

# Stereochemistry of the Concerted S<sub>N</sub>2' Reaction of 3-Chloropropene: A Theoretical Study

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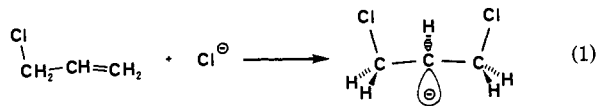
**Abstract:** The preferred stereochemistry and regiochemistry of allylic nucleophilic substitution has been examined by employing ab initio molecular orbital calculations. Complete optimizations of the transition states for S<sub>N</sub>2, anti-S<sub>N</sub>2', and syn-S<sub>N</sub>2' attack by Cl<sup>-</sup> on 3-chloropropene were carried out (4-31G). The calculated relative energies of these transition structures are 0.0, 7.8, and 14.9 kcal/mol, respectively. These data suggest that syn-S<sub>N</sub>2' nucleophilic addition is the least favored of the three possible pathways when the nucleophile is Cl<sup>-</sup>. However, the syn pathway is preferred when NH<sub>3</sub> is the attacking nucleophile. An analysis of the frontier molecular orbitals suggests that a concerted S<sub>N</sub>2' reaction is a feasible pathway, but we see no inherent theoretical reason to suggest that a syn-S<sub>N</sub>2' reaction is favored on the basis of stereoelectronic effects. The observed stereochemistry is more likely due to secondary bonding interactions or a result of participation of the *g*egenation in the transition state.

One of the most fundamental reactions in organic chemistry is nucleophilic substitution at carbon. There are no conceptual difficulties in considering the interaction of a nucleophile (e.g., Cl<sup>-</sup>) with an "electrophilic center" such as a carbon-halogen bond (e.g., CH<sub>3</sub>Cl). However, nucleophilic attack at vinylic carbon immediately invokes concern since the basic initial reaction presumably involves the repulsive interaction of two nucleophiles. The S<sub>N</sub>2' reaction of allylic substrates constitutes such an example. Both the stereochemistry of reaction and the question of concertedness of bimolecular nucleophilic displacement with allylic rearrangement has remained a point of controversy since the inception of the S<sub>N</sub>2' reaction.<sup>1</sup> There are three possible trajectories for nucleophilic displacement with an allylic substrate: the incoming nucleophile (:NUC) may initiate a direct anti-S<sub>N</sub>2 displacement of the leaving group (L) from saturated carbon (path a) or approach the π-bond at C<sub>γ</sub> with either an anti (path b) or a syn (path c) relationship to the nucleofuge (Figure 1).

The first experimental documentation of predominant syn-S<sub>N</sub>2' stereochemistry was reported by Stork.<sup>2a</sup> This inspired the theoretical community to search for a justification for this intriguing observation despite the fact the cyclohexyl system employed had an inherent conformational bias for a syn addition.<sup>1a</sup> Early theoretical studies used frontier molecular orbital (FMO) arguments<sup>3,4</sup> in support of the observed syn stereochemistry while orbital symmetry methods suggested a preferred anti pathway.<sup>5a</sup> Burgess and Liotta<sup>5b</sup> have used orbital distortion techniques to explain general syn stereochemistry, although they suggested that nucleophiles with a low-lying acceptor orbital (e.g., RS<sup>-</sup>) may proceed via an anti transition state with an attendant increase in the S<sub>N</sub>2/S<sub>N</sub>2' ratio. Ab initio molecular orbital calculations prompted Epiotis<sup>6a</sup> to propose an anti mode of substitution for anions and a syn pathway for neutral nucleophiles as a result of electrostatic interactions and nonbonded attractions in the tran-

sition state. Syn stereochemistry has also been suggested with use of the model reaction of hydride ion adding to propene.<sup>6b</sup> Huckel calculations<sup>6c</sup> were consistent with either syn (N, O, Cl) or anti (C, S) pathways, depending upon the nucleophile.<sup>6b</sup> The theoretical studies to date are far from conclusive and offer no clear preference for syn vs. anti stereochemistry in the S<sub>N</sub>2' reaction.

We were initially biased toward a syn-S<sub>N</sub>2' pathway since this would be a logical extension of our theoretical studies on the syn-E<sub>2</sub>-elimination reaction where we have advocated the necessity for an anti carbanionic transition state.<sup>7</sup> The syn addition of Cl<sup>-</sup> to allyl chloride could conceivably produce an sp<sup>3</sup> carbanion at C<sub>2</sub> that is anti to both chlorine atoms (eq 1), affording maximum hyperconjugative stabilization by mixing with the σ\*<sub>C-Cl</sub> orbitals.



Employing microscopic reversibility concepts, anti addition of Cl<sup>-</sup> at C<sub>γ</sub> affording a nonplanar carbon at C<sub>β</sub> (eq 1) must involve inversion of configuration prior to elimination of Cl<sup>-</sup> from C<sub>α</sub>. This would also be a tenable argument if a discrete carbanionic intermediate were involved in the syn-S<sub>N</sub>2' displacement. A similar rationale has recently been reported by Houk<sup>6b</sup> and Stohrer.<sup>6d</sup> However, we now report that we can find no theoretical justification for a preferred syn-S<sub>N</sub>2' orientation. Stereoelectronic arguments suggest that both syn and anti concerted S<sub>N</sub>2' nucleophilic substitutions are intrinsically viable pathways. The observed stereochemistry in S<sub>N</sub>2' reactions is very likely determined by secondary bonding interactions. The question of the regiochemistry of nucleophilic attack on an allyl substrate has not been tested theoretically and is, therefore, another primary objective of the present study.

