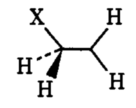
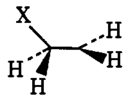
Superjacent Orbital Control. An Interpretation of the Anomeric Effect

Sir:

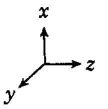
Hyperconjugation leads to different stable geometrical conformations for the $XCH_2-CH_2^+$ and $XCH_2-CH_2^-$ ions.[1] If X is more electronegative than H, the cation adopts an eclipsed conformation while the anion prefers a bisected conformation. The orbital interactions which determine these preferences involve the terminal p orbital and the π- and π^*-type orbitals of XCH_2. However, the specific interactions are different in cations and in anions. Let orbital p lie at energies ΔE and ΔE^*, respectively, from the X-unperturbed π_y and $\pi_y{}^*$ orbitals, and let the X-perturbed (π_x, $\pi_x{}^*$) pair be shifted by (μ,λ) relative to the unperturbed pair. The symmetry properties of the orbitals lead to the interactions shown here. In the cation (two electrons) the energy in either conformation is equal to twice the stabilization of the π orbital *via* its interaction with p. If a common matrix element h is assumed for this interaction, the relative energies are approximately (neglecting overlap) $-2h^2/\Delta E$ (*eclipsed*) and $-2h^2/(\Delta E + \mu)$ (*bisected*).[2]

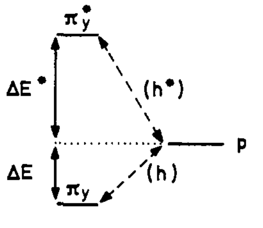


eclipsed

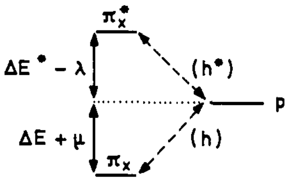


bisected





Eclipsed



Bisected

In anions (four electrons) there are two effects, which both favor the same conformation. One of these is the *repulsive*, p ↔ π interaction. Since orbitals p and π are both occupied, their interaction is net destabilizing.[3] If the p ↔ π overlap integral is S

$$E(\text{repulsive}) = -4Sh + 2S^2(E_\pi + E_\text{p}) \qquad (1)$$

The other effect is *attractive* and arises from the stabilization of the occupied p orbital through its interaction with the π^* orbital. If h^* is a common matrix element for this interaction[2]

$$E(\text{attractive}) = -2(h^* - S^*E_\text{p})^2/(E_{\pi^*} - E_\text{p}) \qquad (2)$$

or approximately $-2h^{*2}/\Delta E^*$ (*eclipsed*) *vs.* $-2h^{*2}/(\Delta E^* - \lambda)$ (*bisected*). Realistic estimates of eq 1 and 2 accounting for the unsymmetrical nature of the (π,π^*) orbital energy pattern and for the slightly larger value of h relative to h^* show the repulsive effect to dominate in the reference ethyl anion.[4] However, similar estimates show the attractive energy to increase rapidly in systems with low-lying π^* orbitals (X more electronegative than H). Moreover, the attractive energy is more sensitive to electronegative substituents than the repulsive energy.[4]

Thus, whereas cation conformations are exclusively controlled by the interaction of the nonbonding level with the "*subjacent*" level,[5] anion conformations are controlled simultaneously by a repulsive interaction with the subjacent level and by an attractive interaction with the "*superjacent*" level. The latter effect may become predominant when X is electronegative.

The anomeric effect[6] is the preference of axial over equatorial C_1 electronegative substituents in pyranose rings. Attempts have been made[6a,c,e,i,7,8] to rationalize this effect on the basis of electrostatic interactions between C_5O-C_1X bond dipoles or between C_5O-C_1X bonded pairs. Altona suggested[9] that donation from the axial *lone pair* of the ring oxygen into the C_1X antibonding orbital stabilizes the axial conformation. Nqr measurements[10] and bond length measurements[9a,b] are compatible with this interpretation. We now show that if due account is made for *the different energies of the two oxygen lone pairs*[11,12] their interaction with the low-lying $\sigma_{CX}{}^*$ orbital leads naturally to the preference for an axial X ligand.

