The following full text is a publisher's version.

For additional information about this publication click this link.
http://hdl.handle.net/2066/169074

Please be advised that this information was generated on 2019-08-26 and may be subject to change.
**Activation Strain Analysis of $S_N2$ Reactions at C, N, O, and F Centers**

Jan Kubelka† and F. Matthias Bickelhaupt*‡§

†Department of Chemistry, University of Wyoming, Laramie, Wyoming 82070, United States
‡Department of Theoretical Chemistry and Amsterdam Center for Multiscale Modeling (ACMM), Vrije Universiteit Amsterdam, De Boelelaan 1083, 1081 HV Amsterdam, The Netherlands
§Institute for Molecules and Materials (IMM), Radboud University, Heyendaalseweg 135, 6525 AJ Nijmegen, The Netherlands

**ABSTRACT:** Fundamental principles that determine chemical reactivity and reaction mechanisms are the very foundation of chemistry and many related fields of science. Bimolecular nucleophilic substitutions ($S_N2$) are among the most common and therefore most important reaction types. In this report, we examine the trends in the $S_N2$ reactions with respect to increasing electronegativity of the reaction center by comparing the well-studied backside $S_N2$ $\text{Cl}^- + \text{CH}_3\text{Cl}$ with similar $\text{Cl}^-$ substitutions on the isoelectronic series with the second period elements $\text{N}$, $\text{O}$, and $\text{F}$ in place of $\text{C}$. Relativistic (ZORA) DFT calculations are used to construct the gas phase reaction potential energy surfaces (PES), and activation strain analysis, which allows decomposition of the PES into the geometrical strain and interaction energy, is employed to analyze the observed trends. We find that $S_N2@N$ and $S_N2@O$ have similar PES to the prototypical $S_N2@C$, with the well-defined reaction complex (RC) local minima and a central barrier, but all stationary points are, respectively, increasingly stable in energy. The $S_N2@F$, by contrast, exhibits only a single-well PES with no barrier. Using the activation strain model, we show that the trends are due to the interaction energy and originate mainly from the decreasing energy of the empty acceptor orbital ($\sigma_{A-\text{Cl}}^*$) on the reaction center A in the order of $\text{C}$, $\text{N}$, $\text{O}$, and $\text{F}$. The decreasing steric congestion around the central atom is also a likely contributor to this trend. Additional decomposition of the interaction energy using Kohn–Sham molecular orbital (KS-MO) theory provides further support for this explanation, as well as suggesting electrostatic energy as the primary reason for the distinct single-well PES profile for the FCl reaction.

1. INTRODUCTION

Understanding chemical reactions and reactivity is one of the central goals of chemistry and, more broadly, all natural science. The ability of molecular species to react and form new, more complex ones is responsible for the evolution and existence of the Universe, Earth, and biological life. In modern society, design and production of new compounds and materials is key for technological advances that help sustain the growing and expanding human population. Fundamental insights into the underlying physical principles behind key chemical processes are therefore critical for future progress in their future development, control, and optimization.

One of the most important prototypes of chemical reactions is bimolecular nucleophilic substitution ($S_N2$, see Scheme 1). Due to its significance, numerous experimental and theoretical studies have been focused on providing detailed, fundamental understanding of the $S_N2$ reactions. Perhaps the best-known model for $S_N2$ reactions is the symmetric, thermoneutral $S_N2$ reaction between the chloride anion and chloromethane, $\text{Cl}^- + \text{CH}_3\text{Cl}$ in the gas phase (Scheme 1).

This reaction proceeds preferentially through backside nucleophilic attack of the chloride anion at the carbon atom ($S_N2@C$) with concerted expulsion of the leaving group. A well-known feature of gas phase $S_N2@C$ reactions is their double-well potential energy surface (PES) along the reaction coordinate, as illustrated in Figure 1. This PES is characterized by a central barrier, provided by a trigonal bipyramidal transition state (TS, see also Scheme 1), that separates two energy minima, associated with the reactant and product ion–molecule complexes (RC and PC).

