The Role of Hyperconjugation In Determining the Stereochemistry of Nucleophilic Epoxidation and Cyclopropanation of Electrophilic Olefins[1]

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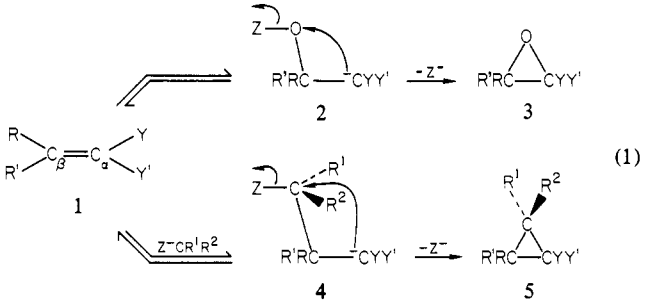
Abstract: The barriers to rotation in a number of β-substituted ethyl anions of the general formula $ZXCH_2CYY'^-$ where X = O, CH_2, and S, Z = Cl, F, H, OH, OCH_3, OCHO, SiH_3, and SH_2^+, and Y and/or Y′ = H, NO_2, and CN were calculated by standard ab initio methods using the STO-3G, 3-21G, 4-31+G, and 6-31G* basis sets. All the carbanions are more stable in the perpendicular conformation (**14**) where the carbanionic lone pairs and the C–X bonds are in the same plane. The barriers to rotation around the C–C^- bonds in the parent $ZXCH_2CH_2^-$ anions, which are a measure of the hyperconjugating ability (HCA) of the C–XZ bond, are as follows (in kcal mol^{-1}, STO-3G): X = O, Z = Cl (29.4) ≫ OCHO (19.8) > F (17.3) ~ OCH_3 (17.1) > OH (16.4) > SiH_3 (14.8) > H (12.4). With X = S the barriers are similar, i.e., Z = Cl (26.1) > H (15.1). The barriers to rotation are much lower for X = CH_2, i.e., Z = H_2S^+ (21.5) > Cl (10.0) > F (4.6) > H (2.3). Electron-withdrawing α-substituents reduce significantly the rotation barriers, i.e., $ClOCH_2CHCN^-$ (11.8) > $ClOCH_2C(CN)_2^-$ (6.3) ≃ $ClOCH_2CHNO_2^-$ (6.6) > $ClCH_2CH_2CHCN^-$ (3.9). Similar rotation barriers are obtained at higher levels of theory. This order of HCA is rationalized by PMO theory. The results of the calculations are used to analyze the stereochemistry of nucleophilic vinylic epoxidation and cyclopropanation. The following conclusions are obtained: (a) the higher the HCA of the C–XZ bond is the higher the stereospecificity; (b) α-electron-withdrawing substituents Y or Y′ lower the stereospecificity; (c) the better the nucleofugality of Z, the higher the stereospecificity; (d) the degree of stereospecificity should be nearly independent of the olefinic β-substituents, particularly for alkyl or aryl substituents; (e) cyclopropanation is much less stereospecific than the corresponding epoxidation. These conclusions, which are based on the hyperconjugation model, are fully consistent with the available experimental data. A unified picture of the stereochemistry of nucleophilic vinylic substitution, epoxidation, and cyclopropanation emerges. Predictions are given for reactions and systems that were not yet investigated.

Nucleophilic epoxidation[3-11] and cyclopropanation[9a,12-16] of electrophilic olefins (**1**, Y and/or Y′ = an electron withdrawing group, e.g., COR, CN, SO_2R) can be accomplished by using anionic oxygen and carbon nucleophiles, ZO^- and $Z^-CR^1R^2$, respectively, where Z is a nucleofuge (leaving group). The mechanisms of the two reactions are analogous and involve a multistep process (eq 1). For example, epoxidation by the most common



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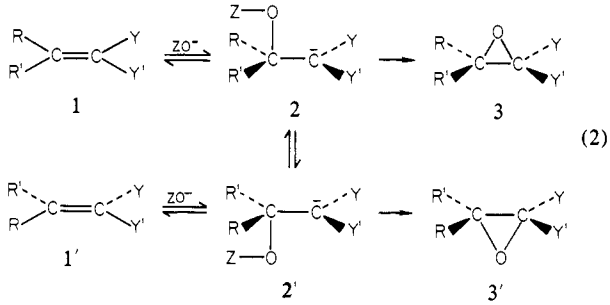
oxidant HOO^- proceeds by an initial nucleophilic attack at C_β of **1** to give the intermediate carbanion **2**, which yields the epoxide **3** by an intramolecular substitution of the carbanionic C_α at oxygen.[10] The reaction with Z = OH[11] or Cl[4a] is first order both in **1** and ZO^- and is retarded by a β-methyl group.[11] Similarly, cyclopropanation proceeds via the carbanion **4**, which cyclizes to **5** by an internal S_N2 reaction with expulsion of Z, which may be a neutral leaving group (e.g., Me_2S) when the nucleophile is an ylide[12,15,16] or a halogen.[13,14]

The stereochemistry of the epoxidation depends on the nature of both the nucleophile and the alkene. Oxidation of enones with alkaline H_2O_2 (Weitz–Scheffer reaction)[3] is usually stereoselective but not stereospecific, giving the same single epoxide from both *E* and *Z* precursors. In some cases this results from a base-catalyzed isomerization of **3** (when Y = H)[17] or from a nucleophilic *E*–*Z* isomerization of **1** to **1′** (eq 2, e.g., (*E*)-MeCH=

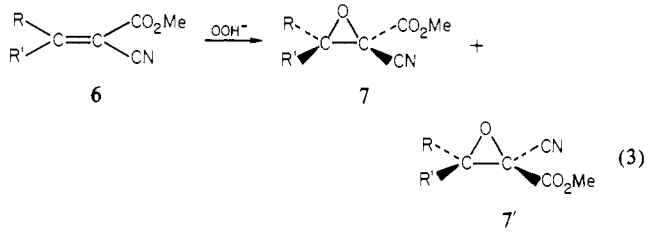


(2)

CMeCOMe)[17] caused by rotation of **2**, which is followed by the expulsion of the nucleophile.[18] However, in most cases stereoselectivity is attributed to a faster internal rotation around the C_α–C_β bond in **2** compared with nucleophilic displacement of Z.[10,11] Consequently, the intermediate isomeric carbanions **2** and **2′** (one enantiomer of each is shown) which are formed by nucleophilic attack on the isomeric olefins **1** and **1′** equilibrate before nucleofuge expulsion, and the ratio of the diastereomeric epoxides **3** and **3′** is exclusively determined by the relative energies of the transition states leading to them (eq 2). When Y = COR″, the isomer with the least hindered carbonyl group (i.e., cis to R when R is smaller than R′) is often the main product even when the trans R′ and Y′ arrangement is sterically more stable.[19]

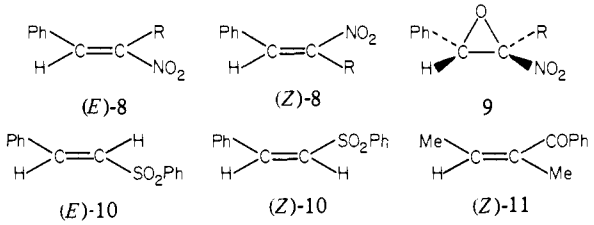
For PhCH=C(Ph)Y, Y = COMe or COPh, this was ascribed to overlap control in the transition state leading to the product.[19] With smaller activating groups than COR, hindrance to overlap control is smaller and steric interactions between other groups dominate. Thus, the least hindered epoxides are the exclusive products in the reactions of (*E*)-PhCH=C(Ph)CHO[20] and of (*Z*)-PhCH=C(Ph)CN.[21] Stereoselectivity was also found with other carbonyl-activated compounds.[22,23] The cyano-activated system **6**, R = H, R′ = Me, gives only **7**; when R = alkyl, R′ = Me, mixtures of **7** and **7′** are formed,[24] and for R = Ph, R′ = H, only **7′** is obtained[25] (eq 3).

Oxidation of the nitroolefins (*E*)-**8** and (*Z*)-**8** with H_2O_2/OH^- gives only epoxide **9** when R = Me.[6] Epoxidation of (*E*)-**8**, R = H or Ph,[7] which gives a single epoxide, may also be stereoselective. Epoxidation of the sulfones (*E*)-**10** and (*Z*)-**10** is stereoselective, yielding the same more stable trans epoxide.[5]



(3)

Electrophilic olefins **1**, Y = H, Y′ = CHO, COMe, $PO(OEt)_2$, can be epoxidized with *tert*-butyl hydroperoxide (Z = OBu-*t*).[10] The stereochemistry is known only for (*Z*)-**10**, which gives a 9:1 ratio of the trans (inverted) to the cis (retained) epoxide.[5] Higher specificity was obtained in the epoxidation of (*Z*)-**10** with *m*-chloroperbenzoate ion (Z = $OOCC_6H_4Cl$-*m*), which gives ≥95% of the cis epoxide.[5] However, epoxidation of (*E*)-**8** and (*Z*)-**8** is stereoselective, giving only **9**.[6]



Epoxidation with hypochlorite ion (Z = Cl) is mostly stereospecific. *cis*- and *trans*-3-arylideneflavanones containing the ArCH=CRCOR′ unit give stereospecifically the retained epoxides.[26] The sulfone (*Z*)-**10** yields exclusively the less stable retained *cis*-epoxy sulfone,[5] and both (*E*)- and (*Z*)-α-cyanocinnamates **6** give in most cases (except when R = Ph, R′ = H) the retained epoxides.[8] However, epoxidation of the nitroolefins (*Z*)-**8** with KOCl yields a ca. 1:1 mixture of the two isomeric nitro epoxides whereas epoxidation of the ketone (*Z*)-**11** with KOCl gives a 4:1 mixture of the retained to the inverted epoxide.[6] In conclusion, the stereospecificity of the epoxidation is reduced when (a) the nucleofuge Z becomes poorer, i.e., in the order Cl > $OOCC_6H_4Cl$-*m* > OH > OBu-*t*[5] and (b) the ability of Y and Y′ to disperse the negative charge increases.

