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S_N2 and Ad_N-E Mechanisms in Bimolecular Nucleophilic Substitutions at Vinyl Carbon. The Relevance of the LUMO Symmetry of the Electrophile[†]

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Abstract: The lowest vacant orbitals of a series of model vinyl systems with substituents of different electron-withdrawing power have been computed at the 3-21G*//3-21G*, 6-31G*//3-21G*, or 6-311G**//3-21G* levels. In situations where the first vacant orbitals with σ and π symmetry at the carbon centers are separated by >0.01 hartree, an almost complete correspondence is found between the symmetry of the lowest orbital and the stereochemical outcome of nucleophilic substitution on the corresponding real substrates. This finding is in line with the assumption that the interaction of the approaching nucleophile with the orbital of π symmetry directs the attack orthogonally to the molecular plane (Ad_N-E mechanism, leading to retention of configuration or stereoconvergence), while that with an orbital with σ symmetry determines the attack in the molecular plane (S_N2-Vin mechanism, leading to inversion of configuration). The situations where this correspondence fails, or the energy gap is smaller, are related to substrates for which no or other mechanisms (nonconcerted or ligand-coupling) have been proposed.

The S_N2 and Ad_N-E mechanisms govern the bimolecular nucleophilic substitutions at the aliphatic and aromatic carbon, respectively, and determine the different courses of the two reactions. Obviously, the two mechanisms are characterized at the electronic level by the same feature: the nucleophile attack occurs at the vacant orbital of the electrophilic substrate which ensures the greatest two-electron stabilizing interaction. This orbital is in most cases the LUMO (energy separation control), but with some substrates the greatest interaction may be with an higher vacant orbital (orbital overlap control).

At the same time, this common feature is responsible for the different courses of the two substitutions. The orbital interaction diagram in Figure 1 illustrates this point.[1,2] The two-electron interaction of the nucleophile HOMO with the electrophile π^* or σ^* LUMO is accompanied by the four-electron interaction with the corresponding π or σ orbitals. φ_1, φ_2, and φ_3 describe the frontier orbitals of the transition state. The φ_2 orbital derives essentially from mixing of the nucleophile HOMO with the electrophile π or σ orbitals, with some contribution from π^* or σ^* orbitals. This orbital will then evolve into an occupied orbital of the detached leaving group (LG), if it is generated from the electrophile σ orbital (S_N2 mechanism), or into the lone pair of the carbanionic intermediate, if it derives from the π orbital (Ad_N-E mechanism).

While the bimolecular aliphatic substitutions occur exclusively by the S_N2 mechanism, and the aromatic ones by the Ad_N-E mechanism, both have been proposed for the substitutions at the vinyl carbon.[3] We will therefore verify the postulated correspondence between the symmetry of the involved orbital of the electrophile and the mechanism with reference to this last reaction.

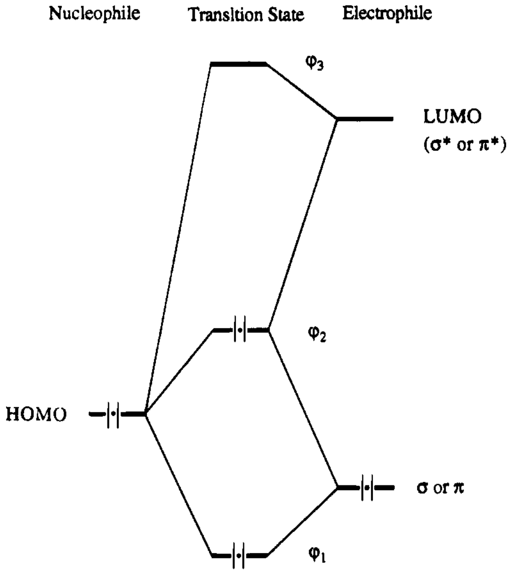

Figure 1. Orbital correlation diagram in nucleophilic substitutions.

In the vast majority of the reactions at the vinyl carbon, the nucleophile attacks orthogonally to the molecular plane yielding, through a tetrahedral intermediate, products with configurational distributions ranging from retention to stereoconvergence (Ad_N-E mechanism in Figure 2).

