Modeling Chemical Reactivity. 4. Regiochemistry and Stereochemistry of Electrophilic Additions to Allylic Double Bonds

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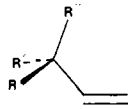
Abstract: The regio- and stereochemistry of electrophilic addition to chiral double bonds incorporated into acyclic molecules is ultimately dictated by no fewer than three factors: (1) the relative equilibrium abundance of available conformational isomers, (2) the relative reactivities of these conformational minima, and (3) the regio- and stereoselectivities of the individual forms. This study examines these three factors theoretically for a selection of allylic alcohols, fluorides, and silanes. Conformational profiles, determined with standard nonempirical molecular orbital methods, suggest that two or more low-energy conformers exist for all molecules considered in this study. Comparisons with available experimental data support the theoretical assignments of ground-state conformations. Assignment of regio- and stereochemistry of electrophilic addition is based on direct evaluation of the relative affinities of diastereotopic olefin faces toward a "test" electrophile. While such an approach appears to provide a sensitive account of the preferred stereochemistry of electrophilic addition to allylic alcohols and silanes, an alternative model, which assumes that electrophilic activity will increase with increasing energy of the substrate HOMO, and furthermore, that addition of an electrophile will occur preferentially onto the face of an olefin on which the HOMO (the π bond) is more heavily localized, does not appear to provide a sensitive or easily interpretable account of reaction stereochemistry in these systems. A detailed analysis of the factors which influence regio- and stereoselectivity of electrophilic additions to chiral allylic double bonds is provided.

Electrophilic additions to carbon–carbon double bonds are among the most utilized reactions in modern synthetic chemistry. The control of regio- and stereochemistry, particularly in conformationally flexible acyclic systems, is of fundamental concern to rational synthesis design. The stereoselectivity of additions to allylic double bonds has attracted considerable interest in the recent literature, and numerous reports of diastereofacial selectivity have appeared.[1]

Stereochemical preferences noted for electrophilic additions generally are not well understood, at least at the level where this understanding can be applied in a predictive manner. For the most part, the explanations that have been advanced to account for observed product stereochemistry in electrophilic additions to allylic double bonds and similar reactions have been based on steric considerations,[2] complexation,[3] or orbital distortion arguments.[4,5]

At least three factors need to be addressed before one can understand (and ultimately predict) the regio- and stereochemistry of electrophilic additions to chiral acyclic olefins. These are the following: (1) the relative abundance of available conformers, (2) the relative electrophilic reactivities of these conformers, and (3) the detailed regio- and stereochemical preferences of any conformational forms which, because of their high equilibrium abundance and/or high reactivity, might contribute significantly to the overall product distribution. For reactions (or calculations) involving conformationally rigid systems, the overall problem is simpler, since product regio- and stereochemistry would depend only on the last of these factors.

In the treatment of acyclic systems, one needs first to establish the relative thermochemical stabilities of all available conformers, which leads to an estimate of relative equilibrium abundances. *Only species which are minima on the conformational energy profile can react*, since only they will be present at equilibrium. For the allylic compounds dealt with here, it has been generally found that only conformers in which a single bond (approximately) eclipses the olefin, i.e.,



are energy minima,[6] although it is not necessary that all such forms correspond to stable structures. Thus, for R, R′, and R″ different, a maximum of three conformations need to be considered. Further complicating the issue is the possibility of conformational minima involving rotation about one or more of the CR bonds. For example, the total conformational profile of 3-buten-2-ol, one of the molecules of interest in the present study, may incorporate as many as nine potential minima, i.e., three conformations involving rotation about the CO bond for each of the three eclipsed arrangements.[7] It should, of course, be noted that the conformational preferences of the transition states for electrophilic addition may be different from those of the reagents. As will be apparent shortly, these need not be considered in the context of the present theoretical treatment.

It is not reasonable to assume that electrophilic addition will occur only onto the lowest energy conformer, or even that it will occur in proportion to the relative equilibrium abundances of the

(1) See, for example: (a) Morrison, J. D.; Mosher, H. S. *Asymmetric Organic Reactions*; Prentice Hall: New York, 1971. (b) Bartlett, P. A. *Tetrahedron* **1980**, *36*, 2. (c) *Aymmetric Synthesis*; Morrison, J. D., Ed.; Academic: New York; Vol. 2, 1983; Vol. 3, 1984. (d) Symposia-in-print, *Control of Acyclic Stereochemistry*: Mukaiyama, T., Ed. *Tetrahedron* **1984**, *40*, 2197–2343.

(2) See, for example: (a) Cram, D. J.; Abd Elhafez, F. A. *J. Am. Chem. Soc.* **1952**, *74*, 5828. (b) Karabatsos, G. T. *Ibid.* **1967**, *89*, 1367. (c) Cherest, M.; Felkin, H.; Prudent, N. *Tetrahedron Lett.* **1968**, 2119, 2205. (d) Corey, E. J.; Snider, B. B. *J. Am. Chem. Soc.* **1972**, *94*, 2549. (e) Pasto, D. J.; Gontraz, J. A. *Ibid.* **1977**, *93*, 6909. (f) Anh, N. T.; Eisenstein, O. *Nouv. J. Chim.* **1977**, *1*, 61. (g) Schmid, G.; Fukuyama, T.; Akasaka, K.; Kishi, Y. *J. Am. Chem. Soc.* **1979**, *101*, 259. (h) Paddon-Row, M. N.; Rondan, N. G.; Houk, K. N. *Ibid.* **1982**, *104*, 7162.

(3) Examples for allylic alcohols and ethers: (a) Dauben, W. G.; Berezin, G. H. *J. Am. Chem. Soc.* **1963**, *85*, 468. (b) Chan, J. H. H.; Rickborn, B. *Ibid.* **1968**, *90*, 6406. (c) Srivastava, R. M.; Sweet, F.; Murray, T. P.; Brown, R. K. *J. Org. Chem.* **1971**, *36*, 3633. (d) Barili, P. L.; Bellucci, G.; Berti, G.; Golfarini, M.; Marioni, F.; Scartoni, V. *Gazz. Chim. Ital.* **1974**, *104*, 107. (e) Matsuki, Y.; Kodama, M.; Itô, S. *Tetrahedron Lett.* **1979**, 2901. (f) Williams, D. R.; White, F. H. *Ibid.* **1985**, 2529.

(4) (a) Inagaki, S.; Fukui, K. *Chem. Lett.* **1974**, 509. (b) Fukui, K. *Theory of Orientation and Stereoselection*; Springer-Verlag: New York, 1975.

(5) (a) Burgess, E. M.; Liotta, C. L. *J. Org. Chem.* **1981**, *46*, 1703 and references therein to earlier work. See also: (b) Anh, N. T. *J. Chem. Soc., Chem. Commun.* **1968**, 1089.

(6) For a review, see: (a) Karabatsos, G. J.; Fenoglio, D. J. *Top. Stereochem.* **1970**, *5*, 167. For a simple explanation, see: (b) Hehre, W. J.; Salem, L. *J. Chem. Soc., Chem. Commun.* **1973**, 754.

(7) A preliminary account of theoretical work on the conformational energy profile of 3-buten-2-ol has appeared: Kahn, S. D.; Hehre, W. J. *Tetrahedron Lett.* **1985**, *26*, 3647.

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stable conformers. Different conformers likely will react at different rates, and a relatively high energy (low abundance) conformer may be largely responsible for the ultimate distribution of products.[8] It is interesting to speculate to what extent conformer stability will parallel conformer reactivity. While it is not unreasonable to expect the high-energy conformers will be more reactive toward electrophiles than low-energy forms, i.e., factors which increase the energy of the incorporated π bond, making it more accessible, should also raise the total molecular energy, the dependence of the energies of other orbitals on conformation is less clear. This issue will be examined.

It remains to establish the regio- and stereoselectivity of reactions of any conformers which, by virtue of high abundance or high reactivity (or both), might contribute significantly. While rationalization of regiochemistry is generally straightforward, stereochemical interpretations are likely to be ambiguous unless restricted to rigid model compounds. The problem again is one of sorting out the contributions of any of the conformers which might be present at equilibrium.

Two different theoretical approaches to the assignment of relative reactivity and reaction regio- and stereoselectivity will be examined in detail in this paper. The more familiar of these, based on FMO theory, has already been extensively applied to the description of reaction regiochemistry, e.g., in Diels–Alder cycloadditions.[9] Its application to reaction stereochemistry is broadly similar; stereoselectivity is related to the degree of asymmetry of the olefin π system, i.e., electrophilic attack will occur on the diastereotopic face on which the π bond is the more heavily concentrated. This follows directly the hypothesis of orbital distortion.[4,5]

The apporoach to electrophilic reactivity and selectivity developed in this paper, while less familiar, is more direct. It assesses stereoselectivity by considering the relative affinities of the diastereotopic olefin faces toward a test electrophile (a proton). The approach allows assessment of relative reactivity and diastereofacial selectivity, as well as provides information about the regioselectivity of electrophilic addition. The application of these techniques, which we collectively term *reactivity models*, to the assignment of the regio- and stereochemistry of electrophilic additions, extends our earlier efforts toward the development of models and modeling strategies for chemical reactivity.[9j,10]

Reactivity models provide an overall view of mechanism, allowing direct comparison of alternative mechanistic routes. Their success depends on mechanistic preferences, i.e., regio- and stereoselectivity, being determined at an early stage in the reaction, before significant electronic and geometrical reorganization has taken place. The approach used here is qualitatively similar to attempts to assign mechanism based on calculation of the energy of the reagent/substrate "supermolecule" at selected geometries.[11] Both differ fundamentally from efforts to calculate directly the properties of reaction transition structures.[2f,12] While the latter offers the advantage that no assumptions about mechanism need to be made, practical considerations presently limit application to very simple systems.

We examine two reactions for which regio- and stereochemical preferences have been determined experimentally. These involve electrophilic additions to chiral allylic silanes and to chiral allylic alcohols and ethers. The first of these, which illustrates electrophilic addition followed by elimination, and which would normally be thought of as representative of an "early transition state", is mechanistically simpler; the overall reaction regio- and stereochemistry is determined upon electrophilic addition. Product regio- and stereochemistry resulting from reactions of allylic alcohols and ethers may either be determined upon initial electrophilic addition or subsequently upon further reaction with an internal or external nucleophile. For the present, we assume the former.

Our assessment of the performance of the two theoretical models to properly account for the observed regio- and stereochemistry of electrophilic additions to allylic double bonds will be carried out in two stages. Comparisons will initially be restricted to rigid systems. This allows separation of inherent regio- and stereochemical preferences, from effects dealing with relative conformer stabilities and reactivities (vide supra). The performance of the theoretical models here (where interpretation of the experimental data is unambiguous) will calibrate their predictive utility for acyclic systems, where conformer stability and reactivity need to be taken into account, and because of this where the available experimental data may be subject to varied interpretation.

A final goal of this paper will be to rationalize both the noted conformational preferences in allylic systems and the regio- and stereochemistry of electrophilic attack on these systems. More precisely, we outline those factors which determine the regio- and stereochemical ccurse of electrophilic additions to chiral allylic double bonds. Our intent, of course, is to provide a basis for extension to systems where experimental (or theoretical) investigations have not as yet been carried out.

Computational Methods

All calculations have been carried out at the single-determinant (Hartree–Fock) level with either the 3-21G split-valence basis set[13] (3-21G(*)[14] for molecules incorporating second-row elements) of the 6-31G* polarization basis set.[15] Optimum geometries have been obtained at the 3-21G (3-21G(*)) level subject only to the constraint that the incorporated olefin maintain a planar skeleton.[16] These are provided in an appendix to this paper. All ab initio calculations have been performed with the GAUSSIAN 85 program system[17] as implemented on a Harris H800 digital computer.

Electrostatic and polarization potentials have been obtained according to methods described earlier[10a] and have been superimposed onto electron-densty surfaces corresponding to $\psi^2 = 0.002$ electron/bohr^3.[18] Further details are provided in an appendix to this paper.

Results and Discussion

Relative Conformational Energies of Molecules Incorporating Allylic Double Bonds. As pointed out in the introduction, the relative equilibrium abundance of available conformers is the first

(8) (a) Curtin, D. Y. *Rec. Chem. Prog.* **1954**, *15*, 111. (b) Seeman, J. I. *Chem. Rev.* **1983**, *83*, 83.

(9) For reviews, see: (a) Herndon, W. C. *Chem. Rev.* **1972**, *75*, 157. (b) Epiotis, N. D. *J. Am. Chem. Soc.* **1973**, *95*, 5621. (c) Houk, K. N. *Acc. Chem. Res.* **1975**, *8*, 361 (1975). (d) Fleming, I. *Fontier Orbitals and Organic Chemical Reactions*; Wiley: New York, 1975. (e) Eisenstein, O.; Lefour, J. M.; Anh, N. T.; Hudson, R. F. *Tetrahedron* **1977**, *33*, 523. (f) Matatoshi, K. *Can. J. Chem.* **1979**, *57*, 2564. (g) Sustmann, R. *Angew. Chem., Int. Ed. Engl.* **1970**, *19*, 779. (h) Gleiter, R.; Bohm, M. C. *Pure Appl. Chem.* **1983**, *55*, 237. (i) Alston, P. V.; Gordon, M. D.; Ottenbright, R. M.; Cohen, T. *J. Org. Chem.* **1983**, *43*, 5051 and earlier papers in this series. (j) Kahn, S. D.; Pau, C. F.; Overman, L. E.; Hehre, W. J. *J. Am. Chem. Soc.* **1986**, *108*, 7381.