Among the most powerful approaches to understanding reactivity is examining trends with respect to some selected properties of the reacting species. Although many trends could be explained using chemical intuition or empirical understanding, when combined with modern quantum chemical calculations it is possible to uncover the details of the electronic structure and its changes associated with the observed trends, thereby providing the fundamental explanations. Bento and Bickelhaupt recently used relativistic DFT calculations together with analysis by the activation strain model to examine
the effects of the nucleophile and the leaving group on methyl chloride (CH₃Cl) SN₂ reactions, both backside and frontside. This study demonstrated that the nucleofiliicity is determined by the electron-donor capability of the nucleophile, while the leaving group ability is associated primarily with the carbon-leaving group bond strength.

The same authors also investigated the SN₂ reactions according to Scheme 1 with the central C atom substituted by heavier group-14 atoms (Si, Ge, Sn, Pb). An interesting feature of the PES for the SN₂@Si, @Ge, @Sn, and @Pb reactions is that the central barrier disappears, giving rise to a single-well reaction profile. They showed that the disappearance of the central barrier is due to the decrease in steric repulsion for the larger atoms along with more stabilizing orbital interactions due to better chloride HOMO/substrate LUMO overlap.

The next level of the quest for a more complete understanding of the SN₂ reactions is the examination of trends with respect to substitutions on atoms other than carbon and its group-14 congeners. Several theoretical reports compare various aspects of SN₂@C reactions to SN₂@N, S, P, O, and S. However, these studies often focus on thermochemistry, molecular geometries, effects of different nucleophiles and/or leaving groups, solvation, or comparison of different computational methods, and few seek a systematic examination of trends with respect to the properties of the central atom and their significance in the SN₂ reactivity. Here we take the first step in this direction by considering on the SN₂ reactions for all substrates of the second period elements that are isoelectronic to the CH₃Cl prototype, namely, NH₂Cl, OHCl, and FCl (Scheme 2). This series provides a potentially very rich model set for understanding the roles of several key factors in the SN₂ reactivity that may be furthermore representative of the corresponding groups of the periodic table. In particular, there is a strong trend of increasing electronegativity from C to F which goes with a more negatively charged electrophilic central atom. Intuitively, one might expect that higher electronegativity will lead to higher barriers due to repulsion with the approaching nucleophile. On the other hand, the valence of the central element decreasing in the same order results in different geometry of the reacting species and transition states, which may manifest itself via geometry strain and steric effects. The resulting PESs are therefore expected to reflect, to a greater or lesser extent, an interplay of both these fundamental contributions. To sort out the roles of each of these individual PES components, we take advantage of the activation strain model, which has been specifically designed for this purpose (see Methods for details), and use this powerful methodology to identify the underlying physical reasons and explanations for the observed trends in the SN₂ reactivity.

2. METHODS

2.1. Computational Details. All calculations were performed with the Amsterdam Density Functional (ADF) program. The molecular orbitals (MOs) were expanded in a large uncontracted set of Slater-type orbitals (STOs) containing diffuse functions, TZ2P. This basis is of triple-ζ quality and has been augmented by two sets of polarization functions: 2p and 3d on hydrogen and 3d and 4f on all heavier atoms. An auxiliary set of s, p, d, f, and g STOs was used to provide a potentially very rich model set for understanding the SN₂ reactivity.