The logical vinyl analogue of the aliphatic S_N2 mechanism is described by the attack of the nucleophile to the vinyl carbon in the molecular plane and from the side opposite to the LG, generating, through a planar tetracoordinate transition state, products with inverted configuration (S_N2-Vin mechanism in Figure 2).[4]

[†] A preliminary account of this work has been presented at the 16th International Symposium on the Organic Chemistry of Sulfur, July 10−15, 1994, Merseburg, Germany.

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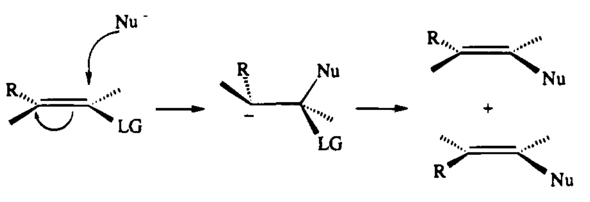
(1) Stohrer, W.-D. *Tetrahedron Lett.* **1975**, 207.

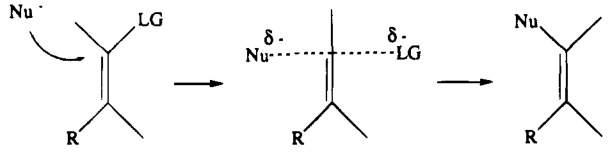
(2) Bach, R. D.; Wolber, G. J. *J. Am. Chem. Soc.* **1984**, *106*, 1401.

(3) Rappoport, Z. *Adv. Phys. Org. Chem.* **1969**, *7*, 1. Modena G. *Acc. Chem. Res.* **1971**, *4*, 73. Stang, P. J.; Rappoport, Z.; Hanack, M.; Subramanian, L. R. *Vinyl Cations*; Academic Press: New York, 1979. Rappoport, Z. *Acc. Chem. Res.* **1981**, *14*, 7. Rappoport, Z. *Reactive Intermediates*; Abramovitch, R. A., Ed.; Vol. 3, Plenum Press: New York, 1983; Chapter 7. Rappoport, Z. *Recl. Trav. Chim. Pays-Bas* **1985**, *104*, 309. Rappoport, Z. *Acc. Chem. Res.* **1992**, *25*, 474.

0002-7863/95/1517-2297$09.00/0



Ad$_N$-E mechanism



S$_N$2-Vin mechanism

Figure 2. The Ad$_N$-E and the S$_N$2-Vin mechanisms for the nucleophilic substitution at vinyl carbon.

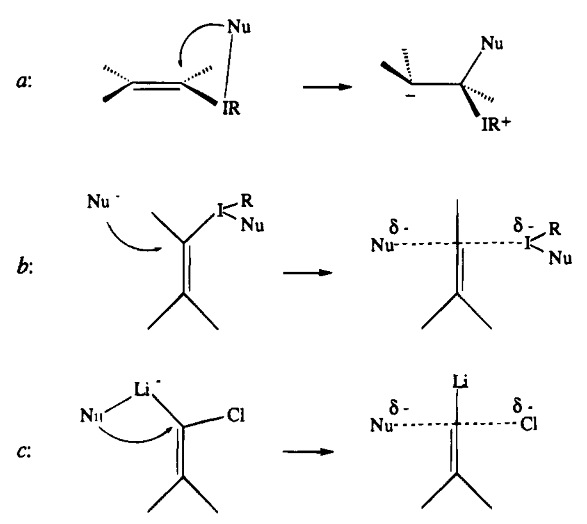


Figure 3. Ligand-coupling mechanisms for the nucleophilic substitutions at vinyl iodonium salts and at 1-chloro-1-lithioethenes occurring with retention (*a*) and with inversion (*b* and *c*) of configuration.