(10) (a) Pau, C. F.; Hehre, W. J. *J. Comput. Chem.*, submitted. (b) Hehre, W. J.; Pau, C. F.; Hout, R. F., Jr.; Francl, M. M. *Molecular Modeling. Computer-Aided Descriptions of Molecular Structure and Reactivity*; Wiley: New York, 1987.

(11) For example, see: (a) Anh, N. T. *Top. Current Chem.* **1980**, *88*, 145. (b) Caramella, P.; Rondan, N. G.; Paddon-Row, M. N.; Houk, K. N. *J. Am. Chem. Soc.* **1981**, *103*, 2438. See also ref 3e.

(12) For example, see (a) Houk, K. N. *Pure Appl. Chem.* **1983**, *55*, 277. (b) Houk, K. N.; Rondan, N. G.; Wu, Y.; Metz, J. T.; Paddon-Row, M. N. *Tetrahedron* **1984**, *40*, 2257. (c) Houk, K. N.; Moses, S. R.; Wu, Y.; Rondan, N. G.; Jäger, V.; Schohe, R.; Fronczek, F. R. *J. Am. Chem. Soc.* **1984**, *106*, 3880.

(13) Binkley, J. S.; Pople, J. A.; Hehre, W. J. *J. Am. Chem. Soc.* **1980**, *102*, 939.

(14) 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.

(15) First-row elements: (a) Hariharan, P. C.; Pople, J. A. *Chem. Phys. Lett.* **1972**, *66*, 217. Second-row elements: (b) Francl, M. M.; Pietro, W. J.; Hehre, W. J.; Binkley, J. S.; Gordon, M. S.; DeFrees, D. J.; Pople, J. A. *J. Chem. Phys.* **1982**, *77*, 3654.

(16) It has previously been noted that asymmetric substitution leads only to slight pyramidalization of the olefin. See: Houk, K. N. *Methods Stereochem. Anal.* **1983**, *3*, 1.

(17) Hout, R. F., Jr.; Francl, M. M.; Kahn, S. D.; Dobbs, K. D.; Blurock, E. S.; Pietro, W. J.; McGrath, M. P.; Steckler, R.; Hehre, W. J. *Quantum Chemistry Program Exchange*; Indiana University: Bloomington, IN, to be submitted.

(18) See: Francl, M. M.; Hout, R. F., Jr.; Hehre, W. J. *J. Am. Chem. Soc.* **1984**, *106*, 563.

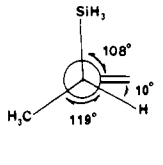
Table I. Conformational Energies and Relative Abundances of Molecules Incorporating Allylic Double Bonds

molecule	description of conformation	relative energy (kcal mol^{-1})[a] 3-21G//3-21G	6-31G*//3-21G
2-silylbut-3-ene			
1a	CH eclipsed	0.0 (73)	0.0 (69)
1b	CC eclipsed	0.6 (26)	0.5 (30)
1c	CSi eclisped	2.3 (1)	2.4 (1)
3-buten-2-ol			
2a	CH eclipsed, OH *trans* to CH_3	1.0 (9)	0.0 (57)
2b	CO eclipsed, OH *trans* to CH_3	0.0 (57)	0.6 (21)
2c	CO eclipsed, OH *trans* to H	0.2 (35)	0.8 (15)
2d	CO eclipsed, OH *trans* to vinyl	1.3 (5)	1.6 (4)
2e	CH eclipsed, OH *trans* to H	3.0 (<1)	1.9 (2)
2f	CH eclipsed, OH *trans* to vinyl	2.6 (<1)	2.7 (1)
2g	CC eclipsed, OH *trans* to H	0.0 (94)[b]	0.0 (86)[b]
2h	CC eclipsed, OH *trans* to vinyl	2.0 (3)[b]	1.4 (8)[b]
2i	CC eclipsed, OH *trans* to CH_3	2.0 (3)[b]	1.6 (6)[b]
2-fluorobut-3-ene			
3a	CF eclipsed	0.0 (97)	0.0 (70)
3b	CH eclipsed	2.1 (3)	0.5 (30)
(*E*)-2-fluoropent-3-ene			
4a	CF eclipsed	0.0 (98)	0.0 (62)
4b	CH eclipsed	2.4 (2)	0.3 (38)
(*E*)-1-cyano-3-fluorobut-1-ene			
5a	CF eclipsed	0.0 (>99)	0.0 (95)
5b	CH eclipsed	3.7 (<1)	1.8 (5)

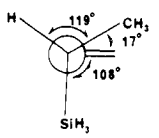
[a] kcal mol^{-1}. 3-21G$^{(*)}$//3-21G$^{(*)}$ and 6-31G*//3-21G$^{(*)}$ for 2-silylbut-3-ene. Relative abundance calculated as $\exp(-E/RT)$ for T = 298 K and normalized to 100% given in parentheses. [b] Not minimum energy forms on the 3-21G potential surface. Energies quoted correspond to geometries in which the CC linkage is constrained to be in the plane of the double bond. Energy of **2g** relative to **2b** at 3-21G//3-21G, 2.5 kcal mol^{-1}; of **2g** relative to **2a** at 6-31G*//3-21G, 1.4 kcal mol^{-1}.

of three factors which needs to be considered in any treatment of the stereochemistry of electrophilic addition to conformationally flexible systems. Relative conformational energies for the molecules dealt with in the present study are provided in Table I. Relative abundances, calculated from $\exp(-\Delta E/RT)$, where ΔE is the energy of a particular conformer relative to the ground-state form and T is taken as 298 K, are also tabulated. These have been normalized so that the total abundance of all conformers is 100%.

The conformational profile calculated at the 3-21G$^{(*)}$ level for 2-silylbut-3-ene (**1**) exhibits three minima. The calculated geometries of the two most stable forms, **1a** and **1b**, deviate significantly from eclipsed arrangements. This is contrary to the usual tendency of single and double bonds to eclipse one another,[6] e.g., in propene. In both structures, the CSi linkage is nearly perpendicular to the CC double bond. The C=CCSi dihedral angle in the ground-state conformer **1a** is calculated to be 108°, and the CH linkage is predicted to be 10° out of the plane of the double bond. A second form, **1b**, 0.6 kcal mol^{-1} above the ground-state conformer according to 3-21G$^{(*)}$ calculations,[19] places the terminal CC linkage 17° out of the double bond plane; here the C=CCSi dihedral angle is 108°. There is some experimental



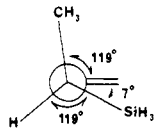
1a



1b

support for these unusual structures. The calculated geometries for these two low-energy conformers are consistent with a microwave structure for the ground state of allylsilane, which shows a C=CCSi dihedral angle of 106.8°;[20] an angle of 103.5° is obtained by the 3-21G$^{(*)}$ calculations for this compound.

The third conformational minimum for 2-silylbut-3-ene (**1c**) is 2.3 kcal mol^{-1} above the ground-state structure at the 3-21G$^{(*)}$ level and places the CSi linkages nearly in the plane of the double bond.



1c

Higher level (6-31G*//3-21G$^{(*)}$) calculations produce the same ordering of conformer energies and nearly identical energy differences. Structure **1b** is predicted to be 0.5 kcal mol^{-1} above **1a**, and **1c** is 2.4 kcal mol^{-1} higher in energy.

It appears, therefore, that two low-energy conformers of 2-silylbut-3-ene will be present in significant abundance at equilibrium. Obviously, successful modeling of the stereochemistry of electrophilic addition will require explicit consideration of at least these two forms. The large energy gap separating conformer **1c** from the other two forms indicates that this structure will not be present in high abundance at equilbrium.

While there appears to be no experimental data relating to the relative conformational energies of 2-silylbut-3-ene, there is information on allylsilane itself. Microwave,[20a,b] electron diffraction,[20c] and infrared and Raman[20d] studies have been interpreted in terms of a single conformer in which the CSi linkage is (approximately) perpendicular to the plane of the double bond. This conformational preference is also consistent with the observation that the first ionization potential in trimethylallylsilane (corresponding to loss of an electron from the π orbital) is 0.8 eV lower in energy than that in trimethylvinylsilane. This difference may be explained in terms of interaction of π_{CC} and σ_{CSi} (leading to an increase in the energy of the former) which is possible only in conformers of the allylsilane in which the CSi linkage is perpendicular to the plane of the double bond.[21] The failure to observe a second form (with the CSi linkage and C=C coplanar) is consistent with the results of both 3-21G$^{(*)}$//3-21G$^{(*)}$ and 6-31G*//6-21G$^{(*)}$ calculations, which show significant energy separations of 2.2 and 2.1 kcal mol^{-1}, respectively.

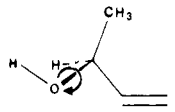
The situation for 3-buten-2-ol (**2**) in much more complex, because internal rotation about both the CO and CC single bonds is possible.[7] This complication gives rise to the possibility of nine different stable conformers, three for each of the CO, CC, and CH linkages eclipsing the carbon–carbon double bond. In fact, only six of these appear to exist on the 3-21G energy surface;

(19) The experimental energy difference between the ground-state CH eclipsed and CC eclipsed conformers of 1-butene is approximately 0.2 kcal mol^{-1}. (a) Bothner-By, A. A.; Naar-Colin, C.; Gunther, H. *J. Am. Chem. Soc.* **1962**, *84*, 2748. (b) Bothner-By, A. A.; Gunther, H. *Discuss. Faraday Soc.* **1962**, *34*, 127. (c) Kondo, S.; Hirota, E.; Morino, Y. *J. Mol. Spectrosc.* **1968**, *28*, 471.

(20) (a) Imachi, M.; Nakagawa, J.; Hayashi, M. *J. Mol. Struct.* **1983**, *102*, 403. An earlier report from the same group suggested a dihedral angle of 103.5° [(b) Hayashi, M.; Imachi, M.; Saito, M. *Chem. Lett.* **1977**, 221], closer to the value of 102 ± 1° obtained by electron diffraction [(c) Beagley, B.; Foord, A.; Moutran, R; Roszondai, R. *J. Mol. Struct.* **1977**, 117]. The results of an infrared and Raman study show a C=CCSi dihedral angle of between 90 and 120°: (d) Ohno, K.; Toga, K.; Murata, H. *Bull. Chem. Soc. Jpn.* **1977**, *50*, 2870.

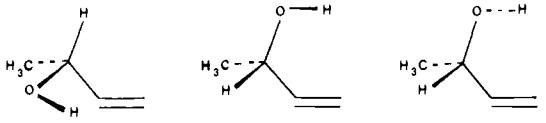
(21) This is commonly known as the "β-silyl" effect. For experimental support, see: Wiedner, U.; Schweig, A. *Angew. Chem., Int. Ed. Engl.* **1972**, *11*, 146.

missing are forms in which the bond to the terminal methyl group eclipses the olefinic linkage.



Because of their possible role as models for cyclic allylic alcohols, calculations on conformers in which the terminal methyl group has been constrained to eclipse the double bond have also been performed.[22]

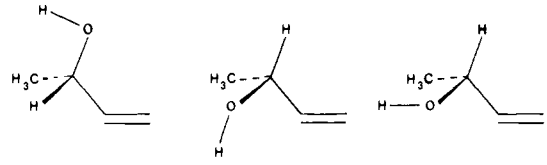
The most stable conformer of 3-buten-2-ol at the 6-31G*//3-21G level is one in which the CH linkage eclipses the CC double bond, **2a**. Slightly higher in energy are two conformers, **2b** and **2c**, with the CO bond eclipsing the olefin; these are less stable by 0.6 and 0.8 kcal mol^{-1}, respectively.



2a **2b** **2c**

A microwave spectrum of 3-buten-2-ol has been interpreted in terms of **2a** as the ground-state conformer, with **2b** being 0.52 kcal mol^{-1} higher in energy.[23] The present (6-31G*//3-21G) results are in complete accord. Several prominent unassigned transitions in the spectrum have led the experimental investigators to leave open the possibility of other stable conformers.[23] Structure **2c** seems an obvious choice.

The calculations indicate that the hydroxlyic hydrogen in each of the three lowest energy conformers of 3-buten-2-ol is positioned above the CC π bond. This is also the case for the two conformers which have been detected in the microwave study, and it has been interpreted as indicative of intramolecular hydrogen bonding in these forms.[23] Stabilization from hydrogen bonding may be rationalized in terms of qualitative molecular orbital arguments. Two-electron interaction of σ^*_{OH} with π_{CC} (Figure 1, left) lowers the energy of the allylic π bond, presumably making it less ammenable to electrophilic attack. The relatively high energies of the remaining conformers (**2d–f**) are presumably due to unfavorable overlap of the oxygen lone pair(s) with the CC double bond. Molecular orbital arguments show this as a four-electron



2d **2e** **2f**

interaction (Figure 1, right), the net result of which is a raising of the energy of the allylic π bond. An increase in reactivity toward electrophiles should result. Were hydrogen bonding important, the conformational profiles and reactivity patterns of allylic ethers would be expected to differ somewhat from that for 3-buten-2-ol, i.e., conformers analogous to **2a–c** should be disfavored due to steric crowding. In fact, calculations suggest that the profiles for 3-buten-2-ol and for 2-methoxy-3-butene are qualitatively very similar[24] and, therefore, suggest the relative unimportance of intramolecular hydrogen bonding in the alcohol.