2.2. Analysis of the Potential Energy Surfaces. Insight into how the activation barriers arise is obtained through activation strain analyses of the various SN₂ reactions. The activation strain model is a fragment approach to understanding chemical reactions, in which the height of reaction barriers is described in terms of the original reactants. Thus, the potential energy surface ΔE(ζ) is decomposed, along the reaction coordinate ζ, into the strain ΔEstrain(ζ) associated with deforming the individual reactants plus the actual interaction ΔEint(ζ) between the deformed reactants:

$$\Delta E(\zeta) = \Delta E_{\text{strain}}(\zeta) + \Delta E_{\text{int}}(\zeta)$$  (1)
The strain \( \Delta E_{\text{strain}}(\zeta) \) is determined by the rigidity of the reactants and by the extent to which groups must reorganize in a particular reaction mechanism, whereas the interaction \( \Delta E_{\text{int}}(\zeta) \) between the reactants depends on their electronic structure and on how they are mutually oriented as they approach each other. It is the interplay between \( \Delta E_{\text{strain}}(\zeta) \) and \( \Delta E_{\text{int}}(\zeta) \) that determines if and at which point along the \( \zeta \) a barrier arises. The activation energy of a reaction \( \Delta E^\ddagger = \Delta E(\ddagger) \) consists of the activation strain \( \Delta E^\ddagger_{\text{strain}} = \Delta E_{\text{strain}}(\ddagger) \) plus the TS interaction \( \Delta E^\ddagger_{\text{int}} = \Delta E_{\text{int}}(\ddagger) \):

\[
\Delta E^\ddagger = \Delta E^\ddagger_{\text{strain}} + \Delta E^\ddagger_{\text{int}}
\]

In the graphical representations shown below, \( \zeta \) is then projected onto the stretch of the central atom—leaving group (A–Cl, A = C, N, O, and F) bond, which is generally one of the dominant components of the reaction coordinate and undergoes a well-defined change from an intact to a dissociated bond.

The interaction \( \Delta E_{\text{int}}(\zeta) \) between the strained reactants is further analyzed in the conceptual framework provided by the Kohn–Sham molecular orbital (KS-MO) model,\(^{44-49} \) according to which it is decomposed into three physically meaningful terms:

\[
\Delta E_{\text{int}}(\zeta) = \Delta V_{\text{distat}}(\zeta) + \Delta E_{\text{Pauli}}(\zeta) + \Delta E_{\text{elstat}}(\zeta)
\]

The term \( \Delta V_{\text{distat}} \) corresponds to the classical electrostatic interaction between the unperturbed charge distributions of the deformed reactants and is usually attractive. The Pauli repulsion \( \Delta E_{\text{Pauli}} \) comprises the destabilizing interactions between occupied orbitals and is responsible for any steric repulsion (see ref. 44 for an exhaustive discussion). The orbital interaction \( \Delta E_{\text{elstat}} \) accounts for charge transfer (interaction between occupied orbitals on one moiety with unoccupied orbitals of the other, including HOMO–LUMO interactions) and polarization (empty–occupied orbital mixing on one fragment due to the presence of another fragment).

The activation strain analysis was performed with the aid of the PyFrag program\(^{30} \) at discrete points on the reaction coordinate, sampled from the computed IRC paths (see above), except Cl– + FCl, where due to the absence of a TS a relaxed energy scan (linear transit) along the F–Cl bond was used.

3. RESULTS AND DISCUSSION

3.1. Reaction Profiles. The computed energies of the reaction complexes (RC), transition states (TS), and transition complex (TC) with respect to the free reactants are summarized in Table 1. Also shown in Table 1 are the A–Cl distances (where A stands for the central atom; A = C, N,

<table>
<thead>
<tr>
<th>Reaction</th>
<th>CH3Cl</th>
<th>NH2Cl</th>
<th>OHCl</th>
<th>FCl</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \Delta \dot{E}(\text{RC}) )</td>
<td>–9.2</td>
<td>–15.9</td>
<td>–23.5</td>
<td></td>
</tr>
<tr>
<td>( \Delta \dot{E}(\text{TS}) )</td>
<td>–0.3</td>
<td>–9.2</td>
<td>–11.3</td>
<td></td>
</tr>
<tr>
<td>( \Delta \dot{E}(\text{TC}) )</td>
<td></td>
<td></td>
<td>–16.8</td>
<td></td>
</tr>
<tr>
<td>A–Cl (R)(^{*})</td>
<td>1.790</td>
<td>1.766</td>
<td>1.711</td>
<td>1.654</td>
</tr>
<tr>
<td>A–Cl (RC)</td>
<td>1.835</td>
<td>1.786</td>
<td>1.705</td>
<td></td>
</tr>
<tr>
<td>A–Cl (TS)</td>
<td>2.351</td>
<td>2.286</td>
<td>2.176</td>
<td></td>
</tr>
<tr>
<td>A–Cl (TC)</td>
<td>2.085</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\(^{*}\)Computed at ZORA-OLYP/TZ2P. R = reactants; RC = reaction complex; TS = transition state; TC = transition complex (for FCl).