The stereochemistry of cyclopropanation when Z = halogen is sometimes complicated by the isomerization of the initially formed cyclopropane. When this is avoided by appropriate substitution, a single precursor olefin yields two isomeric cyclopropanes in a ratio that is dependent on the solvent and the activating group.[13] These reactions are clearly not stereospecific. Attractive interaction between the activating group Y and the positive end of the dipole of an electron-withdrawing group R^1 or R^2 on the nucleophilic moiety was invoked.[13d] Similarly, cyclopropanation of an *E*:*Z* mixture of *i*-PrC(Me)=C(CN)CO_2Et with $BrC(CN)_2^-$ gave a single isomer in a stereoselective but not a stereospecific reaction.[14a] Strong evidence for a carbanionic intermediate in a related reaction was recently reported.[14d]

A more common nucleophilic cyclopropanation involves nucleophilic ylides, especially sulfur ylides, where intermediate **4** (Z = $^+SR_2$[3]) is a zwitterion.[12,15,16] In many such reactions a single isomeric precursor gives a single cyclopropane in an apparent stereoselective reaction,[12x–z,15d–f,16a] whereas in other cases an identical mixture of cis and trans cyclopropanes was obtained from either of the isomeric olefins.[16a] For example, both diethyl maleate and fumarate give the trans-substituted cyclopropane with a chiral oxosulfonium methylide,[15d] and in the former reaction partial isomerization to the fumarate takes place.[15d] An oxosulfonium methylide gives a 1:1 mixture of the corresponding cyclopropanes with either (*E*)- or (*Z*)-1,2-diphenylvinyl sulfone.[15c] However, partial stereospecificity was observed in a few cases. Reaction of $Ph_2{}^+S^-CMe_2$ with dimethyl fumarate at low temperature gives exclusively the trans cyclopropane, whereas dimethyl maleate gives

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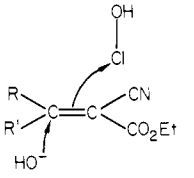
a 7:1 cis/trans mixture.[15b] Likewise, complete retention with the fumarate and formation of a 2:1 trans/cis mixture with the maleate were obtained with $Me_2{}^+S^-CHCO_2Et$.[15f]

The accepted epoxidation mechanism with HOO^- follows eq 2, where the **2** ⇌ **2′** equilibration is faster than cyclization. This leads to a stereoselectivity that is reasonable in view of the poor nucleofugality of OH. However, the retention stereospecificity in epoxidation with ClO^- requires a faster cyclization than internal rotation.[5] However, Robert and Foucaud[8] suggested an alternative concerted thermolecular reaction, which via transition-state **12** gives stereospecifically a chlorohydrin that cyclizes stereospecifically.



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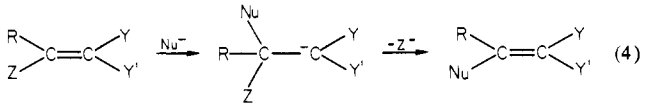
The nonstereospecific cyclopropanation is attributed to formation of a long-lived carbanion or a zwitterion. The conformational stabilities of these intermediates provide a rationale for the observed stereochemistry.[16a]

The stereochemistry of epoxidation and of nucleophilic vinylic substitution (eq 4) is almost identical. Stereoconvergence[27] is



(4)

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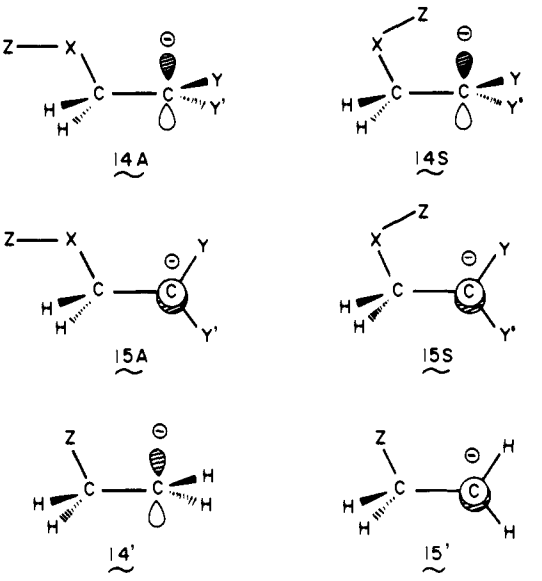
observed[28] with poor nucleofuges Z (e.g., OPh, F),[29] but the reaction is stereospecific, leading to retention,[28] with good nucleofuges (e.g., Cl) except for highly activated olefins (e.g., when Y = NO_2) that generate long-lived carbanions **13**.[1,30]

We have suggested recently on the basis of MO calculations that the stereospecificity in these substitution reactions is due to a high rotation barrier in the intermediate carbanion **13**,[31a] e.g., 16.7 kcal mol^{-1} in $ClCH_2CH_2^-$.[31a] We attributed these high barriers to a net stabilizing hyperconjugation between the occupied 2p(C^-) orbital and the β-C-substituent bond orbitals, which is maximal when these orbitals are in the same plane. As the hyperconjugation with the nucleofuge (Z in **13**) is usually the strongest, the initially formed carbanionic conformer rotates by 60° in order to maximize the hyperconjugative interactions and retention results.[31a] Similar qualitative arguments were suggested by others.[31b] We believe that hyperconjugation also determines the stereospecificity of the epoxidation with ClO^- and that it is a major contributing factor to the other stereochemical results given above. In the present paper we use MO calculations for estimating the barriers to rotation in the intermediates of epoxidation (**2**) and cyclopropanation (**4**). These results are then used to rationalize the available data and for further predictions.

Results and Discussion

Computation Method. We have used standard ab initio methods[32] for calculating a number of model β-substituted ethyl anions of the general formula $ZXCH_2CYY^-$, where X = O, S, and CH_2 and Y and/or Y′ = H, CN, and NO_2. Most of the calculations were performed for X = O. Eight substituents Z were studied, i.e., Z = Cl, F, H, OH, OCH_3, OCHO, SiH_3, and H_2S^+. For each carbanion we have studied two conformations, **14A** and **15A** (Chart I) with respect to the central C–C^- bond. In the perpendicular[33a] conformations **14** the carbanionic lone pair (i.e., the 2p(C^-) orbital) is in the same plane as the C–X bond, while in the eclipsed[33b] conformations **15** these orbitals are in perpendicular planes. In some cases we have also calculated two conformations with respect to rotation around the X–Z bond for each carbanion **14** or **15**, i.e., **14A** and **15A** (anti) where the ZXCC dihedral angle is 180°, and **14S** and **15S** (syn) where this angle is 0°.

Chart I[a]



[a] X = O, S, and CH_2; Z = Cl, F, H, OH, OCH_3, OCHO, SiH_3, and $^+SH_2$; Y = Y′ = H, CN and NO_2.

Calculations were carried out at several levels of sophistication. The carbanions were first calculated with the minimal STO-3G basis set using standard geometries[34] (denoted as STO-3G/STAN.). For the most stable conformation of type **14** (**14A**) and of type **15** (**15A**),[35] we have carried out full geometry optimizations at the minimal STO-3G basis set[36a] (i.e., STO-3G//STO-3G) except for the C–H bond lengths and for the carbanionic center, which was kept planar. Single point calculations at the optimized STO-3G structures were then carried out with the split-valence 3-21G basis set[36b] (i.e., 3-21G//STO-3G) and in some cases also with the polarized 6-31G* basis set[36c] (i.e., 6-31G*//STO-3G). For Z = F, H, and OH we have also used the diffused 4-31+G basis set, which is particularly suitable for anions.[37] $ClOCH_2CHCN^-$, $ClOCH_2C(CN)_2^-$, $ClOCH_2CHNO_2^-$, and $ClCH_2CH$-

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(32) The GAUSSIAN 80 series of programs were used: Whitesides, R. A.; Binkley, J. S.; Krishnan, R.; De Frees, D. J.; Schlegel, H. B.; Pople, J. A. Program No. 406, QCPE, Indiana University, Bloomington, In.
(33) These conformations are often referred to as (a) perpendicular and (b) planar.
(34) For the $OCH_2CH_2^-$ fragment we have used the following parameters: C–C^- = 1.487, C–O = 1.43, C–H = 1.065, $^-$C–H = 1.09 Å; ∠HC^-H = 120.0, ∠OCC^- = 109.47, ∠HCH = 109.47°. The ZOC bond angles and the bond angle within the Z fragment were fixed at 109.47°. The bond lengths (Å) associated with Z were as follows: Z = H, O–H = 0.96; Z = F, O–F = 1.355; Z = Cl, O–Cl = 1.738; Z = OH, O–O = 1.48; O–H = 0.96; Z = SiH_3, O–Si = 1.686; Si–H = 1.421. See also Table I.
(35) With Z = H conformations **14S** and **15S** are the most stable, but geometry optimizations were carried out for **14A** and **15A**.
(36) (a) First row: Hehre, W. J.; Stewart, R. F.; Pople, J. A. *J. Chem. Phys.* **1969**, *51*, 2657. Second row: Hehre, W. J.; Ditchfield, R.; Stewart, R. F.; Pople, J. A. *Ibid.* **1970**, *52*, 2769. (b) First row: Binkley, J. S.; Pople, J. A.; Hehre, W. J. *J. Am. Chem. Soc.* **1980**, *102*, 939. Second row: Gordon, M. S.; Binkley, J. A.; Pietro, W. J.; Hehre, W. J. *Ibid.* **1982**, *104*, 2797. (c) First row: Hariharan, P. C.; Pople, J. A. *Theor. Chim. Acta* **1973**, *28*, 213. Second row: 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.
(37) Chandrasekhar, J.; Andrade, J. G.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1981**, *103*, 5609.