The apparent preference for eclipsing of the CH linkage in 3-buten-2-ol and related allylic alcohols and ethers (over eclipsing of the CO bond) is more difficult to rationalize, although several

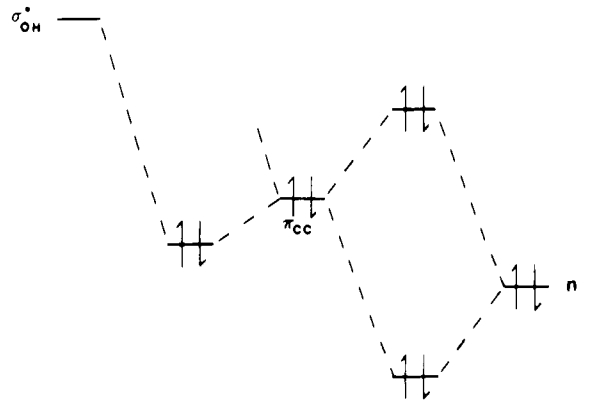


Figure 1. Interaction of valence orbitals on allylic alcohols. Stabilization of π_{CC} by two-electron interaction with σ^*_{OH} (left-hand side) and destabilization by four-electron interaction with an oxygen lone pair (right-hand side).

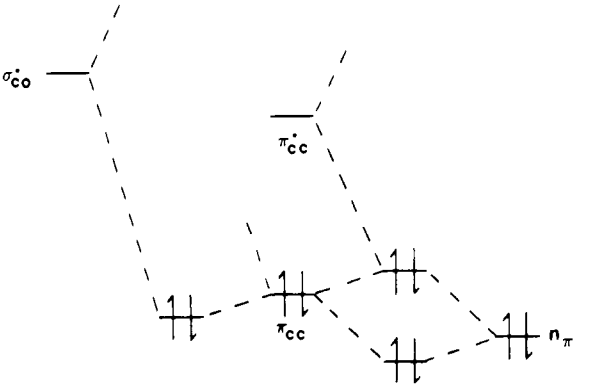


Figure 2. Interaction of valence orbitals on allylic alcohols. Stabilization of π_{CC} by two-electron interaction with σ^*_{CO}, possible in conformers where the C—O and C=C bonds are not coplanar (left-hand side); stabilization by interaction of both π_{CC} and π^*_{CC} with lone pairs on oxygen, maximum in conformers where C—O and C=C are coplanar (right-hand side).

explanations have been advanced in the literature.[12c,23,25,26] In terms of simple orbital arguments, the preference for **2a** over **2b** and **2c** may be seen to follow from the energetically favorable mixing of σ^*_{CO} and π_{CC}, which is possible only with the CO linkage *skew* to the double bond.[27] As shown on the left-hand side of Figure 2, this interaction should lower E_π, and thereby deactivate the olefin toward electrophilic attack. On the other hand, coplanarity of the C=C and CO bonds allows effective mixing of π_{CC} and π^*_{CC} and the π type lone pair on oxygen, resulting in a stabilized "homoallylic anion" (Figure 2, right). Concomitant

(22) These should model cyclopentenols where $\omega_{C=CCC} \simeq 5°$ quite well. Work in progress will provide more accurate models for cyclohexenols where $\omega_{C=CCC} \simeq 15°$.

(23) Smith, Z.; Carballo, N.; Wilson, E. B.; Marstokk, K.-M.; Møllendal, J. *J. Am. Chem. Soc.* **1985**, *107*, 1951.

(24) Part 6: Kahn, S. D.; Hehre, W. J. *J. Am. Chem. Soc.*, following in this issue.

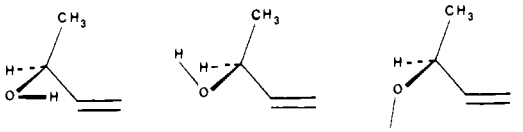
(25) (a) Bothner-By, A. A.; Castellano, S.; Ebersole, S. J.; Günther, H. *J. Am. Chem. Soc.* **1966**, *88*, 2466. (b) Tronchet, J. M. H.; Xuan, T. N. *Carbohydr. Res.* **1978**, *67*, 469. (c) Lessard, J.; Saunders, J. K.; Viet, M. T. P. *Tetrahedron Lett.* **1982**, *23*, 2059. (d) Gonnella, N. C.; Nakanishi, K.; Martin, V. S.; Sharpless, K. B. *J. Am. Chem. Soc.* **1982**, *104*, 3775. See also: (e) Stork, G.; Kahn, M. *Tetrahedron Lett.* **1983**, *24*, 3951.

(26) (a) Giese, B.; Bartman, D. *Tetrahedron Lett.* **1985**, *26*, 1197. (b) Chamberlin, A. R.; Mulholland, R. L., Jr. *Tetrahedron* **1984**, *40*, 2297. (c) Cha, J. K.; Christ, W. J.; Kishi, Y. *Ibid.* **1984**, *40*, 2247. (d) Chamberlin, A. R.; Dezube, M.; Dussault, P.; McMills, M. C. *J. Am. Chem. Soc.* **1983**, *105*, 5819. (e) Still, W. C.; Barrish, J. C. *Ibid.* **1983**, *105*, 2487. (f) Rossiter, B. E.; Verhoeven, T. R.; Sharpless, K. B. *Tetrahedron Lett.* **1979**, 4733. (g) Raiter, M.; Castaing, M.; Godet, J.; Peryre, M. *J. Chem. Res. (S)* **1978**, 179. (h) Bellucci, G.; Bianchini, R.; Ingrosso, G.; Mastrorilli, E. *Gazz. Chim. Ital.* **1978**, *108*, 643. (i) Chantemps, P.; Pierre, J.-L. *Tetrahedron* **1976**, *32*, 549. (j) Tanaka, S.; Yamamoto, H.; Nozaki, H.; Sharpless, K. B.; Michaelson, R. C.; Cutting, J. D. *J. Am. Chem. Soc.* **1974**, *96*, 5254. (k) Chamberlain, P.; Whitham, G. H. *J. Chem. Soc. (B)* **1970**, 1382.

(27) (a) Similar reasoning has been used to rationalize variances in π-ionization energies in allyl alcohol and several cyclic allylic alcohols. See: Brown, R. S.; Marcinko, R. W. *J. Am. Chem. Soc.* **1978**, *100*, 5721. (b) For a discussion of the conformational preferences, and their causes, in allyl alchol, see: Aspiala, A.; Lotta, T.; Murto, J.; Räsänen, M. *J. Chem. Phys.* **1983**, *79*, 4183. (c) Kao, J.; Katz, T. *J. Mol. Struct.* **1984**, *108*, 229.

with the lowering of E_n will be the raising of E_π; this suggests olefin activation. It follows that electron-rich allylic alcohols (ethers) will adopt conformations with the CO bond approximately perpendicular to the plane of the double bond, thereby facilitating π^*_{CO}–π_{CC} overlap, and that electron-poor olefins will assume conformations with the CO bond in plane, thereby delocalizing the oxygen lone pair into the double bond. There is supporting experimental evidence that the conformational preferences of allylic alcohols are quite sensitive to substitution on the olefin. In particular, it has been found that electron-withdrawing groups favor conformations in which the CO linkage eclipses the double bond, while electron-releasing substituents preferentially stabilize arrangements in which the CO bond is *gauche* to C=C.[25]

As previously mentioned, conformers of 3-buten-2-ol in which the terminal methyl group eclipses the double bond are not energy minima at the 3-21G level. This contrasts with the conformational profile for 1-butene, where the methyl eclipsed structure is a local minimum.[19] Artificially constrained structures, **2g–i**, have been examined here because of their use as models for cyclic allylic alcohols and ethers.[22] As expected on the basis of previous



2g **2h** **2i**

comparisons, conformer **2g** (in which the hydroxyl hydrogen is *trans* to the allylic CH bond) is the most stable of the three; this allows "hydrogen bonding" with the olefin π orbital, or it alternatively reduces the interaction between the lone pairs on oxygen and the π bond to a minimum. The two remaining conformers, **2h** and **2i**, are higher in energy (1.4 and 1.6 kcal mol^{-1} above **2g** at the 6-31G*//3-21G level). "Hydrogen bonding" is not possible here, and unfavorable interaction between the oxygen lone pairs and the allylic π bond should be at a maximum.

Because of the complexity of the conformational energy surface for 3-buten-2-ol, specifically with regard to the position of the hydroxylic hydrogen, calculations have been performed on the closely related allylic fluoride, 2-fluorobut-3-ene (**3**). The theory has also been applied to (*E*)-2-fluoropent-3-ene (**4**) and (*E*)-1-cyano-3-fluorobut-1-ene (**5**) in order to assess the effect which electron-donor and acceptor substituents, respectively, have on relative conformer energies. All three systems exhibit two minima conformational profiles (analogous to the situation in 3-buten-2-ol for rotation about the CC bond).

According to both (3-21G//3-21G and 6-31G*//3-21G) levels of calculation, the lowest energy form of 2-fluorobut-3-ene (**3a**) has the carbon fluorine linkage (approximately) eclipsing the double bond. Structure **3b**, in which CH eclipses the double bond, is 0.5 kcal mol^{-1} higher in energy at the 6-31G*//3-21G level.

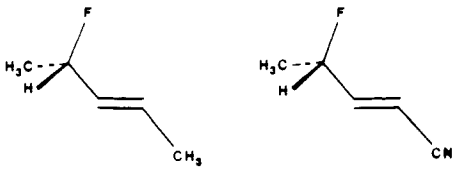
3a **3b**

Although there appear to be no experimental data on 2-fluorobut-3-ene, the closely related molecule, allyl fluoride, has been the subject of extensive experimental work. Both CF and CH eclipsed conformers have been detected by microwave[28] and infrared/Raman[29] spectroscopy, both of which experiments assign the former as the ground-state structure. According to the microwave study,[28] the second form, in which a CH linkage lies approximately in the double bond plane, is only slightly (0.17 kcal mol^{-1}) higher in energy; the more recent infrared/Raman work[29] suggests a somewhat larger difference (0.75 kcal mol^{-1}). The energy separation suggested by the 6-31G*//3-21G calculations (2.2 kcal mol^{-1}) is in reasonable accord with the experimental data.

(28) Hirota, E. *J. Chem. Phys.* **1965**, *42*, 2071.
(29) During, J. R.; Zhen, M.; Little, T. S. *J. Chem. Phys.* **1984**, *81*, 4259.

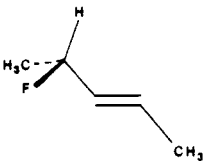
These comparisons suggest that the (6-31G*//3-21G) calculations on 2-fluorobut-3-ene provide a more reasonable description of relative conformational energies and that two low-energy (abundant) forms likely exist. Moreover, the similarities of the conformational profiles of the allyl fluorides and alcohols validates our use of the former to model the latter.

6-31G*//3-21G calculations for (*E*)-2-fluoropent-3-ene (**4**) and (*E*)-1-cyano-3-fluorobut-1-ene (**5**) assign the conformer in which the CF linkage eclipses the double bond as the ground-state form, i.e., structures **4a** and **5a**, respectively. Methyl substitution at



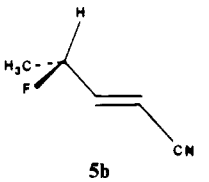
4a **5a**

the β olefin position in 2-fluorobut-3-ene has little effect on the relative conformational energies. The "CH eclipsed" conformer in (*E*)-2-fluoropent-3-ene (**4b**) is predicted to be 0.3 kcal mol^{-1} above the ground state, "CF eclipsed" form, compared to an energy



4b

difference of 0.5 kcal mol^{-1} in the unsubstituted system, **3**. This result is in agreement with the simple orbital arguments advanced in discussion of 3-buten-2-ol, where it was suggested that substitution by methyl (an electron donating group) should raise the energy of the π orbital and, therefore, increase its stabilizing interaction with σ^*_{CO} (σ^*_{CF}). Furthermore, the orbital arguments are also consistent with the greatly increased separation between the ground state (CF eclipsed) and higher energy conformers of (*E*)-1-cyano-3-fluorobut-1-ene (**5b**) (1.8 kcal mol^{-1} relative to 0.5 kcal mol^{-1} in **3**). The cyano substituent is obviously able to stabilize the "homoallylic anion" character of the ground-state form, **5a**.



5b

In summary, it is evident that more than a single comformer of 3-buten-2-ol is energetically accessible. Given the likelihood that the ground-state form is not the most reactive species, i.e., that the π bonds in the low-energy conformers **2b** and **2c** should be more labile toward electrophiles than that in **2a**, and that those in the higher energy forms **2d–f** should be even more reactive, it would appear that any analysis of product stereochemistry based solely on the ground-state species is not likely to be appropriate. On the basis of our model studies with allyl fluorides, it may be concluded that the conformational preferences in allyl alcohols will be sensitive to substitution. In particular, it is to be expected that electron-withdrawing groups will favor conformations with the CO bond eclipsing π_{CC}, whereas electron-releasing groups should enhance the ground-state preference for CH eclipsing the double bond.