As inversions of configuration are seldom observed, the S$_N$2-Vin mechanistic hypothesis has been neglected for a long time. Only one theoretical study has appeared, assessing a large energetic preference for the orthogonal attack over the in-plane alternative.[5] Subsequent theoretical investigation have then focused on the Ad$_N$-E mechanism.[6] However, a recent theoretical paper, at a sophisticated computational level, reports that the in-plane approach of chloride ion onto the α-carbon of vinyl chloride is feasible, with a transition state lower in energy than the carbanionic intermediate derived from the orthogonal approach.[7]

The S$_N$2-Vin mechanism has been reconsidered as a rational for the inversions of configuration observed in a limited number of occasions.[8,9] The best documented case is the nucleophilic attack at irenium ions (either well characterized isolated substrates, thiirenium[10] and selenirenium ions,[11] or proposed intermediates, iodirenium[12] and vinylidenephenonium ions[13]). Recently, the rearrangement of di-*tert*-butylthiirenium ions into thietium ions was proved to be concerted and to occur via an intramolecular S$_N$2-Vin mechanism.[14] At variance, thiirene-1,1-dioxide is opened by strong nucleophiles with retention of configuration and then with the Ad$_N$-E mechanism.[15]

Other situations of predominant or complete inversion at the vinyl carbon are represented by the solvolysis of some vinyl triflates,[16] the nucleophilic substitutions of the tetrahaloethylenes with thiolate ion,[17] and of some vinyl iodonium salts with chloride ion.[18] On the other hand, the substitutions at monohaloethylenes occur with total or partial stereoconvergence[19] and other vinyliodonium salts with an electron-withdrawing β-substituent undergo nucleophilic substitution with retention.[20] A last occurrence of configurational inversion is provided by the nucleophilic substitution of 1-chloro-1-lithioethenes with *t*-BuLi.[21]

The mechanisms for these latter substitutions are not clearly assessed. The solvolysis of vinyl triflates undergo inversion of configuration only preferentially. The S$_N$2-Vin mechanism, which requires exclusive inversion, was then ruled out and a nonconcerted ion pair mechanism was proposed, with a detached but not yet removed LG, screening one side of the vinyl cation.[16c] The mechanism of nucleophilic substitution in 1,2-dibromo-1,2-difluoroethylenes by thiolate ion was not firmly stated: inversion of configuration was observed, but the possibility of a thermodynamic reequilibration was not ruled out.[17] Also the mechanism for substitution at vinyliodonium salts is not certain. For the inversion of configuration of vinyliodonium salts without a β-electron-withdrawing substituent, a ligand coupling mechanism was proposed,[18,22] where the nucleophile complexes on iodine (Figure 3). Similarly, the ligand coupling mechanism was proposed for the substitution of 1-chloro-1-lithioethenes, with the nucleophile *t*-BuLi complexing at the Li atom (Figure 3).[21b,23]

Finally, in-plane nucleophilic substitutions with inversion of configuration are observed in the case of the participation of a nucleophilic β-group in the solvolyses of vinyl substrates, which leads to irenium intermediates.[24] In this instance however, the internal nucleophile is constrained to the in-plane attack by the geometry of the system.

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(4) Gold, V. *J. Chem. Soc.* **1951**, 1430.

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

(6) Cohen, D.; Bar, R.; Shaik, S. S. *J. Am. Chem. Soc.* **1986**, *108*, 231, and papers cited therein.

(7) Glukhovtsev, M. N.; Pross, A.; Radom, L. *J. Am. Chem. Soc.* **1994**, *116*, 5961.

(8) Rappoport, Z. *Tetrahedron Lett.* **1978**, 1073.

(9) Capozzi, G.; Lucchini, V.; Modena, G. *Rev. Chem. Intermed.* **1979**, *4*, 347.

(10) Capozzi, G.; Lucchini, V.; Modena, G.; Scrimin, P. *Tetrahedron Lett.* **1977**, 911. Lucchini, V.; Modena, G. Valle, G.; Capozzi, G. *J. Org. Chem.* **1981**, *46*, 4720.

(11) Schmid, G. H.; Garratt, D. G. *Chem. Scr.* **1976**, *10*, 76.