## Method of Calculation

We initially chose to study the reaction of Cl<sup>-</sup> with allyl chloride because the symmetry inherent in the possible transition states for the three "degenerate" nucleophilic substitutions (S<sub>N</sub>2, anti S<sub>N</sub>2', and syn S<sub>N</sub>2') would greatly simplify both the computations and the analysis of the resultant molecular orbitals. Geometry optimization, using energy gradients, of 3-chloropropene and its accompanying transition states afforded the structures given in Figure 2. The gauche conformation of 3-chloropropene was maintained throughout. Fortunately, this structure is very close to the most stable conformer of allyl chloride in both the gas and liquid phases.<sup>8</sup>

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(6) (a) Yates, R. L.; Epiotis, N. D.; Bernardi, F. J. *J. Am. Chem. Soc.* **1975**, 97, 6615. (b) Caramella, P.; Rondan, N. G.; Paddon-Row, M. N.; Houk, K. N. *J. Am. Chem. Soc.* **1981**, 103, 2438. Houk, K. N.; Paddon-Row, M. N.; Rondan, N. G. *J. Mol. Struct.* **1983**, 103, 197. (c) Cheng, N.; Zhou, B. *J. Fengi Kexue Zuebao* **1982**, 2, 119; *Chem. Abstr.* **1982**, 97, 197541. (d) Stohrer, W. D. *Angew. Chem., Int. Ed. Engl.* **1983**, 22, 613.

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Table I. Relative Energetics for Allylic Nucleophilic Substitution Reactions (kcal/mol)

	STO-3G		4-31G	
	$E_{\text{tot}}$ , au	$\Delta E$	$E_{\text{tot}}$ , au	$\Delta E$
chloride anion	-454.48042		-459.02641	
3-chloropropene (1)	-569.65872	0.0	-575.31162	0.0
$S_N2$ T.S. (2)	-1024.13063	+5.3	-1034.35154	-8.48
<i>syn</i> - $S_N2'$ T.S. (3)	-1024.13949	-0.2	-1034.32773	+6.46
<i>anti</i> - $S_N2'$ T.S. (4)	-1024.14282	-2.3	-1034.33905	-0.66
ammonia	-55.45542		-56.10669	
2-propenaminium cation (5)	-170.40294	0.0	-172.21502	0.0
<i>syn</i> - $S_N2'$ T.S. (6)	-225.82708	+19.6	-228.29494	+16.80
<i>anti</i> - $S_N2'$ T.S. (7)	-225.83344	+15.6	-228.29629	+15.95
chloride anion + 5	-625.11414	0.0	-631.41831	0.0
ammonia + 1	-624.88336	+144.8	-631.24143	+111.0
<i>syn</i> - $S_N2'$ T.S. (8)	-625.04383	+44.1		
<i>anti</i> - $S_N2'$ T.S. (9)	-625.02565	+55.5		

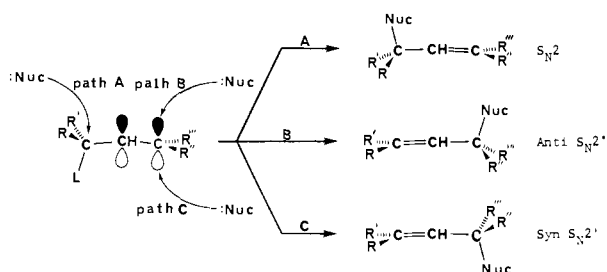


Figure 1. The pathways for nucleophilic displacement with an allylic substrate.

Our computational methods utilized standard molecular orbital theory.<sup>9</sup> The geometries of 3-chloropropene and its three symmetrical transition states (2-4) were optimized with both STO-3G and 4-31G basis sets. The symmetrical  $S_N2'$  displacements (6 and 7) involving ammonia are at the same level of approximation. The optimized geometries are given in Figure 3 and the relative energies are given in Table I. The unsymmetrical *syn*- $S_N2'$  transition-state structure for  $\text{NH}_3$  displacing  $\text{Cl}^-$  from 3-chloropropene (8) was fully optimized with an STO-3G basis set, but an anti transition structure (9) does not exist in the gas phase, presumably as a result of the excessive charge separation as one proceeds along the reaction coordinate. This structure was therefore optimized with the C-Cl and C-N bond distances maintained at the same values as those calculated for the *syn* transition structure 8 (Figure 4). In both 8 and 9 the heteroatoms were held at a  $90^\circ$  dihedral angle to the alkene plane and one N-H bond was maintained at a  $180^\circ$  dihedral angle to the C-C bond.

### Results and Discussion

Examination of the calculated relative energies of the transition structures for  $\text{Cl}^-$  displacement on 3-chloropropene (Table I) suggests that the transition state for direct  $S_N2$  displacement at the "electrophilic" allylic carbon is exothermic relative to reactants by 8.48 kcal/mol (4-31G).<sup>11</sup> Significantly, this reaction coordinate

(path a) is energetically favored over the *anti*- $S_N2'$  reaction (path b) by 7.8 kcal/mol and is 14.9 kcal/mol lower in activation energy than the *syn*- $S_N2'$  displacement (path c). When the 4-31G split valence basis was augmented with a set of diffuse p functions on chlorine,<sup>12a</sup> the *anti*- $S_N2'$  transition state was 18.8 kcal/mol lower in energy than 3. With inclusion of all valence and virtual orbitals, the electron correlation was calculated by Moller-Plesset perturbation theory<sup>12b</sup> to second order (MP2/3-21G) and the energy difference between 3 and 4 was reduced to 4.6 kcal/mol. This is the first direct comparison that we are aware of concerning the energetics of the  $S_N2$  vs. the  $S_N2'$  pathways. It is gratifying to see that the (gas phase) calculations are consistent with experimental observations where the major pathway for allylic substrates in solution is typically the classical  $S_N2$  nucleophilic displacement.