O, F) at the respective stationary points. The corresponding reaction profiles are superimposed in Figure 2. Our ZORA-OLYP/TZ2P computations show that all the model reactions proceed via a Cl–A–Cl symmetric transition structure which is either a labile transition state (for A = C, N, O) or a stable intermediate transition complex (for A = F). Furthermore, there is a systematic trend in the energy of this symmetric TS or TC relative to the reactants: among A = C, N, O, and F, it decreases from –0.3 to –9.2 to –11.3 to –16.8 kcal mol\(^{-1} \) respectively (Table 1).

The Cl– + CH3Cl reaction exhibits the characteristic double-well PES involving local minima corresponding to the reaction complexes (RC) and a central barrier for the transition state (TS), in line with previous studies.\(^{17,19,51} \) The energy profiles for NH2Cl and OHCl reactions are qualitatively similar, but significantly lower in energy (Table 1). Specifically, the RCs are respectively 7 and 25 kcal mol\(^{-1} \) lower, while the TSs are 9 and 23 kcal mol\(^{-1} \) below the computed values for the CH3Cl + Cl– system (all values relative to the reactants). The height of the reaction barrier with respect to the RC, however, does not follow the same trend. It is computed to be 9, 7, and 12 kcal mol\(^{-1} \) for the reactions with CH3Cl, NH2Cl, and OHCl, respectively.

By contrast, the Cl– + FCl reaction profile is qualitatively different, with only a single minimum corresponding to the symmetric [Cl–F–Cl]\(^{-} \) transition complex and no separate, asymmetric RC. The TC is stable by 17 kcal mol\(^{-1} \) compared to the individual reactants (Table 1). This species features a strong halogen bond and electron-rich hypervalent fluoride.\(^{52} \) Similar single-well profiles were identified for Sn2 substitutions on heavier group-14 atoms: Si, Ge, Sn, and Pb.\(^{19} \) In fact, under certain conditions, they may also exist for Sn2 substitution on carbon.

Another trend apparent from Table 1 is the systematic decrease in bond distances between the central atom and the Cl– leaving group for both RC and transition structure (TS or TC) in the order C, N, O, and F. The differences are somewhat greater for the TS (by ~0.02 Å) and also decrease more significantly from Sn2@N to Sn2@O than from Sn2@C to Sn2@N, by about 0.04 Å for both RC and TS. The trend continues for the Sn2 substitution at F although, as mentioned above, no asymmetric RC exists, only a stable TC. In this stable [Cl–F–Cl]\(^{-} \) complex the F–Cl bond lengths are greater than in the RCs for the other compounds. However, when compared...
to the TS, the bond again shortens from O–Cl to F–Cl (Table 1).