(12) Bassi, P.; Tonellato, U. *J. Chem. Soc., Perkin Trans. 2* **1974**, 1283.

(13) Stang, P. J.; Dueber, T. E. *J. Am. Chem. Soc.* **1977**, *99*, 2602. Stang, P. J. *Acc. Chem. Res.* **1978**, *11*, 107.

(14) Lucchini, V.; Modena. G.; Pasquato, L. *J. Am. Chem. Soc.* **1993**, *115*, 4527.

(15) Yoshida, Y.; Komatsu, M.; Ohshiro, Y.; Agawa, T. *J. Org.Chem.* **1979**, *44*, 830.

(16) (a) Clarke, T. C.; Kelsey, D. R.; Bergman, R. G. *J. Am. Chem. Soc.* **1972**, *94*, 3626. (b) Summerville, R. H.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1972**, *94*, 3629. (c) Summerville, R. H.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1974**, *96*, 1110. (d) Clarke, T. C.; Bergman, R. G. *J. Am. Chem. Soc.* **1974**, *96*, 7934.

(17) Shainyan, B. A.; Rappoport, Z. *J. Org. Chem.* **1993**, *58*, 3421.

(18) Ochiai, M.; Oshima, K.; Masaki, Y. *J. Am. Chem. Soc.* **1991**, *113*, 7059.

(19) Rappoport, Z.; Topol, A *J. Am. Chem. Soc.* **1980**, *102*, 406. Rappoport, Z.; Gazit, A. *J. Org. Chem.* **1985**, *50*, 3184. Rappoport, Z.; Avramovitch, B. *J. Org. Chem.* **1982**, *47*, 1397.

(20) Ochiai, M.; Oshima, K.; Masaki, Y. *Tetrahedron Lett.* **1991**, *32*, 7711. Ochiai, M.; Oshima, K.; Masaki, Y.; Kunishima, M.; Tani, S. *Tetrahedron Lett.* **1993**, *34*, 4829.

(21) (a) Duraisamy, M.; Walborsky, H. M. *J. Am. Chem. Soc.* **1984**, *106*, 5035. (b) Topolski, M.; Duraisamy, M.; Rachon, J.; Gawronski, J.; Gawronska, K.; Goedken, V.; Walborsky, H. M. *J. Org. Chem.* **1993**, *58*, 546.

(22) Oae, S.; Uchida, Y. *Acc. Chem. Res.* **1991**, *24*, 202.

(23) Kocienski, P.; Barber, C. *Pure Appl. Chem.* **1990**, *62*, 1933.

(24) Burighel, A.; Modena, G.; Tonellato U. *J. Chem. Soc., Perkin Trans. 2* **1972**, 2026.

The preference of the nucleophilic substitutions at irenium rings for the S_N2-Vin mechanism has been empirically attributed[8,9] to the strain relief of the ring opening process (the ring is maintained in the tetrahedral intermediate generated by the Ad$_N$-E mechanism) and to the synergic involvement of a positively charged LG, which detaches as a neutral particle.

We think that a more comprehensive rationalization for the mechanistic preference of the substitution at vinyl carbon would be offered by the analysis of the symmetry properties of the LUMO (or, more generally, the attacked vacant orbital) of the electrophile. This analysis will not tell anything about the eventual heterolytic process which will lead to charged species.

Results and Discussion

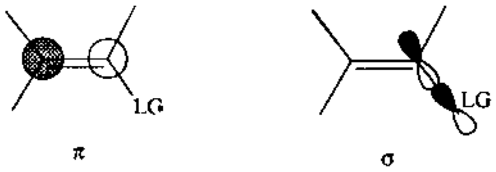
The geometries of the model substrates presented in Table 1 have been optimized *ab initio* at the 3-21G* level.[25,26] The 6-31G*[27] and 6-311G**[28] basis sets for Br and I are not available. Thus the energies of the lowest vacant orbitals with π or σ symmetry of models **3**, **7**, **8**, **9**, and **10** are given at the 3-21G* level, while those of the other models have been recalculated with the two more expanded basis sets. In order to discuss results obtained at a uniform computational level, we have also calculated with the latter procedure dichlorodifluoroethylenes **7a** and **8a** as models for the nucleophilic substitution at dibromodifluoroethylenes[17] and vinylchloronium ions **9a** and **10a** as models for the reaction at vinyliodonium salts.[18,20]