Relative Electrophilic Reactivities and Regio- and Stereoselectivities of Molecules Incorporating Allylic Double Bonds. The description of regio- and stereoselectivities of molecules incorporating allylic double bonds, based on frontier molecular orbital theory, assumes that electrophilic attack will occur where the π bond is most heavily concentrated. As detailed in Appendix A

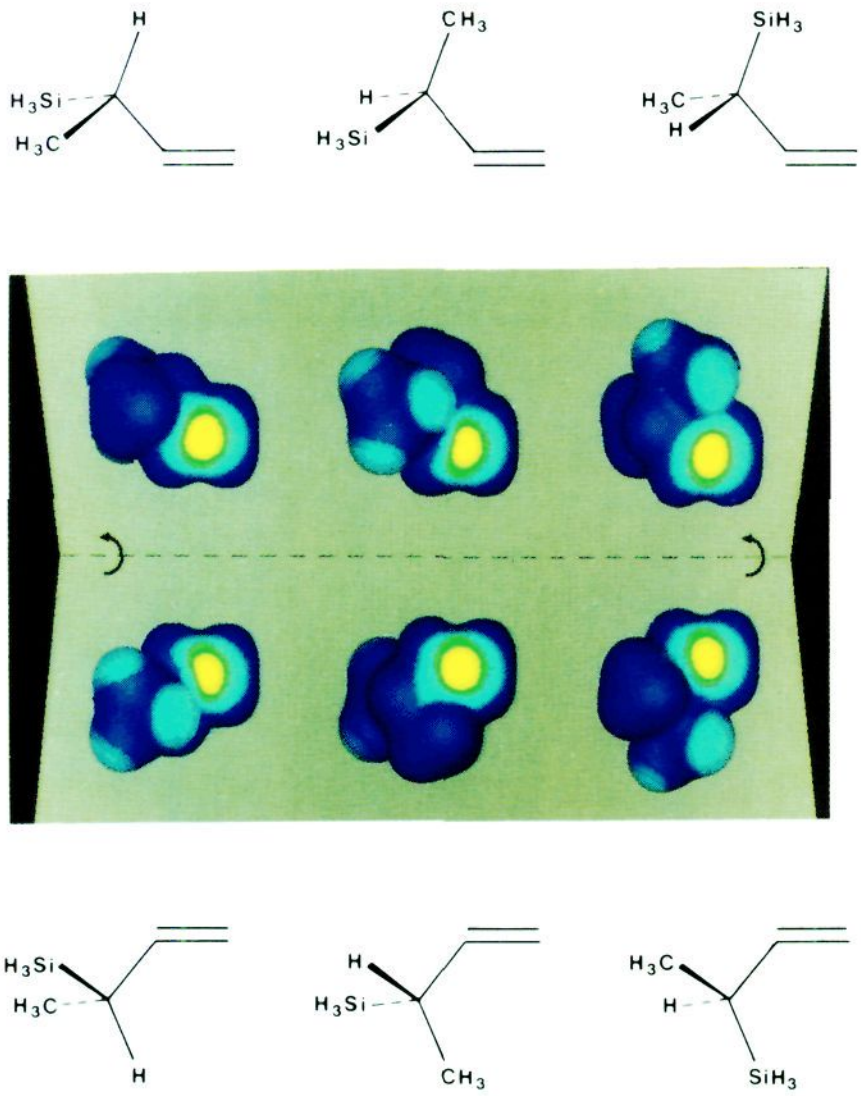


Figure 3. Electrostatic potentials for conformers of 2-silyl-but-3-ene: **1a** (left), **1b** (middle), and **1c** (right). Upper and lower images: **1a**, CH_3 up (top), SiH_3 up (bottom); **1b**, SiH_3 up (top), H up (bottom); **1c**, H up (top), CH_3 up (bottom). Scale: −30 kcal mol^{-1} (red) to 0 kcal mol^{-1} (blue). 3-21G(*)//3-21G(*).

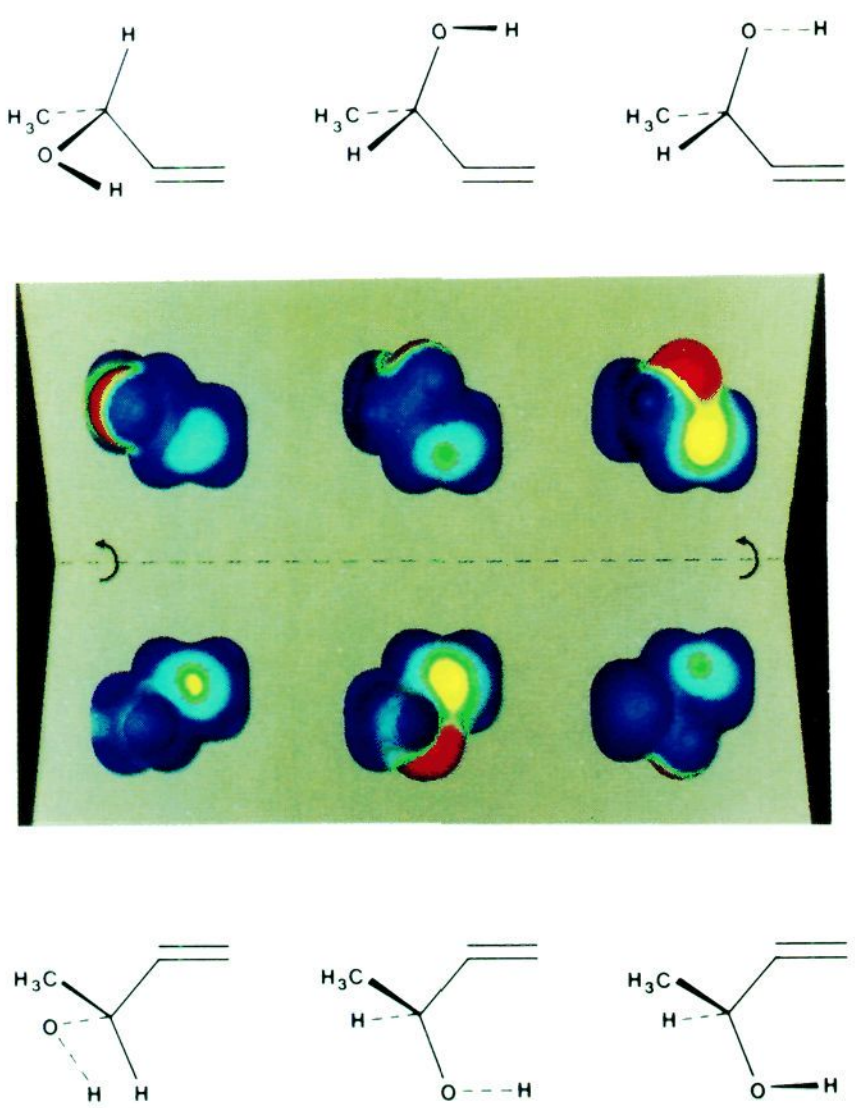


Figure 4. Electrostatic potentials for three low-energy conformers of 3-buten-2-ol: **2a** (left), **2b** (middle), and **2c** (right). Upper and lower images: **2a**, OH up (top), CH_3 up (bottom); **2b**, H up (top), CH_3 up (bottom); **2c** H up (top), CH_3 up (bottom). Scale: −30 kcal mol^{-1} (red) to 0 kcal mol^{-1} (blue). 3-21G//3-21G.

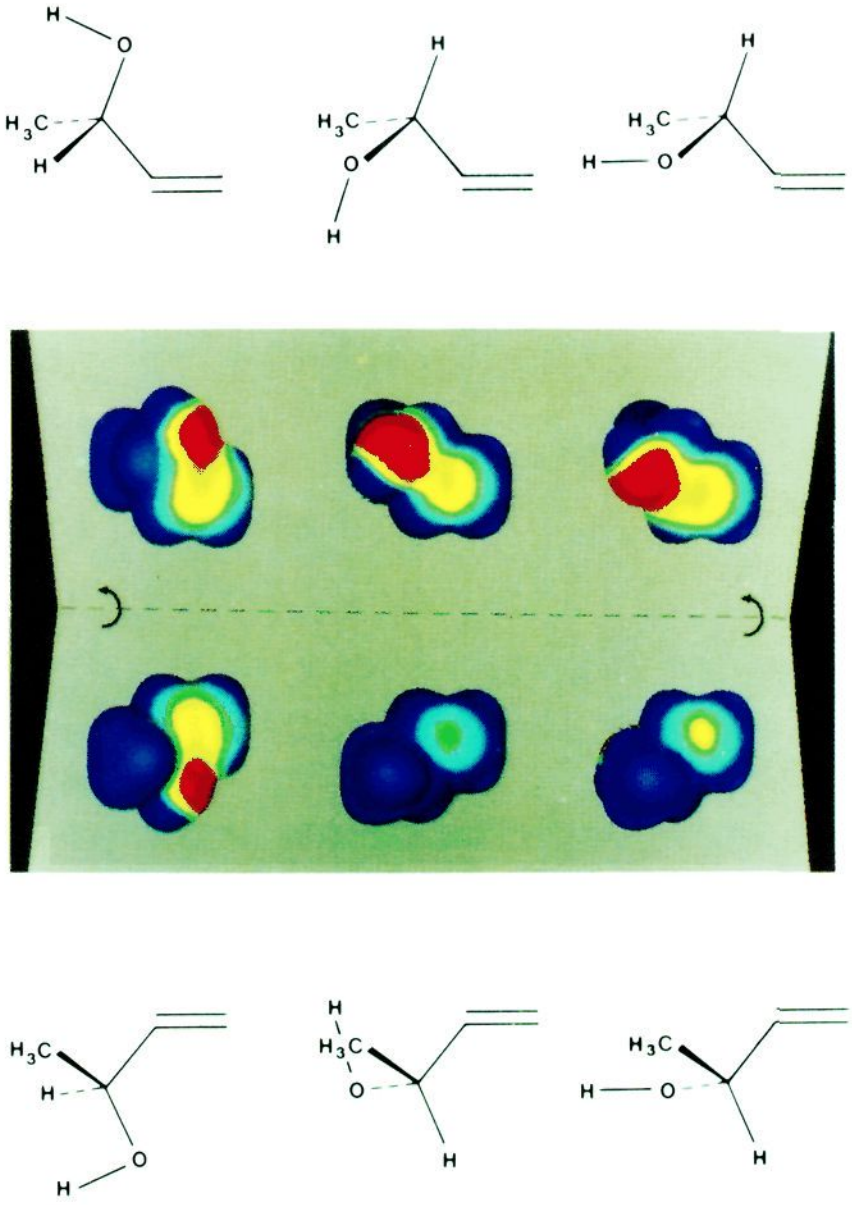


Figure 5. Electrostatic potentials for three high-energy conformers of 3-buten-2-ol: **2d** (left), **2e** (middle), and **2f** (right). Upper and lower images: **2d**, H up (top), CH_3 up (bottom); **2e**, OH up (top), CH_3 up (bottom); **2f**, OH up (top), CH_3 up (bottom). Scale: −30 kcal mol^{-1} (red) to 0 kcal mol^{-1} (blue). 3-21G//3-21G.

of this paper, such an approach does not distinguish the diastereotopic faces of allylic double bonds sufficiently to enable the fundamental underlying reactivity preferences to be uncovered, and predictions of stereoselectivity based on "non-equivalent orbital extension"[4,5] should be viewed with some caution.

An alternative method for describing relative reactivity as well as regio- and stereoselectivity of electrophilic additions to chiral olefins involves comparison of potentials for "test" electrophiles mapped onto quantum-mechanical electron-density surfaces (see Appendix B for an operational discussion of the methods employed). In the simplest model, to be considered initially, and usually termed the *electrostatic potential*,[30] the energy accounts only for coulombic interactions between a point charge (a proton) and the substrate; redistribution of the substrate electron density, transfer of charge from the substrate to the test electrophile, and nuclear relaxation are not allowed for. The effects which *polarization* of the substrate electron distribution has on the results of the simple electrostatic model is described in Appendix C of this paper.

Information regarding relative electrophilic affinities of different substrates may be conveyed either visually, by direct inspection of the reactivity information as superimposed onto the substrate electron-density surface, or by constructing average potentials. Comparisons for different olefin positions give rise to assignment of preferred regiochemistry, i.e, the more negative the potential, the greater the attraction for electrophiles. For chiral molecules,

(30) For recent reviews, see: (a) Scrocco, E.; Tomasi, J. *Adv. Quantum Chem.* **1978**, *11*, 115. (b) *Chemical Applications of Atomic and Molecular Electrostatic Potentials*, Politzer, P., Truhlar, D. G., Eds.; Plenum: New York, 1981.

the diastereotopic faces of the double bond would be expected to react with electrophiles at different rates. Here, comparison of relative reactivities and relative regioselectivities of different systems will be in terms of the more reactive face of a given substrate. Assignment of the more reactive face will itself lead to the assignment of preferred reaction stereochemistry.

Electrostatic potentials corresponding to the diasterotopic faces of the three stable conformers of 2-silylbut-3-ene are shown in Figure 3. Colors near the red end of the visible spectrum represent maximum attraction of the substrate for the test electrophile, while those near the blue represent mimimum attraction. Electrostatic potentials for all three conformers are visually similar. This is confirmed by the average "atomic" potentials[31] provided in Table II.

Averaging over terminal and internal olefin carbons, we found the average atomic potentials for the more reactive faces of the three conformers of 2-silylbut-3-ene are similar. On this basis, their reactivity toward electrophiles should be comparable. The reactivity models indicate a preference for attack onto C_1 for all three conformers.

The reactivity models leave little doubt as to the preferred direction of electrophilic attack in these systems. The full images (Figure 3) do not, however, provide a convenient means for quantifying the degree of stereoselectivity expected for a particular system, or for comparisons of stereoselectivities among different systems. These tasks are better dealt with by the tabulated average potentials for each of the diastereotopic faces (Table II).