In a recent MNDO study of the reaction of chloride ion with allyl chloride, Dewar<sup>13</sup> has concluded that the  $S_N2'$  reaction takes place in steps. He suggested that formation of the new C-Cl bond took place without activation to form an intermediate in which the old C-Cl bond was almost intact. Thus, MNDO calculations indicate the  $S_N2'$  reaction to be a two-step process with formation of the new bond preceding rupture of the old one. Our results (4-31G) on the *syn*- $S_N2'$  transition state 3 suggest that a symmetrical transition structure with identical C-Cl bonds (24% C-Cl bond elongation) represents a maximum on the reaction coordinate. A deviation in  $r_{\text{C-Cl}}$  of  $\pm 0.03$ , 0.06, and 0.12 Å resulted in a small but continuous decrease in energy. To confirm this, the full set of vibrational frequencies were calculated by using analytical second derivatives at the STO-3G level for both 3 and 4. In each case only one imaginary frequency was found, suggesting that both symmetrical structures are true transition states. We feel that it is highly unlikely that extensive bonding between two such "nucleophilic" species can ensue without some elongation of the carbon-leaving group bond. Although this is feasible in the gas phase, such a bonding interaction would very likely be attended by some energy of activation in solution.

With the *anti*- $S_N2'$  transition structure the partial negative charges of the chloride ions are opposed to one another, and this dipole effect could be partially responsible for its lower energy. A similar effect is seen in the symmetrical transition structures arising from  $S_N2'$  "degenerate" displacement of  $\text{NH}_3$  from the allyl ammonium cation 5. The anti transition state 7, where the positively charged heteroatoms are anti, is 0.9 kcal/mol (4-31G) lower in energy than the *syn*- $S_N2'$  activated complex 6. In contrast, *syn*- $S_N2'$  displacement of  $\text{Cl}^-$  from 3-chloropropene by  $\text{NH}_3$  is favored over anti by approximately 11 kcal/mol (STO-3G). Unfortunately, the geometry of the latter structure was not fully optimized because a transition structure could not be attained, presumably due to charge separation. Thus it would appear that, at least in the gas phase, Coulombic interactions play an important

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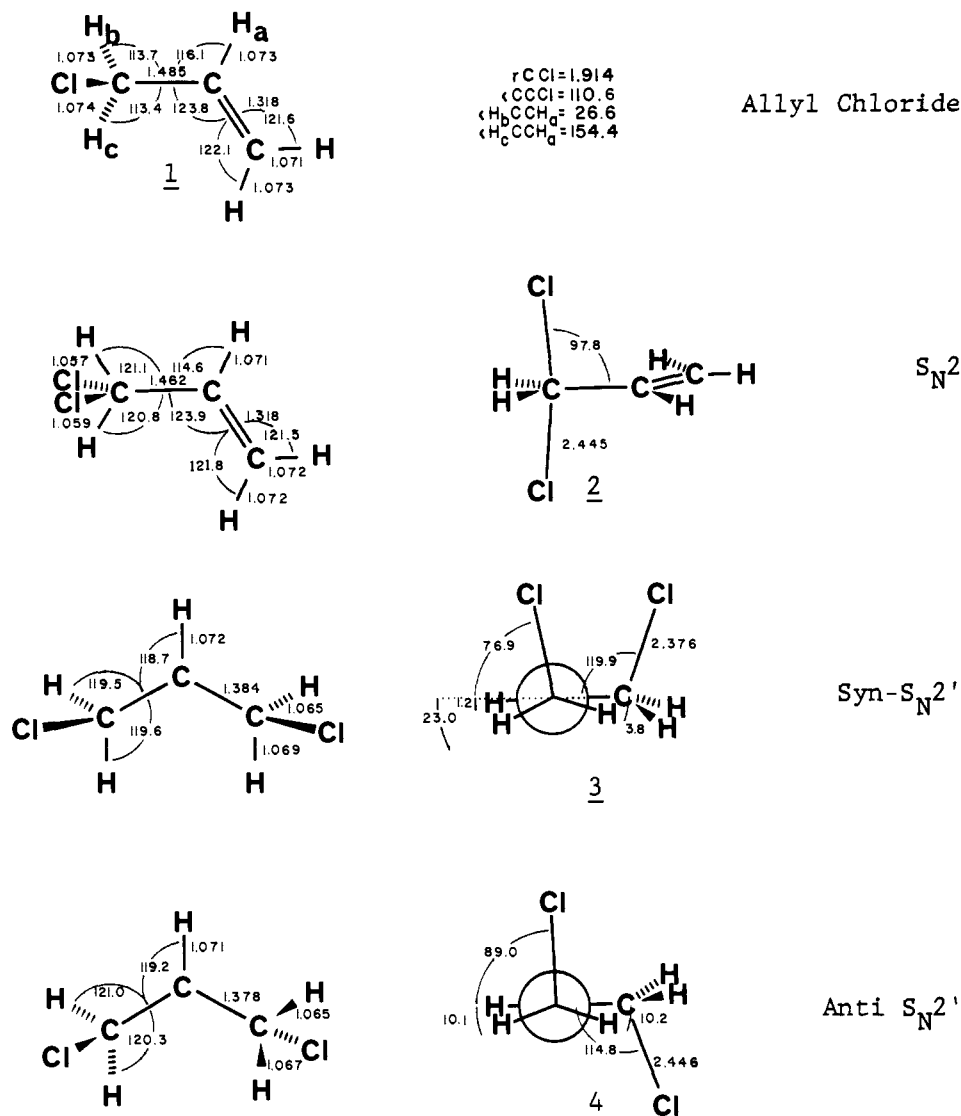
(9) All geometry optimizations used ab initio gradient methods employing the GAUSSIAN 80 series of programs.<sup>10</sup> The chlorine atom in 3-chloropropene was held perpendicular to the plane of the ethylene moiety. Relaxation of this geometry constraint led to a dihedral angle  $\text{Cl-C-C-H}_\alpha$  of  $65.7^\circ$  and a relative stabilization of only 0.67 kcal/mol (STO-3G).