Let n be the p-type oxygen lone pair and n′ the σ-type lone pair.[12] The orientations of n and n′ relative to the C_1X and C_1H bonds are shown in I (C_1X axial)

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[1] R. Hoffmann, L. Radom, J. A. Pople, P. v. R. Schleyer, W. J. Hehre, and L. Salem, *J. Amer. Chem. Soc.*, **94**, 6221 (1972). The orbital energy patterns are not always as simple as in this reference or in the scheme above. For X = Cl, for example, the $3p_y$ lone pair of chlorine pushes π_y *below* π_x while $\pi_y{}^*$ is raised even higher relative to $\pi_x{}^*$. Accordingly, the eclipsed conformation is favored by only 0.6 kcal/mol in the chloroethyl cation (thanks to the larger p,π_y matrix element) while the bisected conformation is favored by 15.7 kcal/mol in the anion.

[2] In fact, the matrix element of p with π_x is smaller than that with π_y (while that with $\pi_x{}^*$ is larger than that with $\pi_y{}^*$). A simple calculation shows that these changes simply *double* the conformational preference due to the energy differences alone.

[3] L. Salem, *Proc. Roy. Soc., Ser. A*, **264**, 379 (1961); K. Müller, *Helv. Chim. Acta*, **53**, 1112 (1970). We are dealing here with *exclusion* repulsion.

[4] Details will be published elsewhere (L. Salem, *Chem. Biochem. Reactiv., Proc. Int. Jerusalem Symp., 6th, 1973*, in press.

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[8] S. Wolfe, A. Rauk, L. M. Tel, and I. G. Csizmadia, *J. Chem. Soc. B*, 136 (1971).

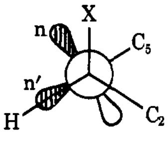
[9] (a) C. Altona, Ph.D. Thesis, University of Leiden, 1964, p 117; (b) C. Romers, C. Altona, H. R. Buys, and E. Havinga, *Top. Stereochem.*, **4**, 39 (1969), in particular pp 73–77 and Figure 18; (c) for a similar effect in FCH_2-OH, see L. Radom, W. J. Hehre, and J. A. Pople, *J. Amer. Chem. Soc.*, **94**, 2371 (1972); (d) electron delocalization, dipole–dipole interactions, and steric effects have been considered together by G. A. Jeffrey, J. A. Pople, and L. Radom, *Carbohyd. Res.*, **25**, 117 (1972).

[10] (a) E. A. C. Lucken, *J. Chem. Soc.*, 2954 (1959); (b) P. Linscheid and E. A. C. Lucken, *Chem. Commun.*, 425 (1970); (c) J. F. A. Williams, *Trans. Faraday Soc.*, **57**, 2089 (1961); (d) J. F. A. Williams, *Tetrahedron*, **18**, 1477 (1968); (e) S. David and L. Guibé, *Carbohyd. Res.*, **20**, 440 (1971).

[11] For OH_2 see (a) F. O. Ellison and H. Shull, *J. Chem. Phys.*, **23**, 2348 (1955); (b) T. H. Dunning, R. M. Pitzer, and S. Aung, *J. Chem. Phys.*, **57**, 5044 (1972); (c) C. R. Brundle and D. W. Turner, *Proc. Roy. Soc., Ser. A*, **307**, 27 (1968); (d) M. I. Al-Joboury and D. W. Turner, *J. Chem. Soc. B*, 373 (1967).

[12] In tetrahydropyran, photoelectron studies show the σ-type lone pair to be at least 1.35 eV below the p-type lone pair (P. D. Mollère and H. Bock, private communication to the authors). See also D. W. Sweigart and D. W. Turner, *J. Amer. Chem. Soc.*, **94**, 5599 (1972).

and II (C_1X equatorial). The bond ↔ lone-pair interactions each involve four electrons and X is electronegative. Let us consider then the attractive interactions between the two lone-pair orbitals and the two empty orbitals σ_{CX}^* and σ_{CH}^*. The important interactions are shown with dotted arrows and the corresponding energies are approximately[13]



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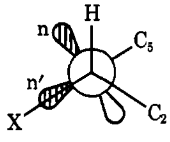