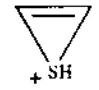
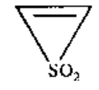
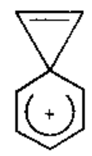
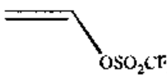
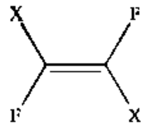
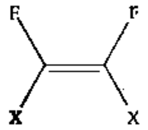
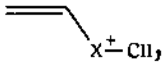
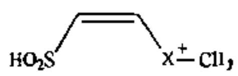
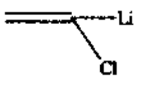
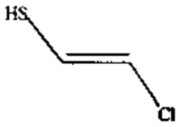
The results are collected in Table 1. The π or σ marks refer to the local symmetry at the vinyl carbons and have been associated to the proper vacant orbital by examination of the orbital surfaces displayed on the computer screen. It may be noticed that in some instances the ordering of the vacant orbitals depends on the basis set. We are confident that the ordering is trustworthy when an energy gap >0.01 hartree is reproduced with two different basis sets. We would extend this criterion also to models calculated with only one basis set.

One first point emerges from the inspection of Table 1. In accordance with the general belief, in some substrates the lowest vacant orbital with a definite density at the C−C double bond (generally the LUMO) possesses π symmetry, but in other substrates this orbital has, unexpectedly, σ symmetry. It is tempting to verify whether the orientation of this orbital determines the approaching direction of the nucleophile and the substitution mechanism, i.e., whether substrates with π LUMO give retention or stereoconvergence, and those with σ LUMO undergo inversion. This hypothesis implies that the nucleophile attack is determined more by the two-electron stabilizing interaction than by the four-electron destabilizing one, and that within the former interaction the energy gap control dominates over the orbital overlap control.

The hypothesis is completely fulfilled in the case of entries **1**−**5** of Table 1. In substrates **1**, **3**, and **4** the LG bearing a positive charge (i.e., it eventually detaches as a neutral species) lowers the vacant orbital of σ symmetry more than the orbital of π symmetry, and even below the level of this latter, by an amount >0.01 hartree. Thus these substrates are predicted to

Table 1. Energies (Single Line, 3-21G*//3-21G*; First Line, 6-31G*//3-21G*; Second Line, 6-311G**//3-21G*; hartree) of the Lowest Vacant Orbitals (LUMO and LUMO + 1, Unless Otherwise Indicated) with π and σ Symmetry for a Series of Model Vinyl Electrophiles



		LUMO (symmetry)	LUMO+1 (symmetry)
1		$-0.0991\ (\sigma)$ $-0.1046\ (\sigma)$	$-0.0865\ (\pi)$ $-0.0954\ (\pi)$
2		$0.0953\ (\pi)$ $0.0819\ (\pi)$	$0.1908\ (\sigma)$ $0.1878\ (\sigma)$
3		$-0.1265\ (\sigma)^a$	$-0.0815\ (\pi)^b$
4		$-0.1335\ (\sigma)$ $-0.1395\ (\sigma)$	$-0.0601\ (\pi)$ $-0.0713\ (\pi)$
5		$0.1611\ (\pi)$ $0.1454\ (\pi)$	$0.2078\ (\sigma)$ $0.1824\ (\sigma)^a$
6		$0.1483\ (\pi)$ $0.1328\ (\pi)$	$0.1987\ (\sigma)$ $0.1811\ (\sigma)^c$
7 (X = Br)		$0.1226\ (\sigma)$	$0.1421\ (\pi)$
7a (X = Cl)		$0.1541\ (\pi)$ $0.1411\ (\sigma)$	$0.1592\ (\sigma)$ $0.1445\ (\pi)$
8 (X = Br)		$0.1355\ (\sigma)$	$0.1391\ (\pi)$
8a (X = Cl)		$0.1521\ (\pi)$ $0.1422\ (\pi)$	$0.1698\ (\sigma)$ $0.1504\ (\sigma)$
9 (X = I)		$-0.1181\ (\sigma)$	$-0.0276\ (\pi)^b$
9a (X = Cl)		$-0.0357\ (\sigma)^a$ $-0.0462\ (\pi)^a$	$-0.0339\ (\pi)^b$ $-0.0435\ (\sigma)^b$
10 (X = I)		$-0.0995(\sigma)$	$-0.0853(\pi)$
10a (X = Cl)		$-0.0869(\pi)$ $-0.0964(\pi)$	$-0.0481(\sigma)^b$ $-0.0565(\sigma)$
11		$0.0610\ (\sigma)^a$ $0.0476\ (\sigma)^a$	$0.1512\ (\pi)^e$ $0.1195\ (\pi)^e$
12		$0.1511\ (\pi)$ $0.1371\ (\pi)^a$	$0.1849\ (\sigma)^b$ $0.1971\ (\sigma)^d$