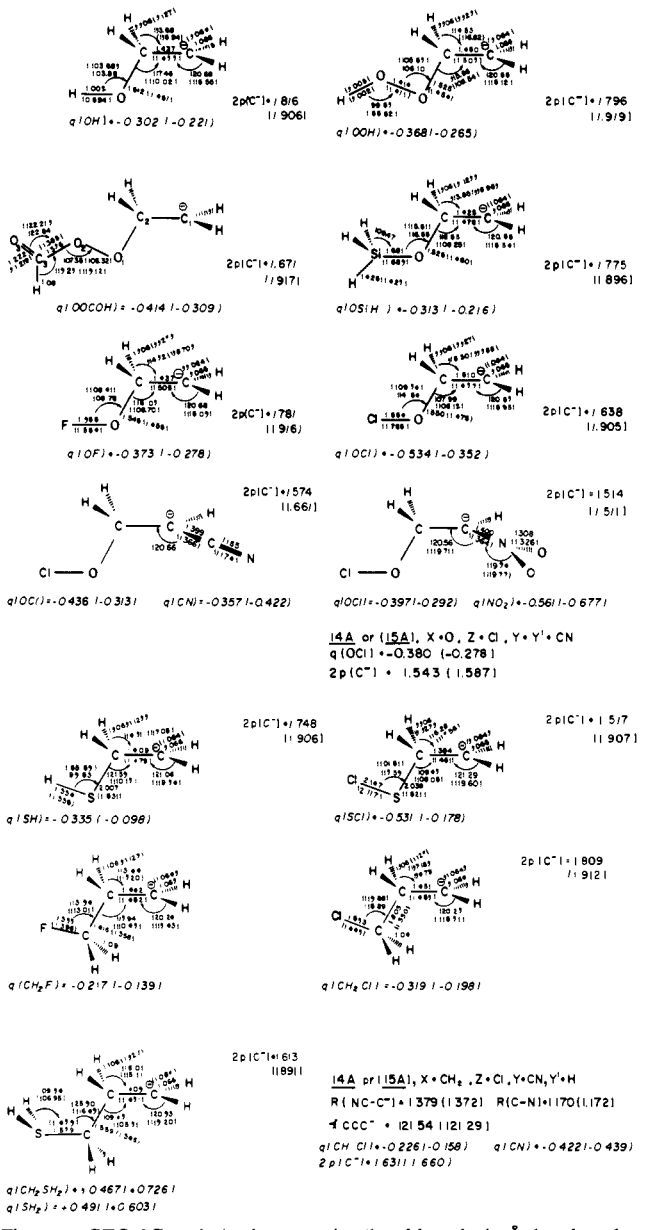


Figure 1. STO-3G optimized geometries (bond lengths in Å, bond angles in deg), total atomic charges of the XZ fragments and the populations of the 2p(C^-) orbitals of various $XZCH_2CYY'^-$ anions in conformations **14A** and **15A**. Values in parentheses are for conformations **15A**.

CN^- were also calculated at STO-3G by using the optimized geometries of $ClOCH_2CH_2^-$ and $ClCH_2CH_2CH_2^-$ respectively, but with optimization of the CN and the NO_2 groups.

Computation Results. The optimized structures of the carbanions are shown in Figure 1, and their total and relative energies are given in Table I. The β-oxycarbanions (**14**, X = O), which were studied in the greatest detail, are analyzed first.

Several conclusions can be drawn from Table I: (a) The perpendicular conformations **14** are more stable than the corresponding eclipsed structures **15**. (b) The most stable structure of all the carbanions (except for Z = H) is **14A**, in which the carbanionic 2p(C^-) orbital, the C–C, the C–O, and the O–Z bonds are arranged in a W alignment. (c) The barriers to rotation around the central C–C^- bond (i.e., the energy difference (**15A**–**14A**)) are substantial and follow the order Cl ≫ OCHO > F ~ OCH_3 > OH > SiH_3 > H.

These results can be understood in terms of simple PMO theory.[38] The concept of hyperconjugation (HC)[39] that was used

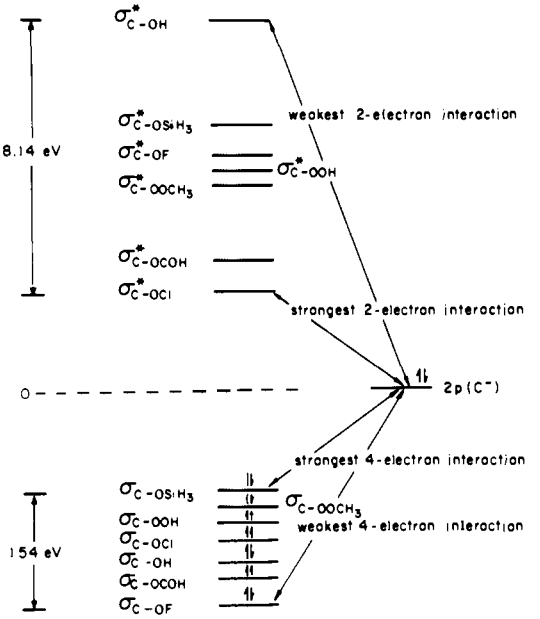


Figure 2. Schematic hyperconjugative interaction diagram (based on STO-3G calculations) between the carbanionic 2p(C^-) orbital and the orbitals of the C–OZ bonds in various $ZOCH_2CH_2^-$ carbanions.

extensively in recent years to account for a variety of stereoelectronic effects[40-42] is particularly useful. Most relevant is our suggestion that HC is an important factor in determining the stereochemistry of nucleophilic vinylic substitution.[31a] HC is described as resulting from the interaction between an empty (i.e., in carbenium ions) or a filled orbital (i.e., in carbanions, amines, etc.) and the β-bonds.[38,39] More specifically, anionic HC in $ZCH_2CH_2^-$ results from interaction between the carbanionic lone pair and the adjacent σ_{C-Z} bond. Two major interactions that involve the 2p(C^-) orbital should be considered: (a) A stabilizing two-electron interaction with the empty σ^*_{C-Z} that depends on the energy separation (ΔE) between the interacting orbitals and on their overlap. The smaller ΔE and the larger the overlap, the greater is the stabilizing effect.[38] (b) A four-electron destabilizing interaction with the filled σ_{C-Z} bonding orbital. This interaction is usually assumed to become more destabilizing as the sum of the energies of the interacting orbitals is less negative (i.e., higher in energy).[38b] This four-electron interaction is believed to be less important than the two-electron interaction.[38b,41h] Consequently, in most cases the overall interaction between the filled 2p(C^-) orbital and β-C–Z bonds is stabilizing.

In the perpendicular conformations (**14'**) the orbitals of interest (i.e., the 2p(C^-) and the σ_{C-Z} bond) are in the same plane and both the two- and the four-electron interactions are maximal. In the eclipsed conformations (**15'**) these orbitals are orthogonal, their interaction is nil, and the 2p(C^-) orbital interacts (i.e., hyper-

(38) (a) Fleming, I. "Frontier Orbitals and Organic Chemical Reactions"; Wiley: London, 1976. (b) Epiotis, N. D.; Cherry, W. R.; Shaik, S.; Yates, R. L.; Bernardi, F. *Top. Curr. Chem.* **1977**, *70*, 1.

(39) Hoffmann, R.; Radom, L.; Pople, J. A.; Schleyer, P. v. R.; Hehre, W. J.; Salem, L. *J. Am. Chem. Soc.* **1972**, *94*, 6221.

(40) For leading older references see: (a) Dewar, M. J. S. "Hyperconjugation"; Ronald Press: New York, 1962. (b) Holtz, D. *Prog. Phys. Org. Chem.* **1971**, *8*, 1.

(41) For more recent references see: (a) Apeloig, Y. *J. Chem. Soc., Chem. Commun.* **1981**, 390. (b) Deslongchamps, P. *Tetrahedron* **1975**, *31*, 2463; *Heterocycles* **1977**, *7*, 1271. (c) Kost, D.; Raban, M. *J. Am. Chem. Soc.* **1982**, *104*, 2960 and references therein. (d) Lehn, J. M.; Wipff, G. *Ibid.* **1980**, *102*, 1347. (e) Jeffrey, G. A.; Pople, J. A.; Binkley, J. S.; Vishreshwara, S. *Ibid.* **1978**, *100*, 373. (f) Kaloustain, M. K.; Khouri, F. *Ibid.* **1980**, *102*, 7579. (g) Pross, A.; Radom, L. *Aust. J. Chem.* **1980**, *33*, 241. These authors have shown that with electropositive substituents such as Li and BH_2 that posses empty acceptor orbitals direct 1,3-interactions are also important. (h) Andreetti, G. D.; Bernardi, F.; Bottoni, A.; Fava, A. *J. Am. Chem. Soc.* **1982**, *104*, 2176. (i) Thibblin, A.; Ahlberg, P. *Ibid.* **1977**, *99*, 7926. (j) Ahlberg, P. *Chem. Scr.* **1980**, *15*, 121. (k) Bingham, R. C. *J. Am. Chem. Soc.* **1975**, *97*, 6743. (l) Schleyer, P. v. R.; Kos, A. J. *Tetrahedron*, in press.

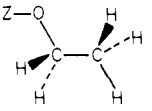
(42) For an alternative viewpoint arguing that HC is of minor importance see ref 40b and also see: Streitwieser, A., Jr.; Berke, C. M.; Schriver, G. W.; Grier, D.; Collins, J. B. *Tetrahedron Suppl. 1* **1981**, 345.

Table I. Total (in hartrees) and Relative Energies (kcal mol^{-1}) of $ZXCH_2CYY'^-$ Anions in Conformations 14A and 15A

	method							
	STO-3G/STAN[a]		STO-3G/STO-3G[b]		3-21G/STO-3G		6-31G*/STO-3G	
compd[c]	total[d]	rel[e]	total[d]	rel[e]	total[d]	rel[e]	total[d]	rel[e]
14A, X = O; Z = H	−151.236 82	0.0 (4.2)[f]	−151.250 26	0.0	−152.499 86	0.0 (0.0)[o,p]	−153.352 67	0.0
15A	−151.218 49	11.5 (4.5)[g]	−151.230 55	12.4	−152.478 02	13.7 (14.5)[o,p]	−153.331 74	13.1
14A, X = O; Z = OH	−225.048 04	0.0	−225.070 59	0.0	−226.880 64	0.0 (0.0)[o,q]	−228.128 27	0.0
15A	−225.021 83	16.4	−225.044 40	16.4	−226.849 81	19.3 (18.2)[o,q]	−228.099 85	17.8
14A, X = O; Z = SiH_3	−438.039 80	0.0	−438.055 23[h]	0.0	−441.097 70	0.0		
15A	−438.020 58	12.1	−438.031 64	14.8	−441.069 35	17.8		
14A, X = O; Z = F	−248.677 64	0.0 (11.4)[f]	−248.691 19	0.0	−250.758 94	0.0 (0.0)[o,r]	−252.118 53	0.0
15A	−248.653 54	15.1 (10.6)[g]	−248.663 57	17.3	−250.722 61	22.8 (21.7)[o,r]	−252.086 07	20.4
14A, X = O; Z = Cl	−605.262 41	0.0 (27.1)[f]	−605.235 08	0.0	−609.226 09	0.0	−612.232 99	0.0
15A	−605.223 68	24.3 (38.7)[g]	−605.281 97	29.4	−609.171 36	34.3	−612.186 98	28.9
14A, X = O; Z = OMe			−263.659 31[i,j]	0.0	−265.699 59	0.0		
15A			−263.632 05[i,j]	17.1	−265.667 54	20.1		
14A, X = O; Z = OCHO			−336.335 66[i,k]	0.0	−339.009 75	0.0		
15A			−336.304 14[i,k]	19.8	−338.971 26	24.2		
14A, X = O; Z = Cl; Y' = NO_2			−806.076 29[l]	0.0				
15A			−806.065 78[l]	6.6				
14A, X = O; Z = Cl; Y' = CN			−695.904 78[l]	0.0	−700.502 13	0.0		
15A			−695.885 88[l]	11.8	−700.473 50	18.0		
14A, X = O; Z = Cl; Y = Y' = CN			−786.502 52[l]	0.0				
15A			−786.492 43[l]	6.3				
14A, X = S; Z = H			−470.601 53	0.0	−473.660 09	0.0	−476.038 20	0.0
15A			−470.577 51	15.1	−473.617 38	26.7	−476.007 79	19.1
14A, X = S; Z = Cl			−924.666 40[m]	0.0	−930.426 42	0.0		
15A			−924.624 79	26.1	−930.348 80	48.7		
14A, X = CH_2; Z = Cl			−570.019 04	0.0	−573.628 77	0.0		
15A			−570.003 06	10.0	−573.610 13	11.7		
14A, X = CH_2; Z = F			−213.443 48	0.0	−215.204 72	0.0		
15A			−213.436 17	4.6	−215.199 72	3.1		
14A, X = CH_2; Z = Cl; Y = H; Y' = CN			−660.665 55[l]	0.0				
15A			−660.659 36[l]	3.9				
14A, X = CH_2; Z = SH_2^+			−509.718 69[m,n]	0.0	−512.892 72	0.0		
15A			−509.684 47	21.5	−512.862 09	19.2		