Electrophilic attack onto the two low energy conformers of 2-silylbut-3-ene, **1a** and **1b**, is indicated to occur *anti* to the silyl group. The preference is very large in structure **1b**, where hydrogen is in competition, and somewhat smaller in the ground-state conformer, **1a**, where the choice is between methyl and silyl substituents. A very small stereochemical preference is noted for the remaining (highest energy) conformer, **1c**; here, the electrophile prefers to enter *anti* to the methyl group (*syn* to hydrogen).

Reactivity models for the nine conformers of 3-buten-2-ol allow definitive assignment of preferred stereochemistry of electrophilic addition. Full images for the diastereotopic faces of the three most stable conformers **2a–c** are provided in Figure 4; those for the remaining three conformational minima, **2d–f**, are provided in Figure 5.[32] Atom averaged potentials are given in Table II. The situation is fairly complex, and our treatment is divided into two sections: (a) the six stable conformers, **2a–f**, as a model for electrophilic additions to acyclic allylic alcohols and ethers, and (b) the three non-minimum-energy forms, **2g–i**, as a model for additions in cyclic or otherwise rigidly held systems.[22] The latter topic already has been briefly addressed in a preliminary communication.[32]

As previously mentioned, the three lowest energy conformers of 3-buten-2-ol, **2a–c**, have the hydroxylic hydrogen positioned more-or-less directly over the allylic double bond. While this type of conformation gives rise to the possibility of significant stabilization, e.g., "hydrogen bonding",[23] it effectively shields the face of the olefin *syn* to the hydroxyl hydrogen, and it gives rise to the *anti* preference for electrophilic addition. It is electrostatic repulsion between the electrophile and the positively charged hydroxylic hydrogen which dictates reaction stereoselectivity, and it results in attack *syn* to methyl in conformers **2a** and **2b** and *syn* to the allylic hydrogen in **2c**. Note that attack onto **2a** and **2c** would occur at the opposite diastereotopic face as addition to **2b**. In all three cases, the noted stereochemical preferences are sizable.

The three high-energy conformers of 3-buten-2-ol, **2d–f**, are all significantly more reactive than any of the low-energy structures, **2a–c**. Thus, this is a situation where the most abundant conformers are not those which are most reactive. A balance needs to be struck in order to ascertain the ultimate distribution of products. This problem will be addressed in the next section. While the distribution of conformers in allylic ethers *might be expected* to be different than that in the corresponding alcohols, conformers analogous to **2a–c** in which the ether alkyl group is positioned over the double bond should still be less reactive than forms like **2d–f**. The ether alkyl group in the former set of conformers should effectively shield the double bond from the electrophile.

Electrophilic addition in **2d** is predicted to occur onto the face of the olefin away from the methyl group. The magnitude of this preference is not large, a result which is not unexpected; methyl and hydrogen are not greatly different as substituents. While the observed stereochemical preference might be assigned a steric origin, it should be recalled that the "test" electrophile is a point charge (a proton), and as such it has no physical size. It is unfounded, therefore, to conclude that the noted stereoselectivities are a result of minimizing steric crowding (between regent and substrate). Instead, we prefer to interpret this result as suggesting that a CH bond is better able to stabilize the nascent positively charged center than a CC linkage, i.e., hyperconjugation.[33]

Sizable stereochemical preferences are again found in conformers **2e** and **2f**. Recall that these are forms in which a lone pair on oxygen is disposed to interact with the π bond. The proximity of the oxygen lone pairs not only raises the energy of the π bond, making it more accessible to electrophilic attack, but also directs that attack onto the olefin face involved in the interaction. Notice from the full images (Figure 4) how facial reactivity in conformers **2b** and **2c** "follows" the oxygen lone pairs. This has previously been suggested as evidence of complexation of the electrophile onto the oxygen lone pairs in advance of reaction with the π bond.[3]

Electrostatic potentials for the three non-minimum-energy conformers of 3-buten-2-ol, **2g–i**, show similar features. The surfaces describing electrophilic attack onto the olefin face away from the CO bond are nearly identical, while the electrostatic potentials corresponding to addition onto the other diastereotopic face are sensitive to the conformation of the OH bond. Here, the two conformers, **2h** and **2i**, in which an oxygen lone pair is positioned "over the double bond" are indicated to be much more reactive than the arrangement, **2g**, in which the OH linkage is overhead.

Use of these conformers as models for electrophilic addition in cyclic allylic alcohols and ethers requires that a balance be struck between relative equilibrium abundance and relative reactivity. Here, conformers **2h** and **2i**, which favor electrophilic attack *syn* to oxygen, contribute only 14% to the total population (according to 6-31G*//3-21G calculations). As before, these are considerably more reactive than the "ground-state" structure, **2g**. Again, cyclic allylic ethers of the form modeled by **2g** would still be expected to be unreactive relative to ethers analogous to **2h** or **2i**, due to the effective shielding of the otherwise reactive olefin face by the ether alkyl group.

Electrostatic potentials for the diastereotopic faces of the two stable conformers of 2-fluorobut-3-ene are also included in Table II. As previously commented, these present a similar but simpler picture of stereoselectivity than seen in the related allylic alcohol. Absent are complications associated with the conformation of the hydroxyl group. Electrophilic addition in the ground-state conformer, **3a** (in which the CF linkage is nearly coplanar with the double bond), is indicated to occur preferentially onto the side of the olefin away from the alkyl group. The preference is small (as it was for the analogous allylic alcohol, **2d**) and is indicative of the similar environment which hydrogen and methyl exhibit to an approaching electrophile. Again, a steric explanation is tempting, although we interpret this result in electronic terms (vide supra). A much greater degree of stereodifferentiation is suggested

(31) The averaging procedure has been described in detail elsewhere.[9j]

(32) A preliminary account of the electrophilic reactivity of conformers of 2-silylbut-3-ene and 3-buten-2-ol with the CC linkage in the plane of the double bond (modeling cyclic systems) has already appeared. Electrostatic potential surfaces for structures **2g–i** are included. Kahn, S. D.; Pau, C. F.; Hehre, W. J. *J. Am. Chem. Soc.* **1986**, *108*, 7396.

(33) The relative importance of CH and CC hyperconjugation has not been clearly resolved in the literature. For a recent discussion, see: Sunko, D. E.; Hehre, W. J. *Prog. Phys. Org. Chem.* **1983**, *14*, 205 and references therein.

Table II. Average Electrostatic and Total (Sum of Electrostatic and Polarization) Potentials for Chiral Olefins[a]

molecule and comformation	face	average electrostatic potential				average total potential[b]			
		C_1	C_2	average[c]	difference[d]	C_1	C_2	average[c]	difference[d]
2-silylbut-3-ene									
1a	CH_3 up	−16.7	−12.3	−14.5	4.3	−26.8	−25.0	−25.9	1.8
	SiH_3 up	−16.3	−6.4	−11.4	9.9	−27.0	−20.9	−24.0	6.1
	difference	0.4	5.9	3.1		−0.2	4.1	2.0	
1b	SiH_3 up	−8.5	−6.7	−7.6	1.8	−19.4	−21.5	−20.5	−2.1
	H up	−17.1	−13.5	−15.3	3.6	−27.5	−25.6	−26.6	1.9
	difference	−8.6	−6.8	−7.7		−8.1	−4.1	−6.1	
1c	H up	−16.5	−11.8	−14.2	4.7	−26.5	−23.7	−25.1	2.8
	CH_3 up	−15.9	−12.2	−14.1	3.7	−25.9	−24.8	−25.4	1.1
	difference	0.6	−0.4	0.1		0.6	−1.1	−0.3	
3-buten-2-ol									
2a	OH up	−8.8	3.4	−2.7	12.2	−17.9	−7.5	−12.7	10.4
	CH_3 up	−12.0	−10.0	−11.0	2.0	−22.7	−21.4	−22.1	1.3
	difference	−3.2	−13.4	−8.3		−4.8	−13.9	−9.4	
2b	H up	−9.6	−4.3	−7.0	5.3	−18.9	−15.0	−17.0	3.9
	CH_3 up	−17.6	−13.8	−15.7	3.8	−27.4	−25.7	−26.6	1.7
	difference	−8.0	−9.5	−8.7		−8.5	−10.7	−9.6	
2c	H up	−18.4	−12.8	−15.6	5.6	−27.6	−23.4	−25.5	4.2
	CH_3 up	−9.2	−3.9	−6.6	5.3	−18.6	−15.4	−17.0	3.2
	difference	9.2	8.9	9.0		9.0	8.0	8.5	
2d	H up	−23.0	−16.4	−19.7	6.6	−32.9	−27.8	−30.4	5.1
	CH_3 up	−20.4	−16.3	−18.4	4.1	−29.5	−27.2	−28.4	2.3
	difference	2.6	0.1	1.3		3.4	0.6	2.0	
2e	OH up	−17.8	−22.0	−19.9	−4.2	−26.9	−32.5	−29.7	−5.6
	CH_3 up	−10.9	−7.4	−9.2	3.5	−20.6	−19.2	−19.9	1.4
	difference	6.9	14.6	10.7		6.3	13.3	9.8	
2f	OH up	−20.5	−27.4	−24.0	−6.9	−29.6	−38.5	−34.1	−8.9
	CH_3 up	−13.8	−11.1	−12.5	2.7	−23.6	−22.9	−23.3	0.7
	difference	6.7	16.3	11.5		6.0	15.6	10.8	
2g	OH up	−8.2	2.7	−2.8	10.9	−17.7	−8.3	−13.0	9.4
	H up	−11.8	−8.3	−10.1	3.5	−21.3	−19.0	−20.2	2.3
	difference	−3.6	−11.0	−7.3		−3.6	−10.7	−7.2	
2h	OH up	−21.8	−32.8	−27.3	−11.0	−31.2	−44.2	−37.7	−13.0
	H up	−13.6	−8.7	−11.2	4.9	−23.0	−19.5	−21.3	4.5
	difference	8.2	24.1	16.1		8.2	24.7	16.4	
2i	OH up	−16.8	−20.5	−18.7	−3.7	−26.1	−30.8	−28.5	−4.7
	H up	−11.4	−7.0	−9.2	4.4	−20.9	−17.7	−19.3	3.2
	difference	5.4	13.5	9.5		5.2	13.1	9.2	
2-fluorobut-3-ene									
3a	H up	−15.2	−9.3	−12.3	5.9	−24.4	−19.5	−22.0	4.9
	CH_3 up	−13.6	−8.6	−11.1	5.0	−23.1	−20.0	−21.6	3.1
	difference	1.6	0.7	1.2		1.3	0.5	0.4	
3b	F up	−13.0	−15.1	−14.1	−1.9	−22.0	−25.5	−23.8	−3.5
	CH_3 up	−7.7	−4.6	−6.2	3.1	−17.4	−16.3	−16.9	1.1
	difference	5.3	10.5	7.9		4.6	9.2	6.9	
(*E*)-2-fluoropent-3-ene									
4a	H up	−13.6	−11.5	−12.6	2.1	−23.6	−22.8	−23.2	0.8
	CH_3 up	−12.1	−10.7	−11.4	1.4	−21.2	−21.6	−21.4	−0.4
	difference	1.5	0.8	1.2		2.4	1.2	1.8	
4b	F up	−11.6	−18.4	−15.0	−6.8	−22.4	−29.7	−26.1	−7.3
	CH_3 up	−6.2	−6.3	−6.3	−0.1	−17.7	−18.9	−18.3	−1.2
	difference	5.4	12.1	8.7		4.7	10.8	7.8	
(*E*)-1-cyano-3-fluorobut-1-ene									
5a	H up	−0.7	8.2	3.8	8.9	−12.2	−4.5	−8.4	7.7
	CH_3 up	1.0	8.6	4.8	7.6	−11.0	−5.1	−8.1	5.9
	difference	1.7	0.4	1.0		1.2	0.6	0.3	
5b	F up	1.9	4.2	3.1	2.3	−9.5	−8.6	−9.1	0.9
	CH_3 up	6.5	11.2	8.9	4.7	−5.7	−2.7	−4.2	8.0
	difference	4.6	7.0	5.8		3.8	5.9	4.9	

[a] kcal mol^{-1}. 3-21G//3-21G (3-21G(*)//3-21G(*) for 2-silylbut-3-ene). [b] Discussed in Appendix C to this paper. [c] $(C_1 + C_2)/2$. [d] $C_1 - C_2$.

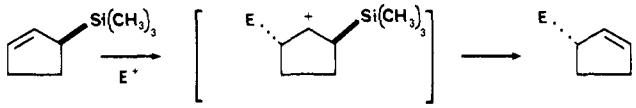
by the reactivity models for the higher energy conformer, **3b**, where an incoming electrophile prefers to approach the olefin on the same side as the CF bond (analogous to the situation in the alcohols **2e** and **2f**). The similarity in the reactivities of 2-fluorobut-3-ene and 3-buten-2-ol reinforces our choice to model the alcohol with the halogen system.

Model studies on allyl fluorides permit us to predict the effect which substitution will have on the reactivity and regio- and stereoselectivity of allylic alcohols. According to the models, substitution of an electron-releasting group, e.g., methyl, at C_1 increases the regio- and stereochemical preferences of the most reactive conformers, i.e., those with CH eclipsing the double bond,

while it has little effect on the stereochemical biases in less-reactive conformers, i.e., with the "CO bond" in the plane of the olefin. Surprisingly, methyl substitution is suggested to do little to increase overall reactivity toward electrophiles. On the other hand, replacement of a C_1 hydrogen with a strong electron-withdrawing group, e.g., cyano, significantly deactivates the double bond toward attack by electrophiles. Concomitant with deactivation is a lessening of diastereofacial bias; the direction of the stereochemical preference remains unchanged.

