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Is S_N2 Substitution with Inversion of Configuration at Vinylic Carbon Feasible?

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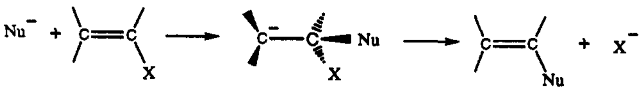
Nucleophilic vinylic substitution often proceeds via an addition–elimination pathway, initiated by nucleophilic attack at the π-bond.[2,3] This may involve a multistep pathway via one or more carbanion intermediates, such as that indicated in Scheme 1, or a single-step process when substituents reduce the lifetime of the carbanion intermediate(s) to zero.[2c,d] Both the stepwise and the concerted processes normally lead to retention of configuration, though when the carbanion intermediate is long-lived, partial or complete stereoconvergence may result.[2,3]

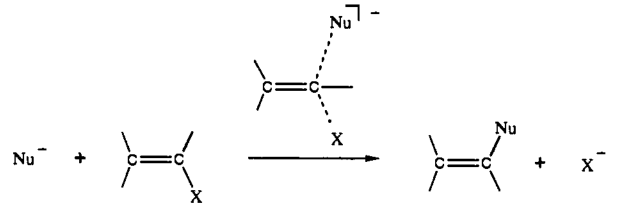
The concerted *in-plane* S_N2 pathway, which involves backside attack at carbon through a planar transition state and results in inversion of configuration (Scheme 2), is quite rare at sp^2 centers, in marked contrast to the situation for sp^3 centers. It has only been postulated to occur in intramolecular processes, in which the nucleophile is constrained to attack in-plane, or when the leaving group is bound to the second terminus of the double bond.[4] In the absence of these special circumstances, in-plane intermolecular S_N2 attack on an unactivated sp^2 carbon is considered to be a high-energy pathway and has not been proposed to date. When complete or predominant inversion of configuration has been observed in simple vinyl systems, it has been attributed to attack on ion pairs (rather than on the neutral substrate),[5] or left unresolved.[6]

Early theoretical studies appeared to support this general view. Extended Hückel calculations for hydride ion attack on ethylene indicated the barrier for the in-plane S_N2 pathway to be 326 kJ mol^{-1}, while the barrier for attack on the π-system was found to be just 75 kJ mol^{-1}.[7] Indeed, the large difference has been considered sufficient grounds for ruling out the in-plane σ–pathway, and as a result subsequent theoretical studies[8] have only considered the π–pathway.[9]

Scheme 1



Scheme 2



In the present communication, we report high-level calculations on the $Cl^- + CH_2{=}CHCl$ reaction that question the current view. Our results indicate that, in the gas phase, in-plane σ-type S_N2 substitution with inversion at an unactivated sp^2 carbon *is actually energetically preferred to the out-of-plane* π-pathway.

Standard *ab initio* molecular orbital calculations[10] were carried out with the use of the GAUSSIAN 92 program.[11] Energies were computed using a G2-type procedure[12] but with MP2/6-31+G(d) geometries and HF/6-31+G(d) frequencies. We denote this level of theory as G2(+). Our more important results are summarized in Figure 1. Full details will be presented elsewhere.[13]

Our energy surface for Cl^- exchange reveals two discrete pathways, one describing an in-plane σ-pathway with inversion of configuration, and the other, an out-of-plane π-pathway with retention of configuration (Figure 1). Attack by Cl^- on $CH_2{=}CHCl$ initially involves the formation of a loose ion–molecule complex **1** in which the incoming Cl^- is located in the plane of the alkene. The reaction may then proceed via the σ-pathway or the π-pathway. The *lower* energy route is through the planar C_{2v} structure **2**, which corresponds to the transition structure for in-plane S_N2 substitution, and has an intrinsic barrier (relative to the complex **1**) of 136.5 kJ mol^{-1}. The alternative out-of-plane pathway leads to transition structure **3**, in agreement with the ideas of Stohrer on the nature of the concerted π-pathway,[8a] and has a barrier of 178.9 kJ mol^{-1}. Thus, in-plane attack via **2** is 42.4 kJ mol^{-1} more favorable than the out-of-plane pathway via **3**.[14]

No two-step pathway via a carbanion intermediate was found. The β,β-dichloroethyl anion, the potential intermediate in the multistep process (Scheme 1), is found to be unstable, collapsing in all unconstrained geometry optimizations to the loose complex **1**. Our results for the $Cl^- + CH_2{=}CHCl$ reaction suggest that, in the gas phase, nucleophilic substitution at unactivated vinyl carbon by halide ion is a single-step process, initiated by either σ-attack or π-attack, rather than a multistep process involving carbanionic intermediates.

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(2) (a) Rappoport, Z. *Adv. Phys. Org. Chem.* **1969**, *7*, 1. (b) Modena, G. *Acc. Chem. Res.* **1971**, *4*, 73. (c) Rappoport, Z. *Acc. Chem. Res.* **1981**, *14*, 7. (d) Rappoport, Z. *Acc. Chem. Res.* **1992**, *25*, 474.