[a] See ref 34. [b] Fully optimized except that the carbanionic center (C_1) was kept planar and the C-H bond lengths were held at the optimized values in 14A and 15A, X = O, Z = H. [c] Y = Y' = H unless otherwise stated. [d] In hartrees. [e] In kcal mol^{-1}. [f] The energy of 14S relative to that of 14A. [g] The energy of 15S relative to that of 15A. [h] The silyl group was kept tetrahedral. [i] The geometry of the $OOCH_2CH_2^-$ fragment was held at the optimized values 14A (or 15A), X = O, Z = OH. [j] The CH_3-O bond lengths and the CH_3-O-O bond angle were optimized. The optimized values are 14A (15A) CH_3-O = 1.442 (1.440) Å and 14A (15A) ∠CH_3-O-O = 104.1° (103.6°). The methyl group was kept tetrahedral, and its C-H bond lengths were held at 1.093 Å. [k] The O_2-C_3 and the C_3-O_3 bond lengths and the C_3-O_2-O_1, O_3-C_3-O_2, and H-C_3-O_2 bond angles were optimized (Figure 1). [l] The optimized geometries of 14A (or 15A), X = O (or X = CH_2), Z = Cl, were used, except that the geometries of Y and Y' were fully optimized. [m] The S-C-C angle was held at 109.47°; see footnote 52a. [n] The S-C-C angle was held at 109.47° and the C-S^+ bond length was held at 1.879 Å; see footnote 52b. [o] At 4-31+G/STO-3G. [p] Total energy: 14A = −153.178 42, 15A = −153.155 31 hartrees. [q] Total energy: 14A = −227.852 28, 15A = −227.823 34 hartrees. [r] Total energy: 14A = −251.830 96, 15A = −251.796 34 hartrees.

conjugates) only with the β-C–H bonds. Calculations and qualitative arguments show that anionic HC is stabilizing if the β-substituent is more electronegative than hydrogen[41] (see, however, ref 41g). In $ZCH_2CH_2^-$, the rotation barriers around the C–C$^-$ bonds, which measure the hyperconjugative ability (HCA) of Z, increase roughly with the increasing electronegativity of Z in the order Z = F ~ OH > NH_2 > CH_3.[31,41g] A β-OH substituent has a relatively high HCA, ranging from 11.5 to 14.5 kcal mol^{-1}, depending on the basis set and the geometry (Table I). Replacing the hydroxylic hydrogen in $HOCH_2CH_2^-$ by Z is expected to a first approximation to affect the HCA of the β-C–O bond moderately and less than in $ZCH_2CH_2^-$ since regardless of the identity of Z, the main hyperconjugative interactions occur with a C–O bond. However, Z inductively shifts the energies of the σ_{C-O} and the σ^*_{C-O} orbitals and thus perturbs the HCA of the C–O bonds. In fact, the HCAs of the OZ groups span over a large range, i.e., from 12.4 to 29.4 kcal mol^{-1} and follow the order OCl ≫ OOCHO > OF ~ $OOCH_3$ > OOH > $OSiH_3$ > OH (Table I).[43] This is indeed the expected order if the rotation barriers are determined mainly by HC. Thus, a qualitative correlation exists between the calculated rotation barriers in $ZOCH_2CH_2^-$ and the σ^*_{C-O} orbital energies in the corresponding neutral **16**[44] (Figure 2). The calculated energies of the σ^*_{C-OZ}



16

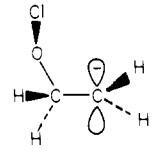
orbitals in **16**[44,45] (STO-3G, hartrees), follow the order Z = Cl (E = 0.2630) < Z = OCHO (E = 0.3001) < Z = OCH_3 (E = 0.4058) < Z = OH (E = 0.4131) < Z = F (E = 0.4490) < Z = SiH_3 (E = 0.4734) < Z = H (E = 0.5594). Thus, roughly the

(43) This scale is based mainly on the 6-31G* caluclations except for Z = OCHO, OCH_3, and SiH_3, where only STO-3G calculations are available.

(44) The anti (i.e., ∠ZOCC = 180°) fully staggered conformations were calculated. Standard geometries were used (i.e., C–C = 1.54, C–O = 1.43, and C–H = 1.09 Å, and all angles were kept tetrahedral). The Z–O bond lengths were fixed at 1.74, 1.36, 1.48, and 1.70 Å for Z = Cl, F, OH, and SiH_3, respectively. For Z = OCH_3, C–O = 1.43 and C–H = 1.09 Å. For Z = OCHO, O–C = 1.36, C=O = 1.22, C–H = 1.08 Å, and bond angles of 120° around the carbonyl were used. The Si–H and O–H bond lengths were 1.421 and 0.96 Å, respectively.

(45) The σ^*_{C-O} and the σ_{C-O} orbitals are delocalized. In **16**, Z = Cl, F, and OH, for example, the σ^*_{C-O} orbitals mix strongly with the lone pairs on the Z atoms. This orbital mixing is especially large for Z = Cl, which possess the highest lying lone pairs. Orbital mixing with the σ^*_{C-O} orbitals is, however, weaker than with the σ_{C-O} orbitals so that the σ^*_{C-O} orbitals can be identified easily.

lower the energy of the σ^*_{C-OZ} orbital, the stronger is the stabilizing two-electron interaction in **14** and the higher is the HCA(Z) and the rotation barrier around the C–C$^-$ bond (Table I and Figure 2). The destabilizing four-electron interaction is more difficult to analyze,[46] because the C–O orbitals are mixed strongly with other orbitals (mainly with the lone pairs on Z) so that several orbitals have significant C–O bonding character.[45] The highest C–O bonding orbitals in **16** that possess also a significant coefficient at C_1 follow the order (STO-3G, hartrees) Z = SiH_3 (E = −0.3505) > Z = OCH_3 (E = −0.3581) > Z = OH (E = −0.3686) > Z = Cl (E = −0.3839) > Z = H (E = −0.3963) > Z = OCHO (E = −0.4053) > Z = F (E = −0.4072). The four-electron interaction is expected to be more destabilizing the higher the energy of the σ_{C-O} orbital (Figure 2).[38,39,46] On the basis of the four-electron interactions alone the barriers to rotation in **14**, X = O, are expected to decrease in the order Z = F > OCHO > H > Cl > OH > OCH_3 > SiH_3. This is not the trend that we find. Apparently, the destabilizing four-electron interactions play a secondary role[47] and may modify the magnitude of the rotation barriers. For example, the rotation barriers in **14**, X = O, Z = OH, is by 2.6 kcal mol^{-1} lower than in **14**, X = O, Z = F (Table I), although the energy of the σ^*_{C-O} orbital in **16**, Z = OH, is considerably lower than in **16**, Z = F. The stronger attractive two-electron interaction in **14**, X = O, Z = OH, compared with **14**, X = O, Z = F, is apparently counterbalanced by the stronger repulsive four-electron interaction in the former. The exceptionally strong effect of the remote chlorine on the rotation barrier around the C–C$^-$ bond (i.e., 28.9 kcal mol^{-1} at 6-31G*) results primarily from the very low energy of the σ^*_{C-OCl} orbital, which at STO-3G is 4.16 and 8.14 eV lower than those of σ^*_{C-OOH} and σ^*_{C-OH}, respectively (the energy difference between σ^*_{C-OF} and σ^*_{C-OH} is only 3.00 eV). In addition, a strong 1,3-interaction exists between the 2p(C$^-$) orbital and the low-lying σ^*_{O-Cl} orbital.[48] In **14**, X = O, Z = F, such 1,3-interactions are both much smaller. The importance of the 1,3-2p(C$^-$)–σ^*_{O-Cl} interaction is reflected in the exceptionally high barrier for rotation around the C–O bond in $ClOCH_2CH_2^-$. Rotation of the chlorine by 90° to conformation **14O**, where the O–Cl bond and the 2p(C$^-$) orbital are orthogonal



14O

and do not interact, requires 16.7 kcal mol^{-1} compared with only 8.2 kcal mol^{-1} in **15** (STO-3G). Other factors contribute to the exceptionally high HCA of the C–OCl bond: (a) the high polarizability of chlorine;[49] (b) the destabilizing four-electron interaction, which is relatively weak when Z = Cl since the highest σ_{C-O} orbital is concentrated at oxygen so that the orbital coefficient at C_1 is small. A similar large effect of a remote chlorine is found in the corresponding **14**, X = CH_2, Z = Cl[50] (vide infra).