For completeness, in Table 2 we present the thermochemistry activation parameters for the studied reactions, calculated for 1 atm, 298.15 K. The trends in the activation thermodynamic energy (i.e., electronic energy plus ZPVE plus thermal energy of translation, rotation, and vibration) and enthalpy parallel the electronic energy presented in Table 1. All $\Delta H^\ddagger$ are negative, implying that the reaction rates would exhibit an anti-Arrhenius behavior in the gas phase, i.e., they would decrease with the increasing temperature. The activation entropies (given as $-T\Delta S^\ddagger$) is essentially constant for CH$_3$Cl, NH$_2$Cl, and OHCl reactions, and only 1 kcal mol$^{-1}$ lower for the FCl, yielding quantitatively very similar progression in the activation Gibbs free energies. Note, however, that there is a qualitative difference: the $\Delta G^\ddagger$ for the Cl$^-$ + CH$_3$Cl reaction is slightly positive, therefore presenting an actual activation barrier, while all others are negative. Thus, at low-pressure conditions, the gas-phase SN$_2$ substitution at C still experiences an entropy bottleneck whereas gas-phase SN$_2$ substitution at N, O, and F proceeds spontaneously. Note that at higher pressure, as energy dissipation becomes important, the central barrier (i.e., relative to the RC or TC) becomes decisive.

At first sight, the mechanism behind the above trends may not be entirely obvious. Why should the relative energy of the TS or TC go down, if the nucleophile attacks a more electronegative and thus more negatively charged (vide infra) central atom if one goes from $A = C$ to $A = N$, O, and F? On the other hand, intuitively, a more electronegative central atom may also be conceived more electrophilic and prone to interact with the lone pair of an incoming nucleophile. As pointed out above, however, there may be yet another important contribution to the energetics and, consequently, shapes of the PES, from the structural strain. In the next section we employ the activation strain model to analyze the various SN$_2$ reaction profiles and provide sound physical explanations for the observed trends.

### 3.2. Activation Strain Analyses

As detailed in Methods, the activation strain analysis$^{5,15}$ decomposes the total $\Delta E(\zeta)$ of the model reactions along the reaction coordinate $\zeta$, into the strain $\Delta E_{\text{strain}}(\zeta)$ component associated with deforming the individual reactants plus the actual interaction $\Delta E_{\text{int}}(\zeta)$ between the deformed reactants. The analysis results of the studied reactions are presented in Figures 3 and 4. Figure 3 shows the activation strain diagrams for each particular reaction, while Figure 4 overlays the strain $\Delta E_{\text{strain}}(\zeta)$ (Figure 3a) and interaction $\Delta E_{\text{int}}(\zeta)$ (Figure 3b) energies for direct comparison. For easier reference the positions of the transition states are also indicated.

It is evident from both Figures 3 and 4, but perhaps more from the latter, that the observed trends in the PES profiles are associated mostly with the interaction energy (Figure 4b) rather than the strain (Figure 4a). In Table 3, we list the values of the $\Delta E_{\text{strain}}$ and $\Delta E_{\text{int}}$ at the TS or, for SN2@F, TC. Although the strain energy does destabilize the TS of the Cl$^-$ + CH$_3$Cl with respect to NH$_2$Cl and OHCl ones by $\sim$5 kcal mol$^{-1}$, the latter two have virtually the same TS strain energy and the Cl$^-$ + FCl reaction complex has again slightly higher strain, counter to the progression in the total energy (Figure 2). These differences in the $\Delta E_{\text{strain}}$ correlate well with the order of $A$–Cl bond dissociation energies, that is, stronger bonds go with more destabilizing strain curves (Table 4).$^{18}$

By contrast, the interaction energies (Figure 4b, see also Table 3) show a very clear trend of stabilization in the order of C, N, O, F. The explanation can be found from the examination of the dominant frontier orbital interaction between the occupied Cl$^-$ 3p AO and the backside lobe of the empty $\sigma^*_{A–Cl}$ orbital.$^{19}$ As shown in Figure 4, the $\sigma^*_{A–Cl}$ energy monotonically decreases with the increasing electronegativity of the central atom, respectively, for along C, N, O, and F. This reflects the decreasing orbital energy of the central atom’s 2p AOs in this order. The monotonic decrease of the $\sigma^*_{A–Cl}$ orbital energy along CH$_3$Cl, NH$_2$Cl, OHCl, and FCl causes the HOMO–LUMO gap $\Delta \epsilon$ between nucleophile Cl$^-$ 3p AO and substrate $\sigma^*_{A–Cl}$ to become smaller and thus the orbital interactions to become more stabilizing. This is what we see in the systematic trend in interaction curves, in perfect agreement with the relationship $\Delta E_{\text{int}} \sim \frac{\Delta \epsilon}{\Delta \epsilon_1}$, where $S$ represents the overlap integral (Table 4) and $\Delta \epsilon$ is the energy difference between the interacting orbitals.$^{24}$ Note that the orbital overlap, shown in Table 4 for the TS (TC), decreases slightly with the increasing electronegativity of A (with the exception of N and O), consistently with the generally greater wave function