(10) Binkley, J. S.; Whiteside, R. A.; Krishnan, R.; Seeger, R.; DeFrees, D. J.; Schelegel, H. B.; Topiol, S.; Kahn, L. R.; Pople, J. A. *Q.C.P.E.* **1981**, *13*, 406.

(11) (a) We did not search for a stable gas-phase cluster to base our barrier upon since it would only be meaningful if the nucleophile preferred to be on the reaction trajectory in the cluster. For example, the cluster for  $\text{Cl}^-$  and  $\text{CH}_2\text{Cl}$  exists at a minimum 16.4 kcal/mol below the reactants, and the barrier for the  $S_N2$  displacement is 5.5 kcal/mol above the structure.<sup>11b</sup> Thus, the activated complex is actually 10.9 kcal/mol lower in energy than the reactants. The experimentally observed barrier in such reactions is largely due to solvation effects. Our "activation barriers" should only be used for relative comparisons. (b) For a recent theoretical discussion, see: Wolfe, S.; Mitchell, D. J.; Schlegel, H. B. *Can. J. Chem.* **1982**, *60*, 1291.

(12) (a) Schaefer, H. F., III, Ed. "Methods of Electronic Structure Theory"; Plenum: New York, 1977; Chapter 1, p 25. (b) Pople, J. A.; Seeger, R.; Krishnan, R. *Int. J. Quant. Symp.* **1977**, *11*, 149.

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**Figure 2.** Optimized geometry (4-31G) of 3-chloropropene (1) and the transition states for  $S_N2$  (2), syn- $S_N2'$  (3), and anti- $S_N2'$  (4) displacement by chloride ion.

role in determining the preferred geometry at the transition state. Similar conclusions were reached by Epiotis on the basis of both ab initio and CNDO/2 computations.<sup>6a</sup> The magnitude of these Coulombic repulsions in the syn transition state 3, as manifested in an essentially zero total Mulliken overlap population between the two chlorine atoms, is not in evidence. However, the C-C-Cl bond angles and dihedral angles (Figure 2) are suggestive of a slight repulsive interaction. The transition states for displacement of  $NH_3$  (6 and 7) come much later along the reaction coordinate than that for  $Cl^-$  substitution (3 and 4) as evidenced by the percent of C-N (46%) and C-Cl (26%) bond elongation relative to that of reactants (5 and 2). The longer C...NUC bond distance can be attributed to the greater HOMO-HOMO interaction of the lower lying lone pair on nitrogen with the alkene  $\pi$ -bond.

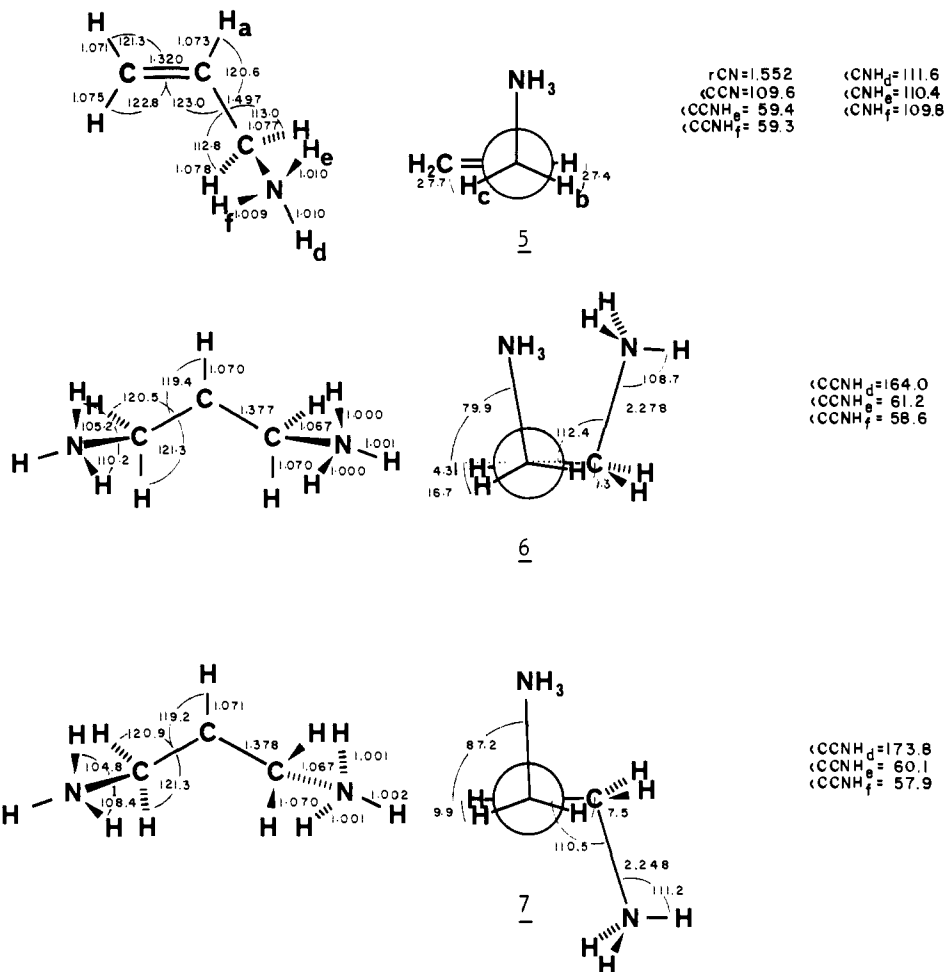
We now turn our attention to a comparative frontier molecular orbital (FMO) analysis of the direct nucleophilic displacement at saturated carbon to the four-bond concerted displacement at vinylic carbon. It has been known for many years that nucleophilic attack on a saturated carbon is accelerated by the presence of an adjacent multiple bond.<sup>14</sup> Hence, the rate of displacement with allylic and benzylic substrates is faster than that with a corre-