[a] LUMO + 1. [b] LUMO + 2. [c] LUMO + 3. [d] LUMO + 4. [e] LUMO + 5.

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(25) *Spartan 3.0* program running on a IBM RS/6000 workstation; distributed by Wavefunction, Inc., Irvine, CA 92715.

(26) The 3-21G* basis set includes d-functions for second and higher row elements. First row: Binkley, J. S.; Pople, J. A.; Hehre, W. J. *J. Am. Chem. Soc.* **1980**, *102*, 939. Second row: Gordon, M. S.; Binkley, J. S.; Pople, J. A.; Pietro, W. J.; Hehre, W. J. *J. Am. Chem. Soc.* **1982**, *104*, 2797. Pietro, W. J.; Francl, M. M.; Hehre, W. J.; DeFrees, D. J.; Pople, J. A.; Binkley, J. S. *J. Am. Chem. Soc.* **1982**, *104*, 5039. Third and forth row, main group: Dobbs, K. D.; Hehre, W. J. *J. Comput. Chem.* **1986**, *7*, 359.

(27) First row: Hehre, W. J.; Ditchfield, R.; Pople, J. A. *J. Chem. Phys.* **1972**, *56*, 2257. Hariharan, P. C.; Pople, J. A. *Chem. Phys. Letters* **1972**, *16*, 217. Second row: Francl, M. M.; Pietro, W. J.; Hehre, W. J.; Binkley, J. S.; Gordon, M. S.; De Frees, D. J.; Pople, J. A. *J. Chem. Phys.* **1982**, *77*, 3654.

(28) First row: Krishnan, R.; Binkley, J. S.; Seeger, R.; Pople, J. A. *J. Chem. Phys.* **1980**, *72*, 650. Second row: McLean, A. D.; Chandler, G. S. *J. Chem. Phys.* **1980**, *72*, 5639.

undergo nucleophilic substitution with inversion, what is actually observed. Substrates **2** and **5**, with a LUMO with π symmetry, will favor the orthogonal attack and are reported to actually react by the Ad$_N$-E mechanism.[15,19]

The comparison of entries **5** and **6** shows that the nucleofugality of a neutral LG has a negligible effect on the relative energies of the first vacant orbitals with σ or π symmetry. The triflate moiety is a particularly good LG,[29] but not so much as good at selective orbital lowering. Thus the predominant inversion observed in the solvolysis of these substrates is better explained by the suggested[16c] heterolytic process and the in-plane attack of the nucleophile to the resulting ion pair. The orbital energies in entry **6** suggest that the attack on carbon of a strong nucleophile in a nonpolar solvent would be orthogonal; this reaction has not been experimentally tested yet.