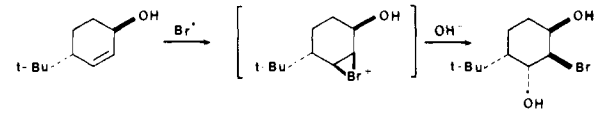
In summary, the reactivity models clearly indicate both regio- and stereochemical preferences for electrophilic addition onto chiral allylic double bonds and the extent to which these preferences vary with conformation. It has also been found that substitution (on the olefin) by electron-releasing groups, e.g., methyl, not only leads to overall activation toward electrophilic addition but also results in enhanced regio- and stereoselectivity. In contrast, substitution by electron-withdrawing groups, e.g., cyano, leads to both deactivation and a reduction in stereoselectivity.

Experimentally Observed Regio- and Stereoselectivities in Electrophilic Additions to Allylic Double Bonds. Comparison with Theoretical Results. Conformationally Rigid Systems. As pointed out in the introduction, the two general cases chosen for investigation here, i.e., additions involving allylic silanes and allylic alcohols and ethers, follow different pathways to eventual (isolated) products. Electrophilic addition to allylic silanes, illustrated schematically below for 1-(trimethylsilyl)cyclopent-2-ene, is followed by elimination, i.e.,

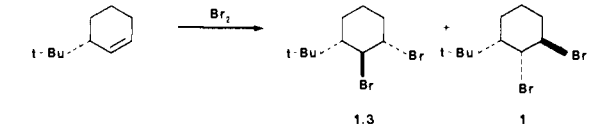


As written, both the overall (product) regio- and stereochemistry *must be determined* upon initial electrophilic addition. As indicated above, the noted preference in conformationally rigid systems is for attack at the terminal olefin position and *anti* to the silyl group. Other examples, i.e., in cyclic compounds where geometrical relationships are fixed, are provided in Table III; these show the same general trends. The situation here should be satisfactorily modeled by the conformer in 2-silylbut-3-ene in which the methyl group lies (approximately) in the plane of the double bond, i.e., **1b**. The reactivity models (Table II) clearly reproduce the observed regio- and stereochemical preferences.

Interpretation of the experimental data for electrophilic additions in allylic alcohols (and ethers) is more complicated. As illustrated below for addition of HOBr to a "locked" allylic alcohol, cyclohexenol, overall product regio- and stereochemistry may be influenced not only by the initial electrophilic addition but also by the subsequent nucleophilic step.[34]



Bromine addition to the parent 3-*tert*-butylcyclohexene is almost entirely stereorandom.[35]



While we are aware that stereoelectronic effects may be important in electrophilic additions of cyclohexene,[36] discussion is deferred.

In this example, and in most cases involving similar rigid systems (further examples are provided in Table III), electrophilic addition occurs preferentially *syn* to the hydroxyl substituent. Subsequent nucleophilic addition of hydroxide, onto the β carbon opposite to the bromine, suggests that the intermediate bromonium ion (or bromonium ion like transition state) has been skewed toward the α carbon. This situation should be properly modeled by conformers of 3-buten-2-ol in which the terminal methyl group has been *constrained* to lie in the plane of the double bond,[22,37] i.e., **2g–i**.

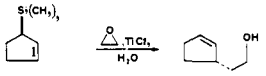
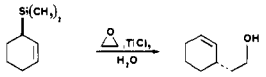
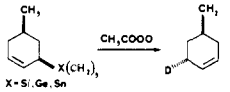
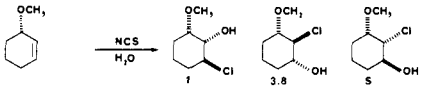
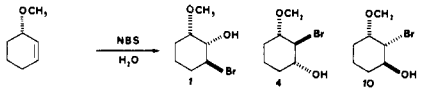
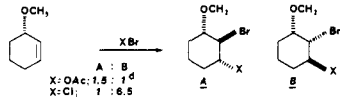
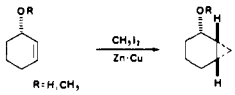
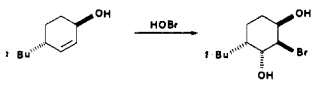
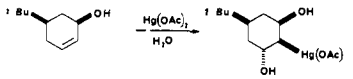
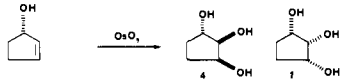
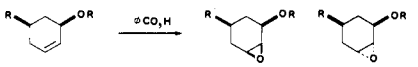
According to the reactivity models (Table II), the lowest energy conformer among the three constrained systems, **2g**, favors electrophilic attack *anti* to the OH group. This form is, however, predicted to be significantly less reactive than either of the alternative structures, **2h** and **2i**, both of which show strong preferences for electrophilic attack *syn* to oxygen and onto the α carbon. With the exception of osmylation and the epoxidation of allylic acetates (ethers), all of the reactions of allylic alcohols and ethers provided in Table III result in products formed by addition of the electrophile *syn* to the oxygen-containing functionality. This result is quite remarkable in light of the varied array of electrophiles represented. Further, the fact that allyl alcohols and allyl ethers exhibit identical stereochemical preferences allows another salient feature of the underlying mechanism to be elucidated. As commented earlier, the "ground-state" conformer for our model cyclic system (**2g**) is one in which the hydroxylic hydrogen is situated directly over the CC π bond. It is to be expected that, because allyl ethers would shield an olefin face more effectively than a hydroxylic hydrogen, conformers analogous to **2g** would continue to be much less reactive relative to the alternative structures analogous to **2h** and **2i**, i.e., ethers of the form **2g** will be as unimportant in determining the product distributions in electrophilic addition reactions as the analogous alcohols have been shown to be. Given that the reactivity models suggest that the stereochemical bias afforded **2g** is opposite those of **2h** and **2i**, it can be reasoned that the less abundant but *much* more reactive forms **2h** and/or **2i** and their ether analogues will dictate product distributions for both sets of electrophilic additions.

Stereochemical results for osmium tetroxide oxidation of allylic alcohols appear to be inconsistent with the remaining body of data in Table III. Permanganate oxidations also exhibit similar stereoselectivities.[26c,38] It is not surprising that H^+ (our test electrophile) is an inadequate model for reagents such as OsO_4 and MnO_4^-. Treatment of coulombic interactions alone would certainly lead to a classification of these reagents as nucleophiles and not electrophiles![39] Indeed, the noted preference of the model for addition *anti* to the OH functionality is consistent with the results of a previous study where H^- was used as a test reagent.[40] Further study is necessary in order to properly model additions involving these reagents.

Another apparent discrepancy between the results of the reactivity models and experiment involves peracid epoxidation of allylic acetates (and ethers). While epoxidation of allylic alcohols proceeds *syn* to OH (in accord with the conclusions of the reactivity models), allylic acetates (and ethers) are best characterized as nonselective to this form of epoxidation reaction. This difference in behavior between two so closely related classes of reactions is evidence for hydrogen bonding between the hydroxylic hydrogen and the peracid in the transition state.[4d] Along with OsO_4 and

(34) Kahn, S. D.; Chamberlin, A. R.; Hehre, W. J., research in progress.
(35) Barili, P. L.; Bellucci, G.; Marioni, F.; Morelli, I.; Scartoni, V. *J. Org. Chem.* **1972**, *37*, 4353.
(36) (a) Goering, H. L.; Abell, P. I.; Aycock, B. F. *J. Am. Chem. Soc.* **1952**, *74*, 3588. (b) Goering, H. L.; Sims, L. L. *Ibid.* **1955**, *77*, 3465. (c) Shoppee, C. W.; Akhtar, M. I.; Lack, R. E. *J. Chem. Soc.* **1964**, 877. (d) Readio, P. D.; Skell, P. S. *J. Org. Chem.* **1966**, *31*, 753, 759. (e) Bellucci, G.; Berti, G.; Ingrosso, G.; Mastrorilli, E. *Tetrahedron Lett.* **1973**, 3911.
(37) The use of the methyl eclipsed conformers ($\omega_{C=CCC} = 0°$) approximates the axial ($\omega_{C=CCC} = 15°$) and the equatorial ($\omega_{C=CCC} = -15°$) conformers of α-substituted cyclohexenes. Work is currently in progress to ascertain the validity of this approximation.
(38) For example, see: Lance, D. G.; Szarek, W. A.; Jones, J. K. N.; Howarth, G. B. *Can. J. Chem.* **1969**, *47*, 2871.
(39) For references to the mechanism of cis hydroxylation with OsO_4 and $KMnO_4$, see: Schröder, M. *Chem. Rev.* **1980**, *80*, 187.
(40) Kahn, S. D.; Hehre, W. J., research in progress.

Table III. Comparison of Experimental Regio- and Stereochemistry for Electrophilic Additions to Cyclic Compounds with Assignments from Reactivity Models

reaction	experimental ref[a]	experimental regiochemistry[b]	experimental stereochemistry[c]	reactivity models regiochemistry[b]	reactivity models stereochemistry[c]
	1	C_1	*anti*	C_1	*anti*
					
	2	C_1	*anti*	C_1	*anti*
	3	C_2 (major)	*syn* (major)	C_2	*syn*
	4	C_2 (major)	*syn* (major)	C_2	*syn*
	5	C_2	*syn* (major)	C_2	*syn*
	6		*syn*		*syn*
	7	C_2	*syn*	C_2	*syn*
	8	C_2	*syn*	C_2	*syn*
	9		*anti* (major)		*syn*
	10				*syn*
R′ = H; R = H	10:1		*syn* (major)		
R′ = H; R = $COCH_3$	1:1.3		*anti* (major)		
R′ = *t*-Bu; R = H	24:1		*syn* (major)		
R′ = *t*-Bu; R = $COCH_3$	1:1.2		*anti* (major)		
R′ = H; R = CH_3	1:1.7	11	*anti* (major)		

[a] References to experimental work: (1) Hayashi, T.; Kebeta, K.; Yamamota, T.; Tamao, K.; Kumada, M. *Tetrahedron Lett.* **1983**, *24*, 5661. (2) Wickham, G.; Kitching, W. *J. Org. Chem.* **1983**, *48*, 614. (3) Langstaff, E. J.; Hamanaka, E.; Neville, G. A.; Moir, R. Y. *Can. J. Chem.* **1967**, *45*, 1907. (4) Bannard, R. A. B.; Casselman, A. A.; Hawkins, L. R. *Ibid.* **1965**, *43*, 2398. (5) Bellucci, G.; Berti, G.; Bianchini, R.; Ingrosso, G.; Mastrorilli, E. *Gazz. Chim. Ital.* **1976**, *106*, 955. (6) Poulter, C. D.; Freidrich, E. C.; Winstein, S. *J. Am. Chem. Soc. 92*, 6892 and references therein. (7) Reference 26h. (8) Reference 26k. (9) Reference 26c. (10) Chamberlain, P.; Roberts, M. C.; Whitham, G. H. *J. Chem. Soc.* (*B*) **1970**, 1374. (11) Reference 3d. [b] Position of attack of electrophile with respect to the directing group (–$SiMe_3$ or –OR). [c] Diastereotopic face attacked with respect to the directing group. [d] The addition of BrOAc appears to be anomalous. See also, Table IV.

MnO_4^- oxidations, the epoxidation of allylic acetates and ethers serves as a reminder of the complexities which often arise in real systems.

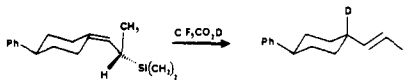
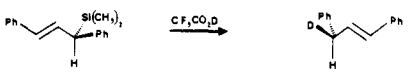
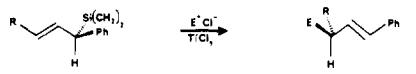
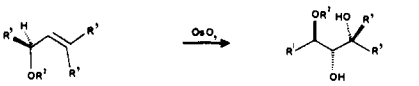
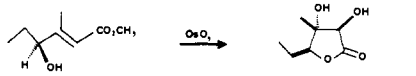
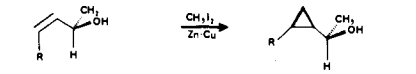
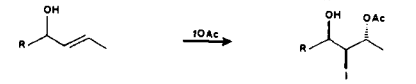
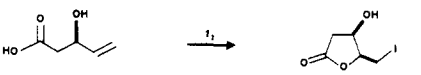
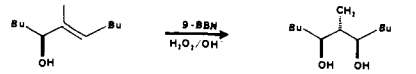
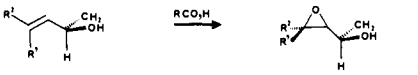
In summary, the reactivity models are in accord with the experimental observation that electrophiles add β and *anti* to allyl silanes. Additions to cyclic allylic alcohols (and ethers) may be interpreted as proceeding through the less abundant but much more reactive conformers (modeled by **2h** and **2i**) in which the oxygen functionality directs *syn*.

Conformationally Flexible Systems

As has been previously discussed, elucidation of the regio- and stereoselectivities of electrophilic additions to conformationally flexible, acyclic systems requires detailed knowledge of relative conformer abundances and reactivities, as well as insight into the stereo- and regiochemical preferences of the individual conformers. Thus, as is apparent from the representative experimental data provided in Table IV, any account of the observed product distributions resulting from additions to acyclic systems must necessarily be intimately intertwined with a description of conformational profile. This complication makes generalizations even more difficult than in cyclic systems. Indeed, our primary purpose here is more to *identify* and, if possible, *quantify* those factors which ultimately contribute to the control of product distributions, rather than to predict detailed regio- and stereochemistries on a case by case basis.