Hyperconjugation is also reflected in the geometries and the charge distributions of the β-substituted anions. According to the HC model, the 2p(C$^-$)–σ^*_{C-O} interaction, which represents a transfer of electrons into an antibonding orbital, is expected to cause a lengthening of the C–O bonds accompanied by a parallel shortening of the C–C$^-$ bonds in conformations **14** but not in **15**. Indeed, C–O bond lengths are longer and C–C$^-$ bonds are shorter in **14** than in **15** (Figure 1). The pronounced antiphase relationship of the C–O and the C–C$^-$ bond lengths strongly suggests that these changes are manifestations of the same phenomenon (i.e., HC). The O–Z bond lengths are also longer in **14** compared with **15**, but the differences are smaller than in the C–O bonds. HC is expected to be accompanied by a net charge transfer from the 2p(C$^-$) orbital to the σ^*_{C-OZ} orbital. Indeed the population of the 2p(C$^-$) orbital decreases as the HCA of the OZ groups increases (Figure 1). The lowest population (1.66 electrons) is found in **14**, X = O, Z = Cl, and the highest (1.85 electrons) in **14**, X = O, Z = H.[51] The contrast with the eclipsed conformations is striking. In **15**, X = O, the population of the 2p(C$^-$) orbital is ca. 1.94 electrons regardless of substituent Z.[51] Similarly, the total charge on the OZ group is higher in conformation **14** than in **15** (Figure 1). The other anions (i.e., X = S, CH_2) behave similarly (Figure 1). In the isoelectronic amines (e.g., FCH_2NH_2), charge transfer to fluorine is very small.[41c] Apparently, HC is accompanied by significant charge transfer only in charged species. We note that Streitwieser et al. have criticized the use of Mulliken population analysis and showed that the integrated spatial populations around the fluorine atom in conformations **14′** and **15′** of $FCH_2CH_2^-$ are nearly the same.[42] These authors argue that these conformations differ in the extent of polarization of the electrons rather than in direct charge transfer.

Rotation around the C–O bond was examined for **14**, X = O, with Z = Cl, F, and H. The anti structures (i.e., ∠ZOCC = 180°) are most stable for Z = F and Cl in both the perpendicular (**14A**) and the eclipsed (**15A**) conformations. For Z = H, on the other hand, the syn conformations (**14S**, **15S**, X = O) are more stable. The syn–anti energy differences in **14A**, X = O, Z = F or Cl, are very high, ca. 11–27 kcal mol^{-1}. The major reason for the lower stability of the syn conformations (with Z = F, Cl) is the electrostatic repulsion between the CH_2^- unit and the negatively charged Z substituent. In **14**, X = O, Z = H (or **15**, X = O, Z = H), on the other hand, the syn conformation is stabilized by electrostatic attraction between the positively charged hydroxylic hydrogen (+0.16) and C$^-$ in **14S**, X = O, or the cis hydrogen of the CH_2^- unit in **15S**, X = O.

The discussion above and the main conclusions regarding the $ZOCH_2CH_2^-$ anions apply also to the other β-substituted anions in Table I (i.e., **14**, X = S, CH_2). The rotation barriers in these anions are determined primarily by the HCA of the C–X bonds: those in $HOCH_2CH_2^-$ and $HSCH_2CH_2^-$ are 13.1 and 19.1 kcal mol^{-1}, respectively, at 6-31G*. Similarly, the rotation barrier in $ClSCH_2CH_2^-$ is 26.1 kcal mol^{-1}, only 3.3 kcal mol^{-1} lower than in $ClOCH_2CH_2^-$.[52a] An unsubstituted C–C bond has a poor HCA: the rotation barrier in $H_3C-CH_2CH_2^-$ is only 2.1 kcal mol^{-1} (STO-3G/STAN.).[31a] Attachment of an electron-withdrawing substituent as in **14**, X = CH_2, Z = Cl, F, or $^+SH_2$, increases the rotation barriers around the C–C$^-$ bonds, but they remain considerably lower than in the corresponding $ZOCH_2CH_2^-$.[52b] For

(46) The four-electron destabilizing interaction in conformation **15** between the 2p(C$^-$) orbital and the π type orbitals of the $ZOCH_2$ fragment are undoubtly larger than the 2p(C$^-$)–σ_{C-OZ} interactions in conformation **14**. However the energies of the π_{CH_2} (and of the 2p(C$^-$)) orbitals are the same regardless of Z, and therefore the energies of the σ_{C-OZ} orbitals and not those of the π_{CH_2} orbitals are assumed to be important in comparing different carbanions.[38,39,41] This assumption is correct only to a first approximation, because Z effects the energy of the 2p(C$^-$) and the π_{CH_2} orbitals inductively (see, for example: Wolfe, S.; Mitchell, D. J.; Schlegel, H. B.; Minot, C.; Eisenstein, O. *Tetrahedron Lett.* **1982**, *23*, 615).

(47) Similar conclusions were reached by others for various stereoelectronic effects.[38,41] See also: (a) Kost, D.; Zeichner, A.; Sprecher, M. S. *J. Chem. Soc., Perkin Trans. 2* **1980**, 317 (in particular pages 322–323). (b) Wolfe, S.; Whangbo, M.-H.; Mitchell, D. J. *Carbohydr. Res.* **1979**, *69*, 1. (c) Cowley, A. H.; Mitchell, D. J.; Whangbo, M.-H.; Wolfe, S. *J. Am. Chem. Soc.* **1979**, *101*, 5224 and references therein.

(48) For example, $E[\sigma^*_{O-Cl}(HOCl)] - E[\sigma^*_{C-O}(CH_3OH)]$ = 8.5 eV (STO-3G).

(49) The importance of the polarizability of the β-substituent was emphasized by Streitwieser et al.[42]

(50) Lehn, J. M.; Wipff, G. *Tetrahedron Lett.* **1980**, *21*, 159.

(51) Similar results were reported for the $ZCH_2CH_2^-$ anions using standard geometries.[41g]

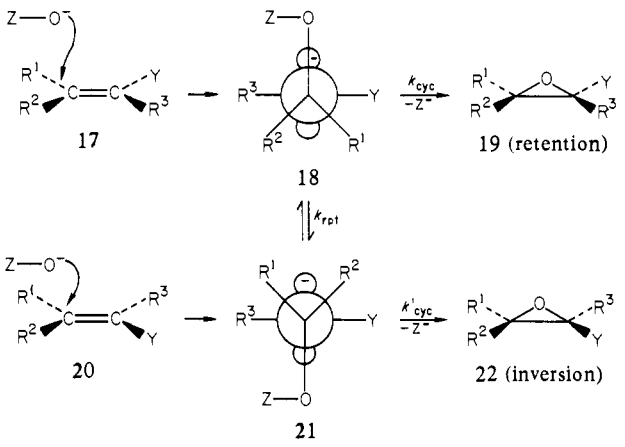
(52) (a) This is the lower limit for the HCA(C–SCl). Upon full optimization $ClSCH_2CH_2^-$ collapses to a bridged structure, and the HCA(C–SCl) was estimated by fixing the SCC bond angle at 109.47° (Table I). (b) Upon full geometry optimization **14**, X = CH_2, Z = $^+SH_2$, collapses to a structure that resembles a loose complex between cyclopropane and H_2S. This probably results from the fact that in the gas phase charge separation is unfavorable and **14**, X = CH_2, Z = $^+SH_2$, tends therefore to dissociate to neutral fragments. In solution, however, charged species are stabilized by solvation. Furthermore, we are interested (see below) in stabilized α-substituted carbanions that have smaller tendency to cyclize and dissociate than the parent carbanion. The HCA of the C–$CH_2{}^+SH_2$ bond was calculated by fixing the CCC($^+SH_2$) angle at 109.47° and the C–S$^+$ bond length at 1.879 Å (taken from the corresponding **15A**).

example, the value in $ClCH_2CH_2CH_2^-$ is 10.0 kcal mol^{-1} compared to 29.4 kcal mol^{-1} in $ClOCH_2CH_2^-$.[53] As in the oxy series (**14**, X = O), the rotation barrier is lower with fluorine, i.e., 4.6 kcal mol^{-1} in **14**, X = CH_2, Z = F, than with chlorine (i.e., 10 kcal mol^{-1} in **14**, X = CH_2, Z = Cl). The rotation barrier in the zwitterion **14**, X = CH_2, Z = $^+SH_2$, is 21.5 kcal mol^{-1}.[52b] This high HCA is expected for a C–C bond that is attached to a positively charged, strongly electron-withdrawing group such as $^+SH_2$. In this case also the anti-conformation **14A** is more stable than the syn-conformation **14S**, although the opposite charges are closer to one another in the latter. Apparently, **14S** is destabilized relatively to **14A** by steric interactions and by repulsion between the sp(C$^-$) and the 2p(S) lone pairs.

Electron-withdrawing substituents on the α-carbanionic center (i.e., in $ZOCH_2CYY'^-$) reduce significantly the rotation barriers around the central C–C$^-$ bonds. The barrier in $ClOCH_2CH_2CN^-$ is 11.8 kcal mol^{-1} compared with 29.4 kcal mol^{-1} for $ClOCH_2CH_2^-$ (STO-3G, Table I). Additional cyano substitution reduces the barrier further to 6.3 kcal mol^{-1} in $ClOCH_2C(CN)_2^-$. The rotation barrier in $ClOCH_2CHNO_2^-$ is similar (6.6 kcal mol^{-1}, STO-3G). With substituents that have a moderate HCA such as $ClCH_2$ the rotation barriers in the stabilized anions are small, e.g., 3.9 kcal mol^{-1} in **14**, X = CH_2, Y = CN, Y' = H, and Z = Cl (STO-3G). It is reasonable that substitution of the α-hydrogen by CN or NO_2 groups will lower the rotation barriers of the other anions of Table I to a similar extent. The major reason for this dramatic lowering of the rotation barriers is that charge delocalization by the α-substituent reduces the demand for charge dispersal by the OZ groups. For example, Figure 1 shows that the population of the 2p(C$^-$) orbital in $ClOCH_2C(CN)_2^-$ (**14A**) is 1.54 electrons, considerably lower than in **14A**, $ClOCH_2CH_2^-$ (1.64 electrons). The rates of nucleophilic attacks on activated olefins RR'C=CYY', which are determined mainly by charge delocalization to the α-substituent in the intermediate carbanion, also follow qualitatively the order of the calculated barriers: i.e., the reactivity order for Y,Y' is CN,CN ≳ NO_2,H > CN,H ≫ H,H.[9a,28b,54]

Finally, we comment on the reliability of the calculations. MO calculations are usually less reliable for anions than for neutral and positively charged systems.[55] However, recent studies showed that geometries, relative energies, and especially rotation barriers can be calculated with reasonable accuracy even at simple levels of theory.[55a] The calculated rotation barriers around the C–C$^-$ bonds (**14** → **15**) are indeed not sensitive to the size of the basis set or to the choice of geometries (Table I). For example, the **14A** → **15A**, X = O, Z = Cl, rotation barrier is 29.4, 34.3, and 28.9 kcal mol^{-1} at STO-3G, 3-21G, and 6-31G*, respectively. The other anions behave similarly. In general, the STO-3G and the 6-31G* values are similar while the 3-21G values are higher by several kcal mol^{-1} (Table I). Most important, with all the basis sets the HCA(C–XZ) order is the same. Furthermore, the rotation barriers in **14**, X = O, Z = OH, F, or H, at 4-31+G[37] are not significantly different from the 3-21G values (Table I). The 4-31+G basis set includes a set of diffuse functions that dramatically improve the reliability of the calculations for anions.[37,56] We believe that the entire evidence supports strongly the reliability of the calculations. We stress, however, that the calculations describe the isolated anions in the gas phase. The barriers to rotation are determined by HC, which depends on the charge in the 2p(C$^-$) orbital. Charge delocalization by substituents (vide supra), by the solvent, or by counterions is therefore expected to reduce these rotation barriers. Indeed, the barriers to rotation

Scheme I



in the allyl anion increase as the interaction with the counterion M^+ is weakened along the series M = $Li^+ < K^+ < Cs^+$.[57] Thus, the gas-phase barriers should be regarded as upper limits to the barriers in solution. However, in the same solvent and with the same counterion the order of HCAs for different C–XZ bonds is expected to be the same in solution and in the gas phase.