sponding saturated compound.<sup>14c</sup> This is due to the ability of a multiple bond to delocalize the developing negative charge on the carbon atom at the site of reaction by resonance or conjugation.<sup>14d</sup> This enhanced reactivity is further augmented in  $\alpha$ -carbonyl derivatives.<sup>15a</sup> We recently concluded<sup>15b</sup> that the enhanced reactivity of an  $\alpha$ -chlorocarbonyl compound to  $S_N2$  attack by a nucleophile ( $:NUC$ ) is due to an "allylic"  $\pi$ -bond interaction of the periplanar Cl-C...NUC moiety with the polarizable carbonyl group.

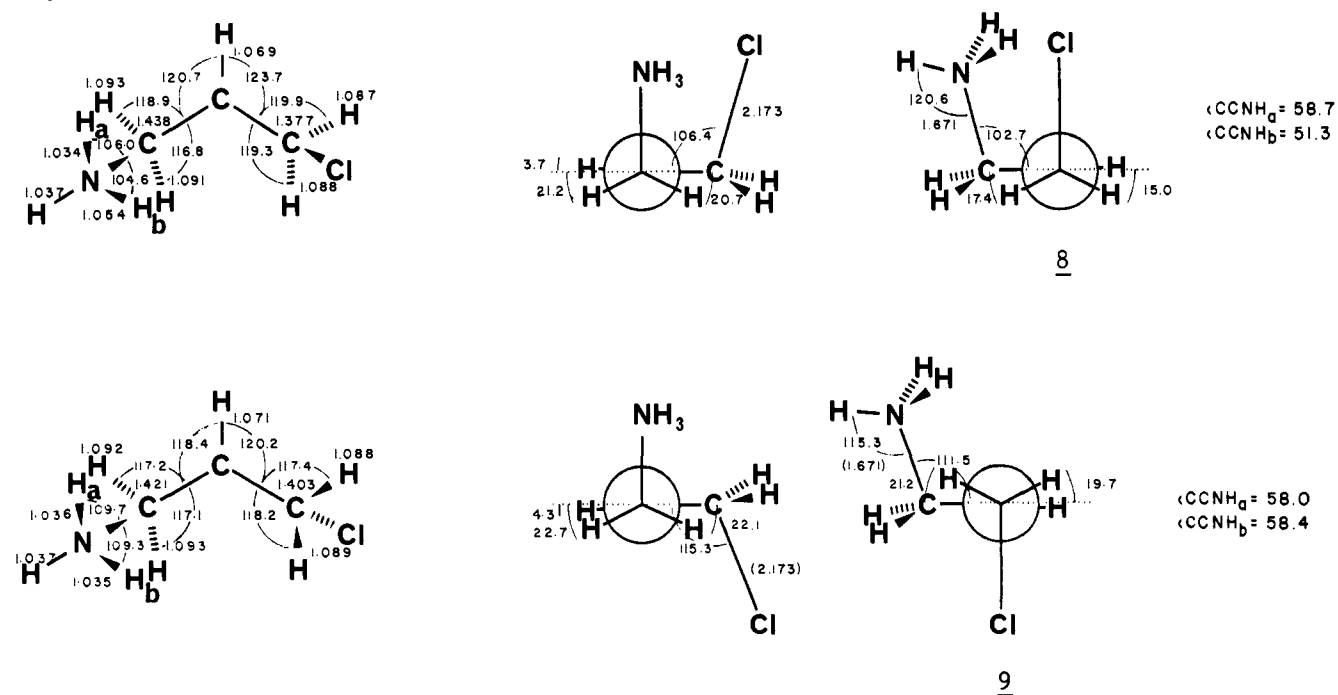
An understanding of the symmetry of the FMO's in the three possible transition states for allylic nucleophilic substitution is vital to an analysis of the requisite orbitals involved in these related reactions early on the reaction coordinate; the "effective HOMO" consists of the lone pair (n) of the nucleophile antibonding to the electrophilic carbon. This molecular orbital is the ( $n-\sigma_{C-X}$ ) upper combination of the four-electron interaction that mediates all such reactions. The increase in energy of this "developing MO" is simultaneously counteracted by its stabilizing two-electron interaction with the antibonding  $\sigma^*$  orbital (LUMO) of the carbon-leaving group bond. At the transition state for the  $S_N2$  reaction (2), where the two chlorine atoms are identical by symmetry considerations, the net bonding interaction summed over

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(15) (a) Bartlett, P. D.; Trachtenberg, E. N. *J. Am. Chem. Soc.* **1958**, *80*, 5808. (b) Pross, A.; Aviram, K.; Kliks, R. C.; Kost, D.; Bach, R. D. *Nouv. J. Chim.*, accepted for publication. [The calculated (4-31G) barrier for this nucleophilic displacement is 19.0 kcal/mol.]



