



## Alkyl chlorides as hydrogen bond acceptors

Janos Nadas, Sinisa Vukovic, Benjamin P. Hay\*

Chemical Sciences Division, Oak Ridge National Laboratory, Oak Ridge, TN 37831-6119, USA

### ARTICLE INFO

#### Article history:

Received 1 February 2012

Received in revised form 15 February 2012

Accepted 23 February 2012

Available online 3 March 2012

#### Keywords:

Hydrogen bonding

Alkyl chloride

Weak interactions

MP2

### ABSTRACT

To gain an understanding of the role of an alkyl chloride as a hydrogen bond acceptor, geometries and interaction energies were calculated at the MP2/aug-cc-pVDZ level of theory for complexes between ethyl chloride and representative hydrogen donor groups. The results establish that these donors, which include hydrogen cyanide, methanol, nitrobenzene, pyrrole, acetamide, and *N*-methylurea, form X–H···Cl hydrogen bonds (X = C, N, O) of weak to moderate strength, with  $\Delta E$  values ranging from  $-2.8$  to  $-5.3$  kcal/mol.

© 2012 Elsevier B.V. All rights reserved.

### 1. Introduction

Given their relatively strong and highly directional nature, hydrogen bonding interactions have played a key role in supramolecular chemistry [1–4]. Although most prior hydrogen bond studies have focused on oxygen and nitrogen acceptor molecules, it is known that alkyl chlorides can also function as hydrogen bond acceptors [5–7]. The evaluation of solution 1:1 hydrogen bond complexation constants reveals that alkyl chlorides form weak, but measurable adducts with hydrogen bond donors such as phenols [8,9]. Investigations of the Cambridge Structural Database (CSD) [10] are consistent with these observations [11–14]. A large number of X–H···Cl contacts are observed at distances,  $d$ , ranging between 2.5 and 2.9 Å [11,12], within the van der Waals (vdW) contact radius of 2.95 Å [15], and therefore, consistent with an attractive interaction. The X–H···Cl angles,  $\theta_1$ , exhibit a wide range (90–180°) of values [11–13], but exhibit a tendency to become more linear at shorter  $d$ , characteristic of hydrogen bonding. Finally, the contacts cluster around H···Cl–C angles,  $\theta_2$ , of 90–130° displaying a directional preference that is consistent with hydrogen bonding as opposed to vdW contact [12,13].

Since the establishment of X–H···Cl as a weak hydrogen bond, it has been exploited in crystal engineering [16], used to rationalize crystal packing [17,18], accredited for ligand binding in proteins [19], and observed in synthetic receptors binding halogenated guests [20]. Our interest in this topic was motivated by the question of whether X–H···Cl hydrogen bonds could be exploited as binding interactions within receptors that recognize mustard

blister agents. These agents have structures composed of a central heteroatom, either S or N, decorated with two 2-chloroethyl substituents [21,22]. By utilizing X–H···Cl hydrogen bonding interactions it should be possible to design receptors that bind mustards through multiple hydrogen bond contacts as shown in Fig. 1. The computer-aided design of such receptors using a *de novo* structure-based approach [23] requires prior knowledge of *optimal* spatial positioning of donating groups in order to maximize hydrogen bonding.

Experimental evidence supports the existence of X–H···Cl hydrogen bonds, but fails to give a clear picture of optimal geometric parameters and it does not provide a quantitative assessment of their strength. Earlier theoretical studies of X–H···Cl interactions involve complexes between chloromethanes and formic acid [24,25], water [26,27], hydrogen peroxide [28,29], dimethylformamide [30], and nitrosyl hydride [31], as well as in thiazoles containing intramolecular C–H···Cl interactions [32]. However, all the reported minima in these studies possess additional and unrelated weak interactions between the interacting molecules causing accompanying structural deformations, making it difficult to identify the geometric preferences associated with the X–H···Cl hydrogen bond or to quantify the magnitude of the interaction energies individual interactions.

Herein, we use electronic structure calculations to gain a better understanding of the alkyl chloride as a hydrogen bonding acceptor. Optimized geometries are reported for complexes between chloroethane, EtCl, and a selection of hydrogen bond donors shown in Fig. 2. EtCl was chosen to mimic the chloroethyl substituents found in mustard blister agents and the hydrogen bond donors were selected as they represent typical groups that could be used in a receptor molecule. These complexes are shown to exhibit X–H···Cl

\* Corresponding author. Tel.: +1 865 574 6717; fax: +1 865 574 4939.