Application of the PMO Model to the Epoxidation and Cyclopropanation Reactions. (a) Epoxidation. Nucleophilic epoxidation is believed to proceed by the two-step carbanionic mechanism of Scheme I. The ZO^- nucleophile approaches the olefin **17** in a plane perpendicular to the molecular plane.[58] The carbanion is therefore formed initially in a perpendicular conformation (**18**) analogous to **14**, where the 2p(C$^-$) C–OZ HC is maximal. We assume that compounds **18** have planar carbanionic centers because nucleophilic epoxidation and cyclopropanation occur mostly with electrophilic alkenes that are activated by good π-acceptor α-substituents (e.g., **17**, Y = CN, COOR, NO_2, Ph, etc). A planar geometry at C_α is essential for an efficient overlap between the 2p(C$^-$) orbital and the acceptor π* orbital of Y. Calculations confirm that CH_2CN^-, $CH_2NO_2^-$, and CH_2CHO^- are planar.[37] Our analysis and stereochemical predictions remain, however, unchanged even if **18** is pyramidal.

We have shown above that if $R^1 = R^2 = H$, **14A** is the most stable conformer of **18** so that **18** represents an intermediate on the reaction hypersurface. When $R^1 = R^2 \neq H$ the most stable conformer is determined by the HCAs for all three substituents, but in most cases the HCA of the C–OZ bond dominates and the first-formed species **18** is an intermediate. In conformations of type **14A** the nucleophilic 2p(C$^-$) orbital, the electrophilic oxygen, and the nucleofuge Z are perfectly aligned for an internal S_N2 displacement of Z, which leads to the epoxide. Thus, cyclization of **18** leads to epoxide **19** with retained (i.e., cis R^1 and Y as in **17**) configuration. Likewise, **20** gives **22** via **21** (Scheme I). Rotation around the central C–C$^-$ bond competes with cyclization. Rotation of **18** gives the isomeric carbanion **21**, which can cyclize to the "inverted" epoxide **22** (Scheme I). Consequently, the stereochemistry of nucleophilic epoxidation is determined by the relative activation energies for rotation around the C–C$^-$ bond and for cyclization. The reaction is highly stereospecific if internal rotation in **18** (cf. k_{rot}) is significantly slower (i.e., the rotation barrier is high) than nucleophilic displacement of Z^- (cf. k_{cyc}, k'_{cyc}). A pair of *E*- and *Z*-olefins should give two different retained isomeric epoxides (i.e., **17** → **19**, **20** → **22**). However, if the rotation **18** → **21** is faster than ring closure and the **18** → **21** equilibrium is established before nucleofuge expulsion, then complete stereoconvergence (i.e., formation of identical **19**:**22** mixtures from either **17** or **20**) should be observed.

The rotation barriers **18** → **21** are determined by the HCAs of the C–OZ, C–R^1, and C–R^2 bonds, by the nature of Y and

(53) A somewhat higher barrier of 12.9 kcal mol^{-1} (STO-3G) was reported[50] for $ClCH_2CH_2CH_2^-$. However, this reflects the energy difference between **14A**, X = CH_2, Z = Cl, and a structure in which the $ClCH_2$ group is rotated by 120°.[50]

(54) (a) Rappoport, Z.; Hoz, S. *J. Chem. Soc., Perkin Trans. 2* **1975**, 272. (b) Shenhav, H.; Rappoport, Z.; Patai, S. *J. Chem. Soc. B* **1970**, 469.

(55) For reviews see: (a) Radom, L. "Modern Theoretical Chemistry"; Schaefer H. F., III, Ed.; Plenum Press: New York, 1977; Vol. 4, p 333. (b) Hopkinson, A. C. *Prog. Theor. Org. Chem.* **1977**, *2*, 194. (c) Simons, J. *J. Am. Rev. Phys. Chem.* **1977**, *28*, 15.

(56) Chandrasekhar, J.; Andrade, J. G.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1981**, *103*, 5612.

(57) Thompson, P. B.; Ford, W. T. *J. Am. Chem. Soc.* **1979**, *101*, 5459.

(58) Stozier, R. W.; Caramella, P.; Houk, K. N. *J. Am. Chem. Soc.* **1979**, *101*, 1340.

R^3 and by the eclipsing steric interactions of the α- and the β-substituents. If steric effects are assumed to be relatively small (vide infra), then rotation barriers in **18** can be estimated from Table I and eq 5.[31a,59] In eq 5 θ is the angle of rotation ($\theta = 90°$ for **18** and 0° for **15**), and V_{OZ}, V_{R^1} and V_{R^2} are the HCAs of the C–OZ, C–R^1, and C–R^2 bonds, respectively, which are given by the **14** → **15** rotation barriers (e.g., at STO-3G V_{OCl} = 28.9 and 11.8 kcal mol^{-1} for R^3 = H and Y = H or CN, respectively). The rotation barriers are given by the energy difference between the highest and the lowest $E(\theta)$ values. In most cases studied R^1 and R^2 = alkyl or aryl, which have very low HCA (e.g., 2.1 kcal mol^{-1} for Me),[31a] and their contribution to the rotation barriers in **18** is therefore small. Furthermore, according to eq 5 rotation of **18** that increases the HC contribution of one substituent (e.g., that of R^1 in a clockwise rotation) necessarily reduces the contribution of the other substituents, so that in most cases the V_{R^1} and the V_{R^2} terms nearly cancel. Thus, the rotation barriers in **18** are essentially due to the C–OZ bonds.

$$E(\theta) = 0.5V_{OZ}(1 + \cos 2\theta) + 0.5V_{R^1}(1 + \cos [2(\theta + 120)]) + 0.5V_{R^2}(1 + \cos [2(\theta + 240)]) \quad (5)$$

The relative barriers to ring closure and the intramolecular displacement of Z are dependent on the nucleofuge Z. We have not attempted to calculate the barriers to intramolecular displacement of Z[60] because the reliability of our calculations for such nonisodesmic reactions is expected to be poor.[61] Furthermore, solvation may strongly affect the nucleofugality of Z so that the calculated order of nucleofugalities of different Z^- in the gas phase probably does not apply in solution. Fortunately, a qualitative knowledge of the nucleofugality order of the groups Z is sufficient for the following analysis.

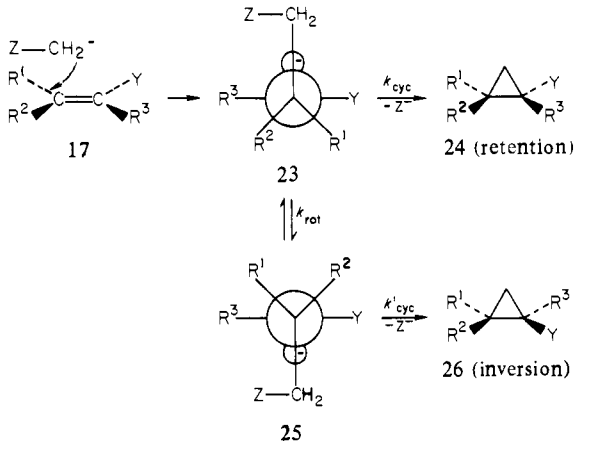
Our theoretical model which is based on HC leads to the following predictions regarding the stereochemistry of nucleophilic epoxidation:

(a) The stereospecificity of epoxidation for a particular set of substituents R^1, R^2, R^3, and Y is higher the higher the HCA of the C–OZ bond is. This is because a higher HCA of OZ increases the rotation barrier in the intermediate carbanion and thus lowers k_{rot}. The dependence of stereospecificity on the nucleofuge is therefore expected to decrease in the order $ClO^- > OCHOO^- > FO^-$, $MeOO^-$, HOO^- (Table I).

(b) α-Substituents (Y and R^3) that stabilize the carbanion reduce the rotation barrier in **18** (Table I), increase k_{rot}, and should therefore lower the stereospecificity of epoxidation with a particular nucleophile.

(c) The better the nucleofugality of Z, the higher is k_{cyc} and the higher is the stereospecificity. Both HCA (C–OZ) and the nucleofugality of Z are related to the electronegativity of Z, and in most cases they change in a parallel fashion. The higher the nucleofugality of Z, the higher is the HCA of the C–OZ bond, and the two effects reinforce each other in determining the stereochemistry. This raises the question whether the stereochemistry can be explained by the different nucleofugalities of the Z groups without invoking HC.[62]

Scheme II



(d) The degree of stereospecificity should be in most cases nearly independent of the substituents R^1 and R^2, because R^1 and R^2 are usually alkyl or aryl groups for which HCA (C–OZ) ≫ HCA (C–R^1), HCA (C–R^2) (Table I). Furthermore, with most nucleophiles the rotation barriers that are imposed in **18** by HC with the C–OZ bonds are considerably higher than the expected eclipsing steric effects that are associated with R^1 and R^2 (except when they are very bulky). For example, rotation of **18** by 90°, which relieves the R^1–Y (or the R^2–R^3) steric interactions, simultaneously excludes the HC interaction with the OZ group and introduces an ZO–Y (or ZO–R^3) interaction. A rough estimate of the steric interactions in the eclipsed conformers of **18** (i.e., $\theta = 0 + 60n$) along the route **18** → **21** can be obtained from the following values (in kcal mol^{-1}) of steric repulsions between two R groups in representative cis-olefins: 0.75 (Me, Me), 3.10 (Ph, Ph), 3.92 (Me, *t*-Bu), 7.79 (*t*-Bu, Ph), 10.51 (*t*-Bu, *t*-Bu).[63] It is therefore clear that at least in epoxidation with ClO^- (HCA = 28.9 kcal mol^{-1}) the HC stabilization energy overrides the steric term even with bulky R groups. This is true also (except for extremely bulky R^1, R^2, and R^3) for moderately stabilized carbanions such as $ClOCH_2CHCN^-$ (rotation barrier = 11.8 kcal mol^{-1}). Steric effects are expected to be more important, with a consequent lower stereospecificity, in ClO^- epoxidations of highly activated olefins that give anions such as $ClOCR^1R^2C(CN)Y^-$ (Y = CN, NO_2, CO_2R, etc.), where HC imposes relatively low barriers (e.g., 6.3 kcal mol^{-1} in $ClOCH_2C(CN)_2^-$), or in the epoxidation of less activated olefins with nucleophiles such as HOO^- that have a considerably lower HCA than ClO^-.