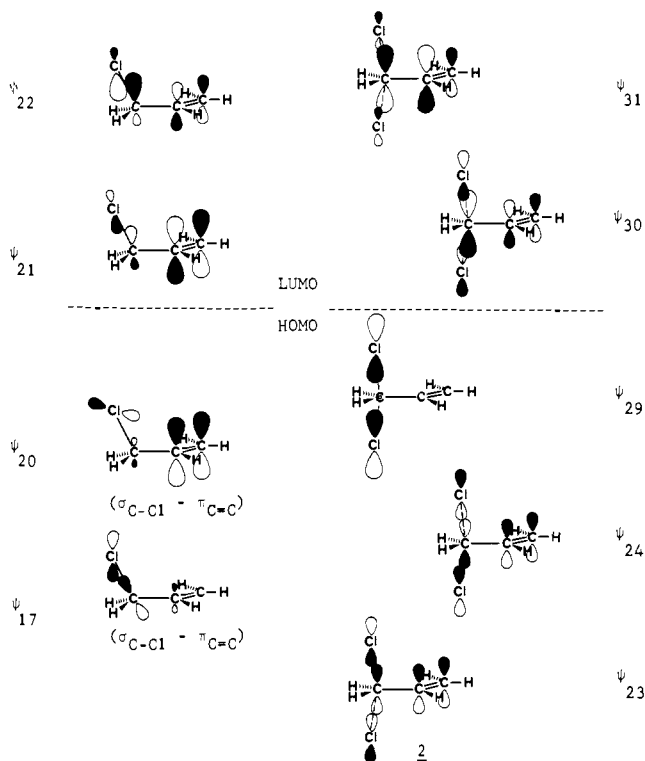
**Figure 3.** Optimized geometry (4-31G) for the 2-propenamium ion **5** and the transition states for syn- $S_N2'$  (**6**) and anti- $S_N2'$  (**7**) displacement by  $\text{NH}_3$ .



**Figure 4.** Optimized geometry for the transition state for the syn- $S_N2'$  displacement of chloride ion from 3-chloropropene by  $\text{NH}_3$  and the partially optimized transition structure for anti- $S_N2'$  displacement.

all occupied molecular orbitals must be identical for the two C-Cl bonds. At this point on the reaction surface, symmetry precludes a p-orbital contribution to the central atom in HOMO, since this MO must be symmetrically disposed about either side of the

symmetry plane in transition state **2**. These arguments also exclude any participation of the carbon 2s orbital in the NHOMO ( $\psi_{24}$ ) of Figure 5. The stabilizing influence of the molecule in its conjugated conformation is in evidence in the lower lying



**Figure 5.** Frontier molecular  $\pi$  orbitals of 3-chloropropene and the symmetrical transition state for the  $S_N2$  displacement of chloride ion from 3-chloropropene.

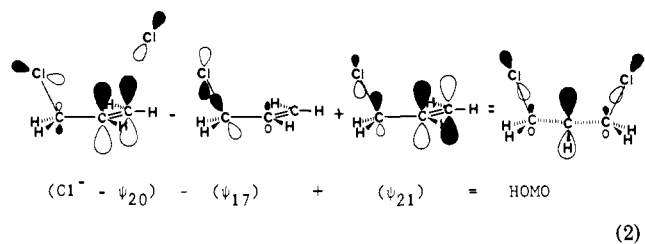
bonding ( $\sigma$ - $\pi$ ) combination ( $\psi_{23}$ ). This is the only occupied MO on the principal axis of reaction that can result in a lowering of the activation energy for  $S_N2$  displacement on an allylic substrate.

The  $S_N2'$  reactions involve nucleophilic attack at vinylic carbon, and the essential FMO interactions are more complex. An understanding of the department of the frontier orbitals of 3-chloropropene is an obvious prerequisite to using a fragment orbital approach to describe the transition state for an  $S_N2'$  reaction. The pertinent molecular orbitals of 3-chloropropene are shown in Figure 5. The occupied orbitals of this allylic system may be formally constructed by a  $\sigma$ - $\pi$  conjugative interaction between two filled orbitals. The lower lying bonding MO ( $\psi_{17}$ ) and the upper filled antibonding combination ( $\psi_{20}$ ) of the  $\sigma_{C-Cl}$  bond with the  $\pi$ -bond of the alkene constitute an "asymmetric" allylic system. The virtual orbitals ( $\psi_{21}$  and  $\psi_{22}$ ) may be derived from a similar interaction of the  $\sigma^*$  and  $\pi^*$  molecular orbitals.