(3) (a) Shainyan, B. A. *Russian Chem. Rev.* (*Engl. Transl.*) **1986**, *55*, 511. (b) Minkin, V. I.; Simkin, B. Y.; Minyaev, R. M. *Quantum Chemistry of Organic Compounds—Mechanisms of Reactions*; Springer Verlag: Berlin, 1990.

(4) (a) Rappoport, Z. *Tetrahedron Lett.* **1978**, 1073. (b) Lucchini, V.; Modena, G.; Pasquato, L. *J. Am. Chem. Soc.* **1993**, *115*, 4527.

(5) (a) Summerville, R. H.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1974**, *96*, 1110. (b) Clarke, T. C.; Kelsey, D. R.; Bergman, R. G. *J. Am. Chem. Soc.* **1972**, *94*, 3626.

(6) (a) Shainyan, B. A.; Rappoport, Z. *J. Org. Chem.* **1993**, *58*, 3421. (b) Ochiai, M.; Oshima, K.; Masaki, Y. *J. Am. Chem. Soc.* **1991**, *113*, 7059.

(7) Kelsey, D. R.; Bergman, R. G. *J. Am. Chem. Soc.* **1971**, *93*, 1953.

(8) (a) Stohrer, W.-D. *Tetrahedron Lett.* **1975**, 207. (b) Miller, S. I. *Tetrahedron* **1977**, *33*, 1211. (c) Apeloig, Y.; Rappoport, Z. *J. Am. Chem. Soc.* **1979**, *101*, 5095. (d) Texier, F.; Henri-Rousseau, O.; Bourgois, J. *Bull. Soc. Chim. Fr.* **1979**, 86. (e) Bach, R. D.; Wolber, G. J. *J. Am. Chem. Soc.* **1984**, *106*, 1401. (f) Cohen, D.; Bar, R.; Shaik, S. S. *J. Am. Chem. Soc.* **1986**, *108*, 231. (g) Rappoport, Z.; Avramovitch, B.; Karni, M.; Apeloig, Y. *Isr. J. Chem.* **1989**, *29*, 267.

(9) We refer to any out-of-plane pathway as a π-pathway, even though σ-mixing will occur to varying extents. The in-plane pathway is, however, pure σ.

(10) Hehre, W. J.; Radom, L.; Schleyer, P. v. R.; Pople, J. A. *Ab Initio Molecular Orbital Theory;* Wiley: New York, 1986.

(11) Frisch, M. J.; Trucks, G. W.; Head-Gordon, M.; Gill, P. M. W.; Wong, M. W.; Foresman, J. B.; Johnson, B. G.; Schlegel, H. B.; Robb, M. A.; Replogle, E. S.; Gomperts, R.; Andres, J. L.; Raghavachari, K.; Binkley, J. S.; Gonzalez, C.; Martin, R. L.; Fox, D. J.; DeFrees, D. J.; Baker, J.; Stewart, J. J. P.; Pople, J. A. *GAUSSIAN 92*; Gaussian Inc.: Pittsburgh, PA, 1992.

(12) Curtiss, L. A.; Raghavachari, K.; Trucks, G. W.; Pople, J. A. *J. Chem. Phys.* **1991**, *94*, 7221.

(13) Glukhovtsev, M. N.; Pross, A.; Radom, L. To be submitted.

(14) Examination of the dividing surface between **1** and **1′** in which the two C–Cl bond lengths are constrained to be equal shows that **2** and **3** (both shown rigorously by our frequency calculations to be first-order saddle points) are separated by a structure that lies approximately 50 kJ mol^{-1} above **3** (calculated at the G2(+)(MP2) level). The reaction pathways via **2** and **3** are thus discrete. Note that optimizations starting from **2** or **3**, seeking a minimum energy structure, lead in both cases to the complex **1**. The G2(MP2) procedure is described in the following: Curtiss, L. A.; Raghavachari, K.; Pople, J. A. *J. Chem. Phys.* **1993**, *98*, 1293.