E-mail address: [haybp@ornl.gov](mailto:haybp@ornl.gov) (B.P. Hay).

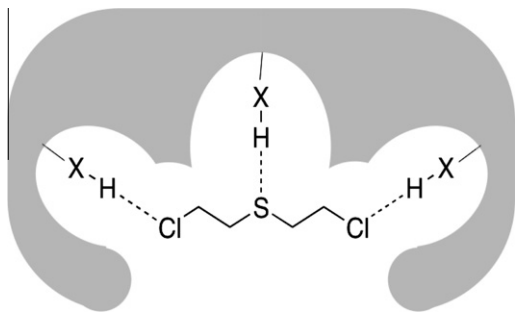


Fig. 1. Strategy for a receptor that captures sulfur mustard through hydrogen bonding interactions.

contacts characteristic of weak to moderate hydrogen bonding interactions, with  $\Delta E$  values ranging from  $-2.8$  to  $-5.3$  kcal/mol.

## 2. Methodology

Electronic structure calculations were carried out with the NWChem program [33,34] using second order Møller-Plesset perturbation theory (MP2) [35]. After initial investigation of potential energy surfaces using the 6-31+G\* basis set, geometries of the complexes, donors, and acceptors were optimized separately using the augmented correlation consistent double- $\zeta$  basis set (aug-cc-pVDZ) [36]. This level of theory is known to give accurate geometries and energies for hydrogen bonded complexes [37–39]. Frequency calculations were performed at the same level of theory to verify that geometries were minima and to obtain the zero-point ( $\Delta E_{ZPE}$ ) and thermal energy ( $\Delta E_{thermal}$ ) corrections needed for the calculation of enthalpies at room temperature. Binding energies were calculated as follows:  $\Delta E = E(\text{complex}) - E(\text{donor}) - E(\text{EtCl})$ . Binding enthalpies were calculated as follows:  $\Delta H = \Delta E + \Delta E_{ZPE} + \Delta E_{thermal} + \Delta(PV)$ , where  $\Delta(PV) = nRT = -0.593$  kcal/mol at 298.15 K ( $n = -1$ ). Electron density and molecular orbital isosurfaces were rendered with ECCE [40].

## 3. Results and discussion

The initial objective of this study was to locate all minima for complexes between EtCl and hydrogen bond donors that contained an X–H...Cl hydrogen bond. The question arose as to how to position the donor groups and not miss any minima. Prior crystallographic and theoretical studies [11–13,24–32] provide an indistinct picture of the preferred hydrogen bonding geometry with EtCl, in other words, complexes exhibiting less than precisely defined ranges for: H...Cl distances of  $2.5 < d < 2.9$  Å, X–H...Cl angles of  $90 < \theta_1 < 180^\circ$ , and H...Cl–C angles of  $90 < \theta_2 < 130$ . In accord with the behavior of hydrogen bonds [7,14,41], the optimal X–H...Cl angle,  $\theta_1$ , should tend toward  $180^\circ$ . The intrinsic direc-

tionality at the Cl acceptor atom, which is characterized by the H...Cl–C angle,  $\theta_2$ , and the C–H...Cl–C dihedral angle,  $\phi$ , is less clear. To probe the nature of this Cl acceptor directionality, a potential energy surface was generated by placing HCN around EtCl and performing constrained optimizations. Keeping  $\theta_1$  locked at  $180^\circ$ , a total of 56 initial hydrogen bonding poses were generated by varying  $\theta_2$  and  $\phi$ . Constraining  $\theta_1$ ,  $\theta_2$ , and  $\phi$ , geometry optimizations at the MP2/6-31+G\* level of theory yielded the potential energy surface shown in Fig. 3.