The nucleophilic interaction  $Cl^-$  with allyl chloride must obviously involve orbital mixing of its filled molecular orbital with all four of the "allylic" molecular orbitals of the allyl system. This is especially true in this case since the calculated energy of  $Cl^-$  (-0.0877 au), in the gas phase, is close enough to both the LUMO (+0.1219 au) and the HOMO (-0.3762 au) so that both the two- and the four-electron interactions must be taken into consideration early on the reaction coordinate. In those reactions where the HOMO of the nucleophile is initially substantially closer to LUMO (i.e., a HOMO-LUMO dominant reaction)<sup>16</sup> the HOMO level of the nucleophile drops early on the reaction coordinate as a consequence of two-electron stabilization and an early transition state may be anticipated. However, in principle, the relative energy of the HOMO ( $Cl^-$ ) should not be affected until late along the reaction coordinate due to the approximate balance between the two- and four-electron interactions.<sup>16</sup> The decrease in energy of HOMO ( $Cl^-$ ) is greatest for the  $S_N2$  transition state as a result of the more repulsive interaction that accompanies an  $S_N2'$  reaction (Figure 6) and the greater ion-dipole attraction of the C-Cl bond. In all three transition states 2-4, the HOMO of 1 rises both as

a consequence of a four-electron interaction and an attendant Coulombic repulsion (Figure 6).

Finally, a comparison between the pertinent frontier orbitals involved in the anti- and syn- $S_N2'$  reaction is in order. There is a striking resemblance between the five molecular orbitals that encompass the principal axis of reaction for both of these controversial transition states (Figure 7) despite the fact that one is syn and the other anti. All of the corresponding molecular orbital pairs have virtually identical atomic orbital coefficients. Consequently, the symmetry (phasing) of these resulting molecular orbitals must be derived from a similar balance of two- and four-electron interactions. The HOMO ( $\psi_{29}$ ) in both transition structures 3 and 4 consists largely of a planar "carbanion" at  $C_2$ . By applying the principle of atomic orbital coefficient cancellation,<sup>16</sup> the origin of this rather unusual frontier molecular orbital may be understood by consideration of the mixing of  $Cl^-$  with the following FMO's of 1:  $\psi_{17}$ ,  $\psi_{20}$ , and  $\psi_{21}$  (eq 2). The HOMO



orbital of the syn transition state 3 should exhibit atomic orbital cancellation at  $C_1$  and  $C_3$  as a result of both the four- and two-electron interactions depicted in eq 2. In a similar fashion, the lack of any atomic orbital coefficient at  $C_2$  in  $\psi_{24}$  (Figure 7) is a reflection of the admixture of fragment orbitals  $\psi_{17}$  and  $\psi_{20}$  in allyl chloride. The lowest lying occupied MO ( $\psi_{23}$ ) provides a stabilizing "allylic" interaction for both orientations of the approach of the nucleophile. The occupied nonbonding ( $\psi_{24}$ ) and antibonding ( $\psi_{29}$ ) molecular orbitals of the transition states clearly reflect the symmetry of an "allylic anion".

Another revealing feature of the syn- and anti- $S_N2'$  transition states is the similarity in the relative changes of the energies of the fragment orbitals as they evolve into their two respective transition states (Figure 6). The order of the activation energies for the  $S_N2$  and the anti- and syn- $S_N2'$  pathways (-8.48, -0.66, +6.46 kcal/mol) are in the same relative order as the level of the HOMO of the transition states. The ultimate level of  $\psi_2$ , which is the HOMO in this three molecular orbital EFMO model, is determined by a delicate balance between the magnitude of two- and four-electron interactions.<sup>17</sup> In the present case, the destabilization attributable to the four-electron interaction should be greater for the addition of an amine, with a relatively low-lying HOMO, than for an anionic nucleophile possessing a lone pair at a higher energy and closer to the LUMO. The relative mixing of these frontier orbitals will also determine the position of the transition state along the reaction coordinate and the exo- or endothermicity of the reaction in accordance with a corollary<sup>16</sup> to the Hammond postulate.

### Summary

One conclusion that can be reached from this theoretical study is that with a nucleophile with a relatively high lying HOMO (e.g.,  $Cl^- = -0.0877$  au) the  $S_N2'$  reaction cannot compete energetically with the direct  $S_N2$  process in accord with experiment.<sup>1</sup> The activation barrier in such cases is due largely to the extensive bond reorganization that attends an endothermic reaction and should not be completely attributable to the four-electron interactions involved in  $S_N2'$  reactions. Our theoretical results also suggest that with transition states involving either negatively (3 and 4) or positively (6 and 7) charged heteroatoms, an anti juxtaposition

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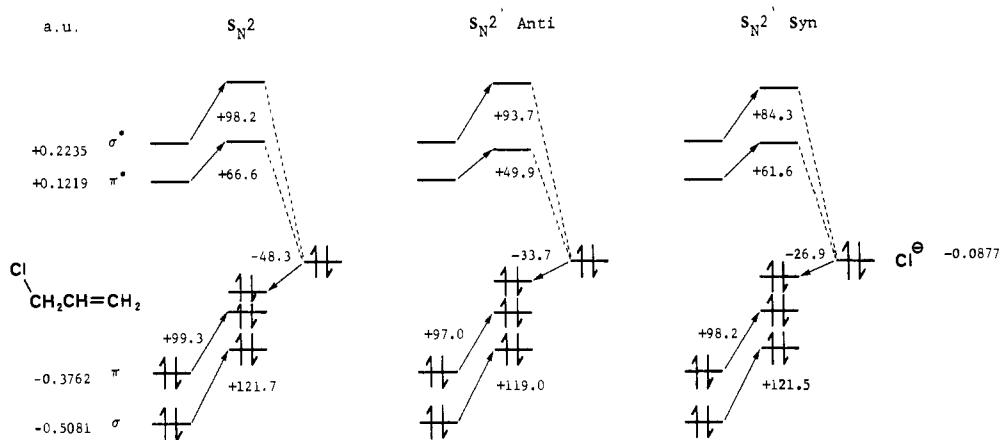


Figure 6. A comparison of the FMO energy changes (kcal/mol) involved in the transition states for nucleophilic displacement of chloride ion from 3-chloropropene.