0002-7863/94/1516-5961$04.50/0

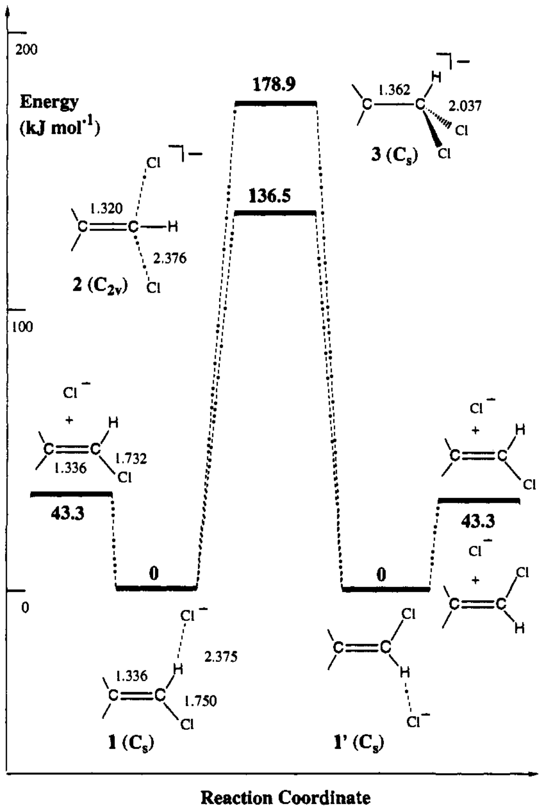

Figure 1. Schematic energy profile for the identity S_N2 reaction of Cl^- with $CH_2{=}CHCl$, calculated at the G2(+) level showing the two possible pathways: in-plane attack via **2** with inversion of configuration, and out-of-plane attack via **3** with retention of configuration. Bond lengths are in angstroms.

The above results for Cl^- exchange appear to be general. Our preliminary calculations show that in-plane backside attack with inversion of configuration is also the preferred pathway for the $Br^- + CH_2{=}CHBr$ and $I^- + CH_2{=}CHI$ reactions.[13]

It is of interest to speculate whether or not our gas-phase predictions will carry over into solution. Noting that the negative charge in transition state **3** is more delocalized (over the C–C bond *and* the two Cl atoms) than in **2** (where it resides mainly on the two Cl atoms), a simplistic analysis would suggest that, in solution, **2** might be further stabilized relative to **3**. Accordingly, one might expect that the gas-phase preference for the in-plane S_N2 reaction (via **2**) will be maintained in solution.

The present results lead naturally to the following question: Given the unexpected energetic preference for σ-attack (with inversion) over π-attack (with retention) in vinyl systems, why it is that the π-route for substitution is the one that is experimentally predominant? Several points need to be noted in this regard.

(a) The calculated intrinsic barrier for the in-plane S_N2 attack of Cl^- on $CH_2{=}CHCl$ (136.5 kJ mol⁻¹) is substantially larger than the intrinsic barrier for the S_N2 attack of Cl^- on CH_3Cl (55.5 kJ mol⁻¹ at the G2(+) level;[15] 55.2 ± 8.4 kJ mol⁻¹ experimentally[16]), so that in-plane σ-attack at unactivated vinyl centers is not expected to be a particularly facile process.

(b) Due to the relatively large barrier for substitution at an *unactivated* sp^2 center, nucleophilic substitution at vinyl carbon is normally observed experimentally for *activated* systems. Since it is much easier to activate systems toward an addition–elimination pathway by stabilizing the carbanionic intermediate, than toward S_N2 substitution (where no intermediates are formed), appropriately activated systems are likely to react via addition–elimination pathways which involve π-attack, and not via in-plane S_N2. Similarly, stabilization of the potential carbocationic intermediate will result in an S_N1 mechanism being followed.

(c) When unactivated vinyl systems with good leaving groups—potential candidates for in-plane S_N2 reactions—were studied experimentally,[5,6] it was found that substitution proceeded with *predominant* inversion of configuration (up to 90%) for simple vinyl triflates,[5] with apparent *complete* inversion of configuration for 1,2 dibromo-1,2-difluoroethylene,[6a] and with *complete* inversion of configuration for simple vinyliodonium salts.[6b] In all three cases, the in-plane S_N2 pathway was not considered a likely mechanistic pathway. In the case of the vinyl triflates, the S_N2 pathway was considered unlikely due to the fact that inversion was not complete, and the result was attributed to nucleophilic attack on ion-pair intermediates.[5] For the substitution of 1,2-dibromo-1,2-difluoroethylene, uncertainty regarding the significance of the product isomer distribution precluded definite conclusions, while for the vinyliodonium salts, both the ion-pair mechanism and the direct S_N2 route were considered unlikely, and the complete inversion of configuration was left unexplained. *In all cases, however, the in-plane S_N2 route was considered unlikely on the basis of the perception that S_N2 attack with inversion at vinylic centers is a high-energy pathway and is higher in energy than out-of-plane π-attack.*

In the light of our theoretical study, which suggests the in-plane pathway for an unactivated substrate to be the lower energy process, we believe that the above experimental data[5,6] need to be reappraised. Consideration of our theoretical results and the experimental data on simple vinyl systems suggests that *in-plane S_N2 reaction with inversion of configuration at unactivated vinylic carbon may be feasible both in the gas phase and in solution.* Further work to evaluate the importance of steric and solvation factors in influencing the competition between in-plane and out-of-plane pathways would assist in defining the scope of the in-plane S_N2 pathway.

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(15) Glukhovtsev, M. N.; Pross, A.; Radom, L. To be submitted.

(16) Barlow, S. E.; Van Doren, J. M.; Bierbaum, V. M. *J. Am. Chem. Soc.* **1988**, *110*, 7240.