Over the entire potential surface optimized H...Cl distance ranged from 2.5 to 2.8 Å. The most stable geometries occur at  $\theta_2 = 105^\circ$ . The potential surface is shallow around this value, where changes of  $\pm 15^\circ$  in  $\theta_2$  increase the energy by  $< 0.2$  kcal/mol for  $\phi \geq 90^\circ$ . This is consistent with the  $90$ – $130^\circ$  range observed in crystal structures [12,13]. At  $\theta_2 = 105^\circ$ , the energy was virtually independent of  $\phi$ , exhibiting a variation of only  $\pm 0.05$  kcal/mol over the entire range of  $0$ – $180^\circ$ . Hydrogen bonding to the chlorine atom acceptor in EtCl was favorable with binding energies,  $\Delta E$ , values ranging between  $-1.8$  and  $-3.5$  kcal/mol, except when HCN sterically clashed with the  $\text{CH}_3$  group of EtCl at  $\theta_2 = 75^\circ$  and  $\phi = 0^\circ$ .

The potential energy surface shown in Fig. 3 provided a basis for generating the initial geometries for possible hydrogen bonded complexes between EtCl and the donor groups shown in Fig. 2. Using the geometric parameters  $d = 2.5$  Å,  $\theta_1 = 180^\circ$ , and  $\theta_2 = 105^\circ$ , each hydrogen bond donor was placed around EtCl at  $\phi$  values of  $0^\circ$ ,  $30^\circ$ ,  $60^\circ$ ,  $120^\circ$ , and  $180^\circ$ . Multiple initial geometries were generated at each  $\phi$  value by rotation about the X–H bond and in the case of acetamide and N-methylurea, by variation of the N–H group that contacts the Cl atom. Starting from initial geometries generated as described above, full geometry optimizations resulted in the location of the 18 structures shown in Fig. 4. Absence of imaginary frequencies confirmed 1–18 to be minima on the MP2/aug-cc-pVDZ potential surface. Table 1 presents the binding energies, structural parameters, and other properties associated with these complexes.

Complexes 1–18 exhibit several common properties characteristic of hydrogen bonding interactions [7,14,41]. First, these complexes have  $\Delta E$  values ranging from  $-4.18$  to  $-8.85$  kcal/mol ( $\Delta H$  values from  $-2.85$  to  $-7.51$  kcal/mol), consistent with the presence of specific bonding interactions between the donor and acceptor in addition to vdW. Second, each complex has a close,  $2.4$ – $2.7$  Å, contact between a donor X–H hydrogen and the chlorine atom acceptor of EtCl. Third, consistent with the formation of a hydrogen bond, complex formation is accompanied by a red shift in the X–H stretching frequency. With the exception of the weakest complex, 7, where the red shift is small,  $-5$   $\text{cm}^{-1}$ , these frequency shifts are significant, ranging from  $-25$  to  $-68$   $\text{cm}^{-1}$ .

As observed in prior study of complexes formed between chloromethane and various donor groups [24–32], each complex

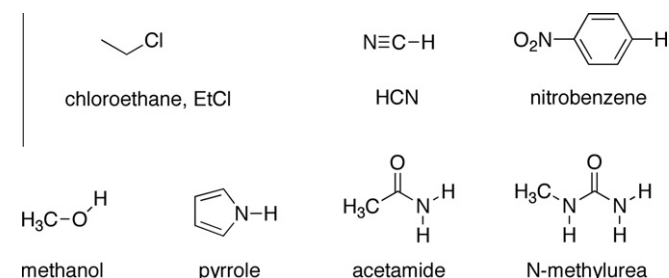


Fig. 2. Hydrogen bond acceptor, EtCl, and the six hydrogen bond donors investigated in this study.

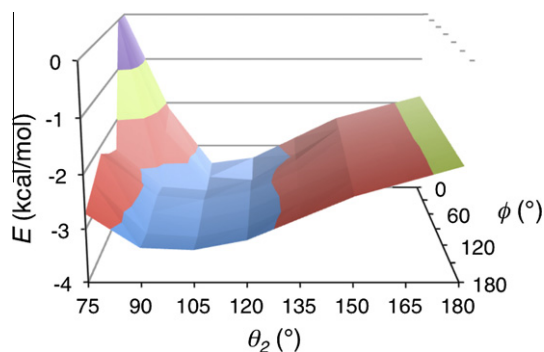


Fig. 3. Potential energy surface generated by plotting  $\Delta E$  versus  $\theta_2$  and  $\phi$  for the hydrogen bond formed between HCN and EtCl.

Download English Version:

<https://daneshyari.com/en/article/5394729>

Download Persian Version:

<https://daneshyari.com/article/5394729>

[Daneshyari.com](https://daneshyari.com)