All examples cited for electrophilic additions to allylic silanes have in common the formation of an E double bond. As indicated in Table IV, this preference could result either from addition of an electrophile *syn* to the silyl group from a conformer analogous to **1b** or alternatively from electrophilic addition *anti* to silicon from a structure analogous to **1a**. Reactivity model and experimental results with cyclic systems (where assignment of conformation is unambiguous) suggest the latter, namely that elec-

Table IV. Interpretation of Experimental Regio- and Stereochemistry for Electrophilic Additions to Acyclic Allylic Compounds

reaction	ref[a]	regiochemistry[b]	stereochemistry[c]	"reactivity" model prediction
	1	C_1	CH *cis*; SiR_3 *anti* CC *cis*; SiR_3 *syn*	*(C_1)
	2	C_1	CH *cis*; SiR_3 *anti* CC *cis*; SiR_3 *syn*	*(C_1)
	3	C_1	CH *cis*; SiR_3 *anti* CC *cis*; SiR_3 *syn*	*(C_1)
	4		CO *cis*; H *syn* CH *cis*; OR *anti*	*d*
	5		CO *cis*; H *syn* CH *cis*; OH *anti*	*d*
	6		CH *cis*; OH *syn* CO *cis*; H *anti*	*
	7	C_2	CH *cis*; OH *syn* CO *cis*; H *anti*	*(C_2)
	8	C_1	CO *cis*; H *syn* CH *cis*; OH *anti*	*(C_1)
	9	C_2	CH *cis*; OH *syn* CO *cis*; H *anti*	*(C_2)
	10		CH *cis*, OH *syn* CO *cis*, H *anti*	*

[a] References to experimental work: (1) Fleming, I.; Terrett, N. K. *J. Organomet. Chem.* **1984**, *264*, 99. (2) Hayashi, T.; Ito, H.; Kumada, M. *Tetrahedron Lett.* **1982**, *23*, 4605. (3) Hayashi, T.; Kouishi, M.; Ito, H.; Kumada, M. *J. Am. Chem. Soc.* **1982**, *104*, 4962. (4) Reference 26c. (5) Reference 25e. (6) Reference 26g. (7) Reference 26b. (8) Reference 25d. (9) Reference 26e. (10) Reference 26f,i,j. [b] Position of attachment of electrophile with respect to the directing group. [c] Diastereotopic face attacked. [d] See text for discussion.

trophiles will add onto the face of the olefin away from the silyl substituent. This interpretation is further supported by the fact that in the model system, structure **1a** is more abundant (Table I) and nearly as reactive (Table II) as the alternative conformer **1b**.

Electrophilic additions to acyclic allyl alcohols and ethers comprise a more diverse class of reactions than those involving allylic silanes. Representative experimental data (Table IV) suggest that reaction is most likely to occur from either of two stereochemically distinct conformations, i.e., additions *syn* to OH (OR) from a conformer in which an allylic CH bond eclipses the olefin plane yield products of opposite relative stereochemistry than additions from the side of hydrogen from a conformer in which C–O eclipses the olefin plane. The situation would be further complicated except for our previous findings which suggest that only those allylic alcohol conformers in which the hydroxylic hydrogen is not properly disposed to shield the otherwise more reactive olefin face are likely to contribute significantly to the overall distribution of products, and further that such structures are likely to be the most reactive forms open to allylic ethers. Further discussion will focus on these conformers (modeled by **2d–f** in 3-buten-2-ol) and not on the more abundant but *much* less reactive alternatives (modeled by **2a** to **2c**).

Hydroboration, iodo-acetate formation, and treatment with CH_2I_2/Zn·Cu (Simmons–Smith reaction) each result in products which are consistent with reaction from allylic alcohol conformations in which a CH linkage eclipses the double bond (modeled by **2e** and **2f**); electrophile addition is from the same side of the olefin as the OH substituent. In contrast, the major stereoisomer arising from iodo lactonization would seem to be properly accounted for by addition *syn* to hydrogen in a conformer in which the CO bond eclipses C=C (modeled by **2d**). Given the similarity of the iodo-acetate and iodo-lactonization reactions, it might be speculated that other factors influencing relative conformer stabilities and/or reactivities need to be addressed.[41]

As was previously the case for reactions of cyclic systems, interpretation of the stereochemical preferences for osmium tetroxide oxidation of acyclic allylic alcohols and presumably peracid epoxidation of allylic ethers[42] is probably best deferred until more appropriate models for these reagents have been developed.

Conclusions and Interpretations

A number of conclusions follow direclty from the research described in this paper:

Frontier molecular orbital theory, while elegant for its simplicity, does not provide a sensitive or unambiguous account of the preferred stereochemistry of electrophilic additions to double bonds in chiral molecules (see Appendix A). Bond polarizations calculated from ab initio 3-21G (3-21G(*)) wave functions are generally very small and often change with olefin position. In contrast, reactivity models in which the relative affinities of the diastereotopic faces of a chiral olefin toward a test electrophile

(41) Part 7: Chamberlin, A. R.; Mulholland, R. L., Jr.; Kahn, S. D.; Hehre, W. J. *J. Am. Chem. Soc.*, in this issue.

(42) There appears to be no experimental data on peracid epoxidations of acyclic allyl ethers or allyl acetates.

(H^+) are evaluated directly are sensitive to the detailed asymmetric enfironment and are generally interrpretable in an unambiguous fashion.

Reactivity models provide a clear indication of the regio- and stereochemistry of electrophilic additions to allylic double bonds, as a function of conformation. The most abundant and most reactive conformer in allyl silanes, typified here by 2-silylbut-2-ene, is that in which the allylic CH linkage (approximately) eclipses the double bond, with the methyl and silyl groups above and below the olefin plane. Electrophilic attack is indicated to occur preferentially at the β carbon and *anti* to silicon, in accord with experimental observation. We interpret this result in terms of the tendency of the approaching electrophile to avoid regions of high positive charge, i.e., the SiH_3 group, rather than due to polarization of the π bond because of its asymmetric environment.

The situation in allylic alcohols is more complicated due to the fact that the most abundant conformers are not the most reactive. Indeed, the most stable conformers of our model compound, 3-buten-2-ol, have the otherwise more reactive diastereotopic face, i.e., *syn* to OH, deactivated either as a result of "hydrogen bonding" between the hydroxylic hydrogen and the π bond or through shielding effects. Because the electrophilic reactivities of allylic ethers (where conformers analogous to the "hydrogen-bonded" forms in allylic alcohols should be deactivated) are very similar to those of the corresponding alcohols, we hypothesize that the highly reactive conformers (which are not disposed to have the olefin "shielded") will, in fact, dictate the overall product distribution in both systems. The reactivity models indicate that electrophilic addition to conformers of 3-buten-2-ol in which the allylic CH linkage eclipses the double bond occurs preferentially at the α carbon and *syn* to oxygen, in accord with experimental data on rigidly held systems. Again, we account for this preference in terms of simple electrostatic arguments, i.e, favorable association of an incoming electrophile with the lone pairs of oxygen, rather than due to polarization of the π system. Conformers of 3-buten-2-ol with oxygen in plane are suggested by the reactivity models to exhibit small preferences for electrophilic addition *anti* to methyl, consistent with either steric considerations or inherent differences between CH and CC bonds to stabilize a nascent positive charge (hyperconjugation).

Our attempts to model the regio- and stereoselectivity of electrophilic additions to allylic alcohols serve to elucidate those factors which need to be addressed explicitly. At the very least these include relative conformer abundance and reactivity and the regio- and stereochemical biases of the individual conformers. More generally, information about the reagent and mechanism (location of the transition state along the reaction coordinate) will need to be considered in any comprehensive treatment of factors which influence electrophilic additions to the broad class of olefins discussed herein. Pursuant of empirical rules, continued efforts are in progress in our laboratories.

Appendix A. Analysis of Relative Electrophilic Reactivities and Regio- and Stereoselectivities by Frontier Molecular Orbital Theory

Within the framework of the FMO model, the reactivity of a substrate toward an electrophile should increase with decreasing energy separation between the substrate HOMO and the LUMO on the electrophile.[9d] Relative reactivities for different conformers should, therefore, parallel relative HOMO energies. Data for the three stable conformers of 2-silylbut-3-ene (**1**), for the nine possible arrangements of 3-buten-2-ol (**2**), and for the two stable conformers of each of 2-fluorobut-3-ene (**3**), (*E*)-2-fluoropent-3-ene (**4**), and (*E*)-1-cyano-3-fluorobut-1-ene (**5**) are provided in Table V. These have been obtained from 3-21G//3-21G wavefunctions (3-21G(*)//3-21G(*) for 2-silylbut-3-ene).

Both low-energy conformers of 2-silylbut-3-ene, **1a** and **1b**, are indicated to have the same HOMO energy. Since both structures should be significantly populated at equilibrium (Table I), both should contribute significantly to overall electrophilic reactivity. The HOMO of the thrid conformer, **1c**, is predicted by the 3-21G(*) calculations to be approximately 10 kcal mol^{-1} lower in energy, causing this species to be less reactive toward electrophiles than the two lower energy (more abundant) conformers. As previously noted, the carbon–silicon linkage in both low-energy structures, **1a** and **1b**, is almost perpendicular to the CC π bond. In these arrangements, the high-energy CSi σ bond, which because of electronegativity differences is primarily localized on carbon, interacts with the higher-energy CC π bond (Figure 6). The result is a raising of the energy of the latter,[43] making it more reactive toward electrophiles. Such an interaction is no longer significant in the remaining conformer, **1c**, where the CSi σ bond and CC π bond are nearly coplanar, a result for which there is experimental support. Specifically, the lowest ionization potential in trimethylallylsilane (in which the carbon–silicon linkage is *presumed* to be nearly perpendicular to the olefin plane) is

Table V. Energies and Coefficients of Highest Occupied Molecular Orbitals in Chiral Olefins[a]

molecule and conformation	HOMO energy (kcal mol^{-1})	function	HOMO coefficient[b] C_1	C_2
2-silylbut-3-ene				
1a	−220	p_π	0.364	0.328
(CH_3 up)		s	0.012	−0.006
1b	−220	p_π	0.368	0.325
(SiH_3 up)		s	−0.005	0.009
1c	−230	p_π	0.378	0.357
(H up)		s	0.002	−0.013
3-buten-2-ol				
2a	−235	p_π	0.373	0.347
(OH up)		s	−0.019	0.041
2b	−230	p_π	0.369	0.361
(H up)		s	0.000	0.021
2c	−231	p_π	0.368	0.363
(H up)		s	0.005	−0.046
2d	−224	p_π	0.363	0.365
(H up)		s	0.002	−0.010
2e	−235	p_π	0.371	0.352
(OH up)		s	−0.002	0.009
2f	−230	p_π	0.372	0.349
(OH up)		s	−0.001	−0.009
2g	−237	p_π	0.373	0.345
(OH up)		s	−0.018	0.048
2h	−232	p_π	0.374	0.352
(OH up)		s	0.006	−0.012
2i	−236	p_π	0.371	0.354
(OH up)		s	0.001	0.015
2-fluorobut-3-ene				
3a	−234	p_π	0.364	0.369
(H up)		s	0.002	−0.010
3b	−240	p_π	0.370	0.358
(F up)		s	−0.003	0.001
(*E*)-2-fluoropent-3-ene				
4a	−223	p_π	0.358	0.369
(H up)		s	0.002	−0.003
4b	−228	p_π	0.351	0.381
(F up)		s	−0.003	0.011
(*E*)-1-cyano-3-fluorobut-1-ene				
5a	−244	p_π	0.343	0.321
(H up)		s	−0.004	0.010
5b	−247	p_π	0.349	0.309
(F up)		s	0.000	0.000

[a] 3-21G//3-21G (3-21G(*)//3-21G(*) for 2-silylbut-3-ene). [b] The coefficients listed correspond to the "outer" component of the respective valence atomic orbital. [c] Not a minimum on the 3-21G conformational profile.

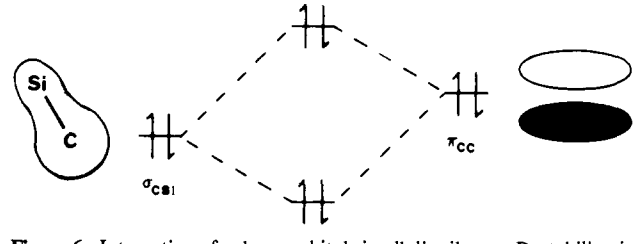


Figure 6. Interaction of valence orbitals in allylic silanes. Destabilization of π_{CC} due to four-electron interaction with σ_{CSi}.

(43) This has previously been noted. See: Chan, T. H.; Fleming, I. *Synthesis* **1979**, 761.

approximately 21 kcal mol^{-1} less than that in trimethylvinylsilane, where the CSi linkage lies in the plane of the double bond.[21] In summary, on the basis of both its relatively equilibrium abundance and the relative reactivity of its π bond, the highest energy conformer of 2-silylbut-3-ene would not be expected to play an important role in the overall electrophilic reactivity of acyclic allyl silanes.