<table>
<thead>
<tr>
<th>Table 2. Thermochemistry of Activation (in kcal mol$^{-1}$) for the Studied SN$_2$ Reactions$^a$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reaction</td>
</tr>
<tr>
<td>$\Delta U^\ddagger$</td>
</tr>
<tr>
<td>$\Delta H^\ddagger$</td>
</tr>
<tr>
<td>$-T\Delta S^\ddagger$</td>
</tr>
<tr>
<td>$\Delta G^\ddagger$</td>
</tr>
</tbody>
</table>

*aComputed at ZORA-OLYP/TZ2P for 1 atm, 298.15 K.*

Figure 3. Activation strain analysis of the SN$_2$ reaction profiles. Total energy (black), decomposed into strain (blue) and interaction (red) components plotted as a function of the A–Cl stretch coordinate with respect to its equilibrium value for (a) Cl$^-$ + CH$_3$Cl reaction (A = C), (b) Cl$^-$ + NH$_2$Cl reaction (A = N), (c) Cl$^-$ + OHCl reaction (A = O), and (d) Cl$^-$ + FCl reaction (A = F). The pale blue vertical lines indicate the position of the transition state.
Figure 4. Comparison of the strain and interaction energies for the studied SN2 reactions. (a) Strain energy and (b) interaction energy plotted as a function of the A−Cl stretch coordinate with respect to its equilibrium value for Cl− + CH3CI reaction (black lines), Cl− + NH2Cl reaction (red lines), Cl− + OHCl reaction (blue lines), and Cl− + FCl reaction (pink lines). The solid circles indicate the positions of the transition states, the pink square for Cl− + FCl the position of the transition complex.

Table 3. Activation Strain Analysis (in kcal mol−1) at the TS of the Studied SN2 Reactions

<table>
<thead>
<tr>
<th></th>
<th>Cl− + CH3−Cl</th>
<th>Cl− + NH2−Cl</th>
<th>Cl− + OH−Cl</th>
<th>Cl− + F−Cl</th>
</tr>
</thead>
<tbody>
<tr>
<td>ΔEi</td>
<td>0.1</td>
<td>9.2</td>
<td>11.8</td>
<td>16.8</td>
</tr>
<tr>
<td>ΔEstrain</td>
<td>31.6</td>
<td>25.7</td>
<td>26.1</td>
<td>27.7</td>
</tr>
<tr>
<td>ΔEint</td>
<td>−31.9</td>
<td>−34.9</td>
<td>−37.9</td>
<td>−44.5</td>
</tr>
</tbody>
</table>

*Computed at the ZORA-OLYP/TZ2P level.

Table 4. Properties of the Substrates in Studied SN2 Reactions: A−Cl Bond Strengths (in kcal mol−1), σA−Cl Orbital Energy (in eV), and A Atomic Charge (in au)