Reactions controlled mainly by HC should give retention of configuration, whereas reactions that are controlled by steric effects should lead to equilibration of the carbanions **18** and **21** before nucleofuge expulsion and hence to stereoconvergence. In the latter case, the product composition is determined by the relative stabilities of the transition states for nucleofuge expulsion from **18** to **21**. If one of these transition states is sterically favored, then one olefin will give retained epoxide whereas the isomeric olefin will give an inverted epoxide. Either steric repulsion or steric attraction[64] may be responsible for the product distribution.

(b) Cyclopropanation. The considerations above are also applicable to cyclopropanation where the attacking nucleophile is ZCH_2^- and the related isomeric carbanions and cyclopropanes are **23** and **25**, and **24** and **26**, respectively (Scheme II). Table I shows that most of the calculated rotation barriers in β-ZCH_2-substituted carbanions (e.g., **23**) are less than half than in the corresponding β-ZO-substituted carbanions (e.g., **18**). Consequently, the stereospecificity in cyclopropanation should be generally much lower than in the corresponding epoxidations, and in most cases retention is not expected. Cyclopropanation with sulfur ylides may exhibit stereospecificity as the HCA(C–

(59) This equation includes only the 2-fold component of a more general equation suggested by the following: Radom, L.; Pople, J. A. *J. Am. Chem. Soc.* **1972**, *94*, 2371.

(60) In the gas-phase these barriers are probably low because the expulsions of Z^- from **18** are very exothermic. For example, the reaction $ZOCH_2CH_2^- \rightarrow c\text{-}C_2H_4O + Z^-$ are exothermic at 6-31G* by 93.1 and 39.5 kcal mol^{-1} for Z = Cl and OH, respectively. Two carbanions ($ClSCH_2CH_2^-$ and $H_2S^+CH_2CH_2CH_2^-$) collapse upon optimization to cyclic structures.

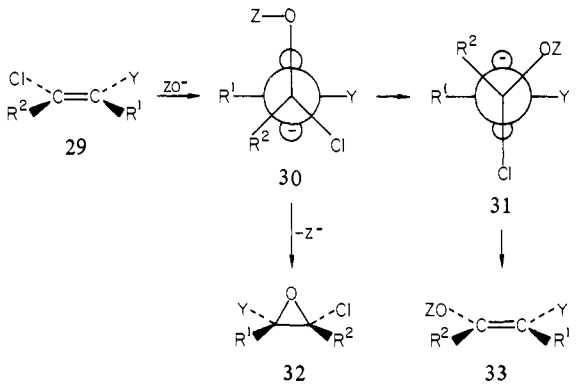
(61) See, for example: (a) Radom, L.; Hehre, W. J.; Pople, J. A. *J. Am. Chem. Soc.* **1971**, *93*, 289. (b) George, P.; Trachtman, M.; Brett, A. M.; Bock, C. W. *J. Chem. Soc., Perkin Trans. 2* **1977**, 1036 and references therein.

(62) The available data do not allow separation of the total effect to contributions from HC and from nucleofugality. Unfortunately, such dissection presents experimental difficulties. For example, a nucleophile with high HCA(C–OZ) and low nucleofugality of Z is expected to give a retained epoxide if HC is product controlling. An example is NCO^-, for which we calculate a rotation barrier around the C–C^- bond in **18**, Z = CN, of 29.7 kcal mol^{-1}. However the nucleofugality of CN^- is so low that epoxidation by NCO^- does not occur.

(63) Yates, K.; McDonald, R. S. *J. Org. Chem.* **1973**, *38*, 2465.

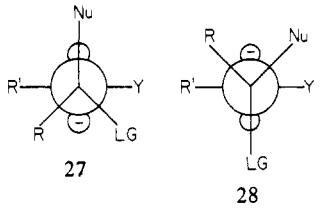
(64) Hoffmann, R.; Levin, C. C.; Moss, R. A. *J. Am. Chem. Soc.* **1973**, *95*, 629.

Scheme III



$CH_2{}^+SH_2$) = 21.5 kcal mol^{-1} is relatively high. Stabilization of the carbanion by electron-withdrawing Y and R^3 substituents or by polar solvents should lower the stereospecificity further. Stereospecificity may be observed only with very good nucleofuges where k_{cyc} is extremely high. Steric effects are expected to be in general more important for cyclopropanation than for epoxidation.

(c) Cyclization vs. Nucleophilic Vinylic Substitution. HC controls the barriers to internal rotation and the stereochemistry in both nucleophilic cyclization and nucleophilic vinylic substitution.[31a] A two-step cyclopropanation is most likely since nucleophilic attack with simultaneous nucleofuge (LG) expulsion is unlikely. Moreover, the initially formed carbanions with parallel 2p(C$^-$) and C–OZ or C–CH_2Z orbitals (e.g., **18**) are the more stable conformers, and internal rotation leads to energy increase. In contrast, in nucleophilic vinylic substitution the nucleofuge (most commonly Cl$^-$ or Br$^-$) that has a considerably higher HCA than the other β-substituents forms a 60° angle with the developing 2p(C$^-$) orbital in the initially formed carbanion (i.e., **27**). Since



internal rotation to **28**, which reduces this angle, increases the carbanion stability, nucleophilic attack and 60° rotation may be concerted.[31] A strong support for a multistep substitution is the initial formation of a carbanion at a local minimum so that a nonsimultaneous rotation will be required before C–LG bond cleavage.

The calculations show that this may be achieved in systems where HCA(C–β-substituents) > HCA(C–LG). Carbanionic nucleophiles have lower HCA than Cl (Table I), and hence they don't fulfill this requirement. However, since usually HCA(C–OZ) > HCA(C–Cl), a conformation with a parallel C–OZ group and 2p(C$^-$) orbital (e.g., **27**, Nu = OCl) will be favored over an isomer rotated by 60° (e.g., **28**, Nu = OCl).[65] The consequences are discussed below.

Reaction of ZO$^-$ with the chloroalkene **29** gives initially carbanion **30** (Scheme III). Counterclockwise rotation in **30** reduces the hyperconjugative interactions of both Cl and OZ and increases HC overlap with R^2, whereas clockwise rotation reduces the HC overlap for R^2 and OZ but increases that for Cl. The fate of **30** depends on the relative nucleofugalities and HCAs of C–Cl compared with C–OZ and on the HCA of C–R^2. As HCA(C–OZ) is usually greater than HCA(C–Cl), the rotation **30** → **31** is endothermic. If Z is a good nucleofuge (e.g., Cl) cyclization to the retained epoxide **32** is likely to be faster than rotation to **31**, which leads to the retained substitution product **33** (Scheme III).[66]

The nucleofugality of the oxygen-bound chlorine in a 1,3-cyclization should differ from that of a carbon-bound chlorine in a 1,2-carbanionic elimination.[67] The observed retention in epoxidation by ClO$^-$ indicates that chlorine expulsion is relatively fast.

Formation of **32** in the epoxidation of **29** by ClO$^-$ will indicate that a nucleophilic reaction on an activated vinyl halide can proceed without chlorine expulsion. This is unprecedented since this reaction usually leads to substitution.[27,28] Since the same carbanion is probably involved in the substitution and the epoxidation, formation of **32** will argue strongly for a multistep nucleophilic vinylic substitution.

The hyperconjugative stabilization in **30** compared with **31**, and consequently, the preference for formation of **32** over **33**, should increase on reducing the electron-withdrawing ability of Y and R^1. This conclusion is important since the concertedness or the stepwise nature of the vinylic substitution was especially questioned for moderately or slightly activated systems.[28a] If a concerted substitution competes effectively with a stepwise epoxidation, than **33** may be formed in excess. With highly activating Y and R^1 the rotation barrier is expected to be low, enabling **30** ⇌ **31** equilibration and formation of either **32** or **33**.

Comparison of the Observed Stereochemistry with the Theoretical Predictions. (a) Epoxidation. Epoxidation with ClO$^-$ is usually stereospecific, leading to retention,[5,6,8,26] in line with our theoretical predictions. The observed retention is due to a combination of two effects. The rotation barrier around the C–C$^-$ bond in **18** is highest for Z = OCl (Table I), and Cl$^-$ is the best nucleofuge, leading to the condition $k_{cyc} > k_{rot}$. There is no need to invoke transition-state **12** to account for the stereospecificity.[8] Even with highly activated systems (e.g., **6**), where the carbanion is expected to be long-lived, the rotation barrier (e.g., 6.3 kcal mol^{-1} in $ClCH_2C(CN)_2^-$)[68] is apparently high enough to prevent rotation and thus isomerization. Additional stabilization of the carbanion lowers further the rotation barrier[69] and epoxidation of (*Z*)-**8** (R = Ph), which is activated by α-NO_2 and α-Ph groups, leads to partial stereoconvergence.[6] Likewise, stereoconvergence is also found in substitution of (*E*)- and (*Z*)-α-iodo-β-nitrostilbenes.[30]

For epoxidation with other ZO$^-$ nucleophiles (Z = *m*-ClC_6H_4COO, *t*-Bu, HO), HCA(C–OZ) < HCA(C–OCl), and the order of nucleofugalities is Z$^-$ < Cl$^-$. Therefore, retention stereospecificity is less likely. The best nucleofuge among these Z groups is *m*-$ClC_6H_4COO^-$, which is expected to have a high HCA of ca. 20 kcal mol^{-1} as indicated by the rotation barrier of 19.8 kcal mol^{-1} in the model anion **14**, X = O, Z = OCHO (Table I). Consequently, high stereospecificity is expected for *m*-$ClC_6H_4COOO^-$, at least in moderately activated systems. Indeed, epoxidation of (*Z*)-**10** yields ≥95% of the retained epoxide.[5] However, the much more activating nitro group reduces the rotation barrier sufficiently so that epoxidation of either (*E*)-**8** or (*Z*)-**8** yields only the single epoxide **9**.[6]

Epoxidation with HOO$^-$ is expected to be the least stereospecific since the rotation barrier with Z = OH is the lowest among the values for the Z groups calculated, being ca. half of that with Z = OCl. Moreover, HO$^-$ is a poorer nucleofuge than Cl$^-$.[70] In

(65) Conformations **27** or **28** are not necessarily the most stable. A conformation in which both Cl and OZ form an angle of ca. 30° with the 2p(C$^-$) orbital may be favored in some cases. According to eq 5 (neglecting steric effects) this occurs when 0.5HCA(C–LG) > 0.25HCA(C–Nu) + 0.25HCA(C–R). For example, in **27**, R = R′ = H, Nu = OCl, LG = Cl, eq 5 using V_{OCl} = 29.4 and V_{Cl} = 16.7 kcal mol^{-1} shows that the conformation with a 30° dihedral angle between the 2p(C$^-$) orbital and the nucleophile is 1.0 and 10.5 kcal mol^{-1} more stable than conformations **27** and **28**, respectively.