Of the three low-energy (most abundant) conformers of 3-buten-2-ol, **2a–c**, the HOMO energies of the latter pair, in which the CO linkage lies roughly in the plane of the double bond, are somewhater higher than that of **2a** in which the CH linkage eclipses the π bond. Clearly, the geometry in which C=C and C—O are coplanar allows maximum interaction between a lone pair on oxygen and the CC π bond, leading to a maximal splitting of the two levels. As a result, the energy of the lone pair is lowered, while that of the π bond (the HOMO) is raised. Thus, while the ground-state conformer, **2a**, would not be expected to be the most reactive, both structures **2b** and **2c** must be considered in analyzing the stereoselectivity of electrophilic additions in acyclic compounds.

Interestingly, the conformation of the OH linkage in structures **2b** and **2c** does not allow for interaction of the higher energy π-type oxygen lone pair with the olefin π bond. In stark contrast, conformer **2d**, while only a minor contributor to the total equilibrium population (4% according to 6-31G*//3-21G calculations), has a highly energetic HOMO. Its role in determining product distributions in electrophilic additions to acyclic systems is difficult to predict a priori; high reactivity must somehow be balanced with low equilibrium abundance.

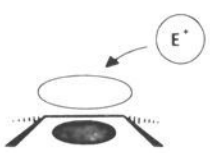
The FMO arguments also suggest that structure **2g**, the lowest energy conformer of 3-buten-2-ol with the CC linkage constrained to lie in the plane of the double bond, is not the most reactive of the three such forms. The HOMO energy of conformer **2h** is higher. Here too, a balance between equilibrium abundance and reactivity needs to be found in order for the eventual product distribution to be properly described.

The HOMO energies corresponding to the ground-state conformers of 2-fluorobut-3-ene (**3**), (*E*)-2-fluoropent-3-ene (**4**), and (*E*)-1-cyano-3-fluorobut-1-ene (**5**) are in each case higher than that for the remaining conformer. Thus, in these cases the more abundant species should also be the more reactive.

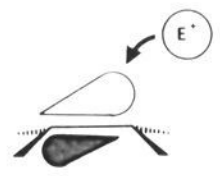
HOMO coefficients for 2-silylbut-3-ene and 3-buten-2-ol, also provided in Table V, allow assignment of the regiochemistry of electrophilic addition in these systems, i.e., electrophilic attack will occur preferentially at the site with the larger HOMO coefficient. On this basis, electrophilic attack for all three conformers of 2-silylbut-3-ene should occur preferentially at C_1, the largest preferences being for the two low-energy conformers, **1a** and **1b**.

According to the FMO model, the ground-state conformer of 3-buten-2-ol, **2a**, also shows a favoring for electrophilic attack onto C_1. The same preference (and approximately the same magnitude of preference) is also noted for the two higher energy forms, **2e** and **2f**, in which the CH linkage also lies (roughly) in the plane of the double bond. On the other hand, conformers **2b–d** with the CO bond in plane show only slight regiochemical preferences (**2b** and **2c** for addition onto C_1, **2d** for preferential attack onto C_2). Given that these three structures are moderately abundant and (according to their HOMO energies) among the most reactive of the 3-buten-2-ol conformers, the prediction of the FMO model with regard to the overall regiochemistry of electrophilic addition is not entirely clear. The situation is similar for 2-fluorobut-3-ene, where the more abundant and more reactive conformer, **3a**, exhibits little preference for electrophilic attack onto one carbon or the other.

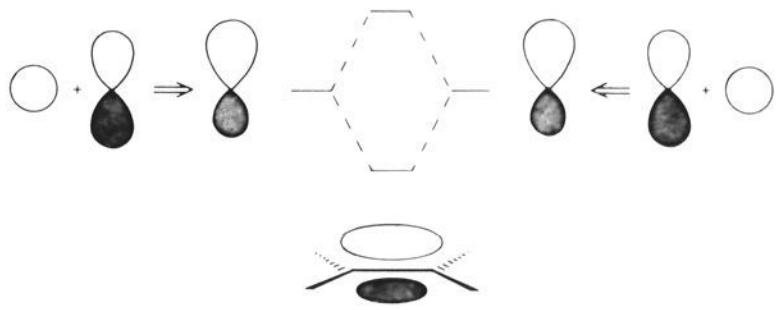
The FMO model suggests that electrophilic addition onto a chiral olefin should occur preferentially from that side in which the π bond is the more heavily localized.



This follows simply from the fact that stabilization afforded the electrophile increases as the square of its overlap with the π orbital on the substrate.[44] If, because of an inherent asymmetric environment, one side of the π orbital extends further into space than the other, it will better overlap with the approaching electrophile, and therefore afford the forming bond a greater degree of stabilization. This reasoning is identical with that employed in the application of FMO theory to the description of regiochemistry. Indeed, complete analysis of orbital size and shape provides information about both regio- and stereochemistry, i.e., the π bond in a chiral olefin will not only be directed toward one face or the other, but each face will itself be polarized toward one side or the other.

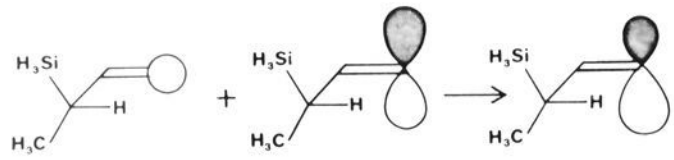


Polarization above or below the "plane" of a double bond incorporated into a chiral molecule is effected by mixing of valence s symmetry functions into the out-of-plane p orbitals, i.e,

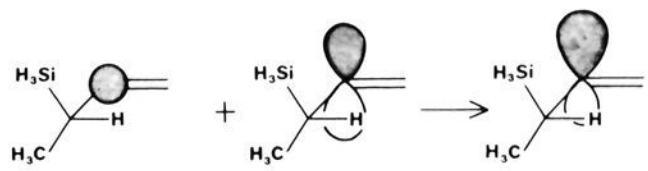


the larger the ratios of s to p orbital coefficients, the greater the degree of bond polarization. While it is difficult to predict on first principles the direction and magnitude of the polarization (as a function of the detailed asymmetric environment),[5] it is easy to extract this information from quantitative molecular orbital calculations in the form of the relative signs and weightings of any contributions which "in-plane" functions make to the olefinic π bond.[45] Data are provided in Table V for the three stable conformers of 2-silylbut-3-ene, for all nine forms of 3-buten-2-ol, and for the two stable conformers for each of 2-fluorobut-3-ene, (*E*)-2-fluoropent-3-ene, and (*E*)-1-cyano-3-fluorobut-1-ene.

The results for 2-silylbut-3-ene are not easily interpretable; π orbital polarizations for all three conformers are small,[46] and change both in magnitude and in sign with olefin position. The s orbital at C_1 in the ground-state conformer, **1a**, admixes with the p orbital to result in polarization away from the silyl group.



As the p orbital coefficient at C_1 is larger than at C_2 (vide supra), the conclusion of the FMO model is that electrophilic attack should occur here and *anti* to the silyl group. Note, however, that the relative signs of the s- and p-orbital coefficients at C_2 are the reverse, resulting in polaization of the π bond away from methyl.



Electrophilic attack here should occur *syn* to the silyl group. The calculated stereochemical preferences are reversed in the second low-energy conformer, **1b**. Attack onto C_1 (leading to the favored regioproduct) should occur *anti* to the silyl group, while addition onto C_2 should proceed with *syn* stereochemistry. Finally, electrophilic attack onto the highest energy conformer of 2-silylbut-3-ene (**1c**) is suggested by the FMO analysis to proceed with little stereochemical preference onto C_1 and *syn* to the methyl group at C_2.

The noted π-bond polarizations for the various conformers of 3-buten-2-ol (**2**) are also very small. According to the sign of the s orbital coefficient, the polarization at C_1 in **2a** is toward the methyl group (away from OH), whereas that of C_2 is in the opposite manner and to a somewhat greater degree. Obviously, assignment of preferred stereochemistry in this system on the basis of π orbital polarization is not without ambiguity. Essentially no facial preferences are displayed in the orbital coefficients at C_1 in conformers **2b–d** in which the carbon–oxygen linkage lies in the double bond plane. It is not possible to assign stereochemistry unambiguously on the basis of these data. On the other hand,

(44) This follows from simple perturbation molecular orbital theory. For discussions, see ref 12c and the following: (a) *Chemical Reactivity and Reaction Paths*, Klopman, G., Ed.; Wiley: New York, 1984. (b) Dewer, M. J. S.; Dougherty, R. C. *The PMO Theory of Organic Chemistry*; Plenum: New York, 1985.

(45) For pictorial representations of molecular orbitals, see: (a) Jorgensen, W. L.; Salem, L. *The Organic Chemists Book of Orbitals*; Academic: New York, 1970. (b) Hout, R. F., Jr.; Pietro, W. J.; Hehre, W. J. *A Pictorial Approach to Molecular Structure and Reactivity*; Wiley: New York, 1984.

(46) This has previously been noted. See ref 16.

the small preferences which are seen at C_2 suggest electrophilic attack *anti* to methyl in **2b** and *syn* to methyl in **2c** and **2d**. The noted preferences in **2d** (the conformer with the highest HOMO energy and presumaby the most reactive) are also very small; were this species to play a major role in the overall process, the FMO model would be at a loss to indicate stereochemistry.

Stereochemical preferences in the three conformers serving as models for cyclic allylic alcohols and ethers are also small and, except for that in structure **2i**, also change with regiochemistry. Attack onto C_1 (the preferred regiochemistry) of the most stable conformer **2g** is indicated to occur from the side of hydrogen, while addition onto C_1 in structure **2h** is suggested to be from the side of the OH group. The highest energy form, **2i**, shows no preference at C_1. Insignificant orbital polarizations are also noted of all stable conformers for all three allylic fluorides.

Supplementary Material Available: Appendices B (The Construction and Application of Chemical Reactivity Models), C (Improved Treatments of Electrophilic Reactivity. The Role of the Polarization Potential), and D (Calculated Equilibrium Structures) (10 pages). Ordering information is given on any current masthead page.

Modeling Chemical Reactivity. 5. Facial Selectivity in Diels–Alder Cycloadditions

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Contribution from the Department of Chemistry, University of California, Irvine, California 92717. *Received August 5, 1985. Revised Manuscript Received December 23, 1985*

Abstract: Diastereofacial selectivity in Diels–Alder cycloadditions involving chiral dienes and dienophiles is influenced by electrostatic interactions, independent of topological distortions involving the participating molecular orbitals. Modeling studies indicate that for reactions involving electron-rich dienes and electron-deficient dienophiles, addition occurs preferentially onto the diene face which is the more reactive toward electrophiles and onto the face of the dienophile which is the more reactive toward nucleophiles. Comparisons with available experimental stereochemical data are favorable except for reactions involving bridgehead dienophiles, where steric factors may come into play. Rules for the assignment of the reactive diene and dienophile diastereotopic faces are presented.

The simultaneous creation of four contiguous chiral centers continues to spur development in Diels–Alder cycloaddition chemistry.[1] Recent reports[2-12] have shown that allylic substitution on a diene or dienophile with heteroatom functionality effects marked diastereofacial selectivity in the ensuing carbon–carbon bond-forming reaction, and moreover, in at least one case, that "equivalent" diene and dienophile substitutions result in opposite stereochemical biases.[2a] Previous discussions of diastereofacial selective Diels–Alder cycloadditions have relied on simple steric arguments[13] or alternatively on topological distinctions involving the relevant frontier oribitals,[14,15] i.e., the HOMO on the diene and LUMO on the dienophile. In light of recent experience, which suggests that FMO theory is an ineffective tool for the elucidation of reaction regiochemistry[15a] and stereochemistry,[15b-d] we approach the latter class of arguments with considerable skepticism. The purpose of this paper is to suggest an alternative rationale for the observed diastereofacial selectivity in Diels–Alder cycloadditions and to provide a set of simple rules allowing predictive assignments to be made for new systems. Our developments are founded on the matching of complementary energy surfaces for the two cycloaddends and have resulted from our continuing efforts to develop simple and broadly applicable models for chemical reactivity.[16,17] They provide a consistent rationale for the complementary selectivities observed upon diene and dienophile substitution.

Discussion

It has been established that the observed regiochemistry of Diels–Alder cycloadditions of electron-rich dienes and electron-

(1) (a) Desimoni, G.; Tacconi, G.; Bario, A.; Pollini, G. P. *Natural Products Synthesis through Pericyclic Reactions*, ACS Monograph no. 180, American Chemical Society, Washington, DC, 1983. (b) Petrizilka, M.; Grayson, J. I. *Synthesis* **1981**, 753.

(2) (a) Franck, R. W.; Argade, S.; Subramanian, C. S.; Frechet, D. M. *Tetrahedron Lett.* **1985**, *26*, 3187. (b) Franck, R. W.; John, T. V. *J. Org. Chem.* **1983**, *48*, 3269. (c) Franck, R. W.; John, T. V.; Olejniczak, K. *J. Am. Chem. Soc.* **1982**, *104*, 1106. (d) Franck, R. W.; John, T. V. *J. Org. Chem.* **1980**, *45*, 1170.

(3) Boger, D. L.; Patel, M.; Takusagawa, F. *J. Org. Chem.* **1985**, *50*, 1911.

(4) (a) Yoshida, K.; Grieco, P. A. *Chem. Lett.* **1985**, 155. (b) Grieco, P. A.; Zelle, R. E.; Lis, R.; Finn, J. *J. Am. Chem. Soc.* **1983**, *105*, 1403.

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