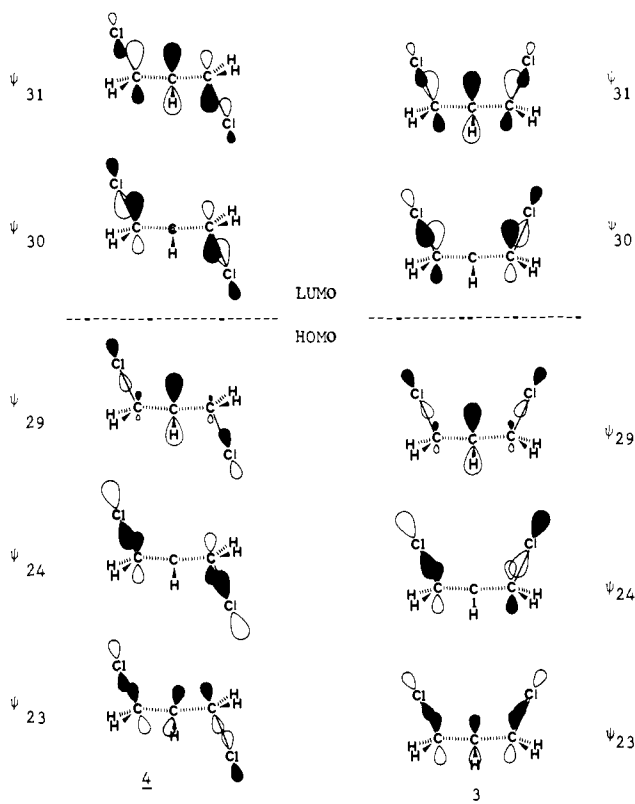


Figure 7. Frontier molecular  $\pi$  orbitals for the symmetrical transition states for anti- and syn- $S_N2'$  displacement of chloride ion from 3-chloropropene.

of the charged fragments should be preferred (in the gas phase). The separation of identically (partially) charged moieties in an anti transition state should also be observed in solution. With an unsymmetrical transition state involving oppositely charged heteroatoms, the calculated energy differences suggest that a syn transition state should be preferred. Stork<sup>2d</sup> has shown that a thiolate anion does prefer to add, very largely or possibly entirely, anti in the  $S_N2'$  reaction with a departing mesitoate from an acyclic system. In a very clever experiment using a deuterium-labeled unbiased acyclic allyl chloride, Magid<sup>18</sup> established the syn stereospecificity of the  $S_N2'$  reaction with a secondary amine. We feel that this observation is due to hydrogen bonding and Coulombic effects and is not due to an inherent stereoelectronic preference for syn- $S_N2'$  addition. The HOMO-HOMO interactions that dominate the syn- and anti- $S_N2'$  pathways are comparable, and we see no electronic bias for a syn pathway. Although

at the outset an "unprovoked attack by a nucleophile at the  $\gamma$  position of an allylic system" may seem intellectually unreasonable,<sup>19</sup> we have suggested<sup>16b</sup> that the HOMO-HOMO interaction is responsible for frontier orbital narrowing that elevates a filled orbital, the "effective HOMO", closer to the LUMO. In the presence of an antibonding orbital of proper symmetry, such four-electron interactions can exert a **stabilizing influence** on the enthalpy of activation. It should be recalled that the orbital splitting resulting from the mixing of two filled orbitals is essentially isoenergetic as a consequence of the stabilizing effect of the bonding combination ( $\psi_1$ ) that is lowered in energy, **that is, the enthalpic effect of  $\psi_1$  drives the reaction.** On the basis of our results, an  $S_N2'$  reaction can take place in the gas phase. We, therefore, advocate that the concerted  $S_N2'$  reaction is a feasible reaction pathway when a good polarizable nucleophile is involved. With highly substituted allylic compounds that require vigorous reaction conditions, the intermediacy of an allylic cation or intimate ion pair<sup>2c,d</sup> in a nonconcerted pathway is very likely. In fact, a great many  $S_N2'$  reactions probably follow a two-step pathway.<sup>1c,d</sup>

In the brief history of classical physical organic chemistry, few reactions have stirred the imagination of both the experimental and theoretical chemists to the extent noted with the  $S_N2'$  reaction. We feel that the theoretical rationale resulting in an infatuation with a preferential syn- $S_N2'$  reaction was unfounded. These theoretical predictions were largely based upon ground-state FMO considerations. Implicit in such an analysis is the assumption that the ground-state orbitals will reflect those of the transition state. We found no evidence to support such arguments. In order to recognize those factors that control the ratio of syn-/anti- $S_N2'$  products, by either mechanism, we should perhaps learn from our experiences with  $E_2$  elimination reactions. Certainly the syn/anti dichotomy in that area of chemistry was quickly reduced to a discussion of cation-anion base pair effects once the importance of the bonding influence of the cation to both the base and the leaving group was recognized.<sup>20</sup> The preferred syn- $S_N2'$  reaction with amines is very likely a simple consequence of hydrogen bonding or Coulombic interactions in the transition state.

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