The synergic effect of many electron-withdrawing neutral groups, as in perhaloethylenes **7**, **7a**, **8**, and **8a** is more determining: the orbital with local σ symmetry is lowered near or even below the level of the π orbital. The orbital energies of the 1,2-dibromo-1,2-difluoroethylenes **7** and **8** have been estimated at the unsophisticated 3-21G* level; nevertheless the LUMO σ symmetries offer a rational for the observed inversion of configuration. The energy gap with π LUMO + 1 orbital meets the trust criterion in the case of the trans isomer **7**; it is less satisfactory for the cis isomer **8**. The 1,2-dichloro-1,2-difluoro substrates **7a** and **8a** are decidedly poor models for the behavior of actual dibromoethylenes.

The σ symmetry at the α-carbon atom of the LUMO of vinyliodonium ion **9** correctly predicts the inversion of configuration observed with the actual salt.[18] Similarly, the β-sulfonylvinyl iodonium **10** maintains a LUMO with σ symmetry, which however contrasts the experimental finding of retention of configuration.[20] The symmetries and energies of the relevant vacant orbitals of vinylchloronium **9a** and **10a**, although obtained with better basis sets, do not clarify the problem. The energy gap between π and σ orbitals in **9a** is not decisive, and the correct prediction given by **10a** may be questioned by the inadequacy of the model.

On the other hand, the alternative ligand-coupling mechanism[18,22] may be supported by the models **9**, **9a**, **10**, and **10a**, which display a LUMO with relevant density at the positive Cl or I atom. The complexes with the nucleophile bound at the halogen atom may then evolve into the substitution product with inverted (mechanism *a* in Figure 3) or retained configuration (mechanism *b*).

The 3-21G* optimized structure of 1-chloro-1-lithioethene **11** gives a distorted molecule, with an almost linear C−C−Li arrangement, in accordance with the crystal structure of a 1-bromo-1-lithio substrate[30] (which is however solvated at Li by other donor molecules). The LUMO of **11** is associated with the Li atom; the lowest vacant orbital at the electrophilic carbon is the LUMO + 1, with σ symmetry. Thus the nucleophile is predicted to attack in the molecular plane with inversion, as observed.[21] The σ symmetry of LUMO + 1 is to be associated with the quasi vinyl cation nature of **11**. Also in this instance, the LUMO of **11** displays some density at the electropositive Li atom, which may account for the ligand-coupling mechanism which has been indeed proposed (Figure 3).[21b,23]

The structure **12** models an intramolecular substitution with the nucleophile constrained in the molecular plane. The symmetry allowed interaction is with the σ LUMO + 2, while an external nonconstrained nucleophile would interact with the lower π LUMO. This may imply a degree of anchimeric assistance in vinyl substitution lower than that in aliphatic substitutions. However, experimental findings have revealed that the anchimeric assistances provided by the β-thio group are similar for the two substitutions.[24,31]

Conclusions

The nucleophilic substitutions at vinyl carbon occurring with exclusive configurational inversion are very rare, and only for some of them the S$_N$2-Vin mechanism can be unambigously proposed. Because of the limited number of examples, it is not easy to recognize the factors which would favor this or the alternative Ad$_N$-E mechanism. At least for unambigous situations, our analysis shows that the mechanistic preference is determined by the symmetry at the α-carbon of the lowest involved vacant orbital.

Until recently, the S$_N$2-Vin mechanism has been almost unanimously rejected on the basis of empirical and theoretical considerations. The concertedness of this process has been demonstrated only recently by the internal nucleophilic displacement which converts di-*tert*-butylthiirenium ions into thietium ions.[14] This mechanism receives now a theoretical support, by the demonstration that the S$_N$2-Vin transition state for a model reaction is energetically accessible,[7] and by this work, which presents a rationalization in terms of frontier orbital interactions.

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(29) Modena, G.; Tonellato, U. *Adv. Phys. Org. Chem.* **1971**, *9*, 246.

(30) Boche, G.; Narsch, M.; Mueller, A.; Horms, K. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1032.

(31) Goering, H. L.; Howe, K. L. *J. Am. Chem. Soc.* **1957**, *79*, 6542. McManus, S. P.; Sedaghat-Herati, M. R.; Harris, J. M. *Tetrahedron Lett.* **1987**, *28*, 5299.