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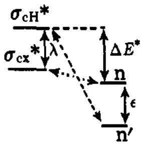

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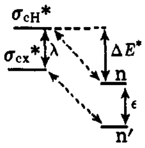

II

$$\mathrm{I}\left\{\begin{array}{ll}(\text{for n}) & -2h^{*2}/(\Delta E^* - \lambda)\\ (\text{for n}') & -2h^{*2}/(\Delta E^* + \epsilon)\end{array}\right.$$

$$\mathrm{II}\left\{\begin{array}{ll}(\text{for n}) & -2h^{*2}/\Delta E^*\\ (\text{for n}') & -2h^{*2}/(\Delta E^* + \epsilon - \lambda)\end{array}\right.$$

Orbital n favors I while orbital n′ favors II. The differential energy in favor of I is $4h^{*2}\lambda\epsilon/(\Delta E^*)^3$, where $2h^{*2}\lambda/(\Delta E^*)^2$ can be approximated by the energy difference between eclipsed and bisected conformations of $XCH_2-CH_2^-$ (15.7 kcal/mol for X = Cl[1]), the splitting ϵ is 17 kcal/mol (*an initio* calculation on tetrahydropyran), and ΔE^* is of the order of 160 kcal/mol.[14] The conformational preference is then ∼3.3 kcal/mol for X = Cl. The experimental value is 2.7 kcal/mol,[9b] while an STO-3G *ab initio* calculation on 1-chlorotetrahydropyran yields a conformational preference of 1.2 kcal/mol (identical bond lengths in the two conformations) and 3.7 kcal/mol (relaxed bond lengths).

In highly polar solvents, orbitals n and n′ are both stabilized, whence an increase in ΔE^* and a decrease in conformational preference, as observed.[15]

We have not examined the repulsive energies corresponding to eq 1 and we cannot rule out the possibility that the preference for I is due to a smaller repulsion energy. However, this is unlikely since a calculation similar to the previous one—keeping only the four largest orbital interactions and choosing a common pair of (h, S) values—yields zero conformational preference. The observed solvent effect also argues against any exclusion–repulsion control. Indeed, it can be shown[4] that the repulsive energy change with substitution (H → X), for any individual (nonbonding orbital, subjacent orbital) pair, is independent of the energy gap between the orbitals. Thus, superjacent orbital control by the C_1X antibonding orbital, as first suggested by Altona, and the energetic nonequivalence of the oxygen lone pairs seem to be significant factors in determining the anomeric effect.

For X less electronegative than H, the same superjacent orbital interactions favor II (equatorial X) over I, thereby providing at least some rationalization for the *reverse* anomeric effect.[16]

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(13) Overlap seems to discriminate only slightly between I and II (whence the common value of h^*). For instance, $\langle n|\sigma_{CCl}^*\rangle = 0.062$ in I while $\langle n'|\sigma_{CCl}^*\rangle = 0.052$ in II.

(14) This number is chosen as half the natural frequency (13.5 eV) of electronic excitation $\sigma_{CH} \rightarrow \sigma_{CH}^*$ for an isolated C–H bond (J. W. Raymonda and W. T. Simpson, *J. Chem. Phys.*, **47**, 430 (1967)).

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Conformational Limitation for the Applicability of the Taft E_S Parameters

Sir:

The steric parameters obtained from the linear free-energy relationship (eq 1) proposed by Taft, for the

$$\log k/k_0 = E_S \qquad (1)$$

evolution of rate constants in acid-catalyzed hydrolysis of esters,[1] have been applied to a wide variety of reactions.

These parameters have been subjected, however, to various criticisms; among the most important ones are: the lack of accounting for the difference in hyperconjugative ability between the various alkyl groups[2] and the close relation between E_S and σ^* observed by Russian workers.[3]

It is noteworthy, however, that in spite of these criticisms the E_S parameters have a surprisingly large range of applications such as: organic reactivity,[4] spectroscopy,[5] enzymatic catalysis,[6] and drug design.[7] Moreover, Charton has shown, in a recent statistical analysis, that the E_S parameters are a function only of the van der Waals radii.[8,9]

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