<table>
<thead>
<tr>
<th></th>
<th>CH3−Cl</th>
<th>NH2−Cl</th>
<th>OH−Cl</th>
<th>F−Cl</th>
</tr>
</thead>
<tbody>
<tr>
<td>BDE</td>
<td>−84.2</td>
<td>−63.4</td>
<td>−58.6</td>
<td>−65.3</td>
</tr>
<tr>
<td>σA−Cl</td>
<td>−5.13</td>
<td>−6.96</td>
<td>−8.95</td>
<td>−11.08</td>
</tr>
<tr>
<td>QMO(A)</td>
<td>−0.031</td>
<td>−0.143</td>
<td>−0.152</td>
<td>−0.072</td>
</tr>
<tr>
<td>Δen</td>
<td>−0.61</td>
<td>−0.12</td>
<td>0.28</td>
<td>0.82</td>
</tr>
<tr>
<td>S</td>
<td>0.215</td>
<td>0.174</td>
<td>0.183</td>
<td>0.131</td>
</tr>
</tbody>
</table>

*Computed at ZORA-OLYP/TZ2P. Bond dissociation energy. VDD atomic charge. \(^{14}\) Pauling electronegativity difference of central atom relative to Cl. \(^{15}\) Overlap integral between HOMO (3p) of Cl− and LUMO (σ*A−Cl) of each substrate at the TS (TC).

That the orbital interaction is indeed the dominant contribution to the ΔEint trend is further confirmed by the examination of the decomposition of ΔEtot according to our quantitative analysis associated with the KS-MO model \(^{14-49}\) (see Methods). The individual components, ΔE_Pauli, ΔV_distr, and ΔE_int are overlaid for all four studied SN2 reactions in Figure 5. Both the Pauli repulsion term (ΔE_Pauli, Figure 5a) and the electrostatic interaction (ΔV_distr, Figure 5b) oppose the trend; although the ΔV_distr(ζ) curves appear nearly superimposable, the shifted TS positions in fact result in less stabilizing ΔV_distr(ζ) contributions from C to N, O, and F. The ΔEint (Figure 5c) is the only term that decreases in this order and, thanks to its magnitude (note different scales on the Figure 5 panels), results in the overall progression of the ΔEtot.

Another factor that may possibly contribute to the computed trends in the ΔEtot for the studied series of the SN2 reactions is the diminishing steric congestion around the reaction center due to the fewer substituent hydrogen atoms in CH3Cl, NH2Cl, OHCl, and FCl, respectively. In earlier, detailed analyses, the combination of more favorable steric and orbital interactions was found to be responsible for the disappearance of the central barrier in SN2@Si as well as heavier group-14 atoms. \(^{19}\) Furthermore, Pierreffie et al. explicitly tested the role of...
of the steric congestion by hydrogens bound to the central carbon for a series of Cl\textsuperscript{−}-induced S\textsubscript{2}2@C reactions with CH\textsubscript{3}Cl, CH\textsubscript{2}Cl\textsuperscript{−}, CHCl\textsuperscript{−}, and CCl\textsuperscript{−} which have the same number of central atom bound hydrogens as our model series. They found that the central activation barrier becomes systematically lower with the decreasing number of hydrogens bound to the central atom and vanishes completely for the CCl\textsuperscript{−}, paralleling our result for S\textsubscript{2}2@F.

Finally, the difference in shape between the PES for S\textsubscript{2}2@C, S\textsubscript{2}2@N, and S\textsubscript{2}2@O and that for S\textsubscript{2}2@F is also codetermined by the strength of the hydrogen bonds that promote the occurrence of a stable RC and PC. Note that the relative energy of the S\textsubscript{2}2@F TC complex exactly fits the trend of the TS energetics for the other reactions: the symmetric TS or TC systematically decreases in energy relative to the RC energy, behaves less systematically. This is because it is dependent not only on the trend in stability of the symmetric transition species (TS or TC) but also on the stability or even the availability of the Cl−···H−AH\textsubscript{2−}Cl hydrogen bond in the RC or PC. This hydrogen bond becomes stronger as the H−A bond becomes more polar, along Cl−···H−CH\textsubscript{3}Cl, Cl−···H−NHCl, and Cl−···H−OCl (see Table 1 and Figure 2). The hydrogen bonding in the RC (and PC) for S\textsubscript{2}2@N and S\textsubscript{2}2@O is evident from the geometries where, in contrast to the RC for S\textsubscript{2}2@C, the Cl− clearly aligns with the N−H or O−H bond. This pronounced H-bonding interaction is reflected also in the distinct downward curvature of the AErot (Figure 4b) below d(A−Cl) of ~0.1 Å for S\textsubscript{2}2@N and S\textsubscript{2}2@O. But it ceases to exist as soon as there is no hydrogen-bond donor anymore, namely, for FCl; and so vanishes the RC and PC in the case of S\textsubscript{2}2@F.