(66) The probability for cyclization could increase by using, for example, OBr$^-$ while retaining a chlorine-bound carbon.

(67) Edwards, J. O.; Pearson, R. G. *J. Am. Chem. Soc.* **1962**, *84*, 16.

(68) The calculated barrier for $ClOCH_2C(CN)_2^-$ is probably somewhat lower than for $ClOCH_2C(COOCH_3)CN^-$ since an α-cyano carbanion is more stabilized by an additional cyano group than by an additional methoxycarbonyl group. (a) Patai, S.; Rappoport, Z. *J. Chem. Soc.* **1962**, 392; (b) Rappoport, Z.; Topol, A. *J. Chem. Soc., Perkin Trans 2*, **1975**, 763.

(69) The rotation barrier in $ClOCH_2C(NO_2)Ph^-$ is expected to be lower (ca. 4–5 kcal mol^{-1}) than in $ClOCH_2CH(NO_2)^-$ (i.e., 6.6 kcal mol^{-1}, Table I) because the α-phenyl is expected to stabilize further the carbanion.

this case $k_{rot} > k_{cyc}$ even for mildly activated systems, and the product ratio is determined exclusively by the relative energies of the transition states leading to the diastereomeric epoxides. Stereoselectivity but not stereospecificity is often observed.[5-7,10,19-23] The HCA (C–OOBu-*t*) ~ HCA (C–OOH) (cf. HCAs of C–OOMe, C–OOH in Table I) and *t*-BuO^- is probably a somewhat poorer nucleofuge than HO^- due to electron donation by the alkyl group. Low stereospecificity is therefore expected in epoxidation with *t*-$BuOO^-$ as is indeed observed for (*Z*)-**10**.[5]

Comparison of data in Table I with experimental results shows that stereoconvergence is expected for systems where the calculated gas-phase rotation barriers in the intermediate carbanions are ≤5–6 kcal mol^{-1}. Significant stereospecificity is expected for barriers of ca. 8–10 kcal mol^{-1} and high stereospecificity for barriers ≥ca. 12 kcal mol^{-1}.[71]

The theoretocial model and the data of Table I also predict the stereochemistry for systems that were not yet studied experimentally. For example, a very low stereospecificity (if at all) is predicted for epoxidation with FO^- (i.e., HCA (C–OF) ~ HCA (C–OOH)) or for thiirane formation in the reaction of electrophilic olefins with HOS^- and HSS^-. However, ClS^- is predicted to be a highly specific reagent. Nucleophilic attack on hypochloroolefins ClOC(R) = CYY′ is predicted to give the epoxide with retained configuration. We hope to test some of these predictions.

(b) Cyclopropanation. In general, due to the low HCAs of the C–CH_2Z bonds (Table I) lower stereospecificity is predicted for cyclopropanation with $ZR^1R^2C^-$ compared with epoxidation with the corresponding ZO^-. Indeed, in the single case where both *E*- and *Z*-olefins were cyclopropanated with a bromocarbanion, complete stereoconvergence was observed.[14a] However, the system was strongly activated by both an α-CN and an α-CO_2Et group, and the stereochemistry with less activated systems is still unknown. An efficient generation of the nucleophile $^-CZR^1R^2$ requires a highly electron-withdrawing R^1 and/or R^2, thus reducing the nucleofugality of Z = halogen of carbanion **4**, relative to that in simple alkyl halides.

Cyclopropanation with sulfonium, sulfoxonium, phosphonium, and other ylides involves poorer nucleofuges than the halogens, as judged by data on carbanionic 1,2-eliminations.[72] However, when these groups are in system **4**, $R^1 = R^2$ = H, they may be better nucleofuges than halogens in **4**, Z = halogen and $R^1 = R^2$ = electron-withdrawing groups. The rotation barrier in $H_2{}^-CCH_2CH_2{}^+SH_2$, the model for the ylides, is relatively high (21.5 kcal mol^{-1}) similar to that in $H_2{}^-CCH_2OCHO$. Thus according to the calculations, cyclopropanation with ylides may be stereospecific. In a few cases complete or partial stereospecificity was indeed observed.[15b,f] However, stereoconvergence is observed with most of the systems studied,[12x-z,15d-f,16a] and in many cases[16a] there is not sufficient data to distinguish between stereospecific and stereoselective behavior. This is the one case in which the HC model seems to fail. However, we emphasize that predictions for the reactions with ylides are expected a priori to be less reliable than for the other nucleophiles.[52b] First, the computational experience with zwitterions is very limited. Second, extrapolation of the gas-phase results to solution is less reliable since solvation is probably more important for zwitterions than for carbanions. Solvation of the H_2S^+ group will lower its electron-withdrawing ability and thus its HCA.

Stereospecific cyclopropanation may be achieved only with Z groups that are both strong electron withdrawing and excellent nucleofuges. A possible nucleofuge that may give retention in cyclopropanation of slightly electrophilic olefins is the triflate (trifluoromethanesulfonate, OTf) group. However, elimination of TfO^- from the carbanion $TfO^-CR^1R^2$ to give vinylidene carbene may compete favorably with its nucleophilic attack on the double bond.[73]

Conclusions

The stereochemistry of nucleophilic epoxidation of electrophilic olefins by ZO^- nucleophiles can be rationalized by a combination of two effects. The probability for retention stereospecificity increases when the hyperconjugating abilities of the C–OZ bond and the nucleofugality of Z increase and diminishes as the α-substituents become more electron withdrawing. Comparison of the calculated HCA(C–OZ) values, which decrease along the series Z = OCl ≫ OOCHO > OF ~ $OOCH_3$ > OOH > $OSiH_3$ > OH, with the experimental observations enables one to make rough predictions of the stereochemistry of epoxidation for various ZO^-/olefin combinations.

Epoxidation with ClO^- is predicted to give mostly retention stereospecificity even with highly activated olefins, whereas partial or complete retention is predicted for the epoxidation of slightly activated olefins with *m*-$ClC_6H_4COOO^-$. Stereoconvergence is predicted in epoxidations of most electrophilic olefins with HOO^- and FO^-, except probably for very slightly activated olefins.[28a]

Stereoconvergence is expected for most nucleophilic cyclopropanations. However, stereospecificity may be observed in reactions of slightly activated systems with ylides at low temperature or with carbanions substituted by extremely good anionic nucleofuges.

Similar considerations can be used to predict the stereochemistry in cyclizations to other three-membered rings and to cyclization via 1,3-eliminations. Nucleophilic formation of aziridines with $ZRNH^-$ is known.[74] The unknown cyclizations using ZS^- nucleophiles are predicted to exhibit similar stereospecificity to that of the corresponding epoxidation. Finally, a competition between internal cyclization and vinylic substitution that proceeds via the same carbanionic intermediate may provide strong evidence for the multistep nature of the nucleophilic vinylic substitution.

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Registry No. 14A (X = 0; Z = H), 71857-15-3; **14A** (X = 0; Z = OH), 84824-62-4; **14A** (X = 0; Z = SiH_3), 40110-53-0; **14A** (X = 0; Z = F), 84824-63-5; **14A** (X = 0; Z = Cl), 84824-64-6; **14A** (X = 0; Z = OMe), 84824-65-7; **14A** (X = 0; Z = OCHO), 84824-66-8; **14A** (X = 0; Z = Cl; Y′ = NO_2), 84824-67-9; **14A** (X = 0; Z = Cl; Y′ = CN), 84824-68-0; **14A** (X = 0; Z = Cl; Y = Y′ = CN), 84824-69-1; **14A** (X = S; Z = H), 71857-18-6; **14A** (X = S; Z = Cl), 84824-70-4; **14A** (X = CH_2; Z = Cl), 74279-92-8; **14A** (X = CH_2; Z = F), 84824-71-5; **14A** (X = CH_2; Z = Cl; Y = H; Y′ = CN), 84824-72-6.

(70) Epoxidation by H_2O_2 in the presence of sodium tungstate is faster than with H_2O_2 alone, requires lower activation, and is stereospecific with maleic and fumaric acids (Payne, G. B.; Williams, P. H. *J. Org. Chem.* **1959**, *24*, 54) or with (*Z*)-MeCH=$CHPO_3H_2$ (Christensen, B. G.; Leanza, W. J.; Beattie, T. R.; Patchett, A. A.; Arison, B. H.; Ormond, R. E.; Kuehl, F. A.; Albers-Schonberg, G.; Jardetzky, O. *Science (Washington, D.C.)* **1969**, *166*, 123). It was suggested that the active nucleophile attacking C_β is the peroxytungstate anion HWO_5^- (i.e., Z = HWO_4). This anion will be a better leaving group than OH^-, but the HC stabilization will probably be lowered, due to electron donation by the metal to the oxygen.

(71) If the rotation barrier around the C–C^- bond in the intermediate carbanion is assumed to be 7 kcal mol^{-1}, then the rate constant of this process is ca. 10^7 s^{-1} at 25 °C (Eyring equation, assuming that $\Delta S^* = 0$). We have estimated that with such rotation barriers stereoconvergence or moderate stereospecificity prevails in epoxidation with ClO^-. Thus, the rate constant for the cyclization of intermediates such as **18**, Z = Cl, Y and R^3 electron-withdrawing groups, can be estimated to be roughly 10^6–10^7 s^{-1}.

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