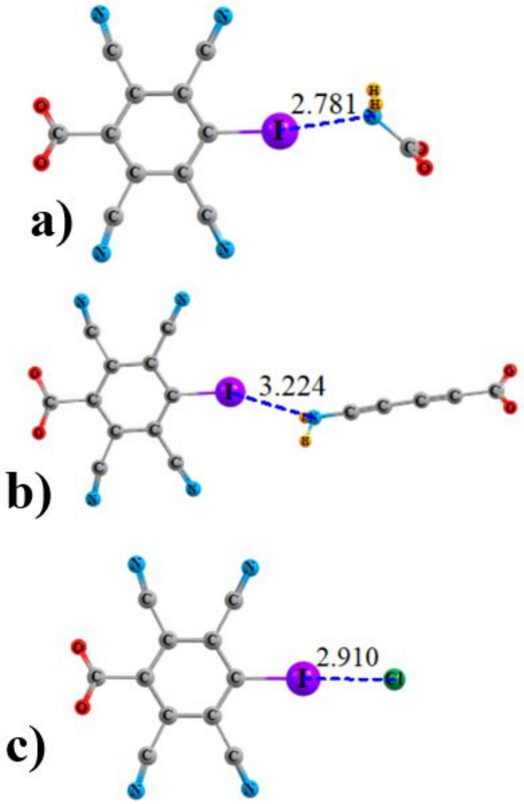

Fig 4. Optimized geometries of complexes involving substituted phenyl Lewis acid with a) 2, b) 4, and c) Cl bases. Distances in Å.

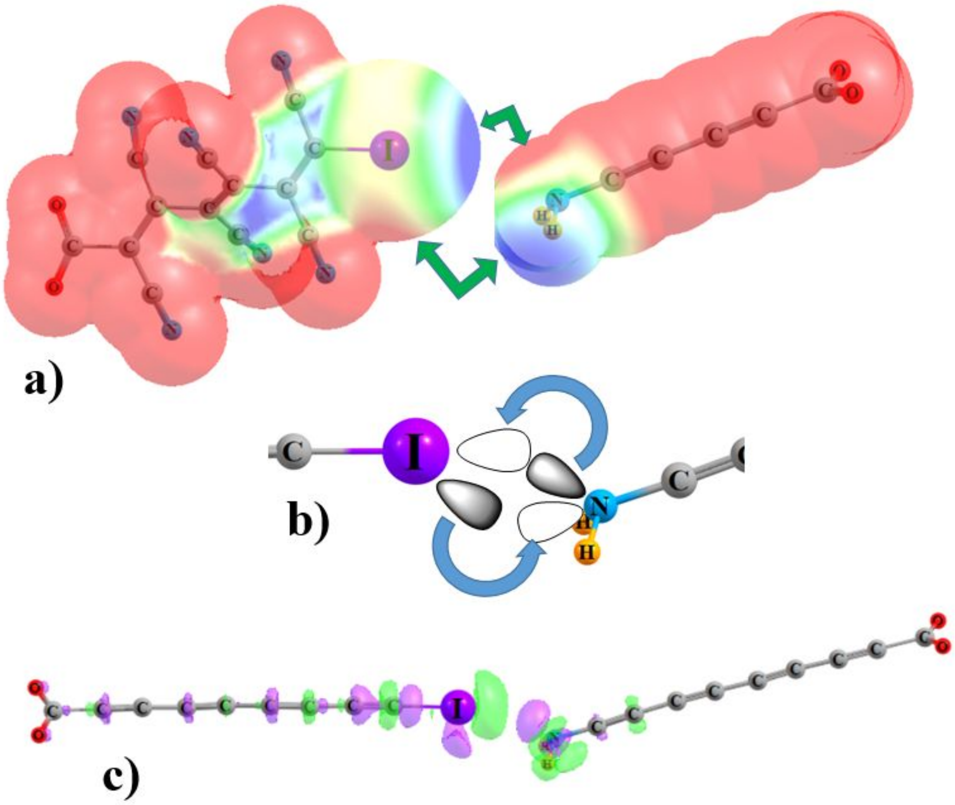

Fig 5. a) MEPs of Lewis acid and base where red and blue indicate respectively the most and least negative regions. b) Charge transfer interactions between occupied (grey) and vacant (white) orbitals of Lewis acid and amine base. c) Density difference map of alkyne 8-8 dimer where purple and green colors designate gain and loss of density, respectively; shown for ±0.0005 a.u. contour.

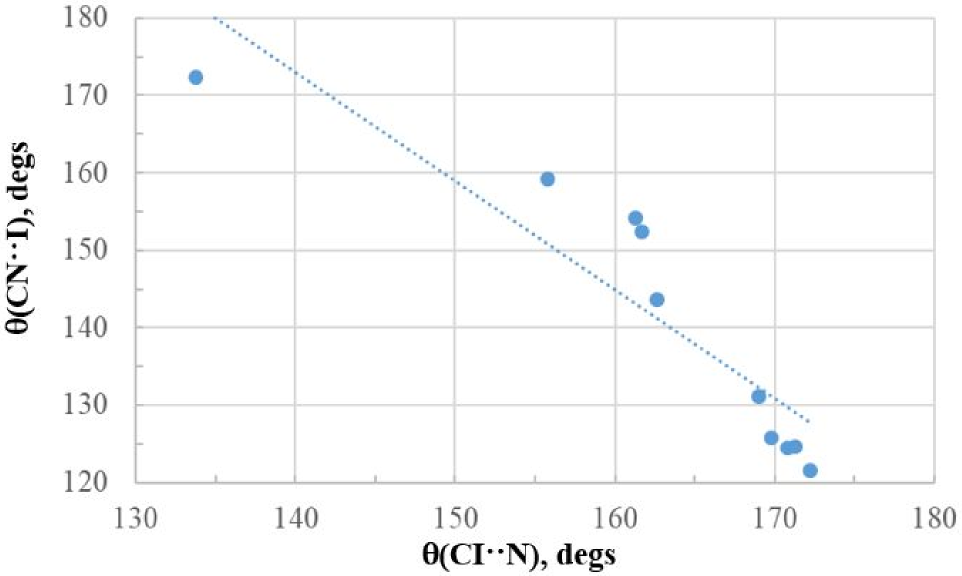

Fig 6. Correlation between θ(CI··N) and θ(I··NC) angles in complexes involving amine bases.