4. CONCLUSIONS

The analyses of the S\textsubscript{2}2 reactions of Cl− + CH\textsubscript{3}Cl, NH\textsubscript{2}Cl, OHCl, and FCl based on relativistic density functional theory reveal a consistent trend, whereby the overall reaction barriers decrease with the decreasing number of hydrogens bound to the central atom, with the exception of FCl, which likewise become increasingly stabilized the more electro-negative the central atom, with the exception of FCl, which yields a single-well PES with no central barrier.

Analyses based on the activation strain model show that the trend is entirely due to the increasingly stabilizing interaction energy between nucleophile and substrate, with minimal contribution from the geometric strain. The origin of this trend lies predominantly (albeit not exclusively) in the lower energy of the unoccupied acceptor orbital (σ\textsuperscript{⁎}A−C\textsubscript{1}) as the electronegativity of the substitution center A (= C, N, O, and F) increases. This σ\textsuperscript{⁎}A−C\textsubscript{1} orbital-energy lowering leads to a stronger HOMO−LUMO orbital interaction with the 3p lone-pair orbital of the Cl− nucleophile.

These results underline the importance of the reaction center electronegativity and orbital interactions in shaping the S\textsubscript{2}2 reaction profiles. They also demonstrate the great utility of relativistic DFT calculations and activation strain analyses for understanding the fundamentals of chemical reaction mechanisms.

ASSOCIATED CONTENT

Supporting Information
The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.jpca.6b12240.

AUTHOR INFORMATION

Corresponding Author
Fax: +31-20-59 87629. E-mail: FM.Bickelhaupt@vu.nl.

ORCID

F. Matthias Bickelhaupt: 0000-0003-4655-7747

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

We thank The Netherlands Organization for Scientific Research (NWO-CW and NWO-EW) and NWO’s Planetary and ExoPlanetary Sciences (PEPSci) Program for financial support.

REFERENCES


(11) Ren, Y.; Wei, X.-G.; Ren, S.-J.; Lau, K.-C.; Wong, N.-B.; Li, W.-K. The Alpha-Effect Exhibited in Gas-Phase S\textsubscript{2}2@N and S\textsubscript{2}2@C Reactions. J. Comput. Chem. 2013, 34, 1997−2005.


(13) van Bochove, M. A.; Swart, M.; Bickelhaupt, F. M. Nucleophilic Substitution at Phosphorus Centers (S\textsubscript{2}2@P). ChemPhysChem 2007, 8 (17), 2452−2463.


(16) van Bochove, M. A.; Swart, M.; Bickelhaupt, F. M. Nucleophilic Substitution at Phosphorus (S\textsubscript{2}2@P): Disappearance and Reappearance of Reaction Barriers. J. Am. Chem. Soc. 2006, 128, 10738−10744.

(17) Bickelhaupt, F. M.; Baerends, E. J.; Nibbering, N. M. M. The Effect of Microsolvation on E2 and S\textsubscript{2}2 Reactions: Theoretical Study...


(20) Bento, A. P.; Bickelhaupt, F. M. Nucleophilic Substitution at Silicon (S2@Si) via a Central Reaction Barrier. J. Org. Chem. 2007, 72, 2201−2207.


(31) Baerends, E. J.; Sola, M.; Bickelhaupt, F. M. Ab Initio and DFT Benchmark Study for Nucleophilic Substitution at Carbon (S2@C) and Silicon (S2@Si). J. Comput. Chem. 2005, 26, 1497−1504.
